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ABSTRACT SUPPLEMENT

ACR Convergence 2023

November 10–15, 2023

San Diego, CA

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Abstract Number: 0001

Loss of the Complement Regulator CD55 Alters Marginal Zone B Cell Homeostasis

Iris Lee[1], Sonam Verma[2], Ivana Ling[2], Christine Pham[3] and Peggy Kendall[2], [1]Washington University in St. Louis, St. Louis, MO, [2]Washington University, Saint Louis, MO, [3]Washington University, St. Louis, MO

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Complement and B cells are implicated in the pathophysiology of rheumatoid arthritis, an autoimmune disease characterized by synovial inflammation. Loss of complement regulator CD55 leads to delayed onset of inflammatory arthritis in the collagen-induced mouse model of arthritis (CIA).[1] Marginal zone (MZ) B cells, an innate-like B cell population, serve as first responders to blood-borne pathogens by rapidly differentiating into antibody producing plasmablasts, and are important initiators of CIA.[2] Whether and how CD55 regulates MZ B cells in CIA pathogenesis is unknown.

Methods: We examined naïve and sorted MZ B cell populations in 3-5 week-old and 10-12 week-old CD55-/- and compared to wildtype (WT) C57BL/6 mice using flow cytometry, immunofluorescence, bromodeoxyuridine (BrdU) incorporation, and bulk RNAseq. Differential gene expression analysis was performed, followed by Gene Sequence Enrichment Analysis (GSEA).

Results: We found that loss of CD55 decreased the number of MZ B cells in 10-12 week-old, but not 3-5 week-old mice. The precursors to MZ B cells were unchanged at both endpoints, indicating that loss of MZ B cells was not due to failure of MZ B cell differentiation. *En vivo* BrdU incorporation showed no difference between CD55-/- and WT, indicating MZ B cell differences are not due to loss of proliferative capacity. Differential gene expression analysis showed decreased expression of genes involved in preventing apoptosis in MZ B cells of CD55-/- compared to WT mice (*HSP90b1*, *STIP1*, *AHSA1*, and *FKBP4*). GSEA showed decreased expression of cell cycle/cell survival pathways in CD55-/- cells relative to WT. Flow cytometry revealed that CD55-/- MZ B cells had corresponding increases in activated caspase-3 and caspase-7.

Conclusion: Loss of CD55 led to increased reactive oxygen species and activation of caspases in MZ B cell populations, which may prevent the normal expansion of the MZ B cell subset over time. These studies suggest a role for the complement regulator CD55 in MZ B cell homeostasis and survival. Future experiments are aimed at defining whether loss of CD55 impacts MZ B cell survival through complement dependent or independent mechanisms.

Disclosure: I. Lee: None; **S. Verma**: None; **I. Ling**: None; **C. Pham**: Insmed, 1, 9; **P. Kendall**: None.

Abstract Number: 0002

Population Pharmacokinetic and Pharmacodynamic Analyses of Obexelimab in Healthy Volunteers and in Patients with Rheumatoid Arthritis or IgG4-Related Diseases

Xiaodong Wang, Rachel Kirk, Simon Lowry and Hua Mu, Zenas BioPharma, Waltham, MA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Obexelimab is a novel bifunctional antibody that inhibits B-cells, CD19-expressing plasma cells, and plasmablast activity and has the potential to provide clinical benefits across multiple autoimmune disorders. The purpose of this analysis was to 1) develop a population pharmacokinetics (PK) and pharmacodynamics (PD) model of obexelimab from clinical studies following intravenous (IV) or subcutaneous (SC) administration; and 2) conduct simulations using this PK/PD model to support the proposed obexelimab Phase 3 dosing regimen in patients with immunoglobulin G4-related disease (IgG4-RD).

Methods: A population PK/PD model, which described obexelimab serum PK and PD [absolute B cell (ABC) count or CD19 receptor occupancy (RO)] following single and multiple IV or SC administration to healthy subjects, and IV administration to patients with rheumatoid arthritis (RA) or IgG4-RD, was established based on 4 clinical studies: 1) a first-in-human, single-ascending dose study with obexelimab in healthy volunteers (0.03 to 10 mg/kg IV); 2) a multiple-ascending dose study in patients with RA (0.3 to 10 mg/kg every other week); 3) an open-label study assessing the effect of obexelimab on disease activity in patients with IgG4-RD (5 mg/kg or 90/180 mg IV every other week); and 4) a PK and relative bioavailability study of obexelimab given IV or SC (125 to 375 mg SC or 250 mg IV every other week or 125 mg SC weekly).

Population PK analyses were performed using nonlinear mixed effects modeling software (NONMEM®). The final population PK/PD model was used to simulate obexelimab PK exposures and changes in ABC counts and in CD19 RO following various SC dosing regimens.

Results: A population PK/PD model was successfully developed which described the PK (concentrations) and PD (both ABC and CD19 RO) of obexelimab following single and multiple IV or SC administration to healthy subjects, and patients with RA or IgG4-RD. The final PK model was a two-compartment model with first-order absorption for SC administration and first-order elimination. Intrinsic and extrinsic subject factors were assessed as covariates in population PK full model development. These covariates included ethnic-related covariates such as race, body weight, age, and gender. The population PK analysis demonstrated that none of these ethnic-related covariates impacted the PK of obexelimab.

The PD simulation predicts a 250 mg SC weekly dosing will achieve the complete (~100%) CD19 RO and the maximum reduction in ABC count of approximately 50% of baseline during the entire dosing interval. Following discontinuation of the 250 mg SC weekly dosing, approximately 8 and 10 weeks is required for CD19 RO and ABC counts to return to baseline levels, respectively.

Conclusion: The population PK analysis of obexelimab demonstrates the ethnic insensitivity of obexelimab PK. Robust RO and PD following 250 mg SC weekly further supports clinical development of obexelimab to treat B-cell mediated autoimmune diseases.

Disclosure: X. Wang: None; **R. Kirk**: None; **S. Lowry**: Zenas bio, 3; **H. Mu**: None.

Abstract Number: 0003

Expanded Extrafollicular B Cells Were Improved by RTX in IgG4-related Disease

Yusho Ishii[1], Aakriti Alisha Arora[1], Scott Jenks[1], Iñaki Sanz[2] and Arezou Khosroshahi[1], [1]Emory University, Atlanta, GA, [2]Emory University School of Medicine, Atlanta, GA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: IgG4-related disease (IgG4-RD) is an immune-mediated disease characterized by fibrotic masses with expansion of $IgG4^-$producing plasma cell in multiple organs such as pancreas, lacrimal and salivary glands, and retro-peritoneal tissues. Antibody secreting cells (ASC) such as plasmablasts expand in peripheral blood in IgG4-RD, resulting in high titer of serum IgG4 in active state.

ASC accumulated in extrafollicular masses, suggesting that B cell precursors of ASC may differentiate through extrafollicular pathways. However, the detail of B cell profile in IgG4-RD remains unclear. Clinically, IgG4-RD responds very well glucocorticoid and B cell depleting therapy, but the change of B cell profile including extrafollicular B cells after these treatments are unknown.

Methods: IgG4-RD patients were enrolled from Emory IgG4-RD Clinic. Disease activity was assessed by IgG4-RD responder index. Fresh and frozen peripheral blood mononuclear cells (PBMCs) were stained by 3 sets of antibody panels and analyzed by flow cytometer. The first cohort used fresh PBMCs and a simple B cell panel (n: 11 healthy control (HC), 13 inactive and 12 active IgG4-RD). The second cohort and third cohort used the same frozen PBMCs with an extended B cell panels (n: 10 HC, 10 or 11 RTX-naïve and 13 RTX-treated (6-51 months after RTX) IgG4-RD).

Results: Analysis of cohort 1 focused on the difference of B cell profile by disease activity. IgD and CD27 double negative (DN) B cells were increased, and unswitched memory B cells (USM) were reduced in active patients. However, IgG4-RD patients were split into the high or low proportion of DN B cells in $CD19^+$ B cells. In DN B cells, DN2 ($CD19^{+/++}$/$CD38^-$/$CD27^-$/IgD^-) expanded, while DN1 ($CD19^{+/++}$/$CD38^{-/+}$ $CD27^-$/IgD^-) were decreased, resulting in high DN2+DN3/DN1 ration in IgG4-RD. In 2nd and 3rd cohorts, we compared HC, RTX-naïve and -treated IgG4-RD. increased DN2 ($CD19^+$/$CD27^-$/IgD^-/$CD11c^+$/$CD21^-$) and reduced USM ($CD19^+$/$CD27^+$/IgD^+) were consistent with 1st cohort though DN B cells did not expand. In addition to DN2, increased ASC, DN3 ($CD19^+$/$CD27^-$/IgD^-/$CD11c^-$/$CD21^-$) and $CD11c^+$switched memory (SWM) B cells also were observed. Moreover, these expanded populations in IgG4-RD were repressed by RTX treatment. In $CD3^+$ T cells, CD4/CD8 ratio was elevated in IgG4-RD, and this ratio was reverted by RTX.

Conclusion: Extrafollicular effector B cells including DN2, DN3, $CD11c^+$ SWM and ASC were expanded in IgG4-RD. Intriguingly, this abnormal expansion was mostly reverted by RTX treatment, consistently with a good clinical response. In addition to B cells, elevated CD4/CD8 ratio was also normalized by RTX. These results suggest that promoted extrafollicular pathway-derived B cell might be a precursor of tissue-infiltrating plasma cell in IgG4-RD.

Disclosure: Y. Ishii: None; **A. Arora**: None; **S. Jenks**: None; **I. Sanz**: None; **A. Khosroshahi**: Horizon Therapeutics, 1, 2.

Abstract Number: 0004

CD22 X CD79b Bispecific Ab Potently Inhibits B Cell Activation and Plasmablast Accumulation

Timothy Burwell[1], Jeffrey Hall[1], Suzanne Cole[2], Sarah Tursi[1], Isabelle Baribaud[3], Kyle Bednar[1], Naresh Kumar[1], Julie Carman[1], Navin Rao[2] and **Edith Janssen**[2], [1]Janssen Research and Development, LLC, Spring House, PA, [2]Janssen Research & Development, LLC, Spring House, PA, [3]IGM Biosciences, Inc., Doylestown, PA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: B cells contribute to the development and progression of autoimmune diseases through multiple mechanisms. Consequently, modulating B cell activation, B cell effector function, and plasmablast development holds great therapeutic potential. CD22 (Siglec-2) is an inhibitory receptor selectively expressed on B cells and has been shown to inhibit BCR downstream signaling. Here we tether CD22 to the B cell receptor (BCR) with a CD22 x CD79b bispecific Ab (bsAb) to potently inhibit B cell activation, proliferation, cytokine production, Ig production, and plasmablast accumulation.

Methods: Binding of the bsAb to different B cells was analyzed by flow cytometry using directly conjugated-bsAb. Potential for *in vitro* antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC) was assessed in PBMC cultures in the presence of fresh serum. Impact on BCR downstream signaling upon IgM cross-linking was determined by phospho-flow of p-Syk and p-PLCg in purified B cells. PBMC and B cells were used to assess inhibitory capacity of the bsAb on B cell activation, proliferation, and cytokine production upon IgM cross-linking. PBMC from 15 RA patients and 17 matched healthy donors (HD) were used to verify inhibitory potential in rheumatologic disease.

For *in vivo* pharmacology studies, CD34+ reconstituted NSG mice were dosed as indicated, and serum IgM, frequency and composition of B cells and plasmablasts (spleen, blood), and splenic B cells functionality upon IgM cross-linking were assessed at indicated time points.

Results: Our CD22xCD79b bsAb showed strong, selective binding to all CD22 expressing B cell subsets without *in vitro* depletion. The bsAb potently inhibited the phosphorylation of BCR downstream signaling molecules Syk and PLCg upon IgM cross-linking, which correlated with significant reductions in B cell proliferation and cytokine production. Moreover, our bsAb potently inhibited the activation of B cells in PBMC from both HD and RA patients (CD69, CD83, CD86).

In vivo treatment of CD34+NSG mice with the bsAb showed a potent, dose-dependent reduction in serum IgM levels, concomitant with profound reductions of plasmablasts in the blood and spleen. In addition, splenic B cells from treated animals showed a significant dose-dependent reduction in their capacity to produce proinflammatory cytokines upon IgM cross-linking *in vitro* (IL-6, IL-8, CCL3, CCL4, CCL22).

Conclusion: Together this data shows that our CD22xCD79b bsAb is a potent inhibitor of B cell activation *in vitro* and *in vivo*, making it a promising approach for the treatment of autoimmune diseases with a pathogenic B cell component.

This work was supported by Janssen R&D, LLC

Disclosure: T. Burwell: Janssen, 3; **J. Hall**: Janssen, 3; **S. Cole**: Janssen, 3; **S. Tursi**: Janssen, 3; **I. Baribaud**: Janssen, 3; **K. Bednar**: Janssen, 3, 11; **N. Kumar**: Janssen, 3; **J. Carman**: Janssen, 3, 11; **N. Rao**: Janssen, 3, 11; **E. Janssen**: Janssen, 2, 11.

Abstract Number: 0005

Obexelimab Inhibits B Cell Activation and May Interfere with B Cell Chemotaxis in IgG4-Related Disease

Thomas Guy[1], Hang Liu[2], Vinay Mahajan[2], Cory Perugino[3], Zachary Wallace[4], Shauna quinn[5], Allen Poma[6], Debra Zach[7], John Stone[8] and Shiv Pillai[9], [1]Ragon Institute of MGH, MIT and Harvard, Cambridge, MA, [2]Ragon Institute, Cambridge, MA, [3]Massachusetts General Hospital, Boston, MA, [4]Massachusetts General Hospital, Newton, MA, [5]Zenas Biopharma, New York, NY, [6]Zenas Biosciences, New York, NY, [7]Exagen, Vista, CA, [8]Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Concord, MA, [9]Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Obexelimab is a bifunctional, non-cytolytic, humanized monoclonal antibody that binds CD19 and ligates FcγRIIb with high affinity. Data from a phase 2 clinical trial of patients with IgG4-related disease (IgG4-RD), a chronic immune-mediated fibro-inflammatory disease, demonstrated rapid, and sustained clinical improvement, including complete remission in most patients following treatment with obexelimab. Although not shown to drive rapid apoptotic death of B cells, obexelimab treatment does result in an approximate 50% reduction in circulating B cell numbers, as well as near complete reduction in circulating plasmablasts. We have shown that obexelimab dampens the activation of BTK in B cells, easily ascribable to the loss of PIP3 that would result from the predicted activation by FcgRIIb of the SH2-domain containing inositol phosphatase SHIP-1. Here, we aimed to examine the changes in gene expression induced by obexelimab in B cells from treated patients with IgG4-RD to better understand its mechanism of action.

Methods: Peripheral blood was collected from patients with IgG4-RD before and after treatment with obexelimab (two days after the eighth dose). PBMCs were isolated using standard density gradient centrifugation. Naïve ($CD19^+IgD^+CD27^-$) and memory ($CD19^+IgD^-CD27^+$) B cell populations were FACS purified and used for subsequent ATAC-sequencing (N = 3 with 3 technical replicates for each sample) and RNA-sequencing (N = 16).

Results: We observed many changes in gene expression and chromatin accessibility attributed to treatment with obexelimab in naïve B cells. RNA sequencing identified 775 genes upregulated and 808 genes downregulated in post- compared to pre-obexelimab treated B cells. ATAC sequencing analysis identified 1040 increased and 708 decreased differentially accessible genes in post- versus pre-obexelimab treated B cells. Gene ontology biological process analysis of ATAC sequencing were consistent with altered cytoskeleton organization, chemotaxis and migration. In addition, nucleotide and purine metabolic processes were impacted after treatment. Furthermore, KEGG pathway analysis demonstrated key components of actin cytoskeleton regulation associated with altered phosphoinositide regulation. Gene ontology biological process analysis of RNA-seq data aligned with ATAC-seq analysis, confirming alteration of cell-cell adhesion and cytoskeletal pathways.

Conclusion: Collectively, these chromatin accessibility and transcriptromic data suggest that reciprocal changes in PIP3 and PI(3,4)P2 dependent events induced by obexelimab on B cells alter B cell activation and migration. Paired with the previous published data demonstrating attenuation of BCR signalling, obexelimab not only reduces PIP3-dependent BCR-induced BTK activation in B cells from IgG4-RD patients but could also enhance PI(3,4)P2 phosphoinositide-mediated B cell

migration, possibly causing sequestration of B cells. Together, these two mechanisms may eliminate the potential of pathogenic, self-reactive B cells to respond to self-antigen, migrate out of secondary lymphoid organs, and infiltrate inflamed tissues.

Disclosure: T. Guy: None; **H. Liu**: UCB, 3; **V. Mahajan**: None; **C. Perugino**: Horizon Therapeutics, 2; **Z. Wallace**: BioCryst, 2, Bristol-Myers Squibb(BMS), 5, Horizon, 1, 2, 5, MedPace, 2, Novartis, 1, PPD, 2, Sanofi, 1, 5, Shionogi, 1, Visterra, 1, 2, Zenas, 1, 2; **S. quinn**: Zenas BioPharma, 3, 10, 11; **A. Poma**: Zenas BioPharma, 3; **D. Zach**: Exagen, 3, 11; **J. Stone**: Abvie, 2, Amgen, 1, 2, Argenx, 2, Aztrazeneca, 2, Bristol Myers Squibb, 2, 5, Celgene, 2, Chemocentryx, 2, Chugai, 2, GSK, 2, Horizon Therapeutics, 1, 2, 5, InflaRx, 2, IQVIA, 1, 2, Kyverna, 2, Mirabio, 2, NIH, 5, Novartis, 2, PPD, 2, Prometheus, 2, Q32, 2, Regeneron, 2, Roche-Genentech, 2, Roivant, 2, Sanofi, 2, 5, Spruce Biosciences, 2, Star Therapeutics, 2, Steritas, 12, Chair, Scientific Advisory Board (no fiduciary responsibilities), ZenasBio, 2; **S. Pillai**: Abpro Inc, 1, BeBio, 1, Octagon Therapeutcis, 1.

Abstract Number: 0006

Preclinical Characterization of a Novel anti-CD40 Antagonist Antibody-glucocorticoid Conjugate with Superior Preclinical Efficacy and Favorable Safety Profile

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Glucocorticoids (GCs) are the first-line anti-inflammatory treatment for many autoimmune diseases, but long-term systemic administration of GCs is associated with unwanted side effects, which may be overcome by targeted delivery of GCs via antibodies. The CD40-CD40L costimulatory pathway regulates a wide array of immune cell effector function. The blockage of CD40/CD40L pathway is effective in autoimmune diseases such as Sjögren's syndrome, but exhibits limited efficacy in severe disease such as systemic lupus erythematosus (SLE). We generated a first-in-class anti-CD40 antibody-glucocorticoid conjugate (anti-CD40 conjugate) that allowed the targeted delivery of GCs to the corresponding immune cells, while blocking CD40/CD40L pathway simultaneously. Here we describe the preclinical characterization of this novel antibody-glucocorticoid conjugate.

Methods: The targeted delivery of GCs was measured by using a CD40-expressing GC reporter cell line. Inhibitory activity of the anti-CD40 conjugate was evaluated in human B and dendritic cells under CD40L stimulation. In addition, Fc-dependent effector functions, including antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC), were assessed by co-culturing natural killer (NK) cells or complement proteins with CD40-expressing cell lines. By using human-CD40-transgenic mice, the efficacy of anti-CD40 conjugate was determined in T cell-dependent antibody responses (TDAR) model and skin graft model. Furthermore, a 4-week GLP repeated-dose toxicity study in cynomolgus monkeys was conducted to evaluate the *in-vivo* safety.

Results: The anti-CD40 conjugate displayed GC receptor activity after being internalized via the membrane CD40 and inhibited CD40L-induced activation of human B or dendritic cells. The anti-CD40 antibody is a humanized antagonist antibody with Fc-silencing mutation to eliminate Fc-dependent effector functions and therefore is unable to mediate ADCC and

CDC.We proved that the anti-CD40 conjugate blocked the generation of KLH-specific antibodies in TDAR model. Compared to the anti-CD40 antibody or the combination of anti-CD40 antibody with GC treatment, the anti-CD40 conjugate supported a longer survival of the transplanted skin tissues in the skin graft model. Further, the repeated-dose toxicity study in cynomolgus monkeys showed that the anti-CD40 conjugate was safe and generally well tolerated up to 75 mg/kg. We did not observe adverse effects in cardiovascular, respiratory, and neurobehavioral endpoints. Reduced follicle size and suppression of germinal center in lymph nodes and spleen were seen with immunophenotyping and histology.

Conclusion: Overall, these data demonstrate that the novel anti-CD40-glucocorticoid conjugate has a promising efficacy and safety profile in preclinical models and support the clinical application in diverse autoimmune diseases, including organ transplantation, systemic lupus erythematosus, etc.

Disclosure: D. wang: Jiangsu Hengrui Pharmaceuticals Co., Ltd., 3; **W. Ren**: Jiangsu Hengrui Pharmaceuticals Co., Ltd., 3; **l. su**: Jiangsu Hengrui Pharmaceuticals Co., Ltd., 3; **y. lin**: Jiangsu Hengrui Pharmaceuticals Co., Ltd., 3; **c. liao**: Jiangsu Hengrui Pharmaceuticals Co., Ltd., 3.

Abstract Number: 0007

Targeting NF-κB Signalling in B Cells from ANCA-associated Vasculitis Impairs B Cell Biology as a Potential Novel Target

Ana Merino-Vico[1], Jan Piet van Hamburg[1], Paul Tuijnenburg[1], Aram Al-Soudi[1], Carlo Bonasia[2], Boy Helder[1], Abraham Rutgers[2], Wayel H. Abdulahad[2], Coen A. Stegeman[2], Jan-Stephan Sanders[2], Laura Bergamaschi[3], Paul A. Lyons[3], Theo Bijma[2], Laura Van Keep[1], Kirsten wesenhagen[1], Aldo Jongejan[1], Henric Olsson[4], Niek De Vries[1], Taco W. Kuijpers[1], Peter Heeringa[2] and **Sander Tas**[5], [1]Amsterdam University Medical Centers, Amsterdam, Netherlands, [2]University Medical Center Groningen, Groningen, Netherlands, [3]University of Cambridge, Cambridge, United Kingdom, [4]AstraZeneca, Gothenburg, Sweden, [5]Amsterdam UMC, locatie AMC, Utrecht, Netherlands

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: B cells have gained increased interest in ANCA-associated vasculitis (AAV) research, as the treatment of this autoimmune disease with rituximab (an anti-CD20 B cell targeted therapy) resulted in beneficial clinical outcomes. Despite its advantages, this treatment strategy results in long-term B cell depletion and fails in the targeting of long-lived plasma cells, rendering an unmet need for more reversible and combined B and plasma cell targeting approaches to achive long-term (drug-free) disease remission. This aim may be fullfilled upon targeting essential signaling pathways for B cell biology. The NF-κB signalling pathways regulate fundamental B and/or plasma cell responses, downstream of various B cell surface receptors, including the B cell receptor, CD40, and TLRs, making them potential targets. Furthermore, alterations in NF-κB have been described in other autoimmune diseases and in B cell malignancies. Our research aims to study the potential effects of inhibition of NF-κB signalling on B cell responses in general, and more specifically on plasmablast differentiation and (auto)antibody production in B cells from AAV patients as a novel therapeutic approach.

Methods: Memory B cells were obtained from patients with AAV and healthy donors (HD), and gene expression profiles were generated by RNA-sequencing. Functional assays were performed culturing PMBCs from AAV patients and HD with stimuli mimicking T cell-dependent (anti-CD40/IL-21) and T cell-independent (CpG/IL-2) conditions. Pharmacological inhibitors of NF-κB inducing kinase (NIK, non-canonical pathway) and Inhibitor-of-κB-kinase-β (IKKβ, canonical pathway) were

added to the cultures. Downstream NF-κB signalling was determined by Western blot. After 6-day cultures, B cell proliferation and differentiation were determined by flow cytometry, and ELISA was performed for detection of (auto)antibody production.

Results: Memory B cells from AAV patients with active disease had an upregulated expression of NF-κB-associated genes compared to patients in remission and HD. Targeting of NIK and IKKβ in AAV and HD B cells effectively inhibited downstream non-canonical or canonical NF-κB signalling, respectively. NIK and IKKβ inhibition significantly reduced B cell proliferation in both stimulatory conditions in functional assays. In addition, NK and IKKβ inhibitors attenuated B cell differentiation into plasmablasts and antibody production, including anti-proteinase-3 (PR3) autoantibodies. Interestingly, the effects of NIK inhibition appeared to be B cell-specific, remdering T cell proliferation unaffected.

Conclusion: These data reveal that NF-κB-associated genes were highly expressed in memory B cells from AAV patients with active disease and that interfering with NF-κB signalling inhibits essential B cell responses that are important in the autoimmune process. These findings suggest that targeting NF-κB, particularly NIK, may be a more reversible and B cell directed novel treatment modality for AAV.

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Abstract Number: 0008

Differential Induction of Anti-Muscarinic Type-3-Receptor Antibodies by Immunization with 4-Hydroxy-2-nonenal-Modified Ro60 in BALB/c Mice

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren's Disease is an autoimmune condition in which patients exhibit decreased salivary/lacrimal gland function and express autoantibodies that target the 60k molecular weight Ro autoantigen. Published works have proposed autoantibodies that target M3R as potential clinical markers for **Sjögren's** Disease. Our studies show that 4-hydroxy-2-nonenal (lipid oxidation byproduct) immunized rabbits develop antibodies against G-protein-coupled acetylcholine receptor muscarinic-type-3-receptor (M3R) second (ECL2) and third (ECL3) extracellular loops. We hypothesized that there will be a differential induction of antibodies against ECL2 or ECL3 dependent on the degree of 4-hydroxy-2-nonenal (HNE)-modification of Ro60 in BALB/c mice.

Methods: Five groups of BALB/c mice were used in this study. Group I was immunized with Ro60. Groups II to IV were immunized with Ro60, modified with 0.4 mM (low), 2 mM (medium) and 10 mM (high) HNE respectively. Group V controls received Freund's adjuvant. Antibodies to M3R ECL2 (amino acids 213-228) and ECL3 (amino acids 514-527) were detected by multiple antigenic peptide ELISA using sera from the immunized mice.

Results: Immunization with unmodified Ro60 induced a rapid and differential intermolecular epitope spreading to the second loop of M3R, but not to the third loop. Bleed 2 sera from Group 1 mice immunized with unmodified Ro60 had an average reactivity of OD_{405} 0.69±0.3 to ECL2 peptide, while Group 2 mice immunized with low HNE-Ro60 showed an average reactivity of OD_{405} 0.58±0.21. The medium HNE-Ro60 immunized mice (Group 3) had the highest reactivity (OD_{405} 1.02 ±0.39), and the Freund's control group (Group 5) had the lowest reactivity (OD_{405} 0.01±0.06), while Group 3 mice immunized with high-HNE-Ro60 had a reactivity of OD_{405} 0.25±0.11 to the ECL2 peptide. The anti-ECL2 antibody levels induced in the medium HNE-Ro60 group was significantly higher than the levels induced by immunization with unmodified Ro60 ($p< 0.0003$). The anti-ECL2 levels correlated well with the induction of anti-Ro60 and anti-La antibodies in the mice immunized with medium HNE-Ro60. A similar trend was observed in Bleed 6 of the five experimental groups, with the medium HNE-Ro60 immunized group having significantly higher anti-ECL2 antibody levels compared to Ro60 immunized group ($p< 0.0005$). However, there was no significant induction of antibodies to ECL3 in any of the groups for both bleeds.

Conclusion: We found a differential induction of antibodies against the second extracellular loop of M3R, with Group 3 mice immunized with medium HNE-Ro60 developing significantly higher reactivity when compared to all other groups. Such a differential intermolecular epitope spreading may have significant implications for developing a deeper understanding of the progression of autoimmunity in Sjögren's Disease.

Disclosure: B. Kurien: None; **D. Dave**: None; **M. Tsaliki**: None; **V. Lewis**: None; **R. Scofield**: None.

Abstract Number: 0009

Impact of Psilocybin on Peripheral Cytokine Production

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Cytokines & Cell Trafficking Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Psilocybin is a psychedelic drug with potential therapeutic effects in patients with mood and substance use disorders. Little is known about its impact on the immune system. In alignment with previous research showcasing psilocybin's influence on cortical and subcortical brain regions, we hypothesized a connection between these enduring personality changes to alterations in the immune system. Psilocybin, known for its psychoactive properties, has shown potential in increasing positive personality traits and reducing stress and anxiety in previous studies. Our current research considers psilocybin's potential anti-inflammatory properties, given its role as a serotonin 2A (5-HT2A) receptor agonist. The existing literature suggests that 5-HT2A activation could play a key role in regulating cytokine responses, thereby influencing the immune system.

Methods: Sera from 91 participants were included from our three prior randomized controlled clinical trials (RCTs). Multiplex immunoassay pro-inflammatory cytokine panels (Meso-Scale Discovery) were used to examine the serum from participants in three separate RCTs wherein a range of doses of psilocybin were administered (methods reported previously). Participants represented a range of clinical histories including those with no-known health problems/long-term meditation practice, depression, anxiety, and cancer (various types). Linear mixed models with random effects for each participant were fit to determine relative cytokine levels both before and at various time points after psilocybin administration.

Table 1. Description of 91 participants in three separate studies.

	Mean (SD)	N (%)
Study #1 (n = 35)		
Age in years, mean (SD)	55.0 (12.1)	
Male, N (%)		16 (46%)
Study #2 (n = 25)		
Age in years, mean (SD)	38.9 (12.6)	
Male, N (%)		9 (36%)
Study #3 (n = 31)		
Age in years, mean (SD)	57.3 (9.9)	
Male, N (%)		14 (45%)

SD, standard deviation; N, number

Results: In our linear models, sera collected ≤1-week post-psilocybin revealed increased levels of IL-8 (β=0.164, 95% CI (0.10, 0.23); p=0.004) and TNF-α (β=0.10 (0.05, 0.15); p=0.027). At ≥4-week time points compared to baseline, there was a relative increased level of IL-10 (β=0.08 (0.04, 0.12); p=0.035) and IFNα (β=0.259, 95% CI (0.11, 0.41); p=0.035).

Conclusion: This preliminary study indicates that psilocybin may have impacts on peripheral cytokine concentrations., There was a transient increase in pro-inflammatory cytokine production ≤1-week post-psilocybin followed by delayed anti-inflammatory cytokine production at ≥4 weeks. More broadly, peripheral cytokine production does appear to be altered

Table 2. Differences between cytokine measures after exposure to psilocybin in 91 participants from three separate studies. Only study #2, 3 had delayed (≥4 weeks) time points (n=56). Regression coefficients are for comparing log transformed cytokine concentrations, adjusted fo study.

		Regression coefficient relative to measures before psilocybin		
Measurement time	**Cytokine (pg/mL)**	**Estimate**	**95% CI**	**p**
Within 1 week post-psilocybin	IFNα	0.040	(-0.07, 0.16)	0.676
	IL-10	0.038	(0.00, 0.07)	0.197
	IL12p70	0.015	(-0.01, 0.04)	0.481
	IL-13	0.013	(-0.05, 0.08)	0.811
	IL-1β	0.033	(-0.02, 0.08)	0.433
	IL-2	-0.041	(-0.08, 0.00)	0.271
	IL-4	0.003	(-0.03, 0.03)	0.903
	IL-6	0.095	(0.04, 0.15)	0.056
	IL-8	0.164	(0.10, 0.23)	**0.004**
	TNFα	0.101	(0.05, 0.15)	**0.027**
≥4 weeks post psilocybin	IFNα	0.259	(0.11, 0.41)	**0.035**
	IL-10	0.080	(0.04, 0.12)	**0.034**
	IL-12p70	0.023	(-0.01, 0.05)	0.385
	IL-13	-0.055	(-0.13, 0.03)	0.416
	IL-1β	0.038	(-0.03, 0.10)	0.476
	IL-2	-0.079	(-0.13, -0.02)	0.092
	IL-4	0.013	(-0.02, 0.05)	0.685
	IL-6	0.080	(0.00, 0.16)	0.204
	IL-8	0.090	(0.00, 0.18)	0.210
	TNFα	0.097	(0.03, 0.17)	0.092

CI, confidence interval; IL, interleukin; IFN, interferon; TNF, tumor necrosis factor

Table 3. Differences between cytokine measures after exposure to psilocybin in 91 participants based on study, estimated with linear regression having a random participant intercept. Regression coefficients are for comparing log transformed cytokine concentrations. *Note, study #1 did not have delayed follow up time points.

	≤1 week Post-Psilocybin			≥4 week Post-Psilocybin		
Cytokine	**Estimate**	**95% CI**	**p**	**Estimate**	**95% CI**	**p**
Study #1*						
IFNα	0.055	(-0.24,0.35)	0.716	-	-	-
IL-10	0.089	(0.00, 0.176)	0.051	-	-	-
IL-12p70	0.034	(-0.04, 0.11)	0.390	-	-	-
IL-13	-0.018	(-0.12, 0.08)	0.725	-	-	-
IL-1β	0.043	(-0.04, 0.12)	0.306	-	-	-
IL-2	0.004	(-0.06, 0.07)	0.902	-	-	-
IL-4	0.001	(-0.01, 0.01)	0.862	-	-	-
IL-6	0.166	(0.02, 0.32)	**0.032**	-	-	-
IL-8	0.303	(0.09, 0.52)	**0.007**	-	-	-
TNFα	0.205	(0.06, 0.35)	**0.009**	-	-	-
Study #2						
IFNα	0.047	(-0.25, 0.34)	0.760	0.098	(-0.20, 0.04)	0.519
IL-10	-0.022	(-0.05, 0.01)	0.171	-0.003	(-0.03, 0.03)	0.861
IL-12p70	0.00	(-0.01, 0.015)	0.955	-0.003	(-0.02, 0.01)	0.643
IL-13	0.028	(-0.01, 0.07)	0.165	0.013	(-0.03, 0.05)	0.525
IL-1β	0.027	(-0.18, 0.23)	0.795	0.047	(-0.16, 0.25)	0.656
IL-2	0.021	(-0.01, 0.05)	0.195	0.009	(-0.02, 0.04)	0.558
IL-4	0.010	(-0.13, 0.15)	0.886	0.025	(-0.11, 0.16)	0.721
IL-6	0.69	(-0.12, 0.26)	0.481	0.057	(-0.133, 0.25)	0.558
IL-8	0.087	(-0.09, 0.26)	0.334	0.005	(-0.12, 0.23)	0.545
TNFα	0.051	(-0.07, 0.172)	0.407	0.006	(-0.12, 0.13)	0.924
Study #3						
IFNα	-0.064	(-0.50, 0.37)	0.771	0.489	(0.09, 0.89)	**0.020**
IL-10	-0.016	(-0.19, 0.16)	0.857	0.148	(-0.02, 0.31)	0.081
IL-12p70	-0.013	(-0.12, 0.10)	0.820	0.049	(-0.05, 0.15)	0.358
IL-13	0.084	(-0.29, 0.46)	0.659	-0.142	(-0.49, 0.20)	0.425
IL-1β	0.001	(-0.08, 0.08)	0.988	0.031	(-0.04, 0.11)	0.420
IL-2	-0.208	(-0.46, 0.04)	0.105	-0.215	(-0.45, 0.02)	0.073
IL-4	-0.003	(-0.02, 0.02)	0.742	-0.002	(-0.02, 0.02)	0.819
IL-6	-0.020	(-0.19, 0.15)	0.819	0.073	(-0.08, 0.23)	0.355
IL-8	-0.005	(-0.16, 0.15)	0.950	0.066	(-0.08, 0.21)	0.381
TNFα	-0.063	(-0.26, 0.13)	0.531	0.168	(-0.01, 0.35)	0.077

IQR, interquartile range; IL, interleukin; IFN, interferon; TNF, tumor necrosis factor

by psilocybin administration. . Further research is required to understand psilocybin's broad immunologic impacts on cytokine concentrations in the central nervous system and innate immune signaling. Despite certain limitations, these findings underscore the need to further investigate psilocybin's influence on the immune system.

Disclosure: D. DiRenzo: None; **F. Barrett**: Gilgamesh Pharmaceuticals, 2, Heffter Research Institute, 4, MindState Design Labs, 1, WavePaths Ltd, 1; **J. Perin**: None; **E. Darrah**: None; **L. Christopher-Stine**: None; **R. Griffiths**: None.

Abstract Number: 0010

A Potential Mechanism for Major Adverse Cardiac Events Associated with JAK Inhibitors: JAK Inhibitor Withdrawal Causes Urokinase Release by Primed STAT Signaling

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Cytokines & Cell Trafficking Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren's Disease (SjD) has high glandular IFNg levels, associated with disease activity and lymphoma risk. We showed that IFNg-stimulated minor salivary gland (SG)-mesenchymal stromal cells (MSCs) produced CXCL-9, -10, and -11 through JAK2→STAT1 phosphorylation. Chemokine production and STAT1 phosphorylation by SG-MSCs were inhibited by the JAK1/2 inhibitor, ruxolitinib, a potential promising therapy for SjD. Using culture adapted SG MSC as an in vitro rosetta stone of SG-resident parenchymal cells, we investigated the IFNg →JAK/STAT biochemical response of SG-MSCs to FDA approved JAK inhibitors.

Methods: We treated human SG-MSCs with IFNg and JAK1/2 inhibitors. The JAK inhibitors included ruxolitinib and baricitinib, which bind the JAK conformation poised to phosphorylate its STAT substrates (kinase active conformation). We also studied the novel JAK inhibitor, CHZ868, which binds the kinase inactive JAK conformation. We performed western blotting of cell lysates, probing for JAK1/2 or STAT1/3. We performed RNA sequencing and confirmed results with qPCR and ELISA. ANOVA or paired t-tests were used to calculate p-values across multiple variables.

Results: We determined that ruxolitinib treatment *increased* phospho JAK1 (pJAK1) and phospho JAK2 (pJAK2) of IFNg-stimulated SG-MSCs in a dose-dependent manner (Fig 1a-b). pSTAT1 and pSTAT3 were suppressed by ruxolitinib upon treatment (Fig 1c-d). Discontinuation of ruxolitinib resulted in decreased pJAK1/2 (Fig1e). We found a marked and rapid *increase* of pSTAT1 upon discontinuation of ruxolitinib and baricitinib, but not CHZ868 (Fig 1f). Next, we wanted to determine the downstream effects of this pSTAT cascade. We performed RNA-seq of three conditions: 1) IFNg throughout; 2) IFNg with ruxolitinib, discontinue ruxolitinib, and collect conditioned media 3 hours later; 3) IFNg with CHZ868, discontinue CHZ868, and collect conditioned media 3 hours later. We found that ruxolitniib withdrawal was associated with increased PLAT and PLAU expression when compared to IFNg treatment or CHZ868 discontinuation (Fig 2a-b). We confirmed that PLAU (plasminogen activator, urokinase [uPA]) increased in response to ruxolitinib discontinuation but not in control or CHZ868 discontinuation by qPCR (Fig 3a-b) and ELISA (Fig 3c).

Conclusion: Our findings suggest that ruxolitinib and baricitinib bind the active phosphorylated form of JAK and lead to a paradoxical cellular accumulation of functionally defective pJAK. Upon inhibitor withdrawal, the primed pJAKs are derepressed and initiate a pSTAT signaling cascade, ultimately resulting in high levels of uPA. In contrast, CHZ868, which binds the inactive JAK kinase conformation, does not lead to pJAK accumulation, a pSTAT cascade, or uPA production. CHZ868 does not cause this phenomenon. High uPA, associated with human atherosclerotic plaques, might cause proteolysis and plaque rupture. In conclusion, JAK1/2 inhibitors that bind the active pJAK configuration, but not those that bind the inactive JAK configuration, increase STAT signaling on withdrawal. This signaling results in high uPA and might promote plaque rupture (Fig 3d).

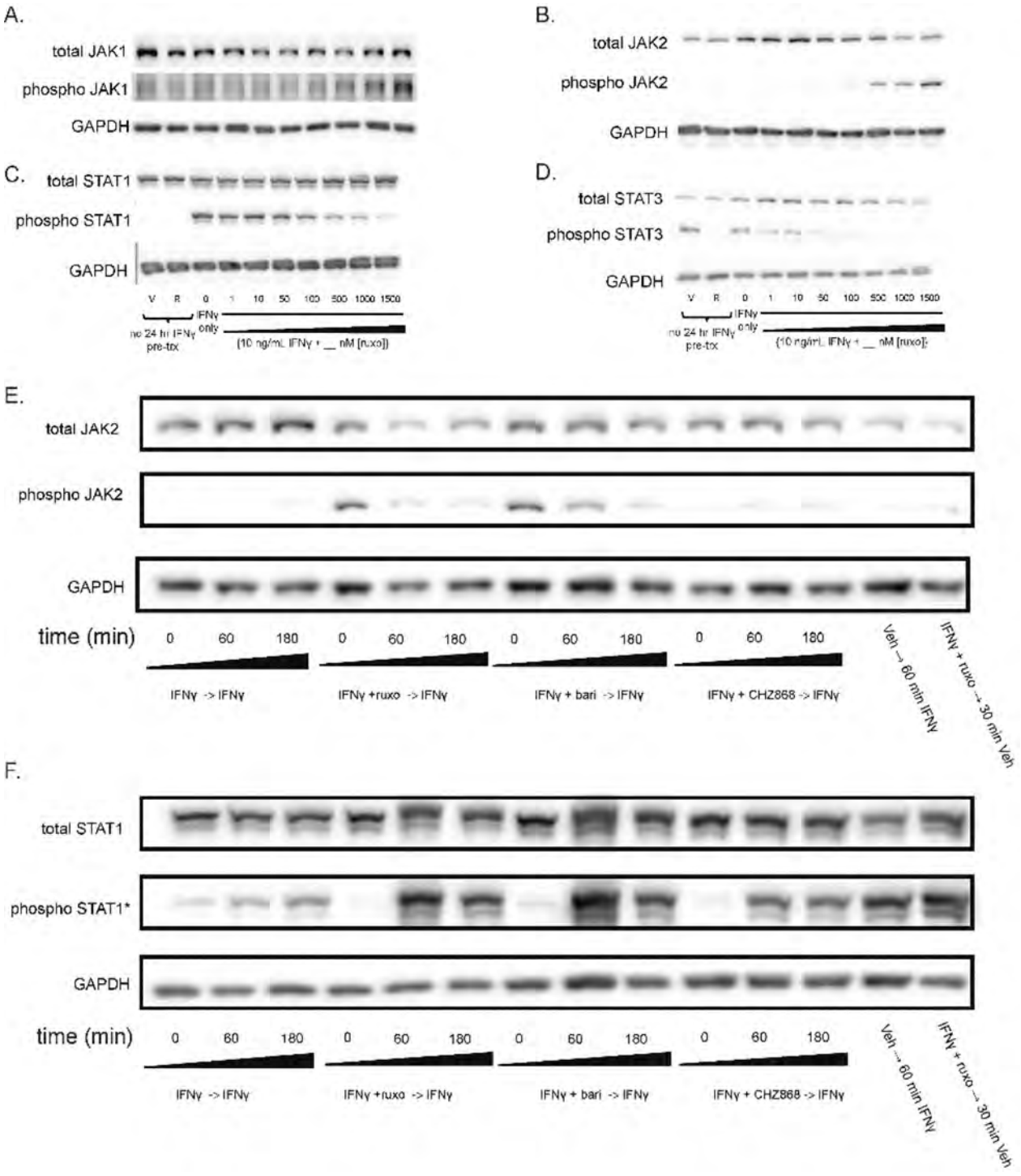

Figure 1. Withdrawal of ruxolitinib and baricitinib, but not CHZ868 causes transient increased phospho STAT1. We treated salivary gland-derived MSCs with vehicle, IFNγ (10 ng/mL), ruxolitinib (1000 nM), baricitinib (1000 nM) or CHZ 868 (1000 nM). A)Total JAK1 remains stable with increasing concentrations of ruxolitinib whereas phospho JAK1 increases with increasing ruxolitinib concentrations; B) total JAK2 peaks at 50 nM ruxolitinib, subsequently decreasing, whereas phospho JAK2 increases with ruxolitinib concentration; C) Total STAT1 remains stable with increasing ruxolitinib concentrations, whereas phospho STAT1 is inversely correlated with ruxolitinib dose; D) Total STAT3 decreases with increasing ruxolitinib concentrations, whereas phospho STAT3 is inversely correlated with ruxolitinib dose; E-F) MSCs treated with IFNγ alone served as controls in lanes 1-4. After treatment of MSCs with IFNγ and either ruxolitinib, baricitinib, or CHZ868 for 24 hours, we withdrew each JAKI and harvested cells at 15-180 minutes. Phospho JAK decreases with ruxolitinib withrawal as expected. Total STAT1 remains stable, whereas phospho STAT1 increases with ruxolitinib withdrawal, peaking at 60 minutes post-withdrawal. A similar trend is seen with baricitinib withdrawal, but not CHZ868 withdrawal.

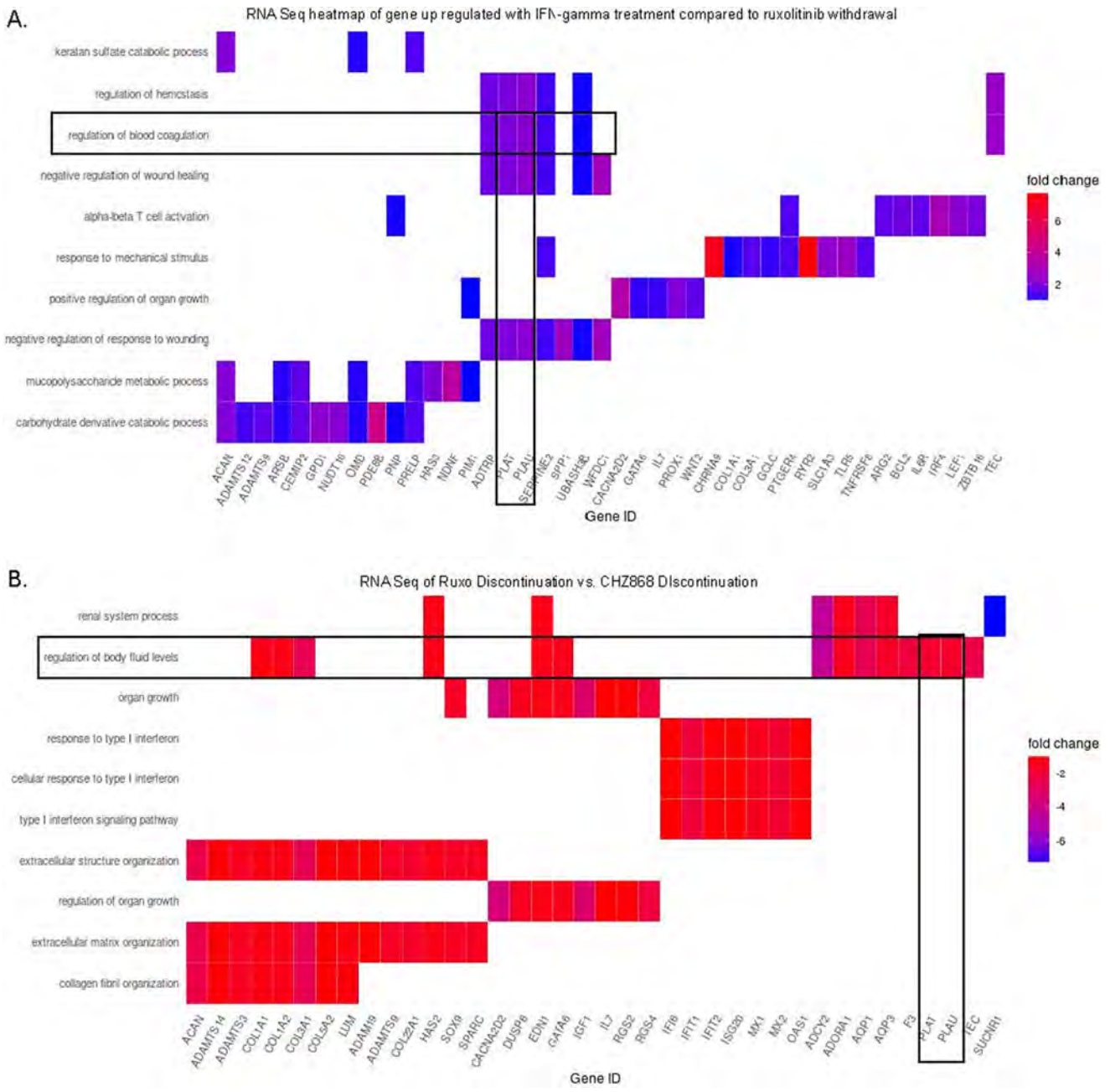

Figure 2. RNA Sequencing identifies PLAT and PLAU and genes differentially regulated upon ruxowithdrawal. Salivary gland MSCs were treated with IFNγ (10 ng/mL), ruxolitinib (1000 nM), or CHZ 868 (1000 nM) and then the either ruxolitinib or CHZ868 were withdrawn. Cells were harvested 6 hours later for RNA Sequencing. A) Compared to continuous IFNγ treatment, ruxolitinib withdrawal causes differential expression of genes associated with keratin sulfate, hemostasis, coagulation, wound healing, T cell activation, response to mechanical stimulus, organ growth, wounding response, mucopolysaccharide metabolic process, and carbohydrate derivative catabolic process. Genes associated with blood coagulation include PLAT and PLAU; B) Ruxo withdrawal compared to CHZ868 withdrawal revealed differential expression of genes related to renal systems, body fluid, organ growth, type I interferon response and signaling pathway, extracellular structure/matrix, and collagen fibril organization. PLAT and PLAU were upregulated in the ruxo withdrawal compared to CHZ868 withdrawal.

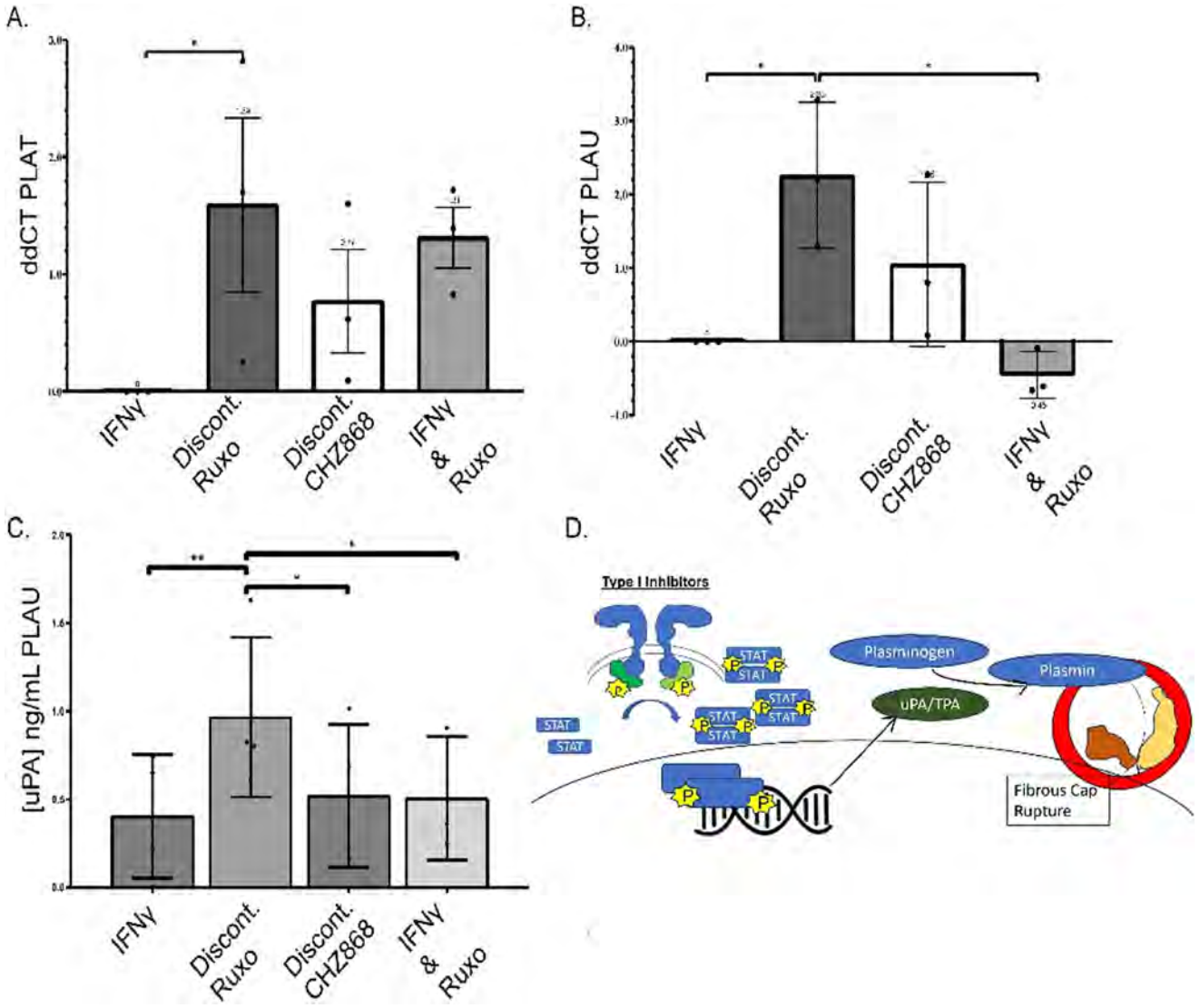

Figure 3. Confirmation that PLAU (plasminogen activator, urokinase [uPA]) increases after type I withdrawal. MSCs were treated with IFNγ (10 ng/mL), ruxolitinib (1000 nM), or CHZ 868 (1000 nM). Withdrawal was performed by treating cells with IFNγ plus JAKI, removing the JAKI by washing cells, and adding back media with IFNγ. After three hours, conditioned media were collected. A-B) qPCR of PLAT (plasminogen activator, tissue type) and PLAU show ruxo withdrawal increases expression of these genes compared to controls. This response was more prominent with PLAU than PLAT; C) uPA ELISA of conditioned media from cells treated with IFNγ treatment, ruxo discontinuation, CHZ868 discontinuation, or continued treatment with IFNγ and ruxolitinb

Disclosure: S. McCoy: Bristol-Myers Squibb(BMS), 2, Horizon, 2, Kiniksa, 2, Novartis, 2, Otsuka/Visterra, 2, Target RWE, 2; **I. Gurevic**: None; **j. Galipeau**: None.

Abstract Number: 0011

Clock Gene Bmal1 Promotes Transcriptional Activity of NF-κB to Regulate Production of Inflammatory Mediators in RA-FLS

Hikari Tsukamoto[1], Kenta Kaneshiro[2], Kohsuke Yoshida[1], Koji Tateishi[3], Yasuhiro Terashima[3], Nao Shibanuma[4], Yoshitada Sakai[5] and Akira Hashiramoto[1], [1]Kobe University Graduate School of Health Sciences, Kobe, Japan, [2]Kobe University Graduate School of Health Sciences, Osaka, Japan, [3]Kohnan Kakogawa Hospital, Kakogawa, Japan, [4]Kobe Kaisei Hospital, Kobe, Japan, [5]Kobe University Graduate School of Medicine, Kobe, Japan

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Cytokines & Cell Trafficking Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA), an autoimmune polyarthritis characterized by 'tumor-like' proliferation of RA fibroblast-like synovial cells (RA-FLS), has characteristic symptoms such as "morning stiffness of joints" related to circadian rhythms. Furthermore, the concentrations of inflammatory cytokines such as TNF-α, IL-6, and IFN-γ in sera of RA patients is also known to peak at midnight, prior to arthritic symptoms in the morning. Circadian rhythms in individual cells are regulated by the expressions of clock genes (*Bmal1*, *Clock*, *Per*, and *Cry*). We previously reported that TNF-α increased the expression of *Bmal1* in RA-FLS which induced osteochondral destruction via production of inflammatory mediators. It has been reported that BMAL1 binds to NF-κB/p65 in breast cancer cells, leading to promotes MMP-9 transcription (Wang et al. Cancer Cell Int, 2019, 19:182), however, it remains unclear how Bmal1 is involved in the pathogenesis of RA. In this study, we examined the function and the mechanism that Bmal1 contributed the productions of inflammatory mediators in RA-FLS under cytokine stimulations.

Methods: After transfected *Bmal1*/siRNA, RA-FLSs were stimulated with or without TNF-α (20 ng/ml), IL-1β (20 ng/ml) or IFN-γ (20 ng/ml) for 32 hours to examine the expressions of inflammatory mediators; CCL2, IL-6, MMP-3 by qPCR. Next, we investigated NF-κB/p65 activity and an interaction between BMAL1 and NF-κB/p65 by immunofluorescence and co-immunoprecipitation. Total protein was extracted from RA-FLS to analyze the expression of phospho-p65/total p65 by western blotting.

Results: Under stimulation of TNF-α and IL-1β, the mRNA expression of CCL2 were significantly suppressed by silencing *Bmal1*. Similarly, under stimulation of IL-1β and IFN-γ, silencing *Bmal1* suppressed the mRNA expressions of IL-6 and MMP-3, respectively (Fig 1). Under fluorescence observations, NF-κB/p65 translocated into the nucleus following TNF-α and IL-1β stimulation though it appeared to be suppressed by silencing *Bmal1*. Stimulation with IFN-γ had no effect on p65 (Fig 2). Furthermore, BMAL1 was combined with p65 (Fig 3-a), and a phosphorylation of p65 was suppressed by silencing *Bmal1* under stimulations with TNF-α (Fig 3-b).

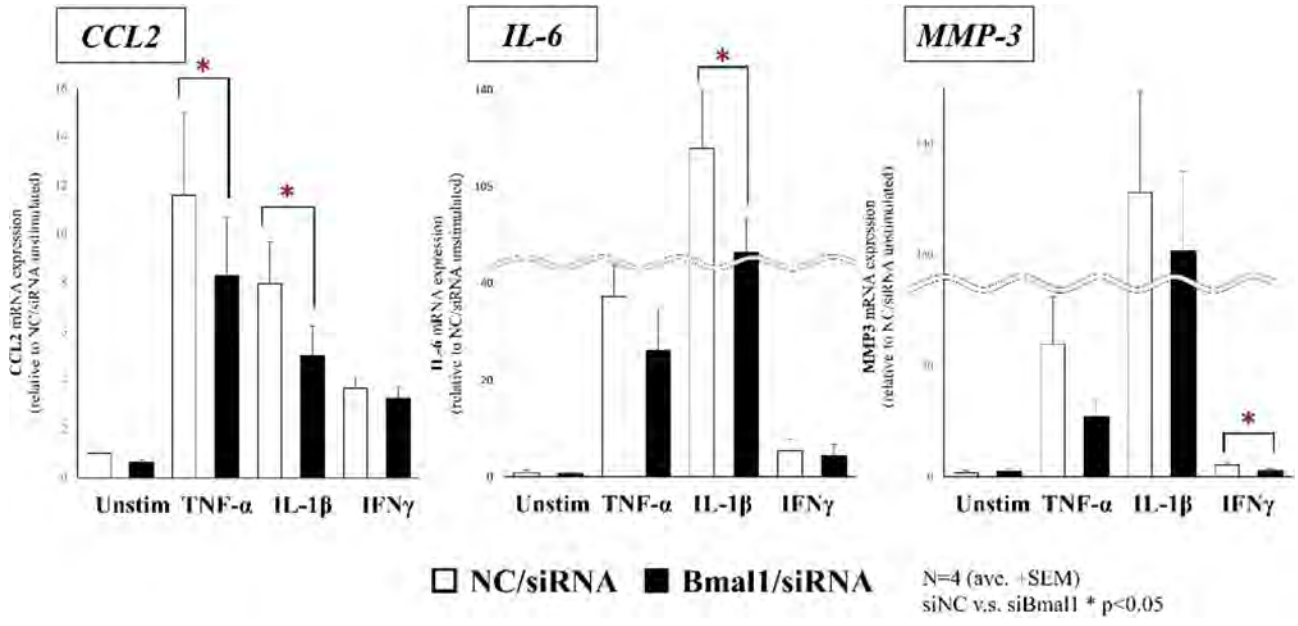

Fig 1

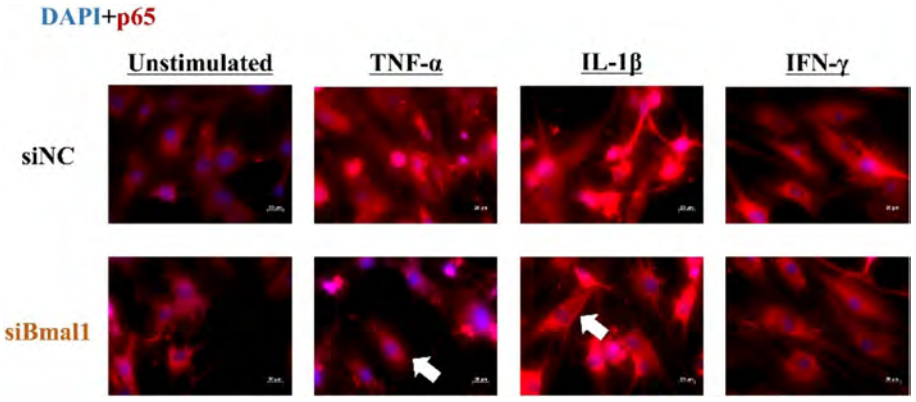

Fig 2

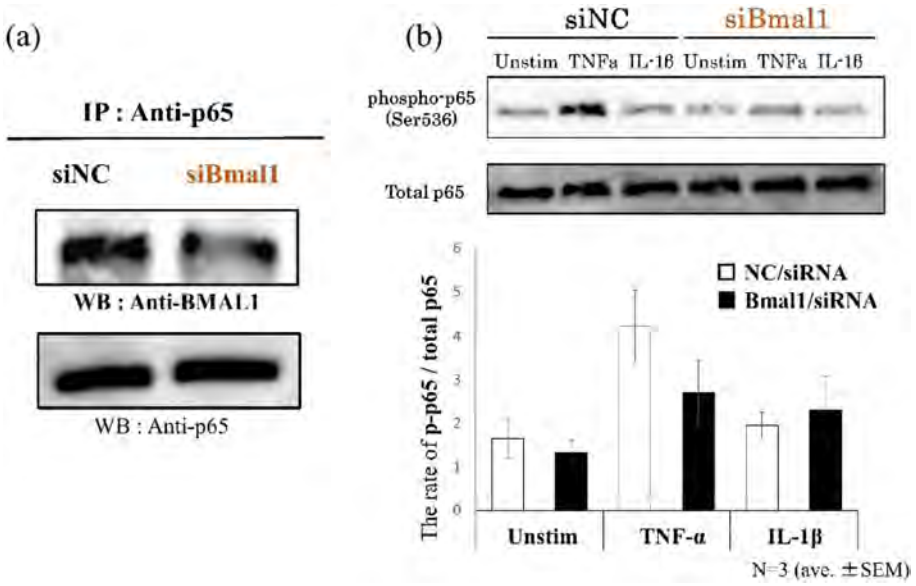

Fig 3

Conclusion: The results indicated Bmal1 promoted the phosphorylation and nuclear translocation of p65 via forming the complex, subsequently contributing to the production of inflammatory mediators in RA-FLS, which might consequently induce osteochondral destruction in RA.

Disclosure: H. Tsukamoto: None; **K. Kaneshiro**: None; **K. Yoshida**: None; **K. Tateishi**: None; **Y. Terashima**: None; **N. Shibanuma**: None; **Y. Sakai**: None; **A. Hashiramoto**: Eli Lilly, 5.

Abstract Number: 0012

Immune-cell Derived Cytokines Synergistically Interact to Drive Synovial Fibroblast Invasive Function and Metabolic Capacity

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Engineering, Trinity College Dublin, Dublin, Ireland, [4]Molecular Rheumatology Department, Trinity Biomedical Sciences Institute, Trinity College Dublin, Ireland EULAR Centre for Arthritis and Rheumatic Diseases, St Vincent University Hospital, University College Dublin, Dublin, Ireland, [5]Molecular Rheumatology Department, Trinity Biomedical Sciences Institute, Trinity College Dublin, EULAR Centre for Arthritis and Rheumatic Diseases, St Vincent University Hospital, University College Dublin, Dublin, Ireland, [6]EULAR Centre for Arthritis and Rheumatic Diseases, St Vincent University Hospital, University College Dublin, Dublin, Ireland, [7]St.Vincent's University Hosp, Dublin, Ireland, [8]Trinity College Dublin, Dublin, Ireland

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Cytokines & Cell Trafficking Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA) encompass two of the most common forms of Inflammatory Arthritis. While common pathogenic mechanisms are involved in driving inflammation in both arthropathies there are significant differences, including the presence/absence of autoantibodies, immune-cell infiltrates, molecular signaling, enthesitis and response to therapy. Therefore, the aim is to identify unique mediators that drive differential synovial fibroblast (FLS) populations and function in RA vs PsA, with implication for the inflammatory responses.

Methods: Single cell (Sc) RNAseq was performed on RA and PsA synovial cell suspensions and FLS populations were then defined by advanced bioinformatic analysis. Subsequently, primary RA FLS were cultured with IL-1β (1ng/ml), TGF-β (10ng/ml), or a combination of both. Analysis of key FLS activation and functional markers was performed by flow cytometry, and secreted pro-inflammatory cytokines and matrix metalloproteinases were quantified by ELISA/MSD multiplex assays. Metabolic capacity was assessed using the Seahorse-XFe-technology and fluorescence-lifetime imaging (FLIM) and glycolytic genes were quantified by real-time PCR. mRNA expression of mitochondrial fission/fusion proteins (DRP1/MFN1/MFN2) and endoplasmic reticulum (ER) stress proteins (XBP1S/BIP/ATF6) were quantified by real-time PCR and immunofluorescent staining was utilized to examine ER stress.

Results: ScRNAseq analysis demonstrated 11 distinct FLS populations in RA and PsA, with FAPα+THY1+ invasive FLS enriched in RA patients. ScRNAseq receptor-ligand interactions demonstrated that T cell-derived TGF-β and macrophage derived IL-1β synergistically drive the transcriptional profile of these FAPα+THY1+ invasive FLS in RA. We further demonstrated at a functional level that IL-1β and TGF- β synergistically interact to promote secretion of pro-inflammatory cytokines IL-6, IL-8, and MCP-1, the growth factor VEGF (all $p< 0.05$), cell surface expression of the adhesion molecule ICAM-1 ($p< 0.01$), in addition to secretion of MMP3 ($p< 0.05$), with no synergistic effects observed for MMP1, CXCR3, CXCR4 and CXCR5. Furthermore, this synergistic interaction also altered the metabolic profile of the RA FLS, towards a more glycolytic phenotype, with synergistic induction of basal glycolysis ($p< 0.05$), proton efflux rate ($p< 0.05$), % PER from glycolysis ($p< 0.05$) and compensatory glycolysis ($p< 0.001$), which supports their invasive phenotype. Significant increases were also observed in key glycolytic markers GLUT-1, HIF1A and PKM2 (all $p< 0.05$) and ER stress genes XBP1S, BIP and ATF6. In parallel, a reduction in mitochondrial size ($p< 0.05$) which was associated with an increase mitochondrial fission protein DRP-1 ($p< 0.05$) with no effect observed for fusion proteins MFN1/MFN2 was demonstrated.

Conclusion: Distinct FLS subtypes were identified in RA and PsA, the invasive phenotype of which were driven by synergistic interactions between T-cell and macrophage derived cytokines. Blocking specific immune-stromal cell interactions may offer new therapeutic intervention in RA and PsA.

Disclosure: Ó. Tynan: None; **A. Floudas**: None; **N. Neto**: None; **M. Monaghan**: None; **S. Wade**: None; **D. Anton**: None; **C. Orr**: None; **D. Veale**: None; **U. Fearon**: None.

Abstract Number: 0013

A Proliferating T Cell Signature in Blood Is Associated with Response to JAK Inhibitor Therapy in Rheumatoid Arthritis Patients

Mehreen Elahee[1], Kathryne Marks[2], Ifeoluwakiisi Adejoorin[2], Lin Chen[2], Derrick Todd[2], Jonathan Coblyn[2], Elena Massarotti[2], Susan Ritter[2], Michael Weinblatt[3], Daniel Solomon[4] and Deepak Rao[2], [1]University of Pittsburgh Medical Center, Pittsburgh, PA, [2]Brigham and Women's Hospital, Boston, MA, [3]Harvard Medical School, Waban, MA, [4]Brigham and Women's Hospital, Newton, MA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Genetics, Genomics & Proteomics Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: There are multiple DMARDs available to treat rheumatoid arthritis (RA) yet there are no widely used predictive biomarkers to guide selection of a specific DMARD. We hypothesize that immunophenotyping of blood immune cells will provide potential biomarkers associated with response to specific DMARDs. We profiled circulating lymphocytes in RA patients before and after treatment with JAK inhibitors (JAKi) or anti-TNF (aTNF) to identify immune cell features associated with treatment response.

Methods: We applied single-cell RNA sequencing (scRNA-seq) and mass cytometry to PBMCs from RA patients before and after treatment with JAKi (scRNAseq n=19, mass cytometry n=27) or aTNF (scRNAseq n=9, mass cytometry n=32) as prescribed by treating physician. RA patients met ACR/EULAR 2010 classification criteria, and treatment response was ascertained by CDAI and medical record review. T cell subsets were identified by unsupervised analysis and specific populations were validated by biaxial gating. Wilcoxon paired tests were used for comparison between the timepoints and Mann-Whitney was used to compare responders vs non-responders.

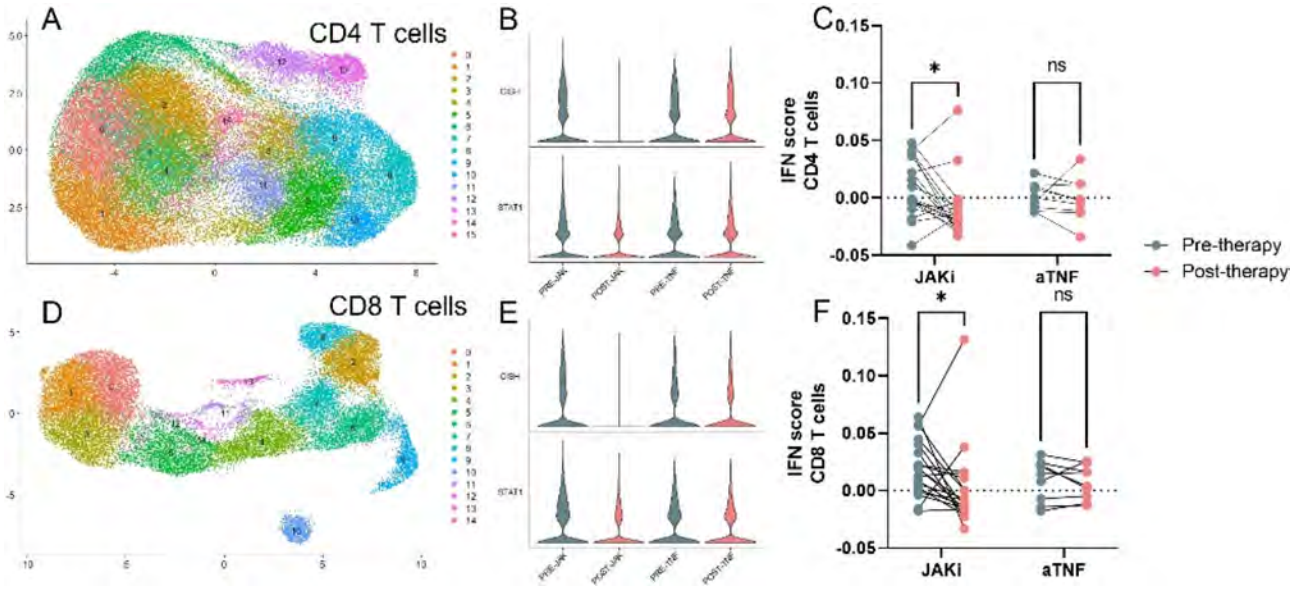


Figure 1. A) UMAP visualization of single cell RNA sequencing of CD4 T cells. B) Expression of CISH and STAT1 in CD4 T cells before and after JAKi or aTNF therapy. C) IFN gene module score in CD4 T cells of each sample before and after JAKi or aTNF therapy. D)UMAP visualization of single cell RNA sequencing of CD8 T cells. E)Expression of CISH and STAT1 in CD8 T cells before and after JAKi or aTNF therapy. F) IFN gene module score in CD8 T cells of each sample before and after JAKi or aTNF therapy.

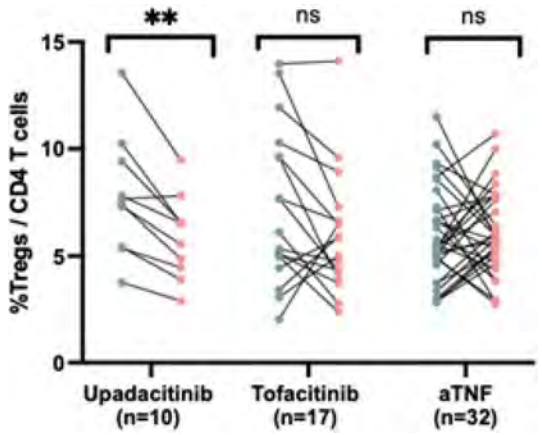


Figure 2. Frequency of regulatory T cells (CD25+FoxP3+) in CD4+ T cells as measured by mass cytometry. Frequencies are shown before and after upadicitinib, tofacinitib, or anti-TNF therapies (**p<0.001 by Wilcoxon signed-rank test).

Results: Comparison of lymphocytes from RA patients before and after treatment with JAKi by scRNA-seq revealed changes in lymphocyte transcriptomic signatures, including reduction in JAK signaling-associated genes such as CISH, SOCS2, and STAT1 and reduction in interferon-stimulated genes, consistent with effective JAK inhibition. These changes occurred similarly in JAKi responders and non-responders, yet they were not observed in the aTNF-treated cohort. Comparison of lymphocyte populations pre- and post-JAKi treatment revealed several changes in T cell composition, including a reduction in a regulatory T cell (Treg) subset following treatment with upadacitinib but not tofacitinib or aTNF. Comparing pre-treatment samples from responders and non-responders, we observed higher frequencies of a PD-1^{hi} CD4 T peripheral helper (Tph) cell cluster and an activated CD8 T cell cluster in JAKi responders compared to non-responders at baseline. Both of these cell clusters had high expression of the proliferation marker Ki67 and increased expression of a gene signature associated with proliferation. These proliferating clusters did not differ between responders vs non-responders in the aTNF-treated cohort.

Unsupervised analysis of mass cytometry data from a larger cohort of JAKi-treated patients similarly identified a reduced Treg frequency in patients treated with upadacitinib and higher frequency of Ki67$^+$ HLA-DR$^+$ Tph cells and Ki67$^+$ HLA-DR$^+$ CD8 T cells specifically in JAKi responders compared to non-responders, but not in the aTNF-treated cohort. Cells in the JAKi responder-associated clusters were characterized by expression of CD38 and PD-1. Biaxial gating on Ki67 and HLA-DR reproduced results from unsupervised clustering.

Conclusion: Broad lymphocyte immunophenotyping revealed a signature of proliferating lymphocytes in blood that was enriched in JAKi responders but not aTNF responders. These results suggest that cellular features detectable in blood may be leveraged as predictive biomarkers and may distinguish likelihood of response to different DMARD therapies.

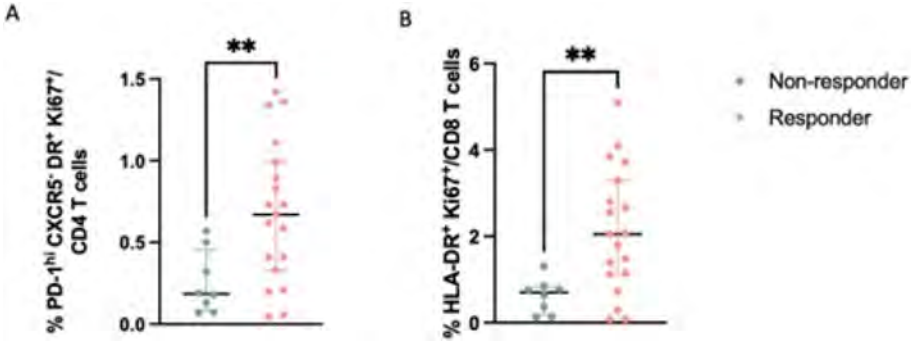


Figure 3. A) Frequencies of PD-1hiCXCR5-HLA-DR+Ki67+ CD4 T cells in responders and non responders to JAKi as measured by mass cytometry (**p<0.001 by Mann-Whitney) B) Frequencies of HLA-DR+Ki67+ CD8 T cells in responders and non responders to JAKi as measured by mass cytometry (**p<0.001 by Mann-Whitney).

Disclosure: M. Elahee: None; **K. Marks**: None; **I. Adejoorin**: None; **L. Chen**: None; **D. Todd**: None; **J. Coblyn**: None; **E. Massarotti**: None; **S. Ritter**: Pfizer, 3; **M. Weinblatt**: Abbvie, 2, 5, Aclaris, 2, Amgen, 2, Aqtual, 5, Bristol Myers Squibb, 2, 5, Canfite, 11, Corevitas, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, 2, Glaxo Smith Kline, 2, Horizon, 2, Inmedix, 11, Janssen, 5, Johnson and Johnson, 2, Pfizer, 2, Prometheus Laboratories, 2, Rani, 2, Revolo, 2, Sanofi, 2, Sci Rhom, 2, Scipher, 2, 11, Set Point, 2, UCB, 2; **D. Solomon**: CorEvitas, 5, Janssen, 5, Moderna, 5, Novartis, 5; **D. Rao**: Astra-Zeneca, 2, Bristol-Myers Squibb, 2, 5, GlaxoSmithKlein(GSK), 2, Hifibio, 2, Janssen, 5, Merck, 5, Scipher Medicine, 2.

Abstract Number: 0014

The 330 Genetic Risk Loci of Systemic Lupus Erythematosus (SLE) Now Known Are Consonant with Multiple Causal Mechanisms Involving Epstein-Barr Virus (EBV)-Encoded Transcription Co-factors (TFs) in EBV-Infected B Cells

Viktoryia Laurynenka[1], Xiaoting Chen[2], sreeja Parameswaran[2], Leah Kottyan[2], Matthew Weirauch[2], Iouri Chepelev[3], Kenneth Kaufman[3] and John Harley[3], [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [3]US Department of Veterans Affairs Medical Center, Cincinnati, OH

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Association of EBV infection with SLE, data suggesting an anti-EBNA1 molecular mimicry fostering SLE autoimmunity, and mechanisms in EBV infected B cells support a model for EBV inducing SLE autoimmunity and clinical illness (Figure 1).

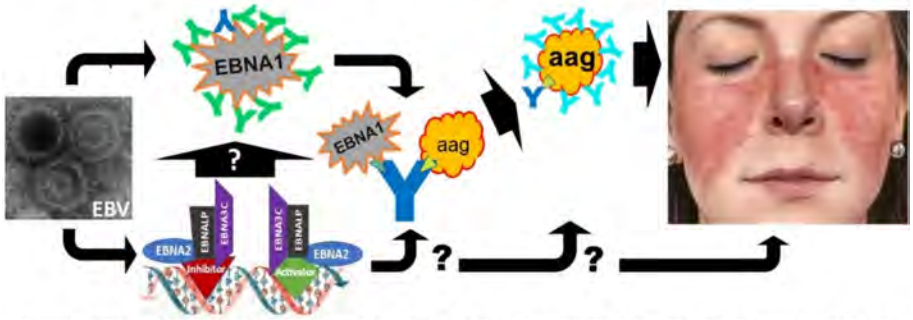
Methods: Literature review identified SLE risk loci at $p< 5x10^{-8}$. We curated 9,862 ChIP-seq (Chromatin ImmunoPrecipitation with DNA sequencing) datasets from 1,339 transcription factors (TFs) in 3,531 "cellular sources" and assessed TF binding to DNA with Multimode RELI (Regulatory Element Locus Intersection (modified from PMID: 29662164)).

Results: 330 SLE risk loci ($p< 5x10^{-8}$) were published prior to 2023. Of these, 255 are found in East Asians (EAS), 106 in Europeans (EU), 11 in African-Americans, and 18 in mixed Americans. 77 of 330 have been established at $p< 5x10^{-8}$ in ≥3 separate studies. 40 of the 330 loci are established independently in both EAS & EU ancestries. KEGG analysis of candidate target genes and genes located near the top variant of the 330 loci, show strong associations related to, among others, IFNγ, IL-12, IL-23, B-cell receptor, & EBV pathways ($6.1< OR< 16$, $10^{-30}< p_a< 10^{-8}$).

Enrichment of TFs binding to SLE loci, with disequilibrium to $r^2>0.8$, using ChIP-seq datasets separately in EAS & EU ancestries, reveals that 200 (14.9%) of 1,339 tested TFs found in 1,871 (19.0%) of the 9,862 TF ChIP-seq datasets are associated with SLE loci at $p_c< 10^{-6}$ in both ancestries. The TF dataset association ranks are highly similar in EAS & EU ancestries ($r=0.73$ (Spearman), $p< 0.0001$) (Figure 2).

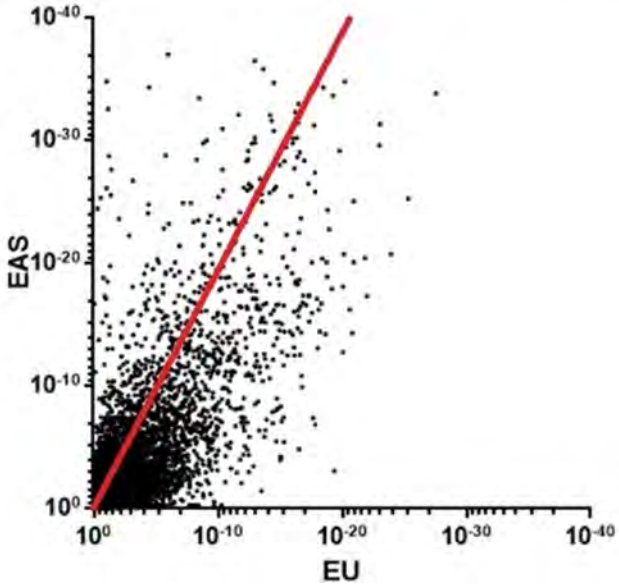
Of the 3,531 cellular sources, EBV-infected and transformed human B cells are most closely associated with both the EAS & EU risk loci ($OR >19$, $p< 10^{-300}$), compared to all other cellular sources, even including B cells that are not EBV-infected. The proportions of significant ($p_a< 10^{-6}$) TF ChIP-seq datasets in all other tested infections are negatively associated in aggregate ($OR< 0.17$, $p< 5.3x10^{-34}$), as are cellular sources with no known infection ($OR< 0.36$, $p< 3x10^{-112}$).

Figure 1. Pathogenesis model for SLE incorporating anti-EBNA1 & EBV-encoded TFs: EBNA2, EBNA3C, & EBNALP. (agg=autoantigen)



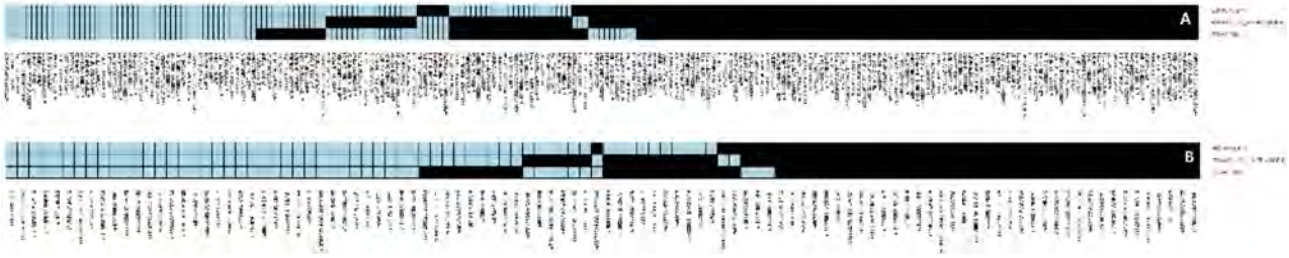
Images courtesy of NIAID (left) & Mayo Foundation (right), all rights reserved. Figure is not otherwise published.

FIGURE 2. P-values for the association of TF DNA binding of 9,862 ChIP-seq datasets with the SLE risk loci of EAS and EU ancestries using multimode RELI.



Of the associated host DNA binding of TFs at $p_a < 10^{-6}$, EBNA2, EBNALP, & EBNA3C, all EBV-encoded Latency III expression products, are separately associated ($2.1 < OR < 2.6$, $p < 10^{-11}$) with the SLE risk loci in both EAS & EU ancestries (Figure 3). At $OR > 3.2$, $p \leq 10^{-4}$, human TFs, known to form super-enhancers in EBV-infected, Latency III expressing transformed B cells, are

Figure 3. Intersection plots (colored boxes) of EBNA2, EBNA3C, & EBNALP ChIP-seq datasets with SLE risk loci for EAS (Panel A) and EU (Panel B) ancestries.



enriched among the significant TF ChIP-seq datasets, compared to uninfected B cells independently at the EAS & EU loci. When the SLE risk loci bound by all 3 of the most closely associated EBV-encoded TF datasets in EBV transformed B cells are removed (see Figure 3), then >95% of formerly significant ($p_a < 10^{-6}$) TF ChIP-seq data sets are no longer significant in either the EAS or EU ancestry, which would also be true for many of the significant human-encoded TF datasets.

Conclusion: The genetic mechanisms of SLE appear similarly dependent upon EBV-encoded TF gene regulation operating in EBV-transformed B cells in both EAS and EU ancestries. The distortion of gene expression, possibly driven through EBV-encoded TFs, is present in both EAS and EU ancestries and potentially important in the pathogenesis of SLE.

Disclosure: V. Laurynenka: None; **X. Chen**: None; **s. Parameswaran**: None; **L. Kottyan**: None; **M. Weirauch**: None; **I. Chepelev**: None; **K. Kaufman**: None; **J. Harley**: None.

Abstract Number: 0015

Genetic Predisposition to a Positive Antinuclear Antibody Test Is Not Associated with Increased Risk of Disease

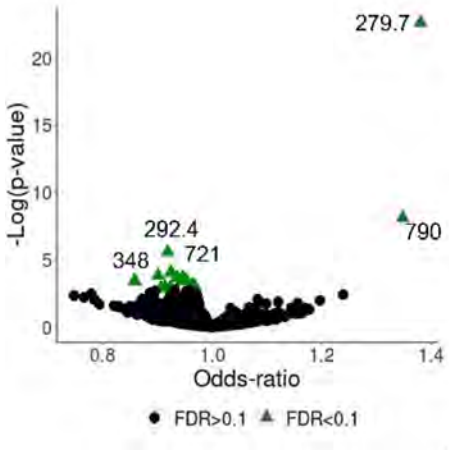
Gul Karakoc[1], Ge Liu[1], Jacy Zanussi[2], Cecilia Chung[2], Jorge Gamboa[1], Jonathan Mosley[1], Nancy Cox[1], C. Michael Stein[1] and **Vivian Kawai**[1], [1]Vanderbilt University Medical Center, Nashville, TN, [2]University of Miami, Miami, FL

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Antinuclear antibodies (ANA) are biomarkers that are frequently used in the diagnosis of common autoimmune (AI) disorders, but are also present in ~12-20% of general population. Several small studies have suggested that a positive ANA test (ANA+) is associated with adverse outcomes such as cardiovascular events, cancer, and infections in the general population, but results have been inconsistent. To define the clinical consequences of ANA+, and mitigate confounding and reverse causation related with clinical testing for ANA, we used a genetic approach to test the hypothesis that a predisposition for ANA+ is associated with adverse clinical outcomes.

Methods: In BioVU, a DNA biobank linked to the de-identified electronic health record system at Vanderbilt, we studied participants of European ancestry (defined by principal components [PCs] and HapMap reference) who had genome-wide SNP genotyping performed on the Illumina Infinium MEGA® Array. We performed a genome-wide association analysis (GWAS) for ANA+ using individuals who had been tested for ANA as part of their clinical care but did not carry a diagnosis of SLE or other common AI diseases. The GWAS used an additive model, and the results were used to develop a polygenic risk score for positive ANA (PRS_{ANA+}) using Bayesian framework with continuous shrinkage. The PRS_{ANA+} was then calculated among BioVU participants not included in the GWAS analysis. A phenome-wide association study (PheWAS) using the PRS_{ANA+} as a predictor was performed adjusting for sex, median age, and 5 PCs of ancestry. For each condition, cases were participants having two or more phecodes for that condition and controls were those with not closely related phecode. Individuals with only one phecode for the condition were excluded. Phecodes with less than 100 cases were excluded to assure power. A false discovery rate (FDR) adjusted P-value < 0.05 was considered significant.

Results: There were 5,081 participants included in the GWAS, and ~7.6 million SNPs were included in the PRS_{ANA+}. The PheWAS was performed in 89,486 individuals and used 1220 phecodes. There were 10 phecodes significantly associated with the PRS_{ANA+} at FDR≤0.05. Providing proof of concept, the top clinical associations with the PRS_{ANA+} were phecodes



PheCode	Description	OR	LCI	UCI	p	FDR
279.7	Other immunological findings	1.38	1.30	1.47	2.4E-23	2.95E-20
790	Nonspecific findings on blood examination	1.35	1.22	1.49	8.5E-09	5.19E-06
292.4	Altered mental status	0.92	0.89	0.95	2.7E-06	1.10E-03
721	Spondylosis and allied disorders	0.92	0.89	0.96	8.1E-05	0.02
348	Other conditions of brain	0.90	0.85	0.95	1.4E-04	0.03
740.9	Osteoarthrosis NOS	0.95	0.92	0.97	2.0E-04	0.04
721.1	Spondylosis without myelopathy	0.94	0.90	0.97	2.0E-04	0.04
783	Fever of unknown origin	0.95	0.93	0.98	3.0E-04	0.05
454	Varicose veins	0.86	0.79	0.93	3.5E-04	0.05
401.2	Hypertensive heart /renal disease	0.94	0.91	0.97	4.1E-04	0.05

Figure: Phenome wide association study of genetic predisposition for a positive antinuclear antibody test. Triangles in green depict significant associations at FDR ≤0.05. All significant associations at FDR≤0.05 are described in the table on the right and sorted by P-value.

related to an abnormal immunological test: "Other immunological findings" and "Nonspecific findings on blood examination" with an odds-ratio (OR)≥1.3 (P < 5.0E-05). The remaining 8 associations had an inverse association (OR < 1.0) and included neurological and back pain-related conditions, fever of unknown origin, hypertensive heart and/or renal diseases (Figure).

Conclusion: A polygenic risk score for ANA+ that captures the genetic predisposition for a positive ANA test was associated with a decreased risk for osteoarthritis, spondylosis, hypertensive renal and/heart disease, and neurological disorders. There was no evidence that a genetic predisposition to a positive ANA test was associated with an increased risk of autoimmune, cardiovascular, or other disease.

Disclosure: G. Karakoc: None; **G. Liu**: None; **J. Zanussi**: None; **C. Chung**: None; **J. Gamboa**: None; **J. Mosley**: None; **N. Cox**: None; **C. Stein**: None; **V. Kawai**: None.

Abstract Number: 0016

Role of TP53 in Inflammatory Reprogramming of Rheumatoid Arthritis Synovial Fibroblasts

Anil Singh and Salahuddin Ahmed, Washington State university, Spokane, WA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: TP53, a tumor-suppressor protein known as the guardian of the genome, plays a critical role in regulating genomic stability and cellular function. When TP53 function is lost, it can lead to uncontrolled cell division and the development of tumors. Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic inflammation and the destruction of joints. In the synovial microenvironment of RA, hyperplastic fibroblasts form a structure called pannus, which resembles a tumor. The downregulation of TP53 is influenced by TNF-α and IL-1β, two inflammatory molecules involved in RA.

Methods: We conducted RNA-seq analysis on human rheumatoid arthritis synovial fibroblasts (RASFs) to investigate the impact of TP53 loss in the synovial microenvironment. TP53 was transiently knocked down using siRNA. Additionally, we employed Gene Ontology studies, ELISA, and Western blot analyses to assess the effects of TP53 loss on inflammatory responses, specifically in the presence of TNF-α and IL-1β. These experiments utilized at least three donor lines of RASFs, with statistical significance set at $p< 0.05$.

Results: Our findings reveal that RASFs exhibit a significant (>40%) decrease in endogenous TP53 levels compared to normal synovial fibroblasts (NSFs). Proinflammatory conditions, such as treatment with IL-1β and TNF-α, further reduce TP53 expression in RASFs by more than 35% within 30 minutes (N=3, $p< 0.05$). RASFs display higher endogenous expression of the MDM2 E3 ubiquitin ligase, responsible for TP53 degradation. Inhibition of p38 MAPK restores TP53 levels, suggesting the involvement of MAPK pathways in TP53 stability. Inhibition of TAK1 and the ubiquitin-proteasome system rescues TP53 loss in response to IL-1β stimulation (N=3, $p< 0.05$). Subcellular fractionation reveals TP53 loss in both the cytoplasmic and nuclear compartments. RNA sequencing analysis identifies 241 differentially regulated genes in TP53-knockdown RASFs (N=3, $p< 0.05$), including an upregulation of inflammatory gene signatures. Gene ontology studies confirm the inflammatory phenotype of RASFs following TP53 loss. These findings suggest that TP53 loss predisposes RASFs to inflammation and may contribute to the progression of rheumatoid arthritis.

Conclusion: This study provides insights into how RASFs are predisposed to proinflammatory reprogramming through selective loss or gain of TP53 functions, affecting resistance to apoptosis and proliferation in response to inflammation during the progression of rheumatoid arthritis. The identification of gene networks, protein factors, and epigenetic changes involved in this process will facilitate the development of novel targeted therapies, enabling a deeper understanding of fibroblast-directed molecular events with significant clinical implications in precision medicine.

Disclosure: A. Singh: None; **S. Ahmed**: None.

Abstract Number: 0017

Xist Ribonucleoproteins Promote Female Sex-biased Autoimmunity

Diana Dou[1], Yanding Zhao[1], Julia Belk[1], Yang Zhao[1], Kerriann Casey[2], Derek Chen[1], Rui Li[1], Bingfei Yu[1], Suhas Srinivasan[1], Brian Abe[1], Katerina Kraft[1], Ceke Hellström[3], Ronald Sjöberg[4], Sarah Chang[5], Allan Feng[5], Daniel Goldman[6], Ami Shah[7], Michelle Petri[6], Lorinda Chung[8], David Fiorentino[9], Emma Lundberg[10], Anton Wutz[11], Paul Utz[5] and Howard Chang[1], [1]Center for Personal Dynamic Regulomes and Program in Epithelial Biology, Department of Dermatology, Stanford University School of Medicine, Stanford, CA, [2]Department of Comparative Medicine, Stanford University, Stanford, CA, [3]Autoimmunity and Serology Profiling, Division of Affinity Proteomics, Department of Protein Science, KTH Royal Institute of Technology, SciLifeLab, Stockholm, Sweden, [4]Department of Protein Science, SciLifelab, KTH Royal Institute of Technology, Stockholm, Sweden, [5]Department of Medicine, Division of Immunology and Rheumatology, Stanford University School of Medicine, Stanford, CA, [6]Department of Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Timonium, MD, [7]Department of Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Ellicott City, MD, [8]Department of Medicine, Division of Immunology and Rheumatology, Stanford University School of Medicine, Woodside, CA, [9]Department of Dermatology, Stanford University School of Medicine, Menlo Park, CA, [10]Departments of Bioengineering and Pathology, Stanford University, Stanford, CA, [11]Department of Biology, Institute of Molecular Health Sciences, Swiss Federal Institute of Technology, ETH Hönggerberg, Zurich, Switzerland

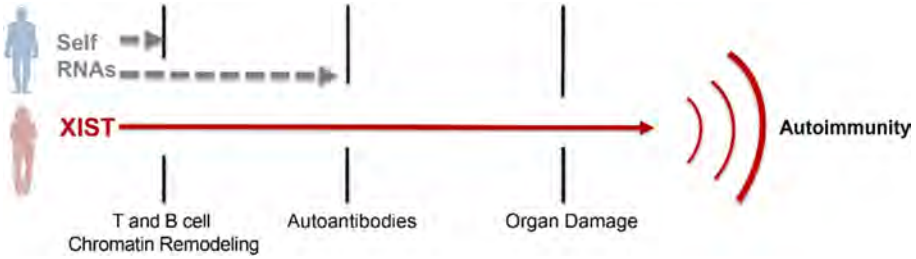
SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Genetics, Genomics & Proteomics Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM



Proposed model of XIST ribonucleoproteins (RNPs) in autoimmune progression: Autoreactivity to Xist RNPs first causes changes in the chromatin landscape impacting genomic accessibility and changes in lymphocyte gene expression programs prior the development of autoantibodies. Prolonged self-reactive activity damages organs in the final stages of autoimmunity.

Background/Purpose: Autoimmune diseases disproportionately affect females more than males. The XX sex chromosome complement is strongly associated with susceptibility to autoimmunity. *Xist* long noncoding RNA (lncRNA) is expressed only in females to randomly inactivate one of the two X chromosomes to achieve gene dosage compensation. The *Xist* lncRNA complexes with numerous proteins associated with autoimmune diseases as autoantigens. The goal of our study is to determine whether the *Xist* ribonucleoprotein (RNP) complex is a driver for female-biased autoimmunity.

Methods: We developed a unique transgenic mouse to confer inducible expression of a non-silencing form of *Xist* in male animals. We assessed disease severity/progression in *Xist*-expressing/non-expressing mice in the pristane-induced systemic lupus erythematous (SLE) model using ATAC-seq, RNA-seq and single cell multiomic analyses of splenic immune cells, histopathology of physical disease markers in tissue sections, and serum autoantibody levels. We screened ChIRP-MS datasets to develop an *XIST* protein antigen array to test autoimmune disease patient serum for reactivity to XIST complex proteins.

Results: Inducible transgenic expression of *Xist* in male mice introduced *Xist* RNP complexes and sufficed to produce autoantibodies. Male SJL/J mice expressing transgenic *Xist* developed more severe multiorgan pathology in pristane-induced model of lupus than wild-type males. *Xist* expression in males reprogrammed T and B cell population and chromatin states to more resemble wild type females. Human autoimmune disease patients displayed significant levels of autoantibodies to multiple components of the *XIST* RNP.

Conclusion: *Xist* is a sex-specific lncRNA that scaffolds ubiquitous RNP components to drive sex-biased immunity.

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Abstract Number: 0018

Alternative Splicing and Expected Protein Changes in Muscle Biopsies from Different Types of Idiopathic Inflammatory Myopathies

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Alternative splicing of mRNA results in important biological impacts with increasing evidence implicating it in the pathology of autoimmune diseases. However, it is understudied in idiopathic inflammatory myopathies (IIM).

Methods: We studied alternative splicing in 152 muscle biopsies from IIM patients and controls. Patients included subgroups with myositis-specific autoantibodies including (anti-Jo1, anti-HMGCR, anti-SRP, anti-NXP2, anti-TIF1g, anti-Mi2, anti-MDA5), and inclusion body myositis (IBM). RNA sequencing data were aligned to the reference genome (GRCh38.p13), then alternative splicing events were quantified using SplAdder. Expected protein changes were identified and visualized using RiboSplitter. The percent spliced-in (PSI) was calculated as reads supporting isoform 2 divided by total reads supporting either isoform per event. We used an alpha of 0.05 and adjusted p values for multiple comparisons. Statistically significant events were filtered based on magnitude of difference to detect events more likely to be biologically meaningful. Finally, we identified outlier splicing events with PSI difference of 3 times the interquartile range, when compared to all other IIM and control samples.

Results: There were hundreds of statistically significant alternative splicing events in each IIM subgroup vs controls. Overall, there were 337 events (in 265 protein coding genes) with larger delta PSI. For each subgroup, we subtracted events that were also present in other subgroup comparisons, resulting in a smaller list of altered splicing that is unique to each subgroup (Table 1). We discovered unique splicing in two patients with anti-SRP myositis where exons 7 and 8 of SRP72 were skipped leading to loss of a tetratricopeptide repeat region (Fig 1A) that is involved in protein binding. SRP72 encodes one of the 6 protein subunits of the signal recognition particle (SRP). An intron retention event in the anti-Jo1 subgroup introduced a stop codon after exon 9 of FBXO9 that would result in a truncated protein (Fig 1B). Patients with HMGCR were more likely to express isoform 1 of an event in EWS RNA binding protein 1, skipping exons 8 and 9 (Fig 1C). One patient with TIF1g, and two with NXP2 had 49, 26, and 10 outlier events, respectively. One of the TIF1g outlier events was an alternative 5´event in

Table 1. Frequencies of statistically significant alternative splicing events in muscle biopsies from myositis patients. NT= Normal tissue

Myositis subgroup	Statistically significant vs NT	Events with larger differences vs NT	Unique events
Anti-Jo1	395	107	22
Anti-HMGCR	566	68	16
Anti-SRP	207	39	8
Anti-NXP2	236	65	11
Anti-TIF1g	215	55	10
Anti-Mi2	428	101	22
Anti-MDA5	307	57	18
IBM	382	80	16

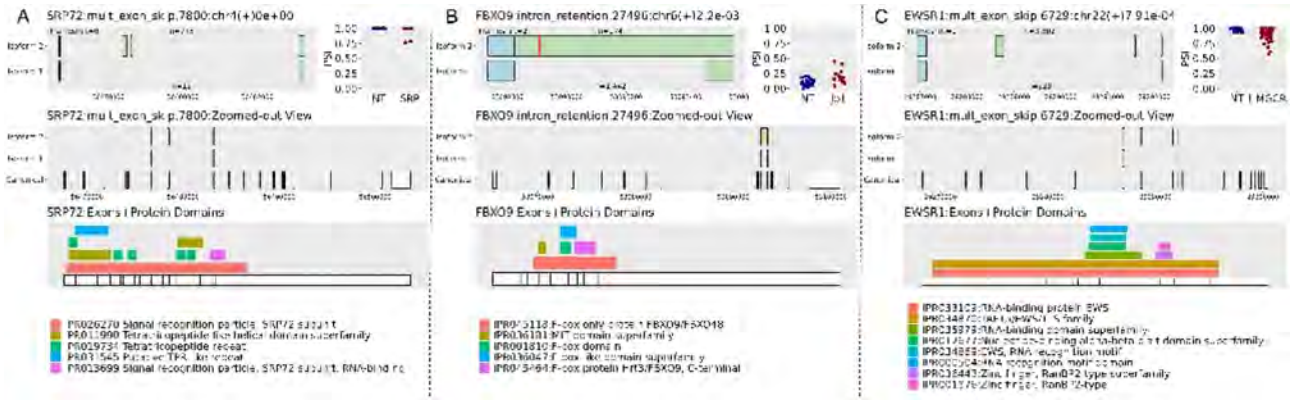

Fig 1. Illustrations of select alternative splicing events in muscle biopsies from myositis patients. Top left figure shows a zoomed-in view of the alternative splicing event. The title includes gene name, event ID, chromosome, strand, and adjusted p value. n is the number of reads supporting isoform 1 or 2. Red lines represent the first stop codon per isoform. Light blue exons indicate same protein product, while light green indicate altered peptides when translated. Top right figure shows percent-spliced in (PSI) of isoform 2 by myositis subgroup and normal tissue (NT). Middle figure shows a zoomed-out view of the alternative splicing event with complete exons of the canonical transcript. Bottom figure shows exons aligned with protein domains of the gene. Panels A, B, and C illustrate three events in SRP, Jo1, and HMGCR subgroups, respectively

the muscle-specific phosphofructokinase gene resulting in a longer 12th exon with introduction of a stop codon that would disrupt the C-terminal phosphofructokinase domain and conserved site (Fig 2A). Additionally, there was a single event that only appeared in two patients with IBM where the 15th exon of ankyrin 2 was skipped, which corresponds to an ankyrin repeat domain (Fig 2B).

Conclusion: We present results of a systematic unbiased search of alternative splicing in IIM muscles. Splicing events that are unique to a myositis subgroup are more likely to be relevant to disease pathology since they were not differentially present in any other subgroup. We discovered a unique event in SRP72 in the anti-SRP subgroup, connecting a genomic feature

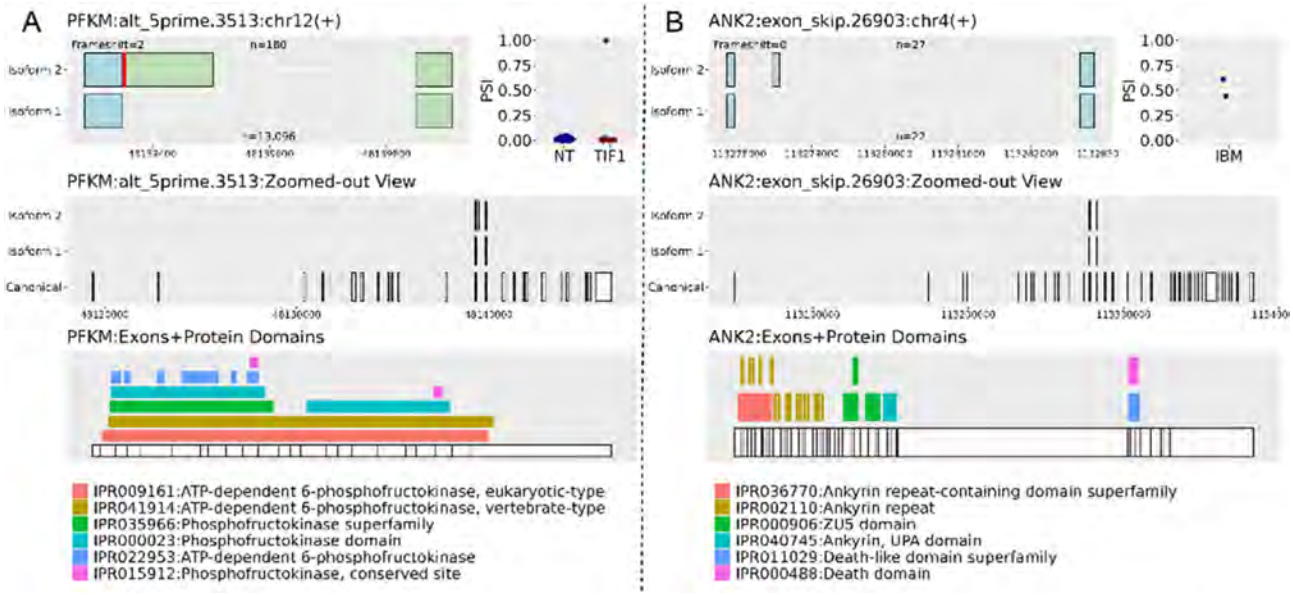

Fig 2. Alternative splicing events in muscle-specific phosphofructokinase and ankyrin 2 genes in muscle of myositis patients. Top left figure shows a zoomed-in view of the alternative splicing event. The title includes gene name, event ID, chromosome, strand, and adjusted p value. n is the number of reads supporting isoform 1 or 2. Red lines represent the first stop codon per isoform. Light blue exons indicate same protein product, while light green indicate altered peptides when translated. Top right figure shows percent-spliced in (PSI) of isoform 2 by myositis subgroup and normal tissue (NT). Middle figure shows a zoomed-out view of the alternative splicing event with complete exons of the canonical transcript. Bottom figure shows exons aligned with protein domains of the gene. Panel A illustrates an outlier event in TIF1 subgroup. Panel B illustrates an event only seen in inclusion body myositis (IBM)

to the disease's specific autoantibody. A few patients expressed roughly two thirds of the total outlier events, suggesting generally perturbed splicing in these patients.

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Abstract Number: 0019

Use of High-plex Data Reveals Novel Insights into the Temporal Artery Processus of Giant Cell Arteritis

Simon Parreau[1], Elsa Molina[2], Stéphanie Dumonteil[1], Radjiv Goulabchand[3], Thomas Naves[4], Melanie Bois[5], Anne-Laure Fauchais[1], Eric Liozon[6], Marie-Odile Jauberteau[4], Cornelia M. Weyand[7] and Kim-Heang Ly[1], [1]Dupuytren Hospital, Limoges, France, [2]Next Generation Sequencing Core, Salk Institute for Biological Studies, La Jolla, CA, [3]University of California San Diego, La Jolla, CA, [4]INSERM U1308, Limoges, France, [5]Mayo Clinic, Rochester, MN, [6]Department of Internal Medicine, University Hospital of Limoges, Limoges Cedex, Limoges, France, [7]Mayo Clinic School of Medicine and Stanford University, Rochester, MN

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Uncover the key coding genes to define new biomarkers or pathways associated with GCA by performing the first *in situ* spatial profiling characterization of molecular actors involved in temporal arteries from GCA patients in comparison to normal arteries.

Methods: From human formalin-fixed paraffin-embedded temporal artery biopsy samples (GCA n=9; controls n=7), we performed a whole transcriptome analysis by using NanoString GeoMx Digital Spatial Profiler (DSP) (2). A total of 59 individual regions of interest (ROIs) were created within each of the 4 layers for each individual artery. After ROIs collection and library construction, samples were sequenced on the Illumina NovaSeq 6000 platform and reads were digitally quantified and normalized using GeoMx DSP Data Analysis software. Differential expressed genes (DEGs) (fold change >2 or < -2, p-adjusted < 0.05) were compared for each layer, to build a spatial and pharmacogenomic network in disease course.

Results: Overall, we found that most of the transcriptome studied (12076 genes) was upregulated in GCA arteries. Precisely, 350, 340, 142 and 5 DEGs were found in intima, media, adventitia, and perivascular tissue respectively. Enrichment analysis highlighted that inflammation/immune-related functions and vascular remodeling were significantly limited to intima and media layers. Upregulated immune-related functions concerned macrophage differentiation & T cell, B cell, complement activations. Regarding vascular remodeling pathways, we found an upregulation of: (i) collagen metabolic process and fibroblast proliferation concerning the 3 artery layers, (ii) angiogenesis & epithelial cell migration in intima and media layers, (iii) smooth muscle cell proliferation & ossification in intima layer. Our pharmacogenomic network analysis identified genes that could potentially be targeted by immunosuppressive drugs currently approved or new immunotherapies.

Conclusion: Our findings provide the first *in situ* spatial profiling characterization of molecular actors involved in GCA which is essential for the discovery of potential new therapeutic targets to cure this disease. The differential spatial upregulation of genes involved in inflammatory process and vascular remodeling suggests a differential chronological involvement of each layer of the artery.

Disclosure: S. Parreau: NanoString Technologies Inc., Seattle, WA, 5; **E. Molina**: NanoString Technologies Inc., Seattle, WA, 5; **S. Dumonteil**: None; **R. Goulabchand**: None; **T. Naves**: None; **M. Bois**: None; **A. Fauchais**: None; **E. Liozon**: None; **M. Jauberteau**: None; **C. Weyand**: None; **K. Ly**: None.

Abstract Number: 0020

The Inflammatory Proteome in Sjögren's Syndrome Identifies New Biomarkers and Relevant Clinical Subgroups

José Miguel Sequí-Sabater[1], Carlos Perez-Sanchez[2], Clarissa Meoni[3], Tomás Cerdó-Ráez[4], Maria del Carmen Abalos-Aguilera[5], Desiree Ruiz Vilchez[5], Francisco Cepas[4], Nuria Barbarroja[6], Alejandro Escudero[7], Mª Angeles Aguirre[8], Chary Lopez-Pedrera[9] and Lorenzo Beretta[10], [1]Agencia Valenciana de Salut/ Hospital Universitari de la Ribera/ Unitat de Reumatología, Gandía, Spain, [2]IMIBIC, Córdoba, Spain, [3]Ospedale Policlinico di Milano, Milan, Italy, [4]Maimonides Institute for Biomedical Research (IMIBIC), Córdoba, Spain, [5]Rheumatology Department, Reina Sofia University Hospital/ Maimonides Biomedical Research Institute of Cordoba (IMIBIC), Córdoba, Spain, [6]University of Cordoba, Córdoba, Spain, [7]SAS, Córdoba, Spain, [8]Reina Sofía University Hospital/ Rheumatology Department, Córdoba, Spain, [9]IMIBIC - Reina Sofia Hospital, Córdoba, Spain, [10]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di MIlano, Milan, Italy

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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Primary Sjögren's syndrome (pSS) is an autoimmune disease characterised by glandular involvement of the eye and salivary glands, leading to xerostomia and xerophthalmia. In addition, this involvement can damage other organs such as the lung, kidney, central and peripheral nervous system. Sustained inflammatory activity can lead to non-Hodgkin's lymphoma. At present, our knowledge of the molecular alterations underlying different clinical phenotypes is still limited.

We aim to characterise the circulating inflammatory profile of pSS patients, using next-generation proteomic studies, in order to identify new biomarkers and distinctive clinical subgroups.

Methods: In an 89 SSp patients cohort from a multicentre study between Ospedale Maggiore Policlinico in Milan and Hospital Reina Sofia in Cordoba, a 92 inflammation-related serum proteins panel was analysed using the innovative Proximity Extension Assay (PEA, Olink) technology. In parallel, a comprehensive clinical profile was performed, including measures of activity (ESSDAI), cumulative damage (SSDDI), patient-reported damage (ESSPRI), health-related quality of life (HRQoL) questionnaires for general health (SF-36), patient-reported damage (ESSPRI), as well as main clinical complications and the prevalence of circulating autoantibodies.

Unsupervised clustering analysis (ward's method) was applied to identify subgroups of patients based on their proteomic profile; associations with clinical and laboratory variables were performed by means of ANOVA and Fisher's test.

Results: Unsupervised clustering analysis in pSS patients distinguished three groups based on their inflammatory profile. Clusters 1 and 3 had a well characterized proteomic profile (high and low expression, respectively) Further analyses showed that the biological profile well mirrored clinical characteristics: Cluster 1, the most inflammatory, showed higher prevalence of interstitial lung disease, arthritis and aphthous ulcers, higher ESSDAI activity index and lower SF36 physical function score; cluster 3, had the lowest prevalence of symptoms.

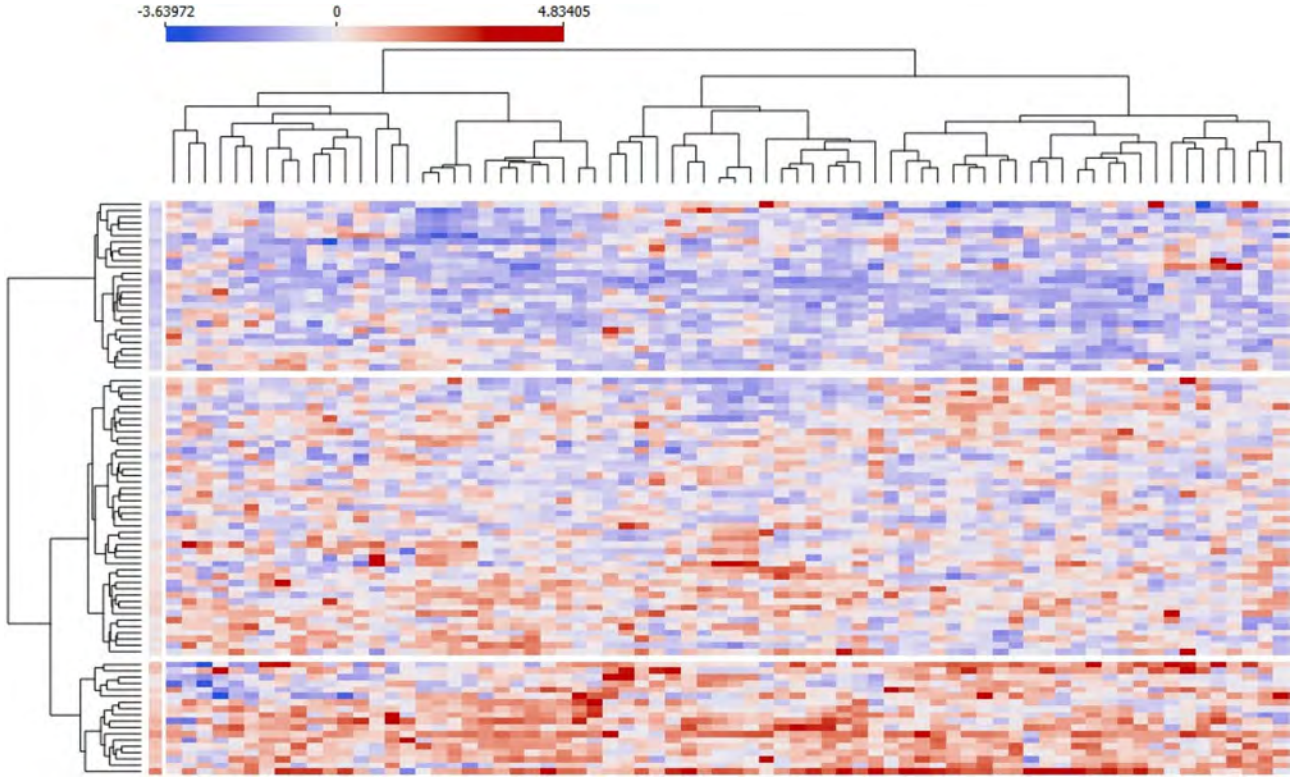

Figure 1: Analysis of the inflammatory proteome highlighting 3 distinct clusters

43 differentially expressed proteins were identified among clusters. Cluster 1 highlighted chemokines (MCP-1, CXCL11, CXCL9, CCL4, SLAMF1, MCP-4, CCL11, CCL19, CCL3, CXCL10, X4E-BP1, IGN-gamma, MCP-2, CASP-8, CCL20), growth factors (VEGF-A, TGFb-1, TGF-α, FGF-23, GFG-21, HGF, CSF-1), interleukins (IL8, IL6, IL17C, IL18, IL10Ra, IL10Rb, IL18R1, IL12b, TNFSF14, TNF, TNFRSF9, TNFB), membrane proteins (CD8A, CDCP1, OPG, PDL1, CD5,

CD40) and enzymes (uPA, MMP1, ADA). These alterations could be associated with an increased invasive capacity of immune cells. Furthermore, these proteins levels correlated with clinical ESSDAI, highlighting their potential as biomarkers of disease activity.

Conclusion: The analysis of the circulating inflammatory profile of pSS patients, using new high-throughput proteomic technologies, allows the identification of distinctive molecular signatures associated with relevant clinical profiles. Identifying novel biomarkers of activity has the potential to significantly enhance the precision and personalization of disease monitoring for this condition.

Table 1: Clinical features

Clusters	*1* (n=18)	*2* (n=44)	*3* (n=27)	p^{+}
	Mean±S.D	Mean±S.D	Mean±S.D	
ESSDAI	10.06± 7.7	8.3± 7.5	5.04± 5.28	0,047
Clinical ESSDAI	11.28±9.1	9.39± 8.7	5.22± 5.67	0,031
Initial ESR	45.94± 33,32	22.17± 14.98	15.73± 13.89	1,79E-05
SF36 Physical function	49.17± 30.450	59.1± 30.38	76.30± 25.89	0,007
	n (%)	n (%)	n (%)	
Arthritis	7 (38.9%)	4 (9.1%)	2 (7.4%)	0,009
Interstitial Lung Disease	4 (22.2%)	4 (9.1%)	0 (0%)	0,032
Aphtous ulcers	6(33.5%)	4 (9.1%)	2 (7.4%)	0,042

$^{+}$ Significance according to ANOVA and Chi2/Fisher Test

Disclosure: J. Sequí-Sabater: None; **C. Perez-Sanchez**: None; **C. Meoni**: None; **T. Cerdó-Ráez**: None; **M. Abalos-Aguilera**: None; **D. Ruiz Vilchez**: None; **F. Cepas**: None; **N. Barbarroja**: None; **A. Escudero**: None; **M. Aguirre**: None; **C. Lopez-Pedrera**: None; **L. Beretta**: None.

Abstract Number: 0021

Shared Genetic Susceptibility Between Rheumatoid Arthritis and Bipolar Disorder: Analyses from Genome-Wide Association Studies

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) has been associated with bipolar disorder (BD) in epidemiological studies, including a recent Mendelian randomization analysis. This study aims to prioritize candidate genes that contribute to the shared genetic susceptibility between these two conditions, using data from genome-wide association studies (GWAS).

Methods: We obtained the summary statistics of the most recent GWAS in RA (PMID: 36333501, 22,350 cases and 74,823 controls) and BD (PMID: 34002096, 41,917 cases and 371,549 controls) of European ancestry. First, we performed linkage disequilibrium score regression (LDSC) to estimate the genetic correlation between the two conditions. We then conducted a cross-trait GWAS meta-analysis in RA and BD to identify shared genetic loci, using a fixed-effect model with METAL software. An additional analysis was carried out reversing the effect direction of BD to detect genetically associated loci with opposite effects. Next, we performed Bayesian genetic colocalization analysis between RA and BD in loci that were significant in the cross-trait GWAS meta-analysis ($p < 5x10^{-8}$) to predict whether the shared genetic susceptibility was due to the same causal single-nucleotide polymorphisms (SNPs). To evaluate the functional consequences of the discovered signals, loci that were significant in cross-trait meta-analysis and predicted to share the causal SNPs (pp.H4 > 70%) were selected for colocalization with tissue-specific expression quantitative trait loci (eQTL) from the Genotype-Tissue Expression (GTEx), as well as plasma-based protein quantitative trait loci (pQTL) from the Atherosclerosis Risk in Communities (ARIC) dataset. We prioritized genes that colocalized with QTL signals of tissues relevant to RA and BD.

Results: Our analysis showed a modest negative genetic correlation between the two conditions (r_g = - 0.1183, se = 0.0315, p = 0.0002). Two genomic loci, near rs112219496 (same effect direction, meta-analysis $p = 1.35 \times 10^{-10}$, pp.H4 = 91.2%) and rs1569723 (opposite effect direction, meta-analysis p-value = 2.22×10^{-13}, pp.H4 = 98.9%), were significant in the cross-trait GWAS meta-analysis and colocalized between RA and BD (Table 1). The genomic locus near rs112219496 colocalized with pQTL and eQTLs for *CILP2* in plasma, lung, and brain tissues. The genomic locus near rs1569723 colocalized with eQTLs for *CD40* in the lung and brain tissues (Figure 1).

Conclusion: This study uncovers a complex relationship between the genetic susceptibilities of RA and BD. By implementing post-GWAS analyses, we identified *CILP2* and *CD40* as being associated with both RA and BD. Interestingly, *CILP2* exhibited the same effect direction in both conditions, while *CD40* demonstrated the opposite effect direction.

Table 1: Cross-trait meta-analysis of RA and BD and colocalization results of the regions +/- 500 kb of lead SNPs identified in cross-trait meta-analysis.

SNP	Position (hg19)	A1	Meta		RA		BD		PP.H4
			β	p	β	p	β	p	
Signals showing aligned effect in the cross-trait meta-analysis									
rs112219496	19:19358086	A	0.078	1.35E-10	0.092	5.79E-07	0.070	6.36E-08	91.2%
Signals showing opposing effect in the cross-trait meta-analysis									
rs1569723	20:44742064	A	0.073	2.22E-13	0.103	2.82E-12	-0.054	3.90E-07	98.9%

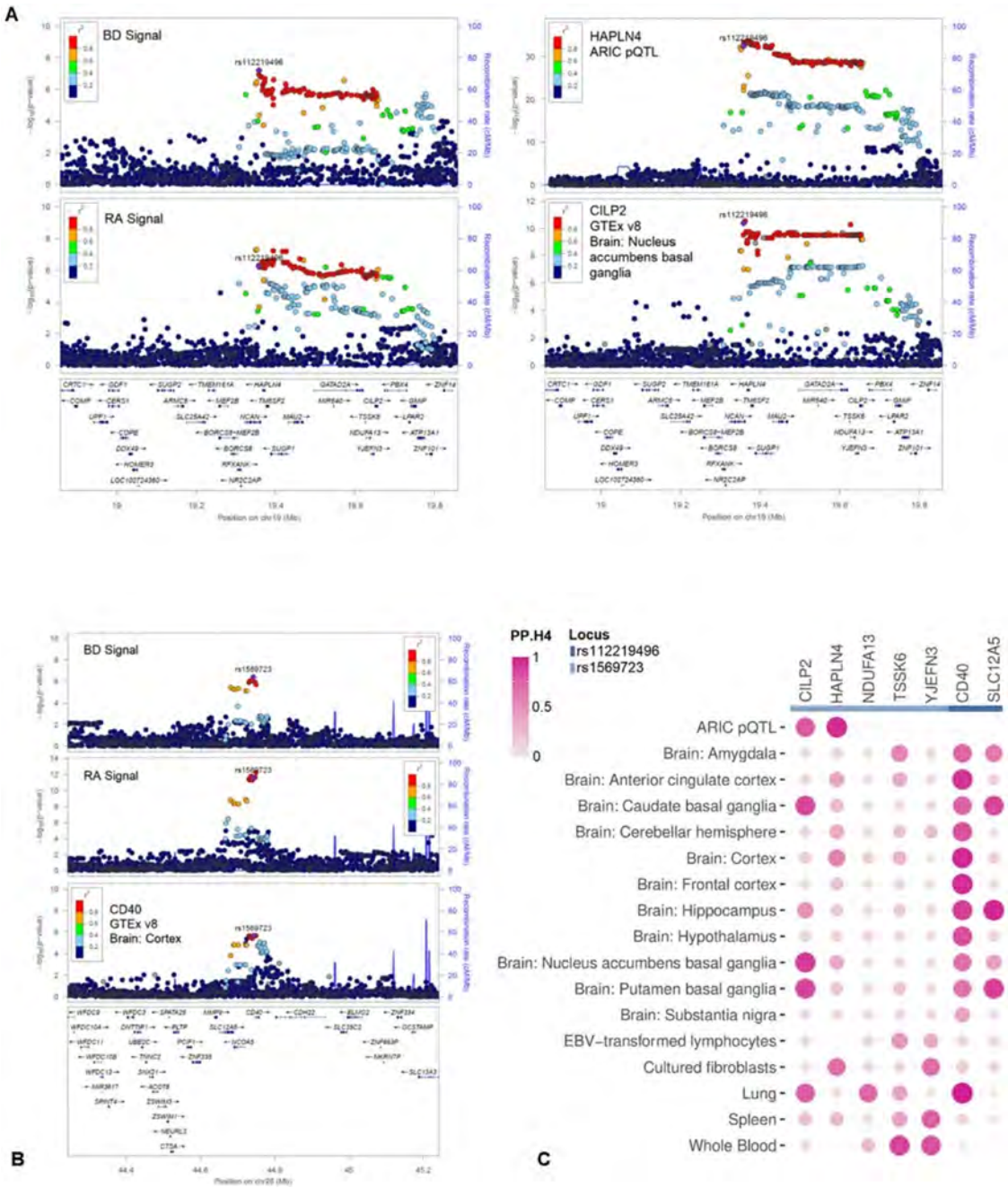

Figure 1: (A) LocusZoom plots of the region near rs112219496 with RA, BD, pQTL for HAPLN4 and eQTL for CILP2. (B) LocusZoom plots of the region near rs1569723 with RA, BD and eQTL for CD40. (C) Colocalization analysis with pQTLs and eQTLs across various tissues; each row represents a tissue, and each column denotes a gene. The color gradient from violet red to grey signifies the probability of GWAS loci and eQTLs sharing the same causal variant (PPH4).

Disclosure: J. Zheng: None; **R. Ni**: None; **N. Barjaktarovic**: None; **Y. Luo**: None.

Abstract Number: 0022

Validation of a Transcriptomic-Based Machine Learning Model to Establish the Endotype of SLE Patients

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: We previously developed a novel machine learning (ML) pipeline leveraging analysis of gene expression data to identify subsets of SLE patients with common molecular patterns of disease, endotypes[1]. These molecular subsets had significant differences in clinical characteristics, the frequency of subsequent flares, and clinical responsiveness to a lupus biologic, tabalumab. The current study makes use of the ML classifier to determine endotype membership in an independent validation cohort of SLE patients.

Methods: Gene expression by RNA-sequencing of whole blood and clinical metadata were collected from 91 SLE patients from two clinical trials (NCT03626311 and NCT03180021). Patients met ACR classification criteria of SLE and patients from one trial had renal biopsies at the time gene expression was measured. A random forest classifier trained on 2183 lupus patient gene expression profiles was used to predict endotype membership of the 91 patients. Lupus Cell and Immune Score (LuCIS), a continuous score measuring the extent of modular immunologic abnormalities determined by ridge-penalized logistic regression, was also calculated for each patient.

Results: The ML prediction of independent SLE patients into endotypes yielded eight subsets with molecular patterns mirroring those found previously in a development and testing cohort of 3166 patients (Figure 1). Endotypes were designated A-H, with A representing the group with the least number of transcriptional lupus-related aberrancies and H representing the group with the greatest immunologic perturbations. Groups H, A, C, and E were comprised of the greatest number of patients whereas B and G were small and underrepresented in this cohort. Endotype H contained the greatest number of patients with proliferative lupus nephritis (LN) whereas no patient with LN was found in subset A or B. Serum complement differed among the subsets, with the more immunologically active having lower levels. LuCIS values reflected the immunological activity of the subsets but did not correlate with SLEDAI, although they were moderately, inversely correlated with serum C3 and C4 levels (Figure 2). Eight patients had moderate/severe flares during the six months of the trials, of whom all had elevated LuCIS scores at baseline.

Conclusion: A novel endotyping pipeline based on transcriptional profiles and ML accurately identified patient endotypes in new datasets. Patients in the endotypes with the least immunologic activity did not have proliferative nephritis and also experienced no lupus flares during the subsequent six months. Endotyping SLE patients based on gene expression profiles can provide important prognostic information and provide novel molecular insights in support of personalized management.

1. Kim YH, Park MR, Kim SY, Kim MY, Kim KW, Sohn MH. Respiratory microbiome profiles are associated with distinct inflammatory phenotype and lung function in children with asthma. J Investig Allergol Clin Immunol. 2023 Jun 1:0. doi: 10.18176/jiaci.0918. Epub ahead of print. PMID: 37260034.

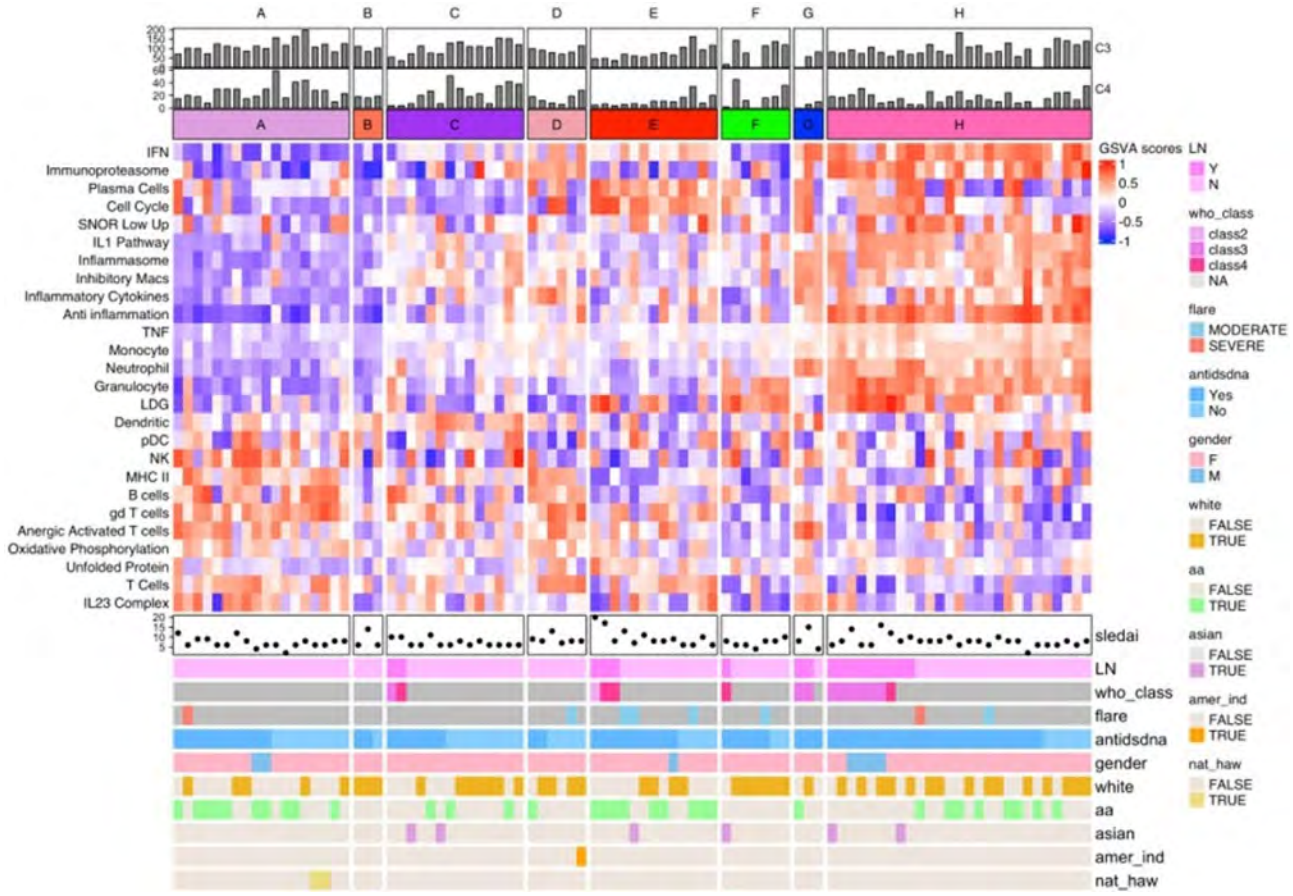

Figure 1. Identification of Endotypes Among 91 SLE Patients Molecular subsets identified by a random forest algorithm using gene set variation analysis (GSVA) enrichment scores of 26 immune/inflammatory modules. Clinical metadata for each patient (x-axis) was annotated as shown. Heatmap constructed in R using the ComplexHeatmap package.

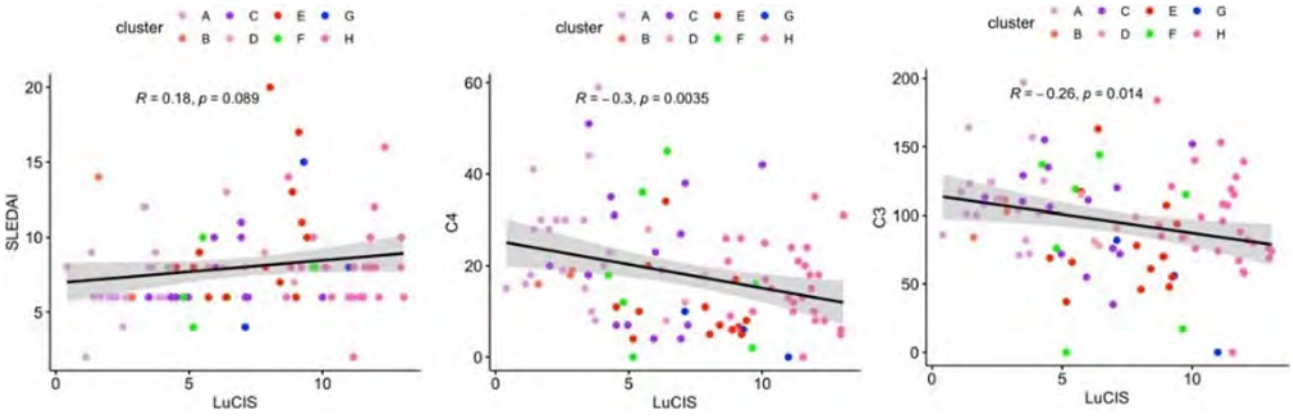

Figure 2. LuCIS Correlations with Clinical Data Pearson correlations of LuCIS values with baseline clinical characteristics. Each data point is colored by endotype membership. Plots were constructed in R using the ggplot2 package.

Disclosure: E. Hubbard: None; **P. Bachali**: None; **K. Kingsmore Allison**: None; **A. Grammer**: None; **P. Lipsky**: None.

Abstract Number: 0023

Proteomic Analysis of Plasma-derived Extracellular Vesicles Renders Glutathione Peroxidase 3 a Biomarker for Dermatomyositis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

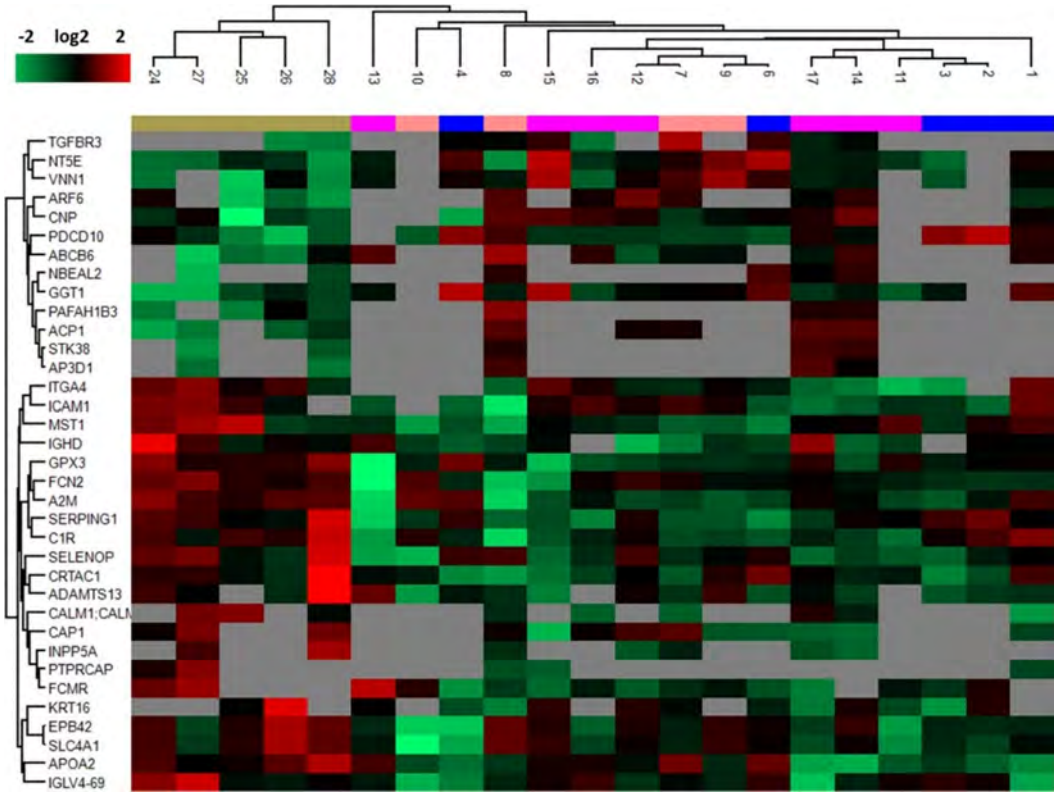
Session Title: Genetics, Genomics & Proteomics Poster

Session Type: Poster Session A

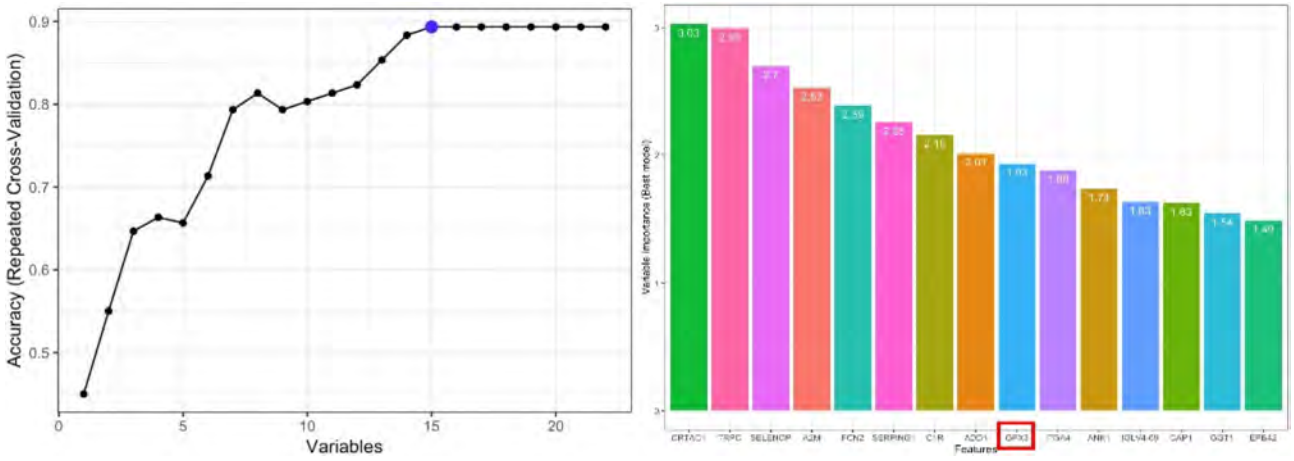
Session Time: 9:00AM–11:00AM

Background/Purpose: Extracellular vesicles (EVs) have been implicated in autoimmune disease pathogenesis. Plasma-derived DNA containing EVs have been shown to induce STING-mediated proinflammatory responses in dermatomyositis (DM), but their protein content is not well characterized (Li Y et al. Plasma-derived DNA containing-extracellular vesicles induce STING-mediated proinflammatory responses in dermatomyositis. Theranostics. 2021 May 21;11(15):7144-7158).

Methods: We collected EVs from plasma of 16 DM patients and 5 controls. EVs were isolated using sequential ultracentrifugation and size- exclusion chromatography, and their content analyzed by mass spectrometry (LC-MS/MS in DIA mode). Over-representation analysis was conducted via http://webgestalt.org based on KEGG,GO and Reactome databases.



Differentially expressed proteins.

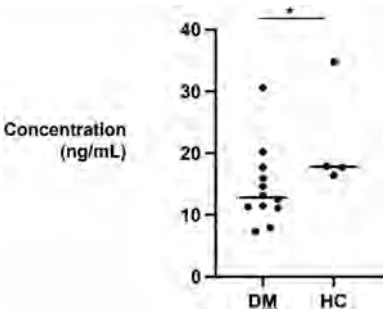


Biomarker prediction. Recursive random forest feature selection predicts a group of 15 proteins to have optimal predictive value for disease state and (left panel) and lists them with top-down probability scores (right panel).

Protein biomarkers that distinguish patients with DM from controls were assessed using the random forest algorithm. GPX3 abundance was validated in a second cohort by ELISA and data was analyzed by the Mann Whitney test.

Results: Sixty-seven proteins were uniquely detected in the patient cohort. Thirty-five proteins were significantly differentially expressed, of which 13 were upregulated and 22 downregulated. Over-representation analysis found unique and upregulated proteins enriched for myeloid mediated immunity, glutathione metabolism, nucleic acid synthesis and vesicle transport pathways. Downregulated proteins were enriched for the classical and lectin complement pathways. The diminution of complement components in vesicles may reflect its abundance in target tissues but may also reflect host inability to circulate these molecules to damaged tissue, which in a chronic stage of disease may have a protective role. The antioxidant enzyme glutathione peroxidase 3 (GPX3) was significantly less abundant in patients' EVs compared to controls ($p = 0.04$) and was assessed by machine learning to be amongst a group of proteins that distinguish patients from controls. GPX3 is a well-known biomarker of certain types of cancer, where its downregulation is correlated with higher inflammatory burden and increased cell proliferation (Nirgude S, Choudhary B. Insights into the role of GPX3, a highly efficient plasma antioxidant, in cancer. Biochem Pharmacol. 2021 Feb;184:114365). A similar mechanism may apply to DM patients, that may be susceptible to oxidative stress due to defective transport of GPX3 by EVs. Alternatively, its lower abundance in EVs may indicate the exhaustion of GPX3 in chronic inflammation.

Conclusion: Our findings indicate GPX3 as biomarker of disease in DM and underlines the importance of oxidative stress in disease mechanism. This finding, along with a growing body of evidence, suggests roles for EVs as disease biomarkers and prompts further mechanistic studies to elucidate the role of GPX3 transport by EVs not only in plasma, but also in muscle and skin.



GPX3 abundance. EVs isolated from healthy control plasma contained more GPX3 than EVs isolated from dermatomyositis patients, as indicated by ELISA performed on a second validation cohort of patients and controls. *$p<0.05$.

Disclosure: A. Baniel: None; **M. Ogawa-Momohara**: None; **M. Bashir**: None; **R. Pandya**: None; **J. Kleitsch**: None; **F. Chin**: None; **M. Liu**: None; **V. Werth**: AbbVie, 2, Amgen, 2, 5, Anaptysbio, 2, Argenx, 5, AstraZeneca, 2, Biogen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Corbus, 5, CSL Behring, 2, 5, EMD Serono, 2, Galderma, 2, Genentech, 5, Gilead, 2, 5, GlaxoSmithKline, 2, Horizon Therapeutics, 5, Idera, 2, Incyte, 2, Janssen, 2, Kyowa Kirin, 2, Lilly, 2, MedImmune, 2, Medscape, 2, Merck, 2, Nektar, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Principia, 2, Regeneron, 5, Resolve, 2, 2, Rome Therapeutics, 2, 5, Sanofi, 2, Ventus, 5, Viela, 2, 5, Xencor, 2.

Abstract Number: 0024

Detection of Synovial Signatures in Peripheral Blood of Patients with Rheumatoid Arthritis via a Novel Blood-Based DNA Capture Assay

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In rheumatoid arthritis [RA], synovial biopsies were shown to guide therapy selection[1]. However, biopsies require special training for clinicians and are semi-invasive for patients. Blood-based tests are a common procedure in clinical practice. Prior research failed to capture synovial signals in RA patients via blood because of the limited circulation of synovial-specific biomarkers and the dilution of molecular signals within the bloodstream. The study aims to investigate synovium-specific transcriptomic signal in blood plasma by employing a novel DNA capture platform to comprehensively analyze and characterize the molecular signatures in RA.

Table 1. Patient demographic characteristics

	Number of patients	Number of samples	White, %	Female, %	Age	
					Range	Mean
Overall, including:	191*	229	63.3%	67.9%	19 – 88	53.6 (16.63)
Rheumatoid Arthritis* **	89	89	58.4%	86.5%	28 - 66	57.0 (14.20)
Non-RA:	102	140	67.7%	51.8%	19 - 88	50.6 (18.06)
Healthy controls	29	66	42.3%**	53.6%	20 – 63	42.6 (12.15)
Ankylosing spondylitis	13	13	84.6%	30.8%	28 – 66	50.5 (14.80)
Crohn's Disease	10	11	80.0%	30.0%	23 – 87	55.7 (21.97)
Psoriasis	18	18	66.7%	50.0%	27 – 70	46.1 (13.74)
Psoriatic arthritis	10	10	70.0%	50.0%	46 – 88	65.8 (11.62)
Ulcerative colitis	10	10	70.0%	50.0%	19 – 67	33.9 (16.03
Osteoarthritis	12	12	91.7%	91.7%	47 – 87	73.3 (10.46)

* One patient did not have demographic characteristics recorded but was included in the sample because plasma and healthy status were known.
** Race was not known for three patients in the *healthy control* group.
*** Among RA patients, 70% were seropositive and 96% were biologic-naïve.

Table 2. Methodological definitions

Metric	Definition	Interpretation
Receiver operating characteristic (ROC)	A graph showing the performance of a classification model at all classification thresholds. This curve plots two parameters: True Positive Rate (Y-axis) and False Positive Rate (X-axis).	Steepest curvature indicates the most accurate test.
Area under the curve (AUC)	UC measures the entire two-dimensional area underneath the entire ROC curve (think integral calculus) from (0,0) to (1,1). The AUC ranges 0–1.	The closest AUC approaches 1, the higher test accuracy is.
Sensitivity	The degree to which a test accurately identifies the presence of a condition (e.g., RA). It is expressed as a percentage of true positive predictions over the sum of true positive and false negative predictions.	Highest sensitivity indicates best ability to accurately detect the presence of condition (e.g., RA).
Specificity	The degree to which a test accurately identifies the absence of a condition (e.g., OA). It is expressed as a percentage of true negative predictions over the sum of true negative and false positive predictions.	Highest specificity indicates best ability to accurately detect the absence of condition (e.g., OA)

Table 3. Synovial fibroblast genes identified within synovial signatures

- Interleukin 6 (IL6),
- Matrix metalloproteinases (MMP1, MMP9, MMP13, MMP16, MMP17), collagen genes (COL3A1, COL4A1, COL4A4, COL5A2, COL6A1, COL8A1, COL10A1, COL11A1, COL12A1, COL21A1, COL22A1, COL24A1)
- Tissue inhibitor of metalloproteinases 3 (TIMP3),
- Transforming growth factor beta (TGFB1, TGFB2) and its receptor (TGFBR2),
- Cathepsin K (CTSK),
- Fibronectin 1 (FN1),
- A disintegrin and metalloproteinase domain-containing protein 12 (ADAM12),
- Vascular endothelial growth factor C (VEGFC),
- Notch 1 (NOTCH1). The remaining 58% of the features showed significant enrichment of immune cell types, including, CD4+ and CD8+ T-cells, B-cells, and macrophages.

Methods: Plasma samples (n=229) from 89 individuals meeting 2010 ACR/EULAR classification criteria for RA, 62 with inflammatory conditions, 12 with OA, and 29 healthy controls (Table 1) were processed using a blood-based assay that enriches for non-hematopoietic signals. The epigenome atlas, comprised of 600,000 features, was evaluated using bootstrap methods to select features that robustly differentiate RA from non-RA samples to generate a candidate list of genomic feature locations. These were mapped to genes and compared to the reported pathways[2] identified in whole blood and synovial tissue of patients with RA. A machine-learning training used 5-repeat 10-fold cross validation of the candidate features that have overlapping genes with synovial pathways. The training generated the average area under the curve (AUC) and performance metrics (sensitivity and specificity; Table 2)

Results: Participants had a mean (standard deviation, SD) age of 53.6 (16.63) years and were mostly female (67.9%) and white (63.3%; Table 2). The RA patients were mostly seropositive (70%) and biologic-naïve (93%). In the list of identified genomic features, 88% overlapped with synovium pathway genes and 30% with blood pathway genes. Within identified synovial signatures, 42% represent synovial fibroblast genes (Table 3); the remaining 58% of the features showed significant enrichment of immune cell types, including, CD4+ and CD8+ T-cells, B-cells, and macrophages.

Conclusion: The developed non-invasive DNA capture assay identified synovium-specific gene expression signatures in blood plasma of RA patients. Further clinical research is needed to validate these synovial signatures and confirm the clinical utility of the developed classification system.

1. Humby F, et al. (2019); PMID: 30878974
2. Rychkov D, et al. (2021); PMID: 34177888

Note: both Dr. Shadick and Dr. Weinblatt are last authors.

Disclosure: P. Taylor: AbbVie, 2, Biogen, 2, Eli Lilly, 2, Fresenius, 2, Galapagos, 2, 5, Gilead Sciences, 2, GSK, 2, Janssen, 2, Nordic Pharma, 2, Pfizer Inc, 2, Sanofi, 2, UCB, 2; **J. Antonova**: Aqtual, Inc., 2; **J. Geis**: Aqtual, Inc., 3, 11; **K. Dilger**: AQTUAL, 3, 10, 11; **D. Chernoff**: Aqtual, Inc., 2, Reflexion Pharma, 2, 11, SetPoint Medical, 3, 11; **D. Abdueva**: Aqtual, Inc., 3, 4, 8, 10, 11; **N. Shadick**: Abbvie, 5, AQtual, 5, Bristol-Myers Squibb(BMS), 5, Janssen, 5; **M. Weinblatt**: Abbvie, 2, 5, Aclaris, 2, Amgen, 2, Aqtual, 5, Bristol Myers Squibb, 2, 5, Canfite, 11, Corevitas, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, 2, Glaxo Smith Kline, 2, Horizon, 2, Inmedix, 11, Janssen, 5, Johnson and Johnson, 2, Pfizer, 2, Prometheus Laboratories, 2, Rani, 2, Revolo, 2, Sanofi, 2, Sci Rhom, 2, Scipher, 2, 11, Set Point, 2, UCB, 2.

Abstract Number: 0025

Relationship Between Genetic Variants in Cannabinoid Receptor 2 and Self-Reported Effectiveness of Cannabis for Pain Management in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Cannabinoid receptor 2 (CB2) is a member of the cannabinoid receptor family and is encoded by the CNR2 gene. CB2 receptors are found primarily in immune cells, and their activation exerts anti-inflammatory effects. Genetic variants in CNR2 have been linked to pain, autoimmune disorders, and depression. The objective of this study was to examine relationships between CNR2 variants and self-reported effectiveness of cannabis in the treatment of RA-related pain.

Methods: Data were provided by adults with RA participating in FORWARD, The National Databank for Rheumatic Diseases, who provided blood samples and reported the use of cannabis or cannabis-derived products for the purpose of treating arthritis-related pain. Genotyping was performed with the Illumina Infinium Global Screening Array platform, and CNR2 variants with minor allele frequencies greater than 0.05 were included in this analysis (SNPs rs4625225, rs7512349, and rs9424399). Multivariable logistic regression was used to determine whether the presence of the minor allele in each variant was associated with self-reported effectiveness of cannabis in managing RA-related pain. Models were adjusted for age, sex, race, cigarette smoking history, RA duration, BMI, glucocorticoid use, NSAID use, opioid use, Rheumatic Disease Comorbidity Index (RDCI), history of depression, and Patient Activity Scale-II (PAS-II).

Results: A total of 134 participants met inclusion criteria, of whom 79 (59%) found cannabis effective in treating their RA-related pain. Respondent characteristics are presented in Table 1 and genotype distributions of the three variants are presented in Table 2. Adjusted models indicated that for all three variants, the presence of at least one copy of the minor allele was associated with reduced odds (rs4625225 OR [95% CI] = 0.34 [0.14, 0.79], p=0.013; rs7512349 0.26 [0.11, 0.64], p=0.003; rs9424399 0.28 [0.12, 0.69], p=0.005) of finding cannabis effective for pain management, compared to those homozygous for the major allele. (Figure 1).

Table 1. Characteristics of study participants by self-reported effectiveness of cannabis in RA pain management.

Characteristic	Not Effective n=55	Effective n=79
Age, years, mean (SD)	68.9 (9.7)	64.3 (10.9)
Female, %	88.9	92.4
White race, %	94.5	91.0
Hx cigarette smoking, %	41.8	40.5
RA duration, years, mean (SD)	25.1 (13.5)	24.8 (11.7)
BMI, kg/m^2, mean (SD)	28.7 (6.6)	27.5 (6.3)
Glucocorticoid use, %	25.5	14.1
NSAID use, %	27.3	30.8
Opioid use, %	20.0	20.5
RDCI, 0-9, mean (SD)	2.2 (1.8)	2.2 (2.0)
Hx depression, %	54.5	73.4
PAS-II, 0-10	3.7 (1.9)	4.4 (2.1)

BMI=body mass index; NSAID=non-steroidal anti-inflammatory drugs; RDCI=Rheumatic Disease Comorbidity Index; PAS-II=Patient Activity Scale II

Conclusion: Our results indicate that the perceived effectiveness of cannabis in the treatment of RA-related pain varies significantly by CNR2 genotype. The three variants appear to be in linkage disequilibrium and are also all silent, so a related variant not assessed by the array used in this study may be causative of the identified relationship. These results highlight the possible impact of genetic variations on the therapeutic potential of cannabis for arthritis pain management, which may be relevant for personalized medicine as legalization and medicinal use of cannabis continue to become more widespread in the United States. Further research is warranted to confirm these findings, to elucidate the underlying mechanisms, and to better understand the relationships between CB2 and pain, cannabis use, and any potential immunomodulatory effects.

Table 2. Genotype distributions of the investigated CNR2 variants.

Variant	Genotype	n (%)
rs4625225	TT	83 (62)
	TC	48 (36)
	CC	3 (2)
rs7512349	TT	89 (66)
	TC	43 (32)
	CC	2 (1)
rs9424399	AA	88 (66)
	AG	43 (32)
	GG	3 (2)

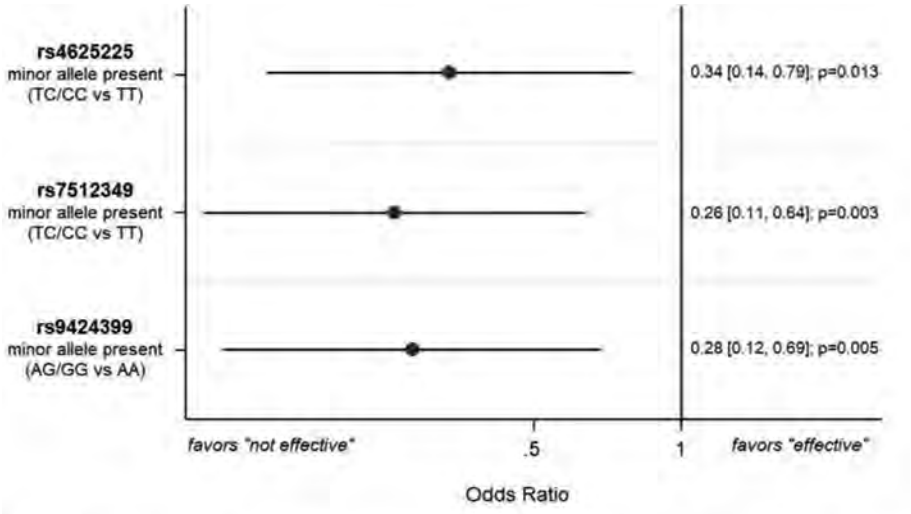

Figure 1. Adjusted odds ratios and 95% confidence intervals for each minor allele's association with reported effectiveness of cannabis in treating RA-related pain. Each model was adjusted for age, sex, white race, cigarette smoking history, calendar year, RA duration, BMI, glucocorticoid use, NSAID use, opioid use, Rheumatic Disease Comorbidity Index (RDCI), history of depression, and Patient Activity Scale II (PAS-II).

Disclosure: K. Wipfler: None; **J. Zeiger**: None; **A. Cornish**: None; **K. Michaud**: None.

Abstract Number: 0026

Mapping Cellular Landscape of Esophageal Epithelium in Systemic Sclerosis Using Single-cell Transcriptomics

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Esophageal involvement is one of the strongest predictors of early mortality in individuals with systemic sclerosis (SSc). Individuals with SSc and esophageal involvement typically suffer from chronic acid reflux and dysphagia due to loss of esophageal motility. However, the pathogenesis of esophageal dysmotility in SSc is still poorly understood.

Recently, studies have demonstrated that esophageal epithelial cells (EECs) in the mucosa may play a more central role in the pathogenesis of SSc esophageal dysmotility than previously thought. Most studies implicating EECs, however, have been performed in mice or in vitro, and molecular analyses in humans have so far been limited to bulk tissues using microarrays with inadequate controls. In this study, we performed a thorough transcriptomic investigation of the SSc esophageal epithelium in humans using single-cell RNA sequencing (scRNA-seq) to determine whether distinct molecular and cellular changes in EECs contribute to impaired motility of the esophageal wall in SSc.

Methods: We performed scRNA-seq of paired proximal and distal esophageal mucosa biopsies from 10 individuals with SSc and 6 healthy controls (HCs). We also evaluated samples from 4 individuals with gastroesophageal reflux disease (GERD) to distinguish primary SSc effects from secondary reflux effects. We further assessed esophageal motility (normal, weak, absent) in individuals with SSc using functional lumen imaging probe panometry and high-resolution manometry. Cells were encapsulated using the 10X Genomics Chromium platform and sequenced on the Illumina Novaseq 6000. Reads were aligned and quantified using Cell Ranger v6.1.2 and cell-specific gene expression was analyzed using Seurat v4.3.0.

Results: ScRNA-seq generated 12.4 billion reads from 434,582 cells across 40 sequenced samples. Following quality control, we annotated 230,720 EECs according to their differentiation state (basal, suprabasal, superficial). Overall proportions of basal, suprabasal, and replicating EECs were similar across conditions, but SSc and GERD samples had significantly fewer terminally differentiated, superficial cells than HCs. Differential gene expression analyses revealed dysregulated gene sets dependent on condition, biopsy region, and EEC layer. A surge of gene dysregulation in the transition from suprabasal to superficial states was observed in both SSc and GERD. We then modeled EEC differentiation as a continuous metric based on cumulative average expression of layer-specific markers and identified genes with condition-dependent expression trends as a function of EEC differentiation, highlighting genes uniquely dysregulated in SSc, including those correlated with esophageal dysmotility.

Conclusion: Esophageal dysmotility in SSc is associated with cellular and molecular changes in EECs distinct from secondary reflux effects. This work serves as an atlas for the human esophageal epithelium in SSc to direct future efforts to identify actionable targets for treatment.

Disclosure: M. Dapas: None; **H. Makinde**: None; **T. Therron**: None; **M. Clevenger**: None; **C. Wei**: None; **M. Karns**: None; **K. Aren**: None; **D. Carlson**: Medtronic, 2, 6, 12, license agreement; **A. Soriano**: None; **L. Muhammad**: None; **J. Pandolfino**: Medtronic, 2, 6; **H. Perlman**: None; **D. Winter**: Pfizer, 2; **M. Tetreault**: None.

Abstract Number: 0027

Association of *HLA-DRB1* and *ANKRD55/IL6ST* Regions with Polymyalgia Rheumatica Diagnosis: A Genome Wide Association Study from UK Biobank and FinnGen

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: The existing literature on the genetics of polymyalgia rheumatica (PMR) is limited to candidate gene studies with small sample sizes. There is a need for larger genetic studies in PMR to investigate genetic associations throughout the whole genome. In this study, we aimed to perform a genome wide association study (GWAS) of PMR in the UK Biobank and compare our results with the FinnGen cohort.

Methods: UK Biobank is a cohort study of around 500,000 individuals from United Kingdom. The study collected genomic information on all participants which include 850,000 measured variants with over 90 million imputed variants using reference databases. The genetic data is linked with patient's clinical record through International Classification of Diseases

(ICD)-10 in addition to procedure and treatment codes. Patients with ICD-10 codes M31.5 Giant cell arteritis with polymyalgia rheumatica and M35.3 Polymyalgia rheumatica were included as cases. Controls were drawn from the same cohort in 1:20 case-control fashion and matched with regards to age, sex, and ancestry. The genome wide association analysis was performed using PLINK 2.0 software through firth logistic regression using age, sex and first 5 principal components (PC) as covariates. Single nucleotide polymorphisms (SNP) were filtered to include those with mean allele frequency greater than 5% and imputation quality score greater than 0.95. Summary statistics for GWAS in the FinnGen cohort was downloaded from the most recent publicly available data release. The FinnGen GWAS was performed by defining individuals with ICD-10 code M35.3 as cases and using REGENIE software with a two-step associated test utilizing firth logistic regression and having sex, age, first 10 PCs and genotyping batch as covariates.

Results: There were 1890 and 3501 patients of PMR in the UK Biobank and FinnGen respectively. In the GWAS analysis in the UK Biobank, 2460 variants in the MHC locus at chromosome 6 passed the genome wide significance level at $5x10^{-8}$ and our quality filters. Our top hit was rs34535888, a SNP close to *HLA-DRB1* gene. In the FinnGen, the top hit was rs34434863, a variant close to *HLA-DRB1* gene. Outside of the MHC locus, only rs7731626, an intronic variant at the *ANKRD55* gene passed genome-wide significance. Prior literature shows that the *ANKRD55* variants affect the expression of the neighboring gene IL6ST in various immune cells. There were three further loci with genome wide suggestive association (< $1x10^{-6}$) in either UK Biobank or FinnGen, but none of these variants were replicated in both cohorts (Table 1). When we restricted the

Table 1. Associations of genetic variants with polymyalgia rheumatica in the UK Biobank and FinnGen cohort

								UK Biobank (n=1890)			FinnGen (n=3501)	
SNP	Chr	Pos	Type	Gene	Minor allele	INFO	MAF (%)	OR (95% CI)	p-value	MAF (%)	OR (95% CI)	p-value
rs34535888	6	32,561,527	intergenic	*HLA-DRB1*	C	0.99	19%	1.7 (1.6-1.9)	4×10^{-47}	15%	1.6 (1.5-1.6)	4×10^{-47}
rs34434863	6	32,559,673	intergenic	*HLA-DRB1*	G	0.95	31%	1.6 (1.5-1.7)	7×10^{-36}	33%	1.5 (1.4-1.5)	6×10^{-52}
rs7731626	5	55,444,683	intronic	*ANKRD55*	A	1	37%	0.8 (0.8-0.9)	5×10^{-7}	28%	0.8 (0.8-0.9)	3×10^{-10}
rs181962435	19	3,311,155	intergenic	*CELF5*	G	0.98	33%	1.2 (1.1-1.3)	5×10^{-7}	ND**	ND**	ND**
rs34233615	18	33,038,896	intergenic deletion	*INO80C*	G	0.95	8%	1.0 (0.9-1.2)	0.5	7%	0.8 (0.7-0.9)	$5x10^{-7}$
rs77441332	4	141,399,202	intergenic	*LOC100507639*	G	0.99	5%	0.9 (0.7-1.0)	0.06	6%	0.8 (0.7-0.9)	$6x10^{-7}$

SNP, single nucleotide polymorphism. Chr, chromosome. Pos, position per Genome Reference Consortium Human Build (GRCh37). OR, odds ratio. CI, confidence interval. MAF, minor allele frequency in the UK Biobank. INFO, imputation quality score in the UK Biobank. ND, not done.
**rs181962435 was not genotyped in the FinnGen cohort but three proxy LDs rs10416424 (r^2 0.9), rs28432971 (r^2 0.8), rs28418831 (r^2 0.8) were not associated with PMR.

Table 2. Association of genome-wide significant single nucleotide polymorphisms with PMR subgroups in the UK Biobank

								PMR without RA (n=1760)		PMR without GCA (n=1737)	
SNP	Chr	Pos	Type	Gene	Minor allele	MAF (%)	INFO	OR (95% CI)	p-value	OR (95% CI)	p-value
rs34535888	6	32,561,527	intergenic	*HLA-DRB1*	C	19%	0.99	1.8 (1.6-1.9)	$1x10^{-46}$	1.7 (1.6-1.8)	$2x10^{-42}$
rs34434863	6	32,559,673	intergenic	*HLA-DRB1*	G	19%	0.95	1.6 (1.4-1.7)	$2x10^{-33}$	1.6 (1.4-1.7)	$6x10^{-33}$
rs7731626	5	55,444,683	intronic	*ANKRD55*	A	37%	1	0.8 (0.8-0.9)	$6x10^{-6}$	0.8 (0.8-0.9)	$5x10^{-6}$

SNP, single nucleotide polymorphism. Chr, chromosome. Pos, position per Genome Reference Consortium Human Build (GRCh37). OR, odds ratio. CI, confidence interval. MAF, minor allele frequency. INFO, imputation quality score in the UK Biobank. PMR, polymyalgia rheumatica. RA, rheumatoid arthritis. GCA, giant cell arteritis.

analysis to patients without concomitant RA or GCA diagnosis in the UK Biobank, the effect sizes were similar albeit with larger p-values (Table 2).

Conclusion: In this study, we report the first genome-wide association analysis of patients diagnosed as PMR in the population from the UK Biobank and FinnGen cohorts. We show that *HLA-DRB1* and *ANKRD55/IL6ST* regions are associated with PMR diagnosis. Both regions have strong biological plausibility due to previous research implicating *HLA-DRB1* variants in genetic susceptibility to PMR and the evidence for the role of IL-6 in the disease pathogenesis.

Disclosure: M. Hocaoglu: None; **J. Mikdashi**: None; **J. Perry**: None; **C. Hong**: None.

Abstract Number: 0028

Adenosine Deaminase 2 Is Expressed as a Short Isoform Lacking Deaminase Activity in the Endothelium: Implications for DADA2 Vasculitis

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SESSION INFORMATION
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Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Deficiency of adenosine deaminase 2 (DADA2) is an autosomal recessive condition caused by biallelic variants in the Adenosine deaminase 2 (ADA2) gene. Clinical manifestations are broad, but a vasculitis phenotype is widely recognised. Although ADA2 expression is conventionally associated with myeloid cells, a recent report identified expression in endothelial cells (ECs) and demonstrated Interferon (IFN) β induction in the absence of ADA2. The current study aimed to investigate the expression and role of ADA2 in the endothelium.

Methods: ADA2 transcript expression was explored across different tissues and cell types using Blueprint, GTEX and in-house short and long read RNA-seq datasets. Findings were validated by qRT-PCR, immunoblot and an ADA2 activity assay in primary human umbilical vein and aortic ECs (HUVEC, HAEC) and the pro-monocytic cell line U937.

Endothelial colony forming cells (ECFC) were cultured from peripheral blood mononuclear cells (PBMCs) isolated from patients with DADA2 and healthy donors, following our established protocols.

Results: We identified 3 human ADA2 isoforms: ADA2 201 and 203, the classically described myeloid derived isoforms (511 amino acids, aa) and ADA2 202 which was predicted to encode a shorter protein lacking a signal peptide and part of the deaminase domain (270 aa) (Fig 1A). In contrast to 201 and 203, the 202 isoform appears widely expressed across tissue types but absent from immune cells (Fig 1B & C).

Analysis of RNA-seq data identified 202 as the sole ADA2 transcript expressed in ECs (Fig 2A). This was confirmed by qPCR using transcript-specific primers: 202 was the predominant isoform in ECs and 201/203 in PBMCs and U937 (Fig 2B).

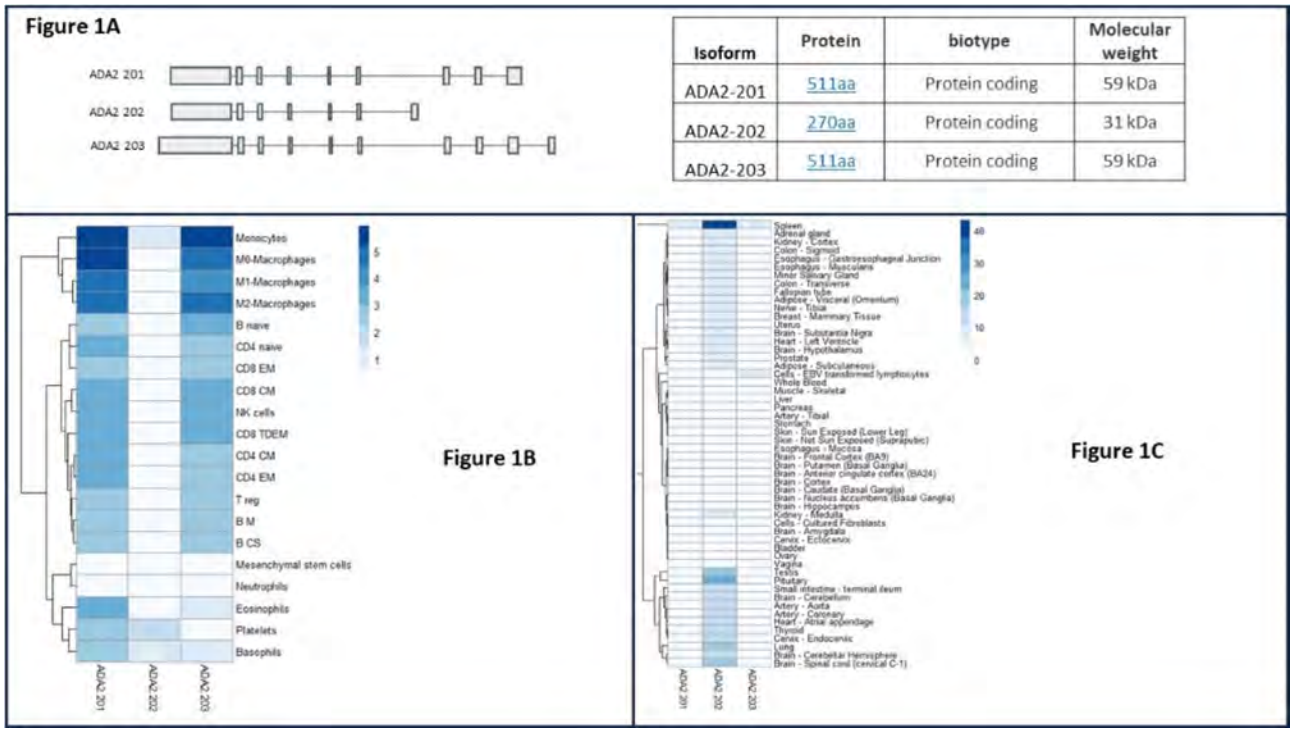

Figure 1A – 3 ADA2 isoforms exon map. Figure 1B – Blueprint blood database demonstrating ADA2 isoform expression in blood cells. Figure 1C – GTEX data demonstrating ADA2 isoform expression in tissues.

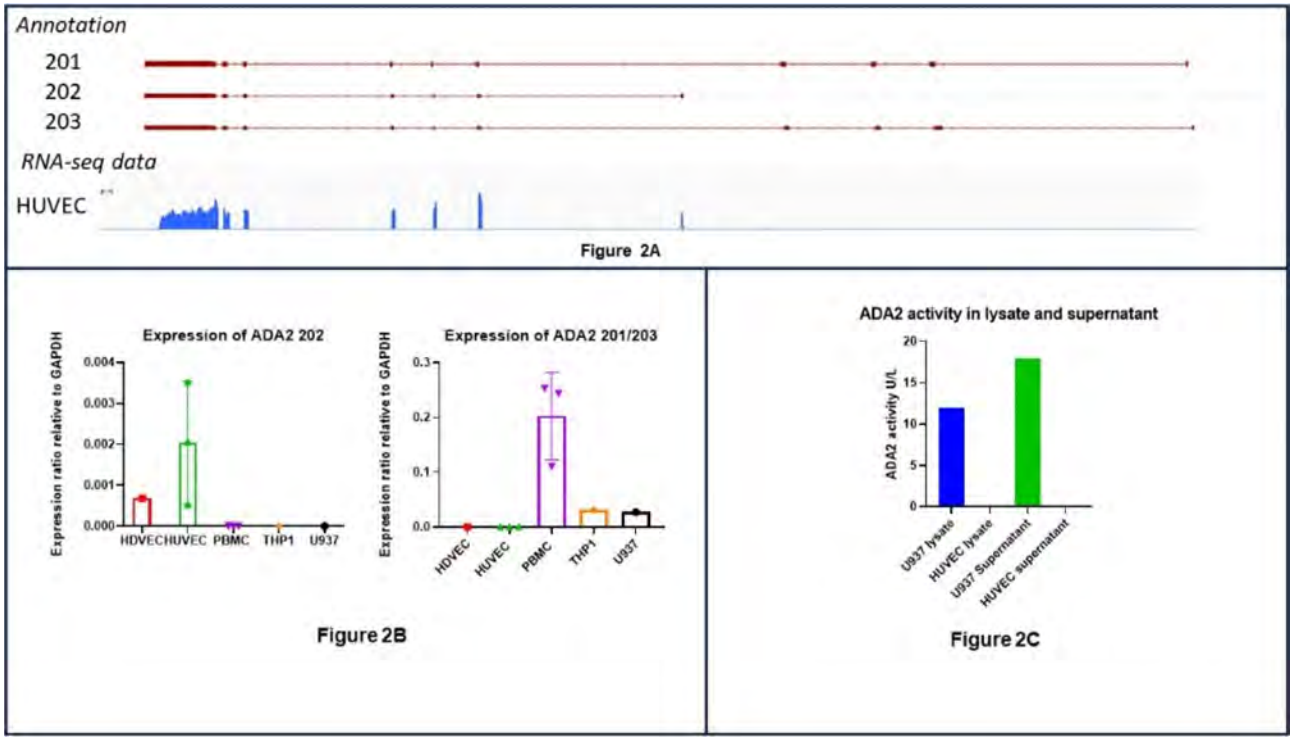

Figure 2A – signal plot from our own RNAseq in Human Umbilical Vein Endothelial Cells (HUVEC) showing ADA2 202 transcript expression. Figure 2B - RT-qPCR demonstrating expression of ADA2 202 and ADA2 201/203 in different cell types. Human Dermal Vascular Endothelial Cells (HDVEC), Human Umbilical Vein Endothelial Cells (HUVEC), Peripheral Blood Mononuclear cells (PBMC), THP1 – monocyte cell line, U937 – pro-monocytic cell line. Figure 2C – ADA2 enzymatic activity in lysate and supernatant from U937 and HUVEC

Figure 3A – Volcano plot demonstrating differentially expressed genes with ADA2 KD in HUVEC. Figure 3B – Table demonstrating gene set enrichment pathway analysis. NES – normalised enrichment score. FDR – false discovery rate.

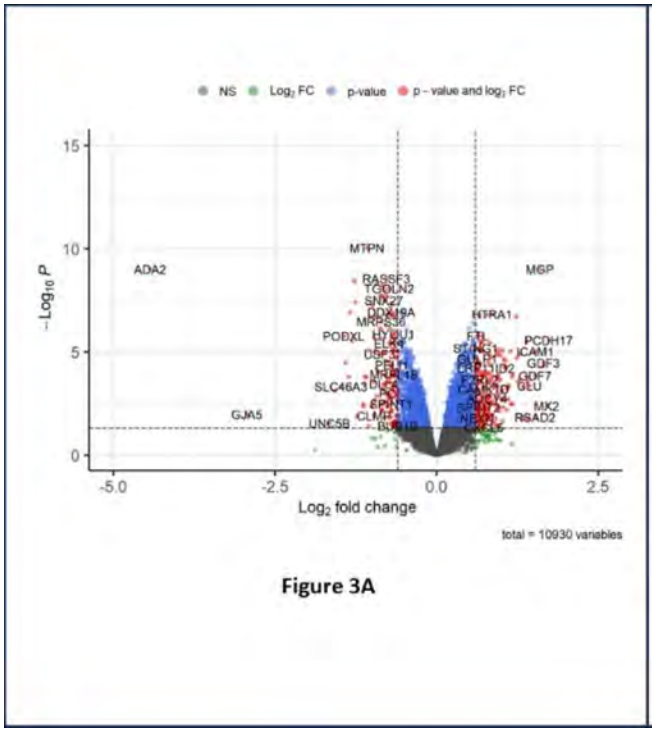

Figure 3A

Pathway	NES	FDR
Interferon alfa response	1.85	0.000
Interferon gamma response	1.67	0.005
Coagulation	1.58	0.022
TNFα signalling via NFκB	1.57	0.018
Epithelial Mesenchymal transition	1.56	0.017
Apoptosis	1.52	0.026
Inflammatory response	1.47	0.031

Figure 3B

Despite the presence of ADA2 202 mRNA, no protein or deaminase activity were detected in HUVEC or HAEC lysates or supernatants (Fig 2C). Overexpression of 201 isoform demonstrated deaminase activity and protein secretion as expected; in contrast 202 was enzymatically inactive, not secreted and retained in the insoluble protein fraction.

Since 202 was expressed at the mRNA but not protein level, we explored a possible regulatory function by siRNA knockdown (KD) in HUVEC (90% KD achieved). ADA2 KD resulted in dysregulation of 352 genes and enriched inflammatory (IFN, TNF), coagulant and apoptotic signalling suggesting an important role for 202 in endothelial homeostasis (Fig 3B).

Consistent with this, initial ECFC analysis demonstrated a lower proliferative and more inflammatory phenotype in DADA2 compared to healthy donor ECFC, characterised by increased ICAM-1, VCAM-1 and IFN-related gene expression (n=4 per group).

Conclusion: Endothelial ADA2 is expressed exclusively as the shortened 202 transcript but its protein form is undetectable. Artificially overexpressed 202 accumulated in the insoluble protein fraction, lacked deaminase activity and thus appeared non-functional. ADA2 knockdown in ECs led to upregulation of inflammatory apoptotic gene expression, potentially indicating a role for 202 in endothelial homeostasis as a non-coding RNA. Given its widespread tissue expression, genetic variants affecting 202 could have implications for understanding the heterogenous manifestations of DADA2.

Disclosure: A. Porter: None; **R. Maughan**: None; **C. Pericleous**: None; **L. Kabir**: None; **R. Stratton**: Aurinia Pharmaceuticals Inc., 5, Riptide Bioscience Inc., 5; **D. Haskard**: None; **P. Lee**: None; **T. Youngstein**: None; **J. Mason**: None.

Abstract Number: 0029

Post-translationally Modified Fibrinogen Activated Macrophages Drive the Expression of Fibrotic Genes in Human Lung Fibroblasts

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SESSION INFORMATION

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Session Title: Genetics, Genomics & Proteomics Poster

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Background/Purpose: Cellular interactions between alveolar macrophages (MΦ) and human lung fibroblasts (HLFs) contribute to excessive pro-inflammatory and pro-fibrotic responses in rheumatoid arthritis interstitial lung disease (RA-ILD), leading to pulmonary fibrosis. Our laboratory has previously shown that malondialdehyde-acetaldehyde (MAA) and citrulline (CIT) modifications co-localize in the lung tissue of RA-ILD patients. However, the mechanism by which MAA and CIT

Inflammation:

	MΦ-SN:				Direct antigens:			
Genes	FIB	FIB-MAA	FIB-CIT	FIB-MAA-CIT	FIB	FIB-MAA	FIB-CIT	FIB-MAA-CIT
CD36	1.0	5.9	3.9	9.4	1.0	1.1	2.0	1.3
C8A	1.0	6.2	5.6	7.8	1.0	-1.2	-1.5	-2.2
BST2	1.0	6.2	2.2	6.7	1.0	1.1	-1.1	-1.1
BMP10	1.0	3.6	1.7	6.0	1.0	-1.2	1.0	1.0
MMP9	1.0	4.4	3.5	4.7	1.0	1.1	1.3	-1.0

Initiation:

	MΦ-SN:				Direct antigens:			
Genes	FIB	FIB-MAA	FIB-CIT	FIB-MAA-CIT	FIB	FIB-MAA	FIB-CIT	FIB-MAA-CIT
CETP	1.0	6.2	4.6	[illegible]	1.0	-1.2	-1.6	1.2
CD36	1.0	5.9	3.9	9.4	1.0	1.1	2.0	1.3
LRP2	1.0	6.7	3.0	2.8	1.0	-7.6	-1.5	-2.3
PDGFRB	1.0	3.6	2.3	3.6	1.0	-1.3	-1.6	1.1
PLCG2	1.0	2.7	2.3	3.6	1.0	1.3	1.2	1.2

Modification:

	MΦ-SN:				Direct antigens:			
Genes	FIB	FIB-MAA	FIB-CIT	FIB-MAA-CIT	FIB	FIB-MAA	FIB-CIT	FIB-MAA-CIT
TJP2	1.0	7.4	3.7	7.4	1.0	-1.9	-1.2	-1.4
MMP9	1.0	4.4	3.5	4.7	1.0	1.1	1.3	-1.0
VAV1	1.0	3.4	3.6	4.5	1.0	-1.1	-1.1	-1.0
COL6A3	1.0	1.9	1.8	3.3	1.0	-1.0	-1.3	-1.1
MMP10	1.0	2.4	2.0	2.9	1.0	-1.0	1.1	1.0

Proliferation:

	MΦ-SN:				Direct antigens:			
Genes	FIB	FIB-MAA	FIB-CIT	FIB-MAA-CIT	FIB	FIB-MAA	FIB-CIT	FIB-MAA-CIT
CD36	1.0	5.9	3.9	9.4	1.0	1.1	2.0	1.3
PIK3R5	1.0	3.7	1.9	7.7	1.0	-1.2	1.4	1.5
LRP2	1.0	6.7	3.0	2.8	1.0	-7.6	-1.5	-2.3
BMP10	1.0	3.6	1.7	6.0	1.0	-1.2	1.0	1.0
MMP9	1.0	4.4	3.5	4.7	1.0	1.1	1.3	-1.0

Figure 1. Representative top 5 genes from Nanostring Human Fibrosis Panel for mRNA levels of inflammation, initiation, modification, and proliferation fibrosis markers from stimulated HLF cells. HLF cells were stimulated with either supernatants from modified antigens-treated U937 cells or with directly modified antigens. The data is represented as the relative quantity (Rq) of fibrosis markers. The blue color represents an increase in mRNA levels, while the yellow color represents a decrease.

modified proteins alter cellular interactions between MΦ and HLFs has not been well delineated. The purpose of this study was to identify fibrotic gene expression and activation of signaling pathways by HLFs in response to: 1) macrophage supernatants (MΦ-SN) collected post-stimulation with MAA and/or CIT modified fibrinogen (FIB); or, 2) direct stimulation with MAA and/or CIT modified FIB.

Methods: Primary HLFs were treated with either MAA and/or CIT modified FIB or with MΦ-SN collected from PMA-activated U-937 cells following stimulation with MAA/CIT modified FIB. RNA was isolated 8-hours post-treatment and evaluated for the expression of 770 genes using the NanoString® Human Fibrosis Panel. The top 30 genes with the highest values for fold increase (compared to FIB or MΦ-SN^{FIB}) were categorized into four stages (inflammation, initiation, modification, and proliferation) in the Nanostring® software based on their role in the fibrotic pathway, with several genes exerting influence on multiple pathways. Additionally, HLFs were evaluated by Western Blot for phosphorylation of signaling pathways involved in fibrosis.

Results: Treatment ofHLFs with MΦ-SN upregulated pro-fibrotic genes in all 4 pathways beyond the effects of direct antigen stimulation (Fig.1). For inflammatory genes, exposure of HLFs to MΦ-SN$^{FIB\text{-}MAA\text{-}CIT}$ yielded the highest mRNA fold increase vs. other groups. The top 5 inflammatory genes expressed following stimulation with MΦ-SN$^{FIB\text{-}MAA\text{-}CIT}$ vs. MΦ-SN^{FIB} were CD36 (9-fold; critical in fibroblast activation), C8A (8-fold; component of complement system), BST2 (7-fold; bone marrow stromal antigen), BPM-10 (6-fold; bone morphogenic protein belonging to TGF-b family), MMP9 (5-fold; plays a role in matrix remodeling). The top genes for initiation, modification, and proliferation upregulated in the MΦ-SN$^{FIB\text{-}MAA\text{-}CIT}$

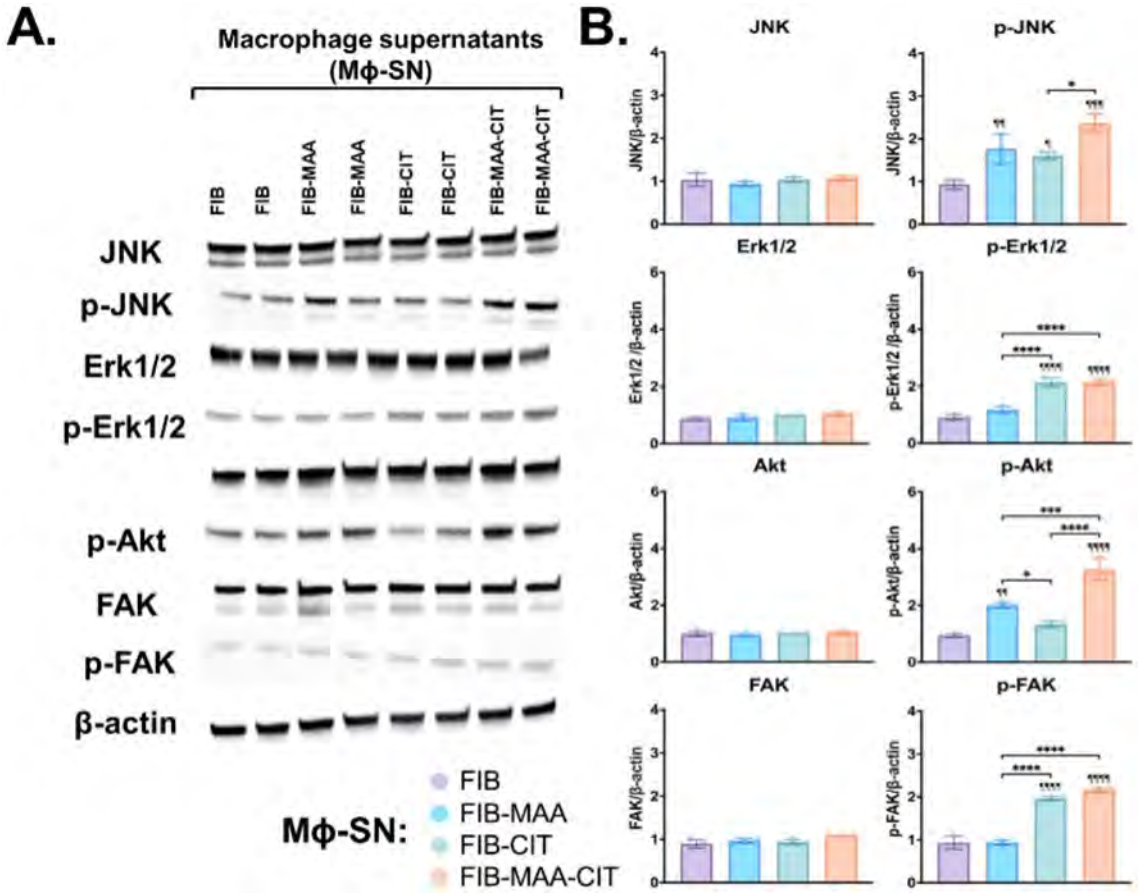

Figure 2. Phosphorylation of fibrosis signaling pathways in stimulated HLF cells. HLF cells were incubated with MΦ-SN for 90 minutes. MΦ-SN were collected from U-937 activation with the modified fibrinogen antigens. (A) Representative Western Blots of HLF lysates probed with signaling molecule antibodies. (B) Densitometry of normalized values (mean with SEM) to β-actin of signaling molecules. Comparisons made to FIB are illustrated above each bar: ¶¶¶¶p<0.0001; n=3. Only significant differences between groups are illustrated: ***p<0.001, ****p<0.0001.

group were; CETP (14-fold), TJP2 (7-fold), and CD36 (9-fold), respectively. HLFs treated with MΦ-SN$^{FIB\text{-}MAA\text{-}CIT}$ in comparison to MΦ-SN$^{FIB\text{-}MAA}$ and MΦ-SN$^{FIB\text{-}CIT}$ showed an increased expression of phosphorylated; (p-) JNK ($p < 0.001$ vs. MF-SN^{FIB}), p-Erk1/2 ($p < 0.0001$), p-Akt ($p < 0.0001$), and p-FAK ($p < 0.0001$) (Fig.2). Direct antigen stimulation did not upregulate any of the signaling pathways examined (data not shown).

Conclusion: Our studies demonstrate that HLF interaction with MΦ released mediators, particularly those initiated by exposure to dually modified antigens, are necessary to engage all 4 relevant pathways involved in fibroblast-mediated pulmonary fibrosis that characterizes RA-ILD. Identification of MΦ released soluble factors may serve as an important mediator of the inflammatory and fibrotic processes underlying RA-ILD pathogenesis and could serve as a potential novel target for treatment.

Disclosure: N. Aripova: None; **M. Duryee**: None; **C. Hunter**: None; **B. Butler**: None; **A. Nelson**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **J. O'Dell**: None; **J. Poole**: AstraZeneca, 12, I have received no monies. I received anti-IL-33 monoclonal antibody from AstraZeneca for animal research sutdies.; **G. Thiele**: None; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9.

Abstract Number: 0030

A Pathogenetic Model of IgG4-related Disease Developed from Familial IKZF1 and UBR4 Gene Variants

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
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Background/Purpose: Most autoimmune diseases are polygenic, frequently with more than 100 gene variants contributing to genetic predisposition. Given this complexity, conclusions on disease mechanisms are generally difficult to draw. Monogenic autoimmune diseases, while rare, offer a unique opportunity to develop models that enable a more mechanistic understanding of the disease process. Here, we have identified a family with IgG4-related disease (IgG4-RD) and dominant atopic features. All three affected members shared mutations in the IKZF1 (c. 548G >A, p. Arg183His) and UBR4 (c. 12537T >A, p. Cys4179Ter) genes, suggesting that either one of them or the combination of both conferred disease with high penetrance. *UBR4* encodes a ubiquitin ligase involved in protein degradation, *IKZF1* the transcription factor IKAROS.

Methods: PBMCs from patients and healthy controls were phenotyped by mass cytometry and flow cytometry. The influence of the variants on the transcriptome and proteome was determined and confirmed by gene silencing. In functional studies, T cell receptor signaling, T cell activation and polarization were examined in patient-derived T cell lines. Gene silencing and forced overexpression of candidate molecules was used to confirm their role in disease-relevant pathways and construct a model of distorted T cell activation and T cell differentiation due to the variants' functions.

Results: Consistent with previous findings in non-hereditary IgG4-RD, all three patients had a prominent Th2 bias as determined by cytokine production, transcription factor expression and chemokine receptor profiles. The *UBR4* mutation caused truncation resulting in reduced function. The *IKZF1* mutation was mapped to the DNA-binding domain, predicting increased transcriptional regulation. Flow studies showed increased CD45 levels in all patients' T and B cells. Consistent with

increased CD45 phosphatase activity, LCK phosphorylation at inhibitory and stimulatory sites were reduced. Unexpectedly, TCR signaling and T cell activation were upregulated in patients. Despite reduced LCK activity, the enhanced TCR signaling was SRC family kinase (SFKs) dependent. After further examination of SFKs, FYN abundance was identified to be upregulated in the patients. In contrast to its inhibitory effect on LCK, CD45 abundance activated FYN, which resulted in augmented T cell activation. Mechanistically, the *IKZF1* mutation resulted in increased binding to the FYN promoter and elevated transcription of FYN. The *UBR4* mutation affected CD45 levels post-transcriptionally by preventing its lysosomal degradation. The hyperactivity of FYN not only reduced the threshold for T cell activation but also accounted for the increased Th2 polarization by phosphorylating JunB.

Conclusion: We identified variants of the *IKZF1* and *UBR4* genes in familial IgG4-RD. The two mutations synergize to promote the expression and activity of the kinase FYN in T and B cells. Increased FYN activity induces unopposed T cell activation and enhances Th2 differentiation. Based on this disease model, we propose several molecular targets that can be explored for therapeutic interventions in IgG4-RD and possibly other atopic diseases.

Disclosure: Q. Liu: None; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Chemocentryx, 1, 6, Eli Lilly, 5, kiniksa, 5; **M. Koster**: None; **C. Weyand**: AbbVie/Abbott, 1, Bristol-Myers Squibb(BMS), 1, Gilead, 1; **J. Goronzy**: AbbVie/Abbott, 1, Bristol-Myers Squibb(BMS), 1, Gilead, 1.

Abstract Number: 0031

A Systematic Approach for Identifying Causal Variants and Their Target Genes on JIA Risk Haplotypes

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

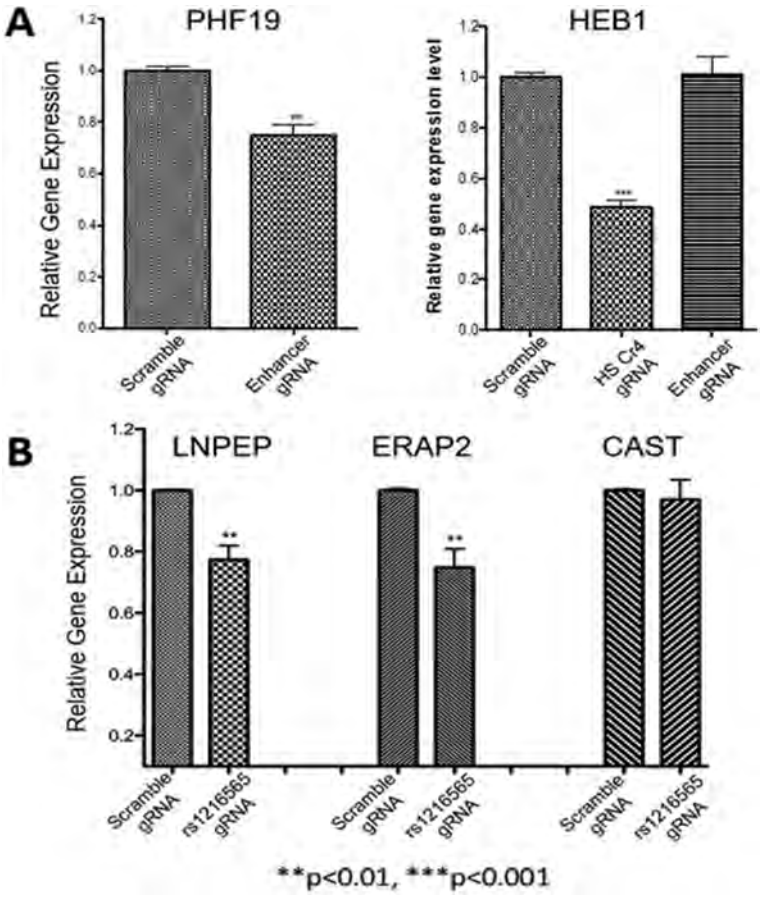
Background/Purpose: GWAS have identified multiple genetic regions that confer risk for juvenile idiopathic arthritis (JIA). However, identifying the single nucleotide polymorphisms (SNPs) that drive disease risk has been impeded by the fact that the SNPs used to identify risk loci are in linkage disequilibrium (LD) with hundreds of other SNPs. Since the causal SNPs remain unknown, it is difficult to identify target genes, and thus use genetic information to elucidate disease biology and inform patient care. We have therefore developed a functional genomics pipeline to identify causal variants and their target genes on JIA risk haplotypes.

Methods: We designed 180 bp oligonucleotides ("oligos") representing 7,312 SNPs in LD with the tag SNPs on JIA risk loci (r^2 = 0.80).Oligos were bar coded and cloned into a green fluorescence protein (GFP)-carrying plasmid vector behind a minimal promoter. We transfected our oligo libraries into myeloid K562 cells to conduct a massively parallel reporter assay (MPRA) in which GFP expression for each of the 7,312 SNPs was compared to the common allele. We then used 3D chromatin data to identify the chromatin loops harboring the enhancers carrying SNPs that screen positive on MPRA. We used K562 cells stably transfected with the epigenome editing enzyme dCas-KRAB and gRNAs across the enhancer regions in the *TRAF1* and *LNPEP/ERAP2* loci, inducing dCas-KRAB with doxycycline and using qrtPCR to query expression levels of genes within the same chromatin loops.

Results: We identified n=44 SNPs that showed a significant difference in gene expression (FC $\geq$ 2.0, FDR = 0.05) when compared to the common allele. After stimulating K562 cells with IFNγ (250 ng/ml), we identified an additional 42 SNPs that showed significant effects on gene expression that were not identified in unstimulated cells. In many cases, we identified multiple alleles on the same haplotype, although these alleles were not necessarily within the same functional element (e.g., intergenic vs intronic enhancers). Ablating the intergenic enhancer harboring rs10985080 on the *TRAF1* haplotype using CRISPRi significantly reduced the expression of *PHF1*, but not *C5*, which is in the same chromatin loop. Using a similar approach for an intergenic enhancer in the *LNPEP/ERAP2* locus, we found reduced expression of both *LNPEP* and *ERAP2* but not *CAST*.

Conclusion: We demonstrate proof-of concept for identifying causal variants on JIA risk haplotypes based on observed functional properties that distinguish them from the SNPs in which they are in LD. We also demonstrate that, once these variants are identified, target genes can be quickly identified using publicly available 3D chromatin data and additional functional assays such as CRISPRi.

Disclosure: K. Jiang: None; **t. liu**: None; **R. Tewhey**: None; **S. Kales**: None; **Y. Park**: None; **J. Jarvis**: None.



CRISPi identifies target genes of enhancers harboring JIA-associated variants detected on MPRA. (A). gRNAs used for epigenome editing experiments. The scrambled gRNA is a non-targeting negative control gRNA. For each experiment, 4 gRNAs were targeted to the functional regions of intergenic enhancers in the TRAF1 locus and the ERAP2/LNPEP locus. (B) Attenuation of the intergenic enhancer at the TRAF1 locus significantly reduced expression of PHF19, but not C5 (not shown). Off-target effects are monitored by showing that these gRNAs have no effect on HBE1 expression, but that gRNAs directed to an enhancer known to regulated HBE1 attenuates expression. Bar graphs summarize the results of 4 independent experiments. (C) Attenuating the intergenic enhancer in the LNPEP/ERAP2 locus reduces expression of both LNPEP and ERAP2, but not the adjacent gene, CAST, nor the HBE1 gene (not shown). In each experiment, scrambled versions of the gRNAs had no effect on expression of the putative targets. **p<0.01; ***p<0.001.

Abstract Number: 0032

Quantification of the Escape from X Chromosome Inactivation with the Million Cell-scale Human Blood Single-cell RNA-seq Datasets Reveals Heterogeneity of Escape Across Immune Cells and Escape in the Autoimmune Disease Conditions

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SESSION INFORMATION
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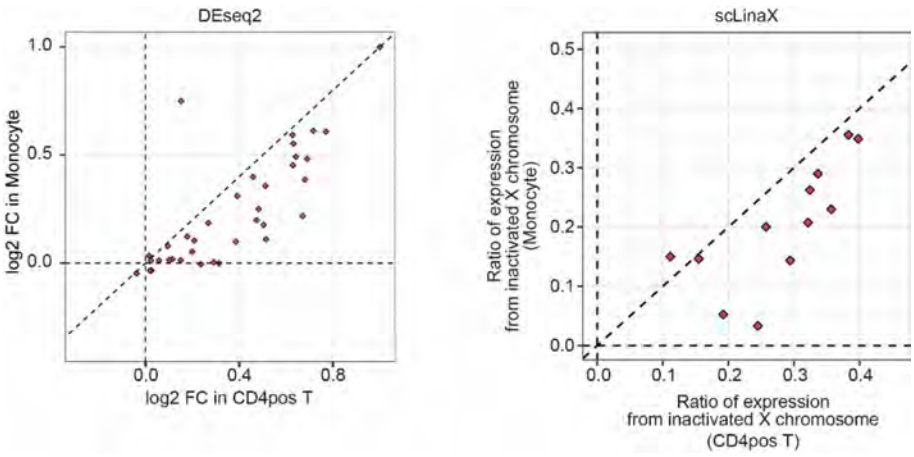
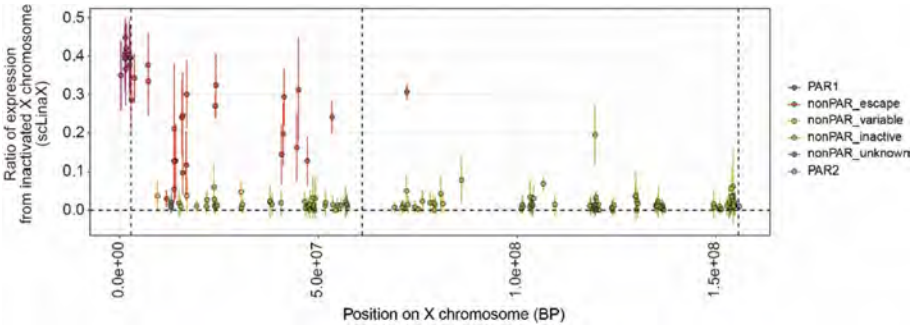
Background/Purpose: Understanding the differences in the immune system between sexes is important to elucidate the pathogenesis of autoimmune diseases which are more prevalent in females than males. One of the two X chromosomes of females is silenced through X chromosome inactivation (XCI) to compensate for the difference in the X chromosome dosage between sexes. There exist several genes which 'escape' from XCI, which could contribute to the differential gene expression between sexes. The differences in the escape across cell types are still poorly characterized, especially across immune cell types, even though a large number of immune-related genes are located on the X chromosome. Although previous studies suggested that abnormal escape of a few immune-related genes could contribute to autoimmune diseases, systematic evaluation of the association between escape and autoimmune diseases has not been conducted.

Methods: We investigated the escape across immune cell types utilizing the largest scale scRNA-seq datasets



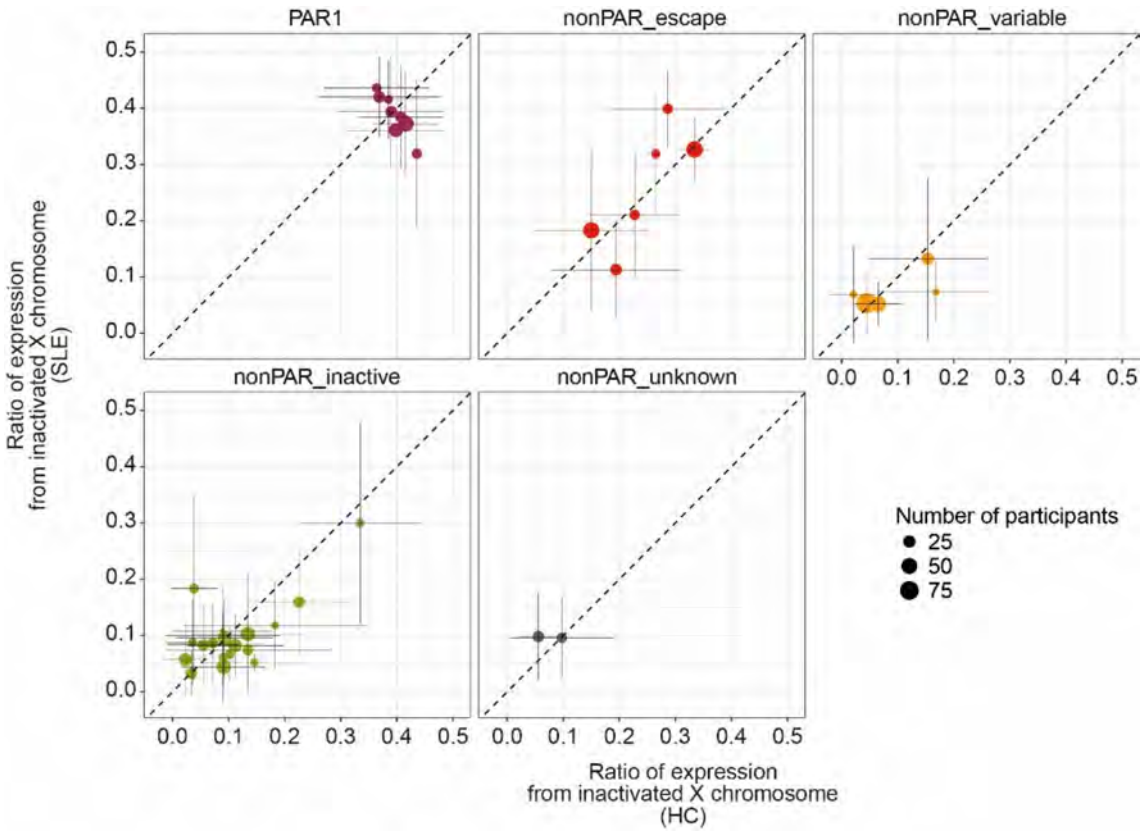
Degree of escape tended to be higher in lymphoid cells than in myeloid cells. The plots indicate the result of the comparison of log2 fold changes in the DEG analysis (left) and the ratio of the expression from the inactivated X chromosome (right) between CD4 positive T cells (x-axis) and monocytes (y-axis). The dashed lines indicate y = x.



The scLinaX successfully detected the escape from the inactivated X chromosome for the previously reported escapee genes. A plot indicating the ratio of the gene expression from inactivated X chromosome quantified by scLinaX (y-axis) and the positions on the X chromosome (x-axis). The color of the points indicates whether the genes escape from the X chromosome inactivation or not based on the previous literature. The error bar indicates the standard deviations.

(1) ~1,000,000 peripheral blood mononuclear cells (PBMCs) from 489 East Asian participants (Asian Immune Diversity Network), (2) ~1,000,000 PBMCs from 147 Japanese (72 COVID19 patients and 75 healthy participants) (3) ~1,000,000 PBMCs from 162 systematic lupus erythematosus patients and 99 healthy participants including East Asian and European.

We performed differential expression gene (DEG) analysis between sexes across immune cell types. In addition, we newly developed a method, **s**ingle-**c**ell **L**evel **ina**ctivated **X** chromosome mapping (**scLinaX**), which directly quantifies gene expression from the inactivated X chromosome (Xi). Although the previous studies required plate-based scRNA-seq data



Comparison of the ratio of the gene expression from inactivated X chromosome between healthy control (HC) subjects (x-axis) and systemic lupus erythematosus (SLE) subjects (y-axis). The error bar indicates the standard deviations.

which had rich per-cell information at the cost of throughput and cost efficiency for analyzing escape, scLinaX could be applied to the droplet-based scRNA-seq data which are high throughput and widely used.

Results: DEG analysis for each immune cell type revealed that degree of female-biased expression of escapee genes was stronger in lymphocytes than in myeloid cells (**Figure 1**). The scLinaX successfully detected the gene expression from the Xi for the previously reported escapee genes (**Figure 2**). The scLinaX revealed the stronger degree of escape in lymphocytes than in myeloid cells suggesting that difference in escape makes the heterogeneity of sex-associated differential gene expression across cell types (**Figure 1**). We also found several genes which had female-biased expression while showing little evidence of the escape in scLinaX analysis, emphasizing the limitation of DEG analysis and the importance of complementary analysis, such as the scLinaX. We evaluated the association between diseases (e.g. SLE) and escape and found little evidence of association, suggesting that abnormal escape in disease conditions might be not common but rather specific for a limited set of reported genes and cell types (**Figure 3**).

Conclusion: As demonstrated with several public datasets, scLinaX could be applied to a wide variety of scRNA-seq datasets. This study would contribute to expanding the current understanding of the XCI and escape and their contribution to autoimmune diseases.

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Abstract Number: 0033

A Novel Transcriptome-Based Machine Learning Pipeline Predicts Phenotypes of Lupus Patients

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SESSION INFORMATION
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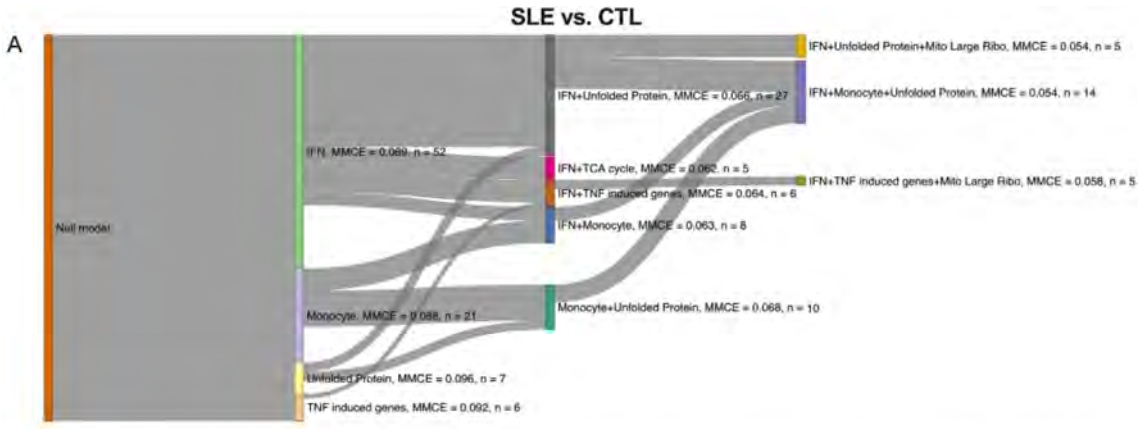
Background/Purpose: Gene expression analysis coupled with machine learning (ML) holds the promise of identifying subsets of patients with heterogeneous diseases, such as systemic lupus erythematosus (SLE), a multi-organ autoimmune disease with known diversity in both clinical presentation and gene expression profiles. However, phenotype prediction based on gene expression has often relied on the performance of individual genes without a systems biology context. To address this, we created an interpretable ML approach to predict clinical phenotype of SLE patients in a non-invasive manner using blood transcriptomic profiles.

Methods: We developed a sequential grouped feature importance algorithm to assess the performance of gene sets, including those identifying immune and metabolic pathways and cell types known to be abnormal in SLE, in predicting the presence of lupus as well as disease activity and organ involvement. We normalized, merged, and batch-corrected publicly available datasets and created six ML models to predict SLE from healthy controls (CTL), inactive SLE from CTL, active from inactive SLE, lupus nephritis (LN) from CTL, LN from non-renal lupus, and rheumatoid arthritis (RA) from SLE.

Results: The SGFI algorithm first selects the best gene set to predict phenotype for the model, and then sequentially adds in additional gene sets if they improve the performance of the model (Figure 1A). SGFI provides a way to reduce the high dimensionality of transcriptomic datasets meaningfully, as it incorporates prior knowledge of biology into the data while also selecting pathways in an unbiased manner, leading to biologically informative conclusions. After feature selection, the best gene set combination was found via 10-fold cross validation on the train set and then evaluated on the test set (Figure 1B-D). We then performed gene set variation analysis to examine how these pathways differ across clinical phenotypes (Figure 1E). Gene sets related to interferon, tumor necrosis factor, the mitoribosome, and anergic/activated T cell were the



B

Features	No. genes	F1	Accuracy	Sensitivity	Specificity	AUC
Genes from *IFN*, *TNF induced genes*, and *Mito Large Ribo*	189	0.828	0.929	0.934	0.906	0.979

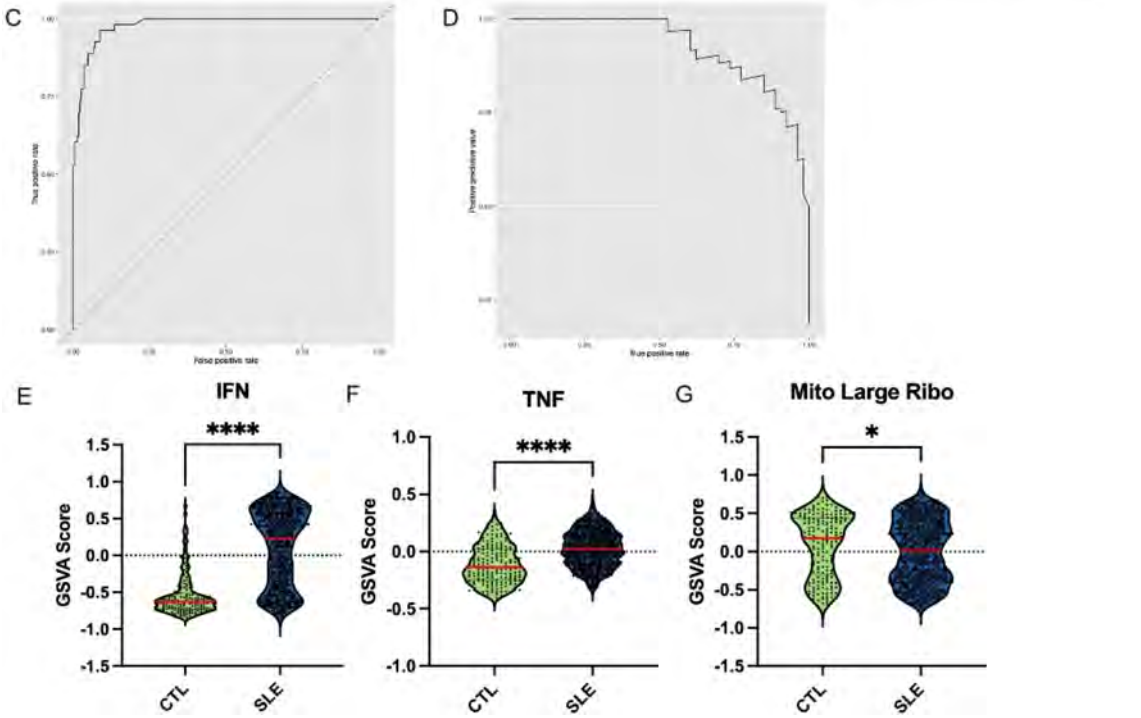


Figure 1. Results from the SLE vs. CTL ML pipeline. A) Sankey plot of the results from feature selection. Feature groups chosen in five or more subsamples are shown in the plot. Feature groups are separated by the symbol, '+'. The average mean misclassification error (MMCE) of each combination across the subsamples and the number of subsamples (n) that module was shown is next to the gene sets. B) Results from evaluation of the final model on the test set. C) Receiver operating characteristic and D) precision-recall curves of final model on the test set. GSVA results of E) interferon (IFN), F) large subunit of mitoribosome (Mito Large Ribo), and G) tumor necrosis factor induced genes (TNF).

Table 1. Summary of the accuracy metrics in the six machine learning models constructed for different patient classification problems.

Classification problem	Gene sets	No. genes	F1	Accuracy	Sensitivity	Specificity	AUC
SLE vs. CTL	*IFN, TNF induced genes, and Mito Large Ribo*	189	0.828	0.929	0.934	0.906	0.979
Inactive SLE vs. CTL	*IFN and Anergic/Activated T Cells*	39	0.857	0.911	0.929	0.868	0.965
Active SLE vs. Inactive SLE	*IFN*	30	0.869	0.824	0.711	0.884	0.842
LN vs. CTL	*IFN and TNF induced genes*	143	0.848	0.831	0.929	0.731	0.943
LN vs. NRL	*IFN and Mito Large Ribo*	80	0.888	0.847	0.732	0.904	0.894
RA vs. SLE	*IFN and TNF induced genes*	147	0.925	0.942	0.963	0.910	0.989

best predictors of phenotype in all classifications (Table 1). The ML models created with those genes as features had excellent performance with AUCs ranging from 0.842 to 0.989 and accuracies of 0.824 to 0.942 (Table 1).

Conclusion: A novel feature selection approach combined with interpretable ML performs extremely well in predicting SLE phenotypes and in separating patients with lupus from both normal and those with RA. Moreover, since interpretable ML can be used to suggest potential causal relationships, these results point to associations between the molecular pathways identified in each model and manifestations of SLE pathogenesis. This innovative ML approach can help improve recognition of SLE phenotypic subsets and additionally be applied to other diseases and tissues.

Disclosure: E. Leventhal: None; **A. Daamen**: None; **A. Grammer**: None; **P. Lipsky**: None.

Abstract Number: 0034

Genome-Wide Association Study for Loci Associated with Positive Antinuclear Antibodies in a Large Hospital Biobank

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SESSION INFORMATION
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Background/Purpose: Antinuclear antibodies (ANA) to intranuclear particles are found in the blood of people with and without autoimmune diseases. To our knowledge, only 1 past genome-wide association study (GWAS) has sought to identify genetic factors related to ANA positivity, reporting association with HLA-DR in a Japanese population (Terao C. et al *Arthritis Rheum* 2014). Dissecting the genetic basis for ANA positivity would allow new insights into susceptibility to autoimmunity.

Methods: We employed data from the Mass General Brigham Biobank, containing linked electronic health records and genotyping (Illumina's Multi-Ethnic Genotyping Array or Global Screening Array chips) for >65,000 consented patients. We identified subjects with genotyping and results for either hep2 or ML immunofluorescence ANA assays (1989-2022). ANA+, those with ≥1 result of ≥ 1:80 titer, were compared to ANA-, those with no positive ANA results. After quality control, we imputed using the Haplotype Reference Consortium, excluding variants with imputation score < 0.5. Classical HLA alleles and amino acids for HLA genes were imputed with SNP2HLA using TopMed HLA data as reference. We restricted analyses to those with predicted European ancestry (1000 Genomes EUR group; 82% of biobank subjects). Diagnostic codes identified 8 autoimmune diseases: systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), scleroderma (SSc), Sjogren's

Table 1. GWAS for ANA Positivity (≥1:80 titer) vs. Negativity: Top results from the Mass General Brigham Biobank among those of European genetic ancestry (N=12,875)

GWAS top associations

Chrom osome	Base position	Ref. allele	Alternate allele	dbSNP ID	Nearest gene	Minor Allele frequency	Beta	SE	OR (95%CI)	p
6	32115185	G	A	rs3134951	N/A	0.20	0.19	0.03	1.2 (1.1-1.3)	1.6E-09
6	32204657	G	A	rs3134925	N/A	0.14	0.22	0.04	1.2 (1.2-1.3)	1.7E-09
6	32204684	G	T	rs3134924	N/A	0.14	0.22	0.04	1.2 (1.2-1.3)	1.7E-09
6	32205867	A	G	rs3130303	N/A	0.14	0.22	0.04	1.2 (1.2-1.3)	1.7E-09
6	32201279	G	C	rs6918888	N/A	0.14	0.22	0.04	1.2 (1.2-1.3)	1.9E-09
6	32205942	C	T	rs6901158	N/A	0.14	0.22	0.04	1.2 (1.2-1.3)	1.9E-09
6	32187637	G	T	rs8192589	*NOTCH4*	0.12	0.23	0.04	1.3 (1.2-1.3)	2.1E-09
6	32122472	C	A	rs3096696	*PPT2*	0.20	0.19	0.03	1.2 (1.1-1.3)	2.2E-09
6	32123973	C	G	rs3130281	*PPT2*	0.20	0.19	0.03	1.2 (1.1-1.3)	2.2E-09
6	32128290	T	C	rs2395099	*PPT2*	0.20	0.19	0.03	1.2 (1.1-1.3)	2.2E-09

HLA analysis top associations

	Base position	Type *	Allele	Reference Amino Acid	Alternate AA		Beta	SE	OR (95%CI)	p
6	32631060	HLA	DQB1:0201				0.23	0.04	1.3 (1.2-1.3)	9.2E-11
6	31323293	HLA	B:0801				0.22	0.04	1.2 (1.1-1.3)	4.3E-08
6	31323293	HLA	B:08				0.22	0.04	1.2 (1.1-1.3)	4.4E-08
6	31324710	AA	B_9	D	others		0.22	0.04	1.2 (1.1-1.3)	4.4E-08
6	32551951	AA	DRB1_73	G	A		0.15	0.03	1.2 (1.1-1.2)	1.0E-07
6	32631060	HLA	DQB1:02				0.16	0.03	1.2 (1.1-1.2)	1.3E-07
6	32632703	AA	DQB1_52	L	P		0.16	0.03	1.2 (1.1-1.2)	1.3E-07
6	32632718	AA	DQB1_47	F	Y		0.16	0.03	1.2 (1.1-1.2)	1.3E-07
6	32632721	AA	DQB1_46	E	V		0.16	0.03	1.2 (1.1-1.2)	1.3E-07
6	32632775	AA	DQB1_28	S	T		0.16	0.03	1.2 (1.1-1.2)	1.3E-07
6	32552063	HLA	DRB1:0301				0.2	0.04	1.2 (1.1-1.3)	2.3E-07
6	32552063	HLA	DRB1:03				0.2	0.04	1.2 (1.1-1.3)	2.5E-07
6	32551939	AA	DRB1_77	N	T		0.19	0.04	1.2 (1.1-1.3)	4.6E-07
6	31324536	AA	B_67	F	others		0.14	0.03	1.2 (1.1-1.2)	6.1E-07

AA: amino acid sequence; HLA: classical HLA alleles

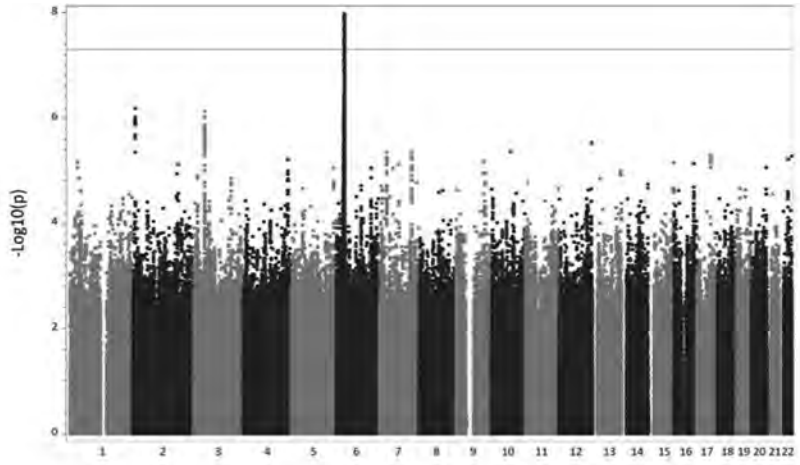

Figure 1. Manhattan Plot for GWAS for ANA positivity (ANA+ 1:80 vs. negative) with threshold for genome-wide significance at p= 5×10^{-8}, showing a strong signal in chromosome 6.

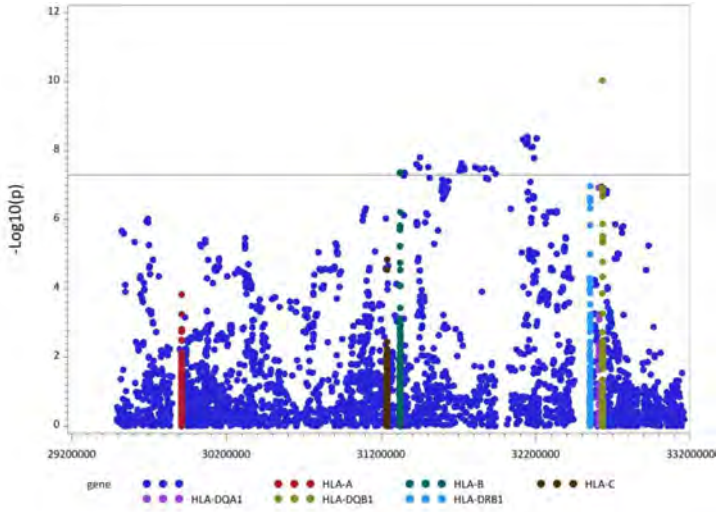

Figure 2. Manhattan Plot for association for ANA positivity (ANA+ 1:80 vs. negative) in the HLA region, with threshold for genome-wide significance at p= 5×10^{-8}, showing a strong signal in HLA-DQB1.

syndrome, mixed connective tissue disease (MCTD), multiple sclerosis (MS), primary biliary cirrhosis (PBC), and autoimmune thyroid disease (ATD). GWAS for ANA + vs – was done in PLINK2, with logistic regression adjusted for age, sex and 4 genetic principal components. We also tested for associations with HLA alleles and amino acids, adjusting for these variables.

Results: We studied 12,875 subjects with ANA and genotyping results: 7,035 ANA + vs. 5,840 ANA -. The female/male ratio was similar in both groups: 62.9% female in ANA+ vs. 62.1% in ANA- (p 0.39). Patients who were ANA+ were older than the ANA- (56.1 ± 15.8 vs. 52.1 ± 15.2 years, p< 0.0001). Overall, by billing codes, SLE, RA, SSc, Sjogren's syndrome, MCTD, MS, PBC and ATD were present in 538, 1425, 159, 370, 65, 354, 63 and 408 subjects (with ANA+ proportions 71%, 55%, 78%, 74%, 82%, 55%, 63%, and 62% respectively).Of ANA+ patients, 33% had ≥1 of the 8 autoimmune diseases, as did 19% of ANA- patients. 8,073,314 SNPs with MAF >=0.01 were included. The strongest GWAS association with ANA+ was for rs3134951 on chromosome 6 in the HLA region with OR 1.2 (95% CI 1.1-1.3, p 1.6×10^{-9}) (**Table 1, Figure 1**). HLA region association analysis revealed *HLA-DQB1:0201* allele had strong association with OR 1.3 (95% CI 1.2-1.3, p 9.2×10^{-11}). *HLA-DRB1:03* and *HLA-B:08* alleles also had significant associations (**Figure 2**). We identified 2 suggestive novel loci for ANA +, one in LOC105373419 gene (rs60343674) and the other in *ABHD5* gene (rs12489159). (**Figure 1)**

Conclusion: These results confirm that *HLA-DRB,* as well as newly identified *HLA-DQB1* and *HLA-B,* are strong genetic factors predisposing to ANA positivity in this European ancestry population. We are pursuing stratified analyses by ANA pattern and titer, sex, and autoimmune disease.

Disclosure: J. Cui: None; **J. Yee**: None; **L. Liang**: None; **J. Ellrodt**: None; **E. Oakes**: None; **H. Guan**: None; **K. Costenbader**: Amgen, 2, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Eli Lilly, 2, Exagen Diagnostics, 5, Gilead, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5.

Abstract Number: 0035

Using Genotyping and Functional Data from Monocytes to Identify Risk-Driving SNPs on JIA Risk Haplotypes

Emma Haley[1], gilad Barshad[2], Adam He[2], Edward J Rice[3], Elizabeth Crinzi[1], Marc Sudman[4], Susan Thompson[5], Charles G Danko[3] and James N Jarvis[6], [1]Jacobs School of Medicine and Biomedical Sciences, Buffalo, NY, [2]Cornell University, Ithaca, NY, [3]Baker Institute of Animal Health Cornell University, Ithaca, NY, [4]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [5]Cincinnati Children's Hospital Medical Center/University of Cincinnati College of Medicine, Blue Ash, OH, [6]University at Buffalo Jacobs School of Medicine, Buffalo, NY

SESSION INFORMATION

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Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: GWAS have identified multiple genetic regions that confer risk for juvenile idiopathic arthritis (JIA). However, identifying the single nucleotide polymorphisms (SNPs) that drive disease risk has been impeded by the fact that the SNPs that identify risk loci are in linkage disequilibrium (LD) with hundreds of other SNPs. Since the causal SNPs remain unknown, it is difficult to identify target genes, and use genetic information to inform patient care. GWAS are also unable to identify the cells impacted by disease-driving variants. We have shown that disease-driving variants on JIA haplotypes are likely to impact monocytes and macrophages. We therefore used genotyping and functional data in primary human monocytes/macrophages to nominate disease-driving SNPs on JIA risk haplotypes and identify their likely target genes.

Methods: We identified JIA risk haplotypes using Immunochip data from Hinks et al (Nature Gen 2013) and the meta-analysis from McIntosh et al (Arthritis Rheum 2017), setting r^2 at 0.80.We used existing genotyping data from 3,939 children with JIA and 14,412 healthy controls to identify SNPs that: (1) were situated within open chromatin in multiple immune cell types and (2) were more common in children with JIA than the controls ($p< 0.05$).We next identified those SNPs that occured within regulatory regions. We intersected the chosen SNPs (n=846) with regions of bi-directional transcription initiation characteristic of non-coding regulatory regions detected using dREG to analyze GROseq data. Finally, we used MicroC data to identify gene promoters interacting with the regulatory regions harboring the candidate causal SNPs.

Results: From the list of n=846 SNPs, we identified 190 SNPs that overlap with dREG peaks in monocytes and126 SNPs that overlap with dREG peaks in macrophages. Of these SNPs, 101 were situated within dREG peaks in both monocytes and macrophages, suggesting that these SNPs exert their biological effects independent of the cellular activation state. MicroC data in monocytes identified 20 genes/transcripts whose promoters interact with the enhancers harboring the SNPs of interest and therefore are the likely target genes. These included genes known to regulate interferon responses (*IRF1, ERAP2*) and well as genes broadly associated with leukocyte activation (*JAK1, PIK3CG*).

Conclusion: We demonstrate that SNPs on JIA risk haplotypes that are candidate causal variants can be further screened using functional data such as GROseq. This screening process identifies a finite number of candidate causal SNPs, the majority of which are likely to exert their biological effects independent of cellular activation state in monocytes. Three dimensional chromatin data generated with MicroC identifies the genes likely to be influenced by these SNPs. These studies demonstrate the importance of investigations into the role of innate immunity in JIA.

Disclosure: E. Haley: None; **g. Barshad**: None; **A. He**: None; **E. Rice**: None; **E. Crinzi**: None; **M. Sudman**: None; **S. Thompson**: None; **C. Danko**: None; **J. Jarvis**: None.

Abstract Number: 0036

Using Genotyping and Chromatin Data in CD4+ T Cells to Nominate Causal Variants on JIA Risk Haplotypes and to Identify Their Target Genes

Emma Haley[1], gilad Barshad[2], Kaiyu Jiang[3], Adam He[2], Edward J Rice[4], Marc Sudman[5], Susan Thompson[6], Elizabeth Crinzi[1], Charles G Danko[4] and James N Jarvis[7], [1]Jacobs School of Medicine and Biomedical Sciences, Buffalo, NY, [2]Cornell University, Ithaca, NY, [3]University at Buffalo, Buffalo, NY, [4]Baker Institute of Animal Health Cornell University, Ithaca, NY, [5]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [6]Cincinnati Children's Hospital Medical Center/University of Cincinnati College of Medicine, Blue Ash, OH, [7]University at Buffalo Jacobs School of Medicine, Buffalo, NY

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

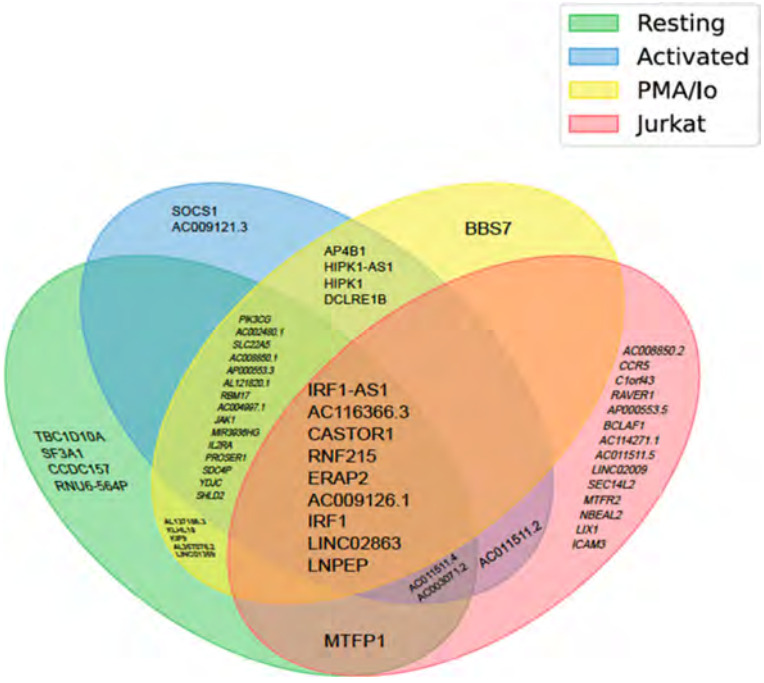
Session Title: Genetics, Genomics & Proteomics Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: GWAS have identified multiple genetic regions that confer risk for juvenile idiopathic arthritis (JIA). However, identifying the single nucleotide polymorphisms (SNPs) that drive risk has been impeded by the fact that the SNPs that identify risk loci are in linkage disequilibrium (LD) with hundreds of other SNPs. Since the causal SNPs remain unknown, it is difficult to identify target genes or use genetic information to inform treatment. GWAS are also unable to identify the cells whose function is impacted by the disease-driving variants. We used genotyping and functional data in primary human CD4+ T cells to nominate disease-driving SNPs and identify their likely target genes.

Methods: We identified JIA risk haplotypes using Immunochip data from Hinks et al (Nature Get 2013) and McIntosh et al (Arthritis Rheum 2017), setting r^2 at 0.80.We used existing genotyping data from 3,939 children with JIA and 14,412 healthy controls to identify SNPs that were present within open chromatin in multiple immune cell types and more common in children with JIA than the controls ($p < 0.05$) .We next sought to identify those SNPs most likely to occur within regulatory



Venn diagram showing the overlap of genes interacting with enhancers harboring candidate causal SNPs on JIA risk haplotypes. Results from Jurkat T cells, commonly used in models of T cell activation, are shown for comparison.

regions in both resting and activated human primary CD4+ T cells by overlaying the chosen SNPs (n=846) with bi-directional transcription initiation characteristic of non-coding regulatory regions detected using dREG to analyze precision run-on sequencing (PROseq) data. Finally, we used MicroC to detect gene promoters interacting with the regulatory regions harboring the candidate causal SNPs.

Results: We identified 138 SNPs situated within dREG peaks in resting CD4+ T cells, 119 in PMA-stimulated CD4+ T cells (2 hr stimulation), and 150 that occurred in dREG peaks in CD3-CD28-IL2-stimulated CD4+ T cells (7 days' stimulation). We identified n=74 SNPs that appeared in dREG peaks under all 3 conditions, suggesting that their biological effects are exerted on both resting and activated cells, while those unique to activation phases (20 in resting cells, 20 in PMA-activated cells, and 39 in CD3-CD28-IL2-activated cells) may exert their effects only under specific biological conditions. MicroC studies identified n=41 genes that interacted with enhancers harboring the candidate causal SNPs in resting CD4+ T cells, n=39 in CD4+T cells activated with ionomycin and PMA (30 min) and n=38 in CD4+ T cells activated with CD3/CD28/IL2 (7 days).There was considerable overlap in these gene sets, as shown in the figure, while other gene-enhancer interactions were cell-state-specific.

Conclusion: We demonstrate that SNPs on JIA risk haplotypes that are seen more frequently in patients than controls can be further filtered by their presence within functional regulatory elements (detected by PROseq) in primary human CD4+ T cells. Some of these regulatory elements are unique to the activation state of the cells, supporting the idea that some SNPs may exert their biological effects only in specific biological contexts. Finally, we demonstrate that newer methods for querying 3D chromatin structures (e.g., MicroC) can crisply identify the genes influenced by regulatory elements harboring these SNPs, and, thus, the immunological processes impacted by disease-driving genetic variants.

Disclosure: E. Haley: None; **g. Barshad**: None; **K. Jiang**: None; **A. He**: None; **E. Rice**: None; **M. Sudman**: None; **S. Thompson**: None; **E. Crinzi**: None; **C. Danko**: None; **J. Jarvis**: None.

Abstract Number: 0037

New Histological Approach in Spatial Transcriptomics Implicates Glandular Cell Involvement in Pathophysiology of Sjögren's Disease

Paulina Czarnota[1], **Rick Wilbrink**[2], Bhuwan Khatri[1], Anna Stolarczyk[1], Cherilyn Pritchett Frazee[1], Chuang Li[1], Caleb Marlin[1], Kyle Wright[3], Kandice Tessneer[1], Lida Radfar[4], Judith James[1], Robert Scofield[1], Indra Adrianto[5], Astrid Rasmussen[1], Joel Guthridge[1], A. Darise Farris[1] and Christopher Lessard[1], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]University Medical Center Groningen, Groningen, Netherlands, [3]University of Oklahoma Health Sciences Center, Oklahoma City, OK, [4]University of Oklahoma College of Dentistry, Oklahoma City, OK, [5]Henry Ford Health, Detroit, MI

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: 10X Visium spatial transcriptomics evaluates gene expression in a 50μm tile coordinate of a sectioned tissue, yielding heterogeneous cell sampling. Spatial PCA algorithm was developed using homogenous tissue types with distinct boundaries to identify like tissue regions and determine the cellular context of spatial coordinates for spatial transcriptomic analyses [1]. However, it is less effective at differentiating like tiles from heterogenous tissue types such as the minor salivary gland; the target tissue of Sjögren's disease (SjD). This study introduces a novel approach, HistoPCA, that connects pathologically annotated and segmented images with spatial coordinates derived from minor salivary gland biopsies to group like tiles based on similar cellularity.

Methods: Histopathological images of minor salivary gland biopsies were annotated based on tissue type (fibrosis, glandular, inflammatory, fat), then annotations were combined with spatial coordinates using the novel HistoPCA algorithm. Image segmentation was used to obtain cell numbers in tiles and combined with pseudo-color percentages associated with certain tissue types to perform unsupervised KMeans clustering. Differential expression (DE) between SjD cases and controls was analyzed using pseudo-bulk gene expression, then analyzed by Ingenuity Pathway Analysis (IPA).

Results: HistoPCA and UMAP with KMeans clustering outperformed Spatial PCA (Adjusted Rand Index (ARI) of 0.52 vs 0.51), identifying four distinct clusters in minor salivary gland. Despite distinct features such as inflammation in Cluster 1 (21% inflammatory, 32% fibrosis, and 23% glandular tiles) and increased glandular involvement in Cluster 3 (0% inflammatory, 48% fibrosis, and 41% glandular tiles), DE and pathway analyses showed similar patterns of dysregulation in SjD cases (n=28) compared to controls (n=16). As a positive control, elevated interferon signatures were observed in all SjD cases and anti-Ro positive SjD cases (n=19) compared to controls across all clusters [2]. Additional immune pathways (T cell receptor, Th1, Th2, and IL-4 signaling, etc.) were also upregulated in SjD cases while CTLA4, IL-10, and IL-12 signaling pathways were downregulated.

Conclusion: HistoPCA is a novel approach that uses histopathological and segmentation data to successfully group like tiles from spatial transcriptomic analysis of heterogeneous tissues, e.g., minor salivary gland. Cluster annotation of HistoPCs (principal components), followed by pseudo-bulk DE and pathway analyses identified four clusters with dysregulated immune pathways in SjD.Further, dysregulation of immune pathways in Cluster 3, which was devoid of tiles associated with inflammation, indicates potential glandular involvement in SjD pathogenesis. Future analyses within spatial contexts will provide additional insights into the role of different cell/tissue types in SjD pathobiology of the salivary gland.

References:

[1] Shang L, et al. Nat Commun. (2022); 13:7203
[2] Hjelmervik TOR, et al. Arthritis Rheum (2005);52(5):1534-44

Disclosure: P. Czarnota: None; **R. Wilbrink**: None; **B. Khatri**: None; **A. Stolarczyk**: None; **C. Pritchett Frazee**: None; **C. Li**: None; **C. Marlin**: None; **K. Wright**: Scopio Labs, 1; **K. Tessneer**: None; **L. Radfar**: None; **J. James**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 2, Novartis, 2, Progentec Biosciences, 5; **R. Scofield**: Merck/MSD, 2, Pfizer, 1; **I. Adrianto**: None; **A. Rasmussen**: None; **J. Guthridge**: None; **A. Farris**: Janssen Research and Development, LLC, 5; **C. Lessard**: Janssen, 5.

Abstract Number: 0038

Specific Binding of Uric Acid to NDFIP1 Associates with Hyperuricemia-induced Ferroptosis

Qiunan Zhu[1], Hiroshi Arakawa[2], Yoshiyuki Shirasaka[2] and Ikumi Tamai[2], [1]Kanazawa University, Kanazawa, Japan, [2]Faculty of Pharmaceutical Sciences, Kanazawa University, Kanazawa, Japan

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Hyperuricemia (HU) is reported as a risk factor for gout and associates with diverse diseases, including ulcerative colitis (UC), while its mechanism remains unclear. In this study, we aim to explain UA effect based on the hypothesis that UA-binding proteins function as UA sensors and regulate various physiological processes.

Methods: UA-binding proteins were detected by proteomics following a pull-down assay with UA-binding beads and human colorectal Caco-2 cells homogenate. Specific binding of these candidate binding proteins was confirmed by binding assay with *in vitro* synthesized proteins using cell-free method. UA was exposed to the cells after filtering by 0.2 μm filter to avoid UA crystals. The cellular levels of iron, ROS, and lipid peroxidation (MDA) were measured with FerroOrange, CellROX®, MDA assay kit, respectively.

Results: Six proteins were found to be potential to bind to UA by pull-down assay. Specific binding of UA to these proteins was confirmed by binding assay using *in vitro* synthesized proteins, where NDFIP1 showed the highest binding rate (Fig. 1). Binding domain was narrowed down by binding assay with UA-binding beads and *in vitro* synthesized partial NDFIP1 protein. To find the binding sites, docking simulation of AlphaFold2-predicted NDFIP1 and UA was carried out. As a result, intracellular C-terminal sequences of NDFIP1 was suggested as UA-binding region.

Exposing UA to Caco-2 cells caused cell death and the viability decreased with increasing UA concentration (Fig. 2A). In addition, as UA significantly increased intracellular iron, ROS and MDA level (Fig. 2B-D), suggesting that high UA level could induce ferroptosis, which is associated with UC.

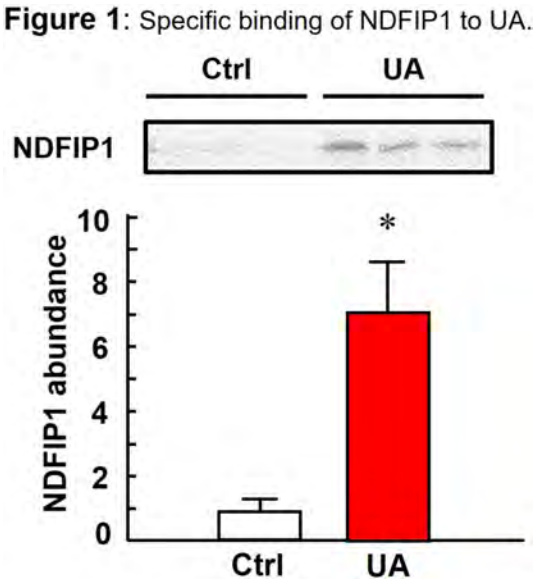


Figure 1. Specific binding of NDFIP1 to UA. NDFIP1 bound to UA-binding beads was approximately 7 times as much as that of control.

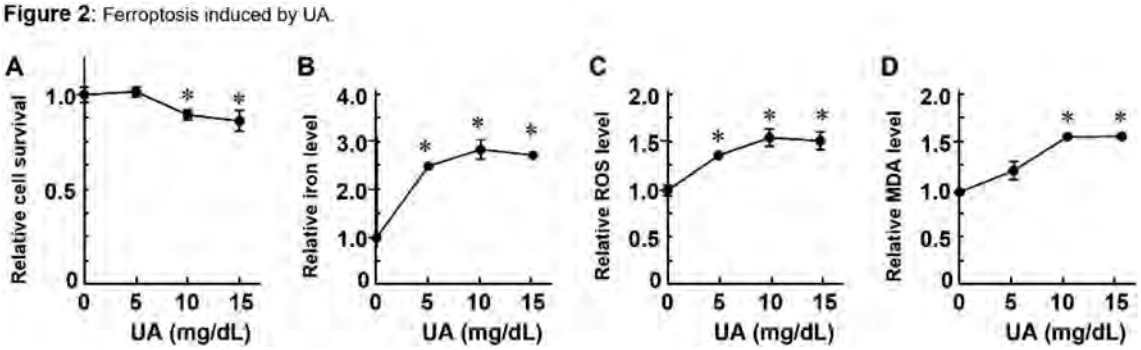


Figure 2. Ferroptosis induced by UA. Exposing UA to Caco-2 cells caused cell death (A) and led to higher intracellular iron (B), ROS (C), and MDA (D) levels.

Figure 3: Effect of UA on DMT1 expression.

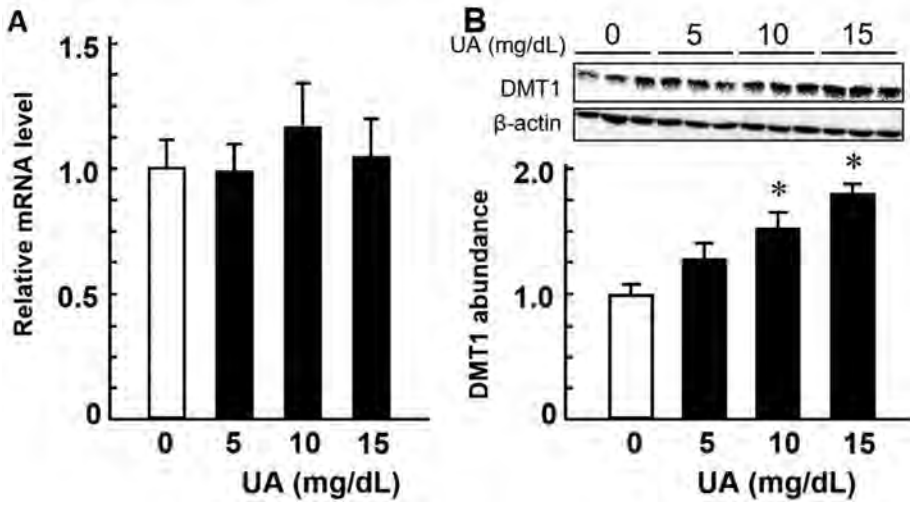


Figure 3. Effect of UA on DMT1 expression. Exposing UA to Caco-2 cells increased DMT1 protein expression significantly (B), but not the mRNA level (A).

Since NDFIP1 is known as a ubiquitin ligase adaptor and promotes ubiquitination of DMT1 (divalent metal transporter 1, an iron transporter), mRNA and protein expressions of DMT1 were measured as Fig. 3, where UA increased DMT1 protein significantly but not mRNA level.

Exposure of DMT1 blocker 2 reduced UA-induced ferroptosis. Furthermore, knockdown of NDFIP1 by transfecting siRNA lowered the difference of ferroptosis level between UA exposed and control groups.

Conclusion: NDFIP1 was found as UA binding protein and was suggested as a UA sensor that regulates HU-induced ferroptosis by modulating DMT1.

Disclosure: Q. Zhu: None; **H. Arakawa**: None; **Y. Shirasaka**: None; **I. Tamai**: None.

Abstract Number: 0039

Enrichment of Rare Variants of Hemophagocytic Lymphohistiocytosis Genes in Systemic Juvenile Idiopathic Arthritis

Mariana Correia Marques[1], Danielle Rubin[1], Emily Shuldiner[2], Mallika Datta[1], Elizabeth Schmitz[1], Alexei Grom[3], Dirk Foell[4], Marco Gattorno[5], John Bohnsack[6], Rae Yeung[7], Sampath Prahalad[8], Elizabeth Mellins[9], Jordi Anton Lopez[10], Claudio Len[11], Sheila Oliveira[12], Patricia Woo[13], Seza Ozen[14], INCHARGE Consortium[1], Zuoming Deng[15] and Michael Ombrello[1], [1]National Institute of Arthritis & Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [2]Department of Biology, Stanford University, Stanford, CA, [3]Division of Rheumatology, Cincinnati Children`s Hospital, Cincinnati, OH, [4]University Hospital Münster, Münster, Germany, [5]UOC Reumatologia e Malattie Autoinfiammatorie, Genoa, Italy, [6]University of Utah, Salt Lake City, UT, [7]The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada, [8]Emory University School of Medicine, Children's Pediatric Institute, Atlanta, GA, [9]Stanford University, Stanford, CA, [10]Pediatric Rheumatology Department, Hospital Sant Joan e Deu, Barcelona University, Barcelona, Spain, [11]São Paulo Federal University, São Paulo, Brazil, [12]Universidade Federal do Rio de Janeiro, Rio De Janeiro, Brazil, [13]University College London, London, United Kingdom, [14]Hacettepe University Medical Faculty, Ankara, Turkey, [15]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD

SESSION INFORMATION

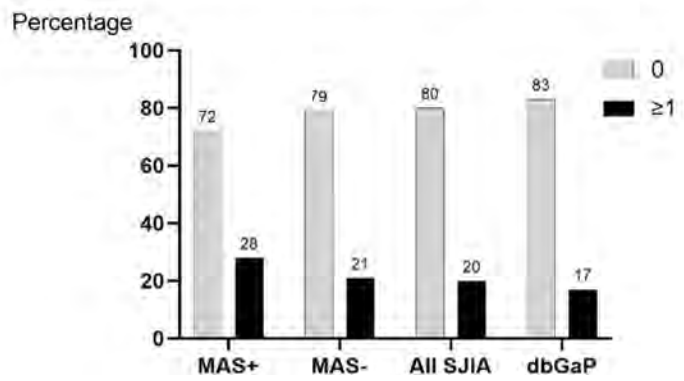
Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic juvenile idiopathic arthritis (sJIA) is a complex inflammatory condition of childhood. It can be complicated by macrophage activation syndrome (MAS), a secondary form of hemophagocytic lymphohistiocytosis (HLH). Studies have identified an enrichment of HLH variants in sJIA patients with MAS compared with those without it. However, the role of these variants in sJIA in general is not known. The goal of our study is to determine whether rare variation in HLH genes contributes to the risk of developing sJIA.

Methods: Targeted sequencing of HLH genes (*LYST, PRF1, RAB27A, STX11, STXBP2, UNC13D*) was performed in sJIA subjects with European ancestry from the International Childhood Arthritis Genetics Consortium cohort using Illumina Nextera Custom Capture Assays and Illumina sequencers. Data processing and quality control were performed using a Genome Analysis Toolkit-based pipeline. Variants were filtered to retain high-quality, protein-altering variation on Ensembl canonical transcripts and stratified by minor allele frequencies (MAF). Healthy control exomes were extracted from the database for genotypes and phenotypes (accession number: phs000280.v8.p2). Rare variant association testing (RVT) was done with sequence kernel association test (SKAT). A burden test was also performed with the SKAT package. Significance was defined as $p < 0.05$ after 100,000 permutations.

Results: Sequencing data from 524 sJIA cases were jointly called and harmonized with exome-derived target data from 2952 controls. Subjects were excluded if they had a monogenic disease (n=6), dissimilar genetic ancestry (39 cases, 22 controls), or > 10% missingness (6 controls). Analysis of the remaining 479 sJIA cases revealed 71 rare HLH gene variants, including recurrent ultra-rare (MAF < 0.001) variants in *LYST* and *UNC13D*.We also observed 2 people in the sJIA cohort who had the *STXBP2* mutation Ala429Val, which has been associated with secondary HLH and severe Covid. RVT comparing the variant distributions of sJIA cases and controls revealed a significant association with rare (MAF < 0.01) variants of *STXBP2* (p=0.019) and ultra-rare variants of *STXBP2* (p=0.006) and *UNC13D* (p=0.045). Sub-analysis of patients with known MAS status showed that the distribution of rare variants of *UNC13D* was different in 32 sJIA patients with MAS than in 90 without it (p=0.0047) or 2930 controls (p=0.03). There was an increased frequency of individuals with ≥1 rare HLH variants in all sJIA groups compared to the controls (Figure 1), with sJIA patients with a history of MAS having the highest frequency. Similarly, the full cohort (p=0.009) and those with MAS (p=0.025) had a higher burden of HLH variants than controls, whereas those without MAS did not (p=0.12).

Figure 1. Percentages of Individuals with Rare HLH Variants in Each Subgroup



HLH: hemophagocytic lymphohistiocytosis, MAS: macrophage activation syndrome, sJIA: systemic juvenile idiopathic arthritis, dbGaP: database of Genotypes and Phenotypes

Conclusion: We found that the association of HLH variants with sJIA is not purely linked to MAS. *STXBP2* was significantly associated with sJIA while showing no association with MAS. Moreover, the frequency of HLH gene variants trended higher in MAS-negative sJIA than in control subjects. As seen in prior studies, *UNC13D* was associated with MAS. Taken together, this suggests that HLH variants may play a role in the pathophysiology of sJIA in general, and not only in MAS.

Disclosure: M. Correia Marques: None; **D. Rubin**: None; **E. Shuldiner**: None; **M. Datta**: None; **E. Schmitz**: None; **A. Grom**: Novartis, 2, 5, Pfizer, 2, 5, Sobi, 2, 5; **D. Foell**: Boehringer, 6, Novartis, 5, 6, Sobi, 5, 6; **M. Gattorno**: Novartis, 5, 6, Sobi, 5, 6; **J. Bohnsack**: AbbVie/Abbott, 5, Janssen, 5, Sobi, 5; **R. Yeung**: Pfizer, 6; **S. Prahalad**: None; **E. Mellins**: Codexis, 5, Genentech, 5, GlaxoSmithKlein(GSK), 5; **J. Anton Lopez**: None; **C. Len**: None; **S. Oliveira**: None; **P. Woo**: None; **S. Ozen**: None; **I. Consortium**: None; **Z. Deng**: None; **M. Ombrello**: None.

Abstract Number: 0039.5

Cytokine-induced Transcriptome Modification Elucidates the Similarity and Dissimilarity Across 10 Immune-related Diseases

Haruka Takahashi[1], Hiroaki Hatano[2], Masahiro Nakano[3], Haruka Tsuchiya[4], Mineto Ota[4], Tomohisa Okamura[5], Keishi Fujio[4] and Kazuyoshi Ishigaki[6], [1]Laboratory for Human Immunogenetics, RIKEN Center for Integrative Medical Sciences and Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, [2]Laboratory for Human Immunogenetics, RIKEN Center for Integrative Medical Sciences, Tokyo, Japan, [3]Laboratory for Autoimmune Diseases, RIKEN Center for Integrative Medical Sciences, Tokyo, Japan, [4]Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, [5]Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo and Department of Functional Genomics and Immunological Diseases, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, [6]RIKEN, Tokyo, Japan

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Abnormal cytokine regulation is the fundamental pathology of immune-mediated diseases (IMDs). Clinical transcriptome data has a potential to monitor real-time cytokine pathway activities of each IMD patient and guide treatment choices. However, multiple confounders including immunosuppressive therapies and experimental batch effects obscures the biologically relevant signals underlying clinical transcriptome data. The aim of this study is i) to establish an analytical strategy to accurately quantify cytokine pathway activities excluding the confounder effects and ii) elucidate the similarity and dissimilarity across 10 immune-related diseases by applying our strategy to the clinical transcriptome database.

Methods: We utilized the ImmuNexUT database, the largest open-access database of clinical transcriptome data with 28 FACS-sorted immune cell subsets obtained from 10 IMDs: SLE, idiopathic inflammatory myopathy (IIM), SSc, MCTD, SS, RA, Behcet's disease (BD), adult-onset Still's disease (AOSD), ANCA-associated vasculitis (AAV), and Takayasu arteritis (TAK) (Figure 1). Using the combination of supervised and unsupervised approaches, we learned the cytokine-induced transcriptome alterations from a large-scale in-vitro cultured fibroblast experiments stimulated by eight cytokines: IFN-α, IFN-γ, TNF-α, IL-1β, IL-6/sIL-6R, IL-17, IL-18 and TGF-β1 (n=506 samples in total). We then transferred the knowledge to the clinical transcriptome data. To mitigate the different statistical power due to unbalanced sample sizes across 10 IMDs, we applied the multivariate adaptive shrinkage approach.

Results: We first took an unsupervised approach and conducted the principal component analysis (PCA) of the cytokine-stimulated fibroblast datasets to learn the transcriptome axes reflecting multiple cytokine signatures. We then projected clinical transcriptome data onto the PC space and confirmed that IMDs were separated by cytokine signatures, with a pronounced shift in SLE. We next took a supervised approach and detected the IMD- and cytokine-related transcriptome signatures from both datasets. By jointly analyzing both signatures simultaneously, we successfully characterized the transcriptome similarity and dissimilarity across 10 immune-related diseases from a viewpoint of cytokine-related signatures. The cytokine signatures grouped IMDs into two clusters: the autoimmune diseases (MCTD, SLE, IIM, SSc, RA and SS) and autoinflammatory diseases (BD, AAV, and TAK).

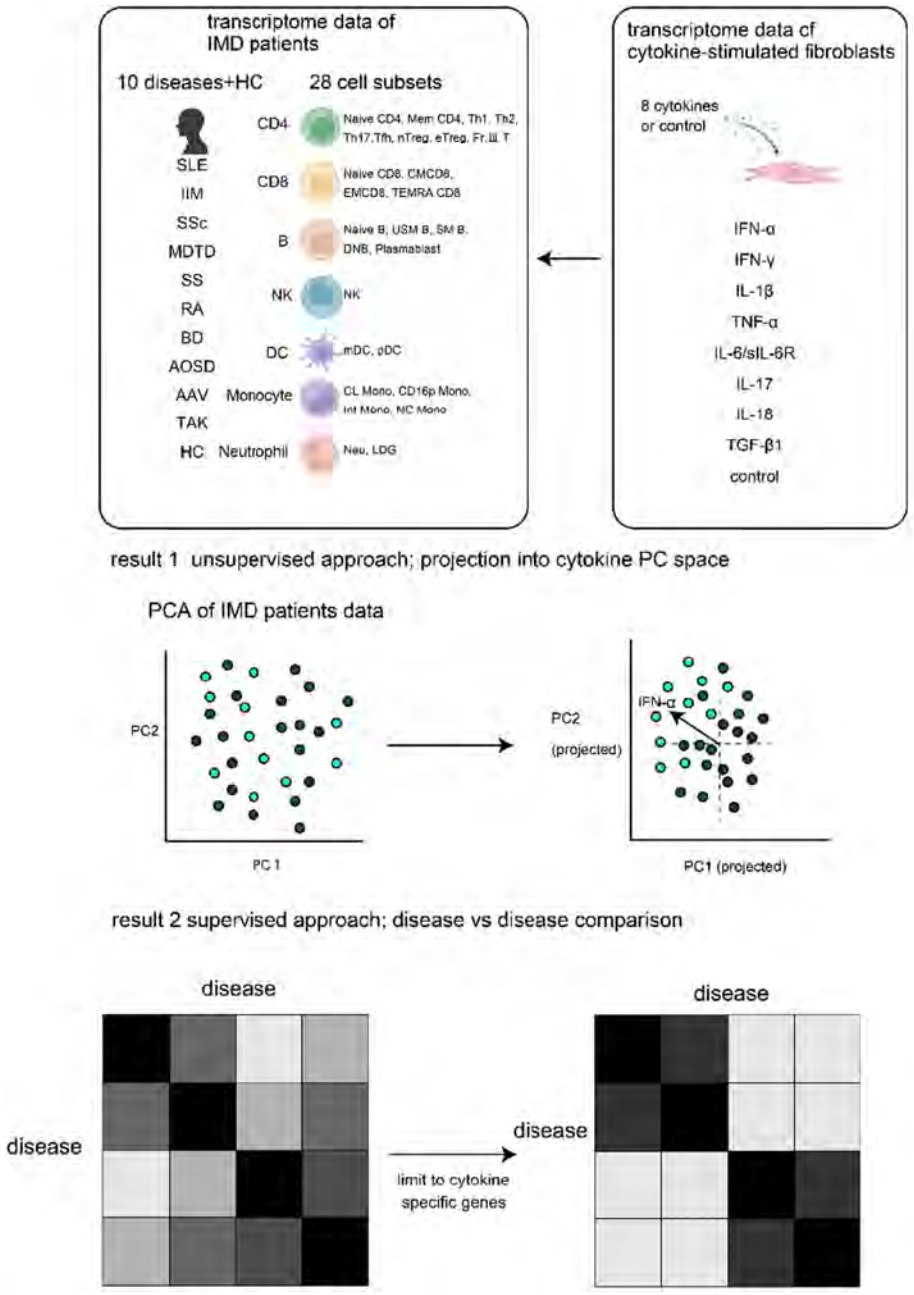


Figure 1. The overview of datasets and analytical strategies. We analyzed transcriptome data of 10 immune-related diseases using the knowledge obtained from transcriptome data of cytokine stimulated fibroblasts. We utilized both unsupervised and supervised approaches.

Conclusion: Our new analytical strategy successfully detected cytokine-related transcriptome characteristics of 10 IMDs, which would be a foundation to elucidate the IMD pathology.

Disclosure: H. Takahashi: None; **H. Hatano**: None; **M. Nakano**: None; **H. Tsuchiya**: None; **M. Ota**: Chugai, 12, MO belonged to the Social Cooperation Program, Department of functional genomics and immunological diseases, supported by Chugai Pharmaceu; **T. Okamura**: Chugai Pharmaceutical., 12, belong to the Social Cooperation Program, Department of Functional Genomics and Immunological Diseases, supported by Chugai Pharmaceutical.; **K. Fujio**: AbbVie/Abbott, 6, Asahi Kasei, 5, 6, Astellas, 6, AstraZeneca, 6, Ayumi, 6, Bristol-Myers Squibb(BMS), 5, 6, Chugai Pharmaceutical., 5, 6, Daiichi-Sankyo, 6, Eisai, 5, 6, Eli Lilly, 5, 6, Janssen, 6, Novartis, 6, Ono, 6, Pfizer, 6, Sanofi, 6, Tanabe Mitsubishi, 5, 6, Tsumura, 5; **K. Ishigaki**: None.

Abstract Number: 0040

Non-canonical NF-κB Signalling Is Required for Extrathymic AIRE Expression and Immunoregulatory Molecules in Cells of the Dendritic Lineage

Guus van Laar[1], Leonie Huitema[1], Boy helder[1], Joanna Fergusson[1], Hergen Spits[1], Jan Piet van Hamburg[1] and Sander Tas[2], [1]Amsterdam University Medical Centers, Amsterdam, Netherlands, [2]Amsterdam UMC, locatie AMC, Utrecht, Netherlands

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: (0040–0064) Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The transcription factor Autoimmune Regulator (AIRE) is crucial for the establishment of central tolerance in the thymus. Recently, peripheral $CD45^+$ extrathymic AIRE-expressing cells (eTACs) have been identified, which share features with antigen presenting cells, such as dendritic cells (DCs). Although, nuclear factor (NF)-κB signaling has been implicated in thymic AIRE expression, stimuli and pathways that induce extrathymic AIRE expression are hitherto unknown. We aimed to unravel the molecular mechanisms underlying the regulation of extrathymic AIRE expression in eTACs and DCs.

Methods: Confocal imaging was performed on secondary lymphoid tissues, including tonsils and lymph nodes to identify and characterize eTACs. Second, we employed a novel sorting strategy to isolate DCs and eTACs from tonsil tissue for RNA-sequencing (seq) to generate transcription profiles. To study the regulation of AIRE, monocyte-derived DCs (moDCs), DCs and eTACs were stimulated by anti-CD40 to induce NF-κB activation. Gene transcription and protein expression levels of AIRE, indoleamine-2,3-dioxygenase (IDO), programmed death ligand-1 (PD-L1) and non-canonical NF-κB signalling components were detected by real time-PCR, flow cytometry, Western blot and/or confocal microscopy. Activation of NF-κB signalling was modulated by siRNA-mediated silencing or using a small molecule inhibitor (SMI) of activating kinases.

Results: In human tonsil and lymph node tissue $AIRE^+$ cells were identified, which displayed DC characteristics, including MHCII and CD40, but were relatively low for CD11c. Bioinformatic analysis on RNA-seq derived gene expression profiles of sorted eTACs and DCs from tonsil tissue revealed an increased expression of AIRE and immunoregulatorygenes, including IDO and PD-L1 in eTACs compared to DCs. In addition, the expression of genes implicated in non-canonical NF-κB signaling, including NIK and CD40, were significantly higher in eTACs compared to DCs. CD40 stimulation has been shown to

be critical for IDO production by moDCs. CD40-stimulation of moDCs resulted in the activation of non-canonical NF-κB signaling, which was accompanied by upregulation of AIRE, IDO and PD-L1 expression. Interestingly, the induction of AIRE expression was abrogated by siRNA-mediated silencing of NF-κB-inducing kinase (NIK) . Likewise, CD40 stimulation of sorted eTACs and DCs resulted elevated AIRE, IDO and PD-L1 expression levels. Subsequently, modulation of NIK via an SMI resulted in the abrogation of AIRE, IDO and PD-L1 expression in eTACs and DCs. In contrast, specific modulation of canonical NF-κB signaling had no significant effects on AIRE, IDO and PD-L1 expression in CD40-stimulated eTACs and DCs.

Conclusion: Collectively, our data demonstrate that AIRE expression, as well as the expression of the immunoregulatory molecules IDO and PD-L1 in eTACs and DCs can be induced through CD40 stimulation in a non-canonical NF-κB signaling dependent manner. These findings concerning the regulation of AIRE and immunoregulatory molecule expression may point towards a novel role of eTACs in peripheral tolerance.

Disclosure: G. van Laar: None; **L. Huitema**: None; **B. helder**: None; **J. Fergusson**: None; **H. Spits**: None; **J. van Hamburg**: None; **S. Tas**: None.

Abstract Number: 0041

Interactions Between Synovial Fibroblasts and Macrophages: Implications for Tissue Remodeling in Chronic Inflammatory Diseases and Macrophage Differentiation in Response to the Immune Microenvironment

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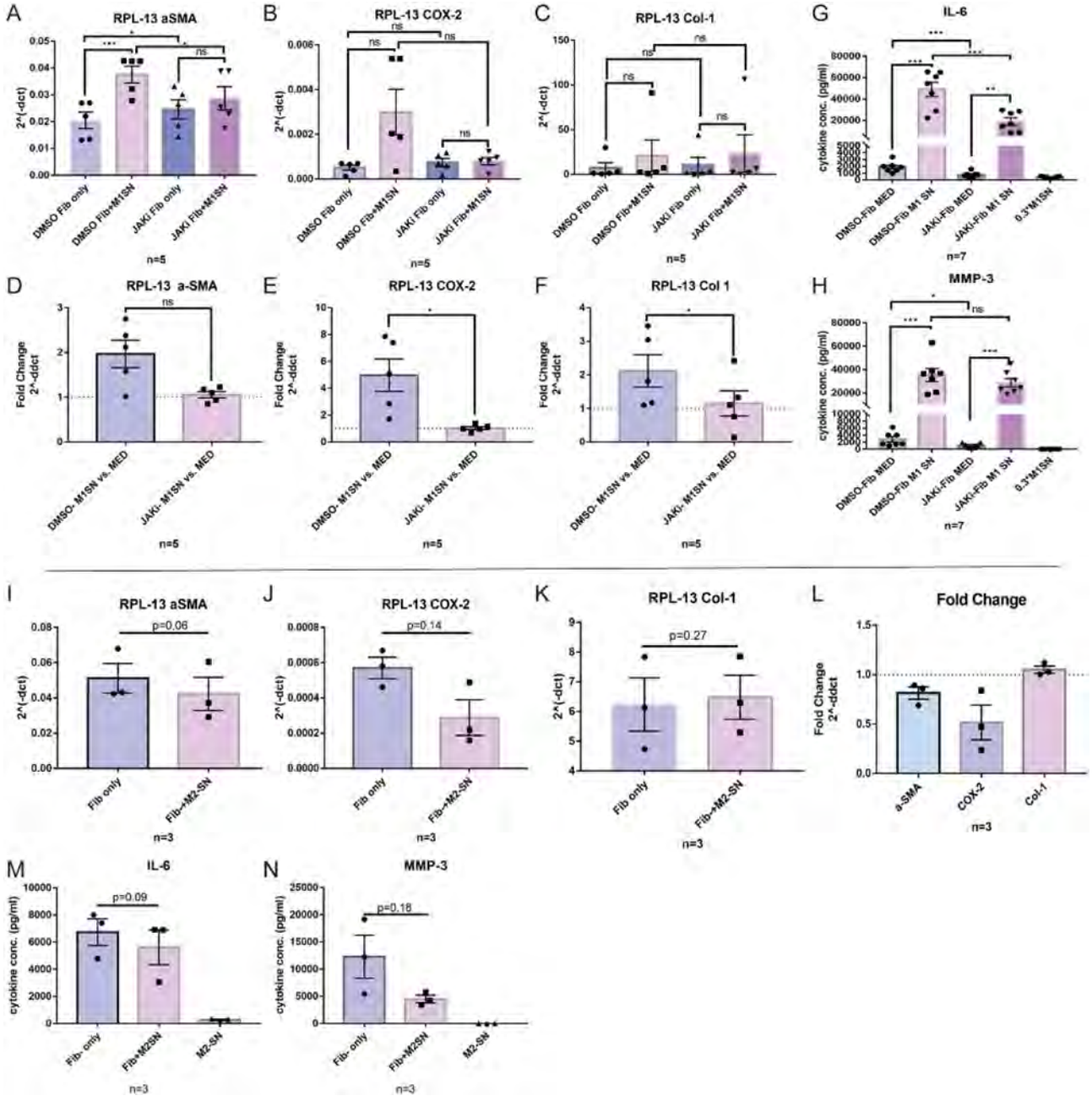
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: (0040–0064) Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

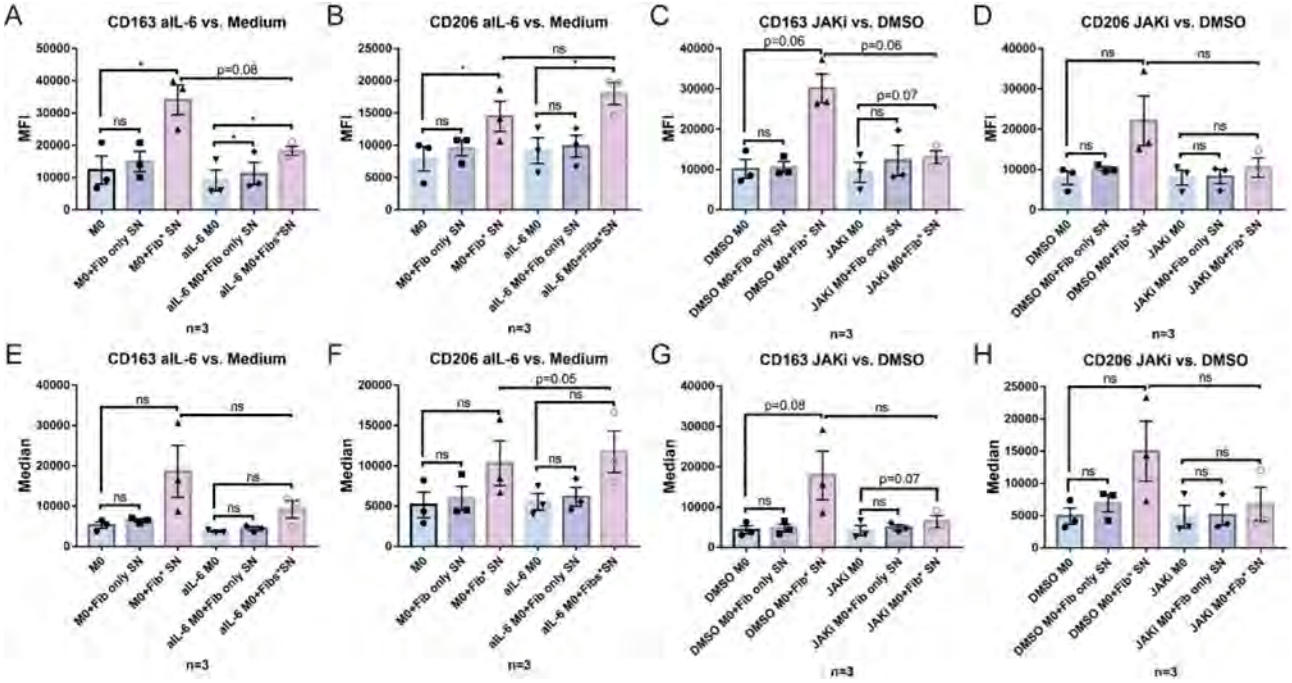
Background/Purpose: Activated macrophages (Mph) can be subdivided in at least 2 major subgroups according to their polarization into classical pro-(M1-Mph) or anti-inflammatory (M2-Mph) subtypes. Together with fibroblasts they are considered key mediators of tissue remodeling in chronic rheumatic diseases. Mph possess high plasticity and it is suggested that an imbalance of M1/M2 Mph polarization might contribute to aberrant activation of fibroblasts (Fib) during tissue remodeling and destruction, like in rheumatoid arthritis (RA). However, the causes of disrupted M1/M2 homeostasis are still not clear. We conducted a project in order to investigate the interactions between synovial fibroblasts and differentiating and polarized macrophages in vitro.

Methods: Macrophages were differentiated from purified monocytes out of peripheral blood from healthy donors and polarized into M1 and M2 Mph over several days. Expression of CD80 TNFa and IL-12 were considered representative for M1 and expression of CD163, CD206 and IL-10 for M2. Fib isolated from osteoarthritis (OA) patients at passage 4-8 were co-cultured with cell culture supernatant (SN) of polarized M1/M2-Mph. Similarly, Fb-SN was added to differentiating Mph. For some experiments Fib were pre-stimulated with TNFa/IL1b to induce a proinflammatory RA-like phenotype. Fib read-out included cytokine and MMP secretion and transcriptional expression of key markers COX-2, COL-1 and aSMA.

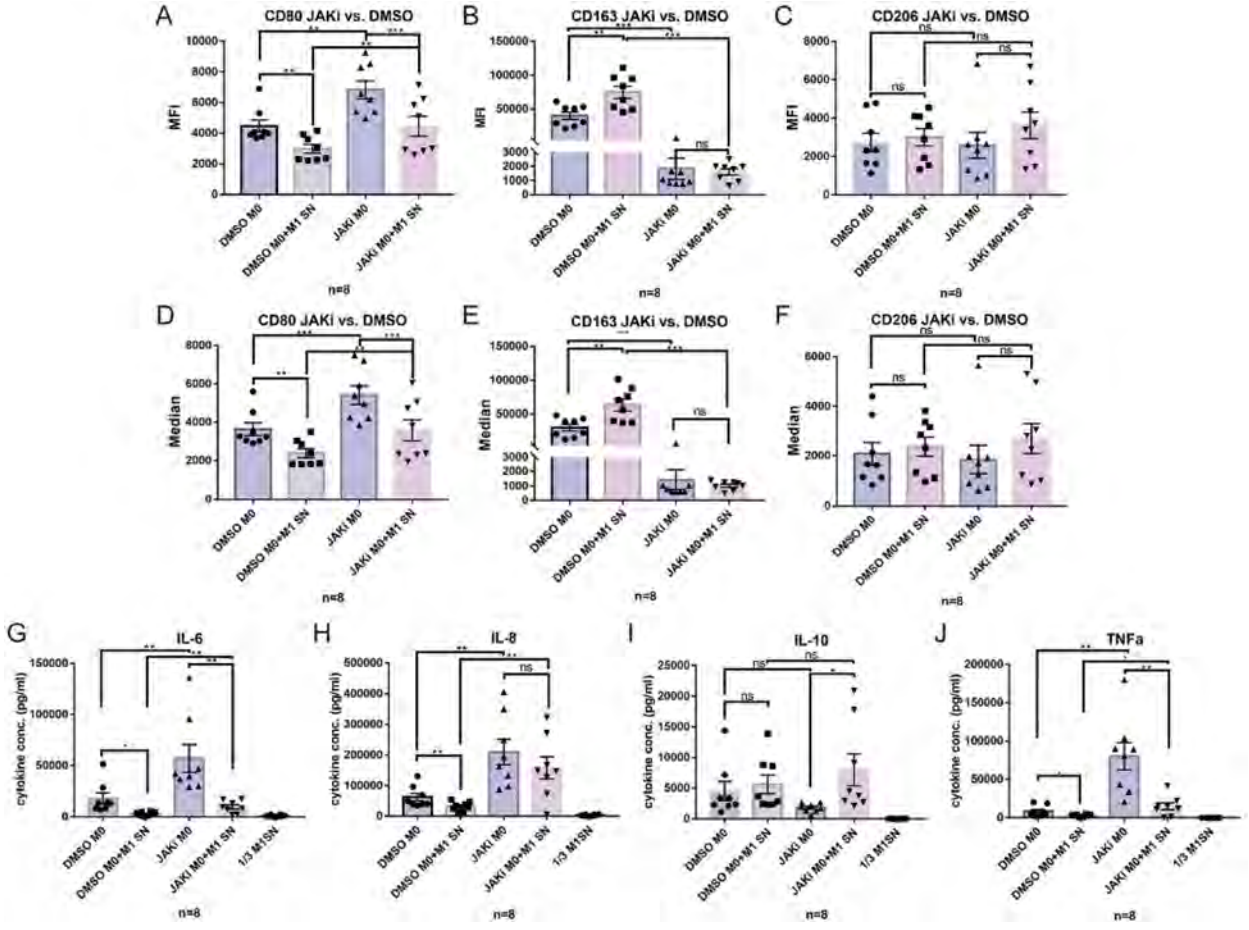
Results: M1-SN had both pro-inflammatory and pro-fibrotic effects on Fib, as evidenced by upregulation of COX-2, aSMA and COL-1. In addition, M1-SN induced a significant upregulation of IL-6 and MMP-3 in Fib. These effects were significantly suppressed in presence of the selective JAK inhibitor (JAKi) Upadacitinib. M2-SN slightly downregulated IL-6, MMP-3, COX-2 and aSMA expression. SN from TNFa/IL-1b pre-stimulated Fib induced a polarization of undifferentiated M0 Mph towards the M2 phenotype as evidenced by expression of high levels of CD163, CD206 and IL-10. Addition of an anti-IL-6 receptor Ab (tocilizumab) and JAKi both inhibited development of this anti-inflammatory phenotype. M0 polarization towards M2 was also induced by M1-SN: CD163 was significantly upregulated by M1-SN, while IL-6, IL-8 and TNFa were evidently downregulated by M1-SN. On the other hand, JAKi forcefully suppressed the effects of M1-SN on M0 Mph.



The Effects of M1/M2 Mph Supernatant on Synovial Fibroblasts in Vitro



The Effects of TNFa/IL1b Pre-stimulated Synovial Fibroblasts Supernatant on M0 Mph in Vitro



The Effects of M1 Mph Supernatant on M0 Mph in Vitro

Conclusion: Polarized Mph have s strong modulatory effect on the Fibs. On the other hand, pre-activated pro-inflammatory Fib and polarized M1 themselves have also a significant effect on Mph polarization, supporting M2 differentiation. JAKi abrogate proinflammatory and profibrotic responses in Fib, while JAKi and anti-IL-6 also inhibited differentiation of Mph into M2, thereby pointing to a new functional aspect of this Immunomodulator.

Disclosure: J. Li: None; **Y. Cai**: None; **X. Guan**: None; **M. Ewald**: None; **L. Tykocinski**: None; **H. Lorenz**: None; **T. Tretter**: None.

Abstract Number: 0042

Effect of the Inflammatory Microenvironment Induced by Monocytes on Fibroblasts and Modulatory Action of Human Dental Pulp Stem Cells

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: (0040–0064) Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The pathophysiology of viral infection is related to elevated levels of inflammatory cytokines therefore also of the excessive activation of monocytes. Prolonged inflammation can cause fibrosis, a process involving the accumulation of fibrous connective tissue and excess of extracellular matrix (ECM). The effector cells of fibrosis are myofibroblasts, an activated phenotype of fibroblasts. Monocytes can be modulated in their action by the release of paracrine factors from adult stem cells. Human dental pulp stem cells (hDPSCs) appear to be cells of low immunogenicity and easily isolated. The aim of this study was to observe the action exerted by monocytes in an inflammatory and profibrotic environment of viral induction and the effect on fibroblasts, as well as the modulating role of hDPSCs on monocytes and consequently on fibrosis.

Methods: An in vitro model of fibroinflammation was set up using human fibroblasts and monocytes isolated respectively from the skin and blood of healthy donors. Monocytes were activated with an imidazoquinoline (CL097) to simulate a viral infection and then characterized by cytofluorimetric analysis. Fibroblasts were treated with activated monocyte conditioned medium and the effect was verified by real-time PCR and western blot. Monocytes and hDPSCs were then co-cultured for 48 hours. Subsequently, the fibroblasts were treated for different times with the conditioned medium obtained from the co-cultures. The expression level of the main inflammatory mediators and profibrotic factors was determined by real-time PCR, western blot, immunofluorescence and ELISA immunoassay.

Results: Already after 48 hours of treatment with the conditioned medium of activated monocytes, a significant increase in the expression of proinflammatory cytokines (IFNγ, IL-6 and *IL-1β*), immunomodulatory genes (*CD55, COX2, CCL2* and *HLA-DRB1*), *Col1A1* and metalloproteinase 2 (*MMP2*) was observed in fibroblasts, while only prolonged exposure to the conditioned medium for seven days induced an increase in the other profibrotic genes *FN1*, *ICAM1* and *αSMA* (IFNγ $p < 0,05$, the others $p < 0,0001$) (FIG.1).

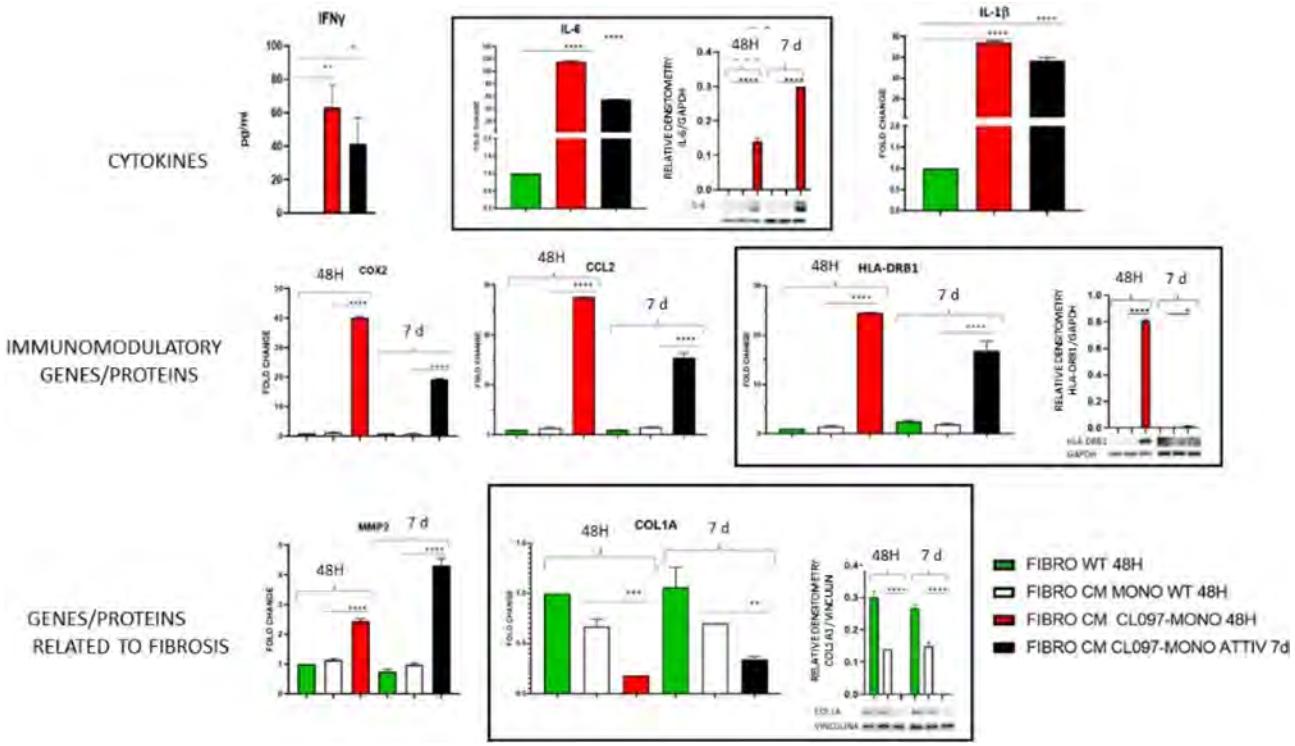

FIGURE 1 FIBROBLASTS TREATED FOR 48 HOURS OR 7 DAYS WITH CONDITIONED MEDIUM OF MONOCYTES ACTIVATED OR NOT WITH CL097

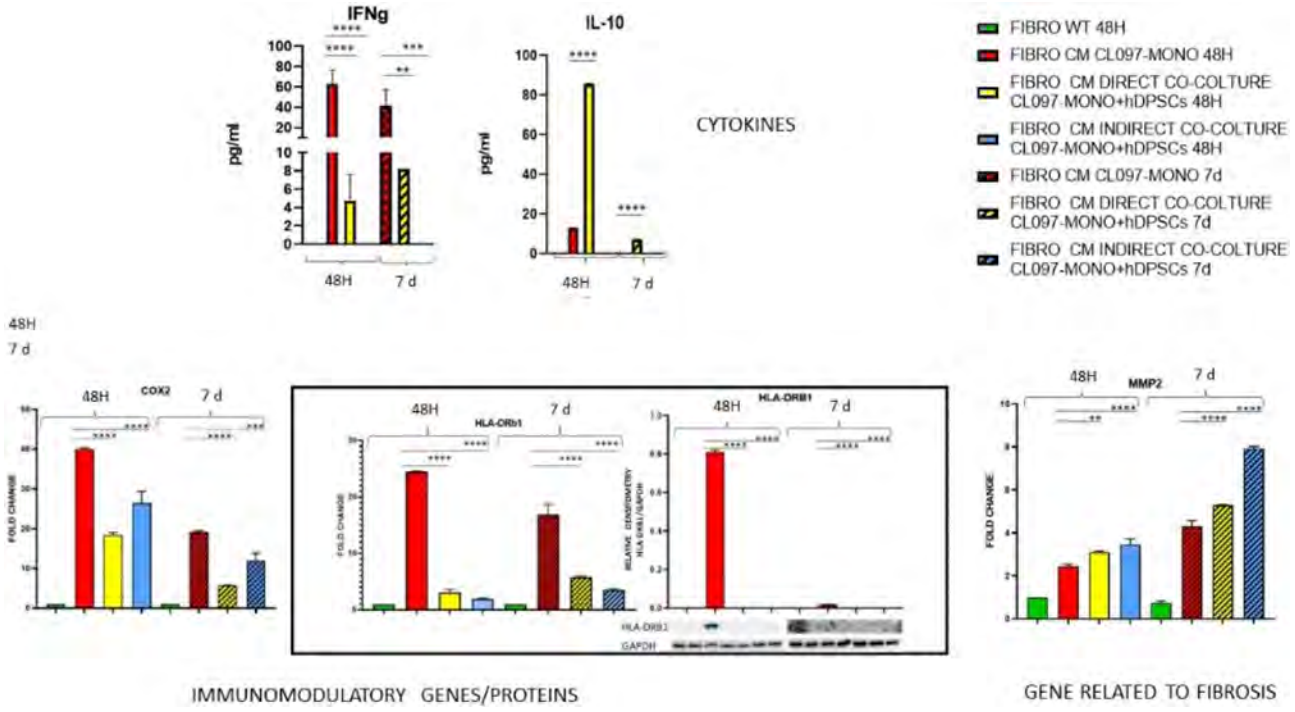

FIGURE 2 FIBROBLASTS TREATED FOR 48 HOURS OR 7 DAYS WITH CONDITIONED MEDIUM OBTAINED FROM DIRECT/INDIRECT CO-COLTURE OF CL097-MONOCYTES + hDPSCs

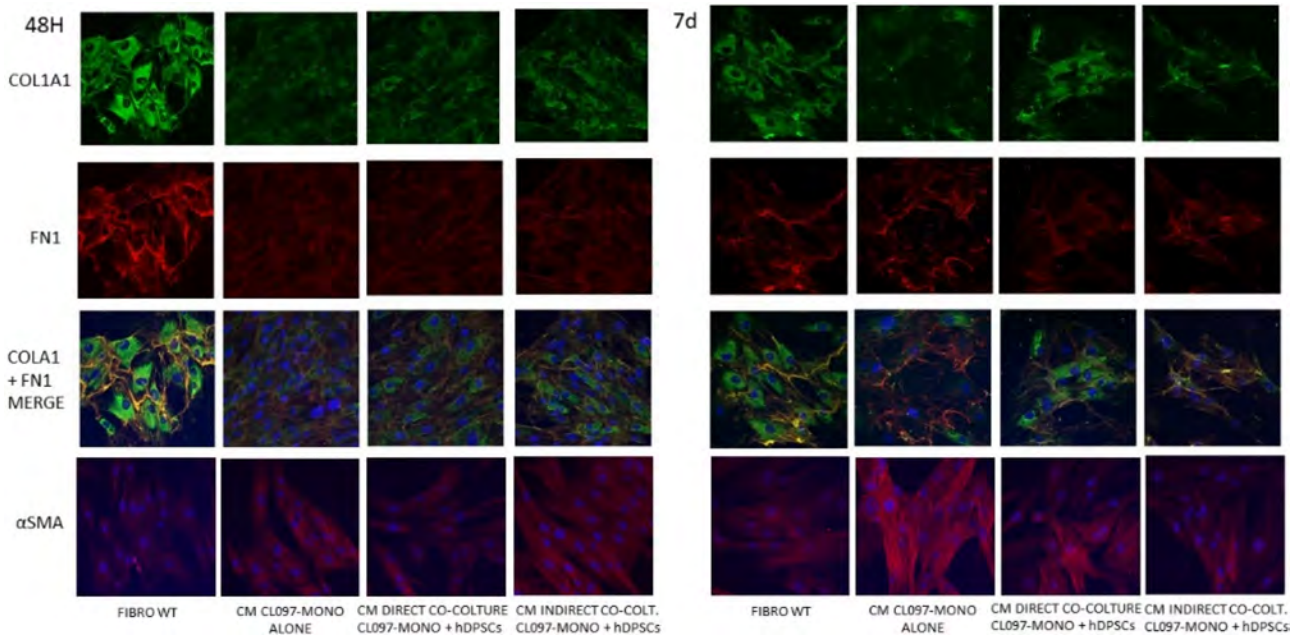

FIGURE 3 FIBROBLASTS TREATED FOR 48 HOURS OR 7 DAYS WITH CONDITIONED MEDIUM OF DIRECT/INDIRECT CO-COLTURE OF CL097-MONOCYTES + hDPSCs. COL1A1, FN1 AND αSMA PROTEINS WERE REVEALED IN FIBROBLASTS BY IMMUNOFLUORESCENCE

Treatment for 48 hours of fibroblasts with the conditioned medium of activated monocytes maintained in co-culture with hDPSCs induced a reduction in the expression of *COX2* ($p < 0{,}001$) and *HLA-DRB1* ($p < 0{,}0001$), an increase in the expression of *MMP2* ($p < 0{,}0001$) and *Col1A1* ($p < 0{,}05$), decrease in IFNγ ($p < 0{,}001$) and increase in IL-10 ($p < 0{,}0001$) secreted by fibroblasts, effect which persisted even after 7 days of treatment (FIG.2, 3).

Conclusion: The induction of a viral-type inflammatory environment by activated monocytes results in the early overexpression of proinflammatory cytokines and immunomodulatory genes and subsequently profibrotic genes in fibroblasts. The anti-inflammatory effects exerted by hDPSCs on monocytes are revealed in the indirect modulation of the immune response of fibroblasts by downregulation of HLA-DRB1, COX2, IFNγ and upregulation of IL-10. hDPSCs also exert antifibrotic and ECM remodeling effects by inhibition of αSMA and increased expression of Col1A1 and MMP2. The next step will be to evaluate the role of hDPSCs secretoma in inflammatory conditions to modulate the fibrotic process.

Disclosure: M. Maccaferri: None; **A. Pisciotta**: None; **G. Carnevale**: None; **C. Salvarani**: None; **E. PIGNATTI**: None.

Abstract Number: 0043

Assessing the Ability of Human Dental Pulp Stem Cells to Modulate the Macrophages Phenotype

Monia Maccaferri, Alessandra Pisciotta, Gianluca Carnevale, Carlo Salvarani and **ELISA PIGNATTI**, University of Modena and Reggio Emilia, Modena, Italy

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: (0040–0064) Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Macrophages have been found to have a key role in Rheumatoid Arthritis. Depending on the microenvironment, macrophages exist in a dynamic functional state which could be mainly grouped in a pro-inflammatory state (M1 macrophages) and an anti-inflammatory state (M2 macrophages). *In vitro*, these conditions can approximately be reproduced by means of cytokines such as lipopolysaccharide (LPS) and IFNγ for M1 classically polarized macrophages or IL-4 and IL-13 for M2 alternatively polarized macrophages. Human dental pulp stem cells (hDPSCs) are adult stem cells which have been found to exert immunomodulatory functions both by cell-to-cell contact and in a paracrine way. The aim of our study was to assess the ability of hDPSCs to modulate the phenotype of human macrophages.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from buffy coats by density-gradient centrifugation. PBMCs were differentiated to macrophages for 7 days in RPMI supplemented with M-CSF to obtain M0 macrophages. M0 macrophages were then polarized for 48 hours to M1 with LPS and IFNγ and to M2 macrophages with IL-4 and IL-13. hDPSCs were seeded at 1:1 ratio both directly on macrophages and into Transwell insert for indirect co-culture. Macrophages in direct co-culture with hDPSCs were separated with human anti CD14 micro beads. Protein expression was measured by Western Blot. Gene expression was assessed by RT-PCR.

Results: Surface markers expression analysis showed that M1 macrophages were *CD80*$^{+}$, *HK2*$^{+}$, *HLA-DRB1*$^{+}$($p < 0.0001$). Following co-culture, *CD80* and *HLA-DRB1* gene expression was further increased ($p < 0.0001$) (Fig. 1a), data were also confirmed by protein expression (Fig. 1b). M1 macrophages showed elevated expression of the transcriptional regulators *JAK-1*, *-2*, *-3,STAT3*, *NF-kB* and of pro-inflammatory cytokines (*IL-6*, *TNFα*, *IL-1β*, *IFNγ*) levels ($p < 0.0001$) (Fig. 2). They also express elevated levels of the immune modulators *IDO*, *PD-L1* and *ICAM-1* confirmed by protein expression (Fig. 3a, -b) and, of *Fas-L* and *COX2* (Fig. 3a). The indirect co-culture enhanced the expression of *STAT3*,

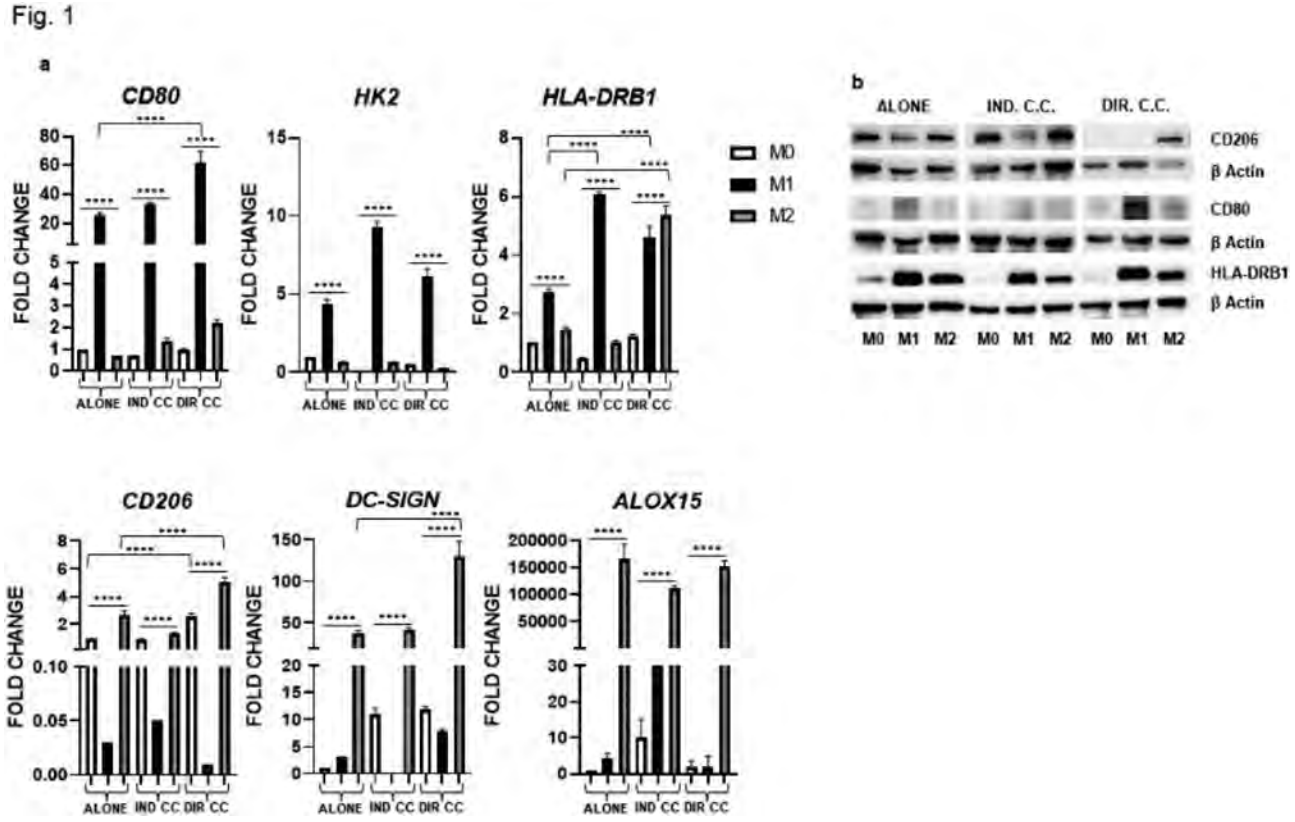

Figure 1. Macrophages markers expression. a) Relative mRNA expression. M0 macrophages alone is the control group used to normalize data (considered 1) expressed as fold change. ****p<0.0001. b) Representative western blot depicting proteins immune-probed. β-actin levels were used as loading control. Indirect co-culture (IND CC), direct co-culture (DIR CC).

Fig. 2

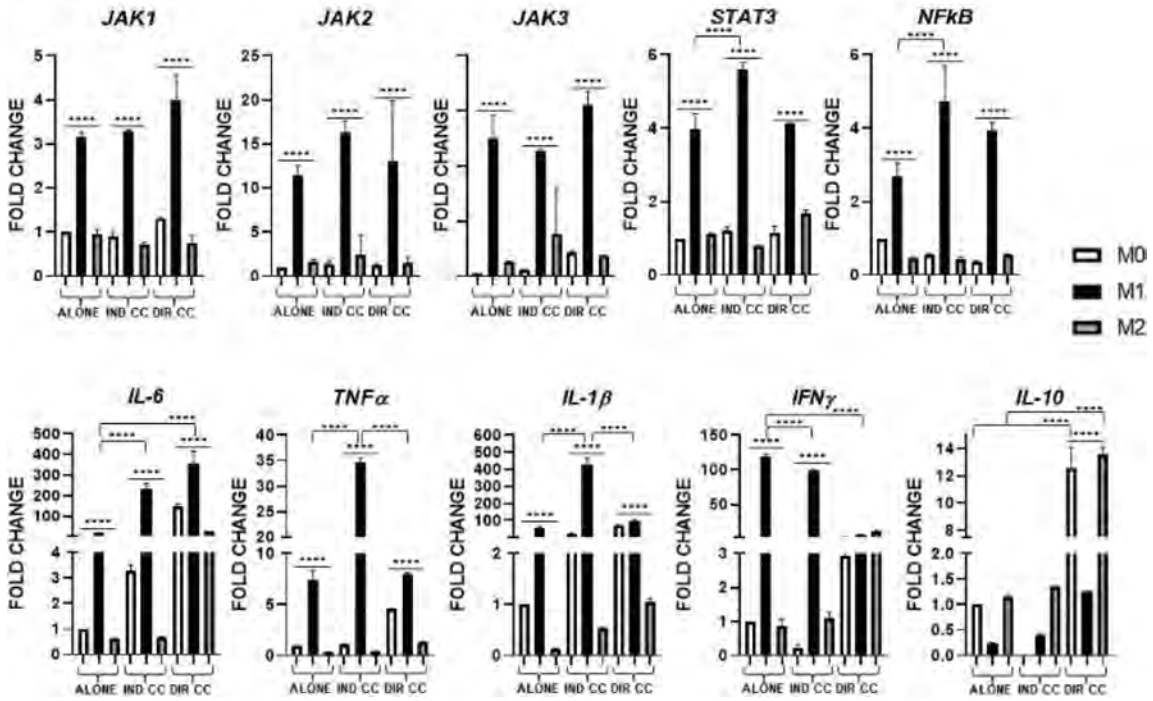

Figure 2. Transcriptional regulators and cytokines expression calculated as fold change. ****p<0.0001. Indirect co-culture (IND CC), direct co-culture (DIR CC).

Fig. 3

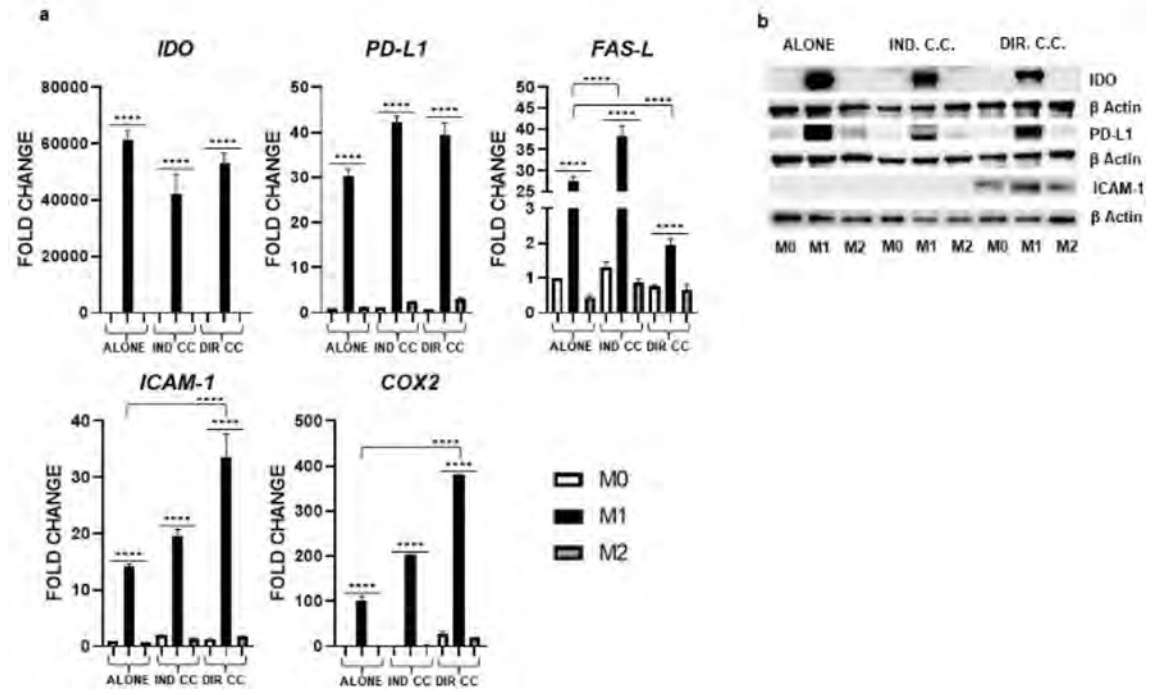

Figure 3. Immune-modulator expression. a) Relative mRNA expression as fold change. b) Representative western blot lanes. ****p<0.0001. Indirect co-culture (IND CC), direct co-culture (DIR CC).

NF-kB, *IL-1β, IL-6, Fas-L* and decreased *IFNγ* expression ($p < 0.0001$) (Fig. 2, 3). The direct co-culture increased *IL-6,-ICAM-1* and *COX2* expression and diminished *IFNγ* and *Fas-L* expression ($p < 0.0001$) (Fig. 2, 3). M2 macrophages were *CD206*$^{+}$*, DC-SIGN*$^{+}$ *and ALOX15*$^{+}$ and only the direct co-culture was able to enhance the *HLA-DR, CD206*, *DC-SIGN* and *IL-10* expression ($p < 0.0001$) (Fig. 1, 2). The direct co-culture increased the expression of *CD206* and *IL-10* in M0 non-polarized macrophages too ($p < 0.0001$) (Fig. 1, 2).

Conclusion: The biological factors secreted by hDPSCs supported the macrophages response to inflammation activating the STAT3 and NF-kB pathways and, in contrast, enhancing the inhibitory membrane molecule FasL expression. The cell-to-cell contact was shown to be the best immunomodulatory way reducing the IFNγ expression in inflammatory condition. Further, in presence of anti-inflammatory cytokines, hDPSCs directly promoted the polarization of M0 macrophages towards M2 phenotype and enhanced IL-10 expression which is a key cytokine in limiting the host immune response.

Disclosure: M. Maccaferri: None; **A. Pisciotta**: None; **G. Carnevale**: None; **C. Salvarani**: None; **E. PIGNATTI**: None.

Abstract Number: 0044

Aberrant Mevalonate Metabolite Farnesyl Pyrophosphate-Induced Neutrophil Hyperactivation in Behçet's Disease Pathogenesis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: (0040–0064) Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Menghao Zhang[1], Na Kang[2], Xin Yu[1], Wanli Liu[2] and Wenjie Zheng[1], [1]Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, Beijing, China, [2]Beijing Key Lab for Immunological Research on Chronic Diseases, School of Life Sciences, Institute for Immunology, Tsinghua University, Beijing, China

Background/Purpose: Behçet's disease (BD) is a chronic vasculitis characterized by polymorphonuclear neutrophils (PMNs) hyperactivation with unknown etiology. The over-productions of neutrophil extracellular traps (NETs) and pro-inflammatory cytokines are increasingly implicated in BD (Clin Immunol. 2023; 250:109318). Aberrant metabolic intermediates have been identified as endogenous danger signals to elicit natural immune responses (Trends Endocrinol Metab. 2020; 31:712-724), yet relevant mechanisms in BD remained unexplored. Farnesyl pyrophosphate (FPP) is a key isoprenoid intermediate in the mevalonate (MVA) pathway that triggers pro-inflammatory responses (Sci China Life Sci. 2015; 58:328-35) and cell death (PLoS Biol. 2021;19:e3001134). Thus, we aimed to reveal the immunometabolic aberrations of BD, and highlight the pathogenic implications of FPP in BD-PMN hyperactivation.

Methods: Focusing on immunometabolism, we integrated and analyzed our published data of serum lipidomics and peripheral blood immunocyte transcriptomics. Transcriptomic analysis and qRT-PCR validated the enhanced MVA pathway and suggested its metabolite FPP accumulated in BD-PMN.To elucidate the involvement of the MVA pathway in BD-PMN hyperactivation, we intervened with its key enzymes using appropriate inhibitors and agonists (Fig 2). We assayed the level of FPP in serum and PMN from BD and HC by targeted mass spectrum, and clinical correlations by Pearson correlation analysis. We stimulated PMNs with FPP, and measured their production of pro-inflammatory cytokines by qRT-PCR and NETs by

immunofluorescence. Then, we stimulated vascular endothelial cells (VECs) with the supernatant from FPP-stimulated PMNs and measured the expression of activation/injury markers in the VECs by qRT-PCR.

Results: Our multi-omics analysis revealed that steroid biosynthesis was significantly elevated in BD serum, with consistent metabolic aberration noted only in PMN (Fig 1A-1B), particularly in cholesterol biosynthesis (Fig 1C). More precisely, the upregulation of enzymes upstream of FPP suggested the enhanced MVA pathway and accumulated intermediate FPP (Fig 2). Furthermore, FPP was confirmed to be the key component of the MVA pathway promoting PMN activation, as its inhibition decreased PMN cytokine productions (zoledronic acid, $p< 0.0001$), while its metabolism inhibition had facilitative effects (BPH-652, $p< 0.0001$), and vice versa (FIN56, $p< 0.0001$). FPP was overexpressed in BD serum ($p=0.0022$) and PMN ($p=0.0397$), and positively correlated with BD disease activity. Notably, FPP specifically promoted PMN to produce proinflammatory cytokines and NETs in a dose-dependent manner, further damaging VECs and leading to the

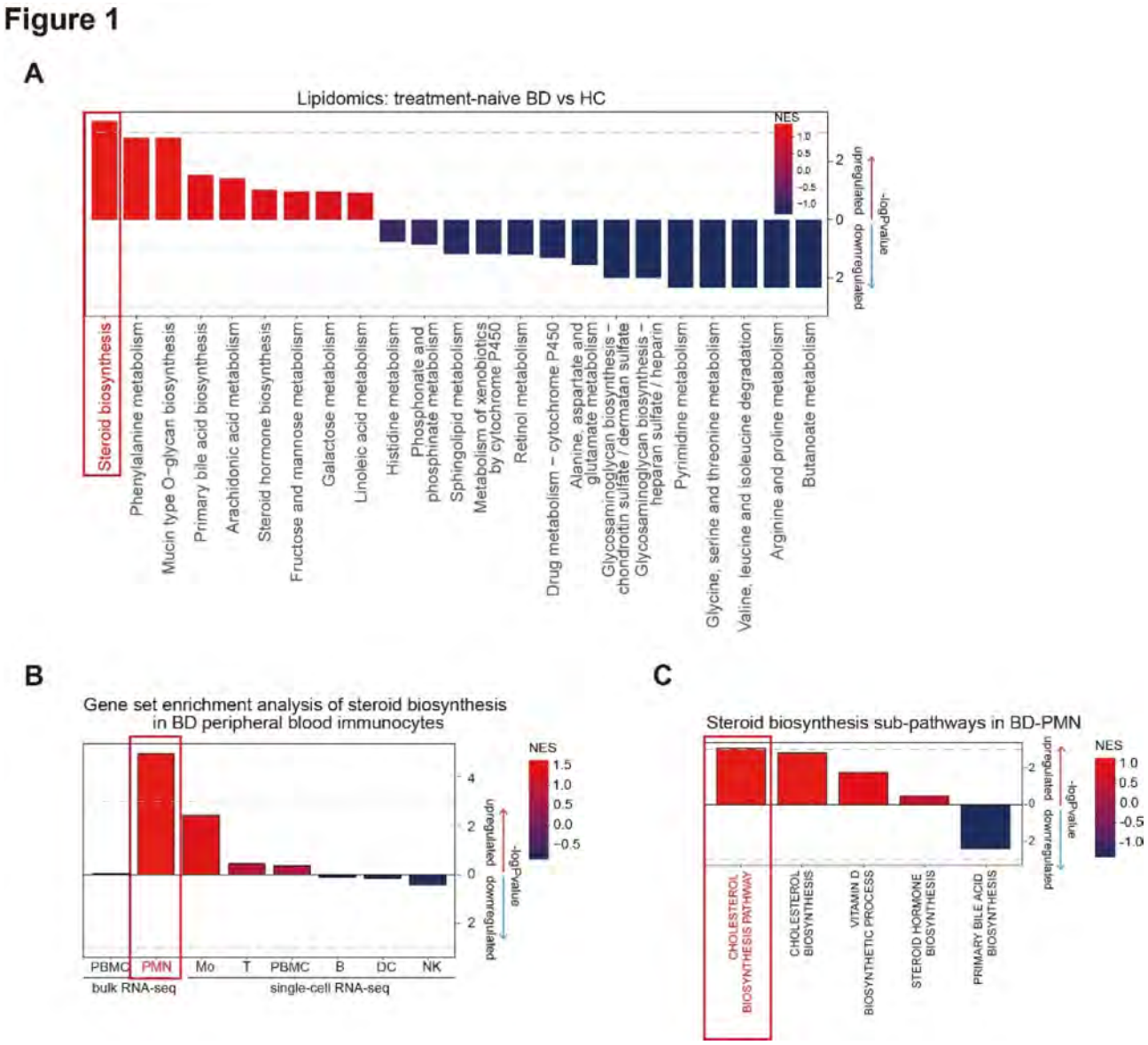

Figure 1: Elevated Steroid Biosynthesis in BD Serum and PMN. A: Lipidomic analysis between treatment-naïve BD and HC serum. B: Gene Set Enrichment Analysis (GSEA) of steroid biosynthesis pathway in BD and HC peripheral blood immunocytes, including bulk RNA-seq of PBMC (GSE198533), PMN (GSE205867) and single-cell RNA-seq of PBMC (GSE198616). C: GSEA of steroid synthesis sub-pathways, such as bile acids, steroid hormones, vitamin D, and cholesterol synthesis, in BD and HC PMN (GSE205867).

overexpression of molecules related to inflammation (TNF-α, p< 0.0001), adhesion (ICAM-1, p=0.0006), and permeability (VEGF, p=0.0004). And BD-PMN was hyper-responsive to FPP (Fig 3).

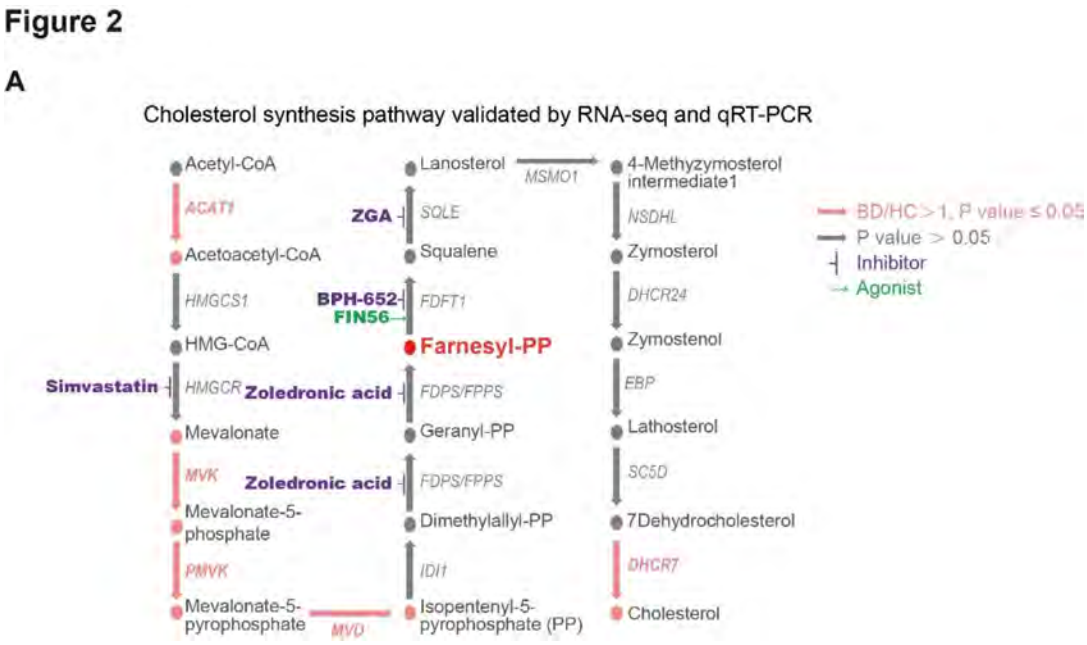

Figure 2: Aberrant Mevalonate Pathway in BD-PMN. A: A schematic diagram of the cholesterol biosynthesis pathway. Enzymes with significantly elevated expression levels in BD-PMN, as verified by both RNAseq and qRT-PCR (N = 20), were marked in red. Potential agonists and inhibitors were highlighted with green and purple arrows, respectively.

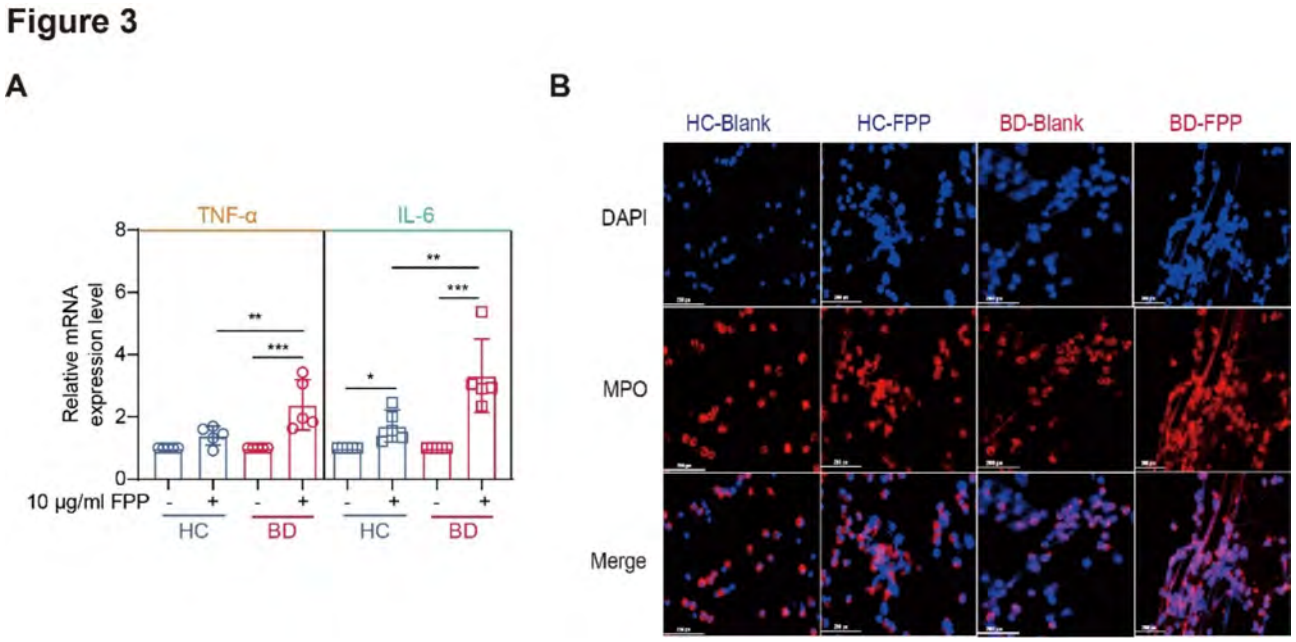

Figure 3: FPP Enhances Pro-Inflammatory Cytokine Production and NETosis in PMNs, with Hyper-Responsiveness in BD-PMN. A: qRT-PCR measurement of TNF-α and IL-6 expression levels in PMNs from BD (red), and HC (blue), after stimulation with 10 μg/ml FPP (N=5). *, p<0.05; **, p<0.01; ***, p<0.001; B: Representative immunofluorescence staining diagrams of 60 μg/ml FPP-induced NETosis in PMNs from BD and HC, showing MPO (red) and DAPI-stained nuclei (blue); scale bar = 50 μm. MPO: Myeloperoxidase.

Conclusion: Overall, our study revealed the aberrant immunometabolic profiles of BD and highlighted the effect of FPPon promoting PMN hyperactivation, providing insight into the potential of targeting FPP for BD treatment. Further investigations are in progress to elucidate the mechanisms.

Disclosure: M. Zhang: None; **N. Kang**: None; **X. Yu**: None; **W. Liu**: None; **W. Zheng**: None.

Abstract Number: 0045

Discovery and Characterization of a Selective, Orally Bioavailable PAD4 Inhibitor to Target NETs Driven Autoimmune and Inflammatory Diseases

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: (0040–0064) Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Protein arginine deiminases (PAD) 4 is an enzyme that catalyzes the conversion of protein-embedded arginine to citrulline. It is essential for neutrophil extracellular traps (NETs) formation which is implicated in multiple immune-mediated pathological conditions. Importantly, PAD4 deficiency does not lead to increased infection of immune suppression, suggesting that PAD4 is an attractive therapeutic target for autoimmune and inflammatory diseases. However, the development of a drug-like PAD4 inhibitor has been challenging. Here, we report the discovery and characterization of a potent, selective and orally bioavailable small molecule PAD4 inhibitor.

Methods: By leveraging Computer Accelerated Rational Design (rCARD^{TM}) and Structure-Based Drug Discovery (SBDD) platforms, we rationally designed and synthesized a small molecule RGT-691. The biochemical activities against PAD4 and PAD2 were measured by ammonia release assays using BAEE as the substrate. The cellular activity was determined by inhibition of citrullination of histone 3 (Cit H3) in differentiated HL-60 cells stimulated with calcium ionophore (A23187). The absorption (MDCK based permeability assay and kinetic solubility), distribution (free fraction in plasma), and metabolism (liver microsomes, hepatocytes, plasma stability) were characterized in *in vitro* assays. The pharmacokinetic study was performed in preclinical species to evaluate the exposure and bioavailability. Proof-of-mechanism study was performed using the LPS challenged airway inflammation mouse model in which the bronchial alveolar lavage fluid (BALF) was collected to measure the concentration of Cit H3 and pro-inflammatory cytokines as efficacy readouts.

Results: The biochemical and cellular activities of RGT-691 were determined. Its IC_{50} in PAD4 ammonia release assay is 46 $\pm$ 12 nM; while its IC_{50} against PAD2 is > 10 mM. It demonstrated a cellular IC_{50} of 22 $\pm$ 11 nM in A23187 stimulated differentiated HL-60 cells. The binding mode of RGT-691 with PAD4 was determined at 2.8 Å by crystallography, providing structural basis for the high potency and selectivity of RGT-691 for PAD4. RGT-691 demonstrated moderate permeability and good solubility. PK studies in mice showed good drug exposures via oral dosing and achieved desired efficacious exposure. In LPS induced airway inflammation model, RGT-691 potently inhibited neutrophil trafficking to lung, reduced the level of dsDNA and Cit H3. Furthermore, it suppressed the pro-inflammatory cytokines including TNF-a and IL-6 in a dose-dependent manner.

Conclusion: In summary, RGT-691 is a potent, selective, orally bioavailable small molecule PAD4 inhibitor which provides therapeutic opportunities in multiple NETs-driven autoimmune and inflammatory diseases.

Disclosure: M. Yang: None; **s. feng**: None; **y. wen**: None; **X. ren**: None; **H. Li**: None; **l. yao**: None; **Z. xie**: None; **W. zhong**: None.

Abstract Number: 0046

Circulating Monocytes in RA, SSc, and SLE Have Radically Altered and Unique Transcriptional & Epigenetic Profiles

Kieran Woolcock[1], Nila Servaas[2], Maarten van der Kroef[2], Stephen Delaney[3], John Cole[1], Aridaman Pandit[2] and Carl Goodyear[1], [1]University of Glasgow, Glasgow, United Kingdom, [2]University Medical Center Utrecht and Utrecht University, Utrecht, Netherlands, [3]Research and Early Development, Respiratory and Immunology (R&I), BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: (0040–0064) Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA), Systemic lupus erythematosus (SLE), and Systemic sclerosis (SSc) are all systemic rheumatic autoimmune diseases with a dysregulated myeloid compartment. Monocytes are poised to rapidly mobilise in large numbers to sites throughout the body, where they provide pro-inflammatory or pro-resolving roles. A key and unaddressed question is are circulating monocytes similarly perturbed on the transcriptional and epigenetic level across different rheumatic diseases. Despite the extensive research in the field, it is still poorly understood how these profiles influence the response to stimuli in disease environment. Understanding this may help understand how monocytes respond at disease sites and how this varies across different conditions. To comprehensively profile monocytes, we performed paired RNA-Seq and ChIP-Seq of activating histone 3 lysine 4 tri-methylation (H3K4me3), and repressive histone 3 lysine 27 tri-methylation (H3K27me3), modifications.

Methods: Fresh peripheral blood samples were collected from active RA patients (DAS28 > 2.7), SLE patients (1997 ACR criteria), SSc (ACR/EULAR 2013 criteria), as well as age- and gender-matched healthy controls (HC). SSc patients were subdivided into diffuse cutaneous (dcSSc), limited cutaneous SSc (lcSSc), and early SSc (eaSSc) subsets. CD14+ monocytes were isolated from peripheral blood and genome-wide profiling of RNA (HC, n=15; RA, n=9; SLE, n= 10; dcSSc, n=10; lcSSc, n=10; eaSSc, n=10), H3K4me3 (HC, n=20; RA, n=20; SLE, n=8; dcSSc, n=9; lcSSc, n=8; eaSSc, n=10), and H3K27me3 (HC, n=15; RA, n=10; SLE n=8, dcSSc, n=9 ; lcSSc, n=7; eaSSc, n=10) was performed. Statistical significance was determined using an adjusted $p < 0.05$ & absolute log2fold > 0.58 for RNA-Seq or an adjusted $p < 0.05$ for ChIP-Seq.

Results: We observed substantial differentially expressed genes (DEGs) in RA monocytes in comparison to HC (3,504 DEGs), whereas much fewer transcriptional changes were observed in SLE and SSc subsets. Similarly, much greater changes were seen in active H3K4me3 profiles in RA in comparison to HC (3,141 differential peaks), than those seen in SLE and SSc subsets (50 and 10, respectively). Moreover, the majority (~65%) of increased H3K4me3 peaks in RA were bivalent; contained a repressive H3K27me3 peak with either no or very low transcriptional expression. Notably, the H3K27me3 profile in RA was comparable to those seen in HC. This was also the case lcSSc and SLE. In contrast,

numerous increases in repressive H3K27me3 peaks were identified in dcSSc and eaSSc (424 and 647, differential peaks respectively).

Conclusion: We found that systemic rheumatic diseases displayed a range of transcriptional and epigenetic profiles. Of note, we identified that in RA, there is an abundance of active H3K4me3 modifications that occur in repressed (H3K27me3) and transcriptionally inactive loci. We propose that the increased epigenetic activation of bivalent genes in RA could prime these monocytes for activation within the diseased joint microenvironment and could subsequently detrimentally contribute to disease pathogenesis.

Disclosure: K. Woolcock: None; **N. Servaas**: None; **M. van der Kroef**: None; **S. Delaney**: AstraZeneca, 3; **J. Cole**: None; **A. Pandit**: ; **C. Goodyear**: Abbvie, 6, AstraZeneca, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 5, Eli Lilly, 5, Galvani, 2, 5, GlaxoSmithKlein(GSK), 5, Istesso, 5, Janssen, 5, MedAnnex, 2, 5, Medincell, 2, MiroBio, 5, Revolo, 5, UCB, 5, 6.

Abstract Number: 0047

Identification of Specific Monocyte Epigenetic Signatures in Sarcoidosis and Tuberculosis

Marie Robert[1], Nader Yatim[2], Arthur Mageau[3], Nicolas Charles[4], Tiphaine Goulenok[2], Tom Dott[1], Violaine Saint Andre[1], Darragh Duffy[1] and Karim Sacre[3], [1]Institut Pasteur Paris, Paris, France, [2]Assistance Publique Hopitaux de Paris, Paris, France, [3]Université Paris Cité, Paris, France, [4]INSERM, Paris, France

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
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Background/Purpose: Sarcoidosis is an inflammatory disease characterized by granuloma tissue lesions that most commonly affect the lungs, but can target any other organ. While the cause of sarcoidosis and the mechanisms underlying granuloma formation and progression are still unknown, the disease shares many similarities with tuberculosis, including histological characteristics, organ tropism and clinical presentation. We hypothesized that circulating monocytes from patients with sarcoidosis or tuberculosis may retain a specific epigenetic signature, distinguishing from healthy controls and each disease.

Methods: To test this, we performed genome-wide epigenetic profiling of circulating monocytes from newly diagnosed patients with tuberculosis or sarcoidosis using the CUT&Tag technology, and assessed the acetylation of lysine 27 of histone 3 (H3K27Ac) (the most appropriate histone mark to identify enhancers of expressed genes).

Results: Using unbiased principal component analysis (PCA) of genome-wide histone H3K27Ac profiles we identified genomic regions that specifically separated sarcoidosis patients, from tuberculosis patients and healthy donors (**Figure 1**). There were 648 H3K27Ac enriched regions of the genome in sarcoidosis as compared to tuberculosis, while 203 regions were H3K27Ac depleted ($log_2FC > 0.3$ or < 0.3, adj-$p < 0.1$). Interestingly, the genes associated with these regions can discriminate sarcoidosis from tuberculosis patients.

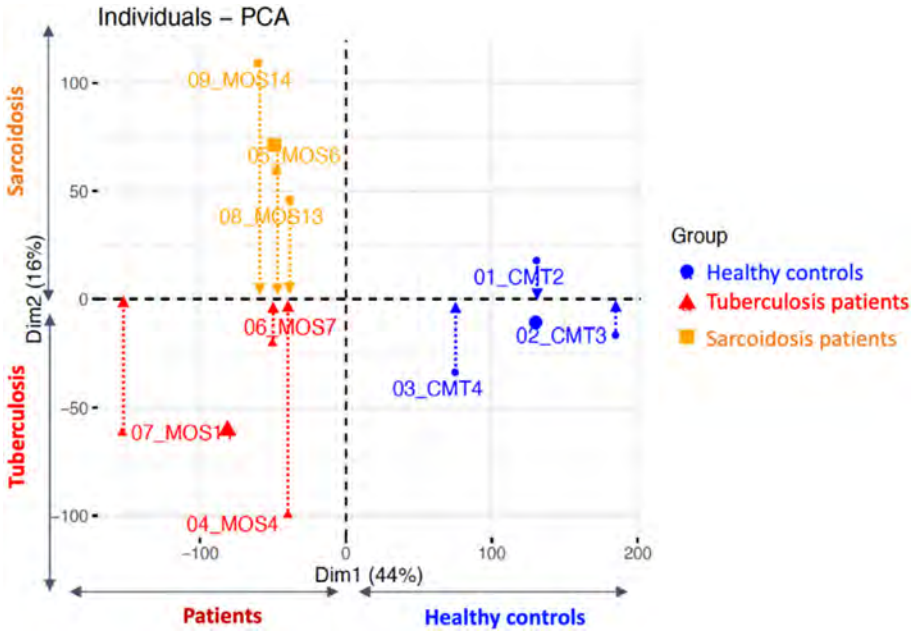

Figure 1. Unbiased principal component analysis (PCA) of genome-wide histone H3K27Ac profiles using CUT&Tag technology.

Conclusion: Our findings provide evidence that there are distinct monocyte epigenetic signatures associated with sarcoidosis and tuberculosis, and raise new and challenging perspectives on the role played by trained immunity in inflammatory diseases. Ongoing work will extend this analysis and integrate with additional immune phenotyping and functional assays for a more comprehensive understanding of sarcoidosis.

Disclosure: M. Robert: None; **N. Yatim**: Hi-Bio, 2; **A. Mageau**: None; **N. Charles**: argenx, 2, 5, Onward Therapeutics, 2; **T. Goulenok**: None; **T. Dott**: None; **V. Saint Andre**: None; **D. Duffy**: Roche, 5, Sanofi, 5; **K. Sacre**: None.

Abstract Number: 0048

Monosodium Urate Crystals Activate an Immune Tolerance Program That Restrains the Activation of Inflammatory Signaling in Macrophages During Gout Flares

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
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Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is the most frequent form of inflammatory arthritis, with episodes of self-resolving acute inflammation in the joint caused by the deposition of monosodium urate crystals (MSUc). MSUc activates a battery of transcription factors and epigenetic regulators in macrophages during gout flares, which orchestrates a unique inflammatory and metabolic program. Much effort has been put into understanding the role of cytokine and inflammatory mediators, including

inflammasome activation during gout flares. However, the mechanisms underlying the activation of a resolution program and the induction of immune tolerance in macrophages during the resolution phase of gout flares remain unknown.

Methods: We stimulated bone marrow-derived macrophages (BMDM) with LPS or MSUc for 10 min, 30 min, one hour, two hours and five hours and performed RNA-Seq. We primed BMDM with MSUc before stimulation with LPS for five hours and performed RNA-Seq. We incubated BMDM with the conditioned media of BMDM stimulated with MSUc before stimulation with LPS and performed RNA-Seq and promoter scanning analysis on the differentially expressed genes.

Results: We found that stimulation of BMDM with MSUc leads to a divergent response compared to that observed in BMDM stimulated with LPS (Figure 1A). Furthermore, the genes that are uniquely upregulated by LPS are significantly downregulated in BMDM stimulated with MSUc (Figure 1B, left), and the genes uniquely upregulated by MSUc are significantly downregulated in BMDM stimulated with LPS (Figure 1B, right). This data indicates that MSUc downregulates the transcriptional program induced by LPS.

Furthermore, we found that priming the BMDM with MSUc ablates the effect of LPS (Figure 2A, grey square). Interestingly, a similar effect is observed when BMDM are primed with MSUc, but we let the BMDM rest without MSUc for one, two, five and eight hours (Figure 2A, grey square). This data indicates that MSUc signaling ablates the signaling induced by LPS by activating a macrophage immune memory program.

We next investigated whether a non-cell autonomous activation mediates the anti-inflammatory program by MSUc in neighbouring cells. We incubated BMDM for one, two and eight hours with the conditioned media of BMDM stimulated with MSUc, before stimulation with LPS. Interestingly, the media conditioned by cells stimulated with MSUc abrogates the BMDM response to LPS (Figure 2B, grey square).

In addition, we demonstrated that MSUc activates the BHLHE/circadian clock and LXR TF while reducing interferon response factor activity (Figure 3A-F).

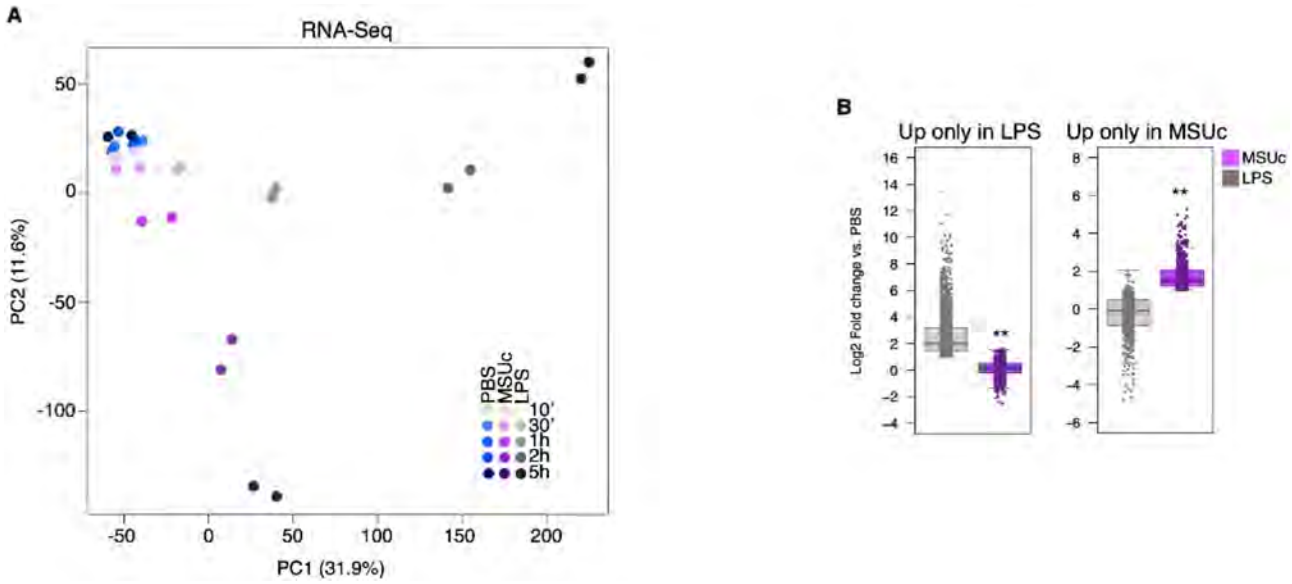

Figure 1. MSUc activates a distinct transcriptional program in macrophages (A) Principal component analysis of RNA-Seq experiment of BMDM stimulated with PBS, LPS or MSUc at various time points (n=2/condition). (B) Boxplot showing the genes uniquely upregulated by LPS (left) or MSUc (right) and their degree of expression in BMDM stimulated with LPS or MSUc (n=2/condition). Except for RNA-Seq experiments, Student's T-test was used to calculate statistical significance.

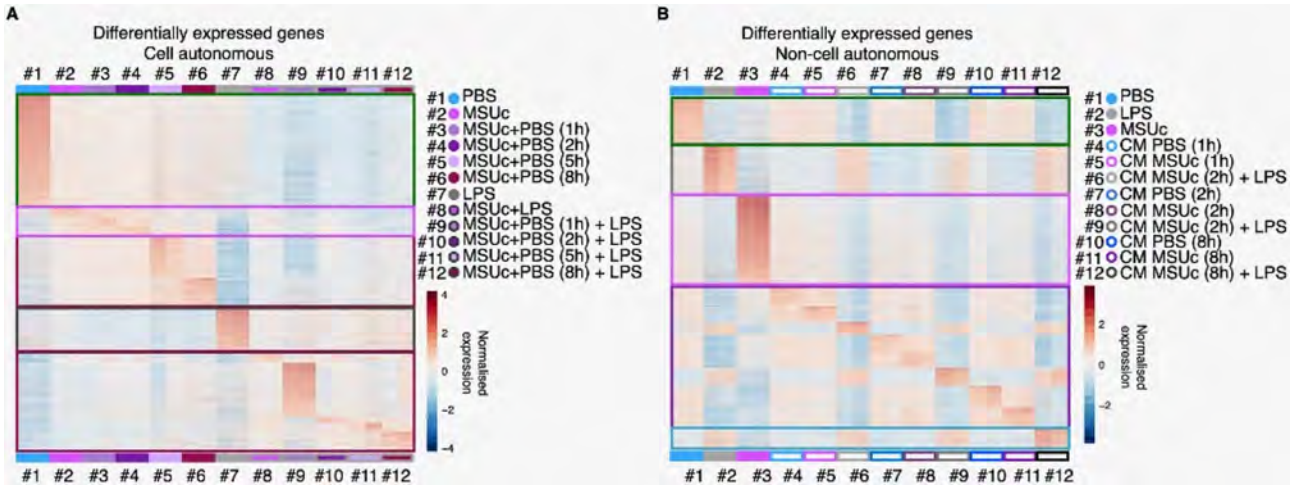

Figure 2. MSUc signaling ameliorates the effect of LPS and activates an immune memory program in macrophages. (A) Pheatmap of differentially expressed genes of BMDM stimulated with LPS or MSUc under various conditions (n=2/condition). (B) Pheatmap of differentially expressed genes of BMDM stimulated with LPS or MSUc or conditioned media from BMDM stimulated with MSUc under various conditions (n=2/condition). MSUc +PBS (1h, 2h, 5h or 8h)= BMDM stimulated with MSUc, culture media was removed, and fresh media without MSUc was added for 1h, 2h, 5h or 8h, respectively. CM= conditioned media. Except for RNA-Seq experiments, Student's T-test was used to calculate statistical significance.

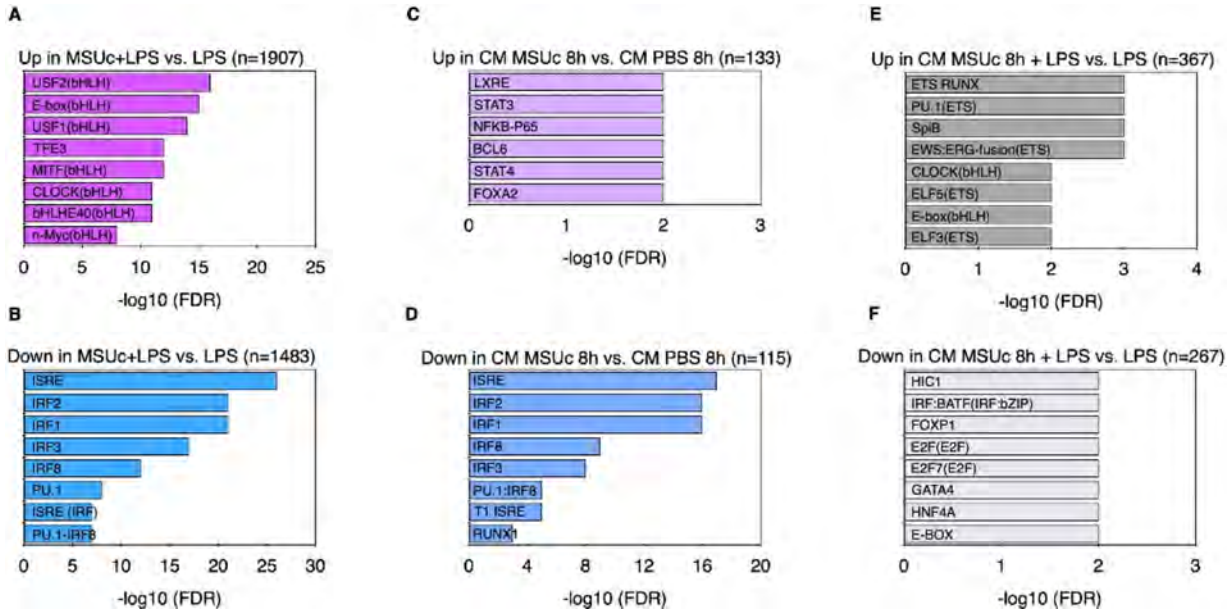

Figure 3. MSUc leads to the activation of the BHLHE/Circadian clock transcription factor and reduces the activity of interferon response factors. (A-F) HOMER analysis of the promoter of differentially expressed genes at various conditions from experiments shown in Figure 2. CM= conditioned media.

Conclusion: Our data indicate that MSUc activates an anti-inflammatory, pro-resolution program with immune memory properties governed by BHLHE/circadian clock TF and abrogates interferon response factors.

Disclosure: M. Alishala: None; **S. Calderon**: None; **A. Chen**: None; **M. Guma**: None; **C. glass**: None; **I. Cobo**: None.

Abstract Number: 0049

Soluble Uric Acid Is an Endogenous Inhibitor of CD38

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: (0040–0064) Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: CD38 is the main NAD^+-degrading enzyme that plays a key role in innate immunity, aging, cancer, and metabolic disorders. Pharmacological inhibition of CD38 has been proposed as a promising strategy for various diseases, including rheumatic diseases. Recently, we and another laboratory demonstrated that monosodium urate (MSU) crystals upregulate the protein expression of CD38 to promote inflammation. In the present study, we aim to clarify the effect of soluble uric acid (sUA) on CD38 and explore its unique role in purine metabolic pathways.

Methods: In enzyme assays, recombinant hCD38, and homogenates or crude membrane fractions of cells and tissues were used as enzyme sources, nicotinamide guanine dinucleotide (NGD) and epsilon-NAD^+ were used as substrates for the measurement of CD38 activity. In metabolic assays, NAD^+ was incubated with recombinant hCD38 in the presence or absence of sUA or other CD38 inhibitors. Then, NAD^+ concentrations in the reaction buffers were measured by LC-MS/MS.

Results: sUA directly inhibited the hydrolase and cyclase activities of CD38. Kinetic analysis revealed that sUA is a non-competitive inhibitor of CD38, suggesting its binding to the allosteric sites of CD38. The inhibitory effects of sUA on CD38 activity were reversible. The precursors and metabolite of sUA hardly inhibited the enzymatic activity of CD38. A structural comparison using analogs revealed that 1,3-dihydroimidazol-2-one is the main functional group for CD38 inhibition, although the adjacent uracil-like heterocycles are also essential. Metabolic assays using NAD^+ as substrate also confirmed the direct inhibitory effect of sUA on CD38. In addition, these findings were further verified by several physiological and pathological models in WT and CD38 KO mice.

Conclusion: sUA directly inhibits CD38 via a reversible non-competitive mechanism, and the inhibitory effect is restricted to sUA in purine metabolic pathways. These findings may promote understanding of sUA physiology, and the development of CD38 inhibitors. The opposite effects of sUA and MSU crystals on CD38 may explain why rapid urate lowering increases the risk of gout flares in the initiation of therapy.

Disclosure: S. Wen: None; **H. Arakawa**: None; **S. Yokoyama**: None; **Y. Shirasaka**: None; **H. Higashida**: None; **I. Tamai**: None.

Abstract Number: 0050

Anti-Citrullinated Histone Antibody CIT-013, a Dual Action Therapeutic for Neutrophil Extracellular Trap Associated Autoimmune Disease

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SESSION INFORMATION
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Session Title: (0040–0064) Innate Immunity Poster
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Background/Purpose: Neutrophil extracellular traps (NETs) contribute to the pathophysiology of multiple inflammatory and autoimmune diseases (Chirivi *et al*., 2021; DOI: 10.1038/s41423-020-0381-3). Targeting the NETosis pathway has demonstrated significant therapeutic potency in various disease models. Here we describe a first in class monoclonal antibody (CIT-013) with high affinity for citrullinated histones H2A and H4 which inhibits NET formation and reduces tissue NET burden *in vivo* with significant anti-inflammatory consequences. CIT-013 is currently in phase 1 clinical trials with phase 2a studies in RA due to commence in 2024.

The objective of the current study was to further unravel CIT-013's mode of action. Questions which we wanted to answer are: 1) How and when does CIT-013 interfere with the NETosis pathway?; and 2) what is the faith of CIT-013 opsonized NETs and NETting neutrophils? Furthermore, we investigated whether CIT-013's epitope is expressed in rheumatoid arthritis (RA) synovial tissue.

Methods: *In vitro* life imaging studies using neutrophils and macrophages in combination with monovalent as well as bivalent CIT-013 have been performed to investigate CIT-013's mode of action. An *in vivo* lung inflammation mouse model was used to investigate CIT-013's effect on NET burden as well as phagocytic macrophages. Finally, the presence of CIT-013's epitope in human RA synovial tissues have been investigated using immunohistochemistry techniques.

Results: Detection of CIT-013 epitopes in RA synovium provides evidence that RA is an autoimmune disease with excessive citrullinated-NETs that can be targeted by CIT-013. We show that CIT-013 acts upon the final stage of NET formation, binding to its chromatin epitopes when plasma membrane integrity is compromised to prevent NET release. Bivalency of CIT-013 is necessary for NETosis inhibition. In addition, we show that CIT-013 binding to NETs and netting neutrophils enhances their phagocytosis by macrophages. Furthermore, we demonstrate that a mouse variant of CIT-013 reduces tissue NET burden *in vivo* at least in part through enhanced macrophage phagocytosis.

Conclusion: Since NETs contribute to the pathophysiology of many immune mediated inflammatory diseases, including autoimmune diseases such as RA, CIT-013's unique ability to both inhibit NET release and enhance NET clearance indicates the importance of this first in class therapeutic antibody as a new emerging therapy.

Disclosure: M. van der Linden: Citryll BV, 3, 12, STOCK APPRECIATION RIGHTS; **S. Kumari**: Citryll BV, 3, 12, STOCK APPRECIATION RIGHTS; **D. Montizaan**: Citryll BV, 3, 12, STOCK APPRECIATION RIGHTS; **S. van Dalen**: Citryll BV, 3, 12, STOCK APPRECIATION RIGHTS; **A. Kip**: Citryll BV, 3, 12, STOCK APPRECIATION RIGHTS; **M. FOSTER**: Citryll BV, 2, Ermium Therapeutics, 2; **I. Reinieren**: None; **E. Neubert**: None; **L. Erpenbeck**: None; **T. Bruurmijn**: Citryll BV, 3, 12, STOCK APPRECIATION RIGHTS; **P. van Zandvoort**: Citryll BV, 3, 12, STOCK APPRECIATION RIGHTS; **P. Vink**: None; **E. Meldrum**: Citryll BV, 3, 12, STOCK APPRECIATION RIGHTS; **H. van Es**: Citryll BV, 1, 4, 12, STOCK APPRECIATION RIGHTS; **R. Chirivi**: Citryll BV, 3, 12, STOCK APPRECIATION RIGHTS.

Abstract Number: 0051

$CD14^+CD64^+$ Classical Monocytes Are the Main Producers of IL-23 at the Enthesis

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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: IL-23 is a key cytokine involved in diseases such as psoriasis, psoriatic arthritis and spondyloarthropathies (SpA) and inflammatory bowel disease.IL-23 is produced by activated monocytes, dendritic cells and neutrophils. Guselkumab, IL-23 p19 subunit inhibitor binds to native FcR1 (CD64) but Risankizumab, another p19 blocker, has a mutated Fc domain and lacks this binding. Entheses are relatively avascular sites and may be difficult for antibody penetration and normal entheseal macrophages have inducible IL-23 protein expression. In this work we investigated the phenotype and functionality of normal and activated entheseal macrophages to explore CD64 expression and which monocyte population had predominant IL-23 expression.

Methods: Immune cell populations were flushed from spinous process; samples were obtained from patients undergoing surgery for spinal decompression with no known chronic inflammation. Cells are sorted into two populations $CD64^+$ and $CD64^-$, sorting was gated on live cell and $CD3^+$ depleted. The populations that were sorted are $CD64^+CD14^+CD16^-$ and $CD64^-CD14^-CD16^+$. Cells were cultured for 48hrs with LPS (100ng/ml) & IFN-γ (50ng/ml) and then assessed for IL-23 production by ELISA and cells phenotyped to assess their CD64 profile (N=4). Single cell sequencing has been performed on bone and soft tissue from the enthesis following collagenase digest and CD64 expression identified (N=4).

Results: Sorting profiles indicated that the $CD64^+$ cells were $CD14^+CD16^-$ and $CD64^-$ cells were $CD14^-CD16^+$, the enthesis showed some cells that are $CD64^+$ have intermediate CD14 expression (Figure 1). Following 48hrs in culture cells maintained their respective CD64 expression profile confirming that CD64 expression does not fluctuate upon cell activation (Figure 2). Analysis of the supernatant reveals that IL-23 expression distinctly comes from the $CD64^+CD14^+$ cells from the enthesis and predominantly from the PBMCs following activation with LPS & IFN-γ (Figure 2). Single cell analysis confirms

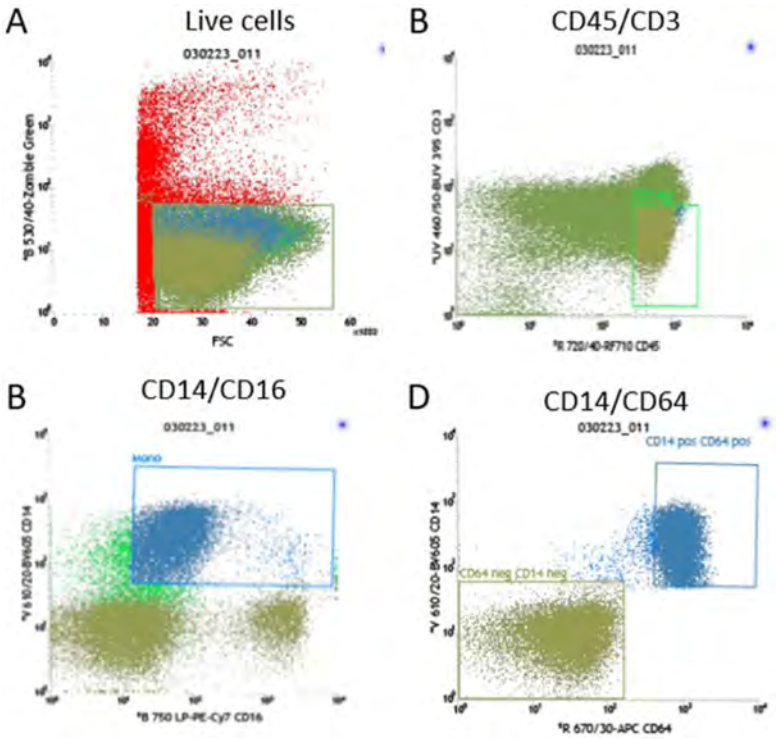

Figure 1: Gating strategy for sorting CD64+ and CD64- cells. Cells flushed from the spinous process are stained for cell sorting using the panel of markers: Live/dead-Zombie Green, CD45-RF710, CD3-BUV395, CD14-BV605, CD16-PE-Cy7 & CD64-APC. The gating strategy uses FSC/SSC to remove the granulocytes and then gates on the live cells (A), from the live cell population the CD3+ cells are gated out (B) which we have shown previously to be CD64 negative. Cells are then separated by CD14 and CD16 (C), the CD64+ cells collected are CD14+ as shown in the bottom left plot and the CD64- cells are CD14- (D).

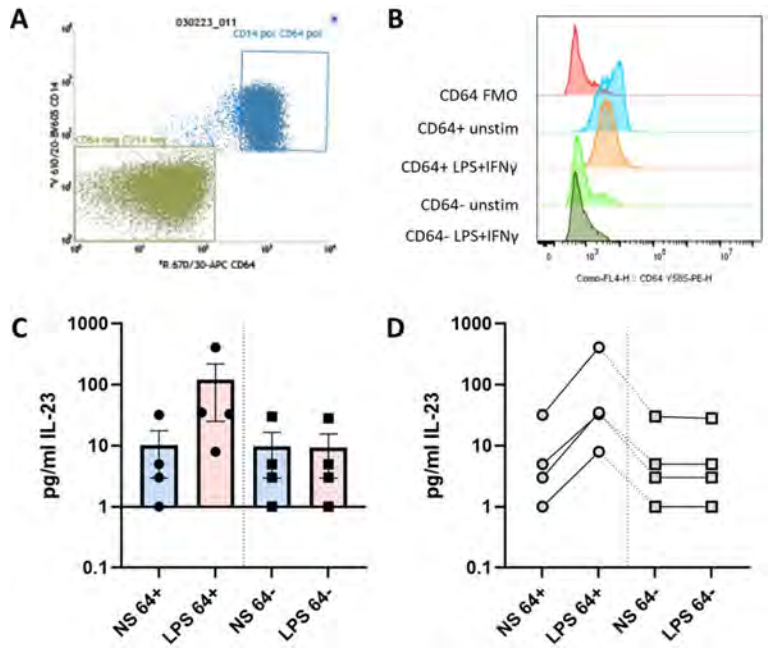

Figure 2: IL-23 production is from activated entheseal monocytes. Sorting of entheseal CD64+ cells correlated with CD14 positivity and CD64- cells correlated with CD14 negativity (A), these two cell populations were put into culture for 48hrs stimulated with LPS (100ng/mL) and IFN-γ (50ng/mL) or with no stimulation. After 48hrs in culture CD64 profiles were reassessed by flow cytometry (B), from both CD64+ and CD64- populations, expression was compared to a CD64 FMO. Supernatants collected after 48hrs were assessed via ELISA to measure the levels of IL-23 Nf4 (C), each of the four donors was plotted and shows levels of IL-23 for each condition follows the same trend (D).

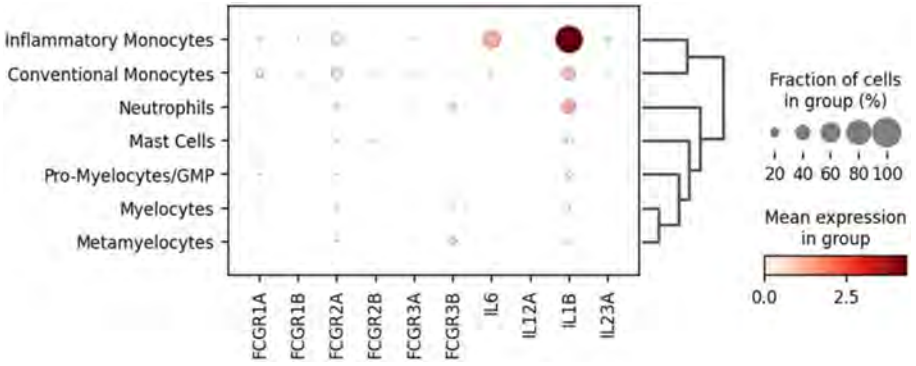

Figure 3: Singe-cell sequencing reveals gene expression for FCGR1A/B and IL23A is only present in the monocyte populations. Single-cell sequencing was performed on spinal entheseal bone and soft tissue, samples were prepared by performing a collagenase digest. Bone and soft tissue were analysed, and cluster analysis reveals that the FGR1A and FCGR2A genes which encode for CD64 are present in approximately 20% of the conventional and inflammatory monocytes, this also correlates with expression of the IL23A gene encoding for IL-23 Nf4. Together this data confirms what has been seen at the protein level.

that CD64 expression is found on the conventional and inflammatory monocytes which makes up approximately 20% of the cell population and even in health a proportion of these cells had IL23A gene expression which encodes the P19 subunit (Figure 3).

Conclusion: In this work, we have shown that $CD64^{+}CD14^{+}$ conventional monocytes are the main producers of IL-23 at the axial enthesis. This has been confirmed by flow cytometry and single cell analysis showing that these make up approximately 20% of the total cell population. Given that the key entheseal cell producing IL-23 also expresses CD64, the receptor for the rapid removal of Guselkumab bound IL-23 at the enthesis. These findings highlight that there could be differences between Guselkumab and Risankizumab in IL-23 neutralisation at the key enthesis territory.

Disclosure: N. McDermott: None; **T. Macleod**: None; **A. Altaie**: None; **L. Straszynski**: None; **R. Dunsmuir**: None; **V. Borse**: None; **P. Loughenbury**: None; **D. Simone**: None; **S. Sansom**: None; **C. Buckley**: None; **D. McGonagle**: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Janssen, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0052

Possible Involvement of TLR4 in the Pathogenesis of Primary Sjögren's Syndrome Through Induction of the Expression of BAFF Receptor, BR3 in Peripheral Monocytes

Keiko Yoshimoto[1], Yumi Ikeda[1], Katsuya Suzuki[2], Hiroyuki Fukui[1], Kotaro Matsumoto[1], Masaru Takeshita[1], Tsutomu Takeuchi[3] and Yuko Kaneko[4], [1]Keio University School of Medicine, Tokyo, Japan, [2]Keio University, Shinjuku, Japan, [3]Keio University School of Medicine and Saitama Medical University, Tokyo, Japan, [4]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan

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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Toll-like receptors (TLRs) play a pivotal role in innate immune system and chronic inflammation in autoimmune diseases. It has been reported that signaling pathways via TLRs, such as TLR2, TLR3, TRL4, TLR7 and TLR9 are involved in onset and/or development of primary Sjögren's syndrome (pSS), and that immune cells expressing TLRs, such as macrophages, dendritic cells, monocytes and B cells play a crucial role in the pathogenesis of the disease. We reported that elevated expression of BAFF receptor, BR3, in peripheral monocytes in pSS patients is correlated with clinical parameters of the patients and is involved in abnormal B cell functions. Therefore, clarification of regulatory mechanisms of the BR3 expression in monocytes is required not only for elucidation of pathogenesis of pSS, but also for search for therapeutic targets of the disease. In this study, we investigated possible involvement of signaling through TLRs in the enhanced expression of BR3 in peripheral pSS monocytes.

Methods: The expression levels of CD14, CD16, BR3 and TLRs in peripheral monocytes from pSS patients (n = 67) and healthy controls (HC; n = 19) were analyzed by FACS.The mRNA levels of BR3 and TLR4 in the monocytes were analyzed by quantitative PCR (qPCR). The serum level of S100A9, one of the ligands for TLR4, was measured by ELISA. PBMCs were stimulated with LPS or S100A9 for 3 days and the expression level of BR3 in the cells was analyzed by FACS.

Results: FACS analysis revealed that the expression of TLR4 was significantly higher in $CD14^{++}CD16^{+}$ cells (intermediate monocytes, IM) than that of $CD14^{++}CD16^{-}$ (classical monocytes) and $CD14^{+}CD16^{++}$ (non-classical monocytes) in pSS. Interestingly, not only the proportion of BR3-positive cells, but also that of TLR4-positive cells among IM was significantly higher in pSS than that of HC ($p < 0.001$ for BR3 and TLR4). The data is consistent with the results with qPCR. In addition, the proportion of TLR4-positive cells was significantly and positively correlated with that of BR3-positive cells only in pSS ($p < 0.01$). Notably, TLR4 ligands such as LPS or S100A9 enhanced the BR3 expression in peripheral monocytes. It may be noteworthy that the serum level of S100A9 was significantly higher in pSS than HC ($p< 0.001$) and the proportion of TLR-positive cells among IM was significantly correlated with the S100A9 level in pSS ($P < 0.05$).

Conclusion: Our results together with the data that the BR3 expression level is correlated with clinical parameters of pSS collectively suggest that TLR4 signaling pathways are involved in the pathogenesis of pSS.

Disclosure: K. Yoshimoto: None; **Y. Ikeda**: None; **K. Suzuki**: None; **H. Fukui**: None; **K. Matsumoto**: None; **M. Takeshita**: None; **T. Takeuchi**: AbbVie, 2, 5, 6, AYUMI, 5, Bristol-Myers Squibb, 6, Chugai, 2, 5, 6, Daiichi Sankyo, 5, Eisai, 5, 6, Eli Lilly Japan, 2, 6, Gilead, 2, 6, Janssen, 6, Mitsubishi-Tanabe, 2, 5, 6, ONO, 5, Pfizer Japan, 6, Taiho, 2; **Y. Kaneko**: AbbVie/Abbott, 1, 6, Ashai Kasei Pharma, 1, 6, Astellas Pharma, 1, 6, AstraZeneca, 1, 6, AYUMI Pharmacutia, 1, 6, Bristol-Myers Squibb(BMS), 1, 6, Chugai-Pharm, 1, 6, Eisai, 1, 6, Eli Lilly, 1, 6, Gilead Sciences Inc., 1, 6, GlaxoSmithKlein(GSK), 1, 6, Janssen Pharmaceutical KK, 1, 6, Novartis, 1, 6, Pfizer, 1, 6, Tanabe Mitsubishi Pharma, 1, 6, UCB Japan, 1, 6.

Abstract Number: 0053

Nintedanib Downregulates the Profibrotic M2 Phenotype of Macrophages Obtained from Systemic Sclerosis Patients Affected by Interstitial Lung Disease

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a systemic autoimmune connective tissue disease, characterized by microvascular damage, alteration of immune response and progressive fibrosis of skin and internal organs, including lungs (1). The lung involvement, either interstitial lung disease (ILD) or pulmonary arterial hypertension, contributes to the highest mortality of SSc patients (1).

Macrophages, primarily alternatively activated (M2) macrophages, seem to have a profibrotic role in SSc, being fundamental cells of the immune inflammatory infiltrate of skin and lungs (3).

M2 macrophages express specific surface markers such as mannose receptor (CD206), macrophage scavenger receptors (CD204 and CD163), and functional markers, including the MER proto-oncogene tyrosine kinase (MerTK). Moreover, they release profibrotic cytokines and growth factors, including interleukin-10 (IL10) and transforming growth factor-β1 (TGFβ1) (2).

Nintedanib is an intracellular tyrosine kinase inhibitor targeting several fibrotic mediators such as the receptors of platelet-derived growth factor, fibroblast growth factor, vascular endothelial growth factor, and colony-stimulating factor 1 (3).

To investigate the capability of nintedanib to downregulate the profibrotic M2 phenotype of cultured monocyte-derived macrophages (MDMs) obtained from SSc-ILD patients.

Methods: Monocytes isolated from the peripheral blood of nine female SSc-ILD patients (mean age 64±14 years) were differentiated into MDMs with phorbol myristate acetate (5ng/ml). Cultured SSc-ILD MDMs were maintained in growth medium without any other stimulation (untreated cells) or treated with nintedanib (0.1 and 1μM) for 3, 16 and 24 hours. SSc-ILD patients fulfilled the 2013 ACR/EULAR criteria for SSc diagnosis (during their standard diagnostic procedures and untreated with nintedanib, glucocorticoids or tocilizumab) and were enrolled after obtaining patients informed consent and Ethical Committee approval.

Gene and protein expression of CD204, CD163, CD206, MerTK and IL10 were evaluated by quantitative RT-PCR and Western blotting. TGFβ1 level was evaluated in the conditioned medium by ELISA.

The statistical analysis was carried out using non-parametric Wilcoxon test.

Results: In cultured SSc-ILD MDMs, nintedanib 0.1 and 1μM significantly downregulated the gene expression of CD204, CD206, CD163 and MerTK after 24 hours of treatment compared to untreated cells. Nintedanib also significantly downregulated gene expression of MerTK and IL10 after 16 hours of treatment compared to untreated cells.

In cultured SSc-ILD MDMs, nintedanib 0.1 and 1μM significantly reduced the protein synthesis of CD204, CD206, CD163, MerTK and the TGFβ1 production after 24 hours of treatment compared to untreated cells.

Conclusion: Nintedanib seems to downregulate the M2 phenotype and the profibrotic activity of cultured MDMs obtained from SSc-ILD patients, through the reduction of the gene expression and protein synthesis of CD206, CD163, MerTK, TGFβ1 and IL10.

References. 1 Cutolo M, et al. Expert Rev Clin Immunol. 2019;15:753-64. 2 Lescoat A, et al. Curr Opin Rheumatol. 2021;33:463-70. 3 Hilberg F, et al. Cancer Res. 2008;68:4774–82.

Disclosure: S. Soldano: None; **P. Montagna**: None; **E. Gotelli**: None; **A. Cere**: None; **R. Campitiello**: None; **S. Paolino**: None; **C. Pizzorni**: None; **A. Sulli**: None; **V. Smith**: Boehringer Ingelheim, 2, 5, 6, 12, Support for travel, Galapagos, 6, Janssen-Cilag, 1, 2, 5, 6; **M. Cutolo**: Amgen, 5, Boehringer Ingelheim, 5, Bristol-Myers Squibb, 5, Lab. Baldacci, 5.

Abstract Number: 0054

RA Monocytes and Monocyte-Derived Macrophages Display Heightened Inflammatory Responses, Reduced Endocytic Capacity and Distinct TET Expression Compared to PsA Monocytes

Success Amaechi[1], Megan Hanlon[2], Alyssa Gilmore[2], Dumitru Anton[2], Mary Canavan[3], Sonia Sundanum[4], Carl Orr[5], Douglas Veale[6], Viviana Marzaioli[7] and Ursula Fearon[8], [1]Trinity College Dublin, Mullingar, Ireland, [2]Molecular Rheumatology Department, Trinity Biomedical Sciences Institute, Trinity College Dublin, EULAR Centre for Arthritis and Rheumatic Diseases, St Vincent University Hospital, University College Dublin, Dublin, Ireland, [3]Molecular Rheumatology Department, Trinity Biomedical Sciences Institute, Trinity College Dublin, EULAR Centre for Arthritis and Rheumatic Diseases, St Vincent University Hospital, University College Dublin, School of Biochemistry & Immunology, Trinity Biomedical Sciences Institute, Trinity College Dublin, Dublin, Ireland, [4]EULAR Centre for Arthritis and Rheumatic Diseases, St Vincent University Hospital, University College Dublin, Dublin, Ireland, [5]Saint Vincent's University Hospital, Dublin, Ireland, [6]St.Vincent's University Hosp, Dublin, Ireland, [7]Trinity College Dublin and University College Dublin, Dublin, Ireland, [8]Trinity College Dublin, Dublin, Ireland

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: RA and PsA share various pathogenic features, while also displaying significant differences at the clinical, cellular and molecular levels. In this study, we investigate the inflammatory capacity of RA and PsA monocytes and monocyte-derived macrophages (MO-MACs), in addition to other effector functions.

Methods: Peripheral blood mononuclear cells (PBMCs) were obtained and $CD14^+$ monocytes isolated from RA and PsA patients and assessed under *ex vivo* and LPS-stimulated conditions. MO-MACs were generated via 7-day stimulation with M-CSF (50ng/mL) and polarised to M1 and M2. Inflammatory responses (IL-6, IL-1β, TNF-α, CXCL9-11, SLAMF1-7) were assessed by Real-time PCR (RT-PCR). Frequency of monocyte subsets and expression of activation (CD40) and macrophage signature markers (CD64, CD163, CD206, SLAMF7) were assessed by flow cytometry. Endocytosis assays were performed on monocytes and MO-MACs. Demethylation genes TET1-3 were assessed by RT-PCR. Finally, monocytes were cultured with a methylation inhibitor (RG108) and activator (budesonide), and pro-inflammatory responses assessed.

Results: Significant increases in LPS-induced expression of IL-6, IL-1b and CXCL9-11 (all $p< 0.05$) were observed in RA compared to PsA monocytes. Expression of SLAMF1 and 2 were significantly increased in LPS-induced RA and PsA monocytes, with SLAMF4 significantly decreased (all $p< 0.05$). Heightened responses for SLAMF7 were observed in RA vs PsA monocytes ($p< 0.05$).The increased pro-inflammatory response of LPS-stimulated monocytes in RA vs PsA was paralleled by a significant decrease in monocyte endocytic capacity, an effect that was more pronounced for RA ($p< 0.01$). Analysis of monocyte-derived macrophages demonstrated that both RA and PsA retain the hyper-inflammatory phenotype of their

precursor cell. Expression of IL-6, CXCL9 and CXCL11 were significantly higher in RA MO-M1 (all $p< 0.05$), whereas IL-1b was higher in PsA ($p< 0.05$). Heightened responses for SLAMF7 were observed for RA MO-M1 ($p< 0.05$), in contrast to SLAMF2 which was significantly increased in PsA MO-M1 ($p< 0.05$). Similarly to monocytes, endocytic capacity was reduced in RA compared to PsA M0 macrophages. RA PBMCs exhibited decreased classical ($CD14^+CD16^-$) but increased intermediate ($CD14^+CD16^+$) monocyte frequencies compared to PsA, though non-classical monocytes ($CD14^-CD16^+$) frequencies were comparable. Frequencies of CD64, CD163, CD206 and SLAMF7 were higher in all RA monocyte subsets compared to PsA, suggesting that RA monocytes have a primed pro-inflammatory macrophage phenotype. Finally, we demonstrated increased expression of methylation markers TET2 in RA monocytes ($p< 0.05$) and of TET3 in PsA monocytes ($p< 0.05$). Budesonide decreased the expression of IL-6, TNF-a and IL-1b in *ex vivo* and LPS-stimulated monocytes.

Conclusion: Monocytes are inherently more pro-inflammatory and activated than PsA monocytes, an effect that is maintained following differentiation into macrophage. The distinct inflammatory pre-programming of monocytes may also involve altered epigenetic alterations.

Disclosure: S. Amaechi: None; **M. Hanlon**: None; **A. Gilmore**: None; **D. Anton**: None; **M. Canavan**: None; **S. Sundanum**: None; **C. Orr**: None; **D. Veale**: None; **V. Marzaioli**: None; **U. Fearon**: None.

Abstract Number: 0055

Elevated LINE-1 Expression in SLE Keratinocytes Leads to LINE-1 Reverse Transcriptase-dependent Type I Interferon Responses

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Long Interspersed Element-1 (LINE-1) are retrotransposable DNA elements that make up ~17% of the human genome, and their role in health and disease is still being evaluated. Published studies have suggested that LINE-1 may contribute to the development and progression of autoimmune diseases such as lupus by triggering the type I interferon (IFN) production via activation of the innate immune system through nucleic acid sensing pathways. Additionally, studies have shown that lupus patients have higher level of LINE-1 in kidneys and blood compared to healthy controls, but expression of LINE-1 in SLE skin, where type I IFN signatures are dominant, has not been studied. We thus examined LINE-1 RNA and protein expression in lupus patient skin biopsies, and the impact on inflammatory signals upon a LINE-1 reverse transcriptase (RT) inhibitor in cellular and murine models.

Methods: All human subjects gave informed, written consent for the study. Formalin-fixed, paraffin embedded skin sections from non-lesional, non-sun exposed and UVB-treated skin were examined for changes in interferon-stimulated gene (ISG) expression via RNA-seq, LINE-1 ORF1p and phospho-STING via immunohistochemistry, and for LINE-1 *ORF1* and *ORF2* transcripts by RNA-scope. A novel, potent LINE-1 RT inhibitor, RPT-A, was characterized using LINE-1 RT enzyme assay, cellular LINE-1 retrotransposition assay, a cellular model of Aicardi-Goutières syndrome, and a UV-irradiated keratinocyte model. To investigate its impact on type I interferon pathway in lupus settings, we assessed its activity in regulating ISGs

in UV-irradiated keratinocytes from lupus patients and healthy controls by RNA-seq. We also studied the impact of RPT-A on disease in a TREX1 knockout interferonopathy mouse model.

Results: Non-lesional biopsies from SLE skin exhibit increased ORF1p protein and increased ORF2 transcript staining and a concurrent increase in phospho-STING staining, suggestive of activation of nucleic acid sensing pathways. UV stimulation increased expression of LINE-1 transcript and protein in both healthy control and SLE skin. Tri-phosphorylated form of RPT-A inhibited enzymatic activity of LINE-1 RT with an IC_{50} of 0.03 μM. RPT-A inhibited cellular LINE-1 retrotransposition, decitabine-induced interferon response in TREX1 deficient THP-1 cells, and UV-induced phospho-TBK1 in human HaCaT keratinocytes. LINE-1 knockdown with shRNA and siRNA in the THP1 and HaCaT cells mimicked the inhibitory effect of RPT-A. Keratinocyte cell lines derived from lupus patients pre-treated with RPT-A exhibit reduced ISGs upon UV irradiation in a dose-dependent fashion. Further, 5-6 week old TREX1 knockout mice dosed with RPT-A orally once a day for 28 days exhibited reduced serum anti-dsDNA antibodies, reduced myocardial ISGs and reduced immune infiltrates in the heart and kidney.

Conclusion: LINE-1 RNA and protein are increased in SLE skin and is induced by UV exposure. Inhibition of LINE-1 RT activity results in decreased ISG expression and improved disease activity in a murine interferonopathy model. Inhibition of LINE-1 reverse transcriptase holds promise as a novel therapy for diseases in which type I IFNs drive disease.

Disclosure: W. Miao: Rome Therapeutics, 3; **D. Rios**: Rome Therapeutics, 3; **M. Gharaee-Kermani**: Rome Therapeutics, 5; **C. Dobry**: Rome Therapeutics, 5; **A. Jaroszewicz**: Rome Therapeutics, 3; **C. Arisdakessian**: Rome Therapeutics, 3; **E. Garcia-Rivera**: Rome Therapeutics, 3; **N. Hafeez**: Rome Therapeutics, 3; **B. Desrosiers**: Rome Therapeutics, 3; **J. Floro**: Rome Therapeutics, 3; **J. Steranka**: Rome Therapeutics, 3; **M. Fromer**: Rome Therapeutics, 3; **D. Zaller**: Rome Therapeutics, 3; **J. Kahlenberg**: AstraZeneca, 1, Bristol-Myers Squibb(BMS), 2, 5, EMD Serano, 2, exo therapeutics, 2, Gilead, 2, GlaxoSmithKlein(GSK), 1, horizon Therapeutics, 2, Janssen, 5, Pfizer, 2, ROME Therapeutics, 2, 5, Rome Therapeutics, 5, Ventus Therapeutics, 2, 5.

Abstract Number: 0056

The Activation of cGAS-STING Pathway in Systemic Lupus Erythematosus

Jie An[1], Stephen Wilson[2], Jill Henault[3] and Keith Elkon[1], [1]University of Washington, Seattle, WA, [2]Bristol Myers Squibb, Cambridge, MA, [3]Bristol Myers Squibb, Acton, MA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The majority of patients with SLE show a striking Type I Interferon (IFN-I) signature in their peripheral blood. Although this signature can be generated by immune complex activation of Toll Like Receptors (TLRs) in vitro, the in vivo mechanisms are not known. Using ex vivo derived peripheral blood mononuclear cell (PBMC) samples from patients, we previously showed that another IFN-I pathway, called cGAS-STING, is activated in ~15% of SLE patients. In the present study, our aims were i) to determine the frequency of cGAS-STING activation in additional SLE cohorts as well as patients with Sjogren's syndrome; ii) to perform longitudinal studies of cGAS-STING positive (cGAMP+) SLE patients; and iii) to evaluate whether activation of downstream pathways such as phospho-STING (P-STING) could be detected.

Methods: The following groups were studied: Healthy Controls (HC) (n=25), SLE (n=52), primary Sjögren's syndrome (SS) (n=20), and secondary SS (SLE/SS) (n=8). SLE disease activity was determined by the SLEDAI. PBMCs were purified from blood by Ficoll density gradient centrifugation and the cells were lysed with sonication. cGAMP concentrations were quantified with 2'-3' cGAMP ELISA kit (Cayman Chemical). Phosphorylated STING and total STING protein were measured with Homogeneous Time Resolved Fluorescence (HTRF) Phospho-STING Ser366 and Total STING Cellular detection Kit. Results were expressed as the ratio of P-STING to STING.

Results: When compared to HC, the new cohorts of SLE patients had a significant increase of cGAMP concentration in PBMCs ($p < 0.05$). There was no statistically significant increase in cGAMP concentrations in SS and SLE/SS PBMC compared to HC. The concentrations of cGAMP in PBMC from SLE patients were also higher compared to SS ($p < 0.01$) but not SLE/SS.The overall frequency of detection of cGAMP by ELISA was 17% in SLE, 0% in SS, and 25% in SLE/SS patients. When longitudinal studies were performed in 6 SLE patients who had tested positive for PBMC cGAMP, 3 of the 6 SLE patients (50%) showed cGAMP positivity on at least two different occasions whereas the other 3 SLE patients only showed cGAMP positivity in their initial clinic visit. Of note, the SLEDAI score and cGAMP level from one patient showed same trend of continued decrease over the course of three different clinic visits. Although no statistically significant difference in the P-STING/STING ratio determined by the HTRF assay was detected when SLE, SS and SLE/SS were compared to HC, it is of interest that SLE patients with higher cGAMP expression also had higher P-STING/STING ratios.

Conclusion: Detection of both cGAMP and phospho-STING in new cohorts of SLE patients confirm activation of the cGAS-STING pathway in a proportion of SLE patients and indicate that the cGAS-STING pathway likely contributes to IFN-I production in SLE. Longitudinal detection of cGAMP in 50% of cGAMP+ patients suggest that activation of this pathway may be persistent. Further defining the molecular mechanisms responsible for activation of the cGAS-STING pathway will contribute to our understanding of IFN-I stimulation and targeted approaches to inhibit cGAS-STING pathway activation may be a useful therapeutic strategy in a subset of SLE patients.

Disclosure: J. An: None; **S. Wilson**: Bristol-Myers Squibb(BMS), 3; **J. Henault**: Bristol-Myers Squibb(BMS), 3; **K. Elkon**: None.

Abstract Number: 0057

GM-CSF receptor/SYK/JNK/FOXO1/CD11c Signaling Enhances Cell Migration to Promote Atherosclerosis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

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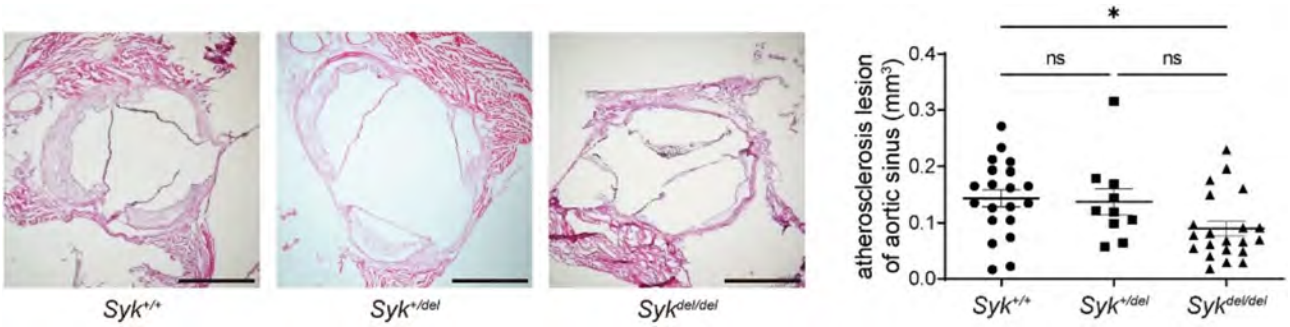
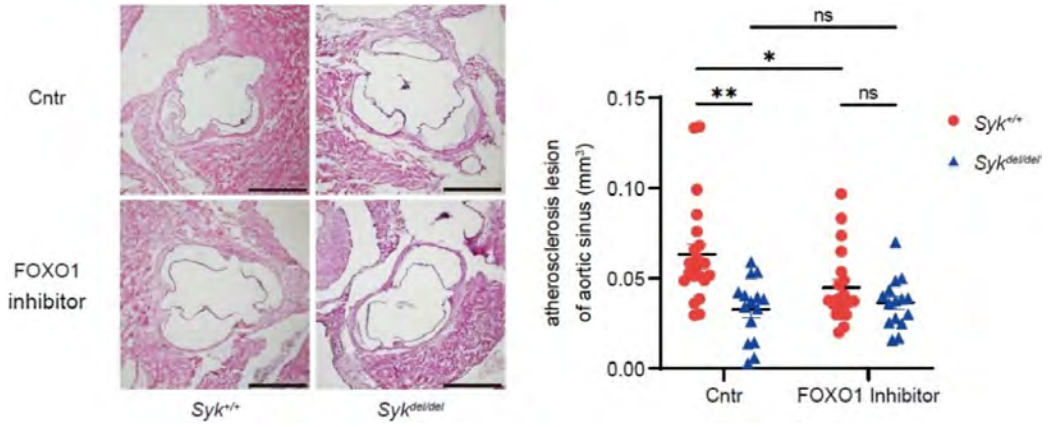
Background/Purpose: Atherosclerosis involves both dyslipidemia and chronic inflammatory disease; however, lipid-lowering agents do not completely eliminate the risks of cardiovascular events. In addition, chronic systemic inflammatory diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are complicated by atherosclerosis. This mutual relationship suggests that a shared physiological pathway might regulate inflammatory responses in both atherosclerosis and inflammatory diseases. Interestingly, spleen tyrosine kinase (SYK), an enzyme abundantly expressed in hematopoietic cells, is involved in atherosclerosis, RA, and SLE. We aimed to identify a shared therapeutic target related to *Syk* for atherosclerosis and inflammatory diseases.

Methods: To determine whether SYK is involved in atherosclerosis through the inflammatory response and elucidate the mechanism of SYK signaling, we utilized *Syk*-knockout atherosclerosis-prone mice. Cell migration capacity was assessed using wound scratch and transwell migration assays. RNA-seq, flow cytometry, and adhesion assay were performed to identify a cell migration-related gene. We investigated the transcription factor that regulates the identified cell migration-related gene using reporter assays and flow cytometry. Additionally, we identified a molecule downstream of SYK signaling that mediates the transcription factor's activity using flow cytometry. Furthermore, we evaluated whether the inhibition of the transcription factor could suppress the identified cell migration-related gene in monocyte and ameliorate atherosclerosis.

Results: Our results revealed that *Syk*-knockout mice exhibited reduced atherosclerosis. Wound scratch and transwell migration assays showed reduced cell migration in *Syk*-knockout bone marrow-derived macrophages (BMDM). RNA-seq analysis demonstrated decreased expression of CD11c, an adhesion molecule involved in inflammatory cell infiltration, in



SYK promotes atherosclerosis in mice



FOXO1 inhibitor suppresses atherosclerosis in mice

Syk-knockout bone marrow monocytes. Peripheral monocytes from *Syk*-knockout mice also exhibited reduced CD11c expression. Bocking CD11c protein resulted in inhibited adhesion capacity. A reporter assay showed SYK associated with approximately 1,000 upstream of the CD11c transcription starting site. The in silico analysis predicted forkhead box protein O1 (FOXO1) might bind to the predicted sequences by the reporter assay. The inhibitor of FOXO1 suppressed the CD11c expression of granulocyte–macrophage colony-stimulating factor receptor (GM-CSF) primed BMDM using flow cytometry. In addition, the inhibition of c-Jun amino-terminal kinase (JNK) suppressed the CD11c expression of GM-CSF primed BMDM. Finally, the FOXO1 inhibitor reduced the CD11c expression of bone marrow and peripheral monocyte and mitigated atherosclerosis in mice.

Conclusion: We discovered the GM-CSF receptor/SYK/JNK/FOXO1/CD11c signaling pathway. FOXO1 could be a novel potential therapeutic target for atherosclerosis and inflammatory diseases.

Disclosure: D. Tsukui: None; **K. Yoshitaka**: None; **H. Kono**: AbbVie/Abbott, 6, Asahikasei Pharm, 5, 6, Asteras Pharm, 6, Ayumi Pharm, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Chugai Pharm, 5, 6, Gilead, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, Kissei, 2, 6, Pfizer, 6, Tanabe Mitsubishi, 6, UCB, 6.

Abstract Number: 0058

Macrophage Extracellular Traps Induced by Monosodium Urate or Calcium Pyrophosphate Crystals Form Independently of NLRP3 Inflammasome Activation

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SESSION INFORMATION
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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Monosodium urate (MSU) and calcium pyrophosphate (CPP) crystals are potent inducers of inflammation by activation of the inflammasome in neutrophils phagocytosing the crystals and undergoing cell death by extracellular trap formation (NETosis), resulting in flares of gout or pseudogout. However, crystal deposition does not always lead to inflammatory flares. Whether there are homeostatic mechanisms preventing activation of the inflammasome in the presence of crystal deposits is unclear. We have investigated the role of extracellular trap formation of macrophages (MET) stimulated with MSU and CPP crystals.

Methods: MET formation was assessed in THP-1 cells, differentiated with phorbol-12-myristate-13-acetate (PMA), and human monocytes from healthy donors, isolated by magnetic bead separation and differentiated in vitro with GM-CSF or M-CSF respectively, to obtain M1 and M2 macrophages. Macrophages were stimulated with MSU and CPP crystals with or without priming with IFNg/LPS. METs were detected by DNA staining with SytoxGreen and Hoechst and immunostaining of citrullinated Histone 3 and myeloperoxidase and subsequently quantified with an automated imaging system. IL-1b production was measured by ELISA. To assess the dependence of METosis on NLRP3, macrophages were stimulated in the presence or absence of inhibitors of NLRP3, caspase 1 and in THP-1 cells deficient for NLRP3 and gasdermin D

(GSDMD). In addition, MET formation was assessed in peritoneal cavity macrophages of C57BL6/c and caspase-1/-11^{KO}, NRLP3^{KO} and GSDMD^{KO} mice.

Results: THP-1 cells were able to release MET after both MSU and CPP crystal stimulation independent of priming with LPS/IFNg. Whereas crystal stimulation of primary human monocytes did not lead to MET formation, in vitro differentiated M1 and M2 macrophages released METs upon stimulation with crystals. In contrast, crystal stimulation alone did not result in IL-1b production but required LPS/IFNg priming in M1 macrophages, whereas M2 did not secrete IL-1b irrespective of priming. Using pharmacological inhibitors of NLRP3 and Caspase 1/4 did not inhibit MET formation after crystal stimulation. Likewise, MET were found in crystal stimulated THP-1 cells deficient for NLRP3 and GSDMD. Furthermore, MET formation could be detected in peritoneal macrophages from wild type C57BL6/c as well as NLRP3, Caspase-1 and GSDMD deficient mice, documenting independence of inflammasome activation in tissue resident macrophages.

Conclusion: We report the novel observation of MSU and CPP crystal induced formation of MET. METosis required differentiation of monocytes to M1 or M2 macrophages, was independent of inflammasome activation and did not induce IL-1b secretion in the absence of priming with LPS/IFNg. These results suggest that MET formation may represent an alternative mechanism by which macrophages may trap crystals without provoking pyroptosis and inflammatory flares.

Disclosure: D. Daoudlarian: None; **A. Tiaden**: None; **S. Giaglis**: None; **U. Walker**: None; **P. Broz**: None; **T. Maningold**: None; **D. Kyburz**: Abbvie, 1, 5, Eli Lilly, 1, 6, Janssen, 1, 6, Novartis, 1, 6, Pfizer, 1.

Abstract Number: 0059

GM-CSF by Natural Killer Cells Drives Inflammatory Arthritis in HIV-Infected Humanized Mice

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Human immunodeficiency virus (HIV) remains a significant life-threatening agent and burden on public health. Lesser studied and understood aspects of HIV include HIV-associated inflammatory arthritis and the role NK cells and cytokines like GM-CSF have on its development. By utilizing humanized mice with human cytokine knockins that better support a human immune system than other models, we studied HIV-associated arthritis to better understand its development and progression.

Methods: MISTRG-IL15 mice (human M-CSF/GM-CSF, IL-3, SIRPα, TPO, RAG2 -/-, IL2rg-/-, and IL-15 knocked into the respective endogenous mouse loci) were reconstituted with CD34+ hematopoietic stem cells obtained from human fetal cord blood. After checking for engraftment after 6-8 weeks, we infected reconstituted mice with HIV. Synovial tissues were obtained from the knee joints of the hind limbs at different time points and processed into single cell suspensions. Intercellular staining was performed on cells incubated with PMA/Ionomycin for 4 hours and then permeabilized and fixed for flow

cytometry. NK cells were defined as CD3-CD56+. Histochemistry was also performed on hind paws that were fixed in 4% paraformaldehyde. Samples were then sectioned and stained with H&E for histologic analysis. Studies also involved depletion of NK cells and macrophages, Antiretroviral therapy (ART), and viral strains with unique tropisms.

Results: The majority of humanized MISTRG-IL15 mice developed inflammatory arthritis after HIV infection. Significant increases in total inflammatory cells and NK cells were seen in the synovial tissue throughout the course of infection. GM-CSF producing NK cells also increased throughout the course of HIV infection. Late in the course of infection, IFNγ- and granzyme B-producing NK cells increased, along with a pro-inflammatory environment in the synovial tissue. Histologic analysis showed increased cellular infiltrate in the synovium by at 8 weeks of infection with erosive changes. ART eliminated cellular infiltration while cessation of therapy resulted in return of cellular infiltration in synovial tissue. Use of a chemokine receptor-tropic HIV virus that does not infect macrophages (X4-tropic) showed reduced pro-inflammatory cytokine production by NK cells, strongly suggesting HIV-infected macrophages induced the NK cell changes. Depletion of NK cells resulted in blockade of development of inflammatory arthritis.

Conclusion: We have found a unique role of GM-CSF produced by NK cells contributing to the development of HIV-associated inflammatory arthritis in our unique mouse model. In addition to providing a model to study arthritis induced by other human pathogens, findings from such studies will provide mechanistic understanding of inflammatory arthritis.

Disclosure: C. Sungur: None; **L. Yang**: None; **L. Shan**: None; **w. Yokoyama**: None.

Abstract Number: 0060

Serpin B1 Modulation of Immune Complex-Mediated Neutrophil Activation and NET-formation Requires Its Chymotrypsin-like Inhibitory Activity

Ting Wang[1], Philip Pemberton[2] and **Christian Lood**[1], [1]University of Washington, Seattle, WA, [2]Redd Pharmaceuticals, Belmont, CA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoantibody-antigen complex-driven formation of neutrophil extracellular traps (NETs) is a major contributing factor to the pathophysiology and clinical manifestations of many different autoimmune diseases including SLE and RA. Inhibition of NET formation improves outcomes in animal models of autoimmune diseases. It has been previously shown that a neutrophil-resident proteinase inhibitor, serpin B1 (sB1) can regulate NET formation mediated by several agonists. However, it is currently unknown if sB1 can block immune complex (IC)-mediated NET formation. This study was designed to determine if sB1 can inhibit IC-mediated NET formation and if so, explore the molecular basis of the inhibition.

Methods: Recombinant forms of wild-type and variant sB1 that lacked protease-inhibitory activity or specifically inhibited elastase-like (neutrophil elastase [hNE], proteinase 3 [hPR3]) or chymotrypsin-like (e.g. cathepsin G [hCatG]) neutrophil serine proteases (NSP's) were tested for their ability to block NET formation driven by RNP-containing ICs. In brief, human neutrophils were incubated in poly-L-lysine-coated tissue culture plates for 60 minutes in the presence of select reagents at

varying concentrations prior to addition of ICs, PMA or A23187. After 4 hours of incubation, NETs were detached with micrococcal nuclease and analyzed for DNA content by staining with sytox green and peroxidase activity using the synthetic substrate TMB. Relative surface levels of CD66b, CD11b, and CD63, as well as ROS production, on treated neutrophils were measured by flow cytometry. Data were analyzed by FlowJo (Tree Star, Inc.).

Results: sB1 variants lacking protease inhibitory activity were unable to block NET formation. In contrast, the sB1 protein that could specifically inhibit chymotrypsin-like proteinases blocked NET formation whereas the sB1 protein that could specifically inhibit elastase-like proteinases did not. Consistently, the specific neutrophil elastase inhibitor had limited effect on NET formation, whereas the specific small molecule hCatG inhibitor also blocked NET formation providing further evidence implicating hCatG in the process of IC-driven NET formation. An oxidation resistant sB1 variant (C344A) effectively inhibited IC-mediated NET formation and was the only agent tested that significantly increased the levels of all three adhesion/activation markers on the surface of activated neutrophils. In addition, it significantly boosted intracellular ROS production.

Conclusion: sB1 can inhibit IC-mediated NET formation and does so in a hNE- and hPR3- independent manner. Our evidence is the first to suggest that hCatG released during neutrophil activation is directly involved in triggering IC-mediated NET formation. Future studies are needed to determine the role of sB1 on other neutrophil effector functions, including phagocytosis, adhesion and trafficking.

Disclosure: T. Wang: None; **P. Pemberton**: Redd Pharmaceuticals Inc, 3, 4, 8, 10; **C. Lood**: Amytryx, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Citryll, 2, Eli Lilly, 5, Gilead, 5, Horizon Therapeutics, 5, Pfizer, 5, Redd Pharma, 5, 11.

Abstract Number: 0061

Discovery of a RIPK2 Scaffolding Inhibitor for the Treatment of Joint Autoimmune Diseases

Marta Wlodarska[1], Chad Van Huis[2], Florian Hoss[3], Rosana Meyer[1], Xiaokang Lu[2], Dominik Koelmel[2], Brian Sanchez[2], Chuck Lesch[2], Alissa Telling[2], Martin Minns[1], Nneka Mbah[2], Isabelle Lacan[1], Robert Aversa[1], Charles Lesburg[1], Carmen Yu[2], Stephen Soisson[1], Natalie Dales[1], Darryl Patrick[1], Anthony Opipari[2], Shifeng Pan[4] and Luigi Franchi[2], [1]Odyssey Therapeutics, Boston, MA, [2]Odyssey Therapeutics, Ann Arbor, MI, [3]Odyssey Therapeutics, Frankfurt, Germany, [4]Odyssey Therapeutics, San Diego, CA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Receptor interacting protein kinase 2 (RIPK2) is a key signaling node for inflammation caused by peptidoglycan (PGN). In the intestine, RIPK2 integrates signaling originating from the microbiota and amplifies pro-inflammatory responses. Hence, blocking RIPK2 is an attractive strategy to treat inflammatory bowel disease. Since peptidoglycan is present in the serum and joints in patients with rheumatic diseases and is thought to drive sterile inflammation, RIPK2 inhibitors may also be a novel approach to treat rheumatoid arthritis, osteoarthritis, and spondyloarthritis. While the kinase function of RIPK2 is dispensable for downstream signaling, its ability to recruit and activate

the E3 ubiquitin ligase, XIAP, is critical for RIPK2 ubiquitination and signal transduction. On this basis, we developed a RIPK2 scaffolding inhibitor that binds to RIPK2, prevents interaction with XIAP, and blocks proinflammatory responses in vitro and in vivo.

Methods: Direct inhibition of RIPK2 scaffolding with XIAP was demonstrated using surface plasmon resonance and a cellular nanoBRET assay. Inhibitory activity was evaluated by NF-kB dependent gene expression in NOD1 and NOD2 reporter cell lines and cytokine production in primary human cells stimulated with PGN fragments or Toll like receptor (TLR) ligands. Potency and selectivity was compared to GSK-559, a RIPK2 kinase inhibitor, and efficacy of the Odyssey RIPK2 scaffolding inhibitor in vivo was evaluated in a PGN-challenge mouse model.

Results: RIPK2 scaffolding inhibitor blocks the binding of recombinant XIAP with RIPK2 in vitro and in cells. RIPK2 scaffolding inhibitor blocks MAPK pathway activation, NF-kB activation, and cytokine production (e.g., TNF, IL-23, and TL1A) in human monocytes and macrophages stimulated with PGN fragments, but not TLR ligands. We observed a synergistic cytokine response in human monocytes stimulated by both NOD1/2 and TLR ligands. This synergistic response is blocked by treatment with a scaffolding inhibitor, but not a RIPK2 kinase inhibitor. Oral administration of the RIPK2 scaffolding inhibitor dose-dependently reduced production of TNF, IL-6, and MCP-1 in response to PGN.

Conclusion: We describe a potent and selective RIPK2 scaffolding inhibitor and demonstrate that blocking scaffolding is necessary to maximally inhibit RIPK2 activation in response to the microbiota. These data show the therapeutic potential of using a RIPK2 scaffolding inhibitor to prevent pathogenic responses to microbiota from which inflammatory intestinal and rheumatic diseases originate.

Disclosure: M. Wlodarska: None; **C. Van Huis**: None; **F. Hoss**: None; **R. Meyer**: None; **X. Lu**: None; **D. Koelmel**: None; **B. Sanchez**: None; **C. Lesch**: None; **A. Telling**: None; **M. Minns**: None; **N. Mbah**: None; **I. Lacan**: None; **R. Aversa**: None; **C. Lesburg**: None; **C. Yu**: None; **S. Soisson**: Merck/MSD, 3, 11; **N. Dales**: None; **D. Patrick**: None; **A. Opipari**: Odyssey Therapeutics, 3; **S. Pan**: None; **L. Franchi**: Odyssey Therapeutics, 3, 11.

Abstract Number: 0062

Differential Metabolic Profiles, Activation and Circadian Dynamics in Rheumatoid Arthritis and Psoriatic Arthritis Circulatory Monocytes

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: While Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA) share many features, they are distinct in clinical presentation and molecular profile. As monocytes are crucial innate effector cells, we investigate metabolic reprogramming of circulating monocytes in RA and PsA, and pathways involved in activation, circadian rhythm and mitochondrial dynamics.

Methods: PBMCs and CD14^{+} monocytes were isolated from RA and PsA patients. Frequency of monocyte subsets and immune/metabolism markers (PDL-1, HIF1a, pS6, TLR2 and pAKT) on specific subsets were assessed by flow cytometry. Metabolic analysis was performed on basal and LPS stimulated monocytes by RT-PCR, Seahorse-XFe-technology and mitotracker assays. In parallel, genes involved in circadian rhythm (BMAL1, PER1, PER2) and mitochondrial fission and fusion (DRP1, MFN1) and related effectors (RORα and NFIL3) were assessed by RT-PCR.

Results: Baseline ECAR following LPS stimulation was induced, with minimal effect observed for OCR, resulting in a significant shift of RA and PsA monocytes towards glycolysis ($p< 0.05$). A significant reduction in max respiratory capacity and ATP synthesis was also observed for PsA vs RA (all $p< 0.05$). Differential expression of PDL-1, pS6 and HIF1α were observed between RA and PsA monocytes, with inverse expression observed between classical and intermediate sub-populations. LPS modulated key metabolic genes HIF1α ($p< 0.001$) and NDufB5 ($p< 0.05$), an effect more prominent in RA monocytes. Supporting mitochondrial dysfunction in RA, LPS stimulation induced mitochondrial fission regulator DRP1 in RA ($p< 0.0001$), but not PsA. For circadian rhythm genes, LPS-stimulation inhibited BMAL1($p< 0.05$) and PER1 ($p< 0.001$) in both RA and PsA, with reduction in PER2 only observed in PsA ($p< 0.05$). Finally, downstream effectors RORα and NFIL3 were increased with LPS in RA monocytes, with no effect observed for PsA.

Conclusion: RA and PsA CD14+ monocytes display a shift towards a glycolytic phenotype. Metabolic/immune markers are differentially expressed between RA and PsA monocytes, expression of which are inversed in classical vs intermediate monocytes. Altered regulation of genes involved in circadian rhythm suggest differences in the cellular clock, and effect that was more pronounced in RA compared to PsA monocytes. This was paralleled by altered mitochondrial dynamics, with significant induction of mitochondrial fission regulator DRP1 in RA monocytes. Taken together, this data, supports differential metabolic dysregulation and activation of RA and PsA monocytes, effects that may involve changes in the cellular clock, inducing monocyte pathogenic mechanisms.

Disclosure: A. Gilmore: None; **S. Amaechi**: None; **M. Hanlon**: None; **D. Anton**: None; **C. Orr**: None; **V. Marzaioli**: None; **D. Veale**: None; **U. Fearon**: None.

Abstract Number: 0063

Investigating Macrophage Repopulation in the Synovium

Jessica Maciuch[1], Yidan Wang[2], Slim Fourati[1], Harris Perlman[1] and Deborah Winter[3], [1]Northwestern University, Chicago, IL, [2]Northwestern University, Hanover Park, IL, [3]Northwestern University, Skokie, IL

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis (RA) is an autoimmune disease characterized by chronic inflammation of the joints. Macrophages are a key mediator of pro-inflammatory signaling, contributing to inflammation and subsequent joint destruction seen in RA. Recent research has revealed that macrophages in the joint synovium exhibit phenotypically distinct subpopulations, which may diverge in contributing towards either RA pathogenesis or potential remission. There is a need to further understand how synovial macrophage subpopulations are repopulated after disruption to better characterize varying phenotypic trajectories.

Methods: Bone marrow chimeras (BMC) were generated by transplanting cells from CD45.1 mice (donor) into CD45.2 mice (recipient) that were irradiated with shielded ankle joints. Ankle joints were extracted from BMC controls (day 0) and those treated with clodronate-laden liposomes (day 7) to deplete circulating monocytes. CITE-seq was performed on sorted synovial macrophages (CD45+CD11b+CD4-CD8-Ly6G-SiglecF-NK1.1-CD64+ cells) using the 10x Chromium instrument and processed using the CellRanger pipeline. Clustering, differential gene expression analysis, and pathway analysis was performed using Seurat and fgsea for each timepoint separately and combined. Trajectory analysis was performed using Monocle after merging day 0 and day 7 data.

Results: Distinct macrophage subpopulations were seen in both day 0 and day 7 samples. MHCII genes (H2-Eb1, H2-Ab1, H2-Aa) were differentially expressed in CD45.1-enriched clusters at day 0. For both timepoints, clusters of synovial lining macrophages (CX3CR1+) were CD45.2-enriched. Genes associated with toll-like receptor signaling pathways (Tlr2, Tlr7, Tlr8) marked CD45.2-enriched clusters at day 0. Genes coding for Ap1 (Jun), a major transcription factor regulating the pro-inflammatory program of macrophages, were repressed at day 7 compared to day 0. Macrophages at day 7 differentially expressed genes coding for metalloproteases (Mmp12, Mmp14, Mmp19) implicated in extracellular matrix degradation, suggesting heightened migratory capacity. Enrichment for pathways associated with extracellular matrix interactions were confirmed in our trajectory analysis from day 0 to day 7.

Conclusion: These results suggest the existence of transcriptional heterogeneity among macrophages in the synovium, as well as changes over time following disruption. Future experiments will test how macrophage repopulation is altered under inflammatory conditions.

Disclosure: J. Maciuch: None; **Y. Wang**: None; **S. Fourati**: None; **H. Perlman**: None; **D. Winter**: Pfizer, 2.

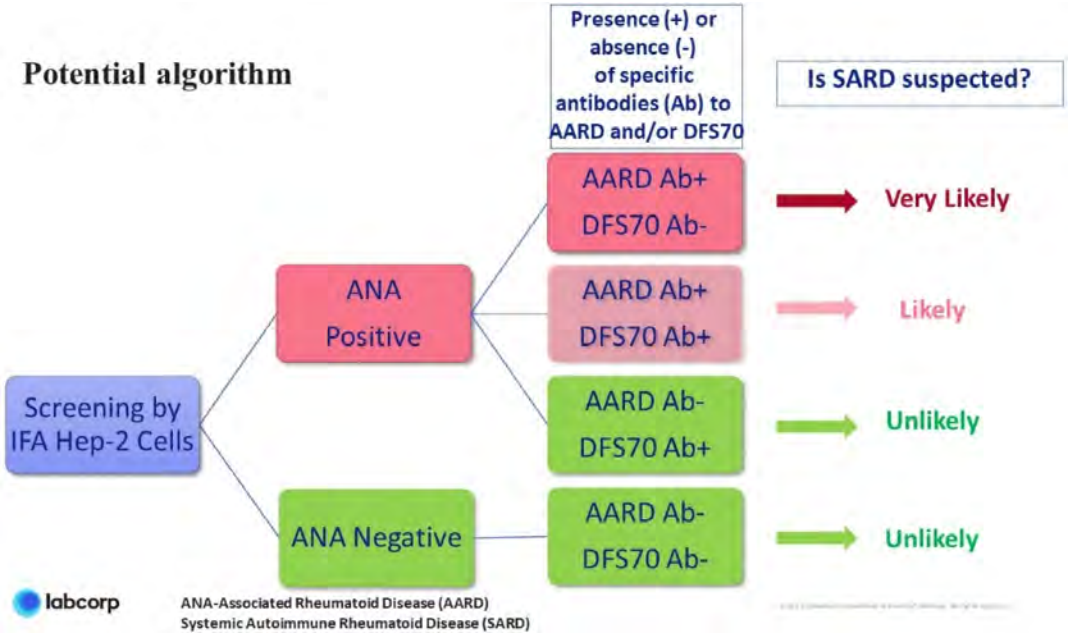
Abstract Number: 0064

Correlation of Anti-DFS70 Autoantibodies by ELISA with HEp-2 Cells DFS Pattern by IFA

Vincent ricchiuti[1], Michael Nappi[2], Kelly Chun[2], Ajay Grover[1] and Rubio Punzalan[2], [1]Labcorp, Dublin, OH, [2]Labcorp, Calabasas, CA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The discovery and characterization of the dense fine speckled (DFS, ICAP AC-2) nuclear pattern of antinuclear autoantibodies (ANA) detected in HEp-2 cells by indirect immunofluorescence assay (IFA) more than 20 years ago has transformed our view on ANA testing. Anti-DFS70 antibodies are associated with this DFS pattern by IFA while their clinical associations remain an immunological enigma. Unlike other ANA, there is a growing body of evidence that anti-DFS70 antibodies, when present in high titers and in isolation (i.e. in the absence of any accompanying autoimmune disease-specific antibodies) are useful to aid in the exclusion of systemic autoimmune rheumatic diseases (SARD), also called ANA-associated rheumatic diseases (AARD). The correlation between the DFS pattern by IFA observed through HEp-2 cells and the presence of anti-DFS70 antibodies detected by enzyme-linked immunosorbent assay (ELISA) has been



the subject of increasing interest in autoimmune research. This study provides supporting evidence of the significant association between the DFS pattern by IFA and anti-DFS70 antibodies by ELISA and offers a potential algorithm to triage patients to exclude SARD/AARD.

Methods: 150 positive and 20 negative serum specimens for DFS pattern by HEp-2 cells by IFA, (Sprinter XL/EuroPattern, Euroimmun, NJ), were analyzed for presence of anti-DFS70 antibodies by ELISA (QuantaLyzer 3000, Werfen CA). The agreement of the DFS70 by ELISA was established by direct comparison of results with those generated by an established or reference method HEp-2 cells DFS pattern by IFA.

Results: When compared, samples between DFS pattern by HEp-2 cells IFA and anti-DFS70 antibodies by ELISA yielded an agreement of 97.1% (95% confidence intervals of 93.1-98.7%), McNemar's Test Chi Square of p >0.999, with a relative sensitivity of 98.0% and a specificity of 90.0%.We propose the following potential algorithm to triage patients with or without SARD/AARD (see figure).

Conclusion: This study demonstrated that accurate reading of DFS pattern by HEp-2 IFA identification provided a significant rate of anti-DFS70 antibodies detected by ELISA. The correlation between the DFS pattern by HEp-2 IFA observed and the presence of anti-DFS70 antibodies detected by ELISA could provide valuable insights into autoimmune diseases. The combined use of these techniques allows for a more comprehensive assessment of autoantibody profiles, aiding in accurate classification, prognosis, and personalized treatment strategies. Further research is needed to elucidate the clinical implications and significance of this anti-DFS antibodies in different conditions.

Disclosure: V. ricchiuti: None; **M. Nappi**: LabCorp, 3; **K. Chun**: None; **A. Grover**: None; **R. Punzalan**: None.

Abstract Number: 0066

Mitochondrial Dysfunction and Fatigue in Sjögren's Disease

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren's disease (SjD) is a chronic, autoimmune condition with diminished lacrimal and salivary gland secretion leading to keratoconjunctivitis sicca and xerostomia, respectively. In addition, subjects with SjD experience significant fatigue. We hypothesized that SjD subjects have mitochondrial dysfunction and that fatigue will be associated with mitochondrial dysfunction in a subset of subjects with SjD.

Methods: Seventeen SjD subjects and eight age-matched subjects underwent a fasting blood draw and completed fatigue questionnaires (Bowman's SjD, Fatigue Impact Scale, Multidimensional assessment of fatigue, Centers for Epidemiological Studies-Depression Scale, Fatigue Severity Scale, The Rheumatology Attitudes Index or Helplessness Score, Modified Health Assessment, Validation of the Functioning in Chronic Illness Scale, SLEEP 1, and SLEEP 2). T cells were purified through negative selection using Miltenyi Biotech B and T cell isolation kit and analyzed for mitochondrial oxygen consumption rate and extracellular acidification rate (glycolysis) using the Seahorse XF24 assay. Mitochondrial macrostructure of PBMC's isolated from SjD or control subjects was analyzed using transmission electron microscopy.

Results: There was no significant difference in the ages of the controls and the SjD subjects (52.25 years ± 3.21 vs 59.88 years ± 3.17 respectively, p=0.17) and there were no age-related changes in the oxygen consumption rate. However, we observed significantly decreased basal, ATP-linked, and maximal respiration as well as reserve capacity in the T cells of SjD subjects compared to controls. We found that scores from the Bowman fatigue questionnaire correlated the best with basal oxygen consumption (r^2=0.34, p=0.014), ATP-linked respiration (r^2=0.36, p=0.011), maximal respiration (r^2=0.491, p=0.0017), and reserve capacity (r^2=0.486, p=0.0019) in SjD. Scores from the general fatigue category (pain/discomfort) related to the question "the worst problem with pains, the worst discomfort I've experienced in 2 weeks" provided most of the power for these associations. Scores from Bowman mental fatigue questionnaire showed a trend towards correlating with ATP-linked respiration (r2=0.22, p=0.0588). Fatigue Severity Scale scores correlated only with mitochondrial reserve capacity in SjD (r^2=0.244, p=0.044). Transmission electron microscopy studies clearly show swollen mitochondria in the lymphocytes from SjD, with the cristae appearing to be prominently disorganized compared to mitochondria from the control.

Conclusion: Mitochondrial dysfunction, associated with fatigue, appears to be a significant problem in SjD.

Disclosure: B. Kurien: None; **R. Wood**: None; **G. Pharaoh**: None; **J. Cavett**: None; **V. Lewis**: None; **B. Shylesh**: None; **L. radfar**: None; **A. Rasmussen**: None; **C. Lessard**: Janssen, 5; **A. Farris**: Janssen Research and Development, LLC, 5; **K. Sivils**: Janssen, 3; **K. Koelsch**: None; **H. Van Remmen**: None; **R. Scofield**: None.

Abstract Number: 0067

Dimethyl Fumarate Modulates T Cell Metabolism and Function in Systemic Lupus Erythematosus Patient Samples

Loren Kell[1], Samuel Taylor[2], Kavina Shah[2], Roel De Maeyer[2], Debajit Sen[2], Madhura Castelino[2], Jo Cambridge[2], David Isenberg[2], Maria Leandro[3], Arne Akbar[2] and **venkat Reddy**[2], [1]University College London, Oxford, United Kingdom, [2]University College London, London, United Kingdom, [3]University College London/UCLH, London, United Kingdom

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Activated T cells make a significant contribution to inflammation in systemic lupus erythematosus (SLE). We know that cellular metabolism regulates the activation of T cells. Evidence from patients with multiple sclerosis indicates that dimethyl fumarate (DMF), an electrophile, targets cellular metabolism to modulate CD4+T cell activation and function.

Here, we investigated whether DMF modulates T cell metabolism and function in samples from patients with SLE in a series of in vitro experiments.

Methods: All experiments were performed using isolated T cells from freshly drawn whole blood samples from patients with SLE. T cells were isolated using negative selection using Stem cell or Miltenyei magnetic bead separation kit. Isolated T cells were activated with anti-CD3 and IL-2 and incubated with either DMF at 25μM concentration or DMSO alone for three or seven days at 37°C and 5% CO_2 before harvesting.

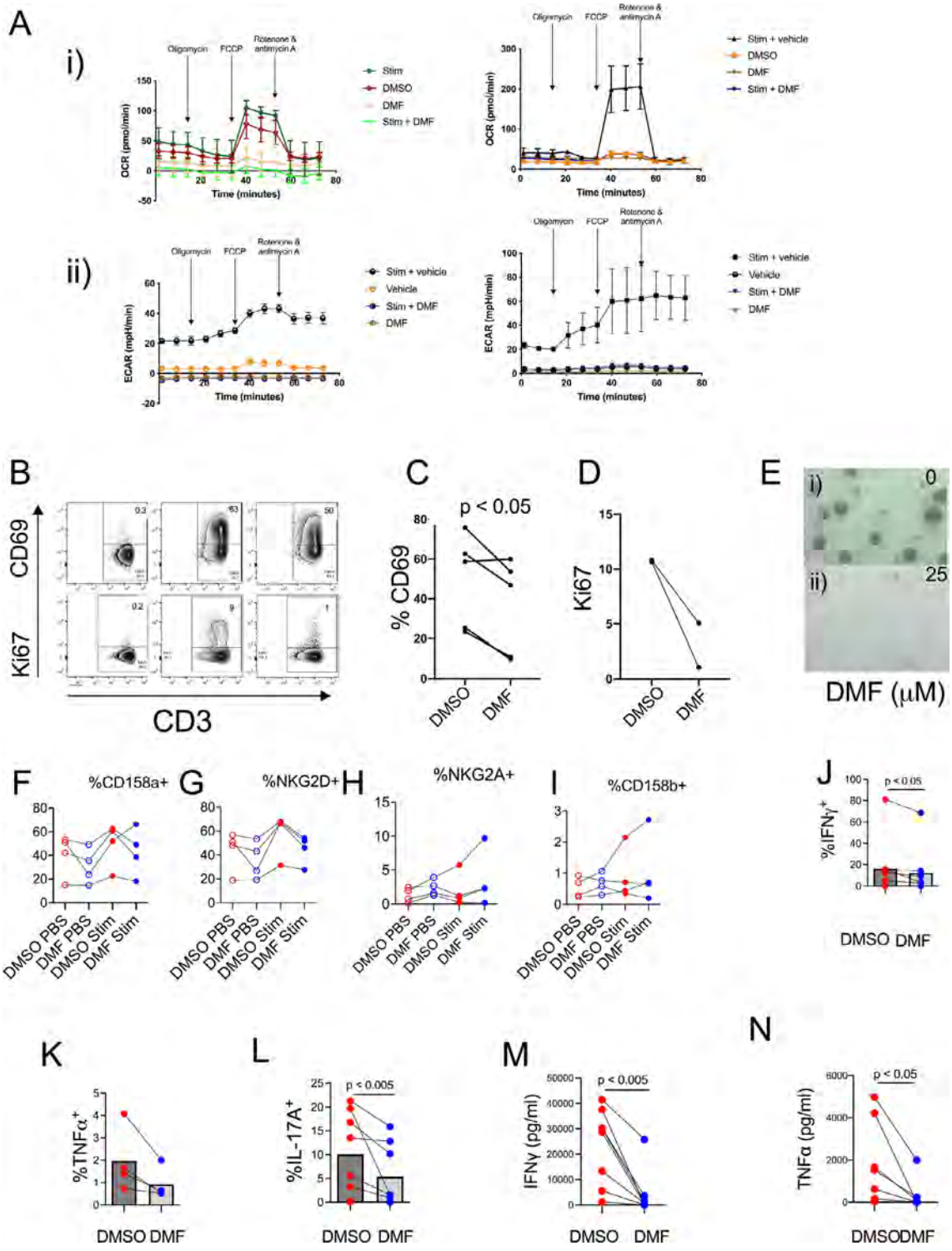
Results: In Seahorse experiments, after three days of incubation dimethyl fumarate (DMF) inhibited Figure A-i) the oxygen consumption rate (OCR) and A-ii) extra cellular acidification rate (ECAR) in isolated T cells when compared with samples incubated with vehicle, dimethyl sulfoxide (DMSO). Our results revealed that DMF significantly inhibited: 1) aerobic glycolysis and oxidative phosphorylation in activated T cells from patients with SLE (n=4) (Figure A- i and ii), in vitro; 2) T cell activation and proliferation as assessed by a reduction in the frequency of CD69 (n=4) and D) Ki67 (n=2) positivity, respectively (Figure B-E); 3) Collectively, these results suggest that DMF inhibits T cell activation and proliferation in samples from patients with SLE.

After 7 days of incubation, DMF significantly inhibited the expression of activating NK receptors CD158a and NKG2D on T cells whereas there was a trend toward enhancing the expression of inhibitory NK receptors NKG2A and CD158b (Figure F-I).

After 7 days of incubation, DMF significantly reduced intracellular expression of IFN-γ, TNF-α, IL-17 and secretion of pro-inflammatory cytokines IFN-γ and TNF-α in supernatants (Figure J – N).

Conclusion: Our preliminary data indicated that DMF modulates metabolic programming to inhibit activation, proliferation, and secretion of proinflammatory cytokines from T cells patients with SLE.

DMF inhibits glycolysis and effector functions of CD4+ T cells from patients with SLE. All experiments were performed using isolated T cells from freshly drawn whole blood samples from patients with SLE. T cells were isolated using negative selection using Stem cell or Miltenyei magnetic bead separation kit. Isolated T cells were activated with anti-CD3 and IL-2 and incubated with either DMF dissolved in 0.0025% DMSO to achieve 25μM concentration or DMSO alone for three or seven days at 37°C and 5% CO2 before harvesting. A-I) In Seahorse experiments, after three days of incubation dimethyl fumarate (DMF) inhibited the oxygen consumption rate (OCR) and A-ii) extra cellular acidification rate (ECAR) in isolated T cells when



compared with samples incubated with vehicle, dimethyl sulfoxide (DMSO). These results revealed that DMF significantly inhibited aerobic glycolysis and oxidative phosphorylation in activated T cells from patients with SLE (n=4), in vitro. B) Flow cytometry gating strategy to analyse for activated T cells CD3+CD69+ and proliferating T cells CD3+Ki67+. C) After three days of incubation, DMF significantly inhibited T cell activation and proliferation as assessed by a reduction in the frequency of CD69 (n=4) and D) Ki67 (n=2) positivity, respectively. E-i) After 7 days of incubation, the density of T cells at 10 X magnification in flat bottom wells without DMF was higher than E-ii) in the well in the presence of DMF. Collectively, these results suggest that DMF inhibits T cell activation and proliferation in samples from patients with SLE. After 7 days of incubation, DMF significantly inhibited the expression of activating NK receptors F) CD158a and G) NKG2D on T cells whereas DMF seemed to have a trend toward enhancing the expression of inhibitory NK receptors H) NKG2A and I) CD158b. After 7 days of incubation, DMF significantly reduced intracellular expression of J) IFN-γ, K) TNF-α, L) IL-17 and secretion of pro-inflammatory cytokines M) IFN-γ and N) TNF-α in supernatants. Thus our preliminary data indicated that DMF modulates metabolic programming to inhibit activation, proliferation and secretion of proinflammatory cytokines from T cells patients with SLE.

Disclosure: L. Kell: None; **S. Taylor**: None; **K. Shah**: None; **R. De Maeyer**: None; **D. Sen**: None; **M. Castelino**: None; **J. Cambridge**: None; **D. Isenberg**: None; **M. Leandro**: Roche Basel, 1; **A. Akbar**: None; **v. Reddy**: None.

Abstract Number: 0068

Anti-TNFR2 VHH Agonistic Antibodies Promote and Stabilize Treg Immunosuppressive Activity

Lee Kim Swee[1], Julia Knopf[1], Tomasz Próchnicki[1], Paul-Albert König[1], Alexander Kirchhoff[1], Laura Preiß[1], Ferdinand Huber[1], Annegrit Seifried[1], Olga Murawjew[1], Fabienne Baumann[1], Jessica Assis[1], Sonja Hennemann[1], Felix Kolbe[1], Helena Schnell[1], Thomas Orlik[1], Kevin Blanco Valle[1], Alissa Telling[2], Brian Sanchez[2], Anthony Opipari[2], Tobias Stuwe[1], Stephen Soisson[3] and **Luigi Franchi**[2], [1]Odyssey Therapeutics GmbH, Frankfurt am Main, Germany, [2]Odyssey Therapeutics, Ann Arbor, MI, [3]Odyssey Therapeutics, Boston, MA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Regulatory T cells (Treg) are a population of lymphocytes with immunosuppressive function. Activation and expansion of Treg is an attractive therapeutic approach for autoimmune diseases currently being evaluated clinically. In addition to inducing Treg activation and expansion, an effective Treg-directed therapy needs to generate cells with a stable immunosuppressive phenotype that is resistant to conversion to T effector function under inflammatory conditions. Nevertheless, current clinical approaches to stimulate Treg to treat autoimmunity expand Treg by increasing homeostatic proliferation (e.g., via IL-2 muteins) without improving Treg stability.

TNFR2 agonism induces Treg proliferation and activation. We hypothesized that TNFR2 stimulation will also increase Treg stability based on the phenotype of TNFR2 knockout mice in which Treg are unstable and convert into effector cells. To test this hypothesis, we developed multivalent anti-TNFR2 VHH proteins with agonist activity on TNFR2 and assessed their impact on Treg proliferation, activation, immune suppressive function and stability compared to IL-2 muteins.

Methods: VHHs specific for human TNFR2 were obtained by immunization of alpacas, followed by panning of phage-display VHH libraries against recombinant protein. VHH binding to TNFR2 was characterized by surface plasma resonance and flow cytometry. VHH identified as binders were formatted as multivalent fusion proteins. Human naïve Treg treated with anti-TNFR2 VHH or IL-2 mutein (PT-101) were evaluated to detect effects on proliferation, activation, suppressive function and stability in inflammatory conditions. The effects of anti-TNFR2 VHH agonists on spleen lymphocyte population in human TNFR2 knock in mice were assessed by flow cytometry 5 days after a single injection.

Results: Agonistic TNFR2 VHH induced the expansion of naïve human Treg, increased the expression of activation markers and stimulated suppressive effects against CD4+ T effector cells. Consistent with these in vitro findings, administration to mice increased Treg by 3-fold, without increasing conventional effector T cells. TNFR2 VHH constructs, but not IL-2 muteins, increased human Treg stability in the presence of proinflammatory cytokines based on sustained presence of FOXP3 bright cells and prevention of conversion of Treg into IL-17A- or IFNg-secreting cells.

Conclusion: Anti-TNFR2 VHH agonistic proteins are effective at expanding Tregs that have a more stable immunosuppressive phenotype compared to IL-2 muteins and may provide a durable and disease modifying therapy for multiple autoimmune diseases.

Disclosure: L. Swee: Boehringer-Ingelheim, 3; **J. Knopf**: Evotec, 3, Merck KgaA, 2; **T. Próchnicki**: IFM Therapeutics, 3; **P. König**: None; **A. Kirchhoff**: None; **L. Preiß**: Octapharma, 3; **F. Huber**: Octapharma, 3; **A. Seifried**: Octapharma, 3; **O. Murawjew**: None; **F. Baumann**: None; **J. Assis**: Hipolabor, 3; **S. Hennemann**: Octapharma, 3; **F. Kolbe**: None; **H. Schnell**: None; **T. Orlik**: Octapharma, 3; **K. Blanco Valle**: None; **A. Telling**: None; **B. Sanchez**: None; **A. Opipari**: Odyssey Therapeutics, 3; **T. Stuwe**: Octapharma, 3; **S. Soisson**: Merck/MSD, 3, 11; **L. Franchi**: Odyssey Therapeutics, 3, 11.

Abstract Number: 0069

All-*trans* Retinoic Acid (atRA) Enhances FoxP3 Protein Stability Under Inflammatory Conditions Through Altering the FoxP3 Protein-interactome

William Willis[1], shane Bruckner[2] and wael Jarjour[2], [1]Ohio State University, Reynoldsburg, OH, [2]Ohio State University, Columbus, OH

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Treg cells play a central role in the tolerance of self-antigens and prevention of autoimmune disease. FoxP3 is a Treg-specific transcription factor that plays a critical role in Treg differentiation and function. The vitamin A metabolite all-*trans* retinoic acid (atRA) has a wide range of biological activity including cellular differentiation and proliferation. Previous studies have shown that atRA regulates Treg stability under inflammatory conditions and promotes plasma-derived Treg development in-part through regulating FoxP3 gene expression. Although these transcriptional effects have been characterized, post-transcriptional effects of atRA on FoxP3 protein stability have not been investigated. The aim of the present study was to test the hypothesis that atRA suppresses FoxP3 protein degradation under pro-inflammatory conditions through altering FoxP3 protein-protein interactions.

Methods: To examine the effect of atRA on FoxP3 protein levels in the absence of FoxP3 transcriptional regulation, FoxP3 was genetically fused to an N-terminal HaloTag reporter protein (Promega) and expressed in the immortalized T lymphocyte jurkat cell line under control of the human cytomegalovirus (CMV) promoter. cDNAs encoding HaloTag and FoxP3 or HaloTag alone were assembled into a lentiviral expression vector via In-Fusion cloning technology (Takara) and transfected into 293T cells to produce VSV-G pseudotyped virus for cell transductions. Halo-FoxP3 and Halo-control expressing cells were then selected with puromycin, creating stable cell lines for experiments. FoxP3 protein levels were assessed in the presence or absence of atRA with IL-6 or IL-1β alone or in combination by Western blot. To characterize the effect of atRA on FoxP3 protein interactions, Halo-FoxP3 was isolated and purified from cell lysates with HaloLink resin (Promega). FoxP3-interacting proteins were then eluted from the resin, digested with trypsin and profiled by nano LC-MS/MS with a Waters M-Class HPLC system interfaced to a ThermoFisher Fusion Lumos mass spectrometer. The resulting Mascot DAT files were parsed into Scaffold (Proteome Software) for validation and filtering to create non-redundant FoxP3-interacting protein lists for each sample.

Results: atRA increased Halo-FoxP3 protein levels in the Halo-FoxP3 expressing cells. In contrast, both IL-6 and IL-1β alone or in combination induced Halo-FoxP3 protein degradation without affecting Halo levels in the Halo-control cells. However, concomitant treatment with atRA abrogated IL-6/IL-1β-induced FoxP3 degradation. Profiling of FoxP3-interacting proteins in cell lysates from Halo-FoxP3 expressing cells by LC/MS-MS indicated that atRA treatment had extensive effects on FoxP3 protein-protein interactions, which included suppression of IL-6/IL-1β-induced interaction with the 26S proteasome and a novel FoxP3-interacting E3 ubiquitin ligase, RNF213.

Conclusion: These results suggest that in addition to previously characterized transcriptional mechanisms, atRA may suppress FoxP3 degradation under inflammatory conditions through preventing interaction with RNF213, a novel FoxP3-interacting E3 ubiquitin ligase.

Disclosure: W. Willis: None; **s. Bruckner**: None; **w. Jarjour**: None.

Abstract Number: 0070

Activation of Joint CD8+ T_{RM} Localize Autoantibody Mediated Arthritis

Sahar Lotfi-Emran, Nicole Koziol and David Masopust, University of Minnesota, Minneapolis, MN

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
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Session Time: 9:00AM–11:00AM

Background/Purpose: In humans, upper respiratory infections have been associated with onset of Rheumatoid Arthritis. In mice, following viral infection, CD8+ T cells take up residence in joints and a portion become tissue resident memory cells (T_{RM}). As these CD8+ T_{RM} are not specific for a Rheumatoid Arthritis specific self-peptide, it is not clear if they contribute to disease activity. In the mouse uterus, re-activation of CD8+ T_{RM} increases the permeability of the tissue to circulating antibodies. Utilizing the K/BxN serum transfer model, we demonstrate that local activation of CD8+ T_{RM} generates persistent clinical arthritis at that site.

Methods: C57BL/6 mice received adoptive transfer of OT-1 transgenic CD8+ T cells, whose cognate antigen is SIINFEKL peptide. The next day, they are infected with vesicular stomatitis virus encoding SIINFEKL. Acute infection resolves over the course of a few weeks, virus is cleared, but tissues are persistently populated by OT-1 CD8+ T_{RM}. These mice are OT-

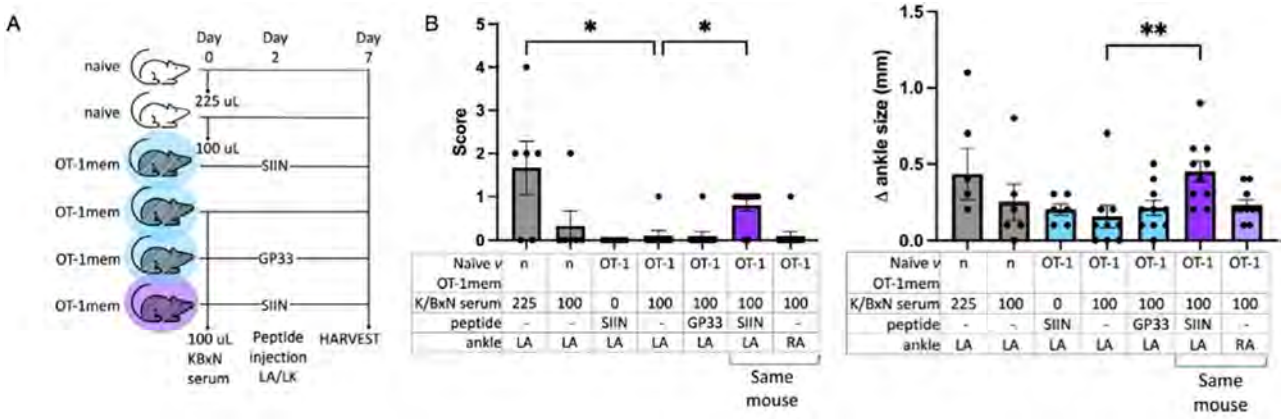

Figure 1. OT-1 CD8+ TRM activation in joints generates persistent clinical inflammation following K/BxN serum transfer arthritis. OT-1mem mice were generated by adoptive transfer of OT-1 cells followed by infection with VSV-OVA. OT-1 transgenic TCR recognizes the SIINFEKL peptide of ovalbumin and OT-1 cells rapidly expand and respond to VSV-OVA. 30+ days after infection, and well after clearance of virus, OT-1mem mice retain OT-1 TRM in tissues. OT-1mem and naive mice receive limited dose of K/BxN arthritogenic serum such that naive mice develop minimal disease. Two days after K/BxN serum, some mice receive SIINFEKL peptide or irrelevant peptide GP33 injections into left ankle and knee. Clinical disease activity is assessed daily by standardize scoring (0, no inflmmation, to 3, maximal swelling and ankylosis) and caliper measurements of ankles from malleolus to malleolus. A, Illustrated experimental groups. B, Left ankle score and change in ankle size. Two separate experiments. *p<0.05, **p<0.01ANOVA followed by Kruskal-Wallis comparison of each OT-1mem group to OT-1mem that received only K/BxN serum.

1mem mice. Naïve and OT-1mem mice receive dose limited volumes of arthritogenic serum from K/BxN mice. Two days later, they receive an injection of SIINFEKL peptide in their left ankle and left knee to reactivate OT-1 T_{RM}. Ankles were scored for severity of clinical inflammation (0, no swelling/redness; 1, mild swelling/redness +/- swollen digits; 2, moderate swelling/redness; and 3, maximal swelling/redness with ankylosis) and their size was measured by calipers daily (from lateral to

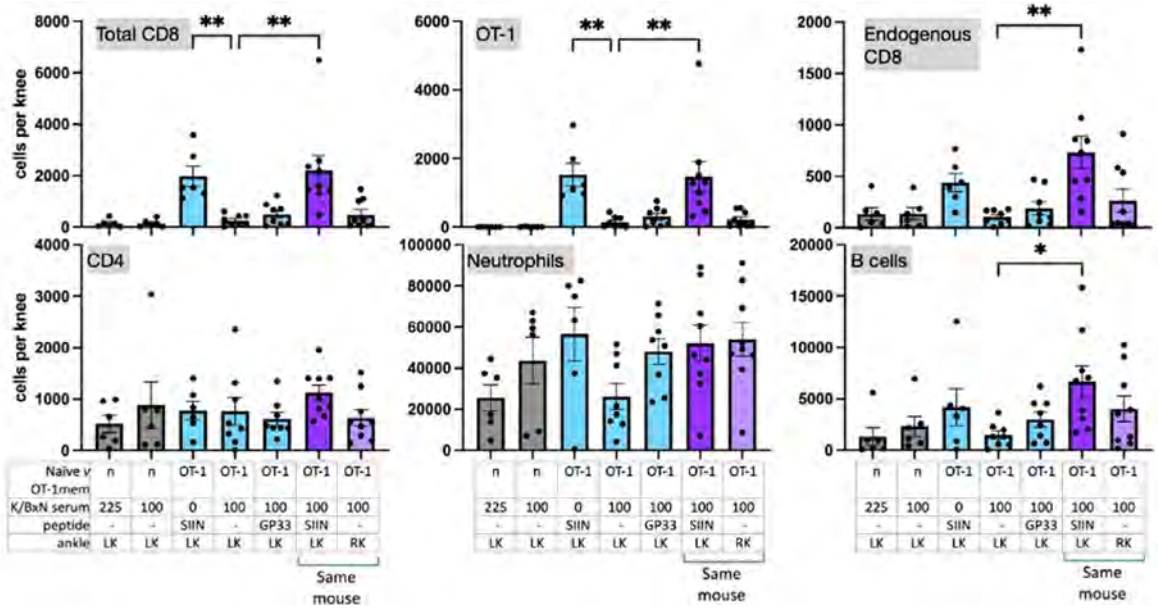

Figure 2. OT-1 CD8+ TRM activation locally increases CD8+ T cells and B cells at the the joint. Figure 1A illustrated experimental groups. Mouse knees were collected following intravascular staining, tissues were disaggregated in collagenase and DNAse solution, a single cell suspension was obtained, stained, and evaluated by flow cytometry with bead based counting to estimate total per tissue. Bead based counts for total CD8+ T cells, OT-1 CD8+ T cells, and non-OT-1 (endogenous) CD8+ T cells are shown in addition to CD4+ T cells, neutrophils (Ly6G+), and B cells (B220+). *p<0.05, **p<0.01ANOVA followed by Kruskal-Wallis comparison of each OT-1mem group to OT-1mem that received only K/BxN serum.

medial malleolus). After seven days, mice were sacrificed following intravascular stain injection, ankles fixed and decalcified for histology, and knees collected and processed to a single cell suspension for flow cytometry. (See Figure 1A for illustration of experimental groups.)

Results: Persistent clinical inflammation and increased size was found in the left ankle of OT-1mem mice that received K/BxN serum and injection of SIINFEKL, but not their right ankle, not in the left ankle of memory mice injected with an irrelevant peptide GP33, and not in the left ankle of memory mice that received SIINFEKL. (Figure 1B) By flow cytometry, the left, but not right, knee of memory mice that received K/BxN serum and injection of SIINFEKL contained significantly more OT-1 cells, endogenous CD8+ T cells, and B220+ B cells compared to Ot-1mem mice that received only K/BxN serum. This was not true of the left knee of OT-1mem mice that received K/BxN serum and left knee injection with GP33, nor the left knee of OT-1mem mice that received only SIINFEKL injection. (Figure 2)

Conclusion: Persistent clinical inflammation is dependent on both K/BxN serum and local activation of virus specific joint CD8+ T_{RM} and characterized by increased number of OT-1 transgenic CD8+ T cells, endogenous CD8+ T cells, and B220+ B cells. Thus, 'bystander,' virus specific, CD8+ T_{RM} activation can localize systemic autoantibody mediated processes to the joint.

Disclosure: S. Lotfi-Emran: None; **N. Koziol**: None; **D. Masopust**: None.

Abstract Number: 0071

Sex Based Differences in Morphological and Functional Niches of the Human Thymus, Identified by Non-supervised Spatial Transcriptomic Profiling, May Underlie Sex Bias in Autoimmune Disease

Viktoria Hennings, Anneke van Dijk, Andri Lemarquis, Christina Lundqvist and **Olov Ekwall**, University of Gothenburg, Gothenburg, Sweden

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Females exhibit a more robust response to both self- and non-self-antigens than males which manifests as higher prevalence of autoimmune disease, eg. rheumatic diseases, and more effective response to infection in females. Both hormonal and genetic differences have been suggested as underlying factors, but the precise mechanisms that lead to sex-based differences in immune responses remain unknown. We hypothesize that a sex bias in thymic central tolerance induction is of importance for the female predominance in autoimmune diseases.

Methods: The 10X Genomics Visium Spatial Transcriptomic method was applied on fresh frozen human thymic tissues from girls (n=2) and boys (n=2), age 4 months. RNAseq data was acquired, and after quality control and filtering, approximately 3000 spots per section were analyzed using the Scanpy toolkit (Fig 1a). After integration of data using Harmony, unsupervised spatial clustering (Leiden_0.1) identified distinct regions that translated to the main functional and morphological compartments of the human thymus; medulla and cortex, which was validated by the expression of marker genes (Fig 1 b, c).

Results: Differential gene expression analyses of the medullary compartment identified sex-biased expression of genes and biological pathways of key importance in central tolerance induction such as chemotaxis, negative selection and regulatory T cell formation (Fig 1 d, e). Interestingly, we also found that the female medullary compartment showed a more pronounced pro-inflammatory milieu with upregulated type 1 and type 2 interferon gene signatures. Further sub-clustering of the medulla showed heterogenicity in this compartment, identifying spatial niches with differences both in cellular composition, spatial organization and functional characteristics.

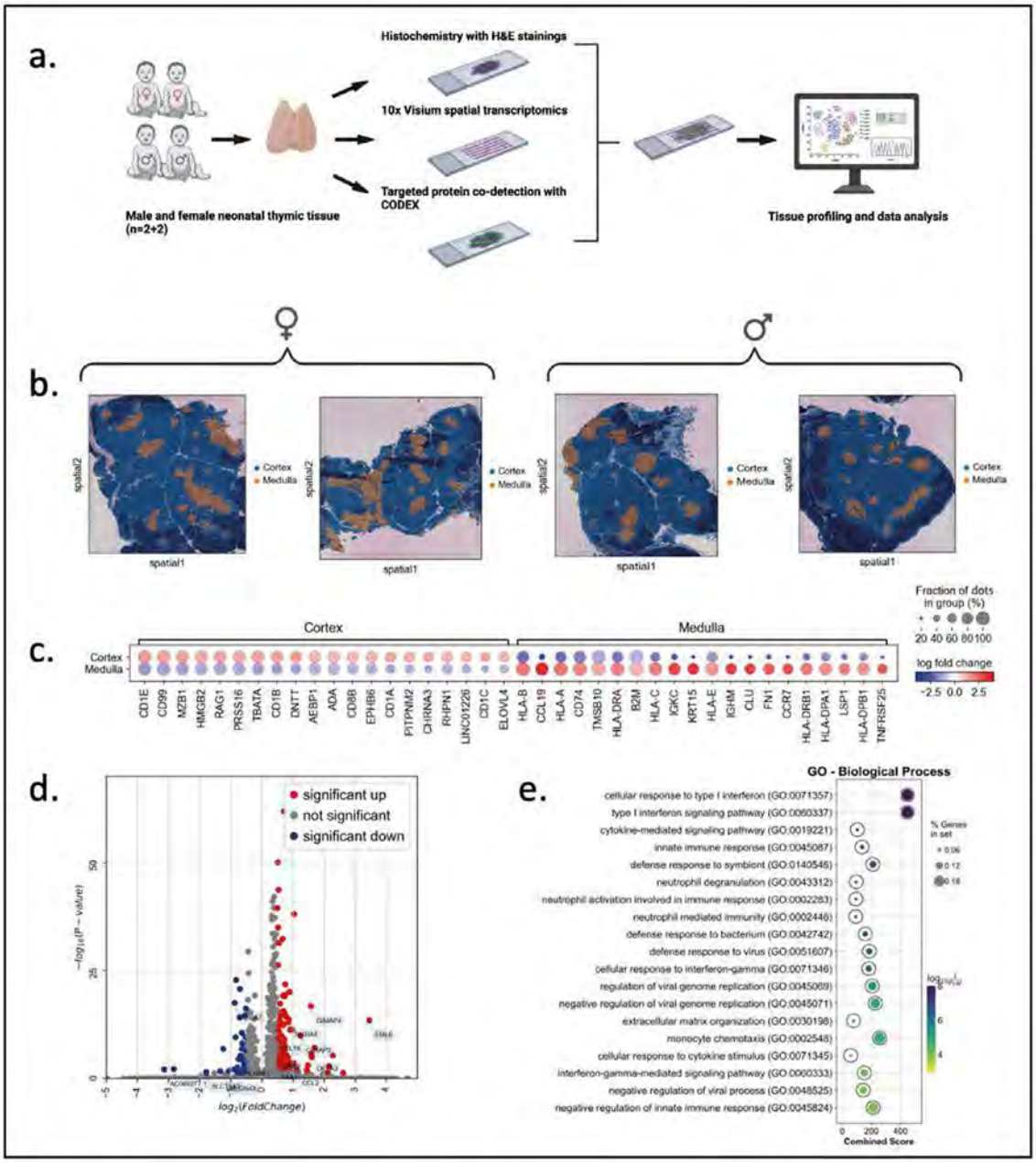

***Figure 1**. Project workflow (a). Unsupervised clustering identified cortical and medullary regions (b), which was validated using marker genes (c). Volcano plot showing the up- and downregulated genes in the female medulla (d). GO-term analysis identified biological pathways upregulated in the female medulla (e).*

Conclusion: The results expand our knowledge regarding the functional and spatial organization of the human thymus and strengthen the importance of sex-biased thymic central tolerance induction a possible explanation for the observed higher prevalence of autoimmune disease in females.

Disclosure: V. Hennings: None; **A. van Dijk**: None; **A. Lemarquis**: None; **C. Lundqvist**: None; **O. Ekwall**: None.

Abstract Number: 0072

Circulating T-cell Immunosenescence Is High in Patients with Immune-Mediated Inflammatory Diseases (IMIDs) and Is Associated with Interferons

Marie Naingeon[1], **Samuel Bitoun**[2], Matthieu roulleaux Dugage[1], Caroline de Oliveira[1], Caroline Berthot[1], Xavier Mariette[3], Nathalie Chaput[1] and Gaetane Nocturne[4], [1]LIO, Department of Medicine, Gustave Roussy Université Paris Saclay, Villejuif, France, [2]CHU Bicêtre APHP, Le Kremlin-Bicêtre, France, [3]Université Paris-Saclay, Le Kremlin-Bicêtre, France, [4]APHP, Le Kremlin-Bicêtre, France

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Immunosenescence is a global remodeling of immune functions that has been first described with aging. It can also occur in pathologies associated with chronic antigenic stimulation and notably cancer. High proportion of circulating senescent CD8+ T cells (T_8sen, CD3+CD8+CD28-CD57+KLRG1+ cells) is observed in more than 25% of the patients with advanced non–small cell lung cancer (aNSCLC) and has been associated with resistance to immune checkpoint blockers. The mechanisms leading to accumulation of T_8sen are still only partially understood. Chronic inflammation is a potential driver. Here we sought to assess the level of T_8sen in patients with IMIDs, its dynamic under TNF inhibitors (TNFi) and the link with the plasmatic concentration of different cytokines.

Methods: T_8sen have been identified by flow-cytometry on fresh whole blood samples from 68 patients with IMIDs [25 with rheumatoid arthritis (RA), 23 with spondyloarthritis (SA) and 20 with Sjogren disease (Sjo], 228 patients aNSCLC and 25 healthy volunteers (HV). Patients with RA and SA were evaluated at baseline and 3 months after TNFi initiation. Baseline plasmatic concentrations of IFNα2a, IFN-β, IFNγ, IFNλ1, and IP-10 were quantified using MSD technology. Associations between proportions of T_8sen and categorical or continuous variables were performed by Mann–Whitney test and Pearson coefficient, respectively.

Results: Patients with IMIDs harbor higher levels of T_8sen compared to aNSCLC patients and HV (Figure 1 left panel). The median level [Q1-Q3] of T_8sen was of 26.34% [16.75-47.33] in IMIDS patients compared to 22.18% [12.41-33.84] in aNSCLC patients and 12.11% [5.56-21.28] in HV. Among the three IMIDs, T_8sen rates were higher in patients with Sjo (Figure 1, right panel). We did not observe any significant correlation between T_8sen and diseases characteristics at baseline. Importantly, TNFi initiation did not modulate T_8sen levels in RA and SA patients. Interestingly, we observed significant positive correlations between plasmatic IFN- λ1, IFN- γ and IP-10 with the levels of T_8sen (Figure 2).

Conclusion: Patients with IMIDs exhibit high levels of T8sen cells that exceed those observed in patients with lung cancer. This senescence is not altered under TNFi treatment and appears to be primarily driven by IFNs. The link between T_8sen and the evolution of the disease as well as with the response to treatment remains to be evaluated. Likewise, since T_8sen is

mainly driven by IFNs, it would be important to evaluate the effect of anti-IFN treatments and JAK inhibitors on senescence with potential implications in autoimmunity and cancer.

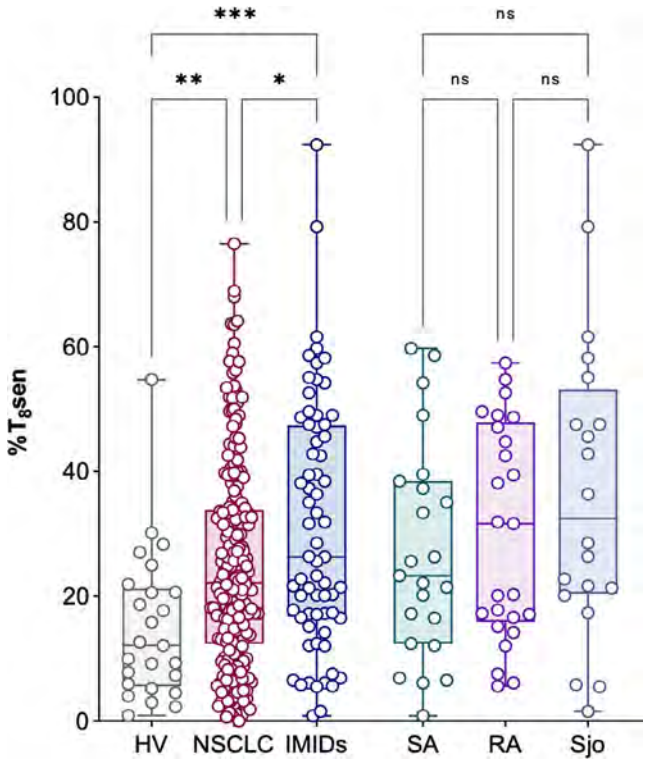

Figure 1. Percentage of senescent CD8+ T (T8sen) cells in patients with AID compared to HV and aNSCLC (right panel) and between AID types. HV : healthy volunteers, NSCLC: advanced lung cancer, IMIDs: immune-Mediated Inflammatory Diseases, SA: spondyloarthritis, RA : rheumatoid arthritis, Sjo: Sjogren disease.

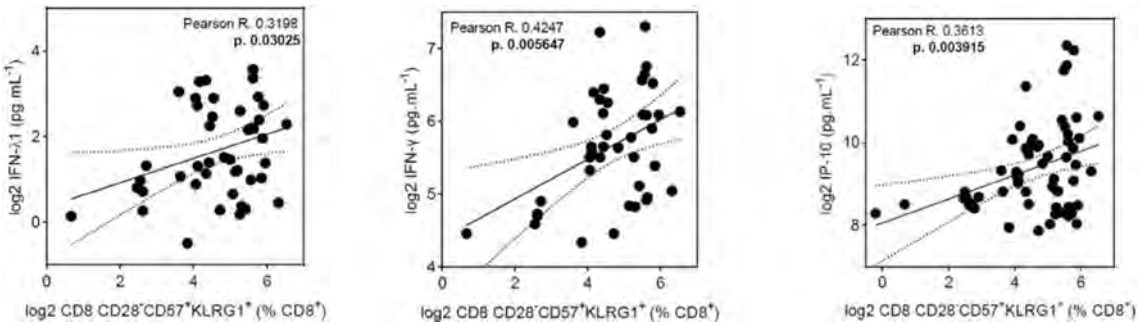

Figure 2. Correlation of IFNλ1, IFN- γ and IP-10 plasmatic levels with the percentage of senescent CD8+ T cells in patients with autoimmune diseases.

Disclosure: M. Naingeon: None; **S. Bitoun**: None; **M. roulleaux Dugage**: None; **C. de Oliveira**: None; **C. Berthot**: None; **X. Mariette**: AstraZeneca, 2, 6, BMS, 2, 6, Galapagos, 2, 6, GSK, 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **N. Chaput**: None; **G. Nocturne**: None.

Abstract Number: 0073

PD-1hi Cells Are Highly Present in the Rheumatoid Joint, and Express Regulatory Capacities

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Programmed death 1 (PD-1) is an immune checkpoint receptor expressed by activated T cells, and of major importance in maintaining peripheral tolerance. Expression of PD-1 has been associated with T cells exhaustion, plasma cell differentiation and bone homeostasis. With emerging treatments engaging the PD-1 pathway in Rheumatoid Arthritis (RA) this pathway is of continued interest.

We aimed to investigate PD-1hi T cells from RA synovial fluid (SF).

Methods: SF was collected from RA patients with disease flare (n=7). Cells were stained for flow and sorted in CD3+ PD-1hi/PD-1lo populations. Post sorting, bulk RNA seq was performed, and cells were stimulated with antiCD3/CD28. Cytokines in the supernatants were investigated using V-plex multipanel assay. Supernatants were added to fibroblast cultures and the osteoblast cell line SaOs-2.

Results: Evaluated by flow cytometry, PD-1+ cells represented 42% of CD4+ T cells and 34% of CD8+ T cells in the SF. When comparing co-expression of checkpoint receptors and transcription factors between PD-1hi and PD-1lo CD4+ T cell; Tigit, Tim3 and NFAT were all increased in PD-1hi (all $p < 0.05$), Lag-3 was slightly elevated ($p=0.07$), whereas TCF1 and TOX expression did not differ. These differences were not observed between PD-1hi and PD-1lo CD8+ T cells.

Post sorting, RNAseq revealed PD-1hi and PD-1lo cells to cluster separately. In PD-1hi cells, gene expression corresponded to structural signatures, including tubulin binding and cytoskeletal motor activity ($p < 0.01$). Genes related to peripheral T helper cells, including *IL21* and *CXCL13* were highly upregulated (all $p< 0.05$) The gene *PHEX* was highly expressed (log2

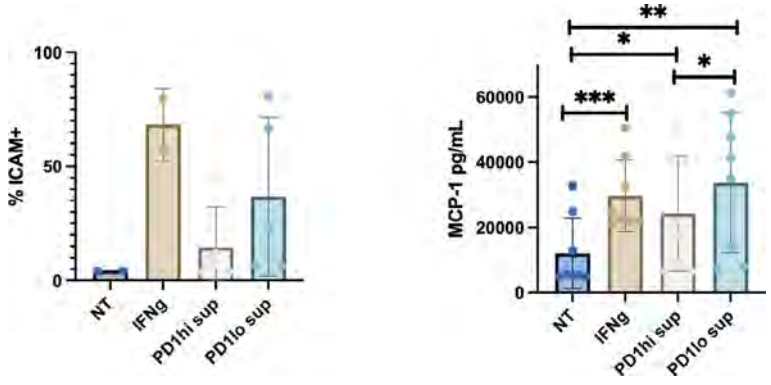
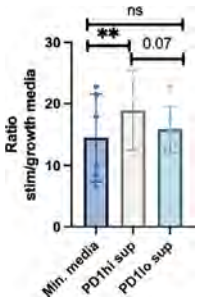


Figure 1: Left: Expression of ICAM on fibroblasts after culturing with PD-1 hi/PD-1lo supernatant. IFNg used as a positive control. Right: MCP-1 production measured in the supernatant from fibroblasts after culturing with PD-1 hi/PD-1lo supernatant. IFNg used as a positive control.



Mineralization measured in the SaOs-2 osteoblast cell line after culturing with PD-1hi and PD-1lo supernatant. Data are normalized to the cell line in growth media.

fold change=5.2), suggesting an association with bone mineralization. The signature in PD-1lo cells was associated with immune activation genes ($p < 0.005$). Stimulating cells with CD3/CD28 post sorting resulted in lower production of IL-2, IFNg, TNFa, IL-8, IL-10, IL-13, IL-12, and IL-1b from PD-1hi cells compared to PD-1lo. The supernatant from PD-1hi cells only slightly activated fibroblasts, whereas the PD-1lo supernatant significantly activated fibroblasts, as measured by by MCP-1 production and surface ICAM expression (fig 1). When adding the PD-1hi and PD-1lo supernatant to osteoblast cultures, bone mineralization was significantly increased by the PD-1hi supernatant (fig 2).

Conclusion: PD-1hi cells are present in the synovial joint. They are not exhausted but express multiple checkpoint receptors, suggesting regulatory capacities. They could play a central role in structural maintenance through effects on fibroblasts and osteoblasts.

Disclosure: S. Rask: None; **C. Andersen**: None; **M. Hvid**: None; **K. Ravnskjær**: Thermo Fisher, 3; **B. Deleuran**: None; **S. Greisen**: None.

Abstract Number: 0074

Distinct PD-1 Receptor Engagement Leads to Different Pharmacodynamic Effects

Yevgeniya Orlovsky, Melissa Swiecki, Kimberly Colby, Changbao Liu, Josephine Wixted, Olesya Chornoguz, Navin Rao, Edith Janssen and **Ling-Yang Hao**, Janssen Research & Development, LLC, Spring House, PA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: T cells play an important role in the development and progression of many autoimmune diseases. Inhibition of T cells and their effector mechanisms has therefore been an area of great therapeutic interest. PD1 (CD279) is a CD28/CTLA4 family coinhibitory receptor that is mainly found on activated lymphocytes. Ample evidence links the PD1 pathway to autoimmune diseases, ranging from genetic evidence, correlations between PD1 expression and disease severity in patients, and autoimmune-like immune-related adverse events (irAE) from blocking PD1 pathway therapies in oncology. Consequently, the activation of the PD1 pathway through agonist antibodies holds promise as a therapeutic

approach in autoimmune disease. With the first PD1 targeting drugs entering the rheumatoid arthritis clinical trial space, there is a need to increase our understanding of the mechanistic underpinnings of agonist PD1 antibody (Ab) on T cells to support further drug development. Here we assess the impact of various Ab configurations on the potential of novel PD1 Ab to inhibit T cell activation *in vitro*.

Methods: PD1 Abs were assessed for affinity and capacity to interfere with endogenous ligands interaction. Selected anti-PD1 reagents were expressed with different molecule configurations and tethering partners. Naïve and activated CD4+ T cells were cultured with soluble or scaffold/bead-bound PD1 Abs and anti-CD3 to determine inhibitory potential on proliferation and cytokine production. Antigen stimulation-based studies in PBMC were used to assess impact in a multi-cellular setting. Potential to promote Treg development was assessed in naïve CD4+ T cells stimulated with anti-CD3 coated beads and recombinant interleukin 2.

Results: In purified T cell assays, several of the anti-PD1 molecules showed clear impact of tethering on the agonist capacity. Importantly, inhibition of T cell function and Treg development was observed when the PD1 Abs were bound to the same scaffold (cis), but not on separate scaffolds (trans). Some PD1 Abs that showed agonism in the purified T cell assay failed to do so in the PBMC assay, and some architectures, such as the PD1xCD4 tetrapod, shifted from agonist to antagonist.

Conclusion: Our data indicate that more potent agonist effects correlated with close proximity engagement of PD1 and T cell receptor. Therefore, strategies that preserve or enhance the natural behavior of PD1 localization to immune synapses are likely to yield more successful agonists.

Disclosure: Y. Orlovsky: Janssen, 3; **M. Swiecki**: Janssen R&D, 3; **K. Colby**: Janssen, 3; **C. Liu**: Janssen, 3; **J. Wixted**: Janssen, 3; **O. Chornoguz**: Janssen, 3; **N. Rao**: Janssen, 3, 11; **E. Janssen**: Janssen, 2, 11; **L. Hao**: Janssen, 3.

Abstract Number: 0075

Proteomic, Transcriptomic, and T-Cell Receptor (TCR) Profiling of Synovial Integrin-Expressing (InEx) T Cells in Axial Spondyloarthritis (axSpA)

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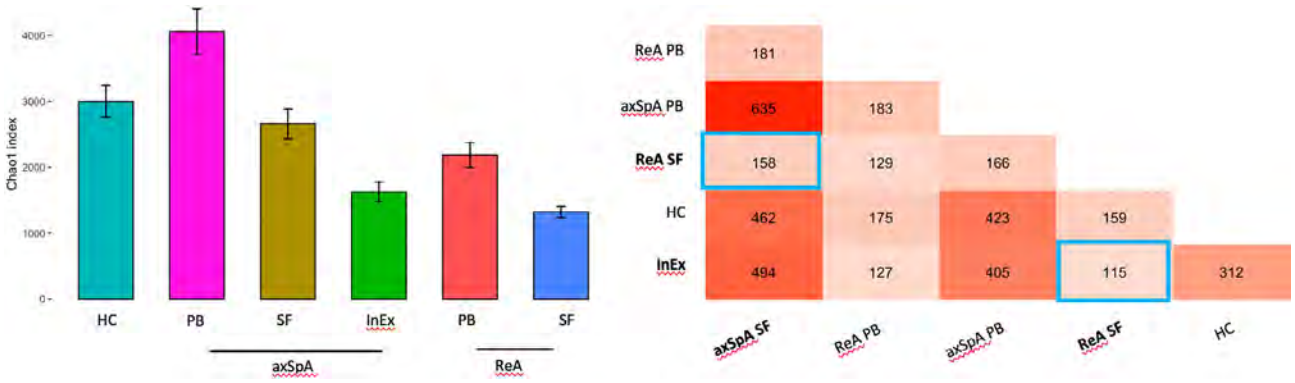
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The strong clinical and genetic associations between axial spondyloarthritis (axSpA) and inflammatory bowel disease (IBD) underscore the pathogenic role of the gut-joint axis. The prevailing arthritogenic peptide hypothesis suggests that CD8+ T cells mount an immunological response upon recognition of a self or microbial arthritogenic peptide at inflammatory sites such as the gut. This could result in a clonal expansion of these cells, ultimately leading to their aberrant migration to other sites such as the joint. We previously identified a subpopulation of pathogenic mature CD8+ T cells in the axSpA synovial fluid (SF), expressing CD103+ and CD49a+ integrins (InEx cells). The expression of integrins on InEx cells

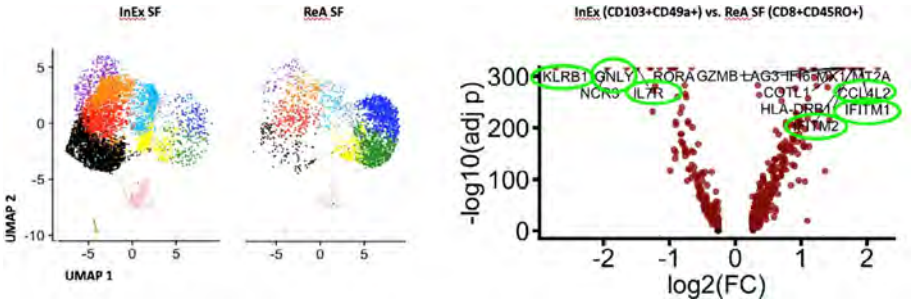
implicates their role in aberrant migration between the gut-joint axis. Whether InEx cells recognize an arthritogenic peptide remains unclear. We hypothesize that InEx cells may incite and perpetuate chronic inflammation in axSpA. To this end, we characterized their T-cell receptor (TCR) repertoire and gene expression profile.

Methods: Patients fulfilling the ASAS classification for axSpA were recruited (n=4). Active joint effusion from these patients is reflective of active joint inflammation which coincided with high disease activity (BASDAI >4). We isolated peripheral blood mononuclear cells (PBMCs) and synovial fluid mononuclear cells (SFMCs), followed by FACS-sorting of mature CD8+ T cells and InEx cells. Subsequently, single-cell TCR (both α and β chains) and RNA sequencing were performed on these cell types. An HLA-B27+ reactive arthritis (ReA) sample were used as a comparison since it is the paradigm for antigen-driven inflammation initiated in the gut. Mature CD8+ T cells from ReA PBMCs and SFMCs were also FACS-sorted. These were all compared to HLA-B27+ healthy controls (n=4).

Results: The InEx TCR repertoire from axSpA patients was less diverse than mature CD8+ T cells from axSpA PBMCs or SFMCs, indicating a clonally expanded population. The TCR V/J pairings from the β chain in InEx cells confirm existing literature. Interestingly, their TRBV9/TRBJ2-3 usage was also found in mature CD8+ T cells from ReA SFMCs. Assessing the TCR V region from paired α/β chains revealed that the InEx cells shared similar usage with mature CD8+ T cells from ReA PBMCs or SFMCs: TRBV20-1/TRAV1-2, TRBV6-1/TRAV1-2, and TRBV6-2/TRAV1-2. Further, the CDR3 region of the β chain in InEx cells differed from mature CD8+ T cells from ReA SFMCs by only three amino acids. On a transcript level, InEx cells differed from ReA mature CD8+ T cells based on elevated genes such as *CCL4L2*, *IFITM1*, and *IFITM2*, and downregulated genes such as *IL7R*, *GNLY*, and *KLRB1*.



Left panel displaying the Chao1 index, a measure of TCR repertoire diversity, stratified by sample type. Right panel displaying the overlapping alpha and beta TCR chain gene usage of the V region. Highlighted in blue boxes are features similar between InEx and ReA SF and axSpA SF (mature CD8+ T cells) and ReA SF. HC = healthy controls, PB = peripheral blood, SF = synovial fluid.



Left panel displaying transcriptome profile of InEx vs mature CD8+ ReA SFMCs on UMAP plots. Genetic profile of InEx cells cluster differently to ReA SF. Right panel displaying differently expressed genes between the two groups, with most informative genes circled in green. UMAP = Uniform Manifold Approximation and Projection. SF = synovial fluid.

Conclusion: These observations suggest that the autoimmune mechanism employed by InEx cells could be mediated by HLA-B27+. This may enable them to incite inflammation similarly to ReA due to potential recognition of similar peptides, ultimately driving the selection of specific T cell clones. However, InEx cells' ability to perpetuate inflammation may be distinct from ReA due to a varied transcriptome. This has important implications for therapeutic designs attempting to target integrin blockade in axSpA.

Disclosure: Z. Qaiyum: None; **M. Tang**: None; **R. Inman**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Sandoz, 2.

Abstract Number: 0076

Characterizing GMCSF Producing T-cells in Rheumatoid Arthritis and Effect of Methotrexate on Them

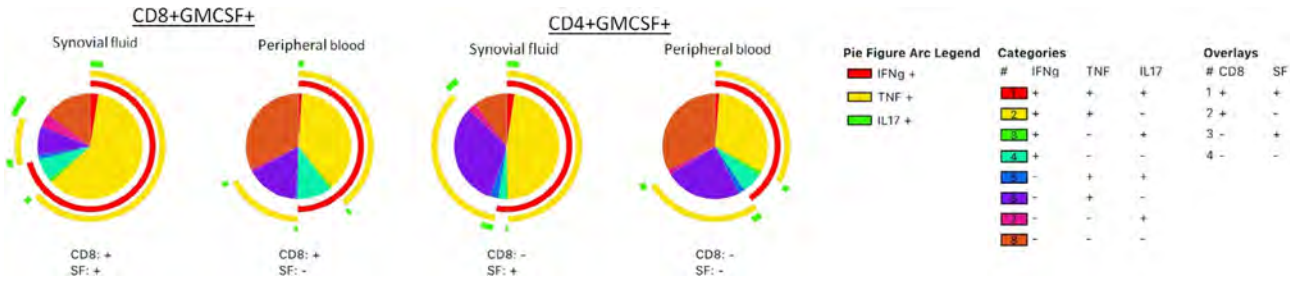
AASTHA KHULLAR[1], Varun Dhir[2], Leishangthem Bidyalaxmi[1], Chandra Bhushan Prasad[3], Sankar Jayaprakash[1], Siddharth Jain[4], Biman Saikia[1], Aman Sharma[5], Shefali Sharma[6], Ashok Kumar Yadav[1], Shankar Naidu[1] and Sanjay Jain[7], [1]PGIMER, Chandigarh, India, [2]PGIMER, CHD, INDIA, Chandigarh, India, [3]Healthway Hospital, Goa, Zuarinagar, India, [4]AIIMS, Delhi, India, [5]PGIMER, Chandigarh, India, Chandigarh, India, [6]PGIMER< Chandigarh, Chandigarh, India, [7]Post Graduate Institute of Medical Education and Research, Chandigarh, India

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Background: GMCSF producing T-cells may be implicated in the pathogenesis of autoimmune diseases like rheumatoid arthritis (RA), multiple sclerosis (MS) and psoriatic arthritis. Few studies reported higher frequencies of CD4+GMCSF+ T-cells in the MS lesions and RA synovial fluid; however, there is no data on CD8+GMCSF+ T-cells. Thus, we planned to assess their frequencies in blood and synovial fluid, and characterize based on polyfunctionality, phenotype, cytotoxic ability and the effect of methotrexate on them.

Methods: The frequency of GMCSF producing CD8 and CD4 T-cells was assessed by stimulation with PMA/Ionomycin, followed by immunostaining and flowcytometry. Subsequently, polyfunctionality for other cytokines (TNFα, IFNγ and IL-17), memory/naïve phenotype and perforin/granzyme expression was also assessed by flowcytometry

Results: Enrichment of GMCSF producing T-cells was found in the synovial fluid, with elevated frequencies of both CD8+-GMCSF+ T-cells (5.8, 3.9%, p= 0.0045) and CD4+GMCSF+ T-cells (8.5, 4.5%, p=0.0008) compared to peripheral blood. These cells were characterised as extremely polyfunctional, with higher frequencies of triple cytokine positive GMCSF +TNFα+IFNγ positive CD8 T-cells (81, 36%, p=0.049) and CD4+GMCSF+TNFα+IFNγ+ (48, 32%, p=0.01)) in synovial fluid



compared to blood. Majority of GMCSF producing T-cells had an effector memory (EM) phenotype, besides CD8+GMCSF+ T-cells also having increased expression of granzyme B. After MTX treatment, there was a significant reduction in circulating CD4+ T-cells producing GMCSF (4.6% to 2.9%, p= 0.0014) and a similar trend was seen in the CD8 T (3.7% to 2.9% p= 0.068) cells.

Conclusion: Synovial fluid enrichment with GMCSF producing CD8 T-cells (and CD4 T-cells) was observed, demonstrating elevated polyfunctionality and granzyme B expression with majority belonging to EM phenotype. Upon treatment with methotrexate a reduction in the frequencies of these cells was found.

Disclosure: A. KHULLAR: None; **V. Dhir**: None; **L. Bidyalaxmi**: None; **C. Prasad**: None; **S. Jayaprakash**: None; **S. Jain**: None; **B. Saikia**: None; **A. Sharma**: None; **S. Sharma**: None; **A. Yadav**: None; **S. Naidu**: None; **S. Jain**: None.

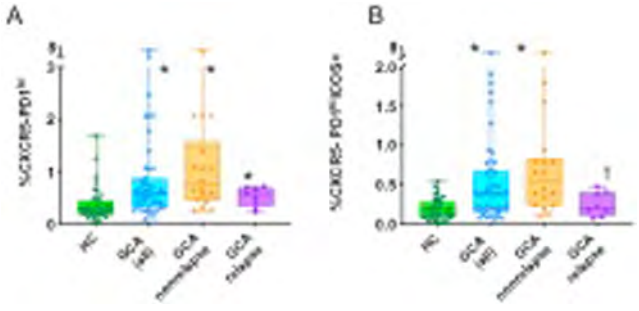
Abstract Number: 0077

Circulating CD4+CXCR5-PD-1^{hi}ICOS+ Cells Are Elevated in Patients with Newly Diagnosed Giant Cell Arteritis and Associate with the Clinical Outcome

Maria-Eugenia Miranda-Carus[1], Beatriz Nieto-Carvalhal[1], Irene Monjo[2], Mariela Uyaguari-Morocho[1], Irene Casado-Juárez[3], Alejandro Balsa[4] and Eugenio De Miguel[4], [1]Hospital Universitario La Paz - IdiPAZ, Madrid, Spain, [2]University Hospital La Paz, Madrid, Spain, [3]Hospital La Paz - IdiPAZ, Madrid, Spain, [4]Hospital Universitario La Paz, Madrid, Spain

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Giant cell arteritis (GCA) is a large-vessel granulomatous vasculitis. It is characterized by the presence at the inflamed arterial walls, of activated PD-1+ CD4 T cells; this contrasts with observations indicating that a defect of PD-1 signaling is implicated in the pathogenesis of GCA. A population of CD4+CXCR5-PD-1^{hi} cells, termed Tph cells, has been described at the inflamed synovium and peripehral blood of patients with Rheumatoid Arthritis, and seem to play a pathogenic role in this condition. Our objective was to study the frequencies of circulating total Tph (cTph) and activated ICOS+Tph (cICOS+Tph) cells in the peripheral blood of patients with newly diagnosed GCA (nGCA) and examine whether they are related with the clinical outcome.



Methods: This is a prospective non-interventional study performed on consecutive patients referred to our ultrasound (US) GCA fast track clinic, in whom newly diagnosed GCA (nGCA) was clinically confirmed (2022 ACR/EULAR criteria) over a period of 18 months. Peripheral blood was drawn immediately upon confirmation and after obtaining written informed consent. For each patient, an age and gender-matched healthy control (HC) was also studied. PBMCs isolated by Ficoll- Hypaque gradient were stained with antibodies to CD3, CD4, CD45RA, CD45RO, CXCR5, ICOS, PD-1, and examined by flow cytometry. Patients were treated with standard therapy according to clinical response.

Results: A total of 48 nGCA patients were included (mean age 81,5 years, 50.0 % female). As compared with HC, nGCA patients presented at baseline with an increased frequency of cTph and cICOS+Tph cells. Among the 26 patients who could be followed up for 12 months (the remaining 22 have been diagnosed less than 12 months ago),8 experienced a relapse (2018 EULAR recommendations; symptoms plus: elevation of acute phase reactants and/or positive US). Interestingly, the basal frequency of cICOS+Tph cells had been significantly lower in patients who relapsed as compared with those who did not; the frequency of cTph cells also tended to be lower in relapsing subjects but the difference with non-relapsing patients was not statistically significant.

Conclusion: Newly diagnosed GCA patients demonstrate an increased frequency of cTph and cICOS+Tph cells. Lower basal proportions of cICOS+ Tph cells are associated with relapse.

Disclosure: M. Miranda-Carus: Bristol-Myers Squibb(BMS), 5, Gebro Pharma, 5; **B. Nieto-Carvalhal**: None; **I. Monjo**: Amgen, 6, Gedeon Richter, 6, Janssen, 6, Novartis, 6, Roche, 6, UCB, 6; **M. Uyaguari-Morocho**: None; **I. Casado-Juárez**: None; **A. Balsa**: AbbVie/Abbott, 1, 2, 5, 6, Bristol-Myers Squibb(BMS), 1, 5, Eli Lilly, 1, 5, 6, Merck/MSD, 1, 5, Novartis, 5, Pfizer, 1, 5, 6, UCB, 1, 5, 6; **E. De Miguel**: None.

Abstract Number: 0078

Circulating CD4+CXCR5+PD-1^{hi} Follicular Helper T Cells Are Elevated in Patients with Rheumatoid Arthritis and Predict Treatment Response to Abatacept or TNF Blockers

Maria-Eugenia Miranda-Carus[1], Beatriz Nieto-Carvalhal[1], Irene Monjo[2], Mariela Uyaguari-Morocho[1], Alejandro Villalba[3], Laura Nuño[1], Diana Peiteado[1], Elisa Fernández[1], Sara García-Carazo[1] and Alejandro Balsa[4], [1]Hospital Universitario La Paz - IdiPAZ, Madrid, Spain, [2]University Hospital La Paz, Madrid, Spain, [3]Rheumatology Department, La Paz University Hospital, Madrid, Spain, [4]Hospital Universitario La Paz, Madrid, Spain

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: CD4+CXCR5+PD-1^{hi} follicular helper (Tfh) T cells dwell in the germinal centers (GCs), help B cells, and are implicated in Rheumatoid Arthritis (RA) pathogenesis. Circulating counterparts of Tfh (cTfh) cells are expanded in patients with autoimmune conditions and their frequencies seem to correlate with the pool of GC Tfh cells. Abatacept (ABT), interfering with costimulation, can restrain Tfh cell generation and the role of Tfh cells may be pre-eminent in patients with higher cTfh cell frequencies. Therefore, our objective was to examine a). The effect of treatment escalation with TNF blockers (TNFb) or ABT, on the cTfh cell frequency in RA, and b). The relation of baseline cTfh cells with the clinical response.

Methods: Peripheral blood was drawn from seropositive RA patients with an incomplete response to csDMARDS (n=41) who initiated, according to routine clinical practice, TNFb (n= 19) (10 Etn, 3 Adal, 3 Certo, 2 goli, 1 Ifx) or ABT (n= 22). cTfh cell frequencies were determined by flow cytometry of freshly isolated PBMCs at the basal visit and 12 months (12M) after treatment escalation. Age and gender-matched healthy controls (HC) were also studied at both time points (n=41).

Results: a). As compared with HC, RA patients receiving csDMARDs showed increased frequencies (fr.) of cTfh and activated ICOS+ cTfh cells (a-cTfh). A significant improvement of disease activity(ΔDAS28 >2.0) was seen in all of the patients at 12M. The cTfh cell fr. did not vary in patients receiving TNFb but it dropped down to HC levels in those receiving ABT. The fr. of a-cTfh cells was significantly reduced in both groups; however, in the TNFb group it remained above HC whereas in the ABT group it dropped down to HC levels. b). In the ABT group, the baseline fr. of cTfh and a-cTfh had been higher for patients who went on to achieve remission at 12M (12Mr), as compared with those who remained active (12Ma) [Tfh logistic regression OR for remission 25.3,95% CI (12.2-39.8); ROC AUC 0.94(0.83-1), p< 0.0005]; as stated above, the 12M fr. were no longer elevated; in addition there were no differences between the 12Ma and 12Mr subjects. Conversely, in the TNFb group, the baseline fr. of cTfh and a-cTfh had been lower for 12Mr as compared with 12Ma patients [Tfh OR for not achieving remission 8.5 (4.3-15.5); ROC AUC 0.77(0.54-0.99), p< 0.05]; furthermore, the 12M fr. showed the same pattern: they had not significantly changed, persisted elevated above HC and remained lower in 12Mr as compared with 12Ma patients. The baseline cTfh cutoff fr. for achieving remission in the ABT group was >0.35% (sensitivity 92.7%, specificity 90%). The baseline cTfh cutoff fr. for not achieving remission in the TNFb group was >0.44% (sensitivity 67.7%, specificity 90%).

Conclusion: ABT but not TNFb, is able to curtail cTfh cell numbers in RA, suggesting that costimulation blockade can restrain germinal center overactivity. Higher baseline cTfh cell frequencies predict a good response to ABT and at the same time, a poor response to TNFb. Therefore, immunophenotyping of patients with an incomplete response to csDMARDs can facilitate a personalized therapeutic strategy for treatment escalation.

Disclosure: M. Miranda-Carus: Bristol-Myers Squibb(BMS), 5, Gebro Pharma, 5; **B. Nieto-Carvalhal**: None; **I. Monjo**: Amgen, 6, Gedeon Richter, 6, Janssen, 6, Novartis, 6, Roche, 6, UCB, 6; **M. Uyaguari-Morocho**: None; **A. Villalba**: None; **L. Nuño**: None; **D. Peiteado**: None; **E. Fernández**: None; **S. García-Carazo**: None; **A. Balsa**: Abb-Vie/Abbott, 1, 2, 5, 6, Bristol-Myers Squibb(BMS), 1, 5, Eli Lilly, 1, 5, 6, Merck/MSD, 1, 5, Novartis, 5, Pfizer, 1, 5, 6, UCB, 1, 5, 6.

Abstract Number: 0079

CD4 T Cell Repertoire Features in RA Patients with High-risk HLA-DRB1 Alleles

Amit Lakhanpal[1], Kazuyoshi Ishigaki[2], Anvita Singaraju[1], Alejandro Kochen[3], Miriam Fein[1], Soumya Raychaudhuri[4] and Laura Donlin[1], [1]Hospital for Special Surgery, New York, NY, [2]RIKEN, Tokyo, Japan, [3]Yale School of Medicine, New Haven, CT, [4]Brigham and Women's Hospital, Boston, MA

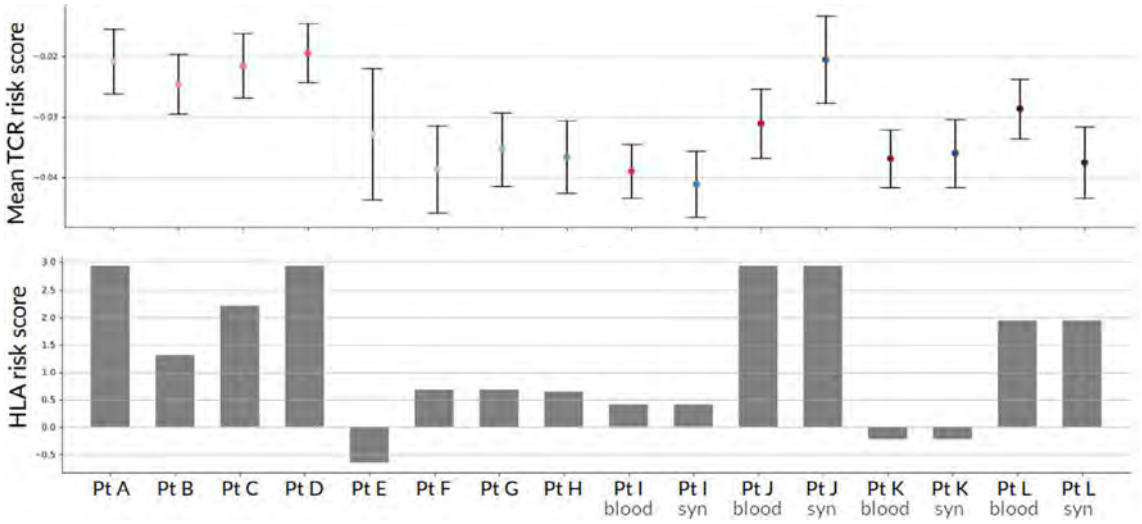
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: A role for CD4 T cells in RA pathology is supported by the effectiveness of T cell therapies, genetic studies implicating T cell gene regulation, and association with specific MHC Class II HLA-DRB1 alleles. Using expansive healthy cohorts, Ishigaki *et al* (Nat Gen 54:393-402 (2022)) previously identified CD4 T cell receptor (TCR) repertoire features associated with the presence of HLA-DRB1 RA risk alleles. These features can be combined into a TCR risk score. This TCR risk score included a positive association with high risk HLA alleles and specific amino acids in certain positions of the CDR3 region (for example, negative charged residues at position 110). Here, we computed TCR repertoire risk scores for 12 RA patients. Understanding these properties would have implications for our conception of the underpinnings of RA pathology.

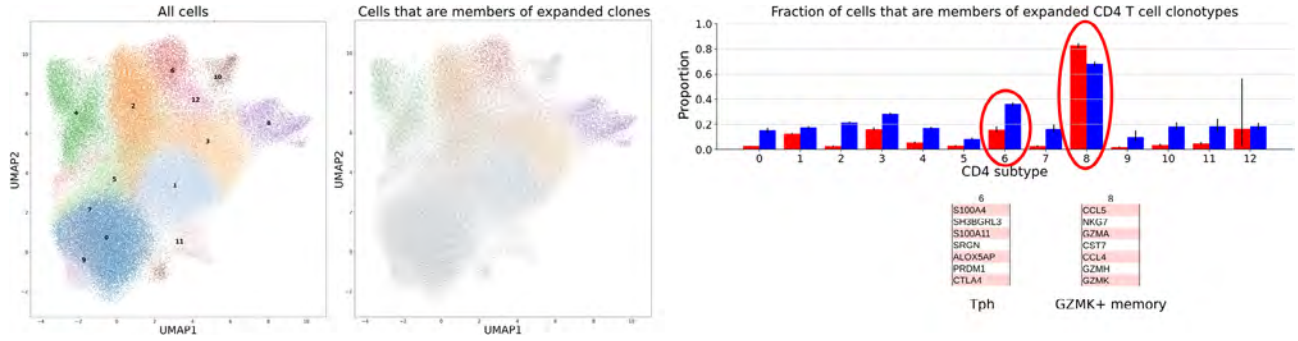
Methods: We obtained synovial tissue (n=8) and blood (n=8) from patients satisfying either the 1987 or 2010 ACR/EULAR RA classification criteria, with informed consent and IRB approval. We flow-sorted CD4 T cells and applied single-cell transcriptome and T-cell receptor sequencing (10X platform). We used our custom computational pipeline, implemented with scanpy, to assign CD4 transcriptional subtypes. We quantified TCR repertoire including clonal expansion and the Ishigaki *et al* TCR risk score, We also inferred HLA-DRB1 genotypes (using arcasHLA) from which HLA-RA risk scores were computed. ~5,000-9,000 cells per sample were analyzed.

Results: Across 12 RA patients, the TCR repertoire risk score positively correlated with the HLA-RA genetic risk score in each subject [Fig 1]; the degree of association is similar to that seen in the large-scale healthy cohorts. Three patients had the highest possible HLA-risk score (~3.0), due to both HLA-DRB1 copies containing the highest scoring risk alleles, which were all shared-epitope alleles. Notably, these patients also demonstrated the highest TCR risk score across their repertoires. For patients from which we had paired blood and synovial tissue CD4 T cells, the patient with the maximal HLA risk score demonstrated a larger overall TCR repertoire risk score in the synovium. Examining features of clonal CD4 T cell populations, we noted a preponderance of cells from expanded clones within two specific CD4 subsets, the T peripheral helper (Tph) and GZMK+ memory CD4 cells [Fig 2].

Conclusion: Our study has defined TCR receptor repertoire patterns that associate with high-risk HLA-DRB1 alleles in RA patients. Indeed, we now show that having two risky HLA-DRB1 alleles increases the total number of risk-associating T cell clones. Given the low frequency of clone sizes for CD4 T cells in general, the total number of risky T cell clonotypes may be a new marker of increased RA risk and argue for a broader repertoire-wide view of CD4 T cell involvement in RA rather than singular antigenic focused hypotheses. Future studies on these particular clones in high-risk repertoires may become highly relevant in further understanding RA disease etiology and treatment.



For each sample, the average of the TCR risk score (with standard error bars) in the upper plot, and the HLA risk score of the corresponding subject in the lower plot. Shades of red in the upper plot denote a blood origin of the sample, while shades of blue denote a synovial origin. Across all samples, there is a general tendency toward higher mean TCR risk score with higher HLA risk score. Looking within the paired samples (the rightmost 8 bars), there is no consistent relationship between the TCR risk score based on blood or synovial origin of the CD4 cells



Two-dimensional UMAP projection of high-dimensional scRNAseq data demonstrates quality of unsupervised Leiden clustering to isolate distinct CD4 T cell subtypes (by color, far left). Combining scRNAseq data with TCR repertoire data allows identification of cells belonging to CD4 T cell clonotypes that show evidence of expansion (i.e., a clonotype that appears more than once across data from all cells) (colored dots on right-side UMAP) The table summarizes genes found to be characteristic of the CD4 subtypes in which the most clonal expansion was observed, based on the scRNAseq data (circled in bar plot above, blue bars for synovium, red bars for blood). Based on those marker genes, two of the CD4 subtypes are identifiable as previously distinguished populations, T peripheral helper cells (Tph) and GZMK+ memory CD4 cells

Disclosure: A. Lakhanpal: None; **K. Ishigaki**: None; **A. Singaraju**: None; **A. Kochen**: None; **M. Fein**: None; **S. Raychaudhuri**: AbbVie, 6, Janssen, 1, Mestag, Inc, 2, 8, Pfizer, 1, Sanofi, 1, Sonoma, 1, 8; **L. Donlin**: Bristol-Myers Squibb(BMS), 2, Stryker, 2.

Abstract Number: 0080

Pharmacological Inhibition of PRMT5 Demonstrates Broad Efficacy in Multiple Preclinical Models of Autoimmunity and Inflammation by Suppressing Th1, Th17 and TNF-Mediated Inflammatory Responses

Neha Bhagwat[1], Kumar Penmetsa[2], Matt Devalaraja[3], Suzana Marusic[4], Cornelia M. Weyand[5], Shozo Ohtsuki[6], Peggy Scherle[1] and Kris Vaddi[1], [1]Prelude Therapeutics, Inc, Wilmington, DE, [2]Thermo Fisher Scientific, Philadelphia, PA, [3]Nipuna Therapeutics, Waltham, MA, [4]Hooke Laboratories LLC, Lawrence, MA, [5]Mayo Clinic School of Medicine and Stanford University, Rochester, MN, [6]Mayo Clinic College of Medicine and Science, Stanford University School of Medicine, Rochester, MN

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

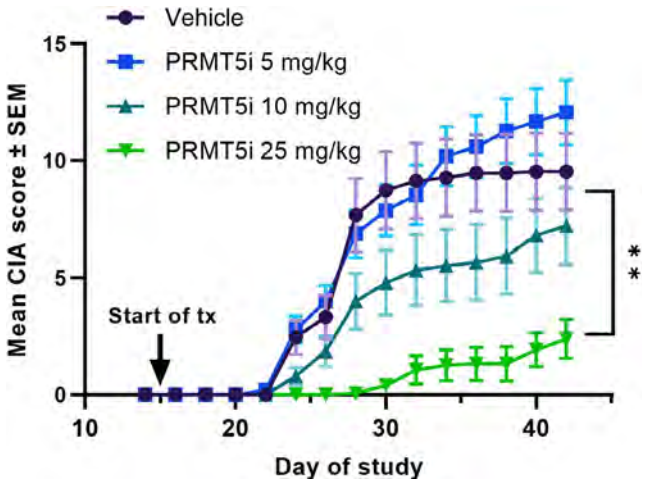
Background/Purpose: Protein arginine methyltransferase 5 (PRMT5) is the major type II PRMT that catalyzes the formation of symmetrical dimethyl arginine (SDMA) on protein substrates and is involved in the regulation of key inflammatory genes. In particular, PRMT5 plays an essential role in T cell homeostasis and activation-induced expansion by maintaining cytokine signaling. It has been shown to promote inflammatory T-cell responses, particularly those driven by Th1 and Th17 cells. Therefore, targeting PRMT5 with selective inhibitors offers a novel therapeutic approach to target T-cell mediated autoimmune and inflammatory disorders. We have previously reported that treatment with selective small-molecule inhibitors of PRMT5 leads to potent suppression of pro-inflammatory cytokines in preclinical models of acute graft-vs-host disease and myeloproliferative neoplasms. We therefore evaluated the effects of novel, selective and orally bioavailable PRMT5 inhibitors in rodent models of T-cell-driven autoimmunity and inflammation.

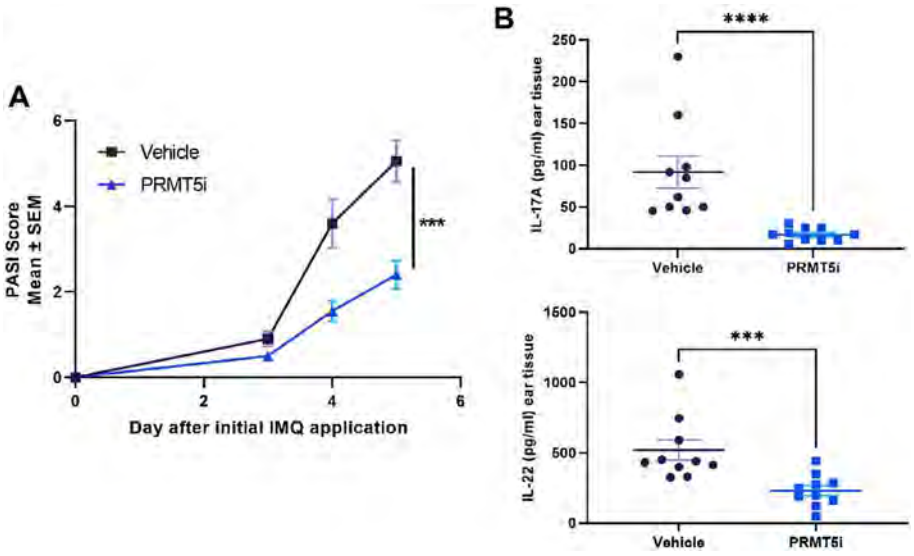
Methods: Orally administered PRMT5 inhibitors (PRMT5i) were evaluated in vivo in several rodent models including an MRL/lpr model of systemic lupus erythematosus, an imiquimod (IMQ)-induced model of psoriasis, a CIA mouse model of rheumatoid arthritis, an experimental autoimmune neuritis (EAN) rat model, and a human artery/NSG mouse chimera model of giant cell arteritis (GCA). In vitro, proliferation (Ki67), IFNγ and IL-17 production was measured in healthy human CD4+ T cells following stimulation and treatment with PRMT5i.

Results: In vitro, PRMT5i treatment significantly inhibited T-cell proliferation and differentiation of Th1 and Th17 cells. Consistent with these effects, PRMT5i treatment of MRL/lpr mice led to significant, dose-dependent reduction of disease severity including reduction in proteinuria, anti-dsDNA antibodies in serum, kidney pathology and key serum cytokines such as TNF, IFNγ and BAFF. Treated animals showed decreased pro-inflammatory CD4+ cells and increased Tregs in kidneys and spleens compared to vehicle controls. In addition, PRMT5i were efficacious at reducing disease severity (PASI score) in the IMQ-induced psoriasis model. Inhibitor treated animals had significantly lower IL-17A and IL-22 serum concentrations compared to vehicle controls. In the CIA model, PRMT5i administration reduced disease incidence and severity in a dose-dependent manner. PRMT5i treatment in a rat model of EAN also resulted in significant reduction of disease severity as evidenced by reduced inflammatory infiltration and higher myelination of peripheral neuronal tissue. Finally, in a humanized mouse model of GCA, treatment with PRMT5i reduced inflammatory mononuclear cell infiltration in the blood vessel wall and reduced levels of IFNγ and IL-21 compared to either vehicle or prednisolone treated animals.

Conclusion: PRMT5 inhibitors were highly effective in suppressing Th1, Th17 and IFNγ-mediated immune responses in a number of preclinical models of human autoimmune diseases at well-tolerated doses. These data support the potential development of PRMT5i as a therapy for inflammatory and autoimmune diseases.

PRMT5 inhibitors show dose-dependent efficacy in a mouse CIA model.





Oral administration of PRMT5i shows (A) significant improvement in erythema and skin thickness (represented by PASI score) and (B) reduction in key cytokines in ear tissue in an IMQ-induced psoriasis model.

Disclosure: N. Bhagwat: Prelude Therapeutics, Inc, 3; **K. Penmetsa**: Prelude Therapeutics, Inc, 2; **M. Devalaraja**: Prelude Therapeutics, Inc, 2; **S. Marusic**: None; **C. Weyand**: AbbVie/Abbott, 1, Bristol-Myers Squibb(BMS), 1, Gilead, 1; **S. Ohtsuki**: None; **P. Scherle**: Prelude Therapeutics, Inc, 3; **K. Vaddi**: Prelude Therapeutics, Inc, 3, 4.

Abstract Number: 0081

RA Disease Activity Influence the Frequency and Phenotype of Citrulline Reactive CD4 T Cells in DRB1*04:04 ACPA+ RA Patients

Cliff Rims[1], Anne Hocking[1], Sylvia Posso[1], Bernard Ng[2], Jeffrey Carlin[3], Jane Buckner[4] and Eddie James[4], [1]Benaroya Research Institute, Seattle, WA, [2]Veteran Affairs, Seattle, WA, [3]Virginia Mason Medical Center, Seattle, WA, [4]Benaroya Research Institute at Virginia Mason, Seattle, WA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The presence of ACPA in RA signifies an immune response toward citrullinated auto-antigens in disease pathogenesis and persistence. RA is a T cell mediated disease based on response to T cell directed therapy, enrichment of T cells in the joint, and association with HLA class II alleles.DRB1*04:01 cit-epitopes have been well described originating from auto-antigens aggrecan, cartilage intermediate layer protein (CILP), α-enolase, α-fibrinogen, and vimentin. Despite DRB1*04:04 inclusion among the shared epitope alleles and over-representation in RA, literature identifying

DR0404 restricted cit-epitopes have been scarce. The purpose of this study was to determine antigen specificities and to describe the character of DR0404 cit-reactive CD4 T cell responses in RA.

Methods: RA and control subjects were recruited with informed consent and sampled through the IRB approved Benaroya Research Institute (BRI) rheumatic disease and control registries. All subjects had at least one copy of the HLA-DRB1*04:04 allele. All RA subjects met the 2010 ACR criteria for RA, were ACPA+, and represented a range of characteristics that included duration of disease, therapy treatment, and disease activity at the time of draw.

Cit-peptides were designed starting from antigens reported in the literature to be associated with RA, synthesized based on predicted binding to DR0404 using a calculation matrix, and binding is confirmed using a competition assay. The peptides were assessed for immunogenicity using a 14-day in-vitro peptide stimulation assay using cognate-peptide loaded DR0404 tetramers to report response. T cell clones that target cit-peptides were isolated from responders. Finally, to characterize cit-specific CD4 T cells, blood from 23 RA and 20 healthy DR0404 subjects were stained with a multi-color cit-tetramer panel along with antibodies to determine CD4 subtype.

Results: A 74 cit-peptide library from aggrecan, CILP, α-enolase, α-fibrinogen, and vimentin was synthesized based on results from a DR0404 cit-prediction binding matrix. Next, a competition assay confirmed 23 peptides as DR0404 binders. All 23 peptides elicited an immune response in RA PBMC using a 14 day in-vitro stimulation assay and 6 clones were isolated and verified using tetramers. These results were used to create a multi-color 13 tetramer DR0404 ex-vivo panel where PBMC was stained from RA and healthy subjects. Ex-vivo analysis revealed all RA subjects having detectable cit-specific CD4 T cells whose memory cells consisted of either CXCR3+ or CCR4+. The frequency of memory cit-specific CD4 T cells was elevated among RA subjects with high disease activity and also enriched of Th1 and Th2 lineage.

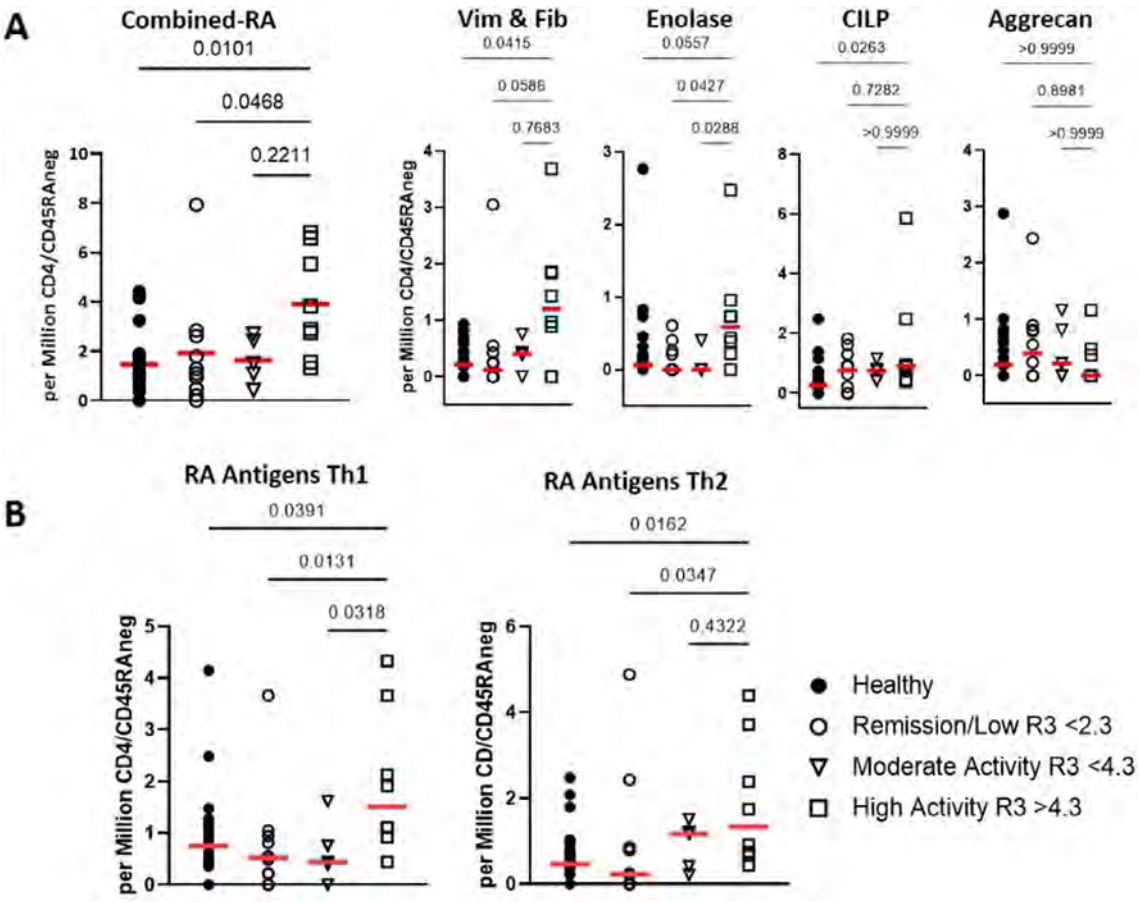
Conclusion: These findings identify novel DR0404 restricted cit-epitopes and provide tools to capture and interrogate cit-reactive CD4 T cells in patients with RA and those at-risk for disease. In particular, we show cit-reactive T cell frequency and it's inflammatory subsets are influenced by disease activity using a multiplexed tetramer assay, which can be used to better understand the interplay of antigen specificities and phenotypes in the pathogenesis of RA.

Ex-vivo tetramer panel of citrulline peptides

Antigen	Position (aa #)	Sequence
Aggrecan	3	TLLWVFVTL(CIT)VITAAVTV
Aggrecan	82	KEVVLLVATEG(CIT)V(CIT)VN
Aggrecan	153	IVFHY(CIT)AIST(CIT)YTLDF
Enolase	3	ILKIHA(CIT)EIFDS(CIT)GN
Enolase	11	IFDS(CIT)GNPTVEVDLF
Enolase	326	K(CIT)IAKAVNEKSCNCL
CILP	297	ATIKAEFV(CIT)AETPYM
CILP	982	GKLYGI(CIT)DVXSTRDR
Vimentin	418	SSLNL(CIT)ETNLDSL
Vimentin	59	GVYAT(CIT)SSAV(CIT)L(CIT)SSVPGVR
Vimentin	66	SAV(CIT)L(CIT)SSVPGVR
Fibrinogen	209	AKDLLPS(CIT)D(CIT)QHLPLIK
Fibrinogen	712	DYLHLLTQ(CIT)GSVL(CIT)V
Influenza	97	VKLYRKLKREITFHGAKEIS

Ex-vivo subject demography

	Rheumatoid Arthritis (n=23)	Healthy Control (n=20)
Median Age at Draw (Range: Min-Max)	56 yrs. (32-82 yrs.)	42.5 yrs. (22-64 yrs.)
Male/Female (number of subjects)	7/16	7/13
Disease Duration (mean±sd)	10.2 yrs. ± 9.1 yrs.	
Early RA (0-5yrs) (number of subjects)	8	
Established RA (>5yrs) (number of subjects)	15	
Disease Activity Score (RAPID3*) (number of subjects)	23	
Near remission (0 – 1.0)	2	
Low activity (1.3 – 2.0)	8	
Moderate activity (2.3 – 4.0)	5	
High activity (4.3 – 10.0)	8	
Not Reported	0	
Therapy at Draw (% of RA cohort)**		
DMARDS	78.3%	
Biologics	39.1%	



RA disease activity influence the frequency and phenotype of citrulline CD4 T cells. (A) The frequency of CD45RA-negative tetramer cells were analyzed based on RA subjects RAPID3 score outcome (Near-Remission/Low <2.3; Moderate activity <4.3; and High activity >4.3) along with healthy subjects. RA subjects with high disease activity were those with the highest frequency compared to healthy subjects among citrulline antigens combined, alpha-enolase, CILP, vimentin, and fibrinogen. (B) The dominant phenotype of citrulline antigens among high RA active disease are Th1 and Th2 type cells respectively. The p-values of both A and B were calculated using Kruskal-Wallis test.

Disclosure: C. Rims: None; **A. Hocking**: None; **S. Posso**: None; **B. Ng**: None; **J. Carlin**: None; **J. Buckner**: Bristol-Myers Squibb(BMS), 2, gentibio, 1, 10, 11, hotspot therapeutics, 2, Janssen, 2; **E. James**: Bristol-Myers Squibb(BMS), 5, Janssen, 5, Novartis, 5, Provention Bio, 5.

Abstract Number: 0082

A VAV1-Directed Molecular Glue Degrader, MRT-6160, Reduces Joint Inflammation in a Collagen-Induced Arthritis Autoimmune Disease Model

Adam Cartwright[1], Foram Desai[2], Sophia Nguyen[2], Alexandra Trouilloud[2], Elisa Liardo[1], Daric Wible[2], Ilaria Lamberto[2], Bradley Demarco[2], Chris King[2], Debora Bonenfant[1], Sharon Townson[2], Owen Wallace[2], Filip Janku[2], Laura McAllister[1], Alison Paterson[2] and **Marisa Peluso**[2], [1]Monte Rosa Therapeutics, Basel, Switzerland, [2]Monte Rosa Therapeutics, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: VAV1 is a member of the VAV family of guanine nucleotide exchange factors (GEFs) and plays a critical role in mediating T- and B-cell receptor activity. VAV1 expression is primarily restricted to immune cells, positioning it as an attractive target for the treatment of inflammatory and autoimmune diseases. In knockout mice and human-based CRISPR screens, *VAV1/Vav1* loss has been linked with reduced T- and/or B-cell function. Despite being a well-validated target for T- and/or B-cell mediated autoimmune disease, VAV1 has remained undruggable to date using small molecule inhibitor approaches. MRT-6160 is a highly selective first-in-class oral VAV1-targeting molecular glue degrader (MGD), which induces proteasomal degradation of VAV1 through formation of a ternary complex with the E3 ligase cereblon. We propose that targeting VAV1 will have broad therapeutic implications in a variety of autoimmune disorders driven by the underlying dysregulation of T- and B-cells, including rheumatoid arthritis.

Methods: Human cells were treated with MRT-6160 and profiled for VAV1 levels and selectivity. To determine effects of MRT-6160-mediated VAV1 degradation on lymphocyte function, pharmacodynamic and functional readouts were assayed in TCR- and BCR-stimulated purified human T- and B-cells. To test pharmaco-kinetics and -dynamics of MRT-6160 *in vivo*, healthy mice were treated with a single oral administration of MRT-6160 followed by assessment of compound and VAV1 levels in multiple tissues over time. The *in vivo* activity of MRT-6160 was evaluated in the collagen-induced arthritis (CIA) autoimmune disease setting where female DBA/1 mice were immunized on day 0 (intravenously) and boosted on day 21 (subcutaneously) using chicken type II collagen emulsified in complete or incomplete Freund's adjuvant respectively. Following disease onset (average clinical score of ~1.5), mice were randomized into treatment groups and orally administered vehicle or 10 mg/kg MRT-6160 daily. In positive control groups, mice were administered either 1 mg/kg dexamethasone (daily via intraperitoneal injection) or 500 μg anti-TNF (three times weekly via intraperitoneal injection). Mice in all treatment groups were dosed for a duration of 20 days and assessed daily for body weight and clinical signs of arthritis in all four paws.

Results: MRT-6160-mediated selective degradation of VAV1 attenuated TCR- and BCR-mediated activation and function in primary human T- and B-cells. *In vivo*, oral dosing of MRT-6160 elicited Vav1 degradation across multiple tissues in a dose-dependent manner. Over the course of 20 days dosing in the CIA autoimmune disease setting, MRT-6160 significantly decreased disease progression and endpoint clinical scores (3.2±2.6) compared to vehicle (12.5±4.0) and was comparable to anti-TNF (4.4±3.7).

Conclusion: The VAV1-targeting MGD MRT-6160 attenuates disease progression in the autoimmune CIA model with a therapeutic treatment regimen. This warrants further investigation of MRT-6160 in a clinical setting.

Disclosure: A. Cartwright: Monte Rosa Therapeutics, 3, 11; **F. Desai**: Monte Rosa Therapeutics, 3, 11; **S. Nguyen**: Monte Rosa Therapeutics, 3, 11; **A. Trouilloud**: Monte Rosa Therapeutics, 3, 11; **E. Liardo**: Monte Rosa Therapeutics, 3, 11; **D. Wible**: Monte Rosa Therapeutics, 3, 11; **I. Lamberto**: Monte Rosa Therapeutics, 3, 11; **B. Demarco**: Monte Rosa Therapeutics, 3, 11; **C. King**: Monte Rosa Therapeutics, 3, 11; **D. Bonenfant**: Monte Rosa Therapeutics, 3, 11; **S. Townson**: Monte Rosa Therapeutics, 3, 4, 11; **O. Wallace**: Monte Rosa Therapeutics, 3, 4, 11; **F. Janku**: Monte Rosa Therapeutics, 3, 4, 11; **L. McAllister**: Monte Rosa Therapeutics, 3, 11; **A. Paterson**: Monte Rosa Therapeutics, 3, 11; **M. Peluso**: Monte Rosa Therapeutics, 3, 11.

Abstract Number: 0083

Expression of mRNA Vaccine Antigen in Hematopoietic Cells Is Necessary for Induction of Optimal Vaccine-Specific CD4$^+$ T Cell Responses

Julia Rood[1], Stephanie Suh Kyung Yoon[2], Mary O'Mara[3], Mary Kate Heard[3], Chaitali Bhadiadra[3], Nhu Le[3], Christabel Ameyaw Baah[3], Norbert Pardi[4] and Laurence Eisenlohr[1], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]School of Engineering and Applied Science, University of Pennsylvania, Philadelphia, PA, [3]Children's Hospital of Philadelphia, Philadelphia, PA, [4]Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: mRNA vaccines are safe and remarkably effective, but rare cases of vaccine-induced autoimmunity have been reported, particularly in patients with underlying inflammatory disease. Mechanistic insight into such cases is limited by the fact that little is known of the proximal events leading to CD4$^+$ T cell priming after mRNA vaccination. Vaccine antigen derived from cells at the immunization site, such as muscle cells, is presumed to activate CD4$^+$ T cells through uptake by antigen presenting cells (APCs) and processing via the classical exogenous pathway. However, APCs themselves efficiently produce mRNA-encoded antigen, and in analogous viral infection models, virus-specific CD4$^+$ T cell responses are driven primarily by endogenous antigens presented via non-classical pathways. We investigated whether a similar phenomenon underlies CD4$^+$ T cell responses to mRNA vaccines.

Methods: We developed a series of mRNA vaccines that encode a model viral protein (influenza nucleoprotein, NP), followed by specific microRNA (miR) targeting sequences that allow for differential expression of vaccine antigen in different cell types. Three different NP-miR mRNA constructs were generated. "NP-miR142t" contains the targeting sequence for hematopoietic-specific miR-142, leading to inhibition of NP expression within hematopoietic cells – and thus reliance on exogenous antigen for presentation to CD4$^+$ T cells. "NP-miR206t" contains the targeting sequence for muscle cell-specific miR-206, thus excluding NP expression from muscle cells and forcing APCs to rely primarily on endogenous antigen. A control "NP-scrambled" construct contains scrambled miR binding sites that are not targeted by any miRs. Cell-type specificity of miR targeting was validated *in vitro* by flow cytometry and Western blot. Mice were immunized intramuscularly with mRNA encapsulated in lipid nanoparticles to evaluate NP-specific CD4$^+$ T cell responses *in vivo*.

Results: Mice immunized with NP-miR142t demonstrated significantly lower frequencies of NP-specific $CD4^+$ T cells by both IFNg ELISpot and tetramer staining, compared to mice immunized with NP-scrambled, suggesting that antigen expressed within hematopoietic cells is critical to the $CD4^+$ T cell response. Immunization with NP-miR206t resulted in only a modest reduction in NP-specific $CD4^+$ T cells, despite significantly decreased NP protein levels within muscle.

Conclusion: Optimal $CD4^+$ T cell activation by mRNA vaccines requires antigen expression in APCs and other hematopoietic cells, suggesting that endogenous antigen presentation is a major driver of the $CD4^+$ T cell response. Contrary to the prevailing paradigm, exogenous vaccine antigen derived from muscle and other cells may not be the primary source of antigen activating vaccine-specific $CD4^+$ T cells. Future studies will expand upon these findings to determine how restriction of antigen source – and therefore processing via exogenous or endogenous pathways – impacts adaptive immune responses to mRNA vaccines more broadly.

Disclosure: J. Rood: None; **S. Yoon**: None; **M. O'Mara**: None; **M. Heard**: None; **C. Bhadiadra**: None; **N. Le**: None; **C. Ameyaw Baah**: None; **N. Pardi**: None; **L. Eisenlohr**: None.

Abstract Number: 0084

Excess IL-18 Protects from Experimental Autoimmune Encephalomyelitis Mainly via Preferential Augmentation of Suppressor/Regulatory over Autoreactive T-cell Function

Jeremy Morrissette[1], Vinh Dang[2], Jemy Varghese[2], Zachary Lanzar[1], Junior Nguyen[2], Emily Landy[3], Anastasia Frank-Kamenetskii[4] and Scott Canna[2], [1]University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA, [2]Children's Hospital of Philadelphia, Philadelphia, PA, [3]University of Pittsburgh, Pittsburgh, PA, [4]CHOP/UPENN, Philadelphia, PA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Interleukin 18 (IL-18) is an inflammasome-activated cytokine that canonically amplifies interferon-gamma (IFNg) production and cytotoxicity by CD8 T-cells (CD8Ts) and Th1 CD4 T-cells (CD4Ts). It is inhibited by the circulating high affinity antagonist, IL-18 binding protein (*Il18bp*). In certain contexts, IL-18 amplifies non-Th1 responses including Th2, Th17, and Treg. Despite its likely pathogenic role in autoinflammation, clinical observations suggest a possible immunoregulatory role in CD4T-mediated autoimmunity. We sought to understand the role of excess IL-18 in the mixed Th1/17 experimental autoimmune encephalomyelitis (EAE) model of central nervous system autoimmunity.

Methods: EAE was induced via immunization with a complete Freund's adjuvant/Myelin Oligodendrocyte Glycoprotein peptide (MOG^{35-55}) emulsion and pertussis toxin in the following mice: mice deficient in Il-18bp ($Il18bp^{-/-}$), with transgenic overproduction of mature IL-18 (Il18tg), transgenic for a T-cell receptor recognizing MOG^{35-55} (2D2 mice), and relevant controls . EAE was monitored by daily clinical scoring of ascending paralysis. Cell number and cellular protein phenotype were determined by flow cytometry.

Results: We hypothesized that systemic excess IL-18, would amplify autoreactive T-cell activation and lead to more severe EAE, but both $Il18bp^{-/-}$ and Il18tg mice were profoundly protected from EAE (Fig. 1). Protection from EAE in $Il18bp^{-/-}$ mice depended on IFNg. Draining lymph nodes and spleens from $Il18bp^{-/-}$ mice showed a modest increase in IFNg-producing

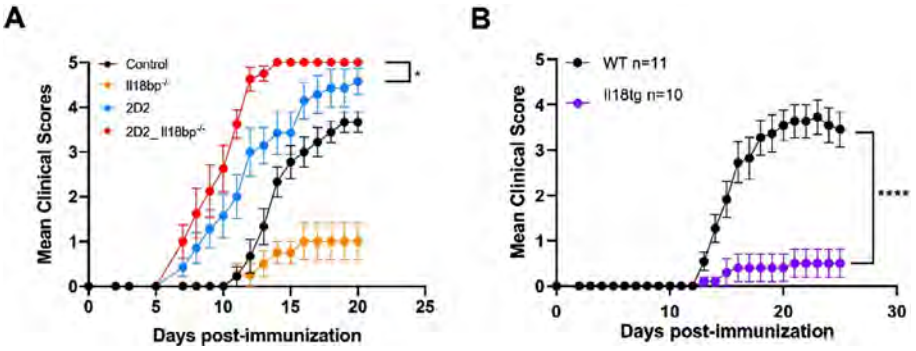


Figure 1: Excess IL-18 protects against EAE development with a physiologic T cell repertoire. Il18bp-/-, 2D2, 2D2;Il18bp-/- (A), or Il18tg (B) mice underwent EAE immunization on day 0 with daily clinical EAE scoring compared to WT control mice.

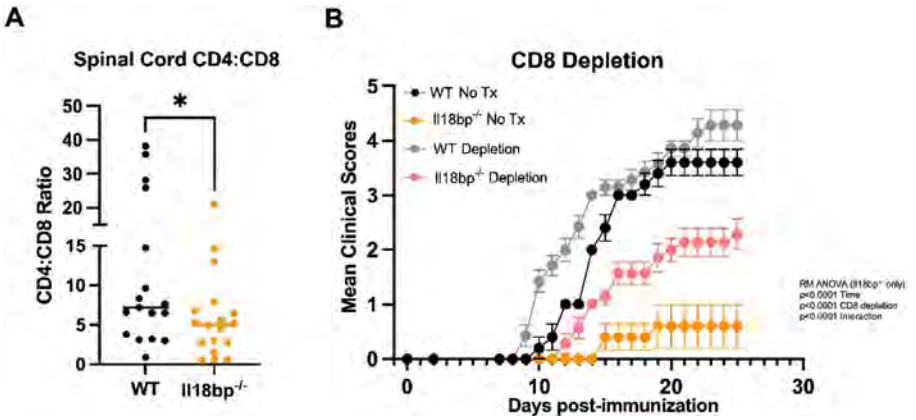


Figure 2: Excess IL-18 enriches CD8 T cells and depends on CD8 T cell function for protection. Spinal cords were analyzed by flow cytometry from WT and Il18bp-/- mice at peak disease (day 19 to 21) and the ratio of CD4 to CD8 T cells is represented (A). Mean clinical EAE score of WT and Il18bp-/- mice receiving isotype control (LIF2 Rat IgG2b) or CD8 depleting antibody (YTS169.4) q3d starting on day 0 (B).

CD4Ts and equivalent IL-17-producing CD4Ts. Spinal cords demonstrated fewer CD4T cells but comparable markers of Th function/polarization on a per-cell basis. There was increased infiltration of CD8Ts relative to CD4Ts in spinal cords of $Il18bp^{-/-}$mice (Fig. 2A). 2D2 mice have an abundance of MOG autoreactive CD4Ts and very few CD8Ts (due to allelic exclusion). Paradoxically, $Il18bp^{-/-}$;2D2 mice developed more severe EAE than control 2D2 mice (Fig.1A), suggesting that an increase in precursor autoreactive CD4Ts and/or loss of CD8Ts switches the effect of excess IL-18 from protective to pathogenic. Sensitivity to EAE was restored in $Il18bp^{-/-}$mice only after transfer of >5 million autoreactive 2D2 CD4Ts. Further, ex vivo culture with IL-18 improved CD8Ts ability to inhibit EAE while CD8-depletion substantially, but incompletely, diminished protection in $Il18bp^{-/-}$ mice (Fig.2B).

Conclusion: These data suggest the IL-18 can amplify both autoreactive CD4T and previously described CD8 T suppressor cells but the latter dominate with a physiologic T cell repertoire. Excess IL-18 may function to preferentially augment CD8T suppressor function to clear autoreactive CD4T and mediate protection in EAE. This may inform novel strategies to amplify endogenous suppressive T cells or enhance cellular therapeutics in the treatment of autoimmune diseases.

Disclosure: J. Morrissette: None; **V. Dang**: None; **J. Varghese**: None; **Z. Lanzar**: None; **J. Nguyen**: None; **E. Landy**: None; **A. Frank-Kamenetskii**: None; **S. Canna**: Apollo Therapeutics, 2, Novartis, 12, Site PI for industry-sponsored trial, PracticePoint CME, 6, Simcha Therapeutics, 2, Sobi, 6.

Abstract Number: 0085

Fibroblasts Promote Upregulation of Cannabinoid Type 2 Receptor on Inflammatory Cells in Dermatomyositis

DeAnna Diaz[1], Muhammad Bashir[1], **Rohan Dhiman**[2], Avital Baniel[1], Julianne Kleitsch[1], Rachita Pandya[1], Meena Sharma[1], Thomas Vazquez[1], Ming-Lin Liu[2], Mariko Momohara[2] and Victoria Werth[3], [1]Philadelphia VAMC, Philadelphia, PA, USA and Department of Dermatology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, [2]University of Pennsylvania, Philadelphia, PA, [3]University of Pennsylvania and Corporal Michael J. Crescenz VAMC, Philadelphia, PA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Dermatomyositis (DM) is a chronic, systemic autoimmune disease affecting the skin, muscle, and lungs. The activation of CB2R has been shown to reduce several, key proinflammatory cytokines implicated in DM. Our group has previously shown that CB2R expression was significantly increased in in DM skin compared to blood, possibly due to increased production of local inflammatory cytokines. CB2R stimulation alleviates inflammatory response by down-regulating the expression of TNF-α, IL31, IFN-γ, and type I interferon expression in the early stage of inflammation and reducing the infiltrated inflammatory cells. Having more CB2R on inflammatory cells will lead to enhanced effects of a CB2R agonist. We hypothesized that fibroblasts (FBs) in the skin may play an important role in upregulating CB2R on inflammatory cells within the skin. Dermal fibroblasts produce and organize the extracellular matrix of the dermis. They also communicate with each other and other cell types. Therefore, we sought to examine the role of FBs in CB2R activation.

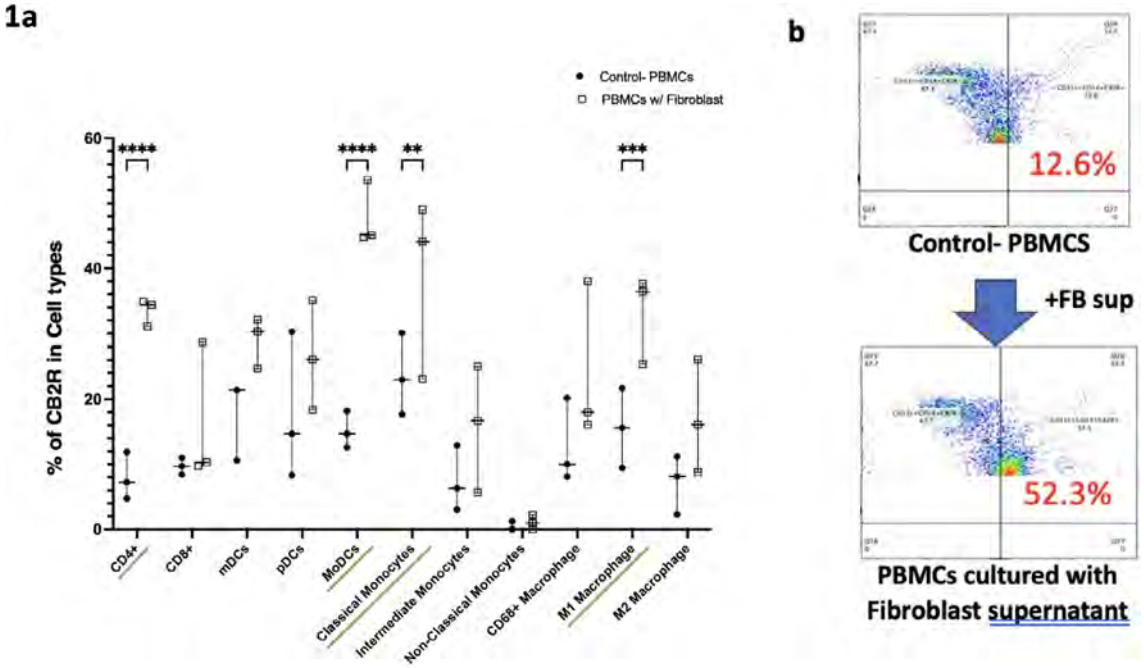


Figure 1. (a) Flow cytometric analysis showing % of CB2R when PBMCS were cultured with fibroblast supernatant. (b) Representative figure in a single DM pt. demonstrates a higher percentage of CB2R on PBMCs cultured with fibroblast supernatant than control.

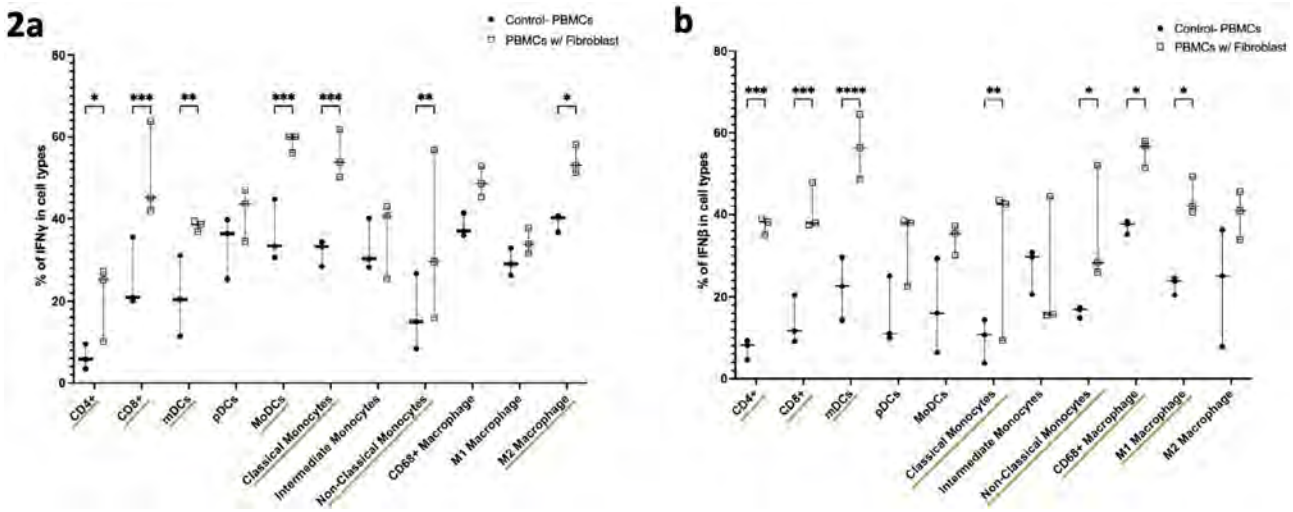


Figure 2. Flow cytometric analysis showing % of IFNγ and IFNβ when PBMCS were cultured with fibroblast supernatant.

Methods: DM PBMCs, which typically have minimal CB2R expression, were cultured with medium with or without human FB supernatant. PBMCs from DM patients were cultured for 24 hrs with control medium at 1:1 dilution with or without fibroblast supernatant retrieved from a 6 well plate of 40-50% confluent primary fibroblast. We then utilized multiplexed flow cytometry to further analyze the expression of CB2R and inflammatory cytokines on 12 cell lineages.

Results: When comparing PBMCs cultured with and without FB supernatant, cells cultured with FB supernatant had a significant increase in CB2R expression on CD4+ T cells ($p < 0.0001$), monocyte-derived dendritic cells (moDCs) ($p < 0.0001$), classical Monocytes (CM) ($p < 0.001$), and M1 Macrophages ($p < 0.0001$). (Figure 1a) There was also a significant increase in inflammatory cells cytokines. When comparing PBMCs cultured with and without FB supernatant, cells cultured with FB supernatant had a significant increase in intracellular IFNγ and IFNβ expression in CD4+ T cells ($p < 0.01$);$p < 0.001$), CD8+T cells ($p < 0.001$; $p< 0.001$), CD11c+ cells ($p < 0.001$; $p< 0.0001$), moDCs in IFNγ ($p < 0.0001$), CMs ($p < 0.0001$; $p< 0.001$), and macrophages ($p < 0.01$). (Figure 2a-b). There was also a significant increase in inflammatory cells cytokines such as TNFα, IL31 and IL4 in CD4+ T cells, moDCs, CD11c+ myeloid dendritic cells, CMs and CD68+ macrophages (data not shown).

Conclusion: These data suggest fibroblasts play a role in increasing CB2R on inflammatory cells, as well as stimulate production of cytokines in DM skin. This suggests that drugs that activate CB2R, leading to downregulation of proinflammatory cytokines, may have enhanced efficacy in the skin due to FB-induced local upregulation of CB2R on inflammatory cells in the skin.

Disclosure: D. Diaz: None; **M. Bashir**: None; **R. Dhiman**: None; **A. Baniel**: None; **J. Kleitsch**: None; **R. Pandya**: None; **M. Sharma**: None; **T. Vazquez**: None; **M. Liu**: None; **M. Momohara**: None; **V. Werth**: Abbvie, 2, Amgen, 2, 5, Anaptys-Bio, 2, Argenx, 5, AstraZeneca, 2, Biogen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Corbus, 5, CSL Behring, 2, 5, EMD Serono, 2, Galderma, 2, Genentech/Roche PI, 5, Gilead, 2, 5, GSK, 2, Horizon Therapeutics, 5, Janssen, 2, Kyowa Kirin, 2, Lilly, 2, Merck, 2, Nektar, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Regeneron, 5, Rome Therapeutics, 2, 5, Sanofi, 2, Ventus, 5, Viela, 2, 5, Xencor, 2.

Abstract Number: 0086

Optimizing PD-1 Agonist Signaling with Membrane Proximal Binding of Rosnilimab, a Clinical Stage PD-1 Agonist IgG1 Antibody

Stephen Parmley, Benjamin Szylyk, Richard Frank, Matthew Hsu, Polina Brodsky, Cailin Sibley, Paul Lizzul and Martin Dahl, AnaptysBio, San Diego, CA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Checkpoint antagonist therapeutics have transformed the field of oncology while advancing the understanding of adequate checkpoint activity in preventing autoimmunity. Checkpoint agonism represents a promising and expanding class of therapies for the treatment of autoimmune diseases, including rheumatoid arthritis (RA), where unmet needs persist despite available therapies. The characteristics that confer agonistic properties to an antibody targeting a checkpoint receptor is an evolving science. Binding to membrane proximal regions of suppressive receptors, together with Fc interactions with receptors on opposing cells, can contribute to tight immune synapse formation between the immune cell and antigen presenting cell. This has been proposed to improve potency of agonistic signaling by excluding activating phosphatases from the immune synapse and promoting receptor clustering. Optimization of these characteristics results in improved agonism and depletion carrying the potential for restoration of immune balance and differentiated clinical efficacy. Rosnilimab has been engineered to leverage these important characteristics. It is a PD-1 agonist antibody with an IgG1 backbone designed to optimize inhibitory signaling through the PD-1 receptor and to deplete PD-1-high pathogenic T cells. It is currently in clinical development for RA and other inflammatory conditions.

Methods: Mutations were targeted to surface exposed regions of the PD-1 extracellular domain where antibodies are likely to bind. Surface plasmon resonance of PD-1 structural mutants were used to locate the epitopes of PD-1 agonist molecules. Membrane proximal and distal binding antibodies were studied in *in vitro* functional assays to assess T cell proliferation and antibody-dependent cellular toxicity (ADCC).

Results: Epitopes of agonistic antibodies were mapped to locations on the PD-1 receptor. The membrane proximal epitope location of rosnilimab was confirmed and binding epitopes for other reference antibodies were identified. Rosnilimab and a membrane distally binding antibody (Reference 1 Antibody) were selected for comparison in functional assays. Rosnilimab demonstrated better inhibition of T cell proliferation and depletion of PD-1+ T cells compared to Reference 1 Antibody, consistent with the hypothesis that membrane proximal binding improves agonistic activity and target cell depletion.

Conclusion: By therapeutically targeting and leveraging natural immune regulatory mechanisms to modulate the pathogenic T cells driving disease, there is an opportunity to dampen the inflammatory cycle and restore immune balance via agonism. Rosnilimab binds to a membrane proximal region of the PD-1 receptor, resulting in optimized inhibition of T cell proliferation, inhibition of cytokine signaling, and PD-1-high T cell depletion. These mechanistic data, robust Phase 1 healthy volunteer safety, PK and translational PD data, and recognized persistent unmet needs in the treatment of RA provide rationale for an ongoing global Phase 2 dose-ranging study of rosnilimab in RA patients.

Disclosure: S. Parmley: AnaptysBio, 3, 11; **B. Szylyk**: AnaptysBio, 3, 11; **R. Frank**: AnaptysBio, 3, 11; **M. Hsu**: AnaptysBio, 3, 11; **P. Brodsky**: AnaptysBio, 3, 11; **C. Sibley**: AnaptysBio, 3, 11; **P. Lizzul**: AnaptysBio, 3, 11; **M. Dahl**: AnaptysBio, 3, 11.

Abstract Number: 0087

Immune Checkpoint Inhibitor Therapy Expands an Activated, anti-PD-1 Drug-bound CD8 T Cell Population That Is Clonally Linked in Blood and Synovial Fluid of ICI-arthritis Patients

Kathryne Marks[1], Anvita Singaraju[2], Runci Wang[3], Ifeoluwakiisi Adejoorin[1], Miriam Fein[2], Michael Postow[4], Karmela Kim Chan[2], Anne Bass[5], Laura Donlin[2] and Deepak Rao[1], [1]Brigham and Women's Hospital, Boston, MA, [2]Hospital for Special Surgery, New York, NY, [3]Renji hospital, Shanghai Jiaotong University, Pudong Xinqu, China, [4]Memorial Sloan Kettering Cancer Center, New York, NY, [5]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitor (ICI) therapies used to treat cancer can induce immune related Adverse events (irAEs) such as ICI-induced arthritis (ICI-arthritis). We have previously identified a cytotoxic, CD38^{hi}CD127^{-} CD8 T cell population that is expanded in the joints of ICI-arthritis patients and characterized by an IFN signature. The extent to which these cells can also be found in the circulation and their potential relationship to T cells in inflamed joints has been unclear. In this study we assessed T cell phenotypes in the circulation following ICI therapy and the clonal relationship between anti-PD-1-bound CD8 T cells in the joints and circulation of ICI-arthritis patients.

Methods: We applied mass cytometry on PBMCs from patients with advanced melanoma in the ADAPT-IT trial who received nivolumab plus ipilimumab, with analysis of PBMC pre-treatment and post-2 cycles (n = 48; 31 with paired pre/post samples) . An anti-IgG4 antibody was included to detect nivolumab (an IgG4 antibody) bound on the cell surface. Separately, bulk TCR sequencing was performed on memory CD8 T cells from paired blood and synovial fluid samples of 3 ICI-arthritis patients.

Results: Unbiased clustering and differential abundance analysis of T cell populations in PMBC from before and after treatment identified several changes in T cell populations, including an increase of a GZMB+ CD8 T cells subset (p=0.0002), a FoxP3+CD25+ regulatory CD4 T cell subset (p< 0.0001) and a CCR6+CD161+ Th17 cell subset (p=< 0.0001). The most dramatic change observed across all PBMCs was a significant induction of CD38^{hi}CD127^{-} CD8 and CD4 T cells

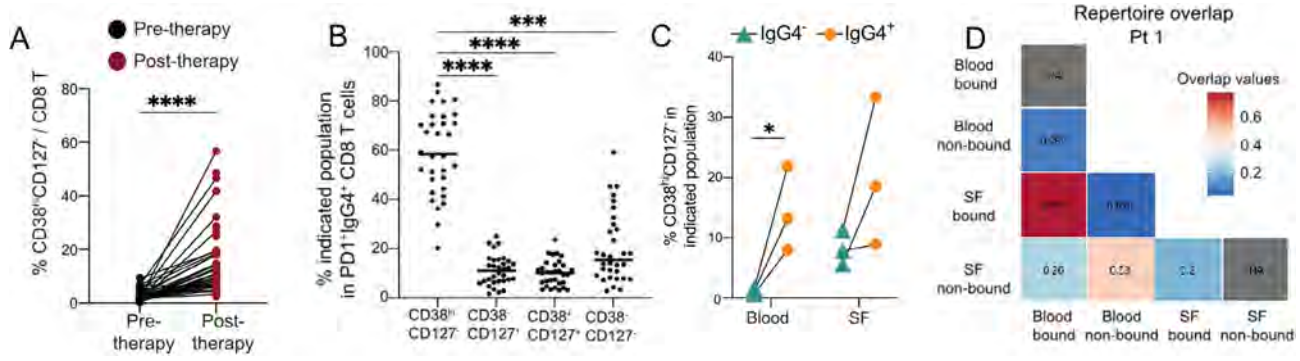


Figure 1.(A) Frequency of CD38hiCD127- CD8 T cells before and after combination ICI therapy. (B) Frequency of anti-PD-1-bound CD8 T cells divided by their expression of CD38 and CD127. (C) Frequency of CD38hiCD127- CD8 T cells in IgG4+ or IgG4- CD8 T cells in either blood or synovial fluid of ICI-arthritis patients. (D) Representative plot of Morisita index values for each comparison demonstrating the repertoire overlap of patients in (C).

($p< 0.0001$,$p< 0.0001$) (Fig 1A). Both the CD8 and CD4 $CD38^{hi}$ T cells were often bound by anti-PD-1 therapy and were Ki67+, indicating that they are proliferative (Fig 1B).

We further investigated the anti-PD-1 drug-bound CD8 T cells in paired blood and synovial fluid samples of those with ICI-arthritis. In both blood and synovial fluid, $CD38^{hi}CD127^{-}$ CD8 T cells were more frequent in anti-PD-1-bound samples than non-drug-bound samples (Fig 1C). In ICI-arthritis patients, anti-PD-1 drug-bound CD8 T cells in blood had marked clonal overlap with drug-bound CD8 T cells in synovial fluid (Fig 1D). There was minimal overlap between drug-bound cells in the synovial fluid and non-drug-bound cells in blood.

Conclusion: $CD38^{hi}CD127^{-}$ CD8 T cells are expanded following ICI therapy and exhibit clonal overlap in the synovial fluid and circulation of ICI-arthritis patients. These results suggest that anti-PD-1 therapy directly targets CD8 T cells to induce $CD38^{hi}$ cytotoxic CD8 T cells. Further, drug-bound, activated cells in the circulation may provide a unique view into the activated T cell populations that accumulate within joints of ICI-arthritis patients.

Disclosure: K. Marks: None; **A. Singaraju**: None; **R. Wang**: None; **I. Adejoorin**: None; **M. Fein**: None; **M. Postow**: Bristol-Myers Squibb(BMS), 2, 5, Chugai, 2, Eisai, 2, Merck/MSD, 2, 5, Nektar, 2, Novartis, 2, 5, Pfizer, 2, Replimune, 2; **K. Chan**: None; **A. Bass**: None; **L. Donlin**: Bristol-Myers Squibb(BMS), 2, Stryker, 2; **D. Rao**: AstraZeneca, 2, Bristol-Myers Squibb, 2, 5, GlaxoSmithKlein(GSK), 2, Hifibio, 2, Janssen, 5, Merck, 5, Scipher Medicine, 2.

Abstract Number: 0088

SLAMF4 Orchestrates the Pathological Cytotoxic Response of $CD4^{+}$ T Cells in Rheumatoid Arthritis

Megane Lacaud[1], Houda-Ghozlane Bouzidi[1], Magali breckler[1], Delphine Lemeiter[2], Luca Semerano[3], Marie-Christophe Boissier[3], Natacha Bessis[4] and **Jerome Biton**[2], [1]Inserm UMR 1225, Université Sorbonne Paris Nord, Bobigny, France, [2]Inserm UMR 1125, Université Sorbonne Paris Nord, Bobigny, France, [3]Inserm UMR 1125, Université Sorbonne Paris Nord; Assistance Publique-Hôpitaux de Paris, Rheumatology department, Avicenne Hospital, Bobigny, France, [4]Inserm UMR 1125, Université Sorbonne Paris Nord, Bobigny, France

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: $CD4^{+}$ $Foxp3^{-}$ conventional T cells (Tconv) play a key role in the inflammatory process involved in rheumatoid arthritis (RA). Recent studies, aided by a substantial advance in available technologies (RNA sequencing, multiparameter flow cytometry and mass cytometry), identified additional $CD4^{+}$ T cell subpopulations that are expanded or dysregulated in RA. It notably included peripheral helper (T_{PH}) T cells ($PD\text{-}1^{hi}$ $CXCR5^{-}$) and cytotoxic $HLA\text{-}DR^{+}$ $CD27^{-}$ $CD4^{+}$ T cells ($CD4^{+}$ CTLs). Regarding pro-inflammatory Tconv, a major remaining objective is to identify additional parameters that support their pathological functions, and then to focus on those that are therapeutically targetable. Among the receptors potentially capable of upregulating the Tconv response, SLAMFs (Signaling lymphocytic activation molecule) represent a family of nine receptors. In RA, our objectives were to determine whether SLAMF receptors are involved in the establishment of the Tconv pro-inflammatory response.

Methods: In RA, we used a multiparametric approach, including multiple flow cytometry panels, cells sorting, RNA sequencing, and various bioinformatics analysis to immuno-phenotyped Tconv from peripheral blood (PB) and synovial fluid (SF). SLAMFs expression was determine among four Tconv subpopulations with different activation status (naive, central memory, effector memory and terminally differentiated effector $CD4^+$ T cells). To assess the inflammatory tropism of Tconv subpopulations, CCR5 expression was studied. The transcriptome of $SLAMF4^+$ $CCR5^+$ Tem was compared to that of their $SLAMF4^-$ counterpart using RNA sequencing. Unpaired and paired data were analyzed usinga parametric test or a non-parametric test according to data distribution. In analyses involving more than 2 comparisons, appropriate post-hoc comparisons were systematically used. Correlations between quantitative parameters were assessed using the Spearman test.

Results: In RA, the study of SLAMF expression among four Tconv subpopulations from peripheral blood (PB), showed that effector memory $CD4^+$ T cells (Tem, $Foxp3^-$ $CCR7^-$ $CD45RA^-$) overexpressed SLAMF4 in patients with active disease. This association was restricted to Tem co-expressing SAP and the chemokine receptor CCR5 (figure 1 a-b). Moreover, RNAseq experiments,

Figure 1:

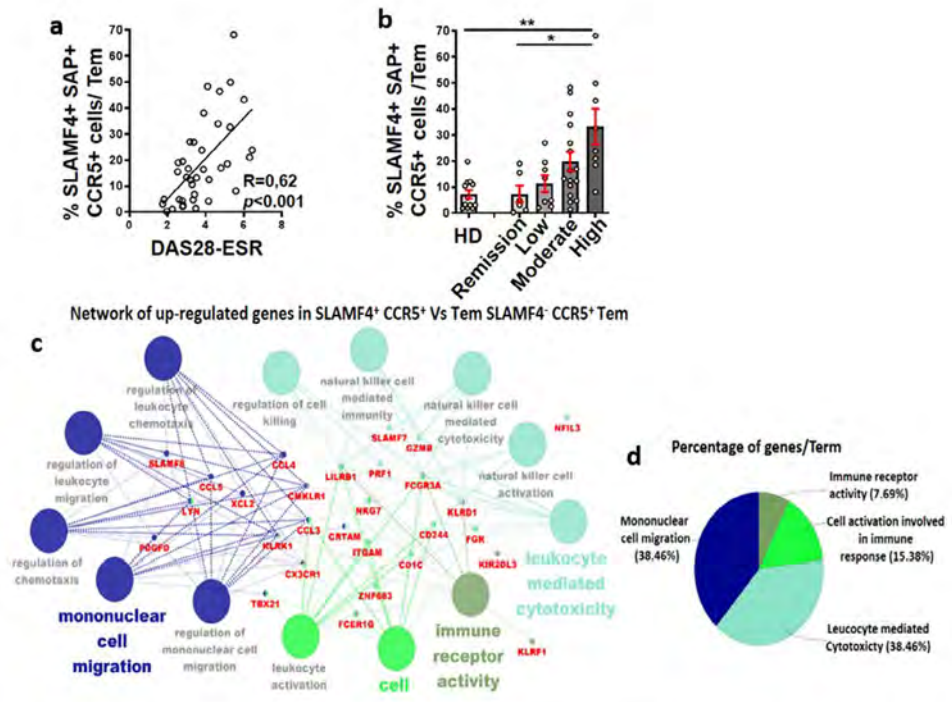


Figure 1: $SLAMF4^+$ effector memory T cells represent a subpopulation of Th1 like cytotoxic Tem associated with RA activity. (a-b) Flow cytometry experiments were performed using PBMCs from RA patients (n=38) and from HD (n=12). **(a)** Spearman correlation between the DAS28-ESR and the % of $SLAMF4^+$ SAP^+ $CCR5^+$ cells among Tem (RA patients). **(b)** % of $SLAMF4^+$ SAP^+ $CCR5^+$ cells among Tem in PBMCs from HD and RA patients according to disease activity defined using DAS28-ESR. A Kruskal-Wallis test was applied. **(c-d)** RNAseq experiments were performed from sorted $SLAMF4^+$ $CCR5^+$ and $SLAMF4^-$ $CCR5^+$ Tem from PBMCs of RA patients (n=4). The Wald test with the contrast function and the Benjamini-Hochberg FDR control procedure were used to identify the differentially expressed genes. A FDR <0.05 and a log2(Fold change) >1 were used as cutoff to determine differentially expressed genes (DEGs). **(c)** Enriched functions and pathways of the 100 most significantly up-regulated genes in $SLAMF4^+$ $CCR5^+$ Vs $SLAMF4^-$ $CCR5^+$ Tem. The network of pathways was created using the ClueGo and CluePedia plugins in Cytoscape. The most significant term of each group appeared in bolt. **(d)** Pie chart showing the most significant terms. *p<0.05 and **p<0.01.

Figure 2 :

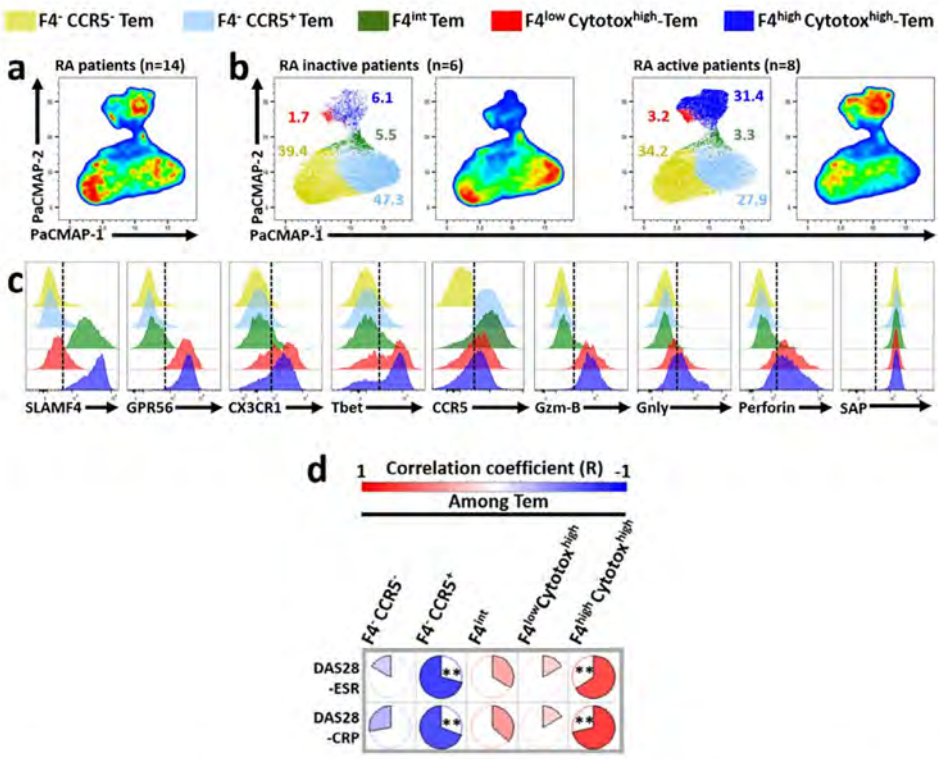


Figure 2: CD4⁺ SAP⁺ CCR5⁺ CTL subpopulations need to express SLAMF4 to be related to RA activity. (a-d) Flow cytometry experiments were performed using PBMCs from RA patients (n=14). **(a)** PaCMAP analysis was done among CD3⁺ CD4⁺ Foxp3⁻ CD45RA⁻ CCR7⁻ cells using concatenated flow cytometry files from 14 RA patients. Cell subsets were determined among Tem (CD3⁺ CD4⁺ Foxp3⁻ CD45RA⁻ CCR7⁻ cells) by the expression of SAP, SLAMF4, GPR56, CX3CR1, Tbet, CCR5, granzyme-B, granulysin and perforin, using the FlowSOM algorithm. **(b)** Same PaCMAP projections as in **(a)**, showing cell subset distribution and frequency in patients according to RA activity (Inactive RA: DAS28-CRP≤3.2; Active RA: DAS28-CRP>3.2). **(c)** Mono-parametric histograms showing the expression of SLAMF4, GPR56, CX3CR1, Tbet, CCR5, granzyme-B, granulysin and perforin among the different Tem subsets identified in **(b)**. **(d)** Graphical representation of Spearman correlations between RA activity (DAS28-ESR and DAS28-CRP) Vs % of F4⁻ CCR5⁻ Tem (gold population in b), % of F4⁻ CCR5⁺ Tem (light blue population in b), % of F4^{int} Tem (green population in b), % of F4^{low} Cytotox^{high}-Tem (red population in b) and % of F4^{high} Cytotox^{high}-Tem (dark blue population in b) among Tem. **(d)** A Spearman test was applied. (**p<0.01 and ***p< 0.001).

followed by gene set enrichment analysis (GSEA),clearly identified that SLAMF4⁺ CCR5⁺ Tem from RA patients corresponded to a subpopulation of Th1-like CD4⁺ CTLs (figure 1 c-d). Based on the differential expression of cytotoxicity markers, multiparameter flow cytometry data identified distinct SAP⁺ CCR5⁺ cytotoxic Tem subpopulations. Remarkably, among them, only those highly expressing SLAMF4 were related to RA activity (figure 2). Finally, our data showed that in the synovial fluid (n=8), SLAMF4⁺ Tem represented the only CD4⁺ T cell subpopulation that maintained a significant expression of granzyme-B and perforin.

Conclusion: By providing a comprehensive immunoprofiling of the cytotoxic CD4⁺ T cell response in RA, our study identified SLAMF4^{high} SAP⁺ CCR5⁺ CD4⁺ effector memory T cells as the main cytotoxic subpopulation involved in this disease.

Disclosure: M. Lacaud: None; **H. Bouzidi**: None; **M. breckler**: None; **D. Lemeiter**: None; **L. Semerano**: None; **M. Boissier**: Sandoz France, 5; **N. Bessis**: None; **J. Biton**: None.

Abstract Number: 0089

Pre-Clinical Characterization of MTX-101, a Novel Bispecific CD8 Treg Modulator with the Potential to Restore CD8 Treg Functions in Patients with Rheumatological Autoimmune Diseases

Daniel Patton, Meghan Maurer, Nadine Morgan, Minh Pham, Daniel Boster, Justin Huard, Cathy Tan, Rachael Fasnacht, Monica Childs, Gleda Hermansky, Alex Chen, Susan Julien, Jennifer Gardell, Cathy McMahan, Courtney Crane and Kristine Swiderek, Mozart Therapeutics, Seattle, WA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In healthy individuals, CD8 Treg activation leads to selective elimination of aberrantly activated self-reactive CD4 T cells to maintain immune balance. The CD8 Treg network appears dysfunctional in autoimmune diseases and insufficient to kill self-reactive CD4 T cells, in part due to expression of inhibitory KIR2DL1/2/3 that serves as an autoimmune checkpoint. We have developed MTX-101, a bispecific CD8 Treg modulator targeting CD8 and KIR2DL1/2/3, which are co-expressed on the surface of CD8 Treg cells. MTX-101 selectively binds CD8 Treg and enhances their killing of self-reactive CD4 T cells by blocking KIR2DL1/2/3 binding to its ligand. Enhanced CD8 Treg function prevents self-reactive CD4 T cell expansion and inflammation, without increasing unwanted immune cell activation or pro-inflammatory cytokines.

Methods: To determine the applicability of MTX-101 to the treatment of rheumatologic autoimmune disorders, we evaluated PBMCs derived from patients with systemic lupus erythematosus (SLE), Sjögren's, ankylosing spondylitis, and psoriatic arthritis for KIR2DL1/2/3 expressing CD8 Treg. We observed that KIR2DL1/2/3 expressing CD8 Treg are present in all patients including in patients without active disease. Immunophenotyping and functional analysis suggest that CD8 Treg are impaired in these patient populations, showing reduced responsiveness to stimulation and expression of proteins critical to CD8 Treg functions relative to healthy donor CD8 Treg.

Results: We used human PBMCs and tissue resident immune cells to demonstrate selective binding to and activation of CD8 Treg of MTX-101. In vitro and in mouse models engrafted with human immune cells, MTX-101 increased cytolytic capacity, activation, and prevalence in healthy donor and autoimmune patient-derived CD8 Treg. In a model of acute inflammation, we observed CD8 Treg binding in peripheral blood and tissues, a reduction in inflammatory cytokines, reduced tissue pathology, and delayed onset of disease in mice treated with MTX-101. Pharmacokinetic and tolerability studies performed using IL-15 transgenic humanized mice, in which human lymphocytes engraft at physiologic ratios, demonstrated a half-life of 11.5 days following a single dose, and selective CD8 Treg binding and expansion, without unwanted immune cell activation or pro-inflammatory serum cytokines in animals treated with doses up to 10 mg/kg. Treatment with MTX-101 reduced the prevalence of activated CD4 T cells, and selectively increased the Granzyme B content and prevalence of the CD8 Treg population, but not of non-Treg CD8 T cells or NK cells, which may serve as clinical biomarkers.

Conclusion: Collectively, our data suggest that MTX-101-mediated disruption of the inhibitory autoimmune checkpoint KIR2DL1/2/3 can improve CD8 Treg dysfunctions observed in patients with rheumatologic autoimmune diseases to support durable re-balancing of the immune system.

Disclosure: D. Patton: None; **M. Maurer**: None; **N. Morgan**: None; **M. Pham**: None; **D. Boster**: None; **J. Huard**: None; **C. Tan**: None; **R. Fasnacht**: None; **M. Childs**: None; **G. Hermansky**: None; **A. Chen**: None; **S. Julien**: None; **J. Gardell**: None; **C. McMahan**: None; **C. Crane**: None; **K. Swiderek**: None.

Abstract Number: 0090

Reduced Frequency of RORγt+ Regulatory T Cells Is Associated with Secukinumab Response in Axial Spondyloarthritis

Addison Pacheco[1], Michael Tang[1], Sinead Maguire[2], Melissa Lim[1], Fataneh Tavasolian[3], Zoya Qaiyum[4] and Robert Inman[1], [1]University Health Network, Toronto, ON, Canada, [2]Toronto Western Hospital, Toronto, ON, Canada, [3]Krembil Research Institute, University Health Network, Toronto, ON, Canada, [4]Krembil Research Institute, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthritis (AxSpA) is an inflammatory disease that predominantly affects the spine and the sacroiliac joints. Dysregulation of Type 3 immunity has been implicated in AxSpA pathogenesis, as AxSpA is characterized by overactive IL-17A-producing cells, including Th17 and γδ T cells. Therapeutically, biologics such as secukinumab, that target the cytokine IL17A, have demonstrated improved clinical outcomes in a significant percentage of patients. Despite this translational success, there is a gap in understanding how type 3 immunity is regulated and normalized by secukinumab. Our study aims to measure the frequencies of type 3 pro-inflammatory and anti-inflammatory cell subsets in AxSpA patients following secukinumab treatment and to discriminate these profiles between responders and non-responders. We hypothesized that patients that respond to secukinumab are able to reduce the frequency of IL-17A producing cell subsets by normalizing the frequency of CD4+ regulatory T cells (Tregs).

Methods: 65 Patients with AxSpA treated with secukinumab were recruited to the study. Peripheral mononuclear cells (PBMCs) were collected at baseline prior to treatment, and at 16- and 24- week post-treatment. Flow cytometry analysis of several IL-17A-producing cell subsets was used to assess differences in frequency between responders (n=13) and

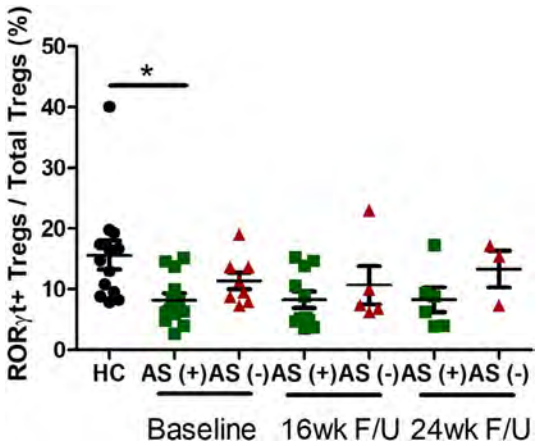


Figure 1. Analysis of RORyt+ Tregs in the Periphery of AxSpA patients. Dot plots represent frequencies of RORyt+ Tregs from PBMCs of Healthy Control (HC) and Axial Spondyloarthritis (AS) patients. Data represent 13 healthy controls, 13 secukinumab responders (green squares), and 7 nonresponders (red triangles). *p<0.05 significant by Mann-Whitney test. Frequencies analyzed using FlowJo 10.8.0 and plotted using GraphPad Prism 5.

nonresponders (n=7) during secukinumab treatment.Age and sex-matched healthy controls (n=13) were used to compare the frequencies of cell subsets in patients to a control population sample. Transcripts from FACS-sorted mature CD45RO +CD4s were measured in secukinumab responders (n=8) and nonresponders (n=7) using NanoString.

Results: Compared to baseline, we found no difference in the Treg frequencies relative to total CD4+ T cells in patients after secukinumab treatment. However, baseline frequencies of RORγt+ Tregs in PBMC of AxSpA patients that responded to secukinumab treatment were significantly reduced by 47.1% compared to healthy controls (Fig 1, $p< 0.05$). The frequency of RORγt + Tregs negatively correlated with BASDAI ($r(18)=-0.4751$, $p< 0.05$). At 16 and 24 weeks after treatment, the frequencies of RORγt+ Tregs in AxSpA responders appeared unchanged compared to baseline frequency. Secukinumab treatment had a significant effect on IL17+FOXP3+CD4 frequency (Fig 2, $p< 0.05$) but none on IL17+RORγt+CD4s frequency ($p=0.138$).When compared to secukinumab nonresponders, secukinumab responders had a significant downregulation of OAS2, IFI44L and OAS1 in mature CD4s (Fig 3). Gene ontology pathway analysis indicate that these genes are involved in viral response.

Conclusion: In AxSpA, frequencies of IL-17A-producing FOXP3+CD4+ cells correspond to clinical improvement after secukinumab treatment. Frequencies of RORγt+ Tregs were significantly decreased in AxSpA patients compared with controls. This subset correlates with clinical activity and may be an informative biomarker with diagnostic potential for AxSpA. These findings underscore the importance of regulating type 3 immunity to control inflammation in AxSpA patients.

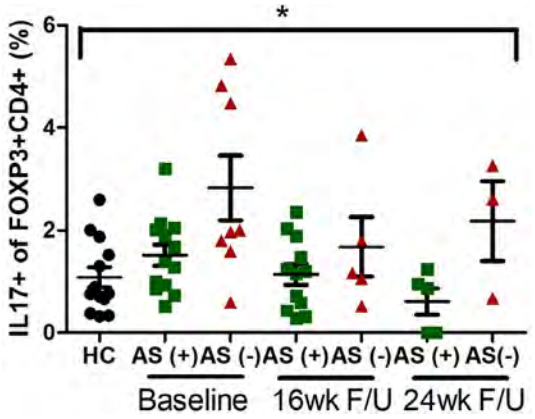


Figure 2. Analysis of IL17+FOXP3+CD4s in the Periphery of AxSpA patients. Dot plots represent frequencies of IL17+ FOXP3+CD4s relative to FOXP3+CD4s in PBMCs of Healthy Control (HC) and Axial Spondyloarthritis (AS) patients. PBMCs were stimulated with PMA and ionomycin for 5 hours. Data represent 13 healthy controls, 13 secukinumab responders (green squares), and 7 nonresponders (red triangles). *p<0.05 significant by Kruskal-Wallis test. Frequencies analyzed using FlowJo 10.8.0 and plotted using GraphPad Prism 5.

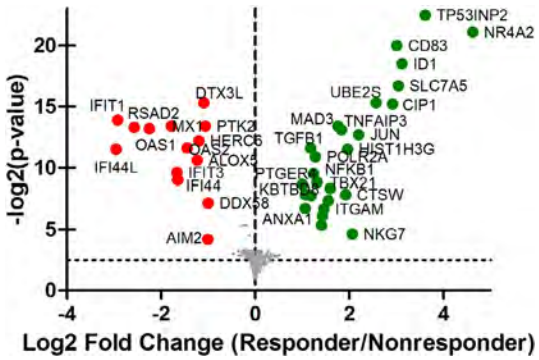


Figure 3. Nanostring Analysis Comparing Transcripts of CD45RO+ CD4s from Secukinumab Responders and Nonresponders. Volcano plot represents differentially regulated genes unique to secukinumab responders/non-responders quantified by NanoString analysis. Green (higher in responder) and red (higher in non-responder) dots represent genes with a log2 fold change above 1.5 and a –log2(p-value) of 4. Figure created using GraphPad Prism 5.

Disclosure: A. Pacheco: None; **M. Tang**: None; **S. Maguire**: None; **M. Lim**: Aria Pharmaceuticals, 5; **F. Tavasolian**: None; **Z. Qaiyum**: None; **R. Inman**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Sandoz, 2.

Abstract Number: 0091

Impaired X-Chromosome Inactivation Maintenance in T Cells Is Associated with Features of Reduced Disease Severity in a Toll-Like Receptor 7-Driven Model of Systemic Autoimmunity

Nikhil Jiwrajka[1], Zowie Searcy[2], Claudia Lovell[2], Natalie Toothacre[2], Katherine Forsyth[2] and Montserrat Anguera[2], [1]Divison of Rheumatology, Department of Medicine, Hospital of the University of Pennsylvania, Phildelphia, PA, [2]Department of Biomedical Sciences, University of Pennsylvania School of Veterinary Medicine, Philadelphia, PA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Many systemic autoimmune rheumatic diseases, including systemic lupus erythematosus (SLE), Sjögren's syndrome, and systemic sclerosis are highly female-biased. Although these diseases are more prevalent in females, disease severity is often greater in affected males. Transcriptional profiling of tissues from patients with these diseases has consistently revealed a prominent Type 1/2 interferon (IFN)-stimulated gene signature (ISG). The mechanisms by which sex modulates IFN-associated inflammatory responses in autoimmunity is unclear. The X chromosome contains several genes with roles in immune functions and IFN signaling, and our lab has shown that females with SLE exhibit impaired maintenance of X-chromosome inactivation (XCI) in circulating B and T cells. We therefore sought to determine how perturbed XCI maintenance in T cells modulates susceptibility to an inducible model of systemic autoimmunity using a toll-like receptor 7 (TLR7)-driven model associated with a strong ISG signature.

Methods: Female wild-type C57BL/6, CD4cre^{+}Xist$^{+/+}$ (n= 12; "WT"), and CD4cre^{+}Xist$^{fl/fl}$ (n=4; "Xist CKO") mice were treated topically with Imiquimod cream (IMQ; a TLR7 agonist; n=9) or Cetaphil lotion (VEH; n=7), thrice weekly for 10 weeks. Serum, spleen, kidney, and lung tissue were harvested upon euthanasia and processed for autoantibody quantitation, flow cytometry, and histology.

Results: Chronic IMQ treatment resulted in marked splenomegaly, T-cell activation, autoantibody production, and dermal, pulmonary, and renal inflammation. IMQ-treated Xist CKO mice tended to exhibit less splenomegaly and autoantibody production, fewer activated CD4^{+} and CD8^{+} T cells, and more Foxp3^{+} (X-linked) regulatory T cells (Tregs) compared to their WT counterparts. Xist CKO mice also tended to exhibit a greater proportion of Tregs expressing *Cxcr3*, an X-linked chemokine receptor integral for chemotaxis to sites of Type 2 interferon-mediated inflammation that has been shown to variably escape XCI.

Conclusion: These initial data suggest that impaired XCI maintenance in T cells may modulate Type 1/2 interferon-associated inflammation through an expansion of Foxp3^{+} Tregs, resulting in a less severe phenotype in this TLR7-driven model. Though further validation of these findings in larger experimental cohorts is required, our studies could provide new insights into factors influencing disease severity in female-biased autoimmune diseases associated with strong ISG signatures.

Disclosure: N. Jiwrajka: None; **Z. Searcy**: None; **C. Lovell**: None; **N. Toothacre**: None; **K. Forsyth**: None; **M. Anguera**: None.

Abstract Number: 0092

Multi-omics Immune Profiling of Cytotoxic T Cells from Ankylosing Spondylitis Patients Identified a Subset of Clonally Exapnded CTLs That Evade Immune Exhaustion

Michael Tang[1], Zoya Qaiyum[2], Melissa Lim[1] and Robert Inman[1], [1]University Health Network, Toronto, ON, Canada, [2]Krembil Research Institute, Toronto, ON, Canada

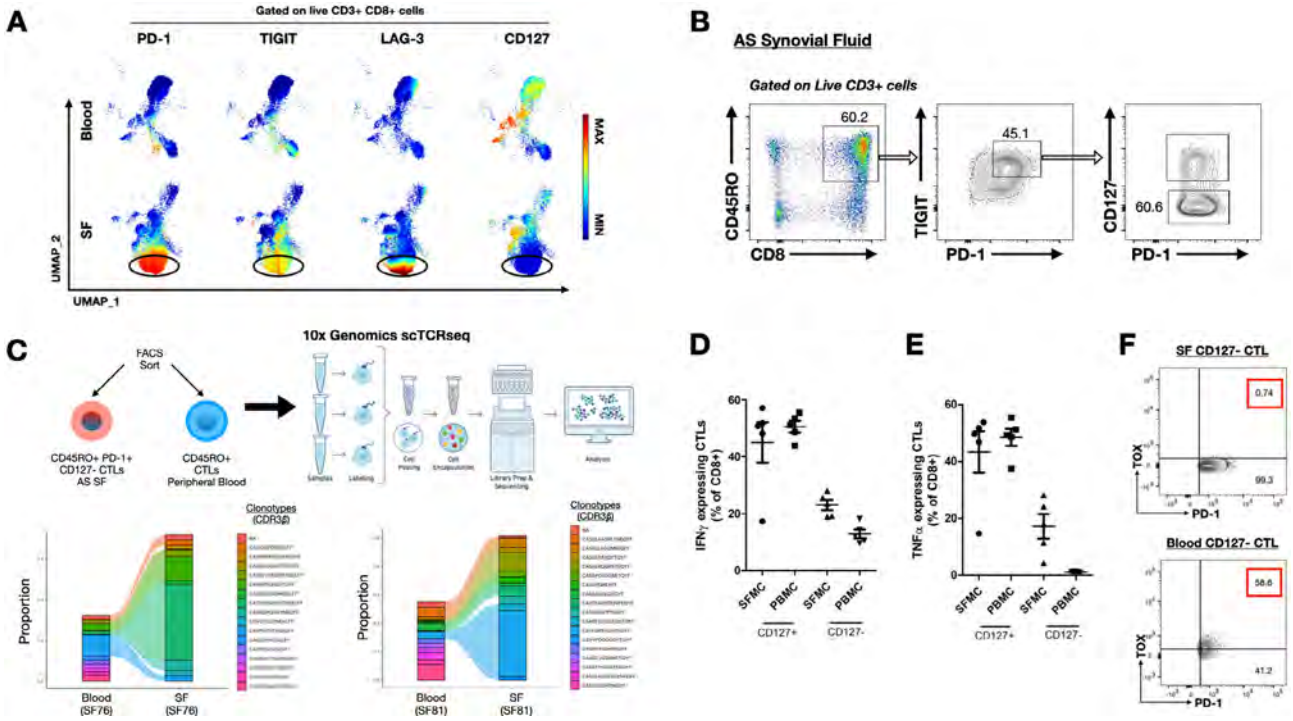
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Sustained chronic inflammation in the spine and of the sacroiliac joints is a key feature in Ankylosing Spondylitis (AS). A central role of CTL involvement in AS inflammation is supported by recent discoveries of chronically activated CTLs with distinctive cytotoxic and integrin expression profiles enriched at sites of inflammation. Yet, the immunophenotype of the CTL compartment which may perpetuate AS inflammation has not been fully defined. The microenvironment that is conducive to AS chronic inflammation is reminiscent to settings found in chronic viral infection and cancer. Here, we seek to unravel the complex heterogeneity of CTLs in AS patients to determine whether CTLs in AS are truly immunologically exhausted. We hypothesize that a loss of CTL immune homeostasis and evasion of T cell exhaustion contribute to autoinflammation in AS.

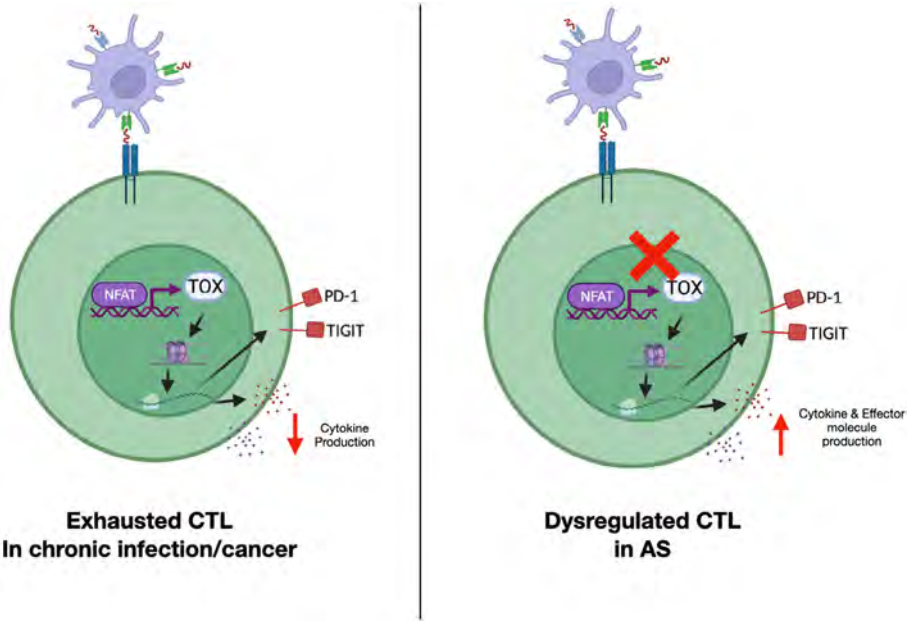
Methods: 8 pairs of PBMCs and SFMCs from patients with active (mean BASDAI=8) Axial Spondyloarthritis meeting the ASAS classification criteria were analysed. Additionally, age and sex-matched healthy control PBMCs (n=18) were analysed. We applied multi-omics single-cell immune profiling strategies to delineate the complex heterogeneity of CTLs in AS. Mass cytometry (CyTOF) of PBMCs and SFMCs was used to simultaneously measure protein expression of more than 30 surface and intracellular markers. Single-cell RNA sequencing (scRNAseq) and T cell receptor sequencing (scTCRseq) of FACS-sorted mature CTLs were used to immune profile AS CTL transcriptome and to perform clonal andTCR diversity analyses.

Results: Unsupervised clustering analysis of CyTOF data identified a subset of CTLs that co-express checkpoint receptors PD-1, TIGIT, and LAG-3 in SF CTLs of AS patients; while these markers are downregulated in the peripheral CTLs compared to healthy controls, implicating CTL dysregulation. This subset of SF CTLs downregulates CD127 expression, while retaining the capacity for CTL effector functions including the ability to express granzyme B, perforin and produce IFNγ and TNFαupon stimulation. Additionally, CD8+ T cell tissue residency markers (CD103, CD69, and CD49a) are highly upregulated in this subset of SF CTLs. scRNAseq of FACS-sorted CD45RO+ PD-1+ TIGIT+ CTLs revealed that transcripts that are normally expressed in canonically exhausted CTLs (e.g. *CD244, HAVCR2, ENTPD1, NT5E, TOX*) are downregulated. Differential gene analysis revealed that the top 5 genes (*IFI6*, *MX1*, *ISG16*, *MT2A*, *IFITM1*) upregulated in these cells are related to the interferon signalling pathway. Single cell TCR sequencing demonstrated that this CTL subset is clonally expanded at sites of inflammation. Intracellular flow cytometry confirmed that this CTL subset downregulated the master transcription factor regulating T cell exhaustion- TOX, suggesting that these CTLs are not truly immunologically exhausted.

Conclusion: Multi-omics immune profiling of CTLs from AS patients identified a subset of clonally expanded CTLs in SF that appear to resist immune exhaustion, while retaining classical cytotoxic capacities. This findings implicates that dysregulation of T cell exhaustion and homeostasis could potentially exacerbate AS autoinflammation.



Mass cytometry and single cell TCR sequencing identified a population of clonally expanded SF CTL that evades immune exhaustion. A) Live CD3+ CD8+ cells from single file representations of paired AS SFMC and PBMC (n=8) were entered into the UMAP algorithm for high dimensional analysis of immune checkpoint molecules. UMAP projections display expression levels of indicated surface molecules. B) Representative flow cytometric analyses of CD127+ and CD127- PD-1+ TIGIT+ CTL from SF of AS patient. C) Schematic workflow of single cell TCR sequencing. Mature CD45RO expressing CTLs were sorted from matched SFMC and PBMC from 2 AS patients. Alluvial plots demonstrating proportion of clonotypes based on amino acid sequences of CDR3b chains of CTLs from blood and SF of 2 AS patients. D-E) Cytokine release assay; CD127+ and CD127- PD-1+ TIGIT+ CTLs were FACS sorted from paired SFMC and PBMC samples, then stimulated with PMA/ionomycin for 4 hours in the presence of Brefeldin A. Intracellular IFNg and TNFa were measured by flow cytometry. Graphs display proportion of CD8+ T cells expressing the cytokines. F) Flow cytometric analysis to quantify frequency of TOX+ CD127- PD-1+ CTL.



Dysregulation of CTLs in AS synovial fluid. In contrast to canonically exhausted CTLs in settings of chronic inflammation such as chronic viral infection and cancer, a distinct subset of CTLs expressing classical immune checkpoint markers appear to resist immune exhaustion, retain effector functions, and progressively perpetuate autoinflammation in AS.

Disclosure: M. Tang: None; **Z. Qaiyum**: None; **M. Lim**: Aria Pharmaceuticals, 5; **R. Inman**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Sandoz, 2.

Abstract Number: 0093

Single Cell RNA-seq and Mass Cytometry Reveal a Cytotoxic CD8 Effector T Cell Population Associated with Interstitial Lung Disease in Systemic Sclerosis Patients

Ye Cao[1], Takanori Sasaki[2], Richard Ainsworth[3], Kim Taylor[4], Nunzio Bottini[5], Mehreen Elahee[6], Edy Kim[7], Francesco Boin[3] and Deepak Rao[7], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [3]Cedars-Sinai Medical Center, Los Angeles, CA, [4]University of California San Francisco, San Francisco, CA, [5]University of California, San Francisco, CA, [6]University of Pittsburgh Medical Center, Pittsburgh, PA, [7]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a major cause of morbidity and mortality in systemic sclerosis (SSc). We aimed to identify features of circulating immune cells associated with SSc-ILD to develop biomarkers and to find treatment targets of SSc-ILD.

Methods: We employed single cell RNA-seq (scRNAseq) using cryopreserved peripheral blood mononuclear cells (PBMC) from 20 SSc patients without ILD and 38 SSc patients with ILD and implemented covarying neighborhood analysis (CNA) to identify cell features associated with SSc-ILD. Detailed surface maker expression was also examined using mass cytometry (CyTOF) with a 39-marker panel using PBMC from 18 controls, 53 SSc patients with ILD and 29 SSc patients without ILD. Differentiation paths and inducing factors were explored through RNA velocity analysis and in-vitro culture.

Results: A broad analysis of the scRNAseq dataset across mononuclear cells highlighted a significant enrichment in a specific CD8 T cell phenotype, captured as CD8 T cell cluster 2, in patients with ILD compared to those without ILD. This cluster expressed *CD8A* and *GZMB* but not *CD27* or *GZMK* (Figure 1A). T cell receptor repertoire analysis indicated cluster 2 was clonally expanded, suggesting the antigen recognition of this CD8 T cell population in SSc-ILD (Figure 1B). In parallel, analysis of an overlapping set of PBMC samples by mass cytometry demonstrated that CD57+ CD27- CD56- CD45RO+ CCR7- effector memory CD8 T cells (CD57+ TEM) were significantly increased in the SSc-ILD cohort (Control: 0.74%, SSc without ILD: 1.42%, SSc with ILD: 2.71%), suggesting that a similar CD8 T cell population associated with SSc-ILD was captured by scRNAseq and mass cytometry. In contrast to CD57+ TEM cells, TEMRA were not statistically different between SSc patients with and without ILD. Independent flow cytometry analysis confirmed that CD57+ TEM highly expressed GZMB but not GZMK. On the contrary, CD57- CD27+ TEM (CD57- TEM) expressed GZMK but not GZMB, indicating there are two distinct populations in CD8 TEM. RNA velocity analysis of CD8 T cell clusters suggested that CD57+ TEM may differentiate from CD57- TEM (Figure 2). In-vitro culture experiments demonstrated that type I IFN facilitates differentiation from CD57- TEM to CD57+ TEM that highly produce GZMB (Figure 3).

Conclusion: ScRNAseq and mass cytometry analyses revealed that a cytotoxic effector memory CD8 T cell subset is expanded in SSc-ILD, and that a type I IFN signal may drive differentiation towards this phenotype.

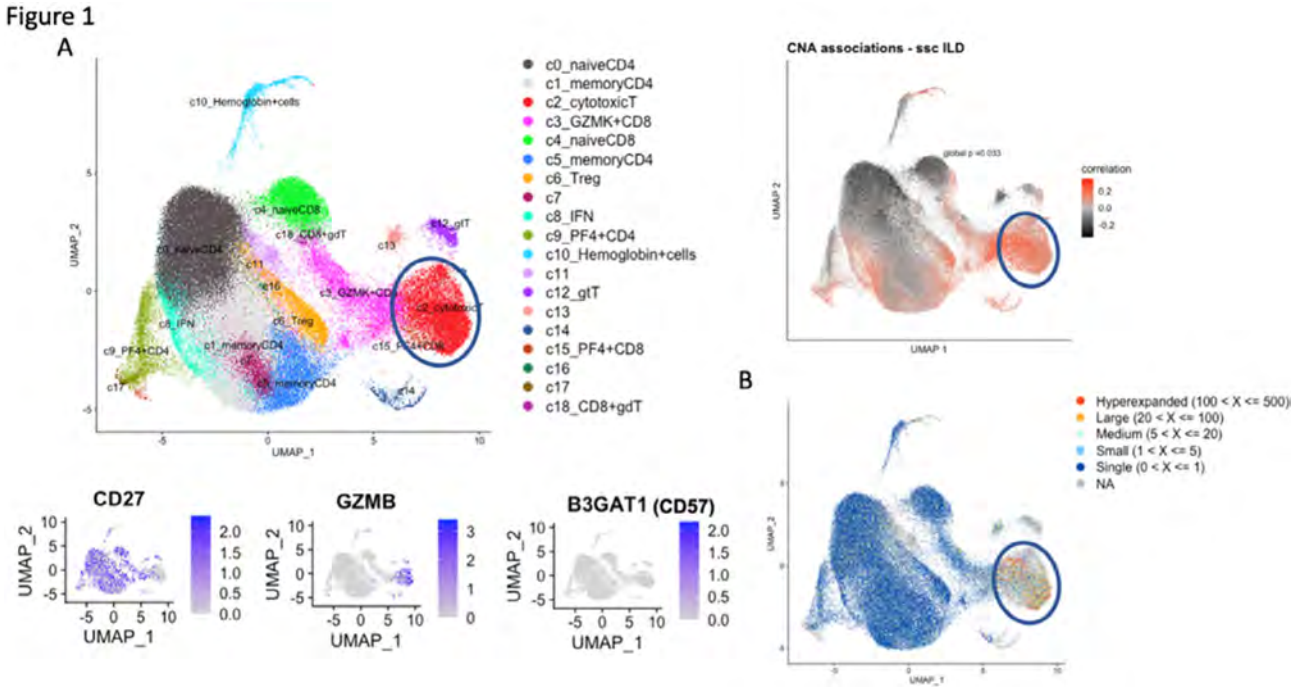


Figure 1. scRNAseq analysis of our SSc-ILD cohort. A. Covarying neighborhood analysis indicated cluster 2 is associated with lung disease in SSc, which expressed GZMB and B3GAT1 (CD57) but not expressed CD27. B. T cell receptor repertoire analysis demonstrated cluster 2 is a clonally expanded population.

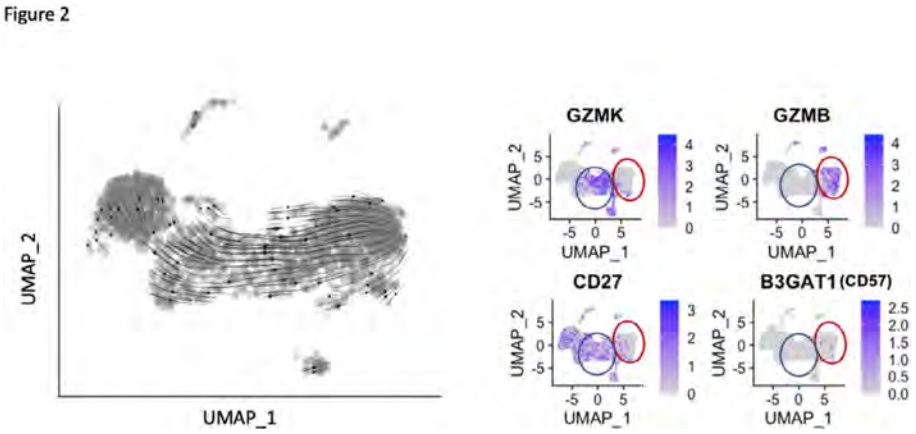


Figure 2. Differentiation pathway analysis of CD57+ TEM. RNA velocity analysis of CD8 T cell clusters indicated that CD57+ TEM (red circle) is differentiated from CD57- TEM (blue circle).

Figure 3

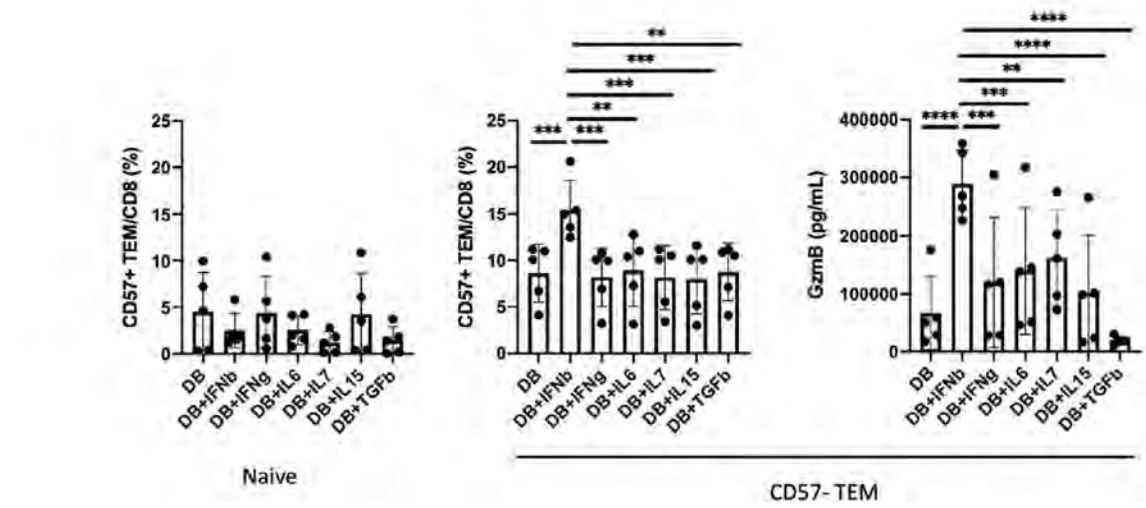


Figure 3. Type I IFN promotes differentiation from CD57- TEM to CD57+ TEM. Proportion of CD57+ TEM after 4 days culture of Naïve or CD57-TEM from 5 different donors with CD3/CD28 + cytokine stimulation. Granzyme B production was assessed by ELISA using culture supernatant after 4 days of culture of CD57- TEM with CD3/CD28 + cytokine stimulation. P value was calculated by One-Way repeated measures ANOVA.

Disclosure: Y. Cao: None; **T. Sasaki**: None; **R. Ainsworth**: None; **K. Taylor**: None; **N. Bottini**: Thirona Bio, 2; **M. Elahee**: None; **E. Kim**: Bayer, 5, Novartis, 12, Spouse is employee; **F. Boin**: None; **D. Rao**: AstraZeneca, 2, Bristol-Myers Squibb, 2, 5, GlaxoSmithKlein(GSK), 2, Hifibio, 2, Janssen, 5, Merck, 5, Scipher Medicine, 2.

Abstract Number: 0094

Granzyme K Elicits a New Pathway for Complement Activation in RA Synovium

Anna Helena Jonsson[1], Carlos Donado[2], Erin Theisen[2], Dominique Jones[1], Aparna Nathan[3], Fan Zhang[4], Accelerating Medicines Partnership (AMP): RA/SLE[1], Soumya Raychaudhuri[1] and Michael Brenner[2], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [3]Harvard Medical School, Boston, MA, [4]University of Colorado, Aurora, CO

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: T cells are major drivers of rheumatoid arthritis (RA) pathogenesis. While most research has focused on CD4+ T cells, we have found that $CD8^+$ T cells – specifically granzyme K (GzmK)-expressing CD8 T cells – are strikingly abundant in inflamed RA synovium as well as other tissues affected by autoimmune disease. Unlike granzyme B (GzmB), GzmK does not cleaves caspases to induce target cell apoptosis, and the function of GzmK in inflamed synovium and other tissues is unclear. Here, we describe that GzmK is continuously released from CD8+ T cells and activates a new

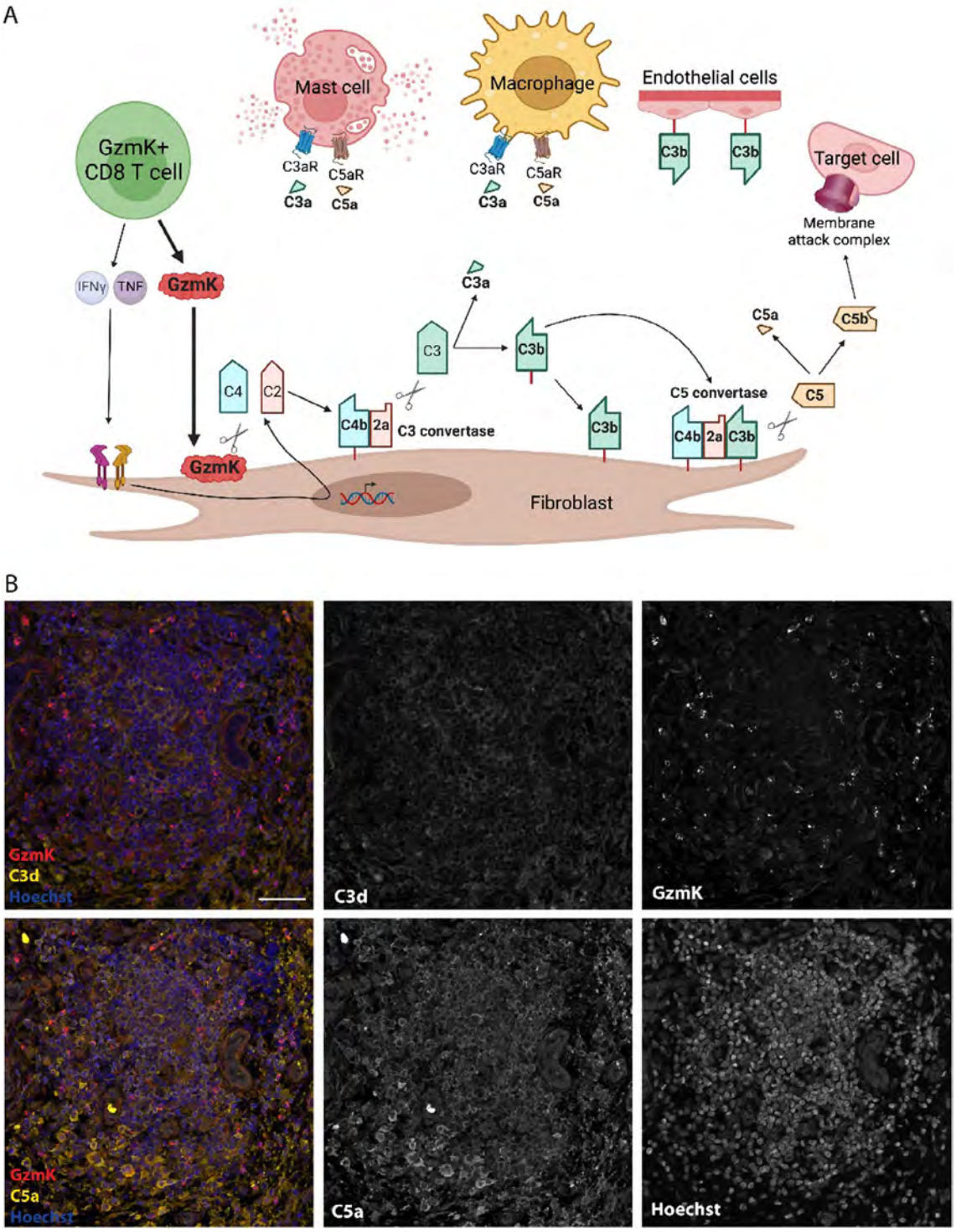


Figure 1. Granzyme K activates a new complement pathway in rheumatoid arthritis synovial tissue. (A) Illustration of the new pathway of complement cleavage activated by GzmK. (B) RA synovial tissue stained for GzmK, C3d, C5a, and Hoescht nuclear stain and imaged by confocal microscopy.

complement pathway, opsonizing target cells and releasing anaphylatoxins C3a and C5a that recruit and activate innate immune cells. In inflamed RA synovium, we find complement fragments C3d and C5a in proximity to GzmK^{+} CD8 T cells, supporting a role for this complement activation mechanism *in vivo*.

Methods: We incubated recombinant enzymatically active GzmK with serum-purified complement fragments to investigate the molecular effects of GzmK on complement proteins. We measured cleavage of C2, C3, C4, and C5 using Western blots. We used flow cytometry to assess C3b and terminal complement complex (TCC) deposition on cell membranes. We performed multicolor immunofluorescence microscopy of human rheumatoid arthritis synovial tissue to assess complement activation and deposition relative to GzmK$^+$ CD8+ T cells.+

Results: GzmK is expressed by a wide range of T cells and innate-like lymphocytes in human synovial tissue and fluid in RA and in other autoimmune and inflamed tissues. Resting GzmK$^+$ CD8+ T cells continuously release GzmK, which binds to negatively charged residues on cell surfaces. Synovial fibroblasts express complement components C2, C3, and C4, and this production is amplified by T cell-associated cytokines IFNγ and TNF. GzmK cleaves C4 to C4b and C2 to C2a to form an active C3 convertase (C4b + C2a) that cleaves C3 to C3a and C3b, which covalently deposits on cell membranes due to the surface localization of GzmK. These complement fragments then form the C5 convertase C4b2b3b, ultimately leading to release of biologically active anaphylatoxin C5a and surface deposition of the terminal complement complex (C5b-C9) (Figure 1A). Using multicolor immunofluorescence microscopy, we find complement products C3/C3d and C5a in proximity to GzmK+ CD8+ T cells in inflamed RA synovium (Figure 1B).

Conclusion: GzmK activates a novel complement pathway that is independent of the classical, alternative, and lectin pathways of complement activation. GzmK can cleave locally generated complement components to generate C3a, C3b, C5a, and terminal complement complex, which promote inflammatory cell recruitment and antigen uptake. In inflamed RA synovium, C3/C3d and C5a deposition occurs near GzmK$^+$ cells, supporting the *in vivo* relevance of this new mechanism of complement activation. Together, these findings reveal a new pro-inflammatory in RA that is likely active in other autoimmune diseases as well.

Disclosure: A. Jonsson: None; **C. Donado**: None; **E. Theisen**: None; **D. Jones**: None; **A. Nathan**: None; **F. Zhang**: None; **A. Medicines Partnership (AMP): RA/SLE**: None; **S. Raychaudhuri**: AbbVie, 6, Janssen, 1, Mestag, Inc, 2, 8, Pfizer, 1, Sanofi, 1, Sonoma, 1, 8; **M. Brenner**: 4FO Ventures, 2, GlaxoSmithKlein(GSK), 2, Mestag Therapeutics, 2, 11, Third Rock Ventures, 2.

Abstract Number: 0095

Kynurenine Is a Proinflammatory Metabolite That Activates a Positive Feedback Loop of Rab4A-dependent CD98 Expression and mTORC1 and mTORC2 Activation in SLE

Thomas Winans[1], Nick Huang[1], Joshua Lewis[1], Xiaojing Wang[1], Tamas Faludi[1], Daniel Krakko[2], Laurence Morel[3] and Andras Perl[4], [1]SUNY Upstate Medical University, Syracuse, NY, [2]North Carolina State University, Raleigh, NC, [3]University of Texas health San Antonio, San Antonio, TX, [4]SUNY, Syracuse, NY

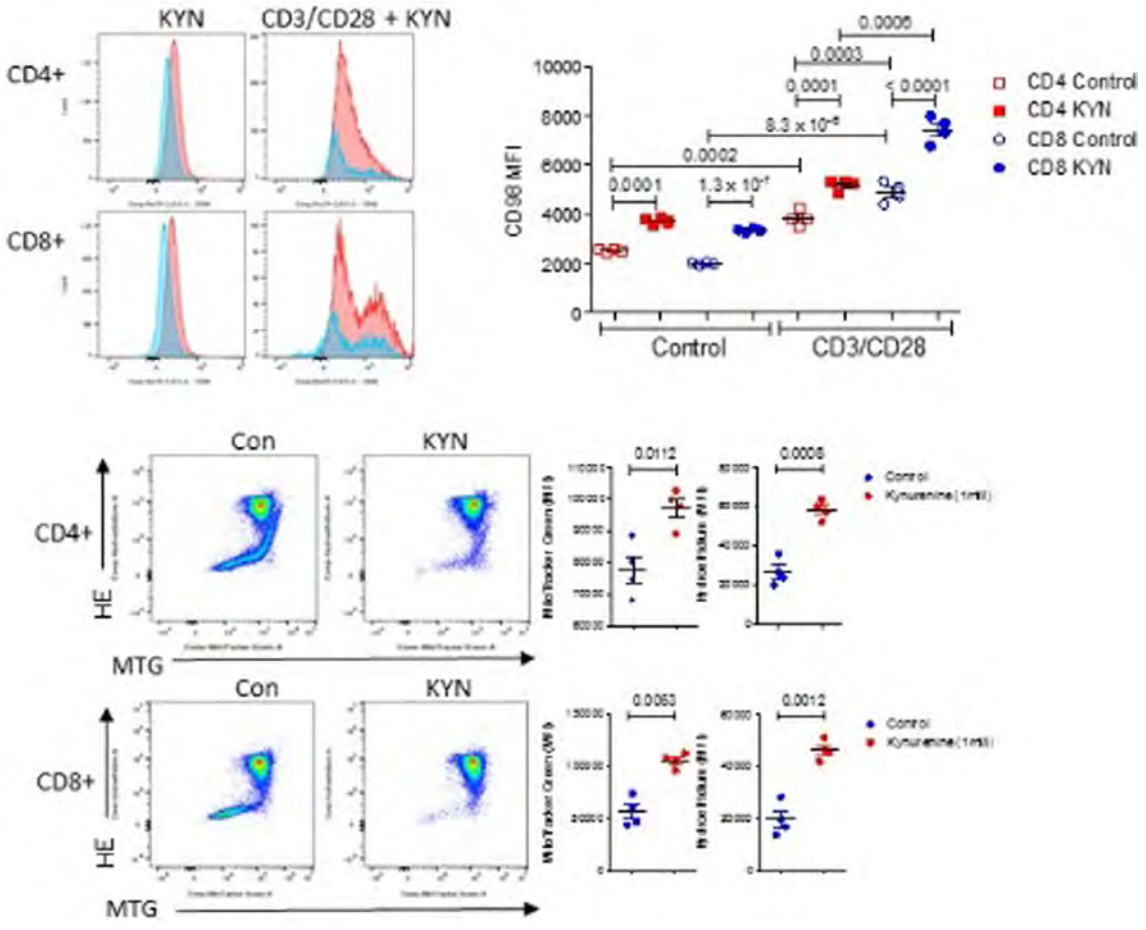
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The kynurenine (KYN) pathway has been linked to disease pathogenesis in patients with systemic lupus erythematosus (SLE) (https://pubmed.ncbi.nlm.nih.gov/26366134/). Genetically enforced overexpression of Rab4A activates the mechanistic target of rapamycin in SLE patients (https://pubmed.ncbi.nlm.nih.gov/31805010/. The present

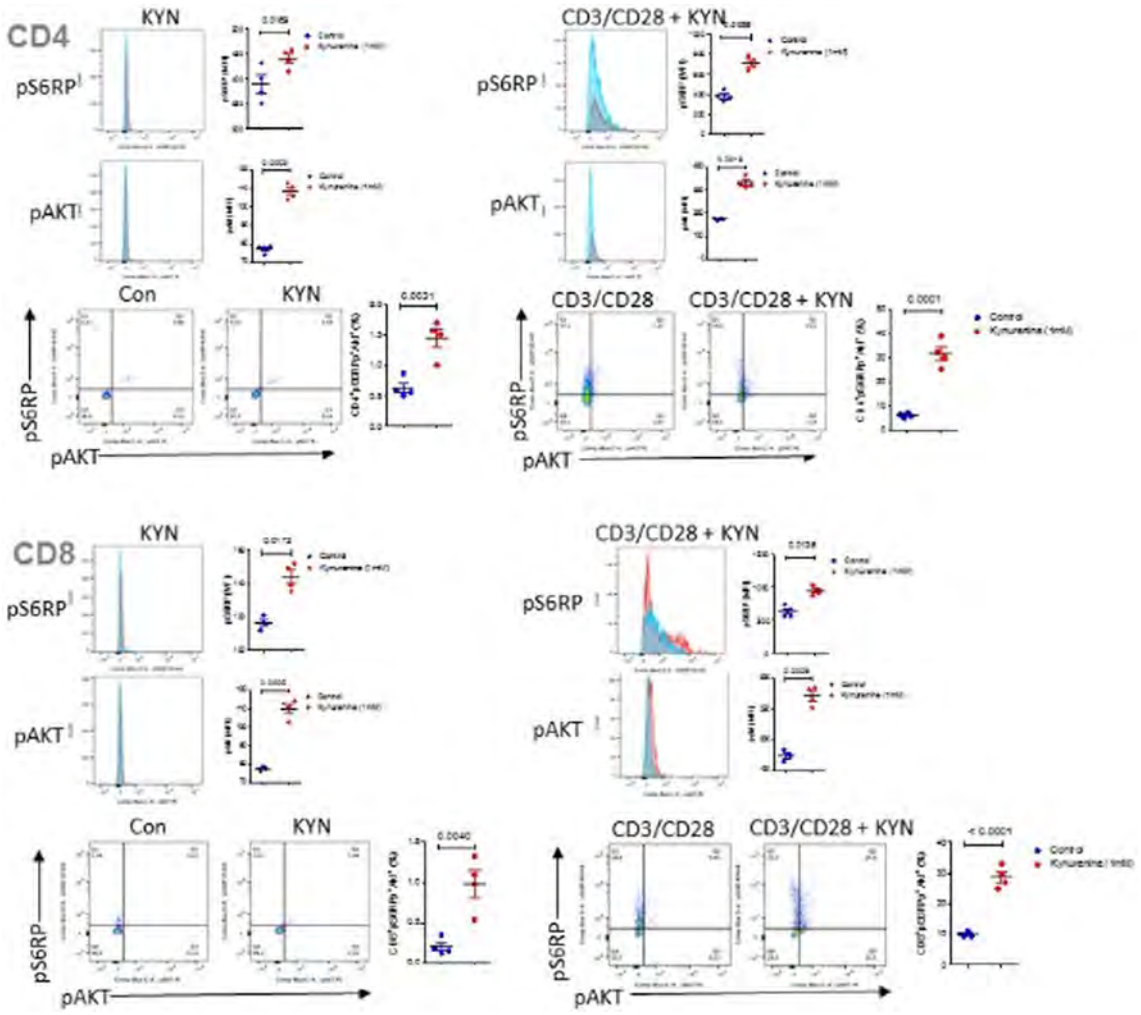
study was initiated to determine the pro-inflammatory mechanism of action of KYN in lupus-prone SLE1.2.3 triple congenic mice on the C57Bl/6 background (B6.TC) carrying constitutively active Rab4A^{Q72L} alleles (Rab4AKI) or lacking Rab4A in T cells (Rab4AKO).

Methods: KYN levels were measured within T cells and sera of mice carrying wild-type (WT), Rab4AKI and Rab4AKO alleles in female C57Bl/6 (B6) control mice and lupus-prone B6.TC mice using LC/MS. The effects of KYN on expression of its receptor CD98 and activation of mTOR complexes 1 (mTORC1, via pS6RP) and 2 (mTORC2, via pAkt) were studied by flow cytometry. Splenocytes were cultured *in-vitro* for 72 hours with or without KYN along with or without concurrent stimulation with lipopolysaccharide (LPS) or CD3/CD28. Mitochondrial mass and reactive oxygen species (ROS) were measured by flow cytometry using mitotracker Green (MTG) and hydroethidine (HE).

Results: KYN was accumulated in T cells and sera of B6.TC/Rab4A^{Q72L} female mice that exhibited increased expression of CD98 and activation mTORC1 and mTORC2 relative to B6.TC and B6.TC/Rab4A^{KO} controls. In C57Bl/6 splenocytes, KYN increased CD98 expression in CD4 and CD8 T cells (CD4 Unstim: FC=1.48, p=0.00012, CD8 Unstim: FC=1.68, p=2.1E-5, CD4 Stim: FC=1.36, p=0.00069, CD8 Stim: FC=1.51, p=0.00058) and significantly increased both mTORC1 (CD4 Unstim: FC=1.13, p=0.0169, CD4 Stim: FC=1.86, p=0.0086 CD8 Unstim: FC=1.24, p=0.0172, CD8 Stim: FC=1.49, p=0.0136) and mTORC2 (CD4 Unstim: FC=1.41, p=0.0003, CD4 Stim: FC=1.91, p=0.0018, CD8 Unstim: FC=1.42, p=0.0005, CD8 Stim: FC=1.55, p=0.0006). KYN increased mitochondrial mass (CD4 Stim: FC=1.25, p=0.0112, CD8 Stim: FC=1.87, p=0.0053) and ROS production (CD4 Stim: FC=2.2, p=0.0008, CD8 Stim: FC=2.34, p=0.0012) in both CD4 and CD8 T cells following KYN and CD3/CD28-stimulation.



MFIs of CD98 expression in response to KYN only or concurrent KYN and CD3/CD28 stimulation. Metabolic dyes mito-tracker green and hydro-ethidine dot plots after 72 hour stimulation with KYN and CD3/CD28.



Flow cytometry dot plots and histograms of mTORC1 and mTORC2 downstream phosphorylated substrates, pS6RP and pAkt.

KYN also expanded CD19+CD11c+ age-related B cells (ABCs) with or without LPS. KYN activated mTORC1 (CD19+: FC=1.15, p=0.012, ABCs: FC=1.97, p=0.0019) and mTORC2 (CD19+: FC=6.289, p=1.21E-5, ABCs: FC=3.70, p=0.00165) and CD98 expression (ABCs: FC=2.06, p=0.0144). Remarkably, the expression of CD138, a plasma cell marker, was also increased by concurrent LPS and KYN treatment (FC=2.76, p=0.001).

Conclusion: This study suggests that KYN accumulation in lupus-prone T cells causes a CD98-KYN-mTOR positive feed-back loop which is enhanced by Rab4A activation, conferring secondary KYN-mediated expansion of ABCs and plasma cells. The Rab4A-CD98/mTOR/KYN positive feed-back loop may represent a mechanistic target for therapeutic intervention in SLE.

Disclosure: T. Winans: None; **N. Huang**: None; **J. Lewis**: None; **X. Wang**: None; **T. Faludi**: None; **D. Krakko**: None; **L. Morel**: None; **A. Perl**: None.

Abstract Number: 0096

Performance Assessment of Lupus Anticoagulant Tests Using Taipan and Ecarin Snake Venom Clotting Times: An International Study from Antiphospholipid Syndrome Alliance for Clinical Trials and International Networking (APS ACTION) Core Laboratories

Maria Efthymiou[1], Ian Mackie[1], Rohan Willis[2], Vittorio Pengo[3], Danieli Andrade[4], Elisa Bison[3], Olga Amengual[5], Zurina Romay-Penabad[6], Yuichiro Fujieda[5], Maria Laura Bertolaccini[7], Doruk Erkan[8], Hannah Cohen[9] and On Behalf Of APS ACTION[10], [1]University College London, London, United Kingdom, [2]University of Texas Medical Branch, Galveston, TX, [3]Department of Cardiac-Thoracic-Vascular Sciences and Public Health University of Padova, Padova, Italy, [4]University of São Paulo, São Paulo, Brazil, [5]Hokkaido University, Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Sapporo, Japan, [6]Antiphospholipid Standardization Laboratory, Division of Rheumatology, University of Texas Medical Branch, TX, [7]King's College London, London, United Kingdom, [8]Hospital for Special Surgery, New York, NY, [9]University College London Hospitals NHS Foundation Trust, London, United Kingdom, [10]on behalf of APS ACTION, New York, NY

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Antiphospholipid Syndrome Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus anticoagulant (LA) test performance is critical for APS diagnosis and management. However, variability remains a challenge in LA testing, particularly in anticoagulated samples, with the activated partial thromboplastin time and dilute Russell's viper venom time (DRVVT) the most commonly used tests. The prothrombin-activating Taipan snake venom time (TSVT) screening test and Ecarin clotting time (ECT) confirmatory test are insensitive to vitamin K antagonists (VKA) and may offer improved LA detection. APS ACTION is an international research network involving 34 centres, a prospective registry and repository, and five core laboratories (CL) worldwide. The aim of this study was to evaluate the performance of the TSVT/ECT in VKA-anticoagulated samples between APS ACTION CLs and examine agreement in LA status with the DRVVT.

Methods: Four CL (A-D) used the same analyser, protocol, and lot of reagents. The manufacturer's cut-off values for TSVT/ECT were verified in each CL using plasmas from at least 40 healthy normal subjects, to determine normal ranges for TVST, ECT and TVST/ECT ratios (Diagnostic Reagents Ltd). Results were normalised with pooled normal plasma (PNP), while equal volume mixtures of patient and PNP were tested to confirm the presence of an inhibitor. George King LA Positive plasma and IL LA Negative control plasma (Werfen) were used for quality control (QC). In a validation exercise, each CL tested six positive and six negative blinded VKA-anticoagulated samples, previously identified as such, with status confirmed by a second CL. VKA-anticoagulated samples were also tested with DRVVT Screen and Confirm (Werfen) in 50:50 mixtures with PNP. A precision study was also performed, testing LA-positive and LA-negative QC plasma x 6 in the same run, to determine intra-assay variability.

Core Laboratory:	A		B		C		D	
		50:50 PNP		50:50 PNP		50:50 PNP		50:50 PNP
TSVT ratio	0.92-1.08	0.94-1.06	0.92-1.12	0.96-1.10	0.98-1.16	0.95-1.10	0.92-1.07	0.95-1.10
ECT ratio	0.92-1.08	0.97-1.03	0.86-1.08	0.93-1.13	0.90-1.07	0.81-0.90	0.93-1. 08	0.81-0.90
TSVT/ECT ratio	0.89-1.11	0.93-1.07	0.95-1.17	0.92-1.08	0.96-1.22	1.13-1.27	0.88-1.10	1.13-1.27

Results: Precision and agreement were acceptable in all CL for both positive and negative control plasma [Coefficient of Variation (CV) 0.7-5%]: CV for clotting times ≤2.5% for LA Negative control plasma and ≤4% for George King LA Positive plasma, CV for TSVT/ECT < 4% for all CLs All CL confirmed the manufacturer's reference range with minor differences (Table 1). All CL correctly identified the six positive and six negative blinded LA samples (CL D identified one LA positive sample as equivocal). In the ongoing patient sample testing phase of this study, 134 VKA anticoagulated samples showed an overall 66.4% agreement between DRVVT and TSVT/ECT LA status. When results were subcategorised according to INR, agreement was 70.6% for INR <2.0, 66.6% for INR 2.0-3.0, 75.7% for INR 3.0-4.0, and 42.9% for INR >4.0. Of the 45 overall samples with a disagreement between DRVVT and TSVT/ECT, 80% were identified as positive with TSVT/ECT.

Conclusion: LA testing in VKA-anticoagulated samples using the TVST/ECT has been established in four international APS ACTION CL. LA status determined to be negative with DRVVT but positive with TSVT/ECT might be due to dilution of the inhibitor in the 50:50 mixture in the DRVVT, required for clotting factor level normalisation. Preliminary results suggest that the TVST/ECT could provide an adjunctive test to DRVVT testing without the need for mixing studies and with high specificity.

Reference ranges for TSVT, ECT and TSVT/ECT established by the four Core laboratories, presented as normalised ratios. Manufacturer's reference range: TSVT ratio=0.93-1.10, ECT ratio=0.90-1.10. Abbreviations: TSVT: Taipan snake venom time, ECT: Ecarin snake time

Disclosure: M. Efthymiou: Alexion, 1, Immune Tolerance Network (ITN), 1; **I. Mackie**: None; **R. Willis**: None; **V. Pengo**: Werfen group, Milan, Italy, 6; **D. Andrade**: None; **E. Bison**: None; **O. Amengual**: None; **Z. Romay-Penabad**: None; **Y. Fujieda**: None; **M. Bertolaccini**: None; **D. Erkan**: Abbvie, 1, ACR/EULAR, 5, APS ACTION, 12, Executive Committee Co-chair, Argenx, 1, Aurinia, 6, Chugai, 1, Exagen, 5, GSK, 5, 6, NIH-NIAID, 5, Up-To-Date, 9; **H. Cohen**: argenx, 1, Roche, 1, Technoclone (paid to University College London Hospital (UCLH) Charity), 6, UCB Biopharma (paid to UCLH Charity), 2; **O. Of APS ACTION**: None.

Abstract Number: 0097

Transient Ischemic Attack in Antiphospholipid Antibody-positive Patients: Retrospective and Prospective Results from the AntiPhospholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking (APS ACTION) Clinical Database and Repository ("Registry")

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SESSION INFORMATION

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Session Title: Antiphospholipid Syndrome Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1: Baseline Characteristics of Antiphospholipid Antibody (aPL)-positive Patients with Transient ischemic attack (TIA) with/without History of Thrombosis

	History of TIA without Thrombosis (N:22)*	History of TIA and Thrombosis (N: 70)**	P Value
Concomitant Lupus	5 (23%)	16 (23%)	1.0
Thrombosis			
Arterial	N/A	59 (84%)	N/A
Venous	N/A	29 (41%)	N/A
Small vessel	N/A	10 (14%)	N/A
Pregnancy Morbidity* **	6 (27%)	16 (23%)	0.78
Other APS Manifestations			
Livedo reticularis/racemosa	1 (5%)	17 (24%)	0.06
Thrombocytopenia	0	9 (13%)	
Hemolytic Anemia	0	5 (7%)	
Skin ulcer	0	2 (3%)	
aPL-Nephropathy	0	3 (4%)	
Valve Disease	2 (9%)	18 (26%)	0.07
Cognitive dysfunction	1 (5%)	6 (9%)	1.0
White matter lesions	6(27%)	28 (40%)	0.32
Baseline CVD Risk factors			
Hypertension	6 (27%)	37 (53%)	*0.05*
Diabetes	0	6 (9%)	-
Hyperlipidemia	10 (45%)	34 (49%)	0.81
Obesity	5 (23%)	22 (31%)	0.59
Smoking Ever	8 (36%)	29 (41%)	0.80
Renal disease	0	6 (9%)	-
aPL Profile			
Triple aPL+	6 (27%)	25 (36%)	0.60
Double aPL+	4 (18%)	26 (37%)	0.12
Single aPL + (LA Only)	9 (41%)	9 (13%)	*0.01*
Single aPL + (aCL or $a\beta_2$GPI)	3 (14%)	9 (13%)	1.0
Medications Baseline:			
Anticoagulation +/- anti-platelet	14 (64%)****	65 (93%)****	0.002
Antiplatelet agent alone	8 (36%)	5 (7%)	0.002
Hydroxychloroquine	11 (50%)	40 (57%)	0.62
Statin	10 (45%)	37 (53%)	0.62

* 14/22 with one TIA and 8/22 with >1 TIA; ** 48/70 with one TIA and 22/70 with >1 TIA; ***Based on the Updated Sapporo APS classification Criteria; ****: all received warfarin or low-molecular weight heparin except one patient who received fondaparinux. **CVD:** cardiovascular disease, **LA:** lupus anticoagulant, **aCL/aβ2GPI**: anticardiolipin antibody / Anti-β_2-Glycoprotein-I Antibody

Background/Purpose: APS ACTION Registry aims to study the course of disease in antiphospholipid antibody (aPL)-positive patients. Although transient ischemic attack (TIA) can develop in aPL-positive patients, the ascertainment of TIA can be challenging due to the need to exclude other conditions, e.g., complex migraine with aura or seizure. Our primary objective was to analyze the clinical characteristics of persistently aPL-positive patients who were reported to have had "TIA" prior to recruitment and/or during prospective follow-up.

Methods: The registry inclusion criteria are positive aPL based on the Updated Sapporo APS Classification Criteria within one year prior to enrollment. Patients are followed every 12±3m with clinical data and blood collection. Firstly, we retrospectively compared the baseline characteristics of patients with a history of TIA among those without or with a history of imaging-confirmed thrombosis (at any time prior to registry entry). Secondly, in patients who completed 1-10 year follow up, we prospectively analyzed those with new onset TIA, which was defined as "a transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction lasting less than 24 hours" (confirmation status by a neurologist is also recorded).

Table 2: Follow-up Characteristics of 11 Antiphospholipid Antibody (aPL)-positive Patients with New Transient Ischemic Attack (TIA)

	History of TIA Without Thrombosis (N: 2/22)	History of TIA and Thrombosis (N: 5/70)	No History of TIA (N: 4/759)
Sociodemographic			
Female	2	3	4
White	2	4	2
Mean Age (Registry Entry)	49.5±4.5	50.8±9.2	36.2±6.2
Concomitant Lupus	0	2	2
Baseline Thrombosis			
Arterial	N/A	4	2
Venous	N/A	2	2
Follow-up Thrombosis			
Arterial (Before/After TIA)	0	0/1	0/1
Venous (Before/After TIA)	0	0	0
Pregnancy Morbidity*	0	2	0
aPL Profile			
Triple aPL+	0	0	0
Double aPL +	1	5	0
Single aPL + (LA)	0	0	3
Single aPL + (aCL or $a\beta_2$GPI)	1	0	1
**Additional Risk factors ** **			
Hypertension	1	4	1
Diabetes	0	1	0
Hyperlipidemia	2	1	1
Obesity	0	4	2
Smoking ever	2	2	1
Renal disease	1	1	0
Family Hx of early CVD	1	1	0
Sedentary lifestyle	0	5	4
MTHFR Polymorphism	0	1	1
*Hormone Replacement/ OCP	0	1	0
Medications at Recurrence			
Anticoagulation +/- anti-platelet	2	5	4
Antiplatelet agent alone	0	0	0
Hydroxychloroquine	1	4	3
Statin	2	2	1

*Based on the Updated Sapporo APS classification Criteria; **Concomitant cardiovascular disease (CVD) and venous thrombosis risk factors at the time of event. **LA:** lupus anticoagulant, **aCL/ aβ2GPI:** anticardiolipin antibody/ Anti-β_2-Glycoprotein-I Antibody, **OCP:** oral contraceptive preparation

Results: As of April 2023, 1,166 patients were included in the registry and 92 (8%) had a history of TIA at enrollment: 22/92 (24%) without and 70/92 (76%) with history of imaging confirmed arterial/venous thrombosis. *Of 22 TIA patients without history of thrombosis* (mean age 54.8 ± 11, female 17 [77%], White: 20 [91%]), 15 (68%) were confirmed by a neurologist. *Of 70 TIA patients with history of imaging-confirmed thrombosis* (mean age 56.7 ± 11, female 39 [56%], White: 48 [69%], arterial thrombosis 59 [84%], and venous thrombosis 29 [41%]), 46 [66%] were confirmed by a neurologist. At baseline, TIA patients without thrombosis were more likely to receive antiplatelet agent alone and have single LA positivity, whereas TIA patients with history of imaging-confirmed thrombosis were more likely to have hypertension and receive warfarin (Table 1). During the prospective follow up of 92 patients with a history of TIA (mean follow-up: 4.5 ± 3.0 years), seven new TIA were reported: a) two (9%) in 22 patients with no history of thrombosis (1.41 per 100 patient-years), and b) five (7%) in 70 patients with history of thrombosis (2.71 per 100 patient-years) (Table 2). In addition, four of 759 (0.5%) patients with no history of TIA at baseline and who completed at least one year follow-up developed a TIA during the mean follow-up of 5.12 years (0.09 per 100-patient years).

Conclusion: In our large international cohort of persistently aPL-positive patients, 8% were reported to have history of "TIA" at the registry entry. The TIA recurrence rate during follow-up was 7-8%; however, the new TIA rate was less than one percent. Approximately two-thirds of patients without a history of imaging-confirmed thrombosis were treated with anticoagulation; all patients with recurrent/new TIA during the follow-up were on anticoagulation. Our findings underscore the need for well-designed controlled studies of TIA in aPL-positive patients with strict definitions.

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Abstract Number: 0098

Predictors of Mortality in Antiphospholipid Antibody Positive Patients: Prospective Results from Antiphospholipid Syndrome Alliance for Clinical Trials and International Networking (APS ACTION) Clinical Database and Repository "Registry"

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SESSION INFORMATION

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Session Title: Antiphospholipid Syndrome Poster
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Background/Purpose: APS ACTION "Registry" was created to study the natural course of disease over 10 years in persistently antiphospholipid antibody (aPL)-positive patients with/without other systemic autoimmune diseases. Our objective was to determine the mortality rate as well as the causes and predictors of mortality in aPL-positive patients with/without APS classification.

Methods: A web-based data-capturing system is used to store patient demographics, history, and medications. The inclusion criteria are positive aPL according to the Updated Sapporo Classification Criteria tested within one year prior to enrollment. Patients are followed every 12 ± 3m with clinical data and blood collection. In this prospective analysis, firstly we analyzed descriptively the causes of death (based on investigators' reports) for patients reported as "deceased" during the follow-up. Secondly, we compared the clinical and laboratory characteristics of deceased versus non-deceased patients using the adjusted Cox proportional hazards model and calculated the survival probability by Kaplan-Meier Model based on different age groups.

Table 1: Associations Between Baseline Characteristics at Registry Entry and Mortality in the APS Action Cohort, Adjusted for Age

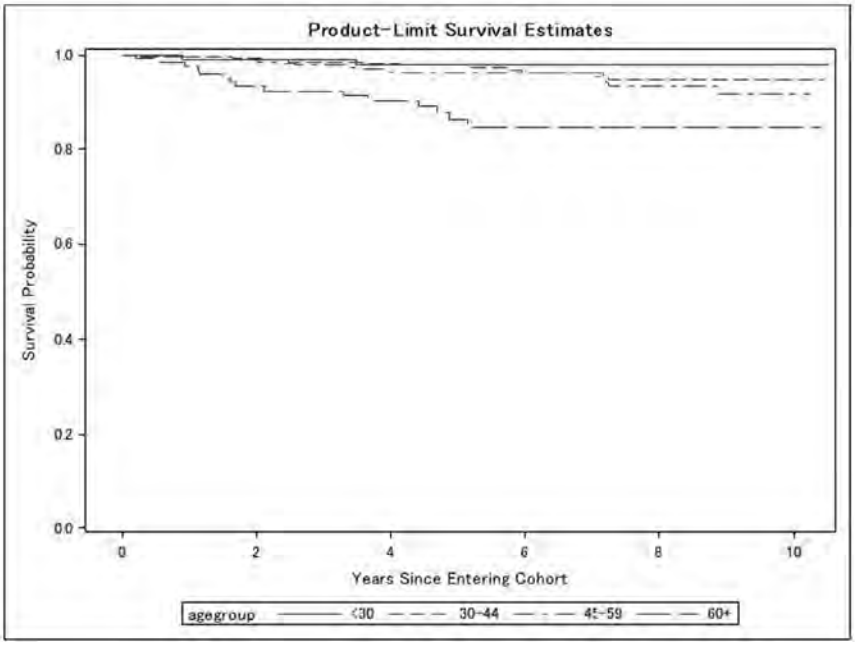
Baseline Characteristics N: 963	Hazard Ratio (95% CI)	P-value
Arterial Thrombosis (AT) (n: 327, 34%)	**2.99 (1.56,5.74)**	**.0010**
Venous Thrombosis (VT) (n: 408, 42%)	1.24 (0.67,2.32)	.4908
AT or VT (n: 630, 65%)	**4.20 (1.49,11.8)**	**.0066**
Microvascular APS (MAPS) (n: 82, 9%)*	1.60 (0.67,3.84)	.2937
Catastrophic APS (CAPS) (n: 11, 1%)	**5.87 (1.35,25.4)**	**.0180**
MAPS or CAPS (n: 93, 10%)	1.79 (0.79,4.08)	.1662
Active Thrombocytopenia (n: 53, 6%)**	1.85 (0.65,5.27)	.2462
Triple aPL positive (n: 323, 34%)	0.74 (0.37,1.49)	.4012
Cardiovascular Risk Factors (564, 59%)* **	**2.85 (1.23,6.58)**	**.0144**
Other Autoimmune Diseases (381, 40%)	**2.85 (1.52,5.36)**	**.0011**
Hydroxychloroquine (n: 459, 48%)	1.57 (0.84,2.92)	.1579
Statins (229, 24%)	1.73 (0.88,3.40)	.1143
Corticosteroids (204, 21%)	1.94 (0.98,3.81)	.0556

*Mostly lung, skin, and/or kidney disease; ** Platelets persistently < 100,000 x10^9/L; ***Hypertension, diabetes, hyperlipidemia, obesity, nephrotic range proteinuria, chronic or end-stage renal disease, and/or current smoking.

Table 2: Independent Associations Between Baseline Characteristics at Registry Entry and Mortality in the APS Action Cohort, Adjusted for Age and Each Other for the Four Strongest Predictors

Patient Characteristic	Hazard Ratio (95% CI)	P-value
Arterial Thrombosis	2.94 (1.50,5.76)	.0017
Catastrophic APS	2.52 (0.57,11.3)	.2248
Other Autoimmune Diseases	2.97 (1.56,5.63)	.0009
Cardiovascular Risk Factors	2.43 (1.04,5.71)	.0414

Figure 1: Kaplan Meier Curves for Survival Probability Based on Different Age Groups (see results for the estimated 5-year survival probabilities; 10-year survival probabilities were not calculated due to limited information)



Results: As of May 2023, of 1,174 patients recruited, 215 (18%) were excluded due to incomplete follow-up data. Of the remaining 963 (mean age at registry entry: 53.0 ± 13.3, female: 723 [75%], and White: 657 [68%]), 43 (5%) were reported as deceased after a median follow-up of 5.3 years (interquartile range 2.4 to 7.9). The main causes of death (not mutually exclusive) were: infection (15, 35%), thrombosis (9, 21%), and malignancies (8, 19%). Based on the univariate analysis, history of arterial thrombosis or catastrophic APS (CAPS), selected baseline cardiovascular disease (CVD) risk factors, baseline active thrombocytopenia, and concomitant systemic autoimmune disease (SAID) were significantly more common in deceased patients, compared to non-deceased (data not shown). Based on the Cox proportional hazards model adjusted for age, arterial thrombosis, CAPS, CVD risk factors combined, and SAID were significantly and independently associated with mortality (Tables 1 and 2). Estimated 5-year survival probabilities starting from the registry entry (by age groups) were 0.98 (95% CI 0.92-0.99), 0.98 (0.95-0.99), 0.96 (0.93-0.98), and 0.86 (0.77-0.92) for ages < 30 (n:119), 30-44 (n: 362), 45-59 (n: 340), and >60 (n: 142), respectively (Figure 1).

Conclusion: Based on analysis of the largest multi-center international prospective cohort of persistently aPL-positive patients, the mortality rate was 5% after a median follow-up of five years. The estimated 5-year survival probability decreased with age; lowest (0.86) for patients over 60 years old at registry entry. History of arterial thrombosis, catastrophic APS, CVD risk factors, and concomitant systemic autoimmune diseases independently predicted future mortality

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Abstract Number: 0099

Cell-bound Complement Activation Products in Antiphospholipid Antibody-positive Patients Without Other Systemic Autoimmune Diseases

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SESSION INFORMATION

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Background/Purpose: Based on animal models, complement activation is part of Antiphospholipid Syndrome (APS) pathogenesis. However, studies investigating complement activation in antiphospholipid antibody (aPL)-positive patients are limited. Our objective was to analyze complement activation in subgroups of aPL-positive patients, using complement 3/4 (C3, C4) andcell-bound complement activation products (CB-CAPs)(B-lymphocytes [BC4d], erythrocytes [EC4d], and platelets [PC4d]).

Methods: Persistently aPL-positive (>12 weeks apart; last within six months (m) prior to entry) adult patients without other systemic autoimmune diseases (SAID) were enrolled in a single center study. For those with aPL-related manifestations, i.e., microvascular APS (MAPS), thrombotic APS (TAPS), obstetric APS (OAPS), thrombocytopenia(TP) (< 150x109/L), and/or hemolytic anemia (HA),at least one event within five years prior to enrollment was required. Selected exclusion criteria wereactive infection, cancer, and corticosteroids >20mg/d. Blood and clinical data were collected at baseline; a subgroup of

Table 1: Complement Activation Markers in Persistently Antiphospholipid Antibody (aPL) Positive Patients without Other Systemic Autoimmune Diseases, Baseline Results Overall and by aPL Profile

#abnormal/# tested or Mean (SD)	Total (n: 33)	Triple aPL (LA, aCL & aB_2GPI) (n:21)*	Single LA or Double aPL (LA & aCL or aB_2GPI) (n:5)**	Double aPL (aCL & aB_2GPI) (n: 5)	Single aPL (aB_2GPI) (n:2)
aPL Details & aCL/aB_2GPI Isotype	N/A	IgG +/- M: 20 IgM Alone: 1	LA Alone: 4 LA + aCL IgG: 1	IgM: 5	IgG: 1 IgM: 1
C3 (<81 mg/dl)	4/31 (13%)	3/18	1/5	0	0
Mean C3 (mg/dL)	113.6 (32.1)	105.4 (35.0)	129.3 (38.6)	114.3 (20.3)	126.0 (34.8)
C4 (<13 mg/dl)	4/31 (13%)	3/18	1/5	0	0
Mean C3 (mg/dL)	25.2 (8.8)	22.7 (10.0)	27.3 (6.2)	25.5 (7.8)	34.5 (0.4)
BC4d (61-100 MFI)[a]	1/29 (3%)	1/18	0	0	0
BC4d (101-200 MFI)[b]	6/29 (21%)	6/18	0	0	0
BC4d (>200 MFI)	0	0	0	0	0
Mean BC4d (MFI)	47.5 (44.8)	61.0 (52.0)	28.0 (17.8)	28.0 (17.4)	17.5 (4.9)
EC4d (15-30 MFI)[c,d]	7/33 (21%)	7/20	0	0	0
EC4d (31-75 MFI)[e]	2/33 (6%)	2/20	0	0	0
EC4d (>75 MFI)[f]	2/33 (6%)	2/20	0	0	0
Mean EC4d (MFI)	18.2 (25.4)	25.7 (30.3)	8.6 (3.8)	4.9 (0.8)	4.8 (1.8)
PC4d (10-15 MFI)[g]	2/32 (6%)	1/20	1/4	0	0
PC4d (16-20 MFI)	1/32 (3%)	1/20	0	0	0
PC4d (>20 MFI)[h]	9/32 (28%)	7/20	2/4	0	0
Mean PC4d (MFI)	38.3 (104.6)	26.8 (35.1)	154.9 (282.8)***	5.1 (2.0)	3.0 (0)

Positive 61-200 mean fluorescent intensity (MFI), 15-75 MFI, and 10-20 MFI, and **strongly positive** above 200 MFI, 75 MFI, and 20 MFI for BC4d, EC4d, and PC4d, respectively. *Two patients with no C3/C4 and BC4d results. ** Two patients with no BC4d results, and one with no PC4d result. *** Based on four samples with levels of 6 MFI, 11.5 MFI, 23 MFI, and an outlier of 579 MFI. [a] Six month (m) repeat BC4d was in the same range (SR) (1 of 1 tested); [b] 6m BC4d SR (2/2); [c] 6m EC4d SR (3/4) and 31-75 range (1/4); [d] 12m EC4d SR (1/3), negative (1/3), and 31-75 range (1/3); [e] 6m EC4d SR (2/2); [f] 6m EC4d SR (1/1); [g] 6m PC4d negative (2/2), and 12m PC4d SR (1/2) and negative (1/2); and [h] 6m PC4d SR (3/5) and negative (2/5), and 12m PC4d SR (1/1).

patients completed 6-12mfollow-up(Table 1 footnote). Positive aPLwas defined as positive lupus anticoagulant (LA) test, anticardiolipin antibody (aCL) IgG/M ≥ 40 ELISA units, and/or aβ2GPI IgG/M ≥ 40 ELISA units. C3/C4 were measured by turbidimetry and CB-CAPs by quantitative flow cytometry. Following a descriptive analysis of baseline results based on aPL profiles and clinical phenotypes, C3/C4 and CB-CAPswere correlated (Pearson).

Results: Between 8/20 and 11/22, 33 patients(female 23 [70%], mean age 50.6+12.5, White 30 [91%]) were enrolled. Four of 31 (13%) had decreased C3/C4, while 7/29 (24%)had elevated BC4d (no strong positivity [SP]), 13/33 (33%) EC4d (2% SP), and 12/32 (37%) PC4d (28% SP). Based on different aPL profiles, all patients with decreased C3/C4 or elevated BC4d, EC4d, and PC4d had triple aPL positivity, or LA positivity with/without aCL or aβ2GPI(additionally, higher mean EC4d and PC4d levels were observed in these groups) (Table 1).Based on different aPL clinical phenotypes, the number of patients with strongly positive EC4d and PC4dwere proportionally higher (14% and 36%) in those with MAPS/TP/HA, compared to those with TAPS (0 and 18%) or no APS (0 and 29%) (additionally higher mean EC4d and PC4d levels were observed in the former group) (Table 2).There was a weak correlation between C3/C4 and CB-CAPs, especially for PC4d (r=-0.098 and 0.068 for C3 and C4, respectively) (Figure 1).

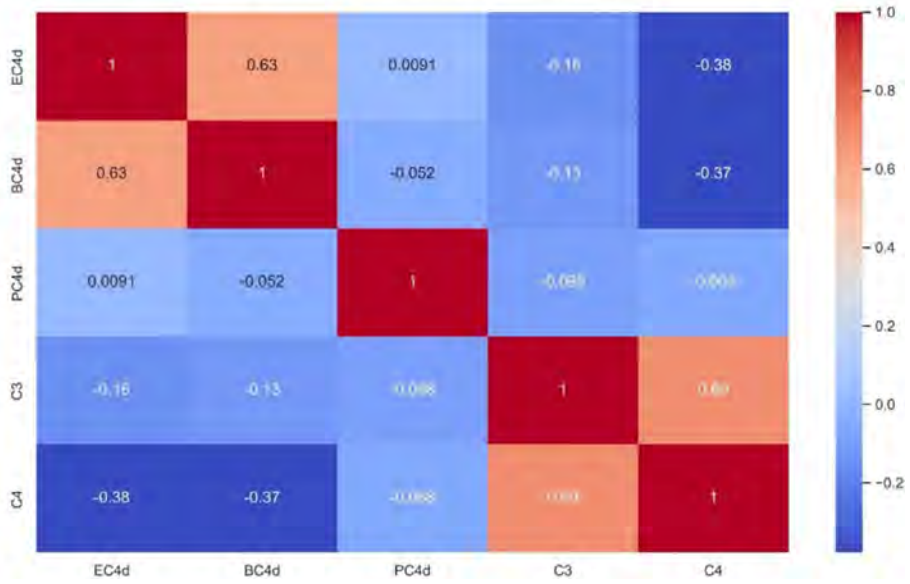
Conclusion: Assessment of complement activation in persistently aPL-positive patients without other SAID demonstrated that13%, 24%, 33%, and 37% had abnormal baseline C3/C4, BC4d, EC4d, and PC4d, respectively; all in patients with triple aPL-positivity, or LA-positivity with/without aCL or aβ2GPI. Number of patients with strongly positive EC4d and PC4d were proportionally higher (14% and 36%) in those with MAPS, thrombocytopenia, and/or hemolytic anemia. Given the higher

Table 2: Complement Activation Markers in Persistently Antiphospholipid Antibody (aPL) Positive Patients without Other Systemic Autoimmune Diseases, Baseline Results Overall and by Clinical Phenotype

#abnormal/# tested or Mean (SD)	Total (n: 33)	MAPS* (n:14)**	TAPS*** (n: 12)****	No APS (n: 7)
C3 (<81 mg/dl)	4/31 (13%)	2/12	1/12	1/7
Mean C3 (mg/dL)	113.6 (32.1)	117.1 (31.6)	123.4 (34.9)	97.1 (27.8)
C4 (<13 mg/dl)	4/31 (13%)	2/12	1/12	1/7
Mean C4 (mg/dL)	25.2 (8.8)	27.7 (8.8)	28.5 (8.6)	17.7 (4.3)
BC4d (61-100 MFI)	1/29 (3%)	1/12	0	0
BC4d (101-200 MFI)	6/29 (21%)	4/12	1/10	1/7
BC4d (>200 MFI)	0	0	0	0
Mean BC4d (MFI)	47.5 (44.8)	48.6 (45.1)	42.8 (49.5)	53.5 (43.3)
EC4d (15-30 MFI)	7/33 (21%)	2/14	2/12	3/7
EC4d (31-75 MFI)	2/33 (6%)	1/14	1/12	0
EC4d (>75 MFI)	2/33 (6%)	2/14	0	0
Mean EC4d (MFI)	18.2 (25.4)	27.1 (36.4)	12.9 (11.7)	9.8 (5.7)
PC4d (10-15 MFI)	2/32 (3%)	0	2/11	0
PC4d (16-20 MFI)	1/32 (6%)	0	0	1/7
PC4d (>20 MFI)	9/32 (28%)	5/14	2/11	2/7
Mean PC4d (MFI)	38.3 (104.6)	62.2 (151.6)	23.4 (37.2)	9.8 (8.5)

Positive 61-200 mean fluorescent intensity (MFI), 15-75 MFI, and 10-20 MFI, and **strongly positive** above 200 MFI, 75 MFI, and 20 MFI for BC4d, EC4d, and PC4d, respectively.
*Includes (not mutually exclusive) MAPS (lung [active: 1, inactive: 3]; kidney [active: 2, inactive: 1, suspected with abnormal kidney function: 3]; and skin [inactive 1]), thrombocytopenia [baseline 100-149 x10^9/L: 5; inactive: 3), and/or hemolytic anemia (active: 1, inactive: 1). 13/14 also had Thrombotic APS and 1/14 also had Obstetric APS (OAPS). ** Two patients with no C3/C4 and BC4d results. ***4/12 also with OAPS. ****Two patients with no BC4d and one with no PC4d results.

Figure 1: Complement Activation Markers Correlated to Serum Complement C3 and C4 Levels
(Pearson's correlation coefficient (r) is shown with darker red shades representing strong positive correlations and darker blue shades representing strong inverse correlations between biomarkers [two patients did not have C3, C4, and BC4d, and one did not have PC4d results])



percentage of aPL-positive patients with abnormal CB-CAPs vs C3/C4, and the poor correlation between CB-CAPs and C3/C4, our study generates the hypothesis that CB-CAPs have a role in measuring disease activity in aPL-positive patients.

Disclosure: D. Erkan: Abbvie, 1, ACR/EULAR, 5, APS ACTION, 12, Executive Committee Co-chair, Argenx, 1, Aurinia, 6, Chugai, 1, Exagen, 5, GSK, 5, 6, NIH-NIAID, 5, Up-To-Date, 9; **J. Vega**: None; **T. O'Malley**: Exagen, 3, 11, 12, Shareholder; **A. Concoff**: Exagen, 3, 4, 12, Shareholder, Pacira Biosciences, Inc., 2, United Rheumatology, 4.

Abstract Number: 0100

The Clinical Relevance of Different Antiphospholipid Antibody Profiles in Pediatric Rheumatology Patients

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The clinical relevance of different antiphospholipid antibody (aPL) profiles, including low level anticardiolipin (aCL) and anti β_2-glycoprotein-I (aβ_2GPI) antibodies, is ill-defined in the pediatric population. The purpose of this project is to describe the demographic, clinical, and laboratory characteristics of aPL "positive" pediatric patients based on different aPL profiles.

Methods: In this single center retrospective cohort study, based on the screening of our pediatric (age ≤18yo) rheumatology electronic medical records (2016—2022), we identified patients who had at least one "positive" aPL (lupus anticoagulant [LA], aCL IgG/M, or aβ_2GPI IgG/M) result. First, we grouped patients based on initial high- (LA positive and/or aCL/aβ_2GPI

IgG/M≥40U [ELISA]) vs low- (LA negative and aCL/aβ$_2$GPI IgG/M 20-39U) risk aPL profiles to evaluate subsequent aPL testing frequency and results. Secondly, we descriptively analyzed the demographic and clinical characteristics of patients with persistently positive (at least 12 weeks apart) aPL results based on different aPL profiles.

Results: Of 113 aPL "positive" patients identified, 56 (50%) were excluded as they had very low aCL/aβ$_2$GPI IgG/M positivity (above laboratory normal range but < 20U). Of the remaining 57 patients (female: 48 [84%], lupus classification: 21 [37%]), 35 (61%) had an initial high-risk profile and 22 (39%) had an initial low-risk profile. Based on the subsequent aPL results available in 42/57 (74%) patients, 26/28 (93%) in the high-risk, and 5/14 (36%) in the low-risk group remained still positive (Table 1). Of these 31 patients with persistent aPL positivity, thrombosis occurred in eight (26%) patients with high-risk aPL profile and in none with low-risk aPL profile; other aPL-related manifestations were reported in 15 (48%) patients with persistent aPL positivity (Tables 2 and 3). Of 26 patients without persistent aPL results (repeat test either negative or not available), none developed thrombosis, one had livedo reticularis, and two had migraines.

Conclusion: An initial low-risk aPL profile (negative LA and aCL/aβ$_2$GPI IgG/M levels 20-39U) is persistent in only approximately one-third of the pediatric patients, which was not associated with thrombosis in our cohort. Meanwhile, a high-risk profile defined as LA positivity and/or aCL/aβ$_2$GPI IgG/M levels ≥ 40U is persistent in 90% of pediatric patients, about a third of

Table 1: Follow-up Antiphospholipid Antibody (aPL) Results in 57 Patients with at Least One High- or Low-risk aPL Profile

	Initial LA+ and/or aCL/aβ$_2$GPI ≥ 40U (n:35)	Initial LA- and aCL/aβ$_2$GPI 20-39U (n:22)
Mean Follow up (+/- SD) (y)	4.49 ± 4.9	3.05 ± 2.9
Subsequent aPL positive / # of patients with repeat aPL	26/28 (93%)	5/14 (36%)
• Repeat LA positive / Initial LA positive	18/28 (64%)	N/A
• Repeat aCL/aβ$_2$GPI positive / Initial aCL/aβ$_2$GPI positive	19/23 (83%)	5/14/(36%)

LA: lupus anticoagulant; aCL: anticardiolipin antibody; and aB2GPI: anti-beta-2 glycoprotein-I antibody

Table 2: Demographic, Clinical, and Laboratory Characteristics of 31 Patients with Persistent High- or Low-risk Antiphospholipid Antibody (aPL) Profiles

	Triple aPL Positive (n:10)	LA with/without aCL or aβ$_2$GPI (n:11)	aCL and/or aβ$_2$GPI (n:10)
aCL/aβ$_2$GPI Level			
aCL/aβ$_2$GPI IgG/M 20-39U	2 (20%)	2 (18%)	6 (60%)
aCL/aβ$_2$GPI IgG/M ≥40U	8 (80%)	2 (18%)	4 (40%)
Demographics			
Mean Age	13.7 ± 4.64	13.7 ± 4.64	13.8 ± 4.34
Female	8 (80%)	8 (80%)	9 (90%)
White	6 (60%)	7 (64%)	5 (50%)
Lupus Classification	6 (60%)	6 (60%)	5 (50%)
Thrombosis	5 (50%)	2 (18%)	1 (10%)*
Other aPL Manifestations	4 (40%)	8 (73%)	3 (30%)
Thrombocytopenia**	1	3	1
Autoimmune Hemolytic Anemia	2	1	2
Cardiac Valve Disease	-	1	-
Livedo Reticularis/Racemosa	1	1	1
Skin Ulcers	-	1	-
Migraines***	2	2	-
Chorea ***	1	-	-

* In a patient with aCL IgM > 40U initially, then 20-30U on repeat testing; **Platelets <150,000 /ul twice with no other diagnosis; *** controversial aPL-related manifestations, which may be more relevant in pediatric population. LA: lupus anticoagulant; aCL: anticardiolipin antibody; and aB2GPI: anti-beta-2 glycoprotein-I antibody

Table 3: Demographic and Clinical Characteristics of Eight Persistently Antiphospholipid Antibody (aPL) Positive Patients with Thrombosis

Age	Sex	Associated Autoimmune Disease	Thrombotic Manifestations	APS Related Non-thrombotic Manifestations*	aPL Profile**
16	F	-	DVT/PE	-	LA aCL IgM high aβ2GPI IgM high
17	F	SLE	Intracardiac thrombus	Cardiac valve disease	LA
12	F	-	Intrahepatic IVC thrombus, PE, popliteal artery thrombosis	Thrombocytopenia, AIHA, livedo racemosa	LA
12	F	SLE	Renal thrombotic microangiopathy	AIHA, livedo reticularis, migraine	LA aCL IgG 20-39U & IgM >40U aβ2GPI IgM >40U
18	F	SLE	DVT	Migraine	aCL IgG >40U
14	F	SLE-Like Disease	DVT (x2), PE	-	LA aCL IgG >40U aβ2GPI IgG >40U
17	M	-	Superficial vein thrombosis	Migraine	LA aCL IgM >40U aβ2GPI IgG >40U
16	F	-	DVT (x2)	-	aCL IgM >40U

*Non-thrombotic manifestations were included if they were not attributable to another diagnosis; **aPL profile at time of first event F: Female; DVT: Deep venous thrombosis; PE: Pulmonary embolism; IVC = inferior vena cava; SLE: systemic lupus erythematosus; AIHA: autoimmune hemolytic anemia. LA: lupus anticoagulant; aCL: anticardiolipin antibody; and aB2GPI: anti-beta-2 glycoprotein-I antibody

whom had history of thrombosis, and half had non-thrombotic aPL-related manifestations. Our results underscore the need for a large-scale international effort to better characterize the aPL-related manifestations in pediatric patients with persistent high-risk aPL-profiles, which can eventually guide the development of future pediatric-specific APS classification criteria.

Disclosure: J. Pandya: None; **K. Onel**: None; **D. Erkan**: Abbvie, 1, ACR/EULAR, 5, APS ACTION, 12, Executive Committee Co-chair, Argenx, 1, Aurinia, 6, Chugai, 1, Exagen, 5, GSK, 5, 6, NIH-NIAID, 5, Up-To-Date, 9.

Abstract Number: 0101

Non-Criteria Antiphospholipid Antibodies and Calprotectin as Potential Biomarkers in Pediatric Antiphospholipid Syndrome

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Antiphospholipid Syndrome Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: While classification criteria for pediatric APS are not yet available, recent research suggests pediatric APS patients are unique, and many present with extra-criteria manifestations as their primary clinical features. Criteria aPL may identify classical APS manifestations, but a clinically actionable biomarker for features unique to pediatric APS is not yet available. Here, we aimed to evaluate the presence, clinical associations, and potential mechanistic roles of non-criteria aPL and circulating NETs markers in pediatric APS patients.

Methods: Children with APS (n=19), venous thrombosis without APS (VT, n=20), systemic lupus erythematosus without aPL (SLE, n=11), and healthy controls (n=13) were evaluated for nine different types of aPL by Werfen assays (**Table 1**). Calprotectin, a well-known marker of circulating neutrophil extracellular traps (**NETs**), was measured in plasma using the Human S100A8/S100A9 heterodimer DuoSet ELISA (R&D). Univariate logistic regression was used to identify potential clinical associations. A platelet viability dye-based assay was performed to assess the potential impact of calprotectin on platelet survival (**Fig 2A**).

Table 1. Prevalence of antiphospholipid antibodies in children with APS (n=19)

aPL	Number positive (manufacturer's threshold)	%	Number positive (titer ≥40 U)	%
aCL IgG*	7	37%	5	26%
aCL IgM*	5	26%	3	16%
aCL IgA	1	5%	1	5%
aβ2GPI IgG*	8	42%	5	26%
aβ2GPI IgM*	9	47%	5	26%
aβ2GPI IgA	1	5%	1	5%
aPS/PT IgG	11	58%	11	58%
aPS/PT IgM	13	68%	13	68%
anti-D1 IgG	10	53%	9	47%
Lupus anticoagulant*†	16	84%		
Any non-criteria aPL	15	79%	15	79%

*Current adult APS classification criteria aPL, remaining are non-criteria aPL

†Lupus anticoagulant as determined by clinical laboratory data

aPL=antiphospholipid antibodies; aCL=anticardiolipin; aβ2GPI=anti-beta-2 glycoprotein I; aPS/PT=anti-phosphatidylserine/prothrombin; anti-D1=anti-Domain 1 of beta-2 glycoprotein I

Manufacturer's thresholds:

- aCL IgG/M/A ≥ 20 GPL/MPL/APL
- $a\beta_2$GPI IgG/M/A ≥ 20 SGU/SMU/SAU
- aPS/PT IgG/M ≥ 30 arbitrary units
- anti-Domain 1 IgG ≥ 20 arbitrary units

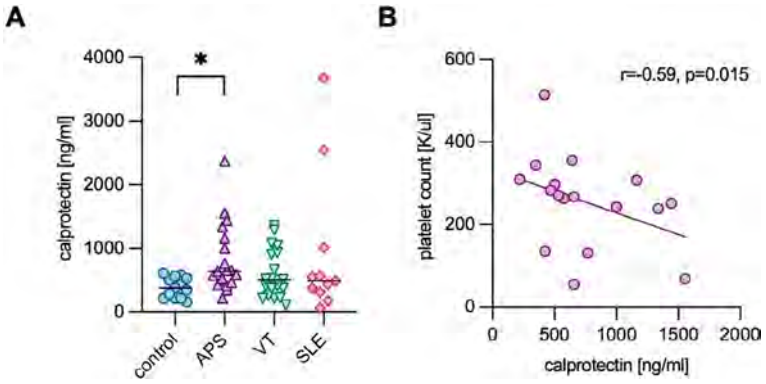

Figure 1. Calprotectin in pediatric APS plasma. A, Levels of calprotectin were measured in patients with pediatric APS, pediatric venous thrombosis (VT), pediatric SLE, and healthy pediatric controls. Calprotectin levels were compared with healthy controls by the Kruskal-Wallis test adjusted for multiple comparisons by Dunn's method; *p<0.05. B, Correlation between circulating calprotectin and platelet count in pediatric APS patients. Spearman's correlation coefficient was calculated and is shown in the panel.

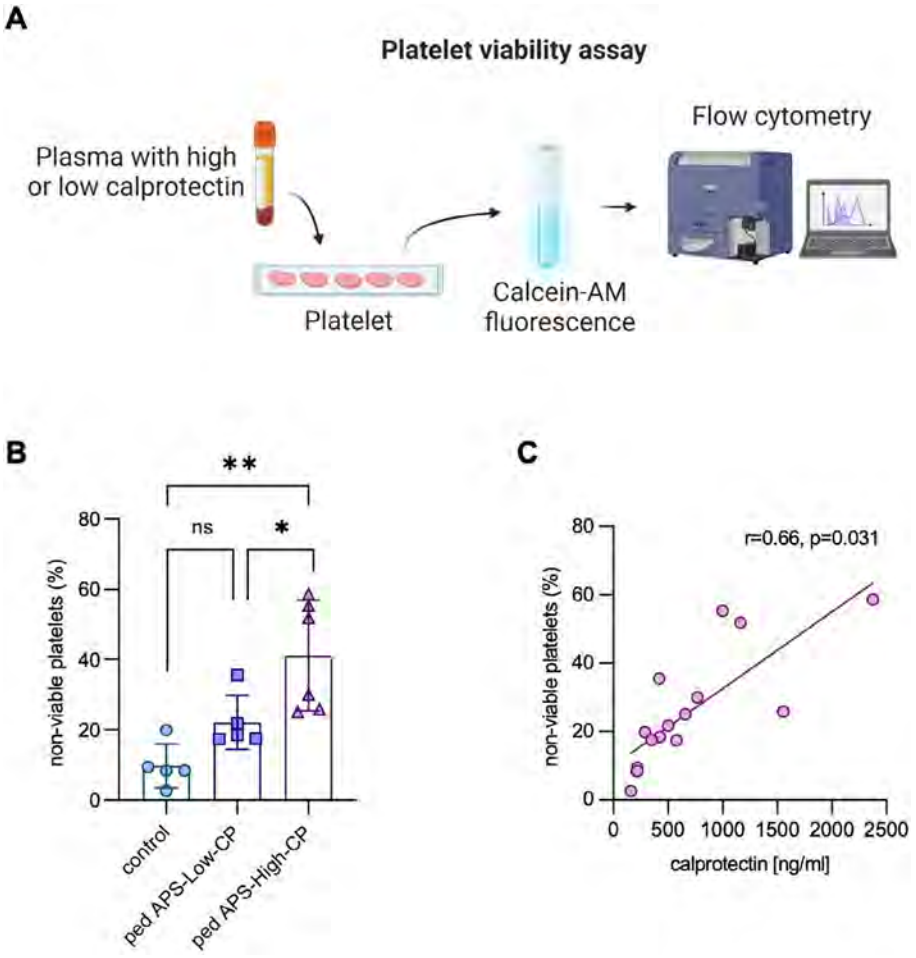

Figure 2. Effect of calprotectin on platelet viability. A, Schematic illustration of platelet viability assay. Created at www.biorender.com. B, Healthy donor platelets were incubated with 5% plasma from pediatric APS patients with low calprotectin, pediatric APS patients with high calprotectin, or pediatric controls. Platelet viability was measured by flow cytometry using Calcein-AM dye. The percentage of non-viable platelets was then compared between groups by the Kruskal-Wallis test adjusted for multiple comparisons by Dunn's method (*p<0.05, **p<0.01, ns=not significant). C, Calprotectin levels from pediatric APS patients were positively correlated with the percentage of non-viable platelets (r=0.66, p=0.031).

Results: Among the 19 pediatric APS patients (median age of 13 [range 3 to 18]), 74% were female, and 58% had primary APS. Most (89%) had experienced at least one venous thrombosis, and four had recurrent thrombotic events. The remaining two children with APS exhibited extra-criteria manifestations, persistent aPL, and a clinical diagnosis of APS. Almost half (47%) had at least one extra-criteria manifestation. Interestingly, 79% of pediatric APS patients had at least one non-criteria aPL at ≥40 units (**Table 1**). Aside from lupus anticoagulant, aPS/PT IgG and IgM were the most prevalent aPL followed by anti-D1 IgG. Univariate logistic regression demonstrated that positive anti-D1 (p=0.0109), positive aPS/PT IgG ($p < 0.0001$), and IgM ($p < 0.0001$) were significantly associated with venous thrombosis. Positive anti-D1 IgG (p=0.0116) and aPS/PT IgG (p=0.0116)/IgM (p=0.0321) were also associated with extra-criteria manifestations such as thrombocytopenia. Increased levels of calprotectin, which is a marker of NETs, were detected in children with APS (**Fig 1A**). Calprotectin levels correlated moderately with levels of aPS/PT IgM (r=0.49, p=0.0345) and absolute neutrophil count (r=0.63, p=0.0079), whereas they were negatively correlated with hemoglobin (r=-0.74, p=0.0189) and platelet count (r=-0.59, p=0.0150) (**Fig 1B**). Mechanistically, plasma from pediatric APS patients with high calprotectin levels impaired platelet survival *in vitro* in a dose-dependent manner (**Fig 2A-B**), and APS calprotectin levels correlated with decreased platelet viability (**Fig 2C**).

Conclusion: Our study suggests non-criteria aPL and circulating calprotectin were highly prevalent among pediatric APS patients and associated with extra-criteria manifestations more common in pediatric APS. The role of non-criteria aPL and calprotectin as clinically actionable biomarkers that might enable earlier diagnosis and inform targeted therapy for some pediatric aPL-positive patients warrants further evaluation.

Disclosure: E. Sloan: None; **K. Kmetova**: None; **N. Somanathapura**: None; **L. Kluge**: None; **E. Chong**: None; **C. Hoy**: None; **S. Yalavarthi**: None; **J. Madison**: None; **C. Sarosh**: None; **L. Walters**: None; **J. Baisch**: None; **J. Turnier**: None; **V. Pascual**: None; **T. Wright**: None; **J. Knight**: Jazz Pharmaceuticals, 2; **A. Zia**: Sanofi, 1, Takeda, 1; **Y. Zuo**: None.

Abstract Number: 0102

The Subtype and Prognosis of Acute Myocardial Infarction in Antiphospholipid Syndrome Patients

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Acute myocardial infarction (AMI) can be divided into coronary artery disease (MICAD) or nonobstructive coronary arteries (MINOCA) according to the severity of artery stenosis on coronary angiography. Antiphospholipid syndrome (APS) can present with AMI, but the subtype and prognosis of these patients were not fully understood.

Methods: A single-center study was conducted based on the APS cohort in Peking Union Medical College Hospital. According to coronary angiography, AMI patients were classified as MICAD (≥50% stenosis) or MINOCA(<50% stenosis). Baseline and follow-up data were compared to identify differences between the two subgroups. Cox analysis was used to find prognostic factors associated with AMI recurrence.

Results: The study enrolled 36 APS-AMI patients underwent coronary angiography, 26 (72%) patients were diagnosed with MICAD and 10 (28%) patients with MINOCA. Comparison between the two subgroups showed MINOCA patients were more likely to present in APS secondary to SLE than MICAD (70% VS 23.1%, p=0.018), and less likely to comorbid with previous atherosclerotic cardiovascular disease (ASCVD) (0 VS 50%, p=0.006). Anti-cardiolipin antibody (aCL) was more common in MINOCA (100% VS 65.4%, p=0.039). Treatment strategies were different, MINOCA patients tended to receive glucocorticoid (80% VS 26.9%, p=0.007), immunosuppressant (80% VS 26.9%, p=0.007), hydroxychloroquine (100% VS 26.9%, p=0.000) and anticoagulation (90% VS 42.3%, p=0.022), while MICAD patients were more likely to receive revascularization (47.6% VS 0%, p=0.002). 2 (5.5%) patients died and 13 (36.1%) patients experienced a relapse of AMI during a mean follow-up time of 42.25 months. Recurrence occurred only in MICAD group (13/26, 50%), over 60% (8/13) had recurrence more than once. Hydroxychloroquine was found to be a protective factor for AMI recurrence by Cox analysis [HR (hazard ratio) = 0.106, CI (confidence interval) = 0.014-0.823, p= 0.032], only 1 (5.8%) patient on hydroxychloroquine relapsed. While 66.7% (10/15) patients received revascularization suffered AMI recurrence caused by stent stenosis/thrombus, and the HR of recurrent AMI with revascularization therapy was 4.041 (CI = 1.087-15.021, p = 0.037).

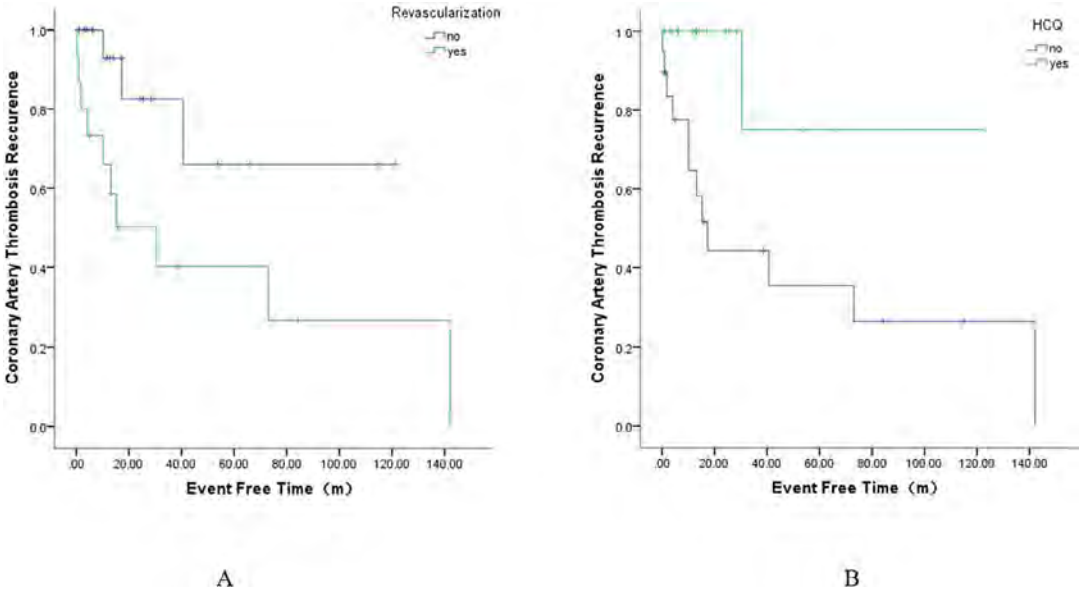

Figure 1. Kaplan-Meier curve of AMI recurrence in APS-AMI patients. (A) Recurrence in patients with revascularization and without. HR = 4.041, CI = 1.087-15.021, p = 0.037. (B) Recurrence in patients with hydroxychloroquine and without. HR=0.106, CI=0.014-0.823, p=0.032.

Table 1.Baseline characteristics and follow-up information of APS patients with AMI

	APS-AMI N=36	APS-MICAD N=26	APS-MINOCA N=10	p
Female, n/%	16 (44.4)	10 (38.5)	6 (60.0)	0.285
AMI onset Age (y), mean±SD	41.09±15.65	42.19±15.83	38.24±15.6	0.754
Disease duration of APS (m) , mean±SD	31.34±56.08	33.72±60.57	25.14±44.49	0.605
AMI as initial (<3m), n/%	20 (55.6)	13 (50)	7 (70)	0.456
Secondary APS, n/%	13 (36.1)	6 (23.1)	7 (70.0)	**0.018**
Traditional CVD risk factor				
Obesity, n/%	7 (19.4)	5 (19.2)	2 (20.0)	1.000
Smoking, n/%	17 (47.2)	13 (50)	4 (40)	0.717
Hypertension, n/%	12 (33.3)	11 (42.3)	1 (10)	0.115
Diabetes, n/%	2 (5.6)	2 (7.7)	0 (0)	1.000
Hyperlipidemia, n/%	11 (30.6)	10 (38.5)	1 (10)	0.127
Previous ASCVD, n/%	13 (36.1)	13 (50)	0 (0)	**0.006**
APS diagnosis				
Venous thrombosis, n/%	17 (47.2)	12 (46.2)	5 (50)	1.000
Arterial thrombosis, n/%	11 (30.6)	6 (23.1)	5 (50)	0.224
Pregnancy morbidity, n/%	2/16 (12.5)	1/10 (10.0)	1/6 (16.7)	0.464
LA, n/%	30 (83.3)	21 (80.8)	9 (90)	0.655
β2GP1-IgG/M, n/%	31 (86.1)	22 (84.6)	9 (90)	1.000
aCL-IgG/M, n/%	27 (75)	17 (65.4)	10 (100)	**0.039**
Triple positivity, n/%	21 (58.3)	13 (50.0)	8 (80.0)	0.142
AMI diagnosis				
STEMI, n/%	21 (58.3)	15 (57.7)	6 (60.0)	0.510
NSTEMI, n/%	12 (33.3)	8 (30.8)	4 (40.0)	
Treatment				
Glucocorticoid, n/%	15 (41.7)	7 (26.9)	8 (80.0)	**0.007**
Hydroxychloroquine, n/%	17 (47.2)	7 (26.9)	10 (100)	**0.000**
Immunosuppressant, n/%	15 (41.7)	7 (26.9)	8 (80.0)	**0.007**
Anticoagulation therapy, n/%	20 (55.6)	11 (42.3)	9 (90.0)	**0.022**
Antiplatelet therapy, n/%	33 (91.7)	25 (96.2)	8 (80.0)	0.181
Revascularization (PTCA/PCI), n/%	10 (27.8)	10 (47.6)	0 (0)	**0.002**
Prognosis				
Follow-up time (m) , mean±SD	42.25±47.75	46.45±51.04	31.31±38.01	0.577
AMI Recurrence, n/%	13 (36.1)	13 (50.0)	0 (0)	**0.006**
Event free time (m) , mean±SD	28.56±36.55	27.45±36.68	31.31±38.01	0.680

Conclusion: APS AMI patients can be divided into two subgroups with different clinical and prognostic characteristics. Hydroxychloroquine can prevent relapse, while revascularization therapy has a high risk for AMI recurrence.

Disclosure: J. Curtis: AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, CorEvitas, 2, 5, Eli Lilly and Company, 2, 5, Janssen, 2, 5, Myriad, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **K. Gavigan**: Global Healthy Living Foundation, 3; **W. Nowell**: AbbVie/Abbott, 2, 5, Amgen, 5, Janssen, 2, 5, Scipher Medicine, 5; **D. Curtis**: Global Healthy Living Foundation, 3; **D. Ali**: Global Healthy Living Foundation, 3; **X. Liu**: None; **K. Makaroff**: None; **C. Almario**: None; **C. Khalil**: None; **S. Choi**: None; **B. Spiegel**: Alnylum, 5, Amgen, 5, Ardelyx, 1, Ferring, 1, Ironwood, 1, 5, Takeda, 1, 5.

Abstract Number: 0103

Criteria and Non-criteria Antiphospholipid Autoantibodies Screening in Women with Unexplained Fetal Death, Pre-eclampsia And/or Fetal Growth Restriction: A Cross-sectional Study

Tiphaine Goulenok[1], Clothilde Gros[1], Arthur Mageau[2], Tiphaine Barral[1], Pascale Roland Nicaise[1], Marie Helene Saint Frison[1], Margot Bucau[1], Valerie Vivier[1], Valentine Marie Ferre[2], Agnes Bourgeois Moine[1], Thomas Papo[2] and Karim Sacre[2], [1]Assistance Publique Hopitaux de Paris, Paris, France, [2]Université Paris Cité, Paris, France

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Antiphospholipid syndrome (APS) is a cause of pregnancy morbidity. Late pregnancy morbidity occurs in up to 25% of pregnant women with APS and may be the presenting manifestation of the autoimmune disease. We recently showed that aPL testing was performed in only 20% patients who displayed late pregnancy morbidity consistent with obstetrical APS. We aimed to determine the frequency of criteria and non-criteria anti-phospholipid (aPL) autoantibodies in patients admitted for unexplained fetal death (UFD), pre-eclampsia (PE) and/or fetal growth restriction (FGR).

Methods: All consecutive patients with UFD, PE and/or FGR followed in the department of Obstetrics, Bichat Hospital, University of Paris, Paris, between January 2019 and December 2021 were screened. Only patients with available serum stored from the index pregnancy were included. Patients with previously known APS or twin pregnancy were excluded. Testing for aPL autoantibodies included anti-cardiolipin (aCL), anti-β2GPI (aβ2GPI), anti-phosphatidylethanolamine (aPE), anti-phosphatidylserine/prothrombin (aPS/PT) IgG/IgM and anti-annexin V IgG. When available, placenta specimens were analysed by a pathologist blinded to the aPL status. All clinical characteristics, pregnancy features, and comorbidities were extracted from electronic medical records.

Results: Overall 167 (32 (28.8-35.7) years) patients with UFD (n=28; 16.8%), PE (n=60; 35.9%) and/or FGR (n=105; 62.9%) were screened for aPL autoantibodies. Moderate titers of aPL autoantibodies were detected in 33 (n=33/167, 19.8%) patients. aPL autoantibodies were non-criteria aPE IgG/IgM in most cases (n=28/33, 84.8%). aPS/PT IgG/IgM were found in 11 (n=11/33, 33.3%) cases and aCL or aβ2GP1 IgG/IgM in 4 (n=4/33, 12.1%). Multivariable logistic regression model showed that aPL autoantibodies were mostly associated with UFD (OR 4.37 [1.72-11.20], p=0.002), PE ≤34th week of gestation (3.22 [0.86-11.90], p=0.070) and chronic deciduitis (8.03 [0.89-67.2], p= 0.060) (Tables 1 and 2).

Conclusion: The frequency of aPL autoantibodies, mostly aPE, is high in patients with late pregnancy morbidity and may qualify obstetrical APS

Table 1. Characteristics of patients according to aPL status Analysis was performed on variables collected in the 167 patients screened for aPL autoantibodies. aPL, antiphospholipid autoantibodies; IMIDs, immune-mediated inflammatory diseases; VTE, Venous Thromboembolic Event; BMI, body mass index; OR, odds ratio; CI, confidence interval. Age is expressed as median [1st quartile- 3rd quartile]. *univariable and **multivariable logistic regression analysis.

	aPL positive n=33	aPL negative n=134	OR * [95% CI]	p-value	OR ** [95% CI]	p-value
Age at pregnancy, years	33 [26.0-35.6]	32 [29.0-35.7]	0.96 [0.90-1.04]	0.320	0.96 [0.89-1.04]	0.330
Active smokers, n (%)	4 (12.1)	17 (12.7)	0.95 [0.3-3.04]	1.000	0.58 [0.13-1.98]	0.120
Alcohol consumption, n (%)	1 (3.0)	0 (0)	-	0.198		
Comorbidities, n (%)						
IMIDs	4 (12.1)	9 (6.7)	1.92 [0.55-6.67]	0.290		
High blood pressure	0 (0)	13 (9.7)	-	0.074		
Chronic kidney disease	1 (3.0)	6 (4.5)	0.67 [0.08-5.76]	1.000		
Diabetes	6 (18.2)	33 (24.6)	0.68 [0.26-1.79]	0.499		
BMI ≥25	18 (54.5)	58 (43.3)	1.57 [0.73-3.38]	0.329		
Previous VTE	1 (3.0)	6 (4.5)	0.67 [0.08-5.76]	1.000	0.76 [0.04-5.12]	0.810
Pregnancy history, n (%)						
Primigravida	17 (51.5)	63 (47.0)	1.2 [0.56-2.57]	0.697		
Previous pregnancy						
Unexplained fetal death	2 (6.1)	6 (4.5)	1.38 [0.27-7.17]	0.658		
Preeclampsia	2 (6.1)	11 (8.2)	0.72 [0.15-3.42]	1.000		
Fetal growth restriction	2 (6.1)	20 (14.9)	0.37 [0.08-1.67]	0.253		
Index pregnancy						
Unexplained fetal death	12 (36.4)	16 (11.9)	4.20 [1.74-10.2]	0.003	4.37 [1.72-11.20]	0.002
Preeclampsia	10 (30.3)	50 (37.3)	0.73 [0.32-1.66]	0.545		
≤34th week of gestation	6 (18.2)	12 (9.0)	2.26 [0.78-6.56]	0.205	3.22 [0.86-11.90]	0.070
Fetal growth restriction	15 (45.4)	90 (67.2)	0.41 [0.19-0.89]	0.027		
≤34th week of gestation	3 (9.1)	15 (11.2)	0.79 [0.21-2.91]	1.000	0.64 [0.11-2.68]	0.570

Table 2. Characteristics of placental lesions according to aPL antibodies screening Analysis was performed on variables collected in the 121 patients with available placenta specimens. Small placenta weight for age defined as <25e percentile; retroplacental hemorrhage included retroplacental hemorrhage or basal decidual hematoma; distal villous hypoplasia defined by hypoxic ischemic villi > 50 %; chronic villitis included low grade, high grade or para basal villitis; massive perivillous fibrin deposition defined by perivillous fibrinoids deposits > 25 % OR, odds ratio; confidence interval; aPL, antiphospholipid autoantibodies. Age is expressed as median [1st quartile- 3rd quartile]. *univariable and **multivariable logistic regression analysis.

	All n=121	aPL positive n=17	aPL negative n=104	OR* [95% CI]	p-value	OR** [95% CI]	p-value
Gestational weeks at delivery, median	37.5 [35.5-39]	37.1 [33.2-38.2]	37.5 [36.0-39.0]	1.02 [0.92-1.13]	0.667	1.03 [0.93-1.15]	0.56
Maternal vascular malperfusion, n (%)							
Decidual arteriopathy	19 (15.7)	2 (11.8)	17 (16.3)	0.68 [0.14-3.25]	1		
Infarcts	35 (28.9)	5 (29.4)	30 (28.9)	1.03 [0.33-3.18]	1		
Retroplacental hemorrhage	14 (11.6)	4 (23.5)	10 (9.6)	2.89 [0.79-10.57]	0.109		
Distal villous hypoplasia	13 (10.7)	3 (17.6)	10 (9.6)	2.01 [0.49-8.21]	0.391		
Fetal vascular malperfusion, n (%)							
Stem vessel obliteration	4 (3.3)	1 (5.9)	3 (2.9)	2.10 [0.21-21.45]	0.459		
Villous stromal-vascular karyorrhexis	2 (1.6)	0 (0.0)	2 (1.9)	0.00 [-]	1		
Intramural fibrin deposition	5 (4.1)	1 (5.9)	4 (3.8)	1.56 [0.16-14.86]	0.537		
Thrombosis	0 (0.0)	0 (0.0)	0 (0.0)	-	1		
Avascular Villi (>15)	22 (18.2)	3 (17.6)	19 (18.3)	0.96 [0.25-3.68]	1		
Inflammation, n (%)							
Chronic villitis	13 (10.7)	3 (17.65)	10 (9.6)	2.01 [0.49-8.21]	0.391		
Chronic intervillositis	5 (4.1)	0 (0.0)	5 (4.8)	0.00 [-]	1		
Chronic deciduitis	5 (4.1)	2 (11.8)	3 (2.9)	4.49 [0.69-29.12]	0.144	8.03 [0.89-67.2]	0.060
Chorioamnniotis	13 (10.7)	0 (0.0)	13 (12.5)	0.00 [-]	0.210		
Funisitis	9 (7.4)	0 (0.0)	9 (8.6)	0.00 [-]	0.357		
Others, n (%)							
Delayed villous maturation	7 (5.8)	0 (0.0)	7 (6.7)	0.00 [-]	0.591		
Massive perivillous fibrin deposition	7 (5.8)	0 (0.0)	7 (6.7)	0.00 [-]	0.591		
Chorangiosis	33 (27.3)	3 (17.6)	30 (28.8)	0.53 [0.14-1.98]	0.397		

Disclosure: T. Goulenok: None; **C. Gros**: None; **A. Mageau**: None; **T. Barral**: None; **P. Roland Nicaise**: None; **M. Saint Frison**: None; **M. Bucau**: None; **V. Vivier**: None; **V. Ferre**: AstraZeneca, 6, Gilead, 12, Congress accomodation, Moderna, 6; **A. Bourgeois Moine**: None; **T. Papo**: None; **K. Sacre**: None.

Abstract Number: 0104

Cluster Analysis of Antiphospholipid Antibodies Associated Adverse Pregnancy Outcome Patients: Based on a 13-year Longitudinal Cohort Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Antiphospholipid antibodies (aPLs) play a pivotal role in the etiology of adverse pregnancy outcomes (APOs). (1) Women with persistently aPLs positivity present heterogeneous clinical manifestations and APOs. We aimed to stratify aPLs positivity patients with APOs and assess the subsequent pregnancy outcomes.

Methods: This was a retrospective study of persistent aPLs positive women cohort in Peking Union Medical College Hospital. Baseline demographic characteristics, clinical manifestation, previous APOs and antibodies profiles were analyzed. Placentae from patients were collected and performed the histopathologic diagnoses during the follow up.

Results: Four clusters among 209 patients with 477 pregnancies were identified. Cluster 1 comprised patients with triple aPLs positivity and demonstrates a high incidence of gestational hypertension (34.92%, P = 0.008) and preterm delivery (20.63%, P = 0.021). Patients in cluster 2 were characterized by lupus anticoagulant (LA) positivity, with high risk of whole

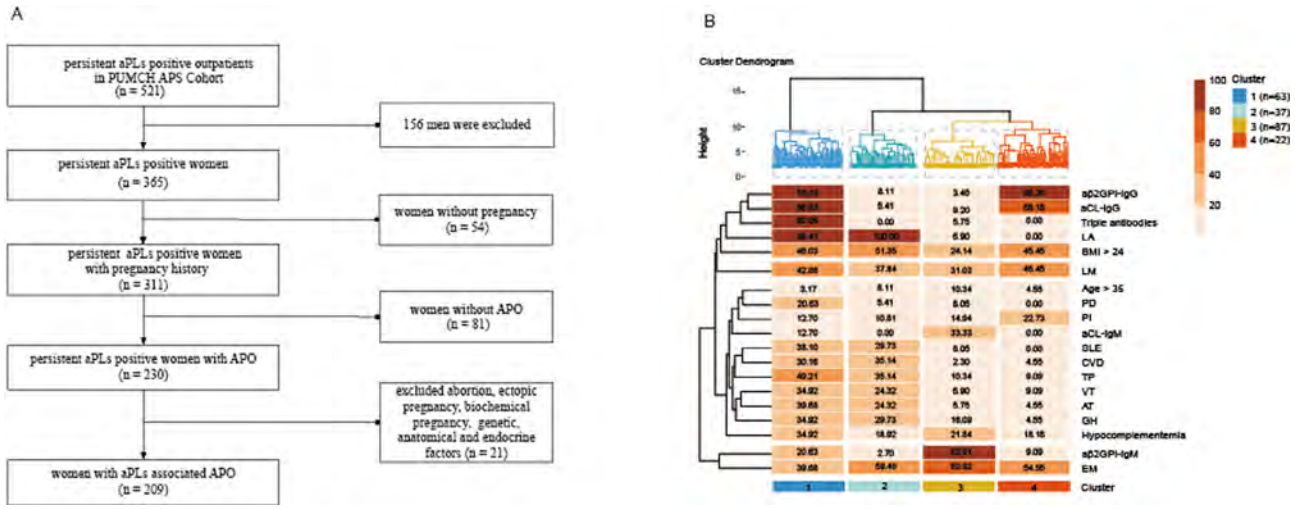

Figure 1. Study flowchart and cluster analysis; A. Study flowchart; B. Cluster analysis

gestational APOs. Cluster 3 included patients with isolated aPLs-IgM isotype combined with early miscarriage (60.92%, P = 0.01). Patients in cluster 4 majorly presented aPLs-IgG isotype combined with placenta insufficiency (22.73%, P = 0.016). During the follow up, the live birth rate in cluster 1 and 2 was only 69.20%. Gestational hypertension was much higher in cluster 1 (15.4%, P = 0.05). Placenta pathology revealed that the patient in cluster 1 exhibited a conspicuous reduction in the number of capillaries present within the placental villi, coupled with hypoplastic chorionic capillaries. The representative placental pathology of the cluster 3 likewise showed a reduced number of stem villi capillaries and slight swelling and degeneration of the endothelium in the stem villi vessels. Placenta in cluster 4 had mildest placental lesions.

Conclusion: In conclusion, our study identified four clusters of patients with aPLs-associated APO. There exists a correlation between specific aPLs isotypes and the occurrence of adverse pregnancy events at different stages of gestation. Triple aPLs positivity is associated with gestational hypertension and preterm delivery. LA positivity is a significant risk factor for the whole gestational APOs. While patients with isolated aPLs-IgM isotype are more likely to have early miscarriage. Patients in cluster 4 majorly present aPLs-IgG isotype combined with placenta insufficiency. The four identified clusters based on

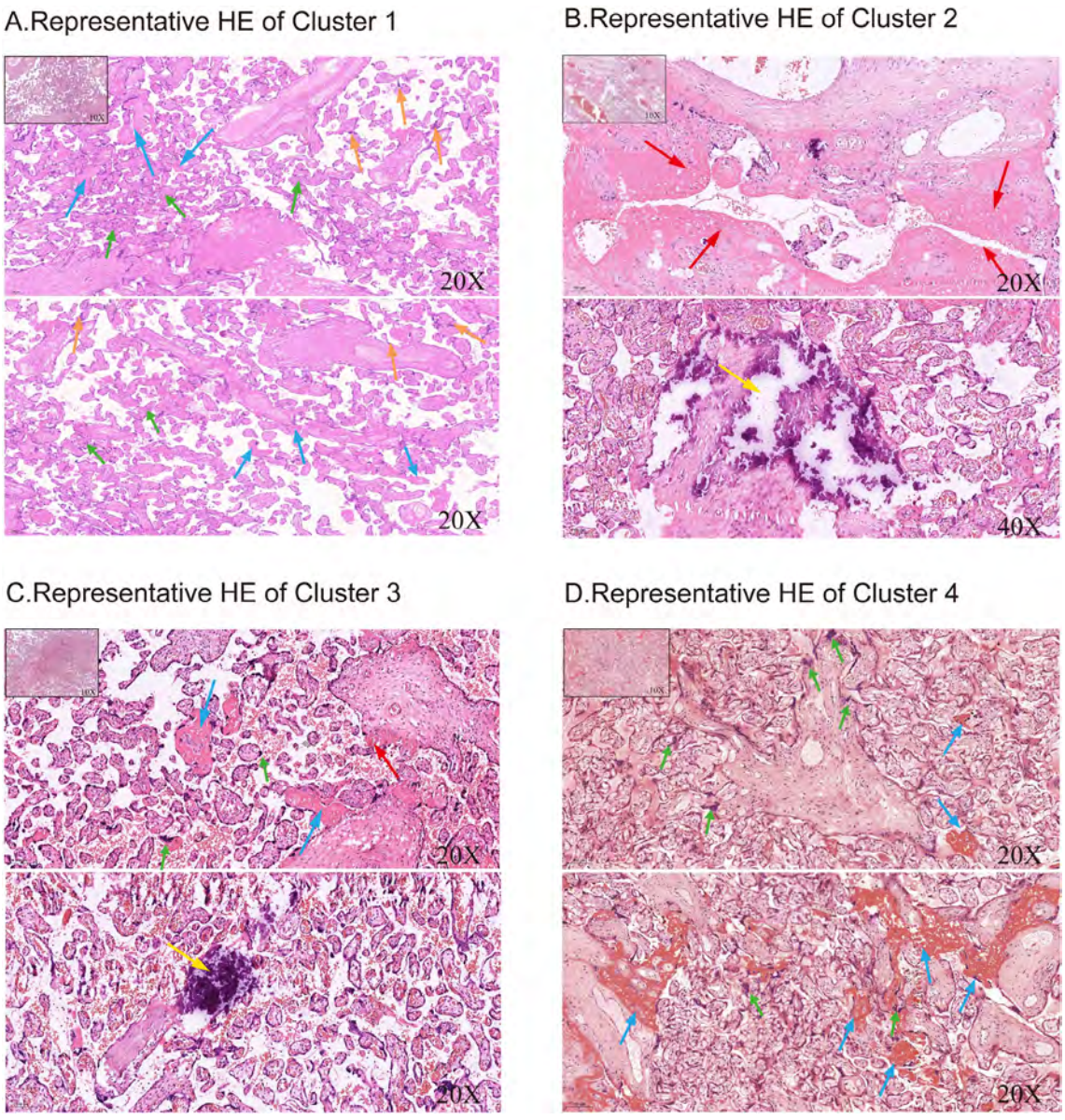

Figure 2. Representative placentae HE of four clusters.

Table 1. Comparison of baseline pregnancy outcomes and antibodies between four clusters

	Cluster 1 *vs* 2 (P value)	Cluster 1 *vs* 3 (P value)	Cluster 1 *vs* 4 (P value)	Cluster 2 *vs* 3 (P value)	Cluster 2 *vs* 4 (P value)	Cluster 3 *vs* 4 (P value)
EM	0.056	**0.010**	0.226	0.879	0.712	0.586
LM	0.622	0.137	0.832	0.461	0.565	0.202
GH	0.594	**0.008**	**0.006**	0.083	**0.020**	0.16
PD	**0.039**	**0.025**	**0.021**	0.604	0.267	0.169
PI	0.207	**0.028**	**0.016**	0.541	0.272	0.356
LA	1	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**	0.345
aCL-IgM	**0.025**	**0.004**	0.105	**< 0.001**	/	**0.002**
aCL-IgG	**< 0.001**	**< 0.001**	**0.001**	0.722	**< 0.001**	**< 0.001**
β2GPI-IgM	**0.013**	**< 0.001**	0.334	**< 0.001**	0.549	**< 0.001**
β2GPI-IgG	**< 0.001**	**< 0.001**	0.714	0.362	**< 0.001**	**< 0.001**

Table 2. Newly pregnancy outcomes in four clusters

	Cluster 1 (n=26)	Cluster 2 (n=13)	Cluster 3 (n=27)	Cluster 4 (n=8)	P1	P2	P3	P4	P5	P6
Age of new pregnancy	32.46±3.54	34.91±2.77	34.33±3.81	33.00±3.71	0.1	0.08	0.71	0.66	0.21	0.4
Live birth	18(69.20%)	9(69.20%)	22(81.50%)	8(100.00%)	1	0.35	0.15	0.44	0.13	0.32
EM	5(19.20%)	3(23.10%)	5(18.50%)	0	1	1	0.31	1	0.26	0.32
LM	1 (3.80%)	1(7.70%)	0	0	1	0.49	1	0.33	1	/
GH	4 (15.40%)	0	0	0	0.3	**0.05**	0.55	/	/	/
PD	4(15.40%)	3(23.10%)	2(7.40%)	0	0.7	0.42	0.55	0.31	0.26	1
PD < 34ws	1(3.80%)	1(7.70%)	1(3.70%)	0	1	1	1	1	1	1
LDA	22(84.60%)	10(76.90%)	26(96.30%)	8(100.00%)	0.7	0.19	0.55	0.09	0.26	1
LWMH	16(61.50%)	6(46.20%)	16(59.30%)	5(62.50%)	0.5	1	1	0.51	0.66	1
HCQ	25(96.20%)	10(76.90%)	23(85.20%)	6(75.00%)	0.1	0.35	0.13	0.66	1	0.6
Pred	10(38.50%)	6(46.20%)	5(18.50%)	1(12.50%)	0.7	0.14	0.23	0.13	0.17	1

Table 3. Comparison of pregnancy outcomes before and after enrollment

	Total pregnancy outcome	Pre-entry pregnancy outcomes	New-onset pregnancy outcomes	P value
Total	477	403	74	
Live birth	128 (26.83%)	71 (17.60%)	57 (77.00%)	**<0.0001**
Fetal Death	349 (73.17%)	332 (82.40%)	17 (23.00%)	**<0.0001**
Early miscarriages	184 (38.57%)	171 (42.40%)	13(17.60%)	**<0.0001**
Late miscarriages	131 (27.46%)	129 (32.00%)	2 (2.70%)	**<0.0001**
Preterm delivery	42 (8.81%)	30 (7.40%)	12 (16.20%)	**0.02**
Severe/mild preterm delivery 32w≤-<37w	25 (5.24%)	16 (4.00%)	9(12.20%)	**0.01**
Early preterm delivery 28w≤-< 32w	13 (2.73%)	11 (2.70%)	2 (2.70%)	1
Extremely preterm delivery <28w	4 (0.84%)	3 (0.70%)	1 (1.40%)	0.49
Still birth	7 (1.47%)	7 (1.70%)	0 (0)	0.6
Placental abruption	7 (1.47%)	6 (1.50%)	1 (1.40%)	1
PROM	13 (2.73%)	5 (1.20%)	8 (10.80%)	**<0.0001**
Oligoamnios	13 (2.73%)	7 (1.70%)	6 (8.10%)	**0.01**
FGR	10 (2.10%)	7 (1.70%)	3 (4.10%)	0.37
GH total	62 (13.00%)	59 (14.60%)	3 (4.10%)	**0.01**
Only hypertension	35 (7.34%)	34 (8.40%)	1 (1.40%)	**0.04**
PE/Eclampsia	27 (5.66%)	25 (6.20%)	2 (2.70%)	0.41
HELLP	5 (1.05%)	4 (1.00%)	1 (1.40%)	0.57
HELLP < 34w	4 (0.84%)	3 (0.70%)	1 (1.40%)	0.49
HELLP > 34w	1 (0.21%)	1 (0.20%)	0 (0)	1

Abbreviation: P1: P value of Cluster 1 *vs* Cluster 2; P2: P value of Cluster 1 *vs* Cluster 3; P3: P value of Cluster 1 *vs* Cluster 4; P4: P value of Cluster 2 *vs* Cluster 3; P5: P value of Cluster 2 *vs* Cluster 4; P6: P value of Cluster 3 *vs* Cluster 4; EM Early miscarriage; LM Late miscarriage; GH Gestational hypertension; PD preterm delivery; LDA Low dose aspirin; LWMH Low weight molecule heparin; HCQ Hydroxychloroquine; Pred prednisone; PROM premature rupture of membranes; FGR fetal growth restriction; GH gestational hypertension; HELLP hemolytic anemia elevated liver function and low platelet count syndrome

clinical and laboratory features showed distinct differences in pregnancy outcomes and placental damage. These findings suggest that an individualized risk stratification approach to the management of persistent aPLs positive women may improve pregnancy outcomes, taking into consideration the clinical phenotype and placental pathology.

1. Branch DW, Silver RM, Blackwell JL, et al. Outcome of treated pregnancies in women with antiphospholipid syndrome: an update of the Utah experience. Obstetrics and gynecology. 1992;80(4):614-20

Disclosure: Y. Long: None; **J. zhao**: None; **M. Li**: None; **X. Tian**: None; **x. Zeng**: None.

Abstract Number: 0105

Characterization of B-Cell Subsets in Antiphospholipid Syndrome Patients: Implications for Disease Phenotype and Pathogenesis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Primary antiphospholipid syndrome (PAPS) is an autoimmune disorder characterized by the presence of pathogenic autoantibodies. The key immune cell subsets change in PAPS patients remains unclear.

Methods: We enrolled 35 primary APS (PAPS) patients fulfilling the 2006 Sydney criteria, five antiphospholipid antibody (aPLs) carriers, and 10 healthy controls (age-, gender-matched). Peripheral blood mononuclear cells (PBMCs) were analyzed using Mass Cytometry (CyTOF) with 42 markers to identify immune cell subsets. Plasma cytokine profiling of 55 PAPS patients was performed using the procartaPlex 65 panel assay. Peripheral B cells from PAPS patients and healthy individuals were isolated for RNA sequencing (RNAseq). Flow cytometry and RT-qPCR were used to validation. FlowJo and R software packages were utilized for CyTOF data analysis.

Results: Our study investigated that APS patients had a significant difference in peripheral blood subtype distribution . Using CD19 as a baseline for dimensionality reduction clustering, we identified 20 subgroups of B cells (Figure 1). Naïve B cells, characterized by IgD+CD27-CD38+CD24+, were the predominant B cell subset in APS patients (C14, 21.04%), while plasmablasts accounted for 1.55%. C01 and C02 subpopulations within B cells were significantly increased in the peripheral circulation of patients (C01: 1.89±1.68 vs 0.58±0.41, P=0.02; C02: 2.16±1.78 vs 0.71±0.67, P=0.015; Figure 2). Both were characterized as IgD-CD27- double negative B cells, with C01 expressing high levels of CD11c and Tbet, which are a subset of age-associated B cells (ABC). In APS patients, C01 cells showed a positive correlation with ESR. C02 showed a positive association with β2GPI IgG expression in patients without extra-criteria organ involvement. We further validated these findings by expanding the sample size and analyzing an additional 23 APS patients using flow cytometry (Figure 3A). The results demonstrated a significant increase in DN B cells in APS patients, along with a marked increase in the CD11cTbet signaling intensity of DN B cells (Figure 2). This suggests that DN cells, especially ABC cells, may be involved in the sustained production of high levels of aPLs in APS patients. Interestingly, we found that the C19 (IgD-CD27++CD38+++CD24-) plasmablasts showed a negative correlation with the production of IgG subtype antibodies in OAPS patients, which contrasts with TAPS patients. This suggests that different mechanisms may be involved in B cell participation in APS with different phenotypes.

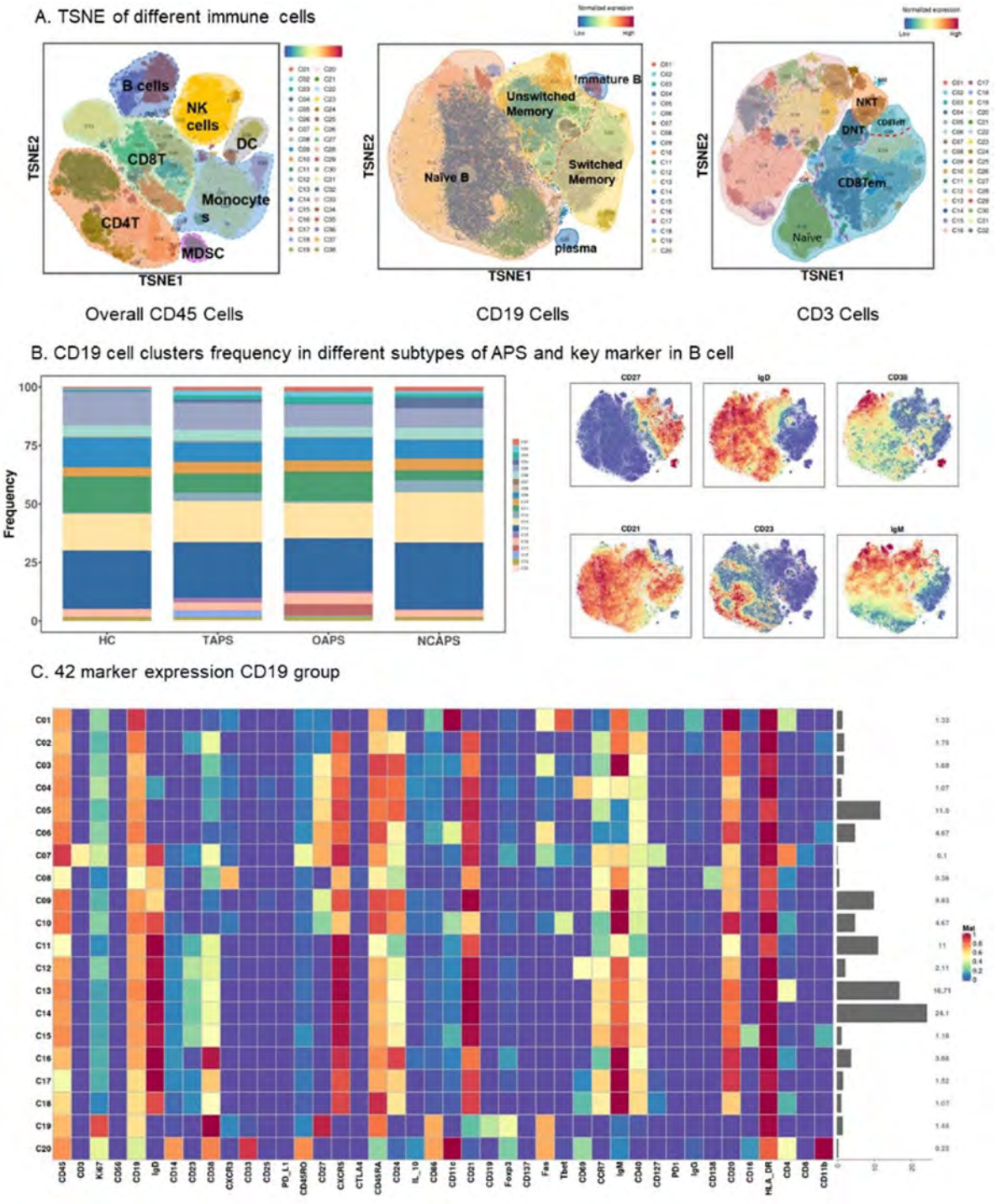
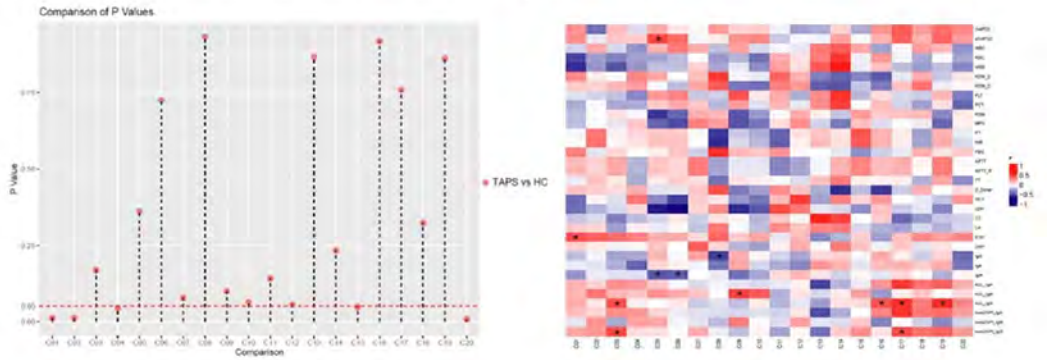


Figure 1. Distribution of peripheral blood immune cells and expression of key markers in patients with APS.

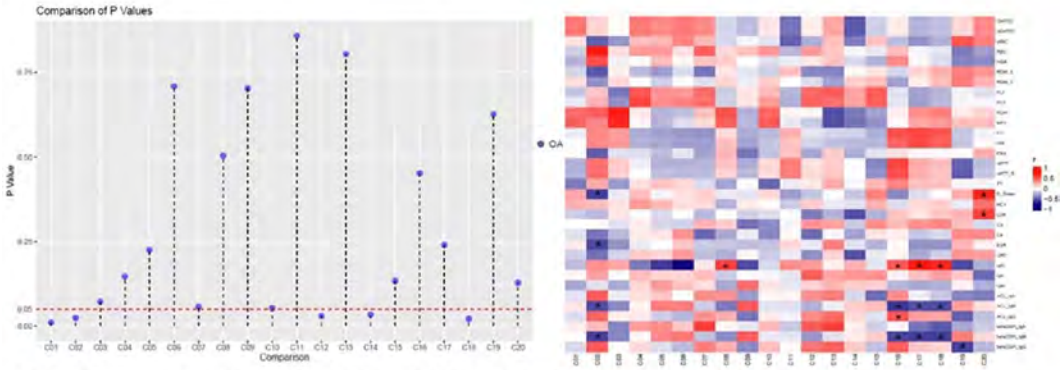
Based on the results of plasma cytokine analysis, we observed elevated expression of BLC/CXCL13 and BAFF in the plasma of APS patients. We then identified upregulation of TNFRSF13B, a gene associated with the Transmembrane activator and CAML interactor (TACI) protein by RNAseq. Furthermore, GSEA analysis revealed activation of the MAPK and NF-κB pathways within B cells (Figure 3B).

Figure 2. CD19 cell types and clinical characteristics

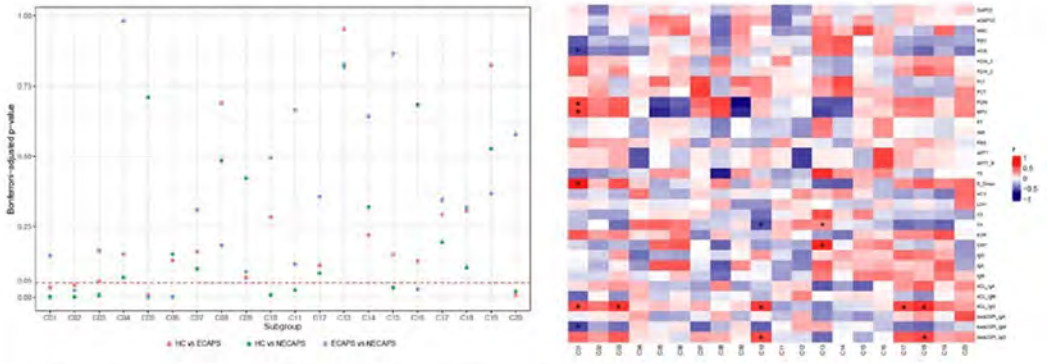
A. B-cell subtype differences and clinical correlation in TAPS patients



B. B-cell subtype differences and clinical correlation in OAPS patients



C. B-cell subtype differences and clinical correlation in extra-criteria manifestation APS patients



D. Different expression of plasma cytokines in patients APS patients

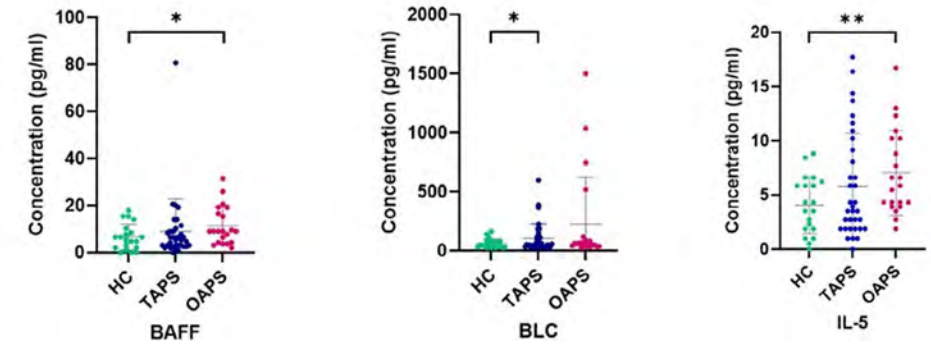
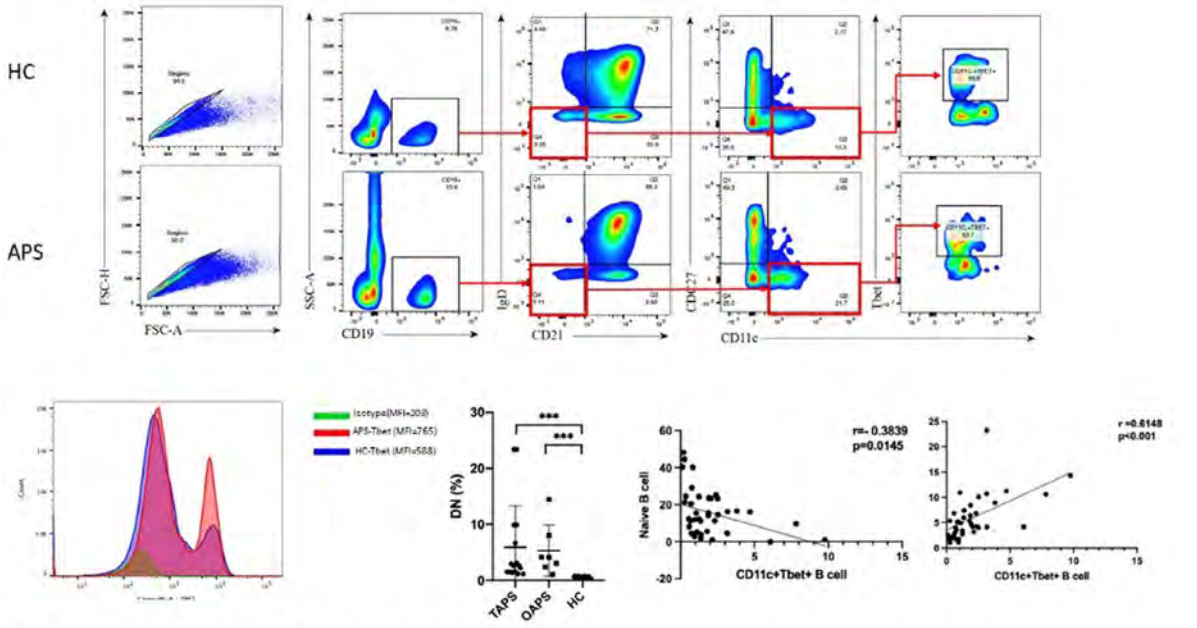


Figure 2.. CD19 cell types and clinical characteristics

Figure 3. Validation and GSEA analysis

A. Gating strategy of CD11c⁺ Tbet+ in peripheral blood of APS patients and healthy donors



B. B cell RNAseq and GSEA analysis APS patients

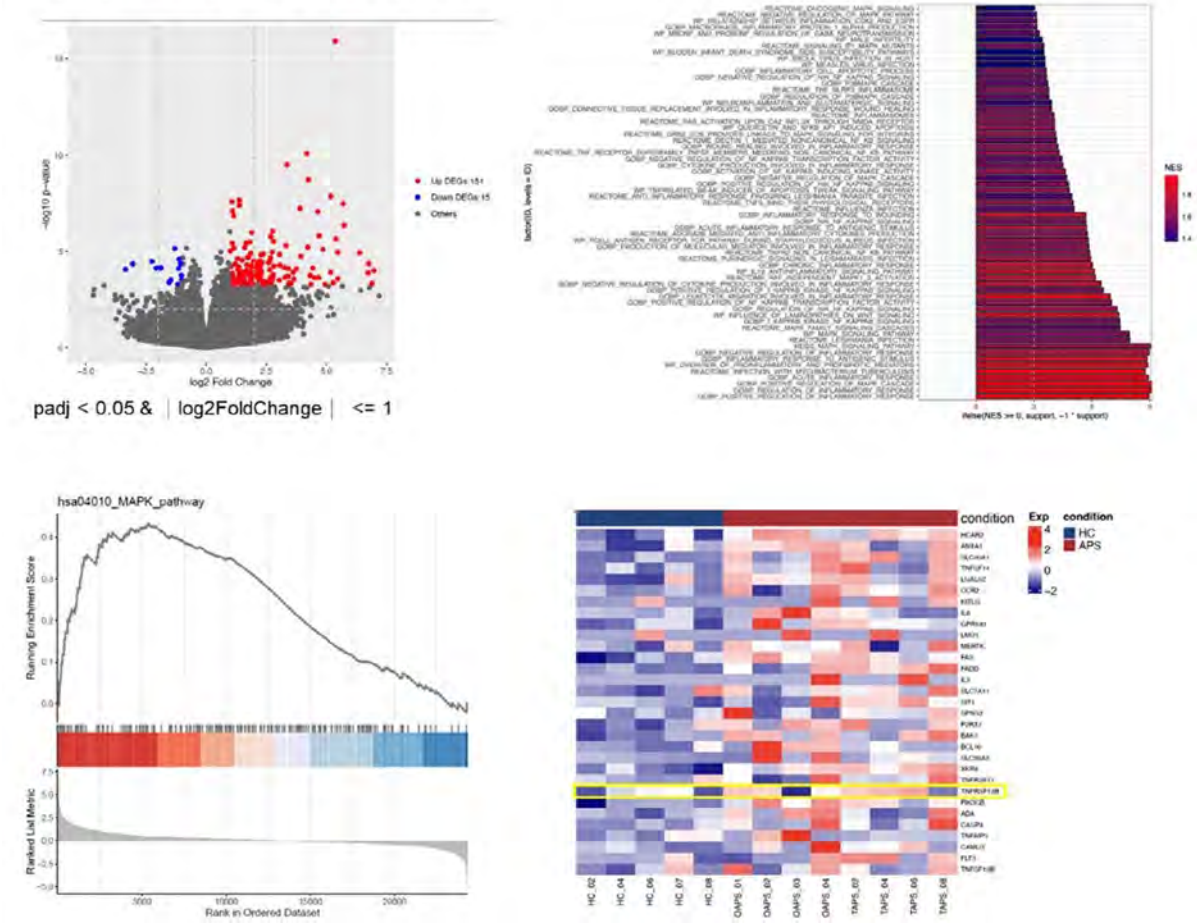


Figure 3. Validation and GSEA analysis.

Conclusion: Double-negative B cells are significantly higher in APS patients, where ABC cells may play a role in aPLs production. The aberrant differentiation and maturation of B cells in APS patients may be triggered by TACI downstream cascade.

Disclosure: Y. Long: None; **J. zhao**: None; **M. Li**: None; **X. Zeng**: None.

Abstract Number: 0106

Positive Antiphospholipid Antibodies Are Associated with a Higher Risk of Cerebral Microbleeds

Junna Ye[1], Yijun You[2], Zhuochao Zhou[2], Fan wang[2], Jingyi Wu[2] and Chengde Yang[2], [1]Ruijin Hospital affiliated to Shanghai Jiaotong University School of Medicine, Shanghai, China, [2]Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Persistent presence of antiphospholipid antibodies (aPLs) are important thrombosis-related laboratory parameters, as well as an indication of anticoagulation use which usually cause higher bleeding risk. Cerebral microbleeds (CMBs) are strongly associated with both bleeding propensity and ischemic events. Till now, the correlation between aPLs and CMBs remained unclear.

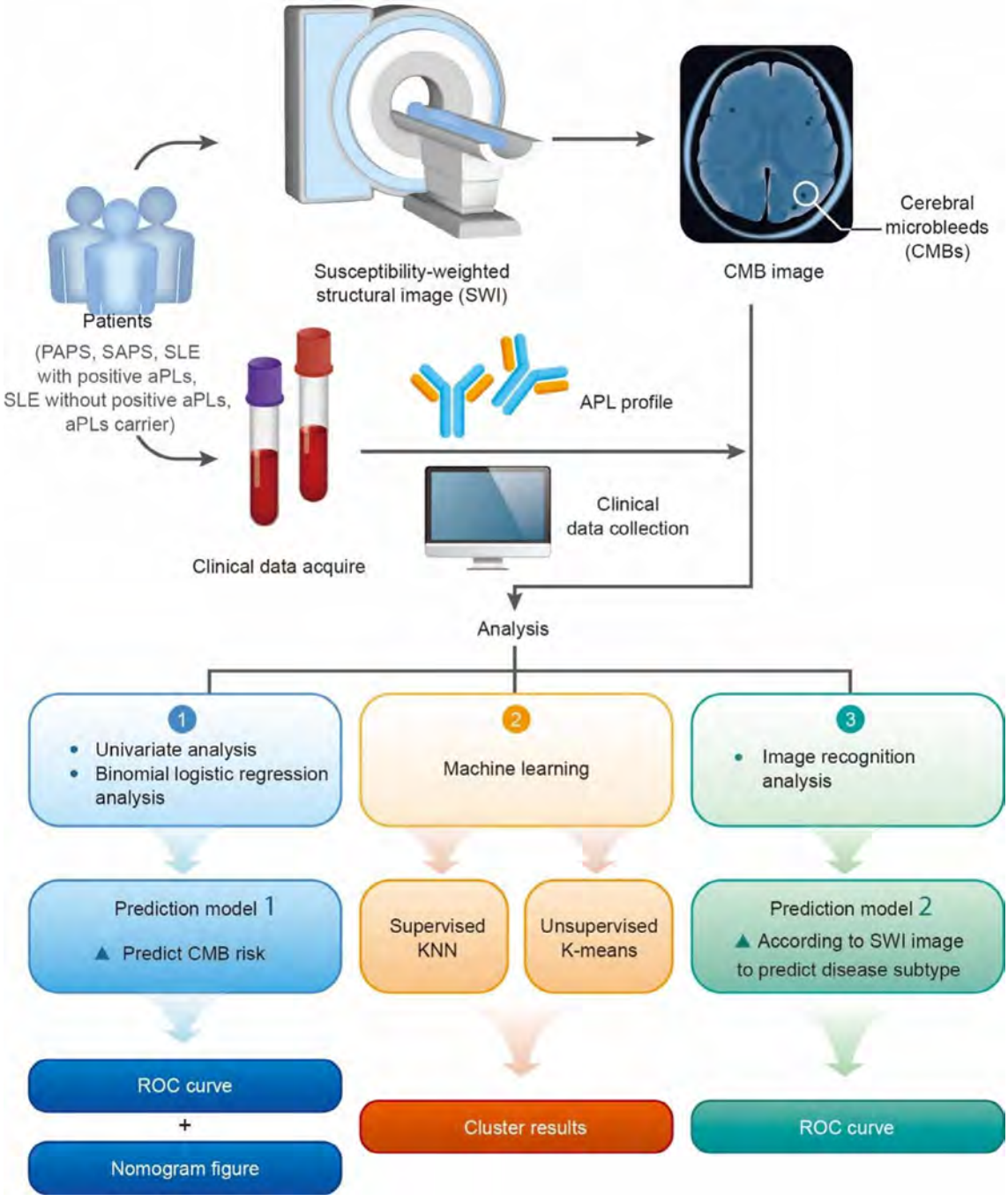
Methods: 31 primary antiphospholipid syndrome (APS), 50 secondary APS, 19 systemic lupus erythematosus (SLE) with positive aPLs, 44 SLE without positive aPLs and 16 aPLs carriers were enrolled from 2018 to 2021 in the Department of Rheumatology and Immunology in Ruijin Hospital. Clinical data, aPLs profile and susceptibility-weighted imaging(SWI) data were collected. Statistical analysis, machine learning, and image recognition analysis were performed from September 2022 to December 2022. Univariate and binomial logistic regression (prediction model 1) analysis was performed to investigate the risk factors of CMBs. Differences in CMBs between those with or without aPLs were analyzed by machine learning (supervised K-Nearest Neighbor (KNN) classification and unsupervised K-means clustering analysis) in SLE patients. Then, an image recognition analysis (prediction model 2) was conducted to build a model to predict the disease subtypes. Receiver operating characteristic (ROC) curve and nomogram representation of the binomial logistic regression analysis for CMBs risk and ROC curve of the image recognition analysis were set up. The area under the curve (AUC) was calculated to reflect the model performance. The results of machine learning were visualized by dimension reduction.

Results: Anti-cardiolipin antibody (aCL) IgG, lupus anticoagulant (LA), and apL-positive number showed a significant difference in the univariate analysis. In prediction model 1 (AUC=0.86), LA played an important role ($p< 0.05$, OR(95%CI): 1.31–13.24). The results of machine learning illustrated that SLE patients with positive aPLs had more CMBs numbers, more CMBs sites, and the possibility of infratentorial region hemorrhage. In addition, prediction model 2 (AUC=0.81) possessed good accuracy to predict the disease subtypes.

Conclusion: APLs were closely related to CMBs, of which LA played the most important role. It could be considered to screen CMBs by SWI in aPLs-positive patients.

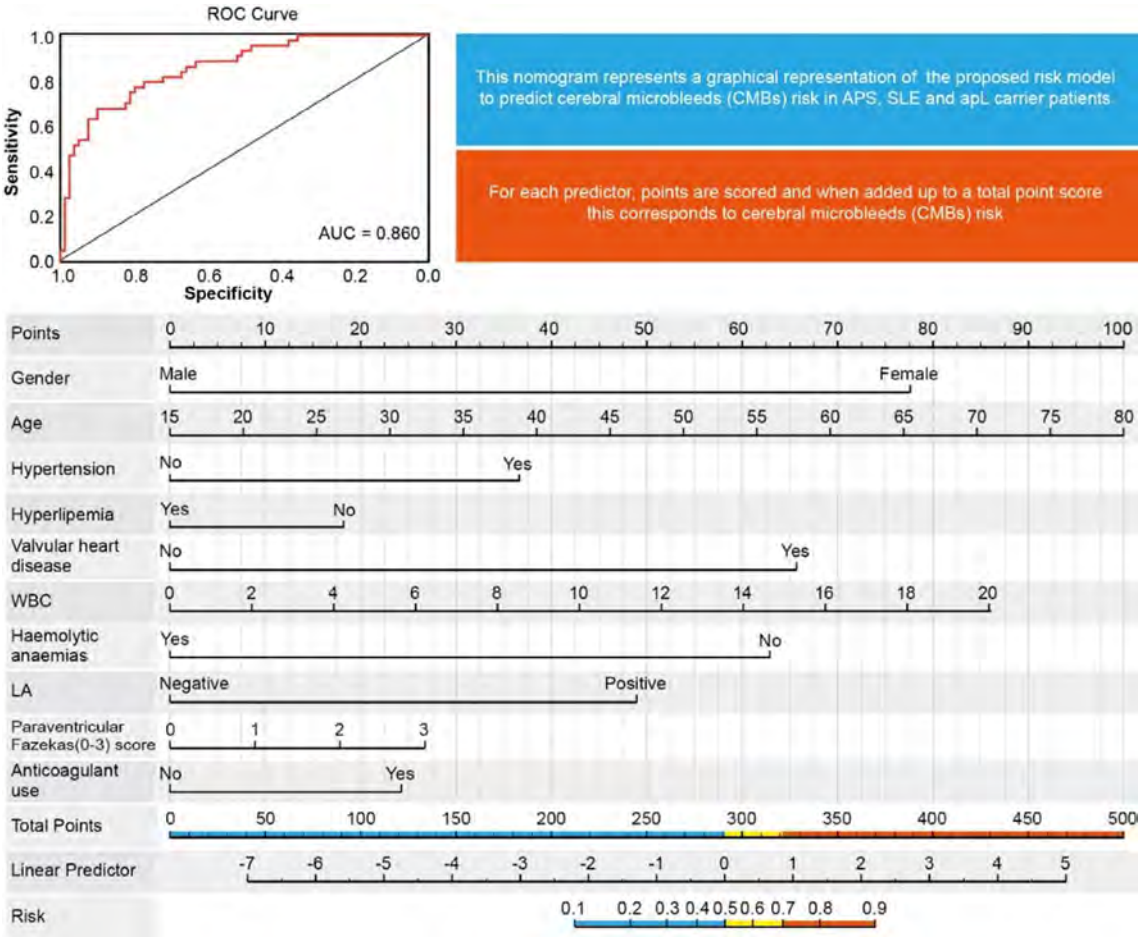
Workflow and analytical plans of this study. First, the study subjects were divided into CMBs group and no-CMBs group. A univariate analysis was conducted to identify the different variables between the two groups. Further binomial logistic regression analysis was performed to explore the risk factors correlated with CMBs, and prediction model 1 was built to predict the probability of CMBs occurrence based on the risk factors. Second, we investigated the correlation between aPLs and CMBs in SLE patients using machine learning. Finally, image recognition analysis was conducted to build prediction model 2 to predict the disease type by algorithm-based integration of the location and number of CMBs.

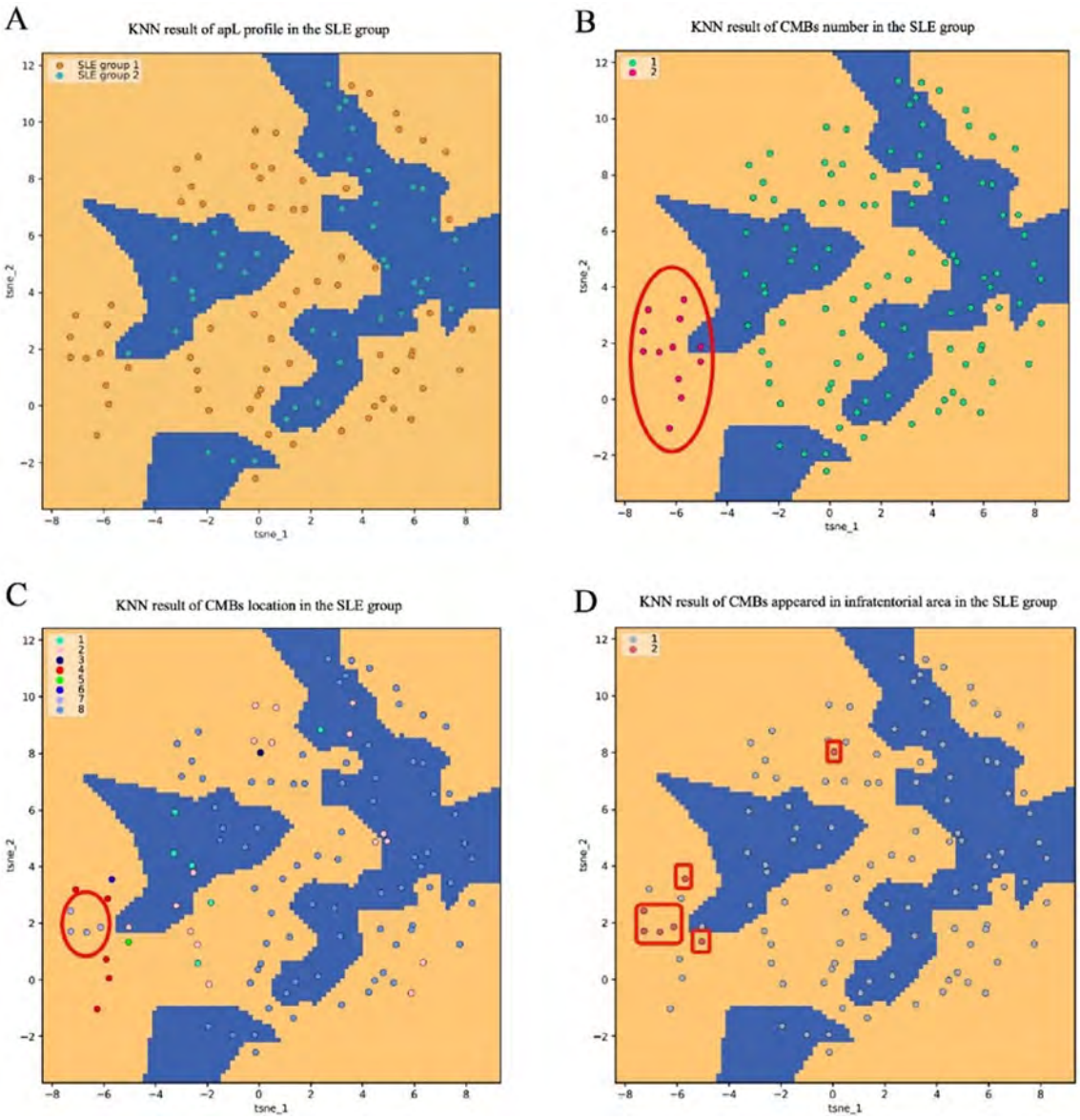
ROC curve and nomogram representation of the binomial logistic regression analysis for CMBs risk. In the ROC curve, the X-axis presents the specificity, and the Y-axis presents the sensitivity. The area under the curve (AUC) was 0.86. In the nomogram figure, for each predictor, points are scored and then added up to a total point score, which indicated to CMBs



risk. Abbreviations: CMBs: Cerebral microbleeds; ROC: Receiver operating characteristic curve; AUC: Area under the curve; LA: Lupus anticoagulant.

Results of KNN (K-Nearest Neighbor) classification analysis in all the SLE patients. (A) showed that SLE patients were divided into SLE group 1 (including SAPS and SLE patients with positive aPLs) and SLE group 2 (SLE patients without aPLs). Orange dots represented SLE group 1, orange area represents the positive aPLs area, blue dots represented SLE group 2, blue area represents the negative aPLs area. (B) showed the corresponding loci classified according to total CMBs (CMBs total level count from three locations) label. Red dots represented CMBs total number>=2; green dots represented CMBs total number<2. Orange area represents the positive aPLs area, blue area represents the negative aPLs area. Next, the corresponding loci was classified according to the bleeding site of the CMBs. Next, the corresponding loci was classified according to the bleeding site of the CMBs (C). Classification labels: 1=deep area, 2=brain lobes, 3=infratentorial region, 4=both deep area and brain lobes, 5=both deep area and infratentorial region, 6=both brain lobes and infratentorial region, 7=triple places, 8=none of these places. Orange area represented the positive aPLs area; blue area represented the negative aPLs area. (D) demonstrated a separate assessment of the infratentorial region. Orange area represented the positive apLs area; blue area represented the negative apLs area; pink dots represented the patient with CMBs appearing in the infratentorial region; grey dots represented the patient without CMBs appearing in the infratentorial region. Abbreviations: KNN: K-Nearest Neighbor; SLE: Systemic lupus erythematosus; aPLs: Antiphospholipid antibodies: SAPS: Secondary antiphospholipid syndrome; CMBs: Cerebral microbleeds.





Disclosure: J. Ye: None; **Y. You**: None; **Z. Zhou**: None; **F. wang**: None; **J. Wu**: None; **C. Yang**: None.

Abstract Number: 0107

Impact of Antiphospholipid Syndrome on Mortality of Hospitalized Ischemic Stroke Patients: A Retrospective Analysis of the National Inpatient Sample Database 2020

Sami Rabah, Lincoln Medical Center, New York, NY

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Antiphospholipid syndrome (APS) is recognized for its association with an elevated risk of ischemic strokes and other thromboembolic events. This study aims to compare the epidemiology and hospitalization outcomes of ischemic stroke patients with and without a secondary diagnosis of APS using a nationwide inpatient database.

Methods: Patients who were 18 or older, and were hospitalized between January 1, 2020, and

December 31, 2020, with a primary diagnosis of ischemic stroke with and without a secondary diagnosis of antiphospholipid syndrome (APS), were identified from the National Inpatient Sample (NIS) database using the International Classification of Diseases, Tenth Revision (ICD-10) codes. The NIS is the largest publicly available all-payer inpatient care database in the United States. The primary outcome was inpatient mortality, and the secondary outcomes were the length of stay (LOS) and the total hospital charge. The odds ratio was calculated using logistic multivariate regression analysis to adjust for age, race, gender, Charlson comorbidity index, and several high-risk comorbidities.

Results: Out of 503,344 patients admitted with a primary diagnosis of ischemic stroke, 1090 (0.21%) had APS. Ischemic stroke patients with APS were younger (54.3 vs 69.7; p=0.000), had more females (67.8% vs 49%; p=0.000), and had a higher prevalence of prior history of pulmonary embolism (14.22% vs 1.8%; p=0.000), and venous thrombosis (24.31% vs 3%; p=0.000) compared to stroke patients without APS. The APS group had a lower prevalence of diabetes (22.4% vs 39.8%; p=0.000), hypertension (45.8% vs 55.5%; p=0.004), and hyperlipidemia (43.58% vs 54.16 %; p=0.002) compared to Ischemic stroke patients without APS. Other differences in demographic and comorbidity trends were insignificant between both groups.

Table 1: Demographics And Comorbidities Of Ischemic Stroke Patients With And Without Antiphospholipid Syndrome (APS)

	Ischemic Stroke (n=503,344)		
	Without APS (n= 502,254)	With APS (n=1090)	P-value
Mean age (years)	69.7	54.3	0.000
Female	49%	67.80%	0.000
Race			0.051
White	65.60%	58.70%	0.039
Black	17.50%	21%	0.196
Hispanic	8%	13.30%	0.003
Asian	3%	2.20%	0.509
Charleson comorbidity index			0.212
1	13.40%	16.90%	
2	13.50%	13.30%	
≥3	73%	69.70%	
Hypertension	55.50%	45.80%	0.004
Diabetes	39.80%	22.40%	0.000
Hyperlipidemia	54.16%	43.58%	0.002
History of ischemic stroke	15.61%	19.27%	0.164
History of Venous Thrombosis	3%	24.31%	0.000
History of Pulmonary Embolism	1.80%	14.22%	0.000
COVID-19 infection	14.90%	18.30%	0.677
Chronic Kidney Disease	19.39%	22.40%	0.248
Congestive Heart Failure	17.60%	16.50%	0.658
Obesity	15.60%	17.43%	0.459
Atrial Fibrillation/Flutter	11.10%	4.60%	0.358
Smoking	23%	22.40%	0.844

Table 2: Primary and Secondary Hospitalization Outcomes of Ischemic Stroke Patients With and Without Antiphospholipid Syndrome (APS)

	Ischemic Stroke (n=503,344)			
	Without APS (n= 502,254)	With APS (n=1090)	Adjusted odds ratio	P-value
	%	%	(95% Confidence Interval)	
Primary Outcomes				
Inpatient Mortality	3.9%	8.7%	3.19 (1.91- 5.34)	0.000
Secondary outcomes				
			Adjusted mean difference	
Mean Length of Stay, Days	5.13	7.9	2.59 (1.07-4.12)	0.001
Total charge, Mean $	77,192	121,662	40,271 (14,284-66,258)	0.002

Demographics and prevalence of comorbidities are summarized in Table 1.

Ischemic stroke hospitalizations with APS were significantly associated with higher inpatient mortality (adjusted odds ratio [AOR] 3.19; 95% Confidence Interval [CI] 1.91- 5.34; p=0.000),

longer mean length of stay (2.59 more days; CI 1.05-4.12; p=0.001), and higher total hospital charges ($121,662 vs $77,192; CI $14,284-$66,258; p=0.002) compared to ischemic stroke patients without APS.

Primary and secondary hospitalization outcomes are summarized in Table 2.

Conclusion: Patients hospitalized with ischemic stroke and APS had higher inpatient mortality rates, longer hospital stays, and incurred greater hospital charges compared to ischemic stroke patients without APS.

Disclosure: S. Rabah: None.

Abstract Number: 0108

Decoding Antiphospholipid Syndrome Laboratory Test Outcomes in a Large Multicenter Electronic Health Record Database

Emily Balczewski, Wenying Liang, Amala Ambati, Yu Zuo, Karandeep Singh and Jason Knight, University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Electronic health record (EHR) data provide an inexpensive, information-rich tool to study rare diseases like antiphospholipid syndrome (APS). Many such studies rely on structured EHR data, e.g., diagnostic codes, laboratory testing, medication information. As a first step toward assessing the feasibility of using structured EHR data to study APS, we evaluated the presence and positivity of APS antibody testing in a diverse, US-based cohort using the All of Us Research Network Database (AOU).

Methods: Possible APS patients were identified by the presence of SNOMED-CT codes: 26843008 (Antiphospholipid syndrome) and 19267009 (Lupus anticoagulant disorder). Among possible APS patients, APS laboratory tests – anticardiolipin (aCL), anti-beta-2 glycoprotein I (aβ2GPI), and lupus anticoagulant (LA; confirmatory tests only) – were identified with a hand-curated list of LOINC and SNOMED-CT codes. Tests were identified as positive if they had a) a text result indicating positivity (e.g. positive, high, abnormal), b) a numeric result exceeding the normal reported range for that test, or c) a numeric result exceeding 40 if the test lacked a range, but included units of GPL, MPL, SGU, or SMU; negative tests were identified analogously. Tests without text or numeric results, ranges, or units, or tests with units other than those referenced above were classified as indeterminate. T-tests were two-sided with Bonferroni correction.

Results: Out of 372,082 total AOU patients, 883 (2.4 in 1,000) were identified as possible APS patients with demographic characteristics of 74% female, 55% White, and 17% Black, and a mean age of 55. Despite having testing information on 613 (70%) patients, only 434 (49%) had enough data to classify a test as positive or negative. Of these, 245 (28%) had

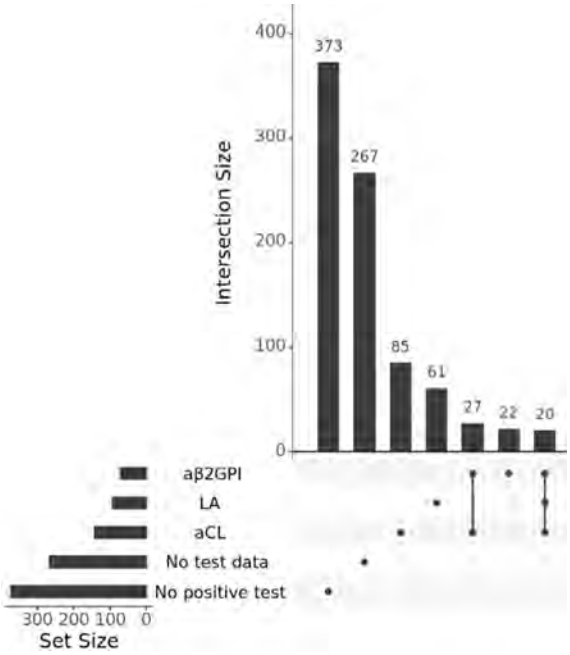


Figure 1. Upset plot of APS antibody testing outcomes by patient. Possible APS patients are sorted into one of the following test outcome categories: no test data, no positive test (i.e., only negative or indeterminate results), or positive test for one or more different APS antibodies. A single patient may have multiple tests within a single category. Categories with fewer than 20 participants are excluded for patient privacy.

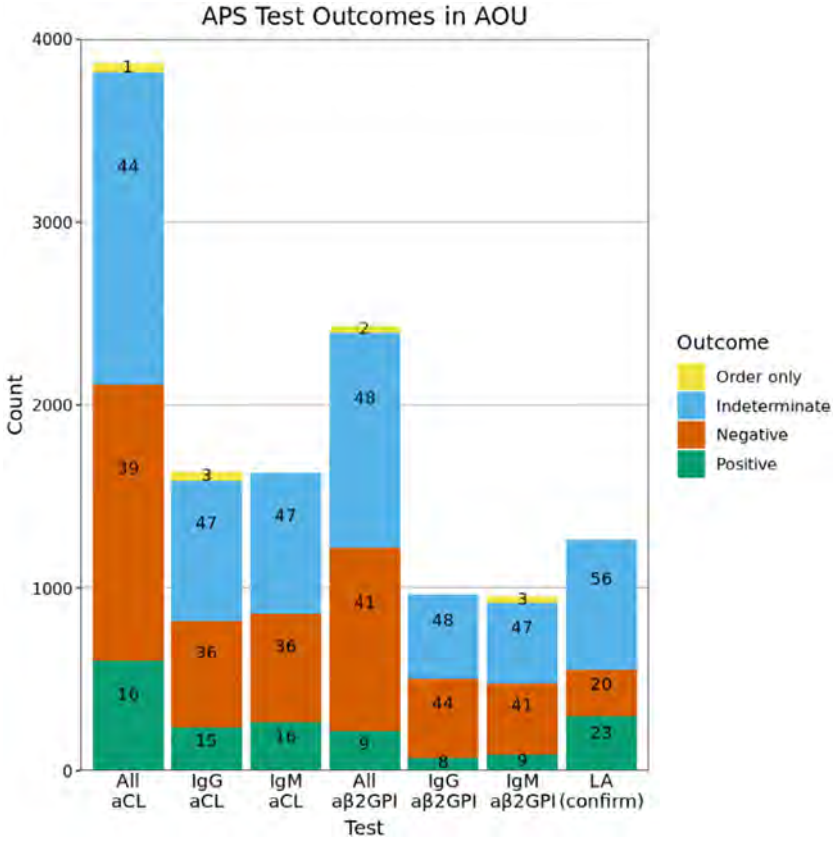


Figure 2. Per-test outcomes of antiphospholipid antibody testing. Outcomes of possible APS patient lab results in the All of Us Research Network Database (AOU). Indeterminate: insufficient data to assess positivity or negativity of test; order only, EHR order without reported results. Labels on bars correspond to a per-bar percentage.

any positive antiphospholipid test (**Figure 1**). Additionally, only 119 (13%) had two positive tests greater than 12 weeks apart, in accordance with APS classification criteria. Despite these low rates of positive tests, possible APS patients had on average 40 rows (i.e., orders and results) of APS test data compared to 1.7 rows among the non-APS patients. Percentages of positive tests were higher for LA (possibly because of its confirmatory nature) than aCL or aβ2GPI; percentages of indeterminate test results were high (44-56%) across all tests (**Figure 2**).

Conclusion: AOU offers one of the largest and most diverse datasets for studying the epidemiology and effects of APS. However, poor data quality can complicate the identification of a robust cohort of APS patients; only 1 in 8 patients with an APS diagnostic code in AOU met the laboratory criteria for APS, despite having an over-enrichment of APS test data compared to the whole database. This result is partially driven by half of all tests having an indeterminate result due to missing data. While improved standardization for testing and documentation could ameliorate data quality issues, creating a "digital phenotype" which combines many and different data types from the EHR will be needed to confidently identify likely APS patients for further study.

Disclosure: E. Balczewski: None; **W. Liang**: None; **A. Ambati**: None; **Y. Zuo**: None; **K. Singh**: Blue Cross Blue Shield of Michigan, 5, Flatiron Health, 1, National Institute of Diabetes and Digestive and Kidney Diseases, 5, Teva Pharmaceuticals, 5; **J. Knight**: Jazz Pharmaceuticals, 2.

Abstract Number: 0109

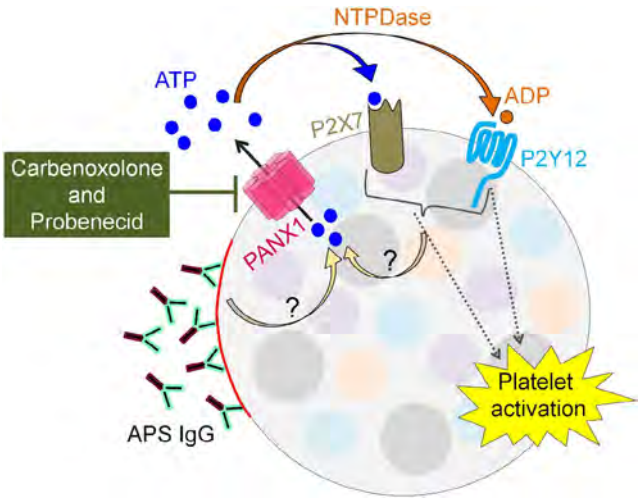
Persistent Prothrombotic Activation of Platelet Pannexin 1 Channels in Antiphospholipid Syndrome

Bruna Mazetto, NaveenKumar Somanathapura, Claire Hoy, Christine Rysenga, Srilakshmi Yalavarthi, Cyrus Sarosh, Caroline Ranger, Katarina Kmetova, Jacqueline Madison, Yu Zuo and Jason Knight, University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Inappropriately amplified inflammatory responses are hallmarks of many diseases, with extracellular ATP often playing a central role in the orchestration of inflammation. Regulated cellular ATP release is mainly through selective anion channels such as pannexin-1 (**PANX1**) channels. When cells are under stress, PANX1 channels may become constitutively opened after the cleavage of the C-terminal regions of channel subunits. While hyperactivated platelets contribute to at least a subset of antiphospholipid syndrome (**APS**)-associated thrombotic events, the most effective way to restrain their activation has remained elusive. Here, we aimed to evaluate the potential role of platelet PANX1 channels in the pathophysiology of APS.

Methods: Extracellular ATP release was evaluated in platelets freshly isolated from patients with positive antiphospholipid antibodies and features of APS (n=51) or from healthy controls (n=16) by standard assay kits and flow cytometry. No patients in this study had concomitant lupus. PANX1 inhibitors included carbenoxolone (**CBX**) and probenecid (**PRB**). In some experiments, platelets were stimulated with standard platelet agonists (thrombin, convulxin, and U46619) or with IgG purified from triple-positive APS patients or healthy controls. The participation of purinergic receptors in ATP-mediated platelet activation was assessed with specific inhibitors of various relevant P2X and P2Y purinergic receptors.



Results: The basal release of ATP from APS platelets was significantly higher than from healthy platelets (median 4-fold, $p< 0.0001$). This ATP release was strongly reduced in the presence of CBX (2-fold reduction, $p< 0.05$). Although the difference between APS and healthy platelets was obscured upon activation with thrombin, ATP release in this context was still prevented by either CBX (3-fold reduction, $p< 0.0001$) or PRB (3-fold reduction, $p< 0.0001$). Beyond thrombin, the PANX1 inhibitors also significantly reduced platelet ATP release in response to the thromboxane mimetic U46619 (2-fold reduction, $p< 0.05$). Interestingly, treatment with APS IgG was even more effective than the standard platelet agonists in opening PANX1 channels (4-fold, $p< 0.0001$) in just 30 minutes. This effect was completely neutralized by CBX treatment (4-fold decrease, $p< 0.01$). Notably, PANX1 channel-dependent ATP release was blunted by blocking either P2Y12 ($p< 0.0001$) or P2X7 ($p< 0.0001$) receptors, suggesting self-perpetuating purinergic pathways for PANX1 activation.

Conclusion: These data highlight the potential role of platelet PANX1 channels in contributing to vascular inflammation in APS by excessive extracellular ATP release. The accumulation of extracellular ATP promotes even further ATP release (and likely platelet activation) via P2Y12 and P2X7 receptors. PANX1 channel blockers such as CBX and PRB could be novel ways to restore platelet homeostasis in APS, potentially restraining thrombosis without a major impact on hemostasis (**-Figure 1**). Experiments are now underway to further evaluate the upstream and downstream signaling partners of activated PANX1 channels in APS platelets.

Illustration of platelet PANX1 channel and downstream purinergic receptors in APS.

Disclosure: B. Mazetto: None; **N. Somanathapura**: None; **C. Hoy**: None; **C. Rysenga**: None; **S. Yalavarthi**: None; **C. Sarosh**: None; **C. Ranger**: None; **K. Kmetova**: None; **J. Madison**: None; **Y. Zuo**: None; **J. Knight**: Jazz Pharmaceuticals, 2.

Abstract Number: 0110

Neutrophil Extracellular Traps as Mediators of Antiphospholipid Antibody-Induced Trophoblast Dysfunction and Fetal Loss

Christine Rysenga, Srilakshmi Yalavarthi, Wenying Liang, Claire Hoy, Cyrus Sarosh, Richard Lieberman, Yu Zuo and Jason Knight, University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Antiphospholipid antibodies (**aPL**) induce obstetric complications associated with placental insufficiency by promoting trophoblast dysfunction and inflammation at the maternal-fetal interface. Neutrophils have been found to play a critical role in aPL-mediated pregnancy loss in mice; however, the role of neutrophil extracellular traps (**NET**s) in obstetric APS has not been well studied. Here, we aimed to characterize the role of NETs in aPL-mediated trophoblast dysfunction and fetal loss, as well as the ability of NET inhibition to prevent these effects.

Methods: IgG was purified from patients with triple-positive APS (referred to as aPL going forward) or healthy controls. To evaluate trophoblast dysfunction, the supernatants of human neutrophils cultured with either aPL or control IgG were transferred onto human first-trimester extravillous trophoblasts (HTR-8/SVneo), and proliferation was quantified after 24 hours by BrdU. In mice (n=10-15/group), obstetric APS was modeled via intraperitoneal injection of aPL (2mg) to WT (C57BL/6) mice on days 0, 3, 6, 9, and 12 of pregnancy. On day 15, plasma was collected, and uteri were dissected to assess fetal resorption frequency. NET inhibition was modeled via knockout of the genes for neutrophil elastase (*Elane-/-*) or peptidylarginine deiminase 4 (*Pad4-/-*). An additional group of WT mice was treated with the irreversible neutrophil elastase inhibitor GW311616A. Circulating NET remnants were quantified as plasma myeloperoxidase-DNA complexes.

Results: In culture, supernatants from aPL-stimulated neutrophils significantly diminished trophoblast proliferation, compared to supernatants from control IgG-stimulated neutrophils (p=0.033) or to aPL alone (p=0.018). In the mouse model, aPL-treated mice experienced higher fetal resorption rates versus mice treated with control IgG (mean 30.1% vs. 13.1%, p=0.006). Plasma NET remnants were also higher in the aPL-treated mice (p=0.003). Compared to the 30% resorption of WT mice, *Elane-/-* mice (8.2% resorption, p=0.006) and *Pad4-/-* mice (9.6% resorption, p=0.04) were protected from aPL-mediated fetal loss. Oral treatment with the neutrophil elastase inhibitor GW311616A also prevented aPL-mediated fetal loss in WT mice (16.4% resorption; p=0.04). Importantly, there was no difference in resorption rates among these groups when treated with control IgG, suggesting a protective effect specific to aPL-mediated loss. Compared to aPL-treated WT mice, plasma myeloperoxidase-DNA complexes levels were 46% lower in aPL-treated *Elane-/-* mice (p=0.012) and 41.5% lower in aPL-treated *Pad4-/-* mice (p=0.006).

Conclusion: In addition to the direct anti-proliferative effect of aPL that has been documented by others, we found that aPL-triggered NETs further reduced normal trophoblast proliferation. In mice, we demonstrated that NET inhibition (by targeting either neutrophil elastase or PAD4) was remarkably effective in preventing aPL-mediated fetal loss and lowering circulating NET levels. Cumulatively, these data suggest that therapies targeting NETs could be effective in preventing APS obstetric morbidities and warrant further study.

Disclosure: C. Rysenga: None; **S. Yalavarthi**: None; **W. Liang**: None; **C. Hoy**: None; **C. Sarosh**: None; **R. Lieberman**: None; **Y. Zuo**: None; **J. Knight**: Jazz Pharmaceuticals, 2.

Abstract Number: 0111

Hippo-YAP1-CCN2 Signaling by Microvascular Endothelial Cells Licenses Vascular Smooth Muscle Cell Proliferation in Antiphospholipid Syndrome

Wenying Liang[1], Allison Billi[1], Srilakshmi Yalavarthi[1], Christine Rysenga[1], Claire Hoy[1], Cyrus Sarosh[1], Yu Zuo[1], Eliza Pei-Suen Tsou[1], Jason Knight[1] and Hui Shi[2], [1]University of Michigan, Ann Arbor, MI, [2]Department of Rheumatology and Immunology, Ruijin Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Some patients with antiphospholipid syndrome (**APS**) are afflicted by an insidious small-vessel vasculopathy that results in the accrual of organ damage over time. While the neotima formation that heralds this vasculopathy is most commonly visualized upon kidney biopsy, other organs such as the brain, heart, and skin may also be at risk. We previously used single-cell RNA sequencing of APS skin biopsies to identify the upregulation of various proliferation-supporting genes in microvascular endothelial cells (**MVECs**). The most notable example was CCN2 (also known as CTGF),

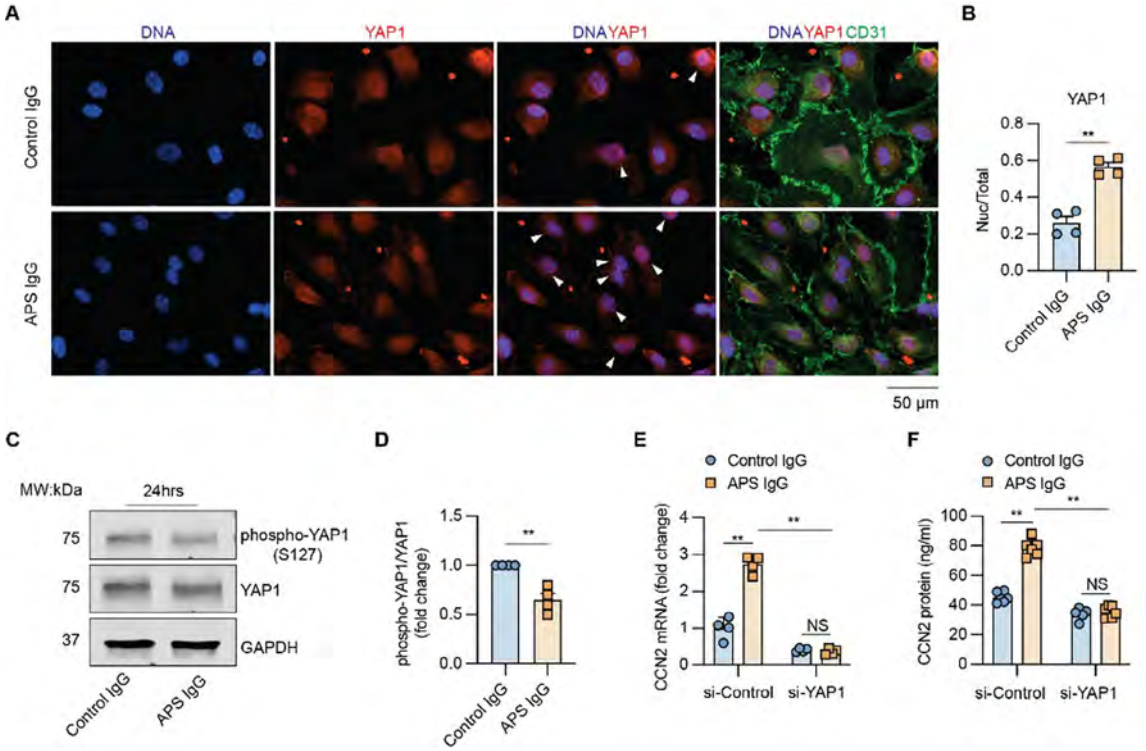


Figure 1. YAP1 mediates APS antibody-induced endothelial cell CCN2 expression. A, Representative images of YAP1 expression (red) in control IgG- or APS IgG-stimulated MVECs (both 100 μg/ml), accompanied by markers of endothelial cells (CD31, green) and nuclear DNA (Hoechst, blue). Arrowheads indicate cells with YAP1 nuclear translocation. Scale bar=50 μm. B, The ratio of cells with YAP1 nuclear translocation in the indicated groups. C, Representative Western blot of phospho-YAP1 (S127) and total YAP1 in control IgG- or APS IgG-stimulated MVECs. D, The band intensity of phospho-YAP1/total YAP1 from four independent western blots was quantified and normalized with GAPDH. MVECs stimulated with control IgG were set as 1. E-F, The relative mRNA and secreted protein levels of CCN2 in control or YAP1-knockdown MVECs stimulated with control or APS IgG. Data are presented as mean ± SEM. Unpaired t-test for B and D. Two-way ANOVA followed by Sidak post hoc analysis for E and F. n=4/group. si-Control, nontargeting small interfering RNA control. si-YAP1, small interfering RNA targeting YAP1. **p < 0.01, NS: not significant.

a classic downstream target of Hippo-YAP1 signaling. Furthermore, the previous bioinformatic analysis demonstrated the potential for strong communication between secreted MVEC ligands such as CCN2 and vascular smooth muscle cells (**VSMC**) receptors—a potentially critical interaction given the important role of VSMC proliferation and migration in neointima formation. Here, we aimed to determine the potential role of the Hippo-YAP1-CCN2 axis in APS micro-vasculopathy.

Methods: Isolated healthy MVECs were cultured with APS patient serum or patient-derived IgG. CCN2 expression was measured by quantitative PCR and ELISA. Immunofluorescence (IF) microscopy and western blotting were used to assess YAP1 signaling. To study cellular communication, human VSMCs were cultured with conditioned media from APS-stimulated MVECs. The proliferation and migration of VSMCs were determined by BrdU-staining and wound-scratch assays, respectively. Finally, CCN2 expression was assessed in kidney biopsies from patients with APS nephropathy by IF microscopy.

Results: Culture of MVECs with APS patient serum or patient-derived IgG led to upregulation of CCN2 mRNA (fold change 2.3 ± 0.3 and 2.8 ± 0.1, respectively, both $p < 0.01$). Concomitantly, secreted CCN2 protein in the supernatant was increased as assessed by ELISA (data not shown). In parallel studies, the activation of the Hippo-YAP1 pathway was confirmed by increased YAP1 nuclear translocation and reduced YAP1 phosphorylation (**Figure 1A-D**). Notably, the knockdown of YAP1 in MVECs abolished APS IgG-induced CCN2 expression and secretion (**Figure 1E-F**). Regarding MVEC-VSMC communication, conditioned media from APS IgG-stimulated MVECs triggered a noncontractile phenotype in VSMCs, accompanied by increased proliferation and migration. These phenotypes were mitigated by the humanized CCN2-blocking antibody, pamrevlumab (**Figure 2**). Finally, kidney biopsies from patients with APS nephropathy showed markedly enhanced CCN2 expression in the thickened intima and media of microvessels, indicating the in vivo relevance of this pathway (**Figure 3**).

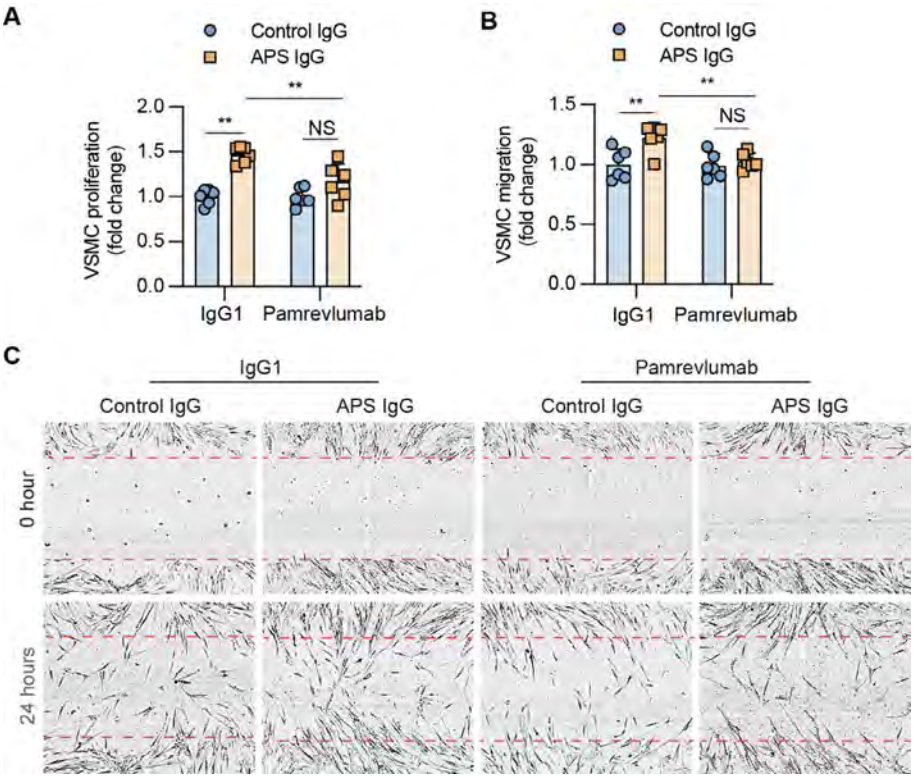


Figure 2. Communication between microvascular endothelial cells (MVECs) and vascular smooth muscle cells (VSMCs) in APS. A-B, Proliferation (A) and migration (B) of VSMCs were quantified and presented as the relative fold change compared to the group stimulated by control IgG1 and conditioned media from control IgG-stimulated MVECs. Migration was quantified by wound confluence (%). C, Representative images of each group at 0 or 24 hours after scratch. Data are represented as mean ± SEM and p values were calculated by two-way ANOVA followed by Sidak post hoc analysis. n=6/group. **$p < 0.01$, NS: not significant.

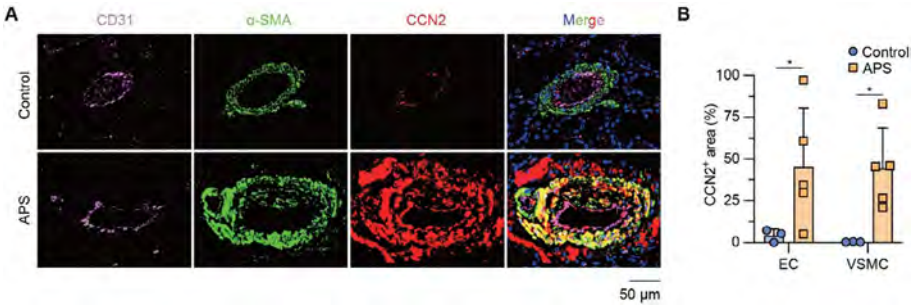


Figure 3. High expression of vascular CCN2 in patients with APS nephropathy. A, Representative images of CCN2 expression (red) in the kidney vessels from healthy controls or APS nephropathy patients. Endothelial cells (CD31+ area) and vascular smooth muscle cells (α-SMA+ area) were labeled in purple and green, respectively. Nuclear DNA was labeled by Hoechst (blue). Scale bar=50 μm. B, The percentage of CCN2+ area in kidney endothelium of indicated groups was calculated as CCN2+CD31+ area/CD31+ area. The percentage of CCN2+ area in kidney vascular smooth muscle cells of indicated groups was calculated as CCN2+α-SMA+ area/α-SMA+ area. Data are presented as mean ± SEM and p values were calculated by two-way ANOVA followed by Sidak post hoc analysis. n=3 for control, n=5 for APS nephropathy patients. *p<0.05. EC, endothelial cell. VSMC, vascular smooth muscle cell.

Conclusion: We found that APS serum and patient-derived IgG triggered YAP1 nuclear translocation in MVECs, which was accompanied by increased CCN2 expression and secretion. The secreted CCN2 was then able to trigger a phenotypic switch in VSMCs toward the migratory and proliferative characteristics that are necessary for neointima formation. Blocking either YAP1 or CCN2 might be a novel approach for the treatment of APS-associated microvasculopathies.

Disclosure: W. Liang: None; **A. Billi**: None; **S. Yalavarthi**: None; **C. Rysenga**: None; **C. Hoy**: None; **C. Sarosh**: None; **Y. Zuo**: None; **E. Tsou**: None; **J. Knight**: Jazz Pharmaceuticals, 2; **H. Shi**: None.

Abstract Number: 0112

Molecular Stratification of Antiphospholipid Syndrome Patients Through Integrative Analysis of the Whole-blood RNA Transcriptome

Amala Ambati[1], Feiyang Ma[1], Katarina Kmetova[1], Sherwin Navaz[1], Claire Hoy[1], Cyrus Sarosh[1], Ajay Tambralli[1], Johann E. Gudjonsson[1], J. Michelle Kahlenberg[1], Jacqueline Madison[1], Ali Duarte-Garcia[2], Jason Knight[1] and Yu Zuo[1], [1]University of Michigan, Ann Arbor, MI, [2]Mayo Clinic, Rochester, MN

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Antiphospholipid syndrome (**APS**) is an acquired thrombo-inflammatory disease associated with diverse clinical manifestations in the setting of persistent antiphospholipid antibodies (**aPL**). Early diagnosis and more targeted therapies would likely improve outcomes, but both are hindered by clinical and pathogenic heterogeneity. There is an urgent need for modern approaches to the diagnosis and endotypic stratification of aPL-positive patients. We aimed to utilize integrative analyses of data derived from the whole-blood RNA transcriptome to cluster aPL-positive patients by gene expression to identify pathogenic pathways that might be therapeutic targets.

Methods: Whole-blood RNA sequencing was performed on 102 patients with primary APS, 29 with secondary APS, and 43 with persistently positive aPL but without "criteria" APS manifestations. Unsupervised machine learning of the whole-blood transcriptome was undertaken. Deconvolution analysis was further used to estimate the different cell types and their abundance in each sample.

Results: We found that aPL-positive patients could be stratified into four major clusters defined by unique gene expression modules (**Fig 1A-B**). Pathway analysis revealed that neutrophil extracellular trap (**NET**) formation, mammalian target of rapamycin (**mTOR**) signaling, and Hippo pathway signaling were top-upregulated pathways among patients in cluster 4. In contrast, patients in cluster 1 tended to have upregulated genes related to cytoplasmic ribosomal proteins, tyrosine metabolism, and fatty acid biosynthesis, amongst other pathways (**Fig 1C**). When looking at the associations between pathway-focused gene expression modules and various extra-criteria clinical manifestations of APS, white matter lesions were associated with

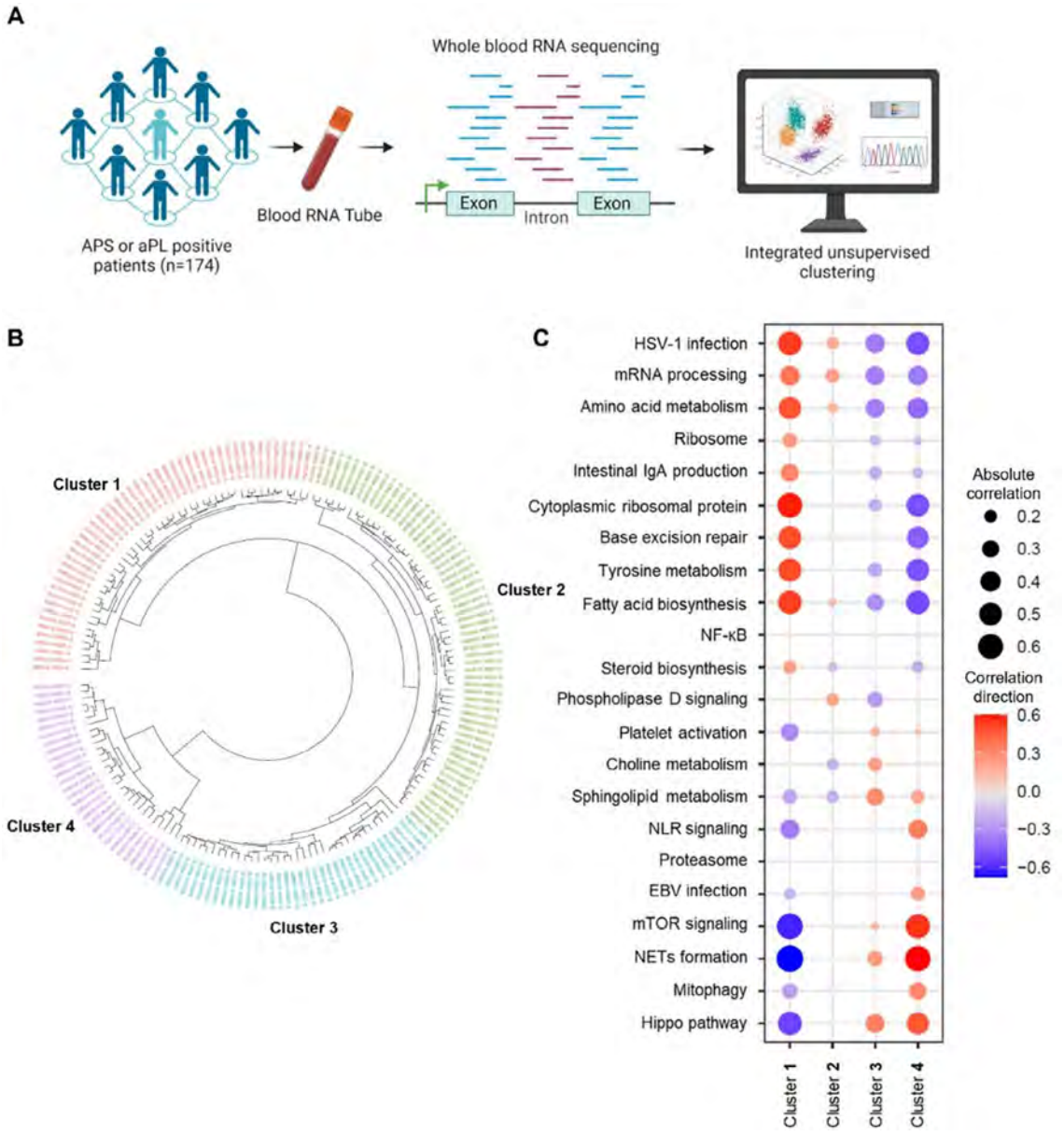


Figure 1. A, Schematic illustration of study design and whole-blood RNA sequencing. The figure was created at www.biorender.com. B, Unsupervised hierarchical clustering was used to stratify aPL-positive patients into four clusters. C, Dot plots demonstrating associations between pathway-specific gene modules and each cluster of aPL-positive patients. Only statistically significant associations are shown.

upregulated NF-κB-related genes (r=0.33, p< 0.0001), and seizures were associated with upregulated choline metabolism-related genes (r=0.2, p=0.009). Meanwhile, cardiac valve disease was associated with NET formation (r=0.18, p=0.02) and the Hippo pathway (r=0.18, p=0.02). Deconvolution analysis demonstrated distinct immune cell type distributions among different clusters of patients (**Fig 2A**). For example, patients in cluster 4 were predicted to have more myeloid cells, such as neutrophils, eosinophils, and dendritic cells. In contrast, patients in cluster 1 had high proportions of lymphoid cells, such as B cells, plasma cells, and CD8 T cells (**Fig 2B**). Our analysis also revealed several significant associations between immune cell types and pathway-focused gene modules, including an association between neutrophils and the Hippo pathway, the mTOR pathway, and NET formation (**Fig 2C**). Clinically, patients in cluster 4 were more likely to have positive testing for anti-beta-2 glycoprotein I IgG, higher absolute neutrophil counts, and increased urine protein-to-creatinine ratio (**Table 1**).

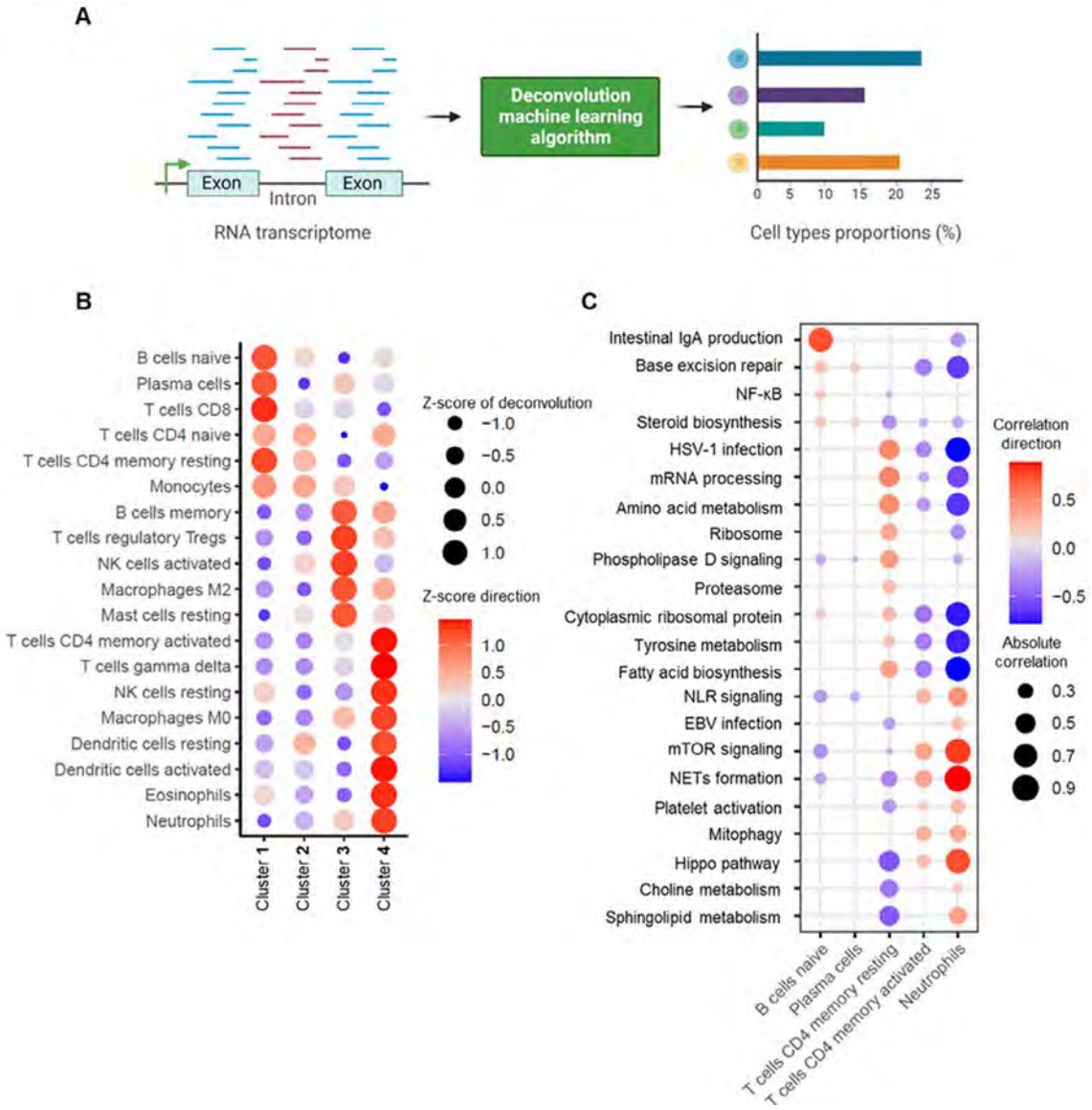


Figure 2. A, Schematic illustration of deconvolution analysis of whole-blood transcriptomic data. Cell type deconvolution was performed using CybersortX with the LM22 (22 immune cell types) as the signature matrix. The figure was created at www.biorender.com. B, Dot plot demonstrating associations between immune-cell types and each cluster of aPL-positive patients. C, Dot plot demonstrating associations between pathway-specific gene modules and immune-cell types. Only statistically significant associations are shown.

Table 1: Clinical and demographic characteristics of aPL-positive patients across four clusters (n=174)					
	Cluster 1 (n=50)	Cluster 2 (n=59)	Cluster 3 (n=36)	Cluster 4 (n=29)	P value
Diagnoses					
Primary APS or +aPL *without* lupus # (%)	36 (72.0%)	47 (80.0%)	23 (63.9%)	20 (69.0%)	**<0.0001**
Demographics					
Age (mean ± SD)	43 ± 13	46 ± 18	46 ± 14	45 ± 17	0.879
Male # (%)	15 (30.0%)	15 (25.4%)	12 (33.3%)	9 (31.0%)	0.859
aPL profile # (%)					
aCL IgG	26 (52%)	40 (67.8%)	26 (89.7%)	22 (75.7%)	0.100
aCL IgM	27 (54%)	26 (44.1%)	12 (33.3%)	11 (37.9%)	0.251
aCL IgA	1 (2%)	2 (3.4%)	3 (8.3%)	2 (6.9%)	0.480
aβ2GPI IgG	29 (58%)	42 (71%)	26 (72%)	26 (90%)	**0.030**
aβ2GPI IgM	26 (52%)	26 (44.1%)	12 (33.3%)	14 (48.3%)	0.377
aβ2GPI IgA	3 (6%)	7 (11.9%)	7 (19.4%)	3 (10.3%)	0.283
aPS/PT IgG	17 (34%)	26 (44.1%)	16 (44.4%)	15 (51.7%)	0.568
aPS/PT IgM	16 (32%)	26 (44.1%)	17 (47.2%)	13 (44.8%)	0.523
anti-D1 of β2GPI IgG	21 (42%)	31 (52.5%)	24 (66.7%)	18 (62.1%)	0.178
Lupus anticoagulant	20 (40%)	34 (57.6%)	21 (58.3%)	16 (55.2%)	0.231
Triple positive	12 (24%)	26 (44.1%)	15 (41.7%)	12 (41.4%)	0.227
Laboratory studies (mean ± SD)					
Neutrophil count (K/µl)	3.29 ± 1.89	4.48 ± 1.91	4.28 ± 0.35	6.29 ± 2.16	**<0.0001**
CRP (mg/dl)	0.32 ± 0.36	0.52 ± 0.54	0.80 ± 0.72	0.69 ± 0.81	0.050
C3 (mg/dl)	74.35 ± 17.62	77.79 ± 17.08	78.76 ± 15.82	76.76 ± 21.28	0.770
C4 (mg/dl)	19.85 ± 4.52	20.38 ± 5.07	20.21 ± 4.54	19.39 ± 6.02	0.871
Platelet count (K/µl)	241.11 ± 78.25	263.35 ± 90.84	221.68 ± 77.97	216.21 ± 73.85	0.074
Creatinine (mg/dl)	1.05 ± 0.65	0.98 ± 0.36	1.03 ± 0.33	1.00 ± 0.47	0.679
Urine protein/creatinine ratio	0.09 ± 0.14	0.41 ± 0.91	0.31 ± 0.52	0.49 ± 0.90	**0.043**
Clinical history # (%)					
Venous thrombosis	22 (44%)	29 (49.2%)	22 (61.1%)	14 (48.3%)	0.469
Arterial thrombosis	10 (20%)	15 (25.4%)	6 (16.7%)	5 (17.2%)	0.492
Pregnancy morbidity	12 (24%)	7 (11.9%)	5 (13.9%)	4 (13.8%)	0.345

SD=standard deviation
aCL=anticardiolipin, aβ2GPI=anti-beta-2 glycoprotein I, aPS/PT=anti-phosphatidylserine/prothrombin, anti-D1=anti-Domain 1
Triple positive= positive LA, positive aCL IgG or IgM, and positive aβ2GPI IgG or IgM

Conclusion: Our study shows, for the first time, that aPL-positive patients can be stratified into four major clusters defined by pathway-focused gene expression modules and predicted immune cell-type compositions. The results obtained in this study are a first step toward the goal of personalized medicine for patients living with APS.

Disclosure: A. Ambati: None; **F. Ma**: None; **K. Kmetova**: None; **S. Navaz**: None; **C. Hoy**: None; **C. Sarosh**: None; **A. Tambralli**: None; **J. Gudjonsson**: Abbvie, 2, 5, Almirall, 2, 5, AnaptysBio, 2, Boehringer Ingelheim, 2, Celgene/BMS, 2, 5, Eli Lilly, 2, 5, Galderma, 2, Janssen, 2, 5, Kyowa Kirin, 5, MiRagen, 2, Novartis, 2, Prometheus Biosciences, 5, Sanofi, 2, SunPharma, 5, TimberPharma, 5; **J. Kahlenberg**: AstraZeneca, 1, Bristol-Myers Squibb(BMS), 2, 5, EMD Serano, 2, exo therapeutics, 2, Gilead, 2, GlaxoSmithKlein(GSK), 1, horizon Therapeutics, 2, Janssen, 5, Pfizer, 2, ROME Therapeutics, 2, 5, Rome Therapeutics, 5, Ventus Therapeutics, 2, 5; **J. Madison**: None; **A. Duarte-Garcia**: None; **J. Knight**: Jazz Pharmaceuticals, 2; **Y. Zuo**: None.

Abstract Number: 0113

Serum Myeloperoxidase (MPO)-DNA Complexes and Serum Calprotectin Differentiate Isolated Thrombotic Antiphospholipid Syndrome from Isolated Obstetric Antiphospholipid Syndrome

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: There is a lack of serum markers to differentiate thrombotic APS (tAPS) and obstetric APS (oAPS). Neutrophil extracellular traps (NETs) are involved in the pathogenesis of antiphospholipid syndrome (APS). This study aims to evaluate the difference of NETs markers between tAPS and oAPS.

Methods: A total of 253 adult patients diagnosed APS and fulfilled Sydney criteria were recruited from the Department of Rheumatology and Immunology at Peking University People's Hospital. Demographic characteristics and clinical features of patients were recorded. Serum concentrations of aPLs, MPO-DNA complexes, cell-free DNA and calprotectin were measured. Results are shown as mean±SD. The results were analyzed by independent t tests, Mann-Whitney U test, and chi-square tests as appropriate.

Results: In comparison to those with oAPS, patients with tAPS had older age (46.89±17.69 vs. 36.95±8.88 years, P< 0.001), higher rate of cardiovascular risk (at least one positive of smoke, coronary heart disease, hypertension, obesity, diabetes, and hyperlipidemia) (65.63% vs. 36.56%, P < 0.001), and lower lymphocyte count (1.51±0.74 vs. 1.77±0.69 10^9/L, P < 0.05) and neutrophil-to-lymphocyte ratio (4.11±3.89 vs. 3.07±2.17 10^9/L, P < 0.05). Both lupus anticoagulant (61.72% vs. 29.63%, P < 0.001), and anti-cardiolipin (61.90% vs. 30.95%, P < 0.001) positivity were higher in patients with tAPS, and there was no significant difference in anti-β2GPI positivity. Compared with oAPS patients, tAPS patients had higher concentration of MPO-DNA complex [1107.77(689.90, 2107.62) vs. 583.62(313.78, 1498.41), ng/ml, P < 0.01) but lower calprotectin (21.22(20.40, 22.60) vs. 22.85(21.43, 24.19), ng/ml P < 0.05), but there was no significant difference in cell-free DNA level in two groups.

Table 1. Demographic characteristics and clinical features and laboratory assessment of patients with isolated obstetric and thrombotic APS

	tAPS(n=160)	oAPS(n=93)	P-values
Age(years) mean ± SD	46.89±17.69	36.95±8.88	< 0.001*
Cardiovascular risk factors, n (%)	105 (65.6)	34 (36.6)	< 0.001*
Hypertension	32 (20)	27 (45.8)	0.123
Coronary heart disease	7 (4.4)	8 (8.6)	0.179
Smoking history, n (%)	15 (9.4)	11 (11.8)	0.528
Diabetes mellitus	16 (10)	10 (10.8)	0.833
Hyperlipidemia	9 (5.6)	12 (12.9)	0.058

*: P< 0.05

Table 2. Laboratory assessment of patients with isolated obstetric and thrombotic APS

	tAPS(n=160)	oAPS(n=93)	P-values
WBC (10^9/L), mean ± SD	7.21 ± 3.92	7.25 ± 3.26	0.946
Neutrophil Count (10^9/L), mean ± SD	4.96 ± 3.40	4.91 ± 2.89	0.917
Lymphocyte Count (10^9/L), mean ± SD	1.51 ± 0.74	1.77 ±0.69	0.012*
NLR, mean ± SD	4.11 ± 3.89	3.07 ± 2.17	0.012*
Anemia, n (%)	56 (37.6)	15 (21.1)	0.020*
Thrombocytopenia, n (%)	64 (42.1)	21 (29.2)	0.077
LA positivity, n (%)	79 (61.7)	24 (29.6)	< 0.001*
ACL positivity, n (%)	91 (61.9)	26 (31.0)	< 0.001*
anti-β2GPI positivity, n (%)	91 (62.8)	46 (51.7)	0.103

a: NLR, Neutrophil-to-lymphocyte Ratio.

*: P< 0.05

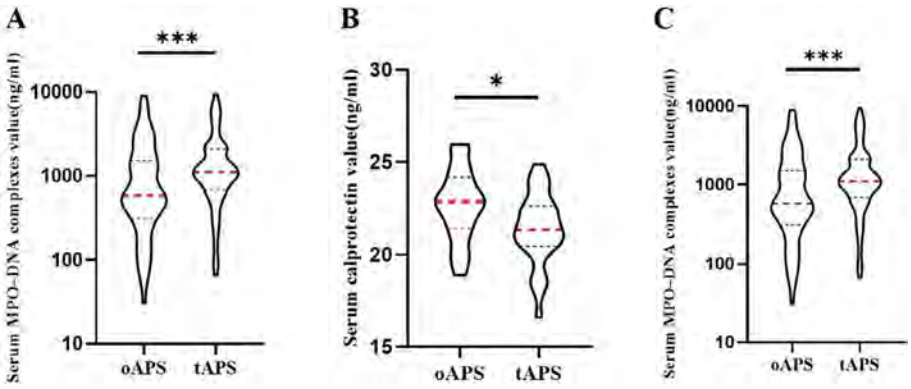

Figure 1. Patients with tAPS had higher level of MPO-DNA complex (A) but lower calprotectin (B). There was no significant difference in cell-free DNA level (C). *P < 0.05, ***P < 0.001 Data are presented as the mean ± SD.

Conclusion: Our data suggest that patients with tAPS had higher level of MPO-DNA complex but lower calprotectin, and higher lupus anticoagulant and anti-cardiolipin. It is worth further research distinct mechanisms of pathogenesis.

Disclosure: R. Liang: None; **R. Yao**: None; **Z. Wang**: None; **W. Pei**: None; **R. Liang**: None; **C. Li**: None.

Abstract Number: 0114

Platelets Are Highly Activated and Could Participate in Immune Abnormality of APS

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Platelets play a pivotal role in the process of coagulation and other biological process. Studies have shown multiple evidences that platelets are highly activated in APS, and have the ability to enhance the activity of other cells like endothelial cells, monocytes, and neutrophils. Emerging evidences have indicated that platelets are more than a part of coagulation process.

Methods: We included 35 patients who fulfilled the 2006 Sydney classification criteria of APS and 18 age, sex matched heathy controls (HC). Activation of platelet was measured by flow cytometry. Reactive oxygen species (ROS) production and mitochondrial respiration was measured. RNA-sequencing was performed.

Results: The baseline characteristics of studied patients are shown in Table 1. Platelet activation was detected by the surface expression of CD62p after gating with CD41a. As presented in Figure 1A, the mean fluorescent intensity of CD62p was significantly increased in APS patients compared with HC ($p< 0.05$) . After stimulated with adenosine diphosphate (ADP, 0.1U/ml) and thrombin (2U/ml), the activation was similar between patients and HC. Previous research showed platelets treated with immune thrombocytopenia plasma was induced to shed GPIbα(CD42b), so we examined the surface expression of CD42b and found no statistic difference (Figure 1B). Then we detected the ROS production (Figure 1C-D) and found that platelets of APS patients both in original state and activated with thrombin produced significantly more ROS than the HC. Then we want to explore if platelets from APS patients contain more mitochondria or it is because the metabolism is more activated. Mitotracker was used to label mitochondria in platelets. As shown in Figure1E, the quantity of mitochondria was similar. We used seahorse analysis to examine mitochondrial respiration and found that maximum respiration was evidently higher in platelets from APS patients (Figure 1F).

Table 1. Baseline demographic, clinical, and laboratory characteristics of study patients.

Characteristics	Study patients (n = 35)
Gender, female, n (%)	17 (50)
Age, year, mean (SD)	39.6 (12.4)
Time since diagnosis, months, median (IQR)	36 (32, 46.5)
BMI, kg/m^2, mean (SD)	25.2 (4.2)
Smoking, n(%)	15 (24.9)
Hypertension, n(%)	4 (11.4)
Diabetes mellitus, n(%)	2 (5.7)
Dyslipidemia, n(%)	2 (5.7)
Thrombosis, n(%)	35 (100)
Arterial thrombosis, n(%)	11 (31.4)
Venous thrombosis, n(%)	27 (77.1)
Pregnancy morbidity, n(%) of female	6 (35.3)
Extra-criteria manifestations, n(%)	9 (25.7)
aPL profile	
aCL, n(%)	22 (62.9)
Anti-β 2GPI, n(%)	22 (62.9)
LA, n(%)	28 (80)
Triple positivity, n(%)	14 (40)
PLT count, $\times 10^9$/L, mean (SD)	189 (76.8)

We performed RNA sequencing in 14 APS patients and 6 age, sex matched HC. 748 differently expressed genes with adjusted p-value < 0.01 and $|\log_2 FoldChange| > 1.5$ were screened and tested enrichment in KEGG pathways (Figure 2). It is evident that multiple immune related pathways were enriched including inflammatory signaling pathways (JAK-STAT, IL-17 signaling pathways) and T cell associated pathways (Th1, Th2, and Th17 differentiation).

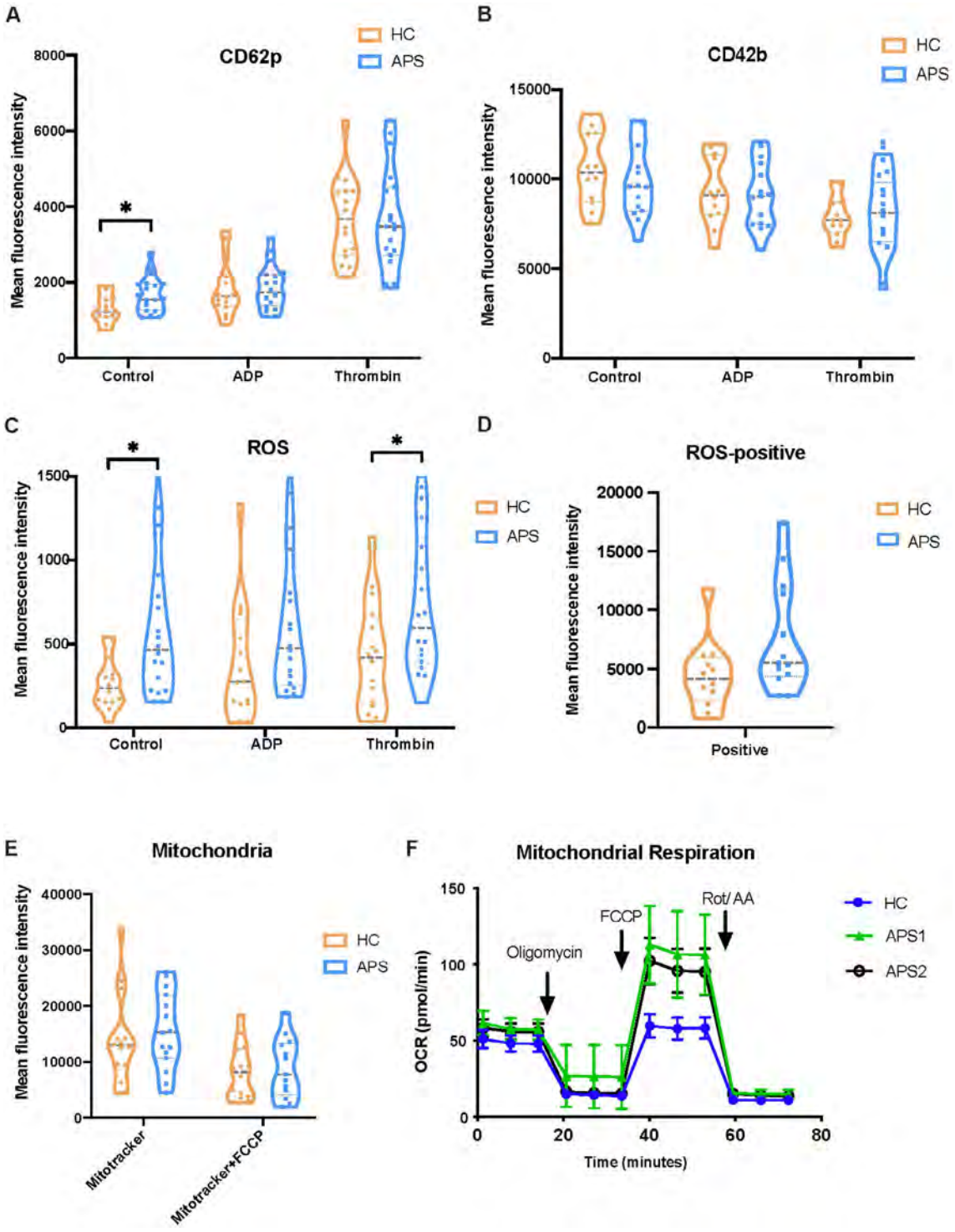

Figure 1. Platelet flow cytometry and mitochondrial respiration of study patients.

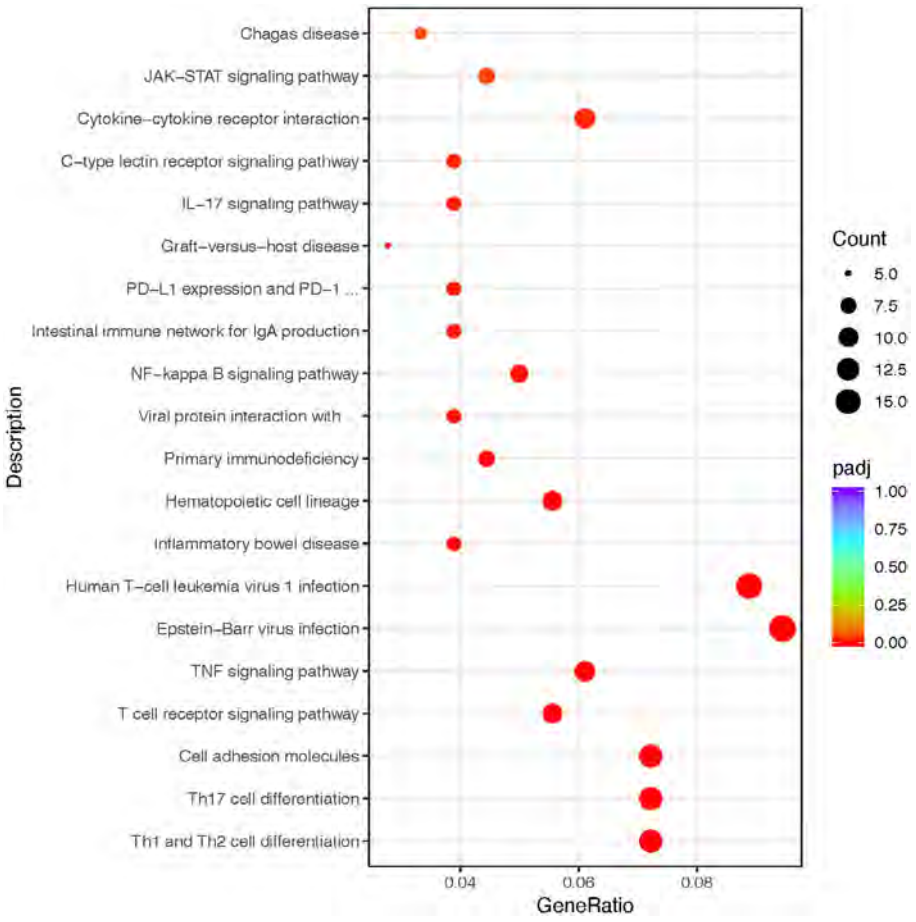

Figure 2. KEGG pathway enrichment of differently expressed genes from platelet RNA sequencing.

Conclusion: Platelet activation and mitochondrial respiration is highly increased in APS. The platelet transcriptome of APS is significantly different from HC. Platelets could interact as immune cells to modulate T cell activity.

Disclosure: Y. Shi: None; **X. Luo**: None; **Q. Chen**: None; **J. zhao**: None; **M. Li**: None; **x. Zeng**: None.

Abstract Number: 0115

Risk Factors of First Thrombosis in Obstetric Antiphospholipid Syndrome

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Antiphospholipid Syndrome Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Limited evidence exists regarding the long-term risk of thrombosis in patients with obstetric antiphospholipid syndrome (OAPS). This study aimed to investigate the clinical features and risk factors associated with the first thrombosis in isolated OAPS patients.

Table 1 Comparison of baseline characteristics, clinical features and treatment between OAPS patients with or without thrombotic events.

	Thrombosis group (n=11)	Non-thrombosis group (n=175)	*P* value
Age at onset (years), mean ± SD	27.6 ± 4.0	31.3 ± 4.8	**0.013**
Disease duration (years), IQR	5.0 (1.0, 25.0)	1.0 (0.3, 3.0)	**0.049**
BMI (kg/m^2), mean ± SD	24.3 ± 4.8	24.4 ± 3.9	0.924
Smoking, n (%)	0 (0)	3 (1.7)	1.000
Cardiovascular risk factors, n (%)			
Hypertension	3 (27.3)	16 (9.1)	0.158
Hyperlipidemia	4 (36.4)	37 (21.1)	0.420
Arteriosclerosis	1 (9.1)	0 (0)	0.059
Diabetes	1 (9.1)	8 (4.6)	1.000
Underlying autoimmune diseases, n (%)			
SLE	6 (54.5)	29 (16.6)	**0.006**
RA	1 (9.1)	12 (6.9)	1.000
SS	1 (9.1)	3 (1.7)	0.572
Clinical manifestations			
Fetal loss, n (%)			
<10 weeks	9 (81.8)	104 (59.4)	0.247
≥10 weeks	4 (36.4)	74 (42.3)	0.943
Abortions (≥3), n (%)	3 (27.3)	24 (13.7)	0.425
Premature birth < 34 weeks, n (%)	4 (36.4)	27 (15.4)	0.164
Pre-eclampsia, n (%)	4 (36.4)	30 (17.1)	0.231
FGR, n (%)	2 (18.2)	23 (13.1)	0.984
Stillbirth, n (%)	1 (9.1)	6 (3.4)	0.888
Thrombocytopenia, n (%)	6 (54.5)	28 (16.0)	**0.005**
Hypocomplementemia, n (%)	9 (81.8)	41 (23.4)	**< 0.001**
Laboratory tests, n (%)			
LA positive	9 (81.8)	74 (42.3)	**0.025**
aβ2GPI positive	8 (72.7)	106 (60.6)	0.629
aCL positive	8 (72.7)	55 (31.4)	**0.013**
Double positive aPLs	0 (0)	24 (13.7)	0.364
Triple positive aPLs	8 (72.7)	30 (17.1)	**< 0.001**
High-risk aPLs	9 (81.8)	93 (53.1)	0.123
Treatment after delivery, n (%)			
LDA	3 (27.3)	111 (63.4)	**0.043**
LMWH	5 (45.5)	123 (70.3)	0.165
LDA+LMWH	3 (27.3)	85 (48.6)	0.170
HCQ	5 (45.5)	135 (77.1)	**0.045**

* P <0.05, compared between the two groups. OAPS, obstetric antiphospholipid syndrome; BMI, body mass index; SLE, systemic lupus erythematosus; RA, rheumatoid arthritis; SS, Sjögren syndrome; FGR, fetal growth restriction; LA, lupus anticoagulant; aβ2GPI, anti-β2-glycoprotein I antibodies; aCL, anticardiolipin antibodies; aPLs, antiphospholipid antibodies; LMWH, low-molecular-weight heparin; LDA, low-dose aspirin; HCQ, hydroxychloroquine.

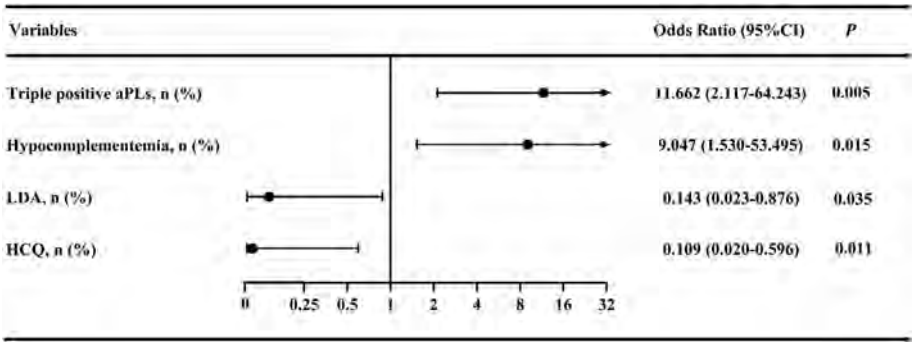

Figure 1 Multivariate logistic regression of first thrombosis in OAPS patients. OAPS, obstetric antiphospholipid syndrome; CI, confidence interval; aPLs, antiphospholipid antibodies; LDA, low-dose aspirin; HCQ, hydroxychloroquine.

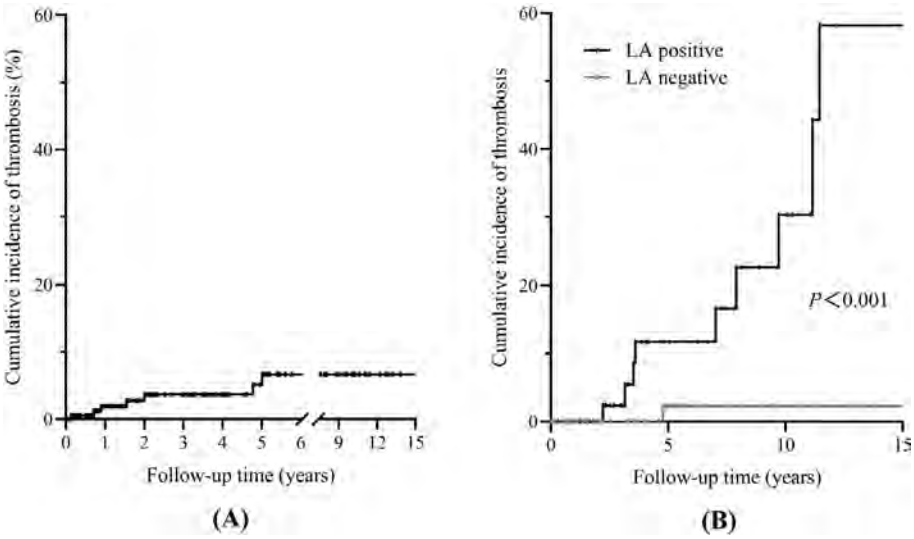

Figure 2 Kaplan-Meier survival analysis. (A) Cumulative incidence of thrombosis in OAPS patients. (B) Cumulative incidence of thrombosis in the LA-negative and LA-positive groups. OAPS, obstetric antiphospholipid syndrome; LA, lupus anticoagulant.

Methods: Clinical and laboratory data from female patients with isolated OAPS were collected. All patients were followed up until the first thrombotic event or until the end of the study. The first thrombotic event during or after delivery was recorded. Logistic regression analysis was used to identify independent risk factors associated with the first thrombosis in isolated OAPS patients.

Results: A total of 186 OAPS patients were included in the study. During a mean follow-up period of 5.4 years, 11 patients experienced thrombotic events, resulting in a 15-year cumulative thrombotic incidence of 6.7%. Triple positive antiphospholipid antibodies [aPLs, odds ratio (OR) = 11.662, 95% confidence interval (CI) = 2.117–64.243, $P = 0.005$] and hypocomplementemia (OR = 9.047, 95% CI = 1.530–53.495, $P = 0.015$) were identified as independent risk factors for the first thrombosis in OAPS patients. Additionally, the use of low-dose aspirin (LDA, OR = 0.143, 95% CI = 0.023–0.876, $P = 0.035$) and hydroxychloroquine (HCQ, OR = 0.109, 95% CI = 0.020–0.596, $P = 0.011$) were associated with a decreased risk of thrombosis.

Conclusion: Triple positive aPLs and hypocomplementemia are risk factors for the first thrombosis in OAPS patients. The use of LDA and HCQ may be associated with a reduced risk of thrombosis.

Disclosure: l. luo: None; **Q. Cai**: None; **x. liu**: None; **Y. Hou**: None; **C. Li**: None.

Abstract Number: 0116

Integrated Metabolomic and Proteomic Analyses Stratified Patients with Antiphospholipid Syndrome According to Their Atherothrombotic Risk

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Antiphospholipid syndrome (APS) is an autoimmune disorder characterized by a hypercoagulable state, leading to arterial, venous, or microvascular thrombosis and accelerated atherosclerosis. Timely diagnosis and accurate monitoring are crucial for optimizing therapeutic interventions.

Methods: A cohort of primary APS patients (n=150) and 43 healthy donors (HD) underwent serum nuclear magnetic resonance (NMR) metabolomics (>250 metabolites, Nightingale) analysis, covering glycolysis metabolites, amino acids, and 130 lipid measures. Serum levels of 92 cardiovascular-related proteins were evaluated using proximity extension immunoassay (PEA, Olink). Extensive clinical and analytical profiling was conducted. Unsupervised hierarchical clustering analyses explored molecular profile contributions to atherothrombotic risk. Additionally, 33 APS patients receiving adjuvant treatment with Ubiquinol (Qred, reduced CoQ10) at 200 mg/day for one month were studied.

Results: APS patients exhibited significant alterations in 53 metabolites compared to healthy donors. These included decreased levels of atheroprotective HDL subsets, sphingomyelins, and phospholipids, as well as increased levels of proatherogenic VLDL subsets and fatty acids. Unbiased hierarchical clustering analysis identified two patient groups with distinct metabolomic profiles. Cluster 2 (C2) patients had a higher prevalence of arterial thrombosis, elevated thrombotic risk score (aGAPSS over 9), and more CV risk factors such as atheroma plaques, dyslipidemia, and hypertension. Molecular analysis revealed 143 deregulated metabolites between clusters, including decreased HDL and increased VLDL and LDL lipoproteins, triglycerides, fatty acids, apolipoproteins (ApoB), glycolysis-related metabolites, and other lipids involved in immune cell activity. Proteomic analysis identified proteins associated with increased cardiovascular risk in these metabolomic clusters. Remarkably, significant correlations were found between deregulated protein and metabolite levels, suggesting their involvement in underlying disease mechanisms. In the *in vivo* study, Qred supplementation partially reversed the altered serum metabolic and proteomic profiles associated with APS-related thrombosis.

Conclusion:

1. "APS patients exhibit distinct metabolomic and proteomic profiles associated with the disease's pathogenesis, partially modifiable by in vivo Qred supplementation.
2. We have identified for the first time a combined metabolomic/proteomic fingerprint able to stratify APS disease according to their thrombotic risk. Ongoing studies will provide further insights into the underlying mechanisms and physiological implications of these alterations, potentially leading to the discovery of diagnostic biomarkers and therapeutic strategies for APS.

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Disclosure: C. Lopez-Pedrera: None; **B. Vellón**: None; **M. Aguirre**: None; **I. Sanchez-Pareja**: None; **L. Muñoz-Barrera**: None; **T. Cerdó**: None; **P. Segui**: None; **C. Merlo-Ruiz**: None; **D. Ruiz-Vilchez**: None; **M. Abalos-Aguilera**: None; **N. Barbarroja**: None; **A. Escudero Contreras**: None; **R. Ortega-Castro**: None; **C. Perez-Sanchez**: None.

Abstract Number: 0117

The Patient Journey to a First Diagnosis of Systemic Sclerosis: Temporal Disease Pattern Identification Using Machine Learning and Data Mining Among US and Japanese Patients

Francesco Del Galdo[1], Yahui Tian[2], Stefano Di Donato[1] and Mario Ehlers[2], [1]University of Leeds - Leeds Institute of Rheumatic and Muskuloskeletal Medicine, Leeds, United Kingdom, [2]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a rare autoimmune disease characterized by skin and organ fibrosis and vasculopathy. The Very Early Diagnosis of SSc (VEDOSS) project (Bellando-Randone S, et al. Lancet Rheum. 2021. 3(12); E834-E843) recently identified the value of predefined red flag symptoms or signs as a stratification tool for the risk of fulfilling the 2013 ACR/EULAR classification criteria for SSc. However, to date, an analysis of symptoms and signs prior to an SSc diagnosis has not been performed. Understanding pre-diagnostic patient pathways can help identify other major signs preceding a diagnosis, identify the burden of very early disease in patients with scleroderma and the potential barriers to early intervention. This study aimed to categorize temporal disease patterns leading to the initial diagnosis of SSc using US and Japanese health insurance claims data.

Methods: Patients with a diagnosis of SSc were identified from two claims databases (Optum® Clinformatics® and JMDC for the US and Japan, respectively). Patients with at least two concordant medical claims associated with SSc (International Classification of Diseases [ICD]-9 710.1, 517.2) on different dates within a 1-year period and who were ≥18 years old at the time of first SSc diagnosis were included. In the US, records were gathered from January 1, 2007 to September 30, 2015, and in Japan from January 1, 2005 to November 30, 2019. ICD codes of the differential diagnostic claims in the 3 years before SSc diagnosis were recorded. Network analysis and sequential pattern mining were used to identify and visualize temporal disease patterns prior to the diagnosis of SSc.

Results: In total, 2550 patients with continuous insurance history for ≥3 years prior to their SSc diagnosis (1765 from the US and 785 from Japan) were analyzed. Mean age at first SSc diagnosis was 61 and 51 years for the US and Japan, respectively. Approximately 80% of patients were female. In the US, the five most common diagnoses prior to SSc were related to fatigue, pain or discomfort, followed by esophageal reflux and chest pain in Japan, the most common diagnoses included upper respiratory infection, gastritis and rheumatoid arthritis (Figures 1a & 2a). In both countries, the mean time to diagnosis was shorter when the presenting complaint was Raynaud's-related (428 days

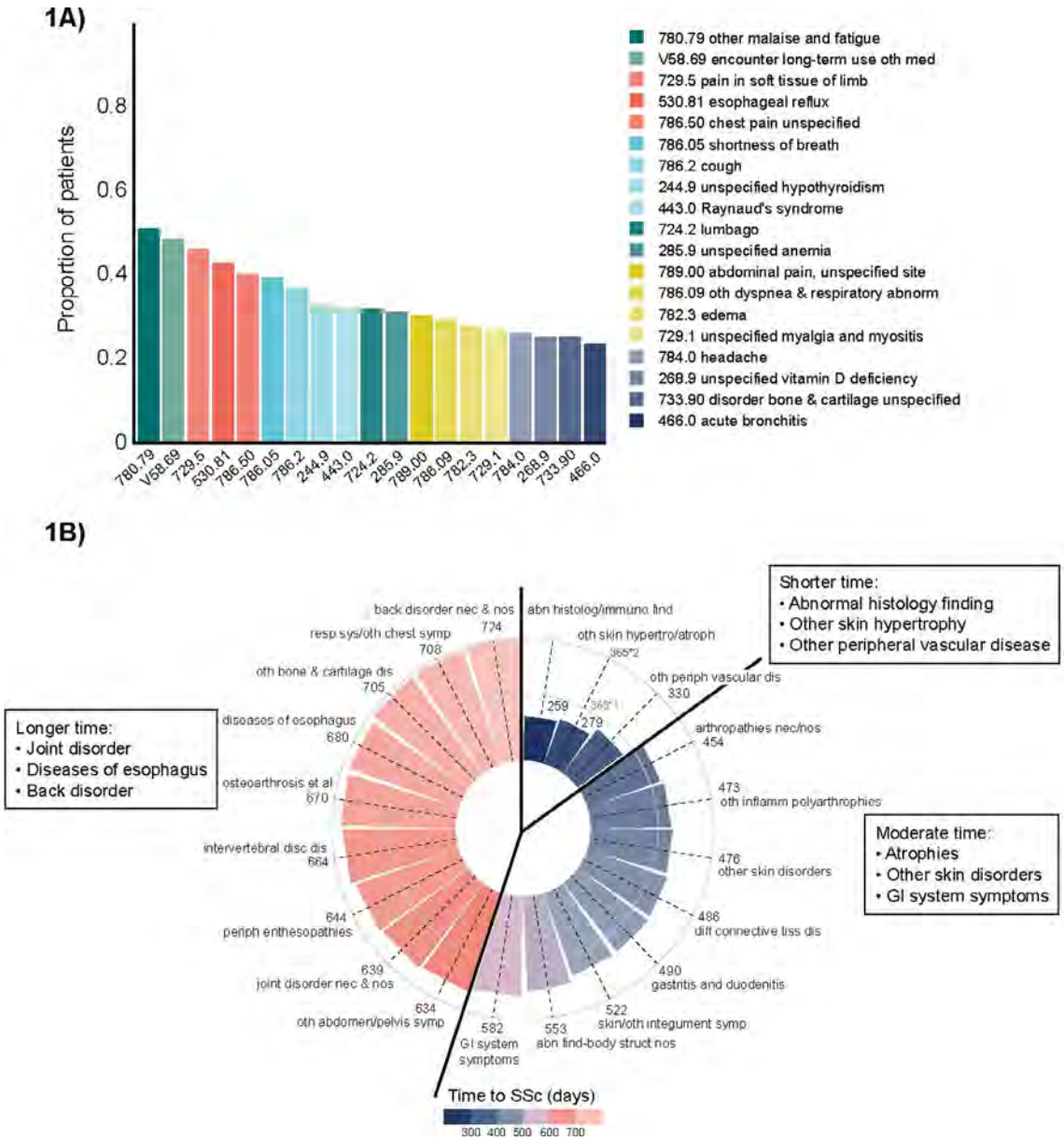


Figure 1. Diagnoses prior to SSc (A) and time to SSc diagnosis (B) in the USA

in the USA and 327 days in Japan), whereas it was almost double this when the complaint was more related to joint pain, fatigue or GI symptoms (Figures 1b & 2b).

Conclusion: Collectively, within the limitations of analyzing data from insurance claims and ICD codes, these real-world data showing a range of diagnoses prior to SSc help to identify the health burden leading to a diagnosis of SSc. These findings suggest that symptoms not directly related to Raynaud's or skin manifestations such as upper GI involvement and joint pain may not be recognized as early signs of SSc. Further deconvolution of the frequency and temporal distribution of symptoms that patients commonly present with prior to being diagnosed with SSc could help identify other "red flags" that physicians should consider when triggering a diagnostic workup for SSc, ultimately improving early detection and long-term outcomes.

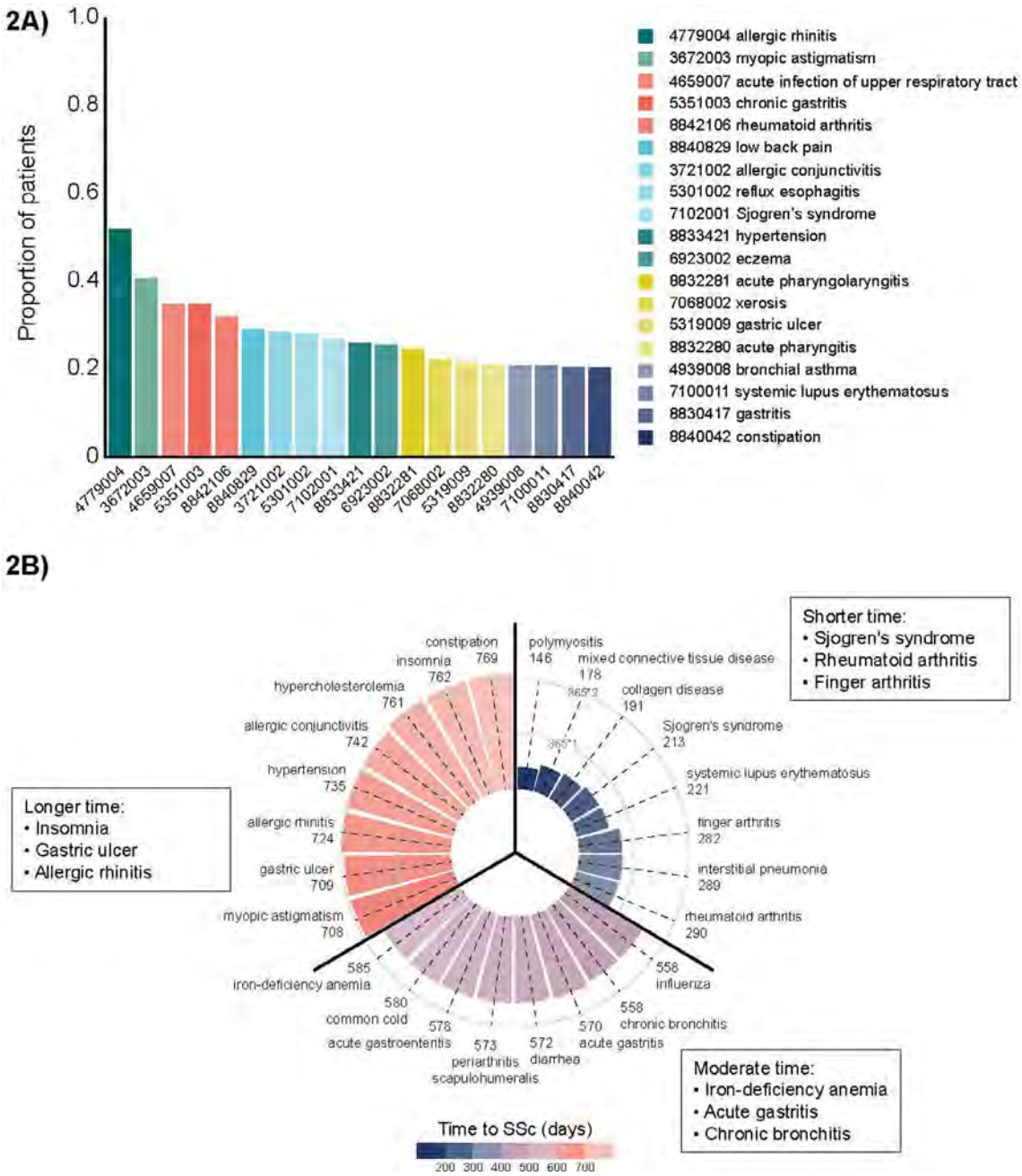


Figure 2. Diagnoses prior to SSc (A) and time to SSc diagnosis (B) in the Japan

Disclosure: F. Del Galdo: AbbVie/Abbott, 5, arxx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, capella, 2, Chemomab, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Mitsubishi-Tanabe, 2, 5; **Y. Tian**: Boehringer Ingelheim, 3; **S. Di Donato**: None; **M. Ehlers**: Boehringer Ingelheim, 3.

Abstract Number: 0118

Physical Performance Among Individuals with Systemic Lupus Erythematosus in a Diverse Population-Based Cohort

Courtney Hoge[1], C. Barrett Bowling[2], Charmayne Dunlop-Thomas[1], Bradley Pearce[1], S. Sam Lim[1], Cristina Drenkard[1] and Laura Plantinga[1], [1]Emory University, Atlanta, GA, [2]Duke University, Durham, NC

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Physical performance is often not measured in clinical settings, despite its association with increased risk of disability, loss of independence, and mortality. Here, we sought to examine the prevalence and correlates of poor physical performance among individuals with systemic lupus erythematosus (SLE) who were recruited from a primarily Black, population-based cohort in Atlanta.

Methods: Participants were recruited for an ancillary study from the ongoing, population-based Georgians Organized Against Lupus (GOAL) cohort of individuals with SLE. Those who had complete Short Physical Performance Battery [SPPB: score range, 0-12; intermediate-low (< 10) vs. high (≥10)] data from either an in-person or a remote study visit (10/8/19-5/12/22) were included. Demographic, clinical, and psychosocial variables were summarized, and the associations [adjusted odds ratios (aOR)] of intermediate-low vs. high physical performance with these characteristics were estimated via multivariable logistic regression.

Results: Among 446 participants (mean age 46.2, 91.7% female, and 82.5% Black), more than half (59.6%) had poor (intermediate-low) overall physical performance (**Figure 1**). Only 7% of the cohort received the maximum score on the lower body strength task, as opposed to 90% and 76% receiving the maximum scores on balance and gait speed tasks, respectively

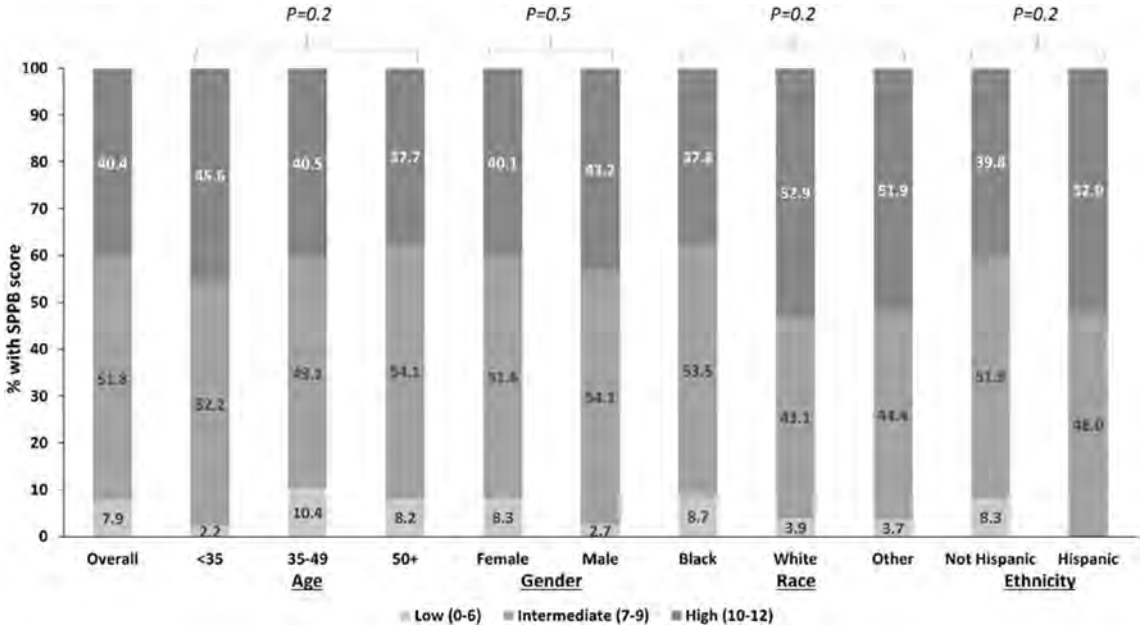


Figure 1. Short Physical Performance Battery scores (range 0-12, higher scores indicating higher levels of physical performance) among study participants, overall and by participant demographics.

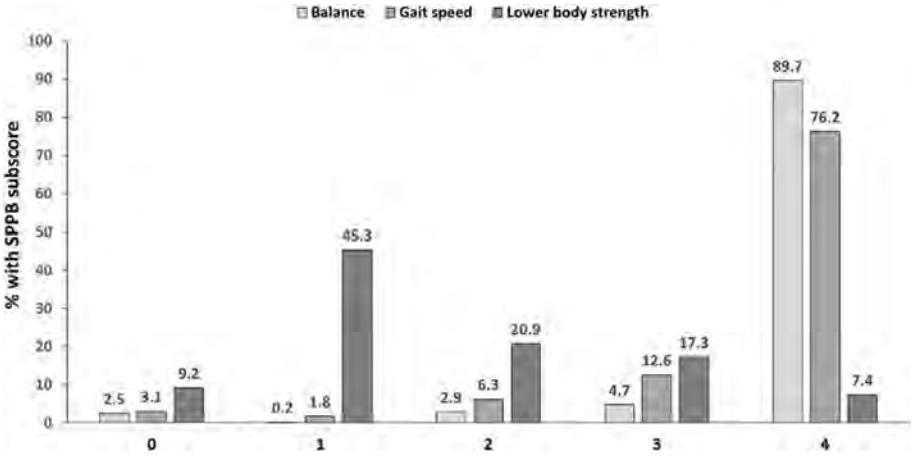


Figure 2. Short Physical Performance Battery subscores (range 0-4, 0=inability to perform task, 4=highest level of performance) for balance, gait speed, and lower body strength (chair stands) among study participants.

Table 1. Associations of intermediate or low (<10) vs. high (10-12) physical performance scores with participant characteristics.

Characteristic	aOR[a] for intermediate-low vs. high SPPB score (95% CI)
Age category	
18-34 vs. ≥50	0.85 (0.23-3.14)
35-49 vs. ≥50	0.92 (0.43-1.98)
Male vs. female gender	0.98 (0.46-2.06)
Race	
White vs. Black	0.59 (0.31-1.11)
Other vs. Black	0.62 (0.27-1.41)
Hispanic vs. not Hispanic	0.95 (0.35-2.55)
Highest level of education completed	
≤High school graduate vs. ≥college graduate	1.71 (0.99-2.96)
Some college vs. ≥college graduate	1.17 (0.74-1.85)
Currently working vs. not	0.69 (0.45-1.05)
SLAQ score, per 1 SD	1.59 (1.27-1.98)
BILD score, per 1 SD	1.38 (1.08-1.77)
Currently taking steroids vs. not	0.95 (0.62-1.45)
BMI, per 1 SD	1.25 (1.01-1.56)
Depressive symptoms T-score, per 1 SD (10 points)	1.23 (0.96-1.58)
Perceived stress score, per 1 SD	1.15 (0.91-1.46)
Fluid cognition T-score, per 1 SD (10 points)[b]	0.57 (0.42-0.77)

BILD, Brief Index of Lupus Damage; BMI, body mass index; SLAQ, Systemic Lupus Activity Questionnaire; SPPB, Short Physical Performance Battery.
[a]Adjusted for age in years, gender, race, visit type (in-person vs. remote), and SLAQ score.
[b]For in-person visits only.

(**Figure 2**). Current employment status and higher cognitive functioning were associated with 31% and 43% lower odds of intermediate-low physical performance (**Table 1**). Higher body mass index, disease activity, and disease burden were associated with 25%, 59%, and 38% higher odds of poorer performance, as were higher depressive symptom and perceived stress scores and lower educational attainment.

Conclusion: In our diverse cohort of individuals with SLE, we found a high burden of low to intermediate physical performance and identified SLE- and non-SLE-related factors associated with poorer performance. Clinicians may use these results to identify patients who are most at risk for suboptimal physical performance and intervene to maintain or improve performance levels, which could delay or prevent associated poor outcomes and help ensure continued independence.

Disclosure: C. Hoge: None; **C. Bowling**: None; **C. Dunlop-Thomas**: None; **B. Pearce**: None; **S. Lim**: None; **C. Drenkard**: None; **L. Plantinga**: None.

Abstract Number: 0119

Mortality-related Health Metrics in Systemic Autoimmune Diseases: An Epidemiological Analysis of a Nationwide Register-based Cohort

Mucong Li[1], Chanyuan Wu[2], Peng Yin[3], Qian Wang[4], Dong Xu[5], Xiaomei Leng[2], Xinping Tian[1], Ali Duarte-Garcia[6], Mengtao Li[1], xiaofeng Zeng[4] and Maigeng Zhou[3], [1]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China, [2]Peking Union Medical College Hospital, Beijing, China, [3]Chinese Center for Disease Control and Prevention, Beijing, China, [4]Department of Rheumatology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China, [5]Department of Rheumatology, Peking Union Medical College, Beijing, China, [6]Mayo Clinic, Rochester, MN

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Epidemiology & Public Health Poster I

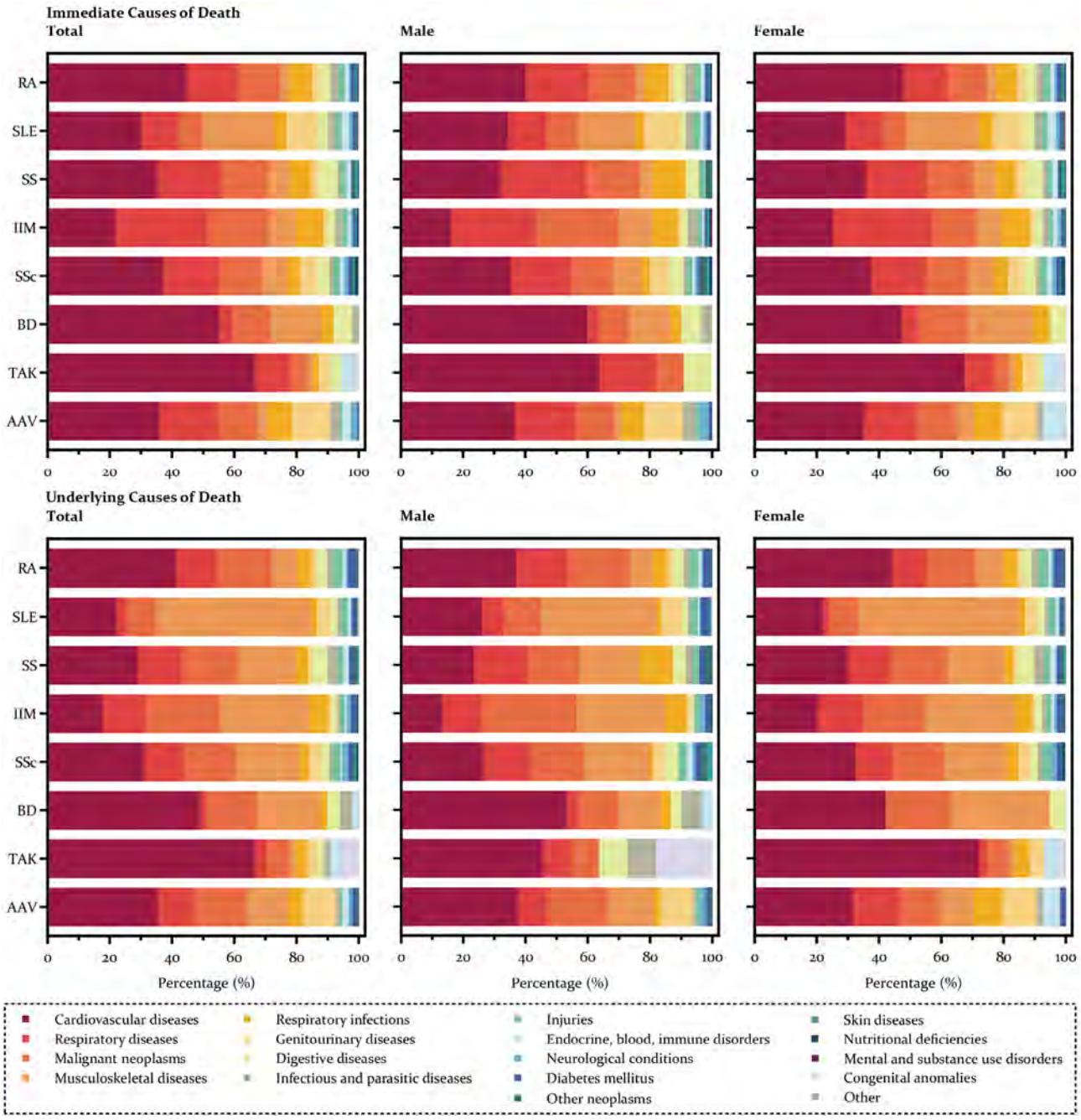
Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic autoimmune diseases (sAIDs) have become leading contributors to premature death. Meanwhile, regional disparities exist in capacity of rheumatology healthcare services delivery. However, no rigorous epidemiological studies have provided an integrated overview of mortality burden of various sAIDs, especially in low-to-middle income countries (LMICs). In this study, we comprehensively analyzed mortality rates, survival probabilities, causes of death, and standardized mortality ratios (SMRs) of eight sAIDs in China and examined the associations between disease burden of sAIDs and development indicators.

Methods: In this nationwide, register-based cohort study, we used data from Chinese Rheumatism Data Center, Nation Mortality Surveillance System, and public databases with a universal coverage of 31 provinces in mainland China between Jan 1, 2011, and Dec 31, 2021. We collected data on patient demographics, clinical status, and vital outcomes of individuals with RA, SLE, SS, IIM, SSc, Behçet's disease (BD), Takayasu's arteritis (TAK), and AAV. Mortality rates, survival probabilities, causes of death, and SMRs were estimated in patients classified by gender, age at disease onset, and area-level socioeconomic status (including a composite indicator, human development index [HDI], and indicators in economy, healthcare, and education).

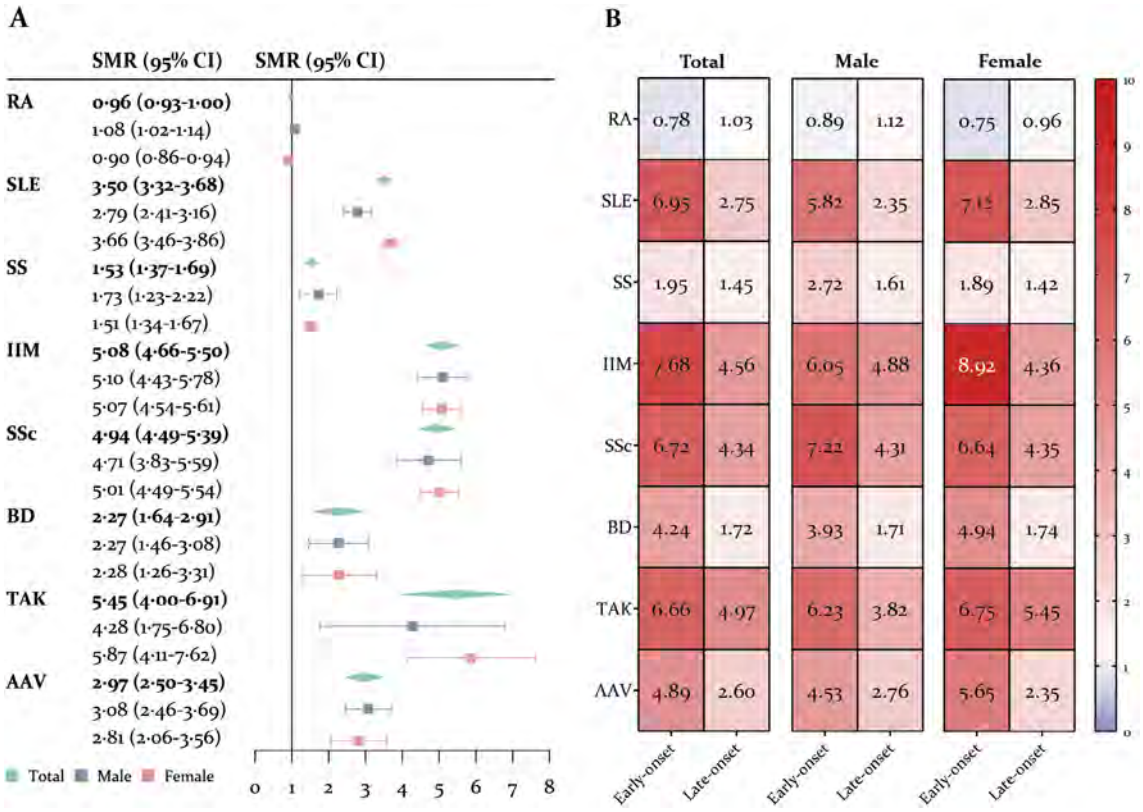
Results: Between 2011 and 2021, 156 862 individuals (87132 with RA, 44658 with SLE, 11668 with SS, 4864 with IIM, 4065 with SSc, 1762 with BD, 1558 with TAK, and 1155 with AAV) were included, with a median duration of follow-up 5.12 (IQR 3.08-8.67) years. AAV, IIM, and SSc were top three diseases with the highest fatality rates and lowest survival rates. Cardiovascular, respiratory (non-infection), musculoskeletal, malignancy, and genitourinary diseases were the leading causes of death (Figure 1). The age-, gender-, and calendar year-adjusted SMR was highest for TAK (5.45, 95%CI 4.00-6.91), followed by IIM (5.08, 4.66-5.50), SSc (4.94, 4.49-5.39), SLE (3.50, 3.32-3.68), AAV (2.97, 2.50-3.45), BD (2.27, 1.64-2.91), SS (1.53, 1.37-1.69), and RA (0.96, 0.93-1.00). Early disease-onset is a risk factor of excess death in patients with sAIDs (Figure 2). Additionally, higher HDI was associated with significant increases in mortality risks in both RA and SLE (SMR ratio 12.24 and 5.15 for 1-unit increase in HDI, $p< 0.001$ and $p=0.080$) patients compared with region-specific general population. More medical institutions (SMR ratio 0.95 for one more medical institution per 10 000 resident population, $p=0.005$) and hospital beds (SMR ratio 0.35 for one more hospital bed per 100 resident population, $p=0.131$) were protect factors of excess mortality in SLE.



Conclusion: The mortality risk in patients with sAIDs can be in substantial excess versus general population, and sAIDs are becoming important contributors to premature mortality in China. Increasing mortality burden associated with sAIDs implied the relative insufficiency of capacity building of diagnosis and treatment in sAIDs in LMICs, raising important need for establishing universal health coverage systems for the affected patients.

Causes of death in systemic autoimmune diseases

Standardized mortality ratios of systemic autoimmune diseases. (A) Point estimates and 95% CIs of standardized mortality ratios (SMRs) in total, male, and female patients are presented for 8 systemic autoimmune diseases. (B) SMRs are presented in early- and late-onset patients with 8 systemic autoimmune diseases, stratified by gender.



Disclosure: M. Li: None; **C. Wu**: None; **P. Yin**: None; **Q. Wang**: None; **D. Xu**: None; **X. Leng**: None; **X. Tian**: None; **A. Duarte-Garcia**: None; **M. Li**: None; **x. Zeng**: None; **M. Zhou**: None.

Abstract Number: 0120

Incidence and Prevalence of Systemic Lupus Erythematosus in Urban China, 2013-2017: A Nationwide Population-based Study

Mucong Li[1], Chaiquan Li[2], Mengzhuo Cao[3], Ke Lu[2], Chanyuan Wu[3], Jiuliang zhao[1], Qian Wang[4], Xinping Tian[1], Xun Tang[2], Mengtao Li[1], xiaofeng Zeng[4] and Pei Gao[2], [1]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China, [2]Peking University, Beijing, China, [3]Peking Union Medical College Hospital, Beijing, China, [4]Department of Rheumatology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Epidemiology & Public Health Poster I

Session Type: Poster Session A

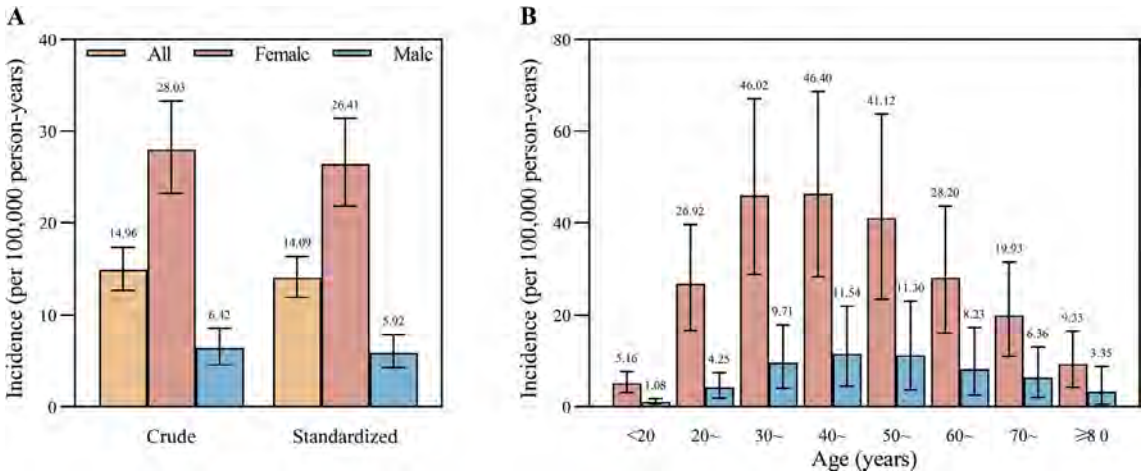
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is becoming a public health concern because of increasing disease and economic burdens. Epidemiological information on SLE, especially its incidence rate, was limited in developing countries. We aimed to investigate the incidence, prevalence, and cost burdens of SLE in urban China.

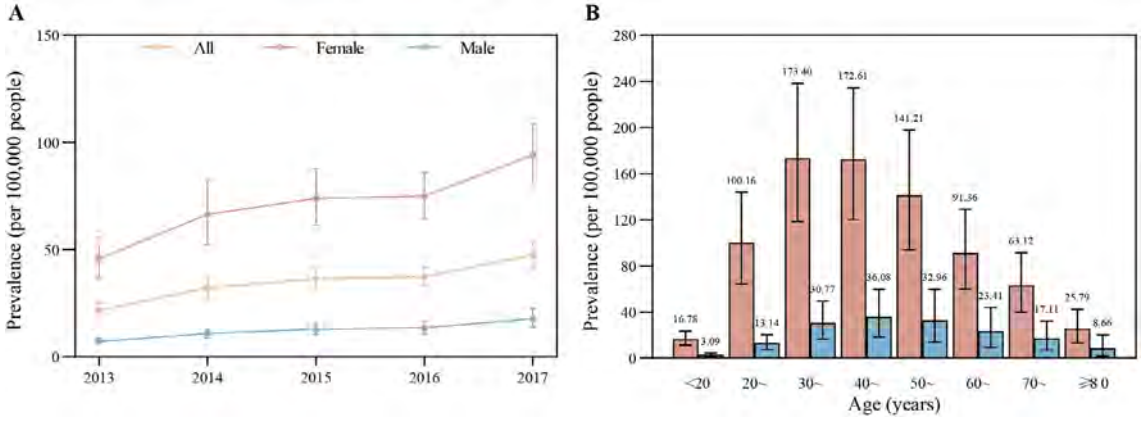
Methods: We conducted a nationwide population-based cohort study using the databases of Urban Employee Basic Medical Insurance and Urban Resident Basic Medical Insurance between 2013 and 2017, covering 23 provinces in China. Incidence and prevalence rates were age- and gender-standardized to China 2010 national census data. Average annual costs and hospital visit times were also calculated.

Results: Total 132,258 patients with SLE were identified during the study period. The mean age was 43.03 (SD, 15.29) years. Overall 81.33% of patients were women. The standardized incidence of SLE in China in 2017 was 14.09 (95%CI, 11.95-16.41) per 100,000 person-years (Figure 1). Women had higher incidence than men (26.41 vs 5.92 per 100,000 person-years). The standardized prevalence in 2017 were 47.61 (95%CI, 41.77-53.83), 94.16 (80.67-108.69), and 17.86 (13.84-22.38) per 100,000 people in overall, female, and male patients (Figure 2). The average annual rates of increase in prevalence were 21.50%, 19.72%, and 25.67% from 2013 to 2017 in overall, female, and male patients. The age-specific incidence peaked at 30-49 years old in women and at 40-59 years old in men. SLE incident and prevalent cases were most common in northwestern and less in south and east China (Figure 3). Additionally, the average estimated annual cost per-capita was US $1,599.34 in SLE patients. Costs of adolescent and young adult patients were the highest among age groups.

Conclusion: SLE population in China is rapidly expanding. Younger age at onset, especially in women, has placed considerable burdens in China. The distinct signatures of different incidence rates with respect to geographic variations were consistent with regions' exposure to ultraviolet radiation in China.



Incidence of SLE in urban China in 2017



Standardized prevalence of SLE in urban China from 2013 to 2017

Standardized incidence and prevalence rates of SLE by regions in China in 2017

Disclosure: M. Li: None; **C. Li**: None; **M. Cao**: None; **K. Lu**: None; **C. Wu**: None; **J. zhao**: None; **Q. Wang**: None; **X. Tian**: None; **X. Tang**: None; **M. Li**: None; **x. Zeng**: None; **P. Gao**: None.

Abstract Number: 0121

High Prevalence of Mental Health Disorders Among Patients with Rheumatoid Arthritis and Systemic Lupus Erythematosus

Jeong Yee[1], Candace Feldman[1], Emily G. Oakes[1], Elizabeth Karlson[1], Jack Ellrodt[1], Laura Kubzansky[2], Karestan Koenen[2] and Karen Costenbader[3], [1]Brigham and Women's Hospital, Boston, MA, [2]Harvard T.H. Chan School of Public Health, Boston, MA, [3]Brigham and Women's Hospital and Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are complex autoimmune diseases associated with pain and decreased quality of life. Mental health conditions related to stress and emotional distress, in particular depression, anxiety, and post-traumatic stress disorder (PTSD), appear to be common among those with these rheumatic diseases, but estimates in large diverse populations are not yet available. We assessed the prevalence of these three mental health conditions among patients with RA and SLE, comparing them to those without in a large and diverse healthcare center-based nationwide cohort.

Methods: We conducted a cross-sectional study within the All of Us Research Program, an ongoing NIH-funded cohort that enrolled US adults age ≥18 from May 6, 2018 - July 1, 2022 (release v7). It includes consented electronic health record (EHR) data for >287,000 people. RA and SLE patients were identified by ≥ 2 International Classification of Diseases (ICD)-9, ICD-10, and Systematized Nomenclature of Medicine (SNOMED) codes >2 months apart but within ≤2 years prior to enrollment. Depression, anxiety, and PTSD were also identified by ICD-9 or-10, and SNOMED codes within 1 year prior to enrollment. Prevalence of each mental health disorder among patients with RA and SLE was compared to age-, sex-, and race/ethnicity-matched patients (1:4 matched). Conditional logistic regression models estimated odds ratios (ORs) for these mental health conditions, adjusting sequentially for socioeconomic factors (Model 1), + smoking, obesity, and other comorbidities (Model 2). Age-stratified analysis was performed for groups aged 18-44, 45-64, and ≥65 years.

Results: After matching for age, sex, and race/ethnicity, we studied 4,370 RA patients, 1,977 SLE patients, and their matched controls (17,479 for RA; 7,908 for SLE) (**Table 1**). Both RA and SLE patients had lower educational attainment, and were less frequently privately insured, and more comorbidities than their matched controls. Compared to controls, RA patients had higher prevalence of depression (24.2 % vs. 11.5%), anxiety (21.4% vs. 11.2%), and PTSD (3.5% vs. 1.6%) (**-Figure 1**). Similarly, compared to controls, SLE patients had higher prevalence of depression (23.6% vs. 11.9%), anxiety (22.8% vs. 12.0%), and PTSD (3.7% vs. 2.1%). **Table 2** shows sequential modeling results. While adjusting for potential confounders, which attenuated the ORs, RA patients vs controls had 1.7-fold (95% CI 1.5-1.9) higher odds of these mental health conditions in fully-adjusted models. For SLE patients, the adjusted OR was 1.9 (95% CI: 1.6-2.4). In the age-stratified analysis, the adjusted ORs were similar in each group, ranging from 1.5 to 1.8 in RA patients and from 1.8 to 2.3 in SLE patients.

Conclusion: Patients with RA and those with SLE had elevated prevalence of mental health conditions related to stress, trauma, and emotional distress than controls in the year prior to their cohort enrollment. These highly prevalent stress-related mental health conditions may complicate the care and treatment of rheumatic diseases. Research is ongoing to understand how mental health treatments affect rheumatic disease outcomes.

Table 1. Demographic and survey data of patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) vs. their matched controls in All of Us (data release v7, through July 2022)

	RA (n=4,370)	Controls for RA (n=17,479)	SMD (Controls vs. RA)	SLE (n=1,977)	Controls for SLE (n=7,908)	SMD (Controls vs. SLE)
Age, mean ± SD, y	59.6 ± 13.5	59.6 ± 13.5	<0.01	50.6 ± 14.2	50.6 ± 14.2	<0.01
Female	3,511 (80.3)	14,043 (80.3)	<0.01	1,802 (91.1)	7,208 (91.1)	<0.01
Race/ethnicity			<0.01			<0.01
Hispanic	799 (18.3)	3,196 (18.3)		482 (24.4)	1,928 (24.4)	
Non-Hispanic Black	751 (17.2)	3,004 (17.2)		602 (30.5)	2,408 (30.5)	
Non-Hispanic Other	212 (4.9)	847 (4.8)		130 (6.6)	520 (6.6)	
Non-Hispanic White	2,608 (59.7)	10,432 (59.7)		763 (38.6)	3,052 (38.6)	
Annual household income < $35,000	1,590 (46.0)	4,795 (33.6)	0.254	811 (53.4)	2,571 (38.8)	0.296
High school graduate or less	1,233 (28.7)	3,881 (22.6)	0.140	571 (29.3)	1,888 (24.3)	0.113
Public health insurance	2,138 (55.2)	6,976 (44.3)	0.221	982 (57.0)	2,912 (40.5)	0.335
Region			0.291			0.373
Northeast	1,748 (40.0)	4,721 (27.0)		695 (35.2)	1,662 (21.0)	
Midwest	932 (21.3)	5,147 (29.5)		399 (20.2)	2,622 (33.2)	
South	569 (13.0)	2,746 (15.7)		361 (18.3)	1,455 (18.4)	
West	1,118 (25.6)	4,851 (27.8)		521 (26.4)	2,165 (27.4)	
Area deprivation index, median (IQR)	0.31 (0.08)	0.31 (0.08)	0.023	0.33 (0.09)	0.32 (0.09)	0.098
Ever smoking history	1,862 (43.8)	6,717 (40.5)	0.067	633 (33.2)	2,705 (36.9)	0.078
Obesity[a]	2,021 (49.1)	5,995 (43.2)	0.117	891 (47.3)	2,624 (49.8)	0.050
Charlson comorbidity index[b]	1.7 ± 2.3	1.0 ± 1.9	0.348	1.8 ± 2.3	0.8 ± 1.7	0.501

RA: rheumatoid arthritis. SMD: standardized mean difference. SLE: systemic lupus erythematosus
[a]Obesity defined by body mass index (BMI) ≥30 kg/m² from enrollment physical measurement data
[b]Charlson comorbidity index was calculated using 16 comorbidities, excluding rheumatic diseases

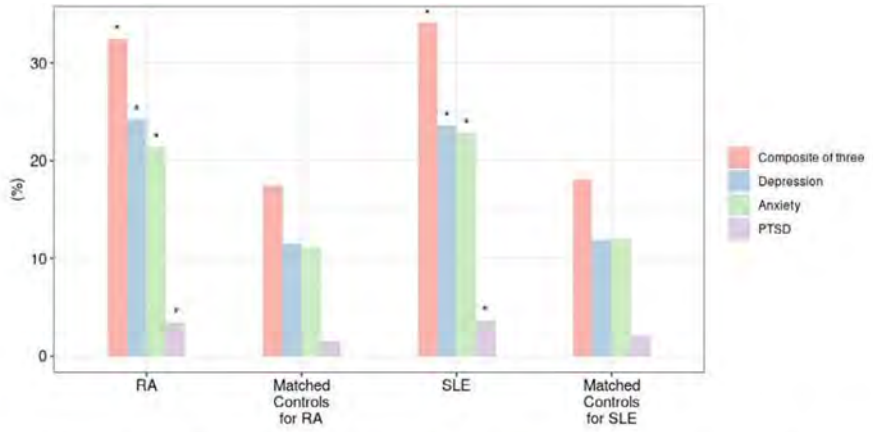


Figure 1. Unadjusted prevalence of three mental health conditions (depression, anxiety and post-traumatic stress disorder, PTSD) in patients with rheumatoid arthritis and systemic lupus erythematosus compared to matched controls in All of Us (v7). RA: rheumatoid arthritis. SLE: systemic lupus erythematosus. *p<0.001.

Table 2. Unadjusted and adjusted odds ratios for prevalence of the three mental health conditions (depression, anxiety, and post-traumatic health disorder, PTSD) and composite conditions among patients with rheumatoid arthritis or systemic lupus erythematosus compared to matched controls in All of Us (v7).

Conditions	Model	Odds ratio (95% CI) for patients with rheumatoid arthritis vs. controls	Odds ratio (95% CI) for patients with systemic lupus erythematosus vs. controls
Depression	Unadjusted	2.49 (2.29-2.71)	2.31 (2.03-2.61)
	Model 1	2.11 (1.88-2.36)	2.08 (1.75-2.48)
	Model 2	1.87 (1.63-2.15)	1.85 (1.46-2.34)
Anxiety	Unadjusted	2.19 (2.01-2.39)	2.20 (1.94-2.50)
	Model 1	1.88 (1.67-2.11)	1.98 (1.66-2.36)
	Model 2	1.60 (1.39-1.84)	1.69 (1.33-2.14)
PTSD	Unadjusted	2.16 (1.77-2.64)	1.83 (1.39-2.42)
	Model 1	1.78 (1.33-2.38)	1.64 (1.07-2.51)
	Model 2	1.49 (1.03-2.16)	1.56 (0.88-2.76)
Composite of three	Unadjusted	2.32 (2.15-2.50)	2.37 (2.12-2.65)
	Model 1	2.00 (1.81-2.21)	2.18 (1.87-2.54)
	Model 2	1.68 (1.49-1.90)	1.93 (1.57-2.37)

Model 1 adjusted for annual household income, education level, insurance type, geographical region, and area deprivation index. Model 2 additionally adjusted for smoking, obesity, and Charlson Comorbidity Index (calculated with 16 comorbidities, excluding rheumatic disease).

Disclosure: J. Yee: None; **C. Feldman**: BMS Foundation, 5, Curio Bioscience, 12, My husband is one of the founders and will receive equity (but has not received anything to date)., OM1, Inc., 2, Pfizer, 5; **E. Oakes**: None; **E. Karlson**: None; **J. Ellrodt**: None; **L. Kubzansky**: None; **K. Koenen**: None; **K. Costenbader**: Amgen, 2, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Eli Lilly, 2, Exagen Diagnostics, 5, Gilead, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5.

Abstract Number: 0122

Depression, Anxiety and Post-Traumatic Stress Disorder in Association with Cardiovascular Disease Among Patients with Systemic Lupus Erythematosus and Rheumatoid Arthritis in the All of Us Research Program

Jeong Yee[1], Emily G. Oakes[1], May Choi[2], Candace Feldman[1], Elizabeth Karlson[1] and Karen Costenbader[3], [1]Brigham and Women's Hospital, Boston, MA, [2]University of Calgary, Calgary, AB, Canada, [3]Brigham and Women's Hospital and Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Epidemiology & Public Health Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular disease (CVD) risk is increased for patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Mental health conditions such as depression, anxiety, and post-traumatic stress disorder (PTSD) are not traditional CVD risk factors but have been associated with CVD risk and are highly prevalent in SLE and RA populations. We assessed the contribution of these 3 mental health conditions related to stress and emotional distress to CVD risk among patients with RA and/or SLE in a large, diverse U.S. cohort.

Methods: We used data from the All of Us Research Program (v7), a NIH cohort with >287,000 adult participants in the U.S. who gave consent for linkage to their electronic health records. RA/SLE patients were identified by ≥2 ICD-9, ICD-10, or SNOMED codes >2 months apart within 2 years of enrollment. We excluded patients with acute myocardial infarction (MI) and stroke at baseline (1 year pre-enrollment). Depression, anxiety, and PTSD were identified by ICD-9/10, and SNOMED codes in the baseline period. The primary outcome was a composite of acute MI, stroke (identified by ICD9/10

and SNOMED codes), and all-cause mortality. Patients were followed until the 1st acute MI, stroke, or death, through 4 years or end of study period (July 1, 2022). Covariates included age, sex, and race/ethnicity, income, educational level, smoking, obesity, and comorbidities. We estimated incidence rates (IRs) and incidence rate ratios (IRRs). Adjusted Cox regression models compared risks of the endpoint of acute MI, stroke, or all-cause mortality among RA/SLE patients with and without these 3 mental health conditions.

Results: We studied 3,825 patients with RA only, 1,862 with SLE (including 383 with meeting both definitions). Among them,1,790 (31.5%) had depression, anxiety, and/or PTSD (**Table 1**). Compared to patients without, those with ≥1 mental health conditions were more likely to be less educated, in a low-income group, to have ever smoked, to be obese, and to

Table 1. Baseline demographic and clinical characteristics of study populations in All of Us Research Program (data release v7, n=5,687)

	RA/SLE patients with mental health conditions[a] (n=1,790)	RA/SLE patients without mental health conditions (n=3,897)	p
Age category, years, (%)			<0.001
18-49	544 (30.4%)	1,065 (27.3%)	
50-64	744 (41.6%)	1,435 (36.8%)	
65-	502 (28.0%)	1,397 (35.8%)	
Female	1,543 (86.2%)	3,208 (82.3%)	<0.001
Race/ethnicity			0.022
Hispanic	356 (19.9%)	757 (19.4%)	
Non-Hispanic Black	348 (19.4%)	839 (21.5%)	
Non-Hispanic Others	78 (4.4%)	226 (5.8%)	
White	1,008 (56.3%)	2,075 (53.2%)	
High school graduate or less	572 (32.0%)	1,009 (25.9%)	<0.001
Annual household income <$35,000	814 (45.5%)	1,281 (32.9%)	<0.001
Ever Smoking	787 (45.3%)	1,444 (38.2%)	<0.001
Obesity[b]	930 (55.9%)	1,685 (45.3%)	<0.001
CVD-related Comorbidities			
Hypertension	1,051 (58.7%)	1,531 (39.3%)	<0.001
Dyslipidemia	789 (44.1%)	1,153 (29.6%)	<0.001
Diabetes	499 (27.9%)	680 (17.4%)	<0.001
Charlson comorbidity index[c]			<0.001
0	490 (27.4%)	1,999 (51.3%)	
1	423 (23.6%)	709 (18.2%)	
2+	877 (49.0%)	1,189 (30.5%)	
Mental health conditions			
Depression	1,305 (72.9%)		-
Anxiety	1,177 (65.8%)		-
PTSD	192 (10.7%)		-
Follow-up, months (mean, SD)	31.2 ± 14.8	30.9 ± 14.6	0.468

PTSD: Post-traumatic stress disorder. RA: rheumatoid arthritis. SLE: systemic lupus erythematosus.
[a] Depression, anxiety, and/or PTSD (≥1 one condition)
[b] Obesity was defined by body mass index (BMI) ≥30 kg/m^2 from physical measurement data.
[c] Charlson comorbidity index was calculated using 16 comorbidities, excluding rheumatic diseases.

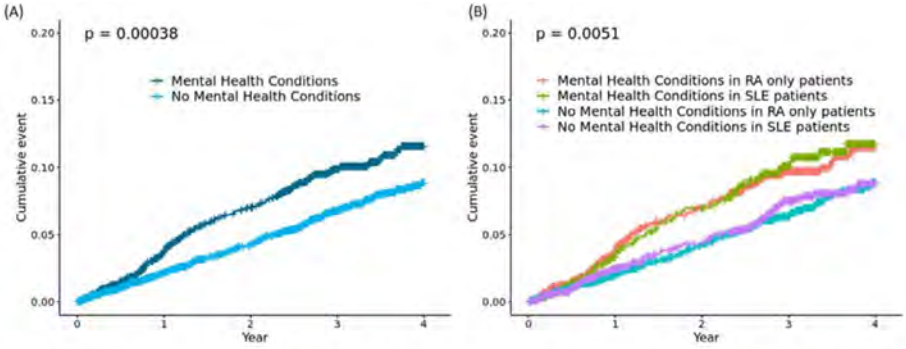


Figure 1. Unadjusted cumulative incidence curves for time to acute MI, stroke, or all-cause mortality for patients with rheumatoid arthritis (RA) and/or systemic lupus erythematosus (SLE), with and without mental health conditions (depression, anxiety, and post-traumatic stress disorder, PTSD) within the All of Us Research Program. (A) Overall analysis. (B) Stratified analysis by disease (patients with RA only and SLE).

Table 2. Hazard ratios for Acute MI, Stroke, or All-cause Mortality Risks for Patients with Mental Health Conditions compared to those without among Patients with Rheumatoid Arthritis and/or Systemic Lupus Erythematosus in the All of Us Research Program, v.7 (14,680 person-years)

	Hazard ratio	95% CI
Model 1	1.52	1.24-1.88
Model 2	1.28	1.02-1.60

Model 1 adjusted for age, sex, race/ethnicity, annual household income, and education level.
Model 2 adjusted for smoking, obesity, and Charlson comorbidity index (calculated with 16 comorbidities, excluding rheumatic disease) in addition to the factors adjusted in Model 1.

have comorbidities. Patients were followed for a mean of 31.0 months (SD 14.7). 155 events (64 MI, 55 strokes and 36 deaths) occurred among RA/SLE patients with mental health conditions in 55,856 person-months (IR 33.3/1000 person-years) vs. 232 (75 MI, 117 strokes and 40 deaths) among those without mental health diagnoses in 120,422 person-months (IR 23.1/1000 person-years; IRR 1.44). The risk of acute MI, stroke, and death was significantly higher among patients with these mental health conditions than without for both RA and SLE (**Figure 1**). After adjustment for smoking, obesity, and Charlson comorbidity index, the HR of incidence of MI, stroke, or all-cause mortality for patients with concomitant mental health conditions was 1.28 (95% CI 1.02-1.60, **Table 2**).

Conclusion: In this large diverse U.S. cohort of patients with RA/SLE without prior CVD events, depression, anxiety and PTSD were associated with increased risk of developing acute MI, stroke, or death. These results suggest greater awareness of increased CVD risk among rheumatic disease patients with concurrent mental health conditions is needed. Research is ongoing to dissect the likely multifactorial causal pathways underlying this relationship.

Disclosure: J. Yee: None; **E. Oakes**: None; **M. Choi**: AbbVie/Abbott, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 6, Mallinckrodt, 2, Merck/MSD, 2, MitogenDx, 2, Organon, 6, Pfizer, 2, 6, Roche, 2, Werfen, 2; **C. Feldman**: BMS Foundation, 5, Curio Bioscience, 12, My husband is one of the founders and will receive equity (but has not received anything to date)., OM1, Inc., 2, Pfizer, 5; **E. Karlson**: None; **K. Costenbader**: Amgen, 2, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Eli Lilly, 2, Exagen Diagnostics, 5, Gilead, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5.

Abstract Number: 0123

Improving Interpretation of Work Outcomes in Patients with Inflammatory Rheumatic Musculoskeletal Disease: General Population Reference Curves for Work Ability and At-work Productivity

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Data on self-reported presenteeism (limitations or reduced work productivity at work) in persons with inflammatory rheumatic and musculoskeletal diseases (iRMD) are challenging to interpret without a population benchmark, as presenteeism likely also occurs in the general working population. Our objective was to establish percentile curves (reference intervals [RI]) for ability and productivity while at paid work in a general working population.

Methods: A cross-sectional study was nested within an ongoing prospective Dutch cohort study on COVID-19, including patients with iRMD and general population controls. Participants with paid work (≥12 working hours/week) reported on work ability (Work Ability Index, range 0-10 [worst-best ability]) and work productivity (Work Productivity and Activity Impairment scale item 5 on productivity loss, range 0-100% [no-complete productivity loss]). A generalized additive model for location, shape and scale parameters (GAMLSS) with a zero-one inflated beta distribution was chosen to assess the association of age, gender, educational level, full- or part time employment and job demands with each presenteeism instrument (work ability, work productivity). Next, GAMLSS was used to establish age-specific RIs percentile curves for controls, stratified by relevant determinants when needed. Finally, the proportion of controls compared to patients with optimal outcomes (work ability=10 and productivity loss=0%) was calculated.

Results: A total of 446 controls were included; 327 (73%) were female, mean age 53 (SD 11) years, 188 (42%) had university education, mean work ability was 8.7 (1.6) [median 9 (IQR 2-10)] and mean at-work productivity loss 11% (25%) [0 (0-100)]. Education influenced work ability as well as work productivity loss. Percentile curves revealed that work ability decreases and productivity loss at work increases with age (Fig 1). While more than 50% of controls reported at least some impairment in work ability, more than 75% indicated having no productivity loss at work. Non-university education was strongly associated with both presenteeism outcomes. Stratification of percentile curves for work ability by education showed high variability in work ability with worse as well as better scores in small proportions of the older (compared to younger) controls (Fig 2). For productivity loss, non-university educated controls experienced increase in productivity loss in the older age groups. Plotting data form 494 patients with iRMD into the percentile curves revealed patients were less likely to have optimal work ability [151/494 (31%) vs 169/390 (43%) in controls] or no productivity loss [305/494 (62%) in patients vs 328/390 (83%) in controls]. Across percentiles, differences between patients and controls were larger for work productivity than work ability independent of age.

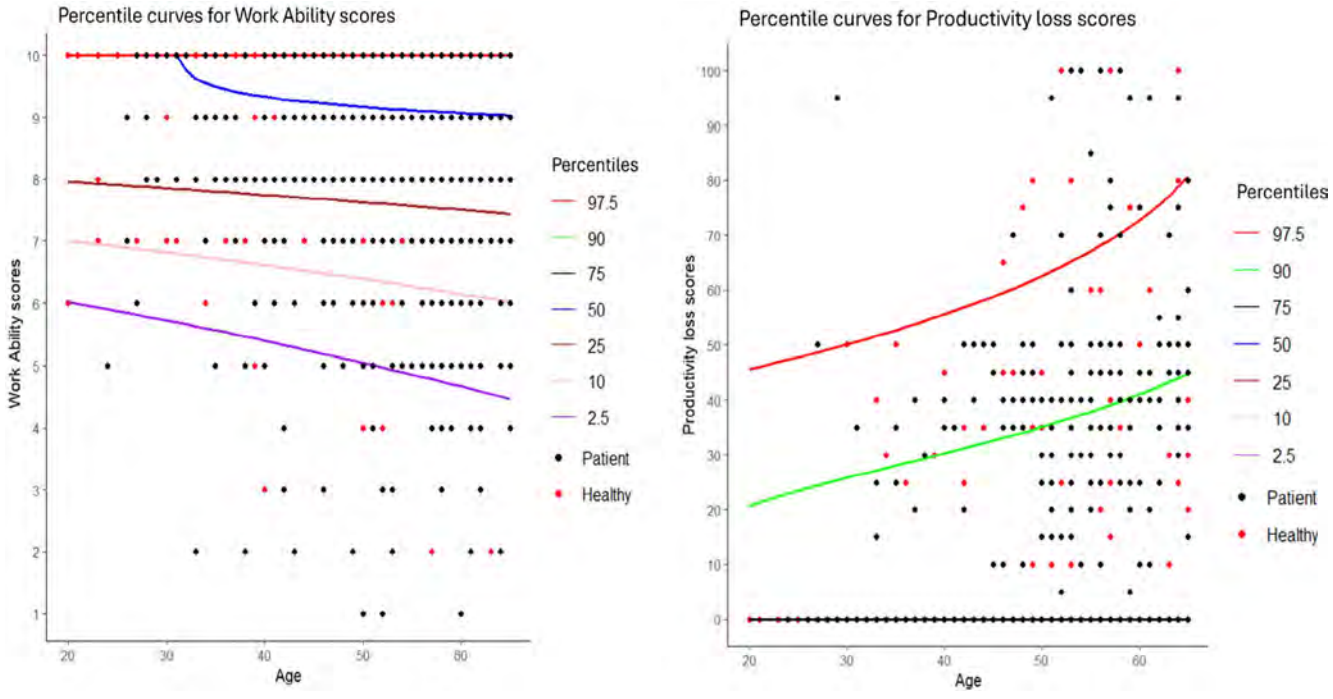


Figure 1. Reference intervals and percentile curves for a) work ability and b) productivity loss at work.

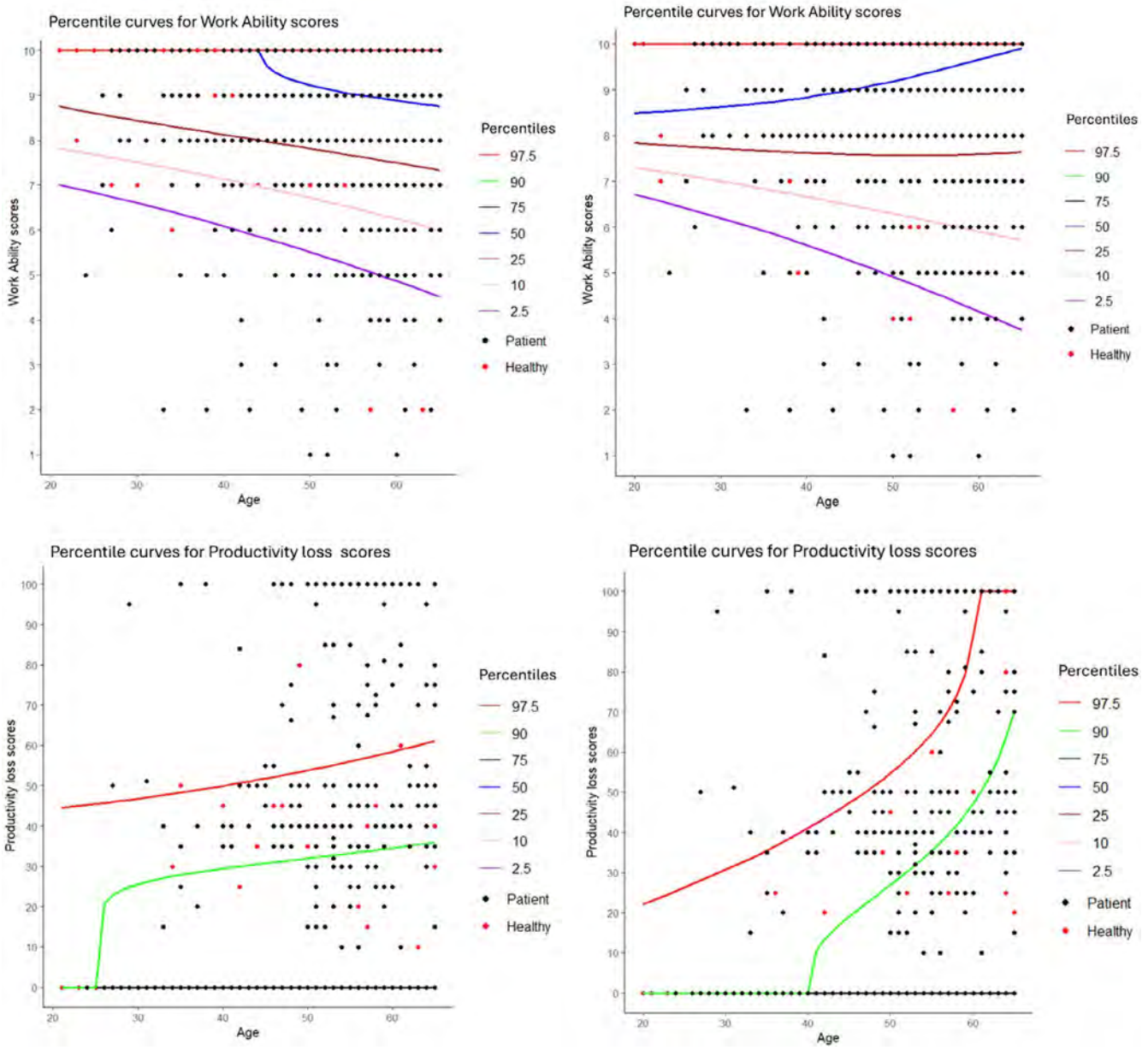


Figure 2. Reference intervals and percentile curves for work ability and productivity loss at work in high educated (left) vs low/middle educated (right) population.

Conclusion: In the general working population work ability and productivity while at work are not perfect, indicating we should be cautious to not overestimate impact of iRMD on presenteeism. Notwithstanding, iRMD had evident impact on presenteeism compared to population controls, and this effect is stronger on productivity (output) than on ability (difficulty).

Disclosure: D. Capelusnik: None; **W. Smeets**: None; **C. Webers**: None; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, Galapagos, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, UCB Pharma, 2, 5; **E. Nikiphorou**: AbbVie/Abbott, 6, Celltrion, 6, Eli Lilly, 6, fresenius, 6, Galapagos, 6, Gilead, 1, 6, Pfizer, 6, Sanofi, 6; **R. Braekers**: None; **L. Boekel**: None; **G. Wolbink**: None; **A. Boonen**: AbbVie, 2, 5, 6, Galapagos, 2, 6, Novartis, 2, 6, Pfizer, 5, 6, UCB Pharma, 2, 6.

Abstract Number: 0124

Utility of the 2019 EULAR/ACR SLE Classification Criteria Score as Predictor for Mortality and Hospitalizations in a Population-Based Cohort: The Lupus Midwest Network

Gabriel Figueroa-Parra[1], Andrew Hanson[2], Alain Sanchez-Rodriguez[3], Jose Meade-Aguilar[1], Cynthia Crowson[3] and Ali Duarte-Garcia[3], [1]Division of Rheumatology, Mayo Clinic, Rochester, MN, [2]Department of Quantitative Health Sciences, Mayo Clinic, Rochester, MN, [3]Mayo Clinic, Rochester, MN

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with SLE experience increased all-cause mortality and have a higher risk of hospitalization than the general population. Recently the classification criteria for SLE were updated resulting in an additive score to classify patients with SLE.

A higher score (≥20) in this classification criteria has been associated with disease severity in populations from referral centers (susceptible to referral bias), but this strategy has not been explored in a community setting. We aimed to assess the utility of the 2019 SLE classification criteria score for predicting mortality and hospitalizations in a population-based cohort of patients with recent SLE classification.

Methods: All incident patients meeting the 2019 EULAR/ACR SLE classification criteria in a population-based cohort between 1976-2018 were included. The EULAR/ACR SLE criteria components were abstracted by retrospective review of medical charts. We used EULAR/ACR score at 1 year from meeting classification. We evaluated the association between a score ≥20 points and mortality and the first unplanned hospitalization using Cox proportional hazards models adjusted for age, sex, and calendar year. Hospitalization data was available starting in 1995, and only incident patients after this were included in the hospitalizations analysis. Additionally, we re-fit multivariable models with EULAR/ACR score included as a penalized spline to explore possible non-linear relationships with outcomes and assess potential cut-off points. Patients were followed until March 2022, death, or lost to follow-up. A p-value < 0.05 was considered statistically significant.

Results: We included 270 patients with SLE. The median age was 45 (IQR 33-60) years; 80% were female and 82% were non-Hispanic White. The median length of follow-up was 9 (IQR 5-16) years. The most common clinical manifestations within 1 year of index date were inflammatory arthritis (66%), leukopenia (47%), and acute cutaneous lupus (25%). 73% were anti-dsDNA positive and 20% had proteinuria (**Table 1**). During follow-up, 68 patients died and 122 experienced unplanned hospitalization. 38% of patients had a score ≥20 points within 1 year of index.

A EULAR/ACR score ≥20 points within the first year of classification were not predictive for mortality (HR 1.42, 95% CI 0.82-2.48; p=0.22) but was for hospitalizations (HR 1.60, 95% CI 1.04-2.46, p=0.031) compared to a score ≤19 points. Assessing the EULAR/ACR score as a continuous predictor, we did not find a statistically significant association with mortality (HR 1.16 per 4-point increase, 95% CI 0.98-1.36, p=0.078), however, we estimated an 18% increase in the hazard for hospitalization (HR 1.18 per 4-point increase, 95% CI 1.06-1.13, p=0.003) (**Table 2**). We did not find any evidence of meaningful non-linear effects between the EULAR/ACR score and mortality (p=0.075) or hospitalizations (p=0.805) that suggested another potential score threshold to test (**Figure 1**).

Table 1. Clinical characteristics of patients with systemic lupus erythematosus.

	N = 270
Age, years, median (IQR)	45 (33-60)
Sex, n (%)	
Female	216 (80%)
Male	54 (20%)
Race/Ethnicity, n (%)	
Non-Hispanic White	222 (82%)
Hispanic/Latino	13 (5%)
Non-Hispanic Asian	20 (7%)
Non-Hispanic Black	9 (3%)
American Indian	0 (0%)
Other/Mixed/Refusal/Unknown	6 (2%)
Length of follow-up, years, median (IQR)	9 (5-16)
EULAR/ACR domain and criteria within 1 year of index*	
Constitutional	
Fever	18 (7%)
Hematologic domain	
Leukopenia	127 (47%)
Thrombocytopenia	58 (21%)
Autoimmune hemolysis	5 (2%)
Neuropsychiatric domain	
Delirium	3 (1%)
Psychosis	1 (<1%)
Seizures	4 (1%)
Mucocutaneous domain	
Non-scarring alopecia	11 (4%)
Oral ulcers	35 (13%)
Subacute cutaneous or discoid lupus	41 (15%)
Acute cutaneous lupus	68 (25%)
Serosal domain	
Pleural or pericardial effusion	45(17%)
Acute pericarditis	22 (8%)
Musculoskeletal domain	
Arthritis	178 (66%)
Renal domain	
Proteinuria >0.5g/24hrs	55 (20%)
Class II or V lupus nephritis	16 (6%)
Class III or IV lupus nephritis	31 (11%)
Immunology domains	
Antiphospholipid antibodies	63 (23%)
Low C3 or C4	100 (37%)
Low C3 and C4	83 (31%)
Anti-dsDNA	196 (73%)
Anti-Smith	61 (23%)

IQR: interquartile range.

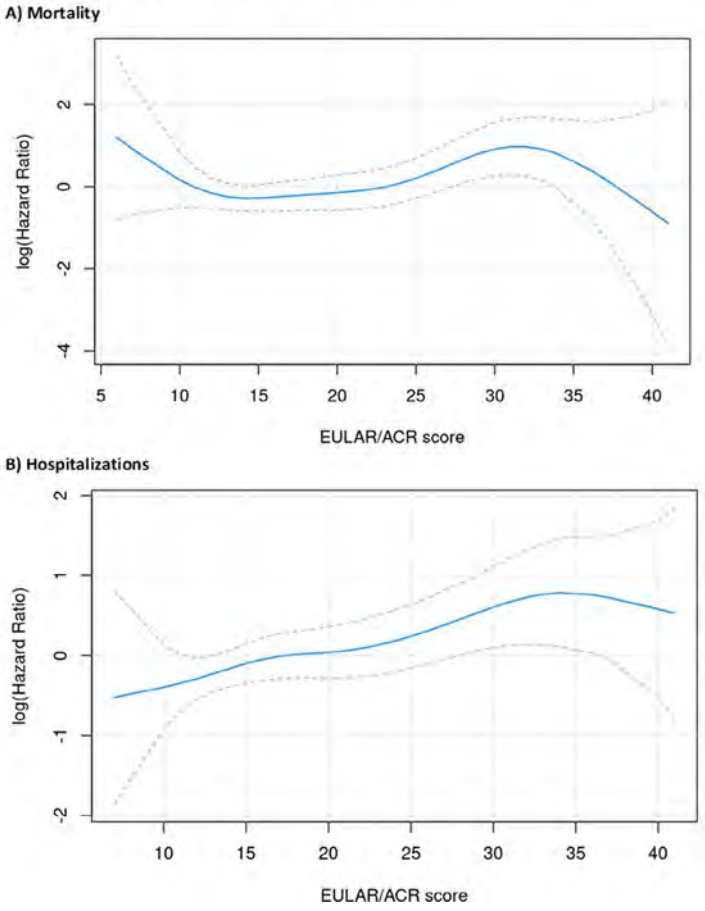
*Including manifestations of patients who died or were lost to follow-up within the first year (n = 13).

Table 2. Association between the 2019 EULAR/ACR SLE classification score (within 1 year) and the outcomes of mortality and hospitalizations among patients with SLE classification in a population-based cohort.

Outcome	Hazard ratio (95% CI)	p-value
Mortality		
EULAR/ACR score ≥20	1.42 (0.82, 2.48)	0.215
EULAR/ACR score, per 4-point increase	1.16 (0.98, 1.36)	0.078
Hospitalizations		
EULAR/ACR score ≥20	1.60 (1.04, 2.46)	0.031
EULAR/ACR score, per 4-point increase	1.18 (1.06, 1.31)	0.003

Conclusion: Among patients with recent SLE classification from a population-based cohort, the EULAR/ACR SLE classification score (≥20 points) was not a useful predictor for mortality compared to patients with SLE from referral centers, but it was predictor for hospitalizations.

Figure 1. Absence of non-linear relationship between the EULAR/ACR SLE classification score and the hazard for mortality and hospitalizations. Suggesting there is no evidence for establishing a threshold.



Disclosure: G. Figueroa-Parra: None; **A. Hanson**: None; **A. Sanchez-Rodriguez**: None; **J. Meade-Aguilar**: None; **C. Crowson**: None; **A. Duarte-Garcia**: None.

Abstract Number: 0125

Decreasing Ischemic Heart Disease, but Increasing Cancer Among the Underlying Causes of Death in Decedents with Lupus Nephritis

snehin Rajkumar[1] and Ram Singh[2], [1]University of California Los Angeles, Irvine, CA, [2]UCLA David Geffen School of Medicine, Los Angeles, CA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with lupus nephritis may die of active systemic lupus erythematosus (SLE) disease, end-stage renal disease (ESRD) and its complications as well as of comorbidities and treatment complications. Previous studies have utilized the national registry of patients with ESRD to examine causes of death in lupus nephritis, identifying

cardiovascular disease and infection as the two leading causes of death. However, the ESRD database may not have information on lupus nephritis patients who may have died of infections or other complications prior to developing ESRD. Furthermore, there are no nationwide population-based studies on causes of death in all, unselected, patients with lupus nephritis across the entire U.S. population.

Methods: We used the Center for Disease Control and Prevention's WONDER database, which compiles data on over 99% deaths from all 50 states and the District of Columbia. We used ICD-10 codes for SLE + a renal condition from the Multiple-Causes-of-Death files to obtain lupus nephritis death counts, overall and by the leading underlying causes of death. We then compared the underlying causes of death in two 10-year periods: 1999-2008 (period 1) versus 2011-2020 (period 2) using the Fisher's exact test.

Results: 4,423 and 4,225 deaths were attributed to lupus nephritis during the first and second 10-year periods, respectively. The 10 leading underlying causes of death in lupus nephritis during 1999-2020 in the decreasing order were SLE (61.5%), diseases of heart (9.7%), renal disease (5.5%), malignant neoplasms (2.2%), septicemia (2.0%), diabetes mellitus (1.6%), cerebrovascular disease (1.4%), chronic lower respiratory disease (0.9%), chronic liver disease (0.8%), and hypertension with hypertensive renal disease (0.7%). The most significant decrease was seen in acute myocardial infarction (102 deaths [2.31%] in period 1 to 45 deaths [1.07%] in period 2, $p< 0.0001$), followed by SLE (64.5% in period 1 to 59.4% in period 2, $p< 0.0001$). Diabetes mellitus (p, 0.002) and chronic ischemic heart disease (p, 0.01) also significantly decreased. However, malignant neoplasms significantly increased from 72 deaths (1.63%) in period 1 to 113 deaths (2.67%) in period 2 (p, 0.0008). Chronic lower respiratory diseases (p, 0.006), chronic obstructive pulmonary disease (p, 0.006), unintentional injuries (p, 0.007), hypertensive renal/heart disease with renal failure ($p< 0.05$), and enterocolitis due to Clostridium difficile ($p< 0.05$) also increased during period 2 compared to period 1. Infections as the underlying causes of death remained unchanged during the study period.

Conclusion: A focus on cardiovascular disease risk in lupus over the past two decades has resulted in decreasing ischemic heart disease as the underlying cause of death in lupus nephritis. However, increased cancers and respiratory diseases and persistent infections among the leading causes of death in lupus nephritis are concerning. Prospective studies are needed to verify these findings and to identify patients at high risk for these complications.

Disclosure: s. Rajkumar: None; **R. Singh**: None.

Abstract Number: 0126

Epidemiology and Retrospective Case-Control Analysis of IIM in the US Veteran Population

Vladimir Liarski, University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Idiopathic Inflammatory Myopathy (IIM) - comprising polymyositis (PM), dermatomyositis (DM), and inclusion body myositis (IBM) - is rare and difficult to study. We sought to study its' epidemiology in the US veteran population – an understudied area.

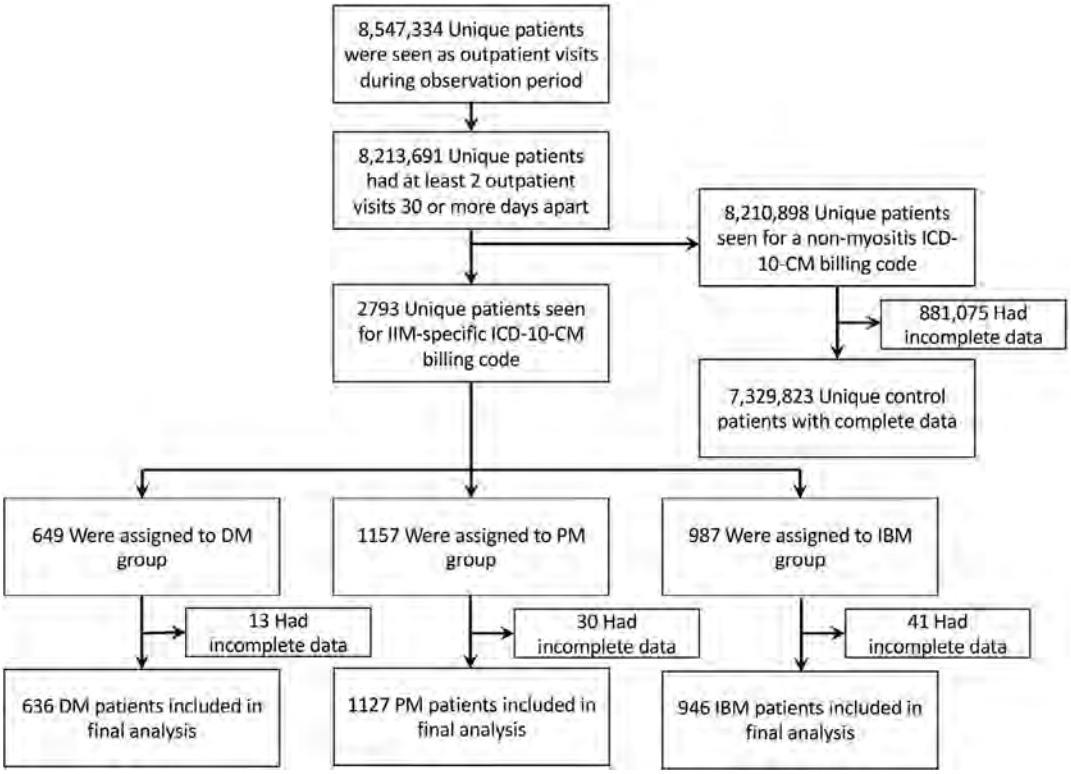


Figure 1.- Overview of study design

Table 1.- Characteristics of patients in final Idiopathic Inflammatory Myopathy cohort.

Characteristic	DM (N = 636)	PM (N = 1127)	IBM (N = 946)
Mean age of cohort (range) - yr	65.0 (27-96)	68.2 (27-104)	75.1 (33-98)
Mean age at first visit (range) – yr	58.2 (25-93)	60.9 (22-100)	69.9 (29-94)
Female sex – no. (%)	130 (20.4%)	132 (12.5%)	23 (2.4%)
Deceased during observation period – no. (%)	116 (18.2%)	307 (27.2%)	365 (38.6%)
Mean age at death (Range) – yr	73 (34-96)	74 (43-104)	77 (48-98)
Race – no. (%)			
White	423 (65.2%)	624 (53.9%)	730 (74.0%)
Black	155 (23.9%)	430 (37.2%)	156 (15.8%)
Native Hawaiian/Pacific Islander	8 (1.2%)	11 (0.9%)	4 (0.4%)
American Indian/Alaska Native	8 (1.2%)	10 (0.9%)	7 (0.7%)
Asian	10 (1.5%)	8 (0.7%)	5 (0.5%)
Other	48 (7.4%)	70 (6.1%)	56 (5.7%)
Presence of ILD – no. (%)	97 (15.2%)	178 (15.8%)	28 (3.0%)
Presence of oncological diagnosis – no. (%)	134 (21.1%)	220 (19.5%)	189 (20.0%)

Table 1. Characteristics of patients in final Idiopathic Inflammatory Myopathy cohort.

Methods: We conducted a retrospective case-control analysis using the Veterans Affairs Corporate Data Warehouse. Cases were identified based on billing data: adults aged 18 to 110, seen between 1/1/2016 and 12/31/2021, with a minimum of two visits denoted by an IIM-specific ICD-10 code. Interstitial Lung Disease (ILD) and oncological comorbidities were identified similarly. DM, PM, and IBM cohorts were randomly matched with age-, sex-, and ethnicity-paired controls on a 3:1 basis. The primary outcome examined was all-cause mortality with secondary outcomes examining the impact of age, sex, and presence of ILD and oncological diagnoses on IIM patient survival.

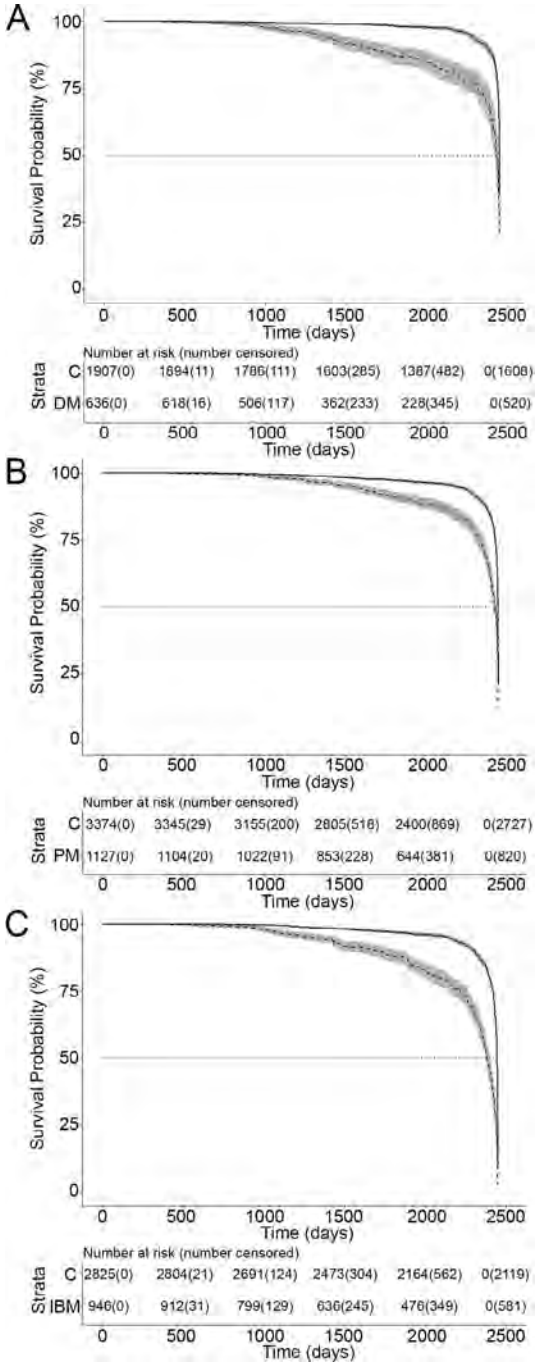


Figure 2.- Kaplan Meier survival plots for dermatomyositis (a), polymyositis (b), and inclusion body myositis (c) matched patient cohort. (a-c) Mean control (solid line) and myositis (dashed line) patient survival, based on all-cause mortality, plotted as labelled with 95% confidence intervals in gray.

Results: Complete data was available for 636 DM, 1127 PM, and 946 IBM patients (**Figure 1**). Calculated prevalence was 79.0 cases of DM/million, 140.9 cases of PM/million, and 120.2 cases of IBM/million. Male:female ratios were lowest for DM at 0.4, intermediate for PM at 0.8, and highest for IBM at 4.2. IBM was the highest prevalence IIM in veterans over 65 (198.5 cases/million). Age-adjusted prevalence was 65.7 cases of DM/million, 91.7 cases of PM/million, and 45.1 cases of IBM/million for individuals over 15. Estimated average annual incidence was 11.8 cases/million for DM (range: 6.1 - 15.4), 13.3 cases/million for PM (range: 4.4 – 20.1), and 12.9 cases/million for IBM (range: 7.4 – 17.7).

The mean age of DM patients (65.0±13.5 years) was similar to the non-IIM VA population (65.1±17.2 years, $p = 0.15$), while the mean ages of PM (68.2±11.9 years) and IBM (75.1±8.9 years) patients were higher ($p < 0.0001$ for both) (**Table 1**). PM had the highest proportion of Black patients (429, 37.2%), with DM (155, 23.9%) also above the non-IIM veteran population (1,296,904, 17.3%, $p < 0.0001$ for both). IBM did not show a significant difference in racial makeup (156, 15.8%, $p = 0.31$).

In terms of comorbidities, only 0.7% (51,158) of the non-IIM VA population had an Interstitial Lung Disease (ILD)-associated ICD-10 code compared to 15.2% (97) of DM, 15.4% (178) of PM, and 2.8% (28) of IBM patients ($p < 0.0001$ for 3 pairwise comparisons). 12.6% (940,933) of non-IIM veterans had an oncological diagnosis, which was significantly lower than rates seen in either IIM group (134, 21.1%; 220, 19.5%; and 189, 20.0% for DM, PM, and IBM respectively, $p < 0.0001$ for 3 pairwise comparisons).

Mean (±SD) survival was 1614.2±620.9 for DM ($p < 0.0001$); 1901.3±563.4 for PM ($p < 0.0001$); and 1789.8±628.2 days for IBM ($p < 0.0001$) versus matched controls (**Figure 2**). Male sex (HR 2.6, $p < 0.017$), older age (HR 2.2, $p < 0.001$) and concurrent oncological diagnosis (HR 2.3, $p < 0.001$) were associated with worse survival in DM while older age was the only factor for PM (HR 2.44, $p < 0.001$) and IBM (HR 1.59, $p < 0.001$) patients. COVID infection or suspected infection had no statistical effect on survival.

Conclusion: All IIMs exhibited decreased survival compared to matched controls. Male sex and concurrent oncological diagnosis were unique poor prognostic factors in DM.

Disclosure: V. Liarski: None.

Abstract Number: 0127

Time Trends, Cumulative Incidence, and Impact on Survival of Interstitial Lung Disease in Systemic Sclerosis: Results from a Population-based Cohort Study

Anukul Karn[1], Sara Achenbach[2], Alicia Hinze[3], Cynthia Crowson[1] and Ashima Makol[2], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Rochester, MN, Rochester, MN, [3]Mayo Clinic - Rochester, MN, Rochester, MN

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiopulmonary complications are the number one cause of mortality in Systemic sclerosis (SSc). We studied the prevalence, cumulative incidence, predictors and impact of interstitial lung disease (ILD) on survival in a recent inception cohort of SSc patients.

Methods: A comprehensive retrospective review of individual medical records was done to assemble a population-based cohort of incident SSc patients from January 1, 2010, through December 31, 2020, who were followed until death, migration from the geographic area, or September 30, 2022. ILD at baseline was identified on high-resolution CT scan, and cumulative incidence of ILD adjusting for competing risk of death was estimated. Cox models were used to examine risk factors for ILD and its time-dependent impact on survival.

Results: We identified 146 incident SSc patients (81% F, 90% Caucasian, mean age = 59.5 ± 13.6 y, mean follow-up 4.8 ± 3.1 y) over the 11-y period. Majority had limited cutaneous SSc (122), followed by diffuse cutaneous SSc (18), and SSc sine scleroderma (6). Anti-nuclear antibody (ANA) was positive in 94% of (134/143) patients, anticentromere in 53%

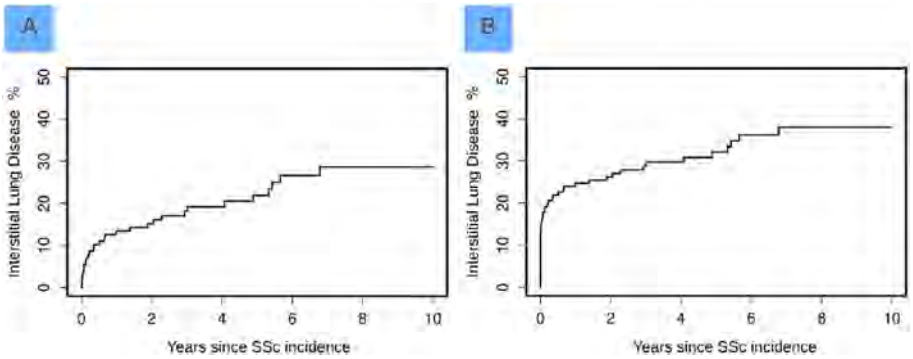


Figure 1. a. Cumulative incidence of Interstitial lung disease (ILD) adjusting for competing risk of death (Excluding 19 patients with ILD prior to index). Twenty-nine of the remaining 127 Systemic sclerosis (SSc) cases had ILD following index date. b. Cumulative incidence of ILD adjusting for competing risk of death (Including 19 patients with ILD prior to index and 29 patients with ILD following index)

Table 1. Risk factors for ILD in SSc (Age-Adjusted Cox Models with Time to ILD following diagnosis)

Parameter	Total (ILD)	HR (95% CI)	p-value
Age per 10-year increase	127 (29)	0.81 (0.62-1.06)	0.13
Male gender	127 (29)	1.24 (0.50-3.05)	0.64
Year of diagnosis	127 (29)	1.05 (0.92-1.19)	0.48
Ever smoked	127 (29)	1.53 (0.73-3.20)	0.26
Current smoker	127 (29)	0.82 (0.19-3.50)	0.79
Body mass index ≥ 30	127 (29)	1.02 (0.98-1.07)	0.33
Skin Involvement (Reference = Limited)	127 (29)		
Skin Involvement = Diffuse		2.15 (0.91-5.07)	0.08
Skin Involvement = Sine scleroderma		--	0.99
Anti-centromere	125 (29)	0.37 (0.17-0.80)	0.01
Anti Scl-70	127 (29)	4.36 (1.72-11.1)	0.002
Anti RNA polymerase III	123 (29)	1.03 (0.39-2.72)	0.95
Anti-nuclear antibody by any method	125 (29)	2.07 (0.28-15.25)	0.48
Nailfold capillary abnormalities (TD)	94 (22)	1.57 (0.64-3.85)	0.33
Telangiectasia (TD)	127 (29)	0.99 (0.47-2.08)	0.98
Digital ulcers/pitting (TD)	127 (29)	2.21 (1.05-4.66)	0.04
Pulmonary arterial hypertension[1] (TD)	127 (29)	5.48 (2.18-13.77)	<0.001
Raynaud's (TD)	127 (29)	1.29 (0.17-9.60)	0.80
Calcinosis (TD)	127 (29)	0.95 (0.22-4.08)	0.95
Scleroderma renal crisis (TD)	127 (29)	2.30 (0.69-7.67)	0.16

*Count of time dependent (TD) variables is at any time point
Interstitial lung disease (ILD), Systemic Sclerosis (SSc)
[1]Pulmonary arterial hypertension: defined based on right heart catheterization with mean pulmonary artery pressure >20 mmHg, or echocardiogram criteria of right ventricular systolic pressure >45 mmHg and tricuspid regurgitant velocity >3.8 m/s.

(77/144), anti-Scl 70 in 11% (16/146), and anti-RNA polymerase III in 18% (25/142). Of 146 patients, 19 (13%) had ILD prior to SSc diagnosis, and 29 (out of remaining 127) developed ILD during follow-up. The cumulative incidence of ILD in SSc (excluding 19 cases with ILD prior to index date) was highest in the initial few years after diagnosis of SSc with 13.4% (95% CI 8.6%-21.0%) at 1 y, 21.9% (95% CI 15.3%-31.3%) at 5 y, and 28.7% (95% CI 20.5-40.3%) at 10 y. Overall, the cumulative incidence of ILD in SSc (including 19 cases with ILD prior to index date was 24.7% (95% CI 18.6-32.8%) at 1 y, 32.1% (95% CI 24.9-41.2%) at 5 y, and 38.0% (95% CI 29.8-48.6%) at 10 y. (**Figure 1**)

Age, gender, and smoking did not affect the risk for the development of ILD in patients with SSc. A higher risk was associated with digital ulcers/pitting (HR 2.21, 95% CI 1.05-4.66; p=0.04) and a trend towards higher risk with diffuse skin involvement (HR 2.15, 95% CI 0.91-5.07; p=0.08). Anti-centromere antibody was a protective factor (HR 0.37, 95% CI 0.17-0.80; p=0.01), while anti-Scl 70 strongly increased the risk for ILD (HR 4.36, 95% CI 1.72-11.1; p=0.002). Pulmonary arterial hypertension (PAH) was also associated with a significantly increased risk of ILD (HR 5.48; 95%CI 2.18-13.77). (**Table 1**)

ILD increased the risk of overall mortality in patients with SSc (HR 3.65, 95% CI 1.72-7.71 adjusted for age, sex and index year). This higher but non-statistically significant risk persisted after adjusting for age, sex, and PAH (as a time-dependent variable) (HR 1.96, 95% CI 0.89-4.33).

Conclusion: ILD is a common visceral complication of SSc and a major contributor to morbidity and mortality in these patients. While it is known to be a complication of 'early' disease, a substantial portion of patients continue to develop ILD between 5-10 years after disease onset. ILD confers a nearly 4-fold higher risk of overall mortality in SSc patients, which may be complicated by co-existing PAH. These findings highlight the importance of thorough pulmonary evaluation not only at diagnosis and in the early years of disease but also during long-term follow-up in SSc patients.

Disclosure: A. Karn: None; **S. Achenbach**: None; **A. Hinze**: None; **C. Crowson**: None; **A. Makol**: Boehringer-Ingelheim, 1, Sanofi-Genzyme, 1.

Abstract Number: 0128

Incidence, Trends, and Determinants of Multimorbidity in Systemic Sclerosis: Data from a Population-based Cohort

Anukul Karn[1], Sara Achenbach[2], Alicia Hinze[3], Cynthia Crowson[1] and Ashima Makol[2], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Rochester, MN, Rochester, MN, [3]Mayo Clinic - Rochester, MN, Rochester, MN

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate the burden, longitudinal trends, and drivers of multimorbidity (MM; the presence of ≥2 morbidities) in patients with Systemic Sclerosis (SSc) vs. age- and sex-matched non-SSc comparators in a community-based incident cohort.

Methods: A population-based cohort of incident SSc patients from Jan 1, 1980, to Dec 31, 2020, were identified and compared to age- and sex-matched comparators (2:1) from the same population. They were followed till death, migration from the geographic area, or Sept. 30, 2022. Data on 21 morbidities identified by the US Department of Health and Human

Table 1. Time to multimorbidity (at follow-up)

Event type	SSc (events)	Non SSc (events)	HR (95% CI)	p-value
DHHS[1]				
Hypertension	116 (48)	269 (104)	1.45 (1.01-2.08)	0.04
Congestive heart failure	180 (44)	398 (29)	3.85 (2.35-6.31)	<0.001
Coronary artery disease	172 (31)	381 (44)	1.91 (1.17-3.12)	0.01
Arrhythmia	154 (71)	369 (113)	1.88 (1.38-2.56)	<0.001
Stroke	185 (26)	397 (32)	2.01 (1.15-3.50)	0.01
Arthritis	125 (58)	318 (112)	1.50 (1.08-2.08)	0.02
Chronic kidney disease	177 (59)	383 (69)	1.83 (1.28-2.63)	0.001
COPD	167 (34)	386 (39)	2.00 (1.24-3.24)	0.01
Osteoporosis	171 (34)	380 (45)	2.13 (1.32-3.43)	0.002
DHHS-MM2+	90 (64)	199 (122)	1.83 (1.34-2.50)	<0.001
DHHS-MM5+	148 (79)	349 (146)	2.00 (1.51-2.64)	<0.001
Charlson Comorbidity Index[2]				
Congestive heart failure	179 (48)	398 (32)	3.86 (2.41-6.18)	<0.001
Peripheral vascular disease	127 (54)	393 (69)	5.65 (3.85-8.31)	<0.001
Cerebrovascular disease	184 (28)	394 (31)	2.25 (1.31-3.85)	0.003
Chronic Pulmonary Disease	153 (52)	357 (47)	3.03 (2.00-4.60)	<0.001
Any renal disease	180 (49)	394 (50)	2.34 (1.55-3.52)	<0.001
Any liver disease	180 (23)	401 (23)	2.25 (1.22-4.16)	0.01
Charlson-MM2+	149 (88)	366 (100)	3.60 (2.67-4.86)	<0.001
Charlson-MM5+	186 (27)	405 (31)	1.44 (0.84-2.47)	0.19

[1]The following DHHS comorbidities did not reach statistical significance: hyperlipidemia, asthma, cancer, dementia, depression, diabetes, substance abuse, and anxiety.
[2]The following Charlson comorbidities did not reach statistical significance: myocardial infarction, dementia, diabetes, and cancer.

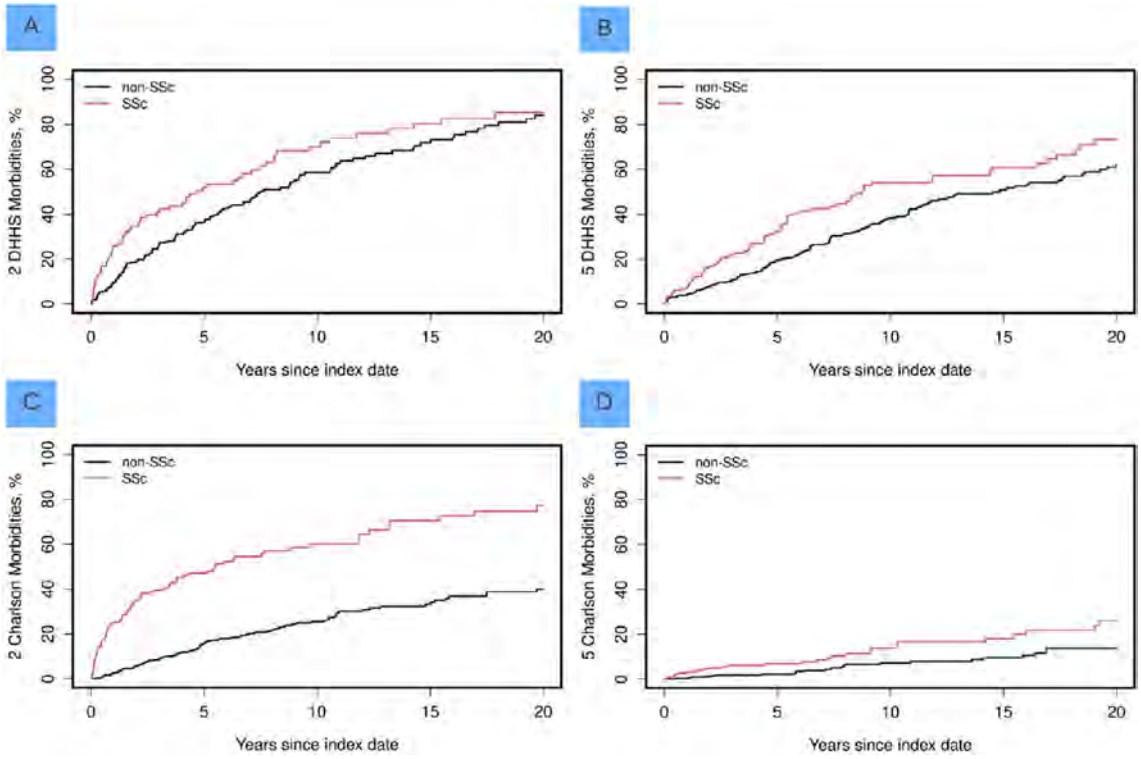


Figure 1. A and B. Cumulative incidence for time to DHHS-MM2+ and DHHS-MM5+ morbidity events adjusted for the competing risk for death. C and D. Cumulative incidence for time to CCI-MM2+ and CCI-MM5+ events adjusted for the competing risk of death. Abbreviations: DHHS (Department of Health and Human Services), MM (Multimorbidity), CCI (Charlson comorbidity index), SSc (Systemic Sclerosis)

Services (DHHS) and 13 morbidities in the Charlson Comorbidity Index (CCI) was retrieved. Cumulative incidence of MM (MM2+) or substantial MM (MM5+; ≥ 5 morbidities) adjusting for the competing risk of death was estimated. Cox models adjusted for age, sex, index year and morbidity count at index date were used to compare cases and comparators. Patients with < 1 year of prior medical history and who met the criteria of event type before the index date were excluded.

Results: We included 189 SSc patients and 408 comparators (mean age 58.2 y, 85% female, 91% white).

The prevalence of cardiac arrhythmia (19% vs 10%, p=0.002), arthritis (34% vs 22%, p=0.002), COPD (12% vs 5%, p=0.007), MI (3% vs 0%, p=0.023), peripheral vascular disease (33% vs 4%, p< 0.001), chronic pulmonary disease (19% vs 13%, p=0.035), and any liver disease (5% vs 2%, p=0.032) were higher at index date, but the prevalence of hyperlipidemia (30% vs 39%, p=0.043) was lower in SSc.

During a mean length of follow-up of 9.7 y (SD 8.7) for non-SSc and 8.5 y (SD 8.0) for SSc, the development of hypertension (HR 1.45; 95% CI 1.01-2.08), congestive heart failure (DHHS: HR 3.85, 95% CI 2.35-6.31; CCI: HR 3.86, 95% CI 2.41-6.18), coronary artery disease (HR 1.91, 95% CI 1.17-3.12), arrhythmia (HR 1.88, 95% CI 1.38-2.56), stroke (HR 2.01, 95% CI 1.15-3.50), arthritis (HR 1.50, 95% CI 1.08-2.08), chronic kidney disease (HR 1.83, 95% CI 1.28-2.63), COPD (HR 2.00, 95% CI 1.24-3.24), osteoporosis (HR 2.13, 95% CI 1.32-3.43), peripheral vascular disease (HR 5.65, 95% CI 3.85-8.31), cerebrovascular disease (HR 2.25, 95% CI 1.31-3.85), chronic pulmonary disease (HR 3.03, 95% CI 2.00-4.60), any renal disease (HR 2.34, 95% CI 1.55-3.52), and any liver disease (HR 2.25, 95% CI 1.22-4.16) were significantly higher in SSc when compared to non-SSc. (**Table 1**)

The risk of development of DHHS MM2+, DHHS MM5+, and CCI-MM2+ was significantly higher in SSc patients vs non-SSc, but CCI-MM5+ was statistically insignificant after adjusting for baseline morbidity count. (**Figure 1 and Table 1**)

Conclusion: There is a high burden of MM and substantial MM in SSc patients at baseline and during the disease course. Witha1.5-4-fold risk of development of cardiopulmonary diseases, 2-fold risk of neurological, renal and liver diseases, and 6-fold risk of peripheral vascular disease in SSc patients during follow-up, there is an urgent need for systematic assessment and management of multimorbidity to reduce healthcare burden and improve prognosis in this population.

Disclosure: A. Karn: None; **S. Achenbach**: None; **A. Hinze**: None; **C. Crowson**: None; **A. Makol**: Boehringer-Ingelheim, 1, Sanofi-Genzyme, 1.

Abstract Number: 0129

Rising Incidence and High Mortality of Systemic Sclerosis: A Population-based Cohort Study (2010-2020)

Anukul Karn[1], Sara Achenbach[2], Alicia Hinze[3], Cynthia Crowson[1] and Ashima Makol[2], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Rochester, MN, Rochester, MN, [3]Mayo Clinic - Rochester, MN, Rochester, MN

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Sclerosis (SSc) is a rare chronic inflammatory disease characterized by immune-mediated dysfunction, vasculopathy and widespread internal organ fibrosis; and the highest case fatality among all rheumatic diseases. We aimed to study trends in incidence and mortality in a physician-diagnosed population-based cohort of SSc patients.

Methods: An inception cohort of incident SSc patients aged ≥18 years with a confirmed physician diagnosis of SSc made by a rheumatologist (supported by compatible clinical presentation, autoantibody testing, and/or appropriate imaging) between Jan 1, 2010, to Dec 31, 2020, was identified based on comprehensive individual medical record review. Fulfillment

Table 1. Clinical Characteristics of Incident Systemic Sclerosis (2010-2020)

Clinical characteristic	Total (N=146)
Mean Age on Index Date, years	59.5 ± 13.6
Sex, Female	118 (81%)
Ethnicity	
Caucasian	131 (90%)
African American	4 (3%)
Hispanic	6 (4%)
Asian	1 (1%)
Others	4 (3%)
Obese (Body mass index≥30 kg/m^2)	49 (34%)
Smoking Status	
Never	80 (55%)
Ex smoker	54 (37%)
Current smoker	12 (8%)
Cutaneous phenotype	
Limited	122 (84%)
Diffuse	18 (12%)
Sine scleroderma	6 (4%)
Systemic Sclerosis related antibodies	
Anticentromere	77/144 (53%)
Anti Scl-70	16/146 (11%)
Anti RNA polymerase III	25/142 (18%)
Raynaud's phenomenon	135 (92%)
Positive Anti-nuclear antibody	134/143 (94%)
Sclerodactyly	80 (55%)
Telangiectasia	69 (47%)
Nailfold capillary abnormalities (37 not done)	63/109 (58%)
Digital ulcers/pitting scars	35 (24%)
Interstitial Lung Disease [1]	19 (13%)
Pulmonary Arterial Hypertension [2]	10 (7%)
Myositis	7 (5%)
Calcinosis*	23 (16%) (7/23 were at baseline)
Inflammatory arthritis*	58 (40%) (32/58 were at baseline)
GI dysmotility*	49 (34%) (15/49 were at baseline)
Scleroderma renal crisis *	11 (8%) (5/11 were at baseline)

*Features appearing at any time during disease course.

[1] Interstitial lung disease: defined based on characteristic findings on high-resolution CT scan of chest.

[2] Pulmonary arterial hypertension: defined based on right heart catheterization with mean pulmonary artery pressure >20 mmHg, or echocardiogram criteria of right ventricular systolic pressure >45 mmHg and tricuspid regurgitant velocity >3.8 m/s

of ACR/EULAR 2013 criteria was ascertained. Patients were followed until death, migration from the geographic area, or Sept. 30, 2022. Incidence rates were age- and sex-adjusted to the 2020 US white population. Survival rates were compared with expected rates in the general population.

Results: A total of 146 incident SSc patients (81% female, 90% White, mean age 59.5 ± 13.6 y) were identified between 2010-2020. A 138 (94.52%) met the classification criteria for SSc. The overall age- and sex-adjusted annual incidence was 23.4 (95% confidence interval = 19.6–27.3) per million population, with a significant increase in incidence over time [SIR (Standardized Incidence Ratio) per 10-year increase=1.92, 95% CI = (1.67-2.20)]. Age-adjusted incidence was 36.7 (95% CI = 30.0-43.3) per million for females and 9.5 (95% CI = 6.0-13.0) per million for males. Thirty patients died during the study period. Patients with SSc had significantly higher mortality compared to the general population, with a standardized mortality ratio of 3.46 (95% confidence interval = 2.34-4.95). (**Table 1 and Figure 1**)

Age, smoking (current and ever), diffuse cutaneous disease, telangiectasias, digital ulcers/pitting and significant internal organ involvement (interstitial lung disease, pulmonary arterial hypertension, renal crisis) were associated with a higher mortality risk. (**Table 2**)

Table 2. Age-Adjusted Cox Models: Risk factors for mortality in SSc (2010-2020)

Parameter	Count of patients with risk factor*	Total (Deaths)	HR (95% CI)	p-value
Age per 10-year increase	--	146 (30)	1.71 (1.21-2.41)	0.002
Male gender	28	146 (30)	1.68 (0.74-3.82)	0.22
Year of diagnosis	--	146 (30)	0.95 (0.82-1.10)	0.51
Ever smoked	66	146 (30)	2.93 (1.33-6.46)	0.008
Current smoker	12	146 (30)	5.23 (2.03-13.43)	<0.001
Body mass index	--	146 (30)	0.98 (0.93-1.04)	0.50
Skin Involvement (Reference = Limited)		146 (30)		
Skin Involvement = Diffuse	18		2.41 (1.01-5.78)	0.05
Skin Involvement = Sine scleroderma	6		1.41 (0.19-10.75)	0.74
Abnormal Nailfold capillaries (TD)	84	109 (15)	2.48 (0.68-8.98)	0.17
Telangiectasia (TD)	100	146 (30)	3.47 (1.41-8.54)	0.007
Digital ulcers or fingertip scars (TD)	54	146 (30)	3.14 (1.51-6.55)	0.002
PAH (TD)	44	146 (30)	7.25 (3.33-15.8)	<0.001
ILD (TD)	48	146 (30)	3.41 (1.66-7.00)	<0.001
Raynaud's (TD)	141	146 (30)	0.91 (0.12-6.89)	0.93
Scleroderma renal crisis (TD)	11	146 (30)	4.00 (1.70-9.38)	0.001

*Count of time dependent (TD) variables is at any time point
PAH (pulmonary arterial hypertension), ILD (Interstitial lung disease)

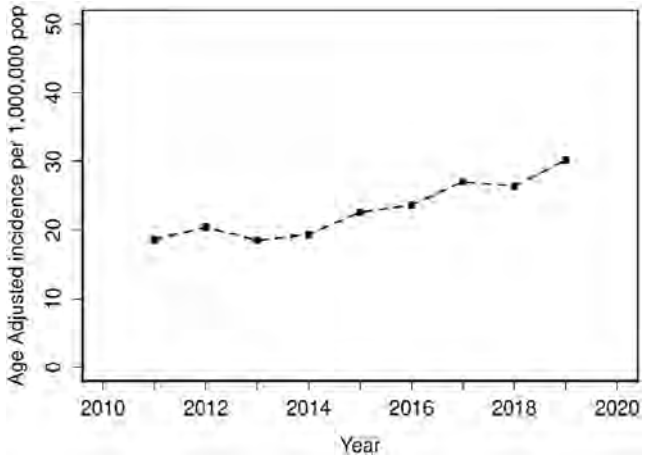


Figure 1. Incidence of Systemic Sclerosis (2010-2020) using 3 year moving averages

Conclusion: In this population-based cohort, the incidence of SSc has been rising, by nearly 2-fold in the last decade. The reasons for this need better understanding but could in part be explained by better recognition of SSc with newer classification criteria. The survival in SSc remains poor, with more than 3-fold higher mortality than the general population with no evidence of improvement over time, highlighting an urgent need for better therapeutics to modify disease activity and course in this morbid disease.

Disclosure: A. Karn: None; **S. Achenbach**: None; **A. Hinze**: None; **C. Crowson**: None; **A. Makol**: Boehringer-Ingelheim, 1, Sanofi-Genzyme, 1.

Abstract Number: 0130

Association of HLA-DRB1 Alleles with Coronary Artery Calcium, Abdominal Aortic Calcium, and Carotid Intima-media Thickness in a Multi-ethnic Community-living Population

Manmeet Kaur[1], Ronit Katz[2], Michael H. Criqui[1], Maripat Corr[3], Wendy S. Post[4], Matthew Budoff[5], Gerald P. Morris[3] and Jan M. Hughes-Austin[3], [1]University of California San Diego, San Diego, CA, [2]University of Washington, Seattle, WA, [3]University of California San Diego, La Jolla, CA, [4]Johns Hopkins University School of Medicine, Baltimore, MD, [5]Harbor-UCLA Medical Center, Torrance, CA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Human leukocyte antigen (HLA) DRB1 alleles with specific common amino acids referred to as the shared epitope (SE) have been linked to endothelial dysfunction in patients with rheumatoid arthritis (RA). However, less is known about the HLA-DRB1 alleles with endothelial dysfunction and subclinical cardiovascular disease (CVD) in people without RA. We aimed to determine associations betweenHLA-DRB1 SE alleles (04:04, 04:05, 04:01, 04:08, 01:01, 14:02, 10:01, 03:01, 03:02) and coronary artery calcium (CAC), abdominal aortic calcium (AAC), and carotid intima-media thickness (cIMT) in a multi-ethnic community-living population.

	Frequency	Coronary artery calcium				Abdominal aortic calcium				Carotid intima-media thickness	
	N (%)	RR (CAC>0)	95% CI	RD	95% CI	RR (AAC>0)	95% CI	RD	95% CI	RD	95% CI
Shared Epitope[1]											
SE +/+ vs SE -/-	75 (8%)	1.19	0.98, 1.43	1.33	0.79, 2.23	1.06	0.93, 1.21	1.02	0.92, 1.14	1.02	0.98, 1.07
SE +/- vs SE -/-	360 (38%)	1.04	0.91, 1.18	0.98	0.70, 1.38	1.04	0.97, 1.12	0.98	0.93, 1.04	0.99	0.97, 1.02
Individual alleles											
04:01	71 (7%)	0.93	0.73, 1.19	0.97	0.51, 1.87	1.10	0.96, 1.25	0.97	0.88, 1.07	0.98	0.94, 1.03
04:04	51 (5%)	1.03	0.81, 1.33	0.82	0.38, 1.78	1.10	0.95, 1.27	1.08	0.98, 1.19	1.02	0.97, 1.08
04:05	27 (3%)	0.98	0.72, 1.33	1.24	0.64, 2.40	**0.76**	**0.58, 0.99**	1.02	0.89, 1.17	1.00	0.94, 1.05
04:08	3 (0.3%)	1.12	0.75, 1.66	0.31	0.03, 3.30	0.87	0.65, 1.17	0.98	0.90, 1.06	1.05	0.86, 1.27
01:01	102 (11%)	0.94	0.78, 1.14	1.41	0.83, 2.38	1.10	0.99, 1.22	0.96	0.87, 1.05	1.04	1.00, 1.09
14:02	15 (1.6%)	1.28	0.90, 1.81	1.70	0.73, 3.94	**1.42**	**1.17, 1.74**	1.10	0.96, 1.26	1.04	0.96, 1.13
10:01	20 (2%)	0.74	0.34, 1.61	**2.63**	**1.17, 5.99**	0.88	0.67, 1.17	0.87	0.67, 1.14	1.02	0.95, 1.09
03:01	150 (16%)	1.22	1.06, 1.41	0.79	0.52, 1.20	1.00	0.91, 1.10	1.00	0.92, 1.08	0.97	0.94, 1.01
03:02	30 (3%)	1.04	0.64, 1.69	2.61	0.94, 7.27	0.85	0.61, 1.19	0.98	0.74, 1.31	1.00	0.95, 1.07

Footnotes:
[1] Total frequense for SE +/- : 521 (55%)
Legend:
Bolded in table represents statistically significant
RR = relative risk
RD = relative difference in Agatston score per increment in risk factor estimated from linear regression with Ln(Agatston score) as the dependent variable, adjusted for all risk factors listed . For example RD of 1.50 represents a 50% increase.

Methods: Within the Multi-Ethnic Study of Atherosclerosis (MESA), a prospective cohort study designed to determine risk factors and progression of subclinical and clinical CVD, a subset of 955 participants who completed the AAC ancillary study and had complete measures of HLA typing and cardiac imaging were evaluated. We defined shared epitope positive, SE(+) for genotypes with the HLA-DRB1 SE alleles listed above; and evaluated associations of SE positivity and each of the individual SE alleles with CAC, AAC, and cIMT. CAC and AAC were evaluated as present vs. absent and as ln(Agatston score) in those with CAC and ACC > 0. cIMT was evaluated in millimeters. We calculated the relative risk (RR) for prevalence of CAC and AAC; and relative difference (RD) for continuous measures of CAC, AAC, and cIMT using linear regression. Our analysis was adjusted for age, sex, race/ethnicity, diabetes mellitus, systolic blood pressure, current smoking, eGFR, current use of anti-hypertensive medications, non-steroidal anti-inflammatory drugs, current use of lipid lowering medications, and IL-6.

Results: Among the 955 MESA participants, 46% were SE(+)—38% carried a single allele and 8% carried two double alleles. Average age was 60±9, 47% were women, and 51% were White, 9% were Asian, 16% were Black, and 24% were Hispanic/Latino. Age, sex, blood pressure, cholesterol, and inflammatory markers (CRP, TNF-α, IL 6), were similar between SE(+) and SE(-) participants, but racial distributions differed where SE(+) had a higher proportion of White (51% vs 38%) and lower proportion of Asian (9% vs 17%) and Black (16% vs 21%) participants. SE positivity was not significantly associated with a higher risk of CAC, AAC, or cIMT. However, individual allele 10:01 demonstrated 2.63-fold higher risk for CAC (95% CI: 1.17-5.99); 14:02 demonstrated 42% higher risk for AAC, (95% CI: 1.17-1.74); and 04:05 demonstrated 24% lower risk for AAC (95% CI: 0.58-0.99).

Conclusion: SE positivity was not associated with higher risk of CAC, AAC, or cIMT in a multi-ethnic community-living population. Alleles 10:01 and 14:02 were associated with a higher risk for CAC and AAC, respectively, and 04:05 with lower risk for AAC.

Associations of HLA-DRB1 alleles with coronary artery calcium, abdominal aortic calcium, and carotid intima media thickness in the Multi-Ethnic Study of Atherosclerosis

Disclosure: M. Kaur: None; **R. Katz**: None; **M. H. Criqui**: None; **M. Corr**: None; **W. S. Post**: None; **M. Budoff**: None; **G. P. Morris**: CareDx, 5, ThermoFisher/One Lambda, 1, 5, 12, travel support; **J. M. Hughes-Austin**: None.

Abstract Number: 0131

Identifying Antinuclear Antibody Positive Individuals at Risk for Systemic Autoimmune Disease: Development and Validation of a Real-Time Risk Model

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Up to 20% of the general population has a positive ANA without having autoimmune disease. Currently, no tools exist to help clinicians interpret the significance of a positive ANA. We developed and validated a risk model that uses readily available data in the electronic health record (EHR) to identify positive ANA individuals at risk for developing systemic autoimmune disease.

Methods: Using a large de-identified EHR, we randomly selected 2000 individuals with a positive ANA (titer ≥ 1:80) to perform chart review to determine if they were diagnosed with a systemic autoimmune disease by a rheumatologist. Non-rheumatic conditions such as autoimmune thyroiditis and autoimmune hepatitis were not counted as cases. Patients with prior diagnoses of systemic autoimmune disease at time of first positive ANA were excluded. *A priori,* we selected variables for the risk model including demographics, billing codes, and labs, previously identified in lupus risk models. We performed logistic regression using the following predictors: age at time of first positive ANA, sex, ANA titer, presence of another autoantibody (i.e. dsDNA), platelet count, and billing codes. A random selection of individuals was set aside for model validation. We assessed model performance in the training and validation sets using c-statistic and calibration curves.

Table 1. Characteristics of positive ANA individuals with vs. without systemic autoimmune disease in the training set.

Characteristics	No systemic autoimmune disease n = 878	Systemic autoimmune disease n = 152	*p* value
Age at positive ANA, years, mean ± SD	47.9 ± 19.3	41.8 ± 21.5	**0.003**
Race % (n) White Black Asian Native American Other	 85% (680) 12% (94) 2% (16) 0.1% (1) 1% (10)	 85% (127) 13% (19) 0% (0) 1% (1) 1% (1)	 0.26
Ethnicity Hispanic	 4% (30)	 1% (2)	 0.13
Gender Female Male	 70% (612) 30% (266)	 84% (127) 16% (25)	 **< 0.001**
ANA titer 1:80 ≥ 1:160	 21% (186) 79% (692)	 11% (16) 90% (136)	 **0.002**
White blood cell count K/uL, mean ± SD	 6.9 ± 3.4	 7.1 ± 3.2	 0.49
Platelet count K/uL, mean ± SD	 229 ± 96	 274 ± 113	 **< 0.001**
Serum creatinine mg/dL, mean ± SD	 1.2 ± 1.0	 0.9 ± 0.6	 **< 0.001**
Ever present autoantibody (i.e. dsDNA, SSA) Yes	 9% (78)	 51% (77)	 **< 0.001**
Total any billing codes, mean ± SD **Count of specific billing codes** (range: 0-9)	3.2 ± 6.2 0.6 ± 0.8	7.3 ± 4.3 0.9 ± 0.9	**0.02** **< 0.001**

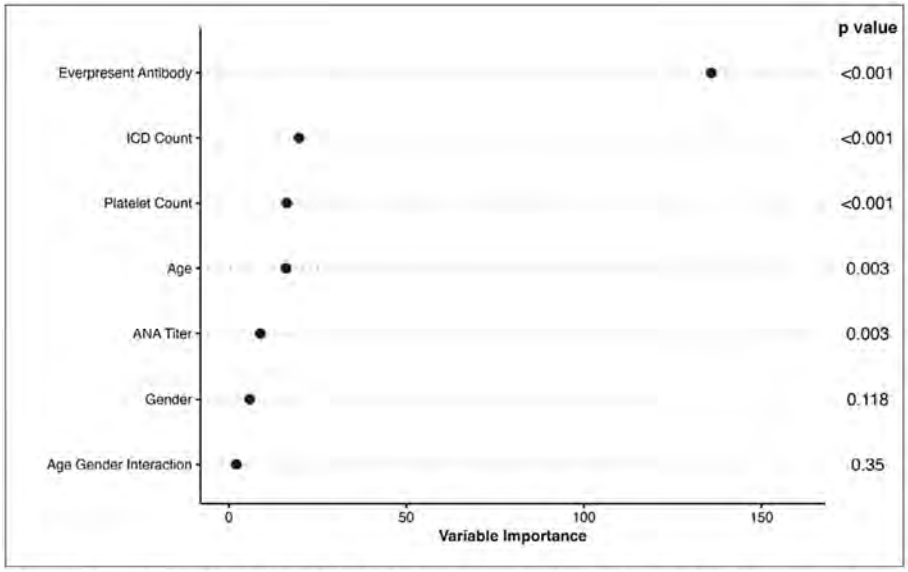

Figure 1. Importance of Variables in ANA Risk Model. The list of variables in the final ANA risk model are shown to the left with p values to the right. The x axis shows variable importance using a Wald statistic. Ever present antibody refers to having a disease-specific autoantibody such as a rheumatoid factor or dsDNA. ICD count refers to billing code category count that ranges from 0 to 9.

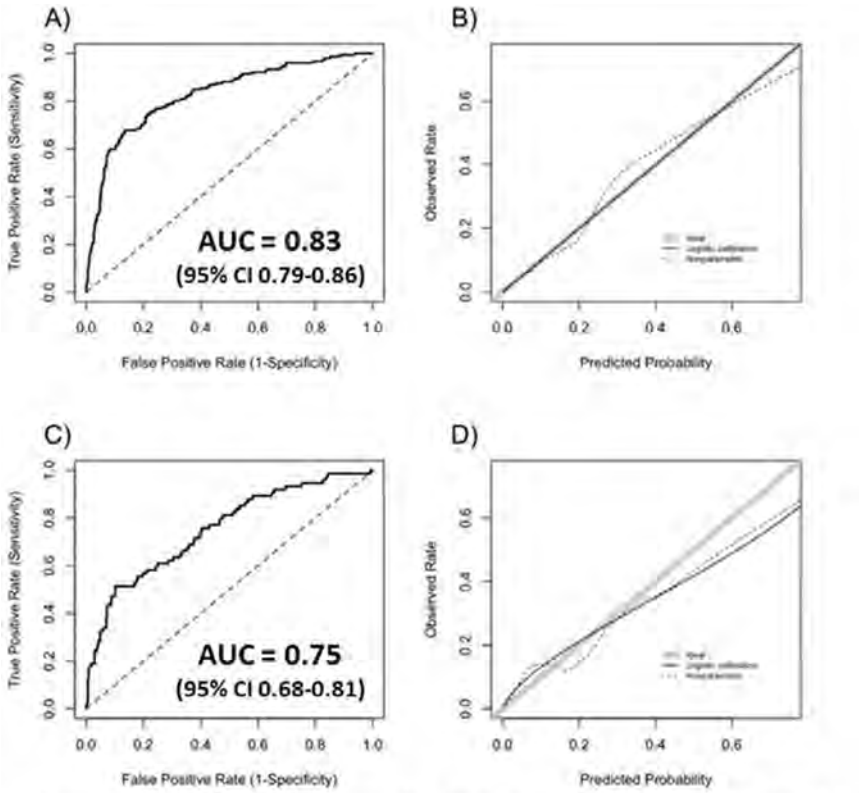

Figure 2. Model performance for training and validation sets. (A) shows ROC for the training set with an AUC 0.83 (95% CI 0.79-0.86). (B) shows the calibration curve with a slope of 1 and intercept of 0 for the training set. Slopes that approach 1, as shown by the shaded grey line, demonstrate ideal calibration, agreement between predicted risk for systemic autoimmune disease and observed rate. (C) shows ROC for the validation set with an AUC 0.75 (95% CI 0.68-0.81). (D) shows the calibration curve for the validation set. Calibration slope was equal to 0.71 and intercept was equal to 0.08.

Results: We assembled training (n = 1030) and validation (n = 449) sets with 15% (n = 152) and 16% (n = 74) having systemic autoimmune disease, respectively. The most frequent systemic autoimmune diseases in the training set were SLE at 18% (n = 28), other at 16% (n = 24), undifferentiated connective tissue disease at 16% (n = 24), and rheumatoid arthritis at 15% (n = 22). Other consisted of psoriatic arthritis/plaque psoriasis and inflammatory bowel disease. Individuals with systemic autoimmune diseases were younger (41.8 ± 21.5 vs. 47.9 ± 19.3 years, p = 0.003), more likely to be female (84% vs. 70%, p < 0.001), have a higher ANA titer (≥1:160 vs. 1:80) (90% vs. 79%, p = 0.002), higher platelet count (274 ± 113 vs. 229 ± 96 K/uL, p < 0.001), more likely to have a disease-specific autoantibody (51% vs. 9%, p < 0.001), and a higher count of the nine billing code categories (scale 0 to 9) compared to individuals without disease (0.9 ± 0.9 vs. 0.6 ± 0.8, p < 0.001) (Table 1). No significant differences were found in race, ethnicity, or white blood cell count. The most important variables in the model included having a disease-specific autoantibody, billing code count, and platelet count (Figure 1). For the training set, model AUC was 0.83 (95% CI 0.79-0.86) with good calibration (Figure 2). For the validation set, model AUC was 0.75 (95% CI 0.68-0.81).

Conclusion: We developed and validated a risk model for systemic autoimmune disease in positive ANA individuals. The model is important because it utilizes readily available EHR data and helps risk stratify positive ANA individuals. In the setting of a national shortage of rheumatologists and frequent referrals for positive ANAs, a risk stratifying tool for positive ANA

individuals is critical. High-risk individuals could be evaluated urgently to prevent delays in diagnosis while low-risk individuals could be reassured.

Disclosure: A. Barnado: None; **R. Moore**: None; **H. Domenico**: None; **S. Green**: None; **A. Camai**: None; **A. Suh**: None; **B. Han**: None; **K. Walker**: None; **A. Anderson**: None; **L. Caruth**: None; **A. Katta**: None; **A. McCoy**: None; **D. Byrne**: None.

Abstract Number: 0132

Feasibility of a Real-Time Risk Model to Identify Antinuclear Antibody Positive Individuals at Risk for Systemic Autoimmune Disease

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Positive antinuclear antibodies (ANAs) cause diagnostic dilemmas for clinicians across multiple specialties. We previously developed and validated a risk model using a de-identified electronic health record (EHR) database to distinguish individuals with positive ANAs who develop systemic autoimmune diseases from individuals who do not. We assessed the feasibility of deploying the risk model in the EHR. We also examined how the model performed in individuals with different systemic autoimmune diseases.

Methods: This logistic regression model contains the following predictors: age at time of first positive ANA, sex, ANA titer, platelet count, billing codes, and presence of another autoantibody (i.e. dsDNA, SSA). The most important variable in the model was presence of another autoantibody. We applied our risk model to data extracted from our EHR-provided data warehouse (Epic Clarity) to assess feasibility of deploying the model in real-time. We calculated risk probabilities for individuals with positive ANAs from 2017-2021. This time period captured an updated ANA titer reporting to the most current data available. Additionally, we combined training (n = 1030) and validation (n = 449) sets from the de-identified EHR. We compared risk scores for individuals in each of the autoimmune disease categories and in individuals without autoimmune diseases. Risk scores are reported as medians with interquartile ranges (IQR) and compared using the Mann-Whitney U test.

Results: We assessed the risk model using Epic EHR data for all individuals with a positive ANA from 2017-2021 (n = 22,234). We observed a similar distribution of risk scores in Epic compared to our model training set that used a de-identified EHR database (Figure 1). Risk scores for positive ANA individuals with and without autoimmune diseases from the combined training and validation sets from the de-identified EHR are shown in Figure 2. Individuals with systemic lupus erythematosus (SLE) had the highest risk scores with a median of 0.481 and IQR of 0.312-0.685 followed by Rheumatoid Arthritis with 0.423 (0.144-0.582). Individuals labeled as other, with predominantly seronegative conditions, had the lowest median risk score of 0.107 (0.061-0.269). Seronegative conditions included plaque psoriasis, psoriatic arthritis, and inflammatory bowel disease. Individuals with seropositive diseases had a higher risk score compared to individuals with seronegative diseases ($p < 0.001$). For individuals without autoimmune diseases, when available alternative diagnoses were documented by rheumatologists, the most frequent diagnoses were fibromyalgia, osteoarthritis, and gout.

Conclusion: To our best knowledge, a risk model that focuses on individuals with positive ANAs and predicts risk for multiple systemic autoimmune diseases does not currently exist. We demonstrate a validated risk model that uses readily available EHR data and can be successfully deployed in the EHR. For future studies, we will assess our risk model prospectively in real-time in the EHR and its impact on time to diagnosis and treatment for autoimmune diseases.

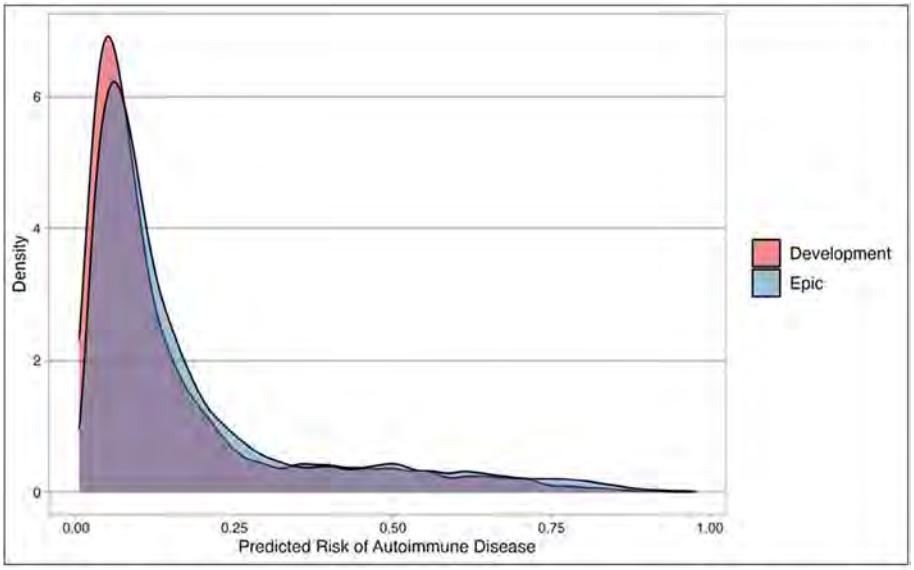

Figure 1. Distribution of risk scores in training set and in the electronic health record (EHR). The density plot shows the distribution of risk scores in our training or development set in the Synthetic Derivative, a de-identified EHR database, (pink) and in our EHR system (EPIC). X axis shows predicted risk for autoimmune disease and y axis density of data.

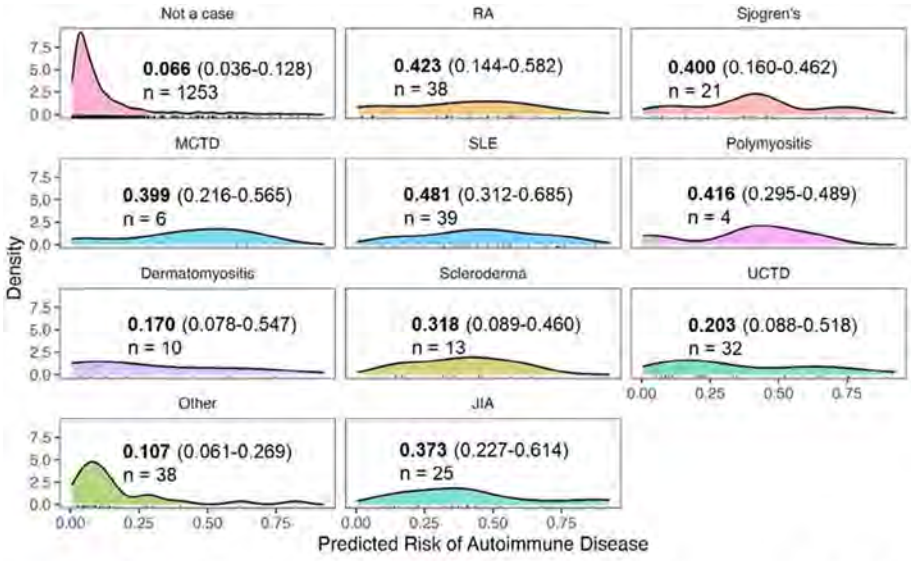

Figure 2. Distribution of risk scores by autoimmune disease type. Data is from a de-identified EHR database that includes training and validation sets. Different colors representing different autoimmune diseases are shown with the disease label above each box. For each autoimmune disease type including subjects without autoimmune disease or not a case, distribution of risk scores with a rug plot on the x axis are shown and density on y axis. Bolded numbers represent median risk score with interquartile ranges in parentheses. RA = rheumatoid arthritis, MCTD = mixed connective tissue disease, SLE = systemic lupus erythematosus, UCTD = undifferentiated connective tissue disease. Other represents seronegative conditions such as plaque psoriasis, psoriatic arthritis, and inflammatory bowel disease. JIA = juvenile idiopathic arthritis.

Disclosure: A. Barnado: None; **R. Moore**: None; **H. Domenico**: None; **S. Green**: None; **A. Camai**: None; **A. Suh**: None; **B. Han**: None; **K. Walker**: None; **A. Anderson**: None; **L. Caruth**: None; **A. Katta**: None; **A. McCoy**: None; **D. Byrne**: None.

Abstract Number: 0133

COVID-19 Vaccination-related Delayed Adverse Events Among Patients with Systemic Lupus Erythematosus: Results from the COVAD Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Epidemiology & Public Health Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1. Socio-demographic and vaccination data of survey respondents. HC: health controls; SLE: Systemic Lupus Erythematosus; nrAID: non-rheumatic autoimmune disease; rAID: rheumatic autoimmune disease.

Variable	Total, n (7203)	(%) (100)	SLE, n (882)	% (12.2)	rAIDs, n (3161)	% (43.9)	nrAIDs, n (426)	% (5.9)	HC, n (2734)	% (38.0)
Age (Me, IQR), years	44 (34-56)	-	39 (31-50)	-	52 (41-62)	-	43 (34-53)	-	38 (30-49)	-
Gender F:M	5310:1799 3:1	-	826:46 18:1	-	2522:602 4.2:1	-	351:70 5:1	-	1611:1081 1.5:1	-
Etnicity n (%)										
African American or of African origin (Black)	336	4.7	89	10.1	146	4.6	4	0.9	97	3.5
Asian	1632	22.7	263	29.8	602	19.0	57	13.4	710	26.0
Caucasian (White)	3039	42.2	274	31.1	1784	56.4	227	53.3	754	27.6
Do not wish to disclose	262	3.6	43	4.9	90	2.8	14	3.3	115	4.2
Hispanic	1200	16.7	114	12.9	283	9.0	83	19.5	720	26.3
Native American/Indigenous/Pacific Islander	53	0.7	12	1.4	17	0.5	4	0.9	20	0.7
Other	628	8.7	80	9.1	224	7.1	34	8.0	290	10.6

Background/Purpose: COVID-19 vaccines have been proven to be safe in healthy populations. However, data on delayed adverse effects (AEs) in people with autoimmune diseases (AIDs), including SLE has been lacking.

Methods: COVID-19 vaccination-related AEs reported longer than 7 days post-vaccination were assessed in the "COVID-19 Vaccination in Autoimmune Diseases 2" (COVAD-2) study in patients with SLE, rheumatic autoimmune diseases other than SLE (rAIDs), non-rheumatic autoimmune diseases (nrAIRDs), and healthy controls (HC). rAIDs included connective tissue diseases, inflammatory myopathies, and inflammatory arthritis, yet not SLE, whereas nrAIDs included inflammatory

Table 2. Effects of COVID-19 vaccination in patients with Systemic Lupus Erythematosus (SLE) vs healthy controls (HCs). Factors included as covariates in multivariable binary logistic regression analysis included age, sex, and ethnicity.

	SLE		HCs		Univariable		Multivariable	
	N 882	% 100	N 2734	% 100	OR (95% CI)	P, value	OR (95% CI)	P, value
Minor ADEs	155	17.6	456	16.7		0.555		
Injection site (arm) pain and soreness	96	10.9	305	11.2		0.800		
Myalgia	73	8.3	164	6.0	**1.4 (1.1-1.9)**	**0.020**		0.079
Body ache	81	9.2	176	6.4	**1.5 (1.1-1.9)**	**0.007**		0.056
Joint pain	73	8.3	120	4.4	**1.9 (1.4-2.6)**	**<0.001**	**1.8 (1.3 – 2.6)**	**<0.001**
Fever	63	7.1	205	7.5		0.700		
Chills	52	5.9	127	4.6		0.137		0.183
Cough	18	2.0	34	1.2		0.084		
Difficulty in breathing or Shortness of breath	24	2.7	33	1.2	**2.3 (1.3-3.9)**	**0.002**	**1.9 – 1.1-3.4)**	**0.031**
Nausea/vomiting	39	4.4	36	1.3	**3.5 (2.2-5.5)**	**<0.001**	**3.0 (1.8 – 5.0)**	**<0.001**
Headache	71	8.0	142	5.2	**1.6 (1.2-2.1)**	**0.002**	**1.5 (1.1 – 2.1)**	**0.012**
Rash	23	2.6	21	0.8	**3.5 (1.9-6.3)**	**<0.001**	**3.4 (1.7 – 6.6)**	**<0.001**
Fatigue	92	10.4	136	5.0	**2.2 (1.7-2.9)**	**<0.001**	**2.0 (1.5 – 2.8)**	**<0.001**
Diarrhoea	21	2.4	33	1.2	**2.0 (1.1-3.5)**	**0.012**		0.066
Abdominal pain	14	1.6	16	0.6	**2.7 (1.3-5.6)**	**0.004**	**2.7 (1.2 – 5.9)**	**0.015**
High pulse rate or palpitations	19	2.2	45	1.6		0.320		
Rise in blood pressure	17	1.9	19	0.7	**2.8 (1.5-5.4)**	**0.001**	**2.7 (1.3 – 5.6)**	**0.009**
Fainting	4	0.5	9	0.3		0.592		
Dizziness	33	3.7	51	1.9	**2.0 (1.3-3.2)**	**0.001**	**2.2 (1.3 – 3.5)**	**0.002**
Chest pain	22	2.5	29	1.1	**2.4 (1.4-4.2)**	**0.002**	**2.3 (1.2 – 4.3)**	**0.009**
Swelling in the extremities	14	1.6	17	0.6	**2.6 (1.3-5.3)**	**0.007**	**2.4 (1.1 – 5.1)**	**0.027**
Weakness and tingling in the feet and legs	28	3.2	49	1.8	**1.8 (1.1-2.9)**	**0.013**		0.093
Pricking or pins and needles sensations in the hands and feet	20	2.3	28	1.0	**2.2 (1.3-4.0)**	**0.005**	**1.9 (1.0-3.7)**	**0.040**
Visual disturbances (loss of vision, blurring of vision, etc.)	20	2.3	21	0.8	**3.0 (1.6-5.6)**	**<0.001**	**3.5 (1.7 – 7.2)**	**0.001**
Bleeding/bruising on the body	15	1.7	9	0.3	**5.2 (2.3-12.0)**	**<0.001**	**3.9 (1.6 – 9.5)**	**0.003**
Petechial rash	8	0.9	5	0.2	**5.0 (1.6-15.3)**	**0.002**	**4.2 (1.1 – 15.5)**	**0.030**
Major ADEs	118	13.4	224	8.2	**1.7 (1.4-2.2)**	**<0.001**	**1.6 (1.2 – 2.0)**	**0.001**
Anaphylaxis	8	0.9	19	0.7		0.525		
Marked difficulty in breathing	24	2.7	42	1.5	**1.8 (1.1-3.0)**	**0.022**	**2.0 (1.1 – 3.5)**	**0.020**
Throat closure	8	0.9	13	0.5		0.143		0.054
Severe rashes	22	2.5	29	1.1	**2.4 (1.4-4.2)**	**0.002**	**2.2 (1.2 – 4.1)**	**0.011**
Hospitalisation	51	5.8	57	2.1	**2.9 (2.0-4.2)**	**<0.001**	**2.2 (1.4 – 3.4)**	**<0.001**

bowel disease and multiple sclerosis, among others. The COVAD-2 study comprised 157 collaborators across 106 countries and was conducted between February and June 2022. An online survey captured self-reported data related to COVID-19 vaccination-associated AEs in SLE, AIDs, and HC. We compared COVID-19 vaccination-related delayed AEs between groups using multivariable binary regression adjusting for age, gender, and ethnicity.

Results: Among 7203 participants, 882 (12.2%) SLE, 3161 (43.9%) rAIDs, 426 (5.9%) nrAIDs, and 2734 (38%) HC were included from a total of 10 783 respondents, with 74% female and 42.2% Caucasian (Table 1). People with SLE were young and middle-aged adults [median age 39 (31–50); rAIDs, 52 (41–62); nrAIDs 43 (34–53); HC 38 (30–49)].

When compared to HC, people with SLE reported higher overall major [OR 1.6 (1.2–2.0)] and minor AEs (Table 2). SLE patients when compared to rAIDS reported more frequent episodes of severe rashes [OR 2.4 (1.3–4.2)], while compared to nrAIDs, SLE individuals reported an increased number of several minor AEs (joint pain [OR 2.4 (1.3–4.3)], fatigue [OR 2.0 (1.2–3.2)], body ache [OR 2.1 (1.2–3.7)]), and hospitalization [OR 2.3 (1.1–4.9)].

Table 3. Effects of COVID-19 vaccination in patients with Systemic Lupus Erythematosus (SLE) and no autoimmune comorbidities vs SLE with rheumatic autoimmune disease (rAIDs). Factors included as covariates in multivariable binary logistic regression analysis included age, sex, and ethnicity.

	SLE		rAIDs		Univariable		Multivariable	
	N 882	% 100	N 3161	% 100	OR (95% CI)	P, value	OR (95% CI)	P, value
Minor ADEs	155	17.6	516	16.3		0.378		
Injection site (arm) pain and soreness	96	10.9	301	9.5		0.229		
Myalgia	73	8.3	223	7.1		0.218		
Body ache	81	9.2	245	7.8		0.167		0.682
Joint pain	73	8.3	242	7.7		0.543		
Fever	63	7.1	188	5.9		0.193		0.724
Chills	52	5.9	153	4.8		0.207		
Cough	18	2.0	49	1.6		0.313		
Difficulty in breathing or Shortness of breath	24	2.7	60	1.9		0.130		0.763
Nausea/vomiting	39	4.4	72	2.3	**2.0 (1.3-3.0)**	**0.001**		0.076
Headache	71	8.0	213	6.7		0.178		0.977
Rash	23	2.6	78	2.5		0.814		
Fatigue	92	10.4	258	8.2	**1.3 (1.0-1.7)**	**0.034**		0.228
Diarrhoea	21	2.4	55	1.7		0.215		
Abdominal pain	14	1.6	43	1.4		0.613		
High pulse rate or palpitations	19	2.2	72	2.3		0.827		
Rise in blood pressure	17	1.9	39	1.2		0.119		0.249
Fainting	4	0.5	11	0.3		0.649		
Dizziness	33	3.7	109	3.4		0.676		
Chest pain	22	2.5	54	1.7		0.129		0.924
Swelling in the extremities	14	1.6	50	1.6		0.991		
Weakness and tingling in the feet and legs	28	3.2	78	2.5		0.245		
Pricking or pins and needles sensations in the hands and feet	20	2.3	68	2.2		0.834		
Visual disturbances (loss of vision, blurring of vision, etc.)	20	2.3	44	1.4		0.065		0.194
Bleeding/bruising on the body	15	1.7	29	0.9	**1.9 (1.0-3.5)**	**0.047**		0.146
Petechial rash	8	0.9	20	0.6		0.385		
Major ADEs	118	13.4	342	10.8	**1.3 (1.0-1.6)**	**0.034**		0.610
Anaphylaxis	8	0.9	22	0.7		0.519		
Marked difficulty in breathing	24	2.7	51	1.6	**1.7 (1.0-2.8)**	**0.031**		0.354
Throat closure	8	0.9	23	0.7		0.589		
Severe rashes	22	2.5	40	1.3	**2.0 (1.2-3.4)**	**0.009**	**2.4 (1.3 – 4.2)**	**0.004**
Hospitalisation	51	5.8	136	4.3		0.064		0.649

Vaccination with ChadOx1 nCOV-19 (Oxford/ AstraZeneca) in SLE patients led to a higher frequency in the incidence of diarrhea compared to other vaccines [OR 2.6 (1.1 – 6.2)], whereas the Moderna vaccine was associated with increased hospitalization frequencies [OR 3.0 (1.6–5.6)].

Patients with active versus non-active SLE reported similar frequencies of COVID-19 vaccine-related delayed minor AEs [17.5% versus 17.6%; OR 1.1 (0.8–1.6)]. SLE patients without autoimmune comorbidities reported fewer major and minor AEs compared to SLE patients with other concurrent rAIDs (Table 3). People with SLE and mental health disorders reported a higher frequency of severe rash [OR 3.2 (1.3–7.5)] and headache [OR 2.2 (1.3–3.6)].

Conclusion: COVID-19 vaccination is linked with increased risks of delayed AEs in patients with SLE compared to HC. Co-existence of rAIDs other than SLE yielded an increased risk for delayed AEs. By contrast, the degree of disease activity did not appear to have an impact.

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Abstract Number: 0134

Stressful Life Events in the Year Prior to Their Diagnosis Are Associated with Adult and Pediatric Systemic Rheumatic Diseases

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Epidemiology & Public Health Poster I

Session Type: Poster Session A

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Background/Purpose: Systemic rheumatic diseases (SRDs) are complex multi-organ immune-mediated disorders that arise from the interaction of environmental exposures in genetically predisposed individuals. Stressful life events have been associated with disease flares and progression, but their impact on SRD development is unclear. This study explored the association between life events, psychosocial stress, and the development of SRD in adult and pediatric siblings discordant for SRDs.

Methods: Life events data from the NIEHS Study of Twins or Siblings Discordant for SRDs was examined in 96 Adults, 129 Children (YC, 1-11 years), and 41 Teen (12-17 years) Probands within 5 years of diagnosis of one of four SRDs, and in their same gender unaffected Siblings (SIBs) and Healthy Controls (HCs), within 5 years of Probands' ages. Life events in the year prior to SRD diagnosis were queried using validated questionnaires, adapted from Paykel's List of Recent Life Events for adults and the Adolescent Perceived Event Scale for YC and Teens. Life events were categorized and rated by

Table 1. Life events questionnaires with scoring system and scale ratings by age group.

Questionnaire	Event Scores* (range)	Stress or Desirability Scale†	Weighted Event Scores‡ (potential range)
Adults, Interview for Recent Life Events§	Total (0-65) Major (0-16) Controllable (0-12) Uncontrollable (0-27) Desirable (0-6) Undesirable (0-40) Highly Stressful (0-65)	0 = "not all all" 1 = "a little stressful" 2 = "somewhat stressful" 3 = "very stressful"	Total (0 - 195) Major (0 - 48) Controllable (0 - 36) Uncontrollable (0 - 81) Desirable (0 - 18) Undesirable (0 - 120)
Young Children, Adolescent Perceived Event Scale‖	Total (0-76) Negative Positive Neutral Highly Undesirable	-2 = Very Bad -1 = Somewhat Bad 0 = Neither Good Nor Bad +1 = Somewhat Good +2 = Very Good	Total (-152 - 152) Negative (-152 - 0) Positive (0 - 152)
	Major (0-23) Negative Positive Neutral		Major (-46 - 46) Negative (-46 - 0) Positive (0 - 46)
Teens, Adolescent Perceived Event Scale‖	Total (0-99) Negative Positive Neutral	-4 = Extremely Bad -3 = Very Bad -2 = Somewhat Bad -1 = Slightly Bad 0 = Neither Good Nor Bad +1 = Slightly Good +2 = Somewhat Good +3 = Very Good +4 = Extremely Good	Total (-396 - 396) Negative (0 - 396) Positive (0 - 396)
	Major (0-26) Negative Positive Neutral		Major (-104 - 104) Negative (-104 - 0) Positive (0 - 104)

* Number of events endorsed, by categories within the year of the Proband's diagnosis of systemic rheumatic disease (SRD), which was also used as a reference date for Siblings and Healthy Controls .
‡ Sum of event ratings endorsed, by categories within the year of SRD diagnosis or reference date.
§ References: Paykel ES, *et al*. Arch Gen Psychiatry, 1975; Paykel ES, *et al*. Psychol Med, 1984
‖ References: Compas BE, *et al*. J Consult Clin Psychol, 1987

Table 2. Multivariate logistic regression of the association of stressful life events with systemic rheumatic disease diagnosis in adult Probands (n= 96) compared to Healthy Controls (n=53).

Stressful Life Event Scores*:	Odds Ratio	95% CI	*P* value
Event Scores:			
Total	1.31	1.11 - 1.53	0.001
Major	2.03	1.00 – 4.10	0.049
Uncontrollable	1.64	1.15 – 2.35	0.007
Undesirable	1.58	1.18 – 2.11	0.002
Highly Stressful	2.10	1.35 – 3.26	0.001
Weighted Event Score:			
Weighted Total Events	1.22	1.11 - 1.36	<0.001
Weighted Major Events	1.51	1.08 – 2.12	0.016
Weighted Uncontrollable Events	1.30	1.09 - 1.56	0.004
Weighted Undesirable Events	1.31	1.11 - 1.54	0.001

* Models were adjusted for age, sex, race/ethnicity, highest educational level, cigarette smoking, time from reference date to study enrollment.

Table 3. Multivariate logistic regression of the association of stressful life events with systemic rheumatic disease diagnosis among pediatric Probands, Siblings, and Healthy Controls.

	Young Children and Teens Combined§ (0-17 years)			Young Children (0-11 years)§		
Life Event Scores*†:	Odds Ratio	95% CI	*P* value	Odds Ratio	95% CI	*P*-value
Event Scores:						
Total Events	0.96	0.92 - 1.00	0.049	0.95	0.91 – 0.98	0.006
Positive	0.96	0.91 - 1.01	0.122	0.96	0.91 - 1.00	0.047
Major Events	0.79	0.66 – 0.95	0.011	0.81	0.70 – 0.94	0.004
Negative	0.69	0.52 – 0.91	0.008	0.80	0.66 – 0.96	0.016
Weighted Event Scores:						
Weighted Positive Events	0.92	0.82 - 1.03	0.161	0.98	0.96 - 1.00	0.060
Weighted Major Events:						
Weighted Major Negative Events	2.25	1.04 – 4.89	0.040	1.19	1.04 – 1.36	0.012

*Models were adjusted for age, sex, race/ethnicity, parental highest level of education, parental cigarette smoking, time from reference date to study enrollment.
† Multivariate logistic regression analysis was not shown in the Teen group, given lack of significant results in the univariate logistic analysis.
§ Young Children: Probands and Sibings (n=129 each), Healthy Controls (n=65); Teens: Probands and Siblings (n=41 each), Healthy Controls (n=16).

their associated stress or desirability (Table 1). The same reference period was used for SIBs and HCs. Pediatric questionnaires were completed by parents. Unconditional and conditional logistic regression were used to calculate odds ratios (OR) of SRD diagnosis.

Results: In adults, the number of total, uncontrollable, undesirable, and highly stressful life events was higher in probands compared to HCs (P values < 0.01–0.03), but there was no difference in the frequency of life events between Probands and SIBs. Perceived stress ratings in the same categories were higher in Probands compared to HCs (P-values < 0.01–0.04). In the YC and Teen combined analysis and in the YC group alone, probands had fewer positive and total life events than HCs (P≤0.04). These events were rated as more desirable by YC HCs than by Probands (P≤0.05). From multivariate logistic regression analyses, adjusted for demographics, time from reference date to study enrollment, and smoking, the number of total, major, uncontrollable, undesirable, and highly stressful life events and their corresponding stress ratings were associated with an increased odds of SRD diagnosis in adult Probands compared to HCs (OR 1.22–2.03, P values ≤0.05, Table 2). The frequencies of total, major negative, and major total events were associated with SRD diagnosis in YC and Teens combined (OR 0.69–0.96, P values ≤0.05, Table 3), and in YC alone. However, higher undesirable ratings for major negative life events were associated with SRD diagnosis in children (OR 2.25, P=0.04).

Conclusion: This retrospective study suggests that negative life events and their stress perception are associated with greater odds for SRD in adult Probands compared to HCs. The relationship between life events and SRD diagnosis is more nuanced in the pediatric group, where more frequent life events were associated with a lower odds of SRD, but a greater perception of undesirability with major negative life events was associated with subsequent SRD diagnosis. These findings support the need for better understanding the role of stress in the development of SRD.

Disclosure: I. Bauer Ventura: None; **M. Goldberg**: None; **A. Schiffenbauer**: Hope, 5; **M. Shi**: None; **R. Volochayev**: None; **S. H. Jackson**: None; **A. Jansen**: None; **N. Bayat**: None; **C. Parks**: None; **C. R. Weinberg**: None; **A. Picardi**: None; **F. Miller**: Argenx, 1, Cabaletta, 1, Pfizer, 2, 2; **L. Rider**: AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Hope Pharmaceuticals, 5.

Abstract Number: 0135

Cancer Incidence and Risk Factors in Patients with Newly Diagnosed Systemic Lupus Erythematosus

Jung-Yong Han[1], Yena Jeon[2], Gaeun Kang[2], Sun-Young Jung[3], Eun Jin Jang[4], Soo-Kyung Cho[5] and Yoon-Kyoung Sung[5], [1]Hanyang University hospital for rheumatic disease, Seongdong-gu, Seoul, South Korea, [2]Department of Statistics, Kyungpook National University, Daegu, South Korea, [3]College of Pharmacy, Chung-Ang University, Seoul, South Korea, [4]Department of Information Statistics, Andong National University, Andong, South Korea, [5]Hanyang University Hospital for Rheumatic Diseases, Seoul, South Korea

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Epidemiology & Public Health Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1. Baseline characteristics of incident SLE patients

Variables	Incident SLE patients (n=5,531)
Age, years	38 ± 16.65
Sex, female	4,961 (89.69)
Payer type	
National health insurance	4,828 (87.29)
Medical aid	672 (12.15)
Charlson comorbidity index	2.48 ± 1.71
Comorbidity	
Hypertension	974 (17.61)
Diabetes mellitus	217 (3.92)
Hyperlipidemia	546 (9.87)
Chronic kidney disease	263 (4.76)
SLE-related comorbidities	2.48 ± 1.71
APS	191 (3.45)
Fibromyalgia	239 (4.32)
Avascular necrosis	76 (1.37)
Interstitial lung disease	127 (2.30)
Lupus nephritis	1,065 (19.26)
Opportunistic infection	58 (1.05)
Viral infection	371 (6.71)
Medication*	
Hydroxychloroquine	3,631 (65.65)
Rituximab	4 (0.07)
Immunosuppressive agent	1,813 (32.78)
Steroid	4,260 (77.02)
NSIADs	3,209 (58.02)
SLE severity	
Mild	348 (6.29)
Moderate	707 (12.78)
Severe	4,476 (80.93)

APS, Anti-phospholipid antibody syndrome, Numerical quantitative data were presented by "mean ± SD" and categorical data were presented by "frequency (%)". *≥1 medication description for the period of 3 months before index date

Table 2. Incidence Rates of site-specific cancer in SLE patients

Site-specific cancer	Observational period (PYs)	No. of events	Incidence rate per 1,000 PYs (95% CI)
All cancer	29,453	156	5.23 (4.40, 6.05)
Solid cancer	29,507	135	4.58 (3.80, 5.35)
Lip, oral cavity and pharynx	29,980	3	0.10 (-0.01, 0.21)
Stomach	29,967	11	0.37 (0.15, 0.58)
Colon and rectum	29,952	16	0.53 (0.27, 0.80)
Liver	29,971	9	0.30 (0.10, 0.50)
Gallbladder etc.	29,990	2	0.07 (-0.03, 0.16)
Pancreas	29,993	2	0.07 (-0.03, 0.16)
Lung	29,985	6	0.20 (0.04, 0.36)
Breast	29,907	22	0.74 (0.43, 1.04)
Cervix uteri	29,936	12	0.40 (0.17, 0.63)
Corpus uteri	29,963	8	0.27 (0.08, 0.45)
Vulva and vagina	29,992	1	0.03 (-0.03, 0.10)
Ovary	29,985	3	0.10 (-0.01, 0.21)
Kidney	29,982	4	0.13 (0.00, 0.26)
Bladder	29,984	2	0.07 (-0.03, 0.16)
Ureter	29,986	1	0.03 (-0.03, 0.10)
Brain and CNS	29,991	2	0.07 (-0.03, 0.16)
Thyroid	29,844	29	0.97 (0.62, 1.33)
Hematologic cancer	29,938	21	0.70 (0.40, 1.00)
Hodgkin lymphoma	29,965	0	0
Non-Hodgkin lymphoma_nodal	29,976	6	0.20 (0.04, 0.36)
Non-Hodgkin lymphoma_extranodal	29,970	10	0.33 (0.13, 0.54)
Myeloma	29,987	2	0.07 (-0.03, 0.16)
Leukemia	29,986	3	0.10 (-0.01, 0.21)

PY, person-year; CI, confidence interval

Table 3. Cox regression model for risk factor in SLE patients

Variables	Univariate HR	p-value	Multivariable HR*	p-value
Age				
10-17	0.27 (0.06, 1.17)	0.08	0.26 (0.06, 1.17)	0.08
18-29	Ref		Ref	
30-39	2.15 (1.61, 4.00)	0.01	2.22 (1.18, 4.18)	0.01
40-49	3.28 (1.83, 5.89)	< 0.01	3.49 (1.91, 6.36)	< 0.01
50-59	4.13 (2.27, 7.50)	< 0.01	4.60 (2.48, 8.54)	< 0.01
60-69	2.82 (1.27, 6.25)	0.01	3.26 (1.45, 7.34)	< 0.01
70-79	5.97 (2.89, 12.35)	< 0.01	7.62 (3.50, 16.58)	< 0.01
Gender				
Male	Ref		Ref	
Female	0.91 (0.54, 1.53)	0.73	0.73 (0.43, 1.22)	0.22
Comorbidities				
Hypertension	1.03 (0.68, 1.58)	0.88	0.56 (0.36, 0.86)	< 0.01
Hyperlipidemia	1.58 (0.97, 2.58)	0.07	1.12 (0.66, 1.92)	0.67
Lupus nephritis	1.34 (0.76, 2.36)	0.31	1.39 (0.92, 2.09)	0.11
Steroid	0.88 (0.62, 1.25)	0.48	1.04 (0.70, 1.55)	0.84
Hydroxychloroquine†	0.77 (0.56, 1.06)	0.11	0.93 (0.65, 1.33)	0.85
Immunosuppressive agents††	0.48 (0.33, 0.69)	< 0.01	0.78 (0.55, 1.12)	0.17

HR, hazard ratio; APS, Anti-phospholipid antibody syndrome. †hydroxychloroquine defined as more than 6 months. ††≥1 medication description before the end of the study.

Background/Purpose: The increased cancer risk in patients with systemic lupus erythematosus (SLE) has received considerable attention. However, there is a lack of studies examining the cancer risk in newly diagnosed SLE patients, and the estimation of risk factors remains inadequate. This study aims to profile cancer incidence and identify risk factors in patients with newly diagnosed SLE.

Methods: From 2008 to 2018, all incident SLE patients were recruited from a comprehensive dataset combining information from the National Health Insurance Service, Health Insurance Review & Assessment Service, and Korea Central Cancer Registry. The study calculated the incidence rates (IRs) per 1,000 person-years (PYs) for site-specific cancers using the Surveillance, Epidemiology, and End Results (SEER) stage classification. Multivariable logistic regression analysis was employed to determine the association between incident SLE patients and risk factors.

Results: A total of 5,531 patients with newly diagnosed SLE were included, with a mean age of 38.0 ± 16.6 years, and 89.7% of them were female. Table 1 shows the baseline characteristics of the study population. During a follow-up period of 29,453 PYs, 156 SLE patients developed cancer. The IRs per 1,000 PYs for all cancers, solid cancers, and hematologic cancers were 5.23 (95% CI 4.40-6.05), 4.58 (95% CI 3.80-5.35), and 0.70 (95% CI 0.40-1.00), respectively. Based on SEER stage, a higher proportion of SLE patients were diagnosed with solid cancers at localized (64 events) and regional (43 events) stages, rather than distal stage (16 events).Site-specific cancers predominantly included thyroid (0.97, 95% CI 0.62-1.33) and breast cancer (0.74, 95% CI 0.43-1.04), followed by colon and rectal (0.53, 95% CI 0.27-0.80), cervix uteri (0.40, 95% CI 0.17-0.63), and stomach cancer (0.37, 95% CI 0.15-0.58) (Table 2). In the multivariable analysis (Table 3), the risk factors associated with cancer development in incident SLE patients were age above 30 years (adjusted hazard ratio [aHR] 2.22, 95% CI 1.18-4.18), whereas hypertension (aHR 0.56, 95% CI 0.35-0.89) was associated with a lower risk of cancer. Medication, such as hydroxychloroquine and immunosuppressive agents, did not correlate with the risk of cancer.

Conclusion: This study provides insights into the cancer incidence characteristics in Korean patients with newly diagnosed SLE over a long follow-up period. The distribution of cancer incidence was predominantly in the early stages, with thyroid and breast cancers being commonly diagnosed. The risk of cancer increased with older age in SLE patients, while there was no clear association between the use of immunosuppressive agents and cancer.

Disclosure: J. Han: None; **Y. Jeon**: None; **G. Kang**: None; **S. Jung**: None; **E. Jang**: None; **S. Cho**: None; **Y. Sung**: Bristol-Myers Squibb(BMS), 5, Eisai, 5, JW Pharmaceutical, 5, Pfizer, 5.

Abstract Number: 0136

The Prevalence and Risk Factors of Retinal Toxicity Associated with Long-term Hydroxychloroquine Use

Sophie Do, Jennifer Du, Jaejin An, Jim Wang and **Antony Lin**, Kaiser SCAL, Fontana, CA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) is commonly used for the treatment of various autoimmune diseases. The medication is generally well-tolerated. However, long-term use after 5 years may increase the risk of retinopathy. One study in 2014 has demonstrated the risk can be as high as 7.5%. Optical Coherence Tomography (OCT) has become a

major modality in screening retinopathy. Our study is to evaluate the prevalence of retinal toxicity among patients using HCQ and to determine various risk factors associated with HCQ-associated retinal toxicity.

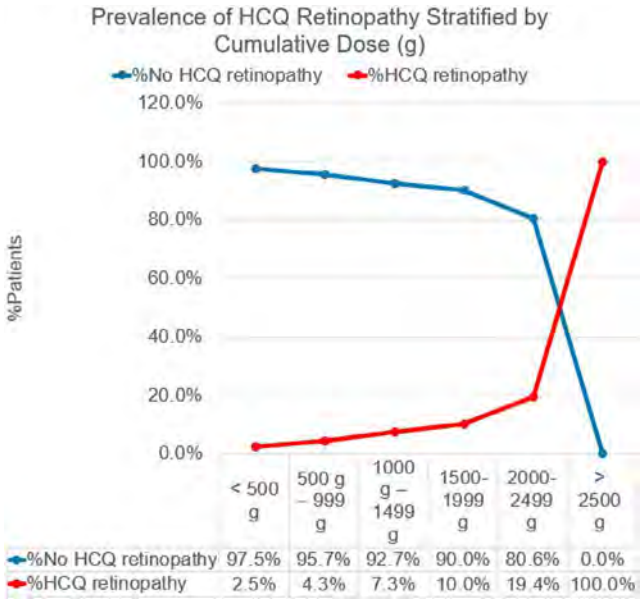
Methods: We performed a retrospective chart review on a cohort of adult patients with long-term use (> 5 years cumulative) of HCQ between January 1st, 2011 to December 31st, 2018 from the Kaiser Permanente San Bernardino County and Riverside Medical Center areas in Southern California, USA. Patients were excluded if they had previous been diagnosed with retinopathy prior to HCQ use, were deceased, or had incomplete OCT exam. Our primary endpoint was the prevalence of patients who developed retinal toxicity detected by OCT, and later confirmed by retinal specialist. Potential risk factors (age, duration of therapy, daily consumption per actual body weight, cumulative dose, confounding diseases and medications) for developing retinopathy were also evaluated. Univariable and multivariable logistic regression analyses were used to determine risk factors associated with retinal toxicity.

Results: Among 676 patients exposed to more than 5 years of HCQ, the overall prevalence of retinal toxicity was 6.8%, and ranged from 2.5% to 22.2% depending on the age group, weight-based dosing, duration of use and cumulative dose. Duration of therapy for 10 years or more increased risk of retinopathy by approximately 5 to 19 folds. Similarly, weight-based dose of 7mg/kg/day or greater was associated with increased risk of retinopathy by approximately 5 times. Patients with cumulative dose of 2000 grams or more had greater than 15 times higher risk of developing retinopathy. Duration of use for 10 years or more (odd ratio 4.32, 95% CI 1.99-12.49), age (odd ratio 1.04; 95% CI 1.01-1.08), cumulative dose of more

Table 2. Hydroxychloroquine Treatment Exposure

	No Retinal Toxicity (N=630)		Retinal Toxicity (N=46)		
	Mean	Std Dev	Mean	Std Dev	p-value
Dose per day (mg)	326.6	96.2	337	92.8	0.479
Dose per kg/day	**4.3**	**1.4**	**4.9**	**1.7**	**0.003**
Duration of use					
Months	**99.3**	**33.4**	**141.5**	**64.5**	**< 0.0001**
Years	**8.3**	**2.8**	**11.8**	**5.4**	**< 0.0001**
Cumulative dose (mg)	**983.2**	**445.2**	**1483.6**	**891.5**	**< 0.0001**

Results: HCQ Treatment Dosage, Duration, and Cumulative Dose



Results: Cumulative Dose of HCQ Therapy Distribution

than 1500 grams(odd ratio 7.4; 95% CI 1.40-39.04) and atherosclerosis of the aorta (odd ratio 2.59; 95% CI, 1.24-5.41) correlated with higher risk of retinal toxicity.

Conclusion: The overall prevalence of retinopathy was 6.8%. Routine OCT screening, especially in patient with hydroxychloroquine use for more than 10 years, daily intake > 7 mg/kg, or cumulative dose > 1500 grams is important in detecting HCQ-associated retinal toxicity.

Disclosure: S. Do: None; **J. Du**: None; **J. An**: AstraZeneca, 5, Bayer, 5; **J. Wang**: None; **A. Lin**: None.

Abstract Number: 0137

Incidence of and Risk Factors for Myelodysplastic Syndromes in Patients with Rheumatologic Diseases

YoungEun Kim[1], **Hansun Song**[1], Wook Jang Seo[2], Jinseok Kim[3], Soo Min Ahn[1], Seokchan Hong[4], Ji-Seon Oh[5], Chang-Keun Lee[6], Bin Yoo[6] and Yong-Gil Kim[1], [1]Department of Rheumatology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea, [2]Department of Rheumatology, Veteran Health Service Medical Center, Seoul, South Korea, [3]Department of Rheumatology, Jeju National University Hospital, Jeju National University School of Medicine, Jeju-si, Jeju-do, South Korea, La Jolla, CA, South Korea, [4]Department of Rheumatology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea, [5]Department of Information Medicine, Big Data Research Center, Asan Medical Center, University of Ulsan College of Medicine, Ulsan, South Korea, [6]Asan Medical Center, Seoul, South Korea

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Myelodysplastic syndrome (MDS) is a hematologic disorder characterized by dysplasia of bone marrow, leading to ineffective hematopoiesis and cytopenia. Despite sporadic reports of associations between rheumatologic diseases and MDS, the exact incidence rate of MDS in these patient populations, and the specific risk factors associated with MDS development, remain unclear. We investigated the incidence rate and risk factors of MDS in patients with rheumatologic disease.

Methods: We conducted a retrospective cohort study of patients who were diagnosed with rheumatologic diseases at a tertiary-care hospital between May 2009 and July 2022 and identified the patients who were subsequently diagnosed with MDS. Patients under 18 years of age and patients with a prior diagnosis of MDS were excluded. Each patient with MDS was matched with five age- and sex-matched controls chosen from the cohort of patients with each specific rheumatologic disease.

Results: During a total follow-up of 55,841 person-years (PY), MDS occurred in 64 patients, yielding an incidence rate of 1.15/1000 PY (median age, 57.0 [IQR, 41.0-69.0]; median duration to MDS diagnosis, 6.5 years [IQR, 3.0-9.0]). In an age- matched analysis, systemic lupus erythematosus (SLE) was a significant risk factor for MDS (adjusted hazard ratio, 2.61 [CI, 1.19–36.06], P=0.01). Refractory cytopenia with multilineage dysplasia was the most common phenotype of MDS (35.9%), and more than half of the patients had karyotypes with favorable prognoses (54.7%). Compared to matched controls, rheumatoid arthritis, SLE, and ankylosing spondylitis patients with MDS had lower levels of hemoglobin at the time

	n	Total observation period (PY)	MDS incidence rate (/1000 PY)	Unadjusted hazard ratio		Adjusted hazard ratio (age)	
				HR (95% CI)	P	HR (95% CI)	P
All rheumatologic diseases†	64	55841	1.15				
Rheumatoid arthritis	22	15991	1.38	0.71 (0.40-1.26)	0.24	0.62 (0.12-3.14)	0.56
Behcet's syndrome	10	6546	1.53	2.26 (0.29-17.68)	0.44	1.51 (0.69-3.32)	0.30
Systemic lupus erythematosus	10	6470	1.54	**2.32 (1.14-4.70)**	**0.02**	**2.61 (1.19-36.06)**	**0.01**
Ankylosing spondylitis	6	2254	2.66	1.48 (0.59-3.69)	0.40	1.61 (0.52-4.99)	0.41
Systemic vasculitis	5	1745	2.87	1.10 (0.10-12.10)	0.94	2.45 (0.20-29.93)	0.48
Adult-onset Still's disease	2	783	2.55	1.39 (0.09-22.21)	0.81	1.43 (0.05-37.98)	0.83
Inflammatory myositis	2	1485	1.35	2.97 (0.18-47.79)	0.44	2.43 (0.06-107.45)	0.65
Sjogren syndrome	2	2650	0.75	1.54 (0.10-24.77)	0.76	1.58 (0.09-27.19)	0.75
Polymyalgia rheumatica	2	2458	0.81	0.64 (0.89-4.68)	0.66	0.59 (0.05-6.55)	0.67
Palindromic rheumatism	1	1847	0.54	-		-	
Relapsing polychondritis	1	126	7.94	-		-	
Antiphospholipid syndrome	1	1092	0.92	-		-	

†All rheumatologic diseases include rheumatoid arthritis, systemic lupus erythematosus, Behcet's disease, relapsing polychondritis, palindromic rheumatism, idiopathic inflammatory myositis, anti-phospholipid syndrome, adult-onset Still's disease, polymyalgia rheumatica, systemic vasculitis, spondyloarthropathy, Sjogren syndrome, psoriatic arthritis, crystal arthropathy, systemic sclerosis, and IgG4-related disease.

of diagnosis of rheumatologic disease. Furthermore, the MDS patients with SLE and Behcet's disease had higher levels of glucocorticoid use in terms of frequency of use or mean dose than the control patients.

Conclusion: SLE is a significant risk factor for MDS among patients with rheumatologic diseases. A lower hemoglobin level at the time of diagnosis of rheumatologic disease was associated with the future development of MDS.

Prevalence of myelodysplastic syndrome in patients with various rheumatologic diseases

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Disclosure: Y. Kim: None; **H. Song**: None; **W. Seo**: None; **J. Kim**: None; **S. Ahn**: None; **S. Hong**: None; **J. Oh**: None; **C. Lee**: None; **B. Yoo**: None; **Y. Kim**: None.

Abstract Number: 0138

Prevalence and Incidence of Sjögren's Syndrome: A Systematic Literature Review

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren's syndrome (SjS) is a chronic autoimmune disease that has been historically categorized into primary (manifesting alone; pSjS) or secondary (appearing alongside another underlying autoimmune condition; sSjS) disease. Recent work has criticized this dichotomy, and instead recommends that SjS be described as a singular disease, with or without comorbidity. Previous literature reviews on the prevalence and incidence of SjS have shown varied estimates and focused on pSjS only. Epidemiological studies on overall SjS are needed to estimate the burden of illness on patients and society. We conducted a systematic literature review to describe prevalence and incidence rates of SjS, with specific focus on key countries, and to investigate geographic variations.

Methods: We searched Embase and MEDLINE® from database inception to 09/27/2022 using predefined search strategies. Gray literature searches were also conducted. Included were studies reporting prevalence or incidence rates of adults with SjS within the United States (US), EU5 (France, Germany, Italy, Spain, and the United Kingdom), China, and Japan.

Results: Of 7,121 abstracts identified from the literature searches, we included 19 studies that reported prevalence of SjS cases within a population, incidence of new cases, or both (Figure 1). We identified various designs: 10 studies were cross-sectional, 7 were retrospective cohort studies, and 2 were prospective cohort studies. Sample size ranged from 341 to 7.2 million participants (median: 25,885 participants). Baseline patient characteristics as well as the population in which prevalence or incidence were measured varied across studies; however, all study samples primarily consisted of female patients, which aligns with the real-world prevalence of SjS.

Prevalence of SjS among the general population (cases per 100,000 persons), reported in 16 studies (table 1), ranged from 13.1 to 103 in the US, from 10.2 to 3300 in Europe, and from 338.8 to 774.4 in Asia. Notably, the upper bound of the European range was from a dated survey with a small sample size; the next highest value was 748.8 cases per 100,000 persons. Prevalence was also calculated among populations with autoimmune disease such as rheumatoid arthritis (29,998 cases per 100,000 persons), systemic lupus (20,341), and multiple sclerosis (up to 12,174); these figures are much higher

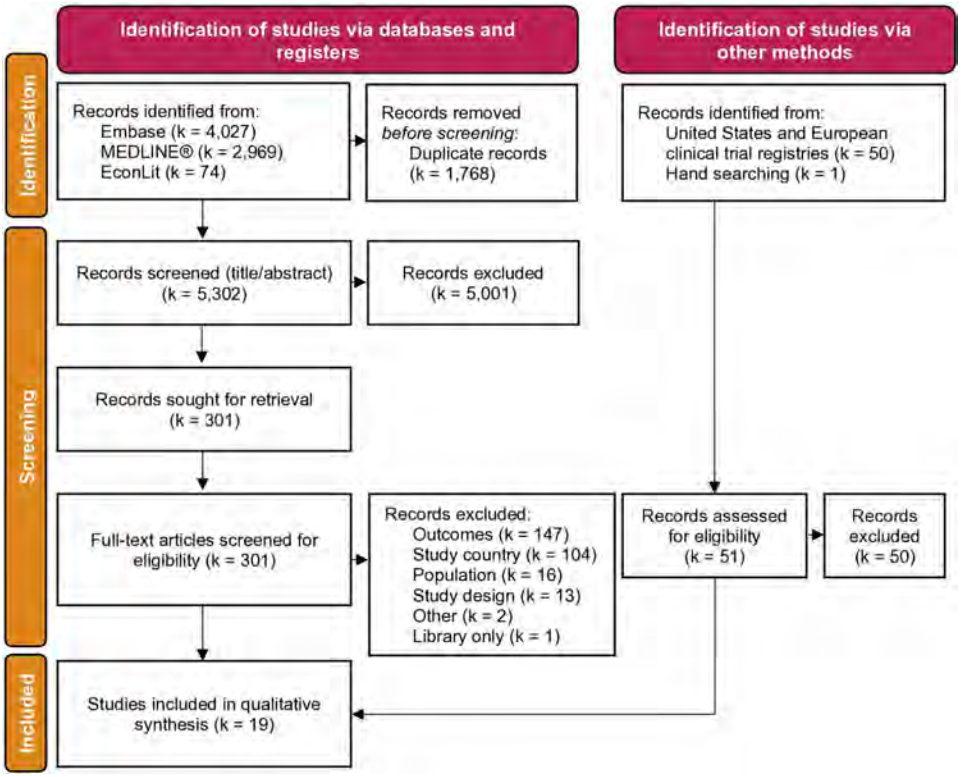

Figure 1. PRISMA flow diagram

Table 1. Prevalence rates of Sjögren's syndrome across included studies

Reference	Group	N	Prevalence, n (%)
Prevalence in the General Population			
Babazade 2015	SjS patients discharged based on administrative health data from the State Inpatient Databases, **US** from 2009-2010	5,539,875	5,463 (0.1%)* or 98.6 per 100,000 persons
Izmirly 2019	pSjS among adults in Manhattan, **US**, physician-diagnosed in 2007	1,585,873	0.01% or 13.1 per 100,000 person-years
Maciel 2017	pSjS in general population of Olmsted County, **US**, physician-diagnosed in 2015	113,306	0.1% or 103 per 100,000 persons
	pSjS in general population of Olmsted County, **US**, diagnosed using classification criteria in 2015	113,306	0.02% or 22 per 100,000 persons
Maldini 2014	pSjS in general population of Greater Paris Area, **France**, using AECG criteria in 2007	1,172,482	133 (0.01%) or 10.2 per 100,000 person-years
	pSjS in general population of Greater Paris Area, **France**, using study-specific enlarged criteria in 2007	1,172,482	203 (0.02%) or 15.2 per 100,000 person-years
Seror 2021	pSjS in general population of **France** from 2011-2018	NR	0.02-0.03% or 22-32 per 100,000 person-years
	pSjS + other autoimmune disease in general population of **France** from 2011-2018	NR	0.02% or 17-22 per 100,000 person-years
Albrecht 2020	SjS in general population of **German** statutory health insurance fund in 2018	7,200,000	53,917 (0.7%) or 748.8 per 100,000 persons
Sardu 2012	SjS in general population in South of Sardinia, **Italy** in 2009	25,885	0.03% or 31.0 per 100,000 persons
Narvaez 2020	SjS in general population of 78 municipalities in **Spain** from 2016-2017	4,916	16 (0.3%) or 325.5 per 100,000 persons
	pSjS in general population of 78 municipalities in **Spain** from 2016-2017	4,916	12 (0.3%) or 250 per 100,000 persons
Thomas 1998	SjS in general population of Manchester, **UK**	341	3.3% or 3300 per 100,000 persons
Zhang 1995	pSjS in general population of a Beijing suburb village, **China**, diagnosed using Modified Fox criteria	2,066	7 (0.3%) or 338.8 per 100,000 persons
	pSjS in general population of a Beijing suburb village, **China**, diagnosed using Copenhagen criteria	2,066	16 (0.8%) or 774.4 per 100,000 persons
Prevalence in Other Populations			
Aggarwal 2015	sSjS in systemic lupus erythematosus patients from the Lupus Family Registry and Repository in the **US**	2,694	548 (20.3%) or 20,341.5 per 100,000 persons
	pSjS in healthy relatives of systemic lupus erythematosus patients from the Lupus Family Registry and Repository in the **US**	7,390	71 (1.0%) or 960.8 per 100,000 persons
Harrold 2020	SjS in rheumatoid arthritis patients, in **US** from 2010-2018	24,528	7,358 (30.0%) or 29,998.4 per 100,000 persons
Miller-Archie 2020	SjS in adults exposed to 9/11 terrorist attack in **US** from 2015-2017	37,135	22 (0.1%) or 59.2 per 100,000 persons
Annunziata 2011	SjS in multiple sclerosis patients receiving disease-modifying drugs, in **Italy** from 2006-2007	230	28 (12.2%) or 12,173.9 per 100,000 persons
	SjS in treatment-naïve multiple sclerosis patients, in **Italy** from 2006-2007	210	14 (6.7%) or 6666.7 per 100,000 persons
Bowman 2004	pSjS in Caucasian females in Birmingham, **UK**	548	2 (0.4%) or 365.0 per 100,000 persons
Hida 2008	SjS in Nagasaki atomic bomb survivors in **Japan** from 2002-2004	1,008	23 (2.3%) or 2281.7 per 100,000 persons

*Value likely represents a mix of incident and prevalent cases. The primary survey used to estimate the prevalence of Sjögren's syndrome covered 4,729 Japan-wide hospital departments. AECG – American-European Consensus Criteria; N – Total sample size; n – Number of patients; NR – Not reported; pSjS – Primary Sjögren's syndrome; SjS – Sjögren's syndrome; sSjS – Secondary Sjögren's syndrome; UK – United Kingdom; US – United States.

than those within the general population. Incidence of SjS was reported in 6 studies (Table 2). Annual incidence rates of pSjS ranged from 3.2 to 5.8 cases per 100,000 person-years within the US, and 0.1 to 4.1 cases per 100,000 person-years in France. Prevalence and incidence data for sSjS were scarce.

Conclusion: Global incidence of SjS ranges from 0.1 to 5.8 cases per 100,000 person-years and prevalence of SjS in the general population ranges from 10.2 to 3300 cases per 100,000 persons. Some of the variations may be related to, in part, the difficulty in diagnosing SjS. Prevalence rates are higher among patients with other autoimmune diseases. Large cohort studies on the prevalence and incidence of SjS alone and SjS associated with other autoimmune diseases are warranted, in particular those that look at treated versus untreated patients.

Table 2. Incidence rates of Sjögren's syndrome across included studies

Reference	Group	N	Incidence, n (%)
Incidence in the General Population			
Izmirly 2019	pSjS among adults in Manhattan, **US**, physician-diagnosed from 2007-2009	1,585,873	3.5 per 100,000 person-years
Maciel 2017	pSjS patients receiving care in the Olmsted Medical Center or affiliate centers within Olmsted County, **US** from 1976-2015	113,306	5.8 per 100,000 person-years
Pillemer 2001	pSjS amongst residents of Olmsted County, **US** from 1976-1992	108,145	3.2 per 100,000 person-years
Albrecht 2020	SjS amongst citizens with statutory health insurance, **Germany** in 2018	7,200,000	102 per 100,000 person-years*
Seror 2021	pSjS in general population of **France** from 2012-2018	NR	0.3-4.1 per 100,000 person-years
	pSjS + other autoimmune disease in general population of **France** from 2012-2018	NR	0.1-2.1 per 100,000 person-years
Incidence in Other Populations			
Nannini 2013	pSjS patients with interstitial lung disease in Olmsted County, **US** from 1976-2005	NR	5.1 per 100,000 person-years

*This value was considered an outlier. The higher value may be explained by the data source being a health insurance database, which may not be representative of the true general population. N – Total sample size; n – Number of patients; NR – Not reported; pSjS – Primary Sjögren's syndrome; SjS – Sjögren's syndrome; US – United States.

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Abstract Number: 0139

Systemic Vasculitides in Portugal and Brazil: Preliminary Results from the Reuma.pt/vasculitis Registry

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The epidemiology of vasculitis varies widely across different geographic areas of the world which may be due to different ethnic and environmental factors. Brazil has a heterogeneous population with influences from Indigenous, African, Asian, and European countries, while Portugal has a very ethnically homogeneous background. This study aims to assess the main differences in the profile of systemic vasculitides between Portugal and Brazil.

Table 1.– Comparison of features in vasculitis patients between Portugal and Brazil.

Variables	Portugal	Brazil	*p*
Behçet's disease			
Females, %	75.5	67.2	0.033*
Age at diagnosis, years	33.3 (25.0-42.3)	33.3 (27.0-40.7)	0.878
Time between symptoms and diagnosis, years	4.00 (1.00-12.00)	0.99 (0.32-4.00)	< 0.0001*
Giant cell arteritis			
Females, %	66.0	80.6	0.076
Age at diagnosis, years	75.3 (69.4-80.4)	68.6 (61.7-75.4)	< 0.0001*
Time between symptoms and diagnosis, years	0.16 (0.05-0.37)	0.43 (0.08-1.83)	0.014*
Takayasu arteritis			
Females, %	85.2	93.9	0.066
Age at diagnosis, years	37.0 (24.3-49.6)	30.3 (23.3-40.4)	0.020*
Time elapsed between symptoms and diagnosis, years	1.16 (0.58-4.61)	1.08 (0.41-4.37)	0.692
Polyarteritis nodosa			
Females, %	56.8	70.0	0.316
Age at diagnosis, years	43.1 ± 17.1	32.3 ± 14.4	0.027*
Time between symptoms and diagnosis, years	1.00 (0.49-2.87)	0.48 (0.29-3.83)	0.463
Granulomatosis with polyangiitis			
Females, %	58.6	60.2	0.818
Age at diagnosis, years	51.5 ± 15.8	43.9 ± 14.2	0,001*
Time elapsed between symptoms and diagnosis, years	0.67 (0.24-3.00)	0.99 (0.29-2.08)	0.600
Microscopic polyangiitis			
Females, %	57.3	75.0	0.239
Age at diagnosis, years	64.3 (54.8-74.1)	58.2 (38.2-74.5)	0.352
Time elapsed between symptoms and diagnosis, years	0.42 (0.10-0.91)	0.33 (0.23-1.58)	0.738
Eosinophilic granulomatosis with polyangiitis			
Females, %	61.0	54.5	0.598
Age at diagnosis, years	54.7 ± 15.8	49.6 ± 11.1	0.176
Time elapsed between symptoms and diagnosis, years	1.56 (0.26-6.50)	2.00 (0.83-4.00)	0.480

Continuous data are presented as median and interquartile range or as mean and standard deviation; * - Flags significant results.

Methods: Collaborative project between the Portuguese and the Brazilian Societies of Rheumatology in which centres from both countries were invited to register data in the vasculitis module of the Rheumatic Diseases Portuguese Register, Reuma.pt/vasculitis. A cross-sectional analysis was performed comparing demographic, ethnic and diagnostic information between Brazilian and Portuguese centres.

Results: A total of 1,955 patients were analysed: 74.2% from 30 Portuguese centres and 25.8% from 7 Brazilian centres. Portuguese patients were predominantly European White (89.2%) and in Brazil the most common ethnic groups with vasculitis were the non-European White (48.3%) and Mestizos (40.1%); 5.4% of all participants were born in other countries. Brazilian patients were younger at the onset of symptoms [35.2 (24.1-46.6) vs.48.1 (27.4-70.1) years; $p< 0.05$]and diagnosis of vasculitis [37.0 (27.6-48.3) vs. 50.8 (32.7-70.4) years; $p< 0.05$] than Portuguese patients, respectively. When analysing individual forms of vasculitis, Brazilian patients with giant cell arteritis (GCA), Takayasu arteritis (TAK), polyarteritis nodosa (PAN) and granulomatosis with polyangiitis (GPA) were significantly younger than Portuguese patients at diagnosis ($p< 0.05$). The proportion of females was higher in Portuguese patients with Behçet's disease (BD) than in Brazilian patients ($p=0.03$). No differences regarding the proportion of females were observed for other vasculitides (Table 1). The most common form of vasculitis in both countries was BD followed by GCA in Portugal and by TAK in Brazil. Regarding ANCA-associated vasculitis, GPA was more common in Brazil and microscopic polyangiitis (MPA) in Portugal. Both countries had similar proportions of patients with PAN and eosinophilic granulomatosis with polyangiitis (EGPA) (Figure 1 and Table 2). Time elapsed between the onset of

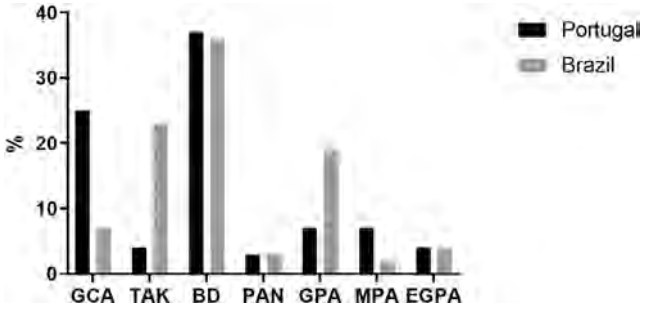

Figure 1.- Frequency of systemic vasculitis in Portugal and Brazil. GCA, giant cell arteritis; TAK, Takayasu arteritis; BD, Behçet´s disease; PAN, polyarteritis nodosa; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; EGPA, eosinophilic granulomatosis with polyangiitis

Table 2.– Frequency of systemic vasculitis in Portugal and Brazil.

Vasculitis	Portugal (n = 1451)	Brazil (n = 504)
Behçet's disease, n (%)	473 (34.2)	180 (35.7)
Giant cell arteritis, n (%)	329 (23.8)	36 (7.1)
Granulomatosis with polyangiitis, n (%)	99 (7.2)	93 (18.5)
Takayasu arteritis, n (%)	54 (3.9)	114 (22.6)
Microscopic polyangiitis, n (%)	96 (6.9)	12 (2.4)
Eosinophilic granulomatosis with polyangiitis, n (%)	59 (4.3)	22 (4.4)
Polyarteritis nodosa, n (%)	44 (3.2)	20 (4.0)
IgA vasculitis, n (%)	38 (2.7)	7 (1.4)
Cryoglobulinemic vasculitis, n (%)	24 (1.7)	4 (0.8)
Cogan syndrome, n (%)	14 (1.0)	0 (0.0)
HCV cryoglobulinemic vasculitis, n (%)	6 (0.4)	1 (0.2)
Antiglomerular basement antibody disease, n (%)	5 (0.4)	1 (0.2)
Kawasaki's disease, n (%)	2 (0.1)	0 (0.0)
Hypocomplementemic urticarial vasculitis, n (%)	2 (0.1)	0 (0.0)

HCV – Hepatitis C virus; n – Number of patients.

symptoms and the diagnosis of GCA was higher in Brazil than in Portugal (p=0.014) while Portugal had a longer interval between the onset of BD symptoms and its diagnosis compared to Brazil (p< 0.05) (Table 1).

Conclusion: In this large multicentre binational study, Portugal and Brazil had a different profile of systemic vasculitis concerning the proportion of GCA and TAK patients, as well as GPA and MPA patients. In addition, both countries had differences in the age of onset, female gender, and ethnicity of patients with systemic vasculitis.

References

Ponte C, et al. *Orphanet J Rare Dis*, 2020.
Watts RA, et al. *Nat Rev Rheumatol*, 2022.

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Extent of Recording of 2019 EULAR/ACR Classification Criteria for Systemic Lupus Erythematosus in a UK Healthcare Database

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The 2019 EULAR/ACR Classification Criteria allow classification of patients with systemic lupus erythematosus (SLE) for research. They reflect updates in current understanding of SLE and their value has been extensively documented in traditional research cohorts. Their functionality in electronic healthcare records is not well established. The purpose of this study was to describe the recording of the 2019 EULAR/ACR Classification Criteria within a UK electronic health database, the Clinical Practice Research Datalink (CPRD) to aid understanding of their utility in research studies in this setting.

Methods: Ethical approval was obtained from the CPRD Independent Scientific Advisory Committee (21_000697). The study period was 01/01/1990 to 31/12/2020. Read code lists were devised to identify adult patients with possible SLE within the CPRD, defined as cases. Codes relating to discoid, tuberculous or drug-induced lupus were excluded. Valid patients within the CPRD without a record of a SLE code were defined as non-cases. EULAR/ACR criteria definitions were adapted for use within the CPRD. Patient records were searched for the presence of criteria items. Descriptive statistics

Table 1. 2019 EULAR/ACR criteria counts in cases and non-cases and odds ratio (with confidence intervals and P value)

	Case (n)	Non case (n)	OR	95% CI	*P*-value
Total	12,376	11,397,308	-	-	-
Fever	128	44509	2.666	2.239,3.173	<0.0001
Delirium	324	133874	11.44	10.4,12.57	<0.0001
Psychosis	205	116822	1.626	1.417,1.867	<0.0001
Seizure	413	157447	1.392	1.386,1.399	<0.0001
Alopecia	1134	249777	4.502	4.235,4.786	<0.0001
Ulcers	954	263568	3.528	3.302,3.77	<0.0001
ACLE	79	1230	59.52	47.39,74.78	<0.0001
Discoid	1990	7996	272.9	258.9,287.7	<0.0001
Joint	3087	461074	44.76	42.95,46.64	<0.0001
Effusion	352	54729	6.067	5.455,6.748	<0.0001
Pericarditis	211	16971	11.63	10.14,13.34	<0.0001
Nephritis	48	1359	32.65	24.47,43.56	<0.0001
APLS Ab	1837	40138	49.32	46.89,51.88	<0.0001
Autoimmune haemolysis	101	4871	19.24	15.79,23.45	<0.0001
Proteinuria	284	9133	29.29	25.99,33.0	<0.0001
DsDNA/ anti-Sm	2956	81516	43.56	41.77,45.42	<0.0001
ANA positive	191	3127	57.12	49.3,66.17	<0.0001
Complement	2007	29356	74.95	71.36,78.73	<0.0001
Leucopaenia	141	6922	25.42	24.49,30.07	<0.0001
Thrombocytopaenia	447	37225	11.44	10.4,12.57	<0.0001

were used to describe the capture of ACR criteria for patients. Odds ratios were used to compare the presence of individual criteria in cases vs non-cases.

Results: 12,376 cases and 11,397,308 non-cases were identified. Counts for each criteria, for both groups, are presented in Table 1. Only 1.5% (n=191) of cases had a record of a positive ANA test. The most common criterion seen for cases was joint involvement (24%, n=3087, and the least common was autoimmune haemolysis (0.8%, n=101). Odds ratios and 95% confidence intervals for the presence of criteria items in cases and non-cases are presented in Table 1. The odds of all EULAR/ACR criteria items were significantly higher in cases than non-cases. This was most pronounced for discoid rash (OR 272.9, 258.9-287.7, $P< 0.0001$) and least for seizure (OR 1.392, 1.386-1.399,$P< 0.0001$).

Conclusion: These data show that the 2019 EULAR/ACR SLE criteria can be identified within the CPRD. The prevalence of these items is lower than those seen in traditional research studies which reflects differences in recording practices between primary and secondary care. Researchers should be cautious when using absolute counts of these items within the CPRD and possibly other primary care databases. Low prevalence of ANA positivity will preclude this as an entry criteria in this setting. The higher odds of criteria in cases compared to non-cases, suggests use of Read codes is likely to identify true SLE cases; combining these with 2019 EULAR/ACR SLE criteria and other parameters may further aid this process.

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In-patient Outcome Difference in Systemic Lupus Erythematous Patient Between Medicare and Non-Medicare Group, a Nationwide Analysis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus is a chronic inflammatory disorder that significantly burdens our health system. The study aimed to understand the difference in in-patient outcomes based on insurance status, especially between Medicare and non-Medicare groups.

Methods: Using National Inpatient Sample databases from 2016 - 2020, we identified patients with underlying systemic lupus erythematosus. Patients were divided into two main groups (with Medicare and with non-Medicare insurance). Our primary outcome of the study was in-patient mortality, length of stay and hospital cost. Multivariate logistic regression, and student t-test were used for analysis using STATA 17.0.

Results: Out of 789,720 SLE admissions, 49.9% were non-Medicare, and 51.1% had Medicare as an insurance. Medicare cohort were older (mean age 62±15.0 vs 44±14.2, P value < 0.001) and predominantly Caucasians compared to Non-Medicare cohort. Medicare cohort was associated with a higher prevalence of Hypertension (74.7% vs 50.4, P value < 0.001), peripheral vascular disease (10.1% vs 4.5%, P value < 0.001), chronic kidney disease (32.4% vs 16.6%, P value < 0.001) and Congestive heart failure (29.5% vs 14.5%, P value < 0.001) when compared to a non-Medicare cohort. However, there were fewer patients with Obesity in Medicare cohort when compared to the non-Medicare cohort (19.1% vs 20.6%, P value < 0.001). In-patient mortality between Medicare and non-Medicare group (10090 vs 6075, OR 0.76, 95% CI 0.68-0.84 P value < 0.001) showed significant better outcome in non-Medicare group. There was higher in-hospital cost in Medicare cohort compared to non-medicare cohort ($17475 vs $17128, P value < 0.001) and slightly longer length of stay in Medicare cohort compared to non-medicare cohort (5.5±6.1 vs 5.2±7.1, P value < 0.001).

Conclusion: This study shows that having a Non-medicare payer is better than Medicare. However, the difference is minimal even though it is statistically significant, so we should assess the clinically significant difference between the two cohorts.

Disclosure: M. Paul: None; **P. Paul**: None; **B. Amgai**: None; **J. Ramos**: None.

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New-Onset Systemic Autoimmune Diseases Following COVID-19 Vaccination – Results from the COVAD Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

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Background/Purpose: We aim to describe the profile of new-onset systemic autoimmune diseases (SAID) developed in individuals following COVID-19 vaccination and to characterize the potential risk factors for their occurrence using a large-scale international survey.

Methods: A retrospective cohort study was conducted among participants who self-reported new-onset SAID in the COVAD-2 study - a global, validated, patient-reported e-survey involving 167 collaborators from 110 countries, to collect data on the long-term safety and tolerability of COVID-19 vaccines in patients with SAID (1). Responses are summarized using descriptive statistics including median (IQR) on the new onset of SAID. Baseline characteristics between those with new-onset SAIDs diagnosed by a rheumatologist and vaccinated healthy controls (HCs) are compared after 1:4 propensity

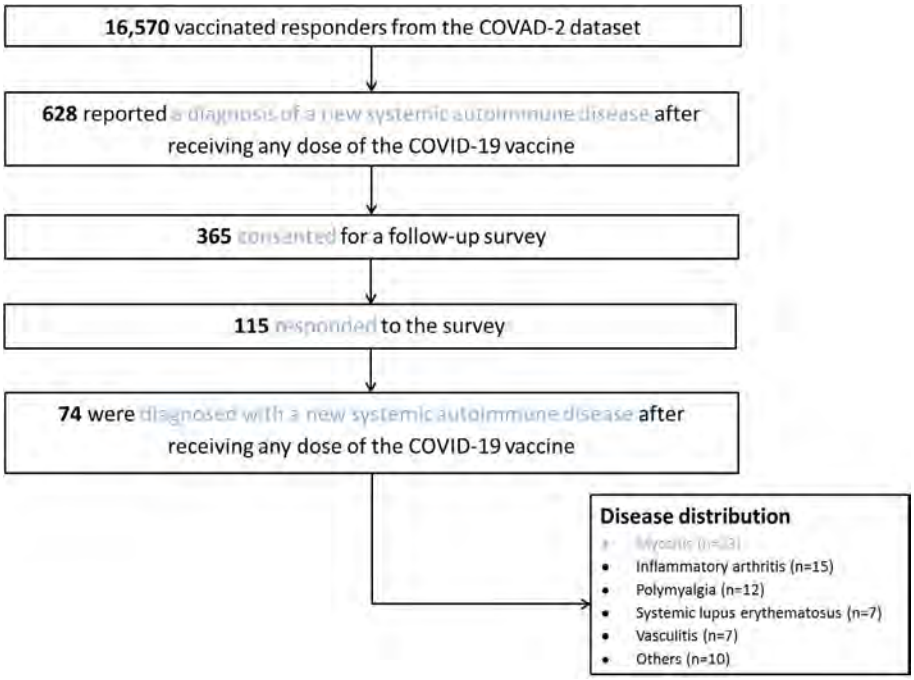

Figure 1. Flowchart showing process of study participants' selection

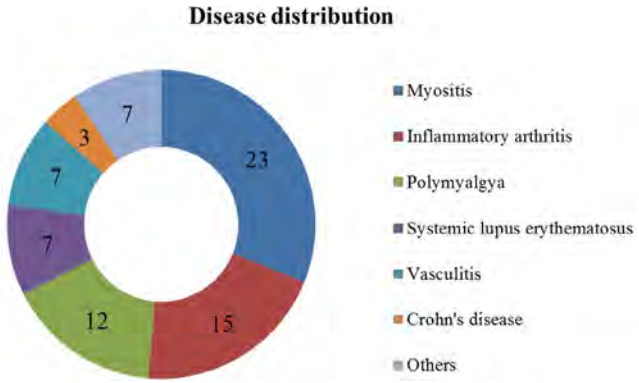

Figure 2. Disease distribution of respondents developing new autoimmune disease after COVID-19 vaccination

score (PS) matched analysis based on age and gender variables. Predictors of new-onset SAIDs were assessed using binary logistic regression adjusting for age, gender, ethnicity, and country by HDI.

Results: Out of a total of 16,570 vaccinated respondents to the COVAD-2 survey, 628 reported a diagnosis of a new-onset SAID after receiving any dose of a COVID-19 vaccine. Of them 365 consented for a follow-up survey and 115 completed the survey. A total of 74 respondents with confirmed diagnosis of new-onset SAID were included in the final analysis (mean age was 52 years (range 18-82 years; SD: 14) and more than three-quarters were females (n=59, 79.7%)) (fig. 1). The most commonly reported new-onset SAIDs were idiopathic inflammatory myopathies (n=23, 31.1%) followed by inflammatory arthritis (n=15; 20.3%) and polymyalgia rheumatica (n=12, 16.2%) (fig. 2). The most commonly received COVID-19 vaccines leading to new-onset SAID were Pfizer (n=37, 37.4%) followed by Moderna (n=32, 32.3%) and then Oxford/AstraZeneca (n=26, 26.3%). The median (IQR) duration from vaccination to symptom onset was 14 (5-30) days. PS matched analysis between vaccinated HCs and new-onset SAIDs showed higher odds of new-onset SAIDs among Caucasians (OR: 5.3; 95%CI: 2.9-9.7; p< 0.001) and mRNA-1273 (Moderna) vaccine recipients (2.7; 1.3-5.3; 0.004) and lower odds among Asians (0.2; 0.1-0.7; 0.011) and BNT162b2 (Pfizer-BioNTech) vaccine (0.3; 0.2-0.7; 0.003) recipients. The predictors of new-onset SAIDs included presence of SAID multimorbidity (1.4; 1.1-1.7; < 0.001), mental health disorders (1.6; 1.3-1.9; < 0.001), and mixed race (2.2; 1.2-4.2; 0.010). Whereas, those with age >60 years (0.6; 0.4-0.8; 0.007), increasing vaccine doses (0.3; 0.2-0.5; < 0.001) and high/medium HDI countries (compared to very high HDI) (0.6; 0.4-0.8; 0.002) reported fewer new onset SAIDs.

Conclusion: This large case-series from the COVAD data set provides the first insights to new-onset SAID following COVID-19 vaccination in a global population. Due to disparity between patient and physician reporting, it is imperative to identify the correct diagnosis in individuals reporting new-onset SAID. Further research is therefore needed to facilitate counselling of individual risks and benefits, particularly if risk could be reduced by different COVID-19 vaccines schedules in predisposed individuals.

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Abstract Number: 0143

Cancer Incidence in Familial Mediterranean Fever

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Background/Purpose: Familial Mediterranean Fever (FMF) is the most common hereditary monogenic fever syndrome characterized by recurrent attacks of fever and polyserositis. Anti-inflammatory drugs, with colchicine being the first-line therapy, have been used in FMF treatment to provide improvement in attacks and prevent amyloidosis, the most serious complication of the disease. Various types of cancer may be observed in FMF patients. This study aimed to evaluate the association between FMF and the risk of cancer, by using the cancer-related outcomes of a cohort of Turkish FMF patients and those of the general Turkish population.

Methods: We retrospectively screened the cancer statistics of our study group consisting of 1734 Turkish FMF patients registered at our division. Data were gathered from patient files, digital records, or from patients themselves verbally. Cancer-related estimates of the Turkish population were published by the Ministry of Health of Turkey in the Turkey Cancer Statistics Report (TCSR), in 2017. Standardized incidence rates (SIR) were calculated to compare the cancer incidences observed in our study group with the expected cancer incidences of the Turkish population. Indirect age adjustment was used,

Table 1. Distribution of cancer types among Turkish Familial Mediterranean Fever patients

Cancer type	Female (n)	Male (n)
BCC[a]	0	1
Breast	7	-
Cervical	2	-
Colorectal	2	1
Endometrial	3	-
Gallbladder	1	-
Hodgkin lymphoma	-	1
Laryngeal	-	1
Leiomyosarcoma	-	1
Lung cancer	1	-
MDS/MPNs[b]	-	3
Malignant melanoma	-	1
Multiple myeloma	1	-
Non-hodgkin lymphoma	1	-
Osteosarcoma	-	1
Peritoneal	1	-
PTC[c]	3	-
RCC[d]	1	1
Testicular	-	1
Total	23	12

[a]: Basal cell carcinoma
[b]: Myelodysplastic/myeloproliferative neoplasms
[c]: Papillary thyroid carcinoma
[d]: Renal cell carcinoma

assuming the TCSR data as standard population outcomes. Considering FMF as a hereditary disorder, the onset of disease exposure was set as the year of birth. Statistical analysis was conducted in the general study group and subgroups based on gender and usage of biological agents (anti-IL-1 and anti-TNF-α drugs). Proportions of patients with a cancer diagnosis were calculated for the analysis of biological agent treatment subgroups. Our study protocol was compliant with the Helsinki Declaration and approved by the local ethics committee.

Results: Females made up 1054 (60.8%) of the patients in our study group . The mean age of the patients was 39.8 ±11.6 years while the mean duration of disease exposure was 15.1±7.43 years. Total follow-up was 68,784 person-years. Malignancy occurred in 35 (2%) patients and 23 (65.7%) of them were female. Breast cancer was the most common cancer type in females (n=7, 30.4%), and among all cancer diagnoses (20%). Males were most frequently diagnosed with myelodysplastic/myeloproliferative neoplasms (n=3, 25%) (Table 1). The incidence of cancer was significantly lower in Turkish FMF patients, compared with the Turkish population [SIR 0.34 (95% CI 0.24-0.46), p< 0.01]. Cancer incidences were decreased among female patients [SIR 0.66 (95% CI 0.43-0.98), p=0.048] and among male patients likewise, but the association didn't reach statistical significance for males [SIR 0.62 (95% CI 0.34-1.06), p=0.096]. No significant difference in risk of cancer was found for patients using anti-IL-1 or anti-TNF-α drugs.

Conclusion: Our findings suggest that Turkish FMF patients have a significantly lower incidence of cancer than the general population of Turkey. Patient characteristics, such as continuous exposure to anti-inflammatory drugs (primarily colchicine) and pathophysiological mechanisms of the disease can be interpreted for the explanation of this association.

Table 2. Subgroup analysis of the association between cancer biologic agent treatment among Turkish Familial Mediterranean Fever patients

Treatment	Cancer Present (n)	Cancer Absent (n)	Proportion of Cancer, (%)	p value[b]
Anti-IL-1[a]				
Female				
Receiving	1	56	1.8	1
Not receiving	22	975	2.2	
Male				
Receiving	1	28	3.4	0.41
Not receiving	11	640	1.6	
Total				
Receiving	2	84	2.3	0.69
Not receiving	33	1615	2	
Anakinra				
Female				
Receiving	1	48	2	1
Not receiving	22	983	2.2	
Male				
Receiving	1	27	3.5	0.4
Not receiving	11	641	1.7	
Total				
Receiving	2	75	2.6	0.67
Not receiving	33	1624	2	
Canakinumab				
Female				
Receiving	1	21	4.5	0.38
Not receiving	22	1010	2.1	
Male				
Receiving	0	4	0	1
Not receiving	12	664	1.7	
Total				
Receiving	1	25	3.8	0.41
Not receiving	34	1674	2	
Anti-TNF α[c]				
Female				
Receiving	0	20	0	1
Not receiving	23	1011	2.2	
Male				
Receiving	1	16	6	0.26
Not receiving	11	652	1.6	
Total				
Receiving	1	36	2.7	0.53
Not receiving	34	1663	2	

[a]: Total of patients receiving at least one of the anti-interleukin-1 drugs, anakinra and canakinumab
[b]: Fischer's exact test is used for calculation with a significance level (α) of 0.05
[c]: Total of patients receiving at least one of the anti-tumor necrosis factor alpha drugs, infliximab, adalimumab, etanercept, golimumab, certolizumab pegol

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COVID-19 Infection in People with Immune Mediated Inflammatory Diseases Who Received SARSCo-V2 Vaccines

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SESSION INFORMATION
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Background/Purpose: Vaccines targeting the SARSCo-V2 virus protect against severe COVID-19 infection. Some immunosuppressive therapies impair SARSCo-V2 vaccine mediated immunogenicity and may increase the risk of severe COVID-19 infection even after vaccination. In people with Immune Mediated Inflammatory Diseases (IMIDs) who received at least one SARSCo-V2 vaccine, we aimed to describe the symptom profile and severity of COVID-19 infections.

Methods: As part of a single-center prospective observational cohort study of patients with diagnosed IMIDs who received SARSCo-V2 vaccines, we collected self-reported data regarding COVID-19 infection (test-confirmed vs suspected vs none), COVID-19 infection severity (ambulatory management, hospitalization, death), infection symptom profile, and risks for SARSCo-V2 virus exposure. Infection symptoms were categorized as constitutional (fever, fatigue), respiratory (rhinorrhea, sore throat, dyspnea, cough, chest pain), gastrointestinal (abdominal pain, nausea, emesis, diarrhea, loss of appetite), neurologic (headache, loss of taste/smell), and dermatologic (rash). IMID treatment was categorized as none vs immunomodulators, vs immunosuppressants, vs biologics/small molecules alone or in combinations. Participants provided blood samples 1, 3, and/or 6 months post each vaccination which were tested for anti-nucleocapsid (NC) IgG reflecting infection mediated immunogenicity and anti -Spike (S), and -receptor binding domain (RBD) IgG reflecting vaccine mediated immunogenicity. We describe the profile of COVID-19 infections across IMIDs.

Results: COVID-19 self-reported infection data was available for 322 participants [Inflammatory Arthritis (IA) N=78; Systemic Autoimmune Rheumatic Diseases (SARDs) N=84; Inflammatory Bowel Disease N=88; Multiple Sclerosis N=72] who were predominantly female (79.8%) white (82.0%) with mean (standard deviation-SD) age 58.3(14.2) years and received a median (range) of 4 (1,5) vaccines (Table). Test-confirmed infections were reported by 64 (20%) participants (p=NS across IMIDs and sexes), viral symptoms by 109 (33.9%), no symptoms by 148 (46%). Those reporting infection were younger than those without infection [(median (interquartile range) years 59.0 (24.9) vs 62.2 (18.9) p=0.03]. Eighteen infections were seronegative for anti-NC a median of 33 days (range 3-178) post diagnosis. Most infections were mild, but 5 people were hospitalized and 3 died from COVID-19 (2 IA, 1 SARDs, age >75 years, with comorbidities and on biologics or IS; 2 were seronegative for anti-S and anti-RBD after 1 or 2 vaccines; 1 had low titers after 3 vaccines). COVID-19 symptoms were similar across IMIDs with constitutional and respiratory symptoms being most common (Figure 1). Of 85 new anti-NC positive infections, 26 were asymptomatic (p=NS across IMIDs). Most participants reported having no risk exposures to SARSCoV2 over the course of the study (Figure 2).

Table: Baseline characteristics of participants IA= Inflammatory arthritis; CTD=Connective tissue disease; IBD=Inflammatory bowel disease; IMIDs=Immune Mediated Inflammatory Diseases MSK=musculoskeletal. 1. depression, anxiety, bipolar disorder, schizophrenia; 2. migraine, epilepsy, transient ischemic attack/stroke)

	IA	SARDs	IBD	MS	Total IMIDs
Female n(%)	66 (84.6)	75 (89.3)	59 (63.4)	60 (83.3)	**260 (79.5)**
Age years mean(SD)	64.0 (12.0)	58.5 (13.6)	56.0 (15.6)	53.3 (15.9)	**59.4 (14.1)**
White N(%)	63 (80.77)	61 (72.62)	80 (86.02)	65 (90.3)	**269 (82.3)**
Comorbidity number Median (range)	2 (0,9)	2 (0,8)	1 (0,9)	2 (0,6)	**2 (0,9)**
Psychiatric disorders [1]	25 (32.1)	35 (42.7)	37 (39.8)	28 (38.9)	**125 (38.2)**
Neurological disorders [2]	10 (12.8)	25 (29.8)	21 (22.6)	14 (19.4)	**70 (21.4)**
Hypertension	33 (42.3)	53 (63.1)	21 (22.6)	20 (27.8)	**127 (38.8)**
Cardiovascular disease	9 (11.5)	6 (7.1)	6 (6.5)	6 (8.3)	**27 (8.3)**
Hyperlipidemia	22 (28.2)	16 (19.05)	18 (19.36)	18 (25.0)	**74 (22.6)**
Lung disease	8 (10.27)	24 (28.57)	15 (16.13)	8 (11.1)	**55 (16.8)**
Diabetes	13 (16.67)	3 (3.57)	3 (3.23)	5 (6.9)	**24 (7.3)**
Kidney disease	2 (2.56)	9 (10.71)	4 (4.3)	0	**15 (4.6)**
Treatment combinations IM + IS Biologics + IM Biologics + IS	 14(17.9) 10(12.8) 4(5.1)	 17(20.2) 0 0	 3 (3.4) 4 (4.5) 7 (8.0)	 0 0 0	 **34 (10.5)** **8 (2.4)** **17(5.3)**
Immunomodulators (IM)	31 (39.7)	41 (48.8)	31 (33.3)	47 (65.3)	**150 (45.9)**
Immunosuppressants (IS)	43 (55.1)	39 (46.4)	18 (19.4)	0	**100 (30.6)**
Biologics/Small molecules	31 (39.7)	5 (6.0)	40 (43.0)	13 (18.1)	**89 (27.2)**
Corticosteroids	7 (9.0)	14 (16.7)	8 (8.6)	0	**29 (8.9)**
None	9 (11.5)	5 (6.0)	20 (21.5)	29 (40.3)	**63 (19.3)**

Conclusion: The symptom profile of COVID-19 is similar across IMIDs and to the general population. A subset of people with IMIDs may not generate robust anti-NC responses to documented COVID-19 infection. This may impact the reliability of surveillance studies relying on these assays.

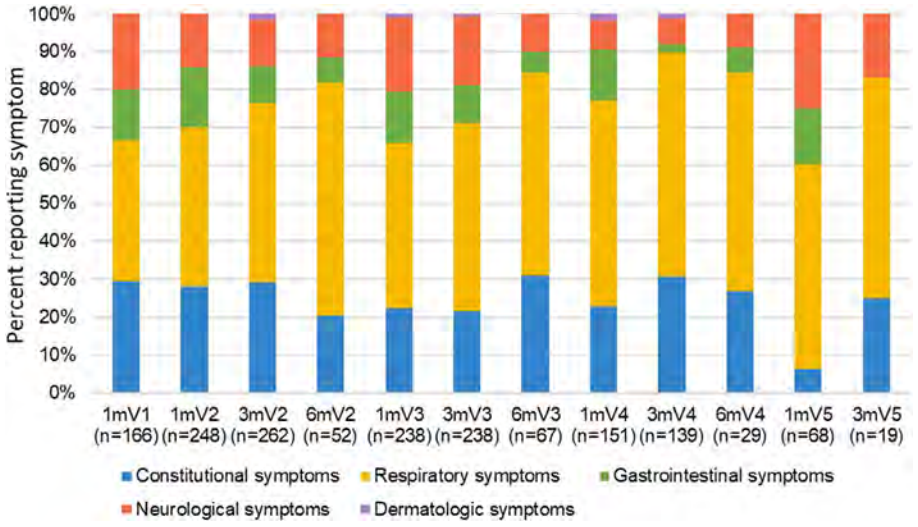

Figure 2. Self-reported symptom profile of COVID-19 infections in vaccinated patients with immune mediated inflammatory diseases V1=vaccine 1; V2=vaccine 2; V3=vaccine3; V4=vaccine 4; V5=vaccine 5 Symptom categories adapted from: Reaney, M., et al. Development of an Item Bank to Assess Patient-Reported Outcomes: Signs, Symptoms, and Impacts of COVID-19. Patient 15, 703–713 (2022).

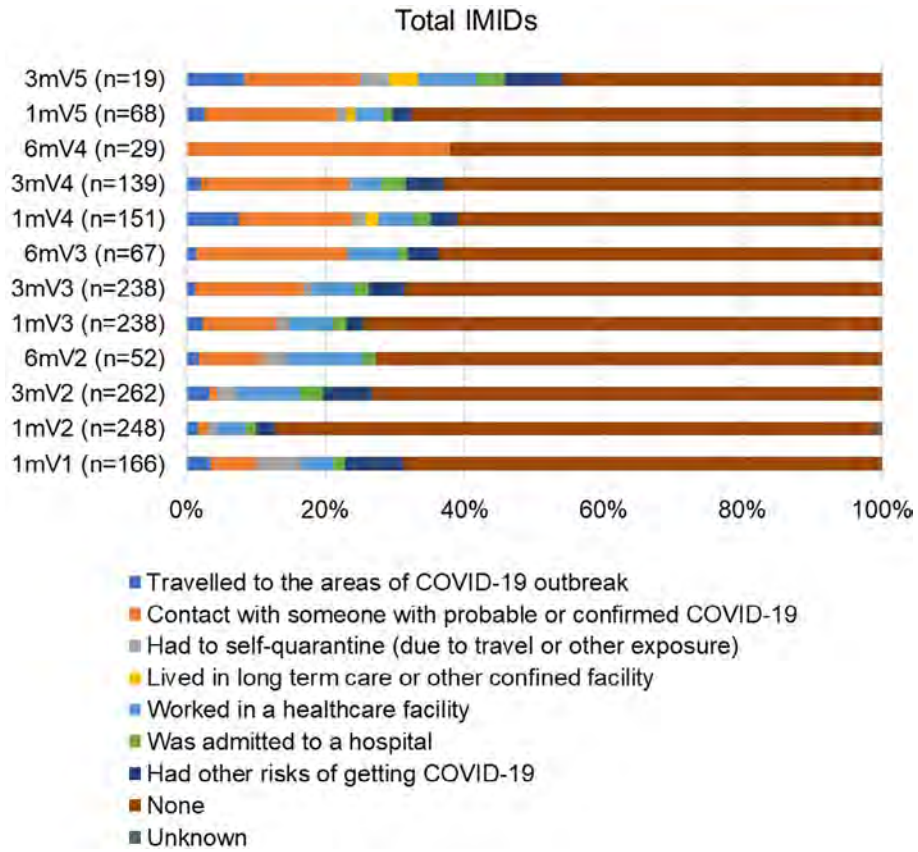

Figure 3.Risk for exposure to SARSCoV2 among vaccinated people with Immune Mediated Inflammatory Diseases

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Abstract Number: 0145

Sexual Health and Function Screening in Patients with Rheumatic Diseases

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SESSION INFORMATION

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Background/Purpose: Rheumatic diseases (RD) can have a negative impact on many aspects of a patient's life, including sexual health. Sexual dysfunction (SD) has been negatively associated with quality of life and disease severity, yet there's still a barrier to the evaluation and assessment of this impact (1). This study aims to evaluate and describe how patients perceive their sexual performance and characterize their demographics.

	Sexual Dysfunction	No	
Total	60	302	
Sex, n (%)			0.071
Femenino	57 (95)	262 (86.8)	
Masculino	3 (5)	40 (13.2)	
Age	38.7 ± 11.2	50.3 ± 7.3	0.001
Marital status, n (%)			0.001
Married	38 (63.3)	147 (48.7)	
Cohabitating	9 (15)	58 (19.2)	
Widow	2 (3.3)	1 (0.3)	
Single	4 (6.7)	81 (26.8)	
Divorced	6 (10)	10 (3.3)	
Separated	1 (1.7)	5 (1.7)	
Education, n (%)			0.048
Elementary	7 (11.7)	51 (16.9)	
Middle School	28 (46.7)	104 (34.4)	
High school	5 (8.3)	70 (23.2)	
Technical career	10 (16.7)	25 (8.3)	
Bachelor's degree	9 (15)	49 (16.2)	
Postgraduate	1 (1.7)	2 (0.7)	
No studies	0	1 (0.3)	
Children, n (%)			0.025
Yes	54 (90)	233 (77.2)	
No	6 (10)	69 (22.8)	

Demographics

	Sexual Dysfunction	No	sig
Total	60	302	
Rheumatic Disease, n (%)			0.176
Rheumatoid Arthritis (RA)	34 (56.7)	150 (49.7)	
Osteoarthritis	5 (8.3)	10 (3.3)	
Systemic Lupus Erythematosus	5 (8.3)	70 (23.2)	
MII	3 (5)	10 (3.3)	
Arthralgias	3 (5)	18 (6)	
Sjögren Syndrome (pSS)	2 (3.3)	9 (3)	
Others	8 (13.3)	32 (11.6)	
Years with diagnosis	5.6 ± 5.8	5.0 ± 5.3	0.476
Fatigue, n (%)			0.333
Yes	57 (95)	294 (97.4)	
No	3 (5)	8 (2.6)	
Menopause (318)	***57***	***261***	<0.001
Yes	42 (73.7)	75 (28.7)	
No	15 (26.3)	186 (71.3)	
ASEX	20.9 ± 3.4	12.0 ± 2.9	<0.001
FACIT	55.5 ± 16.5	60.1 ± 12.9	0.092
HADSA	5.4 ± 5.6	4.5 ± 5.2	0.29
HADSD	2.1 ± 4.3	1.1 ± 2.6	0.075

Clinical characteristics

Methods: We conducted a cross-sectional study in patients with at least one rheumatologic disease at an outpatient rheumatology clinic in at Hospital Universitario Dr. José Eleuterio González. Those without active sexual life, or pregnancy, and those unwilling to answer the questionnaire reliably were excluded. Patients over 18 years old were evaluated from August 2022 to April 2023 with the Arizona Sexual Experiences Scale (ASEX), Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) and Hospital Anxiety and Depression Scale (HADS). Sociodemographic and medical data were collected from patient files.

Results: We included 893 patients. A third (30%) of patients refused to answer and only 40.54 % (362) reported an active sexual life. Sexual dysfunction (SD) was reported in 60 (17%), with a higher prevalence observed in women (95%) than men (5%) (table 1). The mean age in patients with SD was 38.7± 11.2. Being married, younger, and having menopause were associated with a higher prevalence of SD. The most related diagnosis to SD was Rheumatoid Arthritis (n=34, 56.7%) (Table 2) Patients with SD also presented a tendency for depression and fatigue in clinical scales analysis, but not to anxiety. Less education and having children are also associated with SD.

Conclusion: We found a prevalence of SD of 17% in our population. The presence of menopause, a younger age, and offspring was more frequent in patients with SD. Special attention should be take to these factors in the evaluation of sexuality in patients with rheumatic diseases.

References:

1. Zhao S, Li E, Wang J, Luo L, Luo J, Zhao Z, et al. Rheumatoid Arthritis and Risk of Sexual Dysfunction: A Systematic Review and Metaanalysis. J Rheumatol [Internet]. 2018 [cited 2022 Sep 17];45:1375–82. Available from: www.jrheum.org

4. Minopoulou I, Pyrgidis N, Tishukov M, Sokolakis I, Baniotopoulos P, Kefas A, et al. Sexual dysfunction in women with systemic autoimmune rheumatic disorders: a systematic review and meta-analysis. Rheumatology (Oxford) [Internet]. 2022 Aug 11 [cited 2022 Sep 27]; Available from: https://pubmed.ncbi.nlm.nih.gov/35951753/

Disclosure: L. Vega Sevilla: None; **G. Serna-Peña**: None; **D. Flores-Gutierrez**: None; **J. Cardenas-De la Garza**: None; **I. Hernandez Galarza**: None; **D. Galarza-Delgado**: None.

Abstract Number: 0146

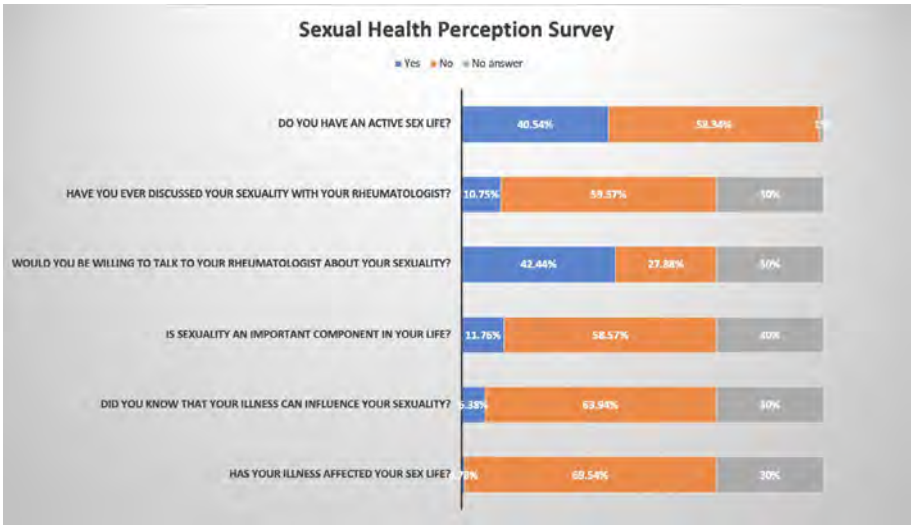
Sexual Health and Self-Perception in Rheumatologic Patients: Has Your Rheumatologist Ever Talked to You About Sexual Health?

Luis Vega Sevilla[1], Griselda Serna-Peña[2], **Diana Paola Flores-Gutierrez**[3], Jesus Alberto Cardenas-De la Garza[4], Dionicio A. Galarza-Delgado[5] and Ivan Hernandez Galarza[6], [1]Hospital Universitario UANL, Garcia, Mexico, [2]Universidad Autónoma de Nuevo León, Guadalupe, Mexico, [3]Hospital Universitario "Dr. José Eleuterio González", Monterrey, Mexico, [4]Hospital Universitario "Dr. José Eleuterio González", San Nicolas, Mexico, [5]Hospital Universitario UANL, Monterrey, Mexico, [6]University Hospital, UANL, San Pedro Garza Garcia, Mexico

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health – Interprofessional Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: There's a high prevalence of sexual dysfunction (SD) in patients with rheumatic diseases (RD). Studies show that it goes from a 36% to a 70%, and still they are not regularly addressed in a routine rheumatologic assessment. Self-perception questionnaires applied to patients with rheumatoid arthritis (RA) have reported that most patients don't share their sexual health concerns with their rheumatologists, even when 32.5% wished their rheumatologist did establish the possibility of doing so. (1)This study aims to describe the prevalence of self-perceived and knowledge of sexual health in patients with RD.

Methods: We conducted a cross-sectional study in patients with at least one rheumatologic disease at an outpatient rheumatology clinic. Those unwilling to answer the questionnaire reliably were excluded. The Sexual Health Perception Survey (SHEPS) was applied and consists of the following questions: 1) Do you have an active sexual life? 2) Have you ever talked



to your rheumatologist about your sexuality? 3) Would you be willing to talk to your rheumatologist about your sexuality? 4) Is sexuality an important component in your life? 5) Did you know that your disease influences your sexuality? 6) Has your disease affected your sexual life? Sociodemographic and medical data were collected from patient files.

Results: We screened 893 patients. A third (30%) of patients refused to answer. Of the 628 patients who answered, 362 (40.5%) had an active sex life, and 105 (11.76) considered sex an important part of their life. While 379 (42.4%) patients reported they are willing to speak to their rheumatologist about their sexuality, only 96 (10.7%) had spoken to their rheumatologist about it. Only 6.3% (57) patients previously knew their rheumatic disease could affect their sexual life, and less than 1% (7) of the patients considered that their rheumatic disease was affecting their sexual life. A higher prevalence of auto-perceived sexual dysfunction (APSD) was observed in women (91.2%) than men (18.9%). Mean (SD) age in patients with self-perceived APSD was 56.14 (22.74). Most related diagnosis to APSD was Rheumatoid Arthritis (n=3).

Conclusion: The SHEPS results show that even when an important percentage of patients are willing to speak to their rheumatologist about their sexuality, only a small percentage has done it. Also, only a few patients knew their rheumatic disease could influence their sexual life, and even a smaller percentage considers it has been affected by it.

References:

1. Østensen M. Sexual and reproductive health in rheumatic disease. Vol. 13, Nature Reviews Rheumatology. Nature Publishing Group; 2017. p. 485–93.
2. Bay LT, Graugaard C, Nielsen DS, Möller S, Ellingsen T, Giraldi A. Sexual Health and Dysfunction in Patients With Rheumatoid Arthritis: A Cross-sectional Single-Center Study. Sex Med. 2020 Dec 1;8(4):615–30.

Disclosure: L. Vega Sevilla: None; **G. Serna-Peña**: None; **D. Flores-Gutierrez**: None; **J. Cardenas-De la Garza**: None; **D. Galarza-Delgado**: None; **I. Hernandez Galarza**: None.

Abstract Number: 0147

Leukotriene Inhibitors Effect on Post-Traumatic Osteoarthritis: A Real-World Evidence Comparative Effectiveness Study

S. Reza Jafarzadeh[1], Matthew Baker[2], Christine E. Peloquin[3], William H. Robinson[4] and David Felson[3], [1]Boston University Chobanian & Avedisian School of Medicine, Boston, MA, [2]Stanford University, Menlo Park, CA, [3]Boston University, Boston, MA, [4]Stanford University, Palo Alto, CA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health – Interprofessional Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Joint injuries frequently lead to post-traumatic osteoarthritis (OA), a disabling condition often affecting young adults, impacting their quality of life and creating substantial economic consequences for society. To fill the therapeutic void, drug repurposing is an attractive alternative to traditional drug development, which is costly and slow-moving. The aim of this work is to assess the effectiveness of leukotriene inhibitors on preventing post-traumatic OA compared with long-acting beta agonists, both of which are commonly used drugs for asthma. Leukotriene inhibitors suppress mast cell products, and data from mouse models suggest that inhibiting mast cell activation and downstream inflammatory processes can prevent OA.

Table 1. Odds of subsequent osteoarthritis and knee replacement in users of leukotriene inhibitors vs. long-acting beta agonists undergoing ACL or meniscal surgery.

Outcome definition	*Odds ratio (95% CI)	
n = 10,973 (prior OA/KR excluded)	**5-year odds**	**10-year odds**
One OA claim	0.96 (0.82, 1.12)	0.81 (0.62, 1.12)
OA claim + NSAID/opioid	0.95 (0.81, 1.12)	0.94 (0.88, 1.01)
OA claim + knee imaging claim	0.99 (0.85, 1.17)	0.86 (0.66, 1.12)
Two OA claims ≥7 days apart	1.03 (0.88, 1.20)	0.96 (0.86, 1.07)
n = 13,800 (only prior KR excluded)		
TKR	0.96 (0.81, 1.12)	0.89 (0.71, 1.12)
Composite OA/KR	0.95 (0.84, 1.08)	0.80 (0.62, 1.03)

* Adjusted for age, sex, geographical region, obesity, a history of chronic kidney disease, diabetes, liver disease, and depression

Methods: Persons with a claim for anterior cruciate ligament (ACL) or meniscal surgery between 2006 and 2020 were drawn from MarketScan Commercial Claims and Encounters (Merative) databases. The date of the surgery claim was defined as the index date. Enrollees were eligible if aged 18-45 years on index date and if they had continuous enrollment for at least 6 months prior to the index date (baseline period) and 12 months after the index date (follow-up period). Additionally, subjects had to be users of leukotriene inhibitors (montelukast, zafirlukast, or zileuton) or an active comparator that consisted of long-acting beta agonists (albuterol, arformoterol, formoterol, indacaterol, olodaterol, salmeterol, terbutaline, or vilanterol) for any duration from the index date up to 6 months after. The study outcomes were identified as claims for OA and/or knee replacement (KR) during the follow-up period, which for OA was the first claim 12 months after the index date to minimize misclassifying trauma as OA. Various definitions of outcome were considered, which included OA claims with and without NSAIDs or opioid prescription or knee imaging (X-ray or MRI) within a year, and a composite outcome of OA and KR. Exclusions consisted of subjects with a history of chronic obstructive pulmonary disease, a prior KR, or a prior OA diagnosis (for OA outcomes only). We used causal inference-based targeted learning estimated through ensemble machine learning to compare incident outcomes among users of leukotriene inhibitors with comparator users within 5 and 10 years, accounting for loss to follow-up by incorporating inverse probability weighting for censoring.

Results: Data included 13,800 persons (50.0% female, mean age = 35.4 [SD = 8.5] years) who underwent ACL/meniscal surgery. Compared with users of long-acting beta-agonists, the odds of KR, adjusted for confounders and loss to follow-up, was about 4% lower at 5 years and 11% lower at 10 years follow-up in users of leukotriene inhibitors undergoing surgery (Table 1). For OA outcomes, the odds of short- and long-term outcomes similarly showed a modest decrease for leukotriene inhibitor users compared with users of comparator drugs, however, estimated confidence intervals crossed the null.

Conclusion: Users of leukotriene inhibitors undergoing ACL or meniscal surgery may have lower odds of post-traumatic OA compared with users of long-acting beta agonists.

Disclosure: S. Jafarzadeh: None; **M. Baker**: Mobility Bio, 8, Nēsos, 2; **C. Peloquin**: None; **W. Robinson**: None; **D. Felson**: None.

Abstract Number: 0148

Recreational Activities in Adults with Rheumatoid Arthritis: Relevance, Difficulty, and Associations with Clinical Outcomes

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health – Interprofessional Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) can limit one's ability to participate in recreational activities. Participation in recreational activities enhances quality of life, yet limited literature addresses recreational activity. The Short-Valued Life Activities (SVLA) questionnaire specifically assesses difficulty with five categories of recreational activities including if accommodations (e.g., extra time, assistance) are needed to participate. Respondents can also indicate if an item is not relevant to their lives, which is a feature absent from many common patient-reported outcomes. The purpose of the study was to (1) describe the relevance and difficulty with recreational activities among adults with RA and (2) examine the association of difficulty with recreational activity with physical function (PF), fatigue, and pain.

Methods: In this cross-sectional study, participants with RA (n=290) completed an online survey regarding their current clinical outcomes and demographic information. Participants were eligible if they were 18 years old or older and received care between 2020-2021 from UNC Rheumatology for RA. We assessed participation in recreational activities using items 5, 7, 10, 11 and 12 from the SVLA (i.e., gardening/yardwork, attending social events, leisure activities, hobbies, and physical recreation). Participants first identified if each item activity was relevant to them. If relevant, they selected their level of difficulty to perform the activity (i.e., none, some, a lot or unable to participate) and if they used an accommodation or not (e.g., extra time, assistance, tools). PROMIS short forms were used to assess physical function, fatigue, and pain interference. For purpose one, we calculated the proportion of the sample who identified each item as relevant, and as relevant and difficult (defined as at least some difficulty or accommodation use). For purpose two, we identified the item that was most frequently relevant and difficult and tested the association of this item with physical function, fatigue, and pain using a general linear model. Significance was set at alpha < 0.05. If the association was significant, Tukey's tests were used to evaluate pairwise differences between groups.

Results: The recreational activities were relevant for most of the sample (86%-95%, Table 1). Physical recreation was the most frequently relevant and difficult activity (75% of the sample). Greater difficulty with physical recreation was associated with worse physical function, fatigue, and pain ($F_{7,282}$ = 20.1 – 41.6, all p < 0.001). Participants who reported no difficulty and no accommodation use with physical recreation had better physical function, fatigue, and pain compared to nearly all other response categories (p< 0.05, Table 2).

Conclusion: Recreational activities were highly relevant and difficult for most adults with RA. Even small increases in difficulty, such as accommodation use, were associated with worse clinical outcomes, suggesting accommodation use could be an early indicator of declining functional abilities. Further research is needed to understand how to best support participation in recreational activity.

Table 1.

Table 1. Proportion of the sample reporting recreational activities as relevant and difficulty

SVLA Item	Total respondents	Proportion who reported the activity as relevant	Proportion who reported the activity as relevant and difficult*
	n	% (n)	% (n)
Gardening/Yardwork	292	86% (252)	66% (193)
Attending social events	290	95% (275)	50% (146)
Leisure activities	290	95% (276)	46% (134)
Hobbies	289	87% (251)	56% (162)
Physical Recreation	290	95% (274)	75% (216)

*difficult indicates any level of difficulty or accommodation use with the activity

Table 2.

Table 2. Association of Physical Recreation Difficulty with Clinical Outcomes

SVLA Item Response to the Physical Recreation Item	n	PROMIS Physical Function t-score Mean (95% CI)	PROMIS Fatigue t-score Mean (95% CI)	PROMIS Pain Interference t-score Mean (95% CI)
No difficulty + no accommodation	58	50.9 (48.8, 53.1)	49.3 (47.8, 50.9)	47.5 (45.3, 49.7)
No difficulty + accommodation use	11	42.3 (37.6, 47.0)*	59.1 (56.3, 62.0)*	58.9 (55.6, 62.1)*
Some difficulty + no accommodation	28	44.9 (42.4, 47.4)*	51.7 (49.3, 54.0)	53.1 (50.3, 55.8)*
Some difficulty + accommodation use	84	42.1 (40.7, 43.5)*	57.3 (55.7, 58.8)*	56.4 (54.8, 58.0)*
A lot of difficulty + no accommodation	4	36.9 (23.5, 50.2)*	54.4 (33.3, 75.5)	56.1 (39.3, 73.0)
A lot of difficulty + accommodation use	67	34.1 (32.8, 35.5)*	62.0 (60.2, 63.9)*	63.5 (62.2, 64.9)*
Unable to do	22	28.7 (26.5, 30.9)*	63.7 (60.6, 66.8)*	66.9 (63.8, 69.9)*
Not relevant	16	37.2 (32.8, 41.6)*	57.8 (53.2, 62.4)*	59.5 (53.9, 65.1)*

*indicates significantly different ($p<0.05$) than 'No difficulty + no accommodation' group in post-hoc testing

Disclosure: S. Novroski: None; **C. Lane**: None; **J. Torrey**: None; **L. Thoma**: None.

Abstract Number: 0149

Impacts of Social Determinants of Health and the Immune System in Adults with Acute-to-Chronic Low Back Pain: An Observational Study

Colleen Burke[1], Michael Brown[2], Kenneth Taylor[2], Stephanie Danyluk[2], Kelley Seebeck[2] and Adam Goode[3], [1]Duke University School of Medicine, Chapel Hill, NC, [2]Duke University School of Medicine, Durham, NC, [3]Duke University, Durham, NC

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health – Interprofessional Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic low back pain (cLBP) is common worldwide yet poorly understood due to the combination of biological, psychological, and sociological factors. An individual's social determinants of health (SDOH) may influence biology by inducing immune responses. While these immune responses likely contribute to the development of cLBP, the mechanisms of how they contribute remain unknown. The purpose of this study is to investigate the relationship between SDOH and the immune system both in individuals who did and did not transition from acute to cLBP.

Methods: Adults (n=26) experiencing acute LBP (< 4 weeks) were recruited from the community. Data was gathered at baseline and 3-month follow-up to determine the participant's low back pain status (i.e., transition to cLBP). Data on SDOH included measures of social connection and social roles, which were measured using the Social Network Index (SNI) recommended by the Institute of Medicine as well as the PROMIS Short Form - Global - Version 1.2 Global Social Activities and Roles Item. We also collected self-reported demographics (i.e., age, gender, and race) and peripheral blood samples.

Peripheral blood mononuclear cell (PBMC) and plasma cytokines were analyzed, and cell-type specific immune activation or tolerance features were analyzed by high dimensional flow cytometry. Multiplex cytokine secretion after PBMC stimulation with innate immune activators were used to measure immune function and tolerance.

Results: Of the social factors, social roles were most associated with immune cell changes and plasma cytokines. Relative to inability to uphold social roles, confidence in one's ability to uphold social roles was associated with lower inflammatory cytokines at baseline and follow-up, lower monocyte expression of TNF at baseline; but higher CD8 T cell proliferation/differentiation and relative increase in monocyte inflammation from baseline to follow-up (Figure 1). For self-reported demographic factors, when sub-grouped by race, White participants had higher inflammatory cytokines in plasma. Several immune cell differences between Black vs White race were observed, including higher levels of B cells; lower monocytes, CD141+ DCs, and regulatory T cells; lower immune suppressing ligands on B cells; and increased markers of T cell differentiation (Figure 1). PBMC functional measurements (i.e., responses to stimulation) revealed similar patterns within each race, wherein individuals who did not transition to cLBP mounted weaker responses than those who did transition to cLBP, possibly indicating immune tolerance/desensitization in participants that do not progress to cLBP (Figure 2).

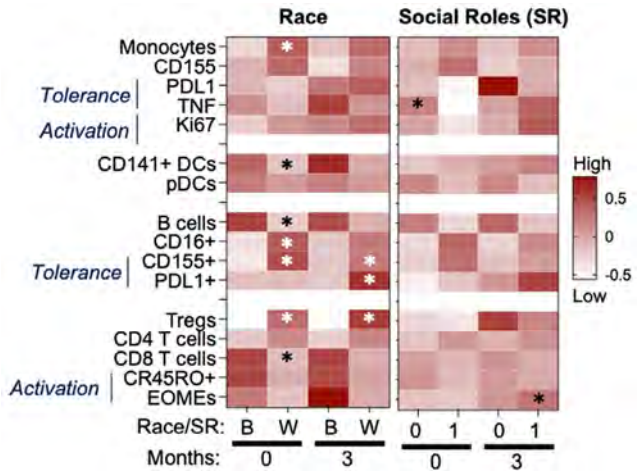

Figure 1. Immunological features on indicated cell types for each time point stratified by race (left) or social roles (SR, right). SR= 0 indicates inability to uphold social roles, SR= 1 indicates ability to uphold with social roles. Asterisks (*) indicate unpaired t-test within time point p<0.05 and heatmaps depict z-scores.

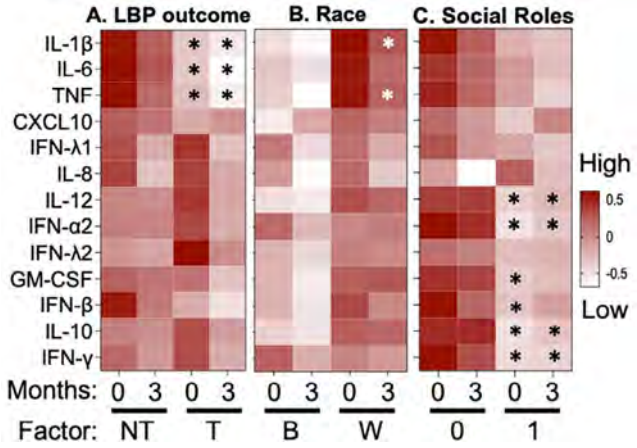

Figure 2. Plasma cytokine differences by LBP outcome (A), race (B), and social roles (C). Plasma cytokine levels at each time point separated by each indicated factor, z-scores for each cytokine are shown; (*) Mann-Whitney test p<0.05 vs by factor at each time point. From left to right: NT= no transition, T= transition to cLBP; B=Black, W- White; 0= inability to uphold social roles, 1= ability to uphold social roles.

Conclusion: SDOH such as race and social roles are associated with immune status and inflammation. Peripheral inflammation is lower in more desirable social factors (connection, roles, and stress) over time, with differences in monocyte inflammation at baseline. Differences in the immune system are observed based on race. While race alone does not explain these differences, it points to the need for further investigation into how SDOH influence the immune system leading to disparities in health outcomes.

Disclosure: C. Burke: None; **M. Brown**: Istari Oncology, 2, 10, Menarini-Stemline, 2; **K. Taylor**: None; **S. Danyluk**: None; **K. Seebeck**: None; **A. Goode**: None.

Abstract Number: 0150

Self-reported Levels of Physical Activity and the Association to Pain, Fatigue, Anxiety and Depression Among Patients with Idiopathic Inflammatory Myopathies

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health – Interprofessional Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with inflammatory diseases such as rheumatoid arthritis exhibit reduced levels of physical activity (PA) compared to the normative population and suffer from anxiety and/or depression. Physical activity at a health-enhancing level can help alleviate these symptoms and other co-morbidities. This study aims to assess the self-reported levels of PA and associations, to depression, anxiety, pain and fatigue among adults with idiopathic inflammatory myopathies (IIM) in Sweden.

Methods: All patients with IIM at the Rheumatology clinic at Karolinska University Hospital have been invited to participate, at a visit or by mail, during 2019-2022. To assess self-reported levels of PA, and screen for anxiety and depression the International Physical Activity Questionnaire – short form (IPAQ) and Hospital Anxiety and Depression Scale (HADS) were used.

Table 1. HADS-A, Hospital anxiety and depression scale - anxiety; HADS-D, Hospital anxiety and depression scale - depression; IPAQ, International physical activities questionnaire - short form; VAS, visual analog scale – 0-100 mm; * = p<0.05; **p<0.01; ***p<0.000; IPAQ is compared between levels, Pain and Fatigue is compared between HADS ≥8 and <8

Table 1. Distribution of patients based on HADS score.

Table 1	HADS-A		HADS-D		Total
	≥ 8, n=62 (25 %)	<8, n=184 (75 %)	≥ 8, n=34 (14 %)	<8, n=212 (86 %)	n = 246
IPAQ-low, n (%)	17 (40)*	26 (60)	14 (33)**	29 (67)	43 (17.5)
IPAQ-moderate and high, n (%)	45 (22)*	158 (78)	20 (10)**	183 (90)	203 (82.5)
Pain, mm-VAS, mean (SD)	38 (28)***	15 (18)***	31 (27)*	19 (22)*	21 (23)
Fatigue, mm-VAS, mean (SD)	50 (27)***	24 (25)***	50 (24)***	27 (27)***	30 (28)

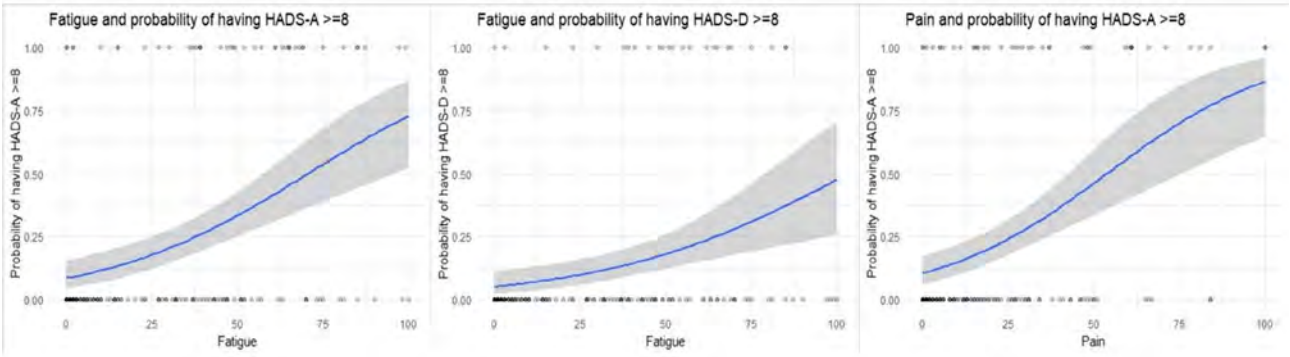


Figure 1. Probability of having a HADS-A as a factor of Fatigue (Panel A) and Pain (Panel B), and probability of having a HADS-D ≥8 as a factor of Pain (Panel C). HADS-A: Hospital Anxiety and Depression Scale for Anxiety, HADS-D: Hospital Anxiety and Depression Scale for Depression

HADS is scored in two sub-scales, one for depression (HADS-D) and one for anxiety (HADS-A). Maximal score is 21 and ≥8 is cut-off for probable depression or anxiety disorder. IPAQ-results were scored as low-PA, (not reaching moderate/high), moderate-PA, (≥600 MET-minutes/week) and high-PA, (≥1500 vigorous or 3000 moderate MET-minutes/week). Pain and fatigue on visual analogue scale (VAS), 0-100 mm were collected from the Swedish Quality Register. Multivariate logistic regression analysis was used to test the association between pain, fatigue, and IPAQ with HADS-A and HADS-D and χ^2 for group differences.

Results: A majority of patients reached or exceeded recommended PA-levels (82.5 %). Anxiety and depression were more prevalent in patients reporting low PA (Table 1). Moderate or high level of PA was associated with a 70 % lower risk of probable depression ($p< 0.01$). Each millimeter worsening in fatigue increased the risk of probable anxiety or depression by 2 % and 3 %, respectively. Each millimeter worsening in pain increased the risk of probable anxiety by 2.5 % (Figure 1).

Conclusion: Physical activity seems to significantly lower the risk of depression. There is an association of worsened pain and fatigue to increased risk of anxiety and worsened fatigue to increased risk of depression. Further, anxiety and depression are more prevalent among those failing to reach moderate/high levels of physical activity.

Disclosure: K. Andreasson: None; **F. Espinosa-Ortega**: None; **H. Sandlund**: None; **H. Alexanderson**: None.

Abstract Number: 0151

Arthritis: A Wealth Gap

Risha Fayyaz[1] and Anum Akhlaq[2], [1]University of Mississippi Medical Center, Flowood, MS, [2]University of Mississippi Medical Center, Jackson, MS

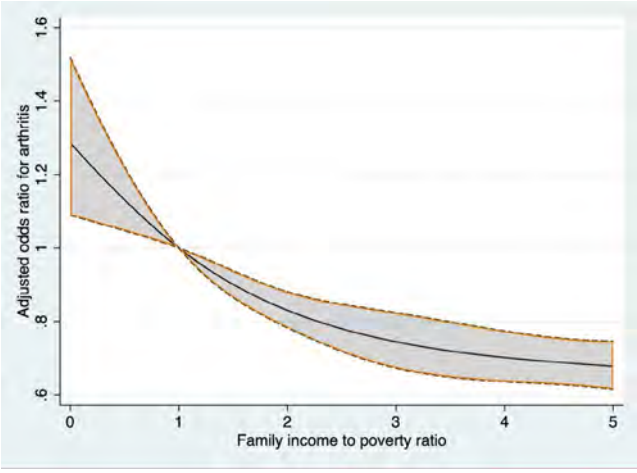
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health – Interprofessional Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Lower socioeconomic status (SES) has been associated with worse health outcomes . Family income is a key component of SES. This study aimed to assess the association of family income with arthritis in the adult population in the United States.

Methods: Data from the National Health and Nutrition Examination Survey (NHANES) from 2005 to 2018 were analyzed. The family income to poverty ratio (FIPR) was used as a measure of SES. FIPR was calculated by dividing family (or individual) income by the poverty guidelines specific to the survey year. FIPR was categorized in 6 levels: FIPR < 1 (for the lowest income), 1-1.9,2-2.9,3-3.9,4-4.9, ≥5 (for highest income). Arthritis was defined by the participants' response to the following question: "Has a doctor or other health professional ever told you that you had arthritis?".

Results: The unadjusted prevalence of arthritis was 24.73% in the lowest income group (FIPR < 1). The prevalence of arthritis decreased with increasing FIPR, and was 23.87% in the highest income group (FIPR ≥ 5). After adjusting for age, race/ethnicity, and sex, the prevalence odds of arthritis were lower in participants with FIPR 1-1.9 (aOR, 95% CI: 0.79 (0.70-0.88), p < 0.001); FIPR 2-2.9: (aOR, 95% CI: 0.66 (0.58-0.75), p < 0.001); FIPR 3-3.9 (aOR, 95% CI: 0.64 (0.55-0.75), p< 0.001); FIPR 4-4.9: (aOR 95% CI: 0.67 (0.57-0.77), p < 0.001), and FIPR ≥5: (aOR, 95% CI: 0.57 (0.50-0.65), p < 0.001).

Conclusion: These findings suggest that lower family income is associated with an increased prevalence of arthritis. Targeted interventions should be directed toward closing this socioeconomic gap which can potentially alleviate the disease burden.



Relationship between FIPR and adjusted odds ratio for arthritis

Disclosure: R. Fayyaz: None; **A. Akhlaq**: None.

Abstract Number: 0152

Long Covid in Persons with Self-Reported Arthritis - Symptoms, Associated Factors and Functional Limitations

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health – Interprofessional Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Long covid, a condition whereby signs and symptoms post covid-19 infection continue for more than 12 weeks and are not explained by an alternative diagnosis, may be more frequent among persons with arthritis. Currently, little is known whether persons with arthritis are at higher risk for long covid and how long covid affects their function. Our objectives are 1) to describe long covid in a cohort of persons with a self-reported history of arthritis who had been diagnosed with covid-19 in terms of frequency, symptoms and associated factors; and 2) to describe change in function in persons with arthritis and long covid compared to pre-covid status, focusing on: perceived global health status, mobility, personal care, participation in daily activities, and employment.

Methods: Among 2764 persons with a confirmed covid-19 diagnosis who responded to an online survey, 171 reported a history of arthritis and formed our study sample. The survey included validated questionnaires: the Newcastle Post-Covid Syndrome Questionnaire and the Covid-19 Yorkshire Rehabilitation Screen. We calculated the frequency of long covid (defined as those still troubled by symptoms) and persistent symptoms, and evaluated associated factors using bivariate analysis and multivariable logistic regression. Among those with long covid, we describe limitations in activity and function in comparison to pre-covid status. Change was calculated by subtracting the current functional score from the pre-covid 19 score and we categorized degree of change as small, moderate and severe.

Results: In our sample, 53.5% were still troubled by symptoms and the most frequent symptoms were: fatigue, myalgia, weakness, breathlessness, low mood, anxiety, and sleep disturbance. Factors associated with long covid were female sex, having been hospitalized for covid, and having at least one other chronic disease. Persons with long covid had substantial declines in function, notably in global health status, usual activities, mobility, personal care, and employment status. For example, 9.3% had major problems with usual activities pre-covid and this proportion rose to 52.5% with long covid. Fatigue was a big problem with 88% reporting a change and 52% reporting the decline as being moderate to severe. Also, 37% reported moderate to severe increase in pain.

Conclusion: Persons with arthritis and long covid have substantial limitations in function compared to pre-covid status. There is a need to implement effective interventions to improve functional status in persons with arthritis and long covid.

Disclosure: D. Ehrmann Feldman: None; **B. Mazer**: None.

Abstract Number: 0153

Diminished Vibration Perception and Greater Pressure Pain Sensitivity Are Associated with Worse Knee Osteoarthritis Outcomes Across Sex and Race

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health – Interprofessional Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Sex and race differences have been observed in clinical outcomes such as patient-reported pain and function in adults with knee OA. However, few studies have examined sex and race differences in vibration sensitivity and pressure pain sensitivity, which may better represent neurophysiological changes suggestive of longer-term symptoms. The purpose of the study was to examine if associations of these neurophysiological assessments with knee OA outcomes differ across sex and race, which may contribute to known sex and race disparities in clinical outcomes.

Methods: Data were from the 2013-2015 follow-up of the Johnston County Osteoarthritis Project. Exposures were vibration perception threshold (VPT) and pressure pain threshold (PPT). VPT was measured using a biothesiometer operating at 120 Hz at the bilateral medial femoral condyle (MFC) and first metatarsophalangeal joint (MTP). PPT was measured on a 0-4 kg scale using a standard mechanical pressure-based dolorimeter operating at 1 kg/sec at the bilateral upper trapezius. Outcomes were frequency of radiographic knee OA (rKOA, defined as Kellgren-Lawrence grade 2–4), Ksx (defined as knee pain, aching, or stiffness on most days of any one month in the last 12 months regardless of rKOA status), symptomatic knee OA (sxKOA, defined as having both rKOA and knee symptoms), and knee pain severity (measured with Knee Injury and Osteoarthritis Outcome Score (KOOS) Pain Subscale) in each knee. We examined cross-sectional associations of the exposures with the outcomes using separate logistic regression models to calculate odds ratios for dichotomous outcomes and log linear models to calculate density ratios for knee pain severity, with 95% confidence intervals. Limb-level models were assessed using generalized estimating equations to account for correlations between limbs and adjusted for relevant covariates (Table 1). Results were presented for the overall sample and separately by sex or race.

Tables and Figures:

Table 1: Cross-sectional Associations of Vibration and Pressure Pain Sensitivity with Knee OA Outcomes

	Overall		Stratified by sex				Stratified by race			
			Women		Men		White		Black	
	Outcome*	aOR or aDR (95% CI)^	Outcome*	aOR or aDR (95% CI)^	Outcome*	aOR or aDR (95% CI)^	Outcome*	aOR or aDR (95% CI)^	Outcome*	aOR or aDR (95% CI)^
VPT at MFC (per 10 volt/s higher)										
rKOA	725 (44.3%)	**1.15 (1.04, 1.27)**	512 (45.8%)	**1.23 (1.09, 1.38)**	213 (41.1%)	0.98 (0.82, 1.17)	460 (42.8%)	**1.14 (1.01, 1.28)**	265 (47.2%)	1.17 (0.98, 1.39)
Ksx	514 (31.4%)	**1.17 (1.06, 1.30)**	385 (34.4%)	**1.15 (1.03, 1.29)**	129 (24.9%)	**1.24 (1.02, 1.51)**	336 (31.2%)	**1.14 (1.01, 1.29)**	178 (31.7%)	**1.25 (1.06, 1.46)**
SxKOA	305 (18.6%)	**1.21 (1.07, 1.38)**	244 (21.8%)	**1.22 (1.07, 1.40)**	61 (11.8%)	1.17 (0.86, 1.60)	183 (17.0%)	**1.18 (1.00, 1.39)**	122 (21.7%)	**1.28 (1.06, 1.54)**
Knee Pain Severity	94.4 (75-100)	**1.10 (1.03, 1.17)**	91.7 (72.2-100)	**1.09 (1.03, 1.17)**	100 (77.8-100)	1.12 (0.97, 1.28)	97.2 (75.0-100)	**1.10 (1.03, 1.18)**	94.4 (72.2-100)	1.10 (0.96, 1.25)
VPT at MTP (per 10 volt/s higher)										
rKOA	725 (44.3%)	1.09 (0.99, 1.21)	512 (45.8%)	1.09 (0.97, 1.24)	213 (41.1%)	1.09 (0.92, 1.29)	460 (42.8%)	1.10 (0.98, 1.24)	265 (47.2%)	1.07 (0.88, 1.29)
Ksx	514 (31.4%)	**1.28 (1.15, 1.42)**	385 (34.4%)	**1.27 (1.11, 1.45)**	129 (24.9%)	**1.29 (1.08, 1.54)**	336 (31.2%)	**1.30 (1.14, 1.48)**	178 (31.7%)	**1.23 (1.04, 1.46)**
SxKOA	305 (18.6%)	**1.27 (1.11, 1.45)**	244 (21.8%)	**1.27 (1.09, 1.48)**	61 (11.8%)	1.26 (0.97, 1.62)	183 (17.0%)	**1.31 (1.12, 1.53)**	122 (21.7%)	1.19 (0.94, 1.49)
Knee Pain Severity	94.4 (75-100)	**1.10 (1.03, 1.18)**	91.7 (72.2-100)	**1.11 (1.03, 1.20)**	100 (77.8-100)	1.08 (0.95, 1.22)	97.2 (75.0-100)	**1.13 (1.05, 1.22)**	94.4 (72.2-100)	1.03 (0.91, 1.17)
PPT (per 1 kg/s lower)										
rKOA	782 (45.6%)	1.08 (0.93, 1.26)	546 (46.9%)	1.05 (0.89, 1.23)	236 (42.8%)	1.45 (0.94, 2.26)	500 (43.7%)	1.05 (0.88, 1.26)	282 (49.6%)	1.14 (0.89, 1.47)
Ksx	530 (30.9%)	1.11 (0.92, 1.34)	400 (34.4%)	1.10 (0.90, 1.34)	130 (23.6%)	1.25 (0.73, 2.14)	349 (30.5%)	1.13 (0.90, 1.43)	181 (31.8%)	1.07 (0.81, 1.42)
SxKOA	324 (18.9%)	1.11 (0.91, 1.35)	259 (22.3%)	1.11 (0.91, 1.36)	65 (11.8%)	1.09 (0.56, 2.11)	193 (16.9%)	1.11 (0.87, 1.41)	131 (23.0%)	1.12 (0.84, 1.50)
Knee Pain Severity	94.4 (72.2-100)	**1.23 (1.12, 1.36)**	91.7 (69.4-100)	**1.21 (1.09, 1.33)**	100 (77.8-100)	**1.50 (1.14, 1.99)**	94.4 (75.0-100)	**1.15 (1.02, 1.29)**	94.4 (69.4-100)	**1.39 (1.20, 1.61)**

* Outcome Frequency [n (%)] or Summary [Median (IQR)]

^ adjusted odds ratio (aOR) or adjusted density ratio (aDR), adjusted for age, sex, race, body mass index, presence of depressive symptoms, presence of any conditions related to peripheral neuropathy, presence of any conditions related to sensation/vibration, prior knee injury; for pain outcomes: Pain Catastrophizing Scale, Tampa Scale of Kinesiophobia-6 were also included

Bold indicates significant association at an alpha level of 0.05.

Results: Of 851 and 862 participants available for the VPT and PPT analysis (mean age 71 years, 2/3 female, 1/3 Black, BMI 31 kg/m^2), 1585 and 1660 knees were used for complete case analysis, respectively. Higher VPT (higher threshold for vibration perception) at the MFC and MTP was associated with the presence of all outcomes. Lower PPT (lower threshold for pain) was associated with greater knee pain severity. Estimates of associations of VPT with all outcomes were similar among women and men but some estimates were less precise (wider confidence interval) among men than women. Estimates for PPT were similar among men and women. Estimates of associations of VPT and PPT with all outcomes were similar among White and Black adults but some estimates were less precise among Black adults than White adults (Table 1).

Conclusion: Diminished vibration perception and greater pressure pain sensitivity were cross-sectionally associated with worse knee OA outcomes. Associations were similar across sex and race groups, suggesting the neurophysiological assessments do not largely inform established sex and race disparities in clinical outcomes.

Disclosure: C. Lane: None; **L. Thoma**: None; **C. Alvarez**: None; **D. Givens**: None; **A. Nelson**: None; **A. Goode**: None; **K. Foucher**: None; **Y. Golightly**: None.

Abstract Number: 0154

Impact of Social Determinants of Health (SDoH) on Survey Response Times Among Lupus Patients

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Epidemiology & Public Health – Interprofessional Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Social determinants of health (SDoH) significantly impact outcomes of Systemic lupus erythematosus (SLE) patients. However, little is known about the influence of SDoH on research participation in this population. We examined whether SDoH are associated with survey response times in a population-based SLE cohort. This is crucial as patient-reported outcomes are fundamental in capturing patient perspectives and informing healthcare interventions.

Methods: Data was sourced from the Georgians Organized Against Lupus (GOAL) 2018-2019 annual patient-reported survey, a population-based cohort study of validated SLE patients established in Atlanta, Georgia. Survey response times and completion methods (mail, web, in-person, and by-phone) were collected. Social Vulnerability Index (SVI), a census tract-based metric linked to participants' home addresses, was used given its compressive characterization of neighborhood-level SDoH. Differences in the mean response times by sociodemographic factors and survey completion methods were tested using two-tailed two-sample t-tests or ANOVA. Associations between response time and SVIs (overall and four thematic SVIs) were explored using linear regression analysis.

Results: 695 participants were included in this analysis. The mean age was 50.3 years old [SD 13.4]. The majority of participants were female (93.5%) and black (81.1%). 11.5% of participants had no insurance, and 39.7% were below the federal poverty level. 188 (27.1%) surveys were completed by mail, 440 (63.3%) by web, and 66 (9.5%) in-person or by-phone (Table). The mean response time was significantly higher for surveys completed by mail than by web (91.0 vs. 52.8, $p< 0.001$). Among the surveys completed by mail, quicker response times were associated with participants with lower

Table: Association of survey response time with sociodemographic factors and social vulnerability index (SVI)

Factors	Category	Overall n=695			Survey Completion Method* By Web(1), n=440			By Mail(2), n=188		
		Count	Mean(SD)	P	Count	Mean(SD)	P	Count	Mean(SD)	P
Gender	Male	45	75.1 (90.4)	0.30	21	52.4 (87.2)	0.98	15	112.5 (100)	0.33
	Female	650	61.6 (83.3)		419	52.8 (81.7)		173	89.1 (88.6)	
Race	1. Black	564	60.1 (84.5)		363	52.8 (83.0)		137	85.7 (93.3)	
	2. White	119	73.7 (78.8)	0.27	71	51.7 (72.1)	0.92	46	109.5 (77.6)	0.24
	3. Other races	12	64.7 (95.3)		6	65.7 (126.7)		5	65.4 (69.9)	
Education attainment	1. HS or less	221	62.1 (86.6)		103	61.0 (94.2)		80	71.6 (91.2)	
	2. Some college	223	61.5 (76.1)	0.95	149	48.4 (70.5)	0.48	56	103.8 (80.6)	***0.037***
	3. College or above	251	63.8 (88.0)		188	51.8 (83.1)		52	107.0 (91.7)	
Age Group	1. 18-34	102	68.5 (100)		70	80.2 (113.1)		13	59.5 (72.3)	
	2. 35-54	330	62.3 (81.8)	0.71	237	54.8 (82.0)	***<0.001***	60	100.9 (82.2)	0.31
	3. 55+	263	60.5 (79.3)		133	34.8 (53.3)		115	89.3 (94.4)	
Work Status	1. Employed	258	58.0 (77.4)		184	46.7 (71.8)		55	106.9 (85.6)	
	2. Off-home	157	66.4 (92.1)	0.51	96	58.1 (92.4)	0.44	50	81.7 (92.7)	0.30
	3. Unemployed	268	65.0 (83.8)		151	55.9 (84.0)		82	86.9 (89.8)	
Insurance Type	1. No insurance	80	61.2 (88.5)		41	65.9 (100.8)		15	88.9 (89.1)	
	2. Private	247	66.8 (89.1)	0.62	186	50.9 (77.3)	0.56	53	127.2 (106)	***0.002***
	3. Federal	365	60.1 (79.2)		210	52.1 (82.3)		120	75.2 (76.9)	
Marital Status	1. Currently married	266	66.8 (84.8)		179	51.8 (78.5)		67	113.3 (91.8)	
	2. Ever married	191	54.4 (68.9)	0.30	103	42.4 (63.4)	0.20	67	69.9 (74.3)	***0.019***
	3. Never married	237	64.4 (93.0)		157	60.9 (95.1)		54	89.4 (98.5)	
Below Poverty	No	419	66.0 (88.7)	0.17	285	50.4 (79.2)	0.43	114	105.9 (100)	***0.004***
	Yes	274	57.0 (75.7)		153	56.9 (87.1)		74	68.0 (63.8)	
Completion Method*	1. Web	440	52.8 (81.9)	***<0.001***	*64 surveys completed in-person and 2 by-phone were excluded from this comparison and further analysis due to underlying bias					
	2. Mail	188	91.0 (89.5)							

Social Vulnerability Index (SVI)	Count	Slope (SE)	P	Count	Slope (SE)	P	Count	Slope (SE)	P
Theme 1): Socioeconomic Status	692	-32.7 (11.5)	***0.0044***	437	-23.4 (14.3)	0.10	188	-84.5 (22.3)	***<0.001***
Theme 2): Household Comp. & Disability	692	-30.8 (11.7)	***0.0085***	437	-18.4 (14.4)	0.20	188	-76.6 (23.4)	***0.001***
Theme 3): Minority Status & Language	692	-31.6 (14.5)	***0.029***	437	-11.2 (18.2)	0.54	188	-70.9 (26.4)	***0.008***
Theme 4): Housing & Transportation	692	-18.9 (11.1)	0.088	437	-16.7 (13.7)	0.22	188	-50.4 (22.8)	***0.028***
Overall Social Vulnerability Index	692	-35.0 (11.5)	***0.0023***	437	-23.7 (14.0)	0.092	188	-96.4 (23.0)	***<0.001***

education (p=0.037), less insurance coverage (p=0.002), a non-married status (p=0.019), and income below the federal poverty level (p=0.004). Survey response times were negatively associated with overall SVI (slope=-96.4, p< 0.001), as well as all of its four subindices: socioeconomic status (slope=-84.5, p< 0.001), household composition & disability (slope=-76.6, p=0.001), minority status & language (slope=-70.9, p=0.008), and housing & transportation (slope=-50.4, p=0.028). No such associations were found in web surveys, though younger participants completed the survey faster online.

Conclusion: Our study shows that SDoH impact mail survey response times in the Georgian SLE population. The overall SVI and all of its subindices are significantly and negatively linked with response times. SDoH's influence on response times varies based on the survey completion method, with insurance, marital, education, and poverty status significant for mail surveys but not web surveys. While requiring web-based surveys would be ideal, mail surveys are unavoidable, especially for those with limited access to technology. Tailored strategies are needed to address SDoH disparities when surveying the SLE populace, especially for underrepresented groups. Further studies are necessary to explore additional interventions to mitigate SDoH-related barriers in SLE patient surveys.

Disclosure: D. Bao: None; **C. Dunlop-Thomas**: None; **C. Drenkard**: None; **S. Lim**: None.

Abstract Number: 0155

Cost Analysis of Subcutaneous Methotrexate Compared to Oral Methotrexate Treatment for Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Health Services Research Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis (RA)patients who switch from oral to subcutaneous methotrexate (MTX) may experience better response to treatment due to increased bioavailability, enhanced tolerability, increased adherence, fewer side effects and better clinical response rates. However, the economic impact of such a switch is unknown. The study objective was to evaluate the incremental cost associated with subcutaneous (Rasuvo®) vs. oral MTX treatment in RA patients.

Methods: A comparative effectiveness study was conducted in adult (18+ years) RA patients on MTX treatment, identified from the Kaiser Permanente Southern California health plan member population. We employed a prospective cohort study design with 1:1 matching of oral vs. Rasuvo® users. After obtaining informed consent, patients completed either a web based or mailed paper survey which recorded their baseline disease activity scores using the MDHAQ's RAPID3 measure. We analyzed direct medical expenditure associated with medical office visits (routine and urgent care), hospital outpatient and ED visits, inpatient and observation stays, pharmacy utilization, laboratory, and radiology utilization during the one-year following the index prescription fill for MTX. To mitigate potential bias due to non-random treatment assignment, we used 2-stage residual inclusion instrumental variables (2SRI) techniques to evaluate the incremental effect of oral MTX vs Rasuvo® on total all cause expenditure as well as subgroups of utilization. Depending on the degree of zero mass, either one part or two part generalized linear model with log link and gamma family distribution with 2SRI correction were specified while confidence intervals were based on 1000 bootstrapped repetitions of these outcome models. Each utilization model adjusted for baseline disease activity (based on MDHAQ survey), duration of RA (early within 2-years of diagnosis); duration of MTX use; age, female sex, white race, Hispanic ethnicity, smoking status, body mass index over 30, income category and Charlson comorbidity index.

Table 1. Baseline Demographics and Disease Activity Levels

	Oral Methotrexate (n = 286)	Rasuvo® (n = 283)
Age (in years) at baseline survey mean (SD)	59 (± 15.0)	55 (± 14.6)
Early RA (%)	27.6%	24.7%
Prior methotrexate use over 2-years (%)	59.1%	25.4%
Female sex (%)	75.2%	90.1%
White race (%)	66.4%	58.3%
Hispanic ethnicity (%)	32.5%	41.3%
Never smoked (%)	65.0%	68.6%
Obese (BMI 30+) (%)	43.7%	45.2%
Low income (%)	19.6%	25.4%
2 or More Charlson comorbidities (%)	23.8%	29.0%
MDHAQ		
Baseline disease activity Remission (Score 3 or Less) (%)	9.90%	4.20%
Low disease activity (score 3.1–6) (%)	17.60%	9.90%
Moderate disease activity (score 6.1–12) (%)	36.60%	32.0%
High disease activity (score 12.1 and up) (%)	35.90%	54.0%

Table 2. Marginal Mean Expenditure and Marginal Difference Between Rasuvo® vs Oral MTX

Cost	Utilization Subgroups Included in Category	Marginal Mean Expenditure (Std Error. of Mean)*@		
		Oral MTX (N=286)	Rasuvo® (N=283)	Marginal Difference between Rasuvo® vs Oral MTX^@@ (95% Confidence Interval)
Total all cause cost	Summation of all subcategories of utiliznition	$8,676 (±1156)	$13,380 (±945)	**$4,704 ($1,758 to $7,650)**
All cause Pharmacy cost	Expenditures for pharmacy fills for any condition	$5,680 (±1163)	$9,903 (±759)	**$4,223 ($1,460 to $6,986)**
Office visits costs	Medical office visit to primary care, or specialist for any condition. Includes all procedures and imaging or laboratory orders associated with that visit	$820 (±103)	$874 (±106)	$54 (-$231 to $338)
Inpatient and Observation Stays Costs	Inpatient stay and observation stay	$1,458 (±4,832)	$1,187 (±3,809)	-$270 (-$11,210 to $10,669)
Emergency department costs	Emergency department visits	$407 (±215)	$504 (±303)	$97 (-$383 to $576)
Urgent care costs	Urgent care department cost	$50 (±35)	$97 (±39)	$47 (-$47 to $140)
Imaging/radiology cost	Imaging orders	$530 (±64)	$698 (±71)	$168 (-$24 to $360)
Laboratory cost	Laboratory tests	$286 (±35)	$282 (±19)	-$4 (-$80 to $71)

##Bold Font indicate statistically significant differences

@ Generalized linear model (GLM) with log link and gamma family distribution which included the first stage residual (2SRI) along with covariates was used to estimate marginal expenditures

@@ Bootstrapping (1000 reps) of GLM was used to estimate the standard errors and for hypothesis testing

*All Models adjusted for baseline disease activity (based on MDHAQ survey), duration of RA (early within 2-years of diagnosis), duration of MTX use, age, female sex, white race, Hispanic ethnicity, smoking status, body mass index over 30, income category and Charlson comorbidity index.

Results: The baseline self-report survey completion rate was 20% (569/2885; oral methotrexate = 286 and Rasuvo® = 283). The mean age of the sample was 57 (±15) years with the majority (83%) of female (Table 1). Rasuvo® arm included a higher proportion of patients with multiple comorbid conditions (29% vs 24%) and who also had higher proportion reporting high disease activity (54% vs 36%) (Table 1). Rasuvo® use was associated with significantly higher all cause total expenditure $4,704 (95% CI $1,758 to $7,650) which was predominantly a result of higher costs associated with all cause pharmacy utilization $4,223 (95% CI $1,460 to $6,986) (Table 2). None of the other subgroups of utilization had statistically significant differences.

Conclusion: In this prospective comparative effectiveness study, patients on subcutaneous methotrexate were associated with higher total cost which was driven by increased pharmacy expenditure.

Disclosure: A. Kawatkar: Medac, 5, 5; **D. Yi**: Medac, 5; **E. Estrada**: Medac, 5; **C. Portugal**: Medac, 5.

Abstract Number: 0156

Factors Associated with Adherence to Cervical Cancer Screening in Ethnically Diverse Women with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Health Services Research Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Women living with systemic lupus erythematosus (SLE) are at an increased risk of infections from human papillomavirus (HPV), and cervical cancer, especially women with higher disease activity who require immunosuppression. The objective of this study was to determine cervical cancer screening rates in women with SLE, and to evaluate their attitudes and beliefs towards screening.

Methods: We conducted a cross-sectional study in which we enrolled consecutive women with a diagnosis of SLE by 2019 ACR criteria. Eligible women were ≥21 years old, without a prior hysterectomy or history of cervical cancer. We collected demographics, clinical characteristics, constructs of the Health Beliefs Model (HBM) (susceptibility, severity, perceived barriers, benefits, cues to action, and self-efficacy) and self-reported last cervical cancer screening (confirmed with the electronic medical record). Our primary outcome was adherence to cervical cancer screening according to the American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines. Multivariable logistic regression models were used to examine the association between the SLE disease activity attributes and the cervical cancer screening and to explore the mediation effect of HBM constructs between disease activity and screening adherence.

Results: We enrolled 130 women with SLE to our study, the majority of whom were Black (35%) or Hispanic (52%), with a median age of 42. The cervical cancer screening adherence rate was 61.5%. Women with higher disease activity (SLEDAI < 6) underwent screening less frequently than those with low disease activity (76% vs 24%, $p < 0.05$). Multivariable logistic regression adjusting for demographics and clinical factors showed higher disease activity had a decreased odds of being screened than low disease activity (aOR 0.24, 95% CI 0.08-0.76, $p < 0.02$). HBM constructs, particularly perceived barriers ($r=-0.30$, $p< 0.01$) and self-efficacy ($r=0.21$, $p< 0.05$) were significantly correlated with the receipt of cervical cancer screening. Multivariable regression models adjusting for covariates and mediation effects of each HBM construct showed that SLE patients with high disease activity had decreased probability of cervical cancer screening ('perceived susceptibility': aOR 0.2548, $p < 0.01$; 'perceived severity': aOR 0.2552, $p< 0.01$; 'perceived barriers': aOR 0.2809, $p< 0.01$; 'perceived benefits': aOR 0.2491, $p< 0.01$; 'self-efficacy': aOR 0.2734, $p< 0.01$; 'cues to action': aOR 0.2602, $p< 0.01$).

Conclusion: Our results show that only 61.5% of women with SLE underwent screening according to ASCCP guidelines. Concerningly, only 24% of those with high disease activity, the highest risk population, had been screened. While some individual attitudes and beliefs partially explained these low rates, low odds for screening remained after adjustment. Our findings indicate the need for ascertainment of cervical cancer screening utilization in this high risk population as needed following ASCCP recommendations.

Disclosure: S. Bruera: None; **S. Bowman**: None; **Y. Huang**: None; **M. Suarez-Almazor**: Celgene, 1, Eli Lilly, 2, Pfizer, 2, Syneos Health, 1; **G. Lo**: None; **E. Chiao**: None; **M. Lopez-Olivo**: None; **S. Agarwal**: None.

Abstract Number: 0157

Discovering the Potential of Digital Biomarkers in the Work Process of the Rheumatology Healthcare Professionals, a Design Thinking Approach; Preliminary Results of the Healthcare Professionals Perspective

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Health Services Research Poster I
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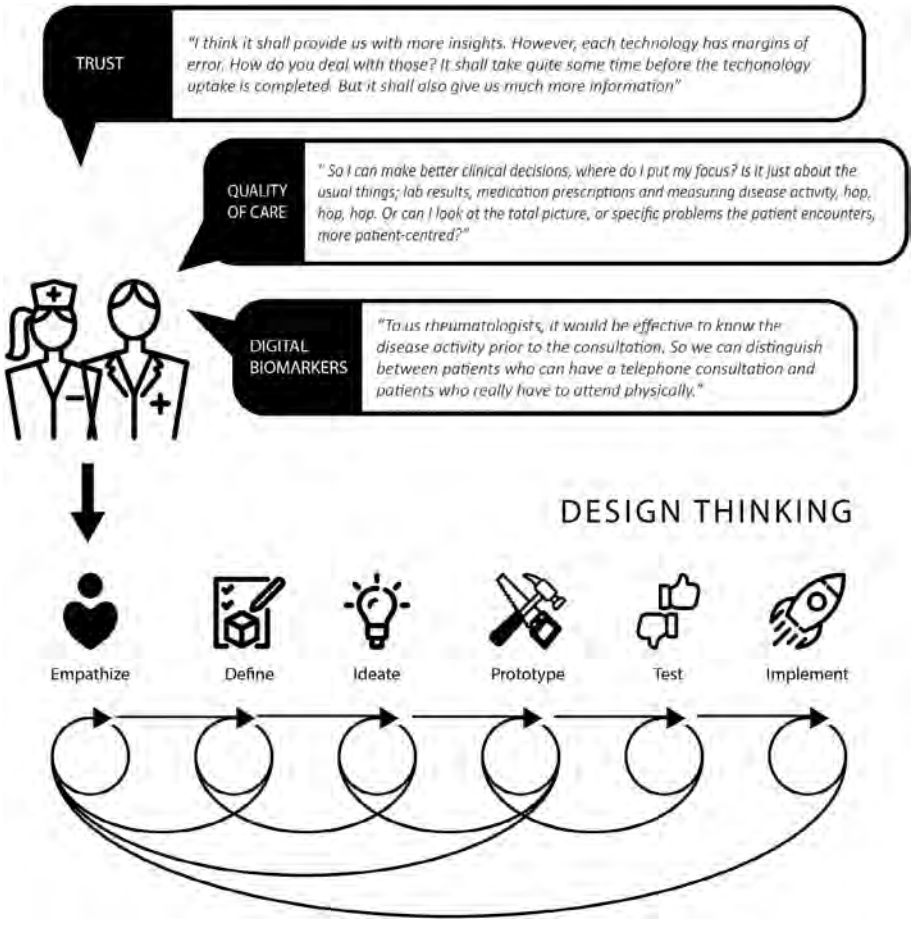
Background/Purpose: During times of social-distancing, in-person outpatient visits were greatly reduced. Health care professionals (HCPs) were dependent on the patient's reported experience of their disease activity in their assessments of the wellbeing and inflammatory state, due to lack of physical assessments. *Digital biomarkers* can support real-world continuous measurements and offer a method for remote quantification of inflammatory joint disease. They are defined as objective, quantifiable, physiological and behavioural data that are collected and measured with digital devices.

This study uncovers the HCPs perspective on current manners of disease activity monitoring, easing their workload and the potential of digital biomarkers.

Methods: A Design Thinking approach is followed for digital biomarker development. It is a human-centered problem solving approach that leverages iteration, empathy and collective idea generation to tackle complex challenges. Semi-structured online focus group discussions were conducted. Pilot 1-1 interviews were executed to assess the interview script. The script is underpinned by the graphical framework for clinical decision making (Charlin 2012) and the theoretical domain framework (Cane 2012). One moderator and three alternating observers facilitated the sessions. All interviews were audio-recorded, transcribed to verbatim and coded.



Quotes of the HCPs and the design thinking process

Results: Six focus groups were organised, with a total of 28 HCPs. Participants were rheumatologists (N= 19, age 47 ± 9, 50% male) and rheumatology nurses (N = 9, age 51 ± 6, 0% male). The main findings about digital biomarkers in relation to current practices were: *Trust;* HCPs felt self-assured about their own abilities of physical evaluation, reading patients and their gut feeling. Trust in flare detection with digital biomarkers and machine learning was low. It was expected that much disease activity is missed and many false-positive flares are detected. Biomarkers should be valid, reliable and sensitive to change. *Innovation should improve quality of care;* No consensus about a golden standard of care exists. HCPs were afraid that with digital biomarkers personal interaction recedes to the background and quality of care is compromised. Personal interaction was marked as essential to raise sensitive topics and stimulate therapy adherence. *Benefits of digital biomarkers;* HCPs enjoyed the delivery of efficient and effective care. They disliked repetition and the high administrative burden. In the HCPs opinion digital biomarkers could establish disease activity prior to the consultation, so time could be spent on what matters to the patient. New technologies should however not add to frustrations and make way for things that really matter.

Conclusion: The following problem statement from the HCPs perspective can be formulated: "In limited time we take many actions. We spend time on both disease and emotional support of our patients. Our workload is high and trivial tasks such as administration take too much of our time. Instead we want to focus on what's relevant to the patient. We are confident about our own abilities and, only if technology is proven to be valuable, valid, reliable and accepted by our patients it can be used in clinical practice."

Disclosure: p. de Groot: None; **J. Luime**: None; **M. Kok**: None; **m. vis**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Dutch Arthritis Foundation, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **i. Tchetverikov**: None.

Abstract Number: 0158

Analyzing User Log Data to Track Provider Use of an EHR-based Dashboard for Rheumatoid Arthritis Outcomes

Lindsay Jacobsohn[1], Emma Kersey[1], Jing Li[1], Catherine Nasrallah[1], Cherish Wilson[2], Cammie Young[3], Cammie Young[3], Alicia Hamblin[1], Jinoos Yazdany[1] and Gabriela Schmajuk[2], [1]University of California San Francisco, San Francisco, CA, [2]UCSF / SFVA, San Francisco, CA, [3]University of California San Francisco, Oakland, CA

SESSION INFORMATION
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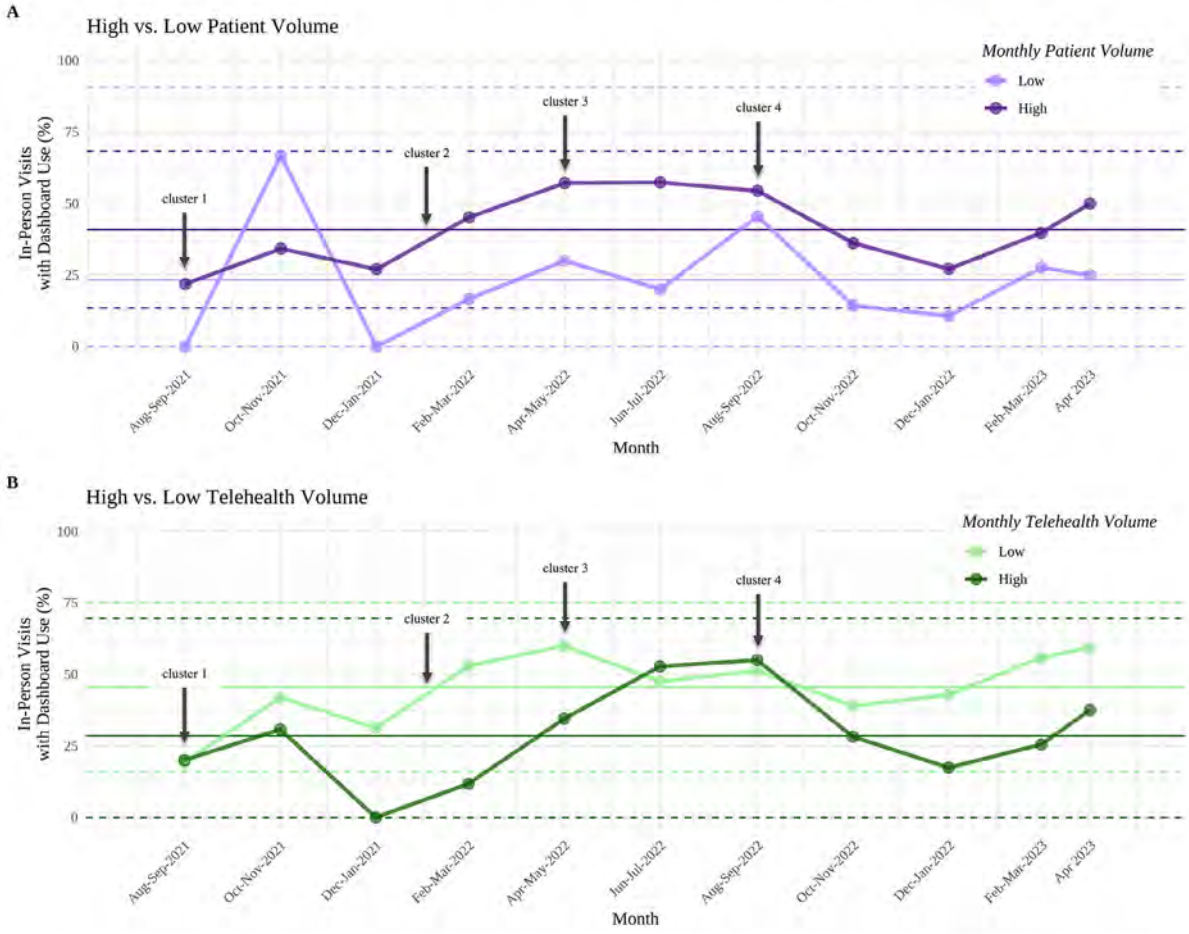
Background/Purpose: We developed an electronic health record (EHR)-based patient-facing sidecar dashboard application to display RA outcomes, including disease activity, functional status, and pain scores over time ("RA dashboard"). User log data is a novel data source that makes it possible to examine provider engagement with technology. We analyzed user log data from the RA dashboard to examine patterns of provider engagement with this health-information technology (IT) tool in the context of a pragmatic clinical trial.

Methods: The RA dashboard was implemented at a single academic rheumatology clinic as part of a stepped-wedge pragmatic trial in which 24 providers were randomized into 4 trial clusters between August 2021 and September 2022. User log data were collected from the initial roll-out through April 2023. The primary outcome was the number of "actions" taken by providers on the dashboard: possible actions included refresh, print, show/hide different sections of the dashboard, and scrolling up/down on the page or backward/forward through historical data. Provider characteristics included level of

Table 1. Characteristics of Providers with Access to the RA Dashboard (N = 24)

Provider Characteristic	*N (%)*
Dashboard Access (Trial cluster, date)	
1 (08/11/2021)	4 (16.7)
2 (02/01/2022)	5 (20.8)
3 (05/02/2022)	5 (20.8)
4 (09/26/2022)	10 (41.7)
Provider Training	
Attending Physician	16 (66.7)
Rheumatology Fellow	7 (29.2)
Physician Assistant	1 (4.2)
Average Patient Visits (N) per Month	
< 10 patients	8 (33.3)
≥ 10 patients	16 (66.7)
Average Telehealth Visits (%) per Month	
Quartile 1 (0 - < 35%)	6 (25.0)
Quartile 2 (35 - < 50%)	6 (25.0)
Quartile 3 (50 - < 58%)	4 (16.7)
Quartile 4 (58+%)	8 (33.3)

Figure. Percent of In-Person Patient Visits with RA Dashboard Use by Provider Characteristics



Panels A and B depict the percent of in-person patient visits with RA dashboard use over the study period by providers with high vs. low patient volume (A) and providers with high vs. low telehealth volume (B). High patient volume was defined as ≥10 patients and high telehealth volume was defined as ≥50% of visits. Each **data point** is the percent of in-person visits with dashboard use during the 2-month period. The **solid horizontal lines** represent the mean (μ) percent of in-person patient visits with dashboard use and the **dashed horizontal lines** represent the upper and lower bounds of the control limits ($\mu \pm 3\sigma$). Data points outside of the control limits are considered outliers, while consecutive data points on either side of the mean line are considered a shift, and consecutive points in a steady increase or decrease are considered trends. **Arrows** indicate dashboard introduction of each of the 4 study clusters.

training, monthly patient volume (for patients with any diagnosis); percent of total visits that were completed via telehealth (video or telephone), and randomization cluster (**Table**). We examined engagement with the dashboard (proportion of visits with at least 1 action) overall, over time, and by provider characteristics using proportions and statistical control charts.

Results: Most providers were attendings with ≥ 10 patient visits per month; 50% of providers performed more than half of their visits via telehealth (**Table**). In total, 2,066 RA visits occurred after the dashboard was rolled out, 998 (48%) of which occurred in-person. Overall, the dashboard was used during 23% of RA patient visits, although this percentage was higher among in-person visits compared to telehealth visits (37% vs. 10%). Among in-person visits with any dashboard actions (N=372), there was a mean (SD) of 15.6 (20.5) actions of any kind. Refresh was the most common action (occurring in 81% of in-person visits with any actions), followed by scrolling up/down (67%) and show/hide (7%). Engagement with the dashboard was relatively stable over time (range 0-30% for all visits; 0-56% for in-person visits over the study period). Providers with ≥ 10 patient visits per month and providers who performed fewer visits via telehealth had more engagement compared to providers with lower patient volumes, and providers with more telehealth, respectively.

Conclusion: User log data is a feasible method to monitor provider engagement with a novel health IT tool in the context of a pragmatic trial. Overall engagement with the RA dashboard was low, although we observed more engagement for in-person visits and among providers with higher patient volumes. Trials of technology need to plan for high variability in provider engagement and consider strategies to include highly engaged providers in order to accurately measure the effect of technology on health outcomes.

Disclosure: L. Jacobsohn: None; **E. Kersey**: None; **J. Li**: None; **C. Nasrallah**: None; **C. Wilson**: None; **C. Young**: None; **C. Young**: None; **A. Hamblin**: None; **J. Yazdany**: Astra Zeneca, 2, 5, Aurinia, 5, Gilead, 5, Pfizer, 2; **G. Schmajuk**: None.

Abstract Number: 0159

Understanding the Economic Impact of Autoimmune Eye Disease in the United States

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
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Session Time: 9:00AM–11:00AM

Background/Purpose: Eye involvement is an important cause of morbidity in rheumatology patients. Inflammatory eye diseases include conditions like scleritis, uveitis, retinitis and orbital inflammation. The complexity of these conditions requires specialized care resulting in significant financial burden for patients and the healthcare system. Identifying this financial burden is the first step towards developing strategies to address it. However, there is a lack of national data for the health care cost associated with inflammatory eye diseases. This study assesses health care cost due to ocular inflammatory diseases using the National Inpatient Sample (NIS), a nationally representative sample of hospital discharges in the United States.

Methods: We have conducted a retrospective analysis of the National Inpatient Sample (NIS) from 2016-2019. Patients with a primary diagnosis of uveitis and ocular inflammation were identified using International Classification of Diseases, Tenth Revision (ICD-10) codes. NIS is the largest all payer database developed by the Healthcare Cost and Utilization Project (HCUP) in the US and is ideal for investigating national estimates for health care cost. Healthcare costs are identified by analyzing aggregate and average hospital charges, aggregate and average hospital cost and length of stay.

Charge is the amount hospital billed and cost is the actual cost of hospital stay. Charges are converted to costs using cost-to-charge ratios based on hospital accounting reports from the Centers for Medicare and Medicaid Services (CMS). Descriptive statistics are used to present the demographics and cost characteristics of patients.

Results: A total of 6105 uveitis and ocular inflammation related hospitalizations were identified in the NIS database from 2016-2019. The average age of patients during the study period ranged between 50-54 years and a higher number of patients were males. The mean length of hospital stay was 6.3 (±.5) days.

The total healthcare costs for uveitis and ocular inflammation related hospitalizations for the years 2016-2019 was $ 82,739,013 and it increased from the years 2016 to 2019. Breakdown of patient demographics, total and aggregate hospital charges, total and aggregate hospital cost and length of stay for individual years from 2016-2019 are shown in the table.

Conclusion: Inflammatory eye diseases impose substantial economic burden on both the patients and the healthcare system. Identifying the financial impact will help patients and healthcare providers in making informed treatment decisions. Further research is necessary to identify the cost-effectiveness of management strategies for inflammatory eye diseases.

Demographics of patients with Uveitis and Ocular inflammation: 2016-2019: National Inpatient Sample.

Demographics of patients with Uveitis and Ocular inflammation: 2016-2019: National Inpatient Sample.

	2016	2017	2018	2019
	Estimate (Standard error)	Estimate (Standard error)	Estimate (Standard error)	Estimate (Standard error)
Number of discharges	1,390 (83)	1,350 (82)	1,510 (87)	1,855 (96)
Number of discharges for Males	750 (42)	760 (41)	745 (44)	1010 (48)
Number of discharges for Females	640 (42)	590 (41)	765 (44)	845 (48)
Average age at admission (in years)	50 (1.4)	54 (1.2)	51 (1.2)	52 (1.1)
Number of discharges in the following racial categories:				
White	775 (40)	750 (40)	830 (43)	905 (47)
Black	265 (33)	255 (32)	295 (34)	400 (39)
Hispanic	195 (29)	230 (31)	235 (31)	290 (35)
Asian or Pacific Islander	60 (17)	30 (12)	15 (9)	60 (17)
Native American	0	0	**	15 (9)
Other	55 (16)	25 (11)	70 (18)	95 (21)

** Values suppressed due cell value of 10 or less.

Health care expenditure for patients with Uveitis and Ocular Inflammation in the United States: 2016-2019: National Inpatient Sample.

	2016	2017	2018	2019
	Estimate (Standard error)	Estimate (Standard error)	Estimate (Standard error)	Estimate (Standard error)
Number of discharges	1,390 (83)	1,350 (82)	1,510 (87)	1,855 (96)
Average Length of Stay (In days)	5.6 (0.33)	6.5 (0.42)	5.9 (0.32)	7 (0.52)
Aggregate hospital charges* (In US $)	66,525,170	72,507,855	65,895,345	118,597,225
Aggregate hospital cost^ (In US $)	16,884,141 (1924031)	17,972,462 (2122834)	19,125,946 (2158514)	28,756,464 (3008420)
Average hospital charge per stay (In US $)	49,278 (3,735)	53,710 (4,384)	59,154 (4,893)	64,107 (4,121)
Average hospital cost per stay (In US $)	13,295 (1064)	14,264 (1151)	14,273 (1045)	17,481 (1394)

*Charges: Amount hospital billed. Aggregate Charges: The sum of all charges for all hospital stays in the U.S.

^Costs: Actual costs of hospital stay.

Charges are converted to costs using cost-to-charge ratios based on hospital accounting reports from the Centers for Medicare and Medicaid Services (CMS).

Health care expenditure for patients with Uveitis and Ocular Inflammation in the United States: 2016-2019: National Inpatient Sample.

Disclosure: K. Chauhan: None; **S. Scaife**: None; **M. Buhnerkempe**: None.

Abstract Number: 0160

Spine and Sacroiliac Joints Findings in Young Males and Females with Chronic Back Pain Undergoing Magnetic Resonance Imaging in Clinical Practice

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Health Services Research Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Magnetic resonance imaging (MRI) is frequently used in patients with chronic back pain (CBP) to diagnose mechanical and inflammatory diseases, including axial spondyloarthritis (axSpA). Recent data suggest sacroiliac joints (SIJ) MRI findings in axSpA may differ according to sex[1]. Whether this holds true for spinal MRI and other causes of CBP is currently unknown. Our aim was to analyze spinal and SIJ MRI findings in young male and female patients with CBP.

Methods: The "Strategy for a Hospital Early Referral in Patients with Axial Spondyloarthritis" (SHERPAS) is a prospective ongoing study recruiting young patients (18 to 40 years) with CBP asked to undergo an MRI of the spine by other specialists different than rheumatologists in a tertiary hospital, starting in September 2021. After inclusion, an additional MRI of the SIJ,

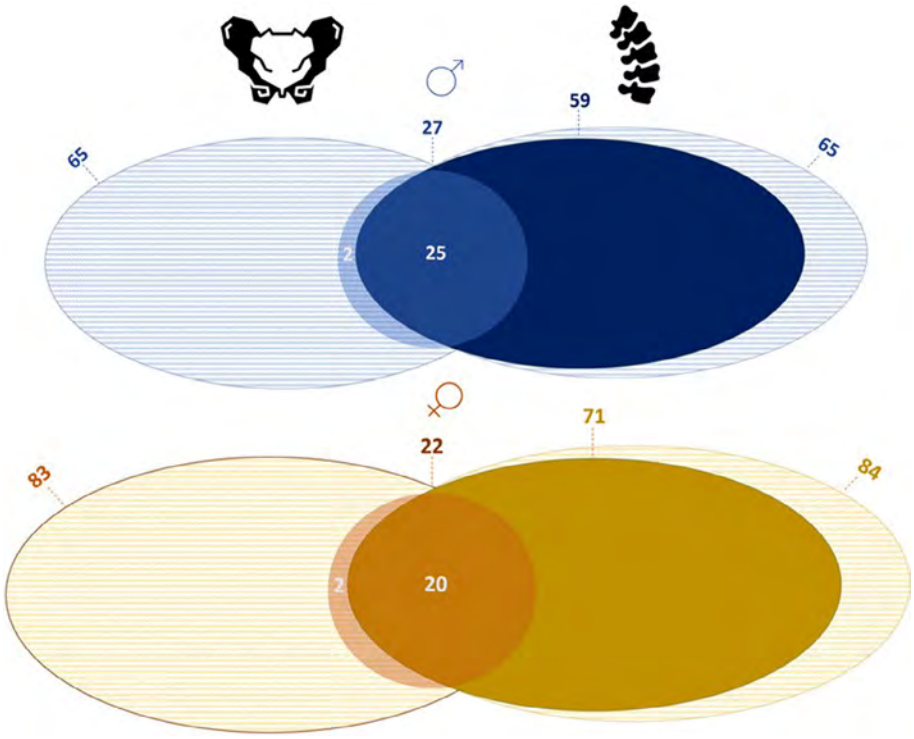

Figure. Patients with any reported finding (structural or inflammatory) in spine or sacroiliac joint magnetic resonance imaging. Colored: any finding. Striped: no findings.

Table. Findings in spinal and sacroiliac joints magnetic resonance imaging

	Total	Male	Female	p-value
Spine MRI	n=149	n= 65	n= 84	
Any finding	130 (87.2)	59 (90.8)	71 (84.5)	0.3
Structural findings	129 (86.6)	58 (89.2)	71 (84.5)	0.3
Spondylolisthesis	5 (3)	3 (4.6)	2 (2.4)	0.6
Spondylolysis	2 (1)	1 (1.5)	1 (1.2)	1
Disc herniation	34 (23)	15 (23.1)	19 (22.6)	1
Disc protrusion	64 (43)	31 (47.7)	33 (39.3)	0.3
Facet joints abnormalities	8 (5)	1 (1.5)	7 (8.2)	0.1
Other	16 (11)	7 (10.8)	9 (10.7)	1
Inflammatory findings	1 (1)	1 (1.5)	0	0.5
No findings	19 (13)	6 (9.2)	13 (15.5)	0.4
Sacroiliac Joint MRI	n=148	n= 65	n= 83	
Any finding	50 (33.5)	27 (41.5)	23 (27.4)	0.07
Structural findings	31 (20.9)	15 (23.1)	16 (19.3)	0.7
Inflammatory findings	11 (7.4)	6 (9.2)	5 (6.0)	0.5
Structural and Inflammatory findings	7 (4.7)	6 (9.2)	1 (1.2)	0.04
No findings	99 (67.8)	38 (58.5)	61 (73.5)	0.08

followed by a rheumatology visit and eligible blood tests were performed. Dataset for this interim analysis was locked in October 2022. The protocol for MRI of the spine used a 1.5T scanner to acquire sagittal T1-weighted turbo spin echo (TSE) and T2- weighted TSE, both for the lateral sides of vertebral bodies, and T2-Multistack. On top of this, an MRI of the SIJ, which involved T1-TSE, T2- weighted SPAIR and short-tau inversion recovery (STIR) sequences, was performed. MRI findings were assessed according to clinical practice by one of the four musculoskeletal radiologists working in the centre, describing the presence of mechanical lesions (spondylolisthesis, spondylolysis, disc herniation, disc protrusion, facet joints abnormalities), inflammatory findings (both SIJ and spine), and SIJ structural findings. For this analysis, results were stratified by sex.

Results: Among152 recruited patients, 85 (55.9%) were female; mean age was 34.2 (5.3) years. Spinal MRI findings were reported in 130 (87.2%) patients, with no differences between sexes (male 90.8% vs female 84.5%, p=0.3). As shown in **Table**, the most frequent diagnosis in both sexes were disc protrusion, followed by disc herniation. Inflammatory spinal findings were detected only in one male patient. No differences were found for any of the spinal lesions. SIJ MRI findings were reported in 49 (33.1%) patients, being numerically more frequently observed in males than females (41.5% vs 26.5%; p=0.08). Concurrence of both structural and inflammatory lesions was more frequently in males (9.2% vs 1.2%, p< 0.05), while no differences in isolate SIJ MRI findings were found between sexes. Overall, 45 (29.6%) patients presented findings both in the spine and SIJ (**Figure**).

Conclusion: In young patients who are requested a spinal MRI by other specialists different than rheumatologists, spinal lesions are reported in most patients, and similarly in males and females. Remarkably, SIJ MRI findings are reported in one out of three patients in this population, being more frequently in males.

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Abstract Number: 0161

Differences and Similarities Between the EULAR/ASAS-EULAR Recommendations and National Recommendations for Treatment of Patients with Psoriatic Arthritis and Axial Spondyloarthritis Across Europe

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Health Services Research Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: National treatment recommendations are often used to optimize patient care and may differ from international recommendations. The aim of this study was to assess differences and similarities between the EULAR and ASAS-EULAR recommendations for the treatment of patients with PsA and axSpA, respectively, versus national PsA and axSpA treatment recommendations across Europe.

Methods: Rheumatologists from 15 European countries (Czech Republic, Denmark, Estonia, Finland, Iceland, Italy, Netherlands, Norway, Portugal, Romania, Slovenia, Spain, Sweden, Switzerland, and the United Kingdom) compared the most recent national treatment recommendations for PsA and axSpA with the "EULAR recommendations for the management of PsA with pharmacological therapies: 2019 update"[1] and the "2016 update of the ASAS-EULAR recommendations for axSpA"[2], in an online survey conducted between October 2021 and April 2022. The study was an initiative of the European Spondyloarthritis Research Collaboration Network (EuroSpA RCN).[3]

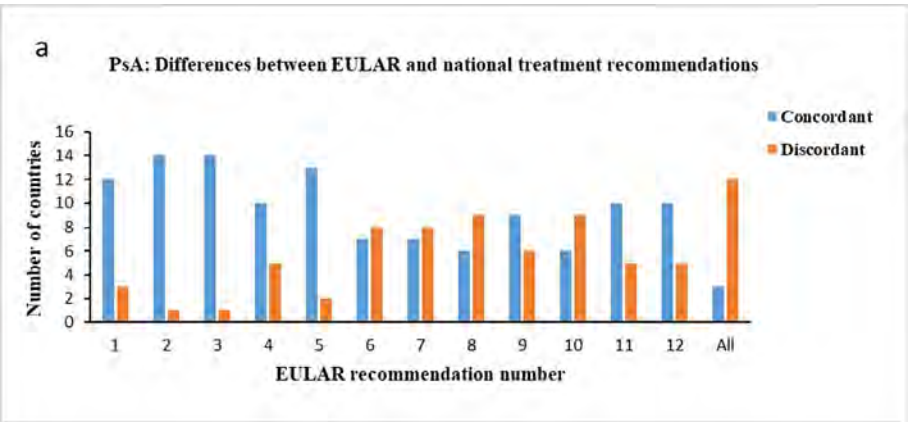

Figure 1a, Differences and similarities between EULAR and national treatment recommendations for patients with PsA

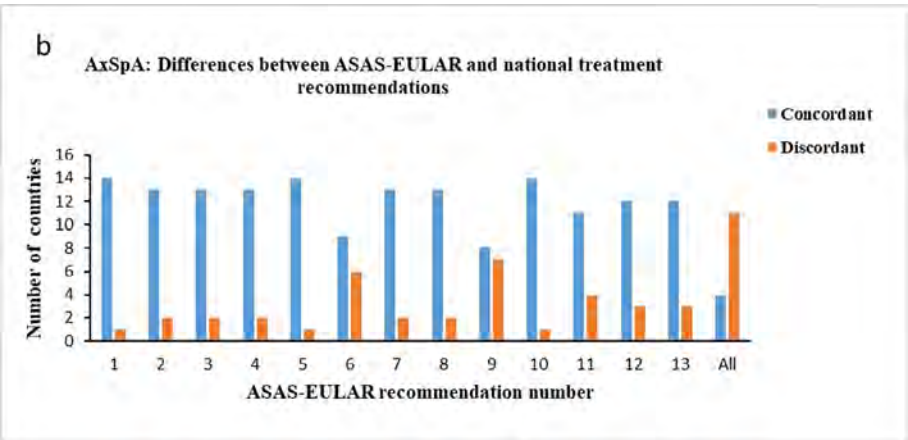

Figure 1b, Differences and similarities between ASAS-EULAR and national treatment recommendations for patients with axSpA

Results: Three countries (Czech Republic, Netherlands, and Spain) followed all EULAR recommendations for treating patients with PsA and four countries (Czech Republic, Italy, Spain, and Switzerland) all ASAS-EULAR recommendations for axSpA. Five countries had no national treatment recommendations for PsA and/or axSpA, but had other rules or regulations to follow, for which the comparisons in this study were performed. In six countries, the national treatment recommendations for PsA predated the 2019 EULAR recommendations and in one country the national treatment recommendations for axSpA predated the 2016 ASAS-EULAR recommendations. More differences were seen between the EULAR and the national treatment recommendations for PsA than between the ASAS-EULAR and the national treatment recommendations for axSpA (Figure 1a,b).

Discrepancies between international and national treatment recommendations included: Entry criteria for start of a biologic/targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD) varied and were the most stringent in Romania, where DAPSA >28 for PsA and BASDAI >6 and ASDAS ≥2.5 for axSpA were required for the start of a bDMARD. Regarding PsA, in two countries (Finland and Switzerland) a conventional synthetic DMARD should be initiated before a b/tsDMARD including in patients with predominantly enthesal or axial disease. In several countries, no preference for interleukin-17 inhibitors was given for PsA patients with significant skin involvement. The positioning of Janus Kinase inhibitors (JAKi) differed across countries, e.g. in Estonia JAKi were indicated after failure of two tumor necrosis factor inhibitors and in Romania JAKi were positioned at the same level as bDMARDs. Phosphodiesterase-4 inhibitors were not in use or not reimbursed in most countries. Analgesics were not specifically mentioned in several of the national treatment recommendations.

Conclusion: Only a few European countries incorporated all EULAR and ASAS/EULAR treatment recommendations in their national recommendations. The potential impact of this on access to b/tsDMARD treatments needs to be further explored.

Disclosure: B. Michelsen: Novartis, 5; **M. Østergaard**: AbbVie, 2, 5, 6, Amgen, 5, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Hospira, 2, 6, Janssen, 2, 6, MEDAC, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Novo Nordisk, 2, 6, Orion, 2, 6, Pfizer, 2, 6, Regeneron, 2, 6, Roche, 2, 6, Sandoz, 2, 6, Sanofi, 2, 6, UCB, 2, 6; **M. Nissen**: AbbVie/Abbott, 2, Eli Lilly, 2, 12, Involved in Clinical Trial, Janssen, 2, Novartis, 6, 12, research funding paid to institution, Pfizer, 6, UCB, 2, 12, funding support to attend EULAR 2023, paid to institution; **A. Ciurea**: None; **B. Moeller**: None; **L. Ørnbjerg**: Novartis, 5; **J. Zavada**: None; **B. Glintborg**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, Sandoz, 5; **A. MacDonald**: Galapagos, 6; **K. Laas**: None; **D. Nordstrom**: AbbVie/Abbott, 2, BMS, 2, Lilly, 2, MSD, 2, Novartis, 2, Pfizer, 2, UCB, 2; **B. Gudbjornsson**: Nordic-Pharma, 6, Novartis, 2, 6; **F. Iannone**: Abbvie, 2, 5, BMS, 2, 5, Janssen, 2, 5, Lilly, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5; **P. Hellamand**: Novartis, 12, Research grant to employer (not to me); **T. Kvien**: AbbVie/Abbott, 1, 2, 6, Bristol-Myers Squibb(BMS), 5, Galapagos, 2, 5, Gilead, 2, grunenthal, 6, Janssen, 2, 6, Novartis, 5, Pfizer, 2, 5, sandoz, 2, 6, UCB, 2, 5, 6; **A. Rodrigues**: AbbVie/Abbott, 5, Amgen, 5, 6, Novartis, 5, Pfizer, 5; **C. Codreanu**: AbbVie/Abbott, 2, 6,

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Abstract Number: 0162

Assessing Reproductive Health Counseling and Provider Attitudes in Rheumatology Post *Roe v. Wade* in Houston, Texas

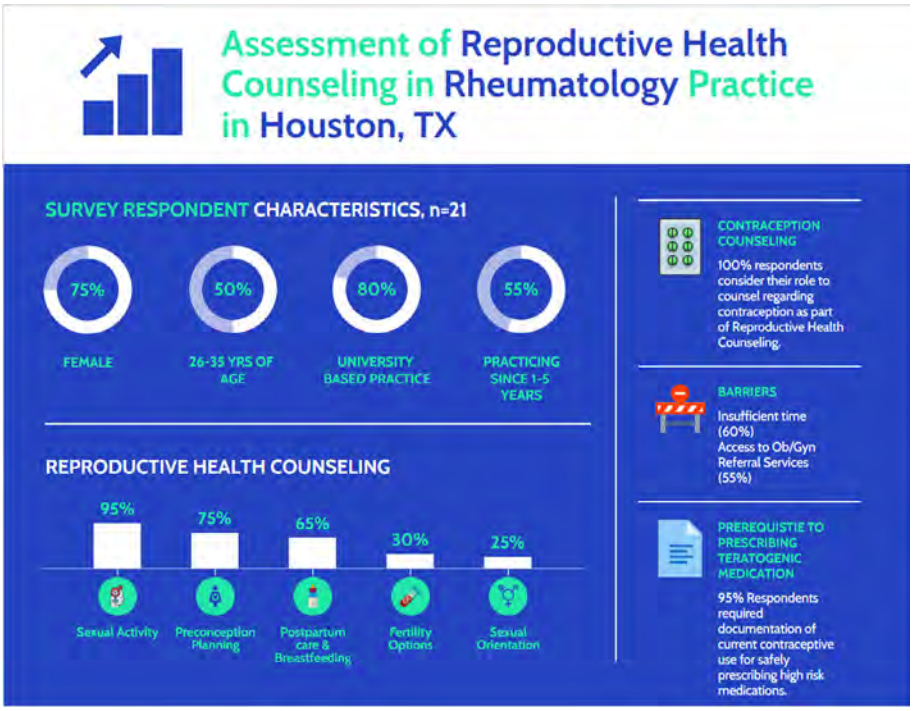
Ruhani Desai and Meera Subash, University of Texas Health Science Center at Houston, Houston, TX

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Health Services Research Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Many rheumatic diseases disproportionately affect women of childbearing age. Advances in the field of rheumatology have led to an increase in targeted treatment agents. Many of these agents have known adverse effects on pregnancy and the developing fetus. At this crossroads of rheumatology and reproductive health, outcomes can be improved by proper planning and education. Guidelines for contraception use based on disease states are available; however, very few studies have evaluated the current rates of contraception counseling and family planning services made available to patients receiving rheumatological care. There are multiple barriers to health care delivery, and with the change in the recent legislature affecting access to abortion services, we hypothesize that more barriers may have been added. We aim to describe current practices for reproductive health counseling in practicing rheumatologists in academic affiliated institutions and describe the barriers to providing such care through an electronic survey.

Methods: A cross-sectional survey designed in REDcap was sent to rheumatologists in the city of Houston associated with academic institutions. The survey inquired about physician demographics, practice characteristics, knowledge and beliefs regarding reproductive health counseling and physician-reported barriers to providing reproductive health. The information from the survey was extracted as de-identified data and analyzed using REDcap.

Results: 59 participants were approached via e-survey. Of the 21 survey responders (35.6%), most were between 26-45 years of age, female physicians in university-based practice. The providers reported they see on an average >30 patients in a week with 25 to 50% these patients being female of reproductive age group. All providers reported it is their role to ask about sexual activity and contraception use. About 60% of physicians reported counseling regarding postpartum and breastfeeding as a part of reproductive health counseling. Only one third (28.6%) considered counseling regarding fertility as part of their role in reproductive health counseling. Most providers (90.5%) reported documentation of current contraceptive use as a requirement before initiation of teratogenic medication - with the same requirement for refill. The common barrier to provide reproductive health counseling was time (61.9%) and the second most common barrier reported was access to OBGYN services (57.1%). Most providers (42.9%) reported medico-legal implications as a barrier since the ruling, while 38.1% noted no changes in barriers since the ruling.



Conclusion: The survey suggests Houston rheumatologists consider reproductive health counseling as an integral part of their role with focus on pregnancy planning, breastfeeding, and postpartum care. Fertility counseling is not considered part of routine counseling. 38.1% respondents noted lack of change in practice or barriers following the legal ruling, which indicates there are existing barriers in the system, which can be optimized to provide comprehensive reproductive counseling. A follow up interview with select survey respondents is planned to define these barriers, beliefs and practices.

Self Reported Survey Results for Reproductive Health Counseling in Rheumatology Practice in Houston, TX

Disclosure: R. Desai: None; **M. Subash**: None.

Abstract Number: 0163

Uncovering Discrepancies: Analysis of Glucocorticoid Exposure Among Patients with Rheumatoid Arthritis in Electronic Health Record Data versus Medicare Claims

Jing Li[1], Julia Kay[1], Sharon Abada[1], Andriko Palmowski[2], Rachael Stovall[1], Jinoos Yazdany[3] and **Gabriela Schmajuk**[4], [1]University of California San Francisco, San Francisco, CA, [2]Charité - Universitätsmedizin Berlin, Berlin, Germany, [3]University of California, General Department of Medicine, Division of Rheumatology, San Francisco, CA, [4]UCSF / SFVA, San Francisco, CA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Health Services Research Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Understanding glucocorticoid (GC) exposure is critical for observational analyses in rheumatology. However, obtaining an accurate measure of GC exposure, including dosage and duration, has been challenging, particularly using electronic health record (EHR) data. In this study, we compared GC medication data derived from the EHRs of 234 rheumatology practices to corresponding Medicare claims for patients with rheumatoid arthritis (RA).

Methods: Data derived from RISE, a national, EHR-enabled registry that passively collects data on all patients seen by participating rheumatology practices, and linked Medicare Part D claims. We included patients ≥ 18 years with RA (≥ 2 visits with RA codes ≥ 30 days apart) with oral GCs documented in both the EHR and Medicare during 2018. We extracted GC records from 3 sources: EHR e-prescriptions (orders), EHR medication lists ("med list"), and Medicare claims. GCs were identified using NDC codes and brand and generic names; all doses were converted to prednisone equivalents. EHR records with missing stop dates (37% of e-prescription records and 86% of med list records) were assumed to last 90 days. GC records from each data source were aggregated to the patient level and daily dose was calculated as the sum of all GC records active on a given day. Daily doses were averaged over 365 days to calculate an average daily dose during 2018.

Table. Characteristics of patients with RA with oral glucocorticoids documented in EHR data and Medicare claims in 2018.

	E-prescription Analysis*	Medication List Analysis**
N	12,537	3,177
Age, mean (SD)	72.3 (8.0)	71.0 (9.3)
Female, N (%)	9521 (75.9)	2454 (77.2)
RISE practice type, N (%)		
Single Specialty Group Practice	10197 (81.3)	1453 (45.7)
Multi-Specialty Group Practice	1326 (10.6)	965 (30.4)
Solo Practitioner	982 (7.8)	737 (23.2)
Health System	32 (0.3)	22 (0.7)
EHR vendor, N (%)		
Nextgen	7653 (61.0)	279 (8.8)
eClinicalWorks	3327 (26.5)	368 (11.6)
GE Centricity	741 (5.9)	163 (5.1)
Allscripts	40 (0.3)	687 (21.6)
eMDs	18 (0.1)	1135 (35.7)
Other EHR	758 (6)	545 (17.2)
Average daily GC dose during 2018 calculated from Medicare claims, median (IQR)	2.5 (0.9-4.8)¶	3.0 (1.2-5.2)¶
Average daily GC dose during 2018 in RISE, median (IQR)	3.1 (1.4-5.1)†	2.5 (1.2-4.9)‡

* The E-prescription analysis included any patients from practices with e-prescriptions available and compared this data to Medicare claims from RISE prescribers only, since e-prescription orders would all come from RISE prescribers.

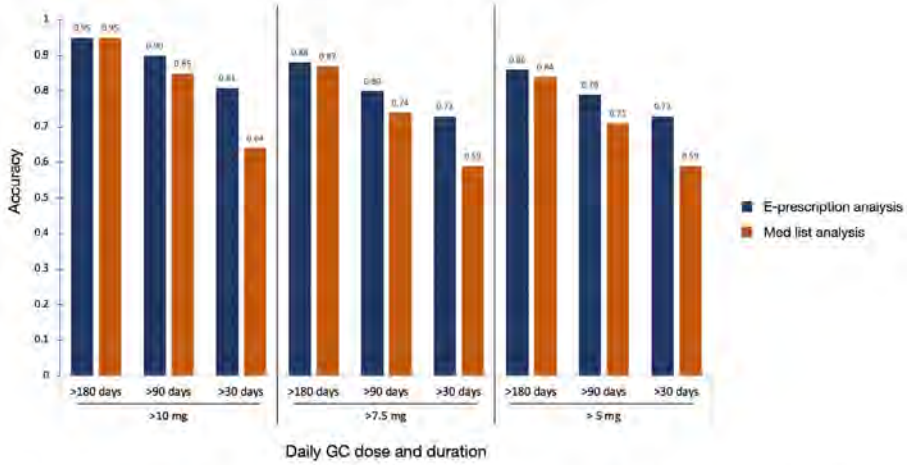
**The Medication List analysis included patients from practices without e-prescriptions available and compared this data to Medicare claims from any prescriber, since patients would report medications taken from any prescriber.

¶ For Medicare Part D records, GC dose was calculated from pill size, quantity dispensed, and days' supply based on established algorithms.

† For EHR e-prescription records, quantity and days' supply were not available, so we used regular expressions to standardize the most common patterns for medication instructions ("sig") (representing ≥ 100 records; 68.7%). Records with sigs that were complex (e.g., tapers; 10.5%), vague ("as directed;" 9.1%), or existed in < 100 records (11.7%) were assumed to be taken once per day.

‡ For EHR medication list records, quantity, and days' supply were not available, nor were medication instructions; therefore all records were assumed to be taken once per day.

Figure. Accuracy of EHR records versus Medicare Part D claims for classifying patients as users (yes/no) of glucocorticoids at different daily doses and durations (EHR e-prescription analysis - blue bars; EHR medication list analysis - orange bars).



Disclaimer: This data was supported by the ACR's RISE Registry. However, the views expressed represent those of the authors, not necessarily those of the ACR.

We compared GC exposure calculated from 1. EHR e-prescriptions with Medicare claims (from RISE prescribers only); and among those patients for whom e-prescription data was not available, 2. EHR med lists with Medicare claims (from any prescriber). We calculated the accuracy of EHR records vs. Medicare claims for classifying patients as users (yes/no) of GC at different daily doses and durations.

Results: We included 12,537 patients with RA in the e-prescription analysis and 3,177 in the med list analysis (Table). Both groups had similar demographics (>75% female, mean (SD) age 72.3 (8.0) years) but most patients in the e-prescription analysis came from practices using NextGen, while the majority in the med list analysis came from practices using eMDs. Nearly all GC records were for prednisone (90%). In the e-prescription analysis, the median average daily GC dose was higher in EHR data compared to Medicare claims (median (IQR) 3.1 mg (1.4-5.1) vs. 2.5 mg (0.9-4.8)); on the contrary, median average daily dose was lower in EHR med lists compared to Medicare claims (median 2.5 mg (1.2-4.9) vs. 3.0 (1.2-5.2)). In both analyses, 83-88% patients had an EHR average daily GC dose within 5 mg of their Medicare dose; 30-40% were within 1 mg. Accuracy for classifying patients as GC users of particular doses and durations based on EHR data varied from 0.59 to 0.95 but was highest for patients receiving >10 mg prednisone daily for durations > 180 days (Figure).

Conclusion: In this national study, we found discrepancies between GC exposure derived from two sources of EHR data (e-prescription orders and medication lists) and Medicare Part D claims among patients with RA. Caution should be exercised when using EHR data to derive GC exposure over short periods but may be suitable for ascertaining GC exposure at higher daily doses taken for longer periods of time.

Disclosure: J. Li: None; **J. Kay**: Pfizer, 12, Own Stock; **S. Abada**: None; **A. Palmowski**: None; **R. Stovall**: None; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, Gilead, 5, Pfizer, 2; **G. Schmajuk**: None.

Abstract Number: 0164

Development and Validation of a Virtual Musculoskeletal Examination Method for Disease Activity Assessment in Rheumatoid Arthritis Patients

Sandeep Yadav, Asna Shaikh and C Balakrishnan, P D Hinduja national Hospital and medical Research centre, Mumbai, India

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Health Services Research Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The rapid adaptation of telemedicine in rheumatology practice brings standardization, reliability and legality challenges. Therefore, it is necessary to develop dependable virtual instruments for the accurate assessment of patients, which are comparable to the standard face-to-face examination. We have developed a virtual musculoskeletal examination, and this communication highlights its usefulness in assessing the disease activity in patients with rheumatoid arthritis (RA).

Methods: Thirty follow-up patients with RA (29 women) attending the rheumatology OPD clinic of a tertiary care hospital were recruited over a month. Disease activity was independently assessed using a novel virtual MSK (Virtual DAS 28 ESR/ CDAI) examination method (Table 1 and 2) and a standard in-person method (DAS 28 ESR/CDAI) by two different examiners blinded to each other's results. (Table 3)To determine test-retest reliability, we used intra-class correlation coefficients, and for the degree of agreement, we used Bland-Altman plots

Results: The reliability of assessments between the two examiners, as judged by inter-class correlation, was excellent for Diease Activity Score of RA (DAS–28 ESR) and Clinical Disease Activity Index (CDAI) (ICC > 0.9), good for the total tender joint count and swollen joint count (ICC 0.75-0.91), and moderate for global physician assessment (0.50-0.75). (Table 3) Thus, the observations of two examiners to calculate disease activity using virtual and standard methods are reliable and reproducible across all measurements, based on an excellent intraclass correlation coefficient. The level of agreement tested using a Bland Altman plot showed that the mean absolute difference (bias) between Virtual DAS ESR 28 and DAS 28 ESR was 0.084 (% 95 CI -0.05782 to 0.2265) with p = 0.2348, which was well below the minimal clinically important difference (MCID) for DAS-ESR, which was 1.2, suggesting an acceptable level of agreement. Similarly, the mean absolute difference (bias) between the Clinical disease activity index (CDAI) and Virtual CDAI was 0.9667 (% 95 CI-0.1705 to 2.1039) with P=0.0927, which was well below the MCID for CDAI, which is 12, suggesting an acceptable level of agreement. There was a significant difference in the level of agreement concerning the total number of swollen joints counted. Thus ,there was an acceptable level of agreement between the two examiners in calculating disease activity virtually and in person using the novel MSK examination method.

Conclusion: Our novel virtual MSK test is consistent and comparable to the in-person assessment of follow-up patients in rheumatoid arthritis with regard to the measurement of disease activity. Although there was some variability in the number of swollen joints, the new approach showed good reliability and an acceptable level of agreement. It is pragmatic, and we recommend its further refinement for routine use in tele-consultancy.

Table 1. Showing method of virtual musculoskeletal examination (MSK) at the Proximal interphalangeal joint (PIP), metacarpophalangeal joint (MCP) and Wrist joint .

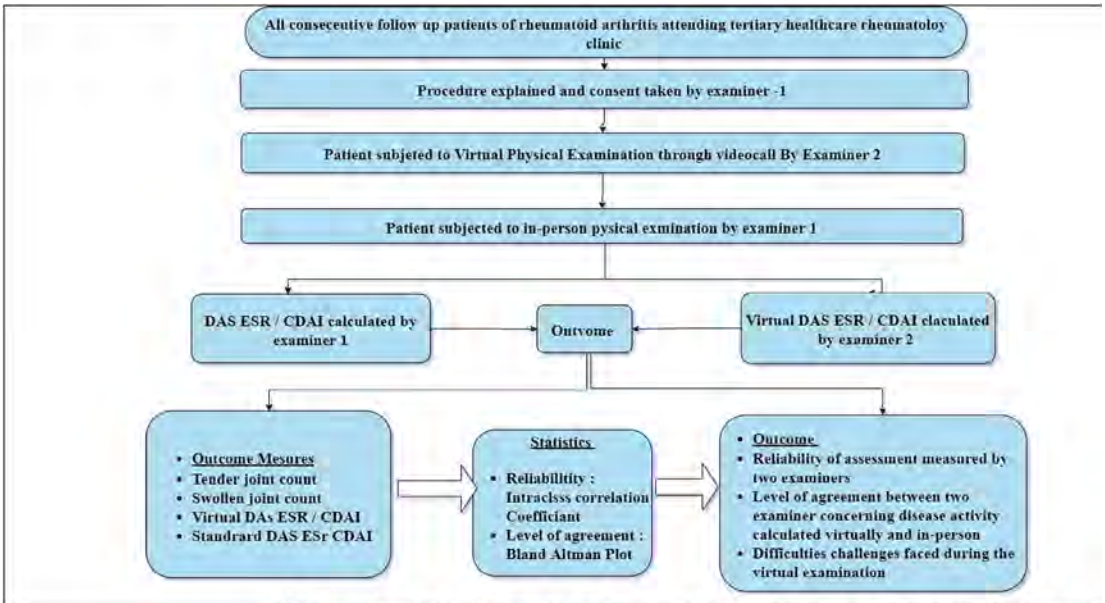
Over aching principle of examination: Common questions about all six joint sets are to be asked while examining the joints.1) All joint manoeuvres are to be mirrored by the examiner and explained simultaneously.2)Which joint is painful? Does the painful joint also stiff in the morning? 3)Which joint is swollen? Does the swollen joint also stiff in the morning? Has the swelling/deformity been new or persisted for over three months?

Method of examination	Defining Tender joint	Defining Swollen Joint
	PIP joint	
LOOK- Virtual inspection of PIP 1 foot from the front camera. **POINT**- Patients point towards the painful PIP. **MOVE**: Patient makes Half claw, and ROM of the joint is assessed. **Press:** Ask the patient to now face his palm in front and press the PIP with another hand, checking for tenderness in the PIP (crack your fingers)	The patient pointing toward the painful PIP Pointed PIP is associated with early morning stiffness > 15 minutes. Associated with pain during ROM and by pressing it with other hands PIP having all three above characters should be considered tender joint	Joints appear swollen on inspection. Pointed PIP is associated with early morning stiffness > 15 minutes. Associated with recent onset (< 3 months).PIP having all three above characters should be considered Swollen
		
	MCP joint	
LOOK: Ask the patient to make a full fist and point both fists towards the screen at 1 foot from the screen. Look for swelling /absent gutter between MCP, deformity, and decreased ROM. **Point**: Patient points toward the painful MCP **Move**: Patient makes full Fist. ROM of a joint is assessedPress: Press the Fist of one hand with the others	The patient pointing toward the painful MCP Pointed MCP is associated with early morning stiffness > 15 minutes. Associated with pain during ROM and aggravated by pressing it on other hands MCP having all three above characters should consider tender joint.	Joints appear swollen on inspection Pointed MCP is associated with early morning stiffness > 15 minutes. Associated with a recent-onset (< 3 months) decrease in ROM MCP having all three above characteristics should consider swollen
		
	Wrist	
LOOK- Ask the patient to face the back of the wrist towards the screen 1 foot from the screen. Look for swelling, an asymmetry between bilateral wrists and deformity. **POINT:** Ask the patient to point to a painful wrist. **MOVE**: Ask the patient to Form a prayer or "Namaste" sign keeping your elbows as high as possible/with support on a flat surface, and then make an inverted prayer or "inverted Namaste" with the back of your hand touching each other. Look for asymmetry /deformity / bony prominences/decreased ROM.	The patient is pointing toward the painful wrist. The pointed wrist is associated with early morning stiffness > 15 minutes. Associated with pain during ROM and aggravated by namaste sign. A wrist having all three above characteristics should consider a tender joint.	Wrist joints appear swollen on inspection. The pointed wrist is associated with early morning stiffness > 15 minutes. Associated with recent-onset (< 3 months) decrease in ROM on Namaste sign. A wrist with all three above characteristics should be considered a swollen joint.
		

Table 2. Showing method of virtual musculoskeletal examination (MSK) at the elbow joint ,Shoulder and Knee joint .

ELBOW JOINT		
LOOK- patient seated 3 feet from the screen was asked to extend his elbow completely and look for asymmetry, visible swelling, and bony prominences **POINT** - Ask the patient to point to the side of the painful elbow and the site of the pain. **MOVE**- Ask the patient to sit laterally 3 feet from the screen and ask to flex and extend the elbows to check for the ROM.**Press:** Ask the patient to press the flexed elbow towards the shoulder and look for pain and ROM.	The patient is pointing toward the painful elbow. The pointed elbow is associated with early morning stiffness > 15 minutes. Associated with pain during ROM and aggravated by pressing towards the elbow by another hand. An elbow having all three above characteristics should consider a tender joint.	The elbow appears joints appear swollen on inspection. The pointed elbow is associated with early morning stiffness > 15 minutes. Associated with recent-onset (< 3 months) decreased ROM and unable to flex completely with other hands An elbow having all three above characteristics should be considered a swollen joint.
		
Shoulder joints		
Screening of the shoulder through the following manoeuvres to check its complete ROM Look for any restriction on ROM. If the whole manoeuvre is performed with pain shoulder joint is likely normal. The shoulder joint is exposed for examination if any pain or restriction is found. **Look** – For visible swelling over the shoulder. **Point**- To the area of maximum tenderness. **Move:** Ask the patient to stand 3 feet from the screen and ask them to mirror the shoulder movement as performed. **Press**: Ask the patient to put the painful shoulder around the neck and over the opposite shoulder and hyper-adduct it with other hands to look for aggravation of pain.	The patient points toward the painful shoulder. The pointed elbow is associated with early morning stiffness > 15 minutes. Associated with pain during ROM and aggravated by pressing towards the shoulder by another hand. A shoulder having all three above characteristics should be considered a tender joint.	The shoulder appears joints appear swollen on inspection The pointed shoulder is associated with early morning stiffness > 15 minutes. Associated with recent-onset (< 3 months) decreased ROM and unable to flex completely with other hands A shoulder with all three above characteristics should be considered a swollen joint.
		
Knee		
Look- Ask the patient to move back from the camera, expose the knee, and point the camera towards the knee in a standing position. Check bilateral for asymmetry, muscle wasting, fixed flexion, swelling or deformity "bow-legged" (varus) or "knock-kneed" (valgus). **Point**- Ask the patient to point towards the painful knee and, if possible, to point towards one medial or lateral site or the whole knee. **Move:** Ask the patient to do one squat and then try to sit on the floor, cross legs, and get up. Look for ROM of the knee joint. **Press:** Ask the patient to put one ankle over the opposite thigh and try to fold it towards the body by grabbing at the ankle.	Patient pointing toward the painful knee The pointed knee is associated with early morning stiffness > 15 minutes. Associated with pain during squatting and aggravated during ankle grab and folding A knee having all three above characteristics should be considered a tender joint. Patient points toward the pain in the knee joint	The knee appears joints appear swollen on inspection The pointed knee is associated with early morning stiffness > 15 minutes. Associated with recent-onset (< 3 months) during squatting, unable to flex completely with other hands by ankle grab The knee joint with all three above characteristics should be considered swollen joint.
		

Table 3.: Showing methodology and mean arithmetic differences across individual joint counts derived from Bland Altman Plot.



		Examiner 1 (In person) Mean ± SD	Examiner 2 (Virtual) Mean ± SD	Bland-Altman Arithmetic difference (95 % Confidence interval)	P value
DAS -28 ESR		4.25±1.16	4.16 ± 1.1	0.08432 (-0.05782 to 0.2265)	0.2348
CDAI		12.7 ± 7.60	11.63 ± 7.0	0.9667 (-0.1705 to 2.1039)	0.0927
Tender joint count		3.20 ± 3.1	3.16 ± 2.7	0 (-0.6202 to 0.6202)	1.0
Swollen joint count		2.53 ± 2.60	1.60 ± 1.79	0.871 (0.3208 to 1.4211)	0.003
Physician Global assessment		3.27 ± 1.7	3.17 ± 1.6	0.06667 (-0.4698 to 0.6032)	0.8012
PIP (0-10)	TJC	0.73 ± 1.22	0.80 ± 1.12	-0.0645 (-0.3313 to 0.2023)	0.625
	SJC	0.80 ± 1.24	0.63 ± 1.06	0.1613 (-0.05252 to 0.3751)	0.1339
MCP (0-10)	TJC	0.66 ± 1.49	0.53 ± 1.13	0.129 (-0.1345 to 0.3926)	0.3253
	SJC	0.90 ± 1.58	0.46 ± 1.04	0.4194 (- 0.1388 to 0.6999)	0.0047
Wrist (0-2)	TJC	0.63 ± 0.71	0.60 ± 0.77	0.03226 (-0.2089 to 0.2734)	0.7866
	SJC	0.33 ± 0.60	0.27 ± 0.52	0.065 (-0.06724 to 0.1963)	0.3253
Elbow (0-2)	TJC	0.27 ± 0.52	0.33 ± 0.60	-0.0645 (-0.2524 to 0.1234)	0.4885
	SJC	0.13 ± 0.34	0.06 ± 0.25	0.06 (-0.02709 to 0.1561)	0.16
Shoulder (0-2)	TJC	0.33 ± 0.66	0.40±0.67	-0.0645 (-0.2524 to 0.1234)	0.4885
	SJC	0.0	0.0		
Knees (0-2)	TJC	0.57 ± 0.67	0.43 ± 0.62	0.09677 (-0.1009 to 0.2944)	0.3253
	SJC	0.36 ± 0.55	0.16 ± 0.46	0.1613 (-0.03040 to 0.3530)	0.096
H0: There is no significant difference between the observations/scores by the two methods.					

Disclosure: S. Yadav: None; **A. Shaikh**: None; **C. Balakrishnan**: None.

Abstract Number: 0165

Hypothyroidism Is Associated with Worse Clinical and Utilization Outcomes After Primary Total Knee Arthroplasty

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Health Services Research Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Limited information is available regarding how medical comorbidities affect the outcomes of total knee arthroplasty (TKA). The association of medical comorbidities with post-TKA outcomes may vary by the primary underlying cause leading to TKA. We evaluated the association of hypothyroidism with TKA outcomes, overall and by the primary diagnoses categorized as knee osteoarthritis (OA), avascular necrosis (AVN), fractures, and inflammatory arthritis including rheumatoid arthritis (RA), or spondylarthritis (SpA) (ankylosing spondylitis (AS), psoriatic arthritis (PsA)).

Methods: We identified all patients in the 2019 national inpatient sample (NIS) that received primary TKA and stratified them based on primary diagnoses. The population was stratified into knee OA (N=529,621), traumatic arthritis (N=7,690) and inflammatory arthritis (RA, AS, or PsA; N=1,175) and other diagnoses. Hypothyroidism was determined using secondary diagnoses. We assessed clinical and healthcare utilization outcomes as endpoints using multivariable-adjusted regression analyses adjusted for race, age, sex, hospital bed size, census region and teaching status.

Results: Total cohort population was 563,381 Mean age was 67.18 years, 61.6% were female, and mean length of stay was 2.12 days.

Overall, hypothyroidism was associated with increased adjusted odds of non-routine discharge, blood transfusion, acute renal failure (ARF), and anemia ($p \leq 0.037$ each). In the knee OA cohort, hypothyroidism was associated with increased adjusted odds of non-routine discharge, ARF, and anemia ($p \leq 0.025$ each). Hypothyroidism was not associated with any complications or adverse patient outcomes in the traumatic or inflammatory arthritis cohorts.

Conclusion: Hypothyroidism impacts TKA outcomes, particularly in patients with knee OA. These findings hold crucial implications for patient care and guidance for orthopedic surgeons, emphasizing the necessity for thorough preoperative evaluations and care plans. By better understanding these risks, we can enhance patient outcomes and streamline surgical protocols.

Table-1: Baseline Hospital and Patient Characteristics with hypothyroidism who underwent primary total knee Arthroplasty (TKA) in the National Inpatient Sample (2019, N=532736)

Variable	Non-Hypothyroidism (N=496735; 83.9%)	Hypothyroidism (N=95155; 16.1%)	Overall (N=591891)	p value
Age (mean ± SD years)	66.81 ± 0.057	69.03 ± 0.077	67.18 ± 0.055	<.001
Length of Stay (mean ± SD days)	2.11 ± 0.027	2.25 ± 0.035	65990.90 ± 944.043	<.001
Total Charges (mean ± SD dollars)	65930.54 ± 948.854	66288.43 ± 998.225	2.12 ± 0.027	0.4
In-hospital mortality	130 (0.0%)	40 (0.0%)	170 (0.0%)	<.001
Underlying Condition (N,%)				<.001
Osteoarthritis	439925 (93.9%)	89695 (94.5%)	529621 (94.0%)	
Traumatic Arthritis	6930 (1.5%)	760 (0.8%)	7690 (1.4%)	
Inflammatory arthritis[1]	960 (0.2%)	215 (0.2%)	1175 (0.2%)	
Other	20605 (4.4%)	4290 (4.5%)	24895 (4.4%)	
Sex (N,%)				<.001
Male	198730 (42.4%)	17875 (18.8%)	216605 (38.4%)	
Female	269660 (57.6%)	77085 (81.2%)	346745 (61.6%)	
Number of Obese Patients	155175 (33.1%)	33430 (35.2%)	188605 (33.5%)	<.001
Number of Morbidly Obese Patients	47570 (10.2%)	11030 (11.6%)	58600 (10.4%)	<.001
Race (N,%)				<.001
White	365285 (80.1%)	79740 (86.5%)	445026 (81.2%)	
Black	41795 (9.2%)	3760 (4.1%)	45555 (8.3%)	
Hispanic	28955 (6.3%)	4935 (5.4%)	33890 (6.2%)	
Asian or Pacific Islander	7500 (1.6%)	1295 (1.4%)	8795 (1.6%)	
Native American	2330 (0.5%)	440 (0.5%)	2770 (0.5%)	
Other	10195 (2.2%)	2015 (2.2%)	12210 (2.2%)	
Charlson Comorbidity (N,%)				<.001
0	261305 (55.8%)	47520 (50.0%)	308825 (54.8%)	
1	132635 (28.3%)	28695 (30.2%)	161330 (28.6%)	
2	41065 (8.8%)	10160 (10.7%)	51225 (9.1%)	
3	19035 (4.1%)	4650 (4.9%)	23685 (4.2%)	
4	6580 (1.4%)	1830 (1.9%)	8410 (1.5%)	
≥5	7800 (1.7%)	2105 (2.2%)	9905 (1.8%)	
Insurance Type (N,%)				<.001
Medicare	262420 (56.1%)	62550 (65.9%)	324970 (57.7%)	
Medicaid	20970 (4.5%)	2925 (3.1%)	23895 (4.2%)	
Private Insurance	163970 (35.0%)	26615 (28.1%)	190585 (33.9%)	
Self-Pay	2980 (0.6%)	610 (0.6%)	3590 (0.6%)	
No Charge	200 (0.0%)	25 (0.0%)	225 (0.0%)	
Other	17405 (3.7%)	2155 (2.3%)	19560 (3.5%)	
Patient Disposition (N,%)				<.001
Routine	191140 (40.8%)	34815 (36.7%)	225955 (40.1%)	
Transfer to Short-term Hospital	1030 (0.2%)	210 (0.2%)	1240 (0.2%)	
Transfer Other[2]	70120 (15.0%)	18255 (19.2%)	88375 (15.7%)	
Home Health Care (HHC)	205735 (43.9%)	41620 (43.8%)	247355 (43.9%)	
Against Medical Advice (AMA)	235 (0.1%)	20 (0.0%)	255 (0.0%)	
Died	130 (0.0%)	40 (0.0%)	170 (0.0%)	
Median Household Income for ZIP Code (N,%)				<.001
0-25th percentile	104650 (22.6%)	19835 (21.2%)	124485 (22.4%)	
26th-50th percentile (median)	119405 (25.8%)	24695 (26.4%)	144100 (25.9%)	
51st to 75th percentile	126615 (27.4%)	26110 (27.9%)	152725 (27.5%)	
76th to 100th percentile	111425 (24.1%)	23065 (24.6%)	134490 (24.2%)	
Census Division of Hospital (N,%)				<.001
New England	26185 (5.6%)	4660 (4.9%)	30845 (5.5%)	
Middle Atlantic	70281 (15.0%)	13565 (14.3%)	83846 (14.9%)	
East North Central	74675 (15.9%)	15960 (16.8%)	90636 (16.1%)	
West North Central	44739 (9.6%)	9090 (9.6%)	53829 (9.6%)	
South Atlantic	86955 (18.6%)	17515 (18.4%)	104470 (18.5%)	
East South Central	30210 (6.4%)	6290 (6.6%)	36500 (6.5%)	
West South Central	50575 (10.8%)	11090 (11.7%)	61665 (10.9%)	
Mountain	32290 (6.9%)	7455 (7.9%)	39745 (7.1%)	
Pacific	52510 (11.2%)	9335 (9.8%)	61845 (11.0%)	
Location/teaching status of hospital (N,%)				0.986
Rural	47130 (10.1%)	9595 (10.1%)	56725 (10.1%)	
Urban nonteaching	109516 (23.4%)	22155 (23.3%)	131671 (23.4%)	
Urban teaching	311775 (66.6%)	63210 (66.6%)	374985 (66.6%)	
Complications (Post-operative)[3]				
Need for blood transfusion	5225 (1.1%)	1440 (1.5%)	6665 (1.2%)	<.001
Prosthetic complications	1920 (0.4%)	530 (0.6%)	2450 (0.4%)	0.005
Post-procedural infection	375 (0.1%)	75 (0.1%)	450 (0.1%)	0.961
Complications (Cumulative)[4]				
Acute renal failure	8900 (1.9%)	2355 (2.5%)	11255 (2.0%)	<.001
Myocardial infarction	420 (0.1%)	95 (0.1%)	515 (0.1%)	0.671
Pulmonary embolism	850 (0.2%)	280 (0.3%)	1130 (0.2%)	<.001
Deep vein thrombosis	1640 (0.4%)	340 (0.4%)	1980 (0.4%)	0.868
Anemia	59960 (12.8%)	13935 (14.7%)	73895 (13.1%)	<.001
Pneumonia	790 (0.2%)	195 (0.2%)	985 (0.2%)	0.264

[1]Includes rheumatoid arthritis, spondylarthritis, ankylosing spondylitis and psoriatic arthritis

[2]Includes Skilled Nursing Facility (SNF), Intermediate Care Facility (ICF), Another Type of Facility

ICD-10 CM codes: Acute Renal Failure (N17.x), Myocardial Infarction (I21.x), Anemia (D62), Pneumonia (J18.9, J15.9, J22.x), Pulmonary Embolism (I26.x), Deep Venous Thrombosis (DVT; I82.x), Prosthetic Complication (T84.010A, T84.012A, T84.012A, T84.013A, T84.018A, T84.019A, T84.020A, T82.021A, T84.022A, T84.023A, T84.028A, T84.029A, T84.090A, T84.091A, T84.092A, T84.093A, T84.098A, T84.099A, M96.65, M96.661,M96.662, M96.669, M96.671, M96.672, M96.69, M97.02XA, M97.11X1, M97.12XA), Post-Procedural Infection (T84.50XA, T84.51XA, T84.52XA, T84.54XA, T84.59XA, T81.4)

ICD-10 PCS codes: Blood Transfusion (302*)

[3]Only initial encounter ICD-10 codes selected

[4]Complications may include pre-operative conditions

Table-2: Multivariable-adjusted association of Hypothyroidism with clinical outcomes of patients who underwent primary total knee arthroplasty (TKA), stratified by underlying diagnosis

	Osteoarthritis (N=529621)		Traumatic arthritis (N=7690)**		Inflammatory arthritis[1] (N=1175)***		Other (N=24895)		Total (N=563381)	
Variable	aOR (95% CI)	p	aOR (95% CI)	p	aOR (95% CI)	p	aOR (95% CI)	p	aOR (95% CI)	p
Length of Stay (> 2 days)	1.014 (0.972-1.058)	0.522	1.132 (0.729-1.758	0.581	1.861 (0.851-4.071)	0.12	1.261 (1.052-1.511)	0.012	1.027 (0.985-1.071)	0.216
Total Cost (Charges above median)	1.038 (0.995-1.082)	0.086	0.930 (0.632-1.369)	0.712	0.709 (0.354-1.417)	0.33	1.193 (0.983-1.448)	0.074	1.040 (0.998-1.084)	0.061
Mortality	0.882 (0.298-2.608)	0.82	*		*		1.065 (0.219-5.176)	0.938	1.088 (0.468-2.529)	0.846
Non-routine discharge	1.093 (1.049-1.139)	<0.001	0.984 (0.659-1.468)	0.936	1.260 (0.565-2.810)	0.572	0.911 (0.754-1.102)	0.338	1.086 (1.043-1.131)	<0.001
Complications (Post-operative)[3]										
Need for blood transfusion	1.168 (0.995-1.370)	0.057	0.849 (0.141-5.105)	0.858	0.845 (0.172-4.163)	0.836	1.130 (0.821-1.557)	0.453	1.161 (1.014-1.329)	0.03
Prosthetic complications	0.838 (0.551-1.276)	0.411	*		*		1.115 (0.825-1.507)	0.479	1.059 (0.842-1.331)	0.626
Post-procedural infection	0.998 (0.389-2.558)	0.996	*		*		1.079 (0.485-2.399)	0.852	1.131 (0.629-2.031)	0.681
Complications (Cumulative)[4]										
Acute renal failure	1.295 (1.148-1.460)	<0.001	1.482 (0.418-5.257)	0.543	2.317 (0.270-19.914)	0.444	1.310 (0.937-1.831)	0.114	1.303 (1.163-1.460)	<0.001
Myocardial infarction	0.809 (0.438-1.495)	0.499	*		*		0.759 (0.160-3.602)	0.728	0.805 (0.457-1.419)	0.453
Pulmonary embolism	1.371 (0.976-1.926)	0.069	*		*		1.342 (0.616-2.923)	0.459	1.349 (0.988-1.841)	0.06
Deep vein thrombosis	0.976 (0.732-1.303)	0.871	8.380. (0.328-214.363)	0.199	*		0.736 (0.295-1.836)	0.511	0.962 (0.729-1.269)	0.781
Anemia	1.062 (1.007-1.119)	0.025	0.936 (0.594-1.473)	0.775	1.503 (0.460-4.908)	0.5	0.954 (0.775-1.173)	0.654	1.055 (1.003-1.110)	0.037
Pneumonia	0.995 (0.661-1.496)	0.979	*		*		0.900 (0.337-2.398)	0.832	0.982 (0.677-1.425)	0.924

[1]includes rheumatoid arthritis, spondylarthritis, ankylosing spondylitis and psoriatic arthritis

*removed from multivariate regression due to missingness

**multivariate analysis did not control for race due to quasi-complete separation

**multivariate analysis did not control for hospital census division due to quasi-complete separation

ICD-10 CM codes: Acute Renal Failure (N17.x), Myocardial Infarction (I21.x), Anemia (D62), Pneumonia (J18.9, J15.9, J22.x), Pulmonary Embolism (I26.x), Deep Venous Thrombosis (DVT; I82.x), Prosthetic Complication (T84.010A, T84.012A, T84.012A, T84.013A, T84.018A, T84.019A, T84.020A, T82.021A, T84.022A, T84.023A, T84.028A, T84.029A, T84.090A, T84.091A, T84.092A, T84.093A, T84.098A, T84.099A, M96.65, M96.661,M96.662, M96.669, M96.671, M96.672, M96.69, M97.02XA, M97.11X1, M97.12XA), Post-Procedural Infection (T84.50XA, T84.51XA, T84.52XA, T84.54XA, T84.59XA, T81.4)
ICD-10 PCS codes: Blood Transfusion (302*)

[3]Only initial encounter ICD-10 codes selected

[4]Complications may include pre-operative conditions

Disclosure: S. Chandrupatla: None; **K. Rumalla**: None; **J. Singh**: Other, 2, 6, 11, 11, 12, Adaptimmune Therapeutics, GeoVax Labs, Pieris Pharmaceuticals, Enzolytics Inc., Seres Therapeutics, Tonix, Charlotte's Web, 12, Atai life sciences, kintara therapeutics, Intelligent Biosolutions, Acumen pharmaceutical, TPT Global Tech, Vaxart pharmaceuticals, Atyu biopharma, 12, speaker's bureau of Simply Speaking, other, 12, received institutional research support from Zimmer Biomet Holdings. JAS received food and beverage payments from Intuitive Surgical Inc./Philips Elec, Other, 12, Schipher, Crealta/Horizon, Medisys, Fidia, PK Med, Two labs Inc., Adept Field Solutions, Clinical Care options, Clearview healthcare partners, Putnam.

Abstract Number: 0166

Annual Economic Burden for Patients with Familial Hypophosphatemia in the United States

Zhiyi Li[1], Elizabeth Marchlewicz[2], Danae Black[2], Hana Schwartz[2], Yang Zhao[1] and Erik Imel[3], [1]Kyowa Kirin North America, Bedminster, NJ, [2]Merative, Cambridge, MA, [3]Indiana University School of Medicine, Indianapolis, IN

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Health Services Research Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Familial hypophosphatemia (FH) is most commonly due to phosphate regulating endopeptidase X-linked (*PHEX*) gene mutations resulting in renal phosphate wasting, which leads to rickets, osteomalacia and other musculoskeletal consequences. X-linked hypophosphatemia, the most common form of FH, may be treated with burosumab.

However, the healthcare utilization and economic burden of FH among burosumab-naïve patients has not been characterized in the United States (US). This study aimed to examine healthcare utilization and costs for burosumab-naïve patients with FH, compared with demographically matched controls without FH.

Methods: Using the Merative™ MarketScan® Commercial and Medicare US administrative claims databases, patients with ≥1 diagnosis code for FH (ICD10:E83.31) between 1/1/2018-12/31/2021, and continuous database enrollment for 12-months pre-and post-index were identified. The index date was defined as the date of the first FH diagnosis. FH patients were demographically matched 1:3 to non-FH control patients based on age group (0-11, 12-17, 18-29, 30-39, 40-40, 50-64, 65+), sex, geographic region, payer, and index year. Healthcare utilization and costs were assessed in the 12-month post-index period and adjusted to 2021 dollars using the medical care component of the Consumer Price Index. The Charlson Comorbidity index (CCI) score was reported in the 12-month pre-index period as a measure of baseline health status. Results were reported overall and stratified by age groups.

Results: Matched burosumab-naïve FH patients (n=570) and non-FH controls (n=1,710) were 57.0% female, 53.0% with an index year in 2018-2019, and with a mean (standard deviation [SD]) age of 47.2 (19.9) and 46.2 (18.3) years (10.4%, 76.2%, and 13.5% were < 18, 18-64, and 65+ years respectively). Baseline CCI score was significantly greater among FH patients than controls (1.9 [2.6] vs. 0.2 [0.9], $P< 0.001$). Annual all-cause healthcare utilization was greater among FH patients compared with controls: inpatient (IP) admissions (60.4% vs. 4.3%), emergency room (ER) visits (51.6% vs. 15.7%), and outpatient (OP) pharmacy (95.8% vs. 71.1%) (all $P< 0.001$). FH patients also had a higher mean number of IP admissions (1.2 [1.8] vs. 0.1 [0.3]), ER visits (1.3 [2.1] vs. 0.2 [0.6]), and OP pharmacy prescriptions (36.8 [32.1] vs. 8.3 [14.8]) (all $P< 0.001$). Annual mean total healthcare costs were significantly higher among FH patients than controls ($118,770 [$316,629] vs. $5,627 [$18,381]), driven by greater IP costs ($67,671 [$277,681] vs. $1,526 [$12,268]), OP costs ($35,347 [$86,914] vs. $3,154 [$11,026]), and OP pharmacy costs ($15,753 [$86,994] vs. $947 [$4,379]) (all $P< 0.001$). Similar trends were observed among age-stratified FH patients and non-FH controls.

Conclusion: FH patients incur substantially higher healthcare utilization, costs, and comorbidity burden compared with non-FH controls.

Disclosure: Z. Li: Kyowa Kirin North America, 3; **E. Marchlewicz**: Merative, 3; **D. Black**: Merative, 3; **H. Schwartz**: Merative, 3; **Y. Zhao**: Kyowa Kirin, 3; **E. Imel**: Kyowa Kirin, 2.

Abstract Number: 0167

Healthcare Resource Utilization Associated with Tumor-Induced Osteomalacia: Review of Patient Histories Prior to Entry in Clinical Trial UX023T-CL201

Suzanne Jan de Beur[1], Thomas Carpenter[2], Kathryn Dahir[3], Erik Imel[4], María Belén Zanchetta[5], Angela Williams[6], **Zhiyi Li**[7], Matthew Sharp[6] and Ben Johnson[6], [1]Johns Hopkins University School of Medicine, Baltimore, MD, [2]Yale School of Medicine, New Haven, CT, [3]Vanderbilt University Medical Center, Nashville, TN, [4]Indiana University School of Medicine, Indianapolis, IN, [5]Universidad del Salvador, Buenos Aires, Argentina, [6]Kyowa Kirin International, Marlow, United Kingdom, [7]Kyowa Kirin North America, Bedminster, NJ

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Health Services Research Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Tumor-induced osteomalacia (TIO) is an ultra-rare paraneoplastic disorder, characterized by renal phosphate wasting due to increased production of fibroblast growth factor 23 (FGF23). Chronic hypophosphatemia causes the accumulation of severe musculoskeletal morbidities, and delays in diagnosis are common, which can lead to considerable healthcare resource use (HCRU). The objective of this study is to estimate HCRU from histories of adults with TIO not curable by surgery, prior to enrollment in the UX023T-CL201 burosumab phase 2 trial.

Methods: Histories of the 14 TIO patients enrolled in UX023T-CL201 were assessed independently by two reviewers. Data related to clinical events directly associated with HCRU were extracted and categorized.

Results: Mean age of TIO subjects enrolled in the trial was 56.9 ± 10.3 years (range 33-68); 57% (8) were male. Mean time between first symptoms and TIO diagnosis was 4.2 ± 4.1 years (range 0.1-13.2); mean time since diagnosis was 13.7 ± 13.0 years (range 0.7-35.8). Tumors were identified in 71% (10) patients, with surgical removal attempted in 64% (9).

Subjects underwent a mean of 11.1 ± 13.2 tumor investigations (range 1-46). The most frequent were magnetic resonance imaging (mean 4.9 ± 7.5 per patient; range 0-29), positron emission tomography/computed tomography (mean 1.9 ± 5.3; range 0-20), octreotide scan (mean 1.4 ± 2.3; range 0-7), and computed tomography (mean 1.3 ± 1.8; range 0-5).

All patients had a history of active vitamin D treatment, and 93% (13) had a history of oral phosphate treatment, with a mean duration of 10.4 ± 12.5 (range 0.3-35.0) and 10.5 ± 12.2 years (range 1.2-35.0), respectively.

History of fracture was reported in 93% (13) patients, with a mean of 5.4 ± 6.8 fractures per patient (range 0-28). The most frequently reported fracture locations were the ribs (mean 1.6 ± 3.3 fractures; range 0-13), foot/ankle (mean 1.0 ± 2.1; range 0-8), and femur (mean 0.7 ± 0.9; range 0-2).

Orthopedic procedures included spinal laminectomy in 21% (3) subjects, spinal corpectomy in 14% (2) subjects, and hip and knee arthroplasty in 14% (2) subjects each.

Conclusion: TIO is associated with substantial HCRU resulting from diagnosis, attempted tumor localization/removal, and disease management.

Disclosure: S. Jan de Beur: Amgen, 2, Ascendis Pharma, 2, Inozyme Pharma, 2, Kyowa Kirin, 2, Mereo BioPharma, 5, Ultragenyx, 2, 5; **T. Carpenter**: Kyowa Kirin, 2, Ultragenyx, 2, 5, Viridian Therapeutics, 2; **K. Dahir**: Alexion/AstraZeneca, 2, 5, Ultragenyx, 2, 5; **E. Imel**: Kyowa Kirin, 2, Ultragenyx, 2, 5; **M. Belén Zanchetta**: Adium, 2, Amgen, 2, Ultragenyx, 2; **A. Williams**: Kyowa Kirin International, 3; **Z. Li**: Kyowa Kirin North America, 3; **M. Sharp**: Kyowa Kirin International, 3; **B. Johnson**: Kyowa Kirin International, 3.

Abstract Number: 0168

What Are the Characteristics of a Cost-Effective Psoriatic Arthritis Biomarker Test? An Early Health Technology Assessment

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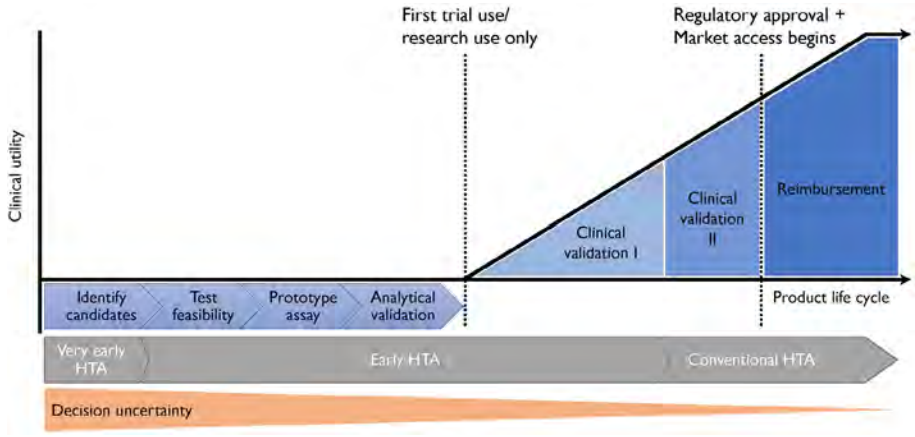
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Health Services Research Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

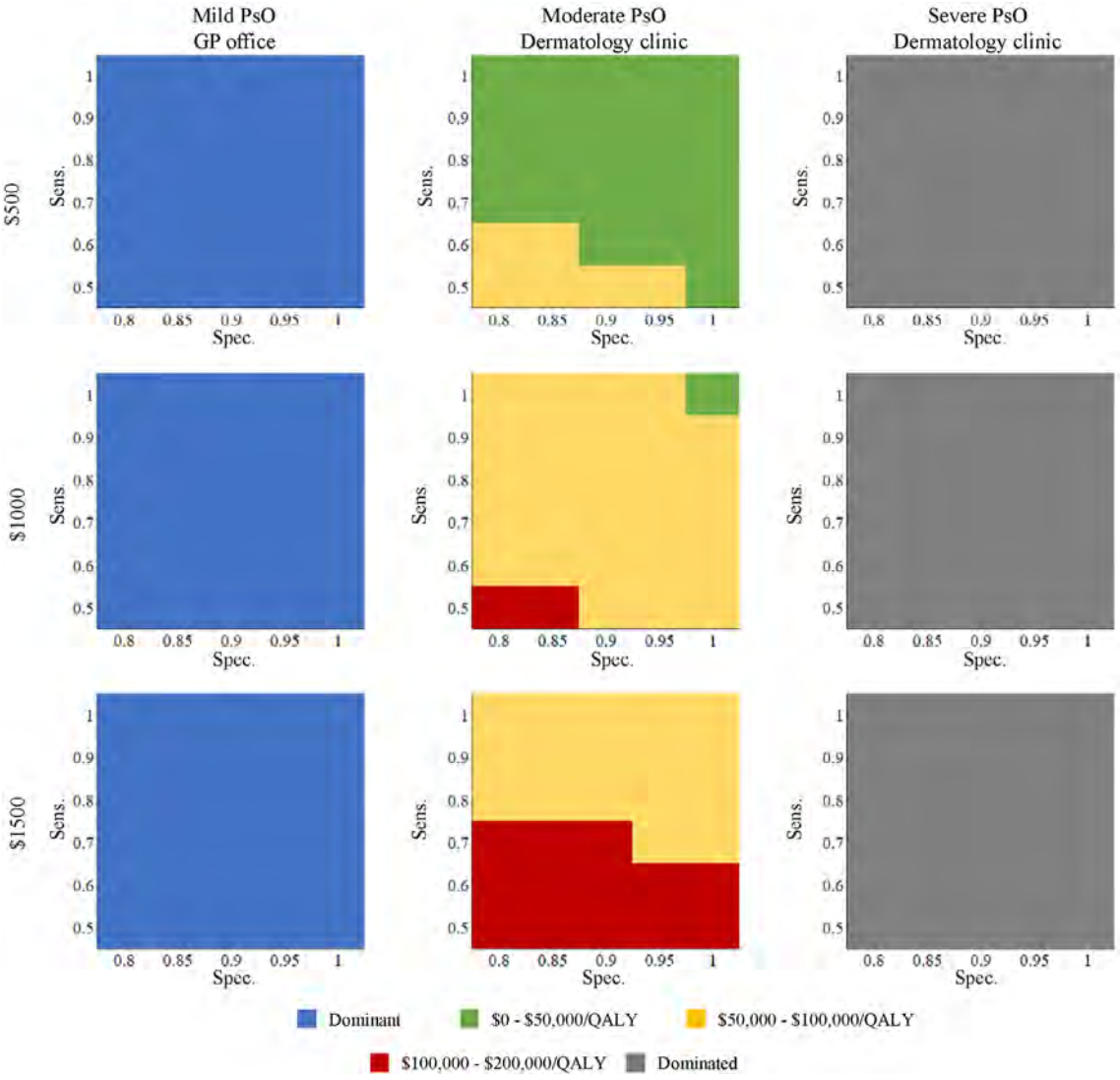
Background/Purpose: Initiating treatment in patients with psoriasis (PsO) who have unrecognized Psoriatic arthritis (PsA) may slow disease progression and improve long-term outcomes. Several candidate biomarkers are currently being studied to identify patients with unrecognized PsA. A biomarker test will ultimately only be successful if it is used – not just because of its clinical utility, but also its value which leads to reimbursement by payors. With product development process for biomarkers being expensive and subject to uncertainties, Early Health Technology Assessment (eHTA) can help indicate the commercial potential of a product to guide decisions in development decision-making. This study aimed to identify the required performance metrics that potential PsA biomarkers would need to achieve in order to be considered cost-effective.

Methods: We developed further an existing Markov model informed by literature and expert opinion. The model followed a cohort of patients aged 45-years with moderate PsO seen at a dermatology clinic and in which PsA was prevalent but unrecognized. In the biomarker arm, candidate biomarker tests were assumed to be administered at baseline, and patients who screened positive would accept combination conventional Disease-Modifying Antirheumatic Drug (cDMARD) and biologic treatment to slow disease progression. In the current practice are, patients with PsA were assumed to be clinically detected. Disease progression was modeled as linear changes in Health Assessment Questionnaire (HAQ) and PASI scores. We assumed a range of values for sensitivity, specificity, and biomarker price based on currently development progress. The time horizon was 40 years. Scenario analyses considered biomarker use in patients with mild and severe PsO separately.

Results: In the base case, using a biomarker test with a sensitivity of 70%, specificity of 80% and a price of $500 was associated with increased cost of $817.49 and additional 0.02 QALY per patient compared to no screening (ICER $47,566.29). Multi-way analyses showed that sensitivity could be as low as 60% and considered cost-effective if specificity was at least 88% and the biomarker was priced at $500. At a price of $1,000, only a near perfect test would be considered cost-effective. Model results were sensitive to the HAQ progression under combination treatment, cDMARD costs, and the



The product development stages of biomarker tests and timing of economic evaluation models assessing product viability. Clinical validation I and II reflect retrospective and prospective trial/study designs, respectively. Adapted from Ijzerman and Steuten (2011)



assumed start time of biologic DMARD treatment. Using a biomarker test in patients with mild PsO seen in primary care was a dominant strategy while screening in patients with severe PsO seen at a dermatology clinic was a dominated strategy (more benefit at less cost) compared to no screening.

Conclusion: This eHTA found that future PsA biomarker tests can be considered cost-effective if they can achieve modest performance, are used in a patient population with moderate PsO, and priced appropriately. Results support the continued product development of biomarker tests, and provide thresholds to guide decision-making on which biomarkers to pursue.

Two-way sensitivity analysis plots showing incremental cost-effectiveness ratios for combinations of sensitivity and specificity at three price points for a hypothetical biomarker test used in three patient populations. Abbreviations: GP = General practitioner, PsO = Psoriasis, Sens. = Sensitivity, Spec. = Specificity, QALY = Quality-adjusted life-years.

Disclosure: N. Bansback: None; **A. Tam**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, Gilead Sciences, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5; **V. Kulasingam**: None; **E. Spackman**: None; **V. Chandran**: AbbVie, 1, 5, 6, Amgen, 1, 5, 6, AstraZeneca, 3, Bristol-Myers Squibb (BMS), 1, 6, Eli Lilly, 1, 5, 6, Janssen, 1, 6, Novartis, 1, 1, 6, UCB, 1, 2.

Abstract Number: 0169

Added Value of Anti-HMGCR and Anti-SRP Antibodies in the Diagnosis of Immune Mediated Necrotizing Myopathy: An Outcome and Cost Comparison from the USA Perspective

Alejandro Figueroa-Lara[1], **Mary Ann Aure**[2] and Carmen Andalucia[1], [1]Werfen, San Diego, CA, [2]Werfen, Chula Vista, CA

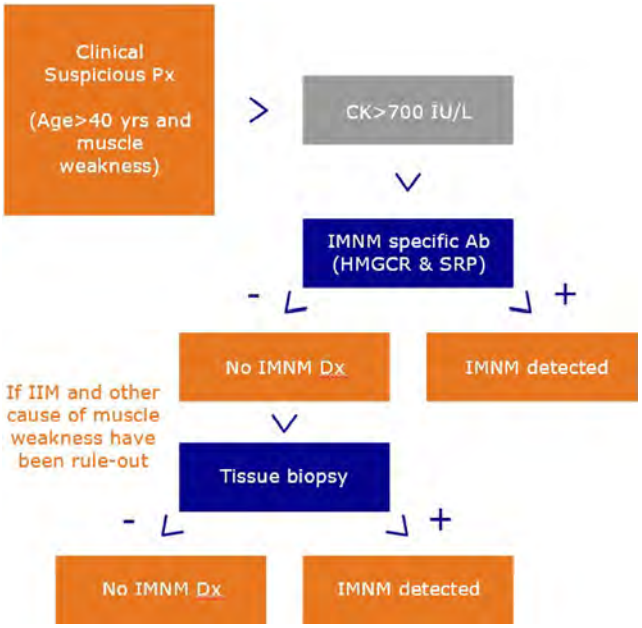
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Health Services Research Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Immune-mediated necrotizing myopathies (IMNM) is a subgroup of immune-mediated myopathies (IMM). The diagnosis of IMNM relied on the presence of proximal muscle weakness, high levels of creatinine kinase (CK) and myofiber necrosis assessment through muscle biopsy. In 2018, the European Neuromuscular Centre (ENMC) recommended running anti-HMGCR and anti-SRP tests on patients with suspected IMNM and if the results were negative, then patients will undergo muscle biopsy for a diagnostic confirmation. Clinical practice is moving gradually towards ENMC diagnosis criteria, but no economic analysis has been done yet. This study assessed the economic consequences of following the ENMC guidelines through a cost-effectiveness analysis of IMNM when specific biomarkers are added in the diagnostic algorithm.

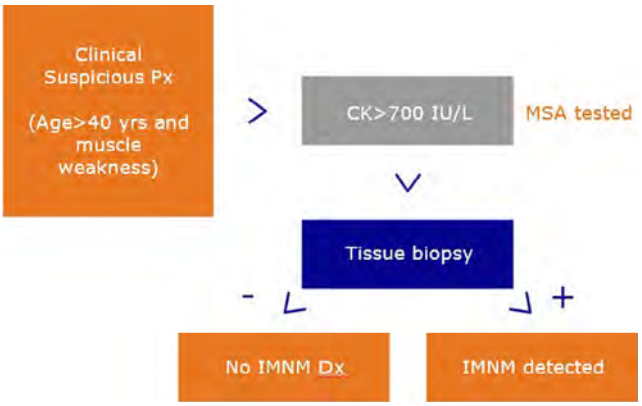
Methods: A decision tree model was designed to simulate a 1,000 hypothetical cohort of patients ≥40 years old with proximal muscle weakness and elevated creatine kinase levels under two interventions: 1) anti-HMGCR + anti-SRP + muscle biopsy (in seronegative cases); and 2) direct muscle biopsy (assumed as current clinical practice). Model parameters were derived from systematic literature review. The prevalence of IMNM was 8% based on a secondary care setting US study. Health related quality of life parameters were measured through utilities of phlebotomy and muscle biopsy. Direct medical costs were standardized to 2022 US dollars (therefore, this analysis did not include patient cost e.g., transport to the healthcare center, loss of productivity). Sensitivity analyses were conducted to assess changes in model output by varying several input data.

Results: The serological intervention was associated with a decreased of 79 muscle biopsies. Therefore, the cost per IMNM correctly diagnosed decreased by 83% ($2001). The cost per suspected IMNM patient decreased $160. Quality of life parameter is 8% higher in the serological intervention compared to the biopsy intervention. Results were sensitive to the IMNM prevalence, and the cost of biopsy and serological tests. In a clinical setting with a 1% IMNM prevalence, the cost-effective alternative is muscle biopsy, unless its cost is above $2,400 and the anti-HMGCR test cost is between $10-$15. At an 8% prevalence the serological intervention is more cost-effective unless the anti-HMGCR test cost is above $35 and cost of biopsy is above $600. At prevalence ≥19% the serological intervention is dominant at any anti-HMGCR test cost and muscle biopsy cost.

Conclusion: Our findings suggest that adding anti-HMGCR and anti-SRP test in the diagnostic algorithm of inflammatory idiopathic myopathies, as recommended by ENMC, results in less invasive diagnostic procedures a therefore having patients with a higher quality of life, at a lower cost. Confirmation of these economic results using real-world data is warranted.



Description of intervention 1



Description of intervention 2

Disclosure: A. Figueroa-Lara: Werfen, 3; **M. Aure**: Werfen Autoimmunity, 3, 3; **C. Andalucia**: Werfen S.A, 3.

Abstract Number: 0170

Gender Equity Amongst Rheumatology Professionals: Preliminary Findings of the Coalition for Health and Gender Equity E-survey (CHANGE Group)

Lisa Traboco[1], Pavel Ovseiko[2], Sarah Dyball[3], Tayyeba Khursheed[4], ALEJANDRA BABINI[5], Asgar Ali Kalla[6], Catherine Hill[7], Debashish Danda[8], Dzifa Dey[9], Elena Nikiphorou[10], Ghita Harifi[11], Ho SO[12], Humeira Badshah[13], Ihsane Hmamouchi[14], Joan Marie Von Feldt[15], Júlia Boechat Farani[16], Mariana Peixoto Guimarães[17], Kanon Jatuworapruk[18], Laura Andreoli[19], Nelly Ziade[20], PENELOPE PALOMINOS[21], Qian Wang[22], Ran Nakashima[23], Syed Haq[24], Wilson Bautista-Molano[25], Yoshiya Tanaka[26], Grace Wright[27], Vikas Agarwal[28], Laura Coates[29] and Latika Gupta[30], [1]University of the Philippines - Manila, St Luke's Medical Center - Bonifacio Global City, Paranaque, Manila, Philippines, [2]Radcliffe Department of Medicine, University of Oxford, Oxford, United Kingdom, [3]University of Manchester, Stockport, United Kingdom, [4]Pakistan institute of Medical Sciences, Islamabad, Pakistan, [5]Hospital Italiano Cordoba, Cordoba, Argentina, [6]Department of Medicine, University of Cape Town, Cape Town, South Africa, [7]The Queen Elizabeth Hospital, Woodville, Australia, [8]Christian Medical College & Hospital, Vellore, India, [9]University of Ghana Medical School, Rheumatology Unit Department of Medicine and Therapeutics, Korle bu Teaching Hospital, Accra, Ghana, [10]King's College London, London, United Kingdom, [11]HBMC, Dubai, United Arab Emirates, [12]The Chinese University of Hong Kong, Hong Kong, China, [13]Dr Humeira Badsha Medical Center, Dubai, United Arab Emirates, Dubai, United Arab Emirates, [14]Rheumatology Unit, Lalla Aicha Temara Hospital, Temara, Morocco, [15]University of Pennsylvania, Pennsylvania, PA, [16]Division of Rheumatology, Hospital Santa Casa de Misericórdia de Juiz de Fora, Juiz de Fora, Brazil, [17]Santa Casa de Misericórdia de Belo Horizonte, Belo Horizonte, MG, Brazil, [18]Thammasat University, Pathumthani, Thailand, [19]University of Brescia, Brescia, Italy, [20]Saint-Joseph University, Beirut, Lebanon, [21]Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil, [22]Department of Rheumatology and Clinical Immunology, Chinese Academy of Medical Sciences (CAMS), Peking Union Medical College Hospital, The Ministry of Education Key Laboratory, National Clinical Research Center for Dermatologic and Immunologic Diseases, Beijing, China, [23]Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, [24]BSM Medical University, Dhaka, Bangladesh, [25]University Hospital Fundación Santa Fe de Bogotá, Bogotá, Colombia, [26]University of Occupational and Environmental Health, Kitakyushu, Japan, [27]Grace C Wright MD PC, New York, NY, [28]Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow, India, [29]University of Oxford, Oxford, United Kingdom, [30]Royal Wolverhampton Trust, Wolverhampton/ University of Manchester, United Kingdom

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Health Services Research Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: There is growing attention to gender inequity within rheumatology with persistent challenges in achieving pay parity, career progression, & access to leadership roles. In order to promote rheumatology as a career & improve job satisfaction, we need to understand the current gender climate & develop potential solutions.

Methods: The CHANGE e-survey is a cross-sectional self-reported survey, adapted from the GEAR taskforce. It was available in 6 languages, & distributed to rheumatology organizations & social media, until April 2023. Descriptive statistics were used, & survey responses were compared by gender.

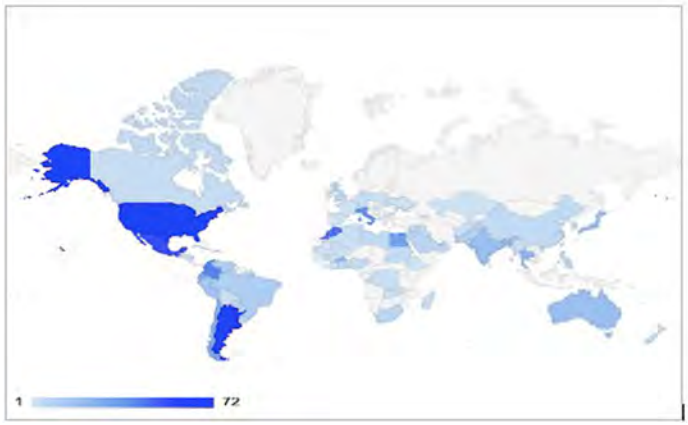
Results: Of 782 respondents, 682 had complete data & were analyzed. There were 205 male & 479 females (M:F 1:2.5), of age 35 (37-55) years from 83 countries (Figure 1) Two-thirds were rheumatologists (65%) the rest were allied healthcare professionals. Half were academics (59%) & 73% worked full time. 49% of respondents worked within the public sector & median career duration was 18 (11-29) years

Women were working in the public sector (52%) while men were distributed in the public (42%) & private sectors (43%). Both male and female respondents reported working >40 hours per week & having active leadership (55%) and academic roles (58%). Internationally, there was no difference between participation by men vs women, but at national & local levels there was more participation by women. (national: 514 vs 1043, p=0.04; local: 498 vs 962 , p=0.02) 30% of women, and 57% of men reported equal division of roles, whereas 50% of women reported these roles to be carried out predominately by women, compared with 30% of men. The most common family caretaking responsibilities were caring for children (F=57%, M=36%, p=0.41). 14% of women reported more than two responsibilities compared with 10% of men (p=0.001). 62% of women report taking previous parental leave compared with to 22% of men

Notably, both genders report a negative impact of having children on their career (10% vs. 2%); women were more likely to report a lack of career advancement opportunities due to family commitments (49 % vs. 35%). Bullying was reported by both genders, with 84% experiencing ongoing bullying. Perceived gender discrimination is described in figure 3; women reported feeling that they were 'less likely to receive a promotion' (p=0.04), to not be 'groomed for leadership positions' (p=0.05), receive less remuneration (p=0.012), assigned 'below expertise' tasks (p=0.05) & deal with an intimidating work environment (p=0.007). Women reported discrimination more common from older colleagues (p=0.03), nurses (p=0.04), patients (p=0.03) & administrators (p=0.019).

The most common recommendations were conference related, including no 'male-only panels' and family-friendly rheumatology conferences. Other suggestions include country specific support, writing & presentation skills training. 13% of women reported a desire to increase visibility of female role models

Conclusion: This e-survey is the first in rheumatology to highlight challenges faced by female rheumatologists globally. The results of the e-survey will be used to investigate the drivers of these inequities, as well as develop strategies and interventions to promote gender equity.



Method and Global Distribution

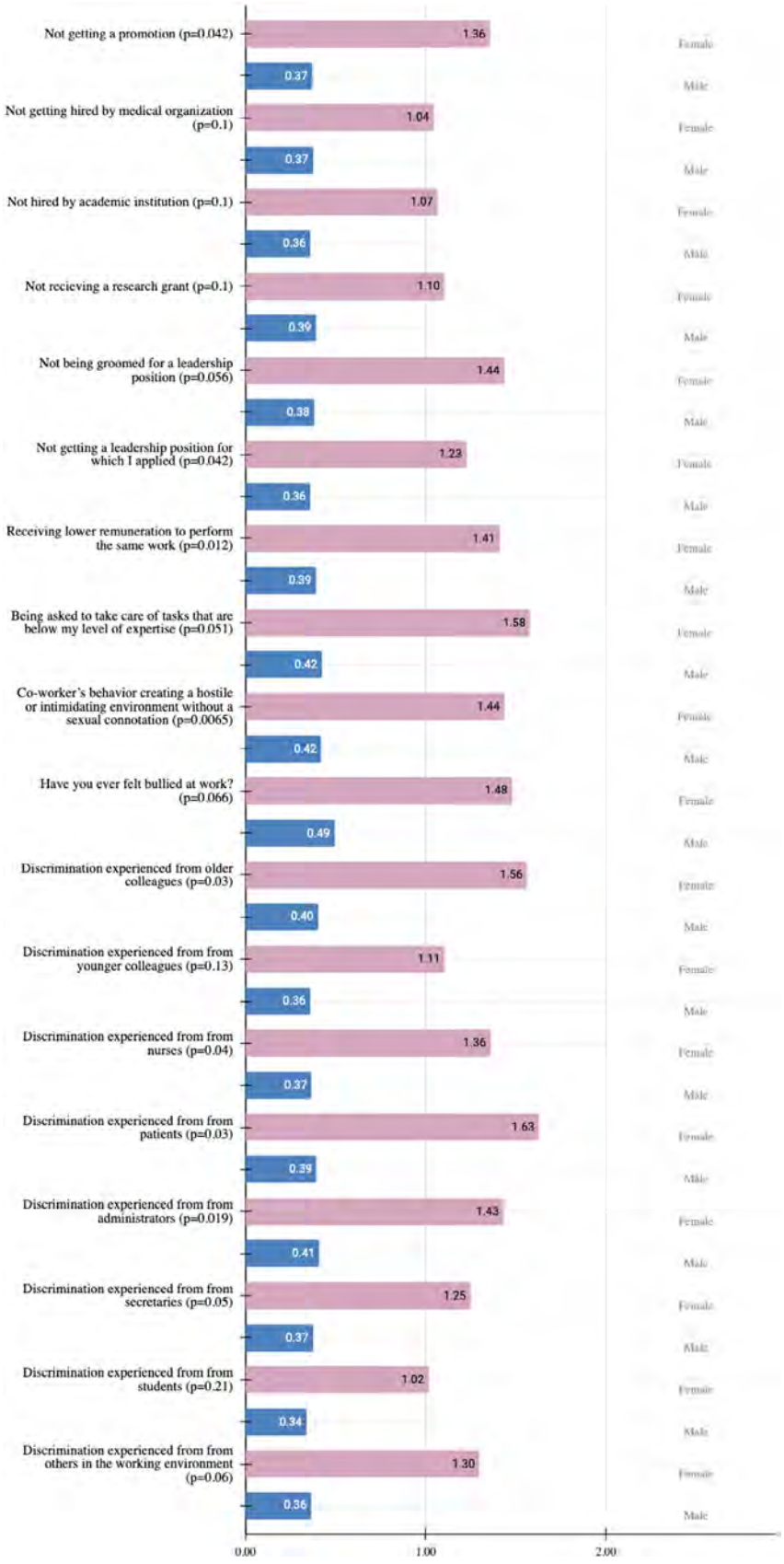

Not getting a promotion (p=0.042)
1.36
Female
0.37
Male
Not getting hired by medical organization (p=0.1)
1.04
Female
0.37
Male
Not hired by academic institution (p=0.1)
1.07
Female
0.36
Male
Not recieving a research grant (p=0.1)
1.10
Female
0.39
Male
Not being groomed for a leadership position (p=0.056)
1.44
Female
0.38
Male
Not getting a leadership position for which I applied (p=0.042)
1.23
Female
0.36
Male
Receiving lower remuneration to perform the same work (p=0.012)
1.41
Female
0.39
Male
Being asked to take care of tasks that are below my level of expertise (p=0.051)
1.58
Female
0.42
Male
Co-worker's behavior creating a hostile or intimidating environment without a sexual connotation (p=0.0065)
1.44
Female
0.42
Male
Have you ever felt bullied at work? (p=0.066)
1.48
Female
0.49
Male
Discrimination experienced from older colleagues (p=0.03)
1.56
Female
0.40
Male
Discrimination experienced from from younger colleagues (p=0.13)
1.11
Female
0.36
Male
Discrimination experienced from from nurses (p=0.04)
1.36
Female
0.37
Male
Discrimination experienced from from patients (p=0.03)
1.63
Female
0.39
Male
Discrimination experienced from from administrators (p=0.019)
1.43
Female
0.41
Male
Discrimination experienced from from secretaries (p=0.05)
1.25
Female
0.37
Male
Discrimination experienced from from students (p=0.21)
1.02
Female
0.34
Male
Discrimination experienced from from others in the working environment (p=0.06)
1.30
Female
0.36
Male
0.00
1.00
2.00
Mean percieved discrimination

Table 1. Intervention Recommendations

Conference Intervention	F		M	
No male-only panel pledge at rheumatology conferences and events	238	40.55%	60	26.20%
Family- and child-friendly rheumatology conferences and events	349	59.45%	169	73.80%
Organizational Intervention				
Establishing a Society/Network of Gender equity in Rheumatology (GEAR)	155	11.14%	59	12.09%
#SheLeadsRheumatology or similar social media campaign	99	7.11%	27	5.53%
Gender-balanced committees, working groups, and task-forces	246	17.67%	75	15.37%
Policies on gender-balanced organizational funding	152	10.92%	52	10.66%
Gender balanced editorial boards and peer-review in rheumatology journals	181	13.00%	45	9.22%
Engaging national rheumatology groups to develop country-specific support	233	16.74%	118	24.18%
Social media campaign promoting female leadership in the scientific population	164	11.78%	42	8.61%
Social media campaign promoting gender equity in the civil population	162	11.64%	70	14.34%
Skills Training				
Leadership skills training	179	10.51%	72	10.68%
Speaking, scientific writing, presentation, communication skills training	255	14.97%	118	17.51%
Effective training on career planning/pathways	198	11.63%	76	11.28%
Promotion and salary negotiation training	185	10.86%	79	11.72%
Support on grant writing applications	126	7.40%	48	7.12%
High-impact scientific writing masterclasses	172	10.10%	78	11.57%
Effective work-life balance management training	239	14.03%	87	12.91%
Unconscious bias and/or implicit bias training (expose people to their implicit biases, provide tools to adjust automatic patterns of thinking, and ultimately eliminate discriminatory behaviors)	149	8.75%	53	7.86%
Promoting gender-sensitive clinical practice, research, and training	200	11.74%	63	9.35%
Work Intervention				
Peer-to-peer mentorship programmes	174	10.88%	87	15.26%
Senior sponsorship programmes	126	7.88%	58	10.18%
Personality insights, e.g. Insights Discovery®	89	5.57%	31	5.44%
Raising awareness of gender equity issues in rheumatology	144	9.01%	50	8.77%
Involving men in advancing gender equity	138	8.63%	45	7.89%
Increasing visibility of female role models	203	12.70%	35	6.14%
Implementation of result-based compensation model including patient satisfaction	155	9.69%	62	10.88%
Promotion of civil society sensibilization on gender equity subject	130	8.13%	43	7.54%
Flexibility of working hours (WITHOUT workload reduction) to care to family needs	230	14.38%	81	14.21%
Flexibility of working hours (WITH workload reduction) to care to family needs	186	11.63%	66	11.58%

Intervention Recommendations

Disclosure: L. Traboco: None; **P. Ovseiko**: None; **S. Dyball**: Eli Lilly, 5, Novartis, 5, UCB, 5; **T. Khursheed**: None; **A. BABINI**: None; **A. Kalla**: None; **C. Hill**: None; **D. Danda**: None; **D. Dey**: None; **E. Nikiphorou**: AbbVie/Abbott, 6, Celltrion, 6, Eli Lilly, 6, fresenius, 6, Galapagos, 6, Gilead, 1, 6, Pfizer, 6, Sanofi, 6; **G. Harifi**: None; **H. SO**: None; **H. Badshah**: None; **I. Hmamouchi**: None; **J. Von Feldt**: None; **J. Farani**: None; **M. Peixoto Guimarães**: None; **K. Jatuworapruk**: None; **L. Andreoli**: None; **N. Ziade**: Abbvie, 6, Boehringer-Ingelheim, 6, Eli Lilly, 6, Janssen, 6, Newbridge, 6, Novartis, 6, Pfizer, 6, Pierre Fabre, 6, Roche, 6, sanofi, 6; **P. PALOMINOS**: None; **Q. Wang**: None; **R. Nakashima**: None; **S. Haq**: None; **W. Bautista-Molano**: None; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer-Ingelheim, 6, Chugai, 5, 6, Eisai, 5, 6, Eli Lilly, 6, Gilead, 6, GSK, 6, Mitsubishi-Tanabe, 5, Pfizer, 6, Taiho, 6, Taisho, 5, 6; **G. Wright**: AbbVie, 2, 6, Amgen, 2, 6, Association of Women in Rheumatology, 4, AstraZeneca, 2, 6, Bristol Myers Squibb, 5, Eli Lilly, 2, 6, Gilead Sciences, 5, GSK, 2, 6, Janssen, 2, 5, 6, Novartis, 2, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 6; **V. Agarwal**: None; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, Bristol Myers Squibb, 2, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead Sciences, 2, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake, 2, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **L. Gupta**: None.

Abstract Number: 0171

A Conceptual Framework to Characterize the Indirect Burden of Systemic Lupus Erythematosus (SLE): Findings from Qualitative Patient Interviews

Vibeke Strand[1], Prajakta Masurkar[2], Jennifer Reckleff[3], Taylor Schwartz[4], Alison Silverstein[4], Jennifer Osborne[4], Josie Lloyd[4], Brian Leinwand[4], Elaine Karis[5], Fatima Barbar-Smiley[6] and Karen Costenbader[7], [1]Stanford University, Portola Valley, CA, [2]Amgen, Inc., Atlanta, GA, [3]Amgen, Inc., Westlake Village, CA, [4]Inovalon Insights, Bowie, MD, [5]Amgen, Inc., Colts Neck, NJ, [6]Amgen, Inc., Dublin, OH, [7]Brigham and Women's Hospital and Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Health Services Research Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1. Demographic and disease characteristics of SLE patients who were interviewed via teleconference

Characteristics	SLE patient cohort (N = 20) n (%)
Age group	
18-29	1 (5%)
30-39	8 (40%)
40-49	7 (35%)
50-64	3 (15%)
65 or older	1 (5%)
Gender	
Female	19 (95%)
Male	1 (5%)
Race/ethnicity*	
African American/Black	9 (45%)
Asian	1 (5%)
Caucasian/White	8 (40%)
Hispanic/Latino	5 (25%)
Marital status	
Single, never married	5 (25%)
Married or domestic partnership	11 (55%)
Divorced	4 (20%)
Annual household income	
$50,000 or less	3 (15%)
$50,000 to $99,999	11 (55%)
$100,000 or more	6 (30%)
Location of residency	
Urban	4 (20%)
Suburban	15 (75%)
Rural	1 (5%)
Cohabitants (not mutually exclusive)	
Parent(s)/parent(s)-in-law	4 (20%)
Spouse/partner	14 (70%)
Child(ren)	10 (50%)
Roommate(s)	2 (10%)
Caretaker	1 (5%)
Self only	1 (5%)
Health insurance status (not mutually exclusive)	
Insurance through employer	14 (70%)
Medicare (including Medicare Advantage)	7 (35%)
Medicaid	2 (10%)
Other government program (e.g., TRICARE, VA, OPM)	3 (15%)
Flares experienced over the previous 12 months	
0	3 (15%)
1-3	10 (50%)
4-6	2 (10%)
7 or more	5 (25%)
Ever diagnosed with lupus nephritis	
Yes	9 (45%)
No	10 (50%)
Not sure	1 (5%)

*Not mutually exclusive as patients may have selected more than one category; OPM = Office of Personnel Management, SLE = systemic lupus erythematosus; VA = Veterans Affairs

Background/Purpose: SLE is a chronic autoimmune disorder that affects multiple organs and leads to a variety of symptoms, including joint pain, fatigue, and skin rashes, that significantly impact patients' lives. Despite the known increased risk of morbidity and mortality in affected populations, there has been limited research about the impact of SLE on a patient's daily life, such as career achievements, social/leisure activities, and family dynamics. A qualitative study was conducted to examine the impact of SLE on daily life from a patient's perspective and to develop a conceptual framework for overall impact.

Methods: A literature review was conducted to identify domains of interest to discuss in the interviews. A semi-structured interview guide was developed to gather patients' perspectives on previously identified areas of SLE impact and identify other ways in which SLE affects daily life. Twenty adult patients with SLE consented to teleconference interviews to discuss how SLE impacted their lives. Transcripts were then analyzed to identify themes. Based on literature review and patient interviews, a preliminary conceptual framework was developed for understanding the indirect burden of SLE on patients.

Results: The literature review identified 10 domains of interest which were used as the topics of the in-depth interviews: career/education, social impact, physical activity, cost (direct/indirect), patient burden, family planning, treatment preference, clinical perspective, family burden, and mental health. Of the patients interviewed, a majority were female (95%), aged 30-39 years (40%), African American/Black (45%), and had employer-based insurance (70%) (**Table 1**). Over half of the patients reported ≥1 flare in the previous 12 months. Content analysis of interview transcripts revealed 8 domains based on patients' perceptions of how SLE impacts their daily lives (percentage of patients reporting): physical activity/mobility

Table 2. Themes that emerged from in-depth patient interviews (N = 20)

Major themes	Example patient quotes
Education/career	*"The first year I went to college, I was really anti-social. And I had a lot of symptoms, like skin rashes and weight gain from the steroids, and I just kind of felt like that freak show... it was kind of hard to stay... to keep up with school, with my lupus being so active."*
Productivity	*"My lupus symptoms were preventing me from potential career [advancement] because I knew I wasn't able to take on more responsibility of a higher role."*
	"Usually during the week I wouldn't do much after work just because I was tired."
Other indirect costs	*"...heat pads, creams, ointments, and things like that."* *"For me, I'm a huge reader, so the cost of entertaining myself... different aids can look like different things to different people. I'm home all day. I kinda need Netflix. You know, so things like that start adding up."*
Caregiver burden	*"My husband had to help me get dressed... he had to put my backpack on. I couldn't do [it]."*
Daily life	*"If someone is going out to the park, I gotta make sure it's a park that has shade and/or chairs because I get tired, or I'll bring stuff.* *"I [missed] Christmas once before, [and] my birthday because I was in the hospital..."*
Mental health	*"Mentally, it's taking me to a really dark place, not like a dark place where I would ever hurt myself or anything, but I've become really negative, really angry all the time, because I'm just like, [why] am I so sick?"*
Social and family life	*"Even for an event not even long term, even like a month or a couple weeks away, I don't like to make plans with friends."*
Future planning	*"I feel like the whole discussion was very difficult in terms of family planning and in terms of, you know, what is it gonna look like if I do get pregnant and then having the conversation of, like, what is it gonna look like postpartum?"*

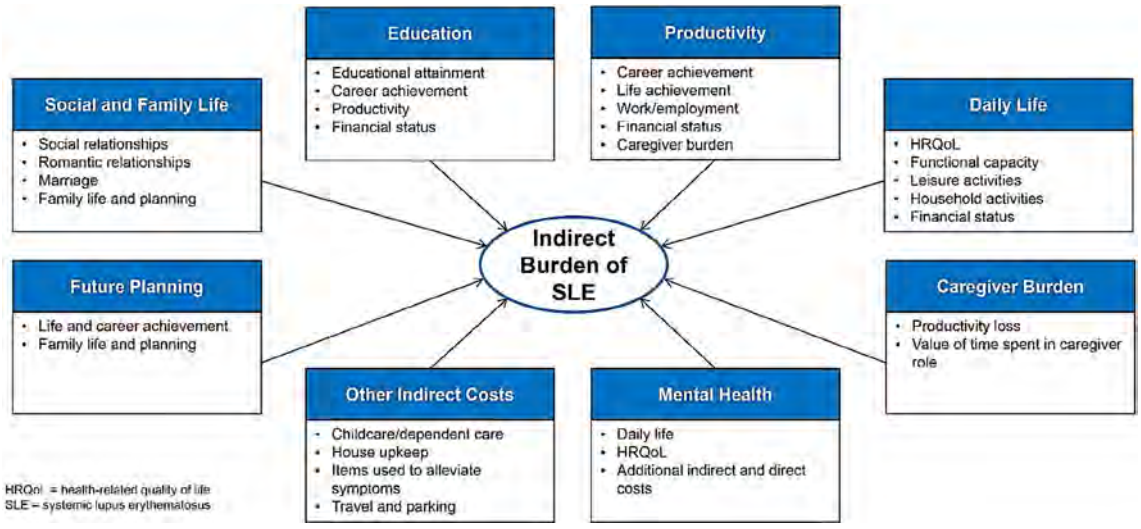


Figure 1. A Conceptual Framework for Understanding the Indirect Patient Burden of SLE

(20%), reduced flares (15%), ability to work (10%), relationships/social life (45%), mental health (20%), fatigue (15%), inflammation/pain (20%), and direct/indirect healthcare costs (15%) (**Table 2**). Patients reported that the overall burden of SLE persisted despite treatment and increased with flares. The conceptual framework illustrates domains identified from the literature review and patient interviews (**Figure 1**). Previously studied domains included productivity, daily life, caregiver burden, and mental health. However, education, family/social lives, future planning, and other indirect costs were newly identified as domains that have not been well characterized.

Conclusion: Based on the literature review and in-depth patient interviews, a conceptual framework was developed for understanding the numerous factors contributing to the impact of SLE on patients' lives in 8 discrete yet interrelated domains. Data reflecting the patient-centered burden of SLE in the literature are limited, especially with respect to the impact on education, family/social lives, future planning, and indirect costs. Future research should target these evidentiary gaps to better establish a holistic view of patient-centered SLE burden.

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Abstract Number: 0172

Barriers and Strategies to Enhance Patient Research Partner Involvement in Rheumatology Research: A Systematic Literature Review

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Health Services Research Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Patient research partners (PRPs) participate in research teams and provide unique and valuable input. Their integration as equal partners is recommended (1). However, PRP involvement still faces significant challenges that need to be addressed (2). This study aimed to assess PRPs' roles, identify barriers to their involvement, and propose strategies to improve involvement.

Methods: A systematic literature review was conducted in PubMed/Medline, focusing on studies reporting PRP involvement in rheumatology published between 2017 and January 2023. Keywords such as "patient research partner," "patient expert," "patient and public involvement (PPI)", and relevant acronyms (PRP, PPI) were used. Data collection encompassed quantitative and qualitative data on PRP definition, roles, added value, and barriers and facilitators to their involvement. The analysis included descriptive statistics for quantitative data (frequencies, n%) and inductive thematic analysis for qualitative data.

Concept	Barriers	Strategies to Enhance Patient Involvement
Emotional and Personal Factors	• Emotional burden • Fatigue • Need to accommodate PRP needs • Lack of trust • Time constraints	• Provide a supportive environment • Provide flexibility and accommodations • Allocate adequate resources • Provide ongoing feedback
Communication and Relationship	• Feeling unheard • Power imbalance • Inconsistent and poor communication • Loss of confidentiality	• Coordinator to facilitate PRP involvement • Open and transparent communication • Clarify patient roles, expectations and objectives
Training and Support	• Inadequate training and support of PRP • Lack of resources and compensation of PRP • Lack of awareness about PRP involvement among researchers • Overburdening of PRPs	• Provide training to PRP and researchers • Recognition of PRP contributions and encouragement • Increase awareness
Research Process	• Anxiety about delays • Time commitment for researchers • Forced changes in working practice • Challenges to recruit PRPs	• Establish realistic timelines • Address recruitment challenges • Build trust through open
Collaboration and Engagement	• Lack of PRP diversity • Discrepancies in views • Uncertainty in incorporating patient experience	• Ensure diversity of PRPs • Involve PRPs from project inception with clear roles • Discuss diverging perspectives

Results: A total of 1481 studies were identified, 108 full-text articles were assessed for eligibility, and 53 were included. Among these, 69% were qualitative studies, reviews, opinion papers, or reports, with 62% published in rheumatology journals. Geographically, 50% of the studies were from Europe, and 31% from North America. 60% of articles reported a definition of PRPs identifying terms such as ''equal partnership'', ''active engagement'', and ''collaboration with researchers''. When PRP involvement was reported, the number of PRPs per project ranged 1 to 4 in 51% of the articles and more than 5 PRPs in 25% of the articles. Various roles of PRPs were described ranging from research partners to patient advocates, advisors, and patient reviewers. PRPs were reported to be involved in all phases of research in 30% of papers, from the conception, conduct to the implementation of outcomes. Barriers to PRP involvement (Table 1) included emotional and personal factors, communication and relationship challenges, inadequate training and support, difficulties following the research process and pace, as well as collaboration and engagement issues. Effective strategies to enhance PRP involvement (Table 1) included early involvement, a supportive environment, effective communication and trust, and providing support and training for PRPs and researchers.

Conclusion: This systematic literature review identified barriers and proposes solutions to enhance PRP involvement in rheumatology research. Addressing these barriers and implementing effective strategies is crucial for meaningful PRP involvement. Further efforts are needed to promote and facilitate patient engagement in research to ensure its relevance and impact.

References

1) de Wit MP, et al. European League Against Rheumatism recommendations for the inclusion of patient representatives in scientific projects. Ann Rheum Dis. 2011.
2) Studenic P et al. Unmet need for patient involvement in rheumatology registries and observational studies: a mixed methods study. RMD open. 2019.

Disclosure: K. Aouad: None; **M. de Wit**: Celgene, 2, Eli Lilly, 2, Janssen, 2, Pfizer, 2, UCB Pharma, 2; **M. Elhai**: AstraZeneca, 12, Travel to Congress support, Janssen, 12, Congress support; **D. Benavent**: Abbvie, 5, Galapagos, 6, Janssen, 6, Novartis, 5, Roche, 6; **H. Bertheussen**: None; **J. Primdahl**: None; **C. Zabalan**: None; **P. Studenic**: None; **L. Gossec**: AbbVie, 2, 12, Personal fees, Amgen, 2, Biogen, 5, BMS, 12, Personal fees, Celltrion, 12, Personal fees, Eli Lilly, 5, 12, Personal fees, Galapagos, 12, Personal fees, Janssen, 12, Personal fees, MSD, 12, Personal fees, Novartis, 5, 12, Personal fees, Pfizer, 12, Personal fees, Sandoz, 5, 12, Personal fees, UCB Pharma, 5, 12, Personal fees.

Abstract Number: 0173

Review of Published Literature Reporting Economic Burden of Treatment Switching in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Health Services Research Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: For rheumatoid arthritis (RA) American College of Rheumatology (ACR) recommends the *treating to target* approach, starting with conventional synthetic antirheumatic drugs (DMARDs). ACR advises as many switches as necessary to achieve the target. Patients may switch therapy because of adverse reactions, response failure, or non-medical

(e.g., economic) reasons. Prior research has reported that treatment switching is associated with increased healthcare burden and costs, however a summary of the published literature is lacking. We aimed to summarize published literature reporting clinical and economic burden of treatment switching in RA.

Methods: We used PubMed and desktop search to identify literature reporting healthcare resource use (HCRU) or costs associated with treatment switching in RA patients. Keywords: RA AND treatment switch* AND [HCRU OR cost].

Results: The PubMed search yielded 100 titles; 48 were selected for abstract review, 16 selected for full-text review (8 articles excluded as not relevant). Three articles were identified via desktop search.

Eleven articles reported research conducted in USA (n=9; commercial claims), Sweden (n=1), and Italy (n=1). Nine articles reported results for RA only; two reported RA within a mix of inflammatory conditions. Outcomes were for patients who switched therapy after initiating oral methotrexate (n=1), first biologic DMARD (n=5), biologic DMARD (n=4), or first targeted DMARD (biologic or JAKi; n=1).

After treatment initiation, treatment switch was reported in 12%-18% patients (8% in one study) within 1 year and 30% within 2 years (Figure 1). Treatment switching was associated with 5%-51% increase in adjusted all-cause healthcare costs (Figure 2). One study (Vanderpoel, et al., 2019) reported switching to be associated with increased adjusted HCRU: hospitalization (adjusted odds ratio [aOR]: 3.03; P< 0.05), emergency department use (aOR: 1.73, P: NS), and outpatient visits (aOR: 1.05, P: NS).

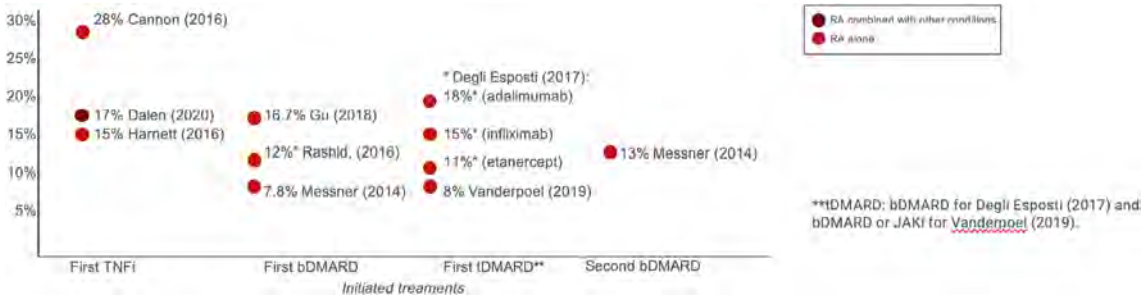

Figure 1. Rates of treatment switching reported in the literature

Figure 2. Adjusted total healthcare costs treatment costs for RA patients who switched therapy at least once (switchers) or twice (twice switchers) within 12 months post-initiation in comparison with alternatives, defined as persisters (A) or non-switchers (B)

Within studies, risks of bias included: reporting of unadjusted estimates (failing to account for between-group differences; n=3), combining RA with other inflammatory conditions (n=2), combining outcomes [switchers and discontinuers (n=1) and non-switchers into one group (n=5)]. All studies had bias towards reporting data from US commercial databases (all prior to 2016), mostly biologic DMARD; few studies reported HCRU.

Conclusion: Published literature consistently reported frequent therapy switching in RA. The switching was associated with increased HCRU and costs, highlighting the health economic need for prognostic markers of sustained response. Additional research is needed to report contemporary trends, outcomes in Medicare and Medicaid, and trends outside of the US.

References:

Degli Esposti, et al. (2017); PMID:28053549
Cannon, et al. (2016); PMID:27352377
Dalen, et al. (2020); PMID:32647910
Gu, et al. (2018); PMID:30020745
Harnett, et al. (2016); PMID:26401963
Rashid, et al. (2016); PMID:26766553
Vanderpoel, et al. (2019); PMID:31122662
Messner, et al. (2014); PMID:24575891
Wolf, et al. (2017); PMID:28363696
Lee, et al. (2017); PMID:28465768
Shahabi, et al. (2019); PMID:30653389

Disclosure: P. Taylor: AbbVie, 2, Biogen, 2, Eli Lilly, 2, Fresenius, 2, Galapagos, 2, 5, Gilead Sciences, 2, GSK, 2, Janssen, 2, Nordic Pharma, 2, Pfizer Inc, 2, Sanofi, 2, UCB, 2; **J. Antonova**: Aqtual, Inc., 2.

Abstract Number: 0174

Evaluation of Healthcare Utilization in Members with Rheumatoid Arthritis, Psoriatic Arthritis, and Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Health Services Research Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Healthcare utilization is increasing among patients with rheumatic diseases. While several studies have assessed healthcare utilization in rheumatoid arthritis (RA) patients, few studies have assessed utilization among psoriatic arthritis (PsA) and systemic lupus erythematosus (SLE) patients. The objective of this study was to examine healthcare utilization trends among patients with RA, PsA, or SLE.

Methods: This was a cohort study of fully insured commercial or Medicare members of a large national health plan between 1/1/2018 and 1/1/2023. Members ≥ 18 years old were included if they had at least 2 visits for RA (ICD-10 code: M05 or M06), PsA (L40.5), or SLE (M32) during the study period. Members were excluded if they did not maintain continuous

Table 1. Demographic characteristics

Variable	Overall N=109,006	PSA N(%) = 13,160 (12.1)	RA N(%) = 80,724 (74.1)	SLE N(%) = 15,122 (13.9)	P-Value
Gender, n (%)					<0.001
F	77483 (71.1)	6880 (52.3)	57555 (71.3)	13048 (86.3)	
M	31523 (28.9)	6280 (47.7)	23169 (28.7)	2074 (13.7)	
Age, mean (SD)	57.7 (15.5)	53.7 (13.7)	59.6 (15.2)	51.2 (15.7)	<0.001
Age, median [Q1,Q3]	59.0 [47.0,69.0]	54.0 [44.0,63.0]	61.0 [50.0,70.0]	51.0 [39.0,63.0]	<0.001
Age category, n (%)					<0.001
18-45	23719 (21.8)	3592 (27.3)	14487 (17.9)	5640 (37.3)	
46-55	21812 (20.0)	3417 (26.0)	15016 (18.6)	3379 (22.3)	
56-65	27796 (25.5)	3529 (26.8)	21167 (26.2)	3100 (20.5)	
66-75	22089 (20.3)	1933 (14.7)	18123 (22.5)	2033 (13.4)	
>75	13590 (12.5)	689 (5.2)	11931 (14.8)	970 (6.4)	
Person time (months), mean (SD)	24.2 (14.5)	24.1 (14.8)	24.2 (14.4)	24.4 (15.0)	0.087
Person time (months), median [Q1,Q3]	21.0 [12.0,34.0]	21.0 [12.0,33.0]	21.0 [12.0,34.0]	21.0 [12.0,34.0]	0.095
Charlson Comorbidity Index, mean (SD)	3.1 (2.8)	1.7 (2.4)	3.3 (2.8)	3.0 (2.6)	<0.001
Charlson Comorbidity Index, median [Q1,Q3]	2.0 [1.0,4.0]	1.0 [0.0,2.0]	2.0 [1.0,5.0]	2.0 [1.0,4.0]	<0.001
Depression, n (%)	32209 (29.5)	3531 (26.8)	23744 (29.4)	4934 (32.6)	<0.001
Region, n (%)					<0.001
Midwest	19177 (17.6)	2257 (17.2)	14630 (18.1)	2290 (15.1)	
Northeast	31385 (28.8)	3792 (28.8)	23258 (28.8)	4335 (28.7)	
South	45990 (42.2)	5207 (39.6)	34403 (42.6)	6380 (42.2)	
West	12454 (11.4)	1904 (14.5)	8433 (10.4)	2117 (14.0)	
SES Index, n (%)					<0.001
Very Low	15440 (14.2)	1453 (11.0)	11717 (14.5)	2270 (15.0)	
Low	35477 (32.5)	4007 (30.4)	26773 (33.2)	4697 (31.1)	
Medium	31219 (28.6)	3811 (29.0)	23071 (28.6)	4337 (28.7)	
High	20024 (18.4)	2826 (21.5)	14360 (17.8)	2838 (18.8)	
Very High	6846 (6.3)	1063 (8.1)	4803 (5.9)	980 (6.5)	

eligibility for 6 months before or after entrance into the study, had multiple conditions of interest, or had missing socioeconomic status (SES) data. Healthcare utilization metrics were examined as use of telemedicine, emergency room (ER), or inpatient services and were identified by place of service codes on medical claims. ER and inpatient claims were aggregated by day and are presented by days utilizing the service. Utilization rates were calculated based on total person years observed in each cohort and the sum of telemedicine claims. ER days and inpatient days are presented as claims or days per 100 person years observed. Rate differences and rate ratios were calculated with 95% confidence intervals (CI) with direct bivariable cohort comparisons. Continuous variables were assessed with analysis of variance or Kruskal-Wallis tests; categorical variables were assessed with the Chi^2 test. P-values < 0.05 are significant, except for cohort comparisons of rate ratios, where the Bonferroni correction was applied and $p< 0.005$ is considered significant.

Results: Of the 109,006 members included in this study, 80,724 (74.1%) had RA, 15,122 (13.9%) had SLE, and 13,160 (12.1%) had PsA. Table 1 demonstrates significant differences in baseline demographics between disease states, with RA members being older (mean age (standard deviation (SD)): 59.6 (15.2) vs. 53.7 (13.7) and 51.2 (15.7) years in PsA and SLE members, respectively; $p< 0.001$) and having more comorbidities at baseline (mean Charlson Comorbidity Index (SD): 3.3 (2.8) vs. 1.7 (2.4) and 3 (2.6) in PsA and SLE members, respectively; $p< 0.001$). Tables 2 and 3 demonstrate the differences in healthcare utilization between disease states. In general, SLE members utilized all healthcare services more than PsA and RA members, except for inpatient services compared to RA members (rate ratio (95% CI): 0.973 (0.963-0.983); $p< 0.005$). Members with RA utilized ER and inpatient services significantly more than PsA members but utilized telemedicine services less ($p< 0.005$).

Table 2. Healthcare utilization by rheumatic condition

Utilization metric	Overall N=108,063	PSA N(%) = 13,024 (12.1)	RA N(%) = 80,048 (74.1)	SLE N(%) = 14,991 (13.9)	P-Value
Telemedicine users, n (%)	32990 (30.3)	4780 (36.3)	22343 (27.7)	5867 (38.8)	<0.001
Telemedicine claims in users, mean (SD)	14.6 (27.3)	13.7 (25.1)	14.2 (26.5)	16.7 (31.4)	<0.001
Telemedicine claims in users, median [Q1,Q3]	6.0 [3.0,15.0]	6.0 [3.0,14.0]	6.0 [3.0,15.0]	7.0 [3.0,18.0]	<0.001
Telemedicine (claims per 100 PY), rate (95% Confidence interval)	218 (217.9-219.1)	248.5 (246.6-250.4)	194.8 (194.2-195.5)	317.9 (315.9-319.9)	<0.001
ER users, n (%)	43885 (40.3)	4162 (31.6)	32947 (40.8)	6776 (44.8)	<0.001
ER days in users, mean (SD)	3.0 (3.9)	2.5 (2.8)	3.0 (4.0)	3.2 (4.4)	<0.001
ER days in users, median [Q1,Q3]	2.0 [1.0,3.0]	2.0 [1.0,3.0]	2.0 [1.0,3.0]	2.0 [1.0,4.0]	<0.001
ER (days per 100 PY), rate (95% Confidence interval)	59.1 (58.8-59.4)	39.3 (38.5-40)	60.3 (59.9-60.6)	70 (69-70.9)	<0.001
Inpatient users, n (%)	27335 (25.1)	2331 (17.7)	21041 (26.1)	3963 (26.2)	<0.001
Inpatient days in users, mean (SD)	10.1 (18.8)	7.7 (13.0)	10.4 (18.8)	10.2 (21.7)	<0.001
Inpatient days in users, median [Q1,Q3]	4.0 [2.0,10.0]	3.0 [1.0,8.0]	4.0 [2.0,11.0]	4.0 [2.0,10.0]	<0.001
Inpatient (days per 100 PY), rate (95% Confidence interval)	125.8 (125.4-126.3)	67.7 (66.7-68.7)	134.3 (133.8-134.9)	130.7 (129.4-132)	<0.001

Table 3. Healthcare utilization rate ratios by rheumatic condition

Rate Ratios (95% CI)	RA vs. PSA	SLE vs. PSA	SLE vs. RA
Telemedicine claims	0.784 (0.777-0.791)*	1.279 (1.266-1.292)*	1.631 (1.62-1.643)*
ER days	1.535 (1.504-1.566)*	1.782 (1.74-1.824)*	1.161 (1.144-1.178)*
Inpatient days	1.984 (1.954-2.015)*	1.93 (1.896-1.965)*	0.973 (0.963-0.983)*

Conclusion: Members with SLE utilize significantly more healthcare services compared to RA and PsA members. In this current study it is not clear what other factors are influencing these utilization patterns. Further studies of healthcare utilization are needed in these patients.

Disclosure: J. Park: CVS Health, 3, 11; **W. Rutter**: CVS Health, 3, 11; **E. Avalos-Reyes**: AstraZeneca, 11, CVS Health, 3, 11, GlaxoSmithKlein(GSK), 11, Haleon, 11, Johnson & Johnson, 11, Moderna, 11, Novavax, 11, Pfizer, 11, Viatris, 11; **C. Liu**: CVS Health, 3, 11; **W. Cavers**: Amedisys Inc, 11, Baxter, 11, Conmed Corp, 11, CVS Health, 3, 11; **D. Verbrugge**: CVS Health, 3, 4, 11; **K. Johnson**: CVS Health, 3, 4, 11, HC Technology Patent, 10.

Abstract Number: 0175

Predicting Cost-Related Medication Non-Adherence in US Adults with Chronic Arthritis: A Machine Learning Approach

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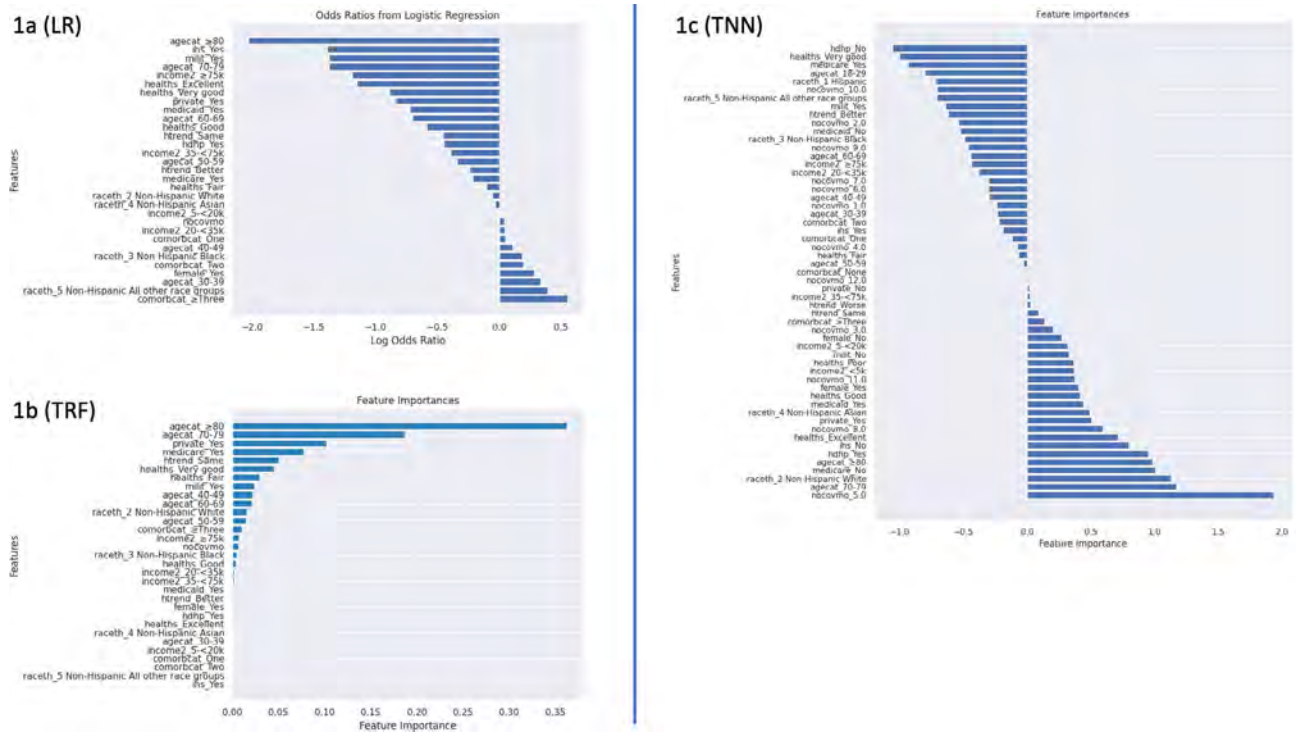
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Health Services Research Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Cost-related medication non-adherence (CRN) occurs when patients are unable to follow their prescribed medication regimen due to financial constraints, such as high costs or lack of insurance coverage. This situation often leads patients to skip doses, take lower dosages, or delay refilling their prescriptions, resulting in negative health outcomes. Accurately predicting CRN is crucial for allocating resources effectively to those who are at higher risk. The objective of this study was to utilize machine learning classifiers to predict CRN in a nationally representative sample of US adults with chronic arthritis.

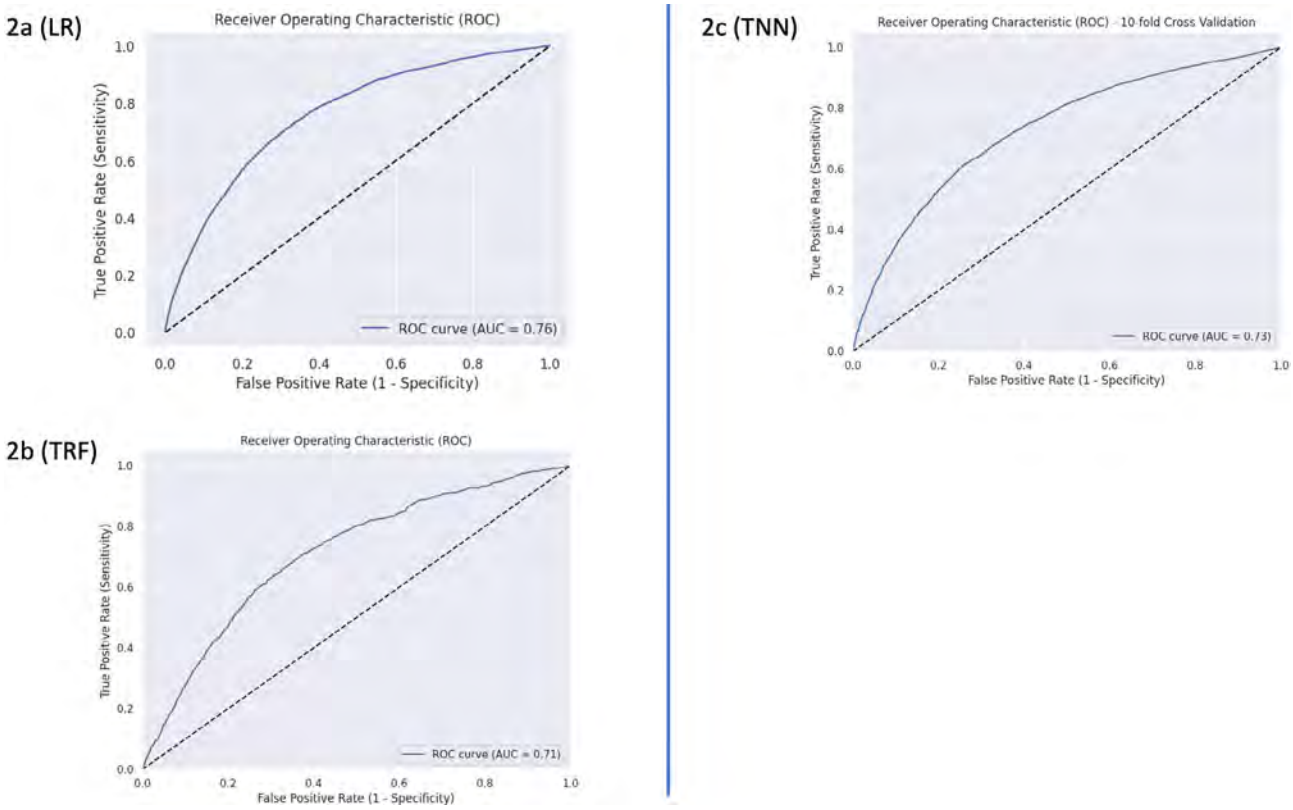
Methods: Data from the National Health Interview Survey (NHIS) collected between 2013 and 2018 were analyzed. Logistic regression (LR), tuned random forest (TRF), and tuned neural network (TNN) classifiers were employed to predict CRN using various demographic and health-related factors, including gender, race/ethnicity, age, health coverage attributes, self-

Table 1. Characteristics of the machine learning classifiers used to predict CRN.

Classifier	Key Features	Optimization Method	Optimized model settings
Logistic Regression (LR)	A linear model that predicts the relationship between predictors and an outcome. It is commonly used for binary classification tasks.	Standardization of features using StandardScaler	Standard
Tuned Random Forest (TRF)	An ensemble method that combines multiple decision trees to make predictions. It is effective for handling complex relationships and interactions.	Grid search for hyperparameter optimization	n_estimators=300; max_depth=3, max_features=0.5
Tuned Neural Network (TNN)	A non-linear model capable of capturing complex relationships between predictors and the outcome. It is suitable for tasks involving intricate interactions.	Grid search for hyperparameter optimization	alpha=0.1, hidden_layer_sizes=(50,)



Machine learning classifier inputs (features) with the most important in predicting CRN. 1a: Logistic regression (LR). 1b: Tuned random forest (TRF). 1c: Tuned neural network (TNN).



Receiver operating characteristic (ROC) curves for the machine learning classifiers. 1a: Logistic regression (LR). 1b: Tuned random forest (TRF). 1c: Tuned neural network (TNN).

reported health status, and comorbidity burden. The characteristics of the models are summarized in Table 1. Feature importance plots were utilized to assess the significance of each input in predicting CRN. Additionally, model performance was evaluated using five-fold cross-validation, and the results were visualized using receiver operating characteristic (ROC) curves.

Results: The study included 23,952 participants with chronic arthritis, among whom 4,632 (19.33%) experienced CRN. The LR classifier identified advanced age as having the smallest odds ratio, while a high comorbidity burden had the largest odds ratio (Figure 1a). Similarly, the TRF classifier indicated that advanced age was the most influential factor, followed by having private or Medicare coverage (Figure 1b). The TNN classifier identified the absence of a high-deductible health plan (HDHP) as the most significant predictor of not having CRN; on the other hand, a lapse in health coverage emerged as the most influential factor in predicting the presence of a CRN (Figure 1c). All three classifiers demonstrated comparable prediction powers, with areas under the curve (AUC) of 76%, 71%, and 73% for LR, TRF, and TNN classifiers, respectively (Figure 2).

Conclusion: Our classification models exhibited promising performance with AUC values close to three-fourths. These AUC values were obtained using five-fold cross-validated test sets, indicating robustness. However, further enhancements are necessary to improve prediction accuracy. Nevertheless, this study highlights the potential of machine learning classifiers in identifying patients at higher risk of CRN.

Disclosure: A. Ara: None; **M. Chenoweth**: None; **C. Scannell**: None.

Abstract Number: 0176

Impact of Social Determinants of Health Factors on Medication Adherence in Members with Rheumatoid Arthritis, Psoriatic Arthritis, and Systemic Lupus Erythematosus

Jean Park, W. Cliff Rutter, Elisea Avalos-Reyes, Chen Liu, Will Cavers, Dorothea Verbrugge and Kjel Johnson, CVS Health, Woonsocket, RI

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Healthcare Disparities in Rheumatology Poster I: Lupus
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Social determinants of health (SDOH) have a significant impact on the health outcomes of many chronic conditions, including rheumatoid arthritis (RA), psoriatic arthritis (PsA) and systemic lupus erythematosus (SLE). The purpose of this study is to assess the impact of SDOH on adherence in RA, PsA and SLE patients.

Methods: In this cohort study of fully insured commercial and Medicare members of a large national health plan between 1/1/2018 and 1/1/2023, members ≥ 18 years old were included if they had at least 2 visits for RA (ICD-10 code: M05 or M06), PsA (L40.5), or SLE (M32) during the study period and received medication therapy for their disease. Members were

Table 1. Demographic characteristics

Variable	Overall N=50817	PSA N(%) = 8161 (16.1)	RA N(%) = 35573 (70)	SLE N(%) = 7083 (13.9)	P-Value
Gender, n (%)					<0.001
F	37222 (73.2)	4160 (51.0)	26712 (75.1)	6350 (89.7)	
M	13595 (26.8)	4001 (49.0)	8861 (24.9)	733 (10.3)	
Age, mean (SD)	55.9 (14.7)	51.6 (12.7)	58.4 (14.3)	48.7 (14.7)	<0.001
Age, median [Q1,Q3]	57.0 [46.0,66.0]	52.0 [43.0,60.0]	59.0 [49.0,68.0]	48.0 [38.0,59.0]	<0.001
Age category, n (%)					<0.001
18-45	12003 (23.6)	2518 (30.9)	6451 (18.1)	3034 (42.8)	
46-55	11332 (22.3)	2379 (29.2)	7287 (20.5)	1666 (23.5)	
56-65	14018 (27.6)	2210 (27.1)	10387 (29.2)	1421 (20.1)	
66-75	9034 (17.8)	839 (10.3)	7491 (21.1)	704 (9.9)	
>75	4430 (8.7)	215 (2.6)	3957 (11.1)	258 (3.6)	
Person time (months), mean (SD)	26.4 (15.5)	25.5 (15.6)	26.5 (15.3)	26.8 (16.0)	<0.001
Person time (months), median [Q1,Q3]	23.0 [13.0,38.0]	22.0 [12.0,35.0]	23.0 [13.0,38.0]	23.0 [13.0,39.0]	<0.001
Charlson Comorbidity Index, mean (SD)	2.8 (2.6)	1.5 (2.1)	3.1 (2.7)	2.8 (2.4)	<0.001
Charlson Comorbidity Index, median [Q1,Q3]	2.0 [1.0,4.0]	1.0 [0.0,2.0]	2.0 [1.0,4.0]	2.0 [1.0,4.0]	<0.001
Depression, n (%)	9945 (19.6)	1406 (17.2)	7020 (19.7)	1519 (21.4)	<0.001
Region, n (%)					<0.001
Midwest	9961 (19.6)	1376 (16.9)	7462 (21.0)	1123 (15.9)	
Northeast	12853 (25.3)	2246 (27.5)	8696 (24.4)	1911 (27.0)	
South	21298 (41.9)	3228 (39.6)	15104 (42.5)	2966 (41.9)	
West	6705 (13.2)	1311 (16.1)	4311 (12.1)	1083 (15.3)	
SES Index, n (%)					<0.001
Very Low	6823 (13.4)	902 (11.1)	4851 (13.6)	1070 (15.1)	
Low	16612 (32.7)	2414 (29.6)	12015 (33.8)	2183 (30.8)	
Medium	14601 (28.7)	2350 (28.8)	10243 (28.8)	2008 (28.3)	
High	9581 (18.9)	1803 (22.1)	6432 (18.1)	1346 (19.0)	
Very High	3200 (6.3)	692 (8.5)	2032 (5.7)	476 (6.7)	

excluded if they did not maintain continuous eligibility 6 months before or after entrance into the study, had multiple conditions of interest, or had missing socioeconomic status (SES) data. Medication adherence was measured using proportion of days covered (PDC), defined as the number of days with medication coverage divided by the number of days between index date into the study and the exhaust date of the last prescription. Adherence was defined as PDC ≥ 0.8. Continuous variables were assessed with analysis of variance or Kruskal-Wallis tests; categorical variables were assessed with the Chi^2 test. Logistic regression was used to examine the impact of SDOH factors on medication adherence; p-values < 0.05 are significant.

Results: Of the 50,817 members included in this study, 35,573 (70%) had RA, 7,083 (13.9%) had SLE, and 8,161 (16.1%) had PsA. There were significant differences (Table 1) in baseline demographics between disease states, with RA members being older (mean age [standard deviation (SD)]: 58.4 [14.3] vs. 51.6 [12.7] and 48.7 [14.7] years in PsA and SLE, respectively; p< 0.001) and more ill at baseline (mean Charlson Comorbidity Index [SD]: 3.1 [2.7] vs. 1.5 [2.1] and 2.8 [2.4] in PsA and SLE, respectively; p< 0.001). Adherence was high during this study (mean PDC [SD]: 0.88 [0.19]). RA members had the highest PDC (mean [SD]: 0.88 [0.19] vs. 0.87 [0.18] and 0.85 [0.21] compared to PsA and SLE members, respectively; p< 0.001). In regression analysis, RA members were more likely to be adherent compared to PsA members (odds ratio [OR, 95% confidence interval (CI)]: 1.19 [1.02-1.39]); SLE was not associated with changes in adherence (Figure 1). Other factors associated with increased adherence include male gender (OR [95%CI]: 1.15 [1.10-1.21]); cancer diagnoses (OR [95%CI]: 1.07 [1.00-1.15]); and increasing age. Factors associated with decreased adherence were: low SES compared to high SES (OR [95%CI]: 0.89 [0.81-0.97]); liver disease (OR [95%CI]: 0.75 [0.66-0.86]); cardiovascular disease (OR [95%CI]: 0.92

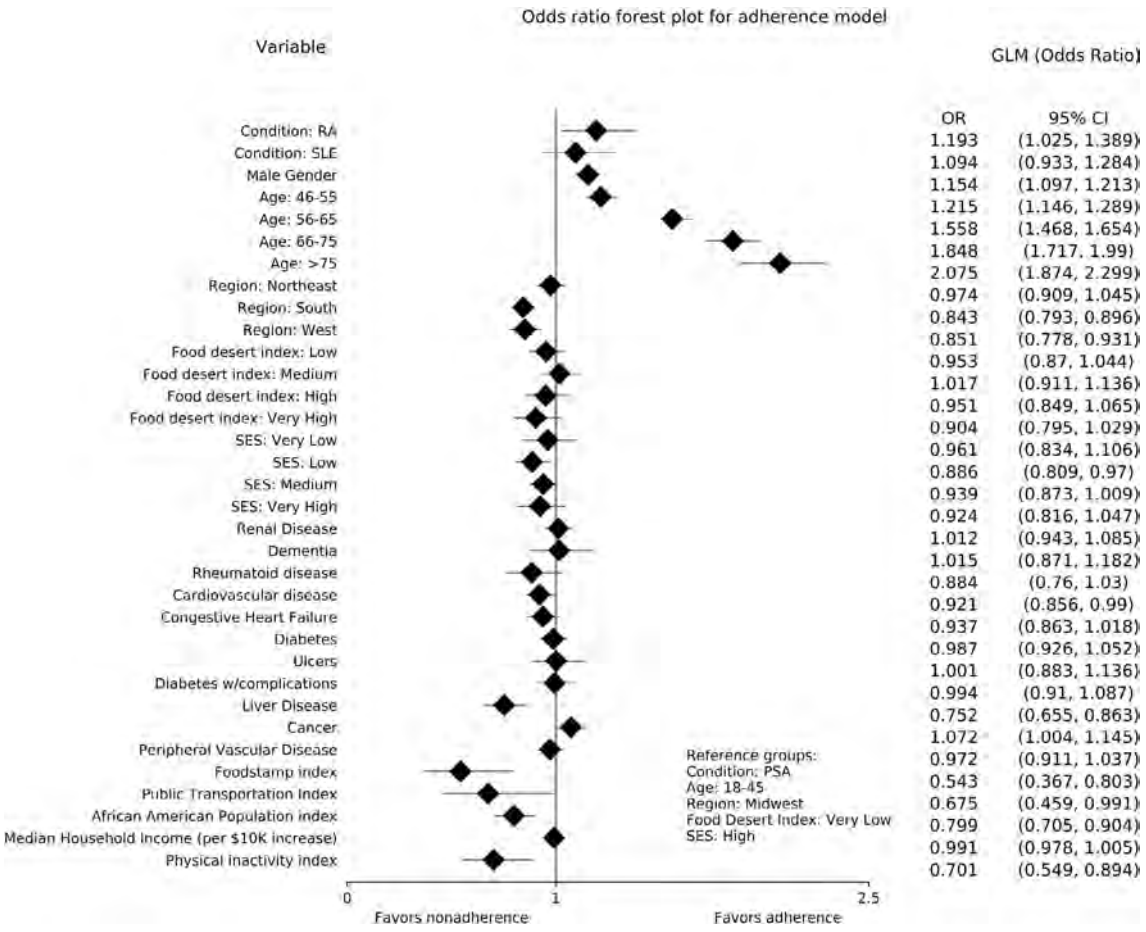


Figure 1. Variables associated with medication adherence

[0.86-0.99]); increases in food stamps (OR [95%CI]: 0.54 [0.37-0.80]), public transportation (OR [95%CI]: 0.68 [0.46-0.99]), African American population (OR [95%CI]: 0.80 [0.71-0.90]), and physical inactivity (OR [95%CI]: 0.70 [0.55-0.89]) indices.

Conclusion: Members with RA had significantly higher rates of adherence compared to members with PsA and SLE. SDOH factors associated with decreased adherence included SES, increases in food stamps, public transportation, African American population, and physical inactivity indices.

Disclosure: J. Park: CVS Health, 3, 11; **W. Rutter**: CVS Health, 3, 11; **E. Avalos-Reyes**: AstraZeneca, 11, CVS Health, 3, 11, GlaxoSmithKlein(GSK), 11, Haleon, 11, Johnson & Johnson, 11, Moderna, 11, Novavax, 11, Pfizer, 11, Viatris, 11; **C. Liu**: CVS Health, 3, 11; **W. Cavers**: Amedisys Inc, 11, Baxter, 11, Conmed Corp, 11, CVS Health, 3, 11; **D. Verbrugge**: CVS Health, 3, 4, 11; **K. Johnson**: CVS Health, 3, 4, 11, HC Technology Patent, 10.

Abstract Number: 0177

Cost-Related Medication Non-Adherence Among US Adults with Chronic Arthritis: Trends, Comparisons, and Disparities

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Healthcare Disparities in Rheumatology Poster I: Lupus
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

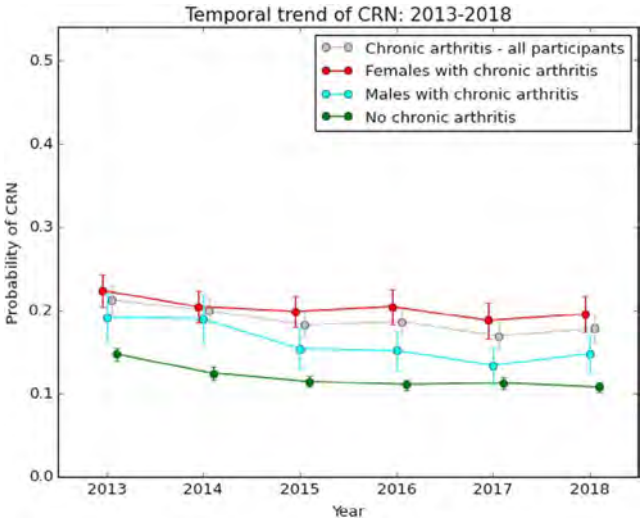
Background/Purpose: Cost-related medication non-adherence (CRN), a measure of drug affordability, refers to a patient's inability to adhere to a prescribed medication regimen due to high medication costs or lack of insurance coverage. Financial burden may lead patients to skip doses, reduce dosages, or delay refilling their prescriptions, which can have negative effects on their health outcomes. In this study, we aimed to investigate CRN in a nationally representative sample of US adults with chronic arthritis.

Methods: We utilized data from the National Health Interview Survey (NHIS) spanning the years 2013 to 2018. By applying survey weights, we calculated the proportion of individuals experiencing CRN among those with and without chronic arthritis of any type. We also calculated the proportion of CRN among individuals with cancer (any type), diabetes mellitus (any type), and heart disease (any type) as comparison groups. Additionally, we calculated the proportion of CRN in subgroups based on gender and race/ethnicity. To ensure accurate calculations, we limited the denominator samples to individuals who received at least one prescription drug. Significant differences were determined using 95% confidence intervals. Data analyses were performed using Stata and Python.

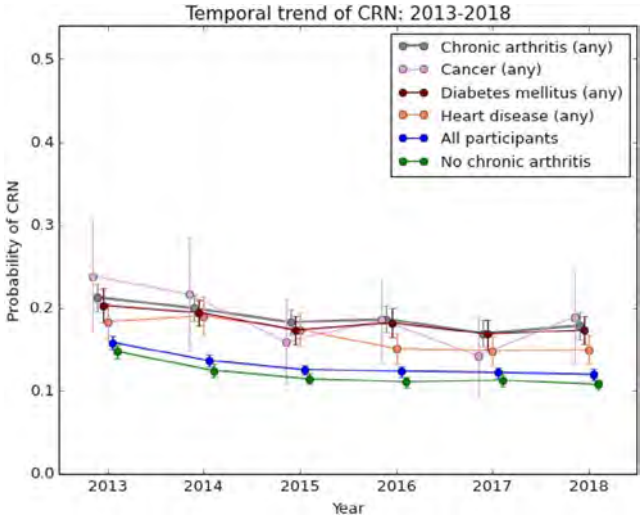
Results: The study included 163,579 participants without chronic arthritis and 26,534 participants with chronic arthritis, of which 17,840 were females with chronic arthritis. Among those with chronic arthritis, there were 19,047 non-Hispanic Whites, 3,917 African Americans/Blacks, 2,497 Hispanics, 625 Asians, and 421 individuals belonging to other races/ethnicities. From 2013 to 2018, the likelihood of experiencing CRN showed a downward trend among individuals with chronic arthritis (21.26% vs. 17.83%, $p< 0.05$) as well as those without chronic arthritis (14.72% vs. 10.76%, $p< 0.05$). CRN was consistently higher across all years in individuals with chronic arthritis versus those without, and the likelihood of experiencing CRN in this group was comparable to that of individuals with cancer and diabetes (Figure 1). Throughout 2013 to 2018,

females with chronic arthritis were significantly more likely to experience CRN than males, and the gender disparities in CRN widened during this period (Figure 2). Furthermore, African Americans/Blacks and Hispanics exhibited trends indicating a higher likelihood of experiencing CRN compared to non-Hispanic Whites and Asians. Nonetheless, those differences were not statistically significant throughout all the years analyzed. (Figure 3).

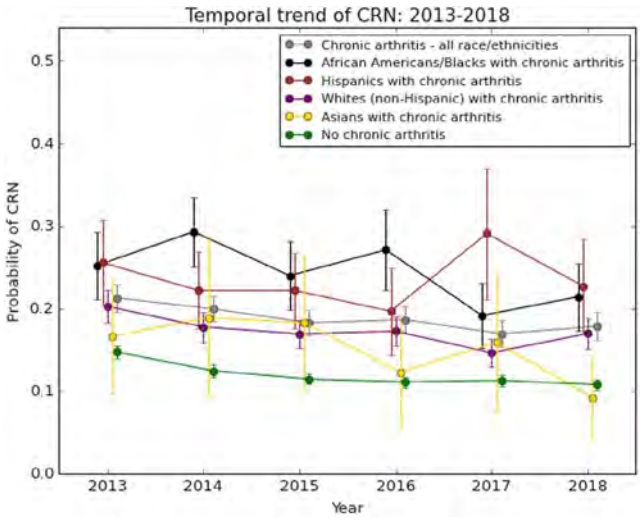
Conclusion: The likelihood of experiencing CRN is gradually decreasing among individuals with and without chronic arthritis. However, individuals with chronic arthritis have a similar likelihood of experiencing CRN compared to those with cancer and diabetes mellitus. Furthermore, our findings raise concerns about potential gender and racial/ethnic disparities in the risk of CRN among US adults with chronic arthritis. In light of these findings, it is crucial to conduct further research and implement targeted policy solutions to address such disparities, ensuring equitable access to affordable medications for all individuals with chronic arthritis.



Comparison of CRN among participants with and without chronic arthritis, as well as those with cancer, diabetes, and heart disease (any type).



Comparison of CRN among females and males with chronic arthritis.



Comparison of CRN among participants with chronic arthritis from various racial/ethnic backgrounds.

Disclosure: A. Ara: None; **M. Chenoweth**: None; **C. Scannell**: None; **J. FitzGerald**: None.

Abstract Number: 0178

Traditional and Lupus-Specific Risk Factors for Cardiovascular Events Among Patients with Systemic Lupus Erythematosus

Saloni Patolia, Dulaney Wilson, Jim Oates and Diane L. Kamen, Medical University of South Carolina, Charleston, SC

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Healthcare Disparities in Rheumatology Poster I: Lupus
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Even among young women with systemic lupus erythematosus (SLE), accelerated atherosclerosis and coronary artery disease are common complications. Traditional risk scoring methods underestimate cardiovascular (CV) risk in patients with SLE, highlighting the need to account for both traditional and lupus-specific risk factors. Our goal is to evaluate the influence of traditional and lupus-specific risk factors on CV outcomes, and examine potential health disparities in these outcomes, among patients with SLE.

Methods: Data was obtained from an ongoing IRB-approved longitudinal single-center registry of patients with SLE and non-SLE population-matched controls. Demographics, medical / social history, and SLE characteristics (if applicable) was obtained from interviews, exams, and medical record review. Disease damage was determined by SLICC/ACR Damage Index ("any damage" if score ≥1).Descriptive analyses, Pearson's chi-squared testing, two-sample t-tests, and multivariable logistic regression were performed as appropriate.

Results: 854 patients with SLE and 663 non-SLE population-matched controls were included in our study. Compared to the controls, the risk of myocardial infarction (MI) was higher among SLE patients (OR 10.53, p< 0.01) and risk of stroke was higher among SLE patients (OR 18.55, p< 0.01), adjusted for age, race, and gender.

Age of SLE diagnosis and current age were both lower among Black patients compared to non-Black patients (**Table 1**), with no significant difference in disease duration. Significantly higher rates of hypertension, lupus nephritis (LN), disease damage and steroid use were observed among Black patients, and a higher rate of smoking was observed among non-Black patients. Diabetes, hypertension, and hyperlipidemia were associated with higher risk of stroke and MI in univariate analysis (each $p < 0.01$). In a multivariate model of the risk among patients with SLE of either a stroke or MI, highest odds were for hypertension (OR 5.24, $p< 0.01$), adjusted for age, race, gender, education, smoking, hyperlipidemia, diabetes, steroid use, and nephritis.

Table 1. Characteristics of study participants comparing Black and non-Black patients with SLE

Characteristics	All patients with SLE N = 854	Black patients with SLE n = 623	Non-Black patients with SLE n = 231	P-value
Current age (mean years +/- SD)	50.2 (15.8)	49.1 (15.3)	53.5 (16.7)	**<0.01**
Age of SLE diagnosis (mean years +/- SD)	31.1 (13.9)	30.1 (12.8)	34.0 (16.6)	**<0.01**
Childhood-onset SLE (%)	16.0	16.2	15.6	NS
Female (%)	91.0	90.7	91.8	NS
Graduated high school (%)	85.2	75.6	81.0	**0.01**
Health insurance coverage (%)	74.0	76.2	68.0	NS
Ever smoker (%)	25.1	20.9	36.4	**<0.01**
Hypertension diagnosed (%)	49.9	55.9	33.8	**<0.01**
Hyperlipidemia diagnosed (%)	18.6	19.1	17.3	NS
Diabetes diagnosed (%)	11.0	12.4	7.4	NS
Stroke diagnosed (%)	10.2	10.8	8.7	NS
Myocardial infarct diagnosed (%)	4.0	3.4	5.6	NS
Lupus nephritis diagnosed (%)	28.2	32.7	16.0	**<0.01**
History of ESRD / Dialysis (%)	10.7	12.8	4.8	**<0.01**
Any SLE disease damage (%)	60.3	63.3	51.7	**<0.01**
High SLE disease damage (%)	32.6	36.1	22.9	**<0.01**
Ever steroid use (%)	73.7	79.3	58.4	**<0.01**

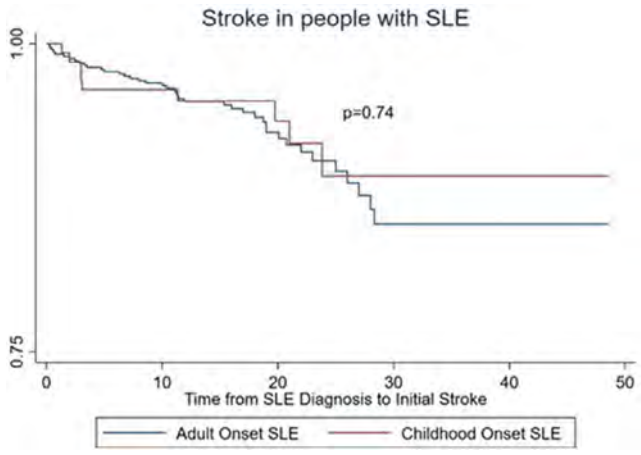


Figure 1. Percent event-free survival over time (in years) from SLE diagnosis to initial stroke comparing adult onset to childhood onset SLE

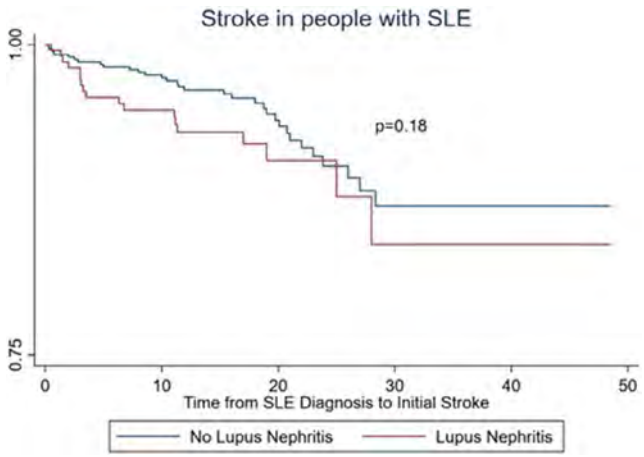


Figure 2. Percent event-free survival over time (in years) from SLE diagnosis to initial stroke comparing lupus nephritis patients to those without lupus nephritis

In multivariate regression models those with childhood onset SLE had a similar mean length of time between SLE onset to stroke compared to adult onset SLE (**Figure 1**), but the stroke age was younger for childhood-onset SLE (23.3 ±10.5 vs 43.3 ±13.8, p< 0.01). Age of MI was also younger for childhood-onset SLE (22.1 ±7.5 vs 47.1 ±11.2, p=0.01). Those with LN had a younger stroke age (32.5 ±14.6 vs 45.0 ±13.5, p< 0.01) and a shorter time to initial stroke compared to those without LN (**Figure 2**).

Conclusion: We found an increased prevalence of CV indicators and CV outcomes among patients with SLE at a significantly younger age compared to population controls, which is even more striking among patients with childhood onset SLE. Continued racial disparities in several important lupus and CV outcomes were evident, highlighting the need to identify and address care gaps for these high-risk patients. Continued progress in understanding what underlies these outcomes will support needed well-informed clinical interventions in risk factor modification for patients with SLE.

Disclosure: S. Patolia: None; **D. Wilson**: None; **J. Oates**: None; **D. Kamen**: None.

Abstract Number: 0179

Social Disparities and Pathology Markers at Lupus Nephritis Diagnosis Predict Worse Kidney Outcomes

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Healthcare Disparities in Rheumatology Poster I: Lupus
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: At diagnosis, a typical 30-year-old with lupus nephritis (LN) already has 10-fold higher chronic kidney disease (CKD) risk than peers and LN is a leading cause of end-stage kidney disease (ESKD) in young patients. Moreover, Black race is associated with a 6-fold higher risk of developing LN associated ESKD suggesting interactions between biological, socio-economic, and pathological factors can accelerate CKD progression and ESKD risk in

LN. Examining early risk factors and interactions between socio-economic and biological factors can improve precision in identifying high-risk patients, yet these are under-examined in LN. Thus, we examined socio-economic and biological factors at LN diagnosis, and pathological markers in index kidney biopsies as predictors of CKD progression and ESKD among a longitudinal inception LN cohort.

Methods: Data including demographics, social factors, comorbidities, LN therapy, and pathology reports at LN diagnosis were abstracted from adult LN patients who underwent index kidney biopsy between 1994-2021. We abstracted LN chronicity and activity indices from index kidney biopsy slides and reports, and re-read biopsy slides to grade renal arteriosclerosis (ASCL) by calculating percent luminal narrowing. We measured two outcomes: a) time to CKD progression defined as a sustained decrease in eGFR ≥30% below the baseline, confirmed by ≥3 values for ≥ 3 months and progression to CKD stage ≥2 (eGFR < 90); b) time to ESKD with up to 12 years follow-up. Cox hazards models and Kaplan Meier (KM) survival analyses were used to examine whether socio-economic factors and pathology markers such as ASCL and activity and chronicity indices predict CKD progression and ESKD.

Results: Among 173 incident adult patients with LN, 75% were female and 35% were from Black and other racial groups. Mean age at LN diagnosis was 38±17 years, and 46% had public or no insurance. Mean renal ASCL (percent luminal narrowing), activity, and chronicity indices were 23%, 2.2, 1.9, respectively.

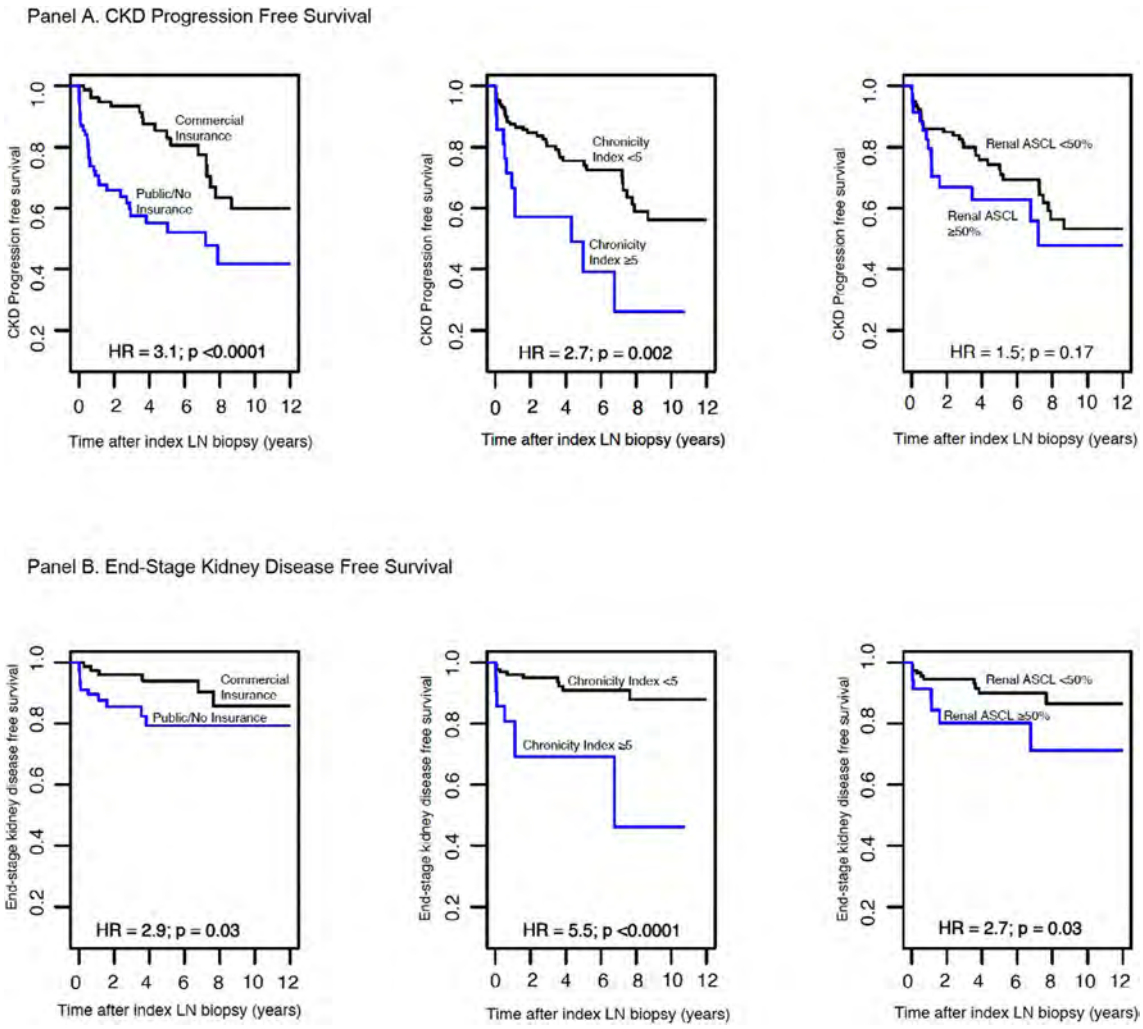

Figure 1. Kaplan Meier Curve shows: Panel A. CKD progression defined as kidney function impairment with sustained decrease in eGFR by 30% and eGFR <90 (CKD stage ≥2); Panel B. ESKD occurrence over 12-year follow-up period after LN diagnosis.

Table 1. Cox models showing risk factors at LN diagnosis of CKD progression defined as kidney function impairment with sustained decrease in eGFR by 30% and eGFR <90 (CKD stage ≥2) (Moroni et al., Kidney360, 2022)

Table 1. Cox models showing risk factors at LN diagnosis of CKD progression defined as kidney function impairment with sustained decrease in eGFR by 30% and eGFR <90 (CKD stage ≥2) (Moroni et al., Kidney360, 2022)

Variables at LN Diagnosis	Unadjusted HR (CIs)	p-value	Adjusted HR* (CIs)	p-value
Age per 10 years	1.001 (0.98, 1.02)	0.91	0.98 (0.95, 1.01)	0.16
Female	1.03 (0.53, 2.0)	0.94	1.03 (0.47, 2.3)	0.94
Black/Other Race or Hispanic Ethnicity	1.7 (0.92, 3.1)	0.09*	2.0 (0.91, 4.3)	0.09*
Public/No Insurance	**3.1 (1.7, 5.6)**	**0.0002**	**2.2 (1.1, 4.7)**	**0.03**
Area Deprivation Index per 10 percentile increase	1.01 (0.99, 1.02)	0.60	-	-
Smoker, Ever	1.1 (0.34, 3.6)	0.87	-	-
GFR per 10 ml/min/m^2 decrease	1.06 (0.97, 1.2)	0.22	-	-
Nephrotic syndrome, yes	**2.0 (1.02, 3.9)**	**0.045**	1.1 (0.48, 2.3)	0.91
Hypertension, yes	1.2 (0.67, 2.3)	0.51	-	-
Diabetes, yes	1.2 (0.43, 3.5)	0.71	-	-
LN Class - Non-proliferative	1.1 (0.55, 2.0)	0.86	-	-
LN Class - Overlap	0.82 (0.37, 1.8)	0.61	-	-
Chronicity index per 1 point increase	**1.3 (1.1, 1.5)**	**<0.0001**	**1.4 (1.2, 1.7)**	**<0.0001**
Activity index per 1 point increase	1.04 (0.95, 1.1)	0.39	-	-
Renal ASCL per 10% increase	1.1 (0.97, 1.2)	0.20	-	-
Severe Renal ASCL ≥50%	1.5 (0.81, 2.8)	0.20	-	-
High dose steroids use, yes	1.45 (0.82, 2.9)	0.19	-	-
Mycophenolate exposure per 1 year increase	0.81 (0.36, 1.8)	0.62	-	-
Chronic steroid use, yes	**1.8 (1.001, 3.3)**	**0.05**	1.8 (0.84, 4.0)	0.13
HCQ exposure per 1 year increase	0.96 (0.91, 1.02)	0.18	-	-
ACE-I/ARB use, yes	0.91 (0.51, 1.6)	0.76	-	-

**Full model includes all socio-demographics, LN chronicity index, and other variables with p-value <0.1 on univariable analysis. Statistically significant values (p <0.05) in bold font. +Trend towards significance.*

A total of 49 patients developed CKD progression over 12 years after LN diagnosis. KM survival curves highlighted accelerated CKD progression in patients with public or no insurance and LN chronicity index ≥5 (Fig. 1A). Patients with public or no insurance had 2-fold higher risk of CKD progression (Adjusted HR 2.2; Table 1). Increase in LN chronicity determined 40% higher CKD progression (Table 1).

Next, 19 patients developed ESKD. KM survival curves noted higher ESKD risk in patients with public or no insurance, severe renal ASCL, and LN chronicity index ≥5 at diagnosis (Fig. 1B). In a limited multivariable model, not including LN chronicity, severe renal ASCL was associated with 2.7 fold higher ESKD risk (Table 2). However, after including LN chronicity, only LN chronicity was associated with 40% higher ESKD risk (Table 2).

Conclusion: Socioeconomic barriers such as public or no insurance at diagnosis were the strongest, independent risk factor of CKD progression to stage ≥2. Additionally, higher LN chronicity in diagnostic biopsies was associated with greater ESKD risk. Future CKD prevention efforts should focus on patients with socioeconomic barriers and those with high LN chronicity index at LN diagnosis to improve outcomes in LN.

Table 2. Cox models showing risk factors at LN diagnosis for end-stage kidney disease (ESKD) over 12 years follow up.

Table 2. Cox models showing risk factors at LN diagnosis for end-stage kidney disease (ESKD) over 12 years follow up.

Variables at LN Diagnosis	Unadjusted HR (CIs)	p	Limited Model* Adjusted HR (CIs)	p	Full Model** Adjusted HR (CIs)	P
Age per 10 years	1.0 (0.97, 1.03)	0.99	1.0 (0.97, 1.03)	0.87	0.97 (0.93, 1.01)	0.14
Female	0.79 (0.28, 2.2)	0.65	1.1 (0.36, 3.1)	0.92	1.3 (0.34, 4.6)	0.74
Black/Other Race or Hispanic Ethnicity	1.4 (0.53, 3.8)	0.48	1.3 (0.45, 3.5)	0.66	2.1 (0.72, 6.1)	0.18
Public/No insurance	**2.9 (1.1, 7.7)**	**0.036**	-	-	2.1 (0.72, 6.2)	0.18
Area Deprivation Index per 10 percentile increase	1.0 (0.97, 1.01)	0.33	-	-	-	-
Smoker, Ever	0.88 (0.28, 2.8)	0.83	-	-	-	-
GFR per 10 ml/min/m^2 decrease	**1.2 (1.1, 1.4)**	**0.004**	-	-	1.2 (0.99, 1.23)	0.06+
Nephrotic syndrome, yes	1.4 (0.46, 4.4)	0.54	-	-	-	-
Hypertension	0.92 (0.31, 2.7)	0.88	-	-	-	-
Diabetes	0.77 (0.1, 6.0)	0.80	-	-	-	-
LN Class - Non-proliferative	1.9 (0.71, 5.1)	0.20	-	-	-	-
LN Class - Overlap	0.30 (0.04, 2.4)	0.26	-	-	-	-
Chronicity index per 1 point increase	**1.5 (1.2, 1.8)**	**0.0002**	-	-	**1.4 (1.1, 1.8)**	**0.019**
Activity index per 1 point increase	1.0 (0.85, 1.2)	0.91	-	-	-	-
Renal ASCL per 10% increase	**1.2 (1.02, 1.3)**	**0.027**	-	-	-	-
Renal ASCL Threshold						
≥15%	2.1 (0.81, 5.4)	0.13	-	-	-	-
≥25%	2.3 (0.90, 5.8)	0.08+	-	-	-	-
≥50%	**2.7 (1.1, 7.01)**	**0.04**	**2.7 (1.001, 7.3)**	**0.049**	1.05 (0.29, 3.7)	0.94
High dose steroids use	2.1 (0.67, 6.3)	0.21	-	-	-	-
Mycophenolate duration per 1 year increase	0.96 (0.85, 1.1)	0.59	-	-	-	-
Chronic steroid use, yes	1.6 (0.60, 4.04)	0.37	-	-	-	-
HCQ exposure per 1 year increase	0.99 (0.91, 1.1)	0.88	-	-	-	-
ACE-I/ARB	1.5 (0.52, 4.4)	0.45	-	-	-	-

**Limited model includes age, sex, race, and renal arterial luminal narrowing of 50% or more. **Full model includes all socio-demographics and other variables with p-value <0.1 on univariable analysis. +indicates a trend towards statistical significance. Statistically significant values (p <0.05) in bold font. +Trend towards significance.*

Disclosure: S. Garg: None; **B. Astor**: None; **A. Raval**: None; **S. Lim**: None; **W. Zhong**: None; **S. Panzer**: None; **B. Rovin**: AstraZeneca, 2, 5, Aurinia, 2, 5, Biogen, 2, F. Hoffmann-La Roche Ltd, 2, Genentech, 2, GlaxoSmithKlein(-GSK), 2, Novartis, 2; **C. Bartels**: Pfizer, 5.

Abstract Number: 0180

Multiplicative Impact of Adverse Social Determinants of Health on Outcomes in Lupus Nephritis: A Meta-analysis and Systematic Review

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Healthcare Disparities in Rheumatology Poster I: Lupus

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus results in 58% more organ damage in people of Black race in the US compared to African descendants living in 11 other developed countries. This highlights that social determinants of health (SDH) likely contribute to disparities in LN outcomes in the US. However, the overall burden of adverse SDHs on LN outcomes and how each SDH domain contributes to observed health disparities have not been fully examined. In the absence of such information, health disparities between racial/ethnic groups may be interpreted as inherently "biological" or "cultural" differences. Thus, there is a need to understand the underlying mechanisms explaining how SDHs influence outcomes and contribute to health disparities in LN to advance equity. Objectives of this systematic review and meta-analysis were to: 1) determine the odds of poor LN outcomes in patients with i) any adverse SDHs, and ii) specific SDH domains; 2) develop a framework for the multidimensional impact of SDH on LN outcomes.

Methods: A comprehensive search was performed using MeSH headings and keywords (e.g., lupus nephritis, insurance, poverty, neighborhood socio-economic status, death, etc.) in Medline, Embase, CINAHL and Web of Science. We included observational and interventional studies on human subjects measuring associations between SDHs and LN outcomes. Risk of bias was assessed using standard tools for all studies.

We examined pooled odds of severe LN outcomes (primary outcome) including mortality, end-stage kidney disease (ESKD), or cardiovascular disease (CVD) in patients with and without any adverse SDHs using a random effects model. Additionally, we calculated the pooled odds of poor outcomes by each SDH domain: individual (e.g., race, insurance), healthcare (e.g., fragmented care, hospital experience), community (e.g., neighborhood socioeconomic status), and behavioral (e.g., smoking) (Fig. 1). Heterogeneity was assessed using I^2.

Results: Among 531 manually reviewed abstracts, 31 met inclusion. Only 13 studies comparing LN outcomes in patients with and without adverse SDHs were included in the meta-analysis. Overall 92% of studies had low risk of bias. The pooled odds of poor outcomes (death, ESKD, or CVD) in patients with any adverse SDHs were 45% higher compared to those without any adverse SDHs (OR 1.45, 95% CI 1.10-1.91, p = 0.008, I^2 85%, Fig. 2). Among the four SDH domains, 64% and 77% higher odds of poor outcomes were noted in patients with adverse SDHs in individual and healthcare domains (OR 1.64, 95% CI 1.13-2.39, I^2 92%; OR 1.77, 95% CI 1.2-3.0, I^2 0%; Fig. 3A-D). Our framework highlighted a multiplicative impact of adverse SDHs in different domains on poor LN outcomes (Fig. 1). As illustrated in Fig. 1, patients of Black race with fragmented care and public insurance had 12-fold higher odds of mortality/ESKD.

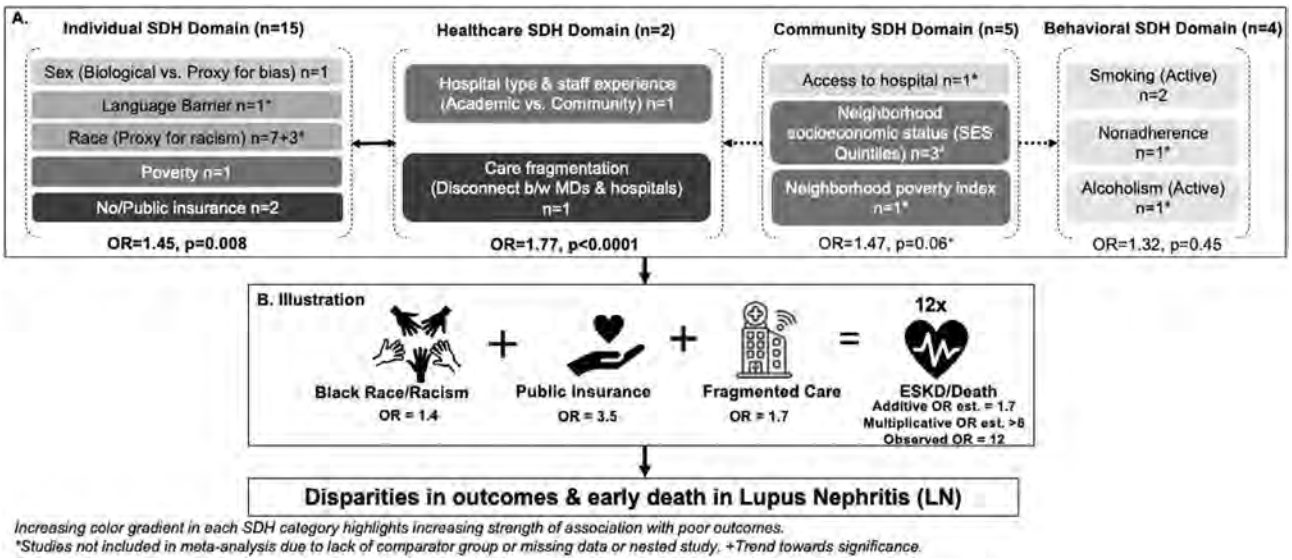

Figure 1. Conceptual model highlighting the impact of adverse individual, community, healthcare, and behavioral SDHs on severe LN outcomes. Data in row B. illustrate multiplicative effects of SDH on LN outcomes.

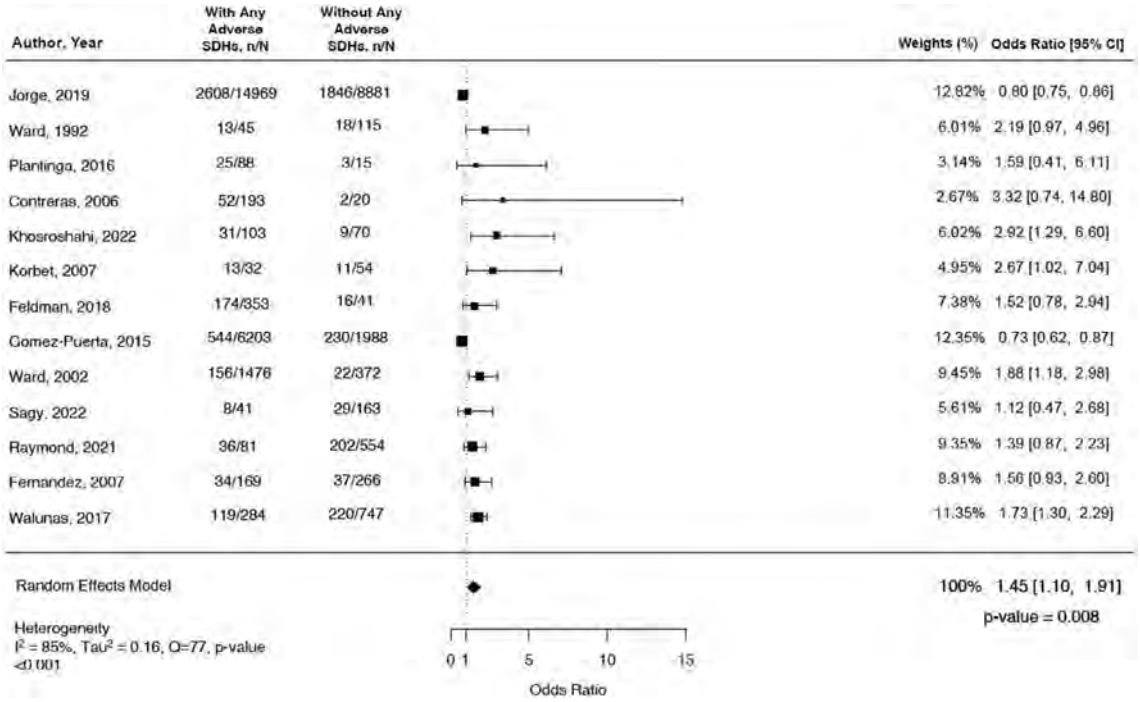

Figure 2. Forest plot showing the odds of ESKD or death in patients with or without any adverse social determinants of health

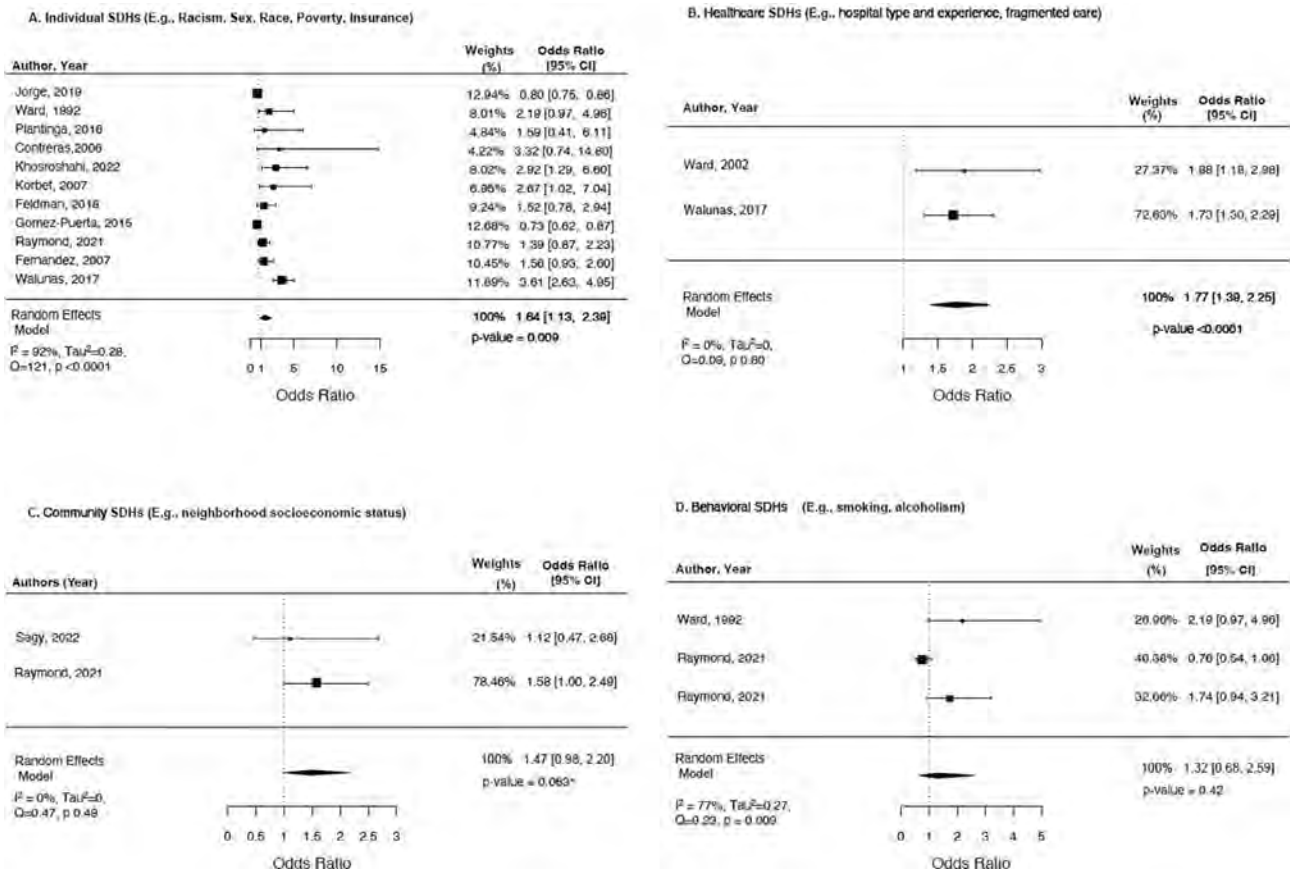

Figure 3. Forest plot showing the odds of ESKD or death with or without adverse social determinants of health in each SDH domain

Conclusion: Our study reports a strong negative impact of adverse SDHs on LN outcomes, with the worst impact in patients with adverse individual and healthcare SDH domains. Moreover, having adverse SDHs in ≥2 domains had a multiplicative impact leading to 12-fold higher odds of poor outcomes, widening health disparities in LN. These findings could guide future health-equity focused interventions to address outcome disparities in LN.

Disclosure: S. Garg: None; **B. Boderman**: None; **N. Sweet**: None; **D. Montes**: None; **B. Astor**: None; **S. Lim**: None; **C. Bartels**: Pfizer, 5.

Abstract Number: 0181

Increased Prevalence of and Acute Hospital Events Among Medicare Systemic Lupus Erythematosus Patients Living in Socially Vulnerable Counties in the United States

Emily Cosentino, John Pearce and Jim Oates, Medical University of South Carolina, Charleston, SC

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Healthcare Disparities in Rheumatology Poster I: Lupus
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is more prevalent and has greater adverse health outcomes in women, minorities, and individuals with low socioeconomic status (SES), particularly in Medicaid populations. These associations have not been reported in the Medicare population of older or disabled individuals. Our purpose is to analyze the association between environments of social vulnerability and SLE prevalence and acute hospital events in a Medicare population within the United States.

Table 1. Demographics of the total Medicare SLE population with 2 or more ICD-10 codes at least 30 days apart

Characteristics	Frequency (n)	Percentage
Sex		
Male	11,806	10.7%
Female	98,771	89.3%
Race/Ethnicity		
White	75894	68.6%
Black	24838	22.5%
Hispanic	4474	4.0%
Asian	1755	1.6%
Native American	960	0.87%
Other	1590	1.4%
Unknown	1066	1.0%
Age		
19-49	20520	18.6%
50-64	29611	26.8%
65-74	38419	34.7%
75-80	12786	11.6%
80+	9241	8.6%
Total	110577	100%

Table 2. Spearman's correlation r values and 95% confidence intervals between prevalence of SLE, ER visit rates, and hospitalization rates with SVI themes rank, themes, and subthemes.

	R values	95% Confidence Intervals (2-tailed)
Prevalence:		
SVI rank	0.408	0.363 to 0.452
Themes:		
Theme 1: Socioeconomic Status	0.431	0.386 to 0.473
Theme 2: Household Composition & Disability	0.364	0.317 to 0.410
Theme 3: Minority Status & Language	0.135	0.082 to 0.187
Theme 4: Housing Type & Transportation	0.135	0.082 to 0.187
ER visits:		
SVI rank	0.222	0.168 to 0.274
Themes:		
Theme 1: Socioeconomic Status	0.227	0.174 to 0.279
Theme 2: Household Composition & Disability	0.224	0.170 to 0.276
Theme 3: Minority Status & Language	0.122	0.067 to 0.176
Theme 4: Housing Type & Transportation	-0.009	-0.065 to 0.047
Hospitalization Rates:		
SVI rank	0.113	0.051 to 0.174
Themes:		
Theme 1: Socioeconomic Status	0.130	0.068 to 0.191
Theme 2: Household Composition & Disability	0.096	0.034 to 0.157
Theme 3: Minority Status & Language	0.075	0.013 to 0.137
Theme 4: Housing Type & Transportation	-0.010	-0.072 to 0.052

Table 3. Logistic regression modeling of the relationship between SVI subtheme variables and SLE prevalence and ER visit rate.

Prevalence:

Variables	Beta	t	Sig.	95% CI for B
Minority	0.301	6.390	<0.001	0.058 to 0.110
No HS Diploma	0.180	4.966	<0.001	0.037 to 0.085
Age 17 or Younger	0.104	3.867	<0.001	0.018 to 0.056
Civilian with Disability	0.108	2.700	.007	0.009 to 0.056
Percent Uninsured	0.138	4.178	<0.001	0.002 to 0.006
Crowding	-0.088	-2.940	.003	-0.065 to -0.013
Age 65 or Older	-0.146	-4.301	<0.001	-0.067 to -0.025
Multi-Unit Structures	-.141	-5.012	<0.001	-0.093 to -0.041
Limited English	-0.174	-5.323	<0.001	-0.115 to -0.053

ER Visits:

Variables	Beta	t	Sig.	95% CI for B
Single-Parent Households	0.111	3.521	<0.001	0.127 to 0.445
Below Poverty	0.087	2.468	0.014	0.029 to 0.257
Mobile Homes	0.086	2.347	0.019	0.010 to 0.220
Age 65 or Older	-0.067	-2.125	.0.034	-0.206 to -0.008
Multi-Unit Structures	-0.060	-1.853	0.064	-0.304 to 0.009
Limited English	-0.063	-2.134	.033	-0.305 to -0.013

Methods: This was a cross-sectional study utilizing the Centers for Disease Control and Prevention (CDC)/Agency for Toxic Substances and Disease Registry (ATSDR) Social Vulnerability Index (SVI) and Lupus Research Alliance Lupus Index Medicare data at a county level. Individuals enrolled in fee-for-service Medicare in 2016 who were diagnosed with SLE by 2 or more ICD-9 codes 30 or more days apart were included. We examined the association between the prevalence of and acute hospital event rates among SLE patients and overall, SVI rank, 4 themes, and 15 subthemes within each county.

Results: The Medicare SLE population was primarily composed of female and White patients (Table I). Using ranked correlation, SVI themes and each of subthemes 1-4 were positively correlated with SLE prevalence, especially themes 1 and 2 (SES and Household Composition and Disability) (Table II). Themes 1 and 2 were positively correlated with ER visits, while theme 4 (Household type and Transportation) was negatively associated with ER visits (Table II). SVI themes and hospitalization rates were the least strongly correlated, however themes 1,2 and 3 (Minority and Non-English-speaking) were positively correlated, while theme 4 was negatively correlated (Table II). In backward stepwise logistic regression analysis, several subthemes were important in the models of prevalence and ER visit rates (Table III). SLE Prevalence was the variable most strongly correlated with SVI themes.

Conclusion: These findings mirror those from studies of SLE prevalence and ED visits in Medicaid populations as well as COVID prevalence and heat-exposure ED visits in socially vulnerable non-SLE patients. This suggests that environments of social vulnerability are an independent risk factor, but the elements of the environments (social stress, toxins, infrastructure, and proximity to care providers) that may drive risk are not addressed by this study. To our knowledge, no other study has examined SLE prevalence and acute hospital events within the Medicare population. These findings inspire the hypothesis that risk models can be used as a tool to identify at risk populations for strategic intervention to reduce disparities in outcomes.

Disclosure: E. Cosentino: None; **J. Pearce**: None; **J. Oates**: None.

Abstract Number: 0182

Impact of Neighborhood-level Child Opportunity on Disease Activity in Children with Lupus

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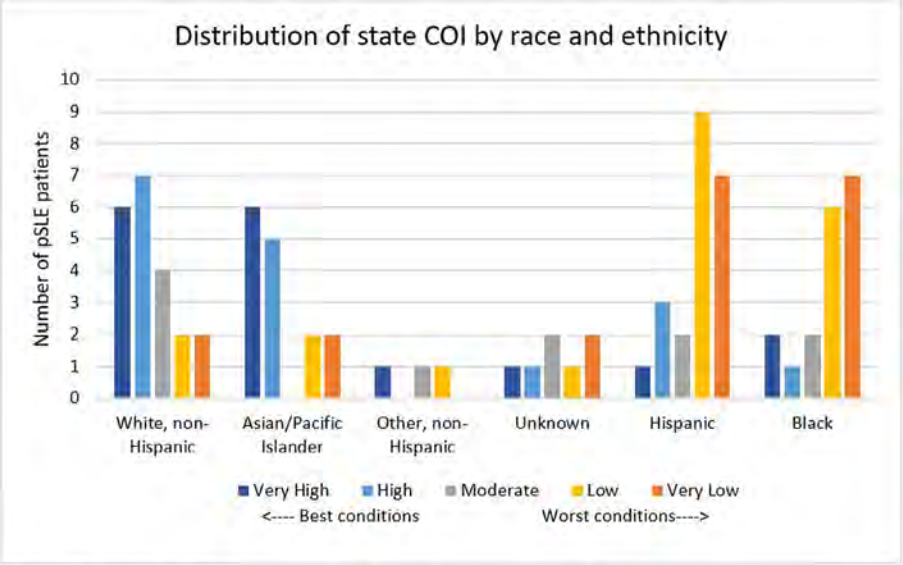
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Healthcare Disparities in Rheumatology Poster I: Lupus
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Racial disparities in outcomes of pediatric SLE (pSLE) have persisted over time. This may be mediated by structural racism, which segregates children belonging to minority groups into neighborhoods with lower childhood opportunity, defined as resources and conditions that promote healthy childhood development across domains of education, socioeconomics, and physical environment. We determined whether lower neighborhood-level opportunity associates with greater disease activity at initial SLE presentation or over time.



Methods: We conducted a cohort study of children newly diagnosed with SLE between 2016-2022, inclusive, in the Boston Children's Hospital Lupus Registry. The index visit was the first inpatient or outpatient rheumatology encounter with a physician diagnosis of SLE. The primary outcome was the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K). Geocoded addresses were linked to the Child Opportunity Index 2.0 (2015) by census tract and categorized as: very high, high, moderate, low, or very low opportunity, based on national and state level rankings. Median SLEDAI-2K at the index visit for children in each state-ranked COI category was compared to those living in very high COI areas using Wilcoxon rank sum tests. Associations between COI and disease activity over time were estimated using linear mixed effects models adjusted for time, insurance status, nephritis and neurologic involvement at presentation; additional covariates tested included age at SLE onset, sex assigned at birth, race and ethnicity, non-English primary language, and initial SLEDAI-2K.

Results: We included 644 visits with calculable SLEDAI-2K scores, comprised by 86 patients with pSLE, with a median of 7 visits/patient [2-11] during the study period. The majority of Black (13/18, 72%) and Hispanic children (16/22, 73%) lived in low or very low state-ranked COI areas, whereas a 62% of Non-Hispanic White and 73% of Asian children lived in high or very high COI areas (**Figure 1**). In this cohort, nationally ranked COI was skewed towards very high (37%) and high (16%) average opportunity (**Table 1**). Children living in low opportunity areas ranked within state had higher SLEDAI scores at initial presentation compared to patients living in very high opportunity areas (median 14 [6-22] vs. 7 [4-8.5], p=0.03). Living in census tracts with moderate, low or very low COI (vs. very high) associated with significantly higher SLEDAI-2K over time compared to living in very high COI areas, both with or without adjustment for time, insurance status, race and ethnicity, and major organ involvement (Table 2). There was a significant test of trend (p=0.001). Results were similar when adjusting for initial SLEDAI-2K at presentation.

Conclusion: For children with pSLE in an area of the U.S. with high average opportunity levels, lower relative neighborhood-level childhood opportunity associated with higher SLE disease activity at initial presentation to care and during follow-up, independent of initial disease severity. Area-level conditions, among other factors in lower resourced areas, may mediate inequitable outcomes of pSLE at numerous points, including initial access to subspecialty care and after establishing care.

Table 1. Characteristics of Newly Seen Children with SLE in the BCH Lupus Registry (2016-2022)

	N = 86
Age at index SLE visit, median (IQR)	15.2 (12.8 - 17.0)
Female sex	70 (81%)
Race and ethnicity	
Asian/Pacific Islander	15 (17%)
Black	18 (21%)
Hispanic	22 (26%)
Other, non-Hispanic	3 (3%)
Unknown	7 (8%)
White, non-Hispanic	21 (24%)
Hispanic country of origin	
Central American	1 (5%)
Dominican American	2 (9%)
Puerto Rican American	4 (18%)
Mexican American	1 (5%)
South American	5 (23%)
Unknown	9 (41%)
Non-English primary language	13 (15%)
Insurance status	
Private	45 (52%)
Public	40 (47%)
Uninsured	1 (1%)
Childhood Opportunity Index, State Rank	
Very High, n (%)	17 (20%)
High	17 (20%)
Moderate	11 (13%)
Low	21 (24%)
Very Low	20 (23%)
Childhood Opportunity Index, National Rank	
Very High	32 (37%)
High	14 (16%)
Moderate	14 (16%)
Low	12 (14%)
Very Low	14 (16%)
Initial SLEDAI-2K at presentation, median (IQR)	9.0 (5.0 - 18.0)
Most recent SLEDAI-2K, median (IQR)	2.0 (2.0 - 6.0)
Hospitalized at index visit	30 (35%)
Nephritis at presentation*	33 (38%)
Neurologic involvement at presentation*	9 (10%)

*Onset confirmed within 3 months of index visit

Table 2. Association between relative childhood opportunity within state and disease activity over time among children with pSLE followed at Boston Children's Hospital, 2016-2022

	Univariable^			Multivariable		
	β	95% CI	p	β	95% CI	p
Child Opportunity Index						
Very High		*(reference)*				
High	1.5	[-0.7, 3.8]		1.4	[-0.5, 3.3]	
Moderate	3.0	[0.6, 5.5]	*	2.7	[0.7, 4.7]	**
Low	3.9	[1.8, 6.0]	***	3.7	[2.0, 5.4]	***
Very Low	2.7	[0.7, 4.7]	**	2.9	[1.3, 4.6]	**
Insurance status						
Public	1.2	[-0.4, 2.8]		1.4	[-0.1, 3.0]	
Private		*(reference)*				
Other/Uninsured	2.1	[1.0, 3.2]	***	1.6	[0.0, 3.2]	
Race						
Asian	2.3	[-0.4, 5.1]		1.1	[-0.7, 2.9]	
Black	1.8	[-0.2, 3.8]		-1.2	[-3.4, 1.1]	
Hispanic	1.0	[-0.9, 3.0]		-1.7	[-3.5, 0.1]	
Other, non-Hispanic	-0.8	[-3.0, 1.4]		-0.4	[-3.7, 2.9]	
Unknown	1.7	[-2.2, 5.6]		-1.0	[-3.8, 1.9]	
White, non-Hispanic		*(reference)*				
Non-English language	0.7	[-1.5, 2.9]				
Age at SLE onset	-0.2	[-0.4, 0.1]				
Male sex	0.5	[-1.0, 2.1]				
Nephritis at presentation	3.8	[2.4, 5.2]	***	3.1	[1.7, 4.5]	***
Neurologic involvement at presentation	4.2	[1.8, 6.6]	***	3.4	[1.6, 5.2]	***
Initial SLEDAI-2K at presentation	0.1	[0.0, 0.2]	**			
Time (month)	-0.3	[-0.4, -0.2]	***	-0.3	[-0.4, -0.2]	***
Time-squared	0.004	[0.002, 0.006]	***	0.004	[0.003, 0.006]	***

Linear mixed effects models with random slope and random intercept, robust variance estimators for N=86 patients with 644 evaluable visits

^ All models adjusted for follow-up time and time-by-time interaction

*p<0.05; ** p<0.01; *** p<0.001

Disclosure: J. Chang: None; **G. Alonzi**: None; **E. Smitherman**: None; **P. Patel**: AbbVie/Abbott, 12, Site Principal Investagator, Pfizer, 12, Site Principal Investigator; **G. Morgan**: None; **L. Huie**: None; **K. Costenbader**: Amgen, 2, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Eli Lilly, 2, Exagen Diagnostics, 5, Gilead, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5; **M. Son**: None.

Abstract Number: 0183

Barriers and Facilitators to Recruiting Underrepresented Participants for Clinical Trials: Insights from the Lupus Clinical Investigators Network (LuCIN)

Tessa Englund[1], Christine Lee[2], Julie Hsieh[2], Richardae Araojo[2], Julia Mariano[1], Emily McCormick[3], Stacie Bell[4], Albert Roy[5] and Saira Sheikh[1], [1]University of North Carolina at Chapel Hill, Chapel Hill, NC, [2]U.S. Food and Drug Administration, Silver Spring, MD, [3]Thurston Arthritis Research Center, Chapel Hill, NC, [4]Lupus Therapeutics, Lakewood, CO, [5]Lupus Research Alliance, New York, NY

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Healthcare Disparities in Rheumatology Poster I: Lupus

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Despite greater prevalence of lupus among diverse, racial and ethnic minority populations, marked gaps exist between populations affected by lupus and those enrolled in clinical trials. Sponsored by the Lupus Research Alliance, the Lupus Clinical Investigators Network (LuCIN) is the largest lupus clinical trials network in North America, comprised of 57 leading academic institutional sites across the US and Canada. This study aimed to describe and discuss prominent barriers and potential solutions to support recruitment and participation in lupus clinical trials conducted through the LuCIN network.

Methods: Data from the LuCIN annual survey of site investigators and research staff (site representatives) collected between March and July 2022 were prepared for analysis. The survey included questions to assess perspectives and practices around clinical trial recruitment. Descriptive statistics were computed to identify the most common barriers and facilitators to recruitment and retention of patients in lupus clinical trials.

Results: Completed survey responses were collected from representatives of 55 LuCIN sites. When asked about sources of patient referrals at their site, most respondents reported receiving patient referrals to LuCIN clinical trials from physicians within their institution (94.5%), while referrals from external community clinicians were reported by 52.7% of respondents. The most frequently reported barriers to LuCIN clinical trial recruitment were restrictive inclusion/exclusion criteria (89.1%), participant mistrust in research (38.2%), and a lack of referrals from healthcare providers (32.7%). Approximately half (49.1%) of sites reported that they had not received training on recruitment of underrepresented patients in clinical trials. When asked about the barriers to establishing a plan to improve recruitment of diverse participants, over half of site

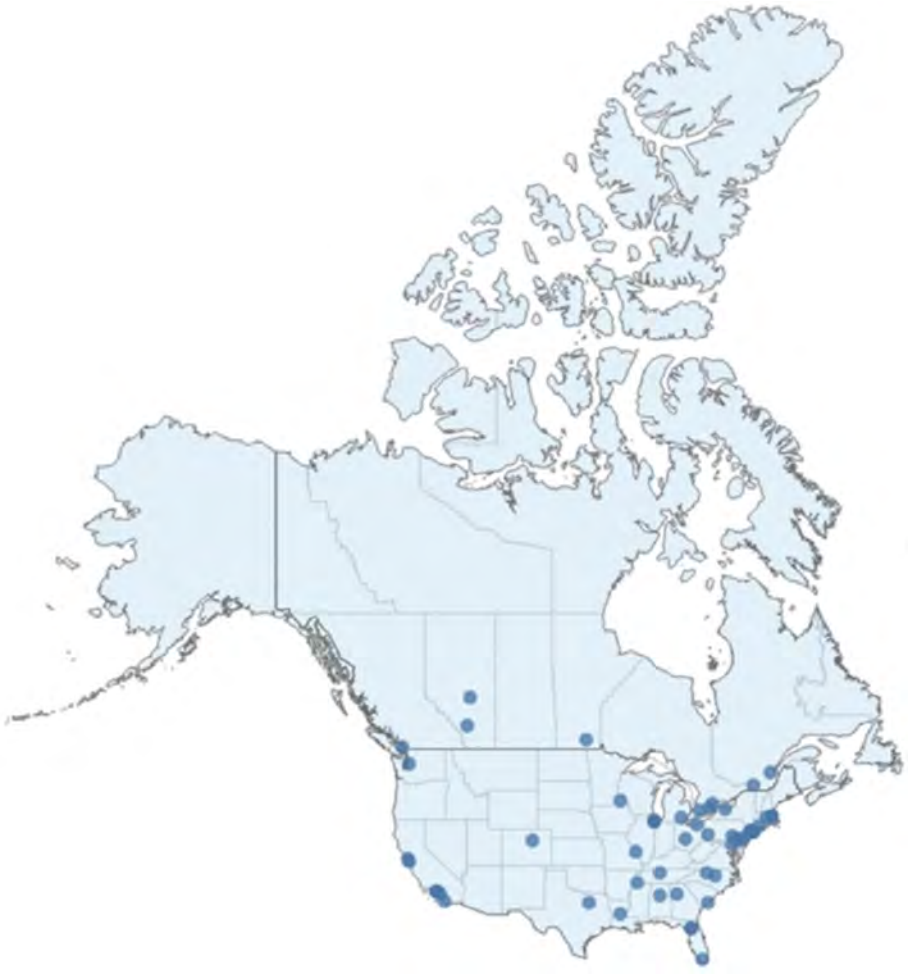


Figure. LuCIN annual survey respondent site locations (n=55 site representatives)

Table. Selected LuCIN site survey respondent characteristics and perspectives on clinical trial recruitment (n=55 site representatives)

Survey Question	n	%
Do you receive patient referrals from the following? Check all that apply.		
Physicians at your institution	52	94.5%
Community providers	29	52.7%
We do not receive any patient referrals	2	3.6%
There are several barriers to recruiting participants for clinical trials/research studies at a given institution. Please select the top 3 barriers your institution faces while recruiting participants.		
Lack of email/phone response	13	23.6%
Lack of participant awareness of clinical trials	12	21.8%
Participant mistrust in research	21	38.2%
Poor attendance at clinics	6	10.9%
Lack of recruitment staff	12	21.8%
Lack of funding for advertisements, translation, or other study related needs	6	10.9%
Restrictive inclusion/exclusion criteria	49	89.1%
Health care providers not referring patients	18	32.7%
Lack of cultural/diversity training	1	1.8%
Competing clinical trials/studies that are recruiting the same type of participants	11	20.0%
Has your site received training for recruitment of underrepresented groups in clinical trials?		
Yes	28	50.9%
No	27	49.1%
What are the barriers to setting up a plan to increase diversity of participants recruited into clinical trials/research studies? Check all that apply.		
Lack of appropriate staff to carry out a plan	20	36.4%
Lack of cultural/diversity training	5	9.1%
Lack of funding for this type of planning and program development	32	58.2%
Lack of time	31	56.4%
What recruitment methods below have you found to be the most effective in recruiting eligible participants for clinical trials? Check all that apply.		
Incentives	21	38.2%
More time to answer participants' questions about the study	17	30.9%
Healthcare provider referral or recommendation	43	78.2%
Conversation with other individuals living with lupus	13	23.6%
Shorter informed consent documents	13	23.6%
The support/backing of their health care provider	37	67.3%
Text messages	5	9.1%
Calls	15	27.3%
Emails	12	21.8%
Brochures	13	23.6%
Posters	6	10.9%
Bulletin Boards	1	1.8%
Recruitment Events	2	3.6%
Online Advertisements	9	16.4%

respondents identified a lack of funding (58.2%) and time (56.4%) as barriers. The patient recruitment strategies respondents most frequently identified as effective approaches included healthcare provider referrals or recommendation (78.2%), support/endorsement from patients' healthcare providers (67.3%), study incentives (38.2%), and additional time to answer potential participants' study-related questions (30.9%).

Conclusion: This work provides valuable insights into key barriers and facilitators reported by sites to the recruitment of underrepresented participants into lupus clinical trials conducted through LuCIN. Findings underscore the need to support opportunities for effective provider-patient communication, as well as engagement between academic and community practices, to improve access and referrals to lupus clinical trials. Future research is needed to explore how these barriers and facilitators relate to clinical trial participation outcomes among underrepresented patients. By understanding these

challenges and leveraging successful recruitment strategies, LuCIN clinical trial sites can promote equity in clinical trial participation among underrepresented groups and further advance lupus research.

Disclosure: T. Englund: None; **C. Lee**: None; **J. Hsieh**: None; **R. Araojo**: None; **J. Mariano**: None; **E. McCormick**: None; **S. Bell**: None; **A. Roy**: None; **S. Sheikh**: AstraZeneca, 2, Aurinia Pharmaceuticals Inc., 2, Biogen, 2, GSK, 1, 1, 2, Lilly USA, 2, Pfizer, 5.

Abstract Number: 0184

Material Need Insecurities Are Associated with Worse Patient-Reported Outcomes Among Individuals with SLE

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Healthcare Disparities in Rheumatology Poster I: Lupus
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Lower socioeconomic status is associated with greater disease activity and mortality in systemic lupus erythematosus (SLE); however, mechanisms driving this are yet to be understood. Qualitative research suggests that material need insecurities, such as concerns about housing, food, or medical costs, impair patients' ability to manage SLE, exacerbating the effects of poverty. We describe the prevalence of food, housing, SLE healthcare, and financial insecurity in an SLE cohort and test their associations with patient-reported outcomes (PROs).

Methods: Data were derived from a statewide SLE epidemiology study involving a cohort of individuals with physician-confirmed SLE. Food, housing, healthcare, and financial material need insecurities were assessed by validated screening tools. PROs were obtained via PROMIS, Neuro-QoL, Patient Health Questionnaire-8, and General AnxietyDisorder-7 instruments. Poverty was defined as household income ≤125% of the federal poverty limit.Lower education was defined as less than a bachelor's degree. The association of material need insecurities with PROs was assessed by multivariable linear regression models adjusting for demographics, lupus characteristics, and comorbidities. We examined the relationship between insecurities with poverty and education via unadjusted ANOVA and by including interaction terms in the adjusted regression model.

Results: Among 252 participants, 53.6% had at least one insecurity (Table 1). Insecurities were highly prevalent, and more common in those with poverty and lower education (79.3% vs. 44.8% of those with low vs. higher incomes, respectively, had any insecurities and 71.7% vs. 39.1% of those with lower vs. higher education, respectively, had any insecurities). Unadjusted analyses examining the relationship between material need insecurities and PROs revealed significant differences in all PROs between those with and without any material needs insecurity and by the number of insecurities. In the unadjusted models of the insecurity-poverty groups, overall significant differences between groups were noted for each PRO. In each case, the post-hoc means test after ANOVA analyses indicated differences between one or both insecurity groups (either "insecurity + no poverty" or "insecurity + poverty") and the no insecurity + no poverty group. Similar results were noted for the insecurity-education group analysis (Table 2). Adjusted multivariate analyses revealed that participants with any

Table 1: Cohort Characteristics

Sociodemographic characteristics	Mean ± SD or % (n)
Age, years	49.7 ± 13.4
Female	90.5 (228)
Race and ethnicity *	
Asian	30.6 (77)
Black	9.9 (25)
Hispanic	23.4 (59)
White	33.3 (84)
Other	2.8 (7)
Income below poverty	11.5 (29)
Education below college degree	15.5 (39)
Married	57.0 (143)
Housing, financial, food, or SLE care insecurity	53.6 (135)
Patient-reported outcomes (PROs)	
PROMIS Physical Function	47.2 ± 9.8
PROMIS Pain Interference	53.3 ± 9.7
PROMIS Fatigue	52.9 ± 10.6
PROMIS Sleep Disturbance	51.2 ± 9.2
NeuroQoL Cognitive Function	47.3 ± 9.7
PHQ-8 (depressive symptoms)	5.3 ± 4.5
GAD-7 (anxiety)	4.3 ± 4.4
General health characteristics	
Number of comorbid conditions	2.0 ± 1.7
Obesity (BMI ≥ 30)	25.0 (63)
SLE-related	
SLE disease duration (years)	22.4 ± 10.7
SLE disease damage (BILD)	2.5 ± 2.4
Medications	
High-dose glucocorticoids	13.9 (35)
Immunosuppressives	51.2 (129)

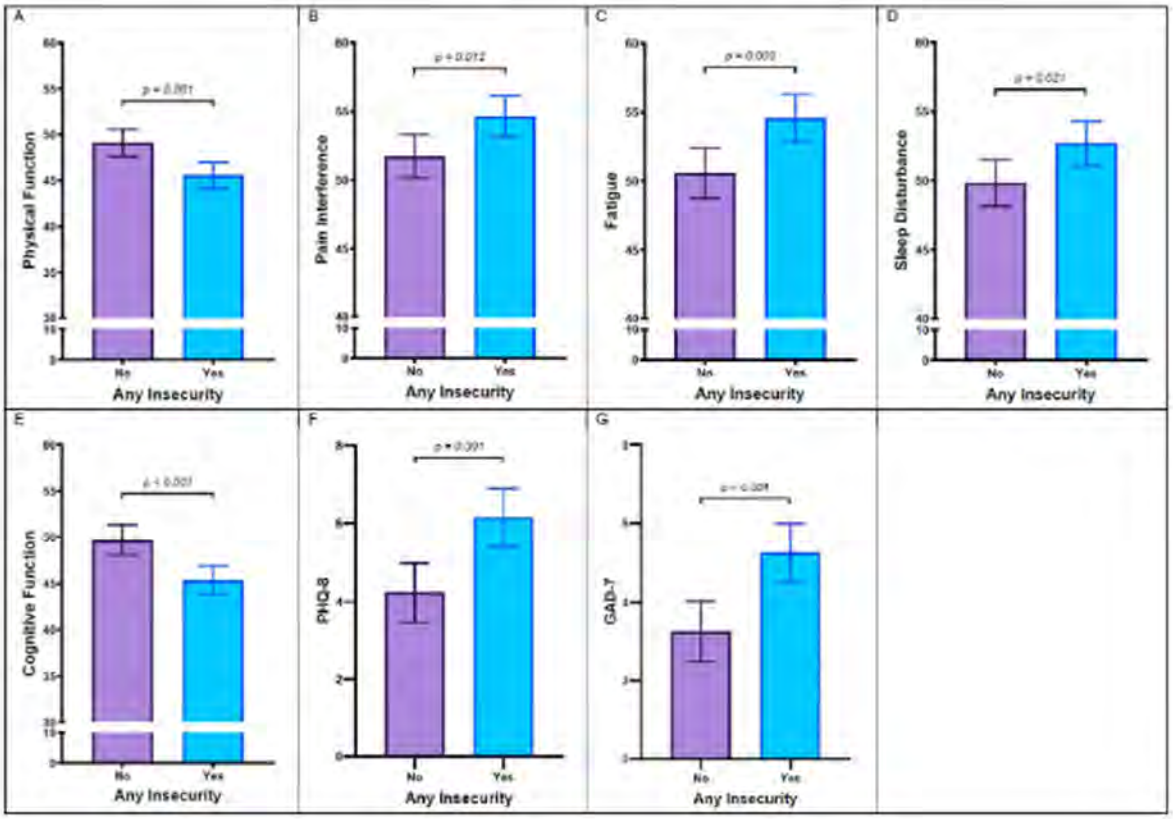
* Race and ethnicity categories are mutually exclusive.
BILD = Brief Index of Lupus Damage; BMI= body mass index; GAD-7= General Anxiety Disorder-7; PHQ-8= Patient Health Questionnaire-8; PROMIS= Patient-reported Outcomes Measurement Information System; SLE= systemic lupus erythematosus

Table 2: Unadjusted differences in patient-reported outcomes by insecurities, income, and education

	Physical Function[a]	Pain Interference[b]	Fatigue[b]	Sleep Disturbance[b]	Cognitive Function[a]	Depression[b]	Anxiety[b]
Any insecurity							
No (n = 117)	50.4 ± 0.7	50.7 ± 9.2	49.5 ± 10.0	49.4 ± 9.0	50.2 ± 8.9	3.9 ± 4.0	2.9 ± 3.6
Yes (n = 135)	44.4 ± 8.9	55.5 ± 9.5	55.8 ± 10.2	53.3 ± 9.1	44.8 ± 8.8	6.5 ± 4.6	5.5 ± 4.7
p	<0.0001	<0.0001	<0.0001	0.0008	<0.0001	<0.0001	<0.0001
Number of insecurities							
0 (n = 117)	50.4 ± 0.7	50.7 ± 9.2	49.5 ± 10.0	49.4 ± 9.0	50.2 ± 8.9	3.9 ± 4.0	2.9 ± 3.6
1 (n = 63)	*46.1 ± 9.3	*54.6 ± 9.5	*55.1 ± 10.8	52.6 ± 9.2	*46.0 ± 9.9	*6.2 ± 4.6	*4.7 ± 4.1
≥2 (n = 72)	*42.9 ± 8.4	*56.3 ± 9.6	*56.3 ± 9.7	*54.0 ± 9.0	*43.8 ± 7.8	*6.8 ± 4.6	*6.2 ± 5.1
p	<0.0001	0.0002	<0.0001	0.0024	<0.0001	<0.0001	<0.0001
Poverty							
No (n = 206)	48.0 ± 9.7	52.7 ± 9.5	52.3 ± 10.7	51.2 ± 8.9	47.8 ± 9.3	5.1 ± 4.4	4.2 ± 4.3
Yes (n = 29)	42.1 ± 8.6	57.0 ± 10.1	55.3 ± 10.6	52.2 ± 11.3	44.8 ± 9.6	6.2 ± 5.5	5.2 ± 4.9
p	0.002	0.02	0.17	0.59	0.10	0.24	0.26
Lower education (<college degree)							
No (n = 138)	49.5 ± 9.5	51.4 ± 9.5	51.6 ± 10.6	50.6 ± 8.4	48.3 ± 9.2	4.7 ± 4.2	3.7 ± 4.1
Yes (n = 113)	44.3 ± 9.3	55.6 ± 9.4	54.6 ± 10.4	52.8 ± 10.0	46.0 ± 9.3	6.1 ± 4.8	5.0 ± 4.7
p	<0.0001	0.0005	0.03	0.06	0.04	0.01	0.02
Any insecurity x income							
No insecurity + no poverty (n = 106)	51.0 ± 9.4	50.1 ± 8.1	49.1 ± 10.0	49.8 ± 8.7	50.6 ± 8.8	3.6 ± 3.5	2.9 ± 3.6
No insecurity + poverty (n = 6)	41.9 ± 10.6	58.6 ± 11.5	56.4 ± 10.2	45.3 ± 13.2	45.9 ± 10.7	8.2 ± 8.3	2.8 ± 3.8
Insecurity + no poverty (n = 100)	*44.8 ± 9.1	*55.4 ± 9.4	*55.6 ± 10.5	52.7 ± 9.0	*44.9 ± 8.8	*6.7 ± 4.7	*5.5 ± 4.6
Insecurity + poverty (n = 23)	*42.1 ± 8.2	*56.7 ± 10.0	55.0 ± 10.9	54.0 ± 10.4	*44.5 ± 9.6	5.6 ± 4.6	*5.8 ± 5.1
p	<0.0001	<0.0001	<0.0001	0.018	<0.0001	<0.0001	<0.0001
Any insecurity x education							
No insecurity + higher education (n = 84)	51.8 ± 9.2	49.6 ± 8.9	49.1 ± 9.9	49.9 ± 8.5	50.6 ± 9.1	3.8 ± 3.8	3.0 ± 3.7
No insecurity + lower education (n = 32)	*46.5 ± 10.1	53.8 ± 9.4	50.7 ± 10.6	48.5 ± 10.5	48.9 ± 8.7	4.3 ± 4.8	2.8 ± 3.4
Insecurity + higher education (n = 54)	*45.8 ± 9.0	*54.2 ± 9.7	*55.3 ± 10.7	51.6 ± 8.4	*44.8 ± 8.3	*6.1 ± 4.5	*4.9 ± 4.4
Insecurity + lower education (n = 81)	*43.4 ± 8.9	*56.4 ± 9.4	*56.0 ± 9.9	*54.5 ± 9.4	*44.8 ± 9.3	*6.8 ± 4.7	*5.9 ± 4.9
p	<0.0001	<0.0001	<0.0001	0.002	<0.0001	<0.0001	<0.0001

Data are mean ± SD. Differences in group means were tested with t-tests or analyses of variance.
* Significantly different from "No insecurity, income>poverty/high education" group based on post-hoc means test.
[a] Higher scores reflect better outcomes
[b] Higher scores reflect worse outcomes

Figure: Adjusted marginal means from multivariable analysis, by any insecurity



Adjusted means (95% confidence interval) calculated from multivariable linear regression analyses controlling for age, sex, race and ethnicity, marital status, education, income, comorbid conditions, obesity, disease duration, disease damage, high glucocorticoid use, and immunosuppressive use·

P values from multivariable linear regression, compared to no insecurities group

PHQ-8 = Patient Health Questionnaire, measure of depressive symptoms; GAD-7 = Generalized Anxiety Disorder questionnaire

insecurity had significantly worse scores across all PROs measured (Figure); individuals with more insecurities had worse PROs. There were no statistically significant interactions between insecurities and poverty or education.

Conclusion: Having any material need insecurity was associated with worse outcomes for patients with SLE regardless of poverty or education. Findings provide insight into mechanisms by which social risk factors can affect SLE outcomes and underscore the need for provider awareness of these modifiable factors and knowledge of relevant resources for interventions.

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Abstract Number: 0185

Classifying Individuals with Rheumatic Conditions as Financially Insecure Using Electronic Health Record Data and Natural Language Processing: Algorithm Derivation and Validation

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Healthcare Disparities in Rheumatology Poster I: Lupus

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Social determinants of health (SDoH) such as financial insecurity contribute to disparities in rheumatic disease care and outcomes but are not routinely included in structured electronic health record (EHR) data, (e.g., ICD-10 billing codes). SDoH described in clinical notes are not readily extractable and therefore cannot be easily incorporated into research studies. We leveraged natural language processing (NLP) to extract terms related to financial insecurity and used machine learning models to develop and validate an algorithm to identify individuals with this critical SDoH.

Methods: We randomly selected 600 patients from 20,395 with rheumatic or musculoskeletal conditions enrolled in an integrated care management program (iCMP) between 1/1/12-10/18/21. iCMP provides care for medically and psychosocially complex patients. The study team (social epidemiologists, pediatric and adult rheumatologists, bioinformaticians) defined the construct "financial insecurity" using nominal group technique. Reviewers (MTC, SU, CHF) operationalized this definition with manual EHR reviews to establish the gold standard. Individuals were classified as having definite, possible, or no financial insecurity in separate training and validation cohorts. We constructed a context-driven lexicon containing terms for financial insecurity using data from PubMed, the Unified Medical Language System, and previous EHR reviews (Table 1). All available notes were then processed using NLP with the context-driven lexicon. We developed models using logistic regression, LASSO regression, and random forest, trained on EHR-based review of cases of financial insecurity (definite or definite and possible combined) and determined the performance metrics for each model.

Table 1. Terms and Phrases Selected for Use in Models to Classify Individuals as Ever Financially Insecure Based on Their Presence in Clinical Notes

Can't Afford	AFFORD.N*, CAN.T.AFFORD, CANNOT.AFFORD, DIFFICULTY.AFFORDING, UNABLE.TO.AFFORD
Enough Money	ENOUGH.MONEY.N, FINANCIAL.LIMITATIONS, NO.MONEY
Financial Difficulties	FINANCIAL.DIFFICULTIES, FINANCIAL.HARDSHIP, FINANCIAL.HARDSHIPS, FINANCIAL.ISSUES, FINANCIAL.ISSUE
Financial Resources	FINANCIAL.RESOURCES.N, JOB.LOSS, LIMITED.INCOME, LIMITED.FINANCIAL.RESOURCES, LOSS.OF.EMPLOYMENT, LOSS.OF.INCOME, LOW.INCOME, LOWER.INCOME, NO.INCOME, ONLY.INCOME
Financial Stress	FINANCIAL.STRESS, FINANCIAL.STRUGGLES, STRUGGLING.FINANCIALLY, FINANCIAL.STRESSES
Financial Stressor	FINANCIAL.STRESSOR, FINANCIAL.STRESSORS
High Copay	HIGH.COPAY, HIGH.CO.PAY, HIGH.COPAYMENTS, HIGH.COPAYMENT, HIGH.CO.PAYS
Pay Rent	PAY.RENT.N, PAY.RENT, RENT.BURDEN, RENTAL.ASSISTANCE, RENTAL.ASSISTANCE.N, PAYING.RENT, PAYING.RENT.N
Public Housing	PUBLIC.HOUSING, SUBSIDIZED.HOUSING
Voucher	VOUCHER, VOUCHERS, WELFARE
Eviction	EVICTION
Financial Concerns	FINANCIAL.CONCERNS
Financial Situation	FINANCIAL.SITUATION

*"N" indicates that the feature is negated in context (e.g., AFFORD.N means "can't afford").

Results: Among 600 identified patients, we excluded 62 due to lack of notes, clear rheumatologic diagnoses, or iCMP enrollment confirmation (N=538). 245,142 notes were processed from the training (N=366) and validation cohorts (N=172). Financial insecurity was present among 100 individuals (27%) in the training cohort and 63 (37%) in the validation cohort (Table 2). All models (logistic regression, LASSO, random forest) classifying the presence of financial insecurity performed similarly regardless of the algorithm used, with logistic regression models achieving the overall highest positive predictive value (PPV) of 0.98. (Table 3). The logistic regression models had specificities ranging from 0.94-0.98, sensitivities

Table 2: Baseline Characteristics of Patients with Rheumatic of Musculoskeletal Conditions in the Training and Validation Cohorts (N=538)

Characteristics/Variables	**Training Cohort** (N=366)	**Validation Cohort** (N=172)
Financial Insecurity Present	100 (27)	63 (37)
Age – Mean (SD)	72.5 (13.0)	75.7 (13.4)
Sex - N (%)		
Male	141 (39)	62 (36)
Female	225 (61)	110 (64)
Race - N (%)		
White	288 (79)	143 (83)
Black	38 (10)	12 (7)
Asian	3 (1.7)	2 (0.5)
Not Disclosed	8 (2.2)	5 (2.9)
Other	30 (8.2)	9 (5.2)
Ethnicity - N (%)		
Hispanic	35 (10)	14 (8)
Not Hispanic	293 (80)	147 (85)
Unavailable/Other	38 (10)	11 (6)
Rheumatic/Musculoskeletal Condition – N (%)		
Connective Tissue Diseases+	18 (4.9)	8 (4.7)
Crystalline arthritis	55 (15)	17 (9.9)
Inflammatory Arthritis	58 (16)	16 (9.3)
Osteoarthritis	155 (42)	91 (53)
Polymyalgia Rheumatica	19 (5.2)	8 (4.7)
Other*	61 (17)	32 (19)
SDoH - Financial Insecurity– N (%)		
Financial - Definite	100 (27)	63 (37)
Financial - Possible	89 (24)	32 (19)
Primary Insurance - N (%)		
Medicaid	20 (5.5)	11 (6.4)
Medicare	310 (85)	133 (77)
Commercial	21 (5.7)	18 (10)
Other	10 (5.8)	15 (4.1)

+Includes systemic lupus erythematosus, Sjogren's syndrome, mixed connective tissue disorder, systemic sclerosis
*Includes sarcoidosis, vasculitis, dermatomyositis and undifferentiated rheumatic conditions

Table 3: Model Performance for Definite and Definite and Possible Financial Insecurity

Definite Financial Insecurity Models			
	Logistic Regression	**Lasso Regression**	**Random Forest**
Sensitivity	0.27 (0.17, 0.37)	0.29 (0.19, 0.38)	0.29 (0.19, 0.38)
Specificity	0.98 (0.84,1.00)	0.98 (0.84, 1.00)	0.98 (0.84, 1.00)
PPV	0.89 (0.76, 1.00)	0.9 (0.77, 1.00)	0.9 (0.77, 1.00)
Definite and Possible Financial Insecurity Models			
	Logistic Regression	**Lasso Regression**	**Random Forest**
Sensitivity	0.54 (0.50, 0.58)	0.20 (0.08, 0.32)	0.48 (0.46, 0.51)
Specificity	0.94 (0.80, 1.00)	0.99 (0.84, 1.00)	0.96 (0.82, 1.00)
PPV	0.91 (0.78, 1.00)	0.95 (0.81, 1.00)	0.94 (0.80, 1.00)

PPV=Positive Predictive Value

ranging from 0.27-0.54 and PPVs of 0.89-0.91. LASSO regression models had specificities ranging from 0.98-0.99, sensitivities of 0.20-0.29, and PPVs of 0.90-0.95. The random forest models had specificities ranging from 0.96-0.98, sensitivities of 0.29-0.48, and PPVs of 0.90-0.94.

Conclusion: Using a context-driven general lexicon for financial insecurity, NLP enabled the development of algorithms to classify individuals with terms or phrases indicative of financial insecurity in free-text EHR notes. These models with high positive predictive values could be leveraged to identify patients with this SDoH for future health equity interventions.

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Abstract Number: 0186

Retention in Rheumatology Care and on Hydroxychloroquine and SLE Outcomes by Neighborhood Disadvantage: A Medicare Cohort Study of Acute Care and Kidney Failure

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Healthcare Disparities in Rheumatology Poster I: Lupus

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Gaps in systemic lupus (SLE) care are believed to contribute to higher kidney failure (ESKD), acute care use, mortality, and disease damage in US patients who are Black or disadvantaged. Such disparities in HIV declined >20% by addressing key care steps. We hypothesized that, SLE retention in care by visits or labs would differ by neighborhood disadvantage. We also examined how gaps in SLE care associate with ESKD, acute care, or death to inform actions to reduce disparities.

Methods: This cohort study used a 20% US Medicare sample of patients ≥18 yrs with >12 mos of Medicare A-B in 2013-14 (subset: Part D). SLE was identified by validated criteria: 1 SLE hospital code, 1 rheumatologist code, or 2+ SLE codes 2 mos apart. Baseline comorbidity was measured 6 mos prior. Over 6 mos, 4 care steps were examined: 1) visit retention: ≥ 1 rheumatology visit; 2) lab retention: a C3, C4 or a double-stranded DNA test (two if nephritis); 3) HCQ use: any HCQ claim; and 4) HCQ adherence: >80% of days covered. Outcomes included acute care (emergency or hospital visits) or death, ESKD or death followed until end of data, 12/31/2014. We assessed for disparities by racial identity and neighborhood disadvantage area deprivation index (ADI) quintile. Cox proportional hazards models were used to report hazards ratios (HR) and 95% confidence intervals (CI) for 2 outcomes by 4 care steps controlling for covariates.

Results: Among 15,395 patients with SLE, 88.6% were female and 17.4% identified as Black (Table 1). Overall, 27.9% had prior Medicaid; 35.2% of Black identifying patients lived in the most disadvantaged ADI quintile neighborhoods. Patients living in high ADI (more disadvantage) had 16% lower visit retention (44.5% vs 60.8%, p< 0.001 Table 2), lower lab retention

Table 1. Characteristics of Medicare patients with SLE by rheumatology visit retention (n=15,395)

		Overall SLE	Visit Retained n = 8,106 (52.65%)	Not Visit Retained n = 7,289 (47.35%)	p
Age (mean, [SD])		63.65, [13.98]	63.15 ,[13.65]	64.20, [14.32]	<0.001
18-39		6.72%	7.01%	6.39%	
40-64		35.54%	35.26%	35.86%	0.280
65 plus		57.74%	57.74%	57.74%	
Sex	Female	88.59%	89.81%	87.24%	<0.001
Race/Ethnicity	White	71.71%	69.97%	73.63%	
	Black	17.39%	17.99%	16.72%	
	Asian	1.71%	2.07%	1.31%	<0.001
	American Indian	0.85%	0.58%	1.15%	
	Other/Unknown	1.31%	1.70%	0.88%	
	Hispanic	7.03%	7.69%	6.30%	
Medicaid ever		27.90%	24.75%	31.40%	<0.001
Medicaid reason	Disability	54.59%	53.31%	56.02%	<0.001
RUCA	Urban	68.34%	71.39%	64.95%	
	Large City/ town	10.04%	9.60%	10.52%	<0.001
	Rural	11.89%	10.86%	13.03%	
	Isolated	9.74%	8.15%	11.50%	
ADI neighborhood disadvantage quintile					
Least	1-20	17.75%	20.44%	14.75%	
	21-40	21.01%	21.84%	20.09%	
	41-60	22.07%	22.27%	21.84%	<0.001
	61-80	21.31%	19.90%	22.87%	
Most	81-100	17.88%	15.56%	20.46%	
HCC comorbidity score		1.81, [1.32]	1.62, [1.14]	2.02, [1.47]	<0.001
Diabetes mellitus		34.36%	31.16%	37.91%	<0.001
CKD		31.94%	29.48%	34.67%	<0.001
Anxiety		33.90%	29.19%	39.14%	<0.001
Depression		50.49%	46.03%	55.45%	<0.001
Tobacco use		19.81%	14.82%	25.37%	<0.001
Fibromyalgia & pain		52.58%	52.23%	52.97%	0.369
Baseline Nephrology visit		8.50%	9.78%	7.07%	<0.001
Acute care use or death		5,376 (34.92%)	2,428 (29.95%)	2,948 (40.44%)	
ESKD or death		1,598 (10.38%)	636 (7.84%)	962 (13.20%)	

*P values calculated using ANOVA for numeric variables & chi-square for categorical. Abbreviations: RUCA = rural-urban commuting area, ADI = area deprivation index, HCC= Hierarchical Condition Category, COPD = chronic obstructive pulmonary disease, CKD = chronic kidney disease.

(13% vs 26.6%, p< 0.001), received less HCQ (39.1 vs 42.5%, p=0.029), and 5.2% lower HCQ adherence (19.4% vs 24.6%, < 0.001) than less disadvantaged neighborhoods. Black patients experienced slightly more visit retention (52% vs 51.4%, p=0.577), lab retention (16% vs 14.4%, p=0.042), and more HCQ use (44.4% vs 39.8%, p< 0.001), but lower HCQ adherence (20.5% vs 24.3%, p< 0.001) than White patients.

Overall, 34.9% received acute care or died over 1 year; rates were 10.5% higher without visit retention (Table 1). 10.4% experienced ESKD or death; rates were 5.4% higher without visit retention. Adjusted Cox models showed that all care retention steps predicted lower acute care or death (HR 0.70-0.84, all p< 0.001, Table 3) and most retention steps predicted

Table 2. Percent Retention & Treatment by Area Deprivation Index (ADI) Quintile and Racial Group
n=15,395 for visits and labs, n=10,880 Part D for HCQ items

Table 2a. Retention & Treatment by ADI Quintile

	ADI Least Disadvantaged	ADI Most Disadvantaged*	p-value
Rheumatology visits	60.8	44.5	<0.001
Lab: C3C4 or dsDNA serology	21.6	13	<0.001
Hydroxychloroquine (HCQ) any	42.5	39.1	0.029
HCQ 80% medication adherence	24.6	19.4	<0.001

Table 2b. Retention & Treatment by Race

	White	Black	p-value
Rheumatology visits	51.4	52	0.577
Lab: C3C4 or dsDNA serology	14.4	16	0.042
Hydroxychloroquine (HCQ) any	39.8	44.4	<0.001
HCQ 80% medication adherence	24.3	20.5	<0.001

*Top ADI disadvantage quintile is most disadvantaged.

Table 3. Hazard ratios of acute care and ESKD or death by care step
n=15,395 for visits and labs, n=10,880 Part D for HCQ items

	Unadjusted hazard ratio	95% CI	p	Full Model Hazard Ratio	95% CI	p
Acute care or death						
Visit retention	0.66	(0.63, 0.70)	< 0.001	0.84	(0.79, 0.89)	< 0.001
Lab retention	0.60	(0.55, 0.65)	< 0.001	0.70	(0.64, 0.76)	< 0.001
Any HCQ	0.66	(0.61, 0.70)	< 0.001	0.82	(0.77, 0.88)	< 0.001
80% HCQ adherence	0.66	(0.61, 0.71)	< 0.001	0.80	(0.73, 0.87)	< 0.001
ESKD or death						
Visit retention	0.55	(0.50, 0.61)	< 0.001	0.78	(0.70, 0.87)	< 0.001
Lab retention	0.62	(0.53, 0.73)	< 0.001	0.81	(0.69, 0.95)	0.009
Any HCQ	0.65	(0.57, 0.73)	< 0.001	0.88	(0.78, 1.00)	0.058
80% HCQ adherence	0.58	(0.49, 0.68)	< 0.001	0.73	(0.63, 0.86)	< 0.001

Full model includes: age, sex, race/ethnicity, Medicaid status, disability, RUCA, ADI quintile, HCC score, diabetes, CKD, anxiety disorder, depression, tobacco use, fibro pain fatigue, and baseline nephrology visit.
Abbreviations: ESKD=end stage kidney disease; HCQ=hydroxychloroquine; HCC=hierarchical condition category comorbidity; CKD=chronic kidney disease. Associations persisted conditioned on visit retention (data not shown).

lower ESKD or death (HR 0.73-0.81, all p< 0.05, except any HCQ, p=0.058). Lab retention associated most with reduced acute care/death HR 0.70 (0.64, 0.76); HCQ adherence most strongly associated with lower ESKD/death, HR 0.73 (0.63, 0.86).

Conclusion: Lupus outcomes correlated with lupus visits and labs, with strongest associations between SLE labs and acute care-free survival. HCQ 80% adherence most strongly correlated with ESKD-free survival. Care varied more by ADI than race alone, supporting ADI use in ACR quality reporting, and a need for new care strategies to advance health equity using a social determinants lens to improve SLE outcomes.

Disclosure: C. Bartels: Pfizer, 5; **A. Yu**: None; **F. Elwert**: None; **A. Gilmore-Bykovskyi**: None; **W. Powell**: None; **S. Garg**: None; **A. Kind**: None.

Abstract Number: 0187

Advancing Health Equity with Lupus Stakeholders to Close Care Gaps and Disparities

Shalvi Parikh[1], Monica Messina[1], Shivani Garg[1], Sancia Ferguson[2], Edmond Ramly[3], Andrea Gilmore-Bykovskyi[4], Katrina Phelps[5] and **Christie M. Bartels**[6], [1]Department of Medicine, University of Wisconsin School of Medicine and Public Health, Madison, WI, [2]University of Wisconsin, Madison, WI, [3]Department of Family Medicine and Community Health, University of Wisconsin School of Medicine and Public Health, Madison, WI, [4]University of Wisconsin School of Medicine and Public Health, Madison, WI, [5]School of Nursing, University of Wisconsin-Madison, Madison, WI, [6]University of Wisconsin, School of Medicine and Public Health, Madison, WI

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Healthcare Disparities in Rheumatology Poster I: Lupus

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) care and outcomes are associated with significant racial and socioeconomic disparities in the US, particularly among young Black and Hispanic/Latina women. We previously identified disparities, including gaps in SLE retention in care (defined as a rheumatology clinic visit or lupus-specific lab test every 6 months) and hydroxychloroquine (HCQ) use and adherence. We sought to address these modifiable gaps in SLE care by adapting intervention approaches from other chronic diseases. We engaged patients and healthcare community stakeholders to garner input to prioritize actionable steps and intervention strategies to reduce disparities in SLE retention in care and HCQ use to improve outcomes and equity.

Methods: We recruited SLE experts and stakeholders, including patients, providers, and advocates (State Public Health Department, Lupus Foundation, and the American College of Rheumatology) to adapt intervention strategies from other chronic conditions to be tested in SLE. The patient advisory board (PAB; n=8) included patients with SLE representing racial,

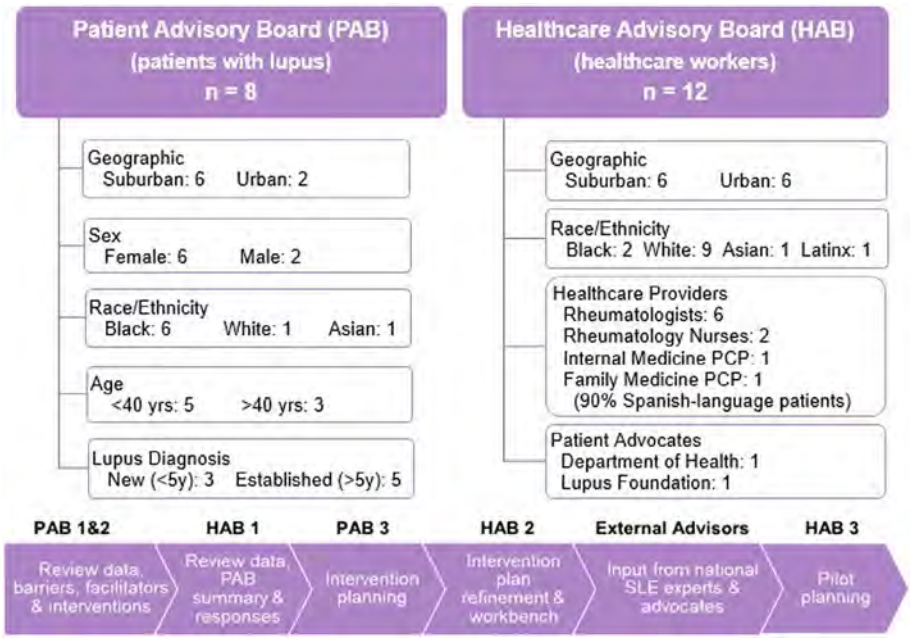

Figure 1. Focus Group Demographics and Meeting Schedule

geographic, age, and sex diversity (**Figure 1**). PAB insights were presented to a healthcare advisory board (HAB; n=12) of 6 rheumatologists, 2 rheumatology nurses, 2 primary care providers, and 2 patient advocates (**Figure 1**). The HAB reviewed prior findings on SLE care gaps and evaluated proven interventions for a pilot. Each group had 3 virtual meetings of 90 minutes (total=6) scheduled to be alternating and iterative. Sessions were audio-video recorded and analyzed using direct content analysis with NVivo software (Melbourne, AU).

Results: The PAB discussed several barriers to SLE retention in care and HCQ, categorized as: labs, visits, and medication adherence (see **Table 1** quotes and meta-themes). Facilitators were similarly identified and grouped (**Table 1**). The main evidence-based interventions considered were electronic health record (EHR) workbench decision support (e.g., HIV Fast-Track) that cues staff action upon missed visits and labs; shared decision making; and patient navigators (**Table 2**). All HAB members and 5 of 8 PAB members supported implementing EHR workbench decision support. PAB and HAB members also suggested including a patient navigator as a supplement to answer patient questions and address challenges in scheduling, medication dosing, and cost barriers, among others. Among HAB members, 8 of 12 recommended EHR workbench decision support as high-impact and low-effort; while 7 of 12 rated patient navigator as high-impact but high-effort.

Table 1. Selection of Patient Identified Barriers (B) and Facilitators (F) to Labs, Visits, and Medication Adherence with List of Predominant Meta-themes

Labs	B	"I'm a 24-hour caregiver…so I have to be real cognizant of…hours for the labs…Are they going to be closed when I get there?" "[Also, labs] charge different amounts of money…I'm rubbing my nickels together…down the street versus…5 miles…to save $20…I have to make those kinds of decisions." [Pt-3, established patient]
	B	"[MyChart results] can be difficult…to understand…can be tricky to read." [Pt-4, established patient]
	F	"[MyChart] will give you like some kind of range…I always like to…double check the levels. And I do a lot of Googling…I like to remind my rheumatologist…if we are not doing labs…if I feel like I need them, I'll really push." [Pt-5, young patient]
Visits	B	"[Sometimes] you'd have to travel 4 hours to get treatment. But…if you don't feel comfortable with them…you're not going to ask questions, you're not going to let them know what's going on." [Pt-1, established patient]
	F	"Your own personal healthcare is so important…you need to drive back to [academic center] or whatever…prioritize yourself…get your visits in." [Pt-1, established patient]
Med Plans	B	"[But] some of the medications are very, very expensive…we will use the [flexible spending] card, but I'm on so many medications…that money don't last all year" [Pt-6, young, newly diagnosed patient] "[The] price of the medication varies…all the time…it's never the same…" [Pt-3, established patient]
	B	"[It] would be really awesome if they would let you make an [eye] appointment the same day…the eye doctor keeps moving all their times…I'll try to refill my pills and they'll be like, well, 'you have to schedule your eye exam because you haven't been there in a year'…if they could straighten out their scheduling…" [Pt-5, young patient (idea supported by 2 established patients)]
	F	"Pharmacists told me about GoodRx [app]…After a while, I couldn't afford that either. So I actually ditched my medication insurance and now I buy all my pills online…doctors don't know how much these things cost." [Pt-5, young patient]
PREDOMINANT META-THEMES Access to Expert Care ● Burden of Disease & Adverse Effects ● Cost Communication & Rapport ● Motivation & Understanding ● Time & Transportation		

Table 2. Patient and Healthcare Members' Reactions to Proposed Evidence-Based Interventions

EHR Workbench Decision Support (e.g., HIV FastTrack) 	**DEFINITION**: EHR alerts flag those who have not had a rheumatology visit or SLE labs for >6mos; +/- medication gap flags. Staff outreach to patients for clinic visits, labs or medication adherence.
	PATIENT: "I like the FastTrack idea…sounds good to me because lupus fog attacks me all the time…I understood it, it was self-explanatory…it works…it's doable…" [Pt-4, established patient]
	PATIENT: "I just might forget…not in my immediate purview…to do get my labs done…so I would appreciate something like that." [Pt-3, established patient]
	PATIENT: "[W]hatever's going to take for me to make sure that I'm up on…my appointments or refills." [Pt-8, newly diagnosed patient]
	PROVIDER: "[It's] quite possible from a technology standpoint…doesn't cost a lot to be able to do something like that…I love the idea of pairing them…maybe leverage the technology to identify who needs outreach…a human connection as the outreach-er…has more potential to be impactful." [PCP-2, urban center]
Patient Navigator 	**DEFINITION**: Personal help with barriers (e.g., cost, transportation) by a nurse, pharmacist, social worker, scheduler, or other (e.g., insurance navigator); consistent person with some medical and resource knowledge in SLE.
	PATIENT: "My insurance…had one…nurse…[who] would call me like every couple of months, just to see if there was something I needed…I wasn't required to use them, but they were available if I needed them…always the same nurse…make it available, but not a requirement." [Pt-1, established patient]
	PATIENT: "I used to have a pharmacist call me…switch the pills around so that I wouldn't be taking so many in the morning…it's time to take the medicine, she might remind me…we had a good rapport…feels more personal." [Pt-4, established patient]
	PROVIDER: "[N]avigators that could also facilitate transportation…basically try to cover all the needs that patients can have as…obstacles…besides reminding someone that they need labs and visit…that would have even more impact…it may also require a little bit more resources." [PCP-1, suburban center, majority Spanish-language patients]
	PROVIDER: "[Navigator is] even high impact than FastTrack…just advocating…so people higher up who are going to decide the resources allotted to the clinic…making them understand why such a navigator is required [as] it is a very high impact factor…[that] will definitely sort the patient in the right way." [Rheum-1, suburban center]

Many discussed that the two could be complementary, recommending EHR workbench decision support first, followed by patient navigator. Indicators for additional support recommended by HAB members were social determinants of health, missed labs or clinic visits, and frequent acute care.

Conclusion: Patient and healthcare stakeholders endorsed implementing EHR workbench decision support, potentially followed by a patient navigator, to reduce disparities and care gaps in SLE. An external advisory board of national SLE leaders is advising scalability for a larger study, and the findings will inform addressing key gaps and unique factors in SLE.

Disclosure: S. Parikh: None; **M. Messina**: None; **S. Garg**: None; **S. Ferguson**: None; **E. Ramly**: None; **A. Gilmore-Bykovskyi**: None; **K. Phelps**: None; **C. Bartels**: Pfizer, 5.

Abstract Number: 0188

Association Between Area Deprivation Index and Organ Damage Accumulation in a Statewide Incident Lupus Cohort

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

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Session Type: Poster Session A

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Background/Purpose: Systemic Lupus Erythematosus (SLE) is a heterogenous systemic autoinflammatory disease that disproportionately effects young women and minoritized populations. Disparities are multifactorial with genetic, hormonal, and environmental contributors. Literature has implicated the role of social determinants of health, specifically low individual socioeconomic status (SES) not just with SLE risk, but also cumulative SLE end organ damage due to disease and consequences of therapy. The area deprivation index (ADI) describes neighborhood social risk by integrating 17 census block factors that correlate with many disease outcomes. We hypothesized that patients with incident SLE in more disadvantaged ADI neighborhoods would more rapidly accumulate damage compared to more advantaged ADI groups.

Methods: This observational cohort study included incident SLE patients from three systems representing urban, suburban, and rural patients across one state. Abstractors manually validated incident SLE cases that fulfilled the 1997 American College of Rheumatology (ACR) and 2012 SLE International Collaborating Clinics (SLICC) criteria. Sociodemographic data and diagnoses related to end organ damage through 2020 were manually abstracted. We used the original US ADI publication to produce ADI rank quintiles. Time to damage, as defined by abstracted events of the SLICC/ACR Damage Index, was assessed at SLE diagnosis and through death or study end (12/31/2020). We used Cox regression to estimate survival curves of time to first damage event from SLE diagnosis stratified by ADI to test our hypothesis.

Results: In a total cohort of 611 incident lupus cases, 524 had complete data. Table 1 shows 88% female and 88% White patients with a low proportion in the most disadvantaged US ADI group. Of those in the most disadvantaged ADI, 67% came from the urban system. Figure 1A shows survival curves of patients from the urban system demonstrating a trend of reduced damage-free survival within the most disadvantaged ADI (median 806 days) compared to those more advantaged (least disadvantaged median 1100 days; log rank insignificant). Total cohort survival (Figure 1B) showed no significant association by ADI. Table 2 shows multivariable hazards with no significance by ADI; significance for age, smoking, and baseline renal disease.

Conclusion: While many studies have investigated associations between individual SES and SLE, ours is among the first to investigate the relationship between neighborhood SES, measured by ADI, and damage in incident SLE. In contrast to our hypothesis, ADI was not statistically associated with damage-free survival. The urban cohort demonstrated the expected reduced damage-free survival trend in the most disadvantaged ADI, suggesting high neighborhood disadvantage may impact SLE damage. Limitations include risk of sampling bias with the small sample size of the most disadvantaged ADI group. Furthermore, neighborhood-level factors may be distinct between urban vs non-urban areas; more research is needed to determine if or how neighborhood disadvantage impacts outcomes in SLE.

Table 1. Statewide Incident Lupus Cohort Demographics

		Incident SLE n=611 (%)
SLE by ACR Criteria		89.85
SLE by SLICC Criteria		87.73
Age at SLE diagnosis (mean, SD)		45.63 (16.14)
Late onset (≥50)		36.82
SLE duration (median, IQR)		3.07 (5.75)
Sex		
Female		88.18
	Male	11.82
Race	White	79.87
	Black	15.55
	Asian	3.11
	Other/Unknown	0.82
Hispanic		2.95
Medicaid ever		32.90
Payor type	Commercial	57.94
	Medicaid	8.84
	Medicare	18.99
	Other/Unknown	14.24
Cohort site	Rural	24.39
	Suburban	18.00
	Urban	57.61
ADI quintile		
	1st (most disadvantaged)	9.34
	2nd	15.38
	3rd	19.96
	4th	36.45
	5th (least disadvantaged)	18.86
Smoking		13.26
CCI (mean, SD)		0.66 (1.23)
Antiphospholipid syndrome		13.74
Renal disease		32.41

Abbreviations: ADI – Area Deprivation Index; CCI – Charlson Comorbidity Index

Figure 1. Damage-Free Survival Curves by Area Deprivation Index (ADI). 1st ADI is most disadvantaged.
A. Urban Cohort B. Statewide Cohort

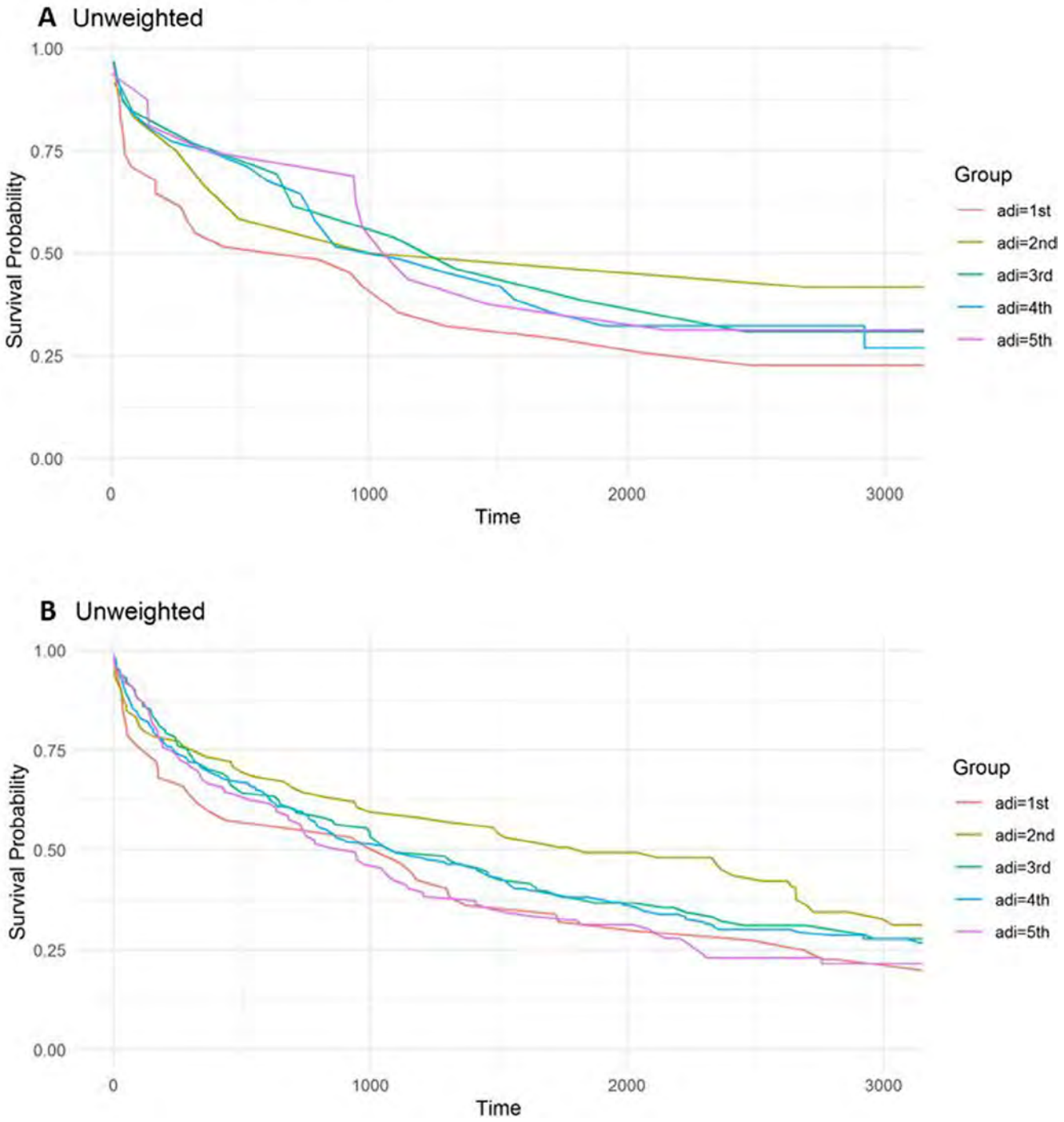

Figure 1. Damage-Free Survival Curves by Area Deprivation Index (ADI). First ADI is most disadvantaged. A. Urban Cohort B. Statewide Cohort

Table 2. Adjusted Hazard Ratios for Time to First SLE Damage Event

		Damage event adjusted hazard ratio (95% CI)
Age		1.03 (1.02, 1.05)
Late onset (≥50)		0.95 (0.64, 1.40)
Sex	Female	0.97 (0.67, 1.41)
Race	White	ref
	Black	1.42 (0.95, 2.13)
	Asian	0.94 (0.50, 1.75)
	Other/Unknown	0.62 (0.14, 2.67)
Hispanic		0.82 (0.41, 1.67)
Medicaid ever		1.16 (0.84, 1.59)
Payor type	Commercial	ref
	Medicaid	0.96 (0.57, 1.62)
	Medicare	0.96 (0.67, 1.36)
	Other/Unknown	1.20 (0.70, 2.04)
RUCA	Urban	ref
	Suburban Area	1.25 (0.89, 1.74)
	Large Town Area	0.96 (0.64, 1.43)
	Small Town & Isolated Rural Areas	1.06 (0.62, 1.81)
ADI quintile		ref
	1st (most disadvantaged)	
	2nd	1.06 (0.58, 1.95)
	3rd	1.14 (0.64, 2.04)
	4th	1.06 (0.60, 1.88)
	5th (least disadvantaged)	1.26 (0.69, 2.31)
Ever smoker		1.30 (1.03, 1.65)
CCI (1 unit change)		0.98 (0.88, 1.09)
Antiphospholipid Syndrome		1.15 (0.82, 1.61)
Renal disease		1.58 (1.22, 2.06)
Baseline damage index		1.04 (0.98, 1.11)

Abbreviations: ADI – Area Deprivation Index; CCI – Charlson Comorbidity Index; RUCA – Rural-Urban Commuting Area

Disclosure: J. Katz: None; **B. Sutherland**: None; **A. Yu**: None; **J. Cormier**: None; **Y. Jiang**: None; **D. Gazeley**: None; **F. Elwert**: None; **C. Bartels**: Pfizer, 5.

Abstract Number: 0189

Influence of Social Support on Systemic Lupus Erythematosus (SLE) Outcomes in a Health Disparity Population

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Healthcare Disparities in Rheumatology Poster I: Lupus

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: SLE disproportionately impacts African American women. Social support may have a positive impact in SLE and as such could potentially reduce disease burden. However, the relationship between social support and SLE disease outcomes has not been investigated in African American female patients with SLE. The goal of this study is to evaluate the relationship between social support and disease outcomes using data from validated participant questionnaires.

Methods: In this study of African American women, we examined differences in social support between healthy controls and patients with SLE and associations with disease severity among the patients. Social support was measured using the validated Medical Outcomes Study-Social Support (MOS-SS) survey. The physician assessed SLE Disease Activity Index (SLEDAI) and the patient reported Brief Index of Lupus Damage (BILD) were used to assess SLE severity. Associations between SLE status and overall MOS-SS score as well as the MOS-SS support domains were analyzed using a series of Wilcoxon rank-sum tests. Hodges-Lehmann estimation was used to calculate the confidence intervals for the difference in medians. Among participants with SLE, associations between MOS-SS score with disease activity (SLEDAI) and with patient reported organ damage (BILD) were evaluated using Spearman's rank correlation. All analyses were performed on RStudio v4.0.3.

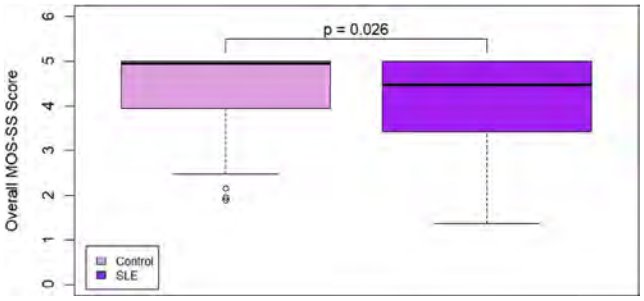

Figure 1. Distribution of overall MOS-SS score by disease status. Boxes in the plots show the median, 25th, and 75th percentiles for the overall MOS-SS scores by disease status. Whiskers extend to 1.5 times the interquartile range (IQR), with measurements outside 1.5 times the IQR being represented by open circles.

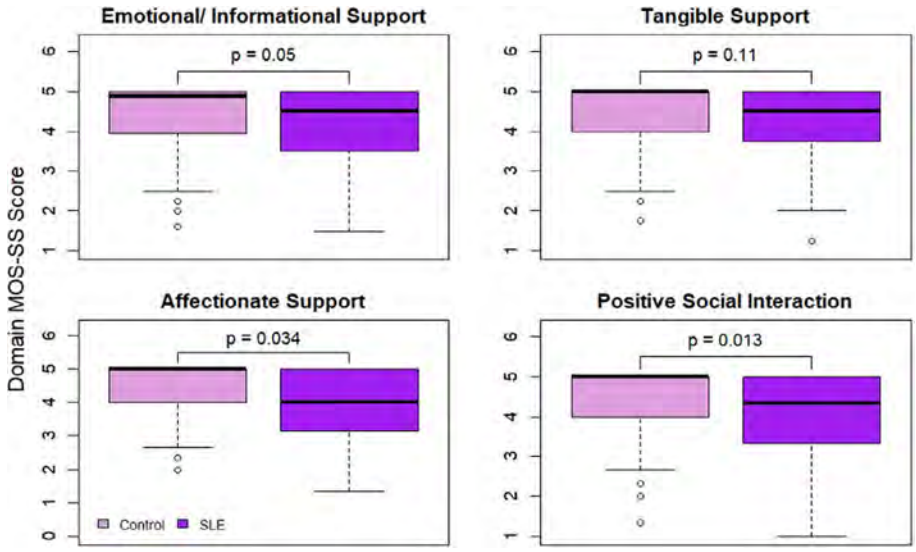

Figure 2. Distribution of MOS-SS score by disease status for each support domain of the MOS-SS. Boxes in the plots show the median, 25th, and 75th percentiles for the overall MOS-SS scores by disease status. Whiskers extend to 1.5 times the interquartile range (IQR), with measurements outside 1.5 times the IQR being represented by open circles.Figure 2: Distribution of MOS-SS score by disease status for each support domain of the MOS-SS. Boxes in the plots show the median, 25th, and 75th percentiles for the overall MOS-SS scores by disease status. Whiskers extend to 1.5 times the interquartile range (IQR), with measurements outside 1.5 times the IQR being represented by open circles.

Table 1. Descriptive statistics for overall MOS-SS score and each support domain for the MOS-SS by disease status. Median (IQR) and difference in medians reported. + Only 69 SLE cases had complete MOS-SS questions applicable for the emotional/ informational domain. ^ Only 68 SLE cases and 59 controls had complete MOS-SS questions applicable for the affectionate support domain. ~ Only 59 controls had complete MOS-SS questions applicable for the positive social interaction domain.

	Controls (n=70)	SLE Cases (n=60)	Difference in Medians (95% CI)	p-value
Overall MOS-SS Score, Median (IQR)	4.95 (3.97 – 5)	4.46 (3.45 – 5)	-0.11 (-0.47, 0)	0.026
Emotional/Informational Support, Median (IQR) +	4.89 (0.94 – 5)	4.5 (3.5 – 5)	-0.12 (-0.38, 0)	0.05
Tangible Support, Median (IQR)	5 (4 – 5)	4.5 (3.8 – 5)	0 (-0.25, 0)	0.11
Affectionate Support, Median (IQR) ^	5 (4 – 5)	4 (3.17 – 5)	0 (-0.67, 0)	0.034
Positive Social Interaction, Median (IQR) ~	5 (4 – 5)	4.33 (3.33 – 5)	-0.33 (-0.67, 0)	0.013

Results: This study was comprised of 70 SLE patients and 60 healthy controls, all self-identified African American females. SLE patients had significantly lower overall MOS-SS scores compared to healthy controls ($p = 0.026$); the distribution of overall MOS-SS scores by disease status is seen in Figure 1. When considering the MOS-SS support domains, SLE patients had significantly lower scores for the emotional/informational support, affectionate support, and positive social interaction domains ($p \leq 0.05$ for all three groups). No notable difference between SLE patients and healthy controls was found for the tangible support domain. Figure 2 shows the distribution of MOS-SS score by disease status for each support domain of the MOS-SS. Table 1 shows the median (IQR) and difference in medians for the overall MOS-SS and each support domain of MOS-SS. Among SLE patients, a significant association was found between overall MOS-SS score and physician reported disease activity (using SLEDAI), such that SLE patients with higher SLEDAI scores have lower MOS-SS scores ($\rho = -0.36$, $p = 0.0003$). No significant association was found between patient reported organ damage (BILD score) and overall MOS-SS score ($p = 0.48$).

Conclusion: This study found significant differences in the overall MOS-SS score between SLE patients and healthy controls and furthermore, the groups differed for the emotional/ informational support, affectionate support, and positive social interaction domains. Among the SLE participants, a significant inverse correlation between SLEDAI total score and overall MOS-SS score was also observed. The potential clinical relevance of these findings suggests that targeted interventions to improve social support could potentially improve SLE outcomes, though further research is needed.

Disclosure: S. Smith: None; **C. Mattila**: None; **L. Ueberroth**: None; **L. King**: None; **D. Kamen**: None; **P. Ramos**: None; **b. wolf**: None.

Abstract Number: 0190

Racial Disparities in Self-reported Extent and Reasons for Nonadherence in SLE

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SESSION INFORMATION

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Background/Purpose: Medication nonadherence is common in SLE and disproportionately affects Black patients. Nonadherence leads to increased hospitalizations, morbidity, and mortality and is a modifiable factor that can reduce racial disparities in SLE outcomes. To better recognize nonadherence and address adherence barriers, we previously adapted and validated a self-reported measure of *extent of nonadherence* and *reasons for nonadherence* called Domains of Subjective Extent of Nonadherence (DOSE- nonadherence-SLE) (Figure 1). In this study, we examined frequencies of reasons for nonadherence to explore possible item reduction and reasons that disproportionately affect Black patients.

For one reason or another, many people can't or don't always take all of their medications as prescribed. We want to know how often you have missed your lupus pills. If you took your pills later than usual, do not count it as a missed dose.

Over the past 7 days...	None of the time	A little of the time	Some of the time	Most of the time	Every time
I missed my medicine(s).	☐	☐	☐	☐	☐
I skipped a dose of my medicine(s).	☐	☐	☐	☐	☐
I did not take a dose of my medicine(s).	☐	☐	☐	☐	☐

People miss doses for various reasons. Please tell us which reasons contribute to you missing a dose of your lupus pills. We recognize that the past 7 days may not represent what you do over longer time periods. However, we are only interested in the past 7 days. When responding, please think only about your lupus pills.
Skip this section if you have not missed any lupus pills.

Over the past 7 days, I missed my lupus pills...	Not at all				Very Much
.....because they **cost too much.**	☐	☐	☐	☐	☐
.....because I **could not fill** the medicine on time.	☐	☐	☐	☐	☐
.....because I **forgot,** or I was **busy.**	☐	☐	☐	☐	☐
.....because I **do not have a regular schedule.**	☐	☐	☐	☐	☐
.....because the **medication instructions were hard to follow.**	☐	☐	☐	☐	☐
.....because I **needed to take them with food but could not eat** at the time.	☐	☐	☐	☐	☐
.....because I had a **hard time swallowing** them.	☐	☐	☐	☐	☐
.....because I take **too many pills.**	☐	☐	☐	☐	☐
.....because they caused **side effects.**	☐	☐	☐	☐	☐
.....because I am **worried about possible side effects.**	☐	☐	☐	☐	☐
.....because I am **worried that they would affect my ability to have children in the future.**	☐	☐	☐	☐	☐
.....because my **family or friends suggested I not take them.**	☐	☐	☐	☐	☐
.....because I **heard that someone had a bad experience** taking them.	☐	☐	☐	☐	☐
.....because I am **worried that my doctor did not prescribe the right medicine** for me.	☐	☐	☐	☐	☐
.....because **I feel that nothing will get better** even if I take my lupus pills.	☐	☐	☐	☐	☐
.....because **I do not understand** why I need to take my lupus pills.	☐	☐	☐	☐	☐
.....because **I felt well.**	☐	☐	☐	☐	☐
.....because **when I skip a dose, I don't feel any difference.**	☐	☐	☐	☐	☐
.....because **I thought the lupus medicine was not working.**	☐	☐	☐	☐	☐
.....because **I was feeling too sick** to take my lupus pills.	☐	☐	☐	☐	☐
.....because I was **too tired** to take my lupus pills.	☐	☐	☐	☐	☐
.....because I was **too stiff** to take my lupus pills.	☐	☐	☐	☐	☐
.....because **I had no one to help me** with my lupus pills.	☐	☐	☐	☐	☐
.....because I felt **too depressed** to take my lupus pills.	☐	☐	☐	☐	☐
.....because I am **tired of taking medicines every day.**	☐	☐	☐	☐	☐

I missed my lupus pills for another reason not listed above: _____

Of the reasons listed above (on this page), circle 3 that you feel are the biggest challenges for you.

Figure 1. DOSE-Nonadherence-SLE survey

Methods: Patients from an academic clinic who met ACR or SLICC criteria for SLE and were prescribed ≥1 SLE medication completed demographic information and the DOSE-Nonadherence-SLE survey, which measures the extent of and reasons for nonadherence over the past 7 days. We limited the analysis to include only patients who self-identified as Black or White race due to small numbers of patients who self-identified as belonging to other races. We compared racial differences in reasons for nonadherence using Chi squared or Fisher's exact tests. We used step-wise multivariable logistic regression to examine factors independently associated with reasons that differentially affected Black patients.

Results: A total of 282 surveys were completed (median age 47, 90% female, 57% Black, 94% HCQ, 48% MMF, 13% AZA, 10% MTX). Black compared to White patients were more likely to be single, working full time, have annual household income < $50,000, and less like to have private insurance (Table 1).

Rates for nonadherence were 53% among Black patients compared to 38% among White patients (p=0.01). The most common reasons for nonadherence were "I forgot or I was busy" (69%), "I was too tired" (33%), and "I am tired of taking medicines every day" (32%). The least common reasons were missing doses due to "the medication instructions were hard to follow" (4.6%), "my family or friend suggested I not take them" (4.5%), and "I heard that someone had a bad experience taking them" (1%).

Most reasons for nonadherence were reported at similar rates by Black and White patients (Table 2). However, Black compared to White patients were more likely to report missing doses due to "I felt well" (31% vs 7%, p=0.004) and "I am worried that the medicine would affect my ability to have children in the future" (9% vs. 0, p=0.08), whereas White patients were more likely to report missing doses due to "I felt too depressed" (24% vs. 9%, p=0.048) and "I had no one to help me" (15% vs 4%,

Table 1. Sociodemographic characteristics of patients.

Patient characteristics		All (n=282)	White (n=122)	Black (n=160)	P-value
Age, median (IQR)		46 (35-57)	49(36-60)	45 (36-56)	**0.04**
Gender, female		90%	88%	91%	0.3
Hispanic		3%	2%	4%	0.6
Marital status					**<0.001**
	Single	31%	13%	44%	
	Married or living with partner	53%	73%	38%	
	Divorced	14%	9%	17%	
	Widowed	3%	5%	1%	
Insurance					
	Private insurance	56%	68%	47%	**<0.001**
	Medicaid/Medicare	37%	31%	41%	0.1
	Military	9%	7%	9%	0.5
Income					**<0.001**
	up to $15k	17%	7%	25%	
	15-50K	38%	26%	47%	
	50-75K	17%	19%	14%	
	75-100K	10%	11%	9%	
	100-150K	12%	25%	3%	
	>150K	6%	12%	2%	
Employment					**0.003**
	Full time	61%	51%	70%	
	Part time	11%	11%	11%	
	Retired	17%	19%	15%	
	Home maker	2%	2%	1%	
	Do not plan to work	9%	18%	2%	
On disability		28%	25%	31%	0.3
Rate of nonadherence*		46%	38%	53%	**0.01**

*Based on the DOSE-Nonadherence-SLE survey

Table 2. Comparing reasons for nonadherence between nonadherent Black and White patients

I missed my lupus pills because...	All (n=112)	White (n=41)	Black (n=71)	p-value
I forgot or I was busy	69%	68%	69%	0.9
I was too tired	33%	33%	33%	1
I was tired of taking medicines every day	32%	36%	30%	0.5
I needed to take them with food but could not eat at the time	27%	22%	30%	0.5
I do not have a regular schedule	25%	21%	26%	0.7
I felt well	23%	**7%**	**31%**	**0.004**
when I skip a dose I don't feel any difference	23%	24%	23%	1
I am worried about possible side effects	23%	26%	21%	0.6
they caused side effects	21%	25%	19%	0.4
I could not fill the medicine on time	20%	20%	20%	1
I take too many pills	18%	17%	19%	1
I feel that nothing will get better even if I take them	18%	19%	17%	0.8
I was too stiff	17%	24%	13%	0.2
I felt too depressed	14%	**24%**	**9%**	**0.048**
I was feeling too sick	13%	20%	10%	0.2
I still felt so bad I thought the medicine was not working	12%	17%	9%	0.2
I had a hard time swallowing them	11%	12%	10%	0.8
I had no one to help me	8%	15%	4%	0.08
I do not understand why I need to take them	6%	3%	9%	0.4
I am worried that my doctor did not prescribe the right medicine for me	6%	5%	7%	1
it cost too much	6%	5%	7%	1
I am worried that they would affect my ability to have children in the future	5%	0	9%	0.08
the medication instructions were hard to follow	4.60%	7%	3%	0.4
my family or friends suggested I not take them	4.50%	7%	3%	0.4
I heard someone had a bad experience taking them	1%	0	1%	1

p= 0.08). After adjusting for other demographic factors, nonadherent due to feeling well was dependently associated with Black race (OR 15, p=0.001).

Conclusion: While busyness and forgetting, physical fatigue, and pill fatigue commonly affect all patients, Black patients were much more likely to report missing doses due to feeling well, and there is a trend that Black patients were more concerned about medication effects on fertility. These represent unique opportunities to improve adherence for Black patients. Our results also suggest that some items can be eliminated to reduce response burden due to their low frequencies.

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Abstract Number: 0191

Reproductive Health Discussions Between Rheumatology Providers and Systemic Lupus Erythematosus Patients: A Survey of English and Spanish-Speaking Patients

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Healthcare Disparities in Rheumatology Poster I: Lupus

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1. Demographics of Female Systemic Lupus Erythematosus Patients

Demographic Variables (N = 61)	Frequency (%)/Median (IQR)
Age (years)	34.0 (16.0) (min=20, max=50)
Race	
White	22 (41.5%)
Black/African American	2 (3.8%)
Asian American	6 (11.3%)
American Indian/Alaska Native	0
Native Hawaiian/Pacific Islander	0
Mixed race	2 (3.8%)
Prefer not to state	7 (13.2%)
Other	14 (26.4%)
Ethnicity	
Hispanic	51 (83.6%)
Non-Hispanic	10 (16.4%)
Preferred Language for Medical Care	
English	43 (70.5%)
Spanish	17 (27.9%)
Other	1 (1.6%)
Education Level	
Less than high school	8 (13.3%)
High school diploma or equivalent	31 (51.7%)
Technical/vocational training	11 (18.3%)
Bachelor's degree	10 (16.7%)
Master's degree or above	0
Marital Status	
Never married	32 (53.3%)
Married/in a domestic partnership	20 (33.3%)
Widowed	0
Divorced or separated	5 (8.3%)
Prefer not to state	3 (5.0%)
Nativity (place of birth)	
In United States	34 (56.7%)
Outside of United States	26 (43.3%)
Religious Affiliation	
Catholic	32 (53.3%)
Denomination of Christianity not Catholic	16 (26.7%)
Other religious group	4 (6.7%)
No religious affiliation	8 (13.3%)
Sexual Activity	
Never sexually active with a male partner	9 (15.3%)
Have been sexually active with a male partner but not currently active	17 (28.8%)
Currently sexually active with a male and trying to get pregnant	1 (1.7%)
Currently sexually active with a male and trying to AVOID a pregnancy	21 (35.6%)
Currently sexually active with male and neither trying to get pregnant or avoid it	11 (18.6%)
Methods of Contraception	
Abstinence or not sexually active with a male partner	14 (23.0%)
Natural methods	3 (4.9%)
Barriers or spermicidal methods	17 (27.9%)
Short-acting birth control	4 (6.6%)
Long-acting reversible birth control	10 (16.4%)
Sterilization	3 (4.9%)
None – I don't use any kind of contraception	15 (24.6%)

Background/Purpose: Systemic lupus erythematosus (SLE) primarily affects women of childbearing age, with a higher burden in non-Caucasian populations. Due to the increased risk of adverse pregnancy outcomes in SLE, especially among non-Caucasian patients, it is essential for rheumatologists to engage patients in reproductive health discussions. Our study aims to gain insight into the conversations surrounding reproductive health between rheumatology providers and a primarily Hispanic SLE population, with a focus on disparities between English-speaking and Spanish-speaking populations.

Methods: A 28-question survey based on the American College of Rheumatology 2020 Reproductive Health Guideline was developed, covering contraception, preconception counseling, and pertinent peri-partum issues. The survey was offered in either English or Spanish to female patients with SLE between the ages of 18 – 50, at a safety-net outpatient rheumatology clinic in urban Los Angeles. Data were presented using frequency (%) or median (IQR) and evaluated using Fisher's exact or Wilcoxon rank sum test, as appropriate.

Results: From March 15 2023, to May 16 2023, 61 surveys were collected. Response rate was 92%. Participants identified as Hispanic (84%), with 71% expressing an English-language preference (Table 1). For all respondents who reported being sexually active with a male partner, 29% denied use of any kind of birth control, and only 25% noted effective contraception (long-acting reversible contraception or sterilization) (Table 1). Approximately 60% of all patients who sought pregnancy after SLE diagnosis took hydroxychloroquine (Table 2). However, while 73% of English-survey respondents noted that a rheumatologist advised them to be on hydroxychloroquine during the pre-conception/pregnancy period, only 60% of Spanish-speaking individuals were given the same counsel (Table 2). English-language respondents reported a significantly higher frequency of conversations in the past one year regarding contraception and pregnancy planning compared to Spanish-speaking respondents (72% vs. 33% and 76% vs. 39%, respectively; Table 2).

Conclusion: This study highlights the importance of thorough reproductive health discussions for patients with SLE, especially in a primarily Hispanic population. For a population known to have high rates of teratogenic medication use and/or poorly controlled disease activity, suboptimal contraception was common. Some disparities between the English and Spanish speaking population include the English-speaking population had a higher rate of conversations surrounding contraception and pregnancy in the past one year, compared to the Spanish speaking patients. This suggests potential barriers in the Spanish-speaking patient population. Hydroxychloroquine use during pregnancy or for those trying to conceive was low, although only patients who ever attempted to conceive or had a pregnancy after SLE diagnosis answered this question.

Table 2. Pre-conception questions by survey language(1) Numbers represent frequency (column percent). *While 17 respondents noted that they prefer receiving medical care in Spanish, only 14 of these elected to take the Spanish language survey (1)Some respondents did not answer all questions (2)Due to branching logic, not all participants answered each question and not all cells will add to the full study population. Individuals who did not attempt and/or experience a pregnancy after SLE diagnosis did not answer questions about hydroxychloroquine use during the pre-conception period or pregnancy.

Variable	Survey Language Group		p-value
	English Survey (n=47)	Spanish Survey* (n=14)	
In the past one year, my lupus doctor has had at least one discussion regarding contraception with me			0.020
No	13 (28.3%)	8 (66.7%)	
Yes	33 (71.7%)	4 (33.3%)	
In the past one year, my lupus doctor has asked what my plans are, if any, for pregnancy			0.018
No	11 (23.9%)	8 (61.5%)	
Yes	35 (76.1%)	5 (38.5%)	
My lupus doctor has told me that I should take hydroxychloroquine when I'm trying to become pregnant or when I'm pregnant[1]			0.613
No	4 (26.7%)	2 (40.0%)	
Yes	11 (73.3%)	3 (60.0%)	
I took hydroxychloroquine during pregnancy or when I was trying to get pregnant[2]			0.999
Yes, I was already on it and continued it	8 (53.3%)	3 (60.0%)	
Yes, I was not already on it but started	1 (6.7%)	0	
No, stopped taking when I found out/was trying	1 (6.7%)	1 (20.0%)	
No, I was not taking it and did not start	3 (20.0%)	1 (20.0%)	
Other	2 (13.3%)	0	

Further research should explore ways of optimizing reproductive health conversations, especially regarding hydroxychloroquine and contraception use, in the management of Hispanic SLE populations.

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Abstract Number: 0192

Demographic and Clinical Factors That Contribute to Clinical Study Enrollment in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

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Background/Purpose: Participation in clinical trials is part of treatment for many patients with chronic diseases. However, patients with systemic lupus erythematosus (SLE), especially those of African American and Hispanic descent, have been reluctant to participate in clinical trials. Qualitative research identified patient, provider, community, and study design factors as the main reasons for this hesitancy. Concerted efforts to increase awareness of and engagement in SLE clinical trials are underway. We evaluated factors associated with challenges to clinical research enrollment in the Columbia University (CU) and Albert Einstein College of Medicine (AECOM) lupus cohorts in New York City (NYC) that serve the low socioeconomic status communities of Washington Heights and the Bronx.

Table 1. Demographic and Clinical Factors Among SLE Patients (n=163)

	Enrolled in the study (n=103)	Refused (n=35)	Clinical Trial Participants (n=25)	p-value
Demographics				
Age (mean ± SD)	40.35 ± 14.09	38.57 ± 12.64	37.84 ± 12.46	0.627
Female (n, %)	94, 91%	29, 83%	23, 92%	0.344
African American (n, %)	38, 37%	14, 48%	5, 20%	0.252
Ethnic Hispanic (n, %)	62, 60%	16, 53%	7, 28%	0.113
Income, $ (mean ± SD)	53535 ± 22037	50514 ± 24315	77378 ± 42968	**0.001**
Years Since SLE Diagnosis (mean ± SD)	8.93 ± 9.21	10.11 ± 7.83	12.04 ± 7.48	0.266
SLE Organ Involvement				
Arthritis (n, %)	86, 84%	25, 71%	24, 96%	**0.043**
Mucocutaneous (n, %)	69, 67%	24, 69%	22, 88%	0.114
Lupus Nephritis (n, %)	28, 27%	9, 26%	5, 20%	0.766
Medication				
Hydroxychloroquine (n, %)	91, 88%	29, 83%	24, 96%	0.298
Corticosteroid (n, %)	27, 26%	5, 14%	14, 56%	**0.001**
MMF, MPA, AZA (n, %)	47, 46%	15, 43%	5, 20%	0.064
Fibromyalgia (n, %)	17, 17%	1, 3%	0, 0%	**0.013**
Admissions in the Past Year (mean ± SD)	1.36 ± 1.50	1.09 ± 1.82	0.52 ± 0.96	**0.044**
Office Visits in the Past Year (mean ± SD)	2.99 ± 2.15	2.63 ± 2.07	4.76 ± 3.35	**0.001**

Methods: This study sponsored by the U.S. Department of Health and Human Services, Office of Minority Health, plans to enroll 200 patients in an engagement program modeled after the Lupus Research Alliance Patient Advocates for Lupus Studies (PALS) program. SLE patients were invited to participate during routine clinic visits. Patients were apprised of the study in detail and their decision to participate or refuse was recorded. Socio-demographics and disease characteristics were collected. Data from recent therapeutic clinical trial participants was included for comparison. One-way ANOVA was used to detect differences among the 3 groups: enrolled in the study, refused participation and clinical trial participants.

Results: Of the 138 patients asked to participate, 103 (74.6%) agreed while 35 (25.4%) refused. Additionally, 25 clinical trial participants were included. Participants enrolled in the educational sessions, demonstrating willingness to engage in clinical trial education, were more likely to have been admitted during the past year (1.36 vs 1.09 vs 0.52, p=0.044) and have co-morbid fibromyalgia (17% vs 3% vs 0%, p=0.013). While there were more African American and Hispanic patients in the education study groups, these differences did not reach statistical significance. Detailed data is summarized in Table 1. The major reasons for refusal were lack of interest in clinical trials (17, 49%), time constraints (14, 40%) and negative prior experiences relating to clinical trials (4, 11%). Clinical trial participants were more likely to have arthritis (84% vs 71% vs 96%, p=0.043), mucocutaneous manifestations (67% vs 69% vs 88%, p=NS) and be on steroids (26% vs 14% vs 56%, p=0.001) as required for inclusion in clinical trials. Also, the clinical trial group displayed a higher zip-code median income (54K vs 51K vs 77K, p=0.001) and more rheumatology office visits in the past year (2.99 vs 2.63 vs 4.76, p=0.001).

Conclusion: These data suggest that people's intention to participate in clinical research is influenced by disease severity (admissions and office visits), patient factors (income and co-morbid fibromyalgia) and study design (arthritis, steroid use). It is difficult to ascertain if racial and ethnic factors affect the current study enrollment. More data is needed to confirm the role of these factors and additional qualitative data will help identify factors that affect a patient's decision at the individual level.

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Abstract Number: 0193

Social Vulnerability Associations with Mortality in a Lupus Cohort

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SESSION INFORMATION
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Background/Purpose: The goal of this study is to identify characteristics of socially vulnerable environments associated with increased mortality in a South Carolina systemic lupus erythematosus (SLE) cohort.

Methods: Address, demographic, medication use, and SLE International Collaborating Clinics (SLICC) disease damage data were gathered prospectively from patients and their medical record enrolled in the Medical University of South Carolina's (MUSC's) lupus registry that met SLE criteria. Death certificate data for patients in the cohort were obtained from the

state Department of Health. Standardized mortality ratios (SMR) were calculated using expected mortality rates from the CDC WONDER database, and characteristics between deceased and living patients were compared. The cohort was linked with geospatial analysis to publicly available census tract contextual data, which was CDC's Social Vulnerability Index (SVI). Then, we applied spatial regression models to assess associations between neighborhood characteristics and SLE outcomes after controlling for age, sex, education, disease characteristics and also examined effect modification of each characteristic by presence of disease damage

Table 1.- SLE Cohort Demographics & Clinical Characteristics Associated with mortality

Table 1. Demographic and clinical characteristics of cohort				
	Total N=717	Deceased N=102	Alive N=615	p value
gender				
Female	652 (90.9)	88 (86.3)	564 (91.7)	0.08
Male	65 (9.1)	14 (13.7)	51 (8.3)	
age at baseline	38.1 ±14.9	41.6 ±17.1	37.5 ±14.4	0.01
Age group (years) at dx				
Missing	12 (1.7)	1 (1.0)	11 (1.8)	0.28
<20	169 (23.6)	28 (27.5)	141 (22.9)	
20-30	207 (28.9)	29 (28.4)	178 (28.9)	
30-40	145 (20.2)	14 (13.7)	131 (21.3)	
40+	184 (25.7)	30 (29.4)	154 (25.0)	
Disease duration	17.1 ±9.0	14.8 ±9.3	17.5 ±8.9	0.004
Age at lupus onset	31.2 ±14.0	32.2 ±16.0	31.1 ±13.6	0.43
Race				
White	165 (23.0)	14 (13.7)	151 (24.6)	0.02
Black	552 (77.0)	88 (86.3)	464 (75.4)	
Nephritis				
No	422 (58.9)	54 (52.9)	368 (59.8)	0.19
Yes	295 (41.1)	48 (47.1)	247 (40.2)	
SLICC Damage Index (SDI) score				
Total SDI	1.9 ±2.5	3.3 ±3.1	1.7 ±2.2	<0.01
Missing	33 (4.6)	4 (3.9)	29 (4.7)	
0	259 (36.1)	17 (16.7)	242 (39.3)	<0.01
1	133 (18.5)	18 (17.6)	115 (18.7)	
2	90 (12.6)	14 (13.7)	76 (12.4)	
3	69 (9.6)	14 (13.7)	55 (8.9)	
4	39 (5.4)	8 (7.8)	31 (5.0)	
5	35 (4.9)	6 (5.9)	29 (4.7)	
6	21 (2.9)	4 (3.9)	17 (2.8)	
7	13 (1.8)	8 (7.8)	5 (0.8)	
8	7 (1.0)	1 (1.0)	6 (1.0)	
9	8 (1.1)	5 (4.9)	3 (0.5)	
10	1 (0.1)	0 (0.0)	1 (0.2)	
11	5 (0.7)	1 (1.0)	4 (0.7)	
13	1 (0.1)	1 (1.0)	0 (0.0)	
14	1 (0.1)	1 (1.0)	0 (0.0)	
16	1 (0.1)	0 (0.0)	1 (0.2)	
20	0 (0.0)	0 (0.0)	1 (0.2)	
SDI score				
missing	33 (4.6)	4 (3.9)	29 (4.7)	
Zero	259 (36.1)	17 (16.7)	242 (39.3)	<0.01
1+	425 (59.3)	81 (79.4)	344 (55.9)	

Table 2.- Social Vulnerability Variable Effect Modification on Mortality based on presence or absence of SDI

Damage	Variable	Estimate	SE	Z	p-value
0	Age >65	-0.11	3.45E-02	-3.2665613	1.09E-03
0	EP_PCI	0.00	2.06E-05	-3.2091779	1.33E-03
0	Unemployed	-0.15	5.70E-02	-2.657105	7.88E-03
0	Single Parent	-0.09	3.73E-02	-2.3016163	2.14E-02
0	Theme 2	-1.45	6.59E-01	-2.2000333	2.78E-02
0	Limited English	-0.56	2.62E-01	-2.1230722	3.37E-02
0	Multinunit	-0.05	2.68E-02	-1.9964248	4.59E-02
0	Disability	-0.07	3.31E-02	-1.9829973	4.74E-02
1	Minority	0.02	6.42E-03	3.4630702	5.34E-04
1	No Highschool Diploma	0.04	1.83E-02	2.2938205	2.18E-02
1	No Vehicle	0.04	1.81E-02	2.277449	2.28E-02
1	Crowded Home	0.15	6.69E-02	2.2305625	2.57E-02
1	Poverty	0.02	1.21E-02	2.0608628	3.93E-02
1	Theme 1	0.96	4.74E-01	2.021387	4.32E-02
1	Theme 3	1.13	5.30E-01	2.1296975	3.32E-02
1	Theme 4	0.94	4.82E-01	1.9591219	5.01E-02
1	Total Theme	0.88	4.67E-01	1.8824017	5.98E-02

Results: 712 subjects were included in the final analysis, and 102 died before the study data cutoff. The total SMR adjusted for age, race, and gender was 12.29 (95% CI 9.97-14.61). Of the deceased, there was a statistically significant increased mortality in association with self-identified Black race (p=0.02), with high vulnerability census tracts, and total, renal-related, and steroid-related SLICC damage index (SDI) of 1 or more (p< 0.01) and a reduced mortality associated with hydroxychloroquine use. Black patients had higher SDI compared to White patients. Patients with SDI of 1 or more were at increased risk of mortality if they lived in a minority neighborhood, had no high school diploma, had low socioeconomic status, or spoke English less than well

Conclusion: Mortality and SDI were significantly greater in Black patients, which, as race is a social construct, prompted evaluation of socially vulnerable environments using SVI which found an increased risk of mortality in socially vulnerable census tracts and this effect was greater in patients with disease damage. The cause of this association is not known. However, the significant association between socially vulnerable environments and mortality suggests the need to study environmental factors that influence the high rate of mortality among lupus patients in SC and should prompt awareness. The significant association between hydroxychloroquine and lower mortality is consistent with other prospective cohort studies and reinforces the current guidelines regarding its use in SLE.

Disclosure: S. Carter: None; **D. Wilson**: None; **S. Minkin**: None; **D. Dillon**: None; **B. Murray**: None; **J. Pearce**: None; **J. Oates**: None.

Abstract Number: 0194

Reproductive Health Conversations with a Primarily Hispanic Systemic Lupus Erythematosus Population: Influences and Barriers

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Healthcare Disparities in Rheumatology Poster I: Lupus
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease most commonly seen in women of childbearing age, with a greater burden in non-Caucasian populations. The American College of Rheumatology (ACR) published guidelines in 2020 to inform a shared decision-making process on reproductive health management between patients and their physicians. However, there is little data as to how these guidelines are experienced by patients in the "real world" setting, and specifically by Hispanic patients, who have high rates of poor SLE outcomes. Our patient survey assesses influences on and barriers to reproductive health conversations and explores how a predominantly Hispanic SLE population obtains reproductive health information.

Methods: A 28-question survey was distributed in either English or Spanish to female patients with SLE ages 18 - 50 in our outpatient urban Los Angeles rheumatology clinic. Questions focused on four areas – contraception, preconception counseling, pregnancy management, and medication safety – and were informed by the ACR guidelines. The majority of the

Table 1. Demographic and clinical characteristics for all 61 patient respondents

Characteristics	Frequency (%)/ Median (IQR)
Age (years)	34.0 (16.0) (min=20, max=50)
Race	
White	22 (41.5%)
Black/African American	2 (3.8%)
Asian American	6 (11.3%)
American Indian/Alaska Native	0
Native Hawaiian/Pacific Islander	0
Mixed race	2 (3.8%)
Prefer not to state	7 (13.2%)
Other	14 (26.4%)
Ethnicity	
Hispanic	51 (83.6%)
Non-Hispanic	10 (16.4%)
Preferred Language for Medical Care	
English	43 (70.5%)
Spanish	17 (27.9%)
Other	1 (1.6%)
Education Level	
Less than high school	8 (13.3%)
High school diploma or equivalent	31 (51.7%)
Technical/vocational training	11 (18.3%)
Bachelor's degree	10 (16.7%)
Master's degree or above	0
Marital Status	
Never married	32 (53.3%)
Married/in a domestic partnership	20 (33.3%)
Widowed	0
Divorced or separated	5 (8.3%)
Prefer not to state	3 (5.0%)

questions were multiple choice. Patients were not required to answer all questions and branching logic was used depending on patients' unique reproductive history. Data were presented using frequency (%) or median (IQR) and evaluated using Fisher's exact or Wilcoxon rank sum test, as appropriate.

Results: From March 15, 2023 to May 16, 2023, 61 surveys were collected (Table 1). Response rate was 92%. 40% of patients noted that the rheumatologist was most likely to initiate a conversation about reproductive health-related topics; 31% reported that patient and rheumatologist were equally likely to initiate such a conversation, and 19% noted never having any such conversation (Table 2).86% of respondents believed that their rheumatologist had sufficient expertise to answer questions about the effect of SLE on contraception use and pregnancy planning, however, this was observed more frequently in the English survey (91%) compared to the Spanish survey (69%) (p = 0.062) (Table 3). 56% of patients identified that there were difficulties with reproductive health care discussions, most commonly noting: "I don't think it's safe for me to become pregnant" (19.7%), and "my lupus doctor has suggested that I talk with an OBGYN instead" (18%). Respondents noted their top three sources for reproductive health information as their rheumatologists (73.8%), the internet (32.8%), and their OBGYN (16.4%) (Table 2).

Conclusion: Our data show that most respondents of our primarily Hispanic SLE population in a safety-net clinic rely on the rheumatologist as a crucial source of reproductive health information. However, more than half reported that there were difficulties with reproductive health conversations, including patients' perception about the safety of pregnancy, and rheumatologists deferring to OBGYNs. Furthermore, *nearly 20% noted never having a reproductive health conversation with a*

Table 2. Influences on reproductive health conversations (given the total N for this table)

Survey Question	Frequency (%)
My lupus doctor has enough information to answer questions I have about lupus and its effect on contraception or pregnancy[1]	
No	8 (13.6%)
Yes	51 (86.4%)
What makes it hard to discuss contraception and pregnancy questions with your lupus doctor?[2]	
Not enough time in my appointment	2 (3.3%)
My lupus doctor suggested I talk to OB-GYN instead	11 (18.0%)
There is a language barrier between doctor and me	1 (2.1%)
I don't think my lupus doctor knows enough about contraception or pregnancy	3 (4.9%)
I don't feel comfortable talking about these issues with my lupus doctor	1 (1.6%)
I don't think it's safe for me to become pregnant	12 (19.7%)
I don't think these topics are relevant or important to me	4 (6.6%)
Other	5 (8.2%)
None	27 (44.3%)
Who is most likely to initiate a conversation about reproductive health-related topics during an appointment with your lupus doctor?[1]	
I am	6 (10.3%)
My lupus doctor is	23 (39.7%)
My lupus doctor and I are equally likely to initiate a conversation	18 (31.0%)
My lupus doctor and I have never discussed reproductive health-related topics	11 (19.0%)
Where do you get most of your information regarding lupus and reproductive health?[2]	
My lupus doctor	45 (73.8%)
My OB-GYN	10 (16.4%)
Another doctor	5 (8.2%)
Significant other	3 (4.9%)
Family member	6 (9.8%)
Friends	0
Lupus support group	4 (6.6%)
Information found on an internet site	20 (32.8%)
Social media	6 (9.8%)
Television	0
Other	2 (3.3%)

[1]Some respondents did not answer all questions
[2]Respondents were able to select more than one option

Table 3. Barriers and contraception discussion by survey language group

Survey questions	Survey Language Group		p-value
	English Survey (n=47)	Spanish Survey* (n=14)	
My lupus doctor has enough information to answer questions I have about lupus and its effect on contraception or pregnancy[1]			0.062
No	4 (8.7%)	4 (30.8%)	
Yes	42 (91.3%)	9 (69.2%)	
Where do you get most of your information regarding lupus and reproductive health?[2]			
My lupus doctor	37 (78.7%)	8 (57.1%)	0.369
My OB-GYN	7 (14.9%)	3 (21.4%)	0.999
Another doctor	4 (8.5%)	1 (7.1%)	0.999
Significant other	1 (2.1%)	2 (14.3%)	0.369
Family member	3 (6.4%)	3 (21.4%)	0.370
Friends	0	0	——
Lupus support group	3 (6.4%)	1 (7.1%)	0.999
Information found on an internet site	20 (42.6%)	0	0.018†
Social media	6 (12.8%)	0	0.578
Television	0	0	——
Other	2 (4.3%)	0	0.999

Numbers represent frequency (column percent)
*While 17 respondents noted that they prefer receiving medical care in Spanish, only 14 of these elected to take the Spanish language survey.
†Adjusted for multiple comparisons using Benajmini-Hochberg correction
[1]Some respondents did not answer all questions
[2]Respondents were able to select more than one option

rheumatologist. Given the above, effective interventions to improve evidence-based reproductive health conversations between Hispanic patients with SLE and rheumatologists should be investigated.

Disclosure: Z. Zaheer: None; **M. Delgado**: None; **J. Rodman**: None; **J. Simard**: None; **S. Lee**: None; **L. Wise**: Astra-Zeneca, 6, Aurinia Pharma, 2, 6, GlaxoSmithKlein(GSK), 6.

Abstract Number: 0195

Assessing Cardiovascular Risk in Black and Latino Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Healthcare Disparities in Rheumatology Poster I: Lupus
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular disease (CVD) is a major cause of mortality among patients with systemic autoimmune disease. Patients with systemic lupus erythematosus (SLE) exhibit accelerated cardiovascular disease compared with age matched healthy controls. While Black and Latino patients with SLE have worse autoimmune disease than white patients, understanding of SLE-associated CVD in these marginalized patients has been limited by the exclusion of Black and Latino patients from these studies. We aim to assess cardiovascular risk in Black and Latino patients with SLE.

Methods: Retrospective cohort study of patients enrolled in a single center SLE natural history study. Healthy volunteers and patients with SLEwho had cardiac CT imaging from 2003-2023 were selected for review. Variables of interest were obtained at the time of imaging, and include coronary artery calcium score (CAC), patient demographics, statin use,

Framingham CVD risk factors, and laboratory parameters (total cholesterol, HDL). Data were analyzed by Wilcoxon rank sum test or Fisher's exact test when appropriate, and a p-value < 0.05 was considered statistically significant.

Results: There were 61 healthy and 141 SLE patients available for review. Of the patients with SLE, 89% were women and the average age at the time of imaging was 45 years. 27% identified as Black/African American and 33% identified as Hispanic Latino. CAC was present in 26% of the SLE patients with a mean CAC score of 49.9, while in healthy controls, CAC was present in 5% of volunteers with a mean CAC score of 2.6. Hypertension was present in 47.5% of healthy controls and 68% of SLE patients (p=0.007). Comparison of other CVD risk factors including obesity, any smoking history, cholesterol level, and diabetes mellitus did not reveal any significant differences between groups. Mean HDL was 58.5 in SLE patients without significant differences between groups. Use of statin in SLE patients with an elevated CAC score was 16%.

	Healthy	SLE	p-value
Sample size	61	141	
Age at imaging	42.2 +/- 11.2	44.9 +/- 10.5	0.1
Biologic sex % female	51 (83.6)	126 (89.4)	0.25
Race/ethnicity (n, %) Asian Black/African American Hispanic or Latino Multiracial Non-Latino White	 3 (4.9%) 10 (16.4%) 20 (32.8%) 1 (1.64%) 25 (41%)	 13 (9.2%) 38 (26.9%) 47 (33.3%) 2 (1.42%) 38 (26.9%)	 0.19
CAC present (n, %) Asian	1	7 (4.96%)	1
Black/African American	1	9 (6.4%)	0.66
Hispanic or Latino	0	9 (6.4%)	0.04*
Multiracial	0	0	--
Non-Latino White	1	12 (8.5%)	0.01*
CAC score (mean +/- sd) Asian	9 +/- 15.6	31.1+/- 55.1	0.67
Black/African American	7.7 +/- 24.3	23.7 +/- 72.5	0.39
Hispanic or Latino	0	25.2 +/- 109.8	0.03*
Multiracial	0	0	N/A
Non-Latino White	1.1 +/- 5.3	120 +/- 396	0.009*
Overall			
BMI >30 Asian	2	0	
Black/African American	2	13	0.47
Hispanic or Latino	3	16	0.14
Multiracial	0	1	
Non-Latino White	3	10	0.34
Hypertension Asian	2	7	1
Black/African American	4	26	0.14
Hispanic or Latino	8	31	0.05*
Multiracial	0	2	--
Non-Latino White	14	28	0.17
Overall			

Conclusion: Our preliminary findings describe a multi-ethnic cohort of patients with SLE. CAC was present in 26% of affected patients and 5% of healthy controls. CAC was more prevalent and higher in white patients compared to Black and Latino patients. While hypertension was more prevalent patients with SLE, many other traditional risk factors were not present. We found that Black and Latino patients with SLE had significantly lower mean CAC scores when compared to non-Latino white patients. Our findings may indicate that calcium scores are not as reliable of a risk factor to guide secondary prevention in Black and Latino patients with SLE. It may be that Black and Latino patients have more non-calcified plaque burden when compared to non-Latino white patients with SLE. Further study is needed to examine mechanisms to explain these differences and replicate our findings in larger groups. These findings begin to address CVD health disparities in marginalized populations by providing additional information on SLE-associated CVD in Black and Latino patient

Disclosure: G. Gonzalez: None; **Z. Manna**: None; **A. Fike**: None; **J. Chu**: None; **s. Hasni**: AstraZeneca, 5; **B. Dizon**: None.

Abstract Number: 0196

Limited Regulatory T Cell Response in Post-Chikungunya Viral Arthritis: A Therapeutic Opportunity?

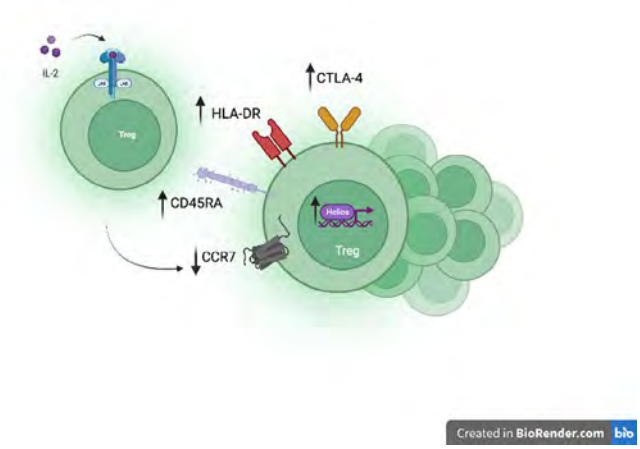
Aileen Chang[1], Sarah Tritsch[1], Carlos Herrera[1], Liliana Encinales[2], Andres Cadena[3], Wendy Rosales[4], Evelyn Mendoza[5], Samuel Simmens[1], Richard Amdur[6], Paige Fierbaugh[1], Abigale Proctor[1], Alfonso Sucerquia[1], Christopher Mores[1], David Boyle[7], Gary Firestein[7] and Gary Simon[1], [1]George Washington University, Washington, DC, [2]Allied Research Society, Barranquilla, Colombia, [3]Clinica de la Costa, Barranquilla, Colombia, [4]Universidad Libre, Barranquilla, Colombia, [5]Universidad Libre, Bogotá, Colombia, [6]Northwell, Washington, DC, [7]University of California San Diego, San Diego, CA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The objective was to define the relationship between chronic chikungunya (CHIKV) post-viral arthritis disease severity, interleukin (IL)-2, and T cell subsets in order to determine if arthritis therapies targeting enhanced regulatory T cell (Treg) activity such as low-dose IL-2 may provide benefit.

Methods: Participants with CHIKV arthritis were recruited from Colombia from 2019–2021. Arthritis disease severity was quantified using the Disease Activity Score (DAS)-28 and an Arthritis-Flare Questionnaire adapted for CHIKV arthritis. Plasma cytokine concentrations (IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12p70, IL-13, interferon-γ and tumor necrosis factor (TNF)) were measured using a Meso Scale Diagnostics assay. Peripheral blood Treg subsets were measured using flow cytometry.

Results: Among participants with CHIKV arthritis (N=158),IL-2 levels and frequency of Tregs were low. Increased arthritis disease activity was associated with higher levels of inflammatory cytokines (IL-6, TNF and CRP) and immunoregulatory cytokine IL-10 without increases in IL-2 ($p< 0.05$). Increased arthritis flare activity was associated with higher Treg frequencies ($p< 0.05$) without affecting Teff frequencies, Treg/Teff ratios and Treg subsets. Finally, elevated levels of IL-2 were correlated with increased Treg frequency, percent Tregs out of $CD4^+$ T cells, and Treg subsets expressing immunosuppressive markers, while also correlating with an increased percent Teff out of live lymphocytes ($p< 0.05$).



Conclusion: CHIKV arthritis is characterized by increased inflammatory cytokines and deficient IL-2 and Treg responses. Greater levels of IL-2 were associated with improved Treg numbers and immunosuppressive markers, suggesting that low-dose IL-2 therapies targeting enhanced Treg activity may be a plausible objective for further investigation.

Increasing IL-2 in chikungunya arthritis is associated with increased Treg numbers and expression of immunomodulatory markers. Herein we report that higher levels of IL-2 in chikungunya arthritis patients were associated with greater numbers of Tregs. Greater IL-2 was also associated with enhanced expression of CTLA-4, which suppresses effector T cell activation by decreasing antigen presenting cell costimulatory function (CD80/CD86). Additionally, higher IL-2 levels of IL-2 were associated with higher expression of HLA-DR, which functions in Treg activation; CD45RA, found in resting Tregs; and Helios, a transcription factor that acts on the Foxp3 promotor to increase immunosuppressor function. Last, increased IL-2 levels correlated with decreased CCR7, whose deficiency permits Treg retention in inflamed tissue.

Disclosure: A. Chang: None; **S. Tritsch**: None; **C. Herrera**: None; **L. Encinales**: None; **A. Cadena**: None; **W. Rosales**: None; **E. Mendoza**: None; **S. Simmens**: None; **R. Amdur**: None; **P. Fierbaugh**: None; **A. Proctor**: None; **A. Sucerquia**: None; **C. Mores**: None; **D. Boyle**: None; **G. Firestein**: Eli Lilly, 5; **G. Simon**: None.

Abstract Number: 0197

Development of a Chikungunya Arthritis Disease Activity Score

Aileen Chang[1], Samuel Simmens[1], Hugh Watson[2], Richard Amdur[3], Andre Siqueira[4], Abigale Proctor[1], Sarah Tritsch[1], Carlos Herrera[1], Liliana Encinales[5], Alfonso Sucerquia[1], Alejandro Jaller[1], Juan Jose Jaller[6], Kennedy Amaral[7], Gary Simon[1], Larry Moreland[8], Andres Cadena[9] and Gary Firestein[10], [1]George Washington University, Washington, DC, [2]Evotec, Lyon, France, [3]Northwell, Washington, DC, [4]Fiocruz, Rio, Brazil, [5]Allied Research Society, Barranquilla, Colombia, [6]Reumatologos SAS, Barranquilla, Colombia, [7]Institute of Diagnostic Medicine of Cariri, Pernambuco, Brazil, [8]University of Colorado, Denver, CO, [9]Clinica de la Costa, Barranquilla, Colombia, [10]University of California San Diego, San Diego, CA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Infection-related Rheumatic Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Tender Joint	Left	Right
Shoulder		
Elbow		
Wrist		
MCP 1		
MCP 2		
MCP 3		
MCP 4		
MCP 5		
PIP 1		
PIP 2		
PIP 3		
PIP 4		
PIP 5		
Knee		
28 Joint Total		
Ankle		

Stiffness

Circle the number that best describes the STIFFNESS you have felt due to your chikungunya arthritis in the last week:

No stiffness 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extreme stiffness

How to score the CHIK-DAS

Variable	Value
DAS-28 Tender Joint Score	
Ankle Tenderness Score	
Stiffness Score	
C-reactive Protein (CRP) (mg/dL)	
CHIK-DAS + CRP = .219 + .067 x Stiffness Score + .235 x Ankle Tenderness + .015 x DAS28 Tender Joint Count + .021*CRP	
CHIK-DAS = .262 + .069 x Stiffness Score + .248 x Ankle Tenderness + .015 x DAS28 Tender Joint Count	

CHIK-DAS Interpretation

With and without CRP	Disease Activity
<0.22	Remission
0.23 to 0.75	Mild
.75 to 1.29	Moderate
≥1.30	High

Background/Purpose: Chikungunya virus is an alphavirus spread by mosquitos that causes a debilitating chronic arthritis that has no standard treatment to date. The objective of this expert group was to develop a measure of chikungunya arthritis that would be useful for clinical trials and patient care.

Methods: A group of chikungunya experts, rheumatologists and biostatisticians identified component measures for evaluation for inclusion in a chikungunya arthritis disease activity score (CHIK-DAS). Utilizing data from a Colombian cohort of chikungunya arthritis patients (N=84), linear regression was used to identify the components that were independently associated with patient reported outcomes assessing disability, pain, physical and mental quality of life and mobility. A preliminary instrument was developed and assessed for internal consistency and test-retest reliability. Cutoffs for grading disease severity were determined.

Results: A CHIK-DAS was developed including a 30 tender joint count and a stiffness item in a form with and without CRP. Disease activity was defined as remission (< 0.22), mild (< 0.75), moderate (0.75-1.29) and severe (≥1.30) disease.

Conclusion: The CHIK-DAS may be used as a specific measure of disease activity in chikungunya arthritis in clinical trials and patient care. This metric should be further validated in additional cohorts.

Chikungunya Disease Activity Score (CHIK-DAS). The items 30 tender joint count including the 28 joints from the DAS-28 and the ankle joints and a stiffness score with and without C-reactive protein. The 28 joints included in the DAS-28 are the bilateral shoulders, elbows, wrists, metacarpophalangeal, proximal interphalangeal and knees.

Disclosure: A. Chang: None; **S. Simmens**: None; **H. Watson**: Evotec, 3; **R. Amdur**: None; **A. Siqueira**: None; **A. Proctor**: None; **S. Tritsch**: None; **C. Herrera**: None; **L. Encinales**: None; **A. Sucerquia**: None; **A. Jaller**: None; **J. Jaller**: None; **K. Amaral**: None; **G. Simon**: None; **L. Moreland**: Boehringer-Ingelheim, 12, member of independent Data Safety Monitoring Board, Celltrion, 12, member of independent Data Safety Monitoring Board; **A. Cadena**: None; **G. Firestein**: Eli Lilly, 5.

Abstract Number: 0198

Improving Vaccination Uptake of Herpes Zoster in Young Rheumatic Disease Patients Ages 18-49 Using Specialty Pharmacy Partnership

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Herpes zoster (HZ), also known as shingles, causes an estimated one million cases annually in the United States. Many studies have shown that the risk for herpes zoster infection is higher in inflammatory rheumatic diseases (IRDs) and those who are immunocompromised (IC). The severity of herpes zoster correlates with underlying immunosuppression, also seen in immunosenescence. The rate of Shingles in our young IRD patients is similar to a healthy 65-year-old with a rate of 8-10 per thousand patient years. Some immunosuppressants (IS) especially JAKs further increase this risk.

Shingrix, approved in 2017 for adults over 50 years old, a non-live recombinant herpes zoster vaccine (RZV) is administered in two doses. In July 2021, the indication was expanded by the Federal Drug Association (FDA) to include patients eighteen years and older with IRDs or on IS. The purpose of our study was to study the prevalence of RZV in our young IRD cohort and to evaluate methods to increase vaccination rates, including utilization of the specialty pharmacy.

Methods: The patient cohort was collected utilizing the electronic medical record reporter system (EMRRS). All patients 18-49 years old who were seen in rheumatology clinic from July 2021 to mid-April 2022 were included to determine current RZV vaccination rates and eligibility. Eligibility criteria included young IRD patients and IC.

After determining which patients required RZV, the team coordinated with the specialty pharmacy to ensure a central location for inoculation and to keep a record of vaccinated patients. In addition, it ensured that patients would receive a reminder to return for the second dose of RZV. The pharmacists were provided with a list of eligible patients and the patients were given a flyer with pharmacy information. In addition, patients were electronically sent a copy of the flyer through the online patient portal or through email.

Cross-sectional analysis using EMRRS from July 2022 to June 1, 2023 was utilized by investigators to determine new eligible patients and the percentage of patients age 18-49 years old seen in rheumatology clinic that had received vaccination.

Results: A total of 1,009 patients ages 18-49 years old were seen in rheumatology clinic since the FDA expanded the indication for RZV. Of those patients, 458 were eligible to receive the vaccine. Prior to intervention, only two (0.2%) patients had received partial vaccination due to previous disseminated zoster infection. To date, 35.5% of eligible patients had been vaccinated, with 109 (23.8%) patients having received two doses of the vaccine and 58 (12.7%) patients having received the

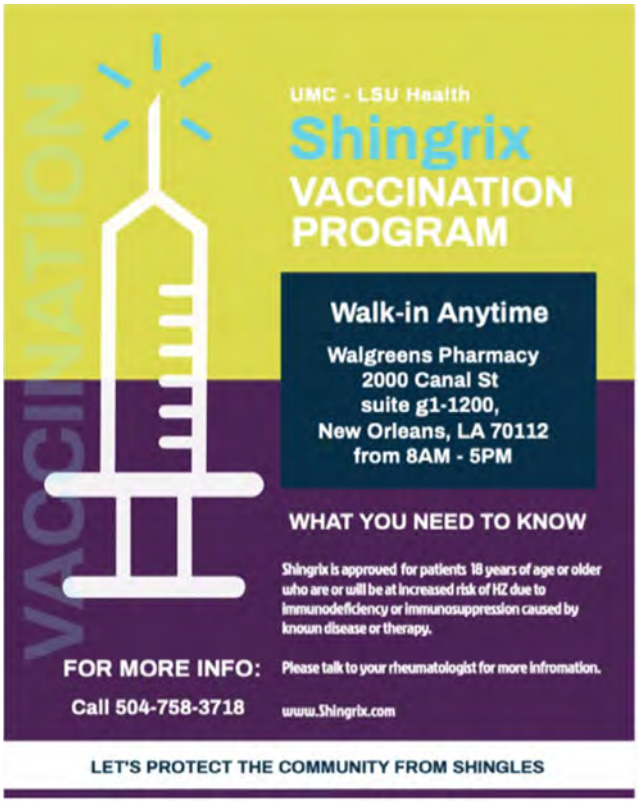

Figure 1. Shingrix Vaccination Patient Flyer

first vaccine dose. A majority of those receiving full vaccination were completed in the specialty pharmacy. The goal is to have 80% of eligible patients seen in rheumatology to be vaccinated.

Conclusion: RZV vaccination uptake has been markedly improved in our 18-49 years old eligible IRD patients, from 0.2% in April 2022 to 35.5% as of June 1, 2023. Even though the FDA may approve new guidelines, uptake is delayed, especially in the younger patient populations. The combination of multiple reminder avenues along with the coordination of specialty pharmacy proved successful in vaccinating eligible patients.

Disclosure: S. Lindsey: None; **B. Hill**: None; **S. Sheth**: None; **A. Loghmani**: None.

Abstract Number: 0199

Experience in Real-World Conditions of the Effectiveness of the Vaccine Against Herpes Zoster Virus

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
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Session Time: 9:00AM–11:00AM

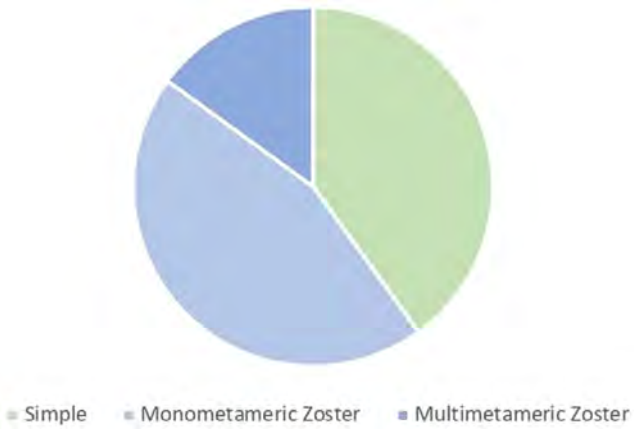
Background/Purpose: Herpes zoster infection is due to the reactivation of the varicella-zoster virus (VZV), having a high prevalence in elderly and immunocompromised patients. Since the beginning of 2022, a new vaccine that prevents herpes zoster virus reactivation has been approved and commercialized. However, there are few studies analyzing its effectiveness in real-world conditions.

Our purpose is to analyze the incidence and rate of herpes zoster disease in a population at risk due to suffering from rheumatic diseases and therefore being subsidiary of receiving VZV vaccination.

Methods: A retrospective observational study of patients who started treatment with JAK inhibitors from 2013 to 2022 was performed. Demographic and clinical features were collected from the electronic clinical history. Vaccination of patients against VZV was analyzed, as well as the incidence of herpes simplex (HSV) and herpes zoster reactivation before and after January 2022, date on which the vaccination program began. In addition, the rate of the VZV disease was calculated based on the follow-up time for both vaccinated and unvaccinated patients and was adjusted by exposure in events/100 patients-year (E/100 PY).

	Total of patients (n=236)
Age - years (sd)	62.45 (8.2)
Female sex - n (%)	188 (79.66%)
Diagnosis - n (%)	
RA	179 (75.84%)
PsA	28 (11.86%)
AS	14 (5.93%)
Others	10 (4.23%)
JIA	5 (2.11%)
Comorbidities - n (%)	
Dyslipidemia	69 (29.23%)
Arterial hypertension	65 (27.54%)
Smoking	40 (16.95)
Mellitus diabetes	22 (9.32%)
Vaccination	
No	206 (87.29%)
Yes	30 (12.71%)

Demographic and clinical characteristics of the patients.



Frequency of Herpes Virus infection.

Results: 236 patients with an indication for vaccination against VZV due to being treated with JAK inhibitors were included, of whom the majority diagnosis was Rheumatoid Arthritis (n=179). Their demographic and clinical features are shown in the following table. 30 patients were vaccinated against VZV (12.71%). An incidence of 20 herpes cases was observed in unvaccinated patients, of them, 8 corresponded with HSV and 12 with VZV. 3 of the VZV reactivations were of multimetameric involvement (see graph). No cases of herpes were found in the vaccinated population. The unvaccinated patients were followed up for 3500 months, remaining with a herpes rate in this population of 4.12 E/100 PY. The total follow-up of vaccinated patients was 102 months, with a herpes rate of 0 E/100 PY.

Conclusion: An incidence of 12 VZV is observed in unvaccinated patients compared to an incidence of 0 in vaccinated patients. The herpes rate in non-vaccinated patients was 4.12 E/100 PY compared to 0 E/100 PY in vaccinated patients. Therefore, we conclude that the herpes zoster vaccine shows its effectiveness in our population but it would be necessary to carry out more studies in the future with a longer follow-up time.

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Abstract Number: 0200

Herpes Zoster Prevalence in Patients with Rheumatic Diseases

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Herpes zoster (HZ) is a painful rash that is commonly known as shingles. People that had a primary infection caused by the varicella-zoster virus known as chicken pox can present herpes zoster at any age.[1] The infection manifests as a vesicular rash with the characteristic of following a dermatomal pattern followed by postherpetic neuralgia. Herpes zoster is commonly observed in the elderly and immunocompromised populations such as patients with autoimmune diseases or malignancies. On average HZ incidence in a normal population is 1.2 to 4.9 cases per 1000 person per year; however, herpes incidence is multiplied in those with autoimmune diseases.[2]

Methods: We conducted a cross-sectional study that included consecutive patients with RD who were ≥ 18 years attending the rheumatology service in a northeast referral hospital in Mexico. We excluded patients who refused to participate. The following data was collected between December 2022 to May 2023: demographics, medical history, and RD diagnosis. We applied a paper-based questionnaire and reviewed medical records to identify HZ events in patients with RD, demographics, onset, recurrence, vaccination status, and hospital admissions related to HZ and HZ-related factors.

Results: A total of 182 patients with RD were screened for HZ. Patients with HZ had a median and IQR age of 57 (48.5 – 69). Thirty-three (18.13%) patients reported an HZ event; of which 14 (42.4) had their first HZ event over more than 10 years ago. Thirty-two (96.97%) were treated with antivirals, 3 (9.09%) were hospitalized due to severe disease, and 31 (93.94%) were not vaccinated against HZ. Regarding rheumatic diseases 9 (32.1) SLE patients, 20 (17.5) RA patients, and 2 (12.5%) OA patients had HZ. (See Tables 1 and 2).

Conclusion: Herpes zoster events are six folded in patients with rheumatic diseases. The prevalence of HZ-events is higher in patients with autoimmune diseases, specifically in those with SLE. The frequency of HZ events and severe disease can be prevented through vaccination; however, the vaccine may not be accessible to everyone.

Table 1. Demographic characteristics in patients with rheumatic diseases

	HZ n = 33	No Hz n = 149
Age, median (IQR)	57 (48.5 – 69)	51 (44 – 59.5)
Sex, n (%)		
○ Female	29 (87.9)	139 (93.3)
○ Male	4 (12.1)	10 (6.7)
Age at the first HZ event, n (%)		
○ Less than a year	4 (12.1)	
○ 1 to 5 years	7 (21.2)	-
○ 6 to 10 years	8 (24.2)	
○ More than 10 years	14 (42.4)	
Recurrent HZ infection, n (%)	4 (12.1)	-

HZ, herpes zoster; IQR, interquartile range

Table 2. Herpes zoster infection per rheumatic disease group

	RA n = 114	SLE n = 28	OA n = 16	Others n = 24
HZ Infection, n (%)	20 (17.5)	9 (32.1)	2 (12.5)	2 (8.3)
Recurrent zoster infection, n (%)	2 (1.75)	1 (6.3)	1 (6.3)	0
HZ Symptoms, n (%)	20 (17.5)	8 (28.6)	2 (12.5)	2 (8.3)
Confirmed diagnosis by a physician, n (%)	19 (16.7)	9 (32.1)	2 (12.5)	0
HSV immunization, n (%)	0	2 (7.1)	0	0
Postherpetic neuralgia, n (%)	0	0	0	0
Antiviral treatment, n (%)	19 (16.7)	9 (32.1)	2 (12.5)	2 (8.3)

HZ, herpes zoster; RA, rheumatoid arthritis; Systemic lupus erythematosus; OA, osteoarthritis; Others: Primary Sjögren syndrome, dermatomyositis, scleroderma, vasculitis mixed connective tissue disease and vasculitis. HPV, human papilloma virus; HSV, herpes simplex virus.

1. Yun H, Yang S, Chen L, Xie F, Winthrop K, Baddley JW, et al. Risk of Herpes Zoster in Autoimmune and Inflammatory Diseases: Implications for Vaccination. Arthritis Rheumatol. 2016;68(9):2328-37.
2. Chen HH, Chen YM, Chen TJ, Lan JL, Lin CH, Chen DY. Risk of herpes zoster in patients with systemic lupus erythematosus: a three-year follow-up study using a nationwide population-based cohort. Clinics (Sao Paulo). 2011;66 (7):1177-82.

Disclosure: R. Castillo-de la Garza: None; **J. Esquivel-Valerio**: None; **E. Campos-Tinajero**: None; **A. Carrazco Chapa**: None; **G. García Arellano**: None; **A. De Leon-Perez**: None; **P. Gamez-Siller**: None; **D. Galarza-Delgado**: None.

Abstract Number: 0201

Tolerability and Safety of Recombinant Zoster Vaccine in Patients with Inflammatory Rheumatic Musculoskeletal Diseases - A Prospective Longitudinal Study over 12 Months

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SESSION INFORMATION
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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Herpes zoster (HZ) is common in the elderly, with a lifetime risk of 25%. The primary risk factors for HZ are advanced age and immunosuppression. The aim is to describe the safety of recombinant zoster vaccine in patients with inflammatory rheumatic and musculoskeletal diseases (RMD)

Methods: Adult patients with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), and giant cell arteritis (GCA) were prospectively enrolled in this ongoing study. Data on demographics, vaccination, RMD diagnosis, disease activity, immunosuppressive treatments, flares, and zoster breakthrough infections were collected at months 0, 2, 3, 6 and 12. Safety assessments were performed at 2, 3, 6, and 12 months. A flare was defined as change in ASDAS ≥ 0.9 for axSpA, change in DAS-28 >1.2 for RA, or clinical signs for GCA and/or CRP ≥ 0.5 mg/dl and/or ≥30 mm. Descriptive analyses were performed

Results: 81 patients were enrolled, of whom 21 (25.9%) had a history of HZ (Table 1). All patients received RZV at month 0 and 66 patients at month 2. Safety assessments in 66, 56, 48, and 5 patients at month 2, 3, 6 and 12, respectively. A total of 87, 68, 15, 8 AEs were reported in 53, 37, 13, and 6 patients, respectively. Localized AEs (n=97 (67.0%)) were more common than generalized AEs (n=48 (33.1%)). Pain at the injection site (55 (30.9%)) was the most common AE, followed by fatigue (20 (11.2%)), musculoskeletal pain (19 (10.7%)), fever (14 (7.9%)), redness at the injection site (10 (5.6%)), and swelling at the injection site (7 (3.9%)). Serious adverse events (AE) were reported in 8 patients (3 RA, 5 GCA), none of which were vaccine-related. No patient reported an AE of special interest. 5, 4, 5 and 2 episodes of self-reported disease worsening were reported by patients at months 2, 3 and 6, respectively, 12 but none met predefined flare criteria. However, 3 patients (2 GCA, 1 RA) were hospitalized as a result. No episodes of HZ occurred during follow-up

Variable	RA (n=32)	AxSpA (n=29)	GCA (n=20)
Age	54.6 (12.2)	45.5 (10.2)	73.3 (6.8)
Sex, female (No., %)	18 (56.3)	9 (31.0)	14 (70.0)
History of zoster (No., %)	8 (25.0)	3 (10.3)	11 (55.0)
CRP, mg/dl	0.5 (0.7)	0.7 (1.2)	0.2 (0.3)
Prednisolone, mean dosage mg/dl	6.4 (8.2)	0	14.1 (15.6)
csDMARD(No., %)	29 (90.6)	0	8 (40.0)
bDMARD(No., %)	23 (71.9)	23 (79.3)	8 (40.0)
tsDMARD(No., %)	6 (18.8)	6 (20.7)	0
Physician global	0.94 (1.5)	1.5 (1.6)	0.8 (1.5)
Patient global	3.6 (2.4)	3.5 (2.1)	3.9 (2.6)
Pain	3.4 (2.5)	3.2 (2.3)	3.6 (2.6)
Disease activity	DAS-28 2.6 (1.4)	ASDAS 2.1 (0.9)	NA
Physical function	FFbH 77.4 (21.7)	BASFI 3.5 (2.7)	FFbH 71.2 (23.3)

Patients and disease characteristics

Conclusion: Most patients tolerated RZV well with few reports of flare and serious AEs. The majority of AEs occurred within a few days of vaccination. These findings are reassuring for rheumatologists and potential vaccine recipients and support confidence in the safety of RZV in patients with RMD

Disclosure: I. Andreica: AbbVie/Abbott, 1, 6, Amgen, 1, 6, AstraZeneca, 1, 6, Chugai, 6, Novartis, 1, 6, Sobi, 1, 6, UCB, 1, 6; **G. Chierergo**: None; **S. Reale**: None; **B. Wilde**: None; **S. Tsiami**: None; **D. Kiefer**: None; **P. Sewerin**: AbbVie, 2, 5, 6, Biogen, 2, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 5, 6, Chugai, 2, 5, 6, Hexal, 2, 6, Janssen-Cilag, 2, 5, 6, Lilly, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, Sanofi-Genzyme, 2, 6, Swedish Orphan Biovitrum, 2, 6, UCB, 2, 5, 6; **H. Kavruk**: None; **D. Karagkiozidou**: None; **B. Guminski**: None; **A. Kribben**: None; **X. Baraliakos**: AbbVie, 2, 6, BMS, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, 6, UCB, 2, 6; **J. Braun**: None; **U. Kiltz**: AbbVie, 2, 5, 6, Amgen, 5, Biocad, 2, 6, Biogen, 5, Bristol-Myers Squibb(BMS), 2, 5, Chugai, 2, 6, Eli Lilly, 2, 6, Fresenius, 5, Gilead, 2, 5, GlaxoSmithKline (GSK), 5, Grünenthal, 2, 6, Hexal, 5, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, onkowiessen.de, 2, 5, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Viatris, 2, 5.

Abstract Number: 0202

Analysis of the Effects of Immunosuppressive Therapy on Herpes Zoster Events After Each of Three Doses of the BNT162b2 mRNA Vaccine in Patients with Spondyloarthritis (SpA)

Tal Gazitt[1], Noa Hayat[2], Amir Haddad[2], Joy Feld[3], Nili Stein[2], Idit Lavi[2], Ilan Feldhamer[4], Arnon Dov Cohen[5], Walid Saliba[2] and Devy Zisman[2], [1]Carmel Hospital, Haifa, Israel, [2]Carmel Medical Center, Haifa, Israel, [3]Carmel and Zvulun Medical Centre, Haifa, Israel, [4]Chief Physician's Office, Clalit Health Services, Tel Aviv, Israel, [5]Ben-Gurion University of the Negev, Beer-Sheva, Israel

SESSION INFORMATION
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Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The importance and efficacy of mRNA COVID-19 vaccination in coping with the pandemic are well established, but inconsistencies remain in the data regarding side effects, especially in patients with rheumatic diseases treated with immunosuppressive therapy.

We aimed to assess the effect of immunosuppressive therapy on the incidence of Herpes Zoster (HZ) in patients with psoriatic arthritis (PsA) and ankylosing spondylitis (AS) after each of the three doses of the BNT162b2 mRNA vaccine compared to HZ incidence in a similar time period two years prior to vaccination.

Methods: The database of Clalit Health Services, the largest health care provider of approximately 4.7 million members in Israel, was retrospectively analyzed for patients with a diagnosis of PsA and AS starting from 12/2018 and who later received 3 doses of the BNT162b2 mRNA vaccine in a national vaccination campaign from 12/2020-12/2021. For each individual, data on demographic, socioeconomic, and selected chronic comorbidities, as well as use of glucocorticosteroids, conventional/ biologic/ targeted-synthetic disease-modifying anti-rheumatic drugs (DMARDs) and previous HZ vaccination status were retrieved.

The incidence of HZ events was calculated during the 6 weeks following each of the three mRNA COVID-19 vaccine doses and compared to a similar time period within this group of patients two years prior by NcNemar test, and also relative to fully-vaccinated controls from the general population matched by sex and age at 1:10 ratio. For each SpA patient, multivariable logistic regression was used to assess for any association between DMARD use within 3 months prior to each HZ event and HZ reactivation risk relative to SpA patients not on these medications.

Results: The study population consisted of 6460 SpA patients, 4648 (72.0 %) with PsA, 1812 (28.0%) with AS and 115 (1.8%) with both PsA and AS with a mean age of 57.6±15.0 years, of whom 3107 (48.1%) male. Of SpA patients, 18.2% (n=1173), 35.5% (n=2293), and 1.2% (n=79) were on cDMARDs, bDMARDs, and tsDMARDs, respectively. The incidence of HZ events was higher among SpA patients in comparison to the general population both pre- (p=0.004) and post- (p=0.027) mRNA COVID-19 vaccination, even after controlling for multiple covariates, with no significant difference in HZ reactivation occurring in the PsA vs AS subgroups pre- and post mRNA vaccination. The number of HZ events was not increased in SpA patients with HZ events who received bDMARDs (p=0.372), TNF-α inhibitors in particular (p=0.095), or cDMARDs (p=0.365) in comparison to patients not on these medications (too few HZ cases occurred in patients on tsDMARDs to allow for statistical analysis).

Conclusion: The risk of HZ after each one of the three BNT162b2 mRNA vaccine doses was not increased in PsA and AS patients compared to a similar time period two years prior to vaccination, and was not influenced by the type of DMARD used.

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Abstract Number: 0203

Projecting the Impact on Clinical Outcomes in ANCA-Associated Vasculitis of Delaying Retreatment with Rituximab for Vaccine Optimization

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SESSION INFORMATION
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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rituximab (RTX) is effective for maintaining remission in ANCA-associated vasculitis (AAV) but increases risks for vaccine-preventable severe infections and reduces the immune response to vaccination. There is uncertainty regarding risks and benefits of holding RTX to improve vaccine efficacy by permitting B cell repopulation (e.g., seasonal flu, COVID-19). We used the previously validated microsimulation model, AAV-Sim, to project the clinical impact of delaying treatment with RTX in people with AAV in remission.

Methods: We evaluated 2 strategies: (1) **Continuous B cell depletion** with routine RTX retreatment; or (2) **Permissive B cell repopulation** with RTX delayed for 4 weeks to optimize vaccination, then resuming RTX. At model start, individuals are in remission, B cell depleted, and have an eGFR ≥45ml/min. They are assigned demographics, ANCA type, and other characteristics based on probabilities, and transition monthly between active (e.g., major/minor relapse) or inactive AAV states. They are monitored monthly for B cell repopulation and are at risk for severe infection, end-stage renal disease (ESRD), or death. Transition rates are stratified by demographic and disease-specific characteristics (**Table 1**). We projected the primary outcomes of relapse-free remission and vaccine optimization over 12 months. We defined vaccine optimization as: B cell repopulated, retreatment delayed, and no relapse prior to vaccination. We performed sensitivity analyses to identify influential factors.

Results: Permissive B cell repopulation (Strategy 2) would be associated with lower relapse-free survival than continuous B cell depletion (Strategy 1) (81.0% vs 95.9%). However, 72.8% of patients would be optimized for vaccination in Strategy 2, whereas none would be optimized in Strategy 1 (**Figure 1**). Minimal differences between strategies would occur in model-projected new renal involvement, ESRD, and death. Varying B cell repopulation rates and ANCA type would strongly influence relapse-free survival. Relapse-free survival in Strategy 2 would be higher in MPO-ANCA+ vs PR3-ANCA+ across B

Table 1: Input Parameters for AAV-Sim Stratified by Treatment Strategy

Input Parameter	Base Case Value		
Baseline Cohort Characteristics[1]			
Age (mean [SD], years)	60.6 (13.0)		
Male (%)	58.2%		
PR3-ANCA (N, %)	58.0%		
Renal Involvement (N, %)	71.1%		
Relapse (monthly probability)[1-6]	**Permissive B Cell Repopulation**		**Continuous B Cell Depletion with RTX**
	B Cells Detected*	No B Cells Detected	
PR3-ANCA Major Relapse	0.026412	0.013158	0.00171
PR3-ANCA Minor Relapse	0.046489	0.023521	0.00292
MPO-ANCA Major Relapse	0.013158	0.006601	0.00085
MPO-ANCA Minor Relapse	0.023521	0.046489	0.00143
B Cell Repopulation[7]	0.174596		N/A
Severe Infection (monthly probability)[1, 2]			
Active Disease^	0.00944		0.00944
Inactive Disease	0.00419		0.00785
Risk of New Renal Involvement with Major Relapse	0.10		0.10
End-Stage Renal Disease (monthly probability)			
Active Disease			
History of Renal Involvement	0.00966[8]		
No History of Renal Involvement	*Age- and sex-stratified*[9]		
Inactive Disease			
History of Renal Involvement	*2.0 * Age- and sex-stratified*[9]		
No History of Renal Involvement	*Age- and sex-stratified*[9]		
Mortality (monthly probability)			
Active Disease	*SMR of 2.5 * age- and sex-stratified*[10]		
Inactive Disease	*SMR of 1.5 * age- and sex-stratified*[10]		
ESRD	*Age- and sex-stratified*[9]		
Severe Infection	*Age- and sex-stratified*[11]		

*Risk of relapse stratified by B cell status based on assumption that B cell repopulation associated with 2-fold increased risk of relapse. ^Risk of severe infection in active disease is the same in both strategies because treatment will be similar for active disease in both strategies. RTX: Rituximab; CDC: Centers for Disease Control and Prevention; USRDS: United States Renal Data System; HCUP: Healthcare Cost and Utilization Project; SMR, standardized mortality ratio; References: 1. Charles P, et al. Ann Rheum Dis. 2018;77(8):1143-9. 2. Smith RM, et al. Ann Rheum Dis. 2020;79(9):1243-9. 3. Guillevin L, et al. N Engl J Med. 2014;371(19):1771-80. 4. Lionaki S, et al. Arthritis Rheum. 2012;64(10):3452-62. 5. Hogan SL, et al. Ann Intern Med. 2005;143(9):621-31. 6. Walsh M, et al. Arthritis Rheum. 2012;64(2):542-8. 7. Stone, et al. NEJM 2010;363:221. 8. Rhee RL, et al. Arthritis Rheumatol. 2016;68(7):1711-20. 9. United States Renal Data System. 2020 USRDS Annual Data Report. 2020. 10. Arias E, Xu J. United States Life Tables, 2017. 11. HCUP

cell repopulation rates (range, 85.0%-89.4% [difference 4.4%] vs 72.7%-80.3% [difference 7.6%], respectively) (**Figure 2**). Further, a greater portion of MPO- vs PR3-ANCA+ patients would have vaccine optimization across scenarios (range, 58.6%-87.9% vs 51.0%-78.5%, respectively).

Conclusion: A strategy that permits B cell repopulation would be associated with a higher risk of relapse but would optimize many patients for vaccination. ANCA type (i.e., relapse risk) and B cell repopulation rates strongly influence these risks and benefits. A strategy of permissive B cell repopulation may be more acceptable in MPO-ANCA+ AAV and people with faster B cell repopulation. B cell repopulation rates had a stronger influence on model-projected relapse-free survival in PR3- than MPO-ANCA+ AAV. To further weigh the risks and benefits of each strategy, the downstream effects of vaccination (e.g., infection severity) will be incorporated in future steps. These findings highlight the importance of improving biomarkers of relapse risk and determining predictors of B cell repopulation rate.

Figure 1: The Impact of Two Strategies for Management of Remission in ANCA-Associated Vasculitis on Relapse-Free Survival (1A), Vaccine Optimization (1A), and Other Key Outcomes (1B)

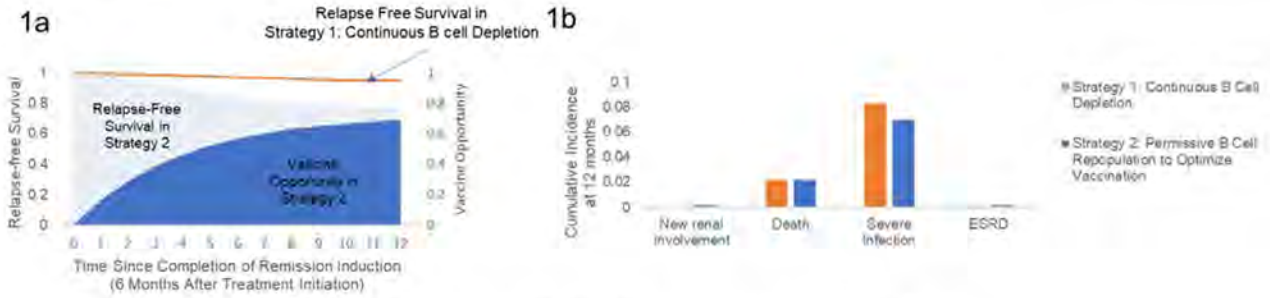

Figure 1a reflects relapse-free survival and vaccine optimization in a population with baseline features similar to those enrolled in MAINRITSAN 2. The solid line reflects the relapse-free survival with continuous B cell depletion with rituximab (Strategy 1). Because there is RTX retreatment to maintain continuous B cell depletion in Strategy 1, there is no vaccine optimization with this strategy. The patterned shade reflects relapse-free survival if B cells are permitted to repopulate to optimize vaccination (Strategy 2). The solid shade reflects vaccine optimization if B cells are allowed to repopulate and retreatment delayed (Strategy 2). Figure 1b reflects the cumulative incidence at 12 months of other key outcomes.

Figure 2: The Impact of ANCA Type and B Cell Repopulation Rates on Relapse-Free Survival and Vaccine Optimization

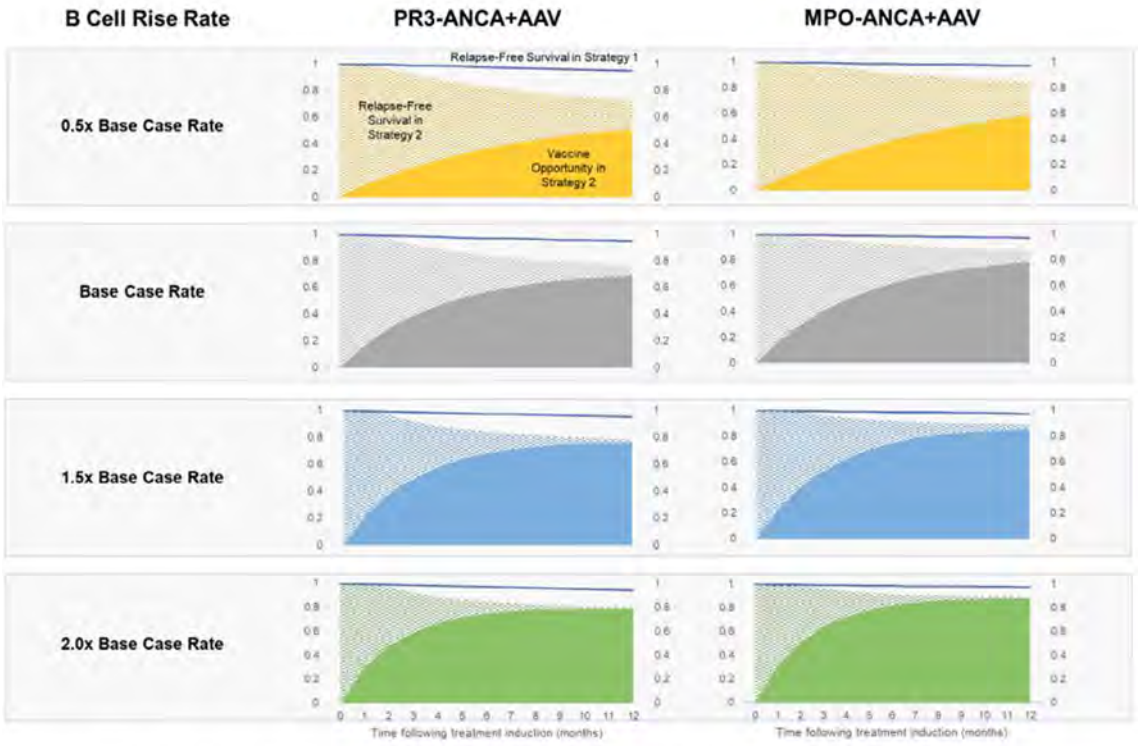

Figure 2 reflects relapse-free survival and vaccine optimization with varied B cell repopulation rates in PR3-ANCA+ and MPO-ANCA+ AAV. The solid line in each figure reflects the relapse-free survival with continuous B cell depletion with rituximab (Strategy 1). Because RTX is used to maintain continuous B cell depletion, there is no vaccine optimization in Strategy 1. The patterned shade reflects relapse-free survival if B cells are permitted to repopulate and RTX retreatment is delayed to optimize vaccination (Strategy 2). The solid shade reflects vaccine optimization if B cells are allowed to repopulate (Strategy 2). AAV: ANCA-associated vasculitis.

Disclosure: Z. Wallace: BioCryst, 2, Bristol-Myers Squibb(BMS), 5, Horizon, 1, 2, 5, MedPace, 2, Novartis, 1, PPD, 2, Sanofi, 1, 5, Shionogi, 1, Visterra, 1, 2, Zenas, 1, 2; **A. Wu**: None; **S. Srivatsan**: None; **N. Patel**: Arrivo Bio, 2, Chronius Health, 2, FVC Health, 2; **J. Sparks**: AbbVie, 2, Amgen, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, 5, Gilead, 2, Inova Diagnostics, 2, Janssen, 2, Optum, 2, Pfizer, 2, ReCor, 2; **E. Miloslavsky**: None; **H. Choi**: Ani, 2, Horizon, 2, 5, LG, 2, Protalix, 2, Shanton, 2; **P. Merkel**: None; **J. Stone**: Abvie, 2, Amgen, 1, 2, Argenx, 2, Aztrazeneca, 2, Bristol Myers Squibb, 2, 5, Celgene, 2, Chemocentryx, 2, Chugai, 2, GSK, 2, Horizon Therapeutics, 1, 2, 5, InflaRx, 2, IQVIA, 1, 2, Kyverna, 2, Mirabio, 2, NIH, 5, Novartis, 2, PPD, 2, Prometheus, 2, Q32, 2, Regeneron, 2, Roche-Genentech, 2, Roivant, 2, Sanofi, 2, 5, Spruce Biosciences, 2, Star Therapeutics, 2, Steritas, 12, Chair, Scientific Advisory Board (no fiduciary responsibilities), ZenasBio, 2; **E. Hyle**: UpToDate.com, 9.

Abstract Number: 0204

Risk of Severe Infections Associated with Immunoglobulin Deficiency Under Rituximab Therapy in Immune Mediated Inflammatory Diseases

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Literature data on the increased risk of severe infection regarding hypogammaglobinemia related to RTX in IMID are controversial and sparse. We proposed to evaluate the risk of severe infections in patients with IMID treated with RTX who presented Ig deficiency (prevalent or acquired).

Methods: We conducted an observational, retrospective single-center study retrieving all patients with at least one infusion of RTX in the department of Rheumatology (CHU Montpellier) between January 1st and December 31st 2017. We included all patients treated for an IMID (rheumatoid arthritis, systemic lupus erythematosus, ANCA-associated vasculitis, primary Sjögren syndrome, inflammatory myopathy, scleroderma, mixt connective diseases, cryoglobulinemia vasculitis and overlap syndrome) with at least one Ig assay performed during follow-up. Patients were followed-up at least12 months after the last infusion of RTX or until the occurrence of a severe infection or death occurring within 12 months after the last infusion of RTX or until the end of the study (May 31st 2020).Ig deficiency was defined as a rate of IgG, and/or IgA and/or IgM lower than the laboratory thresholds. Then, we categorized patients with prevalent Ig deficiency (before the first infusion of RTX), acquired Ig deficiency (normal Ig assays before the first infusion of RTX and with an occurrence of at least one Ig deficiency during follow-up), and patients with normal Ig level from the first infusion to the end of follow-up.

Results: Three hundred and eleven patients were included. Nine patients had undatable Ig deficiency. Twenty-nine patients (9,4%) had prevalent Ig deficiency. As compared with patient with normal Ig level at baseline, concomitant treatment with glucocorticoids (p=0,03) and with a higher daily dose at baseline (p=0,01) were associated with a prevalent Ig deficiency. Sixty-eight patients (22,0%) acquired an Ig deficiency after the first infusion of RTX. A longer time of follow-up and a higher cumulative dose of RTX, the type of IMIDs (SLE and AAV) and concomitant treatment with IS or GCs at baseline, diabetes mellitus and obesity were associated with the occurrence of an Ig deficiency (Table 1). Forty-three patients (14,3%) developed a severe infection within 12 months after the last infusion of RTX. Severe infections occurred more frequently in patients with prevalent Ig deficiency but without any stastistical difference with patient with normal Ig level (Table 2). In multivariate

analysis, only chronic pulmonary disease, a higher daily dose of GCs and a higher mean DAS28-CRP during follow-upwere still associated with an increased risk of severe infection (Table 3). In a time-dependant analysis, Ig deficiency in patient treated with RTX, wether acquired or prevalent, was not associated with an increased risk of severe infection (adjusted HR 1.04 [0.5-2.3], p=0.92).

Table 1.: Baseline and follow-up characterisitics of patients with IMIDs receiving RTX, in the whole cohort, and comparison of patient with acquired Ig deficiency and normal Ig level.

Patients (n)	**All patients (311)**	**Ig deficiency at the end of follow-up**		
		Acquired (68)	**No (205)**	**p**
Age (years), mean (SD)	57.9 (12.5)	57.1 (12.8)	57.6 (12.6)	0.78
Female, n (%)	248 (79.7)	51 (75)	170 (82.9)	0.18
Duration of follow-up (months), mean (SD)	66.6 (84.0)	84.2 (41.5)	62.9 (99.0)	**< 0.001**
Rheumatoid Arthritis, n (%)	264 (84.9)	55 (80.9)	178 (86.8)	0.13
Systemic Lupus Erytematosus, n (%)	13 (4.2)	6 (8.9)	6 (2.9)	**0.02**
ANCA-Associated Vasculitis, n (%)	8 (2.6)	4 (5.9)	3 (1.5)	**0.03**
Others IMIDs, n (%)	23 (7.3)	3 (4.4)	18 (8.8)	0.31
Charlson index, mean (SD)	2.1 (1.5)	2.4 (1.7)	2.0 (1.4)	0.13
Cardiovascular disease, n (%)	42 (13.5)	10 (14.7)	25 (12.2)	0.92
Chronic pulmonary disease, n (%)	86 (27.6)	19 (27.9)	58 (28.3)	0.62
History of neoplasia, n (%)	64 (20.6)	16 (23.5)	40 (19.5)	0.29
Obesity (BMI > 30 kg/m²), n (%)	57 (18.3)	19 (27.9)	31 (15.1)	**0.004**
Diabetes Mellitus, n (%)	40 (12.9)	14 (20.6)	20 (9.7)	**0.03**
Tobacco exposure, n (%)	122 (39.2)	32 (47.1)	76 (37.1)	0.98
Previous severe infection (12 months), n (%)	18 (5.8)	3 (4.4)	11 (5.4)	0.49
Combination with csDMARDs, n (%)	193 (62.1)	41 (60.3)	127 (61.9)	0.61
Combination with ImmunoSuppressor, n (%)	14 (4.5)	8 (11.8)	4 (1.9)	**0.001**
Concomitant treatment with GCs, n (%)	178 (57.2)	45 (66.2)	110 (53.6)	**0.04**
Cumulative dose of RTX (g), mean (S.D.)	9.2 (4.9)	12.8 (4.7)	8.3 (4.6)	**< 0.001**
Mean DAS28 during follow-up, mean (SD)	3.5 (1.3)	3.2 (0.9)	3.6 (1.3)	**0.004**

Table 2. Incidence of severe infections according to Ig level.

Patients (n)	All patients (311)	Prevalent Ig deficiency (29)	Acquired Ig deficiency (68)	Normal Ig level (205)
Severe infection within 12 months after the last infusion of RTX, n (%)	45 (14.5)	7 (24.1)	7 (10.3)	31 (15.1)
Exposure, PY	1726.6	107.9	477.4	1074
Incidence rate (/100 PY)	2.6	6.5	1.5	2.8
Risk of severe infections, compared with patients with normal Ig levels during the entire follow-up, adjusted HR [CI95]*, p	NA	1.8 [0.8-4.2], p=0.15	0.4 [0.5-0.99], p=0.05	Ref.
Risk of severe infections, compared with patients with normal Ig levels during the entire follow-up, adjusted HR [CI95]*, p	NA	1.3 [0.5-3.4], p=0.53	0.3 [0.1-1.2], p=0.09	Ref.

PY = patients-year; RR = relative risk ; CI 95 = confidence interval with 95%

* Multivariate model, adjusted on the type of IMID, chronic pulmonary disease, diabete mellitus, previous treatment with immunosuppressor, combination with immunosuppressor at baseline, glucocorticoids at baseline, daily dose of glucocorticoids during follow-up, mean-DAS 28-CRP during follow-up .

Table 3. Risk factors associated with severe infection within 12 months after the last RTX infusion in the whole population of study (multivariate analyses).

	Multivariate analysis	
	aHR [95CI]	p
IMID		
- Rheumatoid Arthritis	Ref.	NA
- Systemic Lupus Erythematosus	0.9 [0.2-4.1]	0.86
- ANCA associated vasculitis	NA	NA
- Others IMIDs	1.9 [0.5-7.7]	0.37
Comorbidities		
- Chronic pulmonary disease	2.3 [1.2-4.5]	0.01
- DM	1.1 [0.4-3.0]	0.77
Treatment and disease activity		
- Previous treatment with immunosuppressor	1.2 [0.5-2.7]	0.63
- Combination with immunosuppressor	0.6 [0.1-4.7]	0.63
- Concomitant treatment with glucocorticoids	1.1 [0.4-2.8]	0.9
- Mean daily dose of GCs during follow-up	1.2 [1.1-1.3]	0.001
- Mean DAS28-CRP during follow-up	1.3 [1.002-1.7]	0.05
Acquired Ig deficiency	1.3 [0.5-3.4]	0.53
Prevalent Ig deficiency	0.3 [0.1-1.2]	0.09

aHR = adjusted Hazard Ratio, in multivariate analysis by Cox model , adjusted on the type of IMID, chronic pulmonary disease, diabete mellitus, previous treatment with immunosuppressor, combination with immunosuppressor at baseline, glucocorticoids at baseline, daily dose of glucocorticoids during follow-up, mean-DAS 28-CRP during follow-up and the type of immunoglobulin deficiency

Conclusion: We did not observe an increased risk of severe infection in RTX-induced Ig deficiency. In case of Ig deficiency, RTX management should be discussed on a case-by-case basis, according to an individual assessment of the infectious risk, especially when GCs therapy is used and chronic lung diseases are present.

Disclosure: C. Rempenault: None; **C. Lukas**: Abbvie, 2, 6, Amgen, 2, 6, Biogen, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche Chugai, 2, 6, UCB, 2, 6; **L. Tardivon**: None; **C. Daien**: None; **B. Combe**: AbbVie, 2, 6, BMS, 6, Celltrion, 2, Eli Lilly, 1, 2, 6, Galapagos, 2, 6, Gilead, 2, Janssen, 2, 6, MSD, 6, Nordic Pharma, 5, Novartis, 1, Pfizer, 6, Roche-Chugai, 2, 6; **P. GUILPAIN**: None; **J. MOREL**: None.

Abstract Number: 0205

Changes in Serum Rheumatoid Factor Following Eradication of Hepatitis C Virus Infection with Interferon or Direct Antiviral Therapy

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Infection-related Rheumatic Disease Poster

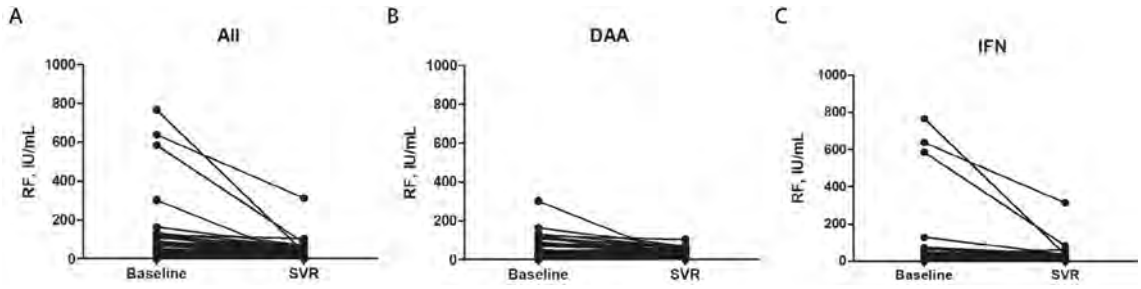
Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

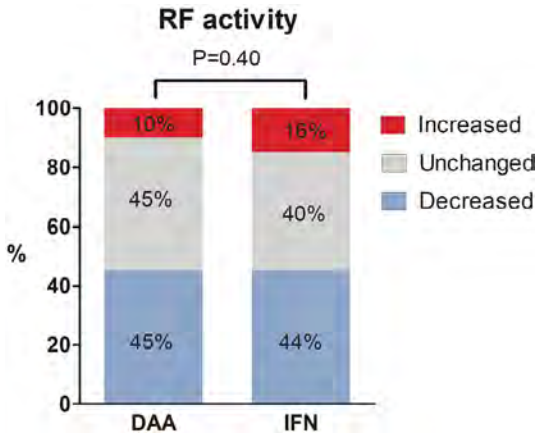
Background/Purpose: Chronic hepatitis C virus (HCV) infection is associated with autoimmune extrahepatic manifestations including increased production of autoantibodies such as rheumatoid factor (RF). Prior to the advent of direct-acting antivirals (DAAs), HCV infection was treated with pegylated interferon (Peg-IFN) which is known to induce or exacerbate autoimmunity. It remains unclear whether HCV eradication was associated with reduction in autoantibodies, and whether results would differ between IFN-based and IFN-free regimens. In our research, we aimed to investigate changes in serum RF following viral eradication in patients with chronic HCV infection who were treated with either Peg-IFN or ribavirin plus DAA.

Methods: This is a retrospective cohort study of adult HCV patients treated at a teaching hospital in Taiwan. All patients had detectable HCV RNA at baseline (BL) and achieved sustained virological response (SVR) documented 12 or 24 weeks after treatment. Serum level of IgG RF was measured using latex immunoassay with a measurement of 15 IU/mL or above defining seropositivity. The changes from BL to SVR were analyzed and the results were compared between patients treated with IFN-based regimens and those with IFN-free DAAs. Subgroup analyses according to age, sex, presence of cirrhosis, HCV genotype, and BL ANA titer were performed.

Results: This study enrolled 297 patients (median age 59; 48.5% female). Among them, 78 (26.3%) were RF-positive by qualitative serology at BL. This number decreased to 49 (16.5%) at SVR-12 or -24 ($P < 0.001$). Quantitatively, the median level of serum RF in the study cohort also decreased from 1.6 IU/mL (IQR undetectable (UD)-15.8) to UD (IQR, UD-6.6 IU/mL) ($P < 0.001$). Significant reductions in serum RF were observed in both treatment groups. The proportion with RF seropositivity decreased from 24.3% to 15.4% ($P = 0.001$) in patients treated with IFN-free agents ($n = 214$) and from 31.3% to 19.3% ($P = 0.006$) in patients treated with IFN-based regimens ($n = 83$), without significant difference between these two groups ($P = 0.40$).



Changes of serum rheumatoid factor (RF) level from baseline to sustained virological response (SVR) in all patients (panel A, left), patients treated with interferon-free (panel B, middle) or interferon-based regimens (panel C, right).



Comparison of changes in rheumatoid factor (RF) activity between interferon-free and interferon-based treatment groups.

Table 1 Baseline characteristics of chronic HCV infected patients treated with DAA and interferon-based regimens

	All (n=297)	DAA (*n* = 214)	IFN (*n* = 83)
Age	59 (48-67)	62 (54, 69)	49 (41, 58)
Female, *n* (%)	144 (48.5)	123 (57.5)	21 (25.3)
Cirrhosis, *n* (%)	50 (16.8)	47 (22)	3 (3.6)
AST, U/L	60 (40-97)	57 (36.8, 97.3)	63 (45, 97)
ALT, U/L	72 (44-119.5)	65 (39.8, 117.3)	95 (53, 137)
Bilirubin, mg/dL	1.0 (0.8-1.3)	1.0 (0.9, 1.3)	0.9 (0.7, 1.1)
White blood cell count, $10^3/\mu l$	5.9 (4.9-7.2)	5.7 (4.7, 6.9)	6.4 (5.1, 7.5)
Hemoglobin, g/dL	14.3 (13-15.4)	14.1 (12.8, 15.1)	14.8 (13.8, 16)
Platelet count, $10^3/\mu l$	181 (142-226)	175 (140, 226)	196 (148, 225)
Creatinine, mg/dL	1.0 (0.9-1.2)	1.0 (0.9, 1.3)	1.1 (0.9, 1.2)
HCV-RNA, log IU/mL	6.29 (5.49, 6.77)	6.28 (5.59,6.75)	6.30 (4.99, 6.80)
Genotype, *n* (%)			
1	170 (57.2)	132 (61.7)	38 (45.8)
2	99 (33.3)	65 (30.4)	34 (41.0)
3	4 (1.3)	1 (0.5)	3 (3.6)
6	24 (8.1)	16 (7.5)	8 (9.6)
Fibrosis 4 score	2.3 (1.5-4)	2.7 (1.7, 4.4)	1.7 (1.3, 2.7)
ANA, *n* (%)			
<1:40	276 (92.9)	194 (90.7)	82 (98.8)
1:40-1:80	13 (4.4)	12 (5.6)	1 (1.2)
1:160-1:640	8 (2.7)	8 (3.7)	0
SMA, *n* (%)			
<1:20	265 (89.2)	188 (87.9)	77 (92.8)
1:20-1:40	29 (9.8)	24 (11.2)	5 (6.0)
1:80-1:160	3 (1.0)	2 (0.9)	1 (1.2)

ALT, alanine aminotransferase; ANA, antinuclear antibody; AST, aspartate aminotransferase; DAA, direct-acting antiviral agents; HCV, hepatitis C virus; IFN, interferon; SMA, anti-smooth muscle antibody.

Baseline characteristics of chronic HCV infected patients treated with DAA and interferon-based regimens

Serum RF level decreased significantly between BL and SVR-12 or -24 in all subgroups, including age ≥ 59 (n = 150; 1.0 vs. UD IU/mL, P < 0.001), age < 59 (n = 147; 2.6 vs. 1.2 IU/mL, P < 0.001), males (n = 153; 2.1 vs. UD IU/mL, P < 0.001), females (n = 144; 1.2 vs. UD IU/mL, P < 0.001), with cirrhosis (n = 50; 0.7 vs. UD IU/mL, P < 0.001), without cirrhosis (n = 247; 1.9 vs. UD IU/mL, P < 0.001), genotype 1 (n = 170; 0.8 vs. UD IU/mL, P < 0.001), non-genotype 1 (n = 127; 2.3 vs. UD IU/mL, P < 0.001), and with BL ANA < 1:40 (n = 276; 1.4 vs. UD IU/mL, P < 0.001), except for patients with BL ANA ≥ 1:40 (n = 21; 3.0 vs. 1.3 IU/mL, P = 0.064).

Conclusion: We found that both the serum RF level and proportion of RF seropositivity significantly decreased after the eradication of HCV infection, regardless of whether the patients were treated with IFN-free or IFN-based regimens. We further analyzed different subgroups of participants and observed similarly significant reductions in serum RF in all subgroups, except for patients with ANA titers higher than 1:40 at BL. These findings indicate that effective treatment for HCV could reduce the production of RF and may alter autoimmunity in patients with chronic HCV infection.

Disclosure: J. Lo: None; **Y. Tsai**: None; **C. Tseng**: AbbVie/Abbott, 6, Bayer, 6, Bristol-Myers Squibb(BMS), 6, Gilead, 6, Merck/MSD, 6; **Y. Hsu**: AbbVie/Abbott, 6, 12, Support for attending meetings and/or travel, Bristol-Myers Squibb(BMS), 6, Gilead, 1, 6, 12, Support for attending meetings and/or travel, Roche, 6; **S. Hsieh**: None.

Abstract Number: 0206

Risk of Hepatitis B Virus Reactivation in Patients with Rheumatoid Arthritis Receiving JAK Inhibitor or IL-6 Inhibitor: A Systematic Review and Meta-Analysis

Akhil Sood, Janice Lin and Neha Shah, Stanford University, Palo Alto, CA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Due to the use of immunosuppressants, patients with rheumatic diseases are at increased risk for Hepatitis B virus (HBV) reactivation. B-cell depleting agents and TNF-α inhibitors are known to be associated with increased risk of HBV reactivation. The risks of other biologic/targeted synthetic DMARDs are not well understood. Both Janus Kinase (JAK) inhibitors and Interleukin-6 (IL-6) inhibitors interfere with the IL-6 pathway, which is critical in the control of underlying HBV infection. We thus conducted a systematic review and meta-analysis on the incidence of HBV reactivation in patients with rheumatoid arthritis receiving JAK inhibitor or IL-6 inhibitor.

Methods: We systematically searched Pubmed/Medline and Embase from January 1, 2010-May 1, 2023, to identify eligible studies that examined Hepatitis B virus (HBV) reactivation among RA patients receiving L-6 inhibitor (Tocilizumab or Sarilumab) or JAK inhibitor (Baricitinib, Tofacitinib, Upadacitinib). Studies with information on RA patients with chronic (HBsAg +/anti-HbcAb+) or previously resolved (HBsAg-/anti-HbcAb+) status were included. Information on medication and interval of monitoring for HBV reactivation were also obtained. Hepatitis B reactivation was defined as > 10-fold increase HBV DNA level from baseline or positive HBV DNA which was previously negative. Meta-analysis was performed using R statistical software.

Results: The meta-analysis included 16 studies comprised of RA patients with previously resolved (n= 547) or chronic (n= 46) HBV infection. The proportion of users of JAK inhibitors among previously resolved HBV infection was 63% (n=362) and chronic HBV was 59% (n=27). Serial monitoring for HBV viral load and liver function tests ranged from every 4 weeks to 6 months. Among those with previously resolved HBV infection, the pooled incidence rate for HBV reactivation was 0.76% [95% CI 0.0017 – 0.0335]. In the subgroup analysis, users of JAK inhibitors showed lower reactivation rate compared to IL-6 inhibitors (0.2% vs 1.9%). Among those with chronic HBV infection, the pooled incidence rate for HBV reactivation was 26% (95% CI 0.14 – 0.44] with lower rate of HBV reactivation among those on JAK inhibitors compared to IL-6 inhibitors (19% vs 37%).

Conclusion: In this systematic review and meta-analysis, the risk of HBV reactivation among RA patients with previously resolved HBV infection was relatively low; however, the risk was higher among HbSAg carriers. In both groups, the use of JAK inhibitors was associated with lower risk of HBV reactivation compared to the use of IL-6 inhibitors. Additional studies with larger cohorts are still necessary to better inform rheumatologists managing these patients with underlying Hepatitis B infection.

Disclosure: A. Sood: None; **J. Lin**: None; **N. Shah**: None.

Abstract Number: 0207

Role of *Pneumocystis Jirovecii* Pneumonia Prophylaxis with Trimethoprim-Sulfamethoxazole Among Patients with Autoimmune Inflammatory Diseases Receiving High-Dose Glucocorticoids: A Systematic Review and Meta-Analysis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Available immunosuppressive treatments for autoimmune inflammatory rheumatic diseases (AIRD) might increase the risk for opportunistic infections, such as *Pneumocystis jirovecii* pneumonia (PJP). Prophylactic trimethoprim-sulfamethoxazole (TMP/SMX) is often prescribed to prevent the occurrence of PJP among patients with AIRD. We calculate the incidence of PJP, PJP-related mortality, and TMP/SMX-related adverse events among patients with AIRD who received a prednisolone dose equivalent of ≥20 mg/day.

Methods: We searched PubMed and EMBASE for multiple-arm studies evaluating the efficacy and safety of TMP/SMX prophylaxis in individuals with AIRD. We stratified different prophylactic dose regimens of TMP/SMX in two groups: a "low-dose" group if the weekly dosage was lower than the equivalent of 400/80 mg/day, and a "standard-dose" group if the weekly dosage was equal or higher than the equivalent of 400/80 mg/day.

Results: Nine studies, performed in Japan, Korea, Thailand, and India, provided data on 1,438 individuals with AIRD receiving TMP/SMX and 1,605 individuals with AIRD not receiving prophylaxis. Studies were published between 2013 and 2021 and participants were followed from 3 to 12 months (77.75% for more than 6 months). At least one TMP/SMX treatment arm (i.e., "standard-dose", "low-dose" or both) was present in any included study. Specifically, eight studies included participants grouped in our "standard-dose" group, 6 studies included participants grouped in our "low-dose" group and 5 studies included participants that received no prophylaxis. The relative risk of PJP was 76% lower (Relative Risk 0.24; 95% CI: 0.07-0.79) among participants who received prophylactic TMP/SMX at any dose, compared to patients who did not receive any prophylaxis. The incidence of PJP for the initial 3-12 months of high-dose glucocorticoid treatment among patients who received no prophylaxis (2.95%, 95% CI: 0.65-6.46%) was significantly higher compared to the incidence of PJP among patients who received "standard-dose" (0.00%, 95% CI: 0.00-0.37%, p-value=0.009) or "low-dose" (0.00%, 95% CI: 0.00-0.04%, p-value=0.003) TMP/SMX. PJP-related mortality was 0.62% (95% CI: 0.00-1.98%) among individuals who

Table 1.Baseline characteristics of included studies

Study	Type	Location	Setting	Enrollment	AIRD	Follow-up	TMP/SMX Group	Treatment	Patient Number
Ganu et al. 2021	Prospective	India	Outpatient /Inpatient	2017-2018	SLE		No prophylaxis	No prophylaxis	162
Ganu et al. 2021	Prospective	India	Outpatient /Inpatient	2017-2018	SLE		Standard dose	800/160 qd OR 800/160 tiw	66
Harada et al. 2021	Retrospective	Japan	Inpatient	2004-2018	Multiple	6 months	Standard dose	400/80 qd OR 800/160 tiw	145
Harada et al. 2021	Retrospective	Japan	Inpatient	2004-2018	Multiple	6 months	Low dose	400/80 tiw	75
Honda et al. 2021	Retrospective	Japan	Inpatient	2003-2018	Multiple	4 months	No prophylaxis	No prophylaxis	61
Honda et al. 2021	Retrospective	Japan	Inpatient	2003-2018	Multiple	4 months	Low dose	Doses lower than 400/80 mg qd	376
Park et al. 2017	Retrospective	Korea	Outpatient /Inpatient	2004-2015	Multiple	1 year	No prophylaxis	No prophylaxis	1260
Park et al. 2017	Retrospective	Korea	Outpatient /Inpatient	2004-2015	Multiple	1 year	Standard dose	400/80 qd OR 800/160 tiw	262
Takenaka et al. 2013	Retrospective	Japan	Inpatient	2010-2011	Multiple	6 months	Standard dose	400/80 qd	28
Takenaka et al. 2013	Retrospective	Japan	Inpatient	2010-2011	Multiple	6 months	Low dose	10% escalation q3d up to 400/80 mg qd	13
Utsunomiya et al. 2020	RCT	Japan	Inpatient	2012-2015	Multiple	1 year	Standard dose	400/80 qd	58
Utsunomiya et al. 2020	RCT	Japan	Inpatient	2012-2015	Multiple	1 year	Low dose	200/40 qd OR 10% escalation qw from 40/8 mg qd up to 200/40 mg qd	114
Waki et al. 2021	Retrospective	Japan	Inpatient	2000-2020	AAV	6 months	No prophylaxis	No prophylaxis	43
Waki et al. 2021	Retrospective	Japan	Inpatient	2000-2020	AAV	6 months	Standard dose	400/80 qd OR 800/160 tiw	40
Waki et al. 2021	Retrospective	Japan	Inpatient	2000-2020	AAV	6 months	Low dose	Doses lower than 400/80 mg qd	167
Vananuvat et al. 2011	Retrospective	Thailand	Outpatient /Inpatient	2006-2007	CTD	>3 months	No prophylaxis	No prophylaxis	79
Vananuvat et al. 2011	Retrospective	Thailand	Outpatient /Inpatient	2006-2007	CTD	>3 months	Standard dose	400/80 qd	59
Yamamoto et al. 2014	Prospective	Japan	Inpatient	2009-2011	Multiple	1 year	Standard dose	400/80 qd	18
Yamamoto et al. 2014	Prospective	Japan	Inpatient	2009-2011	Multiple	1 year	Low dose	400/80 biw	17

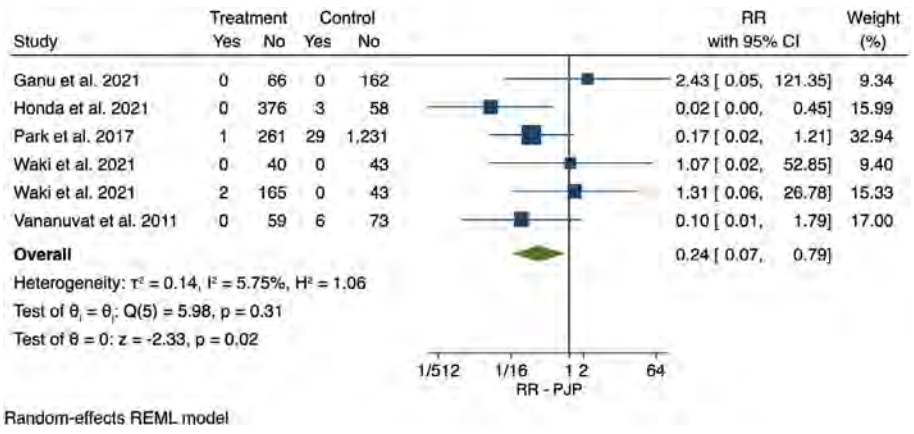

Figure 1.Relative risk of Pneumocystis jirovecii pneumonia among patients receiving trimethoprim-sulfamethoxazole prophylaxis compared to patients not receiving prophylaxis.

received no prophylaxis and 0.00% among patients who received "standard-dose" (95% CI: 0.00-0.06%, p-value=0.073) or "low-dose" TMP/SMX (95% CI: 0.00-0.00%, p-value=0.038). We found the incidence of any TMP/SMX-related adverse event was 23.59% (95% CI: 9.77-40.88%) among patients who received "standard-dose" TMP/SMX and 24.06% (95% CI: 11.90-38.63%) among patients who received "low-dose" TMP/SMX, a non-significant difference (p-value=0.946).

Conclusion: Among individuals with AIRD who were included in studies evaluating the use of prophylactic TMP/SMX, the risk for PJP was lower among participants who received TMP/SMX compared to participants who did not receive prophylaxis. The rate of TMP/SMX-related adverse events did not differ among the low-dose and standard-dose TMP/SMX subgroups. Clinical trials evaluating the efficacy and safety of different prophylactic TMP/SMX dose regimens with long term follow-up are needed to study TMP/SMX utility for preventing PJP among patients with AIRD.

Disclosure: A. Vassilopoulos: None; **S. Vassilopoulos**: None; **F. Shehadeh**: None; **M. Kalligeros**: None; **E. Mylonakis**: BARDA, 5, Basilea, 1, Chemic Labs/KODA Therapeutics, 5, Cidara, 5, Leidos Biomedical Research Inc./NCI, 5, NIH/NIAID, 5, NIH/NIGMS, 5, Pfizer, 5, Regeneron Pharmaceuticals, Inc., 5, SciClone Pharmaceuticals, 5.

Abstract Number: 0208

Pneumocystis Jirovecii Pneumonia (PJP) Prophylaxis (PPX), Investigating the Practice Patterns of Providers for Patients on Chronic, High-Dose Immunosuppression in a Rural Integrated Health System

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: PJP is an opportunistic fungus causing significant morbidity and mortality in immunocompromised patients. Guidelines describe PJP PPX indications among non-HIV infected individuals with cancer and solid organ transplant; however, this is lacking for individuals with rheumatic diseases requiring immunosuppression. General consensus reveals PJP PPX should be considered in patients receiving medication associated with lymphodepletion, likely to cause defects in cell-mediated immunity. Examples include prednisone 20mg or greater, monoclonal antibodies (anti-CD52 alemtuzumab and anti-CD20 rituximab), alkylating agents (cyclophosphamide), and checkpoint inhibitors (pembrolizumab, nivolumab, durvalumab). We conducted a restrospective analysis investigating the percentage of patients, within our rural system, who received appropriate PJP PPX when on immunosuppression and if discrepancies exist among specialties. We aim to determine the incidence of PJP and if PPX causes a reduction in infection risk.

Methods: A retrospective chart review of the electronic medical record was performed for adult patients from 2016-2021 prescribed immunosuppression in the form of prednisone ≥ 20mg for at least 4 weeks or any duration of alemtuzumab, cyclophosphamide, durvalumab, nivolumab, pembrolizumab, and rituximab. Prescribers within rheumatology, hematology/oncology, neurology, pulmonology, dermatology, nephrology, and gastroenterology were included. Exclusion criteria included HIV, solid organ transplant, and active cancer. Forms of PJP PPX included TMP/SMX, atovaquone, dapsone, or inhaled pentamidine. PJP diagnosis was included if occurred within one year of immunosuppression. A chi-square test

Table 1. The proportion of patients with PPX prescriptions did differ by department (chi-square test: p < .0001). Rheumatology had the highest proportion (32.2%), followed by hematology/oncology (19.7%) and neurology (1.8%). The grouping designated "other" consisted of small sample size specialties including nephrology (n = 11), dermatology (n = 3), and unspecified.

	Hematology/Oncology (N = 66)	Neurology (N = 113)	Rheumatology (N = 118)	Other (N = 18)	Total (N = 315)	P-value
PVP prophylaxis prescribed, n (%)						<.0001
No	53 (80.3%)	111 (98.2%)	80 (67.8%)	8 (44.4%)	252 (80.0%)	
Yes	13 (19.7%)	2 (1.8%)	38 (32.2%)	10 (55.6%)	63 (20.0%)	

Table 2. This table consists of the pairwise odds ratio estimates and their 95% confidence intervals from a logistic regression model with PPX prescription as the outcome and department as the predictor. Rheumatology prescribed PPX significantly more than neurology, but rheumatology did not have significantly increased PPX rates compared with hematology/oncology or the "other" category. All departments prescribed PPX more frequenly than neurology.

	Odds Ratio	95% CI	P-Value
Hematology/Oncology vs Neurology	13.61	(2.97, 62.50)	0.0008
Other vs Neurology	69.37	(12.94, 371.88)	< .0001
Rheumatology vs Neurology	26.36	(6.18, 112.45)	< .0001
Other vs Hematology/Oncology	5.10	(1.68, 15.47)	0.0040
Rheumatology vs Hematology/Oncology	1.94	(0.94, 3.98)	0.0716
Other vs Rheumatology	2.63	(0.96, 7.20)	0.0596

and logistic regression model were used to compare PPX prescriptions by department. Odds ratio and 95% confidence intervals are reported.

Results: We identified a cohort of 16,500 individual patients with 52,409 prescription encounters. Two PJP cases occurred in individuals not on PPX but prescribed the following: (rituximab and prednisone 40mg) and (rituximab and prednisone 80mg). Initial review of alemtuzumab, cyclophosphamide, durvalumab, nivolumab, pembrolizumab, and rituximab produced 315 patients and 2,508 prescription encounters with 20% of patients receiving PPX. The proportion of patients prescribed PPX differed by department (p < .0001) with the following: rheumatology 32.2%, hematology/oncology 19.7%, and neurology 1.8%. Pairwise odds ratio estimates and 95% confidence intervals from a logistic regression model demonstrated that rheumatology prescribed PPX significantly more than neurology (odds ratio, 26.36 [95% CI, 6.18-112.45], p < .0001). Review of prednisone prescription encounters is still ongoing, with percentage of appropriate PPX and risk reduction analysis to be included at final presentation.

Conclusion: PJP carries significant morbidity and mortality for patients on immunosuppression; however, PPX is highly underutilized in our rural health care system. Further investigation is needed to identify factors leading to low PPX rates and determining the incidence and severity of adverse effects from PPX, as these often influence prescriber practices.

Disclosure: A. Bobak: None; **E. Pimentel**: None; **J. Jackson**: None; **C. Gray**: None; **H. Srinivasan**: None; **A. Berger**: None; **D. Bulbin**: AbbVie/Abbott, 2, 6, Alexion, 2, 6, Amgen, 2, 6, Novartis, 2, Sanofi Genzyme, 6.

Abstract Number: 0209

Safety of Bivalent SARS-CoV-2 Vaccines as a Second Booster Dose in Arthritis Patients on Immunosuppressive Therapies

Hilde Ørbo[1], Ingrid Jyssum[1], Anne Therese Tveter[1], Ingrid Christensen[1], Joseph Sexton[1], Kristin Hammersbøen Bjørlykke[2], Grete B. Kro[3], Tore Kvien[1], Gunnveig Grødeland[4], Ludvig A. Munthe[5], Siri Mjaaland[6], John Torgils Vaage[5], Espen Haavardsholm[1], Kristin Kaasen Jørgensen[2], Sella Provan[7], Silje Watterdal Syversen[1] and Guro Goll[1], [1]Center for Treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway, [2]Department of Gastroenterology, Akershus University Hospital, Oslo, Norway, [3]Department of Microbiology, Oslo University Hospital, Oslo, Norway, [4]Department of Immunology, Oslo University Hospital, Oslo, Norway, [5]Department of Immunology, Oslo University Hospital, Oslo, Norway, [6]Norwegian Institute of Public Health, Oslo, Norway, [7]Diakonhjemmet Hospital, Oslo, Norway

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Infection-related Rheumatic Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Safety and efficacy of updated bivalent vaccines, containing both the original vaccine variant of SARS-CoV-2 Spike and either Omicron variants BA.1 or BA.4/5, are of particular interest in arthritis patients on immunosuppressive therapies. With the continuous emergence of new viral variants, it is important to evaluate whether updated vaccines induce more adverse events in this patient group. The objective of this study was examine if a second booster dose with updated bivalent vaccine increases the risk of adverse events, compared to the first booster dose with monovalent vaccines.

Methods: The prospective Nor-vaC study investigates vaccine responses in patients with immune mediated inflammatory diseases using immunosuppressive therapies (1). The present analyses included arthritis patients who received two booster doses. Patients received available vaccines according to the Norwegian vaccination program. The current recommendation

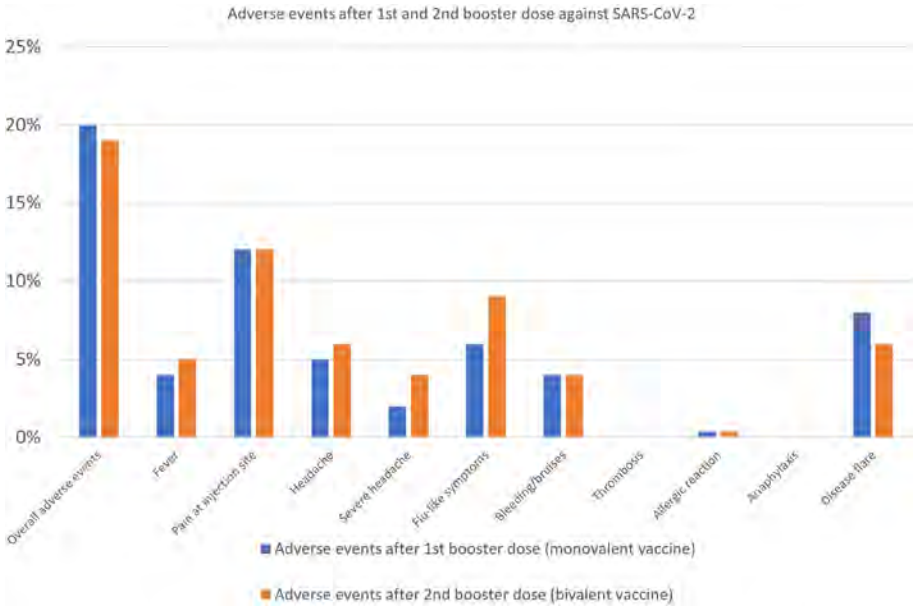

Figure: Adverse events after bivalent vaccine as a 2nd booster dose compared to a monovalent vaccine as a 1st booster dose.

in the Norwegian arthritis population is a three-dose primary vaccination series followed by two booster doses. Adverse events following vaccines doses were self-reported through questionnaires. Adverse events following the first (monovalent) and second (bivalent) booster were compared with McNemar's test.

Results: Between 7th of July 2021 and 6th of December 2022 a total of 243 arthritis patients (127 rheumatoid arthritis, 65 psoriatic arthritis, 51 spondyloarthritis) on immunosuppressive therapies (Table) received a first, monovalent (BNT162b2, mRNA-1273) and a second, bivalent booster dose (BNT162b2 (WT/OMI BA.1), mRNA-1273.214, BNT162b2 (WT/OMI BA.4/BA.5)). Adverse events were recorded within two weeks in all patients (Figure). In total, 45 vs 49 (19% vs 20 %) patients reported any adverse event after a second, bivalent booster dose, compared to the first, monovalent booster, respectively. There was no significant difference in adverse events overall (p= 0.57). The most common adverse events after the second booster were pain at injection site (12 %), flu-like symptoms (9 %) and headache (6 %). No new safety signals emerged. A total of 15 (6 %) patients reported a disease flare after receiving the second, bivalent booster, compared to 21 (8 %) after the first, monovalent booster.

Table: Demographic characteristics and immunosuppressive medication in patients receiving a 1st monovalent and a 2nd bivalent booster dose.

Characteristics	**Patients, n (%)**
Total	243
Age (years), median (IQR)	61 (52-67)
Female	152 (63)
Immunosuppressive medication	
TNFi mono[a]	75 (31)
TNFi combo[a+b]	72 (30)
Methotrexate	62 (26)
Rituximab	9 (4)
IL-inhibitors[c]	6 (2)
JAK-inhibitors[d]	11 (5)
Other[e]	8 (3)
1st booster	
BNT162b2	106 (44)
mRNA-1273	137 (56)
2nd booster	
BNT162b2 (WT/OMI BA.1)	65 (25)
BNT162b2 (WT/OMI BA.4/BA.5)	120 (47)
mRNA-1273.214 (WT/OMI BA.1)	58 (23)

Results in n (%) unless otherwise specified.
[a]Tumor necrosis factor inhibitors: infliximab, etanercept, adalimumab, golimumab, certolizumab pegol.
[b]Combination therapy: methotrexate, sulfasalazine, leflunomide, azathioprine.
[c]Interleukin inhibitors: tocilizumab, secukinumab.
[d]Janus kinase inhibitors: filgotinib, baricitinib, upadacitinib, tofacitinib.
[e]Other: abatacept, sulfasalazine, leflunomide, azathioprine.

Conclusion: There was no difference in adverse events between the monovalent, first booster, and the bivalent, second booster, indicating that bivalent vaccines are safe in this patient group.

Reference:

1. Syversen S.W. et al Arthritis Rheumatol 2022

Disclosure: H. Ørbo: None; **I. Jyssum**: None; **A. Tveter**: None; **I. Christensen**: None; **J. Sexton**: None; **K. Bjørlykke**: Janssen-Cilag, 6; **G. Kro**: None; **T. Kvien**: AbbVie/Abbott, 1, 2, 6, Bristol-Myers Squibb(BMS), 5, Galapagos, 2, 5, Gilead, 2, grunenthal, 6, Janssen, 2, 6, Novartis, 5, Pfizer, 2, 5, sandoz, 2, 6, UCB, 2, 5, 6; **G. Grødeland**: AstraZeneca, 1, Bayer, 6, Sanofi, 6, ThermoFisher, 6; **L. Munthe**: Celgene, 6, Novartis, 6; **S. Mjaaland**: None; **J. Vaage**: None; **E. Haavardsholm**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Eli Lilly, 2, Gilead, 2, Pfizer, 6, UCB, 6; **K. Jørgensen**: Bristol-Myers Squibb(BMS), 6, Roche, 6; **S. Provan**: None; **S. Syversen**: AstraZeneca, 1; **G. Goll**: AbbVie/Abbott, 1, 6, Galapagos, 1, 6, Novartis, 6, Pfizer, 1, Union Chimique Belge, 1, 6.

Abstract Number: 0210

Longitudinal T Cell Responses to a Series of Four SARS-CoV-2 Vaccine Doses or COVID-19 in Patients on TNF Inhibitors

Hilde Ørbo[1], Asia-Sophia Wolf[2], Kristin Hammersbøen Bjørlykke[3], Sarah E. Josefsson[2], Guri Solum[2], Ingrid Fadum Kjønstad[4], Ingrid Jyssum[1], Ingrid Christensen[1], Anne Therese Tveter[1], Joseph Sexton[1], Grete B. Kro[5], Gunnveig Grødeland[6], Tore Kvien[1], Jørgen Jahnsen[3], John Torgils Vaage[7], Espen Haavardsholm[1], Sella Provan[8], Hassen Kared[9], Ludvig A. Munthe[7], Kristin Kaasen Jørgensen[3], Silje Watterdal Syversen[1], Siri Mjaaland[2] and Guro Goll[1], [1]Center for Treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway, [2]Norwegian Institute of Public Health, Oslo, Norway, [3]Department of Gastroenterology, Akershus University Hospital, Oslo, Norway, [4]National Institute of Public Health, Oslo, Norway, [5]Department of Microbiology, Oslo University Hospital, Oslo, Norway, [6]Department of Immunology, Oslo University Hospital, Oslo, Norway, [7]Department of Immunology, Oslo University Hospital, Oslo, Norway, [8]Diakonhjemmet Hospital, Oslo, Norway, [9]Department of Immunology, Oslo University Hospital, Oslo, Norway

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: T cells are critical for control of viral infection with SARS-CoV-2, but knowledge is lacking on cellular immune responses following repeated vaccination and breakthrough infection in immunosuppressed patients. The objective was to examine longitudinal T cell responses across diagnoses, following vaccine series and COVID-19 in patients on tumor necrosis factor inhibitors (TNFi).

Methods: The prospective, observational Nor-vaC study included patients with arthritis (spondyloarthritis, rheumatoid arthritis, psoriatic arthritis) or inflammatory bowel disease (IBD) (ulcerative colitis, Crohns disease) on immunosuppressive therapies. Here, we included patients on TNFi mono- or combination therapy immunised with up to four SARS-CoV-2 vaccine doses with or without breakthrough infection, collecting peripheral blood mononuclear cells (PBMCs) 2-4 weeks after each immunisation. Samples were incubated with SARS-CoV-2 spike, nucleocapside or membrane peptides. The percentage of responding T cells was measured by flow cytometry.

Results: Between February 2021 and December 2022, 144 patients on TNFi (monotherapy n=86 (60%), combination with methotrexate or azathioprine n=58 (40%)) were included (median age 48 years [IQR 33-57]; 51% women) (Table).

The proportions of arthritis vs IBD patients with CD4 responses after 2 vaccine doses were 75% (12/16 patients) vs 86% (25/29), and after 3 doses 83% (10/12) vs 93% (28/30). In total, 80% (4/5) of arthritis patients showed further increases in CD4 responses after a 4th vaccine dose.

Conversely, 81% (13/16) of arthritis patients vs. 55% (16/29) of IBD patients had CD8 T cell responses after two doses, and 67% (8/12) vs. 62% (18/29) after three doses. A 3rd and 4th dose induced higher CD8 responses compared to the previous dose in 55% (6/11) and 100% (5/5) of arthritis patients.

Arthritis patients had lower T cell responses than IBD patients after the 3rd dose; median CD4 response 0.024% [IQR 0.009-0.036] vs 0.098% [IQR 0.040-0.182], p=0.0004; median CD8 response 0.003% [IQR 0.001-0.016] vs 0.044% [IQR 0.009-0.140], p=0.0032 (Figure). This difference remained robust after adjusting for age and sex, p< 0.001, but was no longer detected after the 4th vaccine dose.

Breakthrough infection elicited increased T cell responses across all diagnoses to spike (p< 0.0001), and to nucleocapsid (p=0.002) and membrane proteins (p=0.001) compared to unstimulated T cells.

Also, Spike-specific T cell responses increased compared to the 3rd dose (median CD4 T cell response 0.18% vs. 0.06%, p=0.003; CD8 T cell response 0.08% vs. 0.01%, p< 0.0001), but to a lesser extent compared to the 4th dose (median CD4 response 0.18% vs. 0.12%, p=0.05; CD8 response 0.08% vs. 0.05%, p=0.26).

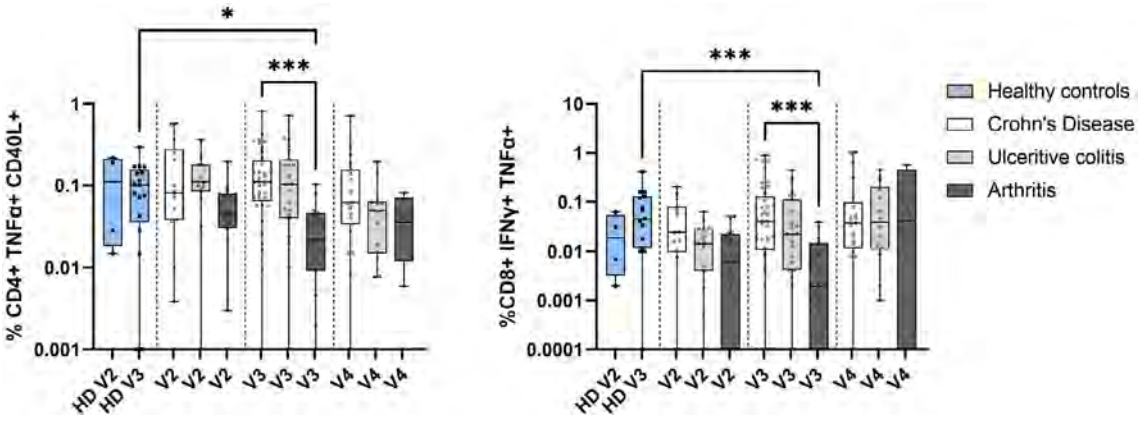

Figure: CD4- and CD8-responses in patients and healthy controls.

Table: Characteristics of patients providing T-cells after vaccine doses and after COVID-19.

Disease, n (%)	Patients in total[a] (n=144)	Two vaccines (n=49)	Three vaccines (n=86)	Four vaccines (n=44)	Hybrid immunity[b] (n=62)
Rheumatoid arthritis (RA)	9 (6)	5 (10)	7 (8)	2 (5)	3 (5)
Spondyloarthritis (SpA)	13 (9)	10 (20)	10 (12)	2 (5)	2 (3)
Psoriatic arthritis (PsA)	3 (2)	2 (4)	2 (2)	1 (2)	0
Crohns disease (CD)	73 (51)	18 (37)	44 (51)	27 (61)	31 (50)
Ulcerative colitis (UC)	46 (32)	14 (29)	23 (27)	12 (27)	26 (42)

[a]Sampled at minimum one timepoint

[b]3 or 4 vaccine doses, followed by COVID-19

Conclusion: Patients on TNFi show improved cellular responses following each immunisation, with infection generating a strong and broad T cell response. Arthritis patients had significantly lower cellular responses compared to IBD patients after three vaccine doses, but with no difference after the 4th dose. These results support giving a 4th vaccine dose to TNFi-treated patients, with particular benefit for arthritis patients.

Disclosure: H. Ørbo: None; **A. Wolf**: None; **K. Bjørlykke**: Janssen-Cilag, 6; **S. Josefsson**: None; **G. Solum**: None; **I. Kjønstad**: None; **I. Jyssum**: None; **I. Christensen**: None; **A. Tveter**: None; **J. Sexton**: None; **G. Kro**: None; **G. Grødeland**: AstraZeneca, 1, Bayer, 6, Sanofi, 6, ThermoFisher, 6; **T. Kvien**: AbbVie/Abbott, 1, 2, 6, Bristol-Myers Squibb(BMS), 5, Galapagos, 2, 5, Gilead, 2, grunenthal, 6, Janssen, 2, 6, Novartis, 5, Pfizer, 2, 5, sandoz, 2, 6, UCB, 2, 5, 6; **J. Jahnsen**: AbbVie/Abbott, 1, 6, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 1, 6, Galapagos, 1, 6, Gilead, 1, 6, Janssen, 1, 6, Pfizer, 1, 6, Roche, 1, 6, Sandoz, 1, 6, Takeda, 1, 6; **J. Vaage**: None; **E. Haavardsholm**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Eli Lilly, 2, Gilead, 2, Pfizer, 6, UCB, 6; **S. Provan**: None; **H. Kared**: None; **L. Munthe**: Celgene, 6, Novartis, 6; **K. Jørgensen**: Bristol-Myers Squibb(BMS), 6, Roche, 6; **S. Syversen**: AstraZeneca, 1; **S. Mjaaland**: None; **G. Goll**: AbbVie/Abbott, 1, 6, Galapagos, 1, 6, Novartis, 6, Pfizer, 1, Union Chimique Belge, 1, 6.

Abstract Number: 0211

COVID-19 Outcome and Association to Anti-Spike Antibody Levels in Patients on Immunosuppressive Therapy; A Prospective Cohort Study

Hilde Ørbo[1], Ingrid Jyssum[1], Joseph Sexton[1], Anne Therese Tveter[1], Ingrid Christensen[1], Kristin Hammersbøen Bjørlykke[2], Grete B. Kro[3], Tore Kvien[1], Ludvig A. Munthe[4], Gunnveig Grødeland[5], Siri Mjaaland[6], Espen Haavardsholm[1], John Torgils Vaage[4], Kristin Kaasen Jørgensen[2], Sella Provan[7], Silje Watterdal Syversen[1] and Guro Goll[1], [1]Center for Treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway, [2]Department of Gastroenterology, Akershus University Hospital, Oslo, Norway, [3]Department of Microbiology, Oslo University Hospital, Oslo, Norway, [4]Department of Immunology, Oslo University Hospital, Oslo, Norway, [5]Department of Immunology, Oslo University Hospital, Oslo, Norway, [6]Norwegian Institute of Public Health, Oslo, Norway, [7]Diakonhjemmet Hospital, Oslo, Norway

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Infection-related Rheumatic Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with immune-mediated inflammatory diseases (IMIDs) on immunosuppressive therapies have attenuated vaccine responses and are prone to severe infections. Knowledge of COVID-19 outcome following vaccine and hybrid immunity, and identification of protective anti-Spike antibody concentrations are important to further develop vaccine strategies in this vulnerable patient group. The objectives of this study were to investigate the outcomes of COVID-19 in a large cohort of IMID patients compared to healthy controls, and in association to anti-Spike antibody concentrations and vaccine status.

Methods: In this prospective observational study, adult patients with IMID on immunosuppressive therapies were followed from February 15., 2021, to February 15., 2023. Throughout the study, patients and controls reported data regarding COVID-19 through questionnairs. COVID-19 related hospital admissions were recorded from The Norwegian Patient Registry. Anti-Spike antibodies were assessed 2-4 weeks following vaccination and COVID-19.

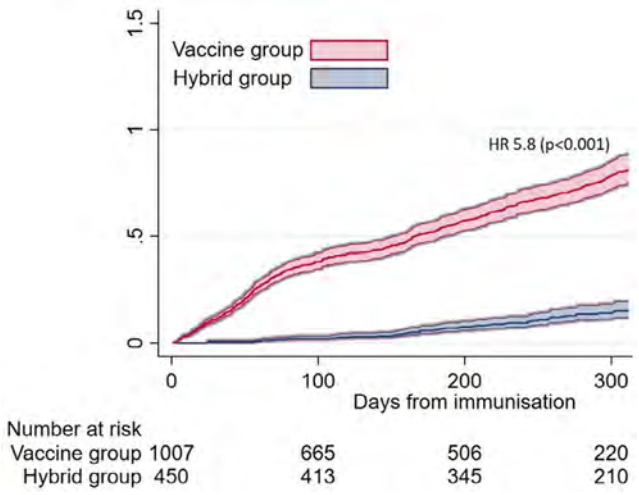

Figure: Cumulative hazards of COVID-19 in Vaccine group (four vaccine doses) vs Hybrid group (three vaccine doses plus COVID-19).

Results: A total of 1729 IMID patients with a documented COVID-19 history were included in the present analyses. 1140 (66%) of patients and 236 of 350 (67%) healthy controls (HC) reported COVID-19,the majority (85%) within the Omicron era. COVID-19 reinfection was reported in in 141 (12%) patients and 32 (14%) HC (p=0.66).

Compared to hybrid immunity (COVID-19 after a 3rd dose), the risk of COVID-19 was six times higher following vaccine series only (HR 5.8 (95% CI [4.4, 7.7]), p< 0.001) (Figure). Anti-Spike antibody concentrations < 6000 BAU/ml were predictive of COVID-19 after three (HR 1.4 (95% CI [1.1, 1.74]), p=0.01) and four vaccine doses (HR 1.3 (95% CI [1.02, 1.6]), p=0.04) and in hybrid immunity (HR 4.5 (95% CI [1·9, 10·7]), p=0.001).

In the entire cohort, the median anti-Spike antibody concentration after the 2nd vaccine dose was 2114 BAU/ml (732, 5749), after the 3rd dose 5897 BAU/ml (1939, 9761), after the 4th dose 7924 BAU/ml (3785, 15049) and following hybrid immunity 23505 BAU/ml (11423, 37007).

Hospitalisation due to COVID-19 (severe disease) occurred in 22 (2%) patients, (9 (41%) before any vaccination) and no HC. Four patients were admitted to intensive care. Prior to hospitalisation, the median anti-Spike antibody concentration was 444 BAU/ml (IQR 31-1634). Hospitalised patients with severe disease were older than non-hospitalised (median age 61 years (IQR 48-74) vs. 54 (42-64), p=0.04) and had a higher frequency of comorbidities (19/22 (86%) vs. 474/1118 (42%), p=0.02). No COVID-19 related deaths occurred.

Prolonged COVID-19 (symptoms >14 days) were reported by201 (18%) patients compared to 29 (12%) HC (p=0.05). The risk of prolonged disease was higher in the vaccine group compared to the hybrid group (HR 10.7 (95 % CI [4.8, 23.8]) p< 0.001)

Conclusion: IMID patients and healthy controls had a comparable occurrence of COVID-19, prolonged disease and reinfection. However, severe disease developed only in the patient group. Hybrid immunity protects against COVID-19 and prolonged disease. A high anti-Spike antibody concentration protects against COVID-19, supporting the role of repeated vaccination in IMID patients on immunosuppressive therapy.

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6; **G. Grødeland**: AstraZeneca, 1, Bayer, 6, Sanofi, 6, ThermoFisher, 6; **S. Mjaaland**: None; **E. Haavardsholm**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Eli Lilly, 2, Gilead, 2, Pfizer, 6, UCB, 6; **J. Vaage**: None; **K. Jørgensen**: Bristol-Myers Squibb(BMS), 6, Roche, 6; **S. Provan**: None; **S. Syversen**: AstraZeneca, 1; **G. Goll**: AbbVie/Abbott, 1, 6, Galapagos, 1, 6, Novartis, 6, Pfizer, 1, Union Chimique Belge, 1, 6.

Abstract Number: 0212

The Impact of Immunosuppression on the Humoral Immunogenicity of SARS-CoV-2 mRNA Vaccines in SLE

Rebecca Sadun[1], Dan Crair[2], Emmanuel B Walter[3], Jennifer Rogers[1], Megan Clowse[4], Amanda Eudy[5], Kai Sun[1], Jayanth Doss[1], Lisa Criscione-Schreiber[6], Sarah Valencia[2] and M. Anthony Moody[6], [1]Duke University, Durham, NC, [2]Duke Human Vaccine Institute, Durham, NC, [3]Duke Human Vaccine Institute, Duke University School of Medicine, Durham, NC, [4]Duke University, Chapel Hill, NC, [5]Duke University, Raleigh, NC, [6]Duke University School of Medicine, Durham, NC

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The ACR's COVID-19 Vaccine Guidance recommends all patients with rheumatic diagnoses be vaccinated against SARS-CoV-2. The predominant SARS-CoV-2 vaccines used in the United States are based on mRNA technology. Little is known about the immunogenicity of the SARS-CoV-2 mRNA vaccines in patients with SLE, many of whom are on immune suppressing medications. This study sought to determine the humoral immunogenicity of two doses of the SARS-CoV-2 mRNA vaccines made by Moderna and Pfizer/BioNTech in SLE patients, stratified by immunosuppression.

Methods: We obtained biobanked serum from SLE patients and healthy control patients whose blood was drawn 14-180 days following dose #2 of a SARS-CoV-2 mRNA vaccine. ELISA was performed using anti-wild-type spike protein ectodomain S1+S2. Area under the curve (AUC) was calculated for each individual. An AUC threshold of 2.0 was established to distinguish between responders and non-responders (Figure 1).

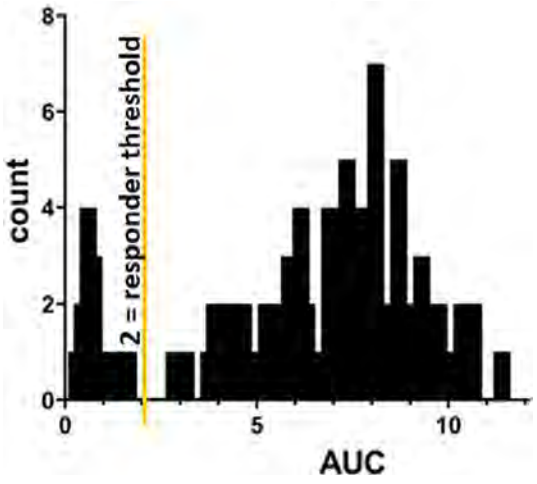

Figure 1. Histogram depicting the distribution of anti-spike antibody areas under the curve (AUC) in SLE patients (n=87), which formed the basis for establishing the responder threshold of 2.0, at which 13 SLE patients (15%) were determined to be non-responsive.

Results: Of the SLE patients (n=87), 23 (26%) were on no SLE therapy or HCQ monotherapy, 44 (51%) were on a DMARD and ≤7.5mg of prednisone, and 20 (23%) patients were on a biologic (rituximab=3, belimumab=11) and/or high-dose prednisone. Figure 2 depicts concomitant use of DMARDs and belimumab. As summarized in Table 1, the AUC for SLE patients was not significantly lower than for healthy controls (n=12): median AUC of 7.09 (range 0.34-11.45) versus 7.30 (range 5.89-8.65). The median AUC for SLE patients on no lupus medications or hydroxychloroquine monotherapy was 7.44 (range 0.34-10.52), with only one patient (4%) being classified as a non-responder. Ten (23%) of the SLE patients on DMARDs were non-responders, with mycophenolate and methotrexate having the biggest impact on AUC: seven (35%) of the patients on mycophenolate were non-responders (AUC median = 5.31; p=0.008), and 30% of the patients on methotrexate were non-responders (AUC median = 7.28; p=0.31). Three (15%) of the SLE patients on biologics and/or high-dose prednisone were non-responders, including two of the 11 belimumab patients (18%), one of whom was on concomitant

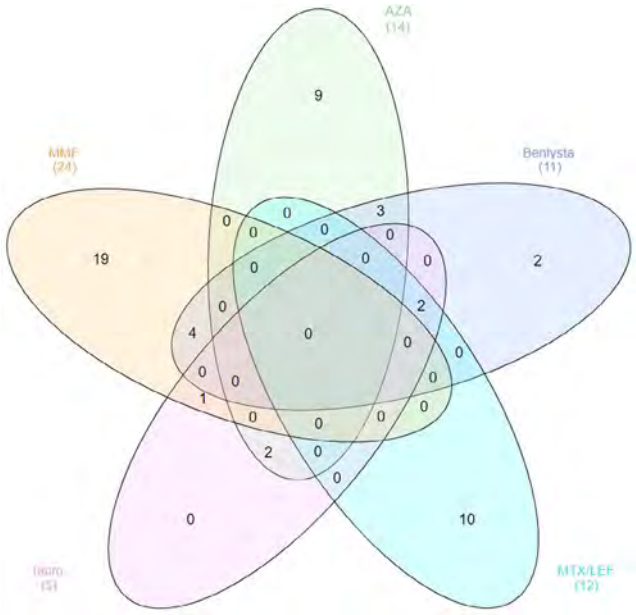

Figure 2. Concomitant use of belimumab (Benlysta) and DMARDs (AZA=azathioprine; LEF=leflunomide; MTX=methotrexate, MMF=mycophenolate; Tacro=tacrolimus).

Table 1. Serologic responses, quantified as areas under the curve (AUC) for healthy controls, patients on insignificant immunosuppression (HCQ group encompasses patients on no medication or hydroxychloroquine monotherapy), and patients on a variety of immune suppressing medications (MMF=mycophenolate; MTX=methotrexate (n=9) and leflunomide (n=1); AZA=azathioprine; RTX=rituximab). Many of the patients on belimumab were also on >10 mg of prednisone daily. P-values were calculated in reference to the HCQ group.

	Healthy Controls (n=12)	All SLE (n=87)	HCQ (n=23)	MMF (n=20)	MTX (n=10)	AZA (n=10)	Belimumab (n=11)	RTX (n=3)
Non-Responders	0 (0%)	13 (15%)	1 (4%)	7 (35%)	3 (30%)	0 (0%)	2 (18%)	0 (0%)
AUC Mean	7.71	6.23	6.99	4.80	5.89	6.67	5.77	4.68
AUC Median	7.30	7.09	7.44	5.31	7.28	6.14	6.10	4.67
AUC Range	5.89-8.65	0.34-11.45	0.34-10.52	0.50-10.34	0.44-11.45	3.09-9.65	0.51-8.35	3.73-5.65
AUC StDev	1.03	2.90	2.22	3.32	3.95	2.15	2.34	0.96
p-value (HCQ=ref)	0.35	0.08	n/a	**0.008**	0.31	0.70	0.16	0.09

mycophenolate, and the other on high-dose prednisone (20 mg daily). All three rituximab patients were classified as responders, although the median AUC (4.67) and mean AUC (4.68) were the lowest of any medication (range 3.73-5.65). The number of days between dose #2 and serum sample collection did not correlate with AUCs: the 13 non-responders were on average 66 days out from dose #2, whereas responders were on average 80 days out from dose #2.

Conclusion: SLE patients on certain immune suppressing medications, most notably mycophenolate, produce less SARS-CoV-2 anti-spike antibodies after receiving two doses of an mRNA vaccine. Neutralization assays and cell-based studies are necessary to understand the full picture of vaccine immunogenicity in SLE; nevertheless, decreased serologic response in SLE patients on certain medications should prompt studies exploring whether holding medications like mycophenolate will enhance the immunogenicity of SARS-CoV-2 and other vaccines.

Disclosure: R. Sadun: None; **D. Crair**: None; **E. Walter**: Clinetic, 5, Iliad Biotechnologies, 2, Moderna, 5, Najit biotechnologies, 5, Pfizer, 5, Sequiris, 5, Vaxcyte, 1; **J. Rogers**: Amgen, 2, Ampel Biosolutions, 1, AstraZeneca, 6, Aurinia, 1, Eli Lilly, 1, Exagen, 5, GlaxoSmithKlein(GSK), 2, Immunovant, 2, 5; **M. Clowse**: Exagen, 5, GlaxoSmithKlein(GSK), 2, 5, Immunovant, 5, UCB, 2, 5; **A. Eudy**: Amgen, 2, Exagen, 5, GlaxoSmithKlein(GSK), 5, Immunovant, 5, Pfizer, 5; **K. Sun**: AstraZeneca, 6; **J. Doss**: None; **L. Criscione-Schreiber**: GlaxoSmithKlein(GSK), 5, UCB, 5; **S. Valencia**: None; **M. Moody**: None.

Abstract Number: 0213

When Should I Get My Next Booster? Active Surveillance of COVID-19 Breakthrough Infections in Canadian Patients with Immune-Mediated Inflammatory Diseases

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Infection-related Rheumatic Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Breakthrough COVID-19 infections are still a risk after vaccination and may be more common in patients with immune-mediated inflammatory diseases (IMIDs) than in the general population. Previous studies on breakthrough infections in IMID relied on retrospective databases; however, these are subject to limitations on COVID-19 test availability, making it hard to determine true infection prevalence as asymptomatic cases may have gone untested. We performed active surveillance of breakthrough COVID-19 infections, analyzing saliva samples via quantitative polymerase chain reaction (qPCR) in vaccinated individuals with IMIDs (systemic lupus erythematosus, rheumatic arthritis, psoriatic arthritis, spondylarthritis, inflammatory bowel disease, and scleroderma).

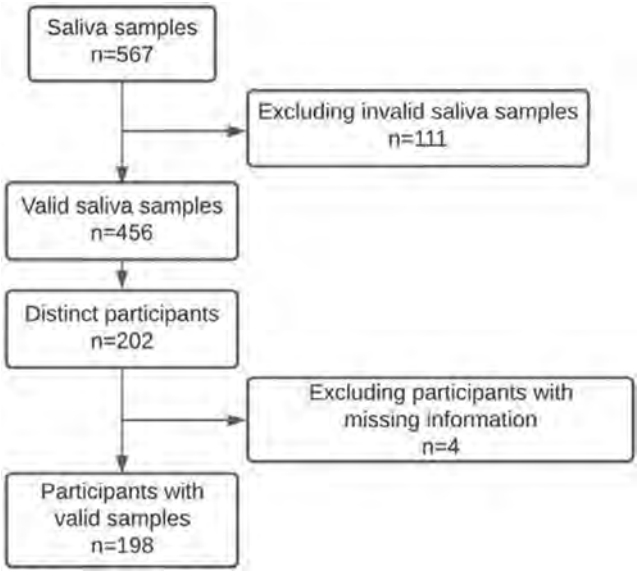

Figure 1. Participants and samples

Table 1. Baseline characteristics for individuals contributing saliva for COVID-19 PCR testing

Characteristic	N=198
Age (years), mean (SD)	56.6 (13.4)
Female, N (%)	152 (76.8%)
Caucasian, N (%)	168/196 (85.7%)
Autoimmune Diagnosis (primary), N (%)	
SLE	54/195 (27.7%)
RA	92/195 (47.2%)
PsA	38/195 (19.5%)
SpA	2/195 (1.0%)
IBD	3/195 (1.5%)
SSC	6/195 (3.1%)
IMID Duration (years), median (IQR)*	10.9 (4.9-21.8)
Immunosuppressed[1], N (%)	129/195 (66.2%)
Vaccination Status*, N (%)	
1 Dose	7(3.5%)
2 Doses	35 (17.7)
3 Doses	77 (38.9%)
4 Doses	51 (25.8%)
5 Doses	28 (14.1%)
Province Distribution, N (%)	
BC	21 (10.6%)
ON	30 (15.2%)
QC	147 (74.2%)

*n=176

[1] Immunosuppressive medications, including: Methotrexate, Leflunomide, Azathioprine, Mycophenolates, Cyclophosphamide, Cyclosporine, Adalimumab, Certolizumab, Etanercept, Golimumab, Infliximab, Rituximab, Abatacept, Anakinra, Secukinumab, Tocilizumab, Tofacitinib, Ustekinumab, Glucocorticoids
Patients with missing values for a medication were considered to not use it.

Methods: Adults with IMID were recruited from Canadian clinics and registries between September 2022 and March 2023 and asked to self-collect saliva samples monthly. Samples underwent batch qPCR testing, with each sample being tested twice, to qualitatively detect SARS-CoV-2 nucleic acids indicators (N1 and N2).

Results: To date, 202 patients have been enrolled, providing 458 valid samples (Fig. 1, Table 1). Most (66.2%) were on immunomodulatory medications, and the majority (78.8%) had received 3 or more vaccine doses. Only 5% of participants (n=10/202) met the N1 and N2 thresholds required to confirm COVID-19 positivity. Given the small number of positive results, we were unable to ascertain significant differences between demographic factors, including age, sex, immunosuppression, or vaccination status. However, participants who tested positive had a median time since their last vaccination that was considerably longer (278 days) than those who tested negative (165 days) (95% CI for difference,18-205). The majority (three-quarters) of positive saliva samples occurred in patients who were beyond 217 days of their last vaccine.

Conclusion: A 5% COVID-19 breakthrough infection rate aligns with a Canadian population-based cohort where breakthrough infections occurred in 5.4%-6.5% of fully vaccinated IMID patients (1). In our sample, those with breakthrough infections had a longer median time since vaccination (by 112 days), corroborating the currently held belief that protection against COVID wanes in the 3-4 months post-vaccination and beyond. Most infections occurred 7-8 months after the last vaccine dose. These findings will help patients, clinicians, and other stakeholders with decision-making in 2023-2024 and beyond.

Reference

Widdifield J, Kwong JC, Chen S, Eder L, Benchimol EI, Kaplan GG, et al. Vaccine effectiveness against SARS-CoV-2 infection and severe outcomes among individuals with immune-mediated inflammatory diseases tested between March 1 and Nov 22, 2021, in Ontario, Canada: a population-based analysis. The Lancet Rheumatology [Internet]. 2022 Apr 14; Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9009845/

Disclosure: J. Tan: None; **J. Avina-Zubieta**: None; **J. Lee**: None; **P. Fortin**: AbbVie, 1, AstraZeneca, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Roche-Genentech, 1; **I. Colmegna**: None; **L. Gonzalez Arreola**: None; **C. Berger**: None; **M. Larche**: None; **C. Hitchon**: Astra Zeneca, 1, Pfizer, 5; **D. Richards**: None; **N. Lalonde**: Greenwish Life Science, 11, Merck/MSD, 11, Mind Medicine, 11, Predictmedix, 11, Takeda Pharma, 11, Tilray Brands, 11; **S. Bernatsky**: None.

Abstract Number: 0214

COVID-19 Vaccine Uptake, Hesitancy, and Flare in a Large Rheumatology Practice Network

Emily Holladay[1], Amy S. Mudano[2], Fenglong Xie[2], Patrick Stewart[3], Lesley E. Jackson[1], Maria I. (\"Maio\") Danila[4], Kelly Gavigan[5], W. Benjamin Nowell[6], Shilpa Venkatachalam[7] and Jeffrey Curtis[1], [1]University of Alabama at Birmingham, Birmingham, AL, [2]Illumination Health, Hoover, AL, [3]Illumination Health, Birmingham, AL, [4]University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL, [5]Global Healthy Living Foundation, Upper Nyack, NY, [6]Global Healthy Living Foundation, Nyack, NY, [7]Global Healthy Living Foundation, New York, NY

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: COVID-19 vaccine uptake in autoimmune and inflammatory rheumatic disease (AIIRD) patients is an area of concern to rheumatologists and other providers. These patients are at a greater risk of infection and COVID-19-related complications due to underlying conditions and therapies. The purpose was to ascertain COVID-19 vaccine and booster uptake, reasons for hesitancy, and self-reported flare in a large rheumatology practice-based network (PBRN).

Methods: A tablet-based survey was deployed as part of routine care in 104 rheumatology practices who were members of the Excellence Network in RheumatoloGY (ENRGY) PBRN during 12/2021- 12/2022. Patients were asked about COVID-19 vaccine status and why they might not receive a vaccine or booster. Patients reporting no vaccine receipt were asked additional questions about why they did not receive the vaccine and were categorized as vaccine-hesitant. Receipt of the primary series of vaccines and a response of "not planning to" or "not sure "when asked about getting additional vaccine or booster doses defined booster-hesitant patients. We used descriptive statistics to explore the differences between vaccination status and vaccine/booster hesitancy, comparing AIIRD to non-AIIRD patients. We used multivariable logistic regression to estimate adjusted odds ratios (aOR) with confidence intervals (CI), examining the association between vaccine uptake and AIIRD status, and self-reported flare/disease worsening and AIIRD status.

Results: Of 61,158 respondents (99.9% completion rate), 89% reported at least one dose of vaccine; of the vaccinated, 68% reported at least one booster (Table 1). AIIRD patients were 32% less likely to receive a vaccine (aOR: 0.68; 95% CI: 0.65, 0.72) and 10% less likely to receive a booster (aOR: 0.90; 95% CI: 0.87, 0.94) versus non-AIIRD patients (Table 2).

Table 1: Characteristics of rheumatology patients and most recent COVID-19 vaccine status

	Overall Cohort		AIIRD		Non-AIIRD	
	61158		27613		33545	
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated
n	54695	6463	24149	3464	30546	2999
Age, Years						
Mean (SD)	62.8 (14.7)*	55.5 (14.8)*	62.6 (14.1)*	55.3 (14.3)*	62.9 (15.2)*	55.7 (15.3)*
Race, N (%)						
White	38145 (69.7)*	4732 (73.2)*	17090 (70.1)*	2547 (73.5)*	21055 (68.9)*	2185 (72.9)*
Black or African American	4912 (9.0)*	523 (8.1)*	2230 (9.2)*	273 (7.9)*	2682 (8.8)*	250 (8.3)*
Asian	1264 (2.3)*	55 (0.9)*	574 (2.4)*	31 (0.9)*	690 (2.3)*	24 (0.8)*
Other	5868 (10.7)*	624 (9.7)*	2548 (10.6)*	345 (10.0)*	3320 (10.9)*	279 (9.3)*
Declined to specify	3445 (6.3)*	470 (7.3)*	1401 (5.8)*	244 (7.0)*	2044 (6.7)*	226 (7.5)*
Missing	1061 (1.9)	59 (0.9)	306 (1.3)	24 (0.7)	755 (2.5)	35 (1.2)
Sex, N (%)						
Female	42645 (78.0)	5072 (78.5)	18200 (75.4)	2650 (76.5)	24445 (80.0)	2422 (80.8)
Ethnicity, N (%)						
Not Hispanic or Latino/a	35898 (65.6)	4378 (67.7) †	16450 (68.1)	2390 (69.0)	19448 (63.7)†	1988 (66.3)†
Hispanic or Latino/a	6271 (11.5)†	700 (10.8)†	2733 (11.3)	394 (11.4)	3538 (11.6)†	306 (10.2)†
Declined to specify	5072 (9.3)†	655 (10.1)†	2160 (8.9)	355 (10.3)	2912 (9.5)†	300 (10.0)†
Missing	7454 (13.6)	730 (11.3)	2806 (11.6)	325 (9.4)	4648 (15.2)	405 (13.5)

AIIRD = autoimmune and inflammatory rheumatic diseases. SD = standard deviation.
*p<0.0001.
†p=0.03.

Table 2: Multivariable adjusted odds ratios for receiving any dose of the primary COVID-19 series (n=54695) and a COVID-19 booster dose (n=37411)

	Adjusted Odds Ratios for Receiving a Dose of Vaccine (95% CI)*	P-value	Adjusted Odds Ratios for Receiving a Booster (95% CI)*	P-value
Disease (AIIRD vs. Non-AIIRD referent)	**0.68 (0.65, 0.72)**	<0.0001	**0.90 (0.87, 0.94)**	<0.0001
Race (vs. White as referent)				
Asian	**3.45 (2.58, 4.61)**	<0.0001	**2.07 (1.80, 2.37)**	<0.0001
Black or African American	1.38 (1.24, 1.53)	0.51	0.99 (0.93,1.06)	0.8
Declined to Specify	0.99 (0.86, 1.13)	<0.0001	0.96 (0.88, 1.05)	0.4
Other	1.27 (1.11, 1.45)	0.06	0.97 (0.89, 1.06)	0.5
Ethnicity (vs. Non-Hispanic or Latino/a as referent)				
Hispanic or Latino/a	**1.18 (1.04, 1.33)**	0.03	1.03 (0.95, 1.11)	0.5
Declined to Specify	1.04 (0.94, 1.16)	0.5	0.97 (0.90, 1.04)	0.4
Age, 5 years	**1.18 (1.17, 1.19)**	<0.0001	**1.21 (1.20, 1.21)**	<0.0001

AIIRD = autoimmune and inflammatory rheumatic diseases. CI = confidence interval.
*Adjusted for all significant demographic variables.

Table 3: Reasons for primary series COVID-19 vaccine hesitancy (n=13950*) and booster hesitancy (n=21164†) among study participants

	Vaccine hesitancy 13950*	Booster hesitancy 21164†
There isn't enough long-term safety data on the COVID-19 vaccine or booster	3933 (28.2)	2426 (11.5)
I am concerned about side effects	3216 (23.1)	3674 (17.4)
I am concerned a COVID-19 vaccine will cause a flare of my health condition	2274 (16.3)	2193 (10.4)
I plan to wait and see if the COVID-19 vaccines and boosters are safe	1648 (11.8)	2334 (11.0)
I do plan to get the COVID-19 vaccine	1023 (7.3)	-
The COVID-19 vaccine or booster may not be effective for people like me	632 (4.5)	559 (2.6)
The vaccine could give me COVID-19 infection	445 (3.2)	-
I have not been told by my doctor when to get a dose or an additional dose of the COVID-19 vaccine	295 (2.1)	4926 (23.3)
I don't believe I need a vaccine or another dose of the COVID-19 vaccine	237 (1.7)	3497 (16.5)
I don't trust COVID-19 vaccines	209 (1.5)	-
I am concerned that the COVID-19 vaccine could modify my DNA	23 (0.2)	-
I am concerned the COVID vaccine might affect me being able to have healthy children	15 (0.1)	-
I had a bad reaction to the COVID-19 vaccine	-	1555 (7.4)

*Patients could answer with more than one response and some patients answered the question multiple times. The number of vaccine-hesitant patients is 7341. Vaccine hesitancy response choices were updated throughout the study.
†Patients could answer with more than one response. The number of booster-hesitant patients is 11058.

A greater proportion of AIIRD patients were vaccine-hesitant (14% vs. 10%; p< 0.0001) and booster-hesitant (21% vs. 16%; p< 0.0001) compared to non-AIIRD patients. Among those who were vaccine hesitant (n=7,341), safety concerns (28%) and side effects (23%) were the main reasons for vaccine hesitancy, while among those who were booster hesitant (n=11,058), lack of recommendation from the physician was the primary factor for booster hesitancy (23%) (Table 3). Of those who received a vaccination, 23% of patients reported experiencing symptoms consistent with reactogenicity or a flare/disease worsening following their most recent vaccination. AIIRD patients did not have increased odds of self-reported flare/worsening disease compared to non-AIIRD patients (aOR: 0.99; 95% CI: 0.94, 1.05). Among the vaccine-hesitant and booster-hesitant, 12% and 39% later reported receiving a respective dose.

Conclusion: A meaningful proportion of vaccine- and booster-hesitant patients eventually received vaccination or booster doses, suggesting that future interventions tailored to AIIRD patients to encourage vaccination or booster use may be fruitful.

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Abstract Number: 0215

Effectiveness of Three Doses of SARS-CoV-2 Vaccines in Brazilian Patients with Systemic Vasculitides: Preliminary Results of a Real-life Prospective Cohort

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Infection-related Rheumatic Disease Poster

Session Type: Poster Session A

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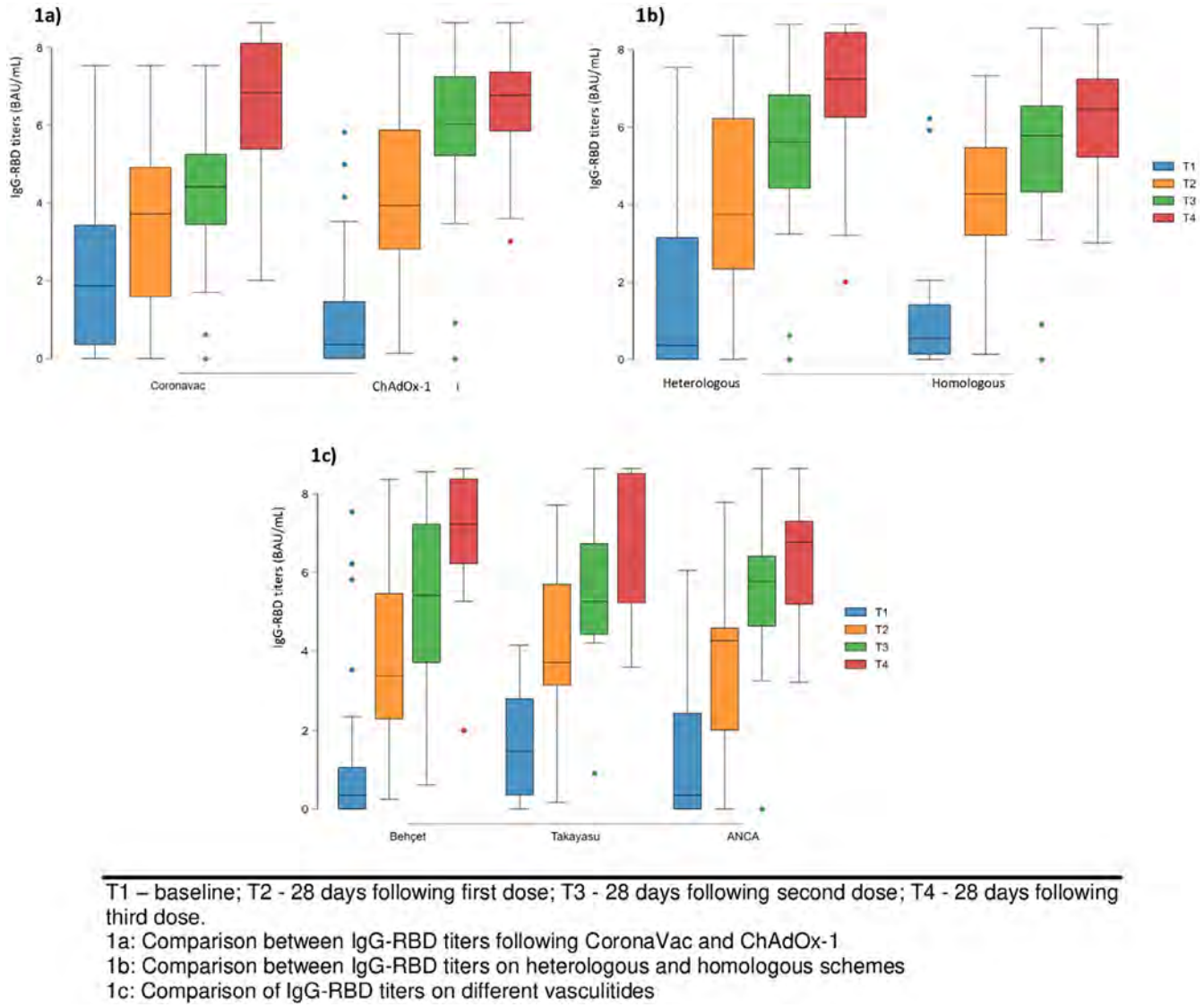
Background/Purpose: Vaccine platforms, number of doses, and immunosuppressive drugs can influence the immunogenicity after SARS-CoV-2 vaccination in individuals with immune-mediated rheumatic diseases. Considering the heterogeneity of systemic vasculitides and their phenotypic variations according to geographic localization, there is still limited data about the immunogenic response in this population, with most studies focusing on homologous vaccine platforms. Furthermore, concerns regarding vaccine-induced vasculitides and potential disease relapse have affected vaccine hesitancy in these patients. This study evaluated the effectiveness of three doses (booster dose) of SARS-CoV-2 vaccines and the occurrence of disease relapse in systemic vasculitides.

Methods: We enrolled 99 patients with systemic vasculitides in a Brazilian multicentric prospective cohort, a subgroup of the SAFER study (Safety and Efficacy on COVID-19 Vaccine in Rheumatic Disease). All patients met international classification/diagnostic criteria for their respective diseases. Studied vaccines were inactivated SARS-CoV-2 (CoronaVac), adenoviral vectored (ChAdOx1/AstraZeneca and Ad26.COV2-S/Janssen), and mRNA (BNT162b2/Pfizer–BioNTech). The measurement of serum IgG levels against SARS-CoV-2 spike protein receptor-binding domain (IgG-RBD) using a chemiluminescence test (Abbott-Laboratories, IgG II Quant assay) assessed the immunogenicity. We collected serum samples at baseline and 28 days after each vaccine dose, with simultaneous assessment of disease activity scores, COVID-19 infections, and adverse events.

Results: Seventy-four patients received a single vaccine dose, 65 received two doses, and 59 completed the full vaccination regimen. Most patients received ChAdOx-1 (n = 36) or CoronaVac (n = 25) for the first two doses. The most administered booster dose was Pfizer–BioNTech. Behçet's disease (BD), Takayasu arteritis, and antineutrophil cytoplasmic antibody (ANCA) associated vasculitis were the most frequent diagnosis in this cohort. Up to 49% of the patients had no comorbidities. Notably, none of the patients received Rituximab at baseline. ChadOx-1 achieved higher antibody titers than CoronaVac after two doses (p=0.002), but this difference disappeared after the booster dose (Table 1). Seropositivity rates tended to be higher in the heterologous vaccine group compared to the homologous three-dose scheme (Table 1). Immunogenicity was similar across different forms of vasculitis (Figure 1-c). No increase in disease relapse rates was observed in any form of vasculitis. No severe relapses or serious adverse events were reported.



T1 – baseline; T2 - 28 days following first dose; T3 - 28 days following second dose; T4 - 28 days following third dose.
1a: Comparison between IgG-RBD titers following CoronaVac and ChAdOx-1
1b: Comparison between IgG-RBD titers on heterologous and homologous schemes
1c: Comparison of IgG-RBD titers on different vasculitides

Figure 1. Serum IgG-RBD geometric means at baseline and following each vaccine dose (BAU/mL)

Conclusion: In this Brazilian multicentric prospective cohort, the booster dose elicits a similar immune response in all patient groups, despite the initial difference in IgG-RBD titers after two doses of ChAdOx-1 and CoronaVac. Although a heterologous vaccine regimen showed a potential trend towards a more robust humoral response, this was not statistically significant, likely due to sample size limitations. Notably, the three-dose scheme was safe for all systemic vasculitides, with no increased disease activity observed.

Geometric means of IgG-RBD titers following different vaccines and different schemes of vaccination in Brazilian patients with systemic vasculitis

Table 1 - Geometric means of IgG-RBD titers following different vaccines and different schemes of vaccination in Brazilian patients with systemic vasculitis

CoronaVac vs. ChAdOx-1				
Log IgG-RBD	Total	CoronaVac	ChAdOx-1	*p*
	n=61	N=25	n=36	
Baseline, Mean (SD)	1.43 (1.86)	2.10 (2.20)	1.01 (1.50)	**0.027**
28 days following first dose, Mean (SD)	3.90 (2.27)	3.44 (2.10)	4.23 (2.36)	0.2
28 days following second dose, Mean (SD)	5.24 (2.19)	4.06 (2.08)	5.97 (1.94)	**0.001**
28 days following third dose, Mean (SD)	6.57 (1.65)	6.45 (2.00)	6.64 (1.46)	0.71
Heterologous vs. Homologous				
Log IgG-RBD	Total n=59	Heterologous n=40	Homologous n=19	*p*
Baseline, Mean (SD)	1.48 (2.04)	1.62 (2.16)	1.19 (1.81)	0.46
28 days following first dose, Mean (SD)	3.99 (2.38)	4.04 (2.45)	3.86 (2.24)	0.82
28 days following second dose, Mean (SD)	5.35 (2.18)	5.44 (2.20)	5.16 (2.20)	0.66
28 days following third dose, Mean (SD)	6.74 (1.60)	7.01 (1.58)	6.14 (1.52)	0.073

RBD – receptor-binding domain; SD – standard-deviation; n - number of patients

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Abstract Number: 0216

High Immunogenicity of mRNA Covid-19 Vaccine Booster in Immune Mediated Inflammatory Disease

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Infection-related Rheumatic Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with immune-mediated inflammatory disorders (IMIDs) have an inherently heightened susceptibility to infection and may be considered high risk for COVID-19, yet IMID populations were initially excluded from vaccine efficacy studies. We have previously shown that: (1) at 3 months post vaccination, IMID patients on background

Table 1. Baseline characteristics of cohort at 12 months post initial vaccination.

Characteristic	Healthy (n =23)	Patients (n=83)	p-value
Age- mean (SD)	51.6 (12.9)	55.3 (14.6)	0.290
Female- n (%)	13 (56.5)	25 (30.1)	0.316
Race- n (%)			0.049
White	14 (60.9)	62 (74.7)	
Black	0 (0.0)	8 (9.6)	
Asian	9 (39.1)	10 (12.0)	
Other	0 (0.0)	3 (3.6)	
Hispanic ethnicity- n (%)	1 (4.3)	6 (7.2)	1.000
Primary IMID - n (%)			
Psoriasis and/or Psoriatic Arthritis	–	39	
Rheumatoid Arthritis	–	28	
Ankylosing Spondylitis	–	4	
Other*	–	12	
Long term medication- n (%)			
Methotrexate	–	42	
Other oral DMARD#	–	18	
Tumor necrosis factor inhibitor	–	40	
Janus kinase inhibitors	–	2	
Interleukin 17 blockers	–	9	
Interleukin 23 blockers^	–	3	
CD-20 depleting therapy	–	2	
Glucocorticoids	–	5	
Prior COVID-19 infection- n(%)	5 (21.7)	18 (21.7)	1.000
Adequate response at 4W	22 (95.7)	65 (78.3)	0.067
Adequate response at 3M	22 (95.7)	58 (69.9)	0.012
Adequate response at 6M	15 (65.2)	45 (54.2)	0.476
Adequate response at 12 M	23 (100.0)	81 (97.6)	1.000
Spike specific SARS-COV-2 Ab Titers	16,757.7 (2332.2)	17,005.1 (4959.7)	0.716
Received at least 1 "booster" prior to 12M	23 (100.0)	79 (95.2)	1.000
Days since last booster	78.4 (30.6)	129.8 (56.4)	0.003

[1]IMID denotes immune mediated inflammatory disease, DMARD disease modifying anti-rheumatic drug
*Vasculitis, dermatomyositis, adult onset stills disease, sarcoidosis, and polymyalgia rheumatic, inflammatory bowel disease
#Leflunomide, sulfasalazine azathioprine, hydroxychloroquine, mercaptopurine.
^Includes interleukin 12/23 blockers.

methotrexate (MTX) were less likely to achieve an adequate humoral response compared to healthy controls and IMID patients on other immunomodulatory medications and (2) at 6 months, those on MTX, tumor necrosis factor inhibitors (TNFis), or combination MTX-TNFi therapy were less likely to maintain an adequate humoral response. The objective of this study was to extend the characterization of the humoral immune response to mRNA COVID-19 vaccines in patients with IMID on immunomodulatory treatment to 12 months post vaccination.

Methods: Established patients with IMID and healthy controls at NYU receiving COVID-19 vaccination were assessed for humoral immune response at 4/5 weeks, 3 months, 6 months, and 12 months post first vaccine dose. Humoral response was assessed by testing IgG antibodies against the S1 domain of the spike protein of SARS-CoV-2. In line with our prior studies, adequate response was defined as greater than 5,000 RU/ml (although no titer is known to indicate immunity). Patient characteristics were summarized using means, standard deviations, and percentages as appropriate. Chi squared tests of independence and Fisher's exact tests were used for categorical variables between groups; Kruskal-Wallis tests for continuous variables as appropriate.

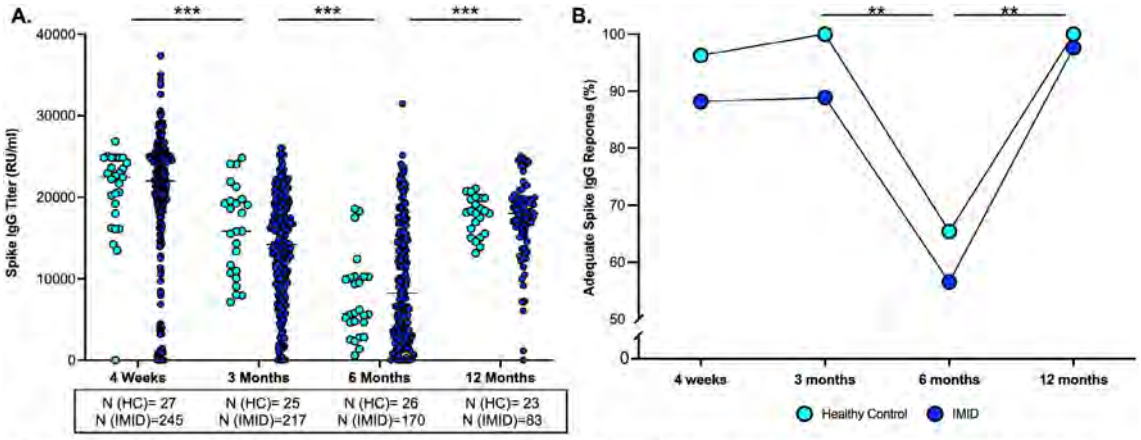

Figure 1. Anti-SARS-CoV-2 IgG levels by (A) titer and (b) percentage achieving an adequate response over time. IgG titers were significantly different at each subsequent timepoints. Percentage achieving an adequate response stayed stable between 4 weeks (96% healthy controls, 88% IMID) and 3 months post vaccination (100% healthy controls, 89% IMID) but dropped significant by 6 months (65% healthy controls, 57% IMID). At 12 months, after receiving a "booster" dose of the SARS-CoV-2 vaccination (red syringe), almost all participants demonstrated an adequate response (100% healthy controls, 97.6%% IMID). ** p< .01, *** p < 0.001.

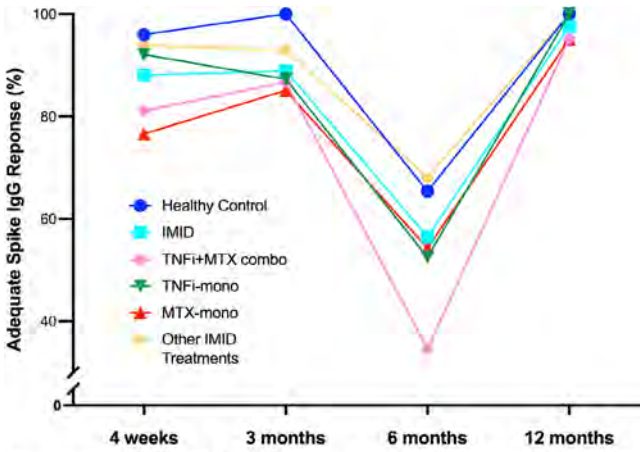

Figure 2. Percentage of IMID patients achieving an adequate response to SARS-CoV-2 vaccination by medication use. At 6 months, combination MTX+TNFi usage was associated with the lowest vaccination response (34.6%). At month 12, there was no difference observed due to medication use.

Results: By 12 months, 23/23 of the healthy controls and 79/83 of the participants with IMIDs received a supplemental dose of the COVID19 booster (Table 1). Participants with IMID were an average of 130 days since the booster dose at the time of phlebotomy (compared to 78 days in the healthy controls). All healthy controls and 81/83 IMID participants achieved an adequate humoral response and there was no difference in antibody titer levels (Figure 1). Antibody titer levels did not correlate with time since booster dose (r= -0.18, p=0.12). Of the 17 patients who had an initial non-response at week 4, all but one demonstrated an adequate response at 12 months. Additionally, there was no difference in response rate or antibody titer level by medication use (Figure 2).

Conclusion: Here, we demonstrate the immunogenicity of a COVID-19 booster dose, regardless of medication use and even in patients who did not initially mount a response. While there is no antibody titer that correlated with clinical efficacy, these findings highlight the importance of a supplemental dose in patients with IMID. Larger scale studies and those looking at the bivalent booster shot are needed to confirm and better understand these findings.

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Abstract Number: 0217

Safety and Efficacy of Tixagevimab/Cilgavimab (Evusheld) in Autoimmune Inflammatory Rheumatic Disease Patients – a Prospective Multicenter Open-label Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune inflammatory rheumatic disease (AIIRD) patients treated with rituximab (RTX) are at risk for severe COVID19 infection, and a blunted humoral response to SARS-CoV-2 vaccines. Evusheld (AZD7442) was a combination of tixagevimab and cilgavimab, indicated for COVID19 prevention in immunosuppressed patients.

We aimed to assess the safety and efficacy of Evusheld in AIIRD patients treated with rituximab or other immunosuppressive medications.

Methods: This prospective open label longitudinal study was conducted in February-December 2022 in 3 Israeli medical centers (Tel Aviv Sourasky, Rambam, and Carmel medical centers).

Consecutive AIIRD patients over 18 years, treated with RTX or other immunosuppressive medications, and qualifying for Evusheld administration were offered to participate in the study. Patients who refused to receive Evusheld were offered to take part as a control group. The participants were followed up to 10 months after receiving the 1st 300 mg dose of Evusheld (n=78). The control group (n=39) patients were followed for the same period of time after enrollment.

Data regarding adverse events, disease activity, and COVID19, were collected 3 days and 2 weeks after enrollment, and then every month until the end of the study.

Results: The age of participants was 63.3±13.1 (mean±standard deviation (SD) years, 77.39% were females. RA was the main indication for RTX treatment (n=65, 56.52%).

Table 1. Demographic and clinical characteristics of autoimmune inflammatory rheumatic disease patients in the Evusheld and control groups Categorical variables are presented by number (percent); continuous variables are presented by mean±standard deviation, except age which is presented by median (range). Tx, treatment; ab, antibody.

Variable	Evusheld group n=76	Controls n=39	p-value
Age, years	66 (24-89)	66.5 (38-81)	0.7128
Female sex	57 (75)	32 (82.05)	0.535
Rituximab tx ever	74 (97.37)	37 (94.87)	0.6034
Prednisone tx at study entry	32 (42.67)	19 (48.72)	0.676
Prednisone average dose in mg/day	14.516±27.006	21.868±45.736	0.5292
Mycophenolate tx	4 (5.33)	0 (0)	0.2972
Anti S1/S2 ab levels at study entry	16.98±29.52 N=23	43.93±49.85 N=23	**0.0321**
mRNA vaccination pre-study entry	76 (100)	37 (97.37)	0.3333
COVID-19 infection pre-study entry	22 (28.95)	20 (51.28)	**0.0315**
Rheumatic disease diagnosis			0.5263
Rheumatoid arthritis	40 (52.63)	25 (64.1)	
ANCA-associated vasculitis	12 (15.79)	6 (15.38)	
Idiopathic inflammatory myopathies	7 (9.21)	1 (2.56)	
Systemic lupus erythematosus	5 (6.58)	2 (5.13)	
Systemic sclerosis	9 (11.84)	2 (5.13)	
IgG4-related disease	0 (0)	1 (2.56)	
Primary Sjogren's syndrome	1 (1.32)	0 (0)	
Other	2 (2.63)	2 (5.13)	
COVID-19 after study entry	23 (30.26)	11 (28.21)	0.9895

Table 2. Adverse events reported by direct questioning in each visit after receiving Evusheld from day 3-month 3

Visit	Adverse event, number/total reports (%)
Day 3	Injection Site Pain 3/76 (3.95) Headache 2/76 (2.63) Chest Pain 1/76 (1.32) Diarrhea 1/76 (1.32) Myalgia 1/76 (1.32) Arthralgia 1/76 (1.32)
Week 2	Injection Site Pain 1/27 (3.7) Cough 1/27 (3.7) Malaise 2/27 (7.41) Myalgia 1/27 (3.7) Arthralgia 2/27 (7.41)
Month 1	Dyspnea 1/33 (3.03) Diarrhea 1/33 (3.03)
Month 2	Pruritus 2/24 (8.33) Chest Pain 1/24 (4.17) Diarrhea 1/24 (4.17)
Month 3	Diarrhea 1/72 (1.39) Constipation 1/72 (1.39)

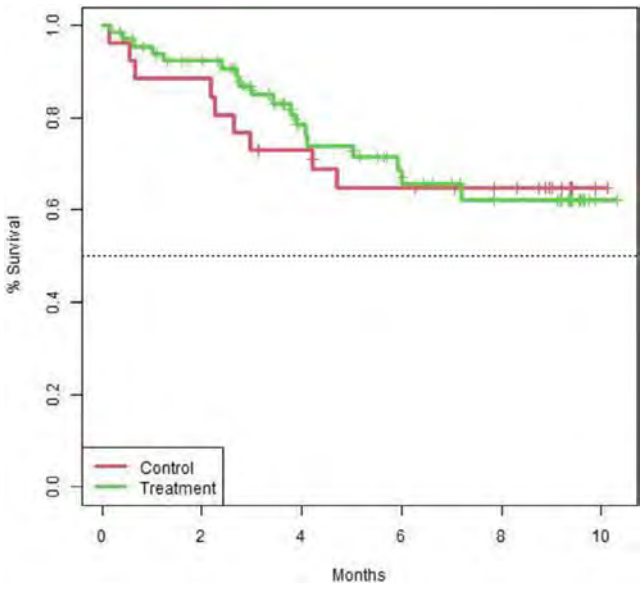

Figure 1. survival analysis of COVID-19 infection cases in the Evusheld (green) and control (red) groups during the study period. P=0.8151

The Evusheld treated group was similar to the controls in regard to age, sex, AIIRD diagnoses, immunosuppressive treatment, and rate of mRNA vaccination (table 1). However, control group participants had a higher rate of previous COVID19 (51.28% vs. 28.95%, p=0.0315, respectively), and higher anti-S1/S2 antibody titers at study entry, compared to controls (43.93±49.85 vs. 16.98±29.52, p=0.0321, respectively).

Adverse events were reported in 17.11% (n=13), most of them within 3 days following Evusheld administration, and all were mild (table 2). Injection site reactions included only pain and were reported by 3.95% of participants receiving Evusheld.

During the study, 15 patients were hospitalized, at a similar rate among the groups (10 (26.3%) Evusheld and 5 (21.7%) controls, p=0.92). One female RA patient, treated with abatacept and prednisone, died 47 days after receiving Evusheld, due to deterioration of rheumatoid lung, not considered related to the use of Evusheld.

Disease activity was generally stable and low, during the study for all indications.

The rate of COVID19 during the study was similar between the groups (n=23, 30.3% Evusheld, n=11, 28.2% controls, p=0.99) (figure 1). Three severe infections were reported in the Evusheld group including one lethal critical COVID19 in 47 years old SSc patient who received Evusheld 6 months previously, and another 2 severe COVID19 cases. Moderate COVID19 was reported in 3 patients –2 of them were in the control group.

Conclusion: Evusheld was safe in patients with AIIRD treated with B-cell depleting or other immunosuppressives medications, that commonly fail to efficiently respond to active/mRNA vaccination. Nevertheless, Evusheld did not prove efficacious in preventing omicron and post-omicron COVID19 in general, and severe disease in particular.

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Abstract Number: 0218

Incidence and Risk Factors for Breakthrough COVID-19 After Tixagevimab/Cilgavimab Among Patients with Systemic Autoimmune Rheumatic Diseases

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SESSION INFORMATION
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Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: During the height of the COVID-19 pandemic in the United States, tixagevimab/cilgavimab (Evusheld), a combination of monoclonal antibodies directed against the SARS-CoV2 spike protein, received emergency use authorization (EUA) for use as pre-exposure prophylaxis (PrEP) against COVID-19. However, little is known regarding real-world experience with PrEP in patients with systemic autoimmune rheumatic diseases (SARDs). We aimed to determine the incidence of and risk factors for breakthrough COVID-19 after tixagevimab/cilgavimab among patients with SARDs.

Methods: We conducted a retrospective cohort study of patients with SARDs at a large U.S. healthcare system. We identified all patients who received tixagevimab/cilgavimab as PrEP between 1/2/2022 and 11/16/2022. The index date was the date of the first dose of tixagevimab/cilgavimab. We collected demographics, medications, prior COVID-19, and SARS-CoV2 spike antibody levels prior to index date from electronic query. SARD diagnoses, the presence of additional PrEP indications (e.g., prior organ transplant, active cancer treatment), and COVID-19 course were confirmed by medical record review. The primary outcome was breakthrough COVID-19 confirmed by polymerase chain reaction or an antigen test reported to a physician. Censoring occurred at earliest of breakthrough COVID-19, death, or end of study (November 16, 2022). We used multivariable Cox regression models adjusting for baseline factors to identify risk factors for breakthrough COVID-19.

Results: We identified 444 patients with SARDs who received tixagevimab/cilgavimab (mean age 62.0 years, 78.2% female, 79.3% white) (**Table 1**). The most common SARD diagnoses were rheumatoid arthritis (43.7%), systemic lupus erythematosus (14.9%), and ANCA-associated vasculitis (11.7%). There were 83 (18.7%) breakthrough COVID-19 cases, of which 8 (1.8%) required hospitalization and 1 (0.2%) died (**Table 2**). The overall incidence rate was 31.5 per 1000 person-months (95% CI 24.70, 38.24). Older age was inversely associated with breakthrough COVID-19 (adjusted hazard ratio [aHR] 0.86 per 10 years, 95% CI 0.75, 0.99). Higher baseline spike antibody levels were associated with lower risk of breakthrough COVID-19 (aHR 0.42, 95% CI 0.18, 0.99 for spike antibody levels >200 units vs. < 0.4 units). CD20 inhibitor users had a similar risk of breakthrough COVID-19 (aHR 1.05, 95% CI 0.44, 2.49) compared to patients on conventional synthetic DMARDs (**Table 3**).

Conclusion: In this study spanning the period of viral neutralizing abilityfor tixagevimab/cilgavimab, we found that patients with SARDs had frequent breakthrough COVID-19 after PrEP, but the proportion of severe COVID-19 was low. Further, we found no associations between DMARD type, including anti-CD20 inhibitors, with the risk of breakthrough COVID-19. Older age and higher baseline spike antibody level were protective against breakthrough infection, highlighting the continued

Table 1. Baseline demographic and clinical characteristics of SARD patients at time of initial tixagevimab/cilgavimab receipt

Characteristic	SARD patients who received tixagevimab/cilgavimab (n=444)
Age (mean, SD)	62.0 (14.0)
Female, %	78.2
Race, %	
White	79.3
Black or African American	8.3
Asian	5.2
Other or unknown	7.2
Additional tixagevimab/cilgavimab indications, %	
History of solid organ or bone marrow transplant	10.4
Active cancer treatment	6.1
Other immune-mediated inflammatory disease*	3.8
Primary immunodeficiency	0.7
Previous COVID-19 infection before index date, %	18.9
Spike antibody level categories, units	
Spike level < 0.4**	34.9
Spike level ≥ 0.4 - 200	15.1
Spike level >200	24.1
Missing	25.9
SARD diagnosis, %	
Rheumatoid arthritis	43.7
Systemic lupus erythematosus	14.9
ANCA-associated vasculitis	11.7
Polymyalgia rheumatica and/or giant cell arteritis	4.5
Psoriatic arthritis	3.8
Systemic sclerosis	3.2
Sjogren's disease	2.9
Idiopathic inflammatory myositis	2.7
Immunomodulatory medications, %	
Biologic DMARDs	67.1
CD20 inhibitor	48.7
TNF inhibitor	8.3
Targeted synthetic DMARDs (JAK inhibitor)	2.5
Conventional synthetic DMARDs	65.1
Methotrexate	22.1
Mycophenolate mofetil / mycophenolic acid	20.5
Antimalarials	19.1
Calcineurin inhibitor	14.2

* Includes multiple sclerosis, inflammatory bowel disease, and other inflammatory conditions that require immunosuppression but not typically treated by rheumatologists

**CD-20 inhibitor users who had no measured spike antibody levels (n = 87) were imputed to have spike antibody levels < 0.4 units

Abbreviations: ANCA, antineutrophil cytoplasmic antibody; DMARD, disease-modifying antirheumatic drug; IQR, interquartile range; JAK, Janus kinase; SARD, systemic autoimmune rheumatic disease; SD, standard deviation; TNF, tumor necrosis factor

need for a multimodal approach (e.g. shielding behaviors, vaccinations) to prevent COVID-19 in this vulnerable population as newer generation PrEP monoclonal antibodies against SARS-CoV2 are being developed.

Table 2: Breakthrough COVID-19 outcomes after tixagevimab/cilgavimab among patients with systemic autoimmune rheumatic diseases

Outcome	SARD patients who received tixagevimab/cilgavimab (n=444)
COVID-19 cases, n (%)	83 (18.7%)
Severe COVID-19	8 (1.8%)
Hospitalizations	8 (1.8%)
Deaths	1 (0.2%)
Time from index date to infection, days (mean, SD) (n=83)	148.8 (81.9)

Table 3. Associations of baseline demographic and clinical factors with COVID-19 breakthrough after tixagevimab/cilgavimab receipt

Variable	COVID-19 cases	Person-months	Incidence rate per 1000 person-months (95% CI)	Multivariable HR* (95% CI)
Age (per 10 years)	83	2,637.6	31.5 (24.7, 38.2)	**0.86 (0.75, 0.99)**
Sex				
Female	62	2,047.9	30.3 (22.74, 37.8)	1.00 (Ref)
Male	21	589.7	35.6 (20.4, 50.9)	1.13 (0.67, 1.90)
Spike antibody level before index date				
<0.4	36	1,089	33.1 (22.3, 43.9)	1.00 (Ref)
0.4 to 200	14	405.4	34.5 (16.4, 52.6)	0.94 (0.45, 1.96)
>200	9	551.6	16.3 (5.7, 27.0)	**0.42 (0.18, 0.99)**
Missing	24	591.6	40.6 (24.3, 56.8)	0.93 (0.40, 2.17)
Previous COVID-19 before index date				
No	72	2,167.2	33.2 (25.6, 40.9)	1.00 (Ref)
Yes	11	470.4	23.4 (9.6, 37.2)	0.66 (0.35, 1.25)
DMARD use				
csDMARD only**	8	321.0	24.9 (7.7, 42.2)	1.00 (Ref)
MMF	13	354.6	36.7 (16.7, 56.6)	1.45 (0.59, 3.60)
CD20 inhibitor	42	1,460.5	28.8 (20.1, 37.5)	1.05 (0.44, 2.49)
Other b/ts DMARD	18	443.1	40.6 (21.9, 59.4)	1.89 (0.83, 4.32)
No DMARD	2	58.3	34.3 (0.0, 81.9)	1.55 (0.31, 7.72)

*Adjusted for age, sex, calendar date, spike antibody level, DMARD use, previous COVID-19
**csDMARD other than MMF
Abbreviations: b/ts DMARD, biologic and targeted synthetic disease-modifying antirheumatic drug; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HR, hazard ratio; MMF, mycophenolate mofetil

Disclosure: Y. Kawano: None; **X. Wang**: None; **N. Patel**: Arrivo Bio, 2, Chronius Health, 2, FVC Health, 2; **G. Qian**: None; **E. Kowalski**: None; **K. Bade**: None; **K. Vanni**: None; **A. Medicines Partnership (AMP): RA/SLE**: None; **Z. Williams**: None; **C. Cook**: None; **S. Srivatsan**: None; **Z. Wallace**: BioCryst, 2, Bristol-Myers Squibb(BMS), 5, Horizon, 1, 2, 5, MedPace, 2, Novartis, 1, PPD, 2, Sanofi, 1, 5, Shionogi, 1, Visterra, 1, 2, Zenas, 1, 2; **J. Sparks**: AbbVie, 2, Amgen, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, 5, Gilead, 2, Inova Diagnostics, 2, Janssen, 2, Optum, 2, Pfizer, 2, ReCor, 2.

Abstract Number: 0219

Safety and Efficacy of Pre-Exposure Prophylaxis with Tixagevimab/Cilgavimab (Evusheld) in Patients with Autoimmune Diseases and Renal Involvement Who Received Rituximab

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients on B-cell depleting agents may have a suboptimal response to vaccination, placing them at a higher risk of contracting SARS-CoV-2 or suffering from a more severe prognosis. Indeed, available data on pre-exposure prophylaxis with tixagevimab/cilgavimab (Evusheld) in subjects with glomerular diseases (GD) who received rituximab is limited.

Methods: We conducted a prospective study analyzing the safety and efficacy of tixagevimab/cilgavimab for pre-exposure prophylaxis in patients with GD who received rituximab in the previous 12 months. Rate of symptomatic infections and hospitalizations were compared to patients with GD treated with rituximab who refused to receive tixagevimab/cilgavimab.

Results: Tixagevimab/cilgavimab was administered to 22 patients (12 females, mean age 58,4±19,6 years) with GD diagnoses including membranous nephropathy, lupus nephritis, ANCA-associated vasculitis and focal segmental glomerulosclerosis. No patient treated with tixagevimab/cilgavimab experienced symptomatic infection with SARS-CoV-2 during the follow-up (mean observation time follow-up was 112 ± 23 days), while 11 out 28 controls (39,3%) reported a symptomatic infection (p=0,001), requiring hospitalization in 2 cases. Reported adverse events were mild, namely self-limiting headache (4), discomfort at the injection site (3), flu-like symptoms/myalgia (3), and fever (1). No serious adverse event, (e.g., cardiac events, anaphylaxis) was reported.

Conclusion: Pre-exposure prophylaxis with tixagevimab/cilgavimab (Evusheld) seems safe and lowering of about 40% the risk of symptomatic SARS-CoV-2 infection in vaccinated subjects with GD who received anti-CD20 therapy. Possible applications in the subset of patients who need immunosuppressive therapy, especially with Rituximab, in a pandemic setting might be envisaged.

Disclosure: S. Sciascia: None; **M. RILAT**: None; **R. FENOGLIO**: None; **S. FODDAI**: None; **M. RADIN**: None; **I. CECCHI**: None; **g. cinnirella**: None; **p. crosasso**: None; **m. guidetti**: None; **A. BARINOTTI**: None; **s. baldovino**: None; **E. MENEGATTI**: None; **D. Roccatello**: None.

Abstract Number: 0220

Paxlovid (Nirmatrelvir Plus Ritonavir) in Patients with Underlying Rheumatological Diseases, in Preventing COVID-19 Related Hospitalization and Death

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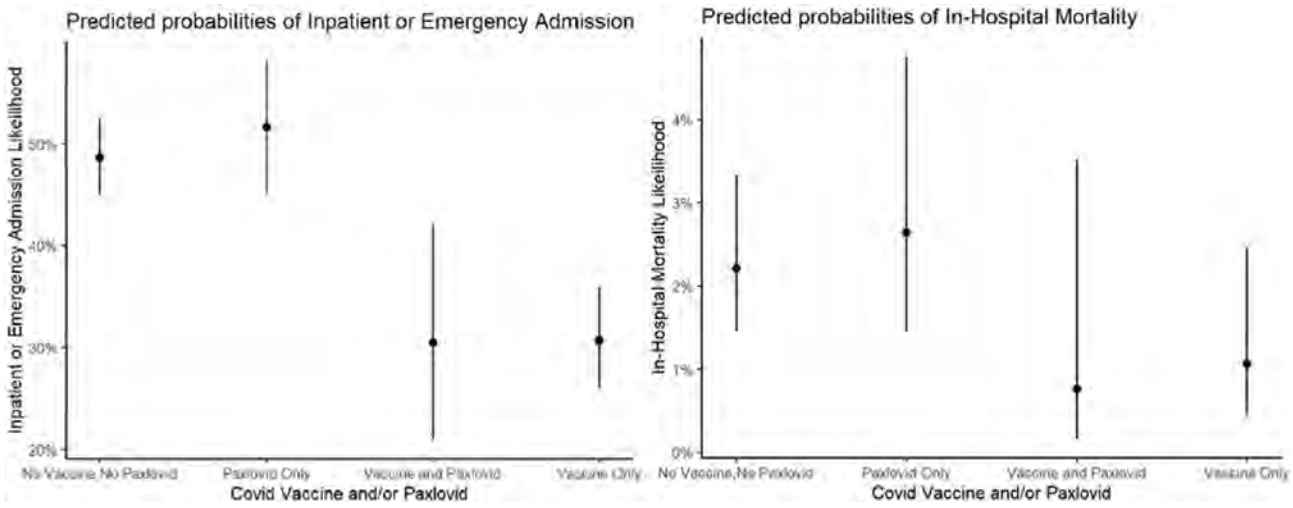
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The benefits of antiviral therapy in the COVID-19 patients with underlying rheumatic disease with or without immunosuppression are not entirely clear. The goal of this study is to determine the utility of Paxlovid in patients with rheumatological diseases (inpatient and outpatient) in preventing COVID-19 associated hospital admissions and mortality. By preventing severe COVID-19 infection, we can potentially avoid any long-term breaks of immunosuppressive agents and disease flares in these patients.

Methods: This is an Institutional Review Board approved, retrospective study in which participants were identified as patients with diagnosis of a rheumatological condition based on ICD-9 and/or ICD-10 codes who presented to either the inpatient or outpatient setting at the University of Kentucky Hospitals between January 1, 2020, and September 30, 2022. Baseline characteristics of patients included in this study are shown in Table-1. Outcomes of interest were in-hospital mortality related to COVID-19 and inpatient or emergency admission due to COVID-19. All statistical tests were two-sided and statistical significance was defined as p-value < 0.05. All analyses were done in R programming language, version 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria). For both outcomes, two logistic regression models were employed with odds ratios (OR) obtained. The first model considered patients' Paxlovid prescription status conditional on their COVID-19 vaccine status. The second model considered patients' Paxlovid prescription status conditional on their COVID-19 vaccine status while adjusting for prednisone prescription status, obesity, and diabetes diagnosis.

CHARACTERISTICS	UNTREATED PATIENTS (N=1926)	PATIENTS TREATED with PAXLOVID (N=461)	TOTAL PATIENTS (N= 2387)
AGE			
Mean	52.6 (17.4)	52.4 (18.2)	52.6 (17.6)
GENDER			
Male	633 (32.9%)	167 (36.2%)	800 (33.5%
Female	1293 (67.1%)	294 (63.8%)	1587 (66.5%)
RACE			
White	1648 (85.6%)	384 (83.3%)	2032 (85.1%)
African American	237 (12.3%)	69 (15.0%)	306 (12.8%)
Other	16 (0.8%)	3 (0.7%)	19 (0.8%)
DIABETES	1290 (67.0%)	323 (70.1%)	1613 (67.6%)
OBESITY	1401 (72.7%)	329 (71.4%)	1730 (72.5%)
OUTPATIENT	74 (35.0%)	142 (30.8%)	816 (34.2%)
INPATIENT	1252 (65.0%)	319 (69.2%)	1571 (65.8%)
COVID-19 VACCINATION	1461 (75.9%)	375 (81.3%)	1836 (76.9%)
Rheumatological disease****	2387 (100%)	2387 (100%)	2387 (100%)

****Ankylosing spondylitis, gout, juvenile rheumatoid arthritis, Still's disease, adult-onset lupus erythematosus, SLE (systemic lupus erythematosus), polymyalgia rheumatica, pseudo gout, psoriatic arthritis, psoriatic spondylitis, Raynaud's syndrome w/o gangrene, Reactive arthritis (Reiter's), R/A w/ rheumatoid arthritis w/o organ or systems involvement, Sjögren's disease, spondylosis with myelopathy, Wegener's granulomatosis, Bechet's syndrome, fibromyalgia



Results: A total of 2,387 patients were reviewed in this retrospective analysis (inpatient, outpatient including tele-medicine). All these patients had diagnosis of rheumatological diseases and COVID-19 based on ICD-09 and ICD-10 codes. COVID-19 vaccination was received by 1,836 patients (76.9%); only Paxlovid prescription was received by 461 patients (18%). Patients who received both COVID-19 vaccination and Paxlovid were 86 (3.6%). We discovered that Paxlovid used alone in unvaccinated recipients was associated with lowering the rate of hospitalization or emergency room visit but was not statistically significant (OR = 1.12; CI:0.86 – 1.48; p = 0.392). However, concomitant use of both Paxlovid and COVID–19 vaccination in patients was associated with a lower likelihood of hospitalization and emergency room visit (OR = 0.46; CI: 0.27 – 0.78; p = 0.004). Additionally, Paxlovid only was not found to be associated with reduced mortality related to COVID-19 (OR = 1.2; CI: 0.65 – 2.09; p = 0.535). Similarly, the use of Paxlovid in vaccinated patients suggested decreased mortality due to COVID-19 but was not significant (OR = 0.34; CI: 0.05 – 1.35; p = 0.185) (Figure 2).

Conclusion: This study demonstrates that Paxlovid provides protection in immunosuppressed patients with rheumatological diseases against severe COVID-19–associated outcomes resulting in emergency room visit and inpatient admission, significantly so in vaccinated individuals. Further studies are needed to investigate this within a larger patient population.

Characteristics of the Patients at Baseline

Showing predicted probabilities of Inpatient or Emergency Admission for All Predictors on the left and mortality on the right.

Disclosure: F. Javed: None; **T. Mangino**: None; **P. Piranavan**: None.

Abstract Number: 0221

Post-COVID-19 Autoimmune Serologies and Immunophenotypes

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmunity after COVID-19 infection has been reported. We examined connective tissue disease (CTD) symptoms and autoantibodies, SARS-CoV-2 serologies, and T and B cell immunophenotypes (found in rheumatoid arthritis, systemic lupus erythematosus, and scleroderma in past studies), by the early vs. late COVID-19 pandemic waves. We hypothesized that patients who had COVID in earlier (3/1/2020- 1/31/2021) vs. later (2/1/2021-9/1/2021) waves would have higher prevalence of new CTD symptoms, autoantibodies, and abnormal immunophenotypes.

Methods: We identified patients COVID-19 PCR positive from 3/1/2020-9/1/2021 in the Mass General Brigham system. Eligible participants ≥18 years old and ≥1-month post-COVID-19 with no prior history of CTD received the CTD Screening Questionnaire (CSQ; Karlson EW, 1995) to complete. Subjects who returned questionnaires were invited for a blood draw. Subjects were tested for 27 autoimmune and 3 SARS-CoV-2 serologies, and for T peripheral helper cells (TpH), T follicular helper cells (TfH), age-related B cells (ABCs), and plasmablasts (PBs) proportions by flow cytometry. We tested for associations between clinical variables, serologies, and immunophenotypes (% total CD4 T cells for TpH and TfH; % total CB19 B cells for ABC and PB) using t-tests, Chi-square, and multivariable logistic regression, adjusting for age, race, sex. A heatmap of the multidimensional data was generated to elucidate underlying patterns.

Results: 324 of 2,935 screening questionnaires (11%) were returned; 80 eligible subjects participated. Baseline demographics and clinical data are shown in **Table 1** by early vs. late COVID-19 wave. 17 subjects were vaccinated at infection, all in the later pandemic; 10 subjects were hospitalized for COVID-19. Among those in earlier vs. later COVID waves, a higher proportion were CSQ+ (35% vs. 17%, p 0.12), and more were ANA+ (44% vs. 13%, p 0.009) (**Table 2**). Lupus anticoagulant was positive in 11% of early vs. 4% of late COVID, p 0.38. Having ≥1 positive autoantibody was found in 77% of early vs. 74% of later COVID subjects, p 0.76. After adjustment for age, race, and sex, having early (vs. late) COVID variants was associated with increased risk of ANA positivity (MV OR 4.55, 95%CI 1.16, 16.67). The heatmap revealed more variety of autoantibody positivity in early COVID, with more antibodies to cardiolipin IgG, B2GP1 IgM, C1q, CCP3, PMScl, PR3, Scl70, while Jo-1 and MPO were only present in later COVID waves. No clear patterns were seen in T and B cell phenotypes (**Figure 1**).

Table 1. Baseline Subject Demographic and Clinical Data ≥ COVID-19 Infection

	Early COVID-19/ Early Treatment, 3/1/2020-1/31/2021 (n=57)	Early Vaccination/ Delta Wave/ Omicron Wave/Post Omicron, 2/1/2021- 9/1/2021 (n=23)	p
Vaccinated at COVID-19, %	0	17 (73.9)	<0.0001
Severe COVID-19 (hospitalized), %	6 (10.5)	4 (17.4)	0.40
Age at COVID-19, years, mean (SD)	50.8 (15.4)	46.3 (15.6)	0.25
Female, %	47 (82.5)	15 (65.2)	0.09
Self-reported racial group			0.86
White, %	44 (77.2)	18 (78.3)	
Black, %	6 (10.5)	2 (8.7)	
Other, %	7 (12.3)	3 (13.0)	
Smoking status			0.41
Ever, %	12 (21)	3 (13)	
Never, %	45 (79)	20 (87)	
Body mass index, mean kg/m² (SD)	28.86 (6.05)	27.84 (5.68)	0.50

Table 2. Follow-up Clinical Data, Serologies, and Immunophenotyping Post-COVID-19 Infection			
	Early COVID 19/Early Treatment (n=57)	Early Vaccination/ Delta Wave/ Omicron Wave/Post Omicron (n=23)	p
Age, years, mean (SD)	51.8 (15.2)	46.9 (15.8)	0.20
Vaccinated at blood draw, %	51 (89.5)	21 (91.3)	0.80
Time from COVID-19 to blood, mean days (SD)	380.0 (188.6)	207.4 (107.5)	<0.0001
CSQ positive, %	20 (35.1)	4 (17.4)	0.12
CTD-Related Autoantibodies			
ANA ≥ 1:80 by IFA on hep2 cells, %	25 (43.9)	3 (13.0)	0.009
Anti-DSF70, %	7 (12.3)	2 (8.7)	0.64
Lupus anticoagulant, %	6 (10.5)	1 (4.4)	0.38
Anticardiolipin IgM, %	14 (24.6)	3 (13.0)	0.25
Anticardiolipin IgG, %	3 (5.3)	0	0.26
Anti-Beta-2 glycoprotein1 IgG, %	0	0	
Anti-Beta-2 glycoprotein1 IgM, %	4 (7.0)	0	0.19
Anti-phosphatidylserine/prothrombin IgG	6 (10.5)	1 (4.4)	0.38
Anti-phosphatidylserine/prothrombin IgM	27 (47.4)	11 (47.8)	0.97
Anti-dsDNA	2 (3.5)	1 (4.4)	0.86
Anti-CCP, %	2 (3.5)	0	0.36
ANCA, %	0	1 (4.4)	0.11
AntiPR3, %	2 (3.5)	0	0.36
AntiScl70, %	1 (1.8)	0	0.52
AntiC1q, %	3 (5.3)	0	0.26
Anti-U1RNP, %	3 (5.3)	4 (17.4)	0.08
Anti-histone, %	0	0	
Anti-Jo-1, %	0	1 (4.4)	0.11
Anti-ribosome,%	0	0	
Anti-Sm, %	0	0	
Anti-Sm-RNP, %	0	0	
Anti-PM-Scl, %	1 (1.8)	0	0.52
Anti-CENP-B, %	0	0	
Anti-PCNA,%	0	0	
Anti-Ro52, %	0	0	
Anti-SSA-Ro60, %	0	0	
Anti-SSB-La, %	0	0	
Any CTD-related autoantibody, %*	44 (77.2)	17 (73.9)	0.76
SARS CoV2 serologies			
Anti-Nucleocapsid	32 (56.1)	19 (82.6)	0.03
Anti-Receptor Binding Domain (RBD)	56 (98.3)	23 (100)	0.52
Anti-Spike 1	52 (91.2)	23 (100)	0.14
Immunophenotyping**			
TfH, % mean (SD)	1.68 (1.89)	1.71 (1.72)	0.95
TpH, % mean (SD)	1.56 (1.20)	1.98 (2.01)	0.35
ABC, % mean (SD)	3.37 (2.31)	4.30 (2.98)	0.14
PB, % mean (SD)	1.27 (1.93)	0.91 (0.93)	0.28

CSQ= Connective Tissue Disease screening questionnaire (Karlson EW, 1995); SD= standard deviation; CTD= connective tissue diseases; ANA= antinuclear antibody; Anti-DFS70= anti-dense fine speckled 70 antibody; IgM= immunoglobulin M; IgG= immunoglobulin G; Anti-dsDNA= anti-double stranded DNA antibody; Anti-CCP= anti-cyclic citrullinated peptide antibody; ANCA= antineutrophil cytoplasmic antibodies; AntiPR3= anti-proteinase 3 antibody; Anti-Sm= anti-Smith; Anti-Sm-RNP= anti-Smith ribonucleoprotein antibody; Anti-PM-Scl= anti-polymyositis/scleroderma antibody; Anti-CENP-B= anti-centromere proteins B antibody; Anti-PCNA= anti-perinuclear anti-neutrophil cytoplasmic antibodies; RBD= receptor binding domain; TfH= T follicular helper cell; TpH= T peripheral helper cell; ABC= age-associated B cell; PB= plasmablast *Some patients had multiple autoantibodies **reported as mean of % of total CD4+ T cells or total CD19+B cells

Conclusion: Although a small study without controls, infection in earlier vs. later COVID was associated with more ANA positivity and autoimmune rheumatic disease symptoms (latter non-significantly). Heatmap analyses elucidated increased prevalence of other autoantibody positivity in the earlier wave. These results raise the possibility that more virulent SARS-CoV-2 strains circulating in the early pandemic and pre-vaccine availability were more immunogenic and more likely to result in autoantibody production.

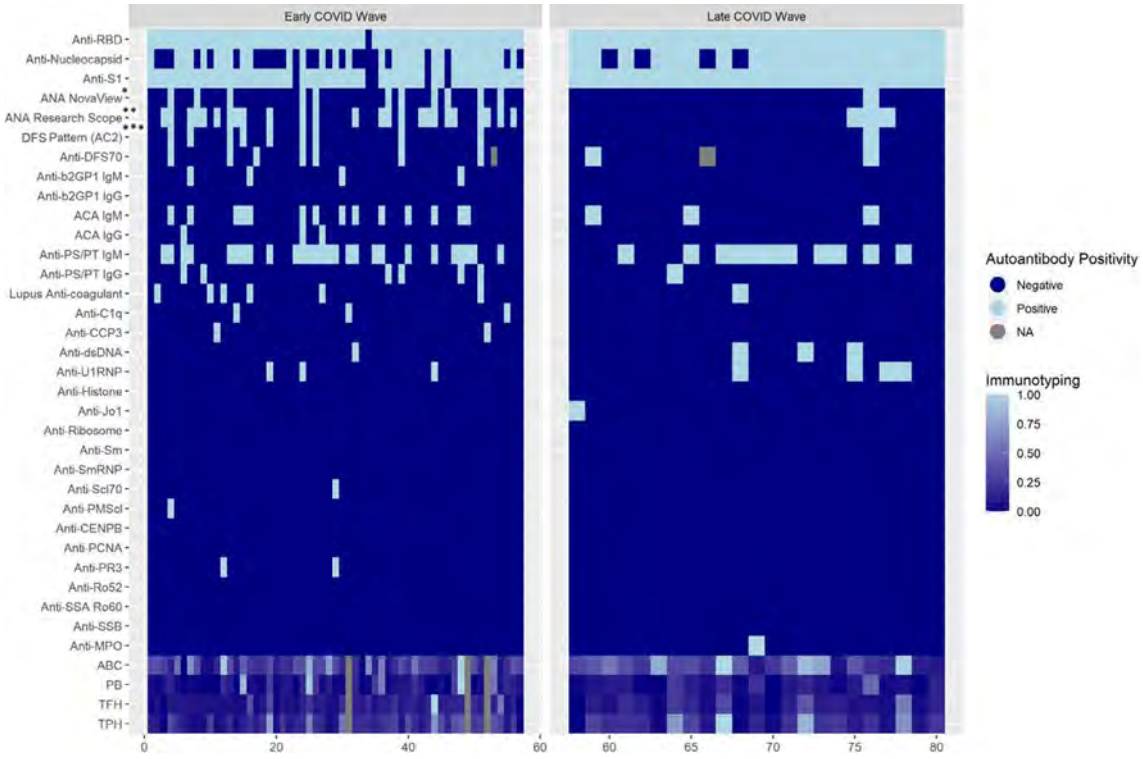

Figure 1. Hierarchical heatmap clustering of autoantibody and immune profile results among 80 subjects following COVID-19 infection stratified by COVID-19 wave (early vs. late). ANA= antinuclear antibody; Anti-DFS70= anti-dense fine speckled 70 antibody, IgM= immunoglobulin M; IgG= immunoglobulin G; Anti-dsDNA= anti-double stranded DNA antibody; Anti-CCP= anti-cyclic citrullinated peptide antibody; ANCA= antineutrophil cytoplasmic antibodies; AntiPR3= anti-proteinase 3 antibody; Anti-Sm= anti-Smith; Anti-Sm-RNP= anti-Smith ribonucleoprotein antibody; Anti-PM-Scl= anti-polymyositis/scleroderma antibody; Anti-CENP-B= anti-centromere proteins B antibody; Anti-PCNA= anti-perinuclear anti-neutrophil cytoplasmic antibodies; RBD= receptor binding domain; TfH= T follicular helper cell, TpH= T peripheral helper cell, ABC= age-associated B cell, PB= plasmablast; *ANA NovaView is read by automated digital immunofluorescence assay microscope, **ANA research scope is manual ANA interpretation by experienced laboratory technician, ***DFS AC-2 is nuclear dense fine speckled antinuclear antibody pattern associated with anti-DFS70 antibody

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Abstract Number: 0222

Predictors of Adverse Prognosis Following Hospitalization for COVID-19 Infection in Patients with Immune Mediated Inflammatory Diseases Treated with Rituximab

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rituximab (RTX) is widely used in immune mediated inflammatory disease (IMID) patients refractory to conventional treatment. Previous studies have indicated that RTX in IMID patients may lead to more severe COVID-19 disease outcomes. This study aims to characterize outcomes of hospitalized COVID-19 patients with IMIDs who received RTX treatment.

Methods: In this single center retrospective observational study, we included IMID patients with prior RTX use who got COVID-19 infection April 2021 to April 2023. COVID-19 was diagnosed by rRT-PCR assay detecting SARS-CoV-2 RNA. The demographics, serum markers, and medical outcomes were systematically reviewed from the electronic health records.

Table 1

Table 1. Demographics. Characteristics of IMID patients with prior Rituximab use, hospitalized with COVID-19 infection

Characteristics	N = 32
Age, median (IQR)	52 (44, 58)
Age < 50	15 (47%)
Age 50 - 65	11 (34%)
Age > 65	6 (19%)
Female	24 (75%)
Comorbidities [1]	21 (70%)
Body Mass Index (kg/m²), median (IQR)	22.9 (20.4, 26.7)
< 20	6 (19%)
20-30	20 (62%)
> 30	6 (19%)
Stationary IMID Disease Status [2]	21 (66%)
Viral RNA Cycle Threshold (Ct) [3], median (IQR)	19.4 (17.5, 21.5)
COVID-19 Severe Disease	16 (50%)
Viral Shedding Duration (Day) [4], median (IQR)	29 (17, 55)
Delayed Viral Shedding [5]	27 (84%)
Very Delayed Viral Shedding [6]	16 (50%)
Subsequent Re-infection < = 3 Months	11 (35%)
All-Cause Mortality [7]	13 (41%)
IMID Diagnosis	
ANCA vasculitis	2 (6.2)
Adult onset Still's Disease	1 (3.1%)
Rheumatoid arthritis	1 (3.1%)
Dermatomyositis	3 (9.4%)
IgG4-related disease	1 (3.1%)
Sjogren syndrome	4 (12%)
Systemic lupus erythematosus	3 (9.4%)
Spodyloarthropathies	5 (16%)
Immune thrombocytopenia	1 (3.1%)
Non-criteria antiphospholipid syndrome	4 (12%)
Autoimmune thyroid disease	3 (9.4%)
Pemphigus	2 (6.2%)
Mixed connective tissue disease	1 (3.1%)
Systemic sclerosis	1 (3.1%)

1. Comorbidities included interstitial lung disease, COPD, asthma, coronary artery disease, congestive heart failure, stroke, type 2 diabetes mellitus, hypertension, cancer, chronic kidney disease.
2. Stationary IMID disease status is defined as the absence of switch or add-on glucocorticoids, conventional synthetic/target synthetic DMARDs or biologics within 180 days prior to the COVID-19 diagnosis.
3. Sampled from nasopharyngeal swab test.
4. Viral shedding duration was defined as the interval between COVID-19 diagnosis and the first negative result in a rRT-PCR test or antigen test.
5. Delayed viral shedding was defined as a positive rRT-PCR test > = 14 days after COVID-19 diagnosis.
6. Very delayed viral shedding was defined as a positive rRT-PCR test > 28 days after COVID-19 diagnosis.
7. All-cause mortality included mortality during hospitalization and in 6 months.

Table 2.

Table 2. Results. Association of laboratory markers at COVID-19 diagnosis, medication, Rituximab use and outcomes, grouped according to COVID-19 disease severity, very delayed viral shedding status and all-cause mortality.

Outcomes / Laboratory Markers*	COVID-19 Disease Severity			Very Delayed Viral Shedding			All-Cause Mortality		
	Severe (N = 15)	Non-severe (N= 12)	p-value *	> 28 Days (N = 15)	< = 28 days (N = 12)	p-value *	Mortal (N = 12)	Alive (N = 15)	p-value *
Serum/Baseline									
Albumin[1] (g/dL)	3.85 (3.42, 4.28)	4.22 (4.05, 4.46)	0.051	4.10 (3.58, 4.32)	4.15 (3.81, 4.46)	0.500	3.90 (3.44, 4.31)	4.20 (3.88, 4.43)	0.200
CRP[2] (mg/dL)	0.32 (0.06, 1.08)	0.16 (0.09, 0.37)	0.700	0.32 (0.08, 0.89)	0.16 (0.06, 0.76)	0.700	0.08 (0.03, 0.55)	0.32 (0.13, 0.94)	0.150
Serum/At COVID-19 Diagnosis									
IgG (mg/dL)	615 (505, 806)	866 (770, 1108)	0.075	591 (486, 740)	927 (782, 1139)	0.004	603 (499, 822)	829 (728, 1048)	0.130
IgA (mg/dL)	101 (62, 158)	160 (117, 242)	0.053	89 (62, 158)	160 (129, 288)	0.010	95 (76, 146)	162 (112, 242)	0.059
Lymphocyte (k/ul)	546 (378, 783)	558 (492, 1407)	0.300	562 (363, 926)	550 (492, 956)	0.600	531 (370, 904)	553 (480, 911)	0.700
Albumin (g/dL)	3.2 (2.70, 3.45)	3.7 (3.58, 3.95)	0.004	3.30 (3.15, 3.70)	3.65 (3.18, 3.73)	0.500	3.30 (3.00, 3.62)	3.70 (3.20, 3.75)	0.300
CRP (mg/dL)	5.4 (2.6, 8.9)	2.3 (1.4, 7.1)	0.200	3.0 (1.5, 5.6)	6.5 (1.8, 10.2)	0.200	4.2 (2.0, 8.2)	3.0 (1.8, 8.0)	> 0.9
Ferritin (ng/mL)	992 (483, 1594)	260 (199, 639)	0.014	758 (394, 1386)	425 (226, 758)	0.200	654 (292, 1293)	578 (241, 955)	0.800
D-dimer (mg/L)	1.3 (0.7, 3.3)	0.4 (0.3, 1.0)	0.045	0.7 (0.3, 2.0)	0.8 (0.4, 1.7)	0.800	0.9 (0.3, 2.8)	0.7 (0.3, 1.6)	0.600
Outcomes / Medication	**COVID-19 Disease Severity**			**Very Delayed Viral Shedding**			**All-Cause Mortality**		
	Severe (N = 16)	Non-severe (N= 16)	p-value *	> 28 Days (N = 16)	< = 28 days (N = 16)	p-value *	Mortal (N = 13)	Alive (N = 19)	p-value *
COVID-19 related Medication									
Glucocorticoid[3] (mg/kg/day)	0.45 (0.35, 0.48)	0.31 (0.22, 0.36)	0.001	0.41 (0.34, 0.48)	0.33 (0.22, 0.41)	0.035	0.41 (0.36, 0.46)	0.31 (0.22, 0.41)	0.027
Remdesevir	11 (69%)	7 (44%)	0.285	10 (62%)	8 (50%)	0.722	9 (69%)	9 (47%)	0.289
Paxlovid	5 (31%)	7 (44%)	0.715	5 (31%)	7 (44%)	0.715	3 (23%)	9 (47%)	0.267
Molupiravir	4 (25%)	2 (12%)	0.654	3 (19%)	3 (19%)	1.000	4 (31%)	2 (11%)	0.193
Tocilizumab	7 (47%)	4 (27%)	0.449	8 (53%)	3 (20%)	0.128	4 (33%)	7 (39%)	1.000
Baricitib	12 (75%)	10 (67%)	0.704	13 (81%)	9 (60%)	0.252	10 (77%)	12 (67%)	0.696
Outpatient Clinic Medication									
Glucocorticoid[4] (mg/kg/day)	0.13 (0.04, 0.22)	0.18 (0.08, 0.22)	0.571	0.12 (0.04, 0.22)	0.17 (0.12, 0.22)	0.584	0.13 (0.04, 0.23)	0.17 (0.07, 0.21)	0.686
Colchicine	5 (31%)	1 (6.2%)	0.174	4 (25%)	2 (12%)	0.651	5 (38%)	1 (5.3%)	0.029
Hydroxychloroquine	15 (94%)	14 (88%)	1.000	15 (94%)	14 (88%)	1.000	12 (92%)	17 (89%)	1.000
Methotrexate	3 (19%)	14 (88%)	0.432	4 (25%)	5 (31%)	1.000	1 (7.7%)	8 (42%)	0.050
Sulfasalazine	1 (6.2%)	3 (19%)	0.593	1 (6.2%)	3 (19%)	0.593	1 (7.7%)	3 (16%)	0.629
Leflunomide	6 (38%)	4 (25%)	0.703	5 (31%)	5 (31%)	1.000	4 (31%)	6 (32%)	1.000
Baricitinib	3 (19%)	3 (19%)	1.000	5 (31%)	1 (6.2%)	0.172	4 (31%)	2 (11%)	0.193
Outcomes / Rituximab Use[5] median (IQR)	**COVID-19 Disease Severity**			**Very Delayed Viral Shedding**			**All-Cause Mortality**		
	Severe (N = 14)	Non-severe (N= 16)	p-value *	> 28 Days (N = 15)	< = 28 days (N = 15)	p-value *	Mortal (N = 11)	Alive (N = 19)	p-value *
RTX-COVID-19 Interval[A] (Days)	82 (14, 131)	46 (16, 102)	0.690	93 (16, 127)	30 (15, 76)	0.430	93 (24, 142)	36 (12, 106)	0.230
RTX Cumulative Dose[B]	12 (6, 15)	12 (4, 18)	0.770	14 (9, 18)	8 (4, 16)	0.065	14 (10, 18)	8 (4, 17)	0.140

* Wilcoxon rank sum test; Fisher's exact test; Pearson's Chi-squared test
1. Median albumin level within the three months before COVID-19 diagnosis
2. The most recent CRP level before COVID-19 diagnosis
3. Average daily glucocorticoid dose (prednisone equivalent) per body weight in the first 2 weeks after COVID-19 diagnosis; median (IQR)
4. Average daily glucocorticoid dose (prednisone equivalent) per body weight in the past 4 weeks before COVID-19 diagnosis; median (IQR)
5. RTX-COVID-19 interval was defined as the time between the last Rituximab infusion and the COVID-19 diagnosis

A. Only included complete cases (N = 27).
B. Only included cases with RTX infusion < 365 days before COVID-19 diagnosis (N = 30)

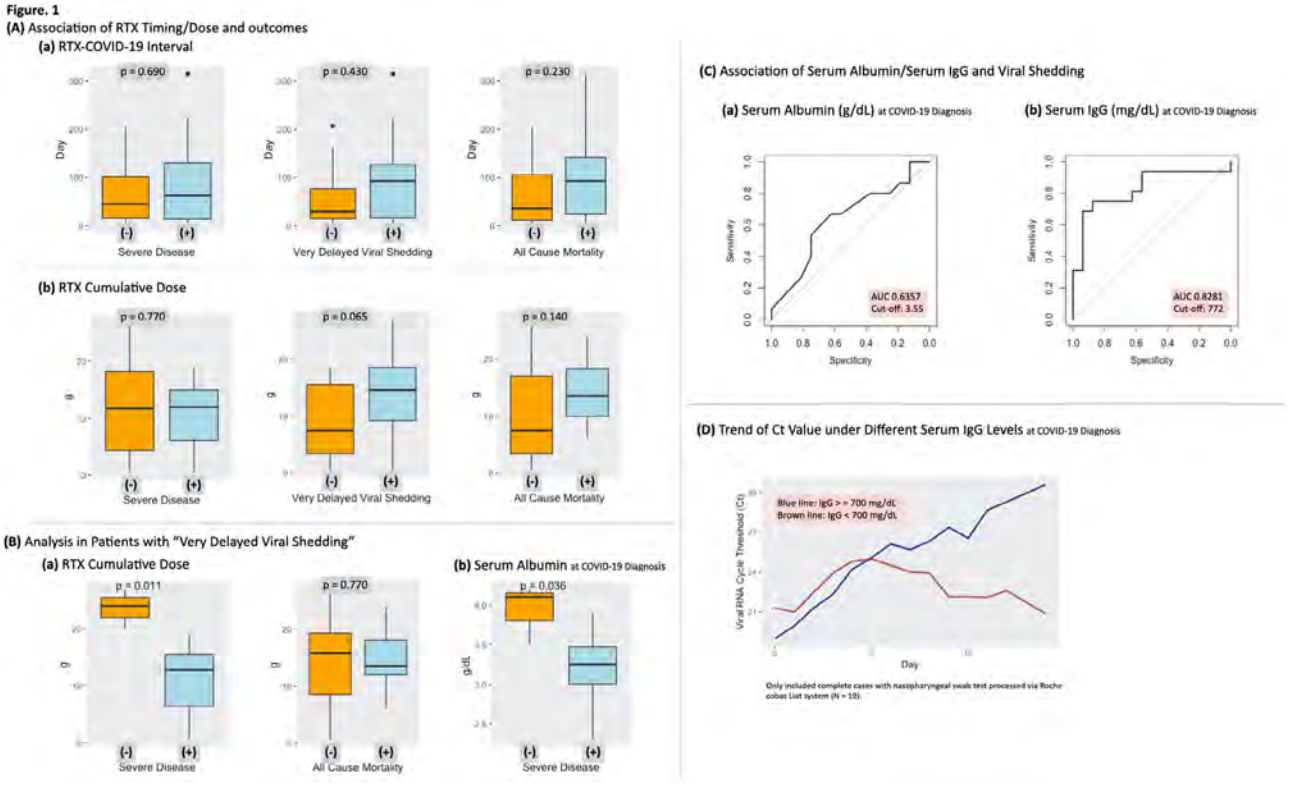

Figure 1.

Average daily glucocorticoid dose (prednisone equivalent) per body weight (mg/kg/day) in the first 2 weeks after infection was adopted for analysis. We proposed the concept "very delayed viral shedding", which referred specifically to a positive rRT-PCR result exceeding 28 days after diagnosis. COVID-19 disease severity was assessed per WHO classification. Outcomes included severe disease, very delayed viral shedding, and all-cause mortality (during hospitalization and in 6 months). For each outcome, we conducted univariate analysis and multivariate logistic regression. All analyses were conducted via R software.

Results: A total of 32 IMID inpatients were included. Their characteristics are shown in Table 1. Sixteen (50.0%) had severe disease, 16 (50.0%) had very delayed viral shedding, and 40.6% died. Factors associated with outcomes are shown in Table 2. Lower baseline serum albumin (OR 0.100, 95% CI: -5.209 to -0.253), higher serum ferritin at diagnosis (OR 1.003, 95% CI: 5x10-4 to 0.006), and higher glucocorticoid dosage (OR 5.318, 95% CI: 0.798 to 2.544) were associated with severe COVID-19 disease. Lower serum IgG at diagnosis (OR 0.994, 95% CI: -0.012 to -0.002) and higher glucocorticoid dosage (OR 2.875, 95% CI: 0.102 to 2.010) were associated with very delayed viral shedding. Routine outpatient colchicine use (OR 16, 95% CI: 0.593 to 5.983) and higher glucocorticoid dosage (OR 3.170, 95% CI: 0.176 to 2.131) were associated with mortality.

The time interval between the last RTX treatment and COVID-19 diagnosis, as well as the cumulative RTX dosage, were not associated with poor outcomes (Figure 1). However, higher cumulative dose tended to be associated with very delayed viral shedding. In patients with very delayed viral shedding, lower serum albumin levels at diagnosis, but not cumulative RTX dose, predicted severe disease. Although the viral cycle threshold (Ct) values increase during antiviral course, in the low serum IgG group, the Ct values wane as antiviral discontinued, potentially correlating with a subsequent poor prognosis (Figure 1D).

Conclusion: Lower serum albumin, higher serum ferritin and increased glucocorticoid dose, are indicative of severe inflammation. Our results suggest that severity of inflammation, rather than Rituximab dose or timing, is associated with poor outcomes. Future research should focus on determining the most optimal glucocorticoid dose for these patients, and whether extended antiviral treatment improves outcomes for those with low serum IgG.

Disclosure: P. Lai: None; **T. Chang**: None; **S. Lan**: None; **C. Cheng**: None; **C. Lu**: None; **S. Hsieh**: None.

Abstract Number: 0223

Severity and Risk Factors of Hospitalization of Omicron in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: There is still lack of data on the prognosis of patients with RA who have been infected with SARS-Cov-2 Omicron variant, a new strain with relatively low pathogenicity but high transmissibility. The aim of our study was to evaluate the factors influencing the infection of patients with RA and the COVID-19 outcomes.

Methods: Patients who were infected after December 5, 2022 were collected. The demographic characteristics, comorbidities, clinical profile, medication of RA, and treatment from 1107 patients with RA and 2800 controls were analyzed. The $\chi 2$ test, Fisher exact test for class variables, and Mann-Whitney U test were used for continuous variables. The independent correlation factors of hospitalization were estimated using multivariate-adjusted logistic regression.

Table 6 The risk factors of COVID-19 outcomes in patients with RA*

Characteristics /Medication	OR (95% CI) Unadjusted	*P* value	OR (95% CI)-ad Adjusted age and sex	*P* value	OR (95% CI)-Ad Adjusted age, sex, BMI, comorbidities and COVID-19 vaccination, glucocorticoid and DMARDs	*P* value
Age (years)	**1.03 (1.01-1.06)**	**0.009**	**1.03 (1.01-1.06)**	**0.010**	1.03 (0.99-1.08)	0.136
≥65 years**	**2.25 (1.04-4.87)**	**0.041**	**2.24 (1.03-4.88)**	**0.043**	2.23 (0.65-7.65)	0.200
Sex						
Female	0.87 (0.33-2.27)	0.769	0.98 (0.37-2.60)	0.971	0.77 (0.22-2.76)	0.693
BMI (kg/m^2)	1.06 (0.97-1.15)	0.189	1.06 (0.97-1.16)	0.190	1.04 (0.90-1.20)	0.583
Comorbidities	**2.51 (1.17-5.36)**	**0.018**	2.10 (0.96-4.57)	0.063	1.83 (0.82-4.11)	0.141
COVID-19 vaccine	**2.23 (1.21-4.54)**	**0.011**	**2.31 (1.19-4.52)**	**0.014**	**0.46 (0.24-0.98)**	**0.046**
HAQ score	**2.51 (1.48-4.27)**	**0.001**	**2.07 (1.16-3.71)**	**0.014**	1.74 (0.94-3.22)	0.076
Glucocorticoid	**1.99 (1.01–3.89)**	**0.045**	**2.00 (1.02–3.92)**	**0.045**	**3.24 (1.13-9.29)**	**0.029**
cDMARDs	0.83 (0.32–2.18)	0.708	0.83 (0.31–2.20)	0.701	0.58 (0.16–2.15)	0.418
Hydroxychloroquine	0.54 (0.25–1.20)	0.131	1.06 (0.39–2.82)	0.911	1.11 (0.52–2.61)	0.806
Methotrexate	0.92 (0.47–1.77)	0.791	0.90 (0.47–1.75)	0.763	1.13 (0.40–3.22)	0.816
Leflunomide	1.27 (0.63–2.56)	0.511	0.97 (0.37–2.58)	0.956	0.52 (0.14–2.01)	0.347
Sulfasalazine	1.04 (0.24–4.46)	0.955	1.04 (0.24–4.49)	0.954	1.38 (0.15–12.60)	0.775
Iguratimod	1.14 (0.51-2.52)	0.756	1.04 (0.47-2.33)	0.922	1.24 (0.36-4.27)	0.738
bDMARDs	0.58 (0.24–1.41)	0.232	0.58 (0.24–1.41)	0.227	0.87 (0.23–3.24)	0.831
Etanercept	0.82 (0.25–2.73)	0.751	0.73 (0.22–2.43)	0.602	0.71 (0.09–5.77)	0.752
Adalimumab	0.63 (0.15–2.65)	0.526	0.86 (0.16–2.90)	0.603	0.98 (0.12–8.10)	0.984
Certolizumab	-		0.98 (0.37–2.59)	0.967	-	
Infliximab	6.79 (0.74-62.31)	0.090	7.52 (0.80–71.18)	0.078	41.57 (0.51,3408.36)	0.097
Abatacept	-		0.99 (0.37-2.61)	0.975	-	
Others	1.16 (0.15-8.82)	0.887	1.09 (0.14–8.39)	0.933	2.60 (0.59–8.07)	0.138
tsDMARDS	1.57 (0.78–3.17)	0.210	0.98 (0.37–2.59)	0.962	2.40 (0.83–6.99)	0.107
Tofacitinib	1.62 (0.77–3.40)	0.205	1.52 (0.72–3.20)	0.275	2.36 (0.74–7.36)	0.140
Baricitinib	1.19 (0.28–5.10)	0.815	1.43 (0.33–6.20)	0.636	2.01 (0.22–18.36)	0.536
Herbal drugs	1.89 (0.87-4.08)	0.107	1.51 (0.68-3.32)	0.311	1.00 (0.26-3.78)	0.994
Tripterygium glycosides	1.17 (0.35-3.90)	0.801	0.86 (0.25-2.92)	0.810	0.59 (0.07-5.01)	0.629
Total glycoside of paeony (TGP)	1.93 (0.66-5.64)	0.229	1.62 (0.55-4.78)	0.384	0.65 (0.08-5.38)	0.686
NSAIDs						
Diclofenac sodium	0.65 (0.15-2.77)	0.563	0.59 (0.14-2.53)	0.477	0.48 (0.06-3.99)	0.498
Ibuprofen	0.39 (0.05-2.86)	0.351	0.32 (0.04-2.36)	0.261	0.67 (0.08-5.45)	0.706
Indometacin	6.79 (0.74-62.31)	0.090	6.18 (0.65-58.56)	0.113	-	
Loxoprofen Sodium	2.17 (0.82-5.75)	0.120	2.01 (0.75-5.37)	0.164	1.10 (0.13-9.04)	0.930
Celecoxib	2.13 (0.91-4.98)	0.081	1.79 (0.76-4.23)	0.187	2.51 (0.70-9.05)	0.167
Others	1.49 (0.19-11.45)	0.703	1.61 (0.21-12.56)	0.646	-	

Abbreviations: RA,rheumatoid arthritis; DMARDs, Disease Modifying Anti-Rheumatic Drugs; cDMARDs, conventional DMARDs; bDMARDs, biologic DMARDs; tsDMARDs,target synthetic DMARDs ;NSAIDs, Nonsteroidal Antiinflammatory Drugs

* Reference group: no

** Reference group: < 65 years

Results: Compared with the control group, patients with RA had significantly higher rates of COVID-19 symptoms. For all patients infected the COVID-19, RA (adjusted OR=2.69, 95%CI 1.37-5.29; p=0.004), older age (adjusted OR=1.03, 95% CI 1.01-1.05; p=0.012) and the use of glucocorticoid (adjusted OR=3.24, 95%CI 1.13-9.29; p=0.029) resulted in higher hospitalization rates. Scheduled vaccination (adjusted OR=0.46, CI 0.24-0.98; p=0.046) was a protective factor in patients with stable RA, who have a low hospitalization rate. Nevertheless, disease-modifying antirheumatic drugs (DMARDs) and non-steroidal anti-inflammatory drugs (NSAIDs), which in some studies had to a certain extent on hospitalization rates in RA patients infected with COVID-19 to a certain extent, were not significantly associated with hospitalization in our study.

Conclusion: RA is a risk factor for increased hospitalization in patients with COVID-19, and glucocorticoids is a risk factor for hospitalization in RA patients.

Disclosure: Y. Wang: None; **m. zhang**: None; **S. Zang**: None; **l. luo**: None; **C. Li**: None; **J. He**: None; **z. li**: None.

Abstract Number: 0224

Risk Factors and Outcomes for Repeat COVID-19 Infection Among Patients with Systemic Autoimmune Rheumatic Diseases: A Case-control Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: As initial COVID-19 infections become nearly ubiquitous and the available prevention and treatment strategies evolve, patients with systemic autoimmune rheumatic diseases (SARDs) may be particularly vulnerable to repeat infections due to immunosuppression. However, no studies have investigated the risk factors and outcomes of repeat COVID-19 infections among patients with SARDs.

Methods: We performed a case-control study investigating risk factors and outcomes of repeat COVID-19 infections among SARD patients at a large healthcare system. All COVID-19 infections were systematically identified from positive PCR tests, patient-reported rapid antigen tests, or physician referral (3/15/2020 through 10/17/2022). SARD diagnosis was confirmed by a medical record review. The index date was the date of repeat COVID-19 infection, defined as a second infection >60 days after the initial infection. Controls had one COVID-19 infection as of their assigned index date (verified by medical record review and survey) and were matched to cases (up to 3:1) by date of first infection and duration between first infection and index date. We collected demographics, lifestyle, comorbidities, SARD features, and COVID-19 characteristics at initial infection and index date by medical record review. We used conditional logistic regression to identify associations with repeat COVID-19 infection, adjusting for potential confounders. We described the severity of repeat COVID-19 infection among cases.

Results: Among 2,203 SARD patients with COVID-19, we identified 76 cases with repeat COVID-19 infection (80.3% female), matched to 211 matched controls (78.2% female) with no repeat infection. The most common SARD was RA, followed by psoriatic arthritis/spondyloarthritis and SLE (**Table 1**). At first infection, cases were younger (mean 49.5 vs. 60.6 years, p< 0.0001), less likely to have hypertension (32.9% vs. 46.9%, p=0.034), and less likely to have been hospitalized for COVID-19 (13.2% vs. 26.1%, p=0.021) than controls. At index date, cases were more likely than controls to be on antimalarials (26.3% vs. 13.3%, p=0.0090) or rituximab (18.4% vs. 6.2%, p=0.0017), but less likely to be on mycophenolate mofetil (0% vs. 10.4%, p=0.0008; **Table 2**). In the multivariable model, rituximab use vs. non-use (OR 3.44, 95%CI 1.27-9.33), younger age (OR 0.66 per 10 years, 95%CI 0.54-0.81), and methotrexate use vs. non-use (OR 2.31, 95%CI 1.12-4.79) were associated with repeat COVID-19 infection (**Table 3**). Among those with repeat COVID-19 infection, 5 (6.6%) were hospitalized and there were no deaths.

Table 1. Demographics, lifestyle factors, and comorbidities at first infection for cases (SARD patients with repeat COVID-19) and matched* controls (SARD patients with exactly one COVID-19 episode).

	Cases – SARD patients with repeat COVID-19 (n=76)	Controls – SARD patients with exactly one episode of COVID-19 (n=211)	p-value
Demographics			
Age at first infection, years (mean, SD)	49.5 (16.1)	60.6 (16.3)	**<0.0001**
Female sex, n (%)	61 (80.3%)	165 (78.2%)	0.71
Race, n (%)			
White	58 (76.3%)	152 (72.0%)	0.18
Black	10 (13.2%)	30 (14.2%)	
Asian	1 (1.3%)	9 (4.3%)	
Other	7 (9.2%)	11 (5.2%)	
Duration between first infection date and index date (median, IQR), days*	254 (149, 528)	239 (140, 533)	0.99
Lifestyle factors			
Smoking, n (%)			
Never	49 (64.5%)	112 (53.1%)	0.15
Past	21 (27.6%)	83 (39.3%)	
Current	4 (5.3%)	16 (7.6%)	
Body mass index, kg/m^2 (mean, SD)	28.1 (6.4)	28.7 (6.5)	0.52
Comorbidities, n (%)			
Hypertension	25 (32.9%)	99 (46.9%)	**0.034**
Diabetes mellitus	8 (10.5%)	41 (19.4%)	0.077
Coronary artery disease	7 (9.2%)	17 (8.1%)	0.76
Cancer	1 (1.3%)	18 (8.5%)	**0.017**
Interstitial lung disease	2 (2.6%)	14 (6.6%)	0.11
Most common SARD types, n (%)			
Rheumatoid arthritis	22 (29.0%)	61 (28.9%)	0.99
Psoriatic arthritis and spondyloarthritis	12 (15.8%)	25 (11.9%)	0.38
Systemic lupus erythematosus	10 (13.2%)	22 (10.4%)	0.52
COVID-19 vaccination, n (%)			
Unvaccinated or pre-vaccine	35 (46.1%)	102 (48.3%)	0.73
Partially vaccinated	4 (5.3%)	9 (4.3%)	0.75
Two doses mRNA or one dose J&J	15 (19.7%)	50 (23.7%)	0.48
Additional doses	22 (29.0%)	50 (23.7%)	0.37
COVID-19 Severity, n (%)			
Outpatient	66 (86.8%)	156 (73.9%)	**0.021**
Hospitalized	10 (13.2%)	55 (26.1%)	
Hospitalized, needed oxygen	4 (5.3%)	24 (11.4%)	0.058
Mechanical ventilation	1 (1.3%)	4 (1.9%)	0.39

*Matching factors were calendar date (+/-7 days) of first infection and duration between first infection and index date (+/-7 days).

Table 2. Characteristics at index date (repeat COVID-19 date for cases; and assigned date for matched* controls with exactly one COVID-19 episode).

	Cases – SARD patients with repeat COVID-19 (n=76)	Controls – SARD patients with exactly one episode of COVID-19 (n=211)	p-value
Tixagevimab/cilgavimab use, n (%)	8 (10.5%)	12 (5.7%)	0.16
Disease activity, n (%)			
Remission or low	58 (76.3%)	133 (63.0%)	0.92
Moderate or severe	14 (18.4%)	31 (14.7%)	
Unknown	4 (5.3%)	47 (22.3%)	
Glucocorticoid use, n (%)			
No	59 (77.6%)	154 (73.0%)	0.84
Yes	15 (19.7%)	42 (19.9%)	
Conventional synthetic DMARDs and immunosuppressants			
Methotrexate	20 (26.3%)	36 (17.1%)	0.081
Antimalarials	20 (26.3%)	28 (13.3%)	**0.0090**
Sulfasalazine	3 (4.0%)	5 (2.4%)	0.23
Leflunomide	1 (1.3%)	5 (2.4%)	0.34
Mycophenolate mofetil	0 (0.0%)	22 (10.4%)	**0.0008**
Azathioprine	2 (2.6%)	4 (1.9%)	0.31
Calcineurin inhibitor	1 (1.3%)	2 (1.0%)	0.43
Biologic DMARDs			
TNF inhibitors	19 (25.0%)	48 (22.8%)	0.69
Rituximab	14 (18.4%)	13 (6.2%)	**0.0017**
Belimumab	3 (4.0%)	1 (0.5%)	0.054
Abatacept	2 (2.6%)	5 (2.4%)	0.32
IL-6 inhibitors	4 (5.3%)	5 (2.4%)	0.13
IL-17, IL-12/23, and IL-23 inhibitors	4 (5.3%)	2 (1.0%)	**0.039**
IL-1 inhibitors	0 (0.0%)	2 (1.0%)	0.54
Targeted synthetic DMARDs			
JAK inhibitors	1 (1.3%)	6 (2.8%)	0.29
Apremilast	0 (0.0%)	0 (0.0%)	-
IVIG	1 (1.3%)	2 (1.0%)	0.43

*Matching factors were calendar date (+/-7 days) of first infection and duration between first infection and index date (+/-7 days).

Table 3. Multivariable odds ratios for repeat COVID-19 case status.

Covariate	Multivariable* OR (95%CI) for repeat COVID-19
Rituximab use at index date (vs. non-use)	**3.44 (1.27, 9.33)**
Age per 10 years	**0.66 (0.54, 0.81)**
Methotrexate use at index date (vs. non-use)	**2.31 (1.12, 4.79)**
Female (vs. male)	0.98 (0.48, 2.00)
Comorbidity count (per comorbidity)	1.05 (0.84, 1.32)
Rheumatoid arthritis (vs. other SARD types)	1.01 (0.52, 1.97)
Glucocorticoid use (vs. non-use)	1.54 (0.73, 3.26)
bDMARD use other than rituximab at index date (vs. non-use)	1.53 (0.80, 2.93)
Symptom count at first infection (per symptom)	1.06 (0.92, 1.23)
Hospitalization at first infection (vs. outpatient)	0.54 (0.23, 1.25)
Partially vaccinated at index date (vs. unvaccinated)	1.84 (0.17, 19.63)
Two doses mRNA or one dose J&J at index date (vs. unvaccinated)	1.46 (0.48, 4.48)
Additional vaccine doses at index date (vs. unvaccinated)	2.06 (0.75, 5.61)

*Conditioned on matching factors (calendar date [+/-7 days] and duration between first infection and index date [+/-7 days]).

Conclusion: In this first study to examine risk factors and outcomes of repeat COVID-19 infection among SARD patients, we identified rituximab use, methotrexate use, and younger age as potential risk factors for repeat COVID-19. While some of the findings may be due to risk mitigation behavior differences, these factors may be useful to raise awareness of repeat COVID-19 risk for patients and clinicians. Reassuringly, there were no deaths and the hospitalization rate was low among those with repeat COVID-19 infection.

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Abstract Number: 0225

Breakthrough SARS-Cov-2 Infection and Disease Flares in Patients with Rheumatoid Arthritis: Result from COVAD E-Survey Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Infection-related Rheumatic Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Existing studies have shown that disease activity of patients with rheumatoid arthritis (RA) may surge after COVID-19 infection. However, factors associated with disease flares remain unknown. This study aimed to identify factors associated with breakthrough infection and disease flares in patients with RA following COVID-19 infection.

Methods: We selected patients with RA from an online e-survey data from the COVAD study. Demographic data, patient reported outcomes, comorbidities and pharmacologic treatments were extracted from the database. Disease flare-up was derived from the e-survey database. Factors associated with disease flare-up were determined by multivariable logistic regression analysis.

Results: In total, 1928 patients with RA were extracted from the COVAD database. Older age, Caucasian ethnicity, comorbidities with chronic kidney disease and asthma, were associated with COVID-19 breakthrough infection. Moreover, younger age (odds ratio, OR: 0.98, 95% CI: 0.96 – 0.99, p< 0.001), ethnicity other than Asian, tuberculosis (OR: 3.80, 95% CI: 1.12 – 12.94, p=0.033), treatment with methotrexate (OR: 2.55, 95% CI: 1.56 – 4.17, p< 0.001), poor global physical health (OR: 1.07, 95% CI: 1.00 –1.15, p=0.044) and mental health (OR: 0.91, 95% CI: 0.87 –0.95, p< 0.001) were independent factors associated with disease flares in patients with RA.

Table 1. Factors associated with breakthrough COVID-19 infection in patients with RA By Chi-square test or ANOVA test. *p<0.05, **p<0.01 #infliximab, adalimumab, certolizumab, golimumab, etanercept +tofacitinib, baricitinib, upadacitinib

Test positive for COVID	No (n= 1269)	Once (n=585)	Twice and More (n=74)	p value
Age	52.15±13.88	48.67±13.00	46.58±12.31	<0.001**
Gender				0.377
Female	1120 (88.3%)	522 (89.2%)	62 (83.8%)	
Male	149 (11.7%)	63 (10.8%)	12 (16.2%)	
Ethnicity				<0.001**
Caucasian (White)	571 (46.4%)	302 (53.9%)	43 (58.9%)	
Asian	313 (25.4%)	73 (13.0%)	11 (15.1%)	
African American or of African origin	88 (7.2%)	36 (6.4%)	5 (6.8%)	
Hispanic	128 (10.4%)	84 (15.0%)	6 (8.2%)	
Native American/Indigenous/Pacific Islander	14 (1.1%)	3 (0.5%)	1 (1.4%)	
Mixed	55 (4.5%)	21 (3.8%)	3 (4.1%)	
Other	61 (5.0%)	41 (7.3%)	4 (5.5%)	
Disease duration (years)	15.95±21.02	17.65±24.19	15.65±20.73	0.864
Number of COVID-19 vaccine dose	3.00±0.77	2.98±0.78	2.91±0.84	0.700
Comorbidities				
Asthma	131 (10.3%)	69 (11.8%)	15 (20.3%)	0.026*
Chronic Kidney Disease	26 (2.0%)	12 (2.1%)	1 (1.4%)	0.916
Chronic Liver Disease	12 (0.9%)	7 (1.2%)	1 (1.4%)	0.852
Chronic Obstructive Pulmonary Disease	39 (3.1%)	15 (2.6%)	8 (10.8%)	0.001**
Interstitial Lung Disease	46 (3.6%)	20 (3.4%)	1 (1.4%)	0.581
Coronary Heart Disease / Ischemic Heart Disease	20 (1.6%)	10 (1.7%)	1 (1.4%)	0.962
Diabetes mellitus	80 (6.3%)	38 (6.5%)	10 (13.5%)	0.053
Hyperlipidemia	154 (12.1%)	69 (11.8%)	9 (12.2%)	0.978
Hypertension	248 (19.5%)	111 (19.0%)	18 (24.3%)	0.550
Tuberculosis	7 (0.6%)	7 (1.2%)	0 (0.0%)	0.238
Medication				
Glucocorticoid	78 (6.1%)	35 (6.0%)	2 (2.7%)	0.477
Methotrexate	81 (6.4%)	45 (7.7%)	8 (10.8%)	0.242
Hydroxychloroquine	26 (2.0%)	17 (2.9%)	1 (1.4%)	0.445
Sulfasalazine	19 (1.5%)	7 (1.2%)	1 (1.4%)	0.877
Leflunomide	14 (1.1%)	5 (0.9%)	0 (0.0%)	0.601
Rituximab	8 (0.6%)	4 (0.7%)	0 (0.0%)	0.779
Anti TNF agents#	17 (1.3%)	13 (2.2%)	0 (0.0%)	0.197
JAK inhibitors+	8 (0.6%)	4 (0.7%)	0 (0.0%)	0.779
PROMIS Global Physical Health	13.56±2.16	13.76±2.00	13.49±2.35	0.089
PROMIS Global mental health	12.53±3.30	12.50±3.36	11.81±3.66	0.199

Table 2. Factors associated with disease flare in patients with RA after COVID-19 infection. By Logistic regression. *p<0.05, **p<0.01. #infliximab, adalimumab, certolizumab, golimumab, etanercept +tofacitinib, baricitinib, upadacitinib

	Univariate			Multivariable		
	OR	95%CI	p value	OR	95%CI	p value
Age	0.98	(0.97-0.99)	<0.001**	0.98	(0.96-0.99)	<0.001**
Gender						
Female	Reference					
Male	0.76	(0.46-1.24)	0.268			
Ethnicity						
Asian	Reference			Reference		
Caucasian	3.73	(2.15-6.47)	<0.001**	4.33	(2.43-7.72)	<0.001**
African American or of African origin	4.13	(2.02-8.46)	<0.001**	3.64	(1.73-7.64)	0.001**
Hispanic	3.45	(1.78-6.66)	<0.001**	3.71	(1.88-7.34)	<0.001**
Native American/Indigenous/Pacific Islander	1.50	(0.19-12.01)	0.704	1.52	(0.18-12.60)	0.697
Mixed	2.87	(1.17-7.02)	0.021*	2.94	(1.18-7.34)	0.021*
Other	2.65	(1.16-6.09)	0.021*	2.83	(1.21-6.64)	0.017*
Comorbidities						
Asthma	1.49	(0.99-2.25)	0.057	1.21	(0.78-1.90)	0.394
Interstitial Lung Disease	1.89	(0.99-3.58)	0.053	2.01	(1.00-4.04)	0.051
Tuberculosis	3.41	(1.06-10.97)	0.040*	3.80	(1.12-12.94)	0.033*
Medication						
Glucocorticoid	1.98	(1.20-3.25)	0.007**	1.26	(0.71-2.23)	0.425
Methotrexate	2.80	(1.82-4.31)	<0.001**	2.55	(1.56-4.17)	<0.001**
Hydroxychloroquine	2.90	(1.44-5.84)	0.003**	1.78	(0.76-4.18)	0.186
Anti TNF agents#	3.72	(1.68-8.24)	0.001**	2.33	(0.94-5.77)	0.066
JAK inhibitors+	4.27	(1.27-14.29)	0.019*	2.93	(0.80-10.78)	0.106
PROMIS global physical health	1.07	(1.00-1.15)	0.044*	1.09	(1.00-1.18)	0.040*
PROMIS global mental health	0.91	(0.87-0.95)	<0.001**	0.91	(0.87-0.95)	<0.001**

Conclusion: Our study highlights the necessity for rheumatologists to recognize potential predictors of RA flare-up following COVID-19 infection. Proactive strategies are recommended for managing high-risk RA patients.

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Abstract Number: 0226

Relationships Among Parameters of Mineral Metabolism and Bone Turnover During Acute COVID-related Hospitalization and Subsequent Follow Up: A Pilot Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammatory conditions can exert direct adverse effects on bone metabolism, via increased bone resorption with inadequate compensatory bone formation. COVID-19 has been associated with high levels of inflammation, particularly in patients with severe disease. However, data exploring the impact of COVID-related inflammation on mineral metabolism and skeletal health are scarce. We aimed to explore the relationship between parameters of bone metabolism during acute COVID-related hospitalization and subsequent follow up.

Methods: We carried out a pilot study to analyze serum and plasma samples collected from a subgroup of patients ≥60 years who were enrolled in a larger longitudinal cohort of patients hospitalized with COVID-19 in a single U.S. healthcare system during 7/2020-7/2021. Patients for whom biospecimens were collected during hospitalization were subsequently invited for an in-person follow up encounter at 6-9 months post-hospitalization. IL-6, intact PTH (iPTH), total 25-hydroxy vitamin D (25OHD) and Collagen Type I C-Telopeptide (CTx) were measured at baseline and 6-9 months. Descriptive statistics and Pearson correlation analysis were used to assess the relationship between IL-6 and biomarkers of bone metabolism and turnover.

Results: 12 patients were enrolled in this pilot study with a mean age of 72.6±8 years, and a mean BMI of 35.9±12 kg/m^2; 66% were male. Median iPTH levels at the baseline and follow up were 55.2 (IQR 39.5-143.9) and 70.7 (IQR 50.4-111.3) pg/mL, respectively, with 50% of patients evidencing frankly elevated PTH levels both during hospitalization and 6-9 months later. Mean baseline and follow up 25OHD levels were 27±9.2 and 26.5±11.4 ng/mL (p=0.91); mean baseline and follow IL-6 levels were 7.3±3.9 and 5.3±3.2pg/mL (p=0.18) and mean baseline and follow up CTx levels were 0.297±0.189 and 0.467±0.439 ng/mL (p=0.23). Correlation analysis demonstrated a moderate negative correlation at baseline between

IL-6 and 25OHD (r=-0.4) and CTx (r=-0.5), and moderate positive correlation between IL-6 and iPTH (r=0.4). There was also a moderate positive correlation between IL-6 and iPTH 6-9 months after hospitalization (r=0.5).

Conclusion: In this study, half of the patients enrolled had increased levels of iPTH both during hospitalization and 6-9 months later. Furthermore, we observed a consistent positive correlation between IL-6 and iPTH levels at both time points. Interestingly CTx levels were inversely correlated with IL-6 levels in our sample, despite elevated iPTH levels. Larger prospective studies are warranted to better elucidate the impact of COVID-19 on bone metabolism.

Disclosure: D. Cabrera: None; **C. Wong**: None; **A. Santoro**: None; **C. Simpson**: None; **K. Insogna**: None; **M. Geda**: None; **A. Cohen**: None; **A. Hadjuk**: None; **L. Ferrante**: None; **E. Hsieh**: None.

Abstract Number: 0227

Associations of DMARDs with Post-Acute Sequelae of COVID-19 in Patients with Systemic Autoimmune Rheumatic Diseases: A Prospective Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Post-acute sequelae of COVID-19 (PASC, or "long COVID") is defined by the CDC as COVID-19 symptoms persisting for ≥28 days after infection. Patients with systemic autoimmune rheumatic diseases (SARDs) may be at higher risk for PASC due to their underlying disease and immunosuppressive medications. Disease-modifying antirheumatic drugs (DMARDs), particularly CD20 inhibitors, have been associated with severe COVID-19, but the effect of DMARD use on PASC risk is unclear. Therefore, we investigated the association of baseline DMARD use and PASC among patients with SARDs.

Methods: We invited all SARD patients with COVID-19 within a large healthcare system to participate in a prospective study. Participants completed a survey ≥28 days after confirmed COVID-19 infection, and we analyzed surveys completed from 3/11/2021 to 5/5/2023. The survey collected data on demographics, SARD characteristics, COVID-19 vaccination status, DMARD use at COVID-19 diagnosis, and COVID-19 symptoms and disease course. We categorized DMARD classes by mechanism of action; those taking combination DMARDs were classified by hierarchy of targeted therapy. PASC was defined by any symptom associated with COVID-19 that persisted for ≥28 days. We used logistic regression to estimate odds ratios (OR) for PASC by DMARD class, adjusting for potential confounders.

Results: We analyzed 501 patients with SARDs and COVID-19 (mean age 52.7 years, 80.2% female), of which 208 (42%) had PASC. The most common SARD type was inflammatory arthritis (53.7%), followed by connective tissue disease (21.6%). Participants with PASC were more likely to be female (88.0% vs. 74.7%, p=0.0002), less likely to have had additional COVID-19 vaccine doses beyond the primary series (45.2% vs. 55.0%, p=0.031), and more likely to be infected with

Table 1. Baseline characteristics at time of COVID-19 diagnosis according to PASC status among patients with systemic autoimmune rheumatic diseases (n=501).

Characteristic	Overall (n=501)	PASC* (n=208)	No PASC (n=293)	p-value
Demographics				
Mean age at COVID-19, years (SD)	52.7 (15.6)	52.7 (15.7)	52.8 (15.5)	0.94
Female, n (%)	402 (80.2%)	183 (88.0%)	219 (74.7%)	**0.0002**
Race, n (%)				
White	425 (84.8%)	180 (86.5%)	245 (83.6%)	0.37
Black	27 (5.4%)	9 (4.3%)	18 (6.1%)	0.38
Asian	21 (4.2%)	6 (2.9%)	15 (5.1%)	0.22
Other or unknown	28 (5.6%)	13 (6.3%)	15 (5.1%)	0.59
Median comorbidity count (IQR)	1 (0, 2)	1 (0, 2)	1 (0, 2)	0.59
SARD type, n (%)				
Inflammatory arthritis	269 (53.7%)	113 (54.3%)	156 (53.2%)	0.81
Connective tissue disease	108 (21.6%)	47 (22.6%)	61 (20.8%)	0.63
Vasculitis	46 (9.2%)	17 (8.2%)	29 (9.9%)	0.51
Multiple	40 (8.0%)	18 (8.7%)	22 (7.5%)	0.64
Other	38 (7.6%)	13 (6.3%)	25 (8.5%)	0.34
DMARD use (hierarchy), n (%)**				
No DMARD	113 (22.6%)	47 (22.6%)	66 (22.5%)	0.99
csDMARDs only	140 (27.9%)	55 (26.4%)	85 (29.0%)	0.53
TNF inhibitors	126 (25.2%)	42 (20.2%)	84 (28.7%)	**0.031**
JAK inhibitors	21 (4.2%)	11 (5.3%)	10 (3.4%)	0.30
CD20 inhibitors	39 (7.8%)	23 (11.1%)	16 (5.5%)	**0.021**
Non-TNFi and non-CD20i bDMARDs	62 (12.4%)	30 (14.4%)	32 (10.9%)	0.24
Vaccination status at time of COVID-19, n (%)				
Unvaccinated or partially vaccinated	88 (17.6%)	43 (20.7%)	45 (15.4%)	0.12
2 mRNA doses or 1 J&J dose	158 (31.5%)	71 (34.1%)	87 (29.7%)	0.29
Additional doses	255 (50.9%)	94 (45.2%)	161 (55.0%)	**0.031**
Calendar time of COVID-19, n (%)				
3/1/2020 to 12/16/2021 (pre-Omicron variants)	221 (44.1%)	111 (53.4%)	110 (37.5%)	**0.0004**
12/17/2021 to 5/8/2023 (Omicron variants)	280 (55.9%)	97 (46.6%)	183 (62.5%)	
Acute COVID-19 severity, n (%)				
Hospitalized	41 (8.2%)	29 (13.9%)	12 (4.1%)	**<0.0001**
Not hospitalized	460 (91.8%)	179 (86.1%)	281 (95.9%)	
Median time from COVID-19 to survey completion, days (IQR)	165 (84, 276)	160.5 (80, 295.5)	165 (86, 245)	0.35

*PASC is defined by the CDC as any COVID-19 symptom persisting for ≥28 days.

**Combination DMARDs were classified by hierarchy of targeted therapy in the order of biologic/targeted synthetic DMARD and csDMARDs only.

bDMARD, biologic disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DMARD, disease-modifying antirheumatic drug; JAK, janus kinase; PASC, post-acute sequelae of COVID-19; SARD, systemic autoimmune rheumatic disease; TNF, tumor necrosis factor; J&J, Johnson & Johnson-Janssen.

pre-Omicron variants (53.4% vs. 37.5%, p=0.0004) compared to participants without PASC. Participants with PASC were also less likely to be on TNF inhibitors (20.2% vs. 28.7%, p=0.031) and more likely to be on CD20 inhibitors (11.1% vs. 5.5%, p=0.021). Participants with PASC were more likely to have been hospitalized for COVID-19 (13.9% vs. 4.1%, p< 0.0001). There were no statistically significant differences in age, race, comorbidity count, SARD type, and other DMARD classes, when comparing those with and without PASC (**Table 1**). After adjusting for comorbidity count, vaccination status, SARD type, and calendar time of infection, SARD patients using CD20 inhibitors had an OR for PASC of 2.61 (95%CI 1.19-5.73) compared to those on conventional synthetic DMARDs (**Table 2**).

Conclusion: In this prospective study, SARD patients on CD20 inhibitors at COVID-19 onset had increased risk for PASC. This analysis extends previous studies linking CD20 inhibitors with acute COVID-19 severity and suggests vigilance is needed to prevent COVID-19 and monitor for PASC in this vulnerable population. Mechanisms linking B cell depletion with PASC risk may include persistent infection, dysregulated immune response following acute infection, and acute COVID-19 severity from impaired humoral immunity.

Table 2. Associations of baseline use of disease-modifying antirheumatic drugs with PASC risk (n=501).

DMARD class	n PASC outcomes (% within DMARD class)	Unadjusted OR (95%CI)	Multivariable* OR (95%CI)
No DMARD	47/113 (41.6%)	1.10 (0.66, 1.82)	1.22 (0.70, 2.12)
csDMARDs only	55/140 (39.3%)	1.0 (Ref)	1.0 (Ref)
TNFi	42/126 (33.3%)	0.77 (0.47, 1.28)	0.93 (0.52, 1.68)
JAKi	11/21 (52.4%)	1.70 (0.68, 4.27)	1.77 (0.66, 4.72)
CD20i	23/39 (59.0%)	**2.22 (1.08, 4.58)**	**2.61 (1.19, 5.73)**
Non-TNFi and non-CD20i biologics	30/62 (48.4%)	1.45 (0.79, 2.65)	1.72 (0.89, 3.31)

*Adjusted for age, sex, comorbidity count, vaccination status (unvaccinated or partially vaccinated, 2 mRNA doses or 1 J&J, additional doses), SARD type, and calendar time.

bDMARD, biologic disease-modifying antirheumatic drug; CI, confidence interval; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; DMARD, disease-modifying antirheumatic drug; JAKi, janus kinase inhibitor; OR, odds ratio; PASC, post-acute sequelae of COVID-19; SARD, systemic autoimmune rheumatic disease; TNFi, tumor necrosis factor inhibitor.

Disclosure: R. Venkat: None; **X. Wang**: None; **N. Patel**: Arrivo Bio, 2, Chronius Health, 2, FVC Health, 2; **Y. Kawano**: None; **A. Schiff**: None; **E. Kowalski**: None; **C. Cook**: None; **K. Vanni**: None; **G. Qian**: None; **K. Bade**: None; **A. Saavedra**: None; **S. Srivatsan**: None; **Z. Williams**: None; **Z. Wallace**: BioCryst, 2, Bristol-Myers Squibb(BMS), 5, Horizon, 1, 2, 5, MedPace, 2, Novartis, 1, PPD, 2, Sanofi, 1, 5, Shionogi, 1, Visterra, 1, 2, Zenas, 1, 2; **J. Sparks**: AbbVie, 2, Amgen, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, 5, Gilead, 2, Inova Diagnostics, 2, Janssen, 2, Optum, 2, Pfizer, 2, ReCor, 2.

Abstract Number: 0228

A Comprehensive Retrospective Analysis of Polymyalgia Rheumatica in Long COVID Patients at an Academic Medical Center in the Midwest

Hanan Ibrahim[1] and Alireza Meysami[2], [1]Henry Ford Health System (HFHS), Detroit, MI, [2]Henry Ford Health, Detroit, MI

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Polymyalgia Rheumatica (PMR) is an inflammatory disorder that predominantly affects older adults. Incidence peaks at 70-80 years old [1] and is more common in people of Scandinavian and northern European descent [2]. Patients have widespread pains, stiffness, and muscle tenderness. The annual incidence is 64 per 100,000 population. Incidence is higher in females with a mean of 74 years [3].

While the exact cause of PMR is unknown, emerging research suggests a potential association between PMR and environmental triggers such as vaccination and infections [4]. It has been postulated that viral infections can incite an aberrant immune response, activating autoimmune processes [5]. Since the start of the coronavirus disease 2019 (COVID) pandemic, studies have suggested that the infection might trigger an inflammatory state, leading to an autoimmune response [6,7].

In our descriptive analysis, we look at patients who were referred to our academic Rheumatology clinics for long COVID symptoms. We also try to address how patients who develop PMR following COVID infection may differ from long COVID patients who do not.

Methods: This is a retrospective study in an academic rheumatology clinic, 132 adults (age >18 years) patients with an initial referral for persistent symptoms post-COVID infection (fatigue, myalgia, joints pains, stiffness, abnormal labs, rash) diagnosed between March 2020 and July 2021 were included using the unified record system at our institute. All patients had a documented positive COVID polymerase chain reaction test before the first rheumatology office visit.

Numeric variables were summarized using means and standard deviations or using medians and intra-quartile ranges. Categorical variables were summarized by counts and percentages. Numeric variables were compared by t-tests or Wilcoxon rank sum tests. Categorical variables were compared by chi-square or Fishers exact tests.

Results: Thirty of 132 patients had persistent arthralgia, stiffness, and myalgias and were diagnosed with long COVID syndrome prior to their rheumatology clinic visit.

Eight of 30 patients were diagnosed with PMR. Patients with PMR had a higher mean age (79 vs 59, $p< 0.001$), and a higher median ESR (48.5 vs 12.0, $p=0.013$). No statistically significant difference between the two groups regarding gender, ethnicity, severity of initial COVID infection, duration of symptoms, and Rheumatoid factor (RF) positivity was detected. (Table 1)

All 8 patients with PMR diagnosis were responsive to steroid taper and achieved remission within one year. One patient required steroid-sparing medication (Leflunomide). Two patients had newly diagnosed neoplasms within 1 year (uterine cancer and chronic myeloid leukemia).

Conclusion: Our study was consistent with patients having long-COVID symptoms experiencing a higher incidence of PMR. As might be expected with the small sample size, there was no statistical difference in demographic characteristics between our PMR population and those without PMR. We aim to stimulate further investigation into the etiology, pathogenesis, and potential therapeutic interventions for PMR and related autoimmune disorders triggered by COVID.

Disclosure: H. Ibrahim: None; **A. Meysami**: None.

Abstract Number: 0229

Vegetable Consumption and Regular Exercise Are Associated with Better Quality of Life in Gout

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout, which is a prevalent form of inflammatory arthritis, is generally considered to be more effectively managed through medication. Besides of maintaining medication, they were required to modify their life style habits including eating habits. Because some gout patients failed to control their disease due to improper lifestyle. Improper lifestyle can affect the gout patient's quality of life.

The Gout Impact Scale (GIS), a part of the Gout Assessment Questionnaire 2.0, is an instrument measuring the gout-specific health-related quality of life (HRQOL). Recently, GIS was translated in to Korean, K-GIS was validated. There have been recommendations for lifestyle changes as well as medication to control gout. So far, there were no research revealing the correlation life style habits and GIS. Therefore, we aimed to evaluate the relationship of GIS and gout patient's life style habit in this study.

Table 1. Baseline characteristics of patients

Variable	Patients (N =232)
Age, years	55.08 (17.69)
Male, n (%)	210 (90.50)
Height, cm	168.90 (8.02)
Weight, kg	75.97 (14.85)
Body mass index, kg/m^2	26.47 (3.99)
Education, n (%)	
Low	110/215 (51.20)
High[a]	105/215 (48.80)
Current working, n (%)	142/230 (61.7)
Smoking, n (%)	
Current	57/226 (25.22)
Ever	85/226 (37.61)
Never	84/226 (37.17)
Current alcohol, n (%)	146/231 (63.20)
Comorbidities, n (%)	
Hypertension	114 (48.9)
Diabetes	42 (18)
Dyslipidemia	68 (29.2)
Cardiovascular disease	23 (9.87)
Liver disease	6 (2.6)
Chronic kidney disease	29 (12.4)
Kidney transplantation	0 (0)
Malignancy	23/231 (10.00)
Concomitant medications, n (%)	
Diuretics	48 (20.60)
Losartan	8 (3.43)
Aspirin	24 (10.3)
Disease duration, years	4.97 (6.41)
Presence of tophi, n (%)	51/211 (24.17)
Presence of erosion on X-ray, n (%)	51/152 (33.60)
Present acute gout flare, n (%) (more than twice per year)	178/223 (79.80)
Frequency of acute flare previously, n (%)	
0	11/219 (5.00)
1-2	84/219 (38.4)
3-5	72/219 (32.9)
6-10	34/219 (15.5)
>10	18/219 (8.2)
Urate-lowering therapy, n (%)	204/225 (90.7)
Allopurinol	35/225 (15.56)
Febuxostat	150/225 (66.67)
Benzbromarone	21/225 (9.33)
Febuxostat + benzbromarone	1/225 (0.44)
Anti-inflammatory prophylaxis, n (%)	
Steroid	54 (23.28)
NSAIDS	83 (35.78)
Colchicine	134 (57.76)
Serum urate, mg/dL	8.63 (1.90)
Serum creatinine, mg/dL	1.10 (0.35)
eGFR, mL/min/1.73m^2	78.91 (26.42)

Values are mean (SD) or number (%).
[a]Bachelor's degree or higher
eGFR, estimated glomerular filtration rate

Methods: Patients with gout aged ≥18 years who fulfil the 2015 classification criteria for gout with necessity of ULT are enrolled. The case report form (CRF) lists demographic and clinical data, comorbidities, lifestyle habits, medications, quality of life (on the gout impact scale), the score on Gout Impact Scale (GIS), laboratory results, and radiological findings.

Results: The study included 232 patients, and the baseline characteristics of the patients were described in the **Table 1**. The mean scores for each GIS subscale (mean ± SD) were as follows: 80.27 ± 18.63 for gout concern overall; 64.39 ± 21.47 for gout medication side effects; 47.20 ± 13.28 for unmet gout treatment needs; 55.27 ± 26.56 for well-being during attack; 61.63 ± 22.28 for gout concern during attack.

Table 2. Discriminative life style properties of the Gout Impact Scale according to the gout-specific

	Gout Impact Scale				
	Gout concern overall	Gout medication side effects	Unmet gout treatment needs	Well-being during attack	Gout concern during attack
Alcohol					
Never (n=46)	82.88 (17.75)	69.17 (22.71)	47.28 (12.68)	58.30 (23.82)	66.71 (19.28)
Ever (n=39)	79.97 (20.94)	62.50 (20.68)	47.22 (13.01)	58.23 (23.28)	66.28 (20.11)
Current (n=146)	79.51 (18.31)	63.39 (21.22)	47.16 (13.63)	53.53 (28.15)	59.22 (22.87)
P value	0.57	0.24	1	0.44	0.05
Coffee					
< once/d (n=90)	81.81 (18.02)	64.44 (24.21)	48.61 (13.76)	59.12 (27.61)	63.76 (22.02)
≥ once/d (n=141)	79.29 (19.01)	64.35 (19.53)	46.28 (12.93)	52.77 (25.65)	60.71 (21.90)
P value	0.32	0.98	0.2	0.08	0.31
Soft drink					
< 3 times/w (n=188)	78.97 (18.95)	63.46 (20.98)	46.55 (12.78)	55.04 (26.46)	62.26 (21.73)
≥ 3 times/w (n=42)	85.57 (16.24)	67.99 (23.39)	50.00 (15.29)	55.99 (27.56)	59.38 (22.48)
P value	*0.04	0.22	0.13	0.84	0.44
Meat consumption					
< 3 times/w (n=133)	78.08 (19.97)	62.31 (21.82)	46.84 (13.01)	55.09 (25.87)	62.69 (21.34)
≥ 3 times/w (n=98)	83.25 (16.28)	67.29 (20.75)	47.68 (13.70)	55.52 (27.61)	60.84 (22.80)
P value	*0.04	0.09	0.64	0.91	0.53
Milk, Dairy consumption					
< 3 times/w (n=180)	80.62 (18.85)	64.06 (21.90)	46.85 (13.42)	55.14 (27.19)	61.70 (23.41)
≥ 3 times/w (n=51)	79.04 (17.98)	65.56 (20.01)	48.47 (12.81)	55.70 (24.52)	62.63 (15.80)
P value	0.6	0.67	0.45	0.9	0.79
Vegetable consumption					
< 5 times/w (n=132)	81.25 (19.33)	66.15 (22.53)	48.04 (13.65)	58.97 (27.09)	66.32 (22.57)
≥ 5 times/w (n=99)	78.95 (17.66)	61.97 (19.80)	46.05 (12.73)	50.26 (25.10)	55.99 (19.70)
P value	0.36	0.15	0.26	*0.02	***0.00
Fruit consumption					
< 5 times/w (n=173)	80.23 (18.98)	65.25 (21.69)	47.72 (13.49)	56.85 (26.45)	63.05 (22.46)
≥ 5 times/w (n=58)	80.37 (17.69)	61.84 (20.79)	45.61 (12.61)	50.60 (26.59)	58.44 (20.13)
P value	0.96	0.3	0.3	0.13	0.17
Exercise					
< 3 times/w (n=166)	81.89 (17.29)	65.93 (21.69)	46.99 (12.65)	57.65 (26.50)	64.98 (22.25)
≥ 3 times/w (n=65)	76.07 (21.29)	60.25 (20.48)	47.75 (14.91)	49.25 (25.95)	53.77 (19.00)
P value	*0.03	0.08	0.7	*0.03	***0.00

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

Table 3. Stepwise multiple linear regression analysis of the K- Gout Impact Scale in gout patients.

	Unstandardized B-coefficient	SE	Standardized β-coefficient	t	*P*	95% CI
Gout concern overall						
Constant	87.49	3.7		23.66	0.00	80.21, 94.78
Exercise	-5.71	2.73	-0.14	-2.1	*0.04	-11.08, -0.34
Well-being during attack						
Constant	67.87	5.34		12.7	0.00	57.33, 78.40
Vegetable consumption	-8.9	3.55	-0.17	-2.51	*0.01	-15.89, -1.90
Gout concern during attack						
Constant	87.92	5.46		16.1	0.00	77.16, 98.68
Vegetable consumption	-9.7	2.81	-0.22	-3.45	**0.001	-15.24, -4.16
Exercise	-9.69	3.11	-0.2	-3.11	**0.002	-15.81, -3.56

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$
SE, standard error; CI, confidence interval

There was a statistically significant difference of gout concern overall subscale in the number of times of soft drink, meat consumption. Also, the number of times of exercise showed difference significantly. The number of times of milk, dairy consumption, vegetables, fruits, alcohol and coffee consumption showed no significant difference. In well-being during gout attack subscale in GIS, number of vegetables consumption and exercise did show difference. Regarding well-being during gout attack, soft drink, meat, milk, dairy, fruits, alcohol and coffee consumption did not show significant results between groups according to the number of times.

In gout concern during attack subscale in GIS, the score was significantly different in vegetable consumption and exercise. **(Table 2).**

In gout concern overall subscale in GIS, the number of times of regular exercise showed a negative linear correlation (B= -5.71, *P*= 0.04). In well-being during attack subscale in GIS, the number of times of vegetable consumption showed a negative linear correlation (B= -8.90, *P*=0.01). In gout concern during attack subscale in GIS, the number of times of vegetable consumption and regular exercise showed a negative linear correlation (B= -9.70, -9.69, respectively) ($P < 0.01$) **(Table 3).**

Conclusion: It has been confirmed that the GIS score is related to specific life style, vegetable consumption, exercise regularly. Based on these results, gout patients can be encouraged to have specific life style habits.

Disclosure: H. DO: None; **K. Moon**: None.

Abstract Number: 0230

Looking Beyond Infections in Job Syndrome: Peripheral Calcium Pyrophosphate Deposition Disease in a Cohort of Patients with Job Syndrome

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Job syndrome or hyperimmunoglobulin E syndrome is an immunodeficiency for which the clinical picture consists largely of frequent infectious complications of the lungs, sinuses, and skin, eczematous cutaneous eruptions, and elevated immunoglobulin E levels starting early in childhood. The condition has been found to occur due mutations most commonly in the STAT3 pathway. Most patients are identified in early child and the disease frequently leads to early fatality due to infectious complication. Patients with Job's syndrome have been living longer due to earlier recognition and more readily accessible genetic testing as well as improved management of infectious complications. As these patients are living longer, new clinical manifestations in the aging Jobs' syndrome patient have been identified including musculoskeletal manifestations such as early onset degenerative joint disease which has been attributed to joint hypermobility.

Methods: We performed a retrospective review of imaging from a cohort of 160 STAT3 HIES patients to determine the prevalence of imaging findings suggestive of calcium pyrophosphate deposition disease (CPPD). Of the 160 patients, we were able to identify 22 patients over the age of 16 years with appropriate hand radiographs and 26 with knee radiographs for review. The median age of patients with findings was 53 and mean age was 47.

Results: We identified radiologic evidence of CPPD including (including narrowing of the 2nd and 3rd metacarpophalangeal joints, chondrocalcinosis) in 6 out of 22 hand radiographs (27%). 26 knee radiographs were reviewed and identified 3 patients with chondrocalcinosis (11%).

Conclusion: As patients with STAT3 HIES are living longer, attention to non-infectious complications associated with this condition is warranted. CPPD may occur at an increased frequency in patients with STAT3 HIES and at a significantly younger age than in the general population. Additional clinical and radiographic monitoring of these patients would help characterize the frequency, age of onset, and severity of this manifestation.

Disclosure: S. Ogbonnaya-Whittlesey: None; **E. Sevim**: None; **D. Kobrin**: None; **s. gupta**: None; **P. DeMarco**: None; **A. Freeman**: None.

Abstract Number: 0231

Febuxostat Dose Requirement for Achieving Target Serum Urate Levels According to Renal Function: A Retrospective Cohort Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Febuxostat clearance is not affected by kidney function, and the risk of adverse events from allopurinol, including fatal hypersensitivity reactions, is higher in patients with renal dysfunction accordingly, febuxostat is preferred for gout patients with chronic kidney disease (CKD). However, few studies have sought to determine the appropriate febuxostat dose required to achieve the target SU level. Therefore, this study aimed to investigate the febuxostat dosage needed to reach the SU target in patients with gouty arthritis, including those with renal impairment.

Methods: We conducted a retrospective cohort study at Asan Medical Center, a tertiary referral hospital in Seoul, South Korea. Of 3153 gout patients who were prescribed febuxostat, 731 patients with an initial SU > 6 mg/dL were included and categorized into three groups based on their estimated glomerular filtration rate (eGFR): chronic kidney disease (CKD) stage 1, stages 2-3, and stages 4-5. The cumulative febuxostat dose was defined as the total dose administered from initiation until the patient reached the target SU (< 6 mg/dL).

Results: The cohort of 731 gout patients had a median age of 52 years (IQR, 41-63) and comprised 667 (91.2%) men. The mean (± standard deviation) SU at febuxostat initiation was significantly higher in the CKD 4-5 group (9.6 [±3.1] mg/dL) than in the other groups (CKD 2-3 group, 8.6 [±1.6]; CKD 1 group, 8.8 [±1.8]; P < 0.001). The proportion of patients who received an initial febuxostat dose of 80 mg was lower in the CKD 2-3 group (30.7%) and CKD 4-5 group (31.7%) than in the CKD 1 group (52.0%). Of the total patients, 626 (85.6%) achieved the SU target after ULT. The proportions of patients who achieved the target SU levels were lower in the CKD 4-5 group (82.0%) than in the CKD 1 group (86.6%) or CKD 2-3 group (86.3%) (P = 0.045). Notably, the cumulative febuxostat dose was significantly lower in the CKD 4-5 group (5.9 g [IQR, 2.5–12.0]) than in the other groups (CKD 2-3, 7.1 g [IQR, 3.5–15.7], P = 0.006; CKD 1, 7.0 g [IQR, 2.7–20.1]; P = 0.010). Furthermore, the CKD 4-5 group had a significant negative correlation with the cumulative febuxostat dosage required to reach the target SU compared to the CKD 1 group (beta -2.334, P = 0.020).

Conclusion: Patients with severely decreased renal function (CKD 4-5) required a significantly lower febuxostat dose to achieve the target SU level.

Febuxostat acquirement to reach target SU level and comparison between patients with CKD 1, 2-3, and 4-5.

	Total (n=731)	CKD 1 (n=204)	CKD 2-3 (n=388)	CKD 4-5 (n=139)	p-value	CKD 1 vs CKD 4-5	CKD 2-3 vs CKD 4-5
SU target achievement, n (%)	626 (85.6)	176 (86.3)	336 (86.6)	114 (82.0)	0.245	**0.043**	**0.045**
Dose escalation before reach target	136 (18.6)	59 (28.9)	62 (16.0)	15 (10.8)	**<0.001**	**0.041**	**0.028**
Patients achieving SU target							
Duration to achieve SU target, months	4.0 (1.9, 9.6)	3.3 (1.8, 11.7)	4.1 (2.1, 9.2)	3.2 (1.4, 7.4)	0.221	0.432	0.054
Median SU at 4 months, mg/dL	6.2 (5.1, 7.2)	6.2 (5.1, 7.3)	6.0 (5.1, 7.1)	6.3 (5.1, 7.2)	0.486	0.270	0.051
Cumulative febuxostat dose, g	7.0 (3.0, 15.7)	7.0 (2.7, 20.1)	7.1 (3.5, 15.7)	5.9 (2.5, 12.0)	0.123	**0.010**	**0.006**
Dose of febuxostat at 4 months, mg	58.3 (25.7, 130.7)	58.5 (22.7, 167.8)	59.3 (29.4, 130.7)	50.0 (21.0, 101.0)	0.093	**0.006**	**0.003**
Percentage change in SU	-41.4 (-51.3, -30.1)	-39.4 (-49.2, -31.1)	-40.2 (-50.0, -29.7)	-47.2 (-58.3, -35.6)	**<0.001**	**<0.001**	**<0.001**
Delta SU, mg/dL	-3.4 (-5.0, -2.4)	-3.3 (-4.8, -2.3)	-3.4 (-4.8, -2.3)	-4.2 (-6.4, -3.0)	**<0.001**	**<0.001**	**<0.001**

Disclosure: Y. Kim: None; **H. Song**: None; **W. Seo**: None; **J. Kim**: None; **S. Ahn**: None; **J. Oh**: None; **Y. Kim**: None; **C. Lee**: None; **B. Yoo**: None; **S. Hong**: None.

Abstract Number: 0232

Incident Gout After Recombinant Zoster Vaccination in Adults Aged ≥65 Years in the USA

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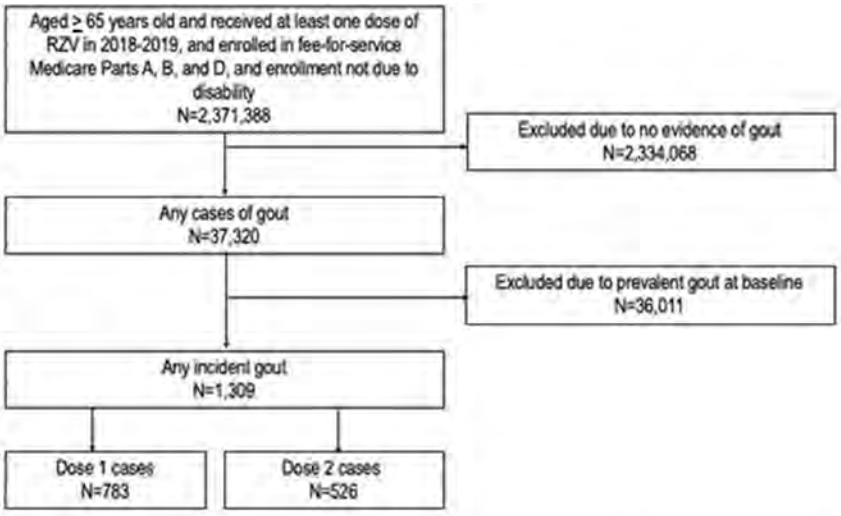
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In pre-licensure clinical trials, numerical differences in gout cases between the recombinant zoster vaccine (RZV) and placebo groups have been observed. However, real-world evidence is limited. Thus, we aimed to estimate the risk of incident gout following RZV exposure using real-world data from a large population of older US adults.

Methods: Using the Centers for Medicare and Medicaid Services Chronic Conditions Warehouse database, a case-only, self-controlled risk interval design was implemented to assess the risk of incident gout in US adults aged ≥65 years. We included adults who were enrolled in fee-for-service Medicare Parts A, B, and D and received at least one dose of the two-dose RZV regimen in 2018–2019 (Figure 1). Incident gout cases in the risk (Days 1–30 following vaccination) or control (Days 31–60 following vaccination) window (Figure 2) were defined by a gout diagnosis in an inpatient or outpatient setting followed by receipt of allopurinol, colchicine, probenecid, or febuxostat within 3 months with no prior evidence of gout diagnosis or medication in the 365 days preceding the incident gout case. Baseline descriptive characteristics in the 12 months up to RZV exposure included age, sex, calendar year–month of RZV vaccination, concomitant preventive immunizations, comorbidities, and health care service utilization. Conditional Poisson regression models estimated the relative risk (RR) of incident gout following any RZV dose in a primary (with censoring at receipt of dose 2) and secondary (30-day fixed control window without censoring) analysis. Sensitivity analyses included 1) a two-dose recipient subgroup with 60–183-day dose

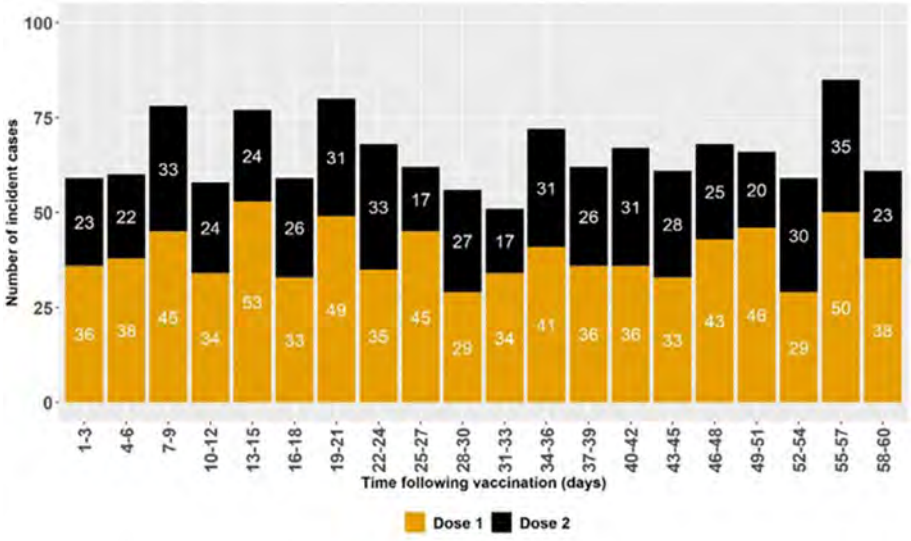


Parts A, B, and D, enrollment in Medicare Parts A (hospital insurance), B (medical insurance), and D (prescription drug coverage); RZV, recombinant zoster vaccine.

CONSORT diagram of the incident gout analytic cohort

spacing; 2) dose 1- and dose 2-specific analysis; 3) a seasonality-adjusted analysis; and 4) a COVID-19 sensitivity analysis excluding incident gout cases on or after December 2, 2019. A temporal scan tested for significant clustering of incident gout cases after vaccination.

Results: We identified 1,309 incident gout cases (Figure 1) who were predominantly White (87%; n=1137) and male (61%; n=801), and aged 70–79 years (55%; n=723). Chronic kidney disease (41%; n=531), diabetes mellitus (36%; n=473), and ischemic heart disease (33%; n=433) were common comorbidities. The majority had no prior hospitalizations (87%;



RZV, recombinant zoster vaccine.

Incident gout cases by dose and day from the RZV index date

Analysis type	Control window length, mean days (SD)	Total cases, n	Risk window cases, n (%)	Control window cases, n (%)	RR (95% CI)
Primary analysis					
Dose 1 and 2 without distinguishing*	29.9 (0.90)	1309	657 (50.19)	652 (49.81)	1.01 (0.90, 1.12)
Secondary analysis					
Fixed 30-day control window, dose 1 and 2 without distinguishing	30.0 (0)	1309	657 (50.19)	652 (49.81)	1.01 (0.90, 1.12)
Sensitivity analysis					
Dose compliant: 60–183-day dose spacing, dose 1 and 2 without distinguishing*	30.0 (0)	971	486 (50.05)	485 (49.95)	1.00 (0.88, 1.14)
Fixed 30-day control window, dose 1 only	30.0 (0)	783	397 (50.70)	386 (49.30)	1.03 (0.89, 1.19)
Fixed 30-day control window, dose 2 only	30.0 (0)	526	260 (49.43)	266 (50.57)	0.98 (0.82, 1.16)
Seasonality-adjusted analysis: dose 1 and 2 without distinguishing*	29.9 (0.90)	1309	657 (50.19)	652 (49.81)	1.01 (0.90, 1.12)
COVID-19 analysis: exclude cases on or after December 2, 2019, dose 1 and 2 without distinguishing*	29.9 (0.93)	1239	622 (50.20)	617 (49.80)	1.01 (0.90, 1.13)

Note: Risk window is Days 1–30 after vaccination, control window starts on Day 31.
*Dose 1 control window censored at receipt of dose 2.
CI, confidence interval; RR, relative risk; RZV, recombinant zoster vaccine; SD, standard deviation.

Risk of incident gout after RZV exposure

n=1,135) or Emergency Department visits (77%; n=1,013), and 9% (n=121) received concomitant influenza vaccine. Of the 1,309 incident gout cases, 1,074 (82%) received two RZV doses. The 783 incident gout cases after dose 1 and the 526 incident gout cases after dose 2 occurred equally in the risk and control windows (Figure 2). In the primary analysis (Table 1), the RR of incident gout was 1.01 (95% confidence interval: 0.90, 1.12). The secondary analysis and all sensitivity analyses produced similar results. The temporal scan did not detect significant clustering of incident gout cases over the 60-day follow-up.

Conclusion: The findings show no statistically significant increased risk of incident gout following receipt of RZV in US adults aged ≥65 years.

Disclosure: S. dosReis: GlaxoSmithKlein(GSK), 5; **C. Zhang**: GlaxoSmithKlein(GSK), 5; **A. Amill-Rosario**: GlaxoSmithKlein(GSK), 5; **A. Johnson**: GlaxoSmithKlein(GSK), 5; **H. Lee**: GlaxoSmithKlein(GSK), 5; **O. Spence**: GlaxoSmithKlein(GSK), 3, 12, stocks; **D. Oraichi**: GSK, 3, 12, Stocks; **H. Seifert**: GlaxoSmithKlein(GSK), 3, 11; **V. Franck**: GlaxoSmithKlein(GSK), 3, 11; **S. Gamble**: GlaxoSmithKlein(GSK), 3, 11, Supernus Pharmaceuticals, Inc, 11; **H. Yun**: GlaxoSmithKlein(GSK), 3.

Abstract Number: 0233

Impaired Anti-oxidant Function of HDL and Its Associated Protein, Paraoxonase-1, in Patients with Gout

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Longitudinal cohorts have described the association between gout and cardiovascular disease (CVD), while other cohort and interventional studies (CANTOS) have shown the impact of inflammatory factors on CV outcomes. Our group has demonstrated that in patients with other Rheumatic Diseases, HDL functions abnormally, promoting oxidation of LDL, rather than being anti-inflammatory. Given the gout-CVD association, we sought to evaluate the function of HDL as well as the activity of its major associated protein, paraoxonase-1 (PON1) in patients with tophaceous (TG) and non-tophaceous gout (G) compared to healthy controls (HC) and subjects with asymptomatic hyperuricemia (ASH).

Methods: Patients meeting ACR-EULAR Gout Classification Criteria were recruited from a single academic center and defined as either G or TG by presence of clinically palpable tophi. HC and subjects with ASH (serum urate > 7 mg/dL in absence of gout) were recruited.

The HDL inflammatory index (HII),is defined by the ability of patient's HDL to prevent oxidation of LDL when added to a cell-free assay and reported as a ratio where levels > 1.0 indicate enhanced oxidation of LDL (pro-inflammatory) and ratios < 1.0 reduce oxidation of LDL (anti-inflammatory).PON1 activity was measured by paraoxanase, arylesterase and lactonase assays using paraoxon, phenylacetate, and dihydrocoumarin as substrates. Hs-CRP levels were measured by the clinical laboratory.

Kruskal-Wallis non-parametric analyses compared HII rank sums across clinical groups. The 5 CV biomarkers were then standardized with mean of 1 and standard deviation of 1. Generalized Linear Models compared unadjusted means across the clinical groups. Finally, multivariate regressions examined the association between gout and the 5 CV biomarkers adjusting for race, age, gender, BMI, hypertension, hyperlipidemia, diabetes, tobacco use, family history of CVD, prior heart disease and presence of kidney disease (Table 1)

Results: Among 136 subjects, mean HII were lowest (most protective) in HC and ASH subjects (0.70 and 0.82 respectively) and highest (least protective) among G and TG patients (1.04 and 1.37 respectively), p-value = 0.0035 for the model and rank sum difference between HC and TG groupsof $p < 0.05$. (Figure 1)

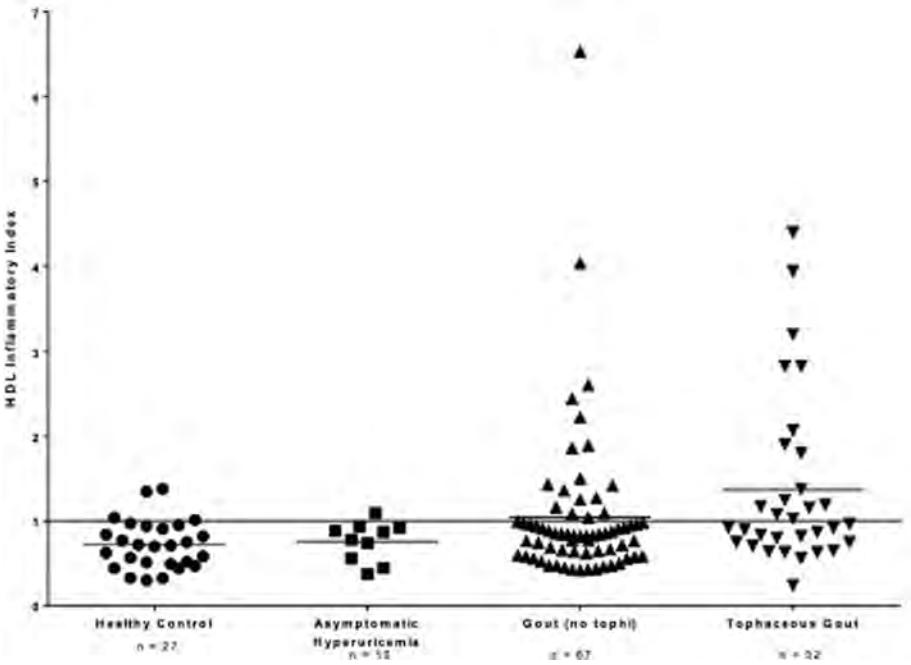

Figure 1. HDL inflammatory index by patient group Legend: HDL = High Density Lipoprotein. P-value = 0.0035 for difference across the groups in ANOVA model. Difference between rank sums for Healthy Controls vs. Tophaceous Gout, p-value < 0.05.

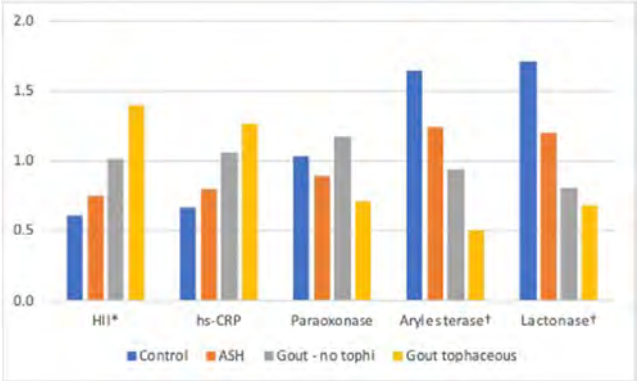

Figure 2. Unadjusted Cardiovascular Biomarkers (standardized) by patient group Legend: HII = High Density Lipoprotein Inflammatory Index, hs-CRP = high sensitivity c-reactive protein, ASH = Asymptomatic Hyperuricemia (urate > 7 mg/dL at time of pro-inflammatory HDL lab) * p = 0.0165, † p < 0.001

Table 1. Multivariate analysis of Cardiovascular Biomarkers Legend: HDL = High-Density Lipoprotein, CV = Cardiovascular, CKD = Chronic Kidney Disease Multivariate models for gout-paraoxonase (p = 0.76) and gout-hs-CRP (p = 0.08) not shown.

	HDL Inflammatory Index		Arylesterase		Lactonase	
	Estimate	p-value	Estimate	p-value	Estimate	p-value
Intercept	0.051	0.91	250.2	**<.0001**	33.4	**0.001**
Gout	0.239	0.17	-60.9	**0.01**	-7.8	0.03
CV risk factors						
Age	0.010	0.17	0.1	0.90	-0.04	0.77
Female	-0.290	0.12	-2.6	0.91	4.0	0.29
Hypertension	-0.180	0.29	9.8	0.66	2.2	0.53
Hyperlipidemia	0.105	0.52	-5.2	0.80	-2.1	0.52
History of Heart Disease (self-reported)	0.044	0.82	13.2	0.59	3.1	0.42
Diabetes	-0.306	0.17	-0.04	1.00	4.3	0.46
Tobacco Use						
Never (referent)						
Remote	-0.094	0.56	53.1	**0.01**	6.2	0.06
Current	1.125	**0.03**	-19.0	0.81	-4.5	0.73
Race						
White (referent)						
Black	0.185	0.59	47.5	0.29	-6.8	0.34
Asian	0.090	0.66	26.2	0.33	1.6	0.70
Other	-0.258	0.35	-37.0	0.35	-12.1	0.06
Chronic Kidney Disease						
None (referent)						
CKD2	-0.027	0.89	-62.4	**0.01**	-9.7	**0.01**
CKD3	0.198	0.43	-96.1	**0.01**	-7.7	0.16
CKD4	0.815	**0.01**	-73.6	**0.10**	-10.4	0.14
BMI	0.009	0.37	1.01	0.40	0.14	0.46

Similarly, standardized, unadjusted PON1 activity as measured by lactonase and arylesterase assays was highest (most protective) in the HC group, decreasing across the patient categories, to the lowest in the TG group ($p < 0.001$ for both lactonase and arylesterase differences across the groups). (Figure 2)

In multivariate analyses, PON1 activity remained most protective (arylesterase and lactonase) among HC and ASH subjects vs. G and TG patients after controlling for above covariates (p = 0.01 and 0.03, respectively). The observed gout-HII association was attenuated (p = 0.17) by the strong renal-HII association. (Table 1)

Conclusion: In this single center analysis of patients with gout (G, TG) compared to HC and patients with ASH, gout was a significant predictor of abnormal antioxidant function of HDL and decreased PON1 activity and suggests a plausible pathway for the inflammatory impact of gout, MSU crystal deposition or hyperuricemia on CVD.

Disclosure: J. FitzGerald: None; **C. Charles-Schoeman**: AbbVie, 2, 5, Alexion, 5, BMS, 2, 5, Boehringer Ingleheim, 2, 5, CSL Behring, 5, Galapagos, 2, Pfizer, 2, 5, Priovant, 2, 5, Recludix, 2; **V. Ranganath**: Bristol-Myers Squibb(BMS), 5, mallinckrodt, 5; **A. Shahbazian**: None; **J. Wang**: None; **M. McMahon**: None.

Abstract Number: 0234

Identifying Optimal Serum Urate Levels to Reduce Gout Flares in Patients Taking Urate Lowering Therapy: A Post-hoc Cohort Analysis of CARES with Consideration of Drop-out

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: ACR gout treatment guidelines recommend a target serum urate (SU) of < 6 mg/dL and anti-inflammatory flare prophylaxis for at least 3-6 months after initiating urate-lowering therapy (ULT). However, optimal targets for SU are not well defined. We investigated gout flare rates based on repeated measurements of SU levels in a randomized controlled trial of ULT, accounting for loss to follow up.

Methods: We performed a secondary analysis using data from the Cardiovascular Safety of Febuxostat or Allopurinol in Patients with Gout (CARES) trial. CARES participants were randomized to febuxostat or allopurinol, titrated for a target SU < 6 mg/dL; 45% did not complete all study visits. Participants received gout flare prophylaxis for 6 months with colchicine 0.6 mg daily or naproxen 250 mg twice daily if colchicine was not tolerated. For this analysis, participants were followed from month 0 (randomization) to the earliest of death, last completed visit (drop out), or end of study. SU levels were assessed at months 0, 3, 6 and then every 6 months and categorized as ≤3.9, 4.0-5.9, 6.0-7.9, 8.0-9.9, and ≥10 mg/dL. The primary outcome was self-reported gout flare in each 3- or 6-month interval. More than 1 flare/interval was permitted if they were separated by ≥14 days. Baseline variables were used to derive inverse probability of censoring weights (IPCW) to account for censoring (drop-out or death). Poisson regression models included stabilized IPCW weights and estimated gout flare incidence rate ratios (IRR) by time-varying SU category, adjusting for change in SU from prior visit, flare prophylaxis, ULT, age, sex, race, body mass index, gout duration, and tophi. Models were performed for months 0-6, 6-12, and 12-72.

Table 1. Association between time-varying serum urate level and gout flare incidence rate ratios (IRR)* in the CARES trial dataset

	Timeframe after starting urate-lowering therapy					
	Months 0-6		Months 6-12		Months 12-72	
Serum urate category (mg/dL)	Gout flare IRR (95%CI)	p value	Gout flare IRR (95%CI)	p value	Gout flare IRR (95%CI)	p value
≤3.9	0.88 (0.67-1.16)	0.36	0.89 (0.73-1.09)	0.27	0.83 (0.70-0.98)	0.03
4.0-5.9	1.00	-	1.00	-	1.00	-
6.0-7.9	0.95 (0.79-1.13)	0.55	0.96 (0.85-1.09)	0.56	1.20 (1.05-1.36)	<0.01
8.0-9.9	1.09 (0.84-1.41)	0.50	0.92 (0.71-1.20)	0.54	1.29 (1.02-1.62)	0.03
≥10	1.24 (0.85-1.79)	0.26	1.16 (0.71-1.88)	0.56	1.92 (1.28-2.87)	<0.01
p for trend		0.22		0.44		<0.01

*Gout flare incidence rate ratios from Poisson models adjusted for stabilized inverse probability of censoring weight (IPCW), absolute change in SU since prior visit, direction of change in SU, urate lowering therapy (febuxostat/allopurinol/none), prophylaxis (colchicine/NSAID/none), age, sex, race (American Indian/Alaska Native, Asian, Black, Native Hawaiian/Pacific Islander, White, Multiracial/other), body mass index, gout duration, tophi (present/absent)

Results: Among 6183 participants in this analysis, median age was 65 (IQR 58-71) years and 84.0% were male. Median follow-up was 32 months. At month 0, median SU was 8.6 (IQR 7.6-9.7) mg/dL. Seventy-one percent achieved SU < 6 mg/dL by month 3, and this percentage increased slightly over time among retained participants (**Figures 1A & 1B**). Gout flare rates were highest during nearly all intervals when SU ≥10 mg/dL and lowest when SU ≤3.9 mg/dL (**Figure 2**). Peak gout flare rates for all SU categories were observed between months 0-3, coinciding with the initiation of ULT and greatest change in SU. A second spike in gout flares occurred in all SU groups between months 6-12, coinciding with discontinuation of prophylaxis (**Figure 2**). In the initial year of ULT, flare rates did not significantly differ between SU groups, but flare rates were consistently highest when SU ≥10 mg/dL. During months 12-72, in adjusted analyses with IPCW weights, a dose-

Figure 1. Serum urate levels over time in the CARES trial dataset.

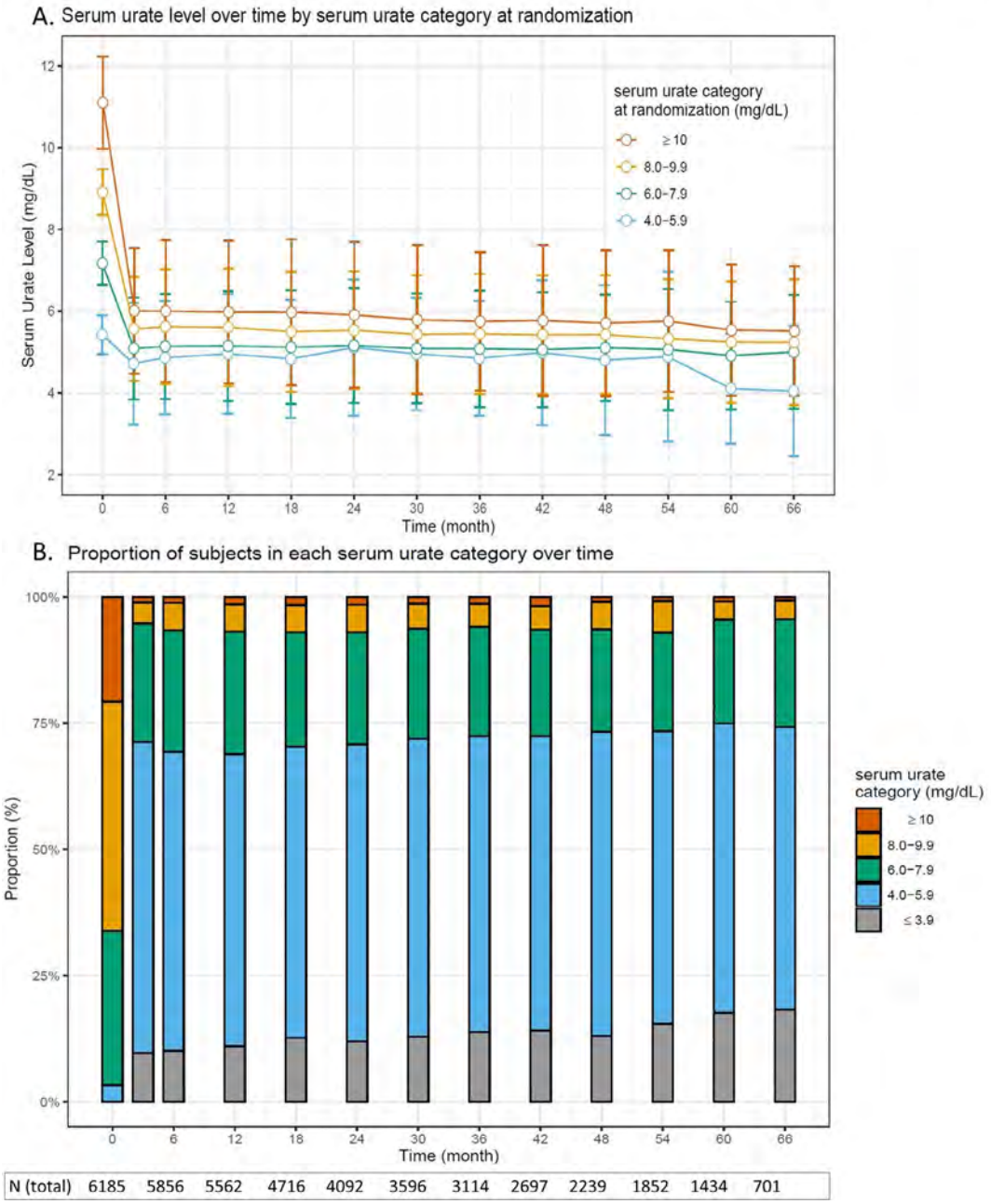
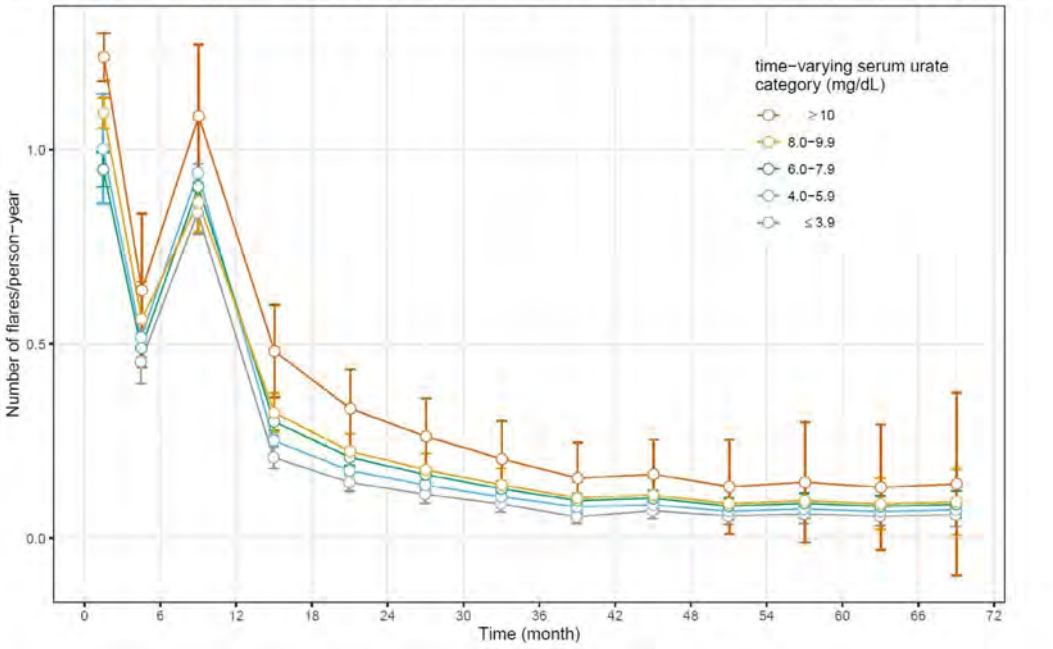


Figure 2. Gout flare rates over time by serum urate category in the CARES trial dataset. Flare rates are adjusted for stabilized inverse probability of censoring weight (IPCW), absolute change in SU since prior visit, direction of change in SU, urate lowering therapy (febuxostat/allopurinol/none), prophylaxis (colchicine/NSAID/none), age, sex, race, body mass index, gout duration, tophi



response relationship was observed between SU category and flare rate. Compared with SU 4.0-5.9 mg/dL, significantly lower flare rates were observed when SU ≤3.9 mg/dL and significantly greater rates when SU ≥10 mg/dL (p for trend < 0.01) (**Table 1**).

Conclusion: Gout flare rates were persistently higher when SU ≥6 mg/dL compared to SU at target after the first year of ULT, after accounting for censoring. These data suggest a potential benefit of achieving very low SU levels (≤3.9 mg/dL) and consideration of a longer duration of prophylaxis to reduce gout flares.

Disclosure: S. Tedeschi: Novartis, 2; **K. Hayashi**: None; **Y. Zhang**: None; **H. Choi**: Ani, 2, Horizon, 2, 5, LG, 2, Protalix, 2, Shanton, 2; **D. Solomon**: CorEvitas, 5, Janssen, 5, moderna, 5, Novartis, 5, UpToDate, 9.

Abstract Number: 0235

Fractures in Patients with Acute CPP Crystal Arthritis versus Matched Comparators in a Large Cohort Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Calcium pyrophosphate deposition (CPPD) disease was positively associated with osteopenia in two large cross-sectional studies, but risk of fractures has not been evaluated. We compared risk of fractures in patients with acute calcium pyrophosphate (CPP) crystal arthritis vs. matched comparators.

Methods: We performed a matched cohort study using electronic health record (EHR) data at a large academic medical center. Patients with at least one episode of acute CPP crystal arthritis, 1991-2017, were matched to comparators without acute CPP crystal arthritis on index date and year of EHR entry; comparators could have other types of arthritis. Index date was the 1st mention of "pseudogout" in notes or 1st synovial fluid analysis with CPP crystals, whichever came first. For the matched comparators, an encounter +/- 30 days was used as the index date. The primary outcome was first fragility fracture (humerus, wrist, hip, or pelvis fracture); secondary outcomes were first fracture at each separate anatomic site. Fragility fractures were identified via published algorithms using diagnosis and procedural codes with positive predictive value >90%. For patients with >1 fracture, only the earliest was included. The baseline period from EHR entry through index date was required to be ≥180 days. Patients with baseline fragility fracture were excluded. Covariates included age, sex, race, smoking, rheumatoid arthritis, hyperparathyroidism, healthcare encounters, multimorbidity index, BMI, oral glucocorticoids, osteoporosis treatment, and proton pump inhibitors. Censoring occurred at the earliest of death, fracture outcome, or last encounter before April 2023. We estimated incidence rates (IR) and IR ratios (IRR) for any fracture and for each anatomic site. Cox models estimated adjusted hazard ratios (HR) for fractures. Sensitivity analyses excluded patients prescribed glucocorticoids, osteoporosis treatment, or with rheumatoid arthritis.

Results: We identified 1148 patients with acute CPP crystal arthritis matched to 3730 comparators. Mean age was 73 years in both cohorts and more than half were female. Glucocorticoids and osteoporosis treatments were more frequent in the acute CPP crystal arthritis cohort than comparators (**Table 1**). Fracture incidence rates were twice as high in the acute CPP crystal arthritis cohort (11.2 per 1000 person-years) vs. comparators (5.6 per 1000 person-years) (**Table 2**). Cumulative incidence curves increasingly diverged, reflecting greater fracture rates in the acute CPP crystal arthritis cohort over time (**Figure 1**). Fracture risk was twice as high in the acute CPP crystal arthritis cohort vs. comparators after adjustment (HR 1.8,

Table 1. Baseline characteristics of patients with acute CPP crystal arthritis and comparators in a large electronic health record cohort study

	Acute CPP crystal arthritis n=1148	Comparators n=3730
Age at index date	72.6 (10.7)	72.5 (12.0)
Female	53.9	58.9
White race	83.1	80.0
Body mass index, kg/m^2 [a]	28.5 (5.0)	27.7 (4.3)
Smoking [b]	13.0	8.2
Healthcare encounters [c]	127.3 (131.1)	56.9 (67.2)
Rheumatoid arthritis [d]	12.5	3.2
Osteoarthritis [d]	58.2	24.9
Hyperparathyroidism [d]	3.5	1.0
Glucocorticoid prescription [e]	18.4	3.7
Osteoporosis treatment [f]	8.2	4.7
Proton pump inhibitor [g]	34.2	15.3
Multimorbidity index [h]	16.0 (16.1)	9.2 (11.6)

Presented as % or mean (SD)
[a] Obtained from the closest available data to index date, and imputed for subjects missing BMI
[b] Defined by ≥1 diagnosis code for smoking and/or prescription for smoking cessation medication before index date
[c] Number of inpatient and outpatient visits, hospitalizations, prescriptions, and laboratory tests
[d] Defined by ≥ 2 diagnosis codes
[e] Oral glucocorticoid prescribed in the 90 days before index date
[f] Bisphosphonate (alendronate, zolendronic acid, ibandronate, etidronate, risendronate, pamidronate), denosumab, raloxifene, or teriparatide prescribed in the 365 days before index date
[g] Prescribed in the 365 days before index date
[h] Weighted multimorbidity score based on ICD-9 codes for 40 chronic conditions (Radner H, et al. Seminars Arthritis Rheum 2015;45:167-73), range 0-156

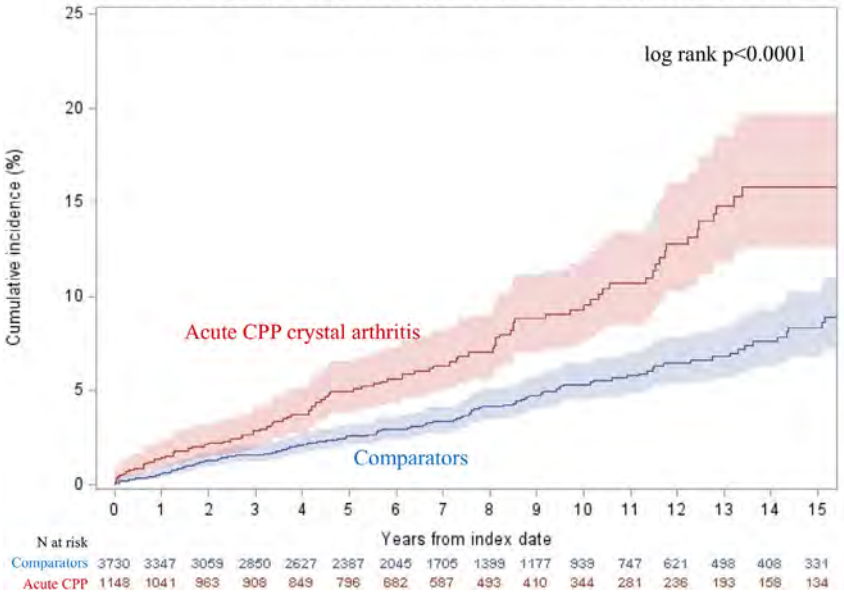
Table 2. Fracture incidence rates (IR), incidence rate ratios (IRR), and adjusted hazard ratios (HR)* in a large electronic health record cohort study

	Acute CPP crystal arthritis cohort n=1148		Comparator cohort n=3730			
	Events	IR/1000 person-years (95% CI)	Events	IR/1000 person-years (95% CI)	Fracture IRR (95% CI)	Adjusted HR* (95% CI)
Any fracture	100	11.2 (10.5, 11.9)	150	5.6 (5.4, 5.7)	2.0 (0.9, 4.3)	1.8 (1.4, 2.4)
Humerus	14	1.5 (1.2, 1.7)	24	0.9 (0.8, 0.9)	1.7 (0.8, 3.5)	1.4 (0.7, 2.8)
Wrist	23	2.5 (2.1, 2.8)	17	0.6 (0.6, 0.7)	4.0 (1.9, 8.3)	3.8 (2.0, 7.4)
Hip	32	3.4 (3.0, 3.8)	61	2.2 (2.1, 2.3)	1.5 (0.7, 3.2)	1.3 (0.8, 2.1)
Pelvis	41	4.4 (4.0, 4.8)	71	2.6 (2.5, 2.7)	1.7 (0.8, 3.6)	1.5 (1.0, 2.3)
Sensitivity analyses comparing risk of **any fracture**† for acute CPP crystal arthritis vs. comparators						
Excluding patients prescribed glucocorticoids						1.6 (1.2, 2.2)
Excluding patients prescribed osteoporosis treatment						1.9 (1.4, 2.5)
Excluding patients with rheumatoid arthritis						1.7 (1.3, 2.3)

* Adjusted for age, sex, race, healthcare utilization, body mass index, multimorbidity index, smoking, rheumatoid arthritis, hyperparathyroidism, oral glucocorticoids in the 90 days before index date, osteoporosis treatment in the 365 days before index date, proton pump inhibitor in the 365 days before index date

Analyses with the outcome of "any fracture" censored patients at the earliest fracture at any site (humerus, wrist, hip, or pelvis fracture), death, or last encounter before April 2023. Analyses of each separate anatomic site censored patients at the earliest fracture at that site, death, or last encounter before April 2023.

Figure 1. Cumulative fracture incidence among patients with acute CPP crystal arthritis and comparators in a large electronic health record cohort study



95% CI 1.4, 2.4); results were similar in sensitivity analyses excluding patients using glucocorticoids, osteoporosis treatments, or with rheumatoid arthritis (**Table 2**).

Conclusion: In this first-ever study of fractures and CPPD, we observed a doubling of fracture risk in patients with acute CPP crystal arthritis. Future studies evaluating bone turnover markers and changes in bone density over time in patients with CPPD are needed.

Disclosure: S. Tedeschi: Novartis, 2; **K. Hayashi**: None; **A. Rosenthal**: None; **J. Marrugo**: None; **S. Fukui**: None; **E. Gravallese**: Associate Editor, New England Journal of Medicine, 3, Co-editor of the textbook Rheumatology, 9, UptoDate, 9; **D. Solomon**: CorEvitas, 5, Janssen, 5, moderna, 5, Novartis, 5, UpToDate, 9.

Abstract Number: 0236

Treatment-emergent Major Adverse Cardiovascular and Thromboembolic Events Were Infrequent During Pegloticase Therapy: Pooled Clinical Trial Findings

orrin Troum[1], Mai Duong[2], Katie Obermeyer[2], Lissa Padnick-Silver[2] and **Brian LaMoreaux**[2], [1]University of Southern California Keck School of Medicine and Providence Saint John's Health Center, Santa Monica, CA, [2]Horizon Therapeutics, Deerfield, IL

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is associated with high comorbidity, including cardiovascular (CV), metabolic, and renal disease,[1] with even higher burden in uncontrolled gout patients (pts).[2] CV (myocardial infarction [MI], stroke) and thromboembolic (VTE) event incidence of 17.34 and 3.65/1000 PY,[3,4] respectively, was reported in gout pts, with higher incidence after flare (CV within 120 days,[3] VTE within 30 days[4]). This link may be from systemic inflammatory consequences of seemingly local gout flares.[5,6] Maintaining serum urate (SU) < 6 mg/dL reduces flares over time.[7] However, initiating urate-lowering therapy (ULT) can induce flare, raising the question of CV/VTE event with ULT initiation. Here, we examine CV/VTE events after pegloticase initiation in this pooled post hoc analysis of clinical trial pts.

Methods: Phase 3,[8] MIRROR OL,[9] and MIRROR RCT[10] pts with ≥1 pegloticase infusion were included (244 biweekly dosing [110 with methotrexate {MTX}], 84 monthly dosing), with focus on biweekly (on-label) pts. All had uncontrolled gout and received flare prophylaxis (FP) ≥1 wk before first dose. Standard pre-infusion prophylaxis was used, including 125 mg IV methylprednisolone or 200 mg hydrocortisone. Gout flare and CV/VTE events were identified using treatment-emergent (TE) AEs during 24 wks of therapy. Flare exposure window was 120 days.[3]

Results: 5/328 pts (1.5%; 4 monotherapy colchicine FP, 1 pegloticase+MTX ibuprofen FP) beginning pegloticase had ≥1 CV/VTE event (cardiac arrest [CA, n=2]; CHF, DVT, MI, TIA [n=1 each]), with all occurring during the flare exposure window (time from first TE flare, range: 18-130 days; time from most-recent TE flare: 3-69 days). 3 CV/VTE events occurred in 244 pts receiving biweekly pegloticase (1.2%, 35.4/1000 PY), with 2 in monotherapy pts (1.5%; CA, CHF) and 1 in a pegloticase+MTX pt (0.9%; CA). 176/244 (72.1%) had ≥1 TE flare. Pts with and without flare were similar but those with flare had more frequent pre-treatment flares (10.9±13.6 vs 5.3±5.7 flares/year [median: 7 vs 3]).

Conclusion: 1.2% of pts had CV/VTE events during biweekly pegloticase therapy, with similar incidence (35.4/1000 PY) to the general gout population (20.99-44.7/1000 PY[3,4,11]) and lower than with XOI initiation (51.8-99.3/1000 PY[12]). All events occurred within the 120 days of flare when pts were at higher risk.[3,4] Of note, pts with TE flares had higher pre-treatment flare rates than those without. Maintaining SU < 6 mg/dL decreases gout flares over time[7] so a treat-to-target approach with ULT may be of critical importance for maintaining gout pt health over the long-term.

References

1. Zhu Y et al. *Am J Med* 2012;125:679-87 e1
2. Francis-Sedlak M et al *Rheumatol Ther* 2021;8:183-97
3. Cipolletta E et al. *JAMA* 2022;328:440-50
4. Cipolletta E et al. *Arthritis Rheumatol* 2023 [ePub]
5. Pillinger M et al. *Arthritis Rheumatol* 2022;74 (sup 9)
6. Wu H et al. *Medicine* 2022;101:e30242
7. Shoji A et al. *Arthritis Rheum* 2004;51:321-5
8. Sundy JS et al. *JAMA* 2011;306:711-20
9. Botson JK et al. *J Rheumatol* 2021;48:767-74
10. Botson JK et al. *Arthritis Rheumatol* 2023;75:293-304
11. Clarison LE et al. *Ann Rheum Dis* 2015;74:642-7
12. Foody J et al. *Am Health Drug Benefits* 2017;10:393-401

Disclosure: o. Troum: Abbvie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb (BMS), 2, 5, 6, Centocor, 5, Corrona, 5, Horizon Therapeutics, 2, 5, 6, Lilly, 2, Novartis, 5, 6, Pfizer, 2, 5, 6, Sanofi-Genzyme, 6; **M. Duong**: Horizon Therapeutics, 3, 12, Stockholder; **K. Obermeyer**: Horizon Therapeutics, 3, 12, Stockholder; **L. Padnick-Silver**: Horizon Therapeutics, 3, 12, Stockholder; **B. LaMoreaux**: Horizon Therapeutics, 3, 12, Stockholder.

Abstract Number: 0237

Oral Urate-Lowering Therapy Use and Efficacy Following Pegloticase Treatment: Findings from a Rheumatology Network Database

Lissa Padnick-Silver[1], Andrew Concoff[2], Hong-Ye Gao[1], Qianhong Fu[1], **Brian LaMoreaux**[1] and N. Lawrence Edwards[3], [1]Horizon Therapeutics, Deerfield, IL, [2]United Rheumatology, Happauge, NY, [3]University of Florida College of Medicine, Gainesville, FL

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Pegloticase, a recombinant pegylated uricase, rapidly reduces serum urate (SU) in patients refractory to/intolerant of oral urate-lowering therapies (ULTs).[1,2] However, pegloticase is generally used for ≤1 year for intensive SU-lowering and subsequent urate burden depletion. Optimal post-pegloticase treatment has not yet been established, but use and efficacy of oral ULTs remains an important unanswered clinical question. This analysis retrospectively examined data from a large US rheumatology database to better understand real-world practice patterns of post-pegloticase oral ULT use and to preliminarily examine post-pegloticase oral ULT efficacy.

Methods: Patients in the UR-NICE data repository who had first pegloticase infusion code (J2507) between 2012 and 2022 were included in analyses. The beginning and end of therapy was defined as the date of first and last pegloticase infusion code, respectively. All patients were in the database for ≥60 days following last infusion. Oral ULT use (allopurinol, febuxostat, probenecid) before and after pegloticase therapy was examined. Patients were also stratified by those that did and did not receive ≥12 infusions (considered as "full course" in prior retrospective studies[3]). Patient characteristics prior to pegloticase therapy were also examined to help characterize the pegloticase-treated population.

Results: 211 patients (77% male; mean[±SD] age: 62.7±12.8 years, BMI: 32.9±7.2 kg/m^2, eGFR: 66.0±24.7 ml/min/1.73m^2 [46% eGFR < 60]) were included. 74% had tophaceous gout and pre-pegloticase SU was 7.9±2.5 mg/dL (n=148). Available inflammatory biomarkers were moderately elevated (median CRP: 3.3 mg/dL [n=114], neutrophil-to-lymphocyte ratio [NLR][4]: 2.9 [n=41]). 141 patients (67%) had pre-pegloticase oral ULT use noted (73% allopurinol, 48% febuxostat, and/or 18% probenecid). Patients received a mean (±SD) of 12.3±12.6 pegloticase infusions (median: 9; 88 [42%] received ≥12), with a 2.2±2.0 wk dosing interval. Following last infusion, 115 patients (55%) began oral ULT (67% allopurinol, 44% febuxostat, and/or 17% probenecid), most (67%) within 30 days of last pegloticase infusion. More patients who received ≥12 infusions had an SU < 6 mg/dL when treated with post-pegloticase oral ULT than those who received < 12 infusions (first post-ULT SU < 6 mg/dL: 78% vs 36%; mean SU: 4.7±3.0 [n=37] vs 7.4±2.9 mg/dL [n=47]).

Conclusion: These pegloticase-treated patients reflected a typical uncontrolled gout population. Two-thirds of patients began oral ULT after pegloticase, most within 30 days of last infusion. Patients who had a longer pegloticase course (≥12 infusions) were more likely to have post-treatment oral ULT efficacy, perhaps because of greater urate burden depletion. These data suggest oral ULTs may be effective after successful pegloticase therapy but further prospective studies are needed to verify our findings and better understand how overall urate burden may influence oral ULT efficacy.

References

1. Sundy JS, et al. *JAMA* 2011;306:711-20.
2. Botson JK, et al. *Arthritis Rheumatol* 2023;75:293-304.
3. Keenan RT, et al. *Semin Arthritis Rheum* 2021;51:347-52.
4. Forget P, et al. *BMC Res Notes* 2017;10:12.

Disclosure: L. Padnick-Silver: Horizon Therapeutics, 3, 12, Stockholder; **A. Concoff**: Exagen, Inc., 3, United Rheumatology, 3; **H. Gao**: Horizon Therapeutics, 12, Paid contractor; **Q. Fu**: Horizon Therapeutics, 3, 12, Stockholder; **B. LaMoreaux**: Horizon Therapeutics, 3, 11; **N. Edwards**: Horizon Therapeutics, 2, United Rheumatology, 12, Medical Policy Committee Member.

Abstract Number: 0238

Adherence to the Gout and Crystal Arthritis Network (G-CAN) Consensus Statements for Gout Nomenclature

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

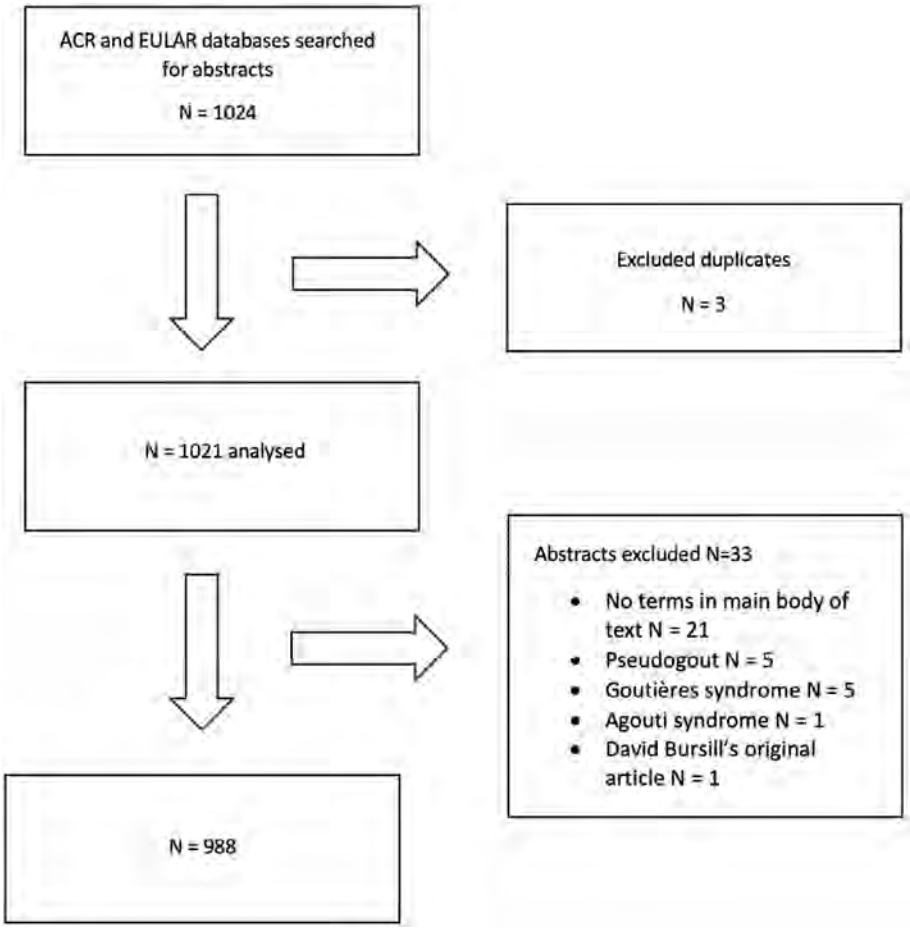

Figure 1. Consort diagram of abstract inclusion criteria

Background/Purpose: Uniform terminology with standardised definitions for the various elements and states of a disease ensure accurate and consistent technical communication. In 2019 the Gout and Crystal Arthritis Network (G-CAN) published consensus statements for the nomenclature of disease elements and disease states in gout. The aim of this study was to determine adherence to the G-CAN consensus statements since publication.

Methods: ACR and EULAR conference abstracts were searched using online databases for the keywords "gout" "urate" "uric acid" "hyperuricaemia" "tophus" and/or "tophi" before and after-publication of the consensus statements (01/01/2016-31/12/2017 and 01/01/2020-31/12/2021 (respectively)). Abstracts were manually searched for labels used to reference gout disease elements and states. Labels were extracted from text, figures, and tables. Use of the G-CAN agreed labels, as well as alternatives, were compared between the two time periods and between abstracts that included a G-CAN consensus statement author and those that did not in 2020/2021. Use of the term 'chronic gout', which G-CAN advised should be avoided, was also compared between the two time periods.

Results: There were 988 abstracts included in the analysis; 596 in 2016/2017 and 392 in 2020/2021. One or more G-CAN agreed labels were used in 445/596 (74.9%) of abstracts in 2016/2017, increasing to 311/392 (79.4%) in 2020/2021 (p=0.006). Use of the agreed labels 'urate', 'gout flare', and 'chronic gouty arthritis' increased between the two periods. There were 219/383 (57.2%) abstracts with the agreed label 'urate' in 2016/2017 compared to 164/232 (70.7%) in 2020/2021 (p=0.001). There were 60/175 (34.3%) abstracts with the agreed label for 'gout flare' in 2016/2017 compared with 57/109 (52.3%) in 2020/2021 (p=0.003). Only 1/35 (2.9%) abstracts used the agreed label for 'chronic gouty arthritis'

in 2016/2017 compared to 6/16 (37.5%) in 2020/2021 (p=0.02). Abstracts with consensus statement authors used the agreed labels in 87.4% of abstracts, compared to 74.5% without in the 2020/2021 period (p< 0.001). Use of the label 'chronic gout' reduced between the two time periods.

There were 29/596 (4.9%) abstracts in 2016/2017 that used the label 'chronic gout' compared with 8/392 (2.0%) abstracts in 2020/2021 (p=0.02).

Conclusion: Use of the G-CAN agreed gout labels has increased but gout nomenclature remains imprecise. Additional efforts are needed to ensure consistent use of agreed nomenclature for gout in the scientific literature.

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Abstract Number: 0239

Incidence and Prevalence of Cardiovascular and Metabolic Diseases Following Gout Diagnosis in the United Kingdom Using the THIN Database

Michael Garshick[1], Haridarshan Patel[2], **ada Kumar**[2], Brian LaMoreaux[2], Lissa Padnick-Silver[2], Louis Dron[3], Vinusha Kalatharan[3], Vivek Verma[3] and Michael Pillinger[4], [1]NYU School of Medicine/NYU Langone Medical Center, New York, NY, [2]Horizon Therapeutics, Deerfield, IL, [3]Cytel Canada Inc., Vancouver, BC, Canada, [4]New York University Grossman School of Medicine, New York, NY

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is a common inflammatory arthropathy characterized by pain, joint swelling, and monosodium urate crystal deposits in joints, organs, and soft tissues.[1] While gout is associated with cardiometabolic disorders, there is limited data on comorbidity burden in gout patients and almost no data on their longitudinal development.[1] This study aimed to estimate the incidence and prevalence of cardiometabolic disease in patients with gout in the United Kingdom (UK).

Methods: Using The Health Improvement Network (THIN) Database (A Cegedim Proprietary Database), a cohort of patients with a first gout diagnosis between January 1, 2003 and December 5, 2021 was analyzed. Patients were excluded if death occurred before first gout diagnosis, last data point was after last data-cut or before first gout diagnosis, the patient was < 18 years old at first gout diagnosis, or there was a prior history of congenital, toxin-related, or infectious cardiovascular disease (CVD). For incidence calculations, patients with prior history of the examined condition were excluded. Patients were followed from gout diagnosis until earliest of death, database disenrollment, or last available data. Gout and outcome diagnoses were identified using Read codes (clinical terminology system used in the UK), with ≥2 codes required ≥30 days apart to minimize identified comorbidity misclassification. Prevalence (in %) and incidence (in % and rate/1,000 person-years [PY]) of gout-associated cardiometabolic diseases (**Table 1**) were calculated. This work uses data provided by patients and collected by the NHS as part of their care and support.

Table 1. Incidence and prevalence of cardiovascular and metabolic diseases following first gout diagnosis in patients from the United Kingdom.

	No. of patients with incident disease n (%)[a]	Incidence rate (per 1000 PY[a])	No. of patients with prevalent disease n (%)[b]
Cardiovascular disease			
≥1 cardiovascular disease	20,779 (25.3)	29.5	118,563 (56.9)
Hypertensive diseases	22,270 (22.7)	26.4	109,452 (52.7)
Ischemic heart diseases	18,615 (12.8)	13.5	39,721 (19.1)
Dysrhythmias (including arrhythmia)	4,699 (2.6)	2.7	7,440 (3.6)
Cerebrovascular diseases	4,144 (2.1)	2.2	5,925 (2.8)
Peripheral vascular diseases	3,102 (1.7)	1.7	4,861 (2.3)
Heart failure	2,630 (1.4)	1.4	4,254 (2.0)
Cardiac valvular diseases	834 (0.4)	0.4	1,031 (0.5)
Pulmonary circulation diseases	420 (0.2)	0.2	473 (0.2)
Conduction disorders	258 (0.1)	0.1	338 (0.2)
Cardiomyopathies	201 (0.1)	0.1	216 (0.1)
Cardiometabolic disease			
≥1 metabolic disease	25,873 (20.0)	23.3	73,744 (35.5)
Dyslipidemia	21,097 (14.9)	17.0	53,996 (26.0)
Type II diabetes mellitus	15,120 (8.6)	9.2	34,473 (16.6)
Non-alcoholic liver diseases	706 (0.3)	0.4	808 (0.39)
Metabolic Syndrome	308 (0.1)	0.2	326 (0.2)

[a]The total number of patients included in analyses varied across comorbidities (patients with prior history of the examined outcome were excluded for incidence calculations, all N≥54,029). [b] N=207,872. Abbreviations: PY, person-years.

Results: A total of 207,872 patients (74.9% male; 47.9% white [N=106,304 with known race]) were included in analyses. At first gout diagnosis, median [interquartile range, IQR] age was 61.7 [49.1, 73.5] years and BMI was 29.0 [25.9, 32.7] kg/m^2. 57.0% had ≥1 CVD code (median [IQR] follow-up: 2.6 [0.7, 8.4] years) and 35.5% had ≥1 metabolic disease code (5.4[1.6, 10.7] years) after gout diagnosis. In patients without a pre-gout cardiovascular code, ≥1 CVD code was identified in 25.3% of patients (median [IQR] follow-up: 8.0 [3.9, 12.8] years) for an overall incidence of 29.5/1000 PY after gout diagnosis. In patients without a pre-gout metabolic disease code, ≥1 metabolic disease code was identified in 20.0% of patients (median [IQR] follow-up: 7.9 [3.8, 12.9] years) for an overall incidence of 23.3/1000 PY after gout diagnosis. The incidence and prevalence of individual conditions are summarized in **Table 1**.

Conclusion: In the first 8 years after initial gout diagnosis, approximately 1 in 4 patients without prior cardiovascular disease developed a new cardiovascular comorbidity and 1 in 5 patients without prior metabolic disease developed a new metabolic comorbidity. Further, the overall prevalence of cardiovascular and metabolic disease was high in this UK gout population, with hypertension and ischemic heart disease of notable frequency among both incident and prevalent cohorts. Comorbidity development over time will be further explored in and compared between controlled and uncontrolled patients to examine potential contributions of gout.

Reference

1. Bardin, et al. *BMCMedicine* 2017;15: 1-10.

Disclosure: M. Garshick: Horizon Therapeutics, 2; **H. Patel**: Horizon Therapeutics, 3, 12, Stockholder; **a. Kumar**: Horizon Therapeutics, 3, 12, Stockholder; **B. LaMoreaux**: Horizon Therapeutics, 3, 12, Stockholder; **L. Padnick-Silver**: Horizon Therapeutics, 3, 12, Stockholder; **L. Dron**: None; **V. Kalatharan**: None; **V. Verma**: None; **M. Pillinger**: Federation Bio, 2, Fortress Biotech, 2, Hikma, 5, Horizon Therapeutics, 2, 5, Scilex, 2, Sobi, 2.

Abstract Number: 0240

Gout: A Gateway to Chronic Opioid Use?

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Painful gout flares often lead to healthcare visits which, based on prior reports, results in the use of opioid therapy for flare management, despite opioids not being a preferred treatment. The use of opioids for flares raises concerns that uncontrolled gout may serve as a "gateway" to chronic opioid use. The objectives of this study were to: 1) compare the risk of initiating chronic opioid use in Veteran's Health Administration (VHA) patients with and without gout, and 2) to examine determinants of initiating chronic opioid use in gout patients.

Methods: We performed a matched cohort study, identifying patients with gout using national VHA data from 1/1999-1/2015 based on ≥2 ICD-9 codes for gout (274.X). Gout cases were matched to patients without gout (up to 1:10) based on birth year, sex, and VA enrollment year, then followed from the index date (fulfillment of gout algorithm) until the earliest of incident chronic opioid use, death, or 5 years after the index date. Individuals with a fill of an opioid in the year prior to the index date were excluded. Chronic opioid use was defined as ³90 cumulative days' supply with at least 2 dispenses occurring in a 6-month window with no gap >32 days. Associations of gout (vs. non-gout) with chronic opioid use were quantified using a cumulative hazard curve and multivariable Cox proportional hazards regression. Associations between patient characteristics and time-to-initiating chronic opioid use among patients with gout were examined in separate analyses. Covariates in both models included race, comorbidities, body mass index (BMI), and smoking status. In the gout-only model, additional covariates included age, sex, Rheumatic Disease Comorbidity Index (RDCI), time-varying serum urate (SU) control (average SU < 6 mg/dL in prior year) and urate-lowering treatment (ULT; ≥2 fills of ULT with ≥90 days covered by dispensing in prior year).

Table 1. The frequency, crude rate and hazard ratios of opioid exposure leading to chronic use in patients with gout (vs. non-gout) *Covariates include age, index year, race (Black/African American, Other, or Missing vs. White), BMI, smoking status (Former, Current, or Missing vs. Never), chronic lung disease, past myocardial infarction, cardiovascular disease, stroke, hypertension, diabetes, fracture, depression, stomach ulcer or cancer.

	Non-Gout (n=3,608,182)	Gout (n=419,837)
Patient initiating chronic opioid use, n (%)	137,497 (3.8)	28,948 (6.9)
Patient years (pt-yrs) of follow-up	14,951,085	1,749,357
Crude Rate (95% CI), per 1,000 pt-yrs	9.2 (9.1-9.2)	16.5 (16.4-16.7)
Unadjusted HR (95% CI)	Reference	1.78 (1.75-1.80)
Adjusted HR (95% CI)*	Reference	1.36 (1.34-1.39)

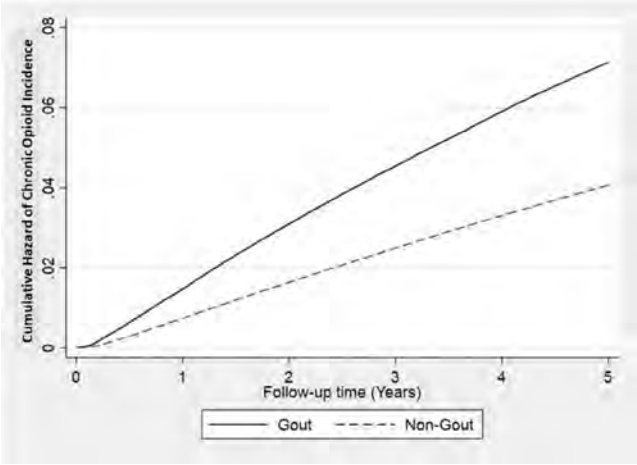


Figure 1. Cumulative hazard of opioid exposure leading to chronic use in patients with gout (vs. non-gout)

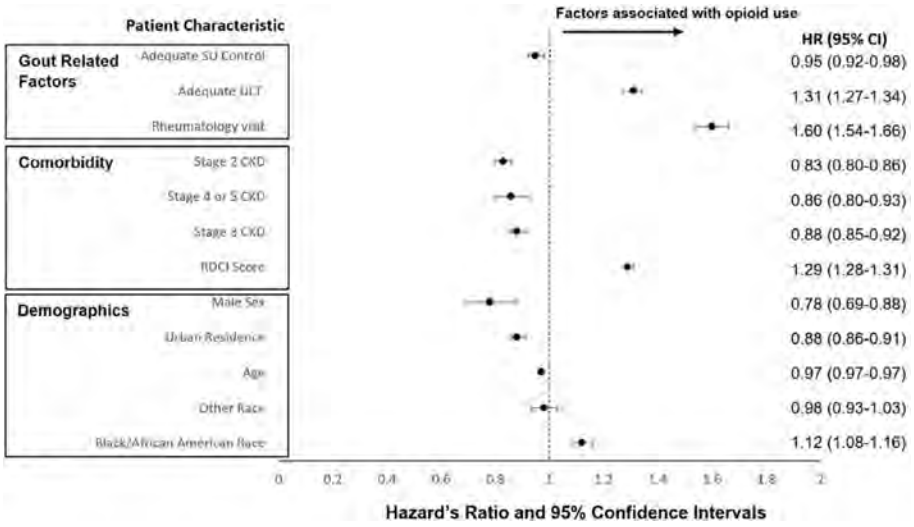


Figure 2. Factors associated with initiating chronic opioid use in patients with gout *All variables in multivariable model with p-value <0.05 are shown in the figure White/Caucasian race was referent value; Other race includes composite of Asian, Native Hawaiian/Pacific Islander, and American Indian; Adequate ULT indicates ≥2 fills of ULT –AND- at least ≥90 days covered by dispensing; Adequate SU control indicates average SU <6 mg/dL; Age reported in years; Rheumatology visit reported as presence of any visit throughout follow up period; RDCI (rheumatic disease comorbidity index) including lung disease, myocardial infarction, other cardiovascular disease, stroke, hypertension, fracture, depression, diabetes mellitus, ulcer or stomach problem, and cancer Abbreviations: urate lowering therapy (ULT), chronic kidney disease (CKD), serum urate (SU)

Results: Over 16.7 million patient-years of follow-up (median follow-up 5 years), 6.9% of gout patients initiated chronic opioids vs. 3.8% of non-gout patients (Fig. 1, Table 1). After adjusting for covariates, patients with gout were significantly more likely than non-gout patients to initiate chronic opioid use (aHR 1.36; 95% CI 1.34 to 1.39). Factors associated with gout-related chronic opioid exposure are summarized in Fig. 2.Among those with gout, factors positively associated with chronic opioid use included Black/African American race, comorbidities, ULT use, and rheumatology encounter. Factors negatively associated with chronic opioid use in those with gout included male sex, CKD, urban residence, SU control, age, and Asian, Native Hawaiian/Pacific Islander, and American Indian race.

Conclusion: In the VHA, we found that patients with gout were 36% more likely than those without gout to initiate chronic opioid use, after accounting for potential confounders, despite opioids not being recommended for management of gout flares. Associations between patient characteristics and time-to-initiating chronic opioid use highlight potential gaps in care,

particularly among underserved Black/African American and rural populations as well as the potential for adequate urate control to reduce the risk of chronic opioid use in gout.

Disclosure: L. Helget: None; **B. England**: Boehringer-Ingelheim, 2, 5; **P. Roul**: None; **H. Sayles**: None; **T. Neogi**: None; **J. O'Dell**: None; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9.

Abstract Number: 0241

Gout Flares During the Initiation and Escalation of Treat-to-Target Urate Lowering Therapy: A Post-hoc Analysis of a Randomized Multicenter Comparative Effectiveness Trial

Austin Barry[1], Lindsay Helget[1], Maria Androsenko[2], Hongsheng Wu[3], Bridget Kramer[1], Jeff Newcomb[4], Mary Brophy[3], Anne Davis-Karim[5], Bryant England[1], Ryan Ferguson[3], Michael Pillinger[6], Tuhina Neogi[7], Paul Palevsky[8], James O'Dell[1] and Ted R Mikuls[9], [1]University of Nebraska Medical Center, Omaha, NE, [2]Department of VA, Newton, MA, [3]Boston VA, Boston, MA, [4]Omaha VA, Omaha, NE, [5]Albuquerque VA, Albuquerque, NM, [6]New York University Grossman School of Medicine, New York, NY, [7]Boston University School of Medicine, Boston, MA, [8]University of Pittsburgh, Pittsburgh, PA, [9]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

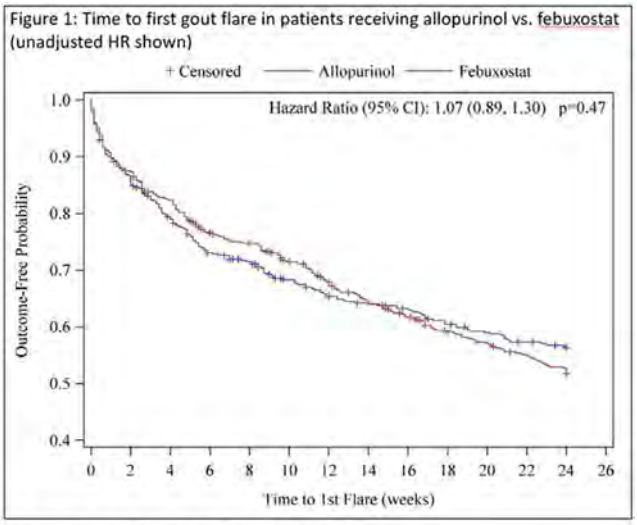
Session Time: 9:00AM–11:00AM

Background/Purpose: Initiating urate-lowering therapy (ULT) in gout is known to precipitate flares, which can lead to decreased adherence and suboptimal outcomes. Until recently, there has been limited data comparing the risk of flare complicating the initiation and escalation of allopurinol and febuxostat, administered as part of a treat-to-target strategy with appropriate anti-inflammatory flare prophylaxis. The STOP Gout study (O'Dell J et al. NEJM Evid, 2022) provided an opportunity to compare flare risk with different agents and to identify predictors for gout flare during ULT initiation and titration.

Methods: The STOP Gout Study was a randomized, double-blind, placebo-controlled, 72-week study comparing allopurinol to febuxostat with a primary outcome of flare occurring during the final study phase (weeks 48-72). This post-hoc analysis evaluated flares occurring during phase 1 (weeks 0-24) when ULT was initiated and titrated towards a serum urate (sUA)

Table 1. ULT dose increases and flares occurring during Phase 1 (weeks 0 to 24).

	Total (N = 940)	Allopurinol (N = 468)	Febuxostat (N = 472)	p-value
ULT dose increases per patient, Median (IQR)	2 (2)	3 (2)	1 (1)	<.001
Total flare rate (95% CI), per 100 pys	217.5 (203.6, 232.3)	209.5 (190.5, 230.4)	225.4 (205.8, 246.9)	0.28
Total flares per patient, Median (IQR)	0 (1)	0 (1)	0 (1)	0.24
Flares per patient, %				0.48
No Flares	55.9	57.9	53.8	
1 Flare	21.6	20.9	22.2	
2-3 flares	16.6	15.0	18.2	
≥4 flares	6.0	6.2	5.7	



goal of < 6 mg/dl (<5 mg/dl if tophi). Flares were assessed at regular intervals and based on patient report. Predictors of flare were examined using multivariable Cox proportional hazards regression with the at-risk period starting at enrollment and extending to the first of: flare, loss to follow-up or withdrawal, death, or the end of phase 1. In addition to ULT (febuxostat vs. allopurinol), baseline covariates included demographics (age, sex, race), gout-specific factors (prophylaxis used, disease duration, tophi, sUA, prior allopurinol use, CRP), and comorbidities (Stage 3 chronic kidney disease [CKD], hypertension, cardiovascular disease [CVD], diabetes, diuretic use, body mass index [BMI], and alcohol use). ULT dose escalation was modeled as a time-varying covariate based on the occurrence of any dose escalation, examining for evidence of ULT-escalation interaction.

Results: Study participants (n=940) were mean age 62.1 years and predominantly male (98.4%); 468 patients received allopurinol, 472 received febuxostat. The mean sUA was 8.5 mg/dL and all participants received prophylaxis (90% colchicine). ULT dose increases and flares experienced during phase 1 are summarized in **Table 1**, with flare rate not differing by treatment. Time to initial flare is shown in **Figure 1**. In multivariable model, there was no association of ULT treatment (aHR 1.14; 95% CI 0.87-1.49), ULT escalation (aHR 1.14; 95% CI 0.90-1.44), prophylaxis type, or comorbidity with flare and no evidence of a ULT-escalation interaction (p=0.66). In the multivariable model, factors associated with increased flare risk during ULT initiation and escalation included younger age (aHR 0.99, 95% CI 0.98-1.00), higher baseline sUA (aHR 1.09; 95% CI 1.01-1.18) and absence of tophi (aHR 0.70; 95% CI 0.54-0.91).

Conclusion: In this analysis of the STOP Gout trial, we observed no difference in flare risk between allopurinol and febuxostat during initiation and titration according to a treat-to-target management strategy using best practice gout flare prophylaxis. Neither the prophylaxis employed, nor the presence of other chronic conditions that frequently accompany gout influenced flare risk following ULT initiation. Few factors were predictive of flare during ULT initiation and titration.

Disclosure: A. Barry: None; **L. Helget**: None; **M. Androsenko**: None; **H. Wu**: None; **B. Kramer**: None; **J. Newcomb**: None; **M. Brophy**: None; **A. Davis-Karim**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **R. Ferguson**: None; **M. Pillinger**: Federation Bio, 2, Fortress Biotech, 2, Hikma, 5, Horizon Therapeutics, 2, 5, Scilex, 2, Sobi, 2; **T. Neogi**: None; **P. Palevsky**: None; **J. O'Dell**: None; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9.

Abstract Number: 0242

Venous Thromboembolism in Patients with Gout in the US

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Venous thromboembolism (VTE), manifested by deep venous thrombosis (DVT) and pulmonary embolism (PE), is a common medical problem with an estimated incidence of 1–2 per 1000 person-years[1]. Patients who develop VTE have high mortality rates of 11–30% per annum[2,3]. While VTE is known to be associated with surgery, immobilization, and cancer (2), some studies have also reported an increased risk of VTE in patients with gout [4-6]. However, there is little nationwide data in the United States (US) on the clinical and economic consequences of VTE in persons with gout. This study examined VTE hospitalizations in patients with gout in the US and estimated their clinical and economic impact.

Methods: The National Inpatient Sample (NIS) is a stratified random sample of all US community hospitals designed to produce national estimates of inpatient utilization, cost, and outcomes. It is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. Unweighted it contains data from around 7 million hospitalizations a year, weighted it estimates around 35 million hospitalizations nationally. We examined all inpatient hospitalizations in the NIS in 2020, the most recent year of available data, with a primary or secondary diagnosis of gout and VTE.

Results: In 2020, there were 32.4 million all-cause hospitalizations in the US, with 19.7 million occurring in persons 45 years or older. Of these, 785,905 hospitalizations occurred in people aged 45 years and over with a diagnosis of gout. This population had a mean age of 71.8 years (95% confidence limits: 71.7–71.9 years) and were more likely to be men (68.8%). Of these hospitalizations, 79,260 (10.1%) also had a concomitant diagnosis of VTE (**Table 1**). As a comparison, only 8.2% of hospitalizations in the general population 45 years or older had a concomitant diagnosis of VTE ($p < 0.001$ compared to persons with gout). Persons with gout and VTE had a mean age of 71.6 years (95% confidence: limit 71.4–71.8 years) and were mostly men (66%, **Table 2**). The average cost of each hospitalization was $76,373 (95% confidence limit $73,343–$79,403), with a total annual national cost of over $6.1 billion.

Conclusion: One out of 10 hospitalizations in persons with gout have a concomitant diagnosis of VTE, with considerable clinical and economic consequences. VTE occurred more frequently in the presence of gout in hospitalized patients over the age of 45 years (1/10 vs. 1/12 patients) and resulted in considerable economic burden. These findings suggest that

Table 1. Venous thromboembolism in gout versus all-cause hospitalizations among men and women 45 years of age or older.

Age (years)	Gender	Hospitalizations with a Diagnosis of Gout N	Hospitalizations with VTE in Persons with Gout n (%)	All-cause Hospitalizations N	All-cause Hospitalizations with VTE n (%)
45-64	Male	165,325	16,710 (10.1%)	416,3365	323,625 (7.8%)
	Female	45,205	5150 (11.4%)	3,519,950	280,900 (8.0%)
≥65	Male	375,685	35,600 (9.5%)	5,756,550	473,905 (8.2%)
	Female	199,650	21,800 (10.9%)	6,300,300	547,550 (8.7%)
All patients ≥45		785,905	79,260 (10.1%)	19,741,255	1,626,055 (8.2%)

VTE, venous thromboembolism.

Table 2. Hospitalizations with a gout diagnosis in patients 45 years of age or older with and without venous thromboembolism.

	Hospitalizations with a Diagnosis of Gout (N=785,905)	Gout Hospitalizations with a VTE (N=79,260)
Age, mean (95% CI)	71.8 (71.7–71.9)	71.6 (71.4–71.8)
Male, n (%)	541,010 (68.8%)	52,310 (66.0%)
Length of hospitalization, days, mean (95% CI)	5.8 (5.7–5.8)	6.4 (6.3–6.5)
Cost of hospitalization, USD, mean (95% CI)	72,533 (70,584–74,483)	76,373 (73,344–79,403)
Medicare	572,575 (72.5%)	59,085 (70.5%)
Medicaid	48,495 (6.1%)	4975 (5.9%)
Private insurance	131,605 (16.7%)	12,305 (14.7%)

CI, confidence interval.

VTE prevention measures and patient education on VTE signs/symptoms may be of particular importance in patients with gout.

References

1. Cushman M, et al. Am J Med 2004;117:19-25.
2. Naess IA, et al. *J Thromb Haem* 2007;5:692-9.
3. Heit JA, et al. *Arch Intern Med* 1999;159:445-53.
4. Sultan AA, et al. *CMAJ* 2019;191:E597-603.
5. Kubota Y, et al. *Thromb Res* 2016;144:144-8.
6. Li L, et al. *Rheumatology (Oxford)* 2020;59:1099-107.

Disclosure: A. Mithal: None; **M. Sehgal**: None; **B. LaMoreaux**: Horizon Therapeutics, 3, 12, Stockholder; **G. Singh**: Horizon Therapeutics, 5.

Abstract Number: 0243

Decreased Incidence of Gout After Kidney Transplant over the Last Decade: An Analysis from a Large Academic Renal Transplant Center

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout has been associated with high rates of morbidity and mortality in kidney transplant (KT) patients with increased bone destruction and associated cardiovascular and kidney disease progression after transplantation. The incidence of gout after transplant has been reported to be 7-13%. [1, 2] Cyclosporine, which has been the mainstay immunosuppressive therapy after KT, has been associated with hyperuricemia and gout; however its use in KT has markedly decreased. [3] There is a paucity of studies comparing the incidence of gout and hyperuricemia in KT patients

Table 1. Demographics of KT patients.

Variables	Number of Patients n=1914, (%)
Gout at any point of time	477 (25%)
Male	1159 (60.6%)
Deceased	262 (13.7%)
Race	
African American	1010 (53%)
Caucasian	794 (41%)
Asian	54 (2.8%)
Latino	44 (2.3%)
Immunosuppression	
Tacrolimus	1904 (99%)
Cyclosporine	78 (4%)
Mycophenolate Mofetil	1905 (99.5%)
Azathioprine	117 (6%)

Table 2. Risk factors associated with gout in patients diagnosed after KT.

Variables	Number of Patients n=71, (%)
Hypertension	71 (100%)
Hyperlipidemia	59 (83%)
Diuretics	62 (87%)
BMI ≥ 30	62 (87%)
Uric acid ≥ 7	35 (49%)
Diabetes Mellitus	52 (73%)

since the adoption of newer immunosuppressive therapies and overall less to no use of cyclosporine. We hypothesize that KT recipients have lower frequencies in incidence of gout with regimens excluding the use of cyclosporine.

Methods: Our population consisted of all patients ages 18 and above who received a KT at our institution between 01/01/2013 and 01/01/2023. We excluded patients with history of gout prior to transplant. Using ICD-10 codes and our institution's medical records informatics software, we identified patients that were diagnosed with gout after receiving KT. Patient demographics and immunosuppressive therapies prior to diagnosis of gout were analyzed. Categorical variables were reported as frequency percentages.

Results: A total of 1914 patients underwent KT since 2013. A majority (60.6%) of the source population for the study were male (Table 1). Out of 1914 patients, 477 patients (25%) were identified to have a concurrent diagnosis of gout at any point of time (before or after KT). Most of the patients developing gout at any point were male (72%), and 228 identified as African American (47.8%). Only 71 out of the remaining 1437 gout-free patients (4.9%) had a new diagnosis of gout after KT. Prior to developing gout, 50 of these 71 patients were on tacrolimus, 2 on cyclosporine, 7 on mycophenolate mofetil, and 2 on azathioprine. Hyperuricemia above 7 mg/dl was appreciated in only 35 out of 71 of these patients (Table 2).

Conclusion: In a large population of patients receiving KT, our study reports an incidence of gout comparable to that of the general population and lower than historical reports in KT patients. Most cases of gout after transplant were seen in patients on tacrolimus, however this is likely a reflection of the overall decrease in use of cyclosporine in general. Further studies are warranted to investigate and characterize the burden of disease associated with gout cases associated with KT over the last decade.

1. Abbott KC, Kimmel PL, Dharnidharka V, Oglesby RJ, Agodoa LY, Caillard S. New-onset gout after kidney transplantation: incidence, risk factors and implications. *Transplantation*. 2005;80(10):1383-1391. doi:10.1097/01.tp.0000188722.84775.af

Baroletti S, Bencivenga GA, Gabardi S. Treating Gout in Kidney Transplant Recipients. Progress in Transplantation. 2004;14(2):143-147. doi:10.1177/152692480401400208
Tedesco D, Haragsim L. Cyclosporine: a review. J Transplant. 2012;2012:230386. doi:10.1155/2012/230386

Disclosure: N. Panchani: None; **A. Gaffo**: None; **V. Kumar**: None.

Abstract Number: 0244

Efficacy and Safety of AR882, a Selective Uric Acid Transporter 1 (URAT1) Inhibitor, in Gout Patients with Various Baseline Characteristics Following 12-Week Treatment in Patients

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: AR882 is a novel, potent, and selective URAT1inhibitor in development for the treatment of gout and tophaceous gout. AR882-202 was a global, multi-center, randomized, double-blinded, 12-week, placebo-controlled phase 2b trial to evaluate the safety and efficacy of AR882 versus placebo in patients with gout. Here, we report the analysis of the efficacy and safety based on various demographics and baseline characteristics.

Methods: The trial recruited 140 gout patients 18 to 75 years of age with eGFR >30 mL/min across 20 sites in the US, Australia, and Taiwan. Subjects were recruited from the US (15 sites), Australia (2 sites) and Taiwan (3 sites), and were randomized into one of three treatment groups at a 1:1:1 ratio. Blood samples were collected every 2 weeks up to 12 weeks to

Table 1.Demographics and baseline characteristics

	Australia (N=30)	Taiwan (N=23)	US (N=87)	All subjects (N=140)
Age (mean, range)	52 (31,73)	46 (24,71)	58 (32,73)	56 (24,73)
Sex				
Female	0	0	9 (10%)	9 (6.4%)
Male	30	23	78 (90%)	131 (93.6%)
Race				
Asian	9 (23%)	23 (100%)	9 (10%)	39 (28%)
Black	0	0	21 (24%)	21 (15%)
White	23 (77%)	0	58 (67%)	79 (56%)
Pacific islander	0	0	3 (3.4%)	3 (3.4%)
Weight (kg)	91.4 (14.9)	84.1 (10.0)	101.3 (18.4)	96.38 (17.8)
BMI (kg/m^2)	30.0 (4.30)	28.7 (3.62)	32.7 (5.05)	31.5 (4.9)
Baseline sUA (mg/dL)	8.48 (1.12)	8.78 (1.24)	8.70 (1.41)	8.61 (1.29)
eGFR (mL/min)				
>=90	22 (73%)	14 (67%)	55 (63%)	92 (65.7%)
60-89	7 (23%)	7 (30%)	23 (26%)	37 (26.4%)
<60	1 (3.3%)	1 (4.8%)	9 (10%)	11 (7.9%)

Table 2. Patient comorbidities across regions

Comorbidities	Australia (n=30)	Taiwan (n=23)	US (n=87)	All subjects (n=140)
Hypertension	4 (13%)	7 (30%)	55 (63%)	66 (47%)
Hyperlipidemia /Hypercholesterolemia	6 (20%)	9 (39%)	34 (39%)	49 (35%)
Chronic kidney disease	8 (27%)	8 (35%)	32 (37%)	48 (34%)
Arthritis (other than gout)	3 (10%)	4 (17%)	25 (29%)	32 (23%)
Diabetes	3 (10%)	2 (9%)	22 (25%)	27 (19%)
Cardiovascular disease	3 (10%)	3 (13%)	15 (17%)	21 (15%)
Lung disease	3 (10%)	1 (4%)	12 (14%)	16 (11%)
Liver disease	2 (7%)	3 (13%)	2 (2%)	7 (5%)

Table 3. Response rate of sUA lowering in patients across regions (per-protocol population)

Region	Treatment	Group N	<6 mg/dL, %	<5 mg/dL, %
Australia	Placebo	6	0	0
	50 mg	9	89	78
N=27	75 mg	12	100	92
Taiwan	Placebo	9	0	0
	50 mg	5	80	40
N=22	75 mg	8	88	88
US	Placebo	27	0	0
	50 mg	22	73	41
N=67	75 mg	18	83	72

monitor sUA levels and safety measures. Efficacy endpoints included the percent of patients who reached a sUA < 6, < 5 mg/dL and lower. Safety data, including vital signs and electrocardiograms, were collected throughout the study.

Results: Baseline characteristics of enrolled participants are illustrated in **Table 1**. The mean baseline sUA level was 8.6 (±1.3) mg/dL and was similar across regions (8.5-8.8 mg/dL), while mean body weights and BMI showed slight regional differences.

Common comorbidities in participants included hypertension, hyperlipidemia, chronic kidney disease, followed by arthritis, diabetes, and cardiovascular disease. The US population had a higher rate of comorbidities than those in Australia and Taiwan (**Table 2**).

In the intent-to-treat population, in the 75 mg group 82% and 73% of patients achieved sUA < 6 and < 5 mg/dL, respectively, and in the 50 mg group, 71% and 45% of patients achieved sUA levels < 6 and < 5 mg/dL, respectively. In the per-protocol population, in the 75 mg group 89% and 82% achieved sUA levels < 6 and < 5 mg/dL, respectively, and in the 50 mg group 78% and 50% achieved sUA levels < 6 and < 5 mg/dL, respectively. Patients in Australia and Taiwan showed slightly higher response rates than those in the US (**Table 3**), likely attributable to the difference in body weight and BMI. Patients with eGFR in the 60-89 mL/min range showed similar response rates to those with eGFR > 90 mL/min, and greater response rates than those with eGFR < 60 mL/min. There were no serious adverse events in AR882 treated patients. The most frequently reported adverse event was gout flare occurring in 30% of patients overall with similar distribution among placebo and AR882 treatment groups. Mild or moderate adverse events including diarrhea, headache, and upper respiratory infection were observed. None of the AEs led to discontinuation of investigational product.

Conclusion: 12-week treatment of AR882 demonstrated safe and efficacious profiles in gout patients with various demographics and baseline characteristics. AR882 may offer improved efficacy and better safety compared to existing therapies in the treatment of patients with gout including those with severe or refractory disease across various demographics and comorbidities.

Disclosure: J. Wei: Abbvie, 2, 5, 6, Amgen, 5, AstraZeneca, 6, BMS, 2, 5, 6, Celgene, 2, Chugai, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 5, 6, Gilead, 5, GSK, 2, 5, Janssen, 2, 5, 6, Novartis, 2, 5, Pfizer, 2, 5, 6, Sanofi-Aventis, 2, SUN pharma, 5, TSH Taiwan, 2, UCB pharma, 2, 5; **R. Fleischmann**: AbbVie, 1, 2, 5, Amgen, 1, 2, 5, Bristol Myers Squibb, 1, 2, 5, Eli Lilly, 1, 2, 5, Galapagos, 1, 2, 5, Galvani, 1, 2, 5, Gilead, 1, 2, 5, GlaxoSmithKline, 1, 2, 5, Janssen, 1, 2, 5, Novartis, 1, 2, 5, Pfizer, 1, 2, 5, UCB, 1, 2, 5, Vyne, 1, 2, 5; **s. Morris**: Arthrosi Therapeutics, 3; **V. Hingorani**: None; **E. Polvent**: Arthrosi Therapeutics, 3; **Z. Shen**: Arthrosi therapeutics, 3; **S. Yan**: Arthrosi Therapeutics, 3; **L. Yeh**: Arthrosi Therapeutics, 3; **R. Keenan**: Arthrosi Therapeutics, 3.

Abstract Number: 0245

Impact of Combined Intervention with Clinical Nurse Specialist in the Management of Cardiovascular Risk in Patients with Gout

Claudia Maria Gomez[1], Patricio Cardoso Peñafiel[1], Jose Antonio Angel-Sesmero[1], Marta Novella-Navarro[2] and Enrique Calvo-Aranda[1], [1]Hospital Universitario Infanta Leonor, Madrid, Spain, [2]Hospital Universitario La Paz, Madrid, Spain

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is associated with increased cardiovascular risk (CVR). Traditional CVR factors (CVRF) are frequently present in patients with gout, further worsening the prognosis. Several studies have shown that clinical nurse specialist (CNS) contributes effectively to the management of gout. To analyze the detection of CVRF in patients with gout in a rheumatology consultation with CNS and to evaluate short-term changes after a targeted approach.

Methods: Patients with gout according to ACR/EULAR 2015 criteria referred from Primary/Specialized Care due to poor control of the disease. At the first visit, demographic and clinical variables were collected: age, sex, smoking, alcohol, duration of gout, tophi, comorbidities, urate-lowering treatment (ULT) and concomitant drugs. A blood test and review of previous were performed, as well as measurement of blood pressure (BP), weight and abdominal circumference. Nurse-managed calls were made to monitor home measurements and check adherence/tolerance to pharmacological (start/adjustment of ULT, antihypertensive, lipid-lowering and antidiabetic drugs) and non-pharmacological approach (gout education, dietary/lifestyle recommendations) initiated, according to EULAR recommendations for CVR management in rheumatic diseases. We count on multidisciplinary collaboration with other specialists. After 6 months, an in-person visit was made with the same measurements to determine potential changes. A descriptive analysis of the sample was performed. Wilcoxon test was used to evaluate the variation in the parameters studied. The outcome variable was determined as improvement vs no improvement of the dependent variable. χ^2 and Mann Whitney U tests were used to evaluate the differences.

Results: Forty patients who met the inclusion criteria were included. Ninety-eight percent were male, with a median age of 66 (58-75) years, severe gout (83% tophaceous, median duration 7 years) and marked presence of CVRF (hypertension 78%, dyslipidemia 55%, smoking 23%, diabetes 23%), some of them previously undetected (10% hypertensive, 3% dyslipidemic, 3% diabetic), and related comorbidities (ischemic heart disease 8%, cerebrovascular disease 5%, chronic kidney disease 20%). Fifty-five percent were not taking ULT and 53% used NSAIDs on a regular basis. At the first visit, ULT was started/adjusted in 95% of patients, antihypertensive in 15%, lipid-lowering drugs in 13%, and anti-diabetes drugs in 8%. At 6 months, there was a significant improvement in sUA and BP, and a non-statistically significant weight reduction (Table). Serum uric acid (sUA) target was achieved in 93% of patients (37/40 < 6 mg/dl, 29/40 < 5 mg/dl). The use of NSAIDs was reduced to 5%. Four out of 9 smokers quit. Systolic BP improved in 73% of patients and diastolic BP in 70%. Dietary

Table. Anthropometric, blood pressure and serum uric acid changes 6 months after the first visit. All variables expressed as median/IQR. BP: blood pressure; sUA: serum uric acid

	Basal	6 months	p
Weight (kg)	87 (77.3-99)	85.4 (77-96.3)	0.79
Abdominal circumference (cm)	107 (102-116)	108 (103-116)	0.81
Systolic BP (mm Hg)	151 (133.3-162.5)	142.5 (124.8-155)	0.02
Dyastolic BP (mm Hg)	88.5 (76.3-95)	78.5 (70-86.8)	0.01
sUA (mg/dl)	7.7 (6.6-8.8)	4.5 (4.1-5.2)	<0.01

and habit modifications, therapeutic adjustments and multidisciplinary care were significantly associated with improved BP (p=0.02).

Conclusion: In patients with difficult-to-treat gout and high CVR, combined intervention with CNS allows substantial short-term changes in CVRF, drastic reduction in NSAID consumption and a high percentage of success in achieving sUA target.

Disclosure: C. Gomez: None; **P. Cardoso Peñafiel**: None; **J. Angel-Sesmero**: None; **M. Novella-Navarro**: Galapagos, 6, Janssen, 5, 6, Lilly, 5, 6, UCB, 5, 6; **E. Calvo-Aranda**: None.

Abstract Number: 0246

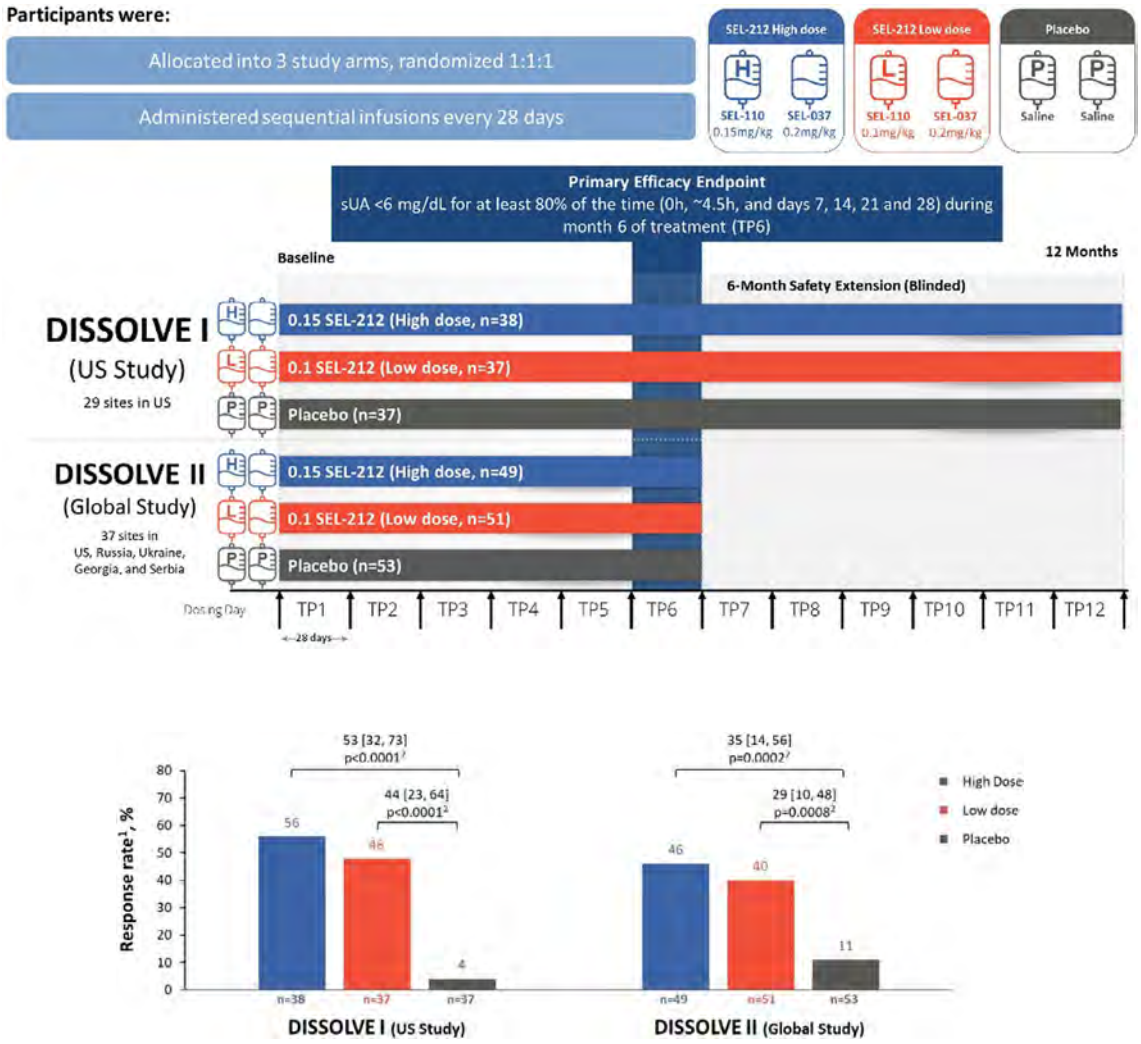
Safety & Efficacy of SEL-212 in Patients with Gout Refractory to Conventional Treatment: Primary Outcomes from Two Randomized, Double Blind, Placebo-Controlled, Multicenter Phase 3 Studies

Herbert Baraf[1], Alan Kivitz[2], Sheri Rhodes[3], Sheldon Leung[4], Olu Folarin[4], Tania Gonzalez-Rivera[5], Joanna Sobierska[5], Jacquie Christie[5], Anand Patel[6], Wesley DeHaan[4], Rehan Azeem[4] and Peter Traber[7], [1]The Center for Rheumatology and Bone Research, George Washington University, Rheumatology, Bethesda, MD, [2]Altoona Center for Clinical Research, Duncansville, PA, [3]Selecta Biosciences, Atlanta, GA, [4]Selecta Biosciences, Inc., Watertown, MA, [5]Swedish Orphan Biovitrum (Sobi), Stockholm, Sweden, [6]Pioneer Research Solutions, Houston, TX, [7]Selecta Biosciences, Gladwyne, PA

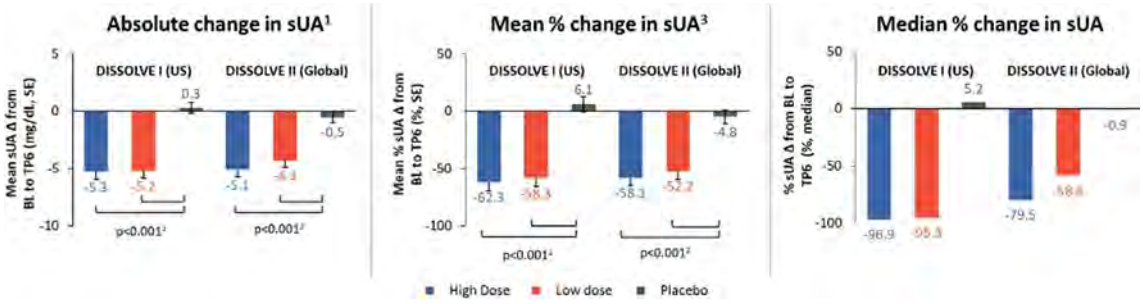
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In patients with refractory gout, the inability to maintain serum uric acid (sUA) levels < 6 mg/dL leads to severe clinical manifestations for which uricase-based therapies can be highly effective, though also immunogenic.[1] SEL-212 is a once-monthly, novel 2-component, uricase-based infusion therapy being investigated in patients with refractory gout. SEL-212 consists of an infusion of tolerogenic nanoparticles containing rapamycin (SEL-110) followed by pegadricase (SEL-037).[2] DISSOLVE I and II (D1 and D2, respectively) evaluated the safety and efficacy of SEL-212 in adults with refractory gout.

Methods: D1 (US) and D2 (Global), were placebo-controlled, double-blind, randomized clinical trials that evaluated two dose levels of SEL-110 (0.15 mg/kg [high-dose] or 0.1 mg/kg [low-dose]) prior to SEL-037 (0.2 mg/kg) infusion. Participants were enrolled if they had ≥ 3 gout flares within 18 months prior to screening or ≥ 1 tophus or a current diagnosis of gouty arthritis, failed to normalize sUA and control symptoms with any xanthine oxidase inhibitor, and were not previously exposed to a pegylated uricase-based therapy. Participants were randomized 1:1:1 between the two doses of SEL-212 and placebo administered intravenously every 28 days for 6 treatments. D1 participants continued in a 6-month blinded extension phase under the initial treatment conditions (Fig. 1). The primary endpoint was defined as the percentage of participants who



DISSOLVE I & II study design.



achieved and maintained sUA < 6 mg/dL for ≥ 80% of the sixth treatment period (TP6). Safety and tolerability were assessed through monitoring of adverse events (AEs).

Results: 112 participants (96% male, 66% ≥ 50 years) were enrolled in D1 and 153 (97% male, 72% ≥ 50 years) in D2. Response rates in all treatment groups were significantly different from placebo ($p \leq 0.0008$), with 56% and 46% of participants responding in the high-dose group and 48% and 40% in the low-dose group for D1 and D2, respectively (Figure 2). The response rates in participants aged ≥ 50 years were 65% and 47% in the high-dose groups and 47% and 44% in the

low-dose groups for D1 and D2, respectively ($p \leq 0.0026$ vs placebo). Across all participants in the treatment groups, sUA levels were significantly reduced from baseline ($p < 0.001$ vs placebo) at TP6 (Figure 3). The safety profile of SEL-212 was favorable, with 3.4% and 4.5% of participants experiencing infusion reactions in the high and low-dose groups, respectively. Reports of gout flares were comparable between treatment groups and placebo. Six participants (3.4%) in the pooled active treatment groups experienced treatment-related serious AEs (n=4 anaphylaxis, n=2 gout flares).

Conclusion: In the DISSOLVE trials, once-monthly treatment with SEL-212 demonstrated statistically significant response rates and reductions in sUA versus placebo. The safety profile of SEL-212 was consistent with that of uricase therapies. Targeted immunomodulation with SEL-212 has the potential to provide a new uricase-based treatment option for patients with gout refractory to conventional therapies.

1. Edwards NL. *Arthritis Rheum* 2008;58(9):2587-90.
2. Sands E, *et al. Nat Commun* 2022;13:272.

Primary efficacy endpoint. (1) The primary endpoint was defined as the percentage of participants who achieved and maintained sUA < 6 mg/dL for at least 80% of the sixth treatment period (TP6). Subjects who dropped from study due to stopping rule, AE, and COVID were considered non-responders. Percentages shown are averaged over multiple imputed datasets for missing sUA for withdrawal of consent, lost to follow-up, and other as per FDA guidance. (2) Difference vs placebo [97.5% CI] and p-value versus placebo group for each treatment group are indicated above each bracket.

Serum uric acid reduction from baseline to treatment period six (TP6). (1) Reduction of mean sUA as computed by subtracting the Baseline (BL) sUA level from the mean sUA during Treatment Period 6 (TP6) defined as the area under the time curve divided by the corresponding time interval. (2) Analysis using ANCOVA model with reduction or percent reduction of mean sUA at TP6 from baseline as dependent variable and randomization stratum and baseline sUA as covariates. Missing values of change or percent change from baseline were multiple imputed by using the Recursively Partitioned Mixture Model. The means of treatment groups are pooled estimates after multiple imputation and 2-sided p-values. (3) Percent reduction mean sUA as computed by subtracting Baseline (BL) sUA level from the mean sUA during TP6 divided by the Baseline and reported as either absolute difference or percent difference.

Disclosure: H. Baraf: Horizon Pharmaceuticals, 5, 6, Swedish Orphan Biovitrum (Sobi), 5, 6; **A. Kivitz**: AbbVie, 6, Amgen, 6, 11, Chemocentryx, 1, Eli Lilly, 6, Fresenius Kabi, 2, Genzyme, 2, Gilead, 2, 11, GlaxoSmithKlein (GSK), 2, 6, 11, Grunenthal, 2, Horizon, 1, 2, Janssen, 1, 2, Novartis, 4, 11, Pfizer, 2, 6, 11, Selecta, 2, Synact, 2, Takeda, 2, UCB, 1, 6; **S. Rhodes**: Selecta Biosciences, 3, 11; **S. Leung**: Selecta Biosciences, 3, 11; **O. Folarin**: Selecta Biosciences, 3, 11; **T. Gonzalez-Rivera**: Swedish Orphan Biovitrum (Sobi), 3; **J. Sobierska**: Swedish Orphan Biovitrum (Sobi), 3; **J. Christie**: GlaxoSmithKlein(GSK), 11, Swedish Orphan Biovitrum (Sobi), 3; **A. Patel**: Lexicon Pharmaceuticals, 6; **W. DeHaan**: Selecta Biosciences, 3, 11; **R. Azeem**: Selecta Biosciences, 3, 11; **P. Traber**: Selecta Biosciences, 3, 11.

Abstract Number: 0247

Risk of Incident Gout Following Exposure to Recombinant Zoster Vaccine in Adults Aged ≥50 Years in the United States

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[4]CVS Health, Blue Bell, PA, [5]Humana Healthcare Research, Inc., Louisville, KY, [6]Optum, Baltimore, MD, [7]Carelon Research, Boston, MA, [8]GlaxoSmithKline, Rockville, MD, [9]GlaxoSmithKline, Wavre, Belgium

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
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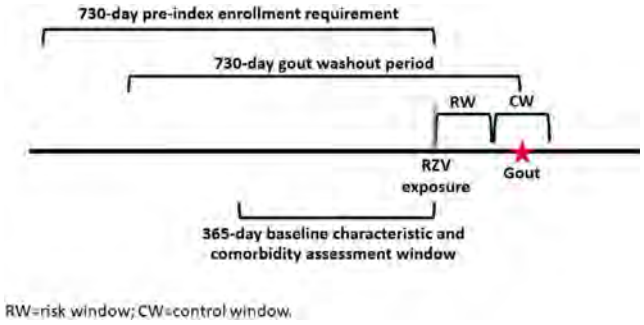
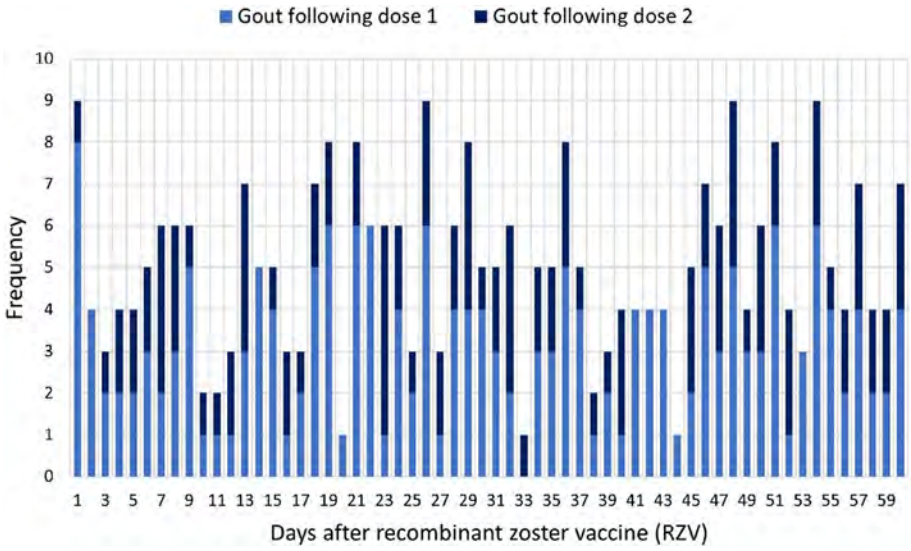
Session Time: 9:00AM–11:00AM

Background/Purpose: Pre-licensure clinical trials for recombinant zoster vaccine (RZV) identified more frequent gout diagnoses among recipients of RZV than placebo; however, these trials were not powered to assess the statistical significance of these differences. The current real-world safety study used administrative claims data from 4 national insurers and 1 regional insurer in the FDA's Sentinel System, a large, distributed data network, to assess whether RZV is associated with an increased risk of new-onset gout among US individuals ≥50 years of age

Methods: This retrospective study used a self-controlled risk interval (SCRI) design (Figure 1). We included health plan members ages ≥50 with RZV exposure followed by incident gout within 60 days: days 1-30 defined the risk window (RW) and days 31- 60 defined the control window (CW). We required 730 days of medical and drug coverage, allowing 45-day gaps, prior to RZV exposure, and 60 days of coverage, with no gaps, after RZV exposure. A conditional Poisson model estimated the risk ratio (RR) of gout in the RW versus CW.



RW=risk window; CW=control window.



Type of analysis	CW length		Total case count	No. cases in RW (%)	No. cases in CW (%)	RR[a] (95% CI)
	Mean (SD)	Median (IQR)				
Primary Analysis						
Includes dose 1 and dose 2[c]	30.0[b] (0.39)	30.0 (30.0 - 30.0)	302	153 (50.7)	149 (49.3)	1.03 (0.81 - 1.29)
Secondary Analysis						
Includes dose 1 and dose 2; 30-day CW for both doses	30 (fixed)	30 (fixed)	302	153 (50.7)	149 (49.3)	1.03 (0.81 - 1.30)
Sensitivity Analysis						
Includes dose 1 and dose 2; Restricted to 2-dose recipients with 60 – 183 days between doses	30 (inherent)	30 (inherent)	235	120 (51.1)	115 (48.9)	1.04 (0.80 - 1.36)
Dose 1 subset	30 (fixed)	30 (fixed)	191	99 (51.8)	92 (48.2)	1.08 (0.80 - 1.45)
Dose 2 subset	30 (fixed)	30 (fixed)	111	54 (48.6)	57 (51.4)	0.95 (0.64 - 1.40)
Seasonality-adjusted primary analysis[d]	30.0[b] (0.39)	30.0 (30.0 - 30.0)	302	153 (50.7)	149 (49.3)	1.03 (0.82 - 1.30)
COVID-19 sensitivity for primary analysis	30.0[b] (0.39)	30.0 (30.0 - 30.0)	293	149 (50.9)	144 (49.1)	1.03 (0.82 - 1.31)

RW=risk window, CW=control window, RR=risk ratio
aRR of gout in the post-RZV RW relative to the CW using conditional Poisson regression.
bMean CW length is less than 30 days but rounds to 30.0.
cDose 1 CW censored at receipt of dose 2
dThe seasonality-adjusted analysis uses the same analytic cohort as the primary analysis, but the offset term of the conditional Poisson model accounts for background gout trends around the calendar date of RZV receipt.

The exposure was receipt of at least one of the two-dose RZV regimen between January 2018 through December 2019, identified by Current Procedural Terminology (CPT) or National Drug Code (NDC). Incident gout was defined as a gout diagnosis followed by a dispensing of allopurinol, colchicine, probenecid, or febuxostat within 3 months, with no gout diagnoses or medications in the 730 days prior. Baseline characteristics (e.g., comorbidities) were evaluated in the 365 days prior to the RZV date.

The primary analysis assessed the risk of new-onset gout following any RZV dose, censoring the dose 1 CW at dose 2 receipt. The secondary analysis assumed uniform 30-day CWs. Sensitivity analyses evaluated dose 1- and dose 2-specific risks, risk among patients compliant with recommended dose spacing of 60–183 days, adjustment for seasonality, and restriction to the pre-COVID era (excluding cases after December 1, 2019).

Results: Among 461,323 members with at least one RZV dose, 302 were eligible for the SCRI analysis, with evidence of new-onset gout within 60 days. The analytic cohort had a mean age of 72.5 years (SD = 8.3); 66% (n=199) were male. The most common comorbidities were diabetes (40%; n=120), chronic kidney disease (38%; n=115), and ischemic heart disease (28%; n=83). Figure 2 illustrates the frequency of gout events for each day of follow-up after dose 1 or 2.

In the primary analysis, 153 (50.7%) gout cases occurred during the RW and 149 (49.3%) during the CW with a RR of 1.03 (95% confidence interval [CI] 0.81-1.29). In the secondary analysis of fixed 30-day CWs, the RR was 1.03 (95% CI: 0.81-1.30). All sensitivity analyses had consistent results, with no statistically significant association of RZV with incident gout (Table 1).

Conclusion: This retrospective safety study found no evidence of a statistically significant increased risk of gout in the 30 days following RZV vaccination relative to a 30-day subsequent control window among a large, diverse national patient population of adults ≥50 years of age.

Illustration of self-controlled risk interval analysis study design for assessment of the risk of new-onset gout following recombinant zoster vaccine (RZV) exposure.

Frequency of gout events on each day of follow-up after recombinant zoster vaccine (RZV) exposure among patients aged ≥50 years with incident gout following RZV dose 1 or dose 2.

Results of primary, secondary, and sensitivity analyses of the risk of new-onset gout following recombinant zoster vaccine (RZV) exposure.

Disclosure: S. Kluberg: None; **A. Simon**: None; **S. Alam**: None; **A. Peters**: None; **C. Horgan**: None; **D. Li**: None; **É. Moyneur**: Pfizer, 2; **R. Platt**: None; **C. McMahill-Walraven**: None; **D. Djibo**: CVS Health, 3, 11; **Q. Ma**: None; **M. Selvan**: None; **C. Pernar**: None; **N. Ziyadeh**: None; **A. Jamal-Allial**: None; **K. Daniels**: AbbVie/Abbott, 7, AstraZeneca, 7, GlaxoSmithKlein(GSK), 7, Pfizer, 7; **O. Spence**: GlaxoSmithKlein(GSK), 3, 12, stocks; **D. Oraichi**: GSK, 3, 12, Stocks; **H. Seifert**: GlaxoSmithKlein(GSK), 3, 11; **V. Franck**: GlaxoSmithKlein(GSK), 3, 11; **S. Gamble**: GlaxoSmithKlein(GSK), 3, 11, Supernus Pharmaceuticals, Inc, 11; **H. Yun**: GlaxoSmithKlein(GSK), 3.

Abstract Number: 0248

In-hospital Treatment, Secondary Prevention, and Mortality After First-ever Acute Myocardial Infarction in Patients with Gout

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with gout are at increased risk of acute myocardial infarction (AMI). However, the clinical course, secondary prophylaxis and mortality after AMI has not been previously studied. The aim of this study is to investigate the in-hospital treatment, secondary prevention, and all-cause and cardiovascular disease (CVD)-related mortality after the first-ever AMI in patients with gout compared to the general population.

Methods: Using data from regional and national population-based registers, we identified all patients in Western Sweden with a diagnosis of gout at both primary and specialty care and a first-ever AMI in the period 2006-2016. Up to five individually matched controls with a first-ever AMI (matched on sex and admission year) were identified as comparators. Follow-up started at the date of admission for the first-ever AMI and ended at death, emigration, or 365 days of follow-up after the AMI, whichever occurred first. The in-hospital treatment and secondary prevention in gout cases and controls were compared by using logistic regression analysis with adjustments for age. Cox regression analysis was used to assess the 1-year mortality with adjustments for age, baseline comorbidities, and medication within 6 months before the start of follow-up.

Results: We identified 1,000 patients with gout and a first-ever AMI (men, 72.7%; mean age, 70.0 years) and 4,740 matched general population comparators (men, 73.5%; mean age, 71.5 years). At admission, patients with gout hade significantly more comorbidities (Table 1). The in-hospital treatment differed significantly between cases and controls. Patients with gout were more likely to receive treatment with diuretics and continuous positive airway pressure (CPAP), and less likely to undergo coronary angiography, percutaneous coronary intervention (PCI), or any primary reperfusion (Table 2). At discharge, patients with gout were less often prescribed statins, and more often

Table 1. Patient characteristics and comorbidities in gout patients and general population comparators at admission for the first-ever AMI.

	Gout cases N=1,000	Controls[§] N=4,740	p-value	OR* (95%CI)
Men, N (%)	727 (72.7)	3,485 (73.5)	0,5925	
Age, mean (SD), years	70.0 (11.6)	71.5 (11.3)	0,0001	
Comorbidities, N (%)				
CHD	284 (28.4)	978 (20.6)	<.0001	1.5 (1.3-1.7)
Hypertension	823 (82.3)	2,661 (56.1)	<.0001	3.6 (3.1-4.3)
Diabetes	309 (30.9)	857 (18.1)	<.0001	2.0 (1.7-2.3)
Obesity	271 (27.1)	793 (16.7)	<.0001	2.0 (1.7-2.3)
Hyperlipidemia	404 (40.4)	1,271 (26.8)	<.0001	1.9 (1.6-2.1)
Renal disease	225 (22.5)	405 (8.5)	<.0001	3.1 (2.6-3.7)
Heart failure	207 (20.7)	406 (8.6)	<.0001	2.7 (2.2-3.3)
Cardiomyopathy	12 (1.2)	24 (0.5)	0.01	2.4 (1.2-4.9)
Atrial fibrillation	212 (21.2)	466 (9.8)	<.0001	2.4 (2.0-2.9)
Smoking	185 (18.5)	1,017 (21.5)	0.03	0.9 (0.7-1.1)
Alcoholism	47 (4.7)	93 (2.0)	<.0001	2.7 (1.9-3.9)
Cerebrovascular disease	205 (20.5)	598 (12.6)	<.0001	1.7 (1.4-2.0)
Thromboembolic disease	19 (1.9)	70 (1.5)	0.33	1.2 (0.7-2.1)
Malingnancy	95 (9.5)	366 (7,7)	0.06	1.2 (1.0-1.6)
Atherosclerotic disease	113 (11.3)	252 (5.3)	<.0001	2.2 (1.7-2.7)
Medication, N (%)				
CVD drugs[¤]	733 (73.3)	2,323 (49.0)	<.0001	2.9 (2.5-3.3)
Anticoagulants	462 (46.2)	1,408 (29.7)	<.0001	2.0 (1.7-2.3)
Allopurinol	350 (35,0)	32 (0.7)	<.0001	78,5 (54.2-113.8)
Colchicine	3 (0.3)	5 (0.1)	0,13	3.2 (0.8-13.3)
Cortisone	149 (14.9)	259 (5.5)	<.0001	2.9 (2.4-3.7)

[§] Matched on sex and admission year.

*Adjusted for age.

[¤] Vasodilator drugs, anti-hypertensive drugs, diuretics, beta-blockers, calcium antagonists, and renin-angiotensin-aldosterone inhibitors

AMI, acute myocardial infarction; CHD, coronary heart disease; OR, odds ratio; CI, confidence interval

Table 2. In-hospital treatment and medication prescribed at discharge after the first-ever AMI in gout patients and general population comparators.

	Gout cases N=1,000	Controls[§] N=4,740	p-value	OR* (95%CI)
In-hospital treatment, N (%)				
Beta blockers iv	107 (10.7)	449 (9.5)	0.23	1.2 (0.9-1.4)
Diuretics iv	232 (23.2)	824 (17.4)	<.0001	1.4 (1.2-1.6)
Anticoagulants iv	657 (65.7)	3,116 (65.7)	0.98	1.0 (0.9-1.1)
Inotropes iv	43 (4.3)	159 (3.4)	0.14	1.3 (0.9-1.8)
Nitrates iv	91 (9.1)	394 (8.3)	0.42	1.1 (0.9-1.4)
Coronary angiography	726 (72.6)	3,734 (78.8)	<.0001	0.8 (0.7-0.9)
Any primary reperfusion	238 (23.8)	1,459 (30.8)	<.0001	0.7 (0.6-0.7)
PCI	231 (23.1)	1,408 (29.7)	<.0001	0.7 (0.6-0.9)
Acute CABG	3 (0.3)	13 (0.3)	0.89	1.2 (0.3-4.0)
CPAP	69 (6.9)	190 (4.0)	0.0001	1.7 (1.3-2.3)
PM/ICD	19 (1.9)	53 (1.1)	0.04	1.7 (1.0-2.8)
Medication at discharge, N (%)				
RAAS inhibitors	709 (70.9)	3,311 (69.9)	0.51	1.1 (0.9-1.3)
Beta blockers	838 (83.8)	4,064 (85.7)	0.11	0.9 (0.7-1.1)
Antiplatelets	938 (93.8)	4,509 (95.1)	0.08	0.8 (0.6-1.1)
Calcium antagonists	217 (21.7)	643 (13.6)	<.0001	1.7 (1.5-2.1)
Digitalis	40 (4.0)	81 (1.7)	<.0001	2.2 (1.5-3.3)
Diuretics	399 (39.9)	1,079 (22.8)	<.0001	2.2 (1.9-2.6)
Nitrates	185 (18.5)	609 (12.8)	<.0001	1.5 (1.2-1.8)
Statins	771 (77.1)	3,963 (83.6)	<.0001	0.7 (0.6-0.9)

[§] Matched on sex and admission year.

*Adjusted for age.

AMI, acute myocardial infarction; iv, intravenous; PCI, percutaneous coronary intervention; CABG, coronary artery by-pass grafting; CPAP, continuous positive airway pressure; PM, pacemaker; ICD, implantable cardioverter defibrillator; RAAS, renin-angiotensin-aldosterone system; OR, odds ratio; CI, confidence interval

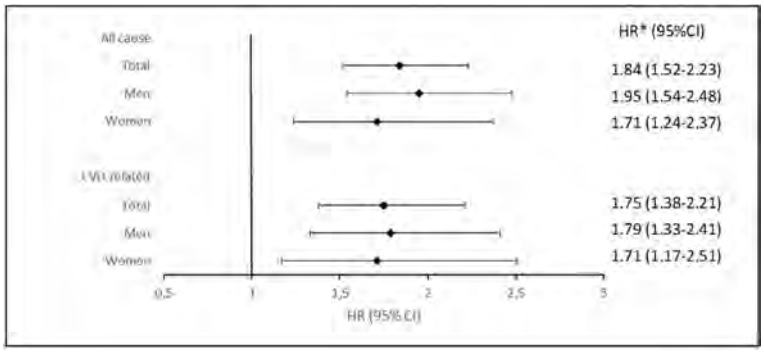

Figure 1. All cause and CVD-related mortality at 1-year after the first-ever AMI in patients with gout compared to the general population. *Adjusted for age, baseline comorbidities, and medication within 6 months before the start of follow-up. HR, hazard ratio; CI, confidence interval; CVD, cardiovascular disease

prescribed nitrates, diuretics, digitalis, and calcium antagonists (Table 2). The prescription of antiplatelets, renin-angiotensin-aldosterone inhibitors, or beta-blockers did not differ significantly between cases and controls (Table 2). The 1-year all-cause and CVD-related mortality was significantly higher in gout patients as compared to the general population (HR, 1.84; 95%CI, 1.52-2.23; and HR, 1.75; 95%CI, 1.38-2.21, respectively) (Figure 1).

Conclusion: Patients with gout were less likely to undergo coronary angiography and PCI during hospitalization for the first-ever AMI and were less likely to be prescribed statins at discharge compared to the general population. The all-cause and CVD-related mortality was significantly higher in patients with gout which might be partly related to differences in in-hospital treatment and secondary prevention.

Disclosure: P. Drivelegka: Horizon, 1; **L. Jacobsson**: Novartis, Eli-Lily and Janssen, 6, Pfizer, Novartis, Eli-Lily and Janssen., 1; **T. Zverkova-Sandström**: None; **M. Dehlin**: None.

Abstract Number: 0249

Comorbidities of Gout: Results from the Korean National Health and Nutrition Examination Survey

Hyemin Jeong and Chan Hong Jeon, Soonchunhyang University Bucheon Hospital, Bucheon, South Korea

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is associated with several comorbidities. The aim of this study was to evaluate the prevalence of comorbidities in Korean adult population with gout.

Methods: Data from 15,935 (weighted n = 39,049,167) participants aged 19 years and older in the Korean National Health and Nutrition Examination Survey from 2019 to 2021 was used for analysis. Weighted prevalence and odds ratios (OR) of comorbidities in individuals with gout were compared with the non-gout population.

Results: The weighted prevalence of gout was 2.1% (weighted n = 808,778). Among individuals with gout, 66.5% had metabolic syndrome, 46.2% had hypertension, 35.6% had dyslipidemia, 19.2% had diabetes, 13.5% had chronic kidney disease (eGFR < 60), 4.1% had myocardial infarction or angina, 3.8% had stroke, and 2.8% hand rheumatoid arthritis. After adjusting for socioeconomic and lifestyle characteristics, gout was independently associated with increased prevalence of metabolic syndrome (male OR 2.0, 95% CI, 1.5-2.8; female OR 3.7, 95% CI 1.5-9.2), hypertension (male OR 2.7, 95% CI 1.9-3.7; female OR 2.5, 95% CI 1.4-4.5), dyslipidemia (male OR 2.0, 95% CI 1.5-2.7; female OR 3.8, 95% CI 1.5-10.0), chronic kidney disease (male OR 4.5, 95% CI 2.7-7.3; female OR 16.2, 95% CI 7.5-34.9), and rheumatoid arthritis (male OR 2.8, 95% CI 1.1-7.1; female OR 3.1, 95% CI 1.1-8.7) compared to the non-gout population.

Conclusion: Gout was associated with several medical comorbidities and rheumatoid arthritis in both males and females. These results suggest that clinicians should prioritize the prevention and management of underlying comorbidities in patients with gout.

Disclosure: H. Jeong: None; **C. Jeon**: None.

Abstract Number: 0250

Validation of Singe-Shot Computational Polarized Microscopy for Crystal Analysis of Synovial Fluid

John FitzGerald[1], Tairan Liu[1], **Chesca Barrios**[1], Bijie Bai[1], Geraldine McCarthy[2], Ann Rosenthal[3] and Aydogan Ozcan[1], [1]University of California Los Angeles, Los Angeles, CA, [2]Mater Misericordiae University Hospital, Dublin, Ireland, [3]Medical College of Wisconsin, Milwaukee, WI

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The gold standard for diagnosis of crystal arthritis relies on the identification of either monosodium urate (MSU) or calcium pyrophosphate (CPP) crystals in synovial fluid by compensated polarized light microscope (CPLM). However, CPLM analysis is labor intensive and depends on experience of the technician. Identifying CPP crystals can be difficult. We previously described single-shot computational polarized light microscopy (SCPLM), that detects MSU and CPP crystals in synovial fluid. This work evaluates the reliability and validity of crystal detection for SCPLM images using crystal experts.

Methods: Microscope slides from patients with CPP or MSU crystals in synovial fluid were obtained and de-identified from the hospital clinical lab. Digital images were acquired using Olympus IX83 microscope, standard objective lens (100x/1.4NA) and either CPLM or SCPLM methodology. Briefly, SCPLM uses a CMOS sensor where each pixel is integrated with a directional polarizing filter with four axes of polarization (0°, 90°, 45°, 135°). SCPLM further combines images from multiple focal depths into a single bright-field fused image.

Table 1. Agreement between Raters for all MSU or CPPD crystals identified by either rater by either method

CPP (n = 280 crystals)

	SCPLM					CPLM			
R1 / R2	Certain	Possible	Negative		R1 / R2	Certain	Possible	Negative	
Certain	89	30	90	209	Certain	44	1	69	114
Possible	3	3	6	12	Possible	1	0	7	8
Negative	16	2		18	Negative	10	6		16
	108	35	96	239		55	7	76	138

MSU (n = 87 crystals)

	SCPLM					CPLM			
R1 / R2	Certain	Possible	Negative		R1 / R2	Certain	Possible	Negative	
Certain	58	5	13	76	Certain	33	1	12	46
Possible	0	0	3	3	Possible	0	0	0	0
Negative	6	1		7	Negative	2	0		2
	64	6	16	86		35	1	12	48

Table 2. Certainty of crystal by Rater and Method ++ = both raters with high certainty about crystal for a specific method

SCPLM	CPLM	CPPD (n = 144)	MSU (n = 69)
++	++	20%	42%
++	Other	60%	48%
Other	++	20%	9%

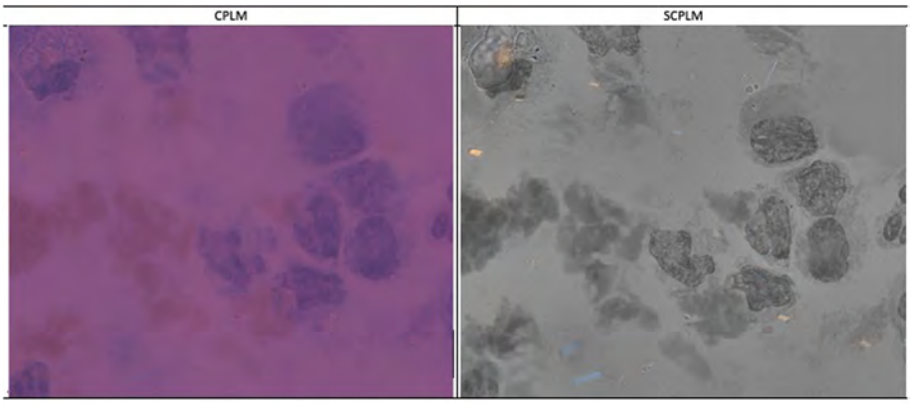

Figure 1. CPLM and SCPLM side-by-side Field of View (100x) Legend: CPLM = Compensated Polarized Light Microscopy. SCPLM = Single-shot Computational Polarized Light Microscopy

In random order, raters were presented paired CPLM images (with analyzer at orthogonal angles) and a single bright-field fused SCPLM image for 67 FOV (including 7 negative controls). For each FOV and each method, each rater recorded their level of certainty (1-5) for each suspect crystal identified and type of crystal. Crystals rated 3 or higher by both raters (++) on either method were included in a high-certainty crystal subset. After rating all of the FOV, raters were presented with side-by-side FOV (CPLM vs. SCPLM) and asked for their preferred image.

Results: 67 FOV were imaged by CPLM and SCPLM methodologies (29 CPP, 31 MSU and 7 negative controls). With an instructed limit of 15 crystals per FOV, 377 unique crystal suspects were identified: 280 CPP, 87 MSU, and 10 uncertain or discrepant crystal identity. (The 10 uncertain/discrepant crystals all came from negative control FOVs.)

Raters identified a higher number of crystals by SCPLM over CPLM for both CPP and MSU. (Table 1) SCPLM identified 239/280 CPP crystals and 86/87 MSU crystals where CPLM identified 138/280 CPP and 48/87 MSU. For SCPLM, there were only 11/239 CPP crystals (4.6%) where neither rater was certain, for CPLM, there were 13/138 (9.4%) where neither rater was certain.

To compare methods, we focused on the 144 CPP and 69 MSU crystals where both raters were certain (++) about the crystal (by at least one method). For 80-90% of included crystals, SCPLM was ++. In contrast, only 40-51% of crystals was CPLM ++. (Table 2) When CPLM was negative, SCPLM was high certain in almost all cases.

Finally, raters subjectively preferred SPCLM over CPLM in side-by-side comparison. Raters were indifferent to method for negative FOVs.

Conclusion: Subjective (rater preference) and objective measures of greater detection and higher certainty were observed for SCPLM images over standard CPLM images, particularly notable for CPP crystals. The digital data associated with these images can be incorporate into an automated scanning platform to provide quantitative reports on crystal counts and morphology perhaps providing greater insight to clinical care.

Disclosure: J. FitzGerald: None; **T. Liu**: None; **C. Barrios**: None; **B. Bai**: None; **G. McCarthy**: PK Med, 2; **A. Rosenthal**: None; **A. Ozcan**: Lucendi Inc, 1, 8, Pictor Labs, 1, 2, 4, 8, 11.

Abstract Number: 0251

Sodium-glucose Cotransporter-2 Inhibitor Initiation, Risk of Recurrent Gout Flares, and Mortality in Patients with Gout and Type 2 Diabetes: A Population-based Cohort Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Recurrent flares are the hallmark of clinical manifestation of gout. Sodium-glucose cotransporter-2 inhibitors (SGLT2i) were associated with a lower risk of incident gout; however, their impact on recurrent flares is unknown. We aimed to examine the relation of SGLT2i vs. active comparators (i.e., glucagon-like peptide-1 receptor agonist or dipeptidyl peptidase 4 inhibitors) to the risk of recurrent gout flares, the first recurrent gout flare, and all-cause mortality among patient with gout and type 2 diabetes.

Methods: Using IQVIA Medical Research Database in the United Kingdom, we identified initiators of SGLT2i and active comparators among gout patients with type 2 diabetes from a United Kingdom primary care database. We conducted cohort studies to examine the relation of SGLT2i vs. active comparators to the risk of recurrent flares, the first recurrent flare, and all-cause mortality using either Poisson regression or Cox-proportional hazards model with propensity score overlap weighting. The primary outcome was the number of recurrent gout flares that were ascertained using recorded codes and prescriptions records. Secondary outcomes were the first recurrent gout flare and all-cause mortality.

Results: During 17,729 person-years of follow-up, 318 recurrent flares occurred in the 1,548 initiators of SGLT2i and 1,714 in the 4,383 initiators of active comparators, respectively. The relative rate of the recurrent flares of SGLT2i vs. active comparators was 0.79 (95%CI: 0.64 to 0.96). Similar results were observed in the relation of SGLT2i to the risk of number of recurrent flares when compared with DPP-4i or GLP-1 receptor agonist, respectively (Table 1). The rate difference (RD) and hazard ratio (HR) of the first recurrent flare for SGLT2i vs. active comparators were -9.2 (95%CI: -18.0 to -0.4) per 1000 person-years and 0.80 (95%CI: 0.64 to 0.98), respectively. All-cause mortality per 1000 person-years was 18.5 for SGLT2i and 24.2 for active comparators, with RD and HR being -5.8 (95%CI: -10.1 to -1.5) per 1000 person-years and 0.72 (95%CI: 0.53 to 0.97) (Table 2).

Conclusion: SGLT2i were associated with a lower risk of recurrent gout flares and mortality than their active comparators in patients with gout and type 2 diabetes. Our findings suggested that SGLT2i have a potential to reduce the burden of recurrent gout flares and narrow the mortality gap between patients with gout and the general population.

Table 1. Risk of recurrent gout flares according to initiation of either SGLT2i or active comparators among patients with gout and type 2 diabetes

	SGLT2i (n=1,548)	Active comparators* (n=4,383)
Event, number of recurrent flares	318	1,714
1	79	338
2	21	109
3	13	51
4	9	36
≥5	13	94
Weighted mean follow-up (years)	2.76	2.70
Weighted rate of event, per 1000 person-years	79.6	99.4
Weighted RD (95% CI), per 1000 person-years	-19.8 (-39.0 to -0.7)	0.0 (reference)
Age, sex, entry-year adjusted RR (95% CI)	0.76 (0.67 to 0.86)	1.00 (reference)
Weighted RR (95% CI)	0.79 (0.64 to 0.96)	1.00 (reference)
	SGLT2i (n=1,829)	**DPP-4i (n=4,113)**
Total number of recurrent flares	428	1,599
Weighted mean follow-up (years)	2.95	2.86
Weighted rate of event, per 1000 person-years	86.7	94.6
Weighted RD (95% CI), per 1000 person-years	-7.9 (-16.7 to 0.9)	0.0 (reference)
Age, sex, entry-year adjusted RR (95% CI)	0.85 (0.75 to 0.95)	1.00 (reference)
Weighted RR (95% CI)	0.84 (0.70 to 1.02)	1.00 (reference)
	SGLT2i (n=2,551)	**GLP-1 receptor agonist (n=787)**
Total number of recurrent flares	539	375
Weighted mean follow-up (years)	2.94	2.91
Weighted rate of event, per 1000 person-years	88.7	143.0
Weighted RD (95% CI), per 1000 person-years	-54.4 (-83.8 to -24.9)	0.0 (reference)
Age, sex, entry-year adjusted RR (95% CI)	0.54 (0.47 to 0.62)	1.00 (reference)
Weighted RR (95% CI)	0.66 (0.51 to 0.84)	1.00 (reference)

n, number; SGLT2i, sodium glucose cotransporter-2 inhibitors; DPP-4i, dipeptidyl peptidase-4 inhibitors; GLP-1, glucagon-like peptide-1; RD, rate differences; RR, relative rate; 95% CI, 95% confidence interval.
*Active comparators consist of dipeptidyl peptidase 4 inhibitors or glucagon-like peptide-1 receptor agonist.

Table 2. Risk of the first recurrent gout flares and all-cause mortality according to initiation of either SGLT2i or active comparators among patients with gout and type 2 diabetes

	SGLT2i (n=1,548)	Active comparators* (n=4,383)
The first recurrent gout flares		
Event, number	135	628
Weighted mean follow-up (years)	2.57	2.46
Weighted rate of event, per 1000 person-years	32.2	41.4
Weighted RD (95% CI), per 1000 person-years	-9.2 (-18.0 to -0.4)	0.0 (reference)
Age, sex, entry-year adjusted HR (95% CI)	0.78 (0.64 to 0.95)	1.00 (reference)
Weighted HR (95% CI)	0.80 (0.64 to 0.98)	1.00 (reference)
All-cause mortality		
Event, number	63	607
Weighted mean follow-up (years)	2.76	2.70
Weighted rate of event, per 1000 person-years	18.5	24.2
Weighted RD (95% CI), per 1000 person-years	-5.8 (-10.1 to -1.5)	0.0 (reference)
Age, sex, entry-year adjusted HR (95% CI)	0.67 (0.51 to 0.89)	1.00 (reference)
Weighted HR (95% CI)	0.72 (0.53 to 0.97)	1.00 (reference)

n, number; SGLT2i, sodium glucose cotransporter-2 inhibitors; RD, rate differences; 95% CI, 95% confidence interval; HR, hazard ratio.
*Active comparators consist of dipeptidyl peptidase 4 inhibitors or glucagon-like peptide-1 receptor agonist.

Disclosure: J. Wei: None; **H. Choi**: Ani, 2, Horizon, 2, 5, LG, 2, Protalix, 2, Shanton, 2; **N. Dalbeth**: Arthrosi, 2, AstraZeneca, 2, Dyve Biosciences, 2, Hikma, 6, Horizon, 2, JW Pharmaceutical Corporation, 2, LG, 2, Novartis, 6, Novotech, 5, PK Med, 2, Protalix, 2, PTC Therapeutics, 2, Selecta, 2, Unlocked Labs, 2; **X. Li**: None; **C. Li**: None; **C. Zeng**: None; **G. Lei**: None; **Y. Zhang**: None.

Abstract Number: 0252

Characterizing Granulomatous Mastitis: A Retrospective, Single-Institutional Case Series of a Racially and Ethnically Diverse Cohort

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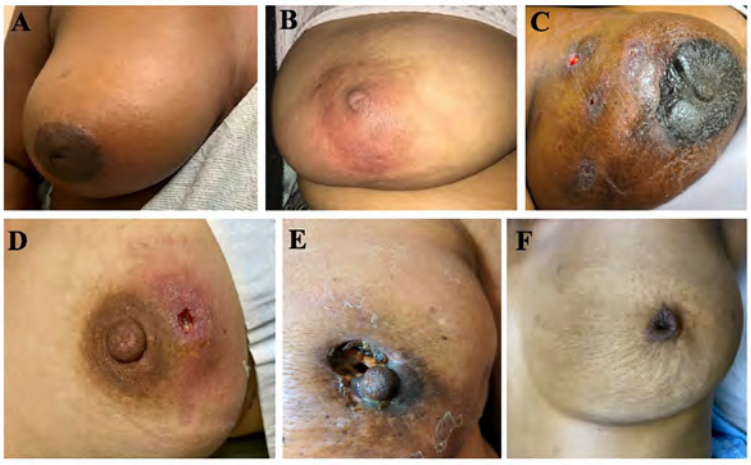
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Granulomatous mastitis (GM) is a rare, chronic, inflammatory breast condition characterized by granulomatous inflammation affecting mainly minority women of childbearing age. Patients present with breast mass and pain that can progress to abscess, fistula, sinus, or ulcer (Figure 1). Pathogenesis of GM is unknown. Hypotheses include autoimmune, inflammatory, infectious, or benign causes. Management includes antibiotics, anti-inflammatory drugs, corticosteroids, disease-modifying anti-rheumatic drugs, biologics, and surgery.

Methods: We performed an IRB-approved retrospective analysis of patients with GM at Montefiore between 1/1/2014-1/1/2023. Inclusion criteria were age greater than 18, diagnosis of GM (clinically diagnosed or biopsy proven). Exclusion criteria were age younger than 18, concurrent alternate breast pathology. We identified 119 patients with GM. No patients fit exclusion criteria.



Various presentations of granulomatous mastitis in African American and Hispanic women. A) Right breast with large area of induration, tenderness, and erythema on the lower medial aspect. B) Right breast with erythematous tender area with some fluctuance in the 6 o'clocl position inferior to the areola. C) Entire right breast firm, indurated, erythematous, and tender to the touch with open sinus. D) Right breast with mass, erythema, and open wound. E) Left breast with open wound secondary to biopsy, with probing depth of 1-2cm, with purulent draining and diffuse induration without erythema. F) Left breast with inverted nipple, mass, and area of dense/fibrous tissue.

Results: 119 patients (118 female, 1 male) with GM were identified. Mean age at diagnosis was 36.29 years (range 20-83). Most patients were minorities (Hispanic/Latino 48.74%, African American 21.01%, Other/Unknown 19.33%, Caucasian 5.88%, Asian 4.20%) and hailed from a broad range of countries (Table 1). Most common comorbidity was obesity (20.17%) and major risk factors included pregnancy within 5 years (52.94%), lactation within 2 years (25.21%), and former/current smoker (18.49%) (Table 1). Most patients experienced unilateral symptoms (76.47%) of breast mass (79.83%), erythema (62.18%), pain (61.345%), and tenderness (50.42%) (Table 2). Mean symptom duration prior to presentation was 53.27 days (range 1-365) and symptom duration prior to diagnosis was 188.96 days (range 3-2555). Of 37 patients with positive bacterial cultures, 67.57 % had *Corynebacterium kroppenstedtii* (Table 2). 84.87% were biopsied and patients not biopsied were diagnosed with a combination of clinical presentation, imaging, and treatment response. Ultrasound, mammogram, and MRI were performed in 109, 82, and 8 patients, respectively. Most common BIRADS score was 4 for ultrasound (33.94%) and for mammogram (31.71%). Antibiotics were prescribed to 84.03% of patients, most

Characteristic	N (%)
Birth Country	
Mexico	12 (10.08)
Ecuador	10 (8.40)
Dominican Republic	6 (5.04)
USA	6 (5.04)
Puerto Rico	4 (3.36)
Peru	3 (2.52)
Other Central & South American countries	5 (4.20)
Bangladesh	3 (2.52)
Yemen	2 (1.68)
Togo	1 (0.84)
Not Reported	49 (41.18)
Comorbidities	
Obesity	24 (20.17)
Hypertension	17 (14.29)
Asthma	13 (10.92)
Anemia	11 (9.24)
Depression	11 (9.24)
Anxiety	8 (6.72)
Prediabetes/diabetes	8 (6.72)
Hypothyroidism	8 (6.72)
Migraine	7 (5.88)
Allergic rhinitis	6 (5.04)
Bipolar disorder	5 (4.20)
Gastroesophageal reflux disorder	4 (3.36)
Latent tuberculosis	3 (2.52)
Hyperthyroidism	2 (1.68)
Vitamin D deficiency	2 (1.68)
Polycystic ovarian syndrome	2 (1.68)
Schizophrenia	2 (1.68)
Alopecia areata	1 (0.84)
Hidradenitis suppurativa	1 (0.84)
Rheumatoid arthritis	1 (0.84)
Sicca	1 (0.84)
No past medical history	48 (40.34)
Risk Factors	
Pregnancy within past 5 years	63 (52.94)
Lactation within past 2 years	30 (25.21)
Current or former smoker	22 (18.49)
History of breast surgery	14 (11.76)
Marijuana use	10 (8.40)
History of breast piercing	7 (5.88)
Family history autoimmune disorders	6 (5.04)
COVID-19 positive prior to symptoms	6 (5.04)
Family history GM	1 (0.84)

Birth countries, comorbidities, and risk factors for patients with GM.

commonly doxycycline (49.00%), bactrim (41.00%), and clindamycin (36.00%). Steroid immunotherapy and methotrexate were prescribed to 69.75% and 14.29% of patients, respectively. Surgical interventions included incision and drainage (43.70%) and excision (12.61%). 3 months, 1 year, and 2 years after symptom onset, 79.81%, 40.38%, and 18.27% of patients had persistent symptoms, respectively. Recurrence occurred in 6 patients.

Conclusion: This is the largest retrospective case series of GM in the United States to date. We stratified comorbidities and risk factors in patients with GM and identified several bacteria previously not reported including *Capnocytophaga ochracea, Serratia marscens, Actinomyces meyeri, Actinomyces neurii, Trueperella bernardiea, Actinotignum unspecified,* and *Proteus mirabalis*. Combining clinical anecdotal evidence with this comprehensive review, we advise physicians caring for young, female, minority patients with breast pain, mass, erythema, or drainage to be mindful for developing GM.

Characteristic	N (%)
Symptoms	
Unilateral	91 (76.47)
Right breast	51 (42.86)
Left breast	40 (33.61)
Bilateral	28 (23.53)
One lesion	65 (54.62)
Few lesions	30 (25.21)
Many lesions	14 (11.76)
Whole breast	10 (8.40)
Mass	95 (79.83)
Erythema	74 (62.18)
Pain	73 (61.34)
Tenderness	60 (50.42)
Induration	39 (32.77)
Drainage	20 (16.81)
Ulceration/open wound	13 (10.92)
Nipple retraction/inversion	10 (8.40)
Warmth	9 (7.56)
Fluctuance	4 (3.36)
Desquamation	2 (1.68)
Bacterial cultures	
No cultures performed	44 (36.97)
Negative result	37 (31.09)
Positive result	37 (31.09)
Corynebacterium kroppenstedtii	25 (67.57)
Propionibacterium acnes	2 (5.41)
Actinobacter baumanni	2 (5.41)
Serratia marscens	2 (5.41)
Capnocytophaga ochracea	2 (5.41)
Methicillin sensitive staphylococcus aureus	2 (5.41)
Corynebacterium amycolaum	1 (2.70)
Trueperella bernardiea	1 (2.70)
Corynebacterium tuberculostearicum	1 (2.70)
Staphylococcus epidermidis	1 (2.70)
Actinomyces meyeri	1 (2.70)
Actinotignum unspecified	1 (2.70)
Staphylococcus lugdunendsis	1 (2.70)
Actinomyces neurii	1 (2.70)
Proteus mirabalis	1 (2.70)

Symptoms and bacterial culture results for patients with GM.

Disclosure: L. Pattison: None; **B. Ayesha**: None; **A. Kumthekar**: None; **M. McEvoy**: None; **B. McLellan**: Laroche posay, 1, Paulas Choice, 1, Pfizer, 5; **I. Gendlina**: None.

Abstract Number: 0253

Clinical Phenotypes in Patients with Isolated Anti-Sm/RNP Common Motif Antibody Positivity, Compared to Those with or Without Associated Anti-RNP Antibody Reactivity

Ruoning Ni[1] and Petar Lenert[2], [1]University of Iowa Hospitals and Clinics, Coralville, IA, [2]University of Iowa Hospitals and Clinics, Iowa City, IA

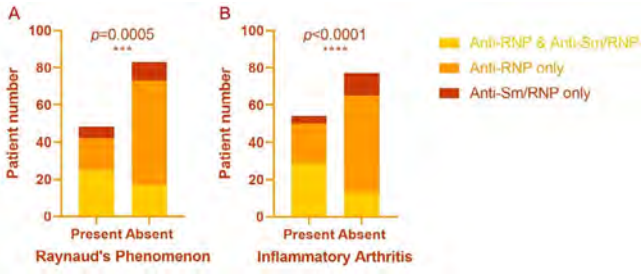
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-ribonucleoprotein (RNP) and anti-Sm/RNP common motif antibodies play a critical role in diagnosing patients with systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD) or other connective tissue disease. Despite some common features between RNP and Sm/RNP antigens, such as sharing a 14-kd-reactive protein, they also carry significant structural differences. Anti-Sm antibodies frequently target B/B', D1 and D3 proteins, whereas anti-RNP antibodies are directed towards 70-kd, A, C proteins. It is already well known that anti-RNP antibodies when presenting alone in patients with MCTD are closely related with Raynaud's phenomenon and relatively rare renal involvement. Rheumatologists encounter patients with positive anti-Sm/RNP common motif antibodies with or without anti-RNP antibodies in different clinical scenarios. However, the clinical phenotype of patients presenting solely with anti-Sm/RNP antibodies, or in association with anti-RNP antibodies remains unknown.

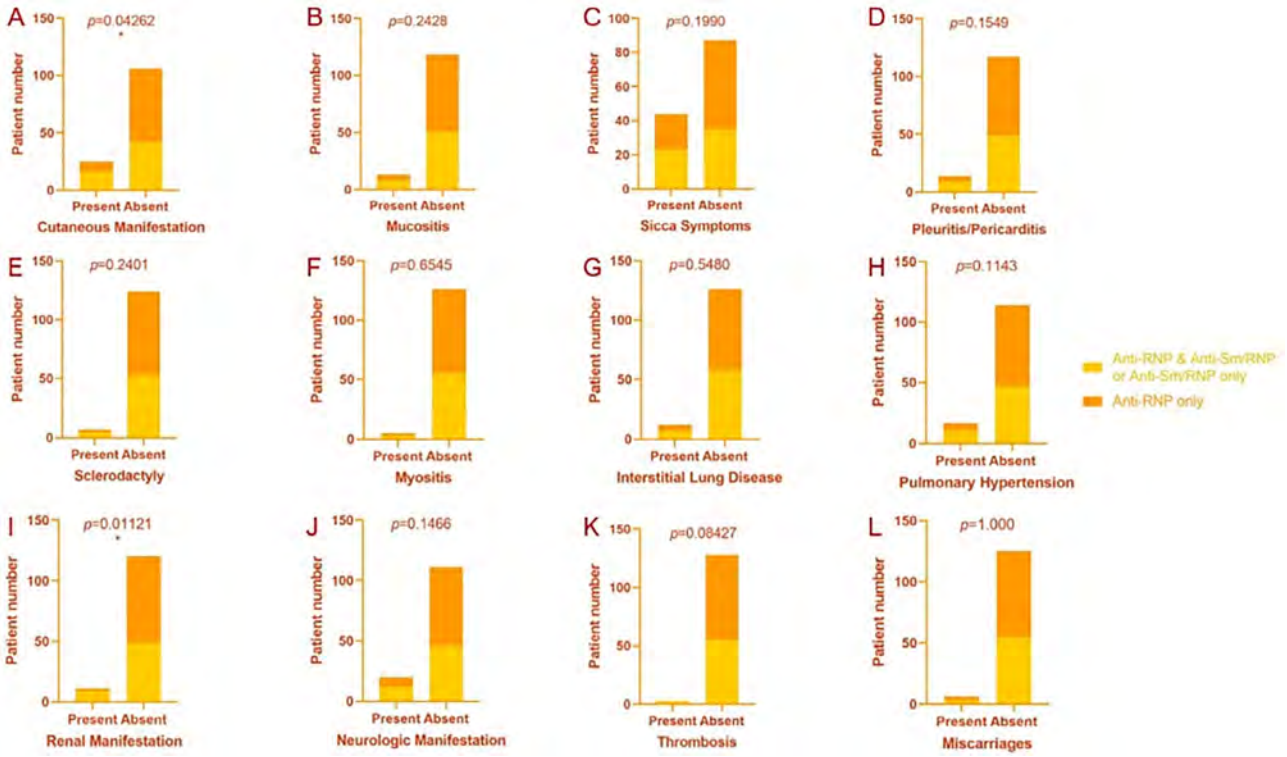
Methods: We obtained approval from the Institutional Review Board at the University of Iowa Hospitals and Clinics and conducted a retrospective cohort study of patients, who tested positive for anti-RNP, and/or anti-Sm/RNP antibodies. The antibody profile was analyzed at the time of diagnosis. All patients were followed up by rheumatology clinic.

All data were retrieved from the existing medical records available through the EPIC database. Data analysis included demographic characteristics, clinical manifestations, organ involvement, disease duration, antibody titers.

Continuous variables were expressed as means ± standard deviation (SD) or median with minimum and maximum range, categorical variables as counts and percentages. Differences between groups were evaluated with the student's t test or Mann-Whitney U test for continuous variables and Chi-square or Fisher's exact test for categorical variables.



Represents the number of patients with and without Raynaud's phenomenon (A) and inflammatory arthritis (B) in patients tested positive for anti-RNP and anti-Sm/RNP, positive for anti-RNP only, and positive for anti-Sm/RNP only.



Represents the number of patients with and without cutaneous manifestations (A), mucositis (B), sicca symptoms (C), pleuritis or pericarditis (D), sclerodactyly (E), myositis (F), interstitial lung disease (G), pulmonary hypertension (H), renal manifestation (I), neurologic manifestation (J), thrombosis (K), and miscarriage (L) in patients tested positive for anti-RNP and anti-Sm/RNP, or anti-Sm/RNP only, or positive for anti-RNP only.

Results: A total of 131 patients were included in the study, of which 42 (32.1%) were tested positive for anti-RNP and anti-Sm/RNP antibodies, 73 (55.7%) positive for anti-RNP antibody only, 16 (12.2%) positive for anti-Sm/RNP only. 91.6% of patients were female and average age at diagnosis at our institute were 45 years old. The rate of inflammatory arthritis was significantly higher in patients positive for anti-RNP and anti-Sm/RNP antibodies than anti-RNP only or anti-Sm/RNP only (69.1% vs. 28.8% vs. 25.0%, $p< 0.0001$), as well as Raynaud's phenomenon (59.5% vs. 23.3% vs. 37.5%, $p=0.0005$). Rash and renal manifestations were significantly more frequent in patients tested positive for anti-Sm/RNP with or without anti-RNP when compared with patients only positive for anti-RNP antibody. There was no significant difference in mucositis, sicca symptoms, pleuritis/pericarditis, sclerodactyly, myositis, interstitial lung disease, pulmonary hypertension, neurologic manifestations, thrombosis, or miscarriages.

Conclusion: The presence of anti-Sm/RNP common motif antibodies was more commonly associated with inflammatory arthritis, Raynaud's phenomenon, and could be associated with rash and renal involvement.

Disclosure: R. Ni: None; **P. Lenert**: None.

Abstract Number: 0254

Microvascular and Cutaneous Assessment in Adult Patients with Hypermobile Ehlers-Danlos Syndrome

Alberto Sulli[1], Francesca Lalli[2], Elvis Hysa[2], Andrea Cere[1], Alessandro Pinelli[2], Silvia Sammorì[1], Emanuele Gotelli[1], Carmen Pizzorni[1], Marco Castori[3], Fransiska Malfait[4], Vanessa Smith[5] and Maurizio Cutolo[6], [1]Laboratory of Experimental Rheumatology and Academic Division of Rheumatology, Department of Internal Medicine, University of Genoa, IRCCS San Martino Polyclinic Hospital, Genoa, Italy, [2]Laboratory of Experimental Rheumatology and Academic

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Hypermobile Ehlers-Danlos syndrome (hEDS) is a hereditary connective tissue disease characterized by joint hypermobility, chronic musculoskeletal pain, and systemic manifestations, primarily caused by defects in collagen synthesis or processing [1]. The microvascular morphology and functional status have not been evaluated in hEDS, as well as dermal thickness (DT) has been little investigated.

The aim of this study was to examine the nailfold microvascular morphological status, assess peripheral blood perfusion (PBP) and measure dermal thickness (DT) in patients with hEDS in comparison with sex and age-matched healthy controls (CNT).

Methods: Twelve patients diagnosed with hEDS (mean age 40±15, 75% females), classified according to the 2017 International Classification Criteria of EDS [2], were included in the study. Twelve age- and sex-matched CNT were also recruited. The Beighton score was calculated for both hEDS patients and CNT, to assess joint hypermobility. The main parameters derived from nailfold videocapillaroscopy (NVC), including dilated capillaries, giant capillaries, microhemorrhages, abnormal capillary shapes, and capillary count, were analysed and compared between the two groups to assess morphological features [3]. Furthermore, the microvascular functional status was evaluated using laser speckle contrast analysis (LASCA), measuring peripheral blood perfusion (PBP) in various regions of interest of the hand. DT was assessed by cross-sectional B-mode scans acquired using a high-frequency 22 MHz ultrasound probe, analysing seventeen different body areas, such as the upper arms, lower arms, trunk, and forehead.

Results: Microhemorrhages were found more prevalent in hEDS patients (25% vs 0%, $p = 0.09$), the capillary number per linear millimetre at the nailfold was slightly higher in hEDS patients than in CNT, as well as the NVC score for abnormal shaped capillaries was slightly lower (less abnormal shaped capillaries) in hEDS patients than in CNT. PBP was similar between hEDS patients and CNT. The DT resulted generally lower in hEDS patients than controls with significant values limited to feet and thorax ($p=0.04$). A statistically significant positive correlation was observed between the Beighton score and the score for microhemorrhages ($r=0.4$, $p=0.05$), as well as between the Beighton score and DT ($r\geq0.5$, $p\leq0.02$) at the level of feet and thorax.

Conclusion: Our study demonstrates that hEDS patients exhibit a morphologically suitable capillary morphology and normal microvascular function during resting conditions. However, there is a increased microvascular fragility in these patients. Additionally, we observed that dermal thickness appears thinner in hEDS patients compared to controls across most skin areas, with significant differences noted in the feet and thorax regions.

References: [1] Malfait F et al.Nat Rev Dis Primers. 2020. [2] Malfait F et al. Am J Med Genet C Semin Med Genet 2017. [3] Smith et al. Autoimmun Rev 2020.

Disclosure: A. Sulli: None; **F. Lalli**: None; **E. Hysa**: None; **A. Cere**: None; **A. Pinelli**: None; **S. Sammorì**: None; **E. Gotelli**: None; **C. Pizzorni**: None; **M. Castori**: None; **F. Malfait**: None; **V. Smith**: Boehringer Ingelheim, 2, 5, 6, 12, Support for travel, Galapagos, 6, Janssen-Cilag, 1, 2, 5, 6; **M. Cutolo**: Amgen, 5, Boehringer Ingelheim, 5, Bristol-Myers Squibb, 5, Lab.Baldacci, 5.

Abstract Number: 0255

Lymphoid Mass in the Inferior Turbinate with IgG4 Producing Cells: A Nasal Manifestation of IgG4-RD or a Distinct Chronic Inflammatory Disease?

Ji In Jung[1], Ju Yeon Kim[2], Jun Won Park[2], Eun Bong Lee[2], Jin Kyun Park[3] and Doo Hee Han[2], [1]Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, South Korea, [2]Seoul National University Hospital, Seoul, South Korea, [3]Seoul National University College of Medicine, Seoul, South Korea

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: IgG4-related disease (IgG4-RD) is a rare, multi-system, fibro-inflammatory disorder characterized by the infiltration of lymphoplasmacytic cells, storiform fibrosis, obliterative phlebitis, and the presence of IgG4-positive plasma cells in affected tissues, accompanied by elevated serum IgG4 levels. In IgG4-RD, sinonasal involvement presents as nasal obstruction, chronic sinusitis, and bleeding. Nasal obstruction may arise from a sessile submucosal mass located in the anterior portion of the inferior turbinate, exhibiting dense lymphocytic lymphoplasmacytic infiltration. We aimed to investigate whether these lymphoid masses in the nasal inferior turbinate represent a nasal manifestation of IgG4-RD or a distinct chronic inflammatory disease entity that has yet to be defined.

Methods: This retrospective study enrolled patients who underwent endoscopy at Seoul National University Hospital between January 2020 and May 2023 due to nasal symptoms, including nasal obstruction or nasal crust. The clinical characteristics and laboratory parameters, such as erythrocyte sedimentation rate (ESR), high-sensitivity C-reactive protein (hs-CRP), and serum IgG4 levels, were evaluated (Figure 1). Biopsies were performed on nasal lymphoid masses exhibiting damaged mucosa features like crusting and bleeding. The diagnosis of IgG4-RD was based on the 2019 classification criteria of IgG4-RD from the American College of Rheumatology/European League Against Rheumatism. All data was analyzed using Chi-square test and Student's t-test.

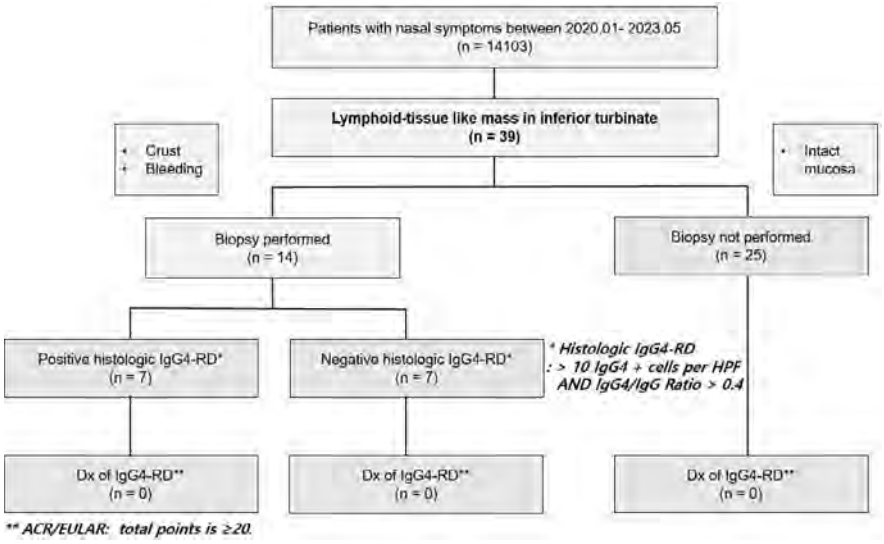


Figure 1. Patient flow

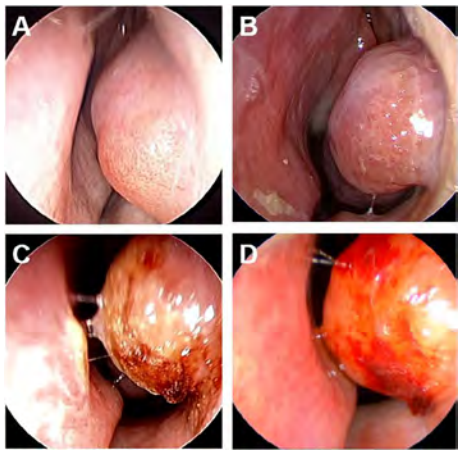


Figure 2. Representative endoscopic findings lymphoid mass. Rhinoscopy reveals yellowish sessile submucosal mass with intact overlying mucosa in the anterior portion of the inferior turbinate - (A,B) Mild and (C,D) severe cases. (D) Overlying mucosa was covered with bloody crust.

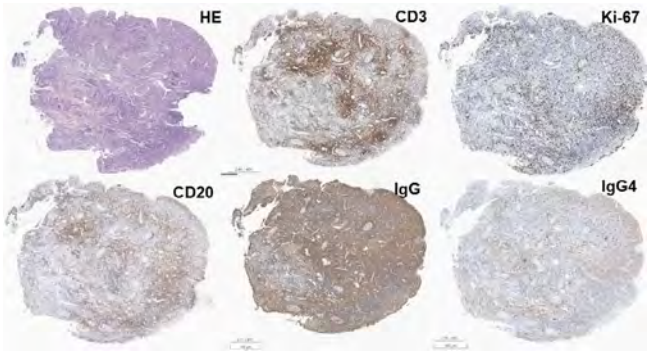


Figure 3. Histology of nasal polyp

Results: In this study, a total of 14103 patients were evaluated for nasal symptoms, and among them, 39 patients presented with lesions resembling lymphoid follicles in the inferior turbinate upon endoscopic evaluation (Figure 2). Among the 14 patients who underwent biopsy, all of them exhibited dense lymphoplasmacytic infiltrates and more than 10 IgG4-expressing plasma cells per high-power field (HPF) (Figure 3). Among these patients, 7 out of 14 (50%) had an IgG4+/IgG+ ratio exceeding 40% and met the histologic criteria for IgG4-RD. However, only 1 patient had elevated serum IgG4 levels. None of the patients were classified as having IgG4-RD based on the EULAR/ACR classification criteria. Patients with significant nasal symptoms who received surgical resection experienced improvement without recurrence of local symptoms.

Conclusion: To the best of our knowledge, this study provides the first comprehensive description of a nasal sessile lymphoid mass located in the inferior turbinate. Our findings indicate that this lymphoid mass, characterized by IgG4+ lymphoplasmacytic infiltration, is likely to represent a distinct disease entity separate from the sinonasal involvement of IgG4-RD. Further study is required to define the optimal treatment and long prognosis.

Disclosure: J. Jung: None; **J. Kim**: None; **J. Park**: None; **E. Lee**: Pfizer, 2; **J. Park**: None; **D. Han**: None.

Abstract Number: 0256

Nintedanib in Combination with Immunosuppressive Agents Improves Forced Vital Capacity in Connective Tissue Disease-associated PF-ILD: A Single-center Study

Yusuke Ushio[1], Risa Wakiya[2], Tomohiro Kameda[2], Shusaku Nakashima[2], Hiromi Shimada[2], Taichi Miyagi[3], Koichi Sugihara[4], Rina Mino[5], Mao Mizusaki[2], Kanako Chujo[6], Ryoko Kagawa[7], Hayamasa Yamaguchi[7] and Hiroaki Dobashi[2], [1]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Miki, Kita District, Kagawa, Japan, [2]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Kagawa, Japan, [3]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Kidagun, Japan, [4]Kagawa University, Miki-cho, Kita-gun, Japan, [5]Kagawa University, Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa, Japan, [6]Kagawa University, Miki, Kita District, Kagawa, Japan, [7]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Miki-cho, Kita-gun, Japan

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Japanese patients with connective tissue disease (CTD) are more likely to have interstitial lung disease (CTD-ILD) than those in Western countries and many CTD-ILDs were treated with various immunosuppressive agents (IS). Recently, nintedanib (NTB), a multitargeted tyrosine kinase inhibitor, has been approved for progressive fibrosing ILD (PF-ILD) including CTD-ILD. However, the efficacy of NTB in combination with IS for CTD-associated PF-ILD (CTD-PF-ILD) is unclear. We aimed to clarify the efficacy and safety of NTB in combination with IS for CTD-PF-ILD under real-world clinical settings, as well as biomarkers reflecting therapeutic efficacy.

Methods: CTD-ILD patients who met the criteria for PF-ILD (Flaherty KR, et al. N Engl J Med. 2019) and received NTB at our institution between 2020 and 2022 were included in this retrospective study. Efficacy of NTB treatment was evaluated by changes in forced vital capacity (FVC (%, mL)) at 6–12 months and the monthly change in FVC (ΔFVC (%/M)) before and after NTB administration. As biomarker reflected of ILD activity, the level of serum KL-6 (Krebs von den Lungen-6) were also analyzed. In addition, the effect of concomitant IS on CTD-PF-ILD was evaluated by comparisons of change in FVC and ΔFVC (%/M) between patients who received new IS after the initiation of NTB (Group A) and those who received only NTB (Group B). Safety was analyzed by the occurrence of adverse events (AEs) considered to be associated with NTB within 12 months.

Results: Twenty-five patients with CTD-PF-ILD (8 males and 17 females) were included in the study. Patient characteristics are shown in Table 1. Among these CTDs complicated with PF-ILD, systemic sclerosis was the most common (9 cases; 36%), followed by myositis (6 cases; 24%). Mean FVC (%) increased from 59.1% to 65.3% and mean FVC (mL) increased from 1666.2 mL to 1821.4 mL at 6–12 months after administration of NTB (Figure 1). ΔFVC (%/M) significantly improved from -0.77%/M before NTB initiation to +0.33%/M after treatment (Figure 2). Serum KL-6 decreased significantly from 1461.6 U/mL to 1145.7 U/mL after 6–12 months of treatment. A significant negative correlation was found between the change of serum KL-6 and FVC (r: -0.7618, p: < .0001). Twelve of the 25 patients had new IS started after NTB initiation (Group A). Rituximab (6 patients) was the most commonly used as IS (Table 1). Twelve patients in Group A had a predominantly higher rate of improvement in ΔFVC (%) than the 13 patients in Group B (+12.1% vs. -0.41%, respectively) (Figure 1). The improvement in ΔFVC (%/M) was also greater in Group A than in Group B, but both groups had suppressed

progressive pulmonary fibrosis (Figure 2). AEs considered to be treatment-related were diarrhea in 13 patients, nausea in 2 patients, elevated liver enzymes in 2 patients, and headache in 1 patient, respectively, and the dose of NTB was reduced in 11 patients. No patient discontinued NTB due to AEs.

Table 1. Baseline characteristics of patients enrolled in this study.

Characteristics	Total, n=25
Age, mean ± SD, years	65.4 ± 10.7
Sex, Female, number (%)	17 (68.0)
Disease duration, mean ± SD, years	8.4 ± 7.9
Former or current smoker, n (%)	12 (50.0)
Primary connective tissue diseases	
Systemic sclerosis, n (%)	9 (36.0)
Polymyositis, Dermatomyositis, n (%)	6 (24.0)
Rheumatoid arthritis, n (%)	4 (16.0)
Microscopic polyangiitis, n (%)	3 (12.0)
Eosinophilic granulomatosis with polyangiitis, n (%)	1 (4.0)
Sjögren's syndrome, n (%)	1 (4.0)
Mixed connective tissue disease, n (%)	1 (4.0)
Laboratory data / Pulmonary function tests	
KL-6, mean ± SD, U/mL	1461.6 ± 961.2
FVC (forced vital capacity)	
% of predicted value, mean ± SD, %	56.8 ± 15.1
mL, mean ± SD, mL	1600.0 ± 600.1
The monthly change in FVC before the initiation of nintedanib, mean ± SD, %/M	-0.77 ± 0.59
Previous immunosuppressive agents prior to the initiation of nintedanib	
Glucocorticoids, number (%)	18 (72.0)
prednisolone equivalent dose, mean ± SD, mg/day	8.9 ± 6.1
Tacrolimus, n (%)	9 (36.0)
Mycophenolate mofetil, n (%)	4 (16.0)
Azathioprine, n (%)	3 (12.5)
Cyclosporine, n (%)	3 (12.0)
Newly added immunosuppressive agents after the initiation of nintedanib	
Rituximab, number (%)	6 (24.0)
Glucocorticoids (≧20mg/day of prednisolone), number (%)	5 (20.0)
Cyclophosphamide, number (%)	2 (8.0)
Abatacept, n (%)	2 (8.0)
Mycophenolate mofetil, n (%)	1 (4.0)
Tacrolimus, n (%)	1 (4.0)

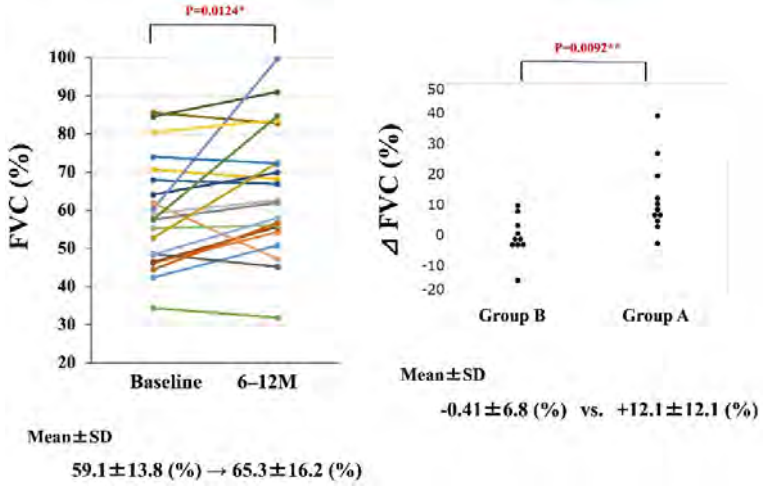


Figure 1. Changes in forced vital capacity (FVC) 6–12 months after the initiation of nintedanib. For statistical analyses * p<0.05, **p<0.01. p value: Wilcoxon signed-rank test, Wilcoxon rank sum test.

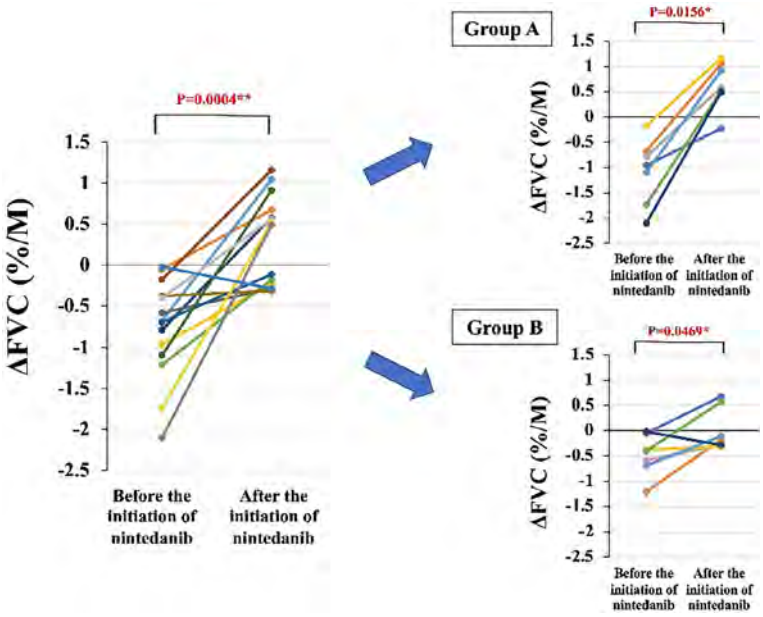


Figure 2. Changes in the monthly change in forced vital capacity (ΔFVC (%/M)) before and after the initiation of nintedanib. For statistical analyses * p<0.05, **p<0.01. p value: Wilcoxon signed-rank test.

Conclusion: NTB for CTD-PF-ILD appeared to be effective and safe in clinical practice. Our results also suggest that the combination of IS, including rituximab, may be more effective for CTD-PF-ILD than NTB treatment alone. Serum KL-6 may be a biomarker reflecting improvement in FVC during treatment with NTB.

Disclosure: Y. Ushio: None; **R. Wakiya**: None; **T. Kameda**: None; **S. Nakashima**: None; **H. Shimada**: None; **T. Miyagi**: None; **K. Sugihara**: None; **R. Mino**: None; **M. Mizusaki**: None; **K. Chujo**: None; **R. Kagawa**: None; **H. Yamaguchi**: None; **H. Dobashi**: None.

Abstract Number: 0257

Activity of IgG4-related Disease Differs Depending on the Presence or Absence of Concomitant Hypocomplementemia

Risa Wakiya[1], Hiroki Ozaki[2], Hiromi Shimada[1], Shusaku Nakashima[1], Taichi Miyagi[3], Yusuke Ushio[4], Koichi Sugihara[5], Mao Mizusaki[1], Rina Mino[6], Kanako Chujo[7], Ryoko Kagawa[4], Hayamasa Yamaguchi[4], Tomohiro Kameda[1] and Hiroaki Dobashi[1], [1]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Kagawa, Japan, [2]Department of Rheumatology, KKR Takamatsu Hospital, Kagawa, Japan, [3]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Kidagun, Japan, [4]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Miki-cho, Kita-gun, Japan, [5]Kagawa University, Miki-cho, Kita-gun, Japan, [6]Kagawa University, Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa, Japan, [7]Kagawa University, Miki, Kita District, Kagawa, Japan

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Hypocomplementemia (HC) is often observed in IgG4-related diseases (IgG4-RD), but there are also IgG4-RD without HC. This study aimed to clarify the difference of characteristics of IgG4-RD in the presence or absence of HC.

Methods: The data of patients diagnosed with IgG4-RD at our institution were retrospectively analyzed, and these patients were divided into two groups: the HC group, which comprised patients with decreased C3 or C4 level (hypocomplementemia), and nonHC group, which comprised patients with normal C3 and C4 levels. The characteristic, affected organs, blood and imaging findings, and treatment course of the patients in both groups were compared. As additional evaluation of IgG4RD feature using imaging modality, fluorodeoxyglucose (FDG)-PET/CT was conducted. The maximum standardized uptake value (SUVmax), metabolic tumor volume (MTV), and total lesion glycation (TLG), which indicate the level of metabolic activity of the tumor, were measured to evaluate disease activity using FDG-PET/CT.

Results: The study enrolled 65 patients. Of these patients, 19 and 46 were included in the HC and nonHC groups, respectively. Table 1 shows the characteristics of patients with IgG4-RD in this study. The HC group had lower hemoglobin levels and platelet counts and higher serum IgG4, IgG, and sIL-2R levels compared than the nonHC group. Moreover, the number of patients requiring treatment was higher in the HC group (17 patients, 89%) than in the nonHC group (28 patients, 61%). Recurrence of IgG4-RD was observed in 3 of the 17 patients in the HC group and 11 of the 28 patients in the nonHC group. Two and three patients in the HC and nonHC groups, respectively, died during the course of this study.

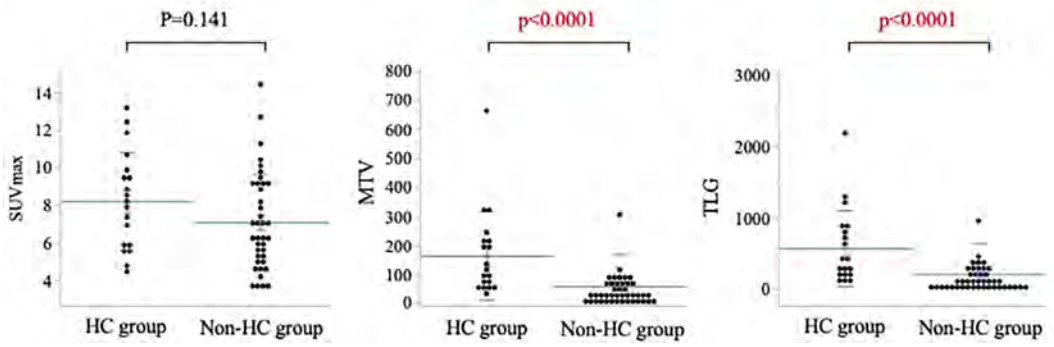
Two of the three index that may reflect IgG4RD activity by analyzed by FDG-PET/CT were significantly higher in the HC group.

Although there was no significant difference in SUVmax between the two groups, the MTV and TLG were significantly higher in the HC group than those of nonHC group (Figure 1).

Table 1. Characteristics of IgG4-RD patients in this study P-values were determined using Mann-Whitney U test or Fisher's exact test.

Characteristics	All (n=65)	HC group (n=19)	nonHC group (n=46)	*P* value
Age, mean (SD), y	65.3(11.6)	69.6 (8.4)	63.5 (12.4)	0.057
Sex, Male : Female, No.	41:24	12:7	29:17	1.000
Serum biomarkers, median[IQR]				
IgG4, mg/dL	458 [226, 792]	713 [412, 2100]	394.5 [201.5, 643.5]	**0.0020**
IgG, mg/dL	1954 [1542, 2975]	3256 [2016, 4580]	1744.5 [1427.8, 2223.5]	**<0.0001**
C3, mg/dL	93 [70.5, 108.5]	56 [41, 67]	104.5 [90.8, 117.3]	**<0.0001**
C4, mg/dL	19 [12, 26]	5 [2, 11]	23 [17.8, 30.3]	**<0.0001**
Soluble IL-2 receptor, U/mL	724 [412, 1326]	1344 [905, 2166.5]	506 [375, 773]	**<0.0001**
White blood cells, /μL	6100 [5145, 7160]	5500 [4740, 6570]	6195 [5390, 7242.5]	0.058
Hemoglobin, g/dL	13.3 [11.6, 14.5]	11.2 [10.3, 12.7]	13.8 [12.7, 15.1]	**<0.0001**
Platelet, $\times 10^4/\mu L$	22.1 [18.2, 26.9]	18.1 [15.9, 21.3]	24 [21.4, 28.5]	**0.0002**
Organs with IgG4-RD, No.(%)				
Lacrimal glands	17 (26.2)	4 (21.1)	13 (28.3)	0.758
Submandibular glands	42 (64.6)	14 (73.7)	28 (60.9)	0.401
Parotid gland	15 (23.1)	6 (31.6)	9 (19.6)	0.340
Pancreas	9 (13.8)	4 (21.1)	5 (10.9)	0.430
Kidney	5 (7.7)	2 (10.5)	3 (6.5)	0.625
Renal pelvis thickening	2 (3.1)	0 (0)	2 (4.3)	
Pulmonary lesion	15 (23.1)	7 (36.8)	8 (17.4)	0.112
Retroperitoneum	8 (12.3)	5 (26.3)	3 (6.5)	**0.041**
Lymph node	53 (81.5)	17 (89.5)	36 (78.3)	0.484

Figure 1



Differences in fluorodeoxyglucose-PET findings of the HC and nonHC groups Maximum standardized uptake value was not significantly different between the groups; however, metabolic tumor volume and total lesion glycation were significantly higher in the HC group than in the nonHC groups. The P-value was determined by performing the Mann–Whitney U test.

Conclusion: The HC group had peripheral blood cytopenia and higher IgG4 level than the nonHC group. Moreover, more patients in the HC group required therapeutic intervention and had a poor prognosis. In assessing the activity of patients with IgG4RD using FDG-PET/CT, HC group had higher disease activity compared with nonHC group.

Disclosure: R. Wakiya: None; **H. Ozaki**: None; **H. Shimada**: None; **S. Nakashima**: None; **T. Miyagi**: None; **Y. Ushio**: None; **K. Sugihara**: None; **M. Mizusaki**: None; **R. Mino**: None; **K. Chujo**: None; **R. Kagawa**: None; **H. Yamaguchi**: None; **T. Kameda**: None; **H. Dobashi**: None.

Abstract Number: 0258

Understanding Monogenic Behçet's Disease Pathophysiology: Impact of Pathogenic Variant L227X Associated with Autoinflammatory A20 Haploinsufficiency on Cellular Survival and Proliferation

Patricia Aires[1], Daniela Pioto[1], Maria Teresa TErreri[2] and **Sandro Perazzio**[3], [1]Universidade Federal de São Paulo (UNIFESP), São Paulo, Brazil, [2]UNIFESP, São Paulo, Brazil, [3]Universidade de Sao Paulo (Unifesp); Universidade de São Paulo (USP); Fleury Laboratories, São Paulo, Brazil

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: A20, encoded by *TNFAIP3*, plays a critical role in NF-κB pathway regulation. A20 haploinsufficiency is a monogenic disorder form of Behçet's disease with a wide spectrum of phenotypic manifestations. This study aimed to establish an in vitro model to investigate the impact of the *TNFAIP3* L227X pathogenic variant on cellular survival and proliferation.

Methods: Jurkat (T cell neoplastic lineage) and THP-1 (monocytic lineage) cells were transfected with a plasmid engineered to express either wild-type (WT) or L227X *TNFAIP3*. A20 protein expression was assessed, and Ki-67 expression was utilized as a measure of cell proliferation. Cell resistance to apoptosis was evaluated using annexin V and propidium iodide

staining (before and after ultraviolet [UV] radiation or anti-CD95 stimulus). Jurkat and THP-1 cells were specifically stimulated with IL-2 + phytohemagglutinin (PHA) and phorbol-miristate-acetate (PMA), respectively. Non-transfected (NT) cells and empty plasmid (EP)-transfected cells served as controls. Flow cytometry was employed for all analyses.

Results: TNFAIP3-L227X transfection reduced A20 protein expression in both THP-1 (MFI=581.0 ± 329.0) and Jurkat cells (763.7 ± 17.32) compared to NT cells (respectively, 1169 ± 51.50 [$p < 0.01$] and 694.5 ± 0.5 [$p < 0.05$], figure 1). THP-1-TNFAIP3-L227X exhibited increased Ki-67 expression after PMA stimulus (19180 ± 4473), in contrast to THP-1-NT cells

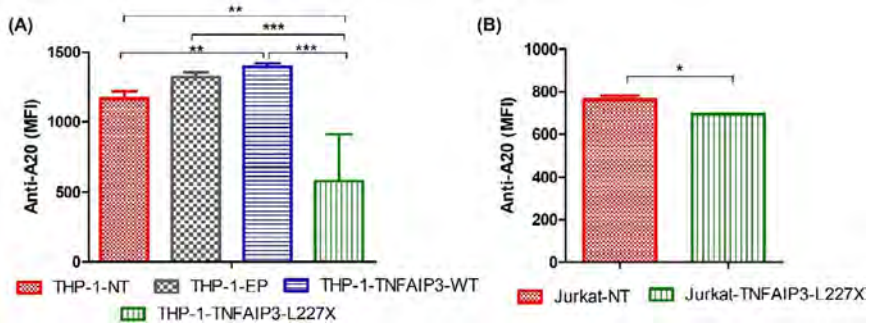


Figure 1: A20 protein expression in THP-1 (A) and Jurkat (B) cells transfected with L227X TNFAIP3 (green), compared to non-transfected cells (red) and cells transfected with WT TNFAIP3 (blue) or empty plasmid (grey). * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

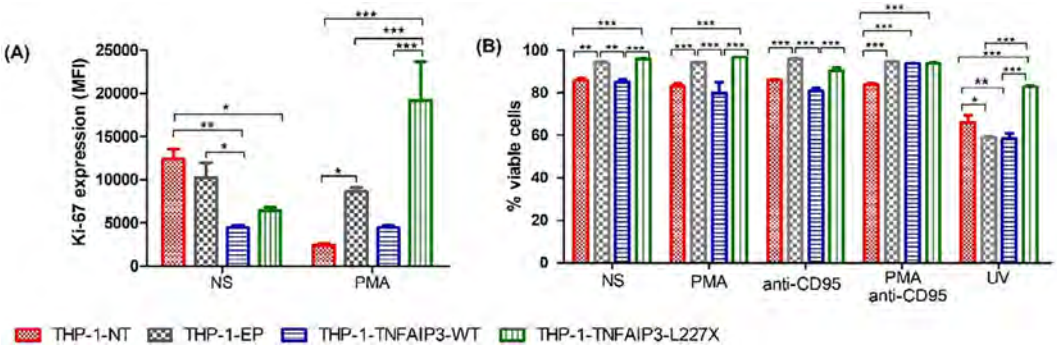


Figure 2: Proliferation rates, determined by Ki-67 expression levels (A) and resistance to apoptosis, determined by percentage of viable cells (B), in THP-1 cells transfected with L227X TNFAIP3 (green), compared to non-transfected cells (red) and cells transfected with WT TNFAIP3 (blue) or empty plasmid (grey). NS = non-stimulated. PMA = phorbol-miristate-acetate. UV = ultraviolet radiation. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

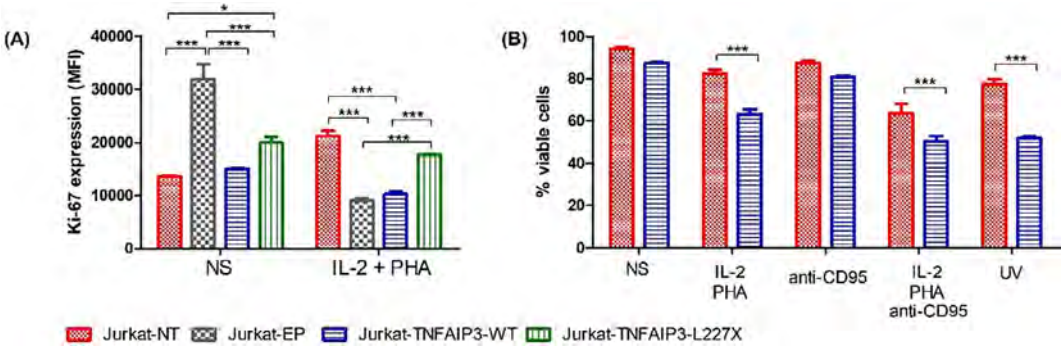


Figure 3: Proliferation rates, determined by Ki-67 expression levels (A) and resistance to apoptosis, determined by percentage of viable cells (B), in Jurkat cells transfected with L227X TNFAIP3 (green), compared to non-transfected cells (red) and cells transfected with WT TNFAIP3 (blue) or empty plasmid (grey). NS = non-stimulated. IL-2 = human interleukin-2. PHA = phytohemagglutinin. UV = ultraviolet radiation. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

(2435 ± 187.4, p< 0.001, figure 2A). Moreover, THP-1-TNFAIP3-L227X cells displayed significantly higher resistance to apoptosis at baseline and when stimulated with anti-CD95 (with or without PMA) or exposed to UV radiation (figure 2B). Jurkat-TNFAIP3-L227X (19960 ± 1048) showed elevated Ki-67 levels at baseline compared to Jurkat-NT cells (13520 ± 249.5, p< 0.05), but not compared to Jurkat-EP cells (31870 ± 2843, figure 3A), which exhibited a substantial baseline increase in Ki-67 expression. Intriguingly, TNFAIP3-WT transfection produced opposite effects, including lower proliferation rates and reduced resistance to apoptosis in both THP-1 (figure 2B) and Jurkat cells (figure 3B).

Conclusion: *TNFAIP3* L227X variant significantly impacts cell survival and proliferation in monocytic and T-lymphoid cell lineages, promoting a predominantly hyperproliferative state. Reduced A20 protein expression in both Jurkat and THP-1 suggests that L227X variant may exert a dominant negative effect on the WT *TNFAIP3* gene. Despite the limitations inherent to this cell model, our results suggest the potential utility of these functional assays for diagnosing patients suspected of harboring *TNFAIP3* genetic variants.

Disclosure: P. Aires: None; **D. Pioto**: None; **M. TErreri**: None; **S. Perazzio**: None.

Abstract Number: 0259

Preliminary Experience with a Novel "Fix" for Deep Epitope and Transcriptional Phenotyping of Fragile Cells from Autoinflammatory Flares

Hallie Carol[1], Emily Landy[2] and Scott Canna[1], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoinflammatory diseases (AID) are characterized by inflammation and immunopathology due to primary defects in the innate immune response. Neutrophils (PMN) feature prominently in the biology of most AID, but show clear differences between AID categories (e.g. mature PMN in *NLRP3*-AID, atypical PMN in proteasome-AID, low-density granulocytes in interferonopathies). However, PMN are excluded in mononuclear cell preparations (e.g. PBMC), do not tolerate freeze/thaw, have low mRNA content, and change dramatically & quickly with treatment. Thus, optimal neutrophil studies require rapid preservation of high-quality samples from unpredictable "flare" timepoints prior to significant pharmacologic intervention. Fixed-cell Indexing of Transcriptomes and Epitopes sequencing (FITEseq) is a novel method for quickly processing and preserving epitope and transcript abundance. We sought to understand which cells were excluded from PBMC preparations, and to pilot the feasibility and quality of whole blood FITEseq in active AID patients.

Methods: Pellets from patient PBMC preparations underwent magnetic red blood cell (RBC) depletion and flow cytometry. 1mL of K-EDTA anticoagulated whole blood from a new-onset Stills-like patient and one healthy control were RBC depleted, fixed (10x Single Cell Fixed RNA Sample Preparation Kit), and stored at -80C. Parallel samples were analyzed by flow cytometry. Libraries prepared using the Chromium human fixed RNA kit, RNA integrity determined by bioanalyzer, libraries quantitated by Qbit and sequenced on NextSeq1000 (P2 reagents, 100 cycles). Analysis was performed using CellRanger7 and visualizations performed using Cellenics.

Results: In addition to CD15+ neutrophils, PBMC pellets variably included monocyte populations, predominantly in patient samples, that would not be included in buffy coats. Whole blood preparation resulted in minimal death or specific loss of neutrophils. Preliminary technical analyses highlighted the importance of timely processing, precise library quantitation, and low-RNA permissive analysis. Contemporaneous Stills-like patient serum showed dramatic total IL-18 and S100A12 elevation. The proportion of neutrophils identified transcriptionally matched well with contemporaneous differential, and was higher in the patient (Fig. 1). Exploratory analysis showed higher expression of granule, S100, and interferon-inducible genes in patient myeloid cells, and CD38 on patient CD8 T-cells.

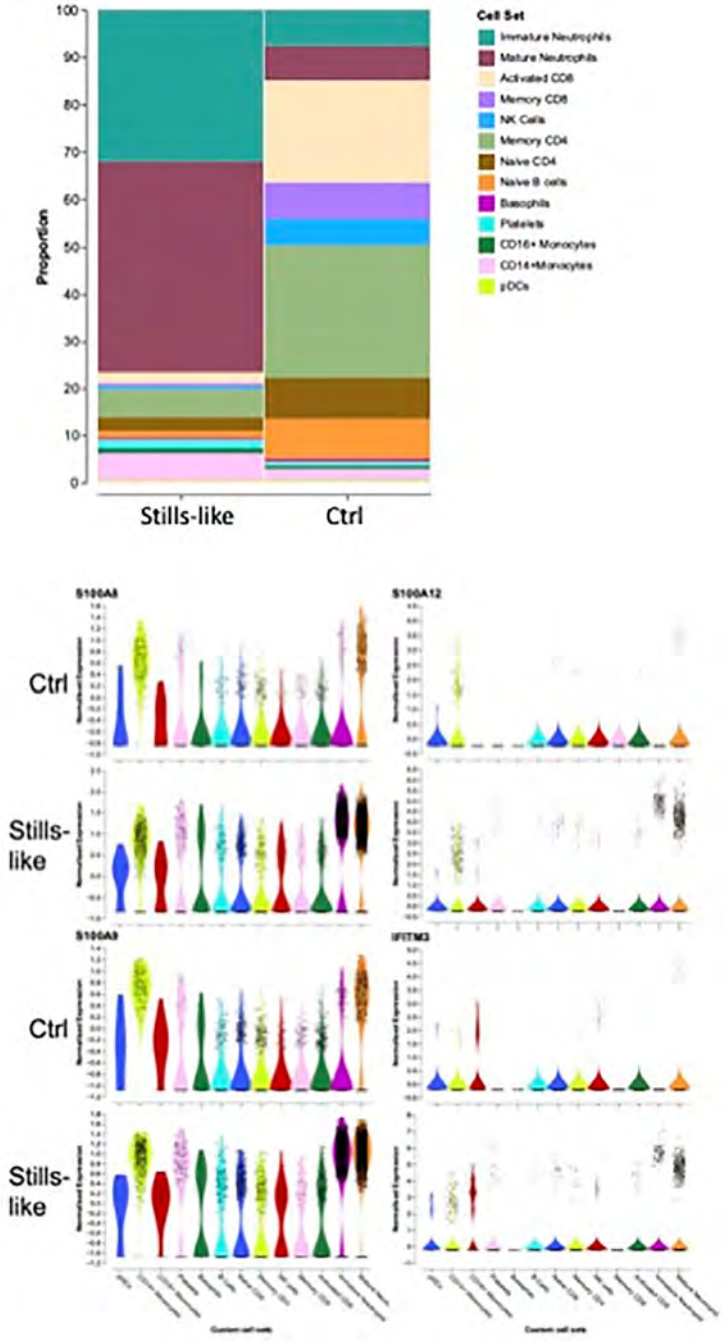


Figure 1: Proportion of total cells sequenced attributed to different cell types. Samples underwent FITE-seq. TOP: proportion of sequenced cells mapped by transcriptional signature to canonical cell types using Cellenics instance. BOTTOM: Violin plots of normalized expression of single cells of candidate genes across these canonical cell types.

Conclusion: Single-cell analysis of fixed whole blood from AID patients is feasible and demonstrates physiologically-relevant alterations in cells omitted in PBMC preparations (including PMN and monocyte populations). FITEseq may be a practical and scalable method of obtaining single-cell protein and transcriptome data from samples containing fragile myeloid cells.

Disclosure: H. Carol: None; **E. Landy**: None; **S. Canna**: Apollo Therapeutics, 2, Novartis, 12, Site PI for industry-sponsored trial, PracticePoint CME, 6, Simcha Therapeutics, 2, Sobi, 6.

Abstract Number: 0260

Phenotypes of the Patients with More Than One Autoinflammatory Gene Variant: Classified Diseases and Mixed Autoinflammatory Disorders (MAID)

Shirkhan Amikishiyev[1], Tuğba Kalaycı[2], Lale Soltanova[3], Yasemin Yalçınkaya[4], Bahar Artim-Esen[1], Murat Inanc[1], Ayla Sahin[2], Sema Sırma Ekmekci[5], Neslihan Abacı[5], Sukru Ozturk[2], Sukru Palanduz[2] and Ahmet Gul[1], [1]Division of Rheumatology, Department of Internal Medicine, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey, [2]Department of Genetics, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey, [3]Department of Internal Medicine, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey, [4]Istanbul University, Istanbul Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, [5]Istanbul University, Aziz Sancar Institute of Experimental Medicine, Department of Genetics, Istanbul, Turkey

Table 1: The genotype and phenotypes of patients who were classified according to Gattorno et. all criteria and phenotype dominancy. *: Pathogenic and likely pathogenic, †: VUS, ǂ: Biallelic VUS, ‡: p.(Pro396Ser) and p.(Arg408Gln)

Case Number	Sex	Current Age	Classification	Major gene	Amino acid change	rs number	Other genes	Amino acid change	rs number	Frequency	Typical clinic	Atypical clinic
1	M	45	FMF	*MEFV* *	p.Met694Val	rs61752717	*NLRP3* †	p.Gln705Lys	rs35829419	0.030266	Duration of episodes 3 days, arthritis, abdominal and chest pain	Neurosensorial hearing loss
2	M	37	FMF	*MEFV**	p.Met694Val	rs61752717	*TNFAIP3* †	c.1233G>T	-	-	Duration of episodes 3 days, arthritis, abdominal pain	Ankylosing spondylitis and Crohn's disease
3	M	72	FMF	*MEFV**	p.Met694Ile	rs28940578	*NLRP3* † *IL10RB* †	p.Gln705Lys c.49+47C>T	rs35829419 -	0.030266 -	Duration of episodes 3 days, abdominal pain, amyloidosis	No
4	M	36	FMF	*MEFV**	p.Met694Val	rs61752717	*TNFAIP3**	p.Thr647Pro	rs142253225	0.001885	Duration of episodes 3 days, abdominal pain	Aseptic meningitis, neurosensorial hearing loss
5	M	32	FMF	*MEFV**	p.Met694Val	rs61752717	*NLRP3* †	p.Thr954Met	rs139814109	0.000740	Duration of episodes 3 days, abdominal pain, amyloidosis	No
6	F	44	FMF	*MEFV**	p.Met694Val	rs61752717	*TNFRSF1A* †	p.Arg283Lys	rs149342980	0.000227	Duration of episodes 3 days, abdominal pain, arthritis, amyloidosis	Splenic, renal, and superior mesenteric artery aneurism, pancytopenia
7	M	56	FMF	*MEFV*	p.Arg408Gln p.Pro369Ser	rs11466024 rs11466023	*NLRP3* †	p.Gln703Lys	rs35829419	0.030266	Duration of episodes 3 days, arthritis, amyloidosis	No
8	F	31	FMF	*MEFV**	p.Met694Val	rs61752717	*LPIN2* †	p.Pro626Ser	-	-	Arthritis	Optic neuritis
9	M	49	FMF	*MEFV*‡	p.Val726Ala p.Met680Ile	rs28940579 rs28940580	*CARD14* †	p.Asp176His	rs144475004	0.000945	Arthritis	Pyoderma gangrenosum, acne, hidradenitis suppurativa
10	M	21	FMF	*MEFV*‡	p.Ser444Leu p.Pro396Ser p.Arg408Gln	rs137947663 rs11466023 rs11466024	*SH3BP2* †	p.Ser444Leu	rs137947663	0.000008	Duration of episodes 3 days, abdominal pain, arthritis	No
11	M	26	FMF	*MEFV**	p.Arg761His	rs104895097	*NOD2* † *TMEM173* †	p.Arg235Cys p.Asn183Ser	rs104895422 rs201277595	0.000121 0.000015	Arthritis	Pyoderma gangrenosum
12	M	57	VEXAS syndrome				*UBA1* † *NLRP7* †	p.Met41Lue p.Cys399Tyr	- rs104895510	- 0.000408	Fever, arthritis, myelodysplastic syndrome, nephritic syndrome, cryoglobulinemic vasculitis, autoimmune hemolytic anemia, immune thrombocytopenia	No
13	M	28	DADA2 HA20	*ADA2**	p.Pro251Leu	rs148936893	*NLRP3* †	p.Gln705Lys	rs35829419	0.030266	Fever, renal AA amyloidosis, multiple thrombotic microaneurysms in celiac, splenic, superior, inferior mesenteric, bilateral renal arteries	No
				*TNFAIP3**	p.Thr647Pro	rs142253225						
14	F	28	DADA2	*ADA2**	p.Gly47Arg	rs202134424	*IKBKB* † *NLRP2* † *NLRP7* † *SERPING1* †	p.Gly555Arg p.Ile532Thr p.Val101Leu p.Ala2Val	rs14901177 rs147222602 rs540923289 rs185342631	- 0.000087 0.000011 0.001115	Fever, rash, cerebrovascular event, neurosensorial hearing loss	No
15	F	41	DADA2				*ADA2* †	p.Lys158AsnfsTer26	rs1317479109	-	Cerebrovascular events (antiphospholipid serology negative)	Systemic lupus erythematosus with arthritis, malar rash, lupus nephritis
							MEFV †	p.Glu148Gln	rs3743930	0.028203		
16	F	27	HA20				*TNFAIP3* † *MEFV* † *NLRP12* † *LPIN2* †	p.Thr647Pro p.Glu520Val p.Glu148Gln p.Gly448Ala p.Lys387Glu	rs142253225 rs769888172 rs3743930 rs104895566 rs104895501	0.001885 0.000019 0.028203 0.00009 0.000960	Fever, aphthous stomatitis, genital ulcers, uveitis, Patergy positivity, cytopenia attacks with hyperinflammation	No

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Background: Systemic autoinflammatory disorders (SAIDs) are including a group of diseases, which are associated with genetic variations resulting in dysregulation of innate immunity and hyperinflammatory response. Pathogenic and likely pathogenic variants in certain genes have been linked to a defined phenotype, but screening of more patients with some autoinflammatory features has been revealing several variants of uncertain significance (VUS), and also patients with variants in more than one autoinflammatory gene. We herein investigated the relationship between phenotype and genotype of the patients who were screened for autoinflammatory genes and identified as carriers of variants in $^{3}2$ genes in a tertiary referral center.

Methods: Methods: Charts of the patients who had been referred to our center with a potential diagnosis of autoinflammatory disorder between April 2019 and January 2023 and the results of their genetic analyses were evaluated. All patients had the results of genetic screening of 22 genes, which were associated with different autoinflammatory disorders, and analyses covered the exons and 10 base pair intron borders of the selected genes and were carried out by using the Ion Torrent platform and Illumina platform.

Results: Results: We evaluated 146 referred patients (60 male, 85 female, mean age 41.0±12.6, range 19-82), and 38 of them (26%) identified as having ≥2 gene variants. By using the recent classification criteria for the autoinflammatory recurrent fevers,[1] eleven out of 38 (28.9%) patients were classified as FMF. Among the patients with the MEFV mutations, the

Table 2: The genotype and phenotypes of patients who were classified according to phenotype dominancy

Case number	Sex	Current age	Pathogenic variant	Likely pathogenic variant	VUS	Amino acid change	rs number	Frequency	Phenotype	Classification
1	F	32	*MEFV* p.Val726Ala rs28940579		*PSTPIP1*	c.517-99A>G	-	-	Fever, aphthous stomatitis, periorbital edema, arthralgia	PFAPA-like
					IL20RB	p.Val108Met	-	-		
2	F	21			*PSTPIP1*	p.Thr68Met	rs201872851	0.000457	Fever, aphthous stomatitis, genital ulcers, folliculitis, rash	PFAPA-like
					TRAP1	c.1165+5G>A	rs373016534	0.000253		
					LPIN2	p.Cys874Phe	rs201160155	0.000227		
3	F	30		*NLRP6* p.Arg799* rs370721274	*NLRP3*	p.Val200Met	rs121908147	0.007864	Diagnosed with Behçet's disease with fever, aphthous stomatitis, genital ulcers, arthritis, and renal transplantation because of FSGS	BD-mimic
					CASP5	p.Ser60Cys	rs572097980	0.000045		
4	M	56			*NLRX1*	p.Glu435Glyfs*40	-	-	Aphthous stomatitis, genital ulcers, Patergy positivity, cerebrovascular event, and diagnosed Behçet^s syndrome	BD-mimic
					IL36RN	p.Pro76Leu	rs139497891	0.000200		
5	F	36			*NLRX1*	p.Trp35Leu	rs985939928	0.000015	Fever, aphthous stomatitis, arthritis (2 weeks attacks)	BD-mimic
					NLRP3	p.Gln705Lys	rs35829419	0.030266		
					CARD14	p.Arg38Cys	rs281875217	0.000008		
6	M	47			*MEFV*	p.Pro369Ser p.Arg408Gln	rs11466023 rs11466024	0.011398 0.012396	Fever, aphthous stomatitis, genital ulcers, splenomegaly, neutropenia	BD-mimic
					FAS	p.*336Tryext*?	rs1258512501	0.000007		
7	F	46			*NLRP3*	p.Val200Met	rs121908147	0.007864	Fever, aphthous stomatitis, headache, myalgia	BD-mimic
					TRAP1	p.Leu638Met	rs147600197	0.000200		
					NLRP13	p.Lys1033*	rs766010573	0.00000		
8	F	28			*ADA2*	p.Met68Ile	rs146597836	0.001734	Fever, aphthous stomatitis, cervical lymphadenitis, pharyngotonsillitis, myalgia	BD-mimic
					NLRP3	p.Gln705Lys	-	-		
					TMEM173	p.Ala97Thr	rs181566154	0.000148		
9	M	33			*NLRP3*	p.Pro317Leu	rs180177462	0.000106	Attacks of fever occurred every week with severe headaches, optic neuritis, and the lesion origin on the left side of the mesial temporal region and extend to the thalamus with heterogeneous contrast involvement and bleeding foci on MRI	BD-mimic
					PSTPIP1	p.Ala353Val	rs200188483	0.000098		

Table 3: The genotype and phenotypes of patients who could not be classified

Case number	Sex	Current age	Pathogenic variant	Likely pathogenic variant	VUS	Amino acid change	rs number	Frequency	Phenotype	Classification
1	F	22	*MEFV* p.Met680Ile Rs28940580		*NLRX1*	p.Arg547Trp	rs145779362	0.005769	Systemic lupus erythematosus with arthritis, malar rash, cytopenia, lupus nephritis, cerebrovascular event, ANA, dsDNA, anti-Ro positive and antiphospholipid serology negative	Unclassified
					TRAP1	p.Arg692His	rs2791	0.027481		
			C1QA p.Gln208* Rs121909581		*NOD2*	p.Arg541Trp	rs576658764	0.000064		
					NLRP13	p.Lue250Pro	-	-		
2	M	42		*MEFV* p.Thr267Ile rs104895081	*PSTPIP1*	c.930-172C>T	-	-	Cerebrovascular event, anterior uveitis	Unclassified
3	M	39			*NLRP3*	p.Val200Met	rs121908147	0.007864	FMF-like clinic with fever, abdomen pain, and high acute phase reactants	Unclassified
					TNFRSF1A	p.Cys158Tyr	-	-		
4	F	23			*MEFV*	p.Glu148Gln	rs3743930	0.028203	Pharyngotonsillitis, cervical lymphadenitis, aphthous stomatitis	Unclassified
					STING1	p.Gly192Val	rs201096097	-		
5	M	22			*TRAP1*	p.Leu638Met	rs147600197	0.000200	Fever, abdominal pain, nausea (4 days attacks)	Unclassified
					LPIN2	p.Pro348Leu	rs34676691	0.001352		
6	F	60			*NLRC4*	p.Lys21Thr	-	-	Acute kidney injury and renal biopsy: noncaseating granuloma	Unclassified
					MEFV	p.Glu148Gln	rs3743930	0.028203		
					PLCG2	p.Tyr648Cys	rs766742207	0.000008		
					IL1R1	p.Gly398Arg	rs34835752	0.001602		
					FAS	c.*296_*297del	rs1337136004	0.000004		
					LPIN3	p.Val292Met	rs772608582	0.000042		
					NLRP14	p.Leu897Pro	rs768724978	0.000094		
7	M	29			*NLRC4*	p.Ala160Thr	rs113631419	0.000744	Fever, abdominal pain, aortitis	Unclassified
					NLRP3	p.Gln705Lys	rs35829419	0.030266		
					PSMB9	c.60+4A>G	rs1385542681	0.00005		
8	F	20			*LPIN2*	p.Lys387Glu	rs104895501	0.000960	Fever, abdominal and chest pain, cervical lymphadenitis, cytopenia (neutropenia)	Unclassified
					NOD2	p.Val162Ile	rs139571975	0.000104		
9	F	48			*TRAF3IP2*	p.Pro100Arg	rs533450897	0.000087	Fever, chest pain, pericarditis	Unclassified
					MEFV	p.Glu148Gln	rs3743930	0.028203		
					SERPINA3	p.Glu109Gly	-	-		
					FAS	p.Glu194Lys	rs56006128	0.001424		
					IL31RA	p.Ile553Asn	rs368179574	0.000023		
					CIITA	p.Ala888Thr	-	-		
10	F	23			*MEFV*	p.Leu110Pro	rs11466018	0.003132	Fever, abdominal pain, aphthous stomatitis, pharyngotonsillitis	Unclassified
					TRAP1	p.Asp685Asn	rs61756352	0.001953		
11	F	48			*MEFV*	p.Arg653His	rs104895085	0.000060	Fever, arthritis attacks	Unclassified
					NOD2	p.Asn852Ser	rs104895467	0.000971		
					PLCG2	p.His193Gln	rs201080992	0.000525		
					CEBPE	p.Arg167His	rs540261393	0.00003		
12	M	37			*MEFV*	p.Glu148Gln	rs3743930	0.028203	Duration of episodes 3 days, arthritis	Unclassified
					NOD2	p.Asp290Gly	-	-		
13	F	20			*MEFV*	p.Gly304Arg	rs75977701	0.001379	Urticarial rash, lymphadenopathy, pancytopenia	Unclassified
					NLRP2	p.Asp417Asn	rs267605682	0.000026		
					CARD14	c.1658+9_1658+11del	rs773281285	0.000026		
					NOD2	p.Leu1007Profs*2	rs2066847	0.013457		
					TNFAIP2	p.Gly39Asp	-	-		

presence of additional variants may have had an effect on the phenotype such as sensorineural hearing loss in those with NLRP3 VUS. Since the Gattorno et al. criteria were aiming only 4 common SAIDs, 5 (13.2%) patients could be diagnosed with VEXAS syndrome (n=1), deficiency of ADA2 (DADA2, n=2), A20 haploinsufficiency (HA20, n=1), DADA2 and HA20 combination (n=1) (Table 1). The remaining patients were grouped as having the PFAPA-like (n=2) and Behçet disease-mimic (n=7) according to their dominant phenotype (Table 2). Thirteen (34.2%) patients could not be classified into any groups (Table 3). Two of these cases had pathogenic and likely pathogenic variants with VUS, and others had between 2-7 different VUS combinations.

Conclusion: Discussion: The criteria developed by Gattorno et al. have some limitations in daily practice since the set includes only CAPS, FMF, TRAPS, and MKD and is not validated in adults. Although those patients with pathogenic variants could be classified by using them, the contribution of additional variants to the phenotype needs further investigation. On the other hand, an important group of adult patients may have unclassified systemic autoinflammatory features mainly associated with a combination of VUS in different genes, and this "mixed autoinflammatory disorder-MAID" phenotype needs to be followed carefully for the evaluation of long-term prognosis.

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Abstract Number: 0261

Deucravacitinib in Plaque Psoriasis: 3-Year Safety and Efficacy Results

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Deucravacitinib, a first-in-class, oral, selective, allosteric tyrosine kinase 2 inhibitor, is approved in multiple countries for the treatment of adults plaque psoriasis. Deucravacitinib was superior to placebo and apremilast in the global, 52-week, phase 3 POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751) trials in plaque psoriasis and is currently being investigated in several immune-mediated diseases and has shown efficacy in phase 2 trials for SLE and PsA. Upon completion of the parent trials, patients could enroll in the POETYK long-term extension (LTE) trial (NCT04036435). In the present LTE analysis, we report safety and efficacy of deucravacitinib up to 3 years (week 148) through data cutoff (June 15, 2022).

Methods: PSO-1 and PSO-2 randomized patients 1:2:1 to oral placebo, deucravacitinib 6 mg once daily (QD), or apremilast twice daily. At week 52, POETYK PSO-1 and PSO-2 patients enrolled in the LTE trial received open-label deucravacitinib 6 mg once daily. Safety was evaluated in patients who received ≥ 1 dose of deucravacitinib via exposure-adjusted incidence rate (EAIR) per 100 person-years (PY). Efficacy outcomes included ≥ 75%/≥ 90% reduction from baseline in Psoriasis Area and Severity Index (PASI 75/90) and static Physician's Global Assessment (sPGA) score of 0 (clear) or 1 (almost clear) with a ≥ 2-point improvement from baseline. Efficacy was reported using modified nonresponder imputation (mNRI) in patients who received continuous deucravacitinib treatment from day 1 of the parent trial and were enrolled and treated in the LTE trial. As-observed results by treatment failure rule imputation were also analyzed.

Results: 1519 patients received ≥ 1 dose of deucravacitinib, with 513 patients receiving continuous deucravacitinib treatment from day 1 in PSO-1/PSO-2 and who were treated in the LTE trial. Cumulative exposure from parent trial randomization was 3294.3 PY for these safety analyses. EAIRs/100 PY were similar, or decreased, from the 2- to 3-year cumulative period, respectively, for adverse events (AEs) (154.4to 144.8), serious AEs (6.1 to 5.5), discontinuation due to AEs (2.8 to 2.4), herpes zoster (0.7 to 0.6), malignancies (0.9 to 0.9), major adverse cardiovascular events (0.4 to 0.3), venous thromboembolism (0.1 to 0.1), and deaths (0.4 to 0.3). Clinical response rates were maintained at week 148 by mNRI (PASI 75, 73.2% [95% CI, 68.7–77.8]; PASI 90, 48.1% [95% CI, 43.2–53.1]; sPGA 0/1, 54.1% [95% CI, 49.1–59.1]), with similar results regardless of data imputation methodology.

Conclusion: Deucravacitinib demonstrated a consistent safety profile through 3 years with no increases in AE or serious AE rates over time and no emergence of new or long-term safety signals. Efficacy was sustained through 3 years in patients treated continuously with deucravacitinib from day 1 in the parent trials. Since it is important to provide long-term safety for this new class of drugs, these findings provide additional support for deucravacitinib having a consistent safety profile and durable efficacy for up to 3 years of use in patients with plaque psoriasis.

Disclosure: A. Armstrong: AbbVie, 5, Almirall, 1, 6, Arcutis, 1, 6, Aslan Pharmaceuticals, 1, 1, 6, 6, Beiersdorf, 1, 6, Boehringer Ingelheim/Parexel, 12, Personal fees, Bristol-Myers Squibb(BMS), 5, Celgene, 12, Personal fees, Dermavant, 1, 6, 12, Personal fees, Dermira, 1, 5, 6, Eli Lilly, 5, EPI Health, 1, 6, Genentech, 12, Personal fees, GSK, 12, Personal fees, Incyte, 1, 6, Janssen, 5, Kyowa Kirin, 5, Leo Pharma, 5, Lilly, 1, 6, Menlo Therapeutics, 12, Personal fees, Merck, 12, Personal fees, Mindera Health, 1, 6, Modernizing Medicine, 12, Personal fees, Nimbus, 1, 6, Novartis, 5, Ortho Dermatologics, 12, Personal fees, Pfizer, 12, Personal fees, Regeneron, 12, Personal fees, Sanofi Genzyme, 12, Personal fees, Science 37, 12, Personal fees, Sun, 1, 6, Sun Pharma, 12, Personal fees, UCB, 5, Valeant, 12, Personal fees; **M. Lebwohl**: Mark Lebwohl is an employee of Mount Sinai and receives research funds from Abbvie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Cara therapeutics, 2; **R. Warren**: AbbVie, 2, 5, 6, Almirall, 2, 5, 6, Amgen, 2, 5, 6, Arena, 2, 6, Astellas, 2, 6, Avillion, 2, 6, Biogen, 2, 6, BMS, 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 5, DiCE, 6, Eli Lilly, 2, 5, 6, GSK, 2, 6, Janssen, 2, 5, 6, LEO Pharma, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sanofi, 2, 6, Sun Pharma, 6, UCB Pharma, 2, 5, 6, Union, 6; **H. Sofen**: AbbVie/Abbott, 5, Amgen, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 1, 2, Eli Lilly, 5, UCB, 5; **S. Imafuku**: AbbVie, 5, Amgen (Celgene), 12, Personal fees, Boehringer Ingelheim, 12, Personal fees, Bristol Myers Squibb, 12, Personal fees, Daiichi Sankyo, 12, Personal fees, Eisai, 5, Eli Lilly, 12, Personal fees, GSK, 12, Personal fees, Janssen, 5, Kyowa Kirin, 5, Leo Pharma, 5, Maruho, 5, Novartis, 12, Personal fees, Sun Pharma, 5, Taiho Yakuhin, 5, Tanabe Mitsubishi, 5, Torii Yakuhin, 5, UCB, 12, Personal fees; **M. Ohtsuki**: AbbVie, 5, 6, Amgen, 5, 6, Boehringer-Ingelheim, 5, 6, Bristol Myers Squibb, 5, 6, Celgene, 5, 6, Eisai, 5, 6, Eli Lilly, 5, 6, Janssen, 5, 6, Kyowa Kirin, 5, 6, Leo Pharma, 5, 6, Maruho, 5, 6, Mitsubishi Tanabe Pharma, 5, 6, Nichi-Iko, 5, 6, Nippon Kayaku, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Sanofi, 5, 6, Sun Pharma, 5, 6, Taiho Pharmaceutical, 5, 6, Torii Pharmaceutical, 5, 6, UCB, 5, 6; **L. Spelman**: AbbVie, 1, 2, 6, Amgen, 2, 6, 12, Investigator, Anacor, 2, 6, 12, Investigator, Astellas, 2, 6, 12, Investigator, AstraZeneca, 2, 6, 12, Investigator, Blaze Bioscience, 2, 6, 12, Investigator, Boehringer-Ingelheim, 2, 6, 12, Investigator, Botanix, 2, 6, 12, Investigator, Bristol Myers Squibb, 2, 6, 12, Investigator, Celgene, 2, 6, 12, Investigator, Dermira, 2, 6, 12, Investigator, Eli Lilly, 2, 6, 12, Investigator, Galderma, 2, 6, 12, Investigator, Genentech, 2, 6, 12, Investigator, GSK, 2, 6, 12, Investigator, Hexima, 2, 6, 12, Investigator, Janssen, 2, 6, 12, Investigator, Leo Pharma, 2, 6, 12, Investigator, Mayne Pharma, 2, 6, 12, Investigator, MedImmune, 2, 6, 12, Investigator, Merck, 2, 6, 12, Investigator, Merck-Serono, 2, 6, 12, Investigator, Novartis, 2, 6, 12, Investigator, Otsuka, 2, 6, 12, Investigator, Pfizer, 2, 6, 12, Investigator, Phosphagenics, 2, 6, 12, Investigator, Photon MD, 2, 6, 12, Investigator, Regeneron, 2, 6, 12, Investigator, Roche, 2, 6, 12, Investigator, Samumed, 2, 6, 12, Investigator, Sanofi Genzyme, 2, 6, 12, Investigator, SHR Pharmacy, 2, 6, 12, Investigator, Sun Pharma ANZ, 2, 6, 12, Investigator, Trius, 2, 6, 12, Investigator, UCB, 2, 6, 12, Investigator, Zai Lab, 2, 6, 12, Investigator; **T. Passeron**: AbbVie/Abbott, 2, 6, Amgen, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 1, 5, 6, Celgene, 6, Eli Lilly, 1, 6, Janssen, 1, 6, Novartis, 1, 6, Pfizer, 6, UCB, 1, 5, 6; **K. Papp**: AbbVie, 1, 2, 5, 6, Akros, 1, 2, 5, 6, Amgen, 1, 2, 5, 6, Anacor, 1, 2, 5, 6, Arcutis, 1, 2, 5, 6, Astellas, 1, 2, 5, 6, Bausch Health/Valeant, 1, 2, 5, 6, Baxalta, 1, 2, 5, 6, Boehringer-Ingelheim, 1, 2, 5, 6, Bristol-Myers Squibb, 1, 2, 5, 6, Can-Fite Biopharma, 1, 2, 5, 6, Celgene, 1, 2, 5, 6, Coherus, 1, 2, 5, 6, Dermira, 1, 2, 5, 6, Dow Pharma, 1, 2, 5, 6, Eli Lilly, 1, 2, 5, 6, Evelo, 1, 2, 5, 6, Forward Pharma, 5, Galapagos, 1, 2, 5, 6, Galderma, 1, 2, 5, 6, Genentech, 1, 2, 5, 6, Gilead, 1, 2, 5, 6, GlaxoSmithKlein, 1, 2, 5, 6, Janssen, 1, 2, 5, 6, Kyowa-Hakko Kirin, 1, 2, 5, 6, LEO Pharma, 1, 2, 5, 6, MedImmune, 1, 2, 5, 6, Meiji Seika Pharma, 1, 2, 5, 6, Merck-Serono, 1, 2, 5, 6, Mitsubishi Pharma, 1, 2, 5, 6, Moberg Pharma, 1, 2, 5, 6, MSD, 1, 2, 5, 6, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, 6, PRCL Research, 1, 2, 5, 6, Regeneron, 1, 2, 5, 6, Roche, 1, 2, 5, 6, Sanofi-Aventis/Genzyme, 1, 2, 5, 6, Sun Pharma, 1, 2, 5, 6, Takeda, 1, 2, 5, 6, UCB, 1, 2, 5, 6; **R. Kisa**: Bristol-Myers Squibb(BMS), 3, 12, Shareholder; **V. Berger**: Bristol-Myers Squibb(BMS), 3, 11; **E. Vritzali**: None; **K. Hoyt**: Bristol-Myers Squibb(BMS), 2; **M. Colombo**: Bristol-Myers

Squibb(BMS), 3, 11; **S. Banerjee**: Bristol-Myers Squibb(BMS), 3, 11; **B. Strober**: AbbVie, 6, 6, Alamar, 6, Almirall, 6, Alumis, 6, Amgen, 6, Arcutis, 6, 6, Arena, 6, Aristea, 6, Asana, 6, Boehringer Ingelheim, 6, Bristol Myers Squibb, 12, Consultancy honoraria, Connect Biopharma, 6, 11, CorEvitas, 6, CorEvitas Psoriasis Registry, 12, Scientific Co-Director (consulting fee), 12, Investigator, Dermavant, 6, 6, Dermira, 12, Investigator, Eli Lilly, 6, 6, Evelo Biosciences, 6, Immunic Therapeutics, 6, Incyte, 6, Janssen, 6, 6, Journal of Psoriasis and Psoriatic Arthritis, 6, Leo, 6, Maruho, 6, Meiji Seika Pharma, 6, Mindera Health, 6, 11, Novartis, 6, Pfizer, 6, Protagonist, 6, Regeneron, 6, 6, Sanofi-Genzyme, 6, 6, Sun Pharma, 6, UCB Pharma, 6, Union Therapeutics, 6, Ventyxbio, 6, vTv Therapeutics, 6; **D. Thaçi**: AbbVie, 1, 2, 5, 12, Investigator, Almirall, 1, 2, 12, Investigator, Amgen, 1, 2, 12, Investigator, Boehringer-Ingelheim, 1, 2, 12, Investigator, Bristol-Myers Squibb(BMS), 1, 2, 12, Investigator, Celltrion, 1, 2, 12, Investigator, Eli Lilly, 1, 2, 12, Investigator, Galapagos, 1, 2, 12, Investigator, Galderma, 1, 2, 5, 12, Investigator, Janssen-Cilag, 1, 2, 12, Investigator, LEO Pharma, 1, 2, 5, 12, Investigator, Novartis, 1, 2, 5, 12, Investigator, Pfizer, 1, 2, 12, Investigator, Regeneron, 1, 2, 12, Investigator, Samsung, 1, 2, 12, Investigator, Sandoz, 1, 2, 12, Investigator, Sanofi, 1, 2, 12, Investigator, Target-Solution, 1, 2, 12, Investigator, UCB, 1, 2, 12, Investigator; **A. Blauvelt**: AbbVie/Abbott, 5, 6, Abcentra, 6, Acelyrin, 12, Clinical study investigator, Aclaris, 6, Affibody, 6, Aligos, 6, Allakos, 12, Clinical study investigator, Almirall, 6, Alumis, 6, Amgen, 5, 6, Anaptysbio, 6, Apogee, 6, Arcutis, 5, 6, Arena, 6, Aslan, 6, Athenex, 5, 6, 12, Clinical study investigator, Bluefin, 6, Boehringer-Ingelheim, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Cara Therapeutics, 6, Concert, 12, Clinical study investigator, CTI Biopharma, 6, Dermavant, 5, 6, EcoR1, 6, Eli Lilly, 5, 6, Escient, 6, Evelo, 6, Evommune, 6, Forte, 6, Galderma, 5, 6, Highlightll Pharma, 6, Incyte, 5, 6, InnoventBio, 6, Janssen, 5, 6, Landos, 6, Leo, 5, 6, Merck/MSD, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Rani, 6, Rapt, 6, Regeneron, 5, 6, Sanofi Genzyme, 6, Spherix Global Insights, 6, Sun Pharma, 5, 6, TLL Pharmaceutical, 6, TrialSpark, 6, UCB, 5, 5, 6, 6, Union, 6, Ventyx, 6, Vibliome, 6, Xencor, 6.

Abstract Number: 0262

Destructive Arthritis in Whipple Disease. a Single-center Case Series of 14 Patients

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

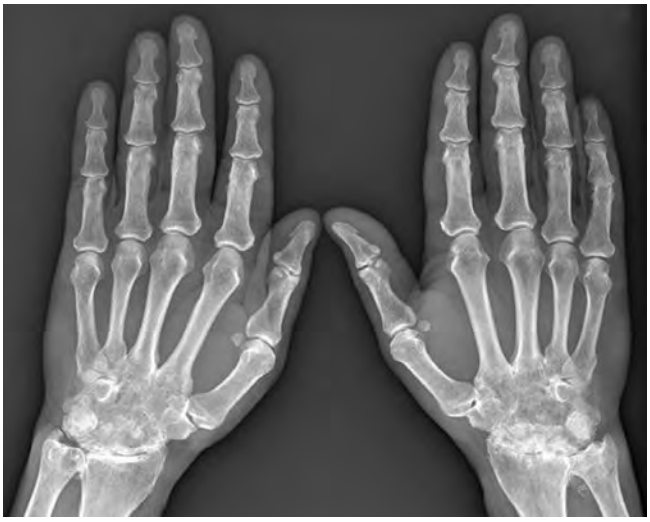
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

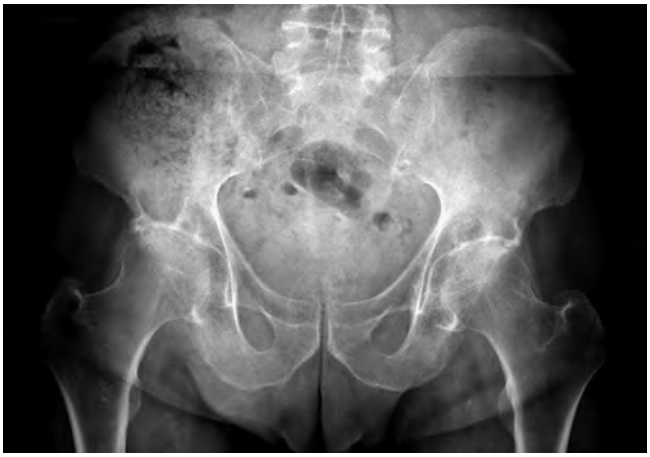
Session Time: 9:00AM–11:00AM

Background/Purpose: Whipple disease is a chronic, curable, systemic bacterial infection caused by *Tropheryma whipplei*. The classic form usually begins with recurrent arthritis, followed years later by weight loss or diarrhea, sometimes associated with fever, lymphadenopathy, neurological, cardiac or ocular signs.[1] Arthritis can occur in isolation for years, which can significantly delay diagnosis and lead to destruction and damage.

Methods: We describe a series of patients with destructive arthritis among those diagnosed with Whipple disease between 2007 and 2023 at our National Referral Center for Rare Systemic Autoimmune Diseases.



Severe bilateral cartilage loss in the radiocarpal, intercarpal, and carpometacarpal joints with ankylosis. The metacarpophalangeal and interphalangeal joints are spared.



Advanced bilateral iliofemoral joint space narrowing with subchondral cysts.

Results: Among a consecutive series of 52 patients diagnosed with Whipple disease during the study period, 48 presented joint manifestations, 14 of whom had destructive arthritis: 13 men and one woman, diagnosed at a mean (SD) age of 65.0 (9.5) years. Their first symptoms appeared at a mean age of 45.3 (12.5) years and consisted of arthritis in 13 (93%). Initially, all patients had intermittent arthritis, usually affecting one large joint at a time, with complete resolution within a week. After a mean of 11.7 (9.7) years, 12 patients developed permanent chronic arthritis with occasional additional flares. At diagnosis, all but one patient had chronically elevated CRP values (mean, 5.4 mg/dL), and neutrophil hyperleukocytosis was present in 67% of patients. Rheumatoid factor was detected in one patient and ACPA testing was negative in all. Radiographs showed narrowing of the carpal or radiocarpal joint in 12 cases (8 bilateral, 4 unilateral) (Figure 1), and global narrowing of the iliofemoral joint space in 10 cases (7 bilateral, 3 unilateral) (Figure 2), with subchondral cysts in 6. Progression to ankylosis occurred in 7 cases, at a late stage of the disease. Small joints were always spared. The diagnosis was made only after a mean delay of 19.7 (11.8) years (range, 5.4-40.1 years) after the first signs of the disease. Only 5/13 patients (38%) had positive PAS staining on duodenal biopsies. The diagnosis was confirmed by positive PCR results for *Tropheryma whipplei* on stool (73%), saliva (73%), and duodenal tissue (83%) samples; 5/8 patients (63%) were PCR positive in synovial fluid, 4/9 (44%) in blood and 3/8 (38%) in cerebral spinal fluid. Eleven patients received doxycycline and hydroxychloroquine, combined in case of CNS involvement (n=4) with sulfadiazine; 3 were treated with trimethoprim-sulfamethoxazole. Dramatic

improvement was observed after administration of antibiotic therapy in all cases, with disappearance of arthritis flares within a few days.

Conclusion: A diagnosis of Whipple disease should be considered in a middle-aged man with unexplained seronegative destructive arthritis of the large joints, especially when preceded by intermittent acute episodes of arthritis and accompanied by persistent elevated CRP levels or leukocytosis, even in the absence of the cardinal manifestations of infection. PCR testing for *Tropheryma whipplei* from saliva and stool samples, or synovial fluid if available, has become the preferred initial diagnostic test. Clinical and biological improvement is often dramatic under antibiotic treatment.

Reference: 1. Puéchal X, *et al*. *N Engl J Med* 2007;356:55-66.

Disclosure: X. Puéchal: None; **P. Blanche**: None; **O. Fogel**: None; **O. Al Tabaa**: None; **R. Ghossan**: None; **X. Ayral**: None; **J. AVOUAC**: AbbVie, 1, 2, 4, 6, BMS, 4, 5, 6, Fresenius Kabi, 4, 5, Galapagos, 1, 2, 4, 6, Lilly, 6, Novartis, 5, 6, Pfizer, 5, 6, Sanofi, 4, 6; **M. Breban**: None; **Y. ALLANORE**: AbbVie/Abbott, 2, Alpine Immunoscience, 5, AstraZeneca, 2, Bayer, 2, Boehringer-Ingelheim, 2, Janssen, 2, Medsenic, 2, 5, Mylan, 2, OSE Immunotherapeutics, 5, Prometeus, 2, Roche, 2, Sanofi, 2.

Abstract Number: 0263

Patient, Disease, and Treatment Factors in Remission of Inflammatory Eye Disease

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Noninfectious inflammatory eye disease (NIIED) is a sight-threatening condition with two-thirds of patients incurring prolonged vision loss due to uncontrolled ocular inflammation. Non-glucocorticoid systemic therapy (NGST) effectively induces and maintains remission in NIIED. However, minimal research exists on the risk factors for requiring long-term NGST for NIIED control or for NIIED relapse after discontinuation of NGST.

Methods: We performed a retrospective chart review of NIIED patients who were evaluated by the Cleveland Clinic Ophthalmology and Rheumatology departments and initiated NGST between January 1, 2014 through December 31, 2018, and had at least 4 years of follow-up prior to December 31, 2022. If treatment was dictated by systemic disease, patients were excluded. Data were extracted from the electronic medical record. The association between patient characteristics and the groups were analyzed through univariate logistic regression.

Results: 94 NIIED patients were included in the study. 78 patients (83.0%) were maintained on NGST throughout the study period, designated as long-term NGST. 16 patients (17.0%) had NGST discontinued due to inactive NIIED, denoted as short-term NGST. NIIED location was significantly different between the two groups (Table 1). Patients with intermediate, posterior, or pan uveitis were more likely to require long-term NGST compared to patients with anterior uveitis (Table 2). Age, sex, race, presence of systemic disease, and treatment with biologic or nonbiologic medication were not significantly

Variable	Level	All (n=94)	Short-Term NGST (n=16)	Long-Term NGST (n=78)	P-value	N
Sex	Male	26 (27.7%)	6 (37.5%)	20 (25.6%)	0.365	94
	Female	68 (72.3%)	10 (62.5%)	58 (74.4%)		
Race	Non-white	21 (22.3%)	1 (6.25%)	20 (25.6%)	0.110	94
	White	73 (77.7%)	15 (93.8%)	58 (74.4%)		
Age at NIIED Diagnosis		44.5 (14.8)	49.1 (18.7)	43.6 (13.7)	0.279	92
Systemic Disease	Yes	41 (43.6%)	5 (31.2%)	36 (46.2%)	0.413	94
Primary Ocular Autoimmune Disease	Yes	58 (63.7%)	12 (80.0%)	46 (60.5%)	0.254	91
NIIED Location	Anterior Uveitis	13 (14.1%)	5 (35.7%)	8 (10.3%)	**0.023**	92
	Intermediate/Posterior/Panuveitis	64 (69.6%)	6 (42.9%)	58 (74.4%)		
	Scleritis	15 (16.3%)	3 (21.4%)	12 (15.4%)		
	Bilateral	12 (80.0%)	2 (66.7%)	10 (83.3%)		
History of Ocular Steroid Implant	Yes	31 (33.0%)	3 (18.8%)	28 (35.9%)	0.300	94
NGST Class	Biologic	35 (37.6%)	6 (37.5%)	29 (37.7%)	1.000	93
	Non-Biologic	58 (62.4%)	10 (62.5%)	48 (62.3%)		
Time from Symptom Onset to NGST Initiation (days)		380 [151;1201]	184 [101;1121]	448 [203;1201]	0.080	93

Short-term NGST (discontinued NGST during study period) and long-term NGST (continued NGST during study period). Continuous variables presented as Median [IQR]. Categorical variables presented as N (column %).

Descriptive comparison of risk factors between Short-Term vs Long-Term NGST groups for NIIED patients. NIIED location was significantly different between the two groups. Patients in the short-term NGST group had earlier initiation of NGST than patients in the long-term NGST group.

different between the groups. However, data trends showed that patients with white race were more likely to require long-term NGST than non-white race; earlier initiation of NGST was more represented in the short-term NGST group which may imply that earlier initiation of NGST confers a greater likelihood of discontinuing NGST due to inactive NIIED. Within the short-term NGST group, 11 patients (68.8%) had inactive NIIED for ≥ 1 year, designated as sustained remission, and 5 patients (31.3%) had relapse of active NIIED < 1 year, designated as intermediate group. NIIED patients with sustained remission tended to be diagnosed at an older age and had earlier initiation of NGST than the intermediate group (Table 3).

Conclusion: This study provides insight into the risk factors for requiring long-term NGST and sustained remission for patients with NIIED. Our results demonstrate that NIIED location of intermediate, posterior, or pan uveitis is a risk factor for requiring long-term NGST. Older age and earlier initiation NGST may be associated with sustained remission of NIIED.

Variable	Level	OR [95%CI]	P-value
Age at Diagnosis		0.76 [0.52;1.13]	0.178
Sex	Female v Male	1.74 [0.52;5.42]	0.354
Race	White v Non-white	0.22 [0.01;1.21]	0.090
Systemic Disease	Yes v No	1.85 [0.60;6.49]	0.291
NIIED Location		5.84 [1.36;25.0]	**0.019**
	Intermediate/Posterior/Panuveitis v Anterior Uveitis		
	Scleritis v Anterior Uveitis	2.38 [0.43;15.5]	0.322
	Intermediate/Posterior/Panuveitis v Scleritis	2.43 [0.43;11.1]	0.288
NGST Class	Non-Biologic v Biologic	1.00 [0.31;3.04]	0.998
Time from Symptom Onset to NGST Initiation (days)		1.00 [1.00;1.00]	0.378

Univariate logistic regression results of risk factors between short-term NGST and long-term NGST groups. Patients with intermediate, posterior, or pan uveitis were more likely to be in the long-term NGST group than patients with anterior uveitis.

Variable	Level	All (n=16)	Intermediate Group (n=5)	Sustained Remission (n=11)	N
Age at Diagnosis		55.5 [33.8;64.2]	28.0 [22.0;35.0]	59.0 [50.0;64.5]	16
Sex	Male	6 (37.5%)	3 (60.0%)	3 (27.3%)	16
	Female	10 (62.5%)	2 (40.0%)	8 (72.7%)	
Race	Non-white	1 (6.25%)	0 (0.00%)	1 (9.09%)	16
	White	15 (93.8%)	5 (100%)	10 (90.9%)	
Systemic Disease	None	11 (68.8%)	4 (80.0%)	7 (63.6%)	16
NIIED Location	Anterior Uveitis	5 (35.7%)	2 (50.0%)	3 (30.0%)	14
	Intermediate/Posterior/Panuveitis	6 (42.9%)	1 (25.0%)	5 (50.0%)	
	Scleritis	3 (21.4%)	1 (25.0%)	2 (20.0%)	
NGST Class	Biologic	6 (37.5%)	4 (80.0%)	2 (18.2%)	16
	Non-Biologic	10 (62.5%)	1 (20.0%)	9 (81.8%)	
Time from Symptom Onset to NGST Initiation (days)		184 [101;1121]	1534 [349;2014]	126 [97.5;220]	16
Treatment Duration (Days)		1108 [669;1500]	1508 [1414;1740]	779 [478;1278]	16
Remission Time (Days)		628 [306;1106]	183 [129;238]	1027 [628;1388]	16

Intermediate Group (relapsed < 1 year after stopping NGST) and Sustained Remission (inactive disease ≥ 1 year off NGST). Continuous variables presented as Median [IQR]. Categorical variables presented as N (column %).

Descriptive comparison of risk factors between patients in the Intermediate v Sustained Remission Groups. The sustained remission group was diagnosed at an older age and had earlier initiation of NGST than patients in the intermediate group.

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Abstract Number: 0264

A Novel Role for Rheumatologists: Managing Idiopathic Granulomatous Mastitis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Idiopathic Granulomatous Mastitis (IGM) is a rare often self-limited chronic inflammatory breast disease of unknown etiology characterized by non-caseating granulomas in breast tissue, affecting primarily women of childbearing age. The diagnosis is made by histological examination after excluding other conditions (particularly malignancy and infections).Management options are limited and include observation, antibiotics, corticosteroids, and methotrexate (MTX). Progression and recurrence are common despite treatment. We present a series of patients referred to a rheumatology practice.

Methods: We reviewed the charts of all patients referred to a rheumatology practice with biopsy-confirmed diagnosis of IGM (2019-2023). Demographics, clinical information, and treatment are summarized in Table 1. For the purpose of this report, we defined improvement as the patients' subjective assessment of their pain/discomfort; the disappearance of discharge; and a reduction/disappearance of the breast mass(es).

Table 1 – IGM patients referred to a rheumatology practice

Pt #	Ethnicity	Age	Side	Initial treatment	Rheumatologist's treatment	F/U (mo)	Outcome
Pt_01	H	23	R	Ab	Pred + MTX	17	No pain or drainage - mass reduced
Pt_02	W	34	L	Ab + Af	Pred + MTX	8	No pain or drainage - mass reduced
Pt_03	H	39	R+L	Pred	MTX	8	No pain or drainage - mass reduced
Pt_04	ME	41	R+L	Pred	MTX	12	Resolved – normal mammogram
Pt_05	H	39	L	Ab	MTX > Adalimumab	15	No pain or drainage - mass reduced
Pt_06	H	48	L	Ab	None	2	No pain or drainage - mass reduced
Pt_07	SA	39	R	Pred	Etanercept	7	No pain or drainage - mass reduced
Pt_08	AA	39	L	Medrol pack	Pred	1	No pain or drainage - mass reduced
Pt_09	SA	36	L	Ab + Pred	MTX	2	No pain or drainage - mass resolved
Pt_10	H	36	R	Ab + Pred	Etanercept	4	No pain or drainage - mass reduced
Pt_11	H	43	R	Pred	Pred	-	Reported improvement – no follow-up
Pt_12	W	42	L	Ab + Pred	Etanercept	4	No pain or drainage - mass reduced
Pt_13	H	37	L	Pred	1 mo Rifampin for TB > Etanercept	-	Reported worsening – no follow-up

Pt = Patient; H = Hispanic; W = White; ME = Middle Eastern; SA = South Asian; AA = African American; R = Right; L = Left; Ab = Antibiotic; Af = Antifungal; Pred = Prednisone; MTX = Methotrexate; F/U = Follow up; mo = Months

Results: Thirteen parous women (median age 39 yrs, range 23 – 48) were referred to us by a breast surgery practice to exclude possible causes for their granulomatous breast masses. Biopsy revealed non-necrotizing granulomas and no malignancy; cultures were negative for bacteria, mycobacteria, and fungi. All patients were otherwise in good health. We obtained ANCA panel, ACE levels, and chest X-ray to gain insights into possible non-caseating granulomatous diseases (*e.g.*, sarcoidosis and ANCA-associated vasculitis). All test results were normal. Previous treatments by the referring breast surgeon, including antibiotics or anti-fungal only (4 patients), antibiotics and corticosteroids (3 patients), and corticosteroids only (6 patients), had failed to induce improvement (as defined above). Only one patient (#6 in table 1) improved with antibiotics alone (after referral) and did not require follow-up; two patients (#8 and #11) improved with continuing corticosteroids; MTX was used in 6 patients, alone (#3. #4, #9), as steroid sparing (#1, #2), or in association with an anti-TNF-α (#5). In 5 patients with persistent or recurrent manifestations (multiple masses, marked drainage, severe pain) we added anti-TNF-α agents (etanercept or adalimumab). Four of the 5 patients (#5, #7, #10, and #12) experienced substantial clinical improvement and the lesions resolved completely (in one case confirmed by mammogram). Patient #13 reported worsening of her symptoms after one dose of etanercept and refused to return for a follow-up appointment.

Conclusion: There are no evidence-based guidelines on the management for IGM. Treatments include observation, antibiotics, systemic or intra-lesional corticosteroids, MTX (alone or as steroid sparing), and rarely surgery. Many patients do not tolerate systemic corticosteroids; MTX is contraindicated in child-bearing women without contraception. Anti-TNF-α agents may represent a safer treatment. The rationale for their use is that by blocking TNF-α, a cytokine that plays a major role in forming and maintaining granulomas, these agents may provide an effective and targeted alternative, making rheumatologists pivotal partners in the management of IGM.

Disclosure: M. Genta: None; **A. DiPasquale**: Impedimed, 1, Simbiosys, 1, Sirius Medical, 1, Stryker, 2.

Abstract Number: 0265

Differential and Combinatorial Mechanism of Action of Golimumab and Guselkumab in Ulcerative Colitis Induction Therapy: IL-23 Blockade Drives Restoration of Normal Epithelium and Mucosal Healing

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The combination treatment of golimumab (GOL), a tumor necrosis factor-alpha (TNFα) antagonist, and guselkumab (GUS), an interleukin (IL)-23 inhibitor was shown to induce higher rates of clinical remission, endoscopic improvement, and histologic remission than each monotherapy in a randomized Phase 2 induction study in TNFα-naïve patients with moderately to severely active ulcerative colitis (VEGA; NCT03662542). Here, we investigated the underlying mechanism of action of GOL, GUS, and the combination (GUS+GOL).

Methods: Colon biopsies were obtained at screening and at Week 12 in patients who received GOL (n=48), GUS (n=52), or GUS+GOL (n=50). Tissue transcriptional profiles were determined with RNA sequencing. Differentially expressed genes were analyzed in the context of cell-type specific transcriptional modules by first defining a gene correlation network and

	Golimumab	Guselkumab	Combination
Numbers of genes up at Week 12	633	495	4,776
Numbers of genes down at Week 12	709	613	4,867
Th17 module: Responder vs Non-Responder Week 12 (p-value)	<0.001	<0.001	<0.001
Th17 module: Responder Week 12 vs Baseline (p-value)	<0.05	<0.001	<0.001
Th17 module: Non-Responder Week 12 vs Baseline (p-value)	NS	0.01	<0.001
Epithelial module: Responder vs Non-Responder Week 12 (p-value)	<0.01	<0.001	<0.001
Epithelial module: Responder Week 12 vs Baseline (p-value)	<0.05	<0.001	<0.001
Epithelial module: Non-Responder Week 12 vs Baseline (p-value)	NS	<0.01	<0.001

P-values associated with GSVA enrichment of biologic modules associated with endoscopic response and at Week 12.

GSVA, gene set variation analysis; NS, not significant

unsupervised network clustering. We then developed a method to create a single-cell-derived co-expression network using published ulcerative colitis single-cell data to provide high resolution gene modules associated with specific cell types and pathways. Gene set variation analysis (GSVA) was used to quantitatively assess changes in specific biologic modules in the context of responder and non-responder analyses.

Results: By Week 12, combination therapy induced a greater magnitude of transcriptional changes in the colon compared with each monotherapy (**Table**). These genes were associated with IL-23/Th17/myeloid-related processes, inflammation, and epithelial homeostasis. Significant changes were observed in Th17 cell and inflammatory epithelial cell modules in patients who achieved endoscopic improvement (subscore 0 or 1) at Week 12 compared with non-responders (**Table**). The magnitude of change relative to baseline was greater in the GUS monotherapy and GUS+GOL arms compared with GOL alone. These changes were consistent with a decrease in crypt destruction in responders at Week 12 as observed by histologic changes in the Geboes score. Genes modulated by GUS+GOL were indicative of greater suppression of inflammation, particularly myeloid cell activation and inflammatory fibroblast development. In contrast, genes modulated by either GUS or GUS+GOL were associated with increased epithelial normalization and decreased Th17 activity compared to GOL alone.

Conclusion: Combination induction with GOL+GUS for 12 weeks drove a greater reduction in inflammation and improvement in epithelial homeostasis compared to each monotherapy, demonstrating differential and complementary mechanisms of action of TNFα and IL-23 blockade. Combination therapy drives a significant increase in the overall magnitude of response with marked improvement in the restoration of normal epithelium.

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Abstract Number: 0266

E-selectin, ICAM-1 and ET-1 Biomarkers Address the Concern of the Challenging Diagnosis of Interstitial Lung Disease in Patients with Autoimmune Diseases

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) constitutes one of the most critical comorbidities in autoimmune diseases (AD), particularly in rheumatoid arthritis (RA) and systemic sclerosis (SSc) [1-2]. Therefore, its early diagnosis is pivotal to avoid irreversible lung damage in these patients. However, no definitive serum biomarkers are available to identify ILD in AD patients. In this sense, lung vasculopathy is one of the essential processes to the development of lung fibrosis [3-4]. Accordingly, we sought to determine if E-selectin, ICAM-1, and ET-1, crucial molecules in endothelial damage, could be helpful screening biomarkers for the detection of AD-ILD$^+$.

Methods: The study objective groups involved 21 patients with RA-ILD$^+$ and 21 patients with SSc-ILD$^+$. Furthermore, we included three comparative groups of patients: 25 with RA-ILD$^-$, 20 with SSc-ILD$^-$ and 21 with idiopathic pulmonary fibrosis (IPF).Serum levels of E-selectin, ICAM-1 and ET-1 were determined by ELISA.

Results: RA-ILD$^+$ patients showed increased levels of E-selectin, ICAM-1 and ET-1 compared to those with RA-ILD$^-$ ($p< 0.01$ in all the cases, **Figure 1A**). Interestingly, the ability of serum E-selectin, ICAM-1 and ET-1 levels to discriminate patients with RA-ILD$^+$ from those with RA-ILD$^-$ were confirmed by performing ROC curves analysis (AUC: 0.78, $p< 0.01$; AUC: 0.72, $p=0.01$; AUC: 0.77, $p< 0.01$, respectively, **Figure 1B**). The optimal cutoff value for E-selectin, ICAM-1 and ET-1 revealing the best sensitivity and specificity was 74.56 ng/mL, 451.70 ng/mL and 1.02 pg/mL, respectively. Furthermore, higher ICAM-1 serum levels were found in patients with SSc-ILD$^+$ compared to those with SSc-ILD$^-$ ($p< 0.01$, **Figure 2A**). Of note, the ROC curve supported a utility of ICAM-1 for differentiating patients with SSc-ILD$^+$ from those with SSc-ILD$^-$ (**Figure 2B**). The AUC was 0.79 ($p< 0.01$) and the optimal cutoff value was 484.70 ng/mL (**Figure 2B**). Moreover, a negative correlation between ET-1 serum levels and both forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) was observed in patients with RA-ILD$^+$ ($r=-0.56$, $p=0.04$ and $r=-0.65$, $p=0.01$, respectively). Likely, E-selectin serum levels were negatively correlated with FVC, FEV1 and diffusing capacity of the lung for carbon monoxide (DLCO) in patients with SSc-ILD$^+$ ($r=-0.64$, $p< 0.01$; $r=-0.56$, $p=0.02$; and $r=-0.56$, $p=0.02$, respectively).

Conclusion: Our findings support a relevant role of E-selectin, ICAM-1 and ET-1 in RA-ILD$^+$ as well as of ICAM-1 in SSc-ILD$^+$, constituting potential screening blood biomarkers of subclinical ILD in AD. Moreover, this study suggests ET-1 and E-selectin as possible indicators of worsening lung function in RA-ILD$^+$ and SSc-ILD$^+$, respectively.

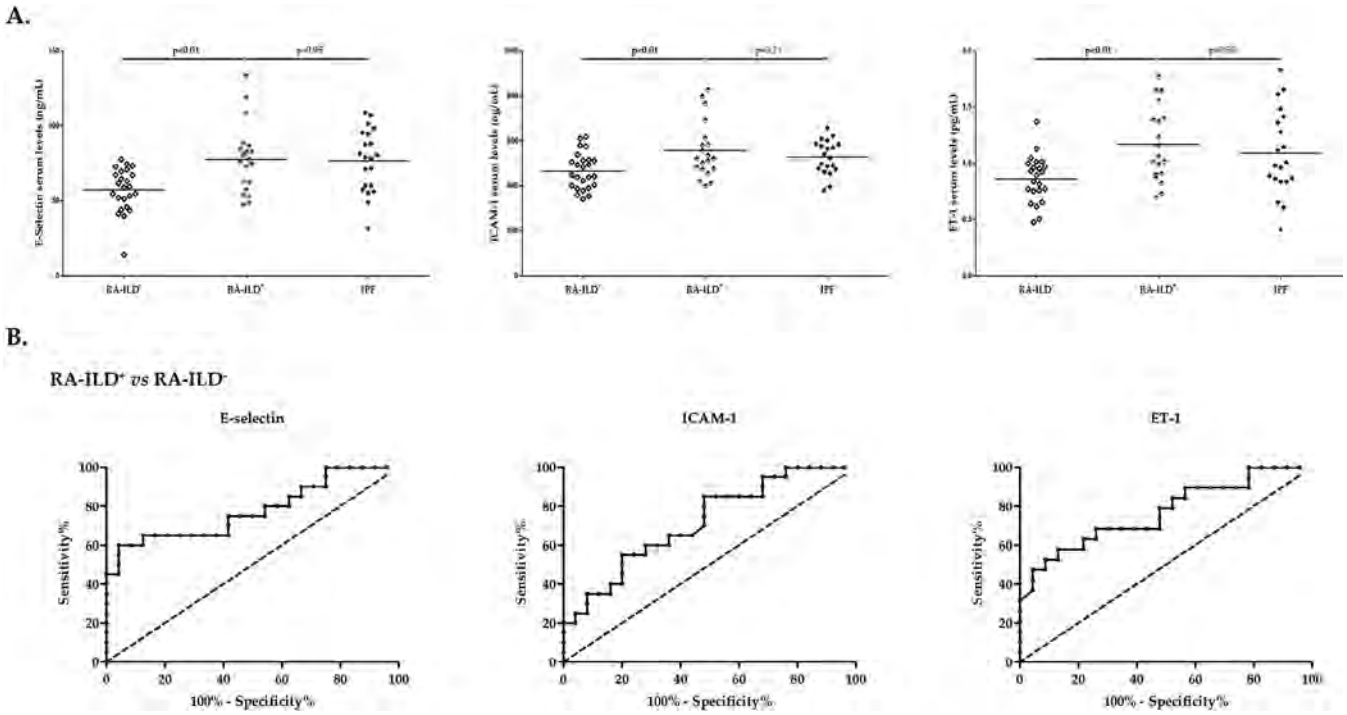

Figure 1. Differences in serum levels of E-selectin, ICAM-1 and ET-1 between patients with RA-ILD+ and those with RA-ILD- and IPF (A), as well as ROC curves analysis for the discrimination of RA-ILD+ from RA-ILD-(B). ICAM-1: intercelullar adhesion molecule 1; ET-1: endothelin 1; RA: rheumatoid arthritis; ILD: interstitial lung disease; IPF: idiopathic pulmonary fibrosis;. Significant results are highlighted in bold.

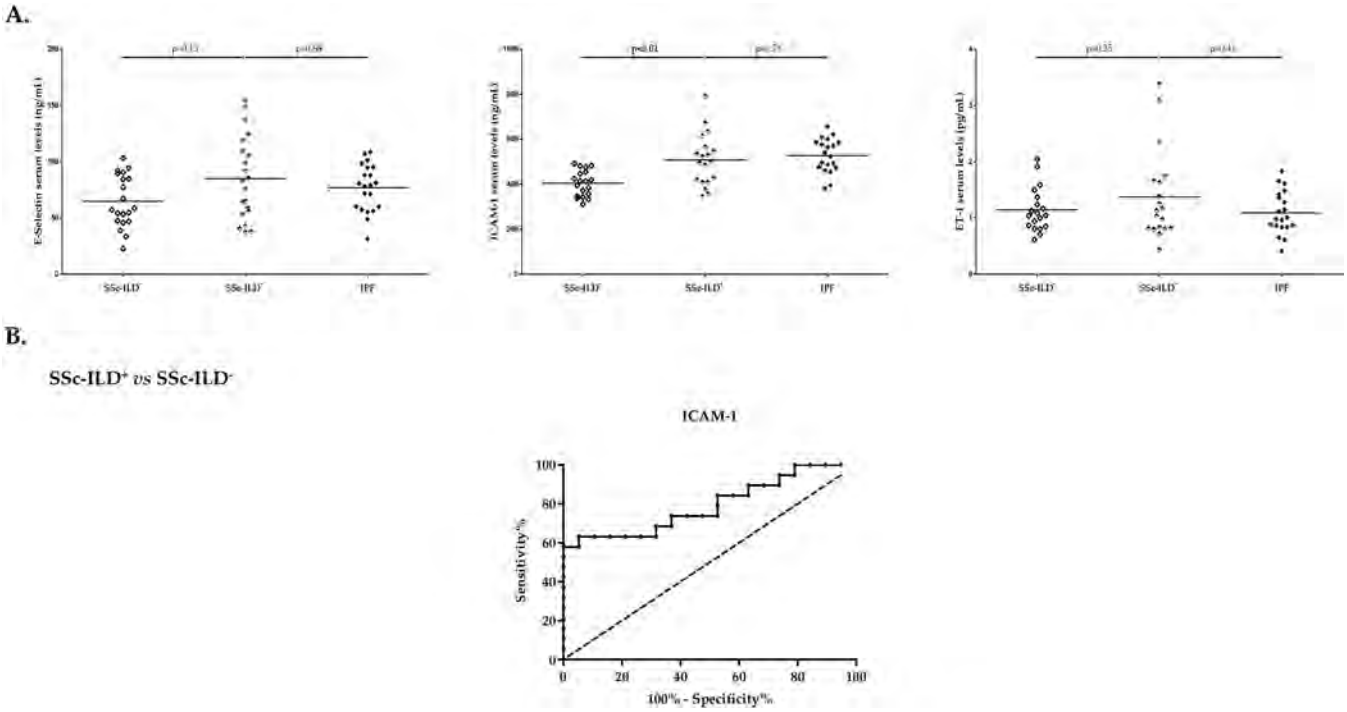

Figure 2. Differences in serum levels of E-selectin, ICAM-1 and ET-1 between patients with SSc-ILD+ and those with SSc-ILD- and IPF (A), as well as ROC curves analysis of ICAM-1 for the discrimination of SSc-ILD+ from SSc-ILD-(B). ICAM-1: intercelullar adhesion molecule 1; ET-1: endothelin 1; SSc: systemic sclerosis; ILD: interstitial lung disease; IPF: idiopathic pulmonary fibrosis;. Significant results are highlighted in bold.

References: [1] J Clin Med. 2019 Nov 21;8(12):2038; [2] Am J Respir Crit Care Med. 2020 Mar 15;201(6):650-660; [3] Ann Rheum Dis. 2021 Feb;80(2):143-150; [4] Int J Mol Sci. 2023 Jan 26;24(3):2405.

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Abstract Number: 0267

Variations in Approach to the Diagnosis and Management of Polymyalgia Rheumatica Among Australian Rheumatologists

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Polymyalgia rheumatica (PMR) is the second-most common inflammatory rheumatic disease but there remains variation amongst rheumatologists in approaches to diagnosis and management. This study aimed to evaluate the perceptions and approaches to PMR in a cohort of Australian rheumatologists.

Methods: Rheumatologist and trainee members of the Australian Rheumatology Association were invited via email to participate in a survey that explored opinions and experience around PMR diagnosis and management.

Results: Responses were received from 79 clinicians, of which 57 (72%) answered the survey to completion. 51% were female, and clinical experience varied from 0-10 years (40%) to over 20 years (26%), with a mix of public hospital work (75%) and private practice (58%). 75% of respondents managed at least one patient with PMR every fortnight.

Regarding PMR presentation and diagnosis, 23% believed that bilateral shoulder involvement is necessary to make a diagnosis of PMR, while 76% believed it occurs "most of the time". 37% believed elevated inflammatory markers are necessary for diagnosis, while 59% acknowledged that inflammatory markers may be normal although an uncommon occurrence. 13% regarded peripheral involvement as preclusion of a PMR diagnosis. Imaging was largely deemed useful in the setting of diagnostic uncertainty (72%).

Regarding treatment, there was a consensus for starting prednisolone at 15 mg (83%) with 75% favoring a 12-month steroid wean. 98% reported having prescribed a steroid-sparing drug in PMR before, with almost half using this in 25-50% of PMR patients. The most common indications for initiating a steroid-sparing drug were first relapse (29%) and second or later relapse (49%), although most would consider it in patients at high risk of steroid side effects (79%). Standard choices

included methotrexate (98%), leflunomide (27%), tocilizumab (13%), and hydroxychloroquine (10%). The majority agreed there is no strong evidence to support the use of methotrexate (86%) or leflunomide (95%).

Regarding monitoring and progress, the most common issues to arise during the disease course included steroid side effects (90%), pain (87%), stiffness (82%), fatigue (79%), and impact on physical function (75%). 48% recognized two distinct patient populations – those who have self-limiting disease which remits within 24 months and those who require lifelong low-dose prednisolone.

Conclusion: Australian rheumatologists had diverse opinions around the diagnostic features of PMR and the role of imaging. Many acknowledged that a diagnosis of PMR might be appropriate even in the absence of bilateral shoulder involvement and abnormal inflammatory markers in contrast to the 2012 EULAR/ACR provisional classification criteria. The majority had initiated a steroid-sparing drug in a PMR patient despite the lacking evidence base. The need for lifelong treatment in some patients was also recognized. Substantial variation existed in other areas of practice.

These findings challenge the classic paradigm of PMR as a self-limiting disease managed with steroid monotherapy, emphasizing the need for standardization of practice and further research into consistent diagnosis and treatment.

Disclosure: V. Yang: None; **J. Ninan**: None; **D. Liew**: None; **H. Keen**: Roche, 6, 12, Conference Support; **C. Hill**: None; **J. Leung**: AbbVie, 1, 6, Eli Lilly, 1, 6, Novartis, 6.

Abstract Number: 0268

Safety and Efficacy of CT-guided Percutaneous Infra-Renal Periaortic Biopsies in Suspected Retroperitoneal Fibrosis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Retroperitoneal fibrosis (RPF) commonly affects the infrarenal abdominal aorta (irAA) and manifests with periaortic soft tissue thickening (pASTT). RPF can be either idiopathic (primary) or secondary. Secondary causes include malignancy and infection and therefore biopsy is advantageous to differentiate etiologies. However, data describing the safety and efficacy of pASTT sampling is limited. The purpose of this study was to assess the safety and efficacy of periaortic biopsies using computed tomography (CT)-guidance among a large single institution cohort of patients with RPF.

Methods: Patients undergoing CT-guided percutaneous pASTT biopsy from June 1, 1999 through September 30, 2022 were identified retrospectively. All patients were required to have radiographic evidence of soft tissue thickening/mass in direct contact with the irAA and have had CT-guided biopsy performed at Mayo Clinic. Patients with biopsies of periaortic lymph nodes or the perivascular space of the iliac vessels or inferior vena cava were excluded. Routine laboratory screening thresholds prior to biopsy included INR < 1.6 and platelet count > 50 x10^9/L). Anticoagulation/antiplatelet agents were held prior to biopsy. Charts were directly reviewed by a physician abstractor. Demographics, biopsy features, and outcomes were collected. Complications were graded based on common terminology criteria for adverse events (CTCAE) with categories 1 and 2 being minor and categories 3-5 considered major.

Table 1: Pre-biopsy suspected diagnosis and post-biopsy confirmed diagnosis following 84 biopsies where CT-guided infra-renal abdominal aorta periaortic soft tissue thickening biopsy was considered sufficient for diagnosis.

Pre-biopsy suspected diagnosis	Post-biopsy confirmed diagnosis	N=73
iRPF	iRPF	45 (54%)
iRPF	IgG4-RD	10 (12%)
iRPF	ECD	1 (1%)
IgG4-RD	IgG4-RD	2 (2%)
Malignancy	iRPF	9 (11%)
Malignancy	IgG4-RD	2 (2%)
Malignancy	Malignancy	1 (1%)
Other (Infection, Sarcoid)	iRPF	3 (4%)
ECD, Erdheim Chester Disease; IgG4-RD, immunoglobulin G subclass 4 related disease; iRPF, idiopathic retroperitoneal fibrosis		

Table 2: Initial suspected diagnosis, ultimate diagnosis, and subsequent procedure performed following initial non-diagnostic CT-guided infra-renal abdominal aorta periaortic soft tissue thickening biopsy (n=11).

Pre-biopsy suspected diagnosis	CT-guided biopsy diagnosis	Ultimate confirmed diagnosis	Reason for inconclusive biopsy	Additional Procedure / Monitoring
Lymphoma	iRPF	iRPF	Concern alternate etiology	Surgical biopsy
Lymphoma	iRPF	iRPF	Concern alternate etiology	Surgical biopsy
Lymphoma	inconclusive	iRPF	Insufficient tissue	Surgical biopsy
Lymphoma	iRPF	Lymphoma	Concern alternate etiology	Repeat CT biopsy
iRPF	inconclusive	iRPF	Insufficient tissue	Clinical monitoring
iRPF	iRPF	iRPF	Concern alternate etiology	Surgical biopsy
iRPF	inconclusive	iRPF	Insufficient tissue	Repeat CT biopsy
IgG4-RD	inconclusive	IgG4-RD	Insufficient tissue	Clinical monitoring
iRPF	iRPF	ECD	Concern alternate etiology	Biopsy alternate site (bone)
iRPF	inconclusive	iRPF	Insufficient tissue	Surgical biopsy
iRPF	inconclusive	iRPF	Insufficient tissue	Clinical monitoring
ECD, Erdheim Chester Disease; IgG4-RD, immunoglobulin G subclass 4 related disease; iRPF, idiopathic retroperitoneal fibrosis				

Results: A total of 83 patients (28 females, 55 males) with 84 biopsies of the pASTT at the level of the irAA were identified. Mean age at biopsy was 58 (range 31-83) years. Biopsy approach was paraspinal in 73 (87%) and anterior abdominal in 11 (13%). Mean number of passes was 5 (range 1-12). A 17/18 gauge needle size was most commonly used (67/84), followed by 19/20 gauge (15/84). One biopsy used a 15/16 gauge device and one report did not specify needle size. Local anesthesia only was used in 18 (21%) biopsies and moderate anesthesia in 61 (73%); anesthesia type was not specified in 5 (6%). Three of 84 (3.6%) biopsy events had minor bleeding at needle entry site. A single (1.2%) patient had a major bleeding complication with left rectus sheath hematoma from anterior abdominal approach requiring embolization of left inferior epigastric pseudoaneurysm. No post procedural infections were observed. Biopsy of the irAA soft tissue was able to confirm a diagnosis following 73/84 (87%) biopsies (Table 1). Among the 11 procedures where the diagnosis was not achieved by initial CT-guided irAA soft tissue biopsy, 6 were due to insufficient tissue for histologic characterization and 5 were due to concern for alternative etiology despite sufficient tissue. Among these 11 cases, 5 had subsequent open surgical biopsy, 2 had repeat CT-guided irAA soft tissue biopsy, 1 had alternative site biopsied and 3 were clinically followed (Table 2).

Conclusion: In this study, percutaneous CT-guided infra-renal pASTT biopsy was considered safe and confirmed diagnosis in 87% of cases. Ultimate diagnosis differed from pre-biopsy suspicion in 34%, highlighting benefit of this procedure.

Disclosure: C. Anderson: None; **M. Guarda**: None; **U. Ghaffar**: None; **T. Atwell**: None; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Chemocentryx, 1, 6, Eli Lilly, 5, kiniksa, 5; **M. Moynagh**: None; **M. Koster**: None.

Abstract Number: 0269

Acute Kidney Injury and Plasma Cell-Rich Acute Interstitial Nephritis in VEXAS Syndrome: An Under-recognized Disease Feature

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: VEXAS syndrome (Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic) is a recently identified autoinflammatory disease with a large variety of disease manifestations. While recurrent fever, auricular chondritis, recurrent venous thromboembolism/thrombophlebitis, inflammatory skin lesions, ocular inflammation and cytopenias have been well-described, understanding of renal manifestations is limited.

Methods: Medical records of all patients with genetically confirmed VEXAS syndrome were reviewed for evidence of AKI or abnormal urinalysis. Patients who met the KDIGO criteria for acute kidney injury (AKI) for at least two consecutive measurements of serum creatinine or cystatin C were considered as having AKI. Biopsy specimens (n = 4) were reviewed by four experienced nephropathologists. Clinical and laboratory features at disease onset and at time of AKI diagnosis were abstracted from direct chart review.

Results: Among a cohort of 69 patients (all men, mean age 71 ± 9) with VEXAS syndrome, 16 (23%) developed AKI (mean age 75 ± 9) at some point during their follow up. A review of urinary findings among patients with AKI revealed microscopic hematuria, mild proteinuria, and pyuria in 100%, 100% and in 82% of cases, respectively. Four patients had undergone renal biopsy for acute kidney injury. One patient had features of peri-tubular capillaritis and has been previously described. Three patients were found to have biopsy confirmation of IN. Clinical features are described in Table 1. A representative biopsy is shown in Figure 1. All three patients had IN (acute in 2 and active chronic in 1) with plasma cell-rich infiltrate and tubulitis.

Table 1: VEXAS patient characteristics

	Case 1	Case 2	Case 3
Sex	Male	Male	Male
Age at onset VEXAS symptoms	87	84	75
Age at VEXAS diagnosis	89	85	76
VEXAS features	Recurrent fever Recurrent uveitis Inflammatory arthritis Macrocytic anemia	Recurrent fever Steroid responsive GGO DVT Macrocytic anemia	Auricular chondritis Recurrent scleritis Neutrophilic dermatosis Inflammatory arthritis Macrocytic anemia
Bone marrow cytoplasmic vacuolization	Yes Erythroid/Myeloid	Yes Erythroid/Myeloid	Yes Erythroid/Myeloid
UBA1 mutation / VAF	p.Met41Thr (87%)	p.Met41Thr (>50%)	p.Met41Thr (78%)
Additional mutations	*DNMT3A p.Arg882Cys (44%)	*TET2 p.Ile1873Thr (6%) *DNMT3A p.Asp529Asn (46%)	None
Labs at VEXAS diagnosis			
MCV, fL (ref: 78-98)	112.2	117.4	111.5
Hgb, g/dL (ref: 13.2-16.6)	11.0	10.7	9.1
Platelets, 10^9/L (ref: 135-317)	240	166	194
Lymphocytes, 10^9/L (ref: 0.9-3.1)	0.32	0.32	0.51
Monocytes, 10^9/L (ref: 0.26-0.81)	0.19	0.13	0.58
Immunoglobulin G4, mg/dL (ref: <121)	12	56.7	28.4
Complement C4, mg/dL (ref: 14-40)	37	25	35

Hgb, hemoglobin; MCV, mean corpuscular volume; VAF, variant allele frequency

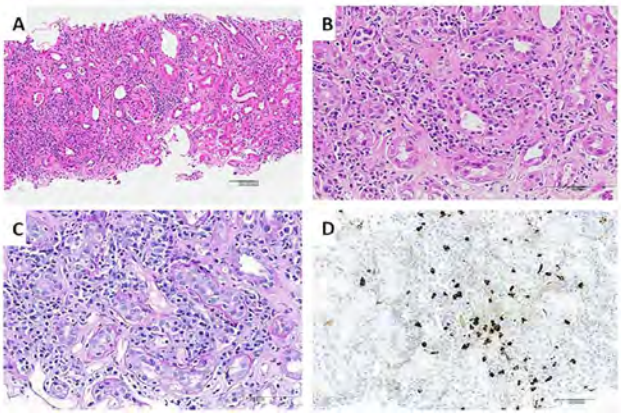

Figure 1: Renal biopsy Case 2. [A] Low power view of renal parenchyma demonstrating diffuse interstitial mononuclear inflammatory infiltrates associated with early fibrosis and tubular atrophy (hematoxylin & eosin, original magnification 100x). [B] High power image shows a plasma cell-rich inflammatory infiltrate (hematoxylin & eosin, original magnification, 400x). [C] High power image of the same region show severe tubulitis with destruction and attenuation of the tubular basement membranes (periodic acid-Schiff, original magnification 400X) . [D] IgG4 stain showing an area with increased numbers of IgG4-positive plasma cells (immunoperoxidase stain, original magnification 400x).

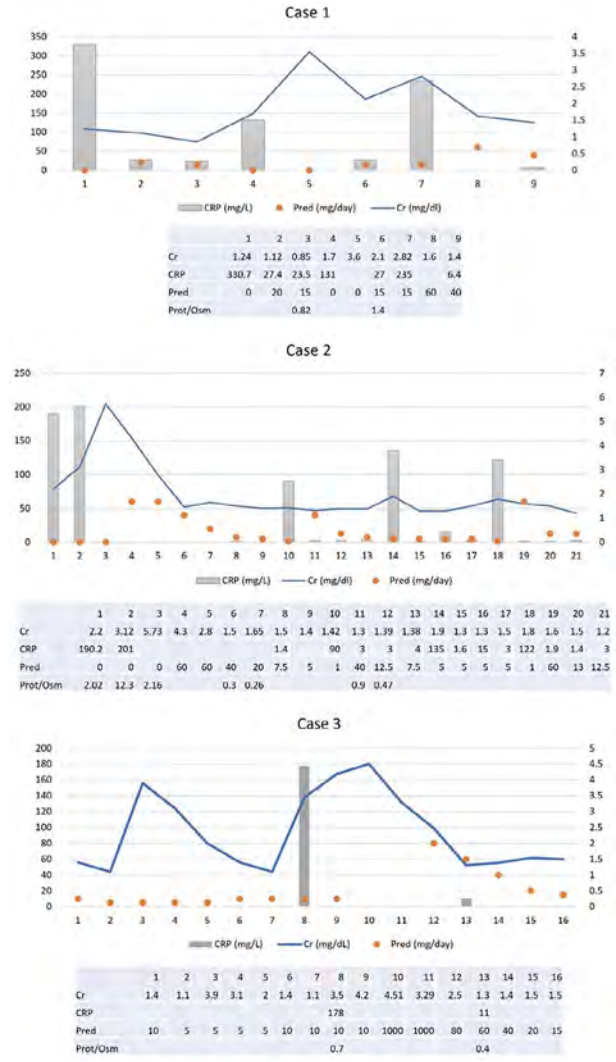

Figure 2: Laboratory trends among patients with VEXAS with Acute Interstitial Nephritis

Two patients had focal increased numbers of IgG4 staining cells (one 30/hpf, one 17/hpf) but the IgG4:IgG was low and no other pathologic features suggestive of IgG4-related disease were seen. None of the patients had clinical or radiographic features of IgG4-RD and all had normal serum IgG4 values. Arteritis, granulomatous inflammation and glomerulonephritis were absent. Immunofluorescence was negative and electron microscopy did not show glomerular or extraglomerular immune deposits. Protein/osmolality ratio was increased at the time of active systemic inflammation and renal compromise. Prednisone was initiated in all patients with biochemical improvement in renal function (Figure 2), however, subsequent decline in renal function corresponded with reduction in prednisone dose below 10-15 mg/day. All three patients carried the p.Met41Thr mutation and two patients had additional clonal hematopoietic mutations (DNMT3A, TET2).

Conclusion: AKI from Plasma cell-rich IN is an under-recognized feature in patients with VEXAS. Physicians should be aware of this complication, which should be considered in patients with VEXAS and acute kidney injury. Prompt treatment with high-dose glucocorticoids can result in improvement of renal function. Further study regarding laboratory and urinary parameters that identify active versus inactive renal disease are needed. Identification of targeted, effective therapy is necessary.

Disclosure: M. Koster: None; **L. HerreraHernandez**: None; **L. Bu**: None; **D. Montes**: None; **S. Nasr**: None; **L. Cornell**: None; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Chemocentryx, 1, 6, Eli Lilly, 5, kiniksa, 5; **M. Patnaik**: None; **A. Mangaonkar**: None; **K. Kalantari**: None.

Abstract Number: 0270

Exploring the Potential of Oral Administration of 5-aminolevulinic Acid/ sodium Ferrous Citrate in Adult-onset Still's Disease: Preclinical Study in Mice and Pilot Investigation in Humans to Assess Efficacy and Safety

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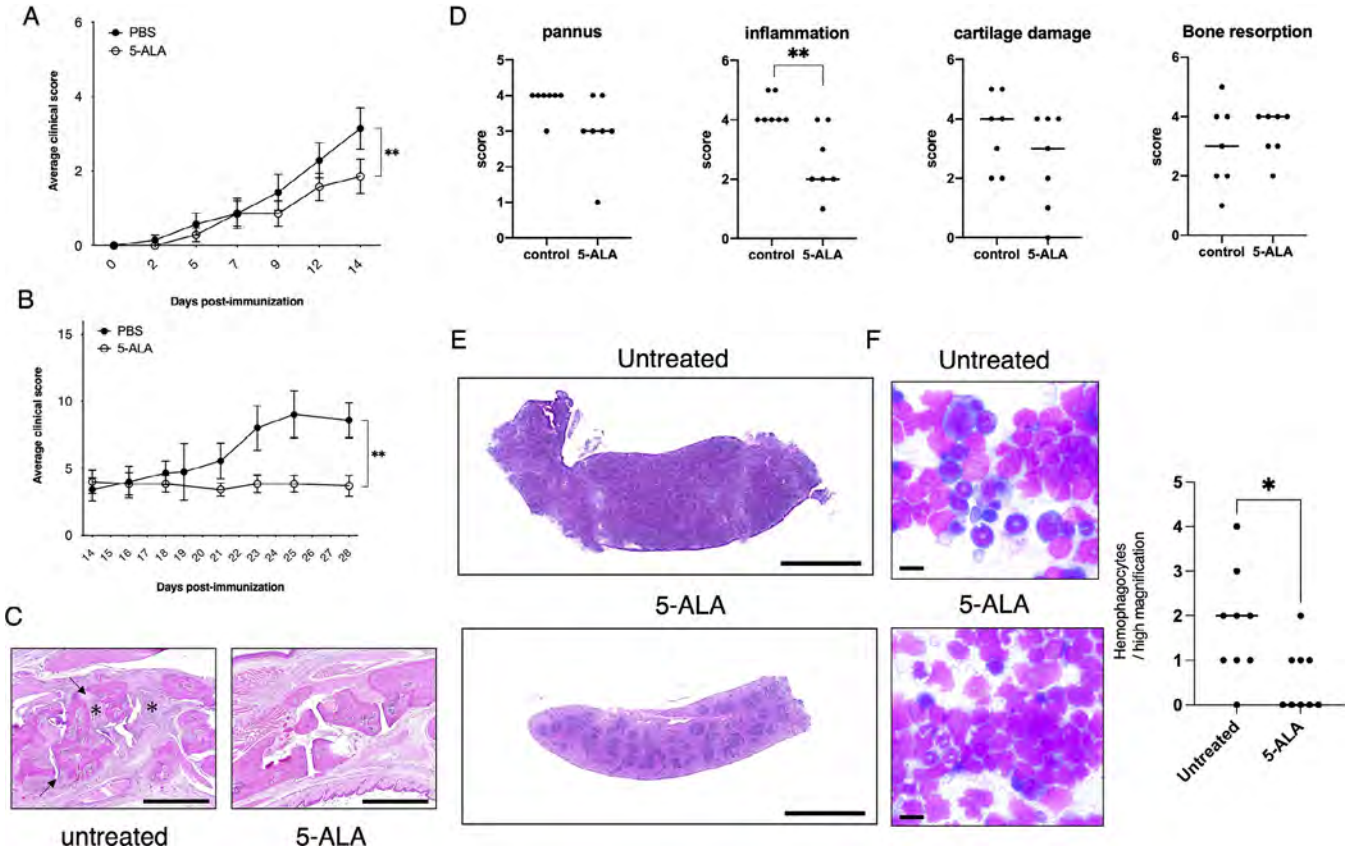
Background/Purpose: The primary objective of this study is to elucidate the therapeutic potential of 5-aminolevulinic acid/ sodium ferrous citrate (5-ALA/SFC) in ameliorating the pathological manifestations associated with adult-onset Still's disease (AOSD), with a specific focus on arthritis and macrophage activation syndrome (MAS). This investigation entails the utilization of mouse models to examine the impact of 5-ALA/SFC on the aforementioned pathologies in AOSD. Additionally, a pilot study involving patients diagnosed with AOSD was conducted to further assess the therapeutic efficacy and safety of 5-ALA/SFC in a clinical setting.

Methods: In this study, mice were subjected to collagen-induced arthritis (CIA) by immunization with type II collagen, and to MAS by repeated administration of stimulating synthetic oligonucleotides containing CpG motifs (CpG-S-ODN) via drinking water. The objective of this investigation was to assess the preventive and therapeutic effects of 5-ALA/SFC on arthritis in CIA mice, as well as its potential to ameliorate hemophagocytosis observed in bone marrow smears of CpG-S-ODN-treated mice. AOSD patients undergoing prednisolone (PSL) treatment were enrolled in an open-label trial, wherein oral



administration of 5-ALA/SFC was conducted. The efficacy and safety of 5-ALA/SFC in facilitating prednisolone tapering were subsequently evaluated.

Results: In both experimental models for arthritis prevention and treatment, the group receiving 5- 5-ALA/SFC exhibited significantly reduced joint scores compared to the control group. Furthermore, in mice treated with CpG-S-ODN, the 5-ALA/SFC group demonstrated a decrease in hemophagocytosis (phagocytosis of red blood cells by immune cells) and splenomegaly (enlarged spleen). The anti-inflammatory properties of 5-ALA/SFC are attributed to its ability to suppress the production of CCL4 and CXCL10 in monocytes and macrophages, while also promoting the induction of M2 macrophages (a type of anti-inflammatory macrophage). These cellular responses contribute to the observed therapeutic effects. In the clinical study, four out of five participants completed the prescribed drug administration, and all patients successfully maintained a tapering regimen of PSL without experiencing any serious adverse events or worsening of symptoms throughout the study duration.

Conclusion: The administration of 5-ALA/SFC holds promise as a viable therapeutic intervention for inflammatory disorders, specifically AOSD. The utilization of 5-ALA/SFC may impart a multifaceted therapeutic impact, encompassing the regulation of arthritis symptoms and the suppression of MAS. Furthermore, our findings provide supporting evidence regarding the safety profile associated with 5-ALA/SFC treatment in individuals diagnosed with AOSD. However, further investigations are warranted to elucidate the underlying mechanisms and evaluate the clinical efficacy of 5-ALA/SFC, which should be pursued in future scientific inquiries.

Disclosure: T. Koga: None; **R. Sumiyoshi**: None; **Y. Tsuji**: None; **K. Kodama**: None; **K. Furukawa**: None; **Y. Endo**: None; **A. Kawakami**: None.

Abstract Number: 0271

Successful Treatment of Refractory IgG4-Related Disease with Tofacitinib: Experiences from 7 Patients

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Our observational cohort study aimed at assessing the effectiveness and safety of the Janus kinase (JAK) inhibitor tofacitinib in refractory IgG4-Related Disease (IgG4-RD).

Methods: Seven patients admitted to the Rheumatology and Immunology Department of Peking University People's Hospital were enrolled. All the patients fulfilled the 2019 American College of Rheumatology(ACR)/ European League Against Rheumatism (EULAR) classification criteria for IgG4-RD. Refractory IgG4-RD was defined to be resistant to conventional treatment of at least 3 months' duration. Patients received tofacitinib twice daily, with simultaneous continuation of immune-suppressants and glucocorticoids. They were followed-up for the shortest 3 months and the longest 12 months by the same medical team. At each visit, IgG4-RD responder index (IgG4-RD RI) [5], physician's global assessment (PGA), serum IgG4 levels (≥201mg/dL) and adverse events (AEs) were measured and assessed. Clinical remission was assessed by evaluating the changes of IgG4-RD RI scores.

Results: The demographic data and clinical features of the seven patients are described in **table 1**. Prednisone were increased from 5-10mg/d to 15-20mg/d in 4 patients with clinical recurrence at entry and the other three received previous steroids dose. Concomitant immunosuppressive treatment was continued or withdrawn. Four patients received clinical remission and two patients achieved serum IgG4 concentration improvement after tofacitinib treatment; one experienced

Table 1 Baseline characteristics, detailed treatment protocol, reduction of corticosteroids and treatment response in patients with IgG4-RD.

Patient No.	Sex	Age (year)	IgG4-RD course (month)	Organ involvement	Previous treatment	Treatment after enrolment	Serum IgG4 Level (RR 3-201mg/dL)	IgG4-RD RI	PGA	Follow-up (month)	Clinical evaluation	Reduction of corticosteroids	Adverse effects
1	M	60s	60	Autoimmune pancreatitis, sclerosing cholangitis, lymphadenopathy	Pred10mg qd+ CYC0.4g q2w	Pred15mgqd+ Tofa 5mg bid	1330	3	5	12	CR	Reduced to 2.5mg qd at the 6th month and stopped at 12th month.	No
2	M	30s	24	Autoimmune pancreatitis, sclerosing cholangitis	Pred15mg qd+ ADA40mg q2w	Pred30mg qd+ Tofa 5mg bid	380	4	8	9	Relapse	Reduced to 7.5mg qd at the 6th month	No
3	M	50s	18	Sialadenitis	Pred10mgqd+ LEF 20mg qd	Pred20mg+ Tofa 5mg bid	431	4	5	3	CR	Reduced to 7.5mg qd at the 3rd month	No
4	M	60s	24	Dacryoadenitis, sialadenitis, dermatitis, lymphadenopathy	Pred10mgqd+ MTX12.5mg qw	Pred15mgqd+ MTX12.5mg qw+Tofa 5mg bid	325	6	5	6	CR	Reduced to 10mg qd at the 6th month	No
5	M	60s	84	Dacryoadenitis, sialadenitis, dermatitis, autoimmune pancreatitis	Pred7.5mg qd+MMF0.5g bid	Pred7.5mg qd+MMF0.5g bid+ Tofa 5mg bid	460	8	6	9	CR	Reduced to 5mg qd at the 3rd month	No
6	M	70s	24	Sialadeniti, dacryoadenitis	Pred5mgqd+ MTX10mg qw+LEF20mg qd	Pred 5mg qd+MTX10mg qw+ Tofa 5mg bid	1250	3	3	3	IgG4 level improvement	No reduction	Yes
7	F	60s	84	Autoimmune pancreatitis, sclerosing cholangitis, sialadenitis	Pred 7.5mg mg qd+MMF0.75g bid	Pred7.5mg qd+ Tofa 5mg bid	437	3	2	9	IgG4 level improvement	Reduced to 5mg qd at the 1st month	No

Abbreviations: ADA, adalimumab; CYC, cyclophosphamide; CR, clinical remission; F, female; IgG4-RD, immunoglobulin G4-related disease; IgG4-RD RI, immunoglobulin G4-related disease responder index; LEF, leflunomide; M, male; MMF, mycophenolate mofetil; MTX, methotrexate; No.,number; Pred, prednisone; PGA, physician's global assessment; RR, reference range; Tofa, tofacitinib; qd, once a day; bid, twice a day; qw, once a week; q2w, once two weeks.

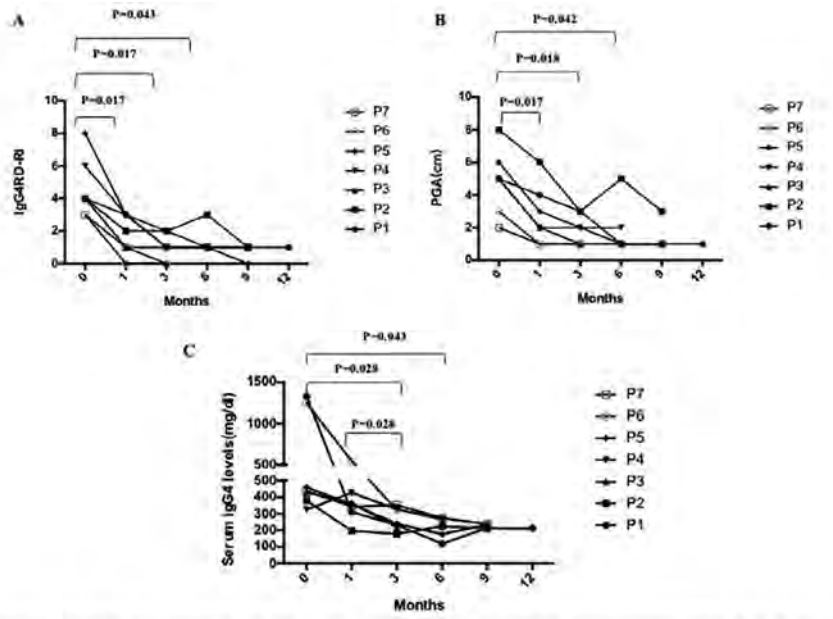

Figure 1. Figure demonstrated the variation trends of IgG4-RD RI **(A)**, PGA **(B)** and IgG4 concentrations **(C)** at baseline, 1st, 3rd, 6th, 9th and12th month on tofa treatment. Statistical analyses were performed using SPSS V.22.0. The p value was two-tailed and defined as significant if <0.05. IgG4-RD RI, immunoglobulin G4-related disease responder index; PGA, physician global assessment; Tofa, tofacitinib.

a flare during the follow-up **(table 1)**. All patients tapered their baseline prednisone dose, with 4 patients receiving doses less than or equal to 5 mg/day, and 1 even withdrawing steroids during the follow-up**(table 1)**. Both IgG4-RD RI score (p=0.017, p=0.017, p=0.043, respectively) and PGA (p=0.017, p=0.018, p=0.042, respectively) were significantly improved at 1st, 3rd and 6th month (**figure 1A, B**). Three patients (Patients 3, 5 and 6) achieved complete remission with IgG4-RD RI scores of 0 during the follow-up. Except the improvement of clinical manifestations, the serum IgG4 levels declined significantly at 3 months (p=0.028) and 6 months (p=0.043) (**figure 1C**). In addition, serum IgG4 levels decreased at 3rd month when compared to their levels at 1st month (p=0.028) (**figure 1C**). The serum IgG4 levels of patient 6 dramatically decreased from 1250mg/dL to 549 mg/dL at 1st month after tofacitinib therapy without steroid increase. Except for one patient who suffered an activation of herpes varicella zoster without serious prognosis, no probable drug-related adverse effect was reported among our other patients enrolled in the study during the follow-up visits **(table 1)**.

Conclusion: Our results proved that tofacitinib was effective for the treatment of refractory IgG4-RD, sparing steroid to reach clinical remission. Tofacitinib offers a promising treatment approach to IgG4-RD. Findings from this study may inform future's studies of other small-molecular targeted drugs for the treatment of IgG4-RD.

Disclosure: H. Zhu: None; **S. Tang**: None; **Y. Li**: None; **F. Sun**: None; **Y. Gan**: None; **H. Ye**: None.

Abstract Number: 0272

Risk Factors for Severe Outcome in Susac Syndrome: A National Cohort Study

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SESSION INFORMATION
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Background/Purpose: Susac syndrome (SuS) is a rare vasculitis affecting the brain, retina and inner ear in young women. Nonreversible hearing loss is the main long-term damage of SuS and requires hearing aids in more than 50% of patients. There are no known predictive factors for poor outcomes in SuS. We aimed to identify risk factors for severe hearing loss in Susac Syndrome.

Methods: SuS patients have been included in the prospective national cohort study (CarESS study) involving 20 different centres in France. CarESS study is an ongoing cohort study that started in December 2011 including all consecutive patients with SuS referred to the French reference center (Department of Internal Medicine, Bichat Claude Bernard Hospital, Paris). SuS was defined either by the triad of encephalopathy with corpus callosum ischemic lesions on brain MRI, cochleo-vestibular damage including sensorineural hearing loss and multiple occlusions of retinal central artery branches and/or retinal vasculitis on retinal fluorescein angiography. Collected data included age, gender, physical examination, fundoscopy, retinal angiography, visual acuity, visual field, audiogram, cerebrospinal fluid, brain MRI and treatment received. The CarESS study was designed with a follow-up at 1, 3 months, 6 months, 12 months after diagnosis and then annually for 5 years and/or in the event of a relapse. Fundoscopy, audiogram, and brain MRI were systematically scheduled at each time-point. The primary outcome was the occurrence of severe hearing loss (HL) at last follow-up. Severe HL was defined as the loss of 70dB in at least one ear *on audiogram or the need for* hearing aids.

Results: Overall, 36 SuS patients were analyzed for the primary outcome. Twenty-four patients (66.7%) were women and the median age at diagnosis was 37.5 [24.5-42.5] years. The triad was complete in 29 (80.6%) patients at disease onset. Thirty-three patients (91.7%) had cochlea-vestibular involvement at SuS diagnosis including tinnitus (n=16), dizziness (n=15), ataxia (n=7) and HL >20dB in at least one ear (n=25). At diagnosis, thirty-two (88.9%), 11 (30.6%) and 7 (19.4%) patients have received steroids, intravenous immunoglobulin and/or immunosuppressive drugs (IS), respectively. After a median follow up of 50.7 [24-73.4] months**,** 20 patients (58.3%) experienced severe HL that occurred a median time of 2.1 [0.3 – 13.6] months after diagnosis. Multivariable logistic regression model showed that odds of severe HL were lower in patients who received IS drugs at diagnosis (OR 0.13 95% CI [0.01-0.93], p=0.041).

Conclusion: Severe hearing loss is frequent in patients with Susac syndrome and associated with the absence of immunosuppressive drugs given at diagnosis. Our findings support the systematic use of immunosuppressive drugs in Susac syndrome to prevent poor outcome, which should be tested in a multicenter prospective randomized trial.

Disclosure: M. Peyre: None; **A. Mageau**: None; **M. Henry Feugeas**: None; **S. Doan**: None; **C. Halimi**: None; **I. Klein**: None; **T. Goulenok**: None; **C. Francois**: None; **M. Chauveheid**: None; **T. Papo**: None; **K. Sacre**: None.

Abstract Number: 0273

Disease Characteristics and Pancreatic Damage in IgG4-Related Disease with Pancreatic Involvement

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
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Background/Purpose: IgG4-related disease (IgG4-RD) is a systemic immune-mediated fibroinflammatory disease that can affect nearly every organ system. Autoimmune pancreatitis (AIP) is among the most common manifestations of IgG4-RD, but data are limited on its disease characteristics in the broader context of systemic IgG4-RD. In addition, the prevalence of exocrine pancreatic insufficiency (EPI) and endocrine pancreatic insufficiency (diabetes mellitus [DM]) in IgG4-related AIP is not well established. We aimed to evaluate disease features and burden of damage due to AIP in a large cohort of patients with IgG4-RD.

Methods: We performed a retrospective study using our large single-center IgG4-RD cohort. Subjects were included if they met ACR/EULAR Classification Criteria for IgG4-RD and were excluded if there were missing data or if AIP presence was unclear. Demographics and overall disease characteristics were compared between subjects with and without AIP using

Table 1. Demographics and disease characteristics in patients with IgG4-RD with and without pancreatic involvement. SD: standard deviation, AIP: autoimmune pancreatitis, ULN: upper limit of normal.

	All	AIP	No AIP	P-Value
N (%)	305 (100)	120 (39)	185 (61)	N/A
Age, years, mean (SD)	65.9 (14.6)	69.3 (14.0)	63.7 (14.6)	**0.001**
Male sex, n (%)	211 (69)	100 (83)	111 (60)	**0.017**
Race, n (%)				
White	220 (72)	88 (73)	132 (71)	0.84
Asian	41 (13)	15 (13)	26 (14)	0.72
Black or African American	14 (5)	4 (3)	10 (5)	0.41
Other	16 (5)	6 (5)	11 (6)	0.73
Unknown/ Not Reported	14 (5)	8 (5)	7 (4)	0.62
Ethnicity, n (%)				
Hispanic	42 (14)	13 (11)	29 (16)	0.27
Not Hispanic	241 (79)	101 (84)	140 (76)	0.42
Not Reported	22 (7)	6 (5)	16 (9)	0.25
Deceased during follow-up, n (%)	22 (7)	11 (9)	11 (6)	0.31
ACR/EULAR Classification Criteria inclusion points, mean (SD)	37.1 (14.6)	42.9 (16.8)	33.4 (11.6)	**<0.0001**
IgG4-RD manifestations, n (%)				
Meninges	7 (2)	3 (3)	4 (2)	0.85
Pituitary Lesion	5 (2)	4 (3)	1 (1)	0.06
Orbits	50 (16)	13 (11)	37 (20)	0.05
Lacrimal glands	101 (33)	38 (32)	63 (34)	0.72
Parotid glands	72 (24)	30 (25)	42 (23)	0.69
Submandibular glands	140 (46)	65 (54)	75 (41)	0.09
Mastoiditis/middle ear disease	3 (1)	2 (2)	1 (1)	0.33
Sinusitis	27 (9)	10 (8)	17 (9)	0.83
Thyroid	8 (3)	2 (2)	6 (3)	0.81
Lymph nodes	75 (25)	32 (27)	43 (23)	0.41
Lungs	68 (22)	31 (26)	37 (20)	0.56
Aorta and large blood vessels	27 (9)	12 (10)	15 (8)	0.29
Heart/pericardium	8 (3)	4 (3)	4 (2)	0.59
Retroperitoneal fibrosis	54 (18)	17 (14)	37 (20)	0.54
Sclerosing mediastinitis	2 (1)	0 (0)	2 (1)	0.24
Sclerosing mesenteritis	6 (2)	2 (2)	4 (2)	0.25
Liver	24 (8)	19 (16)	5 (3)	**<0.0001**
Bile ducts	52 (17)	46 (38)	6 (3)	**<0.0001**
Gallbladder	8 (3)	6 (5)	2 (1)	**0.039**
Kidney	96 (31)	50 (42)	46 (25)	**0.011**
Skin	8 (3)	2 (2)	6 (3)	0.41
Constitutional Symptoms	30 (31)	25 (21)	5 (3)	**<0.0001**
Prostate	26 (9)	17 (14)	9 (5)	**0.007**
Number of organs involved, mean (SD)	3.27 (1.9)	4.41 (2.0)	2.53 (1.5)	**<0.0001**
Peak Serum IgG4 Concentration				
Normal or Unknown	61 (20)	17 (14)	44 (24)	0.07
> 1 and < 2 x ULN	51 (17)	13 (11)	38 (21)	**0.043**
2 – 5 x ULN	73 (24)	28 (23)	45 (24)	0.86
> 5 x ULN	122 (40)	63 (53)	59 (32)	**0.005**
Active disease at baseline evaluation, n (%)	194 (64)	82 (68)	112 (61)	0.40

Table 2. Disease features of active autoimmune pancreatitis.

Feature	N (%)
Clinical and laboratory (n=120)	
Abdominal pain	55 (46)
Jaundice	31 (26)
Fatigue	25 (21)
Nausea/emesis	8 (7)
Diarrhea/changes in stool	32 (27)
Weight loss/anorexia	61 (51)
High lipase	30 (25)
Imaging (n=106)	
Mass	35 (33)
Pancreatic or common bile duct stricture	29 (27)
Peripancreatic halo/ring	21 (20)
Pancreatic enlargement	34 (32)
Increase in T2 signal diffusely	4 (4)

Table 3. Damage due to autoimmune pancreatitis. All values reported as n (%) unless noted otherwise. *Excludes one subject with a known low elastase but unknown concentration. **Clinical EPI was defined by either of the following: 1) weight loss and/or micronutrient deficiency with response to enzyme replacement; or 2) low fecal elastase with symptoms of maldigestion, steatorrhea, or weight loss. One subject had a low fecal elastase that was not quantified.

Endocrine Pancreatic Insufficiency	
Diabetes Mellitus	56/120 (47)
Insulin use	32/56 (57)
Exocrine Pancreatic Insufficiency	
Clinical	
Steatorrhea	20 (17)
Weight loss	60 (50)
Response to enzyme replacement	51 (43)
Laboratory	
Low lipase	60 (50)
Moderately low elastase (<200)	9/49 (18)*
Severely low elastase (<100)	31/49 (63)*
Clinical diagnosis of EPI**	57 (48)
Any evidence of above	102 (85)
Radiologic Pancreatic Damage	
Atrophy	40/106 (38)
Calcification	15/106 (14)
Loss of T1 signal diffusely	12/106 (11)
Iatrogenic Pancreatic Damage	
Partial pancreatectomy (Whipple, modified Whipple, or other)	11 (9)
Functional Pancreatic Damage	
Atrophy, low fecal elastase, or low serum lipase	89 (74)

Chi-square and unpaired T tests for categorical and continuous variables, respectively. For subjects with AIP, we extracted details regarding clinical presentation, laboratory results, and imaging findings representing both active disease and pancreatic damage. For subjects without known EPI and no documented fecal elastase measurements, letters were sent encouraging them to have these performed.

Results: Of 305 eligible subjects, 120 (39%) had pancreatic involvement. Demographics and disease features in patients with and without AIP are shown in **Table 1**. Subjects with AIP were significantly older and more commonly male than those without AIP. Subjects with AIP had significantly more organs involved and higher ACR/EULAR Classification Criteria inclusion points, and they were significantly more likely to have had highly-elevated serum IgG4 concentrations (> 5 x upper limit of normal) than subjects without AIP. Among subjects with AIP, the most common symptoms of active AIP were weight loss or anorexia (51%), abdominal pain (46%), diarrhea or changes in stool (27%), and jaundice (26%); 25% had lipase elevations, and 33% had mass-forming AIP (**Table 2**). Damage due to AIP is summarized in **Table 3**. 47% had DM, 57% of which required insulin. Clinical EPI as defined using stringent criteria was present in 48%, while 85% had any evidence of EPI. Of 49 elastase measurements obtained, 40 (82%) were low. Functional pancreatic damage was present in 74%, defined as low serum lipase, low fecal elastase, or pancreatic atrophy. Eleven (9%) patients had partial pancreatectomies in their diagnostic workups.

Conclusion: Patients with IgG4-RD with AIP are more commonly male and have more extensive and severe disease than those without AIP. Classic acute pancreatitis, manifesting as abdominal pain and high lipase, occurs in a minority of patients with IgG4-related AIP. Features concerning for malignancy, including weight loss, painless jaundice, and pancreatic masses,

are common, and many patients have Whipple procedures as a result. Endocrine and exocrine pancreatic insufficiency are highly prevalent. The burden of clinical and functional pancreatic damage in IgG4-RD is striking and emphasizes the need for early recognition of the disease and prompt initiation of treatment.

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Abstract Number: 0274

A Mix-and-match COVID-19 Vaccination Strategy in Patients with Rheumatic Diseases on Rituximab

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatic diseases (RD) on rituximab (RTX) have increased mortality following COVID-19 and reduced antibody response post-vaccine. We tested whether a mix-and-match strategy using a novel protein subunit vaccine (PSV) is safe and enhances vaccine-specific responses in those who have received $\geq$3 messenger RNA (mRNA) vaccine doses.

Table 1 – Patient characteristics and time intervals between previous dose of rituximab mAb or previous vaccination and repeat vaccine.

	Study Trajectory		
	A - Spikevax®	A - Nuvaxovid®	B - Nuvaxovid®
N	30	13	28
Age (years) - mean (sd)	55 ± 18	55 ± 14	63 ± 13
Sex (female) - N (%)	20 (66.67)	12 (92.31)	20 (71.43)
Ethnicity - N (%)			
White	26 (86.67)	12 (92.31)	28 (100.00)
Other	5 (13.33)	1 (7.69)	0
Systemic Autoimmune Rheumatic Disease N (%)			
Rheumatoid Arthritis	9 (30)	10 (76.92)	12 (42.85)
Systemic Lupus Erythematosus	4 (13.33)	1 (7.69)	1 (3.57)
Inflammatory Immune Myopathies	3 (10)	N/A	4 (14.29)
Systemic Sclerosis	1 (3.33)	N/A	2 (7.14)
ANCA-Associated Vasculitis	11 (36.37)	2 (15.38)	9 (32.14)
Juvenile Idiopathic Arthritis	1 (3.33)	N/A	N/A
Undifferentiated Connective Tissue Disease	1 (3.33)	N/A	N/A
Disease duration (years) - mean (sd)	11.87 ± 9.93	25.85 ± 17.50	12.07 ± 9.07
CD20 Level (10^3/L) - mean (sd)	0.01 ± 0.04	0.01 ± 0.04	0.01 ± 0.02
Interval between vaccination in the study and last dose of anti-CD-20 mAb (months) - mean (sd)	6 ± 1.85	6.87 ± 2.41	5.73 ± 2.41
Interval between vaccination in the study and last dose of COVID-19 vaccine (months) - mean (sd)	8.58 ± 3.17	8.55 ± 2.25	7.56 ± 1.87

Table 2 – Levels of anti-S, anti-RBD, anti-N and titers of neutralizing antibodies pre and 28-days post repeat vaccination.

	Study Trajectory					
	A - Spikevax®		A - Nuvaxovid®		B - Nuvaxovid®	
	Visit 1	Visit 2	Visit 1	Visit 2	Visit 1	Visit 2
Anti-S						
N	30	30	13	13	28	28
Mean	3820.93	5088.77	2544.15	2701.62	4475.21	4304.00
StdDev	4378.08	5265.96	2480.19	2627.97	3941.03	3175.93
ABSENCE	11 (36.67)	9 (30)	5 (38.46)	6 (46.15)	2 (7.17)	2 (7.14)
PRESENCE	19 (63.33)	21 (70)	8 (61.54)	7 (53.85)	26 (92.86)	26 (92.86)
Anti-RBD						
N	30	30	13	13	28	28
Mean	0.85	1.14	0.65	0.82	1.54	1.54
StdDev	0.91	1.07	0.96	0.99	0.80	0.74
ABSENCE	15 (50)	12 (40)	9 (69.23)	7 (53.85)	5 (17.86)	5 (17.86)
PRESENCE	15 (50)	18 (60)	4 (30.77)	6 (46.15)	23 (82.14)	23 (82.14)
Anti-N						
N	30	30	13	13	28	28
Mean	0.17	0.16	0.31	0.28	0.20	0.24
StdDev	0.18	0.16	0.32	0.31	0.24	0.31
ABSENCE	27 (90)	27 (90)	9 (69.23)	10 (76.92)	23 (82.14)	24 (85.71)
PRESENCE	3 (10)	3 (10)	4 (30.77)	3 (23.08)	5 (17.86)	4 (14.29)
NAb Wuhan						
N	30	30	13	13	28	28
Mean	1021.48	2725.63	1818.38	1565.49	2966.58	2410.19
StdDev	2329.78	5547.42	3525.73	2835.72	3098.12	2645.45
NAb BA5						
N	30	30	13	13	28	28
Mean	111.00	399.45	104.60	115.00	133.75	293.17
StdDev	137.58	685.30	65.26	69.17	148.71	654.36

Anti-S = anti-spike antibody; anti-RBD = anti-receptor binding domain antibody; anti-N = anti-nucleocapsid antibody; NAb Wuhan = neutralizing antibody to Wuhan variant; NAb BA5 = neutralizing antibody to BA5 variant.

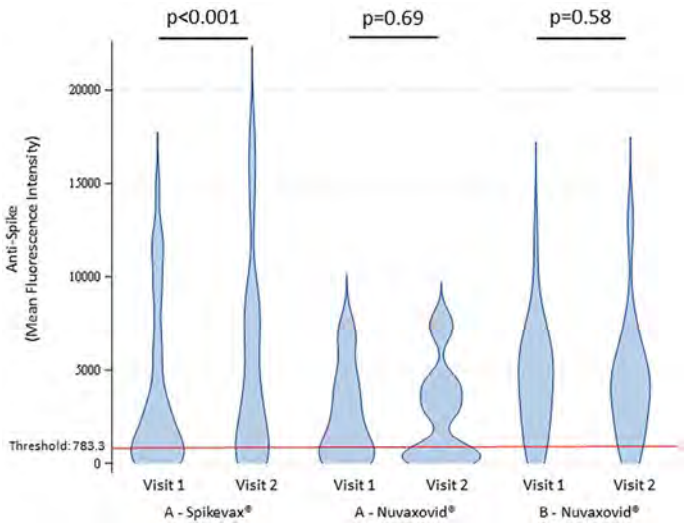

Figure 1. Anti-Spike levels pre and 28 days post-vaccination

Methods: We recruited adults with RDs on RTX post-3rd/4th dose of a mRNA COVID-19 vaccine in an open label, non-randomized, comparative trial. Post-3rd dose participants chose to receive either a 4th dose of mRNA Spikevax® (Moderna mRNA-1273) or PSV Nuvaxovid® (Novavax NVX-CoV2373) vaccines. Patients enrolled post-4th mRNA dose were offered Nuvaxovid®as their 5th. Self-reported reactogenicity at 7 days and adverse events at 28 days were noted. Humoral and cellular vaccine-responses were determined pre and 28 days post-vaccine. We tested for anti-spike (anti-S) by plasma binding on D614G Spike transfected HEK293T cells and measured by flow cytometry, anti-receptor binding domain (anti-RBD) and anti-nucleocapsid (anti-N) by in-house ELISA, and serum neutralizing antibodies (NAbs) using Wuhan and BA.5 pseudotyped lentiviruses. In 19 participants receiving a 4th dose, we tested for spike-specific B, CD4 and CD8 T cell responses by flow cytometry using RBD-B and activation-induced marker (AIM) assays. We used descriptive statistics for demographics, reactogenicity and immunogenicity and ANOVA tests to assess the impact of a booster dose on vaccine-induced immune responses.

Results: Table 1 summarizes data on the first 71 participants (4th dose Spikevax® = 30, 4th dose Nuvaxovid® = 13 and 5th dose Nuvaxovid® = 28). Reactions to the vaccine at 7 days were frequent but not severe. Most common was fatigue, headache, injection site pain and arthralgias. At day 28, five new COVID-19 infections (one requiring hospitalization) and seven disease flares were reported. Table 2 reports anti-S, anti-RBD, anti-N, and NAbs to Wuhan and BA.5. Anti-S levels (Figure 1) were higher in those receiving 5th versus 4th dose. In those to whom we gave a 4th vaccine, we observed higher anti-S levels post mRNA ($p < 0.001$) but this was not clearly seen when the 4th dose was PSV. Most (16/19) of those tested post 4th dose had no detectable RBD B cell responses while three patients had higher B cells numbers and measurable RBD B cell responses. In contrast, the cohort demonstrated good Spike-specific intact and measurable AIM+ CD4 and CD8 T cell responses that did not increase post 4th dose.

Conclusion: Mix-and-match booster dosing was not clearly associated with unusual vaccine reactions, adverse events or disease flares in RTX-treated RD patients. In those who had already received 3 mRNA doses, there was a significant increase in anti-S levels after receiving a 4th mRNA vaccine but not when the 4th vaccine was PSV. Humoral and RBD-B-cell responses increased with a fourth dose. AIM+ CD4 and CD8 T cell responses were intact, showing a disconnect with weak B cell frequencies. We did not see a clear benefit for PSV compared to mRNA booster (after primary mRNA vaccine series) in RTX-treated RD patients. This may have important implications for COVID vaccine strategies in 2023-2024.

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AstraZeneca, 6, Boehringer-Ingelheim, 1, 5, 6, Bristol-Myers Squibb(BMS), 5, Merck, 6, UCB, 5; **N. Richard**: AbbVie/Abbott, 2, 6, AstraZeneca, 2, Eli Lilly, 2, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, UCB, 2; **J. Makhzoum**: None; **A. Mendel**: None; **S. Bernatsky**: None; **M. Dionne**: None; **M. Libman**: None; **G. De Serres**: None; **M. Dieudé**: None; **I. Flamand**: None; **D. Kaufmann**: None; **A. Finzi**: None; **R. Bazin**: None; **I. Colmegna**: None; **P. Fortin**: AbbVie, 1, AstraZeneca, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Roche-Genentech, 1.

Abstract Number: 0275

No Cumulative Effect of Infection Rates in Children Receiving Long-term Canakinumab Treatment in Autoinflammatory Periodic Fever Syndromes − Data from the RELIANCE Registry

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Autoinflammatory diseases (AID) have been treated safely and effectively with the interleukin-1β inhibitor canakinumab (CAN) in controlled trials and routine clinical practice. The most common adverse event reported were infections. In this study infections and infection rates in patients with cryopyrin-associated periodic syndromes (CAPS), familial Mediterranean fever (FMF), hyper-IgD syndrome/mevalonate kinase deficiency (HIDS/MKD) and tumor necrosis factor receptor-associated periodic syndrome (TRAPS) on CAN therapy were investigated in a real-world setting.

Methods: RELIANCE is a prospective, non-interventional, observational study in Germany enrolling pediatric (age ≥2 years) and adult patients with a clinically confirmed diagnosis of AID who routinely receive CAN. Efficacy and safety parameters are recorded at baseline and assessed at 6-month intervals.

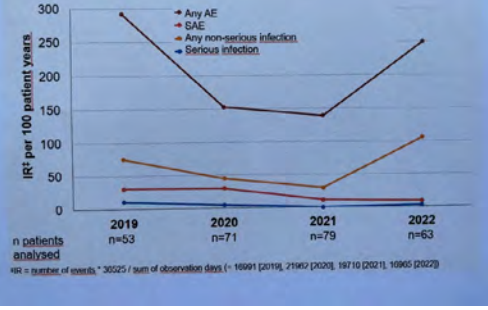
Results: The present interim analysis is based on data from a total of n=232 patients including n=101 (44%) pediatric patients under 18 years diagnosed with autoinflammatory diseases enrolled in the RELIANCE registry. The median duration of CAN treatment before and during study in the pediatric cohort was 4 years (0–15 years).

Between 2017 and 2022, 898 adverse events (AE) were recorded in n=164 patients (71%; Table 1). The incidence rate per 100 patient years (IR) was 163.82. Serious adverse events (SAE) were reported for n=35 patients (15%; 98 events, IR 17.88).

Table 1: Overview of serious and non-serious infections in pediatric patients in the course of the RELIANCE study across all study indications (2019–2022); *In bold: Respiratory tract infections*

Non-serious infections (n)	COVID-19 (24), **nasopharyngitis (19)**, **upper respiratory tract infection (13)**, **bronchitis (5)**, urinary tract infection (2), infection (5), **pharyngitis (3)**, **tonsillitis (6)**, cystitis (2), suspected COVID-19 (3), gastrointestinal infection (3), hand-foot-and-mouth-disease (4), **influenza (4)**, otitis media (2), **sinusitis (1)**, conjunctivitis (3), **respiratory tract infection (1)**, **viral upper respiratory tract infection (3)**, asymptomatic COVID-19, febrile infection, rotavirus infection (2 events each), gastroenteritis, gastroenteritis norovirus, oral herpes, **pneumonia**, pyelonephritis, appendicitis, **atypical pneumonia**, campylobacter gastroenteritis, ear infection staphylococcal, folliculitis, helminthic infection, infection susceptibility increased, **laryngitis**, **rhinitis**, salpingitis, skin infection, tinea infection, **tonsillitis streptococcal**, viral infection, **viral rhinitis** (1 event each)
Serious infections (n)	**Tonsillitis (3)**, gastroenteritis (2), anal abscess (1), genital infection fungal (1), **pneumonia (1)**, **respiratory tract infection viral (1)**, **tonsillitis bacterial (1)**, **tonsillitis streptococcal (1)**, **upper respiratory tract infection (1)**

Figure 1: Overview of adverse events and infection rates in the pediatric cohort of the RELIANCE study across all study indications over time (2019–2022)



During the study, infections occurred in 54.5% of patients (55 patients, 131 AE, including 11 SAE). To closely monitor the impact of long-term CAN treatment on infection rates in pediatric patients, data from a total of n=53, 71, 83 and 80 pediatric patients enrolled in the study in 2019, 2020, 2021, and 2022 were compared (Fig. 1). The IR of non-serious and serious infections in pediatric patients was 75.24 and 10.75 in 2019, and dropped to 44.90 and 4.99 in 2020, and 29.65 and 0.00 in 2021. The IR decrease might be caused by the periods of social distancing during the coronavirus pandemic in 2020 and 2021. In 2022, the IR of non-serious infections increased to 105.50 while the IR of serious infection stayed flat (IR 2.15). The course of upper respiratory tract infections IR in 2019, 2020, 2021, and 2022 was comparable to the IR of non-serious infections: 10.75, 8.32, 1.85, and 10.76. No cumulation of non-serious and serious infections under Canakinumab long-term treatment could be observed in the pediatric cohort.

Conclusion: Interim data of the RELIANCE study confirm that in the pediatric cohort the risk of infections including upper respiratory tract infections does not accumulate over 4 years under CAN treatment.

Disclosure: J. Kuemmerle-Deschner: Novartis, AbbVie, Sobi, 2, 5; **J. Henes**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, GlaxoSmithKlein(GSK), 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **B. Kortus-Goetze**: Novartis, 2; **P. Oommen**: Novartis, 5; **A. Pankow**: None; **T. Kallinich**: Roche, 6; **T. Krickau**: Novartis, 2, 5, 6; **C. Schuetz**: Novartis, 5; **G. Horneff**: GSK, 6, Janssen, 6, MSD, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Roche, 5, 6, Sanofi, 6, Sobi, 6; **I. Foeldvari**: Novartis, 2; **J. Rech**: AbbVie, Biogen, BMS, Chugai, GSK, Janssen, Lilly, MSD; Mylan, Novartis, Roche, Sanofi, Sobi, UCB, 2, 6, Novartis, Sobi, 5; **F. Weller-Heinemann**: None; **A. Janda**: None; **M. Hufnagel**: Novartis, 5; **F. Meier**: Novartis, 6; **F. Dressler**: Abbvie, Mylan, Novartis, Pfizer, 2, Novartis, 5; **M. Borte**: Pfizer, Shire, 5; **I. Andreica**: AbbVie/Abbott, 1, 6, Amgen, 1, 6, AstraZeneca, 1, 6, Chugai, 6, Novartis, 1, 6, Sobi, 1, 6, UCB, 1, 6; **P. Wasiliew**: None; **M. Fiene**: None; **D. Windschall**: None; **M. Krusche**: Chugai, 2, 6; **T. Kuempfel**: None; **J. Weber-Arden**: Novartis, 3; **N. Blank**: Novartis, Sobi, 5, Novartis, Sobi, Lilly, Pfizer, Abbvie, BMS, MSD, Actelion, UCB, Boehringer-Ingelheim, Roche, 2.

Abstract Number: 0276

Disease Control in Patients with Monogenetic Autoinflammatory Diseases Under Canakinumab Treatment – Comparison of 30 Months Interim Data from the RELIANCE Registry

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

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Background/Purpose: Treatment of autoinflammatory periodic diseases (AID) with the interleukin-1β inhibitor canakinumab (CAN) has been shown to be safe and effective in controlled trials and real-world setting. In the RELIANCE registry, long-term safety and efficacy of CAN in patients with cryopyrin-associated periodic syndromes (CAPS), familial Mediterranean fever (FMF), hyper-IgD syndrome/mevalonate kinase deficiency (HIDS/MKD) and tumor necrosis factor receptor-associated periodic syndrome (TRAPS) on CAN therapy were investigated in routine clinical practice.

Methods: The RELIANCE registry is a prospective, non-interventional, observational study in Germany enrolling pediatric (age ≥2 years) and adult patients with a clinically confirmed diagnosis of AID who routinely receive CAN. Efficacy and safety parameters are recorded at baseline and assessed at 6-month intervals. To compare disease control between indications, parameters of 30 months visits were analyzed.

Results: In the present interim analysis, data were included from a total of n=232 patients with a diagnosis of CAPS, FMF, TRAPS and HIDS/MKD enrolled in the RELIANCE registry between October 2017 and December 2022. The median age of the total study cohort was 20.0 years (2–80 years). Most patients (n=198, 85 %) were CAN pre-treated when entering the study and the median duration of total CAN treatment before and during the study was 4 years (0–15 years).

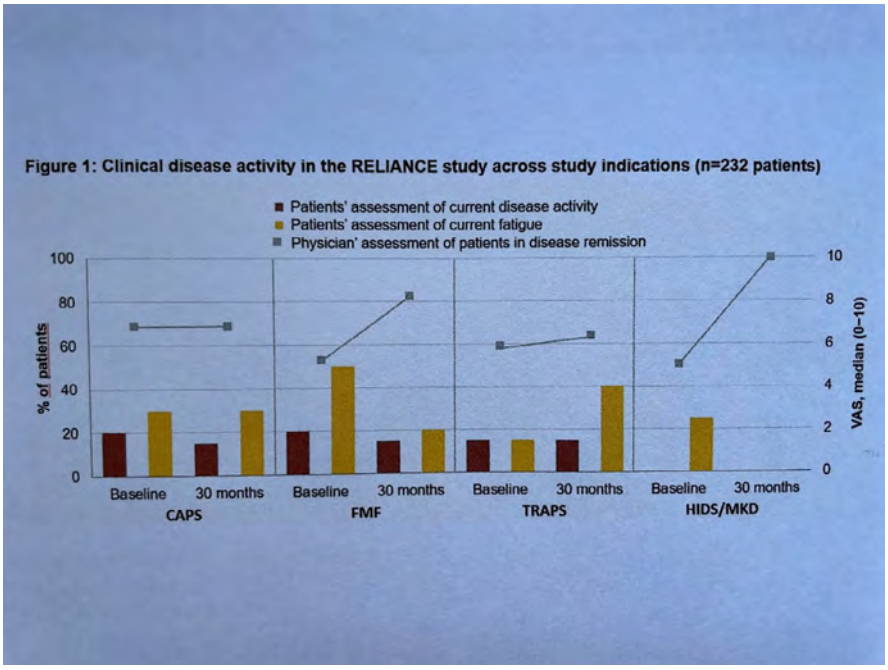

Table 1: Overview of laboratory markers and dose categories in the RELIANCE study across study indications (n=232 patients)

	CAPS		FMF		TRAPS		HIDS/MKD		Significant differences p-value
	Baseline n=107	30 months n=58	Baseline n=96	30 months n=28	Baseline n=21	30 months n=10	Baseline n=8	30 months n=5	
CRP, median (mg/dl) [25 %; 75 % quartiles]	0.1 [0.0; 0.4]	0.1 [0.0; 0.3]	0.2 [0.1; 0.6]	0.1 [0.0; 0.7]	0.2 [0.0; 2.3]	0.1 [0.1; 1.2]	0.2 [0.1; 0.5]	0.2 [0.1; 0.4]	0.465#
SAA, median (mg/dl) [25 %; 75 % quartiles]	0.4 [0.2; 1.1]	0.3 [0.2; 0.6]	0.8 [0.4; 3.1]	0.6 [0.4; 1.5]	0.5 [0.4; 2.8]	0.4 [0.2; 0.8]	0.6 [0.3; 2.3]	1.7 [0.8; 13.3]	0.027#
CAN dose category*, % of patients, less than standard / standard / higher than standard	23 % / 20 % / 58 %		35 % / 41 % / 24 %		33 % / 29 % / 38 %		14 % / 29 % / 57 %		

*Body weight > 40 kg: Standard dose is 150 mg per 8 weeks for CAPS and 150 mg per 4 weeks for any other indication. Body weight ≤ 40 kg: Standard dose is 2 mg per kg per 8 weeks (CAPS) or per 4 weeks (any other indication).

#*Kruskal-Wallis test*

Of 58/28/10/5 CAPS/FMF/TRAPS/HIDS patients with month 30 visits documented, 68/82/63/100% were in disease remission according to physician assessment. Patient-reported median disease activity and fatigue were low (1.5/1.5/1.5/0 and 3/2/4/0 on a 0–10 VAS scale). Inflammation markers (median) were within the limits of normal including neutrophil counts (2975/3420/3262/2897 n/µL). Statistical analysis confirmed similar efficacy across diseases in most parameters.

Even though these outcomes suggest an adequate disease control, an impact of the disease on patient´s social life was reported in 38/22/50/50% and negative influence on mood in 26/6/0/50% of patients.

Conclusion: The interim data of the RELIANCE study confirm sustained disease control of long-term treatment with CAN across all study indications. Even though disease activity measures suggest adequate disease control, patients´ social life and mood were negatively impacted by the disease.

Disclosure: I. Foeldvari: Novartis, 2; **T. Kallinich**: Roche, 6; **N. Blank**: Novartis, Sobi, 5, Novartis, Sobi, Lilly, Pfizer, Abbvie, BMS, MSD, Actelion, UCB, Boehringer-Ingelheim, Roche, 2; **J. Henes**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, GlaxoSmithKlein(GSK), 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **B. Kortus-Goetze**: Novartis, 2; **P. Oommen**: Novartis, 5; **A. Pankow**: None; **T. Krickau**: Novartis, 2, 5, 6; **C. Schuetz**: Novartis, 5; **G. Horneff**: GSK, 6, Janssen, 6, MSD, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Roche, 5, 6, Sanofi, 6, Sobi, 6; **J. Rech**: AbbVie, Biogen, BMS, Chugai, GSK, Janssen, Lilly, MSD; Mylan, Novartis, Roche, Sanofi, Sobi, UCB, 2, 6, Novartis, Sobi, 5; **F. Weller-Heinemann**: None; **A. Janda**: None; **M. Hufnagel**: Novartis, 5; **F. Meier**: Novartis, 6; **F. Dressler**: Abbvie, Mylan, Novartis, Pfizer, 2, Novartis, 5; **M. Borte**: Pfizer, Shire, 5; **I. Andreica**: AbbVie/Abbott, 1, 6, Amgen, 1, 6, AstraZeneca, 1, 6, Chugai, 6, Novartis, 1, 6, Sobi, 1, 6, UCB, 1, 6; **P. Wasiliew**: None; **M. Fiene**: None; **D. Windschall**: None; **M. Krusche**: Chugai, 2, 6; **T. Kuempfel**: None; **J. Weber-Arden**: Novartis, 3; **J. Kuemmerle-Deschner**: Novartis, AbbVie, Sobi, 2, 5.

Abstract Number: 0277

Anti-carbamylated Antibodies in Autoimmunity – Focus on Their Diagnostic and Prognostic Value: A Systematic Review and Meta-analysis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: This is the first systematic review and meta-analysis to examine the prevalence, the diagnostic and the prognostic value of anti-carbamylated protein (CarP) antibodies in the entire spectrum of rheumatic diseases.

Methods: We systematically searched Medline, Embase, the Cochrane Library, PubMed, Scopus and Web of Science databases for studies published before June 2021. Two investigators independently screened manuscripts to evaluate their eligibility, their quality and to extract the relevant data.

Results: A total of 105 full-text articles and 48 abstracts were respectively included for further analysis. Among those, 127 papers were eligible for inclusion in the quantitative meta-analysis. 50% of the studies reported anti-Carp antibodies measured by in-house or commercial ELISA using carbamylated feta calf serum (car-FCS) as antigen. Anti-car-FCS IgG antibodies were most prevalent in RA patients with a pooled sensitivity of 37.34% (meta-analysis using random, I2=60.52%, $p< 0.0001$). A great discrepancy was observed when comparing seropositive and seronegative RA, where pooled sensitivity was 50.27% in seropositive compared to 20.18% in seronegative RA. This trend was confirmed in early RA. The pooled sensitivity in other auto-immune rheumatic diseases was between 15-20%, which was similar to the sensitivity of seronegative RA. Patients with non-inflammatory arthritis such as osteoarthritis had pooled sensitivity of 8.3% which was slightly higher than healthy controls (4.6%). The diagnostic performance of anti-CarP antibodies could be determined in RA for both car-FCS and commercial anti-carbamylated protein ELISA. The area under the summary receiver operator characteristic (ROC) curve of both type was similar, 0.668 and 0.68, respectively. Meta-analysis of correlation coefficient was performed by pooling 8 cohorts of RA assessed by anti-car-FCS ELISA and showed a statistical significant correlation with ACPA ($p< 0.001$). Meta-analysis of association with anti-Carp and risk factors was performed by pooling 9 cohorts of RA patients assessed by anti-car-FCS ELISA and showed a statistical significant association with ever smoker ($p< 0.001$), RF+ ($p< 0.001$) and ACPA+ RA patients ($p< 0.001$).

Conclusion: Anti-Carp antibodies are specifically sensitive in seropositive RA patients and are present with similar sensitivities in seronegative RA and various other inflammatory arthritis such as PsA, SLE and pSS. This could suggest that anti-CarP antibodies may rather reflect a general auto-immune response than a RA-specific immune reaction.

Disclosure: J. Sarrand: None; **D. Parisis**: None; **M. Soyfoo**: None; **P. Sidiras**: None.

Abstract Number: 0278

NOD2 Genotyping Landscape in Yao Syndrome

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
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Background/Purpose: Yao syndrome (YAOS, OMIM 617321) is formerly designated NOD2-associated autoinflammatory disease. A spectrum of NOD2 mutations have been associated with this disease. This study aimed to investigate the NOD2 genetic architecture in YAOS.

Methods: In this retrospective single center study, a large cohort of patients with systemic autoinflammatory diseases (SAIDs) was analyzed in relation to genotyping results. After extensive negative workup for systemic autoimmune and related diseases, genetic testing for periodic fever syndrome 6-gene panel and an extended autoinflammatory disease gene panel was performed at Commercial Diagnostic Molecular laboratories. YAOS was diagnosed based on our published criteria, i.e., the presence of characteristic phenotype and genotype with exclusion of related diseases.

Results: There were 207 patients who carried NOD2 mutations and nearly all were Caucasian with 82% being female. Mean age at diagnosis was 40.7±0.1 years and disease duration at diagnosis was 12.2±12.2 years. Of 207 patients, 179 (86.5%) were diagnosed with YAOS and the remaining were diagnosed with mixed NOD-like receptor associated autoinflammatory disease due to coexistence of mixed genotypes. The genetic profile of patients included in our study showed that patients with two or more NOD2 variants were 26.1% (54/207), rare variants 29.5% (61/207), NOD2 IVS8+158 17.4% (36/207), NOD2 V955I 7.7% (16/207), and combined NOD2 and other SAID gene variants 19.3% (40/207). Based on the Two-hit hypothesis that has been proven true, i.e., one germline mutation and one somatic mutation for monogenic (familial cancer) and some polygenic disorders and our result that approximately 50% of patients carried two or more mutational events, we propose "Two-hit like theory" for the role of NOD2 genetics in YAOS. That is two genetic mutations in the same NOD2 gene or separate genes could be required to cause disease. The combinations could be low frequency variants, low frequency and rare variants, or rare variants only. For a minority of patients with low frequency NOD2 variants only, we assume that another unidentified NOD2 or other SAID gene related variant could be present. The disease has been recently reclassified as the new category of genetically transitional disease (GTD) because of its association with low penetrance variants. GTD refers to disease or disease status straddling monogenic and polygenic, where mutation is necessary but not sufficient to cause disease. GTD highlights the influence of genetic background on disease in concert with environment.

Conclusion: Our study indicates that most patients with YAOS carry two or more gene variants, or rare variants, suggesting Two-hit like hypothesis could be applicable to some cases of autoinflammatory disease. Further study of a large cohort of patients is warranted.

References

Vijg J, et al. Pathogenic Mechanisms of somatic mutation and genome mosaicism in aging. Cell 2020; 182(1): 12-23.
Yao Q, et al. Genetically transitional disease: a new concept in genomic medicine. Trends Genet 2023; 39(2):98-108.
Yao Q, Shen B. A Systematic Analysis of Treatment and Outcomes of NOD2-Associated Autoinflammatory Disease. Am J Med. 2017;130(3):365 e13-365 e18.

Disclosure: H. Nomani: None; **A. Saif**: None; **F. Hwang**: None; **Q. Yao**: None.

Abstract Number: 0279

Therapeutic Exploration of Immune Checkpoint Inhibitor Induced Inflammatory Arthritis *In Vivo*

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite unprecedented clinical success, immune checkpoint inhibitors (ICIs) are associated with immune-related adverse events (irAEs), including arthritis (ICI-arthritis). Management of ICI-arthritis is challenging because immunomodulatory therapy for arthritis should not impede antitumor immunity. Understanding of the mechanisms of ICI-arthritis is critical to overcome this challenge, but the precise pathophysiology remains unknown due to lack of pre-clinical murine models.

Methods: We immunized type II chicken collagen emulsified in Complete Freund Adjuvants. From Day 19, we implemented PD-1 inhibitor or combined CTLA-4 and PD-1 inhibitors (combined ICIs) and measured arthritis score until sacrifice. At sacrifice, we harvested joint (knee), bone (tibia), and serum to perform immunologic, histologic, and micro CT analyses.

Results: Four to five days after initiation of the ICIs, mice started to develop arthritis *de novo*. Clinical and histologic, and micro CT analyses revealed more severe arthritis in mice receiving combined ICIs compared to mice receiving PD-1 inhibitor alone. Importantly, like humans, collagen-specific T helper (Th)17/T cytotoxic (Tc)17 cell signatures were enhanced in inflamed joints of mice with combined ICI arthritis. Kinetic analysis revealed that upon ICI therapy, CII-specific Th1/Tc1 cells undergo plasticity into Th17/Tc17 cells which is correlated with disease severity. Inhibition of cytokines promoting Th17 cell development, function, and/or survival, including IL-1b, IL-6, IL-17A, IL-23 and TNFa, successfully ameliorate arthritis disease progression. Finally, microbial dysbiosis contributes to ICI-arthritis disease pathogenesis by enhancing production of Th17 related cytokines.

Conclusion: By modifying the collagen-induced arthritis model, we observed that mice develop arthritis *de novo* with ICI implementation. This model recapitulates ICI-arthritis and will provide insights of ICI-arthritis disease pathogenesis as well as preclinical supports to develop ideal therapeutic strategies for ICI-arthritis without abrogating ICI-antitumor efficacy.

Disclosure: S. Kim: None; **R. Rico**: None; **N. Turner**: None; **T. Trivedi**: None; **T. Guise**: None; **R. Nurieva**: None.

Abstract Number: 0280

Immunosuppression in the Treatment of Susac Syndrome: A Retrospective Evaluation of the Largest Cohort of Susac Syndrome

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

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Background/Purpose: Susac Syndrome is a rare autoimmune condition causing microvascular occlusions in the brain, retina and inner ear leading to the characteristic triad of encephalopathy, branch retinal artery occlusion (BRAO) and sensorineural hearing loss potentially leading to permanent disability and death if untreated. Approximately 400 cases of Susac Syndrome have been reported since its initial description in the 1970s. Most cases are from small case series utilizing various combinations of immunosuppression with variable outcomes. It is unclear what immunosuppressive regimen is most likely to result in reduced risk of disease flares. The goal of this study is to retrospectively evaluate all Susac Cases in our institution and compare immunosuppressive regimens.

Table 1 Descriptive table for Demographics

Table 1. Patient Characteristics		
Variable	**Level**	**All (n=60)**
Age at Susac admission		33.3 (9.07)
Sex	Male	16 (27.1%)
	Female	43 (72.9%)
Cochlear Implant	None	53 (98.1%)
	Post-SUSAC Index Admission	1 (1.85%)
Immunosuppression Medications	Yes	59 (100%)
IV Methylprednisolone		53 (88.3%)
Prednisone		58 (96.7%)
Cyclophosphamide		15 (25.0%)
IVIG		51 (85.0%)
Rituximab		34 (56.7%)
MMF(3g)		8 (13.3%)
MMF(Other)		42 (70.0%)
Azathioprine		8 (13.3%)
Methotrexate		1 (1.67%)
Tacrolimus		2 (3.33%)
Flare	No Flare	25 (44.6%)
	Flare on Treatment	25 (44.6%)
	Flare not on Treatment	6 (10.7%)

Table 1. Patient Characteristics		
Variable	**Level**	**All (n=60)**
Flare on Combined Treatments		14 (56.0%)
Flare Treatments	Cyclophosphamide	1 (4.00%)
	IVIG	13 (52.0%)
	Rituximab	2 (8.00%)
	MMF(3g)	1 (4.00%)
	MMF(Other)	5 (20.0%)
	Azathioprine	2 (8.00%)
	Methotrexate	1 (4.00%)
Flare Treatments 2	IVIG	3 (21.4%)
	MMF(Other)	11 (78.6%)

Continuous variables presented as Median (IQR). Categorical variables presented as N (column %).

Rates of Flare with Immunosuppression

Methods: A retrospective chart review of 134 patients with Susac Syndrome ICD diagnosis code within our institute's electronic medical record system was performed. The following were recorded: patient demographics, presenting signs/symptoms, whether the full triad of encephalopathy, vision and hearing loss were present, as well as immunosuppressive medications initiated, length of follow up and whether a patient had a flare while on immunosuppression. Flares were defined by objective changes in brain MRI, fluorescein angiography or audiometry in addition to clinical symptoms.

Results: Sixty patients met the European Susac Consortium criteria. The triad of encephalopathy with MRI changes of the corpus callosum, BRAO and hearing loss documented with audiometry were present in 65% of cases. The average age at presentation was 33 years of age and females accounted for 73% of patients. Patients received the following immunosuppressive medications: glucocorticoids 100%, IVIG (85%), mycophenolate mofetil MMF (83%) most patients receiving less than 3 grams daily (84%). Rituximab was given to 56% of patients and cyclophosphamide was given in 25% of cases. Azathioprine, methotrexate or tacrolimus together made up 18% of cases.

Flares were documented in 51% of patients after the initial diagnosis of Susac Syndrome, occurring on average 24 months after disease onset. 74% of patients were on medications at the time of the flare. Flares occurred on the following therapies: IVIG 16 (32%), MMF (< 3 grams) 16 (38%), MMF (3 grams) 1 (12%), Rituximab 2 (5%) and cyclophosphamide 1 (6%).

MMF and Rituximab were two of the more commonly used therapeutics, often in combination with IVIG. MMF overall, had a higher likelihood of experiencing flares when compared to patients on Rituximab (34% vs 5%) (P=0.003). This difference was most pronounced when compared to those on doses of MMF less than 3 grams daily ($P < 0.001$). In our cohort, a patient on MMF (all doses) is 5.8 times more likely to experience a flare compared to patients on Rituximab.

Conclusion: This is the largest cohort of patients suffering from Susac Syndrome. Based upon this single center retrospective cohort analysis, we conclude flares of disease were common over the first two years of follow up. These preliminary data suggest Rituximab may be superior to MMF in maintaining remission. Further study of this rare disease, including prospective controlled trials are needed.

Disclosure: A. Brown: Amgen, 2; **R. Rennebohm**: None; **G. Kharal**: None; **D. Conway**: Arena, 2, Biogen, 5, EMD Serono, 5, Horizon, 5, Novartis, 2; **S. Srivastava**: AbbVie/Abbott, 2, Allergan, 5, Bausch and Lomb, 2, Eyepoint, 2, 5, Eyevensys, 2, 5, Novartis, 2, Regeneron, 2, 5, Santen, 5, Zeiss, 2; **S. Sharma**: AbbVie/Abbott, 2, Alimera, 2, Allergan,

2, Apellis, 2, Bausch and Lomb, 2, Clearside, 2, Eyepoint, 2, Genentech, 2, 5, Gilead, 5, Regeneron, 2, RegenxBio, 2, Roche, 2, 5; **C. Lowder**: None; **L. Calabrese**: AstraZeneca, 6, Bristol-Myers Squibb(BMS), 2, Galvani, 2, Genentech, 2, GlaxoSmithKlein(GSK), 2, sanofi, 2, 6; **R. Hajj-Ali**: Amgen, 2, GlaxoSmithKlein(GSK), 2, uptodate, 9.

Abstract Number: 0281

Is There a Decreased Risk of Developing CF Arthropathy in CF Patients Undergoing Treatment That Targets the F508del Mutation?

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SESSION INFORMATION

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Background/Purpose: Cystic fibrosis (CF) is characterized by mutations within the CFTR (cystic fibrosis transmembrane conductance regulator) gene that result in a defect of the chloride transporter protein in different organs, particularly in the lung. Musculoskeletal symptoms have been reported in up to 29% of CF patients[1], most frequently as recurrent episodes of mono- or polyarthritis in joints of hands and feet. Potent CFTR modulator therapies targeting the F508del mutation in

Table 1. Baseline characteristic of cystic fibrosis (CF) patients.

	CF patients n = 25	CF +Arthropathy n = 6	CF - Arthropathy n = 19	P
Age (years), mean (±SD)	26 ± 5	28 ± 7	25 ± 3	NS
BMI (kg/m2), mean (±SD)	23 ± 4	24 ± 5	22 ± 3	NS
Female sex, n (%)	13/25 (52)	3/6 (50)	10/19 (53)	NS
CF disease characteristics				
PGA (0-10) Tirodness, mean (±SD)	2.6 ± 1.7	3.2 ± 2.3	2.2 ± 1.5	NS
Productive cough ejection > 1 TS, n (%)	3/25 (12)	2/6 (33)	1/19 (5)	NS
Cough, n (%)	9/25 (36)	3/6 (50)	6/19 (32)	NS
Sputum green/yellow, n (%)	10/25 (24)	3/6 (17)	7/19 (21)	NS
Haemoptysis, n (%)	1/25 (4)	0/6 (0)	1/19 (5)	NS
Steatorrhea, n (%)	4/25 (16)	2/6 (33)	2/19 (10)	NS
Nasal airway obstruction, n (%)	10/25 (40)	3/6 (50)	7/19 (37)	NS
Antibiotic since last consultation, n (%)	3/25 (12)	0/6 (0)	3/19 (16)	NS
Diabetes mellitus	6/25 (24)	1/6 (17)	5/19 (26)	NS
CFTR modulator n (%)	22/25 (88)	3/6 (50)	19/19 (100)	0.001
CFTR modulator treatment duration (months), mean (±SD)	11 ± 5	7 ± 9	13 ± 3	0.0280
Chronic colonisation				
Pseudomonas aeruginosa	8/25 (32)	2/6 (33)	6/19 (32)	NS
Staphylococcus aureus	20/25 (80)	3/6 (50)	17/19 (89)	0.0351
Clinical joint characteristics				
PGA (0-10) Pain, mean (±SD)	1.9 ± 2.4	5.0 ± 2.8	0.9 ± 1.2	<0.0001
Arthralgia, n (%)	12/25 (48)	5/6 (83)	7/19 (37)	0.0469
Myalgia, n (%)	5/25 (20)	4/6 (67)	1/19 (5)	0.001
Swollen Joint, n (%)	5/25 (20)	5/6 (83)	0/19 (0)	<0.0001
Tender Joint, n (%)	6/25 (24)	6/6 (100)	0/19 (0)	<0.0001
Morning stiffness (minutes), mean (±SD)	19 ± 60	73 ± 110	3 ± 10	0.009
Squeeze test, n (%)	2/25 (8)	2/6 (33)	0/19 (0)	0.008
FACIT-Fatigue Scale	46 ± 7	45 ± 9	46 ± 6	NS
Laboratory parameters				
ESR (mm/h), mean (±SD)	9 ± 11	22 ± 15	5 ± 4	0.0005
CRP (mg/L), mean (±SD)	4.2 ± 5.1	8.3 ± 3.7	2.8 ± 4.8	0.0181
ACPA, n (%)	1/25 (4)	1/6 (17)	0/19 (0)	NS
ACPA (U/ml), mean (±SD)	22 ± 71	63 ± 136	7 ± 2	NS
Rheumatoid factor IgM, n (%)	3/25 (12)	3/6 (50)	0/19 (0)	0.0023
RF IgM (IU/ml), mean (±SD)	1.9 ± 2.8	4.3 ± 4.6	1.0 ± 0.8	0.0100
Rheumatoid factor IgA, n (%)	2/25 (8)	2/6 (33)	0/19 (0)	NS
RF IgA (IU/ml), mean (±SD)	6.8 ± 14	17 ± 24	3.0 ± 1.9	0.0264
Haemoglobin (g/l), mean (±SD)	145 ± 13	139 ± 9	148 ± 13	NS
Leucocytes (Giga/l), mean (±SD)	7.9 ± 2.5	9.8 ± 3.4	7.2 ± 1.8	NS
IgE (kU/l), mean (±SD)	168 ± 359	391 ± 688	94 ± 127	NS

Fig. 1

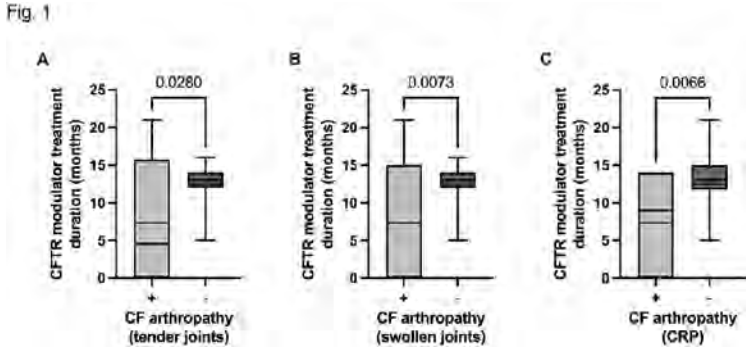
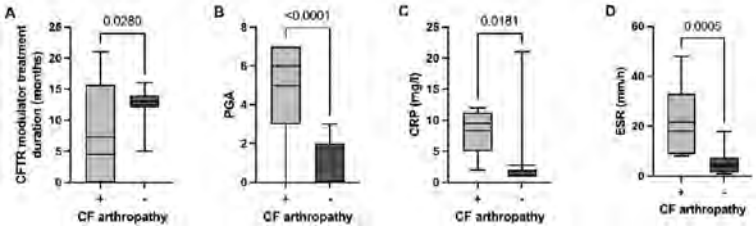


Fig. 2



CF have become available (i.e., Trikafta© - consisting of a triple combination of elexacaftor, tezacaftor, and ivacaftor) that increase CFTR protein availability.

We seek to characterize musculoskeletal symptoms in a cohort of consecutive CF patients.

Methods: 25 CF consecutive outpatients were enrolled in this monocentric, prospective, and cross-sectional cohort study. Rheumatologic evaluation included clinical and laboratory parameters. Data were analyzed by covariance (ANCOVA) models, using the general linear model approach. Correlation analyses were performed calculating nonparametric Spearman correlation rank coefficients.

Results: Baseline characteristics are outlined in Table 1. 22/25 CF patients were under CFTR modulator treatment with a mean treatment duration of 11 ± 5 months. Arthralgias and myalgias were reported in 48% and 20% of patients, respectively. Arthritis, mainly involving small joints, was clinically detected in 6/25 (24%) patients and confirmed by ultrasound (US) in 3/6 patients. Self-reported myalgias, were significantly associated with the presence of swollen joints ($r = 0.7452$, $p < 0.0001$), tender joints, ($r = 0.6674$, $p = 0.0003$), a positive squeeze test ($r = 0.5898$, $p = 0.0019$) and morning stiffness ($r = 0.6556$, $p = 0.0004$) (Table 1). Disease activity as assessed by the SDAI was moderate (mean 18 $\pm$ 3). CCP and rheumatoid factor (RF) were detected in one patient not on CFTR modulator therapy (with PIP synovitis confirmed by US). Two patients on CFTR modulator therapy tested positive for RF. Another patient was seronegative but synovitis was confirmed by US. Of note, longer duration of CFTR modulator therapy was significantly associated with a lower number of tender joints ($r = -0.410$ $p = 0.054$), swollen joints ($r = -0.400$, $p = 0.048$) and a lower CRP ($r = -0.509$, $p = 0.048$) (Fig 1 and Fig 2).

Conclusion: The current cohort study confirms that musculoskeletal symptoms are frequent in adult CF patients. Self-reported myalgias were significantly associated with arthritis mainly involving small joints. Interestingly, longer duration of CFTR modulator therapy was associated with a decreased number of tender and swollen joints in line with the assumption that amelioration of mucosal airway inflammation may decrease the risk of developing CF arthropathy.

References

Ja1. Janssen KMJ et al. Arthritis Res Ther 2015. doi: 10.1186/s13075-015-0690-6

Disclosure: K. Schmiedeberg: None; **A. Walter**: None; **L. Joos**: None; **M. Brutsche**: None; **J. von Kempis**: None; **A. Rubbert-Roth**: AbbVie/Abbott, 2, 6, Amgen, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, 6.

Abstract Number: 0282

DNA Methylation Markers in Peripheral Blood as Effective Diagnostic Biomarkers for Adult-onset Still's Disease

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I

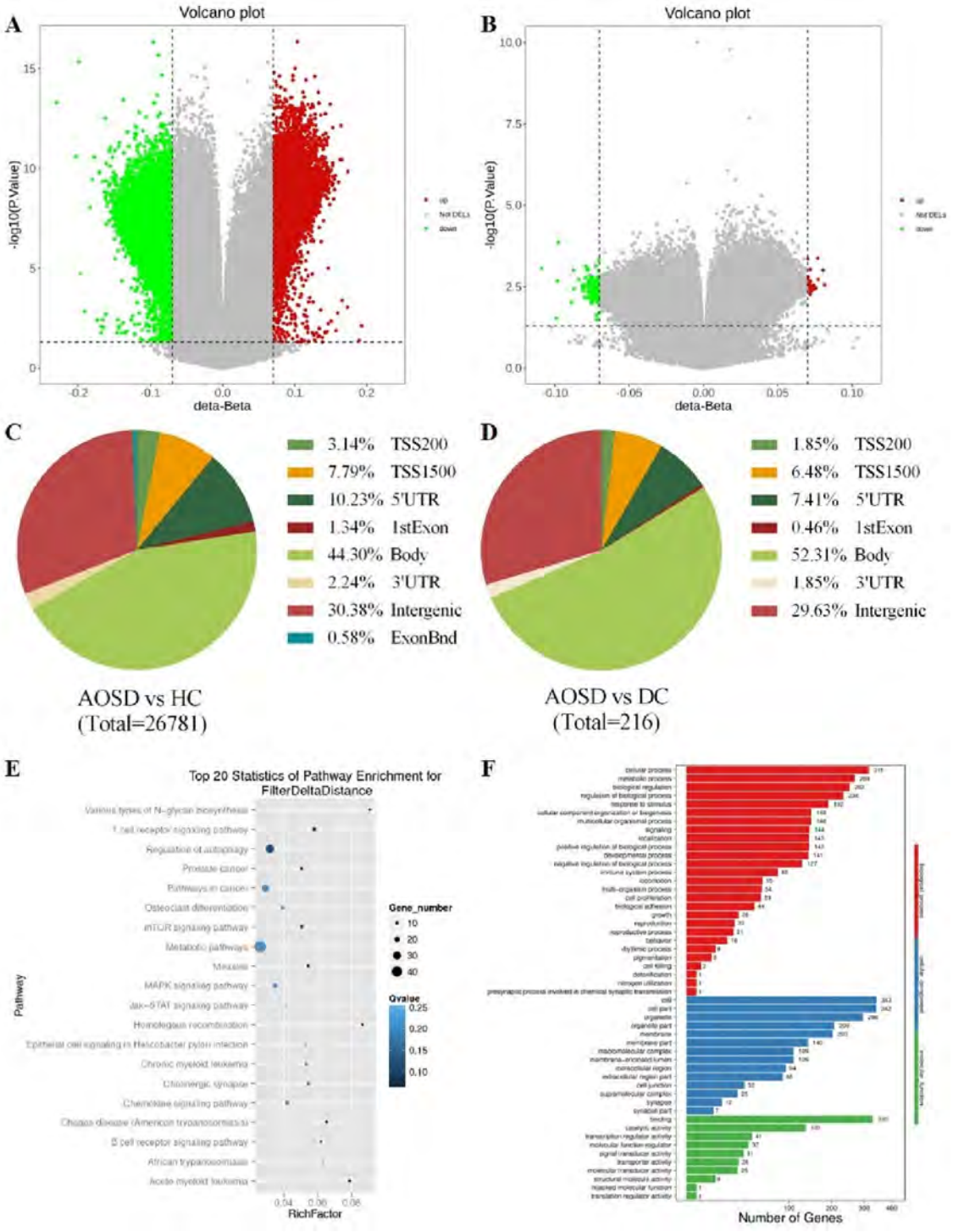
Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Adult-onset still's disease (AOSD) is an auto-inflammatory disease affecting multiple systems. The diagnostic procedures of AOSD are still a challenge. We aimed to find an effective DNA methylation biomarker for AOSD diagnosis in this study

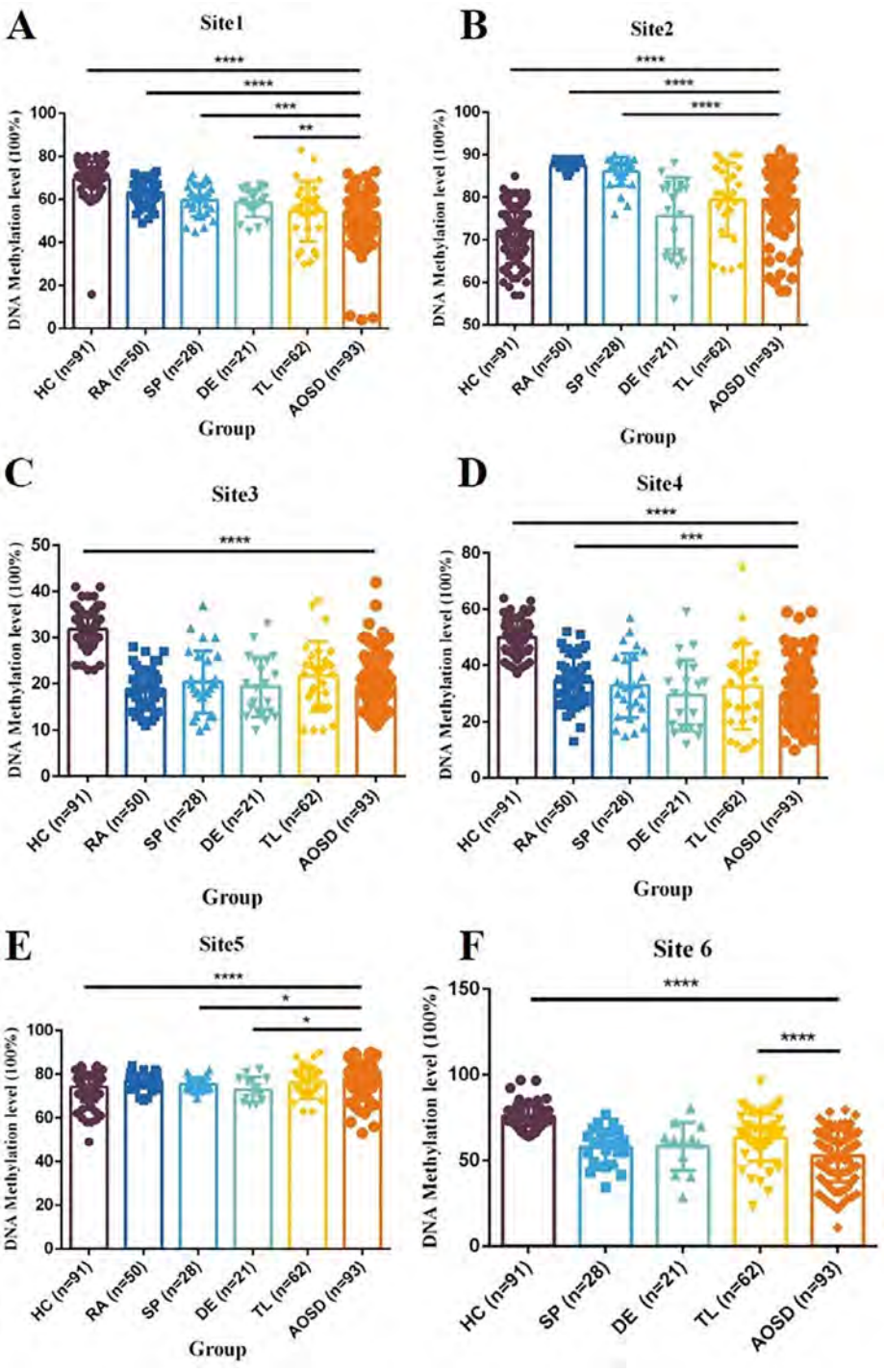
Methods: Differential methylation CpG sites (DMSs) were selected from DNA methylation array comprised of a discovery cohort including 50 AOSD patients, 49 healthy controls (HCs), 24 T cell lymphoma (TL) patients, 24 sepsis (SP) patients and 24 drug eruption (DE) patients. A cohort of 96 AOSD patients, 92 HCs, 50 rheumatoid arthritis (RA) patients, 28 SP patients, 21 DE patients and 62 TL patients was used for validation via pyrosequencing. Subsequently, four logistic regression prediction models were performed.

Results: Nine DMSs were selected from the discovery cohort via the DNA methylation array incorporating Least Absolute Shrinkage and Selector Operation (LASSO). We analyzed the methylation levels of these CpG sites by pyrosequencing in the validation cohort, and calculated four logistic regression prediction models in order to differentiate AOSD from the HCs (AUC: 0.964, sensitivity: 98.5%, specificity: 98.9%), the RA group (AUC: 0.988, sensitivity: 97.8%, specificity: 94%), the SP group (AUC: 0.885, sensitivity: 77.1%, specificity: 92.9%) and the DE group (AUC: 0.842, sensitivity: 72%, specificity: 90.5%) respectively. In addition, the methylation level of cg14887853 could be used to distinguish AOSD (AUC: 0.693, sensitivity: 79.6%, specificity: 59.5%) and active AOSD (AUC: 0.761, sensitivity: 81.5%, specificity: 67.8%) from TL respectively.

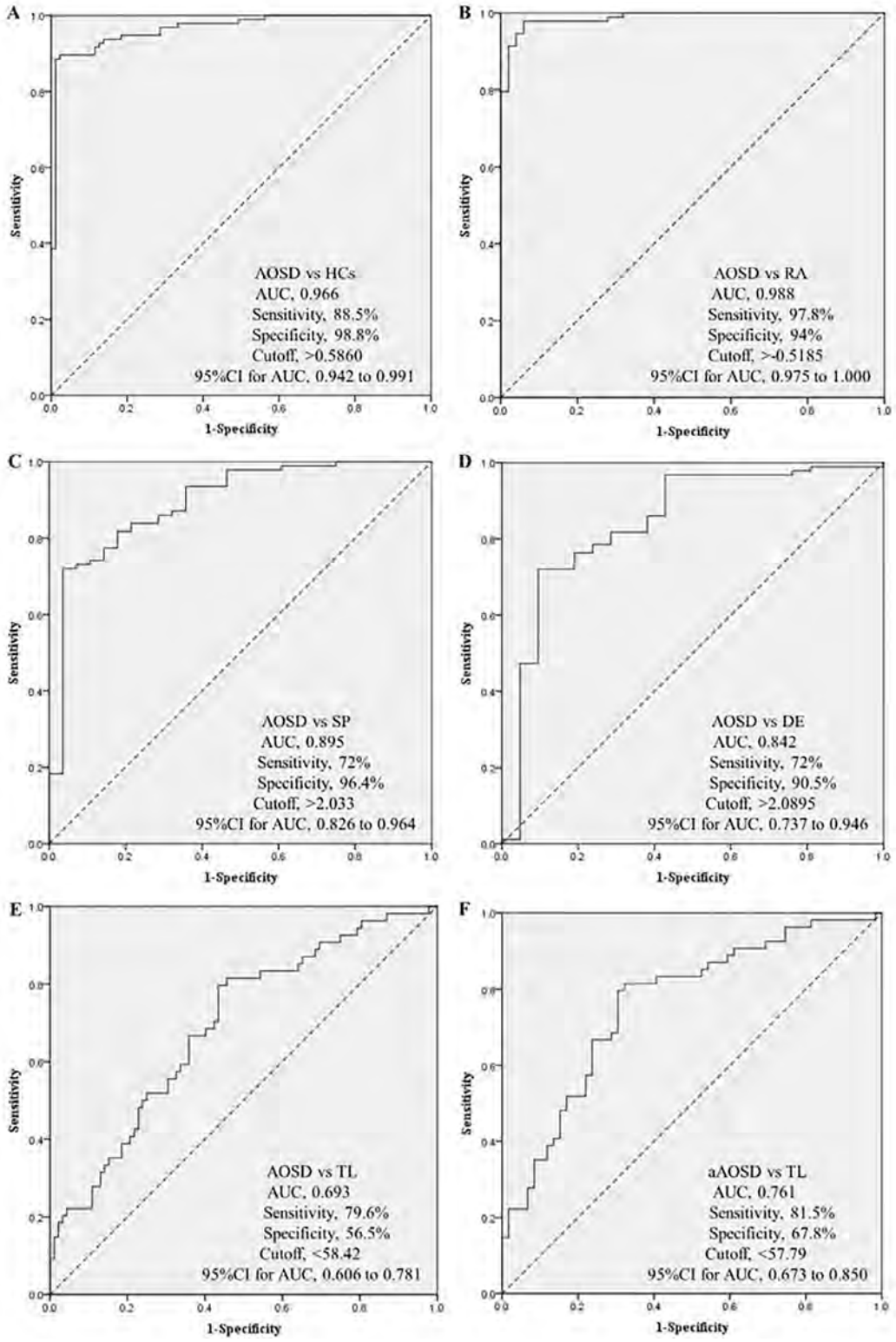


Volcano plots, location information, KEGG pathway analysis and GO analysis of differentially methylated CpG sites (DMSs) in AOSD. A Volcano plot of the distribution of DMSs between AOSD and HC group. B Volcano plot of the distribution of DMSs between AOSD and DC groups. C Location information of DMSs on genome E Top 20 statistic of pathway enrichment of DMSs between AOSD and HC group. F GO analysis DMSs between AOSD and HC group.

Conclusion: The DNA methylation levels of CpG sites can be used as biomarker for diagnosis of AOSD.



DNA methylation level of the identified six differential methylated sites (DMSs) between AOSD and healthy controls (HCs)/ disease controls (DCs) in validation cohort. A It shows that methylation level of Site1 is significantly lower in the blood of AOSD patients than that in HCs, patients with rheumatoid arthritis (RA), patients with sepsis (SP) and patients with drug eruption (DE). B It shows that methylation level of Site2 is significantly lower in the blood of AOSD patients than that in patients with RA and patients with SP, and is significantly higher in the blood of AOSD patients than that in HCs. C It shows that methylation level of Site3 is significantly lower in the blood of AOSD patients than that in HCs. D It shows that methylation level of Site4 is significantly lower in the blood of AOSD patients than that in HCs and patients with RA. E It shows that methylation level of Site5 is significantly higher in the blood of AOSD patients than that in HCs, patients with SP and patients with drug eruption (DE). F It shows that methylation level of Site6 is significantly lower in the blood of AOSD patients than that in HCs and patients with T cell lymphoma (TL).



Receiver operating characteristic (ROC) curves analysis of logistic regression prediction model. A show the ROC curve of the logistic regression prediction model based on Site1, Site3, Site4 and Site5 in patients with AOSD compared with HCs. B show the ROC curve of the logistic regression prediction model based on Site1, Site2, Site3 and Site4 in patients with AOSD compared with patients with RA. C show the ROC curve of the logistic regression prediction model based on Site1, Site2, and Site3 in patients with AOSD compared with patients with SP. D show the ROC curve of the logistic regression prediction model based on Site1, Site3, Site4 and Site5 in patients with AOSD compared with patients with DE. E show the ROC curve of Site 6 in patients with AOSD compared with patients with TL. F show the ROC curve of Site 6 in AOSD patients in active phase compared with patients with TL.

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Abstract Number: 0283

Transcriptomic Profiles in Muscle Biopsies from Systemic Sclerosis Patients with Different Autoantibodies

Maria Casal-Dominguez[1], Jose Cesar Milisenda[2], Iago Pinal-Fernandez[1], Katherine Pak[3], Sandra Muñoz-Braceras[1], Jose Jiram Torres-Ruiz[1], Stefania Dell´Orso[4], Faiza Naz[4], Gustavo Gutierrez-Cruz[4], Shamima Islam[1], Yaiza Duque-Jaimez[2], Ana Matas-Garcia[2], Francesc J Garcia-Garcia[2], Mariona Guitart-Manpel[2], Gloria Garrabou[2], Ernesto Trallero-Araguas[5], Brian Wallit[6], Lisa Christopher-Stine[7], Tom Lloyd[8], Alfredo Guillen-Del-Castillo[9], Carmen Pilar Simeon-Aznar[10], Josep Maria Grau[2], Albert Selva-O'Callaghan[5] and Andrew Mammen[11], [1]Muscle Disease Unit, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [2]Muscle Research Unit, Internal Medicine Service, Hospital Clinic, Barcelona, Spain, [3]National Institutes of Health, Bethesda, MD, [4]National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [5]Systemic Autoimmune Disease Unit, Vall d'Hebron Institute of Research, Barcelona, Spain, [6]National Institute of Neurological Diseases and Stroke, National Institutes of Health, Bethesda, MD, [7]Johns Hopkins University, Baltimore, MD, [8]Johns Hopkins University School of Medicine, Baltimore, MD, [9]Unit of Autoimmune Diseases, Department of Internal Medicine, Hospital Universitario Vall d'Hebron, Barcelona, Spain, [10]Department of Internal Medicine, Systemic Autoimmune Diseases Unit, Hospital Universitario Vall d'Hebronh, Barcelona, Spain, [11]NIH, Bethesda, MD

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The inflammatory myopathies (IM) include dermatomyositis (DM), antisynthetase syndrome (AS), immune-mediated necrotizing myopathy (IMNM), inclusion body myositis (IBM), and overlap myositis (OM), in which IM exists in the context of another rheumatologic disease, such as systemic sclerosis (SSc).

The objective of this study was to define the transcriptomic profiles of muscle tissue from patients with OM-SSc and to compare these with the transcriptomic profiles of muscle tissue from patients with other types of IM as well as healthy volunteers.

Methods: Bulk RNA sequencing was performed on muscle biopsies obtained from(a) OM-SSc patients with defined SSc autoantibodies recognizing PMScl, Scl70, or centromeric autoantigens, (b) patients with DM, AS, IMNM, IBM, and (c) healthy volunteers.

Results: In muscle biopsies from patients with OM-SSc, there was upregulation of genes associated with type I interferon (IFN) signaling (ISG15, MX1), type II IFN signaling (GBP2, PSMB8, IFI30), muscle regeneration (NCAM1, MYH3, MYH8, MYOD, MYOG, PAX7), immunoglobulin production (IGH1, IGH2, IGH3, IGHM, IGHA2), and specific types of immune cells (CD3E, CD4, CD8B, CD14, CD68, CD19, and CD20). The upregulation of these genes was more pronounced in biopsies from patients with OM-SSc who had anti-PMScl autoantibodies compared to those with other SSc autoantibodies. Specifically, the upregulation of type I IFN-associated genes in biopsies from patients with anti-PmScl was intermediate, resembling that observed in biopsies from patients with AS, while type II IFN-associated upregulation was high and comparable in biopsies from patients with AS and IBM. Conversely, structural muscle genes such as MYH1, MYH2, ACTA, and TTN, were downregulated in patients with all types of autoantibody-defined OM-SSc.

Conclusion: Muscle tissue from patients with OM-SSc exhibit significant upregulation of interferon type I and II signaling, immunoglobulin production, muscle regeneration-related genes, and immune cell markers. Notably, these gene expression changes are more pronounced in muscles from patients with SSc who had anti-PMScl autoantibodies compared to those with anti-Scl70 and anti-centromere autoantibodies. These findings contribute to our understanding of the molecular mechanisms underlying SSc and provide insights into potential therapeutic targets.

Disclosure: M. Casal-Dominguez: None; **J. Milisenda**: None; **I. Pinal-Fernandez**: None; **K. Pak**: None; **S. Muñoz-Braceras**: None; **J. Torres-Ruiz**: None; **S. Dell´Orso**: None; **F. Naz**: None; **G. Gutierrez-Cruz**: None; **S. Islam**: None; **Y. Duque-Jaimez**: None; **A. Matas-Garcia**: None; **F. Garcia-Garcia**: None; **M. Guitart-Manpel**: None; **G. Garrabou**: None; **E. Trallero-Araguas**: None; **B. Wallit**: None; **L. Christopher-Stine**: None; **T. Lloyd**: None; **A. Guillen-Del-Castillo**: None; **C. Simeon-Aznar**: None; **J. Grau**: None; **A. Selva-O'Callaghan**: None; **A. Mammen**: None.

Abstract Number: 0284

Phenotyping Calcinosis: A Rare Manifestation of Rare Diseases

Michele Diomedi[1], Federico Fattorini[1], Simone Barsotti[2], Elenia Laurino[1], Chiara Cardelli[1], Linda Carli[1] and Marta Mosca[1], [1]Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy, [2]Internal Medicine, Ospedale di Livorno, Pisa, Italy

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Idiopathic inflammatory myopathies (IIMs) are rare systemic autoimmune disorders, with a pleiotropic clinical picture, specifically characterized from the inflammatory involvement of striate muscles. Calcinosis cutis is a chronic condition, that could be associated with connective tissue diseases, being a source of pain and functional disability. The aim of the study was to evaluate the prevalence of calcinosis in a monocentric cohort of patients with IIMs, exploring possible correlations with clinical variables and quality of life (QoL).

Methods: We retrospectively analyzed medical records of consecutive patients diagnosed with IIM according the EULAR/ACR 2017 criteria, collecting data about demography, subset and duration of disease, organ involvement, serology and comorbidities. QoL and WA were evaluated with Patients Reported Outcomes (PROs): Short-Form 36 Health Survey (SF-36), Functional Assessment of Chronic Illness Therapy Fatigue Subscale (FACIT-F), Health Assessment Questionnaire (HAQ), Work Productivity and Activity Impairment Questionnaire (WPAI), Hospital Anxiety and Depression Scale (HADS). Intergroups comparisons were assessed by using Chi-square, t-test and ANOVA. P values < 0.05 were considered significant.

Results: A total of 176 patients, 116 (65,9%) female, 79 (44,9%) with DM, 74 (42%) with PM, 11 (6,3%) with CADM, 10 (5,7%) with IBM, 2 (1,1%) with JDM were enrolled; 17 of them (9.7%), 12 (70,6%) women, had calcinosis. A statistically significant difference between respectively calcinosis subgroup and the whole cohort was found for the mean age (53,3 ±18,3 years vs 67,6±11,4, $p< 0.001$), the age at disease onset (30,1±16.6 years vs 58.9±12.9, $p< 0.001$), the age at diagnosis (42.1±17.6 years vs 61.6±12.8, $p< 0.001$) and the disease duration (14.2±9.0 years vs 8.7±6.7, $p=0.003$). Taking into account patients' serological profiles, a significant correlation was observed between anti- PMScl100 positivity and calcinosis development ($p=0.007$). The majority of patients with calcinosis, as expected, had a cutaneous involvement ($p< 0.001$) and showed lower values of CPK and aldolase ($p=0.03$). Analysing patients' comorbidities, we found no patient with calcinosis had developed cancer; this result remained significant after correcting for age and disease duration. PROs analysis

showed patients with calcinosis had significantly lower values of both HADS-A, HADS-D and FACIT ($p < 0.03$); accordingly, they had significantly higher values of both Role Emotional and Social Function items of SF36 (p=0.03)

Conclusion: From the analysis of our data, calcinosis seems to be more frequent in younger patients, with an earlier disease onset and with a longer disease duration. Interestingly, we found a significant correlation with anti- PMScl100 antibodies and with a less severe muscle involvement. Notably, we found patients with calcinosis seem to have a significantly lower risk of developing cancer, independently from age. Therefore, even if calcinosis is considered a risk factor for disease severity and QoL compromission, our study highlighted a more favourable clinical profile, with a gain for patients in both their emotional and functional spheres.

Disclosure: M. Diomedi: None; **F. Fattorini**: None; **S. Barsotti**: None; **E. Laurino**: None; **C. Cardelli**: None; **L. Carli**: None; **M. Mosca**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, GlaxoSmithKlein(GSK), 2, Otsuka, 2, UCB, 2.

Abstract Number: 0285

Patient Reported Physical Function, Mental Health, and Treatment Patterns in Dermatomyositis

Lisa Christopher-Stine[1], Julie Paik[1], Brendan M. Johnson[2], Taryn Smith[2], Jolie Feldman[2] and Paul N. Mudd Jr.[2], [1]Johns Hopkins University, Baltimore, MD, [2]Priovant Therapeutics, Durham, NC

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Dermatomyositis (DM) is a rare, debilitating, idiopathic inflammatory myopathy characterized by painful, itchy skin rash and proximal muscle weakness that can significantly impact daily activities and independence. Additional life-threatening manifestations include interstitial lung disease and increased risk of malignancy. The profound impacts of DM and treatment patterns on patient quality of life (QoL) are not yet well-characterized in the literature.

Methods: To capture adult patient perspectives on the impact of DM and frequently used medications on patients' QoL (e.g., physical function, mental health, personal relationships), a 60-question survey was developed via focus groups and adaptations from existing tools. After central IRB review (WCG), members of The Myositis Association with a self-reported diagnosis of DM, 18 – 75 yrs of age, and onset of symptoms ≥ 1 yr were invited to complete the online survey. Responses were collected per the following Likert scales: DM severity rated from "mild" to "very severe" (4-point scale), QoL impact rated from "never" to "always" or "not at all" to "a great deal" (5-point numeric scores). Current medications also were captured. Frequency tables and descriptive statistics were prepared.

Results: Respondents (N=195) predominantly lived in the US (97%), were female (88%), white (82%), with a median age of 57 yrs; 53% and 35% experienced DM symptoms for 3 to 10 yrs or > 10 yrs, respectively.

Arithmetic mean QoL impact scores (out of 5) for patients with mild, moderate, or severe/very severe disease, respectively, were 1.9, 2.7, and 3.6 when asked if DM limits their ability to do things they enjoy; 2.3, 2.6, and 3.2 when asked how often they worry their disease will worsen; and 1.8, 2.4, and 3.4 when asked how often they worry about their disease will limit their

ability to carry out daily activities. Across all QoL endpoints, more than 50% of participants said their social life and relationships are at least somewhat negatively impacted by DM, and that DM limits their ability to perform daily activities (65%) and the ability to climb stairs (63%). Immunosuppressants were most commonly used (72%), then over-the-counter NSAIDS (56%) and oral corticosteroids (48%).84% of respondents use more than 1 medication for DM. Use of steroids increased as disease worsens (35%, 44%, and 65% of mild, moderate, and severe/very severe respondents, respectively). There was also increased use of opioids in respondents with severe/very severe disease (32%), compared to mild/moderate disease (< 10%), despite increased use of intravenous immunoglobulins in this most severe group (35% vs < 20%, respectively). Opioid users most frequently report muscle pain as their most bothersome symptom (63%). Patients using more medications, as well as those using opioids, also reported greater impact of their disease on QoL.

Conclusion: This survey highlights the physical limitations and high emotional burden in patients living with DM. The survey also suggests an unmet need for additional steroid-sparing therapies and novel treatments that address disease pathogenesis. The self-reported use of opioids in the most severely affected patients living with DM has not previously been appreciated.

Disclosure: L. Christopher-Stine: None; **J. Paik**: None; **B. Johnson**: Priovant Therapeutics, 3, 3; **T. Smith**: Priovant Therapeutics, 3; **J. Feldman**: Priovant Therapeutics, 3; **P. Mudd Jr.**: Priovant Therapeutics, 3.

Abstract Number: 0286

Relationship Between High Resolution Computed Tomography(HRCT) Quantitative Scores and Physiological and Clinical Features in Antisynthetase Syndrome Related Interstitial Lung Disease

Sangmee Bae[1], Fereidoun Abtin[2], Grace Kim[3], Daniela Markovic[4], Siamak Moghadam-Kia[5], Chester V. Oddis[6], Lila Pourzand[2], Didem Saygin[6], Daniel Sullivan[7], Koichi Yamaguchi[5], Donald Tashkin[3], Christina Charles-Schoeman[8], Jonathan Goldin[3] and Rohit Aggarwal[6], [1]UCLA Rheumatology, Los Angeles, CA, [2]UCLA Radiological Sciences, Los Angeles, CA, [3]University of California Los Angeles, Los Angeles, CA, [4]UCLA Department of Medicine Statistics Core, Los Angeles, CA, [5]University of Pittsburgh Medical Center Rheumatology, Pittsburgh, PA, [6]University of Pittsburgh, Pittsburgh, PA, [7]UCLA Pulmonology, Pittsburgh, PA, [8]UCLA Medical Center, Santa Monica, CA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: High resolution chest computed tomography (HRCT) plays an important role in the clinical evaluation of interstitial lung disease (ILD) by demonstrating the extent of parenchymal disease and detecting serial changes over time. A quantitative CT scoring method using a computer aided diagnosis system to measure the nature and extent of parenchymal diseases has been used to measure treatment response in the scleroderma lung study II (SLSII). The current study aims to evaluate the association of quantitative CT scores and clinical/physiological disease parameters in a cohort of antisynthetase positive myositis patients with ILD.

Methods: We analyzed 20 patients enrolled at the Abatacept in Myositis Associated Interstitial lung disease (Attack My-ILD) study. Myositis patients with antisynthetase antibodies and active ILD were enrolled across 5 centers and randomized to a double blind placebo period for 24 weeks followed by an open label period for 24 weeks. HRCT were performed at 3 timepoints (week 0, 24, 48) with quantitative scores for extent of ground glass (QGG), fibrosis (QLF), total ILD (QILD) performed

using a computer aided diagnostic system. Pulmonary function tests (forced vital capacity [FVC], diffusing capacity adjusted for hemoglobin [DLCO]), 6 minute walk distance (6MWD), physician/patient reported outcomes (UCSD shortness of breath questionnaire, short form-36 (SF-36), Borg scale, myositis disease activity assessment tool (MDAAT), health assessment questionnaire (HAQ), patient global myositis activity visual analog scale, supplemental oxygen use) were all obtained over

Table 1. Correlations Between Baseline Quantitative CT scores and Baseline Clinical/Physiological Parameters (n=20)

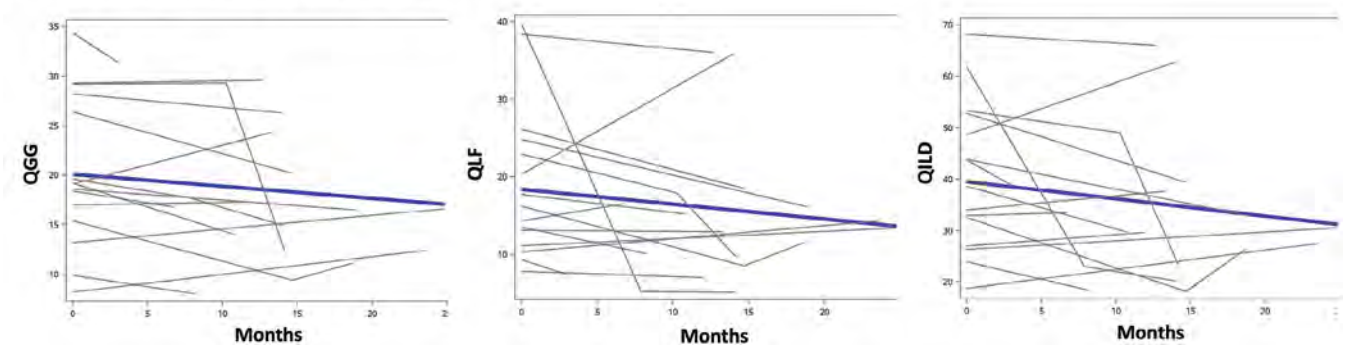
	QGG		QLF		QILD	
	σ	P value	σ	P value	σ	P value
FVC ml	**-0.57**	**0.02***	-0.29	0.28	**-0.54**	**0.03***
FVC %predicted	**-0.60**	**0.01***	-0.30	0.27	**-0.51**	**0.04***
DLCOHg ml	-0.45	0.08	**-0.62**	**0.01***	**-0.64**	**0.01***
DLCOHg %predicted	-0.42	0.10	-0.42	0.11	-0.47	0.07
6MWD	0.01	0.97	**-0.54**	**0.03***	-0.27	0.31
Pulmonary VAS,0-10	0.18	0.50	-0.26	0.34	0.06	0.82
Dyspnea Borg, pre	0.17	0.53	0.09	0.73	0.17	0.53
Dyspnea Borg, post	-0.26	0.36	0.07	0.81	-0.19	0.50
Fatigue Borg, pre	-0.05	0.86	-0.11	0.68	-0.05	0.85
Fatigue Borg, post	-0.09	0.75	0.01	0.98	-0.06	0.85
UCSD dyspnea	0.05	0.86	0.33	0.22	0.21	0.44
O2 use Liters	0.39	0.13	0.13	0.63	0.30	0.26
O2 use yes/no	0.42	0.10	0.06	0.82	0.28	0.29
MD global disease activity VAS, 0-10	0.22	0.42	0.15	0.58	0.30	0.27
Extramuscular global activity, VAS 0-10	0.12	0.65	0.22	0.41	0.27	0.32
MMT8, 0-150	0.38	0.15	0.42	0.11	0.43	0.10
Patient global disease activity VAS, 0-10	0.56	**0.02***	0.34	0.19	0.59	**0.02***
HAQ, 0-3	-0.03	0.91	0.00	0.99	-0.02	0.94
SF-36 domains,						
Physical functioning	-0.34	0.20	-0.54	**0.02***	-0.50	**0.046***
Physical health	0.24	0.38	-0.08	0.76	0.24	0.37
Emotional role functioning	-0.41	0.12	-0.41	0.12	-0.52	**0.04***
Vitality	-0.15	0.57	0.00	0.99	-0.10	0.71
Emotional Wellbeing	-0.18	0.50	-0.18	0.51	-0.22	0.41
Social role functioning	-0.19	0.48	-0.26	0.34	-0.30	0.25
Bodily Pain	-0.54	**0.03***	-0.20	0.46	-0.51	**0.04***
General health perceptions	-0.64	**0.01***	-0.38	0.18	-0.54	**0.045***

Table 2. Associations Between Quantitative CT scores and Clinical/Physiological Parameters Over Time

	QGG		QLF		QILD	
	Mean change (per SD)	P value	Mean change (per SD)	P value	Mean change (per SD)	P value
FVC %predicted	**-4.706**	**0.0004**	**-4.808**	**0.01**	**-9.238**	**0.0005**
FVC ml	**-3.990**	**0.003**	**-3.958**	**0.02**	**-7.783**	**0.002**
DLCOHg, %predicted	**-2.443**	**0.05**	**-4.899**	**0.004**	**-7.201**	**0.005**
DLCOHg, ml	**-3.014**	**0.02**	**-5.439**	**0.001**	**-8.280**	**0.001**
6MWD	0.803	0.41	-0.737	0.61	0.305	0.88
UCSD dyspnea	0.825	0.51	**4.350**	**0.02**	**5.359**	**0.049**
Pulmonary VAS	**1.853**	**0.07**	2.898	0.07	**5.407**	**0.02**

Values reported are mean change per standard deviation estimated using mixed effect models

Figure 1. Quantitative CT scores over time



Blue lines are estimated trajectories of CT scores (QGG, QLF, QILD) over time(months) using mixed effect models

5 timepoints (wk 0, 12, 24, 36, 48). Associations between quantitative CT scores with various physiologic and clinical parameters were analyzed using Spearman's correlations cross-sectionally at baseline, and mixed effect models were used to analyze associations longitudinally over multiple timepoints.

Results: Baseline quantitative CT scores for total extent of ILD (QILD) had strong inverse correlations with baseline FVC and DLCO, while ground glass (QGG) had strong inverse correlations with FVC and fibrosis(QLF) had strong inverse correlations with DLCO (Table 1). Baseline QGG and QILD also correlated with higher scores on patient reported global disease activity and worse health status on several SF-36 domains, whereas QLF correlated with shorter 6MWD and worse physical functioning (Table 1). Using mixed effect models, quantitative CT scores assessed over time demonstrated strong associations between all quantitative CT scores (QGG, QLF, QILD) and both FVC as well as DLCO (Table 2). QLF and QILD scores were also associated with worse scores of respiratory status reported by the patient and physician (UCSD shortness of breath questionnaire and pulmonary VAS on the MDAAT) but were not associated with the 6MWD. The estimated trajectories for quantitative CT scores over time trended towards improved CT scores overall (Figure 1).

Conclusion: Higher quantitative CT scores measuring the extent of ground glass (QGG), fibrosis(QLF), and total ILD (QILD) correlated with pulmonary function tests as well as patient and physician reported outcomes of respiratory status over time in patients with myositis related ILD.

σ Spearman's Rho for correlation coefficient *p<0.05 Abbreviations: QILD, quantitative ILD score on HRCT; QGG, quantitative ground glass score on HRCT; QLF, quantitative fibrosis score on HRCT; FVC, forced vital capacity, DLCO Hg, diffusion capacity adjusted by hemoglobin, UCSD Dyspnea score, University of California San Diego Shortness of Breath Questionnaire with higher scores for worse dyspnea; Pulmonary VAS, pulmonary visual analog scale from the Myositis disease activity assessment tool (MDAAT); Borg scale, Borg scale for dyspnea and fatigue before and after test with higher score indicating more severe symptoms.

Disclosure: S. Bae: None; **F. Abtin**: None; **G. Kim**: MedQIA, 2; **D. Markovic**: None; **S. Moghadam-Kia**: None; **C. V. Oddis**: Boehringer-Ingelheim, 5, Cabaletta, 5, EMD Serono, 5, Novartis, 5, Pfizer, 1; **L. Pourzand**: None; **D. Saygin**: None; **D. Sullivan**: None; **K. Yamaguchi**: None; **D. Tashkin**: None; **C. Charles-Schoeman**: AbbVie, 2, 5, Alexion, 5, BMS, 2, 5, Boehringer Ingleheim, 2, 5, CSL Behring, 5, Galapagos, 2, Pfizer, 2, 5, Priovant, 2, 5, Recludix, 2; **J. Goldin**: MedQIA, 12, Founder; **R. Aggarwal**: Actigraph, 2, Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella Bioscience, 2, Corbus, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Mallinckrodt, 5, Merck, 2, Octapharma, 2, Pfizer, 2, 5, Q32, 5, Roivant, 2, Sanofi, 2, Teva, 2.

Abstract Number: 0287

6-Minute Walk Distance Associates with Physiologic Measures and Physician/Patient Reported Outcomes in Myositis Related Interstitial Lung Disease

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The 6 minute walk distance (6MWD) provides a global evaluation of sub-maximal exercise capacity that is easily performed and highly reproducible, and is used as an outcome measure for ILD. We evaluated the association of 6MWD with physiological, clinical and radiographic measures of interstitial lung disease (ILD) as well as the responsiveness to change in patients with myositis-ILD.

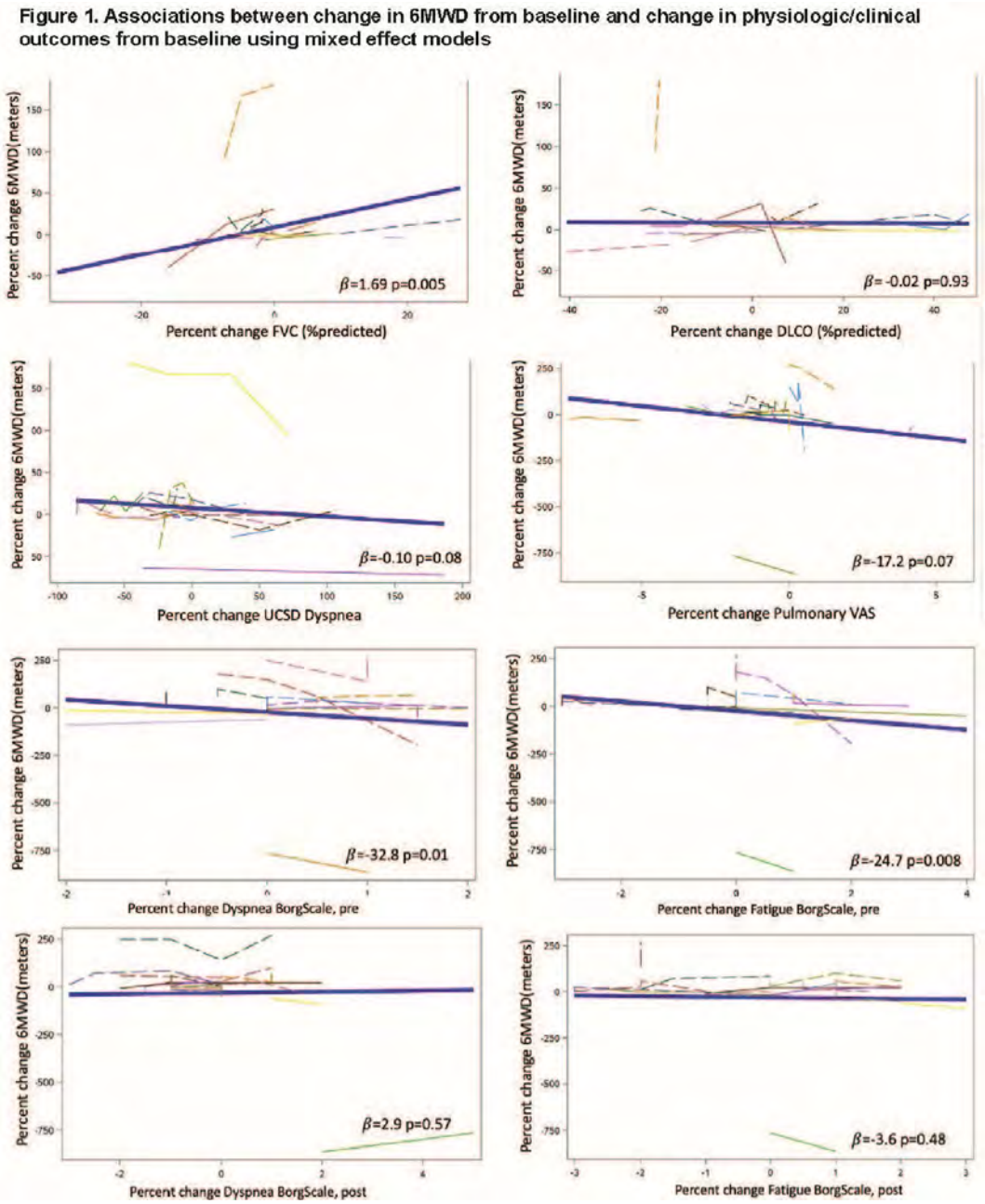
Methods: We analyzed 20 patients enrolled in the Abatacept in Myositis Associated Interstitial lung disease (Attack My-ILD) study. Myositis patients with antisynthetase antibodies and active ILD were enrolled across 5 centers for 24 weeks followed by an open label period for 24 weeks. 6MWD, pulmonary function tests (forced vital capacity; FVC, diffusing capacity adjusted for hemoglobin; DLCOHg), physician/patient reported outcomes (UCSD shortness of breath questionnaire, Borg scale, pulmonary visual analog scale as part of the myositis disease activity assessment tool, supplemental oxygen use) were obtained over 5 timepoints (wk 0, 12, 24, 36, 48) and high resolution CT images were done at 3 timepoints (wk 0, 24, 48) with quantitative scores for extent of ground glass (QGG), fibrosis (QLF), total ILD (QILD) performed using a computer aided diagnostic system previously used in scleroderma ILD. Mixed effect models were used to estimate the associations between 6MWD and various physiologic, clinical and radiographic parameters longitudinally over multiple time points.

Results: Shorter 6MWD was correlated with greater extent of fibrosis on HRCT (QLF) at baseline (r=-0.54, p=0.03) while other variables including physician and patient global myositis disease activity scores, MMT, muscle enzymes, HAQ and SF-36 were not correlated with 6MWD at baseline. Longitudinal 6MWD over multiple timepoints estimated by mixed effect models was significantly correlated with worse longitudinal dyspnea score by the UCSD shortness of breath questionnaire, and worse dyspnea and fatigue on the Borg scale (Table 1). Within each subject, longitudinal 6MWD was positively correlated with longitudinal FVC (Table 1, model 2), although when considering both within subject and between subject effects the correlation was no longer significant (Table 1, model 1). Change in 6MWD from baseline to each time point had significant positive correlations with FVC change from baseline as well as with pre-test Borg scale change from baseline, and similar trends were seen for changes in pulmonary VAS and changes in dyspnea score (Figure 1). We used mixed effect models

Table 1. Associations of longitudinal 6MWD over multiple time points with physiological/radiological/clinical outcome measures using mixed effect models; reported complete model as well as model for only within subject correlations

	Complete model (Model 1)		Within subject correlations (Model 2)	
	Mean change (per SD)	P value	Correlation coefficient r	P value
Age, year	-1.984	0.9422	-	-
QILD, %	4.582	0.8573	-0.03	0.9124
QGG, %	36.333	0.2825	0.02	0.9223
QLF,%	-15.116	0.6288	-0.05	0.8455
FVC(%predicted)	51.534	0.0664	**0.40**	**0.0024**
FVC(ml)	33.391	0.2552	**0.33**	**0.0143**
DLCOHg (% predicted)	-13.265	0.5833	0.07	0.6314
DLCOHg (ml)	-8.343	0.7325	0.04	0.7566
UCSD Dyspnea score(0-120)	**-50.944**	**0.0064**	**-0.27**	**0.0181**
Pulmonary_VAS (0-10)	-16.037	0.3740	-0.08	0.5228
Dyspnea BorgScale, pre (0-10)	**-49.487**	**0.0053**	**-0.30**	**0.0114**
Dyspnea BorgScale, post(0-10)	**-44.969**	**0.0069**	**-0.24**	**0.0440**
Fatigue BorgScale, pre(0-10)	**-67.725**	**0.0002**	**-0.46**	**0.0001**
Fatigue BorgScale, post(0-10)	**-45.164**	**0.0198**	**-0.29**	**0.0144**
O2 use, Liters	-21.602	0.4433	-	-

Model estimate parameters for model 1 are mean change per standard deviation of the specified units and correlation coefficients for model 2. Model 2 was calculated by conditioning between person effects as a fixed effect. Abbreviations: QILD, quantitative ILD score on HRCT; QGG, quantitative ground glass score on HRCT; QLF, quantitative fibrosis score on HRCT; FVC, forced vital capacity, DLCO Hg, diffusing capacity adjusted by hemoglobin; UCSD Dyspnea score, University of California San Diego Shortness of Breath Questionnaire with higher scores for worse dyspnea; Pulmonary VAS, pulmonary visual analog scale from the Myositis disease activity assessment tool (MDAAT); Borg scale, Borg scale for dyspnea and fatigue before and after test with higher score indicating more severe symptoms.



Blue line represents the estimated correlation between percent changes using mixed effect models. Each colored line represents percent change from baseline of each parameter in each subject at multiple time points.

to estimate the trajectories (slopes) of the 6MWD over time for each subject and found estimated slopes correlated with slopes for FVC, dyspnea score and pretest Borg scales for dyspnea and fatigue (Table 2).

Conclusion: Longitudinal measurements of 6MWD reflected parallel changes in FVC as well as patient and physician reported outcomes in patients with myositis ILD.

Table 2. Within person associations between subject specific 6MWD trajectories over time with trajectories of physiologic/clinical outcome measures

	6MWD slope over time	
	Correlation coefficient r	P value
FVC ml	**0.5128**	**0.0208**
FVC%	**0.4346**	**0.0555**
DLCOHg	0.1699	0.4738
DLCOHg %pred	0.1308	0.5825
UCSD Dyspnea	**-0.5790**	**0.0075**
Pulmonary VAS	-0.2075	0.3800
Dyspnea BorgScale, pre	**-0.4782**	**0.0330**
Fatigue BorgScale, pre	**-0.5293**	**0.0164**

Subject specific trajectories over time estimated using the mixed model and correlations between slopes computed using Spearman's correlation

Disclosure: S. Bae: None; **F. Abtin**: None; **G. Kim**: MedQIA, 2; **D. Markovic**: None; **S. Moghadam-Kia**: None; **C. V. Oddis**: Boehringer-Ingelheim, 5, Cabaletta, 5, EMD Serono, 5, Novartis, 5, Pfizer, 1; **L. Pourzand**: None; **D. Saygin**: None; **D. Sullivan**: None; **K. Yamaguchi**: None; **D. Tashkin**: None; **C. Charles-Schoeman**: AbbVie, 2, 5, Alexion, 5, BMS, 2, 5, Boehringer Ingleheim, 2, 5, CSL Behring, 5, Galapagos, 2, Pfizer, 2, 5, Priovant, 2, 5, Recludix, 2; **J. Goldin**: MedQIA, 12, Founder; **R. Aggarwal**: Actigraph, 2, Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella Bioscience, 2, Corbus, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Mallinckrodt, 5, Merck, 2, Octapharma, 2, Pfizer, 2, 5, Q32, 5, Roivant, 2, Sanofi, 2, Teva, 2.

Abstract Number: 0288

Proinflammatory Bioactive Lipid Mediators (BLM) Are Associated with Worse Anti-Oxidant Function of High Density Lipoproteins (HDL) in Patients with Idiopathic Inflammatory Myopathies (IIM)

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Lipid oxidation products produced by artery wall cells under oxidative stress not only regulate immune responses, but their accumulation in HDL are shown to hinder the protective properties of HDL. Our prior work demonstrated that IIM patients had impaired HDL antioxidant function and decreased activity of HDL-associated antioxidant enzyme paraoxonase-1 (PON1), and both correlated with higher disease activity. We hypothesize that higher circulating levels of certain lipid oxidation products that function as proinflammatory bioactive lipid mediators (BLM) will inhibit HDL function and perpetuate vascular damage to enhance IIM disease burden.

Methods: A panel of proinflammatory BLM were assessed from plasma samples of our myositis cohort using liquid chromatography, tandem mass spectroscopy. PON1 activity by paraoxonase, arylesterase, lactonase assays and HDL antioxidant function (HDL inflammatory index, HII) were measured as in prior studies. HDL associated Apolipoprotein A-I(HDL-ApoAI) was measured by sandwich ELISA to assess the major apolipoprotein component of HDL, which normally prevents vessel inflammation. Intercellular cell adhesion molecule-1 (ICAM) and vascular cell adhesion molecule-1 (VCAM) were assessed by ELISA as markers of endothelial dysfunction.

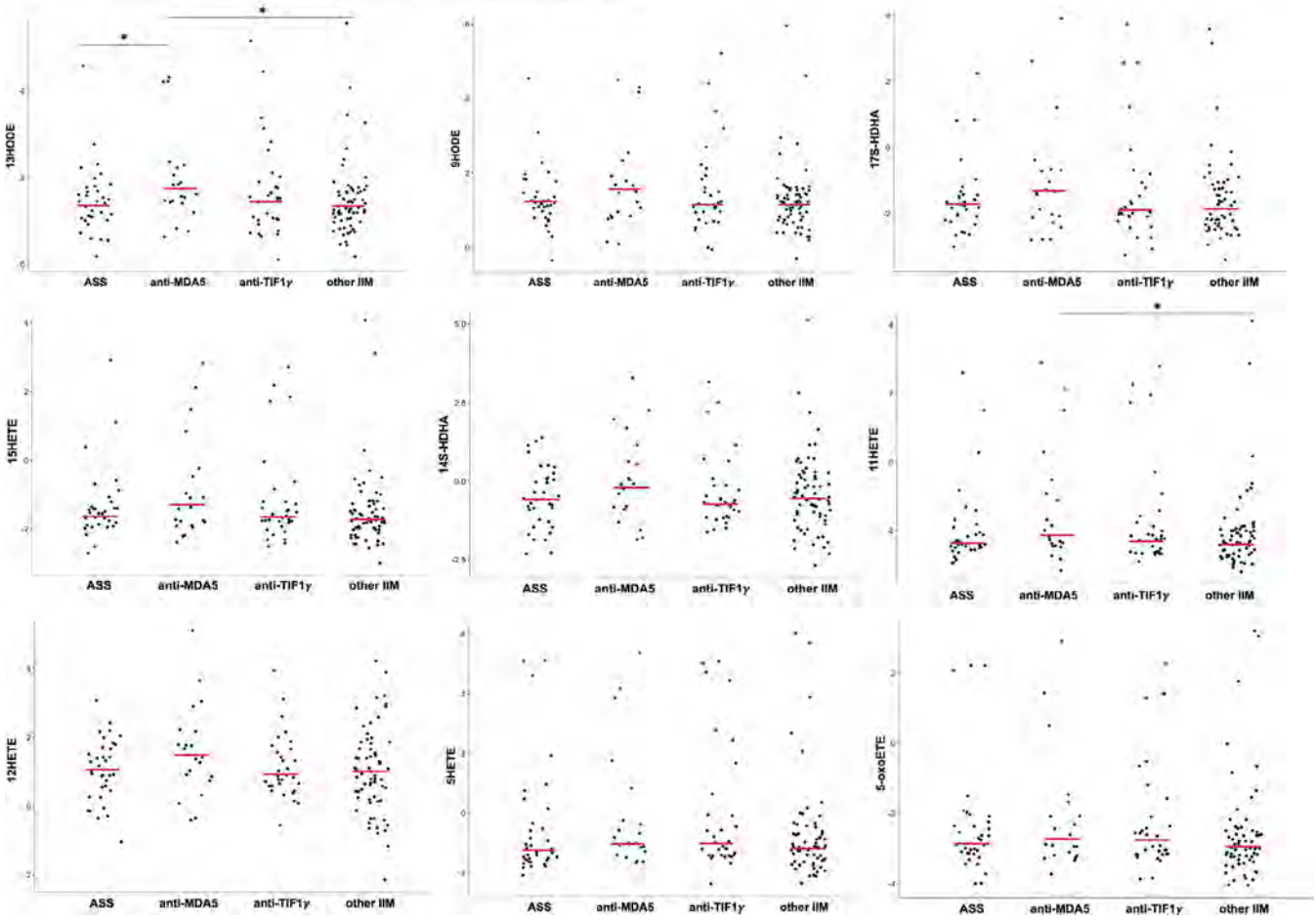
Results: A total of 161 IIM samples were analyzed (Table 1). When grouped by myositis autoantibodies, the anti-MDA5 group had the highest level of all 9 BLM tested with 13HODE and 11HETE showing statistically significant differences (Figure 1). HDL-ApoAI was lowest in anti-MDA5 and PON1 activity was numerically lower in patients with anti-MDA5 or anti-synthetase antibodies (ASS) compared to patients with other myositis antibodies (Table 1). Correlations between BLM and biomarkers of HDL function (HDL-ApoAI, PON1, HII; Table 2) demonstrated that 5HETE, 11HETE, 15HETE correlated with lower HDL-ApoAI and PON1 activity and worse HDL antioxidant function (higher HII). 13HODE, 14S-HDHA, 12HETE also correlated with lower HDL-ApoAI, and 13HODE, 9HODE, 17S-HDHA, and 5-oxoETE correlated with lower PON1 and worse HII. 12HETE also correlated with higher levels of ICAM-1 (r=0.28, p=0.02). Associations between BLMs and measures of myositis disease burden (MD global VAS, CPK, aldolase, hsCRP, ESR) showed 12HETE to have a modest positive correlation with MD global activity score (r=0.16, p=0.047) but otherwise no significant associations were noted. Patients with a history of cancer had numerically higher levels of all BLMs compared to those without cancer, most notably of 17S-HDHA, 15HETE and 5-oxoETE (data not shown). Other clinical characteristics including ILD, arthritis, Raynauds, calcinosis, amyopathic disease and mechanics hands were not associated with the assessed BLMs in our study.

Conclusion: Higher levels of circulating proinflammatory BLM are associated with worse HDL antioxidant function and lower levels of PON1 activity and HDL-ApoA1 in IIM patients. Patients with anti-MDA5 antibodies had the highest level of proinflammatory BLM. Further work is needed to study the relationship between BLM and abnormal HDL function and the mechanism of how they may contribute to IIM disease burden.

	Total IIM (N=161)	ASS (N=37)	MDA5 (N=21)	TIF1gamma (N=33)	Other IIM (N=70)
Age	47 ±15	51 ±15	45± 15	47 ±16	46 ±14
Sex, Female	125(77)	25(67)	12(57)	30(24)	58(83)
Race, White	109(68)	24(65)	12(57)	26(84)	47(67)
Black	18(11)	5(14)	2(10)	1(3)	10(14)
Asian	32(20)	8(22)	7(33)	10(14)	13(19)
Ethnicity, Hispanic	30(19)	7(19)	4(20)	4(12)	15(21)
CV risk factors					
MI	2(1)	1(3)	0	0	1(1)
Stroke	5(3)	1(3)	0	2(6)	2(3)
HTN	35(22)	8(22)	3(14)	8(24)	16(23)
HLD	25(16)	8(22)	2(10)	7(21)	8(11)
Diabetes	18(11)	5(14)	4(19)	1(3)	8(11)
Family history of premature MI	11(8)	2(6)	2(13)	1(4)	6(10)
Ever smoker	30(22)	7(21)	3(19)	4(17)	16(26)
BMI	27 ±6	27± 6	24 ±4	28 ±6	27±6
Total cholesterol, mg/dl	215± 57	14± 51	212± 62	212± 49	218 ±65
LDL-C, mg/dl	127± 49	121 ±45	137± 52	124 ±40	131 ±55
HDL-C, mg/dl	66± 36	66 ±38	52± 21	70 ±21	69 ±43
Triglyceride, mg/dl	183± 207	242± 368	230 ±133*	130 ±67	164 ±137
IIM type, DM #	133(83)	29(78)	21(100)	32(97)	51(73)
PM	28(17)	8(22)	0	1(3)	19(27)
Disease Duration, years	2[1-5]	2[1-8]	1[0-2]**	2[1-7]	2[1-5]
MD global activity VAS, 0-100	45 ±22	47 ±19	49 ±23	43 ±23	42 ±24
MD global damage VAS, 0-100	32 ±22	46 ±18*	35 ±17	15 ±12**	31 ±23
HsCRP, mg/L	1.5[0.5-5.3]	4.9[1-14]**	0.9[0.4-2.6]	1.2[0.5-4.5]	1.4[0.4-4.9]
ESR, mm/hr	23[9-45]	26[10-52]	31[16-53]	18[6-34]	21[9-41]
CPK, U/L	119[62-314]	253[64-861]	57[33-57]**	86[63-122]*	182[76-557]
Aldolase, U/L	6.5[4.9-9.7]	8.7[6.4-26.4]**	5.9[5-7.9]	5.6[3.9-7.6]	6.4[4.9-12.4]
HAQ	0.6[0.03-1.5]	0.6[0.1-1.4]	0.5[0.03-0.8]	0.3[0-0.88]	0.88[0.13-1.63]
ILD #	65(41)	33(89)	17(85)	0	15(22)
Cancer	29(18)	6(19)	2(10)	8(24)	12(17)
Pulmonary hypertension #	10(6)	8(22)	2(10)	0	0
HDL-ApoAI, µg/ml	106[54-995]	119[64-921]	60[20-101]*	101[50-1041]	126[65-1097]
PON1 activity assays, U/mL					
Paraoxonase	650± 450	526 ±351	589 ±443	759 ±568	682± 425
Arylesterase	204± 85	187 ±92	198 ±80	208 ±78	213± 87
Lactonase	15.4± 6.6	13.7 ±7.1	14.0± 6.6	16.1± 7.9	15.8± 6.3
HII	0.5[0.2-0.8]	0.54[0.22-1.02]	0.55[0.19-1.13]	0.42[0.22-0.67]	0.54[0.19-0.88]
VCAM, ng/mL†	2931[2207-3862]	3381[2854-4375]	3042[2638-4700]	2319[1880-3407]**	NA
ICAM, ng/mL	472[368-668]	531[406-764]	573[453-759]	384[329-469]**	NA

ASS, antisynthetase antibody group; MDA5, anti-MDA5 antibody group, TIF1r, anti-TIF1r antibody group; Other IIM, myositis patients with other myositis autoantibodies or no antibodies Values are in Mean± SD, Median[IQR] or n(%) *p<0.05 compared to other IIM group and **p<0.05 compared to all other MSA groups, using student's t-test for values in Mean ±SD, Wilcoxon for values in Median[IQR] #p<0.05 by chi-square for values reported in n(%) †VCAM and ICAM were only done in 69 patients from ASS, MDA5, TIF1 gamma group, none from other IIM group

Figure 1. Proinflammatory BLM levels In Each Myositis Autoantibody Group



BLM units in nl/ml. Values are transformed on the natural logarithmic scale. Lines mark the median *p<0.05 by Wilcoxon test of each pair

Table 2. Correlations with HDL function in IIM (n=161)

	HDL ApoA1			PON1 activity									HII		
				Paraoxonase			Arylesterase			Lactonase					
	r	n	p	r	n	p	r	n	p	r	n	p	r	n	p
13HODE	-0.20	143	0.01*	0.10	154	0.20	-0.17	155	0.03	-0.11	154	0.18	0.14	146	0.09
9HODE	-0.15	143	0.07	0.11	154	0.19	-0.24	155	<0.01	-0.12	154	0.15	0.16	146	0.047*
17S-HDHA(17S-HDoHE)	-0.14	130	0.10	0.15	139	0.08	-0.28	140	<0.01	-0.21	139	0.01*	0.24	132	<0.01*
15HETE	-0.20	142	0.02*	0.11	152	0.16	-0.28	153	<0.01	-0.20	152	0.01*	0.27	145	<0.01*
14S-HDHA(14S-HDoHE)	-0.21	142	0.01*	0.14	152	0.08	-0.07	153	0.37	-0.05	152	0.51	0.12	145	0.16
11HETE	-0.18	143	0.03*	0.15	153	0.06	-0.28	154	<0.01	-0.19	153	0.02*	0.30	146	<0.01*
12HETE	-0.27	143	<0.01*	0.11	154	0.16	-0.03	155	0.73	-0.09	154	0.28	0.12	146	0.14
5HETE	-0.17	143	0.04*	0.16	153	0.05	-0.27	154	<0.01	-0.18	153	0.02*	0.25	146	<0.01*
5-oxoETE	-0.11	142	0.21	0.13	152	0.12	-0.31	153	<0.01	-0.25	152	<0.01*	0.30	145	<0.01*

All BLM, HDL-ApoAI, HII were transformed to the natural logarithmic scale to fit normal distribution. Pearson's correlation was used to test correlations.

Disclosure: S. Bae: None; **A. Shahbazian**: None; **J. Wang**: None; **D. Sulaiman**: None; **D. Meriwether**: None; **s. Reddy**: None; **C. Charles-Schoeman**: AbbVie, 2, 5, Alexion, 5, BMS, 2, 5, Boehringer Ingleheim, 2, 5, CSL Behring, 5, Galapagos, 2, Pfizer, 2, 5, Priovant, 2, 5, Recludix, 2.

Abstract Number: 0289

Markers of Endothelial Damage Are Elevated in Patients with Dermatomyositis Associated Interstitial Lung Disease and Associated with Low Paraoxonase-1 Activity

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Damage to the vascular endothelium is implicated in the pathogenesis of idiopathic inflammatory myopathies (IIM) and its associated interstitial lung disease (ILD), with microvascular involvement most described in the dermatomyositis (DM) subtype. Paraoxonase-1 (PON1) is a high-density lipoprotein (HDL)-associated enzyme that protects the vascular endothelium from damage due to oxidized phospholipids, that is associated with IIM disease activity and presence of severe ILD. We hypothesize that poor PON1 activity is associated with vascular damage evidenced by increased circulating levels of intercellular cell adhesion molecule-1 (ICAM), vascular cell adhesion molecule-1 (VCAM) leading to higher disease burden in DM and DM-ILD.

Methods: We performed a cross-sectional study. Plasma levels of VCAM and ICAM and PON1 activity were analyzed in 83 DM patients with anti-Jo1 (n=24), MDA5 (n=29), and TIF1gamma (n=30) and 28 age and sex matched healthy controls. PON1 activity was measured using the paraoxonase, arylesterase and lactonase assays. VCAM and ICAM levels were measured by ELISA. Multivariate models were adjusted for variables that were significantly associated with the outcome variable in univariate analysis.

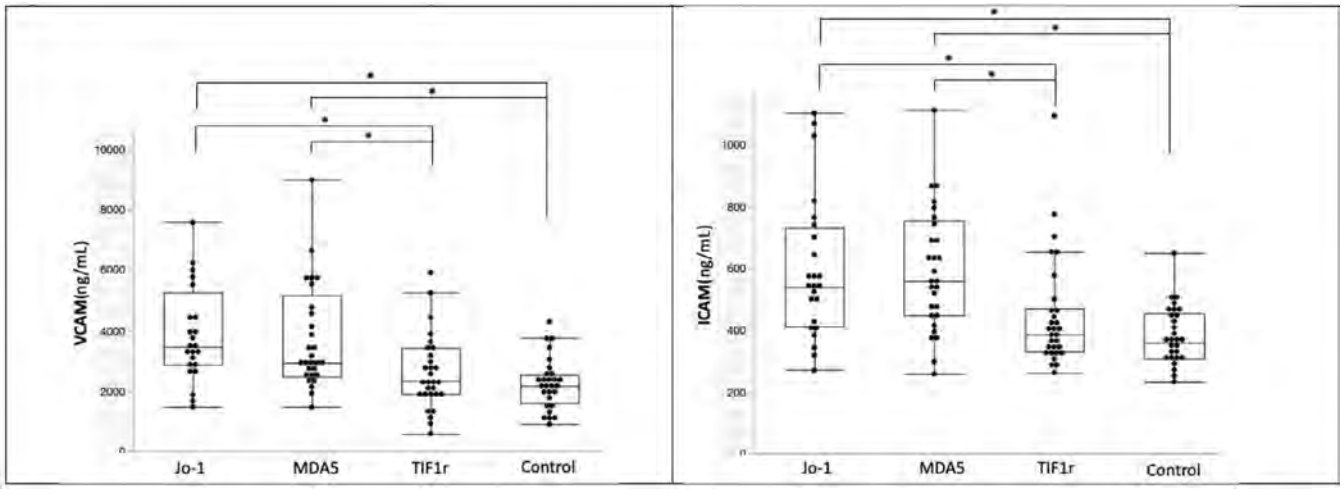

Figure 1. VCAM and ICAM levels in DM patients and Controls (n=111) *p<0.01 by Wilcoxon test Anti-Jo1 (N=24), anti-MDA5 (N=29), anti-TIF1 (N=30) and Age/sex matched healthy controls (N=28)

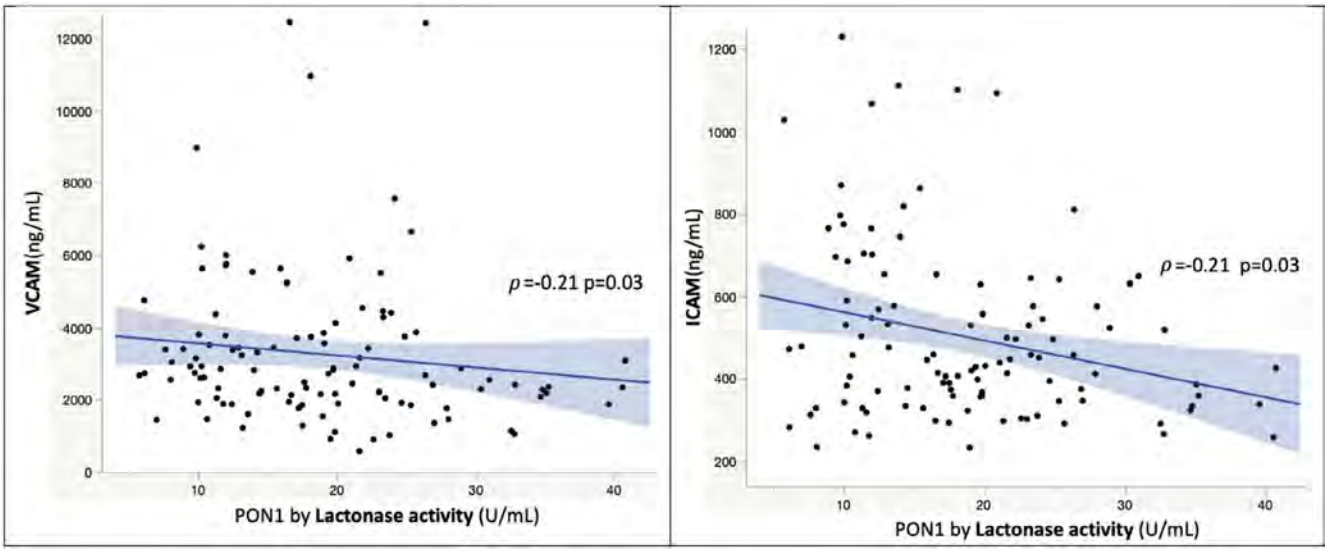

Figure 2. Correlation between PON1 activity by lactonase and VCAM/ICAM levels in DM patients and controls (n=111) Spearman correlation coefficient (ρ) between PON1 by lactonase with VCAM and ICAM levels.

Results: Plasma levels of both VCAM and ICAM were significantly higher in DM patients compared to controls (Figure 1). VCAM and ICAM were particularly higher in the anti-Jo1 and MDA5 positive DM patients compared to the anti-TIF1gamma patients and healthy controls (Figure 1). VCAM and ICAM were both correlated with worse PON1 activity measured by lactonase assay (Figure 2). ICAM remained significantly associated with worse lactonase activity after multivariate adjustment for ESR, triglyceride and Asian race, which were associated with ICAM in univariate analysis. VCAM and ICAM were both significantly higher in DM patients with ILD compared to DM patients without ILD (Table 1). Higher ICAM levels also associated with worse forced vital capacity(FVC), diffusion capacity(DLCO), higher global damage scores, cough, dyspnea, while VCAM was associated with dyspnea and fever (Table 1). Patients on Methotrexate had lower ICAM and VCAM levels compared to those not on methotrexate. In a multivariate logistic model, the presence of ILD remained significantly associated with higher ICAM levels after adjusting for Methotrexate, ESR, disease duration and Asian race.

Conclusion: Plasma VCAM and ICAM were higher in DM patients compared to matched healthy controls, particularly in anti-Jo1/MDA5 ab + patients (compared to TIF1gamma ab + patients) and in DM patients with ILD. ICAM was significantly associated with worse PON1 enzyme activity, suggesting that poor anti-oxidant function of HDL associates with evidence of endothelial activation and damage in DM and DM-ILD. Large prospective studies may be warranted to further evaluate the role of PON1 in the development and propagation of IIM and IIM-ILD.

Table 1. Association between VCAM/ICAM and Clinical/Laboratory characteristics of DM patients (n=83)

Continuous variables		VCAM		ICAM	
		Correlation coefficient ρ	P value	Correlation coefficient ρ	P value
Disease duration, months		0.001	0.99	**-0.24**	**0.03**
CPK, U/ml		-0.01	0.92	-0.01	0.91
Aldolase, U/ml		0.15	0.18	0.23	0.049
MD activity VAS 0-100		0.07	0.51	0.15	0.16
MD activity likert, 0-4		0.05	0.63	0.18	0.10
MD damage VAS, 0-100		0.18	0.10	**0.35**	**0.001**
MD damage likert, 0-4		0.05	0.63	**0.31**	**0.004**
MMT8, 0-150		-0.10	0.48	-0.07	0.62
FVC, % predicted		-0.21	0.12	**-0.42**	**0.0008**
DLCOhg, % predicted		-0.11	0.41	**-0.40**	**0.004**
Prednisone dose, mg/day		0.25	0.03	0.17	0.16
Categorical variables	**N†**	**VCAM**		**ICAM**	
		Variable Yes‡	**Variable No**	**Variable Yes**	**Variable No**
ILD	42	**3350[2730-4939]***	**2557[1923-3687]**	**577[492-764]***	**395[336-509]**
Cancer	15	3273[2324-4375]	2095[2258-4340]	503[342-703]	498[385-638]
Clinical features of DM, ever					
Calcinosis	8	3279[2331-4510]	2879[2303-4121]	490[422-747]	499[370-652]
Hoarseness	17	2935[2455-3996]	2904[2161-4425]	530[335-661]	484[377-661]
Dysphagia	28	3464[2317-5040]	2868[2243-3853]	553[421-702]	447[373-641]
Proximal muscle weakness	69	3089[2308-4437]	2574[2225-3315]	503[386-689]	455[332-634]
Neuropathy	17	3233[2577-4915]	2861[2225-4385]	548[416-662]	466[373-661]
Periungual erythema	20	3039[2207-3971]	2931[2302-4413]	426[330-626]	519[390-700]
Skin ulcerations	13	3438[2203-4993]	2873[2288-3998]	459[382-683]	521[374-661]
Arthritis	54	3119[2419-4481]	2829[2092-3862]	521[395-696]	420[331-646]
Raynaud's	16	3542[2969-4510]^	2829[2172-4121]	449[361-699]	503[375-652]
Mechanics hands	16	3253[1976-4298]	2878[2302-4375]	540[434-626]	459[370-684]
Fever	12	**4012[3192-5657]***	**2829[2171-3853]**	608[487-789]^	459[370-652]
Oral ulcers	8	3093[1578-4595]	2931[2314-4375]	567[414-845]	496[370-652]
Alopecia	18	3155[1875-5720]	2931[2335-3863]	558[373-696]	496[376-652]
Cough	25	3318[2324-4993]	2873[2215-3934]	**628[475-780]***	**427[364-580]**
Dyspnea	55	**3319[2602-4753]***	**2417[1883-2417]**	**531[406-743]***	**386[330-543]**
Respiratory Failure	13	3318[2612-4080]	2861-2225-4446]	643[454-840]^	465[372-633]
Fatigue	33	2748[1982-5231]	3010[2448-3998]	472[382-608]	513[372-697]
Weight loss	18	3687[2614-5550]^	2854[2207-3798]	558[476-710]^	447[368-653]
Myalgias	23	3745[2052-5500]	2861[2305-3729]	529[405-700]	497[359-650]
Dry eyes	9	4121[2455-5922]	2903[2161-3857]	518[414-599]	497[369-687]
Dry mouth	12	3751[2332-5686]	2929[2243-3853]	509[415-565]	496[370-695]
Pulmonary hypertension	5	2929[2047-4269]	2933[2288-4385]	577[423-730]	498[374-652]
CAD/atherosclerosis	6	4997[2676-5983]	2929[2237-3862]	475[382-831]	499[372-653]
IVIG/SCIG	37	3395[2455-4993]^	2824[2051-3822]	472[386-673]	526[364-661]
Mycophenolate	36	2933[2515-4059]	2879[1929-4413]	524[397-684]	472[367-653]
Rituximab	18	3472[2402-5682]	2929[2207-3833]	524[406-668]	496[371-668]
Cyclophosphamide	6	3611[2482-5121]	2929[2273-4248]	659[449-788]	496[371-647]
Azathioprine	4	3314[2967-5340]	2892[2189-4312]	527[365-933]	497[379-653]
Methotrexate	14	**2188[1669-3531]***	**3089[2417-4606]**	**401[319-519]***	**529[386-697]**
Hydroxychloroquine	16	2989[2263-3734]	2935[2302-4460]	466[362-701]	500[375-643]
Prednisone	62	3012[2340-3934]	2679[2030-5618]	511[391-661]	413[336-713]

*p<0.05, ^ is p<0.1 Spearman's correlation for continuous and Wilcoxon rank-sum for categorical variables † N refers to number of patients who has ever had the listed variable as a clinical feature of their myositis ‡ Variable Yes refers to median[IQR] of VCAM/ICAM levels of those with listed variable.

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Abstract Number: 0290

Patient-reported Quality of Life and Working Status Outcomes in Ambulatory Patients with Idiopathic Inflammatory Myopathy

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate the health-related quality of life (HR-QoL), work productivity and activity impairment, and associated factors among patients with idiopathic inflammatory myopathy (IIM).

Methods: This was an observational, cross-sectional study. The 189 ambulatory patients with IIM were recruited from May 2019 to May 2022. HR-QoL was measured by the EuroQol 5-Dimension (EQ-5D). The work productivity and activity impairment (WPAI) questionnaire was used to evaluate work productivity and activity impairment. The IIM-related parameters were assessed by the Manual Muscle Testing-8 (MMT-8), Myositis Disease Activity Assessment Visual Analog Scale (MYOACT), Myositis Damage Index (MDI), Disease Activity Score (DAS), and Physician/Patient Global Assessment (PGA/PtGA). Quantile regression and ordinal logistic regression were performed to identify the factors, considering EQ-5D or WPAI scores as dependent variable, respectively.

Results: Of the 189 IIM patients enrolled, 60% had dermatomyositis, 13% had polymyositis, and 27% had clinical amyopathic dermatomyositis. The median EQ-5D score was 1.00 (0.73, 1.00), 28% were employed, and 45%ofoverall work was impaired due to health problems. EQ-5D values were positively associated with MMT-8, and negatively with MYOACT, DAS, MDI-global, and PGA/PtGA. For the WPAI, activity impairment was associated with lower MMT-8, older onset age, and higher PGA only in 25^{th}–75^{th} percentile. Increased PtGA was associated with increased activity and overall working productivity impairment in most quantiles ($P < 0.05$).

Conclusion: Multiple disease characteristics were associated with reduced HR-QoL or working productivity impairment in patients with IIM, especially for PtGA.

Disclosure: Z. Peng: None; **Y. Wang**: None; **N. Liu**: None; **S. Zhou**: None; **J. zhao**: None; **D. Xu**: None; **M. Li**: None; **c. wu**: None; **Q. Wang**: None.

Abstract Number: 0291

Myopathy Related to Small-to-medium-sized Vessel Vasculitis: Immunopathological Characteristics

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Muscular involvement develops as the initial manifestation of small-sized vessel vasculitis (SV) and medium-sized vessel vasculitis (MV).The musculoskeletal lesion has been found as a crucial biopsy site including the histology of SV and MV unless another suitable organ for a biopsy can be found. However, immunopathological features, including the degree of myofiber damage, in the histology of vasculitic myopathy (VM) have been still unknown, while pathological assessment is an ideal procedure for the definite diagnosis of vasculitis. We elucidated the immunopathological features of skeletal muscle in VM by comparing the immunohistochemical (IHC) findings of skeletal muscle in patients with idiopathic inflammatory myositis (IIM).

Methods: The biopsied skeletal muscle tissues from 15 patients with VM, including antineutrophil cytoplasmic antibody-associated vasculitis and polyarteritis nodosa, and 15 with IIM, including polymyositis and immune-mediated necrotizing myopathy, were used in this study. IHC staining of skeletal muscle was performed as follows: CD56/neural cell adhesion molecule (NCAM) which detects myofiber damage and regeneration, major histocompatibility complex (MHC)-class I,

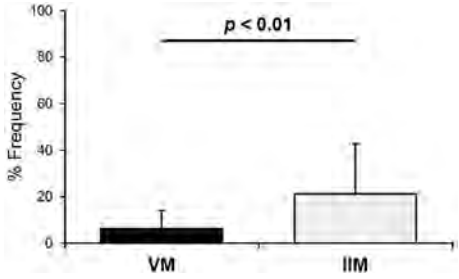

Fig. 1: The frequencies of CD56/NCAM-expressing myofibers in the total myofibers between patients with vasculitic myopathy (VM) and those with idiopathic inflammatory myopathy (IIM).

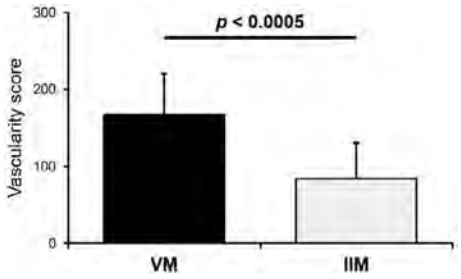

Fig. 2: The vascularity scores in the endomysium areas between patients with vasculitic myopathy (VM) and those with idiopathic inflammatory myopathy (IIM).

C5b-9/membrane attack complex (MAC), and CD31 which is an endothelial cell marker. The vascularity score was defined as the total number of CD31-expressing blood vessels.

The counts and calculations of IHC stained samples and the vascularity scores were performed in the 10 different high-power fields.

Results: The frequency of NCAM-expressing myofibers was significantly lower in patients with VM than in those with IIM ($p < 0.01$) (**Fig. 1**). In addition, the frequency of NCAM-expressing myofibers was positively correlated with serum aldolase levels ($p < 0.01$). The frequency of MHC class I-expressing myofibers was significantly lower in patients with VM than in those with IIM ($p < 0.005$). A lower number of patients with MV had MAC-expressing myofibers on sarcolemma without intracellular staining than those with IIM (33% vs. 80%, $p < 0.05$).Meanwhile, the frequency of patients, who had MAC-expressing capillaries in endomysium areas, was not significantly different between VM and IIM (73% vs. 93%). Significantly higher vascularity scores in the endomysium areas were demonstrated in patients with MV than in those with IIM ($p < 0.0005$) (**Fig. 2**).

Conclusion: Mild myofiber damage, based on the result of less involving NCAM-expressing myofiber, was demonstrated in patients with VM than in those with IIM. Our results suggest that complement component deposits on vessel walls and hypervascularity in the endomysium areas may be immunopathological features of VM.

Disclosure: S. Nomura: None; **Y. Shimojima**: None; **T. Ichikawa**: None; **D. Miyazaki**: None; **D. Kishida**: None; **Y. Sekijima**: None.

Abstract Number: 0292

Comparison of Cardiovascular Risk of Myositis Patients and the General Population

Sabina Oreska[1], Hana Storkanova[1], Jaroslav Kudlicka[2], Vladimir Tuka[2], Ondrej Mikes[2], Zdislava Krupickova[2], Martin Satny[2], Eva Chytilova[2], Jan Kvasnicka[2], Maja Spiritovic[3], Barbora Hermankova[4], Petr Cesak[5], Marian Rybar[6], Karel Pavelka[1], Ladislav Senolt[7], Herman Mann[8], Jiri Vencovsky[1], Michal Vrablik[2] and Michal Tomcik[1], [1]Institute of Rheumatology, Prague, Czech Republic, Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, [2]3rd Department of Internal Medicine, General University Hospital and 1st Faculty of Medicine, Charles University, Prague, Czech Republic, [3]Institute of Rheumatology, Prague, Czech Republic, Department of Physiotherapy, Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic, [4]Department of Physiotherapy, Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic, [5]Department of Human Movement Laboratory, Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic, [6]Department of Biomedical Technology, Faculty of Biomedical Engineering, Czech Technical University in Prague, Kladno, Czech Republic, [7]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Praha, Czech Republic, [8]Institute of Rheumatology, Praha 2, Czech Republic

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
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Background/Purpose: Cardiovascular (CV) risk due to accelerated atherosclerosis and impaired metabolism can be increased in idiopathic inflammatory myopathies (IIM) on behalf of systemic inflammation, limited mobility, and glucocorticoid (GC) therapy. We evaluated CV risk in IIM patients in comparison to healthy controls (HC) and assessed its association with disease-specific features.

Methods: 90 IIM (70 females; mean age 56.6; mean disease duration 5.95 years; dermatomyositis: n=29, polymyositis: n=12, immune-mediated necrotizing myopathy (IMNM): n=20, anti-synthetase syndrome: n=29) and 180 HC (130 females, mean age 54.3) with no history of manifested CV disease (both cohorts). Muscle involvement, disease activity, and tissue damage were evaluated (MMT-8, MITAX, MDI). Comorbidities and current treatment were recorded. All subjects underwent examinations of carotid intima-media thickness (CIMT), pulse wave velocity (PWV), ankle-brachial index (ABI), and body composition (densitometry, bioelectrical impedance analysis), evaluation of the risk of fatal CV events by the Systematic COronary Risk Evaluation (SCORE, for the European population) and its modifications: SCORE multiplied by the coefficient 1.5 (mSCORE), and SCORE2.

Results: Compared to HC, IIM had a significantly higher prevalence of traditional CV risk factors, carotid artery disease (CARD), abnormal ABI, and PWV ($p< 0.05$ for all). After propensity score matching (PSM) using traditional CV risk factors, the prevalence of CARD and pathologic PWV remained significantly higher in IIM ($p< 0.05$ for all), but no significant difference in SCORE was observed. Overall CV risk based on calculated risk (modifications of SCORE) and ultrasound (US) examinations was comparable between IIM ad HC after PSM (CVR-SCORE p=0.457, CVR-SCORE2 p=0.130, CVR-US p=0.126). IMNM patients had the most unfavorable CV risk profile among IIM subtypes. The calculated CV risk scores by SCORE and SCORE2 (in IIM and HC), and mSCORE (in IIM) were reclassified according to CIMT and CARD. SCORE was the most inaccurate in predicting CV risk in IIM, while there was a significantly higher proportion of reclassified patients compared to SCORE2 and mSCORE (p=0.020). Age, disease activity, lipid profile, body composition parameters, and blood pressure were the most significant predictors of CV risk in IIM ($p< 0.05$ for all variables in bivariate analysis). The length of GC therapy was positively associated with an increased count of carotid plaques and overall CV risk (by US examination) ($p< 0.05$ for both).

Conclusion: This cross-sectional cohort study in IIM patients demonstrated a significantly increased risk of subclinical atherosclerosis and CV risk, and also an increased prevalence of traditional CV risk factors compared to HC with comparable age and gender distribution. The most unfavorable findings were seen in IMNM patients. SCORE2 appeared to be the most accurate tool for prediction of fatal CV events in IIM compared to SCORE and mSCORE, although it also underestimates CV risk.

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Abstract Number: 0293

Characteristics and Outcomes of Idiopathic Inflammatory Myositis Associated Interstitial Lung Disease in Rural Appalachia

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SESSION INFORMATION
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Background/Purpose: Interstitial lung disease (ILD) can affect up to 30% of the patients with idiopathic inflammatory myositis (IIM) and contributes significantly towards morbidity and mortality rates. The clinical and radiographic manifestations of IIM-ILD are variable in the affected population. The objective of our study was to recognize the patterns of IIM-ILD and determine the treatment outcomes for these patients specific to the rural Appalachian population of West Virginia.

Methods: A retrospective observational cross-sectional study was performed between January 1, 2012 through August 31, 2022, at a medium sized academic medical facility located in the WV rural Appalachia. 115 patients with IIM were identified through electronic medical record system. Out of these, 29 patients who had coexisting ILD based on radiographic findings and pulmonologist evaluation were included for the final analysis.

Results: Majority of the patients were females (n=22, 76%), never-smokers (n=19, 65%), and had a mean age of 60.17 + 12.92 years. Dyspnea (n=24, 83%) was the most common presenting symptom with mean modified Medical Research Council (mMRC) scale of 2 + 1.2. The mean duration of symptoms at first encounter was 4.57 + 6.66 years. The most common IIM phenotypes were dermatomyositis (n=15, 52%) and polymyositis (n=8, 27.6%). In patients with available serology testing (n=20), anti-Jo1 was present in 55% of the affected population(n=11). Radiographic patterns at presentation (n=27) were indeterminate for usual interstitial pneumonia (UIP) (n=12, 44%), non-specific interstitial pneumonia (NSIP) (n=5, 18%), and UIP (n=3, 11%). Treatment modalities included prednisone (n=20, 69%), azathioprine (n=14, 48%), mycophenolate mofetil (n=13, 45%), and nintedanib (n=2, 7%). Data for mMRC scale, computed tomography (CT), and pulmonary function testing (PFT) before and after treatment was available for 19, 17 and 18 patients respectively. mMRC score improved or remained stable in 89% of patients post treatment (n=17). Similarly, CT findings and PFT improved or remained stable in 59% (n=10) and 67% (n=12) of the patients. Mortality rate during the study period was 21% (n=6).

Conclusion: Dermatomyositis was the most common phenotype and anti-Jo1 was the most observed antibody associated with ILD. Similar findings were reported in larger retrospective cohort studies. The most common radiographic pattern in our cohort was indeterminate for UIP compared to other cohorts with NSIP being the predominant CT finding. While comparing the progression of ILD with other studies based on presenting symptoms, radiographic findings and PFT results, a higher proportion of patients with stable and improved ILD was observed in our study. Despite improvement in the pulmonary disease with treatment, mortality rates were remarkably higher in this cohort compared to other ILD centers. Multiple extrapulmonary factors have been associated with poor prognosis in IIM-ILD, as such, the increased mortality in our cohort may be due to non-pulmonary causes. Further prospective cohort studies are required to evaluate predictors of mortality in IIM-ILD in this region.

Disclosure: F. Rida Ul Jannat: None; **S. Kaur**: None; **B. Balakrishnan**: None; **V. Deepak**: None; **B. Buragamadagu**: None; **R. Salyer**: None; **T. Landis**: None.

Abstract Number: 0294

Tofacitinib Treatment in Rheumatoid Arthritis Is Associated with Increased Lower Limb Muscle Volume: The Rheumatoid Arthritis and Muscle (RAMUS) Study

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SESSION INFORMATION
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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Approximately 1 in 4 people with RA have sarcopenia, defined as generalised loss of skeletal muscle (SKM) strength and mass, resulting in an increased risk of falls, fractures and mortality. Resistance exercise is the most effective treatment for sarcopenia and there is an unmet need for drugs that could augment or replace this, depending on an individual's physical ability. Pooled data from studies investigating tofacitinib for the treatment of RA demonstrated small increases in serum creatinine (SCr) that were not associated with renal impairment and were inversely correlated with fall in CRP. SCr levels are influenced by SKM mass, raising the possibility that tofacitinib has an anti-sarcopenia effect. The Rheumatoid Arthritis and Muscle (RAMUS) study sought to test this hypothesis.

Methods: The RAMUS study is an observational, single-arm study of RA patients commenced on tofacitinib as part of routine care. Enrolment criteria included meeting the 2010 ACR/EULAR classification criteria for RA and >1 sarcopenia risk factor (low appendicular lean mass index, CRP > 5, low grip strength or prolonged sit-to-stand test time). Prior janus kinase

Table 1: Primary, secondary and selected exploratory outcomes from the RAMUS study. Variables with significant change are highlighted in bold. Secondary outcomes underwent multiple test correction using the Benjamini-Hochberg procedure. *Mean (95% confidence interval) and P-value from one-way repeated measures ANOVA. **Median (interquartile range) and P-value from Friedman's test.

	Timepoint			P-value	Adjusted P-value
	Baseline	*1 month*	*6 months*		
Combined thigh and calf muscle volume (L) *	6.86 (6.03 – 7.68)	6.85 (5.98 – 7.71)	7.10 (6.26 – 7.94)	**0.009**	-
Appendicular lean mass index (kg/m²) *	7.41 (6.65 – 8.18)	7.30 (6.62 – 7.98)	7.45 (6.77 – 8.14)	0.61	0.75
Fat mass index (kg/m²) **	13.33 (9.62 – 16.61)	13.07 (9.74 – 17.01)	13.36 (9.68 – 16.86)	0.282	-
Weight (kg) *	81.8 (74.0 – 89.6)	81.6 (74.1 – 89.1)	82.9 (75.5 – 90.3)	0.056	-
Grip strength (kg) *	12.6 (8.2 – 17.0)	15.3 (11.1 – 19.5)	15.8 (11.9 – 19.7)	0.28	0.61
Rapid assessment of physical activity score **	3.5 (2.75 – 5.25)	-	4.5 (3.0 – 6.25)	**0.035**	-
Five times sit-to-stand test (seconds) *	15.5 (14.9 – 27.2)	15.9 (14.2 – 21.9)	15.4 (14.0 – 20.6)	0.53	0.73
Gait speed (m/second) *	0.95 (0.83 – 1.07)	0.97 (0.85 – 1.08)	1.01 (0.88 – 1.14)	0.33	0.61
Disease activity score (28 joints) *	5.14 (4.27 – 6.02)	4.05 (3.15 – 4.95)	4.11 (3.14 – 5.07)	0.003	**0.017**
CRP (mg/L) **	7 (2 – 12)	3 (1 – 6)	3 (2 – 6)	0.219	0.22
ESR (mm/hour) *	28.2 (15.0 – 41.4)	21.8 (13.3 – 30.3)	24.4 (17.3 – 31.4)	0.42	0.66
Serum creatinine (μmol/L)*	62.5 (57.2 – 67.9)	64.1 (58.3 – 70.0)	68.1 (62.1 – 74.2)	0.001	**0.011**
Creatine kinase (IU/L) **	115 (52 – 153)	81 (66 – 131)	105 (86 – 176)	0.28	0.61

(JAK) inhibitor or recent glucocorticoid treatment were not permitted. Assessments were at baseline, 1 and 6 months. The primary outcome was thigh and calf SKM volume determined by quantitative MRI. Whole body composition was measured by DXA. Study procedures are summarised in Figure 1.

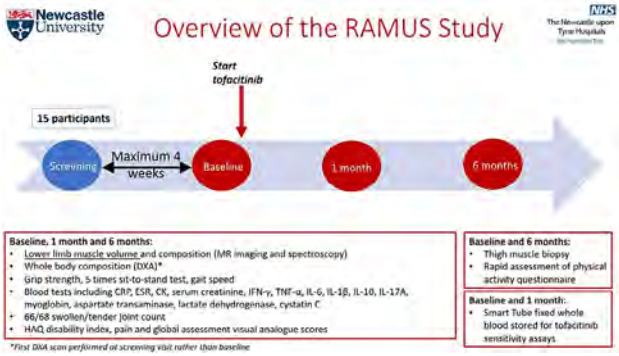

Figure 1: Time points and procedures in the RAMUS study.

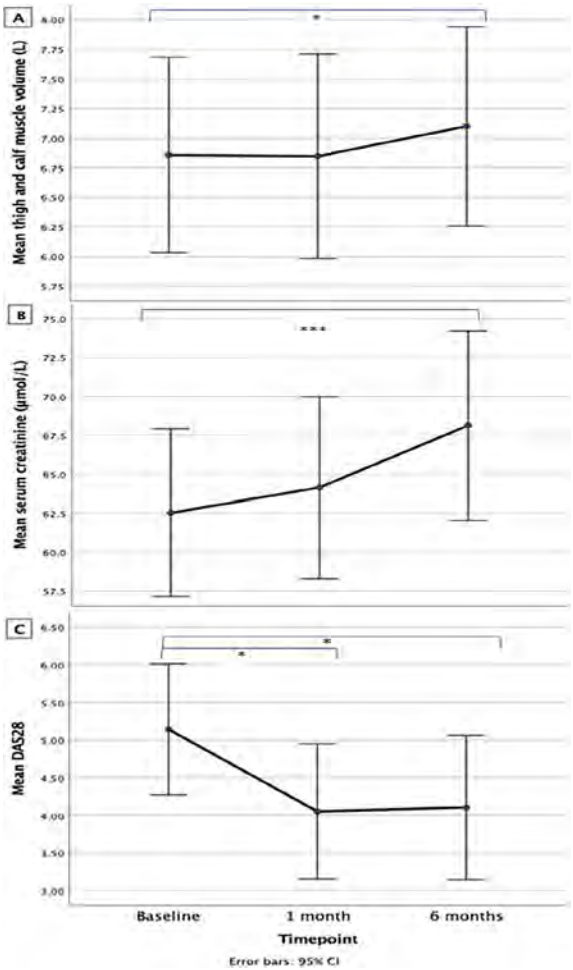

Figure 2: Mean leg muscle volume (A), serum creatinine (B) and DAS28 (C) at each timepoint. Significantly different time points are denoted by * ($p < 0.05$) or *** ($p = 0.001$).

Results: 15 participants aged 41 – 73 years (mean 59) were enrolled (87% female). Median disease duration was 3.1 years (range 1.5 – 24.8) and 60% (n = 9) were seropositive (anti-CCP, RF or both). At baseline, 67% (n = 10) took methotrexate (no other conventional DMARDs were used), 87% (n = 13) were biologic naïve and median BMI was 31.8 kg/m^2. All participants completed the study. 60% (n = 9) had >1 interruption of treatment ranging from 6 – 30 days. At 6 months, increases were observed in lower limb SKM volume (3.5% from baseline), SCr (9.0% from baseline) and self-reported physical activity; changes in disease activity manifested earlier, from 1 month (see Table 1 and Figure 2). 47% (n = 7) achieved a good (n = 3) or moderate (n = 4) EULAR response and 27% (n = 4) achieved ACR20. SKM volume increased significantly in the thigh but not in the calf. The muscle compartment fat fraction did not change. Grip strength, gait speed and fat mass index did not change. There was a trend towards increased weight. SKM volume correlated with grip strength (rs = 0.725, p = 0.003) at baseline. There was no correlation between SKM volume and SCr (either at baseline or in the difference at 6 months).

Conclusion: Treating RA with tofacitinib for 6 months was associated with increased SKM volume, increased SCr and increased self-reported physical activity. Possible mechanisms include a direct anabolic effect of JAK inhibition on SKM, reduced systemic inflammation, improved RA symptoms or a combination of the above. Analysis of SKM tissue samples from participants in the RAMUS study will provide mechanistic insight. These data merit further investigation in the form of a randomised trial to test whether the improvements are specific to tofacitinib and whether combining JAK inhibition with resistance exercise yields greater benefits.

Disclosure: J. Bennett: Pfizer, 5; **K. Hollingsworth**: Astellas Gene Therapies, 2, 5, 7; **A. Pratt**: Gilead, 5, GlaxoSmithKlein(GSK), 5, Pfizer, 5; **M. Egail**: None; **C. Feeney**: None; **V. Di Leo**: None; **R. Taylor**: None; **R. Dodds**: None; **A. Anderson**: None; **A. Sayer**: None; **J. Isaacs**: AbbVie/Abbott, 6, AnaptysBio, 2, Annexon, 2, AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 1, Galapagos, 2, Gilead, 1, GSK, 5, Istesso, 2, Janssen, 5, Kira Biotech, 2, Ono Pharma, 2, Pfizer, 5, Revelo, 2, Sonoma Biotherapeutics, 2, Teijin Ltd, 2.

Abstract Number: 0295

Pneumocystis Jirovecii Pneumonia in Patients with Inflammatory Myopathies

Cody Bruggemeyer[1], Sanket Shah[2], Didem Saygin[3] and Mike Putman[4], [1]Medical College of Wisconsin, Wauwatosa, WI, [2]Medical College of Wisconsin, Milwaukee, WI, [3]University of Pittsburgh, Pittsburgh, PA, [4]Division of Rheumatology, Medical College of Wisconsin, Milwaukee, WI

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Pneumocystis Jirovecii Pneumonia (PJP) is an opportunistic fungal infection with high morbidity and mortality rates. Few studies to date have assessed the incidence of PJP among patients initiating disease-modifying antirheumatic drugs (DMARDs) for idiopathic inflammatory myopathies. The objective of this study was to determine the incidence of PJP among patients receiving treatment for idiopathic inflammatory myopathies.

Methods: Data were derived from the US-based electronic health records database, TrinetX. Patients selected for study inclusion if they had greater than or equal to 2 ICD9-CM or ICD10-CM diagnosis codes for myositis and received at least one prescription for a DMARD . Due to the retrospective and electronic medical records based nature of this study, items from the ACR Classification Criteria were not available. PJP diagnosis was defined as hospitalization with diagnosis of

PJP, any PJP code followed by any PJP treatment, or any diagnostic test positive for PJP. The primary outcome was the incidence of PJP during the first 6 months of initiating DMARD therapy. The secondary outcome was the incidence of PJP during the first 12 months of initiating DMARD therapy. Unadjusted incidence rate ratio and 95% confidence intervals were calculated.

Table 1: Demographic and Clinical Characteristics, n = 6,030	
Age at Diagnosis, mean (SD)	55.0 (14.4)
Gender	
Male	1498 (24.8%)
Female	4532 (75.2%)
Race/Ethnicity	
White	3997 (66.3%)
Black or African American	1030 (17.1%)
Hispanic or Latino	454 (7.5%)
Asian	87 (1.4%)
Other / NA	462 (7.7%)
Comorbidities at Diagnosis	
Admissions during Prior Year, mean (SD)	0.6 (2.0)
Charlson Comorbidity Index	1.5 (1.9)
Obesity	935 (15.5%)
Renal Disease	754 (12.5%)
Liver Disease	633 (10.5%)
Interstitial Lung Disease	611 (10.1%)
Smoking	416 (6.9%)
Congestive Heart Failure	312 (5.2%)
Chronic Obstructive Pulmonary Disease	1294 (21.5%)
Diabetes	1201 (19.9%)
Medications During Index Period	
Methotrexate	2,826 (46.9%)
Azathioprine	1,531 (25.4%)
Mycophenolate Mofetil	1,482 (24.6%)
Hydroxychloroquine	1,194 (19.8%)
Tacrolimus	926 (15.4%)
IVIG	556 (9.2%)
Rituximab	289 (4.8%)
Prophylaxis Prescribed First 30 Days	
Trimethoprim/Sulfamethoxazole	852 (14.1%)
Atovaquone	80 (1.3%)
Dapsone	77 (1.3%)
Pentamadine	30 (0.5%)

Demographics and clinical characteristics

Table 2: Characteristics of patients who developed PJP pneumonia

Patient	Age	Sex	Race/Ethnicity	Comorbidities	Medications	Time to PJP	Death*
1	58.2	F	Hispanic or Latino	None	HCQ, IVIG	103 Days	177 Days
2	43.2	M	Hispanic or Latino	None	IVIG, HCQ, MMF	38 Days	38 Days
3	57.1	M	White	Diabetes, Renal Disease	Tacro	80 Days	Alive
4	71.2	F	White	Interstitial Lung Disease	AZA	23 Days	Alive
5	29.1	F	Hispanic or Latino	Liver Disease, Interstitial Lung Disease	IVIG, rituximab HCQ, MMF	78 Days	Alive
6	36.5	M	White	COPD, Liver Disease	AZA, Tacro, MMF	157 Days	Alive
7	43.1	M	Black or African American	None	AZA, IVIG	42 Days	Alive
8	70.3	F	White	CHF, COPD	Rituximab, IVIG	36 Days	Alive

* Death time restricted to 12-month evaluation period
Abbreviations in Table 2 are defined as follows: COPD - chronic obstructive lung disease, CHF- congestive heart failure, HCQ - hydroxychloroquine, IVIG - intravenous immunoglobulin, MMF - mycophenolate mofetil, Tacro - tacrolimus, AZA - azathioprine

Characteristics of patients who developed PJP pneumonia

Results: This study identified 6,030 patients with myositis who initiated therapy with a DMARD, the most common being methotrexate (2,826, 46.9%), followed by azathioprine (1,531, 25.4%) and mycophenolate mofetil (1,482 ,24.6%). The majority of patients were female (4,532, 75.2%) and white (3,997, 66.3%). The average age at diagnosis of myositis was 55.0 years. A minority (982, 16%) of patients received PJP prophylaxis, the most common of which was trimethoprim/sulfamethoxazole (852, 14.1%). During the first six months of therapy after DMARD initiation, a total of 8 cases of PJP were identified for an incidence rate of 2.9 cases per thousand patient-years. Among the eight patients who developed PJP, four were female, the average age at diagnosis was 51.1 (SD 15.5 years), and 3 had received prophylaxis against PJP. The average time to PJP diagnosis from the index date was 69.6 days (SD 44.7 days). The incidence of PJP among patients with structural lung disease at baseline (defined by chronic obstructive pulmonary disease or interstitial lung disease) was numerically higher as compared to those without lung disease (incidence 5.3 cases vs. 2.0 cases per 1,000 person) with an incident rate ratio of 2.7, 95% (confidence intervals 0.67-10.67). After extending the evaluation period to 1 year after DMARD initiation, no additional cases of PJP were identified, so the 12-month incidence of PJP was 1.45 cases per thousand patient-years.

Conclusion: The incidence of PJP in patients receiving DMARDs for idiopathic inflammatory myopathy was lower than identified in previous literature. It is important to weigh this low incidence rate against potential harms of antimicrobial therapy when deciding to initiate PJP prophylaxis. The risk of PJP in this population may be elevated among patients with structural lung disease.

Disclosure: C. Bruggemeyer: None; **S. Shah**: None; **D. Saygin**: None; **M. Putman**: AbbVie/Abbott, 12, Trial participation, AstraZeneca, 12, Trial participation, Novartis, 2.

Abstract Number: 0296

Does Presence of Anti-SSa and Ro52 Influence the Progression of Interstitial Lung Disease (ILD) in Idiopathic Inflammatory Myopathies (IIM)

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-SSa and Ro52 are commonly present in IIM. We previously reported an association of a more severe early course of IIM-ILD with positive Ro52. The aim of this study was to evaluate if presence of anti-SSa and/or Ro52 is associated with more severe radiological and functional evolution of IIM-ILD over time.

Table 1. Baseline Characteristics of Study Participants

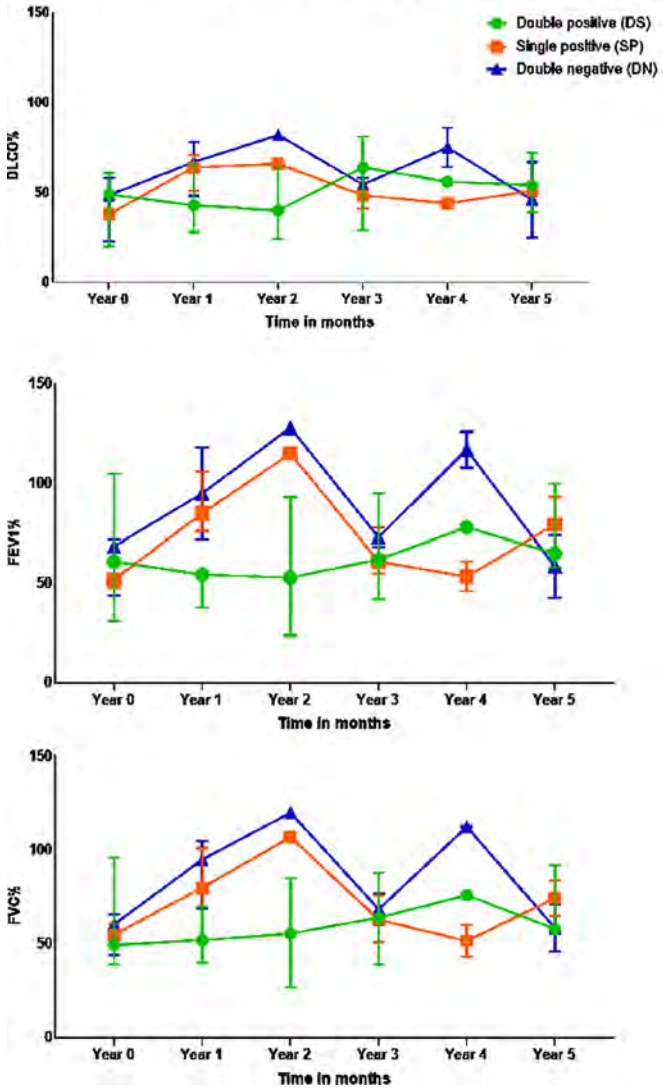
Characteristic	Double Positive Antibody Profile (anti-SSa and anti-Ro52) (N=7)	Single Positive Antibody Profile (anti-SSa or anti-Ro52) (N=6)	Double Negative Antibody Profile (neither anti-SSa nor anti-Ro52) (N=5)
Age - yr (min-max)	57 (44-67)	52 (26-60)	51 (36-83)
Female sex - no. (%)	6 (85.7%)	5 (83.3%)	5 (100%)
Race or ethnic group - no. (%)			
Caucasian	0 (0%)	0 (0%)	3 (60%)
African American	3 (42.9%)	3 (50%)	1 (20%)
Asian/Pacific Islander	4 (57.1%)	2 (33.3%)	1 (20%
Hispanic/Latino	0 (0%)	1 (16.7%)	0 (0%)
Myositis Subset - no. (%)			
Dermatomyositis	3 (42.9%)	2 (33.3%)	2 (40%)
Polymyositis	2 (28.6%)	0 (0%)	0 (0%)
Immune-mediated necrotizing myositis	0 (0%)	1 (16.7%)	0 (0%)
Overlap connective tissue disease	2 (28.6%)	4 (66.7%)	3 (60%)
Additional Myositis Antibody Profile - no. (%)			
Jo-1 ab	2 (28.6%)	1 (16.7%)	0 (0%)
PI-7 ab	0 (0%)	0 (0%)	0 (0%)
PI-12 ab	1 (14.3%)	0 (0%)	0 (0%)
EJ ab	0 (0%)	0 (0%)	1 (20%)
OJ ab	0 (0%)	0 (0%)	0 (0%)
MDA-5 ab	1 (14.3%)	2 (33.3%)	0 (0%)
PM-Scl-100 ab	0 (0%)	0 (0%)	1 (20%)
RNP ab	1 (14.3%)	0 (0%)	0 (0%)
TIF ab	1 (14.3%)	0 (0%)	0 (0%)
Ku ab	1 (14.3%)	0 (0%)	1 (20%)
1st Line Treatment – no. (%)			
Methotrexate	1 (14.3%)	1 (16.7%)	2 (40%)
Mycophenolate Mofetil	4 (57.1%)	3 (50%)	3 (60%)
Azathioprine	1 (14.3%)	1 (16.7%)	0 (0%)
IVIG	2 (28.6%)	0 (0%)	0 (0%)
Rituximab	1 (14.3%)	0 (0%)	0 (0%)
Tacrolimus	0 (0%)	0 (0%)	0 (0%)
*Others:	0 (0%)	0 (0%)	0 (0%)
2nd Line Treatment – no. (%)			
Methotrexate	0 (0%)	0 (0%)	0 (0%)
Mycophenolate Mofetil	0 (0%)	0 (0%)	0 (0%)
Azathioprine	0 (0%)	0 (0%)	0 (0%)
IVIG	1 (14.3%)	1 (16.7%)	1 (20%)
Rituximab	1 (14.3%)	0 (0%)	0 (0%)
Tacrolimus	1 (14.3%)	0 (0%)	0 (0%)
*Others:	0 (0%)	0 (0%)	1 (20%)

Methods: This is a longitudinal analysis of the Northwell Myositis cohort. All patients met 2017 EULAR/ACR IIM classification criteria. ILD diagnosis was validated by manual chart review. Three groups were analyzed: anti-SSa /Ro52 double positive (DP), anti-SSa/ or Ro52 single positive (SP), and both anti-SSa and Ro52 negative (DN). HRCT was scored as improved,

Table 2 - PFT and HRCT data across 3 groups

	Double Positive (DP) (n = 7)	Single Positive (SP) (n = 6)	Double Negative (DN) (n = 5)	*p-value*
Baseline PFT parameters (mean, SD)				
FVC	58.7 (19.0)	65.8 (18.2)	67.2 (22.7)	0.72
FEV1	59.9 (22.6)	65.2 (18.2)	74.2 (27.0)	0.57
DL_{CO}	42.9 (17.3)	49.2 (16.0)	49 (16.5)	0.75
PFT changes (n, %)				
Improved	5 (71.4%)	4 (66.7%)	5 (100%)	
Stable	1 (14.3%)	0 (0%)	0 (0%)	
Worsened	1 (14.3%)	2 (33.3%)	0 (0%)	
Baseline HRCT findings (n, %)				
Groundglass opacities	6 (85.7%)	5 (83.3%)	3 (60%)	
Fibrosis	4 (57%)	1 (16.7%)	2 (40%)	
Honeycombing	1(14.2%)	0 (0%)	0 (0%)	
HRCT changes (n, %)				
Improved	1 (14.3%)	2 (33.3%)	1 (20%)	
Stable	5 (71.4%)	4 (66.6%)	4 (80%)	
Worsened	1 (14.3%)	0 (0%)	0 (0%)	

Figure 1:Longitudinal PFTs Changes in ILD patients



stable or worsened on the last available scan compared to baseline. Serial FVC, FEV1, and DLCO comparisons from baseline to most recent PFT were performed, percent change with annualized relative percent change were calculated. Improvement or worsening on PFTs was defined as an increase or decrease of $\geq$ 10% in 1 PFT parameter with no $\geq$ 5% decrease or increase in other parameters respectively. Descriptive statistics, T-tests, ANOVA tests, Fisher's exact and Spearman's correlation tests were used for statistical analysis.

Results: Baseline demographics and clinical characteristics are reported in **Table 1.** Eighteen patients met inclusion criteria and had > 2 serial HRCT/ PFT of which 7/18 (38.9 %) were DP, 6/18 (33.3%) SP and 5/18 (27.8%) DN. Median follow up was 5 years (range: 1-13).At baseline, PFTs were similar between the groups (**Table 2**). On baseline HRCT, most observed pattern across all groups was groundglass opacities followed by fibrosis (**Table 2**).

Honeycombing was reported in 14.2 % of DP but not seen in SP or DN groups.

HRCT showed improvement in four patients (1 DP, 2 SP and 1 DN), but mostly recorded stability (DP: 71.4%,5/7and SP: 66.6%, 4/6). Nine patients (DP: 71.4%,5/7 and SP: 66.7%, 4/6) improved by PFT criteria while no DN patients improved (p=0.28). Four patients worsened: one by HRCT and 3 by PFT, all were seropositive (2 from SP and 2 from DP), no patients in DN group worsened. FVC or FEV 1 did not improve in seropositive groups, but in DN mean FEV1 improved from baseline 74.2 % to 90.4% (p= 0.04). Mean annualized % change of PFT was not different between groups. Overall DLCO improved in DN group (49% to 63%, p=0.03) and no improvement was seen in DP or SP groups, but weak improvement trend was observed when positive groups were combined (p=0.05). DP group had overall stability across all PFT parameters over the 5 years follow up. In contrast DN and SP groups appeared to have a modest improvement during the first 2 years that was lost by the 5th year follow up. At year 5 the change of all PFT parameters from baseline was not significant in all 3 groups (**Figure 1).**

Conclusion: While we previously reported the patients with diagnosis of IIM associated ILD with Ro52 positive antibodies may have worse outcomes, this study demonstrates that after initial decline of PFT during first 2 years, pulmonary function stabilizes over time irrespective of serological cluster. At the same time patients with negative of SSA/ Ro52 antibodies are more likely to improve over the years as determined by FEV1 and DLCO. HRCT was not sensitive to changes and mostly reported stability.

Disclosure: S. Narain: None; **C. Hu**: None; **M. Liu**: None; **K. Shargani**: None; **G. Marder**: None.

Abstract Number: 0297

Characteristics of Anti-MDA-5 Associated Dermatomyositis in Southern California with a Large Hispanic Population: Case Series

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: There is little to no data about the presentation and clinical course of anti-melanoma differentiation-associated gene-5 antibody (anti-MDA-5) dermatomyositis patients in a primarily U.S. Hispanic population. We describe the clinical presentation and outcomes of anti-MDA-5 dermatomyositis in our urban, majority Hispanic rheumatology patient population.

Methods: This is a multicenter, retrospective case series of patients with anti-MDA-5 dermatomyositis. All patients diagnosed with anti-MDA-5 dermatomyositis and encountered in the clinical setting from June 2015 to March 2023 at four academic medical centers in Los Angeles, California by rheumatologists or dermatologists were included. Demographics and clinical characteristics were obtained. Descriptive statistics were presented using frequency and percent for categorical variables and median (IQR) for continuous variables. Associations between categorical variables were assessed using Pearson's chi-squared or Fisher's exact test, and differences in continuous variables were evaluated using a Wilcoxon rank sum test or Kruskal-Wallis test. All tests were two-sided, and a p-value< 0.05 was considered statistically significant.

Results: A total of 30 patients with at least one positive assay for anti-MDA-5 dermatomyositis with a wide variety of clinical manifestations were included (Table 1). Nearly three-quarters of our patients (73%) were Hispanic. Twenty-one patients (70%) were female, with a median age of 40.5 years (IQR [26, 54]). Five patients were pediatric patients (< 18 years old). Hispanic patients were diagnosed with anti-MDA-5 dermatomyositis at a younger age compared to non-Hispanic patients (median age 37.5 years vs. 56.0 years; p = 0.025) (Table 2). Male patients were more frequently diagnosed with inflammatory arthritis compared to female patients (100% vs. 52.4% respectively; p = 0.027). There were 13 patients (43%) without evidence of myositis. Twenty-five patients (83.3%) had evidence of interstitial lung disease (ILD), and a higher ferritin level was associated with ILD (p = 0.049) (Table 3). There were 6 deaths in our cohort, of which 5 were ascribed to rapidly progressive ILD.

Conclusion: In our primarily Hispanic population of urban Los Angeles, anti-MDA-5 dermatomyositis has a wide spectrum of manifestations, with ILD being one of the most common clinical presentations. On average, Hispanic patients were diagnosed with anti-MDA-5 dermatomyositis at a younger age compared to the non-Hispanic patients in our cohort. Like prior

Table 1

Table 1. Patient Demographics and Clinical Manifestations

Demographics	n=30 (%)
Age at the time of diagnosis	
0-21	5 (17)
21-30	4 (13)
31-40	6 (20)
41-50	7 (23)
51-60	5 (17)
61-70	3 (10)
Sex	
M	9 (30)
F	21 (70)
Ethnicity*	
Hispanic	22 (73)
Non-Hispanic	8 (27)
Clinical features	
Inflammatory Lung Disease (ILD)	25 (83)
RP- ILD	5 (16.6)
Myositis†	17 (57)
Synovitis/Arthritis‡	19 (63)
Common JDM skin findings	
Heliotrope Rash	12 (40)
Gottron's Papules	12 (40)
Facial rash	6 (20)
Nailfold Capillary Changes	6 (20)
Shawl Sign	10 (33)
V sign	4 (13)
MDA-5 specific skin findings	
Palmar Papules	1 (3)
Cutaneous Ulcerations	9 (30)

*Self-reported

†Defined as clinical muscle weakness, elevated muscle enzymes, abnormal electromyogram and/or muscle biopsy results

‡Defined as joint pain, swelling, limited range of motion, and/or morning stiffness

Table 2

Table 2. Clinical variables by Ethnicity

Variable	Ethnicity		p-value
	Non-Hispanic (n=7)	Hispanic (n=22)	
Age at Diagnosis (years)	56.0 (10.0) (min=36, max=61)	37.5 (22.0) (min=5, max=65)	0.025*
Skin Manifestations			0.665
None	2 (28.6%)	2 (9.1%)	
Majority are classic DM/JDM lesions	4 (57.1%)	15 (68.2%)	
Majority are MDA-5 specific	1 (14.3%)	4 (18.2%)	
Both	0	1 (4.6%)	
Myositis			0.667
No	4 (57.1%)	9 (40.9%)	
Yes	3 (42.9%)	13 (59.1%)	
Synovitis/Arthritis			0.999
No	2 (28.6%)	7 (33.3%)	
Yes	5 (71.4%)	14 (66.7%)	
Lung Involvement			0.086
None	0	5 (22.7%)	
ILD	4 (57.1%)	15 (68.2%)	
RP-ILD	3 (42.9%)	2 (9.1%)	
Peak Ferritin	1,790.0 (268.0) (min=810, max=40,000)	478.5 (1,122.5) (min=37, max=9,056)	0.033*
Outcome			0.132
Alive	4 (57.1%)	19 (86.4%)	
Deceased	3 (42.9%)	3 (13.6%)	

Numbers represent median (IQR) for continuous variables and frequency (column percent) for categorical

Table 3

Table 3. Clinical variables by lung involvement

Variable	Lung Involvement			p-value
	None (n=5)	ILD (n=20)	RP-ILD (n=5)	
Age at Diagnosis	23.0 (25.0) (min=14, max=63)	40.5 (20.0) (min=5, max=65)	44.0 (20.0) (min=14, max=61)	0.589
Skin Manifestations				0.848
None	1 (20.0%)	2 (10.0%)	1 (20.0%)	
Majority are classic DM/JDM lesion	3 (60.0%)	13 (65.0%)	4 (80.0%)	
Majority are MDA-5 specific	1 (20.0%)	4 (20.0%)	0	
Both	0	1 (5.0%)	0	
Myositis				0.860
No	3 (60.0%)	8 (40.0%)	2 (40.0%)	
Yes	2 (40.0%)	12 (60.0%)	3 (60.0%)	
Synovitis/Arthritis				0.719
No	2 (40.0%)	6 (30.0%)	2 (50.0%)	
Yes	3 (60.0%)	14 (70.0%)	2 (50.0%)	
Missing	*0*	*0*	*1*	
Peak Ferritin	37.0 (0) (min=37, max=37)	481.0 (1,229.0) (min=190, max=9,056)	1,784.0 (81.0) (min=1,050, max=40,000)	0.049*
Duration of Disease (years)	3.0 (3.0) (min=1, max=9)	2.5 (3.3) (min=0.5, max=11)	0.5 (0) (min=0.5, max=0.5)	0.006*
Outcome				<0.001*
Alive	5 (100%)	19 (95.0%)	0	
Deceased	0	1 (5.0%)	5 (100%)	

Numbers represent median (IQR) for continuous variables and frequency (column percent) for categorical
*Significant at p<0.05

studies, there was an association between higher ferritin level and the presence of ILD. While skin ulceration has been reported to be associated with lung involvement, the association was nonsignificant in our cohort, likely due to the small sample size. This is a first study looking at clinical phenotypes of a primarily Hispanic U.S. population. Larger multi-institutional studies are needed to better understand clinical phenotypes of this population in order to recognize and treat anti-MDA-5 dermatomyositis in a timely manner, especially given the high proportion of amyopathy and ILD.

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Abstract Number: 0298

Accuracy of the 2017 European Alliance of Associations for Rheumatology (EULAR)/American College of Rheumatology (ACR) Classification Criteria and Myositis-Specific Autoantibodies-Based Classification Criteria for Classifying Patients with Idiopathic Inflammatory Myopathy

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Limitations of the 2017 EULAR/ACR classification criteria have been suggested for classifying patients with idiopathic inflammatory myopathies (IIMs) and myositis-specific antibodies (MSAs). On this point, Casal-Dominguez et al recently developed a set of MSAs-based classification criteria that demonstrated perfect sensitivity and specificity (1).

The objective of this study was to determine whether the EULAR/ACR classification criteria and the MSAs-based classification criteria appropriately classify patients with IIMs, differentiating between incident and prevalent cases

Methods: Multicenter cross-sectional study of a cohort of patients included in the Spanish Registry of patients with IIM (Myo-Spain) (2). Patients were classified as incident group (time between diagnosis and study initiation ≤12 months) or prevalent group (>12 months). The accuracy of the classification criteria according of the presence of different MSAs was described. Differences between both groups were tested by Chi-square test. The sensitivity and specificity of the MSAs-based classification criteria was determined. The percent of agreement and the Cohen's Kappa coefficient was used to measured correlations between the EULAR/ACR criteria and the MSAs-based criteria

Results: We included 542 patients with IIM diagnosis, 132 (24.4%) and 410 (75.6%) patients in the incident and prevalent group, respectively. In the overall sample, the diagnosis could be classified with the EULAR/ACR criteria in 284 patients (52.4%) and with the MSAs-based criteria in 344 patients (99.4%). Differentiating by MSAs type, patients were successfully classified by EULAR/ACR criteria as follows: 57.6 % of anti-Jo1-positive patients; 49.3% of MSAs-positive myositis patients (except anti-Jo1 antibody); 52.3% of MSAs-positive myositis patients; 52.5% of patients without MSAs antibodies (table 1). No significant differences were found between the two groups (p >0,05). Regarding MSAs-based classification criteria, patients were successfully classified as follows: 92.1% of anti-synthetase-positive patients and 100% of MSAs-positive (except anti-synthetase antibody) patients (table 2). No significant differences were found between the two groups (p >0,05).The sensitivity and specificity of the MSAs-based criteria were 100% in the incident group and 99.2% and 100%, respectively, in the prevalent group. The percentage of agreement between the EULAR/ACR criteria and the MSAs-based criteria for IIMs was 49.2% in the incident group and 50.9% in the prevalent group. This value was 48.1% and 60.2% in anti-Jo1-positive subgroup (Cohen's Kappa=0).

Table 1: 2017 EULAR/ACR classification criteria for classifying patients with IIMs

	Anti-Jo1-positive	MSAs-positive (except anti-Jo1 antibody)	MSAs-positive	Without MSAs antibodies	All patients
Total (n)	125	221	346	196	542
Classified (n,%)	72 (57.6)	109 (49.3)	181 (52.3)	103 (52.5)	284 (52.4)
No classified (n,%)	53 (42.4)	112 (50.6)	165 (47.69)	93 (47.4)	257 (47.6)
Incident group (n)	27	72	99	33	132
Classified (n,%)	13 (48.15)	35 (48.6)	48 (48.4)	16 (48.4)	64 (48.4)
No classified (n,%)	14 (51.8)	37 (51.3)	51 (51.5)	17 (51.5)	68 (51.5)
Prevalent group (n)	98	149	247	163	410
Classified (n,%)	59 (60.2)	74 (49.6)	133 (53.8)	87 (53.37)	220 (53.6)
No classified (n,%)	39 (39.8)	75 (50.3)	111 (46.1)	76 (46.6)	190 (46.34)

No significant differences were found between groups (p<0.05)
IIMs: idiopathic inflammatory myopathies
MSAs: myositis-specific antibodies

Table 2: MSAs-based classification criteria for classifying patients with IIMs and MSAs

	Anti-synthetase-positive	MSAs-positive (except anti-synthetase antibody)	MSAs-positive
Total (n)	226	120	346
Classified (n,%)	224 (92.1)	120 (100)	344 (99.4)
No classified (n,%)	2 (0.8)	0 (0)	2 (0.5)
Incident group (n)	60	39	99
Classified (n,%)	60 (100)	39 (100)	99 (100)
No classified (n,%)	0 (0)	0 (0)	0 (0)
Prevalent group (n)	166	81	247
Classified (n,%)	164 (98.8)	81 (100)	245 (99.1)
No classified (n,%)	2 (1.2)	0 (0)	2 (0.8)

No significant differences were found between groups (p<0.05)
IIMs: idiopathic inflammatory myopathies
MSAs: myositis-specific antibodies

MSAs-based classification criteria for classifying patients with IIMs and MSAs

Conclusion: The degree of accuracy of the EULAR/ACR criteria for classifying patients with IIM diagnosis was lo, however, the MSAs-based criteria showed excellent diagnostic accuracy. No agreement was found between both classification criteria. Therefore, it seems necessary to review the classification criteria for MII, in which, in addition to including all MSAs, the difficulty in classifying patients without MSAs should be considered.

(1) Casal-Dominguez M et al. Arthritis Rheumatol 2022. (2) Cobo-Ibáñez T et al. Reumatol Clin. 2022.

2017 EULAR/ACR classification criteria for classifying patients with IIMs

Disclosure: T. Cobo: None; **M. Domínguez**: None; **A. Pros**: None; **J. Tandaipán**: None; **L. Nuño**: None; **J. MARTINEZ BARRIO**: None; **V. Jovani**: None; **F. Romero**: None; **M. Ruiz Lucea**: None; **E. Tomero Muriel**: None; **E. Trallero Araguás**: None; **J. Narvaez**: None; **J. Camins Fàbregas**: None; **A. RUIZ ROMAN**: None; **J. Loarce-Martos**: Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Galapagos, 6; **A. Nack**: None; **E. Delgado-Frías**: None; **F. Sivera**: AbbVie/Abbott, 1, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 5, 6, GlaxoSmithKlein(GSK), 6, Novartis, 5, Pfizer, 1, Roche, 5, UCB, 6; **c. Merino**: None; **A. Mas**: None; **A. Gómez Gómez**: Amgen, 6, Janssen, 6, Novartis, 5, Pfizer, 5, UCB, 5, 5; **J. Pego-Reigosa**: None; **M. Martin-Lopez**: None; **J. Valero**: None; **C. carrasco-Cubero**: None; **M. Freire González**: None; **I. Rúa-Figueroa**: AstraZeneca, 5, GSK, 1, 6; **N. Lozano Rivas**: None; **J. Suarez Cuba**: None; **A. Turrión Nieves**: None; **M. Puche Larrubia**: None; **P. Alcocer Amores**: None.

Abstract Number: 0299

Trends and Outcomes of Hospitalized Patients with Idiopathic Inflammatory Myopathy and Venous Thromboembolism: A Nationwide Inpatient Sample Analysis from US (2016-2019)

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Recent evidence suggests increased prevalence of venous thromboembolism (VTE) in patients with idiopathic inflammatory myopathies (IIM). The literature on the clinical implications of VTE among IIM patients remains scarce. We evaluated the recent trends in the mortality rates, length of stay (LOS), and cost of care (COC) of hospitalized patients with IIM with or without VTEs.

Methods: The 2016-2019 Nationwide Inpatient Sample (NIS) database was accessed to identify all adult (18 years and older) IIM patients hospitalized with or without VTE using ICD-10 codes. Baseline demographic characteristics and in-hospital outcomes were compared between the two groups. A multivariate logistic regression analysis was used to calculate the adjusted odds ratio (OR).

Table 1.0 (a) Baseline Characteristics, Mortality and Cost utilizations of inflammatory myositis admitted with or without VTE.

Baseline characteristics	Overall (%) (N=15,165)	No VTE (%) (N= 14,450)	Yes VTE (%) (N=715)	P-value
Mean Age, (Mean ± Standard error) (Years)	65.38 (64.78 - 65.99)	65.41 (64.79 - 66.03)	64.80 (62.29 - 67.31)	0.638
Age (years)				0.267
18-49	15.92	15.99	105	
50-64	23.67	3,420	170	
65-74	28.26	4,035	250	
>= 75	32.15	4,685	190	
Gender				0.246
• Male	53.15	52.91	58.04	
• Female	46.85	47.09	41.96	
Race				0.947
• White	63.27	63.22	64.34	
• Black	19.42	19.41	19.58	
• Hispanic	8.11	8.10	8.39	
• Asian or Pacific Islander	2.14	2.15	2.10	
• Native American	0.66	0.69	0.00	
• Other	6.40	6.44	5.59	
Co-morbidity[a]				
• Obesity	14.64	18.88	14.43	0.127
• Hypertension	68.71	68.79	67.13	0.677
• Diabetes	27.00	27.16	23.78	0.394
• Hypercholesterolemia	36.47	30.77	37.75	0.149
• Heart failure	21.04	21.14	18.88	0.512
• CKD stage 3 or more	9.69	9.72	9.09	0.800
• COPD	12.56	12.70	9.79	0.311
• Smoking	4.45	4.53	2.80	0.328
Hospital characteristics				
Hospital teaching status[c]				0.074
• Non-teaching	22.16	22.46	16.08	
• Teaching	77.84	77.54	83.92	
Hospital location				0.170
• Rural	6.20	6.33	3.50	
• Urban	93.80	93.67	96.50	
In-hospital mortality	4.22	3.98	9.09	0.003
Length of stay (Mean ± Standard error) (Days)	8.17 (7.79-8.55)	7.93 (7.55 - 8.31)	13.10 (10.96 - 15.24)	<0.001
Cost of care (Mean ± Standard error) (USD)	22161.52 (20780.16-23542.89)	21441.79 (20047.29 - 22836.28)	36733.67 (28972.92 - 44494.41)	<0.001

Table 1.0 (b) - Unadjusted and adjusted odds ratios for risk of mortality in inflammatory myositis with VTE.

Mortality (N = 839)		Unadjusted OR	Adjusted OR
With VTE n (%)	Without VTE n (%)		
65 (9.09)	574 (3.90)	2.41(1.32-4.39)	2.04 (1.09 - 3.81)

Table 1.0 (b) Unadjusted and adjusted odds ratio as a measure of effect of inpatient mortality in inflammatory myositis with VTE.

Results: The total number of hospitalized patients with IIM was 15,165 of whom 715 (4.71%) had VTE. There was no significant difference in the baseline characteristics between the two groups concerning age, gender, race, co-morbidities and hospital setting as shown in Table 1.0 (a). The mean age was 64.80 years (62.29-67.71) in patients with VTE with a male predominance (58%). The inpatient mortality rate in patients with VTE was significantly higher than those without (9.09% vs. 3.98%, p< 0.003), with an adjusted OR 2.04 (95% CI 1.09-3.81), Table 1.0 (b). The highest rate of VTE was observed in patients with dermatomyositis, 8.93%, amongst all subtypes of IIM. The mean LOS in patients with VTE was 13.10 days (10.96-15.24) vs 7.93 days (7.55-8.31) in the comparison group (p< 0.001). The mean COC was significantly higher in patients with VTE than those without, $36,733.67 vs $21,441.79 (p< 0.001).

Conclusion: VTE in patients admitted with IIM was associated with significantly higher inpatient mortality, COC and increased LOS. These results may signify the need for appropriate VTE preventive strategies in IIM to improve patient outcomes and impact on the healthcare system.

Disclosure: H. Chaudhary: None; **B. Shrestha**: None; **S. Abi Doumeth**: None; **M. Mattar**: None.

Abstract Number: 0300

Nailfold Videocapillaroscopy in Idiopathic Inflammatory Myopathy Compared with Healthy Controls

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SESSION INFORMATION
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Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
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Background/Purpose: Idiopathic inflammatory myopathies (IIMs) are a group of autoimmune disorders that cause inflammation of the muscle. This includes dermatomyositis and polymyositis. Literature has been strongly supportive of the use of capillaroscopy, particularly in dermatomyositis, for diagnosis and prognosis. However, many studies compare capillaroscopy in IIM to other rheumatic diseases such as scleroderma. There are few studies comparing capillaroscopy in IIM to control populations. We report our findings against a healthy control population who do not have a history of Raynaud's or connective tissue disease.

Methods: Between January 2018 and 2023 we performed capillaroscopy in patients with diagnoses of dermatomyositis or polymyositis following their first visit with active disease. For the primary analysis, we used multivariable linear regression to estimate the difference in mean NVC scores between IIM patients and controls adjusting for age, sex, and smoking history; 95% confidence intervals (CIs) were reported. NVC scores included capillaroscopy density, dilated capillaries, giant capillaries, micro hemorrhages, capillaries ramification, and capillaries disorganization. In the subset of patients with IIM, we explored associations of patient characteristics with NVC scores using single variable linear regression model; regression coefficients and corresponding 95% confidence intervals were reported. All P values are two sided without adjustment for multiple testing. P values less than 0.05 were considered statistically significant.

Table 1. Baseline Characteristics

Characteristic	IIM (N=44)	Control (N=21)
Median age (IQR), years	49 (36, 59)	50 (39, 56)
Race/Ethnicity, n (%)		
White	41 (93%)	16 (76%)
Black or African American	2 (5%)	2 (10%)
Asian	1 (2%)	3 (14%)
Female gender, n (%)	37 (84%)	14 (67%)
History of smoking, n (%)	2 (5%)	7 (33%)
Diagnosis, n (%)		
Dermatomyositis	41 (98%)	
Polymyositis	1 (2%)	

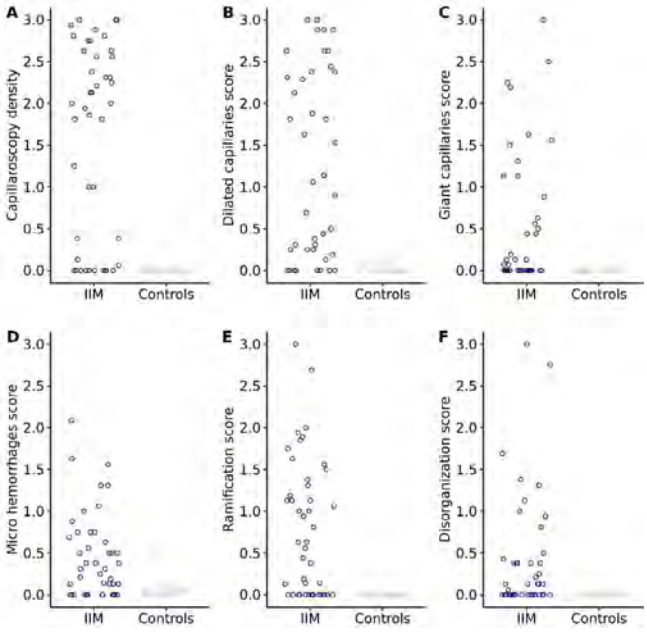

Figure 1. Jitter Plot of Nailfold Videocapillaroscopy Scores Points were jittered horizontally to minimize overlap of points.

Table 2. Single Variable Linear Regression Exploring Associations of Characteristics with Nailfold Videocapillaroscopy Scores in Patients with IIM

		Estimated difference in mean NVC scores (95% confidence interval)					
Factor	N (%) or Median (IQR)	Capillaroscopy Density	Giant Capillaries	Micro Hemorrhages	Dilated Capillaries	Ramification	Disorganization
Any constitutional symptoms (y vs. n)	13/44 (30%)	0.1 (-0.7, 0.8)	0.4 (-0.2, 0.9)	0.2 (-0.2, 0.5)	-0.0 (-0.8, 0.8)	-0.0 (-0.6, 0.5)	0.2 (-0.3, 0.6)
Diminished upper extremity muscle strength (y vs. n)	6/41 (15%)	0.8 (-0.2, 1.8)	**1.1 (0.5, 1.8)**	0.3 (-0.1, 0.8)	1.0 (-0.0, 2.0)	0.4 (-0.3, 1.0)	0.5 (-0.1, 1.0)
Diminished lower extremity muscle strength (y vs. n)	7/41 (17%)	0.0 (-0.9, 1.0)	0.5 (-0.1, 1.2)	0.2 (-0.3, 0.6)	0.3 (-0.7, 1.2)	-0.0 (-0.7, 0.6)	0.2 (-0.3, 0.7)
Associated cancer (y vs. n)	5/44 (11%)	0.6 (-0.5, 1.7)	0.4 (-0.3, 1.2)	0.1 (-0.4, 0.5)	0.4 (-0.7, 1.5)	**0.8 (0.1, 1.6)**	**0.9 (0.3, 1.5)**
CRP (+1), mg/L	3 (3, 3), n=32	0.0 (-0.1, 0.2)	0.0 (-0.1, 0.1)	0.1 (-0.0, 0.1)	-0.0 (-0.1, 0.1)	0.0 (-0.0, 0.1)	-0.0 (-0.1, 0.1)
ESR (doubling), mm/1H	6.0 (2.3, 13.5), n=34	0.1 (-0.1, 0.3)	0.1 (-0.0, 0.3)	0.0 (-0.1, 0.1)	0.1 (-0.1, 0.3)	0.1 (-0.1, 0.2)	0.1 (-0.0, 0.2)
CK (doubling), u/L	102 (71, 175), n=38	-0.2 (-0.4, 0.1)	0.1 (-0.1, 0.2)	-0.0 (-0.2, 0.1)	-0.1 (-0.4, 0.2)	-0.1 (-0.3, 0.1)	-0.0 (-0.2, 0.1)
Aldolase (+1), u/L	5.3 (4.2, 7.6), n=36	0.0 (-0.1, 0.1)	0.0 (-0.0, 0.1)	-0.0 (-0.0, 0.0)	0.0 (-0.0, 0.1)	0.0 (-0.0, 0.1)	0.0 (-0.0, 0.1)
ANA positive (y vs n)	30/44 (68%)	-0.0 (-0.8, 0.7)	0.1 (-0.4, 0.7)	0.1 (-0.2, 0.5)	-0.0 (-0.8, 0.7)	0.1 (-0.4, 0.7)	0.0 (-0.4, 0.5)
SSA-52D positive (y vs n)	12/43 (28%)	0.2 (-0.6, 1.0)	0.2 (-0.4, 0.8)	-0.3 (-0.6, 0.1)	0.1 (-0.7, 0.9)	0.3 (-0.3, 0.8)	0.3 (-0.2, 0.8)
Antisynthetase antibodies (y vs n)	6/43 (14%)	-0.3 (-1.3, 0.8)	-0.1 (-0.8, 0.6)	-0.2 (-0.7, 0.2)	-0.3 (-1.3, 0.8)	-0.4 (-1.2, 0.3)	-0.1 (-0.7, 0.5)
Serology (positive vs. negative)	33/44 (75%)	-0.6 (-1.4, 0.2)	-0.3 (-0.9, 0.2)	-0.1 (-0.4, 0.3)	-0.6 (-1.4, 0.2)	-0.3 (-0.9, 0.3)	0.1 (-0.4, 0.6)

The estimate difference in mean NVC scores and corresponding 95% confidence intervals were estimated from single variable linear regression models. Owing to highly skewed distribution, ESR and CK were transformed on the logarithm scale (base=2) such that a 1 unit increase on the logarithm scale corresponds with a doubling on the original scale.

Results: Baseline characteristics for 44 patients with IIM and 21 controls are shown in Table 1. Patients in the IIM group were more likely to have higher NVC scores compared to controls after adjusting for age, sex, and smoking history (Figure 1).

In Table 2 we explore associations of patient characteristics with NVC scores using single variable linear regression in the subset of patients with IIM. The mean giant capillaries score was 1.1 points higher for those with diminished upper extremity muscle strength (95% CI 0.5 to 1.8 points).IIM patients with associated cancer had mean ramification scores that were 0.8

points higher (95% CI 0.1 to 1.6 points) and mean disorganization scores that were 0.9 points higher (95% CI 0.3 to 1.5 points) than IIM patients without associated cancer.

Conclusion: Nailfold videocapillaroscopy shows statistically significant differences in density, dilation, giant capillaries, micro hemorrhages, ramification, and disorganization when compared with healthy controls. Exploratory analysis suggests there may be a correlation between giant capillary frequency with muscle strength as well as an increase in ramification and disorganization in those with malignancy-related myositis.

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Abstract Number: 0301

Inflammatory Myopathies and Their Relationship with Cancer in a Colombian Cohort

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammatory myopathies (IM) constitute a heterogeneous group of autoimmune muscle diseases. These can occur in isolation, associated with other autoimmune disorders, or as a development of some neoplasia. Different types of IM include dermatomyositis (DM) and polymyositis (PM). Magnetic resonance or electromyography can be helpful in the diagnosis, along with the performance of a biopsy. These entities have a higher risk of occult neoplasms, and cancer is one of the leading causes of death. Therefore, it is essential to understand the clinical, laboratory, and imaging characteristics in patients with IM associated with cancer. Our country's information on this pathology and its association with cancer is limited. Therefore, generating new knowledge and broadening interest in research in this area is essential.

Methods: A descriptive, retrospective, cross-sectional study of a cohort of patients treated at Fundación Valle del Lili in Cali, Colombia, was performed between 2011 and 2022. All participants accomplished the American College of Rheumatology (ACR) criteria for adult inflammatory myopathies, and statistical analyzes were performed using Stata® version 14 (StataCorp, College Station, TX, USA). Quantitative variables were presented as means (standard deviation) or medians (interquartile range).

Results: A total of 112 patients from 2011 to 2022 were included. The patient's median age at inclusion was 47,4 (± 18) years, with age at onset of symptoms of 41,2 (±19,4) years, being all females (100%). The primary inflammatory myopathies diagnosed were dermatomyositis 51 (45,5%), polymyositis 39 (34,8%), and juvenile dermatomyositis 9 (8,1%), which presented a disease evolution time of 48 (120-12) months. Some of the most prevalent clinical characteristics were symmetric weakness 64 (57%), upper limb weakness 63 (56%), myalgias 56 (50%), respiratory distress 31 (27,7%), arthralgia 46 (41%), and rash in Heliotrope 20 (17,9%). Additionally, 42 (37,5%) patients had muscle biopsy confirmation, and a myopathic pattern on EMG was evidenced in 67 (59,8%) individuals. 89 (79,5%) patients were treated with corticosteroids with a weekly dose of 35 (70-5) mg; other treatment included rituximab 33 (29,5%) with 2 (3-1) cycles approximately, azathioprine 40 (35,7%) and methotrexate 18 (16,1%). 13 (11,6%) patients were diagnosed with cancer; thyroid cancer was the most

common 4 (30,8%). The time between myopathy and an oncologic diagnosis was 11 (13-2) months. A bivariate analysis was made evaluating the relationship among cancer and no cancer patients; some variables statistically significant were age (P < 0.01), use of corticosteroids (P < 0.05), Gottron´s papules (P < 0.017), digital ulcers (P < 0.036) and a myopathic

Table 1. Patient characteristics, comorbidities, treatment, and outcomes

Variable	N	n = 112 (%)
Demographics		
Female sex	112	74 (66,1)
Age in years, Mean (SD)*	112	47,4 (18,0)*
Age at onset of symptoms	112	41,2 (19,4)*
Disease evolution time (months)	112	48 (120-12)**
Diagnosis		
Dermatomyositis	112	51 (45,5)
Polymyositis	112	39 (34,8)
Juvenile dermatomyositis	112	9 (8,1)
Other inflammatory myopathies	112	13 (11,6)
Cancer		13 (11,6)
Yes	112	13 (11,6)
No	112	99 (88,39)
Types		
Thyroid cancer	13	4 (30,8)
Skin cancer	13	2 (15,4)
Hematological cancer	13	2 (15,4)
Others	13	5 (38,4)
Time between myopathy and cancer (months)	11	11 (13-2)**
Clinical characteristics		
Symmetric weakness	109	64 (57,1)
Rash in Heliotrope	112	20 (17,9)
Gottron's papules	112	28 (25.0)
Shawl sign	112	21 (18,7)
Dysphagia	112	32 (28,6)
Weight loss	111	20 (17,9)
Calcinosis	110	11 (9,8)
Interstitial lung disease	112	20 (17,9)
Raynaud	112	15 (13,4)
Diagnostic studies		
CPK	108	670,5 (3978,5-129)**
Aldolase	34	7,6 (27,5-4,9)**
AST	105	40 (88,6-24)**
ALT	104	36,5 (99,2-18,9)**
LDH	72	267 (515,3-189)**
Muscle biopsy	106	42 (37,5)
Myopathic pattern on EMG	85	67 (59,8)
Muscle edema on MRI	67	47 (41,9)
Treatment		
Corticosteroid	112	89 (79,5)
Corticosteroid (prednisone) weekly dose (mg)	78	35 (70-5)**
EV immunoglobulin	112	9 (8,0)
Rituximab	112	33 (29,5)
Rituximab cycles	30	2 (3-1)**
DMARDs		
Azathioprine	112	40 (35,7)
Methotrexate	112	18 (16,1)
Cyclophosphamide	112	15 (13,4)
Mycophenolate	112	13 (11,6)
Cyclosporine	112	13 (11,6)
Outcome		
Good evolution	112	98 (87,5)
ICU	112	10 (8,9)
Death	112	4 (3,5)

*Mean (Standard deviation). **Median (Interquartile range). SLE, Systemic lupus erythematosus. RA, Rheumatoid arthritis. EMG, Electromyography. MRI, Magnetic resonance imaging. ICU, Intensive care unit. CPK, Creatin phospholkinase. ALT, Alanine Aminotransferase. AST, Aspartate aminotransferase. LDH, Lactate dehydrogenase.

Patients characteristics, comorbidities, treatment, and outcomes

Table 2. Bivariate analysis

Variable	N	Cancer Yes n = 13 (%)	Cancer No n = 99 (%)	P-value
		Demographics		
Age Mean (Standard deviation)	112	58.8 (19.4)	45.9 (17.4)	**0,014¶**
		Type of myopathy		
Dermatomyositis	112	8 (61,5)	43 (43,4)	0,413†
Polymyositis		3 (23,1)	36 (36,4)	
Juvenile dermatomyositis		0 (0,0)	9 (9,1)	
Other inflammatory myopathies		2 (15,4)	11 (11,1)	
		Treatment		
Use of corticosteroids				
Prednisone	89	2 (25,0)	18 (22,2)	**0,005†**
Prednisolone		2 (25,0)	52 (64,2)	
Methylprednisolone		2 (25,0)	9 (11,1)	
Deflazacort		0 (0)	2 (2.5)	
Hydrocortisone		2 (25,0)	0 (0)	
		Signs and symptoms		
Gottron's papules	112	7 (53,9)	21 (21,2)	**0,017†**
Digital ulcers	111	2 (15,4)	1 (1,0)	**0,036†**
Rash in Heliotrope	112	5 (38,5)	15 (15,2)	0,054†
Weight loss	111	4 (33,3)	16 (16,2)	0,224†
		Diagnostic studies		
Myopathic pattern on EMG	85	5 (50,0)	62 (82,7)	**0,032†**
CPK Median (Quartile 3- Quartile 1)	108	448 (2586-216.5)	787 (3978.5- 129)	0.7139*

† Fisher. *Mann-Whitney. ¶ T-Student. CPK. Creatin phosphokinase. EMG. Electromyography.

Bivariate analysis

pattern on EMG (P < 0.032). In this cohort, 4 (3.5%) patients died because of their underlying disease, and 98 (87.5%) presented a good evolution.

Conclusion: The characterization of patients with inflammatory myopathies and cancer in our country is essential due to its limited information, and it also opens the doors to generate new prospective studies that make it possible to create associations with a more significant statistical impact that guides early interventions in this type of patients.

Disclosure: B. Juan D.: None; **R. Robert**: None; **I. Nieto-Aristizabal**: None; **K. Enriquez**: None; **S. Zura**: None; **A. Echeverri**: None; **A. Hormaza-Jaramillo**: None; **D. Aguirre-Valencia**: None.

Abstract Number: 0302

Remission in Anti-HMGCR Positive Immune-mediated Necrotizing Myopathy Without the Use of Glucocorticoids: A Multicentric Study of 24 Patients

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Statin-induced immune mediated necrotizing myopathy (IMNM) is a subtype of inflammatory myopathy associated with anti-3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) autoantibodies. This condition is characterized by progressive muscle weakness leading to severe disability. Treatment is not well established, but usually includes high doses of glucocorticoids (GCs). Therapeutic effects are often disappointing. Side effects are common and related to the high doses of GCs. Intravenous immunoglobulins (IVIG) may be effective in the treatment of IMNM.

Our aim was to compare two therapeutic protocols in IMNM; **a)** standard therapy including high doses of GCs, and **b)** a GC-free protocol.

Methods: Patients consecutively diagnosed with statin-induced IMNM in our centers from January 2017 to November 2022 and followed for at least 3 months were included.

IMNM was diagnosed according to the definition of the European Neuromuscular International Workshop 2016. Clinical data was extracted retrospectively from the patients' clinical records.

Remission was defined as no disease activity according to 2016 ACR/EULAR response criteria in myositis.

Treatment was assigned to the patients considering the current recommendations and contraindications of the therapies available. In patients with comorbidities that limit the use of glucocorticoids, a steroid-free regime was agreed through a shared decision between the physician and the patient.

Results: We included 24 anti-HMGCR positive patients. Main features and treatment of the patients are summarized in **TABLE**.

A GC-free regimen based on the use of IVIG 2g/kg every month for at least 3 months was used in 5 (20.8%) patients. The remaining received standard treatment including GCs.

At baseline, general demographic data, MMT-8 and CK levels were similar in both groups. Comorbidities were higher in patients treated with the GCs free protocol.

Table: General features of 24 patients diagnosed with HMGCR positive IMNM.

Variables	Total (n=24)	Glucocorticoid group (n=19)	Glucocorticoid-free group (n=5)	P (steroids vs no steroid)
Age (years), mean ± SD	68.2 ± 7.2	69.2 ± 6.9	64.4 ± 8	0.2
Sex (women), n (%)	10 (42)	8 (42.1)	2 (40)	0.7
Comorbidities (n, %)				
- Hypertension	17 (70.8)	13 (68.4)	4 (80)	0.96
- Diabetes mellitus	15 (62.5)	11 (57.9)	4 (80)	0.7
- Cardiovascular disease	7 (29.2)	6 (31.6)	1 (20)	0.96
Analytical values at diagnosis, mean ±SD				
- CK (ukat/L)	114 ± 104	134± 108	40 ± 34	0.07
Treatments, n (%)				
- Intravenous GC	8 (33.3)	8 (42.1)	0	0.2
- Oral GC	19 (79.2)	19 (100)	0	**0,0001***
- MTX	18 (75)	15 (78.9)	3 (60)	0.8
- AZA	3 (12.5)	3 (15.8)	0	0.8
- IVIG	18 (75)	13 (68.4)	5(100)	0,4
- RTX	4 (16.7)	3 (15.8)	1 (20)	0.7
Muscle strength assessment				
- MMT-8 at diagnosis	64.4 ± 12	63.7 ± 10.4	67.3 ± 19.4	0.6
- MMT-8 after treatment	77.6 ± 4.2	77.2 ± 4.6	79.5 ± 1.5	0.3
Remission				
- Patients achieving remission, n (%)	21 (87.5)	16 (84.2)	5 (100)	0.8
- Time to clinical remission (months), mean ± SD	5.2 ± 2.3	5.5 ± 2.5	4.1 ± 1.1	0.2
- Time to CK normalization (months), mean ± SD	4.1 ± 1.6	3.9 ± 1.7	4.9 ± 1.3	0.3

AZA: Azathioprine; CK: Creatine kinase; GC: Glucocorticoids; IVIG: Intravenous immunoglobulins; MTX: Methotrexate; RTX: Rituximab
Upper limit for CK: < 4.7 ukat/L for men and 3.5 ukat/L for women.
*: $p < 0.05$

Remission or low disease activity was achieved in 21 patients (87.5%), including all 5 patients who did not receive GCs (after a mean of 4.1 ± 1.1 months).

However, 3 (15.8%) of the 19 patients receiving glucocorticoids did not achieve remission or low disease activity.

The time to remission or CK normalization was similar in both groups.

Conclusion: In our series of patients with anti-HMGCR positive IMNM, we found that patients can achieve remission without glucocorticoid treatment.

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Abstract Number: 0303

Development of a Human Cytotoxic Myoinjury Model with CD8+ T Cells and Muscle Cells Differentiated from Human Induced Pluripotent Stem Cells

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SESSION INFORMATION

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Background/Purpose: CD8+ cytotoxic lymphocytes (CTLs) play a crucial role in the myoinjury of polymyositis (PM). Nonetheless, conventional treatment for PM depends on high-dose glucocorticoids with or without other nonspecific immunosuppressants. Some patients are refractory to these treatments while others suffer from adverse effects. T cell activity can be suppressed with calcineurin inhibitors but often insufficiently because of their renal toxicity at high dose ranges. Abatacept was effective to PM model of mice, but it could not exhibit its efficacy against idiopathic inflammatory myositis in a phase III clinical trial. Therefore, developing novel therapeutic strategies that is specific to the pathophysiology of PM and safe are still demanded. To further investigate the pathophysiology of PM, which is idealistic to be done with human resource, we aimed to develop an ex vivo model of CTL-mediated myoinjury utilizing muscle cells and regenerative CTLs (rCTLs) derived from human induced pluripotent stem cells (hiPSCs).

Methods: Human iPSCs were established from peripheral blood-derived CD34+ hematopoietic stem and progenitor cells of PM patients, who met the Bohan and Peter criteria. Additionally, HLA-A haplotype analysis of the hiPSC-donors were performed. HLA-A*24:02+ or HLA-A*24:02- hiPSCs were transfected with adoxycycline (Dox)-inducible MyoD vector. After overnight culture with Dox, hiPSCs highly expressing MyoD were sorted and re-cultured to expand in undifferentiation medium without Dox. These cells were differentiated into muscle cells in a differentiation condition with Dox. Human iPSC-derived rCTLs established from WT1-specific primary CTLs were activated by an HLA-A*24:02+ lymphoblastoid cell line presenting a mutant WT1 peptide (mWT1), which binds more strongly to HLA-A*24:02 than the nature WT1 peptide. Activated rCTLs were cocultured with the muscle cells pulsed with mWT1. The cytotoxicity of rCTL was evaluated by fluorescence of calcein released from the pre-labeled muscle cells. Student's t-test and Tukey's test were used for statistical analysis.

Results: Mutant WT1 pulsed muscle cells derived from 2 cell lines of HLA-A*24:02+ hiPSCs were killed by rCTLs, respectively. The cytotoxicity was dependent on the number of rCTLs. In addition, the cytotoxicity was suppressed when mWT1 was not pulsed to the coculture, when tacrolimus was added to the coculture, or when the cocultured muscle cells were derived from HLA-A*24:02- hiPSCs.

Conclusion: By using hiPSCs, we established a human cell-derived cytotoxic myoinjury model, which is MHC class I restricted and antigen-specific. This model would facilitate the analysis on the mechanism of CTL-mediated myoinjury in human and dissect the pathophysiology of PM.

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Abstract Number: 0304

Incidence of Disease Flares Following COVID-19 Vaccination in a Diverse Idiopathic Inflammatory Myopathy Cohort

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
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Background/Purpose: Autoimmune activation in the setting of vaccination against coronavirus disease 2019 (COVID-19) is a well-documented phenomenon in the medical literature. For patients with idiopathic inflammatory myopathies (IIM), there is a concern that vaccinations can cause disease flares. Data regarding this topic in this heterogenous patient population remains sparse. Our aim was to evaluate the incidence of myositis flares in IIM patients following vaccination against COVID-19 in a minority majority cohort.

Methods: Patients from Montefiore Medical Center who met 2017 EULAR/ACR classification criteria for IIM were included in this retrospective cohort study. 152 patient records from the year 2020 onwards were searched for dates of COVID-19 vaccinations and incidence of disease flares, defined as myalgias with elevations in creatine kinase over two times the upper limit of normal within 3 months of vaccination. A bivariate analysis was done in those who were vaccinated to determine possible covariates associated with disease flares, including IIM subtypes, the presence and severity of interstitial lung disease (ILD), and concurrent immunosuppressive therapy.

Results: Of the 152 IIM patients included in this cohort study, 84 (55%) were vaccinated against COVID-19. Of the 84 vaccinated patients, 5 (6%) experienced a disease flare. All flares occurred after the primary vaccine series of either Pfizer (n= 3/5, 60%) or Moderna vaccines (n= 2/5, 40%). There were no statistically significant increases in disease flare incidence in patients with Polymyositis, Dermatomyositis, Amyopathic Dermatomyositis, Mixed or Undifferentiated Connective Tissue Disease, Necrotizing myopathies, or Inclusion Body Myositis. However, there were statistically significant increases in the incidence of disease flares in patients with moderate ILD (p=0.03) and progressive ILD (p=0.05). There were also statistically significant differences noted in the incidence of disease flares in patients taking Rituximab (p= 0.01) and Cyclosporine (p=0.02), while there were no similar trends observed for those on other immunosuppressive agents or those on acute or chronic steroids, as seen in Table 1.

Table 1: Bivariate association of flare with covariates among those COVID vaccinated

Variable	Flare		P-value
	No (n = 79)	Yes (n = 5)	
Mild ILD, n (%)			1.00
No	56 (70.9)	4 (80.0)	
Yes	23 (29.1)	1 (20.0)	
Moderate ILD, n (%)			0.03
No	76 (96.2)	3 (60.0)	
Yes	3 (3.8)	2 (40.0)	
Severe ILD, n (%)			0.36
No	73 (92.4)	4 (80.0)	
Yes	6 (7.6)	1 (20.0)	
ILD unknown, n (%)			NA
No	79 (100.0)	5 (100.0)	
Yes	0 (0)	0 (0)	
ILD progressing, n (%)			0.05
No	65 (82.3)	2 (40.0)	
Yes	14 (17.7)	3 (60.0)	
PM, n (%)	24 (30.4)	3 (60.0)	0.32
DM, n (%)	45 (57.0)	1 (20.0)	0.17
ADM, n (%)	6 (7.6)	1 (20.0)	0.36
MCTD, n (%)	8 (10.1)	1 (20.0)	0.44
Necrotizing, n (%)	13 (16.5)	1 (20.0)	1.00
IBM, n (%)	5 (6.3)	0 (0)	1.00
MTX, n (%)			0.53
uncontrolled	16 (20.3)	2 (40.0)	
controlled	14 (17.7)	0 (0)	
never used	49 (62.0)	3 (60.0)	
MMF, n (%)			0.71
uncontrolled	13 (16.5)	1 (20.0)	
controlled	22 (27.9)	2 (40.0)	
never used	44 (55.7)	2 (40.0)	
MAB, n (%)			1.00
uncontrolled	2 (2.5)	0 (0)	
controlled	1 (1.3)	0 (0)	
never used	76 (96.2)	5 (100.0)	

Table 1: Continued

Variable	Flare		P-value
	No (n = 79)	Yes (n = 5)	
cyclophosphamide, n (%)			1.00
controlled	1 (1.3)	0 (0)	
never used	78 (98.7)	5 (100.0)	
tacrolimus, n (%)			0.12
controlled	1 (1.3)	1 (20.0)	
never used	78 (98.7)	4 (80.0)	
cyclosporine, n (%)			0.02
uncontrolled	1 (1.3)	2 (40.0)	
controlled	1 (1.3)	0 (0)	
never used	77 (97.5)	3 (60.0)	
rituximab, n (%)			0.01
uncontrolled	4 (5.1)	2 (40.0)	
controlled	13 (16.5)	2 (40.0)	
never used	62 (78.5)	1 (20.0)	
IVIG, n (%)			0.35
uncontrolled	13 (16.5)	2 (40.0)	
controlled	17 (21.5)	1 (20.0)	
never used	49 (62.0)	2 (40.0)	
Hydroxychloroquine, n (%)			0.13
uncontrolled	8 (10.1)	2 (40.0)	
controlled	19 (24.1)	1 (20.0)	
never used	52 (65.8)	2 (40.0)	
Steroid use, n (%)			0.11
Limited (<2 yrs), low-mod dose (< 20 mg)	22 (27.9)	0 (0)	
Limited (<2 yrs), high dose (>20 mg	20 (25.3)	0 (0)	
Chronic (>2yrs), low-mod dose (<20 mg)	25 (31.7)	3 (60.0)	
Chronic (>2yrs), high dose (>20 mg)	5 (6.3)	1 (20.0)	
Never used	7 (8.9)	1 (20.0)	

Table 2: Demographics

Variable	COVID vaccinated		P-value
	Yes (n = 84)	No (n = 68)	
Age*, mean (SD)	59.58 (13.19)	63.11 (17.22)	0.17
Sex, n (%)			0.18
Female	66 (78.6)	47 (69.1)	
Male	18 (21.4)	21 (30.9)	
Latinx, n (%)			1.00
Yes	34 (40.5)	27 (39.7)	
No	47 (56.0)	38 (55.9)	
Unk	3 (3.6)	3 (4.4)	
Race, n (%)			0.01
American Indian	2 (2.4)	0 (0)	
Asian	1 (1.2)	5 (7.4)	
Black	43 (51.2)	27 (39.7)	
White	28 (33.3)	17 (25.0)	
Unk	10 (11.9)	19 (27.9)	
PM, n (%)	27 (32.1)	18 (26.5)	0.45
DM, n (%)	46 (54.8)	34 (50.0)	0.56
ADM, n (%)	7 (8.3)	4 (5.9)	0.76
MCTD, n (%)	9 (10.7)	6 (8.8)	0.70
Necrotizing, n (%)	14 (16.7)	6 (8.8)	0.15
IBM, n (%)	5 (6.0)	12 (17.7)	0.02

Conclusion: There were no statistically significant increases in disease activity for IIM patients after COVID-19 vaccination. However, disease flare incidence was increased in IIM patients with moderate or progressive ILD, as well as those taking Rituximab and cyclosporine. More research is needed to further investigate the link between ILD and vaccination-related disease flares. In the meantime, providers should remain vigilant in monitoring for disease activity after COVID-19 vaccination in IIM patients with ILD and those on immunosuppressive agents.

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Abstract Number: 0305

Prevalence and Clinical Significance of anti-Ro52 Antibodies in Antisynthetase Syndrome

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Antisynthetase syndrome (ASSD) is a systemic autoimmune condition characterized by the positivity of anti-aminoacyl-transfer-RNA synthetases antibodies (ARS) and the occurrence of the classic triad, encompassing myositis, arthritis, and interstitial lung disease (ILD).

There is a higher prevalence and increased severity of ILD in patients with ASSD compared to other idiopathic inflammatory myopathies (IIM). The leading prognostic role of ILD in ASSD prompted a focused search for laboratory markers able to predict lung involvement occurrence and progression. ARS specificities have been associated with phenotypically distinct

Table 1. Baseline characteristics

	Anti-Ro52 positive N=32	Anti-Ro52 negative N=24	p
Age (mean ± SD), years	61,8 ± 15	62,4 ± 13	0.879
Women/men (ratio)	22/10	9/15	0.625
Duration of follow-up (mean ± SD), months	63.3 ± 50	54.7 ± 45.5	0.512
Frequency of clinical features			
Fever	7 (22%)	8 (33%)	0.338
Raynaud's phenomenon	11 (34%)	7 (29%)	0.680
Arthritis	15 (47%)	15 (62.5%)	0.246
Mechanic's hands	26 (81%)	11 (46%)	**0.006**
Hiker's foot	5 (16%)	2 (8%)	0.686
Gottron's sign	8 (25%)	1 (4%)	**0.036**
Myositis	18 (56%)	14 (58%)	0.876
Interstitial lung disease (ILD)	29 (91%)	21 (87,5%)	0.708
Chest HRCT pattern of ILD	**N=29**	**N=21**	
Non-specific interstitial pneumonia (NSIP)	23 (79%)	14 (58%)	0.583
Organizing pneumonia (OP) or NSIP superimposed with OP	3 (10,5%)	3 (14%)	
Usual interstitial pneumonia	3 (10,5%)	4 (28%)	
FVC% predicted at ILD diagnosis (mean ± SD)	81,4 ± 27	75,4 ± 14,5	0.448
DLCO% predicted at ILD diagnosis (mean ± SD)	62,4 ± 22	62,4 ± 18	0.995
Need of oxygen therapy at ILD diagnosis	8 (27,5%)	4 (19%)	0.561
Serological parameters			
Positive antinuclear antibodies (ANA)	26 (81%)	17 (71%)	0.516
Myositis-specific antibody			
Anti-Jo1	19 (59%)	10 (42%)	0.189
Anti-PL7 or PL-12	10 (31%)	12 (50%)	0.155
Anti-EJ	3 (9,5%)	2 (8%)	0.892

Table 2. Therapeutic approaches and outcomes

	Anti-Ro52 positive N=32	Anti-Ro52 negative N=24	p
Need of intravenous methylprednisolone boluses	7 (22%)	6 (25%)	0.591
Number of immunosuppressants used (mean ± SD)			
1	20 (62,5%)	15 (62,5%)	0.729
2	7 (22%)	3 (12,5%)	
3	4 (12,5%)	4 (17%)	
4	1 (3%)	0 (0%)	
5	0 (0%)	1 (4%)	
Need of cyclophosphamide	2 (6%)	2 (8%)	0.303
Need of intravenous immunoglobulin (IVIG)	6 (19%)	4 (17%)	0.840
Need of Rituximab	19 (59%)	13 (54%)	0.697
Need of antifibrotic therapy	4 (12,5%)	5 (21%)	0.376
Lung function tests results and response at last follow-up	N=29 (91%)	N = 21 (87,5%)	
FVC% predicted at last follow up (mean ± SD)	92,2 ± 23,6	83,2 ± 29,4	0.246
DLCO% predicted at last follow up (mean ± SD)	61,8 ± 14,3	54,3 ± 20,6	0.151
%pFVC			
Improvement	15 (52%)	8 (38%)	0.318
No change / Stabilization	10 (34%)	8 (38%)	
Worsening	4 (14%)	5 (24%)	
%pDLCO			
Improvement	11 (38%)	7 (33%)	0.163
No change / Stabilization	12 (41%)	8 (38%)	
Worsening	6 (21%)	6 (28,5%)	
Progressive ILD	18 (62%)	13 (62%)	0.691
Need of oxygen therapy at last follow-up	10 (34%)	5 (24%)	0.521
Relapses	9 (28%)	7 (29%)	0.620
Deaths	3 (9,5%)	3 (12,5%)	0.708

subgroups at disease onset. However, it doesn't seem to be significant differences among the groups in the clinical spectrum, time course and prognosis.

Anti-Ro52 antibodies (anti-Ro52) are systemic autoantibodies addressed against the Tripartite motif-containing protein 21 found in several connective tissue diseases and up to 50% of ASSD patients. In patients with other IIM, anti-Ro52 positivity has been associated with a rapid progression (RP) of ILD and a poorer prognosis, whereas its role in ASSD is still uncertain. Our objective was to to assess the prevalence and clinical significance of anti-Ro52 antibodies in a cohort of patients with ASSD.

Methods: Ambispective analysis of clinical, imaging and laboratory characteristics, therapeutic approaches, and outcome of 56 ASSD patients progressively enrolled at our hospital.

Results: We identified 32 anti-Ro52 positive and 24 anti-Ro negative ASSD patients. The prevalence of ILD and myositis at baseline were similar between the two groups. In contrast, some skin lesions (mechanic's hands and Gottron's papules/sign) were significantly more prevalent in anti-Ro52+, whereas arthritis was more frequently seen in anti-Ro negative patients (see Table 1). We did not observe a strong association of co-occurring anti-Ro52 antibodies with any of the ARS.

No differences in oxygen need and ILD patterns, therapeutic approaches, outcome measures, and prognosis were observed (Table 2). Overall mortality was 11% (6 subjects). No differences in mortality, overall and disease-related, between anti-Ro52+ and anti-Ro52- patients were observed. Survival curves were not different at any time point (Log-rank test, p-value 0.608).

Conclusion: Overall, the presence of anti-Ro52 antibodies seems to be related to a higher prevalence of skin lesions, but not with ILD. Although they could affect the clinical characteristics of ASSD, they do not seem to influence the prognosis. No differences in relapses, RP-ILD, or mortality were observed when compared to anti-Ro52 negative patients

Disclosure: J. Narvaez: None; **P. Vidal-Montal**: None; **E. Cañadillas-Sanchez**: None; **P. Maymó**: None; **J. Palacios**: None; **M. Aguilar**: None; **M. Roig**: None; **J. Nolla**: None.

Abstract Number: 0306

Fitbit Is a Valid and Reliable Physical Activity Monitor in Idiopathic Inflammatory Myopathy

Akanksha Sharma[1], shiri keret[2], Raisa Lomanto Silva[3], Tanya Chandra[4], Joel Levin[5], Siamak Moghadam-Kia[3], Chester V. Oddis[6] and Rohit Aggarwal[6], [1]UPMC Mercy Hospital, Pittsburgh, PA, [2]Bnai Zion, Atlit, Israel, [3]University of Pittsburgh Medical Center, Pittsburgh, PA, [4]Georgetown University Hospital, Washington, DC, [5]University of Pittsburgh, Katz Graduate School, Pittsburgh, PA, [6]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Idiopathic inflammatory myopathies (IIM, myositis) are a systemic autoimmune disease leading to debilitating muscle weakness and significant limitations in daily activities. Physical activity monitor (PAM) are validated and recognized measures of the frequency and intensity of physical activities. Given the urgent need for objective, continuous,

longitudinal outcome measures of physical activity and function in myositis, we assessed compliance, reliability, and validity of widely used commercial PAM – Fitbit© in evaluating physical activity in myositis patients.

Table 1. Demographic characteristics of participants

	Total (n=120)	Center-Based Cohort (n=38)	Tele-Research Cohort (n=82)
Age (in years) at Enrollment (Mean± SD)	55.5± 13.4	56.9±12.4	54.9±12.8
Gender			
Female	90 (75%)	28 (73.7%)	62 (75.6%)
Male	30 (25%)	10 (26.3%)	20 (24.4%)
Race			
White	97 (80.8%)	19 (67.9%)	68 (82.9%)
Non-White	15 (12.5%)	7 (25%)	8 (9.8%)
Data Not Available	8 (6.67%)	2 (7.1%)	6 (7.3%)
Myositis Disease Subtype			
Dermatomyositis	62 (51.7%)	20 (52.6%)	42 (51.2%)
Polymyositis	47 (39.2%)	14 (36.9%)	33 (40.2%)
Necrotizing Myopathy	11 (9.1%)	4 (10.5%)	7 (8.6%)

Table 2: Cross-sectional association of Fitbit measures (average daily steps per minute, and average peak cadence) with various myositis outcome measures at baseline.

	Avg steps/ minute			**Avg. peak cadence**		
Parameters	**Beta**	**std.error**	**P-value**	**Beta**	**std.error**	**P-value**
Clinician Reported Outcomes (ClinRO)						
Continuous Measures:						
Skin disease activity (10 cm VAS)	0.8	0.4	**0.02**	1.3	0.5	**0.005**
Constitutional Disease activity (10 cm VAS)	0.02	0.3	1.0	-0.5	0.2	**0.006**
Extra-muscular global (10 cm VAS)	0.9	0.3	**0.003**	0.17	0.2	0.4
MD global disease activity (10 cm VAS)	-0.07	0.2	0.8	-0.3	0.1	**0.03**
Muscle disease activity (10 cm VAS)	-0.2	0.2	0.4	-0.4	0.2	0.005
MMT (0-150)	0.04	0.03	0.08	0.05	0.02	**0.008**
Pulmonary VAS (10 cm VAS)	0.38	0.5	0.4	-0.09	0.3	0.8
Joint disease VAS (10 cm VAS)	1.0	0.6	0.08	-0.1	0.4	0.8
Categorical Measures:						
Arthralgia	0.7	0.778	0.375	-0.396	0.528	0.5
Arthritis	0.8	1.11	0.456	0.747	0.753	0.3
ILD	-1.00	0.99	0.311	-0.340	0.675	0.6
Fatigue	-0.7	0.679	0.324	-1.55	0.434	**0.0006**
Myositis	-2.0	0.683	**0.004**	-1.73	0.450	**0.0002**
Myalgia	-1.3	0.717	0.085	-1.773	0.458	**0.0002**
Patient-Reported Outcomes (PROs):						
Continuous Measures:						
Pain score	-0.3	0.4	0.6	-0.8	0.3	**0.003**
HAQ-DI	-1.2	0.5	**0.01**	-1.8	0.3	4.4
Patient global disease activity	-0.2	0.1	03	-0.4	0.09	**0.00002**
PROMIS physical function – T score	0.1	0.04	**0.006**	0.1	0.02	4.9
Categorical Measures:						
Rashes	1.7	0.7	**0.014**	1.3	0.5	**0.005**
Difficulty breathing	-0.9	1.2	0.5	-0.8	1.0	0.5
Fatigue	-0.02	0.9	1.0	-1.7	0.6	**0.004**
ILD	0.1	1.2	0.9	0.3	1.0	0.8
Joint pain	-0.3	1.0	0.8	-1.3	0.6	**0.02**
Joint swelling	0.6	1.2	0.6	-0.4	0.7	0.5
Muscle pain	0.2	0.7	0.8	-1.0	0.5	**0.04**
muscle weakness	-0.8	0.7	0.3	-1.4	0.5	**0.003**
Functional Outcomes:						
Timed up and go (TUG)	-0.09	0.03	**0.01**	-0.07	0.02	**0.002**
Sit to Stand (STS)	0.3	0.07	**0.0002**	0.3	0.04	1.7
Laboratory Outcome:						
Creatine Kinase (CK)	0.0002	0.0004	0.6	0.0001	0.0002	0.7

Methods: "Myositis Patient Centered Tele-Research (MyPACER)" is a multi-center observational prospective study conducted over 6 months. The study had two cohorts, 1. Tele-Research Cohort (TRC): patients were remotely enrolled from any location in the United States, and 2. Center-Based Cohort (CBC): a traditional cohort with enrollment from the 2 myositis centers. Functional and Patient-Reported Assessments were completed monthly, including a health assessment questionnaire, patient global disease activity, PROMIS-physical function 20 and functional tests timed up-and-go (TUG), and sit-to-stand (STS)). Participants were asked to use their waist-based Fitbit (≥10 hours/day), ≥ 7 days/month. Average steps per minute & Average peak cadence were evaluated using Fitbit data.

Results: 120 IIM patients (mean age 55.5+/- 13.43, 75% females, 80.8% white), who completed baseline visit were enrolled in the study, comprising 82 in the Main TRC group, 21 in Local TRC and 17 in the local CBC (table 1). There were 51.7% DM, 39.2% PM, and 9.1% NM. The TRC and CBC cohorts were similar in demographics and disease subtypes. Age was significantly correlated with the average steps per minute (Ave Step/min) (p=0.01) but not with ave. peak cadence, showing a decrease in steps with advancing age. Gender, race/ethnicity or disease subtypes were not associated with PAM measures.

On data analysis, 90% patients completed at least one valid day on their Fitbit devices. The compliance with Fitbit was very high with participants wearing devices on most days of the week (Ave. = 6.52 days) for the most visits (Ave. 5.73 visits), with similar results for remote or local recruitment. Ave steps per minute and peak cadence showed strong test-retest reliability (r=0.89 and r=0.86, p< 0.0001 & p= 0.0001) and were strongly correlated within-patient. Regarding validity at baseline, ave steps/mins was significantly associated with myositis, skin disease, extra-muscular global, PROMIS physical function and functional tests, HAQ score but not with other myositis core set measures (Table 2).While the ave. peak cadence was significantly associated with MMT-8, physician and patient global disease activity as well as fatigue, myalgia, myositis, TUG, but not with HAQ, CK, and extra-muscular disease activity (Table 2).

Conclusion: In a large IIM cohort, Fitbit physical activity monitor variables demonstrates favorable compliance and psychometric properties with a strong test-retest reliability and association of several patient and physician-reported measures.

Disclosure: A. Sharma: None; **s. keret**: None; **R. Lomanto Silva**: None; **T. Chandra**: None; **J. Levin**: None; **S. Moghadam-Kia**: None; **C. V. Oddis**: Boehringer-Ingelheim, 5, Cabaletta, 5, EMD Serono, 5, Novartis, 5, Pfizer, 1; **R. Aggarwal**: Actigraph, 2, Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella Bioscience, 2, Corbus, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Mallinckrodt, 5, Merck, 2, Octapharma, 2, Pfizer, 2, 5, Q32, 5, Roivant, 2, Sanofi, 2, Teva, 2.

Abstract Number: 0307

Long-term Prognosis and Recurrence in anti-MDA-5 Antibody-positive Dermatomyositis

Jun Nakamura[1], Takao Nagashima[2] and Kojiro Sato[2], [1]Jichi Medical University, Shimotsuke, Japan, [2]Jichi Medical University, Tochigi, Japan

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

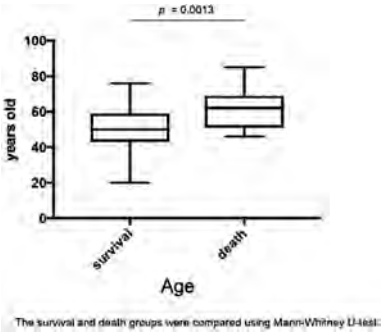
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

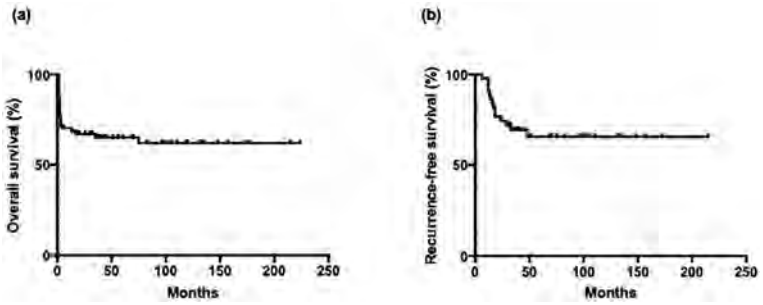
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-melanoma differentiation-associated gene 5 (MDA5) antibody-positive dermatomyositis (DM) is frequently complicated by rapidly progressive interstitial lung disease (ILD) and is life-threatening especially in the early stages. Therefore, triple therapy using glucocorticoid (GC), calcineurin inhibitor (CNI) and cyclophosphamide is recently recommended from the early onset. On the other hand, it has also been known that cutaneous symptoms including skin ulcers, papules on the palmar side, and panniculitis are common and afflict patients. However, the long-term prognosis including not only ILD but also the recurrence of skin symptoms is poorly understood. In this study, we assessed the long-term survival rate and recurrence rate in anti-MDA5 antibody-positive DM.

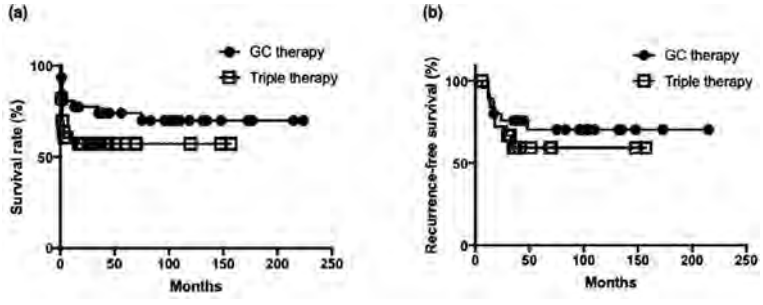
Methods: This retrospective study included patients with anti-MDA5 antibody-positive DM who were admitted to our division from January 2004 to March 2023. Patients who were alive 6 months after the initial hospitalization were classified into the survival group, and those who had died within 6 months were classified into the death group. In addition, the patients were divided into triple therapy (GC, CNI and cyclophosphamide) and GC therapy (GC alone, or GC and CNI). We first analyzed the long-term survival rate in all patients, over 10 years in some patients, and then analyzed it in each group.



The median age of the survival and death group



(a) Survival rate in all patients with anti-MDA5 antibody-positive DM, (b) Recurrence-free survival rate in survival group



(a) Long-term survival rate in Triple and GC therapy, (b) Recurrence-free survival rate in Triple and GC therapy

Results: Sixty-eight patients with anti-MDA5 antibody-positive DM were enrolled, two of whom died of malignant tumors within 6 months of onset and were excluded from the analysis. The median age of the patient was 51.5 (range, 20-85 years), and the number of women was 40 (74%). All but one of the 66 patients had ILD. Forty-seven out of 66 patients (71%) were classified into the survival group and 19 (29%) into the death group. The median age of the death group at onset was significantly higher than that of the survival group (62 and 50 years old, respectively, p = 0.0013, Figure. 1). Survival rate declined rapidly to ∼70% by 13 weeks after admission but did not decline significantly thereafter (Figure 2 (a)). However, a small number of patients died of ILD one to two years after the onset. Long-term follow-up of the survival group showed that dermatomyositis tended to recur until approximately 50 weeks after the initial admission (Figure 2 (b)). The breakdown of recurrence included not only ILD but also exacerbation of skin symptoms such as skin ulcers. Between triple therapy and GC therapy, there was no significant difference in median age (52.5 and 50 years old, respectively, p = 0.1125), female ratio (55.9% and 65.6%, respectively, p = 0.4182) and serum ferritin levels (658.9 ng/ml and 511.9 ng/ml, respectively, p = 0.2519). Furthermore, there was no significant difference in long-term survival and recurrence-free survival between triple therapy and GC therapy (p = 0.18 and 0.49, respectively, Figure 3).

Conclusion: The survival rate of anti-MDA5 antibody-positive DM rapidly declines by three months after onset. When skin symptoms are also taken into account, the recurrence rate remains relatively high until several years after the onset. There was no superiority of Triple therapy over GC therapy with respect to long-term survival and recurrence rate in this study.

Disclosure: J. Nakamura: None; **T. Nagashima**: None; **K. Sato**: None.

Abstract Number: 0308

Burden of Osteoarthritis Attributable to High BMI in 38 OECD Countries: A Benchmarking Analysis

Dhruvkumar Gadhiya[1], Utsav Patel[2], Hiren Chhayani[3], Krushi Shah[3], Sneh Patel[3], Victor Adedara[4], Divya Patel[3] and Hardik Desai[5], [1]St.Luke's University Health, Anderson Campus, Easton, PA, [2]Tulane University, New Orleans, LA, [3]G.M.E. R.S. Medical College, Gandhinagar, Gandhinagar, India, [4]St George's University SOM, True Blue Greneda, True Blue, Grenada, [5]Gujarat Adani Institute of Medical Sciences, Bhuj, India., Bhuj, India

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The burden of osteoarthritis related to high body mass index (BMI) in OECD countries is a significant public health concern. Osteoarthritis is strongly associated with obesity, and the increasing prevalence of obesity in many OECD countries has contributed to the rising burden of osteoarthritis. This study was aim at assessing the Global Burden of Osteoarthritis due to High BMI, in 38 OECD Countries from 1990-2019.

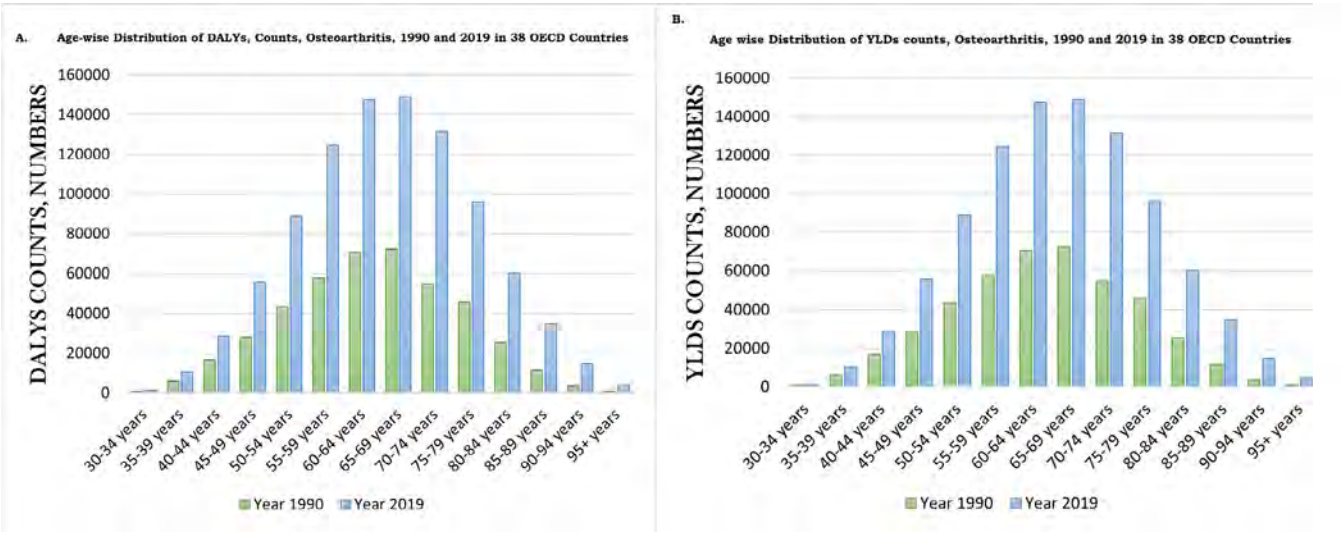
Methods: his study compiled 38 OECD Countries data on the duration of disability caused by osteoarthritis (OA) linked to high BMI from the Global Burden of Disease (GBD) 2019 dataset. The analysis systematically examined the burden of disability attributed to OA in relation to high BMI, considering factors such as age, sex, and annual percentage of change (APC).

Results: There has been a significant increase in the total number of Disability-Adjusted Life Years (DALYs) attributed to Osteoarthritis due to an alarming rise in body mass index (BMI) between 1990 and 2019. The study reveals that the DALYs increased by 116% (95%UI: 102%-144%) during this period, indicating a concerning trend in the burden of the disease.

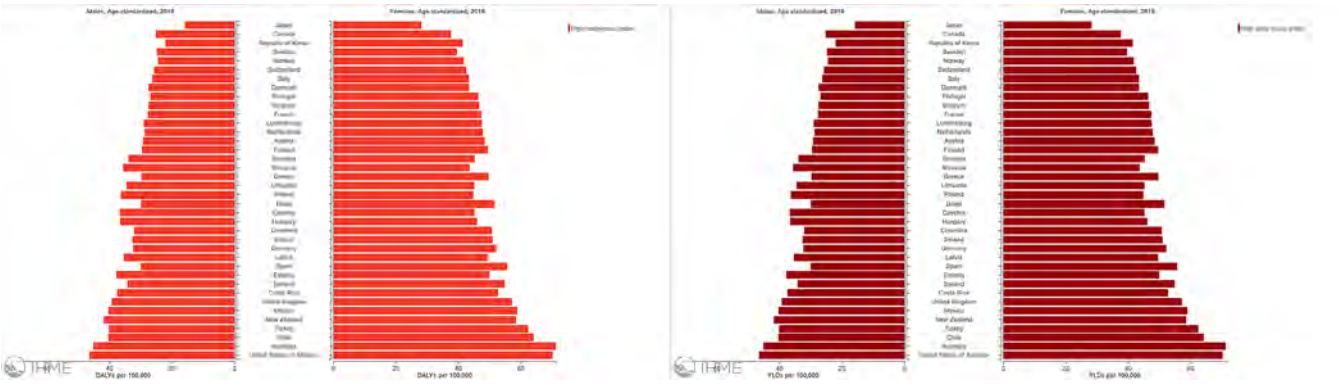
The analysis of age standardized DALYs provides further insights into the impact of Osteoarthritis across different countries. In 2019, the highest age standardized DALYs were observed in the United States, with a rate of 59 per 100,000 individuals (95%UI: 25-128). Following closely behind was Australia, with a substantial burden of Osteoarthritis reflected in the age standardized DALYs.

On the other end of the spectrum, Japan exhibited the lowest age standardized DALYs for Osteoarthritis in 2019, with a rate of 22.44. This suggests a relatively lower burden of the disease in Japan compared to other countries analyzed in the study.

Furthermore, when considering the annual percentage change in DALYs, Australia experienced the highest increase at 47%, indicating a rapid escalation of the disease burden within the population. Chile followed closely behind with a substantial annual percentage change in DALYs. These findings underscore the urgency for targeted interventions and preventive measures to address the rising burden of Osteoarthritis in these countries.



Age-wise distribution of DALYs, Counts, Osteoarthritis, 1990 and 2019 in 38 OECD Countries



Sex wise burden of Osteoarthritis due to High BMI in OECD Countries

Conclusion: The burden of osteoarthritis associated with high BMI in OECD countries is a pressing issue. Combating this burden requires collaborative efforts from policymakers, healthcare providers, and individuals themselves. By promoting healthy lifestyles, early intervention, and evidence-based management strategies, it is possible to reduce the impact of obesity-related osteoarthritis and improve the overall health and well-being of affected individuals and societies.

Disclosure: D. Gadhiya: None; **U. Patel**: None; **H. Chhayani**: None; **K. Shah**: None; **S. Patel**: None; **V. Adedara**: None; **D. Patel**: None; **H. Desai**: None.

Abstract Number: 0309

Efficacy, Safety, Pharmacokinetics and Immunogenicity of Repeated Dosing of GSK3858279 in Patients with Knee Osteoarthritis: A Phase I, Randomized, Double-Blind, Placebo-Controlled Study

Jagtar Singh Nijjar[1], Kathy Abbott-Banner[2], Riju Ray[3], Sam Munoz Vicente[1], Jane H. Bentley[1], Catherine Muya[1], Sarah Siederer[1], Eirini Panoilia[1], Damon Bass[4], Disala Fernando[5] and Edward C. Emery[1], [1]GlaxoSmithKline, Stevenage, United Kingdom, [2]GlaxoSmithKline, Brentford, United Kingdom, [3]GSK Research, Triangle Park, [4]GlaxoSmithKline, Upper Providence, RI, [5]GlaxoSmithKline, Cambridge, United Kingdom

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic pain is an unmet need in osteoarthritis (OA) as current therapies have limited analgesia and side effects. The chemokine CCL17 mediates inflammatory pain and blocking CCL17 (via anti-CCL17 monoclonal antibodies [mAb] or CCL17 knock-out) reduces pain and joint disease in murine arthritis. GSK3858279 is a novel, high affinity, human mAb that functionally inhibits CCL17. The objective of this study is to present efficacy, safety, pharmacokinetic (PK) and immunogenicity data from Part B of a first-in-human, 2-part, phase I, randomized, double-blind, placebo (PBO)-controlled study evaluating GSK3858279 for OA pain (NCT03485365).

Table. Baseline characteristics

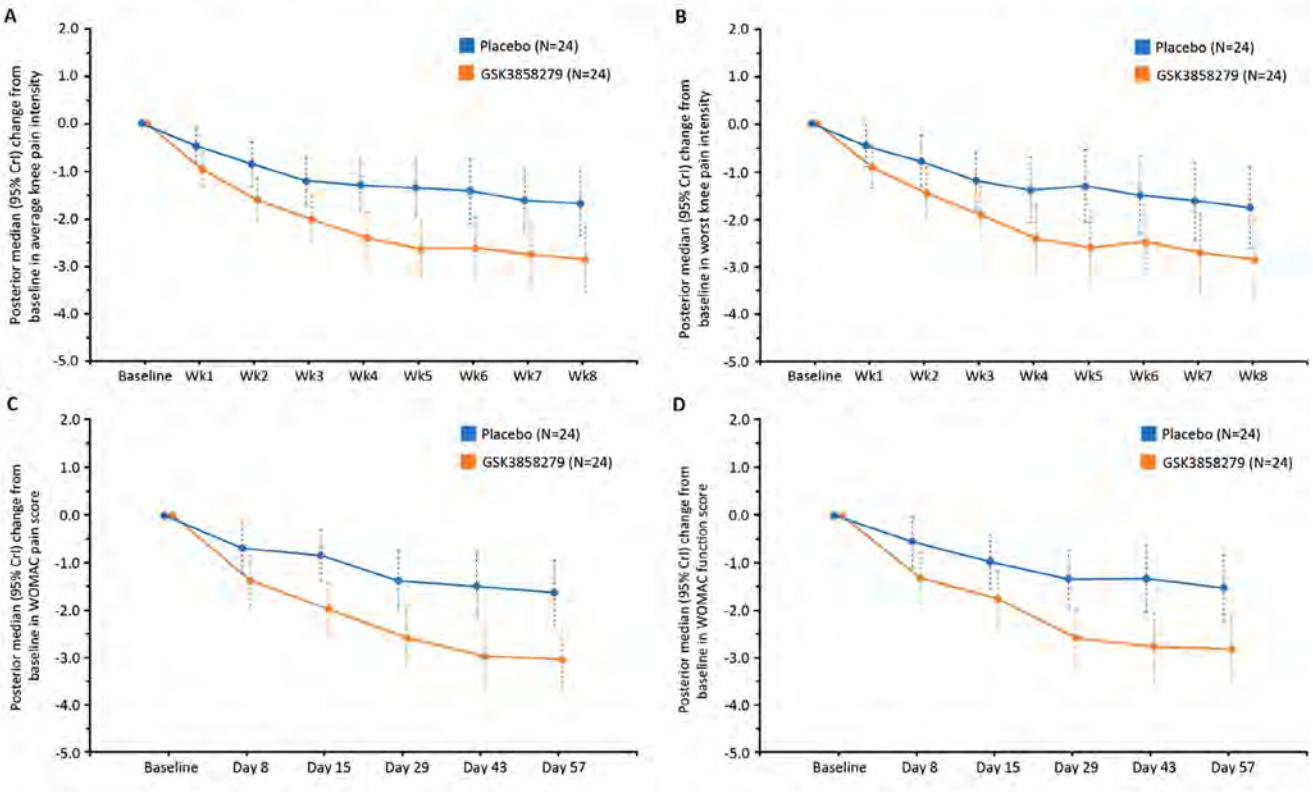
	Placebo (N=24)	GSK3858279 (N=24)	All (N=48)
Male	11 (46)	16 (67)	27 (56)
Age, years	59.0 [51–75]	58.5 [46–74]	59.0 [46–75]
Race			
White	24 (100)	23 (96)	47 (98)
Asian	0 (0)	1 (4)	1 (2)
Body mass index, kg/m^2	28.3 [24–35]	29.7 [23–34]	29.2 [23–35]
Kellgren and Lawrence score			
Grade 2	12 (50)	8 (33)	20 (42)
Grade 3	8 (33)	8 (33)	16 (33)
Grade 4	4 (17)	8 (33)	12 (25)
Average knee pain intensity[a]	5.5 [4.0–7.8]	5.3 [4.0–7.4]	5.3 [4.0–7.8]
Worst knee pain intensity[a]	6.0 [4.0–8.0]	6.2 [4.2–8.6]	6.1 [4.0–8.6]
WOMAC Pain score[a]	5.3 [2.6–9.0]	5.5 [2.8–7.0]	5.4 [2.6–9.0]
WOMAC Function score[a]	5.2 [1.6–9.4]	5.5 [1.7–7.5]	5.4 [1.6–9.4]

Data are *n* (%) or median [range]. [a]11-point numerical rating scale: 0 (no pain/difficulty) to 10 (worst imaginable pain/difficulty). WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Methods: Participants with knee OA per ACR criteria, Kellgren and Lawrence (KL) score ≥2 and average daily pain score 4–9 by 11-point numerical rating scale (NRS), were randomized (1:1) to weekly subcutaneous (SC) GSK3858279 or PBO for 8 weeks. Co-primary endpoints were change from baseline (CFB) to Week 8 in average and worst knee pain intensity. Participants completed a daily pain NRS. Pain medication was prohibited, except paracetamol (≤3g/day) as rescue medication (not 24h before a study visit). Exploratory endpoints included CFB in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and function scores. Samples for analysis of GSK3858279 serum concentration and immunogenicity were collected to Week 20. A Bayesian repeated measures model using non-informative priors was fitted to CFB data; 95% credible intervals (CrI) for treatment differences were calculated.

Results: All 48 participants in Part B completed the study (2 participants in the PBO arm discontinued treatment). Participant characteristics were comparable; however, more participants in the GSK3858279 arm were male and KL grade 4 (**Table**). GSK3858279 was rapidly absorbed after SC administration (median T_{max} ~2 days), with steady concentrations predicted by Week 8. Anti-GSK3858279 Abs were detected in 5/24 (21%) and 1/24 (4%) participants who received GSK3858279 and PBO, respectively; PK profiles for these participants were consistent with profiles in those without anti-drug Abs. For the co-primary endpoints of average and worst knee pain intensity, GSK3858279 showed greater improvement versus PBO at all timepoints (**Figure**). At Week 8, the difference (95% CrI) in CFB for GSK3858279 versus PBO was –1.18 (–2.15, –0.20) and –1.09 (–2.29, 0.12) for average and worst knee pain intensity, respectively (probability of true difference < 0: >99% and 96%). GSK3858279 showed greater improvement in WOMAC pain and function scores versus PBO (**Figure**). At Day 57, the difference (95% CrI) in CFB for GSK3858279 versus PBO was –1.41 (–2.35, –0.46) for pain and

Figure. Posterior median change from baseline in average (A) and worst (B) knee pain intensity score, and WOMAC pain (C) and function (D) score



Average and worst knee pain intensity and WOMAC pain and function were assessed by participants using an 11-point numerical rating scale, where scores range from 0 (no pain/difficulty) to 10 (worst imaginable pain/difficulty). All analyses were performed in the intent-to-treat population using a Bayesian repeated measures model adjusting for treatment, week, baseline and the treatment by week and baseline by week interactions using non-informative priors. (A, B) For each assessment visit, the mean average and mean worst pain scores for the 7 days preceding the visit were calculated for each participant. Data available for n=24 for all visits for GSK3858279, and for n=24 (Baseline, Wks 1 and 2), n=23 (Wks 3, 4 and 6), and n=22 (Wks 5, 7, and 8) for placebo. (C, D) Across the assessed timepoints, data were available for n=22–24 for both GSK3858279 and placebo. CrI, credible interval; Wk, Week; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

–1.29 (–2.28, –0.29) for function (probability of true difference < 0: >99% for both). Adverse events (AE) occurred in 21/24 (88%) and 15/24 (63%) participants, GSK3858279 and PBO, respectively. There were no serious AEs or deaths.

Conclusion: Weekly dosing for 8 weeks with GSK3858279 has clinical activity (improved pain scores) and a favourable safety profile in patients with OA knee pain. These compelling data warrant further study of the effectiveness and safety of GSK3858279 in people with OA pain.

Disclosure: J. Singh Nijjar: GSK, 3, 11; **K. Abbott-Banner**: GSK, 3, 11; **R. Ray**: GSK, 3, 11; **S. Munoz Vicente**: GSK, 3, 11; **J. Bentley**: GSK, 3, 11; **C. Muya**: GSK, 3, 11; **S. Siederer**: GSK, 3, 11; **E. Panoilia**: GSK, 3, 11; **D. Bass**: GSK, 3, 11; **D. Fernando**: GSK, 3, 11; **E. Emery**: GSK, 3, 11.

Abstract Number: 0310

Implementing an Osteoarthritis Management Program to Deliver Guideline-Driven Care for Knee and Hip Osteoarthritis in a U.S. Academic Health System

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: To assess patient outcomes from an Osteoarthritis Management Program (OAMP) situated in an academic medical center.

Methods: Eligibility for this open cohort study included adults with knee or hip osteoarthritis (OA) who attended at least one OAMP visit from 7/1/2017 to 1/15/2021. The OAMP was designed to deliver 1-5 visits across 12 months. A multidisciplinary team provided OA education and self-management; exercise and nutrition; weight loss; pharmacologic management; and assessed mood, sleep, quality of life, and disordered eating patterns. Patient BMI, pain and function were assessed at each visit. Primary patient outcomes included pain rated on the 0-10 Visual Analogue Scale (VAS) and function assessed by the 30-Second Chair Rise test and Timed-Up-And-Go (TUG).

Results: Of the 953 patients attending 2531 visits, most were female (72.6%), older (62.1 ± 10.8), and Caucasian (91.1%). Half (48.5%) were employed and most were insured by Medicare (51.2%) or commercial health insurance (38.8%). Obesity was prevalent (BMI 40.9 ± 10), and bilateral knee OA was the most common diagnosis (42.6%). Assist device use was common (32.95%). Pain changed insignificantly from an average baseline in men of 4.22 ± .177 (0-10 VAS) to 4.78 ± .63 at 12 months. Women also had no significant change in pain. Overweight or obese men had a decrease in BMI over the first 12 months from baseline BMI of 42.25 ± .58 to 40.10 ± .92. Overweight or obese women did not had a significant decrease in weight with baseline BMI 42.22 ± .37 and 12 month BMI 41.28 ± .58. Baseline functional testing scores were lower than normal values for a population of this age, with no significant differences between women and men or after completion of OAMP treatment. Patients with severe baseline pain (7-10 on the VAS) were 94% (95% CI 1.61-2.36) more likely to report decreased pain after OAMP treatment than patients with lower baseline pain. Patients with a starting BMI of 40+ were

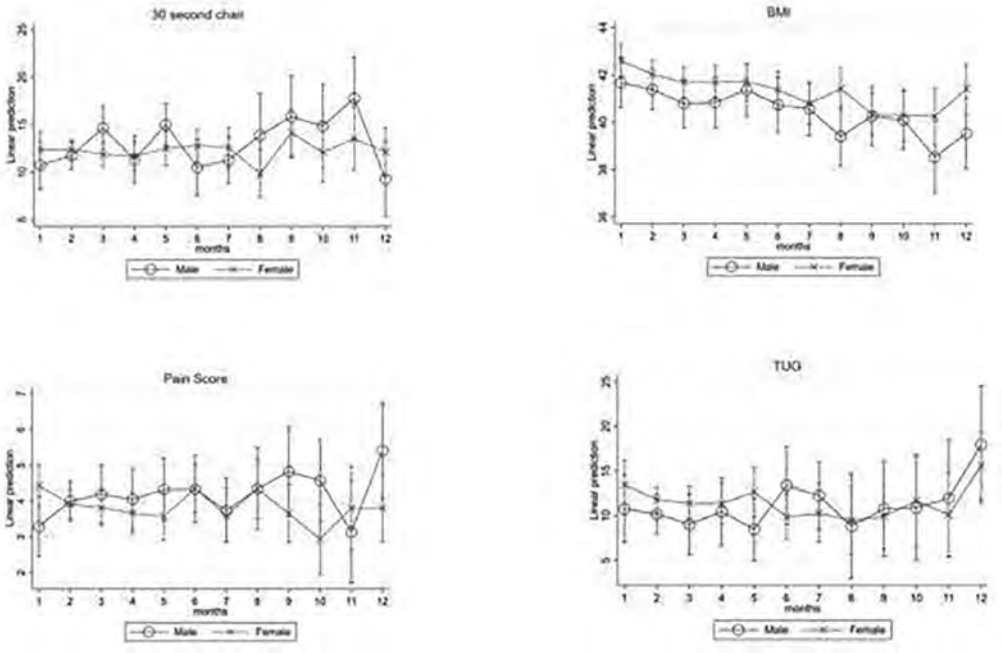

Figure 1. Change in BMI, Pain (0-10 VAS), 30 sec chair rise test, and TUG time from baseline to 12 months.

Table 1. Patient Characteristics at Initial Clinic visit

Table 1. Patient Characteristics at Initial Clinic Visit				
Baseline Characteristic	Total (n=953)	Female (n=692, 72.6%)	Male (n=261, 27.4%)	Test Statistics
Age in years, mean (SD)	62.1 (10.8)	61.9 (10.8)	62.5 (10.5)	p=<0.001
Employment, n (%)				
Working	462 (48.5)	320 (46.2)	142 (54.4)	
Retired	301 (31.6)	218 (31.5)	83 (31.8)	
Disabled	70 (7.3)	53 (7.6)	17 (6.5)	
Unemployed	39 (4.1)	35 (5.05)	4 (1.5)	c2 = 11.9 (4)
Not recorded	81 (8.5)	66 (9.5)	15 (5.7)	p = 0.02
Insurance, n (%)				
Medicare	488 (51.2)	361 (52.2)	127 (48.6)	
Medicaid	51 (5.4)	39 (5.6)	12 (4.6)	
Commercial	370 (38.8)	263 (38.0)	107 (41.0)	c2 = 2.26 (3)
Self-pay	44 (4.6)	29 (4.2)	15 (5.7)	p = 0.51
Osteoarthritis Diagnosis, n (%)				
Unilateral Knee OA	293 (30.8)	224 (32.3)	69 (26.4)	
Bilateral Knee OA	406 (42.6)	302 (43.6)	104 (39.8)	
Unilateral Hip OA	162 (17.0)	103 (14.8)	59 (22.6)	
Bilateral Hip OA	51 (5.3)	33 (4.7)	18 (6.9)	
Knee + Hip OA	26 (2.7)	22 (3.2)	4 (1.5)	c2 = 15.7 (5)
Non Knee or Hip OA	15 (1.6)	8 (1.1)	7 (2.6)	p = 0.007
Body Mass Index, n (%)				
All, mean(SD)	40.9 (10.0)	41.0 (9.9)	40.8 (10.3)	p = 0.82
Visual Analog Scale 0-10 pain ratings by severity categories, mean(SD)	4.44 (2.8)	4.52(2.79)	4.23 (2.80)	p = 0.16
None = 0 n (%)	101 (10.6)	71 (10.3)	30 (11.5)	
Mild = 1-3	250 (26.2)	170 (24.5)	80 (30.6)	
Moderate = 4-6	290 (30.4)	214 (30.9)	76 (29.1)	
Severe = 7-10	239 (25.1)	177 (25.5)	62 (23.7)	c2 = 6.76 (4)
Not recorded	73 (7.7)	60 (8.6)	13 (4.9)	p = 0.15
Timed Up & Go (TUG), mean(SD)				
Seconds to rise, walk 10 feet, return, and sit n=495/953 (51.9%)	12.25 (7.54)	12.56 (7.54)	11.49 (5.37)	z = -2.47
Not recorded, n=458/953 (48.1%)				p = 0.013
30-Second Chair Stand Test, mean(SD)				
Rise and sit repetitions n=495/953 (51.9%)	11.49 (4.78)	11.34 (4.62)	11.88 (5.16)	z = 1.97
Not recorded, 458/953 (48.1%)				p = 0.047

Table 2. Clinic Utilization and Growth. *Psychologist started March 2021. **COVID-19 Clinic Closures 3/9/20-5/31/20. ***Clinic opened July 1, 2017.

	Visits				No Show				Access	cFTE				
	Total Visits	F2F	Phone	Video	Total	F2F	Phone	Video	New Patient Lag	MD	APP	PT	RD	BH
2017***	111	111	0	0	N/A	N/A	N/A	N/A	N/A	0.1	0	0.1	0.1	0.1
2018	658	658	0	0	75 (10.23%)	10.23%	0	0	63 days	0.2	0.2	0.4	0.4	0
2019	863	863	0	0	119 (12.12%)	12.12%	0	0	89.5 days	0.2	0.2	0.4	0.4	0
2020**	730	436	138	156	64 (8.06%)	11.60%	3.50%	1.30%	11.5 days	0.2	0.4	0.6	0.6	0
2021	1829	1498	83	248	153 (7.72%)	8.60%	1.20%	4.20%	32 days	0.2	0.4	0.6	0.6	0.2*
2022	1969	1790	62	117	N/A	6.10%	0	7.10%	39 days	0.2	0.4	0.6	0.6	0.2

60% (95% CI 1.2-2.1) more likely to lose weight than patients with a lower BMI. Patients who did not have health insurance had a shorter treatment duration.

Conclusion: This open cohort study of a guideline-driven OAMP demonstrates that patients with the highest baseline pain and BMI were more likely to experience reductions in pain and BMI respectively. Uninsured patients had the shortest treatment duration. Next steps will be to identify the baseline characteristics of patients who will benefit most from OAMP treatment and to continue exploration of barriers to guideline-recommended care. OA continues to be an under-treated chronic disease and these results an important start to understanding patient outcomes related to OAMP programs within the U.S. healthcare system.

Disclosure: K. Miller: None; **D. Vundamati**: None; **L. Baier**: None; **R. Brown**: None; **T. Yue Yu**: None; **C. Bartels**: Pfizer, 5.

Abstract Number: 0311

Heterogeneity and Natural History of Medial Fixed Joint Space Width in Healthy Knees Among Women and Men: Data from Three Large Cohort Studies

Kent Kwoh[1], Erin Ashbeck[2], Edward Bedrick[1], Yvonne Golightly[3], Zong-Ming Li[1], Jean liew[4], Amanda Nelson[5], Tuhina Neogi[6], Xiaoxiao Sun[1] and Jeffrey Duryea[7], [1]University of Arizona, Tucson, AZ, [2]University of Arizona Arthritis Center, Tucson, AZ, [3]University of Nebraska Medical Center, Omaha, NE, [4]Boston University, Boston, MA, [5]University of North Carolina at Chapel Hill, Chapel Hill, NC, [6]Boston University School of Medicine, Boston, MA, [7]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Radiographic joint space width (JSW) is commonly used to assess structural progression in randomized controlled trials and observational studies of knee osteoarthritis (KOA). No reference standards for healthy knee aging in terms of JSW have been established. Our objective is to establish healthy knee aging norms for medial fixed JSW (fJSW) by estimating sex-specific distribution percentiles in knees without OA (i.e., no osteophytes [i.e., Kellgren-Lawrence grade [KLG] grade 0]) and no frequent knee pain, from age 45 to 90 years.

Methods: We identified x-rays of healthy knees, defined as knees with no evidence of OA (i.e., KLG grade 0) and no reported frequent knee pain (i.e., pain on more than half the days of the past 30 days) from the Johnston County Osteoarthritis Study (JoCoOA), the Multicenter Osteoarthritis Study (MOST), and the Osteoarthritis Initiative (OAI). Participants in all three studies underwent fixed flexion PA knee radiography at baseline and during ~7 years of follow-up for MOST and OAI and between 1999 to 2018 for JoCoOA. We fit a linear mixed model for medial fJSW (x=0.250) with random effects for participants and knees within participants; fixed effects for age as a cubic polynomial, sex, race, and study; and all two-way and three-way interactions to allow for study heterogeneity and differences by sex and race, where age was the metameter of time. Only time-points with KLG=0 x-rays and no participant-reported frequent knee pain were included in the analysis.

Results: The sample consisted of 3,116 participants who contributed 4,670 knees with at least one healthy time point, for a total of 12,347 healthy time point observations, including 2,349 from JoCoOA, 5,760 from MOST, and 4,238 from OAI. Participants self-identified as Non-Hispanic White (83%) and African American (17%), with 58% reporting female sex. Figure 1 shows sex-specific distributions of medial fJSW in healthy knees from age 45 to 90 years, with estimated percentile curves.

Conclusion: The natural history of medial fJSW among healthy knees is gradual loss with age. Women experiencing healthy knee aging had less fJSW than men across the spectrum of age. A large heterogeneity of medial fJSW in healthy knees was observed at all ages between 45 and 90 years. Healthy knee aging reference norms will aid our understanding of the natural history of fJSW.

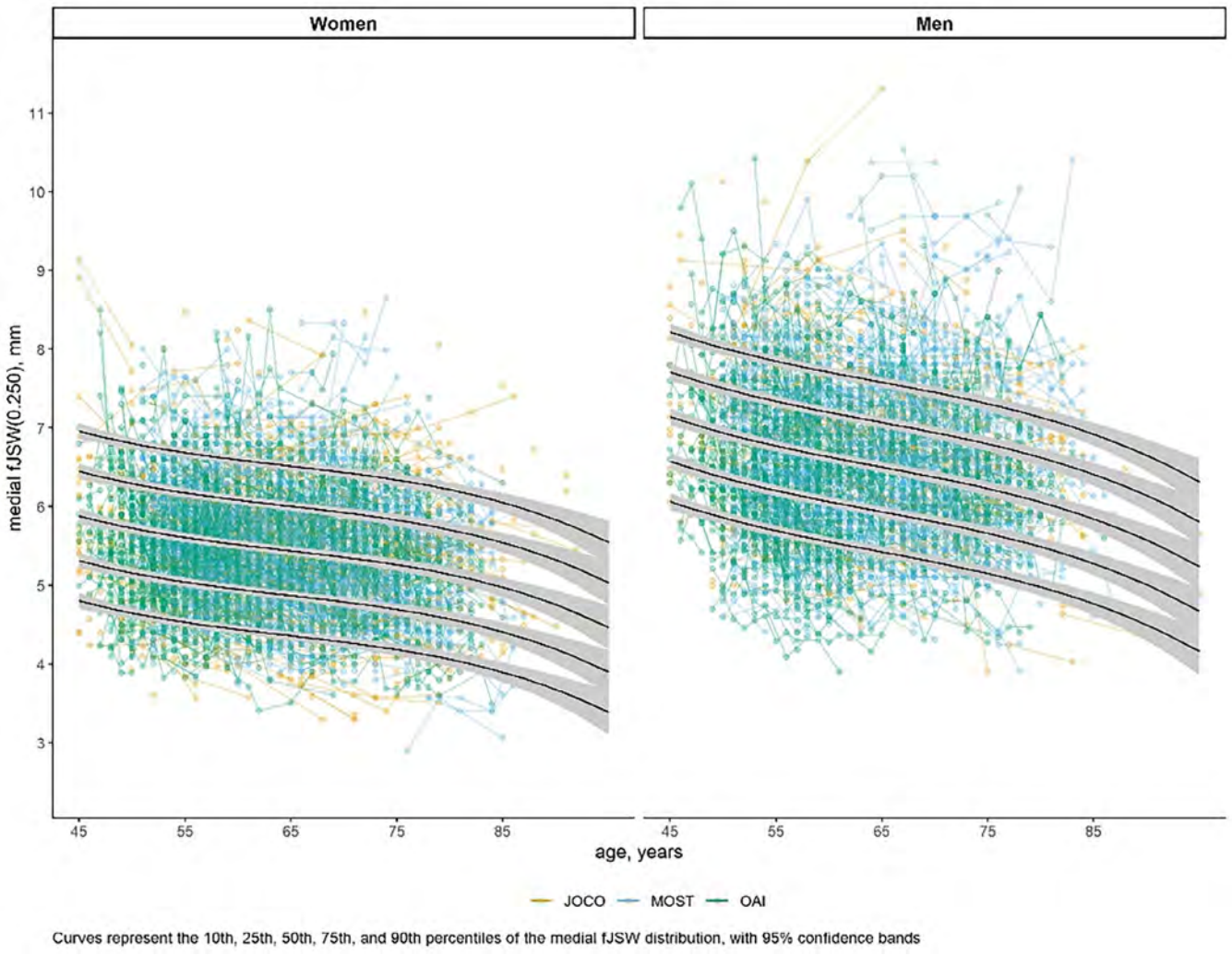

Figure 1. Healthy knees by sex

Disclosure: K. Kwoh: Express Scripts, 2, Kolon Tissue Gene, 12, IDMC, Moebius, 2, Novartis, 1, Trial Spark, 2, Xalud, 1; **E. Ashbeck**: None; **E. Bedrick**: None; **Y. Golightly**: None; **Z. Li**: None; **J. liew**: None; **A. Nelson**: None; **T. Neogi**: None; **X. Sun**: None; **J. Duryea**: None.

Abstract Number: 0312

Frontal Lobe Activation and Gait Alterations During Single- and Dual-task Walking in People with Knee Osteoarthritis: A Functional Near-infrared Spectroscopy Study

Soyoung Lee, Meryem Yücel, Claudio Ferre, Baekdong Cha, Ehyun Kim and Deepak Kumar, Boston University, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Altered gait patterns, including high variability or muscular co-contraction, can increase fall risk and worsen disease progression in people with knee osteoarthritis (OA). However, the neural substrates underlying altered motor performance during walking in this population are unknown. Over-recruitment and reduced frontal lobe capacity during walking with or without a cognitive task have been reported in other populations with gait impairments but have not been examined in knee OA. Our objectives were (1) to assess frontal lobe activation during single- and dual-task walking in people with knee OA and (2) to examine the association of frontal lobe activation with motor and cognitive performance.

Methods: Individuals with symptomatic knee OA (n=20, **Table 1**) completed three tasks, (1) single-task walking (STW) at a self-selected pace for 8 bouts of 30s interspersed with 11-15s standing periods, (2) subtraction by 7 from a 3-digit number while seated (Serial 7), and (3) dual-task walking (DTW), a combination of STW and Serial 7. During these tasks, participants wore a functional Near-Infrared Spectroscopy (fNIRS) device to assess frontal lobe activation and inertial sensors on the trunk and legs for gait assessment. Activation in bilateral superior, middle, and inferior frontal lobes was assessed as the change in oxygenated hemoglobin concentration (HbO) in each task relative to quiet standing or sitting. Motor performance during walking was assessed as step time coefficient of variance (CoV) and gait speed. Cognitive performance was assessed as the percentage of correct counts during serial subtraction. We used repeated measures ANOVA to compare the outcomes between tasks and assessed the correlation between middle frontal lobe HbO and motor and cognitive performance in each task.

Results: Frontal lobe HbO was higher during STW and DTW compared to Serial 7 but not significantly different between STW and DTW (**Figure 1A**). Step time CoV was not different between STW and DTW, but gait speed was lower during DTW; cognitive performance was not different between Serial 7 and DTW (**Figure 1B**). Greater middle frontal lobe HbO was correlated with lower step time CoV during STW and DTW; none of the other correlations were significant (**Figure 2**).

Table1. Participant characteristics

	n=20
Age, (years), Mean (SD)	64.0 (8.9)
Female, n (%)	9 (45.0)
BMI, kg/m^2, Mean (SD)	30.9 (5.6)
KOOS Pain, Mean (SD)	67.5/100 (12.5)
MMSE Score	28.9 (0.8)

SD = standard deviation; KOOS = Knee injury and Osteoarthritis Outcome Score; MMSE = Mini-Mental State Examination.

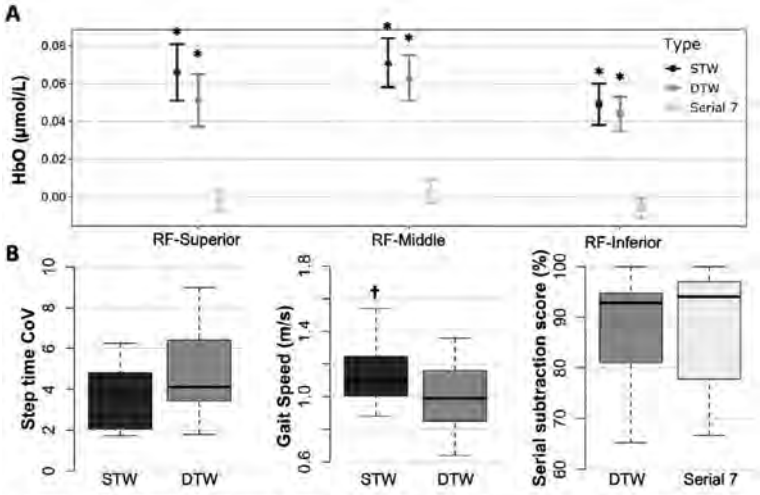

Figure 1. A. Mean and standard error for HbO in all subregions of right frontal lobe in each task. Similar patterns were found in the left side frontal lobe. *Indicates significant difference compared to Serial 7 at $p < 0.05$; HbO: concentration changes in oxygenated hemoglobin. RF: Right frontal lobe. **B.** Distribution of motor and cognitive performance outcomes between tasks. †Indicates significant difference compared to DTW at $p < 0.05$; Middle line in the box = Median; Lower and Upper line of the box = 1st and 3rd quartiles; CoV: Coefficient of Variance = (Standard deviation / Mean)*100; Serial 7 Score (%) = (Number of correct counts / Number of total counts)*100; STW: Single-task walking; DTW: Dual-task walking.

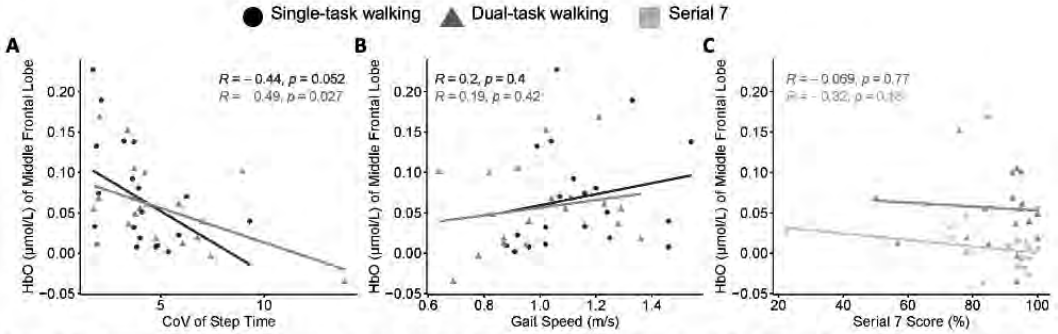

Figure 2. Correlation between bilateral middle frontal lobe HbO and (A) step time CoV during STW and DTW, (B) gait speed during STW and DTW, and (C) serial subtraction score during Serial 7 and DTW. *CoV: Coefficient of Variance; HbO: concentration changes in oxygenated hemoglobin; STW = single-task walking; DTW = dual-task walking*

Conclusion: Greater frontal lobe HbO during STW and DTW vs. Serial 7 suggests a greater need for executive control during walking. This is supported by the correlation between higher frontal lobe activation and lower gait variability (i.e., better motor performance). However, an absence of a further increase in HbO from STW to DTW reflects a lack of additional executive resources (i.e., ceiling effect). This is aligned with prior studies in other populations with gait impairments (e.g., Post-stroke, Parkinson's Disease). It also appears that people with knee OA prioritized the cognitive task during DTW given the deterioration in motor task performance compared to STW but similar cognitive performance compared to Serial 7. This may increase their risk for instability or falls during real-world walking conditions that typically require dual-tasking, and interventions to improve dual-task walking performance may need to be considered.

Disclosure: S. Lee: None; **M. Yücel**: None; **C. Ferre**: None; **B. Cha**: None; **E. Kim**: None; **D. Kumar**: Eli Lilly, 5, Pfizer, 5.

Abstract Number: 0313

The Influence of Pain Catastrophizing on Pain and Function After Knee Arthroplasty for Osteoarthritis

Diana, Xin Hui Chan[1], Seyed Ehsan Saffari[2], Steven, Bak Siew Wong[3], Seng Jin Yeo[1], Vikki Wylde[4], Julian Thumboo[1] and **Ying Ying Leung**[1], [1]Singapore General Hospital, Singapore, Singapore, [2]Center for Quantitative Medicine, Duke-NUS Medical School, National University of Singapore, Singapore, Singapore, [3]Sengkang General Hospital, Singapore, Singapore, [4]University of Bristol, Bristol, United Kingdom

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate the association between pre-operative pain catastrophizing and pain and function outcomes up to one year after knee arthroplasty.

Methods: We used data from a cohort study of patients undergoing primary arthroplasty (either total knee replacement or unicompartmental knee replacement) for knee osteoarthritis. Pain catastrophizing was collected pre-operatively using the Pain Catastrophizing scale (PCS). Other baseline variables included demographics, body mass index, radiographic severity, anxiety, depression, and knee pain and function assessed using the Western Ontario and McMaster University Index (WOMAC). Patients completed the WOMAC at 6- and 12-months after arthroplasty. WOMAC pain and function scores were converted to interval scale and the association of PCS and changes of WOMAC pain and function were evaluated in generalized linear regression models with adjustment with confounding variables.

Results: Of the 1,200 patients recruited into the cohort study, 1136 underwent arthroplasty, 1102 provided data at 6-months post-operative and 1089 provided data at 12-months post-operative. Mean (SD) age of participants was 65.9 (7.0) years, 70% were female, 84% were Chinese, and 92% had a total knee replacement. PCS was associated with a change in WOMAC pain at both 6- and 12-months post-operative after adjustment. PCS was associated with a change in WOMAC function in univariate analysis but not after adjustment in multivariable models.

Table 1. Variables associated with change in WOMAC pain at 6-months.

	Univariate model		Multivariable model	
Variables	β (95% CI)	p value	β (95% CI)	p value
Age	0.04 (0.01, 0.06)	0.015	-	-
Sex (female vs. male)	-0.73 (-1.15, -0.31)	0.001	-0.34 (-0.71, 0.03)	0.071
BMI	-0.07 (-0.11, -0.02)	0.002	0.03 (-0.01, 0.07)	0.142
Education (Secondary or above vs primary)	0.18 (-0.21, 0.58)	0.365	-	-
Radiographic severity (KLs3 vs. KL4)	**-0.75 (-1.15, -0.36)**	**<0.001**	**-0.87 (-1.21, -0.53)**	**<0.001**
UKA vs. TKA	0.08 (-0.63, 0.79)	0.834	-	-
Functional comorbidity index	-0.27 (-0.45, 0.09)	0.003	-0.17 (-0.18, 0.15)	0.838
HADS – anxiety	-0.11 (-0.16, -0.06)	<0.001	0.05 (-0.01, 0.11)	0.122
HADS - depression	-0.16 (-0.22, -0.10)	<0.001	0.03 (-0.05, 0.11)	0.460
Baseline WOMAC total score*	**-0.26 (-0.29, -0.24)**	**<0.001**	**-0.26 (-0.29, -0.23)**	**<0.001**
Pain Catastrophizing scale	**-0.08 (-0.10, -0.06)**	**<0.001**	**-0.02 (-0.04, -0.00)**	**0.024**

Variables with P<0.1 were entered into analysis. *Rasch transformed interval score was used.
Bold: variables statistically significantly associated with outcome of interest in the model
Abbreviations. All figures given as mean (standard deviation) unless specified otherwise.
Abbreviations. BMI: body mass index; CI: confidence intervals; HADS: hospital anxiety and depression scale; KA: knee arthroplasty; KL: Kellgren-Lawrence grading; TKA: total knee arthroplasty; UKA: unicompartmental knee arthroplasty; WOMAC: Western Ontario and McMaster University Index; vs.: versus

Conclusion: In this large cohort study, pre-operative pain catastrophizing was associated with lower improvements in pain at 6-months and 12-months after arthroplasty. Future interventional studies are needed to evaluate if reducing pre-operative pain catastrophizing can improve pain outcomes after arthroplasty.

Disclosure: D. Chan: None; **S. Saffari**: None; **S. Wong**: None; **S. Yeo**: None; **V. Wylde**: None; **J. Thumboo**: None; **Y. Leung**: AbbVie/Abbott, 6, DKSH, 6, Janssen, 6, Novartis, 6, Pfizer, 6.

Abstract Number: 0314

Lack of Systemic Effects from Intra-articular XT-150 for the Treatment of Moderate to Severe Pain Due to OA of the Knee: Safety Results from a Phase 2 Trial

Leonard Kapural[1], Stephen D. Collins[2], Eric Grigsby[3], Mark McBride[4], Jayson Rieger[5], Morgan Stokes[6], **Howard Rutman**[6] and Flavia Cicuttini[7], [1]Center for Clinical Research, Winston-Salem, NC, [2]Xalud Therapeutics, Inc., Chicago, IL, [3]Neurovations Clinical Research, Napa, CA, [4]Instat Clinical Research, Chatham, NJ, [5]PBM Capital, Charlottesville, VA, [6]Xalud Therapeutics, Inc., Berkeley, CA, [7]Monash University, Melbourne, Australia

SESSION INFORMATION
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Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: This study (NCT04124042) was designed to assess the safety, tolerability, and efficacy of XT-150, a non-viral gene therapy, in adult participants with moderate to severe pain due to osteoarthritis (OA) of the knee. XT-150 is a plasmid designed to locally express a proprietary version of the anti-inflammatory cytokine, interleukin (IL)-10. IL-10 has been shown to play a key role in pain reversal but has proven a challenging therapeutic candidate due to its short half-life.[1]

Table 1: Summary of Treatment Administered

	Number (%) of Participants Dosed					
	0.15 – 0.15 mg XT-150 (N=49)	0.15 – 0.45 mg XT-150 (N=47)	0.45 – 0.15 mg XT-150 (N=47)	0.45 – 0.45 mg XT-150 (N=47)	Placebo – 0.15 mg XT-150 (N=48)	Placebo – 0.45 mg XT-150 (N=48)
Stage A						
First dose administered	49 (100.0)	47 (100.0)	47 (100.0)	47 (100.0)	48 (100.0)	48 (100.0)
Dosed per protocol						
Yes	49 (100.0)	46 (97.9)	47 (100.0)	47 (100.0)	48 (100.0)	48 (100.0)
No	-	1 (2.1)[a]	-	-	-	-
Treatment						
0.15 mg XT-150	49 (100.0)	46 (97.9)	-	-	-	-
0.45 mg XT-150	-	1 (2.1)	47 (100.0)	47 (100.0)	-	-
Placebo	-	-	-	-	48 (100.0)	48 (100.0)
Stage B						
Second dose administered	39 (79.6)	41 (87.2)	37 (78.7)	41 (87.2)	43 (89.6)	43 (89.6)
Dosed per protocol						
Yes	39 (79.6)	41 (87.2)	36 (76.6)	41 (87.2)	43 (89.6)	43 (89.6)
No	-	-	1 (2.1)	-	-	-
Treatment						
0.15 mg XT-150	39 (79.6)	-	37 (78.7)	-	43 (89.6)	-
0.45 mg XT-150	-	41 (87.2)	-	41 (87.2)	-	43 (89.6)

a. R035 was randomized to 0.45 mg XT-150 but inadvertently received 0.15 mg XT-150.

Table 2: Summary of Related Treatment-Emergent Adverse Events by Treatment (Total)

	Number (%) of Participants with TEAEs [Number of TEAEs]										
	On or After First Dose and Prior to Second Dose				Post Second Dose						
Preferred Term	0.15 mg XT-150 (N=96)	0.45 mg XT-150 (N=94)	Placebo (N=96)	All Participants (N=286)	0.15 – 0.15 mg XT-150 (N=39)	0.15 – 0.45 mg XT-150 (N=41)	0.45 – 0.15 mg XT-150 (N=37)	0.45 – 0.45 mg XT-150 (N=41)	Placebo - 0.15 mg XT-150 (N=43)	Placebo - 0.45 mg XT-150 (N=43)	All Participants (N=244)
Injection site pain	1 (1.0) [1]	-	-	1 (0.3) [1]	-	-	-	-	-	-	-
Injection site swelling	1 (1.0) [1]	-	-	1 (0.3) [1]	-	-	-	-	-	-	-
Instillation site warmth	-	-	-	-	-	-	-	1 (2.4) [1]	-	-	1 (0.4) [1]
Arthralgia	2 (2.1) [2]	-	-	2 (0.7) [2]	-	-	-	-	-	1 (2.3) [1]	1 (0.4) [1]
Total Related TEAEs	4 (4.2) [4]	-	-	4 (1.4) [4]	-	-	-	1 (2.4) [1]	-	1 (2.3) [1]	2 (0.8) [2]

Abbreviation: TEAE=treatment-emergent adverse event
AEs were graded for severity using the Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 and coded using Medical Dictionary of Regulatory Affairs (MedDRA) Version 23.

Table 3: Overall Summary of TEAEs

	Number (%) of Participants with TEAEs [Number of TEAEs]										
	On or After First Dose and Prior to Second Dose				Post Second Dose						
	0.15 mg XT-150 (N=96)	0.45 mg XT-150 (N=94)	Placebo (N=96)	All Participants (N=286)	0.15 – 0.15 mg XT-150 (N=39)	0.15 – 0.45 mg XT-150 (N=41)	0.45 – 0.15 mg XT-150 (N=37)	0.45 – 0.45 mg XT-150 (N=41)	Placebo - 0.15 mg XT-150 (N=43)	Placebo - 0.45 mg XT-150 (N=43)	All Participants (N=244)
Any TEAEs	30 (31.3) [62]	53 (56.4) [107]	38 (39.6) [114]	121 (42.3) [283]	12 (30.8) [27]	14 (34.1) [18]	18 (48.6) [28]	16 (39.0) [32]	9 (20.9) [15]	18 (41.9) [29]	87 (35.7) [149]
Drug-related TEAEs	4 (4.2) [4]	-	-	4 (1.4) [4]	-	-	-	1 (2.4) [1]	-	1 (2.3) [1]	2 (0.8) [2]
Mild TEAEs	22 (22.9) [36]	36 (38.3) [59]	27 (28.1) [52]	85 (29.7) [147]	6 (15.4) [17]	6 (14.6) [6]	12 (32.4) [16]	8 (19.5) [15]	6 (14.0) [8]	11 (25.6) [14]	49 (20.1) [76]
Mild Drug-related TEAEs	1 (1.0) [1]	-	-	1 (0.3) [1]	-	-	-	-	-	1 (2.3) [1]	1 (0.4) [1]
Moderate TEAEs	14 (14.6) [23]	30 (31.9) [43]	24 (25.0) [49]	68 (23.8) [115]	8 (20.5) [9]	8 (19.5) [10]	8 (21.6) [11]	10 (24.4) [16]	4 (9.3) [6]	10 (23.3) [13]	48 (19.7) [65]
Moderate Drug-related TEAEs	3 (3.1) [3]	-	-	3 (1.0) [3]	-	-	-	1 (2.4) [1]	-	-	1 (0.4) [1]
Severe TEAEs	2 (2.1) [3]	5 (5.3) [5]	8 (8.3) [13]	15 (5.2) [21]	1 (2.6) [1]	2 (4.9) [2]	1 (2.7) [1]	1 (2.4) [1]	1 (2.3) [1]	2 (4.7) [2]	8 (3.3) [8]
Severe Drug-related TEAEs	-	-	-	-	-	-	-	-	-	-	-
Serious TEAEs	2 (2.1) [2]	3 (3.2) [3]	6 (6.3) [7]	11 (3.8) [12]	2 (5.1) [2]	1 (2.4) [1]	1 (2.7) [1]	1 (2.4) [1]	-	1 (2.3) [1]	6 (2.5) [6]
Serious Drug-related TEAEs	-	-	-	-	-	-	-	-	-	-	-

	On or After First Dose and Prior to Second Dose				Post Second Dose						
	0.15 mg XT-150 (N=96)	0.45 mg XT-150 (N=94)	Placebo (N=96)	All Participants (N=286)	0.15 – 0.15 mg XT-150 (N=39)	0.15 – 0.45 mg XT-150 (N=41)	0.45 – 0.15 mg XT-150 (N=37)	0.45 – 0.45 mg XT-150 (N=41)	Placebo - 0.15 mg XT-150 (N=43)	Placebo - 0.45 mg XT-150 (N=43)	All Participants (N=244)
Participant discontinuations due to TEAEs	1 (1.0) [1]	-	-	1 (0.3) [1]	-	-	-	-	-	-	-
Participant discontinuation due to Drug-related TEAEs	-	-	-	-	-	-	-	-	-	-	-
Fatal TEAEs	-	-	-	-	1 (2.6) [1]	-	-	-	-	-	1 (0.4) [1]
Fatal Drug-related TEAEs	-	-	-	-	-	-	-	-	-	-	-

Abbreviation: TEAE=treatment-emergent adverse event

We hypothesize that local expression of IL-10 via gene therapy may be a more appropriate route of administration for sustained effects and has shown acceptable safety profiles and no-anti-IL-10 antibodies in previous clinical and pre-clinical studies.[2]

Methods: We describe safety results from a two-stage double-blind Phase 2 study. Stage A compared 2 active doses of XT-150 to a placebo (phosphate-buffered saline) control arm. Stage B was a 6-month follow-up with the option to randomly receive a single injection of XT-150 at one of two doses (0.15 or 0.45 mg) between Day 180 and Day 330. All intra-articular (IA) injections of XT-150 or placebo were performed under imaging guidance **(Table 1)**. Participants 45-85 years of age had symptomatic knee OA defined as a WOMAC Pain score of ≥8 (out of 20) and Kellgren-Lawrence grade 2 or 3 at screening. After signing the Informed Consent Form (ICF), all were assessed for safety by physical examination, laboratory assessments, vital signs, adverse events (AEs) and serious AEs (SAEs) throughout the study. All participants (N=286) receiving any amount of XT-150 or placebo were included in the safety analysis. Safety data were summarized using descriptive statistics according to a prespecified statistical analysis plan (SAP).

Results: Drug-related AEs in this study were local with no systemic AEs. Local injection drug-related treatment-emergent adverse events (TEAEs) were reported by 6 patients (2%); arthralgia was the most common **(Table 2)**. Overall, XT-150 was generally well tolerated in single and multiple IA injections. No dose-, treatment-, or sequence-related trends were reported for any safety domain for XT-150 **(Table 3)**. The most commonly occurring TEAE for all participants who received active study drug was arthralgia (13% of participants). One unrelated TEAE of Grade 5 intensity, a myocardial infarction, was reported following the second dose in a patient with a history of CVD. SAEs were reported across all arms and treatment sequences with a total of 17 (6%) participants reporting 18 SAEs over the 360-day study period, all of which were considered unrelated to the study treatment. There were no AEs of special interest related to study treatment. Anti-IL-10 antibodies were not detected after single or repeat injections.

Conclusion: Safety data from this study support continued investigation of XT-150 for the management of pain and improvement of physical function in patients with knee OA. The local nature of treatment-related AEs and the absence of treatment-related SAEs support a two-dose regimen of 0.45 mg XT-150 (total dose of 0.9 mg) as safe and well-tolerated for future studies.

1. Kwilasz AJ, et al. Neuropharmacology. 2015;96(Pt A):55-69; 2. Watkins LR, et al. Brain Behav Immun. 2020 Nov;90:155-166.

Disclosure: L. Kapural: Avanos, 1, 5, Gimer, 1, Nalu, 5, Neuralace, 5, Neuros, 1, Nevro, 1, 5, PainTeq, 1, Presidio, 1, Saluda, 5; **S. Collins**: Xalud Therapeutics, Inc., 1, 4, 8, 11; **E. Grigsby**: Eli Lilly, 5, Jointstem, 5, Kolon Tissuegene, 5, Medtronic, 2, 5, Neuros, 5, Sollis Therapeutics, 2, Tenex Health Inc., 2, Xalud Therapeutics, 2; **M. McBride**: None; **J. Rieger**: Xalud Therapeutics, 4, 8, 10; **M. Stokes**: Xalud Therapeutics, 3; **H. Rutman**: Xalud Therapeutics, 3, 11; **F. Cicuttini**: Xalud Therapeutics, Inc., 5.

Abstract Number: 0315

Identification of Calcium Crystals in End-Stage Osteoarthritis with Raman Spectroscopy

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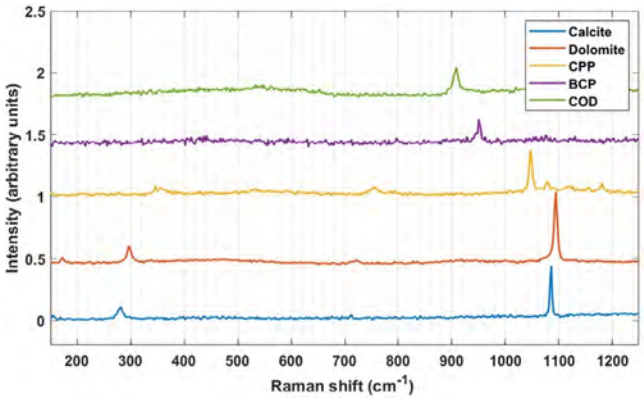
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Calcium containing crystals in osteoarthritis (OA) are of interest as they potentially stimulate the NRLP-3 inflammasome and may become treatable with novel therapeutics. Previous studies demonstrated a presence of calcium pyrophosphate (CPP) and basic calcium phosphate (BCP) crystals in early and advanced OA [1]. Calcium carbonate crystals have been found in cartilage specimens of advanced OA and have recently been shown to potentially occur early in development of cartilage calcification [2].

Methods: Synovial fluid samples from advanced knee OA cases were collected pre-operatively from the Maastricht University Medical Center (MUMC+). The population includes both males and females and all patients were above 18 years of age. Patients gave written informed consent before collection of their synovial fluid. Samples were analyzed with an integrated Raman polarized light microscope. Samples were considered positive for a certain type of crystal if at least one crystal with a distinctive spectrum could be identified.

Results: Calcium containing crystals were present in all (100%) of the 36 samples. 34 (94.4%) of the samples contained calcite (calcium carbonate) crystals. Dolomite (calcium magnesium carbonate) crystals were present in 10 (27.8%) samples, 9 (25.0%) samples contained both types of calcium carbonate crystals. CPP crystals were present in 33.3% of samples. Basic calcium phosphate crystals were present in 9 (25.0%) samples, all of which were hydroxyapatite. Calcium oxalate crystals were present in 7 (19.4%) samples, 3 of which were identified as calcium oxalate dihydrate (COD) and 4 of which were identified as calcium oxalate monohydrate. Most of the samples (80.6%) contained more than one type of calcium crystal, but CPP and BCP were never identified simultaneously in one sample. Raman spectra of identified particles are shown in figure 1.

Conclusion: Calcium containing crystals are common in synovial fluid samples from knee joints in patients with end-stage osteoarthritis. Raman spectroscopy is a novel technique for rheumatology which enables reliable detection and objective identification of crystals such as calcium carbonate. The observation of calcium carbonate (calcite) crystals in synovial fluids of OA patients is novel and a promising subject of further study. Pathways to presentation in synovial fluid and inflammatory properties should be investigated.



Raman spectra of identified calcium containing crystals.

References:

1. Rosenthal, A.K., Crystals, inflammation, and osteoarthritis. Curr Opin Rheumatol, 2011. 23(2): p. 170-3.

2. Casal-Beiroa, P., V. Balboa-Barreiro, N. Oreiro, et al., Optical Biomarkers for the Diagnosis of Osteoarthritis through Raman Spectroscopy: Radiological and Biochemical Validation Using Ex Vivo Human Cartilage Samples. Diagnostics (Basel), 2021. 11(3).

Disclosure: T. Niessink: None; **T. Welting**: Chondropeptix, 8, 10; **M. Janssen**: HCR B.V., 8; **C. Otto**: Hybriscan Technologies B.V., 8; **T. Jansen**: HCR B.V., 8.

Abstract Number: 0316

Relationship of Sensitization to Pain Severity in Patients with Knee Osteoarthritis

Lindsey MacFarlane[1], Hanna Mass[1], Catherine Yang[1], Jose Acosta Julbe[1], Antonia Chen[1], Jeffrey Lange[1], Morgan Jones[1], Faith Selzer[1], Jamie Collins[1], Elena Losina[2] and Jeffrey Katz[1], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Pain in knee osteoarthritis (OA) is multifactorial and influenced by factors including pain sensitization. Most literature on sensitization and OA has contrasted persons with and without OA. We examined the association between knee pain severity and sensitization in a cohort of persons with OA. Further, within individuals with discordant knee pain, we compared sensitization between knees.

Table 1: Sensitization in differing pain levels

	Higher pain (n=44 individuals)	Moderate pain (n=44 individuals)	Lower pain (n=9 individuals)	P-value*
Person level analysis				
Pain pressure threshold wrist (lbs.), mean (SD)	7.5 (3.8)	7.5 (3.3)	8.6 (3.1)	0.50
Temporal summation 3rd digit, mean (SD)	1.5 (1.4)	1.4 (1.6)	0.3 (0.8)	0.01
Central Pain Modulation efficiency (%), mean (SD)	112.1% (29.6)	121.2% (34.0)	131.3 (28.9)	0.045
	Higher pain (n=60 knees)	Moderate pain (n=65 knees)	Lower pain (n=69 knees)	P-value*
Knee level analysis				
Pain pressure threshold knee (lbs.), mean (SD)	10.0 (5.8)	11.5 (5.4)	13.0 (6.1)	0.001
Temporal summation knee, mean (SD)	2.4 (1.7)	1.6 (2.0)	1.7 (1.6)	0.08

Pain pressure threshold range 0-25 lbs
Temporal summation range 0-10
KOOS: Knee injury and osteoarthritis outcome score
SD: standard deviation
NS: not statistically significant
*Person level: ANOVA; knee level: linear mixed effects model

Sensitization in differing pain levels

Table 2: Peripheral sensitization between knees in individuals with discordant levels of pain				
	Knee with higher pain (n=21)	Knee with lower pain (n=21)	Mean Difference (95% CI)	P-value
Knee level analysis				
Pain pressure threshold knee (lbs), mean (SD)	9.3 (6.4)	11.4 (6.6)	2.5 (1.4,3.9)	0.01
Temporal summation knee, mean (SD)	2.7 (1.6)	2.4 (1.8)	1.1 (0.5,1.7)	0.2
KOOS: Knee injury and osteoarthritis outcome score SD: standard deviation				

Peripheral sensitization between knees in individuals with discordant levels of pain

Methods: We recruited patients with knee OA from an orthopedic practice. Knee pain was assessed in each knee using the Knee Injury and Osteoarthritis Outcome Score (KOOS 0-100, 100 best) and categorized into tertiles; higher (< 47 points), moderate (^{3}47 points and < 69), and lower (^{3} 69 points). We considered individuals to have 'discordant pain' if one knee was in the highest tertile and the other in the lowest. Participants underwent quantitative sensory testing (QST) including pain pressure threshold (PPT), temporal summation (TS), and conditioned pain modulation (CPM). We measured PPT at each knee and one wrist. We assessed TS at each knee and 3rd digit. We calculated CPM efficiency as the ratio of mean PPT testing at the wrist before and after the conditioning stimulus (PPT post/PPT pre). Higher TS scores and lower PPT and CPM indicate greater sensitization. We assessed PPT and TS at the knee in knee level analyses and CPM, PPT at the wrist and TS at the digit in person level analyses.

We investigated the relationship between knee pain and sensitization in knee-level and person-level analyses. In person level analyses, we classified individuals into pain tertiles of their most painful knee and examined differences across persons in CPM efficiency, TM at the 3rd digit, and PPT of the wrist. We assessed differences in sensitization between knee pain tertiles using ANOVA. In knee level analyses, we used linear mixed effect models to account for within person correlations. We used paired t-tests to compare differences in QST between discordant knees within an individual.

Results: The sample included 194 knees from 97 participants. Participants had a mean age of 64 years (SD 11), BMI of 30 (SD 8), and 63 (72%) were female. In person level analyses, we observed differences in TS at the 3rd digit across the pain severity tertiles with TS of 1.5 (SD 1.4) in the higher pain group vs 0.3 (SD 0.8) in the lower. We observed small (< 0.5 SD) person level differences across pain tertiles in PPT of the wrist and CPM (Table). In knee level analyses, we observed PPT at the knee increased modestly across pain tertiles. Among the 21 individuals with discordant knee pain, the more painful knee demonstrated modestly lower PPT at the knee (differences < 0.5 SD).

Conclusion: These data support prior research demonstrating greater sensitization in persons with greater knee pain. Our design permitted investigation of sensitization at the knee level. While knees with more pain (across persons and within person), generally had greater sensitization than knees with less pain, the magnitude of these differences was small. The limited influence of sensitization on knee pain in these cross-sectional analyses suggests investigators should have modest expectations of the efficacy of treatments targeting sensitization.

Disclosure: L. MacFarlane: None; **H. Mass**: None; **C. Yang**: None; **J. Acosta Julbe**: None; **A. Chen**: Adaptive Phage Therapeutics, 2, 5, Avanos, 2, BICMD, 2, Convatec, 2, Elute, 5, Ethicon, 2, GLG, 2, Guidepoint, 2, Heraeus, 2, Hyalex, 11, IlluminOss, 11, IrriMax, 2, Osteal Therapeutics, 2, 11, Peptilogics, 2, 11, Pfizer, 2, Smith and Nephew, 2, Sonoran, 11, Stryker, 2, 9; **J. Lange**: Aesulap, 2, OnPoint Kneee, 4; **M. Jones**: Biosplice, 1, 2, Pacira, 5, Regeneron, 1, 2; **F. Selzer**: None; **J. Collins**: None; **E. Losina**: None; **J. Katz**: Biosplice, 5.

Abstract Number: 0317

Long-term Effectiveness of a Lifestyle Program for Osteoarthritis: One-year Follow-up of the "Plants for Joints" Randomized Clinical Trial

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The 16-week Plants for Joints (PFJ) multidisciplinary lifestyle program, based on a whole-food plant-based diet, physical activity, and stress management, significantly reduced The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score compared to usual care in people with hip and/or knee osteoarthritis (OA) and metabolic syndrome.[1,2] The objective was to determine the long-term effectiveness of the PFJ program on pain, stiffness, and function in people with OA.

Methods: People with knee and/or hip OA and metabolic syndrome were randomized to receive the PFJ program in addition to usual care, or the control group which received usual care. After this 16-week RCT period the control group also received the program. After completion of the program all participants were followed-up for one year with biannual visits and 6 adherence-promoting webinars. Medication changes (pain, cholesterol, and diabetes medication) were assessed at one year as an "increase," "stable," or "decrease" compared to baseline. Secondary outcomes included anthropometric and metabolic markers. An intention-to-treat analysis with a linear mixed model was used to analyze within-group differences.

Results: 49 of 64 participants (77%), who completed the initial 16-week clinical trial, completed the one-year follow-up. 84% of participants were female with a mean (SD) age of 63 (6) and body mass index of 33 (5) kg/m^2. In the year after completing the PFJ program the WOMAC score was lower, yet increased slightly again, whereby a mean –7.8-point difference was observed after one year compared to baseline values ($p < 0.001$) (Figure 1). All components of the WOMAC improved significantly compared to before the program (Table 1). Of the 18 participants who completed the follow-up and used pain medication, 11 (61%) decreased or stopped, 3 had stable, and 4 had increased medication. After the 1-year follow-up period

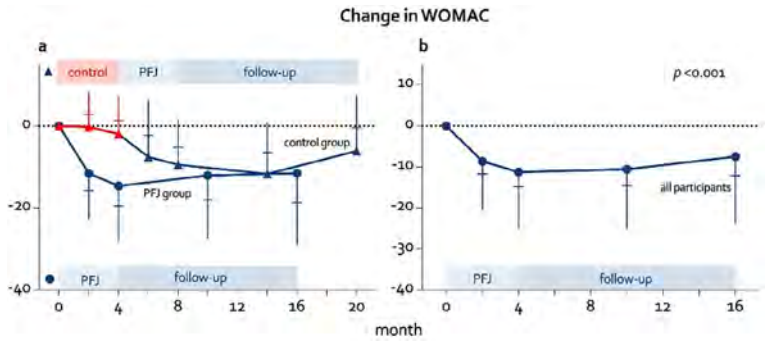

Figure 1. Mean change in WOMAC (a) during the randomized controlled trial phase and one-year follow-up period per trial arm and (b) for the whole cohort before and after completing the lifestyle intervention and one year follow-up.

Table 1. Plants for Joints cohort at start and end of the 16-week intervention period as well as during the one year extension study (6 and 12 months after completing the intervention). Continuous variables reported as mean (SD) when normally distributed or as median [IQR] when skewed. Within-group difference shown between start of the lifestyle intervention and end of the 12-month follow-up determined using the linear-mixed model when model assumptions were met. For variables in which model assumptions were not met (†) a linear-mixed model was performed after log transformation and within group differences were reported as median difference of complete paired values determined using a Wilcoxon test (p-values from the linear mixed model are shown, all were similar to the Wilcoxon test).

	Intervention			Extension study		Within group	
	Start	Halfway	End	6 months	12 months	difference (95% CI)	*p-value*
n=	64	63	62	58	49		
Osteoarthritis measures							
WOMAC total	38.2	29.5	26.9	24.5	30.4	−7.8 (−11.2 to −4.3)	<0.001
WOMAC pain	7.4	5.3	5.1	4.5	5.9	−1.5 (−2.3 to −0.7)	<0.001
WOMAC stiffness	4	3.3	3	2.9	3.5	−0.5 (−1.0 to −0.1)	0.02
WOMAC function	26.8	21	18.9	17.2	21.1	−5.7 (−8.3 to −3.1)	<0.001
Inflammation							
C-reactive protein (mg/l)	1.9	1.5	1.3	1.3	1.4	−0.7 (−1.4 to −0.2)†	0.009
Anthropometric measurements							
Weight (kg)	94.9	92.2	90.2	90.7	93.9	−3.7 (−5.1 to −2.2)	<0.001
Body mass index (kgm-1)	33.3	32.5	31.7	31.5	32.9	−1.3 (−1.7 to −0.8)	<0.001
Waist circumference (cm)	110	105.9	104.6	105.7	107.4	−4.3 (−6.1 to −2.4)	<0.001
Metabolic markers							
HbA1c (mmol/mol)	42.6	40.7	40.3	40.2	40.5	−1.2 (−2.0 to −0.4)	0.003
Fasting blood glucose (mmol/l)	5.8	5.5	5.5	5.4	5.2	−0.4 (−0.6 to −0.2)	<0.001
LDL-cholesterol (mmol/l)	3.6	3.2	3.3	3.3	3.6	−0.1 (−0.3 to 0.2)	0.7
HDL-cholesterol (mmol/l)	1.4	1.4	1.4	1.4	1.4	0.0 (0.0 to 0.1)	0.4
Triglycerides (mmol/l)	1.6	1.4	1.6	1.5	1.4	−0.1 (−0.3 to 0.0)†	0.1
Systolic blood pressure (mmhg)	145	141	144	142	136	−8 (−13 to −3)	0.005
Diastolic blood pressure (mmhg)	91	86	89	86	85	−6 (−9 to −3)	<0.001

weight, waist circumference, HbA1c, CRP, and blood pressure became or remained significantly lower than baseline values, although there was no longer a significant difference in LDL cholesterol. Furthermore, of those completing the follow-up, 3 (33%) and 8 (44%) participants decreased diabetes and cholesterol medication respectively while only 2 participants had increased medication.

Conclusion: The PFJ lifestyle program significantly decreased pain, stiffness, and improved function in people with OA and metabolic syndrome and its effects were largely sustained till one year after program completion with reduced pain medication. Metabolic benefits found after the lifestyle intervention were partially sustained, possibly indicating attenuated adherence to the program in the follow-up.

References

1. Walrabenstein, Trials 2021
2. Walrabenstein, Osteoarthritis and Cartilage 2023

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Abstract Number: 0318

The Association of CT-Detected Intra-Articular Mineralization with MRI-Detected Effusion-Synovitis and Hoffa's Synovitis in Knee OA: The Multicenter Osteoarthritis Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Intra-articular (IA) deposition of calcium crystals (chondrocalcinosis), is common in knee OA. While calcium crystals can cause inflammatory arthritis, their contribution to joint inflammation in OA, as manifested by effusion-synovitis and Hoffa's synovitis on MRI, is unclear. Clarifying the role of calcium crystal deposition in joint-level inflammation would provide improved understanding for the role of targeted cytokine therapy in those with IA mineralization. Prior studies have been limited by use of radiographs to detect chondrocalcinosis. In contrast, CT provides higher sensitivity for detecting IA mineralization as well as identifying potential tissue-specific effects of IA mineralization in OA. We aimed to evaluate the cross-sectional and longitudinal relation of CT-detected IA mineralization to effusion-synovitis and/or Hoffa's synovitis on MRI with the hypothesis that IA mineralization contributes to the worsening of synovitis in OA.

Methods: We included participants from the Multicenter Osteoarthritis (MOST) Study who had knee radiographs, CTs, and MRIs. IA mineralization was assessed on CT at baseline using the Boston University Calcium Knee Score (BUCKS), a semi-quantitative 0-3 scoring of the extent of mineralization in Whole Organ MRI Score (WORMS) subregions. We categorized presence of mineralization as a BUCKS score >0 as follows: 1) anywhere in the knee (including cartilage, meniscus, joint capsule, ligaments); 2) cartilage; 3) meniscus. Effusion-synovitis and Hoffa's synovitis were scored on MRI in one knee using MOAKS at baseline and two years later. For cross-sectional analyses, either effusion-synovitis and/or Hoffa's synovitis were considered present with MOAKS ≥1 in either score. For longitudinal analyses, worsening was defined as an increase of ≥1 in MOAKS, for either effusion-synovitis and/or Hoffa's synovitis scores. We evaluated the relation of IA mineralization to the presence of effusion-synovitis and/or Hoffa's synovitis cross-sectionally and their worsening longitudinally, using binomial regression with generalized estimating equations. Analyses were adjusted for age, sex, and body mass index.

Results: We included 1668 participants (mean age 60±9, 56% female, mean BMI 28.5±5 kg/m^2; 21% knees with radiographic OA) (**Table**). Any IA mineralization was present in 9.2%, effusion-synovitis in 49.1%, Hoffa's synovitis in 29.3%. Overall, 16.7% had worsening of either effusion-synovitis and/or Hoffa's synovitis on MRI at 2 years. The presence of any

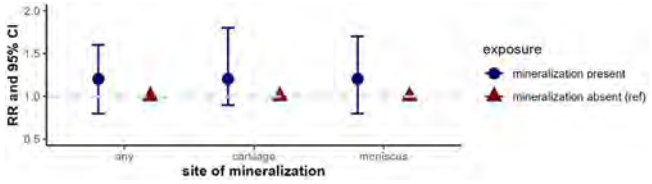

FIGURE: Longitudinal relation of CT-detected intra-articular mineralization, by site, to MRI-detected effusion-synovitis and Hoffa's synovitis worsening over 2 years

Mean (SD) age, years	60.9 (9.1)
% female	56.1
% white	83.9
Mean (SD) BMI, kg/m^2	28.5 (5.0)
KL grade, n knees	
0	1053
1	378
2	298
3	69
4	7
Effusion-synovitis present*, % knees	29.3
Hoffa's synovitis present*, % knees	49.1
Effusion-synovitis and Hoffa's synovitis present*, % knees	29.3

* Effusion-synovitis and Hoffa's synovitis considered present if MOAKS ≥1

TABLE: Baseline characteristics of participants included in this analysis, n = 1668 individuals (1809 knees)

IA mineralization was associated with 30% higher prevalence of effusion-synovitis and/or Hoffa's synovitis cross-sectionally (PR 1.3, 95% CI 1.1-1.5), and 20% higher risk of worsening longitudinally (RR 1.2, 95% CI 0.8-1.6) (**Figure**).

Conclusion: CT-detected IA mineralization in various tissues was modestly associated with effusion-synovitis and Hoffa's synovitis at baseline and with worsening over 2 years. These findings are limited by the sample size.

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Abstract Number: 0319

Knee Flexion Contracture Was Associated with Articular Cartilage Loss in the Central Region but Cartilage Preservation in the Posterior Region of the Tibia: Data from the Osteoarthritis Initiative

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Osteoarthritis – Clinical Poster I
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Session Time: 9:00AM–11:00AM

Background/Purpose: A knee flexion contracture (FC), present in ~1/3 of patients with knee OA[1], is the inability to fully extend the knee[2, 3]. Having a FC means that anterior and middle regions of the tibial articular surface may experience reduced contact with the femur resulting in altered force transmission, a risk factor for cartilage loss[2]. The impact of FC on the articular cartilage regions of the tibia has been studied longitudinally in animals[2], but not humans. We tested for a quantitative longitudinal association between FC and cartilage loss in the tibia in patients with or at-risk of knee OA using MRI data from the Osteoarthritis Initiative (OAI) cohort. We hypothesized that FC would be associated with cartilage loss in tibial anterior and middle regions, which experience reduced load, but cartilage preservation in the posterior regions, where load is maintained.

Methods: 578 participants with baseline knee extension data and MRI at baseline and year 1 were analyzed. Lack of full knee extension to 0° was considered a FC. Cartilage outcomes were measured using 3T knee MRI coronal views[4]. Tibial articular cartilage was segmented into medial and lateral compartments, then further divided into anterior, central, and posterior regions[4]. We looked for associations between the presence of a knee FC, and cartilage thickness or % denuded bone (0mm thickness) over the 1-year period using ANCOVA, controlling for baseline outcomes and relevant covariates.

Results: Table 1 shows participant demographics. In the medial compartment, there was reduced cartilage thickness overall and in the center region, with increased % denuded bone overall and in the center and anterior regions. In the lateral compartment, there was reduced cartilage thickness overall and in the center and posterior regions with increased % denuded bone overall and in the posterior region (Table 2).

Knee FC was associated with increased % denuded bone in the medial center (β=0.465 [0.049,0.881], p=0.029) and preserved cartilage thickness in the medial posterior (β=0.015 [0.004, 0.027], p< 0.001) regions. There was a trend between FC and increased % denuded bone in the lateral anterior region (β=0.203 [-0.020,0.426], p=0.074; Table 3).

Table 1 – Participant demographics

Demographic (n=578)	Mean ± SD
Age (yrs)	61.6±8.9
Contracture	62.3±9.2
No contracture	61.2±8.8
Sex (% female)	59.7
Contracture	53.2*
No contracture	62.9
BMI (kg/m²)	30.7±4.7
Contracture	31.1±4.8
No contracture	30.6±4.7
Kellgren & Lawrence Grade	2.2±0.7
Contracture	2.3±0.7
No contracture	2.2±0.6
Maximum knee extension[a] (°)	0.2±3.9
Contracture	-4.4±2.7
No contracture	1.8±2.7
Knee alignment[b] (°)	-0.4±3.7
Contracture	-0.2±3.6
No contracture	-0.6±3.8
WOMAC Pain	2.3±3.1
Contracture	2.9±3.3**
No contracture	2.1±3.0
WOMAC Function	8.5±10.6
Contracture	10.9±11.7***
No contracture	7.3±9.8
WOMAC Stiffness	1.5±1.5
Contracture	1.8±1.6**
No contracture	1.4±1.5

Contracture group n=190
No contracture group n=388
[a] Negative value indicates degrees lacking from full extension
[b] Valgus has a negative value
* p<0.05 contracture versus no contracture
** p<0.01 contracture versus no contracture
*** p<0.01 contracture versus no contracture

Table 2 – Cartilage thickness and percent denuded bone for all participants

Outcome (n=578)	Baseline [95% CI]	Year 1 [95% CI]	Mean change over 1 year [95% CI]
Medial tibia			
Cartilage thickness (mm)			
Overall	**1.63 [1.60,1.65]**	**1.61 [1.59,1.63]**	**-0.01 [-0.02,-0.01]*** **
Center	**2.08 [2.01,2.12]**	**2.05 [2.01,2.08]**	**-0.03 [-0.04,-0.02]*** **
Anterior	1.45 [1.43,1.48]	1.45 [1.42,1.47]	-0.00 [-0.01,0.00]
Posterior	1.40 [1.38,1.42]	1.40 [1.38,1.42]	-0.00 [-0.01,0.00]
% denuded bone			
Overall	**1.41 [1.08,1.73]**	**1.86 [1.47,2.24]**	**0.45 [0.29,0.62]*** **
Center	**0.52 [0.28,0.76]**	**0.92 [0.54,1.30]**	**0.40 [0.19,0.61]*** **
Anterior	**0.87 [0.40,1.34]**	**1.06 [0.60,1.53]**	**0.19 [0.04,0.35]***
Posterior	0.81 [0.47,1.15]	0.85 [0.53,1.18]	0.04 [-0.05,0.13]
Lateral tibia			
Cartilage thickness (mm)			
Overall	**1.96 [1.93,1.99]**	**1.95 [1.92,1.98]**	**-0.01 [-0.02,-0.01]*** **
Center	**2.97 [2.91,3.03]**	**2.96 [2.90,3.02]**	**-0.01 [-0.03,0.00]***
Anterior	1.64 [1.61,1.67]	1.64 [1.62,1.67]	0.00 [-0.00-,0.01]
Posterior	**1.64 [1.61,1.67]**	**1.63 [1.60,1.66]**	**-0.01 [-0.02,-0.01]*** **
% Denuded bone			
Overall	**1.00 [0.74,1.26]**	**1.07 [0.79,1.34]**	**0.07 [0.01,0.12]***
Center	0.17 [0.05,0.29]	0.23 [0.05,0.42]	0.07 [-0.01, 0.14]
Anterior	0.95 [0.44,1.46]	0.94 [0.43,1.46]	0.01 [-0.11,0.09]
Posterior	**2.97 [2.24,3.70]**	**3.16 [2.39,3.92]**	**0.19 [0.06,0.32]** **

* p<0.05 for mean change difference from baseline to year 1
** p<0.01 for mean change difference from baseline to year 1
*** p<0.01 for mean change difference from baseline to year 1

Table 3 – Repeated measures ANCOVA for contracture interaction with year 1 timepoint

Outcome (n=578)	Mean±SD	Effect size (Beta) [95% CI]	p-value[a]
Medial tibia			
Cartilage thickness (mm)			
Posterior	Baseline		
Contracture	1.43±0.28*		
No Contracture	1.38±0.26		
		0.015 [0.004, 0.027]	<0.001
	Year 1		
Contracture	1.44±0.28**		
No Contracture	1.38±0.26		
% denuded bone			
Center	Baseline		
Contracture	0.55±2.88		
No Contracture	0.51±3.03		
		0.465 [0.049,0.881]	0.029
	Year 1		
Contracture	1.31±6.32		
No Contracture	0.74±3.59		
Lateral tibia			
% denuded bone			
Anterior	Baseline		
Contracture	1.43±0.28*		
No Contracture	1.38±0.26		
		0.203 [-0.020,0.426]	0.074
	Year 1		
Contracture	1.44±0.28*		
No Contracture	1.38±0.26		

Summary of ANCOVA findings for regional effect of contracture

	Medial	Lateral
Anterior	-	↑ % denuded bone (trend)
Middle	↑ % denuded bone	-
Posterior	Cartilage preservation	-

[a] for contracture interaction with year 1 outcome after controlling for baseline outcome and adjusting for age, sex, BMI, knee alignment, baseline KL, WOMAC total score
*p<0.05 contracture vs no contracture
**p<0.01 contracture vs no contracture
***p<0.001 contracture vs no contracture

Conclusion: Knee FC was associated with regional cartilage loss in the center region and preservation in the posterior region of the medial tibia, with a trend towards cartilage loss in the lateral anterior region. Together, these findings are consistent with knee FC negatively impacting regions of the tibia articular cartilage with reduced load. Future studies should evaluate the effects of interventions to maintain full knee range of motion on articular cartilage preservation.

References

1. Campbell 2020
2. Watanabe 2020
3. Ritter 2007
4. Wirth 2009

Disclosure: M. Campbell: None; **O. Laneuville**: None; **G. Trudel**: None.

Abstract Number: 0320

Feasibility and Acceptability of Geniculate Artery Embolization for the Treatment of Painful Knee Osteoarthritis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1. Characteristics of Participants with Knee Osteoarthritis

Characteristics	Median [IQR] or N (%)
Current age (years)	69.00 [61.25, 74.00]
BMI (kg/m^2)	25.95 [23.22, 29.45]
Race	
- Asian	4 (6.1)
- Black or African American	3 (4.5)
- White	55 (83.3)
- Other	4 (6.1)
Ethnicity	
- Hispanic or Latina/x	3 (4.5)
- Not Hispanic or Latina/x	60 (90.9)
- Prefer not to answer	3 (4.5)
Ever tried knee OA pain therapies	
- Medication[1]	62 (93.9)
- Alternative therapies[2]	46 (69.7)
- Supportive therapies[3]	48 (72.7)
- Physical therapy	57 (86.3)
- Other physical activity[4]	65 (98.5)
- Other[5]	56 (84.8)
Willingness to receive geniculate artery embolization procedure as routine clinical care:	
- Definitely willing	25 (37.9)
- Probably willing	33 (50.0)
- Unsure	3 (4.5)
- Probably not willing	5 (7.6)
- Definitely not willing	0 (0.0)
Willingness to participate in geniculate artery embolization randomized controlled trial	
- Definitely willing	16 (24.2)
- Probably willing	23 (34.8)
- Unsure	14 (21.2)
- Probably not willing	11 (16.7)
- Definitely not willing	2 (3.0)
Willingness to participate in geniculate artery embolization randomized controlled trial with procedure guaranteed	
- Definitely willing	18 (27.3)
- Probably willing	23 (34.8)
- Unsure	17 (25.8)
- Probably not willing	5 (7.6)
- Definitely not willing	3 (4.5)
Work situation	
- Working for compensation	34 (51.5)
- Retired	27 (40.9)
- Volunteering, not working due to knee problems, or other	5 (7.6)
Bachelor's degree or higher	55 (83.3)
Pain Catastrophizing	
- Rumination	2.00 [0.00, 4.75]
- Magnification	2.00 [1.00, 3.00]
- Helplessness	2.50 [0.00, 6.75]
- Total score	6.00 [3.00, 13.00]
PROMIS-29 v2.1	
- Anxiety	48.20 [40.30, 56.00]
- Depression	41.00 [41.00, 51.88]
- Fatigue	48.60 [43.10, 53.20]
- Pain Interference	55.70 [53.90, 60.00]
- Physical Function	41.85 [37.20, 45.10]
- Sleep Disturbance	51.40 [42.53, 54.50]
- Ability to Participate in Social Activities	51.80 [47.55, 58.50]
KOOS Knee Survey	
- Symptoms	60.71 [53.57, 71.43]
- Quality of Life	43.75 [25.00, 56.25]
- Pain	58.33 [45.14, 65.97]
- Function in Daily Living	65.44 [55.88, 78.68]
- Sports and Recreation	35.00 [25.00, 55.00]

[1]Includes NSAIDs, COX-2 inhibitors, acetaminophen, viscosupplementation, narcotics, corticosteroid injections, glucosamine, chondroitin, colchicine
[2]Includes herbal remedies, homeopathic medication, yoga, Tai chi, acupuncture, massage, relaxation, meditation, biofeedback, hydrotherapy, aquatic therapy, balneotherapy, electrotherapy, magnetotherapy
[3]Includes knee brace, patellar band, shoe orthotics or inserts, kinesiology taping
[4]Includes walking, swimming, stretching, warm or cold compress, activity modification, other physical activity
[5]Includes periodic rest during the day, platelet-rich plasma, stem cell therapies, weight loss, ultrasound, topical ointments, other therapies

Background/Purpose: There are limited non-surgical options for patients with severe pain due to knee osteoarthritis (KOA). Using geniculate artery embolization (GAE) to infarct hypervascular synovium, a known correlate of pain, has been proposed as a potential novel therapy. However, GAE is invasive and requires a lower extremity angiogram, which may limit its acceptability. Understanding patient-centered acceptability of new therapies is crucial to gauge potential uptake and to estimate enrollment for randomized controlled trials (RCTs). The goal of this study is to evaluate whether GAE is acceptable to patients with painful KOA, and to explore the feasibility of performing an RCT of GAE.

Methods: Patients >50 years with a KOA ICD-10 code (M17.0, M17.1, M17.9) were identified from practices of rheumatologists and physiatrists at a musculoskeletal specialty hospital. Exclusion criteria included Kellgren and Lawrence grade IV, systemic rheumatic disease, prior surgery to the index knee, contemplating arthroplasty, severe comorbidities and a KOOS pain subscale >70. Subjects used a remote viewing platform to watch a 20-minute PowerPoint presentation, which described GAE, including its risks and benefits, and presented a hypothetical sham-controlled RCT (i.e. angiogram with GAE vs. angiogram alone). A trained research assistant conducted the call and was available to answer questions. After completion, the subject was asked whether they would find GAE acceptable in three scenarios: 1) routine clinical care 2) an RCT where 50% of subjects would receive an angiogram but no GAE 3) the same RCT but with the option for the angiogram-only group to receive GAE later.

Table 2. Demographics and Patient-Reported Outcome Measures for Subjects Stratified by Willingness to Receive Geniculate Artery Embolization Procedure As Part of Routine Clinical Care

Characteristics	All (N = 68)	Willing to Receive N = 25 (37.9%)	Probably Willing to Receive or Unsure N = 38 (54.5%)	Probably Not or Definitely Not Willing to Receive N = 5 (7.6%)	p-value
Current age (years), median [IQR]	69.00 [61.25, 74.00]	69.00 [59.00, 72.00]	69.00 [64.00, 74.25]	74.00 [66.00, 74.00]	0.35
BMI (kg/m^2), median [IQR]	25.95 [23.22, 29.45]	27.10 [22.60, 29.50]	25.35 [23.30, 27.75]	27.10 [23.00, 30.00]	0.78
Race, N (%)					0.70
- Asian	4 (6.1)	1 (4.0)	2 (5.6)	1 (20.0)	
- Black or African American	3 (4.5)	2 (8.0)	1 (2.8)	0 (0.0)	
- White	55 (83.3)	21 (84.0)	30 (83.3)	4 (80.0)	
- Other	4 (6.1)	1 (4.0)	3 (8.3)	0 (0.0)	
Ethnicity, N (%)					0.88
- Hispanic or Latina/x	3 (4.5)	2 (8.0)	1 (2.8)	0 (0.0)	
- Not Hispanic or Latina/x	60 (90.9)	22 (88.0)	33 (91.7)	5 (100.0)	
- Prefer not to answer	3 (4.5)	1 (4.0)	2 (5.6)	0 (0.0)	
Bachelor's degree or higher, N (%)	55 (83.3)	20 (80.0)	31 (86.1)	4 (80.0)	0.69
Work situation, N (%)					0.31
- Working for compensation	34 (51.5)	15 (60.0)	17 (47.2)	2 (40.0)	
- Retired	27 (40.9)	10 (40.0)	15 (41.7)	2 (40.0)	
- Volunteering, not working due to knee problems, or other	5 (7.6)	0 (0.0)	4 (11.1)	1 (20.0)	
Pain Catastrophizing, median [IQR]					
- **Rumination**	2.00 [0.00, 4.75]	**2.00 [0.00, 3.00]**	**3.00 [1.00, 7.00]**	**0.00 [0.00, 0.00]**	**0.0055**
- **Magnification**	2.00 [1.00, 3.00]	**2.00 [0.00, 3.00]**	**2.00 [1.00, 3.25]**	**0.00 [0.00, 0.00]**	**0.0306**
- **Helplessness**	2.50 [0.00, 6.75]	**1.00 [0.00, 3.00]**	**4.00 [1.75, 8.25]**	**0.00 [0.00, 0.00]**	**0.0033**
- **Total score**	6.00 [3.00, 13.00]	**5.00 [2.75, 8.25]**	**8.50 [4.75, 19.25]**	**0.00 [0.00, 2.00]**	**0.0016**
PROMIS-29 v2.1, median [IQR]					
- Anxiety	48.20 [40.30, 56.00]	47.90 [40.30, 59.80]	51.40 [40.30, 56.00]	47.90 [40.30, 56.00]	0.90
- Depression	41.00 [41.00, 51.88]	41.00 [41.00, 51.20]	41.00 [41.00, 50.02]	41.00 [41.00, 57.20]	0.60
- Fatigue	48.80 [43.10, 53.20]	46.00 [39.80, 51.00]	48.75 [46.00, 57.10]	48.60 [46.00, 48.60]	0.13
- Pain Interference	56.70 [53.90, 60.00]	55.70 [54.20, 59.00]	57.25 [53.62, 61.30]	53.90 [50.20, 53.90]	0.07
- Physical Function	41.95 [37.20, 45.10]	43.20 [38.20, 45.10]	41.50 [36.10, 44.43]	43.70 [41.40, 45.10]	0.32
- **Sleep Disturbance**	51.40 [42.53, 54.50]	**46.40 [38.40, 52.80]**	**53.40 [47.65, 60.70]**	**44.20 [42.10, 54.50]**	**0.02**
- Ability to Participate in Social Activities	51.80 [47.55, 58.50]	53.50 [47.40, 58.50]	51.80 [45.82, 58.50]	57.00 [54.20, 64.20]	0.21
KOOS Knee Survey, median [IQR]					
- Symptoms	60.71 [53.57, 71.43]	64.29 [50.00, 71.43]	60.71 [52.68, 71.43]	60.71 [57.14, 82.14]	0.71
- Quality of Life	43.75 [25.00, 56.25]	50.00 [31.25, 56.25]	43.75 [23.44, 51.56]	56.25 [56.25, 62.50]	0.10
- Pain	58.33 [45.14, 65.97]	61.11 [41.67, 66.67]	52.78 [46.53, 61.81]	61.11 [61.11, 66.67]	0.25
- Function in Daily Living	66.44 [55.88, 78.68]	73.53 [58.82, 82.35]	63.24 [52.94, 73.90]	86.76 [61.76, 88.24]	0.15
- Sports and Recreation	35.00 [25.00, 55.00]	35.00 [25.00, 55.00]	30.00 [15.00, 50.00]	50.00 [40.00, 55.00]	0.16
Ever tried knee OA pain therapies					
- Medication[1]	62 (93.9)	23 (92.0)	34 (94.4)	5 (100.0)	1
- Alternative therapies[2]	46 (69.7)	19 (76.0)	24 (66.7)	3 (60.0)	0.64
- Supportive therapies[3]	48 (72.7)	19 (76.0)	27 (75.0)	2 (40.0)	0.27
- Physical therapy	57 (86.4)	21 (84.0)	32 (88.9)	4 (80.0)	0.63
- Other physical activity[4]	65 (98.5)	25 (100.0)	36 (100.0)	4 (80.0)	0.07
- Other[5]	56 (84.8)	23 (92.0)	29 (80.6)	4 (80.0)	0.40

[1]Includes NSAIDs, COX-2 inhibitors, acetaminophen, viscosupplementation, narcotics, corticosteroid injections, glucosamine, chondroitin, colchicine
[2]Includes herbal remedies, homeopathic medication, yoga, Tai chi, acupuncture, massage, relaxation, meditation, biofeedback, hydrotherapy, aquatic therapy, balneotherapy, electrotherapy, magnetotherapy
[3]Includes knee brace, patellar band, shoe orthotics or inserts, kinesiology taping
[4]Includes walking, swimming, stretching, warm or cold compress, activity modification, other physical activity
[5]Includes periodic rest during the day, platelet rich plasma, stem cell therapies, weight loss, ultrasound, topical ointments, other therapies

Results: 66 subjects enrolled, median age 69 [IQR: 61-74] years, 83% White, 4.5% Hispanic/LatinX, median BMI 26 [IQR: 23.2-29.5] kg/m^2. Overall, 37.9% would be definitely willing and 50% probably willing to have GAE as a routine clinical intervention; 24.2% would be definitely willing and 34.8% probably willing to participate in a sham controlled RCT; this increased to 27.3% and remained 34.8%, respectively, if GAE was offered to the sham control group later. Those definitely/probably unwilling to have GAE as routine care had lower catastrophizing scores, but they were not clinically meaningfully different. There were no other clinically or statistically significant differences in age, race, ethnicity, BMI, KOOS or PROMIS-29 between those willing or not willing to have GAE in any of the three scenarios.

Conclusion: Approximately 40% of representative patients with painful KOA would be definitely willing to undergo GAE and 24.2% would be definitely willing to participate in a sham-controlled RCT. Guaranteeing access to GAE as part of an RCT may only minimally improve recruitment. These data can inform trial planning. The large proportion of subjects willing to undergo GAE underscores the unmet therapeutic need in this patient population, and similar acceptability across different demographic strata suggests GAE could benefit a wide range of patients with KOA.

Table 3. Demographics and Patient-Reported Outcome Measures for Subjects Stratified by Willingness to Participate in Geniculate Artery Embolization Randomized Controlled Trial

Characteristics	All (N = 66)	Willing to Participate N = 16 (24.2%)	Probably Willing to Participate or Unsure N = 37 (56.0%)	Probably Not or Definitely Not Willing to Participate N = 13 (19.7%)	p-value
Current age (years), median [IQR]	69.00 [61.25, 74.00]	67.50 [59.00, 72.00]	70.00 [65.00, 74.00]	66.00 [61.00, 74.00]	0.38
BMI (kg/m^2), median [IQR]	25.95 [23.22, 29.45]	29.10 [23.57, 30.45]	25.10 [23.30, 27.10]	29.80 [22.50, 31.70]	0.17
Race, N (%)					0.25
- Asian	4 (6.1)	0 (0.0)	3 (8.1)	1 (7.7)	
- Black or African American	3 (4.5)	2 (12.5)	0 (0.0)	1 (7.7)	
- White	55 (83.3)	13 (81.2)	31 (83.8)	11 (84.6)	
- Other	4 (6.1)	1 (6.2)	3 (8.1)	0 (0.0)	
Ethnicity, N (%)					0.43
- Hispanic or Latina/x	3 (4.5)	2 (12.5)	1 (2.7)	0 (0.0)	
- Not Hispanic or Latina/x	60 (90.9)	13 (81.2)	34 (91.9)	13 (100.0)	
- Prefer not to answer	3 (4.5)	1 (6.2)	2 (5.4)	0 (0.0)	
Bachelor's degree or higher, N (%)	55 (83.3)	13 (81.2)	31 (83.8)	11 (84.6)	1
Work situation, N (%)					0.41
- Working for compensation	34 (51.5)	11 (68.8)	17 (45.9)	6 (46.2)	
- Retired	27 (40.9)	5 (31.2)	17 (45.9)	5 (38.5)	
- Volunteering, not working due to knee problems, or other	5 (7.6)	0 (0.0)	3 (8.1)	2 (15.4)	
Pain Catastrophizing, median [IQR]					
- Rumination	2.00 [0.00, 4.75]	2.00 [0.75, 4.00]	2.00 [0.00, 5.00]	2.00 [0.00, 2.00]	0.67
- Magnification	2.00 [1.00, 3.00]	2.00 [1.50, 4.50]	2.00 [1.00, 3.00]	1.00 [0.00, 2.00]	0.28
- Helplessness	2.50 [0.00, 6.75]	2.00 [0.75, 5.75]	3.00 [1.00, 7.00]	2.00 [0.00, 6.00]	0.89
- Total score	6.00 [3.00, 13.00]	6.00 [3.00, 16.50]	6.00 [3.00, 13.00]	5.00 [2.00, 8.00]	0.68
PROMIS-29 v2.1, median [IQR]					
- Anxiety	48.20 [40.30, 56.00]	47.90 [40.30, 61.03]	47.90 [40.30, 56.00]	51.40 [51.40, 56.00]	0.72
- Depression	41.00 [41.00, 51.88]	41.00 [41.00, 52.53]	41.00 [41.00, 48.90]	48.90 [41.00, 57.20]	0.27
- Fatigue	48.60 [43.10, 53.20]	48.00 [38.27, 53.58]	48.60 [43.10, 53.20]	48.70 [48.00, 57.10]	0.68
- Pain Interference	55.70 [53.90, 60.00]	58.20 [56.38, 61.65]	55.70 [53.90, 60.00]	55.70 [53.90, 59.10]	0.40
- Physical Function	41.85 [37.20, 45.10]	41.55 [37.58, 43.70]	43.20 [36.60, 45.10]	42.00 [39.10, 43.70]	0.93
- Sleep Disturbance	51.40 [42.53, 54.50]	45.60 [38.02, 50.67]	52.80 [44.20, 54.50]	53.00 [50.00, 55.80]	0.08
- Ability to Participate in Social Activities	51.80 [47.55, 58.50]	51.80 [47.52, 58.88]	51.80 [46.10, 64.20]	51.80 [51.80, 57.00]	0.98
KOOS Knee Survey, median [IQR]					
- Symptoms	60.71 [53.57, 71.43]	62.50 [37.50, 71.43]	60.71 [53.57, 71.43]	60.71 [53.57, 71.43]	0.73
- Quality of Life	43.75 [25.00, 56.25]	37.50 [25.00, 50.00]	43.75 [31.25, 56.25]	43.75 [31.25, 56.25]	0.61
- Pain	58.33 [45.14, 65.97]	48.61 [37.50, 66.67]	58.33 [47.22, 63.89]	61.11 [52.78, 63.89]	0.66
- Function in Daily Living	65.44 [55.88, 78.68]	63.24 [53.31, 80.15]	69.12 [57.35, 82.35]	61.76 [55.88, 70.59]	0.53
- Sports and Recreation	35.00 [25.00, 55.00]	30.00 [23.75, 43.75]	35.00 [20.00, 55.00]	40.00 [25.00, 60.00]	0.88
Ever tried knee OA pain therapies					
- Medication[1]	62 (93.9)	14 (87.5)	36 (97.3)	12 (92.3)	0.29
- Alternative therapies[2]	46 (69.7)	12 (75.0)	27 (73.0)	7 (53.8)	0.39
- Supportive therapies[3]	48 (72.7)	12 (75.0)	28 (75.7)	8 (61.5)	0.66
- Physical therapy	57 (86.4)	15 (93.8)	31 (83.8)	11 (84.6)	0.71
- Other physical activity[4]	65 (98.5)	16 (100.0)	37 (100.0)	12 (92.3)	0.20
- Other[5]	56 (84.8)	15 (93.8)	30 (81.1)	11 (84.6)	0.58

[1]Includes NSAIDs, COX-2 inhibitors, acetaminophen, viscosupplementation, narcotics, corticosteroid injections, glucosamine, chondroitin, colchicine
[2]Includes herbal remedies, homeopathic medication, yoga, Tai chi, acupuncture, massage, relaxation, meditation, biofeedback, hydrotherapy, aquatic therapy, balneotherapy, electrotherapy, magnetotherapy
[3]Includes knee brace, patellar band, shoe orthotics or inserts, kinesiology taping
[4]Includes walking, swimming, stretching, warm or cold compress, activity modification, other physical activity
[5]Includes periodic rest during the day, platelet-rich plasma, stem cell therapies, weight loss, ultrasound, topical ointments, other therapies

Disclosure: A. Smole: None; **B. Swett**: None; **A. Zhao**: None; **Y. Shea**: None; **S. Gottesman**: None; **D. Sun**: None; **G. Westrich**: Ethicon, 2, 6, Stryker, 1, 2, 5, 6, 9; **M. Alexiades**: Depuy Inc, 5, DJO Inc, 2, 9, Intellijoint Inc, 1, 2; **A. Gonzalez Della Valle**: None; **S. Kishore**: Boston Scientific, 5, Canon Medical Systems, 2, 6, Inari Medical, 2, 6, Intervene, 2, Trisalus Life Sciences, 1, Varian Interventional Systems, 5; **L. Mandl**: Annals of Internal Medicine, 12, Associate Editor, Regeneron Pharmaceuticals, 5, Up-to-Date, 9.

Abstract Number: 0321

Use of Proton Pump Inhibitors and Risk of Hip/knee Joint Replacement Among Patients with Osteoarthritis and Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis and rheumatoid arthritis cause significant joint replacement morbidity. Proton pump inhibitors (PPIs) may contribute to chronic inflammation and joint degeneration due to side effects like hypomagnesemia and gut microbiota dysregulation. However, research on the association between PPI use and joint replacement risk is limited in osteoarthritis and lacks data in rheumatoid arthritis. Our study investigates the link between PPI usage and joint replacement risk in both osteoarthritis and rheumatoid arthritis patients.

Methods: This retrospective analysis included osteoarthritis and rheumatoid arthritis patients diagnosed using ICD10 codes from Northwell Health electronic medical records in 2020-2021. Proton pump inhibitor (PPI) use was confirmed through manual review of medical records. Joint replacement cases (hip/knee) were identified using CPT codes for total hip and knee replacement. Multivariate logistic regression analysis was conducted to compare joint replacement occurrence in PPI users versus non-users, while adjusting for underlying comorbidities. A p-value < 0.05 indicated statistical significance

Results: A total of 1980 patients were included, with 1449 having osteoarthritis and 531 having rheumatoid arthritis. The mean ages were 55.5 and 51.8 years for osteoarthritis and rheumatoid arthritis patients, respectively. Female predominance was observed, with 904 (63%) among the osteoarthritis group and 362 (73%) among the rheumatoid arthritis group. Proton pump inhibitors were taken by 522 osteoarthritis patients (36%) and 175 rheumatoid arthritis patients (33%). Comorbidities that were taken into consideration are tobacco use, alcohol use, coronary artery disease, cerebrovascular accident, peripheral artery disease, diabetes, malignancy, gout, osteoporosis, glucocorticoid use, overweight, obesity, morbid obesity, chronic kidney disease, end-stage renal disease, vitamin D deficiency.

PPI use in individuals with combined osteoarthritis or rheumatoid arthritis significantly increased the risk of joint replacement (OR 1.24, 95% CI 1.10-1.41, $p < 0.0004$). Among those with rheumatoid arthritis alone, PPI users also had a higher risk of joint replacement (OR 1.31, 95% CI 1.13-1.52, $p < 0.0002$). However, there was no significant difference in the risk of joint replacement between PPI users and non-users with osteoarthritis (OR 1.03, 95% CI 0.82-1.28, $p = 0.78$).

Conclusion: In conclusion, our study found that proton pump inhibitors (PPIs) are linked to an increased risk of joint replacement in individuals with combined osteoarthritis or rheumatoid arthritis. This association was significant for patients with rheumatoid arthritis but not for those with osteoarthritis alone. Further research is needed to understand the underlying

Table 1 – Baseline characteristics of osteoarthritis and rheumatoid arthritis patients

Baseline characteristics	Osteoarthritis (n=1449)	Rheumatoid arthritis (n= 531)
Mean age	55.5	51.8
Female gender (%)	914 (63%)	390 (73%)
PPI use (%)	522 (36%)	175 (33%)
Tobacco use (%)	571 (39%)	203 (38%)
Alcohol use (%)	61 (4%)	17 (3%)
Diabetes (%)	462 (31%)	146 (27%)
Coronary artery disease (%)	438 (30%)	136 (25%)
Peripheral artery disease (%)	63 (4%)	19 (3%)
Cerebrovascular accident (%)	34 (2%)	11 (2%)
Malignancy (%)	215 (14%)	64 (12%)
Gout (%)	95 (6%)	25 (4%)
Osteoporosis (%)	120 (8%)	47 (9%)
Glucocorticoid use (%)	31 (2%)	54 (10%)
Overweight (%) (BMI 25-29)	10 (1%)	4 (1%)
Obesity (%) (BMI 30-39)	133 (9%)	37 (7%)
Morbid obesity (%) (BMI > 39)	11 (1%)	3 (1%)
End-stage renal disease (%)	38 (2%)	11 (2%)
Vitamin D deficiency (%)	51 (3%)	15 (2%)
Joint (knee/hip) replacement (%)	33 (2%)	13 (2%)

mechanisms and establish causality. Healthcare providers should consider the potential impact of PPIs on joint health when treating patients with rheumatoid arthritis, aiming to manage comorbidities and reduce the need for joint replacement surgeries.

Disclosure: K. Sangaraju: None; **R. Grovu**: None; **M. Kwark**: None; **E. Cohen**: None; **A. Hassan**: None; **A. Slobodnick**: None.

Abstract Number: 0322

Validation of NICE Criteria for the Diagnosis of Knee Osteoarthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The NICE guideline on osteoarthritis (OA) recommends that adults aged ≥45 should be diagnosed with OA clinically, without investigations, if they have activity-related joint pain and either no morning joint-related stiffness or morning stiffness that lasts no longer than 30 minutes. While the NICE criteria are frequently used and referenced as

diagnostic criteria for OA, they have not been validated. The objective of this study was to validate the NICE criteria for knee OA. This was completed within the context of a larger project focused on identifying and treating OA in people with other chronic conditions.

Methods: This was a diagnostic test study. Reporting was guided by the SIGN checklist. We recruited participants with type 2 diabetes from endocrinology clinics at three academic hospitals in Toronto, Canada. We invited individuals aged ≥45 years with and without self-reported knee pain to participate (aiming for 50% with/without). We excluded individuals with a history of inflammatory rheumatic disease. Participants first self-completed a questionnaire to identify presence of activity-related knee pain and morning joint stiffness ≤30 min (NICE criteria for OA). As history and physical exam is considered the gold standard for making an OA diagnosis, an experienced rheumatologist, blinded to the questionnaire responses, conducted a standardized clinical assessment to identify presence of knee OA (yes, no, possible). A second rheumatologist completed a subset (n=11) of assessments in duplicate for validation of the rheumatologist's assessment. We calculated the sensitivity (sens), specificity (spec), likelihood ratio positive (LR+) and likelihood ratio negative (LR-) of the NICE criteria to detect symptomatic knee OA (yes or possible).

Results: Our study included 91 participants with type 2 diabetes: mean age was 65.9 (SD 8.1) years, 50.6% women, mean BMI 29.1 (SD 6.6) kg/m^2 (Table 1). 50 (54.9%) fulfilled the NICE criteria with a spectrum of illness severity: median (range) pain numeric rating score (0-10) was 5 (1-9). Gold standard assessment identified 51 (56.0%) participants with symptomatic knee OA (yes: n=48, possible [suspected to be early knee OA]: n=3). The sens, spec, LR+, and LR- of NICE criteria for symptomatic knee OA were 86.3%, 85.0%, 5.75, 0.16, respectively (Table 2). Activity-related knee OA ("Do you have pain or aching in one or both of your knee joints that comes on, or is made worse, by activities such as standing, walking, or climbing stairs") alone, without combination with morning stiffness, improved operating characteristics (88.2%, 90.0%, 8.82, 0.12) (Table 3). There was high rheumatologist inter-rater reliability for OA diagnosis (kappa = 0.84).

Conclusion: The NICE criteria have high sensitivity and specificity for detecting symptomatic knee OA. A simplified version, assessing self-reported activity-related knee pain in individuals age ≥45 years, performed slightly better and may be a preferable OA diagnostic tool. This should be validated in other settings. Given purposeful recruiting, this study cannot assess positive and negative predictive values.

Table 1. Characteristics of participants (n=91)

Characteristic	
Age, years, mean (SD)	65.9 (8.1)
Gender (woman), n (%)	56 (50.6%)
Body mass index, kg/m^2, mean (SD)	29.1 (6.6)
Race/ethnicity	
Black	7 (7.7%)
South Asian	7 (7.7%)
Southeast Asian	2 (2.2%)
White	55 (60.4%)
Diabetes treatment	
Diet/exercise only	49 (53.9%)
Oral medications	79 (86.8%)
Insulin	46 (50.6%)
Non-insulin injectable medications	29 (31.9%)
Comorbidities	
Stroke	8 (8.8%)
Heart disease	16 (17.6%)
Gastrointestinal disease	25 (27.5%)
Kidney disease	17 (18.7%)
Respiratory disease	19 (20.9 %)
Anxiety or depression	20 (22.0%)
Fulfill NICE criteria for knee OA, n (%)	50 (55.0%)
Activity-related knee pain, n (%)	51 (56.0%)
Pain NRS (0-10) in those with knee pain, median (range)	5 (1 to 9)

Table 2. Accuracy of NICE criteria

		Rheumatologist diagnosis	
NICE criteria*		+ve	-ve
	+ve	44	6
	-ve	7	34

*NICE criteria: age ≥45 years, activity-related knee joint pain, and morning joint stiffness ≤30 min.

Sensitivity (Sn): 86.3%
Specificity (Sp): 85.0%
Positive likelihood ratio (LR+): 5.75
Negative likelihood ratio (LR-): 0.16

Table 3. Accuracy of patient-reported activity-related knee pain (in individuals ≥45 years)

		Rheumatologist diagnosis	
Activity-related knee pain*		+ve	-ve
	+ve	45	6
	-ve	6	34

*Participants asked: "Do you have pain or aching in one or both of your knee joints that comes on, or is made worse, by activities such as standing, walking, or climbing stairs." All participants were age ≥45 years.

Sensitivity (Sn): 88.2%
Specificity (Sp): 90.0%
Positive likelihood ratio (LR+): 8.82
Negative likelihood ratio (LR-): 0.13

Disclosure: L. King: None; **I. Stanaitis**: None; **V. Hung**: None; **S. Koppikar**: None; **E. Waugh**: None; **L. Lipscombe**: Novo Nordisk, 5; **G. Hawker**: None.

Abstract Number: 0323

A Randomized, Double-blind, Placebo-controlled, Repeat Injection, 52-Week Study to Evaluate the Efficacy and Safety of an Intra-articular Injection (IAI) of CNTX-4975-05 (CNTX) in Subjects with Chronic, Moderate-to-severe Osteoarthritis Knee Pain (MSOAKP) - Study 304

James Connolly, James N Campbell, **Randall Stevens** and Colleen Newman, Centrexion Therapeutics Corporation, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: 30+ million US adults have OAKP. After years of using NSAIDs, analgesics, surgery and IAI, many patients remain with MSOAKP. CNTX is a 1 mg dose of capsaicin for IAI to reduce MSOAKP.

Methods: Efficacy and safety of a two IAI doses of placebo or 1 mg CNTX (Day 1 and at Week 26; ratio capsaicin/placebo 3:2; blinded randomization) were assessed in subjects with chronic, MSOAKP. Subjects were allowed specific MSOAKP concomitant and rescue medications during the study.

Pain was assessed using: a numeric pain rating scale (NPRS [0 – 10; 0 = no pain, 10 worst pain possible]). Subjects had Kellgren-Lawrence (KL) grades 2-4 (radiograph; 0=normal, 4=severe), and met knee OA (KOA) diagnostic criteria. Subjects were blindly randomized. The primary endpoint (Week 12) was the Western Ontario and McMaster Universities Osteoarthritis Index Subscale A (pain). Subjects were also assessed on WOMAC B (stiffness), WOMAC C (function), Numeric Pain Rating Scale (NPRS; 0-10), and Patient Global Impression of Change (PGIC; 0-7).

Key safety included physical exams, vital signs, ECGs, labs and bilateral fixed flexion knee radiographs at screening, and Week 52.

Results: 325 subjects received 1 dose of study drug (140 placebo, 184 CNTX); 243 randomized subjects completed out to Week 52; 89 subjects discontinued (DC) early. DC reasons were subject withdrawal (6.9%), lack of efficacy (6.3%) and other (5.1%). 15 (4.5%) subjects DC prior to Week 12. Mean age 62.8 years (range = 40-84), 61.4% female, 71.3% - not Hispanic or Latino; 70.4% Caucasian and 26.5% Back/African American.

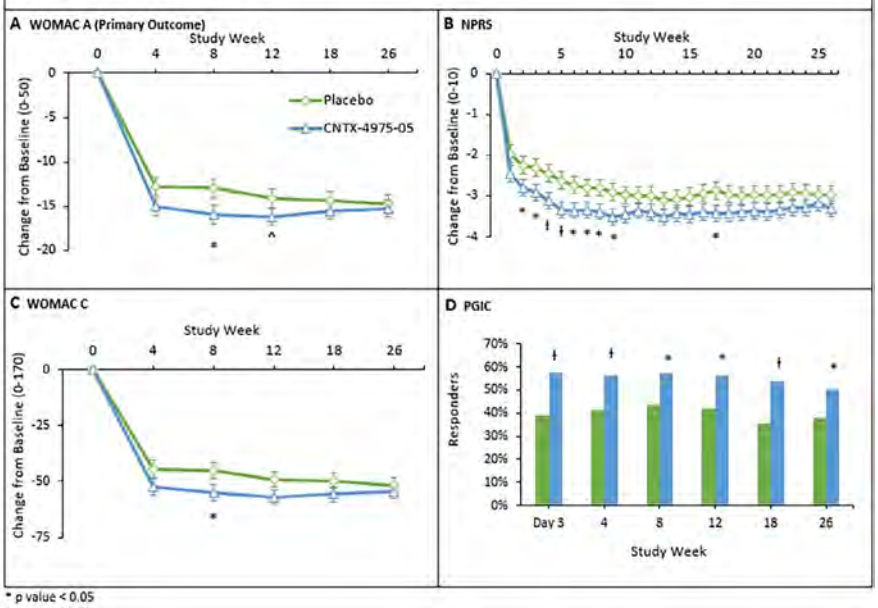
Mean index knee baseline NPRS was 7.0, WOMAC A (0-50 scale; 0 = severe pain) 31.5; WOMAC B (0-20 scale) and WOMAC C (0-170) was 13.2 and 108.8, respectively.

Table 1. Efficacy Outcomes

Outcome	CNTX-304	
	Placebo (n = 140)	CNTX-4975-05 (n = 184)
Primary Outcome^		
WOMAC A Change at Week 12	-14.3 (1.03)	-16.2 (0.96)
Key Secondary Outcomes^		
NPRS Change at Week 12	-2.99 (0.21)	-3.41 (0.2)
WOMAC B Change at Week 12	-5.36 (0.43)	-6.58 (0.4)
WOMAC C Change at Week 12	-49.03 (3.54)	-57.02 (3.31)
PGIC responders at Week 12+	59 (42.1%)	103 (56.0%)*

^ Values in parentheses denote standard error unless otherwise represented
* p value < 0.05
+ PGIC Responder = Much Improved and Very Much Improved

Figure 1. Efficacy Outcomes



* p value < 0.05
† p value < 0.01
^ Endpoint at week 12

Least-squares (LS) mean reduction was greater for CNTX than placebo (–16.20 vs -14.13, respectively; p = 0.0833). The WOMAC B / C, and NPRS were numerically better at nearly all visits through Week 26, and usually better to Week 52, for CNTX relative to placebo. Also, a greater proportion of CNTX subjects were considered PGIC responders at Week 12 and beyond – After the second IAI at Week 26, both pain and function improvements were seen in CNTX vs placebo, up to Week 52. (Table 1 and Figure 1).

There was more transient post injection pain on Day 1 in the CNTX group than placebo. Safety was acceptable out to Week 52 with knee radiographs showing no difference in KOA progression between placebo and CNTX, and no rapidly progressive osteoarthritis.

Conclusion: This study did not meet the primary endpoint. However, the numeric data suggested greater analgesic efficacy through Week 26 in CNTX compared to placebo. CNTX safety was acceptable. The NPRS difference was significant at several timepoints.

Disclosure: J. Connolly: Centrexion Therapeutics Corporation, 3; **J. Campbell**: None; **R. Stevens**: Centrexion Therapeutics Corporation, 3; **C. Newman**: Centrexion Therapeutics Corp, 3.

Abstract Number: 0324

A Randomized, Double-blind, Placebo-controlled, Single Injection, 52-Week Study to Evaluate the Efficacy and Safety of an Intra-articular Injection (IAI) of CNTX-4975-05 (CNTX) in Subjects with Chronic, Moderate-to-severe Osteoarthritis Knee Pain (OAKP) - Study 301

Randall Stevens, James N Campbell, Colleen Newman and James Connolly, Centrexion Therapeutics Corporation, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: 30+ million US adults have OAKP. After years of using NSAIDs and other conservative measures many patients remain with OAKP. CNTX is a 1 mg dose of capsaicin for IAI to reduce OAKP.

Methods: This was a randomized, double-blind, placebo-controlled, 52-week study with 325 subjects dosed, to evaluate the efficacy and safety of a single IAI (at Day 1) of 1.0 mg of CNTX, compared with placebo, in subjects (both sexes) with chronic, moderate-to-severe index OAKP (MSIOAKP). Subjects were allowed specific OAKP concomitant and rescue medications during the study.

Subjects with MSIOAKP using a numeric pain rating scale between 5-9 (NPRS [0 – 10; 0 = no pain, 10 worst pain possible]), Kellgren-Lawrence (KL) grades 2-4 (0-4, Normal to severe by radiographs), and met knee OA (KOA) diagnostic criteria, were blindly randomized on Day 1 to a single IAI of capsaicin or placebo (3:2) into the most painful knee (index). NPRS at Week 12 was the primary outcome measure, with supporting data from the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC; A=pain, B= knee stiffness, C= function) and Patient Global Impression of Change (PGIC; 0-7 scale). Radiographic data was taken of both knees.

Key safety included physical exams, vital signs, ECGs, labs, and fixed flexion radiographs of both knees at Screening, Weeks 12 and 52.

Results: 325 subjects received 1 dose of study drug (136 placebo, 189 CNTX); 262 randomized subjects completed; 70 subjects discontinued (DC) early. Reported reasons for study DC were subject withdrawal (7.2%), lost to follow-up (5.1%), and other (2.1%). 15 (4.5%) subjects DC prior to Week 12. Subjects: Mean age 61.8 years (range = 40-85 years), 63.4% female, 81.5% -not Hispanic or Latino; 65.5% Caucasian and 23.4% Back/African American.

Mean index knee baseline NPRS was 7.07, WOMAC A (0-50 scale; 0 = severe pain) 31.45, WOMAC B (0-20 scale) and WOMAC C (0-170) 13.26 and 106.99, respectively.

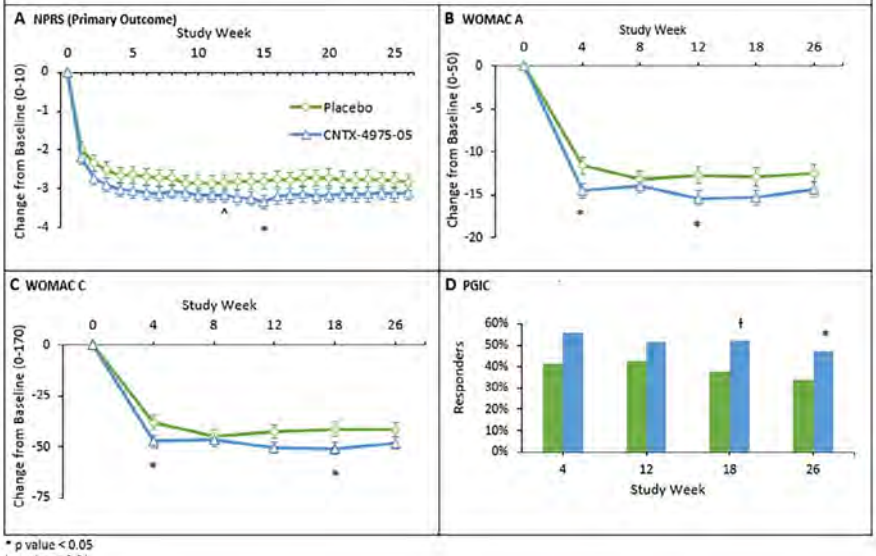
The least squares (LS) mean reduction in the average weekly pain with walking NPRS (0-10) score for the index knee was greater in the CNTX group than in the placebo group (–3.17 vs –2.84, respectively; p = 0.1904). However, the study failed to meet the primary efficacy endpoint. The WOMAC A, B and C subscales, the mean changes from study baseline were numerically better at nearly all visits through Week 26, and usually better to Week 52 for CNTX relative to placebo. Further,

Table 1. Efficacy Outcomes

Outcome	CNTX-301	
	Placebo (N = 136)	CNTX-4975-05 (N = 189)
Primary Outcomes^		
NPRS Change at Week 12	-2.84 (0.21)	-3.17 (0.182)
Key Secondary Outcomes^		
WOMAC A Change at Week 12	-12.72 (1.0)	-15.42 (0.86)*
WOMAC B Change at Week 12	-5.21 (0.45)	-6.15 (0.39)
WOMAC C Change at Week 12	-42.70 (3.42)	-50.49 (2.94)
PGIC responders at Week 12+	58 (42.6%)	98 (51.9%)

^ Values in parentheses denote standard error unless otherwise represented
* p value < 0.05
+ PGIC Responder = Much Improved and Very Much Improved

Figure 1. Efficacy Outcomes



* p value < 0.05
ǂ p value < 0.01
^ Endpoint at week 12

a greater proportion of subjects in the CNTX group were considered PGIC responders at Week 12 and beyond -(Table 1 and Figure 1).WOMAC A (pain) for CNTX was significantly ($p< 0.05$) improved over placebo at week 12.

Overall safety was acceptable and CNTX after treatment Day 1, where there was more transient post injection pain in the CNTX group. Knee radiographs (masked central reading) from Baseline to Week 52 showed no difference in KOA progression between placebo and CNTX, with no rapidly progressive osteoarthritis.

Conclusion: The study did not meet the primary endpoint, though analgesic efficacy through Week 26 in CNTX was numerically superior to placebo. Improvement in WOMAC A at 12 weeks was significantly greater for CNTX compared to placebo CNTX safety was acceptable.

Disclosure: R. Stevens: Centrexion Therapeutics Corporation, 3; **J. Campbell**: None; **C. Newman**: Centrexion Therapeutics Corp, 3; **J. Connolly**: Centrexion Therapeutics Corporation, 3.

Abstract Number: 0325

Understanding the Burden of Cutaneous Lupus: A Subset Analysis from the 2022 World Lupus Federation Global Impact (WLFGI) Patient Survey

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: There is a paucity of data among a global population exploring the burden of CLE on patients, especially as compared to patients with SLE. This has negatively impacted research efforts including the development of new therapeutics specific to CLE. The 2022 World Lupus Federation Global Impact (WLFGI) patient survey assessed multiple aspects of patients' lupus including subsets of disease, therapeutic beliefs, quality of life burden. We utilized the WLFGI survey to characterize the burden of cutaneous disease and the comparative burden on quality of life among patients with self-reported cutaneous lupus compared to systemic lupus erythematosus.

Methods: The 2022 WLFGI survey was a multilingual, anonymous, online survey designed by the World Lupus Federation and disseminated worldwide via email during 3/1/2022-3/22/2023 with 6,704 respondents. 199 respondents had cutaneous lupus (CLE only) compared to 2,929 with systemic lupus with skin involvement (CLE+SLE) and 2,094 with systemic lupus without skin involvement (SLE only). Respondents with incomplete diagnosis data were removed from analysis, however, incomplete responses to questions were included as negative responses. Comparative statistics (odds ratio analysis) was utilized to assess comparative burden of quality of life measures between subgroups.

Results: Patient demographics and clinical manifestations are noted in Table 1. Respondents were more likely to be middle age, female, from the Americas and Europe. Impact on quality of life was observed in all groups, particularly financial insecurity (34%), mental health concerns (38%) and decreased social engagement (60%) (Table 2). There was an additive quality of life burden of 20-80% from cutaneous disease for all quality of life measures except short term disability observed in the CLE

Table 1. Cohort demographics and clinical data by disease subphenotype

	CLE only N (%)	CLE+SLE N (%)	SLE only N (%)	Total N (%)
Total	199 (4)	2929 (56)	2094 (40)	5222
Age				
Early (<18)	2 (1)	36 (1)	27 (1)	65 (1)
Late (>=65)	42 (21)	432 (15)	304 (15)	778 (15)
Middle (18-64)	153 (77)	2443 (83)	1758 (84)	4354 (84)
Unknown age category	2 (1)	18 (1)	5 (0.2)	25 (0.5)
Sex				
Female	179 (90)	2755 (94)	1956 (93)	4890 (94)
Male	18 (9)	136 (5)	109 (5.2)	263 (5)
Self-described	0 (0)	4 (0.1)	12 (0.6)	16 (0.3)
Did not answer	2 (1)	34 (1)	17 (0.8)	53 (1.)
Geographic regions				
Africa	7 (4)	95 (3)	70 (3)	172 (3)
Americas	121 (61)	2025 (69)	1386 (66)	3532 (68)
Asia	6 (3)	93 (3)	87 (4)	186 (4)
Europe	58 (29)	656 (22)	514 (25)	1228 (24)
Oceania	3 (2)	36 (1)	14 (1)	53 (1)
Other	4 (2)	24 (1)	23 (1)	51 (1)
Organ System Involvement				
CNS	10 (5)	883 (30)	465 (22)	1358 (26)
GI	24 (12)	1194 (41)	606 (29)	1824 (35)
Cardiac	12 (6)	718 (25)	467 (22)	1197 (23)
Kidney	12 (6)	963 (33)	963 (46)	1938 (37)
Pulmonary	8 (4)	783 (27)	502 (24)	1293 (25)
Ophthalmologic	32 (16)	1107 (38)	490 (24)	1629 (32)
Musculoskeletal	33 (17)	1492 (51)	871 (42)	2396 (46)
Reproductive	4 (2)	270 (9)	117 (6)	391 (8)

Table 2. Odds ratio and 95% confidence interval of quality of life impacts by disease subphenotype

	CLE only N (%)	CLE+SLE N (%)	SLE only N (%)	Total N (%)	OR (CLE+SLE vs SLE only) (OR, CI)	OR (CLE only vs CLE+SLE) (OR, CI)	OR (CLE only vs SLE only) (OR, CI)
Quality of Life Impacts							
Short term disability	23 (12)	681 (23)	502 (24)	1206 (23)	0.9 (0.8-1.1)	**0.4 (0.3-0.7)**	**0.4 (0.3-0.6)**
Long term disability	16 (8)	859 (29)	524 (25)	1399 (27)	**1.2 (1.1-1.4)**	**0.2 (0.1-0.4)**	**0.2 (0.2-0.4)**
Inability to work	34 (17)	1049 (36)	653 (31)	1736 (33)	**1.2 (1.1-1.4)**	**0.4 (0.3-0.5)**	**0.5 (0.3-0.6)**
Financial insecurity	43 (22)	1090 (37)	629 (30)	1762 (34)	**1.4 (1.2-1.6)**	**0.5 (0.3-0.7)**	**0.6 (0.4-0.9)**
Mental health concerns	63 (32)	1288 (44)	641 (31)	1992 (38)	**1.8 (1.6-2.0)**	**0.6 (0.4-0.8)**	1.0 (0.8-1.4)
Inability to participate in social activities	98 (49)	1935 (66)	1083 (52)	3116 (60)	**1.8 (1.6-2.0)**	**0.5 (0.4-0.7)**	0.9 (0.7-1.2)
Transportation issues	21 (11)	1128 (39)	598 (29)	1747 (33)	**1.6 (1.3-1.8)**	**0.2 (0.1-0.3)**	**0.3 (0.2-0.5)**

+SLE group, compared to the SLE only group. While respondents with cutaneous-limited disease generally had less quality of life burden compared to the SLE-only subgroup, mental health concerns and inabilities to socially engage were notable outliers. About one-third of CLE-only patients reported mental health concerns (32%), similar to the SLE-only population (31%), with CLE+SLE patients having nearly half (44%) reporting mental health concerns, highlighting the significant stigma associated with a potentially disfiguring disease.

Conclusion: This study offers a unique, global insight into the patient-reported burden of CLE +/- SLE. Skin-limited disease appears to carry as high a burden as SLE in several domains of disease impact. The presence of CLE among SLE patients is associated with higher quality of life burden, with particular impact on mental health and social interaction. These data support the need for further research dedicated to CLE and CLE disease-specific therapeutics.

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Abstract Number: 0326

Assessment of Depression in Ankylosing Spondylitis Using Center for Epidemiologic Studies Depression Scale

Yvette Farran[1], Mark Hwang[1], John Reveille[2], Lianne Gensler[3], Accelerating Medicines Partnership Program RA SLE Network[4], Mariko Ishimori[4] and Michael Ward[5], [1]The University of Texas Health Science Center at Houston McGovern Medical School, Houston, TX, [2]The University of Texas Health Science Center, Houston, TX, [3]University of California San Francisco, Department of Medicine, Division of Rheumatology, San Francisco, CA, [4]Cedars-Sinai Medical Center, Los Angeles, CA, [5]National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, US Department of Health and Human Services, Bethesda, MD

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

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Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing Spondylitis (AS) is a chronic inflammatory disease that primarily affects the spine and sacroiliac joints. Depression is a common comorbidity in AS patients and can have a significant impact on their quality of life. The Center for Epidemiologic Studies Depression Scale (CES-D) is a widely used self-report questionnaire for measuring depression in various populations. However, the validity of CES-D in AS patients is unclear.

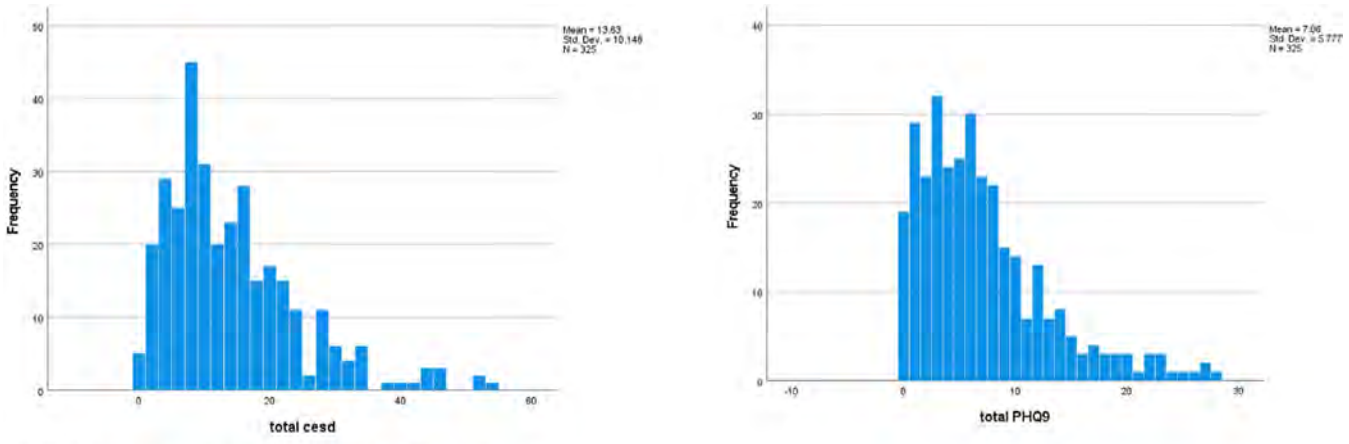

Figure 1. Histograms for total CES-D and PHQ9 score

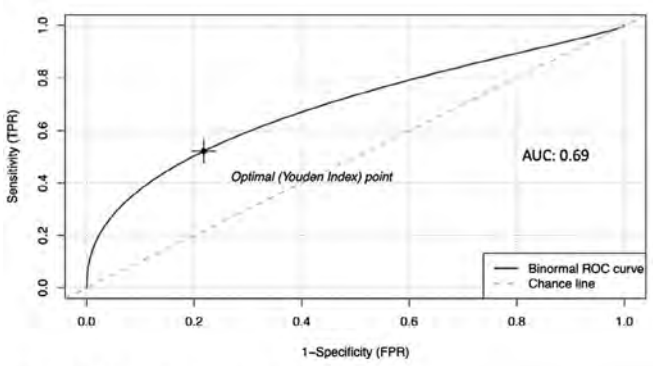

Figure 2A. CES-D vs Self reported Depression

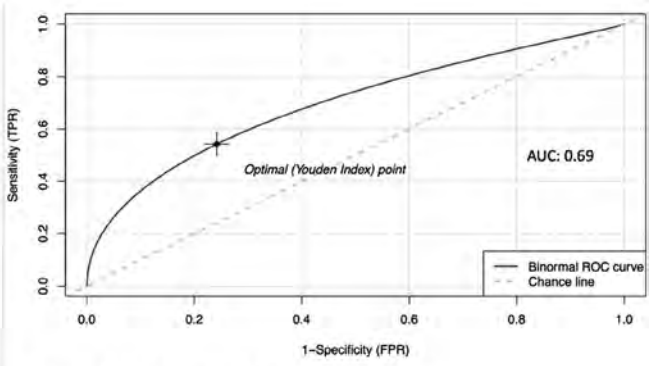

Figure 2B. PHQ9 vs Self reported Depression

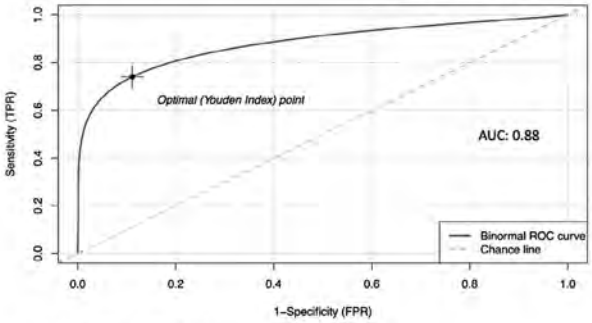

Figure 2C. CES-D vs PHQ9≥10

Methods: We investigated the psychometrics of the CES-D in AS by studying Prospective Study of Ankylosing Spondylitis (PSOAS) observational cohort patients with baseline, concomitant PHQ9 and self-reported depression. Construct validity was examined through convergent and known-groups validity. CES-D and PHQ9 was assessed using Pearson's correlation coefficient. Known groups validity for the CESD was tested using student's t-test comparing patients with and without self-reported depression. To find the optimal cutoffs, ROC curves were made plotting CES-D against Patient reported depression, PHQ9 against Patient report depression and CES-D against PHQ9≥10. The optimal cutoff point was found using Youden's index.

Results: 846 of the patients from the PSOAS cohort had completed CES-D at their initial visit. Of those, 325 had completed CES-D, PHQ-9, and self-reported depression. 25% (83/325) had PHQ9 $\geq$ 10, 34% (112/325) had CES-D $\geq$ 16 and 17% (56/325) had self-reported depression. Of the patients with self-reported depression, the average CES-D score was 19.8 and the average PHQ9 score was 10.7.The CES-D showed strong correlation with PH9 in AS patients ($r > 0.82$, $p < 0.01$) (Figure 1).T-test was significant comparing CES-D scores of AS patients with and without self-reported depression ($p < .01$) with a mean difference of 7.5 (4.6-10.3 95% CI).The ROC curves are shown in Figure 2. AUC's of these ranged from: 0.69-0.88. The optimal cut off point for CES-D in these patients based on Youden's index was 17-18.

Conclusion: In our AS patients, the CES-D scores are valid and have good construct validity. CES-D correlated well with self-reported depression and PHQ9. This suggests that CES-D is valid in this patient population and that a CES-D cutoff of 18, like that found in Rheumatoid Arthritis patients[1], may be a better cutoff value to indicate depression in AS patients.

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Abstract Number: 0327

Self-management Strategies and Self-efficacy in Patients Living with Inflammatory Arthritis: Findings from a Quality Improvement Project in a Tertiary Centre

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The 2021 EULAR guidelines on self-management have made recommendations (rec) to aid with the implementation of self-management strategies in inflammatory arthritis (IA) (1). Their aim is to support patients and encourage a patient-centred care approach which can improve both patient experience and outcomes in IA. Self-management can increase self-efficacy which can in turn improve adherence and outcomes for several self-management strategies (2).

Table 1. Baseline characteristics and areas addressed to patients with IA, based on the EULAR 2021 self-management recommendations *GSE score – Ranges from 10-40, where a higher score indicates more self-efficacy.

	Total	SpA	PsA	RA	p-value
	n=50	n=13	n=12	n=25	
Average Age [mean (SD)]	48 13)	44	48	51	0.29
Gender (Female) N (%)	29 (59) 21 (42)	6 (46) 7 (53)	5 (50) 6 (50)	17 (68) 8 (32)	0.35
DAS [median (IQR)]				4 (3-5)	
BASDAI [median (IQR)]		4 (2-6)			
PSA TJC [median (IQR)]			2.0 (0-10)		
PSA SJC [median (IQR)]			2.0 (0-8)		
Q1 N(%) Patient involvement in care	39 (84.8)	9 (81)	8 (72)	22 (91)	0.33
Q2 N(%) Patient education on their IA and care	30 (66.7)	10 (91)	9 (82)	11 (48)	0.021
Q3 N(%) Goal setting and practical solutions	20 (43)	9 (81)	6 (54)	5 (20)	0.002
Q4 N(%) Physiotherapy / given advice for exercise?	18 (39)	11 (100)	6 (54)	1 (4)	<0.001
Q5 N(%) Lifestyle / healthy behaviour advice given?	25 (54)	9 (81)	5 (45)	11 (45)	0.11
Q6 N(%) Was mental health addressed?	23 (50)	6 (54)	3 (27)	14 (58)	0.22
Q7 N(%) Employment advice given?	14 (30)	7 (63)	4 (36)	3 (12)	0.008
Q8 N(%) Digital health/apps discussed?	15 (32)	4 (36)	4 (36)	7 (29)	0.07
Self-management score [mean (SD)]	4 (2)	6 (2)	4 (3)	3(1)	<0.001
GSE score [median (IQR)]*	14 (12-25)	13 (11-14)	16 (12-26)	26 (23-36)	0.013

The objectives of this project were two fold; 1) to assess the implementation of self-management recommendations into routine clinical care of IA patients at a large tertiary rheumatology centre in London and 2) to explore how implementation (or not) of these recommendations may affect self-efficacy.

Methods: A retrospective analysis of the records of patients attending IA clinics at a large tertiary centre in London was undertaken from January 2022 to November 2022. Inclusion criteria included a diagnosis of either RA, PsA or AS. Specific questions addressing the uptake of the 2021 EULAR recommendations were developed (Table 1). The electronic notes were reviewed by two fellows who additionally interviewed patients via telephone, to explore whether the recommendations were addressed at their clinical encounter with the health care professional. Questions to the patients included specific ones addressing self-efficacy using the validated general self-efficacy (GSE) scale. Comparisons between groups were done with χ^2 tests, paired T-tests and Wilcoxon's Rank sum where appropriate.

Results: Fifty patients were included: 50% with RA, 24% with PsA and 26% with SpA. The mean (SD) age of participants was 48 (13) years. The median DAS was 4 (3-5) in RA, SJC and TJC was 2.0 (0.0-10.0) and 2.0 (0.0-8.0) respectively in PsA patients with the median BASDAI of 4 (2-6) in SpA (Table 1). The median GSE was 14 (12-25), where a higher score indicates more self-efficacy. 78% of patients reported feeling involved in the planning of their care and were made aware of the multidisciplinary team (rec 1). 30% felt they were given enough information on disease management (rec 2). Goals and practical points on physical and psychological interventions (rec 3) were mentioned to 50%. For patients where >50% of the self-management recommendations were addressed the mean GSE was 12.64 compared to a mean of 10.52 when < 50% of self-management recommendations were addressed.

Conclusion: This study demonstrates that self-management recommendations are not fully and consistently addressed in routine clinics. Furthermore, patient self-efficacy was low/moderate suggesting that clinicians need to do better at discussing and supporting self-management strategies to improve self-efficacy which may also improve disease outcomes.

Disclosure: S. Ali: None; **K. Ioasaf**: None; **B. Katie**: None; **A. Rutherford**: None; **S. Steer**: None; **E. Nikiphorou**: AbbVie/Abbott, 6, Celltrion, 6, Eli Lilly, 6, fresenius, 6, Galapagos, 6, Gilead, 1, 6, Pfizer, 6, Sanofi, 6.

Abstract Number: 0328

From Patient Needs to Platform Design: Using Patient Preference to Guide the Development of a Post-Viral Fibromyalgia Management App

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Post-viral fibromyalgia is a chronic condition that can develop in individuals following a viral infection, such as COVID-19. Recent studies have shown that approximately 30% of post-COVID19 patients satisfy the ACR criteria for fibromyalgia, experiencing symptoms such as chronic fatigue, widespread pain, sleep impairment, anxiety and depression.

Digital health interventions have demonstrated efficacy by providing disease monitoring, management and multimodal interventions to chronic pain patients. However, the widespread adoption and adherence to these interventions remain an obstacle. To address these challenges, this study aimed to develop a patient-centered digital health management app tailored specifically for post-viral fibromyalgia patients. By incorporating patient preferences through surveys and conducting usability testing, the study sought to enhance the usability of the app and the engagement of patients. Consequently, improving self-management, leading to improved patient outcomes and a better quality of life.

Methods: This study employed an explanatory design. Patient preference surveys were conducted among individuals recruited from "Long-COVID Schweiz", a post-COVID19 patients association. Usability testing was run with post-viral fibromyalgia patients that were enrolled in the multimodal care program for chronic pain management at the University Hospital of Lausanne (Switzerland).

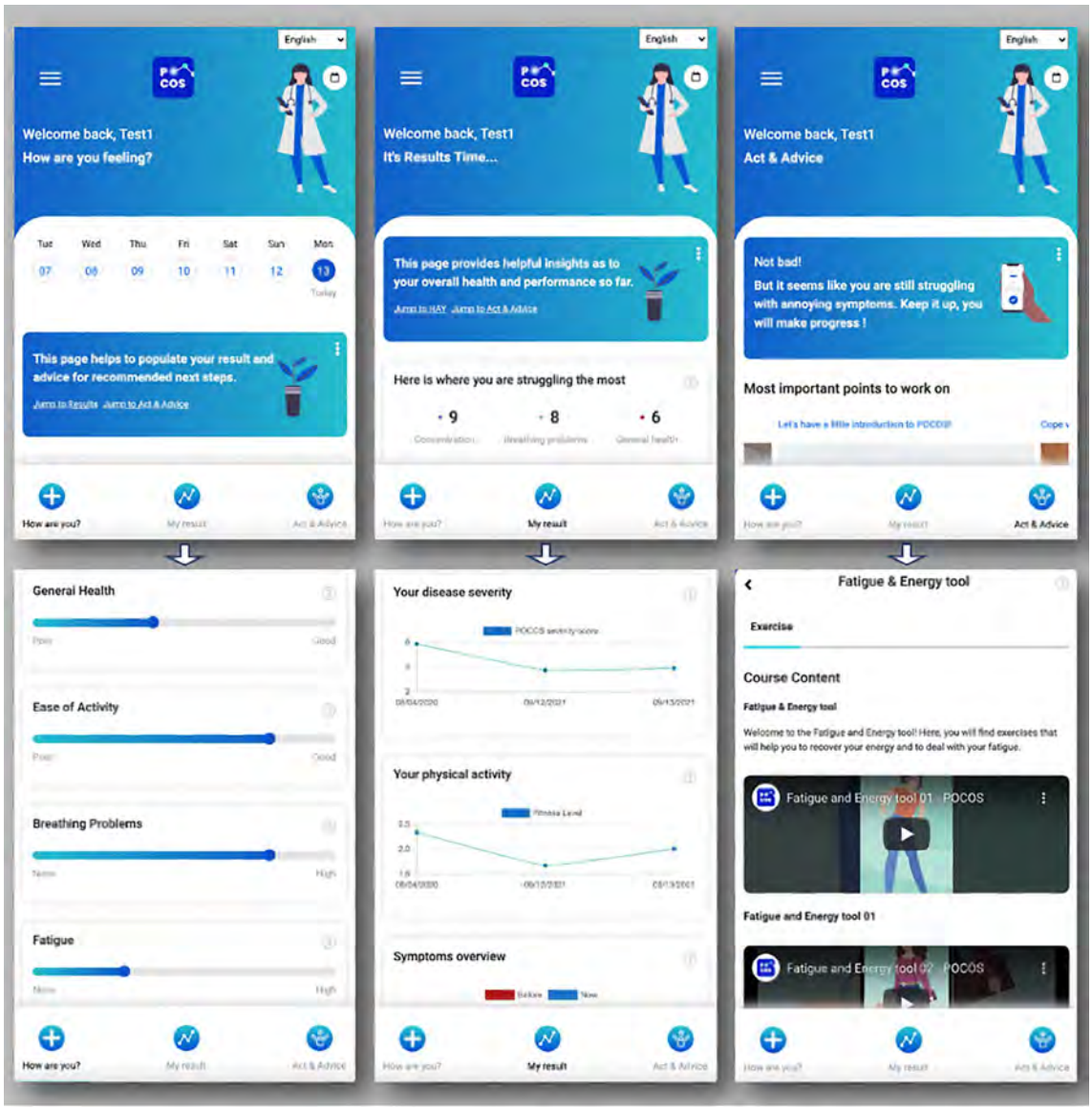

Figure 1: POCOS user interface (app): Left side: 'How are you?', with electronic patient reported outcomes and activity. Middle: 'My result', with monitoring of symptom's activity and health conditions. Right side: 'Act & Advice', with personalized training program, adapted to the user's symptoms.

Data collected from surveys consisted of qualitative preference data related to functional design, interactions with the app, patient reported outcomes, type of monitored data and expected content. Usability testing data under the form of notes, interviews and patients' feedback was collected by observing patients using the newly developed prototype.

Results: The frontend design of the app is shown in Figure 1. Among the 53 patients who responded to patient preference surveys, 90% preferred a regular symptoms list questionnaire over a chatbot to collect patient reported outcomes. Longitudinal symptom evaluation is shown in the "my result" section. 81% of patients expressed their wish that their symptoms are displayed with a benchmark of all other patients and to learn what has helped other patients with similar symptoms. A majority of them were also interested in links to patient communities (63%). Therefore, an anonymized discussion forum has been added. Patients preferred active training programs (63%) and information (59%) over interactive and gamified content (15%).

Among the 6 patients who participated in the usability testing, only 2 showed sufficient understanding of the functionalities and managed to navigate through the app without additional help, revealing the importance of the onboarding process.

Conclusion: Patient preference surveys guided the development of a patient-centric digital health solution, while usability testing identified issues with the onboarding process, requiring further study to investigate the impact of the onboarding on patient adoption and ultimately enhance engagement.

Disclosure: M. Blanchard: Atreon SA, 8; **P. Ming Azevedo**: None; **T. Prétat**: None; **C. Koller**: None; **T. Hügle**: Atreon SA, 8, Curmed, 9, Eli Lilly, 6, Fresenius Kabi, 2, 5, Galapagos, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, Merck/MSD, 6, Pfizer, 6.

Abstract Number: 0329

Factors Associated with Suicidal Ideation Among Patients with Inflammatory Rheumatic Musculoskeletal Disease: A Case-Control Study

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SESSION INFORMATION
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Background/Purpose: Mental health contributes to the morbidity of patients with inflammatory rheumatic musculoskeletal disease (iRMD). Despite extensive research conducted on the prevalence of depressive disorders, limited data on occurrence of suicidal ideation among iRMD patients is available. This study aims to evaluate the prevalence of suicidal ideation in a cohort of iRMD patients and to explore the factors that are associated with suicidal ideation.

Methods: We identified cases from the German osbeservational LORE cohort, consisting of patients with various types of iRMD, who reported suicidal ideations at least weekly (using PHQ-9). These cases were matched in a 1:3 ratio according to age and gender with patients from the same cohort who did not report any suicidal ideations. Patient and disease characteristics such as disease activity, physical function, mental health, and disease severity as well as factors that are reported

to be associated with suicidal ideations, such as previous suicidal attempts, childhood trauma, and personality factors were assessed in a case control study. A standardized clinical interview conducted by a psychosomatic expert was offered to all identified cases. Psychosomatic experts and rheumatologists rated independently whether suicidal ideation was being casual related to iRMD (NRS 0-10, 10 strong confidence in causal relationship). Five questions of the Columbia Suicidal Severity Rating Scale (C-SSRS) were used to assess lifetime suicidal ideation. According to the C-SSRS, patients were

Table1: patient characteristics of subjects with and without suicidal ideation

Variable	Controls (n= 150)	Cases (n=50)
Age, in years	56,5 (10,3)	58,3 (11,1)
Gender, male, n (%)	54 (36)	21 (42)
Family status, married, n (%)	106 (70,7)	32 (64)
Disease duration, in years	9,5 (10,4)	8,7 (8,7)
Disease severity, 4-point Likert scale, ≥severe/very severe, n (%)	4 (2.6)	8 (16)
Suicidal attempts in the past, n (%)	1 (0,7)	16 (32)
Patient global, 0-10 NRS	3,9 (2,4)	5,3 (2,4)
Pain, 0-10 NRS	3,9 (2,6)	5,8 (2,2)
EQ5D, 0-3	0,7 (0,2)	0,4 (0,3)
HADS Depression Scale, 0-21	4,6, (3,9)	14,7, (3,9)
HADS Anxiety Scale, 0-21	4,5 (3,6)	11,6 (4,7)
PHQ-9 depressive syndrome, 0-27	6,0 (5,1)	21,3 (4,6)
PHQ-D, somatoform syndrome,0-26	5,5 (3,7)	11,7 (4,4)
PHQ-D, panic disorder, 0-11	0,3 (0,3)	2,2 (2,5)
CSSRS Suicidal Ideation, lifetime, 0-5	0,4 (0,8)	3,3 (1,4)
ASES Arthritis Self Efficacy Scale,1-10	7,1, (2,1)	3,6, (1,8)
SOP2, Optimism, Pessimism Scale, 0-7	5,3 (1,6)	3,0 (1,7)
I8, Impulsive Behavior		
Urgency,0-8	3,2 (1,2)	3,1 (1,3)
Intent,0-8	4,0 (2,4)	4,4 (1,2)
Endurance,0-8	4,4 (0,8)	3,5 (1,0)
Risk-taking,0-8	3,3 (1,3)	3,0 (1,5)
BFI-10, Big Five Inventory		
Extraversion,0-8	3,1 (1,3)	2,0, (1,4)
Compatibility,0-8	3,1 (1,0)	2,6 (0,9)
Conscientiousness,0-8	3,7 (0,8)	2,6 (1,1)
Neuroticism,0-8	2,2 (1,3)	3,6 (1,1)
Openness,0-8	2,8 (1,0)	2,3 (1,1)
CTQ, Childhood Trauma Questionnaire		
Emotional abuse,0-25	6,2 (2,5)	9,6 (5,1)
Physical abuse,0-25	5,5 (1,9)	8,0 (5,5)
Sexual abuse,0-25	5,3 (1,6)	6,2 (3,8)
Emotional neglect,0-25	4,4 (3,3)	9,0 (4,3)
Physical neglect,0-25	4,9 (2,0)	7,3 (2,8)

stratified into high risk (suicidal intent), moderate risk (suicidal thoughts with methods) and low risk (wish to be dead or non-specific active suicidal thoughts). Factors probably associated with risk of suicidal ideation were investigated using multivariable logistic regression analysis.

Results: We identified a total of 95 cases out of 2960 patients resulting in a prevalence of suicidal ideations of 3.2%. Among these cases, 50 completed the questionnaires, while 150 individuals served as controls. While demographics did not differ between cases and controls patient reported outcome was substantially higher in cases than controls (Table 1). In addition, it was observed that personality factors such as pessimism and neuroticism differed between cases and controls (Figure 1). 25 cases (50%) underwent clinical interviews in a psychosomatic clinic. Confidence in causal relationship between iRMD and suicidal ideation was reported by psychosomatic experts with higher values than by rheumatologists 5.4 (3.5) versus 1.6 (1.6). Predictors for suicidal ideation were shorter disease duration, presence of a somatoform or depressive syndrome, larger impulsivity and neurotic personality (Table 2).

Table 2: Multivariable linear regression with lifetime suicidal ideation, moderate/high vs. Low risk

Characteristic	OR[1]	95% CI[1]	p-value
Age	0.94	0.81, 1.04	0.3
Sex, male	0.56	0.05, 4.47	0.6
Disease duration	0.85	0.69, 0.96	**0.041**
Patient global	0.81	0.47, 1.26	0.4
Disease severity	0.76	0.13, 4.83	0.8
PHQ D, somatoform syndrome	1.63	1.09, 2.88	**0.042**
PHQ-9, depressive syndrome	0.56	0.27, 0.90	**0.049**
PHQ-D, panic disorder	1.04	0.76, 1.40	0.8
I8, Impulsive Behaviour Urgency	2.00	1.06, 4.39	**0.048**
BFI10, Big Five Inventory, Neuroticism	5.39	1.70, 28.3	**0.014**
Family status: Married vs. living alone	3.22	0.42, 30.7	0.3

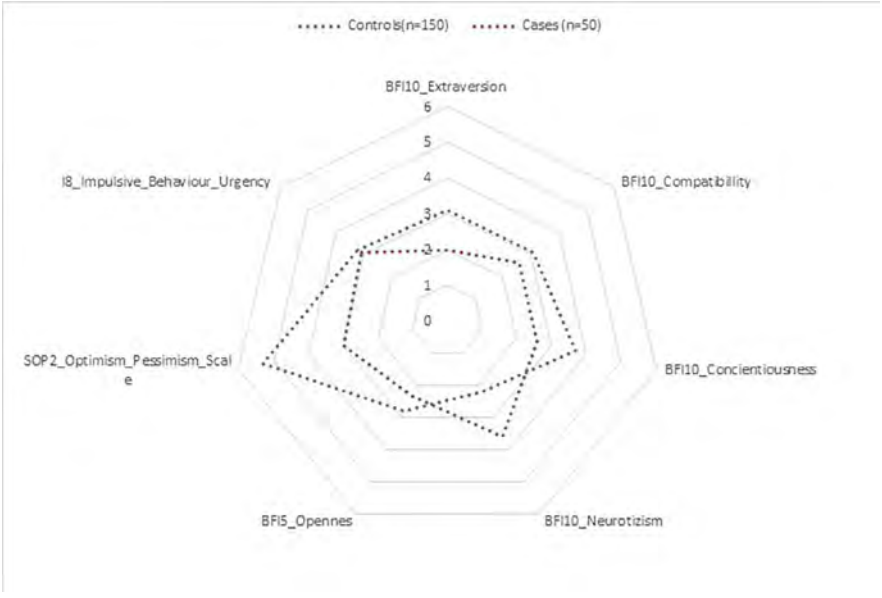

Figure 1: Factors associated with suicidal ideation

Conclusion: A substantial number of patients reported suicidal ideation in our cohort. Of interest, most vulnerable groups were patients with shorter disease duration or a concomitant somatoform or depressive syndrome. Inadequate coping might have influenced the risk for suicidal ideation. Interestingly, known risk factors for suicidal ideation were not identified as such in our study. Larger-scaled studies would be instrumental to unravel further suicidal ideation and its underlying factors.

Disclosure: E. von Schlichting: None; **J. Dieris-Hirche**: None; **I. Redeker**: None; **X. Baraliakos**: AbbVie, 2, 6, BMS, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, 6, UCB, 2, 6; **U. Kiltz**: AbbVie, 2, 5, 6, Amgen, 5, Biocad, 2, 6, Biogen, 5, Bristol-Myers Squibb(BMS), 2, 5, Chugai, 2, 6, Eli Lilly, 2, 6, Fresenius, 5, Gilead, 2, 5, GlaxoSmithKline (GSK), 5, Grünenthal, 2, 6, Hexal, 5, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, onkowiessen.de, 2, 5, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Viatris, 2, 5.

Abstract Number: 0330

Patient-Reported Experiences and Comorbidities in Patients with IgG4-Related Disease with and Without Pancreatic Involvement

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: IgG4-Related Disease (IgG4-RD) is a systemic immune-mediated disease that commonly involves the pancreas in the form of autoimmune pancreatitis (AIP). Despite being one of the most common manifestations of the disease, the burden of abdominal symptomatology experienced by patients with IgG4-related AIP is not well-described.

Methods: We performed a cross-sectional study of patient-reported data using our large, prospective, single-center cohort of patients with IgG4-RD. Subjects were included if they met 2019 ACR/EULAR Classification Criteria. Subjects were excluded if the presence of AIP was unclear from chart review. All eligible subjects were sent surveys that contained questions regarding demographics, disease characteristics, comorbidities, treatment history, and detailed abdominal symptomatology. We compared characteristics between survey responders and non-responders as well as survey responses between patients with and without AIP using Chi-square tests for categorical and unpaired T tests for continuous variables.

Results: Of 327 eligible subjects, 164 (50%) completed surveys; the remainder did not respond to survey invitations, were deceased, or did not have accurate contact information available. Hispanic subjects were less likely to respond to the survey, while subjects with AIP were more likely to respond to the survey than those without; otherwise, demographics were similar between responders and non-responders (**Table 1**).

Disease features and abdominal symptoms in subjects with and without AIP are shown in **Table 2**. Overall, 43% of subjects characterized their general health as either "excellent" or "very good," and 23% reported a cumulative glucocorticoid exposure duration of >1 year. Subjects with AIP more commonly reported having been prescribed insulin, any antihyperglycemic medication, and pancreatic enzyme replacement than those without AIP. Subjects with AIP more frequently experienced

unintentional weight loss, abdominal pain, flatulence, and changes in stool consistency or frequency than those without AIP.

Patient-reported characteristics of abdominal pain are shown in **Table 3**. 38/83 (46%) subjects with AIP reported abdominal pain, and among these subjects, episodic pain was most common (30/38, 79%). 10/38 (26%) reported having experienced episodes of abdominal pain lasting over 6 months, compared with 2/15 (13%) of subjects without AIP who reported

Table 1: Demographics of survey responders vs. non-responders. All values reported as n (%) unless noted otherwise.

	Survey Completed	Survey Not Completed	P-value
N	164 (50)	163 (50)	N/A
Male sex	108 (66)	117 (72)	0.518
Race			
White	129 (79)	108 (66)	0.188
Asian	18 (11)	26 (16)	0.220
Black or African American	5 (3)	9 (6)	0.280
Other	6 (4)	10 (6)	0.311
Unknown/ Not Reported	6 (4)	10 (6)	0.311
Ethnicity			
Hispanic	14 (9)	29 (18)	**0.021**
Not Hispanic	139 (885)	121 (74)	0.286
Not Reported	11 (7)	13 (8)	0.672
Deceased	0 (0)	23 (17)	N/A
Date of diagnosis			
2002-2010	7 (4)	13 (8)	0.175
2011-2015	35 (21)	49 (30)	0.120
2016-2020	84 (51)	75 (46)	0.500
2021-2023	38 (23)	26 (16)	0.140
Disease features			
Number of organs involved	3.4 (1.8)	3.2 (2.0)	0.299
Classification criteria inclusion points, mean (SD)	37.5 (14.0)	36.3 (14.8)	0.473
Pancreatic involvement	83 (51)	57 (35)	**0.031**

Table 2: Patient-reported disease features and abdominal symptoms. *Maximal weight difference defined as difference between highest weight since age 18 years and current weight. **Question on steatorrhea was only asked of subjects who reported changes in stool. AIP: autoimmune pancreatitis; MLS: mean Likert score (1=none, 2=mild, 3=moderate, 4=severe, 5=very severe).

	All	AIP	No AIP	P-value
N	164	83	81	N/A
General health, n (%)				
Excellent or very good	70 (43)	35 (42)	35 (43)	0.919
Good, fair, or poor	94 (57)	48 (58)	46 (57)	0.930
Cumulative glucocorticoid exposure, n (%)	115/144 (80)	51/67 (76)	64/77 (83)	0.639
None	29/144 (20)	16/67 (24)	13/77 (17)	0.351
<1 month	11/144 (8)	6/67 (9)	5/77 (6)	0.594
1-5 months	45/144 (31)	22/67 (33)	23/77 (30)	0.751
6-12 months	26/144 (18)	10/67 (15)	16/77 (21)	0.410
>12 months	33/144 (23)	13/67 (19)	20/77 (26)	0.411
Antihyperglycemic medication use, n (%)	46 (28)	30 (36)	16 (20)	**0.048**
Insulin	26 (16)	19 (23)	7 (9)	**0.022**
Metformin	29 (18)	19 (23)	10 (12)	0.108
Other antihyperglycemics	9 (5)	3 (4)	6 (7)	0.300
Lifetime number of antihyperglycemic classes used	1.5 (0.9)	1.4 (0.6)	1.8 (1.3)	0.18
Current or prior use of pancreatic enzyme replacement, n (%)	35 (21)	34 (41)	1 (1)	**<0.0001**
History of unintentional weight loss, n (%)	71 (43)	47 (57)	24 (30)	**0.0086**
Abdominal symptoms during active IgG4-RD				
Any pain, n (%)	53/163 (33)	38/82 (46)	15/81 (19)	**0.0018**
Bloating, MLS (SD)		2.0 (1.1)	1.8 (1.0)	0.32
Flatulence, MLS (SD)		2.3 (0.9)	2.0 (0.9)	**0.011**
Nausea, MLS (SD)		1.6 (0.9)	1.4 (0.7)	0.10
Number of daily bowel movements, mean (SD)		2.0 (1.2)	1.6 (1.2)	**0.034**
Daily fecal urgency, n (%)	13 (8)	6 (8)	7 (8)	0.95
Other gastrointestinal symptoms, n (%)				
Changes in stool	54/163 (33)	35/83 (42)	19/80 (24)	**0.041**
Steatorrhea (some of the time, often, or all the time)	33/52 (63)	24/34 (71)	9/18 (50)	0.38
Typical Bristol stool form, n (%)				
Type 1: separate hard lumps, like nuts (hard to pass)	3/53 (6)	2/34 (6)	1/19 (5)	0.93
Type 2: sausage-shaped but lumpy	6/53 (11)	2/34 (6)	4/19 (21)	0.12
Type 3: like a sausage but with cracks on its surface	11/53 (21)	6/34 (18)	5/19 (26)	0.51
Type 4: like a sausage or snake, smooth and soft	13/53 (25)	10/34 (29)	3/19 (16)	0.34
Type 5: soft blobs with clear-cut edges (passed easily)	2/53 (4)	1/34 (3)	1/19 (5)	0.68
Type 6: fluffy pieces with ragged edges, a mushy stool	14/53 (26)	11/34 (32)	3/19 (16)	0.26
Type 7: watery, no solid pieces, entirely liquid	4/53 (8)	2/34 (6)	2/19 (11)	0.56

Table 3: Patient-reported abdominal pain characteristics. All questions refer to patient experiences during times of active IgG4-RD. *Among those with abdominal pain, scale: 1=minimal pain, 10=extreme pain; **Among those who take pain medication, scale: 1: no relief, 10: complete relief. AIP: autoimmune pancreatitis.

	AIP	No AIP	P-value
N	83	81	N/A
Abdominal pain, n (%)			
No pain	44/82 (54)	66/81 (81)	**0.031**
Episodic pain	30/82 (37)	12/81 (15)	**0.0062**
Constant pain	8/82 (10)	3/81 (4)	0.14
Average abdominal pain intensity, mean (SD)*	5.2 (2.5)	4.5 (1.4)	0.30
Worst abdominal pain, mean (SD)*	7.0 (2.6)	6.5 (1.6)	0.52
Duration of abdominal pain, n (%)			
A few hours	17/38 (45)	4/15 (27)	0.35
More or less a day	6/38 (16)	2/15 (13)	0.84
More than one week	4/38 (11)	4/15 (27)	0.17
Several weeks	5/38 (13)	2/15 (13)	0.99
Constant mild or moderate pain without discrete episodic pain	3/38 (8)	0/15 (0)	0.28
Constant mild or moderate pain with episodic severe pain	2/38 (5)	3/15 (20)	0.12
Constant severe pain	1/38 (3)	0/15 (0)	0.53
Longest duration of abdominal pain ever experienced, n (%)			
Less than 3 months	22/38 (58)	10/15 (67)	0.71
Between 3 and 6 months	6/38 (16)	3/15 (20)	0.74
Longer than 6 months	10/38 (26)	2/15 (13)	0.37
Exacerbating factors, n (%)			
High-fat meals	19/38 (50)	6/15 (40)	0.63
Stress	17/38 (45)	7/15 (47)	0.93
Alcohol	3/38 (8)	4/15 (27)	0.09
Tobacco	0/38 (0)	0/15 (0)	N/A
Physical activity	3/38 (8)	2/15 (13)	0.56
Relieving factors, n (%)			
Over-the-counter pain medication	13/38 (34)	5/15 (33)	0.96
Rest	12/38 (32)	5/15 (33)	0.92
Fasting or adjusting diet	11/38 (29)	4/15 (27)	0.89
Bowel movement	10/38 (26)	6/15 (40)	0.41
Take pain medication for abdominal pain, n (%)	10/38 (26)	2/15 (13)	0.37
Degree of relief from pain medication, mean (SD)**	5.6 (3.0)	5.0 (3.2)	0.62

abdominal pain (p=0.37). High fat meals and stress were common exacerbating factors in both groups. Numerically more subjects with AIP reported taking pain medication for abdominal pain (26% vs. 13%, p=0.37).

Conclusion: In this large study using patient-reported measures, there was a high burden of symptomatology and comorbidities attributable to IgG4-RD in patients with and without AIP. Patients with AIP experience symptoms and complications attributable to both active pancreatitis (e.g., abdominal pain) and pancreatic insufficiency (e.g., insulin-dependent diabetes, weight loss requiring pancreatic enzyme replacement). These symptoms can have a significant impact on quality of life and should be assessed for and addressed by treating clinicians.

Disclosure: L. Harvey: None; **G. Katz**: None; **Y. Hernandez-Barco**: Nestle Health Science, 1; **A. Fernandes**: None; **A. McMahon**: None; **G. McMahon**: None; **I. Jha**: None; **Z. Wallace**: BioCryst, 2, Bristol-Myers Squibb(BMS), 5, Horizon, 1, 2, 5, MedPace, 2, Novartis, 1, PPD, 2, Sanofi, 1, 5, Shionogi, 1, Visterra, 1, 2, Zenas, 1, 2; **C. Perugino**: Horizon Therapeutics, 2; **J. Stone**: Abvie, 2, Amgen, 1, 2, Argenx, 2, Aztrazeneca, 2, Bristol Myers Squibb, 2, 5, Celgene, 2, Chemocentryx, 2, Chugai, 2, GSK, 2, Horizon Therapeutics, 1, 2, 5, InflaRx, 2, IQVIA, 1, 2, Kyverna, 2, Mirabio, 2, NIH, 5, Novartis, 2, PPD, 2, Prometheus, 2, Q32, 2, Regeneron, 2, Roche-Genentech, 2, Roivant, 2, Sanofi, 2, 5, Spruce Biosciences, 2, Star Therapeutics, 2, Steritas, 12, Chair, Scientific Advisory Board (no fiduciary responsibilities), ZenasBio, 2.

Abstract Number: 0331

Assessment of Patient Adherence to "Sick Day Rules": A Cross-sectional Study of Rheumatology Outpatients Prescribed Immunosuppressive Medications

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SESSION INFORMATION

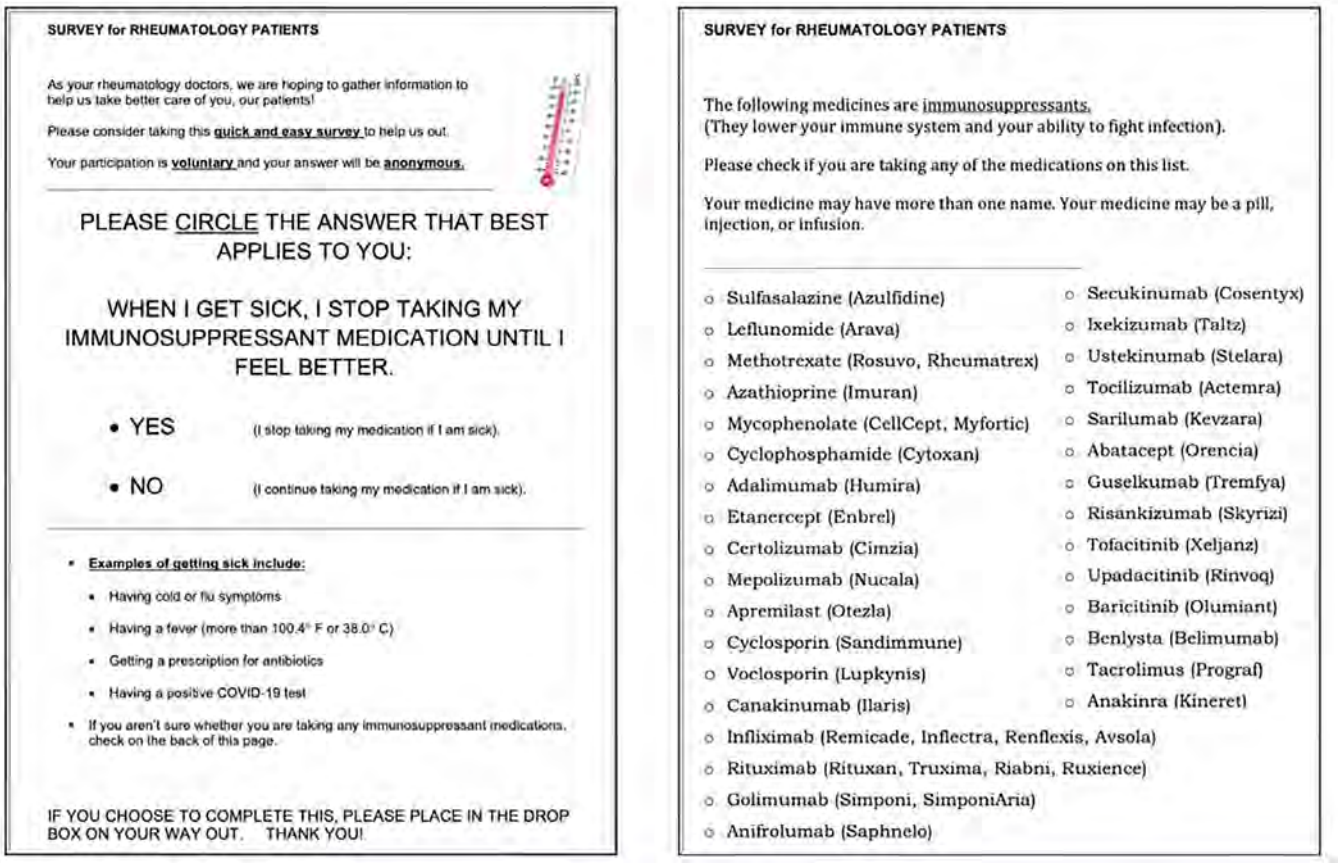
Session Date: Sunday, November 12, 2023

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatology outpatients receiving immunosuppressive medications (IS) inevitably develop acute infections. Expert guidance, in accordance with usual clinical practice, recommends counseling patients on "sick day rules." Patients are recommended to pause IS (with the exception of corticosteroids, which require dose increases) during an acute infection, resuming only when clinically improved. Prior studies have shown poor understanding of "sick day rules" specific to chronic steroid therapy in rheumatology outpatients. [Courtney, 2022]. However, the scope of this problem has not yet been described among the majority of rheumatology outpatients who receive non-steroid IS. Our study aimed to quantify



SURVEY for RHEUMATOLOGY PATIENTS

As your rheumatology doctors, we are hoping to gather information to help us take better care of you, our patients!

Please consider taking this **quick and easy survey** to help us out.

Your participation is **voluntary** and your answer will be **anonymous.**

PLEASE CIRCLE THE ANSWER THAT BEST APPLIES TO YOU:

WHEN I GET SICK, I STOP TAKING MY IMMUNOSUPPRESSANT MEDICATION UNTIL I FEEL BETTER.

- YES (I stop taking my medication if I am sick).
- NO (I continue taking my medication if I am sick).

- **Examples of getting sick include:**
  - Having cold or flu symptoms
  - Having a fever (more than 100.4° F or 38.0° C)
  - Getting a prescription for antibiotics
  - Having a positive COVID-19 test
- If you aren't sure whether you are taking any immunosuppressant medications, check on the back of this page.

IF YOU CHOOSE TO COMPLETE THIS, PLEASE PLACE IN THE DROP BOX ON YOUR WAY OUT. THANK YOU!

SURVEY for RHEUMATOLOGY PATIENTS

The following medicines are immunosuppressants.
(They lower your immune system and your ability to fight infection).

Please check if you are taking any of the medications on this list.

Your medicine may have more than one name. Your medicine may be a pill, injection, or infusion.

- Sulfasalazine (Azulfidine)
- Leflunomide (Arava)
- Methotrexate (Rosuvo, Rheumatrex)
- Azathioprine (Imuran)
- Mycophenolate (CellCept, Myfortic)
- Cyclophosphamide (Cytoxan)
- Adalimumab (Humira)
- Etanercept (Enbrel)
- Certolizumab (Cimzia)
- Mepolizumab (Nucala)
- Apremilast (Otezla)
- Cyclosporin (Sandimmune)
- Voclosporin (Lupkynis)
- Canakinumab (Ilaris)
- Infliximab (Remicade, Inflectra, Renflexis, Avsola)
- Rituximab (Rituxan, Truxima, Riabni, Ruxience)
- Golimumab (Simponi, SimponiAria)
- Anifrolumab (Saphnelo)
- Secukinumab (Cosentyx)
- Ixekizumab (Taltz)
- Ustekinumab (Stelara)
- Tocilizumab (Actemra)
- Sarilumab (Kevzara)
- Abatacept (Orencia)
- Guselkumab (Tremfya)
- Risankizumab (Skyrizi)
- Tofacitinib (Xeljanz)
- Upadacitinib (Rinvoq)
- Baricitinib (Olumiant)
- Benlysta (Belimumab)
- Tacrolimus (Prograf)
- Anakinra (Kineret)

Figure 1. Paper survey (front and back) provided to patients.

the rate of proper adherence to "sick day rules" in a general rheumatology clinic. We hypothesized that we would find a high rate of non-adherence and illuminate a preventable source of patient harm.

Methods: This was a cross-sectional study of outpatients attending general rheumatology clinic visits in spring 2023. Patients who agreed to participate received the one-page document shown in Figure 1. Patients were asked to respond 'yes' or 'no' to the statement: "When I get sick, I stop taking my IS until I feel better." Patients were also asked to select the medications they were currently receiving. Surveys were de-identified. A Spanish-language version of the survey was made available. Any patient currently receiving DMARD therapy was eligible to participate. Exclusion criteria were as follows: no active prescription for a DMARD; active prescription for hydroxychloroquine, colchicine, or corticosteroids only; and inability of the patient (or family member/caregiver present) to read English or Spanish.

Results: 82 patients returned a completed survey. Overall, 32 patients (39%) responded "no," indicating that they would not interrupt IS if they became ill. 73 of 82 patients indicated which medications they were receiving. Among patients receiving biologic DMARD (bDMARD) therapy, apremilast, or JAK inhibitors, 9 of 37 (24%) responded "no" to the survey question. Among patients receiving only conventional synthetic DMARD (csDMARD) therapy, 21 of 36 (58%) responded "no" to the survey question.

Conclusion: Nearly 40% of the patients in our sample receiving IS indicated non-adherence to recommended "sick day rules." Among patients receiving only csDMARD therapy, this proportion rose to 58%. As hypothesized, our findings highlight an area for quality improvement and harm reduction. We observed particularly poor understanding among patients receiving csDMARDs only, even though these patients may still be considerably immunosuppressed. Our study was limited the risk of completion bias, potentially lowering the response rate in patients with poorer health literacy and worse disease control. We plan to intensify patient counseling in our clinic, including posting signage throughout our clinic displaying proper "sick day rules." We will repeat the same survey with a random sample from the same clinic, and we hypothesize that adherence will improve after our intervention.

Disclosure: M. Aksoy: None; **P. Gonzalez Manrique**: None; **H. Greenblatt**: None; **K. Gilek-Seibert**: AbbVie/Abbott, 6.

Abstract Number: 0332

Initial Characterization of a Skin Symptom Questionnaire for Patients with Systemic Sclerosis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Skin disease is a hallmark of systemic sclerosis (SSc). The modified Rodnan skin score (mRSS) is physician performed measurement that assesses the extent and severity of skin thickness. However, it does not capture all of the clinical features of SSc skin disease. Patient-reported outcomes (PROs) can capture patients' perspective. The Scleroderma Skin Questionnaire (SSQ) is a novel PRO which assesses skin symptoms. To date, the SSQ has not been validated, and this study sought to assess the psychometric properties of the SSQ to generate evidence to support its further use.

Methods: We used data from CONQUER (Collaborative National Quality and Efficacy Registry), a multi-center, US-based registry of adults with early limited cutaneous (lc) and diffuse cutaneous (dc) SSc. The SSQ uses a 7-day recall period of 6 items (tight, painful, red, hard, itchy, rigid/stiff), which are graded on a 5-point Likert scale and averaged to obtain a score ranging 0-4 (4=worse). The second part of the questionnaire, the SSQ 6-Month, asks respondents to compare these symptoms to 6-months prior. Internal consistency of the SSQ was determined with Cronbach's α. Baseline response frequencies were used to investigate floor/ceiling effects. The associations between the SSQ and the mRSS and with legacy PROs [Scleroderma Health Assessment Questionnaire (SHAQ), Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29), Patient Global (PtGA), and Physician Global (PGA)] were explored using Pearson's correlations. The SSQ 6-Month was correlated with 6-month changes in mRSS and in legacy PROs using mixed modeling with a bias-corrected confidence interval determined using cluster bootstrapping.

Results: We included 536 participants who completed the mRSS and SSQ (Table 1). The SSQ was higher (worse) in patients with dcSSc compared with lcSSc (1.5 vs 0.9; p< 0.001). The SSQ demonstrated internal consistency (α=0.90) and likely floor effect (Figure 1). At baseline, the SSQ was moderately correlated with the mRSS (r=0.56). The correlation was stronger among individuals with dcSSc (r=0.56) than lcSSc (r=0.22; all p< 0.05).At baseline, the SSQ was strongly correlated with PROMIS-29's physical (r=-0.52) and pain interference (r=0.61), and weakly with PROMIS-29's anxiety (r=0.24) and sleep disturbance (r=0.12; all p< 0.05). For the SHAQ, SSQ correlated strongly to HAQ (r=0.63) and severity score (r=0.61) and weakly to intestinal symptoms, breathing symptoms, Raynaud's attacks, and finger ulcers symptoms (all

TABLE 1: Patient demographics and baseline characteristics

	Overall N = 536	lcSSc[3] N = 166 (31.0%)	dcSSc[4] N = 370 (69.0%)	P-value
Age (years)	52.5 (13.69)*	53.8 (14.08)*	51.8 (13.48)*	0.13[1]
Male	98 (18.3%)	21 (12.7%)	77 (20.8%)	0.02[2]
Digital ulcers	62 (11.7%)	8 (4.8%)	54 (14.7%)	0.00[1]
mRSS[5]	12.8 (10.68)*	4.1 (3.46)*	16.6 (10.54)*	<0.00[1]
SSQ[6]	1.3 (1.07)*	0.9 (0.93)*	1.5 (1.07)*	<0.00[1]

*mean (SD)
[1] Two-sample t-test
[2] Chi-square test
[3] Limited cutaneous systemic sclerosis
[4] Diffuse cutaneous systemic sclerosis
[5] Modified Rodnan Skin Score
[6] Scleroderma Skin Questionnaire

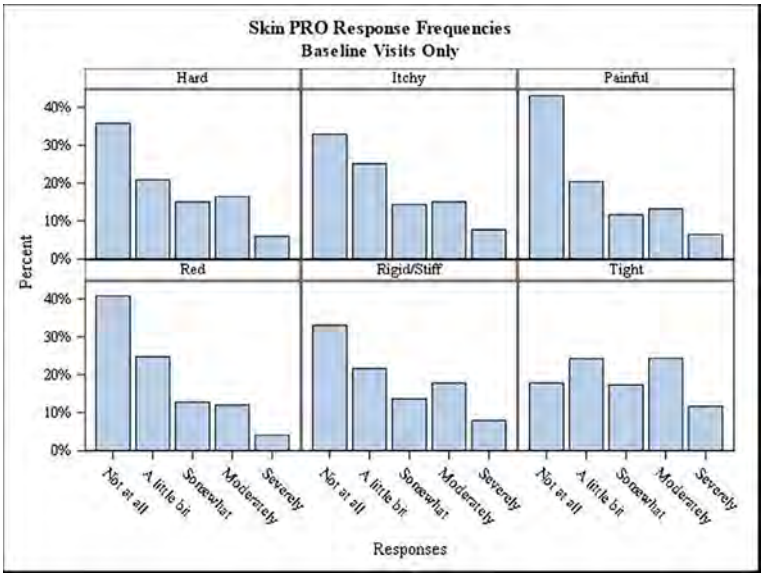

Figure 1: SSQ Response Frequencies at Baseline Visits

TABLE 2: Correlations between SSQ with mRSS and legacy PROs

			SSc Subtype [1,3]		Baseline mRSS [3]		Disease Duration at Baseline [3]	
	Baseline SSQ[5]	SSQ[5] 6-Month[4]	lcSSc[6]	dcSSc[7]	>16	<=16	< 2 Years	≥ 2 Years
mRSS[8]	0.56 (0.5, 0.62)*	0.21 (0.08, 0.33)*	0.22 (0.07, 0.36)*	0.56 (0.49, 0.63)*	0.37 (0.23, 0.49)*	0.27 (0.17, 0.36)*	0.53 (0.43, 0.62)*	0.55 (0.47, 0.62)*
PtGA[9]	0.44 (0.37, 0.51)*	0.11 (-0.04, 0.27)	0.38 (0.24, 0.5)*	0.46 (0.38, 0.54)*	0.35 (0.21, 0.48)*	0.42 (0.33, 0.5)*	0.46 (0.35, 0.56)*	0.38 (0.28, 0.47)*
PGA[10]: Overall Health	0.38 (0.31, 0.45)*	0.09 (-0.02, 0.22)	0.22 (0.07, 0.36)*	0.36 (0.27, 0.44)*	0.2 (0.05, 0.34)*	0.27 (0.17, 0.36)*	0.43 (0.31, 0.53)*	0.31 (0.21, 0.4)*
PGA[10]: Scleroderma Activity	0.46 (0.39, 0.52)*	0.12 (-0.02, 0.25)	0.19 (0.04, 0.33)*	0.45 (0.37, 0.53)*	0.29 (0.15, 0.42)*	0.25 (0.15, 0.34)*	0.49 (0.38, 0.59)*	0.39 (0.29, 0.48)*
PGA[10]: Scleroderma Damage	0.35 (0.27, 0.42)*	0.17 (0.05, 0.31)*	0.08 (-0.07, 0.23)	0.34 (0.25, 0.43)*	0.12 (-0.03, 0.26)	0.18 (0.08, 0.28)*	0.4 (0.28, 0.51)*	0.31 (0.21, 0.4)*
PROMIS-29[11]: Pain Interference	0.61 (0.55, 0.66)*	0.21 (0.05, 0.36)	0.53 (0.41, 0.63)*	0.64 (0.57, 0.7)*	0.55 (0.43, 0.65)*	0.58 (0.5, 0.65)*	0.64 (0.55, 0.72)*	0.57 (0.49, 0.64)*
PROMIS-29[11]: Ability to Participate in Social Roles and Activities	-0.48 (-0.54, -0.41)*	-0.17 (-0.32, -0.02)	-0.38 (-0.51, -0.24)*	-0.5 (-0.58, -0.42)*	-0.41 (-0.53, -0.27)*	-0.45 (-0.53, -0.36)*	-0.51 (-0.61, -0.4)*	-0.42 (-0.51, -0.32)*
PROMIS-29[11]: Physical Function	-0.52 (-0.58, -0.45)*	-0.24 (-0.4, -0.12)	-0.48 (-0.59, -0.35)*	-0.49 (-0.57, -0.41)*	-0.46 (-0.58, -0.33)*	-0.45 (-0.53, -0.36)*	-0.63 (-0.71, -0.54)*	-0.4 (-0.49, -0.3)*
PROMIS-29[11]: Fatigue	0.43 (0.36, 0.5)*	0.14 (-0.01, 0.29)	0.47 (0.34, 0.58)*	0.42 (0.33, 0.5)*	0.48 (0.35, 0.59)*	0.43 (0.34, 0.51)*	0.54 (0.43, 0.63)*	0.35 (0.25, 0.44)*
PROMIS-29[11]: Anxiety/Fear	0.24 (0.16, 0.32)*	0.25 (0.04, 0.42)*	0.22 (0.06, 0.36)*	0.25 (0.15, 0.35)*	0.23 (0.08, 0.37)*	0.22 (0.12, 0.32)*	0.18 (0.04, 0.31)*	0.24 (0.13, 0.34)*
PROMIS-29[11]: Sleep Disturbance	0.12 (0.03, 0.21)*	-0.11 (-0.32, 0.09)	0.07 (-0.09, 0.23)	0.16 (0.06, 0.26)*	0.03 (-0.13, 0.19)	0.13 (0.02, 0.23)*	0.1 (-0.04, 0.24)	0.12 (0.01, 0.23)*
PROMIS-29[11]: Depression/ Sadness	0.4 (0.32, 0.47)*	0.11 (-0.07, 0.27)	0.38 (0.24, 0.51)*	0.4 (0.31, 0.49)*	0.36 (0.21, 0.49)*	0.37 (0.27, 0.46)*	0.37 (0.24, 0.49)*	0.38 (0.28, 0.47)*
SHAQ[12]: HAQ Score	0.63 (0.58, 0.68)*	0.16 (0.01, 0.28)*	0.49 (0.37, 0.6)*	0.64 (0.58, 0.7)*	0.52 (0.4, 0.62)*	0.57 (0.5, 0.63)*	0.65 (0.57, 0.72)*	0.59 (0.52, 0.66)*
SHAQ[12]: Intestinal Score	0.22 (0.14, 0.3)*	0.05 (-0.1, 0.17)	0.27 (0.12, 0.4)*	0.21 (0.11, 0.3)*	0.22 (0.07, 0.36)*	0.23 (0.13, 0.32)*	0.29 (0.16, 0.41)*	0.17 (0.06, 0.27)*
SHAQ[12]: Breathing Score	0.26 (0.18, 0.34)*	0.06 (-0.09, 0.18)	0.26 (0.11, 0.4)*	0.27 (0.17, 0.36)*	0.3 (0.16, 0.43)*	0.23 (0.13, 0.32)*	0.33 (0.21, 0.44)*	0.2 (0.09, 0.3)*
SHAQ[12]: Raynaud's Score	0.38 (0.31, 0.45)*	0.07 (-0.07, 0.22)	0.47 (0.34, 0.58)*	0.34 (0.25, 0.43)*	0.25 (0.1, 0.39)*	0.44 (0.35, 0.52)*	0.36 (0.24, 0.47)*	0.39 (0.29, 0.48)*
SHAQ[12]: Finger Score	0.3 (0.22, 0.38)*	0.01 (-0.09, 0.12)	0.3 (0.15, 0.43)*	0.27 (0.17, 0.36)*	0.18 (0.03, 0.32)*	0.26 (0.16, 0.35)*	0.31 (0.18, 0.43)*	0.27 (0.17, 0.37)*
SHAQ[12]: Severity Score	0.61 (0.55, 0.66)*	0.17 (0.02, 0.32)*	0.5 (0.38, 0.61)*	0.62 (0.55, 0.68)*	0.52 (0.4, 0.62)*	0.58 (0.51, 0.64)*	0.67 (0.59, 0.74)*	0.53 (0.45, 0.6)*

* denotes a significant result at the 0.05 level.
[1] SSc subtype is defined as whether the patient has ever been diagnosed as having diffuse SSc. Otherwise, the patient is assumed to have limited SSc.
[2] Difference in Pearson correlation coefficient, (95% confidence interval)
[3] Based on baseline data only.
[4] Correlation of SSQ 6-Month with 6-month changes in mRSS and in legacy PROs using mixed modeling with a bias-corrected confidence interval determined using cluster bootstrapping.
[5] Scleroderma Skin Questionnaire
[6] Limited cutaneous systemic sclerosis
[7] Diffuse cutaneous systemic sclerosis
[8] Modified Rodnan Skin Score
[9] Patient Global Assessment
[10] Physician Global Assessment
[11] Patient-Reported Outcomes Measurement Information System-29
[12] Scleroderma Health Assessment Questionnaire

p< 0.05). When stratified for SSc subtype, baseline mRSS, and disease duration, similar trends for correlation were seen (Table 2). SSQ 6-Month showed correlation of r=0.21 (p< 0.05) with 6-month change in mRSS and poor correlation with change in legacy PROs (Table 2).

Conclusion: In the CONQUER registry, the SSQ demonstrated internal consistency and moderate correlation with mRSS. The SSQ showed moderate/strong correlations with a subset of legacy PROs. However, the SSQ 6-Month showed weak correlation with change in the mRSS, suggesting either a poor recall for a 6-month time span or a disconnect between the patient perception and the mRSS. This study provides initial characterization of SSQ for future validation.

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Abstract Number: 0333

Ankylosing Spondylitis Patient Perspective on Living with Flares and Impact on Quality of Life

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing spondylitis (AS) leads to symptoms of pain, stiffness, swelling, and fatigue. Patients often report periods of increased symptoms (flares) followed by remission.The purpose of this study was to assess the experience of flares on quality of life from the patient perspective. Improved understanding of the experience of flares may contribute to better treatment and health outcomes.

Methods: In July 2022 an email invitation to an online survey was sent to members of MySpondylitisTeam, a social network of over 88,000 people. 253 members who self-report a doctor's diagnosis of ankylosing spondylitis (AS) completed the 25-question survey.

Results: 94% of members agreed that AS affects their quality of life and 87% agreed that AS makes it hard to do everyday activities. When asked to select the statement that best reflects flare activity in their AS, 44% selected "I have periods of increased symptoms (flares) on and off" and 43% selected "I have flares almost all the time." ***(Figure 1)*** Patients with almost constant flares indicated lower quality of life across a number of measures when compared with those whose flares were "on and off". Significant differences were evident for:

- Negatively affected their relationships with family (79% flares "almost all the time" vs. 48% flares "on and off")
- Made them feel isolated or alone (83% vs. 59%)
- Negatively affected their ability to have an active social life (93% vs. 74%)
- Made them feel stressed, anxious, or depressed (93% vs. 75%) ***(Figure 2)***

Just 27% of those who flare "almost all the time" agreed that they "lead a full life despite having spondylitis", compared 49% for those with flares "on and off". Many also indicated that obstacles to managing AS included pain or feeling unwell, as well as relentless fatigue (82% and 76% respectively). For example, one respondent wrote, "Lots of pain, fatigue. It has had an impact on my family."

Figure 1: Spondyloarthritis Flare Frequency - Among Those With Ankylosing Spondylitis

% Strongly and somewhat agree *My spondylitis…*	Those with AS (Sample=253)	Those with flares "almost all the time" (Sample=110)	Those who flare "on and off" (Sample=111)	*Net difference*
Negatively impacts my family relationships	62%	**79%***	48%	*31 points*
Makes me feel isolated or alone	70%	**83%***	59%	*24*
Interferes with my ability to have an active social life	82%	**93%***	74%	*19*
Makes me feel stressed, anxious, or depressed	82%	**93%***	75%	*18*
Makes it difficult for me to be sexually active	61%	69%	57%	*12*
Makes it hard for me to get around physically	81%	86%	76%	*10*
Makes me less productive at work, school, or home	84%	**91%***	78%	*13*
Makes it difficult to sleep at night	84%	**92%***	81%	*11*
Makes it hard to do everyday activities	87%	**93%***	83%	*10*
Makes it hard for me to exercise or to stay active	88%	92%	86%	*6*
Interferes with my quality of life	93%	95%	90%	*5*

How much do you agree or disagree with each of the following statements? My spondylitis… *95% CI (2-sample *t* test).

Figure 2: Impact on Quality of Life

% Currently taking	Those with AS (Sample=221)	Those with flares "almost all the time" (Sample=98)	Those who flare "on and off" (Sample=98)	*Net difference*
Nonsteroidal anti-inflammatory drug (NSAID)	48%	53%	43%	*11 points*
Biologic drug	46%	36%	**54%***	*18*
Opioid medication	31%	39%	28%	*11*
Disease modifying anti-rheumatic drug (DMARD)	19%	18%	19%	*24*
JAK inhibitor	2%	2%	2%	*0*
Other	25%	26%	22%	*4*

Which of the following are you currently taking to treat spondylitis or your symptoms of spondylitis? Please select all that apply. *95% CI (2-sample *t* test).

Figure 3: Treatments Currently Taking

Additionally, differences also exist with respect to doctor satisfaction and treatment. Fewer were satisfied with the doctor who primarily treats their HS (31% "extremely" or "very" satisfied compared with 42% for those who flare "on and off"). Those who flare "almost all the time" were also less likely to say that doctor "addresses symptoms of spondylitis such as pain or fatigue" (45% compared with 33% for those who flare "on and off").

Interestingly, those who flares were near-constant were significantly less likely to have been prescribed biologics (36% vs. 54% flares "on and off"). Additionally, those with almost constant flares were more likely to be treated with NSAIDs (53% vs. 43% flares "on and off" or opioids (39% vs. 28% flares "on and off") ***(Figure 3)***.

Conclusion: The extensive impact that flares have on AS patients' quality of life suggests that managing symptoms remains an ongoing concern. The obvious physical, emotional, and interpersonal toll that AS has on the lives of patients, combined with ongoing usage of opioids, indicate the need for better disease management and improved health outcomes. Frequent or near-constant flares, combined with the perception that fatigue, pain and feeling unwell act as obstacles to managing AS, is a reminder that better disease control is needed for many patients with AS.

Disclosure: H. Lapidus Glassner: None; **E. Luce**: None.

Abstract Number: 0334

Association of a Self-Report Screening Tool for Sarcopenia (SARC-F) with Functional Status Outcomes in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Sarcopenia, i.e., loss of skeletal muscle mass and strength, has been associated with multiple adverse health outcomes, including mortality. Although limited data suggest that sarcopenia is more prevalent among adults with systemic lupus erythematosus (SLE) across the lifespan relative to comparators, current methods for sarcopenia assessment (e.g., body composition-specific dual energy x-ray absorptiometry) are not widely available. Therefore, we assessed associations of a simple self-report screening tool for sarcopenia (SARC-F) with functional status outcomes in adults with SLE [1].

Methods: We recruited women ≥18 years with validated SLE followed at our hospital. Sociodemographic and SLE disease characteristics, as well as observed and self-report functional status measures (hand grip strength, 4-meter (m) walk test, self-report FRAIL scale, Valued Life Activities self-report disability) were obtained. Participants completed the SARC-F, which includes questions related to strength, assistance walking, rising from a chair, climbing stairs, and falls. Sociodemographic features, SLE disease characteristics, and functional status measures were compared using descriptive statistics between participant groups, with SARC-F scores dichotomized as ≥4 versus < 4 based on established cut points. Pearson correlations and linear and logistic regression were used to evaluate the relationship between the SARC-F as a continuous and dichotomous score with functional status measures, including after adjustment for confounders (i.e., age, race, ethnicity, disease activity, and organ damage).

Results: Of 47 participants, 16 (34%) had SARC-F score ≥4. Participants with SARC-F ≥4 had greater organ damage and worse functional status measures than those with SARC-F < 4 (all p< 0.01). SARC-F continuous scores were significantly correlated with hand grip strength, 4-m walk test, and self-report disability (all p< 0.01) and significantly correlated with all functional status measures (p< 0.01 to p=0.046). Dichotomous SARC-F was significantly associated with 4-m walk test (p< 0.01), including after adjustment for confounders, and there was a trend toward significance with hand grip strength and self-report disability (both p=0.06).

Table 1

Table 1. Sociodemographic and disease characteristics and functional status measures of adults with systemic lupus erythematosus (SLE) with high (≥4) versus low (<4) SARC-F scores

Variable N (%) or mean +/- standard deviation	Overall (N=47)	SARC-F score ≥4 (N=16)	SARC-F score <4 (N=31)	p-value
Age (years)	48.3 (14.5)	47.6 (15.0)	49.6 (14.0)	0.67
Race				<0.01
Asian	6 (13)	0 (0)	6 (19)	
Black or African	14 (30)	4 (25)	10 (32)	
White	14 (30)	2 (12)	12 (39)	
Other	10 (21)	9 (57)	1 (3)	
Declined to state	3 (6)	1 (6)	2 (6)	
Ethnicity				0.25
Hispanic or Latino	17 (36)	8 (50)	9 (29)	
Not Hispanic or Latino	28 (60)	7 (44)	21 (68)	
Declined to state	2 (4)	1 (6)	1 (3)	
Disease characteristics				
SLE duration (years)	19.0 (12.2)	20.3 (11.7)	18.2 (12.6)	0.61
Disease activity[a]	3.6 (3.3)	3.9 (3.7)	3.5 (3.1)	0.70
Organ damage[b]	1.5 (1.8)	2.4 (1.8)	1.0 (1.5)	<0.01
SLE medication use				
Prednisone dose (mg)	10.2 (13.2)	13.9 (16.8)	5.6 (3.3)	0.13
Hydroxychloroquine	39 (83)	13 (81)	26 (84)	0.82
Immunosuppressive[c]	32 (68)	13 (81)	19 (61)	0.16
Functional measures				
Hand grip strength (kg)	15.6 (17.1)	11.3 (6.9)	18.1 (6.2)	<0.01
4-m walk test (s)	5.2 (1.7)	6.6 (2.2)	4.5 (0.8)	<0.01
Valued Life Activities	0.7 (0.6)	1.1 (0.5)	0.5 (0.5)	<0.01
Frailty[d]	12 (26)	11 (69)	1 (3)	<0.01

[a]Safety of Estrogens in Lupus Erythematosus National Assessment-SLE Disease Activity Index
[b]Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index
[c]Methotrexate; azathioprine; mycophenolate mofetil; mycophenolic acid; belimumab; cyclophosphamide; rituximab; tocilizumab; cyclosporine; tacrolimus
[d]FRAIL scale

Table 2

Table 2. Correlation and association of continuous SARC-F score with functional status measures in adults with systemic lupus erythematosus

Functional measure	Correlation coefficient	p-value	Unadjusted parameter estimate (95% confidence interval)	p-value	Adjusted* parameter estimate (95% confidence interval)	p-value
Hand grip strength	-0.48	<0.01	-1.27 (-1.99, -0.56)	<0.01	-1.21 (-2.39, -0.02)	0.046
4-m walk test	0.73	<0.01	0.50 (0.36, 0.65)	<0.01	0.67 (0.37, 0.97)	<0.01
Valued Life Activities	0.65	<0.01	0.14 (0.09, 0.19)	<0.01	0.12 (0.04, 0.21)	<0.01
Functional measure	Correlation coefficient	p-value	Unadjusted odds ratio (95% confidence interval)	p-value	Adjusted* odds ratio (95% confidence interval)	p-value
Frailty	NA	NA	2.03 (1.33, 3.08)	<0.01	2.40 (1.10, 5.21)	0.03

*Adjusted for age, race, ethnicity, disease activity, and organ damage

Table 3

Table 3. Association of dichotomous SARC-F score (≥4) with functional status measures in adults with systemic lupus erythematosus

	Unadjusted parameter estimate (95% confidence interval)	p-value	Adjusted* parameter estimate (95% confidence interval)	p-value
Hand grip strength	-6.81 (-10.84, -2.79)	<0.01	-6.40 (-13.06, 0.26)	0.06
4-m walk test	2.14 (1.22, 3.05)	<0.01	2.30 (0.52, 4.08)	0.01
Valued Life Activities	0.55 (0.22, 0.88)	<0.01	0.47 (-0.02, 0.97)	0.06

*Adjusted for age, race, ethnicity, disease activity, and organ damage

Conclusion: In this exploratory study of adult women with SLE, SARC-F was significantly associated with multiple functional status measures, suggesting that the SARC-F may be a valid point-of-care screening tool for sarcopenia in women with SLE.

Reference: 1. Malmstrom et al. J Cachexia Sarcopenia Muscle 2016;7:28-36.

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Abstract Number: 0335

Meta-Analysis of the Cost-Effectiveness of Social Media Advertising as a Recruitment Tool

Vladislav Tsaltskan[1], Roel Baez[2] and Gary Firestein[1], [1]University of California San Diego, San Diego, CA, [2]UC San Diego Health, San Diego, CA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Recruitment of study participants is challenging and can incur significant costs, particularly for studies of rheumatic disease or other rare conditions. Social media advertising is a promising method for recruiting to clinical studies. This approach may improve cost efficiency by targeting specific populations that are more likely to match a study's criteria. Although individual studies evaluating social media as a recruitment tool have been generally favorable, there are no meta-analyses of its cost-effectiveness.

Methods: Studies evaluating costs of recruitment through social media and non-social media methods were identified on MEDLINE and EMBASE. Articles were screened through a two-step process in accordance with PRISMA guidelines. Cost data was then extracted from included articles, normalized for currency and inflation, and a meta-analysis was performed using the Mantel-Haenszel method. The primary outcome was the relative cost-effectiveness of social media compared to non-social media recruitment, defined as the odds ratio of recruiting a participant per US dollar spent on each method. The secondary outcome was the relative cost-effectiveness of social media recruitment compared only to other online recruitment methods.

Results: After completion of the screening process, 23 studies were included in the meta-analysis. All of the included studies evaluated Facebook as a recruiting tool. Two studies also evaluated Instagram and Twitter, and one study each evaluated Youtube, Reddit, Linkedin, and Snapchat. The sample contained a high degree of heterogeneity, requiring the use of the random effects model. The odds ratio of recruiting a participant through social media advertising compared to non-social media methods per dollar spent was 1.97 [95% CI 1.24-3.00, P = 0.004]. This odds ratio conferred a median advantage over other methods of $45.51 [IQR $13.92-134.81] per enrolled participant for social media compared with $74.89 [IQR $6.57-187.15] per participant for other methods. For the secondary outcome, the odds ratio of recruiting a participant through social media compared to other online methods was 1.66 [95% CI 1.02-2.72, P = 0.04].

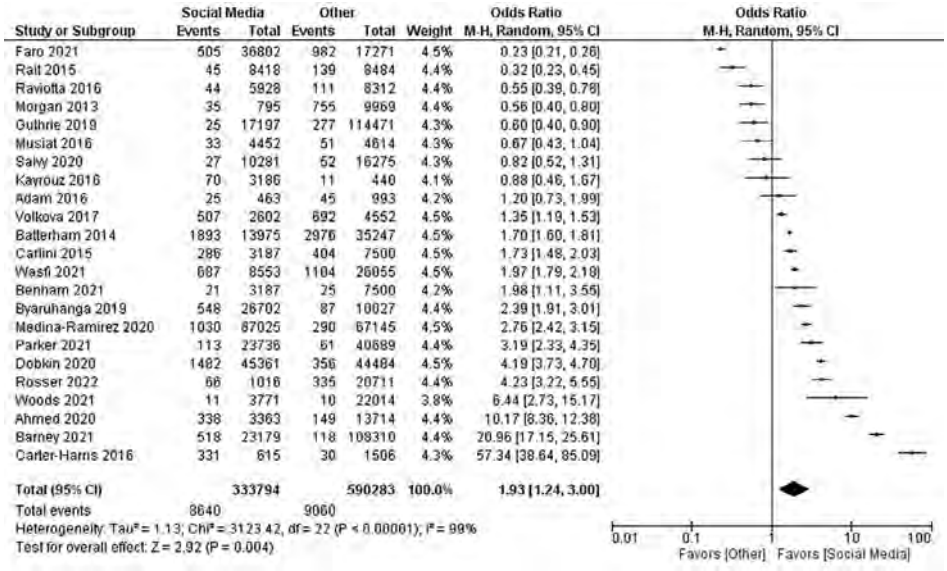

Figure 1: Forest plot of primary outcome.

Conclusion: Social media advertising is approximately twice as cost-effective as other methods of participant recruitment, although the magnitude of cost-effectiveness is varied between studies and populations. Additional data are needed to determine cost-effectiveness for individual rheumatic diseases and for rare conditions. There are also limited data available for newer social media platforms and for difficult-to-reach populations such as non-English speaking or older individuals. However, the data suggest that incorporating social media into clinical research could improve accrual at a lower cost than traditional methods.

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Abstract Number: 0336

Core Signs Associated with the Subtypes of Cutaneous Lupus Erythematosus: Concept Elicitation Interviews with Dermatologists and Rheumatologists

victoria werth[1], Annegret Kuhn[2], Joseph F. Merola[3], Joerg Wenzel[4], Cristina Vazquez-Mateo[5], Sanjeev Roy[6], Erik Thomas[5], Oliver Guenther[7], Ying Sun[7], Alexandra Lauer[7], Almary Guerra Rodriguez[8], Patricia Koochaki[9] and Paul Kamudoni[7], [1]University of Pennsylvania, Wynnewood, PA, [2]Amsterdam University Medical Center, Amsterdam, Netherlands, and University of Münster, Münster, Germany, [3]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [4]University Hospital of Bonn, Bonn, Germany, [5]EMD Serono, Billerica, MA, [6]Ares Trading SA, Eysins, Switzerland, an affiliate of Merck KGaA, Darmstadt, Germany, [7]the healthcare business of Merck KGaA, Darmstadt, Germany, [8]Laife Reply GmbH, Frankfurt am Main, Germany, [9]ICON Clinical Research LLC, Raleigh, NC

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

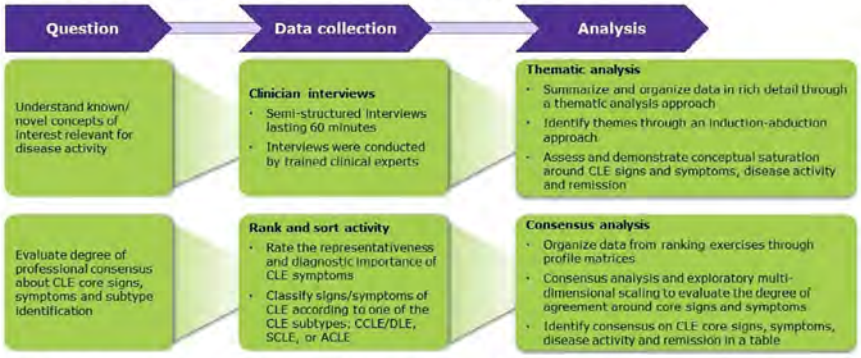
Session Time: 9:00AM–11:00AM

Background/Purpose: Greater understanding of cutaneous signs and symptoms is needed to comprehensively define and measure cutaneous disease activity in lupus erythematosus. Herein, we interviewed dermatologic and rheumatologic experts: (I) to explore perspectives regarding key signs and symptoms for defining disease activity and damage in cutaneous lupus erythematosus (CLE) subtypes (chronic [primarily discoid], subacute and acute [CCLE [DLE]/SCLE/ACLE]) and (II) to explore potential differences and similarities in clinical signs and symptoms across these CLE subtypes.

Methods: This was a non-interventional, mixed-methods research study, integrating qualitative interviews and latent consensus assessments. Board-certified dermatologists (n=11) and rheumatologists (n=10) based in the United States and Europe with ≥5 years' experience in treating CLE were interviewed remotely, using a semi-structured interview guide (Figure 1). Data were evaluated by thematic analysis.

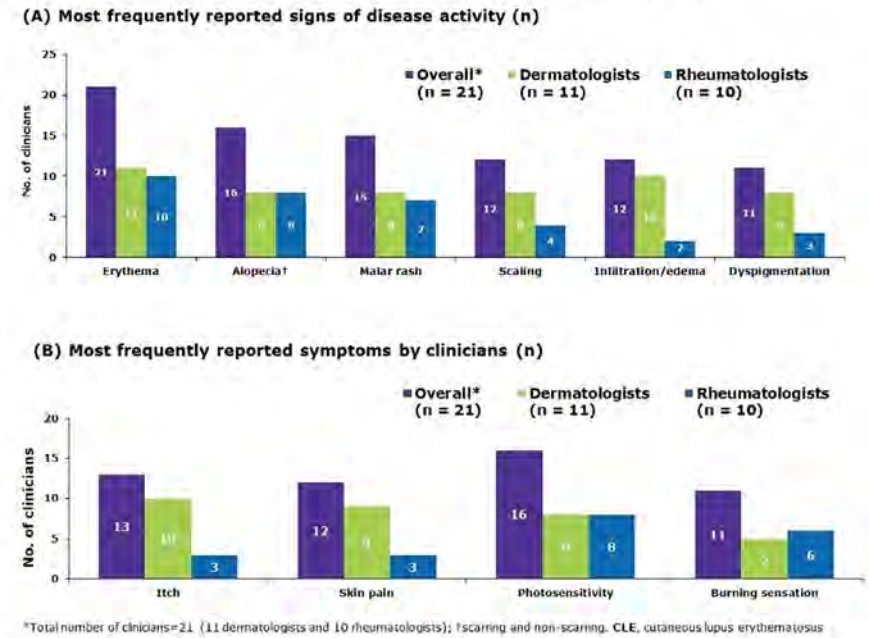
Results: Skin lesions in CLE show a broad spectrum of clinical manifestations and, therefore, it is important to use validated skin scores and to evaluate and distinguish disease activity and damage. The most frequently mentioned signs of disease activity by dermatologists included erythema (11/11) and infiltration/edema (10/11) followed by alopecia (scarring and non-

Figure 1. Methods: Data collection and analysis



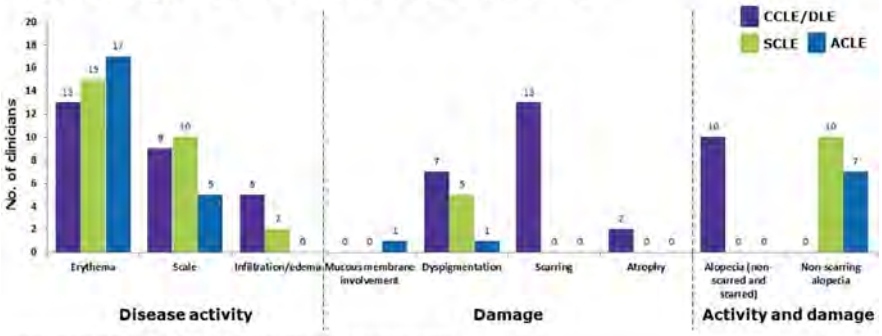
The qualitative interviews were analyzed using MAXQDA 2022, whereas the ranking data were analyzed using consensus analysis in UCINET software. **ACLE**, acute cutaneous lupus erythematosus; **CLE**, cutaneous lupus erythematosus; **CCLE**, chronic cutaneous lupus erythematosus; **DLE**, discoid lupus erythematosus; **SCLE**, subacute cutaneous lupus erythematosus

Figure 2. Most frequently reported signs and symptoms of CLE



*Total number of clinicians=21 (11 dermatologists and 10 rheumatologists); †scarring and non-scarring. **CLE**, cutaneous lupus erythematosus

Figure 3. Signs of CLE subtypes as per clinicians



Total number of clinicians=21 (11 dermatologists and 10 rheumatologists)
ACLE, acute cutaneous lupus erythematosus; **CLE**, cutaneous lupus erythematosus; **CCLE**, chronic cutaneous lupus erythematosus; **DLE**, discoid lupus erythematosus; **SCLE**, subacute cutaneous lupus erythematosus

scarring), malar rash, scaling and dyspigmentation (8/11 for each) (Figure 2A). The rheumatologists also reported erythema (10/10) as the most frequently mentioned signs of disease activity, followed by alopecia (scarring and non-scarring), malar rash, scaling, dyspigmentation and infiltration/edema (Figure 2A). Itch was the most frequently reported symptom by dermatologists (10/11) whereas photosensitivity was the most frequently reported symptom by rheumatologists (8/10; Figure 2B). Erythema and scaling were associated with all subtypes, but infiltration/edema, mucous membrane involvement, alopecia and non-scarring alopecia varied across subtypes (Figure 3). Most clinicians mentioned that CLE progression is often unpredictable, varied across patients and may be influenced by multiple factors including CLE subtype, sun exposure, smoking and medication compliance. The clinical experts characterized remission as the absence of signs and symptoms, with or without medication. CLE remission is negatively influenced by sun exposure and smoking, whereas medication compliance positively impacts duration of remission.

Conclusion: Signs of CLE associated with disease activity may vary across subtypes and must be considered in the definition and measurement of disease activity. Erythema was the most frequently reported sign related to disease activity and was considered relevant across all CLE subtypes.

Disclosure: v. werth: AbbVie, 2, Amgen, 2, 5, Argenx, 2, AstraZeneca, 2, 5, Beacon Bioscience, 2, Biogen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 2, 5, Corcept, 2, Crisalis, 2, CSL Behring, 2, Cugene, 2, Eli Lilly, 2, EMD Serono, 2, Genentech, 2, Gilead, 2, 5, GlaxoSmithKline, 2, Idera, 2, Incyte, 2, Janssen, 2, 5, Kirin, 2, Lupus Research Alliance, 5, MedImmune, 2, Medscape, 2, Nektar, 2, Principia, 2, Resolve, 2, UCB, 2, Viela Bio, 2, 5; **A. Kuhn**: Basilea, 6, Biogen, 2, 6, Eli Lilly, 2, 6, GlaxoSmithKline, 2, 6, Grünenthal, 2, La Roche Posay, 6, Spirig Pharma GmbH, 6; **J. Merola**: AbbVie, 12, Consultant and/or investigator, Amgen, 2, Biogen, 12, Consultant and/or investigator, Bristol Myers Squibb, 2, Dermavant, 12, Consultant and/or investigator, Eli Lilly, 12, Consultant and/or investigator, Janssen, 12, Consultant and/or investigator, LEO Pharma, 12, Consultant and/or investigator, Novartis, 12, Consultant and/or investigator, Pfizer, 12, Consultant and/or investigator, Regeneron, 12, Consultant and/or investigator, Sanofi, 12, Consultant and/or investigator, Sun Pharmaceuticals, 12, Consultant and/or investigator, UCB Pharma, 12, Consultant and/or investigator; **J. Wenzel**: Actelion, 12, Advisory board fees, ArrayBio, 5, Biogen, 12, Advisory board fees, Celgene, 12, Advisory board fees, EMD Serono, 5, GlaxoSmithKline, 5, 12, Advisory board fees, Incyte, 5, Leo Pharma, 5, 12, Advisory board fees, Medac, 12, Advisory board fees, Roche, 5, 12, Advisory board fees, Spirig, 5; **C. Vazquez-Mateo**: EMD Serono, Billerica, MA, USA, 3; **S. Roy**: Ares Trading SA, Eysins, Switzerland, an affiliate of Merck KGaA, Darmstadt, Germany, 3; **E. Thomas**: EMD Serono, Billerica, MA, USA, 3; **O. Guenther**: the healthcare business of Merck KGaA, Darmstadt, Germany, 3; **Y. Sun**: The healthcare business of Merck KGaA, Darmstadt, Germany, 3; **A. Lauer**: The healthcare business of Merck KGaA, Darmstadt, Germany, 3; **A. Rodriguez**: the healthcare business of Merck KGaA, Darmstadt, Germany, 2; **P. Koochaki**: ICON Clinical Research LLC, 3, the healthcare business of Merck KGaA, Darmstadt, Germany, 2; **P. Kamudoni**: the healthcare business of Merck KGaA, Darmstadt, Germany, 3.

Abstract Number: 0337

Impact of Photosensitivity on Quality of Life in Dermatomyositis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Photosensitivity (PS) has been documented in dermatomyositis (DM) with symptoms including aggravation of preexisting cutaneous lesions and abnormal transient erythemal responses (Cheong WK et al. 1994). DM has a large negative impact on quality of life (QoL), and DM skin disease activity has been correlated with poorer QoL (Goreshi R et al. 2011). Yet, the impact of PS specifically on QoL in DM has not been well studied. The aims of this study are to examine the impact of PS on QoL and to determine whether there is a relationship between PS-specific QoL measures and degree of cutaneous disease activity in DM.

Methods: Prospectively acquired data from 401 subjects with either classic DM (CDM) or clinically amyopathic DM (CADM) who completed the Skindex-29+3 was used. The Skindex-29+3 is a modified version of the Skindex-29, a validated measure of skin-specific QoL (Chren MM et al. 1997). Two of the three items added to the Skindex-29 relate to PS, items 31 and 33: "I worry about going outside because the sun might flare my disease" and "My skin disease prevents me from doing outdoor activities". The average of these two items comprises the PS subscale. Item 32, "I am worried about my hair loss", is the third added item in the Skindex-29+3. We compared patient responses to cutaneous disease activity using the Cutaneous Disease Area and Severity Index (CDASI), a validated tool for measuring DM disease (Ahmed S et al. 2020). Subject responses were not normally distributed, and group differences were assessed using the Wilcoxon rank-sum test. All three additional items of the Skindex-29+3 were correlated to CDASI activity scores using Spearman correlations. The three items were also correlated to the symptom, emotion, and function subscales of the Skindex-29+3 using Spearman correlations.

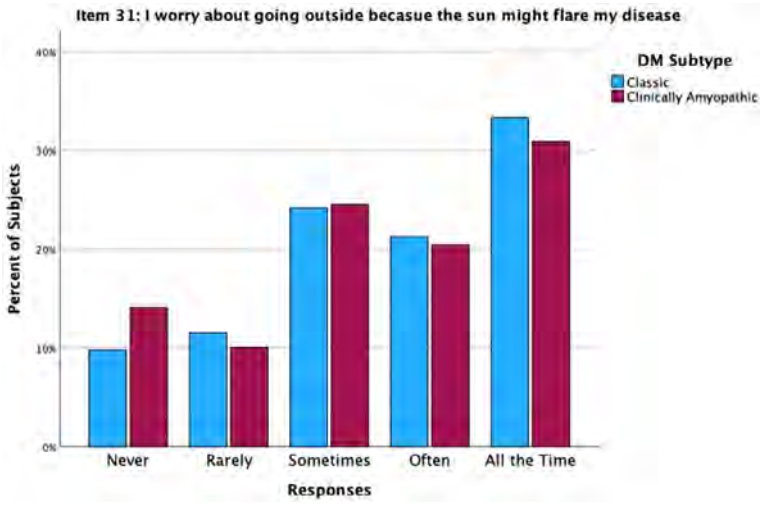

Figure 1. Percent of subject responses to Item 31 by DM subtype

Results: Of 401 subjects, 52% worried "often" or "all the time" about going outside because the sun might flare their disease (Item 31). 42% of subjects reported worrying about their hair loss (Item 32) "often" or "all the time". 39% of subjects reported being prevented from doing outdoor activities (Item 33) "often" or "all the time". There were no significant differences in median responses for Items 31 and 32 between patients with CDM and CADM (p = 0.407, 0.239), but there was a significant difference for Item 33 (p = 0.021), with CDM subjects reporting higher scores. There was a moderate, positive correlation between the PS subscale and both the function and emotion subscales for all subjects (r_s = 0.580, p < 0.001, r_s = 0.527, p < 0.001). There was another moderate, positive correlation between Item 33 and both function and emotion subscales (r_s = 0.611, p < 0.001, r_s = 0.516, p < 0.001). We found a negligible correlation for Items 31, 32, 33, and the PS subscale in relation to CDASI activity scores (r_s = 0.124 p = 0.013, r_s = 0.249 p < 0.001, r_s = 0.183 p < 0.001, r_s = 0.169 p = 0.001).

Conclusion: PS in DM has a significant impact on QoL in CDM and CADM. Concern regarding hair loss is common among subjects with DM. Subjects with CDM experienced greater limitation in participating in outdoor activities when compared to subjects with CADM (p = 0.021). Subjects that experienced greater PS-related concerns and limitations had greater emotional burden and functional impairments.

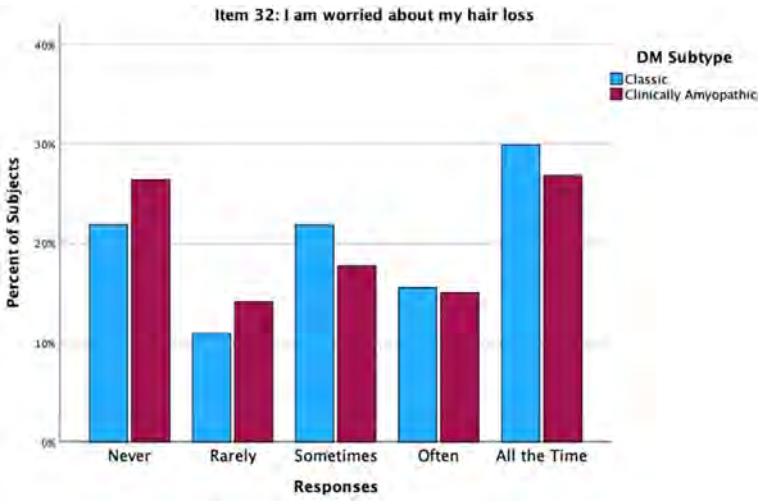

Figure 2. Percent of subject responses to Item 32 by DM subtype

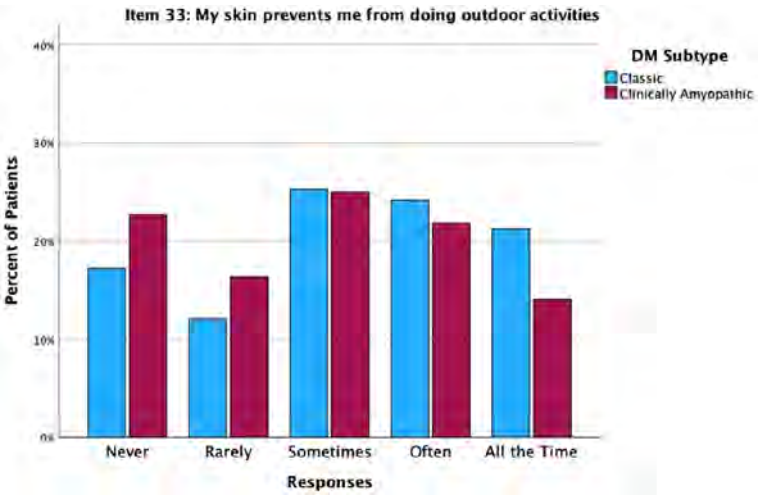

Figure 3. Percent of subject responses to Item 33 by DM subtype. There was a significant difference in the median responses between subjects with classic DM (CDM) and clinically amyopathic DM (CADM), with CDM subjects reporting higher scores (p = 0.021).

Disclosure: K. Gebre: None; **R. Pandya**: None; **J. Kleitsch**: None; **D. Lim**: None; **R. Feng**: None; **v. werth**: AbbVie, 2, Amgen, 2, 5, Argenx, 2, AstraZeneca, 2, 5, Beacon Bioscience, 2, Biogen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 2, 5, Corcept, 2, Crisalis, 2, CSL Behring, 2, Cugene, 2, Eli Lilly, 2, EMD Serono, 2, Genentech, 2, Gilead, 2, 5, GlaxoSmithKline, 2, Idera, 2, Incyte, 2, Janssen, 2, 5, Kirin, 2, Lupus Research Alliance, 5, MedImmune, 2, Medscape, 2, Nektar, 2, Principia, 2, Resolve, 2, UCB, 2, Viela Bio, 2, 5.

Abstract Number: 0338

Comparative Disease Burden in Patients with Rheumatoid Arthritis, Psoriatic Arthritis or Ankylosing Spondylitis: Data from COVAD Patient-reported E-survey

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) and spondyloarthritis (SpA), including either Psoriatic Arthritis (PsA) and Ankylosing Spondylitis (AS), are some of the most commonly diagnosed autoimmune rheumatic diseases in rheumatologists' routine clinical practice. Both can lead to joint destruction and substantial disability. Understanding patients' health and functional status is crucial to provide personalized management strategies to optimize disease control and enhance the quality of life. We aimed to compare disease burden in patients with RA, PsA or AS by assessing Patient-Reported Outcome Measurement Information System (PROMIS) Physical Health, Global Mental Health, Physical Function and Fatigue 4a together with Visual Analogue Scale (VAS) Pain.

Methods: Data were obtained in the international COVID vaccination in autoimmune rheumatic diseases study second e-survey (COVAD study). Demographics, AIRD diagnosis, disease activity, PROMIS Global Physical health, PROMIS Global Mental Health, PROMIS Physical Function SF10 and PROMIS Fatigue 4a scores were extracted from the COVAD study

database. For this study, we only included patients with self-reported RA or spondyloarthritis (either PsA or AS) undergoing active treatment with conventional synthetic disease-modifying anti-rheumatic drugs (DMARDs) and/or biologic DMARDs, who answered all the survey questions. Active disease was defined as the patient's perception of their disease as active in the four weeks before the first dose of COVID-19 vaccination. Analysis of Variance with Bartlett's and Tukey's test was used to compare continuous variables between groups.

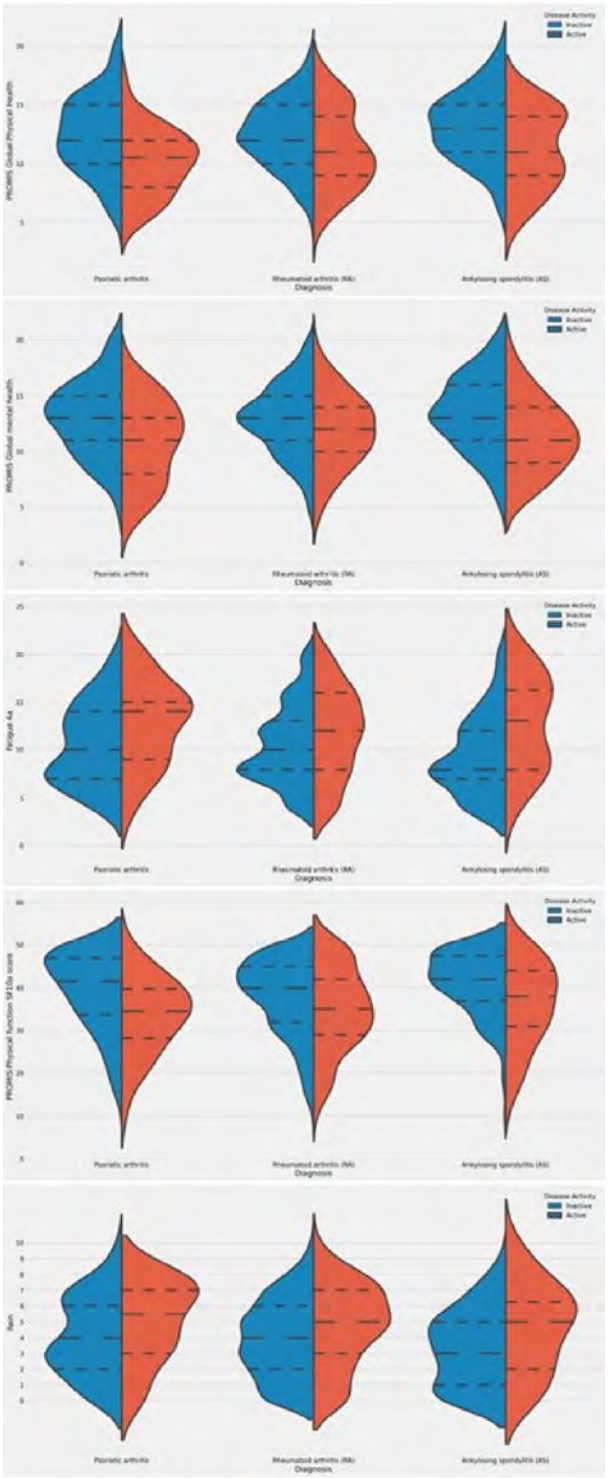

Figure 1. Violin plots showing kernel densities, quartiles and median for Patient-Reported Outcome Measures for patients with RA, PsA and AS, stratified by disease activity status.

Table 1. Patient-Reported Outcome Measures between groups.

Inactive disease							
	AS (n.185)		PsA (n.179)		RA (n.1167)		
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	
PROMIS Global Physical Health	13.13*	2.95	12.43	3.27	12.48	2.90	p=0.01, vs RA
PROMIS Global Mental Health	13.31	3.36	12.97	3.33	12.84	3.17	
PROMIS Fatigue 4a	9.4	4.13	10.58*	4.22	10.45*	4.08	p=0.01, both
PROMIS Physical Function SF10 Score	41.13	7.39	39.27	9.01	37.79*	8.86	p<0.001, vs AS
VAS Pain	3.34	2.39	4.04*	2.50	3.87*	2.45	p=0.01, both
Active Disease							
	AS (n.35)		PsA (n.38)		RA (n.189)		
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	
PROMIS Global Physical Health	11.05	3.19	10.10	2.76	11.24	3.41	
PROMIS Global Mental Health	11.31	3.26	10.84	3.63	11.89	3.30	
PROMIS Fatigue 4a	12.94	4.87	12.84	4.42	11.75	4.68	
PROMIS Physical Function SF10 Score	35.82	9.62	33.52	8.76	34.90	9.80	
VAS Pain	4.68	2.77	5.0	2.54	4.68	2.61	

Results: From January to June 2022, 1907 patients with RA, female 87.62% (1671/1907), with mean age (±SD) 50.95 ± 13.67, 311 patients with PsA, female 67.20% (209/311), with a mean age of 50.42 ± 12.70, and 343 patients with AS, male 63.27% (217/343), with a mean age of 43.13 ± 12.75 years, responded to the COVAD e-survey. When assessed in those with active disease, neither physical health, global mental health, physical function, fatigue, nor pain were different among groups (Table 1, Figure 1). Patients with inactive AS had higher mean global physical health scores than RA patients (13.13 ± 2.93 VS RA 12.48 ± 2.90, p=0.01, Table 1). Nevertheless, those with inactive RA or PsA showed more severe fatigue (PsA 10.58 ± 2.22, RA 10.45 ± 4.08, vs AS 9.4 ± 4.13, p =0.01 for both). Patients with inactive RA also reported poorer physical function and more residual pain than those with AS (37.79 ± 8.86 VS 41.13 ± 7.79, p< 0.001; 3.87 ± 2.45 VS 3.34 ± 2.39, p=0.01, respectively). Similarly, residual pain was perceived as higher in patients with inactive PsA than those with AS (4.04 ± 2.50 VS 3.34 ± 2.39, p=0.01).

Conclusion: The burden of disease is approximately similar in patients with active RA, PsA or AS. However, patients with inactive RA and PsA report a considerably greater disease burden compared to those with AS.

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Abstract Number: 0339

Longitudinal Glucocorticoid Toxicity in Rheumatic Disease Patients (LONG-TOX) and Associations with Quality of Life and Healthcare Resource Utilization: Interim Analysis from a Prospective Cohort

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Glucocorticoids (GCs) continue to be the cornerstone of therapy for many rheumatic diseases, though long-term exposure to GCs has been linked to dozens of potential toxicities. The Glucocorticoid Toxicity Index (GTI) is a validated instrument that quantifies change in GC toxicity longitudinally. The GTI produces two scores: the Cumulative Worsening Score (CWS) and the Aggregate Improvement Score (AIS), which are calculated by evaluation of 9 domains involving clinical, laboratory, and imaging information. We developed a prospective cohort of patients with rheumatic diseases receiving long-term GCs with the goals of assessing longitudinal GC toxicity as measured by the GTI, quality of life (QoL), and healthcare resource utilization to better quantify the personal and societal costs of glucocorticoids.

Methods: We enrolled adults ages 18-89 with any rheumatic disease diagnosis, receiving a GC taper with a starting dose of ≥7.5 mg/day (prednisone or equivalent dose) over an anticipated period of ≥ 3 months. Visits are conducted at baseline, 6, and 12 months and involve assessment of GTI scores, GC use and exposure, patient-reported outcomes including the EQ-5D Visual Analogue Scale [VAS], assessment and quantification of healthcare resource utilization both within Mass General Brigham (MGB) (assessed by an investigator or study coordinator by review of electronic health records) and outside of MGB (assessed by patient survey). Data collection was performed in REDCap and the *Steritas Cloud GTI* app. Patients with available 6-month data are included here. Differences between EQ-5D VAS scores and physician clinic visits were assessed for those with GTI scores above vs. below the median using linear regression, with and without adjustment for disease activity as assessed by Routine Assessment of Patient Index Data 3 (RAPID3) scores. Potential GTI CWS scores ranged from 0 (indicating no toxicity) to 439 (indicating the maximum measurable GC toxicity at 6 months).

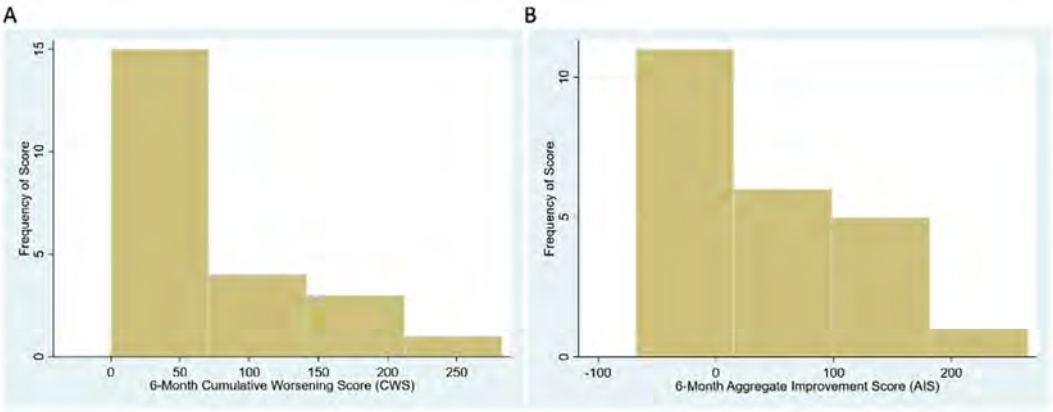

Figure. Glucocorticoid Toxicity Index (GTI) Cumulative Worsening Score (CWS) (A) and Aggregate Improvement Score (AIS) (B) at 6 months.

Table. Differences in healthcare resource utilization and quality of life between those with Glucocorticoid Toxicity Index (GTI) Cumulative Worsening Score (CWS) values above versus below the median.

	GTI CWS above vs. below median, difference (95% CI)	p-value
EQ-5D Visual Analogue Scale		
Unadjusted	3.2 (-1.9, 8.3)	0.21
Adjusted*	2.7 (-2.1, 7.5)	0.26
Physician clinic visits		
Unadjusted	0.0 (-14.8, 14.7)	1.00
Adjusted*	2.1 (-9.8, 14.0)	0.72

Results: Twenty three patients with available 6-month data were included. The 6-month median (IQR) GTI CWS was 63 (29, 121) (Figure). The 6-month median (IQR) GTI AIS was 21 (-19, 113). 21 out of 23 patients (91.3%) had CWS values > 0 at 6 months. The most common individual GTI domains in which patients had an increase in toxicity included Neuropsychiatric (14/23; 61%), Skin (11/23; 48%), Blood Pressure (9/23; 39%), and Body Mass Index (4/23; 17%). The Infection, Myopathy, and Lipid Metabolism domains each indicated toxicity in 3/23 (13%) of patients, and the Glucose Tolerance domain in 2/23 (9%). After adjusting for RAPID3 scores, those with 6-month CWS values > median had 2.7 more clinic visits (p=0.26) and EQ-5D VAS scores that were 2.1 points higher (p=0.72) than those with CWS values < median.

Conclusion: Almost all patients had some degree of GC toxicity at 6 months, based on their GTI scores. Patients with higher GC toxicity had numerically more clinic visits. Quantifying GC toxicity as well as its impact on factors important to both patients and society will be critical to assessing the benefits and cost-effectiveness of steroid-sparing medications moving forward.

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Abstract Number: 0340

Rheumatology Patients' Experiences of a Nationwide Transition to an Adalimumab Biosimilar: A Cross-Sectional Study

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Session Type: Poster Session A
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Background/Purpose: Patients are frequently transitioned to biosimilars to reduce the cost burden of biologics. Brand changes can be daunting for patients who have concerns about biosimilar safety, quality, and anticipate a loss of disease control. Therefore, it is crucial to optimize the transition process for patients. To date, patients' experiences with the transition process have not been explored in detail. This study examined rheumatology patients' experiences of a mandatory nationwide brand change to an adalimumab biosimilar.

Methods: People with rheumatic diseases involved in the adalimumab biosimilar brand change in Aotearoa New Zealand were invited to take part in a nationwide online survey. The transition occurred between March and September 2022 and was expected to enable 380 new patients to receive access to adalimumab. Patients were recruited through patient organizations, a rheumatology clinic, and social media support groups between November 2022 and May 2023. Participants reported their satisfaction with the biosimilar, logistics and supply, information and communication, and availability of support, on a 0-10 scale, with 10 indicating high satisfaction. Open-ended questions explored what did and did not go well during the transition.

Results: The sample consisted of 117 participants (48% with rheumatoid arthritis). The mean [SD] overall satisfaction with the transition was 6.2 [3.2]. Participants were least satisfied with the patient support program (mean [SD] 3.4 [3.3]), support (3.4 [3.5]) and information (3.5 [3.2]) received from patient organizations, and training for the biosimilar device (4.9 [3.8]) during the transition period. Participants were the most satisfied with the ongoing supply of the biosimilar during the transition (8.5 [2.2]), the support received from pharmacists (7.5 [2.9]), and how early they were informed before the transition occurred (6.9 [2.8]). After the transition, participants were less satisfied with the quality of the device, and biosimilar safety, efficacy, and the provision of alcohol wipes and sharps bins ($p < 0.05$ for all). Participants appreciated the citrate-free preservative (less injection pain) and the ease of the device. The lack of alcohol wipes and loss of the bio-originator patient support program were viewed negatively.

Conclusion: Patients reported mixed experiences with the mandatory adalimumab biosimilar transition. Future transitions should ensure the availability of alcohol wipes, sharps bins and a patient support program. Patient support organizations could also assist patients by providing information about the biosimilar and training for the new device.

Disclosure: C. Gasteiger: None; **M. Lobo**: None; **R. Stanley**: None; **L. Wong**: None; **R. Murdoch**: None; **N. Dalbeth**: Arthrosi, 2, AstraZeneca, 2, Dyve Biosciences, 2, Hikma, 6, Horizon, 2, JW Pharmaceutical Corporation, 2, LG, 2, Novartis, 6, Novotech, 5, PK Med, 2, Protalix, 2, PTC Therapeutics, 2, Selecta, 2, Unlocked Labs, 2.

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Patient Perspectives on the Usability of a Rheumatoid Arthritis Patient-reported Outcomes Electronic Health Record-based Dashboard: A Mixed-Methods Study

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Background/Purpose: Shared decision making, health literacy, and effective communication around patient-reported outcomes (PROs) are vital components to a treat-to-target approach in rheumatoid arthritis (RA) patients. To enhance these areas of patient care, we developed an EHR-integrated, patient-facing sidecar dashboard application that displays RA outcomes (disease activity, functional status, pain scores), medications, and lab results for use during clinical visits (**Figure**). The

dashboard was rolled out at an academic rheumatology clinic as part of a stepped-wedge pragmatic randomized trial starting in 2021. This study aimed to assess patient perspectives on the usability of the dashboard using a mixed-methods approach.

Methods: Consecutive RA patients whose clinicians used the dashboard during a visit were invited to complete a survey regarding the usability of the dashboard. Using purposive sampling to ensure that a range of usability perspectives were included, a subset of patients was invited to participate in semi-structured interviews to assess their perceptions of the dashboard. Recorded interviews were transcribed verbatim and thematically analyzed using inductive and deductive techniques.

Results: 181 patients responded to the survey. Most patients (79%) were interested in seeing the dashboard again at a future visit and felt that the dashboard helped them talk to their physician about their RA symptoms (76%) and medications (71%; **Table 1**). Many also reported that the dashboard helped them understand more about their disease (71%) and make better decisions about their RA care (67%).

Figure. Screenshot of the rheumatoid arthritis patient-facing sidecar dashboard application, which incorporated historical and real-time EHR data to display trajectories of RA outcomes.Table 1. Selected patient survey questions examining usability of the RA dashboard (N = 181).

Table 1. Selected patient survey questions examining usability of the RA dashboard (N = 181).

Selected survey questions	N	Yes (%)	Somewhat (%)	No (%)	Unsure (%)
Overall					
Would you like to see the dashboard again at your next visit?	181	79%	NA	8%	13%
Patient-provider communication					
Did the dashboard help you talk to your doctor about your arthritis or your symptoms?	180	76%	15%	8%	2%
Did the dashboard help you talk to your doctor about your medicines?	181	71%	14%	10%	5%
Did the dashboard help you talk about things that are important to managing your disease, other than your medicines?	179	61%	17%	17%	4%
Patient knowledge					
Did the dashboard help you understand more about your arthritis?	178	71%	21%	5%	2%
Did the dashboard help you understand more about why you take certain medicines?	179	60%	16%	18%	6%
Shared decision making					
Did the dashboard help you make better decisions about your arthritis care?	176	67%	19%	10%	5%
Do you think using the dashboard helped your doctor to better understand what's most important to you?	175	46%	21%	22%	11%

Table 2. Patients' perceptions about the dashboard: Results of qualitative interviews.

Themes		Sub-themes	Selected quotes
Perceived Benefits	Patient	Knowledge about disease	*"The dashboard helped me understand something that I didn't really understand before."*
		Visualization of disease progression	*"It's easy to get a quick look at how I've been doing and my progress and whether it's good, bad, or the same."*
		Engagement in care	*"The first time that I was ever shown this tool, I latched onto it because it's about me and my recovery."*
		Motivation	*"It gave me hope that, although I'm not there yet, I'm much better than a year and a half ago. That really empowered me."*
	Physician	Access to individual data	*"It's more beneficial for the doctor as far as her being able to recall testing and things like that."*
		Visualization of disease trajectory	*"It's a great visual summary of the disease progression for the doctor."*
	Interpersonal	Goals of care	*"To make a determination whether to change a medication, I need to know: What does my future look like? What are the risks? How have I been doing on this medication for a period of time? The dashboard's helping me figure that out."*
		Trust	*"It showed professionalism and gave me more confidence in the division, that they're capturing data. They're looking at the data in the right way. There's continuity."*
		Focused discussion	*"It gave us a focus... Sometimes we'll go off on tangents that might not necessarily be productive for my health discussion. The dashboard can help keep it on target."*
Concerns		Design	*"The units seemed to be too complicated. I had to read about them on the facing page. Maybe you could put in parentheses "CDAI"."*
		Content	*"It's subjective in a way when you fill out the form about the pain level…I don't know how accurate these questionnaires are to the doctor."*
		Explanation of content	*"[The doctor] did not [explain it]. That's why I said I didn't understand it."*
		Accessibility offline	*"It would be beneficial for the patient to have access to it, especially when you're asking questions about it and I can't answer everything because I don't have access to the application."*
		Technical difficulties	*"Last time the dashboard wasn't accessible. She was trying hard to get in there, and she couldn't open it."*

Similar themes emerged from the qualitative interviews (N = 27; 89% women, mean age 57 years, 74% with self-reported high health literacy; **see Table 2**). Perceived benefits of the dashboard included visualizing disease progression and changes over time, which engaged patients in their care and increased their motivation to control their disease. Patients valued how the dashboard allowed physicians to conveniently access their RA outcome information. On the interpersonal level, patients noted improved communication around goals of care (disease progression and treatment), and increased trust and confidence in their providers. Despite being comfortable with technology, patients also identified some challenges, including that they found it difficult to understand RA outcomes or the dashboard content without some explanation from physicians. Patients also expressed a wish to access the dashboard in-between visits.

Conclusion: In this mixed-methods study, most patients felt that a sidecar dashboard application enhanced their clinical encounters. Positive feedback from patients suggests that routine use of the dashboard has potential to improve patient engagement in RA care. Patients also suggested specific areas for improvement in accessibility, design, and content, which should be considered to further optimize the dashboard.

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Abstract Number: 0342

Assessing the Known-group Validity of the IDEOM MSK-Q Using Data from the National Psoriasis Foundation Annual Survey

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Background/Purpose: The IDEOM MSK-Q aims to assess MSK symptoms in individuals with psoriatic disease. It consists of 3 subscales: Intensity of MSK Symptom (3 items), Impact of MSK Symptoms (4 items), and Intensity of Fatigue (1 item). This study sought to evaluate the known-groups validity of the IDEOM MSK-Q.

Methods: Data from a cross-sectional survey of a random sample of individuals with psoriasis was used. To determine the known-groups validity of the IDEOM MSK-Q, we compared the IDEOM MSK-Q score among different groups based on: A). Disease status: patients with psoriasis-only vs psoriasis with PEST ≥ 3 vs PsA; B). PEST score: PEST < 3 vs PEST ≥ 3; and C.) Impact of PsA: Psoriatic Arthritis Impact of Disease (PsAID-9) < 4 vs PsAID ≥ 4. ANOVA and ANCOVA, adjusting for age and sex, were used.

Results: A total of 1,453 participants completed the survey. Equal proportions of participants reported a physician given diagnosis of psoriasis-only (47.9%) and psoriasis with concomitant PsA (47.7%), and 4.4% only having PsA. Participants were mostly female (58.4%) with mild psoriasis (52.3% - BSA 3%). Mean participant age was 54.8 (SD ± 15.73). Among all participants, 61% had a PEST score ≥ 3, indicating the potential presence of PsA. Among individuals with PsA and those with psoriasis-only with a PEST score ≥ 3, 65.5% had a PsAID score > 4 (i.e., unacceptable symptom state). For all

participants, mean scores for the for the Intensity of MSK Symptom, Impact of MSK Symptoms, and Fatigue subscales were 18.4 (SD = ± 13.9), 5.0 (SD = ± 3.3), and 5.01 (SD = ± 3.28).

Results comparing the IDEOM MSK-Q subscales among different disease statues groups were statistically significant. Across all subscales, individuals with PsA scored higher than individuals with psoriasis with PEST score ≥ 3, and those with psoriasis-only (Table 1). These differences were maintained when adjusting for age and sex (see Table 1.)

Unadjusted between group comparison based on PEST score (PEST < 3 vs PEST ≥ 3) were statistically significant for the Intensity of MSK Symptom and Impact of MSK Symptoms subscales. Participants who had a PEST ≥ 3 scored higher across all components of the IDEOM MSK-Q (Table 2) compared to PEST < 3. Similarly, unadjusted group comparison based on PsAID score (PsAID ≤ 4 vs PsAID > 4) suggest that individuals at unacceptable symptom state (PSAID > 4) scored higher on all 3 subscales (Intensity of MSK Symptom, Impact of MSK Symptoms , and Fatigue) (Table2). After adjusting for age and sex, comparisons remained statistically significant (see Table 2).

Conclusion: Results from this study suggest that the IDEOM MSK-Q can discriminate between individuals based on disease status, PEST score, and impact of psoriatic arthritis reflecting it has good known group validity.

Table 1 – Known group validity of the IDEOM MSK-Q by disease status.

	Only PsO with PEST < 3 Mean (95% CI)	Only PsO with PEST ≥ 3 Mean (95% CI)	PsA Mean (95% CI)
Unadjusted models			
Impact of MSK Symptoms subscale	7.90*** (6.96 – 8.85)	17.13*** (15.22 -19.03)	22.51*** (21.55 – 23.47)
Intensity of MSK Symptom subscale	1.42*** (.93 – 1.92)	12.08*** (11.10 – 13.07)	15.39*** (14.86 – 15.93)
MSK fatigue subscale	3.33*** (3.06 – 3.60)	5.04*** (4.61 – 5.48)	6.09*** (5.88 – 6.30)
Adjusted models (age and sex)			
Impact of MSK Symptoms subscale	8.00*** (6.61 – 9.38)	16.59*** (14.90- 18.28)	22.52*** (21.64 – 23.40)
Intensity of MSK Symptom subscale	1.34*** (.29 – 2.40)	11.81*** (10.86 – 12.77)	15.36*** (14.86 – 15.86)
MSK fatigue subscale	3.33*** (3.06 – 3.59)	5.02*** (4.63 – 5.41)	6.11*** (5.90 – 6.32)

*** p < 0.001

Table 2 – Known group validity of the IDEOM MSK-Q based on PEST and PsAID-9 scores.

	PEST < 3 Mean (95% CI)	PEST ≥ 3 Mean (95% CI)	PsAID-9 ≤ 4 Mean (95% CI)	PsAID-9 > 4 Mean (95% CI)
Unadjusted models				
Impact of MSK Symptoms subscale	10.83 (9.72 – 11.93)	21.89 (20.99 -22.80)	7.77*** (7.01 – 8.51)	29.76*** (28.95 – 29.56)
Intensity of MSK Symptom subscale	5.27*** (4.78 – 5.76)	15.00*** (14.51 – 15.51)	7.88*** (7.30 – 8.45)	19.01*** (18.53 – 19.49)
MSK fatigue subscale	2.93*** (2.67 – 3.19)	7.67*** (7.50 – 7.83)	2.89*** (2.63 – 3.14)	7.89*** (7.74 – 8.03)
Adjusted models (age and sex)				
Impact of MSK Symptoms subscale	10.98*** (9.726 – 12.240)	21.803*** (20.952- 22.654)	7.90 *** (6.81 – 8.98)	29.65*** (28.90 – 30.39)
Intensity of MSK Symptom subscale	5.99*** (5.38 – 6.60)	14.43*** (13.96 – 14.90)	8.68*** (8.02 – 9.34)	18.83*** (18.35 – 19.32)
MSK fatigue subscale	3.62*** (3.37 – 3.87)	5.93*** (5.74 – 6.13)	3.06*** (2.83- 3.28)	7.81*** (7.65 – 7.97)

*** p < 0.001

Disclosure: L. Perez-Chada: None; **G. Gondo**: None; **J. Merola**: AbbVie, 12, Consultant and/or investigator, Amgen, 2, Biogen, 12, Consultant and/or investigator, Bristol Myers Squibb, 2, Dermavant, 12, Consultant and/or investigator, Eli Lilly, 12, Consultant and/or investigator, Janssen, 12, Consultant and/or investigator, LEO Pharma, 12, Consultant and/or investigator, Novartis, 12, Consultant and/or investigator, Pfizer, 12, Consultant and/or investigator, Regeneron, 12, Consultant and/or investigator, Sanofi, 12, Consultant and/or investigator, Sun Pharmaceuticals, 12, Consultant and/or investigator, UCB Pharma, 12, Consultant and/or investigator; **A. Gottlieb**: Amgen, 1, 2, AnaptysBio, 1, 2, 5, Avotres Therapeutics, 1, 2, Boehringer Ingelheim, 1, 2, Bristol Myers Squibb, 1, 2, 5, Dice Therapeutics, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, MoonLake Immunotherapeutics, 5, Novartis, 1, 2, 5, Sanofi, 1, 2, UCB Pharma, 1, 2, 5, XBiotech, 1, 2.

Abstract Number: 0343

Sjögren's Disease Patient Experiences with Dry Mouth and Content Validity of the Xerostomia Inventory

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Background/Purpose: Xerostomia (dry mouth) is one of the most prevalent symptoms experienced by patients with Sjögren's Disease (SJD). The Xerostomia Inventory (XI) is a 11-item PRO that has been used primarily to assess the impact of xerostomia on oral health in older populations. The purpose of this study was to identify important symptoms and impacts of dry mouth described by SJD patients and explore the content validity of the XI for use in SJD clinical trials.

Methods: US participants with physician-confirmed diagnosis of SJD were recruited in partnership with the Sjögren's Foundation. Combined concept elicitation (CE) and cognitive interviews (CI) were conducted by telephone or online platform with 29 adult patients experiencing dry mouth due to SJD. CE identified dry mouth symptoms and impacts on activities of daily living. During CI, patients completed the XI and discussed the relevance of each item, clarity of wording, ease of completion, response options, comprehensiveness, and relevancy of the recall period. Interviews were audio-recorded, transcribed, and anonymized. A thematic analysis of the CE data was facilitated by MAXQDA software and a codebook developed from patient interviews. An item-matrix tracker was adopted to capture patient comments on the items and other elements of the XI and to record indicated revisions, additions, or deletions based on patient feedback.

Table 1. Selected Patient Descriptions of Dry Mouth

*"Well, I guess what the Sahara Desert feels like, and **cottonmouth** and everything else you could describe. And it makes it difficult to talk at times; you constantly **bite the inside of your cheek** because there's no saliva. So, if I don't have water I have a **hard time talking**, and I have a **hard time eating**" (Patient 045)*
*"You **can't swallow your food; I can't swallow pills**; I have **difficulty eating dry things**, yeah, just **reading out loud, speaking**. " (Patient 029)*
*"Your **lips are burning**, everything is burning. " (Patient 009)*
*It's like when I drink water or something it's almost as if it **dries up as soon as it gets into my mouth**. It feels like things evap—**liquid evaporates in my mouth** instead of really ingesting it." (Patient 205)*

Results: The study participants were primarily female (96%), White (79%), had a bachelor's degree or higher (90%), with mean age 62.8 years (range 33-74). Over 70% of patients reported experiencing dry mouth daily or all of the time; symptoms included difficulty swallowing (59%), eating (52%), speaking (62%), having an unquenchable thirst (10%), burning (10%), dry mouth (100%) and dry lips (14%) (Table 1). Patients described coping strategies including use of products like mouthwash, gum, or oral melts (76%), and carrying water with them (35%). Patients found XI instructions easy to understand (95%), easy to respond to (79%), the items relevant to their experiences (68-100%), and response options appropriate (85%). XI concepts mapped moderately well to patient-reported symptoms. Items concerning difficulty eating (96%) and swallowing (91%) were highly endorsed by patients. Concepts reported by patients but not included in the XI were dental issues (62%) and speaking difficulties (62%). 50% of patients reported that items about dryness in other anatomical areas in the XI did not fit with a PRO to assess dry mouth. Patients identified regional colloquialisms that should be modified to more general terms. Patient input provided clear directions for item eliminations, additions, and rewording needed to develop a revised XI that is relevant and measures concepts important to SJD patients.

Conclusion: These findings reveal the array of dry mouth symptoms SJD experience and support the need for a PRO that comprehensively assesses patients' experiences. This study demonstrates the utility of a modified XI for assessing dry mouth experienced by SJD patients. Further research can help assess the content validity of a revised XI for use in SJD.

Disclosure: D. Kruzikas: AbbVie/Abbott, 3, 11; **A. Eldred**: AbbVie/Abbott, 3, 11; **S. Kafka**: AbbVie/Abbott, 3, 11; **J. Church**: Sjögren's Foundation, 3; **K. Hammitt**: Sjögren's Foundation, 3; **P. Koochaki**: ICON Clinical Research LLC, 3, the healthcare business of Merck KGaA, Darmstadt, Germany, 2; **C. O'Donnell**: ICON plc, 3; **W. Thomson**: AbbVie/Abbott, 5.

Abstract Number: 0344

Patient Engagement and Adherence to Digital Study Tasks: WEARable Activity Tracker Study Exploring Rheumatoid Arthritis Patients' Disease Activity Using Patient-Reported Outcome Measures, Clinical Measures, and Biometric Sensor Data (the WEAR Study)

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SESSION INFORMATION

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Background/Purpose: We evaluated participants' adherence to protocol-assigned capture of patient-reported outcomes (PROs) and activity tracker data in the context of an ongoing longitudinal study collecting data from rheumatoid arthritis (RA) patients initiating a new biologic or JAKi.

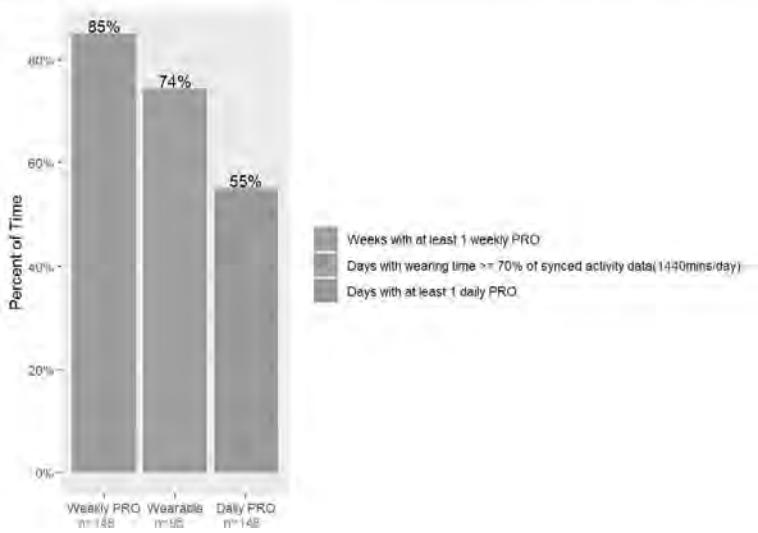
Methods: RA patients in moderate or high disease activity (CDAI >10) and prescribed either upadacitinib (UPA) or adalimumab (ADA) were enrolled during in-office visits at US community rheumatology clinics. To enter the 12-week main study, participants had to successfully complete a 7-day run-in (completion of ≥ 5 of 7 days of daily and weekly PROs) and take their first dose of new treatment within 30 days. Participants completed PROs remotely via app during the main study according to a pre-specified rotating daily assessment schedule that repeated each week and that was anticipated to take 1-3 minutes per day. As an optional component of the study, participants were provided with a Fitbit Versa2 (wearable) device either in clinic or received it by mail.

Table 1. Demographic and clinical characteristics of participants at baseline, by main study eligibility and data completeness (N=299)

	Successfully completed run-in, n=240	Did Not Successfully complete run-in, n=59	Completed main study, n=148	Completed main study and have at least one day wearable data, n=95
Age (years)	52.2 (11.8)	51.2 (12.4)	52.3 (12.0)	51.2 (12.7)
Female (%)	194 (81%)	55 (95%)	117 (79%)	76 (80%)
White (%)	202 (84%)	34 (58%)	122 (82%)	74 (78%)
Currently Employed %	139 (58%)	28 (47%)	84 (57%)	56 (59%)
Years since RA diagnosis	6.7 (8.7)	6.6 (8.2)	7.2 (9.2)	7.2 (9.1)
Osteoarthritis (comorbid) (%)	43 (18%)	17 (29%)	22 (15%)	14 (15%)
Fibromyalgia (comorbid) (%)	35 (15%)	12 (20%)	22 (15%)	8 (8.4%)
Other rheumatic or musculoskeletal condition (comorbid) (%)	184 (77%)	37 (63%)	118 (80%)	77 (81%)
Current RA Treatment				
Biologics +/- csDMARDs (%)	145 (60%)	39 (66%)	93 (63%)	56 (59%)
tsDMARDS +/- csDMARDS (%)	57 (24%)	14 (24%)	34 (23%)	22 (23%)
csDMARDs w/o b/tsDMARDs (%)	70 (29%)	16 (27%)	44 (30%)	31 (33%)
None of the Above	12 (5%)	2 (3%)	6 (4.1%)	3 (3.2%)
Daily/Weekly PROs at Run-in (Baseline)				
Pain (daily, 0-10 NRS)	5.5 (2.6)	6.6 (2.7)	5.3 (2.5)	5.3 (2.4)
Fatigue (daily, 0-10 NRS)	5.9 (2.7)	6.8 (2.6)	5.9 (2.7)	5.8 (2.5)
PROMIS Pain Interference (weekly, T score 0-100)	63.4 (6.5)	64.5 (7.1)	63.6 (6.1)	62.5 (5.4)
PROMIS Physical Function (weekly, T score 0-100)	38.6 (6.5)	36.8 (6.6)	38.4 (6.0)	38.7 (5.6)
PROMIS Fatigue (weekly, T score 0-100)	61.5 (8.6)	62.7 (8.5)	61.9 (8.5)	60.9 (7.8)
PROMIS Sleep Disturbance (weekly, T score 0-100)	58.0 (8.2)	60.9 (7.4)	57.9 (7.4)	57.2 (7.5)
PROMIS Satisfaction with Participation in Discretionary Social Activities (weekly, T score 0-100)	43.4 (7.2)	42.5 (7.2)	43.2 (7.0)	44.0 (6.5)
PROMIS Anxiety (T score 0-100)	57.7 (8.9)	59.0 (9.2)	57.4 (8.7)	56.1 (8.8)
Patient Global (0-10)	5.6 (2.2)	5.3 (2.3)	5.6 (2.2)	5.7 (2.0)
RADAI (0-10)	6.6 (2.1)	7.1 (2.2)	6.6 (2.0)	6.6 (2.0)
CDAI (0-76)	29.1 (15.7)	31.5 (16.4)	29.9 (16.5)	29.7 (17.0)

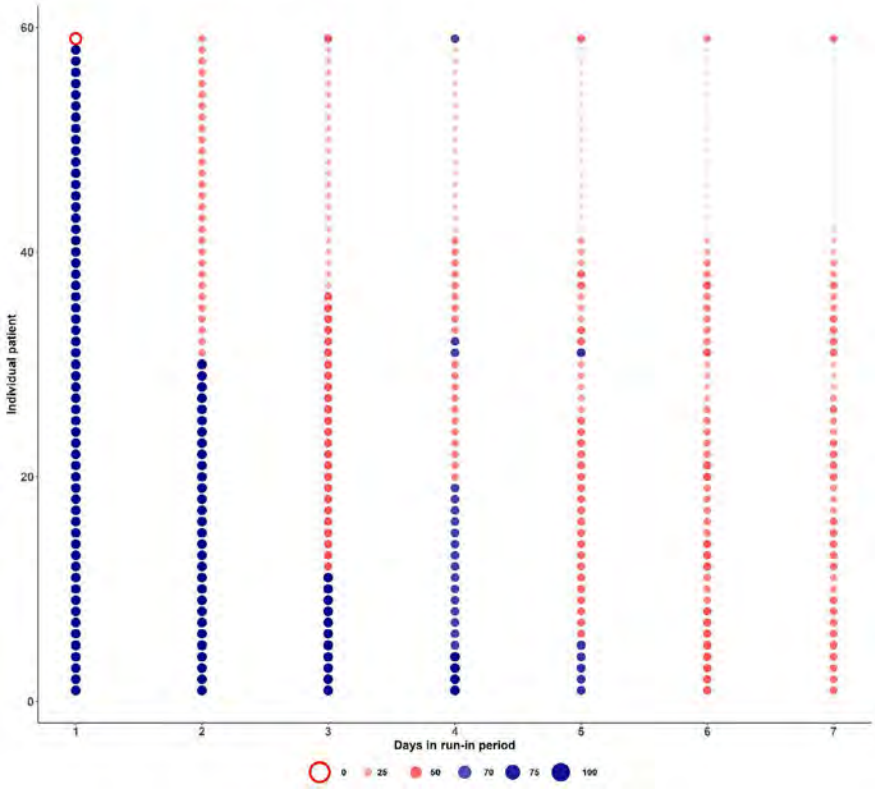
All values shown as mean (standard deviation [SD]), except where indicated as n (percent) Abbreviations: RA, rheumatoid arthritis; DMARDs, disease-modifying antirheumatic drugs; bDMARDs, biologics or biologic DMARDS; csDMARDs, conventional synthetic DMARDs; tsDMARDs, targeted synthetic DMARDs; NRS, numeric rating scale; PROMIS, patient-reported outcomes measurement system; RADAI, rheumatoid arthritis disease activity index; CDAI, clinical disease activity index

Figure 1. Adherence to completing WEAR study tasks by participants providing PRO and wearable data (n=148*)



*n=95 (participants who activated wearable device) for % of days with wearable data PRO = patient-reported outcome

Figure 2. Dot plot of participants who provided one or more day(s) of PRO data during run-in, but did not successfully complete run-in to advance to main study (n=59)



PRO = patient-reported outcome Representative rates of cumulative adherence to data submission show that individuals who did not progress to the main study had a marked drop in adherence as early as day 2. Dot size increases with increasing rate of adherence as shown and at 70% adherence, color of dot changes from red (<70% adherence) to blue (>70% adherence). Each dot in each column represents one participant who did not successfully complete the run-in and advance to the main study (n=59).

Results: A total of 299 patients enrolled and started the run-in. Of these, 240 entered the main study and met all inclusion criteria; at the time of this analysis, 148 participants have successfully completed the main study, with 95 of those (64%) providing both wearable and PRO data. Participants with more pain, fatigue, and worse physical function were more likely to fail the run-in based on inadequate PRO data capture (Table 1). Among the 148 participants who completed the main study, at least once weekly PROs were provided for 85% of weeks (Figure 1), and 83% of participants provided at least once weekly PROs for >= 9 of the 12 main study weeks. Daily PRO data was provided for 55% of days (Figure 1), and 38% of participants provided daily PRO data for at least 70% of all study days. Depending on the day of the week, time taken to complete PRO assessments each day ranged from a median of 1.4 minutes (IQR: 1.1 min – 2.1 min) to 2.1 minutes (IQR: 1.6 min – 3.2 min) among all participants. Among the participants who activated their wearable (n=95 to date), wearable data was provided for 74% of days for >= 70% of each 24-hour period (Figure 1), weekly PRO data was provided for 92% of week, daily PRO data was provided for 59% of days, and 38% of participants provided daily PRO data for at least 70% of all study days. Most patients who failed to meet minimum requirements to successfully complete the run-in did so within 3-4 days of starting the run-in (Figure 2).

Conclusion: Collecting weekly PRO data and daily wearable data for patients on RA treatment is feasible, although requiring daily PROs may be too burdensome in the context of routine care. Building some redundancy into the schedule of patient-generated data capture in order to optimize observations of disease activity and symptom changes over time as part of real-world evidence generation or remote therapeutic monitoring programs is advisable.

Disclosure: W. Nowell: AbbVie/Abbott, 2, 5, Amgen, 5, Janssen, 2, 5, Scipher Medicine, 5; **C. Clinton**: None; **F. Xie**: None; **Y. Su**: None; **L. Stradford**: Global Healthy Living Foundation, 3; **D. Curtis**: Global Healthy Living Foundation, 3; **P. Zueger**: AbbVie/Abbott, 3, 11; **P. Patel**: AbbVie/Abbott, 3, 11; **K. Gavigan**: Global Healthy Living Foundation, 3; **S. Venkatachalam**: Global Healthy Living Foundation, 3; **E. Rivera**: Global Healthy Living Foundation, 3; **J. Curtis**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CorEvitas, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Labcorp, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi/Regeneron, 2, 5, UCB, 2, 5.

Abstract Number: 0345

Jadas10- and cjadas10-based Disease Activity States for Psoriatic Arthritis, Enthesitis-related Arthritis, and Rf+ Polyarthritis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Pediatric Rheumatology – Clinical Poster I: JIA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The measurement of disease activity level is of central importance in the evaluation of the patient with juvenile idiopathic arthritis (JIA). The Juvenile Arthritis Disease Activity Score (JADAS) and its clinical version excluding the acute phase reactant (cJADAS) were validated and are increasingly used in clinical trials and routine practice. To allow score interpretation, cutoffs have been developed and subsequently validated for JADAS10 and cJADAS10 in RF- polyarthritis and oligoarthritis. The need to have cutoffs for other arthritis categories is increasingly evident.

To validate the JADAS10 and cJADAS10 disease activity state cutoffs to separate the states of inactive disease (ID), minimal disease activity (MiDA), moderate disease activity (MoDA), and high disease activity (HDA) in children with RF+ polyarthritis, PsA and ERA.

Methods: JIA children from 49 countries included in the EPidemiology, treatment and Outcome of Childhood Arthritis (EPOCA) study were considered. For PsA and ERA, the decision on whether to use oligoarthritis or polyarthritis cutoffs was based on the most frequent pattern of joint involvement at visit. Discriminative ability was assessed by calculating and comparing in each disease activity state the level of pain (0-10 VAS) and functional ability impairment (measured with the Juvenile Arthritis Functional Ability Score, JAFS, 0-45) and the frequency of patients satisfied with current disease state, starting a new medication, and having morning stiffness. Comparisons of quantitative variables among groups were made by Kruskal-Wallis test; Dunn's test was used to assess differences between pairs of patient groups. Percentage data were compared by chi-squared test or Fisher's exact test. Bonferroni's adjustment was applied to explore post-hoc differences between pairs of patient groups.

Results: 309 children with PsA, 959 with ERA, and 382 with RF+ polyarthritis were included. 88% children with PsA and 91% with ERA had oligoarticular disease, at study visit; therefore, oligoarthritis cutoffs were used for these categories.

The level of pain and functional ability was significantly different among the JADAS-based disease states, with pain and JAFS scores increasing progressively from ID to HDA (Kruskal-Wallis test $p < 0.001$). The percentage of patients who prescribed a new medication, with morning stiffness < 15 minutes, and who were satisfied with current disease state were different in the JADAS-based disease states. Paired comparison showed significant discrimination for most comparisons.

Conclusion: Both the JADAS10 and cJADAS10 cutoffs to define disease activity states validated for oligoarthritis and polyarthritis showed good discriminative validity in RF+ polyarthritis, PsA and ERA. These results preliminarily indicate that available cutoffs might be used for these categories of JIA.

Disclosure: S. Orsi: None; **M. Burrone**: None; **A. Rebollo Gimenez**: None; **F. Ridella**: None; **S. Rosina**: None; **L. Carlini**: None; **I. Rumba-Rozenfelde,**: None; **N. Shafaie**: None; **T. Avcin**: None; **P. Quartier**: AbbVie/Abbott, 2, Amgen, 2, Novartis, 2, Pfizer, 2, Roche, 2; **N. Ruperto**: None; **A. Ravelli**: AbbVie/Abbott, 12, honoraria for consultancies or speaker bureaus from, Novartis, 12, honoraria for consultancies or speaker bureaus from, Pfizer, 12, honoraria for consultancies or speaker bureaus from; **M. Gattorno**: Novartis, 5, 6, Sobi, 5, 6; **A. Consolaro**: AbbVie/Abbott, 6, Pfizer, 6, 12, grants for investigator-initiated research projects.

Abstract Number: 0346

Use, Safety and Persistence of Biosimilars in Adult Patients Diagnosed with Juvenile Idiopathic Arthritis: Results from the Spanish Registry of Adverse Events of Targeted Therapies in Rheumatic Diseases (BIOBADASER)

Juan José Bethencourt[1], Lucia Otero-Valera[2], JAVIER MANERO[3], Eva Perez-Pampin[4], Yanira Pérez Vera[5], SARA MANRIQUE[6], Maria Sagrario Bustabad Reyes[7], Mercedes Freire González[8], Dolores Ruiz-Montesinos[9], Lourdes Mateo Soria[10], Raquel Martín Domenech[11], Manuel Moreno Ramos[12], Fernando Alonso[2] and Isabel Castrejon[13], [1]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [2]Spanish Society of Rheumatology, Madrid, Spain, [3]Department of Rheumatology, Hospital Universitario Miguel Servet, Zaragoza, Spain, [4]Rheumatology Department Complejo Hospitalario Universitario Santiago, Santiago de compostela, Spain, [5]Hospital Universitario Dr Negrín, Las Palmas de Gran Canaria, Spain, [6]Division of Rheumatology, Hospital Regional Universitario Carlos Haya, Malaga, Spain, [7]Hospital Universitario de Canarias, La Laguna, Spain, [8]Rheumatology department, Complexo Hospitalario Universitario A Coruña (CHUAC). Instituto de Investigación Biomédica A Coruña (INIBIC), A Coruña, Spain, [9]Hospital Universitario Virgen Macarena, Sevilla, Spain, [10]HOSPITAL GERMANS TRIAS I PUJOL, Badalona, Spain, [11]Hopsital General de Elda, Alicante, Spain, [12]Hospital Clínico Universitario Virgen dela Arrixaca, Murcia, Spain, [13]Hospital General Universitario Gregorio Marañón, Madrid, Spain

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Pediatric Rheumatology – Clinical Poster I: JIA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease of childhood. The emergence of new biologic agents has led to changes in the prognosis and therapeutic approach for these patients. However, the use of biosimilars in adult patients diagnosed with JIA has not been well studied and more evidence is needed on the safety and persistence of these drugs in this patient population.

The aim of this study was to describe the use and assess the safety and persistence of biosimilar disease-modifying antirheumatic drugs (bsDMARDs) compared with original biologics (bDMARDs) in JIA patients older than 16 years.

	bDMARDs N=183	bsDMARDs N= 130	Total N=313
Age at diagnosis, mean±SD	9.7±4.9	11.2±6.1	10.3±5.5
Age at start treatment, mean±SD	22.6±12.9	25.1±13.4	23.6±13.2
Female, n (%)	118(64.5	79(60.8)	197(62.9)
JIA categories, n (%)			
Oligo/polyarticular	144 (78.7)	103(79.2)	247(78.9)
Related to entesitis	31(16.9)	21(16.2)	52(16.6)
Psoriatic	8(4.4)	6(4.6)	14(4.5)
Biological treatment, n (%)			
Adalimumab	127 (37.2)	85 (56.3)	212 (43.1)
Etanercept	104 (30.5)	44 (29.1)	148 (30.1)
Infliximab	22 (6.5)	19 (12.6)	41 (8.3)
Rituximab	6 (1.8)	3 (2.0)	9 (1.8)
Certolizumab pegol	49 (14.4)	-	49 (10.0)
Golimumab	33 (9.7)	-	33 (6.7)
Reasons for discontinuation, n (%)			
Inefficacy or loss of efficacy	90 (43.1)	29 (52.7)	119 (45.1)
Adverse event	42 (20.1)	10 (18.2)	52 (19.7)
Pregnancy or desire to be pregnant	14 (6.7)	0 (0.0)	14 (5.3)
Loss of patient	4 (1.9)	1 (1.8)	5 (1.9)
Remission	19 (9.1)	1 (1.8)	20 (7.6)
Change for non-medical reasons	5 (2.4)	2 (3.6)	7 (2.7)
Other	29 (13.9)	10 (18.2)	39 (14.8)
Unknown	6 (2.9)	2 (3.6)	8 (3.0)

bDMARDs: original biosimilar disease-modifying antirheumatic drugs; bsDMARDs: biosimilar DMARDs; JIA: Juvenil idiopathic arthritis; SD: standard deviation.

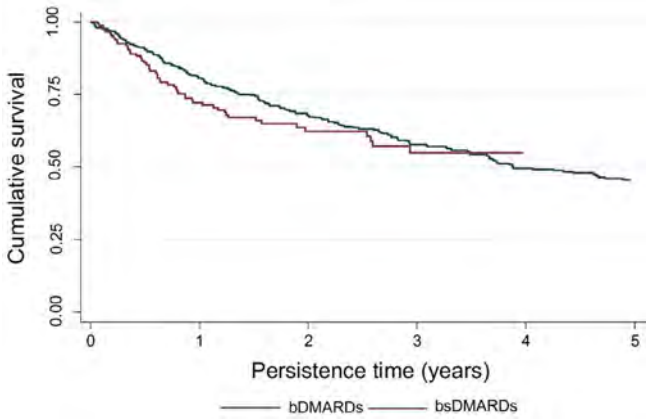
Disease Characteristics, Biologic Therapies, and Reasons for Discontinuation in Adult JIA Patients.

	bDMARDs	bsDMARDs
Total adverse events	400.4 (367.50 - 436.40)	529.6 (444.10 - 631.60)
Serious adverse events	62.4 (50.2-77.6)	51.3 (29.1-90.3)
Fatal	0 (0-0)	0 (0-0)

* Incidence Rate (95% CI) per 1000 Patient-Years

bDMARDs: original biosimilar disease-modifying antirheumatic drugs; bsDMARDs: biosimilar DMARDs.

Incidence rates of adverse events stratified by bDMARDs and bsDMARD*



5-year survival of bDMARD vs. bsDMARD in adult JIA patients.

Methods: Data were obtained from the nationwide prospective registry BIOBADASER (Spanish Registry of Adverse Events of Targeted Therapies in Rheumatic Diseases). All patients diagnosed with JIA and older than 16 years included in the database between 2000 and 2022 were analyzed. Due to the design of the registry, it was not possible to identify each of the JIA subgroups; therefore, we classified them into oligo/polyarticular JIA, enthesitis-related JIA, and psoriatic JIA. Adverse events were coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 13.0. Proportions, means, and standard deviations (SD) were used to describe our population. Drug persistence was calculated using Kaplan-Meier survival curves (KM) until discontinuation for any reason. Incidence rates (IRs) of adverse events and 95% confidence intervals were calculated, and Poisson regression was used to estimate incidence rate ratios (IRRs), adjusting for sex, diagnosis type, age at treatment initiation (≤16 years vs >16 years), and treatment line as confounding variables.

Results: From a total of 313 patients included, 130 (41.5%) patients received bsDMARDs and 183 (58.4%) treatments with bDMRAD. In the bsDMARD group, 43 patients (95.6%) use corticosteroids and 59 patients (96.7%) metotrexate concomitant.Table 1 shows the clinical characteristics, treatment and reason for discontinuation of the studied population according to treatment with bDMARD, bsDMARD and overall. Table 2 shows the IRs for adverse events according to severity. For all adverse events, IR is greater in bsDMARDs compared to bDMARDs, although the latter have a higher IR of serious adverse events. The IRR was 1.33 (95% CI 1.1-1.6) (p=0.004), thus, the risk of adverse events was greater among bsDMARD compared to the original bDMARDs. The KM figure shows that the persistence of bDMARDs and bsDMARDs was similar in the studied population (log rank: 0.78,p-value 0.377).

Conclusion: The most used bsDMARD in adult patients diagnosed with JIA was adalimumab. In this population, there were no differences in 5-year survival rates between bDMARDS and bsDMARDs in JIA adult patients, being ineffectiveness the main reason for discontinuation.

The risk of adverse events was higher in patients treated with bsDMARDs. Although this study allowed us to investigate the long-term safety of biosimilars in JIA, large registries focusing on such patients are needed to better understand rare adverse events.

Disclosure: J. Bethencourt: None; **L. Otero-Valera**: None; **J. MANERO**: None; **E. Perez-Pampin**: None; **Y. Pérez Vera**: None; **S. MANRIQUE**: None; **M. Bustabad Reyes**: None; **M. Freire González**: None; **D. Ruiz-Montesinos**: None; **L. Mateo Soria**: None; **R. Martín Domenech**: None; **M. Moreno Ramos**: None; **F. Alonso**: None; **I. Castrejon**: None.

Abstract Number: 0347

Towards Effective Shared Decision Making - Development and Validation of a Prediction Model for Personalized Probabilities of Side Effects in the Initial Treatment of Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Clinical practice guidelines for Juvenile Idiopathic Arthritis (JIA) emphasize the importance of adapting guideline recommendations to each individual patient through shared decision-making among patients, families, and clinicians. In the initial treatment of non-systemic JIA, a key decision is whether to start NSAIDs and joint injections alone (NSAIDs+/-JI) or in combination with methotrexate (MTX+NSAIDs+/-JI). Effective shared decision making requires patients and families to be informed of reasonable estimates of the likelihood of side effects (SE) with each treatment option. However, there are limited published prediction models for MTX-associated SE and no models comparing MTX+NSAIDs+/-JI

Table 1. Final model for predicting side effects in children with juvenile idiopathic arthritis. The same model calculates risk of side effects with methotrexate (MTX=1) and without (MTX=0)

Predictor	B coefficient (95%CI)
Intercept	1.94 (-1.21, 5.09)
Methotrexate (0=No, 1=Yes)	0.66 (-0.01, 1.33)
Total active joint count	-0.01 (-0.07, 0.04)
Active joint count ≥5	0.26 (-0.65, 1.18)
Male Sex	-0.27 (-0.85, 0.31)
Physician global assessment of disease activity (0 to 10)	-0.03 (-0.19, 0.12)
Disease duration (weeks)	0.00 (0.00, 0.01)
Age (years)	-0.02 (-0.20, 0.16)
Height (cm)	-0.02 (-0.05, 0.02)
Weight (Kg)	0.01 (-0.01, 0.04)
Health related quality of my life scale (0 to 10)	-0.11 (-0.23, 0.02)
Parent global assessment of wellbeing (0 to 10)	0.10 (-0.02, 0.22)
ESR/CRP above normal threshold	0.14 (-0.54, 0.83)
Enthesitis present (0=No, 1=Yes)	0.44 (-0.40, 1.29)
Medication side effects at baseline (0=No, 1=Yes)	1.15 (0.65, 1.65)
Oligoarthritis	-0.19 (-1.18, 0.80)
Polyarthritis RF negative	0.05 (-1.08, 1.18)
Psoriatic arthritis	-0.75 (-2.04, 0.54)
Undifferentiated arthritis	0.35 (-0.65, 1.35)

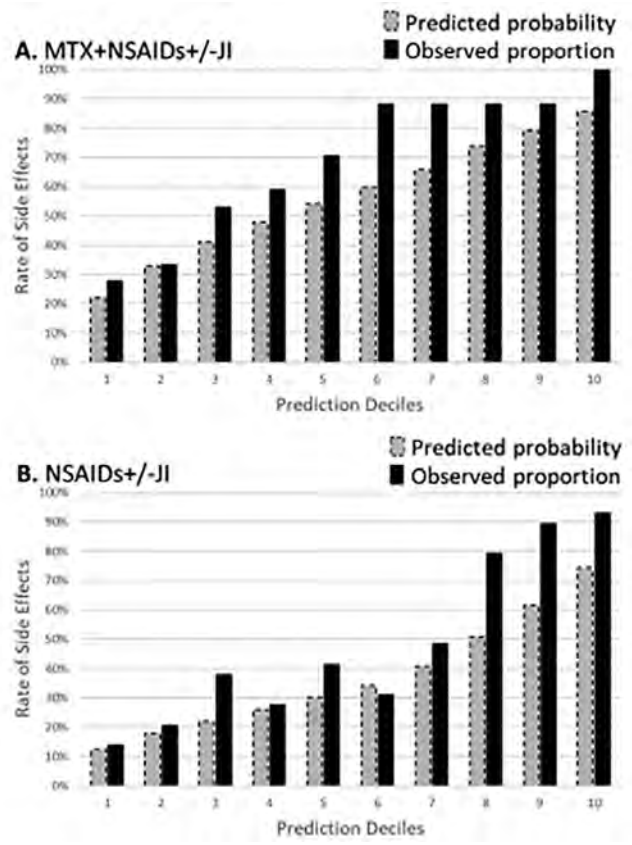

Figure 1. Calibration of prediction models in the validation cohort for probability of side effects for A. MTX+NSAIDs+/-JI and B. NSAIDs+/-JI.

to NSAIDs+/-JI. In this study, we aimed to develop and externally validate a clinical prediction model that provides personalized probabilities of SE comparing NSAIDS+/-JI with and without adding MTX.

Methods: We used data from two Canadian JIA cohorts. Data collected from 2005-2010 in the Research in Arthritis in Canadian Children Emphasizing Outcomes (ReACCh-Out) cohort for model development and data collected from 2017-2020 in the Canadian Alliance of Pediatric Rheumatology Investigators (CAPRI) JIA Registry for external validation. Parents reported SE using standardized lists of symptoms. For model development, we compared various logistic regression models with discrimination accuracy measured with c-index. We measured model calibration by comparing predicted probabilities versus observed rates of SE. Due to the very low frequency of serious SE, models could only predict probabilities for mild-moderate SE. With input from patients, families, and clinicians, we incorporated the models in a Web App that generates a visual aid presenting personalized probabilities of SE when predictor variables are inputted by a clinician.

Results: Patients included for development (n=757) and validation (n=437) had baseline characteristics comparable to most North American JIA inception cohorts. Two-thirds % were female with a median age of 8 years old and more than 75% diagnosed with oligoarthritis, RF-negative polyarthritis or enthesitis related arthritis. The c-indices for the various prediction models in the development cohort were all similar at ~0.67. We chose the final model prioritizing fewer and more easily obtainable variables (Table 1). In external validation, our final model for predicting SE had a c-index of 0.80 (95% CI 0.76, 0.84). Model calibration was acceptable, with similar predicted versus observed SE rates (Figure 1). A Web App was created to present probabilities of SE in pie charts, comparing NSAIDs+/-JI to MTX+NSAIDs+/-JI (Figure 2).

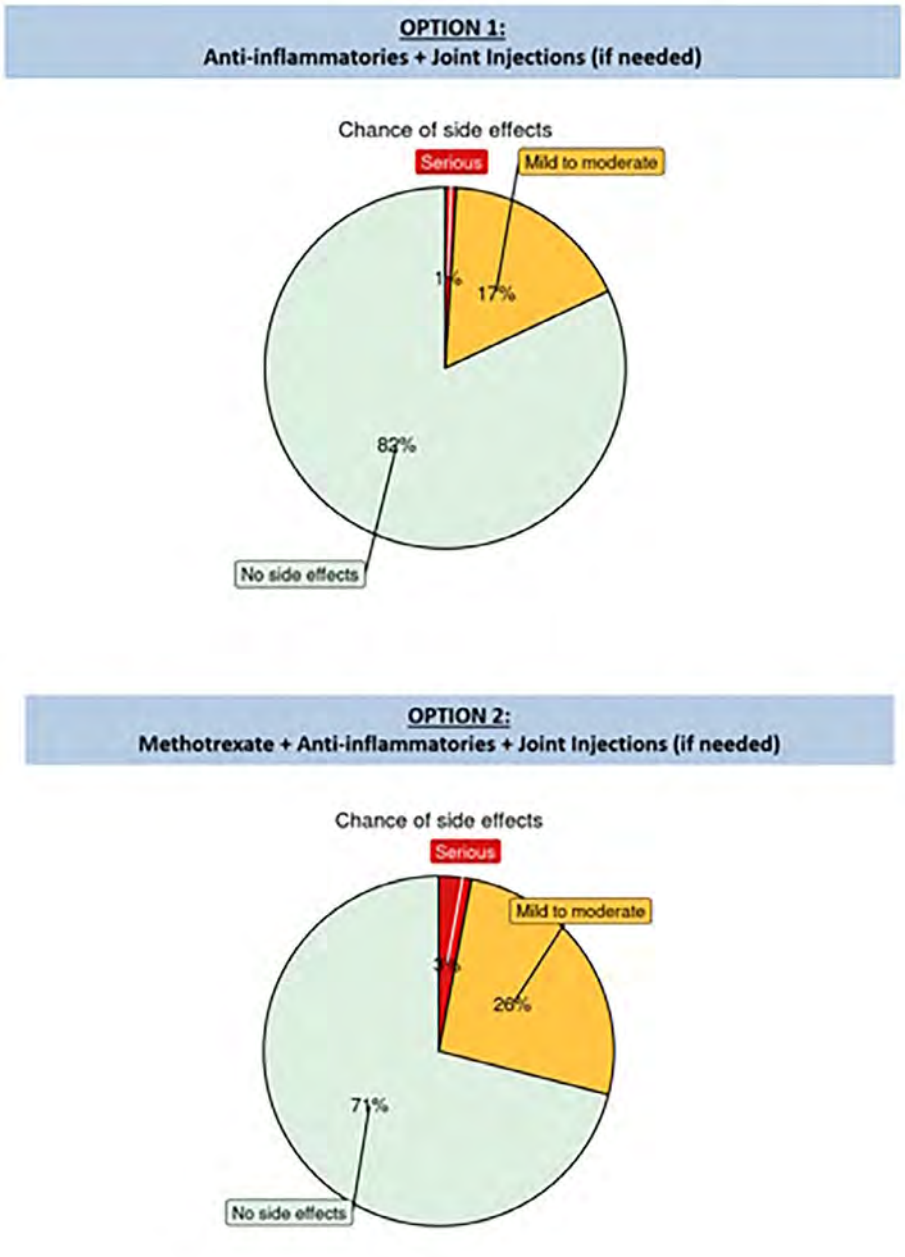

Figure 2. Example of visual representation of predictions for one patient, generated by inputting variables in a Web App.

Conclusion: This study developed and externally validated a prediction model for probability of SE directly comparing two realistic treatment options at the time of JIA diagnosis. Inputting the variables in a Web app will then produce a visual aid to facilitate shared decision-making with families. Future work should add likelihood of treatment response to further aid the decision of choosing an initial treatment option in JIA.

Disclosure: J. Park: None; **T. Loughin**: None; **A. Henrey**: None; **J. Guzman**: None.

Abstract Number: 0348

The Use of Ruxolitinib for Improved Disease Control in Systemic Juvenile Idiopathic Arthritis (sJIA) and Recurrent Macrophage Activation Syndrome (MAS)

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Pediatric Rheumatology – Clinical Poster I: JIA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

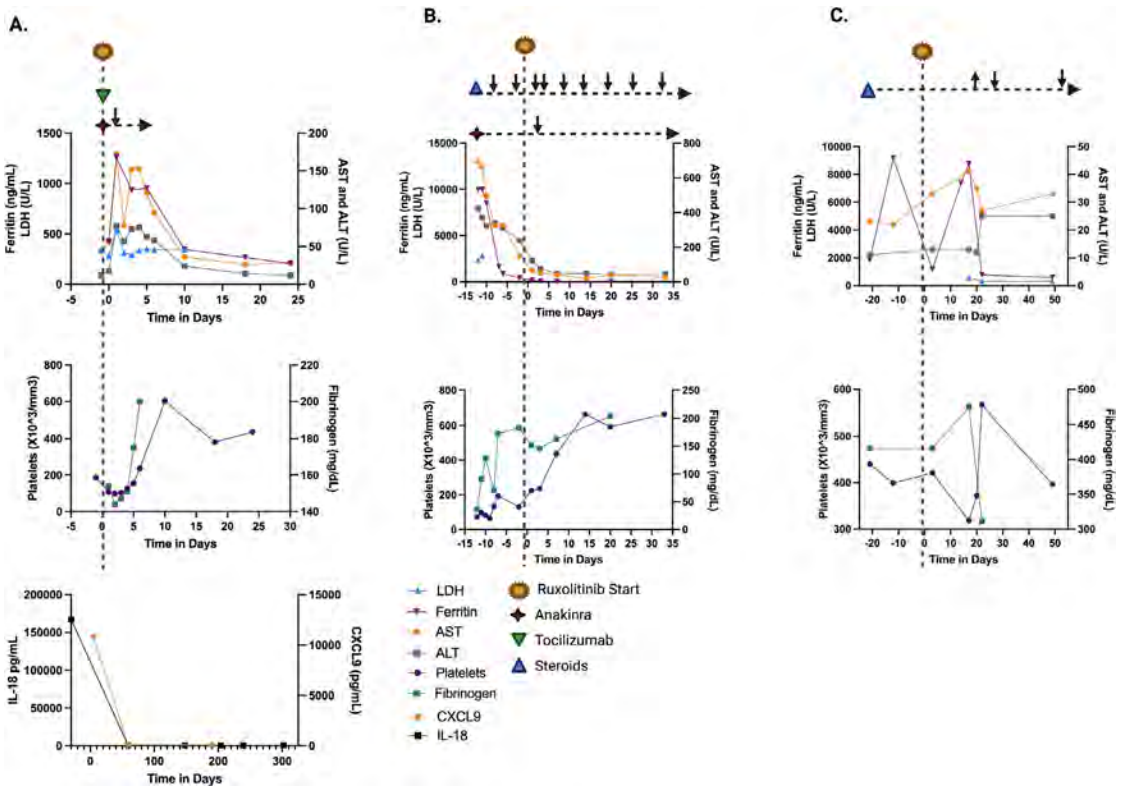


Figure 1. Clinical Details. Day 0 represents first day of ruxolitinib in all patients. Overall, patients had improvement in cytopenias and transaminitis if present. A. On Day 0, patient required ICU admission for MAS with hypotension and fever and was given tocilizumab 800 mg once, ruxolitinib, and anakinra 100 mg q6h (weaned off by day 5). Patient had improvement in ferritin, cytopenias, and transaminitis within 15 days. Patient had significant improvement in IL-18 and CXCL9 levels with continued ruxolitinib monotherapy. B. On day -12, patient was admitted for MAS related to EBV and had initial improvement in ferritin, thrombocytopenia, hypofibrinogenemia and transaminitis with a single dose of rituximab (to aid with EBV clearance), anakinra 12.5 mg/kg/day divided IV q6h and pulse dose steroids (30 mg/kg x 3 days). There was some initial improvement of MAS, but team was unable to wean steroids or anakinra. Ruxolitinib was started which allowed for anakinra to be weaned to 6.25 mg/kg/day SQ dosing by day 3. Patient was discharged on ruxolitinib, anakinra 6.25 mg/kg/day once a day, and 1.5 mg/kg/day prednisolone. While on ruxolitinib, patient continued to tolerate steroid weans as an outpatient. C. Patient was started on ruxolitinib in addition to oral steroids, adalimumab, and mycophenolate for management of SJIA with lung involvement. Patient tolerated slow wean of steroids (methylprednisolone 40 mg/day max to prednisone 15 mg/day) over the course of 4 months. Figure created with GraphPad PRISM and Biorender.

Background/Purpose: The advent of biologics such as IL-1 receptor antagonists has dramatically improved outcomes for children with pediatric rheumatic diseases and hyperinflammation. However, there remains a subset of patients with systemic juvenile idiopathic arthritis (sJIA) who develop life-threatening complications of macrophage activation syndrome (MAS) and interstitial lung disease (ILD) despite treatment with glucocorticoids and IL-1 inhibition. Recent findings point to robust interferon and IL-18 signature as drivers of persistent inflammation in sJIA, suggesting a potential role for inhibition of these pathways using Janus kinase inhibitors, such as ruxolitinib, as a viable therapeutic strategy.

Methods: We completed a retrospective chart review on three patients with sJIA or sJIA-like disease started on ruxolitinib for improved disease control or to allow for glucocorticoid weaning.

Results: Patients ages were 5-15 years of age with 2 females and 1 male (Table 1). Patient A with sJIA-like disease presented with recurrent MAS with fever and hypotension requiring vasopressor support and was treated with ruxolitinib, anakinra, and tocilizumab and MAS was controlled (Figure 1). Anakinra was weaned off prior to discharge home. Ruxolitinib was continued as a single agent and has maintained excellent control of the patient's disease with no further MAS flares or adverse events for the last 10 months. Patient B with previously diagnosed sJIA presented with fulminant MAS secondary to EBV. She was treated with pulse dose steroids and anakinra with some initial stabilization. Ruxolitinib was started due to lack of further improvement in MAS. The addition of ruxolitinib controlled her MAS and steroid and anakinra doses were tapered (Table 2;

Table 1. Patient History, Presentation, and Therapy

	Patient A	Patient B	Patient C
Initial Presentation	Cold autoimmune hemolytic anemia; MAS including hyperferritinemia, cytopenias, hepatosplenomegaly, lymphadenopathy; Uveitis	Arthritis in multiple joints, Systemic inflammation; Fevers; Classic rash	Pleural effusion; Pericardial effusion; Arthritis multiple joints; Elevated ferritin
Age of Initial Presentation	15 years	2 years	17 months
Diagnosis	SJIA-like disease with recurrent MAS and severely elevated IL-18	SJIA	SJIA
Genetic Testing	Primary immunodeficiency, autoimmunity/inflammation, lymphoid malignancy predisposition genetic testing negative for pathogenic variants	None	None
Previous Therapies	Steroid (weaned off 7 months prior presentation) for cold autoimmune hemolytic anemia, anakinra and tocilizumab during MAS flares (last flare 2 weeks prior to presentation). Off all medication at time of last MAS presentation	Stable on every other day anakinra prior to MAS	NSAIDs, steroids, hydroxychloroquine methotrexate, anakinra, and canakinumab. Adalimumab, mycophenolate, and oral steroids were his therapy prior to starting ruxolitinib
Age at Ruxolitinib Initiation	15 years	5 years	10 years
Reason for Starting Ruxolitinib	Single agent to prevent reoccurrence of MAS	To assist with weaning of anakinra and steroids after MAS	Failure of multiple therapies to control disease, development of anti-drug antibodies to adalimumab worsening of SJIA-related lung disease
Current Therapy	Ruxolitinib 20 mg PO BID monotherapy	Anakinra 4.3 mg/kg/dose every other day	Prednisone 0.3 mg/kg/day of PO; Ruxolitinib 25 mg PO BID

Macrophage Activation Syndrome (MAS); Systemic Juvenile Idiopathic Arthritis (SJIA); Interleukin (IL)-18

Table 2. Ruxolitinib Dosing

Patient	A	B	C
Weight (kg)	88.2	18.2	41.1
BSA (m^2)	1.9	1.04	1.48
Starting Medication Dosing	25 mg BID	10mg BID	20mg BID
Weight-based Dosing	0.3 mg/kg/dose	0.5 mg/kg/dose	0.5 mg/kg/dose
BSA-based Dosing	13.5 mg/m^2/dose	10 mg/m^2/dose	13.5 mg/m^2/dose
Titration	Decreased to 20 mg BID	Weaned off	Increased to maximum dose 25 mg

Figure 1). Oral steroids were discontinued 9 weeks after starting ruxolitinib. Ruxolitinib was discontinued at 3 months. Patient was continued on anakinra. Patient C with previously diagnosed sJIA developed sJIA-associated lung disease on canakinumab therapy. Ruxolitinib was added to his therapy (Table 1, 2) due to continued systemic inflammation and inability to wean steroids. Within the 4 weeks the patient reported improvement in joint pain and had no oxygen desaturations with walking. Within 6 weeks, lung function improved with FEV1 increasing from 85% to 91% predicted. Ruxolitinib dose was increased to 25 mg twice a day at 4 months based on patient toleration and to optimize disease control, allowing successful weaning of steroids by 50%. Patients have not had any infectious complications while on ruxoltinib. One adverse event reported was Grade 1 elevated cholesterol. Mean follow-up time is 214 days (146-322). Mean time patients were on ruxolitinib was 189 days (100-322).

Conclusion: Ruxolitinib was well tolerated in these patients with sJIA or sJIA-like disease with no significant adverse events, including cytopenias, transaminitis, or infections. Use of ruxoltinib provided improved disease control as a single agent or in combination with other immunomodulators and allowed reduction of other therapies, such as steroids. Based on our experience, patients may require and can tolerate higher doses than previously used for other indications with titration up and down to affect.

Disclosure: K. Collins: None; **I. Abutineh**: None; **T. Paul**: None; **P. Rai**: None; **G. Schulert**: IpiNovyx, 5, SOBI, 2; **M. Hines**: Incyte, 5.

Abstract Number: 0349

Disease Activity of Juvenil Idiopathic Arthritis in Transitional Care

Karen Carpio Astudillo[1], Daniel clemente Garulo[2], Juan Carlos Lopez-Robledillo[3], Camille Bourgeois Avella[4], Laura Trives Folguera[4], Amparo López López[1], Jose María Alvaro-Gracias[4], Indalecio Monteagudo Sáez[1] and Juan carlos Nieto-Gonzalez[5], [1]Hospital General Universitario Gregorio Marañón, Madrid, Spain, [2]Pediatric Rheumatology Unit, Hospital Niño Jesús, Madrid, Spain, [3]Hospital Infantil Universitario Niño Jesús, Madrid, Spain, [4]Hospital General Universitario Gregorio Marañon, Madrid, Spain, [5]Servicio de Reumatología, Hospital General Universitario Gregorio Marañón, Madrid, Spain

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Pediatric Rheumatology – Clinical Poster I: JIA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile Idiopathic Arthritis (JIA) are a group of heterogeneous arthritis with onset in childhood. According to previous studies, this patients experience an improvement of their disease activity, functionality and even remission as they become young adults [1]. Transitional care units aim to coordinate an uninterrupted follow-up in patients with chronic diseases.[2] Our transitional care unit attend patients from 18 to 25 years old who have been previously diagnosed with any rheumatic disease during childhood. Our primary objective was to describe the disease activity of JIA patients at the transference to our unit and the remission maintenance during follow-up.

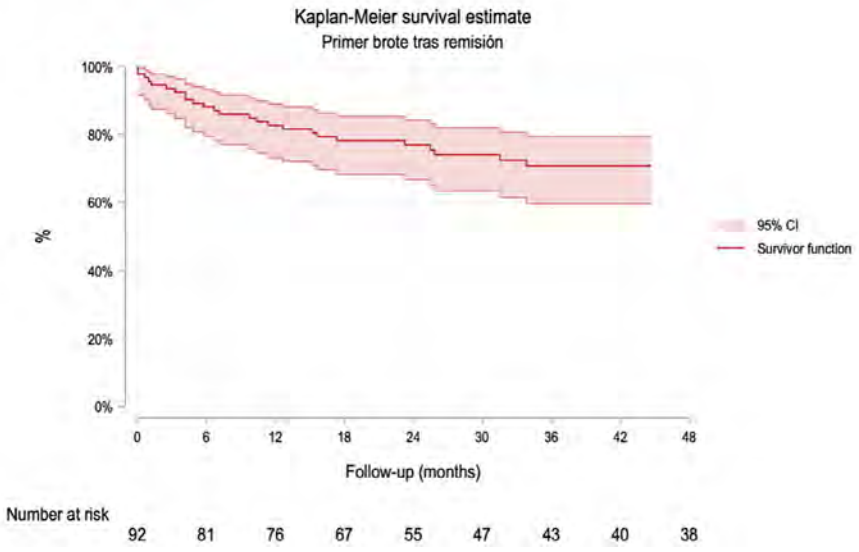
Methods: We conducted an observational retrospective longitudinal study from a cohort of patients with JIA who have been transferred to our transitional care unit. We selected patients with at least one clinical visit and have active follow-up. We collected demographic data, JIA classification, previous treatments and the treatment at time of transfer, articular and ocular flares, remission defined by Wallace criteria[3] and changes in treatment during follow-up.

Results: From December 2016 to December 2021 we received 113 with JIA diagnosis, the mean age at transfer was 19.8 years. Demographic characteristics of patients are shown in Table 1. About 31% of the patients had a flare through the 3 years of follow-up, most of them were women (71.4%). Both oligoarticular (37.1%) and polyarticular (37.1%) and spondyloarthritis (25.7%) had inflamamatory flares in similar proportion.

Table 1. Demographic data from JIA included in the study

	Total (n: 113)	Actives (n:23)	Not Actives (n:90)
Sex (female) n (%)	77 (68.1)	15 (65.2)	62 (68.9)
Age median (SD)	8.22 (5.0)	8.91 (5.1)	8.01 (4.9)
Mean Age at transfer (SD)	19.8 (3.1)	19.18 (1.9)	19.76 (3.3)
sDMARD prior transference (%)	94 (83.2)	22(95.7)	72 (80)
bDMARD prior transference (%)	67 (59.3)	11 (47.8)	56(62.2)
Uveítis	19 (16.8)	8 (16.6)	11 (16.9)
JIA subcategory n (%)			
Oligo persist	39 (34.5)	8 (34.8)	31 (34.4)
Oligo extend	13 (11.5)	1 (4.3)	12 (13.3)
Poly FR -	24 (21.2)	6 (26.1)	18 (20)
Poly FR +	5 (4.4)	1 (4.3)	4 (4.4)
ERA	19 (16.8)	6 (26.1)	13 (14.4)
Systemic	6 (5.3)	0 (0)	6 (6.6)
Psoriatic	7 (6.2)	1 (4.3)	6 (6.6)

Table 2. Kaplan-Meier survival estimate of remission in JIA patients since their transfer to the Transitional Care Unit.



It is important to notice that from 45 patients (38.9%) who had a flare prior to transfer 37.8% had another flare during follow-up. While, 26.5% of the patients who never had a previous flare presented a new flare during this follow-up. Flares during transfer were independent from patient's previous inflammatory activity; and the previous treatment did not influence the risk of flare development.

Conclusion: Flare risk during transfer was independent from previous activity and treatment. The flare frequency was slightly reduced over time (39,8% vs. 31%) (Table 2).

Disclosure: K. Carpio Astudillo: None; **D. clemente Garulo**: Eli Lilly, 5, GlaxoSmithKlein(GSK), 6, Pfizer, 6, Sanofi, 5; **J. Lopez-Robledillo**: None; **C. Bourgeois Avella**: None; **L. Trives Folguera**: None; **A. López López**: None; **J. Alvaro-Gracias**: Abbvie, 2, 6, AstraZeneca, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, GSK, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **I. Monteagudo Sáez**: None; **J. Nieto-Gonzalez**: AbbVie, 2, 6, Amgen, 2, 6, Biogen, 6, Bristol-Myers Squibb(BMS), 6, FAES Farma, 6, Galapagos, 2, GSK, 2, Janssen, 2, 6, Lilly, 6, MSD, 2, 6, Novartis, 6, Pfizer, 6, Roche, 6, Sanofi, 6, UCB, 6.

Abstract Number: 0350

Presentation, Management, and Outcomes of Systemic JIA-Associated Lung Disease: A Single Center Experience

Ana Luiza Altaffer[1], Maria Pereira[2], Marietta De Guzman[2] and Andrea Ramirez[2], [1]Baylor College of Medicine, Texas Children's Hospital, Houston, TX, [2]Baylor College of Medicine, Houston, TX

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a rare and severe complication of systemic juvenile idiopathic arthritis (SJIA) that was recognized relatively recently, and its incidence appears to be rising. Much is still unknown about its optimal management.

Methods: With an institutional review board approval from Baylor College of Medicine, children under 16 years old with SJIA-associated lung disease (SJIA-LD) at Texas Children's Hospital between 2014-2023 were identified. Demographics, clinical features, laboratory, radiographic findings, and therapies were collected and analyzed using standard descriptive statistics.

Results: Six children with SJIA-LD were identified. The median age in years at SJIA diagnosis was 1 (range 0-4), and patients were followed for a median of 30.5 months (range 15-82). There were equal numbers of males and females, most were white (83.3%, vs. 16.7% Black), and most were Hispanic (50.0%, vs. 33.3% not Hispanic and 16.7% not specified). Four patients (66.7%) had no significant medical history prior to SJIA presentation, while 1 patient had Trisomy 21, and another was a former 23-week preterm infant with associated complications, including bronchopulmonary dysplasia with tracheostomy dependence. All patients presented classically with fever, rash, and arthritis; none had respiratory symptoms or clubbing at SJIA diagnosis. The median time from SJIA diagnosis to identification of lung disease was 13 months (range 4-60). Imaging that led to the diagnosis was obtained due to respiratory symptoms in 3 patients (50.0%, of which one occurred in the setting of known rhinovirus) and for asymptomatic screening in 1case (16.7%). Two patients (33.3%) had

incidental ILD on imaging obtained for other reasons. The most frequent pulmonary findings on the initial chest CT were linear opacities (50.0%), while 33.3% had ground-glass opacities. Two patients (33.3%) had pulmonary hypertension, and 1 (16.7%) developed a new oxygen dependence. In addition to corticosteroids, anti-IL1 and anti-IL6 drugs were the most utilized therapies. All patients had their disease course complicated by macrophage activation syndrome (MAS). The disease was difficult to control, and medication changes were common due to disease flares, challenges with the route of administration, infusion reactions, and side effects. At the most recent rheumatology visit, 5 patients (83.3%) were on dual biologic therapy, and 3 patients (50.0%) remained on chronic corticosteroids. No patients died during the study period.

Conclusion: All children in our SJIA-LD cohort were diagnosed with SJIA at an early age and had difficult-to-control disease, including elevated CXCL9 and IL-18 levels. Half of the patients had respiratory symptoms that led to chest imaging, while the other half had no respiratory symptoms. All experienced MAS and required aggressive therapy, often with dual biologics and chronic corticosteroids.

Table 1. Demographics, Clinical Characteristics, and Laboratory Values

Table 1: Demographics, Clinical Characteristics, and Laboratory Values

	N = 6	
Sex, n (%)		
Male	3 (50.0)	
Female	3 (50.0)	
Race, n (%)		
White	5 (83.3)	
Black or African American	1 (16.7)	
Ethnicity, n (%)		
Hispanic or Latino	3 (50.0)	
Not Hispanic or Latino	2 (33.3)	
Not Specified	1 (16.7)	
Age at SJIA diagnosis in years, median (range)	1 (0-4)	
Time from symptom onset to SJIA diagnosis in months, median (range)	5.5 (2-19)	
Time from SJIA diagnosis to identification of lung disease in months, median (range)	13 (4-60)	
Symptoms and exam findings, n (%)	**Presentation**	**Last recorded visit**
Fever	6 (100.0)	2 (33.3)
Arthritis	5 (83.3)	0 (0.0)
Rash	6 (100.0)	2 (33.3)
Lymphadenopathy	5 (83.3)	0 (0.0)
Hepatosplenomegaly	1 (16.7)	0 (0.0)
Respiratory symptoms	0 (0.0)	1 (16.7)
Clubbing	0 (0.0)	3 (50.0)
Lab values, median (range)	**Presentation**	**Last recorded visit**
Ferritin in ng/mL	2,915 (4-3,470)	117 (12-733)[3]
Interleukin-18 in pg/mL	149,883 (8,891-243,436)[1]	12,309 (675-92,829)[3]
CXCL9 in pg/mL	4,264 (n/a)[2]	1,514 (532-1624)[1]
Other features and complications, n (%)		
Macrophage activation syndrome	6 (100.0)	
Pulmonary hypertension	2 (33.3)	
New oxygen dependence	1 (16.7)	
Initial chest CT findings, n (%)		
Lymphadenopathy	4 (66.7)	
Linear opacities	3 (50.0)	
Consolidation	2 (33.3)	
Ground-glass opacities	2 (33.3)	
Pulmonary nodules	2 (33.3)	
Septal thickening	1 (16.7)	
Bronchial wall thickening	1 (16.7)	
Cavitation	1 (16.7)	
Cysts	1 (16.7)	

Legend. 1: documented in 3 patients; 2: documented in 1 patient; 3: documented in 4 patients

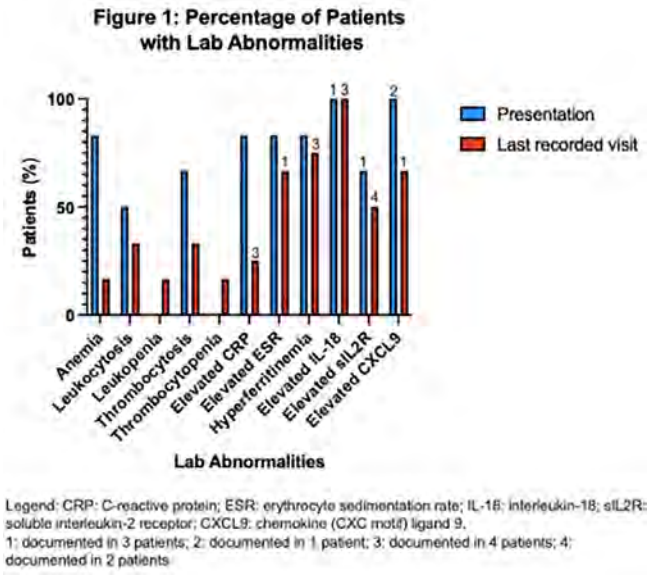


Figure 1. Percentage of Patients with Lab Abnormalities

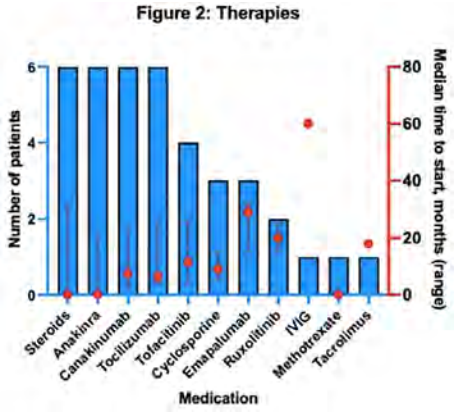


Figure 2. Therapies Used Throughout Disease Course

Disclosure: A. Altaffer: None; **M. Pereira**: None; **M. De Guzman**: None; **A. Ramirez**: None.

Abstract Number: 0351

Needs Assessment Survey of Critical Data Element Completion in Telemedicine Visits for Juvenile Idiopathic Arthritis in the Post-Pandemic Period

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile Idiopathic Arthritis (JIA) affects 1 in 1,000 children in the United States (US). There is a shortage of pediatric rheumatologists across North America and many patients travel lengthy distances to access subspecialty care. Telemedicine is a potential solution to this distance barrier. Although use of telemedicine has substantially increased since the COVID-19 pandemic, questions remain about the role of virtual visits for monitoring of patients with JIA where hands-on assessments have been the cornerstone for care. Surveys from early in the pandemic indicated that critical data elements (CDE) for Treat-to-Target decision making such as active joint count, physician global assessment (PGA) and patient reported outcomes (PROs) were under-reported in telemedicine relative to in-person visits.[1,2] The global aim of this quality improvement effort is to optimize completion of CDE for JIA patients seen via telemedicine, targeting the

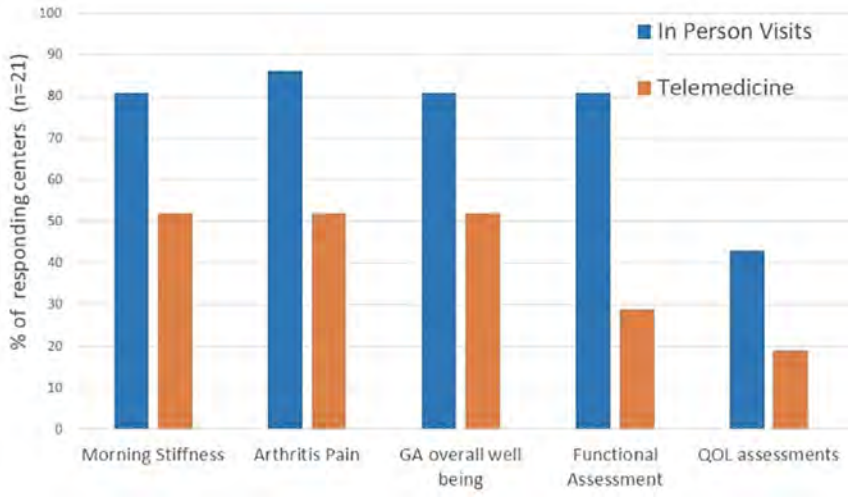

Figure 1: Specific CDE collected during JIA visits by visit modality

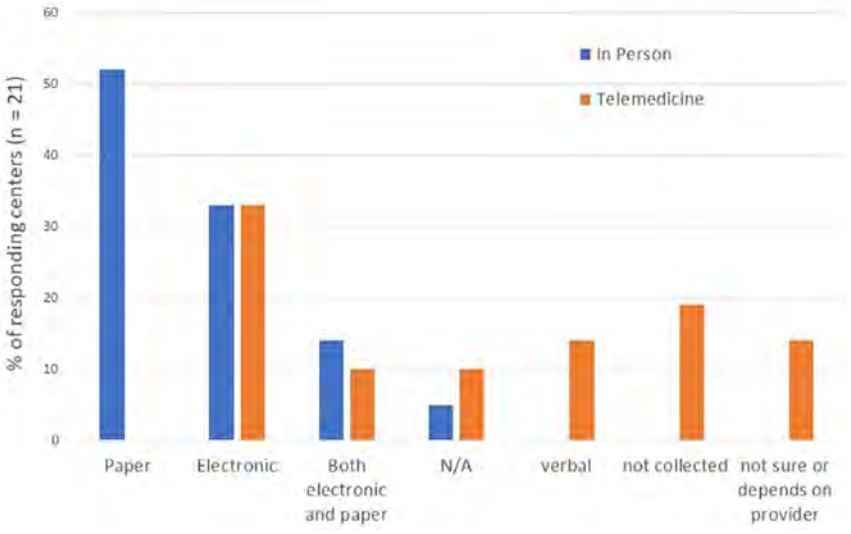

Figure 2: Methods of PRO collection during JIA visits by visit modality

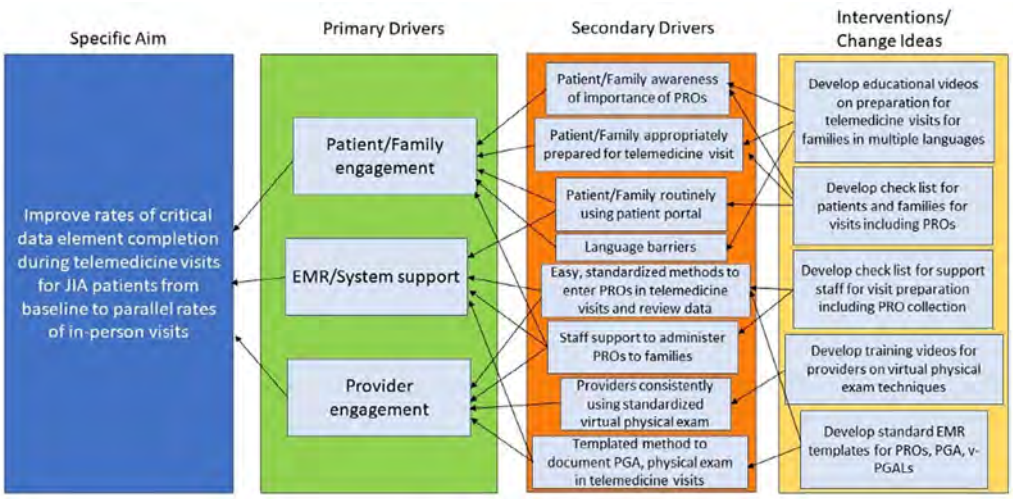

Figure 3: Key Driver Diagram based on PR-COIN network needs assessment survey

same rate as in-person visits. To determine primary drivers of CDE in telemedicine visits as well as to inform ideas for change, we performed a needs assessment of post-pandemic telemedicine practices of the Pediatric Rheumatology Care and Outcomes Improvement Network (PR-COIN) network.

Methods: PR-COIN is a multi-center learning collaborative spanning 24 pediatric centers across the US and Canada. A REDCap survey regarding current telemedicine practices was emailed to the faculty representative for each PR-COIN site in January 2023. Quantitative responses were analyzed with descriptive statistics. Qualitative comments were thematically grouped.

Results: Responses were received from 21/24 sites (88%). Figure 1 demarcates CDE collected by visit modality. Figure 2 notes the methods of PRO collection by visit type. Only 2 sites reported that providers use a standard method to assess active joint counts in telemedicine visits. However, most respondents (15/21) indicated that providers used modifications of the 'video' pediatric Gait Arms Legs and Spine (vpGALS) tool for virtual joint exams.

Reported barriers to CDE collection during telemedicine visits were grouped into three categories of primary drivers: patient engagement, provider engagement and electronic medical record(EMR)/support staff (Figure 3). Opportunities to improve standard collection of CDE included development of educational materials, easy/automated collection methods, enhanced use of support staff, streamlined questionnaires and standardized templates for virtual physical exams.

Conclusion: Despite three years of telemedicine experience, CDE completion for JIA patients in virtual visits lags behind rates for in-person visits. We are currently developing resources including instructional videos, templates and best practices for providers, patients and EMR/support staff to address these gaps. We plan to implement these interventions at network sites using an iterative quality improvement approach and prospectively track rates of CDE completion.

References

1. Goh YI, et al. *Frontiers in Pediatrics*. 2021 Mar 4;9:642460.
2. Ryan ME, et al. *Pediatr Rheumatol Online J*. 2022 Sep 29;20(1):83.

Disclosure: K. Hayward: AbbVie/Abbott, 11, CIGNA/Express Scripts, 11, Merck/MSD, 11, Teva, 11; **Y. Goh**: None; **M. Toth**: None; **J. Leal**: None; **A. Liu**: None; **N. Naik**: None; **J. Singleton**: None; **J. Youn**: None; **E. Morgan**: None.

Abstract Number: 0352

Musculoskeletal Ultrasound Findings in Children with Psoriasis

Laura Nedorezov, Tracy Ting and Patricia Vega-Fernandez, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The presentation of juvenile psoriatic arthritis (JPsA) in children with psoriasis can be insidious and poses a diagnostic challenge. Musculoskeletal ultrasound (MSUS) has emerged in recent years as a sensitive and non-invasive imaging modality to detect joint inflammation. A growing number of evidence has shown that adult psoriasis patients without signs of arthritis have findings of subclinical joint pathology on MSUS. These patients with identified imaging abnormalities are more likely to develop active psoriatic arthritis as demonstrated in longitudinal studies. No such research has been performed among children with psoriasis however, highlighting a critical gap in the understanding of pediatric psoriatic disease. The objective of this investigation is to describe MSUS and nail ultrasound findings in children with psoriasis.

Table 1: Demographics and clinical characteristics of the patients studied.

Characteristic	Total, n = 11
Male/female	7/4
Age (years)[a]	11.8 ± 2.4
Ethnicity, n (%)	
Caucasian	7 (63.6)
African American	3 (27.3)
Asian	1 (9.1)
Body mass index (kg/m^2)[b]	18.5 (5.2)
Disease duration (years)[b]	5.4 (7.9)
Psoriasis subtype[c], n (%)	
Plaque	5 (45.5)
Guttate	3 (27.2)
Scalp	5 (45.5)
Palmoplantar	2 (18.2)
Psoriasis Area and Severity Index[b]	2.4 (5.5)
Nail Psoriasis Severity Index[b]	0 (8.0)
Morning stiffness (minutes)[b]	0 (22.5)
Active joint count, n (%)	0 (0)
Beighton score[d] > 5, n (%)	4 (36.4)
Current treatment[c], n (%)	
Topical corticosteroid	7 (63.6)
Topical vitamin D analog	1 (9.1)
Topical calcineurin inhibitor	1 (9.1)
No treatment	3 (27.3)

[a]Mean ± standard deviation
[b]Median (IQR)
[c]Each patient could have more than one disease subtype or treatment identified.
[d]Measure to assess generalized joint hypermobility.

Methods: Grey-scale (B) mode and power Doppler (PD) mode ultrasound were utilized in this cross-sectional study to evaluate joint, enthesis, and nail findings in pediatric psoriasis patients (< 18 years old) without clinical symptoms of arthritis. Exclusion criteria included acute joint injury, trauma, or joint surgery within the last 3 months, on systemic treatment or oral corticosteroids in the last 2 months, or pregnancy. Each subject underwent a full musculoskeletal exam and sonographic evaluation of seven sites bilaterally: a) joints/nails – fingernails, MCP, and IP joints of the second and third fingers, as well as any finger with psoriatic nail involvement, patella, tibiotalar and subtalar joints, b) entheses – quadriceps, proximal and distal patellar tendon, Achilles, and plantar fascia calcaneal insertion. Ultrasound images were assessed using an established

Table 2: Ultrasound characteristics of the studied nails, n = 61.

Wortsman classification[a]		n (%)
Normal		10 (16.4)
I		11 (18.0)
II		34 (55.8)
III		1 (1.6)
IV		5 (8.2)
Nail parameters		**Mean ± SD**
NP thickness (mm)		0.41 ± 0.11
NB thickness (mm)		1.67 ± 0.22
Matrix thickness (mm)		1.33 ± 0.22
Distal extensor tendon thickness (mm)		0.66 ± 0.16
PD grade[b]	PD signal nail bed n (%)	PD signal nail matrix n (%)
0	30 (49.2)	32 (52.5)
1	21 (34.4)	16 (26.2)
2	7 (11.5)	6 (9.8)
3	3 (4.9)	7 (11.5)

NP: nail plate, NB: nail bed, SD: standard deviation, PD: power Doppler
[a]I – focal hyperechoic involvement of the ventral plate, II – loosening of the borders of the ventral plate, III – wavy plates, IV – loss of definition of both plates (Wortsman X, Jemec GB. Ultrasound imaging of nails. *Dermatol Clin*. 2006;24(3):323-328. doi:10.1016/j.det.2006.03.014)
[b]PD Grade 0 – normal, 1 – confluent signal in < 25% of the area, 2 – confluent signal in >25% and < 50%, 3 – confluent signal in > 50% (Arbault A, Devilliers H, Laroche D, et al. Reliability, validity and feasibility of nail ultrasonography in psoriatic arthritis. *Joint Bone Spine*. 2016;83(5):539-544. doi:10.1016/j.jbspin.2015.11.004)

Table 3: Ultrasound findings of all joint and enthesis sites.

Joints	B-mode, n (%)				PD mode, n (%)
Grade[c]	0	1	2	3	0[d]
Fingers					
MCP joint recess, n = 61	47 (77.0)	12 (19.7)	2 (3.3)	0 (0)	61 (100)
PIP/DIP joint recess, n = 117	81 (69.2)	17 (14.5)	19 (16.3)	0 (0)	117 (100)
Knee, n = 22					
Suprapatellar recess	14 (63.6)	6 (27.3)	2 (9.1)	0 (0)	22 (100)
Medial parapatellar recess	15 (68.2)	6 (27.3)	1 (4.5)	0 (0)	22 (100)
Lateral parapatellar recess	20 (90.9)	2 (9.1)	0 (0)	0 (0)	22 (100)
Ankle, n = 22					
Anterior tibiotalar recess	19 (86.4)	3 (13.6)	0 (0)	0 (0)	22 (100)
Anterior subtalar recess (from medial)	20 (90.9)	0 (0)	2 (9.1)	0 (0)	22 (100)
Posterior subtalar recess (from lateral)	18 (81.8)	3 (13.7)	1 (4.5)	0 (0)	22 (100)
Enthesis, n = 22	**Abnormal B-mode[c], n**				**Abnormal PD mode[d], n**
Quadriceps tendon	0				1
Proximal patellar tendon	0				1
Distal patellar tendon	0				0
Achilles tendon	0				0
Calcaneal plantar fascia	0				1

PD: power Doppler, MCP: metacarpophalangeal, PIP: proximal interphalangeal, DIP: distal interphalangeal
[a]Vega-Fernandez P, Ting TV, Oberle EJ, et al. The MUSICAL pediatric ultrasound examination - a comprehensive, reliable, time efficient assessment of synovitis. *Arthritis Care Res (Hoboken)*. 2021;10.1002/acr.24759. doi:10.1002/acr.24759
[b]None of the joints had PD findings of grade 1, 2, or 3.
[c]Wakefield RJ, Balint PV, Szkudlarek M, et al. Musculoskeletal ultrasound including definitions for ultrasonographic pathology. *J Rheumatol*. 2005;32(12):2485-2487.

pediatric-specific scoring system for the joints and semi-quantitative scoring approach for the nails. Enthesitis was evaluated according to the OMERACT definition. Demographic, clinical, and laboratory information was collected when available.

Results: Eleven patients were included until now. Demographic and clinical characteristics are shown in Table 1. The mean duration of the ultrasound exam was 66 minutes. Ultrasound characteristics of the nails studied are displayed in Table 2, and findings of the joints and entheses are shown in Table 3. 51 nails (83.6%) had abnormal nail plate structure per the Wortsman classification, and roughly 20% of nails had increased PD activity in either the nail bed or nail matrix classified as grade 2 or 3. Eight out of 11 patients (72.7%) had a least one grade 2 finding of synovitis on B-mode, with the PIP/DIP, suprapatellar, and anterior subtalar joint recesses most frequently affected. Two patients (18.2%) had enthesopathy involving the lower extremities identified on PD examination.

Conclusion: Subclinical inflammatory abnormalities of the nails, joints, and entheses were identified utilizing MSUS in children with psoriasis who did not have clinical manifestations of arthritis on exam. Ongoing studies involving additional pediatric psoriasis patients and healthy controls is underway to more clearly elucidate the significance of these findings.

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Abstract Number: 0353

Validation of Claims-based Algorithms for Newly Diagnosed Juvenile Idiopathic Arthritis Using Machine Learning Methods

Patricia Hoffman[1], Lauren Parlett[2], Daniel Beachler[2], Daniel Reiff[3], Sarah McGuire[1], Sonia Pothraj[1], Lakshmi Moorthy[1], Cynthia Salvant[4], Dawn Koffman[5], Sanika Rege[5], Cecilia Huang[5], Matthew Iozzio[5], Kevin Schott[2], Kevin Haynes[6], Amy Davidow[7], Stephen Crystal[8], Tobias Gerhard[5], Brian Strom[9], Carlos Rose[10] and Daniel Horton[4], [1]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, [2]Carelon, Wilmington, DE, [3]University of Alabama at Birmingham, Birmingham, AL, [4]Department of Pediatrics, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, [5]Rutgers Center for Pharmacoepidemiology and Treatment Science, New Brunswick, NJ, [6]Janssen Pharmaceuticals, Raritan, NJ, [7]New York University, New York, NY, [8]Rutgers University, New Brunswick, NJ, [9]Rutgers, State University of New Jersey, New Brunswick, NJ, [10]Thomas Jefferson University, Philadelphia, PA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Administrative claims databases represent important settings for studying large populations with juvenile idiopathic arthritis (JIA), but prior efforts to validate diagnostic algorithms for JIA using administrative data have been limited to potentially non-generalizable settings (e.g., specific clinics or health care systems). We aimed to develop and validate algorithms for new diagnoses of JIA in a large claims database using rule-based and machine learning-based approaches.

Methods: We performed a cross-sectional validation study using US commercial health plan data (2013-2020). We identified children diagnosed with JIA (ICD-9-CM: 696.0, 714, 720; ICD-10-CM: L40.5, M05, M06, M08, M45) before age 18 following ≥12 months of baseline continuous enrollment without JIA diagnosis or immunosuppression. JIA diagnoses were based on 3 previously validated definitions: 1) rheumatologist's diagnosis plus orders for ≥2 specific laboratory tests; 2) ≥2 outpatient diagnoses 8-52 weeks apart; or 3) 1 inpatient diagnosis. Charts from a random subset of subjects meeting each definition were abstracted and independently adjudicated by clinical experts; discrepancies were resolved by a third expert or, where necessary, consensus. Incident JIA was defined as definite or probable JIA diagnosed in the prior 4 months. Using

data from 1 year before through 1 year after first JIA diagnosis, we then created candidate predictor variables from demographics, diagnoses, medications, procedures, and specialty of clinicians diagnosing JIA. After applying a simulation-based balancing method (Synthetic Minority Oversampling Technique, SMOTE), we selected optimal logistic regression regularization hyperparameters using 10-fold cross-validation. Model variables were used to score observations, and sensitivity, specificity, and positive predictive value (PPV) [95% confidence interval (CI)] were assessed at different thresholds of predicted JIA probability.

Results: Of 182 eligible charts reviewed (92 ICD-9-based, 90 ICD-10-based), 133 had definite/probable JIA (ICD-9 64%, ICD-10 82%). Of JIA diagnoses, 90 were incident (ICD-9 90%, ICD-10 50%). Rule-based algorithms had limited PPV for incident JIA (ICD-9 58%, ICD-10 41%) (Table). Use of machine-learning based algorithms enabled excellent discrimination between incident and prevalent JIA (ICD-9 AUC 0.97, ICD-10 AUC 0.88) and between incident JIA and unlikely JIA (ICD-9 AUC 0.99, ICD-10 AUC 0.94) (Figure 1). Specific predicted probability thresholds yielded excellent test characteristics for

Table. Accuracy of rule-based algorithms for incident JIA. ICD, International Classification of Diseases; Inc., incident; JIA, juvenile idiopathic arthritis; PPV, positive predictive value; Prev., prevalent. Numbers of charts are shown by claims-based definition and adjudicated diagnosis. PPV represents the percentage with definite or probable incident JIA among those meeting the claims-based definition. Specific labs eligible for Definition 1 were antinuclear antibody, rheumatoid factor, anti-cyclic citrullinated protein antibody, and HLA-B27.

	ICD-9-based diagnosis					ICD-10-based diagnosis				
Definition	**Charts**	**Inc. JIA**	**Prev. JIA**	**Not JIA**	**PPV, Inc. JIA**	**Charts**	**Inc. JIA**	**Prev. JIA**	**Not JIA**	**PPV, Inc. JIA**
All definitions combined	92	53	6	33	58%	90	37	37	16	41%
Definition 1: ≥1 rheumatologist's diagnosis + ≥2 specific labs	37	28	2	7	76%	35	18	13	4	51%
Definition 2: ≥2 outpatient diagnoses 8-52 weeks apart	52	24	4	24	46%	50	18	24	8	36%
Definition 3: ≥1 inpatient diagnosis	3	1	0	2	33%	5	1	0	4	20%

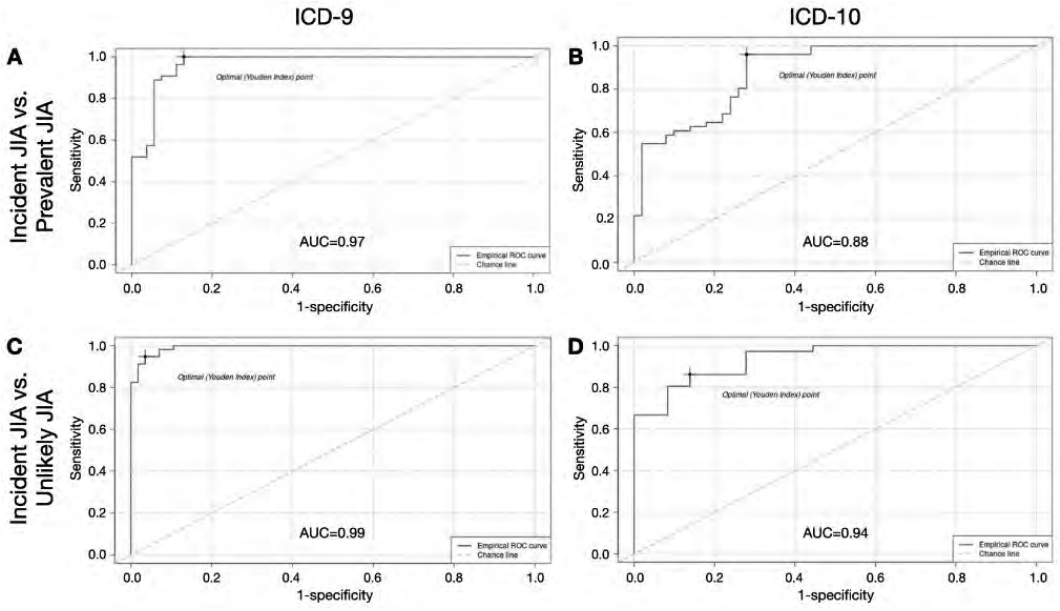

Figure 1. ROC curves for machine learning-based algorithms for incident JIA. AUC, area under the curve; ROC, receiver operating characteristic; ICD, International Classification of Diseases; JIA, juvenile idiopathic arthritis. ROC curves show balance of sensitivity and specificity of machine learning-based algorithms for incident JIA based on comparisons with prevalent JIA (ICD-9 in A, ICD-10 in B) and with unlikely JIA (ICD-9 in C, ICD-10 in D). The Youden Index (dot on ROC curve) represents the maximum value of (Sensitivity + Specificity – 1).

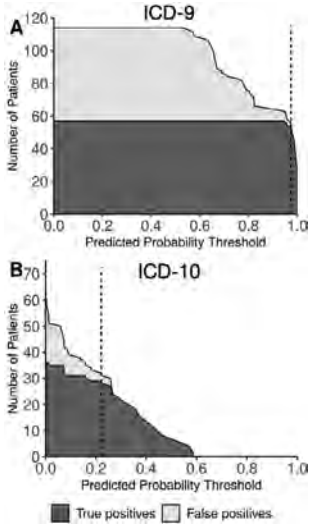

Figure 2. Impact of predicted probability thresholds from machine learning-based models on accuracy of diagnoses of incident JIA compared with unlikely JIA. CI, confidence interval; ICD, International Classification of Diseases; PPV, positive predictive value. Curves show numbers of true positive (dark grey) and false positive (light grey) cases of incident JIA at different thresholds of predicted probability from machine learning-based models comparing children with incident JIA and children unlikely to have JIA based on ICD-9 codes (A) and ICD-10 codes (B). Numbers reflect the total study population, including simulated cases generated by application of a balancing method (Synthetic Minority Oversampling Technique, SMOTE). Threshold values yielding excellent test characteristics (dotted lines) were 0.97 for ICD-9 (sensitivity 95%, specificity 96%, PPV 96% [95% CI 96-100%]) and 0.22 for ICD-10 (sensitivity 81%, specificity 92%, PPV 91% [95% CI 84-97%]).

differentiating incident JIA from unlikely JIA (ICD-9: sensitivity 95%, specificity 96%, PPV 96% [95% CI 96-100%]; ICD-10: sensitivity 81%, specificity 92%, PPV 91% [95% CI 84-97%]) (Figure 2).

Conclusion: Machine learning-based diagnostic algorithms for incident JIA enhanced traditional rule-based algorithms in identifying new diagnoses of JIA using ICD-9 and ICD-10 codes within a large US claims database. External validation of these models is warranted, but these algorithms will facilitate use of administrative data to study JIA diagnosis, management, and outcomes in large populations.

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Abstract Number: 0354

Open-label Phase 3 Study of Intravenous Golimumab in Patients with Polyarticular Juvenile Idiopathic Arthritis: Pharmacokinetics, Effectiveness, Safety, and Immunogenicity over 252 Weeks

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
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Background/Purpose: The phase 3, Intravenous Golimumab in Pediatric Participants with Active Polyarticular-Course JIA Despite MTX (GO-VIVA) study demonstrated that golimumab (GLM) 80 mg/m^2 at Week (W) 0, W4 and Q8W thereafter is well-tolerated and effective in children 2 to < 18 years of age with active polyarticular-course juvenile idiopathic arthritis (pcJIA) despite MTX through W52 (NCT02277444). The pharmacokinetics (PK), immunogenicity, efficacy, and safety of GLM in GO-VIVA participants (pts) who continued into the long-term extension (LTE) through W252 are evaluated.

Methods: Pts from GO-VIVA who continued GLM 80 mg/m^2 IV q8w (max dose 240 mg) after W52 were included. PK and immunogenicity were assessed through W244, and safety was assessed through W252. Efficacy measures included JIA ACR response from baseline (start of GLM), clinical Juvenile Arthritis Disease Activity Score based on 10 joints (cJADAS-10) minimal disease activity (cJADAS-10 MDA), inactive disease (cJADAS-10 ID) and remission (≥ 6 continuous months of cJADAS-10 ID). These were analyzed using an intent-to-treat (ITT) approach through W116, due to a protocol amendment instituted during the LTE that limited efficacy data collected after W116. Non-responder imputation was used for missing data.

Results: Of the 127 pts treated, 112 (88.2%) continued into the LTE, and 69 (54.3%) completed GLM through W244 and had a W252 assessment. The most common reasons for discontinuation of GLM treatment through W244 were adverse event (AE) (19%) and withdrawal of consent (7%). W244 median steady-state trough GLM concentration was 0.61 μg/mL (mean ± SD: 0.66 ± 0.569μg/mL; N=31) vs 0.44 μg/mL (mean ± SD: 0.50 ± 0.455 μg/mL; N=93) at W52, indicating that exposure was maintained over time. Median trough GLM concentrations at W244 were similar across different age categories and body weight quartiles. From W52 to W116, the majority of pts had JIA ACR 30 (72%-77%), JIA ACR 50 (71%-76%), and JIA ACR 70 (62%-68%) responses, and approximately 50% had JIA ACR 90. The majority of pts (≥56%) achieved cJADAS-10 MDA, 41%-49% achieved cJADAS-10 ID, and 28-33% achieved remission. Antibodies to GLM were detected in 56 (44.8%) of pts through W244; the majority of titers were < 1:1000. Of these 56 pts, 35 were positive for neutralizing antibodies (Nab) with an overall incidence of NAb of 31% (35/112). No new or unexpected safety issues were identified through W252. AEs and SAEs were reported in 92.1% and 19.7% of pts, respectively. One death (septic shock) occurred.

Conclusion: PK exposure through the end of the LTE was consistent with that observed through W52. Although analyses were limited by protocol modification, data through W116 suggest a therapeutic benefit with additional treatment and achievement of clinically important endpoints for pts who continued in the LTE. GLM was generally well tolerated with an acceptable long-term safety profile through W252.

Disclosure: N. Ruperto: Ablynx, 2, 6, AstraZeneca-Medimmune, 2, 6, Bayer, 2, 6, Biogen, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb (BMS), 2, 5, 6, Celgene, 5, 12, Personal Fees, Non-Financial Support, Eli Lilly, 2, 5, 6, EMD Serono, 2, 6, F. Hoffman-La Roche, 2, 5, 6, GlaxoSmithKlein (GSK), 2, 5, 6, Janssen, 2, 5, 6, Merck/MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, R-Pharma, 2, 6, Sinergie, 2, 6, Sobi, 2, 5, 6, UCB, 2, 5; **D. Lovell**: Abbott, 2, 6, AbbVie, 2, Amgen, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Canadian Arthritis Society, 1, Celgene, 2, Forest Research, 1, GlaxoSmithKlein(GSK), 2, Hoffmann-La Roche, 2, Janssen, 2, NIH-NIAMS, 1, Novartis, 2, 6, Pfizer, 2, United Bioscience Corporation, 2, Wyeth, 2; **S. Ringold**: Janssen, 3; **X. Xu**: Janssen, 3, 10, 11; **J. Leu**: Janssen, 3, Johnson & Johnson, 11; **E. Lam**: Janssen, 3, 11; **Y. Wang**: Janssen, 3; **A. Martini**: Boehringer-Ingelheim, 2, Eli Lilly, 2, Janssen, 2, Merck/MSD, 2, Novartis, 2, Pfizer, 2; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb (BMS), 2, 5, Celgene, 2, Eli Lilly, 2, 5, EMD Serono, 2, F-Hoffman La Roche, 2, 5, GlaxoSmithKlein (GSK), 2, 5, 6, Horizon, 2, 2, Janssen, 5, Merck, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6.

Abstract Number: 0355

Long Term Safety of Drugs in Systemic Juvenile Idiopathic Arthritis

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SESSION INFORMATION

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Session Title: Pediatric Rheumatology – Clinical Poster I: JIA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Evidence on treatment safety in systemic juvenile idiopathic arthritis (sJIA) is limited. Our objective was to evaluate the safety profile of drugs in the initial 24-months since disease onset.

Methods: Children from Pharmachild were classified into 4 mutually exclusive groups according to the treatment in the first 6 months from sJIA onset. Descriptive data, incidence rates (95% CI), survival curve, log rank test, and Cox multivariate regression model are reported.

Results: A total of 701/992 (71%) sJIA patients were classified as: 1) glucocorticoids (N=161), 2) biologic (b) DMARDS (N=69); 3) conventional synthetic (cs) DMARDs (N=65) and 4) combinations of these drugs (N=406).

In the initial 6 months, bDMARDs and combination therapy had the highest rate of AEs, serious AE and events of special interest. Infections were the most common AEs (N, IR*100PY-95%CI) in bDMARDs group (7, 32.94 [15.70-69.10]). Gastro-intestinal disorders and general disorders were most frequent in the bDMARDs group (6, 28.24 [12.69-62.85]). Kaplan Meier's showed the bDMARDs group experienced more AE and sooner when compared to the other groups (log rank test $p< 0.0001$). The risk of any AE was significantly higher in bDMARDs, hazard ratio (HR) 8.8 (95% CI: 3.5-22.1)

In the following 18 months the number and the risk of any AE was increased in the combination therapy group (HR 4.5; 95% CI: 1.1-18.6).

Conclusion: bDMARDs or combination therapy in sJIA patients was associated with a higher risk of AE in the first six months meanwhile in the following 18 months combination therapy group had the highest risk of AE.

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Abstract Number: 0356

PRINTO Provisional Enthesitis/Spondylitis-Related JIA Criteria: Performance in Youth Classified as Axial Disease in Juvenile Spondyloarthritis

Pamela F. Weiss[1], Timothy G. Brandon[2], Amita Aggarwal[3], RUBEN BURGOS-VARGAS[4], Robert Colbert[5], Gerd Horneff[6], Rik Joos[7], Ronald Laxer[8], Kirsten Minden[9], Angelo Ravelli[10], Nicolino Ruperto[11], Judith Smith[12], Matthew Stoll[13], Shirley Tse[8], Filip Van den Bosch[14], Walter P. Maksymowych[15], Robert Lambert[16], David Biko[2], Nancy A. Chauvin[17], Michael L. Francavilla[18], Jacob Jaremko[15], Nele Herregods[19], Ozgur Kasapcopur[20], Mehmet YILDIZ[21], Hemalatha Srinivasalu[22], Ray Naden[23] and Alison Hendry[24], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]Children's Hospital of Philadelphia, Philadelphia, PA, [3]Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow, India, [4]Hospital General de Mexico, Ciudad de México, Mexico, [5]NIH/NIAMS, Bethesda, MD, [6]Asklepios Klinik Sankt Augustin GmbH, Bonn, Germany, [7]Ghent University, Basel, Switzerland, [8]The Hospital for Sick Children, Toronto, ON, Canada, [9]Charité University Medicine and German Rheumatism Research Center Berlin, Berlin, Germany, [10]Direzione Scientifica, IRCCS Istituto Giannina Gaslini, Genova, Italy, [11]IRCCS Istituto Giannina Gaslini, UOSID Centro Trial, Genova, Italy, [12]University of Wisconsin, Madison, WI, [13]University of Alabama at Birmingham, Birmingham, AL, [14]Department of Internal Medicine and Pediatrics, Ghent University and VIB Center for Inflammation Research, Ghent, Belgium, [15]University of Alberta, Edmonton, AB, Canada, [16]Department of Radiology and Diagnostic Imaging, University of Alberta, Edmonton, AB, Canada, [17]The Cleveland Clinic, Hummelstown, PA, [18]University of South Alabama College of Medicine, Mobile, AL, [19]Ghent University Hospital, Ghent, Belgium, [20]Department of Pediatric Rheumatology, Cerrahpasa Medical School, Istanbul University-Cerrahpasa, Istanbul, Turkey, [21]Istanbul University-Cerrahpasa Department of Pediatric Rheumatology, Istanbul, Turkey, [22]Children's National Hospital, Washington, DC, [23]Auckland City Hospital, Auckland, New Zealand, [24]Te Whatu Ora, Counties Manukau District, Middlemore Hospital, Auckland, New Zealand

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Pediatric Rheumatology – Clinical Poster I: JIA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The Paediatric Rheumatology International Trials Organisation (PRINTO) recently undertook an effort to better harmonize the pediatric and adult arthritis criteria. These provisional criteria are not validated and refinement may be necessary for optimal performance. We aimed to investigate differences amongst youth with clinically diagnosed juvenile SpA who met axJSpA classification criteria who did and did not fulfill the PRINTO provisional enthesitis/spondylitis-related criteria.

Methods: This was a retrospective cross-sectional sample of international youth who had juvenile SpA ascertained by the treating physician. All youth had onset of symptoms prior to age 18 and fulfilled the recently validated axJSpA classification criteria. The axJSpA classification criteria consist of 7 domains: imaging - active inflammation, imaging - structural lesions, pain chronicity, pain pattern, pain location, stiffness, and genetics/family history. A youth with juvenile SpA is classified as having axial disease with a cumulative score of ≥55 (out of 100). To meet the PRINTO criteria for enthesitis/spondylitis-

related arthritis youth must fulfill one of 3 major criteria (Table 1). Data were abstracted from subjects' medical records. All MRI scans underwent central imaging review by at least 2 central raters. Patient demographics, clinical manifestations, and physician and patient-reported outcomes were evaluated using standard descriptive statistics. Differences between groups were compared using Wilcoxon signed-rank test or chi-square as appropriate.

Results: Of 143 patients that met axJSpA criteria, 100 (69%) fulfilled the PRINTO provisional criteria for enthesitis/spondylitis-related arthritis. Thirty-four (23%) did not fulfill any of the 3 major PRINTO criteria due to lack of peripheral disease manifestations. The frequency with which each major and minor criteria were fulfilled is listed in Table 1. Demographics, family history of SpA, location of back pain, and duration of pain were not statistically different between those who did and did not meet PRINTO criteria (Table 2). Those who fulfilled the PRINTO criteria had significantly more morning stiffness lasting ≥15 minutes (p=0.02), peripheral arthritis (p< 0.01), enthesitis (p< 0.01), and HLA-B27 positivity (p=0.02). Patients who did not meet the PRINTO criteria had a significantly higher percentage of pain duration

Table 1. Proportion of JSpA patients with axial disease fulfilling each PRINTO enthesitis/spondylitis-related JIA criterion

PRINTO Criterion		N	N (%)
1. Peripheral arthritis and enthesitis		143	33 (23.1)
	Peripheral arthritis	143	80 (55.9)
	Enthesitis	143	61 (42.7)
2. Arthritis or enthesitis, plus ≥ 3 months of inflammatory back pain and sacroiliitis on imaging		143	56 (39.2)
	Peripheral arthritis or enthesitis	143	108 (75.5)
	≥3 months of inflammatory back pain	143	78 (54.5)
	Sacroiliitis on imaging	143	143 (100.0)
3. Arthritis or enthesitis plus ≥2 of the following: SI joint tenderness; inflammatory back pain; presence of HLA-B27 antigen; acute (symptomatic) anterior uveitis; history of a SpA in a 1st-degree relative.		143	89 (62.2)
	Peripheral arthritis or enthesitis	143	108 (75.5)
	SI joint tenderness	141	95 (67.4)
	Inflammatory back pain	141	94 (66.7)
	Presence of HLA-B27 antigen	136	87 (64.0)
	Acute (symptomatic) anterior uveitis (ever?)	143	8 (5.6)
	History of a SpA in a 1st-degree relative	133	24 (18.1)

Table 2. Clinical features of patients with axial disease

	PRINTO (-)		PRINTO (+)		
	N	N (%) or M(IQR)	N	N (%) or M(IQR)	p-value
Age at reference date	45	14.6 (12.0-16.2)	98	15.2 (12.6-17.0)	0.21
Sex, male	45	26 (57.8)	98	70 (71.4)	0.11
Family history of HLA-B27 disease	44	9 (20.5)	84	20 (23.8)	0.67
Pain					
Sacral/Buttock	45	25 (55.6)	98	39 (39.8)	0.08
Hip/Groin	45	28 (62.2)	98	63 (64.3)	0.81
Insidious onset	36	28 (77.8)	90	80 (88.9)	0.11
Duration					
≥6 weeks	44	41 (93.2)	94	83 (88.3)	0.38
≥12 weeks	44	35 (79.6)	94	54 (57.5)	**0.01**
Stiffness ≥15 minutes	30	13 (43.3)	79	54 (68.4)	**0.02**
Physical exam findings/Patient medical history					
SI pain with deep palpation or FABER/Mennell/ Gaenslen's maneuver	38	19 (50.0)	89	57 (64.0)	0.14
History of peripheral arthritis	45	6 (13.3)	98	74 (75.5)	**<0.01**
History of enthesitis at any location	45	4 (8.9)	98	57 (58.2)	**<0.01**
HLA-B27 positive	44	22 (50.0)	92	65 (70.7)	**0.02**
Polyarticular course of peripheral arthritis	45	2 (4.4)	98	16 (16.3)	0.06
Acute anterior uveitis	45	0 (0.0)	98	8 (8.2)	0.05

Table 3. MRI imaging features of patients with axial disease

	All		PRINTO (–)		PRINTO (+)		
	N	N (%)	N	N (%)	N	N (%)	p-value
Inflammatory lesions							
Inflammation in subchondral bone marrow	143	126 (88.1)	45	38 (84.4)	98	88 (89.8)	0.35
Inflammation at site of an erosion cavity	143	79 (55.2)	45	25 (55.6)	98	54 (55.1)	0.96
Inflammation in SIJ capsule	143	31 (21.7)	45	10 (22.2)	98	21 (21.4)	0.92
Enthesitis outside SIJ	143	31 (21.7)	45	8 (17.8)	98	23 (23.5)	0.44
Unequivocal inflammatory lesions^	141	124 (87.9)	44	38 (86.4)	97	86 (88.7)	0.70
Structural lesions							
Sclerosis	143	66 (46.1)	45	22 (48.9)	98	44 (44.9)	0.66
Erosion	143	117 (81.8)	45	37 (82.2)	98	80 (81.6)	0.93
Fat lesion	143	18 (12.6)	45	3 (6.7)	98	15 (15.3)	0.15
Fat metaplasia in an erosion cavity	143	13 (9.1)	45	2 (4.4)	98	11 (11.2)	0.19
Ankylosis	143	4 (2.8)	45	0 (0.0)	98	4 (4.1)	0.17
Unequivocal structural lesions#	140	121 (86.4)	44	40 (90.9)	96	81 (84.4)	0.30

Legend. ^Unequivocal evidence of inflammatory lesions typical of axial disease: bone marrow edema in ≥3 SI joint quadrants across all SI joint MRI slices. #Unequivocal evidence of structural lesion(s) typical of axial disease: erosion in ≥3 quadrants or sclerosis or fat lesion in ≥2 SI joint quadrants or backfill or ankylosis in ≥2 joint halves across all SI joint MRI slices.

≥12 weeks (p=0.01). There were no significant differences in the prevalence of inflammatory or structural lesions on MRI between the two groups (Table 3).

Conclusion: A third of children classified with axJSpA remain unclassifiable by the provisional PRINTO enthesitis/spondylitis-related criteria. The clinical and imaging manifestations of axial disease were not significantly different between those who did and did not fulfill the provisional PRINTO criteria. The phenotypic differences between those who were and were not classified by the provisional PRINTO criteria are confined to peripheral disease manifestations. Modification of the second major criterion of the PRINTO provisional criteria may facilitate capture of youth with primarily axial disease.

Disclosure: P. Weiss: Eli Lilly, 2, Novartis, 2, Pfizer, 2; **T. Brandon**: None; **A. Aggarwal**: None; **R. BURGOS-VARGAS**: None; **R. Colbert**: None; **G. Horneff**: GSK, 6, Janssen, 6, MSD, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Roche, 5, 6, Sanofi, 6, Sobi, 6; **R. Joos**: None; **R. Laxer**: None; **K. Minden**: Amgen, 6, Medac, 6, Novartis, 6, Pfizer, 6; **A. Ravelli**: AbbVie/Abbott, 12, honoraria for consultancies or speaker bureaus from, Novartis, 12, honoraria for consultancies or speaker bureaus from, Pfizer, 12, honoraria for consultancies or speaker bureaus from; **N. Ruperto**: Ablynx, 2, 6, AstraZeneca-Medimmune, 2, 6, Bayer, 2, 6, Biogen, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb (BMS), 2, 5, 6, Celgene, 5, 12, Personal Fees, Non-Financial Support, Eli Lilly, 2, 5, 6, EMD Serono, 2, 6, F. Hoffman-La Roche, 2, 5, 6, GlaxoSmithKlein (GSK), 2, 5, 6, Janssen, 2, 5, 6, Merck/MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, R-Pharma, 2, 6, Sinergie, 2, 6, Sobi, 2, 5, 6, UCB, 2, 5; **J. Smith**: None; **M. Stoll**: Novartis, 2; **S. Tse**: None; **F. Van den Bosch**: AbbVie, 2, 6, Amgen, 2, BMS, 6, Celgene, 6, Eli Lilly, 2, Galapagos, 2, Janssen, 2, 6, Merck, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB Pharma, 2, 6; **W. Maksymowych**: AbbVie, 2, 5, 6, BMS, 2, 6, Boehringer-Ingelheim, 2, CARE Arthritis Ltd, 4, CARE Arthritis Ltd., 4, Celgene, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **R. Lambert**: Calyx, 2, CARE Arthritis Limited, 2, Image Analysis Group, 2; **D. Biko**: None; **N. Chauvin**: None; **M. Francavilla**: None; **J. Jaremko**: None; **N. Herregods**: None; **O. Kasapcopur**: Novartis, 6, Pfizer, 6; **M. YILDIZ**: None; **H. Srinivasalu**: None; **R. Naden**: None; **A. Hendry**: None.

Abstract Number: 0357

Validation of the Juvenile Spondyloarthritis Disease Activity Index in a Prospective Clinical Trial Setting

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

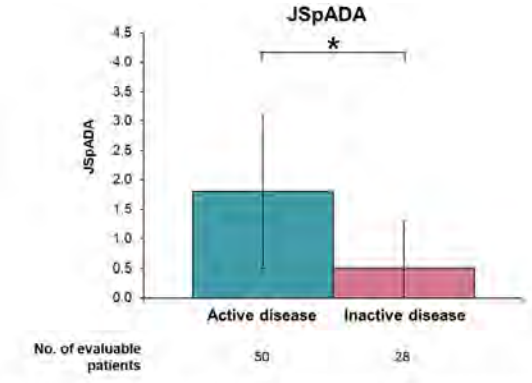
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The juvenile spondyloarthritis disease activity index (JSpADA) is a disease activity assessment tool developed for children with juvenile psoriatic arthritis (JPsA) and enthesitis related arthritis (ERA). This post-hoc analysis investigated the validity of JSpADA for children with ERA and JPsA in a prospective clinical trial setting using data from the JUNIPERA study.

Methods: JUNIPERA (NCT03031782) is a phase 3, placebo-controlled, event-driven withdrawal study investigating the safety and efficacy of secukinumab in pediatric patients with ERA and JPsA. Patients aged 2 to < 18 years who met the International League of Associations for Rheumatology criteria for ERA or JPsA for ≥6 months with active disease (≥3 active joints and ≥1 site of enthesitis) despite treatment with ≥1 non-steroidal anti-inflammatory drug or disease-modifying anti-rheumatic drug were enrolled. Patients received open label secukinumab (75 mg in patients < 50 kg, 150 mg in patients ≥50 kg) weekly for 5 weeks (including Week 0) followed by q4w to Week 12. At Week 12, patients were randomized 1:1 to secukinumab or placebo q4w until disease flare or Week 52. JSpADA consists of 8 equally weighted components (range, 0-8): active joint count, enthesitis count, patient-reported pain, inflammatory markers, morning stiffness, clinical sacroiliitis, uveitis, and back mobility. For this post hoc analysis, the validity of JSpADA was assessed using 3 criteria: discriminatory

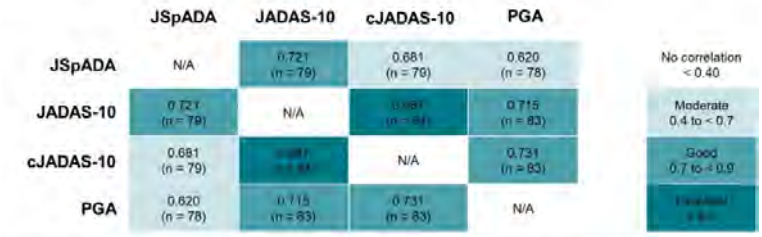


ERA, enthesitis related arthritis; JPsA, juvenile psoriatic arthritis; JSpADA, Juvenile Spondylarthritis Disease Activity; PGA, physician global assessment of disease activity.
* Inactive disease was defined as no joints with active arthritis, CRP level within normal limits, PGA ≤10 mm, absence of patient-reported morning stiffness, and no uveitis; error bars represent SD.
* $P<.0001$

validity based on JSpADA scores at Week 12 among patients with active or inactive disease (defined as no joints with active arthritis, CRP level within normal limits, PGA ≤10, no patient-reported morning stiffness, and no uveitis); convergent validity based on Spearman's correlation between JSpADA and 10-joint Juvenile Arthritis Disease Activity Score (JADAS-10), clinical JADAS-10 (cJADAS-10), and physician global assessment of disease activity (PGA) at Week 12; and responsiveness to change in clinical disease activity based on change in JSpADA scores from Week 12 to Week 52 among patients who had improvement (change in PGA < 0) or worsening (change in PGA >0) of disease activity. Reported *P* values are nominal, and no multiplicity adjustments were made.

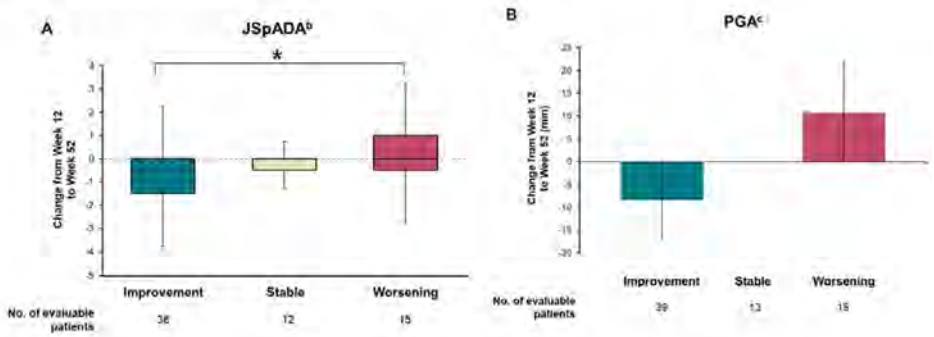
Results: Among the 86 patients included in this analysis, 52 (60.5%) had ERA and 34 (39.5%) had JPsA. At Week 12, patients with active disease had higher mean (SD) JSpADA scores than patients with inactive disease (1.8 [1.3] vs 0.5 [0.8]; *P*< .0001; Figure 1). JSpADA scores showed moderate to good correlation with JADAS-10, cJADAS-10, and PGA scores at Week 12 (Spearman's correlation coefficient; range, 0.62-0.72; Figure 2). Patients with improvements in disease activity from Weeks 12 to 52 as determined by change in PGA scores had greater improvements in mean JSpADA scores over the same time period than patients with worsening in disease activity (–0.8 [1.1] vs 0.4 [1.0]; *P*< .001; Figure 3). Patients with stable disease from Weeks 12 to 52 had minimal change in JSpADA (–0.1 [0.48]).

Figure 2. Spearman's Correlation Coefficients for JSpADA, JADAS-10, cJADAS-10, and PGA Scores for Children with JPsA and ERA at Week 12



cJADAS-10, clinical JADAS-10; ERA, enthesitis related arthritis; JADAS-10, 10-joint Juvenile Arthritis Disease Activity Score; JPsA, juvenile psoriatic arthritis; JSpADA, Juvenile Spondylarthritis Disease Activity; PGA, physician global assessment of disease activity.

Figure 3. Change in (**A**) JSpADA and (**B**) PGA From Week 12 to Week 52 for Children with JPsA and ERA Grouped by Disease Activity[a]



ERA, enthesitis related arthritis; JPsA, juvenile psoriatic arthritis; JSpADA, Juvenile Spondylarthritis Disease Activity; PGA, physicians global assessment of disease activity.
[a] Improvement in disease activity was defined as change in PGA from Week 12 to Week 52 < 0, stable as change in PGA = 0, and worsening as change in PGA > 0.
[b] The horizontal line represents median value, and upper and lower boundaries represent 75th and 25th percentile, respectively. Vertical lines were calculated as the interquartile range × 1.5.
[c] Error bars represent SD.

Conclusion: JSpADA discriminated between active and inactive disease, correlated with other validated disease activity measures, and responded to changes in clinical disease activity in children with ERA and JPsA in the prospective JUNIPERA study.

Disclosure: P. Weiss: Eli Lilly, 2, Novartis, 2, Pfizer, 2; **N. Ruperto**: Ablynx, 2, 6, AstraZeneca-Medimmune, 2, 6, Bayer, 2, 6, Biogen, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb (BMS), 2, 5, 6, Celgene, 5, 12, Personal Fees, Non-Financial Support, Eli Lilly, 2, 5, 6, EMD Serono, 2, 6, F. Hoffman-La Roche, 2, 5, 6, GlaxoSmithKlein (GSK), 2, 5, 6, Janssen, 2, 5, 6, Merck/MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, R-Pharma, 2, 6, Sinergie, 2, 6, Sobi, 2, 5, 6, UCB, 2, 5; **E. Quebe-Fehling**: Novartis, 3, 11; **A. Shew**: Novartis, 3; **L. Pricop**: Novartis, 3, 11; **C. Pieterse**: Novartis, 3; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb (BMS), 2, 5, Celgene, 2, Eli Lilly, 2, 5, EMD Serono, 2, F-Hoffman La Roche, 2, 5, GlaxoSmithKlein (GSK), 2, 5, 6, Horizon, 2, 2, Janssen, 5, Merck, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6.

Abstract Number: 0358

Baseline Clinical Features and Biomarker Profiles of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Systemic Juvenile Idiopathic Arthritis Associated Lung Disease (SJIA-LD) Cohort

Esraa Eloseily[1], Autumn Clark[1], Min-Lee Chang[2], MaryEllen Riordan[3], alan Russell[4], Marc Natter[5], Sherry Thornton[6], Yukiko Kimura[7] and Grant Schulert[1], [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Boston Children's Hospital, Boston, MA, [3]Hackensack Meridian Health, Hackensack, NJ, [4]Duke Clinical Research Institute, Duke, NC, [5]Harvard Medical School, Boston, MA, [6]Cincinnati Children's Hospital, Cincinnati, OH, [7]Hackensack Meridian School of Medicine, New York, NY

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic juvenile idiopathic arthritis (SJIA) associated lung disease (SJIA-LD) is an emerging and life-threatening clinical problem with urgent unmet needs including prevalence, pathogenesis, disease biomarkers, influence of biologics, and outcomes. The objective is to define baseline clinical features and biomarker profiles of patients in the CARRA Registry SJIA-LD cohort.

Methods: Existing or newly enrolled CARRA Registry patients with SJIA and suspected, probable, or definite SJIA-LD were included in the cohort. In addition to standard Registry data, lung disease specific data was obtained using a standardized case report form through REDCap Cloud, and biosamples collected when available. Biomarker profiles were determined from plasma using a custom Luminex panel. This study was approved by the DCRI Reliant IRB and/or IRB of all Registry sites.

Results: 37 patients were enrolled in the SJIA-LD cohort, from 16 CARRA Registry sites in the US. 46% had definite (biopsy-proven), 36% probable, and 18% suspected SJIA-LD. Demographic and clinical features are shown in Table 1. Of those who underwent lung biopsy, all had pulmonary alveolar proteinosis (PAP) and interstitial inflammation, and 40% had collagenous fibrosis. 77% had at least one definite episode of macrophage activation syndrome (MAS)

Table 1: Demographic and clinical features of patients in the SJIA-LD cohort (N=37)

Clinical features	Summary or median
Sex	62% F
Age at enrollment*	4.4 years
Age at LD onset*	3.3 years
Age at SJIA onset*	1 years
LD duration**	0.3 (2.1) years
SJIA disease duration**	1 (2.75) years
SJIA duration at LD diagnosis**	1.6 (1.4) years
Clinical features at LD diagnosis	50% cough 50% clubbing 46% tachypnea 36% dyspnea on exertion 23% digital erythema 18% hypoxemia requiring supplemental oxygen
Baseline chest CT findings	55% ground glass opacities 41% peribronchovascular thickening 41% septal thickening 23% peripheral consolidation 23% hilar adenopathy
Pulmonary function tests	50% abnormal DLCO 50% abnormal spirometry 0% abnormal spot pulse oximetry
Broncho alveolar lavage	19% PAP 8% signs of infection
Parent/patient overall well-being score at most recent visit**	1(2)
Parent/subject assessment of disease activity at most recent visit**	1 (4.5)
Overall SJIA physician global assessment at most recent visit**	0.5 (2.5)
Physician global assessment of lung disease (PGALD) at most recent visit**	3.5 (3.75)
Health Related quality of life at most recent visit	26% excellent 22% very good 35% good 17% fair
Biologics ever used	92% Anakinra 65% Canakinumab 65% Tofacitinib 58% Tocilizumab
DMARDs ever used	46% Methotrexate 19% Mycophenolate mofetil
Currently on oral steroids	81 %

*Median, ** Median (IQR)

(including 64% that met the 2016-SJIA-MAS criteria), 73% had more than one MAS episode, and 32% had subclinical MAS. MAS occurred prior to SJIA-LD diagnosis in 68% and coincided with it in 18%.

Across all patient samples, SJIA-LD patients showed significantly increased plasma levels of IL-6, IL-12, IL-18, CXCL9, CD25, CCL11, CCL17, MCP-1, and MCP-3 compared to healthy pediatric controls. Cluster analysis defined 3 distinct groups of SJIA-LD patients. Group 1 (n=7) showed high levels of TNF, IL-6, IL-17, MCP-1 and 3, CCL11, and CCL17; group 2 (n=8) showed high IL-10, IL-12, IL-18, CXCL9, CXCL10, CD25, and CD163; and group 3 (n=10) showed high CCL15 and CCL25 (Figure 1).

Conclusion: Patients in the CARRA SJIA-LD cohort exhibit a broad spectrum of clinical and radiographic features, disease activity, and treatment approaches. Recurrent MAS was common. Patients with SJIA-LD showed multiple distinct plasma biomarker patterns. As an ongoing prospective cohort study of this emerging disease, we will be able to assess clinical features, longitudinal disease progression and trajectories, as well as associated immune biomarkers and cellular populations.

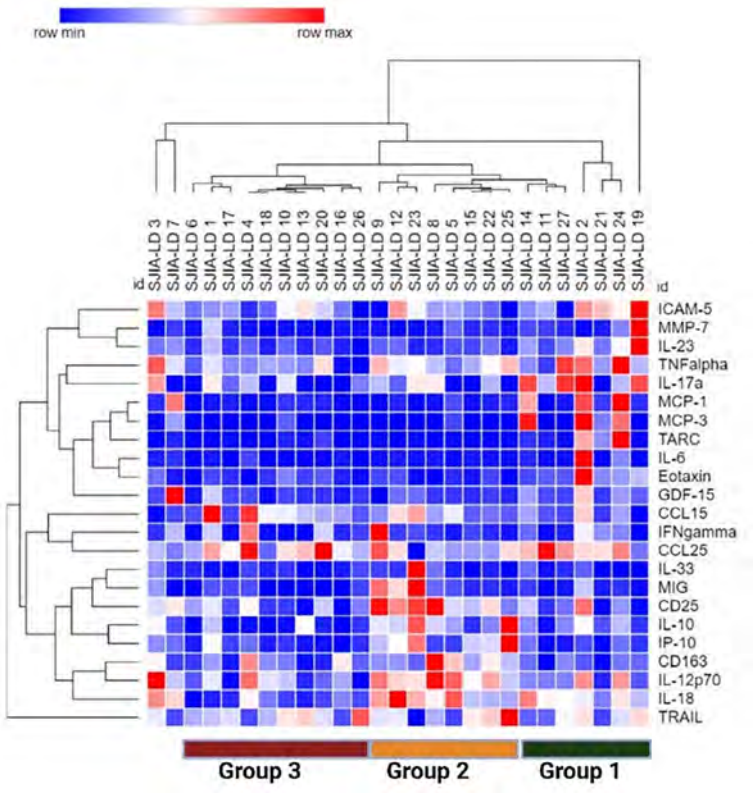


Figure 1: Heatmap showing plasma biomarker levels in SJIA-LD patients

Disclosure: E. Eloseily: None; **A. Clark**: None; **M. Chang**: None; **M. Riordan**: None; **a. Russell**: None; **M. Natter**: None; **S. Thornton**: None; **Y. Kimura**: None; **G. Schulert**: IpiNovyx, 5, SOBI, 2.

Abstract Number: 0359

Clinical Characteristics of Patients with Juvenile Idiopathic Arthritis Who Undergo Adalimumab Drug Level Testing and Anti-Drug Antibody Assessment

Chelsea Vallejos[1], Jennifer Cooper[2] and **Ingrid Pan**[1], [1]Children's Hospital Colorado, Aurora, CO, [2]University of Colorado/Children's Hospital Colorado, Denver, CO

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Pediatric Rheumatology – Clinical Poster I: JIA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Adalimumab therapeutic drug monitoring (TDM) using established trough concentrations is not standard practice in JIA patients, unlike IBD. No specific guidelines outline a therapeutic trough level range or clinical indications for monitoring. The aim of this study was to evaluate our institution's current practice of ordering and utilizing adalimumab trough levels for JIA patients.

Table 1: Baseline Demographics and Clinical Characteristics

Variable	All Patients (n = 64)	ADA positive (n = 30)	ADA negative or not tested (n = 34)
Age (years)	11.6 (6.3, 14.1)	11.5 (6.4, 14.1)	11.8 (7.8, 14.1)
Gender (female)	35 (54.7%)	10 (33.3%)	25 (73.5%)
Race			
Caucasian	47 (73.4%)	23 (76.7%)	24 (70.6%)
African American	3 (4.7%)	2 (6.7%)	1 (2.9%)
American Indian/Alaska Native	2 (3.1%)	0 (0%)	2 (5.9%)
Other/Unknown	12 (18.8%)	5 (16.6)	7 (20.6%)
Ethnicity (Hispanic or Latino)	21 (32.8%)	10 (33.3%)	11 (32.4%)
Weight (kg)	45.0 (28.4, 63.0)	45.0 (28.4, 63.0)	45.0 (28.4, 63.0)
BSA (m^2)	1.4 (1.0, 1.7)	1.4 (1.0, 1.7)	1.4 (1.1, 1.7)
BMI percentile	37.6 (15.1, 69.9)	36.7 (14.6, 70.5)	38.0 (16.6, 70.3)
Presence of uveitis	11 (17.2%)	5 (16.7%)	6 (17.6%)
Disease subtype			
Enthesitis-related	23 (35.9%)	8 (26.7%)	15 (50.0%)
Oligoarticular	22 (34.4%)	12 (40.0%)	10 (33.3%)
Polyarticular, RF (+)	6 (9.4%)	3 (10.0%)	3 (10.0%)
Polyarticular, RF (-)	11 (17.2%)	7 (23.3%)	4 (13.3%)
Undifferentiated	2 (3.1%)	0 (0.0%)	2 (6.7%)
Disease duration at start of adalimumab (months)	7.6 (1.6, 28.3)	7.6 (1.6, 27.6)	7.1 (1.6, 28.5)
Indication for adalimumab drug level testing			
Inadequate initial response to adalimumab	8 (12.5%)	5 (16.6%)	3 (8.8%)
Loss of clinical response to adalimumab[a]	46 (71.9%)	23 (76.7%)	23 (67.6%)
Other	10 (15.6%)	2 (6.7%)	8 (23.5%)

[a]Loss of clinical response defined as recurrence of joint pain, inflammation, or uveitis flare
Abbreviations: ADA = anti-drug antibody, BSA = body surface area, BMI = body mass index

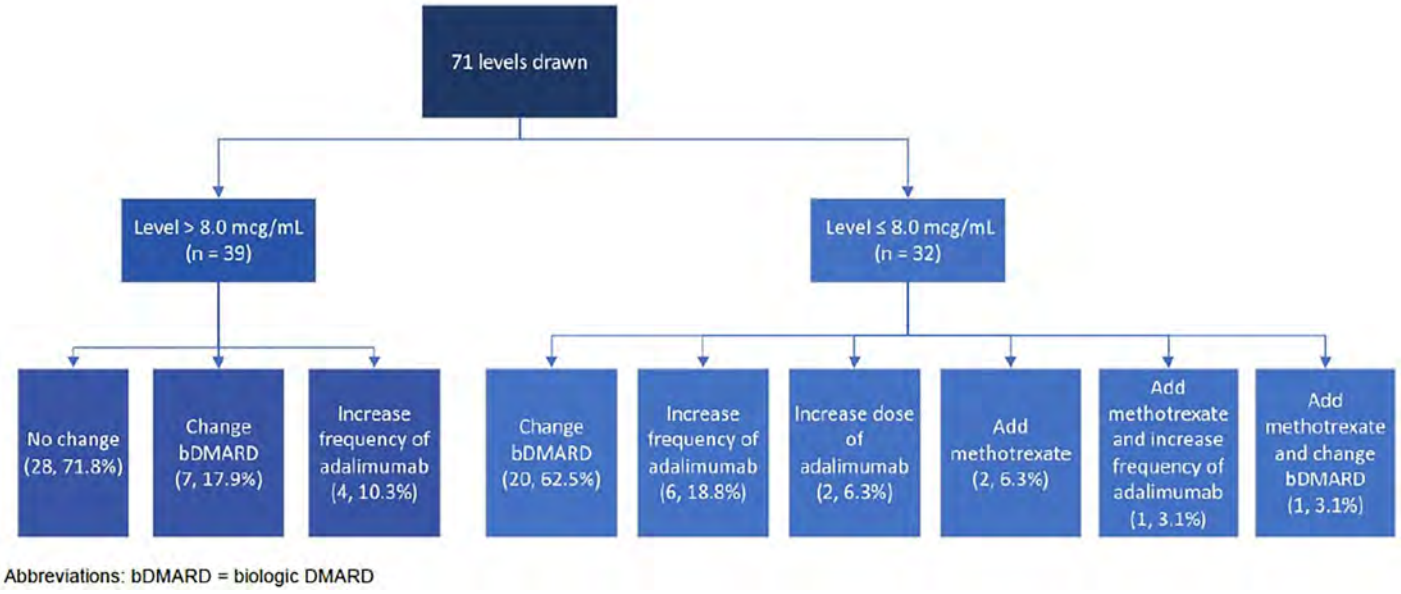
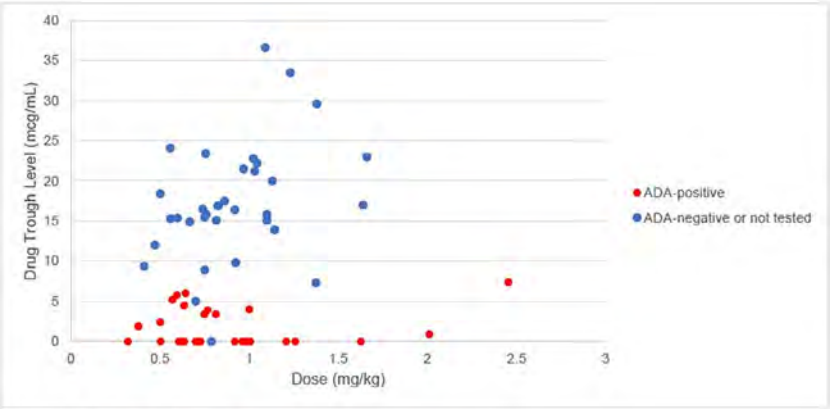


Figure 1: Treatment Changes Based on Adalimumab Trough Level

Methods: Asingle-center, retrospective cohort study was completed using an electronic medical system. Non-systemic JIApatients on adalimumab with a minimum of one adalimumab trough drawn at our institution between 1/1/2019 to1/1/2022were included. Patient data, adalimumab dose and frequency, adalimumab trough levels, anti-drug antibody (ADA) activity, and subsequent treatment decisions were collected. The primary objective was to describe the therapeutic outcomes of drug level assessment in patients with JIA. Secondary objectives included indications for trough level testing, incidence of positive ADA activity, and treatment plan changes. Descriptive statistics were performed.

Results: A total of 64 patients with 71 adalimumab trough levels met study inclusion criteria of which 30 patients were ADA positive and 34 patients were ADA negative or not tested (Table 1).The median age was 11.6 years (6.3, 14.1), predominantly female (35, 54.7%) and Caucasian (47, 73.4%).Enthesitis-related arthritis (23, 35.9%) and oligoarticular JIA (22, 34.4%) were the most common subtypes. Common clinical indications for adalimumab drug level testing included loss



Abbreviation: ADA = anti-drug antibody

Figure 2: Adalimumab Dose vs. Trough Level

of response (46, 71.9%) and inadequate initial response to adalimumab (8, 12.5%). Adalimumab troughs resulted at ≤ 8.0 mcg/mL in 32 (45.1%) measurements leading to ADA testing(Figure 1). Of patients tested for ADA, 30 patients were found to be positive. For patients with a level > 8.0 mcg/mL, the most common treatment decision was no change to therapy (28, 71.8%). Switching to an alternative biologic DMARD was the most common change (20, 62.5%) for ADA tested patients. Trough concentrations did not correlate with the dose of adalimumab that patients received (Figure 2).

Conclusion: No distinguishing patterns associated with ADA development were noted. Most trough concentrations collected were due to loss of clinical response to adalimumab. Assessing adalimumab trough concentrations impacted therapy changes, with switching to an alternative biologic DMARD as the most common practice for adalimumab levels ≤ 8.0 mcg/mL. Adalimumab doses did not correlate with trough concentration. Limitations include small sample size and chart review. Further studies are needed to identify the role of TDM in JIA patients.

Disclosure: C. Vallejos: None; **J. Cooper**: None; **I. Pan**: None.

Abstract Number: 0360

Increasing the Etanercept Dose in Juvenile Idiopathic Arthritis Patients: Does It Help Reaching the Treatment Target? A Post-hoc Analysis of the Best4Kids Randomised Clinical Trial

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Pediatric Rheumatology – Clinical Poster I: JIA

Session Type: Poster Session A

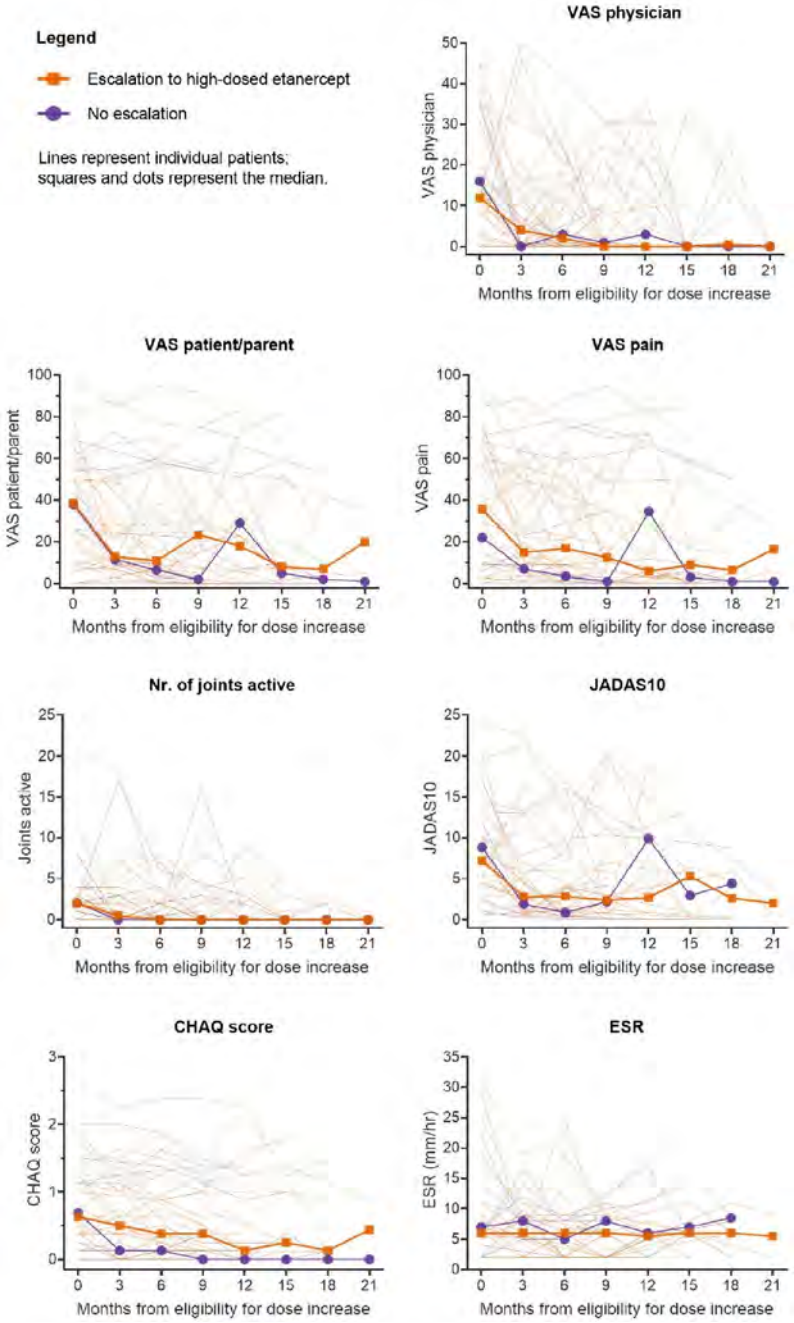
Session Time: 9:00AM–11:00AM

Background/Purpose: The relation between etanercept dose and clinical outcomes of juvenile idiopathic arthritis (JIA) is unclear. Most studies only evaluated doses up to 0.8 mg/kg/week (max 50mg/week),[1] but higher doses are often used off-label in clinical practice. An in-depth description of patients receiving such treatment is lacking. Here, we describe the clinical course of JIA-patients that received high-dose etanercept (1.6 mg/kg/week; max 50mg/week) as part of the Best4Kids trial.

Methods: In a single-blinded treatment-strategy trial, patients with oligoarticular JIA, RF-negative polyarticular JIA or juvenile psoriatic arthritis were randomised across three arms: (1) sequential DMARD-monotherapy (sulfasalazine or methotrexate (MTX)), (2) combination-therapy MTX+6 weeks prednisolone and (3) combination therapy MTX+etanercept.[2]

Figure. Clinical parameters over time after etanercept dose increase (orange) and after not escalating to high-dose etanercept despite eligiblity (purple)

Time-point zero = visit of eligibility for etanercept dose increase



A protocolised treat-to-target approach aiming for inactive disease was used during 24 months follow-up. Treatment was escalated in case of persistent disease-activity or tapered in case of inactive disease. In any treatment-arm patients could eventually escalate from regular to high-dose etanercept alongside MTX 10mg/m^2/week. For comparison we studied patients who did not receive high-dose etanercept due to decisions overriding the trial-protocol by the treating pediatrician and/or the patient/parents.

Results: Of the 94 randomised patients, 32 received high-dose etanercept (69% female, median age 6 years (IQR 4-10), median time from baseline 10 months (7-16), median dose 1.3 mg/kg/week (1.1-1.5)). Follow-up was up to 2 years from baseline (median 24.6 months). Clinical measures of disease-activity decreased largely within 3 months (Figure): median VAS-physician from 12 to 4 (p=0.022), VAS-patient/parent from 38.5 to 13 (p=0.003), VAS pain from 35.5 to 15 (p=0.030), number of active joints from 2 to 0.5 (p=0.12) and JADAS10 from 7.2 to 2.8 (p=0.008). Functional status (CHAQ-score) improved more gradually and ESR remained stable. A comparable pattern of clinical parameters over time was observed in 11 patients (73% girls, median age 8 (IQR 6-9)) who did not escalate to high-dose etanercept despite eligibility according to trial-protocol. In both the high-dose and the comparison group the percentage of patients with inactive disease 6 months after eligibility for dose-increase was 56%. In the high-dose group, 18 out of 32 patients (56%) experienced 26 infectious adverse events (AEs, on average 0.20 events per visit following dose-increase). No serious AEs (SAEs) were recorded after dose-increase. Among the 11 patients who did not receive high-dose etanercept, 4 patients (36%) subsequently experienced 5 infectious AEs (on average 0.11 events per visit); this included one SAE requiring hospitalisation.

Conclusion: Escalation to high-dose etanercept was generally followed by meaningful clinical improvement within 3 months. However, non-escalators experienced comparable improvement. These data do not suggest superior clinical outcomes after etanercept dose increase, while there was a potential trend for more (non-severe) infectious AEs. Larger studies are needed to more closely examine outcomes, adverse events and cost-effectiveness of high dose etanercept.

Disclosure: B. van Dijk: None; **S. Bergstra**: Pfizer, 5; **M. van den Berg**: None; **D. Schonenberg-Meinema**: None; **L. van Suijlekom-Smit**: None; **M. van Rossum**: None; **Y. Koopman**: None; **R. Ten Cate**: None; **C. Allaart**: AbbVie/Abbott, 5; **D. Brinkman**: None; **P. Hissink Muller**: None.

Abstract Number: 0361

Safety of Golimumab Dose Escalation in Pediatric Autoimmunity: A Single Institution Retrospective Experience

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: There is limited data on pediatric golimumab dose escalation, with some data available only in the adult literature. The subcutaneous formulation is not approved for use in pediatric juvenile arthritis. The primary goal of this retrospective analysis was to evaluate for the safety of subcutaneous (SC) golimumab and intravenous (IV) golimumab at escalated doses in children and adolescents with autoimmune diseases. The secondary goal was to gain insight into the efficacy of escalated golimumab dosing in this population.

Table 1. Characteristics, medication details, and side effects of patients initiated on subcutaneous golimumab at age < 18 years and/or receiving escalated subcutaneous dosing. AOM = acute otitis media; IV = intravenous; PNA = pneumonia; SQ = subcutaneous; URI = upper respiratory infection; UTI = urinary tract infection.

	Case 3	Case 5	Case 9	Case 11	Case 12	Case 13
Age at golimumab initiation (years)	19	11	15	13	14	17
Sex	Female	Female	Female	Male	Male	Female
Race/Ethnicity	White	White	Hispanic or Latino	Hispanic or Latino	Hispanic or Latino	White
Rheumatologic Diagnosis	Spondyloarthritis	Oligoarticular JIA	Polyarticular JIA (RF-)	Polyarticular JIA (RF+)	N/A	Psoriatic JIA
Uveitis	No	Yes	Yes	No	Yes	No
Golimumab SQ dosing						
Initial dose	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg
Initial frequency	q4 weeks	q4 weeks	q2 weeks	q4 weeks	q4 weeks	q4 weeks
Duration at initial dosing	3 months	4.5 months	N/A	3 months	N/A	3 months
Max dose	100 mg	100 mg	50 mg	50 mg	50 mg	100 mg
Max frequency	q2 weeks	q2 weeks	q2 weeks	q3 weeks	q4 weeks	q2 weeks
Max total monthly dose	200 mg	200 mg	100 mg	67 mg (average)	50 mg	200 mg
Total duration	21 months	41 months	24 months	44 months	48 months	13 months
Positive response	Yes	Yes	Yes (uveitis only)	Yes	Yes	No
Side Effects						
Mild	Hair loss, fatigue	None	None	None	None	None
Moderate	None	UTI, COVID-19	None	none	COVID-19, URI	Sinus infection, AOM, PNA, COVID-19
Severe	None	None	None	None	None	None

Table 2. Characteristics, medication details, and side effects of patients receiving escalated intravenous golimumab dosing. AGE = acute gastroenteritis; IV = intravenous; SQ = subcutaneous.

	Case 1	Case 7	Case 8
Age at golimumab initiation (years)	19	11	15
Sex	Female	Female	Female
Race/Ethnicity	White	Hispanic or Latino	White
Rheumatologic Diagnosis	Oligoarticular JIA, extended	Oligoarticular JIA	Polyarticular JIA (RF-)
Uveitis	No	Yes	No
Golimumab IV dosing			
Initial dose	2 mg/kg	2 mg/kg	80 mg/m2
Initial frequency	q4 weeks (loading only)	q4 weeks	q4 weeks
Duration at initial dosing	2 months (loading only)	N/A	N/A
Max dose	2 mg/kg	2 mg/kg	80 mg/m2
Max frequency	q4 weeks	q4 weeks	q4 weeks
Max total monthly dose	199 mg	122 mg	113 mg
Total duration	14 months	44 months	4 months
Positive response	Yes	Yes	No
Side Effects			
Mild	None	None	None
Moderate	Thrush, viral AGE	Influenza, COVID-19, psoriasis	None
Severe	None	None	None

Table 3. Characteristics, medication details, and side effects of patients receiving combined intravenous and subcutaneous golimumab dosing. IV = intravenous; SQ = subcutaneous.

	Case 2	Case 4	Case 6	Case 10
Age at golimumab initiation (years)	10	16	17	18
Sex	Female	Female	Male	Female
Race/Ethnicity	White	Hispanic or Latino	White	White
Rheumatologic Diagnosis	Polyarticular JIA (RF-)	Polyarticular JIA (RF+)	Polyarticular JIA (RF-)	Juvenile AS
Uveitis	Yes	No	No	No
Golimumab IV dosing				
Initial dose	2 mg/kg	2 mg/kg	2 mg/kg	1.2 mg/kg
Initial frequency	q8 weeks	q4 weeks	q4 weeks	q8 weeks
Duration at initial dosing	17 months	7 months	9 months (then added SQ)	4 months
Max dose	3.5 mg/kg	3 mg/kg	2 mg/kg	2 mg/kg
Max frequency	q4 weeks	q4 weeks	q4 weeks	q4 weeks
Golimumab SQ dosing				
Initial dose	50 mg	50 mg	100 mg	100 mg
Initial frequency	q4 weeks	q4 weeks	q4 weeks	q4 weeks
Duration at initial dosing	13 months	3 months	N/A	N/A
Max dose	100 mg	100 mg	100 mg	100 mg
Max frequency	q4 weeks	q4 weeks	q4 weeks	q4 weeks
Max total monthly dose	275 mg	256 mg	272 mg	250 mg
Total duration	55 months	8 months	29 months	21 months
Positive response	Yes (uveitis)	No	Yes	Yes
Side Effects				
Mild	None	None	None	Nausea, anorexia
Moderate	Pharyngitis, COVID-19	Bronchitis	COVID-19	None
Severe	None	None	None	None

Methods: Patients were identified by retrospective electronic medical record review from a single center pediatric rheumatology clinic. Inclusion criteria encompassed patients with a rheumatologic disease who were treated with IV or SC golimumab at escalated doses or frequency, SC golimumab in patients under the age of 18 years, or combined SC and IV golimumab regimens. IV doses were considered escalated if patients under the age of 18 years received greater than 80 mg/m2/dose or if patients 18 years or older received greater than 2 mg/kg/dose. Increased dose frequency included those receiving IV golimumab at intervals less than every 8 weeks or SC golimumab at intervals less than every 4 weeks.

Results: Thirteen patients were identified. Ten of the patients were female and the average age at initiation of golimumab was 15 years. Average duration of treatment was 28 months. Twelve patients were treated with golimumab for management of juvenile idiopathic arthritis (JIA), 4 of which had associated uveitis, and 1 patient had uveitis without JIA. Patients had insufficient response or intolerance to an average of 2 disease-modifying antirheumatic drugs (DMARDs) and 3 biologic agents or small molecule drugs before initiating golimumab. Golimumab was the first biologic agent used in 1 patient. Positive clinical response to golimumab, based on patient report and clinician assessment, was seen in 10 patients (76.9%). Three patients discontinued high-dose golimumab due to ineffectiveness and 1 discontinued golimumab due to lack of insurance coverage. None discontinued golimumab due to side effects. Mild side effects were reported in 2 patients, including hair loss, fatigue, nausea and decreased appetite. Two patients developed psoriasis after the initiation of golimumab. Mild infections that were seen during golimumab treatment in 8 patients included upper respiratory tract infections, viral gastroenteritis, urinary tract infections, and 2 lower airway infections. There were no serious adverse events.

Conclusion: Our study suggests that dose escalation of golimumab therapy, and SC golimumab administration, are well-tolerated in pediatric rheumatologic diseases and uveitis, with a safety profile similar to that of other biologic agents. Many of our patients (>70%) had positive clinical responses, suggesting that escalated doses may also be effective in patients with refractory disease.

Disclosure: L. Medrano: None; **A. Hoftman**: None.

Abstract Number: 0362

Adverse Childhood Experiences Are Associated with Disease Outcomes in Youth with Juvenile Idiopathic Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Pediatric Rheumatology – Clinical Poster I: JIA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Adverse childhood events (ACEs) are common in children. ACEs are various stressors, including, but not limited to parental incarceration or food and housing insecurity. Our previous work showed that children with arthritis were more likely to be affected by ACEs than healthy children and children with other chronic diseases. To gain a better understanding of the relationship between ACEs and disease outcomes in Juvenile Idiopathic Arthritis (JIA), we screened JIA enrollees from the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry for ACEs.

Table 1: Categorical ACE Scores and JIA Outcomes

	No ACEs	1 ACE	2-3 ACEs	≥4 ACEs	p value
JADAS (median, IQR)	1 (0, 3)	0 (0, 3)	2 (0, 3)	4 (2, 5)	0.005
Physician Global Assessment					
Minimal (n, %)	70 (69%)	21 (66%)	17 (74%)	5 (42%)	<0.001
Moderate (n, %)	20 (20%)	9 (28%)	4 (17%)	0	
Severe (n, %)	12 (12%)	2 (6%)	2 (9%)	7 (58%)	
Patient/Parent Global Assessment					
Minimal (n, %)	57 (55%)	17 (50%)	10 (40%)	2 (18%)	0.004
Moderate (n, %)	26 (25%)	10 (29%)	10 (40%)	1 (9%)	
Severe (n, %)	20 (19%)	7 (21%)	5 (20%)	8 (73%)	
CHAQ					
Minimal (n, %)	62 (65%)	21 (68%)	11 (44%)	4 (44%)	0.2
Moderate (n, %)	24 (25%)	8 (26%)	9 (36%)	2 (22%)	
Severe (n, %)	10 (10%)	2 (6%)	5 (20%)	3 (33%)	
PROMIS Global Health Index T-score (median, IQR)	42 (40, 46)	44 (40, 46)	37 (34, 43)	37 (34, 40)	0.0006
Pain Intensity (median, IQR)	1 (0, 3)	0 (0, 3)	2 (0, 3)	4 (2, 5)	0.005
PROMIS Pain Interference T-score (median, IQR)	47 (41, 54)	48 (44, 52)	57 (50, 61)	54 (48, 63)	0.005
PROMIS Mobility T-score (median, IQR)	56 (46, 59)	59 (52, 59)	47 (40, 59)	45 (38, 59)	0.1

Bivariate relationships between catgerical ACE scores and JIA outcome variables. JADAS, clinical Juvenile Arthritis Disease Activity Score; CHAQ, Childhood Health Assessment Questionnaire; PROMIS Patient-Reported Outcomes Measurement Information System. Physician and Parent Global Assessments were measured by 10-cm visual analog scales with mild, moderate, and severe defined by 25%-ile, 50%-ile, and 75%ile.

Methods: Patients and their families who met inclusion criteria and consented to the study received an ACE screen at CARRA study visits. For participants < 18 years, parents completed the screen; patients ≥18 years completed ACE screen. Demographic and JIA disease data collected in the CARRA Registry were linked to ACE screen data. ACE scores were categorized as 0, 1, 2-3, and ≥4. JIA outcomes examined included disease activity (JADAS), physical impairment (CHAQ and PROMIS Mobility), physician global assessment, patient/parent global assessment, pain intensity scale, PROMIS Pain Interference, and PROMIS Pediatric Global Health Index. Bivariate analyses were conducted to assess for associations between categorical ACE scores, demographics, clinical characteristics and outcomes. Chi-square and Fisher's exact tests were used for categorical variables and Kruskall-Wallis tests were used for continuous variables.

Results: Among 209 participants screened for ACEs, 130 (62%) had none, 38 (18%) had 1, 28 (13%) had 2-3, and 13 (6%) had ≥4. Categorical ACE scores differed by age ($p< 0.001$), race/ethnicity ($p=0.002$), household income ($p< 0.001$), parental education level ($p=0.01$), health insurance status ($p< 0.001$), Area of Deprivation Index national ranking ($p=0.01$), and estimated poverty rate by zipcode ($p=0.002$). Associations between categorical ACE scores and JIA outcomes are described in Table 1. Higher ACE scores were associated with poorer measures of disease activity (JADAS, physician and patient/parent global assessments), higher pain intensity and pain interference, and a poorer PROMIS Global Health Index. While associations with CHAQ and PROMIS Mobility scores did not meet significance, higher proportions of impaired youth were observed among youth with ACE scores of 2-3 and ≥4.

Conclusion: Higher ACE scores were associated with worse JIA outcome measures including disease activity, pain, global health, and patient/parent and physician global assessments. Further work needs to be done to see whether addressing stress around ACEs in youth with JIA can improved disease outcomes.

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Abstract Number: 0363

Allogenic Hematopoietic Stem Cell Transplant for Children with Refractory Systemic Juvenile Idiopathic Arthritis and sJIA-Associated Lung Disease: 6-month Post-Transplant Outcomes from an International Cohort

Michael Matt[1], Daniel Drozdov[1], Rolla Abu-Arja[2], Shanmuganathan Chandrakasan[3], Kyla Driest[2], Elvira Cannizzaro Schneider[4], Despina Moshous[5], Benedicte Neven[5], Karen Onel[6], Sampath Prahalad[7], Susan Prockop[8], Pierre Quartier[5], Johannes Roth[9], Donna Wall[10], Ulrike Zeilhofer[11], Scott Canna[12], Alexei Grom[1], Grant Schulert[1] and Rebecca Marsh[1], [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Nationwide Children's Hospital, Columbus, OH, [3]Emory University School of Medicine, Atlanta, GA, [4]Universitaetskinderspital Zurich, Zurich, Switzerland, [5]Paris Cité Université and Necker Hospital, Paris, France, [6]Hospital for Special Surgery, New York, NY, [7]Emory University School of Medicine, Children's Pediatric Institute, Atlanta, GA, [8]Division of Hematology-Oncology, Boston Children's Hospital, Boston, MA, [9]University of Ottawa, Ottawa, ON, Canada, [10]The Hospital for Sick Children, Toronto, ON, Canada, [11]Children's Hospital of Zurich, Zurich, Switzerland, [12]Children's Hospital of Philadelphia, Philadelphia, PA

SESSION INFORMATION
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Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Refractory systemic juvenile idiopathic arthritis (sJIA) in children can be complicated by repeated episodes of macrophage activation syndrome (MAS) or sJIA-related lung disease (sJIA-LD). Use of allogenic hematopoietic stem cell transplant (HSCT) has been reported in cases of refractory SJIA; however, there is limited data regarding its use in sJIA-LD. The objective of this study was to determine clinical, inflammatory, and pulmonary outcomes 6 months post-transplant in an international cohort of patients with refractory SJIA, recurrent MAS, and sJIA-LD.

Methods: Thirteen patients with refractory sJIA who underwent allogeneic HSCT from 2018-2022 were identified and analyzed. Information regarding sJIA-related treatments prior to transplant, HSCT conditioning regimens, donor HLA matching, pulmonary function tests and chest imaging, pertinent laboratory values, and transplant complications were collected using a standardized case report form. The study was completed with IRB approval from each institution.

Results: Of the 13 patients who underwent allogeneic HSCT for refractory sJIA, 10 patients had recurrent episodes of MAS, and 9 patients had progressive sJIA-LD. All patients in this study had failed treatment IL-1 and IL-6 blockade and received an average of 8 different agents (range 5-13) prior to HSCT. Many patients had received treatment with Janus Kinase inhibitors or emapalumab. The mean maximum IL-18 level prior to HSCT was 251,398 pg/mL (range 64,840-471,860 pg/mL). Most patients received grafts from 10/10 HLA-matched unrelated donors (n=6), or 9/10 HLA matched unrelated donors (n=3). Two patients received grafts from 5/10 or 7/10 HLA-mismatched related donors. Two patients received a second transplant, one for acute graft failure after 32 days and one for relapsed sJIA after one year with donor chimerism of 100%. Post-transplant complications included graft versus host disease (5 patients), bacteremia (3 patients), HHV6 reactivation, (2 patients), EBV encephalitis, CMV reactivation, and infection-triggered MAS (2 patients). One patient died 120 days after transplant due to CMV pneumonitis and multi-organ failure, and another died at day+133 with steroid dependent graft-versus-host disease and CMV pneumonitis. Six months after final transplant, 80% (10/13) of patients showed a complete clinical response, with no active features of sJIA or MAS without any biologic therapy. All patients with available post-transplant IL-18 data had normalized levels 6 months post-HSCT. Most patients (7/9) with sJIA-LD demonstrated improvement in pulmonary function, including improvements on chest CT, reduced need for supplemental oxygen, and reduced clubbing.

Conclusion: A majority of patients who underwent allogenic HSCT for refractory SJIA, recurrent MAS, or sJIA-LD showed a complete response including improvement in clinical and imaging features of lung disease. HSCT may represent a promising approach for highly refractory sJIA and its complications.

Disclosure: M. Matt: None; **D. Drozdov**: None; **R. Abu-Arja**: None; **S. Chandrakasan**: Sobi, Inc, 1, 2; **K. Driest**: None; **E. Cannizzaro Schneider**: None; **D. Moshous**: None; **B. Neven**: None; **K. Onel**: None; **S. Prahalad**: None; **S. Prockop**: AlloVir, 12, Support for the conduct of clinical trials through BCH, Atara, 10, 12, Support for the conduct of clinical trials through BCH, CellEvolve, 2, Jasper Therapeutics, 12, Support for the conduct of clinical trials through BCH, Pierre Fabre, 2, 6, Regeneron, 6, VOR, 2; **P. Quartier**: AbbVie/Abbott, 2, Amgen, 2, Novartis, 2, Pfizer, 2, Roche, 2; **J. Roth**: None; **D. Wall**: None; **U. Zeilhofer**: None; **S. Canna**: Apollo Therapeutics, 2, Novartis, 12, Site PI for industry-sponsored trial, PracticePoint CME, 6, Simcha Therapeutics, 2, Sobi, 6; **A. Grom**: Novartis, 2, 5, Sobi, 2, 5; **G. Schulert**: IpiNovyx, 5, SOBI, 2; **R. Marsh**: horizon, 1, sobi, 1.

Abstract Number: 0364

Sex Differences in Clinical and Imaging Characteristics of Axial Juvenile Spondyloarthritis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Pediatric Rheumatology – Clinical Poster I: JIA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The extent to which heterogeneity exists in youth with axial disease and juvenile spondyloarthritis (JSpA) is unclear. In a cross-sectional sample of patients classified as axial disease in JSpA (axJSpA) according to recently validated criteria, we tested for differences in clinical and imaging features amongst males and females.

Table 1. Clinical and imaging features of axJSpA by sex

Feature	Female (n=47) N (%) or median (IQR)	Male (n=96) N (%) or median (IQR)	P-value
Demographics			
Age at axial disease evaluation (n=142)	13.7 (12.0, 16.6)	15.2 (13.0, 17.0)	0.14
HLA-B27 (+) (n=136)	20 (44.4)	67 (73.6)	<0.01
SpA in first-degree relative (n=133)	12 (26.1)	12 (13.8)	0.08
Patient-reported symptoms			
Hip or groin pain (n=141)	25 (54.3)	66 (69.5)	0.08
Hip or groin stiffness (n=126)	12 (31.6)	49 (55.7)	0.01
Lumbar/sacral/buttock pain	37 (78.7)	75 (78.1)	0.93
Arthritis/enthesitis history and/or exam			
Enthesitis (n=136)	16 (36.4)	45 (48.9)	0.17
Peripheral arthritis (n=142)	24 (51.1)	56 (58.9)	0.37
Hip arthritis (current or past) (n=136)	19 (45.2)	46 (48.9)	0.69
Tarsitis (current or past) (n=134)	6 (14.3)	14 (15.2)	0.89
SIJ pain with deep palpation (n=127)	23 (57.5)	53 (60.9)	0.72
Abnormal CRP or ESR (n=126)			
≥1x upper limit normal	11 (26.8)	22 (25.9)	0.91
≥2x upper limit normal	12 (29.3)	41 (48.2)	0.04
Patient/physician-reported outcomes			
Patient pain VAS (n=79)	6.0 (3.0, 8.0)	6.0 (3.5, 7.0)	0.71
Patient global assessment VAS (n=73)	6.0 (3.0, 7.0)	5.0 (3.0, 7.0)	0.61
Physician global VAS (n=94)	2.5 (1.0, 5.0)	3.0 (1.0, 4.0)	0.97
MRI inflammatory/structural lesions			
Subchondral bone marrow edema	36 (76.6)	90 (93.8)	<0.01
Inflammation at site of erosion	27 (57.4)	52 (54.2)	0.71
Capsulitis	13 (27.7)	18 (18.8)	0.22
Joint space enhancement	7 (14.9)	9 (9.4)	0.33
Joint space fluid	5 (10.6)	11 (11.5)	0.88
Enthesitis outside SIJ	3 (6.4)	28 (29.2)	<0.01
Erosion	39 (83.0)	78 (81.2)	0.80
Sclerosis	18 (38.3)	48 (50.0)	0.19
Fatty lesion	6 (12.8)	12 (12.5)	0.96
Fat metaplasia in erosion cavity (backfill)	3 (6.4)	10 (10.4)	0.55
Ankylosis	0 (0.0)	4 (4.2)	0.30
Unequivocal SIJ inflammation (n=141)	36 (76.6)	88 (93.6)	<0.01
Unequivocal SIJ structural lesion(s) (n=140)	40 (87.0)	81 (86.2)	0.90
Axial arthritis in JSpA classification score (range 0-100)	76.0 (60.0, 85.0)	79.0 (68.0, 90.0)	0.07

Legend: JIA (juvenile idiopathic arthritis), SpA (spondyloarthritis), CRP (C-reactive protein), ESR (erythrocyte sedimentation rate), VAS (visual analog scale), MRI (magnetic resonance imaging), SIJ (sacroiliac joint). Sample size indicated for each variable if data incomplete. Unequivocal SIJ inflammation defined as bone marrow edema in ≥3 quadrants across all SIJ slices. Unequivocal SIJ structural lesion(s) defined as erosion in ≥3 quadrants or sclerosis or fat lesion in ≥2 SIJ quadrants or backfill or ankylosis in ≥2 joint halves across all SIJ slices (Weiss PF et al. Arthritis Care Res. 2023).

Methods: This was an international cross-sectional study of youth that met the following criteria: 1) Physician diagnosis of JSpA, 2) Symptom onset prior to age 18 years, 3) Fulfilled criteria for axJSpA. Clinical and magnetic resonance imaging (MRI) data were available from the time when axial disease was first identified; these features were compared between males and females using Pearson's chi-squared and Fisher's exact tests for categorical variables, and Wilcoxon rank-sum tests for continuous variables as appropriate. Multivariate logistic regression was used to assess the association of unequivocal inflammatory and structural lesions typical of axial disease on MRI and sex adjusted for HLA-B27 status and degree of inflammatory marker elevation.

Results: 143 patients met inclusion criteria of which 96 (67.1%) were male, 64.0% were HLA-B27 positive, and 18.1% had a family history of spondyloarthritis in a first degree relative. Clinical and imaging characteristics stratified by sex are displayed in **Table 1.** Male patients had significantly greater prevalence of HLA-B27 positivity ($p< 0.01$), hip/groin stiffness ($p=0.01$), inflammatory markers ≥2x the upper limit of normal ($p=0.04$), pelvic enthesitis ($p< 0.01$), subchondral bone marrow edema ($p< 0.01$), and unequivocal sacroiliac joint inflammation on MRI ($p< 0.01$). There were no statistically significant differences between males and females in peripheral disease manifestations (current or history of) or patient-reported measures. After adjusting for HLA-B27 status and degree of inflammatory marker elevation, the odds of unequivocal inflammatory lesions typical of axial disease (OR 5.70, 95% CI 1.51-21.59), pelvic enthesitis outside the sacroiliac joint (OR 5.92, 95% CI 1.48-23.61) and subchondral bone marrow edema (OR 4.92, 95% CI 1.38-18.12) remained significantly higher in males (**Figure 1A**) but there were no differences between sexes with respect to structural MRI lesions (**Figure 1B**). The median axial disease classification score (range 0-100, classification threshold ≥55) was not significantly higher in males.

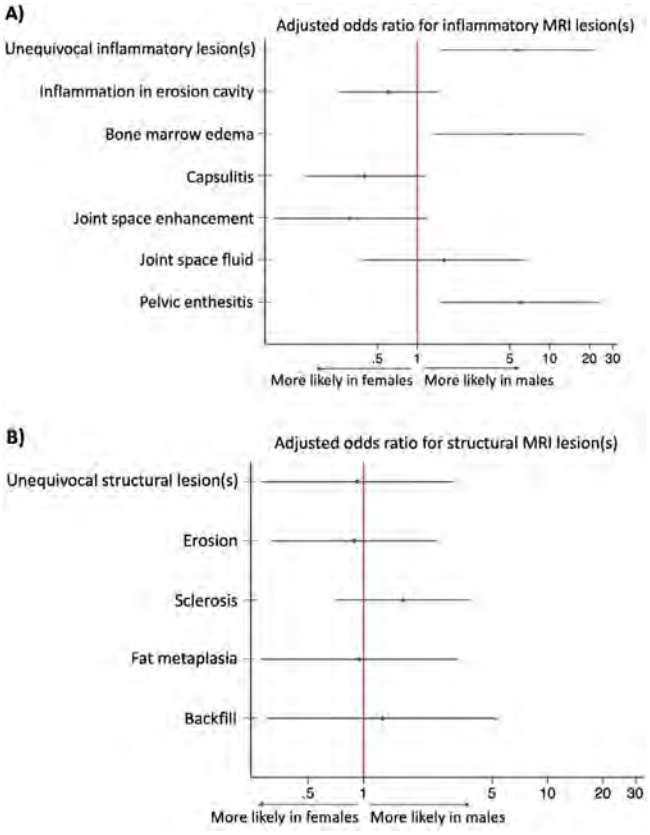

Figure 1. Association of unequivocal (A) inflammatory and (B) structural sacroiliac MRI lesions typical of axial disease and sex, adjusted for HLA-B27 status and degree of inflammatory marker elevation.

Conclusion: In patients with JSpA who met validated criteria for axJSpA the prevalence of HLA-B27 positivity, and serologic and imaging evidence of inflammation were significantly higher in males than females. Further exploration of the mechanisms underlying these differences is warranted, but our findings suggest that stratification by sex should be considered in the design of future studies in axJSpA.

Disclosure: A. Mayer: None; **T. Brandon**: None; **P. Weiss**: Eli Lilly, 2, Novartis, 2, Pfizer, 2; **o. JAXSPERT members**: None.

Abstract Number: 0365

Establishing a Multidisciplinary Registry for Temporomandibular Joint Arthritis in Juvenile Idiopathic Arthritis: Insights into Patient Outcomes and Management Challenges

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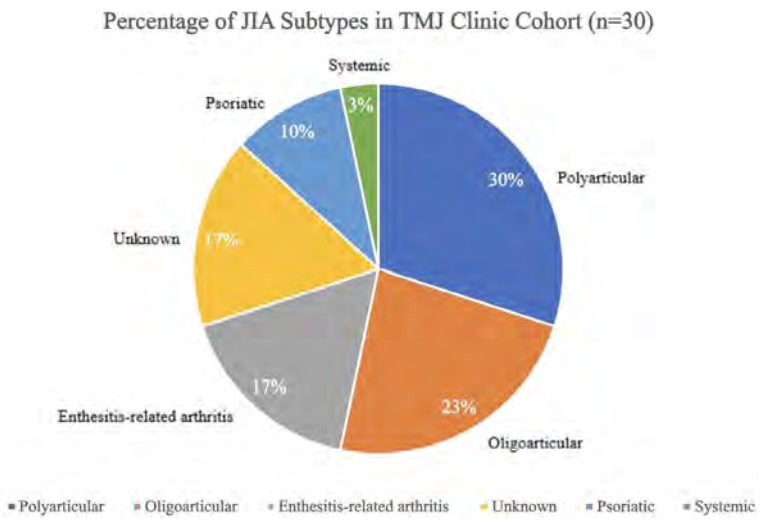
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

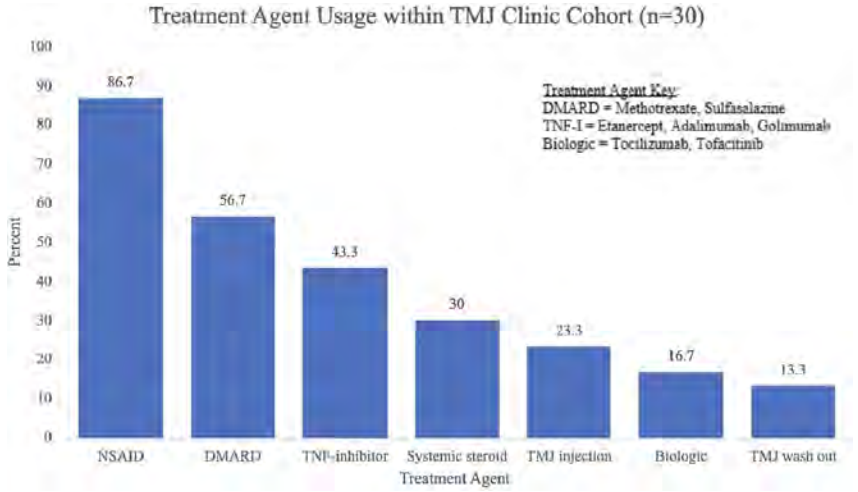
Background/Purpose: Temporomandibular joint (TMJ) arthritis, a condition frequently overlooked in patients with JIA, can result in joint damage if not promptly treated. Such damage presents as pain during joint movement and chewing, as well as mandibular growth abnormalities. Due to minimal symptoms in the early stages, timely diagnosis of TMJ arthritis is challenging without early imaging, often leading to joint damage before detection. This study aims to establish a registry specifically focusing on JIA patients with TMJ involvement. The registry operates within a multidisciplinary clinic, involving pediatric rheumatologists, neuroradiologists, oral maxillofacial surgeons, physical therapists, orthodontists, and pediatric dentists.

Methods: The study enrolled JIA patients referred to the multidisciplinary TMJ clinic for suspected TMJ involvement. Data collection took place during routine care visits, and information was obtained through a combination of prospective and retrospective chart reviews, as well as patient-reported outcomes. The data analyzed in this study were extracted from the participants' initial visit records. Quantitative data was analyzed using descriptive statistics.

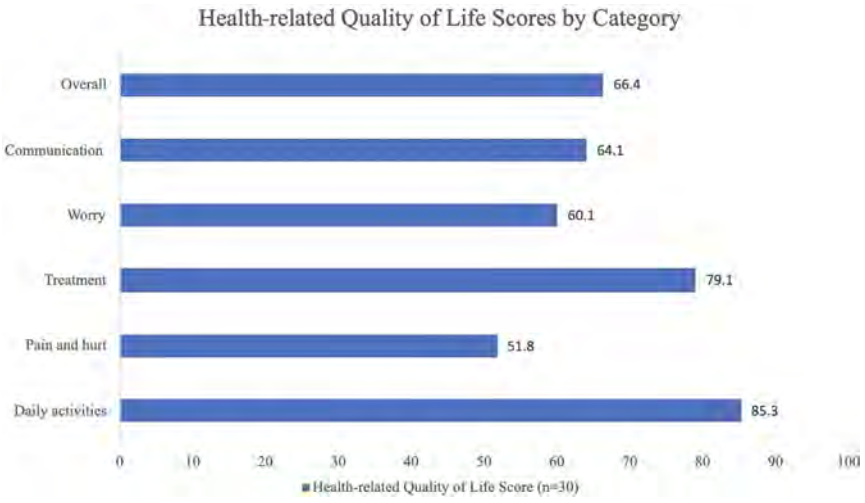
Results: Data from the multidisciplinary TMJ clinic were reviewed involving (n=30) 7 males and 23 females aged 7 to 20 years. The most common diagnoses among participants were polyarticular JIA (30%), oligoarticular JIA (23.3%), and enthesitis-related arthritis (16%) [Figure 1]. The primary reason for referral to the TMJ clinic was jaw, muscle, or neck pain, reported by 86.7% of participants. Before the referral, participants had, on average, tried 2.8 different treatment agents [-Figure 2]. Furthermore, 23.3% of participants had received prior TMJ steroid injections, and 13.3% had undergone a prior TMJ wash-out. Among the 30 patients, 21 had obtained an MRI of their TM joint within 12 months of entering the clinic. During the study visit, participants completed the Pediatric Quality of Life Inventory, a measure of health-related quality of life (HRQOL). The responses were transformed to a 0-100 scale, with higher scores indicating better HRQOL. The average score across all categories (daily activities, pain and hurt, treatment, worry, and communication) was 66.4 [Figure 3]. Participants also reported difficulties in performing various activities based on a patient-specific functional scale. A total of 56 activities were identified, and on average, patients scored 4.9 per activity on a scale of 0 to 10, with 0 indicating complete inability



Percentage of JIA subtypes in TMJ clinic cohort.



Treatment agent usage within TMJ clinic cohort.



Health-related quality of life scores by category.

to perform the activity. Overall, participants reported an average pain intensity score of 3.4/10, and 64% of patients reported affected functionality of their jaws. Additionally, 8 out of the 30 study participants expressed concerns regarding body image.

Conclusion: This data offers valuable insights by capturing outcomes from patients with TMJ arthritis. Our findings indicate that these patients endure TMJ-related pain and experience joint dysfunction that affects their quality of life. The challenges associated with TMJ arthritis highlight the importance of this registry and the ongoing observation of this clinic's cohort.

Disclosure: S. Tarvin: Pfizer, 5, Roche, 5, UCB, 5; **A. Rakestraw**: None; **J. Lee**: None; **N. Matthews**: None; **S. Ballinger**: None; **C. Sparks**: None.

Abstract Number: 0366

Active Joint Acoustic Emissions on the Achilles Tendon: A Digital Biomarker of Enthesitis Related Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile Idiopathic Arthritis (JIA) is a chronic condition in children that causes joint inflammation. Enthesitis-related arthritis (ERA), a subtype of JIA, affects 10-20% of patients and is characterized by enthesitis, leading to substantial joint pain and disability. Diagnosing JIA subtypes is challenging due to insensitive and subjective clinical examinations, patient surveys, non-specific laboratory tests and a lack of pediatric rheumatologists worldwide. Active joint acoustic emission (JAE) sensing, using vibrational stimulation, offers potential to assess the inflammatory status of soft tissues such as the Achilles tendon (AT). Integrating JAEs with machine learning (ML) algorithms can offer valuable insights into tendon health. The aim of this study is to demonstrate the utility of active JAEs as a new digital biomarker for assessing AT involvement in ERA.

Methods: JAEs were recorded from 14 patients diagnosed with JIA that were divided into two subgroups: (1)ERA and symptomatic AT enthesitis (sx ERA), and (2) without ERA and asymptomatic ATs (asx nERA). Symptomatic AT enthesitis was determined by tenderness on clinical examby a physician, while asymptomatic AT showed no tenderness, stiffness, or swelling. To record the JAEs, a setup comprising a miniature vibration motor and an accelerometer was used. The vibration motor provided a harmless input train of burst vibrations, while the accelerometer measured the response of the AT in tiptoe position. The recorded signals were filtered, and 25 bursts were segmented to extract 25 temporal features and the top 3 principal components(PC).Two MLclassifier (logistic regression) was trained using three most salient features and the second and third PCs, respectively. Two subject-wise cross-validation approaches were used to assess the model's generalizability: leave-one-subject-out cross-validation (LOSO-CV) and a 3-fold cross-validation. The latter was performed 10 times with unique combinations to evaluate robustness.

Results: The feature-based LOSO-CV resulted in an 86% accuracy, 83% sensitivity and 88% specificity. The PC-based LOSO-CV resulted in a 71% accuracy, 67% sensitivity and 75% specificity. The corresponding confusion matrices, ROC curves and boxplot of the subject scores are shown in Figure 1. The iterations of the 3-fold cross-validation when

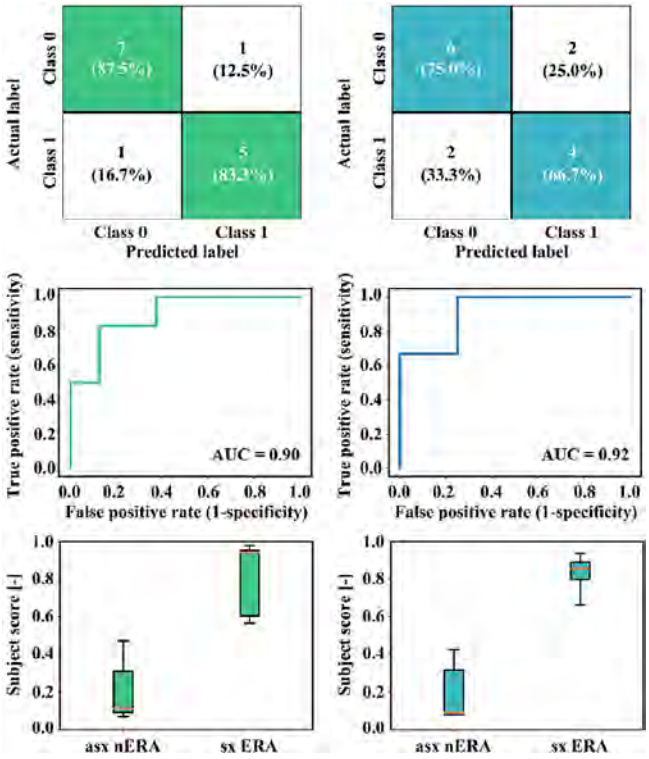

Figure 1 Results of the LOSO-CV. Top row: confusion matrices, middle row: ROC curves, bottom row: box plots of the subjects scores of the correctly predicted subjects generated by the classification algorithm. Left column shows the results of the feature-based classification, right column shows the results of the PC-based classification.

considering the feature-based approach resulted in a 79% mean accuracy (range: 71-93%), a 70% mean sensitivity (range: 50-83%) and an 86% mean specificity (range 75-100%). When considering the PC-based classification, the 3-fold validation resulted in a 76% mean accuracy (range: 64-93%) a 72% mean sensitivity (range: 67-100%) and an 80% mean specificity (range 63-100%).

Conclusion: The presented results lay the foundation in recognizing the potential utility of active JAE technology to identify and label symptomatology on the entheses of the Achilles tendon. While more work needs to be done to increase the sample size and optimize the technology by using training labels validated by gold standard technology, JAEs hold promise as a screening or disease monitoring tool that can be used in clinic or at home and that may help decrease disease morbidity caused by JIA in children.

Disclosure: Q. Goossens: None; **M. Locsin**: None; **E. Moise**: None; **L. Ponder**: None; **O. Inan**: Arthroba, 4, 10, 11; **S. Prahalad**: None.

Abstract Number: 0367

Adolescents and Young Adults Taking Methotrexate: Knowledge and Behaviours

Matthew Sholdice[1], Heather Bollegala[1], Lauren Heessels[1], Meghan Pancucci[1], KAREN BEATTIE[1] and Michelle Batthish[2], [1]McMaster University, Hamilton, ON, Canada, [2]McMaster Children's Hospital, Hamilton, ON, Canada

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: MTX, a first line DMARD, commonly used to treat adolescents and young adults (AYA) with rheumatic diseases (RD), can be hepatotoxic and teratogenic. AYA with RD may face challenges accessing and understanding accurate, reliable information regarding the potential harmful interactions between their medications (e.g., MTX) and certain lifestyle choices they make. The objective of this study was to determine the educational experiences, level of knowledge and informational needs and preferences of AYA taking MTX for RDs, specifically regarding alcohol use and contraception.

Methods: AYA 16-25 years old currently or previously taking MTX completed an anonymous online questionnaire co-designed by AYAs with RD. Links to questionnaires were shared in rheumatology clinics and through patient advocacy groups on social media.

Results: Of 43 respondents, 77% were female, 65% were 19-21 years of age, and 80% had a diagnosis of JIA. In assessing respondent knowledge of MTX, 21% did not know that MTX is a DMARD, 53% were not aware that MTX takes 2-4 months to achieve full effectiveness, 28% did not know that MTX can cause liver damage, and 86% agreed that alcohol should be avoided when taking MTX. The majority (79%) stated that contraception should be used if a female is taking MTX, compared to 64% for a male.

In assessing respondent behaviours, 37% report drinking an average of 1-5 alcoholic drinks weekly, 32% reported drinking ≥3 alcoholic drinks at least once/week, 56% reported that their rheumatologists ask them about their alcohol use at every visit, 21% reported discomfort discussing alcohol use with their rheumatologist, and 18% inaccurately reported alcohol use to their rheumatologist. Past or present sexual activity was reported by 56% of respondents, 93% of which report using contraception. Discomfort discussing sexual activity with their rheumatologist was reported by 28%, and 10% inaccurately reported sexual activity to their rheumatologist. Approximately one quarter were unaware that there is a risk of birth defect while taking MTX.

Respondents reported receiving information about their RD from their rheumatologist/healthcare provider, the internet, and educational pamphlets, which were also their preferred methods of receiving information. One third reported not having access to accurate information regarding managing MTX side effects.

Conclusion: Despite approximately half of AYA reporting drinking alcohol weekly and being sexually active, results suggest almost half of rheumatologists do not routinely discuss these at-risk behaviours with their patients on MTX. Approximately one quarter of respondents reported feeling uncomfortable and/or not being honest with their rheumatologist in discussing alcohol use and sexual activity. Approximately one quarter of AYA report not having access to accurate resources regarding MTX side effects and safe alcohol use. This study identified educational opportunities about MTX for AYAs which can be shared by their rheumatologist/healthcare provider and/or educational pamphlets.

Disclosure: M. Sholdice: None; **H. Bollegala**: None; **L. Heessels**: None; **M. Pancucci**: None; **K. BEATTIE**: None; **M. Batthish**: AbbVie/Abbott, 6, Novartis, 1, Viatris, 1, 5.

Abstract Number: 0368

Surveying Psychological Resilience and Pain in a Cross-Section of JIA Patients

Daniella Schocken and Tracy Ting, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Pain trajectories vary in JIA, with some patients developing chronic pain over the course of their illness. Adaptation and recovery under stressful or traumatic conditions, defined as "psychological resilience," correlates to symptom severity and functioning in other pediatric populations affected by chronic illness. Resilience can be enhanced by therapeutic interventions, making it a potential target for strategies to improve outcomes in disease management. However, psychological resilience has never been studied quantitatively in JIA. This study aimed to apply a validated measure to determine the resilience of children and adolescents with JIA and identify any relationships between pain and resilience in this population.

Methods: 98 children and adolescents with JIA participated in this study, completing the Connor-Davidson Resilience Scale (CD-RISC-25), the PROMIS Pediatric Pain Interference (PPI) Short Form, and the Pain and Symptom Assessment Tool (PSAT). Participants' caregivers provided information regarding participant demographics and psychiatric health history and also completed the CD-RISC-25. Chart review documented participants' case history and clinical status including JIA subtype, date of diagnosis, treatment, pain level, well-being, and active joint count during study participation. Spearman correlation coefficients were calculated to determine relationships between resilience scores and other variables, which were non-parametric. To compare resilience among subgroups of participants, Welch's t-test was used.

Results: Participant resilience scores were normally distributed between 29 and 100 with a mean of 72.93 (sd = 15.96). Comparison of CD-RISC-25 scores to participant age at time of JIA diagnosis (ρ = -0.053, p = 0.60), time elapsed since JIA diagnosis (ρ = 0.10, p = 0.31), and caregiver CD-RISC-25 score (ρ = 0.089, p = 0.38) revealed no statistically significant relationships. Correlations were identified between CD-RISC-25 scores and participants' reported numeric pain intensity rating (ρ = -0.23, p = 0.023), self-assessed well-being (ρ = -0.33, p < 0.001), and PPI (ρ = -0.48, p < 0.001). CD-RISC-25 scores were similar among participants with and without a reported history of depression or anxiety (t = -1.12, p = 0.27). However, for the 18% of participants with PSAT scores consistent with clinical features of juvenile FM (jFM), CD-RISC-25 scores were significantly lower than those seen in the remainder of the study population (t = -3.23, p = 0.0034).

Conclusion: Psychological resilience varied among study participants and was not found to correlate to age at JIA diagnosis, duration of disease, or caregiver resilience. There was no significant difference observed between levels of resilience among participants with and without a reported history of anxiety or depression. In view of the relationships observed between resilience and pain measures among study participants, the differences in resilience of participants with and without clinical features of jFM are compelling. Future research should focus on longitudinal observations to identify whether low psychological resilience may predict the development of secondary FM in JIA patients.

Disclosure: D. Schocken: None; **T. Ting**: None.

Abstract Number: 0369

Trajectory of Progression in Transition Readiness in Adolescents with JIA and jSLE

Dorota Borovsky[1], Lauren Heessels[1], Tania Cellucci[2], Liane Heale[1], Julie Herrington[1], KAREN BEATTIE[1] and Michelle Batthish[2], [1]McMaster University, Hamilton, ON, Canada, [2]McMaster Children's Hospital, Hamilton, ON, Canada

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: For adolescents, the transition from pediatric to adult rheumatology care is associated with increased health risks, poor disease control and loss to follow-up. Optimizing adolescents' ability to manage their own health independently is of utmost importance and ideally begins years before the actual transfer to adult care. Different models of transition programs to improve patient self-management skills have been proposed and implemented, but best-practices have not been identified. We aimed to assess how a multidisciplinary, patient-centred, individualized approach to improving self-management skills affects changes in transition readiness over time among adolescents with JIA and jSLE.

Methods: Patients 14-18 years old with JIA or jSLE seen in the multidisciplinary pediatric rheumatology transition clinic at McMaster Children's Hospital were invited to participate in a prospective study. At each clinic visit, patients are seen by a pediatric and adult rheumatologist together, as well as a nurse, physiotherapist, and child life specialist. Consenting patients completed the Transition-Q, a validated, self-administered 14-item questionnaire which assesses healthcare self-management skills, at consent and at follow-up (FU) clinic visits. Questionnaires are scored from 0-100 with higher scores reflecting higher skills/independence. Responses to individual questions on the TRANSITION-Q identify areas of need and, in partnership with a member of the healthcare team, goals are set for the next clinic visit. Transition-Q scores were determined at baseline and follow-up visits for all participants and then sub-grouped by age and sex. Clinical characteristics (disease duration, disease activity, quality of life) were collected at baseline.

Results: Of 79 participants who completed the Transition-Q at baseline and ≥1 follow-up, 51 (65%) were female and 64 (81%) had JIA (Table 1). Mean (SD) Transition-Q scores improved by 8.0 (12.7) points between baseline and first FU, and 5.9 (10.1) (n=36) between first and second FU. Overall, 75% of males' Transition-Q scores stayed the same or improved from the baseline to first FU compared to 80% of females. Between the baseline and second FU, 92% (n=11/12) of males improved while 96% (23/24) of females improved. Changes in Transition-Q scores for males and females over the first follow-up period are shown in Figures 1 and 2.

Table 1: Baseline Characteristics

	N	Mean (SD)
Age (years)	79	16.0 (1.2)
Disease duration (years)	69	4.0 (3.9)
Transition-Q (max 100)	79	55.9 (14.6)
Peds QL (max 100)	34	80.7 (20.0)
Physician Global Assessment (max 10)	56	0.4 (1.0)
Patient Global Assessment (max 10)	52	1.4 (2.2)
cJADAS (max 30)	43	1.7 (2.5)

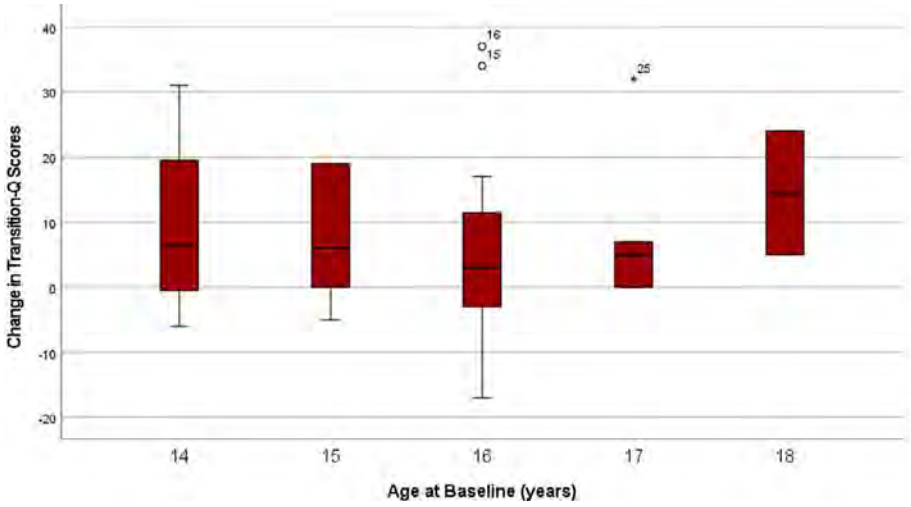

Figure 1: Change in Transition-Q Scores from Baseline to First Follow-Up in Males

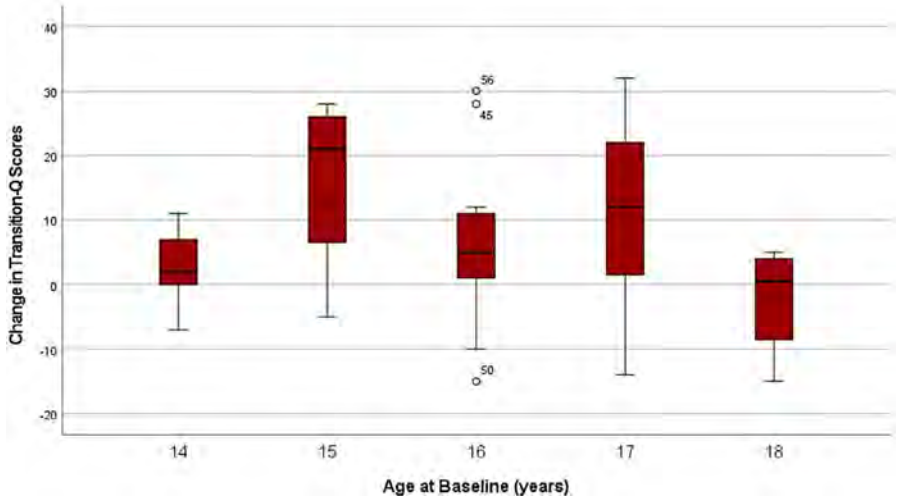

Figure 2: Change in Transition-Q Scores from Baseline to First Follow-Up in Females

Conclusion: In this sample of adolescents with low disease activity, Transition-Q scores improved over time. Males and females do not appear to have the same trajectory of improvement across age groups, and there is considerable variability in improvements within and between age groups. These results suggest that goal setting to improve self-management skills requires an individualized approach within a multidisciplinary clinic. Improvements are evident in adolescents as young as 14, and there is room for ongoing improvement even after adolescents reach 18 years when they transfer to adult care.

Disclosure: D. Borovsky: None; **L. Heessels**: None; **T. Cellucci**: AbbVie/Abbott, 2; **L. Heale**: Novartis, 5; **J. Herrington**: None; **K. BEATTIE**: None; **M. Batthish**: AbbVie/Abbott, 6, Novartis, 1, Viatris, 1, 5.

Abstract Number: 0370

Clinical Disease Manifestations Associated with TNF Inhibitor Non-Response in Juvenile Spondyloarthritis

Melissa Oliver[1], Kelly Mosesso[2], Pamela F. Weiss[3], Robert Colbert[4], Matthew Stoll[5] and **Hemalatha Srinivasalu**[6], [1]Indiana University, Indianapolis, IN, [2]Indiana University School of Medicine, Indianapolis, IN, [3]Children's Hospital of Philadelphia, Philadelphia, PA, [4]NIH/NIAMS, Bethesda, MD, [5]University of Alabama at Birmingham, Birmingham, AL, [6]Children's National Hospital, Washington, DC

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Tumor necrosis factor inhibitors (TNFi) are effective in children with juvenile spondyloarthritis (JSpA) and generally represent the first-line choice for biologic therapy. However, not all JSpA patients respond well to TNFi initially (primary non-response) or respond well but lose efficacy over time (secondary non-response). Children who do not respond to initial TNF inhibition are left with limited options. We aimed to identify the clinical characteristics associated with TNFi non-response in JSpA patients.

Methods: Retrospective analysis of JSpA patients and their response to first TNFi agent enrolled in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry between July 2015 - January 2019. JSpA population included enthesitis-related arthritis, psoriatic arthritis, and undifferentiated spondyloarthritis subtypes. Primary non-response defined as discontinuation of TNFi within the first 3 months of starting. Secondary non-response defined as 1) stopping TNFi AND 2) switching to another biologic or addition of a disease-modifying anti-rheumatic drug (DMARD). Responders were defined those continuing the first TNFi agent for duration of study. Demographic and disease characteristics were compared at 1) baseline visit prior to TNFi start and at 2) time of failure for non-responders or at 4-6 months following TNFi start for responders.

Results: Total of 287 patients met inclusion criteria; 163 TNFi responders and 124 TNFi non-responders. The majority of non-responders were secondary non-responders (91.9%). Median duration prior to initial TNFi failure for non-responders was 274.5 days (IQR:160.5, 433.5). Mean age at TNFi start was 12.5y for non-responders (SD 4.1y) and 12.4y for responders (SD 4.1y) (Table 1). Non-responders were more likely to be female compared to responders, 60.5% vs 48.5% (p=0.04). BMI was higher in non-responders compared to responders, 22.5 vs 21 (p=0.01). Non-responders had more arthritis, enthesitis and sacroiliitis at their baseline visit prior to TNFi start (Table 2) and a post-TNFi start visit (Table 3)

Table 1 Demographics by TNFi response status

Characteristic	Non-responder (N=124)	Responder (N=163)	p value
Sex, Male (n, %)	49 (39.5%)	84 (51.5%)	0.043
Age, y			0.803
Mean (SD)	12.5 (4.1)	12.4 (4.1)	
Race (n, %)			0.706
White	104 (83.9%)	130 (79.8%)	
Black	6 (4.8%)	10 (6.1%)	
Other race	14 (11.3%)	23 (14.1%)	
Not Hispanic or Latino (n, %)	112 (90.3%)	144 (89.4%)	0.593
Positive HLA-B27* (n, %)	37 (30.3%)	53 (34%)	0.773
BMI	22.5 (6.5)	21 (6.3)	0.010

* 18.9% & 19.2% HLA-B27 Not done/Unknown for non-responder & responder group, respectively

Table 2 Clinical characteristics at baseline visit

	Non-responder (N=124)	Responder (N=163)	p value
Active Joint Count Mean (SD)	5.0 (6.3)	4.3 (6.1)	0.072
Active Enthesitis (n, %)	52 (45.2%)	51 (34.2%)	0.070
Active Sacroiliitis (n, %)	37 (29.8%)	29 (17.8%)	0.071
Uveitis (n, %)	6 (4.9%)	3 (2.0%)	0.307
PhGA Mean (SD)	3.2 (2.0)	3.3 (2.4)	0.727
PtGA Mean (SD)	4.6 (2.6)	3.5 (2.5)	0.007
CHAQ Disability Index Mean (SD)	0.7 (0.6)	0.6 (0.6)	0.063

PhGA: Physician Global Assessment; PtGA: Patient Global Assessment

Table 3 Clinical characteristics at post-TNFi start visit

	Non-responder (N=124)	Responder (N=163)	p value
Active Joint Count Mean (SD)	3.0 (6.0)	0.7 (1.7)	<0.001
Active Enthesitis (n, %)	45 (39.8%)	21 (13.9%)	<0.001
Active Sacroiliitis (n, %)	25 (22.9%)	11 (7.6%)	0.001
Uveitis (n, %)	7 (5.7%)	0 (0)	0.003
PhGA Mean (SD)	2.3 (1.9)	0.8 (1.1)	<0.001
PtGA Mean (SD)	4.2 (2.4)	2.1 (2.4)	<0.001
CHAQ Disability Index Mean (SD)	0.6 (0.6)	0.3 (0.5)	<0.001

PhGA: Physician Global Assessment; PtGA: Patient Global Assessment

compared to responders. Following initial TNFi therapy for all the non-responders, most patients switched to 2nd TNFi (60.2%), followed by DMARD (35.2%) then another biologic (4.6%).

Conclusion: JSpA patients who did not respond to initial TNFi had more active disease and more axial involvement at baseline prior to starting therapy. Additionally, the non-responders were found to have higher BMI compared to the responders.

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Abstract Number: 0371

Assessing Methotrexate Adherence in JIA Using Electronic Health Record-Linked Pharmacy Dispensing Data

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Pediatric Rheumatology – Clinical Poster I: JIA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The extent to which lack of adherence to prescribed treatment regimens contributes to differential disease outcomes in JIA – and demographic disparities in these outcomes – is unknown, largely because adherence is challenging to assess. Many methods rely on patient or caregiver report, which tend to overestimate adherence. Pharmacy dispensing data offer an objective means of assessing adherence through metrics such as the medication possession ratio (MPR), which measures the proportion of time a patient has medication available. We aimed to link medication adherence

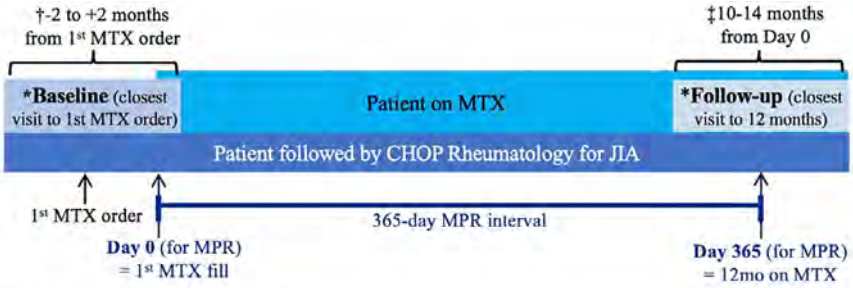

Figure 1. Study design timeline
*Visits from which disease activity data were obtained
†Patients without a visit between -2 and +2 months from the first MTX order were excluded
‡Patients without a visit between the 10- and 14-month window were excluded

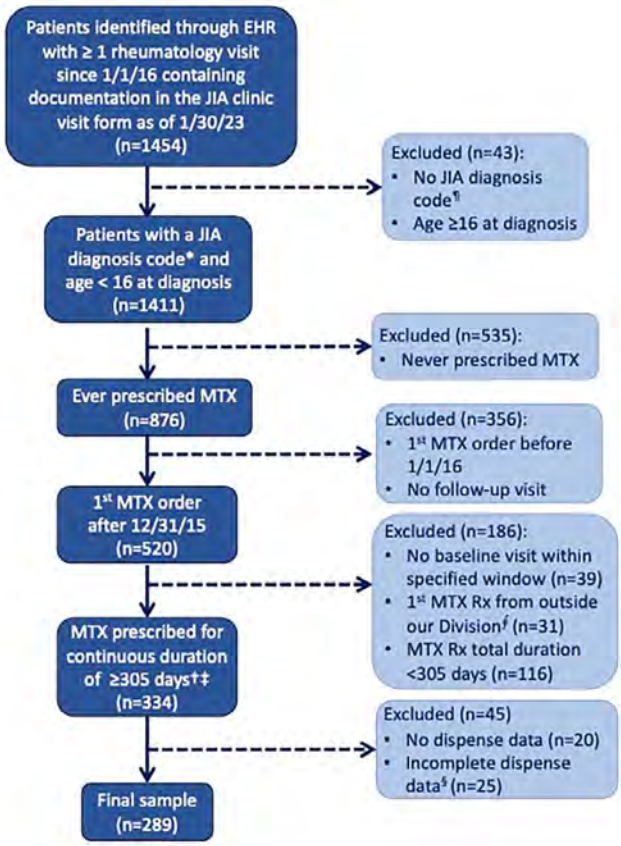

Figure 2. Flow diagram of patient selection into the study sample
*Any diagnosis code within M08, M45, or L40.5
†From prescription orders in the EHR
‡Allowing for 60 days of flexibility to account for follow-up visits that occurred at the 10-month mark
¶Patients with documentation within the JIA visit form but with diagnosis codes of IBD-associated arthritis, reactive arthritis, transient effusion, or Lyme arthritis
ǂOutside institution or different specialty (Gastroenterology, Dermatology)
§Determined by chart review of patients with > 60 days between 1st MTX order and 1st reported dispense

estimates to clinical data in the electronic health record (EHR) to investigate associations between medication adherence, disease activity, and patient characteristics.

Methods: This single-center retrospective cohort study leveraged pharmacy dispensing data from the EHR, provided by Surescripts, to calculate the MPR for MTX for patients with a physician diagnosis of JIA in a large pediatric rheumatology clinic. Surescripts is an information technology company that supports electronic prescriptions and provides this data to subscribing institutions.

All incident users of MTX, treated between January 2016 and May 2022 for ≥12 months with outpatient rheumatology visits within 2 months of the first MTX prescription and after 12 months of follow-up (±2 months) (Figure 1), were included in the sample (Figure 2). MPR was calculated using the total days' supply over a fixed 365-day interval following the initial MTX prescription fill date. Patient-level variables (Table 1), including sociodemographic factors and visit-level clinical factors from the

Table 1. Comparison of baseline characteristics and risk factors between adherence groups

Variable	Mean MPR μ (σ)	Suboptimal adherence (MPR<80%) [n=124]	Optimal adherence (MPR ≥80%) [n=165]	p-value
Age at start of MTX				
<6 years	77.5 (24.5)	42 (33.9)	46 (27.9)	0.30
6-12 years	75.4 (28.8)	45 (36.3)	56 (33.9)	
13+ years	82.8 (21.8)	37 (29.8)	63 (38.2)	
Race/ethnicity				
White	81.3 (24.0)	75 (60.5)	131 (79.4)	
Black	57.7 (29.9)	15 (12.1)	4 (2.4)	
Hispanic / Latino	73.0 (26.7)	16 (12.9)	11 (6.7)	**<0.001**
Asian	71.7 (28.2)	8 (6.5)	4 (2.4)	
Multi-racial / Other	79.4 (23.0)	10 (8.1)	12 (7.3)	
Unknown / Refused / Missing	100.0 (-)	0 (0.0)	3 (1.8)	
Biological Sex				
Female	79.1 (25.8)	84 (67.7)	119 (72.1)	0.44
Male	77.5 (24.4)	40 (32.3)	46 (27.9)	
Insurance Type				
Commercial	81.4 (23.6)	90 (72.6)	141 (85.5)	**0.008**
Public	67.6 (29.1)	34 (27.4)	24 (14.5)	
Nationally Ranked Childhood Opportunity Index		[9 missing]	[14 missing]	
Very Low	52.0 (26.5)	20 (17.4)	2 (1.3)	
Low	74.1 (27.9)	10 (8.7)	8 (5.3)	**<0.001**
Moderate	78.0 (25.6)	12 (10.4)	16 (10.6)	
High	84.6 (20.9)	19 (16.5)	46 (30.5)	
Very High	80.6 (24.2)	54 (47.0)	79 (52.3)	
Baseline disease activity measures				
cJADAS[a] [4/0 missing]	-	μ=8.6 (σ=6.4)	μ=8.4 (σ=6.3)	0.88
Active joint count[b] [1/0 missing]	-	μ=3.6 (σ=5.3)	μ=3.7 (σ=5.6)	0.80
Physician global assessment[c]	-	μ=3.0 (σ=1.9)	μ=3.0 (σ=1.8)	0.69
Patient/parent global assessment[d]	-	μ=3.5 (σ=2.5)	μ=3.8 (σ=2.7)	0.55
Pain intensity score[e]	-	μ=4.1 (σ=2.9)	μ=4.0 (σ=2.8)	0.69
JIA subtype		[1 missing]	[2 missing]	
Oligoarticular persistent	76.0 (26.5)	45 (36.6)	56 (34.4)	
Oligoarticular extended	80.7 (19.2)	6 (4.9)	5 (3.1)	
Polyarticular, RF-positive	78.9 (26.9)	12 (9.8)	15 (9.2)	
Polyarticular, RF-negative	84.6 (19.6)	19 (15.4)	33 (20.2)	0.89
Enthesitis-related arthritis	77.7 (27.8)	22 (17.9)	32 (19.6)	
Systemic	81.8 (31.2)	3 (2.4)	5 (3.1)	
Psoriatic	74.5 (30.6)	7 (5.7)	10 (6.1)	
Undifferentiated	79.1 (20.4)	9 (7.3)	7 (4.3)	
Route of MTX				
Subcutaneous	78.1 (25.8)	79 (63.7)	102 (61.8)	0.81
Oral	79.5 (24.7)	45 (36.3)	63 (38.2)	
MTX monotherapy				
Yes	79.9 (24.1)	74 (59.7)	103 (62.4)	0.71
No	76.5 (27.1)	50 (40.3)	62 (37.6)	
MTX + biologic combination therapy				
Yes	75.8 (26.5)	38 (30.6)	43 (26.1)	0.43
No	79.7 (24.9)	86 (69.4)	122 (73.9)	
Uveitis diagnosis				
Yes	75.2 (26.8)	15 (12.1)	17 (10.3)	0.71
No	79.0 (25.2)	109 (87.9)	148 (89.7)	
Mental health diagnosis				
Yes	82.7 (17.9)	12 (9.7)	14 (8.5)	0.84
No	78.2 (26.0)	112 (90.3)	151 (91.5)	

[a]cJADAS = three-variable clinical Juvenile Arthritis Disease Activity Score (range 0,30); [b]Active joint count (sample range 0,33); [c]Physician global assessment of disease activity visual analog scale (range 0,10); [d]Patient/parent global assessment of disease activity visual analog scale (range 0,10); [e]Pain visual analog scale score (range 0,10)

baseline and follow-up visits, were extracted from the EHR. We dichotomized MPRs into optimal adherence (MPR ≥80%) and suboptimal adherence (MPR < 80%) groups. Patient characteristics were compared between the adherence groups using Fisher's exact test for categorical variables and the Wilcoxon rank sum test for continuous variables.

Results: A total of 289 patients were included in the analysis (Figure 2). There was a mean of 9.4 dispenses per patient (SD 3.7) within the first year. Three patients had only 1 MTX dispense reported. The mean MPR was 84.5% (SD 32.3) and the majority (57.1%) of patients were classified as having optimal adherence. Patient race, public insurance, and a lower childhood opportunity index were associated with suboptimal adherence (Table 1). There were no statistically significant associations between adherence and disease activity at baseline, JIA subtype, route of MTX, concomitant use of biologics, or presence of uveitis or a mental health diagnosis.

Conclusion: Our findings demonstrate socioeconomic disparities in adherence to MTX among a cohort of patients with JIA. This method of linking dispense data to clinical data available in the EHR offers an objective approach to assessing adherence to chronic medications, but it should be validated against other methods. Future analyses will investigate associations between patient characteristics, MTX adherence, and disease activity using multivariable models. Qualitative work exploring patient perspectives on mechanisms that influence medication adherence will inform future adherence-focused interventions.

Disclosure: D. Abel: None; **D. Anderson**: None; **M. Kallan**: None; **L. Utidjian**: None; **J. Chang**: None; **C. Kenyon**: None; **S. Gmuca**: None.

Abstract Number: 0372

Efficacy and Safety of Secukinumab in Juvenile Idiopathic Arthritis: Interim Results from the Extension of the JUNIPERA Trial

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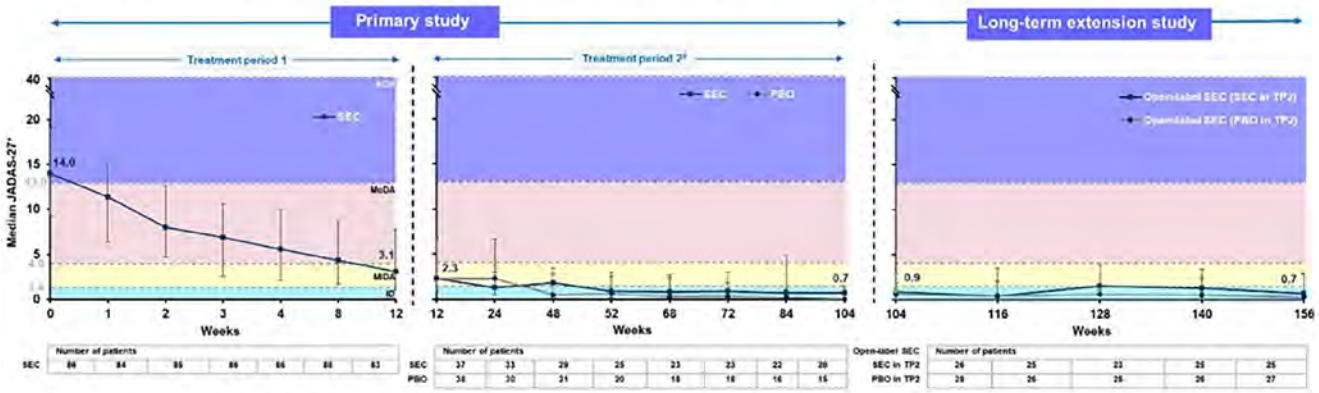
SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Secukinumab has demonstrated efficacy and safety in patients with enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA) categories of juvenile idiopathic arthritis (JIA) for up to 2 years.[1] After completion of a 2-year primary study (JUNIPERA), a long-term extension (LTE) study was conducted to evaluate the continued efficacy

Figure. Median JADAS-27 over time in the primary study (TP1 and TP2) and long-term extension study



*JADAS-27 median cut-off values[a]: ID, 0-1.4; MDA, 1.5-4.0; MoDA, 4.1-13.0; HDA, >13.0. JADAS-27 ranges from 0 to 57 (higher scores indicate more disease activity)

[a]Patients received open-label secukinumab in TP1 and were randomized to received placebo or secukinumab in TP2. Patients with placebo who flared in TP2 of the primary study entered TP3 to receive open-label secukinumab. TP2 data presented here (week 12 to week 104) include only TP2 patients.

The upper and lower error bars represent the third (Q3) and first (Q1) quartiles, respectively.

[a]Trincianti et al. *Arthritis Rheumatol*. 2021;73:1966-1975.

HDA, high disease activity; ID, inactive disease; JADAS-27, Juvenile Arthritis Disease Activity Score in 27 joints; MDA, minimal disease activity; MoDA, moderate disease activity; PBO, placebo; SEC, secukinumab; TP, treatment period.

and safety of secukinumab in patients with ERA and JPsA. Here we report the interim efficacy and safety results of the LTE study.

Methods: In the primary study, a total of 86 patients (2 to < 18 years of age) received secukinumab up to week 12 in the open-label period.[1] JIA American College of Rheumatology (ACR)30 responders at week 12 (n=75) were subsequently randomized to secukinumab (n=37) or placebo (n=38) up to week 100 in study period 2. Those who flared after randomization (secukinumab, n=10; placebo, n=21) received open-label secukinumab in study period 3 up to week 100.[1] A total of 55 of 61 patients who had completed the primary study consented to enter the LTE study, among which 54 patients received secukinumab (subcutaneous; 75/150 mg in patients < 50/≥50 kg) every 4 weeks up to 4 years. Patients whose signs and symptoms were not fully controlled, as judged by the investigator in the LTE study, could have dose escalation of their secukinumab dose from 75 mg to 150 mg or 150 mg to 300 mg. Median Juvenile Arthritis Disease Activity Scores (JADAS)-27 were presented up to week 156 for efficacy, and adverse events (AEs) and serious AEs were presented for the entire treatment period up to the cut-off date (02-Feb-2022).

Results: JADAS-27 in the primary study and in the LTE study are presented in the **Figure**. A total of 19 patients had dose escalation in the LTE study: 8 patients from 75 mg to 150 mg and 11 patients from 150 mg to 300 mg. The overall exposure-adjusted incidence rate per 100 patient-years (PY) of treatment-emergent AEs was 98.4 PY in the entire JIA population. The most commonly reported AEs were nasopharyngitis (n=9, 16.7%) and arthralgia (n=8, 14.8%). One major adverse cardiovascular event, not related to the study drug, and 2 cases of uveitis were reported. No cases of Crohn's disease or deaths were reported, and no patient discontinued treatment due to an AE.

Conclusion: With secukinumab treatment, the JADAS-27 inactive disease status was sustained from week 104 to week 156 in patients with JIA who had completed the 2-year primary study and enrolled in the LTE study. Safety data were consistent with adult and pediatric indications, with no new or unexpected safety signals.

Reference:

1. Brunner HI, et al. *Ann Rheum Dis*. 2023;82(1):154-160.

Disclosure: H. Brunner: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb (BMS), 2, 5, Celgene, 2, Eli Lilly, 2, 5, EMD Serono, 2, F-Hoffman La Roche, 2, 5, GlaxoSmithKlein (GSK), 2, 5, 6, Horizon, 2, 2, Janssen, 5, Merck, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6; **I. Foeldvari**: AbbVie, 2, Bayer, 2, BMF, 2, Bristol-Myers Squibb(BMS), 2, Chugai, 2, Genentech, 2, Medac, 2, Novartis, 2, Pfizer, 2, Sanofi, 2; **E. Alexeeva**: Amgen, 5, 6, Eli Lilly, 5, 6, MSD, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Roche, 5, 6, Sanofi, 5, 6; **N. Ayaz**: None; **G. Schulert**: IpiNovyx, 5, SOBI, 2; **S. Ozen**: None; **A. Popov**: None; **A. Ramanan**: Eli Lilly, 6, Novartis, 6, Roche, 6, Sobi, 6, UCB, 6; **C. Scott**: None; **B. Sozeri**: None; **E. Zholobova**: AbbVie, 6, Novartis, 5, 6, Pfizer, 5, 6, Roche, 6; **S. Chakraborty**: IQVIA, 3, 11; **X. Zhu**: Novartis, 3, 11; **R. Martin**: Novartis, 3, 11; **S. Whelan**: Novartis, 3, 11; **S. Kaur**: Novartis, 3, 11; **L. Pricop**: Novartis, 3, 11; **D. Lovell**: Abbott, 2, 6, AbbVie, 2, Amgen, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Canadian Arthritis Society, 1, Celgene, 2, Forest Research, 1, GlaxoSmithKlein(GSK), 2, Hoffmann-La Roche, 2, Janssen, 2, NIH-NIAMS, 1, Novartis, 2, 6, Pfizer, 2, United Bioscience Corporation, 2, Wyeth, 2; **A. Martini**: AbbVie, 2, 6, Eli Lilly, 2, 6, EMD Serono, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **N. Ruperto**: Ablynx, 2, 6, AstraZeneca-Medimmune, 2, 6, Bayer, 2, 6, Biogen, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb (BMS), 2, 5, 6, Celgene, 5, 12, Personal Fees, Non-Financial Support, Eli Lilly, 2, 5, 6, EMD Serono, 2, 6, F. Hoffman-La Roche, 2, 5, 6, GlaxoSmithKlein (GSK), 2, 5, 6, Janssen, 2, 5, 6, Merck/MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, R-Pharma, 2, 6, Sinergie, 2, 6, Sobi, 2, 5, 6, UCB, 2, 5.

Abstract Number: 0373

Potential Tear-Based Uveitis Biomarkers in Children with JIA: A Pilot Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Children with oligoarticular JIA are at increased risk of developing uveitis. JIA category, ANA positivity, ≤4 years JIA duration, and < 6 years old at diagnosis are known risk factors. Regular ophthalmic examination is important for screening since uveitis is asymptomatic. Tear fluid is easily obtained and has been used for biomarker studies. This pilot study aims to identify potential tear-based inflammatory markers that can differentiate children with JIA who develop uveitis.

Methods: This prospective cohort study at Cincinnati Children's compared children with JIA-associated uveitis (JIA-U) and JIA without uveitis (JIA-no-U) with oligoarticular subtype. Medical charts were reviewed for demographics, uveitis characteristics, ophthalmic examination, and current treatment. Tear fluid was collected by Schirmer strips. We used advanced proteomic strategies (isobaric tag for relative quantitation [iTRAQ] labeling and nanoLC-MS/MS) to quantify proteins in the left eye of patients with JIA-U and JIA-no-U in duplicate. In those with unilateral JIA-U, the affected eye was used. We reported the log of the mean of the ratios derived from two abundance readings per protein for each subject. Based on a Wilcoxon rank sum exact test we considered a P-value < 0.1 to be significant.

Table 1

TABLE 1. DEMOGRAPHICS AND CLINICAL CHARACTERISTICS OF CHILDREN WITH JIA WITH AND WITHOUT UVEITIS.

n (%), unless otherwise specified	TOTAL Cohort (n=28)	JIA-no-U (n=14)	JIA-U (n=14)	p value
DEMOGRAPHIC CHARACTERISTICS				
Female	25 (89.2)	13 (92.8)	12 (85.7)	ns
Age at onset of JIA median (range)	4 (1-8)	4 (2-8)	3 (1-4)	0.049
Age at uveitis diagnosis (yrs)	4 (2-7)	NA	4 (2-7)	ns
Oligo JIA	28 (100)	14 (100)	14 (100)	ns
Race White	27 (96.4)	14 (100)	13 (92.8)	ns
Asian	1 (3.6)	0	1 (7.2)	ns
Ethnicity Non-Hispanic	28 (100)	14 (100)	14 (100)	ns
ANA positivity	18 (64.2)	8 (57.1)	10 (71.4)	ns
Median age at tear collection (range)	11 (5-20)	11 (5-20)	13 (6-18)	
N of patients with active arthritis	11 (39.2)	5 (35.7)	6 (42.8)	ns
UVEITIS CHARACTERISTICS				
Anterior location	14/14 (100)	NA	14 (100)	-
Bilateral involvement	12/14 (85.7)	NA	12 (85.7)	-
Active uveitis at tear collection[A]	3/14 (21.4)	NA	3 (21.4)	-
MEDICATIONS AT TIME OF TEAR COLLECTION				
Topical glucocorticoids	6/14 (42.8)	NA	6 (42.8)	-
Methotrexate	10 (35.7)	4 (28.5)	6 (42.8)	ns
Leflunomide	5 (17.8)	5 (35.7)	0	ns
Infliximab	5 (17.8)	2 (14.2)	3 (21.4)	ns
Adalimumab	3 (10.7)	0	3 (21.4)	ns
Etanercept	2 (7.1)	2 (14.2)	0	ns
Golimumab	1 (3.5)	0	1 (7.2)	ns
Tocilizumab	2 (7.1)	0	2 (14)	ns

[A]Values determined per SUN criteria, *JIA-U* JIA-associated uveitis, *JIA-no-U* JIA without uveitis; ns: non significant. List of abbreviations: JIA-U: juvenile idiopathic arthritis-associated uveitis, JIA-no-uveitis: JIA without uveitis, YRS: years, N: number

Results: Tear samples of 28 JIA patients were collected (14 JIA-U and 14 JIA-no-U). Demographic and clinical characteristics are summarized (Table 1). Thirteen proteins exhibited differences in tears of 14 children with JIA-U and 14 with JIA-no-U (Table 2). Of these, 8 showed a difference at $p \leq 0.05$. All the proteins were higher in the group of JIA-no-U except for cathepsin D. Cathepsin D and Transitional endoplasmic reticulum ATPase have been associated with the retinal pigment epithelium (RPE) and maintaining the blood-retinal barrier (BRB). As 39% of patients had active arthritis at the time of tear collection, we stratified the analysis by arthritis activity as joint inflammation could affect the presence and level of inflammatory mediators (Table 3). A larger number of proteins differentiated patients with JIA-U and JIA-no-U p who had inactive arthritis (Table 3). Specifically, complement 3, apolipoprotein, S100 proteins, transthyretin, and beta-2 microglobulin have been associated with uveitis.

Conclusion: Uveitis is a vision-threatening disease that warrants exploration of techniques for early detection and treatment. The eye is an immune-privileged organ immunologically shielded by the RPE as part of the BRB. We hypothesize that the immune response proteins identified within the tears of JIA-U patients are by-products of inflammation-induced RPE and BRB breakdown, promoting the inflammatory cascade. Tears of children with JIA-U and JIA-no-U display differential expression of proteins, but it seems to be influenced by arthritis activity. Further study in larger cohorts is needed to verify these results.

Table 2

Table 2. Differentially expressed proteins in children with JIA-no-U and JIA-U. Comparison of mean values is indicated by color. Red color reflects higher expression

Protein	JIA U (N =14) log of the mean of the ratio	JIA – no – U (N = 14) log of the mean of the ratio	P value
Alpha-2-macroglobulin	-0.068	0.3358	0.0067
Protein S100-A9	-0.1274	0.1914	0.0091
Thymidine phosphorylase	-0.1136	0.1144	0.0141
Apolipoprotein A-I	-0.0321	0.3302	0.031
Protein S100-A11	-0.0911	0.2171	0.039
Immunoglobulin J chain	-0.0884	0.2398	0.0497
Transthyretin	-0.044	0.193	0.05
Transitional endoplasmic reticulum ATPase	-0.0236	0.1905	0.05
Histone H1.4	0.0166	0.1183	0.062
Immunoglobulin alpha-2 heavy chain	-0.0889	0.2548	0.069
Cathepsin D	0.1002	-0.0453	0.0849
Haptoglobin	-0.0301	0.157	0.0939
Interleukin-1 receptor antagonist protein	-0.0608	0.2259	0.0939

List of abbreviations: JIA-U: Juvenile Idiopathic Arthritis associated uveitis, JIA-no-U: Juvenile Idiopathic Arthritis without uveitis

Table 3

Table 3: Differentially expressed proteins in children with JIA-U and JIA-no-U, stratified by arthritis status. The red color reflects higher expression.

Proteins in patients WITHOUT active arthritis (N = 17)	JIA-U (N=8) log of the mean of the ratio	JIA-no-U (N=9) log of the mean of the ratio	P value
Complement C3	-0.161	0.2043	0.0079
Apolipoprotein A-I	-0.1777	0.4159	0.0079
Alpha-2-macroglobulin	-0.0995	0.4405	0.0111
Protein S100-P	-0.091	0.4196	0.0111
Immunoglobulin gamma-1 heavy chain	-0.0957	0.4614	0.0206
Protein S100-A9	-0.1056	0.2944	0.0274
Cofilin-1	-0.0641	0.2493	0.0274
Profilin 1	-0.0865	0.2755	0.036
Vitamin D-binding protein	-0.0589	0.1227	0.0592
Hemopexin	-0.0827	0.1517	0.0592
Gelsolin	-0.0107	0.1487	0.0592
Ubiquitin-60S ribosomal protein L40	-0.0956	0.2901	0.0592
Adenylyl cyclase-associated protein	-0.1129	0.2247	0.0592
Haptoglobin	-0.1643	0.0764	0.0745
Antithrombin-III	-0.0779	0.2252	0.0745
Transthyretin	-0.0416	0.2486	0.0745
Glucose-6-phosphate isomerase	-0.0731	0.275	0.0745
Protein disulfide-isomerase	-0.0713	0.1773	0.0745
Lysozyme	0.2161	-0.172	0.0745
WD repeat-containing protein 1	-0.1211	0.151	0.0927
Antileukoproteinase	0.1963	-0.109	0.0927
Interleukin-1 receptor antagonist protein	-0.0263	0.2908	0.0927
Transketolase	-0.1011	0.329	0,0927
DNA dC->dU-editing enzyme APOBEC-3A	-0.0778	0.2592	0.0927
Beta-2-microglobulin	0.4255	-0.061	0.0927

Proteins in patients WITH active arthritis (N =11)	JIA U (N=6) log of the mean of the ratio	JIA-no-U (N=5) log of the mean of the ratio	P value
Cystatin-S	-0.340	0.278	0.0519
Zymogen granule protein 16 homolog B	0.0634	0.4903	0.0519
Immunoglobulin J chain	-0.172	0.2701	0.0823
Lactoperoxidase	0.1178	0.4762	0.0823
Lipocalin-1	-0.031	0.364	0.0823

Comparison of log of the mean of the ratio is indicated by color. Red color reflects higher expression. List of abbreviations: JIA-U: Juvenile Idiopathic Arthritis associated uveitis, JIA-no-U: Juvenile Idiopathic Arthritis without uveitis

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Abstract Number: 0374

Actionable Adverse Events in a Real-Practice Cohort of Children with Juvenile Idiopathic Arthritis. Results from the CAPRI Registry

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SESSION INFORMATION

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Session Title: Pediatric Rheumatology – Clinical Poster I: JIA

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Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory rheumatic disease of childhood and most children require long-term treatment. Adverse events (AE) during treatment may negatively influence disease control and quality of life, and may result in permanent harm.

Table 1. Demographics of patients included in the study

Number of patients	721
Female, n (%)	429 (61.2)
Mean age at baseline	9
JIA category, n (%)	
Oligoarthritis	321 (44.5)
Polyarthritis rheumatoid factor negative	131 (18.2)
Polyarthritis rheumatoid factor positive	26 (3.6)
Enthesitis-related arthritis	116 (16.1)
Systemic arthritis	31 (4.3)
Psoriasis arthritis	46 (6.4)
Undifferentiated arthritis	50 (6.9)
Medications, calculated per visit, no. (%)	
Naproxen	1691 (37.6)
Other NSAID	455 (10.1)
MTX PO	957 (21.3)
MTX SC	1041 (23.1)
Other DMARD	137 (3)
Biologics	967 (21.5)
Systemic glucocorticoids	304 (6.8)
Ocular corticosteroids	128 (2.8)
No Medication	841 (18.7)

NSAID, nonsteroidal anti-inflammatory drug; MTX, methotrexate; DMARD, disease modifying anti-rheumatic drug

In this study, we aim to describe the frequency, seriousness and consequences of physician reported actionable AE in an inception cohort of children with JIA, the Canadian Alliance of Pediatric Rheumatology Investigators (CAPRI) JIA Registry.

Methods: For this study, registry data were extracted on December 18, 2021. Recruitment into the CAPRI JIA registry began in February 2017 to prospectively collect information on children within 3 months of JIA diagnosis at 16 participating sites. Core data were collected at every clinic visit including information on actionable AE since previous visit reported by clinicians. An actionable AE was defined as any untoward medical occurrence that requires additional medical visits, investigations, treatment, or a change in arthritis medications, irrespective of its cause. A serious AE was defined as an event that results in death, is life-threatening, requires hospitalization, or results in a significant disability or a congenital anomaly (or requires medical intervention to prevent these).

Results: Patients included in the study were comparable to Western JIA inception cohorts (Table 1). Actionable AE were reported in 261 out of 721 patients (36.2%) at 478 of 4503 visits (10.6%), during a total observation period of 1,207 patient years. The AE rate was 39 per 100 patient years. The serious AE rate was 2.9 events per 100 patient years. The probability that a patient newly diagnosed with JIA will develop an AE during the first year after diagnosis was 34% (95% CI 30-38, Kaplan-Meier estimate). Interestingly, for 67 (25.7%) patients an AE was reported at the study enrolment visit. Most patients (60%) had only 1 visit with an AE but some had multiple visits (range 1-8). The most frequent reported AE were gastrointestinal, primarily nausea and vomiting (n=217, 45.4% of all AE) and abdominal pain (n=51, 10.7%). There were 34 serious AE in 27 patients. The most frequent serious AE were infections with hospitalization (n=9, 0.75 per 100 patient-years), followed by eye surgery (n=5) and gastrointestinal bleed (n=4). There were no reported deaths, malignancies, demyelinating diseases or tuberculosis. More than half (53.8%) of the visits with a reported AE were in patients receiving non-steroidal anti-inflammatory drug (NSAID) either alone or in combination with other medications, most frequently if the combination was

Table 2. List of actionable adverse events

List of adverse events	All/Serious
Most common and/or serious adverse events grouped by system	
Gastro-intestinal symptoms	**315/7**
Nausea/vomiting	217/2
Abdominal pain	51/0
GI bleed	15/4
Epigastric pain	11/0
Mouth ulcers	10/0
Diarrhea	9/0
Appendicitis	1/1
Behavioral symptoms	**39/2**
Mood changes	15/0
Fatigue	8/0
Headaches	7/0
Dizziness	7/0
Anxiety	5/1
Depression	1/1
Cutaneous symptoms	**27/2**
Rash	18/1
Facial edema	2/1
Infections	**14/0**
Musculo-skeletal symptoms	**7/2**
Joint injury	4/1
Fractures	2/1
Respiratory symptoms	**7/1**
Hemoptysis	2/1
Endocrine/metabolic symptoms	**6/3**
Adrenal suppression	2/2
Diabetes type 1	1/1
Laboratory abnormality	**53/2**
Abnormal liver function	28/0
Abnormal blood counts	21/1
Elevated PTT	1/1
Special events	
Anaphylaxis	--
Infection with hospitalization	9/9
Tuberculosis	--
Opportunistic infection	--
Demyelinating disease	--
IBD	1/1
Malignancy	--
GI perforation	--
Complications	
Eye surgery	6/5
Joint surgery	1/0
Macrophage activation syndrome	1/0

with methotrexate. The most common action taken by the clinician reporting an AE was additional treatment (n= 171, 35.8%), followed by stopping medication (n= 122, 25.5%), and by changing dose or route of medication (n= 93, 19.5%).

Conclusion: In our cohort, actionable AE were reported in over a third of JIA patients, but serious AE were rare. Most AE were gastrointestinal and managed with additional treatment. Increasing awareness to these actionable AE is important to improve health outcomes of patients with JIA.

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Abstract Number: 0375

Treatment of Methotrexate Intolerance in Juvenile Idiopathic Arthritis Using Eye Movement Desensitization and Reprocessing (EMDR) Can Be Improved by Bi-lateral Alternating Stimulation Tactile (BLAST) Armbands

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SESSION INFORMATION
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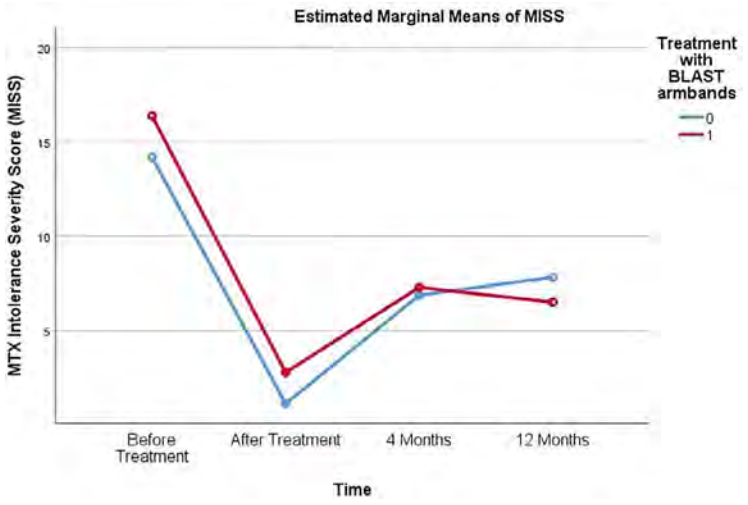
Background/Purpose: Methotrexate (MTX) is commonly used in the treatment of children with juvenile idiopathic arthritis (JIA), and intolerance to the drug frequently leads to discontinuation due to anticipatory and associative gastrointestinal symptoms. Eye Movement Desensitization and Reprocessing (EMDR) is a psychotherapy which has been successfully used in MTX intolerance, however with diminishing efficacy over time. BLAST (bi-lateral alternating stimulation tactile) armbands utilize a similar process to EMDR and have already been used in conjunction with this method.

The aim of this study was to determine if utilization of BLAST armbands could improve and prolong the effect of EMDR on patients with MTX intolerance.

Methods: Consecutive patients admitted to the German Center for Pediatric and Adolescent Rheumatology from October 2016 until March 2023 were included in this study. Inclusion criteria were 1) diagnosis of JIA according to ILAR criteria, 2) age between 8 and 17 years, 3) symptoms of MTX intolerance using the Methotrexate Intolerance Severity Score (MISS) questionnaire and 4) necessity of MTX treatment for at least 6 more months as determined by the treating physician. The standard 8 phase EMDR protocol was adapted for the treatment of MTX intolerance. Treatment started with a structured psychosocial and medical history. Subsequently, five sessions lasting 60 minutes each were held over a time period of 10 – 12 days, concluding with an application of MTX in a clinical setting. The initial 50 patients were treated only with EMDR, as previously published (Höfel et al. Pediatric Rheumatology (2018) 16:11). Subsequent patients were treated with EMDR and BLAST armbands which patients continued to use after the initial treatment sessions.



Estimated marginal means of MISS values over time in the two groups of patients with MTX-Intolerance, treated (1) or not treated (0) with BLAST armbands.

Health-related quality of live was determined using the PedsQL. Measurements of MISS and PedsQL were taken at 4 time points: directly before and after (MISS only) treatment, as well as 4 and 12 months after treatment. Changes in MISS and PedsQL were compared using descriptive statistics and repeated measures ANOVA.

Results: 93 patients with MTX intolerance [median MISS at inclusion: 14 (range 6 - 26)] were included, 50 in group 1 without BLAST armbands and 43 in group 2 which were concurrently treated with BLAST armbands. Directly after treatment, all patients reported marked improvement of MTX intolerance symptoms [group 1: median MISS: 1 (0 – 6), group 2: median MISS: 2 (0 – 11)]. Four months after treatment, median MISS score in group 1 was 5.5 (0-26), and 5 (0-25) in group 2. After 12 months median MISS was 8 (0-33) in group 1, and 6 (0-17) in group 2. A repeated measures ANOVA showed a significant difference between the MISS results ($F(3,105) = 53.7$, $p = .000$). Median quality of life as measured by the PedsQL rose after 12 months from 79.4 to 87.0 in group 1, and from 72.7 to 91.3 in group 2.

Conclusion: Treatment with Eye Movement Desensitization and Reprocessing (EMDR) presents an effective treatment of MTX intolerance, and further significant improvement can be achieved using BLAST armbands. This can facilitate continuation of MTX treatment in patients with MTX intolerance and has the potential to significantly increase quality of life in affected children.

Disclosure: L. Höfel: None; **B. Eppler**: None; **J. Haas**: None; **B. Hugle**: None.

Abstract Number: 0376

Switching Patterns of Biological and Targeted Synthetic Therapies in Juvenile Idiopathic Arthritis

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SESSION INFORMATION

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Background/Purpose: New therapies have improved the therapeutic management of juvenile idiopathic arthritis (JIA), allowing disease control in cases that are refractory or intolerant to methotrexate. However, satisfactory disease control is not achieved in all patients with the first biological and targeted synthetic therapies (ts/bDMARDs) and need switching to another. The choice of ts/bDMARDs for switching is made on an individual basis and influenced by several reasons, mainly the indication for each JIA category, but also previous drug discontinuation causes, concomitant therapy, and comorbidities. Therefore, clinicians are increasingly familiar with the clinical profiles of this treatments and the evidence in halting disease progression. In this study, we aimed to obtain information from real clinical practice about the management of JIA patients to characterize the trends in biologic utilization and switching among JIA categories.

Methods: We conducted a multicentre, observational, longitudinal study of JIA patients, following International League of Associations for Rheumatology (ILAR) classification categories: a) oligoarthritis; b) rheumatoid factor (RF) positive polyarthritis; c) RF negative polyarthritis; d) systemic arthritis; e) psoriatic arthritis; f) enthesitis-related arthritis. Our outcome measure was 'switch' (defined as ≥ 2 ts/bDMARDs courses for therapy). The independent variable was exposure to ts/bDMARDs including: a) TNF inhibitors (infliximab, adalimumab, etanercept, certolizumab, golimumab); b) Other bDMADRs: anti-IL6 (tocilizumab); anti-CTLA4 (abatacept); anti-IL1 (anakinra, canakinumab); anti-IL17 (secukinumab); anti-IL12/23 (ustekinumab); anti-CD20 (rituximab) c) tsDMARDs (tofacitinib). We did a descriptive analysis of the switching, stratified by JIA categories. We also did a bivariate analysis of variables associated with "difficult-to-treat" JIA (≥2ts/bDMARDs with different mechanisms of action)

Table 1. ts/bDMARDs courses and switch among JIA categories.

Oligoarthritis (n=215) N (%)	RF positive polyarthritis (n=16) N (%)	RF negative polyarthritis (n=65) N (%)	Enthesitis-related arthritis (n=39) N (%)	Systemic arthritis(n=44) N (%)	Psoriatic arthritis (n=24) N (%)	
1st ts/bDMARD •Anti-TNF : 99 (100) •Other bDMARDs: 0 •JAKi: 0	1st ts/bDMARD •Anti-TNF : 11 (85) •Other bDMARDs: 2 (15) •JAKi: 0	1st ts/bDMARD •Anti-TNF : 45 (98) •Other bDMARDs : 1(2) •JAKi: 0	1st ts/bDMARD •Anti-TNF : 16 (100) •Other bDMARDs : 0 •JAKi: 0	1st ts/bDMARD •Anti-TNF : 10 (34) •Other bDMARDs : 19 (66) •JAKi: 0	1st ts/bDMARD •Anti-TNF : 21 (100) •Other bDMARDs : 0 •JAKi: 0	
2nd ts/bDMARD •Anti-TNF : 20 (80) •Other bDMARDs : 5 (20) •JAKi: 0	2nd ts/bDMARD •Anti-TNF : 1 (33) •Other bDMARDs : 2 (67) •JAKi: 0	2nd ts/bDMARD •Anti-TNF : 9 (60) •Other bDMARDs : 6 (40) •JAKi: 0	2nd ts/bDMARD •Anti-TNF : 5 (83) •Other bDMARDs : 1 (17) •JAKi: 0	2nd ts/bDMARD •Anti-TNF : 1 (9) •Other bDMARDs : 10 (91) •JAKi: 0	2nd ts/bDMARD •Anti-TNF : 5 (100) •Other bDMARDs : 0 •JAKi: 0	1th switch or 2nd course (n=65)
3nd ts/bDMARD •Anti-TNF : 4 (80) •Other bDMARDs : 0 •JAKi: 1 (20)	3nd ts/bDMARD •Anti-TNF : 2 (100) •Other bDMARDs : 0 •JAKi: 0	3nd ts/bDMARD •Anti-TNF : 4 (67) •Other bDMARDs : 2 (36) •JAKi: 0	3nd ts/bDMARD •Anti-TNF : 1 (100) •Other bDMARDs : 0 •JAKi: 0	3nd ts/bDMARD •Anti-TNF : 1 (17) •Other bDMARDs : 5 (83) •JAKi: 0	3nd ts/bDMARD •Anti-TNF : 2 (100) •Other bDMARDs : 0 •JAKi: 0	2nd switch or 3rd course (n=22)
4nd ts/bDMARD •Anti-TNF : 0 •Other bDMARDs: 1 (100) •JAKi: 0	4nd ts/bDMARD •Anti-TNF : 0 •Other bDMARDs : 0 •JAKi: 1 (100)	4nd ts/bDMARD •Anti-TNF : 0 •Other bDMARDs : 1 (100) •JAKi: 0	4nd ts/bDMARD •Anti-TNF : 0 •Other bDMARDs : 0 •JAKi: 0	4nd ts/bDMARD •Anti-TNF : 2 (67) •Other bDMARDs : 1 (33) •JAKi: 0	4nd ts/bDMARD •Anti-TNF : 1 (50) •Other bDMARDs : 1 (50) •JAKi: 0	3rd switch or 4th course (n=8)
5nd ts/bDMARD •Anti-TNF : 0 •Other bDMARDs : 1 (100) •JAKi: 0	5nd ts/bDMARD •Anti-TNF : 0 •Other bDMARDs : 0 •JAKi: 0	5nd ts/bDMARD •Anti-TNF : 0 •Other bDMARDs : 0 •JAKi: 0	5nd ts/bDMARD •Anti-TNF : 0 •Other bDMARDs : 0 •JAKi: 0	5nd ts/bDMARD •Anti-TNF : 0 •Other bDMARDs : 0 •JAKi: 0	5nd ts/bDMARD •Anti-TNF : 0 •Other bDMARDs : 1 (50) •JAKi: 0	4th switch or 5th course (n=2)

Results: In our cohort of 403 patients with JIA, the mean age at onset was 5.80 ± 4.46 years and 65.84% were females. A total of 235 (58.17%) patients received a bDMARD, with a total of 321 courses. Globally, TNF inhibitors were the most used bDMARDs, with 260 (81%) courses of treatment, although in systemic JIA, as expected, anti-IL1 and anti-IL6 were most used (Table 1). 28% of patients switched bDMARDs and we found a total of 97 ts/bDMARD switches. Of these, 28 (7%) patients met the definition of difficult-to-treat JIA patients. Our analysis identified that systemic JIA was the category with more changes among mechanisms of actions of ts/BDMARDs (p=0.001), representing 39% of the total switches. Long-term disease was also associated with high switching between ts/bDMARDs (p=0.01). Stratified analysis revealed distinct switching patterns in the different JIA categories (Table 1).

Conclusion: In this cohort, approximately a quarter of patients did not respond to the initial ts/bDMARD and need switching to another ts/bDMARD. Our stratified analysis found that the JIA category defines the choice of ts/bDMARD and treatment sequences. This real-world data study can give useful information about treatment patterns and trend for switching in routine clinical practice.

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Abstract Number: 0377

Disease Activity and New Medication Start at Two Consecutive Registry Visits for Patients with Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
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Background/Purpose: The goal of treatment for patients with juvenile idiopathic arthritis (JIA) is inactive or minimal disease activity and escalating medication for active disease is recommended. The goal of this analysis is to assess patterns of disease activity at 2 sequential registry visits and associated new medication start.

Methods: Patients with JIA enrolled in the Childhood Arthritis and Rheumatology Research Alliance Registry, a North American multicenter registry, with complete clinical Juvenile Arthritis Disease Activity Scores (cJADAS) at the 6 month and 12-month registry visits were included. Disease activity at each visit was classified according to cJADAS categories (inactive, minimal, moderate, or high) for either oligo- or polyarticular disease course, regardless of JIA categorization. Patient characteristics were determined at the 12-month Registry visit. The primary outcome was new medication (methotrexate or biologic) start at the 12-month visit determined by a clinical site attestation. Stratifying by the respective pairings of 6- and 12-month cJADAS categories, we examined the association between paired cJADAS values, disease activity, and medication changes.

Table 1: Characteristics of patients with JIA by disease activity patterns at 2 consecutive (6-month and 12-month) registry visits. Values are n (row proportion).

	"Persistent Inactive/Minimal" at both visits (60%)	"Improved" Moderate/High then Inactive/Minimal (12%)	"Worsening" Inactive/Minimal then Moderate/High (10%)	"Persistent Moderate/High" at both visits (18%)
New medication start at 6 month visit				
No	1762 (56%)	639 (20%)	232 (7%)	500 (16%)
Yes	22 (12%)	35 (19%)	40 (22%)	89 (48%)
New medication start at 12 month visit				
No	1724 (54%)	648 (21%)	251 (8%)	534 (17%)
Yes	60 (37%)	26 (16%)	21 (13%)	55 (34%)
Sex				
Male (28%)	515 (56%)	176 (19%)	70 (8%)	164 (18%)
Female (72%)	1269 (53%)	498 (21%)	202 (8%)	425 (18%)
Race/Ethnicity				
White (77%)	1424 (55%)	509 (20%)	202 (8%)	435 (17%)
Other (8%)	120 (48%)	53 (21%)	28 (11%)	51 (20%)
Hispanic (7%)	89 (41%)	57 (26%)	21 (10%)	50 (23%)
Asian (3%)	58 (62%)	16 (17%)	4 (4%)	16 (17%)
Black (3%)	43 (42%)	28 (27%)	7 (7%)	25 (24%)
American Indian/Pacific Islander (1%)	17 (57%)	5 (17%)	4 (13%)	4 (13%)
Middle Eastern (0.3%)	8 (73%)	1 (9%)	1 (9%)	1 (9%)
Decline to Answer (1%)	25 (61%)	5 (12%)	4 (10%)	7 (17%)
ILAR Category				
Oligoarticular (36%)	692 (59%)	227 (19%)	97 (8%)	164 (14%)
RF- polyarticular (31%)	541 (53%)	224 (22%)	80 (8%)	184 (18%)
ERA (10%)	134 (41%)	68 (21%)	36 (11%)	89 (27%)
Psoriatic (8%)	137 (51%)	53 (20%)	25 (9%)	56 (21%)
Systemic (7%)	160 (65%)	38(16%)	17 (7%)	30 (12%)
RF+ polyarticular (6%)	73 (40%)	46 (25%)	13 (7%)	50 (27%)
Undifferentiated (2%)	30 (53%)	11 (19%)	3 (5%)	13 (23%)
ILAR – International League of Associations for Rheumatology, RF – rheumatoid factor, ERA – enthesitis related arthritis, Inactive/Minimal disease activity is clinical Juvenile Arthritis Disease Activity Score (cJADAS) <=4 for oligoarticular course and <=5 for polyarticular course, Moderate/High disease activity is cJADAS >4 for oligoarticular course and >5 for polyarticular course				

Results: Our sample included 3325 patients with JIA: 72% were female, 77% were white, 91% were from the US, and two-thirds had oligoarticular (36%) or rheumatoid factor (RF)- polyarticular JIA (31%). The patterns of disease activity across paired visits were: 54% persistent inactive/minimal, 18% persistent moderate/high, 20% "improved" (moderate/high then inactive/minimal), and 8% "worsening" (inactive/minimal then moderate/high)(Table 1). Only 6% of all patients had a new medication start attested after the 6-month Registry visit and 5% at the 12-month visit. A higher percentage of patients with moderate/high disease activity at the 12-month visit started a new medication (9%) compared to those with inactive/minimal disease activity at the 12-month visit (3%) (X^2 $p< 0.0001$). Of those starting a new medication at the 12-month visit, 37% had persistent inactive/minimal disease activity. Notably, 91% of patients with persistent moderate/high disease activity had no medication change at the 12-month visit.

Conclusion: In a large multicenter registry of patients with JIA, starting a new medication was more common for those with moderate/high disease activity at the 12-month visit, but was still uncommon overall. Interestingly, starting a new medication occurred for some patients with persistent inactive/minimal disease and did not occur for most patients with persistent moderate/high disease activity. Our findings suggest that starting a new medication is not driven by longitudinal disease activity scores. Further study is needed to identify reasons for treatment non-escalation among patients with persistent moderate or high disease activity.

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Abstract Number: 0378

Characteristics of Macrophage Activation Syndrome in Systemic JIA Patients Receiving Anakinra as First-line Treatment

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Pediatric Rheumatology – Clinical Poster I: JIA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Juvenile Idiopathic Arthritis (sJIA) is a severe inflammatory disease with auto-inflammatory characteristics. The introduction of targeted biologic therapies has revolutionized the treatment and as such improved outcomes for children with sJIA. The IL-1 receptor antagonist, anakinra, is used as first-line treatment for sJIA in the Netherlands since 2008 and has been shown to induce and sustain inactive disease with approximately 50% of patients being able to taper and stop within the first year of disease [Ter Haar 2019 PMID: 30848528]. However, also with this strategy, around 25-30% of patients experience a more refractory disease course, necessitating maintenance therapy. Multiple eposodes of Macrophage Activation Syndrome (MAS), a severe complication of sJIA, has been suggested to be one of the refractory sJIA phenotypes [Erkens 2021 PMID: 34635293]. The EULAR/ACR/PRINTO 2016 MAS classification criteria [Ravelli 2016 PMID: 26314788] have been developed to facilitate the diagnosis of MAS in sJIA. However, there is still a scarcity of data on their performance in sJIA patients treated with biologicals. Recent studies indicate that treatment of sJIA with biologicals might change some clinical and laboratory features of MAS [Schulert 2018 PMID: 28499329]. We therefore aimed to describe the (clinical and laboratory) characteristics of sJIA patients who developed MAS while treated with first-line anakinra and to evaluate whether the 2016 MAS classification criteria are still applicable in these patients.

Methods: In this cohort study, we used both retrospective data (2008-2016) as well as data from a nationwide, prospective multicentre cohort study (Early start of Targeted Treatment in Systemic JIA, ESTIS, 2017 onwards) selecting patients who developed MAS during treatment with first-line anakinra. In total, 15 patients were included with at least 1 year of follow up. We described the demographic, clinical, laboratory and immunologic features of MAS in patients started on recombinant IL-1RA therapy as first-line therapy for sJIA.

Results: We included fifteen patients, with a total of sixteen episodes of MAS. The estimated incidence of MAS was 15.6% in the first year after start of anakinra (7/45 in the prospective nationwide, multicentre cohort study ESTIS in the period 2017-2021). Eleven out of the fifteen patients were female. A significant share (11/16 episodes) of the MAS episodes occurred within 2 months after the onset of sJIA and four episodes (4/16, 25%) were triggered by a primo EBV infection at the onset of MAS. All episodes of MAS met the EULAR/ACR/PRINTO 2016 classification criteria for MAS in sJIA.

Conclusion: While first-line treatment with anakinra in sJIA results in high response rates and minimal corticosteroid use, this strategy does not seem to lower the risk or incidence of MAS in SJIA in the first year of disease. The EULAR/ACR/PRINTO 2016 classification criteria for MAS are applicable to patients treated with first-line anakinra. We recommend to

closely monitor the laboratory features from the classification criteria in (female) patients within the first months after the onset of sJIA and suggest to test all patients at the onset of sJIA on EBV status.

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Abstract Number: 0379

Clinical Evolution of Patients Diagnosed of Juvenile Idiopathic Arthritis After the Transitional Care Consultation

Alba Maria Torrat Noves[1], Rebeca Perpiñan Perez[2], Jose Ivorra Cortes[1], Elena Grau Garcia[1], Daniel Ramos Castro[1], Pablo Francisco Muñoz Martínez[3], Laura Mas Sanchez[4], Carmen Riesco Barcena[1], Anderson Victor Huaylla Quispe[1], Samuel Leal Rodriguez[1], Belen Villanueva Mañez[1], Iago Alcantara Alvarez[1], Isabel Martinez Cordellat[1], Luis Gonzalez Puig[1], Rosa Negueroles Albuixech[1], Jose Eloy Oller Rodriguez[1], Elvira Vicens Bernabeu[1], Ernesto Tovar Sugrañes[1], Marta De la Rubia Navarro[4], Hikmat Charia[1], Ines Canovas Olmos[1], Carmen Najera Herranz[1] and Jose Andres Roman Ivorra[5], [1]Rheumatology Department. HUP La Fe, Valencia, Spain, [2]Universidad Catolica de Valencia San Vicente Martir, Valencia, Spain, [3]Rheumatology Department. HUP La Fe, Sagunto, Spain, [4]Rheumatology Department. HUP La Fe, Valéncia, Spain, [5]Hospital Universitari i Politècnic la Fe, Valencia, Spain

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile idiopathic arthritis (JIA) encompasses a group of chronic arthritis that begin in childhood. According to the International League of Associations for Rheumatology (ILAR) criteria, JIA can be divided into seven distinct groups: oligoarthritis, rheumatoid factor (RF) negative and positive polyarthritis, enthesitis related arthritis, psoriatic arthritis, systemic arthritis and undifferentiated arthritis.

Following their visit to the transitional consultation, these patients subsequently undergo clinical follow-up in adult rheumatology.

The objective of this study is to describe the evolution of clinical and analytical findings, as well as treatment data in patients with JIA after the transitional care consultation.

Table 1	Oligoarthritis (n=20)	Enthesitis related arthritis (n=16)	RF negative polyarthritis (n=13)	Systemic arthritis (n=7)	Undifferentiated arthritis (n=6)	RF positive polyarthritis (n=4)	Psoriatic arthritis (n=4)
Diagnosis changes N (%)	2 (10)	-	1(7.7)	1(14.3)	4(66.6)	1(25)	-
New diagnosis	Spondyloarthritis Rheumatoid arthritis	-	Rheumatoid arthritis	Rheumatoid arthritis	Bechet's disease Behçet's disease Psoriatic arthritis Sjögren's disease	Sjögren's disease	-

Diagnosis changes

Table 2	Cumulative incidence at pediatric age N (%)	Cumulative incidence after the transitional care consultation N (%)
Oral/genital thrush	14(20)	5(7.1)
Uveitis	10(14.3)	7(10)
Diarrhea	8(11.4)	4(5.7)
Psoriasis	8(11.4)	4(5.7)
Raynaud phenomenon	6(8.6)	1(1.4)
Antinuclear antibodies (ANA)	40(57.1)	37(52.8)

Cumulative incidence of clinical and analytical manifestations

Table 3	Remission after the transitional care consultation N (%)	New episodes after the transitional care consultation N (%)	Recurrences after the transitional care consultation N (%)
Oral/ genital thrush (n=16)	11(68.7)	2(12.5)	3(18.7)
Uveitis (n=11)	4(36.3)	1(9.1)	6(54.5)
Diarrhea (n=10)	6(60)	2(20)	2(20)
Psoriasis (n=8)	4(50)	-	4(50)
Raynaud phenomenon (n=6)	5(83.3)	-	1(16.6)
ANA (n=42)	5(11.9)	2(4.7)	35(83.3)

Evolution of clinical and analytical manifestations

Methods: Descriptive, longitudinal, and retrospective study conducted on 70 patients diagnosed with JIA based on the ILAR criteria. These patients were followed-up in adult rheumatology consultations after being visited in the transitional consultation at a Spanish tertiary-level hospital. Data pertaining to clinical, laboratory, and treatment aspects were collected from both the adult and transitional consultations.

Results: 70 patients diagnosed of JIA (65.7% women) were included in the study, with a mean age at diagnosis of 9 years old and a mean age at the transitional consultation of 21 years. The average duration of follow-up after the initial diagnosis was 16 years, while the mean duration of follow-up after the transitional consultation was 4 years.

After the transitional consultation, 12.8% of the patients had a change in their diagnosis (table n° 1).

24 patients (34.3%), were lost to follow-up, primarily due to changes in the health department in the majority of cases.

Half of the patients with history of previous uveitis experienced new episodes following the transitional consultation. In contrast, a significant number of patients did not experience recurrences during their follow-up in adult rheumatology appointments (table n ° 3). 100% of the patients who had new flares of uveitis after the transitional consultation had ANA+ in serum.

The frequency of oral and genital thrush, Raynaud phenomenon and diarrhea episodes decreased after the transitional consultation.

Out of the 28 patients who were in remission without treatment during the transitional care consultation, only 1 patient required initiation of therapy during their follow-up in adult rheumatology appointments.

Conclusion: 12.8% of the patients experienced a change in their diagnosis during their follow-up in the adult rheumatology consultation, with the majority of these cases being classified as undifferentiated JIA.

The majority of patients who were in remission without treatment during the transitional consultation did not require treatment during their follow-up in adult rheumatology appointments.

A significant number of patients experienced recurrences of uveitis after the transitional care consultation. However, new cases of uveitis in patients who had not previously experienced episodes were rare during the follow-up in adult rheumatology appointments.

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Abstract Number: 0380

Use of Digital Health Tools to Evaluate Change in Clinical and Patient-Reported Outcomes Among Patients with Rheumatoid Arthritis Initiating Treatment with a JAKi or TNFi

W. Benjamin Nowell[1], Cassie Clinton[2], Fenglong Xie[2], Yuji Su[3], Laura Stradford[1], David Curtis[4], Patrick Zueger[5], Pankaj Patel[6], Kelly Gavigan[7], Shilpa Venkatachalam[8], Esteban Rivera[9] and Jeffrey R. Curtis[3], [1]Global Healthy Living Foundation, Nyack, NY, [2]University of Alabama at Birmingham, Birmingham, AL, [3]University of Alabama at Birmingham and Illumination Health, Birmingham, AL, [4]Global Healthy Living Foundation, San Francisco, CA, [5]AbbVie, Inc., Mettawa, IL, [6]AbbVie, Inc., North Chicago, IL, [7]Global Healthy Living Foundation, Upper Nyack, NY, [8]Global Healthy Living Foundation, New York, NY, [9]Global Healthy Living Foundation, Long Island City, NY

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Although the use of patient-reported outcome (PRO) data has grown more common in the care of people with rheumatoid arthritis (RA), the utility of PRO data captured between visits in relation to traditional, physician-derived measures has not been adequately evaluated. We compared changes over time in PRO data captured on a smartphone app against a physician-derived disease activity measure, the Clinical Disease Activity Index (CDAI).

Methods: RA patients in moderate or high disease activity (CDAI >10) and prescribed either upadacitinib (UPA) or adalimumab (ADA) were enrolled in the study from March 2021 to October 2022 during in-office visits at 28 community rheumatology clinics in the US. Patients were prompted to download the ArthritisPower registry smartphone app to complete PROs at home over a 12-week period. Following a mandatory run-in period to verify willingness to provide PRO data, subsequent at-home data collection included disease activity measures as well as symptom measures from the Patient-Reported Outcomes Measurement Information System (PROMIS). Patients returned for a follow-up clinical visit at approximately 3-4 months (follow-up visits permitted at 2-6 months). Rheumatology clinics provided baseline clinical data including CDAI, years since RA diagnosis, prior medications, and follow-up CDAI. A subgroup analysis was restricted to those who stayed on medication with minimal interruptions. Linear regression models adjusted for baseline CDAI and baseline PRO scores were used to test the correlation between follow-up CDAI and follow-up PRO scores.

Results: Of 299 patients recruited, 240 patients (80%) successfully completed the run-in period, and 205 patients started UPA or ADA within 4 weeks and were eligible. A total of 148 patients ("All" cohort) to date have provided baseline and follow-up clinical and PRO data, and 122 (82%) remained adherent (Table 1). Mean CDAI improved 14.4 units for patients who stayed on the medication (Table 2). Correlations between follow-up CDAI and follow-up PROs ranged from 0.38 – 0.56, the strongest of which were for Patient Global Assessment NRS (R=0.56) and Pain NRS (R=0.47) (Table 3). The adjusted R^2 of the overall model showed that changes in PROs explained 52% of the variability in the change in the CDAI.

Table 1. Baseline Characteristics of WEAR Study Participants

	All	Adherent to Medication*
N	148	122
Age (mean (SD))	52 (12)	52 (12)
Female	117 (79%)	97 (80%)
Race = White	122 (82%)	102 (84%)
Hispanic Ethnicity = Yes	35 (24%)	31 (25%)
Years Since RA Diagnosis		
<2	54 (36%)	44 (36%)
2-5	36 (24%)	32 (26%)
6-10	12 (8.1%)	9 (7.4%)
>10	46 (31%)	37 (30%)
Employment Status		
Employed	84 (57%)	69 (57%)
Unemployed	41 (28%)	35 (29%)
Retired	23 (16%)	18 (15%)
Initiated Upadacitinib [rather than Adalimumab]	93 (63%)	74 (61%)
Previously on csDMARD	128 (86%)	103 (84%)
Previously on Biologic	93 (63%)	76 (62%)
Previously on TNFi	91 (61%)	74 (61%)
Previously on JAKi	34 (23%)	26 (21%)
Clinical Disease Activity Index (CDAI)	29.9 (16.5)	30.0 (16.2)
Patient Global Assessment (0-10 NRS)	5.7 (2.4)	5.9 (2.3)
Pain (0-10 NRS)	6.0 (2.5)	6.0 (2.5)
Fatigue (0-10 NRS)	6.4 (2.7)	6.3 (2.8)
RADAI-5 (0-10)**	6.7 (1.8)	6.6 (1.9)
PROMIS Fatigue (T score 0-100)	63.2 (7.9)	62.9 (7.7)
PROMIS Sleep Disturbance (T score 0-100)	59.6 (7.8)	59.2 (7.8)
PROMIS Pain Interference (T score 0-100)	64.6 (6.7)	64.4 (6.4)
PROMIS Anxiety (T score 0-100)	56.7 (8.5)	57.3 (8.2)
PROMIS Physical Function (T score 0-100)	37.4 (6.3)	37.6 (6.2)
PROMIS Social Activities (T score 0-100)	42.6 (7.1)	42.7 (7.3)

Table 2. Disease Activity Measures and PROs at Follow-up in All Patients and in Patients Adherent to Medication

	All n=148		Adherent to Medication n=122	
	Follow-up Score (mean (SD))	Change from Baseline (mean (95% CI))	Follow-up Score (mean (SD))	Change from Baseline (mean (95% CI))
Clinical Disease Activity Index (CDAI)	16.8 (16.4)	-13.1 (-15.4, -10.7)	15.6 (15.6)	-14.4 (-17.1, -11.7)
Patient Global Assessment (0-10 NRS)	3.4 (2.6)	-2.3 (-2.7, -1.9)	3.3 (2.6)	-2.5 (-3.0, -2.1)
Pain (0-10 NRS)	4.5 (2.7)	-1.5 (-2.0, -1.1)	4.3 (2.8)	-1.7 (-2.2, -1.2)
Fatigue (0-10 NRS)	4.8 (2.7)	-1.6 (2.0, -1.1)	4.7 (2.8)	-1.6 (2.1, -1.1)
RADAI-5 (0-10)*	5.5 (2.3)	-1.1 (-1.5, -0.6)	5.4 (2.3)	-1.2 (-1.6, -0.9)
PROMIS Fatigue (T score 0-100)	57.8 (9.0)	-5.4 (-6.8, -4.0)	57.6 (8.9)	-5.2 (-6.7, -3.8)
PROMIS Sleep Disturbance (T score 0-100)	54.8 (7.9)	-4.8 (-5.9, -3.7)	54.3 (7.9)	-4.9 (-6.2, -3.6)
PROMIS Pain Interference (T score 0-100)	60.5 (7.6)	-4.1 (-5.3, -2.9)	60.1 (7.6)	-4.3 (-5.6, -2.9)
PROMIS Anxiety (T score 0-100)	55.1 (10.1)	-1.6 (2.8, -0.5)	55.6 (9.7)	-1.6 (3.0, -0.3)
PROMIS Physical Function (T score 0-100)	40.3 (7.4)	2.9 (1.9, 3.9)	40.7 (7.5)	3.1 (2.0, 4.2)
PROMIS Social Activities (T score 0-100)	45.3 (8.5)	2.7 (1.5, 4.0)	45.9 (8.6)	3.1 (1.6, 4.6)

Table 3. Correlations Between Follow-up CDAI and PROs at Follow-up, Adjusted for Baseline CDAI and PRO Scores

	All n=148	Adherent to Medication n=122
PRO	**Adjusted Correlation** (correlation coefficient (p-value))	**Adjusted Correlation** (correlation coefficient (p-value))
Patient Global Assessment (0-10 NRS)	0.56 (0.00)	0.53 (0.00)
Pain (0-10 NRS)	0.47 (0.00)	0.44 (0.00)
Fatigue (0-10 NRS)	0.43 (0.00)	0.40 (0.00)
RADAI-5 (0-10)	0.46 (0.00)	0.44 (0.00)
PROMIS Fatigue (T score 0-100)	0.40 (0.01)	0.37 (0.00)
PROMIS Sleep Disturbance (T score 0-100)	0.44 (0.00)	0.42 (0.00)
PROMIS Pain Interference (T score 0-100)	0.44 (0.00)	0.40 (0.00)
PROMIS Anxiety (T score 0-100)	0.38 (0.02)	0.34 (0.01)
PROMIS Physical Function (T score 0-100)	0.40 (0.00)	0.35 (0.03)
PROMIS Social Activities (T score 0-100)	0.41 (0.00)	0.37 (0.00)

CDAI = clinical disease activity index; PRO = patient reported outcome; RADAI = rheumatoid arthritis disease activity index

Conclusion: PROs are useful for tracking RA disease activity over time outside of the clinic setting for patients initiating new treatments, even in the absence of clinician-derived measures.

*Adherence to medication was defined as: still taking upadacitinib or adalimumab at 3-month follow-up and no interruption in taking the medication lasting greater than 3 weeks between enrollment to follow-up; RA = rheumatoid arthritis; csDMARD = conventional synthetic disease modifying anti-rheumatic drug; TNFi = tumor necrosis factor inhibitor; JAKi = Janus kinase inhibitor All categorical data shown as n (%), all continuous data shown as mean (standard deviation [SD]) **RADAI-5 score: 0.0-1.4 for a remission-like state, 1.6-3.0 for mild disease activity, 3.2-5.4 for moderate, and 5.6-10.0 for high disease activity PROMIS measures use a weekly referent; score of 50.0 is US population mean for all adults, 10.0 is equivalent to 1 standard deviation from the mean PRO = patient reported outcome; NRS = Numeric rating scale; PROMIS = patient reported outcomes measurement information system; RADAI = rheumatic arthritis disease activity index

*RADAI-5 score: 0.0-1.4 for a remission-like state, 1.6-3.0 for mild disease activity, 3.2-5.4 for moderate, and 5.6-10.0 for high disease activity PROMIS measures use a weekly referent; score of 50.0 is US population mean for all adults, 10.0 is equivalent to 1 standard deviation from the mean PRO = patient reported outcome; NRS = Numeric rating scale; PROMIS = patient reported outcomes measurement information system; RADAI = rheumatic arthritis disease activity index

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Abstract Number: 0381

Disease Burden, Patient Experiences, and Unmet Needs in Refractory Rheumatoid Arthritis: Insights from 20 Years of Real-World Data

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite major advances in RA treatment, a substantial number of patients (estimated at 6-21%[1]) are refractory to multiple advanced therapies. Well-defined refractory RA (reRA) criteria and thoughtful selection of controls are essential to ensure that observed differences are truly due to refractory disease and not to confounding variables. In this study, we aimed to identify factors associated with reRA and characterize differences in disease burden/patient experiences between reRA and matched nonrefractory controls, from over 20 years of real-world data.

Methods: Data were provided by adults with RA in the FORWARD Databank from 1998 to 2019. Participants with no history of biologic (bDMARD) or targeted synthetic DMARD (tsDMARD) use at study entry but with subsequent exposure to one or more of these advanced therapies were included. The reRA group included participants with exposure to ≥3 advanced therapies during observation, with ≥1 TNF inhibitor (TNFi) and ≥1 tsDMARD or non-TNFi bDMARD. The nonrefractory group included participants with continued use of their first advanced therapy for at least two years, and who never

Table 1. Characteristics of FORWARD participants with RA by reRA status at baseline (initiation of first advanced therapy) and follow up (the point of meeting reRA criteria; matched time point for nonrefractory controls).

	Baseline			Follow Up		
	Nonrefractory	Refractory	p	Nonrefractory	Refractory	p
Demographics						
Age, years	56.7 (11.4)	56.4 (10.9)	0.57	62.7 (12.0)	62.3 (11.5)	0.55
Female, %	88.2	88.2	1	88.2	88.2	1
White, %	92.0	91.2	0.60	92.0	91.2	0.60
Education, years	13.9 (2.4)	14.1 (2.2)	0.08	13.9 (2.4)	14.1 (2.2)	0.08
Rural residence, %	23.1	26.6	0.13	23.1	26.6	0.13
Hx smoking, %	49.7	50.3	0.83	51.9	53.3	0.59
BMI	28.0 (7.2)	28.4 (6.4)	0.30	28.1 (7.4)	28.8 (6.7)	0.08
Duration, years	14.5 (10.3)	14.4 (10.7)	0.87	20.5 (11.3)	20.4 (11.6)	0.87
Concomitant Medications						
Glucocorticoid, %	40.1	46.1	0.03	33.0	47.0	<0.001
csDMARD, %	84.6	85.7	0.58	70.8	71.8	0.68
NSAID, %	64.8	61.6	0.21	43.3	43.8	0.85
Weak opioid, %	22.0	28.2	<0.01	25.8	32.2	0.01
Strong opioid, %	3.8	5.6	0.10	5.9	9.4	0.02
Patient-Reported Outcomes						
Pain VAS, 0-10	3.5 (2.7)	4.3 (2.8)	<0.001	3.7 (2.8)	4.5 (2.6)	<0.001
Fatigue VAS, 0-10	4.2 (2.9)	4.8 (3.0)	<0.001	4.5 (3.1)	5.1 (2.9)	<0.001
Patient Global VAS, 0-10	3.4 (2.5)	4.0 (2.5)	<0.001	3.7 (2.5)	4.4 (2.3)	<0.001
HAQ-II, 0-3	1.0 (0.7)	1.1 (0.7)	<0.01	1.0 (0.8)	1.2 (0.7)	<0.001
PAS-II, 0-10	3.4 (2.2)	4.0 (2.1)	<0.001	3.6 (2.3)	4.3 (2.0)	<0.001
Comorbidities						
RDCI, 0-9	1.4 (1.4)	1.7 (1.5)	<0.01	1.9 (1.6)	2.1 (1.7)	<0.01
Hx pulmonary disorder, %	28.3	26.4	0.45	43.2	45.1	0.49
Hx cardiac disorder, %	17.3	19.4	0.32	32.2	32.7	0.83
Hx fracture, %	16.2	16.8	0.79	27.5	31.6	0.01
Hx depression, %	38.8	41.1	0.37	52.2	55.1	0.28
Hx diabetes, %	9.5	10.4	0.61	18.7	18.4	0.87
Hx cancer, %	16.2	14.5	0.36	29.9	25.1	0.05
Hx GI disorder, %	50.5	57.9	<0.01	66.8	74.4	<0.01
PSD, 0-31	10.3 (7.2)	11.8 (7.5)	<0.001	10.7 (7.7)	12.6 (7.7)	<0.001
Fibromyalgia criteria, %	22.5	28.2	0.02	23.2	32.9	<0.001
Healthcare Interactions						
Rheumatology visits	3.4 (1.9)	3.6 (2.0)	0.13	2.5 (1.7)	3.4 (2.0)	<0.001
Family medicine visits	2.3 (1.9)	2.3 (1.7)	0.56	2.2 (1.8)	2.3 (1.8)	0.40
Gastroenterology visits	0.8 (1.3)	0.8 (1.0)	0.83	0.6 (1.1)	0.7 (1.0)	0.21
Other specialist visits	2.1 (2.3)	2.0 (2.2)	0.53	2.2 (2.2)	2.1 (2.1)	0.44
ER visits	0.7 (0.8)	0.7 (0.9)	0.62	0.6 (0.7)	0.7 (0.8)	0.55
Any hospitalization, %	10.0	11.3	0.44	10.0	13.3	0.06
Hospitalized for infection, %	2.7	1.7	0.20	2.5	3.3	0.34
Healthcare satisfaction, 0-4	2.4 (1.2)	2.0 (1.3)	<0.001	2.3 (1.2)	1.9 (1.2)	<0.001

csDMARD=conventional synthetic DMARD; weak opioid=codeine, tramadol, hydrocodone; strong opioid=morphine, fentanyl, methadone, hydromorphone, oxycodone, oxymorphone; VAS=visual analog scale; PAS-II=Patient Activity Scale II; RDCI=Rheumatic Disease Comorbidity Index; PSD=polysymptomatic distress. Healthcare interactions were in the six month time period preceeding the observation.

exceeded two advanced therapies during observation. Refractory and nonrefractory participants were matched 1:1 on age, sex, RA duration, calendar year, and observation time. Descriptive statistics were calculated at baseline (initiation of first advanced therapy) and at follow up (the point of meeting reRA criteria; matched time point for nonrefractory controls). Significance was assessed with Chi-square and t-tests, as appropriate. Covariates with $p < 0.1$ were included in multivariable logistic regression models for each time point.

Results: Of 6,575 participants who met study inclusion criteria, 718 (10.9%) met reRA criteria. Of those, 692 were matched 1:1 to nonrefractory controls, for a total of 1,384 participants included in the study. In univariate analyses (Table 1), all patient-reported outcomes (PROs) were significantly worse among the reRA group at both time points. Glucocorticoid use, opioid use, Rheumatic Disease Comorbidity Index (RDCI), gastrointestinal (GI) disorder, and polysymptomatic distress (PSD) were also all higher for the reRA group at both time points, and healthcare satisfaction was lower. In multivariable analyses (Figure 1) higher pain, GI disorder, and lower healthcare satisfaction were all associated with future incidence of reRA. Higher education, corticosteroid use, GI disorder, and more rheumatology visits were associated with reRA. History of cancer was associated with nonrefractory status.

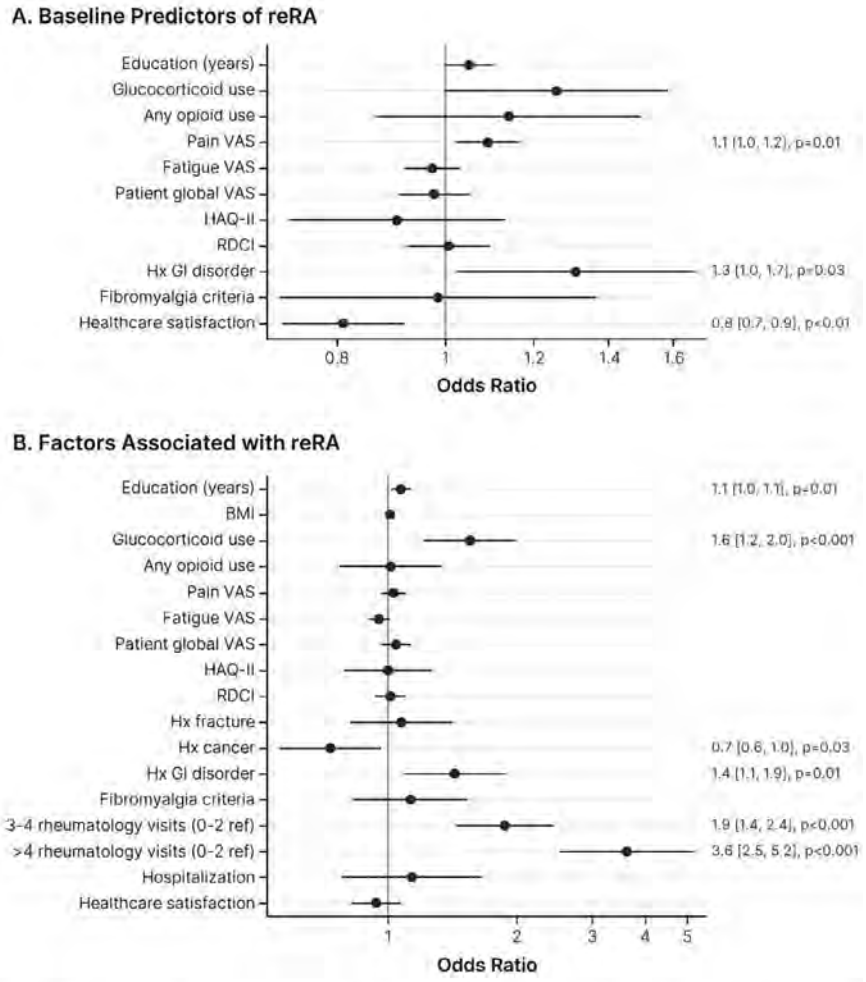

Figure 1. Multivariable logistic regression results for (A) baseline predictors of reRA and (B) factors associated with reRA at the time of meeting reRA criteria. Characteristics with $p<0.1$ in Table 1 were included in each model. Statistically significant ($p<0.05$) covariates have their associated odds ratio [95% CI] and p-value listed. RDCI=Rheumatic Disease Comorbidity Index. Rheumatology visits and hospitalization were within the six month period prior to the observation.

Conclusion: These results demonstrate that reRA is associated with significant disease burden and unmet healthcare needs, as evidenced by lower healthcare satisfaction, higher rates of glucocorticoid and opioid use, greater comorbidity and symptom burdens, and more rheumatology visits. These findings underscore the importance of well-defined reRA criteria and the need for further investigation into this unique RA phenotype to identify targeted treatment strategies and ultimately improve outcomes.

1. Melville, A. R. *et al*. *Drugs***80**, 849–857 (2020)

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Abstract Number: 0382

Heterogeneity Within a "difficult to Treat" Rheumatoid Arthritis Patients Cohort: 36% May Have a More Benign Course and Have Distinct Characteristics at bDMARD or tsDMARD Initiation

Irini Flouri[1], Antonios Bertsias[2], Argyro Repa[2], Nestor Avgoustidis[2], Eleni Kalogiannaki[2], Sofia Pitsigavdaki[3], George Bertsias[4] and **Prodromos Sidiropoulos**[4], [1]University of Crete Medical School, Heraklion, Greece, [2]Rheumatology, Clinical Immunology and Allergy Department, Medical School, University of Crete, Heraklion, Greece, [3]Rheumatology, Clinical Immunology and Allergy Department, Medical School, University of Crete, Crete, Greece, [4]Rheumatology, Clinical Immunology and Allergy Department, Medical School, University of Crete, Greece; Institute of Molecular Biology and Biotechnology, Foundation for Research and Technology Hellas (FORTH), Heraklion, Greece

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Early detection of difficult to treat (D2T) RA patients as well as better characterization of their long-term course represent unresolved issues. Herein we aimed for a detailed analysis of predictors and assessed for heterogeneity of long-term prognosis within D2T patients.

Methods: This was an analysis from "University of Crete Rheumatology Clinic Registry (UCRCR)", a prospective single center study. We analyzed all patients included form May 2000 until April 2022 and applied the EULAR definition of D2T. Univariate and multivariate analysis of sociodemographic and RA-related characteristics at start of first bDMARDs or tsDMARD were analysed as predictors of D2T. Heterogeneity (HAQ and DAS28 trajectories) withing D2T group was analysed during a follow-up period of 60 months applying latent class trajectory analysis.

Results: 251 out of 1264 patients (19.9%) identified as D2T. Female gender, age at 1st biologic, RF negative, higher RDCI scores, Sicca symptoms, disease duration, higher DAS28 and HAQ at baseline and failure to decrease DAS28 >1.2 at 6 months were all associated with D2T grouping ($p < 0.05$). Patients classified as D2T suffered from osteoarthritis, fibromyalgia, dyslipidemia, hypothyroidism and obesity at significantly higher rates compared to non-D2T patients ($p < 0.05$ for all). Latent class trajectory analysis during 60 months of follow-up, indicated that D2T patients do not constitute a homogenous group; interestingly distinct disease activity trajectory groups could be differentiated while ∼36% of them showed a more favorable outcome but never reaching low disease activity (DAS 28 ESR∼ 3.8 at 60 months) (Figure 1).

Table. Univariate comparisons of selected factors between D2T and non-D2T patients

Table. Univariate comparisons of selected factors between D2T and non-D2T patients				
	All	**Non-D2T**	**D2T**	**p-value**
Gender				0.001
Female	1026 (81.2%)	804 (79.4%)	222 (88.4%)	
Male	239 (18.8%)	209 (20.6%)	29 (11.6%)	
Age at 1st biologic Median (min,max; IQR)	60 (15,90;15)	61 (15,90;17)	56 (17,81;14)	0.003
Positive RF	341 (29.8%)	288 (31.9%)	53 (21.7%)	0.002
Fibromyalgia	434 (34.3%)	294 (29.0%)	140 (55.8%)	<0.0001
Osteoarthritis	540 (42.7%)	401 (39.6%)	139 (55.4%)	<0.0001
DAS28-esr at 1st biologic initiation (mean,SD)	5.66 (1.22)	5.59 (1.52)	5.95 (1.15)	<0.0001
DAS28-esr reduction >1.2 within the first 6 months of biologic treatment	375 (46.9%)	312 (50.4%)	63 (35.0%)	<0.0001
mHAQ at 1st biologic initiation (mean,SD)	0.91 (0.73)	0.89 (0.77)	0.97 (0.57)	0.034
Dyslipidemia	448 (38.6%)	376 (37.1%)	112 (44.6%)	0.029
Hypothyroidism	252 (19.9%)	185 (18.3%)	67 (26.7%)	0.003
Obesity	366 (29.0%)	274 (27.0%)	92 (36.7%)	0.003
Xerostomia	100 (7.9%)	71 (7.0%)	29 (11.6%)	0.017
Xeropthalmia	102 (8.1%)	71 (7.0%)	31 (12.4%)	0.005
RDCI Mean (SD)	1.26 (1.42)	1.21 (1.38)	1.45 (1.56)	0.016

D2T: Difficult to treat, IQR: Inter-quartile range, RF: Rheumatoid Factor, RDCI: Rheumatic Disease Comorbidity Index,

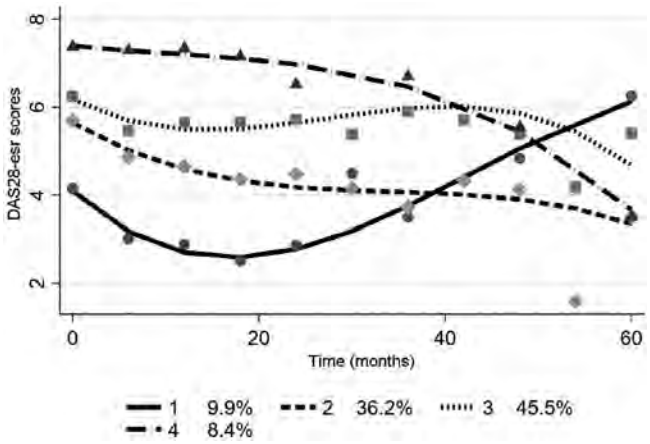

Figure - Latent class trajectory analysis of DAS28-esr over time

Conclusion: D2T patients represent a heterogenous group of RA patients in terms of long-term disease course. Age, comorbidities, inflammatory burden and compromised function at start of bDMARD/tsDMARD may characterize D2T group.

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Abstract Number: 0383

Identification of Contributing Factors to Difficult-to-Treat Rheumatoid Arthritis (D2T RA) in a Cohort of 972 Patients Using a Natural Language Processing (NLP) Approach

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Natural Language Processing (NLP), an interdisciplinary field combining artificial intelligence and language science, has gained significant interest in the medical domain for automated collection and structuring of medical data. In this study, we employed an NLP approach to identify and extract the characteristics of patients with D2T RA from their computerized medical records.

Methods: We conducted a monocentric observational retrospective cohort study in our French hospital. Patients were longitudinally recruited over a 5-year period (2015-2020), and their characteristics were retrieved from their electronic health records spanning 2010-2022. Firstly, we performed an NLP phenotyping tool to identify patients who had at least one hospital stay related to RA between 2015 and 2020. The tool relied on CIM-10 coding and the recognition of specific keywords (e.g., "rheumatoid arthritis" or "ACPA") in the medical records to calculate the patient's probability of meeting the RA phenotype. We subsequently employed a named-entity recognition algorithm to identify all drugs associated with RA from the patients' medical reports. The drugs were then arranged in chronological order based on their appearance, and the date of introduction was approximated as the date of first extraction. D2T RA was defined as the failure of at least two targeted therapies (identified by the algorithm retrieving three or more biologics), thereby allowing us to separate our RA cohort into D2T and non-D2T RA groups. Finally, we used another NLP program employing named-entity recognition to retrieve the characteristics of these patients. Specific keywords related to general variables (sex, age at first stay), disease characteristics (presence of joint erosion, DAS28 activity score), and comorbidities were sought in the medical reports using cumulative extraction. The occurrence of these specific tokens was linked to the presence of the respective variable. Finally, a multivariate logistic regression analysis was performed to assess the relationship between variables and the D2T group.

Results: The phenotyping tool identified 972 RA patients, of which 313 were classified as D2T RA and 659 as non-D2T RA. The presence of joint erosions (OR 2.97 CI95% [2.17; 4.08], p< 0.001) and higher disease activity (median DAS28 3.16 vs 2.89) were associated with the D2T group. Female gender, obesity, smoking, anxio-depression, and fibromyalgia comorbidities showed similar proportions in our two groups. Chronic kidney disease (OR=0.66 CI95% [0.44;1.01], p=0.068), cardiac insufficiency (OR 0.52 CI95% [0.38;0.7], p=0.001), liver insufficiency (OR=0.7 CI95% [0.35;1.4], p=0.39), and a history of malignancy (OR=0.62 CI95% [0.47;0.82], p=0.001) were found in higher proportions in the non-D2T group.

Conclusion: NLP facilitates the automated collection of diverse data directly from medical reports using named-entity recognition algorithms. In this study, we demonstrated its application in identifying potential contributing factors to D2T RA. Enhanced understanding of the mechanisms underlying D2T RA and early detection of contributing factors hold promise for improved outcomes and management in this heterogeneous population.

Disclosure: H. BERGIER: None; **T. Fabacher**: None; **N. Sedmak**: None; **E. Sauleau**: None; **J. Gottenberg**: AbbVie, 2, BMS, 2, 5, Galapagos, 2, Gilead, 2, Lilly, 2, MSD, 2, Novartis, 2, Pfizer, 2, 5.

Abstract Number: 0384

Targeting NET Formation in Early RA Patients; A Spin-off Study from the NORD-STAR

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The formation of neutrophil extracellular traps (NETs) with extrusion of nuclear, granular and cytosolic components from a dying neutrophil, has been described extensively in patients with rheumatoid arthritis (RA), and linked to generation of autoantigens (e.g. citrullinated proteins), inflammation and organ damage. Thus far there have been very few studies describing the effect of treatment in patients with RA on NET formation, and no studies comparing the effects of treatment strategies in (very) early RA. The objective of the study is to assess the effects of different initial treatments on NET formation in patients with early RA.

	Baseline	*Week 12*	*Reduction*	*Week 24*	*reduction*
Calprotectin (ng/mL)	1080 (1718)	231 (326) ***	-79%	214 (274) ***	-80%
Conventional treatment	1222 (2197)	354 (554) ***	-71%	285 (357) ***	-77%
Certolizumab pegol	1166 (1927)	213 (486) ***	-88%	157 (281) ***	-93%
Abatacept	850 (1323)	269 (313) ***	-68%	220 (354) ***	-74%
Tocilizumab	757 (1346)	169 (195) ***	-54%	184 (168) ***	-53%
MPO-DNA (pM)	7185 (2567)	6503 (2694) ***	-9%	6612 (2542) ***	-8%
Conventional treatment	7057 (4052)	6396 (2878) **	-11%	6629 (3092) **	-8%
Certolizumab pegol	7183 (2733)	6492 (3308) *	-10%	6549 (2608) *	-9%
Abatacept	7727 (2512)	7562 (4708)	-2%	6688 (3882) **	-13%
Tocilizumab	6904 (2168)	6120 (1921)	-11%	6509 (2113)	-6%

*Table 1. Results are reported as median (IQR) due to skewedness of the data. Reductions are reported as a percentage reduction compared to baseline. Measurements are marked with * if p<0.05, ** if p<0.01, *** if p<0.001.*

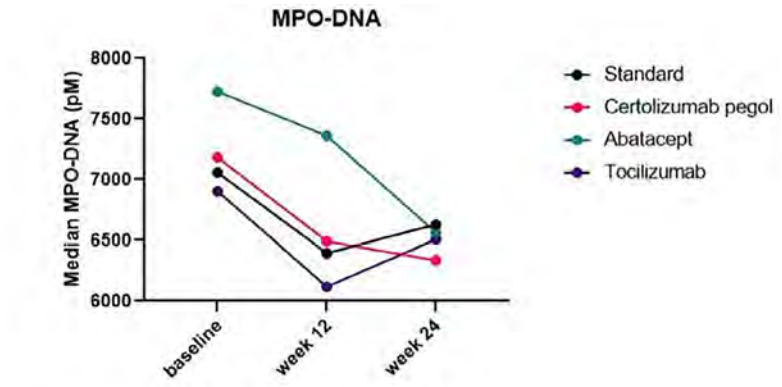

Figure 1:median MPO-DNA over time (pM)

Methods: NORD-STAR is an international, multicenter, open-label, assessor-blinded, phase 4 study where patients with newly diagnosed RA started methotrexate (MTX) and were randomized 1:1:1:1 to a) conventional treatment (either prednisolone tapered to 5mg/day, or sulfasalazine combined with hydroxychloroquine and intra-articular corticosteroids), b) certolizumab pegol, c) abatacept, or d) tocilizumab[1]. This study is a spin-off from the main NORD-STAR study measuring neutrophil biomarkers MPO-DNA (Myeloperoxidase-DNA; NETs) and calprotectin in 24 consecutive Dutch participants and 94 Swedish patients at baseline, 12 weeks and 24 weeks after the start of the treatment. Statistical analysis was done using the Wilcoxon Signed Rank test for paired samples and independent samples median test to compare patients to healthy controls in SPSS version 28.

Results: At baseline patients had elevated levels of NETs and neutrophil activation compared to healthy controls as indicated by calprotectin (median 1080ng/ml vs 133ng/ml, $p< 0.001$) and elevated MPO-DNA (median 7185pM vs 3976pM, $p< 0.001$). Both of the biomarkers decreased significantly at 12 and 24 weeks after treatment in the total group demonstrating reduced neutrophil activity and NET formation. After 24 weeks of treatment, calprotectin was significantly reduced in all groups by up to 93% (Table 1). MPO-DNA showed a more modest reduction of up to 13%, and was relatively similar in all groups, although the reduction in MPO-DNA did not reach statistical significance in the tocilizumab group.

Conclusion: These results indicate highly elevated neutrophil activation and NET formation in recently diagnosed RA patients. All four treatments studied here reduced these detrimental processes within 3 months. The calprotectin reduction seen in this study is in line with an earlier spin-off study[2]. The rapid decline in these markers may have contributed to the minimal radiological progression that was seen in the NORD-STAR trial.

References:

[1] Hetland M et al. BMJ. 2020
[2] Stevens D et al. Ann Rheum Dis. 2022

Disclosure: B. Dijkshoorn: Galapagos, 2, Novartis, 2; **T. Wang**: None; **G. Grondal**: None; **D. Vedder**: None; **A. Rudin**: AstraZeneca, 12, financial support; **D. Nordstrom**: AbbVie/Abbott, 2, BMS, 2, Lilly, 2, MSD, 2, Novartis, 2, Pfizer, 2, UCB, 2; **B. Gudbjornsson**: Nordic-Pharma, 6, Novartis, 2, 6; **K. Lend**: None; **T. Uhlig**: Galapagos, 2, 6, Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **E. Haavardsholm**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Eli Lilly, 2, Gilead, 2, Pfizer, 6, UCB, 6; **M. Hetland**: AbbVie/Abbott, 1, 5, Bristol-Myers Squibb(BMS), 5, Danbio, 12, MLH has chaired the steering committee of the Danish Rheumatology Quality Registry (DANBIO, DRQ), which receives public funding from the hospital owne, Eli Lilly, 5, MEDAC, 6, Novartis, 5, Pfizer, 5, 6, Sandoz, 5, 6; **M. Schrumpf Heiberg**: Roche, 6; **M. Østergaard**: AbbVie, 2, 5, 6, Amgen, 5, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Celgene,

2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Hospira, 2, 6, Janssen, 2, 6, MEDAC, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Novo Nordisk, 2, 6, Orion, 2, 6, Pfizer, 2, 6, Regeneron, 2, 6, Roche, 2, 6, Sandoz, 2, 6, Sanofi, 2, 6, UCB, 2, 6; **K. Horslev-Petersen**: None; **J. Lampa**: None; **R. van Vollenhoven**: AbbVie, 2, 6, AstraZeneca, 2, 5, 6, Biogen, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Galapagos, 2, 5, 6, GlaxoSmithKline, 6, Janssen, 2, 6, MSD/Merck Sharp and Dohme, 5, Novartis, 5, Pfizer, 2, 5, 6, RemeGen, 2, Roche, 5, Sanofi, 5, UCB, 2, 5, 6; **C. Lood**: Amytryx, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Citryll, 2, Eli Lilly, 5, Gilead, 5, Horizon Therapeutics, 5, Pfizer, 5, Redd Pharma, 5, 11; **M. Nurmohamed**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Celgene, 2, 5, 6, Galapagos, 2, 5, Janssen, 2, 5, 6, Menarini, 2, 5, 6, Merck/MSD, 2, 5, 6, Mundipharma, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0385

Heterogeneity of the Joint Location Supports the Importance of Local Factors in Early RA Synovitis : Analysis of the ERA UCLouvain Brussels Cohort

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: ERA is considered to be a systemic disorder, but the role of local factors in driving synovial inflammation is increasingly being recognized. These joint-specific factors may modulate disease phenotype. We will study the spatial distribution of swelling (S), tenderness (T) and erosions in a large cohort of ERA patients to assess the existence of joint patterns. Patients treated with MTX were evaluated after 3 and 6 months for joint swelling (JS).

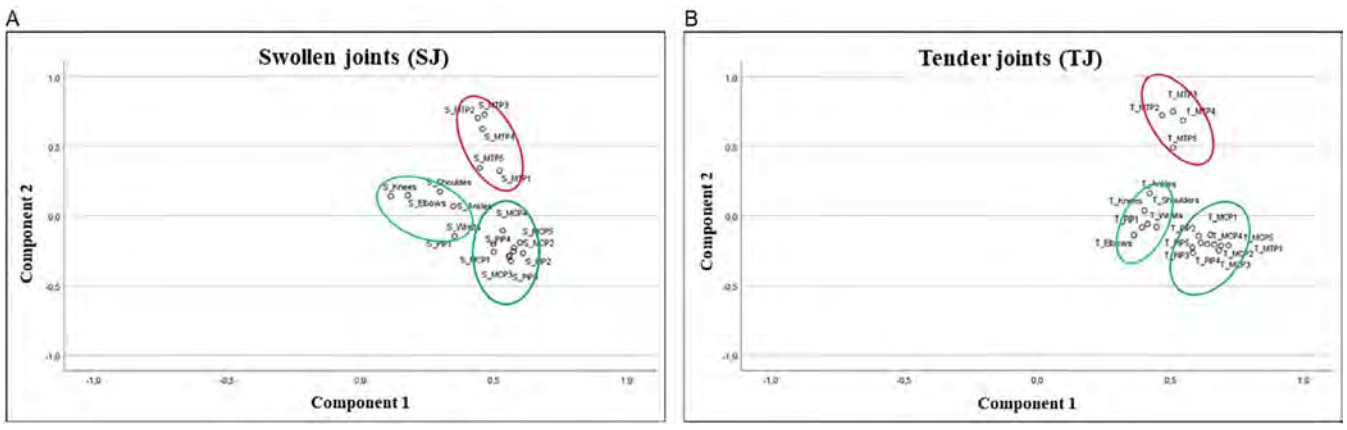

Figure 1 The average spatial distribution of SJ (A) and TJ (B)

Methods: This analysis was based on data from our ERA UCLouvain Brussels cohort. The physician assessed prevalence of baseline SJ and TJ status before DMARD initiation. The association between BL swelling, tender, erosions and disease characteristics was investigated for each individual joint. Remission rates (DAS28-CRP < 2.6) in patients treated with MTX were assessed.

Results: 452 newly diagnosed untreated RA patients were included: mostly female (72.3%), mean age 47.5 years, ACPA/RF positivity 64.8% and 63.3%, erosive disease in 44%, mean DAS28CRP - 4.6 and HAQ - 1.23. In total, 18,080 joints were assessed for swelling and tenderness at baseline, of which 20.4% were SJ and 27.6% were TJ. Wrist was the most frequently S and T joint (in 57% and 50.8% of patients), followed by PIP 2 and 3. Assessment of S and T showed a good correlation for most joints, except for shoulder and MTP1.

We applied PCA on SJ and TJ matrices to assess for potential clusters of joint prone to be concurrently involved in patients (Figure 1). We found three joint clusters: one with MTP1-5, one with hand joints, and one with larger joints. Wrist seemed to locate at the boundaries between fingers and large joints clusters. Analysis for ACPA-positive and ACPA-negative patients found very similar results. The higher rates of bone erosions were observed in the MTP cluster. Erosions were less frequent in the MCP+PIP, and almost absent in large joint, excepted for wrist.

We then divided the patients into 2 subgroups according the swelling for each joint location and compared clinical characteristics. We found that MTP4,5 are more often S in patients younger than 50 years and MCP2-4 in ≥50 years old patients. Swelling in MCP1,3,4 and MTP1,2,5 is associated with erosive disease, whereas swelling of MTPs (MTP1,2,5) is associated with higher frequency of ACPA. Knee swelling more frequently manifest in non-erosive and seronegative disease. Swelling of multiple joints (knee, elbow, shoulder, ankle, wrist, MCP3, PIP 1-2, and MTP5) associates with a higher DAS28CRP, just as higher HAQ score (knee, shoulder, ankle, MCP 1-5, MTP1,5 and PIP1-2).

We analyzed the impact of MTX montherapy on joint swelling. Number of SJs decreased significantly after 6 months: swelling persisted in 36.3%. We found no significant difference in response and JS persistence. We grouped all joints into the previously identified clusters, but no statistical difference in resolution of JS was observed.

Conclusion: This is the first study investigating the spatial distribution of arthritis in a large cohorts of early untreaded RA using unbiased approach. We identify clusters of simultaneously involved joints (hands and fingers cluster, metatarsophalangeal cluster and large joints cluster), supporting the importance of local factors driving synovitis in RA.

Disclosure: L. BRICMAN: None; **c. triaille**: None; **F. Natalucci**: None; **E. Sapart**: None; **T. Sokolova**: None; **A. AVRAMOVSKA**: None; **T. KIRCHGESNER**: None; **P. Durez**: None.

Abstract Number: 0386

Functional Disability and Disease Activity Are Affected by Social Determinants of Health in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The relationship between social determinants of health (SDH) (e.g. income, education, and employment status) and disease outcomes in the RA population is not well documented. We aimed to understand the effect of different SDH on disease activity and functional ability.

Methods: All retrospective data were extracted from the Ontario Best Practices Research Initiative- Rheumatoid Arthritis (OBRI-RA) registry for the period January 2008 to April 2022. We conducted adjusted generalized linear mixed models analysis to investigate the effect of baseline SDH on disease activity, using the Clinical disease activity index (CDAI), and functional disability, using the Health Assessment Questionnaire-disability index (HAQ-DI) at 12 months follow-up. The analysis was completed on multiple imputed.

Results: Two thousand six hundred fifty-one patients were identified with a mean (SD) age of 58.1 years (12.9) and 77.8% were female.

Retired patients (compared to unemployed) had higher improvement (difference =-1.62; 95%CI: --3.11,-0.14)and current smokers (compared to never/past) had lower improvement (difference =0.95; 95%CI: -0.02, 1.92)in disease activity (CDAI) at 12 months.

CDAI LDA/remission was less common current smokers (adj ORs: 0.82; 95%CI: 0.68, 0.99) and more common in females (adj ORs: 1.33; 95%CI: 1.12, 1.58).

Compared to unemployed, employed (difference =-0.24; 95%CI: -0.32,-0.16) or retired patients (difference =-0.16; 95%CI: -0.25,-0.07), those with higher house hold income (>50 vs. ≤ 50 CAD) (difference =-0.10; 95%CI: -0.16, -0.04), and post-secondary education (compared to high school or less) (difference =-0.07; 95%CI: -0.11, -0.02) had greater improvement of physical function (Table 1). Caucasian race (compared to non-Caucasian) and alcohol consumption (compared to never use) were also associated with a positive impact on functional ability. In contrast, currently smokers (compared to never/past) had lower improvements in physical function (difference= 0.08; 95%CI: 0.01, 0.14).

Conclusion: Our study suggests that disease activity and functional disability are affected by different SDH factors at 12 months follow-up. These differences in SDH must be understood and addressed by rheumatologists to provide equitable healthcare for all patients with RA.

Disclosure: M. Movahedi: None; **K. Cui**: None; **G. Tomilnson**: None; **A. Cesta**: None; **x. Li**: None; **C. Bombardier**: None.

Abstract Number: 0387

The Association Between Inflammation, High-Sensitivity Cardiac Troponin T, and Cardiovascular Events in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) have a 1.5x excess risk of cardiovascular (CV) disease compared to the general population, attributed to chronic inflammation. In the general population, detectable levels of high sensitivity cardiac troponin (hs-cTnT) are associated with higher risk of major cardiovascular (CV) events (MACE); while this same relationship is expected in RA, we sought to determine whether inflammation may modify this relationship. The objective of this study was to test the association between hs-cTnT with MACE, and further determine whether this relationship may differ by inflammatory states.

Methods: We studied 185 patients in a longitudinal RA cohort with blood samples and hsCRP measured annually, who experienced either a significant increase in hsCRP low→high or decrease in hsCRP high→low, defined as hsCRP≥10 mg/L, in 2 consecutive annual visits. Subjects on statin therapy or lipid-lowering therapy were excluded. Hs-cTnT, a marker of subclinical myocardial injury and routine lipids were measured at baseline; estimated 10-year atherosclerotic CV risk was also calculated at baseline. The primary outcome, MACE was obtained using medical record review from linked electronic health record (EHR) data. Patients were followed from baseline until MACE, death, last EHR encounter or 15 years,

Table 1. Baseline clinical characteristics of RA patients in the study.

Characteristics	hsCRP low→high cohort **n=101**	hsCRP high→low cohort **n=84**
Age, mean (SD)	59.2 (12.7)	57.6 (12.8)
Female (%)	80	89
RA disease duration, median, IQR	16 [8, 27]	14 [8, 28]
Anti-CCP positive, (%)	69	80
DAS28_CRP, median, IQR	3.22 [2.34, 4.09]	5.18 [3.48, 6.56]
Hs-CRP, median, IQR	4.50 [1.67, 8.13]	28.46 [22.08, 44.o09]
Cardiovascular Risk Factors (%)		
Diabetes Mellitus (%)	1	11
Hyperlipidemia (%)	13	14
Hypertension (%)	30	25
Current Smoker (%)	7.1	4.7
ACC/AHA ASCVD Risk*, median (IQR)	4.77 [2.05, 12.35]	4.08 [1.85, 9.15]
Baseline CV Biomarker Data		
Hs-TnT, median, IQR	10.02 [7.57, 14.90]	8.41 [6.71, 12.24]
Detectable hs-cTnT (%)	45.5	44

Anti-CCP indicates anti-cyclic citrullinated peptide; RA, rheumatoid arthritis; RF, rheumatoid factor; hs-CRP, high-sensitivity C-reactive protein; CDAI, clinical disease activity index; hs-cTNT, high sensitivity troponin

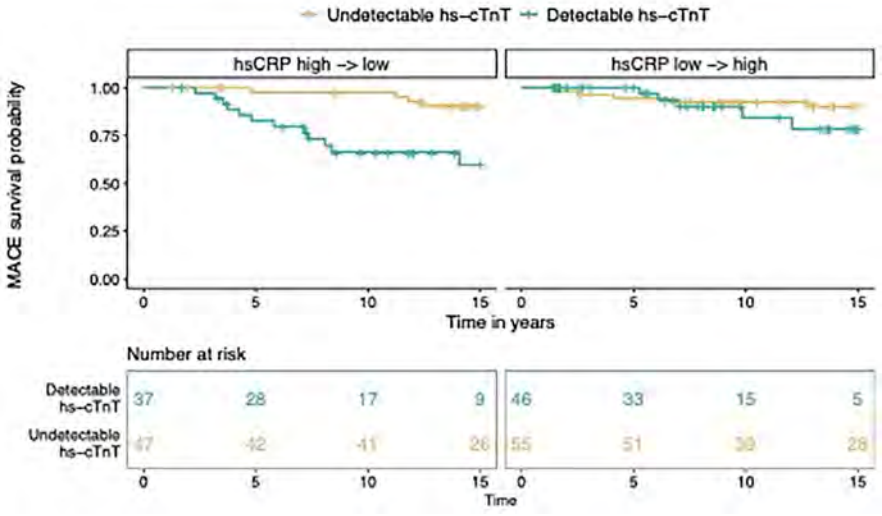

Figure 1. Survival curves for MACE among subjects with and without detectable hs-cTnT at baseline, stratified by cohort: hsCRP high->low cohort and hsCRP low->high.

whichever occurred first. The association between detectable hs-cTnT with MACE were determined using Cox proportional hazards models stratified by cohort status, i.e., hsCRP low→high cohort vs hsCRP high → low cohort; models were further adjusted be CV risk factors including age, sex, hypertension, hyperlipidemia, and smoking.

Results: The mean age was 58 years, 84% female, 74% anti-CCP positive with median RA disease duration of 15 years **(Table 1).** A total of 26 MACE events (14%) occurred during this period. The baseline median hsCRP among the hsCRP low→high cohort was 4.5 mg/dl [IQR 1.7-8.1) and in the hsCRP high→low cohort 28.5 mg/dl [IQR 22-44]. At baseline, in hsCRP low→high cohort, 46% had a detectable hs-cTnT, while 44% were detectable in the hsCRP high→low cohort. Detectable hs-cTnT at baseline was associated with future MACE HR 5.6 (95% CI 1.78-17.6; p=0.003) in the hsCRP high→low cohort with high inflammation at baseline; no association was observed with MACE in the hsCRP low→high cohort with low inflammation at baseline HR 1.84 (95% CI 0.53-6.41; p=0.3) **(Figure 1).** These associations remained after adjusting for CV risk factors.

Conclusion: In this RA cohort with overall low estimated ASCVD risk by standard CV risk scores, detectable hs-cTnT was associated with future MACE independent of traditional CV risk factors among those experiencing a high inflammatory state but not among those in a lower inflammatory state. These findings suggest that hs-cTnT may provide additional info for assessing CV risk among RA patients with overall low estimated ASCVD risk with active inflammation.

Disclosure: B. Weber: Bristol-Myers Squibb(BMS), 1, Horizon Therapeutics, 1, Kiniksa, 1, Novo Nordisk, 1; **D. Weisenfeld**: None; **M. Jeffway**: None; **J. Coblyn**: None; **M. Weinblatt**: Abbvie, 2, 5, Aclaris, 2, Amgen, 2, Aqtual, 5, Bristol Myers Squibb, 2, 5, Canfite, 11, Corevitas, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, 2, Glaxo Smith Kline, 2, Horizon, 2, Inmedix, 11, Janssen, 5, Johnson and Johnson, 2, Pfizer, 2, Prometheus Laboratories, 2, Rani, 2, Revolo, 2, Sanofi, 2, Sci Rhom, 2, Scipher, 2, 11, Set Point, 2, UCB, 2; **N. Shadick**: Abbvie, 5, AQtual, 5, Bristol-Myers Squibb(BMS), 5, Janssen, 5; **M. DiCarli**: Amgen, 2, Gilead, 5, Medtrace, 2, sanofi, 2; **K. Liao**: UCB, 2.

Abstract Number: 0388

Left Ventricular Geometry Abnormalities Are Related to Higher Clinical Activity in Rheumatoid Arthritis Patients

Victor Beltran[1], Iris Colunga[2], Dionicio A. Galarza-Delgado[2], José Ramón Azpiri-López[2], Jesus Alberto Cardenas-De la Garza[3], Rosa Arvizu-Rivera[4], Valeria Gonzalez-Gonzalez[5] and Angel Arias Peralta[6], [1]Rheumatology Service Hospital Universitario "Dr. José Eleuterio González", Monterrey, Mexico, [2]Hospital Universitario UANL, Monterrey, Mexico, [3]Hospital Universitario "Dr. José Eleuterio González", San Nicolas, Mexico, [4]Hospital Universitario \"Dr. José Eleuterio Gonzalez\", Escobedo, Mexico, [5]Universidad Autónoma de Nuevo León, Monterrey, Mexico, [6]Medicine Faculty, Universidad Autonoma De Nuevo Leon, Monterrey, Mexico

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) leading cause of death is cardiovascular (CV) disease. RA patients can develop silent myocardial tissue alterations, which result in changes in left ventricular geometry (LVG) and increase CV morbidity and mortality. Echocardiography is a non-invasive tool that can detect subtle geometrical abnormalities. The purpose of this study is to compare the RA disease activity in patients with and without left ventricular geometry abnormalities

Table 1. Demographic Characteristics (n= 156)			
Variable	Patients with LVG abnormalities (n= 52)	Patients with normal LVG (n= 104)	p
Age (years), mean (±SD)	58.3 (8.2)	54.4 (9.1)	0.009
Women, n (%)	50 (96.2)	97 (93.3)	NS
Comorbidities, n (%)			
Active smoking	6 (11.5)	10 (9.6)	NS
Dyslipidemia	14 (26.9)	39 (37.5)	NS
T2DM	11 (21.2)	18 (17.3)	NS
Hypertension	24 (46.2)	32 (30.8)	NS
Obesity	19 (36.5)	27 (26.0)	NS

This table shows a comparison of demographic characteristics and comorbidities between groups. LVG left ventricular geometry; SD standard deviation; T2DM type 2 diabetes mellitus; NS No significative.

Table 2. Disease characteristics (n= 156)			
Variable	Patients with LVG altered (n= 52)	Patients with normal LVG (n= 104)	p
Disease duration (years), median (IQR)	7.7 (3.4-16.6)	7.4 (2.9-13.7)	NS
DAS28-CRP, median (iQR)	3.4 (2.2-4.5)	2.7 (1.9-3.81)	0.022
Lab work-up, median (iQR)			
CRP (mg/dL)	0.8 (0.5-1.0)	0.5 (0.2-1.0)	0.026
ESR (mm/Hr)	26.0 (16.0-39.7)	21.5 (14.0-35.0)	NS
ACPA (U/mL)	27.1 (2.2-192.7)	42.2 (1.6-199.9)	NS
RF IgG (U/mL)	5.8 (2.0-16.9)	4.0 (2.0-11.9)	NS
RF IgM (U/mL)	123.8 (19.2-200.0)	190.4 (34.9-200.0)	NS
RF IgA (U/mL)	40.5 (6.6-179.8)	66.8 (6.3-200.0)	NS
Treatment, n (%)			
Methotrexate	45 (86.5)	78 (75.0)	NS
bsDMARDs	6 (11.5)	14 (13.5)	NS
Prednisone	38 (73.1)	53 (51.0)	0.008

This table shows a comparison of disease characteristics between groups. LVG left ventricular geometry; iQR interquartile range; CRP C reactive protein; ESR erythrocyte sedimentation rate; ACPA anticitrullinated peptide antibody; RF rheumatoid factor; NS no significative.

Methods: Descriptive, comparative, and cross-sectional study. We enrolled RA patients between 40 and 75 years old who fulfilled ACR/EULAR 2010 classification criteria. The disease activity was evaluated by DAS28-CRP. A transthoracic echocardiography was realized. Normal left ventricular geometry was defined as a left ventricular mass index ≤115 g/m^2 for men and ≤95 g/m^2 for women, and a relative wall thickness ≤0.42. Left ventricular abnormalities were considered as any value higher than normal. Normality was assessed by the Kolmogorov-Smirnov test. Variables were described by central tendency and dispersion measures. Differences between groups were analyzed by chi-squared test and Students' t-test or Mann-Whitney U test, accordingly. Statistical significantly was $p \leq 0.05$.

Results: A total of 158 RA patients were included. Demographic characteristics are presented in Table 1. Patients with LVG abnormalities were older (58.3 vs 54.4 years; *p*=0.009). There were no differences in sex and comorbidities (Table 1). The group with LVG abnormalities had higher disease activity (3.4 vs 2.7; *p*=0.022) and C reactive protein levels (0.8 vs 0.5; *p*=0.026). More patients with abnormalities in LVG used prednisone than those with normal LVG (73.1% vs 51.0%; *p*=0.008). There were no differences in disease duration or serology (Table 2).

Conclusion: RA patients with LVG abnormalities had higher disease activity and C reactive protein levels, and current prednisone use than those with normal LVG. Echocardiography may be a useful tool to detect early and subtle LVG abnormalities, particularly in patients with those characteristics.

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Abstract Number: 0389

The Role of anti-CCP3 Antibodies in anti-CCP2 Antibody Negative Patients with Musculoskeletal Symptoms

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate, in primary care, whether testing anti-CCP3 antibodies in anti-CCP2 negative individuals with musculoskeletal (MSK) symptoms, improved the prediction of inflammatory arthritis (IA)/rheumatoid arthritis (RA) progression.

Methods: A total of 469 anti-CCP2 negative individuals who presented to their general practitioner (GP) with new MSK symptoms were included in this study. All participants underwent baseline anti-CCP3 testing (QUANTA Lite CCP3; Inova Diagnostics) and received a questionnaire 12 months after enrolment assessing their disease status. The GPs of those individuals who reported progression to IA/RA were contacted by a rheumatologist to confirm the diagnosis. Univariate and multi-variate analyses were performed to establish variables associated with disease progression.

Results: Both the progression rate towards IA/RA and the prevalence of anti-CCP3 antibodies in anti-CCP2 negative individuals with MSK symptoms were low. Only 61/469 (13.0%) participants reported disease progression of which 43/61 (70.5%) and 13/61 (21.3%) were confirmed to have a diagnosis of IA and RA, respectively. Anti-CCP3 was positive in only 16/469 (3.4%) anti-CCP2 negative individuals. However, interestingly, in univariate analysis, anti-CCP3 positivity was associated with self-reported progression (p< 0.001) and with a diagnosis of IA (p=0.03), but not with a diagnosis of RA (p=0.37). In contrast, when considering antibody levels, anti-CCP3 differed significantly between progressors and non-progressors (p< 0.0001) for all three categories (self-reported progression, IA and RA diagnosis).

At the manufacturer's cut-off (≥20 units) the sensitivity for progression to IA/RA ranged from 8.0-14.0% with high specificity (≥97.0%). The corresponding odds ratios (OR) ranged from 2.4 (95% CI 0.3-20.0) to 7.8 (95% CI 2.8-21.8). Interestingly, when cut-offs were optimized for F-1 score, lower cut-off values (5 units) significantly increased the OR for progression in all three categories. After correcting for confounding factors (age, gender), in multi-variate analysis anti-CCP3 levels remained significantly associated with diagnosis of RA (p=0.02).

Dx	Age	Gender·(male)	Family·history	CCP3·(≥20·units)
Self-reported	***p*<0.0001**	2.6·(1.5-4.8) ***p*=0.0010**	0.8·(0.4-1.5) *p*=0.45	7.5·(2.3-24.0) ***p*=0.0003**
Rheum-IA	*p*=0.0683	2.3·(1.2-4.6) ***p*=0.0113**	1.1·(0.5-2.2) *p*=0.86	3.5·(1.2-11.0) ***p*=0.03**
Rheum-RA	***p*=0.0006**	1.7·(0.4-6.2) *p*=0.3471	1.5·(0.4-5.4) *p*=0.54	2.4·(0.1-18.6) *p*=0.37

Demographic and serological features and their association with disease progression.

Conclusion: The rate of progression to IA/RA in anti-CCP2 negative individuals with MSK symptoms seen in primary care setting was low over a 12-months follow-up period. Our results showed that anti-CCP3 antibody levels have a potential role in improving prediction in IA/RA progression in anti-CCP2 negative individuals with MSK symptoms. Future studies are warranted to validate the cut-off values for anti-CCP3 antibodies with best prediction accuracy in this population.

Disclosure: A. Di Matteo: None; **K. Mankia**: Abbvie, 6, Eli Lilly, 5, Galapagos, 6, Gilead, 5, Serac Lifesciences, 6; **L. Garcia-Montoya**: None; **J. Nam**: None; **S. sharrack**: None; **M. Mahler**: werfen, 3; **P. Emery**: Boehringer Ingelheim, 2, Eli Lilly, 2, Novartis, 2.

Abstract Number: 0390

Statins Influence the Relationship Between ATP-binding Cassette Transporter A1 (ABCA1)-mediated Cholesterol Efflux and Coronary Atherosclerosis in Rheumatoid Arthritis

George Karpouzas[1], Bianca Papotti[2], Sarah Ormseth[3], Marcella Palumbo[2], Elizabeth Hernandez[3], Maria Pia Adorni[4], Francesca Zimetti[2], Matthew Budoff[1] and Nicoletta Ronda[2], [1]Harbor-UCLA Medical Center, Torrance, CA, [2]University of Parma, Department of Food and Drug, Parma, Italy, [3]The Lundquist Institute, Torrance, CA, [4]Department of Medicine and Surgery, Unit of Neuroscience, University of Parma, Parma, Italy

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
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Session Type: Poster Session A
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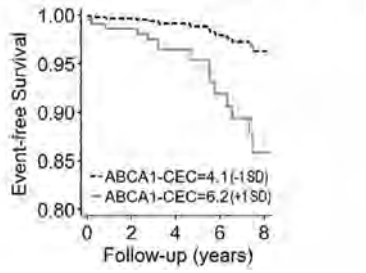
Background/Purpose: Cholesterol efflux capacity (CEC) is the main antiatherogenic function of high-density lipoprotein (HDL). ATP-binding-cassette A1 (ABCA1) membrane transporter initiates cholesterol export from arterial macrophages to pre-β HDL particles fostering their maturation; in turn, those accept cholesterol through ABCG1-mediated export. Impaired pre-βHDL maturation may disrupt the collaborative function of the two transporters and adversely affect atherosclerosis. Statins exert atheroprotective functions systemically and locally on plaque. We here evaluated associations between ABCA1-CEC, coronary atherosclerosis and cardiovascular risk and the influence of statins on those relationships in rheumatoid arthritis (RA).

Methods: Atherosclerosis (noncalcified, partially or fully calcified, low attenuation plaques) was evaluated with coronary computed tomography angiography in 140 patients without cardiovascular disease and reassessed in 99 after 6.9 ±0.4 years. ABCA1-CEC and ABCG1-CEC were measured in J774 macrophages and Chinese hamster ovary cells respectively as previously described. Cox regression evaluated the association between ABCA1-CEC and cardiovascular risk.

Figure 1 ABCA1-CEC associates with cardiovascular risk in RA



Multivariable negative binomial and robust logistic regression tested associations of ABCA1-CEC and its interactions with statin therapy on coronary plaque burden at baseline and its progression respectively.

Results: ABCA1-CEC inversely correlated with ABCG1-CEC (Pearson r= -0.167, p=0.049). ABCA1-CEC (per SD increment) associated with long-term cardiovascular event risk after adjustments for cardiovascular risk score and baseline plaque burden [HR 2.05 (95% CI 1.20-3.48), Figure 1]. There was an interaction of ABCA1-CEC with time-varying statin use (p=0.038) such that current statin use inversely associated with risk only in patients with ABCA1-CEC below the upper tertile. ABCA1-CEC had no main effect on plaque or plaque progression; instead, ABCA1-CEC (per SD) associated with fewer baseline total plaques (adjusted rate ratio [aRR] 0.81, [95%CI 0.65-1.00]), noncalcified plaques (aRR 0.78 [95%CI

Figure 2. Associations of ABCA1-CEC with baseline atherosclerosis outcomes for the total sample and stratified by statin use. Rate ratios derived from negative binomial regression models indicate the percent change in the outcome associated with one standard deviation unit increase in ABCA1-CEC. All models controlled for ASCVD risk score and high-density lipoprotein cholesterol.*Additionally adjusted for waist circumference †Additionally adjusted for waist circumference and age at diagnosis ‡Additionally adjusted for age at diagnosis.

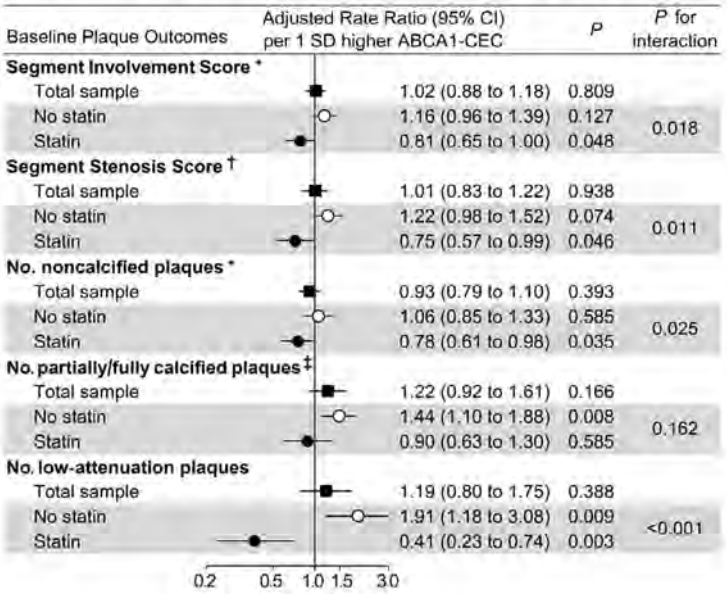
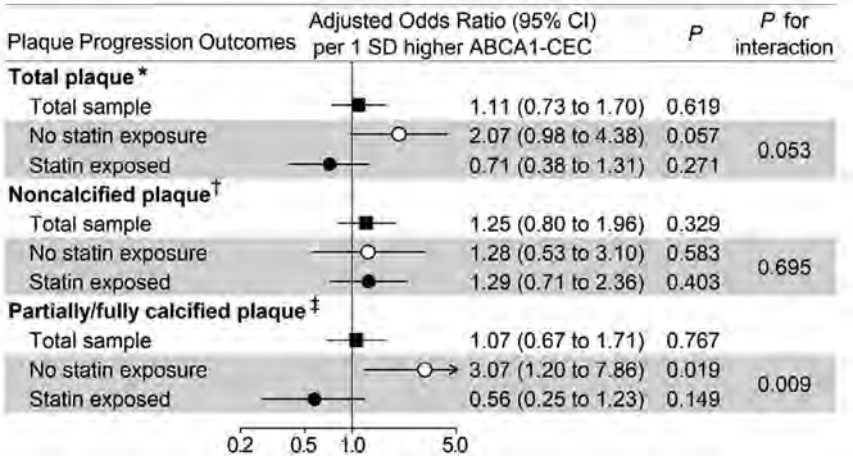


Figure 3. Associations of ABCA1-CEC with coronary atherosclerosis progression for the total sample and stratified by statin exposure during follow-up. Odds ratios derived from binary logistic regression models adjusted for ASCVD risk score, high-density lipoprotein cholesterol, baseline plaque burden, and time between scans *Additionally adjusted for time-averaged C-reactive protein †Additionally adjusted for time-weighted average prednisone dose ‡Additionally adjusted for time-averaged C-reactive protein, waist circumference, and age at diagnosis.



0.61-0.98]), and low attenuation plaques (aRR 0.41 [95%CI 0.23-0.74]) in statin users, and more low attenuation plaques (aRR 1.91 [95%CI 1.18-3.08]) in nonusers (p-for-interaction=0.018, 0.011, 0.025 and < 0.001 respectively, Figure 2). Moreover, ABCA1-CEC (per SD) associated with greater partially/fully-calcified plaque progression (adjusted odds ratio 3.07 [95%CI 1.20-7.86]) only in patients not exposed to statins during follow-up (p-for-interaction=0.009, Figure 3).

Conclusion: In the context of inflammation and impaired pre-β HDL maturation typical of RA, higher ABCA1-CEC may reflect a proatherogenic rather than atheroprotective state, associated with greater coronary atherosclerosis burden, vulnerability and cardiovascular risk. Statin use, by reducing cell cholesterol overload and restoring pre-β HDL maturation may unmask and promote the atheroprotective effect of ABCA1-CEC.

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Abstract Number: 0391

Biologic Use Regulates the Impact of Inflammation on Ischemic Cardiovascular Risk in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic inflammation contributes to enhanced cardiovascular risk in rheumatoid arthritis (RA). Biologic disease modifying antirheumatic drugs (bDMARDs) control inflammation in many conventional synthetic DMARD non-responders and improve outcomes. We explored whether baseline bDMARD use may influence the impact of disease activity and systemic inflammation on long-term cardiovascular risk in RA.

Methods: We studied 4370 patients free of cardiovascular disease upon registration to *An International Cardiovascular Consortium for people with RA* (ATACC-RA) and followed prospectively. Outcomes included (a) major adverse cardiovascular events (MACE) defined as non-fatal myocardial infarction, non-fatal stroke, or cardiovascular death and (b) any ischemic cardiovascular events (CVE) comprising MACE, coronary revascularization, stable angina pectoris, transient ischemic attack and peripheral arterial disease with or without revascularization. Missing data were imputed using multiple imputation with 10 repetitions.

Figure 1 bDMARD use regulates the effect of inflammation on ischemic cardiovascular risk in patients with RA

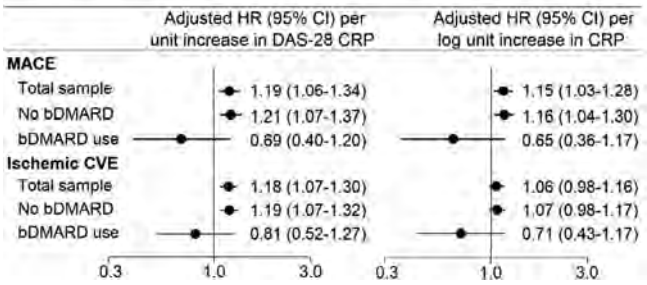
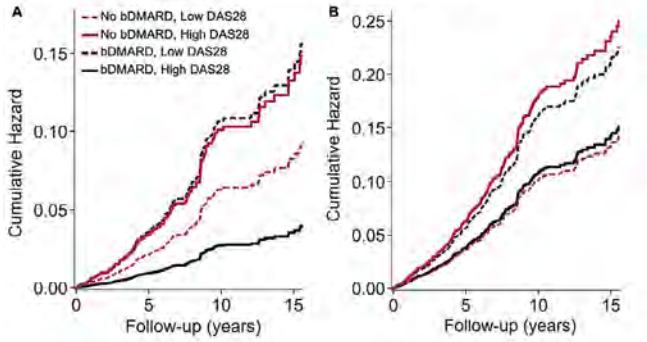


Figure 2 Cumulative probability of (A) Major Adverse Cardiovascular Event (MACE) and (B) any ischemic events in bDMARD users and nonusers at high (+1-SD) and low (-1-SD) baseline DAS28-CRP



Multivariable Cox models stratified by center evaluated the impact of disease activity (DAS28-CRP), inflammation (CRP), bDMARD use and their respective interactions on CVE risk after adjusting for age, gender, hypertension, diabetes, family history, smoking and total cholesterol to high-density lipoprotein ratio. Two corroborating sensitivity analyses were performed; the first included patients enrolled in the cohort on or after January 1, 2000, when bDMARD use became more prevalent. The second used inverse probability of treatment weights to balance differences in bDMARD treated and untreated patients.

Results: Throughout 26,534 patient years, 239 first MACE and 362 total ischemic CVE were recorded. Among bDMARD nonusers, incidence of MACE and any ischemic CVE was 9.3 (95% CI 8.2-10.6) and 14.2 (12.8-15.8) events/1000PY. Rates for bDMARD users were [5.4 (95% CI 2.9-10.1) and 8.2 (5.0-13.6) events/1000PY. In the entire cohort, DAS-28 CRP and CRP(ln) associated with greater risk of MACE [(adjusted hazards ratio [aHR] 1.19 (95%CI 1.06-1.34), p=0.004 and HR 1.15 (1.02-1.28), p=0.017], while for all ischemic CVE the association was significant for DAS28-CRP [aHR 1.1 (95%CI 1.07-1.30)], but not CRP(ln) [aHR 1.06 (0.97-1.16)]. In bDMARD nonusers, higher DAS28-CRP and CRP(ln) associated with greater risk of MACE [aHR 1.21 (95%CI 1.07-1.37), p=0.002 and aHR 1.16 (1.04-1.30), p=0.009]. However, this was not the case in bDMARD users [p-for-interaction= 0.017 and 0.011 correspondingly, Figures 1 and 2]. In contrast, no significant interaction between DAS28-CRP or CRP and bDMARD use on any ischemic CVE risk was observed (p-for-interaction= 0.167 and 0.237 respectively). Both sensitivity analyses yielded similar results.

Conclusion: Conclusion: Higher disease activity and systemic inflammation at baseline associated with greater risk of MACE in bDMARD nonusers but not in users. This may suggest the presence of additional bDMARD-specific benefits directly on atherosclerotic plaque —such as plaque stabilization— above and beyond effects on systemic inflammation.

Disclosure: G. Karpouzas: Janssen, 1, Pfizer, 5, Scipher, 1; **S. Ormseth**: None; **P. Van Riel**: None; **E. Myasoedova**: None; **M. Gonzalez-Gay**: AbbVie/Abbott, 5, 6, Amgen, 5, 6, Pfizer, 5, 6; **A. Corrales**: None; **S. Rantapää-Dahlqvist**: None; **P. Sfikakis**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Boehringer-Ingelheim, 2, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen,

2, 5, Novartis, 2, 5, Pfizer, 2, 5; **P. Dessein**: None; **L. Tsang**: None; **C. Hitchon**: Astra Zeneca, 1, Pfizer, 5; **H. El Gabalawi**: None; **V. Pascual Ramos**: None; **I. Contreras Yañez**: None; **I. Colunga**: None; **D. Galarza-Delgado**: None; **J. Azpiri-López**: None; **S. Rolefstad**: None; **A. Semb**: None; **D. Misra**: None; **E. Hauge**: AbbVie/Abbott, 5, 6, Galapagos, 5, Novartis, 6, Novo Nordic Foundation, 5, 6, Sanofi, 6, Sobi, 6; **G. KITAS**: None.

Abstract Number: 0392

Novel Diagnostic Markers for Rheumatoid Arthritis Including Anti-CarP (Carbamylated Protein), Anti-Sa (Citrullinated Vimentin) and Anti-CEP1 (Citrullinated Enolase Peptide1) Are Frequently Positive in Diagnostic Profiles

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite the diagnostic contribution of Anti-CCP3.1 (cyclic citrillunated peptide) antibody and RF (rheumatoid factor) as classified by the 2010 ACR/EULAR RA criteria, approximately one-third of patients with rheumatoid arthritis (RA) are considered "seronegative." Novel markers, Anti-CarP Anti-Sa, and Anti-CEP1 were recently added in order to improve RA diagnosis and characterization. Citrullination and carbamylation are post-translational modifications, and autoantibodies against citrullinated and carbamylated proteins in RA patients may predict the development of RA and may be associated with more active disease and higher risk of developing joint erosions.

Methods: Serum from 28,575 patient samples was analyzed for RF (Roche Integra/COBAS), Anti-CCP3.1 (QUANTA Lite IgG/IgA), and/or enzyme immunosorbent assay (ELISA) lab-developed tests (LDT) for 14-3-3 eta, Anti-CarP, Anti-Sa, and/or Anti-CEP1 in three RA profiles: RheumAssure (RF, Anti-CCP3.1, 14-3-3 eta), RAdx6 (RF, Anti-CCP3.1, 14-3-3 eta, Anti-CarP, Anti-Sa, Anti-CEP1) and SeroNegRAdx4 (14-3-3 eta, Anti-CarP, Anti-Sa, Anti-CEP1).

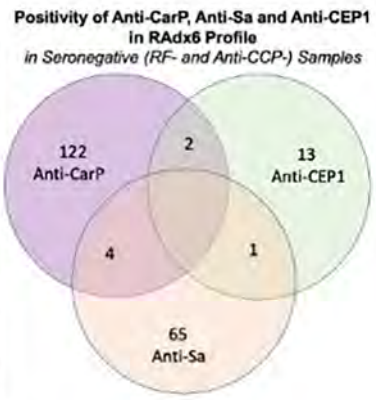
Results: Here, 24,549 RheumAssure, 2672 RAdx6 and 1354 SeroNegRAdx4 were performed and exhibited overall positivity of 28.5%, 35.4% and 19.9%, respectively as shown in Table 1. Novel markers, Anti-CarP, Anti-Sa and Anti-CEP1, added an incremental positivity of 7.7% and 13.5% in RAdx6 and SeroNegRAdx4, respectively. Of note, this additional 7.7%

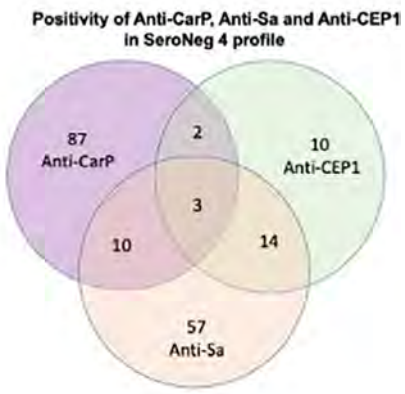
Table 1. Positivity Rates of RA Diagnostic Profiles

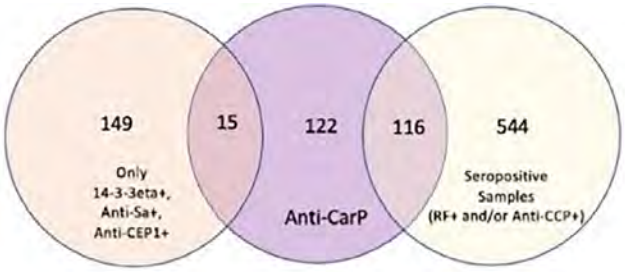
RA Profile	n=	Overall Positivity rate	Positivity rate from conventional markers alone	Incremental positivity from extra marker(s)
RheumAssure (RF, Anti-CCP, 14-3-3eta)	24549	**28.5%**	**24.2%** from RF & Anti-CCP **4.3%** from 14-3-3eta	**N/A**
RAdx6 (RF, Anti-CCP, 14-3-3eta, Anti-CarP, Anti-Sa, Anti-CEP1)	2672	**35.4%**	**24.7%** from RF & Anti-CCP **3.0%** from 14-3-3eta	**7.7%** from Anti-CarP, Anti-Sa, Anti-CarP
SeroNeg 4 (14-3-3, Anti-CarP, Anti-Sa, Anti-CEP1)	1354	**19.9%**	**6.4%** from 14-3-3eta	**13.5%** from Anti-CarP, Anti-Sa, Anti-CarP

Table 2. RAdx6 Positivity Figure 1. Anti-CarP, Anti-Sa & Anti-CEP1 in Seronegative RAdx6 Samples; Figure 2. Anti-CarP, Anti-Sa & Anti-CEP1 in SeroNeg RAdx4 Samples

RAdx6 (RF, Anti-CCP, 14-3-3eta, Anti-CarP, Anti-Sa, and Anti-CEP1)	Count	%
Total	2672	
All negative	1726	64.6%
Any positive (at least one positive)	946	35.4%
Overall RF positivity	559	21.1%
Overall Anti-CCP positivity	307	11.5%
Overall 14-3-3eta positivity	219	8.2%
Overall Anti-CarP positivity	253	9.5%
Overall Anti-Sa positivity	262	9.8%
Overall Anti-CEP1 positivity	137	5.1%
RF positive only	272	13.2%
Anti-CCP positive only	73	3.8%
14-3-3eta positive only	70	2.6%
Anti-CarP positive only	122	4.6%
Anti-Sa positive only	65	2.4%
Anti-CEP1 positive only	13	0.5%
More than one positive	331	12.4%







Overall Anti-CarP positivity	253
Anti-CarP positive only	122
Anti-CarP in Seropositive samples (i.e. RF+ and/or Anti-CCP+)	116
Anti-CarP with only 14-3-3eta+ +/- Anti-Sa+ +/- Anti-CEP1+	15

Figure 3. Anti-CarP Positivity

positivity was seen in 207 (of 2672 total) RAdx6 samples that tested negative for RF, Anti-CCP3.1 and 14-3-3 eta. SeroNegRAdx4 is designed to be useful in patients with high clinical suspicion for RA who have previously tested negative for RF and Anti-CCP. Though clinical histories are not known, almost twice as many, 13.5%, were positive for Anti-CarP and/or Anti-Sa and/or Anti-CEP1. In Table 2, positivity rates of individual markers in RAdx6 are shown where RF was the most frequently positive, followed by Anti-CCP3.1, Anti-Sa, Anti-CarP, 14-3-3 eta, and Anti-CEP1. Concomitant positivity of more than one marker was common, occurring in one third of all positives (331/946, 35.0%). Almost one-quarter (24.7%) of all RAdx6 samples were Seropositive (RF+ and/or Anti-CCP3.1+). In Seronegative samples, the positivity of Anti-CarP, Anti-Sa and Anti-CEP1 (Figures 1 and 2) may be helpful for diagnosis. Figure 3 shows that more than half the time, Anti-CarP is positive in the presence of another RA-specific marker (131/253, 51.8%).

Conclusion: Here, we show the overall positivity rates of three RA profiles. RAdx6 as the most comprehensive RA profile is positive more than one-third of the time. SeroNegRAdx4 offers a potential 20% incremental benefit in diagnosing RA. RF and Anti-CCP3.1 together can detect about a quarter of all positivity observed, but novel markers for RA, Anti-CarP, Anti-Sa and Anti-CEP1, provide additional positivity of 7.7% and 13.5% that may be beneficial in diagnosing early RA and RA in Seronegative patients. Anti-CarP was frequently positive with RF and/or Anti-CCP3.1 and as such, is a useful prognostic marker for erosive disease.

Disclosure: J. Yang: None; **R. Punzalan**: None; **L. Andrew**: None; **M. Nappi**: LabCorp, 3; **V. ricchiuti**: None; **M. Zikry**: None; **K. Chun**: None.

Abstract Number: 0393

Pulmonary Involvement in Patients with Seropositive and ACPA Positive Rheumatoid Arthritis (RA-ILD) – Novel Screening Protocol for Early Detection of Pulmonary Involvement

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Seropositive and ACPA positive Rheumatoid Arthritis (RA) is associated with significant cardiovascular and pulmonary comorbidity. However, screening for early detection of pulmonary involvement especially intestitial lung disease (ILD) in patients with seropositive and ACPA positive Rheumatoid Arthritis is not yet established.

Methods: We included a total of 50 consecutive patients with a confirmed diagnosis of seropositive and ACPA positive Rheumatoid Arthritis without symptoms for or known cardiopulmonary disease. For the purpose of this study, we used a noninvasive radiation-free approach to screen for pulmonary, pleural or vascular manifestation of the disease by means of

Table 1

Deskriptive Kennwerte: RA-ILD (Gesamtstichprobe, n = 43)

	n (valid)	% (valid)	n (NA)	% (NA)	Mean	95%CI (low)	95%CI (high)	SD	SE	Median	25% Quantile	75% Quantile	Min	Max
Age	43	100	0	0	58.5	55.1	61.9	11.3	1.7	57.0	51.5	68.5	28.0	79.0
Disease Duration (yrs)	43	100	0	0	10.1	7.3	12.9	9.4	1.4	6.0	3.0	16.0	1.0	35.0
BMI	43	100	0	0	25.3	23.9	26.7	4.7	0.7	24.1	22.3	27.8	16.8	39.8
ESR (mm/h)	43	100	0	0	10.6	9.0	12.2	5.2	0.8	10.0	10.0	10.0	2.0	28.0
CRP (mg/l)	43	100	0	0	3.7	3.2	4.2	1.7	0.3	2.9	2.9	3.3	2.9	11.7
DAS28 (CRP)	43	100	0	0	2.2	2.0	2.5	0.9	0.1	1.9	1.7	2.6	1.4	4.9
DAS28 (ESR)	43	100	0	0	2.3	2.0	2.6	0.9	0.1	2.0	1.8	2.8	0.6	5.1
CDAI	43	100	0	0	6.2	4.3	8.0	6.2	0.9	4.0	2.0	8.0	0.0	30.0
SDAI	43	100	0	0	6.6	4.7	8.4	6.2	0.9	4.3	2.8	8.3	0.3	30.3
RAID	43	100	0	0	2.3	1.9	2.7	1.3	0.2	2.2	1.3	3.0	0.0	6.3
RADAI	43	100	0	0	2.0	1.6	2.3	1.3	0.2	1.9	1.2	2.8	0.0	5.8
WHO-5	43	100	0	0	73.8	70.7	76.9	10.4	1.6	76.0	68.0	80.0	32.0	92.0
PHQ-4	43	100	0	0	0.6	0.2	1.0	1.4	0.2	0.0	0.0	0.0	0.0	4.0
EQ-5D	43	100	0	0	0.9	0.9	0.9	0.1	0.0	0.9	0.9	1.0	0.7	1.0
MST	43	100	0	0	20.2	13.1	27.3	23.8	3.6	15.0	0.0	30.0	0.0	120.0
FFbh	43	100	0	0	86.4	82.6	90.1	12.5	1.9	88.9	77.8	100.0	47.2	100.0
FACIT-F	43	100	0	0	43.5	41.6	45.3	6.2	0.9	45.0	41.0	47.5	25.0	52.0

Table 2

Forced Vital Capacity 80%

Value	Frequency (n)	Proportion (%)	Proportion valid - cumulative (%)
FVC % <= 80	3	6.98	6.98
FVC % > 80	40	93.02	100.00
NA	0	0.00	NA

pulmonary function tests (PFT), cardiopulmonary exercise test (CPET), echocardiography and pleuro-pulmonary transthoracic ultrasound (LUS).

Results: The data of 43 patients (mean age 58.5 years, 81.4% female, 93.02% non-smokers) were available for this analysis, as data collection is still ongoing. With an average disease duration of 10.1 years and with a mean remission of DAS28 ESR 2.3, DAS28 CRP 2.2 or low disease activity (CDAI 6.2, SDAI 6.6), respectively, depending on the used disease activity score, 34.88 % showed an erosive course. A reduced forced vital capacity (FVC ≤80%) on PFT was shown in 3 patients (6.98%), a reduced CO-diffusion capacity (DLCOc-SB ≤80%) in 14 patients (32.56%). In 39% of patients, we found noticeable changes in LUS, 23% with a pattern consistent with ILD. ILD was suspected in 13% with changes on LUS and additional PFT.

Numerous other RA- and ILD-associated parameters were collected in the present study (table 1 and 2).

Other findings included pleural consolidation suspicious for malignancy and pleural effusion on LUS, severe aortic stenosis in bicuspid aortic valve on echocardiography, severe impaired diffusion capacity due to lung emphysema and obstructive lung disease on PFT.

None of the patients showed signs of pulmonary vascular involvement or cardiac ischaemia on echocardiography or CPET.

Conclusion: In conclusion screening of RA-patients for pulmonary involvement with a non invasive, radiation free screening approach may detect a significant number of asymptomatic patients with signs consistent with pulmonary manifestation of rheumatoid arthritis, along with a variety of other cardiopulmonary comorbidities.

Disclosure: F. Popp: AbbVie/Abbott, 1, Boehringer-Ingelheim, 5; **M. Hoffmann**: Boehringer-Ingelheim, 5; **J. von Kempis**: Boehringer-Ingelheim, 5; **M. Welcker**: Abbvie, 1, 5, 6, Boehringer, 5, 6, GSK, 1, 6, Novartis, 1, 5, 6, Sanofi, 1, 6, UCB, 1; **W. von Wulffen**: Boehringer-Ingelheim, 5; **F. Reichenberger**: Boehringer-Ingelheim, 5.

Abstract Number: 0394

Higher Intakes of Red Meat Are Associated with an Increased Risk of Developing Seropositive but Not Seronegative Rheumatoid Arthritis - Results from a Nested Case-Control Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Healthy eating habits might prevent the development of rheumatoid arthritis (RA). We aimed to examine the relation between adherence to dietary recommendations and the risk of RA.

Methods: A nested case-control study was performed including participants from a population-based survey conducted in 1991-1996. Cases diagnosed with RA from inclusion until December 2016 were identified through register linkage and validated in a structured process. Four controls for each case, matched for sex, year of birth, and year of inclusion, were included. The controls were alive and RA-free when the index person was diagnosed with RA. Diet was assessed using a modified diet history method comprising of a seven-day menu book, a diet history questionnaire, and a complementary diet history interview.

According to the Swedish Dietary Guidelines (SDG) from 2015, a substantial daily intake of vegetables and fruits, fish and wholegrain products is recommended, whereas red meat and added sugars should be limited. Cut-off values for adherence were based on a previously validated Diet Quality Index, except for red and processed meat and added sugars, which were based on the SDG from 2015 and the World Health Organization guidelines from 2015 for sugar intake for adults, respectively.

Table 1. Baseline characteristics.

	RF/anti-CCP positive RA		RF/anti-CCP negative RA	
	Cases (n=204)	Controls (n=816)	Cases (n=101)	Controls (n=404)
Age at screening (years), mean [SD]	56.4 (7.0)	56.0 (6.9)	57.7 (7.3)	57.3 (7.2)
Female, n [%]	161 (78.9)	644 (78.9)	71 (70.3)	284 (70.3)
Formal education ≤8 years, n [%]	90 (47.9)	294 (38.6)	35 (37.2)	157 (42.2)
Current smoker at time of screening, n [%]	76 (40.4)	220 (28.8)	24 (25.3)	89 (23.9)
SDG components, mean (SD)				
Fibre (g/MJ)	2.14 (0.59)	2.24 (0.63)	2.25 (0.67)	2.28 (0.69)
Vegetables and fruits (g/day)	352.9 (157.4)	391.4 (183.3)	383.2 (213.6)	391.6 (194.6)
Fish and shellfish (g/week)	313.1 (206.1)	300.5 (227.1)	348.2 (214.2)	299.6 (248.6)
Added sugar (E%)	9.86 (4.54)	9.63 (4.26)	10.3 (4.19)	10.0 (4.22)
Red and processed meat (g/week)	839.0 (388.4)	759.9 (381.8)	818.7 (544.3)	785.2 (420.0)
Adherence to recommendation, n (%)				
Fibre (≥ 2.4 g/MJ)	53 (28.5)	273 (35.9)	32 (34.0)	123 (33.4)
Vegetables and fruits (≥ 400 g/day)	62 (33.3)	310 (40.8)	37 (39.4)	158 (42.9)
Fish and shellfish (≥ 300 g/week)	88 (47.3)	318 (41.8)	88 (47.3)	150 (40.8)
Added sugar (<10 E%)	109 (58.6)	448 (58.9)	46 (48.9)	205 (55.7)
Red and processed meat (<500 g/week)	24 (12.9)	193 (25.4)	28 (29.8)	86 (23.4)

Table 2. SDG components and the risk of developing RA based on unadjusted conditional logistic regression

		Seropositive RA		Seronegative RA	
		OR	95% CI	OR	95% CI
Compliant with recommendation	Recommendation				
Fibre (g/MJ)	≥ 2.4	0.67	0.44 – 1.00	1.08	0.61 – 1.89
Vegetables and fruits (g/day)	≥ 400	**0.66**	**0.45 – 0.97**	0.79	0.46 – 1.33
Fish and shellfish (g/week)	≥ 300	1.34	0.93 – 1.94	**2.04**	**1.18 – 3.51**
Added sugar (E%)	≤ 10	0.98	0.68 – 1.41	0.64	0.38 – 1.08
Red and processed meat (g/week)	< 500	**0.32**	**0.19 – 0.55**	1.58	0.86 – 2.89
Reported intake, per SD*					
Fibre		**0.80**	**0.65 – 0.98**	0.94	0.73 – 1.21
Vegetables and fruits		**0.74**	**0.61 – 0.91**	0.94	0.73 – 1.21
Fish and shellfish		1.08	0.89 – 1.30	1.24	0.98 – 1.58
Added sugar		1.07	0.90 – 1.28	1.16	0.90 – 1.49
Red and processed meat (g/week)		**1.38**	**1.13 – 1.69**	1.11	0.86 – 1.44

Odds ratio (OR), Rheumatoid arthritis (RA), Standard deviation [SD], Percent of total energy intake (E%), Confidence interval (CI)
* SD for: fibre 0.64 g/MJ; vegetables and fruits 185.6 g/day; fish and shellfish 229.6 g/week; Added sugar 4.28 E%; Red and processed meat; 406.0 g/week

Table 3. SDG components and the risk of developing RA based on conditional logistic regression adjusted for total energy intake, smoking, alcohol (quintiles), leisure time physical activity. All potential misreporters of energy intake were excluded (n=259; 17%).

		Seropositive RA		Seronegative RA	
		OR	95% CI	OR	95% CI
Compliant with recommendation	Recommendation				
Fibre (g/MJ)	≥ 2.4	0.65	0.38 – 1.11	0.90	0.43 – 1.89
Vegetables and fruits (g/day)	≥ 400	**0.59**	**0.36 – 0.97**	0.74	0.39 – 1.40
Fish and shellfish (g/week)	≥ 300	**1.59**	**1.00 – 2.52**	**2.06**	**1.03 – 4.10**
Added sugar (E%)	≤ 10	0.81	0.52 – 1.26	0.52	0.27 – 1.00
Red and processed meat (g/week)	< 500	**0.27**	**0.14 – 0.52**	1.99	0.89 – 4.44
Reported intake, per SD*					
Fibre		0.76	0.57 – 1.02	0.89	0.64 – 1.24
Vegetables and fruits		**0.64**	**0.48 – 0.85**	0.83	0.59 – 1.14
Fish and shellfish		1.08	0.87 – 1.36	1.10	0.83 – 1.47
Added sugar		1.23	0.98 – 1.53	1.05	0.76 – 1.45
Red and processed meat (g/week)		**1.39**	**1.08 – 1.79**	1.13	0.80 – 1.58

Odds ratio (OR), Rheumatoid arthritis (RA), Standard deviation (SD), Percent of total energy intake (E%), Confidence interval (CI)
* SD for: fibre 0.64 g/MJ; vegetables and fruits 185.6 g/day; fish and shellfish 229.6 g/day; Added sugar 4.28 E%; Red and processed meat: 406.0 g/week

Conditional logistic regression analysis was applied to study the relation between fibers, vegetables and fruits, fish, added sugars and red meat, and RA, with exposures treated as dichotomous (compliant with dietary recommendation or not) and continuous variables per standard deviation. Analyses were stratified for seropositive (positive for rheumatoid factor (RF) and/or anti-cyclic citrullinated peptide antibodies (anti-CCP) and seronegative (negative for RF and anti-CCP) RA. Multivariable models were designed in which covariates (smoking, alcohol and leisure time physical activity) that have been associated with both diet and RA were added. All multivariable models were adjusted for total energy intake and excluded potential misreporters of total energy intake.

Results: In the study population, 204 cases of seropositive RA and 101 cases of seronegative RA were identified (Table 1). Recommended intakes of vegetables and fruits (>400 g/week) and red meat (< 500 g/week) were associated with lower risks of seropositive, but not seronegative RA (Table 2), with similar findings in multivariable-adjusted models (odds ratios (ORs) for seropositive RA 0.59; 95% CI 0.36 – 0.97 and 0.27; 95% CI 0.14 – 0.52, respectively) (Table 3). There were corresponding associations with seropositive RA for continuous variables; for red meat OR 1.39 per SD; 95% CI 1.09 – 1.79, for vegetables and fruits OR 0.64 per SD; 95% CI 0.48 – 0.85) (Table 3). Adherence to recommended intake of fish was associated with an increased risk of RA, in particular seronegative disease, although there was no significant linear association with fish intake (Table 2, 3).

Conclusion: Adherence to recommended intakes of red meat as well as vegetables and fruits were associated with a decreased risk of developing seropositive RA. These results indicate that compliance with dietary guidelines may have differential effects on seropositive and seronegative RA.

Disclosure: R. Bäcklund: None; **I. Drake**: None; **U. Bergström**: None; **M. Compagno**: None; **E. Sonestedt**: None; **C. Turesson**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, Pfizer, 6.

Abstract Number: 0395

Prevalence of Objectively Measured Sleep Disturbance in Rheumatoid Arthritis (RA)

Patti Katz[1], Mary Nakamura[2], Sarah Patterson[3] and Katie Stone[4], [1]University of California San Francisco, San Rafael, CA, [2]UCSF/SFVAHCS, San Francisco, CA, [3]University of California San Francisco, Pacifica, CA, [4]University of California San Francisco, San Francisco, CA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Self-reported poor sleep is common in RA, but only a few small studies objectively measuring sleep have been conducted in RA. In general population studies, sleep disorders are associated with poor health outcomes relevant to RA, including lower pain thresholds and higher rates of depression, cognitive impairment, systemic inflammation, and cardiovascular events. We report on the prevalence of objectively-measured sleep disturbances in a longitudinal cohort of individuals with RA.

Methods: Data are from a study of sleep disorders in RA (n=133).At baseline, participants underwent 9 nights of home sleep monitoring. For the first 2 nights, participants wore a WatchPAT™ device (Itamar Medical, Ltd). For the next 7 nights, participants wore an actigraph (GT9X, Actigraph Corp., Pensacola, FL).Participants were followed over 18 months with 3 follow-ups at 6-month intervals. At each follow-up, actigraphs were worn for 7-day periods. WatchPAT monitoring was discontinued early due to the COVID-19 pandemic. The WatchPAT estimates the apnea-hypopnea index (AHI), reflecting the number of apnea or hypopnea episodes/hour of sleep, an indication of obstructive sleep apnea (OSA), and levels and timing of oxygen desaturation (O_2desat). AHI was categorized as normal-mild OSA (< 15) or moderate-severe OSA (≥15). Actigraphs yielded estimates of time in bed, time asleep, and sleep efficiency (SE, time asleep/time in bed).Acceptable SE was defined as ≥85%.Short sleep time was defined as < 7 hours. Analyses examined the frequency of moderate-high OSA, poor SE, and short sleep.

Results: Mean age was 58 ± 13 years, ∼90% female, mean BMI 28 ± 6.Mean disease duration was 16 ± 13 years, self-reported disease activity was relatively low (mean RA Disease Activity Index, RADAI, 3.3 ± 1.9). 31% were currently using glucocorticoids.116 participants had sufficient baseline actigraph data for scoring, 63 completed WatchPAT monitoring, and 58 completed both WatchPAT and actigraph assessments at baseline. Only 9.5% of the sample had normal AHI, while over half had moderate-severe OSA (Table 1).Of those with moderate-severe OSA, fewer than a quarter reported receipt of an OSA diagnosis. 10% had some time at O_2desat < 80%; 40% had >30 minutes with O_2desat < 90%.From actigraphy, mean SE was 83.8% ± 5.7% at baseline, approximately half of participants had SE < 85%, and over half of participants averaged < 7 hours sleep/night; 18% averaged < 6 hours/night (Table 2).Prevalence of poor SE and short sleep was relatively consistent over measurement periods. In the actigraph cohort, 35% had both poor SE and short sleep, 18% had short sleep only, and 16% had poor SE only (Figure 1).Among those with WatchPAT and actigraph assessments, 22% had combined OSA, poor SE, and short sleep. Only 5% had none of the sleep disorders.

Table 1. Characteristics of participants by AHI category (n = 63)

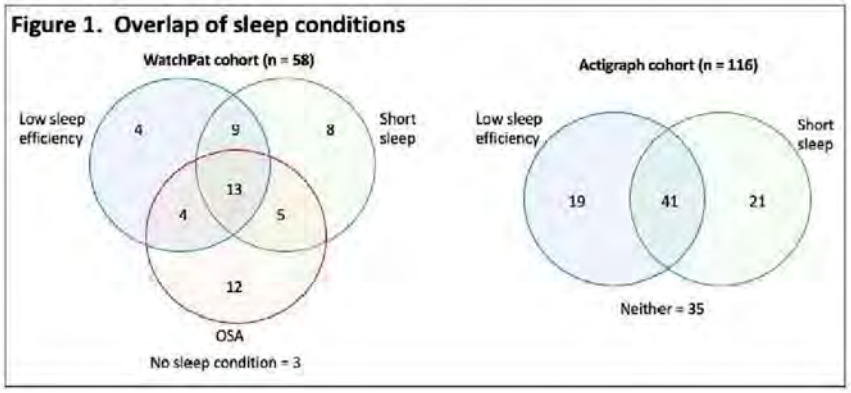
	% (n)	Ever received a diagnosis of OSA, % (n)
Apnea Hypopnea Index (AHI) category		
Normal-mild (>15)	44.4 (28)	3.6 (1)
Moderate-severe (≤15)	55.6 (35)	22.9 (8)
Oxygen Desaturation Index (ODI)		
Any time <80% O_2 saturation	10.3 (6)	
Any time <85% O_2 saturation	43.8% (25)	
>30 minutes <85%	5.3% (3)	
Any time <90% O_2 saturation	76.9% (40)	
>30 minutes	39.6 (23)	
>60 minutes	27.6 (16)	
>120 minutes	13.8 (8)	

Population estimates: General population: 4.2%[1]. Age 60-65: females, 8.2%; males, 14.6%[2].
[1]Ram S, Seirawan H, Kumar S, Clark G. Prevalence and impact of sleep disorders and sleep habits in the United States. Sleep Breath 2010; 14:63-70.
[2]Huang T, Lin B, Mark S, Stampfer M, Laden F, Hu F, Tworoger S, Redline S. Sex differences in the associations of obstructive sleep apnoea with epidemiological factors. Eur Resp J 2018; 51:1702421.

Table 2. Results from Actigraph assessments (n = 116)

	Sleep disturbance	
	Low sleep efficiency (<85%)	Short sleep (<7 hours)
T1 (n = 116)	51.7 (60)	53.5 (62)
T2 (n = 83)	60.2 (50)	57.8 (48)
T3 (n = 64)	48.4 (31)	50.0 (32)
T4 (n = 86)	51.6 (69.8)	59.1 (39)
At any time (n = 116)	69.8 (81)	64.7 (75)
At each measurement time	41.4 (48)	40.5 (47)
% of measurements with disorder	55.6 ± 43.0	53.2 ± 44.3

Figure 1 Overlap among sleep conditions



WatchPAT cohort

One condition only	
• OSA only	12 (21%)
• Low efficiency only	4 (7%)
• Short sleep only	8 (14%)
Two conditions	
• OSA + low efficiency	4 (7%)
• OSA + short sleep	5 (9%)
• low efficiency + short sleep	8 (16%)
All three conditions	13 (22%)
None of the conditions	3 (5%)

Actigraph cohort

Low efficiency only	19 (16%)
Short sleep only	21 (18%)
Both	41 (35%)
Neither	35 (30%)

Conclusion: The majority of this RA sample had at least one sleep disturbance. Given the known association of sleep disturbances with poor health outcomes and potential associations with RA-related factors such as inflammation and disordered cytokine profiles, increased awareness of sleep problems among people with RA may be beneficial. If findings are replicated, screening for OSA may be an important addition to routine care for RA.

Disclosure: P. Katz: None; **M. Nakamura**: None; **S. Patterson**: None; **K. Stone**: None.

Abstract Number: 0396

Hydroxychloroquine Is Associated with a Decreased Risk of Non-alcoholic Fatty Liver Disease in Patients with Rheumatoid Arthritis: A Population-based, Cohort Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a systemic autoimmune inflammatory disease characterized by chronic destructive arthritis and extra-articular involvement. Prior studies showed patients with RA had a high prevalence of NAFLD (35.2% in men with RA and 22.2% in women with RA). Lim et al. suggested that hydroxychloroquine (HCQ) may decrease the risk of NAFLD[1]. The National Health Insurance Research Database (NHIRD) in Taiwan provided nationwide, population-based claim data to facilitate a longitudinal epidemiologic study.

The aim of the study was to assess the association between HCQ and incident NAFLD in a nationwide RA cohort.

Methods: Using the 2000–2020 NHIRD, we identified 41,791 newly-diagnosed RA patients from 2002 to 2020. After excluding patients with diagnoses of liver diseases (acute/subacute necrosis of liver, chronic liver disease, live abscess/sequelae of chronic liver disease, other disorders of liver, hepatitis B, hepatitis C, alcohol related disorders, alcoholic liver disease) on or before the RA diagnosis date (n = 16,223 patients) and patients with missing data of residence of insured amount (n = 4,110), we included 21,458 patients with RA. A time-varying multivariable Cox regression model was applied to estimate the adjusted hazard ratios (aHRs) with 95% confidence interval (CIs) for the association of NAFLD with the use of HCQ after adjusting potential confounders. Subgroup analyses were conducted based on age (≤50, >50 years) and sex.

Results: The mean ± standard deviation (SD) age was 51.9 ± 14.2 years, and the female-to-male ratio was 3.2. 399 (1.86%) patients developed NAFLD during a mean follow-up period of 8.4 years, with an incidence rate of 2.21 x 10^{-3}. Multivariable time-dependent Cox regression analyses showed that HCQ use was associated with a lower risk of NAFLD (aHR, 0.75; 95% CI, 0.60–0.93; p = 0.007). Other significant predictors for the risk of NAFLD included obesity (aHR, 4.63; 95% CI, 1.47–14.59; p = 0.009), defined daily dose (DDD) of NSAID (per incremental DDD: aHR, 1.03; 95% CI, 1.02–1.05; p < 0.001), prednisolone (Pd) equivalent dose > 5 mg/day (reference: without Pd use; aHR, 2.4; 95% CI, 1.86–3.10; p < 0.001) and Pd equivalent dose ≤5 mg/day (reference: without Pd use; aHR, 0.53; 95% CI, 0.40–0.72; p < 0.001). The association between HCQ and NALFD risk was consistent in patients aged ≤50 years and female patients with RA.

Conclusion: This study revealed that using HCQ was significantly associated with a lower risk of NAFLD, particularly in RA patients aged ≤50 years and in female RA patients.

Disclosure: H. Chen: AbbVie/Abbott, 2; **D. CHEN**: None.

Abstract Number: 0397

Obesity Is Associated with Worse Flare Symptoms and Quality of Life in Early Rheumatoid Arthritis: Insights from the RA Flare Questionnaire

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Elevated BMI has been previously associated with lower RA remission rates and underascertainment of swollen joint counts.1,2 However, a knowledge gap persists regarding the potential impact of elevated BMI on the severity of RA flare symptoms and their effects on quality of life (QOL). Our study addresses this gap, evaluating the influence of BMI on RA flare symptoms and QOL.

Methods: Participants with ≥2 swollen joints and Early/Recent Onset RA (symptoms ≤12/≤24 months) were recruited into the Consortium of Early ArThritis CoHorts-USA Study (CATCH-US) at two centers (New York, Baltimore) between December 2014 and May 2023. Baseline characteristics and patient reported outcomes (PROs) were recorded at each visit.

Table 1. Patient Characteristics

		BMI Category			
Characteristic	**Overall** n=134[1]	**Healthy Weight** n=73[1]	**Overweight** n=37[1]	**Obese** n=24[1]	**p-value**[2]
Age	47.3 (35.3, 60.0)	42.0 (33.5, 55.9)	55.6 (44.9, 63.1)	51.2 (42.4, 60.1)	**0.008**
Sex					0.3
Female	114 (85%)	65 (89%)	29 (78%)	20 (83%)	
Male	20 (15%)	8 (11%)	8 (22%)	4 (17%)	
Race					0.3
Asian	16 (12%)	11 (15%)	5 (14%)	0 (0%)	
Black	12 (9.0%)	6 (8.2%)	2 (5.4%)	4 (17%)	
White	95 (71%)	50 (68%)	28 (76%)	17 (71%)	
Other/NA	11 (8.2%)	6 (8.2%)	2 (5.4%)	3 (12%)	
Ethnicity					0.6
Hispanic	18 (13%)	11 (15%)	3 (8.1%)	4 (17%)	
Not Hispanic	116 (87%)	62 (85%)	34 (92%)	20 (83%)	
BMI	24.3 (21.4, 28.6)	21.5 (19.6, 22.9)	27.7 (25.8, 28.7)	33.6 (32.7, 36.6)	**<0.001**
EGA	3.5 (2.0, 5.0)	3.0 (2.0, 5.0)	3.0 (2.0, 5.0)	4.0 (2.8, 6.2)	0.3
CDAI	12.0 (5.1, 19.2)	10.0 (5.5, 17.5)	12.0 (4.0, 18.0)	16.8 (10.8, 30.4)	0.067
CRP	0.7 (0.2, 1.2)	0.4 (0.2, 0.9)	0.8 (0.2, 1.4)	1.0 (0.2, 2.4)	0.14
Seropositivity					0.6
Negative	32 (24%)	15 (21%)	11 (30%)	6 (26%)	
Positive	101 (76%)	58 (79%)	26 (70%)	17 (74%)	
RA-FQ Score[3]	14.0 (7.0, 23.0)	14.0 (8.0, 19.0)	11.0 (4.0, 26.0)	23.0 (11.8, 31.2)	0.059
Pain Subscore	3.0 (2.0, 5.0)	3.0 (2.0, 4.0)	3.0 (1.0, 5.0)	5.0 (2.8, 7.0)	**0.043**
Fatigue Subscore	3.0 (1.0, 5.8)	3.0 (1.0, 5.0)	2.0 (0.0, 5.0)	5.5 (2.0, 7.2)	**0.043**
Stiffness Subscore	3.0 (2.0, 5.0)	3.0 (2.0, 5.0)	3.0 (1.0, 6.0)	5.0 (3.0, 7.2)	0.059
Function Subscore	2.0 (1.0, 4.0)	3.0 (1.0, 3.0)	2.0 (1.0, 5.0)	3.5 (2.0, 6.0)	0.2
Social Participation Subscore	1.5 (0.0, 4.0)	1.0 (0.0, 3.0)	2.0 (0.0, 5.0)	3.5 (0.8, 6.0)	0.11

[1] Median (IQR); n (%)
[2] Kruskal-Wallis rank sum test; Fisher's exact test; Pearson's Chi-squared test
[3] An RA-FQ score ≥15 for ≥7 days indicates an RA flare

Table 2. Multivariable Linear Regression Results for RA-FQ Score and Individual RA-FQ Subscores, displaying Adjusted Betas with 95% Confidence Intervals for all analyzed variables.

			Flare Symptom Subscores						QOL Impact Subscores			
	RA-FQ Score		Pain		Fatigue		Stiffness		Function		Social	
Characteristic	**Beta**[1]	**95% CI**[2]	**Beta**[1]	**95% CI**[2]	**Beta**[1]	**95% CI**[2]	**Beta**[1]	**95% CI**[2]	**Beta**[1]	**95% CI**[2]	**Beta**[1]	**95% CI**[2]
EGA	**2.3*** **	**1.5, 3.1**	**0.43*** **	**0.27, 0.60**	**0.43*** **	**0.23, 0.64**	**0.44*** **	**0.24, 0.64**	**0.44*** **	**0.26, 0.62**	**0.54*** **	**0.35, 0.73**
Age	-0.11*	-0.22, 0.00	-0.02	-0.05, 0.00	-0.03	-0.06, 0.00	-0.01	-0.04, 0.01	-0.03*	-0.06, -0.01	-0.02	-0.04, 0.01
Sex	NA		NA		NA		NA		NA		NA	
Female	—	—	—	—	—	—	—	—	—	—	—	—
Male	0.83	-4.0, 5.7	-0.12	-1.2, 0.91	-0.38	-1.7, 0.91	0.36	-0.87, 1.6	0.82	-0.28, 1.9	0.15	-1.0, 1.3
Race	NA		NA		NA		NA		NA		NA	
Asian	—	—	—	—	—	—	—	—	—	—	—	—
Black	6.8	-0.75, 14	1.6	0.00, 3.2	0.21	-1.8, 2.2	2.0	0.12, 4.0	1.9	0.22, 3.7	0.99	-0.86, 2.8
White	3.9	-1.4, 9.2	0.74	-0.39, 1.9	1.1	-0.33, 2.5	1.4	0.00, 2.7	0.56	-0.65, 1.8	0.15	-1.1, 1.4
Other/NA	8.2	-0.41, 17	1.5	-0.34, 3.4	1.9	-0.36, 4.2	2.5	0.27, 4.7	1.5	-0.51, 3.4	0.86	-1.3, 3.0
Ethnicity	NA		NA		NA		NA		NA		NA	
Hispanic	—	—	—	—	—	—	—	—	—	—	—	—
Not Hispanic	-0.48	-6.3, 5.4	-0.61	-1.9, 0.65	0.38	-1.2, 1.9	0.33	-1.2, 1.8	-0.40	-1.7, 0.93	-0.18	-1.6, 1.3
BMI	**0.38***	**0.09, 0.68**	**0.08***	**0.01, 0.14**	**0.08***	**0.00, 0.16**	**0.08***	**0.01, 0.16**	**0.06**	**-0.01, 0.12**	**0.08***	**0.01, 0.15**

[1] *p<0.05; **p<0.01; ***p<0.001
[2] CI = Confidence Interval

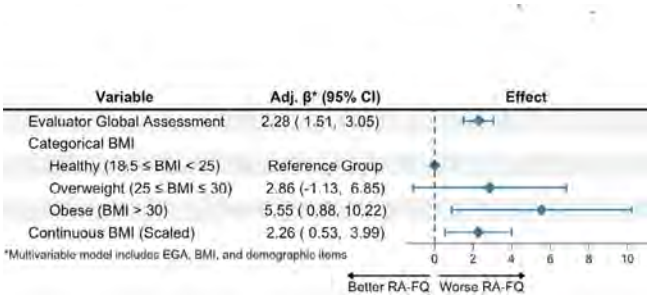

Figure 1. Forest Plot of Adjusted Betas with 95% Confidence Intervals illustrating the impact of Evaluator Global Assessment (EGA) and BMI on RA-FQ scores. BMI is presented as both a categorical and continuous variable; the continuous BMI variable is scaled such that the RA-FQ score is predicted to shift approximately 2.3 points for each standard deviation that the BMI increases/decreases (SD = 5.9).

Flares were determined using the OMERACT RA-Flare Questionnaire (RA-FQ), a PRO that assesses symptoms of Pain, Stiffness, Fatigue, and impacts on Physical Function and Social Participation (items scored from 0 to 10; best to worst); all five scores are summed for an overall score range of 0 to 50. An Evaluator Global Assessment (EGA) score, indicating RA clinical disease activity, was scored by the enrolling rheumatologist between 0 (not active) and 10 (very active). Using a multivariable linear regression model, we tested the correlation between BMI and RA-FQ scores, considering EGA scores and demographic factors as covariates.

Results: Eligible participants (n=134) were mostly female (85%), white (71%), and non-Hispanic (87%); almost half were overweight or obese (46%); median age was 47.3 years and median BMI was 24.3 (**Table 1**). Higher EGA scores ($\beta = 2.3$; $p < .001$) and elevated BMI ($\beta = 0.38$; $p = .01$) emerged as significant predictors of higher RA-FQ scores; EGA was also significantly associated with each RA-FQ subscore, while BMI was significantly associated with four of the five subscores (**-Table 2**). We observed an amplified impact of elevated BMI on RA-FQ scores in obese patients compared to those in healthy weight and overweight categories (**Figure 1**). Age was inversely related to the total RA-FQ score ($\beta = -0.11$; $p = .04$) and Function subscore ($\beta = -0.03$; $p = .01$). No significant associations were found for sex, race, or ethnicity.

Conclusion: Our findings underscore a strong correlation between EGA scores and RA-FQ scores, thereby establishing the concordance of this PRO with clinically assessed disease activity. More importantly, we found that elevated BMI is associated with more severe flare activity and diminished QOL, particularly in obese ERA patients. This result corroborates earlier studies that suggested a systematic underestimation of disease activity in patients with elevated BMI. As such, clinicians should consider patients' BMI and RA-FQ scores when formulating treatment plans for RA flares. Future research will focus on longitudinal analyses to assess the persistence of these associations throughout the course of the disease.

References:

1. Schulman, E., et al, Arthritis Care Res (Hoboken), 2018.**70**(8)

2. Bauer, E.M., et al. BMC Musculoskelet Disord, 2017.18(1)

Disclosure: M. Butler: None; **C. Aude**: None; **C. Bingham**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 2, Janssen, 2, Pfizer, 2, Sanofi, 2; **V. Bykerk**: Abbvie, 2, BMS, 2, Pfizer, 2.

Abstract Number: 0398

Identification of Disease Activity-related miRNAs Through Artificial Neural Network Analysis in Rheumatoid Arthritis

Milena Rodriguez Alvarez[1], Lissette Delgado-Cruzata[2], **Anna Tryfonos**[1], Nickolas Almodovar[2], Toni-Ann Bravo[2] and Naureen Kabani[1], [1]SUNY Downstate Health Sciences University, Brooklyn, NY, [2]The City University of New York, John Jay College, New York, NY

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis (RA) is the result of the complex interplay between genetic, epigenetic, and environmental factors leading to immune dysregulation, synovial membrane inflammation, and disability. MicroRNAs (miRNAs) are non-coding RNA molecules that alter mRNA expression, affecting multiple molecular pathways. Growing evidence suggests that miRNAs are implicated in the onset and development of RA but studies about their association with disease activity are scant. We conducted a pilot study to identify miRNAs differentially expressed in patients with RA and applied Artificial Neural Network (ANN) analysis to build a classificatory model that explored the association between levels of differentially expressed miRNAs and disease activity using Clinical Disease Activity Index (CDAI).

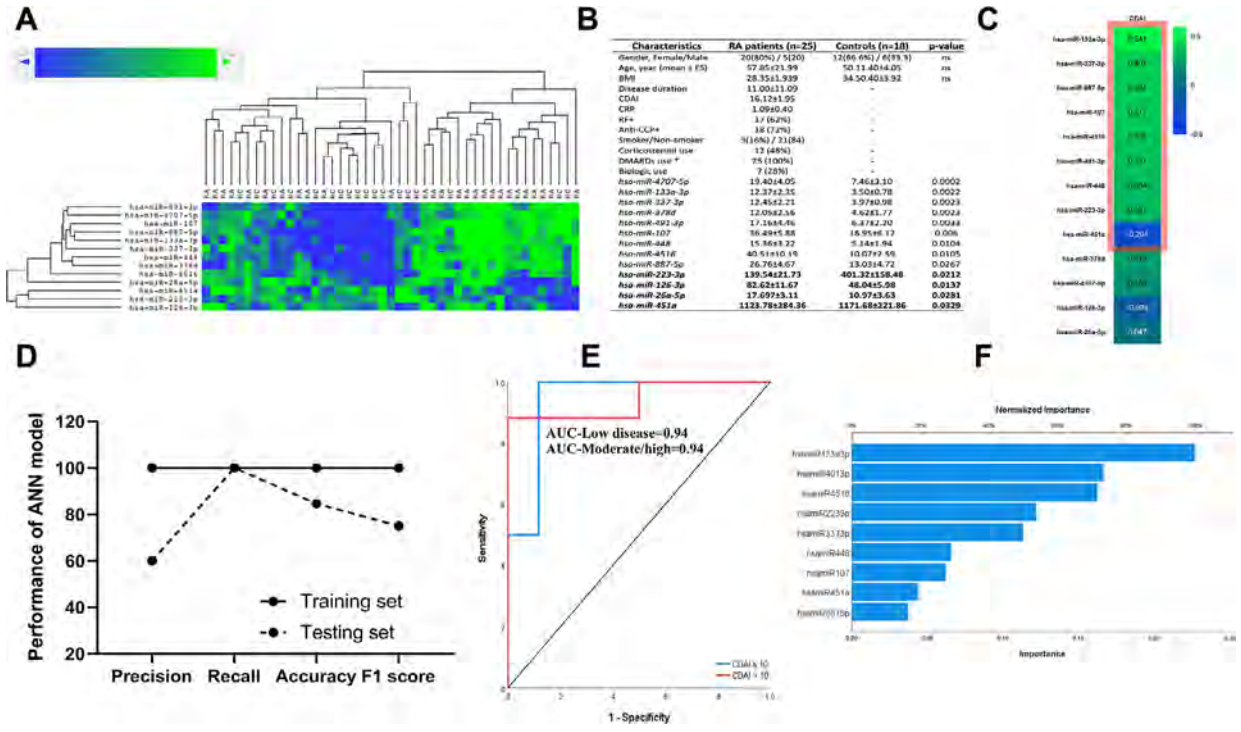

Figure 1: The association of miRNAs with Disease Activity Index in Rheumatoid Arthritis (RA) based on Artificial Neuronal Network (ANN). -A- Unsupervised hierarchical cluster analysis of 13 exosomal miRNA levels in RA patients and healthy controls (HC). -B- Demographics data and miRNA levels in RA patients and HC. -C- Heatmap of Pearson correlation coefficients between 13 miRNAs levels and CDAI numeric values.Statistical significant correlations ($p<0.05$ and/or ES≥0.3) are enclosed in a pink-colored box. -D-. Performance of the ANN model classifying disease activity of RA patients based on miRNAs. -E- ROC curve for the ANN Model and AUC values to predict disease activity levels. -F- Normalized contribution of each miRNAs to the ANN model.

Methods: We recruited 43 subjects, 18 healthy controls (HC), and 25 RA patients. Serum from all participants was collected, exosomes isolated, and miRNAs extracted. Using the Nanostring nCounter miRNA expression panel, levels of 800 miRNAs were determined. We identified 9 miRNAs using nSolver software analysis that had the largest difference (top 10%) between groups and a RA:HC ratio in the top 50%. In subsequent analysis, we also included 4 previously reported RA-relevant miRNAs. The 13 miRNA panel showed good discrimination between RA and HC (Figure 1A). We used the Mann-Whitney t-test to identify mean differences and Pearson correlation to assess the association between miRNA levels and CDAI. ANN analysis was used to build a classificatory model. All analysis was carried out with SPSS v.28, $p \leq 0.05$ was considered statistically significant, and Pearson correlation coefficients were important when $p < 0.05$ and/or the effect size (ES) was moderate or high (ES >0.3).

Results: Of the 13 identified RA-relevant miRNAs in this study (Figure 1A, B), 9 correlated with CDAI (Figure 1C). These 9 miRNAs, ***miR -133a-3p, miR-337-3p, miR -887-5p, miR-107, miR-4516, miR-491-3p, miR-448, miR-223-3p***, and ***miR-451a***, were further selected for the ANN analysis. 70% of the sample was used to train the ANN model and 30% to test it. The training set scored 100% in all performance metrics (Figure 1D), whereas the testing set performed 80% in recall and accuracy, 60% in precision, and 75% in F1 score. The receiver operating characteristic curve (ROC) illustrates the diagnostic ability of the model expressed as low (CDAI≤10) and moderate/high (CDAI >10) disease activity. The area under the ROC curve (AUC) is 0.94 indicating excellent classificatory prediction for the model (Figure 1E). The 4 miRNAs that most contributed to the model were ***miR-133a-3p, miR-491-3p, miR-4516,*** and ***miR-223-3p*** (Figure 1F).

Conclusion: Our study for the first time describes ***miR-133a-3p, miR-491-3p,*** and ***miR-4516*** as differentially expressed in RA. We also described 9 miRNAs not previously correlated with RA disease activity. An ANN model built with these 9 miRNAs had an excellent classificatory capacity for RA patients with low or moderate-high disease activity, therefore providing a new set of potential biomarkers as a starting point to assess RA disease activity and response to treatment in future studies.

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Abstract Number: 0399

Differential Synovial Tissue Enrichment of Oxylipins and Their Mediators Across Rheumatoid Arthritis Trajectory

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I

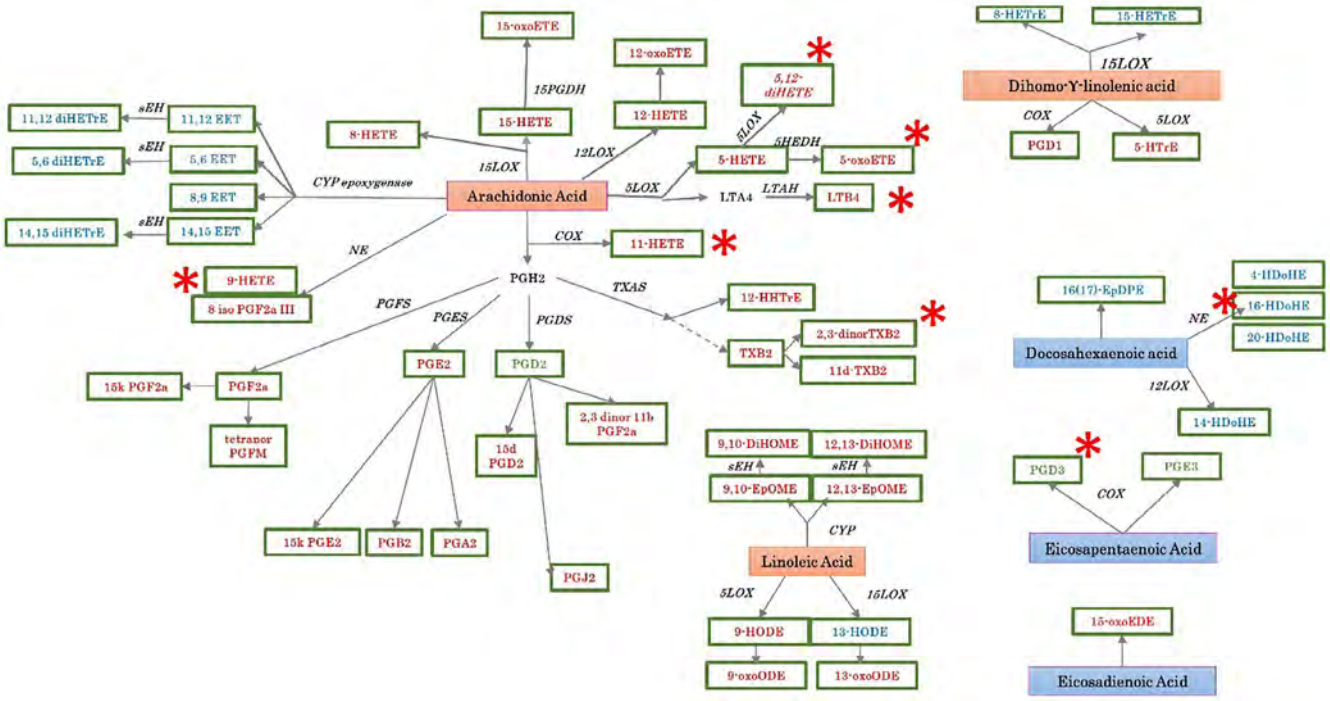
Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Synovial membrane represents the target tissue of Rheumatoid Arthritis (RA) inflammation. Our study aimed to perform a comprehensive quantification of oxylipins and their precursors in synovial tissue specimens of RA patients across disease trajectory.

Methods: 32 patients fulfilling the ACR/EULAR 2010 classification criteria underwent US-guided minimally invasive synovial tissue biopsy of the knee [n=16 patients with DAS28≥4.2 and n=16 patients in sustained (≥12 months) clinical (DAS28≤2.6) and ultrasound remission (Power Doppler negative)]. Oxylipins in synovial tissue were determined by liquid chromatography with tandem mass spectrometry (LC-MS-MS) and were classified into groups according to their precursor: arachidonic acid (AA), LA, ALA, DHA, EPA and DGLA. Moreover, each sample was processed for histology and the synovitis degree was assessed using H&E-based scoring by pathologist blinded on clinical characteristics. Statistical analysis was performed using MetaboAnalyst 5.0 and SPSS software v27.

Results: Among the general panel, 84 different oxylipins were detected in at least one sample and 55 oxylipins remained after eliminating those with less than 50% across the samples (Figure 1). Stratifying RA patients based on the disease status, synovial tissue of active RA was significantly enriched of distinct specialized pro-resolving lipid mediators (SPMs) precursors such as free AA (p=0.0045), free adrenic acid (p=0.0080) and free docosahexaenoic acid (p=0.012) compared to synovial tissue of RA patients in sustained remission. Moreover, considering a threshold ≥4 of oxylipins expression, synovial tissue of active RA showed an 5LOX-derived oxylipins enrichment of 16.087 folds of 5,12-diHETE, 5.7419 folds of LTB4, TXA-derived 34.259 folds of 2,3 dinor TXB2, non-enzymatic -derived 6.192 folds of 16-HDoHE, 5.5097 folds of 9-HETE and, COX-derived oxylipins 4.8275 folds of 11-HETE compared to synovial tissue of RA patients in sustained clinical and ultra-sound remission which was enriched 5.1589 folds of PGD3. Finally, the enrichment of pro-inflammatory SPMs was directly correlated with the histological synovitis degree (R^2=0.473, p=0.006) particularly with the score of synovial hyperplasia (R^2=0.472, p=0.006) and inflammatory infiltrate (R^2=0.466, p=0.007).



Oxylipins observed in at least 50% of the samples by precursor and pathway are shown. Proinflammatory oxylipins are marked on red letters, while anti-inflammatory oxylipins are marked on blue letters. The n-3 polyunsaturated fatty acids (PUFAs) precursors are marked on red squares, while the n-6 PUFAs precursors are marked on blue squares. Those oxylipins with pro and anti-inflammatory reported roles are marked on green letters.

Conclusion: Synovial tissue of RA patients shows a differential enrichment of oxylipins and their precursors which is contingent with the disease status directly mirroring the synovitis degree in terms of synovial hyperplasia and inflammatory infiltrate.

Disclosure: S. Perniola: None; **J. Murillo-Saich**: None; **B. Tolusso**: None; **C. Di Mario**: None; **M. Gessi**: None; **D. Bruno**: None; **L. Petricca**: None; **M. Gigante**: None; **E. Gremese**: None; **M. Guma**: None; **S. Alivernini**: None.

Abstract Number: 0400

Thresholds of Presenteeism Measurement Instruments for Unacceptable Work Participation and Future Adverse Work Outcomes in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Presenteeism is associated with lower work satisfaction and increased risk of future sick leave in rheumatic diseases. It is generally measured on a continuous scale; however, despite a lower precision, identifying persons with a meaningful level of presenteeism can improve interpretation in clinical studies and might be useful in routine practice. Recently, thresholds of meaning for presenteeism instruments were established for axial spondyloarthritis (axSpA). Our objectives were 1) To identify thresholds for presenteeism instruments that reflect unacceptable work status in patients with RA and whether those thresholds could predict future adverse work outcomes; 2) to assess in patients with RA the performance of presenteeism thresholds previously established in axSpA for the same instruments.

Methods: We used data from the 1-year multinational prospective study on Patient-Reported Outcomes in Employment Study in Rheumatoid Arthritis (RA-PROSE). Thresholds to determine when patients consider themselves in unacceptable work status were calculated at baseline for 4 presenteeism instruments (Work Productivity and Activity Impairment

Table. Optimal thresholds for presenteeism measures and patients correctly classified for unacceptable work status and adverse work outcome during 12 months.

	Optimal threshold (SE/SP)	Correctly classified for unacceptable work status n (%)	Correctly classified for AWO during 12 months n (%)
WPAI presenteeism (0-100)	≥30 (89/70)	66 (73)	57 (69)
	≥40 (78/82)	77 (82)	62 (75)
QQ method (0-10)	<8 (67/55)	53 (56)	49 (59)
	<7 (56/64)	59 (63)	57 (69)
WALS (0-3)	≥0.61 (89/59)	51 (62)	44 (61)
	≥0.75 (67/68)	56 (68)	49 (68)
WLQ 25 (0-100)	≥27 (89/77)	53 (57)	45 (55)
	≥29 (77/80)	57 (61)	46 (56)
Pain (0-10)	≥4 (67/68)	64 (68)	61 (73)

The final thresholds are colored in green and correspond to the one's derived from axSpA. For pain measurement there was no axSpA derived threshold.

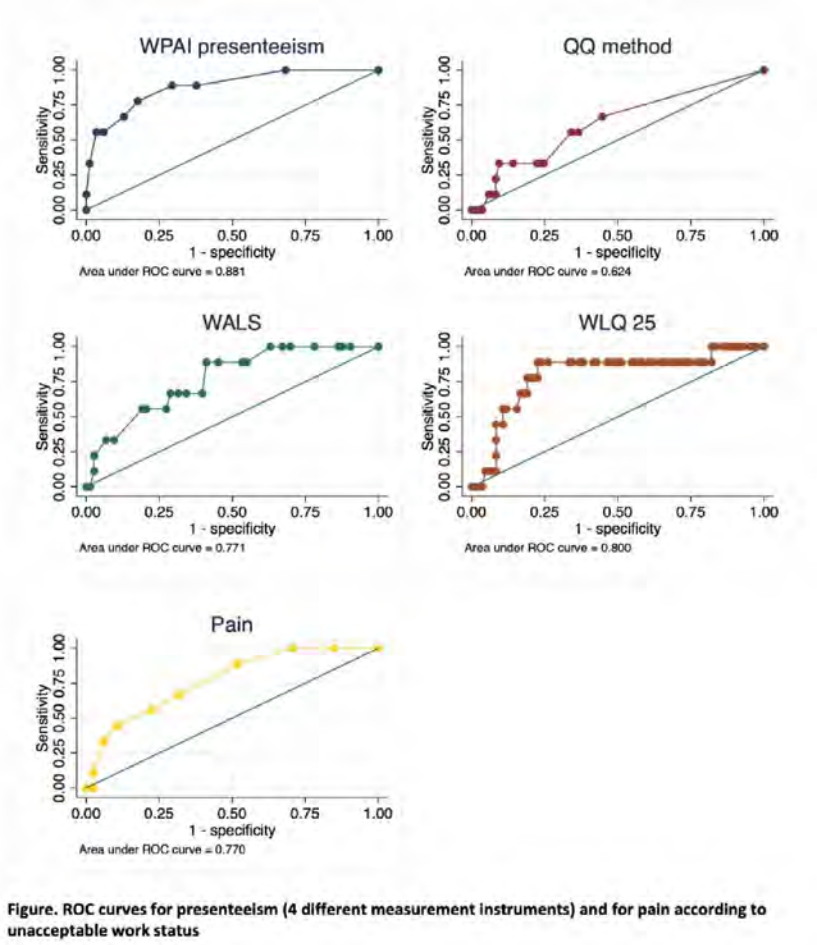

Figure. ROC curves for presenteeism (4 different measurement instruments) and for pain according to unacceptable work status

Figure. ROC curves for presenteeism (4 different measurement instruments) and for pain according to unacceptable work status.

questionnaire -WPAI-, Quality and Quantity method -QQ-, Workplace Activity Limitations Scale -WALS- and Work Limitations Questionnaire -WLQ 25-) and for a patient global assessment of pain.

We created receiver operating characteristic (ROC) using as external criterion addressing one's ability to perform current job satisfactorily. We used different approaches (75th percentile, Youden index, Liu method, nearest to 0.1) to determine the optimal cut-off, while balancing over-under diagnosis (i.e. specificity and sensitivity). Next, accuracy of thresholds to predict future adverse work outcome (AWO) throughout 12 months (defined as sick leave or long-term disability) was assessed. The recently developed presenteeism thresholds for axSpA were also tested.

Results: 105 employed patients were included: 77% females, mean age 48 (SD 9), with a symptom duration of 9.8 (8.7) years. 15% of the patients considered themselves in an unacceptable work status and 7 (8%) had at least one AWO during the 12 months.

All instruments showed good performance vs the external criterion (AUC >0.75) except for the QQ method (AUC 0.62) (figure). The table shows for each instrument (presenteeism and pain) the optimal thresholds and their performance to correctly identify an unacceptable work status and AWO during 12 months for the RA-specific threshold (1st row) and the available axSpA threshold (2nd row). Interestingly, the axSpA thresholds performed better to classify work status as unacceptable and to predict AWO (somewhat lower sensitivity but higher % of correctly classified patients). For adverse work outcome over 12 months, pain and WPAI performed better especially in predicting AWO.

Conclusion: Thresholds for presenteeism and pain representing unacceptable work status have been established for RA. Previously developed thresholds for axSpA showed an even better performance and are therefore the preferred to be used. WPAI performed the best and can be used to identify patients requiring more tailored care in order to avoid future AWO.

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Abstract Number: 0401

Resolution of Swollen Joint Count Is an Important Clinical Objective in Early Rheumatoid Arthritis : Analysis of the UCLouvain Brussels ERA Cohort and Comparison with the Remission Composite Index

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis is a chronic autoimmune disease characterized by persistent joint inflammation. According to international guidelines, the treatment target should aim to reach the remission state or at least the low disease activity (LDA), evaluated through the disease activity score, including DAS28, CDAI, and SDAI. All the disease activity

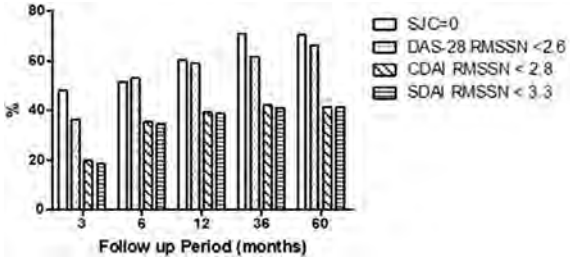

Figure 1. Percentage of patients reaching a SJC=0 and remission status according to DAS28, CDAI, and SDAI definitions up to 5 years of follow-up

composite scores include the swollen joint count (SJC) as the main clinical evaluation. Following this, the ACR/EULAR Boolean criteria were validated with a SJC >1. To the best of our knowledge, no studies have been addressed in the evaluation of no SJC and is association with the other response criteria. The aim of the study is to determine which baseline variables are associated with achieving and maintaining a zero SJC.

Methods: We enrolled RA patients included in the ERA UCLouvain Brussels cohort naïve to DMARDs therapy according to the ACR/EULAR 2010 criteria. Each patient had a complete rheumatological evaluation at baseline and up to 60 months of follow-up. The patient's characteristics including clinical and serological features were collected. The association between swelling, bone erosion, and clinical and disease characteristics was analyzed, aiming at identifying any variables associated with the reaching of SJC=0.

Results: We enrolled 455 RA patients (Male/Female 29.5%/70.5%, medium age 48.8±14.7. At baseline, the mean SJC was 8.70 ±7.44, the mean DAS28 was 4.76±1.38, Age 48.8±14.7, ACPA and RF prevalence was 68.9% and 64.7% respectively. Bone erosions were identified in 45.5% of patients. In figure 1. are reported the percentage of patients reaching a SJC=0 and remission status according to DAS28, CDAI, and SDAI definitions up to 5 years of follow-up. In our cohort at 3 and 6 months, respectively 37.2%, 21.3%, 22.2% and 39.3%, 28.5%, 27.7% of the patients fulfilling DAS28, CDAI or SDAI remission presented at least one SJC. Among all the baseline analyzed features, Baseline Erosion was the strongest predictor of at least one SJ from baseline to 5 years of follow-up: (3 months: 36.2% versus 54.1%; p< 0.001; 6 months: 36.7% versus 54.9%; p< 0.001; 12 months: 39.3% versus 55%; p=0.034; 36 months:43.9% versus 56.2%; p=0.045; 60 months: 47.1% versus 62.8%; p=0.019). Smokers had a lower chance to reach a SJC count at three months (20.8% versus 29.7%; p=0.042), and the female sex had the same association at 60 months of follow-up (65.8% versus 78.2%; p=0.0019). Focusing on long-time follow-up (5 years), including only MTX-treated patients (n=141), the group of subjects who never reached a SJC=0 were characterized by a higher baseline age (52.1±15.7 versus 46.7±15.5; p=0,150), DAS28 (5.08 ±1.38 versus 4.04±1.16; p=0.001), RF prevalence (81.5% versus 62.7%; p=0.08) and baseline erosions (77.8% versus 36.7%; p=0.0004).

Conclusion: We identified an association between baseline disease features and the chance of not reaching a SJC of zero, suggesting how smoking, presence of RF, and baseline erosion may identify a group of patients with clinically persistent joint inflammation, whit a greater risk of not reaching remission. We confirm also that the resolution of SJC is a good practical end point in ERA.

Disclosure: F. Natalucci: None; **c. triaille**: None; **E. Sapart**: None; **L. BRICMAN**: None; **C. VAN MULLEM**: None; **C. Desmet**: None; **S. DIERCKX**: None; **M. DOYEN**: None; **T. Sokolova**: None; **A. AVRAMOVSKA**: None; **P. Durez**: None.

Abstract Number: 0402

Automated Detection and Quantification of Hand Joint Swelling in Rheumatoid Arthritis: Computer Vision, Deep Neural Network Models, and a Potential Biomarker for Disease Activity Monitoring

Marc Blanchard[1], Jules Maglione[2], Cinja Koller[3], Patrick Hermann[4], David Brüschweiler[3], Arnd Kleyer[5] and Thomas Hügle[6], [1]Dept. of Rheumatology, University Hospital Lausanne (CHUV) and University Lausanne, Lausanne, Switzerland, [2]EPFL, Lausanne, Switzerland, [3]Lausanne University Hospital, Lausanne, Switzerland, [4]ATREON SA, Lausanne, Switzerland, [5]University Hospital Erlangen, Erlangen, Germany, [6]Dept. of Rheumatology, University Hospital Lausanne (CHUV) and University of Lausanne, Lausanne, Switzerland

SESSION INFORMATION
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Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: We have previously shown that automated detection and processing of dorsal finger fold patterns from hand photographs can be used as a digital biomarker for joint swelling in rheumatoid arthritis.

In this study, we tested different computer vision and deep learning methods for the automated quantification of dorsal finger folds and diameter of proximal interphalangeal finger joints (PIP) in patients with rheumatoid arthritis. Additionally, the selected model aimed to evaluate the difference in PIP finger joint swelling between healthy individuals and rheumatoid arthritis patients.

Methods: We evaluated the detection and measurement of PIP joint diameter and dorsal finger fold length on hand photographs in 1783 joints of patients with rheumatoid arthritis by canny edge or ridge detection computer vision models or a newly trained convolutional neural network, respectively. The models have been trained to calculate the finger fold index (FFI, potential biomarker for joint swelling), defined as the ratio between pixel length of joint diameter and mean recognized finger folds. In an independent healthy control dataset, the FFI has been calculated to be compared with rheumatoid arthritis PIP joints.

Results: Canny edge and ridge detection were suitable models to detect dorsal finger fold patterns. The prediction of joint diameter and finger fold pixel length was best achieved in a newly trained deep neural network model, where the FFI was predictable in 93% of the images. The accuracy of correct detection of joint diameter measurement was 91%. In 1783 PIP joints of patients with rheumatoid arthritis, the mean FFI was significantly higher than in 168 healthy controls PIP joints (3.42 ± SD 1.04 and 2.15 ± SD 0.68, respectively, p-value < 0.05).

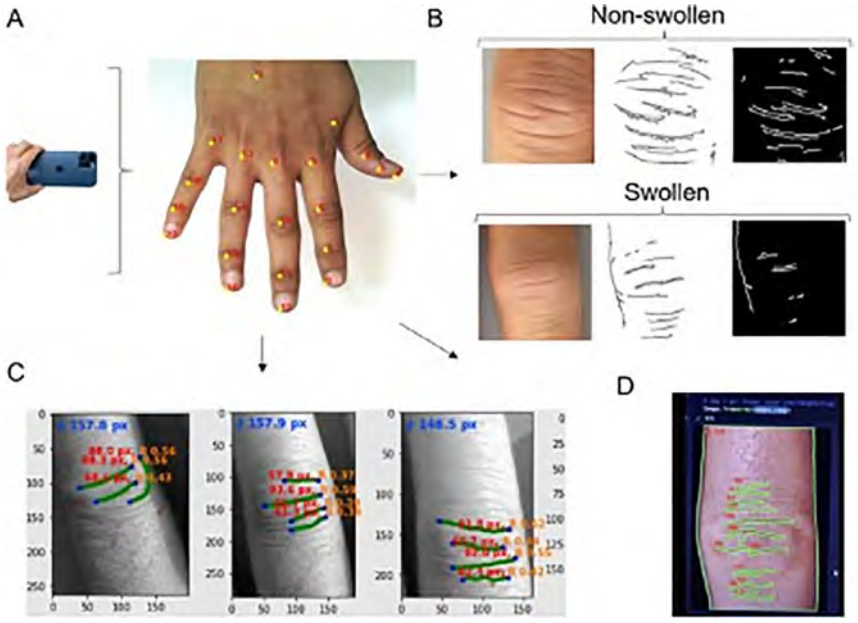

Figure 1: A: Keypoint detection. B: Canny edge detection. C: Metrical analysis with ridge detection. D: Newly trained deep neural network.

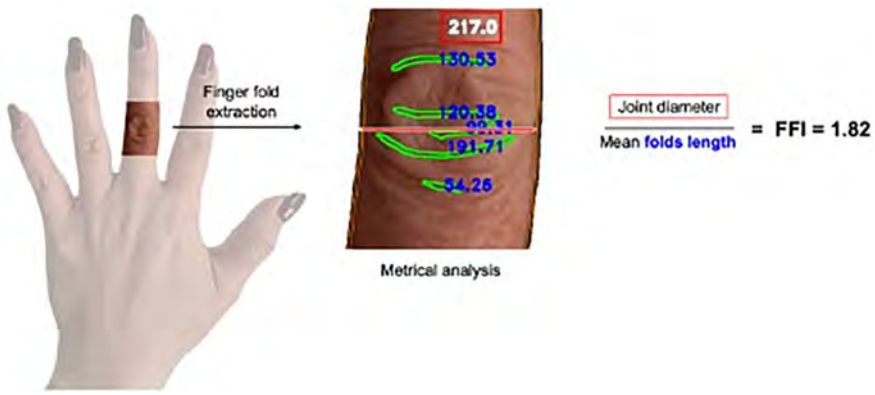

Figure 2: Finger Fold Index (FFI) detection and quantification, from the finger fold extraction (image recognition) to the metrical analysis and calculation (deep neural network).

Conclusion: Finger fold index calculated by a deep neural network model seems a reliable tool for the metrical analysis and thus gradeless detection of swelling in patients with rheumatoid arthritis. Standard deviation for FFI in patients with rheumatoid arthritis was higher than in healthy patients. Therefore, further investigation by stratifying patients into different disease activity levels as well as the correlation of FFI with longitudinal changes of clinical scores on a joint-level and general disease activity is ongoing.

Disclosure: M. Blanchard: Atreon SA, 8; **J. Maglione**: None; **C. Koller**: None; **P. Hermann**: ATREON SA, 4; **D. Brüschweiler**: None; **A. Kleyer**: None; **T. Hügle**: Atreon SA, 8, Curmed, 9, Eli Lilly, 6, Fresenius Kabi, 2, 5, Galapagos, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, Merck/MSD, 6, Pfizer, 6.

Abstract Number: 0403

Disease Activity Is Associated with Frailty in Veterans with Rheumatoid Arthritis

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SESSION INFORMATION

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Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Frailty, defined as an increased vulnerability to stressors and adverse health outcomes, is an emerging concept in RA. Active RA disease gives rise to inflammation, pain, and joint damage leading to functional impairment and morbidity, which cumulatively influences frailty status. However, the association between frailty and RA disease activity is incompletely understood. Given that RA disease activity may impact frailty status but could also be confounded by other health factors, we examined the relationship of disease activity and frailty in a large RA cohort with robust co-variable adjustment.

Methods: A cross-sectional descriptive study was performed on baseline data from the VA Rheumatoid Arthritis (VARA) Registry, a multi-center prospective cohort which began enrolling in January 2003. All participants met ACR criteria for RA. Frailty was measured using the 31-item VA-Frailty Index (VA-FI) which includes diagnostic and procedure codes linked to health-related deficits encompassing morbidity, functional status, cognition and mood, sensory impairment, and other geriatric syndromes from the 3 years prior to enrollment. The VA-FI is a ratio of all deficits and ranges from 0 to 1 with scores >0.2 considered frail. RA disease activity was measured during routine clinical care using the DAS28-ESR. Multivariable logistic regression was used to evaluate the association between frailty and disease activity adjusting for age, sex, disease duration, smoking status, BMI, prednisone use, conventional synthetic DMARD use, and biologic DMARD use, obtained from the registry and linked VA data. Due to collinearity the Rheumatic Disease Comorbidity Index (RDCI) and MDHAQ were not included in the multivariable model.

Results: Of the 2,240 participants studied, 89% were male, mean age was 64.2±10.9 years, mean RA disease duration was 11.1±11.3 years, majority were White (77%), and had moderate RA disease activity (39%). Frailty was observed in 29% of participants at enrollment. Those categorized as frail were older (68.7 vs. 62.3 years), had longer RA disease duration (11.7 vs. 10.9 years), had higher RDCI scores (5.0 vs. 2.7), and higher MDHAQ scores (1.0 vs. 0.8) compared to non-frail participants (Table 1). In the multivariable model, with remission as the reference group, RA disease activity was significantly associated with frailty with the following odds ratios: low disease activity 1.59 (95% CI 1.14-2.21), moderate disease activity 1.65 (95% CI 1.26-2.17) and high disease activity 2.17 (95% CI 1.60-2.94) (p-values all < 0.01) (Table 2). These associations were not attenuated in the adjusted model.

Table 1. Characteristics of the whole cohort and by frailty status measured by the VA Frailty Index. Reported as N (%) or mean (SD).

	Total N = 2,240	Non-frail N = 1,591 (71%)	Frail N = 649 (29%)
Age (years)	64.2 (10.9)	62.3 (11.0)	68.7 (9.3)
Female	246 (11%)	182 (11%)	64 (10%)
Race			
White	1,725 (77%)	1,232 (77%)	493 (76%)
Black	361 (16%)	246 (16%)	115 (18%)
Other	154 (7%)	113 (7%)	41 (6%)
BMI (kg/m^2)			
<18.5	17 (1%)	10 (1%)	7 (1%)
18.5-24.9	507 (23%)	349 (22%)	158 (24%)
25.0-29.9	821 (37%)	618 (39%)	203 (31%)
30.0-34.9	487 (22%)	342 (22%)	145 (22%)
35.0-39.9	188 (8%)	114 (7%)	74 (11%)
≥40	214 (10%)	155 (10%)	59 (9%)
Smoking Status			
Ever smoker	1,727 (77%)	1,207 (76%)	520 (80%)
Never smoker	513 (23%)	384 (24%)	129 (20%)
Anti-CCP*			
Positive	1,535 (77%)	1,131 (79%)	404 (73%)
Negative	448 (23%)	298 (21%)	150 (27%)
RA Disease Duration (years)	11.1 (11.3)	10.9 (10.9)	11.7 (12.2)
RDCI	3.4 (2.0)	2.7 (1.7)	5.0 (1.5)
Medication use			
Prednisone	792 (35%)	535 (34%)	257 (40%)
MTX	1,167 (52%)	861 (54%)	306 (47%)
Biologic	627 (28%)	473 (30%)	154 (24%)
MDHAQ	0.9 (0.6)	0.8 (0.6)	1.0 (0.6)
DAS28-ESR Category			
Remission	551 (25%)	436 (27%)	115 (18%)
Low	341 (15%)	241 (15%)	100 (15%)
Moderate	878 (39%)	611 (38%)	267 (41%)
High	470 (21%)	303 (19%)	167 (26%)

BMI: body mass index, CCP: cyclic citrullinated peptide, DAS28-ESR: disease activity score 28 with erythrocyte sedimentation rate, MDHAQ: multidimensional health assessment questionnaire, MTX: methotrexate, VA-FI: Veterans Affairs Frailty Index; RDCI, Rheumatic Disease Comorbidity Index
*Missing N=257 (12%)

Table 2. Unadjusted (N=2,240) and adjusted (N=2,186) logistic regression models evaluating the relationship between frailty and RA disease activity.

DAS28-ESR Category	OR*	95% CI	p-value	aOR**	95% CI	p-value
Remission	Ref	–	–	Ref	–	–
Low	1.57	1.15-2.15	0.004	1.59	1.14-2.21	0.007
Moderate	1.66	1.29-2.13	<0.0001	1.65	1.26-2.17	<0.0001
High	2.09	1.58-2.76	<0.0001	2.17	1.60-2.94	<0.0001

*Values are odds ratios for predicting frailty.
**Model was adjusted for baseline age, sex, RA disease duration, smoking status, BMI, prednisone use, conventional synthetic DMARD use, and biologic DMARD use.

Conclusion: RA disease activity has a strong, independent association with frailty in Veterans with RA. Point estimates remained consistent between unadjusted and adjusted models suggesting a robust association. Future studies evaluating the longitudinal relationship between these two measures are needed to understand the causal relationships underlying this association and to determine if improving disease activity can impact frailty status.

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Abstract Number: 0404

Persistent Pain and Its Predictors After Start of Anti-TNF Therapy in Rheumatoid Arthritis – Is Line of Treatment Linked to Different Pain Patterns?

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Persisting pain with or without inflammation control is a common and debilitating symptom in rheumatoid arthritis (RA). Concerns have been raised that patients with non-inflammatory pain features might accumulate along the treatment path, but data is limited. The aim of this study was to examine prevalence and dynamics of unacceptable pain and unacceptable pain despite inflammation control (refractory pain), as well as predictors of these pain states, comparing TNF-inhibitor (TNFi) treatment lines in established RA.

Methods: RA patients starting a 1st, 2nd or ≥3rd TNFi treatment line 2004-2009 were identified in the South Swedish Arthritis Treatment Group register: N=993 for a 1st TNFi (77% women, mean age 58y, mean disease duration 10y); N=439 for a 2nd TNFi (83%, 56y, 14y); and N=143 for a ≥3rd TNFi (88%, 58y, 16y). A patient could contribute with data to more than one treatment line. Unacceptable pain was defined as >40 mm on a Visual Analogue Scale (VAS; 0-100 mm), according to the Patient Acceptable Symptom State (PASS),[1]and inflammation control captured through CRP < 10 mg/L combined with ≤1 swollen joint (of 28), as previously described.[2] Frequencies of unacceptable and refractory pain were respectively

assessed at 0, 3, 6, 12 and 24 months and compared between treatment lines by Chi-2 test. Potential predictors at start of each TNFi line were estimated in relation to unacceptable/refractory pain at 24 months by logistic regression.

Results: In patients initiating a 1st TNFi, unacceptable pain decreased from 84% to 42% from therapy start to 24 months. Corresponding figures at 24 months were 49% for a 2nd TNFi (p=0.14 vs. 1st) and 63% for a ≥3rd TNFi (p=0.009 vs. 1st) (Figure). Refractory pain at 24 months was 18%, 24% and 26% for a 1st, 2nd and ≥3rd TNFi (2nd and ≥3rd line treatments

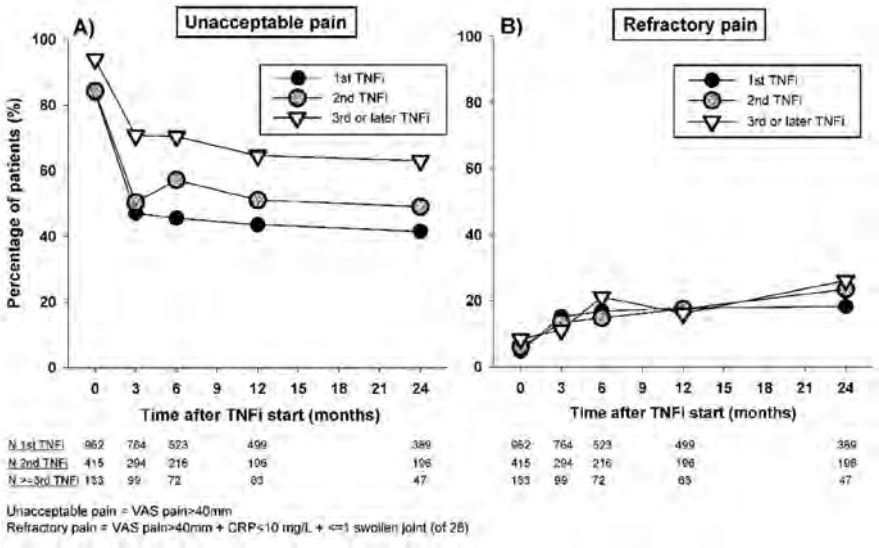

Figure. Frequency of unacceptable pain (A) and refractory pain (B) during 24 months after start of a TNF-inhibitor (TNFi), shown for a 1st, 2nd and ≥3rd TNFi treatment line in RA patients initiating therapy 2004-2009.

Table 1

Table 1. Baseline predictors of unacceptable pain 24 months after start of a TNF-inhibitor

	1st TNFi line				≥2nd TNFi line			
	Univariate		*Multivariate*		*Univariate*		*Multivariate*	
	OR	*P Value*	*OR*	*P Value*	*OR*	*P Value*	*OR*	*P Value*
Sex (women vs. men)	**1.77**	**0.023**	**1.38**	**0.24**	1.76	0.15		
Age (per 10y increase)	0.90	0.83			1.13	0.28		
Disease duration (per 10y increase)	1.04	0.72			1.05	0.74		
TJC (28) (per unit increase)	**1.03**	**0.036**	**1.04**	**0.038**	**1.55**	**0.037**	**1.61**	**0.029**
SJC (28) (per unit increase)	**0.96**	**0.032**	0.96	0.085	1.09	0.72		
CRP (mg/L; per 10 unit increase)	0.92	0.094			0.90	0.17		
ESR (mm/h; per 10 unit increase)	0.93	0.16			0.99	0.85		
VAS pain (per 10 mm increase)	**1.27**	**<0.001**	**1.33**	**<0.001**	**1.38**	**<0.001**	**1.38**	**<0.001**
VAS global (per 10 mm increase)	**1.27**	**<0.001**	**1.32**	**<0.001**	**1.38**	**<0.001**	**1.41**	**<0.001**
Evaluator's global (per unit increase)	0.97	0.86			1.15	0.48		
HAQ (per unit increase)	**3.51**	**<0.001**	**4.65**	**<0.001**	**3.46**	**<0.001**	**4.04**	**<0.001**
EQ-5D utility* (per unit increase)	**0.24**	**<0.001**	**0.17**	**<0.001**	**0.19**	**<0.001**	**0.17**	**<0.001**
Ongoing MTX (yes vs. no)	**0.55**	**0.013**	0.65	0.11	1.46	0.18		
Corticosteroids (yes vs. no)	0.95	0.80			1.14	0.65		
NSAID (yes vs. no)	0.88	0.35			0.93	0.64		

Unacceptable pain: VAS pain >40 mm
Statistically significant estimates (p<0.05) are shown in bold font
Univariably significant predictors were adjusted through multivariate models with adjustment covariates chosen based on subject matter knowledge. Covariates with a correlation ≥0.4 or ≤-0.4 were not introduced in the same model. VAS pain, VAS global, HAQ and EQ5D were adjusted for sex, age, disease duration, SJC and CRP. TJC and SJC were adjusted for sex, age, disease duration and CRP. Ongoing MTX was adjusted for sex, age, disease duration, SJC, CRP and VAS pain. TNFi, tumor necrosis factor inhibitor; OR, odds ratio; CI, confidence interval; TJC, tender joint count; SJC, swollen joint count; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; VAS, visual analogue scale; DAS28, disease activity score with 28 joint count; HAQ, health assessment questionnaire; EQ-5D, EuroQol 5-Dimensions; MTX, methotrexate; NSAID, non-steroid anti-inflammatory drug.

Table 2

Table 2. Baseline predictors of refractory pain 24 months after start of a TNF-inhibitor

	1st TNFi line				≥2nd TNFi line			
	Univariate		*Multivariate*		*Univariate*		*Multivariate*	
	OR	*P Value*	*OR*	*P Value*	*OR*	*P Value*	*OR*	*P Value*
Sex (women vs. men)	1.36	0.35			2.41	0.12		
Age (per 10y increase)	0.96	0.68			0.96	0.75		
Disease duration (per 10y increase)	0.99	0.93			0.95	0.74		
TJC (28) (per unit increase)	1.03	0.11			0.95	0.82		
SJC (28) (per unit increase)	**0.94**	**0.045**	0.96	0.15	**0.93**	**0.028**	0.95	0.13
CRP (mg/L; per 10 unit increase)	**0.83**	**0.026**	**0.81**	**0.042**	0.90	0.17		
ESR (mm/h; per 10 unit increase)	**0.85**	**0.035**	**0.84**	**0.013**	0.89	0.21		
VAS pain (per 10 mm increase)	**1.18**	**0.014**	**1.27**	**0.001**	**1.25**	**0.009**	**1.21**	**0.033**
VAS global (per 10 mm increase)	**1.15**	**0.033**	**1.21**	**0.005**	**1.29**	**0.004**	**1.28**	**0.012**
Evaluator's global (per unit increase)	0.98	0.936			0.77	0.27		
HAQ (per unit increase)	**1.80**	**0.018**	**2.47**	**0.001**	1.54	0.13		
EQ-5D utility (per unit increase)	0.48	0.076			0.45	0.125		
Ongoing MTX (yes vs. no)	0.79	0.43			1.38	0.34		
Corticosteroids (yes vs. no)	1.02	0.95			0.80	0.50		
NSAID (yes vs. no)	0.83	0.20			0.96	1.00		

Refractory pain: VAS pain >40 mm + CRP<10 mg/L + ≤1 swollen joint (of 28)

Statistically significant estimates ($p<0.05$) are shown in bold font

Univariably significant predictors were adjusted through multivariate models with adjustment covariates chosen based on subject matter knowledge. Covariates with a correlation ≥0.4 or ≤-0.4 were not introduced in the same model. VAS pain, VAS global and HAQ were adjusted for sex, age, disease duration, SJC and CRP. SJC was adjusted for sex, age, disease duration and CRP, whereas CRP and ESR were adjusted for sex, age, disease duration, SJC and VAS pain. TNFi, tumor necrosis factor inhibitor; OR, odds ratio; CI, confidence interval; TJC, tender joint count; SJC, swollen joint count; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; VAS, visual analogue scale; DAS28, disease activity score with 28 joint count; HAQ, health assessment questionnaire; EQ-5D, EuroQol 5-Dimensions; MTX, methotrexate; NSAID, non-steroid anti-inflammatory drug.

non-significant vs. 1st line). Higher baseline HAQ and VAS pain/global, more tender joints, and lower EQ-5D utility were associated with a higher risk of 24-month unacceptable pain in patients starting both a 1st and later TNFi treatment lines, in adjusted analyses (Table 1). For refractory pain, higher VAS pain/global were the only significant predictors across treatment lines, while for a 1st TNFi refractory pain was also predicted by lower CRP and ESR, as well as higher HAQ (Table 2).

Conclusion: Unacceptable pain at 2 years follow-up is more frequent in later TNFi treatment lines and almost half of this pain load is due to pain indicative of a non-inflammatory mechanism. Predictors of unacceptable pain are largely stable across treatment lines, while for refractory pain they vary with line of treatment. The results suggest a selection of RA patients with intense pain, including non-inflammatory components, in later TNFi treatment lines. This highlights a need for additional pharmacologic and non-pharmacologic therapies that more specifically target various pain features.

1. Tubach et al. *ArthritisCareRes* 2012;64:1699-707
2. Olofsson et al. *Arthritis Care Res* 2021;73:1312-21

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Abstract Number: 0405

Clinical Features of Anti-Th/To Antibodies-positive Systemic Sclerosis Patients: A Single-center Retrospective Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-Th/To antibodies (Abs) have been reported in patients with systemic sclerosis (SSc). The presence of anti-Th/To Abs is detected in 2-5% of SSc cases and is more frequently observed in the limited cutaneous SSc (lcSSc). In the Japanese population, there is a higher incidence of concurrent gastroesophageal reflux disease (GERD) and interstitial lung disease (ILD), although the severity of these complications tends to be milder compared to European and North American populations. Due to the low expression frequency and few case reports on this Abs, there is no consensus on clinical significance of this Abs.

Methods: Thus, to examine the clinical characteristics of patients with anti-Th/To Abs, we retrospectively identified 10 patients by using the serum immunoprecipitation assays between 2001 and 2021.

Results: Among the anti-Th/To positive cases, only lcSSc was observed, and diffuse cutaneous SSc (dcSSc) was not detected.

Compared to 596 cases of Th/To-negative SSc from our hospital, the modified Rodnan total skin thickness score (mRSS) was significantly lower in the anti-Th/To positive group (2.8 [0-9] vs. 10.1 [0-49], $p < 0.05$). Additionally, there was a significantly higher rate of ILD (8/9 vs. 143/596, $p < 0.01$) and Pulmonary arterial hypertension (PAH) (3/9 vs. 41/596, $p < 0.05$) in the anti-Th/To-positive group compared to the negative group. Although there was no significant difference, GERD was more common in the anti-Th/To positive group (63%) compared to the negative group (44.3%). No cases of renal crisis were observed in patients with anti-Th/To positive SSc.

When compared to 170 SSc patients with anti-topoisomerase antibodies, which are known to be frequently associated with ILD, there was no significant difference. However, the anti-Th/To-positive group had a higher rate of ILD.

Conclusion: In conclusion, patients with anti-Th/To antibodies exhibit mild skin sclerosis but have an increased risk of developing organ complications such as ILD and PAH in the future.

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Abstract Number: 0406

Obesity Is a Risk Factor for Poor Response to Treatment in Early Rheumatoid Arthritis – a NORD-STAR Spin-Off Study

Violetta Dubovyk[1], Gerdur Maria Grondal[2], Bjorn Gudbjornsson[3], Espen A Haavardsholm[4], Marte Schrumpf Heiberg[4], Merete Hetland[5], Kim Hørslev-Petersen[6], Meliha Kapetanovic[7], Alf Kastbom[8], John Lampa[9], Kristina Lend[10], Dan Nordstrom[11], Michael Nurmohamed[12], Milad Rizk[13], Annika Söderbergh[14], Till Uhlig[15], Mikkel Østergaard[16], Ronald van Vollenhoven[12], Anna Rudin[17] and **Cristina Maglio**[18], [1]University of Gothenburg, Gothenburg, Sweden, [2]Department for Rheumatology, Landspitali University Hospital, Reykjavik, Iceland, [3]Centre for Rheumatology Research, University Hospital, Reykjavik, Iceland, [4]Diakonhjemmet Hospital, Oslo, Norway, [5]Copenhagen Center for Arthritis Research, Rigshospitalet, Copenhagen, Denmark, [6]University of Southern Denmark, Odense, Denmark, [7]Lund University and Skåne University Hospital, Lund, Sweden, [8]Linköping University, Linköping, Sweden, [9]Stockholm County, Hässelby, Sweden, [10]Amsterdam UMC, Karolinska Institute, Stockholm, Sweden, [11]Helsinki University Hospital, Helsinki, Finland, [12]Amsterdam University Medical Centers, Amsterdam, Netherlands, [13]Västmanlands Hospital Västerås, Västerås, Sweden, [14]Örebro University Hospital, Örebro, Sweden, [15]Center for Treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway, [16]Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Centre for Head and Orthopaedics, Rigshospitalet; University of Copenhagen, Copenhagen, Denmark, [17]Department of Rheumatology and Inflammation Research, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, [18]Institute of Medicine, University of Gothenburg, Gothenburg, Sweden

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Several therapeutic options are currently available to treat rheumatoid arthritis (RA); however, the response to treatment is highly variable, and not all patients achieve clinical remission. Obesity is suggested to lower the chances of remission, even though a recent observational study has shown that obesity is not associated with reduced response to conventional synthetic anti-rheumatic drugs in patients with early RA. Here, we aim to determine if obesity affects the response to treatment in participants with early RA.

Methods: This report includes 393 Swedish patients from the NORD-STAR study, which is a multicenter, randomized trial on 812 patients with untreated early RA [4]. Participants have been randomized at baseline into 4 arms of treatment: methotrexate combined with (1) prednisolone, (2) certolizumab, (3) abatacept, or (4) tocilizumab. Scores for disease activity and blood samples were measured and collected before randomization and at 24-week follow-up.

Table 1. Disease activity scores and inflammatory parameters at 24 weeks follow-up stratified by baseline BMI. Abbreviations: TJC28, tender joint count; VAS, visual analogue scale of pain; ESR, erythrocyte sedimentation rate.

	BMI (kg/m^2)		
	< 30	≥ 30	P-values
DAS28-ESR	2.2±1.1	2.8±1.2	<0.001
DAS28-CRP	2.1±0.9	2.6±1.0	<0.001
CDAI	5.0±5.3	7.5±6.4	0.001
SJC28	0.7±1.4	0.9±1.4	0.418
TJC28	1.8±3.1	3.0±4.2	0.256
Global VAS, patient, mm	17±18	25±22	<0.001
Global VAS, investigator, mm	8±9	11±11	0.018
ESR, mm/h	11±10	15±16	0.031
CRP, mg/L	2.2±3.1	4.4±7.1	<0.001

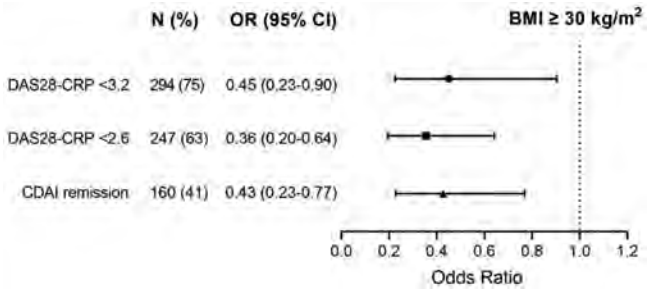

Fig. 1. Multivariable binary logistic regression analysis for response to treatment at 24 weeks according to BMI (reference category: BMI< 30 kg/m2).

Multiple linear regression and binary logistic regression analyses were performed adjusting for sex, baseline age, anti-citrullinated peptide antibody status, current smoking, disease activity score- C-reactive protein (DAS28-CRP), and treatment randomization. The outcomes for this report were: DAS28-CRP ≤3.2 (DAS28-CRP low disease activity), DAS28-CRP ≤2.6 (DAS28-CRP remission) and clinical disease activity index (CDAI) ≤2.8 (CDAI remission).

Results: In total, 75 (19%) participants had obesity at baseline, defined as body mass index (BMI) ≥30 kg/m^2. The percentage of patients with obesity in each treatment group was (1) 25%, (2) 15%, (3) 19% and (4) 19%. At baseline, there were no differences in terms of disease activity indices and inflammation parameters between patients with BMI <30 vs. ≥30 kg/m^2, except for number of swollen joints (SJC28), which was slightly lower in those with obesity (mean±SD, 8±5 vs. 9±5, p=0.018). At 24-week follow-up, patients with obesity had higher disease activity indices and inflammation parameters compared to those with lower BMI (Table 1). Moreover, patients with obesity had a lower chance of achieving response to treatment as measured by DAS28-CRP ≤3.2 (OR 0.5, 95% CI 0.2 - 0.9, p=0.025), DAS28-CRP ≤2.6 (OR 0.4, 95% CI 0.2 - 0.6, p < 0.001) and CDAI remission (OR 0.4, 95% CI 0.2 - 0.8, p=0.006), compared to patients with lower BMI (Fig. 1). BMI-treatment interaction was not significant for any score of disease activity.

Conclusion: In patients with early RA, obesity was not associated with higher disease activity before treatment initiation. However, 24 weeks after treatment, patients with obesity had higher disease activity and lower chances to respond to therapy compared to patients with lower BMI irrespective of treatment.

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Abstract Number: 0407

Meteorological Conditions Contribute to the Joint Ultrasound Findings in Patients with Rheumatoid Arthritis: Kyushu Multicenter Rheumatoid Arthritis Ultrasound Prospective Observational Cohort Study

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SESSION INFORMATION

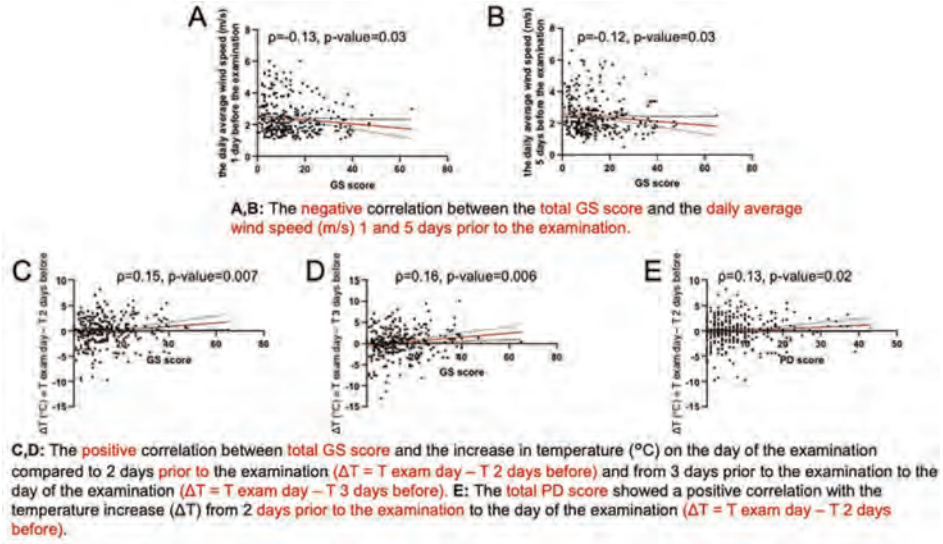
Session Date: Sunday, November 12, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Various environmental factors are involved in the pathogenesis of rheumatoid arthritis (RA), and meteorological conditions such as temperature and atmospheric pressure have also been reported to affect its symptoms. However, studies evaluating its influence based on objective imaging studies are lacking. This study analyzed the correlation between joint ultrasonography scores and meteorological conditions in a multicenter RA cohort to determine whether meteorological conditions contribute to the joint ultrasound findings of RA.



A,B: The negative correlation between the total GS score and the daily average wind speed (m/s) 1 and 5 days prior to the examination.

C,D: The positive correlation between total GS score and the increase in temperature (°C) on the day of the examination compared to 2 days prior to the examination (ΔT = T exam day – T 2 days before) and from 3 days prior to the examination to the day of the examination (ΔT = T exam day – T 3 days before). **E:** The total PD score showed a positive correlation with the temperature increase (ΔT) from 2 days prior to the examination to the day of the examination (ΔT = T exam day – T 2 days before).

Methods: The present study was analyzed from the baseline data from Kyushu Multicenter Rheumatoid Arthritis Ultrasound Prospective Observational Cohort started from 2013. This cohort study recruits active RA patients who require the treatment with biologicalor targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs). Three hundred eight subjects were evaluated by joint ultrasound synovitis scores [22 joints including bilateral 1^{st} -5^{th} metacarpophalangeal (MCP) joints, proximal interphalangeal (PIP) joints, and wrist joints semi-quantitatively examined by grey-scale (GS) and power Doppler (PD) scores from 0 to 3]. The sum of the GS and PD scores was used as an indicator of individual's ultrasound disease activity. Metrological data [daily mean temperature (°C), daily mean-sea-level barometric pressure (hPa), daily mean vapor pressure (hPa), and daily mean wind speed (m/s)] was obtained from the database issued by the Japan Meteorological Agency (JMA). Spearman's rank correlation coefficient was used for the analysis of the correlation between metrological conditions and ultrasonographic scores.

Results: There was a negative correlation between the total GS score and the daily average wind speed 1 and 5 days before the examination (ρ=-0.13, p-value=0.03, andρ=-0.12, p-value=0.03, respectively). The total GS score exhibited a positive correlation with the increase in temperature on the day of the examination compared to 2 days prior to the examination(ΔT = T exam day–T 2 days before,ρ=0.15, p-value=0.007) and from 3 days prior to the examination to the day of the examination(ΔT = T exam day–T 3 days before,ρ=0.16, p-value=0.006). The total PD score showed a positive correlation with the temperature increase (ΔT) from 2 days prior to the examination to the day of the examination(ΔT = T exam day–T 2 days before,ρ=0.13, p-value=0.02).

Conclusion: Our findings suggest that meteorological conditions, specifically low wind speed, and temperature rise, are associated with the joint ultrasound findings of RA patients. Understanding these correlations could aid in better management and treatment of RA by considering the potential climate impact toward RA disease conditions. Further research and studies are warranted to explore the underlying mechanisms and to validate these findings in larger and more diverse cohorts.

Disclosure: M. Umeda: None; **Y. Endo**: None; **T. Michitsuji**: None; **A. Nishino**: None; **S. Kawashiri**: None; **S. Morimoto**: None; **M. Tuboi**: None; **N. Matsuoka**: None; **K. Fujikawa**: None; **A. Mizokami**: None; **Y. Arinobu**: None; **T. Tsuru**: None; **H. Takaoka**: None; **T. Yoshitama**: None; **T. Asano**: None; **J. Ishizaki**: None; **A. Kawakami**: None.

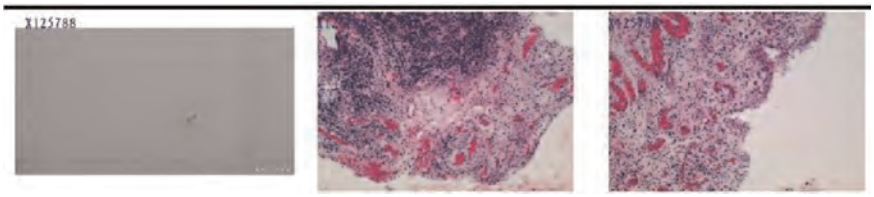
Abstract Number: 0408

The Role of Synovial Biopsy in Evaluating Rheumatoid Arthritis Acitivity in Patients: Findings from a Study of 30 Patients Treated with Adalimumab

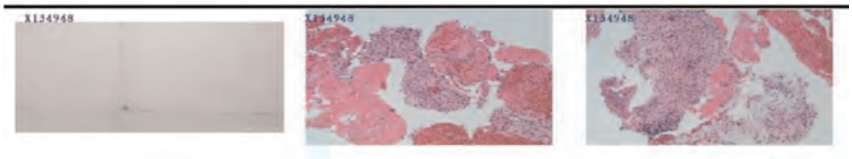
Rui Wu and YIlin Peng, the first affilated hospital of Nanchang University, Nanchang, China

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis(RA)is a chronic autoimmune disease that is characterized by inflammation and destrction of synovial jionts which result in high disabilty. Treat-to-Target is critical to preveting disability and improving outcomes. Accurate evaluation of disease activity is crucial to guide clinical decision-making and develop effective management plan. Synovial biopsy is an emerging tool that can prvide valuable information about the molecular and cellular processes undrlying RA. There is several diffferent types of needles for synovial biopsy. But they maynot be widely available or feasible



F43, acchieved clinical remmision with normal ESR, CRP and high synovial inflammatory score(7 poionts) in right ankel joint synovium which shows proliferation of synovial cells, interstitial edema, neovascularization, lymphoplasmcytic inflitrates, lymphoid tissue hyperplasia, and infiltration (HE).



F62, failed the treatment of adlimumab and MTX with high synovial inflammatory score(6 points) in left knee joint synovium after 3-months adiministration of adalimumab. Under microscope (HE) , it shows proliferation of synovial cells and fibrous tissue, moderate infliltration of lymphoplasmacytic cells, and inflammatory fibrinous exucdate.

for use because of unsuitalbe for small joints or compliated procedure We improved a spring-loaded biopsy needle which can make the procedure easier and safer. This needle now is commonly used in clinical practice in our center. We reports the findings from our study of RA patients treated with adalimumab who underwent synovial biopsy.

Methods: Thrty RA patients who had inadequate response to MTX were treated with adalimumab and assessed using various indicators of disease activity, including DAS28, ESR,CRP, and radiography imaging. Synovial biopsy was also performed to assess the level of synovial inflmmation before and after 3-months administration of adalimumab. The Synovial biopsy scores were compared to the other indicators of disease activity to evaluate their correlation. We improved a novel spring-loaded synovial biopsy needle which can provide more accurate samples. it consists of a small cylindrical outer sheath and an inner stylet that contains a spring-loaded sampling needle. Once the needle is in place, the negative pressure suction mechinism enables the sample to enter the core of the sampling needle and than release the spring which draw back the inner needle and cut sample quickly. The improved synovial biopsy needles provide an easier and safter procedure.

Results: Of the 30 patients, 22 patients responded well to adalimumab, with significant improvement in DAS28, ESR, and CRP levels. But 8 patinets failed to achieve ACR 20. In 22 patients, 6 patients accheive clinical remission with less than 2.6 of DAS 28. Synovial membrane inflammation scores(GSS) were calculated by inflammatory infiltration, stromal activation and synovila lining hyperplasia(0-9). A significant positive correlation between the GSS and DAS28 score was found in RA patients. in 8 patients who failed the treatment of adalimumab, infllltratrion of lymphoplasmcytic cell in the synovial membrane were predominant. But in 4 patiens who accheived clinical remission, GSS sitll remains high level(more than 6).

Conclusion: Our study suggest that a large infiltration of lymphoplasmacytic cells in the synovial mebbrane is a negative predictor for response of adalimumab in RA. Synovial membrane inflammatory scores(GSS) may be a useful tool for assessing disease activity in RA patients and may help indentify patients who need more aggressive treatment even they acchieved clinical remission with DAS 28. The improved spring-loaded synovial biopsy needles can help faciliated more accurate and effective synovial biopsy for assessing disease activity in RA.

Disclosure: R. Wu: None; **Y. Peng**: None.

Abstract Number: 0409

Prevalence of Pulmonary Manifestations in Patients with Newly Diagnosed Rheumatoid Arthritis, Psoriatic Arthritis, and Peripheral Spondyloarthritis

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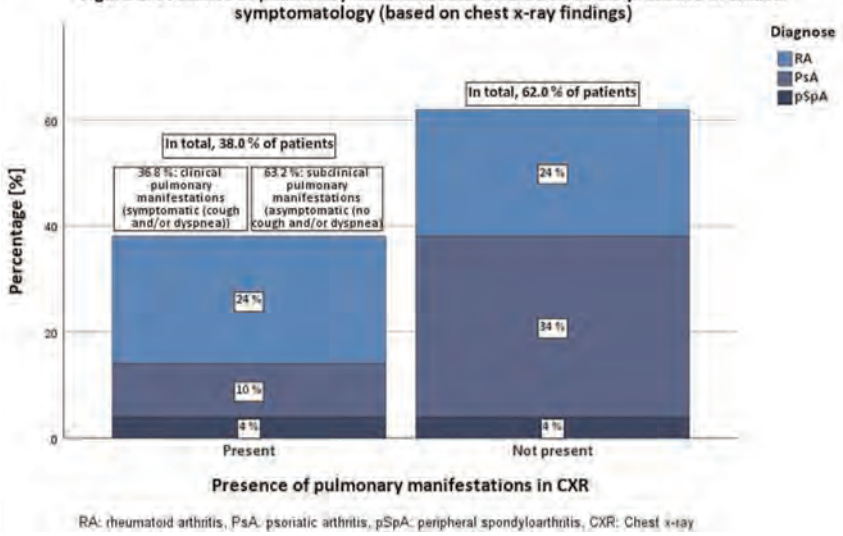
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Pulmonary impairment is a common, yet poorly understood, extraarticular manifestation in rheumatic diseases, which is often inadequately screened and managed. This can result in a substantial increase in morbidity and mortality [1]. While previous studies have mainly focused on rheumatoid arthritis (RA) and to some extent on psoriatic arthritis (PsA), data for patients with peripheral spondyloarthritis (pSpA) are lacking. The aim of this study was to investigate the prevalence of both clinical and subclinical pulmonary manifestations in newly diagnosed patients with RA, PsA, and pSpA. Furthermore, different baseline examination results were compared in order to develop a screening proposal for detecting patients at risk.

Methods: This clinical-prospective, longitudinal cohort study included a diagnostic workup consisting of a questionnaire for patient history, a physical examination, a body plethysmography with diffusion capacity for carbon monoxide (DLCO), a 6-minute walk test, laboratory parameters, and a chest x-ray (CXR) at the time of the initial diagnosis of arthritis disease, and at four additional time points in three-month intervals. This abstract thereby focuses on the baseline characteristics.

Figure 1: Presence of pulmonary manifestations in relation to the presence of clinical symptomatology (based on chest x-ray findings)



RA: rheumatoid arthritis, PsA: psoriatic arthritis, pSpA: peripheral spondyloarthritis, CXR: Chest x-ray

Table 1 Baseline patient characteristics

		Diagnose			
		RA (n = 26)	PsA (n = 24)	pSpA (n = 4)	Control proband (n = 26)
Age [years]	Mean	52.7	46.3	41.3	48.4
	Standard deviation	16.1	12.8	9.0	11.9
Sex	Female	9 (34.6 %)	14 (58.3 %)	1 (25.0 %)	14 (53.8 %)
	Male	17 (65,4 %)	10 (41,7 %)	3 (75,0 %)	12 (46,2 %)
BMI [kg/m²]	Mean	25.1	26.9	26.9	27.0
	Standard deviation	4.1	5.3	8.8	4.1
Smoking	Neversmoker	17 (65.4 %)	14 (58.3 %)	1 (25.0 %)	19 (73.1%)
	Eversmoker	9 (34.6 %)	10 (41.7 %)	3 (75.0 %)	7 (26.9 %)
Chronic cough	Not present	16 (61.5 %)	19 (79.2 %)	2 (50.0 %)	24 (92.3 %)
	Present	10 (38.5 %)	5 (20.8 %)	2 (50.0 %)	2 (7.7 %)
Dyspnea	Not present (NYHA I)	20 (76.9 %)	19 (79.2 %)	2 (50.0 %)	24 (92.3 %)
	Present (NYHA II+)	6 (23.1 %)	5 (20.8 %)	2 (50.0 %)	2 (7.7 %)
Previous pulmonary disease	None	23 (88.5 %)	22 (91.7 %)	3 (75.0 %)	22 (84.6 %)
	Bronchial asthma	2 (7.7 %)	1 (4.2 %)	1 (25.0 %)	1 (3.8 %)
	COPD	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	1 (3.8 %)
	Interstitial lung disease	1 (3.8 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)
	Sarcoidosis	0 (0.0 %)	1 (4.2 %)	0 (0.0 %)	2 (7.7 %)

RA: rheumatoid arthritis, PsA: psoriatic arthritis, pSpA: peripheral spondyloarthritis, BMI: Body Mass Index, NYHA: New York Heart Association, COPD: chronic obstructive pulmonary disease

Results: In total 54 outpatients (26 RA, 24 PsA, 4 pSpA) and 26 age- and gender-matched controls were examined (tab. 1). Pulmonary impairment, in the sense of a morphologically abnormal CXR, was diagnosed in 19 arthritis patients (38.0 %). Of these, 36.8 % suffered from clinical symptoms such as cough and/or dyspnea. However, 63.2 % of the patients presented subclinical, asymptomatic pulmonary abnormalities (fig. 1). The baseline results of several examinations are illustrated in table 2. An elevation of rheumatoid factor (> 14 IU/ml) showed an association with the manifestation of RA (p = .002) as well as with the presence of pulmonary affection (p = .008). In addition, the mean age of patients with pulmonary abnormalities (57.0 ± 12.8 yrs.) differed significantly from that of patients without such abnormalities (43.9 ± 14.3 yrs.), with a p-value of .002. The association between the activity of arthritis disease, assessed by Disease Activity Score in 28 joints using CRP (DAS28CRP), and CXR findings proved to be significant (p = .011). A DAS28CRP less than 3.2 (remission or low disease activity) indicated non-pathological findings in CXR.

Conclusion: The prevalence of pulmonary manifestations was more than one-third and more than two-thirds presented asymptomatic. The high proportion of asymptomatic patients highlights the need for the implementation of a pulmonary screening at the initial diagnosis of arthritis disease. By alerting physicians, especially in the observed age cohort of 57 years with elevated RF levels, morbidity and mortality could be reduced.

Table 2 Findings in different examinations (physical examination, bodyplethysmography with CO diffusion capacity, laboratory parameters)

		Presence of rheumatic disease		Presence of pulmonary disorders in chest x-ray	
		RA[a]/PsA[b]/pSpA[c] (n=54)	Control proband (n=26)	Present (n=19)	Not present (n=31)
Breathing width	Non-pathological (≥ 3 cm)	18 (33.3 %)	20 (76.9 %)	4 (21.1 %)	13 (41.9 %)
	Pathological (< 3 cm)	36 (66.7 %)	6 (23.1 %)	15 (78.9 %)	18 (58.1 %)
Chest excursion	Non-pathological (≥ 8 cm)	31 (57.4 %)	17 (65.4 %)	10 (52.6 %)	17 (54.8 %)
	Pathological (< 8 cm)	23 (42.6 %)	9 (34.6 %)	9 (47.4 %)	14 (45.2 %)
Restrictive lung disease	Not present	39 (84.8 %)	16 (64.0 %)	15 (88.2 %)	21 (84.0 %)
	Present (FVC < 70 %; TLC < 80 %)	7 (15.2 %)	9 (36.0 %)	2 (11.8 %)	4 (16.0 %)
Obstructive lung disease	Not present	46 (100.0 %)	25 (100.0 %)	17 (100.0 %)	25 (100.0 %)
	Present (FEV1/FVC < 70 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)
Emphysema	Not present	39 (86.7 %)	19 (76.0 %)	14 (82.4 %)	23 (95.8 %)
	Present (RV > 140 %)	6 (13.3 %)	6 (24.0 %)	3 (17.6 %)	1 (4.2 %)
Diffusion disturbance	Not present	37 (86.0 %)	21 (91.3 %)	13 (81.3 %)	21 (91.3 %)
	Present (DLCO < 60 %)	6 (14.0 %)	2 (8.7 %)	3 (18.8 %)	2 (8.7 %)
C-reactive protein (CRP)	Non-pathological (≤ 3 mg/l)	19 (35.2 %)	19 (86.4 %)	4 (21.1 %)	13 (41.9 %)
	Pathological (> 3 mg/l)	35 (64.8 %)	3 (13.6 %)	15 (78.9 %)	18 (58.1 %)
Rheumatoid factor (RF)	Non-pathological (≤ 14 IU/ml)	31 (66.0 %)	19 (95.0 %)	6 (37.5 %)	21 (77.8 %)
	Pathological (> 14 IU/ml)	16 (34.0 %)	1 (5.0 %)	10 (62.5 %)	6 (22.2 %)
Anti-citrullinated peptide antibodies (ACPA)	Non-pathological (≤ 8 U/ml)	38 (80.9 %)	20 (100.0 %)	12 (75.0 %)	22 (81.5 %)
	Pathological (> 8 U/ml)	9 (19.1 %)	0 (0.0 %)	4 (25.0 %)	5 (18.5 %)

RA: rheumatoid arthritis, PsA: psoriatic arthritis, pSpA: peripheral spondyloarthritis

Disclosure: L. Winter: None; **D. Skowasch**: None; **M. Weber**: None; **D. Kütting**: None; **C. Behning**: None; **P. Brossart**: None; **S. Petzinna**: None; **V. Schäfer**: None.

Abstract Number: 0410

Usefulness of RAPID3 in Assessing Unmet Needs of Patients with Rheumatoid Arthritis in Remission or with Low Disease Activity -a Multicenter Observational Study: T-FLAG Study-

Mochihito Suzuki[1], Nobunori Takahashi[2], Yasumori Sobue[3], yoshifumi Ohashi[1], Ryo Sato[1], Masataka Maeda[1], Hironobu Kosugiyama[1], yusuke Ohno[1], kenya terabe[4], Shuji Asai[1] and Shiro Imagama[1], [1]Nagoya University Graduate School of Medicine, Nagoya, Japan, [2]Department of Orthopedic Surgery, Aichi Medical University, Nagakute, Japan, [3]Japanese Red Cross Nagoya Daiichi Hospital, Nagoya, Japan, [4]Nagoya University, Nagoya, Japan

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Routine Assessment of Patient Index Data 3 (RAPID3) is a patient-reported outcome (PRO) that can be used to assess the condition of rheumatoid arthritis (RA) patients using only a questionnaire that can be completed in a short time. In previous reports, RAPID3 could be used as an assessment similar to Disease Activity Score 28 (DAS28), a common disease activity assessment [1]. However, there are unmet needs in which patients have low satisfaction with treatment, even though they are in remission according to disease activity assessments such as DAS28. To investigate the cause of this discrepancy, we decided to conduct a study using RAPID3 as a subjective patient assessment. The aime of this study was to investigate the discrepancy between disease activity and RAPID3 in RA patients.

Methods: The data for this study were obtained from the Tsurumai-Frailty and Locomotive Syndrome of Rheumatoid Arthritis for Globalization (T-FLAG), an observational study involving three centers. Of the 638 RA patients who completed the PRO questionnaire in 2022, 455 patients with a DAS28-CRP of low disease activity (LDA) or remission (REM) were enrolled. Disease activity was assessed using the RAPID3, DAS28-CRP. PRO assessment was performed using PtGA, Health Assessment Questionnaire Disability Index (HAQ-DI), Kihon checklist (KCL), and the 25-question Geriatric Locomotive Function Scale (GLFS-25). RAPID3 categories were compared in two groups: REM/LDA, and medium and high disease activity (MDA/HDA). Cutoff values for each PRO were detected using ROC analysis.

Results: The mean age (± standard deviation) was 69±14, female was 72%, disease duration was 12±9, RAPID3 was 3.1 ±4.0, DAS28-CRP was 1.65±0.48, HAQ-DI was 0.31±0.55, and KCL was 6.1±4.4. In the disease activity category, 84.5% of patients had RAPID3 and DAS28-CRP in the same category (The disease activity category of RAPID3 was LDA or REM). There were no significant differences in gender, biological and targeted synthetic disease-modifying antirheumatic

Table 1. Baseline characteristic of patients by RAPID3 category

	Total	RAPID3 REM/LDA	RAPID3 MDA/HDA	P value
N, %	445 (100.0)	376 (84.5)	69 (15.5)	
age, year *	69 ± 14	67 ± 14	72 ± 11	0.004
female, % †	72	73	62	0.080
Disease duration, year *	12 ± 9	11 ± 9	16 ± 10	< 0.01
MTX use, % †	59	63	39	< 0.01
b/ts DMARDs use, % †	38	37	44	0.286
Glucocorticoid use, % †	25	22	39	0.002
History of surgery, % †	15	12	29	< 0.01
RAPID3 *	3.1 ± 4.0	1.7 ± 1.7	10.8 ± 4.1	< 0.01
DAS28-CRP *	1.65 ± 0.48	1.56 ± 0.44	2.14 ± 0.39	< 0.01
CRP *	0.23 ± 0.49	0.23 ± 0.51	0.22 ± 0.31	0.844
TJC *	0.4 ± 0.8	0.4 ± 0.9	0.4 ± 0.7	0.515
SJC *	0.4 ± 1.1	0.4 ± 1.0	0.6 ± 1.6	0.196
PtGA, mm *	10 ± 16	5 ± 7	39 ± 20	< 0.01
PhGA, mm *	9 ± 14	5 ± 7	32 ± 18	< 0.01
Pain VAS, mm *	10 ± 16	5 ± 7	38 ± 21	< 0.01
HAQ-DI *	0.31 ± 0.55	0.20 ± 0.37	0.96 ± 0.84	< 0.01
KCL *	6.1 ± 4.4	5.5 ± 3.9	9.7 ± 5.0	< 0.01
GLFS-25 *	16 ± 16	13 ± 13	32 ± 21	< 0.01

RAPID: Routine Assessment of Patient Index Data; REM: remission; LDA: low disease activity; MDA: medium disease activity; HAD: high disease activity; MTX: methotrexate; b/ts DMARDs: biological and targeted synthetic disease-modifying antirheumatic drugs; DAS28: disease activity score with 28 joint counts; CRP: C-reactive protein; TJC: tender joint count; SJC: swollen jointcount; PtGA: patient global assessment; PhGA: physician global assessment; VAS: visual analog scale; HAQ-DI: Health Assessment Questionnaire-Disability Index; KCL: Kihon checklist for frailty; GLFS-25: the 25-question Geriatric Locomotive Function Scale. * Student's t-test † Chi-squared test

Baseline characteristic of patients by RAPID3 category

drugs, C-reactive protein, tender joint count, swollen joint count between the two groups of REM/LDA and MDA/HAD (Table 1). On the other hand, there were significant differences between the two groups in disease duration (11 vs. 16 years), PtGA (5 vs. 39mm), HAQ-DI (0.20 vs. 0.96), KCL (5.5 vs. 9.7), and GLFS-25 (13 vs. 32). The cutoff values for PRO assessment for different disease activity categories of patients were HAQ-DI 0.375 points, KCL 8 points, and GLFS-25 16 points.

Conclusion: In this study of patients with good disease activity control, 84.5% of patients were found to have a concordance between RAPID3 and DAS28 disease activity categories. The discrepancy between DAS28-CRP and RAPID3 may be due to physical dysfunction (HAQ-DI or GLFS-25) or frailty (KCL). Therefore, it is important to achieve clinical remission and improve PRO in RA treatment as an intervention to address unmet needs.

Disclosure: M. Suzuki: None; **N. Takahashi**: AbbVie/Abbott, 6, Asahi-Kasei, 6, Astellas, 6, Bristol-Myers Squibb(BMS), 6, Chugai, 6, Daiichi Sankyo, 6, Eisai, 6, Eli Lilly, 6, Janssen, 6, Mitsubishi Tanabe, 6, Novartis, 6, Pfizer, 6, Sanofi, 6, UCB, 6; **Y. Sobue**: None; **y. Ohashi**: None; **R. Sato**: None; **M. Maeda**: None; **H. Kosugiyama**: None; **y. Ohno**: None; **k. terabe**: None; **S. Asai**: None; **S. Imagama**: None.

Abstract Number: 0411

The Impact of Patient-reported Outcomes on Boolean 2.0 Remission Criteria in Rheumatoid Arthritis Patients in Real Clinical Practice -a Multicenter Observational Study: T-FLAG Study-

Mochihito Suzuki[1], yoshifumi Ohashi[1], Yasumori Sobue[2], Ryo Sato[1], Masataka Maeda[1], Hironobu Kosugiyama[1], yusuke Ohno[1], kenya terabe[3], Shuji Asai[1] and Shiro Imagama[1], [1]Nagoya University Graduate School of Medicine, Nagoya, Japan, [2]Japanese Red Cross Nagoya Daiichi Hospital, Nagoya, Japan, [3]Nagoya University, Nagoya, Japan

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The Boolean remission criteria proposed by the The American College of Rheumatology (ACR) and the European College of Rheumatology (EULAR) in 2011 are widely used as remission criteria for rheumatoid arthritis (RA) patients.

Until now, Boolean 1.0, which defined as a score 1 for each of TJC28, SJC28, CRP (mg/dl), and a Patient General Assessment (PtGA) ≤ 1 cm, has been used, but there have been concerns about overtreatment due to its too strict criteria. Therefore, Boolean 2.0, which uses a PtGA ≤2 cm, has recently been shown to be more consistent with Simplified Disease Activity Index (SDAI) remission criteria and has been described to be useful in clinical practice. The purpose of this study was to investigate the relationship between Boolean 2.0 remission and Boolean 1.0 remission and patient-reported outcomes (PRO) in RA patients using real clinical data.

Methods: Among 661 patients who visited the RA outpatient clinic between June and August 2022 (T-FLAG study) and whose patient background could be investigated, including Boolean remission, 308 patients who achieved the Boolean 2.0 remission criteria were included; a group of patients achieving Boolean 1.0 and a group of patients meeting the new criteria of The patient group that achieved Boolean 1.0 and the patient group that achieved Boolean 2.0 but not Boolean 1.0 (Boolean 1.0-2-0) were compared, and logistic regression analysis was performed to determine the background of patients

Table 1. Factors associated with baseline characteristics

	Total (n=308)	Boolean 1.0 (n=276)	Boolean 1.0-2.0 (n=32)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
age (years)	68.1 (14.1)	68.4 (14.3)	65.6 (12.7)	1.01 (0.99-1.04)	
female (%)	73.1	72.8	75.0	0.89 (0.39-2.08)	
Disease duration (years)	11.3 (9.0)	10.8 (8.3)	15.9 (13.2)	0.95 (0.92-0.98) *	0.94 (0.91-0.98) *
BMI	22.0 (3.8)	22.0 (3.8)	21.7 (3.5)	1.02 (0.92-1.13)	1.02 (0.92-1.13)
MTX use (%)	64.6	63.4	75.0	0.58 (0.25-1.33)	0.62 (0.26-1.45)
bDMARDs use (%)	29.5	27.5	46.9	0.43 (0.21-0.91) *	0.45 (0.21-0.96) *
tsDMARDs use (%)	6.8	7.2	3.1	2.42 (0.31-18.68)	2.42 (0.31-18.73)
Glucocorticoid use (%)	21.4	21.4	21.9	0.97 (0.40-2.36)	0.91 (0.37-2.23)
seropositivity (%)	80.9	96.8	79.1	0.13 (0.02-0.95) *	0.13 (0.02-0.95) *
DAS28-CRP	1.40 (0.34)	1.36 (0.31)	1.80 (0.36)	0.04 (0.02-0.12) *	0.04 (0.02-0.12) *
TJC	0.12 (0.33)	0.10 (0.30)	0.31 (0.47)	0.25 (0.11-0.58) *	0.25 (0.11-0.60) *
SJC	0.11 (0.32)	0.09 (0.29)	0.28 (0.46)	0.27 (0.11-0.63) *	0.28 (0.12-0.66) *
CRP	0.17 (0.18)	0.16 (0.18)	0.26 (0.23)	0.11 (0.02-0.53) *	0.08 (0.02-0.43) *
PtGA, 0-10 scale	3.3 (4.8)	2.0 (3.1)	14.1 (2.1)	0.00 (0.00-Infinity)	0.00 (0.00-Infinity)
PhGA, 0-10 scale	3.6 (5.9)	2.4 (4.5)	13.7 (7.2)	0.76 (0.70-0.83) *	0.76 (0.70-0.82) *
Pain VAS, 0-10 scale	3.7 (6.0)	2.3 (3.9)	15.6 (7.1)	0.65 (0.57-0.74) *	0.64 (0.56-0.73) *
KCL	5.5 (4.0)	5.4 (4.0)	6.0 (3.6)	0.97 (0.88-1.05)	0.95 (0.86-1.04)
GLFS-25	12.8 (13.6)	12.7 (13.5)	13.5 (14.1)	0.99 (0.97-1.02)	0.99 (0.96-1.02)
HAQ-DI	0.20 (0.44)	0.19 (0.42)	0.36 (0.50)	0.51 (0.27-0.97) *	0.46 (0.23-0.89) *

BMI: Body mass index; MTX: Methotrexate; bDMARDs: biological disease-modifying antirheumatic drugs; tsDMARDs: targeted synthetic disease-modifying antirheumatic drugs; DAS28: disease activity score with 28 joint counts; CRP: C-reactive protein; TJC: tender joint count; SJC: swollen jointcount; PtGA: patient global assessment; PhGA: physician global assessment; KCL: Kihon checklist for frailty; GLFS-25: the 25-question Geriatric Locomotive Function Scale; HAQ-DI: Health Assessment Questionnaire-Disability Index. OR: odds ratio. The adjusted model included variables (age and sex). *$p<0.05$ was considered statistically significant.

Factors associated with baseline characteristics

who achieved Boolean 1.0-2.0. The cutoff values of the factors associated with Boolean 1.0-2.0 were calculated by ROC analysis.

Results: The mean age (± standard deviation) of the 308 patients who achieved Boolean 2.0 remission criteria was 68 ± 14 years, 73% were female, disease duration was 11 ± 9 years, DAS28-CRP was 1.40 ± 0.34, Health Assessment Questionnaire-Disability Index (HAQ-DI) was 0.20 ± 0.44, and KCL was 5.0 ± 4.0 (Table 1). Adjusted for age and gender, disease duration, biological disease-modifying antirheumatic drugs (DMARDs), seropositivity, and HAQ-DI were found to be relevant factors. The the 25-question Geriatric Locomotive Function Scale (GLFS-25), a PRO assessment of physical function, and the Kihon Checklist for Frailty Assessment (KCL) were not significantly associated factors. The HAQ-DI cutoff for achieving Boolean 1.0 was 0.25 points (sensitivity, 81.4%; specificity, 40.6%: AUC, 0.619).

Conclusion: RA patients with Boolean 1.0-2.0 were characterized by long disease duration and high use of biologic DMARDs. In addition, only HAQ-DI was involved as PRO assessment.

Disclosure: M. Suzuki: None; **y. Ohashi**: None; **Y. Sobue**: None; **R. Sato**: None; **M. Maeda**: None; **H. Kosugiyama**: None; **y. Ohno**: None; **k. terabe**: None; **S. Asai**: None; **S. Imagama**: None.

Abstract Number: 0412

COVID Antibody Response to Third Dose Anti-SARS-COV2 mRNA Vaccine in Patients with Seropositive Rheumatoid Arthritis on Immunosuppressive Therapy

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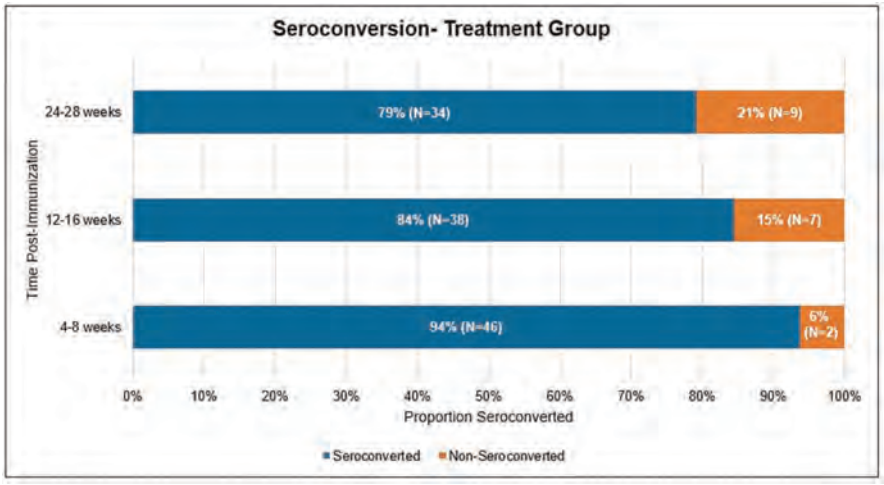
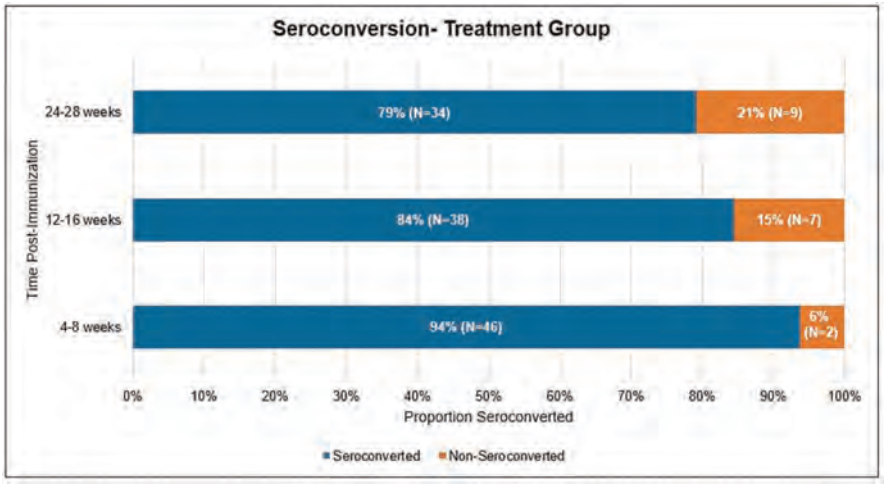
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with immune-mediated inflammatory diseases on immunosuppressive medications are presumed to be at increased risk for hospital admissions and deaths related to COVID-19 infections. The aim of this study was to better characterize seroconversion response to the third dose of COVID-19 vaccine in patients with seropositive rheumatoid arthritis (RA) on various immunosuppressive therapy classes.

Methods: A prospective cohort study recruited patients with RA on immunosuppressive treatment (n=48) to evaluate immune response to the third COVID-19 vaccine compared to the general population (n=164). Patients with RA in the study group were further characterized into three categories based on their active treatment. These groups were patients on either synthetic DMARD alone, DMARD with biologic, or biologic only. Patients received their third dose of the COVID-19 vaccine of either BNT162b2 (Pfizer) or CX-04414 (Moderna). Serum IgG antibody titers to Anti-S1 spike protein were collected in three different time frames, 4-8 weeks post-immunization (phase 1), 12-16 weeks post-immunization (phase 2), and 24-28 weeks post-immunization (phase 3). Seroconversion was defined as antibody titers above 1500 U/ml. 5 patients were lost in follow-up in the treatment group along with 79 in the control group over course of the study. Sample matching analysis was used to better compare the control and study groups.

Results: In our treatment group, 94% (n=46) of patients seroconverted in phase 1, 84% (n=38) in phase 2, and 79% (n=34) in phase 3. In the control group, 71% (n=74) of patients seroconverted in phase 1, 83% (n=85) in phase 2, and 78% (n=66) in phase 3. After sample matching analysis, patients in the treatment group showed higher rates of seroconversion compared to the control group during phase 1 ($p = 0.01$). A decrease in seroconversion rates over time was observed in both groups.





When evaluating patients on different classes of RA medications, patients on synthetic DMARDs with biologics showed lower rates of seroconversion than the other groups. All therapy classes showed decreased seroconversion rates over time.

Conclusion: Our study revealed that patients with RA demonstrated an adequate response to COVID vaccination despite being on immunosuppressive therapies. Immunogenicity decreases over time after the third COVID-19 vaccine in both immunocompromised and general populations as well as across therapy classes. Patients with RA on immunosuppressive therapies still show adequate levels of seroconversion in the early phase (phase 1) similar to the control group.

Disclosure: K. Kovuru: None; **S. Waz**: None; **A. Malik**: None.

Abstract Number: 0413

Transcriptomic Analysis of Peripheral Blood Mononuclear Cells Reveals Pain and Inflammation Specific Alterations in Difficult-to-treat Rheumatoid Arthritis

Lilla Gunkl-Tóth[1], Gábor Sütő[2], Gábor Kumánovics[3], József Kun[4], Péter Urbán[5], Attila Gyenesei[5], Panna Királyhidi[6], Georg Schett[7], György Nagy[8] and Zsuzsanna Helyes[9], [1]Department of Pharmacology and Pharmacotherapy, University of Pécs, Hungary; Eötvös Loránd Research Network, University of Pécs, Chronic Pain Research Group, Budapest, Hungary, [2]Second Department of Medicine and Nephrology-Diabetes Centre, University of Pécs, Pécs, Hungary, [3]Department of Rheumatology and Immunology, Medical School, University of Pécs, Pécs, Hungary, [4]Department of Pharmacology and Pharmacotherapy, Medical School, University of Pécs, Pécs, Hungary; Bioinformatics Research Group, Genomics and Bioinformatics Core Facility, Szentágothai Research Centre, University of Pécs, Budapest, Hungary, [5]Bioinformatics Research Group, Genomics and Bioinformatics Core Facility, Szentágothai Research Centre, University of Pécs, Pécs, Hungary, Pécs, Hungary, [6]Department of Genetics, Cell- and Immunobiology, Semmelweis University School of Medicine, Budapest, Hungary, [7]Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany, [8]Department of Rheumatology and Clinical Immunology, Semmelweis University School of Medicine; Department of Genetics, Cell and Immunobiology, Semmelweis University, Budapest, Hungary; Heart and Vascular Centre, Semmelweis University, Budapest, Hungary, [9]Department of Pharmacology and Pharmacotherapy, Medical School, University of Pécs, Pécs, Hungary; Eötvös Loránd Research Network, University of Pécs, Chronic Pain Research Group, Pécs, Hungary; National Laboratory for Drug Research and Development, Pécs, Hungary

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite novel treatment strategies in rheumatoid arthritis (RA), approximately 20-30% of patients remain symptomatic. The EULAR definition of difficult-to-treat (D2T) RA has recently been published with significant contributions from our research group (1).Many causes can lead to D2T RA, such as degenerative alterations, psychosocial factors like stress and depression, and central nervous system (CNS) dysfunction, including neuroinflammation and subsequent central pain sensitization. Recent literature suggests that peripheral blood mononuclear cells (PBMCs) can reflect the pathophysiological mechanisms of the CNS. Our main goal was to compare the transcriptomic profiles of PBMCs from D2T RA patients and healthy controls (HC) to identify differences in molecules and signaling pathways to reveal the connection between pain and inflammation.

Methods: This study has been conducted in two centers. 14 D2T RA patients, meeting the 2021 EULAR definition for D2T RA, and 11 HCs were included in Pécs, and 34 D2T RA patients and 20 HCs in Budapest, the data analysis for this group is currently under evaluation. Patients were divided into different subgroups based on their inflammatory and pain parameters. Transcriptomic analysis was performed using total RNA isolated from PBMCs through next-generation sequencing, and the results were evaluated using bioinformatics tools. A clinical examination, including psychology and fMRI experiments, was also conducted.

Results: D2T RA patients exhibited several differentially expressed genes compared to HCs, primarily involved in immune cell migration, activation, cytokine- and chemokine-mediated signaling, and neuronal regulation. Thus far, we have identified 35 upregulated genes, including interleukin 15 (IL-15) and chemokine receptor 2 (CCR2), playing an essential role in maintaining inflammation, and Sortilin1, contributing to neuropathic pain. 28 downregulated genes were found, e.g. tumor necrosis factor alpha-induced protein 3, which controls inflammatory responses. Compared to those with high inflammation and low pain, the subgroup of D2T RA patients with high inflammation and high pain exhibited significant differences in their transcriptomic profiles, particularly in the involvement of Type I Interferon and Interferon-β response. The results of the D2T RA subgroup with high pain and low inflammatory parameters revealed potential pain-related genes, such as the cholesterol-phospholipid efflux protein ABCA1 and EIF2AK2 encoding a serine/threonine kinase. Clinical and fMRI results and their correlation with the transcriptomic data are currently under evaluation.

Conclusion: Our analysis revealed many differences in the transcriptomic profiles of different subgroups of D2T RA patients and HCs. Therefore, PBMC transcriptomics proved to be a useful tool for identifying differentially expressed genes associated with pathophysiological mechanisms involved in inflammatory processes and pain sensitization. Confirming hypotheses generated with this unbiased omics approach can facilitate the development of novel therapies.

(1) Nagy G et al. EULAR definition of difficult-to-treat rheumatoid arthritis *Ann Rheum* Dis 2021;80:31-35.

Disclosure: L. Gunkl-Tóth: None; **G. Sütő**: None; **G. Kumánovics**: None; **J. Kun**: None; **P. Urbán**: None; **A. Gyenesei**: None; **P. Királyhidi**: None; **G. Schett**: None; **G. Nagy**: None; **Z. Helyes**: None.

Abstract Number: 0414

Association of a Treat-to-Target Management Approach with Physician and Patient Reported Outcomes Among Real - World Patients with Rheumatoid Arthritis Receiving Advanced Therapy in Europe

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune disease affecting the joints, causing swelling, stiffness, and pain that impact a patient's quality of life. EULAR treatment guidelines suggest using treat-to-target (T2T) for optimal management of RA patients[1] with evidence that T2T is effective when used with advanced therapies (AT)[2]. The clinical benefits of T2T are well studied but evidence for T2T's impact on patient reported outcomes (PROs) is limited. This study aimed to assess the association between T2T, and PROs and clinician reported outcomes (CROs) for RA patients on AT in real world clinical practice.

Methods: Data were sourced from the Adelphi RA XIII Disease Specific Programme™, a cross-sectional survey with retrospective data collection of rheumatologists and their RA patients in France, Germany, Italy, Spain, and the United Kingdom from June 2021 - February 2022. Physicians reported whether a patient was currently on a T2T approach or not. Sensitivity analyses were conducted with T2T defined more stringently, by including patient T2T goals (remission/low disease activity) and consultation frequency (e.g. ≥3 or 4 in the last 12 months) in the definition. PROs were collected through the EQ-5D-5L, EQ-VAS, Health Assessment Questionnaire Disability Index (HAQ-DI) and Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F). CROs included physician perceived disease activity (DAS28 scores: remission = < 2.6; low = 2.6–3.2; moderate = 3.3–5.1; high = >5.1), pain and fatigue (none, mild, moderate, or severe). Multivariate regressions (linear regressions for continuous, ordered logistic regressions for ordinal outcomes) were conducted to assess the impact of T2T on PROs and CROs amongst AT patients. The model was adjusted for age, sex, body mass index, Charlson comorbidity index and physician perceived disease severity at diagnosis.

Results: A total of 971 RA patients were receiving AT at the time of data collection of which 610 (63%) were currently following a T2T approach, of these 72% were female vs 65% who were not on T2T, 90% were white/Caucasian vs 86% and mean (standard deviation) age was 50.6 (12.5) vs 53.1 (13.5) years old, respectively. A T2T approach was associated with significantly higher (better) EQ-5D-5L, EQ-VAS, and FACIT-F scores and lower (better) HAQ-DI scores. Patients on T2T experienced problems with activities of daily living less than patients not on T2T (Table 1). T2T was also associated with significantly greater odds of patients being in physician perceived remission and having no pain (Table 2). Despite the association with better FACIT-F scores, T2T was not significantly associated with less physician perceived fatigue.

Conclusion: T2T in RA was associated with significantly better PROs such as overall and domain scores for EQ-5D-5L, HAQ-DI, and FACIT-F. Patients on T2T reported a greater likelihood of being able to conduct daily activities without difficulties or problems compared to those not on T2T. T2T was also associated with better CROs such as remission and no pain.

Table 1: Associated Impact of T2T on Patient Reported Outcomes

PRO		Expected change associated with T2T	Margin Interpretation (On T2T compared to not on T2T)	p-value
EQ- 5D-5L Utility score[1] (n=324)		0.09	Patients on T2T reported 0.09 points higher EQ-5D-5L scores than patients not on T2T	0.001
EQ-VAS[2] (n=325)		9.32	Patients on T2T reported 9.32 points higher EQ-5D VAS scores than patients not on T2T	0.015
HAQ-DI[3] (n=326)		-0.20	Patients on T2T reported -0.20 points lower disability scores than patients not on T2T	0.022
FACIT-F[4] (n=330)		3.18	Patients on T2T reported lower fatigue (3.18 higher FACIT scores) than patients not on T2T	0.033
		Odds Ratio associated with T2T		**p-value**
EQ-5D-5L Domains*	**Mobility** (n=329): (no problems walking)	3.90	Patients on T2T were 32% less likely to have any problems walking	<0.0001
	Self-Care (n=331): (no problems washing or dressing themselves)	3.08	Patients on T2T were 25% less likely to have any problems washing or dressing themselves	0.002
	Usual Activities (n=330) (no problems doing their usual activities)	2.90	Patients on T2T were 25% less likely to have any problems doing their usual activities	0.001
	Pain/discomfort (n=332) (no pain/discomfort)	2.39	Patients on T2T were 17% less likely to have any pain/discomfort	0.004
HAQ-DI Domains†	**Shampoo your hair** (n=327) (without any difficulty)	2.93	Patients on T2T were 23% less likely to report difficulties with shampooing their hair than patients not on T2T	0.001
	Climb up 5 steps (n=330) (without any difficulty)	2.38	Patients on T2T were 20% less likely to report difficulty with climbing steps than patients not on T2T	0.006
	Wash and dry your body (n=332) (without any difficulty)	2.87	Patients on T2T were 21% less likely to report difficulty with washing/drying their body than patients not on T2T	0.002
	Take a tub bath (n=318) (without any difficulty)	2.24	Patients on T2T were 16% less likely to report difficulty with taking a tub bath than patients not on T2T	0.030
	Get on and off the toilet (n=331) (without any difficulty)	2.18	Patients on T2T were 16% less likely to report difficulty with taking a tub bath than patients not on T2T	0.031
	Open car doors (n=332) (without any difficulty)	2.94	Patients on T2T were 22% less likely to report difficulty with opening car doors than patients not on T2T	<0.0001
	Run errands and shop (n=330) (without any difficulty)	3.71	Patients on T2T were 30% less likely to report difficulty with running errands than patients not on T2T	<0.0001
	Get in and out of the car (n=330) (without any difficulty)	2.19	Patients on T2T were 17% less likely to report difficulty with running errands than patients not on T2T	0.021
	Do chores such as vacuuming and yard work (n = 325) (without any difficulty)	2.08	Patients on T2T were 18% less likely to report difficulty with running errands than patients not on T2T	0.040
FACIT-F Domains‡	**I feel fatigued** (n = 328) (not at all)	2.04	Patients on T2T were 17% less likely to report feeling fatigued than patients not on T2T	0.021
	I feel weak all over (n = 328) (not at all)	1.90	Patients on T2T were 16% less likely to report feeling weak all over than patients not on T2T	0.014
	I need help doing my usual activities (n = 330) (not at all)	2.12	Patients on T2T were 18% less likely to report needing help with their usual activities than patients not on T2T	0.016
	I am frustrated by being too tired to do the things I want to do (n=329) (not at all)	2.39	Patients on T2T were 21% less likely to report being frustrated at being too tired than patients not on T2T	0.004
	I have to limit my social activity because I am tired (n=331) (not at all)	2.48	Patients on T2T were 22% less likely to report having to limit social activity due to tiredness than patients not on T2T	0.007

Only PRO domains with best outcomes and significant values included. PRO key (range): Range in brackets indicates for each PRO whether a higher or lower score is a better outcome for patients 1EQ-5D-5L utility score – Germany Tariff (0.0-1.0)=higher; 2EQ-VAS (1.0-100.0)=higher; 3HAQ-DI (0.0-3.0)=lower; 4FACIT-F (0.0-52.0)=higher. Margin outputs are calculated using the regression equation and are the predictions for each group if all other covariates are at their mean value. Margin outputs were calculated for patients on T2T and those not on T2T and the difference has been reported. Odds ratio >1 shows the patient on T2T is more likely to have the outcome = 1 (positive outcome). PRO domain model outcomes: *EQ-5D-5L: 0 = I have problems' (includes 'Slight problems', 'Moderate problems', 'Severe problems', 'Unable to do') 1 = 'I have no problems'. †HAQ-DI: 0 = With difficulty (includes 'With some difficulty', 'With much difficulty' and 'Unable to do'), 1 = 'Without any difficulty'. ‡FACIT-Fatigue: 0 = Presence of fatigue ('Includes a little bit', 'Somewhat', 'Quite a bit' and 'Very much'), 1 – 'Not at all'.

Table 2: Associated Impact of T2T on Physician Perceived Clinical Status

	Odds Ratio associated with T2T	Margin Interpretation (On T2T compared to not on T2T)	p-value
Physician Perceived DAS-28 Remission (n = 971)	1.48	Patient on T2T were 10% more likely to be in remission than patients not on T2T	0.024
Physician Perceived No Current Pain (n = 971)	1.63	Patient on T2T were 11% more likely to have no current pain than patients not on T2T	0.004
Physician Perceived No Current Fatigue (n = 971)	1.15	Patient on T2T were 4% more likely to have no current fatigue than patients not on T2T	0.351

Odds ratio >1 shows the patient on T2T is more likely to have the outcome = 1 (positive outcome). Margin outputs are calculated are calculated from the regression equation seeing the change in outcome for each treatment, while all other covariates are taken as their mean value

References:

1. Smolen J. et al., Ann. Rheum. Dis 2020;79:685-699.
2. Lampropoulos C. et al., Clin Exp Rheumatol. 2017;35(2):192-200.

Disclosure: D. White: AbbVie, 2, 6, Novartis, 1, 2; **A. Kadakia**: AbbVie/Abbott, 3, 11; **O. Howell**: AbbVie/Abbott, 2, Adelphi Real World, 3; **S. Strengholt**: AbbVie/Abbott, 3, 11; **E. Goddard**: AbbVie/Abbott, 2, Adelphi Real World, 3; **S. Barlow**: AbbVie/Abbott, 2, Adelphi Real World, 3; **T. Takeuchi**: AbbVie, 2, 5, 6, AYUMI, 5, Bristol-Myers Squibb, 6, Chugai, 2, 5, 6, Daiichi Sankyo, 5, Eisai, 5, 6, Eli Lilly Japan, 2, 6, Gilead, 2, 6, Janssen, 6, Mitsubishi-Tanabe, 2, 5, 6, ONO, 5, Pfizer Japan, 6, Taiho, 2.

Abstract Number: 0415

Serious Infections Hospital Admissions and Mortality in Patients with Early Inflammatory Arthritis: Results from a Large UK Cohort

Maryam Adas[1], Bechman Katie[1], Mark Russell[1], Ioasaf Karafotias[1], Deepak Nagra[1], Sam Norton[1], Mark Garton[2] and James Galloway[1], [1]King's College London, London, United Kingdom, [2]The Shrewsbury and Telford hospital NHS trust, Shropshire, United Kingdom

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: To identify risk of serious infections (SI) according to initial treatment strategy, using conventional synthetic disease modifying anti-rheumatic drugs (csDMARD) and corticosteroids, in patients recruited to the National Early Inflammatory Arthritis Audit.

Methods: An observational cohort study design was used. Population included adults in England with new diagnosis of rheumatoid arthritis (RA), all fulfilling ACR/EULAR 2010 criteria, between April 2018-March 2021. Outcome studied was SI defined by infections requiring hospitalisation (primary admission reason/ nosocomial acquisition) or death (SI stated on death certificate), identified using UK National Health Services (NHS) Digital linkage. Hazard ratios were calculated using single failure Cox proportional hazards models, with confounders adjusted models (age, gender, smoking status, comorbidities, social deprivation) and fully adjusted models included disease factors (seropositivity, 28-joint disease activity score/ DAS28). Individuals were considered at risk from date of RA diagnosis and censored at SI event, death, or March 2021 (whichever was earlier).

Results: 20,060 patients with RA were included. Initial DMARD therapy was known for 19,572 patients, of which 11,966 on MTX based strategy, 2789 on csDMARDs combination strategy and 15,319 on corticosteroids. Baseline characteristics categorized by starting (MTX) strategy were: Mean age was 59.6 (+/-15); 62% were female. Smoking status: 20% current; 30% ex-smokers. Comorbidities: 21% hypertension; 9% diabetes; and 10% lung disease. Rheumatoid Factor/CCP antibodies were positive in 69%. At presentation, median scores were 5.1 (interquartile range IQR: 4.3-6.0) for DAS28, 1.1 (IQR: 0.6-1.7) for health assessment questionnaire (HAQ) and 23 (IQR: 16.0-23.0) for musculoskeletal health questionnaire (MSKHQ). There were 519 SI admissions and 17 SI deaths, corresponding to incidence rates per 100 person-years for admissions: 3.19 [95% CI: 2.93-3.48] and deaths: 0.10 [95% CI: 0.06-0.16]. In fully adjusted models, increasing age predicted both SI admissions and deaths. Being a smoker, having comorbidly (i.e diabetes mellitus, lung disease), disease

activity, symptom burden measured by MSKHQ and disability by HAQ all associated with SI admission. For each 1 unit increase in DAS28, the risk of SI increased by 8% (hazards ratio HR 1.08 [95% CI:1.01-1.16]). Seropositivity did not associate with SI. Methotrexate based strategies 0.75 [95% CI:0.62-0.91] and csDMARDs combination therapy 0.7 [95% CI:0.53-0.94] were significantly related to lower SI admissions. In unadjusted models, corticosteroid was associated with higher SI admissions 1.29 [95% CI:1.10 -1.62], but in fully adjusted model association was no longer significant. csDMARDs strategies were not significantly associated with SI deaths in any of the models.

Conclusion: Patient and disease factors at diagnosis appear to an important predictor of SI. Infection risk appears to be greatest in those with higher RA disease activity. An important limitation is that NEIAA registry does capture data on treatment changes over time and steroids data beyond baseline.

Disclosure: M. Adas: None; **B. Katie**: None; **M. Russell**: Eli Lilly, 6, Janssen, 6; **I. Karafotias**: None; **D. Nagra**: AbbVie/Abbott, 6; **S. Norton**: Janssen, 6, Pfizer, 6; **M. Garton**: None; **J. Galloway**: AbbVie, 2, 5, 6, AstraZeneca, 5, Biogen, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0416

Association Between Sleep Disorders and Rheumatoid Arthritis: A Population-based Cohort Study

Rakesh Kumar[1], Edward Lovering[1], Chanakya Kodishala[2], Sara Achenbach[3], Diego Carvalho[1], Cynthia Crowson[1], John Davis[1] and Elena Myasoedova[1], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic Rochester Minnesota, Rochester, MN, [3]Mayo Clinic, Rochester, MN, Rochester, MN

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Some sleep disorders (SD) are more prevalent in patients with chronic inflammatory diseases, such as Rheumatoid Arthritis (RA). However, most of the research has focused on obstructive sleep apnea (OSA), and less is known about other SD (i.e., insomnia, restless legs syndrome [RLS]). The incidence of SD over time is also not well understood. Therefore, we aimed to examine the incidence of sleep disorders in patients with RA vs comparators without RA over time and by serologic status.

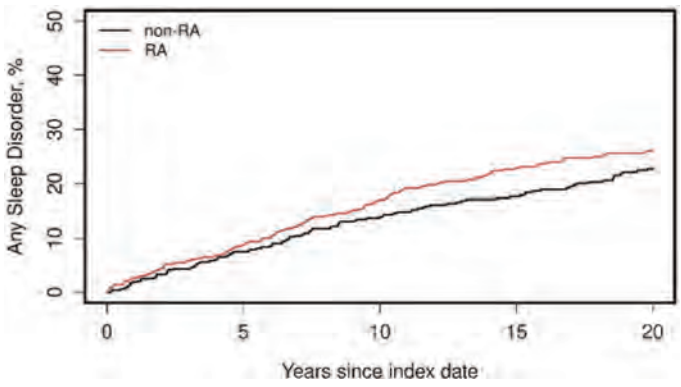

Figure 1. Cumulative incidence of sleep disorders in patients with incident RA in 1980-2009 vs non-RA comparators

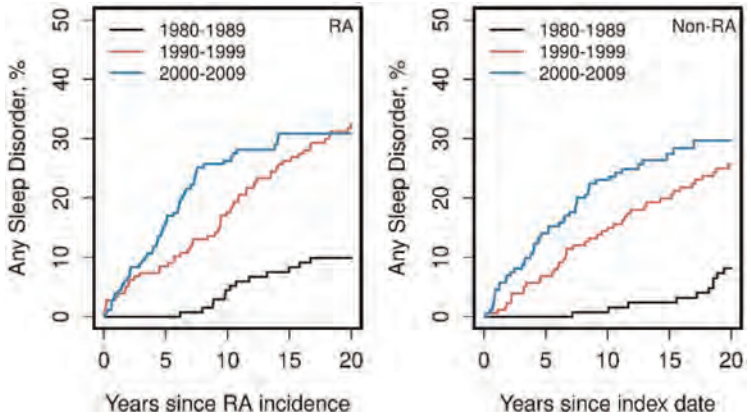

Figure 2. Cumulative incidence of sleep disorders in patients with incident RA in 1980-2009 vs non-RA comparators by decade

Methods: This retrospective population-based cohort study included residents of a geographically defined area, aged ≥50 years when they met 1987 ACR criteria for incident RA in 1980-2009. All these patients were followed until death/ migration or 12/31/2021 and matched 1:1 on age, sex, and calendar year with non-RA comparators. SD were identified based on two ICD 9/10-CM codes and data were abstracted via manual record review. Demographics, medical comorbidities, laboratory data on RA characteristics were collected. We investigated the association between RA and sleep disorders by using Cox models, adjusting for age and sex. P-value < 0.05 was considered significant. All analyses were performed using SAS version 9.4.

Results: A total of 573 patients with RA were studied (mean age 65.5 ±10.3 years, 66% female, 95% White, mean body mass index 28.1 ±6.1 kg/m^2; 62% RF/Anti-CCP positive) along with 573 matched non-RA comparators. At RA incidence/ index date, there were no differences in the prevalence of any SD in patients with RA vs non-RA controls (13% vs 14%, respectively) and by SD subtype: insomnia (6% vs 6%), OSA (7% vs 7%), RLS (2% vs 2%). During a median follow-up of 13.9 years in the RA cohort and 15.1 years in the non-RA cohort, SD developed in 129 patients with and 113 patients without RA. RA patients experienced a borderline increased risk for any SD (age- and sex-adjusted hazard ratio:1.29; 95% CI: 1.00-1.66, p=0.05) (Figure 1). The most common types of SD were OSA and insomnia.

When comparing seropositive and seronegative patients with RA, there was no difference in the development of any SD (HR: 1.17; 0.82-1.67) or OSA (HR: 0.95; 95% CI: 0.59-1.54). However, seronegative patients were more likely to develop insomnia than seropositive patients (HR: 1.81; 95% CI: 1.09-3.03). This association persisted after adjusting for age, sex, smoking and obesity (HR 1.94, 95%CI 1.16-3.27). In addition, the incidence/diagnosis rate of SD increased over time by decade of RA incidence/index date (i.e., 1980-1989, 1990-1999, and 2000-2009) in both cohorts (Figure 2), and this association persisted even adjusting for age, sex, smoking status and obesity.

Conclusion: Our study findings indicate that RA patients tend to experience an increased risk for any SD after the index date. Patients with seronegative RA had significantly higher risk of insomnia compared to seropositive RA patients. The increased incidence rate of SD by decade of RA incidence/ index, likely reflects higher awareness and improved recognition of SD in more recent years. Further research is ongoing by our group to understand the underlying mechanisms for these associations, in order to inform preventive and management options for SD in patients with RA.

Disclosure: R. Kumar: None; **E. Lovering**: None; **C. Kodishala**: None; **S. Achenbach**: None; **D. Carvalho**: None; **C. Crowson**: None; **J. Davis**: Girihlet, 9, Pfizer, 5, Remission Medical, 9; **E. Myasoedova**: None.

Abstract Number: 0417

The Role of Rheumatoid Arthritis Flare in the Risk of Alzheimer's Disease and Related Dementias: A Population-based Cohort Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) have increased risk for Alzheimer's disease and related dementias (AD/ADRD). Recent studies have reported an association between RA disease activity and risk of AD/ADRD, suggesting that inflammation can be an important contributor to this association. It is unknown whether having more RA flares or spending more time in RA flare increases the risk of AD/ADRD incidence. We examined the role of RA flare and remission on the risk of AD/ADRD.

Methods: This population-based study was conducted on an inception cohort of patients with RA who were residents of a geographic area and aged ≥50 years when they met 1987 American College of Rheumatology criteria for RA in 1980-2014 with follow up until 12/31/2019. Flare/remission status was obtained via medical record review. A worsening of disease status requiring initiation/escalation of therapy or a documentation such as 'flare up', 'ongoing' and 'active' in the medical records was considered a 'RA flare'. While remission was defined as absence of disease activity based on documentation such as 'remission', 'quiescent', 'no activity', or swollen and tender joints (≤1) along with normal inflammatory markers. Visits not classified as flare or remission were counted as intermediate activity. Flares were considered to start on the first date they were documented and to resolve halfway to the next visit where the status was changed (definition 1). In definition 2, 'acute flares' were defined to last ≤6 weeks and patients were considered to have intermediate activity from the 6 week point until the next clinical visit. Incident dementia was defined by presence of two ICD9/10 codes for AD/ADRD at least 30 days apart. Cox models with time-dependent covariates were used to assess the association of RA flares with AD/ADRD, adjusting for age, sex and year of RA.

Results: The study included 771 patients with RA (mean age 65.1 years, 65.4% females). During median follow up of 7.7 years, 77 (10%) patients developed AD/ADRD. During a total of 11,085 medical visits (12 median visits per patient), patients were flaring at 3,608 (32.5%) visits and were in remission at 2,631 (23.6%) visits. Median total duration of time spent in RA flare was 46.4 weeks (IQR: 12.9-137.4). Using definition 1, we found no evidence of a higher risk of incident AD/ADRD when in a RA flare vs remission (HR 1.10; 95% CI: 0.63-1.89). Using definition 2, RA flare was associated with a 2-fold higher risk of AD/ADRD (HR 2.00; 95% CI: 0.93-4.27), but this association did not reach statistical significance. When we examined cumulative time spent in each active flare (using either definition of flare) and intermediate activity, we observed a non-

Table: Association between RA flare and time spent in a flare with incident Alzheimer's disease and related dementias.

	Definition 1	Definition 2
Model 1	Hazard Ratio(95% Confidence Interval)	Hazard Ratio (95% Confidence Interval)
Active flare	1.10 (0.63-1.89)	2.00 (0.93-4.27)
Model 2		
Time spent in active flare (per 1 year increase)	1.03 (0.96-1.10)	1.10 (0.97-1.24)
Time spent in intermediate activity (per 1 year increase)	1.05 (0.98-1.12)	1.03 (0.97-1.10)
Remission	1.00 Reference	1.00 Reference

significant trend towards increased risk (3-5% per year time spent in active flare or intermediate activity) of incident AD/ADRD compared to time spent in a state of remission (Table).

Conclusion: Our findings indicate that flares of RA disease activity are common and may have a detrimental effect on cognitive status. More studies are needed to understand the mechanisms underlying the association between RA and AD/ADRD, and whether tight control of inflammation and improved flare management in patients with RA may confer long term cognitive benefits.

Disclosure: C. Kodishala: None; **T. Gunderson**: None; **E. Lovering**: None; **R. Kumar**: None; **C. Crowson**: None; **J. Davis**: Girihlet, 9, Pfizer, 5, Remission Medical, 9; **E. Myasoedova**: None.

Abstract Number: 0418

Synovial Fluid Cell Counts Associated with Joint Histopathology in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: While analysis of synovial fluid white blood cell counts (WBCs) is performed in clinical practice for diagnosing septic arthritis and differentiating noninflammatory from inflammatory forms of arthritis, the connection between features of paired synovial fluid and tissue has not been explored. This study seeks to explore the relationship between paired synovial fluid cell counts, synovial histopathology, clinical features, and disease activity.

Methods: Patients meeting ACR/EULAR 1987 and/or 2010 rheumatoid arthritis (RA) classification criteria were recruited prior to elective total knee arthroplasty. All patients provided written informed consent (HSS IRB # 2014-233). Demographics, RA patient reported outcome measures (PROMs), tender and swollen joints, ESR, CRP, RF, and CCP were collected. Synovial fluid was obtained via arthrocentesis performed immediately before surgery. Absolute and differential cell counts were performed, and synovial histopathology using hematoxylin and eosin (H&E) was performed on tissue. An expert musculoskeletal pathologist scored 14 synovial histologic findings: synovial lymphocytic inflammation, mucoid change, fibrosis, fibrin, germinal centers, lining hyperplasia, polymorphonuclear neutrophils (PMNs), detritus, plasma cells, binucleated plasma cells, Russell bodies, sub-lining giant cells, synovial lining giant cells, and mast cells (available at www.hss.edu/pathology-synovitis). Relationships between synovial fluid and tissue data were measured with Pearson's correlations.

Results: We included 25 patients. Mean age = 68.12 years, mean disease duration = 16.25 years, indicating longstanding disease, mean DAS28-ESR = 4.86 indicating moderate disease activity. Further characteristics of the cohort divided by noninflammatory vs inflammatory synovial fluid (WBC threshold of 2000 cells/microL) are included (Table 1). Synovial fluid WBC was positively correlated with synovial lymphocytic inflammation (SLI), neutrophil infiltration, CRP, and ESR. Of the other synovial histologic features, mucoid degeneration approached significance. Percentage of PMNs in the synovial fluid was positively correlated with PMN infiltration. Percentage of monocytes in the synovial fluid was negatively correlated with PMN infiltration and SLI. Synovial fluid total WBC had no significant correlation with disease activity or PROMs in our cohort. Overview of correlations with associated statistical values included (Table 2, Table 3).

Table 1: Clinical and Histopathologic Characteristics Stratified by Synovial Fluid WBC

	Total (N=25)	WBC<2000 (n=14)	WBC>2000 (n=11)	p – Value*
Demographics and Clinical Features				
Age in years[1]	68.12 (9.7)	68.22 (9.17)	67.98 (10.79)	0.95
Years since diagnosis[1]	15.62 (17.01)	18.53 (20.02)	11.93 (12.1)	0.3
Sex, Female[2]	24 (96%)	14 (100%)	10 (90.9%)	-
RF, Positive[2]	14 (56%)	6 (42.9%)	8 (72.7%)	0.15
CCP, Positive[2]	18 (72%)	9 (64.3%)	9 (81.8%)	0.35
ESR mm/hr[1]	40 (28)	**30 (23)**	**53 (30)**	**0.03**
CRP mg/dL[1]	2.0 (3.0)	**0.6 (0.6)**	**3.7 (3.9)**	**0.008**
DAS28-ESR[1]	5.0 (1.3)	4.9 (1.4)	5.2 (1.1)	0.56
DAS28-CRP[1]	4.3 (1.2)	4.2 (1.4)	4.5 (1.0)	0.53
CDAI[1]	20 (10)	21 (9)	19 (11)	0.55
Synovial Fluid Absolute Cell Count				
WBC Cells/μL[1]	8077 (11,577)	490 (492)	17734 (11756)	-
Synovial Fluid Differential Cell Count				
Polys(%)[1]	55 (26)	35 (25)	68 (19)	**0.002**
Monos(%)[1]	18 (11)	25 (10)	13 (9)	**0.0032**
Lymphs(%)[1]	26 (20)	37 (21)	19 (18)	**0.03**
Synovial Tissue Lymphocytic Inflammation[2] (SLI) n=24				**<0.0001**
None	7 (29.2%)	**7 (53.8%)**	**0 (0%)**	-
Mild	1 (4.2%)	**0 (0%)**	**1 (0.91%)**	-
Moderate	3 (12.5%)	**3 (23.1%)**	**0 (0%)**	-
Marked	7 (29.2%)	**3 (23.1%)**	**4 (36.3%)**	-
Band-like	6 (25%)	**0 (0%)**	**6 (54.5%)**	-
PMN Tissue Infiltration[2] n=24				**<0.0001**
None	10 (41.7%)	**10 (76.9%)**	**0 (0%)**	-
Interstitial	11 (45.8%)	**3 (23.1%)**	**8 (72.7%)**	-
Marked	3 (12.5%)	**0 (0%)**	**3 (27.3%)**	-

1 = mean (SD) 2 = n(%) *Between groups p-value calculated using t-test. RF = rheumatoid factor; CCP = cyclic citrullinated protein; ESR = erythrocyte sedimentation rate; CRP = C Reactive Protein; DAS28 = disease activity score using 28 joints; CDAI = clinical disease activity index; WBC = absolute white blood cell count; Polys% = percentage white blood cells in synovial fluid that are polymorphonuclear neutrophils; Monos% = percentage white blood cells in synovial fluid that are monocytes; Lymphs(%) = percentage white blood cells in synovial fluid that are lymphocytes; PMN = polymorphonuclear neutrophils; Bolded values significant p<0.05

Table 2: Correlations between synovial fluid, synovial histopathology, and blood inflammatory markers using Pearson's Correlation

Absolute Synovial Cell Count			
Variable 1	Variable 2	Adjusted R^2	p - Value
WBC	SLI	0.505	**0.001**
WBC	PMN tissue Infiltration	0.299	**0.009**
WBC	Mucoid Degeneration	0.183	0.01
WBC	CRP	0.338	**0.003**
WBC	ESR	0.238	**0.01**
Differential Synovial Cell Count			
%Polys	Neutrophil tissue infiltration	0.349	**0.02**
%Monos	Neutrophil tissue infiltration	0.294 [Negative Correlation]	**0.03**
%Monos	SLI	0.357 [Negative Correlation]	**0.04**

Table 3: Correlations between synovial fluid WBC and PROMs/disease activity using Pearson's Correlation

Variable 1	Variable 2	Adjusted R^2	p - Value
WBC	DAS28-CRP	0.013	0.27
WBC	DAS28-ESR	-0.013	0.41
WBC	Stiffness	-0.021	0.48
WBC	Pain	-0.035	0.65
WBC	Fatigue	-0.045	0.82
WBC	CDAI	-0.043	0.93

Conclusion: Preliminary results suggest that synovial fluid characteristics are informative and correlate with inflammation in the underlying synovial tissue, but not with disease activity. CRP, present in subclinical synovitis,[1] is strongly correlated with synovial fluid WBC. Further analysis of synovial fluid might increase insight into RA pathophysiology and disease control.

References

1. Orange DE, Agius P, DiCarlo EF, et al. Histologic and Transcriptional Evidence of Subclinical Synovial Inflammation in Patients With Rheumatoid Arthritis in Clinical Remission. *Arthritis Rheumatol Hoboken NJ*. 2019;71(7):1034-1041. doi:10.1002/art.40878

Disclosure: E. Spolaore: None; **E. DiCarlo**: None; **D. Ramirez**: None; **M. Smith**: None; **A. Lakhanpal**: None; **B. Mehta**: Janssen, 1, Novartis, 5; **L. Donlin**: Bristol-Myers Squibb(BMS), 2, Stryker, 2; **S. Goodman**: NIH, 5, Novartis, 5; **D. Orange**: AstraZeneca, 2, Pfizer, 2.

Abstract Number: 0419

No Clinically Relevant Changes in Coagulation Activation Between Patients Initiating TNF-blockers versus JAK-inhibitors

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1: Progression of mean coagulation markers. * Significantly different from baseline, p < 0,05. TNF = tumor necrosis factor, JAK = Janus kinase, F1+2= prothrombin fragment 1+2, VWF= von Willebrand factor, TAT= thrombin-antithrombin complex, FIX= Factor 9, PT = prothrombin time, aPTT = activated partial thromboplastin time.

	Baseline	1 Month	3 Months	6 Months
D-dimer				
TNF	0,99	0,96	0,82	0,68*
JAK	1,05	0,88	1,34	0,88
Fibrinogen				
TNF	4,01	3,44*	3,43*	3,3*
JAK	4,01	3,61	4,03	3,52
F1+2				
TNF	290,46	303,88	317,27	285,21
JAK	290,39	269,24	319,87	289,37
VWF				
TNF	82,56	81,45	77,42	82,74
JAK	100,13	82,00	86,23	62,72
TAT				
TNF	6,81	6,89	8,06	8,06
JAK	4,19	3,54	4,05	3,51
FIX				
TNF	646,86	705,61	848,85	703,32
JAK	456,53	395,40	403,36	848,85
PT				
TNF	9,10	9,14	8,90	9,28
JAK	9,80	9,41	9,39	10,95
aPTT				
TNF	26,17	26,63	16,19	26,47
JAK	27,58	28,37	28,04	28,53

Background/Purpose: Rheumatoid arthritis (RA) is associated with a 2-fold higher risk of venous thromboembolism (VTE) compared with the general population. The immune system and hemostatic system are closely linked by a shared origin. Inflammation affects thrombotic responses by upregulating procoagulants and downregulating anticoagulants and fibrinolysis. Tumor necrosis factor (TNF), an important mediator in the inflammatory pathway, induces a disbalance between the coagulation system and fibrinolytic system, resulting in a hypercoagulable state. In addition, several studies have suggested that some Janus kinase-inhibitors (JAKi) might be associated with an increased risk for VTE. However, the underlying pathogenic mechanisms have yet to be elucidated. Our objective was to compare changes in hemostatic parameters during treatment with TNF-blockers and JAKi in RA.

Methods: Biomarkers for the coagulation system, including D-dimer, fibrinogen, PT, aPTT, F1+2, TAT, F IX and vWF, were prospectively measured in 121 consecutive RA patients: 83 patients treated with aTNF and 38 patients with JAKi. Data were collected at baseline, after 1, 3, and 6 months.

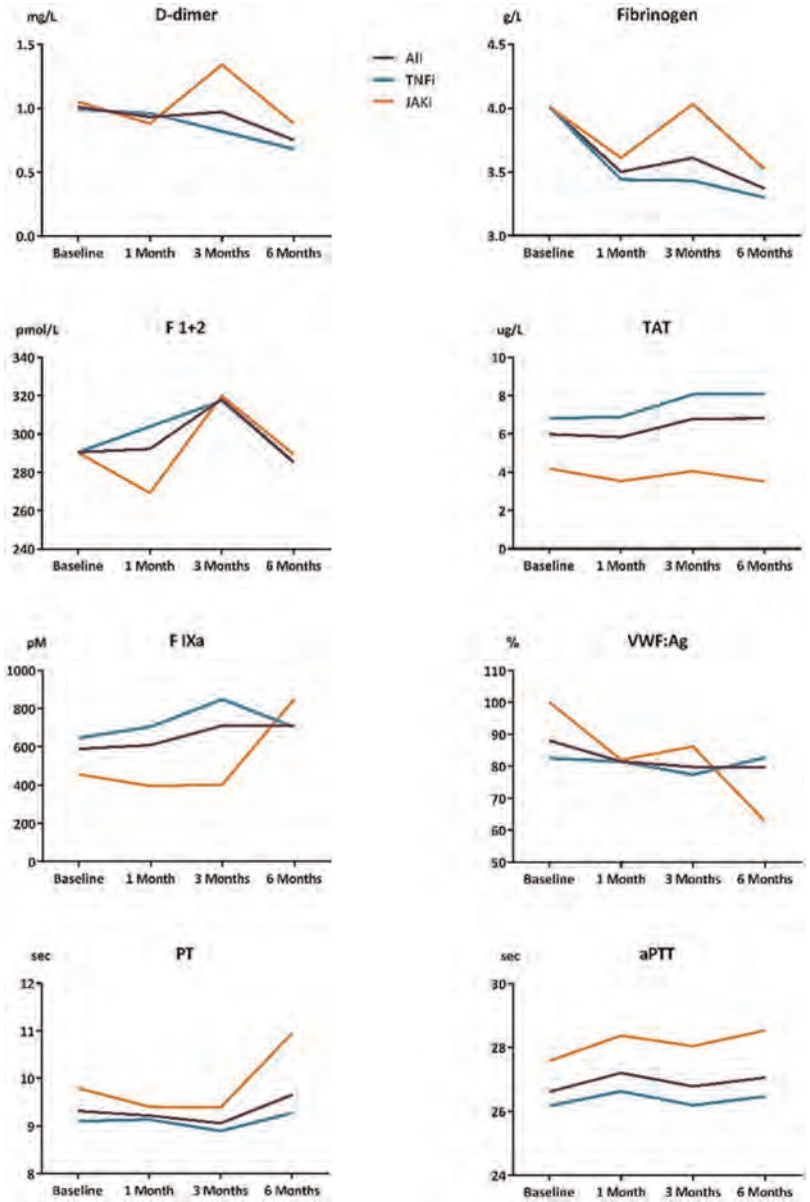

Figure 1: Progression of coagulation markers. F1+2= prothrombin fragment 1+2, VWF= von Willebrand factor, TAT= thrombin-antithrombin complex, FIX= Factor 9, PT = prothrombin time, aPTT = activated partial thromboplastin time.

Results: Mean age for all patients was 57 (±14) years, 76% were female. Mean DAS28-CRP at baseline for TNF-inhibitor group was 3.6 (±1.3) and 4.1 (±1.4) for JAKi group, steadily declining in aTNF users, while decreasing in JAKi users with an intermittent peak at 3 months. Baseline coagulation markers levels were comparable between the groups. D-dimer and vWF levels were slightly higher in the JAKi group (p = 0.30 and p = 0.08, respectively), while F IXa levels were lower (p = 0.17). D-dimer and fibrinogen levels steadily declined in the aTNF group, while fluctuating in the JAKi group, with a peak at 3 months with a subsequent decline thereafter (Figure 1). In aTNF users, TAT increased slightly during follow-up. VWF, PT and aPTT remained relatively stable, while F IXa and F 1+2 showed an increase after 3 months of follow-up, after which they returned to baseline. In JAKi users, D-dimer, fibrinogen, VWF and F 1+2 fluctuated, with a peak after 3 months and then a subsequent decline. F IX and PT initially decreased slightly but increased steadily after 6 months, while TAT and aPTT remained stable during follow-up.

Conclusion: The pro-thrombotic tendency in active RA declined during effective treatment with both aTNF as well as JAKi. A gradually decrease in D-dimer and fibrinogen was seen after 6 months of treatment. The transient increase of coagulation activation in JAKi users at three months coincided with increased disease activity. Altogether, our data suggests that an increased VTE risk in the first six months due to wither treatment aTNF or JAKi seems unlikely. Whether or not the risk increases beyond this time period remains to be investigated.

Disclosure: R. Hansildaar: None; **R. Raadsen**: None; **M. Heslinga**: None; **M. Nurmohamed**: None.

Abstract Number: 0420

Associations and Mortality Impact of Machine Learning-derived Quantitative Computed Tomography Parenchymal Lung Features in Rheumatoid Arthritis and non-RA Comparators in a Multicenter Prospective Cohort of Smokers

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Quantitative computed tomography (QCT) methods have been developed to automatically quantify parenchymal lung features on chest CT imaging. There have been limited investigations of QCT in RA participants and non-RA comparators or studies of the mortality impact of QCT features in RA. We hypothesized that RA would be associated with increased interstitial changes and emphysema, as determined by QCT. We also hypothesized that QCT scoring of interstitial and emphysematous lung changes would identify RA patients at higher mortality risk.

Methods: We investigated associations between RA and QCT features in COPDGene, a multicenter cohort study of current or former smokers that excluded participants with known interstitial lung disease or bronchiectasis. We identified participants with and without RA using RA self-report and DMARD use. We assessed the lung parenchyma in each scan using a

k-nearest neighbors classifier that categorizes regions of interest into normal lung, interstitial changes, or emphysema using the local tissue density and distance from the pleural surface. Interstitial changes were subclassified into reticular, subpleural line, linear scar, honeycombing, centrilobular nodule, nodular, and ground glass. Each feature was summed and standardized to total lung volume. We examined associations between QCT features and RA using multivariable linear regression. We dichotomized participants using the 75th percentile for each QCT feature among non-RA participants and investigated mortality associations by RA status and QCT features using Cox regression. We examined multiplicative interactions between RA and continuous interstitial and emphysema percentages and additive interactions between RA status and >75th percentile of QCT features and mortality.

Results: We analyzed 82 RA cases and 8820 non-RA comparators. RA was associated with a lower percentage of normal lung (85.8% vs. 91.0% p=0.0001), increased interstitial changes (7.0% vs. 4.8%, p< 0.0001) and no statistically significant difference in emphysema (2.6% vs. 1.9%, p=0.09) compared to non-RA comparators. In linear regression analyses adjusted for age, sex, smoking status, pack-years, and body mass index, RA was associated with increased interstitial changes (β=1.7±0.5, p=0.0008) but not emphysema (β=1.3±1.7, p=0.44). The combination of RA and >75th percentile of emphysema had significantly higher mortality compared to both non-RA participants (HR 5.86, 95%CI 3.75-9.13) and RA participants (HR 5.56, 95%CI 2.71-11.38) with < 75th percentile of emphysema. There were statistically significant interactions between RA and emphysema for mortality (multiplicative: p=0.014; additive: attributable proportion 0.53, 95%CI 0.30-0.70, p< 0.0001).

Table 1: Select demographics, lifestyle factors, pulmonary disease, and genetics of RA patients and non-RA comparators at baseline (n=8902).

	RA cases (n=82)	Non-RA comparators (n=8820)
Demographics		
Age at enrollment (years, mean, SD)	64.0 (8.7)	59.5 (9.1)
Female (n, %)	54 (65.9%)	4061 (45.9%)
White Race (n, %)	66 (79.3%)	6025 (68.3%)
Black Race (n, %)	17 (20.7%)	2795 (31.7%)
Lifestyle		
Current Smoker (n, %)	27 (32.9%)	4628 (52.5%)
Past Smoker (n, %)	55 (67.1%)	4192 (47.5%)
Pack-years (mean, SD)	42.2 (18.0)	43.9 (24.7)
BMI (kg/m^2, mean, SD)	30.0 (7.9)	28.7 (6.2)
***MUC5B* promoter variant (rs35705950) genotype**		
GG	61/76 (80.3%)	7120/8305 (85.7%)
GT	15/76 (19.7%)	1122/8305 (13.5%)
TT	0/76 (0.0%)	63/8305 (0.8%)
Chronic obstructive pulmonary disease*		
GOLD Class 0 (no COPD)	44 (53.7%)	4892/8769 (55.8%)
GOLD Class 1	3 (3.7%)	715/8769 (8.2%)
GOLD Class 2	17 (20.7%)	1651/8769 (18.8%)
GOLD Class 3	13 (15.9%)	993/8769 (11.3%)
GOLD Class 4	5 (6.1%)	518/8769 (5.9%)

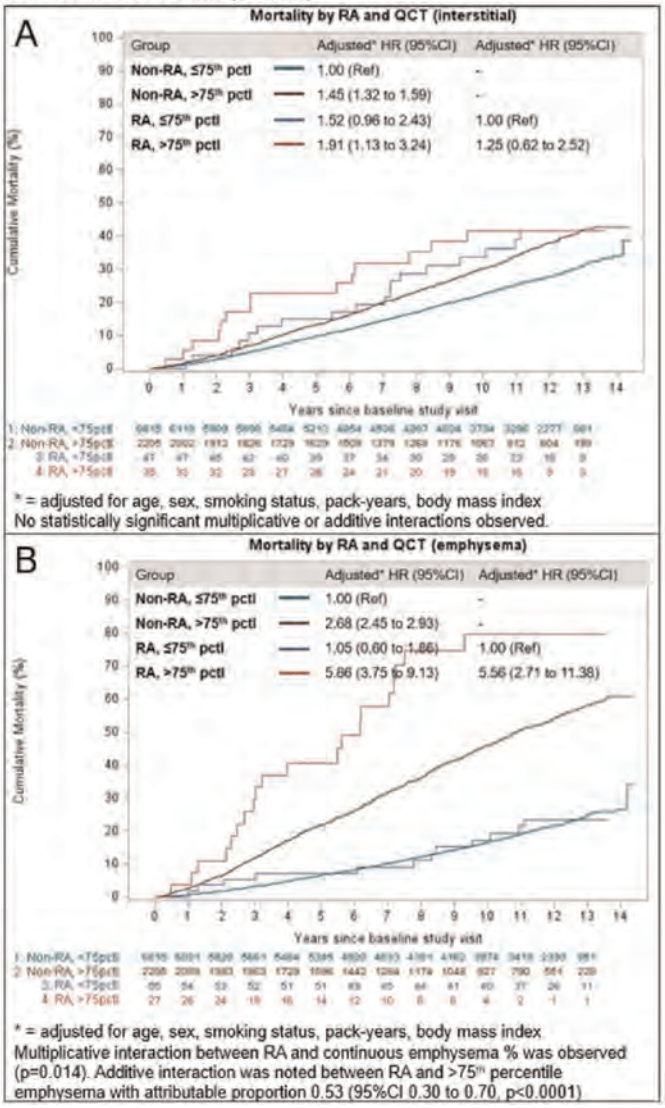
BMI = body mass index; COPD = chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease; ILA = interstitial lung abnormalities; RA = rheumatoid arthritis; SD = standard deviation; SGRQ = Saint George's Respiratory Questionnaire
* = based on GOLD 2007 classification using postbronchodilator FEV_1 and FVC

Table 2: Linear regression of quantitative CT features comparing RA patients and non-RA comparators (n=8902)

Characteristic	Unadjusted β (RA vs. non-RA)	SE	p value	Adjusted* β (RA vs. non-RA)	SE	P value
Normal	-4.67	1.87	0.01	-3.04	1.73	0.08
Interstitial	2.15	0.52	<.0001	1.71	0.51	0.0008
Reticular	1.95	0.47	<.0001	1.55	0.46	0.0008
Subpleural line	0.11	0.03	0.0005	0.08	0.03	0.009
Linear scar	0.04	0.02	0.01	0.03	0.02	0.08
Honeycombing	0.07	0.02	0.0005	0.06	0.02	0.003
Centrilobular nodule	-0.016	0.02	0.28	-0.006	0.01	0.69
Nodular	-0.013	0.04	0.70	-0.005	0.03	0.88
Ground glass	0.0002	0.02	0.99	0.002	0.02	0.93
Emphysema	2.52	1.85	0.17	1.32	1.69	0.43
Centrilobular	2.27	1.77	0.20	1.05	1.66	0.51
Panlobular	0.24	0.20	0.22	0.28	0.20	0.16

* adjusted for age, sex, smoking status (current/past), pack-years, and body mass index.

Figure: Cumulative mortality and hazard ratios stratified by RA/comparator status and < or >=75th percentile of (A) interstitial changes and (B) emphysema quantitative CT features in COPDGene (n=8902)



Conclusion: Using machine learning-derived QCT data in a cohort of smokers, we found that RA was associated with increased interstitial changes, even after adjustment for smoking and other lifestyle factors. The combination of RA and emphysema conferred greater than 5-fold increased mortality.

Disclosure: G. McDermott: None; **K. Hayashi**: None; **M. Moll**: Bayer, 5; **M. Cho**: AstraZeneca, 2, Bayer, 5, GSK, 5, Illumina, 6; **K. Yoshida**: None; **T. Doyle**: None; **G. Kinney**: None; **P. Dellaripa**: None; **Z. Wallace**: BioCryst, 2, Bristol-Myers Squibb(BMS), 5, Horizon, 1, 2, 5, MedPace, 2, Novartis, 1, PPD, 2, Sanofi, 1, 5, Shionogi, 1, Visterra, 1, 2, Zenas, 1, 2; **E. Regan**: None; **G. Hunninghake**: Boehringer-Ingelheim, 2, Chugai Pharamaceuticals, 2, Gerson Lehrman Group, 2; **E. Silverman**: Bayer, 5; **S. Ash**: Boehringer-Ingelheim, 5, Quantitative Imaging Solutions, 8, 10, Verona Pharmaceuticals, 1; **R. San Jose Estepar**: Boehringer-Ingelheim, 5, Chiesi, 6, Imbio, 9, Insmed, 5, Leuko Labs, 2, Lung Biotechnology, 5; **G. Washko**: Boehringer-Ingelheim, 5, Janssen, 2, Novartis, 2, Pulmonx, 2, Quantitative Imaging Solutions, 8, Vertex, 2; **J. Sparks**: AbbVie, 2, Amgen, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, 5, Gilead, 2, Inova Diagnostics, 2, Janssen, 2, Optum, 2, Pfizer, 2, ReCor, 2.

Abstract Number: 0421

Bioinformatics Platform to Study the Genetics of Biologic DMARD Non-responders: Design and Protocol of the RA Non-responders to Treatment (RANT) Study

Gregory McDermott[1], Mary Jeffway[1], Thany Seyok[1], Harrison Zhang[2], Kumar Dahal[1], Dana Weisenfeld[1], Margaret Vella[3], Tracy Johansson[4], Gabriela Schmajuk[5], Kaleb Michaud[6], Cassandra Perry[3], Susanne Churchill[3] and Katherine Liao[1], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [3]Harvard Medical School, Boston, MA, [4]American College of Rheumatology, Atlanta, GA, [5]UCSF / SFVA, San Francisco, CA, [6]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Although the modern RA treatment armamentarium has led to significant improvements in response rates and outcomes, some RA patients inadequately respond to multiple lines of treatment. The ability to study these "treatment refractory" RA patients is limited by small numbers of patients meeting criteria, even at high volume centers. In the cancer field, the general challenge of engaging small patient subsets for research led to the development of a novel "crowdsourced" bioinformatics research platform to recruit and study extreme outlier responses to chemotherapy from multiple sites/sources. Here we report the adaption of this novel platform to study genetic and clinical risk factors for inadequate response to multiple biologic and targeted synthetic DMARD medications (b/tsDMARDs) in RA.

Methods: RA Non-responders to Treatment (RANT) is a "crowdsourced" cohort study (target size n=300) using a bioinformatics platform investigating genetic and clinical predictors of non-response to b/tsDMARD medications. RA patients who have failed two or more b/tsDMARDs (including at least one TNF inhibitor) are eligible. A combination of traditional and

Figure 1: Study design of RANT study

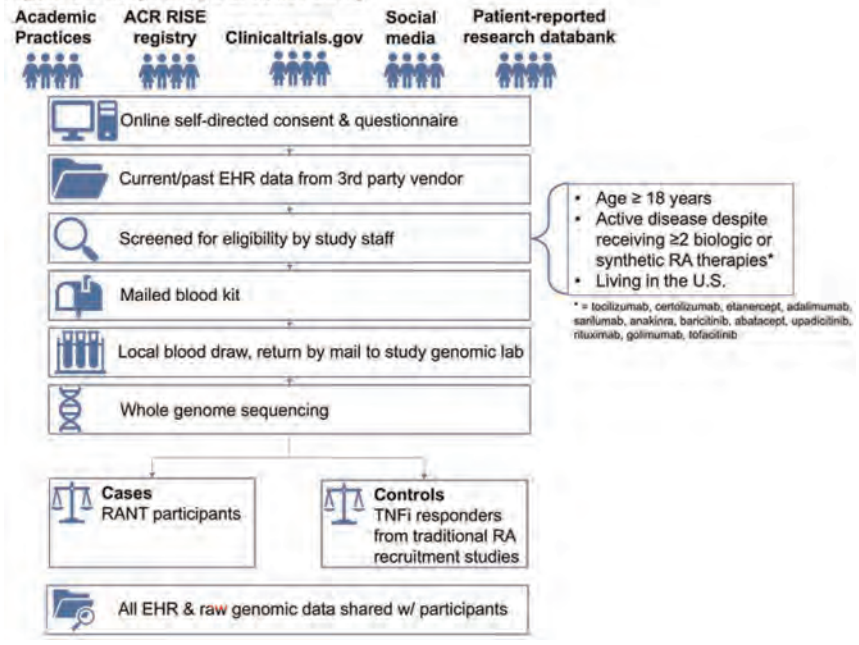


Table 1: Characteristics of RANT study participants and recruitment methods (n=107)

Characteristic	
Age at enrollment (years, mean, SD)	59.8 (12.8)
RA duration (years, mean, SD)	22.0 (12.8)
Female (n, %)	98 (91.6%)
Number of prior b/tsDMARDs (mean, SD)	5.1 (2.2)
Recruitment Method (n, %)	
FORWARD (Patient-reported research databank)	49 (45.8%)
Direct in-person clinic recruitment at academic practices	42 (39.2%)
ACR RISE	8 (7.5%)
Internet search/study website	6 (5.6%)
Clinicaltrials.gov	2 (1.9%)

ACR = American College of Rheumatology; b/tsDMARDs = biologic or targeted synthetic disease modifying antirheumatic drugs; RA = rheumatoid arthritis; SD = standard deviation

multimedia recruitment advertises the study: direct in-person clinic recruitment, dissemination of trial information to patients identified in established RA registries (ACR RISE, FORWARD), and social media publicizing the study to patients and rheumatologists via Twitter and Facebook. Study details are posted for the general public on clinicaltrials.gov.

The study process is detailed in **Figure 1**. Interested patients complete a self-directed online informed consent that includes access to electronic health records though a third-party vendor as well as RA treatment and disease status questionnaires. After study staff confirm eligibility by reviewing patient responses, patients receive a blood sample kit by mail, have blood sample tubes drawn locally, and return the kit by mail to the study genomic lab for whole genome sequencing. Clinical and genetic factors of RA treatment non-responders will be compared to established groups of RA treatment responders from established research cohorts. Patients will receive a copy of their medical records and genetic sequence data.

Results: Baseline characteristics of the first 107 recruited patients are detailed in **Table 1**. The majority were female (91.6%) with mean age 59.8 years and mean RA duration of 22 years. The mean number of b/tsDMARDs prescribed was 5.1 (SD 2.2). The most successful recruitment methods have been through an established patient-reported research databank (45.8%) and direct in-person recruitment of patients in clinic (39.2%).

Conclusion: This protocol describes a "crowdsourced" recruitment and online enrollment/consent procedures to investigate RA treatment non-responders. Similar methods may be useful for investigating rare rheumatology diseases, outcomes, or patient subsets that are difficult to reach or recruit by traditional research methods. Study results will demonstrate the feasibility of these research methods in future rheumatology research and inform the potential clinical and genetic predictors of treatment refractory RA.

Disclosure: G. McDermott: None; **M. Jeffway**: None; **T. Seyok**: None; **H. Zhang**: None; **K. Dahal**: None; **D. Weisenfeld**: None; **M. Vella**: None; **T. Johansson**: None; **G. Schmajuk**: None; **K. Michaud**: None; **C. Perry**: None; **S. Churchill**: None; **K. Liao**: UCB, 2.

Abstract Number: 0422

Electronic Health Record-Based Machine Learning Model for Predicting Disease Activity in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is one of the most prevalent chronic inflammatory diseases in which synovitis gradually leads to polyarthritis and joint destruction. Poor response to initial therapy may contribute to progressive disease activity, high costs, and side effects. Given the explosive growth in the number of electronic health records (EHRs), we constructed machine learning models to predict disease activity and assess the effectiveness of treatment prior to the actual start of treatment.

Methods: This multicenter, prognostic study included 1864 patients with RA from 5 tertiary hospitals in China. Electronic health records (EHRs) were collected from 2016 to 2021. The Peking University People's Hospital (PKUPH) cohort was used for training and internal validation. The multicenter cohort was used for external validation. Multi-dimensional variables arranged sequentially (baseline, 3 months, and 6 months after treatment), including demographic features, laboratory tests, and medication history information, were involved in machine-learning model construction. Different algorithms were selected to predict disease activity 6 months after treatment. External validation involved multicenter participants. The Disease Activity Score in 28 joints-Erythrocyte Sedimentation Rate (DAS28-ESR) ≤ 2.6 was categorized as the primary outcome.

Table 1. The baseline characteristics of the study population Data that are not normally distributed are presented as the medians and interquartile ranges (IQRs) unless otherwise indicated. CRP=C-reactive protein; DAS28=disease activity score using 28 joint counts; ESR=erythrocyte sedimentation rate; TJC28=tender joint count (of 28); SJC28=swollen joint count (of 28); PtGA=patient global assessment of disease activity; RF=rheumatoid factor; Anti-CCP=anti-cyclic citrullinated peptide. * indicates a significant difference.

	PKUPH (n=1629)	Multicenter (n=235)	*P* value
Age, years	51 (43, 59)	49 (40, 60)	0.154
Female, *n* (%)	1353 (83.1)	197 (84.5) (n=233)	0.764
RA duration, months	68.2 (25.8, 128.4)	48 (12.0, 108.0) (n=233)	<0.001*
Clinical evaluations			
DAS28-ESR	5.4 (4.8, 6.2)	6.1 (5.5, 6.7)	<0.001*
TJC28	12 (8, 19)	10 (7, 16)	<0.001*
SJC28	7 (5, 12)	6 (4, 10)	<0.001*
PtGA	60 (50, 70)	70 (60, 75)	0.036*
Laboratory tests			
ESR, mm/h	42.0 (27.0, 63.0)	48.0 (31.0, 72.0)	0.004*
CRP, mg/L	13.5 (5.6, 28.9) (n=1419)	6.2 (2.0, 18.4)	<0.001*
RF, IU/ml	125.0 (44.9, 339.5) (n=1363)	91.1 (26.6, 370.0)	<0.001*
Anti-CCP, IU/ml	193.0 (56.0, 411.1) (n=783)	100.0 (33.7, 242.8)	0.003*

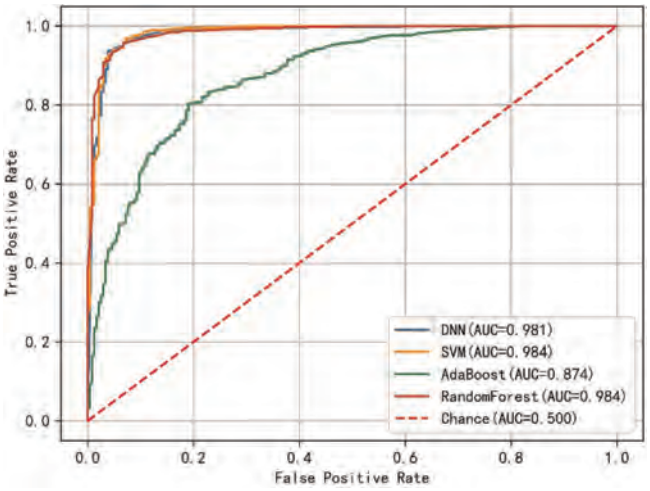

Figure 1. Evaluation of predictive machine learning models using the area under the receiver operating characteristic curve for primary outcome. The area under the receiver operating characteristic curve (AUROC) of machine learning (ML) models is displayed. Different colors were used to represent ML models. The results were attained from tests in the Peking University People's Hospital (PKUPH) cohort. DNN=deep neural network; SVM=support vector machine; AdaBoost=adaptive boosting.

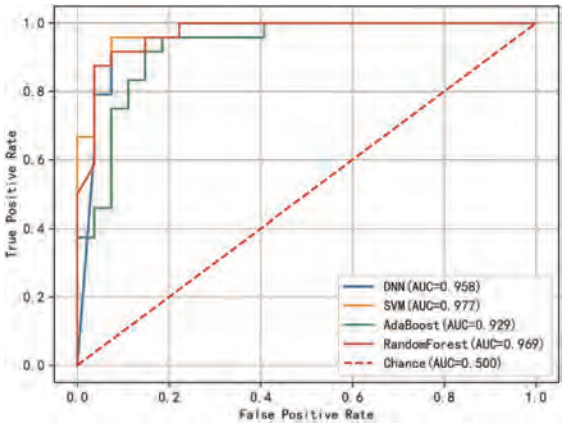

Figure 2. Evaluation of predictive machine learning models using the area under the receiver operating characteristic curve for external validation. The area under the receiver operating characteristic curve (AUROC) of machine learning (ML) models is displayed. Different colors were used to represent ML models. The results were attained from tests in the Peking University People's Hospital (PKUPH) cohort. DNN=deep neural network; SVM=support vector machine; AdaBoost=adaptive boosting.

Results: A total of 1629 patients from Peking University People's Hospital (PKUPH) and 235 multicenter patients were included (number [%] female, 1353 [83.1] vs 197 [84.5]). There were significant differences in disease activity at baseline between the PKUPH and multicenter cohorts at baseline (median [IQRs] DAS28-ESR, 5.4 [4.8, 6.2] vs 6.1 [5.5, 6.7]). For the primary outcome, the best-performing predictive model attained an accuracy of 96.8% and an area under the receiver operating characteristic curve (AUROC) of 0.984 [sensitivity of 98.9%, specificity of 85.2%, positive predictive value (PPV) of 96.9%, and negative predictive value (NPV) of 94.4%]. Notably, in external validation, the best accuracy of 92.7% and AUROC of 0.977 were achieved. We also tested the performance of machine learning models with the secondary outcome (DAS28-ESR >5.1 for high disease activity, >3.2 to ≤5.1 for moderate disease activity, >2.6 to ≤3.2 for low disease activity, ≤2.6 for remission). The DNN model displayed an accuracy of 70.4% and an AUROC of 0.898, which is acceptable.

Conclusion: EHRs including multiple, sequential time nodes can be used to construct and improve machine learning models. Deep learning model can accurately predict the effectiveness of treatment within a moderate sample size. Constructing machine learning models to predict disease activity in patients with rheumatoid arthritis had significant benefits across distinct hospitals.

Disclosure: Z. Yun: None; **C. Li**: None; **Z. Li**: None.

Abstract Number: 0423

Detection of Citrullinated Proteins Recognized by a Novel Chimeric Antigen Receptor T_{reg} Therapy in Both Synovial Fluid and Serum from Patients with Rheumatoid Arthritis

Sara Charmsaz[1], Jeff Tracy[1], Elizabeth Whalen[1], John Bui[1], Anne-Renee van der Vuurst de Vries[1], Vivianne Malmström[2] and Michelle Blake[1], [1]Sonoma Biotherapeutics, Seattle, WA, [2]Karolinska Institutet, Stockholm, Sweden

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is one of the most common autoimmune diseases and despite many therapeutic options, an unmet medical need persists for novel therapies in RA. Protein citrullination is a post-translational modification in which arginine is converted to citrulline through a process mediated by the activity of peptidylarginine deiminase enzymes. Citrullination is an important driver of RA pathogenesis and autoantibodies against citrullinated proteins are observed in majority of RA patients. We have developed a novel autologous chimeric antigen receptor (CAR) Treg therapy, SBT777101, that is designed to suppress inflammation in RA patients by utilizing a targeting domain directed against a subset of citrullinated antigens (Van der vurst de vries, ACR 2022). An enzyme-linked immunosorbent assay (ELISA) was developed to characterize the level of CAR-reactive antigens in RA patients.

Methods: An ELISA assay using a capture antibody derived from the binding domain of SBT777101 was used to measure the level of citrullinated proteins in synovial fluid (n = 176 RA, n = 54 non-RA) and serum (n = 130 RA, n = 15 non-RA). Levels of citrullinated proteins as evaluated by the ELISA assay, were compared to the activity produced by the antigen in a CAR-expressing cell-based assay. Additionally, the level of citrullinated antigens were compared to the levels of inflammatory markers in a set of matched serum and synovial fluid samples (n = 50).

Results: In RA patients with active disease, elevated protein citrullination was detected in 84% of synovial fluid samples and in 48% of serum samples (n = 50 matched synovial fluid and serum). Citrullinated antigen in synovial fluid correlated with levels of the antigen in serum (n = 50, Spearman R = 0.41, $p < 0.05$). The levels were higher by 4.6-fold in synovial fluid compared to serum which was reflected by more activity as detected by the CAR-expressing cell-based assay in synovial fluid. Additionally, levels of CAR-specific citrullinated antigens as measured by ELISA significantly correlated with the level of activity measured in the CAR-expressing cell-based assay (n =50, Spearman R = 0.48, $p < 0.05$) and with several markers of inflammation measured in synovial fluid (TNFα, IL1β, IL6, IL12p70, IP10 and MIP1α) and in serum (CRP and IL6) of these patient samples.

Conclusion: In summary, we were able to detect CAR-reactive citrullinated antigens for SBT777101 in synovial fluid and serum and these levels correlated with ability to activate the CAR in a cell-based assay, and with several inflammatory markers both in synovial fluid and serum. The presence of these CAR-reactive citrullinated antigens and inflammatory markers will be further evaluated in an upcoming planned phase 1 study.

Disclosure: S. Charmsaz: Sonoma Biotherapeutics, 12, Stock holder; **J. Tracy**: Adaptive Biotechnologies, 12, Stock holder, Sonoma Biotherapeutics, 11, 12, Stock holder; **E. Whalen**: Sonoma Biotherapeutics, 3, 11; **J. Bui**: Bristol-Myers Squibb(BMS), 11; **A. van der Vuurst de Vries**: None; **V. Malmström**: Eli Lilly, 1, Janssen, 5, ONO, 1, Pfizer, 5; **M. Blake**: None.

Abstract Number: 0424

Real-World Effectiveness of Upadacitinib in Patients with Moderate/Severe Rheumatoid Arthritis: 6-Month Data from the Observational UPHOLD Study

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Siena, Italy, [8]National Taiwan University Hospital, Taipei, Taiwan, [9]AbbVie, Inc., North Chicago, IL, [10]Pharmacovigilance and Patient Safety, AbbVie, Inc., North Chicago, IL, [11]AbbVie B.V., Mijdrecht, Utrecht, Netherlands, [12]King Abdulaziz University, Jeddah, Saudi Arabia

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The efficacy and safety of upadacitinib (UPA), an oral reversible Janus kinase inhibitor, have been shown in patients (pts) with moderate/severe RA in the SELECT clinical trial program, both as monotherapy and as part of combination therapy[1]. However, real-world (RW) data on UPA in clinical practice are limited. This analysis presents 6-month data on the effectiveness and safety of UPA in pts with moderate/severe RA in RW clinical practice.

Methods: UPHOLD (NCT04497597) is an ongoing, international, observational cohort study of UPA-naïve adults (aged ≥18 years) with moderate/severe RA, who received UPA 15 mg once daily (QD) as per the product label, with the decision to initiate UPA made before study enrollment. This 6-month interim analysis includes data reported between the study start

Table 1. Patient demographics and disease characteristics at upadacitinib initiation

	FAS (N=1715)
Age, years, mean (SD)	57.0 (12.4)
Sex, female, n (%)	1368 (79.8)
RA duration from diagnosis, years, mean (SD)	10.1 (9.1)
Smoking status, n (%)[a]	
Current	316 (18.5)
Former	358 (20.9)
Never	1037 (60.6)
Erosions on X-ray, n (%)[b]	710 (41.4)
RF and/or ACPA positive, n (%)[c]	891 (75.4)
SJC28, mean (SD)	5.6 (5.2)
TJC28, mean (SD)	8.1 (6.4)
DAS28-CRP, mean (SD)	4.6 (1.2)
SDAI, mean (SD)	28.1 (14.0)
CDAI, mean (SD)	26.5 (12.5)
Patient's Global Assessment of Pain (past 7 days), 0–10 NRS, mean (SD)	6.4 (2.2)
Morning stiffness (past 7 days), 0–10 NRS, mean (SD)	5.9 (2.7)
HAQ-DI, mean (SD)	1.3 (0.7)
FACIT-F, mean (SD)	28.1 (11.3)
Presence of cardiovascular risk factors, n (%)[d]	1061 (61.9)
Initiated upadacitinib as monotherapy, n (%)	832 (48.5)
Initiated upadacitinib with *csDMARDs*, n (%)[e]	883 (51.5)
Concomitant medications, n (%)[f]	
Corticosteroids	783 (45.7)
NSAIDs	361 (21.0)
Prior therapies, n (%)[g]	
≥1 csDMARD	1209 (78.8)
≥1 biologic DMARD	978 (63.8)
≥1 targeted synthetic DMARD	275 (17.9)

[a]N=1711. [b]N=1713. [c]Includes patients with ≥1 positive result for either RF or ACPA (N=1181). [d]Risk factors include history of hypertension, diabetes mellitus, high-density lipoprotein cholesterol ≤40 mg/dL in ≥1 measurement before enrollment, low-density lipoprotein cholesterol ≥130 mg/dL in ≥1 measurement before enrollment, and current or former tobacco/nicotine use. [e]N=1359. [f]MTX, n=734. [g]Number of patients who answered 'Yes' for any prior RA therapy (N=1533); patients may have received >1 prior therapy and may be counted more than once.
CDAI, Clinical Disease Activity Index; csDMARD, conventional synthetic DMARD; DAS28-CRP, DAS of 28 joints using CRP; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; FAS, full analysis set; HAQ-DI, HAQ – Disability Index; NRS, numerical rating scale; SD, standard deviation; SDAI, Simplified Disease Activity Index; SJC28, swollen joint count using 28 joints; TJC28, tender joint count using 28 joints.

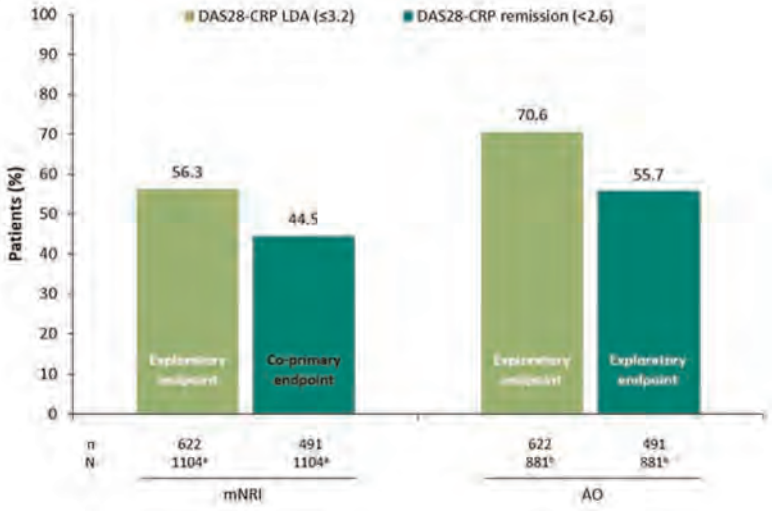
date of Oct 16, 2020 and data cutoff of Apr 20, 2023. The co-primary endpoints are: 1) proportion of pts achieving DAS28-CRP remission (< 2.6) at 6 months, and 2) proportion of pts achieving DAS28-CRP remission at 6 months who continue to receive UPA and maintain remission (or have a ≤0.6-point increase in DAS28-CRP) at 12 months; only the first of these is reported here. Secondary and exploratory efficacy endpoints reported include proportion of pts achieving DAS28-CRP low disease activity (LDA; ≤3.2) at 6 months and change from baseline to 6 months in pt-reported outcomes (PROs). Safety (reported as % of pts with adverse events [AEs]) and PROs (as observed [AO] data) were assessed in the full analysis set (FAS; all pts who received ≥1 UPA dose). DAS28-CRP remission and LDA were analyzed using modified non-responder imputation (mNRI; discontinuations before 6 months for any reason were treated as non-responders) in a

Table 2. Change from baseline to 6 months in PROs (AO analysis)

PRO, mean (SD)	FAS (N=1715)
Patient's Global Assessment of Pain (past 7 days), 0–10 NRS	[N=848] -2.8 (3.46)
Morning stiffness (past 7 days), 0–10 NRS	[N=839] -2.9 (3.16)
HAQ-DI	[N=824] -0.4 (0.66)
FACIT-F	[N=841] 7.6 (11.40)

AO, as observed; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; FAS, full analysis set; HAQ-DI, HAQ-Disability Index; NRS, numeric rating scale; PRO, patient-reported outcome; SD, standard deviation

Figure. Proportion of patients who achieved DAS28-CRP LDA and remission at 6 months (mNRI and AO analyses)



[a]Number of patients in the mFAS population (patients within the FAS who completed 6 months of upadacitinib treatment and had DAS28-CRP data available at 6 months [n=881], and those who discontinued the study before 6 months for any reason [n=223]).

[b]Number of patients who completed 6 months of upadacitinib treatment and had DAS28-CRP data available at 6 months.

AO, as observed; DAS28-CRP, DAS of 28 joints using CRP; FAS, full analysis set; LDA, low disease activity; mFAS, modified FAS; mNRI, modified non-responder imputation.

modified FAS (mFAS; all pts within the FAS who completed 6 months of UPA treatment and had DAS28-CRP data available, and pts who discontinued the study before 6 months for any reason). Remission and LDA at 6 months were also analyzed AO in the mFAS population.

Results: Of the 1732 pts enrolled, 1715 received ≥1 UPA dose (FAS), of whom 223 (13%) prematurely discontinued the study before 6 months. The most common primary reasons for discontinuation were AEs and lack of efficacy (n=72 [4.2%] each). Pt demographics and disease characteristics at UPA initiation are summarized in Table 1. Of the 1104 pts in the mFAS, 44.5% (mNRI) and 55.7% (AO) achieved DAS28-CRP remission at 6 months, and 56.3% (mNRI) and 70.6% (AO) achieved DAS28-CRP LDA at 6 months (Figure). Improvements from baseline to 6 months were observed across PROs (Table 2). AEs reported were: any AE (36.4% of pts), serious AEs (4.5%), serious infection (1.7%; most commonly COVID-19), herpes zoster (2.5%), creatine phosphokinase elevation (0.5%), malignancy excluding non-melanoma skin cancer (NMSC; 0.3%), NMSC (0.4%), venous thromboembolic events (0.4%), and deaths (0.3%). No major adverse cardiovascular events were reported.

Conclusion: The results from UPHOLD suggest that UPA 15 mg QD is effective for the treatment of moderate/severe RAin RW practice, with almost half of pts achieving remission at 6 months. The benefit–risk profile of UPA remains favorable in the RW, consistent with that observed in Phase 3 clinical trials[1].

Reference:

1. Conaghan PG, et al. Drug Saf 2021;44:515–30

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Abstract Number: 0425

Long-term Safety of Rituximab in Rheumatoid Arthritis: A Systematic Review and Meta-analysis

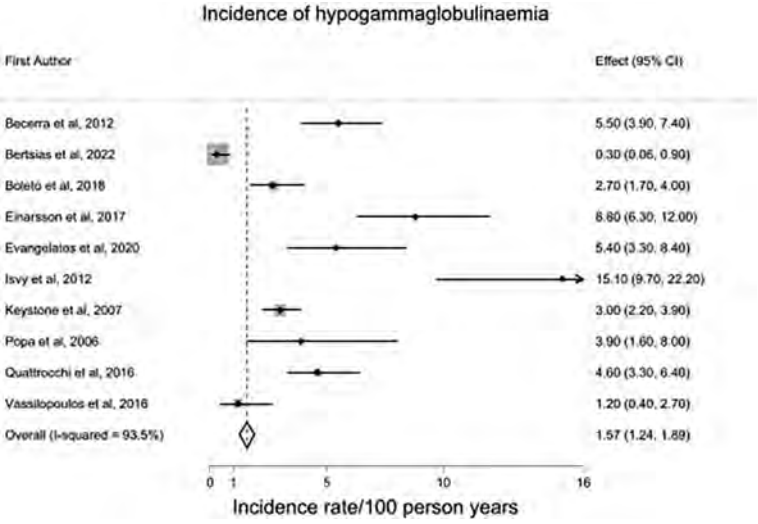
Ioasaf Karafotias, Joshua Rothwell, Maryam Adas, Bechman Katie, Mark Russell, Sam Norton and James Galloway, King's College London, London, United Kingdom

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

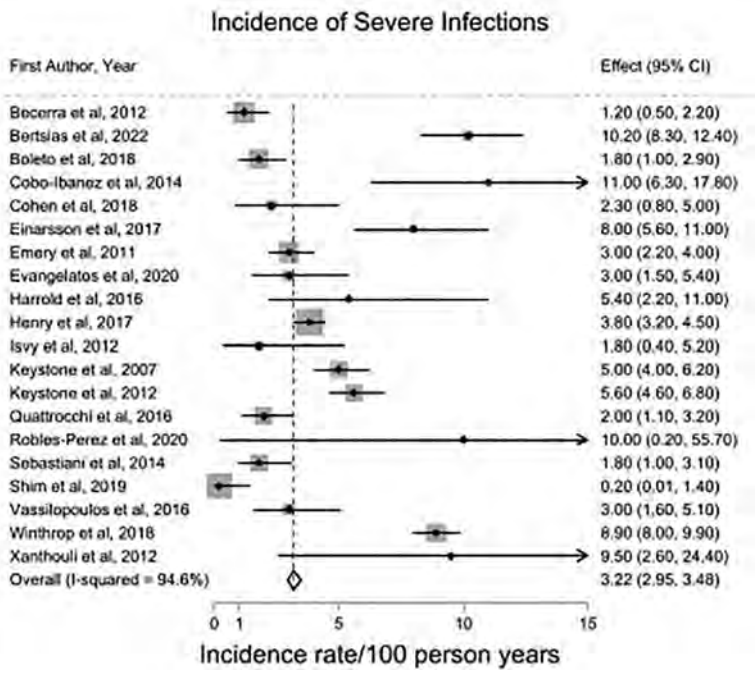
Background/Purpose: Rituximab targets CD20-bearing B cells and is used to treat Rheumatoid Arthritis (RA). Common Variable Immune Deficiency (CVID) is a primary immune deficiency syndrome with immune dysregulation, hypogammaglobulinemia, and recurrent infections. It was hypothesised that iatrogenic B cell depletion could produce a CVID-like phenotype. We sought to evaluate the safety of long-term Rituximab administration in RA patients.

Methods: A systematic review of the Medline/Embase, Web of Science, and Cochrane Library databases was conducted until February 2023. Observational studies in RA populations evaluating the safety of >2 courses of Rituximab, and/or >12 months' exposure to Rituximab were included. Exclusion criteria were case series, short-term exposure to Rituximab, or studies with patients under 16 years of age. Data on adverse events (hypogammaglobulinemia, severe infections, serious adverse events) were extracted. Pooled incidence rates of adverse events were calculated by random-effects meta-analysis.

Results: Twenty-three studies were included, reporting 253 episodes of hypogammaglobulinemia, 964 severe infections, and 1,903 severe adverse events, from a total 19,855 patient-years (PY) exposure. Their pooled incidence rates/100PY were 1.57 [95% confidence interval (95%CI) 1.24-1.89], 3.22 (95%CI 2.95-3.48), and 8.07 (95%CI 7.60-8.54), respectively. Event rates did not increase with longer duration of exposure.



Incidence of hypogammaglobulinemia



Incidence of severe infections

Conclusion: The safety risk of long-term exposure to Rituximab appears to be consistent over time. However, there was high heterogeneity in the outcomes, limited data on use beyond 5 years, and risk of bias was substantial. More research on long-term safety of Rituximab is required to address this.

Disclosure: I. Karafotias: None; **J. Rothwell**: None; **M. Adas**: None; **B. Katie**: None; **M. Russell**: Biogen, 6, Eli Lilly, 5, 6, Galapagos, 6, Menarini, 6, UCB, 5; **S. Norton**: Janssen, 6, Pfizer, 6; **J. Galloway**: AbbVie, 2, 5, 6, AstraZeneca, 5, Biogen, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0426

The Clinical Efficacy of Switching Therapy Between Biological Agents and JAK Inhibitors in the Patients with Rheumatoid Arthritis

Tomokazu Choshi[1], Kenji Mamoto[1], Yutaro Yamada[1], Tadashi Okano[1], Shohei Anno[2], Kazuki Orita[2], Takahiro Iida[3], Masahiro Tada[4], Kentaro Inui[5], Tatsuya Koike[6] and Hiroaki Nakamura[1], [1]Osaka Metropolitan University, Osaka, Japan, [2]Yodogawa Christian Hospital, Osaka, Japan, [3]Koryokai Hospital, Osaka, Japan, [4]Osaka City General Hospital, Osaka, Japan, [5]Saiseikai Nakatsu Hospital, Osaka, Japan, [6]Search Institute for Bone and Arthritis Disease (SINBAD), Shirahama Foundation for Health and Welfare, Shirahama, Japan

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Some patients with rheumatoid arthritis (RA) need switching therapy between biologic agents (Bio) and Janus kinase inhibitors (JAKi) when efficacy of Bio or JAKi is not enough.

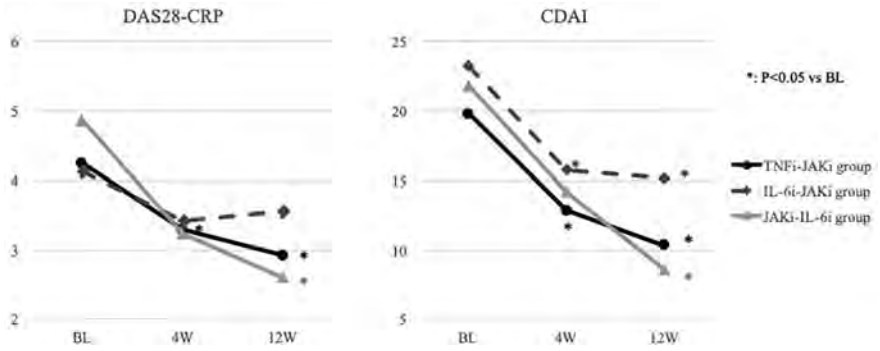


Figure 1: DAS28-CRP and CDAI in three groups for 12 weeks after switching

The aim of this study was to investigate the clinical efficacy of switching therapy between Bio and JAKi in the patients with RA.

Methods: We evaluated inflammatory markers and disease activities for 12 weeks (W) after switching in the patients with RA who received the switching therapy from Tumor Necrosis Factor inhibitors (TNFi) to JAKi (TNFi-JAKi group, N=61; mean age 64.6±12.9 years old), from Interleukin-6 inhibitors (IL-6i) to JAKi (IL-6i-JAKi group, N=33; mean age 64.9±14.7 years old), and from JAKi to IL-6i (JAKi-IL-6i group, N=8; mean age 65.5±14.7 years old).

Results: The mean values of Matrix Metalloproteinase-3 (MMP-3) (ng/ml) of TNFi-JAKi, IL-6i-JAKi, and JAKi-IL-6i groups were 213.5±481.3, 237.5±179.4, and 268.5±138.4 at baseline (BL), and 118.9±126.3 (p=0.148), 183.6 ±192.7 (p=0.279), and 196.2±100.9 (p=0.254) after 4W (vs BL), and 104.0±96.1 (p=0.089), 176.6±120.8 (p=0.123), and 137.4±114.5 (p=0.077) after 12W (vs BL), respectively. The mean Disease Activity Score 28- C reactive protein (DAS28-CRP) of TNFi-JAKi, IL-6i-JAKi, and JAKi-IL-6i groups were 4.22±1.27, 4.13±1.39, and 4.87±1.35 at BL, and 3.28±1.37 (**p< 0.001**), 3.41±1.46 (p=0.805), and 3.24±1.85 (p=0.065) after 4W (vs BL), and 2.99±1.24 (**p< 0.001**), 3.56±1.45 (p=0.115), and 2.60±1.40 (**p=0.005**) after 12W (vs BL), respectively (Figure 1). The mean Clinical Disease Activity Index (CDAI) of TNFi-JAKi, IL-6i-JAKi, and JAKi-IL-6i groups were 19.8±11.8, 23.2±12.7, and 21.8±9.9 at BL, and 12.8±10.4 (**p< 0.001**), 15.7±12.5 (**p=0.020**), and 14.2±13.9 (p=0.228) after 4W (vs BL), and 10.3±9.8 (**p< 0.001**), 15.2±12.6 (**p=0.012**), and 8.6±9.5 (**p=0.017**) after 12W (vs BL), respectively (Figure 1). There were no significant differences in the mean values of MMP-3 for 12W after switching in all groups. The disease activities (both of DAS28-CRP and CDAI) significantly decreased after 4W in TNFi-JAKi group, and after 12W in TNFi-JAKi and JAKi-IL-6i groups (Figure 1). DAS28-CRP and CDAI kept to decrease for 12W after switching in TNFi-JAKi and JAKi-IL-6i groups, however, DAS28-CRP increased and CDAI did not decrease from 4W to 12W after switching in IL-6i-JAKi group (Figure 1).

Conclusion: There have not still been clear indications of the switching therapy between Bio and JAKi in the patients with RA. In this study, it may be considered that the switching therapy from TNFi to JAKi and from JAKi to IL-6i could be effective when RA patients treated with TNFi or JAKi need switching therapy due to insufficient clinical efficacy.

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Abstract Number: 0427

Molecular Characterization of Biologic and Targeted Synthetic DMARDs Effects Through Ex- vivo Studies in Rheumatoid Arthritis Immune Cells

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite advances in rheumatoid arthritis (RA) treatment, a significant proportion of patients (10-30%) fail to respond to current medications, including biologics. A better characterization of the molecular effects promoted by the drugs might contribute to the development of personalized therapeutic strategies.

Methods: Peripheral blood mononuclear cells (PBMC) and neutrophils from 10 active RA patients were cultured (24h and 12h, respectively), with autologous serum and with either, etanercept, sarilumab, or baricitinib (all 10 micromolar). Changes in cell proliferation and adhesion in PBMCs and NETosis-derived products in supernatants of cell cultures were measured with specific commercial kits. Protein expression changes promoted by each drug were evaluated in supernatants using proximity extension assay (PEA) technology (Olink), analyzing a panel of 92 inflammation-related proteins. To identify if the proteomic signatures susceptible to being modulated by the drugs were present in patients with active disease, we analyzed the same inflammatory profile in the serum of 180 RA patients.

Results: TNFi, IL6Ri, and JAKinibs inhibited proliferation and adhesion in PBMCs from 70% of RA patients, being TNFi and JAKinibs more effective than IL6Ri. RA Neutrophils treated with autologous serum underwent NETosis, which was equally prevented by all inhibitors. Autologous serum increased the secretion of inflammatory proteins by RA PBMCs and neutrophils, while each drug promoted specific changes in proteomic signatures. Thus, TNFi, IL6Ri, and JAKinibs reduced different sets of cytokines, chemokines, and growth factors, with only three reduced (IL7, TNF, FGF23) by all three inhibitors. Lastly, analysis of the circulating inflammatory proteome revealed that approximately 60% of active RA patients exhibited at least one altered proteomic signature associated with the one modulated ex vivo by any of the drugs. Particularly 20% of patients exhibited an altered proteomic signature modulated ex vivo by the 3 drugs, 20 % with two of them, and 20% with only one precise drug.

Conclusion: The distinctive cellular and molecular changes promoted by TNFi, IL6Ri, and JAKinibs in ex vivo assays of RA immune cells, were consistent with specific altered serum profiles observed in subgroups of active RA patients. Such observations provide compelling evidence regarding the therapeutic potential of each therapy, as it aligns with the specific molecular profile alterations exhibited by individual patients at baseline.

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Abstract Number: 0428

Real World Patterns of Advanced Therapy Tapering in Early Rheumatoid Arthritis: Data from the Canadian Early Arthritis Cohort

Maria Powell[1], Vivian Bykerk[2], Orit Schieir[3], Marie-France Valois[4], Susan Bartlett[5], Louis Bessette[6], Gilles Boire[7], Carol Hitchon[8], Edward Keystone[9], Janet Pope[10], Carter Thorne[11], Diane Tin[12], Glen Hazlewood[1] and Canadian Early Arthritis Cohort (CATCH) Investigators[13], [1]University of Calgary, Calgary, AB, Canada, [2]Hospital for Special Surgery, New York, NY, [3]McGill University, Montréal, QC, Canada, [4]McGill University, Pointe-Claire, QC, Canada, [5]McGill University, Montreal, QC, Canada, [6]Centre de l'Ostéoporose et de Rhumatologie de Québec, Quebec City, QC, Canada, [7]Université de Sherbrooke, Sherbrooke, QC, Canada, [8]University of Manitoba, Manitoba, MB, Canada, [9]Keystone Consulting Enterprises Inc., Toronto, ON, Canada, [10]University of Western Ontario, London, ON, Canada, [11]Southlake Regional Health Centre, Newmarket, ON, Canada, [12]Centre of Arthritis Excellence, Newmarket, ON, Canada, [13]CATCH, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Recent Canadian treatment recommendations suggest offering to taper of biologic or targeted synthetic therapy to patients with rheumatoid arthritis (RA) after they achieve sustained remission (sREM) or low disease activity (LDA) for at least 6 months. This study sought to describe real-world patterns of advanced therapy tapering in a large pan-Canadian cohort of patients with early RA who would be eligible to taper and identify predictors of which patients are reducing their therapy in routine care.

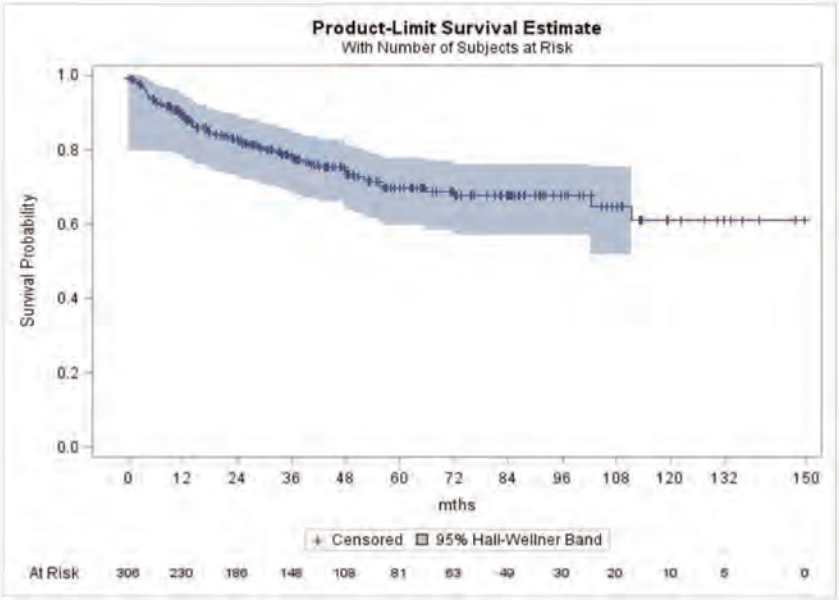

Figure 1: Kaplan Meier Survival Estimates of Time from Rheumatoid Arthritis Sustained Remission or Low Disease Activity to First Advanced Therapy Taper in a Multi-Centre Study Embedded in Routine Care (72 tapered and 234 censored).

Table 1: Multivariable Cox Regression Results - Predictors of Tapering Advanced Therapy in Rheumatoid Arthritis Patients Reaching Sustained Remission or Low Disease Activity in a Multi-Centre Study Embedded in Routine Care (N=306).

Variables	HR	95% CI
Baseline		
Sex: female vs male	0.960	0.556 – 1.660
Education: post-secondary vs. high school degree or less	1.545	0.899 – 2.654
Seropositive (RF or ACPA), %[%]	0.931	0.496 – 1.749
When Sustained Remission / Low Disease Activity First Achieved		
Age, years	1.010	0.990 – 1.029
Disease duration, months	1.001	0.991 – 1.011
Number of Advanced Therapies Tried/Used (>1 vs. 1)	1.080	0.476 – 2.454
Pain (0-10), change of 1	1.004	0.847 – 1.191
Fatigue (0-10), change of 1*	0.852	0.739 – 0.982
Type of advanced therapy		
Non-TNF inhibitor vs TNF inhibitor*	2.732	1.345 – 5.549
JAK inhibitor vs TNF inhibitor	0.750	0.309 – 1.822

[%] % of non-missing
[1] First ever over available follow-up
* $p < 0.05$

Abbreviations
RF (rheumatoid factor)
ACPA (anti-citrullinated protein autoantibodies)
TNF (tumour necrosis factor)
JAK (Janus kinase)

Methods: Data from patients (age >18) enrolled in the Canadian early ArThritis CoHort (CATCH) between January 2007 to August 2022 were analyzed. CATCH is a prospective, observational cohort of patients with early inflammatory arthritis (symptoms < 1 year) treated in rheumatology clinics across Canada. The analysis cohort included patients with a diagnosis of RA according to the 1987 or 2010 ACR/EULAR classification criteria who were prescribed advanced therapy (i.e., tumour necrosis factor (TNF) inhibitors, Janus kinase (JAK) inhibitors, non-TNF inhibitor advanced therapy) and sREM or LDA (using simplified disease activity index or clinical disease activity index) for at least 6 months. Patients were considered taper advanced therapy if they reduced the dose of therapy by at least 25% through dose reduction or dose spacing for a time period of at least 3 months. Survival analysis using the Kaplan-Meier method was used to estimate the median time to taper advanced therapy and Cox regression analysis was used to identify predictors of tapering advanced therapy.

Results: Data were analyzed from 306 RA patients treated with advanced therapy who reached sREM or LDA for at least 6 months. These patients were predominantly white (87%), female (73%), and had seropositive RA (82%) with a mean age of 50 years. At the time of sREM or LDA patients were treated with TNF inhibitors [n=218 (71%)], JAK inhibitors [n=52 (17%)], and non-TNF biologic therapy [n=36 (12%)]. Treatment tapering occurred in 72 (24%) patients and was more frequent for treatment with non-TNF-inhibitors [n=15/36 (42%)] compared to TNF inhibitors [n=51/218 (23%)] or JAK inhibitors [n=6/52 (12%)]. The median time to taper advanced therapy after achieving sREM or LDA was 14 months (IQR: 5, 35 months) (Figure 1). In adjusted Cox regression analyses, treatment with a non-TNF inhibitor was associated with a higher likelihood of tapering (HR: 2.73, 95% CI:1.35, 5.55) and having higher patient reported symptoms of fatigue was associated with a decreased likelihood of tapering (HR 0.89: 95% CI 0.80 – 0.99) (Table 1).

Conclusion: In this real-world study of early RA patients, tapering was attempted in approximately 1 in 4 patients who would be considered eligible based on current recommendations, with a median time of 14 months. Tapering was associated with the type of advanced therapy and was less common in patients with worse fatigue, suggesting real-world decisions to taper are influenced by factors beyond typical measures of RA disease activity.

Disclosure: M. Powell: None; **V. Bykerk**: Abbvie, 2, BMS, 2, Pfizer, 2; **O. Schieir**: None; **M. Valois**: None; **S. Bartlett**: Janssen, 6, Merck/MSD, 2, 6, Novartis, 2, Organon, 1, 6, PROMIS Health Organization, 4, Sandoz, 2, 6; **L. Bessette**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol Myers Squibb, 2, 5, 6, Eli Lilly, 2, 5, 6, Fresenius Kabi, 2, 6, Gilead, 2, 5, 6, JAMP Pharma, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Organon, 2, 6, Pfizer, 2, 5, 6, Sandoz, 2, 6, Sanofi, 2, 5, 6, Teva, 2, 6, UCB, 2, 5, 6, UCBA, 5; **G. Boire**: Eli Lilly, 1, Janssen, 6, Organon, 1, Orimed Pharma, 1, 6, Otsuka, 1, Pfizer, 1, 5, Sandoz, 1, Teva, 1, Viatris, 1, 6; **C. Hitchon**: Astra Zeneca, 1, Pfizer Canada, 5; **E. Keystone**: AbbVie/Abbott, 2, 6, Amgen, 2, 6, celltrion, 2, 6, Eli Lilly, 2, 6, Fresenius Kabi, 2, 6, Pfizer, 2, 6, Samsung Bioepsis, 2, sandoz, 2, 6; **J. Pope**: AbbVie,

1, 2; **C. Thorne**: Abbvie, 1, Biogen, 2, Nordic Pharma, 1, Pfizer, 1, 5, Roche, 1, Sandoz, 1, 2; **D. Tin**: None; **G. Hazlewood**: None; **C. (CATCH) Investigators**: None.

Abstract Number: 0429

Direct and Indirect Effects of Upadacitinib or Adalimumab on Pain in Rheumatoid Arthritis: Results from a Randomized Phase 3 Study

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SESSION INFORMATION
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Session Title: RA – Treatments Poster I
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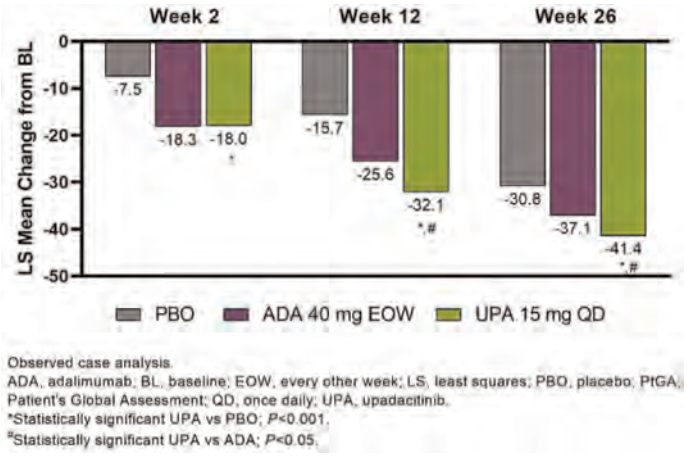
Session Time: 9:00AM–11:00AM

Background/Purpose: Rapid and sustained pain control is an important goal for patients (pts) with rheumatoid arthritis (RA). Control of inflammation in RA does not always eliminate pain, which can have multifactorial causes. Our objective was to assess direct and indirect (ie, by inflammation surrogates) effects of treatment with upadacitinib (UPA) or adalimumab (ADA) vs placebo (PBO) on pain in pts with RA.

Methods: Period 1 of SELECT-COMPARE was a 48-week, randomized, double-blind, phase 3 study with a 26-week PBO-controlled period in pts with RA who had active disease despite methotrexate treatment. Adults (≥18 years) on stable background methotrexate were randomized 2:2:1 to UPA 15 mg once daily, PBO, or ADA 40 mg every other week. Pts with an insufficient response (< 20% improvement in tender joint count [TJC] or swollen joint count [SJC] at week 14, 18, and 22 or if Clinical Disease Activity Index was >10 at week 26) were rescued from PBO to UPA, UPA to ADA, or ADA to UPA; all PBO pts who were not rescued were switched to UPA at week 26. Observed case analysis was performed for change from baseline in Patient's Global Assessment (PtGA) of pain (1–100 mm). A multiple mediator analysis[1] for effect of UPA vs PBO and ADA vs PBO on pain assessed as PtGA of pain or TJC28 was conducted using observed case analysis for week 2 and

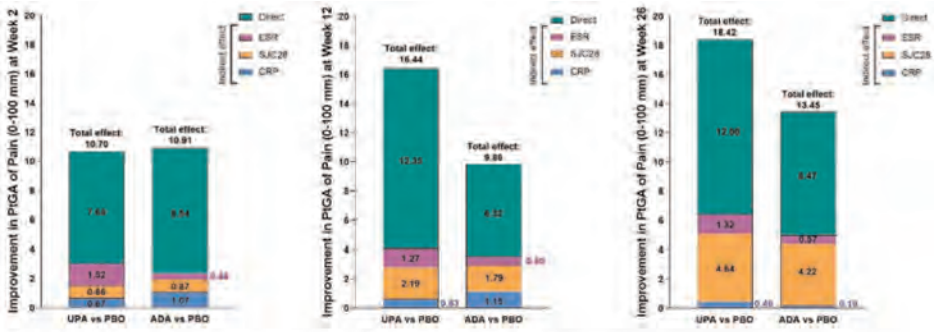


Observed case analysis.
ADA, adalimumab; BL, baseline; EOW, every other week; LS, least squares; PBO, placebo; PtGA, Patient's Global Assessment; QD, once daily; UPA, upadacitinib.
*Statistically significant UPA vs PBO; $P<0.001$.
#Statistically significant UPA vs ADA; $P<0.05$.

Figure 1. Change from Baseline in PtGA of Pain (mm) at Weeks 2, 12, and 26

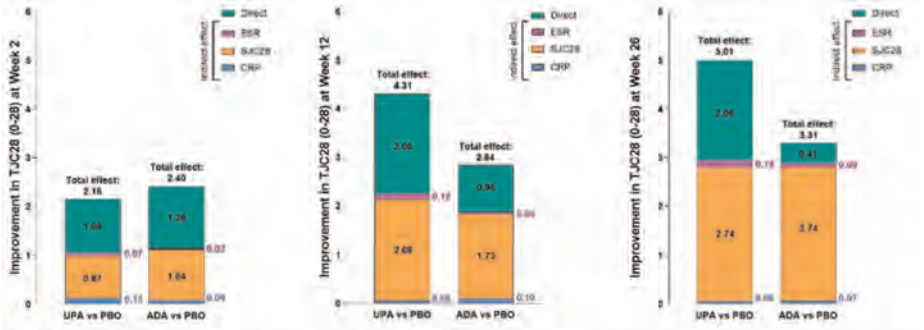
12 analyses and last observation carried forward for data after rescue for the week 26 analysis. Indirect effect of treatment on pain was assessed based on ESR, CRP, and SJC28.

Results: 1629 pts were included in this analysis (UPA, n=651, PBO, n=651, ADA, n=327).PtGA of pain significantly improved with UPA vs PBO from baseline to week 2 (–18.0 [n=639] vs –7.5 [n=624]; *P*< 0.001), week 12 (–32.1 [n=614] vs –15.7 [n=616]; *P*< 0.001), and week 26 (–41.4 [n=478] vs –30.8 [n=305]; *P*< 0.001; **Figure 1**). Improvements in PtGA of pain were also observed with ADA vs PBO at weeks 2 (–18.3 [n=318]), 12 (–25.6 [n=307]), and 26 (–37.1 [n=212]; **Figure 1**). Total and direct effects on PtGA of pain improvement were significantly greater (both *P*< 0.001) with UPA vs PBO as early as week 2 (**Figure 2**) and increased at weeks 12 and 26 (all *P*< 0.001). Total and direct effects on PtGA of pain improvement were also observed with ADA vs PBO (**Figure 2**). Improvement in pain assessed as TJC28 was also significantly greater (all *P*< 0.05) with UPA and ADA vs PBO at weeks 2, 12, and 26; SJC28 showed the greatest indirect effect on pain assessed as TJC28 at weeks 12 and 26 (**Figure 3**). UPA and ADA vs PBO showed similar indirect contributions to improvement in PtGA of pain and TJC28 at weeks 2, 12, and 26, whereas UPA showed a greater direct effect on PtGA of pain and TJC28 at weeks 12 and 26 than ADA (**Figures 2 and 3)**.



Week 2 and 12 data: observed case analysis; week 26 data: LOCF analysis.
ADA, adalimumab; LOCF, last observation carried forward, PBO, placebo; PtGA, Patient's Global Assessment; SJC28, swollen joint count based on 28 joints; UPA, upadacitinib.
Mediation analyses were conducted using the methods of Preacher and Hayes[1]. Estimates for the following effects were generated, controlling for baseline value of PtGA of pain: direct effect of treatment on the outcome of improvement from baseline in PtGA of pain, indirect effects of treatment on the outcome via mediators of change from baseline in ESR/SJC28/CRP, and total effect of treatment on the outcome.

Figure 2. Direct and Indirect Effects of Treatment on Pain Assessed as Improvement in PtGA of Pain at Weeks 2, 12, and 26



Week 2 and 12 data: observed case analysis; week 26 data: LOCF analysis.
ADA, adalimumab; LOCF, last observation carried forward; PBO, placebo; SJC28, swollen joint count based on 28 joints; TJC28, tender joint count based on 28 joints; UPA, upadacitinib.
Mediation analyses were conducted using the methods of Preacher and Hayes[1]. Estimates for the following effects were generated, controlling for baseline value of TJC28: direct effect of treatment on the outcome of improvement from baseline in TJC28, indirect effects of treatment on the outcome via mediators of change from baseline in ESR/SJC28/CRP, and total effect of treatment on the outcome.

Figure 3. Direct and Indirect Effects of Treatment on Pain Assessed as Improvement in TJC28 at Weeks 2, 12, and 26

Conclusion: Both UPA and ADA resulted in rapid and significant improvements in pain vs PBO as early as week 2 in patients with RA. Indirect effects on PtGA or TJC28 pain improvement were similar between UPA and ADA at all time points; however, direct effect on pain was up to two times greater with UPA vs ADA at weeks 12 and 26. These results suggest UPA may be more effective in control of pain, which may be due to either inflammatory or non-inflammatory mechanisms, than ADA in RA.

Reference:[1]Preacher, KJ & Hayes, AF. *Behavior Research Methods,2008;40*(3), 879–891.

Disclosure: P. Taylor: AbbVie, 2, Biogen, 2, Eli Lilly, 2, Fresenius, 2, Galapagos, 2, 5, Gilead Sciences, 2, GSK, 2, Janssen, 2, Nordic Pharma, 2, Pfizer Inc, 2, Sanofi, 2, UCB, 2; **D. Walsh**: AbbVie, 2, Contura International A/S, 2, Eli Lilly, 5, GlaxoSmithKline Research & Development Limited, 5, Orion Corporation, 5, Pfizer, 5; **T. Takeuchi**: AbbVie, 2, 5, 6, AYUMI, 5, Bristol-Myers Squibb, 6, Chugai, 2, 5, 6, Daiichi Sankyo, 5, Eisai, 5, 6, Eli Lilly Japan, 2, 6, Gilead, 2, 6, Janssen, 6, Mitsubishi-Tanabe, 2, 5, 6, ONO, 5, Pfizer Japan, 6, Taiho, 2; **B. Fautrel**: AbbVie, 2, BMS, 2, Chugai, 2, Fresenius Kabi, 2, Galapagos, 2, Lilly, 2, Medac, 2, Nordic Pharma, 2, Novartis, 2, Pfizer, 2, Sobi, 2, UCB, 2; **J. Pope**: AbbVie, 1, 2; **A. Garrison**: AbbVie, 3, 11; **Y. Song**: AbbVie, 3, 11; **S. Penn**: AbbVie, 3, 11; **R. Lippe**: AbbVie, 3, 11; **D. Caballero**: AbbVie, 3, 11; **A. Kavanaugh**: AbbVie, 1, 2, Amgen, 1, 2, BMS, 1, 2, Eli Lilly, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, UCB, 1, 2.

Abstract Number: 0430

A Multicenter, Real-world Clinical Data Study of the Use of JAK Kinase Inhibitors in a Large Cohort of Patients with Rheumatoid Arthritis

Maria Lopez-Lasanta[1], Helena Borrell[1], Meritxell Salles Lizarzaburu[2], Virginia Ruiz-Esquide[3], Daniel Roig[4], Annika Nack[5], Carolina Pérez[6], Julia Bernardez[7], Andrea García[8], Joana Rovira[9], Andrea Cuervo[10], Marta Valls[11], Carmen Garcia[12], Sonia Minguez[13], Rosa Morla[14], Paula Estrada[4], Melania Martinez[15], Conxita Pitarch[16], Noemi Busquets[17], Hye Park[18], Jose A Gomez-Puerta[19], Susana Holgado[20], Nuria Montala[21], Raimon Sanmarti[3], Lourdes Mateo[20], Cesar Diaz[22], Hector Corominas[23] and Georgina Salvador[7], [1]Hospital Universitari Vall d'Hebron, Rheumatology, Barcelona, Spain, [2]C. H. de Manresa - Fundació Althaia, Barcelona, Spain, [3]Hospital Clinic, Rheumatology, Barcelona, Spain, [4]Hospital Moisses Broggi, Rheumatology, Barcelona, Spain, [5]Department of Rheumatology, Hospital Universitari Germans Trias i Pujol, Barcelona, Spain, [6]Hospital del Mar-Parc de Salut Mar, Rheumatology, Barcelona, Spain, [7]Hospital Mutua Terrassa, Rheumatology, Barcelona, Spain, [8]Hospital Sant Pau-Dos de Maig, Rheumatology, Barcelona, Spain, [9]Hospital de Mollet, Barcelona, Spain, [10]Hospital Granollers, Rheumatology, Barcelona, Spain, [11]Hospital Josep Trueta, Rheumatology, Girona, Spain, [12]Hospital de Terrassa, Rheumatology, Barcelona, Spain, [13]Fundació Althaia, Manresa, Spain, [14]Hospital Clinic, Rheumatology, Barcelona, Barcelona, Spain, [15]Hospital Germans Trias i Pujol, Rheumatology, Barcelona, Spain, [16]Hospital Universitari de la Santa Creu i Sant Pau, Rheumatology, Barcelona, Spain, [17]HOSP. GENERAL DE GRANOLLERS, GRANOLLERS, Spain, [18]Hospital Universitari Sant Pau, Rheumatology, Barcelona, Spain, [19]Department of Rheumatology, Hospital Clinic of Barcelona, Barcelona, Spain, [20]Hospital Universitari Germans Trias i Pujol, Rheumatology, Barcelona, Spain, [21]Hospital Santa Maria, Rheumatology, Lleida, Spain, [22]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, [23]Hospital Universitario Sant Pau, Rheumatology, Barcelona, Spain

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The Janus Kinase inhibitors (JAKi) drugs are approved for use in adults with moderate to severe rheumatoid arthritis (RA). Real-world studies are necessary as they provide relevant data that complements the information provided by registration clinical trials.

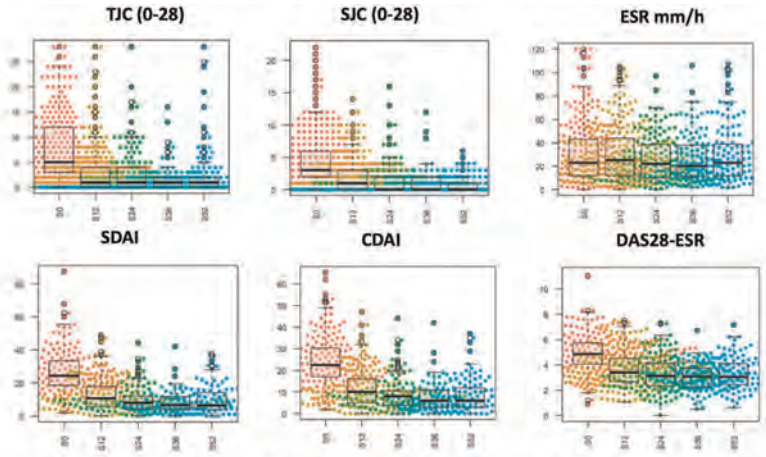


Figure 1. Evolution of parameters and index per week of treatment

For each variable, the mean and standard deviation -mean(sd)- together with the 95% confidence interval for the mean -IC [,] - and the median and interquartile range, median [IQR], were calculated

Table 1. Clinical and epidemiological characteristics of the cohort.

VARIABLE	N (%) [CI 95%]	N
Smoking		248
- No smoker	168 [65.7%] [59.5; 72.0]	
- Smoker	53 [20.6%] [15.7; 26.5]	
- Former smoker	34 [13.7%] [9.7; 18.6]	
HTA	68 [26.6%] [21.1; 32.9]	256
Dyslipemia	69 [27%] [21.6; 32.8]	256
Diabetes Mellitus	18 [7%] [4.2; 10.8]	256
Ischemic Heart Disease	10 [3.9%] [1.9; 7.1]	256
Vertebral fracture	15 [5.9%] [3.3; 9.5]	255
Non- vertebral fracture	26 [10.2%] [6.8; 14.7]	253
Depression	54 [21.2%] [16.2; 26.7]	255
Peptic ulcer	7 [2.7%] [1.1; 5.6]	256
Neoplasia		252
- No	236 [93.7%] [89.8; 96.3]	
- Past	15 [6%] [3.4; 9.6]	
- Active	1 [0.4%] [0; 2.2]	
Non ILD pulmonary disease	31 [12.2%] [8.4; 16.8]	255
Ocular	8 [3.2%] [1.4; 6.2]	254
Degenerative joint disease	65 [25.5%] [20.1; 31.5]	255
Herpes Zoster	15 [6%] [3.4; 9.7]	250
Thrombosis	2 [0.8%] [0.1; 2.8]	255
Extraarticular manifestations		255
- Scleritis/episcleritis	2 [0.8%] [0.1; 3]	
- Pleurisy	4 [1.7%] [0.5; 4.3]	
- Pericarditis	1 [0.4%] [0; 2.2]	
- Vasculitis	2 [0.8%] [0.1; 2.8]	
- Amyloidosis	1 [0.4%] [0; 2.2]	
- ILD	7 [3%] [1.2; 6.1]	
joint prostheses	23 [9.8%] [6.3; 14.4]	234
1 prostheses	14 [60.9%] [38.5; 80.3]	
2 prostheses	6 [26.1%] [10.2; 48.4]	
3 prostheses	1 [4.3%] [0.1; 21.9]	
4 o more	2 [8.7%] [1.1; 28]	
Sjogren syndrome	32 [14.1%] [9.8; 19.3]	227
Dislocation atlanoaxoidea	7 [3%] [1.2; 6.1]	232
Previous bDMARDs	195 [78.3%] [72.8; 83.1]	
Number of bDMARDs, median [IQR]	2 [1,3]	255
Type of bDMARDs		
Anti-TNFi	147 [65.2%] [58.5; 71.5]	
Anti-IL6	79 [30.8%] [25.2; 36.9]	256
Abatacept	72 [28.1%] [22.7; 34.1]	
Rituximab	32 [12.5%] [8.7; 17.2]	
Number of previous csDMARDs, median [IQR]	2 [1,3]	254
Monotherapy	113 [44.1%] [38; 50]	256
csDMARDs combination		
Methotrexate		
Leflunomide	91 [35.5%] [29.7; 41.7]	
Sulfasalazine	57 [22.3%] [17.1; 27.9]	
Hidroxicloroquine	2 [0.8%] [0.1; 2.8]	
	15 [5.9%] [3.3; 9.5]	
Corticosteroid	159 [62.4%] [56.2; 68.3]	255
Have you ever discontinued treatment?	Yes 48 [18.8%] [14.1; 24.3]	254
	No 206 [81.2%] [75.7; 85.9]	
Time of discontinuation	< 1 week 7 [14.6%] [6.1; 27.8]	48
	1-4 weeks 32 [66.7%] [50.8; 79.4]	
	5-8 weeks 9 [18.8%] [8.9; 32.8]	
Herpes Zoster during treatment with JAKi	Yes 11 [5.3%] [2.6; 9.3]	206
	NO 195 [94.8%] [90.7; 97.4]	

bDMARDS: biological Disease-Modifying Antirheumatic Drugs
csDMARDS: conventional Disease-Modifying Antirheumatic Drugs
JAKi: Jak Kinases Inhibitors
ILD: Interstitial Lung Disease

1: n(%) [Exact CI]
2: N mean(sd) [CI95%mean] median(IQR)

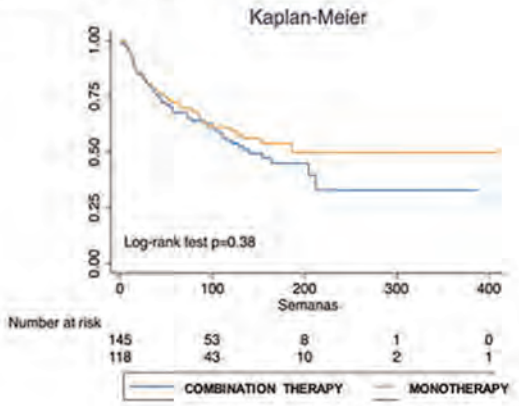
Table 3. Proportion of JAKi responders and non-responders in W12, n=204.

ASSESSMENT CRITERIA		N (%) [exact ci]
DeltaDas28> 1.2		
	Responder	111 (54.4) [47.3; 61.4]
	Non responder	93 (45.6) [38.6; 52.7]
EULAR Response		
	Good/moderate	135 (66.2) [59.2; 72.6]
	No response	69 (33.8) [27.4; 40.8]

Table 4. Proportion of patients in remission, low, moderate or high activity according to CDAI and week of follow-up.

	W12	W24	W36	W52
CDAI	N (%) [Exact CI]			
<2.8	16 (11.2%) [6.5; 17.5]	13 (13.1%) [7.2; 21.4]	14 (20%) [11.4; 31.3]	25 (24%) [16.2; 33.4]
>2.8 ≤ 10	60 (42%) [33.8; 50.5]	61 (61.6%) [51.3; 71.2]	36 (51.4%) [39.2; 63.6]	45 (43.3%) [33.6; 53.3]
>10 ≤ a 22	48 (33.6%) [25.9; 41.9]	18 (18.2%) [11.1; 27.2]	17 (24.3%) [14.8; 36]	29 (27.9%) [19.5; 37.5]
> 22	19 (13.3%) [8.2; 20]	7 (7.1%) [2.9; 14]	3 (4.3%) [0.9; 12]	5 (4.8%) [1.6; 10.9]
N	143	99	70	104

FIGURE 2. Survival of JAKi in monotherapy or combination therapy



Methods: Observational, retrospective, and multicenter study of a cohort of RA patients treated with a JAKi and followed up in n=14 Rheumatology Services, members of the RA Working Group (GT-ARCat) of the Catalan Society of Rheumatology (SCR). Data from patients who underwent JAKi treatment between May 2014 and November 2022 were included. Epidemiological and clinical variables were collected from baseline (S0) to week 52 (S52) of treatment. Analysis of the use of a first JAKi has been performed.

Results: A total of 256 patients (87% women) were included, with a mean age of 57.31 years and a mean time of disease evolution of 12.17 years. The cohort characteristics are detailed in Table 1. 53.5% of the cohort had received baricitinib, 41.8% tofacitinib and 4.7% upadacitinib. No statistically significant differences were observed in the epidemiological and clinical characteristics according to JAKi type. 65.6% of patients had at least one of the following characteristics (age ≥65 years, smoker or former smoker, HT, dyslipidemia, diabetes mellitus, ischemic heart disease, neoplasia, cerebral vascular accident or thrombosis). 36% had undergone ≥ 4 biological therapies (BT). During the follow-up period, treatment with a JAKi was withdrawn in 39.1% (n=100) of the cases included. The main reason for withdrawal was inefficacy in 57% (31% primary, 26% secondary), followed by 26% adverse effects and 17% other reasons. After treatment withdrawal with a JAKi, most patients (31.3%) were started on an anti-TNF drug, followed by an IL6 inhibitor (20.2%) or another JAKi (18.2%). Regarding the efficacy of JAKi treatment, a reduction in activity parameters and indices was observed throughout follow-up period as shown in Figure 1.The proportion of responders at follow-up weeks is detailed in Tables 2 and 3. The comparative analysis between responders and non-responders showed no statistically significant differences in descriptive and disease variables, except for number of previous bDMARDs (2 [RIQ 0.3] vs 2 [RIC 1.4], p=0.041, prior antiTNF use (57.8% vs 76.8%, p=0.011) and rituximab (7.4% vs 23.2%, p=0.003). A higher percentage of patients with DAS28 ≤2.6 was observed in the monotherapy group compared to the combinantion treatment (30.3% vs 17%, p=0.037). The median survival was 3.15 years and higher in monotherapy, although without statistically significant differences, Figure 2.

Conclusion: JAKi have been effective in different RA patient profiles while maintaining a good safety profile. In our cohort, although according to the latest recommendations, the use of JAKi would be limited in more than half of the patients, the withdrawal rate due to adverse effects has been low, although a longer follow-up time would be necessary.

Disclosure: M. Lopez-Lasanta: None; **H. Borrell**: None; **M. Salles Lizarzaburu**: None; **V. Ruiz-Esquide**: None; **D. Roig**: None; **A. Nack**: None; **C. Pérez**: None; **J. Bernardez**: None; **A. García**: None; **J. Rovira**: None; **A. Cuervo**: None; **M. Valls**: None; **C. Garcia**: None; **S. Minguez**: None; **R. Morla**: None; **P. Estrada**: None; **M. Martinez**: None; **C. Pitarch**: None; **N. Busquets**: None; **H. Park**: None; **J. Gomez-Puerta**: AstraZeneca, 6, Eli Lilly, 6, Galapagos, 6, GSK, 6, Janssen, 6, Pfizer, 6, Sanofi, 2; **S. Holgado**: None; **N. Montala**: None; **R. Sanmarti**: None; **L. Mateo**: None; **C. Diaz**: None; **H. Corominas**: None; **G. Salvador**: None.

Abstract Number: 0431

Senescence and Cell Exhaustion in CD4+ and CD8+ Lymphocytes in Rheumatoid Arthritis Patients in Remission Without Treatment

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

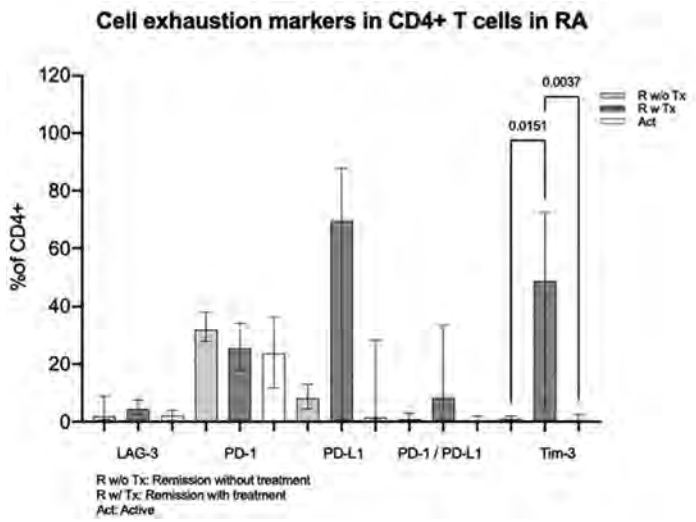
Session Title: RA – Treatments Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: T cells are important among the several risk factors and immunological markers implicated in rheumatoid arthritis (RA). The goal of this study was to look for biological markers of cell exhaustion in CD4+ and CD8+ lymphocytes from RA patients in remission who were not receiving medication.

Methods: A cross-sectional, single-center study was carried out in a tertiary care center in Mexico City. We included 18-year-old patients who met the EULAR/ACR 2010 RA classification criteria. Patients were divided into three groups: G1) remission for 5 years without therapy with DMARDs and/or glucocorticoids; G2) remission on treatment, and G3) active patients. Pregnancy, active infection, cancer, and the presence of other autoimmune diseases (except Sjogren's syndrome) were all exclusion criteria. Relevant clinical and serological parameters were recorded, and a univariate analysis was done with SPSS v29. Flow cytometry with Flow Jo v10 was used to analyze the expression of cell exhaustion markers (CTLA-4, LAG-3, PD-1, PD-L1, and Tim-3).



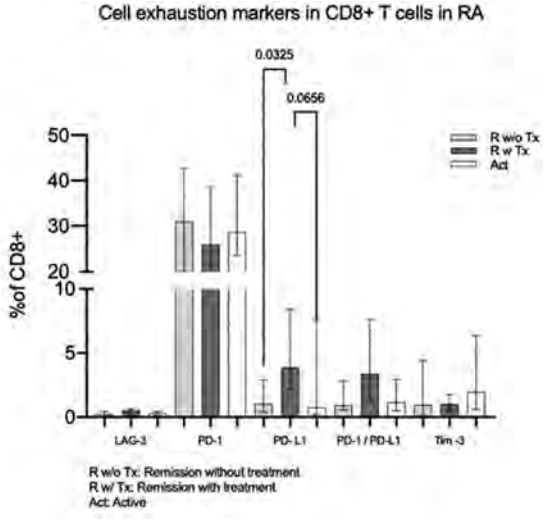


Table 1. Demographic, clinical, laboratory characteristics and treatment of RA patients (n=37).	
Variables	**Total (%) or mean (± SD)**
Age	57.5 (± 12.9)
Female	36 (97.3)
Smoking	5 (13.5)
Hemoglobin (g/dL)	13.53 (± 1.47)
Hematocrit (%)	40.37 (± 3.88)
Leukocytes (10^9/L)	6.38 (± 1.87)
Lymphocytes (10^9/L)	1.60 (± 0.522)
Neutrophiles (10^9/L)	4.28 (± 1.91)
Platelets (10^9/L)	268 (± 81.28)
ESR (mm/hr)	8.22 (±8.32)
CRP (mg/dL)	1.24 (±1.88)
DMARDs	19 (51.3)
MTX	16 (43.2)
HCQ	7 (18.9)
SSZ	5 (13.5)
LFL	5 (13.5)
Group 1	12 (32.4)
Group 2	12 (32.4)
Group 3	13 (35.1)
RA: rheumatoid arthritis, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, DMARDs: disease-modifying antirheumatic drugs, MTX: methotrexate, HCQ: hydroxychloroquine, SSZ: sulfasalazine, LFL: leflunomide.	

Table 2. Comparative analysis between groups				
Variables	**Group 1 (%)**	**Group 2 (%)**	**Group 3 (%)**	**Comparison (p value)**
Smoking	20	60	20	0.367
DMARDs	**0**	**57.9**	**42.1**	**0.001**
HCQ	**0**	**28.6**	**71.4**	**0.032**
MTX	**0**	**62.5**	**37.5**	**0.002**
SSZ	**0**	**20**	**80**	**0.046**
LFL	0	40	60	0.172
RF (UI/mL)	36	28	36	NV
Anti-CCP (U)	36	20	44	0.161
Age	**64.5 (52.75-73)**	**64.5 (52.5-69)**	**49 (41.5-59.5)**	**0.039**
Hemoglobin (g/dL)	**13.86 (12.87-14.57)**	**14.55 (13.87-15.17)**	**12.28 (11.95-13)**	**0.000**
Hematocrit (%)	**41.25 (± 3.88)**	**43.07 (41.82-44.87)**	**37.08 (36.9-38.6)**	**0.000**
ESR (mm/hr)	**4 (2-5)**	**2 (2-5.75)**	**14 (4.5-19)**	**0.034**
CRP (mg/dL)	**0.24 (0.087-0.4675)**	**0.27 (0.2-1.43)**	**1.52 (0.5-2.45)**	**0.008**
RF	198.08 (74.75-317.45)	201.05 (97.8-296.1)	86.61 (34.9-108.85)	0.059
Anti-CCP	234.53 (67.4)-336.12	195.5 (14.1-304)	304.94 (256-343)	0.129
***Data are expressed as number (percentage) or median (interquartile range). Statistical analysis: chi-square test for nominal variables and Kruskal-Wallis test used for numerical variables.** **Values shown in bold represent statistically significant p values.** DMARDs: Disease-modifying antirheumatic drugs, HCQ: hydroxychloroquine, MTX: methotrexate, SSZ: sulfasalazine, LFL: leflunomide, RF: rheumatoid factor, NV: not valuable, anti-CCP: anti-cyclic citrullinated peptide antibody, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein.				

Results: We included 37 patients, 12 (32.4%) of whom were in remission without treatment (G1) and were paired with G2 (32.4%) and G3 (35.1%). The majority (97.3%) were female, the mean age was 57.5 (±12.9) years, and only 5 (13.5%) were smokers. Methotrexate (MTX) was used in 16, hydroxychloroquine (HCQ) in 7, sulfasalazine (SSZ) and leflunomide in 5 each. The mean ESR was 8.22 mm/hr (2-36), and the mean CRP was 1.24mg/dL (0.05-8.74), with no major differences detected between the three groups. When the use of DMARDs was analyzed by group, it was 0%, 57.9%, and 42.1% respectively ($p< 0.001$). HCQ use was higher in G3, with 0% vs 28.6% vs 71.4% ($p=0.032$), while SSZ and MTX were more frequent in G2-3, with 0% vs 20% vs 80% and 0% vs 62.5% vs 31.3%, respectively ($p=0.046$ and $p=0.002$). Other drugs showed no significant differences. Rheumatoid factor was positive in all patients, while anti-cyclic citrullinated peptide antibodies were positive in 90%, 71.4%, and 100%, respectively ($p=0.161$). (Table 1) When comparing numeric values between groups, G3 were younger patients and had higher values of ESR and PCR compared to other groups; with ages 64.5 (52.75-73) vs 64.5 (52.5-69) vs 49 (41.5-59.5) years ($p=0.039$), mean ESR of 4 (2-5) vs 2 (2-5.75) vs 14 (4.5-19) mm/hr ($p=0.034$), and mean CPR of 0.24 (0.0875-0.4675) vs 0.27 (0.2-1.43) vs 1.52 (0.5-2.455) mg/dL ($p=0.008$). Other variables were studied; however, no statistical significance was found. (Table 2)Cell exhaustion markers in CD4+ were higher in G2, except for PD-1, with LAG-3, PD-L1, ratio PD-1/PD-L1, and Tim-3 being significant ($p=0.0052$), whereas in CD8+, only the expression of PD-L1 was significantly different ($p=0.0325$) (Image 1). These findings suggest that G2 induces increased cell exhaustion, and treatment may be the primary determining factor. However, the limited sample size may have an impact on the findings.

Conclusion: To the best of our knowledge, this is the first study that assess multiple markers of cell exhaustion in RA patients, with expression perhaps related to remission and/or treatment. Further research with larger sample sizes is required to confirm our findings.

Disclosure: R. Jiménez-Soto: None; **L. Ilorente**: None; **G. Lima**: None; **L. Alanis Saenz**: None; **A. Gomez Rodriguez**: None; **H. Marin Lopez**: None; **E. Cimé-Aké**: None; **J. Jakez-Ocampo**: None.

Abstract Number: 0432

Predictors of Use, Survival and Safety of Tofacitinib Monotherapy vs. in Combination with CsDMARDs in Daily Clinical Practice

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Different guidelines recommend the use of tofacitinib either in monotherapy or combined with methotrexate (combination therapy) in patients with rheumatoid arthritis (RA) with an inadequate response to conventional synthetic DMARDs (csDMARDs) or biologic DMARDs (bDMARDs). Although the evidence originating from clinical trials does not show notable differences in terms of efficacy and safety with both strategies, data from real life is limited.

To evaluate the frequency, predictors of use and survival of tofacitinib in monotherapy compared with combination therapy in a cohort of patients with RA from daily clinical practice in our country.

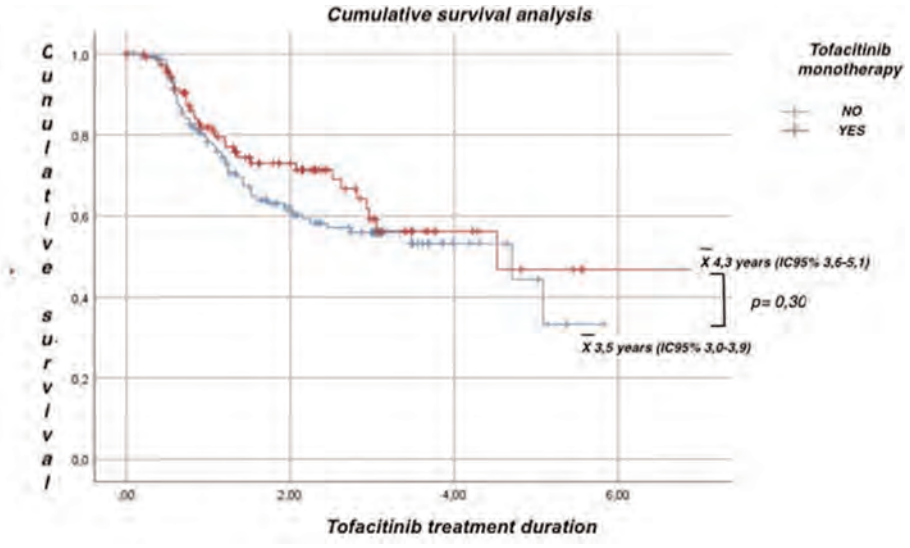
Methods: Longitudinal, observational study which includes a cohort of patients with RA (ACR/EULAR 2010 criteria) from different rheumatology centers who started treatment with tofacitinib. Patients were evaluated at baseline and followed up every six months from the start of medication. Sociodemographic, clinical and treatment data were collected. Chi2 test, Fisher's exact test, Student's T test and Mann Whitney were used according to the nature of the variables. Kaplan-Meier method and the Log Rank test were applied to compare survival of treatment in monotherapy vs. combination therapy. Cox regression analysis was used to evaluate variables associated with lower survival. The incidence of adverse events (AEs) was calculated as events every 100 patients/year (p/y). A $p< 0.05$ was considered significant.

Results: 269 patients were included, 87% female, mean age 56.3 years (SD 13.6), of which 41.3% started treatment with tofacitinib monotherapy. Main reasons for monotherapy use were previous adverse events with csDMARD (16%) and physician's decision (16%). In the univariate analysis, no significant association was found between the use of monotherapy and different sociodemographic and clinical variables. In the multivariate analysis, fewer prior cs-DMARDs combination therapy and prior use of biologic therapy were significantly associated with initiation of tofacitinib monotherapy ($p< 0.05$, both) (table). During follow-up (502.4 patients/year), no statistically significant differences were found in tofacitinib survival between the two groups (figure). Regarding safety, 110 patients (40.9%) had at least 1 AE, the most frequent being infections (57.6%),

	Monotherapy n= 111	Combination n= 158	p
Females, n (%)	98 (88,3)	136 (86,1)	0,7
Age (years), m (SD)	57,4 (12,2)	55,5 (14,5)	0,2
Disease duration (years), *m (IQR)*	12,4 (9,8)	10,6 (8,2)	0,1
Ever Smoking, n (%)	12 (11,4)	26 (17)	0,4
Extra-articular manifestations, n (%)	50 (45)	72 (45,6)	0,9
Rheumatoid nodules, n (%)	22 (19,8)	38 (24,1)	0,4
ILD, n (%)	13 (11,7)	9 (5,7)	0,1
FR positivity, n (%)	95 (85,6)	140 (88,6)	0,4
ACPA positivity, n (%)	96 (90,6)	131 (89,7)	1
Previous therapy with combination of cs-DMARDs	**55 (49,5)**	**103 (65,2)**	**0,01**
Previous therapy with b-DMARDs	**71 (64)**	**81 (51,3)**	**0,04**

*n: number; m: media; SD: standard deviation; *m:* median; IQR: interquartile range; ILD: interstitial lung disease; RF: rheumatoid factor; ACPA: anti-citrullinated protein antibodies; csDMARDS: conventional disease-modifying antirheumatic drugs; b-DMARDs: biologic disease-modifying antirheumatic drugs

Predictors factors of initiation of treatment with tofacitinib monotherapy



Cumulative survival analysis between tofacitinib monotherapy vs. combination therapy

others (16.7%), and gastrointestinal (9.5%). When evaluating the incidence rate (IR) of AEs, no significant differences were found between tofacitinib monotherapy and combination therapy: 47.2 events (100 p/y) (95% CI 38.6-57.5) vs. 38.05 events (100 p/y) (95%CI 31.6-45.7), respectively (p=NS).

Conclusion: In this real-life study, the use of tofacitinib monotherapy was almost 40%, being associated with less prior treatment with csDMARDs and prior use of biologic therapy. Tofacitinib monotherapy demonstrated similar drug survival and safety compared to the use in combination with csDMARDs, and may be a valid option for patients with RA in daily clinical practice.

Disclosure: R. Perez-Alamino: None; **C. Isnardi**: None; **E. Soriano**: AbbVie, 2, 5, 6, Amgen, 6, Bristol-Myers Squibb, 6, Eli Lilly, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Roche, 2, 5, 6, UCB, 5, 6; **L. Lo Giudice**: None; **j. zacariaz hereter**: None; **G. Casado**: None; **V. Caputo**: None; **A. Schmichowski**: None; **C. Romeo**: None; **E. Rivero**: None; **F. Savy**: None; **M. García**: GSK, 6, Janssen, 6, Pfizer, 6; **O. Romano**: None; **H. Maldonado Ficco**: None; **G. Citera**: None.

Abstract Number: 0433

DMARD Initiation in Older Adults with New Diagnosis of Late-Onset Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The number of older adults living with rheumatoid arthritis (RA) is growing as the world population is aging. Up to one-third of the older RA population are diagnosed after the age of 65 and have late-onset RA (LORA) which is characterized by more symptomatic and progressive disease. Older adults with RA are less likely to receive optimal treatment despite disease modifying anti-rheumatic drug (DMARD) being effective and generally well tolerated in older adults. In addition, they are prone to the negative effects of glucocorticoids (GCs) which are symptom relieving but not disease modifying. We evaluated the prevalence of and factors associated with disease modifying anti-rheumatic drug (DMARD) initiation and glucocorticoid (GC) use in older adults with new diagnosis of LORA.

Methods: In this retrospective observational study, we identified adults ≥66 years of age with new diagnosis of LORA using 20% Medicare data from 2008-2017. Information on baseline patient characteristics and DMARD initiation during the first 12 months after LORA diagnosis were collected. Concomitant long-term (>90 days) GC use and GC monotherapy (GC use >180 days without any DMARD) was also evaluated. We performed multivariable logistic regression for factors associated with DMARD initiation.

Results: We identified 33,373 older adults with new diagnosis of LORA in continuous fee-for-service Medicare. Average age at LORA diagnosis was 76.7 (SD 7.6), 75.4% were female, 76.9% were non-Hispanic white, and 35.6% had low-income subsidy. Less than one third (28.9%) were initiated on some form of DMARD during the first 12 months after LORA diagnosis. The proportion of older adults initiated on DMARDs was stable between 2009-2015 and ranged between 26.7-30.8%

(Figure 1). Among those on any DMARD treatment (N=9640), 90.1% were initiated csDMARD only, 2.6% on bDMARD only, and 6.8% on both classes of DMARDs. Concomitant long-term GC use was observed in 44.3% of older adults on DMARDs. Among those without DMARD use (N=23,733), 10.8% were on GC monotherapy alone. In multivariable analyses, DMARD initiation was associated with younger age, fewer comorbidities, absence of low-income subsidy status, adjusting for patient sex and race/ethnicity (Table 2).

Table 1: Characteristics of Medicare beneficiaries with new diagnosis of LORA

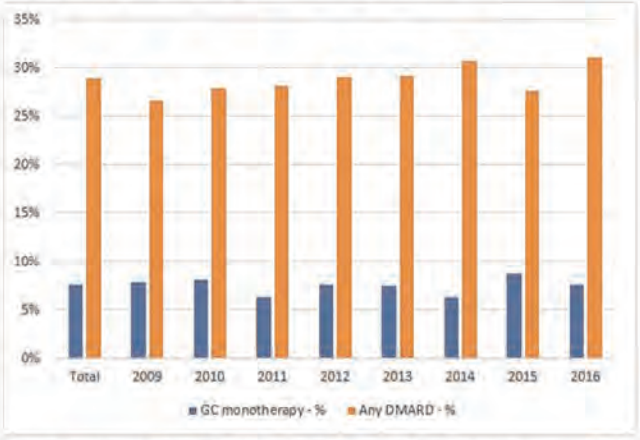
	No DMARD initiation N=23733	Any DMARD initiation M=9640	p-value
Age at diagnosis, mean (SD)	77.6 (7.9)	14.4 (6.3)	<0.0001
Female, n (%)	18079 (76.2)	7081 (73.4)	<0.0001
Race, n (%)			<0.0001
...White	17957 (75.6)	7695 (79.8)	
...Black	2606 (11.0)	818 (8.5)	
Hispanic	2144 (9.0)	694 (7.2)	
Other	1026 (4.3)	433 (4.5)	
Low Income Subsidy, n (%)	9420 (39.7)	2473 (25.5)	<0.0001
Comorbidity, n (%)			<0.0001
<3	9082 (38.3)	4859 (50.4)	
3-5	10196 (43.0)	3768 (39.1)	
≥6	445 (18.8)	1013 (10.5)	

Table 2: Patient characteristics associated with initiation of any DMARD after new diagnosis of LORA among Medicare beneficiaries ≥66 years of age

Variables	OR (95% CI)	
	Unadjusted	Adjusted
Age at dx	0.94 (0.94, 0.95)†	0.95 (0.94, 0.95)†
Female	0.87 (0.82, 0.91)†	0.99 (0.94, 1.05)
Race		
White (Ref)	1	1
Black	0.73 (0.67, 0.8)	0.94 (0.86, 1.03)
Hispanic	0.76 (0.69, 0.83)	1.01 (0.92, 1.11)
Other	0.99 (0.88, 1.11)	1.12 (0.99, 1.26)
Low Income Subsidy	0.52 (0.5, 0.55)†	0.57 (0.54, 0.61)†
Comorbidity		
<3 (ref)	1	1
3-5	0.69 (0.66, 0.73)†	0.81 (0.77, 0.85)†
≥6	0.43 (0.39, 0.46)†	0.54 (0.5, 0.59)†

†statistically significant (adjusted model) with p<0.05

Figure 1: Proportion of older adults with DMARD initiation or glucocorticoid monotherapy (without any DMARDs) after new diagnosis of LORA



DMARD=disease modifying anti-rheumatic drugs, GC=glucocorticoids, GC monotherapy=GC use only for >180 days without any DMARD use

Conclusion: DMARD use in older adults with new diagnosis of LORA is low despite current clinical practice guidelines recommending early aggressive initiation of treatment. Concomitant long-term GC use and GC monotherapy use among those on any DMARDs is common, raising concern for suboptimal DMARD use. Further studies are needed to understand drivers of DMARD use in older adults.

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Abstract Number: 0434

Effects of B/tsDMARDs on Non-inflammatory Pain in Patients with Rheumatoid Arthritis -ANSWER Longitudinal Cohort Study-

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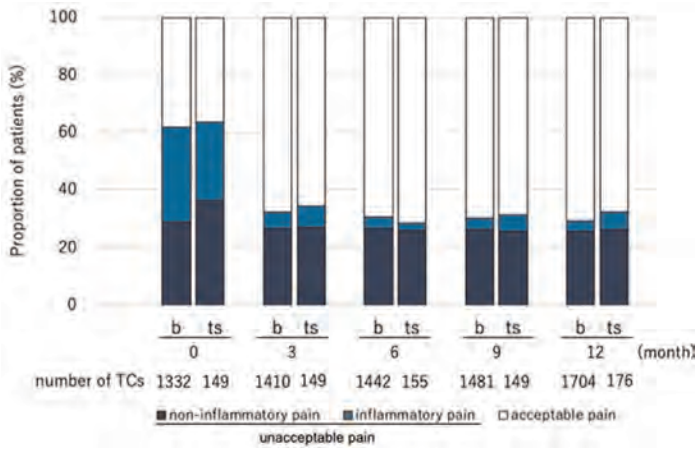
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Non-inflammatory pain (NIP) is one of the remaining issues in rheumatoid arthritis (RA), and some previous studies suggest that 10-20% of patients with RA remain with NIP even after treatment with biological disease modifying anti rheumatic drugs (bDMARDs). Targeted synthetic DMARDs (tsDMARDs) is reported to improve patient-reported-outcomes including pain, but its effect on NIP is unclear. The aim of this study is to investigate whether tsDMARDs can relieve NIP compared to bDMARDs in RA patients in a longitudinal multicenter cohort study.

Methods: RA patients treated with b/tsDMARDs between 2000 to 2022 and continued the same drug for more than 12 months were included in this study. Unacceptable pain (UP) was defined as patient-visual analog scale (VAS) > 40 mm and was classified to two categories; NIP and inflammatory-pain (IP). NIP was defined as UP with C-reactive protein level < 10 mg/liter. We also assigned a strict definition for NIP (sNIP) as NIP with swollen joint count ≦1. IP was defined as UP without fulfilling the NIP definition. We examined the association between the choice of b/tsDMARDs and the persistence of NIP at month (Mo) 12 using logistic regression model. The frequency of NIP, IP and UP at Mo 0, 3, 6, 9 and 12 were also assessed. Confounding factors (age, sex, disease duration, number of previous b/tsDMARDs, smoking status, stage, class, titer of rheumatoid factor and anti-citrullinated protein/peptide antibodies, dose of methotrexate and prednisolone, the use of painkillers and disease activity at baseline) were adjusted



Time-dependent changes in pain of patients treated with b/tsDMARDs

with inverse probability of treatment weighting estimated by generalized propensity score. Missing data were dealt with multiple imputation to calculate generalized propensity score.

Results: Of 1880 treatment courses (TCs), 1704 TCs were treated with bDMARDs and 176 TCs were treated with tsDMARDs. The rate of UP at baseline was 61.8% in bDMARDs and 63.8% in tsDMARDs. These rates decreased significantly to 32.2% in bDMARDs ($p < 0.001$) and 34.2% in tsDMARDs ($p < 0.001$) at Mo 3, respectively, which remained stable at Mo 12. The rates of IP in both bDMARDs and tsDMARDs also significantly declined at Mo 3, and then remained stable at Mo 12. On the other hand, NIP was present in 28.8% of TCs in bDMARDs and 36.2% of TCs in tsDMARDs at baseline, which remained in 25.6% and 26.1% at Mo 12, respectively (figure). Analysis with sNIP did not change the trend. The proportion of NIP in UP was 46.6% in bDMARDs and 56.8% in tsDMARDs at baseline, which increased to 87.5% and 80.7% at Mo 12. There was no statistically significant difference in frequency of NIP at Mo 12 among b/tsDMARDs in both definitions [NIP: adjusted odds ratio (OR) = 0.79 (95% confidence interval (CI) : 0.53-1.18, p = 0.25), sNIP: adjusted OR = 0.73 (95%CI : 0.46-1.14, p = 0.16)].

Conclusion: In RA patients who were able to continue b/tsDMARDs for 12 months, the effects of tsDMARDs against NIP was comparable to that of bDMARDs. The frequency of RA patients with NIP treated with b/tsDMARDs for 12 months remained 25%, while that of IP were decreased.

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Abstract Number: 0435

Changes in Characteristics of Patients Initiating and Discontinuing Advanced Therapies for Rheumatoid Arthritis Following Release of Safety Data

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: RA – Treatments Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The ORAL Surveillance study highlighted risks of cardiac events, thromboembolism (VTE), and cancer associated with Janus kinase inhibitors (JAKi). The aim of this study was to understand the effect that these data have had on practice patterns by describing the characteristics of patients initiating advanced therapies for RA including tofacitinib (TOFA), TNF inhibitors (TNFi), and non-TNFi agents before and after the release of safety data in January 2021 and to evaluate characteristics associated with discontinuation among active users at the time that the data was released.

Table 1. Characteristics of Tofacitinib Initiators Before and After January 2021 Oral Surveillance Press Release

	Before	After	p-value
N	2111	1664	
Demographics			
Age in years, mean (SD)	**64.1 (11.3)**	**63.0 (12.1)**	**<0.01**
Female (%)	**20.8**	**25.9**	**<0.001**
White (%)	**75.3**	**70.0**	**<0.001**
Black (%)	**14.8**	**19.0**	**<0.01**
Rheum visits per year (SD)	**3.1 (2.6)**	**2.4 (2.4)**	**<0.001**
Current smoker (%)	25.7	26.8	0.27
Comorbidities*			
BMI kg/m^2, mean (SD)	30.2 (6.4)	29.9 (6.5)	0.40
RDCI, mean (SD)	**4.6 (2.1)**	**4.4 (2.1)**	**<0.01**
Hypertension (%)	**73.7**	**69.7**	**<0.01**
Hyperlipidemia (%)	**74.5**	**69.0**	**<0.001**
Heart failure (%)	**14.5**	**10.8**	**<0.01**
Coronary artery disease (%)	**33.0**	**24.8**	**<0.001**
Vascular disease (%)	**19.9**	**16.0**	**<0.01**
Cerebrovascular disease (%)	**14.9**	**10.2**	**<0.001**
Venous thromboembolism (%)	10.9	10.3	0.57
Diabetes (%)	47.0	45.6	0.40
Kidney disease (%)	66.6	64.4	0.17
Any Malignancy (%)	21.4	18.6	0.03
Skin cancer (%)	**14.2**	**11.3**	**0.01**
Prostate (%)	5.8	5.8	0.99
Lung (%)	2.1	1.9	0.57
Colon (%)	1.3	1.1	0.61
GI (%)	0.71	0.60	0.68
Lymphoproliferative (%)	1.7	0.8	0.01
COPD or asthma (%)	45.5	42.5	0.07
Liver disorder (%)	22.8	20.4	0.07

*Categorized using Healthcare Cost and Utilization Project Clinical Classification Software

Methods: This was a national, retrospective study of US Veterans with RA receiving advanced therapies between April 2019 through September 2022. This period was divided into two 664-day periods, one before and one after the January 2021 press release. Eligible patients had ≥1 diagnosis code for RA and initiated a TNFi, non-TNFi, or TOFA. Patient characteristics were defined for each therapy initiation including a comorbidity index (RDCI), and individual comorbidities were categorized using Healthcare Cost and Utilization Project Clinical Classification Software. We tested for interaction within regression models to determine whether changes observed in characteristics (standardized differences) for TOFA users were different from changes observed for the other therapies. We also determined the time to discontinuation for active users at the time of the press release, censoring for death and end of follow-up. We used Cox models adjusted for age, sex, and duration on therapy to evaluate for associations between patient characteristics and therapy discontinuation, testing for interactions with TOFA vs. TNFi.

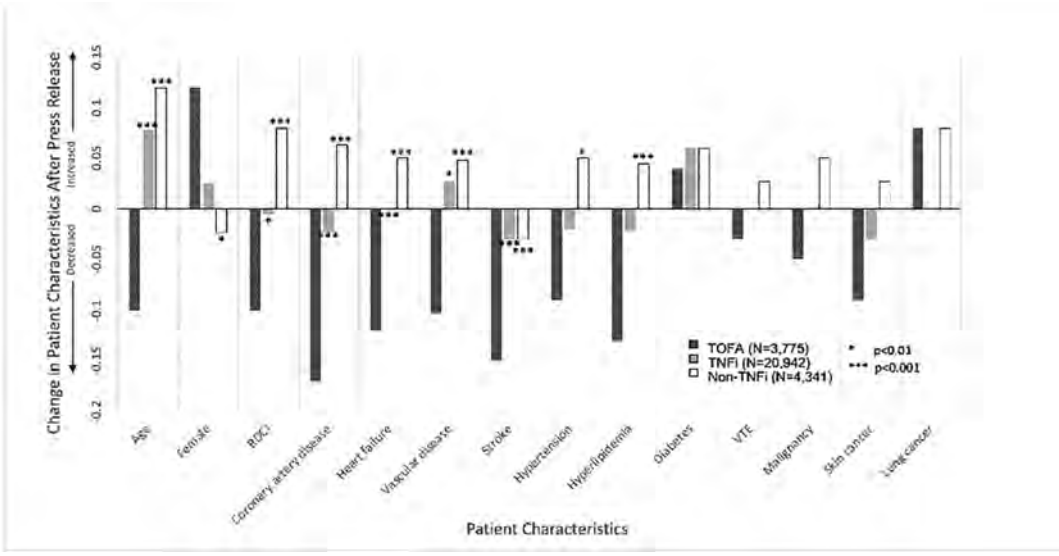

Figure 1. Change in patient characteristics (per 1 SD) by therapy after the January 2021 Oral Surveillance press release. Statistical testing comparing TNFi and non-TNFi therapies to tofacitnib (based on the significance of interaction terms within regression models) are illustrated with asterisks.

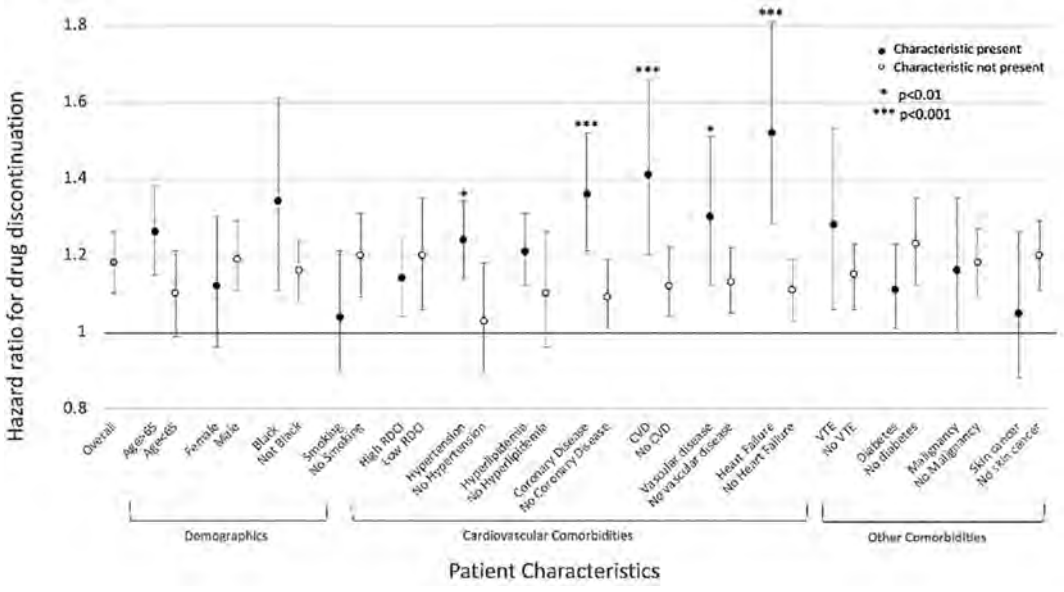

Figure 2. Hazard ratio of discontinuation for tofacitinib compared to TNFi following the ORAL Surveillance press release, stratified by patient characteristic. P-values for multiplicative interactions between tofacitinib and TNFi are illustrated with asterisks. Infliximab and rituximab were excluded because of the length of their dosing cycles.

Results: When comparing patients initiating TOFA before (N=2111) and after (N=1664) January 2021, there were decreases in mean age (64.1 vs 63.0), the proportion of men (20.8% vs 25.9%), mean RDCI score (4.6 vs 4.4), and the proportion with cardiovascular comorbidities and skin cancer (**Table 1**) (all p< 0.01). These changes were significantly different from those observed for patients initiating TNFi or non-TNFi biologic drugs (p for interaction with therapy < 0.05) (**Figure 1**). In contrast, changes in VTE, smoking, and malignancies, including skin cancer, were not significantly different between TOFA initiators and initiators of other therapies. Among active users, the likelihood of discontinuation was higher among TOFA (N=2295, HR: 1.18 [1.10, 1.26], p< 0.001) compared to TNFi (N=12,042). The higher rate of TOFA discontinuation was more pronounced in the presence of cardiovascular comorbidities (**Figure 2**).

Conclusion: Shifts toward younger age, female sex, lower comorbidity, and lower rates of cardiovascular diseases were observed in patients initiating TOFA after the release of safety data. There was a lower proportion of VTE and malignancy as well, which did not reach significance. TOFA users, particularly those with cardiovascular comorbidities, were more likely than TNFi users to discontinue ongoing therapy following the release. These data suggest the ORAL Surveillance trial affected prescribing practices, with particular attention to those at high cardiovascular risk.

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Abstract Number: 0436

Patients with Difficult-to-treat Rheumatoid Arthritis Have Higher Levels of Inflammation on Ultrasound

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: With increasing numbers of advanced therapies, rheumatologists frequently see Rheumatoid Arthritis (RA) patients who have failed ≥2 advanced therapies with different mechanisms of action. The management of difficult-to-treat (D2T)-RA patients is challenging, and there is an unmet need to understand the factors leading to D2T-RA. In this analysis, we aimed to compare the disease characteristics and activity of our D2T-RA patients with other RA patients who are starting a new advanced therapies for having active RA.

Methods: Within the ORCHESTRA Clinic (Ottawa Rheumatology CompreHEnSive TReartment and Assessment) at the Ottawa Hospital, all patients with inflammatory arthritis that are planning to initiate a new advanced therapy are assessed in a standardized fashion. Extensive data regarding disease history, medication exposure and disease activity measures are collected; the comorbidity burden is documented and managed. A protocoled ultrasound (US) of 36 joints is conducted at baseline and three-month intervals, until reaching clinical remission. All joints are scored using the Global OMERACT-EULAR Synovitis Score (GLOESS). For this analysis, the D2T-RA definitions were based on the EULAR definition and

patients falling into this category had failed ≥2 biologics therapies[1]. Here we present the results from a pilot exploratory comparative analysis to identify the differences between the D2T-RA patients with the rest of the cohort.

Results: Among 64 RA patients included the study, 18 (28.1%) fulfilled the definition of D2T-RA. Demographic characteristics were similar between two groups, except female sex being slightly higher in D2T-RA patients and having longer disease duration (table). Seropositivity was similar across groups. DT2-RA patients had statistically significant more deformity in their joints than the rest of the group with higher HAQ scores and numerically more erosive disease. There were no differences between groups in terms of comorbidities, except urate levels being but significantly higher in D2T-RA patients (median (IQR): 319 umol/L (98) vs 256 umol/L (103); p=0.05). Regarding disease activity, D2T patients have numerically higher tender joint counts and CDAI scores. The GLOESS scores of D2T-RA patients on US were significantly higher with a trend to have higher Doppler scores (table).

Conclusion: In our D2T RA population, higher disease activity on US suggests an uncontrolled inflammatory process, which may or may not be complicated by centralized pain mechanisms. A greater portion of D2T patients were females, highlighting the importance of incorporating sex into research and understanding the factors leading to poor response in this group.

Table. Comparison of D2T RA patients with others

		D2T: No (N:46)	D2T: Yes (N:18)	p
Disease Features	**RF positive#**	34 (75.6%)	14 (77.8%)	1.000
	Anti-CCP positive#	27 (61.4%)	13 (72.2%)	0.417
	ESR or CRP elevated#	28 (60.9%)	8 (44.4%)	0.234
	Disease duration (years) *	6 (14)	22.5 (16.8)	**<0.001**
	Erosive disease#	26 (56.5%)	14 (77.8%)	0.114
	Deformities#	12 (26.1%)	11 (61.1%)	**0.009**
	Urate (umol/L)*	256 (103)	319 (98)	**0.050**
Previous therapies *	**Previous number of csDMARDs**	3 (1)	2 (2)	**0.006**
	Previous number of advanced therapies	0 (0)	3 (2)	**<0.001**
Disease activity *				
Clinical	**Duration of morning stiffness (hours)**	0.75 (1.5)	0.5 (1.4)	0.289
	Swollen joint count (28)	5 (4)	6.5 (6)	0.179
	Tender joint count (28)	3.5 (10)	8.5 (10)	0.166
	Swollen joint count (44)	7 (6)	7 (4)	0.389
	Tender joint count (44)	7 (13)	11.5 (9)	0.153
	Patient VAS	5 (4)	6 (3)	0.171
	Physician VAS	5 (3)	5.5 (3)	0.145
	HAQ	1.00 (1.31)	1.375 (1.16)	**0.008**
	CDAI	17.5 (17)	25.5 (13)	0.059
	DAS28ESR	4.08 (1.87)	4.43 (1.19)	0.249
Ultrasound	**Ultrasound: GLOESS score**	27 (18)	48 (42)	**0.016**
	Ultrasound: Doppler score	6 (8.5)	12 (26.5)	0.064

n (%), * median (IQR)

GLOESS: Global OMERACT-EULAR Synovitis Score

Higher urate levels in D2T-RA may be due to increased disease duration, however, it would be noteworthy to look at the impact of urate crystals joint deposition in resistance to therapies. In addition,to date, fibromyalgia status is self-reported by our participants likely resulting in under-reporting. As this is a significant predictor of D2TRA, we will begin completing the Widespread Pain Index/Symptom Severity Scale in our cohort patients to better understand the predictors of D2TRA in our setting.

1.Nagy G.AnnRheumDis.2021

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Abstract Number: 0437

Comparative Safety of Biologic and Targeted Synthetic Disease Modifying Anti-Rheumatic Drugs for Cardiovascular Outcomes in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: RA – Treatments Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1. Baseline characteristics of RA cohort stratified by different drug exposures

Variable	TNFi n=31,008 (71%)	Non-TNFi n=8591 (19%)	JAKi n=4309 (10%)
Age in years (median, IQR)	50 (41, 56)	51 (43, 56)	50 (43, 56)
Female, n (%)	24,078 (78)	6824 (79)	3457 (80)
Geographic region, n (%)			
Northeast	4429 (14)	1443 (17)	691 (16)
North Central	6147 (20)	1669 (19)	775 (18)
South	15,277 (49)	4059 (47)	2216 (51)
West	4686 (15)	1313 (15)	603 (14)
Year of initiating biologic drug (median, IQR)	2016 (2014, 2018)	2016 (2014, 2019)	2019 (2016, 2020)
Days from RA diagnosis to initiating biologic drug (median, IQR)	430 (200, 920)	630 (320, 1250)	650 (350, 1240)
Charlson comorbidity score, n (%)			
1-2	26,376 (85)	6000 (70)	3563 (83)
3-4	3606 (12)	1774 (21)	581 (13)
Frailty score (0 [not at all frail]-1 [severely frail]), median (IQR)	0.14 (0.12, 0.16)	0.15 (0.12, 0.17)	0.14 (0.12, 0.16)
Any hospital admissions, n (%)	2659 (9)	1415 (16)	351 (8)
Any emergency department visits, n (%)	8473 (27)	3084 (36)	1072 (25)
Any opioid prescription fills, n (%)	12,159 (39)	3501 (41)	1548 (36)
Any NSAID opioid prescription fills, n (%)	17,272 (56)	3817 (44)	2422 (56)
Concomitant csDMARDs, n (%)	21,460 (69)	4129 (48)	2812 (65)
Concomitant DMARDs, n (%)	14,289 (46)	3751 (44)	1822 (42)

Abbreviations: IQR: Interquartile range; NSAID: Non-steroid anti-inflammatory drug; TNF: Tumor necrosis factor

Background/Purpose: Concern has arisen over the safety of Janus kinase inhibitors (JAKi) regarding cardiovascular (CV) outcomes in patients with rheumatoid arthritis (RA) with CV risk factors based on results of the ORAL surveillance trial (1). We compared the risk of major adverse cardiovascular events (MACE) between tumor necrosis factor inhibitors (TNFi), non-TNFi, and JAKi among patients with RA.

Methods: We performed a cohort study using Merative MarketScan databases (2012-2021) of RA patients (including those with pre-existing CV risk factors) identified using ≥1 ICD-9/10 codes, age 18-64 years, who initiated treatment with TNFi, non-TNFi, or JAKi. We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for developing MACE (a composite of myocardial infarction, cardiac arrest, sudden death, stroke, percutaneous coronary intervention, coronary artery bypass graft, identified using ICD-9/10 codes and CPT codes) within 2 years of treatment initiation, adjusting for multiple confounders, including age, sex, region, comorbidity index, frailty (2), healthcare utilization, and surrogates for RA severity. Patients could contribute person-years to multiple drug exposures only if drug escalation mimicked typical clinical practice and were censored if they did not fill a prescription of these drugs for >90 days (>180 days for rituximab due to its longer washout period) or their enrollment ended.

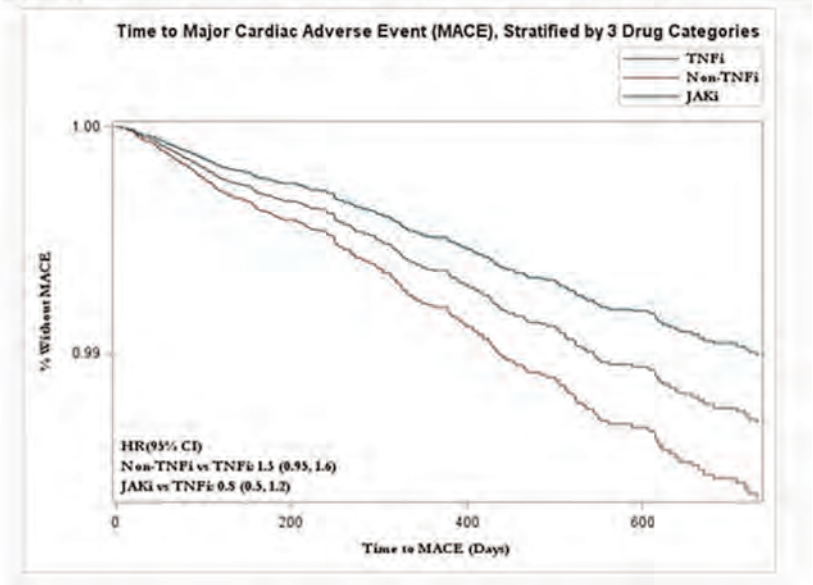
Results: A total of 40,207 patients met eligibility criteria for our study (71% initiated on TNFi, 19% non-TNFi, and 10% JAKi). Most patients were female (78-80%) with the mean age ranging from 47-49 years (Table 1). The median follow-up time was 230 days for TNFi, 190 days for non-TNFi, and 180 days for JAKi. The number of MACE per drug class was highest in non-

Table 2. Number and incidence rate of MACE outcomes within 2 years of initiating biologic drug per 10,000 person-years at risk, stratified by DMARD category

	Raw n of MACE	Incidence rate of MACE /10,000 person-years (95% confidence interval)	Median (IQR) days to MACE (among those with MACE)
TNFi	202 (0.7%)	78 (68, 90)	207 (85, 378)
Non-TNFi	87 (1.0%)	150 (121, 185)	102 (48, 252)
JAKi	20 (0.5%)	66 (40, 102)	180 (94, 271)

Abbreviations: DMARD: disease-modifying antirheumatic drug; JAKi: Janus kinase inhibitors; MACE: Major adverse cardiovascular events; TNFi: tumor necrosis factor inhibitors

Figure 1. Kaplan-Meier curves showing adjusted HR* for incident MACE per different drug class exposures



*Models adjusted for age, sex, Charlson Comorbidity Index, frailty status, healthcare utilization within 12 months prior to starting treatment, days from RA diagnosis to initiating biologic, and disease-modifying antirheumatic drug, nonsteroidal anti-inflammatory drug and opioid fills in 12 months prior to starting treatment and glucocorticoid use 3 months prior to starting treatment)

TNFi exposures (Table 2). In multivariable models, patients taking non-TNFi had an HR (95% CI) 1.3 (0.95, 1.6) compared to those taking TNFi (Figure 1). Patients on JAKi had a similar risk of developing MACE (HR 0.8; 95% CI 0.5, 1.2) compared to those on TNFi, although this was statistically non-significant.

Conclusion: In this large nationwide study, although users of non-TNFi had increased risk of MACE, we did not detect any statistically significant difference overall. However, our study has limitations of residual confounding (e.g., inadequate accounting for RA severity using claims data, the fact that most RA patients initiate treatment with TNFi's before proceeding to non-TNFi's or JAKi's in clinical practice, and the small number of MACE outcomes in the study population). Additional studies with longer follow-up are needed for better assessment of MACE risk to guide clinical care.

References:

1. Ytterberg SR, Bhatt DL, Mikuls TR, Koch GG, Fleischmann R, Rivas JL, et al. Cardiovascular and Cancer Risk with Tofacitinib in Rheumatoid Arthritis. N Engl J Med. 2022;386(4):316-26.
2. Kim DH, Schneeweiss S, Glynn RJ, Lipsitz LA, Rockwood K, Avorn J. Measuring Frailty in Medicare Data: Development and Validation of a Claims-Based Frailty Index. J Gerontol A Biol Sci Med Sci. 2018;73(7):980-7.

Disclosure: X. Sendaydiego: None; **L. Gold**: None; **K. Wysham**: None; **J. liew**: None; **M. Dubreuil**: Amgen, 2, Pfizer, 5, UCB Pharma, 2; **J. Andrews**: None; **P. Reid**: None; **D. Liew**: None; **R. Goulabchand**: Novartis, 2; **A. Singh**: AbbVie/Abbott, 5, Novartis, 5, Pfizer, 5; **G. Hughes**: Janssen, 3; **M. Pioro**: None; **J. Sparks**: AbbVie, 2, Amgen, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, 5, Gilead, 2, Inova Diagnostics, 2, Janssen, 2, Optum, 2, Pfizer, 2, ReCor, 2; **J. Jarvik**: GE Healthcare, 12, Travel reimbursement for Faculty Board of Review for GE-Association of University Radiologists Radiology Research Academic Fellowship (GERRAF), Springer Publishing, 9, Wolters Kluwer/UpToDate, 9; **S. Singh**: None; **N. Singh**: None.

Abstract Number: 0438

Association Between Methotrexate Use and Lymphoma in Rheumatoid Arthritis: A Systematic Literature Review

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis (RA) patients have an increased risk of developing lymphoma compared to the general population. This increased risk is believed to be linked to higher disease activity. Methotrexate (MTX), a commonly used treatment for RA, has the potential to reduce the risk of lymphoma by lowering disease activity. However, existing research on the association between MTX use in RA and lymphoma development presents conflicting results. This study aimed to conduct a systematic literature review to evaluate this association.

Methods: A comprehensive search was performed in PubMed, Embase, and Cochrane Central Register of Controlled Trials on December 9, 2021. The search included observational studies and randomized controlled trials (RCTs) published in English, focusing on the relationship between MTX use in RA and lymphoma development. Case series and reports were

Figure 1. PRISMA flow diagram

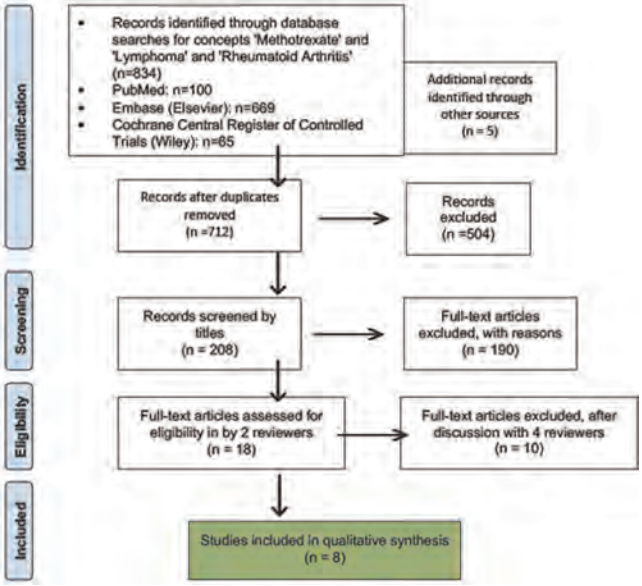

Table 1. Characteristics of the included studies

Author, year	Study location; period	Number of patients with RA	Number of patients with lymphoma	Effect estimates of the association (95% CI)
Bernatsky, 2008	Canada; 1980-2003	23 733	346	OR 1.23 (0.97-1.57)
Hashimoto, 2015	Japan; 2002 - 2012	66,953 patient - years	63	**OR 3.5 (2.0–6.3)**
Hellgren, 2017	Sweden; 1997-2012	12,656	62	RR =0.9 (0.8–1.0)
Kedra, 2021	France; 1971–2016	162	54	-Univariate analysis: OR - 1.0 (0.3 to 3.4); p value 0.97 -Sensitivity analysis: OR - 0.78 (0.10-5.93); p value 1.00
Honda, 2022	Japan; 2011	9815	68	MTX use versus no MTX use based on MTX dose: 0 to 8 mg: **HR: 2.35 (1.25-4.42);** >8 mg: **HR 4.39 (2.07-9.32)**
Setoguchi, 2006	US and Canada; 1994 -2004	7,830	58	bDMARD versus MTX; HR:1.11 (0.51–2.37)
Lee, 2014	151 centers worldwide; 2010- 2013.	958	3	3 lymphomas in Tofacitinib group; 0 in MTX group
Solomon, 2014	US; 2001 -2010	6806	2865 Person-years	TNFI versus MTX; HR- 0.15 (0.01–2.19)

CI- Confidence Interval; OR- Odds Ratio; RR- Relative Risk; MTX- Methotrexate; HR- Hazard Ratio; DMARD- Disease Modifying Antirheumatic Drug; TNFI- Tumor Necrosis Factor Inhibitor; RA- Rheumatoid arthritis

excluded. Data were extracted from the selected articles by two independent authors using a predefined form, with conflicts resolved by a third reviewer. Quality assessments were conducted.

Results: The search process identified 839 articles, out of which only eight met the eligibility criteria (Figure 1). Table 1 summarizes the characteristics of these studies, which predominantly consisted of observational studies, with one RCT included. The sample sizes ranged from 160 to 20,000 RA patients. Five studies reported odds/hazard ratios for lymphoma occurrence in MTX-exposed versus non-exposed patients. Three studies (one of which was an RCT) compared the risk of lymphoma development in RA patients treated with MTX versus other biological DMARDs. Most studies adjusted for various factors, including age, sex, RA disease activity measures, inflammatory markers, concomitant RA medications, cancer risk factors, and RA-related variables. Six of the eight studies found no significant association between MTX use and lymphoma, while two studies from Japan reported a significant positive association. The included studies were of moderate to high quality, but heterogeneity prevented a meta-analysis.

Conclusion: While conflicting data exist regarding the role of MTX in lymphoma development in RA, the majority of high-quality epidemiological studies reviewed did not support an association between MTX use and lymphoma development. Only two studies, both from Japan, indicated a significant association between MTX use and lymphoma development.

Disclosure: S. Alexander: None; **G. Starkebaum**: None; **D. Louden**: None; **G. Hughes**: Janssen, 5; **N. Singh**: None.

Abstract Number: 0439

Humoral Immune Response to 13 Valent-conjugate and 23-valent Polysaccharide Pneumococcal Vaccines in RA Patients Treated with Abatacept: Results of the Open Randomized Controlled Trial VACINA (Vaccination Against Pneumococcal in Naïve Abatacept Rheumatoid Arthritis Patients)

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SESSION INFORMATION
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Background/Purpose: To prevent infections, EULAR recommends to vaccinate RA patients against streptococcal pneumoniae. PCV13 is a T- cell dependent vaccine whereas PPSV23 induces a T-independent humoral response. Abatacept is a biological DMARD that inhibits T cell activation. We hypothesized that the humoral response after PCV13 vaccination may be more affected under abatacept than after PPSV23. To answer this question, we compared the humoral response 1, 6 and 12 months after vaccination with PCV13/PPSV23 or PPSV23 in RA patients starting abatacept

Methods: We conducted a prospective, multicentre, randomized, open-label study in patients with RA according to ACR/EULAR 2010 criteria, active (DAS28 >3,2) under MTX or leflunomide and proposed to start abatacept. Patients were randomized in 2 groups: the first group (G1) was vaccinated with the PPSV23 and the second group (G2) with PCV13 and PPSV23 8 weeks later. Abatacept was initiated at the same time as vaccination. Patients previously treated with rituximab within the last year were excluded. To measure humoral response, serum was collected 4 weeks after the first vaccine and at 6 and 12 months. A patient was considered as responder if there was a two-fold increase of the antibodies titer for at least 3 of 5 serotypes of interest (1, 3, 14, 7F, 19A) which are the most frequently involved in pneumococcal infections. For the primary endpoint, we compared the rate of responders at one month in G1 and G2 using a Chi-Square test (alpha risk 5% and 80% power). For the secondary end points, we compared humoral response at 6 and 12 months between G1 and G2. A logistic regression was used to identify factors associated with the humoral response at 1, 6 and 12 months. Tolerance of the vaccines (injection site reaction and general reaction) was recorded within the first week and later in a patient booklet. Serious adverse events (SAEs) and related to study participation or study vaccine, were recorded at 1, 6 and 12 months.

Results: Eighty patients were included and randomized in the two groups: 40 in G1 and 39 in G2 because of consent withdrawal for one patient. Characteristics of patients are described in **table 1**. Female were more represented in G1 (82.5%) compared to G2 (64.1%). Lymphocyte count was significantly higher in G1 compared to G2: 1841/mm3 (+/-887) vs

Table 1 : Characteristics of patients at inclusion

Variable	Modality	All population N=79	Group1 PPSV23 N=40	Group 2 PCV 13/PPSV23 N=39
Age (years)	Mean (±SD)	59.61 (± 12.59)	58.08 (± 13.74)	61.18 (± 11.24)
Gender	Women	58 (73.42)	33 (82.50)	25 (64.10)
BMI (kg/m²)	Mean (±SD)	26.03 (± 5.09)	26.76 (± 6.17)	25.29 (± 3.62)
Previous pneumococcal vaccine	Yes/ (%)	17 (21.52)	10 (25.00)	7 (17.95)
DAS28 CRP	Mean (±SD)	4.33 (± 0.90)	4.20 (± 0.79)	4.46 (± 1.00)
RF positive	Yes/ (%)	55 (70.51)	30 (75.00)	25 (64.10)
ACPA positive	Yes/ (%)	55 (70.51)	31 (77.50)	24 (61.54)
Erosive RA	Yes/ (%)	47 (61.04)	24 (60.00)	23 (58.97)
Lymphocytes count n/mm3	Mean (±SD)	1822.31 (± 778.25)	2029.73 (± 886.68)	1603.97 (± 579.90)
MTX	Yes/ (%)	63 (79.75)	32 (80.00)	31 (79.49)
MTX dose (mg/w)	Mean (±SD)	15.67 (± 4.52)	15.63 (± 5.12)	15.73 (± 3.88)
Leflunomide	Yes/ (%)	8 (10.13)	4 (10.00)	4 (10.26)
Steroids	Yes/ (%)	33 (41.77)	16 (40.00)	17 (43.59)
Steroid dose (mg/d)	Mean (±SD)	7.77 (± 2.42)	7.50 (± 2.58)	8.03 (± 2.30)

Table 2: Humoral response after PPSV23 and PCV13/PPSV23 vaccinations, at 1, 6 and 12 months after first dose of vaccine (secondary endpoints). mITT=modified intention to treat; PP= per protocol

Primary Endpoint	Total	PPSV23	PCV13	Chi² test p-value	RR [95% CI]
ITTm: Responders at 1 month (n (% col))	34/79 (43.04)	19/40 (47.50)	15/39 (38.46)	0.42	1.24 [0.74 ; 2.06]
PP: Responders at 1 month (n (% col))	26/64 (40.63)	13/32 (40.63)	13/32 (40.63)	1.00	1.00 [0.55 ; 1.81]

Secondary Endpoints	Total	PPSV23	PCV13/PPSV23	Chi2 test p-value	RR [95% CI]
ITTm: Responders at 6 months (n(% col))	35/79 (44.30)	17/40 (42.50)	18/39 (46.15)	0.74	0.92 [0.56 ; 1.51]
ITTm: Responders at 12 months (n(% col))	25/79 (31.65)	16/40 (40.00)	9/39 (23.08)	0.11	1.73 [0.87 ; 3.45]
PP: Responders at 6 months (n(% col))	27/64 (42.19)	12/32 (37.50)	15/32 (46.88)	0.45	0.80 [0.45 ; 1.43]
PP: Responders at 12 months (n(% col))	20/64 (31.25)	12/32 (37.50)	8/32 (25.00)	0.28	1.50 [0.71 ; 3.17]

1603/mm3 (+/-580). In the mITT, the rate of responders was 47.5% in in G1 and 38.46% in G2 with a RR of 1.23 (IC95%: 0.73-2,06) when comparing responders in PPSV23 vs PCV13 groups (**table 2**). At 6 and 12 months, there was no difference between G1 and G2 in mITT and PP analysis. Logistic regression did not identify factors associated with humoral response at 1 and 6 months. At 12 months, gender (being a male vs female) and PPSV23 vs PCV13/PPSV23 were associated with a better response: OR 3,7 [IC95% 1.2-12] and 3,1 [IC95% 1-9.4] respectively ($p< 0.05$) . 17 infections were reported in G1 and 28 in G2 with 3 severe infections but no pneumococcal infection.

Conclusion: In RA patients treated with abatacept combined with csDMARDs (MTX or LEF), the rate of responders is similar at 1-, 6- and 12-months following vaccination with PCV13 or PPSV23.Abatacept does not seem to impact humoral response of PCV13 in the first 6 months following vaccination.

Disclosure: J. MOREL: None; **O. Brocq**: None; **C. Gaujoux Viala**: AbbVie/Abbott, 2, Amgen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, Janssen, 2, Medac, 2, Merck-Serono, 2, Mylan, 2, Nordic Pharma, 2, Novartis, 2, Pfizer, 2, Roche-Chugai, 2, Sandoz, 2, Sanofi, 2, UCB Pharma, 2; **A. Constantin**: None; **S. Lassoued**: None; **E. Dernis**: AbbVie/Abbott, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, Janssen, 2, MSD, 2, Nordic Pharma, 2, Novartis, 2, Pfizer, 2, Roche, 2, Roche-Chugai, 2, Sandoz, 2, Sanofi, 2, UCB Pharma, 2; **C. Richez**: AbbVie/Abbott, 2, 6, Amgen, 6, AstraZeneca, 2, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, 12, receipt of drugs, GlaxoSmithKlein(GSK), 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **C. Lukas**: Abbvie, 2, 6, Amgen, 2, 6, Biogen, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche Chugai, 2, 6, UCB, 2, 6; **C. Daien**: None; **C. Duflos**: None.

Abstract Number: 0440

Baseline T Cell and B Cell-related Markers and HLA-DRB1 Shared Epitope Alleles Predict the Therapeutic Efficacy of Abatacept in Patients with Moderate to Severe Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Abatacept, a CTLA-4-Ig fusion protein, is widely used as a treatment for rheumatoid arthritis (RA). However, data on predictive biomarkers associated with therapeutic response to abatacept is still limited. We conducted this study to identify novel biomarkers to predict the therapeutic efficacy of abatacept in patients with moderate to severe RA.

Methods: A total of 23 RA patients, who had an inadequate response to methotrexate and other conventional DMARDs, were enrolled in this study. Responders (n=10) to abatacept were defined as subjects who achieved ACR50 response at week 24. At baseline, week 6, week 14, and week 24, serum levels of soluble CD25, CD27, CD40L, CD80, CXCL10, CXCL13, IL-21, and PD-1 were measured with ProcartaPlex by Luminex, while serum levels of soluble CD83, CD163, and rheumatoid factor (RF) IgM were determined by ELISA. Peripheral blood mononuclear cells (PBMCs) were isolated and analyzed for changes in different T cell and B cell subsets by flow cytometry at baseline, week 14, and week 24. Patients were

also genotyped for human leukocyte antigen (HLA)-DRB1 shared epitope (SE) alleles and classified as SE2 (≥ 2 SE allele, n=8), SE1 (≥ 1 SE allele, n=19) and SE0 (no SE alleles, n=4).

Results: Levels of sCD25, sCD27, sCD83, CXCL13, sPD-1 and RF IgM were significantly decreased at week 14 and week 24 with the treatment of abatacept when compared to baseline, while IL-21 levels were only decreased at week 14 (Table 1). Subjects treated with abatacept had a significant decline in the frequencies of circulating CD4+CXCR5+PD-1hi follicular helper T (Tfh) cells (p=0.0008 and p=0.0001 respectively) and CD4+CXCR5-PD-1hi peripheral helper T (Tph) cells (p=0.0004 and p< 0.0001 respectively) at week 14 and week 24. There was also a significant reduction in other T cell subsets, including CD4+CD25+CD127- regulatory T (Treg) cells, CD4+CD45RA-CCR7+ central memory T cells, and CD4+-CD45RA-CCR7- effector memory T cells. Abatacept also reduced the frequencies of circulating CD19+IgD-CD27+ class-switched memory (SM) B cells (p=0.0239 and p=0.0237, respectively), CD19+CD27hiCD38hi plasmablasts/plasma (PL) B cells (p=0.0249 and p=0.0108, respectively) and CD19+CD11c+ B cells (p< 0.0001 and p=0.012, respectively) at

Table 1. Levels of serum soluble markers before and after treatment with abatacept. Data are displayed as median (interquartile range). Differences between baseline and post-treatment (week 6, week 14, and week 24) were determined by the Wilcoxon matched-pairs signed rank test. ****p<0.0001, ***p<0.001, **p<0.01 and *p<0.05.

	Baseline	Week 6	Week 14	Week 24
sCD25 (pg/mL)	1368 (2845.6)	1246 (2023) **	909.7 (1626.15) ****	723.3 (1652.3) **
sCD27 (pg/mL)	177 (342.79)	167.7 (288.77)	135.7 (198.11) **	97.08 (185.88) ****
sCD40L (pg/mL)	18.17 (22.329)	21.71 (23.414)	19.18 (17.18) **	15.74 (22.842)
sCD80 (pg/mL)	83.13 (196.06)	121 (265.35)	131.6 (261.7)	109.5 (182.95)
sCD83 (pg/mL)	522.6 (1185.56)	278.1 (1395.23) *	132.4 (801.4) **	126.7 (1038.75) *
sCD163 (pg/mL)	360.6 (239.1)	297.3 (198.2) *	299.5 (216)	344 (215.7)
CXCL10 (pg/mL)	3.66 (15.005)	3.561 (13.6102)	2.731 (6.8991)	2.433 (7.8704)
CXCL13 (pg/mL)	119.1 (188.06)	89.64 (97.73) **	85.27 (83) ***	67.91 (57.83) **
IL-21 (pg/mL)	39.06 (125.8)	23.62 (88.75)	12.48 (54.47) **	0 (45.46)
sPD-1 (pg/mL)	95.21 (64.05)	91.27 (39.53) **	83.46 (31.94) ****	81.03 (34.5) *
RF IgM (IU/mL)	15894 (16520)	15016 (188.06)	13278 (18237) **	12122 (19298) *

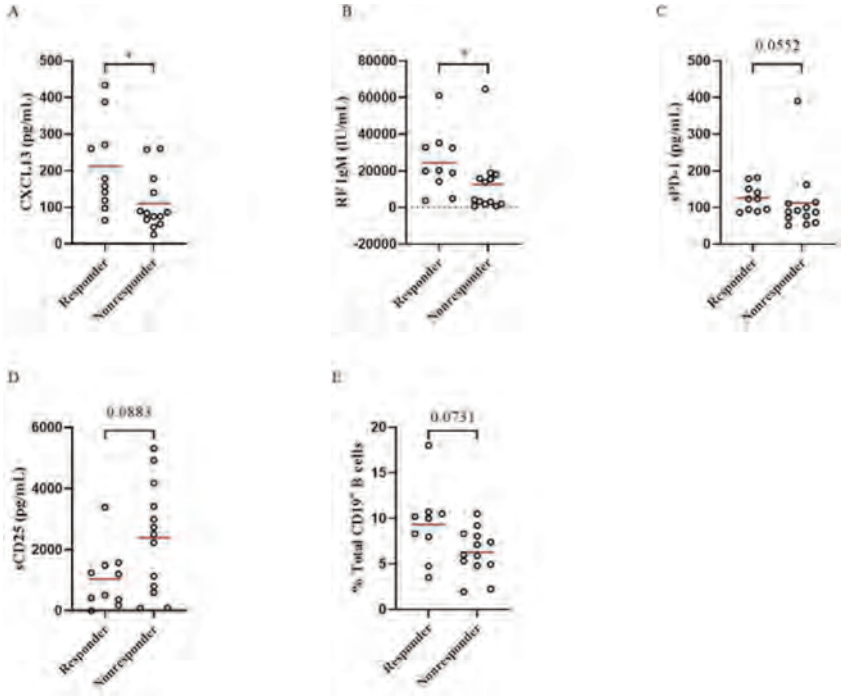

Figure 1. Comparisons in T cell and B cell-related markers between responders and nonresponders. Comparisons of serum levels of CXCL13 (A), RF IgM (B), sPD-1(C), sCD25 (D), and percentages of CD19+CD11c+ B cells (E) in circulation at baseline in patients treated with abatacept. Differences between groups were determined by the Mann-Whitney test. *p<0.05.

week 14 and week 24. Compared to non-responders, baseline levels of CXCL13 (p=0.0178), RF IgM (p=0.0147), sPD-1 (p=0.0552), and the percentages of CD19+CD11c+ B cells (p=0.0731) were higher in the responders, while levels of sCD25 (p=0.0883) tended to be lower in the responders (Figure 1). Responders had a significantly higher percentage of patients with SE2 than non-responders (60% vs 15.38%, p=0.0393). Baseline serum CXCL13 levels were correlated with circulating Tph (r=0.5425, p=0.0075), Treg cells (r=0.4665, p=0.0248), CD19+CD11c+ B cells (r=0.4609, p=0.0309) and RF IgM levels (r=0.6108, p=0.0012).

Conclusion: These findings suggest that baseline CXCL13, RF IgM, sPD-1, CD19+CD11c+ B cell percentages, and HLA-DRB1 shared epitope alleles may be useful markers in predicting response to abatacept in moderate to severe RA patients.

Disclosure: T. Wang: None; **N. Giltiay**: None; **C. Lood**: Amytryx, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Citryll, 2, Eli Lilly, 5, Gilead, 5, Pfizer, 5, Redd Pharma, 2, 5, 11; **B. Han**: None.

Abstract Number: 0441

Outcomes in Patients with Rheumatoid Arthritis Initiating Therapy with Etanercept, Adalimumab, or Janus Kinase Inhibitors

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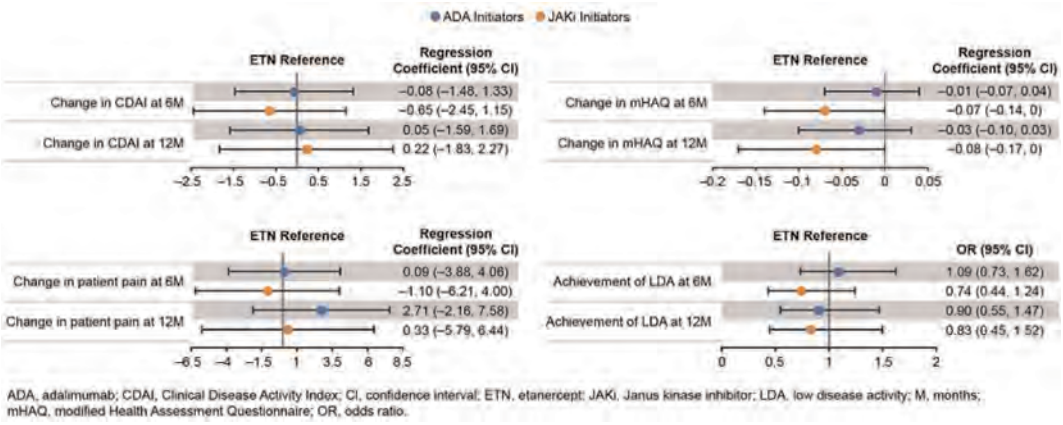
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Ongoing debate exists regarding the optimal sequence of tumor necrosis factor inhibitors and Janus kinase inhibitors (JAKis) in patients with rheumatoid arthritis (RA) as first-line biologic or targeted synthetic disease-modifying antirheumatic drug (b/tsDMARD) therapy following conventional therapies.The aim of this study was to describe

	ETN	ADA	JAKis
Age, years	54.4 (12.8)	55.5 (12.1)	60.9 (12.5)
Female, n (%)	666 (77)	843 (76)	303 (77)
BMI, kg/m^2	30.4 (7.6)	31.3 (7.9)	30.8 (7.6)
Duration of RA, years	5.9 (7.6)	5.8 (7.3)	8.6 (10.0)
BL disease activity[a]			
CDAI	19.9 (14.3)	18.9 (12.7)	18.8 (13.2)
mHAQ	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)
Patient pain[b]	48.0 (28.8)	49.2 (28.5)	45.2 (29.2)
Disease activity decrease from BL at 6M			
CDAI	6.9 (13.6)	6.4 (12.1)	4.7 (12.3)
mHAQ	0.1 (0.4)	0.1 (0.4)	0.1 (0.4)
Patient pain[b]	9.7 (30.2)	10.6 (28.4)	8.9 (29.5)
Disease activity decrease from BL at 12M			
CDAI	7.4 (13.5)	6.1 (13.0)	5.1 (13.0)
mHAQ	0.1 (0.4)	0.1 (0.4)	0.1 (0.4)
Patient pain[b]	8.8 (29.7)	8.7 (30.1)	7.5 (28.6)
Achievement of LDA[c], %			
6M	43.4	41.9	32.5
12M	41.0	39.6	38.3

[a]Baseline for combined population with 6M and 12M follow-up. [b](range: 0–100). [c]CDAI ≤10 among those with moderate or high disease activity at baseline.
Data are mean (SD) unless otherwise specified.
ADA, adalimumab; BL, baseline; CDAI, Clinical Disease Activity Index; ETN, etanercept; JAKis, Janus kinase inhibitors; LDA, low disease activity; M, months; mHAQ, modified Health Assessment Questionnaire; RA, rheumatoid arthritis; SD, standard deviation.

Patient Description at Time of Initiation and Unadjusted Disease Activity Results



ADA, adalimumab; CDAI, Clinical Disease Activity Index; CI, confidence interval; ETN, etanercept; JAKi, Janus kinase inhibitor; LDA, low disease activity; M, months; mHAQ, modified Health Assessment Questionnaire; OR, odds ratio.

Adjusted Mean Differences in Change in Effectiveness and Patient-Reported Outcomes Relative to Etanercept Initiators

baseline characteristics, effectiveness, persistency, and treatment patterns among first-line b/tsDMARD-naive initiators of etanercept (ETN), adalimumab (ADA), or JAKis (tofacitinib, baricitinib, and upadacitinib).

Methods: Data on patients who initiated b/tsDMARD from 11/2012 to 6/2021 were obtained from the CorEvitas RA Registry, a prospective, multicenter, observational, disease-based registry. Patients ≥18 years with rheumatologist-diagnosed RA and 6- and/or 12-months' (M) follow-up were included. We report descriptive statistics at baseline, persistency on therapy, escalation/de-escalation of therapy, details on patterns of drug switching, and effectiveness outcomes using regression models adjusted for baseline covariates (demographic/socioeconomic/lifestyle characteristics, comorbidities, medication history, disease activity, and patient-reported outcomes). Outcomes were evaluated at 6M and 12M follow-up.

Results: First-line initiators of ETN, ADA, and JAKis with baseline and follow-up visits were identified: 803, 984, and 361 patients at 6M, respectively; 589, 749, and 264 patients at 12M, respectively. Baseline characteristics were similar among ETN, ADA, and JAKi initiators with the exception of disease duration, which was longer among first-line JAKi initiators (mean, 8.6 y) versus ETN (5.9 y) and ADA (5.8 y) initiators. Unadjusted mean improvement in Clinical Disease Activity Index (CDAI) was generally similar between groups at 6M and 12M (**Table**). Adjusted effectiveness results were similar at 6M and 12M (**Figure**). At 6M, 68% of ETN, 69% of ADA, and 67% of JAKi initiators remained on the same therapy; at 12M, 53% of ETN, 57% of ADA, and 57% of JAKi initiators remained on the same therapy. The frequency of switching to another b/tsDMARD was similar across initiators.

Conclusion: In this real-world study in patients initiating first-line b/tsDMARD therapy with ETN, ADA, or JAKis, we did not observe differences in clinical effectiveness/patient-reported outcomes and treatment persistency at 6M and 12M after treatment initiation.

Disclosure: D. Pappas: AbbVie, 2, 6, CorEvitas, LLC, 3, 8, 11, Corrona Research Foundation, 4, Novartis, 6, Roche Hellas, 2, 6, Sanofi, 1, 6; **J. O'Brien**: CorEvitas, LLC, 3; **L. Guo**: CorEvitas, LLC, 3; **Y. Shan**: CorEvitas, LLC, 3; **J. Baker**: Bristol-Myers Squibb(BMS), 2, Burns-White, LLC, 2, CorEvitas, LLC, 2, Pfizer, 2; **G. Kricorian**: Amgen, 3, 11; **S. Stryker**: Amgen, 3, 11; **D. Collier**: Amgen, 3, 11.

Abstract Number: 0442

Infliximab Clearance a Predictive Factor of Pharmacokinetic Origin in Relation to Suboptimal Pharmacokinetics and Immunogenicity in United States Based Rheumatology Practices

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Infliximab (IFX) has become a mainstay of treatment of many different immune-mediated inflammatory diseases. With the wide range of IFX dosing and dosing intervals, adjustments are often made on clinical parameters without consideration of IFX pharmacokinetics (PK). Measuring clearance (CL) of IFX may be useful for individual dosage adjustment as higher CL is associated with immunogenicity (antibodies to IFX [ATI]), suboptimal exposure (< 8 mg/L at trough) with resultant insufficient neutralization of inflammatory burden. There is paucity of data supporting the notion that optimal PK is achieved in US patients with rheumatic diseases treated with IFX.

Methods: We interrogated a database from a US based clinical PK laboratory offering IFX monitoring and extracted results from patients with rheumatoid arthritis (RA) or juvenile idiopathic arthritis (based on ICD-10 codes beginning with M05, M06 or M08) and having IFX dosing (range 3-10 mg/Kg) and interdose interval provided on test requisition (range 4-8 weeks). Concomitant use of methotrexate was not available. All patient results were de-identified prior to analysis. Serum IFX was measured using a drug tolerant homogenous mobility shift assay. Serum ATI positive status corresponded to titers > 3.1 U/mL. CL, the volume of serum removed each day (expressed as L/day) from drug, was calculated using nonlinear mixed effect models with Bayesian priors using IFX concentrations and ATI status. Minimal effective concentration commensurate with disease control achieved was set at 8 μg/mL, based on prior convention (1). Lower limit of quantification was 1 μg/mL. The impact of lower (< 0.3 L/day), intermediate (0.3-0.8 L/day) and higher clearance (>0.8 L/day) cutoffs on PK parameters was analyzed using Fisher Exact and logistic regression tests.

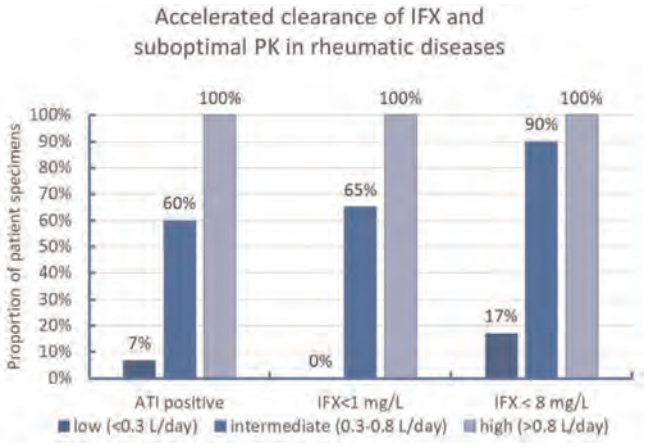

Figure 1

Results: We identified a total of 161 patient specimens ordered by 74 practices and submitted for testing (73% female, mean age =57 [Interquartile range, IQR: 37-69 years]). Median dose was 7.5 mg/Kg normalized to every 8 weeks (IQR: 5-13 mg/Kg every 8 weeks).Median IFX level was 14 μg/mL (IQR: 2.8-28.9 μg/mL), suboptimal exposure (< 8μg/mL) was observed in 36% patients, 22% presented with ATI, 18% had IFX concentration < 1μg/mL. Median CL was 0.231 L/day [IQR: 0.173-0.312 L/day]. Higher and intermediate CL were observed in 2% [3/161] and 25% ([40/161] patient specimens, respectively). Inadequate exposure was observed in most patient specimens having intermediate or high CL and there was little immunogenicity (7%) in the presence of lower CL. In the presence of intermediate or higher CL, there was 47.8 (95%CI: 15.2-150.1) and 23.2 (95%CI: 8.9-60.3) fold higher likelihood of having concentration below 8 mg/L and immunogenicity, respectively (p< 0.001).

Conclusion: This preliminary data suggests that IFX dosing may be suboptimal in a significant proportion of patients with RA and other inflammatory rheumatic diseases. Dose optimization (achieving IFX levels >8 mg/L at trough) might benefit patients who demonstrate inadequate disease control, particularly those who manifest accelerated CL, in part due to immunogenicity.

(1) Mulleman D., et al. Arthritis Res Ther. 2009;11:R178. doi: 10.1186/ar2867

Disclosure: E. Rosenstein: None; **M. Weinblatt**: Abbvie, 2, 5, Aclaris, 2, Amgen, 2, Aqtual, 5, Bristol Myers Squibb, 2, 5, Canfite, 11, Corevitas, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, 2, Glaxo Smith Kline, 2, Horizon, 2, Inmedix, 11, Janssen, 5, Johnson and Johnson, 2, Pfizer, 2, Prometheus Laboratories, 2, Rani, 2, Revolo, 2, Sanofi, 2, Sci Rhom, 2, Scipher, 2, 11, Set Point, 2, UCB, 2; **A. Everts-van der Wind**: Prometheus Laboratories, 3, prometheus laboratories, 3; **J. Conklin**: Prometheus Laboratories, 2; **T. Dervieux**: Prometheus Laboratories, 3.

Abstract Number: 0443

The Potential of an Oral TNFα Inhibitor with TNFR1 Specificity: Results of a Phase 1b Proof-of-mechanism Trial in Psoriasis

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SESSION INFORMATION

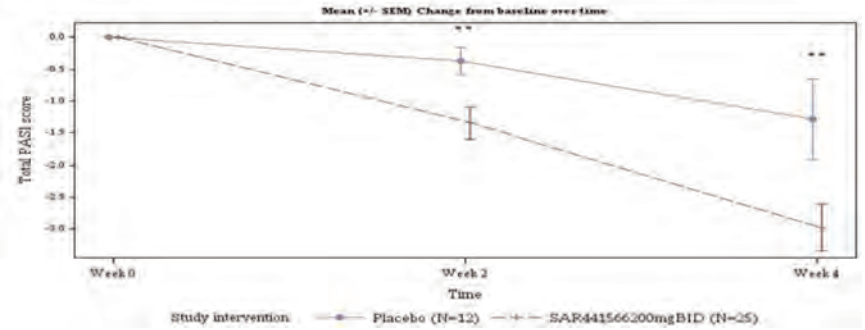
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: TNFα inhibition is a cornerstone of therapy for rheumatologic disease, yet there is no orally administered TNFα inhibitor available. A novel oral TNFα inhibitor (SAR441566) which specifically inhibits TNFR1 signaling is currently in clinical development. In contrast to biologic TNFα inhibitors, this compound preserves homeostatic TNFR2 signaling. Using SAR441566 in a mouse model of RA (collagen induced arthritis), disease improvement similar to biologic TNFα inhibition was observed*. Based on safety, PK and PD characteristics in first-in-human studies, a phase 1 proof-of-mechanism (POM) trial in psoriasis was conducted. The primary objective was to evaluate tolerability and safety, with secondary/exploratory objectives to assess clinical and biomarker response over 4 weeks of treatment.

Methods: The clinical trial was a double-blind, randomized, placebo-controlled, single-center study with SAR441566, an oral TNFα inhibitor. All participants had dermatologist-diagnosed mild-moderate psoriasis. Peripheral blood biomarkers were assessed by ultra-sensitive immunoassay platform.

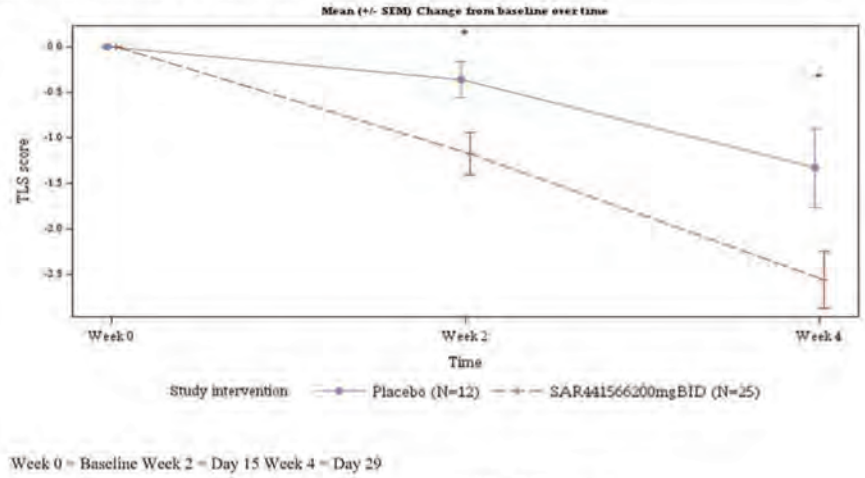
Results: Psoriasis patients recruited to the study randomized to oral TNFα inhibitor (n=26) vs placebo (n=12) were similar in age (μ±SD: 44.2±9.7 vs 40.5±12.5 yrs, p=0.332), race (proportion in %: 96.2 vs 91.7 Caucasian p= 0.565), BMI (26.45 ±2.97 vs 25.98±2.92 kg/m^2, p=0.650), baseline disease severity Investigator Global Assessment (IGA) score (2.42±0.64 vs 2.25±0.45, p=0.407), psoriasis area and severity index (PASI) score (8.91±3.73 vs 7.86±2.53, p=0.382), and target lesion severity (TLS) score (6.83±1.60 vs 7.42±1.40, p=0.280). With regards to safety and tolerability, there were no serious

Figure 1. Time profile of total PASI (psoriasis area and severity index) score for each study intervention group (placebo and SAR441566 200 mg BID)



Comparisons for SAR441566 vs placebo at week 2 demonstrated mean % improvement from baseline (least square means (LSM) ± standard error (SE)) 17.73±2.76 versus 4.12±4.10, with significant improvement from baseline in SAR441566 compared to placebo p= 0.005. Continuous data were summarized using the number of observations available, mean, Standard Deviation (SD), median, standard error of mean (SEM), minimum, and maximum. Categorical and ordinal data were summarized using the count and percentage of participants. Time profile plots and statistical modeling (Mixed model for repeated measures [MMRM]) were used to compare intervention vs placebo. Statistical significance differences between active drug and placebo were reported as a p-value and were calculated either from MMRM model (adjusted mean percentage improvement from baseline) or two-sample t-test for comparing means between the two groups on continuous data or chi-square test for comparing proportions between the two groups on categorical data. p-values <0.05 were considered significant.

Figure 2. Time profile of average TLS (target lesion severity) score for each study intervention group (placebo and SAR441566 200mg BID)

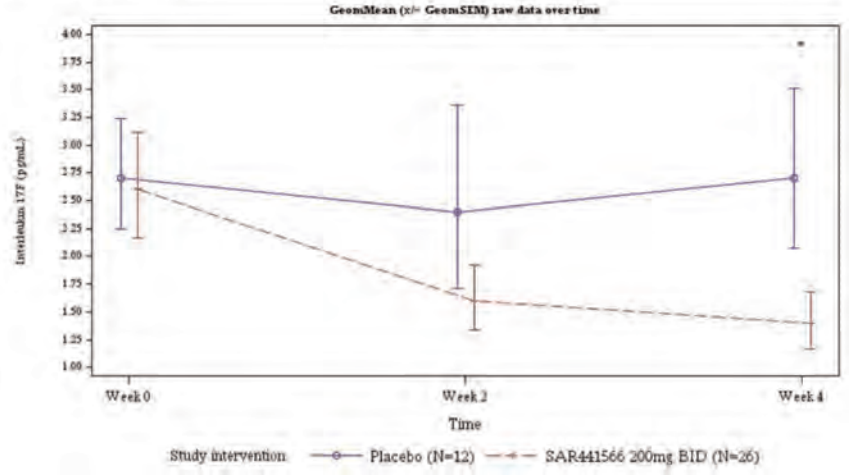


Week 0 = Baseline Week 2 = Day 15 Week 4 = Day 29

*P<0.05, p-value for one-sided test at 5% significance level calculated from MMRM model

Comparisons for SAR441566 vs placebo at week 2 demonstrated adjusted mean % improvement from baseline (least square means (LSM) ± standard error (SE)) 17.06±3.13 versus 6.29±4.68, with significant improvement from baseline in SAR441566 compared to placebo p= 0.032. Statistical significance calculation based on adjusted mean percentage improvement from baseline modeling using Mixed Models for Repeated Measures (MMRM).

Figure 3. Time profile of peripheral blood IL-17F (pg/mL) for each study intervention group (placebo and SAR441566 200mg BID)



Plot shows raw data with geometric mean and geometric standard error. Comparisons for SAR441566 vs placebo at week 2 demonstrated change from baseline in SAR441566, with geometric mean IL17-F levels of 1.65±2.55 vs. 2.39±2.71 pg/mL, p= 0.292, and significant improvement at week 4 1.35±2.55 vs. 2.73±2.44 pg/mL, p= 0.038.

adverse events (SAEs), severe treatment emergent adverse events (TEAEs) or AE of special interest (AESI). All observed TEAEs were grade 1/2 and participants fully recovered. There were few potentially clinically significant abnormalities for vital signs, ECG and laboratory parameters scattered across groups. All were considered not clinically meaningful by the investigator. With regards to clinical response by week 4, patients (N=37) were noted to have significant adjusted mean % improvement in PASI (LSM±SE, 35.09±4.47 vs 15.71±6.33, p=0.009) and TLS (% change 38.18±4.33 vs 20.44±6.18, p= 0.012). The proportion of patients achieving improvement by at least 1 severity level in IGA was 58.3 vs 0%, p=0.003. In addition to improvement in disease severity (PASI and TLS score change from baseline, Figures 1 and 2), Figure 3 depicts improvement in IL-17F.

Conclusion: This phase 1 study demonstrated that this novel oral TNFα inhibitor was safe, well tolerated, and clinically effective, to be further confirmed in larger trials. Limitations include the sample size and homogeneous population. A computational disease platform is being applied to translate psoriasis results to estimate the efficacy of SAR441566 for RA. A phase 2b dose ranging intervention proof-of-concept trial testing efficacy and safety for RA is planned.

*Vugler et al, An orally available small molecule that targets soluble TNF to deliver anti-TNF biologic-like efficacy in rheumatoid arthritis. Front Pharmacol. 2022

Disclosure: A. Fishbein: Sanofi, 3; **M. Nguyen**: Sanofi, 3; **O. Chow**: Sanofi, 3; **T. Matos**: Sanofi, 3; **C. Dreis**: Sanofi, 3; **H. Zhang**: Sanofi, 3; **M. Poirel**: IT & M Stats, 3, Sanofi, 7; **J. Gassenhuber**: Sanofi, 3; **M. Dufault**: Sanofi, 3; **W. Frank-Dietrich**: Sanofi, 2; **L. Perrin**: Sanofi, 3; **M. Rehberg**: Sanofi, 3; **M. Kohlmann**: Sanofi, 3; **N. Nassr**: Sanofi, 3.

Abstract Number: 0444

Safety, Tolerability, and Pharmacokinetics of a Novel Synthetic Disease Modifying Antirheumatic Drug, TCK-276, After Single Ascending Dose in Healthy Subjects and Multiple Ascending Doses in Patients with Rheumatoid Arthritis

Chie Watai[1], Kazuoki Tsuruda[2], **Yoshinori Tsumura**[1] and Daisuke Tasaki[1], [1]Teijin Pharma Limited, Chiyoda City Tokyo, Japan, [2]Teijin America, Inc., Sausalito, CA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: TCK-276 is a highly potent, orally active, and selective cyclin dependent kinase 4/6 (CDK4/6) inhibitor that is in development as a novel synthetic disease modifying antirheumatic drug targeting the hypertrophy of synovial fibroblasts. To investigate the safety, tolerability, and pharmacokinetics (PK) of oral doses of TCK-276, we conducted two phase 1 studies in the United States; one was the single ascending dose (SAD) study in healthy subjects and the other is an ongoing multiple ascending dose (MAD) study in patients with rheumatoid arthritis (RA).

Methods: The SAD study was a single-center, randomized, placebo-controlled, double-blind study, which enrolled 48 healthy subjects into 6 cohorts. Six subjects in each cohort received TCK-276 (5, 15, 50, 100, 150, or 185 mg) and 2 subjects in each cohort (total of 12 subjects) received placebo. The MAD study (NCT05437419) is a multicenter, randomized, placebo-controlled, double-blind study, which is planned to enroll a total of 32 RA patients into 4 cohorts. Six patients in each cohort received TCK-276 and 2 patients in each cohort received placebo for 7 days, respectively.

Results: In the SAD study, 5 subjects (10.4%) experienced 7 treatment-emergent adverse events (TEAEs). All TEAEs were mild. Only one TEAE (headache) was considered possibly related to TCK-276 at 150 mg, and all the other TEAEs were considered either unlikely to be related or unrelated. No action was taken for the TEAEs. There were no deaths, serious TEAEs, or TEAEs leading to discontinuation reported during the study. No clinically significant findings were noted in the clinical laboratory evaluations (clinical chemistry, hematology, coagulation, and urinalysis). After administration of 5 to 185 mg TCK-276, geometric mean C_{max}, $AUC_{0\text{-}inf}$, and $t_{1/2}$ values of TCK-276 ranged from 11.5 to 481 ng /mL, 53.9 to 2260 ng*h/mL, and 3.70 to 13.0 h, respectively. Across the 5 mg to 185 mg dose range, an increase in TCK-276 exposure approximately proportional to dose was observed. In the MAD study, a total of 16 patients have been enrolled as of May 26, 2023; 12 patients received TCK-276 (10 mg/day or 25 mg/day for 7 days) and 4 patients received placebo, respectively. There were no safety concerns identified, and the safety review committee concluded that the study can proceed with the next higher dose. PK profiles in RA patients after administration of 10 or 25 mg/day TCK-276 were confirmed to be similar to those in healthy subjects.

Conclusion: Safety results indicated that TCK-276 was well tolerated at a dose of up to 185 mg for a single administration and up to 25 mg/day over 7 days of administration. In addition, no safety concerns have been observed such as anemia, neutropenia, leukopenia, and thrombocytopenia, which are often observed with other CDK4/6 inhibitors. TCK-276 showed faster elimination than other CDK4/6 inhibitors, which may be related to the observed safety profile. Safety, tolerability, and PK of the higher TCK-276 dose cohorts in the MAD study will be available at the presentation. The safety and efficacy of TCK-276 in the treatment of RA will be further evaluated in a phase 2 trial in the future.

Disclosure: C. Watai: Teijin Pharma Limited, 3; **K. Tsuruda**: Teijin America. Inc, 4; **Y. Tsumura**: Teijin Pharma Limited, 3; **D. Tasaki**: Teijin Pharma Limited, 3.

Abstract Number: 0445

Comparison of the Efficacy, Safety and Immunogenicity of a Proposed Biosimilar MSB11456 with Tocilizumab Reference Product in Moderate-to-severe Rheumatoid Arthritis: Results of a Randomized Double-blind Study

Anna Zubrzycka-Sienkiewicz[1], Maria Misterska-Skora[2], Małgorzata Socik Pojawa[3], Kamilla Klama[4], Martin Ullmann[5], Corinne Petit-Frere[5], **Andras Illes**[5], Peter Baker[5], Joëlle Monnet[5] and Jan Brzezicki[6], [1]Reumatika - Centrum Reumatologil, Warsaw, Poland, [2]Centrum Medyczne Oporów, Wrocław, Poland, [3]MICS Centrum Medyczne Warszawa, Warsaw, Poland, [4]Solumed Centrum Medyczne, Poznań, Poland, [5]Fresenius Kabi SwissBiosimilars, Eysins, Switzerland, [6]Centrum Kliniczno Badawcze, Elbląg, Poland

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Tocilizumab is an anti-interleukin-6 receptor monoclonal antibody indicated for treating rheumatoid arthritis (RA) and other inflammatory diseases. MSB11456 is a proposed biosimilar to US-licensed tocilizumab and EU-approved tocilizumab. It has already shown equivalent pharmacokinetic (PK), pharmacodynamic (PD) safety, tolerability, and immunogenicity profiles to these products given subcutaneously (SC) as a single dose in healthy volunteers. This is a

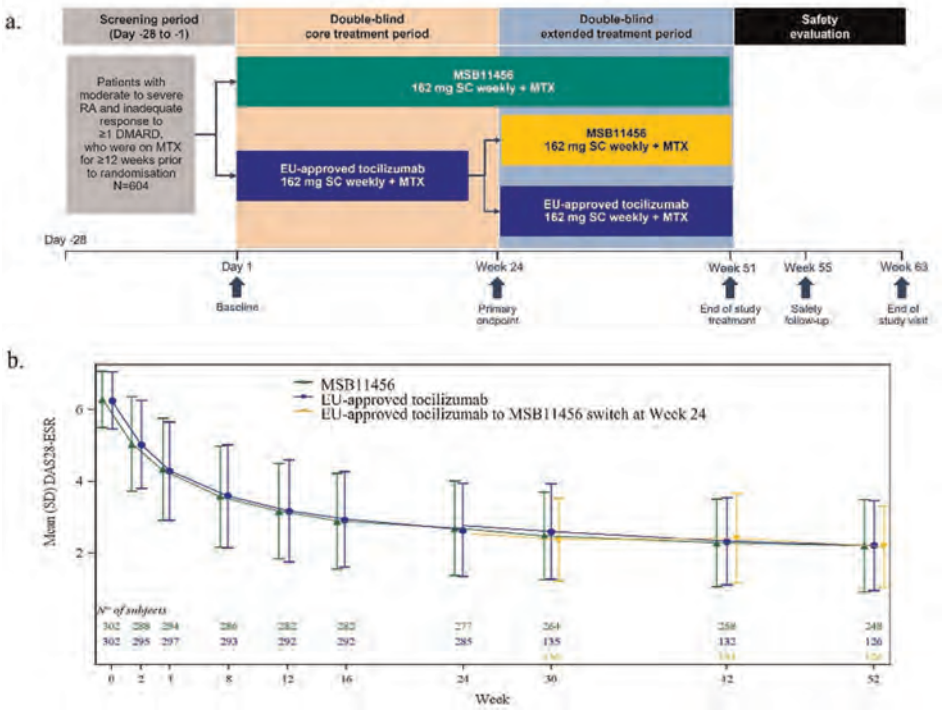


Figure 1: a. Study design; b. Mean DAS28-ESR at various timepoints in patients receiving MSB11456; EU-approved tocilizumab and patients who were switched from EU-approved tocilizumab to MSB11456 at W24 until W52 - All Randomized subjects.

Phase III, multicenter, randomized, double-blind, multiple fixed-dose, parallel group study aiming to compare the efficacy, safety, and immunogenicity of MSB11456 and EU - approved tocilizumab administered SC in patients with moderate-to-severe RA (NCT04512001).

Methods: Patients were randomized to subcutaneous injections of 162 mg MSB11456 or EU - approved tocilizumab for 24 weeks (W). At W24, patients receiving EU-approved tocilizumab were re-randomized to continue their treatment or to switch to MSB11456 up to W52. Those receiving MSB11456 continued MSB11456 until W52. A safety evaluation was conducted up to W63 (Figure 1a).

The primary efficacy endpoint - change from baseline in Disease Activity Score-28 Joint Count (DAS28)-erythrocyte sedimentation rate (ESR) at W24 - was analyzed using analysis of covariance to determine the least squares mean (LSM) difference between MSB11456 and EU-approved tocilizumab; MSB11456 was considered equivalent to EU-approved tocilizumab if the 90% confidence interval (CI) for this difference was entirely within the equivalence interval -0.6 to 0.5. Secondary endpoints were 20% improvement in American College of Rheumatology core set measures (ACR20) at W24 and DAS28-ESR at W12. Additional endpoints included ACR50/70, change in DAS28-C-reactive protein (CRP), Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), evaluation of immunogenicity at various time points up to W55 and safety up to W63.

Table 1: DAS28-ESR - Change from Baseline at Week 24 - (ITT Analysis Set)

Variable Statistic	MSB11456 (N=302)	EU-approved tocilizumab (N=302)	Difference MSB11456 - EU-approved tocilizumab (N=604)
Change from Baseline to Week 24			
LS Mean (SE)[a]	-3.53 (0.106)	-3.54 (0.106)	
95% Confidence Interval[a]	(-3.74, -3.32)	(-3.75, -3.33)	
Number of Imputed Values	25	17	
Difference in Change from EU-approved tocilizumab[a]			
LS Mean Difference (SE)[b]			0.01 (0.104)
90% Confidence Interval[b]			(-0.16, 0.18)

LS = Least squares; SE = Standard error
[a] LS means, standard errors and confidence intervals are from an ANCOVA model based on change from baseline in DAS28-ESR with fixed effects for study drug and previous exposure to biologic treatment for RA [Y / N] and baseline DAS28-ESR as a covariate. Fixed effects were based on IRT.
[b] For the FDA: MSB11456 was considered equivalent to EU-approved tocilizumab if the 90% confidence interval was included in the equivalence interval of [-0.6, 0.5].

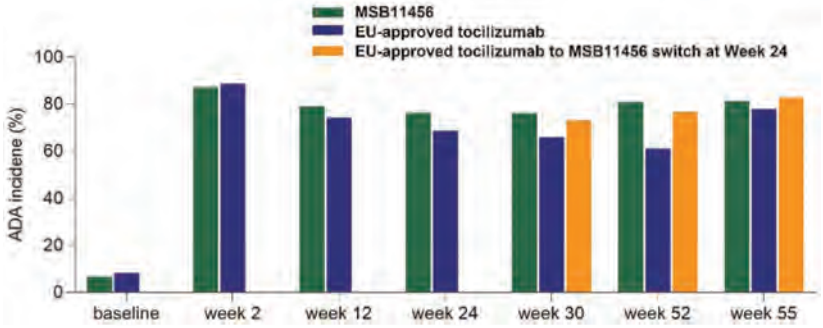


Figure 2: Antidrug antibody (ADA) incidence at various time points in patients receiving MSB11456; EU-approved tocilizumab and patients who were switched from EU-approved tocilizumab to MSB11456 at W24 until W52.

Results: Clinically relevant LSM decreases from baseline in DAS28-ESR were observed as early as W2 and up to W24 with MSB11456 and EU-approved tocilizumab (Figure 1b). As the 90% CI for the LSM difference in the change from baseline in DAS28-ESR between treatments was fully included within the predefined equivalence interval, therapeutic equivalence of MSB11456 and EU-approved tocilizumab was demonstrated (Table 1). The other efficacy endpoint analyses supported this conclusion. Treatment-emergent adverse events (TEAEs) were usually mild or moderate and occurred at similar frequency with both drugs. There were no discernible patterns in terms of the nature, frequency, or other characteristics of serious or treatment related TEAEs to suggest a difference between drugs. Anti-drug antibodies (ADA) incidence was similar among treatment arms (Figure 2). The switch from EU-approved tocilizumab to MSB11456 at W24 had no clinically relevant impact either on efficacy or safety, including immunogenicity.

Conclusion: Equivalent efficacy, and similar immunogenicity and safety profiles of MSB11456 and EU-approved tocilizumab were demonstrated in patients with moderate to severe RA

Disclosure: A. Zubrzycka-Sienkiewicz: None; **M. Misterska-Skora**: None; **M. Socik Pojawa**: None; **K. Klama**: None; **M. Ullmann**: Fresenius Kabi SwissBioSim GmbH, 3; **C. Petit-Frere**: Fresenius Kabi SwissBioSim GmbH, 3; **A. Illes**: Fresenius Kabi SwissBioSim GmbH, 3; **P. Baker**: Fresenius Kabi SwissBioSim GmbH, 3; **J. Monnet**: Fresenius Kabi SwissBioSim GmbH, 3; **J. Brzezicki**: None.

Abstract Number: 0446

Review of Rheumatoid Arthritis Treatment Landscape During the COVID-19 Pandemic

Rachel Connolly[1], MamTing Thoo[2], Elizabeth Baynton[3] and **Denise Baldock**[3], [1]Ipsos, New York, NY, [2]Ipsos SDN BHD, Kuala Lumpur, Malaysia, [3]Ipsos MORI UK, London, United Kingdom

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: During the COVID-19 pandemic, guidelines were amended with respect to the prescribing of biologic/tsDMARD usage to treat rheumatoid arthritis (RA). In addition, regulatory reviews also ensued gauging the safety & risk parameters of Janus kinase inhibitor (JAKi) usage. The purpose of this study was to analyse any biologic/tsDMARD prescribing shifts in RA during this time, and any possible impacts.

Methods: A multi-country, multi-centre, online, medical chart review study of patients with RA was conducted across January – December 2021 ("2021 cohort") and January – December 2022 ("2022 cohort"), among UK, FR, DE, IT & ES rheumatologists in hospitals and private practices were recruited to collect de-identified data on patients who were recently treated with an advanced therapy (biologic/tsDMARD) as part of their usual care. Physicians were screened for practice duration and patient volume. Rheumatologists abstracted current patient treatment, reasons for prescribing treatments and patient disease score information; patient charts are included in the analysis.

Results: The 2021 cohort consists of 383 sampled physicians who reported on 4999 patients in total. The 2022 cohort consists of 422 sampled physicians who reported on 5161 patients in total.

2022 cohort recorded an increase in biosimilar tumour necrosis factor inhibitor (TNFi) usage among reported patients vs 2021 cohort (31% vs 27%). Alternate available mechanisms of action (MoA) to TNFi recorded a decrease in use to 44% (2022) from 46% (2021) among reported patients; JAKi class share showed minimal change from 24% (2021) to 23% (2022).

In reasons for therapy choice cited by the sampled rheumatologists, the % of reported patients with the following driving metrics have increased from 2021 to 2022: cost/insurance (16% vs 19%), patient request (9% vs 12%), long-term efficacy data available (27% vs 31%) and long-term safety data available (26% vs 29%).

Recorded remission status has decreased from 59% in 2021 cohort to 56% in 2022 cohort.

Conclusion: Comparing the two cohorts in this study data has allowed insight into possible prescribing changes that were beginning to come into view throughout the COVID-19 pandemic and while JAKi regulatory reviews were ongoing: increased prescribing of biosimilar TNFis and decreased prescribing of alternate MoAs. The data shows an increasing desire for long-term safety and efficacy data, patient request, and cost/insurance when physicians are choosing the therapy that their patient is going to be treated with. Interestingly, while the prescribing behaviour of sampled physicians has shifted, disease outcomes of reported patients are not necessarily improving. With patients in this study recording lower remission rates, it may be that the treatment shift away from newer MoA therapies are having an influence. It will be critical to monitor the RA treatment landscape for patient outcomes going forward. Further analysis using comparator cohort is warranted.

Disclosure: R. Connolly: None; **M. Thoo**: None; **E. Baynton**: None; **D. Baldock**: None.

Abstract Number: 0447

Glucocorticoid Use in Rheumatoid Arthritis Patients Initiating Biological or Targeted Synthetic Disease Modifying Anti-rheumatic Drugs (b/tsDMARDs) in Real Life: Data from BIOBADASER

Lucia Otero-Valera[1], Jose María Alvaro-Gracias[2], Jerusalem Calvo[3], Cristina Campos[4], Alicia Garcia Dorta[5], Fernando Sánchez-Alonso[6] and **Isabel Castrejon**[7], [1]Spanish Society of Rheumatology, Madrid, Spain, [2]Hospital General Universitario Gregorio Marañon, Madrid, Spain, [3]Reina Sofia University Hospital, Córdoba, Spain, [4]Rheumatology Unit, Hospital General Universitario de Valencia, Valencia, Spain, [5]Rheumatology Unit, Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [6]Fundación Española de Reumatología, Madrid, Spain, [7]Hospital Universitario Gregorio Marañón, Madrid, Spain

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Glucocorticoids are frequently used as bridging therapy for rheumatoid arthritis (RA) patients starting conventional synthetic DMARDs. Both EULAR and ACR guidelines (1,2), recommend to use the lowest effective dose for the shorter duration possible, ideally less than three months. In addition, glucocorticoids are not recommended when starting a b/tsDMARD. We aim to assess glucocorticoid usage after treatment initiation with bDMARDs and JAKi in RA patients in real life.

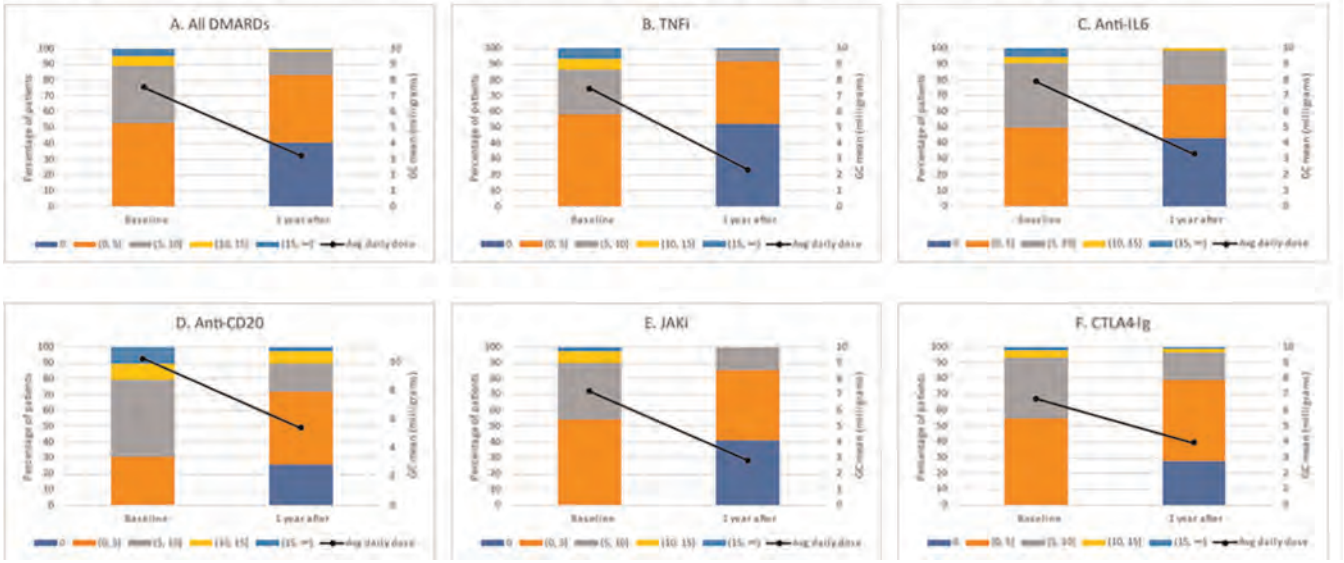
Methods: Data on patients with RA switching from a conventional synthetic DMARD to a first biologic or JAKi enrolled in BIOBADASER 3.0 (a multicenter Spanish Registry on Adverse Events of Advanced Therapies in Rheumatic Diseases) were analyzed. Biologic treatment included TNFi, anti-IL6, anti-CD20, and CTLA4-Ig. Patients with any biologic or JAKi, all in combination with glucocorticoids at therapy initiation were included. As TNFi was the larger group, a random sample was taken for comparison purposes. Descriptive statistics were used to calculate the frequency and average daily glucocorticoid usage according to therapy group, both at baseline and 1 year after treatment initiation. Wilcoxon Singed Rank test was used to compare glucocorticoid dose changes from baseline to 1 year after initiation of the b/tsDMARDs and ANOVA, to compare the mean dose differences across groups.

Results: A total of 432 RA patients met the inclusion criteria and were included in the analysis, 78.2% women, mean age 58.4 (12.2) years old, median disease duration 5.2 years [IQR: 2.1-10.8] and mean DAS28-ESR at baseline 4.72 (1.33). Mean (SD) glucocorticoid daily dose decreased from 7.6 mg (5.8) at baseline to 3.2 (5.5) mg at 1-year follow-up (Figure). Daily dose changes were statistically significant (Wilcoxon Signed Rank test: $p < 0.001$). Mean difference from baseline to one year follow-up was 5.13 for TNFi, 4.59 for anti-IL6, 4.83 for anti-CD20, 4.38 for JAKi, and 2.78 for CTLA4-Ig (ANOVA: p=0.12). The proportion of patients with a decrease in glucocorticoids dose from baseline to one year follow-up after b/tsDMARD initiation was 72.7% for TNFi, 62.2% for anti-IL6, 66.7% for anti-CD20, 67.9% for JAKi, and 60.5% for CTLA4-Ig, and the proportion of patients with no glucocorticoids at one year was 52.1%, 43.2%, 25.6%, 41.1% and 27.9% respectively for each treatment (Table).

Table. Average daily glucocorticoid usage for treatment group

				GC daily doses				
DMARD Drug	**n**		**Mean (SD)**	**No GC [0]**	**[0, 5]**	**(5, 10]**	**(10, 15]**	**(15, ∞)**
TNFi	121	Baseline	7.43 (5.58)	0 (0.0)	71 (58.7)	34 (28.1)	8 (6.6)	8 (6.6)
		1 year after	2.33 (3.49)	63 (52.1)	48 (39.7)	9 (7.4)	0 (0.0)	1 (0.8)
Anti-IL6	74	Baseline	7.89 (7.82)	0 (0.0)	37 (50.0)	30 (40.5)	3 (4.1)	4 (5.4)
		1 year after	3.29 (3.55)	32 (43.2)	25 (33.8)	16 (21.6)	1 (1.4)	0 (0.0)
Anti-CD20	39	Baseline	10.21 (7.41)	0 (0.0)	12 (30.8)	19 (48.7)	4 (10.3)	4 (10.3)
		1 year after	5.38 (5.70)	10 (25.6)	18 (46.2)	7 (18.0)	3 (7.7)	1 (2.6)
JAKi	112	Baseline	7.22 (4.50)	0 (0.0)	61 (54.5)	40 (35.7)	8 (7.1)	3 (2.7)
		1 year after	2.83 (2.85)	46 (41.1)	50 (44.6)	16 (14.3)	0 (0.0)	0 (0.0)
CTLA4-Ig	86	Baseline	6.71 (3.54)	0 (0.0)	47 (54.7)	33 (38.4)	4 (4.7)	2 (2.3)
		1 year after	3.92 (4.21)	24 (27.9)	44 (51.2)	15 (17.4)	2 (2.3)	1 (1.2)
All DMARDs	**432**	Baseline	**7.57 (5.77)**	**0 (0.0)**	**228 (52.8)**	**156 (36.1)**	**27 (6.3)**	**21 (4.9)**
		1 year after	**3.22 (5.48)**	**175 (40.5)**	**185 (42.8)**	**63 (14.6)**	**6 (1.4)**	**3 (0.7)**

Figure. Average daily glucocorticoids usage. A) All DMARDs. B) TNFi. C) Anti-IL6. D) Anti-CD20. E) JAKi. F) CTLA4-Ig



Conclusion: Our data shows that glucocorticoids are frequently used and for longer than 3 months when initiating b/tsDMARDs. Around 2% of patients have glucocorticoid doses over 10mg and 15% over 5mg after one year follow-up. Further studies are necessary to evaluate variables associated with persistent use of glucocorticoids.

References:

1. Smolen JS, et al. Ann Rheum Dis 2023;82:3–18.
2. Fraenkel, L. Arthritis Care & Research 2021; 73: 924–939

Disclosure: L. Otero-Valera: None; **J. Alvaro-Gracias**: Abbvie, 2, 6, AstraZeneca, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, GSK, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **J. Calvo**: None; **C. Campos**: None; **A. Garcia Dorta**: None; **F. Sánchez-Alonso**: None; **I. Castrejon**: Bristol Myers Squibb, 1, 6, Galapagos, 2, GlaxoSmithKline, 1, 6, Lilly, 1, 6, Merck Sharp & Dohme, 6, Pfizer, 1, 2, 6.

Abstract Number: 0448

Cardioprotective Impact of JAKi, Tofacitinib, on CV Risk in Rheumatoid Arthritis: JAKi CV Risk Impact Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: RA patients have at least twice the risk of CVD. In fact, CVD is the leading cause of morbidity and premature mortality in RA. Inflammation driven endothelial dysfunction leads to accelerated atherosclerosis and premature CVD in RA. JAKi, tofacitinib, in human aortic endothelial culture inhibits VCAM-1, ICAM-1, TNF-a, IL-1b. However, tofacitinib increases MACE risk in RA patients with ASCVD.

Impact of Tofacitinib on endothelial function in RA patients with inadequate response to csDMARDs in the absence of conventional CV risk factors or pre-existing CVD needs exploration. Endothelial dysfunction (ED), the " sine qua non" for atherosclerosis appearance, is the key promoter of CVD. ED is a barometer for CV health and a seminal target for reducing cardiovascular (CV) risk in RA.

The objective was to prospectively investigate the impact of Tofacitinib (TOFA) on CV risk in active RA in absence of overt CVD or its risk factors.

Methods: 81 consecutive RA patients meeting 2010 Rheumatoid Arthritis Classification Criteria median age 54 years, 81% female, disease duration 14 years, moderate to high activity (DAS28-5.3) who were non-responders to MTX at least 15 mg/week and/or other synthetic DMARDs free of clinical overt cardiovascular disease were randomized 1:1 to receive TOFA 5 mg bid (n=41) or placebo (n=41) for 12 weeks as an adjunct to existing stable antirheumatic drugs. Primary endpoints included endothelial dysfunction assessed by FMD, using Angiodefender, at baseline and after 12 weeks of treatment and occurrence of MACE and VTE throughout the study. The secondary end points included: DAS28, ESR, CRP, HAQ-DI.

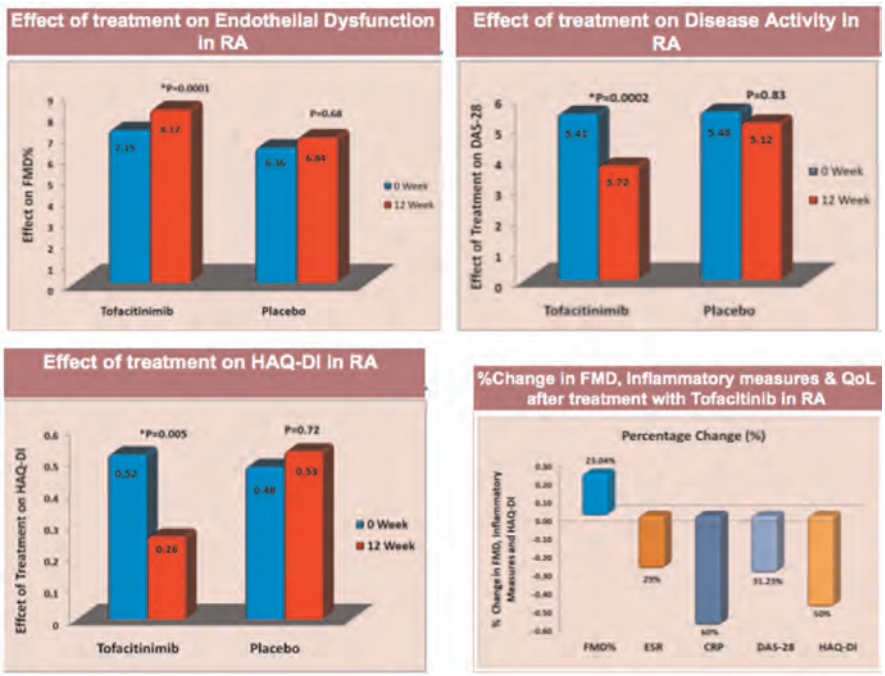

Fig 1. Effect of Tofacitinib treatment on (A) Endothelial dysfunction (B) Disease activity (C) HAQ-DI and (D) % Change

Effect of tofacitinib on 9A) Endothelial Dysfunction (B) Disease Activity (C) HAQ (D) % Change

Results: At baseline, endothelial function was impaired and levels of inflammatory measures were elevated and HAQ-DI was impaired in both groups. After treatment, FMD improved significantly in the tofacitinib group from (6.64 ± 2.13 to 8.17 ± 2.69, p=0.0001) as compared to placebo (6.36 ± 3.01% to 6.84 ± 2.95%, p=0.68) (Fig. 1A). DAS28 (Fig. 1B), ESR and CRP levels improved significantly in tofacitinib group as compared to placebo (p≤0.05). TOFA significantly decreased HAQ-DI (Fig. 1C) values as compared to placebo. There was no MACE or VTE event during the study period in either group. After 12 weeks of treatment, FMD increased by 23.04% where as DAS28, ESR and CRP decreased by 31.23%, 29% and 60% respectively in the TOFA group (Fig 1D). Significant negative correlation was observed between FMD and CRP (0.32, p≤0.05) before and after (r= -0.34, p≤0.05) treatment with TOFA whereas no such correlations were found in placebo group.

Conclusion: TOFA, apart from its anti-inflammatory activity, improves endothelial dysfunction and cardiovascular risk in active RA without clinical overt cardiovascular disease. Thus, JAK inhibition with TOFA has vasculoprotective and cardioprotective effect mediated through anti-inflammatory and probably other mechanisms.

Disclosure: A. Syngle: None; **I. verma**: None; **N. Garg**: None; **K. Chauhan**: None; **S. Patyal**: None; **D. Syngle**: None.

Abstract Number: 0449

Parsing Pathophysiology of Rheumatoid Arthritis-associated Lymphoproliferative Disorders via Whole RNA Transcriptome Analysis: Multi-center Study in Japan

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Lymphoproliferative disorders (LPD) in rheumatoid arthritis (RA) (RA-LPD) have unique pathophysiological features. More than half of the cases of RA-LPD undergo spontaneous regression after the discontinuation of disease modifying anti rheumatic drugs (DMARDs), whereas approximately 33% of these cases relapse. Epstein-Barr virus (EBV) infection is especially involved in the pathophysiology of RA-LPD. The current study was conducted with whole RNA transcriptome analysis using the peripheral blood of patients developing RA-LPD to investigate the pathophysiology of RA-LPD.

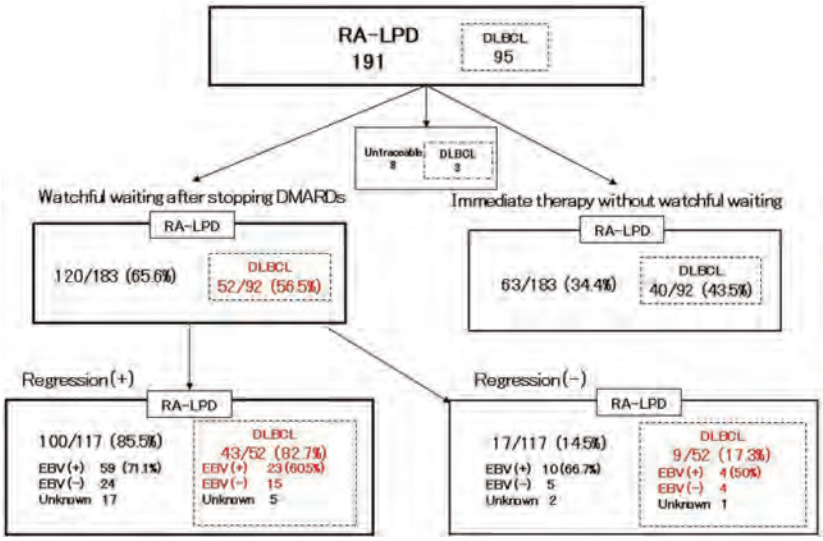

Figure 1. Flow diagram of the study. Cases analyzed in this study are written in red. RA-LPD: lymphoproliferative disorders in rheumatoid arthritis; DLBCL: diffuse large B-cell lymphoma; DMARD: Disease modifying anti rheumatic drug; EBV: Epstein-Barr virus.

Methods: Peripheral blood samples of the patients with RA-LPD were obtained between May 2013 and October 2018 from 30 hospitals in Japan. Whole transcriptome sequencing was performed using the Ion AmpliSeq Human Gene Expression Kit (Thermo Fisher Scientific) and an IonS5 XL sequencer (Thermo Fisher Scientific). The kit covers the expression levels of 20,802 human RefSeq genes (based on UCSC hg19). Differential gene expression analysis was performed by Transcriptome Analysis Console (TAC) software (ver. 4.0.3, Thermo Fisher Scientific) with |FC| > 2-fold difference and at $p < 0.1$. A Gene Set Enrichment Analysis (GSEA) was performed to identify pathways enriched in the Molecular Signatures Database (MSigDB) Hallmark gene set. A nominal p value of < 0.05 and an FDR (false discovery rate) q value of < 0.25 were considered statistically significant.

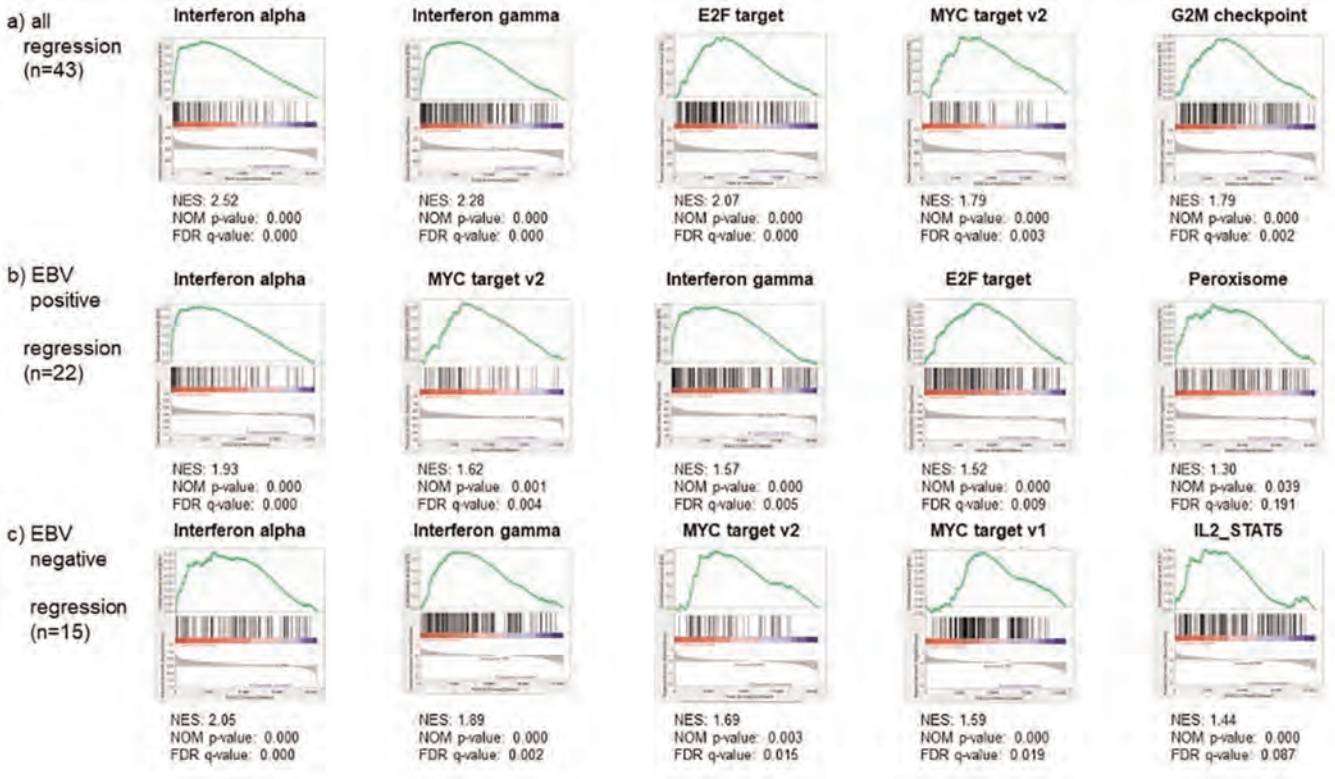

Figure 2. Gene set enrichment analysis (GSEA) in all regression cases (a), regression cases with Epstein-Barr virus (EBV) infection (b), and regression cases without EBV infection (c). Interferon alpha and gamma pathways were upregulated in all regression cases. Interleukin-2- STAT5 was a unique pathway in EBV negative cases.

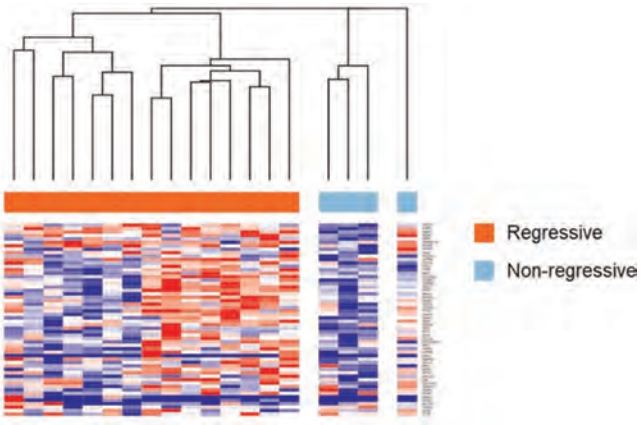

Figure 3. Heatmap showing gene expression related to interleukin 2-STAT5 pathway in cases without Epstein-Barr virus infection. They were highly expressed in regression cases.

Results: In total, 211 cases (191 RA-LPD cases and 20 non-LPD RA cases) were analyzed. The flow diagram of the study is shown in Figure 1. We grouped diffuse large B-cell lymphoma (DLBCL) cases into two groups; regression cases (n = 43), which regressed spontaneously after stopping DMARDs and non-regression cases (n = 9), which did not regress. Gene expression levels were compared between the two groups. GSEA analysis showed that interferon alpha and gamma pathways were enhanced in regression cases (Figure 2a). To investigate mechanisms of regression in EBV-negative cases, we performed further analysis according to EBV infection status. (EBV positive, n= 22; EBV negative, n= 15). The interleukin-2-STAT5 (IL2-STAT5) pathway was enhanced in regression cases without EBV infection, which was suggested to be a unique mechanism for regression in EBV-negative RA-LPD (Figure 2b, c). The heatmap (Figure 3) shows that genes related to IL2-STAT5 were expressed highly in regression cases without EBV infection. Additionally, expression levels of some genes related to the IL2-STAT5 pathway were significantly different between regression and non-regression EBV-negative cases. This result suggests that these genes may serve as new liquid markers for regression in EBV-negative RA-LPD.

Conclusion: The current study showed that interferon-alpha and gamma pathways were upregulated in the regression cases with DLBCL of RA-LPD. Moreover, the study revealed a unique mechanism related to IL2-STAT5 for regression of EBV-negative cases. Our research further suggested new potential markers for regression in EBV-negative cases.

Disclosure: A. TSUJII: None; **K. SAKAI**: Chugai Pharmaceutical, 6, Life Technologies Japan, 6, Qiagen, 6, Takeda Pharmaceutical, 6; **S. OHSHIMA**: None; **Y. SAEKI**: None; **M. YAGITA**: Medical & Biological Laboratories, CO., Ltd, 9, ONK therapeutics, 9; **T. MIYAMURA**: None; **M. Katayama**: None; **Y. HIRAMATSU**: None; **S. HIGA**: None; **F. HIRANO**: None; **K. ICHIKAWA**: None; **N. CHIBA**: None; **T. SUGIYAMA**: None; **A. IHATA**: None; **H. TSUTANI**: None; **K. TAKAHI**: None; **K. MIGITA**: None; **S. MORI**: AbbVie GK, 6, 6, Asahikasei Pharma Corp, 6, Boehringer Ingelheim Japan, 6, Chugai Pharmaceutical Co. Ltd., 6, Chugai Pharmaceutical Co., Ltd., 6, Eli Lilly Japan K.K., 6, Janssen Pharmaceutical K.K., 6, Pfizer Japan Inc., 6, Taisho Pharma Co., Ltd., 6; **N. YOSHIKAWA**: None; **A. UEDA**: None; **S. NAGAOKA**: None; **K. SETOGUCHI**: None; **S. SUGII**: Eisai CO., Ltd., 6, MOCHIDA PHARMACEUTICAL CO>, 6; **A. ABE**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 6; **T. SUGAYA**: None; **H. SUGAHARA**: None; **S. TSUNODA**: None; **N. IIZUKA**: None; **R. YOSHIHARA**: None; **H. YABE**: None; **T. FUJISAKI**: None; **E. MORII**: None; **K. SAITO**: None; **K. Matsui**: None; **Y. TOMITA**: None; **H. FURUKAWA**: None; **S. Tohma**: AbbVie/Abbott, 5, AsahiKASEI Co., Ltd., 6, Chudai Pharmaceutical Co., Ltd., 5, Mitsubishi Tanabe Pharma Corporation, 5, Pfizer Japan Inc., 6; **K. NISHIO**: Amgen, 6, AstraZeneca, 6, Bristol-Myers Squibb, 6, Chugai, 6, DAIICHI SANKYO, 6, Eli Lilly Japan, 5, 6, FUJIREBIO, 6, Guardant Health, 6, Hitachi, 5, Invitae Japan, 6, Janssen Pharmaceutical, 6, Merck Biopharma, 6, MSD, 6, Nichirei Biosciences, 5, Nippon Boehringer Ingelheim, 5, 6, Novartis Pharma, 6, Ono, 6, Otsuka Pharmaceutical, 5, 6, Pfizer, 6, SymBio Pharmaceuticals⊃⊃v, 6, SYSMEX, 5, Takeda, 6, Yakult Honsha, 6; **Y. HOSHIDA**: None.

Abstract Number: 0450

Baricitinib versus TNF-inhibitors in Patients with Active Rheumatoid Arthritis After Failure of CsDMARDs: A Pragmatic, Multicenter, Real-Life Study in a Treat-to-Target Setting

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The EULAR guidelines for Rheumatoid Arthritis (RA) patients advise to use a strategy aiming at a predefined target of disease activity (T2T). If this target is not achieved with csDMARD, adding a TNF-inhibitor (TNFi) or a JAK-inhibitor (JAKi) are advised options in cases with poor prognostic factors, obviously considering contraindications. While randomized clinical trials have provided insight into the relative efficacy and safety of TNFi and JAKi under trial conditions, the generalizability to real-life clinical practice remains unclear.

We aim to demonstrate the non-inferiority (NI) and, in case NI could be shown, subsequent superiority of a T2T strategy using baricitinib versus TNFi, after failure of csDMARDs, in a real-life setting.

Methods: Biologic or targeted synthetic DMARD(b/tsDMARD)-naïve RA patients failing to respond to csDMARDs were eligible if they were pretreated according to T2T principles, had a disease duration ≤5 years and no contraindications to b/tsDMARD. All included patients were treated open label, according the T2T principle, at the discretion of their attending physician with either a TNFi (any type) or baricitinib. Patients were seen at baseline and 12-weekly until final follow-up (48 weeks). Full clinical assessment was performed at each visit and patients completed several PROMs. The primary endpoint was defined as NI of baricitinib versus TNFi with respect to the number of patients achieving ACR50 response at week 12. Subsequently, superiority testing was foreseen in case non-inferiority was shown. For the primary efficacy analysis, the

Table baseline characteristics

		TNFi	Baricitinib	p
		N=102	N=97	
Age		55.2 (13.4)	54.8 (12.0)	0.833
Gender	F	68 (66.7%)	62 (63.9%)	0.796
	M	34 (33.3%)	35 (36.1%)	
Smoking	Never	38 (37.3%)	37 (38.9%)	0.963
	Stopped	39 (38.2%)	36 (37.9%)	
	Yes	25 (24.5%)	22 (23.2%)	
BMI		27.4 (4.93)	26.5 (5.03)	0.209
Disease duration (years)		2.00 [1.00;3.00]	2.00 [1.00;3.00]	0.766
CV	No	74 (72.5%)	76 (78.4%)	0.432
	Yes	28 (27.5%)	21 (21.6%)	
RF	Neg	33 (32.4%)	27 (27.8%)	0.589
	Pos	69 (67.6%)	70 (72.2%)	
ACCP	Neg	37 (36.3%)	27 (27.8%)	0.262
	Pos	65 (63.7%)	70 (72.2%)	
MTX	No	33 (32.4%)	35 (36.1%)	0.686
	Yes	69 (67.7%)	62(63.9%)	
$DAS28_{ESR}$		4.43 (1.06)	4.41 (1.14)	0.911
$DAS28_{CRP}$		4.17 (1.03)	4.08 (1.05)	0.553
TJC		4.00 [2.00;7.00]	4.00 [2.00;7.00]	0.778
SJC		3.00 [1.00;5.00]	3.00 [2.00;4.00]	0.940
BSE		24.0 (19.5)	25.1 (22.1)	0.746
CRP		13.7 (19.1)	12.3 (17.5)	0.581
PG		50.0 (21.3)	51.9 (16.9)	0.501
Wellbeing		61.1 (21.5)	54.1 (22.5)	0.025
Pain		61.5 (24.0)	55.6 (25.0)	0.095
HAQ		12.2 (5.66)	10.9 (6.38)	0.155
SDAI		21.3 (8.89)	20.9 (8.96)	0.769

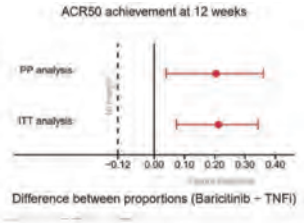

figure 1

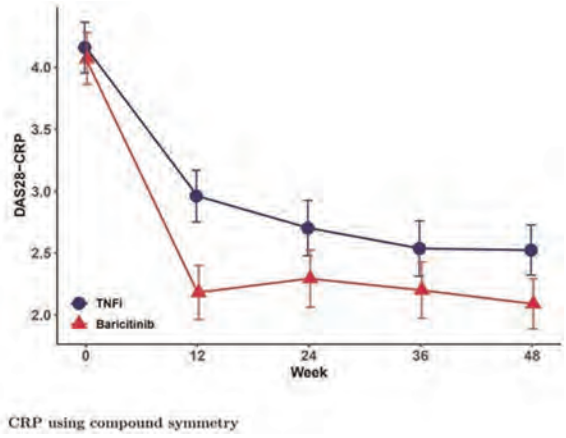

figure 2

ACR50 responses were compared, using 95% confidence intervals calculated using the Wilson score method for the difference in proportions. The non-inferiority margin for baricitinib was set at -12%. Linear mixed models were used to analyze continuous secondary outcomes over the study period of 48 weeks.

Results: 199 patients who received a first dose of either TNFi (n=102) or baricitinib (n=97) were included. Baseline characteristics were comparable between both groups (see table). At 12 weeks, the lower bound of the 95% confidence interval for the difference in the ACR50 response was above zero, in both the per-protocol and intention-to-treat analysis (figure 1). Hence, baricitinib was found to be non-inferior and statistically superior to TNFi in the analysis of the primary endpoint. Moreover, DAS28 remission (DAS28-CRP < 0.6) was achieved in 74% of baricitinib patients compared with 47% of TNFi patients ($p< 0.001$) at 12 weeks. All secondary clinical and PRO -measures over the study period of 48 weeks showed better responses, most often statistically superior, of Baricitinib over TNFi (figure 2 for DAS28-CRP).

Conclusion: Baricitinib was found to be non-inferior as well as superior to TNFi in terms of ACR50 response at 12 weeks in real-world csDMARD refractory RA patients. Analysis of the secondary endpoints on disease activity and PROMs, were consistently in favor of the group that started Baricitinib.

Disclosure: M. Van de Laar: Eli Lilly, 5, 6; **M. Oude Voshaar**: Eli Lilly, 5; **P. ten Klooster**: Eli Lilly, 5; **D. Tedjo**: Eli Lilly, 5; **c. van de laar**: Eli Lilly, 5.

Abstract Number: 0451

Long-term Clinical Profile of Filgotinib in Patients with Rheumatoid Arthritis by Cardiovascular Risk Factors: A *Post Hoc* Subgroup Analysis

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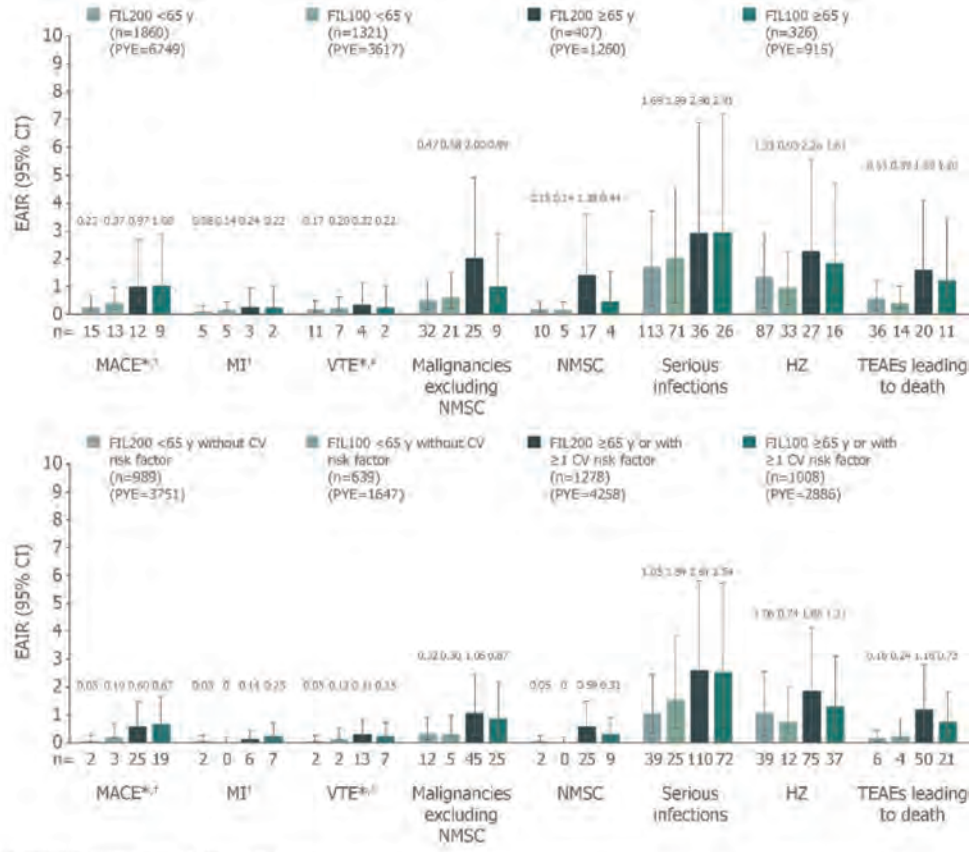
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Filgotinib (FIL) is an oral Janus kinase 1 preferential inhibitor for the treatment of moderate to severe active RA. A previous pooled analysis reported long-term safety and efficacy for FIL 200 mg (FIL200) vs FIL 100 mg (FIL100) in patients (pts) aged ≥ 65 and < 65 y.[1] The objective of this analysis was to report updated long-term safety and efficacy in 4 subgroups of pts with RA (aged < 65 y, ≥ 65 y, < 65 y without cardiovascular [CV] risk, and ≥ 65 y or with CV risk), treated with FIL200 vs FIL100.

Methods: This *post hoc* analysis pooled data from Phase 2 (DARWIN 1–3; NCT01888874, NCT01894516, NCT02065700) and Phase 3 (FINCH 1–4; NCT02889796, NCT02873936, NCT02886728, NCT03025308) trials. Data for long-term extensions (LTEs) were as of May 2, 2022 (DARWIN 3), and May 6, 2022 (FINCH 4). Analyses were by age (< 65 vs ≥ 65 y) and subgroup (< 65 y without CV risk factor vs ≥ 65 y or ≥1 CV risk factor). CV risk factors were: family history of CV disease; history of dyslipidemia, diabetes mellitus or CV disease; hypertension, ischemic vascular conditions, peripheral vascular disease, extra-articular manifestations of RA; or ever smoked. The as-treated analysis set included data for pts receiving ≥1 FIL dose. Exposure-adjusted incidence rates (EAIRs)/100 patient-years of exposure (PYE) of selected adverse events (AEs), and % of pts achieving Disease Activity Score in 28 joints using C-reactive protein (DAS28-CRP) of < 2.6 or ≤ 3.2 through Week 156 in FINCH 4, are reported.

Results: Baseline characteristics by age have been reported.[1] Baseline disease characteristics by age or CV risk factor were similar for disease severity and concurrent treatment. EAIRs for any treatment-emergent AEs (TEAEs) were generally higher in pts aged ≥ 65 (120.40) vs < 65 y (97.86), and higher in pts aged ≥ 65 y or with CV risk (120.45) vs pts aged < 65 y without CV risk (81.83). Pts aged ≥ 65 y, followed by the broader subgroup with CV risk factors (i.e. ≥ 65 y or ≥ 1 CV risk) had higher EAIRs of serious TEAEs and TEAEs leading to discontinuation vs other subgroups, indicating age is a key risk factor alongside other CV risk factors for developing AEs (data not shown). In pts aged ≥ 65 y, lower incidences of malignancies (excluding nonmelanoma skin cancer [NMSC]), NMSC, herpes zoster (HZ) and TEAEs leading to death were observed with FIL100 than FIL200 (**Figure**). In the broader subgroup with risk factors (i.e. aged ≥ 65 y or ≥ 1 CV risk factor), EAIRs of AEs were generally lower vs pts aged ≥ 65 y, indicating greater influence of age. EAIRs of AEs for subgroups (aged < 65 y without CV risk; ≥ 65 y or ≥ 1 CV risk) for FIL200 and FIL100 are shown (**Figure**). Rates of DAS28-CRP < 2.6 or ≤ 3.2 in all subgroups (FINCH 4) were maintained with FIL100 and FIL200 to Week 156 (**Table**).



EAIRs/100 PYE, censored at time of first event.
*MACE and VTE only included positively adjudicated events with a cutoff of April 3, 2022. †MACE comprised CV events leading to death, MI and stroke; for subcategories of stroke and MI, both fatal and non-fatal events were considered. ‡For VTE subcategories, PE, DVT and 'other' were considered.
DVT, deep vein thrombosis; MACE, major adverse cardiovascular event; MI, myocardial infarction; PE, pulmonary embolism; VTE, venous thromboembolism.

Figure. EAIR of AEs by age and CV risk (safety analysis set, as treated)

Table. DAS28-CRP <2.6 and ≤3.2 from LTE baseline to Week 156, by age, CV risk and FIL dose (safety analysis set, observed values)

	<65 y		≥65 y		<65 y without CV risk factor		≥65 y or with ≥1 CV risk factor	
LTE Week	FIL100 n=944	FIL200 n=1256	FIL100 n=255	FIL200 n=274	FIL100 n=419	FIL200 n=640	FIL100 n=780	FIL200 n=890
	Patients achieving DAS28-CRP <2.6 (%)							
Baseline	46.8	54.5	50.8	59.5	48.2	57.4	47.3	54.0
12	49.0	61.3	55.8	62.0	48.8	65.0	51.3	58.9
24	50.5	62.7	55.2	66.3	48.7	64.7	52.9	62.3
48	51.1	64.2	57.8	65.7	51.6	67.2	53.0	62.4
108	54.2	65.0	58.8	70.2	52.3	67.8	56.7	64.3
156	52.9	64.2	58.9	63.5	51.6	62.9	55.4	64.9
	Patients achieving DAS28-CRP ≤3.2 (%)							
Baseline	66.9	73.7	69.8	74.8	68.8	76.3	66.8	72.2
12	66.8	75.7	71.9	74.4	67.3	80.2	68.2	72.1
24	70.4	78.0	70.4	79.2	70.2	80.4	70.5	76.7
48	71.2	79.1	73.3	78.2	71.4	82.3	71.8	76.4
108	70.4	79.8	75.8	82.0	71.2	82.5	71.6	78.3
156	72.0	81.7	77.8	82.6	70.9	81.6	74.5	82.0

No missing data imputation was performed.

Conclusion: This *post hoc* analysis (in pts ≥ 65 y or with ≥ 1 CV risk factor) suggests that age is an important risk factor in the evaluation of the FIL200 safety profile. Future studies are needed to address the relative contribution of age to traditional CV risk factors. In FINCH 4, efficacy was maintained in all subgroups.

Reference:
1. Buch M, et al. Arthritis Rheumatol 2022;74(Suppl 9):0281

Disclosure: M. Buch: AbbVie, 2, 6, 12, All paid to host institution, Boehringer Ingelheim, 2, 6, 12, Paid to host institution, Galapagos, 2, 6, 12, Paid to host institution, Gilead, 2, 5, 6, 12, Paid to host institution, Lilly, 2, 6, 12, All paid to host institution, National Insitute for Health and Care Research (NIHR), 3, 12, Maya H Buch is a National Institute for Health and Care Research (NIHR) Senior Investigator. The views expressed are those of the authors and not nece, Pfizer, 2, 12, Paid to host institution; **J. Gomez-Puerta**: AstraZeneca, 6, Eli Lilly, 6, Galapagos, 6, GSK, 6, Janssen, 6, Pfizer, 6, Sanofi, 2; **G. Burmester**: AbbVie, 2, 6, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Chugai, 6, Galapagos, 2, 6, Lilly, 2, 6, Pfizer, 2, 6, Sanofi, 2, 6; **B. Combe**: AbbVie, 2, 6, BMS, 6, Celltrion, 2, Eli Lilly, 1, 2, 6, Galapagos, 2, 6, Gilead, 2, Janssen, 2, 6, MSD, 6, Nordic Pharma, 5, Novartis, 1, Pfizer, 6, Roche-Chugai, 2, 6; **V. Rajendran**: Galapagos, 3, 11; **P. Stiers**: Galapagos, 3, 11; **P. Van Hoek**: Galapagos, 7; **K. Van Beneden**: Galapagos, 3, 11; **J. Gottenberg**: AbbVie, 2, BMS, 2, 5, Galapagos, 2, Gilead, 2, Lilly, 2, MSD, 2, Novartis, 2, Pfizer, 2, 5; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer-Ingelheim, 6, Chugai, 5, 6, Eisai, 5, 6, Eli Lilly, 6, Gilead, 6, GSK, 6, Mitsubishi-Tanabe, 5, Pfizer, 6, Taiho, 6, Taisho, 5, 6; **D. Aletaha**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Janssen, 2, 6, Lilly, 2, 5, 6, Merck, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6, Sandoz, 2, 6, Sanofi, 5, Sobi, 5; **R. Westhovens**: Celltrion, 2, 6, Galapagos, 2, 6, Gilead, 2, 6; **R. Caporali**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celltrion, 2, 6, Fresenius Kabi, 2, Galapagos, 2, 6, Janssen, 2, 6, Lilly, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, Sandoz, 2, 6, UCB, 2, 6.

Abstract Number: 0452

Real Life Safety and Survival of Targeted Therapies in Arthritis Patients over Age of 65

Elena Grau Garcia[1], Pablo Francisco Muñoz Martínez[2], Laura Mas Sanchez[3], Alba Maria Torrat Noves[1], Daniel Ramos Castro[1], Carmen Riesco Barcena[1], Anderson Victor Huaylla Quispe[1], Iago Alcantara Alvarez[1], Belen Villanueva Mañez[1], Samuel Leal Rodriguez[1], Ines Canovas Olmos[1], Hikmat Charia[1], Marta De la Rubia Navarro[1], Luis Gonzalez Puig[1], Jose Ivorra Cortes[1], Isabel Martinez Cordellat[1], Carmen Najera Herranz[1], Rosa Negueroles Albuixech[1], Jose Eloy Oller Rodriguez[1], Ernesto Tovar Sugrañes[1], Elvira Vicens Bernabeu[1] and Jose Andres Roman Ivorra[4], [1]Rheumatology Department. HUP La Fe, Valencia, Spain, [2]Rheumatology Department. HUP La Fe, Sagunto, Spain, [3]Rheumatology Department. HUP La Fe, Valéncia, Spain, [4]Hospital Universitari i Politècnic la Fe, Valencia, Spain

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Prognosis for chronic inflammatory arthritis is drastically improved over previous decades and older patients are treated with targeted therapies (TTs) (biological or synthetic targeted therapies). Clinical trials provide mainly information about TTs in patients below the age of 65, so real-life studies are needed to provide more information about TTs in patients over 65 years of age.

The aim of the present study was to compare clinical and therapeutic profile of arthritis patients undergoing TTs and to analyze safety and therapeutic survival according to different age groups.

Table1. Comparative analysis of clinical profile of different age groups at the beginning of TTs.

Variable	40-65 years N=719	≥65 years N=219	P-value
	Mean (SD) / n (%)	Mean (SD) / n (%)	
Age at diagnosis (years)	43 (11)	56 (14)	< 0.001
Age at the beginning of treatment (years)	53 (7)	72 (5)	< 0.001
Time from the diagnosis to the beginning of treatment (years)	10 (10)	17 (12)	< 0.001
Treatment duration (months)	73 (66)	52 (52)	< 0.001
Female sex	425 (59.1%)	156 (71.2%)	0.001
Diagnosis:			
• RA	359 (49.93%)	163 (74.43%)	< 0.001
• PsA	168 (23.37%)	22 (10.05%)	< 0.001
• AS	192 (26.7%)	34 (15.53%)	< 0.001
Arterial hypertension	130 (29%)	84 (57.9%)	< 0.001
Diabetes mellitus	47 (10.5%)	32 (22%)	< 0.001
Dislipemia	124 (27.7%)	61 (42.1%)	< 0.001
Malignancy	54 (13%)	27 (22.5%)	0.016
DMARD concomitant			
• No DMARD	355 (49.4%)	79 (36.1%)	< 0.001
• Methotrexate	246 (34.2%)	98 (44.8%)	0.006
• Leflunomide	72 (10%)	22 (10.1%)	0.999
• Others	37 (5.2%)	20 (9.1%)	0.045
Targeted therapies:			
• ANTI-TNF	399 (55.5%)	86 (39.3%)	< 0.001
• ANTI-JAK	114 (15.9%)	33 (15.1%)	0.862
• ANTI-IL17	84 (11.7%)	12 (5.5%)	0.012
• ANTI-IL6	55 (7.7%)	32 (14.6%)	0.003
• Others	67 (9.3%)	56 (25.6%)	< 0.001
Continuing treatment	559 (77.9%)	158 (72.1%)	0.746
Discontinued treatment by:			
Primary non-response	10 (1.4%)	3 (1.4%)	0.895
Secondary non-response	27 (3.8%)	5 (2.3%)	0.401
Other causes	57 (7.9%)	18 (8.2%)	0.999
Adverse events	65 (9.1%)	35 (15.9%)	0.005
• Infection	11 (1.5%)	8 (3.7%)	0.093
• Malignancy	26 (3.6%)	7 (3.2%)	0.932
1st line treatment	444 (61.8%)	99 (45.2%)	< 0.001
Cycling	85 (11.8%)	29 (13.2%)	0.656
Switching	190 (26.4%)	91 (41.6%)	< 0.001

Methods: We performed an observational cross-sectional study in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) patients, older than 40 years old, who started biological or anti-JAK therapy between 2000 and 2022. A comparative analysis and a Kaplan-Meier survival analysis was performed.

Results: 938 patients (62% female) were included in the study, of which 20.3% are PsA, 55.6% RA and 24.1% AS, with a mean age at the beginning of treatment of 57 (10) years and a mean duration of treatment of 68 (64) months. Patients were classified according to the age at the beginning of treatment: 40-65 years and ≥ 65 years of age. 219 patients (23.3%) were over 65 years of age. In table1 we show the comparative analysis between both groups.

Higher proportion of arterial hypertension, diabetes mellitus and dislipemia in patients older than 65 years was observed. Using a logistic regression model, an association between conventional DMARD prescription and patients older than 65 years was found (P< 0.001), being the methotrexate the most used (44.8%). Anti-TNF therapy was the most extended treatment in both groups of patients, and an association between anti-IL6 therapy and older patients than 65 years was observed (P< 0.001). Previous TTs were more frequent in older patients (P=0.002) and treatment duration was lower in

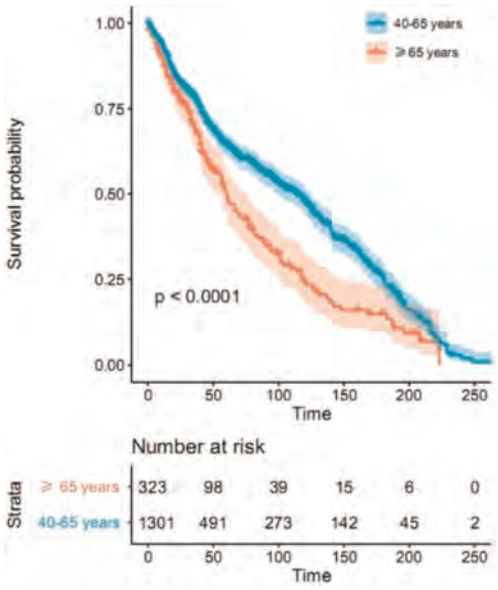


Figure 1

those patients (P< 0.001) (figure1). Adverse events were more commonly found in patients older than 65 years as the reason to TT discontinue (P=0.008), being infections the more frequent.

Conclusion: The use of conventional DMARDs and lower therapeutic survival are more frequent in patients older than 65 years of age.

Adverse events were the main reason of treatment suspension in these patients, with a higher proportion of infections among them in contrast to patients under 65 years old.

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Abstract Number: 0453

Risk of Lung Cancer in Veterans with Rheumatoid Arthritis in Relation to Use of Conventional versus Biologic or Targeted Synthetic DMARDs

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Table 1. Characteristics of the cohort in person-years by DMARD exposure

Characteristic	Person-years on csDMARD only (%)	Person-years on b/tsDMARD (%)
Baseline Age		
18-40	3709 (2.78)	2,944.32 (5.61)
41-60	40,524 (30.35)	25,085.85 (47.77)
61-80	79,303 (59.40)	23,692.31 (45.11)
80+	9,973 (7.47)	797.17 (1.52)
Male	120,030.23 (90)	45,326.84 (86)
Race		
Black	18,145.95 (13.59)	6,198.27 (11.80)
Other	3,136.46 (2.35)	1,331.89 (2.54)
White	101,143.65 (76)	42,071.43 (80)
Missing	11,083.06 (8.30)	2,918.06 (5.56)
Ethnicity		
Hispanic or Latino	5,588.36 (4)	2,416.73 (4.60)
Not Hispanic or Latino	119,691.03 (90)	48,022.44 (91.4)
Missing	8,229.72 (6)	2,080.47 (4)
Cohort Entry		
2002-2007	65,531.74 (49.08)	25,571.25 (48.70)
2008-2013	47,049.41 (35.24)	20,496.76 (39.00)
2014-2019	20,927.96 (15.68)	6,451.64 (12.28)
Baseline BMI		
<18.5	930.72 (0.70)	417.61 (0.80)
18.6-25	24,998.70 (18.72)	9,017.56 (17.17)
25.1-30	44,883.75 (33.62)	16,928.78 (32.23)
30.1+	44,166.95 (33.08)	19,160.21 (36.48)
Missing	18,528.99 (13.88)	6,995.49 (13.32)
Baseline RDCI		
0	25,877.53 (19.38)	14,014.02 (26.68)
1	33,627.91 (25.19)	14,094.80 (26.84)
2	36,158.72 (27.08)	12,765.50 (24.31)
3	20,926.12 (15.67)	6,743.53 (12.84)
4+	16,918.82 (12.67)	4,901.80 (9.33)
Baseline smoking status		
Current or former	51,752.38 (38.76)	21,901.77 (41.70)
Never smoker	29,248.65 (21.91)	10,569.39 (20.12)
Missing	52,508.08 (39.33)	20,048.49 (38.17)
RF or anti-CCP positive	71,834.43 (53.80)	39,236.89 (74.71)

Abbreviations: anti-CCP: anti-cyclic citrullinated peptide; BMI: body mass index; csDMARD: conventional synthetic disease modifying anti-rheumatic drug; b/ts: biologic or targeted synthetic; RDCI: rheumatic disease comorbidity index; RF: rheumatoid factor

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is associated with an increased risk of lung cancer compared to the general population. While smoking is a shared risk factor, little is known about the association between use of disease modifying anti-rheumatic drugs (DMARDs) and development of lung cancer. We undertook this study to evaluate the association between use of conventional synthetic (cs) versus biologic (b) or targeted synthetic (ts) DMARDs and incident lung cancer in patients with RA.

Methods: In this retrospective cohort study, we identified Veterans diagnosed with RA in any United States Veterans Affairs facility from 1/1/2002 and 12/31/2018. Criteria for the presence of RA were: two or more International Classification of Diseases Version 9 or 10 (ICD9 or ICD10) diagnosis codes for RA at least 7 days apart but no more than 365 days apart, and a prescription for a csDMARD within 90 days of the first RA diagnosis (index date). The csDMARDs included in these analyses

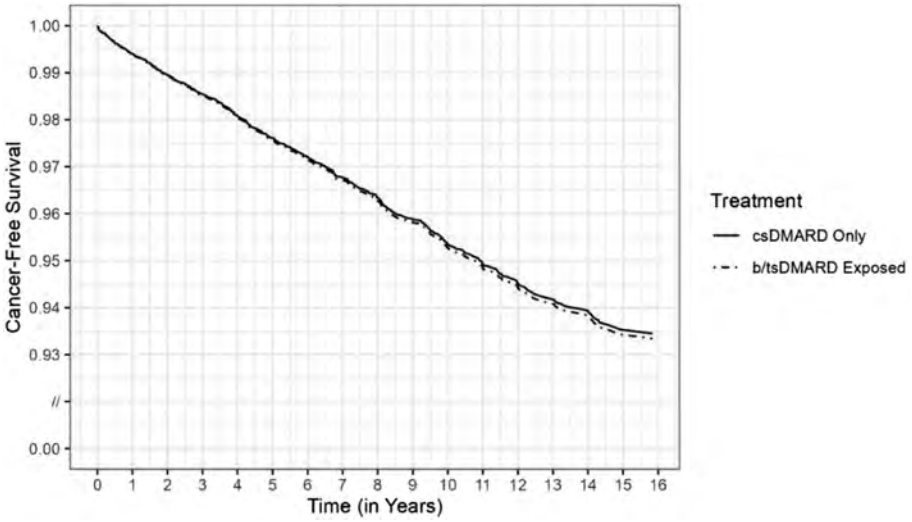

Figure 1. Kaplan Meier curves showing association between use of disease modifying anti-rheumatic drugs and lung cancer.

were: methotrexate, sulfasalazine, leflunomide, and hydroxychloroquine. The bDMARDs included were tumor necrosis factor inhibitors (TNFi) and non-TNFi biologics such as tocilizumab, rituximab, abatacept, and biosimilars; tsDMARDs included tofacitinib and baricitinib. Patients with lung cancer before the diagnosis of RA were excluded. Incident lung cancer was determined by ^{3}2 outpatient ICD9/10 codes, or ^{3}1 ICD9/ICD10/ICDO codes if from inpatient or the oncology raw domain. Drug exposure categories (csDMARD versus b/tsDMARD) were treated as a time-varying variable. Multivariable Cox models were fit to estimate the hazard ratio for developing lung cancer during and following the use of a b/tsDMARD relative to b/tsDMARD-naïve persons adjusting for time-varying age, rheumatic disease comorbidity index (RDCI) and RA interstitial lung disease (RA-ILD, identified using validated administrative algorithms(1)); and baseline sex, race, ethnicity, smoking status, body mass index (BMI), cohort entry (2002-2007, 2008-2013, 2014-2019), rheumatoid factor or anti-CCP positivity, use of opioids, NSAIDs, and steroids. Missing data were imputed using multiple imputation by chained equations.

Results: 26,625 veterans met eligibility criteria, of whom 89% were male and 71% were Non-Hispanic White (**Table 1**). Over a mean (±standard deviation) follow up of 7.0 (±4.5) years, 852 incident lung cancers were detected. The age-standardized incidence among those only on csDMARDs was 4.56 per 1000-person years, compared to 5.33 for those exposed to b/tsDMARDs. In multivariable adjusted models, the hazard ratio for lung cancer in persons who had been treated with a b/tsDMARD was 1.03 (95% confidence interval (CI) 0.87-1.21) relative to those only on csDMARDs (**Figure 1**).

Conclusion: Among Veterans with RA, we observed no evidence of an altered risk of lung cancer associated with different forms of RA treatment. However, incomplete information on cigarette smoking history, along with the relatively short period of follow-up, limit any conclusions that might be drawn.

Reference:

1. England BR, et al. Performance of Administrative Algorithms to Identify Interstitial Lung Disease in Rheumatoid Arthritis. AC&R 2020

Disclosure: N. Singh: None; **A. Peterson**: None; **A. Baraff**: None; **K. Wysham**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **J. Baker**: CorEvitas, 2, Cumberland Pharma, 2, Horizon Pharmaceuticals, 5; **N. Smith**: None; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **N. Weiss**: None.

Abstract Number: 0454

Rheumatoid Arthritis Disease Activity Indices Assess More Than Inflammation: 29%-36% of Patients with Moderate or High DAS28–ESR or CDAI Have 0 or 1 Swollen Joints, but Positive Screens on MDHAQ FAST4 (fibromyalgia Assessment Screening Tool) And/or MDS2 (MDHAQ Depression Screen) Indices

Theodore Pincus[1], Nicholas Rodwell[2] and Rahel Hunter[1], [1]Rush University Medical Center, Chicago, IL, [2]University of New South Wales, Sydney, Australia

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) therapy is recommended to be intensified according to treat-to-target if DAS28 (disease activity score 28) or CDAI (clinical disease activity index) indicate high/moderate (H/M) activity, although exceptions based on shared decisions are recognized. Comorbid fibromyalgia (FM) and/or depression (DEP) may raise DAS28 and CDAI, independent of inflammation, but often are underrecognized in routine care. A multidimensional health assessment questionnaire (MDHAQ) provides validated feasible screening indices for FM and DEP, FAST4 (fibromyalgia assessment screening tool) (ACR Open Rheum 2019;1:516) and MDS2 (MDHAQ depression screen) (Arth Care & Res 2021;73:120), which agree more than 80% with reference standards, on a single MDHAQ, completed by most patients in 5-10 minutes. We hypothesized that some patients in DAS28-ESR or CDAI H/M vs low/remission (L/R) would have 0 or 1 vs ≥2 swollen joint counts (SJC), but positive vs negative MDHAQ FAST4 and/or MDS2 screens.

Methods: A cross-sectional study at a routine care visit included DAS28 and CDAI. Patients competed an MDHAQ to score patient global assessment, fatigue, 0-3.3 DEP query, self-report 0-54 RADAI painful joint count, 60-symptom checklist (Sx), medical history queries, and FAST4 [positive (+) if 3/4: pain VNS ≥6/10, fatigue VNS ≥6/10, RADAI ≥16/54, and/or Sx

	Total (Row%)(Col%)	SJC 0,1 (Row%)(Col%)	SJC≥2 (Row%)(Col%)	FAST4 FM- MDS2 DEP- (Row%)(Col%)	FAST4 FM+ OR MDS2 Dep+ (Row%)(Col%)	SJC 0,1 & FAST4 FM+ OR MDS2 Dep+ (Row%)(Col%)
DAS28-ESR: Total	128	88 (69%) (100%)	40(31%) (100%)	74(58%)(100%)	54 (42%) (100%)	32 (25%) (100%)
Remission/low(R/L)	76(100%) (59%)	63(83%) (72%)	13(17%) (33%)	52 (68%) (70%)	24 (32%) (44%)	17 (22%) (53%)
Moderate/high(M/H)	52(100%) (41%)	25(48%) (28%)	27(52%) (68%)	22 (42%) (30%)	30 (58%) (56%)	15 (50% of FM+ and/or DEP+) (60% of all M/H and SJC 0,1)
Chi-square			P<0.0001		P=0.003	
CDAI: Total 140	140	95(68%) (100%)	45 (32%)(100%)	79(56%)(100%)	61(44%) (100%)	36 (26%) (100%)
Remission/low(R/L)	61(100%)(44%)	55(90%)(58%)	6(10%) (13%)	50 (82%)(63%)	11(18%) (18%)	9 (15%) (25%)
Moderate/high(M/H)	79(100%)(56%)	40(51%)(42%)	39(49%)(87%)	29(37%)(37%)	50(63%) (82%)	27 (54% of FM+ and/or DEP+) (68% of all M/H and SJC 0,1)
Chi-square			P<0.0001		P<0.0001	

Number of RA patients in DAS28-ESR or CDAI remission/low (R/L) vs moderate/high (M/H), swollen joint count (SJC) 0 or 1 vs ≥2 and MDHAQ FAST4 and MDS2 negative (-) vs FAST4 and/or MDS2 positive (+) for fibromyalgia and/or depression; highlighted numbers focus on patients with DAS28- ESR or CDAI M/H and SJC 0 or 1 and/or FAST4+ and/or MDS2+

≥16/60] and MDS2 [+ if a 0-3 DEP query is ≥2 or positive DEP on Sx). The numbers of patients in H/M vs L/R DAS28-ESR and CDAI, SJC 0/1 vs ≥2 and FAST4 + vs negative (-) and MDS2+ vs - status were analyzed using chi-square statistics.

Results: Median age was 61.3 years, median disease duration 10 years, and 75% of patients were female. DAS28-ESR and CDAI M/H vs L/R differed significantly according to SJC, as expected; R/L included 0/1 SJC in 83% of DAS28–ESR and 90% of CDAI ($p< 0.001$) (Table). However, M/H with 0/1 SJC was seen in 25/52 (48%) by DAS28-ESR and 40/79 (51%) by CDAI. DAS28-ESR and CDAI M/H vs L/R also differed significantly according to FAST4 and MDS2 status, somewhat unexpectedly (Table): 68% of DAS28-ESR L/R were FAST4-,MDS2- while 58% of M/H were FAST4+ &/or MDS2+ ($p=0.003$); 50/61 (82%) of CDAI L/R were FAST4-,MDS2-, while 50/79 (63%) of M/H patients were FAST4+ &/or MDS2+ ($p=< 0.0001$) (Table). Patients classified as M/H but with SJC of 0/1 included 15 for DAS28 (50% of 30 M/H and FAST4+ &/or MDS2+, 60% of 25 with M/H and SJC 0/1, and 29% of all 52 M/H patients), and 27 for CDAI (54% of 50 M/H and FAST4+ &/or MDS2+, 68% of 40 with M/H and SJC 0/1, and 34% of all 79 M/H patients) (Table).

Conclusion: Treat-to-target is a useful guideline for most RA patients. However, a sizable majority in H/M DAS28–ESR or CDAI have 0/1 SJC and may not be candidates for therapy escalation. About half of patients with high index scores and 0/1 SJC have comorbid FM or and/or DEP, which can be feasibly screened for with FAST4 and MDS2 indices on a single MDHAQ. Patients with DAS28-ESR or CDAI H/M vs L/R differed significantly in MDHAQ FAST4+ or - and/or MDS2 + or - indices for FM and DEP. Recognition that FM and DEP may elevate RA index scores is analogous to recognition that an elevated ESR may result from a cause other than inflammation. An MDHAQ, completed by most patients in 5-10 minutes, can help rheumatologists interpret RA index scores.

Disclosure: T. Pincus: None; **N. Rodwell**: None; **R. Hunter**: None.

Abstract Number: 0455

Rosnilimab, a Novel PD-1 Agonist Monoclonal Antibody, Inhibits Peripheral T Cell Proliferation and Cytokine Secretion and Reduces Circulating PD-1 High Expressing CD4 and CD8 T Cells: Results from a Phase 1 Healthy Volunteer Clinical Trial

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: PD-1 pathway mutations increase human susceptibility to multiple autoimmune diseases, and insufficient PD-1 signaling can lead to dysregulated T cell responses. By targeting natural immune regulatory mechanisms to modulate immune cells driving disease, there is an opportunity to dampen the inflammatory cycle and restore immune balance. Rosnilimab is a PD-1 agonist antibody designed to inhibit activated T cells for the treatment of inflammatory diseases, including rheumatoid arthritis (RA).The primary objective of this first-in-human (FIH), healthy volunteer (HV) Phase 1 study was to assess the safety and tolerability of single ascending doses (SAD) and multiple ascending doses (MAD) of rosnilimab. Other objectives included the assessment of pharmacokinetic (PK) profile, immunogenicity, and translational

pharmacodynamic (TPD) endpoints (e.g. PD-1 receptor occupancy (RO), reduction in various T cell populations and associated cytokine signaling).

Methods: This study was conducted at a single study center in the United States with 14 cohorts in SAD and 3 cohorts in MAD. Each cohort had 8 participants (6 active, 2 placebo (PBO)). Treatment cohorts were enrolled sequentially in each SAD/MAD phase. Intravenous (IV) and subcutaneous (SC) routes of administration were assessed in the SAD; SC route was assessed in the MAD.

Results: A total of 144 participants were enrolled; 90 randomized to the active SAD cohorts, 18 to the active MAD cohorts, and 30 and 6 randomized to the SAD and MAD PBO cohorts, respectively. All participants were assessed for safety and PD. Rosnilimab was well tolerated, with no dose-limiting toxicities or deaths. Two serious adverse events (SAEs) were reported in the SAD (obstructive pancreatitis in a PBO-dosed participant; COVID-19 infection in a rosnilimab-dosed participant leading to discontinuation; unrelated to treatment).No SAEs were reported in the MAD. TPD activity was rapid with sustained reduction in quantity and functional activity of PD-1+ T cells. Conventional T (Tcon) cells in the periphery expressing PD-1 were reduced, on average through Day 30 in the SAD where full RO was sustained following rosnilimab dosing, by ∼50% in both CD4+ and CD8+ subsets, in a dose-dependent manner and in correlation with RO.This reduction was maximized on PD-1 high expressing T cells, ∼90% reduction relative to baseline. There was no significant impact on the overall total T cell, Tcon or regulatory T (Treg) cell numbers, thereby resulting in an observed bias in favor of Treg:Tcon cell ratio post-dosing. An antigen-specific functional T cell assay measuring *ex vivo* interferon-gamma release in response to antigen challenge was inhibited up to ∼90% relative to baseline within 30 days following a single dose. Rosnilimab has a favorable PK profile consistent with full RO, a two-week half-life, and exposure nearly dose-proportional in both IV and SC dosing.

Conclusion: Rosnilimab demonstrated favorable safety, PK, and TPD activity. These results demonstrate proof of mechanism in humans and support advancing rosnilimab into a phase 2b study in RA.

Disclosure: K. Luu: AnaptysBio, 3, 11; **M. Dahl**: AnaptysBio, 3, 11; **E. Hare**: AnaptysBio, 3, 11; **C. Sibley**: AnaptysBio, 3, 11; **P. Lizzul**: AnaptysBio, 3, 11; **B. Randazzo**: AnaptysBio, 3, 11.

Abstract Number: 0456

The "Topics" in the Electronic Health Record of Rheumatoid Arthritis Patients Before Initiating Targeted Therapies and Association with Future Treatment Course

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
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Background/Purpose: Strong clinical predictors for response to biologic and targeted synthetic disease modifying rheumatic drugs (b/tsDMARDs) in rheumatoid arthritis (RA) have yet to be identified. The majority of studies test associations between individual clinical factors, e.g., age, disease duration, with treatment response. Alternatively, individual variables

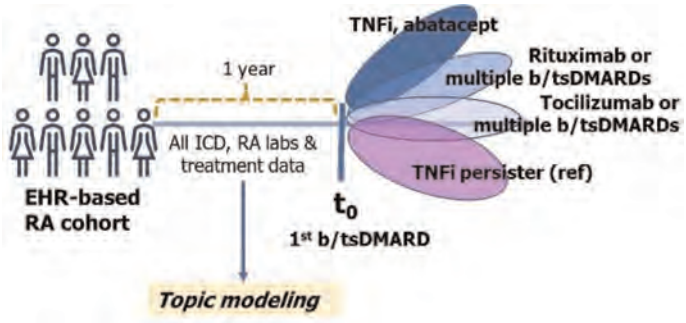

Figure 1. Study design to identify "topics" in an RA cohort using structured electronic health record (EHR) data in the year prior to initiating the 1st b/tsDMARD (t0); subsequent analyses test the associations between the topics and the 4 main treatment patterns after 1st b/tsDMARD identified from a prior study.

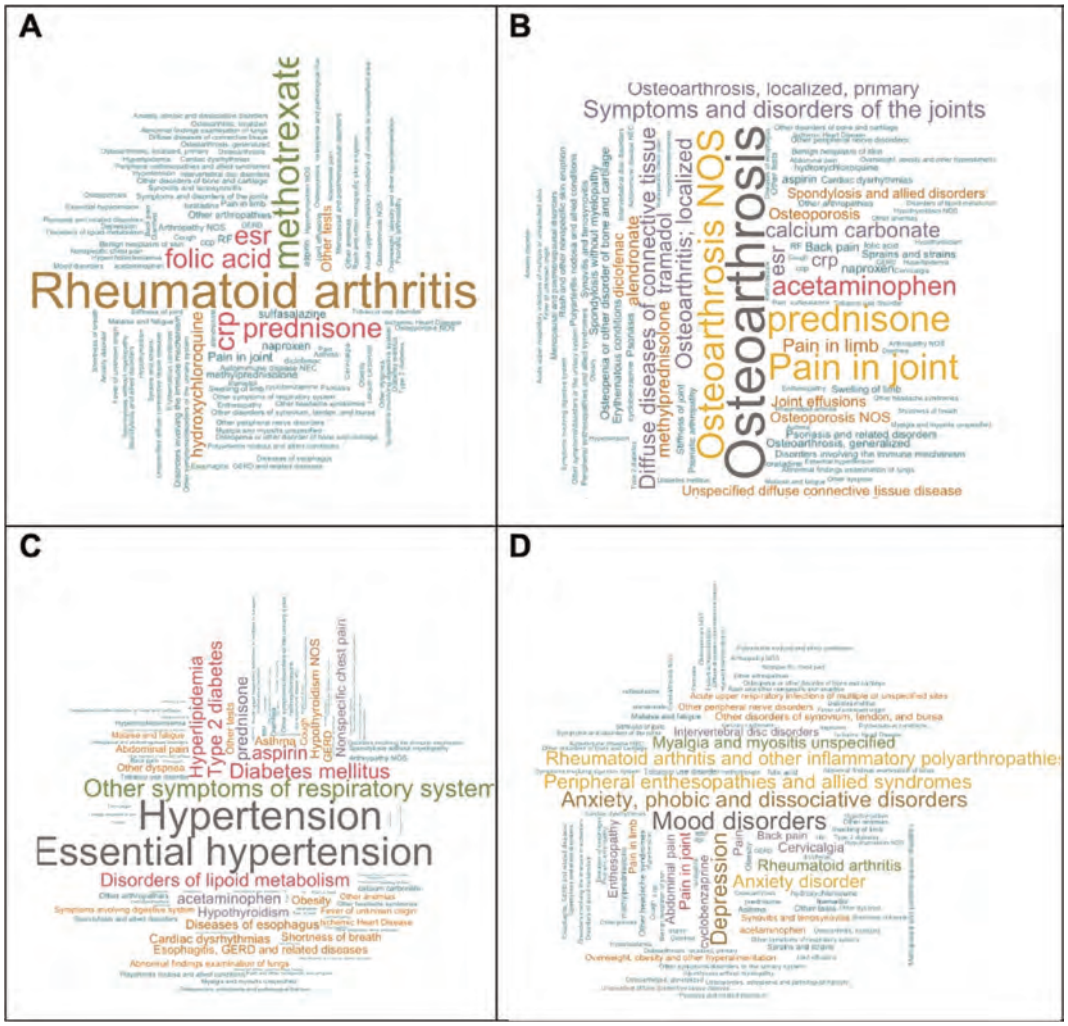

Figure 2. Four main topics identified using all ICD codes, RA-related laboratory data and medications in the year prior to initiating 1st b/tsDMARD named by the predominant features: (A) RA on MTX, (B) arthralgia, (C) hypertension and other CV comorbidities, (D) mood disorders.

can be grouped as a theme or topic, and then tested for association with an outcome, treatment response. Identifying potential topics using a data-driven method can be accomplished using topic modeling. Topic modeling performed on words in a newspaper grouped "music, film, performance" and "market, stock, share" into 2 topics, identifying

Table 1. Association between topics (top row) prior to initiating b/tsDMARD with future RA treatment course.

Treatment course	(A) Early RA		(B) Arthralgia		(C) HTN & CV		(D) Mood disorders	
	OR	p-value	OR	p-value	OR	p-value	OR	p-value
TNFi persisters	REF	-	REF	-	REF	-	REF	-
TNFi to abatacept	1.2	NS	0.56	NS	1.3	NS	0.92	NS
Rituximab	0.18	$1.2x10^{-6}$	1.4	NS	10.3	$1.2x10^{-6}$	0.94	NS
Tocilizumab	0.34	$1.1x10^{-3}$	1.6	NS	3.6	$2.0x10^{-3}$	1.4	NS

NS=not significant

entertainment vs finance-related terms respectively. The objective of this study was to identify the topics in a cohort of RA patients using their electronic health record (EHR) data prior to starting b/tsDMARDs, and to determine the association of these topics to their future b/tsDMARD treatment course.

Methods: We studied subjects from a validated EHR based RA cohort who initiated their 1st b/tsDMARD 2011-2019.In a previously published study, subjects were categorized based on the similarity of their treatment course after their 1st b/tsDMARD: (1) tumor necrosis factor inhibitor (TNFi) persister, (2) TNFi to abatacept, multiple b/tsDMARD and (3) rituximab or (4) tocilizumab (**Figure 1**). Structured EHR data: ICD codes, RA related laboratory data, e.g., anti-CCP, and RA related medication prescription data, e.g., prednisone, methotrexate (MTX), in the year prior to their first b/tsDMARD initiation (t_0) were extracted; all variables had prevalence at least 5%.Latent Dirichlet Allocation (LDA), a topic modeling method, was applied to group the structured EHR data into topics. Multinomial regressions were constructed to test the associations between the 4 topics across the treatment courses in comparison to TNFi persisters (reference group), adjusting for age, sex, self-reported race, and year of 1st b/tsDMARD.

Results: We studied 1102 RA subjects, mean age 53 years, 77% female, 64% rheumatoid factor (rf), 76% were on TNFi at t_0.The LDA model grouped the structured EHR data into 4 main topics: (a) RA on MTX, (b) arthralgia, (c) hypertension (HTN) and cardiovascular (CV) comorbidities, (d) mood disorders (**Figure 2**).Subjects in the RA/MTX topic cluster in the year prior to their 1st b/tsDMARD use had a higher-odds of eventually becoming TNFi persisters compared to those who will belong to the multiple b/tsDMARD/tocilizumab or rituximab groups (**Table 1**). Subjects belonging to the HTN/CV comorbidities topic had a lower-odds of belonging to the TNFi persister group compared to the multiple b/tsDMARD/tocilizumab or rituximab groups. Arthralgias and mood disorders did not associate more strongly with any future treatment course.

Conclusion: Topics derived from the structured EHR data of RA subjects prior to their 1st b/tsDMARD identified 2 topics differentiating future TNFi persisters vs those requiring multiple b/tsDMARDs.Topic modeling can provide an alternative method to study potential predictors for outcomes in RA and other rheumatic conditions.

Disclosure: J. Tang: None; **D. Weisenfeld**: None; **K. Dahal**: None; **L. Wang**: None; **C. Bonzel**: None; **Y. Kawano**: None; **G. McDermott**: None; **T. Cai**: None; **K. Liao**: UCB, 2.

Abstract Number: 0457

Biologic Disease Modifying Antirheumatic Drug Use in Immune Checkpoint Inhibitor-Treated Cancer Patients with Rheumatoid Arthritis: Utilization and Overall Survival

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Background/Purpose: There is a dearth of knowledge around the safety of biologic disease modifying antirheumatic drugs (bDMARDS) in immune checkpoint inhibitor (ICI)-treated rheumatoid arthritis (RA) patients with cancer. The goal of this study was to quantify the association between bDMARD use after ICI initiation and overall survival (OS) in RA patients with metastatic non-small cell lung cancer (mNSCLC), melanoma and urothelial cancer.

Methods: We used a curated Medicare claims dataset that consists of a 100% sample of patients with RA. We included patients ≥ 66 years of age with both a diagnosis of RA and of mNSCLC, melanoma or urothelial cancer, who initiated nivolumab, pembrolizumab or atezolizumab 2015-2019 and who received an intravenous (IV) bDMARD at some time during the year prior to ICI initiation. ICI and DMARD use were identified using J and C codes. We limited the study to IV bDMARDs because the timing of administration can be accurately ascertained. Patients with mNSCLC, melanoma and urothelial cancers were required to have two claims associated with the relevant ICD-9-CM or ICD-10-CM codes. RA was defined as having two claims associated with an ICD-9-CM or ICD-10-CM diagnosis code for RA. Patients who took a specific bDMARD after ICI initiation were compared to patients who took the same bDMARD in the year prior, but not in the year after ICI initiation. Kaplan Meier (KM) curves and cox proportional hazard models (CPHM) (un-adjusted, age and ICI adjusted) were created to measure OS from first ICI initiation. Patients were followed through 12/31/2019 and were censored at time of death or last recorded visit in the database.

Results: A total of 6350 ICI-treated RA patients with mNSCLC, melanoma, and urothelial cancer were identified. Of these, only 466 (7.3%) received an IV bDMARD in the year prior to ICI initiation. 166/466 (35.6 %) took the same DMARD in the 1 year after ICI initiation. Overall median follow up was 186.5 days (IQR 76, 355). Patients who took a bDMARD prior to ICI only were more likely to be female than those who continued/initiated that bDMARD after ICI initiation (63.3% vs 51.2%, p= 0.011) (Table1). Figure 1 displays the KM curves comparing patients who continued/initiated a TNFi after ICI initiation to those who took a TNFi only prior to ICI initiation (1A, log rank p-value 0.02) and a similar analysis for Rituximab (1B; p-value 0.06). In CPHM for mNSCLC, patients who took an IV TNFi only prior to ICI initiation had worse OS than those who continued/initiated a TNFi after ICI initiation (Table 2). Adjusted models for other cancers and other IV DMARDS were not statistically significant.

Conclusion: Few RA patients with mNSCLC, melanoma, and urothelial cancer use IV bDMARDS in the year prior to ICI initiation, even among those who were previously receiving them before their cancer diagnosis. Patients who continued/initiated an IV TNFi after ICI initiation appear to have better OS than patients who take a TNFi only prior to ICI initiation. However, this may reflect unmeasured differences between these two groups, such as the use of concomitant chemotherapy, number of prior cancer treatments or comorbidities, which we will address in further analyses.

Disclosure: D. Jannat-Khah: AstraZeneca, 12, stock ownership, Cytodyn, 12, stock ownershil[, Walgreens Boots Alliance, 12, stock ownership; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, BMS, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Genentech, 2, 5, Janssen, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB Pharma, 2, 5; **F. Xie**: None; **A. Saxena**: AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, G1 Therapeutics, 2, Jazz Pharmaceuticals, 2; **A. Bass**: None.

Abstract Number: 0458

Drug Switching Due to Inefficacy in Rheumatoid Arthritis Patients Treated with Biological and Targeted Therapies. Daily Clinical Experience

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
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Background/Purpose: The treatment of Rheumatoid Arthritis (RA) has undergone an enormous change in the last two decades with the use of biological Disease Modifying Drugs and targeted therapies (ts/bDMARDs). These drugs are widely used in clinical practice, but we have scarce information about the switching between them in these conditions due to inefficacy. Our objective is to evaluate the incidence rate of switching due to inefficacyas well as the factors associated to switching due to inefficacy.

Methods: We conducted an observational longitudinal retrospective study. Subjects: all patients with recent onset RA diagnosed between January 1st 2007 and December 31st 2015 followed in outpatient clinic at Hospital Clinico San Carlos until January 1st 2022, which used any ts/bDMARDs during at least 3 months. Main outcome: Switching of the ts/bDMARD (suspension and change to a different ts/bDMARD) due to inefficacy. Covariables: sociodemographic, clinical and treatment. Statistical analysis: incidence rates of switching due to inefficacy (IR) per 100 patient-years were estimated using survival techniques with their respective 95% confidence interval [CI]. A multivariate Cox regression analysis was used to evaluate the risk factors of switching due to inefficacy. Results were expressed as HR with their 95% CI.

Table 1. Baseline sociodemographic characteristics.

Variables	N= 186
Women, n (%)	152 (81.72)
Age; media ± SD	52.37 ± 13.8
Smokers (n= 177), n (%)	31 (17.51)
Positive rheumatoid factor + (n=184), n (%)	119 (64.67%)
Positive anti-citrullinated protein antibodies + (n=181); n (%)	101 (55.8)
ESR (n=), media ± SD mm/h	41.55 ± 28.42
ts/bDMARDS; n (%)	
TNF inhibitor	213 (61.38)
Rituximab	50 (14.41)
Abatacept	31 (8.93)
IL6 inhibitor	25 (7.20)
JAK inhibitor	28 (8.1)
Combined treatment, n(%)	
Methotrexate	96 (51.61)
NSAIDs	156 (83.87)
Glucocorticoids	66 (35.48)

Table 2. Incidence rates of drug switching due to inefficacy per 100 *patient year in RA patients treated with biological and targeted therapies.

	SWITCHING			
	Patients/year	N	IR	95%CI
Total	918.12	88	9.95	7.77-11.81
By gender				
Female	749.51	80	10.67	8.57-13.28
Male	168.61	8	4.75	2.37-9.49
By age				
< 46 years	407.19	55	13.50	10.37-17.59
47-69 years	424.17	26	6.12	4.17-9.00
> 70 years	86.75	7	8.07	3.85-16.92
By treatment course				
First	614.04	43	7.11	5.27- 9.59
Subsequent	313.82	45	14.35	10.70- 19.20
By concomitant use of corticoids				
No	194.28	14	7.20	4.26-12.16
Yes	723.85	74	10.22	8.14-12.83
By ts/bDMARDS				
TNF inhibitor	618.03	10	9.54	7.39-12.32
Rituximab	148.45	9	23.38	12.58-43.45
Abatacept	42.76	10	23.38	12.58-43.45
IL6 inhibitor	57.48	6	10.43	4.68-23.23
JAK inhibitor	51.38	4	7.78	2.92-20.74

Table 3. Multivariate analysis of drug switching due to inefficacy in RA patients treated with biological and targeted therapies.

	SWITCHING		
	HR	95%CI	P
Age < 46 years	0.98	0.97-1.01	0.22
Male	0.45	0.21-0.98	0.04
≥3 courses of treatment	1.72	1.07-2.76	0.025
By ts/bDMARDs			
TNF inhibitor	1	-	-
Rituximab	0.68	0.33-1.39	0.296
Abatacept	1.78	0.97-3.27	0.060
IL-6 inhibitor	0.79	0.31-1.98	0.61
JAK2 inhibitor	0.70	0.23-2.10	0.52

Results: 186 patients were included (927.86 patient-years), 81.72% were women with a mean age of 52.38±13.80. Characteristics at baseline are shown in table 1. The 186 patients received 347 courses of ts/bDMARD treatment of which 88 were switched due to inefficacy (25.36%) with an IR of inefficacy of 9.58 [7.77-11.81]. The most frequent ts/bDMARD group was TNFi (61.38%), specifically Etanercept (21.90%). IRs of switching due to inneficacy are shown in table 1, we found a higher IR in the female sex (IR 10.67 [8.57-13.28]), younger patients (IR 13.50 [10.37-17.59], subsequent courses of treatment (IR 14.34 [10.70-19.20]), with the concomitant use of corticoids (IR 10.22 [8.14-12.83]), and with the use of certain ts/bDMARDs (IR Abatacept 23.38 [12.58-43.45], IR anti-IL6 10.43 [4.68-23.23], IR anti-TNF 9.54 [7.39-12.32], IR JAKi 7.78 [2.92-20.74], IR Rituximab 6.06 [3.15-11.65]). In the multivariate analysis (table 2) we found a higher risk for switching due to inefficacy in patients receiving the third or posterior course of treatment (HR 1.72 [1.07-2.77]) and a tendency in patients in treatment with abatacept compared to anti-TNF (HR 1.79 [0.98-3.28]); the male sex was a protective factor for switching due to inefficacy (HR 0.46 [0.21-0.98]).

Conclusion: Switching of ts/bDMARDs in daily clinical practice due to inefficacy appears with certain regularity (25.36%) with an estimated IR of 9.58. We have found higher switching rates of ts/bDMARDs due to inefficacy in the female sex, younger patients, subsequent courses of treatment, concomitant use of corticoids as well as with some ts/bDMARDs in specific (Abatacept and anti-IL6). Patients receiving the third or posterior course of treatment had a higher risk of switching due to inefficacy meanwhile the male sex acted as a protective factor; treatment with abatacept seemed to have a higher risk to switching due to inefficacy but it did not reach statistical significance.

Disclosure: M. Rodriguez Laguna: None; **Z. Rosales-Rosado**: None; **C. Vadillo-Font**: None; **J. Otazu-Moudelle**: None; **I. Pérez Sancristóbal**: None; **I. Abasolo**: None.

Abstract Number: 0459

Upadacitinib Monotherapy versus Methotrexate in Patients with Rheumatoid Arthritis: Efficacy and Safety Through 5 Years in the SELECT-EARLY Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: RA – Treatments Poster I
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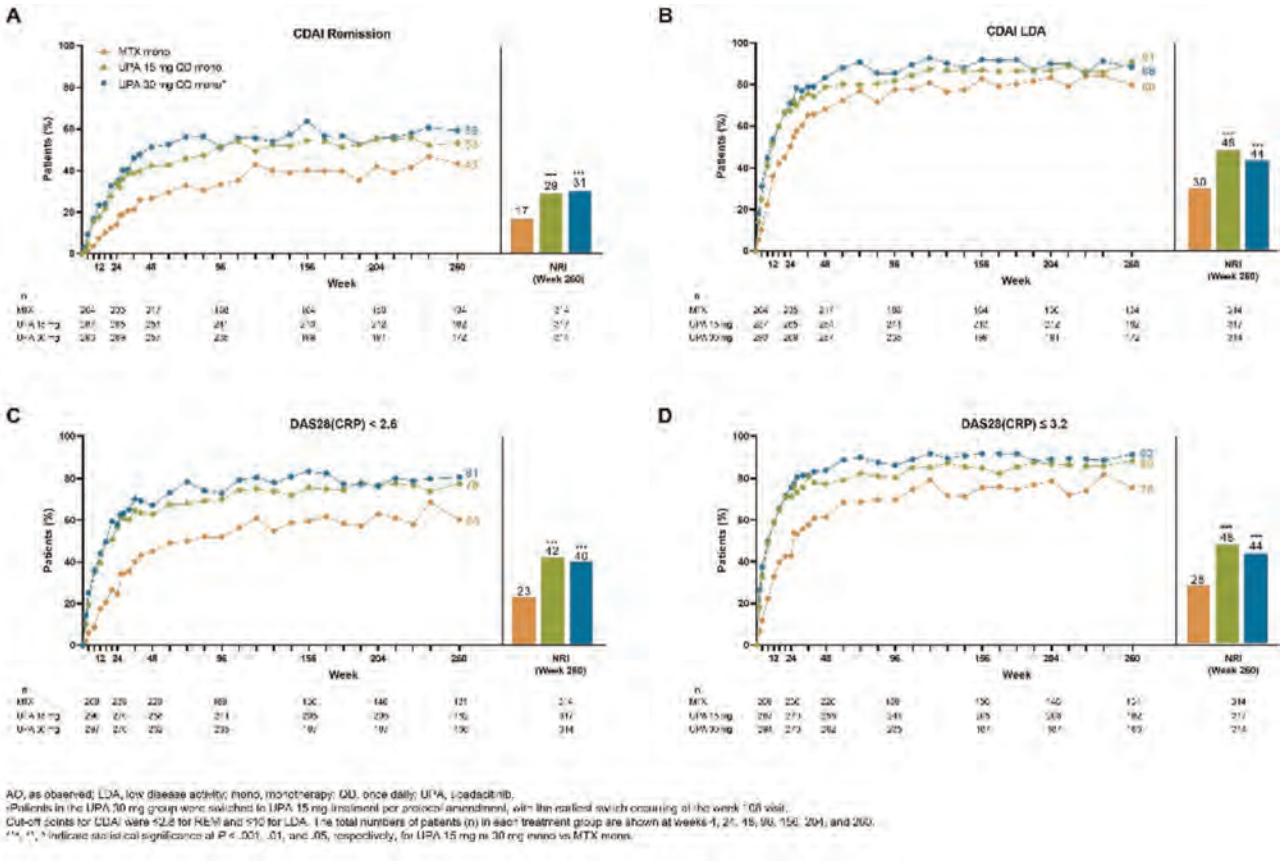
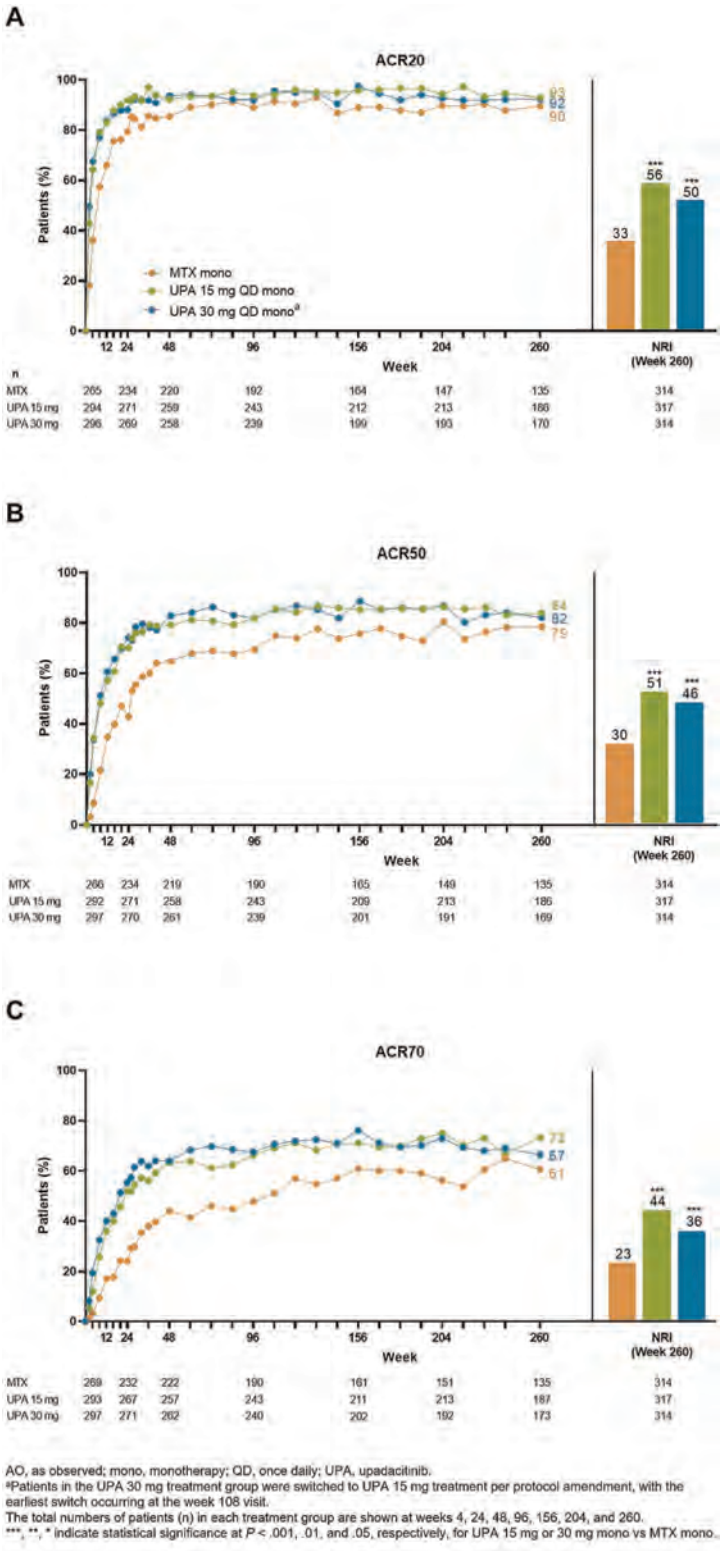
Background/Purpose: To evaluate the efficacy and safety of upadacitinib (UPA) monotherapy vs MTX monotherapy over 5 yrs among MTX-naïve patients with moderately to severely active RA in the long-term extension (LTE) of the phase 3 SELECT-EARLY trial.

Methods: Patients were randomized 1:1:1 to receive once daily UPA 15 mg or 30 mg or MTX (titrated up to 20 mg/wk by wk 8).[1] At wk 26, patients who did not achieve CDAI remission (≤2.8) with < 20% improvement from baseline in TJC or SJC received rescue therapy (addition of MTX to insufficient responders in the UPA groups and addition of UPA 15/30 mg [by re-randomization] to insufficient responders in the MTX group). For patients who did not achieve CDAI remission but had ≥20% improvement in TJC and SJC at wk 26, background RA medications were optimized while patients remained on their original study drug. Per protocol amendment, all patients receiving UPA 30 mg were switched to the approved 15 mg dose, with the earliest switch occurring at wk 108. Efficacy assessments were evaluated over 5 yrs and are reported



AO, as observed; LDA, low disease activity; mono, monotherapy; QD, once daily; UPA, upadacitinib.
*Patients in the UPA 30 mg group were switched to UPA 15 mg treatment per protocol amendment, with the earliest switch occurring at the week 108 visit.
Cut-off points for CDAI were ≤2.8 for REM and ≤10 for LDA. The total numbers of patients (n) in each treatment group are shown at weeks 4, 24, 48, 96, 156, 204, and 260.
*, **, *** Indicate statistical significance at $P < .001$, .01, and .05, respectively, for UPA 15 mg or 30 mg mono vs MTX mono.

Figure 1. Proportions of Patients Achieving CDAI or DAS28(CRP) Disease Activity States Through 5 Years (AO, NRI)



AO, as observed; mono, monotherapy; QD, once daily; UPA, upadacitinib.
[a]Patients in the UPA 30 mg treatment group were switched to UPA 15 mg treatment per protocol amendment, with the earliest switch occurring at the week 108 visit.
The total numbers of patients (n) in each treatment group are shown at weeks 4, 24, 48, 96, 156, 204, and 260.
***, **, * indicate statistical significance at $P < .001$, .01, and .05, respectively, for UPA 15 mg or 30 mg mono vs MTX mono.

Figure 2. Proportions of Patients Achieving ACR20/50/70 Responses Through 5 Years (AO, NRI)

Table. Treatment-Emergent Adverse Event Summary Through 5 Years

Events (E/100 PY)[a]	MTX mono (n = 314; PY = 860.2)	UPA 15 mg QD mono (n = 317; PY = 1062.6)	UPA 30 mg QD mono[b] (n = 314; PY = 741.5)	UPA 15 mg QD mono switched from UPA 30 mg QD mono (n = 181; PY = 292.5)
Any AE	1767 (205.4)	2396 (225.5)	2077 (280.1)	451 (154.2)
Serious AEs	78 (9.1)	111 (10.4)	118 (15.9)	44 (15.0)
Any AE leading to discontinuation of study drug	50 (5.8)	58 (5.5)	57 (7.7)	10 (3.4)
Serious infection	16 (1.9)	34 (3.2)	33 (4.5)	15 (5.1)
Opportunistic infection[c]	1 (0.1)	2 (0.2)	2 (0.3)	1 (0.3)
Herpes zoster	7 (0.8)	41 (3.9)	33 (4.5)	12 (4.1)
Malignancies (excluding NMSC)	8 (0.9)	6 (0.6)	8 (1.1)	5 (1.7)
NMSC	0	4 (0.4)	8 (1.1)	6 (2.1)
CPK elevation[d]	12 (1.4)	68 (6.4)	106 (14.3)	14 (4.8)
MACE (adjudicated)[e]	3 (0.3)	3 (0.3)	4 (0.5)	1 (0.3)
VTE (adjudicated)[f]	5 (0.6)	3 (0.3)	4 (0.5)	1 (0.3)
Neutropenia	15 (1.7)	34 (3.2)	41 (5.5)	11 (3.8)
Lymphopenia	28 (3.3)	17 (1.6)	23 (3.1)	6 (2.1)
Anemia	37 (4.3)	45 (4.2)	28 (3.8)	8 (2.7)
GI perforation (adjudicated)	0	0	4 (0.5)	0
COVID-19	23 (2.7)	34 (3.2)	6 (0.8)[g]	39 (13.3)[g]
All deaths[h,i]	8 (0.9)	6 (0.6)	9 (1.2)	5 (1.7)
Deaths ≤30 days after last dose	1 (0.1)	3 (0.3)	8 (1.1)	3 (1.0)
Deaths >30 days after last dose	7 (0.8)	3 (0.3)	1 (0.1)	2 (0.7)

AE, adverse event; CPK, creatine phosphokinase; GI, gastrointestinal; NMSC, nonmelanoma skin cancer; PY, patient-years; QD, once daily; UPA, upadacitinib.
[a]Treatment-emergent adverse event is defined as any adverse event with an onset date that is after the first dose of study drug, and no more than 30 days after the last dose of study drug. Data include patients receiving UPA or MTX monotherapy, censored at either time of rescue to UPA + MTX or with addition of background conventional synthetic DMARD.
[b]UPA 30 mg exposure was censored at time of dose switch to the approved 15 mg dose. Safety outcomes following the switch from UPA 30 mg to UPA 15 mg are reported separately (last column).
[c]Opportunistic infections exclude herpes zoster and tuberculosis (TB). No cases of TB were reported on MTX monotherapy during the study, while 2 cases were reported for each the UPA 15 mg and 30 mg mono groups.
[d]Most CPK events were asymptomatic and transient.
[e]Defined as cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke
[f]Includes pulmonary embolism and deep vein thrombosis.
[g]Given the timing of the study, the lower rate of COVID-19 observed in the UPA 30 mg group is due to the majority of patients in this group having been switched to UPA 15 mg by the onset of the COVID-19 pandemic (and, conversely, why rates are higher in the UPA 15 mg switched from 30 mg group).
[h]Five of these deaths were COVID-19-related: 2 on UPA 30 mg mono and 3 on UPA 15 mg mono switched from UPA 30 mg mono.
[i]Additionally, 1 death occurred in a patient receiving UPA 30 mg plus background MTX, and 2 deaths (both COVID-19-related) occurred in patients on background MTX who switched from UPA 30 mg to UPA 15 mg.

as observed (AO) for patients who received continuous monotherapy with UPA 15/30 mg or MTX. Results at wk 260 are also reported by randomized group for all patients, applying NRI for patients who were rescued or discontinued, with nominal *P* values. Treatment-emergent adverse events (TEAEs) per 100 patient-yrs were summarized over 5 yrs for those receiving monotherapy.

Results: Of 945 patients randomized and treated, 775 (82%) completed wk 48 and entered the LTE on study drug. Of these 775 patients, 255 (27%) discontinued study drug during the LTE due to the following primary reasons: TEAEs (9%), withdrawal of consent (7%), lack of efficacy (2%), lost to follow-up (3%), or other reasons (6%). Patients receiving UPA consistently demonstrated higher achievement of disease activity targets over 5 yrs compared with MTX (**Figure 1, 2**). In AO analyses, 53%/59% of patients attained CDAI remission with UPA 15/30 mg vs 43% on MTX at wk 260. NRI analyses also showed better CDAI, DAS28(CRP), and ACR/20/50/70 responses with UPA relative to MTX at wk 260 (nominal $P < .001$). Most TEAEs were numerically most frequent in patients receiving UPA 30 mg (**Table**). The rates of serious infections, herpes zoster, CPK elevation, nonmelanoma skin cancer (NMSC), and neutropenia were

numerically higher with UPA than MTX. The overall rates of MACE, VTE, malignancy excluding NMSC, and lymphopenia were comparable across treatments. Rates of death were similar between UPA 15 mg and MTX but numerically higher with UPA 30 mg. Overall, the observed safety profile of UPA over 5 yrs was consistent with earlier results from this trial and the integrated phase 3 safety analysis.[1-3]

Conclusion: UPA 15 mg or 30 mg showed better clinical responses vs MTX in patients with RA throughout the 5-yr trial. Higher rates of several AEs, including serious infection, herpes zoster, and CPK elevation were observed with UPA compared to MTX. When used as monotherapy in MTX-naïve patients, UPA has better long-term efficacy vs MTX and a favorable benefit-risk profile.

References:

1. van Vollenhoven, R et al. *Arthritis Rheumatol* 2020; 72:1607–20
2. van Vollenhoven, R et al. *Ann Rheum Dis*2021; 80:568–59.
3. Cohen, SB et al. *Ann Rheum Dis* 2021;80: 304–11.

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Abstract Number: 0460

Knowledge Related to Fertility and Infertility Treatments Among Women with Systemic Rheumatic Disease

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Reproductive Issues in Rheumatic Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Fertility awareness is low in the population and is influenced by disparities in race, ethnicity, and socioeconomic status. Because systemic rheumatic disease (SRD) contributes to decreased fertility, identifying knowledge gaps and underlying factors among affected women is a key step towards improved counseling on fertility therapies. Here, we use a previously published instrument to determine whether fertility knowledge is affected by having an SRD or by other medical or sociodemographic factors.

Methods: We enrolled women ages 18-65 seen ≥2 times by a Hospital for Special Surgery rheumatologist from 2020-2022 in the Rheumatology Women's Reproductive Health and Wellness Cohort; cohort enrollment is ongoing. This is an interim analysis that includes women aged 18-45 years with self-reported SRD, to whom we administered the Fertility & Infertility Treatment Knowledge Score (FIT-KS) (1). Using descriptive statistics, we compared FIT-KS scores in women with SRD to scores of reproductive-aged women in the general population, as previously published by Kudesia et al. Among women with SRD, we compared those with a total score ≥19 on the FIT-KS ("high scorers") and those who scored < 19 ("low scorers") in terms of sociodemographic, lifestyle, medical, and reproductive factors.

Results: In this interim analysis, 142 reproductive-aged women with SRD completed the FIT-KS, with a median total score of 18 (62% correct out of 29 questions) (Table 1). Compared to women in the general population, women with SRD were more frequently non-White (p=0.04) and Hispanic/Latina (p=0.02), more highly educated (p< 0.01), and less likely to have

Table 1. Fertility awareness among reproductive-aged women with SRD compared to a previously published sample of reproductive-aged women in the general population in the United States of America[1,2]

	SRD Population (N=142)	General Population (N=118)	p-value[3]
Population Characteristics			
Current age, median (IQR)	34 (29, 41)	31 (27, 38)	
Married or partnered	85 (60)	75 (64)	*0.54*
Previous successful pregnancy (live birth)	36 (25)	52 (44)	***0.006***
Race			***0.035***
• White only	105 (74)	101 (86)	
• Non-white (including multiracial)	35 (25)	17 (14)	
Hispanic or Latina ethnicity	14 (10)	3 (3)	***0.017***
Bachelor's degree or higher	131 (92)	74 (63)	***<0.001***
Overall Performance on FIT-KS[4,5]			
Total score, median (% correct)	18 (62)	16 (55)	
Natural fertility sub-score, median (% correct)	14 (67)	13 (62)	
Infertility treatment sub-score, median (% correct)	4 (50)	4 (50)	
Natural Fertility Knowledge[5,7]			
Age of maximal fertility decline ***(35-39)***	69 (49)	46 (39)	*0.12*
Fecundability at age 30 ***(20%)***	50 (35)	39 (33)	*0.71*
Fecundability at age 40 ***(≤5%)***	77 (54)	52 (44)	*0.10*
Miscarriage rate ***(16-25%)***	58 (41)	36 (31)	*0.084*
Lifestyle Risk Factor Knowledge[6,7]			
Smoking ***(T)***	135 (95)	103 (87)	***0.025***
Occasional caffeine intake ***(F)***	116 (82)	88 (75)	*0.22*
Moderate alcohol consumption ***(F)***	73 (51)	63 (54)	*0.65*
Safely conducted pregnancy termination ***(F)***	118 (83)	88 (75)	*0.13*
Obesity ***(T)***	123 (87)	94 (80)	*0.13*
Gonorrhea or Chlamydia infection ***(T)***	125 (88)	90 (76)	***0.013***
Prior use of oral contraceptive pills ***(F)***	103 (73)	75 (64)	*0.16*
Being underweight ***(T)***	138 (97)	92 (78)	***<.001***
Use of certain sexual lubricants ***(T)***	57 (40)	35 (30)	*0.078*
Infertility Treatments Knowledge[6,7]			
IVF success rate at age 35 ***(41-60%)***	30 (21)	17 (14)	*0.16*
IVF success rate at age 44 ***(≤5%)***	64 (45)	37 (31)	***0.024***
IVF twinning rate ***(21-35%)***	36 (25)	37 (31)	*0.28*
Live birth rate per thawed egg after OC ***(≤10%)***	20 (14)	42 (36)	***<.001***

1. The fertility knowledge of women from the general population is based on data previously published by Kudesia et al
2. All results are reported as N (%) unless noted otherwise
3. P-values were derived from chi-squared testing, which was performed if at least 80% of expected values were ≥5
4. Scores are reported as each population's median number of questions answered correctly, with the corresponding percentage of correctly answered questions denoted in parenthesis. Of note, there were a total of 29 questions on the FIT-KS, of which 21 related to natural fertility to comprise the natural fertility sub-score, and 8 related to infertility treatments to comprise the infertility treatment sub-score.
5. Not enough granularity of data was provided regarding the previously published sample of the general population to be able to perform statistical analysis comparing FIT-KS scores between the two populations.
6. Each of the rows in this section of the table represents an individual question on the FIT-KS. Results are presented as the number (%) of individuals in each population who answered the question correctly.
7. Correct answers to each question are denoted in parentheses.

had successful pregnancies (p< 0.01). The SRD population was more aware of the risks of infertility due to smoking (p=0.03), sexually transmitted infections (p=0.01), and being underweight (p< 0.01). Women with SRD were more frequently correct about success rates for in vitro fertilization (IVF) for women older than 44 years (p=0.02) but less frequently correct about success rates per thawed egg after oocyte cryopreservation (OOC) (p< 0.01). Compared to high scorers on the FIT-KS, low scorers were more frequently Hispanic/Latina (p=0.03) and more likely to have considered OOC (p=0.03) (Table 2).

Conclusion: Compared to a previously reported sample of women in the general population, women with SRD performed qualitatively better on the FIT-KS, with greater knowledge of modifiable infertility risk factors and IVF, but less knowledge of OOC. Among women with SRD, those with decreased fertility awareness were more frequently Hispanic/Latina and more open to OOC. Future multivariate analysis is planned, but our results suggest a relationship between demographic characteristics and fertility awareness and highlight important knowledge gaps among women with SRD, particularly related to options for fertility preservation.

Table 2. Characteristics of women with SRD who had high versus low scores on FIT-KS[1]

Variable[2]	High Scorers (N=70)	Low Scorers (N=72)	*p-value*[3]
Sociodemographics and Lifestyle			
Current age (years)			
• 18-29	19 (27)	23 (32)	*0.53*
• 30-39	31 (44)	28 (39)	*0.51*
• 40-45	20 (29)	21 (29)	*0.94*
Race			*0.079*
• White only	57 (81)	48 (67)	
• Non-white (including multiracial)	13 (19)	22 (31)	
Hispanic or Latina ethnicity	3 (4)	11 (15)	***0.026***
Bachelor's degree or higher	65 (93)	66 (92)	*0.56*
Private medical insurance	68 (97)	68 (94)	
Married or partnered	44 (63)	41 (57)	*0.47*
Alcohol use (ever)	63 (90)	62 (86)	*0.48*
Cigarette use (ever)	10 (14)	7 (10)	*0.42*
Medical History			
SRD diagnosis category			
• Inflammatory arthritides[4]	44 (63)	34 (47)	*0.061*
• Lupus and lupus-like conditions[5]	21 (30)	26 (36)	*0.44*
• Vasculitis, myositis, and SSc[6]	2 (3)	8 (11)	*0.055*
• Other autoinflammatory conditions[7]	3 (4)	1 (1)	
• Multiple diagnosis categories	0 (0)	3 (4)	
Disease flare in the last year	49 (70)	50 (69)	*0.96*
Teratogenic medication in the last year[8]	18 (26)	21 (29)	*0.39*
Fertility-Related Attitudes & Experiences			
Seen a gynecologist in the last year	59 (84)	65 (90)	*0.28*
Gynecologic comorbidity present[9]	22 (31)	19 (26)	*0.51*
Previous pregnancy	27 (39)	24 (33)	*0.69*
Previous successful pregnancy (live birth)	22 (31)	14 (19)	*0.070*
Concerned about fertility	31 (44)	36 (50)	*0.60*
Considered egg freezing (ever)	30 (43)	44 (61)	***0.028***
Previous use of other ART[10]	11 (16)	8 (11)	*0.40*

1. A high score was defined as a total score ≥19 on the FIT-KS, which marked the 75th percentile of scores reflected in the general population, as previously published by Kudesia et al.
2. All results are reported as N (%) unless noted otherwise.
3. P-values were calculated using chi-squared testing. Values were only calculated for variables for which at least 80% of the expected values were ≥5.
4. Inflammatory arthritis: Adult Onset Still's Disease, JIA, PsA, RA, spondyloarthritis (i.e. AS, IBD-related arthritis, ReA), inflammatory arthritis - not otherwise specified
5. Lupus and lupus-like conditions: APS, SLE, MCTD, SS, UCTD
6. Vasculitis, myositis, and SSc: Behcet's, myositis (i.e. DM, PM, IBM, or other inflammatory muscle disease), SSc, CREST, vasculitis (including ANCA-associated vasculitis, GCA, Takayasu's vasculitis, PAN)
7. Other autoinflammatory conditions: autoinflammatory syndrome (i.e. CAPS, TRAPS, FMF), IgG-4-related disease, PMR, sarcoidosis
8. Teratogenic medications: CYC, LEF, MTX, MMF, nintedanib, thalidomide, warfarin
9. Gynecologic comorbidities: polycystic ovarian syndrome, endometriosis, uterine fibroids, gynecologic cancer
10. Other ART: oral/injectable medications for ovarian stimulation, intrauterine insemination, and in vitro fertilization

References:

1. Kudesia R, Chernyak E, McAvey B. Low fertility awareness in United States reproductive-aged women and medical trainees: creation and validation of the Fertility & Infertility Treatment Knowledge Score (FIT-KS). Fertil Steril. 2017 Oct;108(4):711-717.

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Abstract Number: 0461

Self-esteem as a Determinant of Sexual Function in SLE Patients

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Reproductive Issues in Rheumatic Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatic diseases, and specifically SLE, present with greater sexual dysfunction than other chronic diseases. Sexual dysfunction (SxD) is multifactorial and comprises disease-related factors, psychological factors, hormonal imbalance, and treatment. Self-esteem has an association with mental and physical health in SLE patients, however, its impact has not been studied as a determinant of SxD.

We aimed to assess the association between body self-esteem, global self-worth and sexual functioning in SLE patients.

Methods: We performed a transversal study in a tertiary care center in Mexico City. Patients ≥18 years old who fulfilled EULAR/ACR criteria for SLE were included. Body self-esteem was assessed by the Body Self-esteem Scale (BSS) and global self-worth by the Rosenberg´s Self-Esteem Scale (RSES). Sexual function was assessed by the CSFQ-14 questionnaire. Disease activity was measured by SLEDAI and disease-associated damage by SLICC index. Relevant demographic, clinical and serological characteristics were recorded. We used univariate and multivariate analysis to assess association between self-esteem and SxD. Statistical analysis was performed using SPSS V.25.

Results: We included a total of 280 patients, in whom self-esteem was analyzed. Most patients were female (87%), the mean age was 41 (±12 years) and mean BMI was 25.6 (±4.9kg/m^2). Mean SLEDAI and SLICC scores were 2.45 (±2.72) and 0.8 points (±1.04), respectively. A correlation between body self-esteem and SxD was found in both genders. Interestingly, the correlation was higher in men than in women (r=0.45, p=0.008 *vs* r=0.25, p=0.0001,

Table 1. Clinical, demographic, and laboratory variables of patients with Systemic Lupus Erythematosus (SLE)

Table 1. Clinical, demographic, and laboratory variables of patients with Systemic Lupus Erythematosus (SLE)			
Variables	**SxD mean ± SD**	**No-SxD mean ± SD**	**Comparison (p value)**
BMI, kg/m2	25.2 ±4.6	26.1±5.5	0.16
PDN dose	4.6 ±8.7	3.8 ±6.1	0.42
Body Attractive (Total AC), points	37.2 ±13.8	46.8±8.6	**<0.0001**
Body Satisfaction (Total SC), points	151.2 ±35.7	162.7±29.1	**< 0.006**
Body self-esteem (EAC), points	188.4 ±44.9	207.9±40.1	**<0.0001**
Global self-worth, points (Rosenberg)	21.8 ±5.0	34.4±6.4	**<0.0001**
SLEDAI score, points	2.4±2.7	2.3±2.5	0.71
SLICC DI, points	0.8 ±1.0	0.6±0.9	0.09
C3 levels, mg/dL	111.6 ±30.3	117.1 ±32.8	0.19
C4 levels, mg/dL	22.1 ±10.3	20.7 ± 10.9	0.34
anti-dsDNA antibodies, IU/mL	151.1 ±752.4	36.1 ±63.5	0.16
*Values shown in bold represent statistically significant p values.			

respectively). In addition, a correlation was established between global self-worth and SxD for both men and women (r=0.4, p=0.006 *vs* r=0.18, p=0.004) respectively. Interestingly, both scales (BSS and RSES) showed a moderate correlation with SxD in men with SLE (r=0.45, p=0.008 and r=0.47, p=0.006, respectively). Although this correlation was also found in women (between BSS, RSES and SxD), it was weaker than in men (r=0.25, p=0.0001 and r=0.18, p=0.004)

Other clinical and laboratory variables were studied, such as prednisone, cyclophosphamide, obesity, depression, body self-esteem, SLEDAI and SLICC damage index; however, no statistical significance was found (Table 1).

The multivariate analysis showed that age (0.96, 95% CI 0.94-0.98, p=0.003), lower RSES score (1.08, 95% CI 1-1.14, p=0.01) and leukocytes (1.19, 95% CI 1-1.40, p=0.02) were independently associated with SxD. Although there was a trend for an association with lower BSS, it did not reach statistical significance (1.00, 95% CI 1-1.15, p=0.055).

Conclusion: To our knowledge this is the first study to evaluate self-esteem (with two different scales) as a determinant of sexual function in SLE patients, showing a greater impact in male population. Given the complexity of sexual function in SLE patients and the various factors that can affect it, it is important to consider additional psychosocial aspects, such as self-esteem, to help us identify and address potential problems early on, leading to better quality of life through timely interventions.

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Abstract Number: 0462

Breastfeeding Intention in Systemic Lupus Erythematosus Patients

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Reproductive Issues in Rheumatic Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Breastfeeding in systemic lupus erythematosus (SLE) has received little attention and the limited data available suggest that women with SLE have lower breastfeeding rates and sustain it for less time than the general population. This study aimed to assess the knowledge about breastfeeding in patients with SLE, estimate the breastfeeding intention rate, and consider the impact that SLE activity and the information on lactation provided by hydroxychloroquine and prednisone patient information leaflets (PILs) could have on breastfeeding intention.

Methods: A cross-sectional study was performed through an anonymous, closed, multiple-choice survey. Outpatients with SLE (meeting EULAR/ACR 2019 classification criteria) treated at a public hospital, aged 18 or older, and of childbearing age were surveyed. The authors conducted the surveys during medical consultations. Personal data (age, level of education) and past pregnancy and lactation experience were collected. Prior knowledge about breastfeeding in SLE was evaluated. Patients were asked about a) their intention to breastfeed in the event of a pregnancy and b) their intention to breastfeed in the event of active SLE. They were requested to read hydroxychloroquine and prednisone PILs and asked whether they thought it was possible to breastfeed while taking these medications. Finally, they were given updated information brochures on the subject. All patients signed written consent forms. The study was approved by the Bioethics Committee.

Results: The survey was answered by 72 patients with a mean age of 34 (SD 9) years old. Thirteen (18%) had at least primary education, 35 (49%) had high school education, and 24 (33%) had higher education. Twenty-nine (40%) had no children, 13 (18%) had had children before being diagnosed with SLE, and 30 (42%) had had at least one child after the diagnosis. Thirty-nine patients (54%) had previous breastfeeding experience.

Table 1: Level of knowledge about breastfeeding in SLE

n :72 patients	Yes	No	Unknown
Is it possible to breastfeed with SLE?	44 (61%)	7 (10%)	21 (29%)
Do SLE medications allow breastfeeding?	24 (33%)	16 (22%)	32 (45%)
Does breastfeeding benefit patients with SLE?	5 (7%)	10 (14%)	57 (79%)
Does breastfeeding with SLE benefit the infant?	25 (35%)	13 (18%)	34 (47%)

In the event of a new pregnancy, 64 patients (89%) would choose to breastfeed. However, in the event of active SLE, 47 patients (65%) would take the best available medication and not breastfeed,19 (27%) would opt for less effective medications that allow breastfeeding, and 6 (8%) would prefer not to take medication and breastfeed.

After reading the prednisone PILs, 47 patients (65%) considered it was possible to breastfeed while taking that drug, but only 20 (28%) said that the same applied to hydroxychloroquine.

Conclusion: Most patients considered it was possible to breastfeed and intended to do so, but this percentage would decrease in the event of active disease. Over 70% of the respondents considered it was unsafe to breastfeed after reading the hydroxychloroquine PIL. Information on breastfeeding should be reinforced for patients with SLE.

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Appropriate Preconception Care Improves Pregnancy Outcomes in SLE Patients

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Reproductive Issues in Rheumatic Disorders Poster I

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Background/Purpose: Pregnancies complicated by systemic lupus erythematosus (SLE) are known to be at high risk for adverse pregnancy outcomes (APOs). Previous studies have shown that active SLE and/or glucocorticoid use were risk factors for APOs. In American College of Rheumatology guideline for reproductive health, the importance for preconception care has been indicated. However, the evidence of the need for preconception care has not well revealed, especially whether it influences pregnancy outcomes. Therefore, we evaluated the impact of preconception care for SLE patients on pregnancy outcomes.

Methods: We used the data of SLE patients who were managed from the planning for pregnancy to delivery from March 2006 to March 2023 in our institution. Preconception care strategy was defined as all of the following: 1) counseling, 2) contraception and control moderate or high disease activity, 3) assessment of risk factors for maternal and fetal adverse event, 4) change to pregnancy-compatible medications. We retrospectively evaluated the associatio

Results: 42 cases in 30 SLE patients were included in our study. The preconception care strategy was completed in 34 cases (81.0%), while the remaining cases resulted in conceiving before completion of preconception care. In preconception care group, mean glucocorticoid dose and the rate of increasing dose of glucocorticoid during pregnancy was significantly lower than non-preconception care group (Table 1, P=0.01, < 0.01). As for disease activity parameters, only SLEDAI at first trimester was significantly lower in preconception care group (Table 2, P=0.01). However, there was no significant difference in other disease activity parameters between these two groups. Table 3 showed pregnancy outcomes with or without preconception care. Mean gestational age at delivery and mean birth weight of newborns was significantly higher in preconception care group (P=0.03 and < 0.01), and the rate of APOs or NICU administration was significantly lower in these group (P=0.04 and 0.03). The rates of preterm birth, low birth weight, or SGA tend to be lower in preconception care group (P=0.06, 0.053, and 0.06).

Table 1. Patients characteristics on preconception care. Values are presented as the mean ± standard deviation or number (%). #Wilcoxon rank sum test; ##Fisher's exact test. *P < 0.05.

	Preconception care (+) (n=34)	Preconception care (-) (n=8)	P value
Mean age at conceive (years old)#	32.9 ± 4.0	31.8 ± 3.8	0.47
Mean disease duration (years)#	11.3 ± 5.9	12.0 ± 4.5	0.74
Nulliparity (n (%))##	21 (61.8)	4 (50.0)	0.69
Glucocorticoid therapy before pregnancy			
Glucocorticoid use (n (%))##	29 (85.3)	8 (100.0)	0.56
Mean glucocorticoid dose (mg/day)#	6.0 ± 3.7	7.6 ± 2.9	0.22
Glucocorticoid therapy during pregnancy			
Glucocorticoid use (n (%))##	30 (88.2)	8 (100.0)	0.57
Mean glucocorticoid dose (mg/day)#	6.0 ± 4.6	11.4 ± 5.5	0.01*
Increased dose of glucocorticoid (n (%))##	2 (5.9)	4 (50.0)	<0.01*
Immunosuppressants use (n (%))##	5 (14.7)	0 (0)	0.56
Hydroxychloroquine use (n (%))##	7 (20.6)	1 (12.5)	1.00
Anticoagulant therapy (n (%))##	9 (26.5)	3 (37.5)	0.67

Table 2. Disease activity parameters on preconception care. Values are presented as the mean ± standard deviation or number (%). #Wilcoxon rank sum test; ##Fisher's exact test. *P < 0.05. SLEDAI: systemic lupus disease activity index; LLDAS: low lupus disease activity status.

	Preconception care (+) (n=34)	Preconception care (-) (n=8)	P value
SLEDAI#			
first trimester	1.1 ± 1.6	3.1 ± 2.7	0.01*
third trimester	0.7 ± 1.4	1.8 ± 2.2	0.10
LLDAS achievement (n(%))##			
first trimester	23 (67.7)	4 (50.0)	0.43
third trimester	18 (66.7)	3 (50.0)	0.64
LLDAS achievement without glucocorticoid dose (n(%))##			
first trimester	29 (85.3)	5 (62.5)	0.16
third trimester	24 (88.9)	4 (66.7)	0.22
C3#			
first trimester	85.7 ± 15.3	81.6 ± 22.9	0.42
third trimester	101.8 ± 20.4	108.8 ± 35.3	0.37
C4#			
first trimester	17.1 ± 4.9	15.6 ± 8.1	0.76
third trimester	18.0 ± 6.6	20.6 ± 12.3	0.77
CH50#			
first trimester	40.2 ± 8.6	35.9 ± 11.1	0.17
third trimester	44.3 ± 10.2	45.3 ± 14.5	0.74
Titer of anti-dsDNA antibody#			
first trimester	4.4 ± 6.8	63.9 ± 103.1	0.18
third trimester	2.9 ± 4.6	25.2 ± 30.0	0.06

Table 3. Pregnancy outcomes on preconception care. Values are presented as the mean ± standard deviation or number (%). #Wilcoxon rank sum test; ##Fisher's exact test. *P < 0.05. NICU: neonatal intensive care unit.

	Preconception counseling (+) (n=34)	Preconception counseling (-) (n=8)	P value
Live birth (n (%))##	27 (79.4)	6 (75.0)	1.00
Mean gestational age at delivery (weeks)#	38.5 ± 1.7	35.0 ± 4.7	0.03*
Mean birth weight of newborns (gram)#	2846.2 ± 482.4	2075.3 ± 766.9	<0.01*
Adverse pregnancy outcomes (n (%))##	12 (38.7)	6 (85.7)	0.04*
Preterm birth (n (%))##	3 (11.1)	3 (50.0)	0.06
Low birth weight (n (%))##	6 (22.2)	4 (66.7)	0.053
Small for gestational age (n (%))##	3 (11.1)	3 (50.0)	0.06
NICU administration (n (%))##	5 (18.5)	4 (66.7)	0.03*

Conclusion: In SLE patients, completing preconception care strategies improved pregnancy outcomes, by reducing glucocorticoid dose during pregnancy and controlling disease activity, especially in SLEDAI. Preconception care is an important therapeutic strategy for SLE patients who hope to pregnancy.

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Abstract Number: 0464

Adverse Pregnancy Outcomes in Sjogren's Disease Compared to Controls: An Interdisciplinary Approach with Maternal Fetal Medicine

Lauren Tesoriero[1], Jennifer Kidd[1], Julie Piccione[1], Izmirly peter[2], Meredith Akerman[1], Steven Carsons[1], Patricia Rekawek[1] and Julie Nusbaum[1], [1]NYU Long Island School of Medicine, Mineola, NY, [2]NYU, New York, NY

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Reproductive Issues in Rheumatic Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Outside of the known association of Ro antibody with congenital heart block (CHB), little is known about adverse maternal outcomes, and even less about neonatal outcomes, in patients with Sjogren's Disease (SjD).Few studies of pregnancy in SjD have been conducted in collaboration with Maternal Fetal Medicine (MFM). With an interdisciplinary approach, we aim to describe maternal and neonatal outcomes of pregnancies in SjD compared to a 1:3 matched control population.

Methods: This was a retrospective cohort study of pregnant patients who had prenatal care and delivered at NYU Langone Hospital-Long Island from 01/2018-12/2022.SjD patients were matched 1:3 with non-SjD controls by gestational age and maternal age. Inclusion criteria for SjD patients were diagnosis by the 2016 ACR/EULAR Criteria or by rheumatologist evaluation, with available pregnancy data. Exclusion criteria for SjD patients were concurrent autoimmune disease (i.e. SLE); antibodies to dsDNA, Smith, or aPL; or unavailable pregnancy records. Controls were excluded if they had major maternal medical comorbidities, major fetal anomalies in pregnancy, prior adverse pregnancy outcome (APO), or delivery elsewhere. Many outcomes of interest are rare, and a composite of grouped outcomes was utilized. All component details of composites are included below (Table 3) and were verified by a MFM specialist. The primary outcome was a composite of APO between the two groups. Secondary analysis included the following composite outcomes: maternal hypertensive, adverse maternal antenatal, adverse delivery, maternal infectious, and adverse neonatal. Statistical analysis of maternal demographics, maternal outcomes, and neonatal outcomes was performed using two sample t-test for continuous variables and Fisher's exact test for categorical variables, with significance p value of < 0.05.

Results: 48 patients were included: 12SjD patients and 36 controls. SjD patients were more likely to be prescribed aspirin (50% vs 5.6%, p = 0.002) and hydroxychloroquine (33.33% vs 0%, p=0.003), while other demographics were comparable (Table 1).The APO composite score was significantly increased in SjD patients (25% vs 2.8% p=0.04) with SjDAPO of 1 preterm birth, 1 fetal growth restriction, and 1 limb anomaly; non-SjD had 1 cardiac anomaly (Table 3).There were no cases of CHB in either group. SjD patients were more likely to be delivered by cesarean delivery(CD) (75% vs 25%, p= 0.004) (Table 2). There were no other significant differences in adverse maternal or neonatal outcomes (Table 2, Table 3).

Table 1: Demographics

Variable	Patients with SjD (n=12)	Non-SjD Controls (n=36)	p-value
Age (years)*	35.58 ± 4.44	34.19 ± 4.20	0.33
Advanced maternal age at birth (age 35 or greater)	6 (50%)	19 (52.8%)	0.87
Body Mass Index (Kg/m^2) *	27.56 ± 4.28	27.07 ± 6.07	0.79
Race			0.67
Asian	1 (8.33%)	1 (2.78%)	
Black or African American	1 (8.33%)	7 (19.44%)	
White	6 (50%)	18 (50%)	
Unknown/other	4 (33.33%)	10 (27.78%)	
Ethnicity			0.54
Non Hispanic	6 (50%)	24 (66.67%)	
Hispanic/Latino	4 (33.33%)	8 (22.22%)	
Unknown	2 (16.67%)	4 (11.11%)	
Pre-pregnancy condition			
Hypertension	0 (0%)	0 (0%)	N/A
Diabetes	0 (0%)	0 (0%)	N/A
Hyperlipidemia	1 (8.33%)	1 (2.78%)	0.44
Coronary artery disease	0 (0%)	0 (0%)	N/A
Chronic kidney disease	0 (0%)	0 (0%)	N/A
In Vitro Fertilization	1 (8.33%)	4 (11.11%)	1
Multiparous	9 (75%)	26 (72.22%)	1
Medications in Pregnancy			
Aspirin	6 (50%)	2 (5.56%)	0.002
Hydroxychloroquine	4 (33.33%)	0 (0%)	0.003
Oral corticosteroids	0 (0%)	0 (0%)	N/A
SjD Antibody Positivity			
SSA	8 (66.67%)		
SSB	6 (50%)		
ANA	7 (58.33%)		
Rheumatoid Factor	2 (16.67%)		

All outcomes reported at n (percent) unless otherwise noted below
*Reported as mean ± standard deviation

Table 2: Delivery Outcomes

Variable	Patients with SjD (n=12)	Non-SjD Controls (n=36)	p-value
Live birth rate	12 (100%)	36 (100%)	N/A
Miscarriage	0 (0%)	0 (0%)	
Intrauterine fetal demise	0 (0%)	0 (0%)	
Mode of Delivery			<0.01
Vaginal	2 (16.67%)	25 (69.44%)	
Operative	1 (8.33%)	2 (5.56%)	
Cesarean	9 (75%)	9 (25%)	
Induction of labor	4 (33.3%)	20 (55.6%)	0.18
Gestational age at birth (weeks)*	38.63 ± 1.48	39.53 ± 0.96	0.13
Preterm birth (prior to 37 weeks)	1 (8.3%)	0 (0%)	0.25
Birth weight (grams)*	3308 ± 455	3404 ± 332	0.60
Intrauterine growth restriction	1 (8.33%)	0 (0%)	0.25
Birthweight less than 2500 grams	0 (0%)	0 (0%)	N/A
Umbilical cord pH (arterial blood gas)*	7.25 ± 0.05	7.24 ± 0.09	0.9687

All outcomes reported at n (percent) except as noted
* Reported as mean ± standard deviation

Table 3: Composite Outcomes

Composite Outcomes	Patients with SjD (n=12)	Non-SjD Controls (n=36)	p-value
Adverse pregnancy[1]	3 (25%)	1 (2.78%)	0.04
Maternal infectious[2]	0 (0%)	0 (0%)	N/A
Maternal hypertensive[3]	3 (25%)	3 (8.33%)	0.156
Adverse delivery[4]	2 (16.67%)	7 (19.44%)	1.000
Adverse maternal antepartum[5]	2 (16.67%)	3 (8.33%)	0.587
Adverse neonatal[6]	0 (0%)	4 (11.11%)	0.560

All outcomes reported as n (percent)
1. **Adverse pregnancy composite:** Miscarriage, intrauterine fetal death, Fetal complication (intrauterine growth restriction and congenital anomalies [cardiac, lung, renal, neurologic, gastrointestinal, genitourinary, limb, hydrops, neural tube defect, thickened nuchal translucency]), Fetal heart block, Preterm birth (gestational age <37weeks)
2. **Adverse infectious composite:** Chorioamnionitis, Endometritis, Mastitis, Wound infection
3. **Maternal hypertensive composite:** Gestational hypertension, Preeclampsia, Eclampsia, HELLP (hemolysis, elevated liver enzyme, low platelet) syndrome, Postpartum preeclampsia
4. **Adverse delivery composite:** 3rd/4th degree laceration, Episiotomy, Cesarean delivery for fetal intolerance of labor, Postpartum hemorrhage, Shoulder dystocia, Placenta accreta spectrum, Retained placenta, Blood transfusion, Hysterectomy, Intensive care unit admission, Maternal death
5. **Adverse maternal antepartum composite:** Venous thromboembolism, Gestational diabetes, Vasa previa, Placenta Previa, Placental abruption
6. **Adverse neonatal composite:** Neonatal intensive care unit admission, Neonatal complications (infection [sepsis, pneumonia, neonatal necrotizing enterocolitis], respiratory problem [mechanical ventilation, RDS], neurologic [seizures, hypoxic ischemic encephalopathy, intraventricular hemorrhage]) Neonatal demise, Birthweight less than 2500 grams, Umbilical cord arterial blood gas pH <7.0, APGAR (appearance, pulse, grimace, activity, and respiration) 5 minute score <7

Conclusion: There was an increased risk of APO in SjD patients compared to controls. No significant difference in neonatal outcomes was noted, adding an important contribution to the limited knowledge of neonatal outcomes in SjD. A significantly increased rate of aspirin use and of CD among patients with SjD was noted and calls for further study. Larger sample size, an interdisciplinary approach with MFM, and the use of rigorous definitions of perinatal outcomes would improve upon our existing knowledge of pregnancy in SjD. Our study suggests that clinicians should consider closer monitoring and early collaboration with MFM specialists for the pregnancies of SjD patients.

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Abstract Number: 0465

The Effects of Post-Dobbs Abortion Policy on Rheumatology Clinical Practice: A Survey of Rheumatologists

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Reproductive Issues in Rheumatic Disorders Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: In June 2022, the U.S. Supreme Court's decision in *Dobbs v. Jackson Women's Health* removed the federal constitutional right to abortion, returning abortion policy to individual states. Approximately one-third of states have since banned or planned to greatly restrict abortion access. We distributed a confidential online survey to a sample of U.S.-based rheumatologists to learn how the *Dobbs* decision might affect clinical practice around teratogen prescribing, abortion referrals, and perceived vulnerability to criminalization.

Methods: This study was designated as exempt by the University of Pittsburgh Institutional Review Board. QR codes to the survey were disseminated in November 2022: 1) at a plenary session about reproductive health at the American College of Rheumatology (ACR) national meeting; 2) via Twitter by study investigators during the ACR national meeting. Results were analyzed by descriptive statistics or chi-square tests, which compared responses by practice in abortion-restricted or protected states.

Results: Most respondents (N=152) identified as female (80.3%), practiced in academic settings (76.3%), and were in their early careers (fellows: 13.2%, < 10 years of independent practice: 47.4%). Approximately 47% of respondents practiced in abortion-restricted states. Half of respondents reported that one or more of their patients had ever become pregnant while using a teratogen (e.g., methotrexate, mycophenolate), and 34% had ever recommended abortion to a patient before *Dobbs*. Rheumatologists in abortion-restricted states were more comfortable referring a patient for abortion without fear of reprisal prior to *Dobbs* than post-*Dobbs* (83.1% and 34.8%, respectively; $p< 0.001$). Rheumatologists in abortion-restricted vs protected states were marginally more likely to report that they had changed or planned to change how often they prescribed methotrexate (13.0% vs 5.3%, p=0.146) and/or mycophenolate (8.7% vs 1.32%, p=0.05) to reproductive-age patients.

Conclusion: Our results suggest that rheumatologists' prescribing patterns may change in the context of the nationwide abortion restriction, particularly in abortion-restricted states; reproductive-age females with rheumatic diseases may therefore have less access to evidence-based treatments such as mycophenolate and methotrexate [2-5]. Limitations of the current study include uncertain representativeness of the sample: the response rate cannot be calculated due to social media dissemination, and rheumatologists who had more interest in reproductive health issues may have been more likely to respond to the survey. Nonetheless, our findings underscore an urgent need for data to inform a concerted public health response that protects the health and well-being of females with rheumatic diseases.

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Abstract Number: 0466

Impact of Postpartum on Patients with Inflammatory Rheumatic Diseases: The P2Rheum Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Reproductive Issues in Rheumatic Disorders Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: There are limited data on the impact of the postpartum period (PP) on the activity of inflammatory rheumatic disorders (IRD), and the data available on the impact of breastfeeding on the activity of IRD are contradictory. The objectives of this analysis were to describe disease activity and treatments received during the PP period and breast-feeding frequency and its possible impact on IRD activity.

Methods: A descriptive study from a French multicenter prospective observational cohort (GR2) studying pregnant women with IRD i.e. rheumatoid arthritis (RA) and spondylarthritis (SpA) confirmed by a rheumatologist was conducted (NCT 02450396). Data were collected during several regular pre-conception visits, visits during pregnancy and visits around 6- and 12-months PP, from October 2014 to October 2022. Disease activity was assessed with DAS28-CRP for RA and

CHARACTERISTICS	SPONDYLOARTHRITIS *N= 124*	RHEUMATOID ARTHRITIS N = 94
Mean age at pregnancy, y (sd)	31.8 (5.0)	32.8 (5.0)
Mean duration of rheumatism, y (sd)	10.3 (6.1)	12.3 (7.7)
Axial SpA (%)	95 (76.6)	
Peripheric SpA (%)	58 (46.8)	
Erosive RA (%)		41/89 (46.1)
RF positive (%)		66/92 (71.7)
ACPA positive (%)		65/92 (70.7)
Parity (%)		
- primiparous	46/59 (78.0)	32/40 (80.0)
- multiparous	13/59 (22.0)	8/40 (20.0)
Vaginal delivery (%)	95/116 (81.9)	60/83 (72.3)
Cesarean section (%)	21/116 (18.1)	23/83 (27.7)
Complication during pregnancy (%)	59/116 (50.9)	46/84 (54.8)
Mean term at delivery (w)	38.9 (1.8)	38.3 (2.1)
Preterm (%)	7/123 (5.7)	17/92 (18)

Legends: Data are expressed in mean and standard deviation (sd) or number and percentages. SpA: spondyloarthritis; RF: rheumatoid factor; ACPA: Anti-citrullinated protein antibody)

	SPONDYLOARTHRITIS				RHEUMATOID ARTHRITIS			
	N	PREGNANCY	POST-PARTUM (M6)	p	N	PREGNANCY	POST-PARTUM (M6)	p
FLARE (%)	118	48 (40.7)	48 (40.7)	0.999	92	40 (43.5)	57 (62.0)	**0.020**
ACTIVITY (%)	71			0.436				0.349
REMISSION		23 (32.4)	27 (38.0)			44 (68.8)	37 (57.8)	
LOW		28 (39.4)	19 (26.8)			7 (10.9)	12 (18.8)	
MODERATE/HIGH		20 (28.2)	25 (35.2)			13 (20.3)	15 (23.4)	
CRP (mg/l)	43	**7.0 [3.3; 13.1]**	**3.2 [1.4; 5.1]**	**0.014**	54	4.8 [2.3; 10.2]	2.6 [1.0; 9.8]	0.371
ESR (mm)	20	21.5 [11.8; 48.4]	9.0 [4.8; 22.5]	0.067	28	**29.0 [16.8; 48.8]**	**14.0 [6.0; 27.5]**	**0.004**
ASDAS-CRP	29	2.3 [1.7; 2.8]	2.2 [1.1; 3.0]	0.865	-	-	-	-
BASDAI	70	2.5 [1.3; 4.0]	2.0 [1.0; 4.0]	0.562	-	-	-	-
DAS28-CRP	-	-	-	-	54	2.1 [1.6; 3.0]	2.4 [1.5; 3.1]	0.409
Breastfeeding (%)	109		20 (18.3)		82		13 (15.9)	

Legends: Data are expressed in median and interquartile or number and percentages. Disease activity was defined for SpA according to BASDAI or ASDAS-CRP: BASDAI < 2 for remission and BASDAI ≥ 4 for high activity; ASDAS-CRP <1.3 for remission, ASDAS-CRP> 1.3 and <2.1 for low activity, ASDAS-CRP> 2.1 for moderate to high activity; DAS28-CRP<2.6, for low activity, DAS28-CRP >2.6 and <3.2, and DAS28-CRP>3.2 for medium to high activity. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; DAS28-CRP: Disease Activity Score based on 28 tender and swollen joints and C reactive protein.

	DELIVERY	RESUMED PP	INITIATED PP
SPA			
bDMARDS (%)	29/124 (23.4)	54/123 (43.9)	2/123 (1.6)
MTX (%)	0/124	6/123 (4.9)	3/123 (2.4)
CORTICOTHERAPIE (%)	5/124 (4.0)		3/123 (2.4)
RA			
bDMARDS (%)	15/92 (16.3)	39/91 (42.9)	6/91 (6.6)
MTX (%)	0/91	30/91 (33.0)	4/91 (4.4)
CORTICOTHERAPIE (%)	12/94 (12.8)		12/94 (12.8)

Legends: Date are expressed in number and percentages. SpA : Spondylarthritis; RA : rheumatoid arthritis; PP : post-partum; bDMARDs : biological Disease-Modifying AntiRheumatic Drugs ; MTX : Methotrexate.

BASDAI and ASDAS for SpA. Flares were defined according to physician judgment. The change in disease activity was investigated by paired Student's t-tests and Mac-Nemar Chi-2 tests for paired data, as appropriate. Subgroup bivariate comparisons by IRD pathology were performed according to patients' breastfeeding status at 6-months PP by Kruskal-Wallis tests for continuous variables and Fisher exact tests for categorical variables. There was no imputation of missing data.

Results: Overall, 218 pregnant patients were analyzed: 124 with SpA and 94 with RA. The mean age was 31.8 ± 5.0 and 32.8 ± 5.0 years, respectively for SpA patients and RA patients (**Table 1**). In SpA patients, there were no significant differences in terms of activity (flares, BASDAI and ASDAS) at 6 months PP compared to during pregnancy. However, CRP level was significantly higher during pregnancy compared to 6 months PP (7 mg/L vs 3.2 mg/L; p = 0.014) (**Table 2**). RA patients presented significantly more flares in the first 6 months PP compared to pregnancy (62.0% vs 43.5% p = 0.02).Disease activity measures were similar between both SpA and RA patients who still breastfed at six months PP and patients who never breastfed or stopped before 6 months.

After one-year PP, among SpA patients, the number of flares were significantly higher than during pregnancy (40.3% vs 13.4%; p < 0.001). For RA patients, the mean activity and the number of flares were not different during pregnancy and at one year PP. Regarding treatment, about 40% of SpA and RA patients resumed bDMARD during PP, mainly in the first month PP (**Table 3**). For SpA, all bDMARDs were TNF inhibitors except for one treatment with belimumab (patient with SpA and systemic lupus erythematosus). For RA, among bDMARDs prescribed, 38/45 (84.4%) were TNF inhibitors (tocilizumab, abatacept and JAK inhibitors were the remaining).

Conclusion: RA patients presented significantly more flares in the first 6 months of postpartum compared to pregnancy while SpA patients remained stable. Yet, in both diseases, only about 40% of the patients resumed bDMARD during postpartum period. Breastfeeding was not associated with an increase or decrease in disease activity in SpA and RA patients.

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Abstract Number: 0467

Cardiovascular Events During Pregnancy: Implications for Adverse Pregnancy Outcomes in Individuals with Autoimmune Rheumatic Diseases and Antiphospholipid Syndrome

Rashmi Dhital, Rebecca Baer and Christina Chambers, University of California San Diego, La Jolla, CA

SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune rheumatic diseases (ARD) and antiphospholipid syndrome (APS) are autoimmune conditions with increased risks of cardiovascular complications as well as negative pregnancy consequences. We recently found significantly higher risks for acute cardiovascular events (CVEs) during pregnancy and postpartum in women with ARD and APS compared to individuals without such conditions. However, the impact of such CVEs on adverse pregnancy outcomes (APOs) is not well known. The primary aim was to compare APOs between individuals with ARDs, primary APS and those without either condition, based on the presence or absence of acute CVEs during pregnancy.

Methods: We used the Study of Outcomes in Mothers and Infants (SOMI) database (2005-2020), an administrative population-based birth cohort in California. The main outcomes were APOs, which included preterm birth (PTB) and small-for-gestational age (SGA). Preterm birth was sub grouped as spontaneous, provider initiated, early preterm birth (< 32 weeks), and late preterm birth (32 – 36 weeks). We compared APOs between individuals with or without acute CVEs during pregnancy, after categorizing them into three groups: those with ARDs, those with primary APS, and those with no ARDs or APS. We calculated relative risks (aRR) and 95% confidence intervals (CIs), adjusting for age at delivery, race/ethnicity, primary payer, maternal education, maternal pre-pregnancy body mass index, preexisting hypertension, preexisting diabetes, hyperlipidemia, smoking, alcohol use, drug use, and depression.

Table 1. Comparison of adverse pregnancy outcomes (APOs) in individuals with or without an acute cardiovascular event during pregnancy, stratified by presence of an autoimmune rheumatic disease (ARD) or primary antiphospholipid syndrome (APS), 2005 – 2020 (n= 7,031,432) *ARD: autoimmune rheumatic disease, APS: antiphospholipid syndrome, CVEs: cardiovascular events, APOs: adverse pregnancy outcomes Risks were adjusted for: age at delivery, race/ethnicity, payer for delivery, maternal education, maternal pre-pregnancy body mass index, preexisting hypertension, preexisting diabetes, hyperlipidemia, smoking, alcohol use, drug use, and depression.

	No ARD or APS (n= 7,004,334)			Any ARD (n=19,340)			Primary APS (n=7,758)		
	With Acute CVEs	Without Acute CVEs	aRR (95% CI)	With Acute CVEs	Without Acute CVEs	aRR (95% CI)	With Acute CVEs	Without Acute CVEs	aRR (95% CI)
	n (%)			n (%)			n (%)		
Sample	17,175 (100.0)	6,987,159 (100.0)		268 (100.0)	19,072 (100.0)		431 (100.0)	7,327 (100.0)	
Adverse Pregnancy Outcomes	4,838 (28.2)	1,063,115 (15.2)	1.6 (1.6, 1.7)	143 (53.4)	5,063 (26.6)	1.8 (1.5, 2.1)	132 (30.6)	1,516 (20.7)	1.3 (1.1, 1.6)
Preterm Birth	3,331 (19.4)	496,394 (7.1)	2.2 (2.2, 2.3)	110 (41.0)	2,977 (15.6)	2.3 (1.9, 2.7)	85 (19.7)	945 (12.9)	1.3 (1.03, 1.6)
< 32 weeks	783 (4.6)	60,151 (0.9)	4.3 (4.0, 4.6)	34 (12.7)	517 (2.7)	4.5 (3.2, 8.5)	16 (3.7)	163 (2.2)	1.4 (0.8, 2.3)
32 – 36 weeks	2,548 (14.8)	436,243 (6.2)	2.1 (2.0, 2.2)	76 (28.4)	2,460 (12.9)	2.1 (1.7, 2.7)	69 (16.0)	782 (10.7)	1.3 (1.02, 1.7)
Spontaneous	2,151 (12.5)	337,885 (4.8)	2.2 (2.1, 2.3)	79 (29.5)	2,042 (10.7)	2.6 (2.1, 3.2)	61 (14.2)	652 (8.9)	1.3 (1.03, 1.8)
Provider initiated	1,053 (6.1)	116,555 (1.7)	3.2 (3.0, 3.4)	28 (10.5)	823 (4.3)	2.6 (1.7, 3.7)	22 (5.1)	268 (3.7)	1.3 (0.8, 2.0)
Small for gestational age	1,954 (11.4)	622,516 (8.9)	1.2 (1.1, 1.3)	52 (19.4)	2,657 (13.9)	1.2 (0.9, 1.6)	61 (14.2)	726 (9.9)	1.3 (1.02, 1.7)

Results: Pregnant individuals with an ARD (26.9%) or primary APS (21.3%) had significantly higher APOs as compared to women without these conditions (15.2%). The presence of acute CVEs during pregnancy further increased the adjusted risk of an APO by 1.8-fold for ARD, 1.3-fold for primary APS and 1.6-fold for those without an ARD or APS. Among individuals with an ARD, more than half (53.4%) with CVEs experienced APOs, compared to 26.6% without CVEs (aRR 1.8, 95% CI 1.5 to 2.1). The increased risk of APOs in ARD pregnancies with CVEs was primarily driven by higher rates of PTB, which was 41.0% in ARD patients with CVEs compared to 15.6% in those without CVEs during pregnancy (RR: 2.3, 95% CI 1,9, 2.7), whereas the rate of SGA was similar among ARD patients with and without CVEs. Among ARD patients with CVEs, 12.7% experienced early PTB, while 2.7% of those without CVEs had early PTB (RR 4.5, 95% CI 3.2 to 8.5) (**Table 1**).

Conclusion: Pregnant individuals with an ARD or APS had higher rates of APOs than those without these conditions. Acute CVEs during pregnancy further increased the risk of an APO, regardless of ARD or APS diagnosis. These findings highlight the need for close monitoring and management of pregnant women, not only for adverse outcomes, but also for cardiovascular risks and events, in order to identify those at the highest risk for adverse outcomes. This need is particularly significant for individuals with ARDs, as 53.4% of our population with an ARD and CVE in pregnancy experienced an APO.

Disclosure: R. Dhital: None; **R. Baer**: None; **C. Chambers**: Amgen, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Genzyme Sanofi-Aventis, 5, Gerber Foundation, 5, Gilead, 5, GlaxoSmithKline, 5, Hoffman La-Roche-Genentech, 5, Janssen Pharmaceuticals, 5, Leo Pharma, 5, Novartis, 5, Pfizer, Inc., 5, Regeneron, 5, Sanofi, 5, Sun Pharma Global FZE, 5, Takeda Pharmaceutical Company Limited, 5, UCB Pharma, USA, 5.

Abstract Number: 0468

Patients with Autoimmune Skin Diseases Are at Increased Risk of Adverse Pregnancy Outcomes

Heejo Keum[1], Bonnie Bermas[2], Shivani Patel[1], Benjamin Chong[1] and Heidi Jacobe[1], [1]University of Texas Southwestern Medical Center, Dallas, TX, [2]UT Southwestern, Dallas, TX

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Reproductive Issues in Rheumatic Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Increased rates of adverse pregnancy outcomes (APOs) have been reported in association with rheumatologic diseases such as systemic lupus erythematosus (SLE), dermatomyositis (DM), and rheumatoid arthritis (RA). However, little is known about pregnancy outcomes in patients with autoimmune skin diseases (ASDs). We aimed to determine the frequency of APOs in patients with ASDs. We hypothesized that similar to rheumatic diseases, patients with ASDs would have a higher frequency of APOs than the general population.

Methods: This case-control study was conducted using the TriNetX US Collaborative Network, a database of electronic medical records of 94 million patients in the United States. Pregnant patients aged 15-44 years between January 1, 2016 and December 31, 2021 were included. Pregnancies were identified using International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) indicating pregnancy endpoints. Cases consisted of patients with at least one ASD diagnosed prior to the end of pregnancy. The ASDs identified were alopecia areata, bullous pemphigoid, cicatricial pemphigoid, dermatitis herpetiformis, cutaneous lupus erythematosus, epidermolysis bullosa acquisita, morphea, pemphigus foliaceus, pemphigus vulgaris, vitiligo, and amyopathic DM. There were 2 control groups: 1) healthy controls without ASDs, SLE, or RA and 2) disease controls defined as patients with SLE or RA. For all cases and controls, patients with hidradenitis suppurativa or other common autoimmune diseases such as Hashimoto's thyroiditis and Type 1 diabetes were excluded. The primary outcomes were APOs defined as spontaneous abortion, gestational hypertension, preeclampsia/

Table 1. Baseline characteristics of patients with ASDs, controls, and disease controls after propensity score matching

Characteristics	Patients with ASDs (N=3,654)	Controls (N=3,654)[1]	SLE (N = 2147)[2]	RA (N = 889)[3]
Age at pregnancy endpoint (mean ± SD)	31.4 (6.3)	(31.4, 6.3)	31.1 (5.8)	33.0 (5.8)
Race, No. (%)				
White	2338 (64%)	2305 (63%)	1261 (59%)	613 (69%)
Black	579 (16%)	583 (16%)	477 (22%)	101 (11%)
Asian	152 (4%)	153 (4%)	47 (2%)	29 (3%)
American Indian or Alaska Native	24 (1%)	25 (1%)	<11 (0.5%)	<11 (1%)
Native Hawaiian or Other Pacific Islander[4]	<11 (0.3%)	<11 (0.3%)	<11 (0.5%)	0
Unknown Race	559 (15%)	584 (16%)	352 (16%)	137 (15%)
Ethnicity, No. (%)				
Hispanic or Latino	693 (19%)	688 (19%)	312 (15%)	163 (18%)
Not Hispanic or Latino	2577 (71%)	2568 (70%)	1550 (72%)	616 (69%)
Unknown Ethnicity	384 (11%)	398 (11%)	285 (13%)	110 (12%)
Comorbidities, No. (%)				
Nutritional anemias	242 (7%)	255 (7%)	141 (7%)	69 (8%)
Hemolytic anemias	161 (4%)	141 (4%)	95 (4%)	24 (3%)
Other anemias	538 (15%)	562 (15%)	333 (16%)	124 (14%)
Thrombocytopenia	83 (2%)	68 (2%)	56 (3%)	12 (1%)
Chronic hypertension	501 (14%)	510 (14%)	304 (14%)	105 (12%)
Diabetes mellitus	409 (11%)	415 (11%)	146 (7%)	49 (6%)
Hypothyroidism	293 (8%)	306 (8%)	138 (6%)	66 (7%)
Hyperthyroidism	41 (1%)	38 (1%)	19 (1%)	<11 (1%)
Chronic kidney disease	224 (6%)	236 (6%)	150 (7%)	44 (5%)
Pulmonary hypertension	22 (0.6%)	22 (0.6%)	12 (0.6%)	<11 (1%)
BMI >= 30 kg/m², No. (%)	875 (24%)	892 (24%)	458 (21%)	197 (22%)
Nicotine dependence, No. (%)	571 (16%)	557 (15%)	278 (13%)	98 (11%)
Alcohol related disorders, No. (%)	158 (4%)	153 (4%)	47 (2%)	23 (3%)

[1] There were 692,860 patients identified as controls before propensity score matching. The controls that were propensity score matched with patients with ASDs are shown here.
[2] Patients with SLE after propensity score matching with patients with ASDs
[3] Patients with RA after propensity score matching with patients with ASDs
[4] Number of patients less than 11 are not specified on TriNetX to protect patient privacy

Table 2. Adverse pregnancy outcomes in patients with autoimmune skin diseases and controls after propensity score matching

Characteristics, No. (%)	Patients with ASDs (N=3,654)	Controls (N=3,654)	RR (95% CI)	P value
Preeclampsia/ eclampsia	358 (9.8)	307 (8.4)	1.2 [1.0-1.3]	0.04
Gestational hypertension	308 (8.4)	265 (7.3)	1.2 [1.0-1.4]	0.06
Gestational diabetes	210 (5.7)	231 (6.3)	0.9 [0.8-1.1]	0.3
Intrauterine growth restriction	106 (2.9)	112 (3.1)	0.9 [0.7-1.2]	0.68
Spontaneous abortion	963 (26.4)	624 (17.1)	1.5 [1.4-1.7]	<0.001
Stillbirth	30 (0.8)	30 (0.8)	1 [0.6-1.7]	>0.99
Preterm premature rupture of membrane	93 (2.5)	100 (2.7)	0.9 [0.7-1.2]	0.61
Preterm birth	110 (3.0)	130 (3.6)	0.8 [0.7-1.1]	0.19

Table 3. Adverse pregnancy outcomes in patients with autoimmune skin diseases and disease controls after propensity score matching

Characteristics, No. (%)	Patients with ASDs (N=2,147)	SLE (N=2,147)	RR [95% CI]	P value	Patients with ASDs (N=889)	RA (N=889)	RR [95% CI]	P value
Preeclampsia/ eclampsia	186 (8.7)	250 (11.6)	0.7 [0.6-0.9]	0.001	80 (9.0)	93 (10.5)	0.9 [0.6-1.1]	0.3
Gestational hypertension	179 (8.3)	154 (7.2)	1.2 [0.9-1.4]	0.15	84 (9.4)	80 (9.0)	1.0 [0.8-1.4]	0.74
Gestational diabetes	109 (5.1)	86 (4.0)	1.3 [1.0-1.7]	0.09	50 (5.6)	50 (5.6)	1 [0.7-1.5]	>0.99
Intrauterine growth restriction	72 (3.4)	118 (5.5)	0.6 [0.5-0.8]	<0.001	25 (2.8)	27 (3.0)	0.9 [0.5-1.6]	0.78
Spontaneous abortion	512 (23.8)	432 (20.1)	1.2 [1.1-1.3]	0.003	217 (24.4)	196 (22.0)	1.1 [0.9-1.3]	0.24
Stillbirth	20 (0.9)	33 (1.5)	0.6 [0.3-1.1]	0.07	10 (1.1)	10 (1.1)	1 [0.4-2.4]	>0.99
Preterm premature rupture of membrane	47 (2.2)	78 (3.6)	0.6 [0.4-0.9]	0.004	13 (1.5)	16 (1.8)	0.8 [0.4-1.7]	0.57
Preterm birth	62 (2.9)	119 (5.5)	0.5 [0.4-0.7]	<0.001	22 (2.5)	37 (4.2)	0.6 [0.4-1.0]	0.05

eclampsia, gestational diabetes, intrauterine growth restriction (IUGR), preterm premature rupture of membranes (PPROM), and preterm birth. Patients with ASDs and controls were 1:1 propensity score matched by age, race, ethnicity, comorbidities, obesity, and substance use. For each outcome, risk ratio (RR) with a 95% confidence interval (CI) was calculated.

Results: 3,654 patients with ASDs were matched to 3,654 healthy controls (Table 1). Patients with ASDs were more likely to have spontaneous abortions (RR=1.5 [1.4-1.7], P< 0.001), and preeclampsia/eclampsia (RR=1.2 [1.0-1.3], P=0.04) than healthy controls (Table 2). When compared to women with SLE, women with ASDs were less likely to have preeclampsia/eclampsia (RR=0.7 [0.6-0.9, p=0.001), have a preterm birth (RR= 0.5 [0.4-0.7], P< 0.001), PPROM (RR=0.6 [0.4-0.9], P=0.004), or an infant with IUGR (RR=0.6 [0.5-0.8], P< 0.001), and more likely to have a spontaneous abortion (RR=1.2 [1.1-1.3], P=0.003). Patients with ASDs had similar risks for APOs as patients with RA (Table 3).

Conclusion: These results suggest that patients with ASDs have increased rates of adverse pregnancy outcomes compared to healthy controls and are similar in risk to RA. In contrast, those with SLE have a greater frequency of APOs indicating that all these groups may benefit from multidisciplinary care with maternal-fetal medicine specialists. Further studies will be helpful to identify mechanisms behind increased risk of adverse pregnancy outcomes in patients with ASDs.

Disclosure: H. Keum: None; **B. Bermas**: None; **S. Patel**: None; **B. Chong**: Biogen Inc, 1, 2, 12, Site PI for Clinical Trial, Bristol-Myers Squibb(BMS), 2, EMD Serono, 2, Horizon Therapeutics, 2; **H. Jacobe**: None.

Abstract Number: 0469

Hydroxychloroquine and Preeclampsia Risk in Lupus Pregnancy: Results from a Large Regional Integrated Health Network

Julia Simard[1], Emily Liu[2], Amadeia Rector[3], Miranda Cantu[4], Daniel Kuo[5], Eliza Chakravarty[6], Maurice Druzin[7], Gary Shaw[7], Michael Weisman[8] and Monique Hedderson[2], [1]Department of Epidemiology & Population Health, Stanford University School of Medicine, Stanford, CA, [2]Kaiser Permanente Division of Research, Oakland, CA, [3]Stanford University, San Francisco, CA, [4]Global Lupus Support Group, Portage, MI, [5]Kaiser Permanente, Redwood City, CA, [6]Oklahoma Medical Research Foundation, Oklahoma City, OK, [7]Stanford University, Stanford, CA, [8]Stanford, Los Angeles, CA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Reproductive Issues in Rheumatic Disorders Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Pregnancies in patients with systemic lupus erythematosus (SLE) are at greater risk of preeclampsia. Hydroxychloroquine (HCQ) is recommended during SLE pregnancy to control disease activity. Some studies have suggested that HCQ may reduce the risk of preeclampsia and hypertensive disorders of pregnancy, although results are conflicting. We studied HCQ use in SLE pregnancy in a large integrated health system to investigate whether HCQ reduces the risk of preeclampsia in a diverse patient cohort.

Methods: SLE was defined as ≥2 coded visits ≥7 days apart (ICD9: 710.0, ICD10: M32.1, M32.9). Individuals with full pregnancy histories derived from the electronic health records occurring in 2011-2020 were included. Data from all healthcare encounters, labs and pharmacy records were accessible. Qualifying SLE-coded encounters were required to occur before last menstrual period date (LMP) prior to pregnancy. We included pregnancies lasting until at least 20 gestational weeks. Pregnancies were considered HCQ-exposed if at least two fills covered the exposure window (3 months pre-LMP through 1st trimester), and unexposed if there were no fills overlapping with this time. Preeclampsia and eclampsia (PE/E) were defined in the pregnancy database and included all ICD-coded visits during pregnancy and labor and delivery documentation. All analyses were stratified by parity (primipara vs multipara). To account for possible confounding by indication, we estimated propensity scores (PS) as a function of age, BMI, race/ethnicity, neighborhood deprivation index, pre-pregnancy morbidity (diabetes, hypertension, nephritis) and medication ((corticosteroids, azathioprine), and antiphospholipid antibody (aPL) status. We estimated risk ratios (RR) and 95% confidence intervals using PS adjusted Poisson regression stratified by parity and by pre-pregnancy hypertension to investigate effect modification.

Results: 18% of SLE pregnancies had a PE/E diagnosis; among primiparous: 24% in HCQ exposed vs 21% in unexposed, and 14% and 15% among multiparous exposed and unexposed, respectively. Approximately 20% of the pregnancies had ≥1 aPL antibody, 16% had pre-existing hypertension, and 20% had a history of nephritis in the study cohort of 399 SLE pregnancies. (Table 1). In PS-adjusted models among primipara we found a null association (1.06, 95% CI: (0.57, 1.97)). Among multipara the RR was 0.76 (0.35, 1.64). Examining effect modification by pre-pregnancy hypertension, we found that among those with pre-pregnancy hypertension, ≥2 HCQ fills (vs no fills) was associated with a RR of 0.70 (95% CI (0.39, 1.25)), compared to RR=1.12 (0.57, 2.20) among those without pre-existing hypertension.

Conclusion: SLE patients using HCQ shortly before and early in pregnancy generally were comparable to those who did not use HCQ, although some small differences were observed. Confounding by disease activity was accounted for by including pre-pregnancy treatment with corticosteroids and azathioprine. We consistently observed RRs near or below the null of 1.0.

Demographics and clinical characteristics for singleton deliveries (live and stillbirth) in patients with systemic lupus erythematosus by HCQ fills (exposed defined as at least two fills overlapping three months pre-LMP through first trimester and unexposed is no fills)

Characteristics		Primipara pregnancies		Multipara pregnancies	
	All pregnancies	HCQ +	HCQ -	HCQ +	HCQ -
	n=399	n=85	n=78	n=94	n=142
Demographic characteristics					
Age at pregnancy in years, median (IQR)	32.7 (29.5, 35.5)	31.2 (28.8, 34.9)	31.0 (26.8, 33.4)	33.2 (30.0, 36.0)	33.9 (30.9, 36.0)
Pre-pregnancy BMI, median (IQR)	24.9 (21.8, 29.6)	24.7 (21.6, 29.2)	25.3 (22.1, 28.6)	24.6 (21.7, 31.1)	25.0 (22.0, 29.7)
Neighborhood deprivation index					
Quartile 1 (Least deprived)	118 (30%)	24 (28%)	22 (28%)	36 (38%)	36 (25%)
Quartile 2	105 (26%)	22 (26%)	23 (29%)	20 (21%)	40 (28%)
Quartile 3	107 (27%)	23 (27%)	19 (24%)	22 (23%)	43 (30%)
Quartile 4 (Most deprived)	69 (17%)	16 (19%)	14 (18%)	16 (17%)	23 (16%)
Insurance Status (Medicaid/Medicare)	57 (14%)	11 (13%)	14 (18%)	12 (13%)	20 (14%)
Morbidities and clinical characteristics					
Pre-existing hypertension	65 (16%)	11 (13%)	17 (22%)	19 (20%)	18 (13%)
Pre-existing diabetes	6 (1.5%)	-**	-**	-**	-**
History of lupus nephritis	80 (20%)	19 (22%)	15 (19%)	22 (23%)	24 (17%)
Positive aPL lab (strict)	74 (19%)	21 (25%)	16 (22%)	14 (15%)	23 (18%)
Pregnancy characteristics and outcomes					
Preterm delivery (<37 weeks)	83 (21%)	17 (20%)	13 (17%)	20 (21%)	33 (23%)
Preeclampsia/eclampsia overall	71 (18%)	20 (24%)	16 (21%)	13 (14%)	22 (15%)
Preeclampsia/eclampsia early onset	22 (5.5%)	5 (5.9%)	6 (7.7%)	5 (5.3%)	6 (4.2%)
Gestational diabetes	28 (7.0%)	4 (4.7%)	3 (3.8%)	7 (7.4%)	14 (9.9%)
Gestational hypertension (>= 20wks GA)	100 (25%)	28 (33%)	22 (28%)	18 (19%)	32 (23%)
Prior preeclampsia	14 (4%)	-	-	6 (19%)	8 (15%)
Medications					
Corticosteroids*	92 (23%)	33 (39%)	13 (17%)	30 (32%)	16 (11%)
Injection or intravenous corticosteroids*	7 (1.8%)	-**	-**	-**	-**
Azathioprine (During pregnancy)	39 (9.8%)	15 (18%)	7 (9.0%)	10 (11%)	7 (4.9%)
Heparin (During pregnancy)	28 (7.0%)	7 (8.2%)	6 (7.7%)	7 (7.4%)	8 (5.6%)
Labetalol (During pregnancy)	47 (12%)	13 (15%)	12 (15%)	11 (12%)	11 (7.7%)

* 6 months pre-pregnancy
** specific numbers removed to reduce identifiability

Demographics and clinical characteristics for singleton deliveries (live and stillbirth) in patients with systemic lupus erythematosus by HCQ fills (exposed defined as at least two fills overlapping three months pre-LMP through first trimester and unexposed is no fills)

Disclosure: J. Simard: None; **E. Liu**: None; **A. Rector**: None; **M. Cantu**: None; **D. Kuo**: None; **E. Chakravarty**: None; **M. Druzin**: None; **G. Shaw**: None; **M. Weisman**: None; **M. Hedderson**: None.

Abstract Number: 0470

Educational Intervention to Increase Contraception Screening and Documentation for Reproductive-Aged Women Seen in an Academic Rheumatology Clinic

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Reproductive Issues in Rheumatic Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Only one-third of reproductive-aged women with rheumatic disease (RD) are prescribed effective contraception, even if prescribed teratogenic medications (Talabi et al. *Arthritis Care Res*. 2019). Contraception counseling and documentation are important steps to improve effective contraception use in at-risk patients; however, in a nationwide study, less than 10% of women with SLE or RA had contraception documented in a structured electronic health record (EHR) field (Clowse et al. *Arthritis Care Res*. 2023). The aim of this quality improvement (QI) initiative was to increase the rate

of provider screening and documentation of contraception use for female patients aged 18-45 seen in an academic rheumatology clinic from our baseline of 11% to 50% by 24 weeks.

Methods: We administered a survey to clinic staff including demographic information, professional credentials and years of experience, and barriers to contraception documentation and desired interventions. We conducted 6 Plan-Do-Study-Act (PDSA) cycles including educational presentations and motivating reminders for clinic staff, devised to address the "vital few" barriers (representing 80% of responses) identified.

The primary outcome measure was the percentage of the study population with contraception use documented in the structured EHR field. The primary balancing measure was the percentage of the study population with smoking status documented in the structured EHR field. The primary process measure was percentage of contraception documenters who

Table. Demographic and Professional Characteristics of Baseline Survey of Rheumatology Clinic Staff

Characteristic	*N (%)*
Sex	
• Female	11 (65)
• Male	6 (35)
Race	
• Asian or Indian subcontinent	5 (29)
• Black	1 (6)
• White	8 (47)
• Other	2 (12)
• Prefer not to answer	1 (6)
Ethnicity	
• Hispanic/Latino	2 (12)
• Not Hispanic/Latino	14 (82)
• Missing	1 (6)
Role	
• MD - Fellow	8 (47)
• PCA	3 (18)
• RN	6 (35)
Years in Role	
• <5 years	12 (71)
• 5-10 years	2 (12)
• 11-20 years	3 (18)
Ever previously entered data in this field?	8 (47)

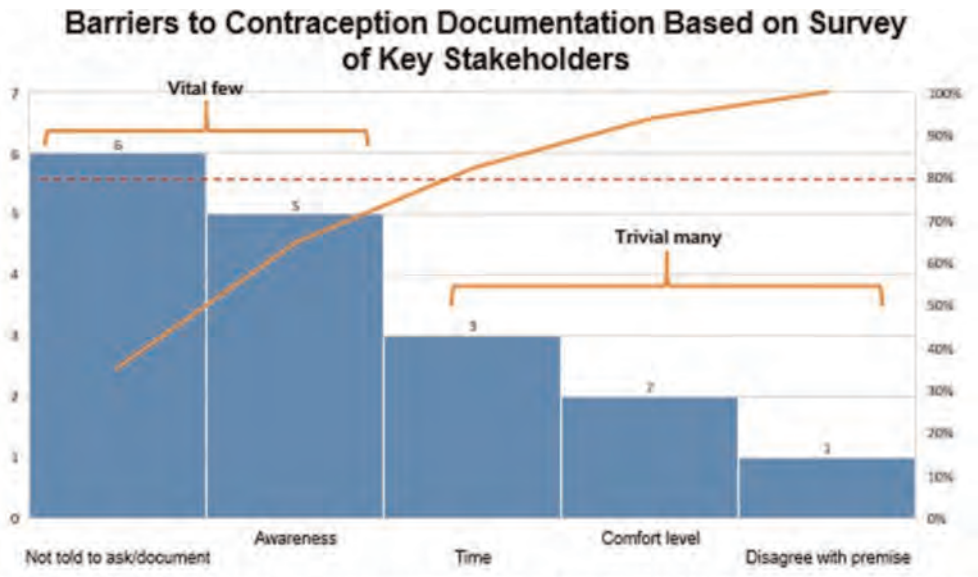

Figure 1. Pareto chart demonstrating responses to survey administered to rheumatology clinic staff at study baseline regarding barriers to contraception screening and documentation.

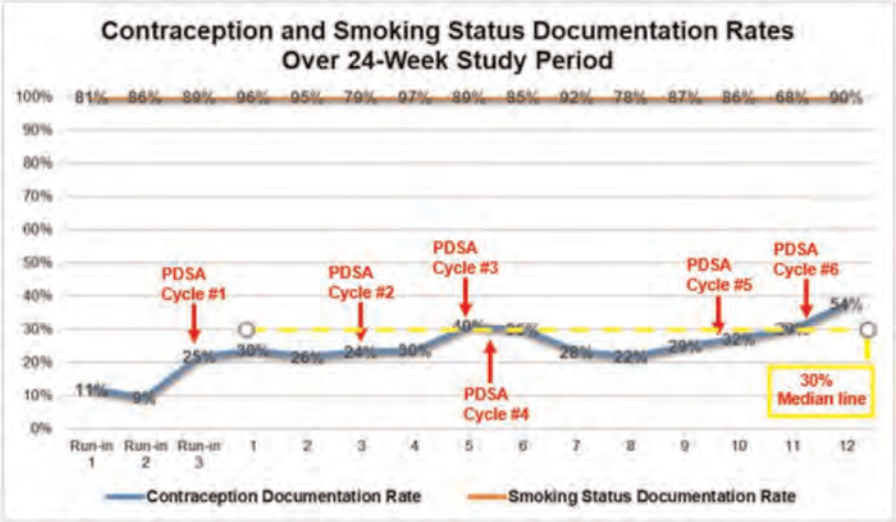

Figure 2. Run chart demonstrating primary outcome measure (i.e. contraception documentation rate) and balancing measure (i.e. smoking status documentation rate) every 2 weeks over 24-week study period.

were non-MD clinical staff, as the intervention focused on this group. We tracked primary outcome, process, and balancing measures at 2-week intervals over 24 weeks; we tracked primary outcome and balancing measures on a run chart.

Results: Baseline survey respondents (n=17) were 65% female; 47% White and 29% Asian/Indian; 82% Not Hispanic/Latino; 53% Registered Nurses/Personal Care Assistants and 47% Rheumatology Fellows [**Table**]. The "vital few" barriers to contraception documentation were not having been told to document this information and lack of awareness of this EHR field [**Fig. 1**]. The intervention most frequently suggested by respondents (47%) was education.

Interventions included an introductory educational session with documentation instruction and scripts to guide screening (PDSA #1), email reminders from nursing leadership (PDSA #2 and #5), and interim educational sessions (PDSA #3, #4, #6). Over 24 weeks, the rate of contraception documentation increased from 11% to 54% (median 30%) and the median smoking status documentation rate was 88% (68%-97% range) [**Fig. 2**]; the median rate of non-MD clinical staff documenters was 92% (70%-100% range).

Conclusion: A multi-cycle educational intervention designed based on key stakeholder feedback led to an increase in the contraception documentation rate from 11% to 54% for reproductive-aged women seen in our rheumatology clinic over 24 weeks. Future phases of this QI initiative will focus on encouraging rheumatologists to provide contraceptive counseling and referrals to women's health providers for patients who are prescribed teratogenic medications.

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Abstract Number: 0471

Knowledge and Misconceptions About Contraception Among Individuals with Inflammatory Arthritis and Lupus-like Diseases

Caroline Siegel[1], Medha Barbhaiya[2], Lucy Masto[1], Amaya Smole[1], Bessie Stamm[1], Jonah Levine[1], Sarah Lieber[2], Lisa Mandl[2], Michael Lockshin[2] and Lisa Sammaritano[2], [1]Hospital for Special Surgery, New York, NY, [2]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY

SESSION INFORMATION
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Background/Purpose: Rheumatologists do not consistently provide contraceptive counseling for patients with systemic rheumatic disease (SRD). As contraception considerations may differ based on SRD, we compared contraception knowledge between individuals with reproductive capacity who have inflammatory arthritis (IA) or lupus-like diseases.

Methods: Women aged 18-65 years seen by a rheumatologist at our academic center ≥2 times from 2020-2022 were enrolled in the Rheumatology Women's Reproductive Health and Wellness Cohort. This analysis included participants who completed a contraception knowledge assessment and self-reported IA or lupus-like disease. We excluded participants >50 years of age and those who self-reported menopause/premature ovarian failure, hysterectomy and/or oophorectomy, and/or infertility. We used descriptive statistics to compare the frequency of correct responses between participants with IA and lupus-like diseases.

Results: Of 812 cohort participants, 658 (81.0%) responded to contraception questions; 249 with reproductive capacity (mean age 36.3 ± 7.5 years; 99.2% self-reporting woman as gender identity) who self-reported IA (n=147) or lupus-like disease (n=102) were included in this analysis. Patients with IA vs. lupus-like diseases were more frequently White race (82.5% vs. 69.7%, p=0.04) and less frequently Hispanic/Latinx ethnicity (7.5% vs. 15.7%, p=0.04). 93.2% reported Bachelor's degree or higher education level and 61.1% were married/partnered, with no differences between groups.

There were no differences in the frequency of correct responses about contraception effectiveness between patients with IA and lupus-like disease. Many participants overestimated the effectiveness of methods with low (1-10%) 1-year failure rates: 50.2% for depot medroxyprogesterone acetate [DMPA], 33.7% for estrogen-containing birth control pill [BCP], patch, or vaginal ring, and 28.1% for the progestin-only pill. In terms of methods with high (11-30%) 1-year failure rates, 66.7% overestimated effectiveness of barrier methods [**Table 1**].

Compared to individuals with IA, those with lupus-like disease more frequently responded "true" (i.e., correct response) that BCPs are contraindicated for women with antiphospholipid antibodies (aPL) (54.9% vs. 30.6%, p< 0.001). Participants with lupus-like disease vs. those with IA less frequently responded "false" (i.e., correct response) that BCPs (81.4% vs. 93.2%, p=0.004) and subdermal implants (82.4% vs. 91.2%, p=0.04) are contraindicated for women with any rheumatic disease [**Table 2**].

Conclusion: In a sample of highly educated individuals with reproductive capacity and IA or lupus-like disease, approximately half responded incorrectly about effectiveness of moderately/highly effective contraceptive methods. Compared to those with IA, more patients with lupus-like disease endorsed SRD-specific contraindications to BCPs: half correctly noted BCPs should not be taken by patients with aPL but one-fifth incorrectly noted BCPs should not be taken by anyone with SRD. Our results highlight important misconceptions about contraception that can inform patient education and counseling efforts.

Table 1. Knowledge about Contraception Effectiveness of Women with IA and Lupus-like Disease

	Overall (N=249)	IA (N=147)[1]	Lupus-like (N=102)[2]	p-value
Correct Responses[3]				
Highly effective methods [<1% 1-year failure rate]				
• **IUD**	154 (61.9)	94 (64.0)	60 (58.8)	0.41
• **Subdermal implant**	135 (54.2)	84 (57.1)	51 (50.0)	0.27
Moderately effective methods[3] [1-10% 1-year failure rate]				
• **Depot medroxyprogesterone acetate (DMPA) shot**	110 (44.2)	64 (43.5)	46 (45.1)	0.81
➢ Overestimated	125 (50.2)	76 (51.7)	49 (48.0)	
➢ Underestimated	14 (5.6)	7 (4.8)	7 (6.9)	
• **Progestin-only pill ("mini pill")**	151 (60.6)	91 (61.9)	60 (58.8)	0.63
➢ Overestimated	70 (28.1)	41 (27.9)	29 (28.4)	
➢ Underestimated	28 (11.2)	15 (10.2)	13 (12.8)	
• **Combined birth control pill, patch, vaginal ring**	138 (55.4)	80 (54.4)	58 (56.9)	0.70
➢ Overestimated	84 (33.7)	50 (34.0)	34 (33.3)	
➢ Underestimated	27 (10.8)	17 (11.6)	10 (9.8)	
Less effective methods[4] [11-30% 1-year failure rate]				
• **Barrier methods**	67 (26.9)	39 (26.5)	28 (27.5)	0.87
➢ Overestimated	166 (66.7)	98 (66.7)	68 (66.7)	
➢ Underestimated	16 (6.4)	10 (6.8)	6 (5.9)	
• **Fertility awareness/ withdrawal**	100 (40.2)	55 (37.4)	45 (44.1)	0.29
➢ Overestimated	54 (21.7)	34 (23.1)	20 (19.6)	
➢ Underestimated	95 (38.2)	58 (39.5)	37 (82.2)	
No birth control[5] [>30% 1-year failure rate]	193 (77.5)	113 (76.9)	80 (78.4)	0.77

1. RA, PsA, SpA, JIA, adult-onset Still's disease, or IA not otherwise specified
2. SLE, APS, SS, MCTD, or UCTD.
3. N (%) of participants who responded correctly to the following question for each contraceptive method: ***"To the best of your knowledge, how likely is it for a woman to become pregnant over the course of one year while using each of the following methods of birth control?"***

Table 2. Knowledge about Contraception Facts and Misconceptions of Women with IA and Lupus-like Disease

	Overall (N=249)	IA (N=147)[1]	Lupus-like (N=102)[2]	p-value
Correct Responses to TRUE Statements[3]				
Condoms can protect against sexually transmitted infections.	228 (91.6)	132 (89.8)	96 (94.1)	0.23
The progestin-only "mini pill" must be taken at the same time every day to work.	214 (85.9)	127 (86.4)	87 (85.3)	0.81
Birth control pills containing estrogen should never be taken by women with antiphospholipid antibodies.	101 (40.6)	45 (30.6)	56 (54.9)	*<0.001*
Correct Responses to FALSE Statements[3]				
IUDs may only be used by women who have delivered a child.	244 (98.0)	146 (99.3)	98 (96.1)	0.16
IUDs may only be used by women who have one partner.	242 (97.2)	143 (97.3)	99 (97.1)	1.0
IUDs cannot be used by women taking immunosuppressive medications.	228 (91.6)	138 (93.9)	90 (88.2)	0.12
Birth control pills containing estrogen should never be taken by women with rheumatology conditions.	220 (88.4)	137 (93.2)	83 (81.4)	*0.004*
Implants placed under the skin for contraception may not be used by women with rheumatology conditions.	218 (87.6)	134 (91.2)	84 (82.4)	*0.04*
Copper-containing IUDs reduced painful or heavy menstrual cycles.	131 (52.6)	77 (52.4)	54 (52.9)	0.93

1. RA, PsA, SpA, JIA, adult-onset Still's disease, or IA not otherwise specified
2. SLE, APS, SS, MCTD, or UCTD.
3. N (%) of participants who responded correctly to the above series of true/false statements regarding indications and contraindications to various contraceptive methods, with the following prompt: ***"To the best of your knowledge, please select 'true' or 'false' for each statement about contraception."***

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Abstract Number: 0472

Contraception Choices in Individuals with Inflammatory Arthritis and Lupus-like Disease Differ Based on Diagnosis and Teratogen Use

Caroline Siegel[1], Medha Barbhaiya[2], Lucy Masto[1], Amaya Smole[1], Bessie Stamm[1], Jonah Levine[1], Sarah Lieber[2], Lisa Mandl[2], Michael Lockshin[2] and Lisa Sammaritano[2], [1]Hospital for Special Surgery, New York, NY, [2]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY

SESSION INFORMATION
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Background/Purpose: Individuals with systemic rheumatic disease (SRD) underutilize effective contraception even when prescribed teratogenic medications. As disease-related factors may impact contraception choice, we evaluated the association between contraception use and both SRD diagnosis and teratogenic medication use in patients with inflammatory arthritis (IA) or lupus-like diseases.

Methods: Women aged 18-65 years seen by a rheumatologist at our academic center ≥2 times from 2020-2022 were enrolled in a Reproductive Health and Wellness Cohort. This analysis included participants with self-reported IA or lupus-like disease. We excluded participants >50 years of age and those who self-reported menopause/premature ovarian failure, hysterectomy and/or oophorectomy, and/or infertility. We used descriptive statistics to evaluate demographics, medications, and contraception use, stratified by disease and teratogenic medication use.

Results: Of 812 cohort participants, 658 (81.0%) responded to contraception questions; 249 with reproductive capacity (mean age 36.3 ± 7.5 years, 99.2% self-reporting woman as gender identity) who self-reported IA (n=147) or lupus-like disease (n=102) were included in this analysis. Patients with IA vs. lupus-like disease were more frequently White (82.5% vs. 69.7%, p=0.04) and less frequently Hispanic/Latinx (7.5% vs. 15.7%, p=0.04). 94.8% had private insurance and 61.5% were married/partnered, with no differences between groups.

Compared to individuals with IA, those with lupus-like diseases less frequently used the birth control pill, patch, or vaginal ring (14.7% vs. 31.5%, p=0.003) and more frequently used barrier methods, fertility awareness or withdrawal (30.5% vs. 17.5%, p=0.02); groups did not differ in terms of permanent contraception, intrauterine device, or subdermal implant use [**Table 1**].

Compared to participants not taking teratogenic medication (n=197), those who were (n=52) more frequently reported that their rheumatologist had ever discussed contraception (44.2% vs. 21.8%, p=0.001) and more frequently reported permanent contraception use (8.0% vs. 1.1%, p=0.02). Of those taking teratogenic medication, 44.0% reported use of barrier methods, fertility awareness/withdrawal, or no contraception; frequency of any reversible method or no contraception use did not differ based on teratogen use [**Table 2**].

Conclusion: Among individuals with IA or lupus-like diseases and reproductive capacity seen in an academic rheumatology center, less than half used moderately/highly effective contraception. Although patients taking vs. not taking teratogenic medication were more likely to have discussed contraception with their rheumatologist, they were no more likely to use effective contraception; nearly half used less effective or no contraception. Compared to patients with IA, those with lupus-like diseases less commonly used estrogen-containing methods and more commonly used less effective contracep-

Table 1. Contraception and Teratogen Use in Women with IA and Lupus-like Disease

	IA (N=147)[1]	Lupus-like (N=102)[2]	p-value
Teratogen Use (current)[3]	33 (22.6)	19 (18.6)	0.47
• Leflunomide	2 (1.4)	0	
• Methotrexate	31 (21.1)	6 (5.9)	
• Mycophenolate	0	10 (9.8)	
• Warfarin	0	3 (2.9)	
Contraceptive Method[4]	**N=143**	**N=95**	
Permanent Contraception	13 (9.1)	5 (5.3)	0.33
• Bilateral tubal ligation	3 (2.1)	0	
• Partner vasectomy	10 (7.0)	5 (5.3)	
Highly Effective Methods[5]	27 (18.9)	21 (22.1)	0.54
• Intrauterine device	25 (17.5)	20 (21.1)	
• Subdermal implant	2 (1.4)	1 (1.1)	
Moderately Effective Methods[5]	45 (31.5)	14 (14.7)	*0.003*
• Birth control pill	41 (28.7)	12 (12.6)	
• Birth control patch	1 (0.7)	0	
• Vaginal ring	3 (2.1)	2 (2.1)	
Less Effective Methods[5]	25 (17.5)	29 (30.5)	*0.02*
• Barrier methods	18 (12.6)	20 (21.1)	
• Fertility awareness or withdrawal	7 (4.9)	9 (9.5)	
No Contraception[5]	33 (23.1)	26 (27.4)	0.45

1. RA, PsA, SpA, JIA, adult-onset Still's disease, or IA not otherwise specified
2. Lupus-like diseases included SLE, APS, SS, MCTD, or UCTD
3. No one reported cyclophosphamide or thalidomide/lenalidomide use.
4. When ≥1 contraceptive method was reported, the method with highest efficacy was counted. No one reported birth control patch or medroxyprogesterone acetate (Depo-Provera) use.
5. **Highly effective**: <1% of women per year will become pregnant with typical use; **moderately effective**: 5-10% of women per year will become pregnant with typical use; **less effective**: 10-30% of women per year will become pregnant with typical use; **no contraception**: >30% of women per year will become pregnant.

Table 2. Contraception Use in Women with IA and Lupus-like Disease Stratified by Teratogen Use

	Teratogen Use (N=52)	No Teratogen Use (N=197)	p-value
RD Diagnosis			0.47
• IA[1]	33 (63.5)	114 (57.9)	
• Lupus-like disease[2]	19 (36.5)	83 (42.1)	
Rheumatologist Discussed Contraception (ever)			*<0.001*
• Yes	23 (44.2)	43 (21.8)	
• No/Don't Recall	29 (55.8)	154 (78.2)	
Contraceptive Method[3]	**N=50**	**N=188**	
Permanent Contraception	4 (8.0)	2 (1.1)	*0.02*
• Bilateral tubal ligation	1 (2.0)	2 (1.1)	
• Partner vasectomy	3 (6.0)	0	
Highly Effective Methods[4]	10 (20.0)	38 (20.2)	0.97
• Intrauterine device	8 (16.9)	37 (19.7)	
• Subdermal implant	2 (4.0)	1 (0.5)	
Moderately Effective Methods[4]	14 (28.0)	45 (23.9)	0.55
• Birth control pill	12 (24.0)	41 (21.8)	
• Birth control patch	0	1 (0.5)	
• Vaginal ring	2 (4.0)	3 (1.6)	
Less Effective Methods[4]	14 (28.0)	40 (21.3)	0.31
• Barrier methods	11 (22.0)	27 (14.4)	
• Fertility awareness or withdrawal	3 (6.0)	13 (6.9)	
No Contraception[4]	8 (16.0)	51 (27.1)	0.11

1. RA, PsA, SpA, JIA, adult-onset Still's disease, or IA not otherwise specified
2. SLE, APS, SS, MCTD, or UCTD.
3. When ≥1 contraceptive method was reported, the method with highest efficacy was counted. No one reported medroxyprogesterone acetate (Depo-Provera) use.
4. **Highly effective**: <1% of women per year will become pregnant with typical use; **moderately effective**: 5-10% of women per year will become pregnant with typical use; **less effective**: 10-30% of women per year will become pregnant with typical use; **no contraception**: >30% of women per year will become pregnant.

tion. Our findings can inform interventions to optimize contraception utilization in patients with SRD by targeting patients prescribed teratogenic medications and those with lupus-like diseases without contraindications to estrogen-based methods.

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Abstract Number: 0473

The Number of Rheumatoid Arthritis Patients Who Give up Pregnancy Due to the Disease Is Decreasing

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SESSION INFORMATION
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Background/Purpose: Biologics have been shown not to be a disruption in pregnancy, and the reproductive health care environment surrounding rheumatoid arthritis patients has improved significantly. In this study, we attempted to assess changes in attitudes toward pregnancy among female rheumatoid arthritis patients of childbearing age using a questionnaire.

Methods: A cross-sectional study using the NinJa database conducted at 49 sites in 2020, a database of RA patients in Japan collected from April 1, 2020 to March 31, 2021. We selected women under 50 years of age who answered a questionnaire on changes in the desired number of children due to the presence of rheumatoid arthritis. Of these, we excluded those who answered that they already had the desired number of children or that they did not want to have children. We compared the percentage of patients who reported that the onset of rheumatoid arthritis had reduced their desire for children in the three groups based on the time of onset of the disease ("before 2000," "2001-2011," and " after 2012"). We also evaluated the stratification by age at onset (24 years and younger, 25 to 34 years, and 35 years and older), the reasons why respondents answered that they wanted fewer children.

Results: Of 15553 patients, 468 were selected, of which 188 were excluded, leaving 280 eligible cases. The number of patients who reported that the onset of rheumatoid arthritis reduced the desired number of children was 57% (20/35) for onset before 2000, 47% (63/133) for onset between 2001 and 2011, and 35% (39/112) for onset after 2012. Within each group, when further divided into three groups according to age at onset, especially in the 25-34 age group, the percentage of patients who reported a reduction in the desired number of children decreased with the time of onset.

We analyzed the reasons for the 122 patients who indicated that they wanted to have fewer children, and found that the most common reason was "I am worried about my ability to take care of my children" (40%: 49 patients). The next most common reason was "I am worried about the effects of the medication on my child" (25%: 30 patients).

Conclusion: In this study, the desired pregnancy outcome was particularly improved in the 25-34 age group, who are likely to be thinking about pregnancy and childbirth in the near future, possibly due to improvements in the treatment environment, such as an increase in the number of drugs available during pregnancy and the accumulation of information on pregnancy complicated by rheumatoid arthritis. On the other hand, the reasons behind the decrease in pregnancy desire may include limitations in physical function and financial burden, which will be an issue to be addressed in the future.

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Abstract Number: 0474

Acute Cardiovascular Events During Pregnancy and Delivery in Patients with Autoimmune Rheumatic Diseases (ARDs): An Analysis of National Inpatient Sample

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Background/Purpose: Systemic lupus erythematosus (SLE), rheumatoid arthritis (RA) & vasculitis are autoimmune rheumatic diseases (ARDs) with systemic involvement. Management of women with ARDs during pregnancy presents unique clinical challenges. Previous studies have indicated that individuals with ARDs are at an increased risk of experiencing significant cardiovascular (CV) events during delivery. Long-term CV risks associated with ARDs are well-documented but less is known about the acute CV complications during delivery. This study aims to investigate the outcomes of CV complications during delivery hospitalizations for women with ARDs.

Methods: NIS (2016-2019) was used to identify delivery hospitalizations among birthing individuals with diagnoses of SLE, RA and systemic vasculitides (medium & small vessel vasculitis) using International Classification of Diseases (ICD-10) codes. The primary outcomes were CV events such as preeclampsia, peripartum cardiomyopathy (PPCM), heart failure (HF), stroke, cardiac arrhythmias and venous thromboembolism (VTE). We also assessed mortality, length of stay and total cost of hospitalization. Statistical analysis was performed in STATA v.17.A multivariable logistic regression model was used to understand the association between ARDs and acute peripartum cardiovascular complications. Statistical significance was defined by the two-sided t-test with a p value < 0.05.

Results: We identified 3,470,086 weighted delivery hospitalizations [mean age 29.14 years, 95% Confidence interval (CI), 29.05-29.24)]. Among them, 5900(0.17%) had SLE, 4895(0.14%) had RA, and 325(0.009%) had vasculitis. After adjusting for age, race, insurance, income and co-morbidities; SLE remained an independent risk factor for peripartum cardiovascular complications such as preeclampsia (OR 1.5; 95% CI, 1.1-2.1), arrhythmia (OR 3.17; 95% CI, 1.73-5.79), and venous thrombosis (OR 8.4; 95% CI, 2.9-22.1). Vasculitides was identified as an independent risk factor for preeclampsia

(OR 4.7; 95%CI, 2-11.3), stroke (OR 513.3; 95% CI, 114-2284), heart failure (OR 24.17; 95% CI, 4.68-124.6) and peripartum cardiomyopathy (OR 66.7; 95% CI, 8.7-509.4. However, RA was found to be a risk factor for pre-eclampisa only(OR 1.5; 95% CI, 1.05-2.1).

The study also revealed significantly higher in-hospital mortality among pregnant women with SLE (0.17% vs. 0.0001%, p< 0.001) and vasculitis (1.54% vs. 0.0001%, p< 0.001) compared to women without ARDs. Individuals with SLE had a longer mean length of hospital stay compared to those without SLE (3.7 days vs. 2.5 days, p< 0.001), as did individuals with vasculitis compared to those without vasculitis (4.7 days vs. 2.5 days, p< 0.001). The mean cost of hospitalization was also

Table 1: Characteristics of hospitalized patients for delivery with and without rheumatic disease

	Rheumatoid Arthritis			SLE			Medium & small vessel vaculitis		
Variables	With RA(n=4895)	Without RA(n=3465191)	p-value	With SLE(n=5900)	Without SLE(n=3464186)	p-value	With vasculitis(n=325)	Without vasculitis(n=3469761)	p-value
Age, mean (years)	31.7	29.1		30.7	29.1		29.2	29.1	
Race n(%)									
White	2890(59.04)	1750614 (50.52)	**<0.001**	2815(47.71)	1754264 (50.64)	0.06	180(50.53)	1921554 (55.38)	0.43
Black	490(10.01)	513888 (14.83)	**<0.001**	1240(26.60)	513046 (14.81)	**<0.001**	50(15.38)	514219 (14.82)	0.89
Hispanic	970 (19.82)	714176 (20.61)	0.5	1100(18.64)	713969 (20.61)	0.13	50(15.38)	715118 (20.61)	0.3
Asian	195(3.98)	200635 (5.79)	**0.01**	325(5.51)	200576 (5.79)	0.71	10(3.08)	200899 (5.79)	0.35
Native american	60(1.23)	24949 (0.72)	0.06	40(0.86)	24942 (0.72)	0.8	5(1.54)	24982 (0.72)	0.4
Other	155(3.17)	147617 (4.26)		225(3.81)	147574 (4.26)	0.4	15(4.62)	147812 (4.26)	0.88
Primary Payer n(%)									
Medicare	165(3.37)	21138 (0.61)	**<0.001**	225(3.81)	21132(0.61)	**<0.001**	10(3.08)	21166 (0.61)	**0.01**
Medicaid	1535 (31.36)	1446717 (41.75)	**<0.001**	2150(36.44)	1446298 (41.75)	**0.002**	110(33.85)	1447931 (41.73)	0.19
Private insurance	3010(61.49)	1814027 (52.35)	**<0.001**	3200(54.24)	1813848 (52.36)	0.19	175(53.85)	1816767 (52.36)	0.81
Self-pay	65(1.33)	81779 (2.36)	**0.04**	75(1.27)	81755 (2.36)	**0.01**	10(3.08)	81886 (2.36)	0.69
Median household income (percentile), n(%)									
0-2	1105(22.57)	948769 (27.38)	**0.0008**	1665(28.22)	948494 (27.38)	0.5	90(27.69)	950021 (27.38)	0.95
25-50	1160(23.7)	903722 (26.08)	0.09	24.92(1470)	903460 (26.08)	0.3	75(23.08)	904914 (26.08)	0.5
51-75	1325(27.07)	826448 (23.85)	**0.02**	1505(25.51)	826208 (23.85)	0.1	75(23.08)	827885 (23.86)	0.88
76-100	1295(26.46)	760609 (21.95)	**0.001**	1203(20.85)	760389 (21.95)	0.4	80(24.6)	761613 (21.95)	0.6
Hospital size n(%)									
Small	885(18.08)	706899 (20.4)	0.09	950(16.1)	706694 (20.4)	**0.0008**	10(3.08)	695340 (20.04)	**0.0005**
Medium	1305(26.66)	1006985 (29.06)	0.12	1405(23.81)	1006692 (29.05)	**0.0005**	85(26.15)	1008313 (29.06)	0.5
Large	2705(55.26)	1751654 (50.55)	**0.007**	3545(60.08)	1751146 (50.55)	**<0.001**	230(70.77)	1753964 (50.55)	**0.007**
Hospital region n(%)									
Northeast	780(15.93)	551658 (15.92)	0.99	1040(17.63)	551498 (15.92)	0.18	60(18.46)	552386 (15.92)	0.5
Midwest	1020(20.84)	722492 (20.85)	0.99	1220(20.68)	722283 (20.85)	0.9	105(32.32)	723445 (20.85)	**0.01**
South	1785(36.47)	1389195 (40.09)	**0.03**	2265(38.39)	1388792 (40.09)	0.33	95(29.23)	1391027 (40.08)	0.06
West	1310(26.76)	802192 (23.15)	**0.01**	1375(23.3)	801959 (23.15)	0.91	65(25)	803250 (23.15)	0.5

Table 2: Complications and hospital resourse use in hospitalized patients for delivery with and without rheumatic disease

	Rheumatoid Arthritis			SLE			Medium and small vesel vaculitis		
Variables	With RA(n=4895)	Without RA(n=3465191)	p-value	With SLE(n=5900)	Without SLE(n=3464186)	p-value	With vasculitis(n=325)	Without vasculitis(n=3469761)	p-value
Complications									
AKI	10 (0.2)	5891 (0.17)	0.8	136 (2.3)	5889 (0.17)	**<0.001**	50 (15.38)	5899 (0.17)	**<0.001**
Pre-eclampsia/Eclampsia	170 (3.47)	75888 (2.19)	**0.007**	225 (3.81)	75866 (2.19)	**0.002**	35 (10.77)	75988 (2.19)	**<0.001**
Stroke	0	0	**0.001**	5 (0.08)	0	**0.004**	20 (6.15)	3 (0.0001)	**<0.001**
Acute heart failure	0	0	0.4	20 (0.34)	0	**0.006**	10 (3.08)	3123 (0.09)	**<0.001**
GHTN	195 (3.98)	107767 (3.11)	0.12	280 (4.75)	107736 (3.11)	**0.0008**	15 (4.62)	107910 (3.11)	0.48
GDM	365 (7.46)	178111 (5.14)	**0.0008**	320 (5.42)	187412 (5.41)	0.67	20 (6.15)	178346 (5.14)	0.71
Arrythmia	20 (0.41)	10049 (0.29)	0.4	70 (1.19)	10046 (0.29)	**<0.001**	10 (3.08)	72518 (0.29)	**<0.001**
Resource use, mean									
Length of stay (days)	2.8(2.7-3.07)	2.5(2.5-2.54)	**<0.001**	3.7(3.4-4.03)	2.5(2.5-2.54)	<0.001	4.7(3.7-5.8)	2.5(2.5-2.54)	**<0.001**
Cost of hospitalization, $	26182 (24175-28188)	23503 (22887-24119)	0.005	34880(30613-39130)	23488(22873-24103)	**<0.001**	74839(50155-99523)	23502(22886-24188)	**<0.001**

higher for pregnant individuals with RA ($26,182 vs. $23,503, p=0.005), SLE ($34,880 vs. $23,488, p< 0.001), and other vasculitis ($74,839 vs. $23,502, p< 0.001) compared to individuals without these diseases.

Conclusion: This study found that SLE & vasculitis were associated with increased risk of cardiovascular complications during pregnancy and delivery along with longer duration of hospital stay and higher cost of hospitalization.

Disclosure: K. Shrestha: None; **P. Subedi**: None; **M. Ghimire**: None; **S. Poudel**: None; **K. Ghimire**: None; **S. Parvatheneni**: None; **M. Dandamudi**: None; **L. Pedraza**: None; **L. Brito**: None; **L. Gandrabur**: None.

Abstract Number: 0475

Prevalence of Endometriosis and Polycystic Ovarian Syndrome in Patients with Rheumatic Diseases in the United States

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Reproductive Issues in Rheumatic Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Endometriosis (ENDO) and Polycystic Ovarian Syndrome (PCOS) are underdiagnosed, often debilitating conditions with unknown etiologies that, like rheumatic diseases, affect reproductive-aged women. Recent studies suggest an association between ENDO across autoimmune diseases; PCOS has not been examined. The purpose of our study is to determine the prevalence and association of these conditions in patients with rheumatologic diseases in a large ambulatory population.

Table 1. Polycystic Ovarian Syndrome and Endometriosis Prevalence by Rheumatic Disease and Age

Rheumatic Disease	PCOS All ages	PCOS 10-49yo	ENDO All ages	ENDO 10-49yo
JIA	10.0%	11.1%	6.3%	2.3%
PsA	5.1%	6.1%	3.5%	3.3%
RA	2.5%	6.8%	3.5%	6.5%
AS	1.3%	28.1%	4.0%	7.9%
SLE	3.7%	6.2%	5.6%	6.2%
CTD	10.3%	27.4%	5.8%	8.1%
Vasculitis	3.3%	5.4%	2.2%	2.7%
IM	3.8%	8.3%	2.1%	2.9%
SD	7.6%	16.9%	5.1%	10.7%
SSc	2.8%	7.1%	2.7%	5.2%
All Rheum Dx of Interest	3.0%	8.6%	3.9%	5.8%
Explorys® Population	1.4%	2.1%	1.0%	1.0%

Juvenile idiopathic arthritis (JIA) Psoriatic arthritis (PsA) Axial spondyloarthritis (AS) Rheumatoid arthritis (RA) Systemic lupus erythematosus (SLE) Mixed or undifferentiated connective tissue disease (CTD) Inflammatory Myositis (IM) Sjogren's disease (SD) Systemic Sclerosis (SSc)

Table 2. Likelihood of Polycystic Ovarian Syndrome or Endometriosis Diagnosis with a Rheumatic Disease

Rheumatic Disease	OR PCOS All Ages (95% CI)	OR PCOS 10-49yo (95% CI)	OR ENDO All Ages (95% CI)	OR ENDO 10-49yo (95% CI)
JIA	7.18 (6.68-7.69)	5.40 (4.99-5.84)	6.53 (5.98-7.12)	2.30 (1.93-2.70)
PsA	3.66 (3.51-3.81)	2.99 (2.82-3.17)	3.71 (3.53-3.89)	3.37 (3.12-3.65)
RA	1.79 (1.76-1.83)	3.33 (3.23-3.43)	3.72 (3.66-3.78)	6.73 (6.53-6.94)
AS	0.96 (0.91 - 1.01)	13.80 (13.34-14.27)	4.14 (4.08- 4.28)	8.12 (7.65-8.60)
SLE	2.70 (2.60-2.776)	3.06 (2.96-3.16)	6.01 (5.89-6.13)	6.42 (6.22-6.63)
CTD	7.40 (6.28-8.71)	13.35 (11.23-15.78)	6.06 (4.86-7.45)	8.24 (6.10-10.87)
Vasculitis	2.36 (2.19-2.54)	2.65 (2.37-2.95)	2.33 (2.13-2.55)	2.77 (2.37-3.22)
IM	2.71 (2.56-2.88)	4.06 (3.71-4.44)	2.22 (2.05-2.39)	3.01 (2.58-3.47)
SD	5.45 (5.12-5.79)	8.22 (7.36-9.16)	5.37 (4.98-5.77)	10.88 (8.50-12.41)
SSc	1.99 (1.85-2.13)	3.48 (3.09-3.90)	2.82 (2.62-3.02)	5.34 (4.65-6.10)
All Rheum disease of Interest	2.21 (2.18-2.24)	4.31 (4.24-4.38)	4.38 (4.33-4.43)	13.34 (13.15-13.54)

Juvenile idiopathic arthritis (JIA) Psoriatic arthritis (PsA) Axial spondyloarthritis (AS) Rheumatoid arthritis (RA) Systemic lupus erythematosus (SLE) Mixed or undifferentiated connective tissue disease (CTD) Inflammatory Myositis (IM) Sjogren's disease (SD) Systemic Sclerosis (SSc)

Methods: Utilizing the secure cloud-based platform, IBM® Explorys®, we conducted a retrospective cross-sectional study of females, ages 10-49, from the United States with PCOS or ENDO and rheumatic diseases using pooled deidentified data from multiple US health-care systems using Epic® electronic medical record platform, collected from 1999 to 2022. Rheumatic diseases examined: Juvenile idiopathic arthritis (JIA) Psoriatic arthritis (PsA) Axial spondyloarthritis (AS) Rheumatoid arthritis (RA) Systemic lupus erythematosus (SLE) Mixed or undifferentiated connective tissue disease (CTD) Inflammatory Myositis (IM) Sjogren's disease (SD) Systemic Sclerosis (SSc).Females in the IBM® Explorys® platform with no rheumatic diseases served as the control group representing the general population. Chi-squared test and odds ratio (OR) were calculated.

Results: RA was present in 1% of the Explorys® population, in line with established epidemiologic data, serving as validation of the data set. The prevalence of PCOS and ENDO in the general population was under 2%, regardless of age.900,600 women had one of the queried rheumatic diseases, with 194,200 ages 10-49. In those with a rheumatic disease, 3% and 3.9% had PCOS and ENDO, in those 10-49 prevalence was 3.9% and 5.8%, respectively. Table 1 contains prevalence for each specific rheumatic disease. SD had the highest ENDO prevalence and SD, JIA, AS, and CTD the highest prevalence of PCOS. There is evidence that there is an association between each unique rheumatic disease or as a whole with ENDO ($p< 0.0001$) and PCOS ($p< 0.0001$).

If age 10-49 with a rheumatic disease, the odds of having PCOS was 4.3 (4.24-4.38) times higher than in the general population with the odds of having ENDO 13.34 (13.15-13.54).In this demographic, SD, AS and CTD had the highest likelihood of both ENDO and PCOS, which can be found in Table 2.Across all ages, JIA and CTD had the highest likelihood of PCOS and ENDO. SLE also had one of the highest likelihoods of having ENDO across all ages.

Conclusion: Increased prevalence and evidence of association exist between rheumatic diseases and both PCOS and ENDO compared to the general population when examined in a large electronic medical record platform. Additionally, there is an increased likelihood of having PCOS or ENDO in all rheumatic diseases analyzed. Future studies are needed to identify the mechanisms contributing to these findings of PCOS and ENDO in patients with rheumatic diseases as well as increased awareness of these underdiagnosed conditions amongst those who care for these patients to aid in their diagnosis and care.

Disclosure: S. Usmani: None; **C. Lavallee**: None; **M. Antonelli**: None; **C. Edens**: None.

Abstract Number: 0476

Factors Associated with the Need for Assisted Reproductive Therapies in a Spanish Cohort of Patients with Rheumatic Diseases

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SESSION INFORMATION
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Session Title: Reproductive Issues in Rheumatic Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatic diseases (RMD) have a lower pregnancy rate, with infertility being one of the main causes. The rate of assisted reproductive therapies (ART) and the factors associated with the need for ART in patients with RMD are not fully identified.

Methods: Retrospective study of patients with RMD followed up in a specialized pregnancy clinic in Madrid, Spain. Patients with RMD who attended the clinic from December 2012 to January 2023 were included. After one year trying to conceive, patients were referred for ART. Each episode of pregnancy counseling was included as a case. Carriers of autoantibodies, anti-Ro and antiphospholipid (aPL) antibodies, without defined disease, were excluded. Factors associated with the need for ART (ART group) were compared with patients who did not require ART (no ART group). Categorical variables were described as proportions and/or percentages, while continuous variables were shown as mean and standard deviation (SD). The Mann-Whitney U test, Student t test and $\chi 2$ test were used to compare data (ART and non-ART groups), when appropriate. A multivariate logistic regression model was plotted to identify factors associated with need of ART.

Results: 259 cases in 202 patients were included. Fifty-two cases, in 39 patients, of autoantibody carriers were excluded. Sixty-one of 259 (23.6%) cases required ART. The main characteristics and univariate analysis are reported in Table 1. The most frequent diagnosis was the combined RA-JIA group (28.6%). There was a low frequency of comorbidities, including previous nephritis, and 62.7% of the cases had never been pregnant. The patients who required ART were older, more frequently with dyslipidemia. A higher rate of patients in the non-ART group had previously delivered a newborn, but there was no difference from prior miscarriage. There were no differences regarding immunosuppressive treatment, but there was a higher prescription of hydroxychloroquine, aspirin, and heparin in the ART group. In the multivariate analysis (Table 2), older age was associated with the need for ART, while previous delivery of a newborn was the main protective factor for not needing ART.

198 (76.4%) cases became pregnant. The pregnancy rate was lower among the ART group (39/61, 63.9%) compared to the no ART group (159/198, 80.3%), p=0.008. Among the 61 (23.6%) cases who did not become pregnant, the main reason in the ART group was ART failure (9/21, 42.9%) and in the no ART group it was the interruption of the desire for pregnancy (17/39, 43.6%) and active disease (8/39, 20.5%), p= 0.03.

Conclusion: In our cohort, the ART rate was 23.5% and maternal age was the main factor associated with the need for ART, while a history of a previous newborn was associated with a lower risk of needing ART.

Table 1: Demographic and Clinical Characteristics

	ART	non-ART	Total cohort	*p* value
Cases, n (%)	61/259 (23.6)	198/259 (76.4)	259/259 (100)	–
Age at 1st visit, mean (SD), years	37.9 (4.1)	35.2 (4.5)	35.6 (4.6)	<0.0001*
BMI, mean (SD)	23.6 (4.1)	23.6 (4.6)	23.6 (4.5)	0.919
Smoke, n (%)				0.913
never	49 (80.3)	154 (77.8)	203 (78.4)	
active	4 (6.6)	15 (7.6)	19 (7.3)	
previous smoker	8 (13.1)	29 (14.6)	37 (14.3)	
Hypertension, n (%)	3 (4.9)	5 (2.5)	8 (3.1)	0.345
Diabetes, n (%)	0 (0)	1 (0.5)	1 (0.4)	0.578
Dyslipidemia, n (%)	3 (4.9)	1 (0.5)	4 (1.5)	0.015*
RMD diagnosis, n (%)				0.718
RA+JIA	18 (29.5)	56 (28.3)	74 (28.6)	
Spondyloarthropathies	10 (16.4)	44 (22.2)	54 (20.8)	
SLE	13 (21.3)	41 (20.7)	54 (20.8)	
APS	6 (9.8)	11 (5.6)	17 (6.6)	
Other autoimmune diseases*	14 (23)	46 (23.2)	60 (23.2)	
Previous nephritis, n (%)	4 (6.6)	8 (4)	12 (4.6)	0.414
Disease duration, days, mean (SD)	3577.8 (5483.7)	2880.6 (4107.6)	3048 (4474.9)	0.29
Time since last flare, days, mean (SD)	1111.8 (1296.5)	704.6 (1093.8)	802 (1155)	0.064
anti-Ro positive, n (%)	11 (18)	28 (14.1)	39 (15.1)	0.454
APL positive, n (%)	19 (31.1)	40 (20.1)	59 (22.8)	0.094
Never pregnant, n (%)	34 (55.7)	98 (49.5)	174 (67.2)	0.394
Previous newborn, n (%)	5 (8.2)	80 (40)	85 (32.8)	<0.0001*
Previous miscarriage, n (%)	25 (40.9)	58 (29.3)	83 (32)	0.087
Pregnancy risk, n (%)				0.612
Low	4 (6.6)	15 (7.6)	19 (7.3)	
medium	14 (23)	57 (28.8)	71 (27.4)	
high	43 (70.5)	126 (63.6)	169 (65.3)	
Corticosteroids at 1st visit, n (%)	19 (31.1)	45 (22.7)	64 (24.7)	0.182
cDMARDS at 1st visit, n (%)	18 (29.5)	51 (25.8)	69 (26.6)	0.562
bDMARDs at 1st visit, n (%)	7 (11.5)	27 (13.6)	34 (13.1)	0.829
Hydroxychloroquine at 1st visit, n (%)	26 (42.6)	42 (21.2)	68 (26.3)	0.001*
Aspirin at 1st visit, n (%)	17 (27.9)	28 (14.1)	45 (17.4)	0.013*
Heparin at 1st visit, n(%)	7 (11.5)	9 (4.5)	16 (6.2)	0.049*

*Other autoimmune diseases: Systemic sclerosis, mixed connective tissue disease, undifferentiated connective tissue disease, Sjogren syndrome, inflammatory myopathies, vasculitis, sarcoidosis, others
aPL, antiphospholipid antibodies; APS, antiphospholipid syndrome; bDMARDS biological disease-modifying anti-rheumatic drugs; BMI, body mass index; cDMARDs, conventional disease-modifying anti-rheumatic drugs; JIA, juvenile idiopathic arthritis; RA, rheumatoid arthritis; RMD, rheumatic diseases; SLE, systemic lupus erythematosus.

Table 2: Multivariate Analysis

	Total cohort (n=198)	
	OR (95% CI)	*p* value
Age at 1st visit, years	1.14 (1.058-1.230)	0.001*
Dyslipemia (ref yes)	0.09 (0.004-1.909)	0.12
Previous newborn (ref no)	0.12 (0.042-0.319)	<0.001*
Hydroxychloroquine (ref yes)	0.57 (0.279-1.182)	0.132
Aspirin (ref yes)	0.45 (0.184-1.083)	0.075
Anticoagulation (ref yes)	0.51 (0.137-1.861)	0.526

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Abstract Number: 0477

Continuing TNFi After Pregnancy Diagnosis in Women with Chronic Rheumatic Inflammatory Diseases Is Not Associated with Worse Obstetrical or Infant Outcomes and Seems to Reduce Risk of Maternal Severe Infection: The Results of the Emulated Target Trial BioGRIC

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Reproductive Issues in Rheumatic Disorders Poster I

Session Type: Poster Session A

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Background/Purpose: Many women with chronic rheumatic inflammatory diseases (CRID) stop tumor necrosis factor inhibitors (TNFi) treatment once pregnancy is confirmed to avoid potential adverse fetal events but taking the risk of inflammatory flare.

The aim of the study was to compare in real life settings the pregnancy outcomes of two treatment strategies among women with CRID: to continue TNFi vs. stop TNFi upon pregnancy diagnosis.

Methods: the French nationwide health insurance database (*Système National des Données de Santé*) was used to emulate a target trial in adult women, with CRID (i.e., rheumatoid arthritis, psoriatic arthritis or spondyloarthritis), having started a singleton pregnancy between 2008 and 2017, and and being treated with TNFi upon pregnancy diagnosis. We compared the frequency of unfavorable pregnancy outcomes (malformations, obstetrical complications, and infections) between the treatment strategies at pregnancy diagnosis, using inverse probability weighted marginal models.

	OUTCOMES	TNFI CONTINUE (N = 584)[$]	TNFI STOP (N=1497)[$]	RELATIVE RISK (CONTINUE VS. STOP) 95% CI
	Live births	505 (86.6%)	1327 (88.6%)	0.9 [0.9 - 1.0]
	Spontaneous abortion (GA < 22 WG or birth weight < 500g)	11 (1.9%)	50 (3.3%)	0.6 [0.3 - 1.2]
	Intrauterine fetal death (GA >=22 WG or birth weight >=500g)	6 (1.1%)	8 (0.5%)	2.0 [0.8- 5.3]
	Medical termination of pregnancy	4 (0.6%)	15 (1.0%)	0.6 [0.2 - 2.4]
	Preterm birth (GA between 22 and 37 among live birth)	37 (6.4%)	108 (7.2%)	0.9 [0.6 - 1.3]
	Small for GA (< 10th percentile)	52 (8.9%)	139 (9.3%)	0.9 [0.7 - 1.4]
	Cesarean delivery	115 (19.8%)	337 (22.5%)	0.9 [0.7- 1.1]
	Eclampsia/Pre-eclampsia	6 (1.0%)	21 (1.4%)	0.7 [0.3 - 1.6]
OBSTETRICAL	Extra-uterine pregnancy	0 (0.0%)	5 (0.3%)	-
	Hospital admission for infection (during pregnancy and 6 weeks post-delivery)	**1 (0.2%)**	**19 (1.3%)**	**0.2 [0.1 - 0.6]**
MATERNAL	Gestational diabetes	59 (10.2%)	155 (10.3%)	0.9 [0.7 - 1.4]
	Major congenital malformation	12/486 (2.5%)	37/1293 (2.9%)	0.9 [0.4 - 1.7]
	Severe infection (requiring hospitalization) during the first year of life	51/486 (10.6%)	119/1293 (9.2%)	1.2 [0.8 - 1.7]
	NCIU admission for more than 48h in infants born after 37 WG	6/486 (1.3%)	24/1293 (1.9%)	0.7 [0.3 - 1.9]
INFANTS				

$: Weighted pseudopopulation; Abbreviations: GA = gestational age; WG = weeks of gestation

Results: A total of 2082 singleton pregnancies of CRID women (579 RA and 1503 SpA) exposed to TNFi 6 weeks after last menstrual period were identified; among them, in 1497 (72%) TNFi was discontinued.

Mean (SD) age of women at the start of pregnancy was 31 (5) years and mean (SD) disease duration was 4 (5) years. Continuation of TNFi was not associated with increased frequencies of unfavorable obstetrical nor infant outcomes, and interestingly, the proportion of maternal severe infections (i.e., requiring hospitalization) was significantly lower in the 'continue' group (1(0.2%) vs. 19 (1.3%), with an adjusted risk ratio = 0.2 [0.1 - 0.6]).

Conclusion: In pregnant women with CRID treated with TNFi until pregnancy diagnosis, unfavorable obstetrical outcomes were not different to those observed when TNFi were maintained, and maternal severe infections were less frequent, when compared with a strategy of stopping TNFi.

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Abstract Number: 0478

The Long-term Neurodevelopmental Outcome of Children Born to Women with Systemic Sclerosis: Assessment Through a Self-reported Questionnaire by the Mothers and Nneuropsychiatric Evaluations of the Children

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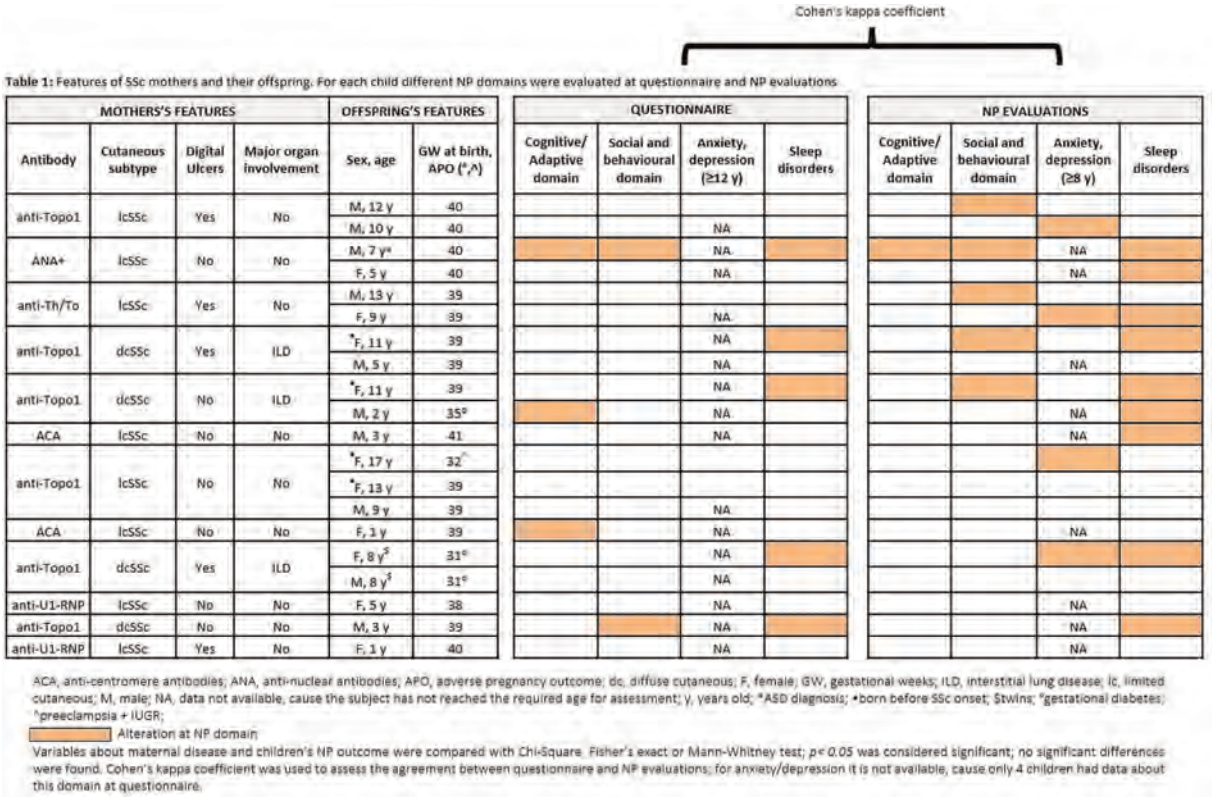
Session Title: Reproductive Issues in Rheumatic Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The long-term neuropsychiatric (NP) outcome of children born to mothers affected by autoimmune diseases (AIDs) represents a controversial topic, with few studies[1-3] reporting a possible increased prevalence of NP alterations. We focused on the neurodevelopment (ND) of children born to Systemic Sclerosis (SSc) mothers, starting with the creation of an ad-hoc questionnaire regarding different aspects of children's ND administered to consecutive SSc mothers in 2021[4]. We further investigated the long-term NP outcome of SSc offspring by offering a comprehensive pediatric NP evaluation.

Methods: SSc mothers (ACR/EULAR 2013 criteria) who previously completed the questionnaire[4] were allowed to have their children aged < = 18 years undergo a clinical NP evaluation including:

Table 1: Features of SSc mothers and their offspring. For each child different NP domains were evaluated at questionnaire and NP evaluations



Cohen's kappa coefficient

Table 1: Features of SSc mothers and their offspring. For each child different NP domains were evaluated at questionnaire and NP evaluations

MOTHERS'S FEATURES				OFFSPRING'S FEATURES		QUESTIONNAIRE				NP EVALUATIONS			
Antibody	Cutaneous subtype	Digital Ulcers	Major organ involvement	Sex, age	GW at birth, APO (*,^)	Cognitive/ Adaptive domain	Social and behavioural domain	Anxiety, depression (≥12 y)	Sleep disorders	Cognitive/ Adaptive domain	Social and behavioural domain	Anxiety, depression (≥8 y)	Sleep disorders
anti-Topo1	lcSSc	Yes	No	M, 12 y	40								
				M, 10 y	40			NA					
ANA+	lcSSc	No	No	M, 7 y*	40			NA				NA	
				F, 5 y	40			NA				NA	
anti-Th/To	lcSSc	Yes	No	M, 13 y	39								
				F, 9 y	39			NA					
anti-Topo1	dcSSc	Yes	ILD	*F, 11 y	39			NA					
				M, 5 y	39			NA				NA	
anti-Topo1	dcSSc	No	ILD	*F, 11 y	39			NA					
				M, 2 y	35°			NA				NA	
ACA	lcSSc	No	No	M, 3 y	41			NA				NA	
anti-Topo1	lcSSc	No	No	*F, 17 y	32^								
				*F, 13 y	39								
				M, 9 y	39			NA					
ACA	lcSSc	No	No	F, 1 y	39			NA				NA	
anti-Topo1	dcSSc	Yes	ILD	F, 8 y§	31°			NA					
				M, 8 y§	31°			NA					
anti-U1-RNP	lcSSc	No	No	F, 5 y	38			NA				NA	
anti-Topo1	dcSSc	No	No	M, 3 y	39			NA				NA	
anti-U1-RNP	lcSSc	Yes	No	F, 1 y	40			NA				NA	

ACA, anti-centromere antibodies; ANA, anti-nuclear antibodies; APO, adverse pregnancy outcome; dc, diffuse cutaneous; F, female; GW, gestational weeks; ILD, interstitial lung disease; lc, limited cutaneous; M, male; NA, data not available, cause the subject has not reached the required age for assessment; y, years old; *ASD diagnosis; •born before SSc onset; §twins; °gestational diabetes; ^preeclampsia + IUGR;

Alteration at NP domain

Variables about maternal disease and children's NP outcome were compared with Chi-Square, Fisher's exact or Mann-Whitney test; $p < 0.05$ was considered significant; no significant differences were found. Cohen's kappa coefficient was used to assess the agreement between questionnaire and NP evaluations; for anxiety/depression it is not available, cause only 4 children had data about this domain at questionnaire.

(1) cognitive/adaptive functioning (Griffiths Mental Development Scales -GMDS-III-; Wechsler Scale for corrected age -WISC-III; Vineland Adaptive Behavior Scales -VABS-II-)

(2) behavioral/social problems (Child Behavior CheckList -CBCL-, fulfilled by the mothers; Youth Self Report -YSR-, for children [3] >=11 years)

(3) anxiety/depression/somatic disorders (Self-administered psychiatric scales for children/adolescents -SAFA-A/D/S- [3] >=8 years)

(4) sleep disorders.

Cohen's kappa coefficient was used to evaluate the agreement between questionnaire answers and NP test results.

Results: 23 SSc mothers reported 39 children aged < = 18 years, 37/39 were proposed for NP evaluation and 20 agreed to be evaluated (F/M 1:1; median age 8 [6-11] years). The mothers had reported at least one alteration in the questionnaire for 7 children (Table 1); one already had a diagnosis of autism spectrum disorder (ASD). At NP evaluations were recorded:

(1) normal scores for cognitive/adaptive functioning in all children, except the one with ASD
(2) an increased risk of developing behavioral/social problems especially in extra-academic/social activities in 3/20 at CBCL and in 3/6 at YSR
(3) an increased risk of developing depression in 4/11
(4) sleep disorders in 9/20

Features of mothers and their offspring are shown in Table 1. The agreement between questionnaires and NP evaluation was moderate for cognitive/adaptive functioning and sleep disorders (k 0.5 and 0.6 respectively) and weak for behavioural/social problems (k 0.2).

Conclusion: At NP evaluation, children born to SSc mothers showed normal cognitive skills but a tendency toward an impairment in the behavioral/social area. Mothers seldom recognized such a difficulty, according to the self-reported questionnaire.

In the setting of preconception counseling, it is important to inform SSc mothers about possible NP symptoms in their children and to seek for a specialist evaluation in case of doubts. Indeed, with the help of specialists, most NP problems can be overcome if detected early.

References.[1]Vinet E. et al. Arthritis Rheumatol.2015; [2]Wojcik S. et al. Arthritis Care Re.2017; [3]Nalli C. et al. Best Pract Res Clin Obstet Gynaecol.2020; [4]Pedretti E. et al. [abstract]Arthritis Rheumatol.2022

The Authors would like to thank the Italian association of SSc patients 'GILS' (Gruppo Italiano Lotta Sclerodermia) for kindly supporting the project.

Disclosure: M. Lazzaroni: None; **E. Pedretti**: None; **L. Moschetti**: None; **M. Bendoni**: None; **L. Visconti**: None; **A. Molinaro**: None; **C. Nalli**: None; **F. Franceschini**: None; **P. Airò**: None; **J. Galli**: None; **E. Fazzi**: None; **A. Tincani**: Galapagos, 6, GSK, 6, UCB, 6; **L. Andreoli**: None.

Abstract Number: 0479

Exploring Reproductive Experiences with Women Enrolled in the Vasculitis Pregnancy Registry

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Reproductive Issues in Rheumatic Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: There are limited data on the reproductive health and experiences of women with vasculitis. This study engaged women with vasculitis to understand their perspectives about pregnancy and breastfeeding.

Methods: The Vasculitis Pregnancy Registry (VPREG) is an international, online, prospective, patient-reported registry within the Vasculitis Patient-Powered Research Network (VPPRN). The VPREG team partnered with the Vasculitis Foundation and patient research partners to develop two qualitative interview guides to prompt discussions of reproductive experiences with i) women who had live births; and ii) women who had non-live births. The guides included closed-ended scale items and open-ended prompts to elicit participant experiences. The interviews, performed by a rheumatologist, explored topics including pregnancy, medication choices to treat vasculitis, disease activity levels, patient-physician relationships, experiences with delivery, and breastfeeding. Participant responses were evaluated using thematic analysis.

Results: The 18 participants were located in North America, ranged in age from 25-43 years, and most had more than one pregnancy (n=11) (**Table 1**). Anti-neutrophil cytoplasmic antibody-associated vasculitis was the most common diagnosis (n=10) followed by Takayasu's arteritis (n=4), Behçet's disease (n=2), IgA vasculitis (n=1), and relapsing polychondritis (n=1). Almost all pregnancies ended in a live birth (n=17).

Table 1. Patient Characteristics among Women with Vasculitis and a History of Pregnancy

Mean age at enrollment (range)	33 years (25-43)
Country of origin	United States: 14 Canada: 4
Type of vasculitis	ANCA-associated vasculitis: 10 (55.6%) *-Granulomatosis with polyangiitis: 8* *-Microscopic polyangiitis: 1* *-Eosinophilic granulomatosis with polyangiitis: 1* Takayasu's arteritis: 4 (22.2%) Behçet's disease: 2 (11.1%) IgA vasculitis: 1 (5.6%) Other/suspected: 1 (5.6%)
First pregnancy	No: 11 (61.1%) Yes: 6 (33.3%) No response: 1 (5.5%)

Figure 1. Women utilized a broad range of resources for information about pregnancy and breastfeeding

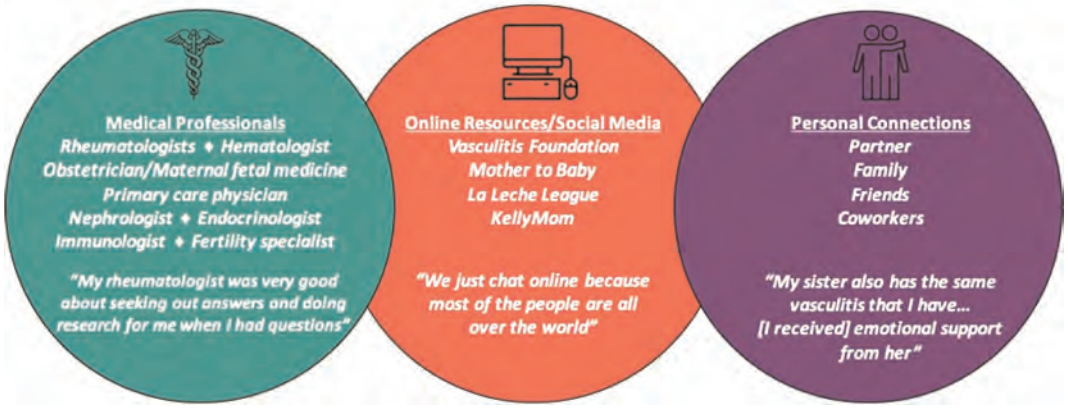


Figure 1 displays the variety of resources patients with vasculitis accessed to gather information about their reproductive health

Figure 2. Emergent themes in the reproductive journey for women with vasculitis

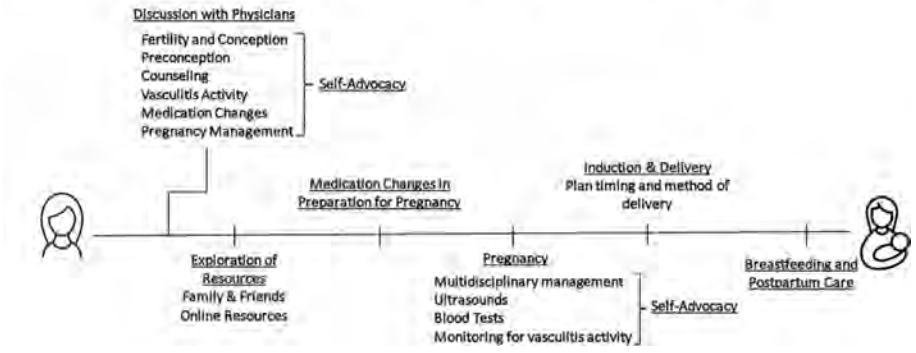


Figure 2 summarizes the emergent themes along the reproductive timeline of patients with vasculitis

Four major themes emerged from interviews: 1) Women sought information about pregnancy from a range of sources, including their physicians, social media, and online forums (**Figure 1**); 2) Women cited discussions with family and physicians as important when deciding about treatment of vasculitis during pregnancy; 3) Women with vasculitis developed skills of self-advocacy during pregnancy to optimize communication between medical providers; and 4) Women with vasculitis had positive reproductive experiences with the majority reporting no flares of vasculitis, feeling "very well", and having "no pain" related to their vasculitis (**Figure 2**). Women who required changes to their medications to pursue their reproductive goals, identified physicians and family members as important participants in these conversations. Women described proactively gathering information about pregnancy and vasculitis from multiple sources, but ultimately decided their physician's perspective was the most influential. All women that used social media and online resources reported it did not impact or determine their reproductive decisions.

Conclusion: Women with vasculitis value the recommendations of their rheumatologists during reproductive healthcare discussions. Self-advocacy was frequently described during pregnancy because women felt they needed to act as liaisons among multiple specialists to ensure proper medical treatment. This study found that patients prioritize their relationships and conversations with physicians when planning for pregnancy.

Disclosure: C. Sims: UCB, 5; **C. Yeung**: None; **H. Tam**: None; **J. Kullman**: None; **A. Eudy**: Amgen, 2, Exagen, 5, GlaxoSmithKlein(GSK), 5, Immunovant, 5, Pfizer, 5; **R. Borchin**: None; **C. Burroughs**: None; **M. Clowse**: Exagen, 5, GlaxoSmithKlein(GSK), 2, 5, Immunovant, 5, UCB, 2, 5; **P. Merkel**: AbbVie/Abbott, 5, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos, 5, Electra, 5, Genentech, 5, GlaxoSmithKlein(GSK), 2, 5, HiBio, 2, InflaRx, 2, 5, Janssen, 2, Jubilant, 2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, Takeda, 2, 5, UpToDate, 9, Visterra, 2.

Abstract Number: 0480

Non-random Sampling in Rheumatology Randomized Controlled Trials: Evidence of Concerning Trial Conduct?

Victoria Le[1], Mats Junek[2], Mike Putman[3], Maximilian Casey[1], Kenrick Manswell[1], Jay Goldsher[1], Elizabeth Nettleton[1], Desh Nepal[1] and Sanket Shah[1], [1]Medical College of Wisconsin, Milwaukee, WI, [2]McMaster University, Hamilton, ON, Canada, [3]Division of Rheumatology, Medical College of Wisconsin, Milwaukee, WI

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Research Methodology – Interprofessional Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Non-random sampling of baseline variables in randomized controlled trials (RCTs) may be due unintentional errors, stratified randomization strategies, or data fabrication. Prior studies have suggested that non-random sampling may occur in up to 15% of RCTs in anesthesiology and have led to high profile retractions of fabricated data. No similar studies have been conducted in the field of rheumatology.

Methods: A PRISMA compliant systematic review was conducted to identify rheumatology RCTs published between 2010 and 2022 and met the following criteria: >20 patients per arm, first publication of trial data, ≥5 extractable variables, 2-5 trial arms, and studied a rheumatic disease. Baseline demographic and clinical variables from randomized arms were extracted. Monte Carlo simulations (50,000 per variable) were performed to calculate p values for individual baseline variables, which

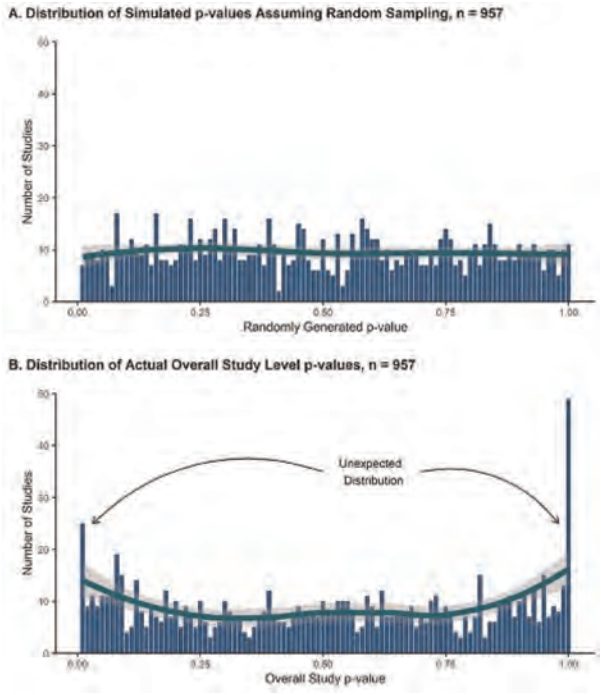


Image 1. (A) Distribution of Simulated p-values Assuming Random Sampling (B) Distribution of Actual Overall Study Level

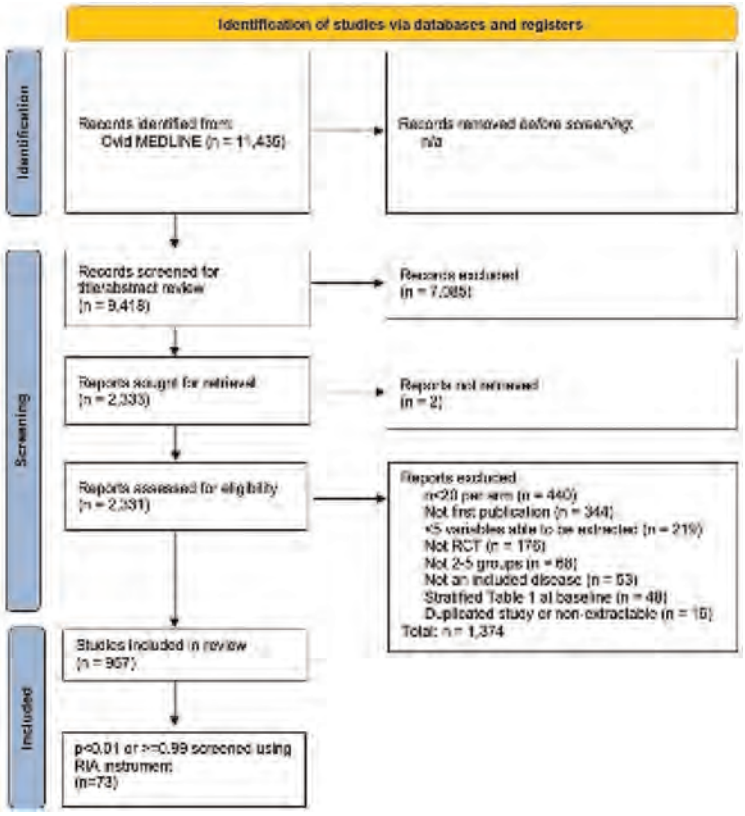


Image 2. Identification of studies via databases and registers

were then used to calculate an overall trial p-value using the Fischer-Stouffer method. The distribution of participant summary p-values, which should be uniform under conditions of true random sampling, was graphed. RCTs with trial p-values ≤ 0.01 or ≥ 0.99 underwent further scrutiny using a modified version of the Research Integrity Assessment (RIA) Checklist. Integrity concerns for individual metrics (No, Some, Significant Concerns) and overall (Low, Moderate, High Concern) were assessed.

Results: We identified 11,435 RCTs, 2,313 of which underwent full text review. Of these, 957 met inclusion criteria, from which 19,799 baseline variables were extracted. A uniform distribution of trial p-values would have produced approximately 19 studies with p values < 0.01 or >0.99; our search identified 73 such studies (Figure 1). Using the RIA checklist, 64 (87.7%) studies were found to be lacking across at least one metric of study integrity. The most common items among trials with high integrity concerns included trials not being prospectively registered (21, 28.8%) and reporting ethics approval number (20, 27.4%). None of the studies were retracted or had letters of concern written. Based on the RIA findings, 28 (38.4%) trials were rated as having a high level of data integrity concerns, 3 (4.1%) had moderate data integrity concerns, and 42 (57.5%) had low data integrity concerns.

Conclusion: Non-random sampling has occurred in nearly 1 out of every 100 rheumatology randomized controlled trials. The majority of studies were assessed as being of low risk of threats to their integrity, but 27 out of 957 studies (2.8%) had moderate to high concern of problematic conduct. Understanding common themes within these studies will assist in identifying areas that require further scrutiny in evidence synthesis and implementation.

Table 1: Summary statistics of threats to individual research integrity based on the Research Integrity Assessment checklist (RIA) and overall assessment by RIA reviewers, n = 73

Table 1: Summary statistics of threats to individual research integrity based on the Research Integrity Assessment checklist (RIA) and overall assessment by RIA reviewers, n = 73

Variable	High concern (n=28)	Moderate concern (n=3)	Low concern (n=42)
Not prospectively registered	21 (28.8%)	2 (2.7%)	50 (68.5%)
Ethics approval number not reported	20 (27.4%)	2 (2.7%)	51 (69.9%)
Registry number not reported	19 (26.0%)	2 (2.7%)	52 (71.2%)
Incomplete or missing flow diagram	17 (23.3%)	0 (0.0%)	56 (76.7%)
Excess in similarity or differences in characteristics of participants (H)	16 (21.9%)	0 (0.0%)	57 (78.1%)
Baseline details insufficient to assess if randomization was done properly (H)	15 (20.5%)	0 (0.0%)	58 (79.5%)
Implausible number of patients recruited within timeframe (H)	14 (19.2%)	0 (0.0%)	59 (80.8%)
Insufficient reporting of the study design, concerns over randomization based on CONSORT items (see comments)	13 (17.8%)	1 (1.4%)	59 (80.8%)
Unrealistic response rate or loss of follow up (H)	12 (16.4%)	0 (0.0%)	61 (83.6%)
Implausible study results (H)	9 (12.3%)	0 (0.0%)	64 (87.7%)
Name and location of the ethics committee not reported	5 (6.8%)	2 (2.7%)	66 (90.4%)
Inconsistency in study and registration dates	4 (5.5%)	1 (1.4%)	68 (93.2%)
Implausible number of authors for the study design	4 (5.5%)	0 (0.0%)	69 (94.5%)
Written informed consent not obtained	4 (5.5%)	0 (0.0%)	69 (94.5%)
Ethics was not reported	3 (4.1%)	1 (1.4%)	69 (94.5%)
Ethics approval not obtained by a nationally recognized ethics committee in the country's trial regulations	3 (4.1%)	0 (0.0%)	70 (95.9%)
Calculation errors	2 (2.7%)	1 (1.4%)	70 (95.9%)
Concerns over plagiarism	2 (2.7%)	0 (0.0%)	71 (97.3%)
Number of participants is inconsistent with randomization method	1 (1.4%)	0 (0.0%)	72 (98.6%)
Discrepancies between data reported in figures, tables, text	0 (0.0%)	0 (0.0%)	73 (100.0%)

Disclosure: V. Le: None; **M. Junek**: None; **M. Putman**: AbbVie/Abbott, 12, Trial participation, AstraZeneca, 12, Trial participation, Novartis, 2; **M. Casey**: None; **K. Manswell**: None; **J. Goldsher**: None; **E. Nettleton**: None; **D. Nepal**: None; **S. Shah**: None.

Abstract Number: 0481

Automatically Detect Finger Joint Center and Angle on Hand X-ray: A Deep Learning Model

Yuan Gao[1], Juan Shan[2], Raj Ponnusamy[2], Jordan Blackadar[3], Carmine Guida[2], Jeffrey Driban[4], Timothy McAlindon[5] and **Ming Zhang**[1], [1]Boston University, Boston, MA, [2]Pace University, New York, NY, [3]Photo Diagnostic System, Boston, MA, [4]Tufts Medical Center, Boston, MA, [5]Tufts Medical Center, Arlington, MA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Research Methodology – Interprofessional Poster

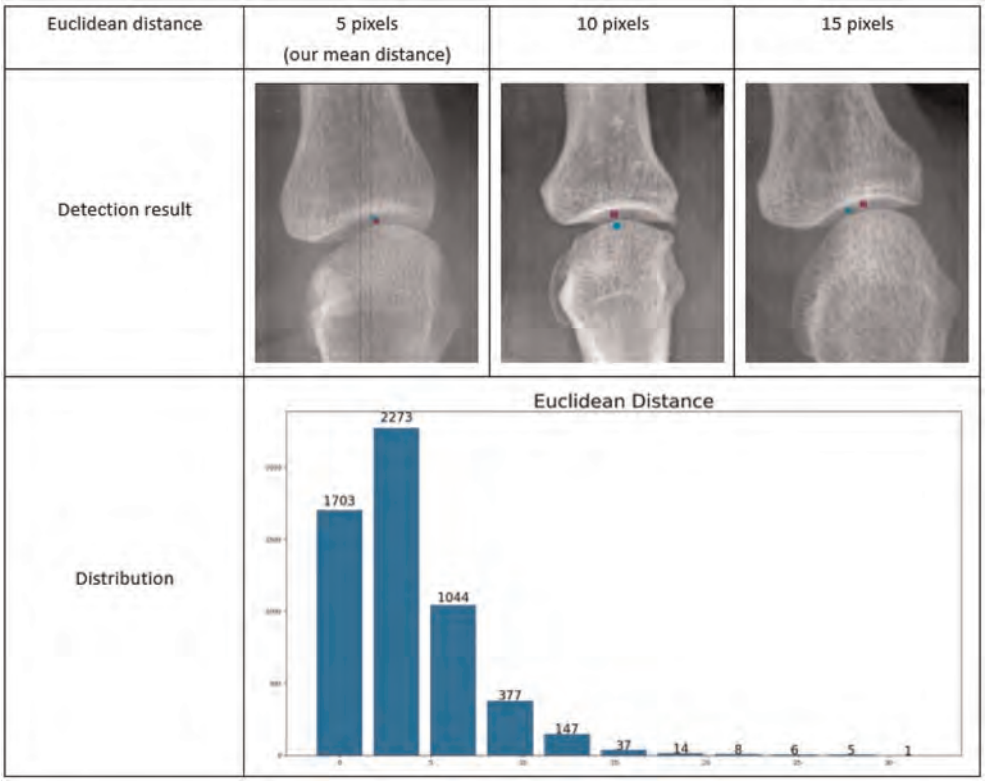
Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

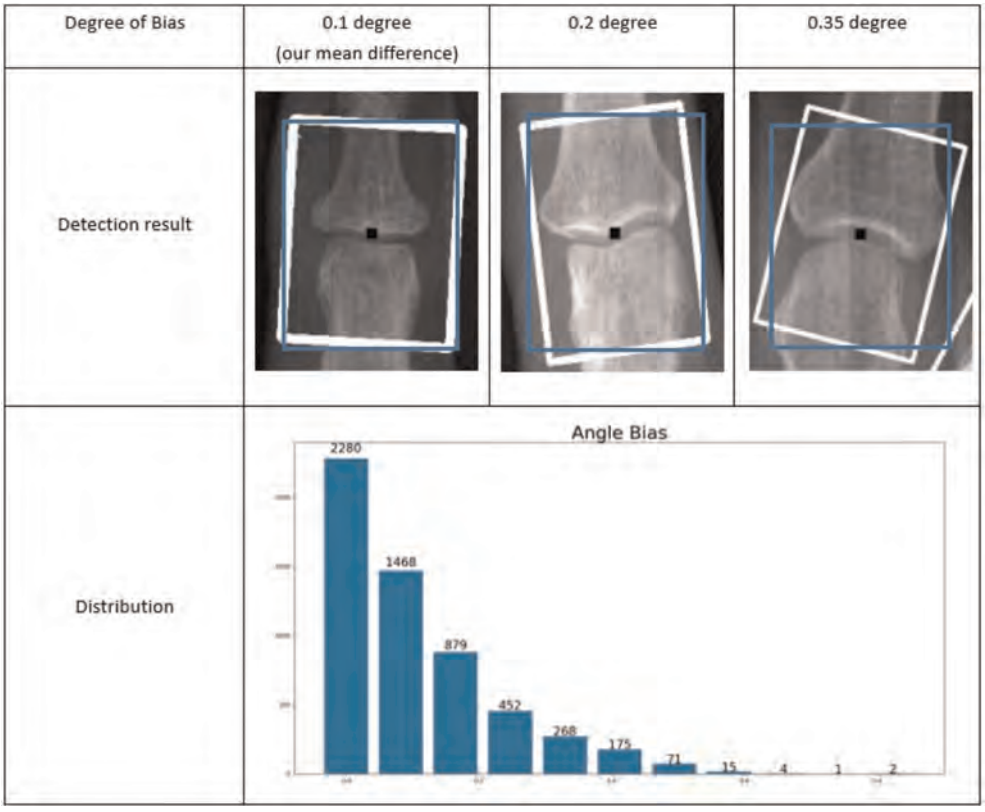
Background/Purpose: Hand osteoarthritis (OA) is the second most common anatomic region for OA. The diagnosis and evaluation of hand OA heavily rely on subjective assessments conducted by experienced physicians, primarily utilizing clinical examinations and radiographs. However, the interpretation of radiographs is prone to considerable variability, leading to challenges in objectively assessing hand OA. This abstract presents the development of an automated approach using deep learning and convolutional neural networks (CNN) to localize joint hand centers and measure angles, offering a potential solution to the Joint Space Width (JSW) estimation and hand OA assessment.

Methods: We selected 3,557 hand X-ray images from the Osteoarthritis Initiative (OAI). Two readers performed manual annotations of the twelve finger joints on each hand, the distal interphalangeal (DIP), proximal interphalangeal (PIP), and metacarpophalangeal (MCP) joints. Each joint was enclosed within a bounding box measuring 180*180 pixels. To enhance the diversity of the training data for the machine learning model, we employed various image augmentation techniques, including rotation, flipping, scaling, cropping, and mosaic. The data was split into training, validation, and test sets in a 7 : 1.5: 1.5 ratio. Utilizing the YOLOv5 architecture, the model was trained for 100 epochs using stochastic gradient descent (SGD) as the optimizer. The model output provided each joint's position in coordinate form, which calculate the rotation and inclination angles of the DIP, PIP, and MCP joints. Specifically, we connected the center points of the DIP and PIP joints to derive the slope as the rotation angle of the DIP joint. Similarly, by connecting the PIP and MCP joints, we obtained the slope representing the rotation angle of the MCP joint. The rotation angle of the PIP joint was computed as the average of these two slopes. Leveraging the joint positions and the computed angles, we selectively cropped image patches from the original hand X-ray images, ensuring the joints were vertically oriented. This vertical orientation is crucial for accurately calculating the joint space width in subsequent steps.

Results: In our evaluation process, our testing set has an average Euclidean distance (between the detection center and human annotation center) of 5.1 pixels (Figure 1). The mean error (absolute distance) in the test set for the angle estimation step is 0.144 degrees (Figure 2). Interestingly, we encountered 21 human annotation errors within the dataset during the initial training of YOLOv5, resulting in a human error rate of 0.5%, while the model successfully identified 5 out of the 6 human errors in the test set, leading to machine error rate of 0.2%. This indicates that our model exhibited a lower error rate than manual annotations.



Examples of Euclidean Distance between the manual label (purple) and computer-generated (green) result



Angle difference between a manual label (white box) and computer-generated (blue box) results

Conclusion: Our deep-learning approach successfully detects each finger joint its rotation angle. Moreover, our model shows a lower error rate than manually labeling the joints. It also exhibits high accuracy and holds promise in reducing inter-observer variability during hand OA evaluation. In future studies, we intend to develop an automatic JSW detection algorithm and explore the correlation between clinical symptoms and JSW.

Disclosure: Y. Gao: None; **J. Shan**: None; **R. Ponnusamy**: None; **J. Blackadar**: None; **C. Guida**: None; **J. Driban**: None; **T. McAlindon**: None; **M. Zhang**: None.

Abstract Number: 0482

Preference and Relative Sensitivity of Indicators Reporting Response Rate in Pharmaceutical Trials of Psoriasis and Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Research Methodology – Interprofessional Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Numerous indicators have been proposed to evaluate the efficacy for randomized clinical trials (RCTs) of psoriasis (Pso) and psoriatic arthritis (PsA), but the comparability and correlation remain unknown. To evaluate the preference and relative sensitivity of the mostly widely used indicators that report response rate, and to provide advice for the primary endpoint selection for Pso and PsA.

Methods: We conducted a systematic search including 3 databases and 4 registries to identify all pharmacological intervention-controlled RCTs of Pso. Bayesian hierarchical linear mixed model assessed the relative discriminations and provided a ranking of these indicators.

Results: Altogether 326 RCTs met our inclusion criteria, with 285 and 65 records on Pso and PsA, respectively. We found evidence of significant differences between indicators. Psoriasis Area and Severity Index (PASI) 50, PASI 75 and Investigator's Global Assessment (IGA) 0,1 were powerful indicators to reveal the pharmacological efficacy in most RCTs of Pso(-Figure 1). In contrast, PASI 125, Dermatology Life Quality Index (DIQI) 0,1 and Numerical Rating Scale (NRS) 4 were not preferred under different circumstances. Additionally, PASI 50, PASI 75 and PASI 90 seemed to be the most effective in nearly all types of pharmacological RCTs of PsA (Figure 2). However, due to their extremely sensitivity, American College of Rheumatology (ACR) 20 was also recommended to avoid exaggerating the therapeutic advantages of interventions. Instead, ACR 50, ACR 70 and Minimal Disease Activity (MDA) were the least sensitive, but they were supposed to be more cautious in evaluating disease changing. Indicator preference was slightly altered by disease severity, intervention type and administration method(Table 1).

Conclusion: The impressionable efficacy discrimination ability of indicators highlights the importance of flexibility and comprehensiveness when choosing primary outcome(s). As for trials that are only evaluated by indicators with extremely sensitivity, attention should be paid to the outcome interpretation to avoid the exaggeration of treatment efficacy.

Table 1. Recommendations for the selection of primary outcome of RCTs for psoriasis and psoriatic arthritis.

Items	Suggested Indicators		Not suggested Indicators	
	Psoriasis	Psoriatic arthritis	Psoriasis	Psoriatic arthritis
Overall	PASI 50 PASI 75 IGA 0,1	PASI 75 PASI 50 PASI 90 ACR 20	PASI 125 DLQI 0,1 NRS-4	ACR 70 MDA ACR 50
Baseline severity of participants				
All	PASI 50 PASI 75	ACR 20 PsARC	PatGA 0,1 IGA 0,1, Reduction≥2	-
Moderate	PASI 75 PASI 50	-	PASI 90	-
Severe	PASI 75	-	DLQI 0,1	-
Mild to moderate	PASI 50 PASI 75 IGA 0,1	ACR 50	PASI 125 PASI 90	-
Moderate to severe	PASI 50 PASI 75 IGA 0,1, Reduction≥2 IGA 0,1	PASI 75 PASI 50 PASI 90 ACR 20	PASI 125 DLQI 0,1 NRS-4	ACR 70 MDA PsARC
Not mentioned	PASI 50 PASI 75 IGA 0,1	PASI 75 PASI 50 PASI 90 PsARC	PASI 125 DLQI 0,1 IGA 0,1, Reduction≥2	ACR 70 ACR 50 MDA
Type of intervention				
Antibodies combined with small molecules	-	PASI 75 ACR 20	-	ACR 70
Antibodies	PASI 50 PASI 75 IGA 0,1, Reduction≥2	PASI 75 PASI 50 PASI 90 ACR 20	PASI 125 DLQI 0,1 PatGA 0,1	ACR 70 MDA ACR 50
Small molecules	PASI 50 PASI 75 IGA 0,1 PatGA 0,1	ACR 20 PsARC PASI 90 PASI 75	PASI 125 DLQI 0,1 PASI 90	ACR 70 ACR 50 MDA
Non-biologics	PASI 75 IGA 0,1 PASI 90	PsARC	PASI 125 DLQI 0,1 IGA 0,1, Reduction≥2	ACR 50
Application method				
Topical	PASI 50 IGA 0,1 PASI 75	-	PASI 125 IGA 0,1, Reduction≥2	-
Systemic	PASI 50 PASI 75 IGA 0,1, Reduction≥2	PASI 75 PASI 50 PASI 90 ACR 20	PASI 125 DLQI 0,1 NRS-4	ACR 70 MDA ACR 50

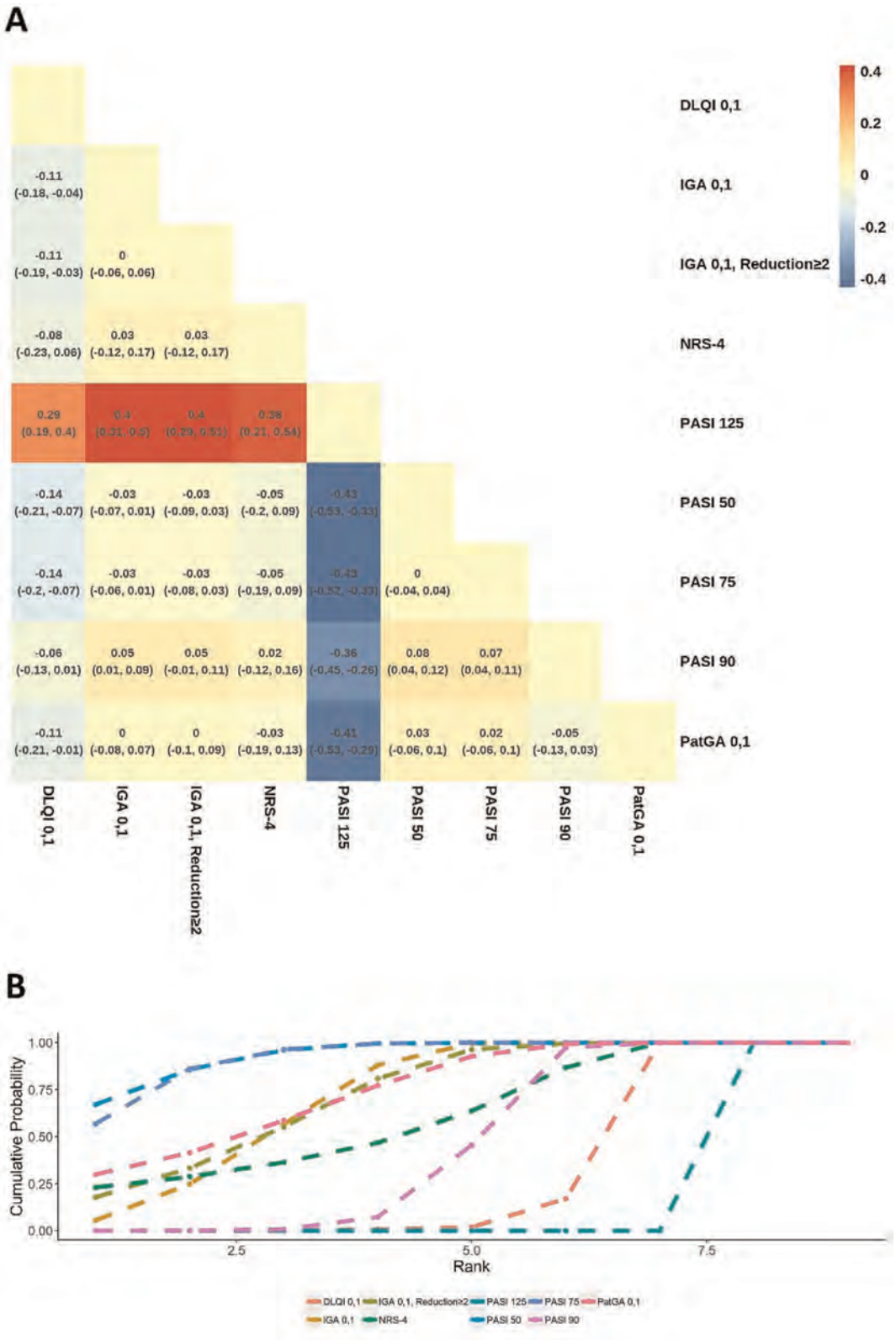

Figure 1. Preference of indicators reporting response rate in pharmacological intervention-controlled RCTs for psoriasis. (A) Bayesian hierarchical linear mixed model estimated effectiveness with 95% uncertainty intervals on indicators reporting response rate in pharmacological intervention-controlled RCTs for psoriasis. (B) The rank of indicators reporting response rate. The sooner an indicator reaches 1, the stronger ability to discriminate treatment efficacy.

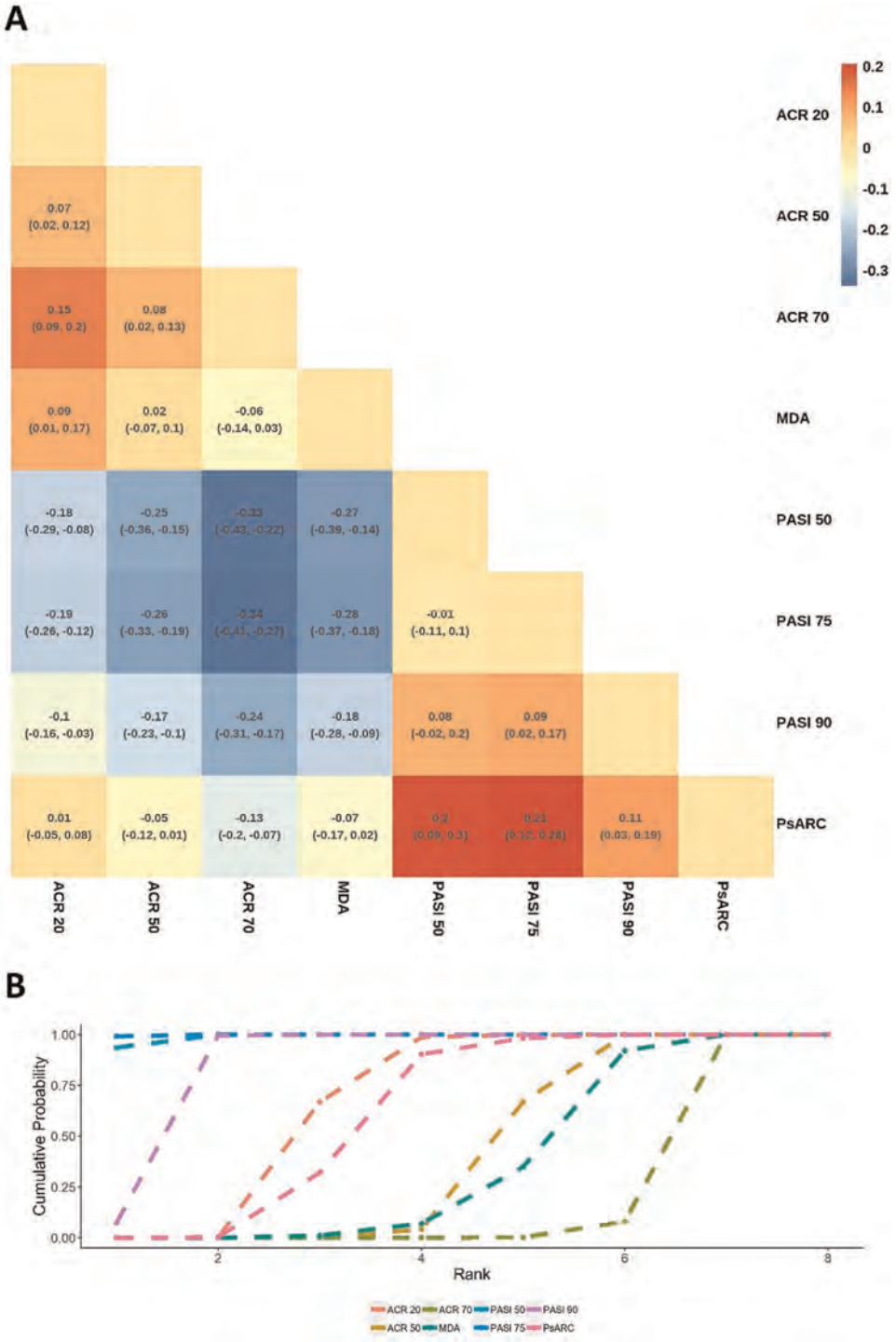

Figure 2. Preference of indicators reporting response rate in pharmacological intervention-controlled RCTs for psoriatic arthritis. (A) Bayesian hierarchical linear mixed model estimated effectiveness with 95% uncertainty intervals on indicators reporting response rate in pharmacological intervention-controlled RCTs for psoriatic arthritis. (B) The rank of indicators reporting response rate. The sooner an indicator reaches 1, the stronger ability to discriminate treatment efficacy.

Disclosure: J. Tian: None; **S. Kang**: None; **D. Zhang**: None; **Q. Lu**: None.

Abstract Number: 0483

The Influence of "Fibromyalgia-ness" on Treatment Response Amongst Patients with Psoriatic Arthritis (PsA). Results from the British Society for Rheumatology Psoriatic Arthritis Register (BSR-PsA)

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Co-morbid fibromyalgia has been shown to be an important influence on non-response in patients with some inflammatory arthritides. Around 1 in 5 patients with PsA have been estimated to have co-morbid fibromyalgia. Here we examine to what extent meeting criteria for fibromyalgia or reporting symptoms typical of fibromyalgia is an important determinant of non-response to a biologic or targeted synthetic (b/ts) DMARD, taking into account other predictors of non-response.

Table. Fibromyalgia and other predictors of treatment response

		Model 1[1] N = 125	Model 2[2] N = 116
Variable		**OR (95% CI)[3]**	**OR (95% CI)[3]**
Polysymptomatic distress (FMness)	0-31	0.66 (0.40, 1.08)[4]	-
FM ACR2016 criteria		-	0.29 (0.08, 0.99)
csDMARD (current)		2.58 (1.01, 6.61)	2.61 (0.92, 7.44)
Patient global score (Arthritis)	0-10	1.27 (1.04, 1.55)	-
Physician global (skin disease activity)	0-10	1.28 (1.05, 1.57)	1.42 (1.10, 1.85)
Symptom duration (joints), years		-	0.79 (0.63, 0.98)
Steroids (current)		0.42 (0.15, 1.13)	0.40 (0.13, 1.24)
Nail onycholysis (current)		-	3.07 (1.11, 8.50)
Index of Multiple Deprivation (Based on area of residence)	Decile 1-4[5]	Reference	Reference
	Decile 5-7	1.36 (0.41, 4.50)	1.58 (0.37, 6.73)
	Decile 8-10	3.15 (1.03, 9.60)	3.46 (1.05, 11.38)
Sensitivity		41.0%	54.6%
Specificity		88.4%	94.0%

[1] Polysymptomatic distress forced into model
[2] FM ACR2016 criteria forced into model
[3] Odds Ratio (per unit increase unless otherwise specified)
[4] Odds Ratio per 5-unit increase in FMness
[5] Least Deprived

Methods: Data included were from BSR-PsA (January 2023 download), a prospective registry of patients with PsA who meet CASPAR criteria, recruited across Great Britain. In this analysis we include those newly commencing a bDMARD/tsDMARD (having not previously taken the same agent). The association between patient characteristics and treatment response (PsARC) was determined by logistic regression. The fibromyalgia polysymptomatic distress score (FMness) (*Model1*) or fibromyalgia 2016 (FM2016) criteria (*Model2*) was forced into the model and then other predictors of poor outcome which improved the fit of the model were determined using a stepwise procedure. There were 12 candidate variables across social/demographic/economic, clinical and patient-reported outcome domains.

Results: 148 patients were included with median age 52 years, 29% male, 52% obese with a median FMness score of 12 and 29% met FM criteria. They had a median disease duration of 7 years, a median Quality of Life score (PsAQoL) of 12, physician global (musculoskeletal and skin) of 5.1, Disease Activity in Psoriatic Arthritis (DAPSA) 34 and 57% had ≥1 comorbidity. Follow-up was at a median of 6 months (IQR 4.9-6.7) at which point 28% fulfilled PsARC. Multivariable regression models showed that patients meeting FM2016 (OR 0.3 95% CI (0.1, 0.99) or with fibromyalgia symptoms (OR 0.7, 95% CI (0.4, 1.1) per 5 unit increase in FMness (Table) were less likely to meet PsARC after accounting for other predictors of response accepted into the model (living in a less deprived area, concurrent therapies, shorter symptom duration, nail onycholysis, poorer physician and patient global measures).

Conclusion: PsA patients with features of fibromyalgia, particularly those meeting current fibromyalgia criteria, commencing b/tsDMARDs, are considerably less likely to meet response criteria, independently of other predictors of outcome. They are likely to benefit from additional management specifically targeted to their fibromyalgia symptoms.

Disclosure: G. Macfarlane: None; **O. Rotariu**: None; **S. Lembke**: None; **F. Sunzini**: None; **G. Jones**: Amgen, 5; **N. Basu**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Pfizer, 5, Roche, 6, Vifor, 2, 5, 6.

Abstract Number: 0484

Higher Levels of High-sensitivity CRP Are Associated with Future Risk of Developing Psoriatic Arthritis Among Patients with Psoriasis: A Prospective Cohort Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Simple and accessible biomarkers that predict the development of psoriatic arthritis (PsA) among psoriasis patients are critically needed to improve early detection of high-risk individuals. High-sensitivity C-Reactive Protein (hs-CRP) is a biomarker of systemic inflammation. We aimed to assess whether higher levels of hs-CRP are associated with risk of future development of PsA among patients with psoriasis.

Methods: We analyzed data from a prospective cohort of patients with psoriasis without PsA at enrollment. Participants were assessed annually by a rheumatologist for signs and symptoms of PsA. Information on patient demographics, psoriasis features, medications and musculoskeletal symptoms was collected using standard protocols. hs-CRP levels were measured in serum samples collected at baseline using standard commercial assays in a hospital laboratory. The differences in

Table 1 - Baseline patient characteristics

Variable	All (N=589)	Developed PsA (N=57)	No PsA (N=532)
Age (years)	47.3 (13.5)	48.6 (12.2)	47.2 (13.7)
Sex: Female	254 (43.1%)	23 (40.4%)	231 (43.4%)
Duration of psoriasis (years)	16.2 (14.4)	20.2 (15.4)	15.7 (14.2)
hsCRP (mg/L)	3.1 (5.5)	5.4 (13.1)	2.9 (3.8)
PASI	5.2 (5.8)	5.2 (4.8)	5.2 (5.9)
Nail lesions (yes)	272 (46.2%)	31 (54.4%)	241 (45.3%)
BMI (kg/m^2)	27.9 (5.9)	28 (5.4)	27.9 (5.9)
Patient pain score (0-10)	1.5 (2.2)	1.7 (2.2)	1.5 (2.2)
FACIT-fatigue	44.7 (7.1)	42.1 (8)	45 (7)
Current Biologic therapy (yes)	35 (5.9%)	5 (8.8%)	30 (5.6%)
Current non-biologic systemic therapy for psoriasis or UV therapy (yes)	396 (67.2%)	33 (57.9%)	363 (68.2%)

*mean (SD) for continuous variables and frequency (%) for categorical variables
BMI- Body mass index; FACIT - Functional Assessment of Chronic Illness Therapy; hsCRP- high sensitivity C reactive protein

Table 2 – Differences in hsCRP levels by patient group

Variable	Mean hCRP level (SD) in mg/L	P value*
Age		
• >50	3.54 (7.1)	0.11
• ≤50	2.81 (3.88)	
Sex		
• Female	**3.92 (7.13)**	**0.004**
• Male	**2.51 (3.68)**	
BMI		
• >30	**4.75 (4.95)**	**<0.001**
• ≤30	**2.45 (5.61)**	
Arthralgia		
• Yes	**4.20 (8.53)**	**0.003**
• No	**2.71 (3.67)**	
Morning stiffness		
• Yes	3.46 (4.58)	0.61
• No	3.08 (5.57)	
Heel pain		
• Yes	4.62 (4.77)	0.46
• No	3.10 (5.49)	
Axial pain		
• Yes	3.00 (3.83)	0.67
• No	3.20 (6.38)	
Psoriatic nail lesions		
• Yes	3.05 (6.36)	0.79
• No	3.17 (4.60)	
Any pain		
• Yes	3.78 (6.95)	0.79
• No	2.54 (3.64)	
On biologic therapy		
• Yes	2.42 (3.17)	0.43
• No	3.17 (5.59)	
On non-biologic therapy or UV therapy		
• Yes	3.25 (6.08)	0.42
• No	2.88 (4.00)	
PASI		
• >10	2.46 (2.50)	0.27
• ≤10	3.21 (5.79)	
FACIT-fatigue		
• >50	3.36 (6.38)	0.19
• ≤50	2.25 (6.39)	

*Student's t-test; Bolded = p<0.05.
BMI= Body mass index; FACIT - Functional Assessment of Chronic Illness Therapy; PASI- psoriasis area and severity index

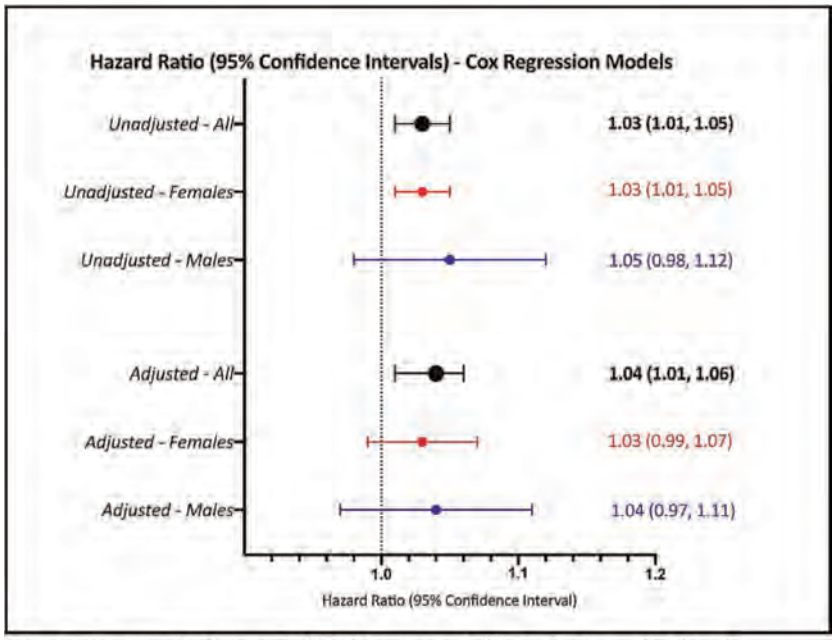

Figure 1: The association between hsCRP and development of PsA by Cox proportional hazards models. Univariate and multivariable regression models adjusted for age, sex, psoriasis duration, PASI, nail lesions, BMI, pain, FACIT-fatigue, use of biologics, and use of non-biologic systemic therapy/UV therapy

average hs-CRP levels were assessed across pre-defined patient groups using t-test. The association between hs-CRP levels and risk of future development of PsA was assessed using multivariable Cox proportional hazards model adjusted for known risk factors for PsA.

Results: A total of 589 patients with psoriasis followed from 2006 to 2019 were analyzed. Mean duration of follow up was 7.5 years. 57 patients developed PsA during the follow up period (incidence of 1.2 events per year). Mean level of hsCRP was 3.1±5.5 mg/L. Patient characteristics are shown in **Table 1**. Significantly higher levels of hs-CRP at baseline were found in patients with arthralgia (4.2±8.53 vs. 2.71±3.67 mg/L), obesity (4.75±4.95 vs. 2.45±5.61 mg/L) and in females (3.92 ±7.13 vs. 2.51±3.68 mg/L); see **Table 2**. Higher hs-CRP levels were associated with future development of PsA in univariate analysis (hazard ratio (HR) 1.03, 95% Confidence Interval (CI) 1.01, 1.05, p=0.002). This association remained significant in the multivariable regression analysis (HR 1.04, 95% CI 1.01, 1.06, p=0.008). Similar effect size was seen in males and females (**Figure 1**). No significant interaction was found between hs-CRP and sex or BMI.

Conclusion: Higher levels of systemic inflammation, as measured by hs-CRP, identify patients with psoriasis at high risk of future development of PsA.

Disclosure: L. Eder: AbbVie, 2, 5, Eli Lilly, 2, 5, Fresenius Kabi, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Sandoz, 5, UCB, 2, 5; **V. Chandran**: AbbVie, 1, 5, 6, Amgen, 1, 5, 6, AstraZeneca, 3, Bristol-Myers Squibb (BMS), 1, 6, Eli Lilly, 1, 5, 6, Janssen, 1, 6, Novartis, 1, 1, 6, UCB, 1, 2; **C. Rosen**: AbbVie/Abbott, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Novartis, 2, UCB, 2; **R. Cook**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, Gilead Sciences, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5.

Abstract Number: 0485

Sex and Treatment-associated Outcomes in Patients with Active Psoriatic Arthritis Treated with Deucravacitinib, an Oral, Selective, Allosteric Tyrosine Kinase 2 Inhibitor, in a Phase 2 Trial

Lihi Eder[1], Alexis R Ogdie[2], Subhashis Banerjee[3], Miroslawa Nowak[3], Thomas Lehman[4] and Philip J. Mease[5], [1]Women's College Research Institute, Division of Rheumatology, University of Toronto, Toronto, ON, Canada, [2]University of Pennsylvania, Philadelphia, PA, [3]Bristol Myers Squibb, Princeton, NJ, [4]Bristol Myers Squibb, Philadelphia, PA, [5]Swedish Medical Center/Providence St. Joseph Health and University of Washington School of Medicine, Seattle, WA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Sex differences have been reported in pathophysiology, clinical manifestations, and treatment responses in several rheumatic diseases, including psoriatic arthritis (PsA).[1] Although PsA is equally prevalent in male and female patients, it is important to understand sex-specific outcomes related to physician assessment of disease activity and patient-reported outcomes (PROs).[1]Previous research also suggests there may be a differential response to therapy with TNF or IL-17 inhibition in male and female patients. Deucravacitinib is a first-in-class, oral, selective, allosteric inhibitor of tyrosine kinase 2 approved in multiple countries for adults with plaque psoriasis.[2,3] Here, we further characterize the effect of deucravacitinib on PsA disease activity by sex as derived from physician assessments and PROs.

Methods: Patients with PsA (N=203) were randomized 1:1:1 to placebo, deucravacitinib 6 mg once daily (QD), or deucravacitinib 12 mg QD in this phase 2 study. Outcomes were reported descriptively by sex. Composite changes in PsA disease activity were assessed by the achievement of ACR 20/50/70 and Minimal Disease Activity (MDA) and by mean changes in Psoriatic Arthritis Disease Activity scores. Mean change from baseline scores were calculated for physician assessments of specific disease domains including both Tender and Swollen Joint Counts, Leeds Enthesitis Index, and Leeds Dactylitis Index. Mean change from baseline scores were calculated for PROs included HAQ Disability Index (HAQ-DI), Patient-Reported Outcomes Measurement Information System (PROMIS)-Fatigue, and Subject Global Assessment of Pain (Pain).

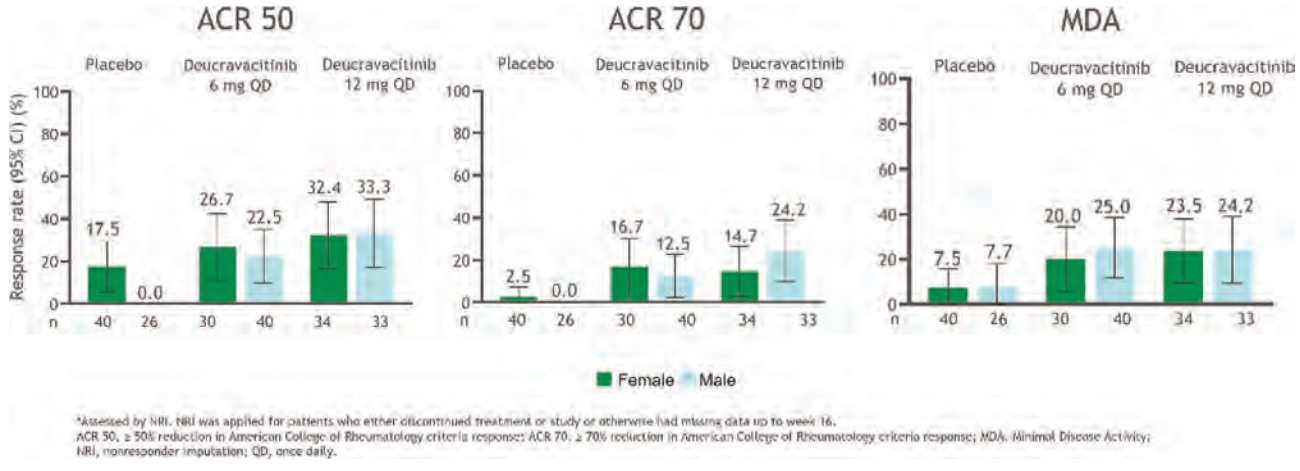

Figure 1. Disease activity measures: ACR 50, ACR 70, and MDA response rate by sex (a)

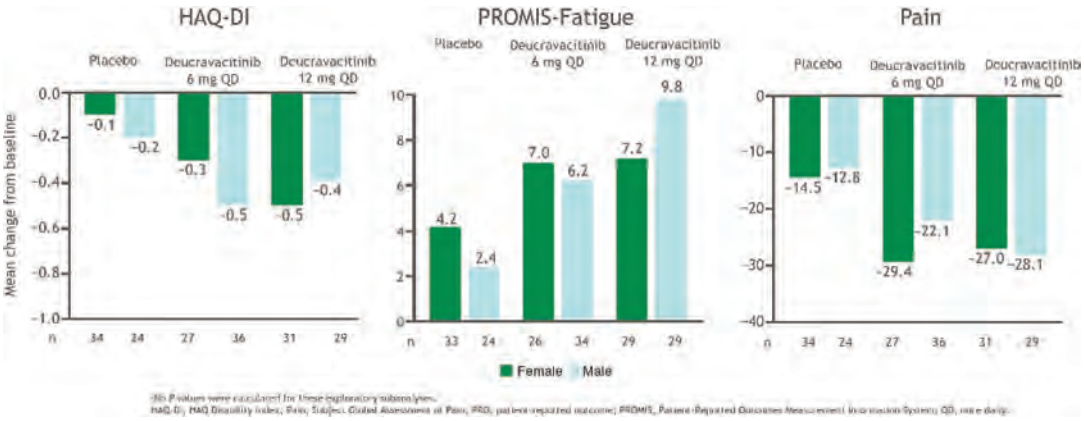

Figure 2. PROs: mean change from baseline in HAQ-DI, PROMIS-Fatigue, and Pain scores by sex (a)

Table. Baseline characteristics

Treatment	Placebo (n = 66)		Deucravacitinib 6 mg QD (n = 70)		Deucravacitinib 12 mg QD (n = 67)	
Sex	Male (n = 26)	Female (n = 40)	Male (n = 40)	Female (n = 30)	Male (n = 33)	Female (n = 34)
Age at disease onset, y						
Median (range)	34.5 (3.0–66.0)	41.5 (16.0–68.0)	35.5 (12.0–67.0)	43.0 (13.0–70.0)	41.0 (21.0–72.0)	39.5 (20.0–69.0)
Duration of disease, y						
Median (range)	3.7 (0.6–21.5)	4.7 (0.7–22.9)	5.8 (0.1–29.5)	4.7 (0.1–42.8)	3.3 (0.6–21.0)	4.5 (0.6–27.7)
Use of MTX at baseline, n (%)						
Yes	13 (50.0)	26 (65.0)	23 (57.5)	12 (40.0)	19 (57.6)	18 (52.9)
No	13 (50.0)	14 (35.0)	17 (42.5)	18 (60.0)	14 (42.4)	16 (47.1)
MTX weekly dose at baseline, mg						
Median (range)	15.0 (10.0–25.0)	16.3 (10.0–25.0)	15.0 (10.0–25.0)	20.0 (7.5–25.0)	15.0 (10.0–25.0)	15.0 (10.0–25.0)
Oral steroid dose at baseline						
Median (range)	4.0 (1.3–8.0)	4.0 (4.0–5.0)	5.0 (2.0–5.0)	4.0 (2.0–4.0)	4.0 (1.3–5.0)	3.5 (2.0–5.0)
Use of NSAID at baseline, n (%)						
Yes	14 (53.8)	28 (70.0)	25 (62.5)	17 (56.7)	23 (69.7)	18 (52.9)
No	12 (46.2)	12 (30.0)	15 (37.5)	13 (43.3)	10 (30.3)	16 (47.1)
No. of biologic DMARDs used prior to first treatment, n (%)						
0	21 (80.8)	34 (85.0)	34 (85.0)	24 (80.0)	30 (90.9)	28 (82.4)
1	5 (19.2)	6 (15.0)	4 (10.0)	6 (20.0)	3 (9.1)	5 (14.7)
2	0	0	2 (5.0)	0	0	0
≥ 3	0	0	0	0	0	1 (2.9)
Use of nonbiologic DMARDs at baseline, n (%)						
Yes	17 (65.4)	27 (67.5)	27 (67.5)	18 (60.0)	22 (66.7)	21 (61.8)
No	9 (34.6)	13 (32.5)	13 (32.5)	12 (40.0)	11 (33.3)	13 (38.2)
Baseline HAQ-DI score						
Median (range)	1.1 (0.0–2.5)	1.5 (0.4–2.5)	1.1 (0.0–2.4)	1.4 (0.1–2.3)	1.3 (0.0–2.9)	1.4 (0.4–2.4)
Individual ACR components at baseline, mean (SD)						
Tender Joint Count	17.23 (11.5)	16.7 (8.7)	16.8 (9.8)	19.8 (10.9)	18.4 (9.6)	20.3 (13.7)
Swollen Joint Count	11.9 (8.1)	9.7 (7.5)	12.2 (6.6)	11.6 (7.6)	10.9 (6.3)	11.7 (11.0)
Subject global assessment of pain	63.0 (19.9)	66.2 (17.2)	59.7 (25.4)	68.7 (14.3)	64.1 (13.7)	63.5 (18.0)
Subject global assessment of disease activity	65.3 (14.6)	66.7 (16.7)	65.5 (19.2)	71.8 (12.5)	62.1 (15.9)	65.1 (15.4)
Physician global assessment of disease activity	70.3 (13.6)	59.5 (14.2)	69.8 (13.5)	66.1 (16.2)	67.1 (12.0)	59.6 (18.7)
HAQ-DI	1.2 (0.6)	1.4 (0.5)	1.2 (0.6)	1.4 (0.5)	1.2 (0.7)	1.4 (0.5)
CRP, mg/L	30.4 (55.4)	13.9 (21.6)	21.7 (28.5)	12.1 (13.4)	18.6 (24.2)	14.6 (19.2)
BSA ≥ 3% at baseline, n (%)						
Yes	24 (92.3)	30 (75.0)	36 (90.0)	23 (76.7)	28 (84.8)	24 (70.6)
No	2 (7.7)	7 (17.5)	4 (10.0)	7 (23.3)	5 (15.2)	9 (26.5)
Not reported	0	3 (7.5)	0	0	0	1 (2.9)
Baseline PASI score in patients with BSA ≥ 3% at baseline, n (%)						
Median (range)	11.5 (1.6–31.4)	5.2 (1.2–18.0)	6.5 (1.6–33.8)	5.2 (1.8–16.4)	6.9 (1.8–31.8)	5.9 (1.4–18.3)

BSA, body surface area; HAQ-DI, HAQ Disability Index; PASI, Psoriasis Area and Severity Index; QD, one daily.

Results: Baseline characteristics were balanced between sexes and are shown in the **Table**. A higher percentage of patients of both sexes treated with deucravacitinib achieved ACR 50, ACR 70, and MDA responses at week 16 compared with placebo (**Figure 1**). In addition, a greater mean change from baseline HAQ-DI, PROMIS-Fatigue, and Pain scores occurred in patients treated with deucravacitinib compared with placebo among both sexes (**Figure 2**). Treatment-associated responses were generally similar between sexes in disease activity assessments and PROs.

Conclusion: Patients treated with deucravacitinib more frequently achieved reductions in disease activity measures and had greater changes from baseline scores for PROs compared with patients who received placebo. Deucravacitinib has comparable effects on PsA disease activity and PROs for the instruments assessed after 16 weeks of treatment in male and female patients.

References:

1. Coates L, et al. *J Rheumatol* 2023; 50:488–496.
2. Armstrong A, et al. *J Am Acad Dermatol* 2023;88:29–39.
3. Strober B, et al. *J Am Acad Dermatol* 2023;88:40–51.

Disclosure: L. Eder: AbbVie, 2, 5, Eli Lilly, 2, 5, Fresenius Kabi, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Sandoz, 5, UCB, 2, 5; **A. Ogdie**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, UCB, 2; **S. Banerjee**: Bristol-Myers Squibb(BMS), 3, 11; **M. Nowak**: Bristol-Myers Squibb(BMS), 3, 11; **T. Lehman**: Bristol-Myers Squibb(BMS), 3; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2.

Abstract Number: 0486

Identifying Serum Metabolomic Markers Associated with Psoriasis Skin Disease Activity

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriasis is a chronic, immune-mediated inflammatory skin disease that affects over 2.5% of the global population. Approximately 25% of psoriasis patients also have a form of inflammatory arthritis called psoriatic arthritis (PsA). Current methods for evaluating skin disease activity, like Psoriasis Area and Severity Index (PASI), are subjective and

prone to intra- and inter-rater variability. A metabolomics-based approach can elucidate psoriatic disease pathogenesis and provide potential objective biomarkers. Therefore, we aimed to use solid phase microextraction (SPME) with liquid chromatography coupled with mass spectrometry (LC-MS) with the hypothesis that serum metabolites are associated with skin disease activity.

Methods: Serum samples from PsA patients (n=151, summary of demographics and disease characteristics shown in Table 1) with active skin disease and a range of PASI scores were selected. Patients were classified into 3 groups of psoriasis activity based on PASI- low (PASI 1-4.8) n=56, moderate (PASI 5-9.8) n=45, and High (PASI 10.1-54.6) n=40. SPME devices were prepared in-house and used to conduct the sample preparation, followed by positive and negative ion mode data acquisition via an untargeted approach using LC-MS. Associations between the levels of each metabolite and PASI scores was evaluated using 8 Machine learning (ML) models including support vector machine (SVM), random forest, and Naïve Bayes (NB) with varied feature sizes of 1-80. These models were summarised using Area Under Receiver Operator Characteristic curves (AUROC) for performance. Statistically significant metabolite features were tentatively identified.

Results: ML models were able to distinguish between low and high PsA severity with Area Under Curve (AUC) score as low as 0.745 for 10 features, and as high as 0.813 for 40 features. Trends were similar for other disease activity comparisons. A SVM model with 10 features were able to predict between low and high severity PsA with AUC = 0.862, and p-value < 0.05. Table 2 provides a summary of the results of the analyses. The features of interest used in best performing models were associated with dysregulation of fatty acid metabolism when predicting between low PASI versus moderate or high PASI.

Table 1: Summary of disease characteristics and patient demographics

Total = 151 patients		
LOW PASI 1-4.8 Ages 18-75	**MODERATE** PASI 5-9.8 Ages 19-73	**HIGH** PASI 10.1-54.6 Ages 22-81
28 M	28 M	28 M
28 F	27 F	12 F
56 TOTAL	55 TOTAL	40 TOTAL

Table 2: Top 10 Tentatively Identified Metabolites for Low vs High PASI Disease Activity

m/z	Ret. Time (min)	Adduct	Monoisotopic Mass	Tentative Identification
412.4147	14.784	$[M+NH4]^+$	394.3811	Ximenic Acid; 1 other hit
546.3528	14.588	$[M+Na]^+$	523.3638	Platelet-activating factor; 6 other hits
544.3373	13.349	$[M+Na]^+$	521.3481	LysoPC(0:0/18:1(9Z)); 5 other hits
116.0708	0.603	$[M+H]^+$	115.0633	Proline
427.1938	5.737	$[M+NH4]^+$	409.1584	dermatan L-iduronate; 1 other hit
496.3397	12.948	$[M+Na]^+$	473.3505	Clupanodonyl carnitine; 5 other hits
373.2735	9.793	$[M+H]^+$	372.2664	Cervonoyl ethanolamide
520.3398	12.332	$[M+H]^+$	519.3325	LysoPC(0:0/18:2(9Z,12Z)); 1 other hit
370.2950	8.204	$[M+NH4]^+$	352.2614	MG(18:3(6Z,9Z,12Z)/0:0/0:0); 8 other hits
289.1409	5.124	$[M+Na]^+$	266.1518	pentadeca-5,7,9-trienedioic acid; 8 other hits

Some metabolites tentatively identified include eicosanoids with anti- or pro-inflammatory properties, like 12-Hydroxyeicosatetraenoic acid, which was previously implicated in joint disease activity in PsA. Other tentatively identified features belong to classes such as bile acid metabolites, oxidized phospholipids, N-acrylamide, and long-chain fatty acids.

Conclusion: An untargeted metabolomics approach was employed to analyze potential differences in serum metabolome of PsA patients of varying skin disease activity. Confirmation and validation of the tentatively identified circulating metabolites should be conducted to reveal potential biomarkers of PsA disease activity.

Disclosure: H. Choksi: None; **S. Li**: None; **N. Looby**: None; **M. Kotlyar**: None; **V. Kulasingam**: None; **I. Jurisica**: None; **V. Chandran**: AbbVie, 1, 5, 6, Amgen, 1, 5, 6, AstraZeneca, 3, Bristol-Myers Squibb (BMS), 1, 6, Eli Lilly, 1, 5, 6, Janssen, 1, 6, Novartis, 1, 1, 6, UCB, 1, 2.

Abstract Number: 0487

A Comparative Study of Serositis Between Inpatients with Psoriatic Arthritis and Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune diseases such as rheumatoid arthritis (RA) and psoriatic arthritis (PsA) can causes erositis including pericarditis and pleuritis. However, the rate of serositis in PsA is not defined, though several case reports have described pleuropericardial involvement. The prevalence of pericarditis in RA ranges from 30% to50%. This study aimed to estimate the frequency of pleuropericarditis in PsA vs RA.

Methods: A retrospective chart review of hospitalized patients with RA and PsA was conducted between 2013 and 2021. The frequencyof pericarditis or pleuritis was compared between RA and PsA patients. This study was approved by the Institutional Review Board of Stony Brook University.

Results: There were a total of 113 inpatients aged 18 and 65 (Table 1). These patients were divided into two groups: 57 patients with RA (Group 1) and 56 with PsA (Group 2). Of the 57 RA patients, 48 patients had pericardial or pleural effusions and 46 were determined to have idiopathic etiology. Of the 56 PsA patients, 42 had pericardial or pleural effusions and 23 were considered idiopathic. Approximately 41% of PsA patients had idiopathic pericardial or pleural effusions as compared with 81% RA patients. This shows a statistically significant difference between the two groups ($P < 0.0001$).

Conclusion: This study suggests that both RA and PsA patients can cause pleuropericarditis, and the frequency of idiopathic etiology in RA may be two-fold higher than PsA. Further study using a larger cohort of patients is warranted to accurately estimate the rate of serositis.

Table 1: comparison of pleuropericardial involvement between psoriatic arthritis and rheumatoid arthritis

Variable	Nmissing	Level	Total (N=113)	RA category (N=57)	PSA category (N=56)	P-value*
Age	0	56 vs 57	54.65±9.69	55.23±10.11	54.07±9.30	0.5279
Gender	0	Female	77 (68.14%)	41 (71.93%)	36 (64.29%)	0.3832
		Male	36 (31.86%)	16 (28.07%)	20 (35.71%)	
Race	0	Caucasian	97 (85.84%)	45 (78.95%)	52 (92.86%)	0.0588
		Other	16 (14.16%)	12 (21.05%)	4 (7.14%)	
Pericardial effusion	0	No	30 (26.55%)	9 (15.79%)	21 (37.50%)	0.0090
		Yes	83 (73.45%)	48 (84.21%)	35 (62.50%)	
Pleural effusion	0	No	29 (25.66%)	15 (26.32%)	14 (25.00%)	0.8728
		Yes	84 (74.34%)	42 (73.68%)	42 (75.00%)	
Idiopathic	0	No	44 (38.94%)	11 (19.30%)	33 (58.93%)	<.0001
		Yes	69 (61.06%)	46 (80.70%)	23 (41.07%)	
Infection-related	0	No	88 (77.88%)	49 (85.96%)	39 (69.64%)	0.0366
		Yes	25 (22.12%)	8 (14.04%)	17 (30.36%)	
Cancer-related	0	No	105 (92.92%)	55 (96.49%)	50 (89.29%)	0.1619
		Yes	8 (7.08%)	2 (3.51%)	6 (10.71%)	
Drug-related	0	No	110 (97.35%)	56 (98.25%)	54 (96.43%)	0.6191
		Yes	3 (2.65%)	1 (1.75%)	2 (3.57%)	

*: For categorical variables, p-values were based on Chi-squared test with exact p-value from Monte Carlo simulation; for continuous variable, p-value was based on Welch's test.
Note: 1. For continuous variable, mean ± standard deviation were reported.
2. Column percentages were reported.

References

1. Movahedian M, et al. Chest pain due to pericardial effusion as initial presenting feature of rheumatoid arthritis: case report and review of the literature. Cardiology research. 2017; 8(4): 161.
2. Esposito M, et al. Resolution of idiopathic recurrent pericarditis in a psoriatic arthritis patient treated with etanercept. European Journal of Dermatology. 2012; 22(1): 151-152.

Disclosure: A. Saif: None; **P. Dongare**: None; **M. Beard**: None; **Y. Liao**: None; **X. Zhang**: None; **Q. Yao**: None; **A. Patnaik**: None.

Abstract Number: 0488

Factors Associated with Work Productivity Among Individuals with Psoriatic Arthritis (PsA) and Psoriasis (PsO): The Role of Patient Reported Outcomes and Disease Severity

Nancy Shadick[1], Kumiko Schnock[2], Vivi Feather[3], Ruogu Li[2], Jing Cui[1], Shivani Patel[2], Sabrina Goutier[1], Muibat Yussuff[2], Lourdes Perez-Chada[2], Michael Weinblatt[4] and Joseph Merola[5], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital, Boston, MA, [3]Mass General Brigham, Boston, MA, [4]Harvard Medical School, Waban, MA, [5]Harvard Medical School, Brigham and Women's Hospital, Newton, MA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with Psoriatic Arthritis (PsA) and Psoriasis (PsO) have an increased rate of work loss due to their disease compared the general population; however, little is known about the impact of their illness on work productivity among those who remain employed. Our goal was to evaluate the differential effect of self-reported disease symptoms and severity on the ability to work.

Methods: Data from study subjects who participated in the Cohort of Psoriasis and Psoriatic Arthritis Registry (COPPAR), a prospective, longitudinal registry of adult subjects with PsA or PsO at a large academic medical center, were analyzed. Demographics and disease characteristics of the study subjects were summarized by diagnosis (PsA vs. PsO) and compared using univariate statistics. Work Productivity and Activity Impairment (WPAI) survey data were collected at baseline and assessed in three binary domains: missed work, impaired work productivity, and impaired daily activity due to their illness. All subjects had disease severity measured by the Psoriasis Area and Severity Index (**PASI**), and self-reported disease

Table 1. Employed Study Subjects' Characteristics in the COPPAR Registry

	PsA (N=113)	PsO (n=67)	*P* value
Age, mean (SD), years	50.9 (10.8)	48.4 (14.7)	0.27
Female, n (%)	50 (44.3)	31 (46.3)	0.79
Race, n (%)			
White	101 (89.4)	55 (82.1)	0.16
Ethnicity, n (%)			
Hispanic or Latino	2 (1.8)	6 (9.0)	0.05
Disease Duration, years (median, IQR)	22 (13, 32)	15 (6, 29)	**0.04**
Current Psoriatic Disease Therapy, n (%)			
Conventional Systemic DMARDs*	20 (17.86%)	4 (6.06%)	**0.03**
Biologic Systemic DMARDs	89 (78.76%)	37 (55.22%)	**<0.001**
Topical Agents	63 (55.75%)	46 (68.66%)	0.09
Clinician Assessments (median, IQR)			
BSA	1 (0, 2)	2 (1, 5)	**<0.001**
PGA	1 (0, 2)	2 (1, 3)	**<0.001**
PASI	0.6 (0, 2.1)	2.4 (0.4, 4.5)	**<0.001**
Patient Self-Reported Symptoms (median, IQR)			
Pain[a]	1 (1, 1)	0 (0, 1)	**<0.001**
Fatigue[b]	1 (1, 2)	1 (0, 2)	0.10
Itch[c]	1 (0, 3)	2 (0, 5)	0.06
Patient Reported Outcomes (median, IQR)			
Skin Global Assessment	8 (5, 9)	8 (5, 9)	0.40
SF-12 Physical	46.30 (36.92, 52.6)	54.78 (47.13, 55.89)	**<0.001**
SF-12 Emotional	52.91 (44.54, 57.84)	51.44 (41.56, 57.1)	0.18
DLQI	2 (0, 5)	3 (0, 7)	0.30
PHQ-8	2 (1, 5)	3 (1, 6)	0.80
PROMIS Anxiety	45.90 (37.10, 54.3)	49.40 (37.10, 54.3)	0.43
EQ-5D	0.82 (0.77, 0.83)	0.84 (0.82, 1)	**<0.001**
WPAI, n (%) #			
Missed Work Hours	18 (15.93%)	13 (19.40%)	0.55
Work Productivity Impaired	50 (44.25%)	17 (25.37%)	**0.01**
Daily Activity Impaired	60 (53.10%)	14 (20.90%)	**<0.001**

SD: Standard Deviation, IQR: Interquartile Range. DMARD: Disease-Modifying Antirheumatic Drug, BSA: Body Surface Area, PGA: Physician's Global Assessment, PASI: Psoriasis Area and Severity Index, SF-12: The 12-Item Short Form Health Survey, DLQI: Dermatology Life Quality Index, PHQ-8: The Eight-Item Patient Health Questionnaire Depression Scale, PROMIS: Patient-Reported Outcomes Measurement Information System, EQ-5D: European Quality of Life- 5 Dimensions, WPAI: Work Productivity and Activity Impairment #Each WPAI element is binary. % Yes are reported.

*Pain is assessed by a 3-level scale pain question in European Quality of life-5D (EuroQol-5D) where 0 represents the patient has no pain or discomfort, and 2 represents that the patient has extreme pain or discomfort. [b]Fatigue is assessed by a 5-level scale question from the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fversion 4) questionnaire where 0 represents that the patient does not feel fatigued at all and 4 represents that the patient feels very tired. [c]Itch is assessed by a numeric itchiness rating scale where 0 represents no itch, and 10 represents the worst imaginable itch.

Table 2: Association between WPAI Scores and Demographic, Disease Severity, and Symptom Related Covariates in the COPPAR Registry

	Multivariate Model*								
	Missed Work Hours			Work Productivity Impaired			Daily Activity Impaired		
Covariates	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Diagnosis (PsA vs. PsO)	0.41	(0.14, 1.24)	0.11	1.98	(0.69, 5.71)	0.21	3.73	(1.39, 10.02)	**0.01**
Pain[a]	2.43	(0.87, 6.82)	0.09	6.94	(2.41, 19.98)	**<0.001**	5.6	(2.16, 14.53)	**<0.001**
Fatigue[b]	2.17	(1.42, 3.3)	**<0.001**	2.39	(1.56, 3.65)	**<0.001**	2.16	(1.45, 3.22)	**<0.001**
Itch[c]	0.99	(0.81, 1.2)	0.89	1.3	(1.07, 1.57)	**0.01**	1.12	(0.94, 1.34)	0.22
PASI[d]	0.96	(0.87, 1.06)	0.40	1.05	(0.92, 1.19)	0.47	1.01	(0.91, 1.13)	0.79

*Adjusted for age, gender, and race. [a]Pain is assessed by a 3-level scale pain question in European Quality of Life-5D (EuroQol-5D) where 0 represents the patient has no pain or discomfort, and 2 represents that the patient has extreme pain or discomfort. [b]Fatigue is assessed by a 5-level scale question from the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F version 4) questionnaire where 0 represents that the patient does not feel fatigued at all and 4 represents that the patient feels very tired. [c]Itch is assessed by a numeric itchiness rating scale where 0 represents no itch, and 10 represents the worst imaginable itch. [d]PASI: Psoriasis Area and Severity Index

symptoms were assessed as the amount of overall pain, degree of skin itch, and fatigue measured on a rating scale. Symptoms and disease severity variables, along with demographics, were tested in logistic regression models to determine their associations with WPAI outcomes.

Results: Of 288 cohort subjects who completed the WPAI survey, 180 (63%) subjects were currently employed (113 PsA and 67 PsO subjects). Study subjects had a mean age of 49.7 years, 45.3% female, and 85.8% White (Table 1). The mean disease duration was 22 years for PsA and 15 years for PsO (p=0.04). PsO subjects had more severe skin disease, while PsA subjects were more likely to be on biologic therapies (Table 1). In univariate analyses, there were no statistically significant differences in missed work between PsA and PsO subjects (15.93% vs. 19.40%, p=0.55), but PsA subjects reported more impaired work productivity (44.25% vs. 25.37%, p=0.01) and impaired daily activities outside of work hours (53.10% vs. 20.9%, p< 0.001). However, the adjusted regression model showed that study subjects who had missed work reported more fatigue ([Odds Ratio (OR)]:2.17, p< 0.001). Study subjects who had impairment in work productivity reported more pain (OR:6.94, p< 0.001), fatigue (OR:2.39, p< 0.001), and itch (OR:1.3, p=0.01). Study subjects who reported daily activity impairment outside of work hours reported more fatigue (OR:2.16, p< 0.001), pain (OR:5.6, p< 0.001) and were more likely to have PsA than PsO (OR: 3.73 p=0.01). Of note, the PASI score was not associated with any of the three WPAI impairment domains.

Conclusion: While employed individuals with PsA reported more impaired work productivity than those employed who had PsO, impairment was driven by pain, itch, and fatigue rather than arthritis diagnosis and skin disease severity. Eliciting these symptoms may help rheumatologists better tailor interventions to improve an individual's capacity to work.

Disclosure: N. Shadick: Abbvie, 5, AQtual, 5, Bristol-Myers Squibb(BMS), 5, Janssen, 5; **K. Schnock**: AbbVie, 5, Bristol-Myers Squibb(BMS), 5; **V. Feather**: None; **R. Li**: None; **J. Cui**: None; **S. Patel**: None; **S. Goutier**: None; **M. Yussuff**: None; **L. Perez-Chada**: None; **M. Weinblatt**: Abbvie, 2, 5, Aclaris, 2, Amgen, 2, Aqtual, 5, Bristol Myers Squibb, 2, 5, Canfite, 11, Corevitas, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, 2, Glaxo Smith Kline, 2, Horizon, 2, Inmedix, 11, Janssen, 5, Johnson and Johnson, 2, Pfizer, 2, Prometheus Laboratories, 2, Rani, 2, Revolo, 2, Sanofi, 2, Sci Rhom, 2, Scipher, 2, 11, Set Point, 2, UCB, 2; **J. Merola**: Abbvie, 2, 12, Investigator, Amgen, 2, 12, Investigator, Biogen, 2, 12, Investigator, Bristol-Myers Squibb, 2, 12, Investigator, Dermavant, 2, 12, Investigator, Eli Lilly, 2, 6, 12, Investigator, Janssen, 2, 12, Investigator, Leo Pharma, 2, 12, Investigator, Novartis, 2, 12, Investigator, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, 12, Investigator, Sun Pharma, 2, 12, Investigator, UCB Pharma, 2, 12, Investigator.

Abstract Number: 0489

Prediction of Low Disease Activity in Patients with Psoriatic Arthritis Treated with Secukinumab in Real World – Data from a German Observational Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA
Session Type: Poster Session A
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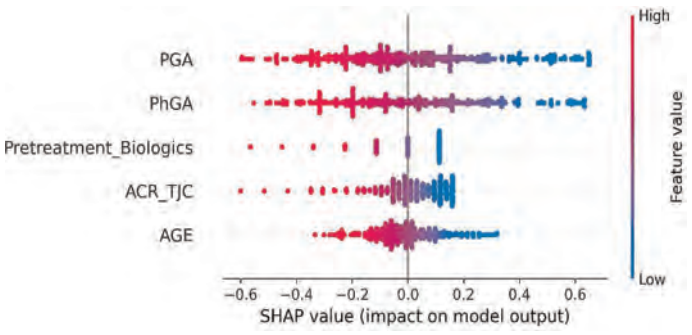
Background/Purpose: Secukinumab (SEC) proved to be an effective treatment for patients with psoriatic arthritis (PsA) in previous randomized clinical trials [1]. There is only limited knowledge on prediction of low disease activity (LDA) and treatment strategy in PsA patients under SEC treatment in routine clinical care.

Using real-world data from the German non-interventional study AQUILA [2], the main objectives were (1) to predict LDA in individual PsA patients treated with SEC through machine learning methods and (2) to identify the most important predictors and their influence on the prediction using explainable artificial intelligence (XAI).

Methods: Data of 1041 PsA patients from the AQUILA study were used. Thirty-three demographic, clinical and treatment parameters at baseline (BL) served as input data to develop prediction models. LDA was defined as physician global assessment (PhGA) ≤ 2 at week (w) 16 (+/- 6 w). Samples were divided into training (70%) and validation (30%) cohorts. Ten different prediction models were applied and compared. Model performance was measured using area under the receiver operating characteristic curve (AUROC) which represents the probability that a randomly selected patient with LDA will have higher prediction to achieve LDA than a patient with moderate/high disease activity. Additionally, sensitivity and specificity of the prediction model were computed and express the proportion of correctly identified patients who reach or don't reach LDA at w16, respectively. Shapley XAI estimated importance and impact of each predictor based on how it affected the change in individual prediction [3].

Results: The most influencing predictor was patient global assessment (PGA) at BL, followed by PhGA, number of pretreatments with biologics, tender joint count and age (Figure 1 A). AUROC of the best prediction model was 0.68 in validation cohort. Sensitivity and specificity were 0.62 and 0.64, respectively. Applied XAI approach showed that lower BL values of



A: Main predictors at baseline and their direction of influence based on Shapley values [3]

B: Explanation of patient-individual prediction of 79% using baseline data

all main predictors have higher probability of reaching LDA at w16. The highest probability was evident in biologic-naive patients (Figure 1 A). The approach also provided visual explanations of patient-individual predictions: Variables with values shown in green color increased probability of reaching LDA at w16, whereas red ones showed the opposite effect (Figure 1 B).

Conclusion: A promising prediction model accuracy of LDA in PsA patients treated with SEC could be reached and validated. Identified main predictors at BL, such as PGA and number of pretreatments with biologics, and their direction of influence on the prediction mostly match the existing clinical knowledge [4]. The analysis showed that XAI can provide useful clinical insights in patient-individual predictions, potentially guiding PsA treatment decisions in future.

Disclosure: A. Vodencarevic: Novartis, 3; **J. Brandt-Juergens**: AbbVie/Abbott, 2, 6, Affibody, 2, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Gilead, 2, Janssen, 2, 6, Medac, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **D. Peterlik**: Novartis, 3; **B. Gmeiner**: Novartis, 3; **U. Kiltz**: AbbVie, 2, 5, 6, Amgen, 5, Biocad, 2, 6, Biogen, 5, Bristol-Myers Squibb(BMS), 2, 5, Chugai, 2, 6, Eli Lilly, 2, 6, Fresenius, 5, Gilead, 2, 5, GlaxoSmithKline (GSK), 5, Grünenthal, 2, 6, Hexal, 5, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, onkowiessen.de, 2, 5, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Viatris, 2, 5.

Abstract Number: 0490

Racial/Ethnic Differences in Psoriatic Arthritis Patient Responses Regarding Disease Burden, Treatment, and Communication with Care Team

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The purpose of this study was to examine differences in perceptions of psoriatic arthritis (PsA) disease burden as well as various aspects of care across racial/ethnic groups.

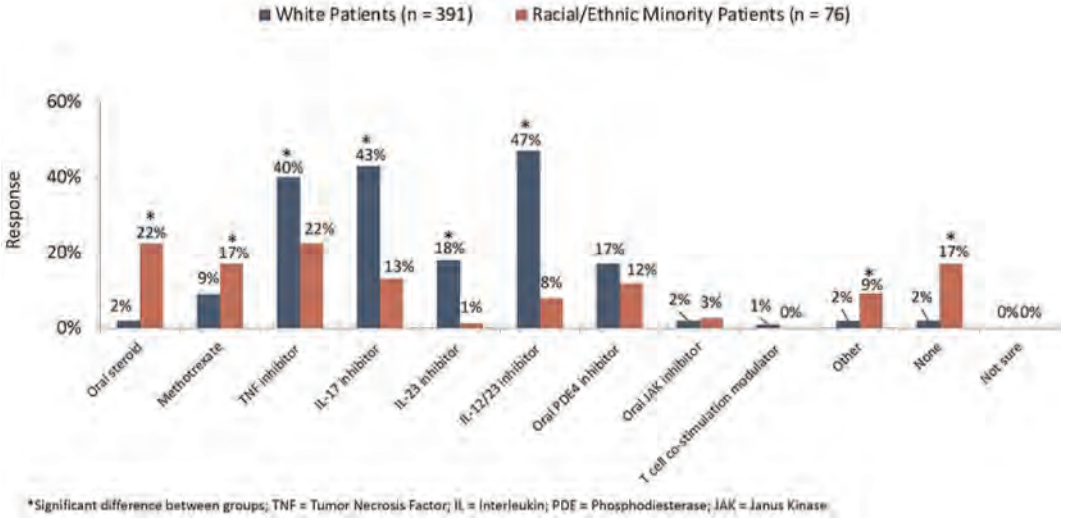
Methods: Survey questions assessing PsA patient insights regarding their disease burden and quality of care were developed. From September to October 2022, surveys were deployed to 455 PsA patients either through a leading advocacy organization email list (n = 420) or an additional national patient survey organization (n = 35). Self-reported race/ethnicity was recorded. If patients selected both "white" and another racial/ethnic group, they were included in both groups in the analysis.*P* values were calculated using the chi-square or Fisher's Exact tests for counts less than 5.

Results: The age of patients ranged from 28 to 91 years. Three hundred ninety-one identified as white and 76 identified with a racial/ethnic minority group (29 African American/Black, 20 Asian/Pacific Islander, 14 Hispanic/Latinx, 8 Native American/Alaska Native, 5 "Other").

Racial/ethnic minority PsA patients were less likely to be diagnosed within 12 months from the onset of symptoms (50% vs 71%; $P < 0.001$) and more frequently uninsured (8% vs. 1%; $P < 0.001$) compared to white patients. Racial/ethnic minority patients more often had self-described severe disease vs. white patients (41% vs. 14%; $P < 0.001$) and extreme impact on quality of life and emotional well-being (25% vs. 6%; $P < 0.001$).

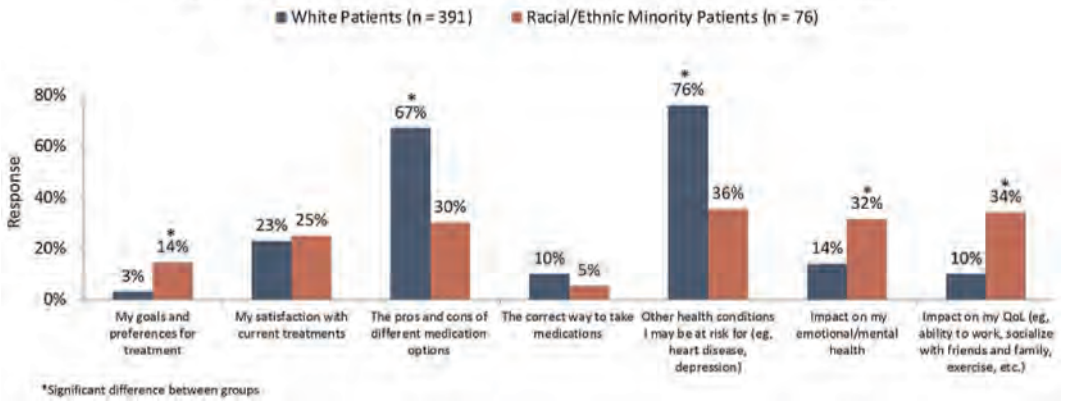
Regarding treatment, racial/ethnic minority PsA patients were less often prescribed a biologic and more frequently received oral glucocorticoids, methotrexate, or no prescription medications compared to white PsA patients (Figure 1). Also less frequent among racial/ethnic minority patients were high levels of knowledge/familiarity with targeted agents such as injectable biologics or oral small molecule inhibitors (42% vs. 81%; $P < 0.001$) and high satisfaction with treatment (39% vs. 77%; $P < 0.001$). Financial barriers to managing PsA were four-fold more common in racial/ethnic minority patients (26% vs. 7%; $P < 0.001$); the difference in concern for risks of medications was similarly significant (29% vs. 3%; $P < 0.001$).

Figure 1. Patients' Response to the Question: "Which Prescription Therapies Are You Currently Taking For PsA?"



*Significant difference between groups; TNF = Tumor Necrosis Factor; IL = Interleukin; PDE = Phosphodiesterase; JAK = Janus Kinase

Figure 2. Patients' Response to the Question: "Which of the Following Do You Wish You Had More Time To Discuss With Your PsA Care Team?"



*Significant difference between groups

Gaps in communication with the PsA care team were also observed. Racial/ethnic minority patients were less likely to feel that they were very/extremely involved in shared decisions regarding their care (60% vs. 82%; $P < 0.001$). When asked what they wished they had more time to discuss with their care team, racial/ethnic minority PsA patients requested various aspects of the impact of the disease as well as goals and preferences for treatment (Figure 2). Notably, the advantages and disadvantages of different treatment options and comorbidities were a lower priority in racial/ethnic minority patients despite a higher percentage of comorbid disease (Figure 2).

Conclusion: These survey findings confirm racial/ethnic disparities across the spectrum of PsA disease from time to diagnosis to treatment, and underscore the dissatisfaction with overall care. There is a need for more time to be spent on educating individuals with PsA to enable shared decisions and improved understanding of therapeutic options.

Disclosure: I. Navarro-Millán: None; **G. Kerr**: AstraZeneca, 2, Aurinia, 6, Horizon, 2, Janssen, 2, Pfizer, 1, Sanofi, 2; **J. Carter**: None; **L. Simone**: None; **M. Nelson**: None.

Abstract Number: 0491

Arthralgia with Risk of Progression to Psoriatic Arthritis in a Large Cohort of Patients: Role of Ultrasound

rodrigo garcía salinas[1], Jonatan Mareco[2], Santiago Ruta[2], RONALD PEREZ[2], Felica Almada[2] and Sebastián Juan Magri[3], [1]Arthritis and Spondyloarthritis Unit, Hospital Italiano de La Plata, National University of La Plata, La Plata, Argentina, [2]Hospital Italiano de La Plata, La Plata, Argentina, [3]Hospital Italiano La Plata, Melchor Romero, Argentina

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The psoriasis- to- psoriatic arthritis (PsA) transition offers a unique opportunity to identify individuals at increased risk of developing PsA and to implement preventive strategies. **Objectives**: To estimate the frequency of arthralgia with risk of progression to PsA (ARP-PsA) in a large cohort of patients and to estimate the incidence of PsA at one year in ARP-PsA patients analyzing clinical, laboratory and imaging predictor variables.

Methods: Prospective cohort study, include patients over 18 years of age who were admitted consecutively for arthralgias, to the¨Reuma-check program. In this, the baseline included: laboratory, X-rays, ultrasound (US) with power Doppler (PD) and clinical interview. Sociodemographic data, clinical and clinimetry (global VAS, joint count, HAQ) were collected. Each evaluator (laboratory, imaging and clinical) were blinded to the data of the other studies. Presence of psoriasis (Pso) and family history (FH) were investigated. Patients with previous diagnosis of PsA were excluded. The ARP-PsA was defined as those patients with arthralgia plus Pso and/or FH. This group was evaluated at one year to estimate if they developed PsA. Statistical analysis: descriptive statistics, Chi2 test, Fisher's exact test, Student's T test and Mann Whitney was performed. A multivariate logistic regression: dependent variable the final diagnosis of PsA at year.

Results: A total of 1419 patients with arthralgia were included between July 2017 and March 2022, 8.4% (95% CI: 7-10) met ARP-PsA criteria. Of these 119 patients 34 developed PsA at 1 year (29%, 95%CI: 20-37). The clinical, laboratory and imaging characteristics between ARP-PsA patients who did and did not develop PsA are shown in table 1 (univariate analysis). Of the ARP-PsA patients who had only Pso (n 32), only family history (n 70) or both combine (n 17) developed PsA at 1 year: 57%, 11% and 53% respectively. Longer duration of psoriasis was associated with the development of

Features	ARP-PsA no PsA (85)	ARP-PsA yes PsA (34)	p	RR (95%IC)
Age (years), mean (SD)	48 (14)	49 (15)	0.9	
Female, %	78	61	0.06	0.4 (0.2-1)
Years of education, median (IQR)	14 (3)	13 (3)		
Time between the onset of symptoms and the baseline visit (months), mean (SD)	13 (30)	18 (30)	0.2	
Smoking, %	36	44	0.4	1.3 (0.6-3)
Cardiometabolic comorbidities, %	40	35	0.6	0.6 (0.3-1.8)
Family psoriasis, %	80	47	>0.001	**0.2 (0.1-0.5)**
Pso + Family history Pso	8	26	**0.008**	**4 (1.3-12)**
Cutaneous psoriasis, %	26	73	>0.001	**8 (3-20)**
Pso duration time (years) median (IQR)	3 (15)	15 (15)	**0.03**	
Patient global VAS (0-100), mean (SD)	50 (23)	60 (15)	**0.04**	
Tender joints (28), median (IQR)	2 (4)	1.5 (3)	**0.05**	
Arthralgia less than one year, %	38	19	**0.04**	**0.4 (0.1-0.8)**
Morning stiffness, %	16	12	0.6	0.7 (0.2-2)
Squeeze test +, %	22	31	0.3	1.5 (0.6-4)
ESR, mean (SD)	17 (13)	18 (16)	0.6	
CRP +, %	21	28	0.6	1.2 (0.8-1.7)
CRP, median (IQR)	1 (2.7)	3 (4)	0.4	
HAQ, median (IQR)	0.5 (0.8)	0.8 (0.75)	0.1	
X-ray bone erosions, %	4	26	**0.004**	**7 (2-28)**
X-ray, joint narrowing, %	25	19	0.5	7 (0.2-2)
Ultrasound synovitis, Tenosynovitis, %	8	12	0.5	1.6 (0.4-6)
Ultrasound synovitis, Gray Scale, %	5	21	**0.01**	**5 (1.3-18)**
Ultrasound synovitis, Power Doppler signal, %	1.3	12	**0.01**	**10 (1.1-98)**
Ultrasound, Enthesopathy findings, %	4	53	>0.001	**25 (6.5-99)**

Clinical, laboratory and imaging characteristics between ARP-PsA patients who did and did not develop PsA

PsA: median years:15 vs 3. In multivariate analysis, the predictor variables for progression from ARP-PsA to PsA at one year were: combination of Pso plus FH (OR: 32; CI 95%: 1.2-1026), synovitis by PDUS (OR: 31; CI 95%: 1.1-967), US enthesopathy findings (OR: 470; CI 95%: 13-1600) and tender joint count (OR 0.2 CI95% 0.05-0.6).

Conclusion: The frequency of patients at risk of progression to PsA (arthralgia plus PsA and/or FH) in our cohort was 8.4%, of whom 29% developed PsA at 1-year follow-up. The main predictor variables were US findings (synovitis and enthesopathy), as well as the combination of Pso plus FH, a lower number of tender joints, and a longer duration of the Pso.

Disclosure: r. garcía salinas: AbbVie, 1, 2, 5, 6, AstraZeneca, 5, Biogen, 5, Bristol Myers Squibb, 1, 2, 5, 6, Genentech, 5, GlaxoSmithKlein, 5, Janssen, 1, 2, 5, 6, Lilly, 1, 2, 6, Merck Serono, 5, Novartis, 1, 2, 6, Roche, 1, 2, 6, Sandoz, 1, 2, 6; **J. Mareco**: None; **S. Ruta**: None; **R. PEREZ**: None; **F. Almada**: None; **S. Magri**: None.

Abstract Number: 0492

Axial Spondyloarthritis in Patients with Late-Onset Chronic Low Back Pain (Older Than 45 Years). Axial Spa or Psoriatic Disease with Axial Involvement?

rodrigo garcía salinas[1], Gisel Reyes[2], Rosario Jaldín Céspedes[2], Felica Almada[2] and Sebastián Juan Magri[3], [1]Arthritis and Spondyloarthritis Unit, Hospital Italiano de La Plata, National University of La Plata, La Plata, Argentina, [2]Hospital Italiano de La Plata, La Plata, Argentina, [3]Hospital Italiano La Plata, Melchor Romero, Argentina

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose:

It is known that patients diagnosed with axSpA do not subsequently meet the classification criteria. The Objectives are: To estimate the diagnostic prevalence of axSpA in patients who started low back pain over 45 years of age and to analyze the clinical, laboratory and imaging differences with patients who started it before that age.

Methods: Methods: Observational and cross-sectional study, which included patients older than 18 years with a diagnosis of axial spondyloarthritis performed between 2017 and 2021. At baseline, all patients underwent: blood tests, HLA B27, X-rays and MRI of the sacroiliac joint, enthesis ultrasound, sociodemographic data, level of education and habits were also recorded. Axial spondyloarthritis symptoms, age of onset, delay to diagnosis, characteristics of low back pain, characteristics of axial spondyloarthritis, NSAIDs intake and response, VAS pain and night pain, morning stiffness time. In addition, BASDAI, BASFI, MASES and HAQ scores were used. The symptom evaluator was unaware of the results of the complementary studies that were collected by another observer. The MRIs recorded the presence of any lesion and classified it into acute (edema) and chronic (fatty changes, erosions, sclerosis, and bone bridges) lesions.

Features	ARP-PsA no PsA (85)	ARP-PsA yes PsA (34)	p	RR (95%IC)
Age (years), mean (SD)	48 (14)	49 (15)	0.9	
Female, %	78	61	0.06	0.4 (0.2-1)
Years of education, median (IQR)	14 (3)	13 (3)		
Time between the onset of symptoms and the baseline visit (months), mean (SD)	13 (30)	18 (30)	0.2	
Smoking, %	36	44	0.4	1.3 (0.6-3)
Cardiometabolic comorbidities, %	40	35	0.6	0.6 (0.3-1.8)
Family psoriasis, %	80	47	>0.001	**0.2 (0.1-0.5)**
Pso + Family history Pso	8	26	**0.008**	**4 (1.3-12)**
Cutaneous psoriasis, %	26	73	>0.001	**8 (3-20)**
Pso duration time (years) median (IQR)	3 (15)	15 (15)	**0.03**	
Patient global VAS (0-100), mean (SD)	50 (23)	60 (15)	**0.04**	
Tender joints (28), median (IQR)	2 (4)	1.5 (3)	**0.05**	
Arthralgia less than one year, %	38	19	**0.04**	**0.4 (0.1-0.8)**
Morning stiffness, %	16	12	0.6	0.7 (0.2-2)
Squeeze test +, %	22	31	0.3	1.5 (0.6-4)
ESR, mean (SD)	17 (13)	18 (16)	0.6	
CRP +, %	21	28	0.6	1.2 (0.8-1.7)
CRP, median (IQR)	1 (2.7)	1 (4)	0.4	
HAQ, median (IQR)	0.5 (0.8)	0.8 (0.75)	0.1	
X-ray bone erosions, %	4	26	**0.004**	**7 (2-28)**
X-ray, joint narrowing, %	25	19	0.5	7 (0.2-2)
Ultrasound synovitis, Tenosynovitis, %	8	12	0.5	1.6 (0.4-6)
Ultrasound synovitis, Gray Scale, %	5	21	**0.01**	**5 (1.3-18)**
Ultrasound synovitis, Power Doppler signal, %	1.3	12	**0.01**	**10 (1.1-98)**
Ultrasound, Enthesopathy findings, %	4	53	>0.001	**25 (6.5-99)**

Tabla 1: Patientes´Features.

Results: Results: One hundred sixteen patients with a diagnosis of axial spondyloarthritis were included, whose characteristics are summarized in Table 1. The prevalence of patients who started low back pain after the age of 45 was 31.28% (95% CI 20-36). The relevant differences were: female sex (51% vs 29% p 0.03), smoking (38% vs 57% p 0.07), psoriasis (42% vs 17% p 0.007), good response to NSAIDs (52% vs 73% p 0.03), HLA-B27 (+) (32% vs %54 p 0.04), more than 4 characteristics of axial spondyloarthritis (35% vs 54% p 0.08), BASFI (5.1 vs 4.5 p 0.05), delay to diagnosis in months (40 vs 93 p 0.002). No differences were found in terms of disease activity and imaging (MRI or X-rays). In the logistic regression analysis, the variables that were independently associated were: male sex (OR 0.2 IC95% 0.06- 0.8), psoriasis (OR 4.8 IC95% 1.1-29), and shorter delay to diagnosis (OR 0.9 IC95% 0.96 -0.99).

Conclusion: The prevalence of diagnosis of axial spondyloarthritis in patients who started low back pain after the age of 45 was 28%. The characteristics of these patients were: female sex, higher frequency of psoriasis, and shorter delay to diagnosis. This study shows that the older age at the onset of low back pain and the association with psoriasis could show a group of patients with axial involvement in the context of psoriatic disease.

Disclosure: r. garcía salinas: AbbVie, 1, 2, 5, 6, AstraZeneca, 5, Biogen, 5, Bristol Myers Squibb, 1, 2, 5, 6, Genentech, 5, GlaxoSmithKlein, 5, Janssen, 1, 2, 5, 6, Lilly, 1, 2, 6, Merck Serono, 5, Novartis, 1, 2, 6, Roche, 1, 2, 6, Sandoz, 1, 2, 6; **G. Reyes**: None; **R. Jaldín Céspedes**: None; **F. Almada**: None; **S. Magri**: None.

Abstract Number: 0493

Axial Disease Activity in Psoriatic Arthritis Is Higher in Patients with Carotid Plaque

Rosa Arvizu-Rivera[1], Valeria Gonzalez-Gonzalez[2], Dionicio A. Galarza-Delgado[3], Iris Colunga[3], José Ramón Azpiri-López[3], Victor Beltran[4], Angel Arias Peralta[5] and Jesus Alberto Cardenas-De la Garza[6], [1]Hospital Universitario \"Dr. José Eleuterio Gonzalez\", Escobedo, Mexico, [2]Universidad Autónoma de Nuevo León, Monterrey, Mexico, [3]Hospital Universitario UANL, Monterrey, Mexico, [4]Rheumatology Service Hospital Universitario "Dr. José Eleuterio González", Monterrey, Mexico, [5]Medicine Faculty, Universidad Autonoma De Nuevo Leon, Monterrey, Mexico, [6]Hospital Universitario "Dr. José Eleuterio González", San Nicolas, Mexico

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Approximately half of the patients with psoriatic arthritis (PsA) present with axial disease. Previously, it was reported that PsA-patients with axial involvement present a higher cardiovascular risk compared with those without the axial disease. Additionally, it has been reported that axial disease is higher in patients with axial spondyloarthropathies, and carotid plaque (CP) identified by ultrasound than in patients without CP. The objective was to compare the Bath Ankylosing Spondylitis Metrology Index (BASMI) between PsA-patients with and without CP.

Methods: A cross-sectional and comparative study that included PsA patients aged 30 to 75 years old who fulfilled the 2006 Classification Criteria for PsA. Patients with previous cardiovascular atherosclerotic disease were excluded. B-mode carotid ultrasound was performed on all patients by a board-certified radiologist blinded to clinical information. Carotid plaque (CP) was defined as a carotid intima–media thickness (cIMT) ≥1.2 mm or a focal narrowing ≥0.5 mm of the surrounding lumen, and an increased cIMT was defined as a value ≥0.8 mm. Axial disease activity was measured using the BASMI in all patients.

Table 1. Demographic characteristics.

Characteristics	PA patients without CP (n=38)	PA patients with CP (n=32)	*p*-value
Age, years, ± SD	52.3 ± 9.4	56.3 ± 12.2	**0.012**
Women, n (%)	20 (52.6)	17 (53.1)	NS
Diabetes, n (%)	4 (10.5)	13 (40.6)	**0.003**
Hypertension, n (%)	15 (39.5)	18 (56.3)	NS
Dyslipidemia, n (%)	15 (39.5)	17 (53.1)	NS
Obesity, n (%)	16 (42.1)	12 (37.5)	NS
Active smoking, n (%)	10 (26.3)	5 (16.1)	NS
Time of evolution, years, median (IQR)	5.5 (3.2-10.2)	6.0 (3.0-14.0)	NS
DAPSA, median (IQR)	13.0 (6.1-19.1)	10.3 (5.3-21.1)	NS
PASI, median (IQR)	0.75 (0.0-2.2)	0.20 (0.0-3.0)	NS
NAPSI, median (IQR)	0.0 (0.0-4.0)	0.0 (0.0-10.0)	NS
BASMI, median (IQR)	2.8 (2.4-3.4)	3.4 (2.4-4.2)	**0.016**

PsA, psoriatic arthritis; SD, standard deviation; IQR, interquartile range; NS, no significative.

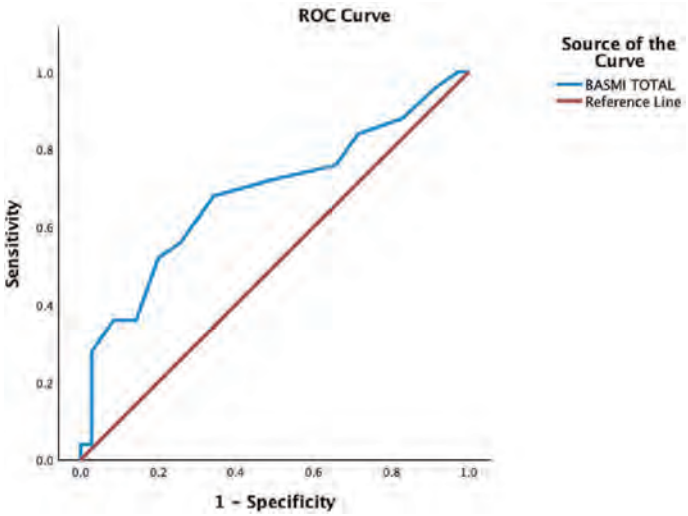


Figure 1. ROC analysis to evaluate the best cut-off point of BASMI to identify CP.

Results: A total of 70 patients with PsA were included, the mean age was 55 ± 11.47, the disease evolution of PsA was 7.95 ± 7.08 years, and the mean BASMI of all patients included was 3.09 ± 0.99. The prevalence of type 2 diabetes mellitus was higher in patients with PsA and CP (10.5% vs 40.6%, *p*=0.003). There was no difference between the prevalence of obesity and other cardiovascular risk factors, including smoking, obesity, hypertension, and dyslipidemia. BASMI was higher in PsA patients with CP in comparison to those patients without CP (3.4 vs 2.8, *p*=0.016). In a subanalysis, the Youden Index between CP and BASMI was assessed to determine the best cut-off point to identify CP, which resulted in a cut-off point of a BASMI of 2.9 with a sensitivity of 68% and a specificity of 65.7% (CI 0.541 - 0.826, *p*=0.012), Figure 1.

Conclusion: Patients with PsA and CP present higher axial disease activity compared to PsA patients without CP. A BASMI of 2.9 or higher may identify patients who would benefit from non-invasive screening for subclinical atherosclerosis.

Disclosure: R. Arvizu-Rivera: None; **V. Gonzalez-Gonzalez**: None; **D. Galarza-Delgado**: None; **I. Colunga**: None; **J. Azpiri-López**: None; **V. Beltran**: None; **A. Arias Peralta**: None; **J. Cardenas-De la Garza**: None.

Abstract Number: 0494

Levels of Atherosclerotic Index of Plasma and Triglyceride Glucose Index in Patients with Psoriatic Arthritis and Carotid Plaque

Dionicio A. Galarza-Delgado[1], Iris Colunga[1], José Ramón Azpiri-López[1], Valeria Gonzalez-Gonzalez[2], **Rosa Arvizu-Rivera**[3], Victor Beltran[4], Angel Arias Peralta[5] and Jesus Alberto Cardenas-De la Garza[6], [1]Hospital Universitario UANL, Monterrey, Mexico, [2]Universidad Autónoma de Nuevo León, Monterrey, Mexico, [3]Hospital Universitario \"Dr. José Eleuterio Gonzalez\", Escobedo, Mexico, [4]Rheumatology Service Hospital Universitario "Dr. José Eleuterio González", Monterrey, Mexico, [5]Medicine Faculty, Universidad Autonoma De Nuevo Leon, Monterrey, Mexico, [6]Hospital Universitario "Dr. José Eleuterio González", San Nicolas, Mexico

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Triglyceride Glucose Index **(**TyG) is a surrogate marker positively correlated with atherosclerotic burden in patients with psoriatic arthritis (PsA). Atherosclerotic index of plasma (AIP) levels have not been evaluated in patients with subclinical atherosclerosis and PsA. The objective was to compare levels of AIP and TGI between PsA-patients with and without carotid plaque (CP).

Table 1. Demographic characteristics.

Characteristics	PsA patients with CP (n=36)	PsA patients without CP (n=52)	*p*-value
Age, years, ± SD	57.7 ± 9.8	54.9 ± 6.3	**0.006**
Women, n (%)	18 (50)	28 (53.8)	NS
Diabetes, n (%)	13 (37.1)	6 (11.5)	**0.005**
Hypertension, n (%)	17 (48.6)	17 (32.7)	NS
Dyslipidemia, n (%)	19 (54.3)	17 (32.7)	**0.045**
Obesity, n (%)	11 (31.4)	22 (42.3)	NS
Active smoking, n (%)	6 (17.6)	12 (23.1)	NS
Time of evolution, years, median (IQR)	7.5 (3.2-16.5)	6.0 (3.5-8.0)	NS
DAS28-CRP, ± SD	2.4 ± 1.3	2.4 ± 1.0	NS
PASI, median (IQR)	0.4 (0.0-4.0)	0.4 (0.0-1.9)	NS
NAPSI, median (IQR)	0.0 (0.0-17.0)	0.0 (0.0-4.5)	NS
DAPSA, median (IQR)	10.1 (4.6-24.8)	13.3 (5.3-22.4)	NS
AIP, median (IQR)	0.48 (0.35-0.78)	0.35 (0.21-0.54)	NS
TGI, median (IQR)	3.9 (3.7-4.3)	3.7 (3.6-3.8)	**0.010**
cIMT, mm, median (IQR)	1.0 (0.8-1.2)	0.5 (0.5-0.6)	**0.000**

PsA, psoriatic arthritis; CP, carotid plaque; SD, standard deviation; IQR, interquartile range; NS, no significative; DAS28-CRP, 28-joint Disease Activity Score based on C-reactive protein; PASI, psoriasis area severity index; NAPSI, nail psoriasis severity index; DAPSA, disease activity in psoriatic arthritis; AIP, atherogenic index of plasma; TGI, triglyceride-glucose index; cIMT, carotid intima-media thickness.

Methods: Cross-sectional study that included PsA-patients aged 40 to 75 years old who fulfilled the 2006 Classification Criteria for PsA. Patients with previous cardiovascular disease were excluded. Carotid ultrasound was performed on all study participants. The presence of carotid plaque (CP) was defined as diffuse carotid intima-media thickness (cIMT) ≥1.2 mm or focal thickness ≥0.5 mm. Subclinical atherosclerosis was defined as the presence of CP or an increased cIMT (≥0.8mm). Cardiovascular disease risk was evaluated using the algorithm: FRS-Lipids. AIP was defined by Log (TG/HDL-C) mg/dL. TGI was defined by Log (Fasting triglyceride (mg/dl) x fasting glucose (mg/dl)/2. The distribution between groups was assessed with the Kolmogorov-Smirnov test. Comparisons with Chi-square or Fisher's exact test and Student's t-test or Mann Whitney's U-test, accordingly. The correlation between the AIP, TGI, cIMT, and FRS-Lipids was assessed by Spearman's correlation coefficient. A value of $p \leq 0.05$ was considered statistically significant.

Results: A total of 88 patients with PsA were included, mostly women (n=46, 52.3%), the mean age was 53 ± 11.3, median disease duration of PsA was 5.0 (3.0-10.7) years. Median AIP was 0.44 (0.31-0.66) and TGI 3.8 (3.6-4.0) of all patients included. The most prevalent cardiovascular risk factor was dyslipidemia (n= 36, 41.4%). Patients with carotid plaque and PsA presented higher TyG compared to the group without carotid plaque (p=0.010). (Table 1).

Table 2. Association between cardiovascular algorithm, cIMT and index.

	AIP	TGI
FRS-Lipids	rs=0.618 *p*=0.000	rs=0.569 *p*=0.000
cIMT	rs=0.254 *p*=0.020	rs=0.271 *p*=0.013

TGI, triglyceride-glucose index; AIP, atherogenic index of plasma; FRS, Framingham Risk Score; cIMT, carotid intima-media thickness.

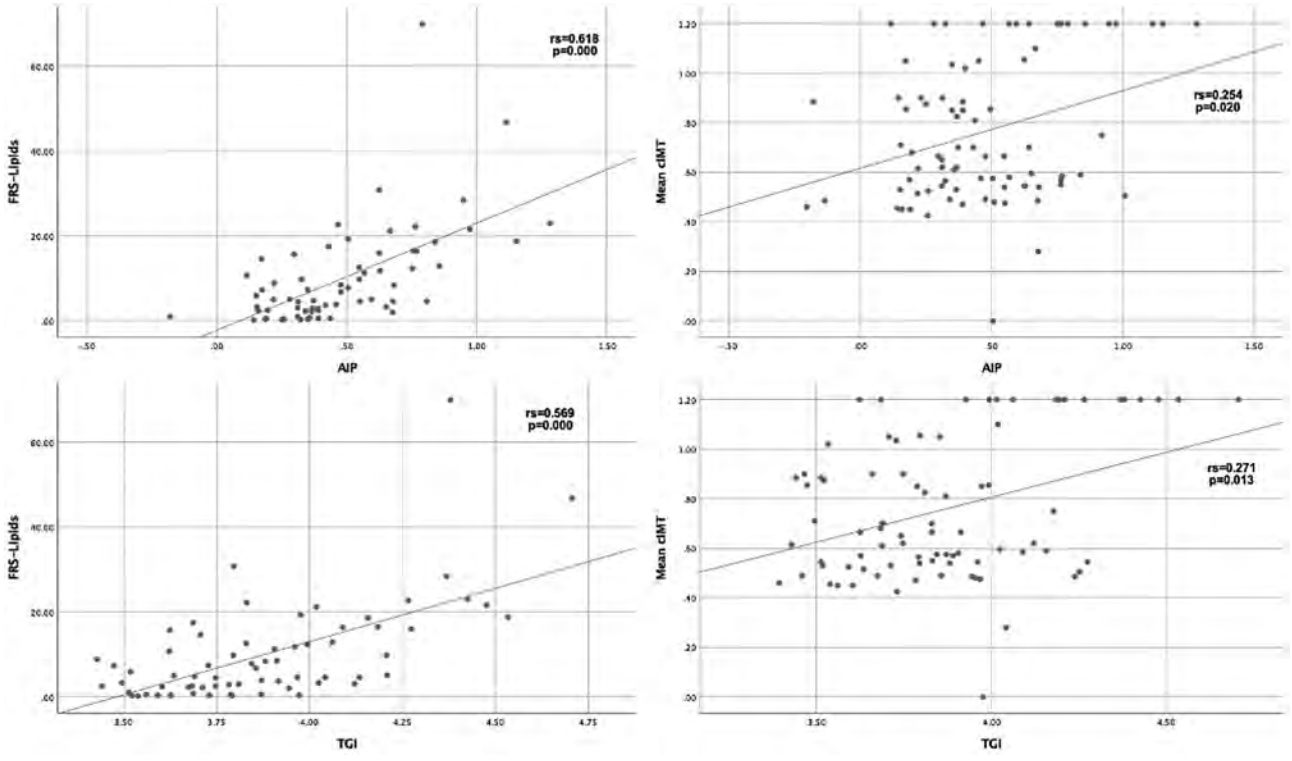


Figure 1. Scatterplots of the association between cardiovascular algorithm, cIMT and index.

Conclusion: AIP is not elevated in patients with PsA and subclinical atherosclerosis. However, TyG levels are increased in PsA-patients and CP. Prospective studies are needed to evaluate the performance of these surrogate markers to predict CV events in these patients.

Disclosure: D. Galarza-Delgado: None; **I. Colunga**: None; **J. Azpiri-López**: None; **V. Gonzalez-Gonzalez**: None; **R. Arvizu-Rivera**: None; **V. Beltran**: None; **A. Arias Peralta**: None; **J. Cardenas-De la Garza**: None.

Abstract Number: 0495

Prevalence of Undiagnosed Inflammatory Bowel Disease in Patients with Spondyloarthritis: EISER Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: EISER is a cross-sectional, multicenter, observational, SER-GETECCU cooperative study involving 13 Spanish hospitals whose main objective was to estimate the prevalence of undiagnosed Inflammatory Bowel Disease (IBD) in patients with spondyloarthritis (SpA), including axial (axSpA) (radiographic axSpA-r and non-radiographic; axSpA-nr) and psoriatic arthritis (PsA).

Methods: We selected patients ≥18 years of age from the NHS Rheumatology Department, SpA diagnosed according to CASPAR criteria for PsA and ASAS for axSpA. Patients under treatment with biologics were excluded. Patients currently treated with systemic steroids or in the previous 30 days were not included. Patients over 50 years of age were included if a colonoscopy wasn't performed in the last three years or, if a colonoscopy was performed but did not meet the criteria of valid colonoscopy.

Patients were recruited by the rheumatologist who collected demographic, clinical and treatment data. A fecal calprotectin (FC) determination was performed using the Quantum Blue rapid test. FC was assessed and all patients with a FC ≥80 µg/g underwent an endoscopic study by the gastroenterologist. Patients in whom the result of the endoscopic study was normal underwent to an endoscopic capsule study or magnetic resonance imaging.

Table 1: Sociodemographic and general data of all patients included in the study.

General and sociodemographic data n (%)	
Number of patients	559
Male	285 (51.0%)
Female	274 (49.0%)
Mean age of participants*	52.2 ± 12.6
Mean age of diagnosis*	42.0 ± 13.2
Mean time of disease progression*	12.3 ± 11.6
Smoking status	
Never	271 (48.5%)
Past	186 (33.2 %)
Current	102 (18.3%)
Alcohol consumption	
No	333 (59.6%)
Yes	226 (40.4%)

*mean ± standard deviation

Table 2: Type and activity of patients enrolled in the study.

Disease information n (%)	
Type Spondyloarthritis (SpA)	
Axial psoriatic arthritis	17 (3.0%)
Peripheral psoriatic arthritis	200 (35.8%)
Mixed psoriatic arthritis	55 (9.8%)
Radiographic Axial Axial Spondyloarthritis	207 (37.0%)
Non radiographic Axial Axial Spondyloarthritis	80 (14.3%)
Spondyloarthritis Baseline Activity (SpA)	
BASDAI*	3.6 ± 2.3
DAPSA*	10.4 ± 8.3
ASDAS_PCR*	2.3 ± 1.0
ASDAS_VSG*	2.4 ± 1.0
Global assessment of the disease between 0 and 10*	4.1 ± 2.7
Quality of life (EuroQol-5D-5L)	
Health status between 0 and 100*	67.5 ± 19.5

*mean ± standard deviation

Results: A total of 559 patients were included, 51.0% of whom were men. The mean age of the participants was 52.2 years, with a mean age at diagnosis of 42 years. Mean time of disease evolution was 12.3 years (Table 1).

Regarding the type of SpA, the most frequent form was axSpA-r (37.0%), followed by peripheral PsA (35.8%; Table 2). Concerning disease activity data in axSpA BASDAI 3.6, ASDAS_PCR 2.3, ASDAS_VSG 2.4 and of patients with PsA DAPSA of 10.4 (Table 2). Global assessment and mean health status reported by patients was 4.1 (0 to 10 scale) and 67.5 (0 to 100 scale; Table 2), respectively.

A total of 47.0% of patients with PsA had FC≥80 μg/g vs. 53% of axSpA (80% axSpA-r vs. 20% axSpA-nr). The mean FC values were higher in the case of axSpA-r (395.06 μg/g) compared to the other groups (305.52 μg/g for the axSpA-nr and 306.19 μg/g for the PsA subgroup).

Overall, 10.0% of the patients had a family history of IBD and 14.6% had clinical manifestations compatible with IBD, the most common clinical manifestations were asthenia (50.0%), abdominal pain (15.6%) and chronic diarrhea (14.1%). A total of 189 colonoscopies were performed (167 in patients with FC≥80 μg/g, of which 39.7% presented some pathological finding, mostly: aphthous ulcers (65.9%), superficial ulcers (20.5%) and mucosal erythema (13.6%), mainly located in terminal ileum (41.3%).

Finally, 23 patients were diagnosed with IBD (4.4%): 22 diagnosed with Crohn's disease (95%), 1 unclassifiable IBD (5%). Of the 23 patients diagnosed with IBD, 17.4% had a family history of IBD, 30.4% had clinical symptoms compatible with IBD and 82.6% had a colonoscopy with some type of pathological finding.

Conclusion: The finding of elevated fecal calprotectin levels in patients with SpA, followed by an appropriate complementary study (endoscopic and/or radiological), allows the detection of a relevant subgroup of patients who meet diagnostic criteria for IBD.

Disclosure: J. Sanz: AbbVie/Abbott, 1, 6, Janssen, 1, 5, 6, Novartis, 6, UCB, 1, 5, 6; **Z. Plaza**: None; **J. Gratacos Masmitja**: AbbVie/Abbott, 1, 6, Amgen, 6, AstraZeneca, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 1, 6, Janssen, 1, 6, Novartis, 1, 6, Pfizer, 1, 6, UCB, 1, 6; **I. Rodríguez -Lago**: None; **E. Trujillo**: None; **I. Marin-Jimenez**: None; **E. Perez-Pampin**: None; **M. Barreiro de Acosta**: None; **A. Aznar Esquivel**: None; **M. Carrillo Palau**: None; **M. Garcia Vivar**: None; **M. Muñoz**: None; **L. Ladehesa Pineda**: None; **E. Iglesias Flores**: None; **c. Merino**: None; **Y. gonzalez-Lama**: AbbVie/Abbott, 1, 6, Janssen, 1, 6, Pfizer, 1, 6; **M. Arévalo Salaet**: None; **X. calvet**: None; **A. Brandy-Garcia**: None; **M. Izquierdo Romero**: None; **S. MANRIQUE**: None; **R. Olmedo**: None; **J. Garcia Llorente**: AbbVie/Abbott, 6, Amgen, 5, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, Faes, 11, galápagos, 6, Gebro pharma, 5, UCB, 5; **S. Pérez**: None; **I. Ros**: Janssen, 6, novartis, 6, Pfizer, 6; **N. Rull**: None; **J. Pinto Tasende**: None; **P. Ucha Abal**: None; **C. González**: None; **F. Rodríguez Martínez**: None; **S. Serrano Ladron de Guevara**: None; **M. Domínguez**: None; **F. Prado**: None; **E. González-Dávila**: None; **A. Gutierrez-Casbas**: None.

Abstract Number: 0496

Higher Values of Atherogenic Index of Plasma Are Correlated with Increased Cardiovascular Risk in Patients with Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The atherogenic index of plasma (AIP) is a predictor of atherosclerosis and coronary heart disease. In patients with systemic lupus erythematosus and rheumatoid arthritis, AIP is correlated with increased cardiovascular risk measured by Framingham's risk score. The correlation between AIP and calculated cardiovascular risk has not been studied in PsA-patients. To evaluate the correlation between AIP and six cardiovascular risk scores in patients with PsA.

Methods: Cross-sectional study that included PsA-patients aged 40 to 75 years who fulfilled the 2006 Classification Criteria for PsA. Patients with previous cardiovascular disease were excluded. AIP was defined by log (TG/HDL-C) mg/dL, and levels ≥0.21 were considered as high AIP. Cardiovascular disease risk was evaluated using 6 algorithms: ACC/AHA 2013, FRS-Lipids, FRS-BMI, RRS, QRISK3, and SCORE2. The Kolmogorov-Smirnov test was performed to evaluate the distribution of variables. The correlation between the AIP and cardiovascular risk algorithms was assessed by Spearman's correlation coefficient. A value of $p \leq 0.05$ was considered statistically significant.

Results: A total of 94 patients with PsA were included, mostly women (n=52, 55.3%), the mean age was 53 ± 11.2, the disease duration of PsA was 5.0 (2.0-10.0) years, and the median AIP of all patients included was 0.49 (0.35-0.67). The median of each algorithm was: FRS-BMI 15.0 (6.7-27.8), FRS-Lipids 7.4 (3.0-16.4), SCORE 1.0 (1.0-3.0), QRISK3 5.6 (2.4-12.5),

Table 1. Correlations between cardiovascular risk algorithms and AIP.

	FRS-Lipids	FRS-BMI	SCORE	RRS	QRISK3	ACC/AHA 2013
AIP	rs=0.619 *p*=0.000	rs=0.427 *p*=0.000	rs=0.341 *p*=0.003	rs=0.538 *p*=0.000	rs=0.460 *p*=0.000	rs=0.641 *p*=0.000

AIP, atherogenic index of plasma; FRS, Framingham Risk Score; BMI, body mass index; RRS, Reynolds Risk Score.

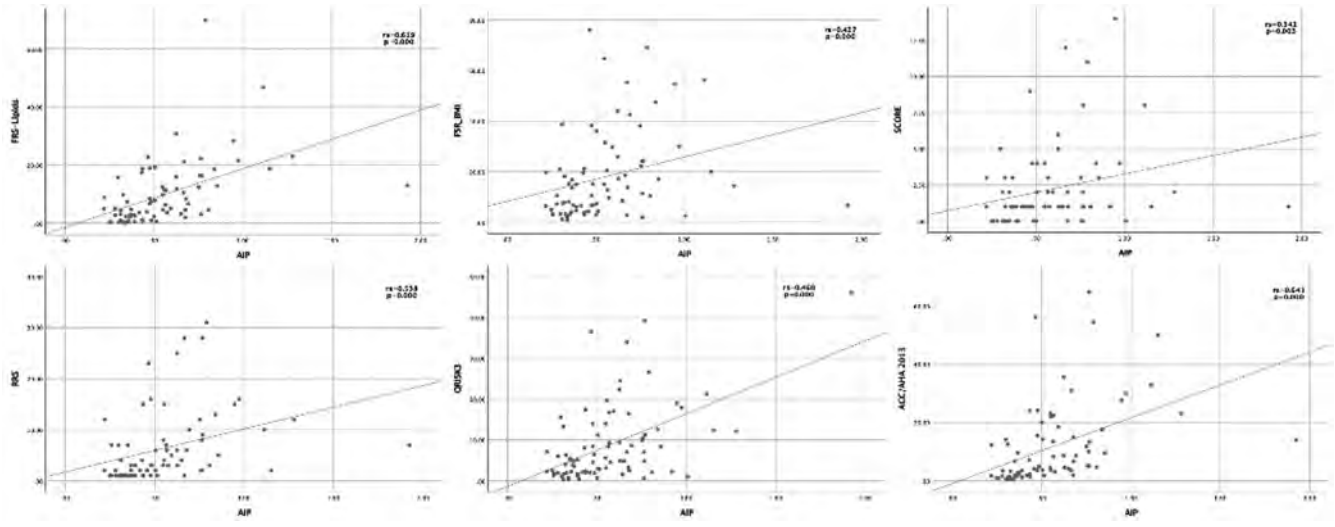

Figure 1. Scatterplots of the correlations between cardiovascular risk algorithms and AIP.

RRS 3 (2.0-7.5) and ACC/AHA 2013 5.3 (2.1-14.5). The most prevalent cardiovascular risk factor was dyslipidemia (n= 41, 43.6%). All cardiovascular risk algorithms presented a high positive correlation between AIP levels and cardiovascular risk. The calculator with the highest correlation was ACC/AHA 2013 (rs=0.641, *p*=0.000). (Table 1 and Figure 1).

Conclusion: In patients with PsA, higher values of AIP are associated with increased cardiovascular risk irrespective of the algorithm used. High AIP values could identify patients who would benefit from a non-invasive evaluation for subclinical atherosclerosis.

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Abstract Number: 0497

Effects and Tolerability of Low to Moderate Biomechanical Stress During Leisure Sport Activity in Patients with Psoriasis and Psoriatic Arthritis

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: International guidelines advise physical activity as complementary measure to drug treatment for patients with RA. However, this can hardly be extrapolated for PsA, for which excessive physical strain areas has been implicated in the pathogenesis of enthesitis (so-called "Deep Koebner phenomenon"). This raises the question whether physical activity should be at all recommended in PsA, and if yes what type of activity and intensity are safe. Hence, determining safe thresholds for exercise in PsA is of high importance. In this context, we aimed to assess the effects of mechanical strain on the entheses of psoriatic patients exposed to low-moderate physical activity through badminton, which exerts considerable mechanical stress on the extremities.

Methods: A prospective study was conducted on a cohort of patients with PsA fulfilling CASPAR criteria and PsO recruited at the department of rheumatology of the Erlangen University Clinic and of the Nürnberg Hospital. Participants underwent physical examination of 29 entheses and US of the entheses at the lateral humeral epicondyle, inferior patellar pole, and Achilles tendon bilaterally before and after a 60-minutes badminton session through two rheumatologists (AH, AK). Two blinded expert readers scored US scans to assess entheseal pathology according to OMERACT criteria (MYM, FF). Data on clinical history, therapy, physical activity habits, disease activity, and pain before and after exercise were collected. A follow-up assessment of pain and adverse events was performed one week afterwards by telephone.

Table 1: Baseline characteristics of PsA and Psoriasis patients

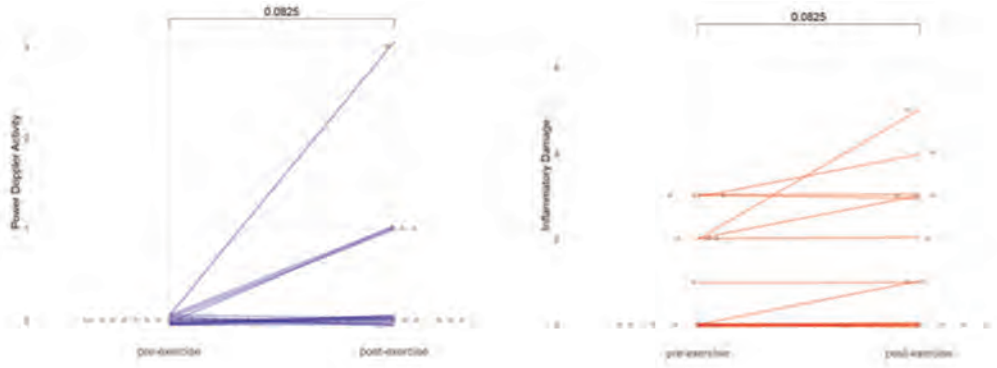
	PsA	Psoriasis
n (% female)	7 (14%)	9 (33%)
age (yrs) (mean (SD))	39,3 (10,3)	44,1 (10,9)
disease duration (mean (SD))	16,9 (14,2)	24,3 (14,8)
smoker status	1/7 (14 %)	3/9 (33%)
BMI (mean (SD))	30,0 (8,6)	23,7 (1,7)
Comorbidities		
comorbidities (>1)	1/7 (14%)	1/9 (11%)
IBD	2/7 (28%)	1/9 (11%)
Uveitis	0/7 (0%)	1/9 (11%)
Frequency of physical activity		
Less than once monthly	2/16	2/16
Once monthly	1/16	0/16
Once to twice weekly	0/16	4/16
More than three times weekly	3/16	4/16
Systemic therapy		
no systemic therapy	1/7 (14%)	6/9 (66%)
csDMARD	1/7 (14%)	-
tsDMARD	2/7 (28%)	1/9 (11%)
TNFi	1/7 (14%)	1/9 (11%)
IL-17i	1/7 (14%)	1/9 (11%)
IL-23i	1/7 (14%)	-
Disease activity		
DAPSA (mean (min;max))	6,1 (0,8; 19,0)	N/A
MDA	5/7 (71,4%)	N/A

PsA: Psoriatic Arthritis; yrs: years; SD: standard deviation; BMI: body mass index; IBD: inflammatory bowel disease; cs/ts/DMARDs: conventional synthetic/targeted synthetic disease modifying antirheumatic drugs; TNFi: tumor necrosis factor alpha inhibitors; IL: interleukin; DAPSA: disease activity in Psoriatic Arthritis score; MDA: minimal disease activity score.

Table 2: Clinical and Ultrasound findings before and after training

	Pre	Post
Tender entheses		
Entheses count, n (%)	12/464 (2,6%)	13/464 (2,8%)
SPARCC, median (IQR)		
MASES, median (IQR)		
LEI, median (IQR)		
Inflammatory changes, n (%)	17 (17,8%)	22 (22,9%)
Hypoechogenicity	14/96	14/96
Thickening	2/96	2/96
Power-Doppler signal	1/96	7/96
Structural changes, n (%)	15 (15,6%)	15 (15,6%)
Calcifications/Enthesiophytes	15/96	15/96
Erosions	0/96	0/96

SPARCC: Spondyloarthritis Research Consortium of Canada enthesitis score; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; LEI: Leeds Enthesitis Index; IQR: interquartile range,



A Paired t-test revealed no significant difference in the frequency of inflammatory changes (p = 0.08) and Power Doppler activity (p = 0.08) in the pre- and post-exercise measurements.

Figure 1: Spaghetti plots depicting the frequency of individual inflammatory ultrasound changes (right panel) and power Doppler ultrasound signals (left panel) before and after training.

Results: Seven patients with PsA and 9 PsO patients were included. A total of 196 grayscale and power Doppler (PD) US scans were acquired. Baseline clinical characteristics are reported in Table 1. After training, no significant change in median VAS pain nor in tender entheses emerged (Table 2). Baseline US showed structural and inflammatory changes in 15/96 and 17/96 entheses, respectively. After training, 4 patients (2 PsA, 2 PsO) developed a grade-1 Power-Doppler at 6 entheses (Figure 1), which remained non-tender. After one week, median VAS pain remained stable (0,5 cm (0,0-3,0)). Only one untreated PsA participant with active disease at baseline experienced new-onset arthritis in three joints. A single adverse event (disc protrusion) was reported by one PsO patient.

Conclusion: Our findings show that low-moderate mechanical strain on entheses, as in the context of leisure physical activity, is likely to be well tolerated by patients with psoriasis and PsA and might not lead to an increase in disease activity. As the only flare in our cohort was observed in an untreated PsA patient, immunomodulatory therapy could possibly offer some protection against mechanically-induced inflammation. Larger controlled studies are needed to validate our findings and define which physical activity thresholds are safe in PsA. Generating this data is crucial to inform management decisions and ultimately develop evidence-based guidelines for physical activity in PsA.

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Abstract Number: 0498

Biological Therapies for Psoriasis and Psoriatic Arthritis- effects on Future Risk Development of Major Adverse Cardiovascular Events (MACE)

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SESSION INFORMATION
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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA
Session Type: Poster Session A
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Background/Purpose: Major adverse cardiovascular events (MACE) are known comorbidities and consequences of psoriasis (PsO) and psoriasis arthritis (PsA). Previous studies underlined the potential of immunomodulatory agents decreasing MACE incidence in patients with PsO and PsA.

We aimed to assess the risk of developing MACE in patients with pre-existing PsO treated with different treatment regimens; topical treatment, methotrexate and biologic disease-modifying anti-rheumatic drugs (bDMARDs), including antiTNFα, anti-IL17 and anti-IL12/23 agents and JAK inhibitors.

Methods: We conducted a retrospective exploratory study using real-world data from the databases of 'Meuhedet', the third-largest Israeli health maintenance organization, covering approximately 1.3 million subjects. A total of 55,780PsO and 5,223 PsA patients were diagnosed between January 2000 and January 2020 and 244,012 healthy controls were included. We performed Cox proportional hazards regression analysis adjusted for factors including sex, body mass index, age at PsO diagnosis, diagnosis of type 2 diabetes mellitus, dyslipidemia, and hypertension. To gain further insight into the

influence of different types of bDMARDs on the risk of MACE, we undertook a comprehensive logistic regression analysis which included the accumulative constatives of the different types of bDMARDs and the mean quantity per month with the same adjustments as in the cox analysis.

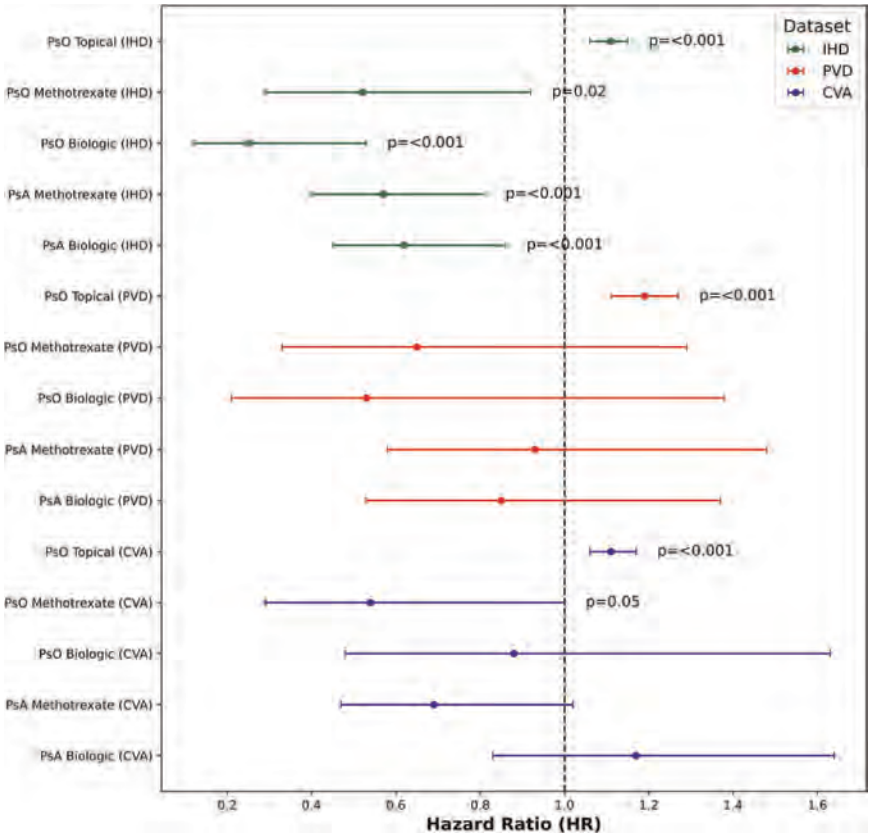
Results: After implementing the exclusion criteria, our study comprised 216,896 participants, with 52,632PsO and 1,592 PsA patients and 162,672 matched controls, contributing a total of 2,261,815 patient-years. PsO and PsA patients treated with methotrexate or bDMARDs showed a significantly lower MACE risk compared to health matched controls (HR: 0.45-0.68, p-value: < 0.001). However, patients receiving topical therapy exhibited a marginally increased MACE risk com-

Combined Univariate and Multivariate Cox Regression Results

	Univariate				Multivariate			
Variable	HR[1]	Lower 95% CI[2]	Upper 95% CI	P-Value	HR	Lower 95% CI	Upper 95% CI	P-Value
PsO Topical	1.13	1.09	1.17	<0.001	1.14	1.10	1.18	<0.001
PsO Methotrexate	0.51	0.33	0.80	<0.001	0.45	0.29	0.70	<0.001
PsO Biologic	0.46	0.29	0.74	<0.001	0.46	0.29	0.74	<0.001
PsA Methotrexate	0.70	0.53	0.92	0.01	0.64	0.48	0.85	<0.001
PsA Biologic	0.66	0.51	0.84	<0.001	0.68	0.53	0.88	<0.001

[1] HR: Hazard ratio

[2] CI: Confidence interval



Green, red, and blue represent data points from 'IHD', 'PVD', and 'CVA' datasets, respectively. Circles symbolize Hazard Ratio (HR) values with lines showing the 95% confidence interval. A black dashed line at HR=1. Data points may have a 'p' value, indicating the HR's statistical significance. Only 'p' values ≤0.05 are shown.

pared to health matched controls (HR: 1.14, p-value: < 0.001) **(Table 1)**. Individual outcomes constituting the composite of MACE, including cerebrovascular accidents, ischemic heart disease, and peripheral vascular disease, showed similar trends**(Figure 1)**.In the logistic regression analysis of PsO and PsA patients exclusively treated with biological treatments, we observed stronger cardioprotective properties of anti-IL-12/23 and anti-IL-17 compared to anti-TNF. Importantly, increased mean monthly quantity of anti-TNF was associated with higher risk of developing MACE (OR=1.12, p=0.042, 95% CI [1.01, 1.24]).In contrast, total quantity of anti-IL 17, anti-IL 12/23, and JAKi reduced risk of developing MACE (OR = 0.98, p = 0.024, CI [0.96, 0.99]).

Conclusion: Our findings suggest that systemic anti-inflammatory treatments for PsO and PsA, including bDMARDs and methotrexate, provide cardioprotective effects. Our study also highlights potential cardiovascular benefits of anti-IL17 and anti-IL12/23 biological agents compared to anti-TNF treatments. This information can assist clinicians and patients in making informed decisions about these therapeutic agents.

Disclosure: A. Dotan: Janssen, 5, 5; **N. Ben-Shabbat**: None; **A. watad**: None; **D. McGonagle**: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Janssen, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **H. AMITAL**: Janssen, 5.

Abstract Number: 0499

Durability of Response Among Patients with Psoriatic Arthritis (PsA) Using Biological or Targeted Synthetic Disease-Modifying Antirheumatic Drugs in the CorEvitas PsA/Spondyloarthritis Registry

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Improvement in both joint and skin manifestations is an important goal in the treatment of psoriatic arthritis (PsA). This study describes durability of 50% improvement in the modified American College of Rheumatology (mACR50) over 24 months and associated factors of response among patients (pts) with PsA initiating biological/targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) in the CorEvitas PsA/Spondyloarthritis Registry – a prospective, non-interventional North American research registry.

Methods: Pts who initiated b/tsDMARDs (March 2013–February 2022) and achieved mACR50 at 6 (±3) months post-initiation were followed until the first occurrence of loss of treatment response (defined as earliest occurrence of b/tsDMARD discontinuation, non-biologic addition, or loss of mACR50), last study visit, or 24 months post-achievement. The mACR50 response measure, which did not require laboratory results, was validated to have high correlation with ACR50 in the CorEvitas registry.[1]

Pt and clinical characteristics, including disease activity and pt-reported outcomes (PROs), were assessed at treatment initiation (index) and time of mACR50 achievement. Percent (95% confidence interval [CI]) maintaining treatment response at 6, 12, 18, and 24 months along with median time to loss of response were reported. Unadjusted proportional hazards

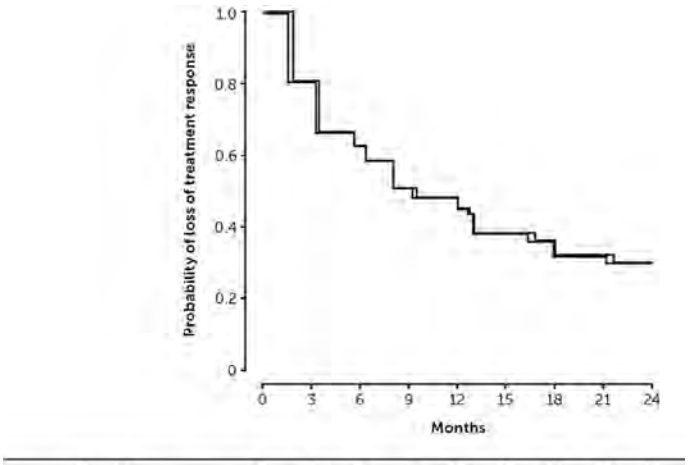
regression models for interval-censored outcomes were used to identify predictors of mACR50 response durability. A multivariable-adjusted regression model was used to calculate hazard ratios (HRs) to evaluate associations between pt characteristics and loss of response over follow-up.

Results: The analysis included 189 b/tsDMARD initiations. Mean (standard deviation [SD]) age was 53.0 (13.3) years. Overall, 52% of pts were female, 89% were white, 86% were overweight/obese, 58% pts were biologic-naïve. Mean (SD) PsA disease duration was 5.9 (7.6) years, with 8.1 (9.3) years since symptom onset.

At mACR50 achievement, improvements in disease activity and PROs were observed. However, 8% of mACR50 achievers still had moderate/high disease activity according to the Clinical Disease Activity Index for Psoriatic Arthritis (cDAPSA) and 20% had not reached Minimal Disease Activity.

Over the 24-month follow-up, 37% (95% CI: 31%, 43%) lost response at 6 months, 52% (95% CI: 45%, 58%) at 12 months, and 70% (95% CI: 65%, 75%) at 24 months (**Figure 1**, **Table 1**). Median time for loss of mACR50 was 9.3 months (95% CI: 7.5, 13.0).

Multivariable-adjusted analysis showed that higher EuroQol-5D (EQ-5D) score at achievement of mACR50 (0.1 unit increase, HR=0.8 [95% CI: 0.67, 0.96]) and having a college education (HR=0.5 [95% CI: 0.30, 0.83]) were associated with lower risk of initial mACR50 loss (**Table 2**).



Months	0	3	6	9	12	15	18	21	24
Number remaining at risk (n)	189	185	155	122	110	92	82	76	72

N= 189. mACR50: 50% improvement in the modified American College of Rheumatology response. Calculation of the mACR50 response correlates with calculation of the ACR50 response, but with the removal of laboratory measures (erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP]).[1]

Figure 1. Kaplan-Meier Curve of Estimated Time Until Loss of mACR50 Treatment Response

Table 1. Description of Time Until Loss of mACR50 Treatment Response

	Months (95% CI) to loss of response			Percent (95% CI) maintaining treatment response			
	25th percentile	Median	75th percentile	6 months	12 months	18 months	24 months
All initiators (N=189)	3.4 (1.8, 3.7)	9.3 (7.5, 13)	NA (21.6, NA)	62.8 (56.6, 69.3)	48.1 (42.1, 54.5)	31.9 (26.7, 37.7)	30.1 (24.8, 35.2)

NA: As 30% maintained response at 24 months (the end of follow-up), the 75th percentile of time to loss of response could not be calculated; mACR50: 50% improvement in the modified American College of Rheumatology response.

Table 2. Hazard Ratios Assessing the Association Between Loss of Treatment Response and Patient and Disease Characteristics

	Unadjusted[a]		Adjusted[b]	
	HR (95% CI)	p value	HR (95% CI)	p value
Demographic Characteristics				
Age at Index Visit				
5-Year Increase	1.05 (0.98, 1.14)	0.175	1.02 (0.92, 1.14)	0.683
Sex (Reference: Male)				
Female	1.18 (0.81, 1.72)	0.389	1.23 (0.78, 1.95)	0.372
Education (Reference: No College)				
College-Educated	0.56 (0.36, 0.86)	0.008*	0.50 (0.3, 0.83)	0.007*
Work Status (Reference: Not Full-Time)				
Full-Time	0.85 (0.58, 1.23)	0.387	0.88 (0.52, 1.49)	0.644
BMI (Reference: Underweight/Normal)				
Overweight	1.11 (0.62, 1.98)	0.732	1.41 (0.56, 3.55)	0.472
Obese	1.08 (0.63, 1.86)	0.775	1.06 (0.44, 2.55)	0.904
Disease Characteristics				
BSA at Response Achievement				
5-Unit Increase	1.21 (0.92, 1.6)	0.181	1.05 (0.98, 1.14)	0.183
Fatigue (VAS-100) at Response Achievement				
5-Unit Increase	1.05 (1.01, 1.09)	0.01*	1.01 (0.96, 1.07)	0.609
EQ-5D at Response Achievement				
0.1 Unit Increase	0.82 (0.72, 0.93)	0.002*	0.80 (0.67, 0.96)	0.018*
Combination Therapy with cDMARD (Reference: Monotherapy)				
Polytherapy	1.14 (0.76, 1.69)	0.532	1.27 (0.92, 1.75)	0.148

*The significance level was set at p<0.05. [a]Univariate model where each predictor was tested one at a time; [b]Models were adjusted for age, sex, college education, work status, BMI, BSA, fatigue, EQ-5D, and combination therapy; model variables were selected based on univariate regression results and clinical knowledge. BMI: body mass index; BSA: body surface area; cDMARD: conventional disease-modifying antirheumatic drug; CI: confidence interval; EQ-5D: EuroQol-5D; HR: hazard ratio; VAS: Visual Analog Scale.

Conclusion: Among pts with PsA who achieved mACR50 after b/tsDMARD initiation, approximately one third lost treatment response at 6 months, and two thirds lost treatment response at 18- and 24-months post-achievement. A higher EQ-5D score, denoting greater health status, was associated with longer durability of mACR50, following the initial response.

References:

1. Greenberg JD et al. Rheumatol 2009;48:686–90.

Disclosure: A. Ogdie: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, UCB, 2; **C. Song**: UCB Pharma, 3, 11; **N. Middaugh**: CorEvitas, LLC, 3; **M. Marchese**: CorEvitas, LLC, 3; **M. Eliot**: CorEvitas, LLC, 3; **S. Beaty**: UCB Pharma, 3, 11; **R. Low**: UCB Pharma, 3, 11; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2.

Abstract Number: 0500

Analysis of the Probability of Retention of Golimumab as a Two-phase Exponential Decay Curve in Rheumatoid Arthritis or Spondyloarthropathies to Identify Patients with Higher Probability of Long-term Retention

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Selecting patients with the highest probability of long-term retention of biological treatments is important from a clinical and cost-effectiveness point of view. In this work, we analyzed the Kaplan-Meier curve of golimumab retention in patients with rheumatoid arthritis (RA) and spondyloarthropathies (SpA, including axial SpA plus psoriatic arthritis [PsA]) fitted to a two-phase exponential decay curve, to identify the moment the curve changes from fast to slow decay, and to study factors related to golimumab retention at that moment, i.e, the patient profiles most likely to retain golimumab in the long term.

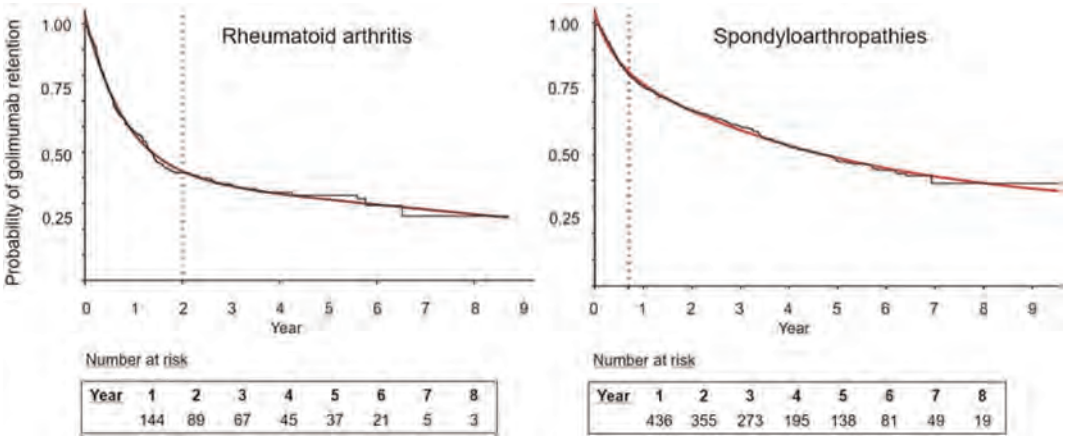
Methods: Data were retrospectively analyzed from the BIOBADASER registry. The Kaplan–Meier retention curve of golimumab was fitted to a two-phase exponential decay curve using GraphPad Prism version 9.3.1 for Windows, and the change in the trend of the curve from fast to slow decay (i.e, from high to low golimumab discontinuation rate) was identified with the formula:

$$Retention_0 - SpanFast = Retention_0\ (Retention_0 - Plateau) * PercentFast * 0.01$$

($Retention_0$ = retention value when time is zero, Plateau = retention value at infinite times, PercentFast = fraction of the span (from $Retention_0$ to Plateau) where the decay is fastest).

Variables associated with retention at the moment of the decay change were studied with Cox-regression analysis. Furthermore, the retention rates at that moment by subgroups of combination of the different variables identified in the Cox regression were calculated. Axial SpA and PsA showed similar curves and were analyzed together as a group (SpA group).

Results: A total of 267 patients with RA and 618 with SpA were included. The Kaplan-Meier curve fitted to a two-phase exponential decay curve for RA and for SpA yielded a coefficient of determination (R^2) = 0.99 and identified month 24 and month 8 as the moment the curve changed from fast to slow decay for RA and for SpA respectively (figure). By Cox regression analysis, second/third line of therapy, older age and use of glucocorticoids at golimumab initiation were associated with golimumab discontinuation at month 24 in RA. In SpA, factors associated with golimumab discontinuation at month 24 in RA. In SpA, factors associated with golimumab discontinuation at month 8 were female sex, second/third line of therapy and disease activity > median at golimumab initiation. Tables 1 and 2 show the retention rates at month 24 (RA) and at month 8 (SpA) stratified by the variables identified in the Cox regression.



Kaplan Meier curve showing probability of golimumab retention. The red line represents the fit of the Kaplan-Meier survival curve to the exponential two-phase decay equation model

Table 1. Retention rate of golimumab at month 24 in RA patients by combination of variables identified in the Cox regression analysis

Line of therapy	Age (years)		Corticosteroids at golimumab initiation	
First line: 54.7 (44.9 – 64.5)	< 45:	51.3 (29.5 – 73.1)	No:	85.7 (59.8 – 100.0)
			Yes:	32.5 (6.8 – 58.2)
	45 – 65:	52.9 (40.6 – 65.2)	No:	63.3 (44.1 – 82.5)
			Yes:	46.5 (30.8 – 62.2)
	≥ 65:	66.7 (42.8 – 90.6)	No:	50.0 (*)
			Yes:	72.7 (46.2 – 99.2)
Second line: 35.1 (23.9 – 46.3)	< 45:	55.6 (23.1 – 88.1)	No:	42.9 (6.2 – 79.6)
			Yes:	(**)
	45 – 65:	36.9 (23.2 – 50.6)	No:	34.8 (14.2 – 55.4)
			Yes:	38.8 (20.4 – 57.2)
	≥ 65:	18.2 (0.0 – 39.6)	No:	22.2 (0.0 – 49.4)
			Yes:	(***)
Third or subsequent line: 34.5 (23.9 – 45.1)	< 45:	64.8 (36.8 – 92.8)	No:	62.5 (20.8 – 100.0)
			Yes:	66.7 (29.1 – 100.0)
	45 – 65:	30.5 (15.6 – 45.4)	No:	32.8 (12.0 – 53.6)
			Yes:	27.8 (7.0 – 48.6)
	≥ 65:	27.5 (10.8 – 44.2)	No:	63.6 (35.2 – 92.0)
			Yes:	12.2 (0.0 – 27.3)

(*) Only four patients in this group. Confidence intervals were not calculated; (**) Only one patient in this group, who reached month 24; (***) This group comprised nine patients, five discontinued golimumab before month 24 and the remaining four were on golimumab therapy but had not reached a follow-up of 24 months at the time of study analysis.

Table 2. Retention rate of golimumab at month 8 in SpA patients by combination of variables identified in the Cox regression analysis

Sex	Line of therapy		Disease activity at golimumab initiation	
Men: 86.0 (82.3 – 89.7)	First line:	91.5 (86.8 – 96.2)	< median:	93.2 (87.5 – 98.9)
			> median:	88.9 (79.7 – 98.1)
	Second line:	86.6 (80.3 – 92.9)	< median:	88.9 (81.1 – 96.7)
			> median:	83.7 (72.7 – 94.7)
	Third or subesquent line:	78.7 (71.1 – 86.3)	< median:	83.0 (72.2 – 93.8)
			> median:	81.5 (71.1 – 91.9)
Women: 75.7 (70.6 – 80.8)	First line:	81.5 (73.1 – 89.9)	< median:	94.1 (86.3 – 100.0)
			> median:	78.9 (66.0 – 91.8)
	Second line:	78.3 (70.1 – 86.5)	< median:	76.5 (62.2 – 90.8)
			> median:	78.0 (66.4 – 89.6)
	Third or subesquent line:	67.7 (58.1 – 77.3)	< median:	80.0 (65.7 – 94.3)
			> median:	64.9 (50.0 – 79.8)

Conclusion: The golimumab retention curve changes from fast to slow decay at month 24 in RA and at month 8 in SpA. After that moment, the rate of golimumab discontinuation slows. The probability of retention of the different patient profiles calculated might allow a better identification of patients with higher probability of retention in the long-term to be treated with golimumab. The study is limited by the low number of patients in several subgroups of RA.

Disclosure: J. Diaz-Gonzalez: None; **L. Cea-Calvo**: Medical Affairs MSD Spain, 3; **E. González-Dávila**: None; **M. Sánchez-Jareño**: Medical Affairs MSD Spain, 3; **M. Pombo Suarez**: Janssen, 6, MSD Spain, 6; **F. Alonso**: None; **I. Castrejon**: Bristol Myers Squibb, 1, 6, Galapagos, 2, GlaxoSmithKline, 1, 6, Lilly, 1, 6, Merck Sharp & Dohme, 6, Pfizer, 1, 2, 6.

Abstract Number: 0501

Multicentre Study of Uveitis in Spondyloarthritis: Prevalence, Characteristics, and Prognosis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Data are still scarce about risk factors predicting the occurrence and course of uveitis in spondyloarthritis (SpA). We aimed to examine associations between demographic, clinical, and/or laboratory characteristics of SpA with the occurrence and the course (including eye damage and recurrence rate) of uveitis.

Methods: Characteristics (at disease diagnosis and ever-present) from all SpA patients in 3 tertiary rheumatology-clinics (1/2018-1/2023) were retrospectively recorded. Comparisons were made between patients with and without uveitis, as well as between subjects with uveitis rate [episodes/year] above the median uveitis rate in the whole cohort and those without persistent uveitis. In multivariable models, age, gender, and variables that were statistically significant in univariate analyses were included.

Results: 264 AxSpA and 369 PsA patients were enrolled. In AxSpA, uveitis occurred in 11.7% and was associated (multivariable analysis) with HLA-B27 (OR = 4.15, 95% CI 1.16-14.80, p=0.028) and ever-present peripheral arthritis (OR 3.05 (1.10 – 8.41, p=0.031;) (Table 1). In PsA, uveitis was reported in 2.7% of patients and was associated with SpA family history (p=0.023; 6.35 (1.29-31.27), axial disease at diagnosis (p=0.038; 5.61 (1.01-28.69) and disease duration (. p=0.004; 1.12 (1.04-1.21) (Table 2). Median uveitis rate was 0.205 for AxSpA and 0.285 for PsA. No associations were found between those above the above rates and demographic/clinical/laboratory characteristics. Permanent vision damage was seen in 16.1% of AxSpA and 30% of PsA patients, all of them with recurrent uveitis.

Conclusion: Uveitis in SpA is associated with specific characteristics. Permanent eye damage is not rare, especially in those with recurrent uveitis.

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Table 1: Comparison of demographic, laboratory, and clinical characteristics between AxSpA patients who developed uveitis and those who did not.

Table 1

	AxSpA		
Feature	Recurrent (n= 17)	Non-recurrent (n= 14)	p-value
Demographics			
Age (years), mean (SD)	52.7 (14.5)	51.8 (16.6)	0.872
Female gender, n (%)	8 (47.0)	6 (42.8)	1.000
BMI, mean (SD)	26.7 (3.9)	25.0 (2.9)	0.253
Family history of SpA, n (%)	5/15 (33.3)	1/11 (9.0)	0.197
Smoking (current), n (%)	8 (47.0)	5/12 (41.6)	1.000
HLA-B27, n (%)	10/12 (83.3)	10/11 (90.9)	1.000
Clinical at Diagnosis			
Peripheral Arthritis, n (%)	2/16 (12.5)	4/10 (40.0)	0.162
Enthesitis, n (%)	0/16 (00.0)	0/10 (00.0)	1.000
Dactylitis, n (%)	0/16 (00.0)	0/10 (00.0)	1.000
Bowel involvement$^{\infty}$, n (%)	0/16 (00.00	1/10 (10.0)	0.384
Clinical (Ever)			
Peripheral Arthritis, n (%)	7 (41.1)	10 (71.4)	0.149
Enthesitis, n (%)	3 (17.6)	5 (35.7)	0.412
Dactylitis, n (%)	0 (0.0)	3 (21.4)	0.081
Bowel involvement$^{\infty}$, n (%)	0 (0.0)	1 (7.1)	0.451
Psoriasis, n (%)	2 (11.7)	2 (14.2)	1.000

AxSpA: axial spondyloarthritis, SD: standard deviation, n: number, ∞ inflammatory bowel disease confirmed by colonoscopy.

Table 2: Comparison of demographic, laboratory, and clinical characteristics between PsA patients who developed uveitis and those who did not.

Table 2

	PsA		
Feature	**Uveitis (n=10)**	**Non-uveitis (n=359)**	**p-value**
Demographics			
Age (years), mean (SD)	46.6 (7.5)	54.7 (13.1)	0.089
Female gender, n (%)	7/10 (70.0)	194/359 (54.0)	0.356
BMI, mean (SD)	24.7 (3.2)	28.6 (5.9)	0.053
Family history of SpA, n (%)	5 (50.0)	43/318 (13.5)	**0.0078**
Smoking (current), n (%)	5 (50.00)	117/331 (35.3)	0.338
HLA-B27, n (%)	3/7 (42.8)	22/125 (17.6)	0.124
Disease duration, mean (SD)	14.8 (9.2)	9.0 (9.1)	**0.012**
Clinical at Diagnosis			
Peripheral Arthritis, n (%)	8 (80.0)	231/286 (80.7)	1.000
Enthesitis, n (%)	3 (30.0)	38/329 (11.5)	0.107
Dactylitis, n (%)	1 (10.0)	31/343 (9.0)	1.000
Axial Disease*, n (%)	6 (60.0)	57/332 (17.1)	**0.0036**
Bowel involvement$^{\infty}$, n (%)	0 (00.0)	3/353 (0.8)	1.000
Clinical (Ever)			
Peripheral Arthritis, n (%)	9 (90.0)	335 (94.3)	0.508
Enthesitis, n (%)	6 (60.0)	98 (27.2)	**0.0333**
Dactylitis, n (%)	5 (50.0)	76 (21.1)	**0.0451**
Axial Disease*, n (%)	6 (60.0)	109 (30.3)	0.076
Bowel involvement$^{\infty}$, n (%)	3 (30.0)	15 (4.1)	**0.0095**

PsA: psoriatic arthritis, SD: standard deviation, n: number, * clinical plus imaging (x-ray or magnetic resonance) evidence, ∞ inflammatory bowel disease confirmed by colonoscopy.

Abstract Number: 0502

Developing Electronic Health Record Algorithms to Accurately Identify Psoriatic Arthritis Patients

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic, progressive inflammatory disease of the skin and musculoskeletal system, affecting over half a million US adults. With relatively uncommon diseases such as PsA, electronic health records (EHR) offer an opportunity to better understand long-term outcomes in the real-world setting. EHR are an efficient and cost-effective tool that allows for the identification of a large number of patients in the real-world setting for clinical and translational research. However, the clinical heterogeneity of PsA along with a lack of clear diagnostic criteria or tests poses a diagnostic challenge. This also translates into a difficulty in identifying PsA patients in the EHR. Identifying PsA patients accurately in the EHR is crucial to study long-term outcomes in PsA in the real-world setting. Therefore, the objective of this study was to develop EHR algorithms to accurately identify patients with PsA.

Methods: We used a de-identified version of Vanderbilt's EHR called the Synthetic Derivative (SD containing ~3.5 million subjects) to identify our PsA cohort. The SD includes longitudinal clinical data over several decades (1993-2021) with all information available in the EHR. We screened the SD for adult patients (≥18 years of age) with one International Classification of Diseases, Ninth or Tenth Revision (ICD 9/10) code for psoriatic arthritis or any psoriatic arthritis keyword in the problem list (**Figure 1**). Of the 5,636 potential PsA cases, we randomly selected 200 for chart review

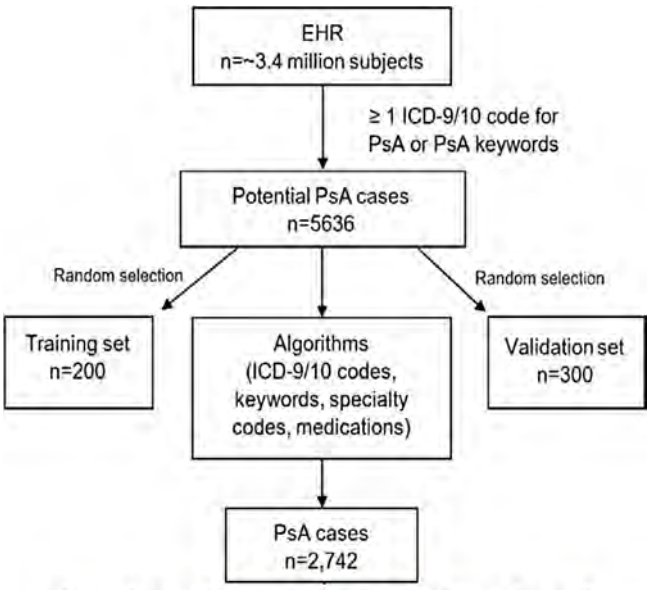

Figure 1. Development of EHR algorithms for PsA
n= number of individual patients

Figure 1. Development of the electronic health record algorithms for psoriatic arthritis

to identify their true disease status and to serve as a training set and a separate random set of 300 as the validation set. A rheumatologist diagnosis of PsA or fulfillment of CASPAR criteria based on manual chart review was used as the reference standard. Potential algorithm components decided *a priori* were ICD 9/10 codes for PsA and psoriasis, ICD 9/10 codes for PsA by rheumatology and dermatology, keywords for PsA in the problem list, and use of disease-modifying antirheumatic drugs (DMARDs). Positive predictive value (PPV) and sensitivity, along with the F-score (harmonic mean of PPV and sensitivity), were calculated.

Table 1. Performance of high-performing algorithms using specialty and medications in addition to PsA ICD 9/10 codes

Algorithm	PPV in training set	PPV in validation set	Sensitivity	F-score (training set)
≥ 4 counts ICD 9/10 counts	90%	93%	71%	0.79
≥ 1 count by a rheumatologist	95%	95%	51%	0.66
≥ 4 PsA ICD 9/10 counts **OR** ≥ 1 count by a rheumatologist	**91%**	92%	**81%**	**0.86**
≥ 4 PsA ICD 9/10 counts **AND** ever DMARD use	91%	93%	67%	0.77

Table 2. Baseline characteristics of the psoriatic arthritis electronic health record cohort (n=2,742)

Baseline characteristics	Mean (SD)
Age, years	50.2 (13.5)
Female, no. (%)	1602 (58.4)
Race, no. (%)	
White	2453 (89.5%)
African American	54 (2.0%)
Hispanic	30 (1.1%)
Asian	28 (1.0%)
Alaskan/Indian	4 (0.2%)
Missing/unknown	189 (6.9%)
No. of PsA ICD codes	15 (16)
BMI (kg/m^2)	29.9 (7.3)
Years of follow-up	8 (5)
PsA Medications Ever*	
Conventional DMARDs	1956 (71.4%)
TNFi	1834 (66.9%)
PDE4	460 (16.8%)
JAKi	112 (4.1%)
IL-17i	504 (18.4%)
IL-23i	109 (4.0%)
Abatacept	111 (4.1%)

SD= standard deviation, PsA= psoriatic arthritis, ICD= International Classification of Diseases, BMI= body mass index
*Adds to more than 100% because these are medication ever used

Results: The best-performing algorithms in the training and validation sets are shown in **Table 1**. Using the best performing algorithm of ≥ 4 PsA ICD 9/10 codes OR at least 1 ICD 9/10 code by a rheumatologist (PPV of 91%, sensitivity 81%, F-score 0.86), we identified 2,742 PsA patients. The mean age of the EHR cohort was 50.2 (SD 13.5), 58.4% female, and the majority (89.5%) were white, with a mean follow-up of 8 (SD 5) years (**Table 2**).

Conclusion: We have successfully developed an EHR algorithm using ICD-9/10 codes, demonstrating a PPV of 92% in internal validation. This rule-based algorithm represents a useful tool for clinical and translational research to identify PsA patients efficiently and accurately in an EHR. The EHR-based PsA cohort will enable longitudinal, de-identified chart review for further sub-phenotyping, and pragmatic clinical studies that pave the way for personalized treatment approaches.

Disclosure: P. Karmacharya: None; **A. Fortier**: None; **G. Sellyn**: None; **A. Ogdie**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, UCB, 2; **L. Crofford**: None.

Abstract Number: 0503

Spinal Inflammation a Dominant Pathology in Psoriatic Arthritis: Characterization and Quantification by *In-Vivo* ^{18}F-FDG Total-Body PET/CT Imaging

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Right and Moll recognized the presence of spinal inflammation/axial disease in psoriatic arthritis (PsA) in their seminal work in 1973. The prevalence of axial disease in patients with PsA varies with disease duration. The Total Body (TB)-PET/CT with the ^{18}F-FDG radiotracer captures glucose metabolism across the entire body, and provides standardized measures as surrogates for degree of inflammation such as SUVmax. The objective of this study was to apply high-sensitivity TB ^{18}F-FDG PET/CT imaging to identify and characterize the spectrum of spinal inflammation in patients with PsA.

Methods: We prospectively recruited 25 PsA patients (6 female, 19 male; mean age of 51.4±16.4 years), as per CASPAR criteria. Among them, 8 patients had inflammatory low back pain (LBP). All subjects underwent a single-time point ^{18}F-FDG TB-PET/CT using 1/5th the standard radioisotope dose (78.2±4.9 MBq) *(Abdelhafez Y,et al .J Nucl Med. 2022(10):1579-1585)*.

Degree of inflammation was quantified by using maximum standardized uptake value ratio corrected by the background level (rSUVmax).Qualitative changes in the joints (atlantoaxial, apophyseal, costovertebral/costotransverse, and sacroiliac) and entheses (cervical/thoracic/lumbar supra- and interspinous ligaments) were also evaluated.

Results: In one or more of the described sites PET imaging demonstrated abnormality in 21 (84%) patients. Notable changes respectively were observed in atlantoaxial **(Figure 1),** apophyseal, costovertebral/ costotransverse, and sacroiliac joints **(Figure 2)** in 15 (60%), 18 (72%), 11 (44%), and 5 (20%) patients in variable combinations.

20% patients(5/25) demonstrated sacroiliitis by PET imaging, among them the involvement was unilateral in three and bilateral but asymmetric in two patients **(Figure 2).** A patient with PsA with inflammatory LBP for >5 years had no evidence of sacroiliitis on MRI but demonstrated unilateral pronounced sacroiliitis on PET.

Increased ^{18}F-FDG uptake suggestive of active inflammation on PET imaging was observed in cervical, thoracic, and lumbar spine enthuses **(Figure 3**) in 14 (56%), 17 (68%), and 15 (60%) patients, respectively. Overall, spinal enthesitis was evident in 80% (20/25) patients.

Quantification of the total spinal inflammatory load (rSUVmax) could be measured in each patient, the summed rSUVmax/patient was on average 7.3±3.1 for all the described sites.

Conclusion: TB-PET/CT scan is an US FDA approved technology. We observed spinal inflammation to be a dominant pathology in PsA : i. Our findings provide direct in-vivo evidence that enthesitis could be the primary pathology for axial inflammation in PsA; spinal enthesitis was observed in 80% of patients. In majority of the patients this pathology was clinically occult, as only about one third of the patients reported back pain. ii. Non-radiographic axial disease in PsA remains unaddressed. Here we have demonstrated this condition in PsA and we provide TB-PET/CT as a biomarker tool to diagnose this

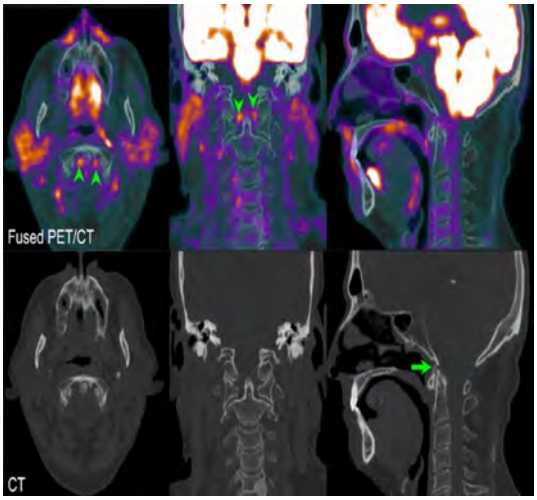

Figure 1. Changes in atlanto-axial articulation. Fused 18F-FDG PET/CT sections (top row) and their corresponding low-dose CT (bottom row) extracted from TB-PET/CT for a 62-year-old man with PsA in axial (left), coronal (middle) and sagittal (right) views. Images demonstrate intense FDG uptake with rSUVmax 1.7 at the alar ligaments (arrowheads) with evidence of ossification of the anterior atlanto-occipital membrane on the CT (arrow).

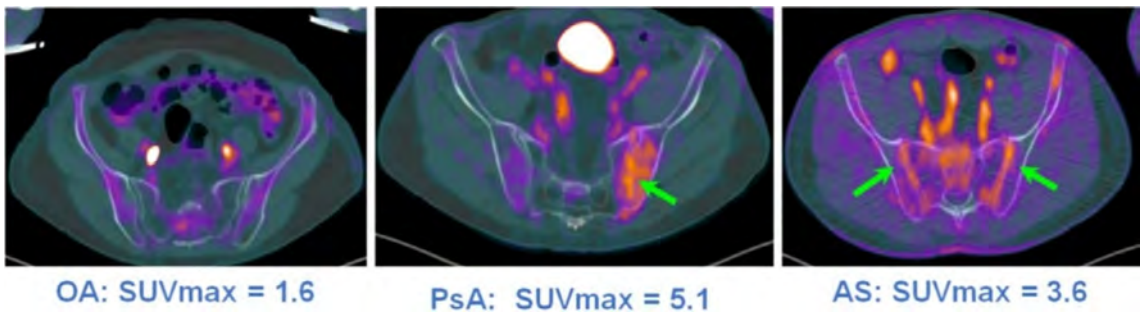

Figure 2. Asymmetric sacroiliac inflammation in Psoriatic arthritis. PET-CT imaging is capable of Identifying and providing in vivo quantitative measures of the degree of inflammation (SUVmax) as shown in this figure. Compared to osteoarthritis (OA) marked unilateral SI joint inflammation can be been in psoriatic arthritis (PsA) and bilateral symmetric inflammation of SI joints in ankylosing spondylitis (AS).

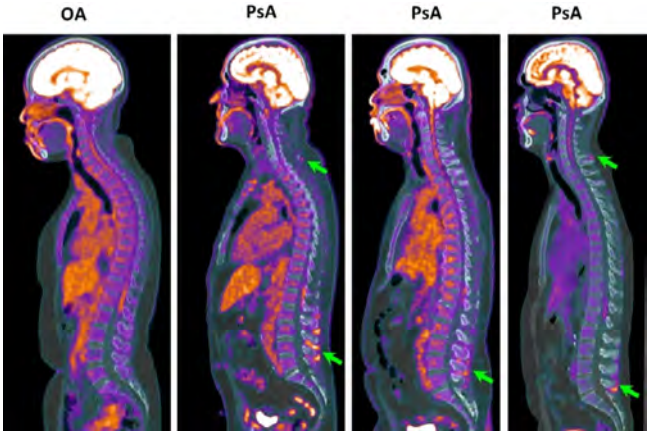

Figure 3. PET-CT in Diagnosis of Psoriatic Arthritis Axial Disease. Enthesitis at multiple levels in the spine (green arrows) with or without sacroiliitis is an interesting finding in the psoriatic arthritis (PsA) patients by total body the PET-CT imaging. Where as in osteoarthritis (OA) spinal inflammation could not be detected. Involvement of the inter-/supra-spinous ligament are marked by the green arrows.

condition. iii. In-vivo TB-PET imaging provided the total inflammatory burden (rSUVmax) of the whole spine thus demonstrating the ability of TB-PET/CT as a quantitative tool for assessing disease severity and for therapeutic response.

Disclosure: S. Raychaudhuri: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, SUN Pharma, 2, 5, 6, UCB, 2, 5, 6; **Y. Abdelhafez**: None; **D. Mazza**: None; **S. Raychaudhuri**: None; **A. Chaudhari**: None.

Abstract Number: 0504

Burden of Disease of Psoriatic Arthritis in Latin America: A Systemic Review of Literature

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA
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Background/Purpose: Psoriatic arthritis (PsA) is a chronic inflammatory pathology that generates a substantial and progressive deterioration of functionality and quality of life. It is associated with comorbidities such as cardiovascular disease, metabolic diseases and a significant compromise of mental health. In Latin America, information regarding the disease is limited. This study reviews the burden of disease (disease activity, function, clinical manifestations, comorbidities, patient-reported outcomes, quality of life, and use of health resources) in adults diagnosed with PsA in Latin America.

Methods: A SLR of the literature was carried out to determine the burden of PA in Latin America, under a qualitative and quantitative approach, following the PRISMA report. Publications in PUBMED, EMBASE, Cochrane Database of Systematic Reviews – CDSR, LILACS, Scielo, Redalyc, conference abstracts and grey literature, were reviewed. The full texts of potentially eligible studies were assessed independently, extracting in each the data requested by a pre-specified data collection

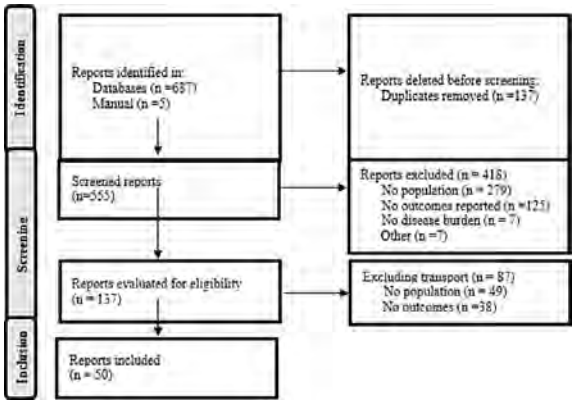

Table 1. Measures of disease activity in patients with psoriatic arthritis in Latin America

I am a student	n	Country	DAS28	BASDAI	CDAI	MDA	NS	PGA
Molina et al[40]. (2007)	148	Argentina	3.51 (SD 1.21)	Biologics 1.8 (SD 1.6) NSAID 4.7 (SD 2.6) DMARD 3.9 (SD 2.3)			2 (IQR 0-4.6)	
Buschiazzo et [41] (2011)	242	Argentina		3,8 (IQR 2-6.1)			12 (SD 11)	
Sampaio-Barros et [42] (2011)	139	Brazil		4.0 (SD 2.5)				
Costa et [43] (2015)	289	Argentina, Brazil, Costa Rica, Chile, Ecuador, Mexico, Peru, Uruguay and Venezuela		4.13 (SD 2.47)				
Oliveira et al[44]. (2015)	39	Brazil		5.27 (SD 2.26)	26.90 (SD 14.80)			
Paniagua et [45] (2015)	87	Argentina					11.2 (SD 6.1)	
Gallino et [46] (2016)	110	Argentina		4,37 (IQR 1,83-6,53)			1,6 (IQR 0,4-4,48)	
Zaffarana et [47] (2017)	110	Argentina		Normal weight 3.8 (SD 2.5) Overweight 3.9 (SD 2.9) Obesity 4.9 (SD 2.8)		Normal weight 5 (SD 23.8) Overweight 10 (SD 20.8) Obesity 4 (SD 9.75)	Normal weight 1.5 1.7) overweight 3.1 (2.8) obesity 2.5 (2.9)	Normal weight 1.2 (SD 1.3) Overweight 2.2 (SD 1.5) Obesity 1.9 (SD 1.7)
da Silva et [48] (2018)	122	Brazil		5,24 (IQR 3,05-6,85)	16,7 (RIC 8,78-32,8)			
Adeodatus et [49] (2021)	76	Brazil	With MS: 3.01 (2.21–4.01) Without MS: 3.17 (1.94–5.05)	With MS: 2 (1.40–5.65) Without MS: 3.85 (2.40–5.70)			With MS: 1.4 (IQR 0–3) Without MS: 0.2 (IQR 0-2.8)	
da Silva et [50] (2021)	114	Brazil		5.41 (SD 2.46)	22.58 (SD 16.46)			
Moraes et [51] (2021)	212	Brazil		5.18 (SD 2.53)	22.54 (SD 16.89)			
Gamonal et [52] (2021)	73	Brazil					17.08 (SD 4.68)	
da Silva et [53] (2022)	130	Brazil						3.4 (SD 2.7)

The values reported with interquartile range (IQR) present the median. The values reported with standard deviation (SD) present the mean. BASDAI Bath Ankylosing Spondylitis Disease Activity Index; DAS28 Disease Activity Score 28-joint counts; CDAI, Clinical Disease Activity Index; SD Standard Deviation; MDA Minimal Disease Activity (MDA); PASI Psoriasis Area Severity Index; PGA Physician's Global Assessment; IQR Interquartile range. MS metabolic syndrome

instrument. Quality was assessed according to the type of study. Risk of bias assessment was performed with the instrument validated for cross-sectional studies, for cohort studies the instrument validated (CLARITY tool) was used. The Joanna Briggs quality tool was used for economic evaluations. To reduce publication bias, we searched grey literature.

Results: We identified 692 references, selecting 50 studies: 41 cross-sectional, 4 economic studies, 4 cohort studies and 1 systematic review. The information comes mainly from Brazil, Argentina and Mexico. The estimated disease prevalence for Latin America ranges from 0.004% to 0.08% (95% CI 0.02–0.20). The disease duration was reported with a mean of 7.2 years (95% CI 6.94-7.52). DAS28 scored between mild to moderate disease activity (mean 3.01–3.51). Lower activity was reported in patients with normal body weight *versus* those who were overweight or obese. Disability assessed using the HAQ-DI reports data of 1.1 ±0.7. Patients treated with biologics had fewer impairments in function than those treated with NSAIDs, without treatment or with DMARD. The SF-12 health survey, report averages of 43 (physical component) and 42-45 (mental component). In a registry, 39.6% of these were employed. The greater the severity of the disease, the lower the employment rate (mild:50%, moderate:38.7%, severe:38.5%). Twelve studies reported frequency of medication use, 30.3% (6.2%-42.5%) receiving corticosteroids, 47.8% (38.5%-82.4%) methotrexate, 38.3% (9.2%-40.6%) leflunomide and 23.5% (8%-56.2%) biologics.

Table 2| Measures of function and disability in patients with psoriatic arthritis in Latin America

I am a student	N	Country	BASFI	HAQ-DI
Molina et [40] (2007)	148	Argentina	Biologics 1.4 (SD 1.8) NSAIDs 3.6 (SD 3.2) DMARD 3 (DE 2.9)	1.03 (SD 0.78)
Buschiazzo et [31] (2011)	242	Argentina	2,5 (IQR 0,7-5,4)	
Sampaio-Barros et al. [33] (2011)	139	Brazil	4.0 (SD 2.9)	
Oliveira et [42] (2015)	39	Brazil		1.30 (SD 0.64)
Gallino et [23] (2016)	110	Argentina	3,55 (IQR 0,92-5,8)	0,75 (IQR 0,16-1,22) *
Lopes et [32] (2017)	90	Brazil		
Zaffarana et [45] (2017)	110	Argentina	Normal weight 2.7 (SD 2.5) Overweight 3.3 (SD 2.7) Obesity 4.4 (SD 2.8)	Normal weight 0.63 (SD 0.6) Overweight 0.71 (SD 0.6) Obesity 0.96 (SD 0.6)
da Silva et [39] (2018)	122	Brazil		1,25 (IQR 0,50-1,75)
Palominos et [25] (2018)	15	Brazil		HAQ>1: 11 (73,1%)
Salario et [53] (2018)	37	Argentina		1.4 non-working group 0.6 Working group
Soriano et [17] (2020)	179	Mexico, Colombia and Argentina		12.9 (SD 17) **
Adeodatus et [44] (2021)	76	Brazil		With metabolic syndrome 1.37 (IQR 0.37–1.62) Without metabolic syndrome 0.87 (IQR 0.25–1.50)
da Silva et [50] (2021)	114	Brazil		1.21 (SD 0.74)
Moraes et [41] (2021)	212	Brazil		1.20 (SD 0.71)
da Silva et [47] (2022)	130	Brazil		0.76 (SD 0.7)

The values reported with interquartile range (IQR) present the median. The values reported with standard deviation (SD) present the mean. Statistically significant differences are presented in bold.

*HAQ Argentinian version. ***Patient-Reported Outcomes Measurement Information System Health Assessment Questionnaire* [PROMISHAQ], range de 0 a 100

BASFI Bath Ankylosing Spondylitis Functional Index, ranges from 0 (no limitation) to 10 (maximum limitation on function); HAQDI Health Assessment Questionnaire Disability Index. range 0 to 3 where higher scores indicate greater deficiency; IQR interquartile range; SM metabolic syndrome.

Conclusion: This study reports a considerable burden of disease in patients with PsA in Latin America, with involvement of quality of life associated with disability in relation to disease activity and its various manifestations. Measurements with validated instruments suggest suboptimal assessment of disease domains, significant functional compromise, loss of productivity, and high frequency of comorbidities, including mental health.

Disclosure: W. Bautista-Molano: None; **L. Ibata**: None; **S. Martinez**: None; **A. Chacon**: None.

Abstract Number: 0505

Factors Associated with Minimal Disease Activity in Psoriatic Arthritis: Insights from a Registry-Based Study

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SESSION INFORMATION
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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Achieving minimal disease activity (MDA) is an important treatment goal in psoriatic arthritis (PsA), as it leads to improved clinical outcomes and quality of life for patients. However, the impact of specific clinical factors and therapies on long-term MDA status requires further investigation. The aim of this study was to identify treatment factors associated with minimal disease activity (MDA) status in PsA patients.

Methods: We utilized data from a tertiary care psoriatic disease biorepository, collecting patient- and physician-reported outcomes and clinical information longitudinally. Adult PsA in the registry for more than one year with at least two evaluations of MDA status were included. A multivariable logistic regression model was constructed to investigate factors associated with long-term MDA status. Candidate predictors included: PsA duration (at the most recent recorded visit), gender, baseline MDA status, number of completed visits in the registry, number of medication regimen switches, and seven medication class-related variables (use of TNFi, IL-17i, IL-12/23i, IL-23i, JAKi, oral DMARD only, and combination biologic and oral DMARD). The outcome of interest was long-term MDA status, defined MDA status at the most recent registry visit. Continuous variables were summarized using medians and IQR, while categorical variables were summarized using counts and frequencies. Model results were presented using odds ratios and 95% confidence intervals for likelihood of being in non-MDA status at the most recent registry visit. All tests were two-sided, assuming an alpha level of 0.05.

Results: The analysis included 164 PsA patients with an average duration of PsA of 20.4 years, of whom 56% were female. Approximately 75% of patients were not in MDA at baseline, while approximately 54% of patients were not in MDA at their most recent evaluation. Baseline MDA status showed the most significant association with long-term MDA status. Patients in MDA at baseline had an 84% lower likelihood of being in non-MDA status at their most recent evaluation compared to patients not in MDA at baseline (OR 0.16, 95% CI: 0.06, 0.46, $p = 0.001$). In other words, patients in MDA at baseline were much more likely to be in MDA long-term. The use of IL-17 inhibitors (OR 3.38, 95% CI: 1.08, 10.59, $p = 0.036$) or oral DMARDs alone (OR 2.51, 95% CI: 1.01, 6.26, $p = 0.048$) during the registry period decreased the likelihood of long-term MDA status. No other medication or continue variable had a significant effect on the final MDA status.

Table 1: Demographic and Disease Characteristics of the PsA Study Cohort

Variable	Level	Total(n=164)	N
PsA Duration. Median [25th:75th]		20.4 [12.7;37.0]	146
Age at PsA Diagnosis. Median [25th:75th]		31.9 [20.3;44.3]	146
Gender. N (%)	Male	72 (43.9%)	164
	Female	92 (56.1%)	
Baseline MDA Status. N (%)	Non-MDA	124 (75.6%)	164
	MDA	40 (24.4%)	
Number of Medication Switches[1]. Median [25th:75th]		1.00 [0.00;2.25]	164
Ever on TNFi. N (%)	No	39 (23.8%)	164
	Yes	125 (76.2%)	
Ever on IL-17i. N (%)	No	131 (79.9%)	164
	Yes	33 (20.1%)	
Ever on IL-12/23i. N (%)	No	147 (89.6%)	164
	Yes	17 (10.4%)	
Ever on IL-23i. N (%)	No	155 (94.5%)	164
	Yes	9 (5.49%)	
Ever on JAKi. N (%)	No	156 (95.1%)	164
	Yes	8 (4.88%)	
Ever on DMARD alone. N (%)	No	101 (61.6%)	164
	Yes	63 (38.4%)	
Ever on Biologic + DMARD. N (%)	No	98 (59.8%)	164
	Yes	66 (40.2%)	
Number of Completed Visits. Median [25th:75th]		4.00 [2.00;5.00]	164
Most Recent MDA Status. N (%)	Non-MDA	89 (54.3%)	164
	MDA	75 (45.7%)	

[1] Number of times medication regimen was different from the prior registry visit

DMARD, disease modifying anti-rheumatic drugs; IL-17i, interleukin-17 inhibitor; IL-12/23i, interleukin-12/23 inhibitor; IL-23i, interleukin-23 inhibitor; JAKi, janus kinase inhibitor; MDA, minimal disease activity; TNFi, tumor necrosis factor inhibitor

Table 2: Analysis of Multivariable Logistic Regression Model Results in the Psoriatic Arthritis Study Cohort

Variable	Level	OR (95%CI)	P-value
PsA Duration (years)[1]	12.7–37	1.19 (0.68, 2.08)	0.538
Gender	F (v M)	1.12 (0.51, 2.46)	0.786
Baseline MDA	MDA (v non-MDA)	0.16 (0.06, 0.46)	0.001
Number of Visits	2–5	1.11 (0.53, 2.35)	0.782
Number of Medication Switches	0–2	1.48 (0.69, 3.2)	0.317
Ever on TNFi	Yes (v No)	1.51 (0.49, 4.63)	0.468
Ever on IL-17i	Yes (v No)	3.38 (1.08, 10.59)	0.036
Ever on IL-12/23i	Yes (v No)	0.68 (0.18, 2.63)	0.576
Ever on IL-23i	Yes (v No)	1.03 (0.18, 5.8)	0.970
Ever on JAKi	Yes (v No)	1.31 (0.23, 7.54)	0.761
Ever on DMARD alone	Yes (v No)	2.51 (1.01, 6.26)	0.048
Ever on Biologic + DMARD	Yes (v No)	1.07 (0.45, 2.56)	0.877

[1] For PsA duration, number of visits, and number of medication switches, OR reflects the IQR increase

IQR, interquartile range; OR, odds ratio

Conclusion: This registry-based study provides insights into factors associated with minimal disease activity in PsA patients. Baseline MDA status is a key predictor of long-term MDA status, emphasizing the importance of achieving early MDA. The use of IL-17 inhibitors and oral DMARD alone were associated with a decreased likelihood of achieving MDA. These findings can assist in risk stratification and guide clinicians in selecting therapies for improved psoriatic disease control.

Disclosure: S. Cheemalavagu: None; **Y. Jin**: None; **M. Husni**: AbbVie, 1, 2, Amgen, 1, 2, Bristol-Myers Squibb, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, UCB, 1, 2.

Abstract Number: 0506

Patient and Physician Global Assessment of Psoriatic Arthritis Disease Activity: High Concordance in an ArLAR Multinational Study

Nelly Ziade[1], Noura Abbas[2], Lina El Kibbi[3], Avin Maroof[4], Bassel Elzorkany[5], Nizar Ani[6], ASAL ADNAN[7], NABAA IHSAN JAWAD AWADH[7], Faiq Gorial[8], Nada Alchama[9], Chafika Haouichat[10], Fatima Alnaimat[11], Suad Hannawi[12], Saed Atawnah[13], HUSSEIN HALABI[14], Manal Al-Mashaleh[15], Laila Aljazwi[16], Ahmed Abogamal[17], laila Ayoub[18], Elyes Bouajina[19], Rachid Bahiri[20], Sahar Saad[21], Maha Sabkar[21], Krystel Aouad[22], Laure Gossec[23] and Ihsane Hmamouchi[24], [1]Saint-Joseph University, Beirut, Lebanon, [2]Saint Joseph University Beirut, Beirut, Lebanon, [3]Specialized Medical Center, Riyadh, Saudi Arabia, [4]Kurdistan University Hawler, Erbil, Iraq, [5]Private (BZRC), Cairo, Egypt, [6]Baghdad College of Medicine, Baghdad, Iraq, [7]Baghdad Teaching Hospital, Baghdad, Iraq, [8]University of Baghdad, Baghdad, Iraq, [9]Ebn Al Nafiss Hospital, Damascus, Syria, [10]Faculty of Medicine El Mahdi Si Ahmed, Blida, Algeria, [11]University of Jordan, Amman, Jordan, [12]Kuwait Hospital, Department of Rheumatology, Dubai, United Arab Emirates, [13]Al ahli hospital, Hebron, Palestine, Hebron, Palestinian Territories, [14]King Faisal Specialist Hospital & Research Centre, Jeddah, Saudi Arabia, [15]Royal Medical Services, Amman, Jordan, [16]Tripoli, Tripoli, Libya, [17]Saudi German Hospital Dubai, Dubai, United Arab Emirates, [18]University of Tripoli, Tripoli, Libya, [19]Farhat Hached Hospital of Sousse, Sousse, Tunisia, [20]Department of Rheumatology, El Ayachi Hospital Medical University, Sale, Morocco, [21]King Hamad University Hospital, Bahrain, Bahrain, [22]Saint George Hospital University Medical Center, Beirut, Lebanon, [23]Sorbonne Université and Pitié Salpêtrière Hospital, Paris, France, [24]Rheumatology Unit, Lalla Aicha Temara Hospital, Temara, Morocco

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: In patients with psoriatic arthritis (PsA), discordance between physicians and patients when assessing disease activity has been described as frequent, mainly in European and North American studies. This discordance may negatively impact treatment adherence and shared decision-making processes. Culture and beliefs influence patients' perceptions of health.

The purpose of this study was to evaluate the concordance between patient- (PGA) and physician-global assessment (PhGA) of PsA disease activity and its association with demographic and disease characteristics in a multinational group of patients from Arab countries.

Methods: This multicentric multinational cross-sectional study was conducted in thirteen Arab countries by the Arab League of Associations of Rheumatology (ArLAR) research group (ARCH). During a single routine visit, patients and physicians rated PsA disease activity on a numeric scale from 0 (no activity) to 10 (worse activity). In addition, demographic and disease data were collected, as well as PGA and PhGA for psoriasis (PsO) activity, Health Assessment Questionnaire (HAQ), Fibromyalgia Rapid Screening Tool (FiRST), Patient Health Questionnaire (PHQ4) and Disease Activity in Psoriatic Arthritis (DAPSA). First, the correlation between PGA and PhGA for PsA and PsO disease activity was assessed statistically

using the Spearman correlation coefficient and graphically using the Bland and Altman method. Second, concordance between the PGA and PhGA PsA activity (defined as a difference between -2 and 2) was calculated and correlated with demographic and disease factors using multivariable binary logistic regression.

Results: The study included 554 patients from thirteen countries: mean age 45 years (SD 13), 57% females, median disease duration four years (IQR 2-9); 89.2% had skin PsO, and 43.5% had nail PsO. The disease was active overall: mean DAPSA was 19.3 (SD 16.1), HAQ 1.1 (SD 0.8), and PHQ4 3.3 (SD 2.9). The screening test for widespread pain was positive in 18.4% of patients (Table 1). The mean PGA for PsA activity was 4.7 (SD 2.5) versus a PhGA of 3.9 (SD 2.4). Similarly, PGA for psoriasis activity was 4.0 (SD 2.8), and PhGA was 3.1 (SD 2.6). The correlation between PGA and PhGA was strong for PsA activity (r= 0.738) (with good agreement on Bland and Altman (Figure 1)) and moderate for psoriasis activity (r=0.613). Among 554 patients' measurements, 358 (84.2%) were in concordance with the physician's global assessment (Figure 2). In the multivariable analysis, concordance was independently associated with a high CRP (OR 2.32 [95%CI 1.33; 4.02] and DAPSA category (better concordance in patients in remission (OR 1.02 (95%CI 1.01; 1.03]).

Table 1. Patients' and disease's characteristics.

Characteristic	N or Mean or Median	% or SD or IQR
Number of patients (N)	554	
Age, years (mean, SD)	45.5	13.2
Gender (N, %)		
- Male	221	39.9
- Female	318	57.4
- Missing	15	2.7
Education (N, %)		
- None	13	2.3
- Elementary	99	17.9
- Secondary	164	29.6
- University	263	47.5
- Missing	15	2.7
BMI category (N, %)		
- Underweight	9	1.6
- Healthy	135	24.4
- Overweight	206	37.2
- Obese	189	34.1
- Missing	15	2.7
Current smoking (N, %)	99	17.9
PsA duration (median, IQR)	4	2 - 9
PsA diagnostic delay (median, IQR)	1	0 - 3
Skin psoriasis (N, %)		
- Yes	494	89.2
- No	45	8.1
- Missing	15	2.7
Nail psoriasis (N, %)		
- Yes	241	43.5
- No	298	53.8
- Missing	15	2.7
Psoriasis duration (median, IQR)	12	6 - 21
PGA for PsA activity (mean, SD)	4.7	2.5
PGA for PsA pain (mean, SD)	4.7	2.7
PGA for psoriasis activity (mean, SD)	4.0	2.8
PhGA for PsA activity (mean, SD)	4.0	2.4
PhGA for psoriasis activity (mean, SD)	3.1	2.6
DAPSA score (mean, SD)	19.3	16.1
HAQ score (mean, SD)	1.1	0.8
PHQ4 total score (mean, SD)	3.3	2.9
FiRST positive screening (5/6) (N, %)		
- Yes	102	18.4
- No	450	81.2

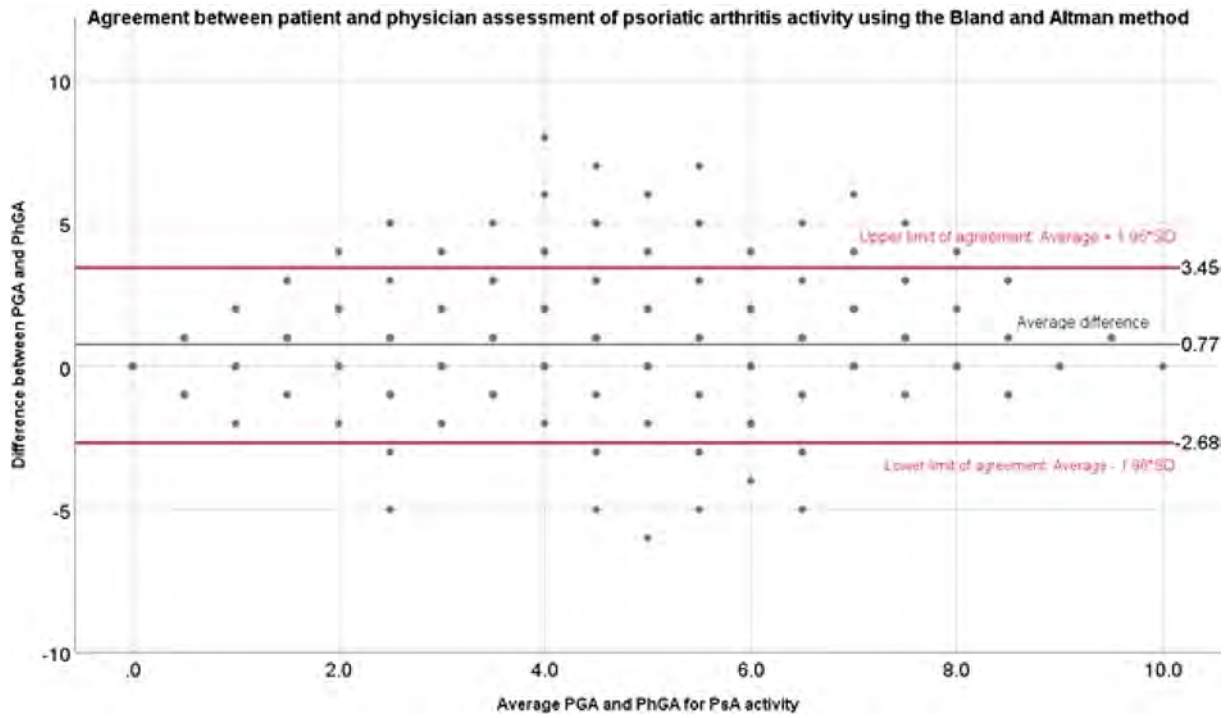

Figure 1. Agreement between PGA (Patient) and PhGA (Physician Global Assessment) of PsA activity using the Bland and Altman plot. Each dot is the difference between PGA and PhGA for a specific patient.

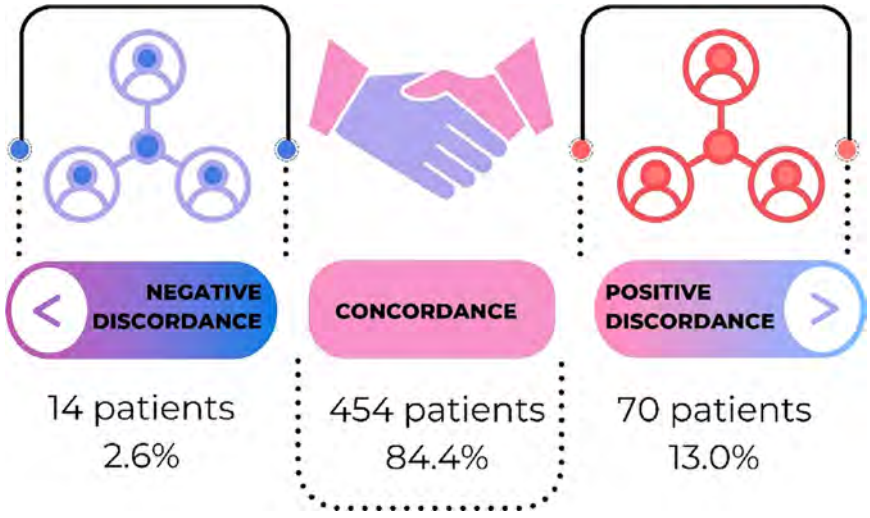

Figure 2. Concordance between PGA and PhGA of PsA activity, defined by a difference (PGA – PhGA) comprised between -2 and +2 (total available = 538 pairs)

Conclusion: In this unselected sample of patients from Arab countries, there was a strong concordance between PGA and PhGA of PsA activity. This raises questions about patient expectations and pain perceptions in Arab countries. Concordance was stronger for PsA than PsO, indicating that rheumatologists may be more comfortable assessing joints than skin. The patient's evaluation of disease activity needs to be taken into account when considering the disease management plan, especially in patients who are not in remission.

Disclosure: N. Ziade: Abbvie, 6, Boehringer-Ingelheim, 6, Eli Lilly, 6, Janssen, 6, Newbridge, 6, Novartis, 6, Pfizer, 6, Pierre Fabre, 6, Roche, 6, sanofi, 6; **N. Abbas**: None; **L. El Kibbi**: None; **A. Maroof**: None; **B. Elzorkany**: None; **N. Ani**: None; **A. ADNAN**: None; **N. AWADH**: None; **F. Gorial**: None; **N. Alchama**: None; **C. Haouichat**: None; **F. Alnaimat**: None; **S. Hannawi**: GSK, 2, 6; **S. Atawnah**: None; **H. HALABI**: None; **M. Al-Mashaleh**: None; **L. Aljazwi**: None; **A. Abogamal**: None; **I. Ayoub**: None; **E. Bouajina**: None; **R. Bahiri**: None; **S. Saad**: None; **M. Sabkar**: None; **K. Aouad**: None; **L. Gossec**: AbbVie, 2, 12, Personal fees, Amgen, 2, Biogen, 5, BMS, 12, Personal fees, Celltrion, 12, Personal fees, Eli Lilly, 5, 12, Personal fees, Galapagos, 12, Personal fees, Janssen, 12, Personal fees, MSD, 12, Personal fees, Novartis, 5, 12, Personal fees, Pfizer, 12, Personal fees, Sandoz, 5, 12, Personal fees, UCB Pharma, 5, 12, Personal fees; **I. Hmamouchi**: None.

Abstract Number: 0507

The Use of PSAID-12 in Remote Monitoring Correlates with In-person Clinical Examination Findings in Psoratic Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patient-reported outcome measures (PROMs) are important tools for evaluating disease activity, functional status, and quality of life in patients with psoriatic arthritis (PsA). The Psoriatic Arthritis Impact of Disease (PSAID) questionnaire is a commonly used PROM. The Psoriatic Arthritis Response Criteria (PSARC) is a composite measure that assesses changes in disease activity based joint pain, swelling and general health. The objective of this study was to assess the correlation between remote PSAID-12 and in-person tender, swollen joint and pain in patients with PsA attending the clinic.

Methods: This study was a cross-sectional, observational study of patients with PsA meeting CASPAR critieria. Patients were recruited consecutively from clinic and completed the PSAID-12 questionnaires 14 days prior to their clinic visit digitally or by paper. Demographic and clinical data, including age, gender, disease duration, medication were collected. The tender (68 joint) and swollen (66 joint) count as well as the Likert Pain Score was conducted in-person in the clinic. The primary outcome was the correlation between PSAID-12 and tender, swollen joint and Likert Pain Score. Descriptive statistics was used to summarise the demographic and clinical characteristics of the study population. Pearson correlation coefficients were calculated to assess the correlation between PSAID-12 and tender joint, swollen joint and pain scores.

Results: The total number of patients in the study was 235. The female:male ratio was 1.0:0.8. The mean disease duration was 27 years (range 2 months to 54 years). The mean age was 52 years (range 18 to 86 years). The number of patients on cs DMARDs were 201/235 (85.5%) and bDMARDs 84/235 (35.7%). The mean PSAID-12 score was 4.1 (SD 2.5). The number of patients in remission (PSAID-12 < 1.4) was 48 (21%), low disease activity (PSAID-12, 1.4- 4) 71 (30%), moderate disease activity (PSAID-12, 4-6.7) was 83 (35%), active disease (PSAID-12 > 6.7) was 33 (14%), tender joint count 11.7 (SD 14.8), swollen joint count 6.1 (SD 10.1) and Likert Pain Score 4.6 (SD 2.6). There was a positive correlation between the pre-clinic PSAID-12 score and the in-person calculated tender joint count ($r=0.58$, $p < 0.05$, figure 1)swollen joint count ($r= 0.51$, $p < 0.05$, figure 2) and the Likert pain score ($r=0.84$, t-score 22.7, $p< 0.05$, figure 3).

Conclusion: This real-world clinic study confirms the findings from the previous PSAID-12 validation studies where the PSAID-12 correlation with Pain VAS was $r = 0.83$, tender joint count was $r = 0.57$ and swollen joint count was $r = 0.40$. Our study has shown very similar results. This provides evidence that the PSAID-12 score may be used as a PROM for remote monitoring

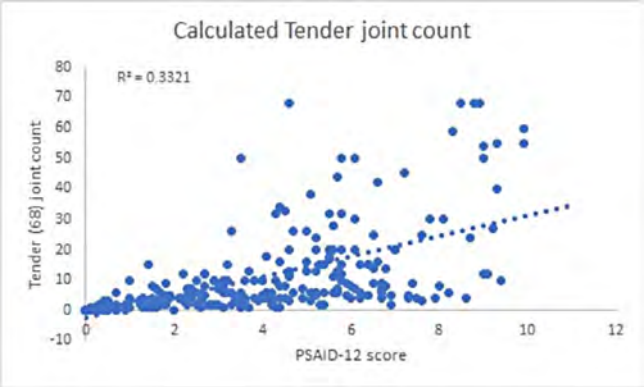


Figure 1. Correlation between remote PSAID-12 and in-person calculated tender (68) joint count

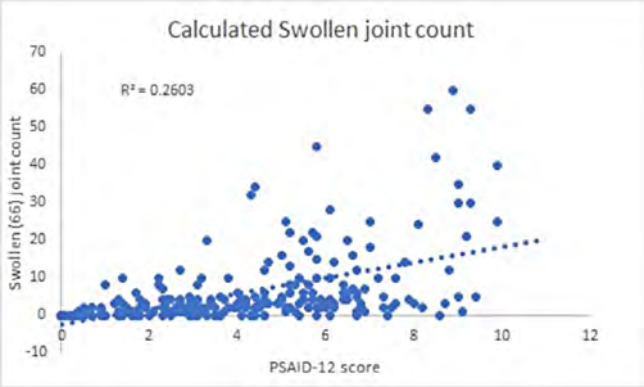


Figure 2. Correlation between remote PSAID-12 and in-person calculated swollen (66) joint count

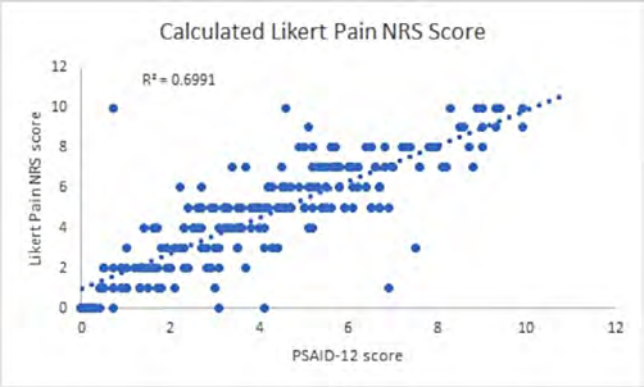


Figure 3. Correlation between remote PSAID-12 and in-person Likert Pain NRS score assessment

during the longer intervals between in-person clinic reviews. Using PSAID-12, one-fifth of patients were in PsA remission and may be suitable for a remote or tele-consultation which will reduce the need to travel to hospital for an in-patient review. The results of this study may help to improve the understanding of the relationship between these remote monitoring and in-person assessments and their utility in clinical practice for assessing disease activity and functional status in patients with PsA.

Disclosure: A. Chan: None; **N. Nwe**: None.

Abstract Number: 0508

Assessment of Pain Outcomes in a Phase 2 Trial of a Selective, Allosteric Tyrosine Kinase 2 Inhibitor, Deucravacitinib, in Patients with Active PsA

Philip J. Mease[1], Lihi Eder[2], Alexis R Ogdie[3], Atul Deodhar[4], Subhashis Banerjee[5], Miroslawa Nowak[5], Jiyoon Choi[6], Thomas Lehman[7] and Vibeke Strand[8], [1]Swedish Medical Center/Providence St. Joseph Health and University of Washington School of Medicine, Seattle, WA, [2]Women's College Research Institute, Division of Rheumatology, University of Toronto, Toronto, ON, Canada, [3]University of Pennsylvania, Philadelphia, PA, [4]Division of Arthritis and Rheumatic Disease, Oregon Health & Science University, Portland, OR, [5]Bristol Myers Squibb, Princeton, NJ, [6]Bristol Myers Squibb, Lawrenceville, NJ, [7]Bristol Myers Squibb, Philadelphia, PA, [8]Stanford University, Palo Alto, CA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Pain is commonly cited by patients with PsA as affecting their daily activities and quality of life and may differ by sex[1]. In addition to neurological pathways, pain signaling involves many cytokines, some of which are tyrosine kinase 2 (TYK2) mediated and involved in PsA pathogenesis. Deucravacitinib is a first-in-class, oral, selective, allosteric inhibitor of TYK2 approved in multiple countries for adults with moderate to severe plaque psoriasis.[2,3] Deucravacitinib was efficacious vs placebo (PBO) in a phase 2 trial in patients with active PsA, and certain cytokine levels associated with pain signaling were reduced with deucravacitinib vs PBO, demonstrating the downstream effects of TYK2 inhibition on these

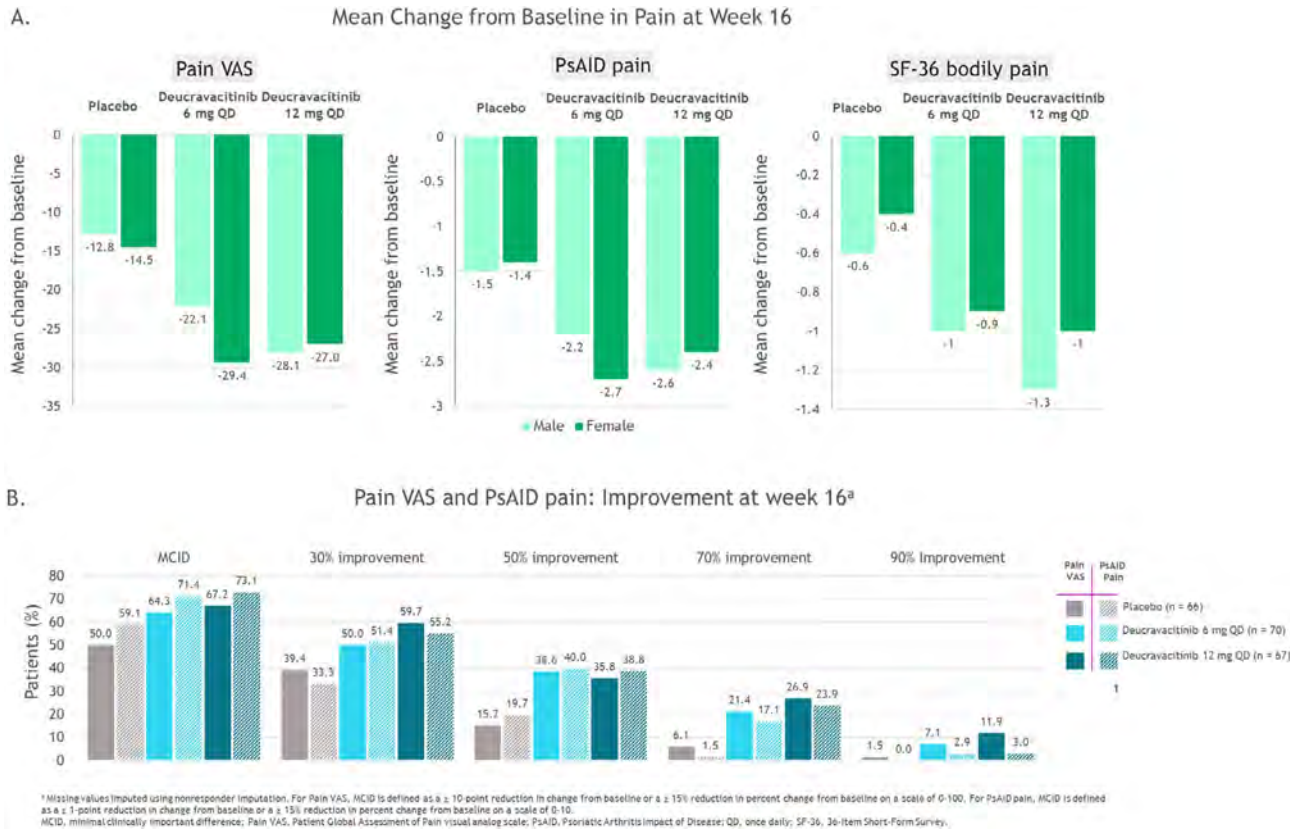


Figure 1. Mean change in pain from baseline (A) and percentage of patients who reported improvements in Pain VAS and PsAID at week 16 (B)

pathways.[4,5] Here, we characterize the effect of deucravacitinib on pain across different instruments by sex, and alignment across those pain instruments, in patients in the phase 2 PsA trial (NCT03881059).

Methods: Patients with PsA (N=203) were randomized 1:1:1 to PBO, deucravacitinib 6 mg once daily (QD), or deucravacitinib 12 mg QD. Three instruments assessed pain up to week 16: (1) Patient Global Assessment of Pain visual analog scale (Pain VAS), scored from 0-100; (2) Psoriatic Arthritis Impact of Disease (PsAID) pain instrument, scored from 0-10; and (3) 36-Item Short Form Survey (SF-36) Bodily Pain questionnaire, in which patients rated their pain on a 6-item scale from "none" to "very severe." Mean change from baseline (BL) in pain scale scores by sex, the proportion of patients who reported meaningful improvements in pain, and correlation among pain scales and disease efficacy measures were evaluated.

Results: Mean Pain VAS score was 64.1, and mean PsAID pain score was 6.4 at BL; scores were similar across groups. At BL, pain assessments strongly correlated with the Psoriatic Arthritis Disease Activity Score (PASDAS) and Patient Global Assessment of Disease Activity **(Table)**. Mean improvements in pain for all 3 measures and percentages of patients reporting improvements in Pain VAS and PsAID pain scores were greater with deucravacitinib compared with PBO **(Figure 1)**.

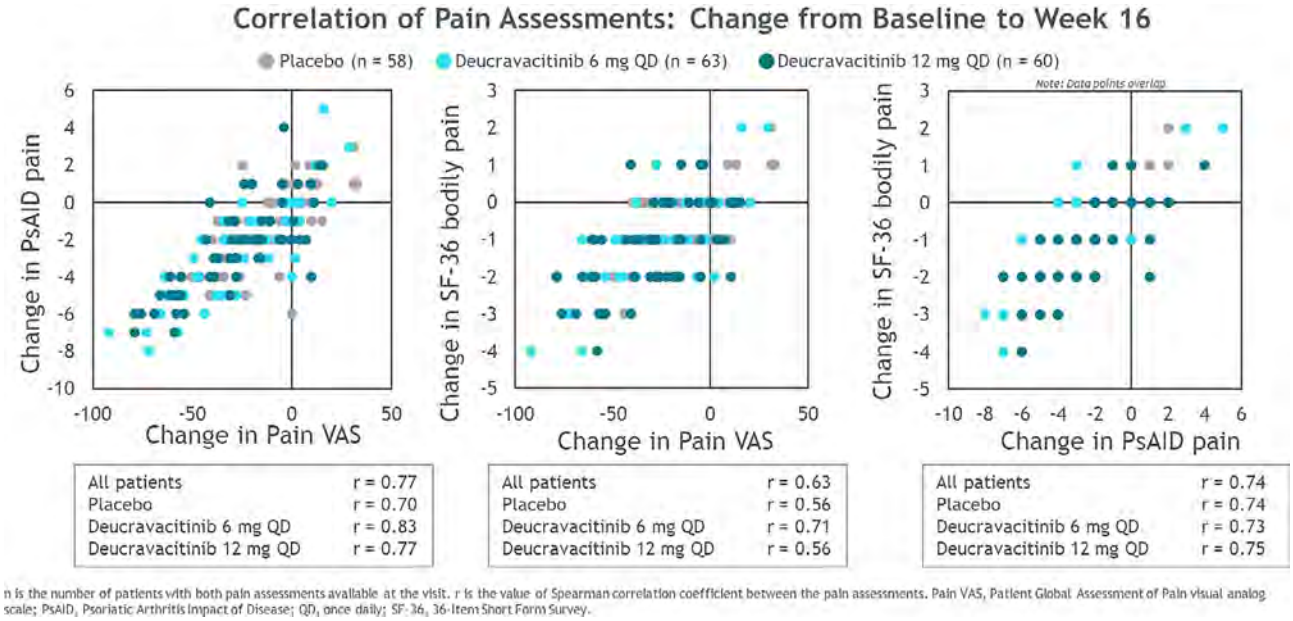


Figure 2. Correlation of pain assessments: Change from baseline to week 16

Table. Correlations between pain assessments at baseline and other baseline disease activity measures

	Pain measurements			Disease activity measurements											
	Pain VAS	PsAID pain	SF-36 bodily pain	PASDAS	PtGA	DAPSA	DAS28	HAQ-DI	TJC	SJC	PGA	CRP	Dactylitis[a]	SPARCC Enthesitis[a]	LEI[a]
Pain VAS	--	0.746	0.655	0.618[b]	0.653[b]	0.495[b]	0.466[b]	0.423[b]	0.351[b]	0.305[b]	0.367[b]	0.190[b]	0.197	0.213	0.072
PsAID pain	0.746	--	0.703	0.602	0.643	0.505	0.495	0.468	0.349	0.349	0.265	0.297	0.220	0.246	0.184
SF-36 bodily pain	0.655	0.703	--	0.511	0.535	0.361	0.401	0.472	0.196	0.262	0.204	0.289	0.173	0.157	0.060

Strength of association:
None: 0.0–0.1
Weak: 0.1–0.3
Medium: 0.3–0.5
Strong: 0.5–1.0

Spearman rank correlation coefficient was used unless otherwise noted. [a]Only in patients with a score of > 0 at baseline. [b]Pearson rank correlation coefficient. CRP, C-reactive protein; DAPSA, Disease Activity in Psoriatic Arthritis; DAS28, Disease Activity Score - 28 joint; HAQ-DI, Health Assessment Questionnaire - Disability Index; LEI, Leed's Enthesitis Index; Pain VAS, Patient Global Assessment of Pain visual analog scale; PASDAS, Psoriatic Arthritis Disease Activity Score; PGA, Physician Global Assessment; PsAID, Psoriatic Arthritis Impact of Disease; PtGA, Patient Global Assessment of Disease Activity; SF-36, 36-Item Short Form Survey; SJC, swollen joint count; SPARCC, Spondyloarthritis Research Consortium of Canada; TJC, tender joint count.

Similar improvements in pain were observed in both male and female patients. Pain assessments correlated with one another both at BL **(Table)** and over time through week 16, with some divergent responses to pain questions also observed **(Figure 2)**.

Conclusion: A higher proportion of patients with PsA treated with deucravacitinib reported clinically meaningful improvements in pain compared with PBO. Patient-reported pain assessments had moderate correlation with one another. No consistent differences were observed between male and female patients in reported mean improvements in pain.

References:

1.Coates L, et al. *J Rheumatol* 2023; 50(4):488–496. 2.Armstrong A, et al. *J Am Acad Dermatol* 2023;88:29–39. 3. Strober B, et al. *J Am Acad Dermatol* 2023;88:40–51. 4.Mease PJ, et al. *Ann Rheum Dis* 2022;81:815–822. 5. FitzGerald O, et al. 2021 ACR Convergence, Abstract 0490; 2021.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2; **L. Eder**: AbbVie, 2, 5, Eli Lilly, 2, 5, Fresenius Kabi, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Sandoz, 5, UCB, 2, 5; **A. Ogdie**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, UCB, 2; **A. Deodhar**: AbbVie, 2, 5, Amgen, 2, Aurinia, 2, Bristol Myers Squibb, 2, 5, Celgene, 5, Eli Lilly, 2, 5, Janssen, 2, 6, MoonLake, 2, 5, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5; **S. Banerjee**: Bristol-Myers Squibb(BMS), 3, 11; **M. Nowak**: Bristol-Myers Squibb(BMS), 3, 11; **J. Choi**: Bristol Myers Squibb, 3; **T. Lehman**: Bristol-Myers Squibb(BMS), 3; **V. Strand**: AbbVie, 2, Alpine Immune Sciences, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, Bayer, 2, Bioventus, 2, Blackrock, 2, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, Celltrion, 2, Citryll, 2, Ermium, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon, 2, Inmedix, 2, Janssen, 2, Kiniksa, 2, Lilly, 2, Merck, 2, MiMedx, 2, Novartis, 2, Omeros, 2, Pfizer, 2, RAPT, 2, Regeneron, 2, R-Pharm, 2, Samsung, 2, Sandoz, 2, Sanofi, 2, Scipher, 2, Setpoint, 2, Sorrento, 2, Spherix, 2, Urica, 2, 4.

Abstract Number: 0509

Assessment of Direct and Indirect Impact on Pain and Fatigue Outcomes in a Phase 2 Clinical Trial of Deucravacitinib, a Selective, Allosteric Tyrosine Kinase 2 Inhibitor, in Patients with Active PsA: A Mediation Analysis

Philip J. Mease[1], Lihi Eder[2], Alexis R Ogdie[3], Atul Deodhar[4], Subhashis Banerjee[5], Ying-Ming Jou[5], Miroslawa Nowak[5], Thomas Lehman[6] and Vibeke Strand[7], [1]Swedish Medical Center/Providence St. Joseph Health and University of Washington School of Medicine, Seattle, WA, [2]Women's College Research Institute, Division of Rheumatology, University of Toronto, Toronto, ON, Canada, [3]University of Pennsylvania, Philadelphia, PA, [4]Division of Arthritis and Rheumatic Disease, Oregon Health & Science University, Portland, OR, [5]Bristol Myers Squibb, Princeton, NJ, [6]Bristol Myers Squibb, Philadelphia, PA, [7]Stanford University, Palo Alto, CA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: PsA

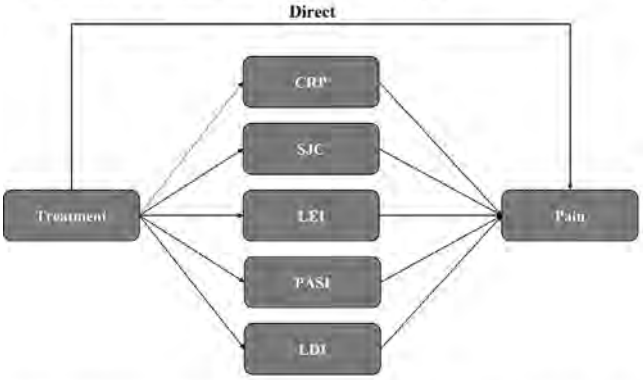
Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Tyrosine kinase 2 (TYK2) is an intracellular kinase involved in key cytokine pathways linked to PsA pathophysiology. Several of these pathways are intertwined with those that mediate pain signaling and fatigue, symptoms that patients with PsA commonly cite as negatively affecting quality of life and daily activities. Deucravacitinib is a first-in-class, oral, selective, allosteric TYK2 inhibitor approved in multiple countries for the treatment of adults with plaque psoriasis. In a phase 2 trial in patients with active PsA, deucravacitinib treatment resulted in a reduction in pain and fatigue as well as the levels of key cytokines, vs placebo (PBO)[1]; deucravacitinib has also demonstrated efficacy vs PBO in patients with SLE receiving standard background therapy. Previous studies have shown the effects of therapeutic interventions on pain may have both direct and indirect contributions. Here, we apply a mediation analysis of data from the phase 2 PsA trial (NCT03881059) to characterize and quantify the potential direct effects of deucravacitinib on pain and fatigue vs. observable indirect effects achieved through improvements in available clinical endpoints associated with inflammation or swelling.

Methods: All data included are from week 16 observations in the phase 2 trial of deucravacitinib (6 mg QD and 12 mg QD pooled) v. PBO in patients (N=203) with active PsA. Improvements in pain and 5 clinical endpoints associated with inflammation or swelling were included in the initial mediation model. These endpoints included C-reactive protein (CRP), swollen joint

Figure 1. Mediation model in the full analysis. Treatment is represented by a binary variable (deucravacitinib 6 mg QD and 12 mg QD pooled vs PBO). Pain was measured by the patient's assessment of arthritis pain



CRP, C-reactive protein; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; PASI, Psoriasis Area and Severity Index; QD, once daily; SJC, swollen joint count.

Figure 2. Direct and indirect effects of deucravacitinib treatment on pain and fatigue in patients with PsA in the refined model

PASI, Psoriasis Area and Severity Index; SJC, swollen joint count.

Table. Direct and indirect effects of treatment on pain and fatigue, and proportion of effect mediated by PASI and SJC

	Pain, %	Fatigue, %
Direct	50.8	48.5
Indirect		
Total	**49.2**	**51.5**
PASI	31.0 (P 0.0246)	34.3 (P 0.0534)
SJC	18.7 (P 0.0553)	16.9 (P 0.1355)

PASI, Psoriasis Area and Severity Index; SJC, swollen joint count.

count (SJC), Psoriasis Area and Severity Index (PASI), Leeds Enthesitis Index (LEI), and Leeds Dactylitis Index (LDI) (**-Figure 1**). The relative contribution of each parameter to the improvement in pain was derived and used to develop a refined model including only those parameters which reached or neared statistical significance. The same methodology was repeated for fatigue.

Results: In the initial model, the strongest indirect mediators of both pain and fatigue with deucravacitinib treatment were SJC and PASI (**Table**). The following parameters were not significantly associated with the mediation of pain or fatigue: CRP, LEI, LDI. In the refined model, the total observable indirect effects of deucravacitinib on pain and fatigue were calculated to be 49.2% and 51.5%, respectively, derived from improvements in SJC and PASI. The remaining, potentially direct, effect on pain and fatigue improvement is calculated to be 50.8% and 48.5% respectively. (**Figure 2**).

Conclusion: Improvements in pain and fatigue in patients with PsA treated with deucravacitinib may be attributable to both direct and indirect mechanisms. PASI- and SJC-mediated improvements in pain and fatigue contributed the most to the observed indirect effects. Further investigation into the potential direct effect of deucravacitinib on pain and fatigue are needed.

Reference: 1. Mease P, et al. *Ann Rheum Dis* 2022; 81:815-822.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2; **L. Eder**: AbbVie, 2, 5, Eli Lilly, 2, 5, Fresenius Kabi, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Sandoz, 5, UCB, 2, 5; **A. Ogdie**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, UCB, 2; **A. Deodhar**: AbbVie, 2, 5, Amgen, 2, Aurinia, 2, Bristol Myers Squibb, 2, 5, Celgene, 5, Eli Lilly, 2, 5, Janssen, 2, 6, MoonLake, 2, 5, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5; **S. Banerjee**: Bristol-Myers Squibb(BMS), 3, 11; **Y. Jou**: Bristol Myers Squibb, 3, 12, Shareholder; **M. Nowak**: Bristol-Myers Squibb(BMS), 3, 11; **T. Lehman**: Bristol-Myers Squibb(BMS), 3; **V. Strand**: AbbVie, 2, Alpine Immune Sciences, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, Bayer, 2, Bioventus, 2, Blackrock, 2, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, Celltrion, 2, Citryll, 2, Ermium, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon, 2, Inmedix, 2, Janssen, 2, Kiniksa, 2, Lilly, 2, Merck, 2, MiMedx, 2, Novartis, 2, Omeros, 2, Pfizer, 2, RAPT, 2, Regeneron, 2, R-Pharm, 2, Samsung, 2, Sandoz, 2, Sanofi, 2, Scipher, 2, Setpoint, 2, Sorrento, 2, Spherix, 2, Urica, 2, 4.

Abstract Number: 0510

Bimekizumab Treatment Improved Key Patient-Reported Symptoms of Axial Spondyloarthritis Including Spinal Pain, Fatigue, and Morning Stiffness: 52-Week Results from Two Phase 3 Studies

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A. In the phase 3 studies BE MOBILE 1 and 2, BKZ demonstrated sustained improvements to Week (Wk) 52 in patients (pts) with active non-radiographic (nr-) and radiographic axial spondyloarthritis (r-axSpA; i.e., AS).[1,2]

Here, we report the impact of BKZ in pts with axSpA on key pt-reported symptoms (spinal pain, stiffness, and fatigue).

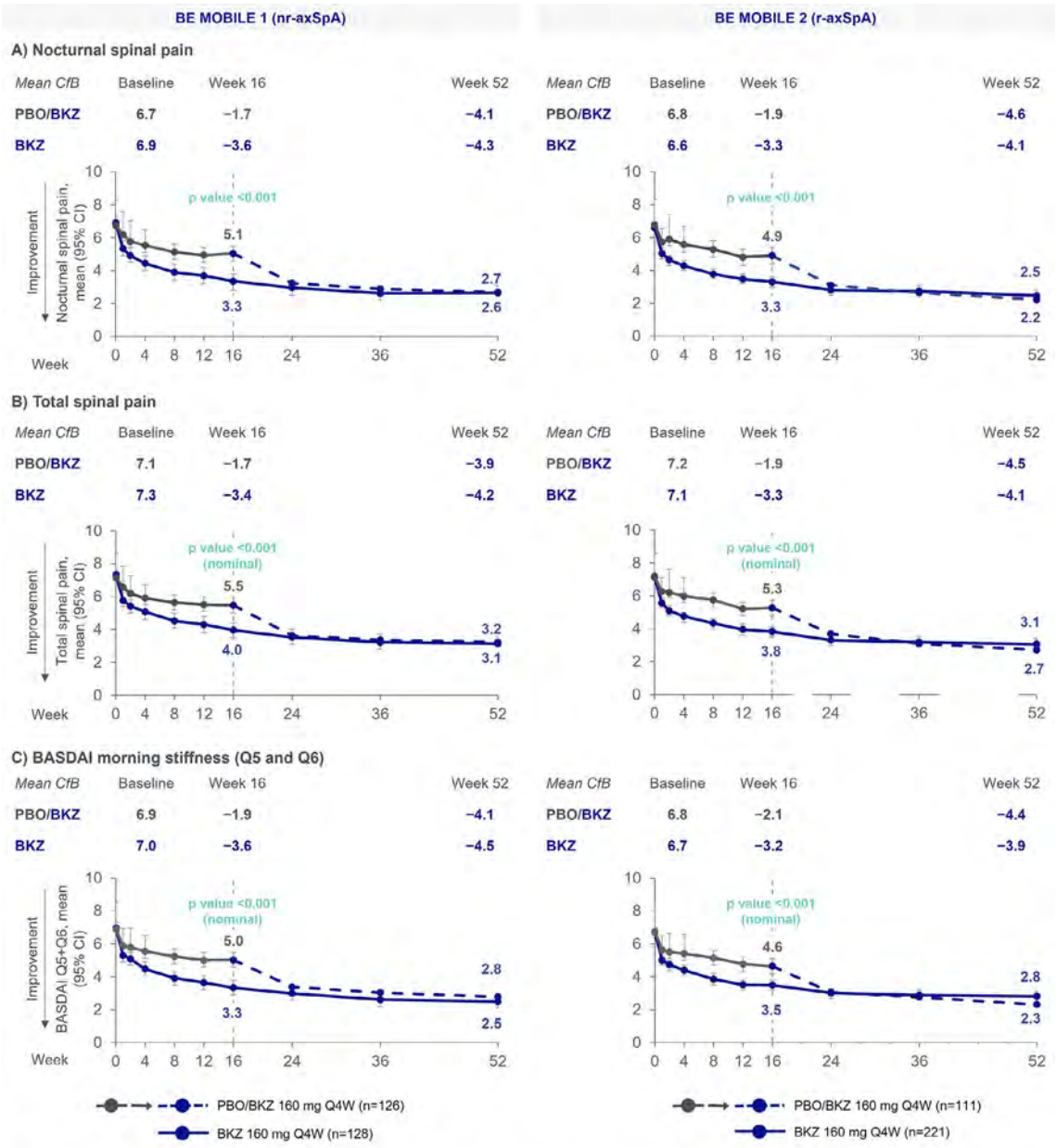
Methods: BE MOBILE 1 (NCT03928704) and 2 (NCT03928743) both comprised a 16-wk double-blind period followed by a 36-wk maintenance period. Pts were randomized to receive subcutaneous BKZ 160 mg every 4 wks (Q4W) or placebo (PBO); from Wk 16 all pts received BKZ 160 mg Q4W.

We report mean nocturnal and total spinal pain, and BASDAI morning stiffness (mean of BASDAI questions 5 and 6), as well as mean change from baseline (CfB) in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue scores to Wk 52; missing values were imputed using multiple imputation. Least squares mean difference (LSMD) is reported for FACIT-F at Wk 16. Proportion of pts achieving low levels of pain (total and nocturnal spinal pain score: ≤2 and ≤4) and a meaningful improvement in fatigue (FACIT-F score: ≥8 point increase from baseline [BL]), analyzed post hoc, are also reported; missing values were imputed using non-responder imputation.

Results: 254 pts with nr-axSpA (BKZ: 128; PBO: 126) and 332 with r-axSpA (BKZ: 221; PBO: 111) were randomized; 86.6% (220/254) and 89.8% (298/332) pts completed to Wk 52, respectively. Across both studies, mean BL scores for all reported outcomes indicated high disease burden (**Figure 1**).

At Wk 16, BKZ-randomized pts achieved greater improvements in mean nocturnal and total spinal pain (nominal), and BASDAI morning stiffness (nominal) vs PBO (all $p < 0.001$; **Figure 1**). Mean scores were further improved to Wk 52 among BKZ-randomized pts and among pts who switched from PBO to BKZ at Wk 16 (PBO/BKZ), responses approached those of BKZ-randomized pts. Similarly, at Wk 16 a higher proportion of BKZ- vs PBO-randomized pts achieved low nocturnal and total spinal scores (**Figure 2**); at Wk 52 these improvements were similar across BKZ-randomized and PBO/BKZ pts.

At Wk 16, BKZ-randomized pts achieved greater improvements in FACIT-F scores vs PBO (mean CfB [nominal p value]: nr-axSpA: 8.5 vs 3.9 [< 0.001]; r-axSpA: 8.4 vs 5.0 [0.015]; LSMD: nr-axSpA: 4.2; r-axSpA: 2.2) with similar improvements at Wk 52 among BKZ-randomized and PBO/BKZ pts (mean CfB: nr-axSpA: 10.9 vs 9.2; r-axSpA: 9.9 vs 9.5). Similarly, a higher proportion of BKZ-randomized pts achieved a ≥8 point improvement from BL compared with PBO at Wk 16 (**Figure 3**);responses at Wk 52 were similar across PBO/BKZ and BKZ-randomized pts.



Randomized set. Multiple imputation. P values calculated at Week 16 for nocturnal spinal pain were part of a hierarchical gatekeeping strategy and used reference-based multiple imputation. P values without any multiplicity adjustment are indicated as nominal p values and should not be used as an indication of statistical significance. Error bars represent 95% CI. Spinal pain scores range from 0–10 with lower scores reflecting better health status. BASDAI morning stiffness score assessed as mean of BASDAI questions 5 and 6; scores range from 0–10 with lower scores reflecting better health status. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BKZ: bimekizumab; CfB: change from baseline; CI: confidence interval; nr-axSpA: non-radiographic axial spondylarthritis; PBO: placebo; Q4W: every 4 weeks; r-axSpA: radiographic axial spondylarthritis.

Figure 1. Improvement in mean (A) nocturnal spinal pain, (B) total spinal pain scores, and (C) BASDAI morning stiffness (questions 5 and 6) to Week 52 (MI)

Conclusion: BKZ treatment resulted in clinically meaningful improvements in spinal pain, morning stiffness, and fatigue to Wk 52 in pts across the full disease spectrum of axSpA, who had a similar and high disease burden at BL. These findings emphasize the benefit of BKZ on clinical symptoms which are important to pts and have a substantial impact on their daily lives.[3]

References:1. van der Heijde D. Ann Rheum Dis 2023;82:515–526; **2.** Boel A. Ann Rheum Dis. 2019;78:1545–9; **3.** Strand V. J Clin Rheumatol 2017;23:383–91.

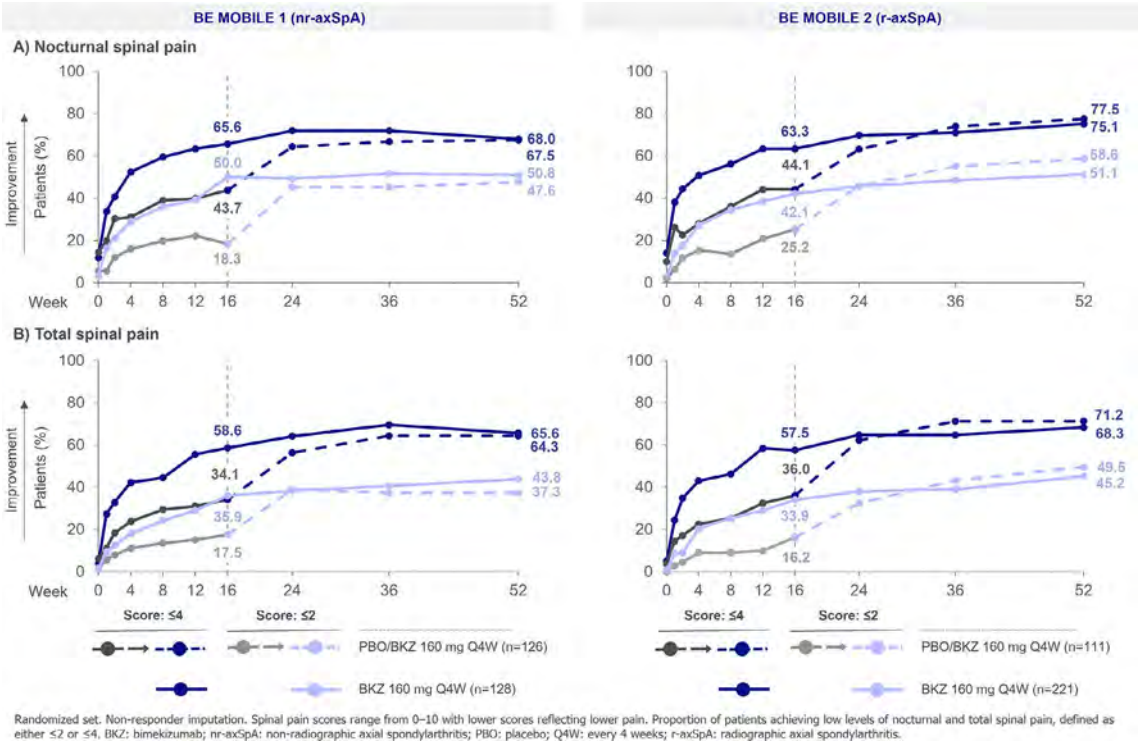


Figure 2. Proportion of patients achieving (A) total and (B) nocturnal spinal pain scores ≤2 and ≤4 to Week 52 (NRI)

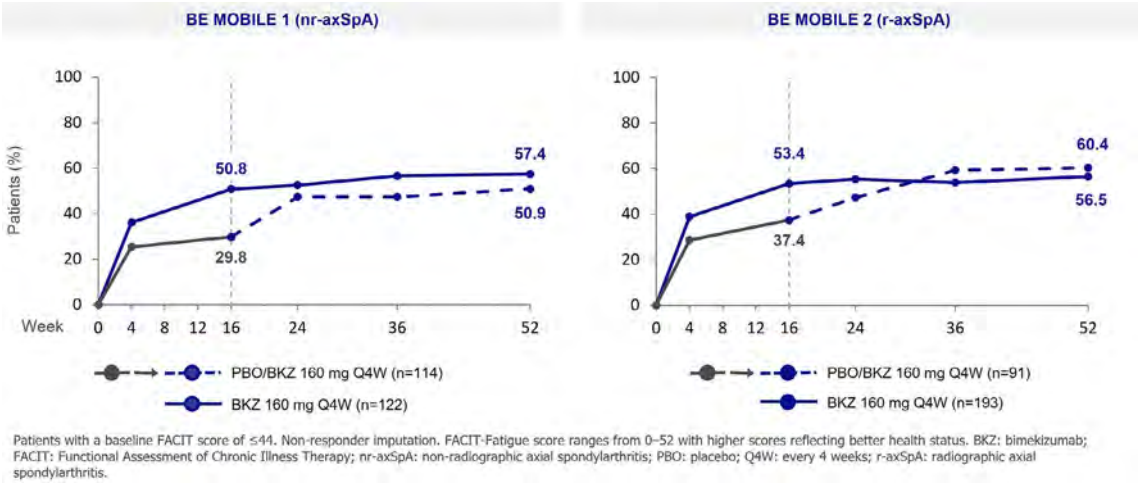


Figure 3. Proportion of patients achieving an increase in FACIT-Fatigue score of ≥8 to Week 52 (NRI)

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2; **M. Dougados**: AbbVie, 2, 5, 6, Eli Lilly, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 3, 5, 6, UCB Pharma, 2, 5, 6; **M. Dubreuil**: Amgen, 2, Pfizer, 5, UCB Pharma, 2; **M. Magrey**: AbbVie, 2, Bristol Myers Squibb, 2, Eli Lilly, 2, Novartis, 2, Pfizer Inc, 2, UCB, 5; **H. Marzo-Ortega**: AbbVie, 2, 6, Biogen, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 5, 6, MoonLake, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Takeda, 2, 6, UCB Pharma, 2, 5, 6; **M. Rudwaleit**: AbbVie, 2, 6, Boehringer Ingelheim, 6, Chugai, 6, Eli Lilly, 2, 6, Janssen, 6, Novartis, 2, 6, Pfizer, 6, UCB Pharma, 2, 6; **C. de la Loge**: UCB Pharma, 2; **C. Fleurinck**: UCB Pharma, 3; **U. Massow**: UCB Pharma, 3; **V. Taieb**: UCB Pharma, 3, 11; **A. Deodhar**: AbbVie, 2, 5,

Amgen, 2, Aurinia, 2, Bristol Myers Squibb, 2, 5, Celgene, 5, Eli Lilly, 2, 5, Janssen, 2, 6, MoonLake, 2, 5, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5.

Abstract Number: 0511

Long-term Safety and Tolerability of Bimekizumab in Patients with Axial Spondyloarthritis and Psoriatic Arthritis: Results from Pooled Phase 2b/3 Studies

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SESSION INFORMATION

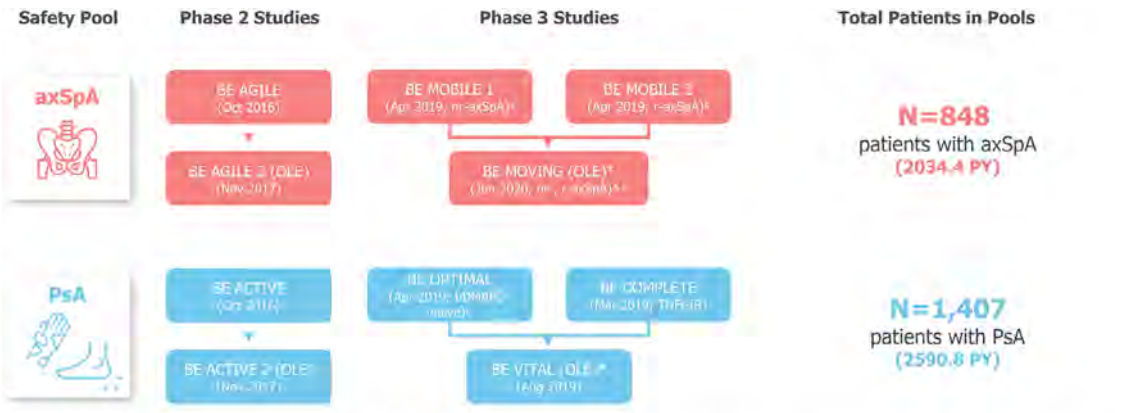
Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A. A previous analysis of pooled safety data from the placebo-controlled period of four phase 3 trials was conducted in patients (pts) with axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) to Week (Wk) 16.[1] Here, we present long-term pooled safety data for BKZ in axSpA and PsA pt populations, across phase 2b/3 trials and all study periods.



Actual study start dates provided. *Study ongoing. [a] Patients with nr-axSpA met ASAS classification criteria. Patients with radiographic sacroiliitis were excluded; [b] Patients with r-axSpA met modified New York criteria and fulfilled ASAS classification criteria, therefore the terms raxSpA and AS may be used interchangeably;[7] [c] BE OPTIMAL also included an adalimumab treatment arm. Patients randomized to this arm are not included in the PsA safety pool. The PsA (and axSpA) safety pool only includes patients who received ≥1 dose of BKZ 160 mg Q4W.

BE AGILE: NCT02963506; BE AGILE 2: NCT03355573; BE MOBILE 1: NCT03928704; BE MOBILE 2: NCT03928743; BE MOVING: NCT04436640; BE ACTIVE: NCT02969525; BE ACTIVE 2: NCT03347110; BE OPTIMAL: NCT03895203; BE COMPLETE: NCT03896581; BE VITAL: NCT04009499.

Abbreviations: AS: ankylosing spondylitis; ASAS: Assessment of SpondyloArthritis international Society; axSpA: axial spondyloarthritis; bDMARD: biologic DMARD; BKZ: bimekizumab; nr-axSpA: non-radiographic axSpA; PsA: psoriatic arthritis; pt: patient; PY: patient-year; Q4W: every 4 weeks; r-axSpA: radiographic axSpA; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; TEAE: treatment-emergent adverse event; TNFi-IR: tumour necrosis factor inhibitor inadequate response; Wk: week.

Figure. Two safety pools (axSpA, PsA) of patients treated with BKZ 160 mg Q4W from phase 2b/3 studies

Table. Summary of TEAEs

	axSpA	PsA
TEAEs[a] n (%) [EAIR/100 PY]	BKZ 160 mg Q4W (N=848; exposure 2034.4 PY)	BKZ 160 mg Q4W (N=1,407; exposure 2590.8)
Any TEAE	752 (88.7) [136.9]	1,170 (83.2) [139.6]
Severe TEAEs	66 (7.8) [3.4]	90 (6.4) [3.6]
Study discontinuations due to TEAEs	54 (6.4) [2.7]	79 (5.6) [3.1]
Drug-related TEAEs[b]	393 (46.3) [28.9]	504 (35.8) [26.7]
Serious TEAEs	97 (11.4) [5.1]	148 (10.5) [6.1]
Deaths	3 (0.4) [0.1]	3 (0.2) [0.1]
Most common TEAEs[c]		
Nasopharyngitis	146 (17.2) [8.2]	180 (12.8) [7.7]
SARS-CoV-2 infection	133 (15.7) [6.8]	201 (14.3) [8.2]
Upper respiratory tract infection	94 (11.1) [5.0]	136 (9.7) [5.6]
Oral candidiasis	70 (8.3) [3.7]	103 (7.3) [4.2]
Headache	56 (6.6) [2.9]	72 (5.1) [2.9]
Diarrhea	48 (5.7) [2.4]	75 (5.3) [3.0]
Safety topics of interest		
Fungal infections	161 (19.0) [9.2]	214 (15.2) [9.2]
Systemic infections[d]	0	0
Fungal infections NEC	75 (8.8) [4.0]	89 (6.3) [3.6]
Candida infections	85 (10.0) [4.5]	131 (9.3) [5.4]
Oral candidiasis	70 (8.3) [3.7]	103 (7.3) [4.2]
Serious infections and infestations	29 (3.4) [1.5]	30 (2.1) [1.2][e]
Active tuberculosis	0	0
Hepatic events[f]	108 (12.7) [5.9]	144 (10.2) [6.0]
>3x ULN ALT or AST	43 (5.1)[g]	59 (4.2)[h]
>5x ULN ALT or AST	15 (1.8)[g]	18 (1.3)[h]
Adjudicated MACE	4 (0.5) [0.2][i]	10 (0.7) [0.4][j]
Malignancies (excluding non-melanoma skin cancer)	5 (0.6) [0.2]	12 (0.9) [0.5]
Neutropenia[k]	11 (1.3) [0.5]	35 (2.5) [1.4]
Adjudicated SIB	3 (0.4) [0.1]	2 (0.1) [0.1]
Injection site reactions	23 (2.7) [1.1]	29 (2.1) [1.1]
Definite or probable IBD	16 (1.9) [0.8]	7 (0.5) [0.3]
Crohn's Disease	7 (0.8) [0.3]	1 (<0.1) [0.0]
Ulcerative Colitis	6 (0.7) [0.3]	2 (0.1) [0.1]
Unclassified	4 (0.5) [0.2]	4 (0.3) [0.2]
Uveitis[l]	25 (2.9) [1.2]	0
With prior history	14 (10.8) [4.6][m]	0
Without prior history	11 (1.5) [0.6][n]	0

Data to the most recent data-cut (July 2022) shown; includes all patients who received ≥1 dose of BKZ 160 mg Q4W. [a] Defined according to MedDRA v19.0. [b] Per investigator assessment; [c] TEAEs occurring in ≥5% of patients in both the axSpA and PsA patient pools, respectively; [d] Defined by omission, non -systemic infections were reported; [e] One serious fungal infection was reported – a 59-year-old female patient with oropharyngeal candidiasis was hospitalized to achieve candidiasis control 10 months and 18 days after initiation of BKZ. BKZ was temporarily discontinued. The infection resolved with antifungal treatment, including fluconazole and clotrimazole. BKZ was restarted approximately one month later; [f] Includes events described as drug -related hepatic disorders, excluding liver neoplasms; [g] n=847; [h] n=1405; [i] Three patients with axSpA experienced cardiac disorders (AMI, ventricular arrythmias, and cardiac arrest); [j] Three patients with PsA experienced an ischemic stroke, while two patients experienced an AMI; [k] Neutropenia includes additional preferred terms identified based on UCB-defined search criteria; [l] Includes the preferred terms uveitis, iridocyclitis and iritis; [m] n=130; [n] n=718. ALT: alanine transaminase; AMI: acute myocardial infarction; AST: aspartate aminotransferase; axSpA: axial spondyloarthritis; BKZ: bimekizumab; EAIR: exposure-adjusted incidence rate; MACE: major adverse cardiovascular event; NEC: not elsewhere classifiable; PsA: psoriatic arthritis; PY: patient-years; Q4W: every four weeks; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; SIB: suicidal ideation or behavior; TEAE: treatment-emergent adverse event; ULN: upper limit of normal.

Methods: We report two pooled analyses, each comprising three phase 2b/3 trials, and their open-label extensions, in pts with active axSpA (non-radiographic [nr]-axSpA and radiographic [r]-axSpA, i.e., ankylosing spondylitis)[2] and active PsA, respectively (**Figure**).[1,3–5]

The number, proportion, and exposure-adjusted incidence rates (EAIRs) per 100 pt-years (PY) of treatment-emergent adverse events (TEAEs) are reported for all pts who received ≥1 dose of BKZ 160 mg every four weeks (Q4W). Data are reported to the most recent data-cut (July 2022) across all treatment periods.

Results: The axSpA and PsA safety pools included 848 pts (2034.4 PY) and 1,407 pts (2590.8 PY), respectively. The most frequently reported TEAEs in pts with axSpA and PsA were nasopharyngitis, SARS-CoV-2 infection, and upper respiratory tract infection (**Table**). See **Table** for safety topics of interest.

Fungal infections were reported in 375 pts (axSpA: 161 [19.0%]; PsA: 214 [15.2%]), leading to discontinuation in 19 pts (7 axSpA [0.8%], 12 PsA [0.9%]); no fungal infections were systemic in nature. Most fungal infections were oral, and the vast majority of oral fungal infections were mild to moderate in severity (axSpA: 162 [99.4%]; PsA: 231 [99.6%]). Two pts experienced severe oral fungal infections (axSpA: 1 [0.1%]; PsA: 1 [0.1%]), which resolved in both cases with treatment. *Candida* fungal infections were seen in a similar proportion of pts with axSpA and PsA (**Table**).

Serious infections and infestations occurred in 59 pts (axSpA: 29 [3.4%]; PsA: 30 [2.1%], **Table**). One serious fungal infection (oropharyngeal candidiasis) was reported in a pt with PsA (1 [< 0.1%]), which resolved with treatment (further details provided in **Table**).

Adjudicated IBD (definite or probable) occurred in 16 pts with axSpA (EAIR/100 PY: 0.8) and 7 pts with PsA (EAIR/100 PY: 0.3). Uveitis occurred in 25 pts with axSpA (EAIR/100 PY: 1.2), while no uveitis cases were reported in pts with PsA (**Table**).

Fourteen pts experienced an adjudicated major adverse cardiovascular event (axSpA: 4 [EAIR/100 PY: 0.2]; PsA: 10 [EAIR/100 PY: 0.4]). Five pts experienced events adjudicated as suicidal ideation/behavior (axSpA: 3 [EAIR/100 PY: 0.1]; PsA: 2 [EAIR/100 PY: 0.1]), while no cases of active tuberculosis were reported (**Table**).

Conclusion: The long-term safety profile of BKZ in pts with axSpA and PsA is consistent with prior studies.[1] As expected, due to inhibition of IL-17, oral candidiasis featured among the safety signals reported.

References: 1. Poddubnyy D. Ann Rheum Dis. 2023;82(suppl 1); **2.**Boel A. Ann Rheum Dis. 2019;78:1545–9; **3.** Baraliakos X. Arthritis Rheumatol. 2022;74(suppl 9); **4.** Ritchlin C. Arthritis Rheumatol. 2022;74(suppl 9); **5.** Merola J. Ann Rheum Dis. 2022;81:167–9.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, MoonLake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 2, UCB Pharma, 2, 6; **A. Orbai**: AbbVie, 5, Amgen, 5, BMS, 2, Janssen, 2, 5, Sanofi, 2, UCB Pharma, 2; **R. Warren**: AbbVie, 2, 5, 6, Almirall, 2, 5, 6, Amgen, 2, 5, 6, Arena, 2, 6, Astellas, 2, 6, Avillion, 2, 6, Biogen, 2, 6, BMS, 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 5, DiCE, 6, Eli Lilly, 2, 5, 6, GSK, 2, 6, Janssen, 2, 5, 6, LEO Pharma, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sanofi, 2, 6, Sun Pharma, 6, UCB Pharma, 2, 5, 6, Union, 6; **C. Fleurinck**: UCB Pharma, 3; **R. Bajracharya**: UCB Pharma, 3, 11; **B. Ink**: AbbVie, 11, GSK, 11, UCB Pharma, 3, 11; **U. Massow**: UCB Pharma, 3; **V. Shende**: UCB Pharma, 3; **J. Shepherd-Smith**: UCB Pharma, 3; **L. Peterson**: UCB Pharma, 3, 11; **K. White**: UCB Pharma, 3, 12, Shareholder; **R. Landewé**: AbbVie, 2, 5, AstraZeneca, 2, BMS,

2, Eli Lilly, 2, Novartis, 2, 5, Pfizer, 2, 5, Rheumatology Consultancy BV, 12, Owner, UCB Pharma, 2, 5; **L. Gensler**: AbbVie, 2, Acelyrin, 2, Eli Lilly, 2, Fresenius Kabi, 2, Janssen, 2, Novartis, 2, 5, Pfizer, 2, UCB Pharma, 2, 5.

Abstract Number: 0512

Factors Associated with Treatment Pathways in Early Axial Spondyloarthritis: A Multistate Analysis of the 10-year Follow-up of the DESIR Cohort

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Current recommendations for the management of patients with axial spondyloarthritis (axSpA) emphasize the need of individualized strategy in the therapeutic decision. Thus, many factors seem to impact this strategy.

The objectives of the study were to describe the therapeutic strategies observed in axSpA, and to assess the factors associated with treatment changes over time.

Methods: This study included patients with axSpA from the French prospective cohort DESIR, with a scheduled 10-year follow-up. A multi-state model with 4 ordered treatment states ("none", "non-steroidal anti-inflammatory drugs (NSAID)", "conventional synthetic DMARD (csDMARD)", "TNF inhibitors (TNFi)") was defined, with 6 possible transitions. Estimation of the restricted mean sojourn times spent in each state from the state occupation probabilities was performed. Then, predictors of those transitions were assessed by multivariable Cox models.

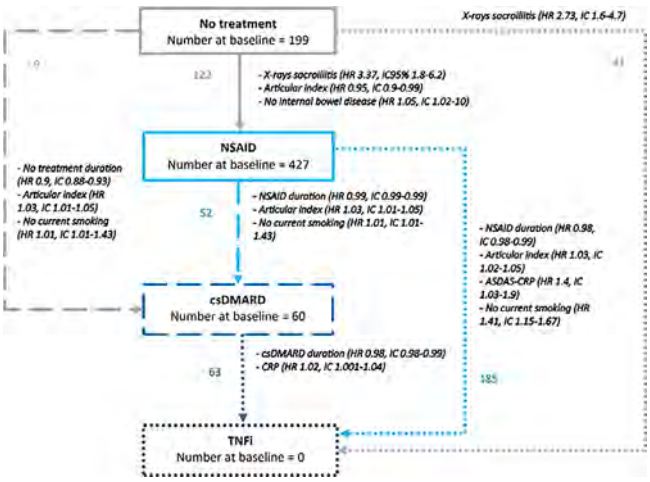

Figure: Multistate model representation. Each arrow corresponds to a possible transition (n=6). Number at baseline denotes the number of patients who started from the state at baseline. The number of events and factors significantly associated with each transition in the multivariable analysis are written near to the corresponding arrow. NSAID refers to non-steroids anti-inflammatory drugs, csDMARD stands for conventional synthetic Disease Modifying Anti-Rheumatic Drug, and TNFi for tumor necrosis factor inhibitors.

Results: 686 (96.9%) of the 708 patients who had more than one visit were analyzed. At cohort entry, 199 (29.0%) were untreated, 427 (62.2%) received NSAID, and 60 (8.7%) received csDMARD and none TNFi.

Over the 10 years of follow-up, patients mostly received NSAID (46.4% of the time) followed by TNFi (24.4% of the time). In multivariable analysis (**figure**), presence of sacroiliitis on radiography, internal bowel disease and articular index were associated with transition to NSAID. Duration in the previous state was often a significant protective factor associated with transition to csDMARD or TNFi. Finally, the several disease activity outcomes were associated with most transitions.

Conclusion: This was the first study using a multistate model to easily represent the different states, detailing the transitions across them, and their associated factors. Different time profiles of axSpA patient management were identified, including abstention up to a significant proportion of patients treated with csDMARD.

Disclosure: E. Portier: None; **S. chevret**: None; **A. Ruyssen-Witrand**: None; **A. Walter-Petrich**: None; **M. Dougados**: AbbVie, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Roche, 2, 5, UCB, 2, 5; **A. Molto**: None.

Abstract Number: 0513

Impact of Pregnancy on Sacroiliac Imaging in Women with Axial Spondyloarthritis: Results of the Analysis of the DESIR Cohort

Elodie Portier[1], Maxime Dougados[2], Adeline Ruyssen-Witrand[3] and Anna Molto[4], [1]Hôpital Cochin, Paris, France, [2]Rheumatology Department, Cochin Hospital; INSERM (U1153): Clinical Epidemiology and Biostatistics, University of Paris, Paris, France, [3]Toulouse University Hospital, Toulouse, France, [4]HOPITAL COCHIN AP-HP, Service de Rhumatologie, Paris, France

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthritis (axSpA) is typically characterized by imaging (radiographs or MRI) abnormalities of the sacroiliac joints (SIJ). Also, inflammatory lesions of the SIJ have been observed in healthy women post-partum. However, the impact of pregnancy on imaging abnormalities in women with axSpA is unknown.

The objective of this study was to evaluate impact of pregnancy on SIJ imaging in patients with early axSpA.

Methods: Women with axSpA from the French prospective cohort DESIR were included, with a follow-up of 5 years. Description of demographic and disease criteria, and SIJ imaging abnormalities at baseline was performed in all women, then according to antecedent of pregnancy. Secondly, changes on imaging over time were analyzed in the 38 women who were nulligravidae at baseline and became pregnant during follow up, using paired-test and then mixed models.

Results: 381 patients were included in the analysis. At baseline, women nulligravidae (142, 37%) were younger and had higher education level than other women with axSpA. Presence of sacroiliitis on MRI and X-ray were more frequent in women nulligravidae (16.9% vs 9.9%, p = 0.046 and 33.8% vs 19.4%, p = 0.0016, respectively) **(table 1).**

Table 1: Imaging characteristics of women with axSpA according to antecedent of pregnancy at baseline, and statistical analysis with Student test or Chi-square (for continuous and binary variables, respectively).

Imaging criteria *Mean (sd) or number (%)*	Nulliparous (N = 142)	Non-nulliparous (N = 232)	P-value*
X-ray criteria			
X-ray sacroiliitis	24 (16.9%)	23 (9.9%)	**p = 0.046**
New York score on right sacroiliac joint	0.72 (1.1)	0.61 (0.95)	NS
New York score on left sacroiliac joint	0.59 (1.02)	0.56 (0.96)	NS
Any erosion in the sacroiliac joints	28 (19.7%)	27 (11.6%)	**p = 0.031**
Any joint widening in the sacroiliac joints	0	2 (0.9%)	NS
Any sclerosis in the sacroiliac joints	27 (19%)	29 (12.5%)	NS
Any partial or total ankylosis in the sacroiliac joints	3 (2.1%)	3 (1.3%)	NS
MRI criteria			
Sacroiliitis on MRI	48 (33.8%)	45 (19.4%)	**p = 0.0016**
SPARCC score	3.6 (6.74)	2.42 (5.12)	NS
≥ 3 fatty lesions on MRI	12 (8.45%)	7 (3.02%)	**p = 0.013**
≥ 3 erosions on MRI	4 (2.82%)	4 (1.72%)	NS
≥ 5 fatty lesions and/or erosions on MRI	11 (7.75%)	5 (2.16%)	**p = 0.0086**
Number of any lesions on sacroiliac joint (0 to 144)	1.65 (3.51)	1.95 (4.55)	NS
Number of enthesitis (0 to 12)	0 (0)	0 (0)	NA
Number of erosions (0 to 40)	0.8 (1.53)	0.71 (1.57)	NS
Number of fatty lesions (0 to 40)	0.96 (9.52)	0.51 (1.74)	NS
Number of sclerosis (0 to 40)	0.125 (0.59)	0.38 (1.26)	**p = 0.03**
Number of partial or total ankylosis (0 to 24)	0.07 (0.64)	0.06 (0.53)	NS

Table 2: Imaging characteristics in women with axSpA who had first pregnancy during follow up, with description before/after delivery and paired-test with Mc Nemar of Student test (for binary and continuous variables, respectively).

Imaging criteria *Mean (sd) or number (%)*	Before pregnancy (N = 38)	After delivery (N = 38)	P-value
Radiographic criteria			
X-ray sacroiliitis	8 (21.1%)	9 (23.7 %)	p = 0.37
New York score on right sacroiliac joint	0.66 (1.06)	0.67 (0.86)	p = 1
New York score on left sacroiliac joint	0.67 (1.07)	0.95 (0.95)	**p = 0.037**
Any erosion in the sacroiliac joints	9 (23.7%)	9 (23.7%)	p = 0.48
Any joint widening in the sacroiliac joints	0	3 (7.9%)	NA
Any sclerosis in the sacroiliac joints	6 (15.8%)	9 (23.7%)	p = 0.13
Any partial or total ankylosis in the sacroiliac joints	1 (2.6%)	2 (5.3%)	p = 0.48
MRI criteria			
Sacroiliitis on MRI	18 (47.3%)	2 (5.2%)	p = 0.074
SPARCC score	3.94 (7.63)	0.39 (0.74)	p = 0.15
≥ 3 fatty lesions on MRI	4 (10.5%)	1 (2.6%)	p = 1
≥ 3 erosions on MRI	1 (2.6%)	0	NA
≥ 5 fatty lesions and/or erosions on MRI	1 (2.6%)	1 (2.6%)	p = 1
Number of any lesions on sacroiliac joint (0 to 144)	1.81 (3.36)	1.8 (2.92)	p = 0.1
Number of enthesitis (0 to 12)	0 (0)	0 (0)	NA
Number of erosions (0 to 40)	0.84 (2.36)	0.42 (0.7)	p = 1
Number of fatty lesions (0 to 40)	0.97 (2.01)	1 (2.02)	p = 0.15
Number of sclerosis (0 to 40)	0 (0)	0.26 (0.86)	p = 0.29
Number of partial or total ankylosis (0 to 24)	0 (0)	0 (0)	NA

When focusing on incident pregnancies, these patients had more sacroiliitis on X-ray and MRI at baseline than patients nulligravidae at the end of follow-up and patients with past pregnancy, but had lower BASFI and ASDAS-CRP. Only left SIJ was statistically different after delivery, with mean scores of 0.67 and 0.95 before and after delivery (**table 2**). No impact of pregnancy on continuous imaging score was found with the different mixed models.

Conclusion: Pregnancy does not seem to aggravate imaging of axSpA women when comparing imaging according to the antecedent of pregnancy. Following axSpA patients who had first pregnancy showed mild increase of left sacroiliitis score on X-ray after delivery, but not enough to be considered as "worsening".

Disclosure: E. Portier: None; **M. Dougados**: AbbVie, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Roche, 2, 5, UCB, 2, 5; **A. Ruyssen-Witrand**: None; **A. Molto**: None.

Abstract Number: 0514

Difficult-to-treat Axial Spondyloarthritis Is Associated with Psoriasis and Comorbidities: Results from a Nationwide Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: An increasing number of targeted therapies are available for the treatment of SpA. However, some patients retain active disease despite several lines of treatment. This has led to the emergence of the concept of difficult-to-treat axial SpA (D2T-axSpA), inspired by similar reasoning in rheumatoid arthritis (D2T-RA). This study aimed to determine the cumulative incidence and identify the factors associated with D2T-axSpA.

Methods: This study used the French National Medico-Administrative Database Système National des Données de Santé (SNDS), which includes administrative data, long-term illnesses (LTIs), outpatient care, medication consumption, and hospitalizations for 97% of the French population. All patients newly benefiting from the LTI #27 "severe spondyloarthritis" with associated diagnostic code M45 (AS), between 2010 and 2013, were included. The use of LTI allowed us to build a cohort of patients with supposedly active disease, the SNDS having no data on disease activity. All patients with active SpA despite NSAID treatment and therefore requiring DMARDs were theoretically newly enrolled in the LTI scheme. The end date of follow-up was December 31, 2018.

Similar to the EULAR definition of D2T-RA, D2T-axSpA was defined as the failure of three biologic/targeted synthetic DMARDs (b/tsDMARDs) or two b/tsDMARDs with different modes of action. Comorbidities and extra-musculoskeletal manifestations (EMM) were identified using previously described algorithms.

A comparison of characteristics between the D2T-axSpA and non-D2T-axSpA groups was performed using t-tests for quantitative variables, and Chi-2 for qualitative variables. Multivariate analysis adjusted for age and b/tsDMARD exposure duration was performed using logistic regression analysis.

Results: 23062 patients were included. 10928 (47.39%) patients received at least one b/tsDMARD during the study period. Uveitis was observed in 82 (0.36 %) patients. This can be explained by the algorithm used, which detects only hospitalized patients. There was also a lack of sensitivity for the detection of smoking and obesity. The rates of other comorbidities and EMM were similar to those reported in previous studies.

During follow-up, 2176 were classified as D2T-axSpA, representing 9.44% of all patients and 19.91% of patients who received at least one b/tsDMARD. To limit selection bias, comparisons were restricted to D2T-axSpA and non-D2T-axSpA patients who had received at least one b/tsDMARD. In the univariate analysis, peripheral involvement and psoriasis were significantly more frequent in the D2T-axSpA group (Table 1). There was a significant increase in smoking, obesity, hypertension, and depression in the D2T-axSpA group. These results were confirmed by the multivariate analysis, with the highest

Table 1: Comparison of sociodemographic characteristics, extra-musculoskeletal manifestations, and comorbidities between D2T-axSpA and non-D2T-axSpA patients who received at least one b/tsDMARD.

Characteristic	D2T-axSpA (n=2176)	Non-D2T-axSpA (n=8752)	p
Sociodemographic characteristics			
Age, mean (SD) years	39.85 (10.61)	39.95 (12.26)	0.72
b/tsDMARD exposition duration, mean (SD) years	**4.87 (2.40)**	**3.87 (2.51)**	**<0.001**
Female sex	**1457 (66.96%)**	**4453 (50.88%)**	**< 0.001**
French social deprivation index, mean (SD)	0.05 (0.88)	0.02 (0.93)	0.21
Aid for the payment of complementary health insurance	18 (0.83%)	93 (1.06%)	0.33
Free complementary health coverage	1337 (61.44%)	5194 (59.35%)	0.07
State medical aid	4 (0.18%)	19 (0.22%)	0.76
Clinical phenotype and extra-musculoskeletal manifestations			
Peripheral symptoms	**280 (12.87%)**	**511 (5.84%)**	**< 0.001**
Psoriasis	**1078 (49.54%)**	**3287 (37.56%)**	**<0.001**
Inflammatory Bowel Disease	251 (11.53%)	980 (11.20%)	0.66
Uveitis	15 (0.69%)	40 (0.46%)	0.17
Comorbidities			
Diabetes	158 (7.08%)	543 (6.20%)	0.14
Dyslipidemia	277 (12.73%)	1012 (11.56%)	0.13
Hypertension	**597 (27.44%)**	**2031 (23.21%)**	**<0.001**
Smoking	**154 (7.08%)**	**437 (4.99%)**	**<0.001**
Obesity	**86 (3.95%)**	**179 (2.05%)**	**<0.001**
Chronic kidney disease	7 (0.32%)	39 (0.45%)	0.42
Atherosclerosis of arteries of extremities	19 (0.87%)	59 (0.67%)	0.32
Depression	**823 (37.82%)**	**1900 (21.71%)**	**<0.001**

Table 2. Multivariate analysis of factors associated with D2T-SpA adjusted for age and duration of exposure to b/tsDMARDs duration.

Characteristic	Odds-ratio (95% CI)	p
Female sex	1.92 (1.73-2.14)	< 0.001
Peripheral symptoms	2.20 (1.87-2.60)	< 0.001
Psoriasis	1.36 (1.23-1.51)	< 0.001
Depression	2.10 (1.88-2.33)	< 0.001
Hypertension	1.22 (1.08-1.38)	< 0.001

OR for peripheral symptoms (Table 2). Analyses restricted to patients fulfilling the definition of D2T-axSpA over a maximum period of 2 years showed similar results (data not shown).

Conclusion: D2T-axSpA affects one in five patients exposed to b/tsDMARDs in this national cohort. D2T-axSpA is more common in women and in patients with peripheral involvement, psoriasis, and depression.

Disclosure: O. FAKIH: None; **M. Desmarets**: None; **B. Martin**: None; **C. Prati**: None; **E. Monnet**: None; **D. Wendling**: None; **f. Verhoeven**: None.

Abstract Number: 0515

Dose Adjustment of Tumor Necrosis Factor Inhibitors Does Not Correlated with Radiographic Progression in Patients with Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Among patients with ankylosing spondylitis (AS) treated with tumor necrosis factor (TNF) inhibitors, tapering the dose of TNF inhibitors may be considered for patients with low disease activity. While several studies have examined the relationship between tapering of TNF inhibitors and disease activity, few have investigated the relationship between tapering TNF inhibitors and radiographic progression. This study aimed to analyze the correlation between the total dose of TNF inhibitors and radiographic progression over a defined period of time, using a defined daily dose (DDD).

Methods: This retrospective study evaluated the electronic medical records of patients with AS between January 2001 and December 2018. The study included AS cohort patients from a single center who had modified Stoker Ankylosing Spondylitis Spinal Score (mSASSS) records for more than 2 years after starting TNF inhibitors. The patients were divided

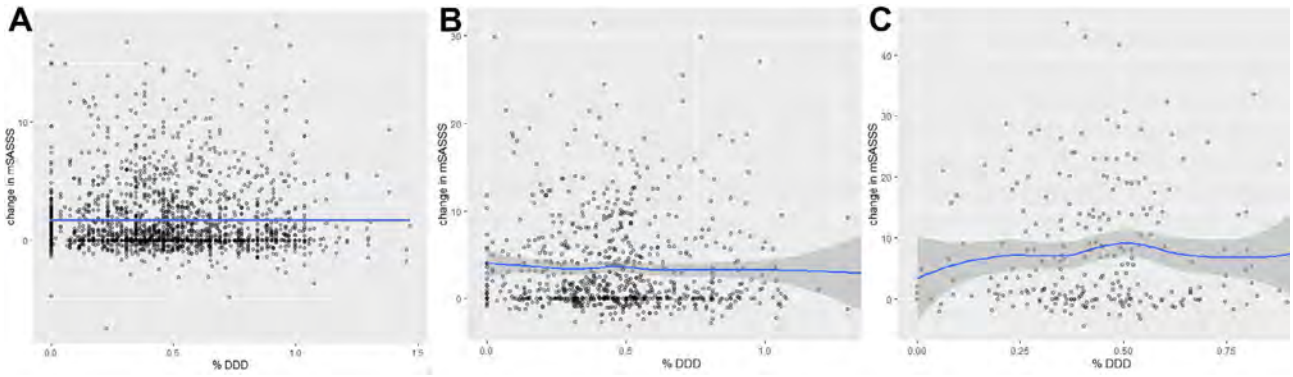

Figure 1. Scatterplot of defined daily dose (%DDD of TNF inhibitors) and change in modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) at each interval (A: 2-year interval, B: 4-year interval, C: 8-year interval)

into follow-up periods of 2 years, 4 years, and 8 years, and the %DDD of TNF inhibitors during each period was calculated. The correlation between the percentage of DDD and changes in mSASSS was analyzed using a linear mixed model at 2-year, 3-year, and 8-year intervals. Subgroup analysis was also performed by dividing the baseline mSASSS into three groups (mSASSS ≤24, mSASSS >24 and ≤48, mSASSS > 48).

Results: A total of 559 patients were included in the study. The Pearson correlation coefficients of %DDD and changes in mSASSS were -0209 for the 2-year interval, -0.0301 for the 4-year interval, and 0.0315 for the 8-year interval (Figure 1). In linear mixed models, %DDD and the changes of mSASSS at 2 years (β=-0.134, 95% CI -0.629 – 0.362), 4 years (β =-0.733, 95% CI -2.258 – 0.792), and 5 years (β=1.235, 95% CI -5.230 – 7.701) were not statistically significant in any interval (p = 0.597, p = 0.345, p = 0.707, respectively).In the subgroup analysis divided by baseline mSASSS, the correlation between %DDD and the changes of mSASSS was not statistically significant.

Conclusion: There was no correlation between the doses of TNF inhibitors and the changes of mSASSS. Although this study was a retrospective, our findings suggest that dose adjustment of TNF inhibitors may not be correlated with radiographic progression in patients with AS.

Disclosure: B. Koo: None; **S. Park**: None; **J. Shin**: None; **S. Iee**: None; **k. Joo**: None; **T. Kim**: None.

Abstract Number: 0516

Drivers of Treatment Intensification in Patients with Axial Spondyloarthritis and High Disease Activity: Results from a Clinical Practice Registry

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In the management of axial spondyloarthritis (axSpA), treatment intensification (TI) is recommended in patients with high disease activity (HDA). However, in practice, in most patients who are in an HDA state, treatment is not changed. Possibly, other factors than disease activity, such as disease impact and acceptability of current health state, drive the decision for TI. Our objective was to explore which patient- and disease-related determinants are associated with TI in axSpA patients with HDA.

Methods: In this cross-sectional observational study, one time point per patient was used from SpA-Net, a multicentre registry for SpA. Only patients in an HDA state (defined as Ankylosing Spondylitis Disease Activity Score [ASDAS]≥2.1) were included. The outcome (TI) was defined as 1) a higher dose or shorter interval of the same drug, 2) a switch of the current drug to another drug or 3) addition of a new drug to the current treatment regime; and only due to inefficacy of the current treatment. Only anti-inflammatory drugs (NSAIDs, conventional synthetic/biologic/targeted synthetic DMARDs [cs/b/tsDMARDs], corticosteroids) were considered. Primary determinants were ASDAS, Assessment of SpondyloArthritis international Society Health Index (ASAS HI) and physician global (PhGA). Education, peripheral symptoms and skin

Table. Logistic regression analyses of treatment intensification in patients with axSpA and ASDAS≥2.1

	Univariable (n=119)			Multivariable physician-centered* (n=111)			Multivariable patient-centered (n=111)		
Variable	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Age, years	0.97	0.94-0.99	0.02	0.97	0.94-1.00	0.07	0.97	0.94-1.00	0.05
Sex, female	1.02	0.48-2.20	0.95	0.84	0.31-2.25	0.72	0.93	0.37-2.32	0.88
ASDAS	1.76	0.96-3.26	0.07	1.65	0.78-3.47	0.19	1.81	0.90-3.62	0.10
PhGA (0-10)	1.92	1.43-2.57	<0.01	1.74	1.24-2.46	<0.01	N/A		
ASAS HI (0-17)	1.05	0.94-1.17	0.36	†§			†§		
Education, high	1.27	0.59-2.77	0.54	†			†		
Peripheral symptoms	4.87	2.03-11.68	<0.01	2.76	0.99-7.70	0.05	5.11	2.00-13.05	<0.01
BSA ≥3%	2.03	0.12-33.44	0.62	†			†		

*PhGA and PASS according to physician were only considered for the physician-centered model, in separate models. Only the PhGA-model is shown here. †Variable with p>0.20 in univariable regression, not included in multivariable model. §Not associated with TI if forced in multivariable model (physician-centered model: OR 0.97 [0.85-1.10], p=0.64; patient-centered model: OR 1.02 [0.90-1.14], p=0.79). BSA, Body Surface Area; N/A, not applicable; PhGA, physician global.

involvement were also considered as determinants. Acceptable symptom state according to patient (PASS-patient) or physician (PASS-physician) were included in sensitivity analyses. The association between determinants and TI was investigated with multivariable logistic regression. Both physician-centered and patient-centered models were generated.

Results: In total, 119 patients in an HDA state were included. Mean age was 50.4 (SD 13.5) years, symptom duration 20.1 (13.2) years and 65 patients (54.6%) were female. The majority were currently in an acceptable state (PASS-patient 57.1%, PASS-physician 66.7%). TI was conducted in 40 patients (33.6%). Patients in which TI was not applied were older, less often employed and more likely to be on biological treatment at time of ASDAS≥2.1. In physician-centered regression analyses, the physician-based determinants were very strong and independent drivers for TI (OR_{PhGA} = 1.74 [95%CI 1.24-2.46]; $OR_{PASS\text{-}physician}$ = 27.0 [4.18-174.0]) while patient-based determinants (ASDAS, ASAS HI, education) were not associated with TI (Table). In patient-centered regression analyses, only peripheral symptoms were associated with TI. PASS-patient was not associated with TI in any of the models (OR = 1.22 [0.34-4.45] when added to the patient-centered model).

Conclusion: In practice, treatment is intensified in only a minority of patients with axSpA and HDA. Physician-centered factors seem to be driving this decision to change treatment, independently of (ASDAS-based) disease activity. Further research is needed to better understand these decisions.

Disclosure: C. Webers: None; **R. Nezam El-Din**: None; **M. Been**: None; **H. Vonkeman**: AbbVie, 5, 6, Boehringer Ingelheim, 5, 6, Galapagos, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6; **A. van Tubergen**: MSD, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, UCB Pharma, 2, 5.

Abstract Number: 0517

Which ASDAS Cut-Off Corresponds Best to Treatment Intensification in Patients with Axial Spondyloarthritis in Daily Practice?

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In patients with axial spondyloarthritis (axSpA) and high disease activity (typically defined as Ankylosing Spondylitis Disease Activity Score [ASDAS]≥2.1), it is recommended to adapt treatment. However, this recommendation is not always followed in practice. The ASDAS was developed for research, and it is unknown how it performs in daily practice. Possibly, the cut-off of 2.1 as currently endorsed is too strict in this setting. Our objective was to investigate which ASDAS cut-off values correspond best with treatment intensification (TI) in practice.

Methods: Data were used from a prospective multicentre Dutch registry for patients with SpA (SpA-Net). Patients with axSpA and ≥1 ASDAS measurement in 2016-2022 were included. TI was defined as 1) higher dose or frequency of the same drug, 2) switch to another drug or 3) addition of a new drug to the current treatment regime; due to inefficacy. Only anti-inflammatory drugs (NSAIDs, conventional synthetic/biologic/targeted synthetic DMARDs [cs/b/tsDMARDs], corticosteroids) were considered. Single patients could contribute multiple TI events. Receiver operating characteristic (ROC) curve analyses were conducted to estimate the ability of ASDAS to discriminate between TI/non-TI (Area Under the Curve [AUC]), and identify the ASDAS cut-off that discriminates best in this real-world population, with corresponding sensitivity and specificity. Analyses were conducted with (1) all observations and (2) the first observation per patient per calendar year.

Results: In total, 328 patients with 2,010 ASDAS measurements were included. Median follow-up was 2.5 (IQR 1.0-4.3) years. Mean age was 50.2 (SD 14.0) years, 149 (45.4%) were female, and mean ASDAS was 2.3 (SD 1.0). Approximately two-thirds of patients (211/328, 64.3%) were on biological/targeted synthetic DMARDs (b/tsDMARDs) at some point during follow-up. TI was applied after 218/2,010 ASDAS measurements (10.8%), and mean ASDAS was higher at TI timepoints than at non-TI timepoints (3.1 [SD 1.0] versus 2.3 [SD 1.0]). When all ASDAS measurements were included for analysis, the AUC was 0.72 (95%CI 0.68-0.75) with an optimal ASDAS cut-off of 2.7 (sensitivity 68%, specificity 66%). Results were similar when only one measurement was used per patient and calendar year (1,069 ASDAS measurements; AUC 0.75, ASDAS cut-off 2.7). Over the years, the ASDAS cut-off was consistently higher than 2.1, however with a decreasing trend (Table).

Conclusion: In daily practice, TI is associated with a higher ASDAS cut-off value than the recommended one (≥2.1). Possibly, rheumatologists believe the recommended cut-off to be too stringent or consider other factors than disease activity when making treatment decisions. Regardless, the cut-off seems to be gradually decreasing, suggesting increased uptake of axSpA management recommendations.

Table. ROC analysis of TI and ASDAS, by calendar year (one measurement per patient per year)

	2016 (n=56)	2017 (n=175)	2018 (n=221)	2019 (n=206)	2020 (n=132)	2021 (n=133)	2022 (n=117)
AUC (95% CI)	0.67 (0.39-0.95)	0.82 (0.73-0.91)	0.75 (0.66-0.84)	0.70 (0.59-0.81)	0.71 (0.59-0.82)	0.73 (0.60-0.86)	0.77 (0.64-0.91)
Optimal cut-off*							
ASDAS	2.34	2.76	2.67	2.70	2.35	2.40	2.53
Sensitivity	0.75	0.78	0.78	0.67	0.94	0.88	0.80
Specificity	0.65	0.76	0.65	0.68	0.56	0.59	0.71

If patients had multiple ASDAS measurements in a calendar year, the first measurement was used. *According to Liu index (maximize product of sensitivity x specificity). AUC, Area Under the Curve; Receiver operating characteristic, ROC; TI, treatment intensification.

Disclosure: C. Webers: None; **R. Nezam El-Din**: None; **M. Been**: None; **H. Vonkeman**: AbbVie, 5, 6, Boehringer Ingelheim, 5, 6, Galapagos, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6; **A. van Tubergen**: MSD, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, UCB Pharma, 2, 5.

Abstract Number: 0518

Tofacitinib Efficacy and Safety in Patients with Ankylosing Spondylitis by Baseline C-Reactive Protein Levels: A Post Hoc Analysis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

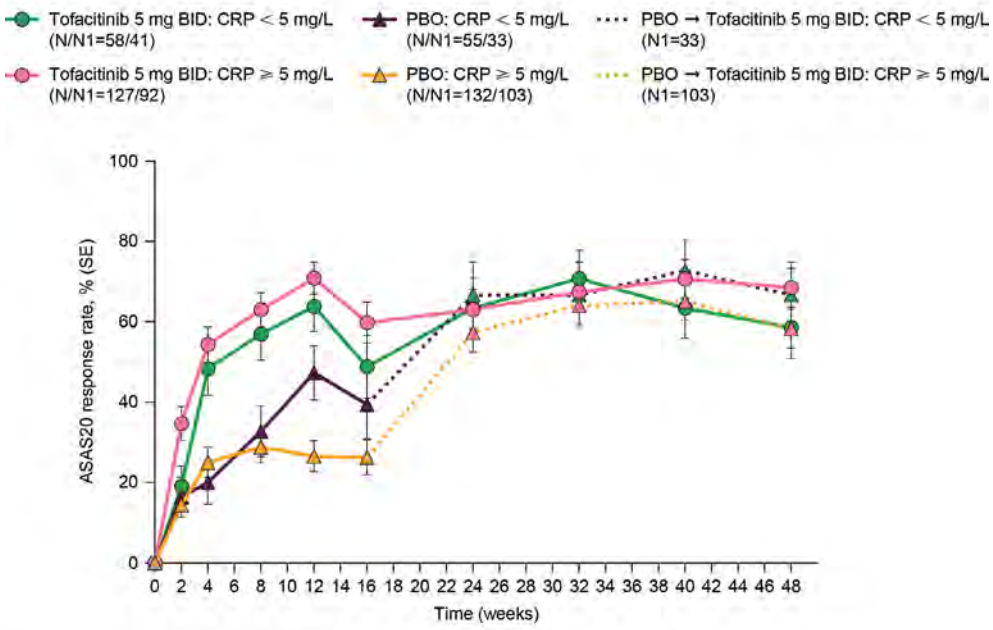
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Elevated baseline (BL) CRP levels can predict treatment response in patients (pts) with AS. Tofacitinib is a Janus kinase inhibitor for the treatment of AS. This post hoc analysis evaluated the impact of BL CRP levels on tofacitinib efficacy and safety in pts with AS.

Fig. ASAS20 response rates over time by BL CRP



ASAS20, Assessment of SpondyloArthritis international Society ≥ 20% improvement; BID, twice daily; BL, baseline; N, pooled pts in P2 and P3 from BL–W16; N1, pts from P3 from W24–48; P, Phase; PBO, placebo; pts, patients; SE, standard error; W, Week

Table. Safety outcomes by BL CRP (NML < 5 mg/L; ELV ≥ 5 mg/L)

	To W16				To W48			
	Tofacitinib 5 mg BID[a]		PBO		All tofacitinib 5 mg BID[b]		All tofacitinib[c]	
n (%) IR[d] [95% CI]	NML N=58	ELV N=127	NML N=55	ELV N=132	NML N=91	ELV N=225	NML N=129	ELV N=291
TEAEs	39 (67.2) 365.4 [259.9, 499.6]	61 (48.0) 222.7 [170.4, 286.1]	27 (49.1) 240.7 [158.6, 350.2]	64 (48.5) 235.4 [181.3, 300.6]	60 (65.9) 188.2 [143.7, 242.3]	138 (61.3) 146.5 [123.1, 173.1]	80 (62.0) 202.5 [160.6, 252.0]	168 (57.7) 155.6 [133.0, 181.0]
SAEs	1 (1.7) 5.6 [0.1, 31.0]	2 (1.6) 5.1 [0.6, 18.6]	0 0.0 [0.0, 21.9]	1 (0.8) 2.5 [0.1, 14.0]	5 (5.5) 7.8 [2.5, 18.2]	3 (1.3) 1.8 [0.4, 5.3]	5 (3.9) 6.6 [2.1, 15.4]	4 (1.4) 2.2 [0.6, 5.5]
All infections	23 (39.7) 158.0 [100.2, 237.1]	28 (22.0) 81.5 [54.2, 117.8]	13 (23.6) 87.9 [46.8, 150.2]	30 (22.7) 83.9 [56.6, 119.8]	37 (40.7) 82.1 [57.8, 113.2]	74 (32.9) 56.7 [44.5, 71.2]	46 (35.7) 84.1 [61.6, 112.2]	86 (29.6) 58.0 [46.4, 71.6]
SIs	1 (1.7) 5.6 [0.1, 31.0]	0 0.0 [0.0, 9.5]	0 0.0 [0.0, 21.9]	0 0.0 [0.0, 9.2]	1 (1.1) 1.5 [0.0, 8.5]	0 0.0 [0.0, 2.2]	1 (0.8) 1.3 [0.0, 7.3]	0 0.0 [0.0, 2.0]
HZ	0 0.0 [0.0, 20.4]	0 0.0 [0.0, 9.5]	0 0.0 [0.0, 21.9]	0 0.0 [0.0, 9.2]	2 (2.2) 3.1 [0.4, 11.1]	3 (1.3) 1.8 [0.4, 5.3]	3 (2.3) 3.9 [0.8, 11.5]	4 (1.4) 2.2 [0.6, 5.5]
Discontinuations due to AEs	1 (1.7) 5.6 [0.1, 31.0]	3 (2.4) 7.7 [1.6, 22.6]	2 (3.6) 11.9 [1.4, 43.0]	2 (1.5) 5.0 [0.6, 18.0]	4 (4.4) 6.1 [1.6, 15.7]	7 (3.1) 4.2 [1.7, 8.7]	4 (3.1) 5.2 [1.4, 13.4]	8 (2.7) 4.3 [1.9, 8.5]

[a]To W12: P2; W16: P3

[b]To W12: P2; W48: P3

[c]P2: tofacitinib 2, 5, or 10 mg BID to W12; P3: 5 mg BID to W48

[d]Pts with events/100 pt-years

AE, adverse event; BID, twice daily; BL, baseline; CI, confidence interval; ELV, elevated; HZ, herpes zoster; IR, incidence rate; n, number of pts with an event within risk period (on treatment); N, number of pts in safety analysis set; NML, normal; P, Phase; PBO, placebo; pt, patient; SAE, serious adverse event; SI, serious infection; TEAE, treatment-emergent adverse event; W, Week

Methods: Post hoc analysis of pooled data from placebo (PBO)-controlled, randomized, double-blind trials (NCT01786668, Phase [P]2, 16 weeks; NCT03502616, P3, 48 weeks) in pts with AS on ≥ 1 dose of tofacitinib or PBO (P3: PBO-treated pts switched to tofacitinib after Week [W]16), by BL CRP: normal (NML) < 5 mg/L; elevated (ELV) ≥ 5 mg/L. Tofacitinib 5 mg twice daily (BID) efficacy was assessed to W12/W16–48 (P3). Endpoints: Assessment of SpondyloArthritis international Society (ASAS) 20/40, Bath AS Disease Activity Index (BASDAI) 50, AS-Disease Activity Score-CRPinactive disease (ASDAS-CRP ID), and least squares mean change from BL (Δ) in nocturnal pain and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F). Safety was assessed to W16 and W48.

Results: Of 372 pts, 30.4/69.6% had NML/ELV BL CRP. Both groups had generally similar BL characteristics; more pts with ELV CRP were male, current smokers, and had prior biologic DMARD use. At W12, ASAS20 response was greater for tofacitinib vs PBO in both groups (Fig); efficacy maintained to W48. At W12, the difference in response from PBO for tofacitinib was numerically greater for ELV vs NML CRP for ASAS20 (44.7% vs 15.9%), ASAS40 (34.6% vs 17.3%), BASDAI50 (33.8% vs 15.3%), ASDAS-CRP ID (9.5% vs 8.2%), Δnocturnal spinal pain (-2.1 vs -1.4), and ΔFACIT-F (5.2 vs 3.5). For tofacitinib, rates of treatment-emergent adverse events and infections to W16 trended numerically higher for tofacitinib vs PBO in pts with NML CRP, but were similar to PBO in pts with ELV CRP (Table). There were few serious adverse events, serious infections, or herpes zoster across groups and no deaths. Limitations: small sample size, differences in BL characteristics.

Conclusion: Regardless of BL CRP, at W12, tofacitinib was more efficacious vs PBO; and across endpoints, the differences in response from PBO for tofacitinib were numerically greater in pts with ELV vs NML CRP. Tofacitinib safety rates were consistent with PBO in pts with ELV CRP, but trended higher for tofacitinib vs PBO in pts with NML CRP.

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Disclosure: A. Deodhar: AbbVie, 2, 5, Amgen, 2, Aurinia, 2, Bristol Myers Squibb, 2, 5, Celgene, 5, Eli Lilly, 2, 5, Janssen, 2, 6, MoonLake, 2, 5, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5; **X. Baraliakos**: AbbVie, 2, 6, BMS, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, 6, UCB, 2, 6; **M. Magrey**: AbbVie,

2, Bristol Myers Squibb, 2, Eli Lilly, 2, Novartis, 2, Pfizer Inc, 2, UCB, 5; **L. Gensler**: AbbVie, 2, Acelyrin, 2, Eli Lilly, 2, Fresenius Kabi, 2, Janssen, 2, Novartis, 2, 5, Pfizer, 2, UCB Pharma, 2, 5; **A. Thorat**: Pfizer Australia, 3, Pfizer Inc, 11; **S. Pemmaraju**: Pfizer Inc, 3, 11; **M. Cadatal**: Pfizer Inc, 3, 11; **P. Nash**: AbbVie, 5, 6, Bristol Myers Squibb, 5, 6, Celgene, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, GSK, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer Inc, 5, 6.

Abstract Number: 0519

Long-Term Safety and Efficacy of Bimekizumab in Patients with Active Ankylosing Spondylitis: 5-Year Results from a Phase 2b Study and Its Open-Label Extension

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Bimekizumab (BKZ), a monoclonal IgG1 antibody, selectively inhibits IL-17F in addition to IL17A. BKZ has demonstrated clinical efficacy and safety up to 3 years (yrs) in patients (pts) with active AS (i.e., radiographic axial spondyloarthritis)[1] in the phase 2b study BE AGILE and its open-label extension (OLE).[2]

Here, we report 5-yr results of BKZ in BE AGILE and its OLE.

Methods: The dose-ranging BE AGILE study (NCT02963506) consisted of a 12-week (wk) double-blind, placebo-controlled period, then a dose-blind period to Wk 48 where pts received BKZ 160 or 320 mg every 4 wks (Q4W).[2] Pts completing Wk 48 were eligible to enter the OLE (NCT03355573) where all pts received BKZ 160 mg Q4W to Wk 256.

Treatment-emergent adverse events (TEAEs; MedDRA v19.0) are reported for BKZ exposure from Wk 0–256. Efficacy is reported from Wk 0–256 for pts enrolled in BE AGILE entering the dose-blind period (dose-blind set [DBS]) and Wk 48–256 for pts enrolled in the OLE with ≥1 efficacy measurement at OLE entry (OLE full analysis set [FAS]). Analyses used non-responder imputation (NRI; pts who did not enter the OLE were considered non-responders from Wk 48), observed case methodology, or multiple imputation (MI).

Results: 296/303 (97.7%) pts randomized in BE AGILE entered the dose-blind period; 265/303 (87.5%) completed to Wk 48. Of 255/303 (84.2%) pts who entered the OLE at Wk 48, and received ≥1 BKZ dose, 202/255 (79.2%) completed to Wk 256.

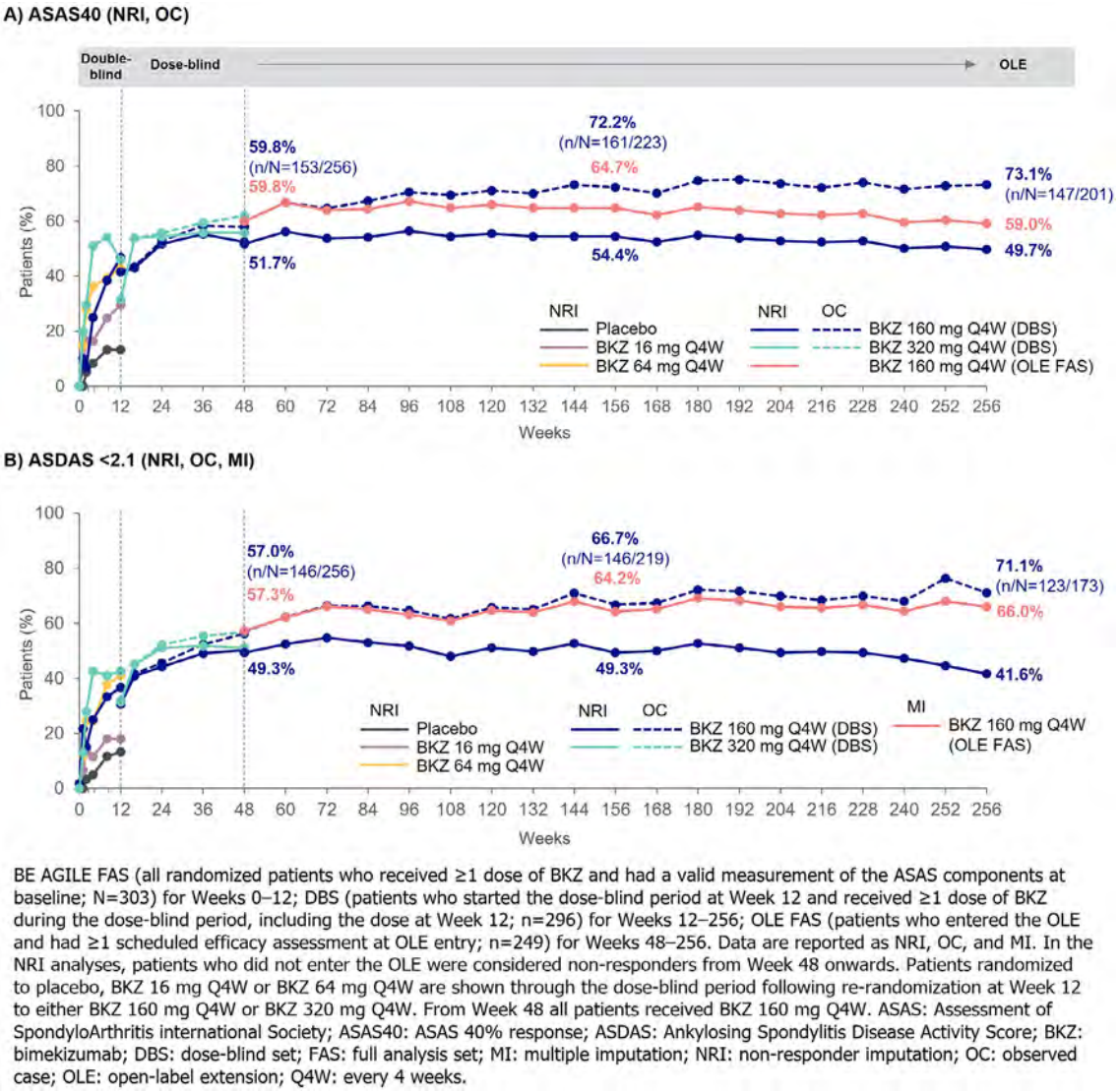
Table. Safety to Week 256 for exposure to BKZ in BE AGILE and the OLE

TEAEs[a] n (%) [EAIR/100 PY]	**BE AGILE and OLE** Weeks 0–256 **Total (N=303; exposure 1,231 PY)**
Any TEAE	289 (95.4) [134.6]
Study discontinuations due to TEAEs	43 (14.2) [3.5]
Drug-related TEAEs	160 (52.8) [21.8]
Serious TEAEs	58 (19.1) [5.2]
Deaths	3 (1.0) [0.2][b]
Safety topics of interest	
Fungal infections[c]	74 (24.4) [7.4]
Candida infections by preferred term[d]	30 (9.9) [2.6]
Oral candidiasis	25 (8.3) [2.2]
Skin *Candida*	4 (1.3) [0.3]
Vulvovaginal candidiasis	2 (0.7) [0.2]
Candida infection	1 (0.3) [0.1]
Oropharyngeal candidiasis	1 (0.3) [0.1]
Serious infections and infestations	17 (5.6) [1.4]
Neutropenia	4 (1.3) [0.3]
Adjudicated SIB	1 (0.3) [0.1]
Injection site reactions	2 (0.7) [0.2]
Definite and probable IBD[e]	10 (3.3) [0.8][f]
With prior history	2 (0.7)
Without prior history	8 (2.6)
Uveitis[g,h]	9 (3.0) [0.7][i]
With prior history	3 (1.0)
Without prior history	6 (2.0)

Safety set. TEAEs occurring on placebo treatment are not included. All patients received BKZ 160 mg Q4W during the OLE (Weeks 48–256) after completing BKZ 160 mg or 320 mg Q4W at Week 48 in BE AGILE.
[a] Defined according to MedDRA v19.0. [b] There was one death in BE AGILE (cardiac arrest) and two in the OLE (cardiac arrest, road traffic accident). Neither were considered treatment related. [c] Other than *Candida* infections, fungal infections included *Tinea* and not elsewhere classified infections, and were localized to the skin, scalp, ear, mouth, tongue, nails, vulva, and feet; none were systemic. [d] All *Candida* infections were mild to moderate, none were systemic. [e] Includes the preferred terms Crohn's disease, colitis ulcerative, and colitis. [f] Four patients had IBD TEAEs in BE AGILE; none of these cases occurred from Weeks 0–12 in patients who were treated with placebo. [g] Includes the preferred terms iritis, iridocyclitis, and uveitis. [h] Uveitis was not a safety topic of interest in this study and is included as an extra-musculoskeletal manifestation. [i] Two uveitis cases occurred during BE AGILE; one case was in a placebo-treated patient during Weeks 0–12. BKZ: bimekizumab; EAIR: exposure-adjusted incidence rate; IBD: inflammatory bowel disease; OLE: open-label extension; PY: patient-years; Q4W: every 4 weeks; SIB: suicidal ideation and behavior; TEAE: treatment-emergent adverse event.

From Wk 0–256, exposure adjusted incidence rates (EAIRs) per 100 pt-yrs were 134.6 for any TEAE and 5.2 for serious TEAEs (**Table**). EAIR of *Candida* infections over 256 wks (2.6) was lower than in Wk 0–48 (7.5).[1] All *Candida* infections were mild or moderate; 1 oral candidiasis event led to discontinuation. No systemic fungal infections were reported. Over 256 wks, EAIRs of serious infections and infestations (1.4) and injection site reactions (0.2) remained low. EAIRs of IBD (0.8) and uveitis (0.7) were also low.

At the OLE entry visit (Wk 48), around half of the DBS (n=296) achieved ASAS40 (51.7%) and ASDAS < 2.1 (49.3%); 49.7% and 41.6% achieved these endpoints at Wk 256, respectively (NRI; **Figure 1**). Similar results were seen in the OLE FAS (n=249) for ASAS40 (NRI; Wk 48: 59.8%; Wk 256: 59.0%) and ASDAS < 2.1 (MI; 57.3%; 66.0%).



BE AGILE FAS (all randomized patients who received ≥1 dose of BKZ and had a valid measurement of the ASAS components at baseline; N=303) for Weeks 0–12; DBS (patients who started the dose-blind period at Week 12 and received ≥1 dose of BKZ during the dose-blind period, including the dose at Week 12; n=296) for Weeks 12–256; OLE FAS (patients who entered the OLE and had ≥1 scheduled efficacy assessment at OLE entry; n=249) for Weeks 48–256. Data are reported as NRI, OC, and MI. In the NRI analyses, patients who did not enter the OLE were considered non-responders from Week 48 onwards. Patients randomized to placebo, BKZ 16 mg Q4W or BKZ 64 mg Q4W are shown through the dose-blind period following re-randomization at Week 12 to either BKZ 160 mg Q4W or BKZ 320 mg Q4W. From Week 48 all patients received BKZ 160 mg Q4W. ASAS: Assessment of SpondyloArthritis international Society; ASAS40: ASAS 40% response; ASDAS: Ankylosing Spondylitis Disease Activity Score; BKZ: bimekizumab; DBS: dose-blind set; FAS: full analysis set; MI: multiple imputation; NRI: non-responder imputation; OC: observed case; OLE: open-label extension; Q4W: every 4 weeks.

Figure 1. Efficacy responses to Week 256

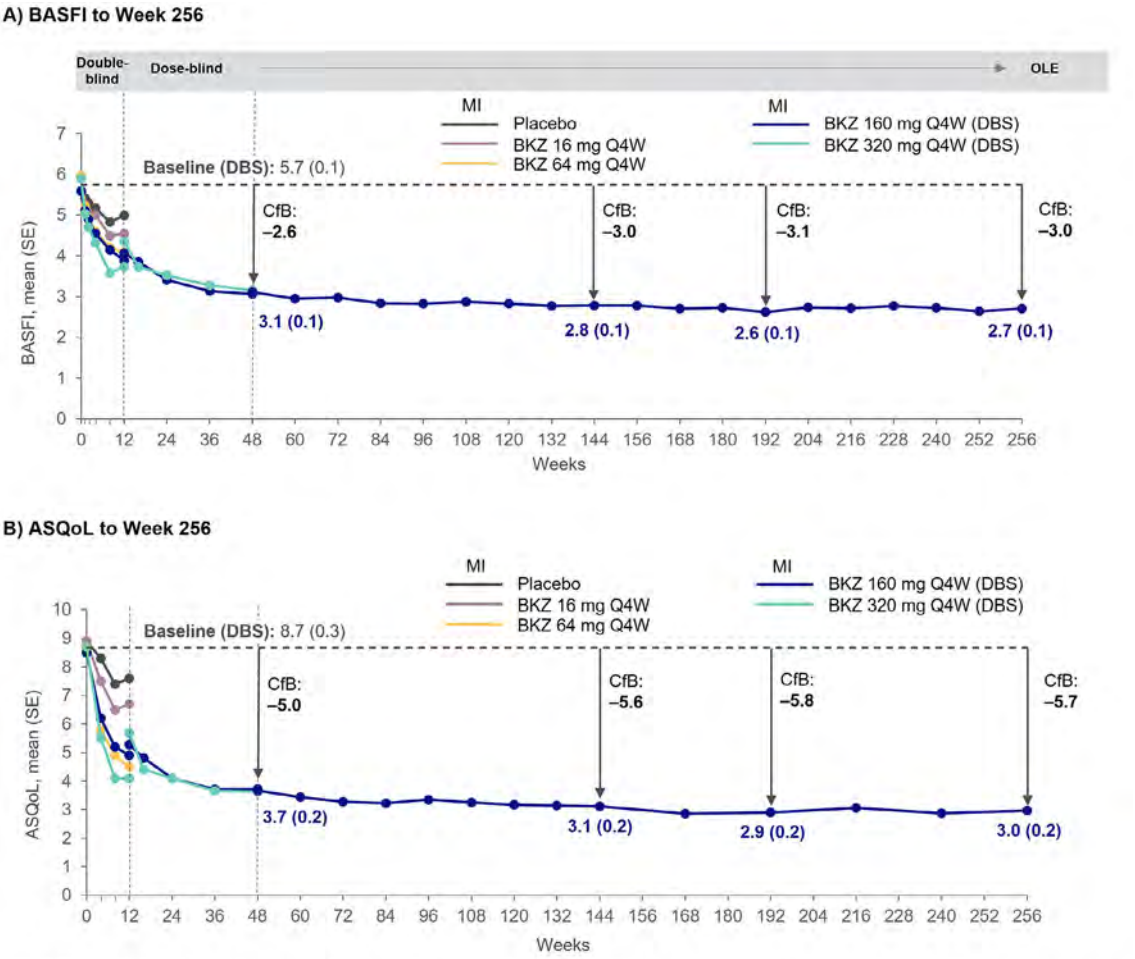
Mean reductions from BL to Wk 48 in ASDAS (3.9 to 2.1) and BASDAI (6.5 to 3.0) in the DBS were sustained or further decreased to 2.1 and 2.5, respectively, at Wk 256 (MI); responses in the OLE FAS from Wk 48 to Wk 256 were similar (MI; ASDAS: 2.0 to 1.9; BASDAI: 2.8 to 2.4).

Mean BASFI and ASQoL improvements from BL to Wk 48 were sustained to Wk 256 in the DBS (MI; **Figure 2**), and from Wk 48 to Wk 256 in the OLE FAS (MI; BASFI: 3.0 to 2.6; ASQoL: 3.3 to 2.6).

Conclusion: The long-term safety profile of BKZ in pts with AS was consistent with previous observations, with no new safety signals identified after 5 yrs of exposure.

Clinical efficacy, including improvements in signs and symptoms, disease activity, physical function, and health-related quality of life, was maintained up to 5 yrs of BKZ treatment. To our knowledge, this is the first report of NRI ASAS40 data up to 5 yrs in pts with AS exposed to novel treatments.

References:1. Boel A. Ann Rheum Dis 2019;78:1545–9; **2.** Baraliakos X. Arthritis Rheumatol 2022;74:1943–58.



BE AGILE FAS (all randomized patients who received ≥1 dose of BKZ and had a valid measurement of the ASAS components at baseline; N=303) for Weeks 0–12; DBS (patients who started the dose-blind period at Week 12 and received ≥1 dose of BKZ during the dose-blind period, including the dose at Week 12; n=296) for Weeks 12–256; OLE FAS (patients who entered the OLE and had ≥1 scheduled efficacy assessment at OLE entry; n=249) for Weeks 48–256. Data are reported as MI. Baseline BASFI and ASQoL are shown for the BKZ 160 mg Q4W DBS. Patients randomized to placebo, BKZ 16 mg Q4W or BKZ 64 mg Q4W are shown through the dose-blind period following re-randomization at Week 12 to either BKZ 160 mg Q4W or BKZ 320 mg Q4W. From Week 48 all patients received BKZ 160 mg Q4W. ASAS: Assessment of SpondyloArthritis international Society; ASAS40: ASAS 40% response; ASDAS: Ankylosing Spondylitis Disease Activity Score; BKZ: bimekizumab; DBS: dose-blind set; FAS: full analysis set; MI: multiple imputation; OLE: open-label extension; Q4W: every 4 weeks.

Figure 2. (A) Physical function and (B) health-related quality of life to Week 256 (MI)

Disclosure: A. Deodhar: AbbVie, 2, 5, Amgen, 2, Aurinia, 2, Bristol Myers Squibb, 2, 5, Celgene, 5, Eli Lilly, 2, 5, Janssen, 2, 6, MoonLake, 2, 5, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5; **V. Navarro-Compán**: AbbVie, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, Janssen, 6, MoonLake, 2, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, MoonLake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 2, UCB Pharma, 2, 6; **L. Gensler**: AbbVie, 2, Acelyrin, 2, Eli Lilly, 2, Fresenius Kabi, 2, Janssen, 2, Novartis, 2, 5, Pfizer, 2, UCB Pharma, 2, 5; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, Galapagos, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, UCB Pharma, 2, 5; **T. Tomita**: AbbVie, 2, 6, Astellas, 6, BMS, 6, Eisai, 6, Eli Lilly, 2, 6, Gilead, 2, Janssen, 6, Kyowa Kirin, 6, Mitsubishi-Tanabe, 6, Novartis, 2, 6, Pfizer, 2, 5; **H. Marzo-Ortega**: AbbVie, 2, 6, Biogen, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 5, 6, MoonLake, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Takeda, 2, 6, UCB Pharma, 2, 5, 6; **C. Fleurinck**: UCB Pharma, 3; **T. Vaux**: UCB Pharma, 3; **U. Massow**: UCB Pharma, 3; **D. van der Heijde**: AbbVie, 2, Bayer, 2, BMS, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GSK, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; **X. Baraliakos**: AbbVie, 2, 6, BMS, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, 6, UCB, 2, 6.

Abstract Number: 0520

How Do Early Disease Activity and Early Clinical Response Associate with Long-Term Outcomes with Ixekizumab in Radiographic Axial Spondyloarthritis?

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The ASAS-EULAR recommendations for the management of axial spondyloarthritis (axSpA) advise that a patient be assessed for biological disease-modifying anti-rheumatic drug (bDMARD) treatment response after at least 12 weeks of treatment[1]. The recommended treatment target for axSpA is inactive disease (ID) or low disease activity (LDA)[2], as together defined by an Ankylosing Spondylitis Disease Activity Score (ASDAS) <2.1[3]. This analysis aimed to explore the association between treatment response at Week (W)12 and W24, and attainment of the ASDAS < 2.1 treat-to-target (T2T) recommendation at W52 in patients with radiographic (r-) axSpA treated with ixekizumab (IXE).

Methods: This post hoc analysis included patients randomly assigned to IXE 80mg every 4 weeks (N=81) from COAST-V (NCT02696785), a Phase 3 trial that investigated the efficacy of IXE in bDMARD-naïve patients with r-axSpA. The proportion of patients who achieved the ASDAS < 2.1 target response at W52 was evaluated among those in ID, LDA, high disease activity (HDA) or very high disease activity (VHDA) at W12 or W24. The proportion of patients who achieved ASDAS< 2.1 at W52 was also measured among those who attained meaningful clinical response at W12 or W24, as defined by a clinically important (CII, ΔASDAS ≥1.1) or a major improvement (MI, ΔASDAS ≥2.0) in ASDAS, improvement of ≥50% in Bath Ankylosing Spondylitis Disease Activity Index score (BASDAI50), or achievement of BASDAI < 4. Patient and disease characteristics are described according to responses at W12 or W24 and W52. Non-responder imputation was used to handle missing data.

Results: Of the 81 patients, 34 (42%) were in ID or LDA at W12 (8 ID, 26 LDA) and most of these patients met the ASDAS < 2.1 target at W52 (ID=100%, LDA=85%; Figure 1A). 47 patients achieved ASDAS CII at W12 and of those, 33 (70%) were in ID or LDA at W52 (Figure 1B). Similarly, most patients who met the ASDAS MI, BASDAI50 or BASDAI< 4 clinical response measures at W12 met ASDAS < 2.1 at W52 (81–94%; Figure 1B). 37 patients (46%) were in ID or LDA at W24 (13 ID, 24 LDA) and of those, 29 (78%) had already achieved ASDAS < 2.1 at W12 (Table 1), and most also met ASDAS < 2.1 at W52 (ID=100%, LDA=79%; Figure 1A). 52 patients achieved ASDAS CII at W24 and among them, 37 (71%) were in ID or LDA at W52 (Figure 1B). Most patients who met the ASDAS MI, BASDAI50 or BASDAI< 4 clinical response measures at W24 met ASDAS < 2.1 at W52 (80–89%; Figure 1B). Patients who did not meet ASDAS < 2.1 at W12 were more likely to be older, female, or with a longer symptom duration versus those who did, and 8 of these 47 patients (17%) subsequently achieved ASDAS < 2.1 at W24 (Table 1). 39 patients were in HDA or VHDA (ASDAS ≥2.1) at both W12 and W24 (Table 1), and 9 (23%) of these patients (11% of the 81 included patients) met the ASDAS < 2.1 target at W52.

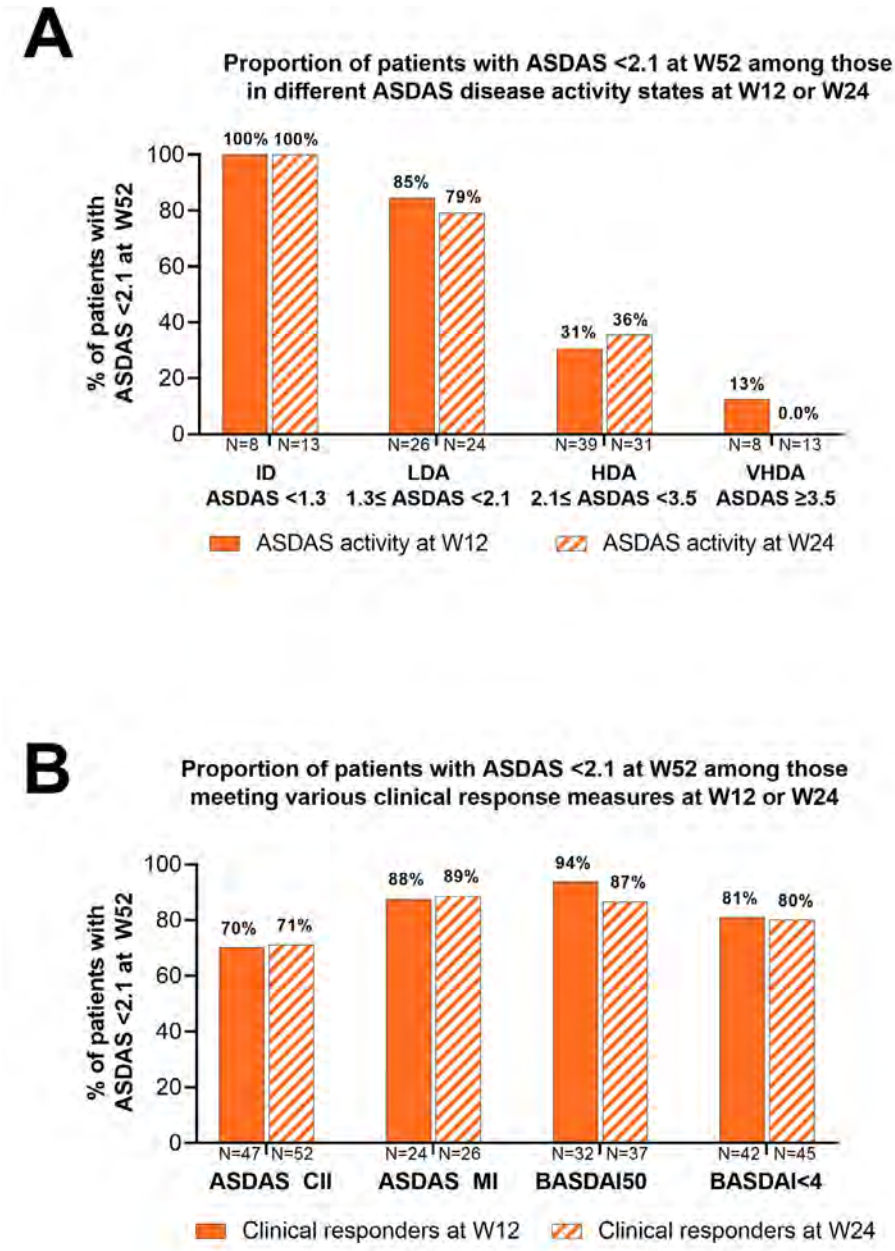

Figure 1. The proportion (%) of IXE-treated patients that achieved ASDAS <2.1 at Week 52 among those meeting specific response criteria at Week 12 or Week 24

Percentage values are rounded. ASDAS <2.1 represents the treatment target of ID or LDA. ASDAS CII is a change ≥1.1 units, ASDAS MI is a change ≥2.0 units. BASDAI50 represents an improvement of ≥50% of the BASDAI score from baseline. A BASDAI score less than 4 is not considered active disease.

Abbreviations: ASDAS= Ankylosing Spondylitis Disease Activity Score; BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; CII=Clinically Important Improvement; HDA=High Disease Activity; ID=Inactive Disease; IXE=ixekizumab; LDA=Low Disease Activity; MI=Major Improvement; VHDA=Very High Disease Activity; W=Week

Conclusion: These data regarding IXE-treated patients with r-axSpA reinforce the current ASAS-EULAR and T2T recommendations, in that those who achieved ASDAS CII or ASDAS < 2.1 at W12 and/or W24 were highly likely to attain the treatment target of ID or LDA at W52.

Table 1. Baseline demographics and disease characteristics of patients that had ASDAS <2.1 or ASDAS ≥2.1 at Week 12 and/or Week 24

	Week 12 ASDAS <2.1 (N=34)		Week 12 ASDAS ≥2.1 (N=47)	
	Week 24 ASDAS <2.1 (N=29)	Week 24 ASDAS ≥2.1 (N=5)	Week 24 ASDAS <2.1 (N=8)	Week 24 ASDAS ≥2.1 (N=39)
Age, years	35.0 (10.1)	38.2 (9.8)	42.1 (11.5)	45.5 (12.3)
Female, n (%)	1 (3.4)	0 (0)	2 (25.0)	10 (25.6)
HLA-B27+, n (%)	28 (96.6)	5 (100.0)	8 (100.0)	34 (87.2)
Symptom duration, years	9.9 (6.6)	14.2 (10.4)	16.2 (13.1)	20.3 (11.8)
MRI-SIJ+, n (%)	15 (51.7)	2 (40.0)	2 (25.0)	8 (20.5)
CRP+, n (%)	21 (72.4)	2 (40.0)	5 (62.5)	24 (61.5)
ASDAS at baseline	3.7 (0.8)	3.5 (0.3)	3.6 (0.7)	3.8 (0.7)
ASDAS at week 12	1.5 (0.4)	1.9 (0.2)	2.5 (0.2)	2.9 (0.4)
ASDAS at week 24	1.4 (0.4)	2.5 (0.3)	1.6 (0.3)	2.9 (0.7)

Data are mean (standard deviation) unless stated otherwise.
Abbreviations: ASDAS=Ankylosing Spondylitis Disease Activity Score; CRP+=SERUM C reactive protein nephelometry >5.0 mg/L, HLA-B27=Human Leukocyte Antigen B 27; MRI-SIJ+=Magnetic resonance imaging of the sacroiliac joints, Spondyloarthritis Research Consortium of Canada score ≥2

References

1. Ramiro SE et al. *Ann Rheum Dis*. 2023; 82(1):19-34
2. Smolen JS et al. Ann Rheum Dis. 2018; 77(1): 3-17
3. Machado PM et al. Ann Rheum Dis. 2018; 77(10): 1539-1540

Disclosure: S. Ramiro: AbbVie, 2, 5, Eli Lilly, 2, Galapagos, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, UCB Pharma, 2, 5; **C. Lukas**: Abbvie, 2, 6, Amgen, 2, 6, Biogen, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche Chugai, 2, 6, UCB, 2, 6; **L. Bessette**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol Myers Squibb, 2, 5, 6, Eli Lilly, 2, 5, 6, Fresenius Kabi, 2, 6, Gilead, 2, 5, 6, JAMP Pharma, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Organon, 2, 6, Pfizer, 2, 5, 6, Sandoz, 2, 6, Sanofi, 2, 5, 6, Teva, 2, 6, UCB, 2, 5, 6, UCBA, 5; **P. Wickersham**: Abbvie, 2, 6, Amgen, 6, AstraZeneca, 2, 6, Eli Lilly, 2, 5, 6, Novartis, 6; **S. Liu-Leage**: Eli Lilly, 3, 11; **T. Panni**: Eli Lilly, 3; **R. Bolce**: Eli Lilly and Company, 3, 11; **B. Janos**: Eli Lilly, 3, 11; **M. Nissen**: AbbVie/Abbott, 2, Eli Lilly, 2, 12, Involved in Clinical Trial, Janssen, 2, Novartis, 6, 12, research funding paid to institution, Pfizer, 6, UCB, 2, 12, funding support to attend EULAR 2023, paid to institution; **J. Wei**: Abbvie, 2, 5, 6, Amgen, 5, AstraZeneca, 6, BMS, 2, 5, 6, Celgene, 2, Chugai, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 5, 6, Gilead, 5, GSK, 2, 5, Janssen, 2, 5, 6, Novartis, 2, 5, Pfizer, 2, 5, 6, Sanofi-Aventis, 2, SUN pharma, 5, TSH Taiwan, 2, UCB pharma, 2, 5.

Abstract Number: 0521

Work Productivity Improved in Patients with Axial Spondyloarthritis Receiving Bimekizumab Treatment over 52 Weeks: Results from Two Phase 3 Studies

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The clinical manifestations of axial spondyloarthritis (axSpA) limit physical function and work productivity, posing an economic burden to patients (pts) and society.[1] Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A, demonstrated sustained efficacy in controlling disease activity up to Week (Wk) 52 in pts with non-radiographic (nr-) and radiographic (r-)axSpA (i.e., AS)[2] in the phase 3 studies BE MOBILE 1 and 2, respectively.[3] This analysis assessed the impact of BKZ on work productivity and activity impairment (WPAI) at Wk 16 and Wk 52 in pts across the full disease spectrum of axSpA.

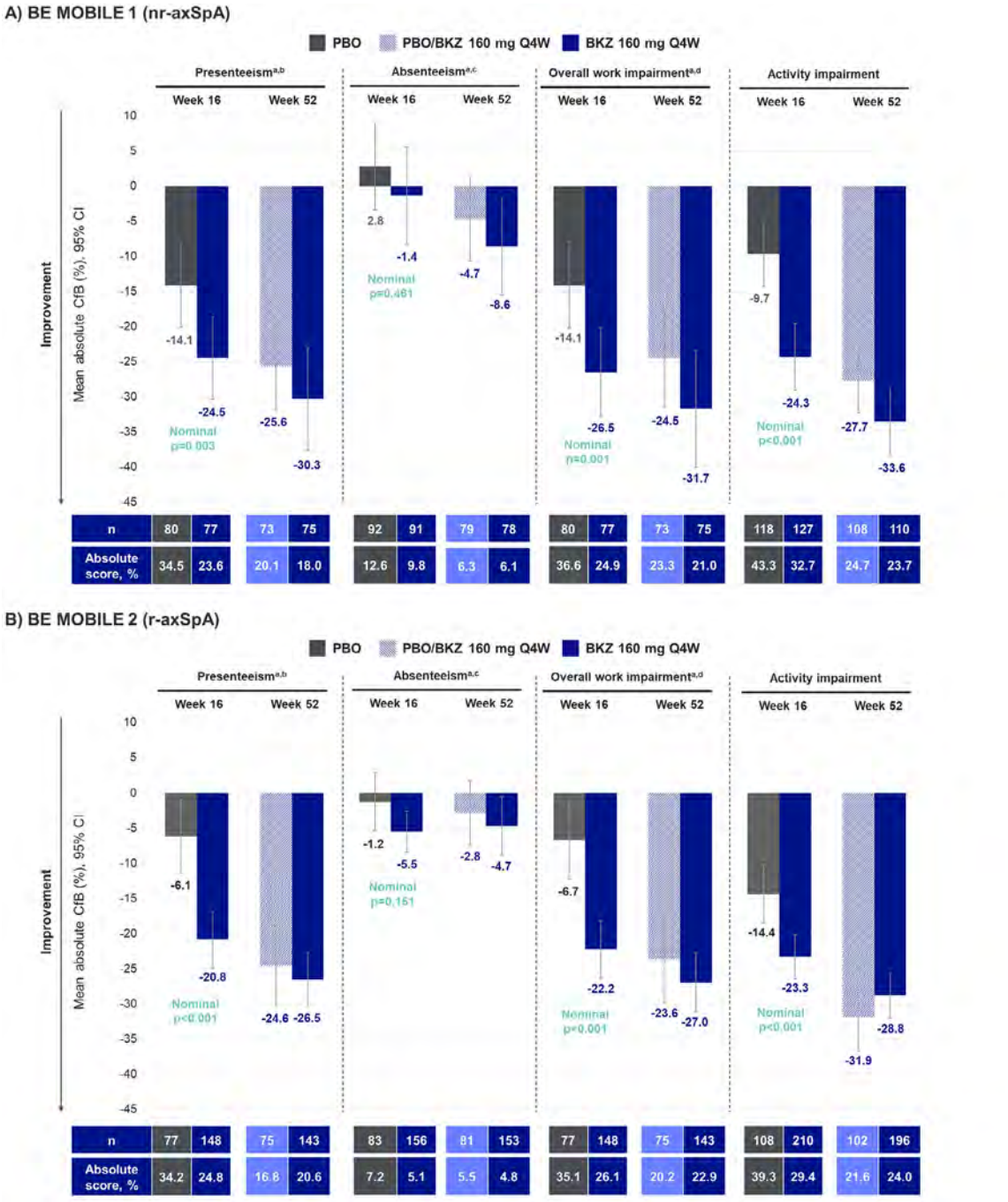
Methods: The parallel BE MOBILE 1 (NCT03928704) and 2 (NCT03928743) studies comprised a 16-wk double-blind period followed by a 36-wk maintenance period.[3] Pts were randomized to subcutaneous BKZ 160 mg every 4 wks (Q4W) or placebo (PBO). All pts received BKZ 160 mg Q4W from Wk 16. We report mean change from baseline (BL) at Wk 16 and 52 in WPAI Specific Health Problem scores,[4] which assess disease impact on pts' impairment while at paid work (i.e., presenteeism), work time missed (i.e., absenteeism, including sick leave), overall work impairment (composite of presenteeism and absenteeism) and daily activity impairment (outside paid work). Observed case data are reported.

Results: Almost 75% of pts were employed at BL (nr-axSpA BKZ: 95/128 [74.2%], PBO: 93/126 [73.8%]; r-axSpA BKZ: 161/221 [72.9%], PBO: 82/111 [73.9%]). Pts had substantial overall work impairment at BL, with presenteeism contributing most to this (**Table**).

Table. Baseline employment and WPAI-SHP item scores (OC)

	BE MOBILE 1 (nr-axSpA)		BE MOBILE 2 (r-axSpA)	
	PBO/BKZ 160 mg Q4W N=126	BKZ 160 mg Q4W N=128	PBO/BKZ 160 mg Q4W N=111	BKZ 160 mg Q4W N=221
Employment, n (%)	93 (73.8)	95 (74.2)	82 (73.9)	161 (72.9)
WPAI-SHP item score, mean % (SD)				
Presenteeism[a,b]	47.1 (20.9) (n=84)	49.2 (25.1) (n=86)	42.3 (23.4) (n=74)	46.1 (24.9) (n=149)
Absenteeism[a,c]	11.6 (26.7) (n=93)	12.8 (25.0) (n=95)	10.9 (26.9) (n=82)	11.5 (23.6) (n=161)
Overall work impairment[a,d]	49.1 (21.5) (n=84)	52.2 (26.6) (n=86)	43.9 (24.5) (n=74)	49.2 (25.6) (n=149)
Activity impairment	53.4 (21.7) (n=126)	57.3 (22.9) (n=128)	54.1 (24.2) (n=111)	53.3 (23.6) (n=221)

Randomized set. OC data reported. WPAI-SHP item scores are expressed as a percentage, with higher numbers indicating greater impairment and less productivity. [a] Absenteeism, presenteeism, and overall work impairment were assessed only in patients who were employed at baseline. [b] Impairment while at paid work due to axSpA; [c] Work time missed due to axSpA. [d] Overall work impairment is a composite of absenteeism and presenteeism. axSpA: axial spondyloarthritis; BKZ: bimekizumab; nr-axSpA: non-radiographic axSpA; OC: observed case; PBO: placebo; Q4W: every 4 weeks; r-axSpA: radiographic axSpA; SD: standard deviation; WPAI-SHP: Work Productivity and Activity Impairment Questionnaire Specific Health Problem.



Randomized set. OC data reported. Error bars represent 95% CI. WPAI-SHP item scores are expressed as a percentage, with a greater reduction indicating greater improvement. Week 16 nominal p values are calculated using ANCOVA with baseline WPAI-SHP item score as covariate and treatment, region and either MRI/CRP classification at baseline (nr-axSpA) or prior TNF inhibitor exposure (r-axSpA) as fixed effects. [a] Absenteeism, presenteeism, and overall work impairment were assessed only in patients who were employed at baseline. [b] Impairment while at paid work due to axSpA; [c] Work time missed due to axSpA. [d] Overall work impairment is a composite of absenteeism and presenteeism. ANCOVA: analysis of covariance; axSpA: axial spondyloarthritis; BKZ: bimekizumab; CfB: change from baseline; CI: confidence interval; CRP: C-reactive protein; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axSpA; OC: observed case; PBO: placebo; Q4W: every 4 weeks; r-axSpA: radiographic axSpA; TNF: tumor necrosis factor; WPAI-SHP: Work Productivity and Activity Impairment Specific Health Problem.

Figure. Mean absolute change from baseline in WPAI-SHP items at Week 16 and Week 52 (OC)

At Wk 16, mean reductions from BL (i.e., absolute improvement) were greater in BKZ- vs PBO-randomized pts for presenteeism (nr-axSpA: –24.5% vs –14.1%, nominal p=0.003; r-axSpA: –20.8% vs –6.1%, nominal p< 0.001), overall work impairment (nr-axSpA: –26.5% vs –14.1%, nominal p=0.001; r-axSpA: –22.2% vs –6.7%, nominal p< 0.001) and activity impairment (nr-axSpA: –24.3% vs –9.7%; r-axSpA: –23.3% vs –14.4%; nominal p< 0.001; **Figure**). Mean improvements in overall work impairment were sustained or further improved to Wk 52 in BKZ-randomized pts (nr-axSpA: –31.7%; r-axSpA: –27.0%); pts who switched from PBO to BKZ at Wk 16 reached similar levels of improvement to BKZ-randomized pts at Wk 52. Similar trends were seen in presenteeism and activity impairment (**Figure**).

Mean BL absenteeism scores were low compared with other WPAI items (**Table**), leaving limited room for improvement. At Wk 16, no clear separation was seen for improvements in absenteeism between BKZ-randomized pts and PBO; this response improved or was sustained in BKZ-randomized pts at Wk 52 (**Figure**). Absenteeism may also have been impacted by the COVID-19 pandemic.

Conclusion: BKZ treatment resulted in substantial improvements in overall work and activity impairment at Wk 16, with further improvements at Wk 52 in pts across the full disease spectrum of axSpA.

References:1. Strand V. J Clin Rheumatol 2017;23:383–91; **2.** Baraliakos X. Arthritis Rheumatol 2022;74(suppl 9); **3.** Boel A. Ann Rheum Dis 2019;78:1545–9; **4.** Hoepken B. Qual Life Res. 2021;30:945–54.

Disclosure: M. Rudwaleit: AbbVie, 2, 6, Boehringer Ingelheim, 6, Chugai, 6, Eli Lilly, 2, 6, Janssen, 6, Novartis, 2, 6, Pfizer, 6, UCB Pharma, 2, 6; **V. Navarro-Compán**: AbbVie, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, Janssen, 6, MoonLake, 2, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6; **A. Deodhar**: AbbVie, 2, 5, Amgen, 2, Aurinia, 2, Bristol Myers Squibb, 2, 5, Celgene, 5, Eli Lilly, 2, 5, Janssen, 2, 6, MoonLake, 2, 5, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5; **M. Dubreuil**: Amgen, 2, Pfizer, 5, UCB Pharma, 2; **M. Mørup**: UCB Pharma, 3; **V. Taieb**: UCB Pharma, 3, 11; **C. de la Loge**: UCB Pharma, 2; **C. Fleurinck**: UCB Pharma, 3; **U. Massow**: UCB Pharma, 3; **T. Vaux**: UCB Pharma, 3; **A. Boonen**: AbbVie, 2, 5, 6, Galapagos, 2, 6, Novartis, 2, 6, Pfizer, 5, 6, UCB Pharma, 2, 6.

Abstract Number: 0522

Effect of Secukinumab versus Adalimumab Biosimilar on Radiographic Progression in Patients with Radiographic Axial Spondyloarthritis: Results from Subgroup Analyses by Baseline Syndesmophytes and C-reactive Protein Status

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: SURPASS, a phase 3b randomized controlled study in patients with radiographic axial spondyloarthritis (r-axSpA), found low spinal radiographic progression over 2 years with no significant difference between the secukinumab (SEC) and adalimumab biosimilar (SDZ- ADL) treatment arms.[1,2] Baseline (BSL) radiographic damage (presence of syndesmophytes) and elevated C-reactive protein (CRP) levels have been identified as predictors of radiographic progression in r-axSpA.[3] This study evaluated the effect of SEC and SDZ-ADL on spinal radiographic progression in subgroups of patients based on the presence of syndesmophytes and elevated high-sensitivity CRP (hsCRP) levels at BSL, from the SURPASS study.

Methods: Biologic-naïve patients with active r-axSpA and with hsCRP ≥5 mg/L and/or ≥1 syndesmophyte(s) on spinal radiographs were randomized (1:1:1) to SEC (150 or 300 mg; dose-blinded) or SDZ-ADL (40 mg; open label). Patients were categorized into the following subgroups at BSL: hsCRP ≥5 mg/L (CRP+), hsCRP < 5 mg/L (CRP–), presence of syndesmophyte(s) (Synd+), absence of syndesmophyte(s) (Synd–), and CRP+Synd+. The proportion of patients with no radiographic progression (change from BSL in modified Stoke Ankylosing Spondylitis Spinal Score [mSASSS] ≤0.5), mean change from BSL in mSASSS, and proportion of patients with no new syndesmophytes(s) in each subgroup at week 104 (all as observed) are reported.

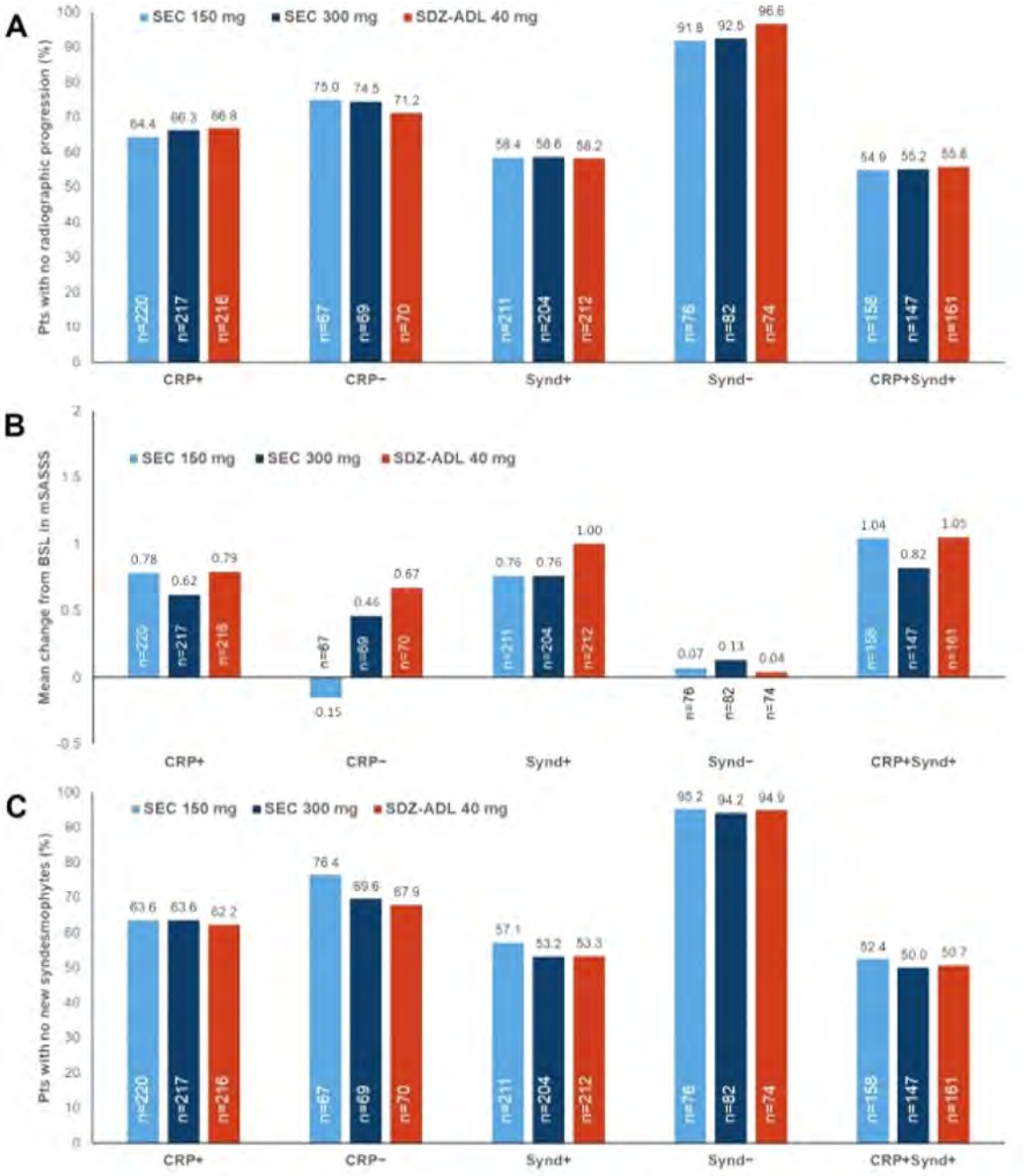
Results: Of the 859 patients, 653 (76%) were CRP+, 627 (73%) were Synd+, and 466 (54%) were CRP+Synd+ at BSL. Demographic and BSL disease characteristics were largely balanced across subgroups and treatment arms, except for the Synd– group in which mean age, proportion of male patients, and mean time since diagnosis were lower than in other subgroups (**Table 1**). All radiographic outcomes at week 104 were similar across treatment arms; however, differences were observed between subgroups irrespective of the treatment arm. The Synd– subgroup followed by the CRP– subgroup showed the least progression in all radiographic outcomes (as indicated by the higher proportion of patients with no radiographic progression and no new syndesmophytes, and lower mean change from BSL in mSASSS), across treatment arms (**Figure 1**). The CRP+Synd+ subgroup followed by the Synd+ subgroup and the CRP+ subgroup had higher radiographic progression compared with the Synd– and CRP– subgroups (**Figure 1**).

Conclusion: Spinal radiographic progression over 2 years was low with no notable difference between SEC and SDZ-ADL arms regardless of the presence or absence of specific predictive factors for progression (syndesmophytes/elevated CRP). Expectedly, patients from subgroups without predictive factors (especially Synd–, followed by CRP–) had lowest rates of radiographic progression. The presence of syndesmophytes is a stronger predictor than the presence of an elevated CRP.

Table 1. Demographic and baseline disease characteristics by subgroup

Characteristics, mean values unless specified otherwise	CRP+ N=653	CRP− N=206	Synd+ N=627	Synd− N=232	CRP+Synd+ N=466
Age (years)	40.7	46.4	45.0	34.2	43.4
Male, %	80.1	73.3	82.1	68.5	84.3
BMI (kg/m²)	27.3	27.2	27.6	26.4	27.6
Time since first diagnosis of r-axSpA (years)	6.3	8.0	7.6	4.3	7.2
mSASSS	16.2	17.8	22.5	0.1	22.5
Number of syndesmophytes	6.8	7.6	9.6	0.0	9.5
BASDAI	7.2	6.9	7.1	7.2	7.2
hsCRP (mg/L)	26.1	2.6	19.9	22.0	25.8
HLA-B27 positive, %	82.4	77.7	81.2	81.5	82.0

CRP+, hsCRP ≥5 mg/L; CRP−, hsCRP <5 mg/L; Synd+, presence of syndesmophyte(s); Synd−, absence of syndesmophyte(s)
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index; HLA-B27, human leukocyte antigen B27; hsCRP, high-sensitivity C-reactive protein; mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score; r-axSpA, radiographic axial spondyloarthritis



BSL, baseline; mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score; Pts, patients; SDZ-ADL, adalimumab biosimilar; SEC, secukinumab
A patient was considered to have a syndesmophyte if at least one reader assessed mSASSS score of ≥2 for any individual vertebral corner

Figure 1. Radiographic outcomes at week 104 by subgroup: A) Patients with no radiographic progression (change in mSASSS ≤0.5), B) Mean change from BSL in mSASSS, C) Patients with no new syndesmophytes

References:

1. Baraliakos X, et al. *Clin Drug Investig*. 2020;40(3):269-78
2. Baraliakos X, et al. *Arthritis Rheumatol*. 2022;74 (suppl 9)
3. Poddubnyy D, et al. *Arthritis Rheum*. 2012;64(5):1388-98

Disclosure: X. Baraliakos: AbbVie, 2, 6, BMS, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, 6, UCB, 2, 6; **D. van der Heijde**: AbbVie, 2, Bayer, 2, BMS, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GSK, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; **P. Machado**: AbbVie/Abbott, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Orphazyme, 2, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 6; **V. Navarro-Compán**: AbbVie, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, Janssen, 6, MoonLake, 2, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6; **L. Gensler**: AbbVie, 2, Acelyrin, 2, Eli Lilly, 2, Fresenius Kabi, 2, Janssen, 2, Novartis, 2, 5, Pfizer, 2, UCB Pharma, 2, 5; **P. Pertel**: Bayer Consumer Health, 3, Novartis, 3; **E. Quebe-Fehling**: Novartis, 3, 11; **A. Readie**: Novartis, 3, 11; **H. Richards**: Novartis, 3, 11; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, MoonLake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 2, UCB Pharma, 2, 6.

Abstract Number: 0523

Bimekizumab Maintained Stringent Clinical Responses Through Week 52 in Patients with Axial Spondyloarthritis: Results from Two Phase 3 Studies

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

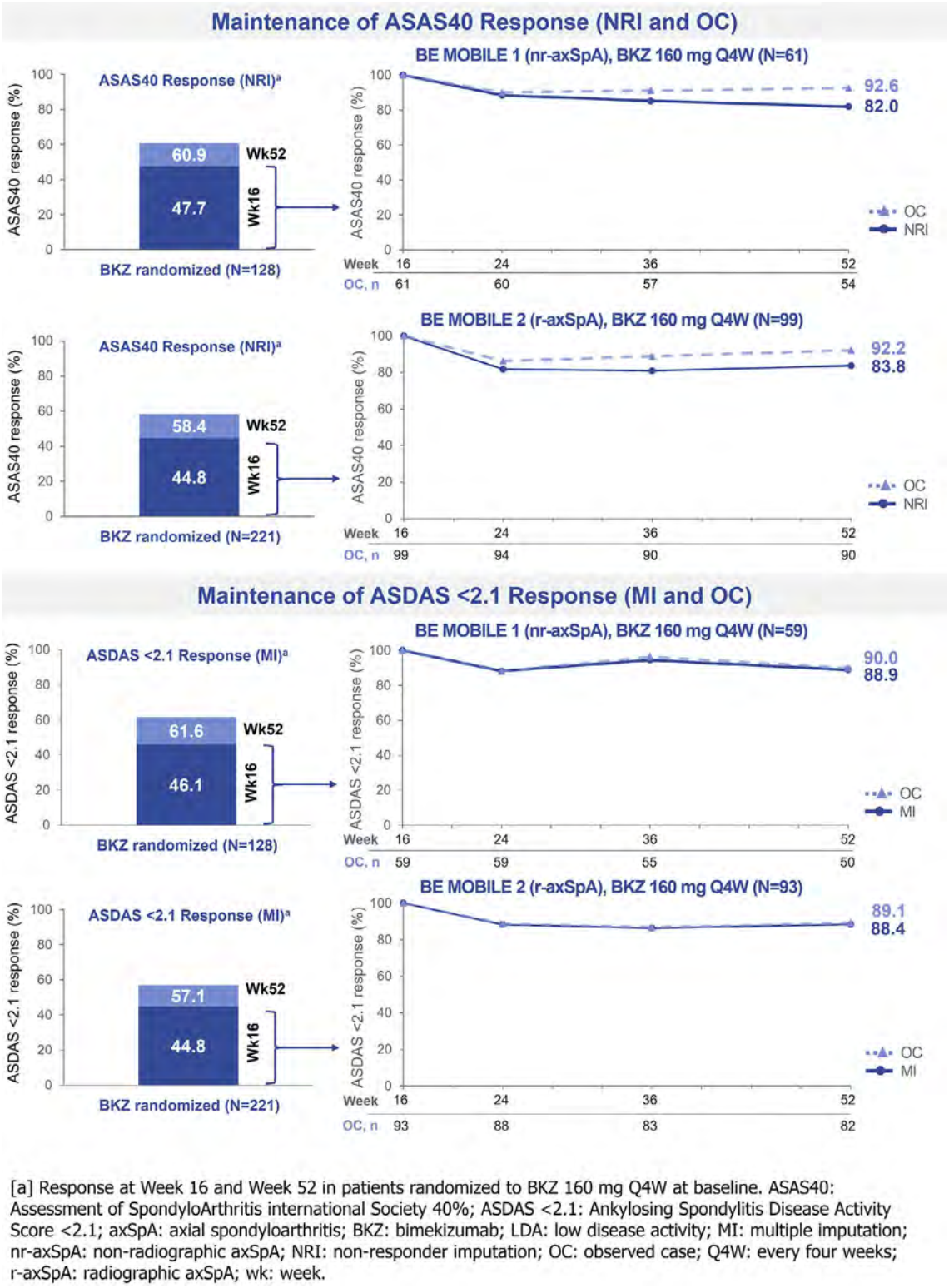
Background/Purpose: Axial spondyloarthritis (axSpA) is a chronic rheumatic disease which requires optimal management and disease control. Patients (pts) can experience loss of response in the long term and maintenance of response is an internationally recommended treatment target.[1]

Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A, has demonstrated sustained clinical efficacy to Week (Wk) 52 in pts across the full disease spectrum of axSpA in the phase 3 studies BE MOBILE 1 and 2.[2]

Here, we report the maintenance of stringent clinical responses through 1 year of treatment with BKZ in pts with non-radiographic axSpA (nr-axSpA) and radiographic-axSpA (r-axSpA, i.e., AS).[3]

Methods: In BE MOBILE 1 (NCT03928704; nr-axSpA; pts met ASAS criteria for axSpA) and BE MOBILE 2 (NCT03928743; r-axSpA; pts fulfilled ASAS and modified New York criteria for r-axSpA), pts were randomized to receive subcutaneous BKZ 160mg every 4 wks (Q4W) or placebo (PBO) to Wk 16. From Wks 16–52, all pts received BKZ 160mg Q4W.[4,5]

Assessment of SpondyloArthritis international Society ≥40% improvement (ASAS40) and Ankylosing Spondylitis Disease Activity Score (ASDAS) < 2.1 (low disease activity [LDA]) or < 1.3 (inactive disease [ID]) responses to Wk 52 were assessed among BKZ-randomized pts who responded at Wk 16. Non-responder imputation (NRI), and multiple imputation (MI) were



[a] Response at Week 16 and Week 52 in patients randomized to BKZ 160 mg Q4W at baseline. ASAS40: Assessment of SpondyloArthritis international Society 40%; ASDAS <2.1: Ankylosing Spondylitis Disease Activity Score <2.1; axSpA: axial spondyloarthritis; BKZ: bimekizumab; LDA: low disease activity; MI: multiple imputation; nr-axSpA: non-radiographic axSpA; NRI: non-responder imputation; OC: observed case; Q4W: every four weeks; r-axSpA: radiographic axSpA; wk: week.

Figure. Maintenance of ASAS40 and ASDAS LDA (ASDAS <2.1) through 52 weeks of BKZ 160 mg Q4W among Week 16 ASAS40 and ASDAS LDA responders, respectively, from BE MOBILE 1 and 2

used for missing ASAS40 and ASDAS data, respectively. Observed case (OC) data and Wk 16 and Wk 52 responder rates for all BKZ-randomized pts (NRI or MI) are also reported.

The number of treatment-emergent adverse events (TEAEs) to Wk 52 are reported for pts who received ≥1 dose of BKZ.

Results: A total of 128 and 221 pts were randomized to BKZ 160mg Q4W in BE MOBILE 1 and 2, respectively. At Wk 16, 47.7% and 44.8% of these pts achieved the primary endpoint, ASAS40, and this increased to 60.9% and 58.4% at Wk 52 (NRI, **Figure**). Of pts that achieved ASAS40 at Wk 16, 82.0% and 83.8% maintained this response at Wk 52 (NRI, **Figure**).

ASDAS LDA was achieved by 46.1% and 44.8% of BKZ-randomized pts at Wk 16 of BE MOBILE 1 and 2, respectively; this increased to 61.6% and 57.1% at Wk 52 (MI, **Figure**). Of pts that achieved ASDAS LDA at Wk 16, 88.9% and 88.4% maintained this response at Wk 52 (MI, **Figure**).

At Wk 16 of BE MOBILE 1 and 2, ASDAS ID was achieved by 18.8% and 16.4% of BKZ-randomized pts, respectively; and this increased to 25.2% and 23.4% at Wk 52 (MI). Among Wk 16 ASDAS ID responders, ASDAS ID was maintained by 79.2% and 75.1% at Wk 24, 85.3% and 71.7% at Wk 36, and 88.0% and 58.7% at Wk 52 (MI).

To Wk 52 of BE MOBILE 1 and 2, 183/244 (75.0%) and 249/330 (75.5%) pts reported ≥1 TEAE whilst receiving BKZ, respectively; 9 (3.7%) and 20 (6.1%) reported serious TEAEs.

Conclusion: Dual inhibition of IL-17F and IL-17A with BKZ provided robust maintenance of stringent clinical responses from Wk 16 to Wk 52 across the full disease spectrum of axSpA.

References:1. Smolen J. Ann Rheum Dis 2018;77:3–17; **2.** Baraliakos X. Arthritis Rheumatol 2022;74 (suppl 9); **3.** Boel A. Ann Rheum Dis 2019;78:1545–9; **4.** Deodhar A. Ann Rheum Dis 2022;81:772–3; **5.** van der Heijde D. Ann Rheum Dis 2022;81:12–3.

Disclosure: F. Proft: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celgene, 2, 6, Eli Lilly, 5, Hexal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 6, UCB Pharma, 2, 5, 6; **D. van der Heijde**: AbbVie, 2, Bayer, 2, BMS, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GSK, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; **X. Baraliakos**: AbbVie, 2, 6, BMS, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, 6, UCB, 2, 6; **J. Ermann**: AbbVie, 2, 5, Boehringer Ingelheim, 5, Janssen, 2, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, UCB Pharma, 2; **C. Fleurinck**: UCB Pharma, 3; **U. Massow**: UCB Pharma, 3; **N. De Peyrecave**: UCB Pharma, 3; **V. Taieb**: UCB Pharma, 3, 11; **A. van Tubergen**: MSD, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, UCB Pharma, 2, 5; **V. Navarro-Compán**: AbbVie, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, Janssen, 6, MoonLake, 2, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6.

Abstract Number: 0524

Efficacy of Certolizumab Pegol in Preventing Anterior Uveitis Flares Compared with Standard Non-Biologic Treatment: A Matched Control Study in High-Risk Patients with Axial Spondyloarthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Acute anterior uveitis (AAU) is the most common extra-musculoskeletal manifestation in axial spondyloarthritis (axSpA), affecting more than a third of patients. However, long-term interventional placebo-controlled studies are lacking due to ethical challenges. This study aimed to evaluate anterior uveitis flares rate in patients with axSpA who are at high risk of recurrent uveitis when treated with the PEGylated Fc-free TNF inhibitor certolizumab pegol (CZP) compared with standard non-biologic care.

Methods: In the C-VIEW study (NCT03020992), CZP was administered to patients with a high risk of uveitis flares (i.e., those with active axSpA, human leukocyte antigen-B27 [HLA-B27] positivity, and a history of recurrent AAU [≥2 AAU flares in total; ≥1 in the year prior to baseline]). This was an open-label, multicenter study where patients received CZP for 96 weeks; data up to Week 48 were used in the present analysis. The number of AAU flares in C-VIEW were compared to those seen in matched high-risk patients with non-biologic standard care from two North American axSpA centers who were followed up for 48 weeks. Inverse probability weighting (IPW) was performed to adjust for potential confounders, followed by Poisson regression, adjusted for follow-up time, to test the effect of treatment with CZP.

Results: A total of 89 patients received CZP and completed the C-VIEW study, while 66 bio-naïve patients (40 from the University of California, San Francisco and 26 from the University of Toronto) qualified as comparator with no exposure to biologic therapy during the 48-week follow-up period. All patients were HLA-B27 positive and had at least one episode of AAU before the baseline visit. Symptom duration and baseline CRP levels were similar in the two groups. Following IPW, there were no statistically significant differences in mean BASDAI and distribution of ASDAS disease activity states at baseline between the CZP treatment and comparator groups. Conventional synthetic DMARD use was similar between groups at baseline and during follow-up. The mean number of AAU flares (mean ± standard deviation) was significantly lower ($p < 0.001$) with CZP (0.42±0.81) than in the matched comparator population (1.3±1.47). In the final model after IPW, there was an 87% reduction in AAU flares ($p \leq 0.001$) associated with CZP treatment (**Table**).

Table. Results of the final model after IPW

	AAU flares, mean (SD)	p value	RR	95% CI	Bootstrap 95% CI
CZP (n=89)	0.42 (0.81)	–	–	–	–
Comparator (n=66)	1.3 (1.47)	**<0.001**	0.13	(0.08, 0.24)	(0.05, 0.33)

IPW was performed to adjust for potential confounders, followed by Poisson regression, adjusted for follow-up time. All patients were HLA-B27 positive and had a history of uveitis with at least one episode in the preceding year. AAU: acute anterior uveitis; CI: confidence interval; CZP: certolizumab pegol; IPW: Inverse probability weighting; RR: relative risk ratio; SD: standard deviation; SE: standard error.

Conclusion: This matched control study supports the benefit of CZP over standard non-biologic treatment in reducing anterior uveitis flares among high-risk patients with axSpA, highlighting its potential as a promising therapeutic option in managing this debilitating ocular manifestation in axSpA.

Disclosure: N. Haroon: AbbVie, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, UCB Pharma, 2; **Z. Baskurt**: None; **T. Chim**: None; **R. Inman**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Sandoz, 2; **D. Paez**: None; **T. Kumke**: UCB Pharma, 3, 11; **R. Tham**: UCB Pharma, 2, 3; **M. Kim**: UCB Pharma, 3, 11; **I. van der Horst-Bruinsma**: AbbVie, 2, 5, 12, Fees for lectures, BMS, 12, Fees for lectures, Eli Lilly, 2, MSD, 2, 5, 12, Fees for lectures, Novartis, 2, Pfizer, 5, UCB Pharma, 2, 5; **L. Gensler**: AbbVie, 2, Acelyrin, 2, Eli Lilly, 2, Fresenius Kabi, 2, Janssen, 2, Novartis, 2, 5, Pfizer, 2, UCB Pharma, 2, 5.

Abstract Number: 0525

Bimekizumab Achieved Sustained Improvements in Efficacy Outcomes in Patients with Axial Spondyloarthritis, Regardless of Prior TNF Inhibitor Treatment: Week 52 Pooled Results from Two Phase 3 Studies

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

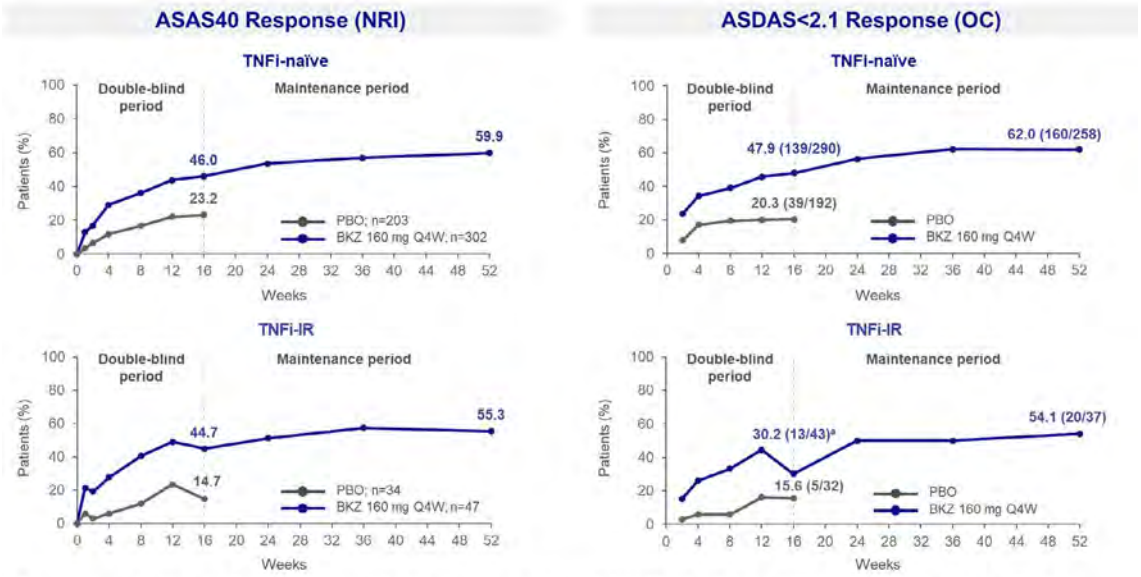
Background/Purpose: In patients (pts) with axial spondyloarthritis (axSpA), tumor necrosis factor inhibitors (TNFi) are the usual first line biologic treatment, yet many pts may experience loss of response over time, and some are intolerant to TNFis.[1] Typically, response to second line biologics is limited in TNFi-inadequate responders (IR).

Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A. In the phase 3 BE MOBILE 1 and 2 studies, BKZ treatment resulted in rapid and sustained improvements in efficacy outcomes through 52 weeks (wks) in pts with active non-radiographic (nr-)axSpA and radiographic (r-)axSpA (i.e., AS).[2,3] In studies of BKZ in psoriatic arthritis, similar efficacy between TNFi-naïve and TNFi-IR pts were observed.[4] Here, we report the efficacy of BKZ in TNFi-naïve or -IR pts with active nr-axSpA and r-axSpA through Wk 52 across multiple key endpoints.

Methods: In BE MOBILE 1 (nr-axSpA; NCT03928704) pts met Assessment of SpondyloArthritis international Society (ASAS) classification criteria and in BE MOBILE 2 (r-axSpA; NCT03928743) pts fulfilled modified New York and ASAS criteria. Pts were randomized to receive subcutaneous BKZ 160 mg every 4 wks (Q4W) or placebo (PBO) then BKZ 160 mg Q4W from Wk 16. This post hoc analysis reports pooled mean efficacy data, including disease activity, MRI inflammation,

physical function, and quality of life (QoL), through Wk 52 of BE MOBILE 1 and 2, stratified by TNFi status (naïve/IR). TNFi-IR pts are defined as those who experienced loss of efficacy, contraindication or intolerance to prior TNFi treatment.

Results: This pooled analysis included 505 TNFi-naïve and 81 TNFi-IR pts. 302/505 (59.8%) TNFi-naïve and 47/81 (58.0%) TNFi-IR pts were randomized to BKZ.



Data are pooled from BE MOBILE 1 and 2. Data reported using OC (ASDAS <2.1) or NRI (ASAS40). Data from PBO-randomized patients not included from Wk 16 onwards. [a] 7 patients were identified as being responders at Week 12 and non-responders at Week 16; all were male and 6 were patients with r-axSpA. Of these participants, 6 became responders again at Week 24. All ASDAS differences in these patients between Week 12 and Week 16 were less than 1. ASAS40: Assessment of SpondyloArthritis international Society 40 response; ASDAS<2.1: Ankylosing Spondylitis Disease Activity Score <2.1; BKZ: bimekizumab; IR: inadequate responder; LDA: low disease activity; NRI: non-responder imputation; OC: observed case; PBO: placebo; Q4W: every four weeks; TNFi: tumor necrosis factor inhibitor.

Figure. Achievement of ASAS40 and ASDAS<2.1 (LDA) over 52 weeks in TNFi-IR and TNFi-naïve patients, pooled across BE MOBILE 1 and 2

Table. Pooled efficacy endpoints across BE MOBILE 1 and 2 in TNFi-naïve and -IR patients

	Week 16				Week 52	
	BE MOBILE 1 and 2 TNFi-naïve		BE MOBILE 1 and 2 TNFi-IR		BE MOBILE 1 and 2 TNFi-naïve	BE MOBILE 1 and 2 TNFi-IR
	PBO N=203	BKZ 160 mg Q4W N=302	PBO N=34	BKZ 160 mg Q4W N=47	BKZ 160 mg Q4W N=302	BKZ 160 mg Q4W N=47
ASDAS-CRP CfB [MI] mean (SE)	−0.7 (0.1)	−1.5 (0.1)	−0.6 (0.1)	−1.6 (0.1)	−1.8 (0.1)	−1.9 (0.2)
BASDAI CfB [MI] mean (SE)	−1.7 (0.1)	−3.0 (0.1)	−1.6 (0.4)	−2.7 (0.3)	−3.6 (0.1)	−3.7 (0.3)
SPARCC MRI SIJ CfB [OC][a] mean (SD)	−0.9 (7.3)[b]	−5.3 (8.4)[c]	1.4 (6.0)[d]	−5.6 (13.4)[e]	−5.9 (9.1)[f]	−6.9 (12.2)[e]
Berlin MRI Spine CfB [OC][a] mean (SD)	−0.2 (1.5)[g]	−1.4 (3.2)[h]	0.4 (1.3)[i]	−0.5 (1.9)[e]	−1.7 (3.6)[j]	−1.2 (2.1)[e]
BASFI CfB [MI] mean (SE)	−1.1 (0.1)	−2.3 (0.1)	−0.5 (0.3)	−2.2 (0.3)	−2.8 (0.1)	−2.9 (0.3)
Nocturnal spinal pain CfB [MI] mean (SE)	−1.7 (0.2)	−3.4 (0.2)	−2.1 (0.5)	−3.3 (0.3)	−4.1 (0.2)	−3.9 (0.3)
ASQoL CfB [MI] mean (SE)	−2.8 (0.3)	−5.1 (0.3)	−2.4 (0.6)	−4.2 (0.6)	−5.8 (0.3)	−4.7 (0.6)

Data are pooled from BE MOBILE 1 and 2. Data reported using OC or MI. Data from PBO-randomized patients not included from Wk 16 onwards. [a] Only patients enrolled in the SIJ and spine MRI substudy and with ≥1 post-baseline record for the respective variable are included; [b] n=95; [c] n=144; [d] n=13; [e] n=15; [f] n=130; [g] n=94; [h] n=140; [i] n=12; [j] n=127. ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score C-reactive protein; ASQoL: Ankylosing Spondylitis Quality of Life; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BKZ: bimekizumab; CfB: change from baseline; IR: inadequate responders; MI: multiple imputation; MRI: magnetic resonance imaging; OC: observed case; PBO: placebo; Q4W: every four weeks; SD: standard deviation; SE: standard error; SIJ: sacroiliac joints; SPARCC: Spondylarthritis Research Consortium of Canada; TNFi: tumor necrosis factor inhibitor.

At Wk 16, the proportion of pts achieving ASAS40 and AS Disease Activity Score (ASDAS)< 2.1 (low disease activity) were higher in BKZ-randomized TNFi-naïve/-IR pts vs PBO. In both TNFi-naïve/-IR continuous BKZ-treated pts, responses were similar and increased to Wk 52 (**Figure**). Similar substantial reductions from baseline in ASDAS-CRP and MRI inflammation by Wk 16 were also achieved with BKZ vs PBO in both TNFi-naïve and IR pts; in continuous BKZ-treated pts this was sustained or further improved through 52 wks. Comparable improvements in physical function, nocturnal spinal pain and ASQoL were observed through 52 wks with BKZ in TNFi-naïve/-IR pts(**Table**).

Conclusion: Across the full disease spectrum of axSpA, BKZ treatment resulted in clinically relevant improvements in key efficacy outcomes vs PBO, including suppression of inflammation and improvements in physical function and QoL, regardless of prior TNFi exposure. The improvements with BKZ at Wk 16 were sustained to Wk 52. **References:1.** Noureldin B. Rheumatology (Oxford). 2018;57(suppl 6); **2.** Boel A. Ann Rheum Dis. 2019;78:1545–9; **3.**Baraliakos X. Arthritis Rheumatol. 2022;74 (suppl 9); **4.** Mease P. Arthritis Rheumatol. 2022;74 (suppl 9).

Disclosure: M. Magrey: AbbVie, 2, Bristol Myers Squibb, 2, Eli Lilly, 2, Novartis, 2, Pfizer Inc, 2, UCB, 5; **M. van de Sande**: AbbVie, 2, Eli Lilly, 5, Janssen, 6, Novartis, 2, 5, 6, UCB Pharma, 2, 5, 6; **M. Breban**: MSD, 5, Novartis, 2, UCB Pharma, 2; **F. Van den Bosch**: AbbVie, 2, 6, Amgen, 2, BMS, 6, Celgene, 6, Eli Lilly, 2, Galapagos, 2, Janssen, 2, 6, Merck, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB Pharma, 2, 6; **C. Fleurinck**: UCB Pharma, 3; **U. Massow**: UCB Pharma, 3; **N. De Peyrecave**: UCB Pharma, 3; **T. Vaux**: UCB Pharma, 3; **X. Baraliakos**: AbbVie, 2, 6, BMS, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, 6, UCB, 2, 6; **H. Marzo-Ortega**: AbbVie, 2, 6, Biogen, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 5, 6, MoonLake, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Takeda, 2, 6, UCB Pharma, 2, 5, 6.

Abstract Number: 0526

Bimekizumab Improved Physical Function and Health-Related Quality of Life in Patients with Axial Spondyloarthritis: 52-Week Results from Two Phase 3 Studies

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

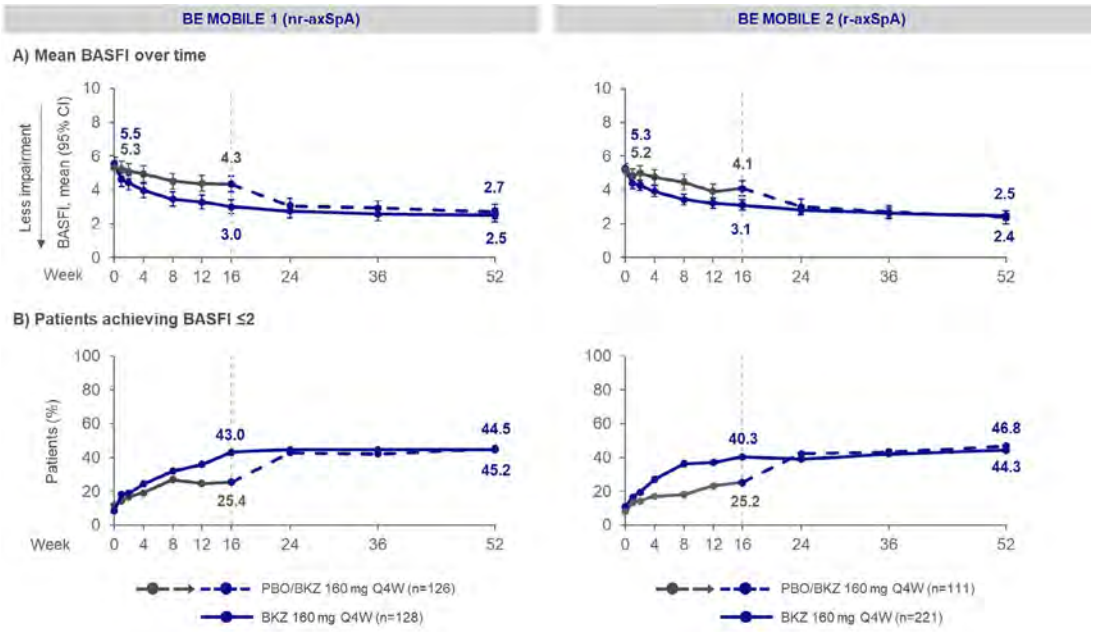
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

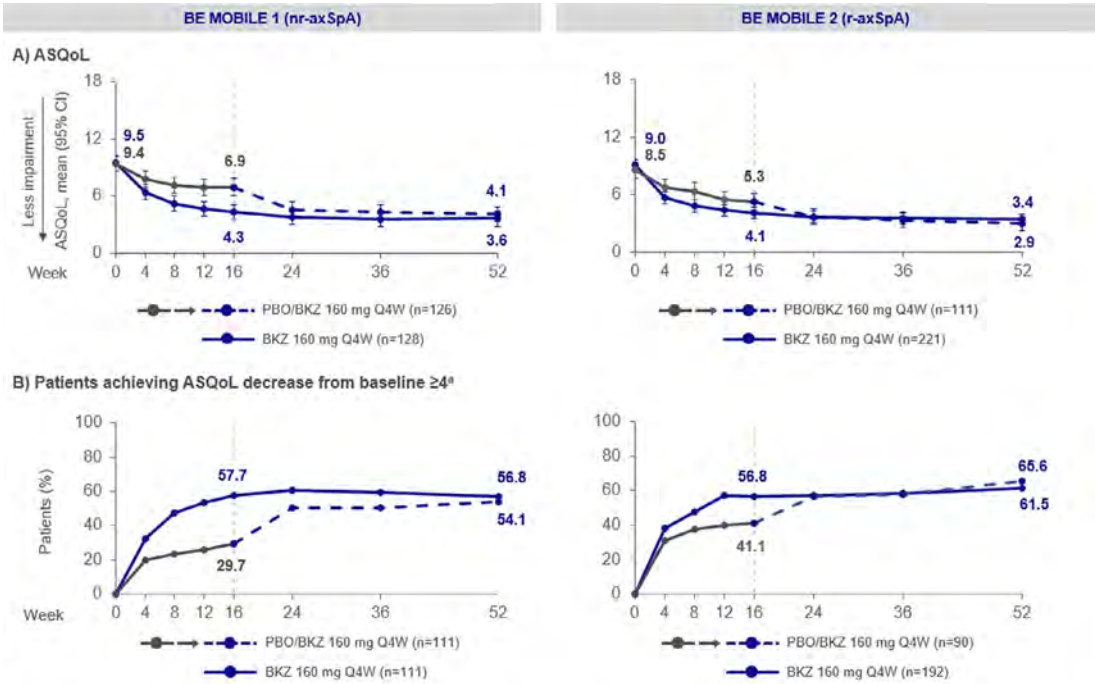
Background/Purpose: Axial spondyloarthritis (axSpA) severely impairs physical function and health-related quality of life (HRQoL).[1] Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A, met all primary and ranked secondary endpoints at Week (Wk) 16 in patients (pts) with axSpA in the phase 3 studies BE MOBILE 1 and 2; efficacy was sustained to Wk 52.[2]

Here, we assess the impact of BKZ on physical function and HRQoL in pts with axSpA to Wk 52.



Randomized set. Mean BASFI reported with MI and proportion of patients achieving BASFI ≤2 with NRI. Error bars represent 95% CI. BASFI scores range from 0–10 with a higher score reflecting greater impact on physical function. BASFI: Bath Ankylosing Spondylitis Functional Index; BKZ: bimekizumab; CI: confidence interval; HRQoL: health-related quality of life; MI: multiple imputation; nr-axSpA: non-radiographic axial spondyloarthritis; NRI: non-responder imputation; PBO: placebo; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis.

Figure 1. (A) Mean BASFI (MI) and (B) proportion of patients achieving BASFI score ≤2 (NRI) to 52 weeks



Randomized set. Mean ASQoL reported with MI and proportion of patients achieving ASQoL improvement ≥4 with NRI. ASQoL scores range from 0–18 with a higher score reflecting greater impact on HRQoL. [a] Reported for patients with baseline ASQoL score ≥4. ASQoL: Ankylosing Spondylitis Quality of Life Questionnaire; BKZ: bimekizumab; HRQoL: health-related quality of life; MI: multiple imputation; nr-axSpA: non-radiographic axial spondyloarthritis; NRI: non-responder imputation; PBO: placebo; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis.

Figure 2. (A) Mean ASQoL (MI) and (B) ASQoL improvement of ≥4 points (NRI) from baseline to Week 52

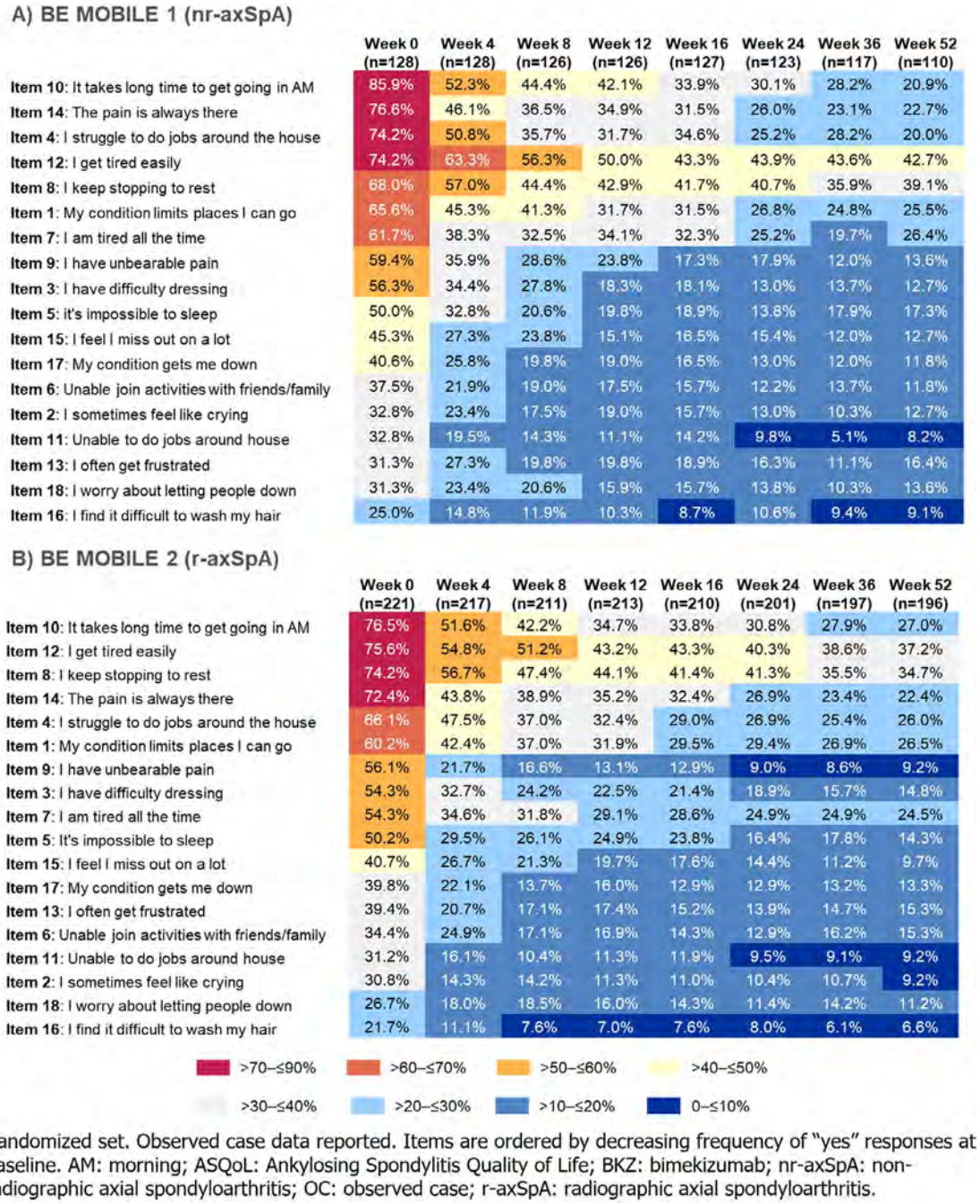


Figure 3. Proportion of BKZ-randomized patients providing "yes" responses to individual ASQoL items (OC)

Methods: BE MOBILE 1 (NCT03928704; non-radiographic [nr-] axSpA) and 2 (NCT03928743; radiographic [r-] axSpA; i.e., AS)[3] were randomized, placebo (PBO)-controlled trials comprising a 16-wk double-blind period followed by a 36-wk maintenance period. Pts were randomized to subcutaneous BKZ 160 mg every 4 wks (Q4W) or PBO; from Wk 16 PBO-randomized pts switched to BKZ 160 mg Q4W (PBO/BKZ). Physical function was assessed by BASFI (0–10) and HRQoL by AS quality of life questionnaire (ASQoL; 0–18).

We report mean BASFI and ASQoL scores to Wk 52 with multiple imputation (MI), and proportion of pts achieving low BASFI score (≤2) and clinically relevant ASQoL improvement (≥4-point reduction from baseline [BL])[4] with non-responder imputation. Proportion of BKZ-randomized pts impacted by each ASQoL item (i.e., responded "yes") to Wk 52 is reported as observed.

Results: 254 pts with nr-axSpA (BKZ: 128; PBO: 126) and 332 with r-axSpA (BKZ: 221; PBO: 111) were randomized. Mean BL BASFI and ASQoL indicated impaired physical function and HRQoL (**Figure 1A, 2A**).

At Wk 16, significantly greater reductions from BL (i.e., improvement) in BASFI and ASQoL were observed in BKZ-treated pts vs PBO ($p< 0.001$; reference-based MI). Mean scores remained low or decreased at Wk 52 in both BKZ-randomized vs PBO/BKZ pts for BASFI (nr-axSpA: 2.5 vs 2.7; r-axSpA: 2.5 vs 2.4) and ASQoL (3.6 vs 4.1; 3.4 vs 2.9; **Figure 1A, 2A**).

A higher proportion of BKZ- vs PBO-treated pts achieved BASFI ≤2 and ≥4 ASQoL reduction from BL at Wk 16; these proportions were sustained or improved to Wk 52, and were similar among BKZ-randomized vs PBO/BKZ pts for BASFI ≤2 (nr-axSpA: 44.5% vs 45.2%; r-axSpA: 44.3% vs 46.8%) and ≥4 ASQoL reduction from BL (56.8% vs 54.1%; 61.5% vs 65.6%; **Figure 1B, 2B**).

ASQoL items impacting ≥66% of BKZ-randomized pts with nr-axSpA and r-axSpA at BL were items 10 (it takes a long time to get going in the morning; 85.9% and 76.5%), 14 (pain is always there; 76.6% and 72.4%), 12 (I get tired easily; 74.2% and 75.6%), 4 (I struggle to do jobs around the house; 74.2% and 66.1%), and 8 (I keep stopping to rest; 68.0% and 74.2%). Reductions from BL were seen in the proportion of pts responding "yes" to each ASQoL item through 52 wks of BKZ treatment; the greatest reductions at Wk 52 were in items 10 (nr-axSpA: –65.0%; r-axSpA: –49.5%) and 14 (–53.9%; –50.0%; **Figure 3**).

Conclusion: BKZ resulted in high proportions of pts achieving improvements in physical function and HRQoL through 52 wks of treatment across the full disease spectrum of axSpA.

References:1. Strand V. J Clin Rheumatol 2017;23:383–91; **2.** Baraliakos X. Arthritis Rheumatol 2022;74(suppl 9); **3.** Boel A. Ann Rheum Dis 2019;78:1545–9; **4.** Hoepken B. Qual Life Res. 2021;30:945–54.

Disclosure: M. Dubreuil: Amgen, 2, Pfizer, 5, UCB Pharma, 2; **K. Gaffney**: AbbVie, 2, 5, 6, Eli Lilly, 2, 5, 6, Gilead, 5, Novartis, 2, 5, 6, UCB Pharma, 2, 5, 6; **J. Kay**: Alvotech Swiss AG, 2, Boehringer Ingelheim, 2, Gilead, 5, Novartis, 5, Organon, 2, Ridgeline Discovery, 2, Samsung Bioepis, 2, Sandoz, 2, Scipher Medicine, 2, UCB Pharma, 2; **V. Navarro-Compán**: AbbVie, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, Janssen, 6, MoonLake, 2, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6; **C. de la Loge**: UCB Pharma, 2; **A. Ellis**: UCB Pharma, 3; **C. Fleurinck**: UCB Pharma, 3; **U. Massow**: UCB Pharma, 3; **V. Taieb**: UCB Pharma, 3, 11; **A. Deodhar**: AbbVie, 2, 5, Amgen, 2, Aurinia, 2, Bristol Myers Squibb, 2, 5, Celgene, 5, Eli Lilly, 2, 5, Janssen, 2, 6, MoonLake, 2, 5, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5.

Abstract Number: 0527

Bimekizumab Treatment Impact on Pain and Fatigue in Patients with Active Psoriatic Arthritis Who Were Biologic DMARD-Naïve or Had Inadequate Response or Intolerance to TNF-α Inhibitors: 1-Year Results from Two Phase 3 Studies

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Pain and fatigue have been identified by patients (pts) as key features of PsA, driving the impact on their health-related quality of life.[1] Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A, has demonstrated meaningful improvements in pain and fatigue outcomes to 16 weeks (wks) vs placebo (PBO) in pts with active PsA.[2,3] In this study, pt-reported pain and fatigue outcomes are reported up to 1 year from two phase 3 studies of BKZ in pts with PsA.

Methods: BE OPTIMAL (NCT03895203) and BE COMPLETE (NCT03896581) were two phase 3 trials assessing BKZ in pts with active PsA who were biologic DMARD (bDMARD)-naïve or had inadequate response or intolerance to 1–2 TNF-α inhibitors (TNFi-IR), respectively. Both trials had a 16-wk double-blind, PBO-controlled phase.

Table. Patient-reported symptoms at Week 40/52

	BE OPTIMAL (bDMARD-naïve)		BE COMPLETE (TNFi-IR)	
Patient-reported symptom	PBO/BKZ 160 mg Q4W (n=281)	BKZ 160 mg Q4W (n=431)	PBO/BKZ 160 mg Q4W (n=133)	BKZ 160 mg Q4W (n=267)
	Week 52		Week 40[a]	
FACIT-Fatigue CfB,[b] mean (SE) [MI]	5.5 (0.5)	5.3 (0.4)	4.4 (0.8)	6.0 (0.6)
FACIT-Fatigue MCID,[c] n (%) [NRI]	139 (53.7)	208 (54.3)	54 (44.6)	146 (58.4)
	Week 52		Week 52	
PtAAP CfB,[d] mean (SE) [MI]	−31.8 (1.8)	−30.4 (1.4)	−29.5 (2.7)	−32.2 (1.8)
PtAAP 30, n (%) [NRI]	188 (66.9)	277 (64.3)	71 (53.4)	178 (66.7)
PtAAP 50, n (%) [NRI]	158 (56.2)	243 (56.4)	56 (42.1)	152 (56.9)
PtAAP 70, n (%) [NRI]	122 (43.4)	183 (42.5)	42 (31.6)	117 (43.8)

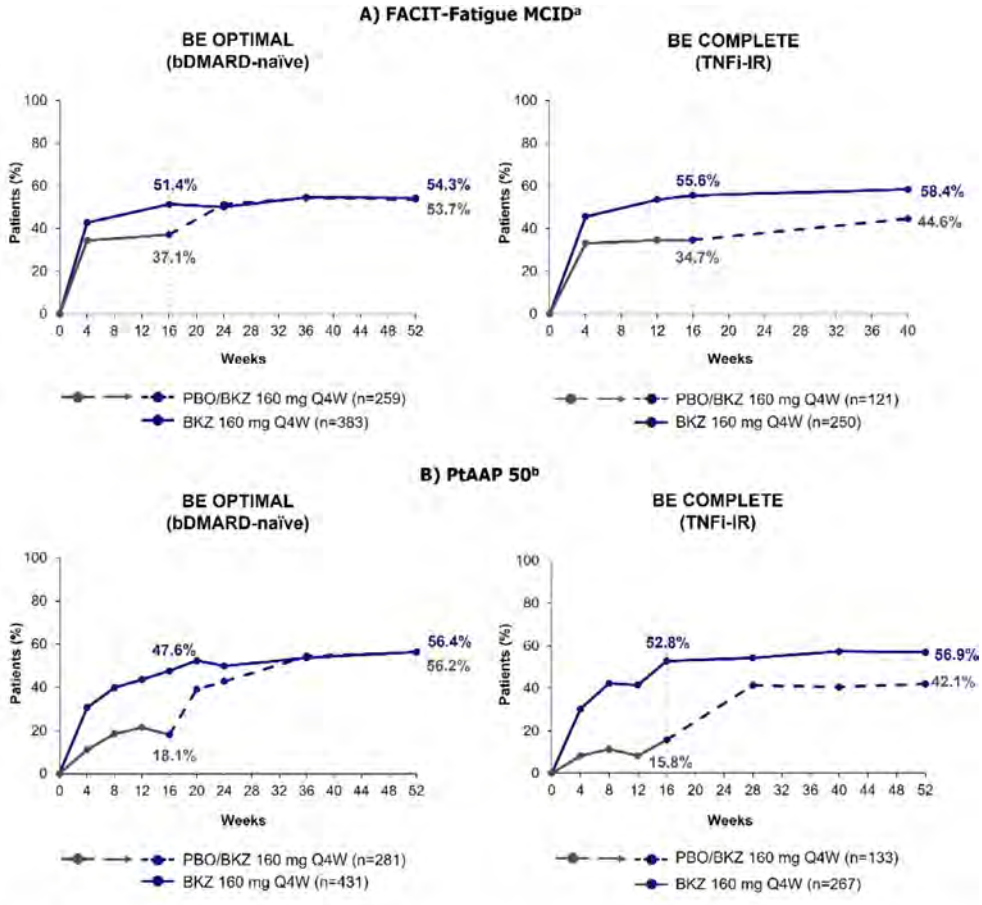
Randomized set. FACIT-Fatigue score ranges from 0 to 52, with 52 being the best possible score. PtAAP 100 mm VAS ranges from 0 to 100, with 0 representing "no pain" and 100 "most severe pain". PtAAP 30/50/70 represent clinically important improvements in patient-reported pain. [a] FACIT-Fatigue values not collected at Week 52; only collected to Week 40 for BE COMPLETE; [b] OC FACIT-Fatigue baseline values (SD): BE OPTIMAL PBO/BKZ 36.0 (10.2) BKZ 37.8 (9.6); BE COMPLETE PBO/BKZ 36.3 (9.9) BKZ 35.3 (10.5); [c] FACIT-Fatigue MCID defined as score increase from baseline ≥4 in patients with FACIT-Fatigue ≤48 at baseline; BE OPTIMAL PBO/BKZ n=259; BKZ n=383; BE COMPLETE PBO/BKZ n=121; BKZ n=250; [d] OC PtAAP baseline values (SD) BE OPTIMAL PBO/BKZ 56.8 (23.2) BKZ 53.6 (24.3); BE COMPLETE PBO/BKZ 61.7 (24.6) BKZ 58.3 (24.2).

bDMARD: biologic DMARD; BKZ: bimekizumab; CfB: change from baseline; FACIT-Fatigue: Functional Assessment of Chronic Illness Therapy—Fatigue; MCID: minimum clinically important difference; MI: multiple imputation; NRI: non-responder imputation; OC: observed case; PBO: placebo; PtAAP 30/50/70: ≥30/50/70% improvement in Patient's Assessment of Arthritis Pain; Q4W: every 4 weeks; SD: standard deviation; SE: standard error; TNFi-IR: inadequate response or intolerance to TNF-α inhibitor; VAS: visual analog scale.

Pts in BE OPTIMAL were randomized 3:2:1 to subcutaneous (sc) BKZ 160 mg every 4 wks (Q4W), PBO, or reference (sc adalimumab [ADA] 40 mg Q2W). At Wk 16, PBO pts switched to receive BKZ until Wk 52 (PBO/BKZ); pts receiving BKZ or ADA continued their dosing until Wk 52. BE OPTIMAL ADA data are not reported here. Pts in BE COMPLETE were randomized 2:1 to sc BKZ 160 mg Q4W or PBO. Along with BE OPTIMAL Wk 52 completers, pts who completed Wk 16 of BE COMPLETE were eligible to enter an open-label extension, BE VITAL (NCT04009499); PBO pts switched to BKZ (PBO/BKZ) on entry (36 wks of BKZ treatment to Wk 52); BE COMPLETE plus BE VITAL is referred to as 'BE COMPLETE' hereafter.

Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) subscale Minimum Clinically Important Difference (MCID; ≥4-point improvement from baseline [BL]) and change from BL (CfB), along with Pt's Assessment of Arthritis Pain (PtAAP) CfB and clinically important improvements (≥30/50/70%), are reported up to 1 year. BE COMPLETE FACIT-Fatigue values were collected to Wk 40 only. Non-responder and multiple imputation (NRI, MI) were used for missing binary and continuous variables.

Results: Overall, 770/852 (90.4%) and 347/400 (86.8%) pts completed Wk 52 of BE OPTIMAL and BE COMPLETE, respectively.



Randomized set. [a] FACIT-Fatigue MCID defined as score increase from baseline ≥4 in patients with FACIT-Fatigue ≤48 at baseline; [b] PtAAP 100mm VAS ranges from 0 to 100, with 0 representing "no pain" and 100 "most severe pain"; PtAAP 50 represents a clinically important improvement in patient-reported pain. bDMARD: biologic DMARD; BKZ: bimekizumab; FACIT-Fatigue: Functional Assessment of Chronic Illness Therapy—Fatigue; MCID: minimum clinically important difference; NRI: non-responder imputation; PBO: placebo; PtAAP 50: ≥50% Improvement in Patient's Assessment of Arthritis Pain; Q4W: every 4 weeks; TNFi-IR: inadequate response or intolerance to TNF-α inhibitor.

Figure. (A) FACIT-Fatigue MCID and (B) PtAAP 50 responders up to Week 40/52 [NRI]

At Wk 16, BKZ-treated pts achieved greater improvements in pain and fatigue outcomes vs PBO pts (**Figure**); improvements were sustained from Wk 16 to Wk 52 on BKZ treatment. For PBO/BKZ pts, pain and fatigue outcomes improved following switch to BKZ (**Table**).

Of pts with FACIT-Fatigue ≤48 at BL, FACIT-Fatigue MCID was achieved by 208/383 (54.3%) BKZ and 139/259 (53.7%) PBO/BKZ pts at Wk 52 in BE OPTIMAL, and 146/250 (58.4%) BKZ and 54/121 (44.6%) PBO/BKZ pts at Wk 40 in BE COMPLETE (**Table**, **Figure**). At Wk 52, PtAAP 50 was achieved by 243/431 (56.4%) BKZ and 158/281 (56.2%) PBO/BKZ pts in BE OPTIMAL, and 152/267 (56.9%) BKZ and 56/133 (42.1%) PBO/BKZ pts in BE COMPLETE.

Conclusion: Treatment with BKZ resulted in sustained improvements in pt-reported pain and fatigue from Wk 16 up to 1 year in both bDMARD-naïve and TNFi-IR pts with active PsA, with clinically meaningful improvements observed in over half of pts. Improvements in pt-reported pain and fatigue were similar between the two studies, demonstrating consistent responses in bDMARD-naïve and TNFi-IR pts.

References:1. Ogdie A. RMD Open 2020;6:e001321;**2.** McInnes IB. Lancet 2023;401:25–37; **3.** Merola JF. Lancet 2023;401:38–48.

Disclosure: M. Husni: AbbVie, 1, 2, Amgen, 1, 2, Bristol-Myers Squibb, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, UCB, 1, 2; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2; **J. Merola**: Abbvie, 2, 12, Investigator, Amgen, 2, 12, Investigator, Biogen, 2, 12, Investigator, Bristol-Myers Squibb, 2, 12, Investigator, Dermavant, 2, 12, Investigator, Eli Lilly, 2, 6, 12, Investigator, Janssen, 2, 12, Investigator, Leo Pharma, 2, 12, Investigator, Novartis, 2, 12, Investigator, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, 12, Investigator, Sun Pharma, 2, 12, Investigator, UCB Pharma, 2, 12, Investigator; **F. Behrens**: AbbVie, 2, 6, Affibody, 2, Amgen, 6, Boehringer-Ingelheim, 2, Celgene, 5, Chugai, 5, Eli Lilly, 6, Genzyme, 6, Gilead Sciences, 2, GSK, 2, 6, Janssen, 2, 5, MoonLake, 2, 6, MSD, 2, 6, Novartis, 6, Pfizer, 2, 5, 6, Roche, 5, Sandoz, 2, 6, Sanofi, 2, 6; **E. Favalli**: AbbVie, 2, 6, Bristol-Myers Squibb (BMS), 2, 6, Celltrion, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB Pharma, 2, 6; **D. McGonagle**: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Janssen, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **W. Tillett**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, GSK, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Ovo Pharma, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma, 2, 5, 6; **S. Tsuji**: AbbVie, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Kyowa Kirin, 2, 6, Novartis, 2, 6, UCB Pharma, 2, 6; **B. Ink**: AbbVie, 11, GSK, 11, UCB Pharma, 3, 11; **R. Bajracharya**: UCB Pharma, 3, 11; **J. Lambert**: UCB Pharma, 3, 11; **J. Coarse**: UCB Pharma, 3, 11; **L. Gossec**: AbbVie, 2, 12, Personal fees, Amgen, 2, Biogen, 5, BMS, 12, Personal fees, Celltrion, 12, Personal fees, Eli Lilly, 5, 12, Personal fees, Galapagos, 12, Personal fees, Janssen, 12, Personal fees, MSD, 12, Personal fees, Novartis, 5, 12, Personal fees, Pfizer, 12, Personal fees, Sandoz, 5, 12, Personal fees, UCB Pharma, 5, 12, Personal fees.

Abstract Number: 0528

Risk of Cardiovascular Disease Associated with Long-term Use of NSAIDs in Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing spondylitis (AS) is associated with increased cardiovascular disease, but there are limited data as to whether prolonged treatment with non-steroidal anti-inflammatory drugs (NSAIDs) increases the cardiovascular risk in AS patients. We aimed to examine the risk of cardiovascular disease associated with long-term use of NSAIDs in a large real-world AS cohort.

Methods: A nationwide population-based cohort of patients with AS and matched controls without AS were analysed. The primary outcome was cardiovascular disease, a composite outcome of ischemic heart disease, stroke, or congestive heart failure. Long-term use of NSAIDs was defined as use of NSAIDs for more than 365 cumulative defined daily doses. The association between long-term use of NSAIDs and incident cardiovascular disease was examined using a multivariable Cox proportional hazards regression model in both AS and non-AS populations.

Results: Among 19,775 patients with AS and 59,325 matched controls without AS, there were 1,663 and 4,308 incident cases of cardiovascular disease, showing an incidence of 16.9 and 13.8 per 1,000 person-years, respectively. Long-term use of NSAIDs increased the risk of cardiovascular disease in non-AS controls (adjusted hazard ratio [aHR], 1.64; 95% CI, 1.48–1.82). In contrast, long-term use of NSAIDs did not increase the risk of cardiovascular disease in AS patients (aHR, 1.06; 95% CI, 0.94–1.20; adjusted for age, sex, socioeconomic status, body mass index, smoking status, hypertension, diabetes, hyperlipidemia, and tumor necrosis factor inhibitor use).

Conclusion: Prolonged NSAID treatment in AS patients may not be as harmful as in the general population regarding cardiovascular risk.

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Abstract Number: 0529

Sex-dependent Differences in Disease Characteristics Do Not Influence Effectiveness of Secukinumab Therapy in Patients with Active Axial Spondyloarthritis in a Non-Interventional Trial (AQUILA)

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Individualized treatment strategies are of high importance in the treatment of patients with axial spondyloarthritis (axSpA). IL-17A inhibition has demonstrated good efficacy on axSpA. Nevertheless, approx. 30% of the patient will not achieve remission after initiation of systemic therapy. Therefore, the identification of patient characteristics leading to higher response rates to bDMARD treatments are important to guide treatment choice and its adjustments in clinical routine care to promote an improved outcome. An adapted machine learning approach (cluster analysis) is used to analyze baseline (BL) patient characteristics to detect clinical patterns of disease activity in axSpA patients treated with secukinumab (SEC) in a non-interventional trial.

Methods: Data from 621 patients enrolled in the German non-interventional AQUILA study with active axSpa, whose first SEC treatment occurred no more than 4 weeks prior to BL, was analyzed. All patients were included, irrespective of treatment response We identified patient groups by applying an extended version of the machine learning method of hierarchical density-based clustering (HDBSCAN) to BL data, where features included patient and disease characteristics variables as well as standardized patient-reported outcome (Table 1).Feature groups with high numbers of missing values were initially excluded, and subsequent clustering was performed to achieve the stepwise integration of all features. At each step, an additional feature group was included in a re-clustering using a complete subset of subjects. This led to a further split of some of the original clusters. For every final cluster, disease activity over the course of the study was visualized including patient and physician-derived assessments.

Results: The machine learning approach resulted in the categorization of 7 clusters of patients and outliers (n=139, cluster -1)(Fig.1). The primary focus of this analysis lies on medially relevant clusters, which exhibit similar characteristics including little prior and ongoing therapy, but differ in their sex (cluster 5: n=89, female; cluster 6: n=172, male, Fig. 2A). While women had a significantly higher subjective ASAS-HI (p=.003, Fig 2B), BASDAI was comparable in both groups at BL. At week

Table 1: Overview of dataset characteristics of 621 axSpA patients at baseline, across all 7 clusters. *Total n can differ from 621 in table, due to missing values; ** Chronic heart failure, stroke, or coronary heart disease

Baseline Criteria	Total n=621*
Age, [years] (median) (n=621)	47.8
BMI, [kg/m²] (median) (n=605)	26.9
Active smokers (n=545)	205
Ex-smokers (n=545)	70
bDMARD-naïve	227
Previous TNF	394
Previous IL-23	4
Previous csDMARDs	212
csDMARDs Concomitant	77
MTX Concomitant	61
Comorbidity: Depression (n=586)	70
Comorbidity: Uveitis (n=603)	35
Comorbidity: Cardiovascular** (n=609)	43
PhGA (median) (n=563)	6.2
PGA (median) (n=378)	6.1
ASAS (median) (n=549)	8.0
CRP [mg/dl] (median) (n=302)	5.0
BASDAI (median) (n= 510)	5.4

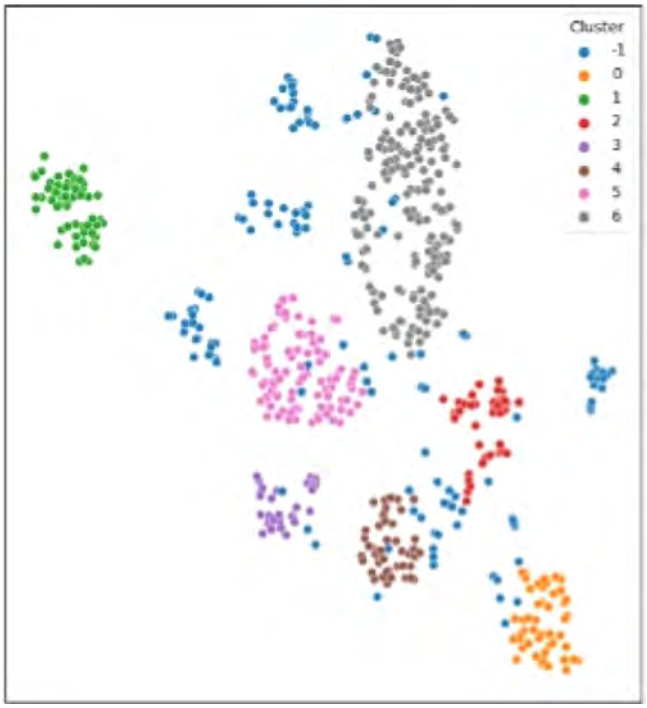

Figure 1 Result of multistage clustering of BL characteristics of 621 active axSpA patients. The clustering reveals 7 clusters and outliers (cluster –1). Important cluster characteristics: 5, predominantly female; 6, predominantly male. The scatterplot of the patient characteristics is created by the dimension reduction TSNE to 2 dimensions and thus has arbitrary units on the axes.

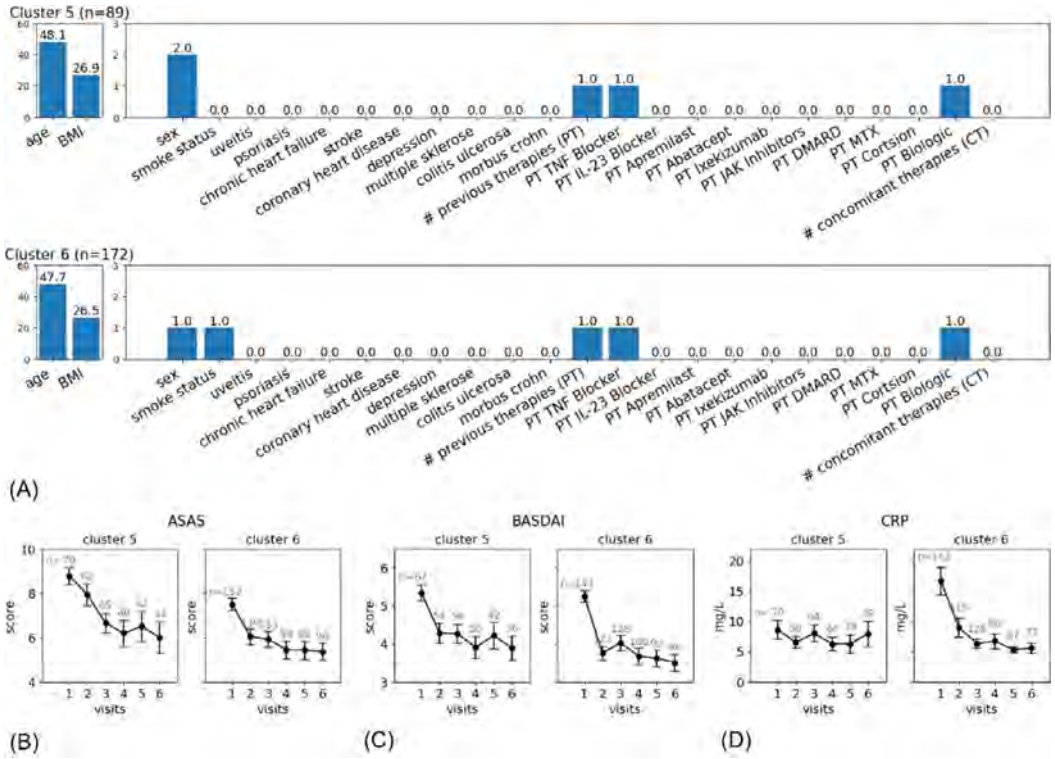

Figure 2 (A) Median BL characteristics of patients of cluster 5 and cluster 6 (B) Mean ASAS with standard error of patients of cluster 5 and cluster 6 over the course of the study up to W52 (visit 6). Cluster 5 has significantly higher values at BL (p=.003). (C) Mean BASDAI with standard error of patients of cluster 5 and cluster 6 over the course of the study up to W52 (visit 6). (D) Mean CRP with standard error of patients of cluster 5 and cluster 6 over the course of the study up to W52 (visit 6). Cluster 6 has significantly higher values at BL (p=.04) and a stronger improvement over trail (BL – V6, p=.001).

52 disease activity (ASAS-HI and BASDAI, Fig 2B, 2D) did not differ significantly between both groups. At BL CRP was significantly higher among male patients (p=.04, Fig 2C) and showed stronger improvement after one year of SEC treatment (p=.001, Fig 2C), leading to a comparable mean outcome (4.0 vs. 3.9).

Conclusion: We present a machine learning approach applied to the heterogeneous axSpA cohort from AQUILA. Differences were found in the two clusters which differ primarily in sex. At BL, female patients had higher subjective ASAS-HI while male axSpA patients showed higher CRP values whereas BASDAI was comparable. No differences in disease activity remain at week 52. This initial difference in disease perception between male and female groups converges to similar outcomes after 1 year of SEC therapy, emphasizing the treatment's effectiveness across sexes.

Disclosure: M. Koehm: Janssen, 2, 5, 6, Novartis GmbH, 2, 5, 6; **M. Klippstein**: Novartis GmbH, 5; **S. Kugler**: Novartis GmbH, 5; **S. Mackay**: Novartis GmbH, 5; **D. Schulz**: Novartis GmbH, 5; **A. Vodencarevic**: Novartis, 3; **G. Wendt**: Novartis GmbH, 3; **D. Peterlik**: Novartis, 3; **U. Kiltz**: AbbVie, 2, 5, 6, Amgen, 5, Biocad, 2, 6, Biogen, 5, Bristol-Myers Squibb(BMS), 2, 5, Chugai, 2, 6, Eli Lilly, 2, 6, Fresenius, 5, Gilead, 2, 5, GlaxoSmithKline (GSK), 5, Grünenthal, 2, 6, Hexal, 5, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, onkowiessen.de, 2, 5, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Viatris, 2, 5; **J. Brandt-Juergens**: AbbVie/Abbott, 2, 6, Affibody, 2, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Gilead, 2, Janssen, 2, 6, Medac, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **F. Behrens**: AbbVie/Abbott, 2, 5, 6, Affibody, 2, Amgen, 2, 5, 6, Bionorica, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Chugai Pharma GmbH, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Genzyme, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Iron4u, 2, 5, 6, Leo, 2, 5, 6, Merck/MSD, 2, 5, 6, Moon-Lake, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sandoz, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0530

Impact of Upadacitinib on Wearable Device-Measured Physical Activity in Patients with Ankylosing Spondylitis from the SELECT-AXIS 2 Trial

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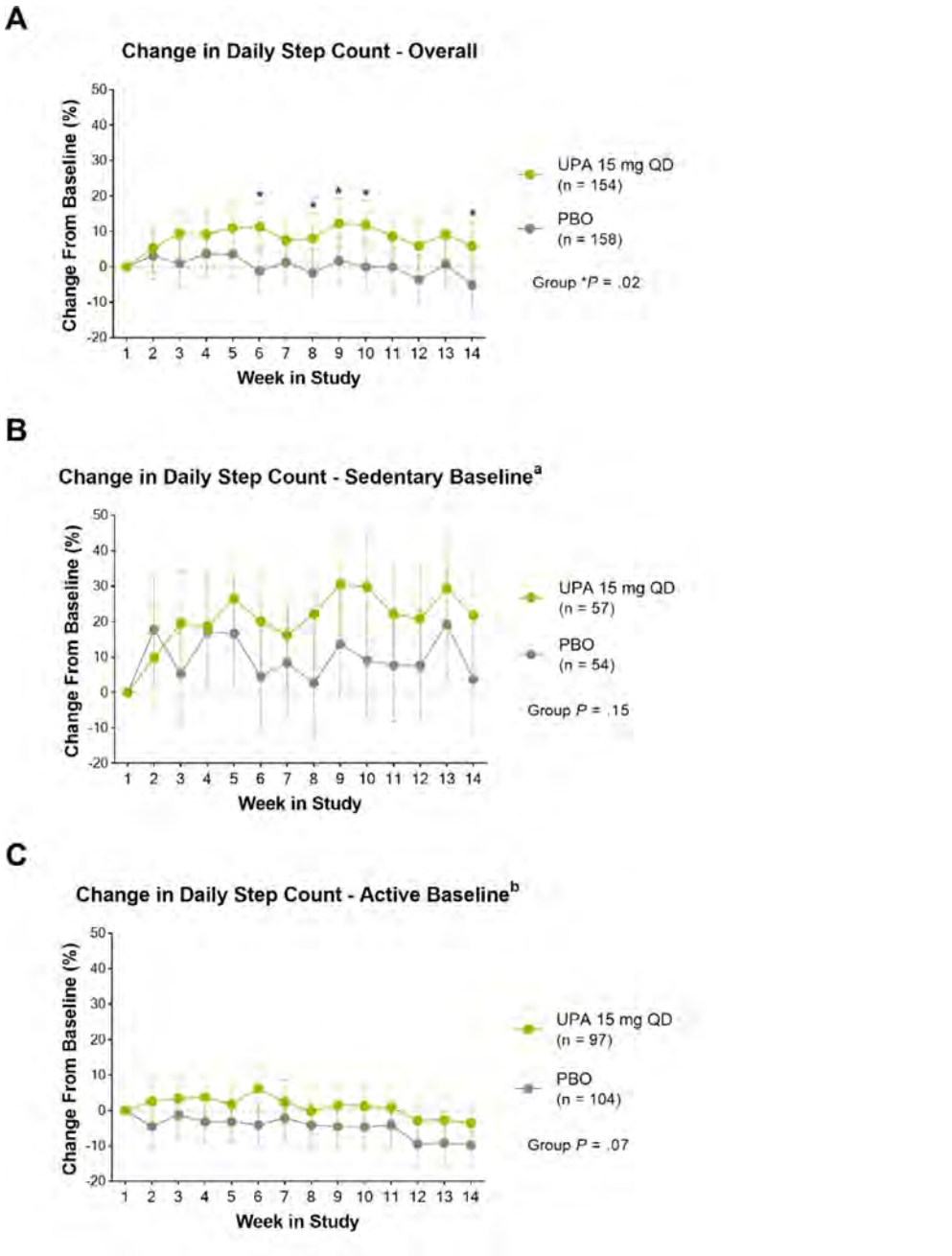
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Physical activity is associated with reduced pain, improved mobility and physical function in people with ankylosing spondylitis (AS) and plays a crucial role in AS management. Despite this, the impact of pharmacologic interventions on physical activity is rarely measured or reported in clinical research. Wearable technology enables passive collection of objective physical activity data. We previously demonstrated high levels of wearable device adherence in patients with active AS in the SELECT-AXIS 2 phase 3 trial and reported this cohort's baseline physical activity patterns.[1] Here, we evaluated the effect of upadacitinib (UPA) vs placebo (PBO) on physical activity in this patient cohort through 14 weeks (wks).

Methods: Patients with active AS with an inadequate response or intolerance to biologic DMARDs (bDMARD-IR) were randomized to receive UPA 15 mg once daily or PBO.[2] As part of the study design, patients were required to wear a medical-grade wrist-worn actigraphy device during the 14-wk, PBO-controlled portion of the study. For inclusion in physical activity

analyses, patients needed to have at least 3 adherent days (defined as 16 hrs per day of device usage) out of the first 7 days after trial entry. The percent change from the first wk of the study (defined as baseline) in mean daily steps was evaluated over 14 wks. Changes in physical activity were also assessed in the subsets of patients who demonstrated an active (≥5000 steps per day per day) or sedentary lifestyle (< 5000 steps per day) at baseline. Group-wise nominal *P* values for



PBO, placebo; QD, once daily; UPA, upadacitinib.
[a]Defined as <5000 steps per day, as previously reported (Tudor-Locke C, et al. *Sports Med*. 2004;34:1–8).
[b]Defined as ≥5000 steps per day.
Group-wise nominal *P* values for comparison of UPA vs PBO groups were calculated by mixed model repeated measures (MMRM) analysis, with comparisons at each week performed by one-way analysis of variance (ANOVA). Fixed effects in the MMRM model included treatment, visit, treatment-by-visit interaction, and baseline step count.
*, indicates nominal statistical significance at *P* <.05 for UPA 15 mg vs PBO.

Figure 1. Percent Change From Baseline in Physical Activity Through 14 Weeks in the SELECT-AXIS 2 Study Cohort

comparison of UPA vs PBO groups through 14 wks were calculated by mixed model repeated measures analysis, with comparisons at each wk performed by one-way analysis of variance.

Results: Of 420 total patients, physical activity data were collected from 394 participants, and 312 (UPA, n=154; PBO, n=158) met minimal adherence criteria based on their first 7 days of study participation. In these patients, adherence was 83.5% of study days through 14 wks.[1] Patients treated with UPA had numerically higher mean daily step counts than those treated with PBO, with an 11-percentage point improvement vs PBO at wk 14 (mean absolute difference of 345 steps per day; $P < .05$) (**Fig 1A**). In patients with a sedentary lifestyle at baseline, a 22% improvement in the mean daily step count was observed with UPA from baseline to wk 14 compared to a 4% improvement with PBO (mean absolute difference of 264 steps per day), although these differences were not significant (**Fig 1B**). Patients with an active lifestyle at baseline also showed numerically better maintenance of their daily step counts over 14 wks with UPA compared to PBO where step counts declined over time (**Fig 1C**).

Conclusion: In bDMARD-IR AS patients, UPA treatment led to numerically greater improvements compared to PBO in physical activity as measured by a wearable device over 14 wks, especially in sedentary patients. These findings support the utility of passively collected actigraphy measurements to monitor the effect of a targeted therapy on physical activity and further exploring possible heterogeneous effects on step count depending on baseline activity.

1. Mease et al. *Ann Rheum Dis*. 2023;82:626.

2. van der Heijde et al. *Ann Rheum Dis*. 2022;81:1515–23.

Disclosure: J. Curtis: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, 5, CorEvitas, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **R. Grainger**: AbbVie, 2, 6, Cornerstones, 6, Janssen, 6, Novartis, 2, Pfizer, 6; **D. Webster**: AbbVie, 3, 11; **J. Shen**: AbbVie, 3, 11; **A. Biljan**: AbbVie, 3, 11; **A. Shmagel**: AbbVie, 3, 11; **P. Wung**: AbbVie, 3, 11; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2.

Abstract Number: 0531

Effects of Anti-tumor Necrosis Factor Treatment on Lipid Profiles in Patients with Ankylosing Spondylitis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate the effects of anti-tumor necrosis factor (anti-TNF) treatment on lipid profiles and identify risk factors for elevated total cholesterol (TC) after the treatment in ankylosing spondylitis (AS) patients.

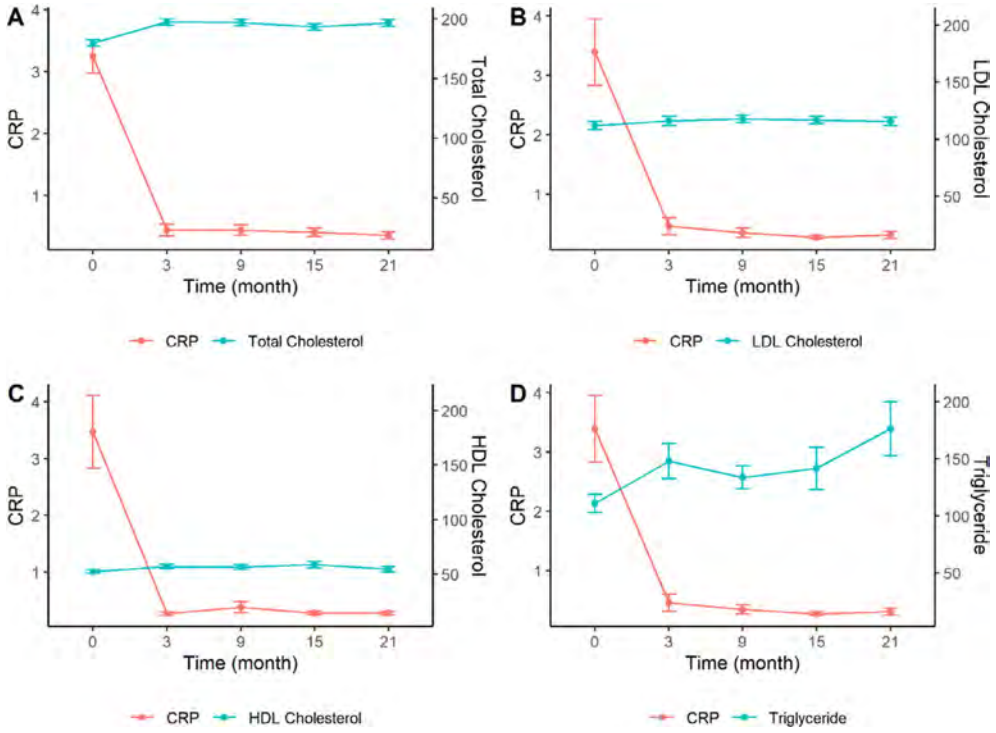

Figure 1. Changes in CRP and lipid particles after anti-TNF treatment. CRP, c-reactive protein; TNF, tumor necrosis factor; HDL, high-density lipoprotein; LDL, low-density lipoprotein

Table 1. Risk factors for increased total cholesterol after 3 months of anti-tumor necrosis factor treatment

	Univariable		Multivariable1		Multivariable2	
	Estimate	*P*	Estimate	*P*	Estimate	*P*
Male (Ref. Female)	1.785	0.661	2.116	0.722	4.822	0.417
Age (years)	0.122	0.436	0.742	0.002	0.720	0.002
Baseline mSASSS	-0.028	0.806				
Initial BASDAI	-0.424	0.735				
CRP (mg/dL)	2.405	<.0001	1.190	0.093		
ESR (mm/h)	0.244	<.0001			0.159	0.033
LDL (mg/dL)	-0.348	<.0001	-0.322	0.001	-0.324	0.001
HDL (mg/dL)	-0.032	0.877				
TG (mg/dL)	-0.089	0.003	-0.047	0.203	-0.041	0.258
Use of anti-TNF agents						
Adalimumab	Reference		Reference		Reference	
Golimumab	-0.154	0.971	10.735	0.139	10.073	0.162
Etanercept	-10.423	0.024	-3.959	0.512	-4.489	0.453
Infliximab	-2.047	0.680	-3.616	0.686	-4.925	0.577

TNF, tumor necrosis factor; mSASSS, modified stoke ankylosing spondylitis spinal score; BASDAI, Bath ankylosing spondylitis disease activity index; CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglyceride;

Methods: A retrospective cohort study analyzed AS patients who received first-line anti-TNF treatment. Patients excluding underage and those on lipid-lowering agents, with at least nine months of follow-up were included. One-way ANOVA with repeated measures assessed the impact of anti-TNF inhibitors on disease activity and lipid profile (TC, Low-density lipoprotein [LDL], High-density lipoprotein [HDL], and triglycerides [TG]). Univariable and multivariable linear regression identified risk factors for elevated TC after 3 months of anti-TNF treatment.

Results: A total of 320 AS patients were enrolled (78.4% male, mean age 34.3 ± 10.8 years). TC and TG levels significantly increased particularly within the first 3 months of anti-TNF treatment, while LDL and HDL levels did not show significant changes. Changes in inflammatory markers and lipid particles (TC, LDL, TG) were strongly correlated over time, but HDL showed no significant correlation. Older age, higher baseline ESR, and lower baseline LDL levels were identified as risk factors for elevated TC after 3 months of anti-TNF treatment.

Conclusion: In AS patients, anti-TNF treatment has been found to increase lipid particles, potentially due to its anti-inflammatory effects. Future research should explore the clinical implications of dyslipidemia, particularly the occurrence of cardiovascular events, following anti-TNF treatment in AS patients.

Disclosure: I. Kwon: None; **b. nam**: None; **N. Choi**: None; **J. Shin**: None; **S. lee**: None; **T. Kim**: None.

Abstract Number: 0532

Factors Associated with Cause-specific Discontinuation of Long-term Anti-tumor Necrosis Factor Agent Use in Patients with Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-tumor necrosis factor (TNF) agents have proven to be effective in treating Ankylosing spondylitis (AS). However, a significant number of patients discontinue or switch their anti-TNF agent for various reasons. Previous studies have been limited in scope, primarily focusing on drug retention rates or utilizing cohorts with short follow-up durations. The objective of this study is to investigate the factors associated with cause-specific discontinuation of long-term anti-TNF agent use in patients with AS.

Methods: AS patients who initiated the first-line anti-TNF agent between 2004 and 2018 and continued the treatment for at least 2 years were enrolled in the study. Patients with concomitant inflammatory bowel disease were excluded. The index date was defined as the date of initiation of the first-line anti-TNF agent, and the observation period lasted until the last visit, discontinuation of the first-line anti-TNF agent, or September 2022. The reasons for discontinuation of the first-line anti-TNF agent were categorized into 1) clinical remission, 2) lack of efficacy, 3) adverse events, and 4) other reasons including loss to follow-up, cost, or reimbursement issues. The cumulative incidence function curve was used to visualize the cumulative

failure rates over time for each specific reason. Univariate and multivariate cause-specific hazard models were utilized to identify factors associated with cause-specific discontinuation of the first-line anti-TNF agent.

Results: A total of 429 AS patients were included in the study, with 121 on adalimumab (ADA), 176 on etanercept (ETN), 89 on infliximab (INF), and 43 on golimumab (GLM). The median overall survival on the first-line anti-TNF agent was 10.6 (7.9-14.5) years. Among the patients, 103 (24.0%) discontinued the first-line anti-TNF agent, with 36 (34.9%) due to

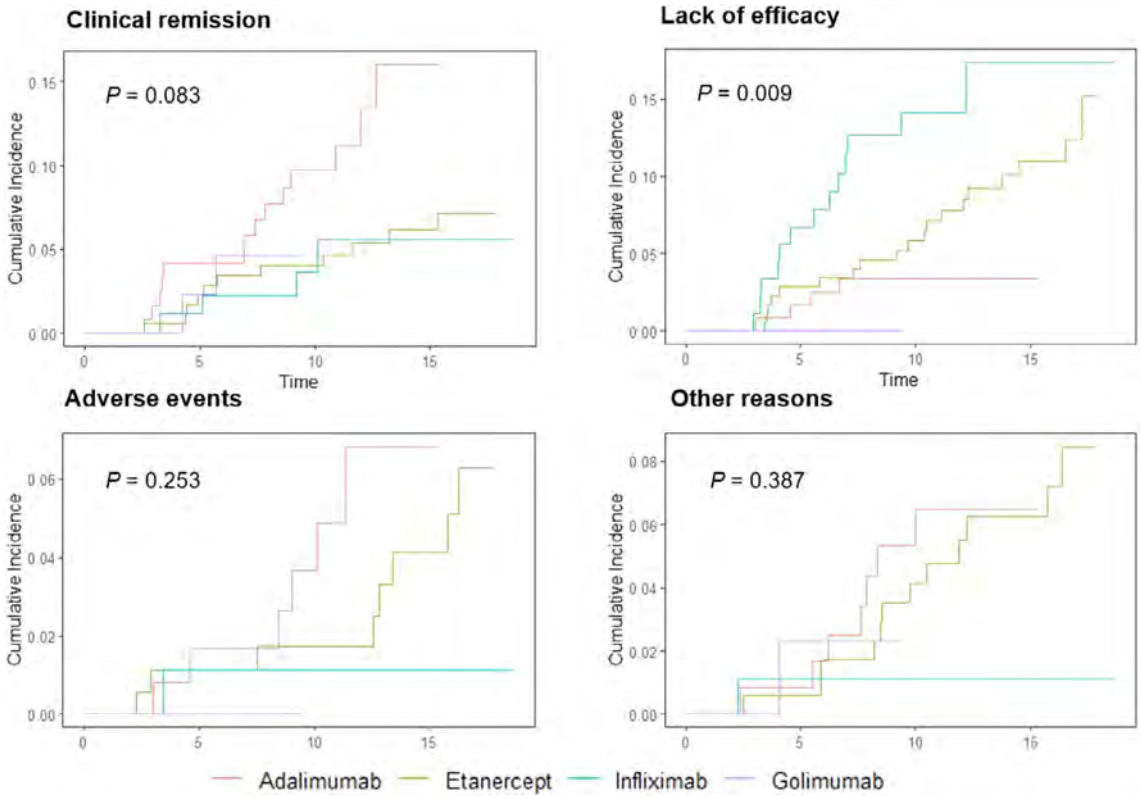

Figure 1. Cumulative incidence function according to anti-TNF agents

Table 1. Multivariable cause-specific hazard model for discontinuation of long-term anti-TNF agent use in AS patients

	Clinical remission		Lack of efficacy		Overall side effect		Infection-related side effect		Other reasons	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Age, years	0.986 (0.947-1.028)	0.516	1.027 (1.000-1.056)	0.052	1.018 (0.969-1.069)	0.486	1.068 (1.020-1.118)	0.005	0.976 (0.916-1.039)	0.445
Male	3.605 (0.460-28.265)	0.222	1.582 (0.494-5.065)	0.440	0.779 (0.145-4.193)	0.771			1.049 (0.119-9.248)	0.966
DzDRT										
< 5yrs	1.930 (0.947-3.932)	0.070	0.801 (0.354-1.811)	0.594	0.260 (0.030-2.250)	0.221			1.627 (0.648-4.083)	0.300
≥ 5yrs	Reference		Reference		Reference				Reference	
Baseline mSASSS					1.018 (0.999-1.038)	0.062	1.024 (0.985-1.064)	0.228		
BASDAI 0m			1.309 (1.037-1.652)	0.023						
CRP 0m							0.827 (0.582-1.176)	0.290		
Uveitis					2.021 (0.697-5.855)	0.195				
Peripheral joint involvement			1.990 (0.982-4.032)	0.056						
Use of biologics										
Adalimumab	Reference		Reference		Reference				Reference	
Etanercept	0.454 (0.208-0.992)	0.048	2.890 (0.981-8.511)	0.054	0.452 (0.163-1.256)	0.128			0.926 (0.362-2.365)	0.872
Infliximab	0.399 (0.127-1.250)	0.115	4.534 (1.452-14.157)	0.009	0.182 (0.022-1.546)	0.119			0.174 (0.021-1.455)	0.107
Golimumab	0.648 (0.144-2.917)	0.572	-	-	-	-			0.853 (0.105-6.964)	0.882
Smoking										
Never									Reference	
Ex									1.464 (0.116-18.472)	0.768
Current									6.218 (1.817-21.279)	0.004

inefficacy, 31 (30.1%) due to sustained clinical remission, 15 (14.6%) due to adverse events, and 21 (20.4%) due to other reasons. Patients treated with ETN had a lower risk of discontinuation due to sustained clinical remission compared to those on ADA (Hazard ratio [HR] 0.45 [0.21-0.99], P=0.048). Higher baseline BASDAI (HR 1.31 [1.04-1.65], P=0.023) and use of INF were associated with a higher likelihood of discontinuation due to inefficacy compared to ADA (HR 4.53 [1.45-14.16], P=0.009). Older age was related to an increased risk of discontinuation due to infection-related adverse events (HR 1.07 [1.02-1.12], P=0.005), and current smoking was a risk factor for discontinuation due to other reasons (HR 6.22 [1.82-21.28], P=0.004).

Conclusion: Several factors influencing cause-specific discontinuation of long-term anti-TNF treatment were identified in our study. Further investigation is needed to understand the underlying reasons for these phenomena. This knowledge is valuable for improving personalized medicine in the management of patients with AS, as it allows for more informed decision-making and the customization of treatment plans based on individual patient characteristics.

Disclosure: b. nam: None; **N. Choi**: None; **B. Koo**: None; **J. Kim**: None; **J. Shin**: None; **S. lee**: None; **k. Joo**: None; **T. Kim**: None.

Abstract Number: 0533

Remission in Axial Spondyloarthritis: Is There a Difference Between NSAIDs and b/tsDMARDs in Daily Practice?

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Randomized-controlled trials (RCTs) done in axial spondyloarthritis (axSpA) patients have shown that remission in axSpA (including nonradiographic axSpA) patients treated without b/tsDMARDs (TNFα blockers, IL-17A blockers, JAK inhibitors)(BIOL) occurs infrequently. Few are known about remission rate (RR) with large cohort in daily clinical practice.

The purpose of this study was to assess the remission rate (RR) in axSpA patients in the real life, and to compare the RR in axSpA patients on NSAIDs to RR for those on BIOL.

Methods: This cross-sectional study reviewed clinical data from a single center from 01/2013 to 01/2023. Last visit available for clinical assessment was evaluated. Disease activity was measured using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and the Ankylosing Spondylitis Disease Activity Score (ASDAS) using the C-reactive protein. Remission was defined as BASDAI < 4 and ASDAS < 1,3.

Results: Data from 873 axSpA patients were reviewed. 529 were men (60.3 %). In the entire cohort, 653 BASDAI and 409 ASDAS were recorded. The RR according to the BASDAI was 46.7% (n =305), and 20.3 % for the ASDAS (n = 83). To look for the treatment-related RR, we stratified by the treatment (NSAIDs vs Biologics). We had 441 patients on NSAIDs

Table: Distribution of ASDAS values in both groups.

	ASDAS < 1.3	ASDAS ≥ 1.3 < 2.1	ASDAS ≥ 2.1 ≤3.5	ASDAS > 3.5
NSAIDs (n = 158)	N = 34 (21.5%)	N = 35 (22.2%)	N = 60 (38%)	N = 29 (18.4%)
BIOL (n = 251)	N = 49 (19.5%)	N = 58 (23.1%)	N = 93 (37.1%)	N = 51 (20.3%)

(250 men, 56.7 %) and 432 on BIOL (279 men, 64.6 %). 287 BASDAI were available for NSAIDs and 366 for BIOL. 132 patients on NSAIDs (46 %) and 173 on BIOL (47.3%) were in remission for BASDAI. Regarding ASDAS (table below), data from 158 patients on NSAIDs and 251 on BIOL were available. Out of them, 34 (21.5 %) and 49 (19.5 %) were in remission for NSAIDs and BIOL respectively. Chi-square test: p = NS.

Conclusion: Based on the ASDAS, The overall RR in our axSpA cohort was around 20%, even in the NSAIDs group. When we added patients on low disease activity (LDA) according to the ASDAS score, the overall proportion of patients with inactive disease or LDA was quite the same in both groups and slightly above 40 %. In daily practice, we should probably better define the remission in axSpA.

Disclosure: F. Natalucci: None; **P. KRUG**: None; **A. DE SOUSA LEITE**: None; **T. Sokolova**: None; **P. Durez**: None; **M. Stoenoiu**: None; **A. NZEUSSEU TOUKAP**: None.

Abstract Number: 0534

Tapering Tofacitinib for Axial Spondyloarthritis in Remission or Low-disease Activity State

Pankti Mehta[1], Sanjo Saijan[2], Justin George[2], Sakir Ahmed[3], Bhowmik Meghnathi[4] and Padmanabha Shenoy[2], [1]King George's Medical University, Mumbai, India, [2]Centre for arthritis and rheumatism excellence, Kochi, India, [3]Kalinga Institute of Medical Sciences, Bhubaneswar, India, [4]Smt. NHL Municipal Medical College and SVP hospital, CIMS Hospital, Ahmedabad, India

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The recent recommendations from EULAR-ASAS for Axial Spondyloarthritis (AxSpA) call for decreasing biologic (b)DMARDs after an extended period of remission. This is especially relevant in underdeveloped countries, where patients pay out of pocket for their healthcare and are exposed to higher risks of opportunistic infections with bDMARD therapy. Despite sharing the same issues of infections and expenses, there is no clear evidence for the tapering strategy of targeted synthetic DMARDs in AxSpA. We aimed to study whether TOFA can be tapered in patients with AxSpa, assess the risk of flares, time to flare, and factors associated with flares.

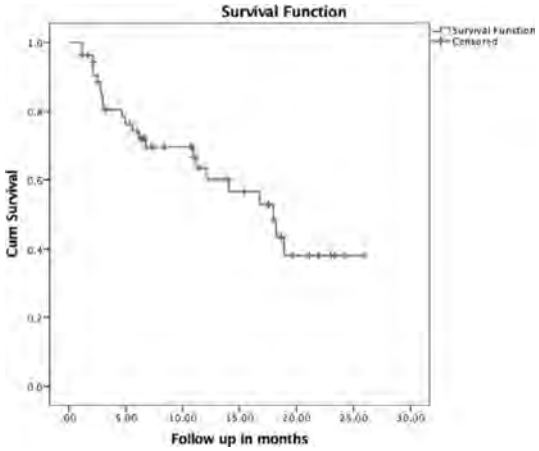
Methods: Patients with AxSpA (ASAS criteria) on tofacitinib (TOFA) in remission or low disease activity (ASDAS CRP < 2.1) state for at least three months, were gradually tapered off TOFA. The drug was tapered at the treating physician's discretion, with each visit accompanied by an evaluation of the disease activity. Co-treatment with conventional(c) DMARDs, but not bDMARDs was permitted. Tofacitinib was resumed at the previous dose in case of flares, defined at the treating physician's discretion.

Flare-free survival was visualized by Kaplan-Meir curves. To determine factors associated with flares, covariates with a p-value of < 0.2 on univariate analysis (age, radiographic disease, cDMARD use in the past, ASDAS CRP > 3.5 at baseline) were included for multivariate Cox regression modelling. Data are expressed as median and interquartile range.

Results: The study included 54 patients, aged 38 years(29.75–46.75), 75% males, and a disease duration of 6 (9–17.5) years. Three-fourths had radiographic disease, and 30 of 44 (68.1%) were HLA-B27 positive. Amongs the extra-articular features,uveitis was observed in 9(16.7%).

Before TOFA initiation, ASDAS-CRP was 3.1(2.4-3.5), 24 (44.4%) had used cDMARDs, and 20 (37%) had used bDMARDs. Reasons for shifting to TOFA were an inadequate response to cDMARD or bDMARD in 36 (66.7%) cases; financial considerations with bDMARD therapy in 14 (26%), and adverse drug reactions in four (7.4%). TOFA was started at a full dose of 70 mg/week in 47 (87%), and 41 (76 %) received concomitant sulfasalazine but no bDMARDs were used with TOFA.

ASDAS CRP was 0.3 (0.9-1.7) at 3 months (3-5.25) of full dose TOFA. During tapering, 23 (42.6%) patients flared, with the median time to flare being 18 months (CI 12.5-23.4)(Figure 1,2). All patients who flared re-attained remission after restoring the TOFA dose to the previous dose.



Kaplan Meir survival analysis with time from onset of TOFA dose tapering and flare as the event

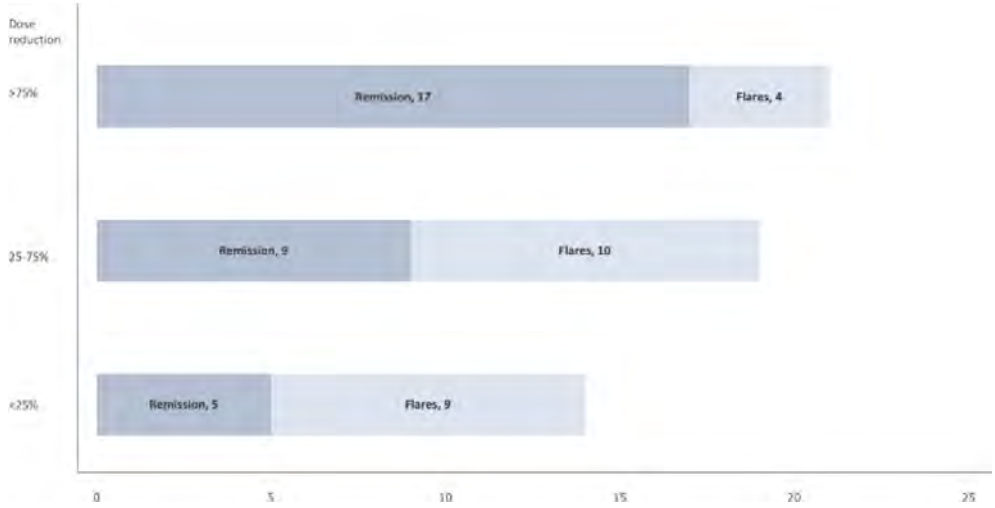


Figure 2: Outcomes stratified by dose tapering of Tofacitinib

At a median of 7.3 months (3-17.4) of TOFA tapering, 39 (70%) were in remission with4 (10.5%) on >75%, 32(84.2%) on 25-75% and 2(5.2%) on >25% of full TOFA dosage.

In multivariate Cox regression, radiographic disease [0.01, 7(1.6-31)], prior cDMARD [0.02, 0.3(0.1-0.8)] and ASDAS CRP >3.5 prior to initiation of TOFA [0.005, 3.4(1.4-8.1)] use were linked with flare.

Conclusion: This real-world data provides proof of concept that TOFA tapering is viable in the management of AxSpA. Flares can be managed by increasing the dose of TOFA to the previous effective level. This can pave the way for randomized controlled studies to determine the optimum tapering strategy, as well as long-term cohort studies to see the effects on radiographic progression.

Disclosure: P. Mehta: None; **S. Saijan**: None; **J. George**: None; **S. Ahmed**: Cipla, 6, DrReddy's, 6, Janssen, 6, Novartis, 6, Pfizer, 6; **B. Meghnathi**: None; **P. Shenoy**: None.

Abstract Number: 0535

Pharmacologic Treatment of Ankylosing Spondylitis in a Large Urban Medical Center: Effects of Socioeconomic Status, Race/Ethnicity and Sex

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing spondylitis (AS) is estimated to affect up to 1,647,500 Americans, resulting in significant disability and lost productivity for affected individuals. Biologic medications reduce disease activity and improve functional outcome in those with AS, but they are expensive and may be difficult to access. Individuals of lower socioeconomic status (SES), minorities (specifically African American or Latinx), and women may be less likely to receive biologic treatment, resulting in poorer functional outcomes The objective of this study was two-fold: 1) to develop a multi-ethnic longitudinal AS cohort for analysis of clinical features, demographics, SES, race/ethnicity, sex and treatment patterns and 2) to analyze the effects of these factors on the prescription of a biologic agent.

Methods: Data from the electronic medical record of an urban academic health system were analyzed between January 1, 2010 and September 12, 2020.Subjects had at least one ambulatory encounter and diagnostic codes of M45 (ICD-10) or 720 (ICD-9). Independent variables included insurance information, address with zip code, race/ethnicity and sex. Social Deprivation Index (SDI) was utilized as a measure of SES. Patients were removed from the analysis if they were in a correctional facility or did not list a residential address in the chart. The dependent variable was prescription of at least one biologic medication. Multivariate logistic regression was performed using R Statistical Programming Software.

Results: Our cohort included 430 patients total; 423 were included in the multivariate analysis. Seven patients were removed due to lack of SDI information. Non-Hispanic Blacks made up 30% of the cohort, with Latinx and Non-Hispanic Whites representing 21% and 30% respectively (Fig 1). Women made up 37% of the cohort (Fig 2). Men were prescribed biologic agents more often than women. Non-Hispanic Blacks and Latinx had increased odds of receiving biologic therapy

compared with Non-Hispanic Whites. Insurance status and SDI did not affect the odds of receiving a biologic agent. The odds of receiving biologic therapy decreased 0.962 (CI 0.946, 0.978) with each year of age (Fig 3).

Conclusion: In a large multiethnic cohort of patients with AS, biologic therapy was prescribed more often for males, Non-Hispanic Blacks and Latinx. Low SES, measured by SDI, and insurance status did not affect the odds of receiving a biologic agent. This study suggests that SES did not prevent patients with AS from receiving biologic therapy. The reasons for differential prescribing by race/ethnicity would benefit from further study.

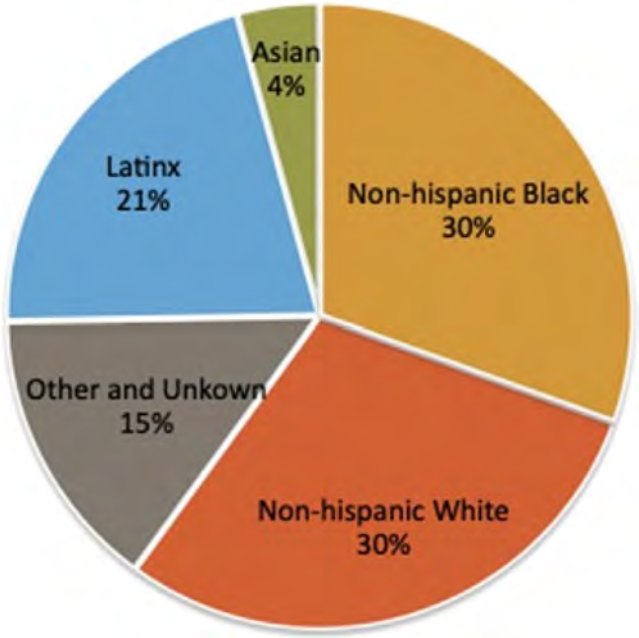

Figure 1. Race/Ethnicity Distribution of Cohort

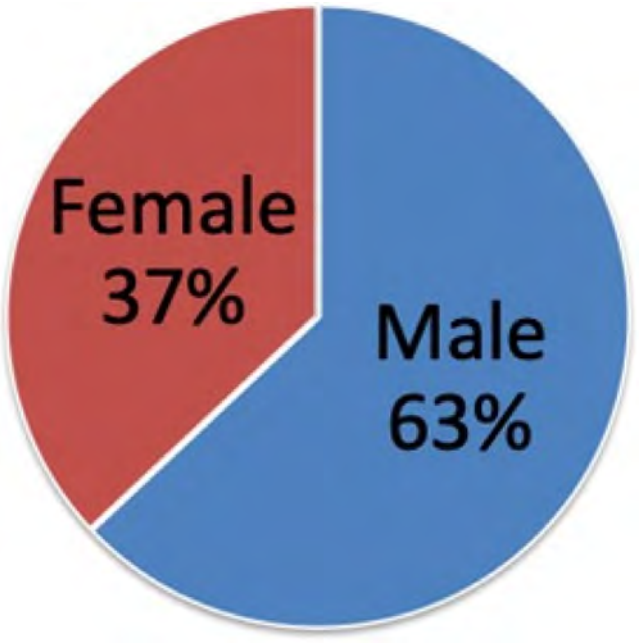

Figure 2. Sex Distribution of Cohort

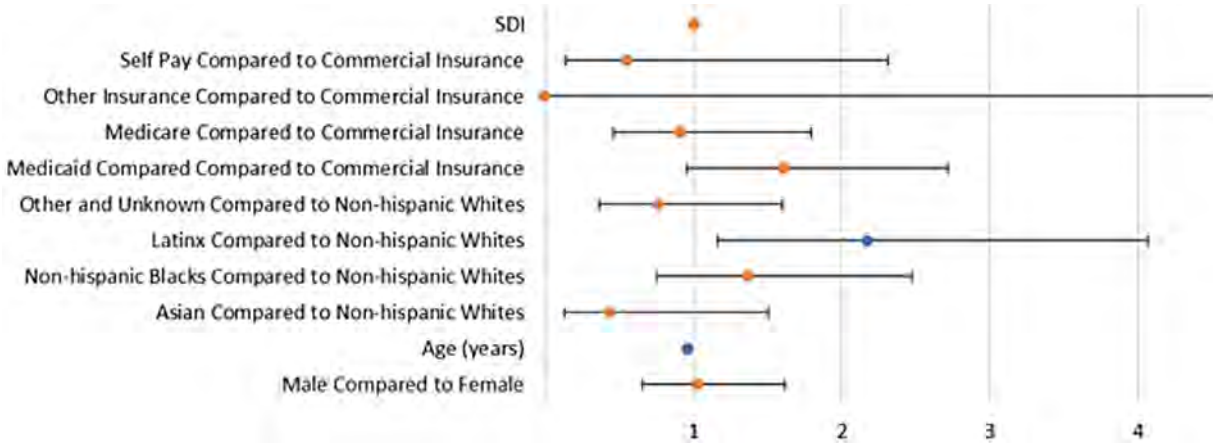

Figure 3. Odds Ratios for Biologic Prescription by Socioeconomic Factors

Disclosure: E. TROY: None; **Z. Chan**: None; **W. GALLANTER**: None; **E. Adams**: None; **M. Al-Awqati**: None; **H. Chang**: None.

Abstract Number: 0536

Asynchronous Tele Consultation by WhatsApp Chatbot in Controlled Axial Spondyloartrhitis Patients Under Biological Therapy: Patients Perspective

Maria Luz Garcia Vivar[1], elena abad plou[2], Natalia Rivera[3], Eva Galindez-Agirregoikoa[1], Eduardo Cuende[4], Ana Rosa Intxaurbe[5], Juan M Blanco Madrigal[1], Lucia Vega-Alvarez[1], Carmen Lucia Garcia-Gomez[6], Maria Enjuanes-Noguero[7], Olaia Fernandez-Berrizbeitia[8], Maria Rosa Exposito Molinero[9], Maria Esther Ruiz Lucea[1], Ignacio Torre Salaberri[5] and iñigo Gorostiza Hormaeche[1], [1]Basurto University Hospital, Bilbao, Spain, [2]Hospital universitario de Basurto, Bilbo, Spain, [3]Biocruces Bizkaia Health Research Institute, Research area, Bilbao, Spain, [4]Basurto University Hospital, Rheumatology, Madrid, Spain, [5]Basurto University Hospital, Rheumatology, Bilbao, Spain, [6]Basurto University Hospital, Rheumatology, Terrassa, Spain, [7]Hospital Universitario de Basurto, Bilbao, Spain, [8]Spanish Health Care Service, Bilbao, Spain, [9]Hospital de Basurto, Bilbao, Spain

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Before COVID pandemic, rheumatologists were not confident with telehealth for the need to adquire new technology, need of specific training and poorer reimbursement (1). Two groups of rheumatoid arthritis (RA) patients have been identified in a study of PROMS-based telehealth use (2): the keen and the reluctant.

Explore the degree of acceptance of asynchronous telehealth followup with whatsapp platform chatbot among our controlled AxSPA patients under biological therapy, and to search for a patient profile more prone to telehealth consultation

Methods: A prospective study with retrospective control was performed, choosing AxSPA patients under biological therapy with stable disease, visited in our center from 01/01 to 30/11/2021. We recruited 62 patients, but finally include 60 (2 quit for personal reasons). We offered them two teleconsultation visits (using their personal mobile), every f4 months, and a presential final visit one year after inclusion. The chatbot sends PROMS (BASDAI, VAS for patient global disease assessment,

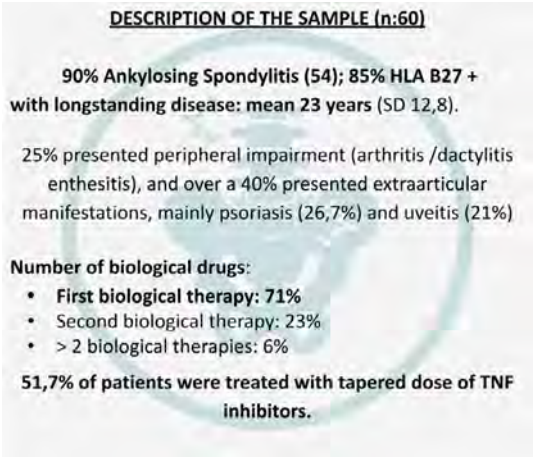

Image 1

ASDAS, and 3 questions for extraarticular disease), and feedback and schedule for the following visits. In the case of lab test or PROMs deviation or when the patient asks for contact, it is phoned by nurse/doctor who solves the question and/or arranges an additional presential visit. We collect patient and disease characteristics (age, gender, educational level, employment, disease activity, duration and treatments), and patient´s satisfaction and preferences in the final visit.

Results: We included 60 patients (Image 1).

At inclusion 93,3% were at remission/LDA by ASDAS/BASDAI-RCP and 4 patients were considered clinically controlled in spite of higher scores. At follow-up 3 patients with reduced dose needed to increase to standard dose of biological drug. There was no worsening from basal to final visits according BASDAI, BASFI, ASDAS-RCP or AsQOL.

Patients final VAS score (1-10) assessment of telehealth consultation was high: mean 9,14 (DS 1,498); 91.7% ≥ 8 and 76.7% ≥ 9.

83,3% preferred telehealth follow-up. There was a trend towards telehealth preferences in higher educational levels, and active working (86% vs 70%) but not statistically significant. We found no correlation with gender, age and disease characteristics tested.

Conclusion: Asynchronous teleconsultation seems promising, not inferior to presential consultation and preferred for follow-up by our AxSpa patients with stable disease with biological drugs . We met some "reluctant patients", that were more inactive working and with lower educational levels, but the differences were not significant. Further reserarch is needed with this telehealth model in other age and disease populations (RA), in order to characterize the reluctant and keen patients.

References:

Muehlensiepen F, et al. Acceptance of Telerheumatology by Rheumatologists and General Practitioners in Germany: Nationwide Cross-sectional Survey Study. J Med Internet Res. 2021 Mar 29;23(3):e23742.
Knudsen LR, et al. Experiences With Telehealth Followup in Patients With Rheumatoid Arthritis: A Qualitative Interview Study. Arthritis Care Res (Hoboken). 2018 Sep;70(9):1366-1372.

Disclosure: M. Garcia Vivar: None; **e. abad plou**: None; **N. Rivera**: None; **E. Galindez-Agirregoikoa**: None; **E. Cuende**: None; **A. Intxaurbe**: None; **J. Blanco Madrigal**: None; **L. Vega-Alvarez**: None; **C. Garcia-Gomez**: None; **M. Enjuanes-Noguero**: None; **O. Fernandez-Berrizbeitia**: None; **M. Exposito Molinero**: None; **M. Ruiz Lucea**: None; **I. Torre Salaberri**: None; **i. Gorostiza Hormaeche**: None.

Abstract Number: 0537

Asynchronous Teleconsultation by WhatsApp Chatbot in Controlled Axial Spondyloartrhitis Patients Under Biological Therapy as a More Sustainable Model Than Face-to-face Classical Consultation

Natalia Rivera[1], elena abad plou[2], Eva Galindez-Agirregoikoa[3], Eduardo Cuende[4], Ana Rosa Intxaurbe[5], Juan M Blanco Madrigal[3], Lucia Vega-Alvarez[3], Carmen Lucia Garcia-Gomez[6], Maria Enjuanes-Noguero[7], Olaia Fernandez-Berrizbeitia[8], Maria Rosa Exposito Molinero[9], Maria Esther Ruiz Lucea[3], Ignacio Torre Salaberri[5], iñigo Gorostiza Hormaeche[3] and Maria Luz Garcia Vivar[3], [1]Biocruces Bizkaia Health Research Institute, Research area, Bilbao, Spain, [2]Hospital universitario de Basurto, Bilbo, Spain, [3]Basurto University Hospital, Bilbao, Spain, [4]Basurto University Hospital, Rheumatology, Madrid, Spain, [5]Basurto University Hospital, Rheumatology, Bilbao, Spain, [6]Basurto University Hospital, Rheumatology, Terrassa, Spain, [7]Hospital Universitario de Basurto, Bilbao, Spain, [8]Spanish Health Care Service, Bilbao, Spain, [9]Hospital de Basurto, Bilbao, Spain

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Before COVID pandemic, telehealth use for the followup of rheumatic disease patients had been limited, but nowadays it appears as a more sustainable model of consultation, as it seems to be time and resources sparing for the patiens and the healthcare system.

Prove that the use of asynchronous telehealth followup with whatsapp platform chatbot among our controlled AS patients under biological therapy, was less time (and resource) consuming for the patient and the system.

Methods: A prospective study with retrospective control was performed, choosing AxSPA patients under biological therapy with stable disease, visited in our centre from 01/01 to 30/11/2021. We recruited 62 patients, but 2 quit for home moving or personal reasons. We offered them 2 teleconsultation visits (using their personal mobile), every 4 months, and a presential final visit one year after inclusion. The chatbot sends PROMS (BASDAI, VAS for patient global disease assessment, ASDAS, and 3 questions for extraarticular disease), and feedback and schedule for the following visits. In case of lab test or PROMs deviation or when the patient asks for contact, it is phoned by nurse/doctor who solves the question and/or arranges an additional presential visit. We collect patient and disease characteristics (age, gender, educational level, employment, disease activity, duration and treatments), patients preferences, and number of presential visits and phone calls from the year previous to inclusion.

Results: We included 60 patients (83,3% men), mean aged 48,22 years (SD 12,128), 36% under 45 years at inclusion. 83.3% were active working and only 10 patients were jobless or retired. They were Ankylosing Spondylitis (AS) (90%), HLA B27 positive (85%) with longstanding disease (mean 23 years, SD 12,8), and were receiving the first (71%), or the second (23%) biological therapy (51,7% tapered anti-TNF). 25% presented peripheral impairment, and over 40% extraarticular manifestations.

At inclusion 93,3% were at remission/LDA by ASDAS/BASDAI-RCP and 4 patients were considered clinically controlled in spite of higher scores. At followup 3 patients with reduced dose needed to increase to standard dose of biological drug, with no other need of treatment change. There was no worsening from basal to final visits according BASDAI, BASFI, ASDAS-RCP or AsQOL. Patients final VAS score (1-10) assesment of telehealth consultation was high: mean 9,14 (DS 1,498) and 83,3% preferred telehealth followup.

In this study we spared 62% presential visits (Only needed 70, 60 scheduled and 12 additional). Patients estimated time needed for presential consultation was 90 +/- 30 minutes including approach to hospital and waiting times. For the health-care team, time needed for whatsapp consultation was 1/3 from the needed for presential consultation.

Conclusion: Asynchronous telehealth followup with whatsapp platform chatbot in our controlled AxSPA patients under biological therapy resulted time sparing for the patient and the system, as it reduces time in presential consultation. The use of this model of telehealth approach in an enviroment different from a clinical study is needed for more precise saving estimates.

Disclosure: N. Rivera: None; **e. abad plou**: None; **E. Galindez-Agirregoikoa**: None; **E. Cuende**: None; **A. Intxaurbe**: None; **J. Blanco Madrigal**: None; **L. Vega-Alvarez**: None; **C. Garcia-Gomez**: None; **M. Enjuanes-Noguero**: None; **O. Fernandez-Berrizbeitia**: None; **M. Exposito Molinero**: None; **M. Ruiz Lucea**: None; **I. Torre Salaberri**: None; **i. Gorostiza Hormaeche**: None; **M. Garcia Vivar**: None.

Abstract Number: 0538

The Challenge of Identifying Difficult-To-Treat Axial Spondyloarthritis in Clinical Practice: Results from La Paz-SpA Cohort

Manuel Juárez[1], Diego Benavent[2], Victoria Navarro-Compán[3], Mariana Díaz-Almirón[4], Marta Novella-Navarro[5], Diana Peiteado[1], Alejandro Villalba[1], Irene Monjo[6], Laura Nuño[7], Alejandro Balsa[5] and Chamaida Plasencia-Rodríguez[5], [1]Rheumatology Department, La Paz University Hospital, Madrid, Spain, [2]Hospital la Paz, Madrid, Spain, [3]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain, [4]Biostatistics Unit, IdiPAZ, La Paz University Hospital, Madrid, Spain, [5]Hospital Universitario La Paz, Madrid, Spain, [6]University Hospital La Paz, Madrid, Spain, [7]Hospital Universitario La Paz - IdiPAZ, Madrid, Spain

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite multiple pharmacological options for axSpA are available, still one out of three patients do not achieve the recommended treatment target (1), highlighting the need to understand better the difficult-to-treat (D2T) axSpA profile. The aim of this study was to identify the characteristics of D2T-axSpA patients compared to "good responders" (GR) and determine predictive factors for D2T-axSpA.

Methods: Data from an observational prospective cohort recruiting consecutively patients diagnosed of axSpA initiating the first bDMARD from La Paz University Hospital between 2004 and 2019 were analysed. Patients were classified as D2T if they failed to at least two b/tsDMARDs or as GR if they continued treatment with the first bDMARD for at least 3 years or stopped it due to disease control. Clinical characteristics, laboratory tests, concomitant treatment and disease activity measures prior to starting the first bDMARD (baseline) and after 6 months were collected. Also, b/tsDMARD courses were registered. Chi-square or Fisher test and unpaired t-student were used for descriptive analyses. Logistic regression models

Table 1. Stratified characteristics. Results are shown as absolute numbers (percentages) or mean ± standard deviation.

	D2T (n=42)	GR (n=59)	p value
Age (years)	40.7±11	44.7±12.4	0.1
Male sex	21 (50)	38 (64.4)	0.1
Current smoking habit	13 (31)	7 (11.9)	<0.05*
Symptom duration until first bDMARD (year)	5.5±7.7	10.5±10.7	<0.01*
HLA-B27 +	27 (64.3)	48 (82.8)	<0.05*
Enthesitis	40 (95.2)	35 (59.3)	<0.001*
IBD	6 (14.3)	2 (3.4)	<0.05*
Comorbidities			
Hypertension	20 (47.6)	15 (25.4)	<0.05*
Dyslipidemia	28 (66.7)	23 (39)	<0.01*
Depression or anxiety	23 (54.8)	14 (23.7)	<0.01*
Fibromyalgia	6 (14.3)	1 (1.7)	<0.05*
Concomitant NSAIDs	35 (97.2)	43 (81.1)	<0.05*
Baseline			
ASDAS	3.6±0.9	3.3±1	0.2
BASDAI	6.4±1.7	5.6±2.1	0.06
BASDAI-spinal pain	7.5±2.1	6.4±2.7	<0.05*
BASDAI-stiffness severity	7.1±2.5	5.9±2.8	<0.05*
BASDAI-stiffness duration	6.1±2.8	4.7±2.7	<0.05*
TJC	4.4±6.7	1.1±2.7	<0.01*
PtGA	70.4±18.7	59.9±22.4	<0.05*
PhyGA	50±20.2	39.9±19.7	<0.05*
6-month			
ASDAS	2.8±1.1	1.6±0.9	<0.001*
BASDAI	5.4±2	3.3±2.1	<0.001*
CRP (mg/L)	5.9±7.9	1.7±2.7	<0.01*

(*): statistically significant differences (p<0.05), IBD: inflammatory bowel disease, NSAIDs: nonsteroidal anti-inflammatory drugs, ASDAS: Ankylosing Spondylitis Disease Activity Score, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, TJC: tender joint count, PtGA: patient global activity, PhyGA: physician global activity, CRP: C-reactive protein.

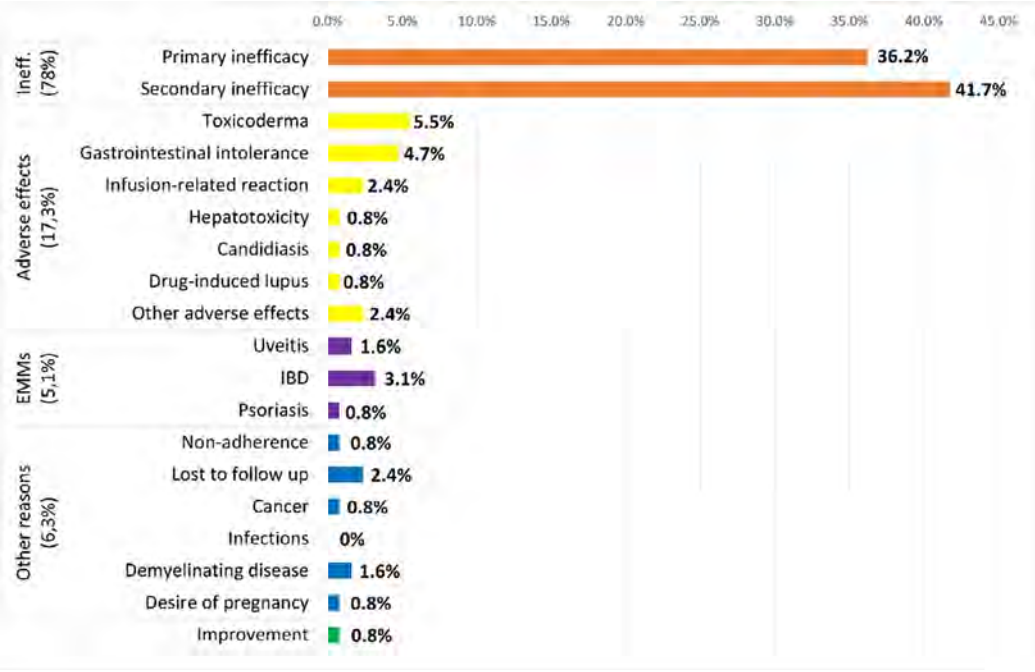

Figure 1. Reasons for b/tsDMARD discontinuation in D2T-axSpA patients.

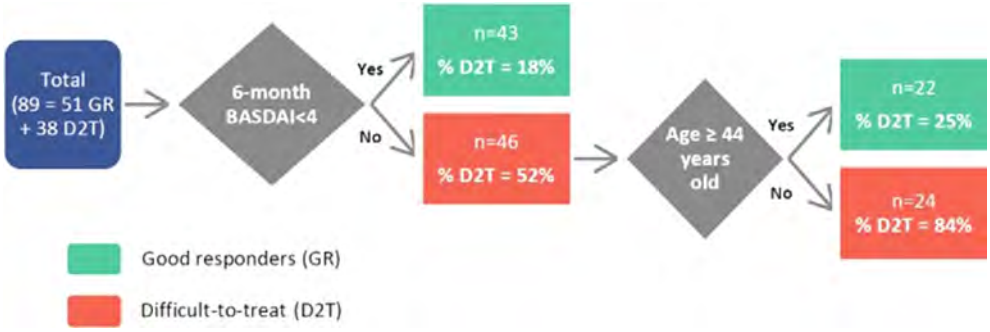

Figure 2. CART predicting probability of D2T-axSpA patients. The value at the terminal node represents the most frequently expected value (D2T vs. GR).

were used to identify associated factors with D2T-axSpA. Finally, a Classification And Regression Tree ('CART') was created to predict D2T-axSpA.

Results: Out of 101 patients included, 42 (41.6%) were classified as D2T and 59 (58.4%) as GR. D2T patients were more frequently HLA-B27 negative and smokers, had significant shorter symptom duration and more enthesitis, IBD, concomitant NSAIDs and comorbidities (hypertension, dyslipidemia, depression or anxiety and fibromyalgia) (**Table 1**). However, no significant differences were found in age, sex, BMI, dactylitis, arthritis, uveitis, psoriasis, concomitant csDMARDs, diabetes mellitus or cardiopathy. Furthermore, while no differences were found for disease activity composite measures (ASDAS, BASDAI) and CRP or ESR at baseline, D2T patients had greater scores in BASDAI questions for pain and morning stiffness, TJC, PtGA and PhyGA. After 6 months of starting the first bDMARD, the scores for all disease activity measures, including ASDAS, BASDAI, CRP and ESR were significantly higher in D2T patients. Reasons for b/tsDMARDs discontinuation in D2T patients are shown in **Figure 1**. Two different multivariable models were obtained due to collinearity between ASDAS and BASDAI/CRP.These multivariable logistic regression models showed that 6-month BASDAI (odds ratio [OR]=1.49, p=0.001) and 6-month CRP (OR=1.15, p< 0.05) or 6-month ASDAS (OR=3.16, p< 0.001) were independently associated with D2T-axSpA. The CART model (**Figure 2**), incorporating 6-month BASDAI and age at diagnosis, demonstrated the best predictive performance, with an area under the curve (AUC) of 0.84 (95% confidence interval 0.87-1).

Conclusion: D2T-axSpA patients often have known predictors of poor therapeutic response (smoking and HLA-B27 negative) and worse response to first bDMARD already after 6 months. Disease activity at this point is independently associated with failure to consecutive b/tsDMARDs. The proposed CART model is simple to apply and useful for predicting D2T-axSpA after 6 months of bDMARD therapy.

References:

1. Smolen JS, et al. Ann Rheum Dis. 2018.

Disclosure: M. Juárez: None; **D. Benavent**: Abbvie, 5, Galapagos, 6, Janssen, 6, Novartis, 5, Roche, 6; **V. Navarro-Compán**: AbbVie, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, Janssen, 6, MoonLake, 2, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6; **M. Díaz-Almirón**: None; **M. Novella-Navarro**: Galapagos, 6, Janssen, 5, 6, Lilly, 5, 6, UCB, 5, 6; **D. Peiteado**: None; **A. Villalba**: None; **I. Monjo**: Amgen, 6, Gedeon Richter, 6, Janssen, 6, Novartis, 6, Roche, 6, UCB, 6; **L. Nuño**: None; **A. Balsa**: AbbVie/Abbott, 1, 2, 5, 6, Bristol-Myers Squibb(BMS), 1, 5, Eli Lilly, 1, 5, 6, Merck/MSD, 1, 5, Novartis, 5, Pfizer, 1, 5, 6, UCB, 1, 5, 6; **C. Plasencia-Rodríguez**: Abbvie, 5, 6, Eli Lilly, 6, Novartis, 5, Pfizer, 5, 6, Roche, 6.

Abstract Number: 0539

Impact of Extreme Baseline BASDAI and/or Maastricht AS Enthesitis Score on Treatment Response to Upadacitinib in Patients with Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Axial SpA (axSpA) and FM manifest with overlapping clinical features such as pain, fatigue, and stiffness, yet their treatment is distinctly different. FM is a comorbidity with axSpA in 4–21% of patients (pts), and extreme BASDAI pain and fatigue scores have been suggested as surrogate markers for FM[1]. The Janus kinase inhibitor upadacitinib (UPA) is approved for the treatment of AS and non-radiographic axSpA (nr-axSpA), and has demonstrated efficacy in pts with axSpA in the Phase 3 SELECT-AXIS 2 study through 14 weeks (wks) of treatment[2,3]. The objective of this post hoc analysis was to compare the baseline (BL) characteristics of pts with extreme or non-extreme BL BASDAI and/or Maastricht AS Enthesitis Score (MASES) and to assess the efficacy of UPA vs placebo (PBO) in these subgroups.

Methods: The SELECT-AXIS 2 program was comprised of 1 study of pts with active nr-axSpA (PBO-controlled for 52 wks) and 1 study of pts with active AS and inadequate response to biologic DMARDs (PBO-controlled for 14 wks). Pts with a concomitant diagnosis of active FM according to the treating physician were excluded. The primary endpoint in both studies was ≥40% improvement in Assessment of SpA international Society score (ASAS40) at wk 14. Subgroup analysis was performed on pooled data: 'extreme BASDAI' was defined as a score of ≥8 for ≥3/5 BASDAI components, and 'extreme MASES' was defined as a score of ≥10; cutoffs reflected the top quartile range of each measure. Demographics and disease characteristics were summarized descriptively. Efficacy measures were evaluated at wk 14 and reported using non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19; statistical comparisons were adjusted for screening high-sensitivity CRP level and study.

Results: Overall, 732 pts were evaluated, including 275 with extreme scores (PBO, n=135; UPA, n=140) and 457 with non-extreme scores (PBO, n=230; UPA, n=227). At BL, of the 275 extreme pts, 232 (84.4%) met BASDAI criteria only, 19 (6.9%) met MASES criteria only, and 24 (8.7%) met both criteria. Compared with non-extreme pts, more extreme pts were female, ≥40 years old, and had higher BL rates of anxiety/depression (validated cutoff scores from EuroQol-5D-5L, 43.9% vs 22.2% for extreme vs non-extreme pts with UPA), pain (Pt's Assessment of Pain, 8.4 and 6.8, respectively), and fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue, 21.7 and 30.5, respectively; Table). Regardless of extreme or non-extreme scores at BL, UPA demonstrated improvement across multiple disease activity outcomes vs PBO at wk 14 including ASAS40 ($p< 0.0001$; Figure). Extreme pts reported a numerically lower efficacy response within both UPA and PBO treatment groups at wk 14 vs non-extreme pts.

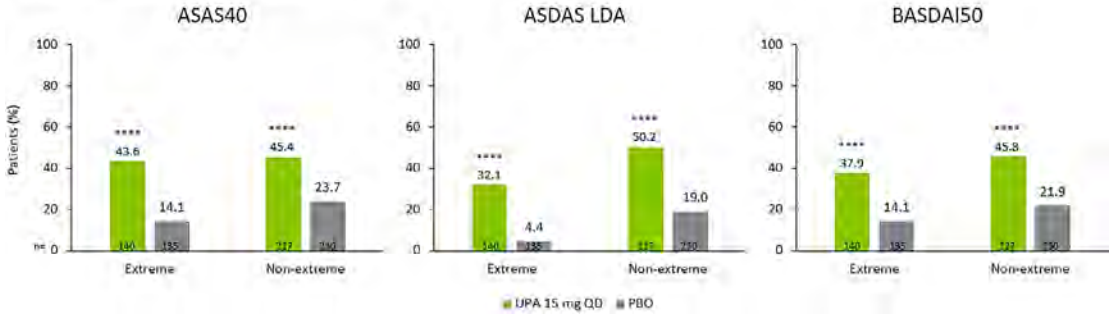
Conclusion: Pts with axSpA and extreme BL BASDAI/MASES reported higher BL rates of anxiety/depression, pain, and fatigue than those with non-extreme scores. UPA demonstrated greater efficacy than PBO among pts with both extreme and non-extreme BL BASDAI/MASES scores.

Table. Baseline demographics of patients from SELECT-AXIS 2 with extreme or non-extreme scores of spontaneous pain or tenderness at baseline

	Extreme[a]			Non-extreme[b]		
	PBO (n=135)	UPA 15 mg QD (n=140)	Total (n=275)	PBO (n=230)	UPA 15 mg QD (n=227)	Total (n=457)
Age, n (%)						
<40 years	51 (37.8)	54 (38.6)	105 (38.2)	107 (46.5)	105 (46.3)	212 (46.4)
≥40 years	84 (62.2)	86 (61.4)	170 (61.8)	123 (53.5)	122 (53.7)	245 (53.6)
Female, n (%)	65 (48.1)	65 (46.4)	130 (47.3)	80 (34.8)	82 (36.1)	162 (35.4)
Prior bDMARDs, n (%)						
No prior bDMARDs	26 (25.2)	18 (18.8)	44 (22.1)	28 (17.7)	31 (18.9)	59 (18.3)
TNF inhibitor	56 (54.4)	55 (57.3)	111 (55.8)	101 (63.9)	99 (60.4)	200 (62.1)
IL-17 inhibitor	8 (7.8)	12 (12.5)	20 (10.1)	16 (10.1)	17 (10.4)	33 (10.2)
Other	13 (12.6)	11 (11.5)	24 (12.1)	13 (8.2)	17 (10.4)	30 (9.3)
Concomitant antidepressants, n (%)	7 (5.2)	8 (5.7)	15 (5.5)	8 (3.5)	8 (3.5)	16 (3.5)
Concomitant anxiolytics, n (%)	5 (3.7)	5 (3.6)	10 (3.6)	8 (3.5)	9 (4.0)	17 (3.7)
Concomitant opioids, n (%)	22 (16.3)	11 (7.9)	33 (12.0)	10.4 (4.3)	4 (1.8)	14 (3.1)
Disease activity outcomes and PROs						
BASDAI score, mean (SD)	8.0 (0.7)	7.9 (1.0)	8.0 (0.9)	6.2 (1.0)	6.1 (1.0)	6.2 (1.0)
MASES (baseline enthesitis), mean (SD)[c]	5.8 (3.7)	5.8 (3.5)	5.8 (3.6)	3.5 (2.3)	4.0 (2.4)	3.7 (2.4)
EQ-5D-5L Anxiety/Depression, n (%)	65 (48.5)	61 (43.9)	126 (46.2)	72 (31.7)	50 (22.2)	122 (27.0)
Pt-Pain, mean (SD)	8.3 (0.9)	8.4 (1.1)	8.3 (1.0)	6.9 (1.2)	6.8 (1.3)	6.8 (1.3)
FACIT-F, mean (SD)[d]	21.6 (7.9)	21.7 (8.5)	21.6 (8.2)	30.5 (9.5)	30.5 (9.1)	30.5 (9.3)

aAS, n=155; nr-axSpA, n=120. bAS, n=264; nr-axSpA, n=193. cExtreme: PBO, n=114; UPA, n=122; total, n=236. Non-extreme: PBO, n=173; UPA, n=151; total, n=324. dExtreme: PBO, n=134; UPA, n=138; total, n=272. Non-extreme: PBO, n=225; UPA, n=223; total, n=448. AS, ankylosing spondylitis; BASDI, Bath Ankylosing Spondylitis Disease Activity Index; bDMARD, biologic disease-modifying antirheumatic drug; EQ-5D-5L, EuroQoL-5D-5L; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; IL, interleukin; MASES, Maastricht AS Enthesitis Score; nr-axSpA, non-radiographic axial spondyloarthritis; PBO, placebo; PRO, patient-reported outcome; Pt-Pain, Patient's Assessment of Pain; QD, once daily; SD, standard deviation; TNF, tumor necrosis factor; UPA, upadacitinib.

Figure. Disease activity outcomes at week 14 in patients with or without extreme scores of spontaneous pain or tenderness at baseline (NRI-MI)



****p<0.0001 for UPA 15 mg vs PBO. ASDAS(CRP) LDA defined as <2.1. Data are based on NRI-MI, adjusted for screening hsCRP level and study. ASAS40, ≥40% improvement in Assessment of SpondyloArthritis International Society score; ASDAS, Ankylosing Spondylitis Disease Activity Score; ASDAS-CRP, ASDAS with CRP; BASDAI50, ≥50% improvement in Bath Ankylosing Spondylitis Disease Activity Index; hsCRP, high-sensitivity CRP; LDA, low disease activity; NRI-MI, non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19; PBO, placebo; QD, once daily; UPA, upadacitinib.

References:

1. Santos-Faria D, et al. Rheumatol Int 2019;39:141–6
2. Deodhar A, et al. Lancet 2022:400;369–79
3. Van der Heijde D, et al. Ann Rheum Dis 2022;81:1515–23

Disclosure: M. Dougados: AbbVie, 2, 5, 12, Contracts, Eli Lilly, 2, 5, 12, Contracts, Novartis, 2, 5, 12, Contracts, Pfizer, 2, 5, 12, Contracts, UCB, 2, 5, 12, Contracts; **D. Bulbin**: AbbVie/Abbott, 2, 6, Alexion, 2, 6, Amgen, 2, 6, Novartis, 2, Sanofi Genzyme, 6; **H. Jones**: AbbVie, 3, 11; **T. Gao**: AbbVie, 3, 11; **A. Shmagel**: AbbVie, 3, 11; **T. Poznanski**: AbbVie, 3; **A. Danve**: AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5; **K. Gaffney**: AbbVie, 2, 5, 6, Eli Lilly, 2, 5, 6, Gilead, 5, Novartis, 2, 5, 6, UCB Pharma, 2, 5, 6.

Abstract Number: 0540

The Impact of Baseline BMI and Physical Activity on Upadacitinib Treatment Response: A Post Hoc Analysis of Patients with Ankylosing Spondylitis from the SELECT-AXIS 2 Study

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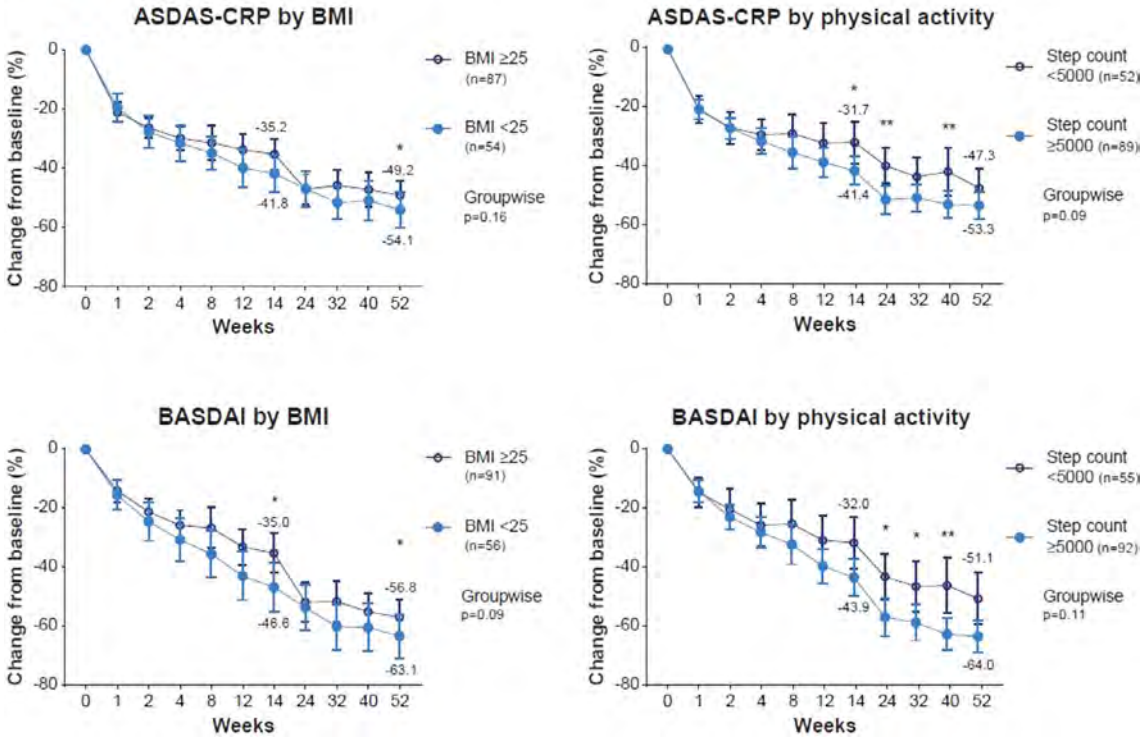
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In patients (pts) with AS, higher BMI has been linked to higher disease activity[1]. However, given that BMI can be a poor indicator of body composition, using BMI alongside digital devices that can measure physical activity (PA) may be a more comprehensive measure of fitness. To better understand the impact of BMI and PA on treatment response, we evaluated outcomes in pts with AS treated with upadacitinib (UPA) 15 mg once daily through 52 weeks (wks) of the Phase 3 SELECT-AXIS 2 trial (NCT04169373), stratified by baseline (BL) BMI and level of PA[2].

Methods: Pts with active AS and inadequate response to biologic DMARDs in SELECT-AXIS 2 were required to wear a wrist-worn actigraphy device that remotely monitored PA during the 14-wk, placebo-controlled portion of the study. In this post hoc analysis, we evaluated Ankylosing Spondylitis Disease Activity Score with CRP (ASDAS-CRP) and BASDAI scores at wk 52 among pts who received continuous UPA for 52 wks stratified by BL PA (inactive [< 5000 steps/day] or active [≥5000 steps/day])[3] and BMI (overweight/obese [BMI ≥25 kg/m^2] or healthy weight/underweight [BMI < 25 kg/m^2]). BL step count was calculated by mean daily step counts for wk 1 in pts with at least 3 days of wearable device adherence, and at least 16 hours/day of wear time. One-way analysis of variance was used to investigate the association of ASDAS-CRP and BASDAI scores at each time point through wk 52 with each BL category; significant variables ($p< 0.05$) were then analyzed using a mixed model for repeated measures. A Student's t-test with Welch's correction was used to assess ASDAS-CRP or BASDAI scores in each combination of BL BMI and PA.

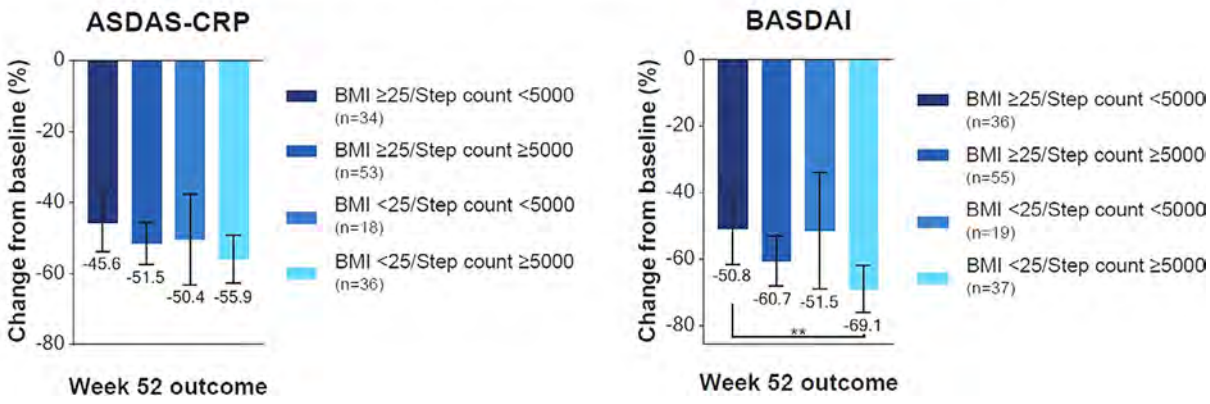
Results: Data were available from 141 pts for ASDAS-CRP and 147 pts for BASDAI who wore the actigraphy device. While no statistical differences in change from BL in ASDAS-CRP or BASDAI were observed between subgroups at wk 52, pts who were healthy weight/underweight or active at BL demonstrated a trend toward greater reduction in ASDAS-CRP and BASDAI scores at most time points from wk 8 onwards vs pts who were overweight/obese or inactive (Figure 1). When BL subgroups were considered concurrently, pts who were healthy weight/underweight and active at BL achieved significantly greater reduction in BASDAI scores over 52 wks vs pts who were overweight/obese and inactive (nominal p< 0.01;

Figure 1. Change from baseline in ASDAS-CRP and BASDAI stratified by baseline BMI or physical activity levels



*p<0.05; **p<0.01. As observed data, excluding missing data due to COVID-19. Error bars denote 95% confidence intervals. ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score with CRP; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index.

Figure 2. Change from baseline in ASDAS-CRP and BASDAI among each stratified combination of baseline BMI and physical activity



**p<0.01. As observed data, excluding missing data due to COVID-19. Error bars denote 95% confidence intervals. ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score with CRP; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index.

Figure 2). No significant differences were reported between pts with any other combination of BL BMI and PA for ASDAS-CRP or BASDAI.

Conclusion: Pts with active AS receiving UPA for 52 wks who were active or healthy weight/underweight at BL generally experienced greater decreases from BL in ASDAS-CRP and BASDAI vs pts who were inactive or overweight/obese. Pts with active AS receiving UPA who were active tended to have numerically greater improvements in disease activity vs pts who were inactive, regardless of BMI. BMI and PA together may offer a more clinically relevant way to determine outcomes than either measure alone.

References:

1. Liew JW, et al. RMD Open 2020;6:e001225
2. Van der Heijde D, et al. Lancet 2022;400:369–79
3. Tudor-Locke C, et al. Appl Physiol Nutr Metab 2013;38:100–14

Disclosure: A. Crowley: AbbVie, 5, 6, AstraZeneca, 2, Eli Lilly, 5, GlaxoSmithKlein(GSK), 6, Horizon, 6, Janssen, 6, Labcorp, 5, Novartis, 2, Set Point Medical, 5, SunPharma, 5, UCB, 2; **L. Siegel**: AbbVie, 2, 6, Amgen, 2, 6, Boehringer-Ingelheim, 2, 6, GlaxoSmithKlein(GSK), 2, 6, Novartis, 2, 6, Sanofi-Genzyme, 2, 6; **P. Wickersham**: AbbVie, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6; **H. Jones**: AbbVie, 3, 11; **D. Webster**: AbbVie, 3, 11; **A. Shmagel**: AbbVie, 3, 11; **A. Biljan**: AbbVie, 3, 11; **U. Kiltz**: AbbVie, 2, 5, 6, Amgen, 5, Biocad, 2, 6, Biogen, 5, Bristol-Myers Squibb(BMS), 2, 5, Chugai, 2, 6, Eli Lilly, 2, 6, Fresenius, 5, Gilead, 2, 5, GlaxoSmithKline (GSK), 5, Grünenthal, 2, 6, Hexal, 5, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, onkowiessen.de, 2, 5, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Viatris, 2, 5; **P. Helliwell**: Janssen, 12, fees for educational services, Novartis, 12, fees for educational services.

Abstract Number: 0541

Treat-to-Target Strategy Implementation in Spondyloarthritis Patients of Real-World Clinical Practice: A Cross-Sectional Single-Center Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Data regarding the adoption of the treat-to-target (T2T) approach aiming at inactive disease (ID), or low disease activity (LDA) in axial (axSpA) and peripheral Spondyloarthritis (perSpA) in real-world clinical practice is scarce. Our aims were to assess the level of disease activity of SpA patients in real-world practice, the extent of T2T strategy implementation and the reasons of possible non-implementation.

Methods: Cross-sectional study of all consecutive patients with SpA who visited the outpatient department or the one-day infusions' clinic of our hospital during a 7-month period (6/2021-12/2021). Detailed patient, disease and treatment characteristics were collected, as well as disease activity of axial (using ASDAS-CRP), peripheral (DAPSA) and extraarticular manifestations. Additionally, physicians filled-in questionnaires regarding treatment intensification or not (and reasons) in patients not in target at the specific visit. Multivariable logistic regression analysis was employed to identify predictors of therapy intensifications in patients not in target.

Results: We analyzed243 patients (54% males; AxSpA:187, perSpA:56)with median (IQR) age of 52 (42-61) and disease duration 4.1 (2.1-12.3) years. The main therapy in the majority of the patients (83%) was a biologic (b-)DMARD.In patients with AxSpA, median (IQR) ASDAS-CRP was 2.4 (1.7-3.1), while in perSpA patients, median (IQR) DAPSA score was 26 (12.4-36.2). Low disease activity or inactive disease (LDA/ID), taking into account axial and/or peripheral as well as extra-articular manifestations was found in 26% and 25% of the patients in AxSpA and perSpA respectively.

Of the patients not having at least LDA (N=181), 82 (45%) had their treatment intensified. Physician-documented reasons of non-intensification are shown in Figure. In multivariable analysis, the type of patients' main therapy [OR(95%CI) for non-bDMARD vs bDMARD:12.2 (4.8-41.4)], physician's VAS score [OR:1.22 (1.10-1.27)]and patients' VAS global score [OR:1.08 (1.02-1.12)]were predicting therapy intensifications in patients not in target.

Conclusion: In this real-world study, the majority of SpA patients had high disease activity levels. T2T strategy was implemented in approximately half of those patients, especially those on non-biologic main therapy and high physician VAS score.

Disclosure: I. Flouri: None; **N. Avgoustidis**: None; **A. Eskitzis**: None; **A. Repa**: None; **K. Pateromichelaki**: None; **S. Pitsigavdaki**: None; **M. Nikoloudaki**: None; **M. Terizaki**: None; **G. Bertsias**: None; **P. Sidiropoulos**: None.

Abstract Number: 0542

Two-Year Treatment Adherence and Clinical Response to Secukinumab Compared to TNF Inhibitors in Axial and Peripheral Spondyloarthritis Patients: A Single-Center Prospective Observational Study

Irini Flouri[1], Argyro Repa[2], Nestor Avgoustidis[2], Sofia Pitsigavdaki[3], Katerina Pateromichelaki[2], Maria Terizaki[2], George Bertsias[4] and Prodromos Sidiropoulos[4], [1]University of Crete Medical School, Heraklion, Greece, [2]Rheumatology, Clinical Immunology and Allergy Department, Medical School, University of Crete, Heraklion, Greece, [3]Rheumatology, Clinical Immunology and Allergy Department, Medical School, University of Crete, Crete, Greece, [4]Rheumatology, Clinical Immunology and Allergy Department, Medical School, University of Crete, Greece; Institute of Molecular Biology and Biotechnology, Foundation for Research and Technology Hellas (FORTH), Heraklion, Greece

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: AxSpA Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-IL17 agent secukinumab (SEC) has been proven effective and is widely used in the treatment of spondyloarthritis (SpA) patients alternatively to tumor necrosis factor inhibitors (TNFis). Our aim was to compare treatment retention and clinical responses at 2 years in SpA patients starting therapy with SEC versus TNFis in routine clinical care.

Methods: This was an analysis from UCRCR Registry, which is a prospective single center study. For the present study we analyzed all consecutive patients with axial (AxSpA) or peripheral SpA (pSpA), including psoriatic arthritis (PsA) starting or switching bDMARD therapy, either a TNFi or SEC from 1/2016 till 12/2022. We excluded patients with IBD-related SpA, patients starting ustekinumab (or apremilast) and patients switching from a bio-originator to a biosimilar TNFi or vice versa. We compared disease activity scores improvement at 6 months using linear regression analysis and treatment retention using Kaplan-Meier survival curves with log-rank test and Cox regression, adjusting for diagnosis (AxSpA vs pSpA,), presence of psoriasis, age, sex, disease duration, treatment line, co-administered csDMARDs (yes/no), smoking status (ever/never) and rheumatic disease comorbidity index (RDCI).

Results: A total of 644 patients with SpA started/switched bDMARD (SEC:214, TNFis:430). SEC was the ≥3rd bDMARD in 49% of patients compared to 31% of TNFis (p< 0.001). AxSpA was the diagnosis in 62% patients starting SEC and 74% starting TNFis while psoriasis was more common with SEC (51% vs 33.5% in TNFis). Monotherapy was more common with

Table 1. Patients' characteristics at baseline

Table 1. Patients' characteristics at baseline (N=644)	Secukinumab N=214	TNFis N=430	p- value
Gender (female), N (%)	135 (63)	274 (64)	0.874
Age, years	52 (44-60)	52 (41-59)	0.077
Symptom duration, years	14 (6-32)	11 (5-26)	**0.026**
Disease duration since diagnosis, years	1 (0-5)	1 (0-4)	0.782
Diagnosis, N (%): AxSpA	132 (62)	319 (74)	**0.001**
Peripheral SpA	82 (38)	111 (26)	
Diagnosis, N (%): AxSpA (non PsA)	97 (45)	267 (62)	**<0.001**
PsA (AxPsA and pPsA)	109 (51)	137 (32)	
Peripheral SpA non PsA, non-IBD	8 (4)	26 (6)	
Extraarticular manifestations, N (%)	115 (61)	180 (51)	**0.024**
Psoriasis, N (%)	110 (51)	144 (33.5)	**<0.001**
Uveitis, N (%)	17 (8.5)	39 (10)	0.500
Peripheral arthritis, N (%)	176 (84)	340 (80)	0.242
Current smokers, N (%)	68 (36)	151 (41)	0.195
Nr of previous csDMARDs	1 (0-2)	1 (0-2)	0.339
Nr of previous bDMARDs	1 (0-3)	1 (0-2)	**<0.001**
Treatment line: 1st or 2nd, N (%)	109 (51)	298 (69)	**<0.001**
3rd or more	105 (49)	132 (31)	
Nr of co-administered csDMARDs	0 (0-1)	0 (0-1)	0.038
Co-administered Methotrexate, N(%)	56 (26)	145 (34)	**0.043**
Monotherapy , N (%)	140 (66)	243 (58)	**0.040**
Co-administered prednisolone, N(%)	17 (8)	44 (10)	0.332
RDCI	1 (0-2)	1 (0-2)	0.719
Total Comorbidities Count	2 (1-4)	2 (1-4)	0.820
No Comorbidities, N (%)	31 (15)	41 (11)	0.149
Fibromyalgia, N (%)	78 (36)	149 (35)	0.653
Obesity, N (%)	69 (34)	134 (35)	0.717
BMI	28 (25-33)	29 (25-33)	0.602
Education >6 years, N (%)	126 (76)	270 (81)	0.200
Employed, N (%)	96 (60)	165 (57)	0.578
Rural residence, N (%)	73 (40)	158 (45.5)	0.195
Follow-up time, months	11 (4-26)	10 (4-21)	0.171

Table 2. Disease activity at baseline

Table 2. Disease activity at baseline	Secukinumab	TNFis	p- value
A. Patients with Axial SpA	**N=132**	**N=319**	
BASDAI (0-10)	6.2 (4.9-7.3)	6.0 (4.8-7.3)	0.698
ASDAS-CRP	3.4 (3.0-3.9)	3.3 (2.8-3.8)	0.345
CRP (mg/dl)	0.4 (0.2-1)	0.4 (0.2-0.9)	0.159
ESR (mm/hr)	21 (11-35)	20 (13-35)	0.779
VAS global (0-100)	70 (60-80)	70 (60-80)	0.272
VAS pain (0-100)	70 (60-80)	70 (60-80)	0.451
Physician's global (0-100)	65 (50-75)	70 (50-75)	0.787
HAQ (0-3)	0.75 (0.5-1.2)	0.9 (0.6-1.1)	0.885
BASFI (0-10)	5.3 (3.7-6.9)	5.5 (2.9-7)	0.918
Tender joint count (0-68) [a]	7 (1-13)	5 (1-12)	0.356
Swollen joint count (0-66) [a]	8 (1-14)	6 (2-12)	0.106
DAS28-ESR [a]	4.2 (3.3-5.3)	4.2 (3.3-5.3)	0.977
DAPSA [a]	29 (18-44)	26 (16-39)	0.094
B. Patients with Peripheral SpA	**N=82**	**N=111**	
DAPSA	37 (26-47)	32 (20-48)	0.739
DAS28-ESR	4.9 (4.2-5.5)	4.6 (3.7-5.6)	0.305
VAS global (0-100)	70 (60-80)	70 (60-80)	0.845
VAS pain (0-100)	70 (60-80)	70 (60-80)	0.948
Physician's global (0-100)	70 (50-75)	64 (50-75)	0.203
HAQ (0-3)	1.0 (0.6-1.1)	0.8 (0.4-1.4)	0.521
Tender joint count (0-68)	9 (3-14)	7 (1-14)	0.245
Swollen joint count (0-66)	10 (4-15)	8 (2-15)	0.266
CRP (mg/dl)	0.3 (0.2-1.5)	0.4 (0.2-1.0)	0.924
ESR (mm/hr)	27 (14-43)	23 (14-40)	0.807

SEC compared to TNFis (66% vs 58%, p=0.04). All other patients' characteristics at baseline, including extraarticular manifestations (except psoriasis), comorbidities' indices and sociodemographics were similar in the two groups. Baseline disease activity in both AxSpA and peripheral SpA was also comparable in patients starting SEC and TNFi.

Unadjusted 2-year treatment retention was higher in patients receiving SEC compared to TNFi both overall (SEC: 60%, TNFi: 45%, p=0.004) and separately in AxSpA (SEC: 59.5%, TNFi: 48%, p=0.039) and pSpA patients (SEC: 61%, TNFi: 36.5%, p=0.020).

In adjusted analysis, SEC administration was an independent predictor for higher bDMARD retention overall [HR (95%CI) =0.61 (0.45-0.84), p=0.002] and separately in AxSpA [HR=0.65 (0.45-0.95), p=0.025] and in pSpA [HR=0.54 (0.31-0.93), p=0.028].

Mean BASDAI and ASDAS improvements at 6, 12, 18 and 24 months of treatment were similar in patients with AxSpA receiving SEC or TNFis [at 6 months, mean(SD) δBASDAI:0.9 (2.2) vs 1.3 (2.2) respectively (p=0.49) and δASDAS: 0.5 (0.9) vs 0.6 (1.0), p=0.75]. Similarly, in patients with pSpA, δDAPSA was comparable in the two groups at all timepoints [at 6 months, mean (SD)δDAPSA: 12.3 (21) vs 8.1 (11), p=0.294]. Adjusted analyses provided similar results to the unadjusted analyses in both axial and peripheral SpA.

Conclusion: In real-world SpA patients, administration of Secukinumab results in similar clinical responses but higher treatment retention compared to TNFis.

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Abstract Number: 0543

Sensitivity of the 2019 European Alliance of Associations for Rheumatology /American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus in a Population-based Cohort; A Study Set in Norway 2000-2015

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: To diagnose Systemic Lupus Erythematosus (SLE), one must understand the phenotype specter and interpret clinical, serological, radiological, and histopathological data, as well as exclude mimicking conditions. As diagnostic criteria for SLE currently are not within reach, patients are selected for research by classification criteria created to define homogeneous SLE-cohorts comparable across studies. This requires high specificity, which typically compromise the sensitivity. The new 2019 European Alliance of Associations for Rheumatology /American College of Rheumatology (ACR) classification criteria for SLE (2019 EA criteria) appears to be significantly more sensitive than the 1997 ACR criteria when applied on cohorts from referral centers/registries, especially for recent onset SLE. However, further studies are needed to confirm this highly promising sensitivity-improvement, not least in population-based SLE cohorts. We established a population-based cohort including all new-onset SLE cases during 1999-2017 in an area of 2.9 million inhabitants in Norway. Then we estimated the sensitivity of 1997 ACR- and 2019 EA criteria for adult cases diagnosed during 2000-2015.

Table 1A Comparative sensitivity of classification criteria in the adult incident SLE study population (2000-2015, N=647) N, number of cases in the study population; n1, number of cases fulfilling the criteria; n2, total number of cases at visit

	1997 ACR criteria % (n_1/n_2)	2019 EA criteria % (n_1/n_2)	95 % CI		p-value
			1997 ACR	2019 EA	
Total					
Time of diagnosis	77.2 (493/639)	91.2 (583/613)	0.74-0.80	0.90-0.93	p<0.001
Two-year follow up	82.5 (506/613)	92.7 (568/613)	0.80-0.86	0.91-0.95	p<0.001
Last visit	85.1 (525/617)	94.2 (581/617)	0.82-0.88	0.92-0.96	p<0.001
Female					
Time of diagnosis	79.1 (423/535)	92.3 (494/535)	0.76-0.83	0.90-0.95	p<0.001
Two-year follow up	83.6 (429/513)	93.6 (480/513)	0.80-0.87	0.91-0.96	p<0.001
Last visit	86.5 (447/517)	94.6 (489/517)	0.84-0.90	0.93-0.97	p<0.001
Male					
Time of diagnosis	67.3 (70/104)	85.6 (89/104)	0.58-0.76	0.79-0.92	p=0.002
Two-year follow up	77.0 (77/100)	88.0 (480/513)	0.69-0.85	0.82-0.94	p=0.041
Last visit	78 (78/100)	92.0 (92/100)	0.70-0.86	0.87-0.97	p=0.006

Table 1B Comparative sensitivity of sex in the adult incident SLE study population (2000-2015, N=647) N, number of cases in the study population; n1, number of cases fulfilling the criteria; n2, total number of cases at visit

	Female % (n_1/n_2)	Male % (n_1/n_2)	95 % CI		p-value
			Female	Male	
1997 ACR criteria					
Time of diagnosis	79.1 (423/535)	67.3 (70/104)	0.76-0.83	0.58-0.76	p 0.009
Two-year follow up	83.6 (429/513)	77.0 (77/100)	0.80-0.87	0.69-0.85	p=0.120
Last visit	86.5 (4477517)	78.0 (787100)	0.84-0.89	0.70-0.86	p=0.030
2019 EA criteria					
Time of diagnosis	92.3 (494/535)	85.6 (89/104)	0.90-0.95	0.79-0.92	p=0.026
Two-year follow up	93.6 (480/513)	88.0 (88/100)	0.91-0.96	0.82-0.94	p=0.051
Last visit	94.6 (489/517)	92.0 (92/100)	0.93-0.97	0.87-0.97	p=0.313

Methods: The cohort included all cases (all ages) ICD-10 coded as SLE in the study area during 1999-2017. All cases were chart-reviewed to confirm/reject SLE diagnosis and assess classification-criteria items at time of diagnosis, and prospectively. At study end, 84% vs. 94% of cases in the total incident cohort fulfilled 1997 ACR- vs. 2019 EA criteria. Applying SLE diagnosis as "gold standard", sensitivity of 1997 ACR- vs. 2019 EA criteria was compared at diagnosis, at two years disease duration, and at study end, in adult incident SLE cases diagnosed during 2000-2015. All tests were two-sided and a 5% significance level was used. We applied 2015 as study end to have complete two-year data, and 2000 as study start as 29 cases diagnosed in 1999 lacked complete follow-up data due to technical reasons.

Results: After chart-review the population-based adult SLE cohort included 647 cases with new-onset disease diagnosed during 2000-2015. In this cohort the 2019 EA criteria showed higher sensitivity than the 1997 ACR criteria at diagnosis (91.2% vs. 77.2 %), also when stratified for sex (Table 1A). The sensitivity of the 2019 EA criteria was also superior to the 1997 ACR criteria after two years disease duration and at end of study, for both female-and male subjects (Table 1A). The sensitivity of the 2019 EA criteria was not significantly different for the female vs. the male population (Table 1B).

Conclusion: We provide new evidence for excellent sensitivity of the 2019 EA criteria for new-onset SLE, from a presumably complete population-based cohort. More than 90% of the SLE-cohort cases met the 2019 EA criteria already at time of diagnosis. Stratified for sex, almost all female subjects meeting the 2019 EA criteria during study period did so at time of diagnosis (91.2 % out of 94.2%). The corresponding numbers for the male population was 85% out of 92%.One possible implication for future clinical studies might be capture of almost all SLE patients early in their disease course, which may have important implications for studies on treatment.

Disclosure: H. Haukeland: UCB, 1; **S. Reppe Moe**: None; **C. Brunborg**: None; **A. Botea**: None; **N. Damjanic**: None; **G. Wivestad**: None; **H. Øvreås**: None; **T. Bøe**: None; **T. Garen**: None; **A. Orre**: None; **H. Sanner**: None; **Ø. Molberg**: None; **K. Lerang**: None.

Abstract Number: 0544

Autoantibodies to dsDNA and Associated Proteins: Association with Proteinuria and Lupus Nephritis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-dsDNA antibodies (ADA) are traditionally measured by ELISA and are associated with Lupus nephritis (LN). Testing by immunoline assay (IL) provides additional information on antibodies to dsDNA, nucleosomes and histones which are all dsDNA associated proteins. Co-positivity for these antibodies in various combinations may have an association with diagnosis of LN, especially proliferative LN. This study aimed to assess if ADA by IL show similar association with proteinuria (i.e. lupus nephritis; LN) and proliferative LN (PRLN) as by ELISA and if co-occurrence with the other 2 antibodies have any impact on association with LN or PRLN.

Methods: Autoantibody profiles on IL and ADA values by ELISA (Euroimmune, Germany) of 2151 Indian SLE patients (F:M=1968:183; mean age=27.56 years) from the INdian SLE Inception Cohort for REsearch (INSPIRE cohort) at baseline were used. Among patients with LN (defined as per EULAR 2019 criteria; n=835), renal biopsy was available for 549 patients (337 PRLN; class III, IV, Mixed class III+IV and IV+V in 117, 149, 45 and 26 respectively). Autoantibodies against dsDNA (by both methods), nucleosomes and histones were tested for association with LN and PRLN either in isolation or in combination. Chi-square test was used to find association of individual and combination of autoantibodies with LN and PRLN. The results are expressed as Odds ratio (95% CI). A p-value< 0.05 was considered significant.

Results: ADA on ELISA and IL tested positive in 1499 (69.68%) and 843 (39.19%) patients respectively. A total of 1685 (78.33%) patients tested positive for ADA by at least one method and 749 (34.82%) patients tested positive by both the methods. Anti-nucleosome and anti-histone antibodies were positive in 950 (44.16%) and 791 (36.77%) patients. ADA results (ELISA & IL respectively) showed significant association with LN (1.55 (1.27-1.88); p< 0.001 & 1.31 (1.1-1.56); p< 0.001) and PRLN (2.64 (1.94-3.59); p< 0.001 & 2.74 (2.16-3.48); p< 0.001) but this association disappeared when re-tested after omitting the co-positivity for anti-nucleosome and anti-histone antibodies. Positivity for the other 2 antibodies either in isolation or in combination also didn't show any association with LN and PRLN.

Double positivity for ADA (IL) and anti-nucleosome antibodies showed a significant association (1.62 (1.06-2.48); p< 0.05) with PRLN. Triple antibody positivity in both the groups (ELISA & IL respectively), showed significant association with LN (1.5 (1.24-1.82); p< 0.001 & 1.45 (1.18-1.78); p< 0.001) and PRLN (2.4 (1.89-3.05); p< 0.001 & 2.73 (2.13-3.49); p< 0.001). (Table-1)

Table – 1. Association of antibodies to dsDNA, nucleosomes and histones (alone or in combination) with proteinuria and proliferative lupus nephritis

Anti-ds DNA	Anti-Nucleosome	Anti-Histone	LN (n=835)	OR (95%CI)	p-value	PRLN (n=337)	OR (95%CI)	p-value
+ (ELISA)	Not taken into account	Not taken into account	628	1.55 (1.27-1.88)	<0.001*	284	2.64 (1.94-3.59)	<0.001*
+ (IL)	Not taken into account	Not taken into account	360	1.31 (1.1-1.56)	<0.001*	202	2.74 (2.16-3.48)	<0.001*
+ (ELISA)	-	-	225	1.13 (0.93-1.38)	0.22	77	0.84 (0.64-1.11)	0.23
+ (IL)	-	-	68	0.96 (0.7-1.31)	0.81	28	0.99 (0.66-1.52)	0.99
+ (ELISA)	+	-	88	0.84 (0.64-1.11)	0.23	42	1.1 (0.78-1.57)	0.58
+ (IL)	+	-	50	0.95 (0.66-1.36)	0.78	30	1.62 (1.06-2.48)	0.035*
+ (ELISA)	-	+	40	1.01 (0.68-1.53)	0.93	16	1.0 (0.58-1.73)	0.99
+ (IL)	-	+	25	1.24 (0.73-2.10)	0.43	13	1.61 (0.86-3.03)	0.14
+ (ELISA)	+	+	275	1.5 (1.24-1.82)	<0.001*	149	2.4 (1.89-3.05)	<0.001*
+ (IL)	+	+	217	1.45 (1.18-1.78)	<0.001*	131	2.73 (2.13-3.49)	<0.001*

ELISA = Enzyme Linked Immunosorbent Assay; IL = Immunoline Assay; LN = Lupus Nephritis (presence of proteinuria); PRLN = Proliferative Lupus Nephritis; OR = Odds Ratio; CI = Confidence Interval

*p-value is significant

Positive predictive value (PPV) of ADA by ELISA for LN vs PRLN were 41.89% & 42.7% respectively as compared to ADA by IL (18.94% & 23.96% respectively). These were lower than the PPV for triple antibody positivity for LN and PRLN for ADA by ELISA (45.99% & 45.78% respectively) and for ADA by IL (24.87% & 27.63% respectively).

Conclusion: Anti-dsDNA antibody positivity in isolation (ELISA or IL) doesn't have any association with LN or PRLN. Their association with LN and PRLN appears only when antibodies to nucleosomes and histones are co-positive with them and the odds of developing renal involvement increase significantly.

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Abstract Number: 0545

Referral Pattern and Factors Associated with Time to Diagnosis for Lupus in India- multicentric Data from the SLE Special Interest Group (SIG) of the Indian Rheumatology Association (IRA)

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SESSION INFORMATION
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Background/Purpose: Early diagnosis remains an unmet need for SLE patients across the world. Reasons for delay in diagnosis differ in various geographic regions and largely depend on accessibility to medical care. We report the time to diagnosis, its determinants and the referral pattern from India.

Methods: Members of the Lupus special interest group developed a questionnaire including a pilot run to understand the referral pattern and variables affecting time to diagnosis of Lupus. Patients fulfilling the SLICC criteria for SLE diagnosed after Jan 2022 were included. All patients provided written informed consent. All centres received permission from their ethics committees. Their socio demographic profile as per modified Kuppuswamy scale(2022), health care referral pattern, organ systems affected and disease related parameters at diagnosis were recorded. The data was categorised into early and late diagnosis based on median time taken for diagnosis and the differences were explored using Chi-square, univariate and multivariate logistic regression.

Results: Nine centres provided data for 348 patients for this study, four were Government university teaching hospitals(n=191), 3 private university teaching hospitals (n=116) and 2 from single specialty clinics (n=41). Figure 1 represents an overview of centres which participated in the current study and the home states from where the patients were enrolled. Patients originated from both rural (48%) as well as urban areas(52%).

Table 1: Sociodemographic and clinical factors associated with early or late diagnosis (n=348)

Variables	Early diagnosis (≤7 months) N 166 (54%)	Late diagnosis (>7 months) N 143 (46%)	P value
Mean age in years (SD)	29 ± 11	28 ± 11	0.6
Gender (females)(%)	156 (55%)	130 (45%)	0.3
Socioeconomic status as assessed by modified Kuppuswamy Scale (2022)			
Education status of patient			
Literate(3,4,5,6,7)	131(56%)	102(44%)	0.05
illiterate(1,2)	22(42%)	31(58%)	
Education status of head of family			
Literate(3,4,5,6,7)	129(56%)	101(44%)	0.10
illiterate(1,2)	33(45%)	40(55%)	
Occupation of Head of family			
Higher level(7,8,9,10)	29(47%)	33(53%)	0.5
Middle level(4,5,6)	84(56%)	67(44%)	
Lower level(1,2,3)	52(55%)	43(45%)	
Monthly family income			
Low income (1)	78(50%)	79(50%)	0.05
Middle income(2,3)	43(52%)	39(48%)	
High income (4,6,10,12)	40(66%)	21(34%)	
Socio Economic status			
Upper class	8(44%)	10(56%)	0.2
Upper middle class	41(67%)	20(33%)	
Lower middle class	55(51%)	52(49%)	
Upper lower class	48(53%)	43(47%)	
Lower class	14(47%)	16(53%)	
Geographic location			
Place of residence (home state)			
South India	134(60%)	90(40%)	0.001
North India	11(31%)	24(69%)	
Eastern states	21(42%)	29(58%)	
Place of residence			
Rural	84(57%)	64(43%)	0.2
Urban	75(49%)	77(51%)	
Referral pattern and Health costs			
Whom did you see first			
Medical Professional	127(54%)	1079(46%)	0.7
Non medical	38(52%)	35(48%)	
Who referred to Rheumatologist			
Medical Professional	135(51%)	129(49%)	0.12
Non medical	6(67%)	3(33%)	
Others	22(69%)	10(31%)	
Health costs covered by			
Self	93(57%)	69(43%)	0.05
Insurance	54(45%)	67(55%)	
Government support	6(75%)	2(25%)	
Employer	6(75%)	2(25%)	
SLE related parameters (at diagnosis)			
Mean SLEDAI 2K(±SD)	12± 7	13± 7	0.6
Organ system affected at diagnosis			
Major (Renal + NPSLE+ others)	136(55%)	113(45%)	0.4
Minor (Skin + Musculoskeletal)	28(48%)	28(52%)	
Renal Lupus	23(40%)	34(60%)	0.02
Comorbidities			
Diabetes Mellitus	8(53%)	7(47%)	>0.9
Hypertension	19(54%)	16(46%)	>0.9
Hypothyroidism	18(62%)	11(38%)	0.3
Cancer	1(33%)	2(67%)	0.6
Tuberculosis	4(80%)	1(20%)	0.4
Miscellaneous			
Family Size			
<4 members	99(55%)	80(45%)	0.5
>5 members	63(51%)	60(49%)	
Marital status			
Married	93(53%)	81(47%)	>0.9
Single/separated	69(53%)	60(47%)	
Employment status			
Employed	31 (56%)	24 (44%)	0.8
Unemployed	134 (54%)	113 (46%)	
No of Earning members			
1	89(51%)	86(49%)	0.4
>1	70(56%)	56(44%)	

Abbreviations: NPSLE- Neuropsychiatric systemic lupus erythematosus, SLEDAI 2K- SLE disease activity Index.

Table 2: Multivariate Analysis - Time taken for diagnosis >7months

Variables	Adjusted Odd Ratio(CI)
Education	
Literate	-
Illiterate	2.28(1.00,5.41)
Place of residence (home state)	
South India	-
North India	5.44(1.87,18.7)
Eastern states	2.13(0.79,5.90)
Renal Lupus	1.87(0.90,3.93)

Figure: Map of India depicting participant centres and states from where patients originated

The mean age of SLE patients was 28.48±10.92 years, 93% were women and 57% were married. The median time to diagnosis was 7 months(IQR 3::18), about one third [92(30.4%)] were diagnosed within 3 months and 55(18.2%) within one month. In about 38%, the diagnosis was beyond 12 months. Renal involvement at diagnosis was observed in 19.3% (69/348).The mean SLEDAI-2k at diagnosis (n=232) was 12.13+ 6.85 and in 33/232(14.2%) SLEDAI was <4.

The mean Kuppuswamy scale was 12.39+6.55 reflective of lower middle class patient population. In the univariate analysis, illiteracy (uOR=1.81, 95%CI:0.99,3.35), renal involvement (uOR=1.87,95%CI:0.90,3.93) and lower family income (p=0.05) were found to be associated with delayed diagnosis.(table1) However, in the multivariate analysis only illiteracy (AOR=2.36,95%CI:1.02,5.66) remained significantly associated with delayed diagnosis.(table2)

The referring practitioners were largely another graduate or postgraduate doctor (87%). No referral was made by a medical field worker. The family size, employment and marital status did not influence the time to diagnosis, however, the regional differences were evident.(p=0.001) Almost half patients were self-financing (56.6%) ,with one-third (36.9%) utilising private medical insurance and < 2% receiving government health insurance.

Conclusion: Very early diagnosis (within 3 months of symptom onset) was made in about a third of SLE patients. Time taken for diagnosis was longer in those with low literacy and differed in geographic regions of our country.

Disclosure: V. Shobha: None; **L. Rajasekhar**: None; **S. V**: None; **A. Rajamurgan**: None; **V. Rao**: None; **S. Nallasivan**: None; **D. Singh**: None; **A. Jain**: None; **A. Singh**: None; **F. George**: None; **S. Malviya**: None; **D. Yadav**: None; **J. Mathew**: None; **A. Aggarwal**: None.

Abstract Number: 0546

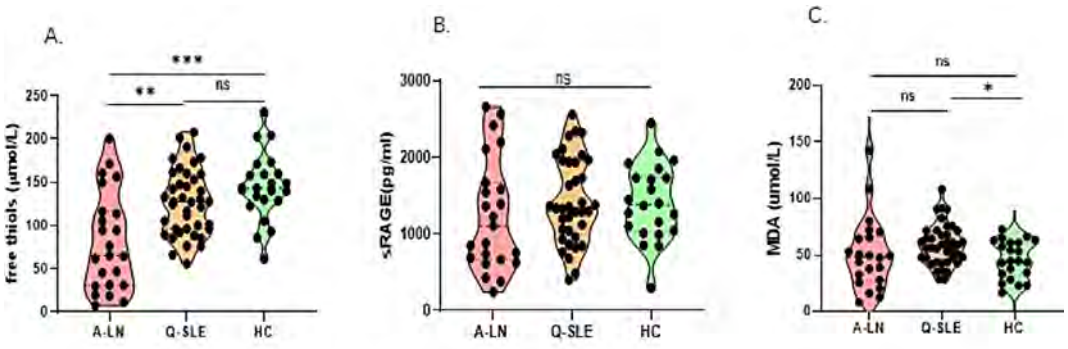
Markers of Oxidative Stress in Systemic Lupus Erythematosus Patients with Nephritis

Lu Liu, Karina de Leeuw, Suzanne Arends, Berber Doornbos-van der Meer, Harry van Goor and Johanna Westra, University Medical Center Groningen, Groningen, Netherlands

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis (LN) is regarded as one of the most severe manifestations of systemic lupus erythematosus (SLE). This inflammation in the kidneys may lead to excessive production of reactive oxygen species (ROS), which can induce oxidative stress, creating a pathogenic loop. Potential biomarkers of oxidative stress are plasma-free thiols, soluble receptors for advanced glycation end-products (sRAGE), and malondialdehyde (MDA). To analyze whether levels of thiols, sRAGE and MDA are different in SLE, and especially in active LN. Moreover, associations between oxidative stress biomarkers and clinical characteristics were investigated.

Methods: Forty-seven SLE patients with quiescent disease (Q-SLE) without renal involvement, 23 SLE patients with active proliferative LN, who previously participated in Dutch Lupus Nephritis studies and 23 healthy controls (HC) were included. Of the SLE patients with active LN follow-up samples were also analyzed. Thiols levels were measured as previously described. sRAGE levels were measured by ELISA. MDA levels were measured by Lipid Peroxidation (MDA) Assay Kit. Clinical parameters, including



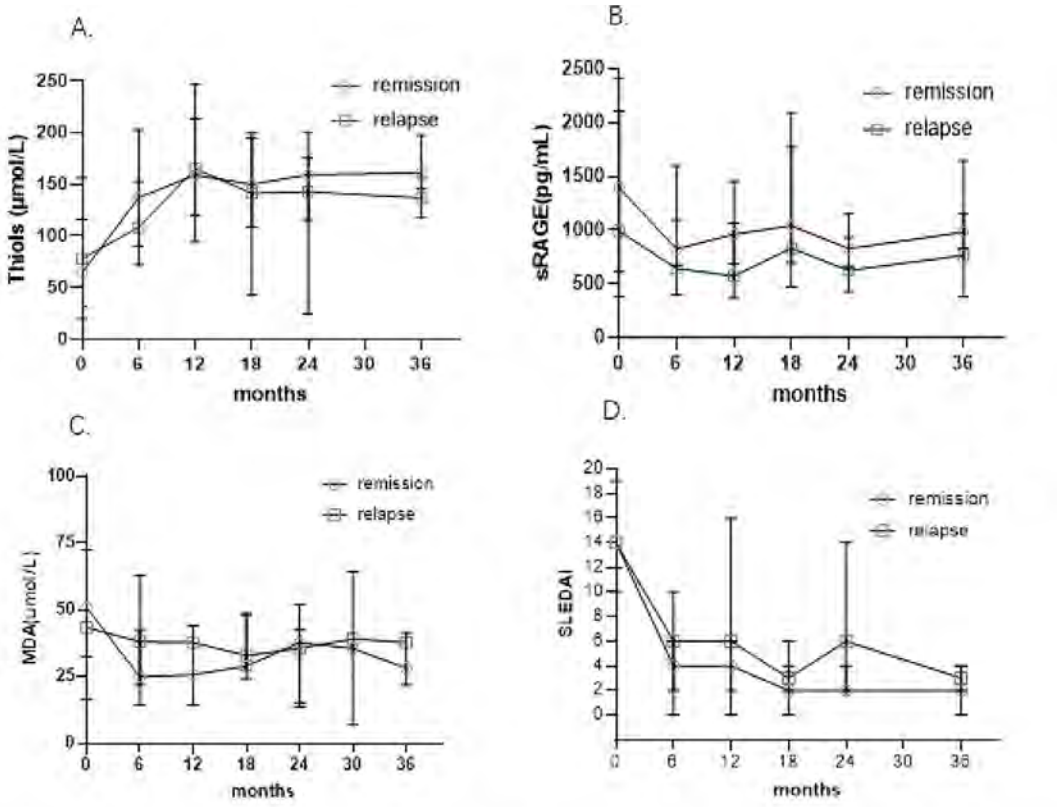
(A) Plasma-free thiols levels. (B) sRAGE levels (C) MDA levels
A-LN: active Lupus Nephritis, Q-SLE: quiescent systemic lupus erythematosus, HC: healthy control.
sRAGE: soluble receptor for advanced glycation end-products, MDA: malondialdehyde

Figure 1. Levels of thiols, sRAGE and MDA at baseline

disease activity using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score, were documented. Longitudinal changes in thiols, sRAGE, and MDA levels were compared to clinical parameters using generalized estimating equations (GEE).

Results: Demographic characteristics are shown in Table 1. Thiols levels were significantly lower in active LN (at baseline) and Q-SLE patients compared to HC (Figure 1A). There was no significant difference in sRAGE levels among the groups (Figure 1B). Q-SLE patients exhibited significantly elevated levels of MDA compared to HC (Figure 1C). In SLE patients with LN, changes over time in thiols, sRAGE, MDA and SLEDAI during the 36-month follow-up are shown in Figure 2. We divided the patients into relapse and remission subgroups, defined as having remission when SLEDAI was < 5 during follow-up. Six patients experienced a flare-up resulting in a recurrence rate of 26%. In the univariate GEE model, changes of thiols were negatively correlated with SLEDAI ($p < 0.001$). Changes in sRAGE and MDA were positively correlated with SLEDAI ($p = 0.035$ and $p = 0.016$, respectively).

Conclusion: Levels of thiols are significantly reduced in patients with Q-SLE and active LN compared to HC. In Q-SLE, levels of MDA were increased compared to HC. During follow-up of SLE patients with LN, thiols levels are significantly negatively correlated to SLEDAI. sRAGE and MDA levels are slightly positively correlated with SLEDAI. These results indicated



(A) Median plasma-free thiols levels; (B) Median sRAGE levels; (C) Median MDA levels; (D) Median SLEDAI levels;
Pink lines represent remission group, green lines represent relapse group; Each dot with vertical lines indicate median with error.
sRAGE: soluble receptor for advanced glycation end-products, MDA: malondialdehyde, SLEDAI: Systemic Lupus Erythematosus Disease Activity Index

Figure 2. Median oxidative stress biomarkers and SLEDAI levels during 36-month follow-up of SLE patients with LN

Table 1. Baseline characteristics of patients and healthy controls

Characteristics	Lupus Nephritis (LN) (n=23)	SLE (n=47)	Healthy controls (n=22)	p value
Age (years)	34 (28- 49)	43 (29- 54)	47 (28- 61)	0.324
Gender (females, n%)	18 (78%)	37 (79%)	18 (82%)	0.947
Systolic blood pressure (mmHg)	120 (110-130)	120 (110-130)	120 (110-120)	0.77
Diastolic blood pressure (mmHg)	80 (70-80)	75 (70-80)	75 (70-80)	0.867
Weight (Kg)	67 (63- 86)	72 (60- 85)	69 (62- 80)	0.859
Thrombocytes (10^9/L)	303 (263- 341)	230 (198- 281)	236 (212- 273)	0.006*
Creatinine (umol/L)	81 (76- 92)	72 (62- 81)	71 (62- 76)	<0.001*
ALAT (U/L)	19 (12- 29)	19 (15- 23)	19 (14- 28)	0.952
Hemoglobin (mmol/L)	8.1 (7.4-8.3)	8.0 (7.7-8.5)	8.3 (8.0-8.9)	0.068
Leukocytes (10^9/L)	9.2 (7.6-12.4)	5.4 (4.4-7.1)	5.6 (4.8-6.2)	<0.001*
Complement 3 (g/L)	0.79 (0.7-1.0)	1.0 (0.8-1.1)	1.06 (0.93-1.20)	0.013*
Complement 4 (g/L)	0.18 (0.1-0.3)	2.0 (2.0-4.0)	0.19 (0.16-0.26)	0.257
SLEDAI score	14 (12-19)	2 (2-4)	N.A.	<0.001*
Anti-dsDNA antibodies (IU/ml)	11.0 (4.8-18.5)	6.0 (1.0-23.0)	N.A.	0.406
Anti-dsDNA (positive, n%)	14 (61%)	21 (45%)	N.A.	0.203

Abbreviations: ALAT: alanine aminotransferase; MDA: Malondialdehyde; N.A.: not applicable

SLEDAI: Systemic Lupus Erythematosus Disease Activity Index.

that SLE patients with or without nephritis have increased oxidative stress levels compared with HC, associated with disease activity. Furthermore, free thiols might be a better biomarker of oxidative stress in LN compared to sRAGE and MDA.

Disclosure: L. Liu: None; **K. de Leeuw**: None; **S. Arends**: None; **B. Doornbos-van der Meer**: None; **H. van Goor**: None; **J. Westra**: None.

Abstract Number: 0547

A Spatially-resolved Single Cell Resolution Atlas of Pediatric Lupus Nephritis Uncovers Complex Interactions Between Stromal and Infiltrating Immune Cells

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The molecular and cellular heterogeneity of human Lupus Nephritis (LN) at the kidney tissue level makes it challenging to identify key disease drivers and therapeutic targets. Single-cell transcriptomics (scRNA-Seq) has advanced our understanding of LN pathogenesis, but tissue dissociation eliminates all spatial information and several rare cell types (such as podocytes) are under-represented using droplet-based scRNA-Seq protocols. Using a technical advance in spatial transcriptomics, we generated a spatially-resolved, single cell resolution atlas of childhood-onset lupus nephritis.

Methods: Using the CosMx Spatial*Molecular Imager* (Nanostring), we generated single cell-resolution spatial transcriptomic data on archived kidney biopsy tissue from 8 pediatric Class III/IV LN patients and 2 health controls.

Results: After data QC and cell segmentation, we identified a total of 447,892 cells, which were assigned to 33 reference cell types (Fig. 1A). Visualizing spatial relationships provided robust evidence of the accuracy of cell annotation, such as the colocalization of fenestrated glomerular endothelial cells, mesangial cells, and podocytes within glomeruli (Fig. 1B, C).

As predicted by the biology of immune complex glomerulonephritis, the proportion of mesangial cells was broadly increased in LN, while relative podocyte numbers declined (Fig. 2A, B). Analysis of differential gene expression demonstrated that SLE induced broad transcriptional changes in resident glomerular cells (Fig. 2C). For example, glomerular endothelial cells downregulate expression of *TEK* (encoding the angiopoietin-1-binding TEK receptor tyrosine kinase), the angiopoietin-1/TEK signal regulator *DUSP1* (Dual Specificity Phosphatase 1), and *CLEC1A*(encoding the C-type lectin domain family 1 member A), suggesting altered glomerular endothelial function and cross-talk with surrounding mesangial matrix. Amongst the upregulated genes in LN mesangial cells, *TAGLN*, encoding transgrelin, is a marker for proliferating mesangial cells responding to

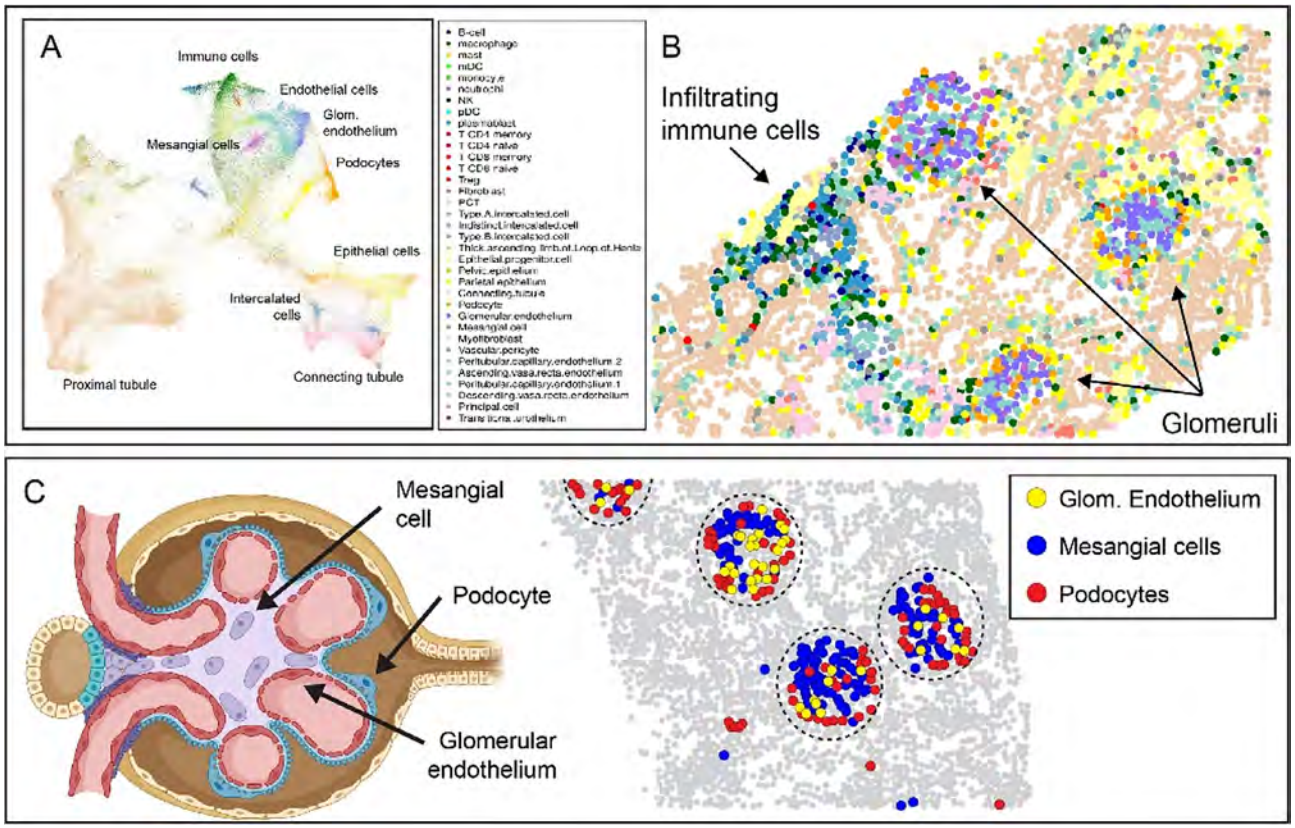

Figure 1: (A) UMAP projection of immune and renal cell subsets in LN. (B) Spatial relationships with each dot indicating a single cell. Arrows denote glomeruli and infiltrating tubulointerstitial immune cells. (C) Left: Illustration showing major glomerular cell types. Right: Glomerular cell types are spatially confined to glomerular structures (dashed circle), with podocytes (red) predominantly located peripherally outside mesangial and endothelial cells. Grey dots: unlabeled cells.

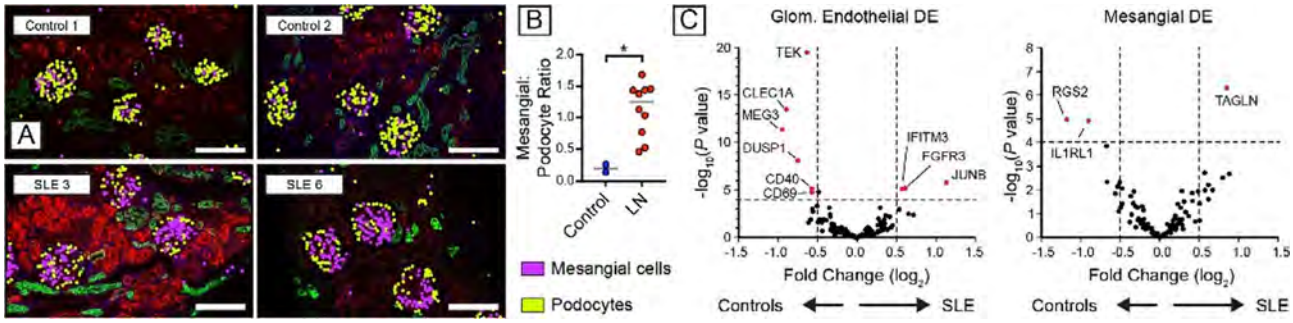

Figure 2: (A) Representative image showing mesangial hypercellularity in proliferative LN relative to controls. (B) Increased mesangial cell:podocyte ratio in LN. (C) Volcano plot showing differentially expressed genes (DEG) in childhood-onset LN relative to healthy controls.

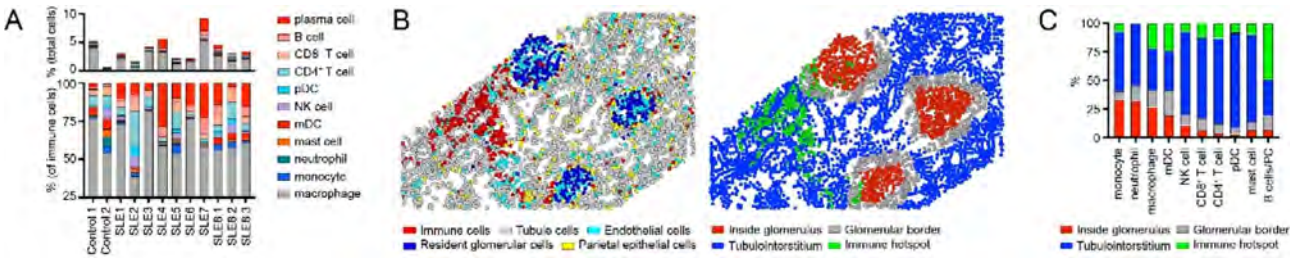

Figure 3: (A) Immune cell distribution in 8 LN patients vs. 2 healthy controls. (B) Image showing the computational identification of kidney regions (defined as: i) inside glomeruli; ii) bordering glomeruli; iii) within the kidney tubulointerstitium; and i) within immune hotspots). Left panel: cell types. Right panel: kidney spatial regions. (C) Distribution of infiltrating immune cells into kidney spatial regions in LN.

tissue injury. Mesangial cells in LN also upregulated collagen molecules (*COL3A1, COL1A2, COL4A1, COL6A*), matrix metalloproteinases and inhibitors (*MMP14, MMP19, TIMP1*), and chemokines (*CSF1*, CXCL9).

Focusing on immune cell infiltrates, LN was characterized by the relative expansion in B cells, plasma cells, and plasmacytoid dendritic cells (pDCs) within the kidney parenchyma (Fig. 3A). Notably, individual immune lineages traffic to specific regions in LN kidneys (Fig. 3B, C), while the transcriptional signatures of these cells also varied as a function of tissue location (not shown).

Conclusion: Spatial transcriptomics is a powerful tool to uncover the heterogeneity of LN. Our data highlight how gene expression in resident kidney cells and infiltrating immune cells varies as a function of both disease state and spatial location. The identification of new pathogenic mechanisms may inform the development of new targeted therapies.

Disclosure: S. Jackson: None; **N. Hasle**: Bristol-Myers Squibb(BMS), 3; **E. Nguyen**: None; **R. Reed**: None; **P. Danaher**: Nanostring, Inc., 3, 11.

Abstract Number: 0548

Clinical and Interferon Biomarkers to Exclude Imminent Autoimmune Disease in ANA Positive Individuals

Md Yuzaiful Md Yusof[1], Sabih Ul-Hassan[1], Zoe Wigston[1], Antonios Psarras[2], Jack Arnold[1], Lucy Carter[3], Paul Emery[4] and Ed Vital[1], [1]University of Leeds, Leeds, United Kingdom, [2]Oxford University, Oxford, United Kingdom, [3]University of Leeds, Hartlepool, United Kingdom, [4]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, and NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Many rheumatologists find it challenging to safely discharge "At-Risk" ANA-positive people at the first visit due to lack of cardinal signs and prediction tools. "Watch and wait" approach is not cost-effective and delay appropriate care of non-immune pathology. We previously showed that higher IFN-Score-B and family history were predictive of progression to meeting classification criteria at 12-months[1]. However, classification criteria may undergo revision and not capture all significant outcomes. Our study objectives were to describe the 3-year outcomes of At-Risk cohort and assess discriminative ability of baseline clinical and IFN-Score-B in predicting various progression endpoints at 1 and 3 years.

Methods: We conducted a prospective cohort study in At-Risk people (ANA-positive ≥1:80, new referral with non-specific symptoms of ≤1 year and treatment naïve). Patients were assessed at baseline, then annually for 3 years. We used multiple RMD classification criteria, including the revised 2019 EULAR/ACR for SLE, and need for therapy, to group patients as below: i) Absolute non-progressor (ANP) (no clinical criteria); ii) Undifferentiated CTD (U-CTD) (≥1 clinical criteria but not full RMD criteria). This group was subdivided into those requiring immunosuppressant (IS) excluding antimalarials only and those who did not; iii) Year 1 progressor (meeting criteria for RMD by 1 year); iv) Late progressor (meeting criteria for RMD in Years 2-3); v) Clinically significant disease (CSD) (progressor OR U-CTD on IS). Bloods were analysed for two IFN-stimulated gene expression scores previously described[2]. Discrimination of single or combined clinical and IFN-Score-B markers were assessed using ROC curve analyses.

Results: Of 148 patients, mean (SD) age was 47 (15) years, 132 (89%) were female, 107 (72%) were Caucasians, 48 (32%) had a family history of RMD, 56 (38%) were anti-dsDNA+ and 8 (6%) had low C3 and/or C4. No. of clinical criteria at baseline were 0 (30%), 1 (64%) and 2 (6%). Outcomes were: Year 1 progressors: 21 (14%) [SLE=14; pSS=6; AS=1]; Late progressors: 12 (8%) [SLE=10; pSS=1; AS=1] of which only 2/12 in Year 3; U-CTD on IS: 8 (5%); U-CTD on antimalarials only: 20 (14%); U-CTD not on therapy: 50 (34%) and ANP: 37 (25%). Thus, 41 (28%) was classified as CSD by 3-year. For the prediction of Year 1 progressor, in addition to baseline IFN-Score-B and family history, multivariable regression showed no. of clinical criteria was associated with increased risk, OR 7.8 (95% CI 1.7-36.3). Table 1 showed that combined baseline

Table 1: Discrimination of single or combined clinical and IFN-Score-B markers

Progression Criteria	No. of Progressors (n/N)	No. of Progressors with available samples (n/N)	AUC (95% CI) for IFN-Score-B Only	AUC (95% CI) for Combined Markers (IFN-Score-B + FH of RMD + No. of Clinical Criteria)	Sensitivity, Specificity	PPV, NPV	Accuracy
Year 1 SLICC Classification	21/148	20/122	0.81 (0.72, 0.91)	0.89 (0.83, 0.96)	45%, 98%	82%, 90%	89%
Year 1 ACR/EULAR Updated Classification	26/148	25/122	0.73 (0.64, 0.81)	0.81 (0.73, 0.91)	36%, 98%	82%, 86%	85%
Year 1 CSD	26/148	24/122	0.76 (0.66, 0.87)	0.86 (0.77, 0.95)	42%, 98%	83%, 87%	87%
Year 3 SLICC Classification	33/148	31/122	0.64 (0.52, 0.76)	0.77 (0.67, 0.87)	29%, 97%	75%, 80%	80%
Year 3 ACR/EULAR Updated Classification	36/148	34/122	0.64 (0.52, 0.76)	0.76 (0.67, 0.86)	26%, 97%	75%, 77%	77%
Year 3 CSD	42/148	40/122	0.59 (0.48, 0.70)	0.74 (0.64, 0.83)	30%, 96%	80%, 74%	75%

markers (IFN-Score-B, family history and no. of clinical criteria) had good accuracy in predicting various definitions of progression at Years 1 and 3 as per AUROC.

Conclusion: About a quarter of At-Risk people developed CSD by 3-year, mostly did so within Year 1. Combined baseline clinical and IFN biomarkers had high specificity and could be used to risk stratify new ANA-positive referrals to rheumatology to exclude imminent or future disease/requirement of immunosuppressant. A validation study with cost-effectiveness analysis of these markers is in progress and would help translate their use in clinical practice.

References: 1. Md Yusof et al. ARD 2018, 2. El-Sherbiny et al. Sci Rep 2018

Disclosure: M. Md Yusof: Novartis, 6, Roche, 6, UCB, 1; **S. Ul-Hassan**: None; **Z. Wigston**: None; **A. Psarras**: None; **J. Arnold**: None; **L. Carter**: UCB, 1; **P. Emery**: Boehringer Ingelheim, 2, Eli Lilly, 2, Novartis, 2; **E. Vital**: F. Hoffmann-La Roche Ltd, 2, Genentech, Inc., 2, Sandoz, 5.

Abstract Number: 0549

Development of Customized Digital Cognitive Assessment Battery: A Pilot Use Case in SLE Patients

Priyanka Srivastava[1] and **Liza Rajasekhar**[2], [1]International Institute of Information Technology, Hyderabad, India, [2]Nizam's Institute of Medical Sciences, Madhapur, India

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Reported prevalence of cognitive dysfunction (CD) in SLE varies from 3%-88%1.Variability may be due to use of tools insensitive to population characteristics like literacy, improper control groups and effect of psychological health. We developed a language agnostic computerized cognitive test battery to evaluate CD in SLE.

Methods: Patients fulfilling the 2012 classification criteria for SLE and their randomly chosen care-givers, attending outpatient services, able to provide written consent and sustain the duration of cognitive testing (CT) were enrolled as cases and controls respectively.

CT included 1 paper-and-pencil Montreal Cognitive Assessment (MoCA), and 4 modified computerized tests: attention network tests (ANT) for executive control; sustained attention to response task (SART) for continuous task performance, picture naming for language proficiency, and n-back for working memory (WM), which used familiar images like truck, bag, fan instead of numbers or colors. Developed with PsychoPy experiment design software, participants' response time and accuracy was recorded. Depression, anxiety, stress, and trait anxiety were assessed using patient health questionnaire (PHQ-9), generalized anxiety disorder scale (GAD-7), perceived stress scale (PSS-4) and short state-trait anxiety inventory (STAI-T) respectively. Institutional Ethics committees approved the study. Scores were compared between groups using Mann Whitney U test with Bonferroni correction.

Results: Twenty-one SLE patients and 20 controls were enrolled. There was no difference in mean age (cases 27.7(6.5) controls 28(8.3) years) between groups. Mean duration of illness in cases was 61.8(42.5) months and mSLEDAI was 0. Table 1 shows mean scores of CT and psychological scales. Cases had reduced commission error (inappropriate

response to a no-go stimulus), and increased accuracy for no-go conditions, but with overall response latency in SART (effect size, r= .43 , -0.43, -0.40 respectively). Cases had significantly higher GAD scores (effect size (r=-0.36) with overall 23% reporting moderate generalized anxiety symptoms. (Figure 1).

Cognitive Task/Subtask	SLE (21)	HC (20)
Age	27.7 (6.5)	28.0 (8.3)
Female (%)	95.2	100
MoCA		
Score	24.8 (3.1)	24.4 (3.2)
Normal (%)	52.38	65.00
SART		
Overall Accuracy (%)	85.7 (7.6)	84.4 (6.9)
Go trials (%)	88.4 (8.3)	88.9 (6.8)
No-Go trials (%)	67.8 (19.7) **	53.6 (20.4) **
Commission Error	32.2 (19.7) **	46.4 (6.8) **
Omission Error	11.5 (8.3)	11.05 (6.8)
Overall Response Time (RT) (ms)	350.9 (41.8) *	318.8 (36.0) *
Go RT (ms)	379.1 (47.8) **	337.6 (41.4) **
No-Go RT (ms)	126.2 (76.7)	169.2 (83.7)
n-Back		
0-back Score	94.8 (7.1)	93.9 (10.4)
0-back d prime	3.1 (1.0)	3.3 (1.2)
0-back Overall RT (ms)	639.3 (102.5)	648.9 (196.3)
1-back Score	89.0 (12.1)	90.7 (13.3)
1-back d prime	3.1 (1.0)	3.3 (1.2)
1-back Overall RT (ms)	708.8 (123.0)	601.50 (170.1)
2-back Score	74.1 (12.9)	78.1 (11.9)
2-back d prime	1.4 (0.8)	1.9 (0.9)
2-back Overall RT (ms)	854.6 (163.5)	762.5 (151.9)
Picture Naming Response Time (ms)	1887.6 (581.8)	1973.3 (782.6)
ANT Response Time (ms)	75.6 (59.5)	74.9 (37.7)
Psychological Health		
PHQ-9	9.0 (6.4)	5.9 (4.3)
GAD-7	7.1 (5.5) *	4.1 (3.9) *
PSS-4	7.0 (2.6)	6.4 (2.8)
STAI-T	10.6 (3.6)	8.8 (3.1)

* denotes $p < 0.05$; ** denotes $p <= 0.01$.
[a] Mean (SD)

Cognitive and psychological task response by SLE and HC group.

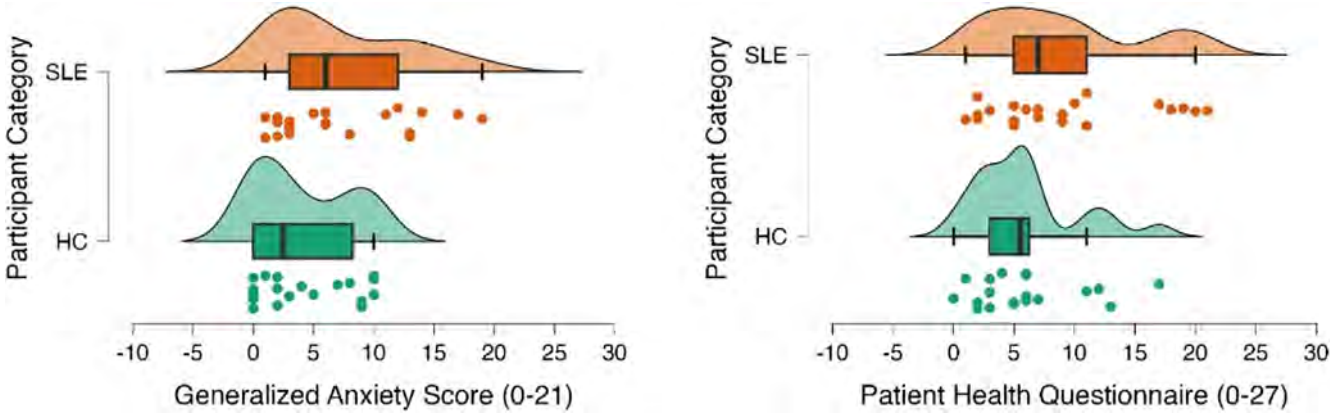

Figure 1. Raincloud plot depicting generalized anxiety disorder score (left panel) and patient health questionnaire score (right panel) . SLE=SLE patients and HC=healthy control.

Conclusion: Unlike previous studies, though patients and caregivers had no difference in MOCA, patients had increased psychomotor latency. After validation in populations with higher literacy and use in larger sample size with proper controls the true prevalence of CD in SLE will emerge.

Reference: 1. Rayes HA Touma Z et al. What is the prevalence of cognitive impairment in lupus and which instruments are used to measure it? A systematic review and meta-analysis. Semin Arthritis Rheum. 2018 Oct;48(2):240-255.

Disclosure: P. Srivastava: None; **L. Rajasekhar**: None.

Abstract Number: 0550

Harnessing Machine Learning to Predict Neuropsychiatric Events in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Neuropsychiatric systemic lupus erythematosus (NPSLE) is linked to increased morbidity, mortality, and adverse health-related quality of life. Early disease, a history of NPSLE, aPL positivity, and high disease activity are considered risk factors for NPSLE. However, there is currently no reliable clinical tool to predict neuropsychiatric flares. Recent advancements in machine learning (ML) have demonstrated great potential in aiding clinical decision-making across various medical disciplines. Therefore, we aimed to assess the reliability and effectiveness of ML applications in predicting NPSLE flares within a large cohort of patients with active SLE, yet no ongoing active severe NPSLE.

Methods: We analysed data from five phase III trials (BLISS-52, BLISS-76, BLISS-NEA, BLISS-SC, EMBRACE) after exclusion of patients with baseline neuropsychiatric BILAG score A (N=3638). Neuropsychiatric flares were defined as a transition from BILAG score C, D, or E to score A or B, or from score B to score A in the neuropsychiatric domain of the classic BILAG index throughout a 52-week long follow-up. After constructing panels of variables based on expert knowledge, we employed ML methodology to develop predictive models utilising the least absolute shrinkage and selection operator (LASSO) as well as multivariable logistic regression analysis. A stratified split was applied to the data to partition the study population into a training (70%; N=2547), and a test set (30%; N=1091). The training set was used in model development while the internal validation was developed by a 10 times 10-fold cross validation. The test set was used for validation of the built model, and the performance of the two models was demonstrated using area under the curve (AUC) of the receiver operating curves (ROC), accuracy with a 95% confidence interval (CI), sensitivity, and specificity metrics.

Results: A total of 105 SLE patients (2.89%) experienced a neuropsychiatric flare during follow-up. Knowledge-driven feature selection included a history of NPSLE, disease duration, aCL positivity, clinical SLEDAI-2K, sex, age, and the use of antimalarials. The LASSO and multivariable logistic regression models demonstrated comparable performance, with an AUC of 0.80 and 0.80, sensitivity of 0.61 and 0.61, and specificity of 0.83 and 0.82, respectively. Moreover, both algorithms exhibited appropriate calibration on the test dataset.

Conclusion: The integration of traditional risk factors for NPSLE into ML-based models can predict neuropsychiatric involvement in SLE with high specificity and modest sensitivity. We herein propose a pragmatic, robust, and highly accurate prediction tool forecasting neuropsychiatric flares in patients with SLE. The utilisation of this ML-based tool holds promising prospects for improving patient care and outcomes in real-world settings.

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Abstract Number: 0551

Monogenic Lupus: Clinical Phenotypes and Genetic Mutations in a Cohort of Pediatric Patients

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Monogenic lupus is associated with specific gene mutations, most commonly reported in TREX1, DNASE1L3, DNASE2, and SAMHD1. However, their phenotypes are not well reported.

Methods: Patients < 16 years of age, satisfying classification criteria for SLE (SLICC 2012) or incomplete lupus1 (ILE)(ANA (titer ≥1:80) and any 1 of acute/ subacute/ chronic cutaneous lupus, oro-nasal ulcers, alopecia, synovitis, serositis, neurologic or renal manifestation or 2 of hematologic, immunologic manifestations, family history of autoimmune rheumatic

Table 1- Genetic Mutations and Lupus Presentation Categories in Study Patients

Nomenclature	Number of patients	Genetic mutation
Complete lupus (fulfilling SLICC classification criteria)	1	C1QA , Exon 3, c.622C>T(p.Gln208Ter)
Incomplete lupus (fulfilling criteria for incomplete lupus)	2	IFIH1,c.281A>G (p.Tyr94Cys) C1QB,Exon 3,c.371C>A (p.Ala124Asp)
Lupus like disease (not fulfilling criteria)	3	DNASE1L3,Exons 1-2,chr3:g.(58207142_58210877)del CFI,Exon 4,c.562G>A (p.Gly188Arg) ACP5 Exon 4,c.407del, (p.Phe136SerfsTer23)

disease (AIRD) or lupus-like disease(LLD) as per treating physicians opinion, in whom a monogenic cause was suspected due to consanguinity in parents, young age of onset, familial history, recurrent infections, skeletal abnormalities were subjected to clinical exome sequence. Data was retrieved from outpatient and inpatient records. Those with pathogenic variants or with variant of unknown significance but with the same mutation identified in parents were analysed.

Results: Clinical exome revealed mutations in 6 of 7 patients tested (Table 1). The mean age of the patients was 5.3 years(range 2-12) and mean duration of follow-up was 10.8 months (range 4- 21). One patient with a mutation in C1QA gene fulfilled the SLICC-CC (acute cutaneous lupus, oral ulcers, myelitis, lupus nephritis). She also experienced recurrent infections (thigh cellulitis and thumb abscess).

Two patients met the criteria for ILE. One had AIHA, ILD, and low complements and shared a heterozygous mutation in the IFIH1 gene with her mother. The other had oral ulcers, discoid rash, and mutation in C1QB mutation.

Three patients had LLD. One had DAH (diffuse alveolar haemorrhage) and mutation in DNASE1L3 gene, another had urticarial skin rash and low complements with a mutation in CFI gene, and third had AIHA (autoimmune hemolytic anemia), leucopenia, and spondyloenchondroplasia with mutation in ACP5 gene. All, except patient with DNASE1L3 mutation, were ANA positive. None had a family history of AIRD.

Conclusion: We report on 6 patients with mutations in C1QA, C1QB, DNASE1L3, CFI, IFIH1, and ACP5. In 3 with known mutations for monogenic lupus (C1QB, DNASE1L3, ACP5) SLE SLICC criteria were not met. One child presented with DAH. Others had lupus-like autoimmune features and features atypical for ILE eg ILD. Monogenic lupus will allow better research into pathways of disease.

Reference: 1.Lambers WM. Incomplete Systemic Lupus Erythematosus: What Remains After Application of ACR and SLICC criteria? Arthritis Care Res 2020;72(5):607–14.

Disclosure: K. Yerram: None; **K. Shanigaaram**: None; **G. Deshpande**: None; **A. Parikh**: None; **A. Ramavath**: None; **N. Gollakota**: None; **R. Manthri**: None; **L. Rajasekhar**: None.

Abstract Number: 0552

The Impact of Antiphospholipid Antibodies on Future Atherosclerotic Cardiovascular Disease Risk in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) suffered from an increasing risk of cardiovascular diseases (23·3 events per 1000 patient-years). Antiphospholipid antibodies (aPLs), including anticardiolipin antibodies (aCL), anti-β2 glycoprotein I antibodies (aβ2GPI), and lupus anticoagulant (LA), increase the risk of thrombotic events in antiphospholipid syndrome, but the impact of aPLs on SLE patients was not yet determined. In this multi-center prospective study, we aimed to determine the association between aPLs and future atherosclerotic cardiovascular disease (ASCVD) risk in SLE.

Methods: Seven aPL isotypes (aCL IgG/IgM/IgA, aβ2GPI IgG/IgM/IgA, and LA) were measured based on international guidelines at SLE diagnosis and during follow-up. Clinical manifestations, disease activity status and organ damage were collected. Future ASCVD events were defined as new onset nonfatal myocardial infarction, nonfatal stroke, coronary or peripheral artery revascularization, or cardiovascular death.

Results: Among the 1573 recruited SLE patients, 525 (33.4%) had positive aPLs. LA had the highest prevalence (324 [20.6%]), followed by aCL IgG (249 [15.8%]), aβ2GPI IgG (199 [12.7%]), aCL IgA (58 [3.7%]), aβ2GPI IgM (83 [5.3%]), aβ2GPI IgA (58 [3.7%]), aCL IgM (92 [5.8%]). 116 (7.37%) patients developed ASCVD during the mean follow-

Table 1. Proportion of ASCVD in SLE patients with different isotypes of aPLs

	ASCVD, n (%)	HR	95% CI	p
Anti-phospholipid antibodies (n=525)				
Anticardiolipin antibodies (n=299)	66(22.1)	6.07	4.19-8.77	<0.001
IgG (n=249)	51(20.5)	4.76	3.29-6.88	<0.001
IgM (n=48)	15(31.3)	4.01	2.32-6.91	<0.001
IgA (n=92)	20(21.7)	2.74	1.68-4.48	<0.001
Anti-β2 glycoprotein I antibodies (n=245)	33 (13.5)	2.38	1.59-3.56	<0.001
IgG (n=199)	29(14.6)	2.72	1.78-4.15	<0.001
IgM (n=83)	1(1.2)	2.30	1.34-3.97	0.002
IgA (n=58)	9(15.5)	2.04	1.03-4.04	0.036
Lupus anticoagulant (n=324)	89(24.7)	7.87	5.31-11.67	<0.001
Risk factors of cardiovascular disease				
Smoking (n=41)	12(29.3)	7.80	4.24-14.35	<0.001
Sex (male) (n=61)	17(27.9)	3.99	2.38-6.69	<0.001
Diabetes mellitus (n=27)	12(44.4)	7.16	3.93-13.50	<0.001
Hypertension (n=117)	34(29.1)	3.11	3.42-7.64	<0.001
Age>50 years old (n=169)	29(17.2)	2.50	1.63-3.83	<0.001
SLEDAI		1.10	1.05-1.13	<0.001

up of 4.51±2.32 years and 92 patients were aPLs positive. In univariate Cox regression analysis, both aPLs (HR=7.81, 95% CI, 5.00-12.24, p< 0.001) and traditional risk factors of cardiovascular disease were associated with future ASCVD events (Table 1). Kaplan-Meier plots suggested a potential trend towards ASCVD in positive versus negative aPLs antibodies. More importantly, anticoagulant or antiplatelet therapy can reduce ASCVD risk in SLE patients with positive aPLs (HR=0.57, 95% CI,0.25-0.93, P=0.026) (Figure 1). In multiple Cox regression analysis, aCL IgG (HR=1.95, 95% CI, 1.25-3.00, p=0.003), aCL IgM (HR=1.83, 95% CI, 1.03-3.20, p=0.039), and LA (HR=5.13, 95% CI 3.23-8.20, p< 0.001) positivity remained independently associated with ASCVD; traditional risk factors for ASCVD, including smoking, gender, age and hypertension, also play an independent role in SLE patients (Figure 2).

Conclusion: SLE patients with positive aPLs, especially positive aCL IgG/IgM and LA, warrant more care and surveillance of future ASCVD events during follow-up. Antithrombotic therapy has a protective effect on future ASCVD.

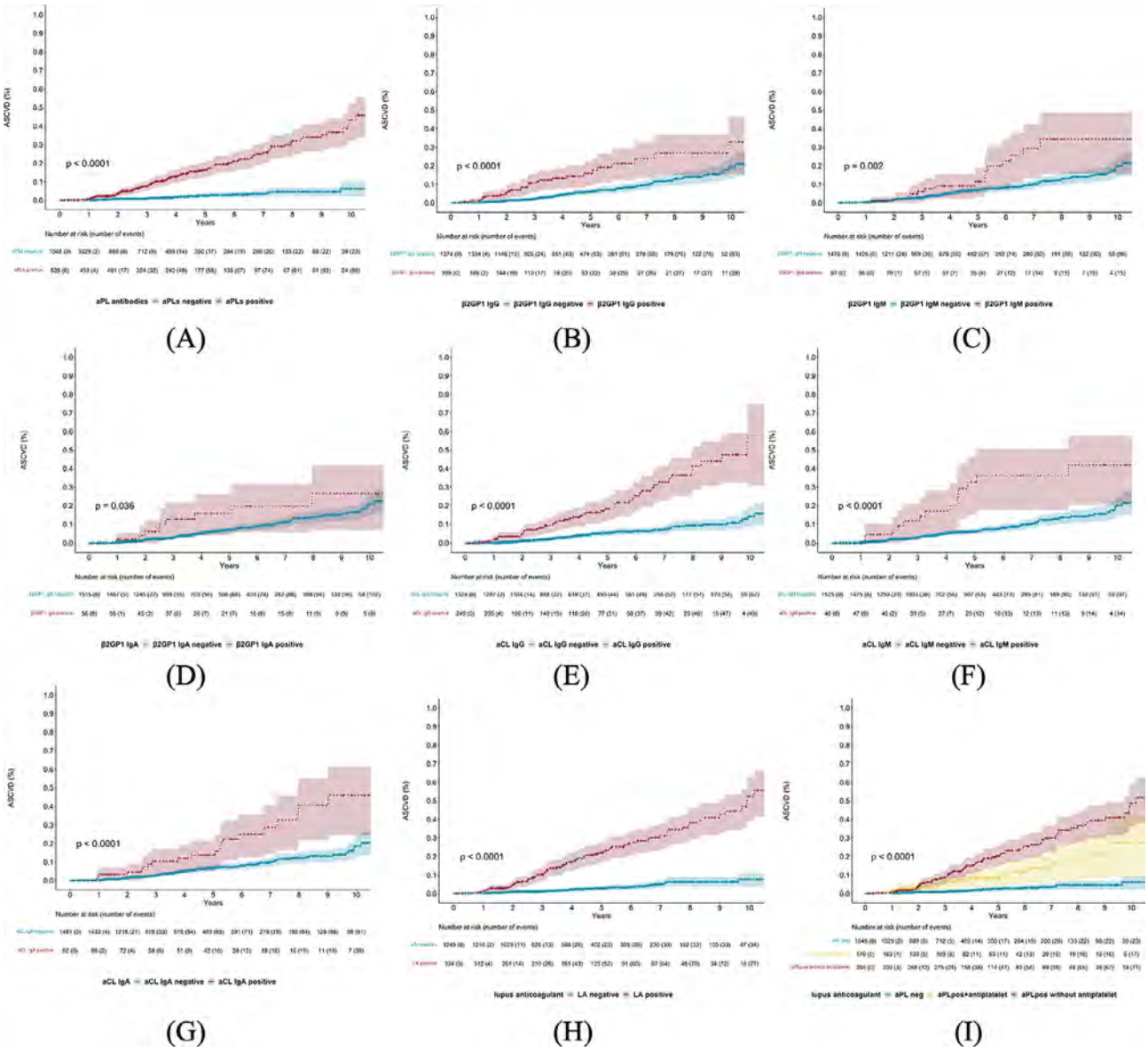

Figure 1. Cumulative probability of ASCVD in patients with or without aPLs (A), aβ2-GPI IgG antibody (B), aβ2-GPI IgM antibody (C), aβ2-GPI IgA antibody (D), aCL IgG antibody (E), aCL IgM antibody (F), aCL IgA antibody (G), and LA (H). (I) Cumulative probability of ASCVD in aPLs negative patients, aPLs positive patients with anticoagulant or antiplatelet therapy, and aPLs positive patients without anticoagulant or antiplatelet therapy.

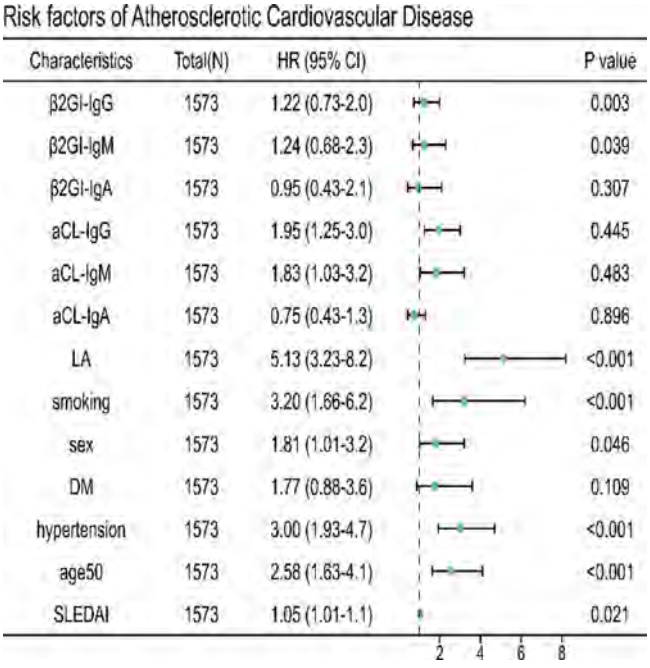

Figure 2. Risk factors of ASCVD in SLE patients.

Disclosure: Y. Ding: None; **C. Huang**: None; **J. zhao**: None; **Q. Wang**: None; **X. Tian**: None; **M. Li**: None; **x. Zeng**: None.

Abstract Number: 0553

Serum Isolevuglandin IgG Antibody Concentrations Are Increased in Patients with Systemic Lupus Erythematosus versus Control Subjects and Associated with Lower 24-hour Blood Pressure

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) have a 2-3-fold increased risk of cardiovascular events. A major risk factor for this is hypertension. We previously demonstrated that downstream products of oxidative stress, isolevuglandins (isoLGs) promote hypertension and autoimmunity in SLE. IsoLGs covalently bind to lysine residues, leading to increased tissue damage, inflammation, and formation of autoantigens. The purpose of this study is to determine if anti-isoLG IgG antibodies are increased in patients with SLE and associated with disease activity and blood pressure (BP).

Methods: This cross-sectional study included 23 SLE and 30 control subjects. Subjects wore an ambulatory BP monitor for 24 hours with diurnal measurements every 15-30 minutes and nocturnal measurements every 30 minutes. Serum-isoLG IgG antibody concentrations were measured using a sandwich ELISA as previously published. One SLE serum sample was

used on all plates to normalize for plate-to-plate variability. Data were compared by chi square (categorical) or Mann-Whitney U (continuous) tests. Correlation was conducted by Spearman rho and linear regression analysis with anti-isoLG IgG antibody concentrations log-transformed to normalize residuals.

Results: Patients with SLE and control subjects were of similar age, race, and sex. Disease activity in SLE patients was low to moderate (mean SLEDAI=4). Most 24-hour BP parameters were significantly elevated in SLE versus control subjects (**-Table 1**). Serum anti-isoLG IgG antibody concentrations were increased in SLE (median [interquartile range]: 1.30 units [0.93, 1.70 units]) versus control subjects (0.91 units [0.73, 1.28 units], P=0.007; **Figure 1**). Anti-isoLG IgG antibody concentrations were significantly inversely associated with office and diurnal systolic BP (**Table 2**) in patients with SLE but were not significantly associated with BP in control subjects or disease activity and damage in SLE (SLEDAI: rho=0.156, C4: rho=-0.320, SLICC: rho=0.338). SLE patients not taking anti-hypertensive drugs were examined separately due to impact of the anti-hypertensives on BP and anti-isoLG IgG antibody concentrations were strongly significantly inversely associated with office and 24-hour BP measurements (**Table 2**). For example, every 20% increase in anti-isoLG IgG concentration was associated with a 10 mmHg decrease in 24-hour systolic BP, P=0.004. This remained significant after adjustment for age (P=0.03).

Conclusion: Serum concentrations of anti-isoLG IgG antibodies are increased in SLE versus control subjects. Anti-isoLG IgG antibody concentrations were inversely associated with 24-hour BP measurements. Given prior mechanistic studies demonstrating that cellular isoLGs promote hypertension, it is possible that in SLE, isoLG antibodies could help clear these hypertension-inducing antigens. Future work will further evaluate this mechanism and the role of anti-isoLG IgG antibodies as markers of BP and cardiovascular risk.

Table 1. Subject demographics and 24-hour blood pressure measurements

	SLE (n=23)	Control (n=30)	P
Age, years	35 [31, 52]	37 [29, 56]	0.56
Race			0.76
Caucasian, #	13 (57%)	24 (80%)	0.17
Black, #	9 (39%)	5 (17%)	
Asian, #	1 (4%)	1 (3%)	
Ethnicity, #non-hispanic	20 (87%)	28 (93%)	0.64
Sex, # female	19 (83%)	25 (83%)	0.99
SLEDAI, units	4 [2, 8]	-	-
SLICC, units	1 [0, 1]	-	-
Lupus nephritis, # ever	8 (36%)	-	-
Hypertension, #	10 (43%)	3 (10%)	0.009
Anti-Hypertensive use, #	10 (43%)	2 (7%)	0.002
Office SBP, mmHg	126 [114, 149]	121 [116, 127]	0.32
Office DBP, mmHg	84 [68, 90]	80 [72, 85]	0.60
24-hr SBP, average mmHg	129 [112, 147]	116 [110, 120]	0.03
24-hr DBP, average mmHg	78 [69, 86]	71 [64, 75]	0.01
Diurnal SBP, average mmHg	130 [115, 145]	119 [115, 125]	0.06
Diurnal DBP, average mmHg	82 [71, 90]	75 [69, 79]	0.04
Nocturnal SBP, average mmHg	114 [100, 141]	104 [97, 110]	0.01
Nocturnal DBP, average mmHg	68 [58, 83]	58 [52, 64]	0.003

Data analyzed by chi square (categorical) or Mann-Whitney U (continuous) tests.

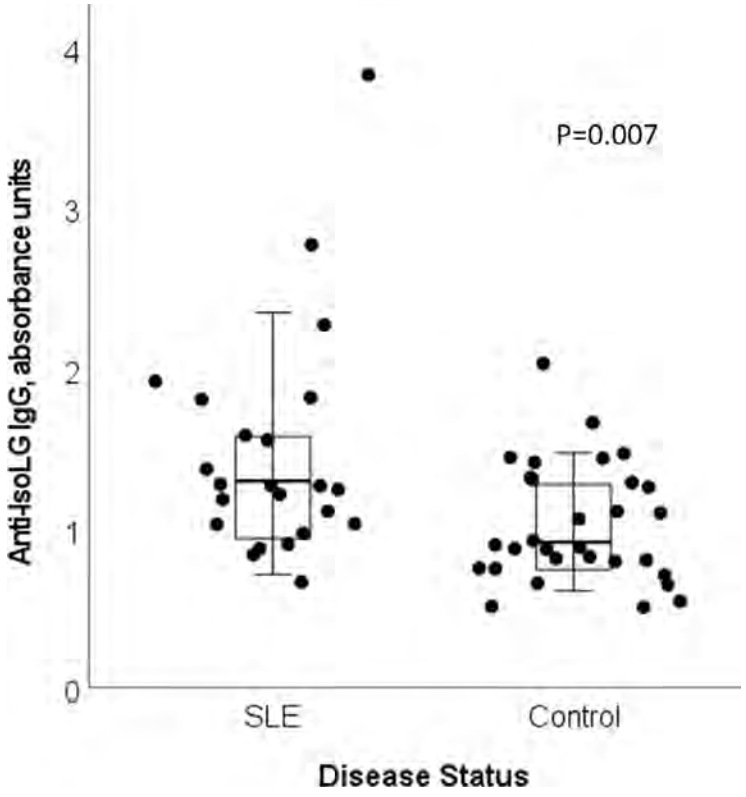

Figure 1. Serum anti-isoLG IgG antibodies are increased in patients with SLE compared to control subjects. Mann-Whitney-U test.

Table 2. Relationship between anti-isoLG IgG concentrations and blood pressure measurements in patients with SLE

	SLE, all (N=23)	SLE, no anti-hypertensive (N=13)
Office SBP, mmHg	-0.418*	-0.740**
Office DBP, mmHg	-0.320	-0.523
24-hour SBP, average mmHg	-0.406	-0.802**
24-hour DBP, average mmHg	-0.307	-0.610*
Diurnal SBP, average mmHg	-0.421*	-0.802**
Diurnal DBP, average mmHg	-0.279	-0.544
Nocturnal SBP, average mmHg	-0.360	-0.731**
Nocturnal DBP, average mmHg	-0.272	-0.456

Data analyzed by Spearman correlation. SBP= systolic blood pressure. DBP= diastolic blood pressure. *P value <0.05, **P value <0.01

Disclosure: A. Phothisane: None; **S. Shaik**: None; **Q. Wu**: None; **O. Posey**: None; **S. Davies**: None; **J. Krishnan**: None; **D. Patrick**: Metabolic Technologies, Inc., 9, 10; **C. Stein**: None; **M. Ormseth**: None.

Abstract Number: 0554

A Refined Disease Activity Immune Index Informed by Select Immune Mediators That Characterizes Clinical Disease Activity in Systemic Lupus Erythematosus

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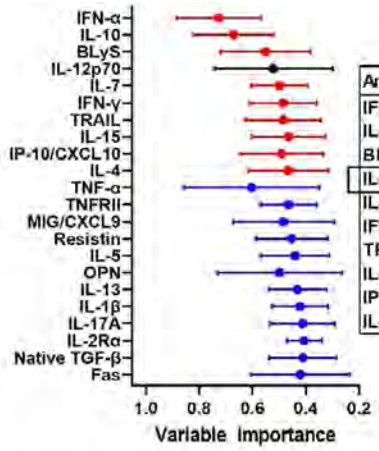
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease marked by varied disease activity, underscored by complex immune dysregulation, including altered immune mediators and accumulation of autoantibody (AutoAb) specificities. This study seeks to determine an optimal panel of analytes that distinguish SLE patients with active disease and refine a Lupus Disease Activity Index (L-DAI).

Methods: We procured samples from patients with classified SLE on dates of low disease activity (< 4, range 0-3, n=162) or active disease (≥4, range 4-30, n=162) defined by the hybrid SLEDAI (hSLEDAI). Race/sex/age-matched healthy control (Ctrl) samples (n=81) were also evaluated. Plasma immune mediators (n=33) were evaluated by microfluidic immunoassay and serum AutoAb specificities, including dsDNA, chromatin, Ro/SSA, La/SSB, Sm, SmRNP, and RNP, were assessed by xMAP assay. The L-DAI is the sum of log-transformed, standardized immune mediators, weighted by the Spearman r correlation coefficient of mediator levels vs. either hSLEDAI scores or number of AutoAb specificities associated with clinical disease activity. Log-transformed mediator levels were further evaluated using random forest applied machine learning modeling to determine an optimal subset of analytes to inform the L-DAI.

Results: As expected, SLE patients with active disease demonstrated differences in clinical and serologic features, as well as increased use steroids. Random forest modeling of immune mediators comparing low vs. active disease, including clinically and/or serologically active vs. quiescent disease and Ctrls informed a variable importance ranking (**Fig. 1**, mean ± SD, top 21 mediators shown). Forward selection (adding mediators to top mediator, IFN-α [red]) and backward elimination (subtracting mediators from total [blue]), in combination with univariate analysis (**Fig. 1**), yielded a combination of 9 mediators (in red, **Fig. 1**) that best informed the L-DAI. The L-DAI 9, whether weighted by hSLEDAI or number of AutoAbs, significantly ($p \leq 0.05$) differentiated SLE patients with Low vs. Active disease, including clinically/serologically active/quiescent disease (vs. Ctrls, **Fig. 2**), with strong correlation between the weightings (Spearman r=0.990, $p < 0.0001$). An average composite L-DAI differentiated SLE patients with low, active, and clinically/serologically active/quiescent disease (vs. Ctrls, **Fig. 3**). There was enhanced distinction of low/moderate/high risk regions for active disease after application of decision curve analysis, with large (>0.8) Cohen's effect size and AUC=0.795 ($p < 0.0001$) in distinguishing clinical/serologic active/quiescent disease activity, and significant correlation (Spearman r=0.407, $p < 0.0001$) with concurrent clinical disease activity (hSLEDAI scores) (**Fig. 3**).



	Case Breakout						Active vs Ctl	Low vs Ctl	Active vs Low
Analyte[a]	Active[b] Mean	SEM	Low[b] Mean	SEM	Ctl Mean	SEM	p-value[c]	p-value[c]	p-value[c]
IFN-α	5.16	0.85	1.67	0.27	0.27	0.06	≤0.0001	≤0.0001	≤0.0001
IL-10	5.5	0.38	4.72	0.84	1.95	0.16	≤0.0001	≤0.0001	≤0.0001
BLyS	1414	77.5	1272	121	608	20.1	≤0.0001	≤0.0001	0.0017
IL-12 (p70)	1.48	0.16	1.16	0.1	1.4	0.32	0.4685	1.0000	0.2206
IL-7	8.48	0.62	7.27	0.27	4.96	0.5	≤0.0001	≤0.0001	0.4686
IFN-γ	3.57	0.91	2.5	0.53	1.06	0.23	≤0.0001	≤0.0001	0.0054
TRAIL	89.9	3.28	78	2.66	67	2.81	≤0.0001	0.0273	0.0024
IL-15	8.82	1.57	4.63	0.42	1.93	0.1	≤0.0001	≤0.0001	0.0030
IP-10/CXCL10	447	55.4	292	32.8	124	11	≤0.0001	≤0.0001	≤0.0001
IL-4	0.36	0.05	0.38	0.04	0.39	0.05	0.1851	1.0000	0.0860

	Case Breakout								CQSQ vs CASQ	CQSQ vs CQSA	CQSQ vs CASA	CASQ vs CQSA	CASQ vs CASA	CQSA vs CASA
Analyte[a]	CQSQ[b] Mean	SEM	CASQ[b] Mean	SEM	CQSA[b] Mean	SEM	CASA[b] Mean	SEM	p-value[c]	p-value[c]	p-value[c]	p-value[c]	p-value[c]	p-value[c]
IFN-α	1.67	0.40	2.34	0.49	1.92	0.40	6.76	1.35	1.0000	0.0272	≤0.0001	0.4155	≤0.0001	0.1309
IL-10	4.8	1.64	3.87	0.45	4.6	0.49	6.88	0.59	1.0000	0.0152	≤0.0001	0.1348	≤0.0001	0.0740
BLyS	1288	230	1229	72.6	1323	130	1510	114	0.2754	1.0000	0.0037	1.0000	0.8361	0.4532
IL-12 (p70)	1.10	0.13	1.52	0.22	1.15	0.17	1.39	0.18	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
IL-7	7.19	0.31	7.08	0.36	7.89	0.62	9.19	0.97	1.0000	1.0000	1.0000	1.0000	0.9776	1.0000
IFN-γ	2.85	1.03	2.91	0.96	1.85	0.35	4.00	1.26	1.0000	0.5567	0.0001	1.0000	0.0033	0.2126
TRAIL	72.3	3.31	81.6	3.41	84.9	4.4	95.1	4.98	0.1791	0.1138	0.0008	1.0000	0.5084	1.0000
IL-15	4.16	0.46	6.18	1.01	5.44	0.91	10.1	2.48	0.3569	0.3316	0.0007	1.0000	0.2485	0.7902
IP-10/CXCL10	249	51.9	288	36.2	305	40.6	585	88.1	0.9719	0.0868	≤0.0001	1.0000	≤0.0001	0.0164
IL-4	0.39	0.05	0.45	0.05	0.32	0.05	0.32	0.07	1.0000	1.0000	0.0390	1.0000	0.0180	0.4281

[a]Soluble mediators (pg/ml)
[b]Active=hSLEDAI≥4; Low=hSLEDAI<4; C=Clinically; S=Serologically; Q=Quiescent; A=Active
[c]Kruskal-Wallis test with Dunn's multiple comparison; significance (***p≤0.05***) with Bonferroni corrected ***p≤0.005***

Figure 1

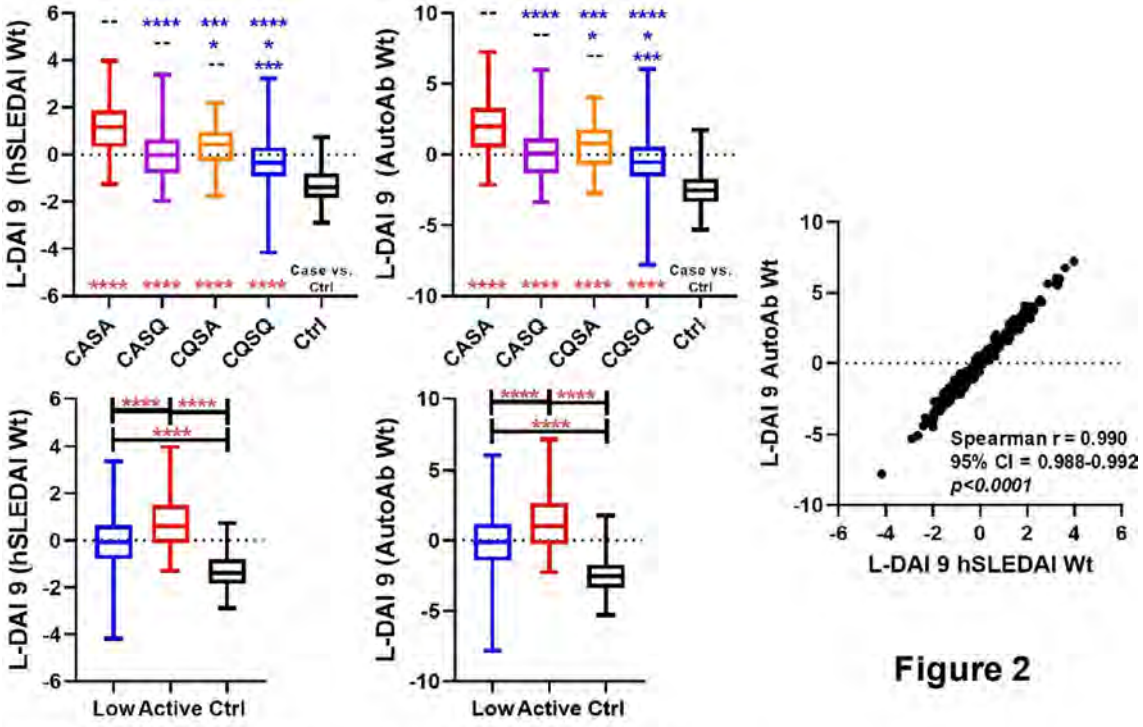
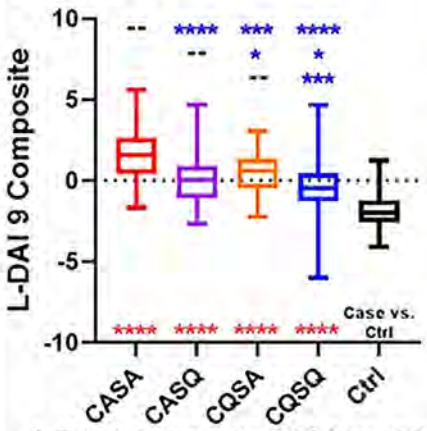
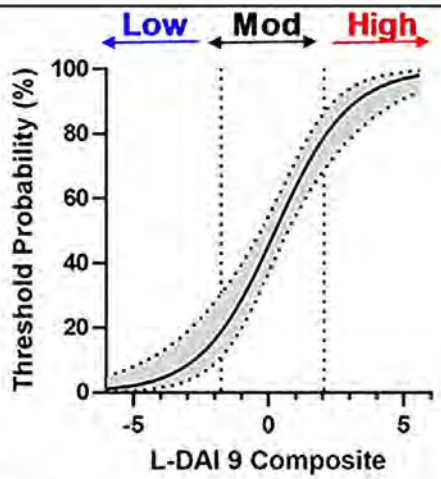


Figure 2

Low=hSLEDAI<4; Active=hSLEDAI≥4 ; C=Clinically; S=Serologically; Q=Quiescent; A=Active
*p<0.05, ***p<0.001, ****p<0.0001 Kruskal-Wallis test with Dunn's multiple comparison.

Figure 3

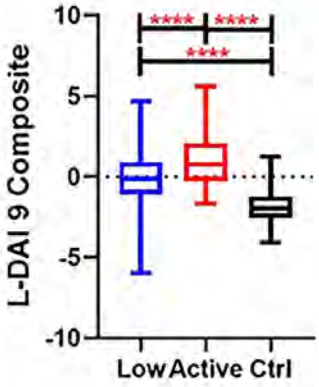


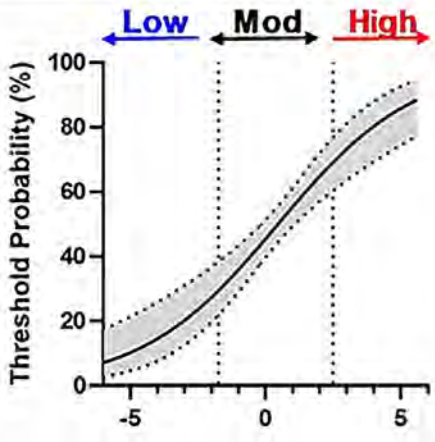


L-DAI 9 Composite CASA vs. CQSQ

AUC (95% CI)	p-value	Effect Size
0.795 (0.727-0.862)	*<0.0001*	1.11

Low Range Cutoff = -1.7577 (19% Threshold Probability)					
OR (95% CI)	***p-value***	**Specificity**	**Sensitivity**	**NPV**	**PPV**
∞ (1.0-∞)	*<0.0001*	0.15	1.00	1.00	0.59
High Range Cutoff = 2.0624 (79% Threshold Probability)					
OR (95% CI)	***p-value***	**Specificity**	**Sensitivity**	**NPV**	**PPV**
7.6 (2.8-19)	*<0.0001*	0.94	0.34	0.54	0.87





L-DAI 9 Composite Low vs. Active

AUC (95%CI)	*p-value*	Pearson r	95% CI	*p-value*	Effect Size
0.673 (0.615-0.731)	*<0.0001*	0.407	0.312-0.494	*<0.0001*	0.613
Low Range Cutoff = -1.7363 (30% Threshold Probability)					
OR (95% CI)	***p-value***	**Specificity**	**Sensitivity**	**NPV**	**PPV**
∞ (6.4-∞)	*<0.0001*	0.12	1.00	1.00	0.53
High Range Cutoff = 2.4928 (69% Threshold Probability)					
OR (95% CI)	***p-value***	**Specificity**	**Sensitivity**	**NPV**	**PPV**
4.5 (2.1-10)	*<0.0001*	0.94	0.21	0.54	0.79

Low=hSLEDAI<4; Active=hSLEDAI≥4 ; C=Clinically; S=Serologically; Q=Quiescent; A=Active

*$p<0.05$, ***$p<0.001$, ****$p<0.0001$ Kruskal-Wallis test with Dunn's multiple comparison.

Conclusion: We have refined the L-DAI to characterize SLE patients with active clinical and/or serological disease vs. those with low/quiescent disease. Treat-to-target approaches using a sensitive and objective biomarker surrogate for clinical disease activity has the potential to help improve clinical disease management and prevent organ damage in SLE.

Disclosure: M. Munroe: Progentec Diagnostics, Inc., 12, Salary Support; **D. Blankenship**: Progentec Diagnostics, Inc., 2; **D. DeFreese**: Progentec Diagnostics, Inc., 3; **A. Holloway**: Progentec Diagnostics, Inc., 3; **M. Purushothaman**: Progentec Diagnostics, Inc., 3, 4; **W. DeJager**: None; **S. Macwana**: None; **J. Guthridge**: None; **S. Kamp**: None; **N. Redinger**: None; **T. Aberle**: None; **E. Chakravarty**: None; **C. Arriens**: AstraZeneca, 1, 5, 6, Aurinia, 6, Bristol-Myers Squibb, 1, 5, Cabaletta, 1, GSK, 1, Kezar, 1, UCB, 1; **Y. Li**: None; **H. Zeng**: None; **S. Dezzutti**: None; **P. Izmirly**: None; **U. Thanarajasingam**: None; **D. Kamen**: None; **J. Buyon**: Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, Related Sciences, 1; **J. James**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 2, Novartis, 2, Progentec Biosciences, 5; **E. Jupe**: Progentec Diagnostics, Inc., 3.

Abstract Number: 0555

Evaluation and Management of the "False Positive" ANA and Undifferentiated Connective Tissue Disease Amongst Rheumatologists

Neha Gupta[1], Sarah Ford[2], Lane Scheiber[2], Tangada Rao[2] and Abhishek Nandan[2], [1]Virginia Commonwealth University Health Systems, Richmond, VA, [2]Virginia Commonwealth University Health Systems; Veterans Affairs Medical Center, Richmond, VA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The management of a positive anti-nuclear antibody (ANA) is one of the most common consultations in rheumatology outpatient practice. The prevalence of a positive ANA in the general population is far greater than that of connective tissue diseases (CTDs), including systemic lupus erythematosus (SLE). There are no guidelines on management of a positive ANA without a clear diagnosis. This study seeks to understand how rheumatologists navigate such scenarios.

Methods: We reached out to 40 practicing rheumatologists using an anonymized, case-based survey using multiple choice questions with branching logic. Demographic information was obtained. We used American College of Rheumatology/European Alliance of Associations for Rheumatology (ACR/EULAR) criteria for SLE to design the cases.

In two cases, patients had a high titer ANA but met no ACR/EULAR criteria for SLE. These cases represent a false-positive ANA (FP-ANA). Two additional cases had patients with low-positive ANA titers, morning-dominant joint stiffness for one hour with a normal musculoskeletal exam, and one ACR/EULAR criteria for SLE. These two cases represent undifferentiated connective tissue disease (UCTD). A final case had isolated thrombocytopenia along with a positive ANA (ITP-UCTD).

Participants were asked if they would obtain ANA sub-serologies or discharge the patient from practice. Of those obtaining sub-serologies, they were asked when follow-up should be arranged, if routine labs are to be obtained at follow-up, and if they would start hydroxychloroquine (HCQ). In each case if sub-serologies were requested, they always returned negative.

Results: 21 out of 40 rheumatologists participated. Work setting: 47% academic, 53% non-academic. Years in practice: 52% with 1-10 years, 24% with 10-20 years, and 24% with more than 20 years. 57% of participants worked in suburban areas. Practice characteristics were not significant in case decision-making.

A mean of 81% of participants in the FP-ANA cases obtained sub-serologies, while the rest chose to discharge the patient without further work-up. Despite negative sub-serologies, 87.5% of participants wished to continue to follow up. One of these cases is detailed in Figure 1.

In all three UCTD cases, all participants obtained sub-serologies. A mean of 55% of participants started HCQ. All participants chose to follow the patient long-term. The ITP-UCTD case is detailed in Figure 2.

Conclusion: Our study suggests that there is substantial variability in how rheumatologists manage the "false-positive ANA" and UCTD. Based on the data, many participants obtain ANA-specific antibodies for a high-titer ANA even when no clinical criteria are met. Most rheumatologists would continue to follow all patients with a positive ANA, although the decision to start HCQ was variable among responders in the cases. Yet, clinical practice guidelines on these practices are lacking. Balancing

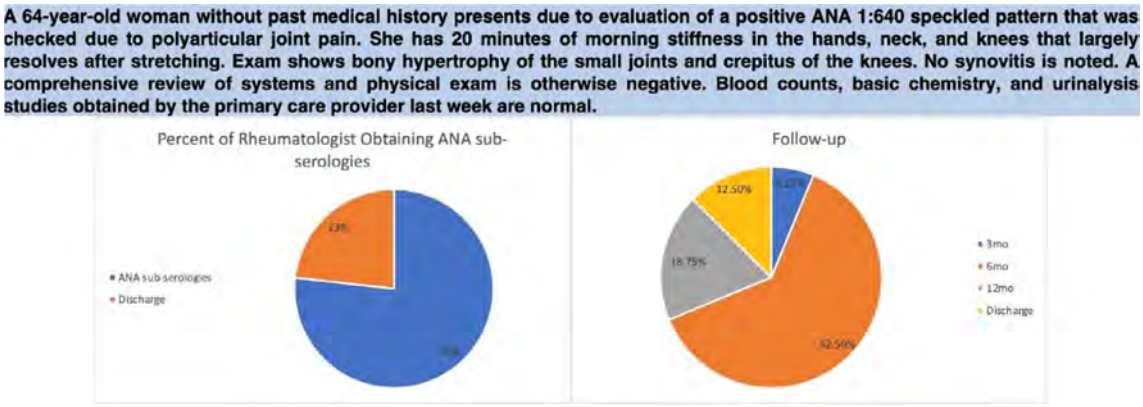


Figure 1: A representative case of a positive ANA patient without ACR/EULAR criteria for CTD. Pie charts show the percentage of participants that would pursue further ANA sub-serologies. Of those obtaining sub-serologies (which returned negative), the additional pie chart shows the distribution of when follow-up was chosen to be arranged.

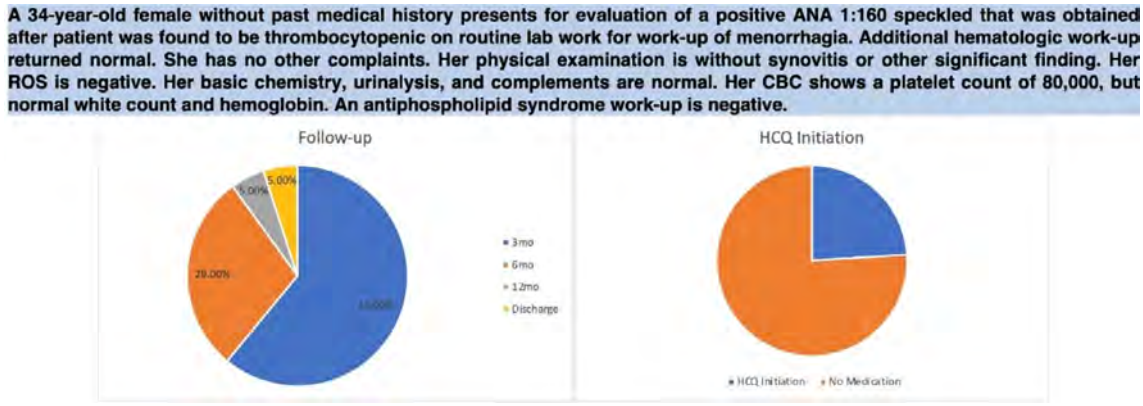


Figure 2: A representative case of a positive ANA patient with thrombocytopenia. All participants chose to obtain sub-serologies, which were negative. Pie charts show the percentage of participants electing to initiate HCQ therapy and the distribution of when follow-up was chosen to be arranged.

the economic costs of continued follow up visits and lab testing in these cases with the risk of developing a defined CTD is a complicated endeavor for most rheumatologists. Further studies and evidence are needed to guide decision making in such scenarios.

Disclosure: N. Gupta: None; **S. Ford**: None; **L. Scheiber**: None; **T. Rao**: None; **A. Nandan**: None.

Abstract Number: 0556

Classical Complement Activation in Lupus Nephritis Correlates with Disease Biomarkers: Results from Two Observational Studies

Edmund Chang[1], Julian Low[1], Noosha Yousefpour[1], Min Bao[1], Jeannette Osterloh[1], Qing Chang[1], Dean Artis[1], Henk-Andre Kroon[1], Yaisa Andrews-Zwilling[1], Maria Dall'Era[2], Ted Yednock[1] and Ann Mongan[1], [1]Annexon Biosciences, Brisbane, CA, [2]University of California San Francisco, San Francisco, CA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis (LN) is an autoantibody-mediated disease that can activate C1q and the classical complement pathway. Pathogenic anti-C1q antibodies (PACAs) are often present, amplifying classical pathway inflammation and contributing to progressive kidney damage. Elevated C4d and reduced C4 are markers of classical complement activation and consumption, respectively. For LN patients in the CLUES/UCSF Study, C4d/C4 ratio positively correlated with PACAs and urine protein-creatinine ratio (UPCR). To validate this correlation, the Sanguine Bio study was conducted.

Methods: Samples were collected from 40 LN patients (plus 20 healthy controls) from the CLUES/UCSF Study and 24 LN patients (plus 10 healthy controls) from Sanguine Bio. In the CLUES/UCSF Study, systemic lupus erythematosus (SLE) diagnoses were confirmed by study physicians according to either of the following definitions: (a) meeting ≥4 of the 11 ACR revised classification criteria for SLE as defined in 1982 and updated in 1997 or (b) meeting 3 of the 11 ACR criteria along with having SLE confirmed by a study rheumatologist. Complement activation and consumption (C4d, C4), exploratory biomarkers in plasma and urine, and UPCR were evaluated.

Results: Sanguine Bio samples from a subset of LN patients demonstrated elevated C4d/C4 compared to healthy controls, indicating classical complement pathway activation (**Figure**). Urinary biomarkers of LN correlated with C4d/C4 ratio in these patients.

Conclusion: In these LN patients, C4d/C4 ratios were elevated and correlated with LN biomarkers in blood and urine, supporting classical complement activity. These data support an ongoing, phase 1b study of ANX009 with the goal of assessing safety, tolerability, and pharmacodynamics of repeat doses of subcutaneous ANX009 with standard of care in adults with LN. ANX009 is an anti-C1q antigen binding fragment targeting LN patients with evidence of classical complement activity (elevated C4d/C4).

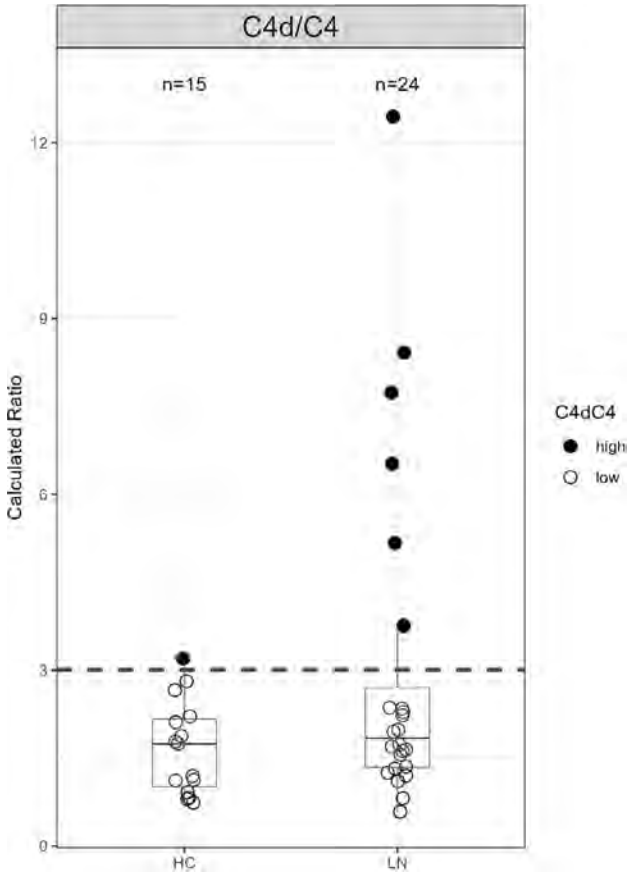


Figure. A Subset of Patients with LN Demonstrated Elevated C4d/C4 Over Healthy Controls

Disclosure: E. Chang: Annexon Biosciences, 3, 8; **J. Low**: Annexon Biosciences, 3, 8; **N. Yousefpour**: Annexon Biosciences, 3, 8; **M. Bao**: Annexon Biosciences, 3, 8, Roche/Genentech, 3, 8; **J. Osterloh**: Annexon Biosciences, 3, 8, FibroGen, Inc., 3; **Q. Chang**: Annexon Biosciences, 3, 8; **D. Artis**: Annexon Biosciences, 3, 8; **H. Kroon**: Annexon Biosciences, 3, 8; **Y. Andrews-Zwilling**: Annexon Biosciences, 3, 8; **M. Dall'Era**: Annexon Biosciences, 2, 5, AstraZeneca, 2, Aurinia, 2, Biogen, 2, GlaxoSmithKlein, 2, 5, Pfizer, 2; **T. Yednock**: Annexon Biosciences, 3, 8; **A. Mongan**: Annexon Biosciences, 3, 8.

Abstract Number: 0557

Longitudinal Evaluation of Cell-bound Complement Activation Products in Patients with SLE

Jennifer Rogers[1], Amanda Eudy[2], Daniel Wojdyla[3], Tyler O'Malley[4], David Pisetsky[5], Roberta Alexander[4], Kai Sun[1], Lisa Criscione-Schreiber[6], Jayanth Doss[1], Rebecca Sadun[1], Mithu Maheswaranathan[6] and Megan Clowse[7], [1]Duke University, Durham, NC, [2]Duke University, Raleigh, NC, [3]Duke Clinical Research Institute, Durham, NC, [4]Exagen, Vista, CA, [5]Duke University Medical Center, Durham, NC, [6]Duke University School of Medicine, Durham, NC, [7]Duke University, Chapel Hill, NC

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Cell-bound complement activation products (CB-CAPs), when part of a multi-analyte assay with algorithm (MAP), are valuable SLE diagnostic biomarkers. Levels of erythrocyte-bound complement activation products have been associated with SLE disease activity. The clinical and serologic phenotype of longitudinal MAP-positive patients has not been well described. Herein, we assessed the relationship between longitudinal MAP results with clinical and laboratory variables.

Methods: This was a longitudinal study of adult SLE patients (2012 SLICC or ACR/EULAR criteria) with ≥2 routine clinic visits from June 2020 to July 2022. Patients completed the polysymptomatic distress scale. The rheumatologist scored the PGA and SLEDAI scores. Autoantibodies including ANA and anti-RNA binding proteins were measured by ELISA. Anti-dsDNA was measured by immunofluorescence using the Crithidia luciliea assay. CB-CAPs were analyzed by flow cytometry. The multi-analyte assay panel (MAP) was determined using a 2-tier algorithm. Chi-square and ANOVA tests were used to analyze differences in demographic and disease history between persistently MAP positive, MAP negative, and patients with changing MAP positivity. Serologies and clinical variables at follow-up visits were compared using generalized linear models.

Results: In this longitudinal cohort of 113 patients with 175 follow-up visits (90% female, 62% Black, mean age 45) 65% were consistently MAP positive, 20% were negative, and MAP positivity changed in 15%. Persistent MAP-positive patients were younger and more often of the Black race. There was no difference in MAP positivity based on disease duration. Significantly more MAP-positive patients met ACR/EULAR criteria and had higher total ACR/EULAR scores. Patients who remained MAP positive were more likely to have a history of acute cutaneous lupus but there was no difference in other historical manifestations between groups (Table 1).

When evaluating longitudinal associations, patients with persistent MAP positivity had higher total SLEDAI scores, but there was no difference in the clinical SLEDAI. Therapy was comparable across groups except for greater use of belimumab, rituximab, and cyclophosphamide in persistent MAP-positive patients. Patients who remained MAP positive reported higher rates of depression, but a similar burden of polysymptomatic distress and fatigue. A greater number of lupus-specific serologies were present in those with MAP positivity (Table 2).

Table 1. Demographics and Disease History of the SLE patient cohort

	Overall Patients (N = 113)	MAP remains positive (N = 73)	MAP remains negative (N = 23)	MAP changing positivity (N = 17)	p-value
Demographics					
Age, mean (SD)	44.6 (14.3)	42.1 (15.0)	47.1 (12.9)	52.0 (10.2)	0.0227
Female	89.4% (101)	87.7% (64)	95.7% (22)	88.2% (15)	0.5485
Black race	61.9% (70)	71.2% (52)	39.1% (9)	52.9% (9)	0.0584
Ethnicity Hispanic	5.4% (6)	4.1% (3)	13.0% (3)	0.0% (0)	0.1488
SLE Disease History					
Duration of disease, mean (SD)	12.7 (9.0)	13.2 (9.0)	12.5 (9.2)	11.0 (9.4)	0.6764
2011 SLICC Criteria	100.0% (113)	100.0% (73)	100.0% (23)	100.0% (17)	na
2019 ACR/EULAR Criteria	94.7% (107)	98.6% (72)	91.3% (21)	82.4% (14)	0.0190
2019 ACR/EULAR Total Score, median (25th - 75th pctls)	21 (16-29)	24 (18-30)	18 (13-21)	19 (16-26)	0.0117
h/o Renal	45.1% (51)	45.2% (33)	34.8% (8)	58.8% (10)	0.3195
h/o Arthritis	67.3% (76)	72.6% (53)	65.2% (15)	47.1% (8)	0.1262
h/o Acute cutaneous SLE	62.8% (71)	68.5% (50)	65.2% (15)	35.3% (6)	0.0373
h/o Discoid SLE	18.6% (21)	21.9% (16)	17.4% (4)	5.9% (1)	0.3057
h/o Serositis	23.9% (27)	26.0% (19)	21.7% (5)	17.6% (3)	0.7385
h/o Neuropsychiatric	5.3% (6)	8.2% (6)	0.0% (0)	0.0% (0)	0.1762
h/o Oral ulcers	54.0% (61)	52.1% (38)	65.2% (15)	47.1% (8)	0.4480
h/o Alopecia	56.6% (64)	56.2% (41)	43.5% (10)	76.5% (13)	0.1135
h/o Hematologic	61.1% (69)	65.8% (48)	39.1% (9)	70.6% (12)	0.0504

Table 2. Serologies, medications, disease activity, and patient symptoms at the longitudinal follow-up visits.

	All Follow-up Visits (N = 175)	MAP remains positive (N = 111)	MAP remains negative (N = 43)	MAP positive to negative (N = 10)	MAP negative to positive (N = 11)	
Serologies						
Anti-dsDNA positive	21.7% (38/175)	34.2% (38/111)	0.0% (0/43)	0.0% (0/10)	0.0% (0/11)	<.0001
Low C3 or C4	14.4% (25/174)	17.3% (19/110)	11.6% (5/43)	0.0% (0/10)	9.1% (1/11)	0.2236
Anti-Sm positive	3.0% (2/66)	5.6% (2/36)	0.0% (0/17)	0.0% (0/7)	0.0% (0/6)	0.4795
Anti-Ro60 positive	46.2% (80/173)	49.5% (54/109)	39.5% (17/43)	50.0% (5/10)	36.4% (4/11)	0.6242
Anti-U1RNP positive	29.3% (49/167)	44.8% (47/105)	0.0% (0/42)	11.1% (1/9)	9.1% (1/11)	<.0001
Anti-C1q	23.4% (41/175)	27.9% (31/111)	14.0% (6/43)	10.0% (1/10)	27.3% (3/11)	0.1785
Medications						
Hydroxychloroquine	83.3% (145/174)	84.5% (93/110)	81.4% (35/43)	70.0% (7/10)	90.9% (10/11)	0.6051
Mycophenolate	31.0% (54/174)	33.6% (37/110)	25.6% (11/43)	20.0% (2/10)	36.4% (4/11)	0.6322
Prednisone	18.4% (32/174)	22.7% (25/110)	9.3% (4/43)	10.0% (1/10)	18.2% (2/11)	0.2010
Belimumab, Rituximab, Cyclophosphamide	13.2% (23/174)	17.3% (19/110)	9.3% (4/43)	0.0% (0/10)	0.0% (0/11)	0.0451
Current Disease Activity						
PGA, mean (SD), N	0.5 (0.5), 175	0.5 (0.5), 111	0.4 (0.4), 43	0.4 (0.5), 10	0.4 (0.5), 11	0.7886
PGA >= 1.5	9.7% (17/175)	11.7% (13/111)	4.7% (2/43)	10.0% (1/10)	9.1% (1/11)	0.5701
SLEDAI, mean (SD), N	2.2 (2.5), 175	2.6 (2.7), 111	1.9 (2.2), 43	0.8 (1.7), 10	0.5 (0.9), 11	0.0120
Clinical SLEDAI, mean (SD), N	1.1 (1.8), 175	1.2 (1.7), 111	1.1 (2.1), 43	0.8 (1.7), 10	0.4 (0.8), 11	0.5125
SLEDAI Renal	7.4% (13/175)	8.1% (9/111)	9.3% (4/43)	0.0% (0/10)	0.0% (0/11)	0.3183
SLEDAI Arthritis	12.0% (21/175)	9.9% (11/111)	18.6% (8/43)	20.0% (2/10)	0.0% (0/11)	0.1466
SLEDAI Rash	17.1% (30/175)	21.6% (24/111)	9.3% (4/43)	0.0% (0/10)	18.2% (2/11)	0.0601
Patient reported symptoms						
Polysymptomatic distress score, mean (SD), N	9.3 (6.7), 159	8.8 (6.7), 99	10.8 (6.6), 40	9.1 (5.1), 10	7.8 (7.3), 10	0.3985
Fatigue (moderate/severe)	48.0% (72/150)	46.4% (45/97)	54.3% (19/35)	55.6% (5/9)	33.3% (3/9)	0.6473
Depression	36.5% (54/148)	45.7% (43/94)	21.6% (8/37)	11.1% (1/9)	25.0% (2/8)	0.0136

Conclusion: Identifying endotypes of SLE is key to advancing personalized medicine. In this cohort of patients with SLE, most patients had static MAP results. MAP results changed between visits in a subset of patients; although there was not a distinct clinical, demographic, or laboratory phenotype in those patients. Patients with consistent MAP positivity reported more depression and had a greater burden of disease activity as measured by the ACR/EULAR score and greater use of biologic and cytotoxic therapy. Combining longitudinal MAP scores with assessments of SLE activity may provide important prognostic information. Larger studies are ongoing to evaluate the relationship between individual CB-CAPs and disease activity.

Disclosure: J. Rogers: Amgen, 2, Ampel Biosolutions, 1, AstraZeneca, 6, Aurinia, 1, Eli Lilly, 1, Exagen, 5, GlaxoSmithKlein(GSK), 2, Immunovant, 2, 5; **A. Eudy**: Amgen, 2, Exagen, 5, GlaxoSmithKlein(GSK), 5, Immunovant, 5, Pfizer, 5; **D. Wojdyla**: None; **T. O'Malley**: Exagen, 3, 11, 12, Shareholder; **D. Pisetsky**: Immunovant, 2, 5; **R. Alexander**: Exagen, 3; **K. Sun**: AstraZeneca, 6; **L. Criscione-Schreiber**: GlaxoSmithKlein(GSK), 5, UCB, 5; **J. Doss**: None; **R. Sadun**: None; **M. Maheswaranathan**: AstraZeneca, 6; **M. Clowse**: Exagen, 5, GlaxoSmithKlein(-GSK), 2, 5, Immunovant, 5, UCB, 2, 5.

Abstract Number: 0558

Elevated Serum Levels of S100A8/A9 Discriminate Systemic Lupus Erythematosus Patients with Cognitive Impairment from Patients Without Impairment

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Cognitive impairment (CI) is one of the most common manifestations of Neuropsychiatric Systemic Lupus **Erythematosus** (NPSLE). Studies have reported that SLE patients with different NPSLE syndromes have alterations in the cerebrospinal fluid or their serum levels of various cytokines and proteases (analytes) that can lead to neuroinflammation. However, studies focused on analytes in CI are scarce. In this study, we investigated the ability of various serum analytes to discriminate SLE patients with CI from those without impairment.

Methods: Two hundred ninety individuals 18-65 years old who met the 2019 EULAR/ACR classification criteria for SLE were included. Cognitive ability was measured by psychometrists utilizing the 1-hr ACR-Neuropsychological Battery (ACR-NB), and the scores were standardized by age and gender to operationally classify patients' performance into CI (z-score of ≤-1.5 in two or more domains) and non-CI. At the time of the neuropsychological assessment patients provided blood samples. The serum levels of nine analytes (IL-6, IL-10, IFN-γ, MMP-9, NGAL, S100A8/A9, S100B, TNF-α, and TWEAK) were determined using ELISA. The data were randomly partitioned into a training (70%) and a test (30%) sets. A predictive regression model was performed to evaluate the measured analytes' ability to discriminate SLE patients with CI from patients without impairment. The optimal cut-off values to discern between CI and non-CI for each analyte were

Table. 1. AUC of measured analytes serum levels to discriminate SLE patients with CI from those without CI.

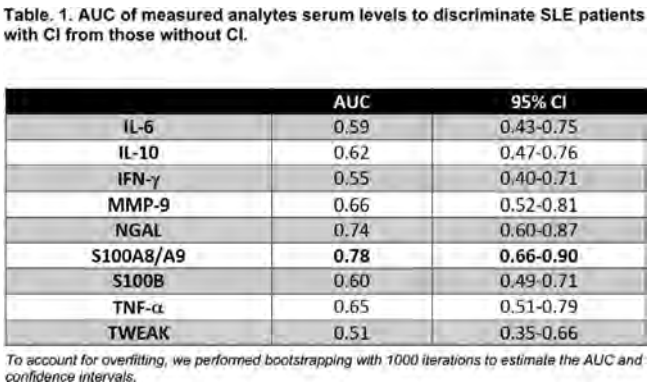

Table. 1. AUC of measured analytes serum levels to discriminate SLE patients with CI from those without CI.

	AUC	95% CI
IL-6	0.59	0.43-0.75
IL-10	0.62	0.47-0.76
IFN-γ	0.55	0.40-0.71
MMP-9	0.66	0.52-0.81
NGAL	0.74	0.60-0.87
S100A8/A9	**0.78**	**0.66-0.90**
S100B	0.60	0.49-0.71
TNF-α	0.65	0.51-0.79
TWEAK	0.51	0.35-0.66

To account for overfitting, we performed bootstrapping with 1000 iterations to estimate the AUC and confidence intervals.

Table 2. MMP-9, NGAL, S100A8/A9, and various combinations ability to discriminate SLE patients with CI from those without CI.

Table 2. MMP-9, NGAL, S100A8/A9, and various combinations ability to discriminate SLE patients with CI from those without CI.

Analyte	Sn (%)	Sp (%)	PPV (%)	NPV (%)
MMP-9 (≥ 78.42 pg/mL)	78	32	71	41
NGAL (≥ 141.47 pg/mL)	42	69	70	35
S100A8/A9 (≥ 2367 ng/mL)	29	**86**	**82**	36
Analyte Combination				
S100 A8/A9 and MMP-9	38	87	86	40
S100 A8/A9 and NGAL	35	74	47	63
S100 A8/A9 and NGAL and MMP-9	15	89	48	61

For those analytes with the highest AUC (MMP-9, NGAL, and S100A8/A9) optimal cut-off values to discern between CI and non-CI were obtained by Youden's index, Sensitivity (Sn), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV).

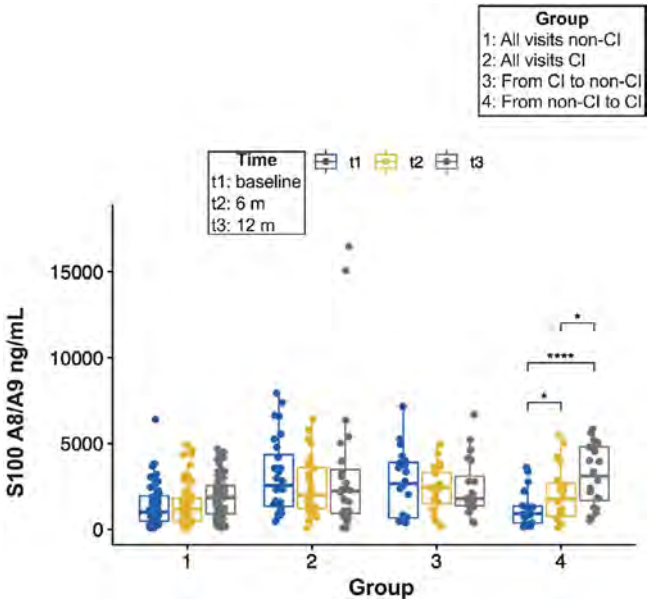

Figure 1. Pairwise comparison of S100A8/A9 serum levels between time points. P-values were adjusted using the Bonferroni multiple-testing correction method. Significant differences are indicated by asterisks (* $p \leq 0.05$, **** $p \leq 0.0001$). Non-significant differences are not displayed.

obtained by Youden's index, and their sensitivity (Sn), specificity (Sp), and predictive values were calculated. For patients that had completed cognitive assessment at 6 and 12 months (n=125, 43%), pairwise comparisons of the S100A8/A9 serum levels between time points were performed.

Results: Of 290 patients, 40% had CI (n=116). Overall, no differences in demographic or clinical characteristics were observed between patients with and without CI. S100A8/A9 had the highest AUC (0.79, 95% CI: 0.66-0.90) (Table 1) and displayed the greatest discriminative ability (Sp 86% and PPV 82%) (Table 2) to differentiate between patients with and without CI. Compared to the predictive ability of S100A8/A9 alone, the improvement of S100A8/A9 combined with other analytes was marginal, except for a mild increase in Sn and Sp with MMP-9 (Table 2). Cognitive status remained unchanged for most of the patients with 6- and 12-month follow-up visits (57 and 28 remained in the non-CI and the CI groups, respectively, whereas 20 with CI changed to non-CI and 20 from non-CI to CI). S100A8/A9 serum levels increased over time in group 4 (from non- CI to CI) and there was a trend to reduced levels from the baseline and 6-month visits to the 12-month visit in group 3 (from CI to non-CI) (Figure 1).

Conclusion: In this large cohort of well-characterized SLE patients, amongst all measured analytes, S100A8/A9 had the greatest discriminatory ability in differentiating between SLE patients with and without CI. Replication of these findings is needed to confirm the utility of S100A8/A9 as a biomarker for CI in SLE. Research into the underlying mechanisms is also needed.

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Abstract Number: 0559

Development of Charlson Comorbidity Index (CCI) Comorbidities and CCI Score in Danish Nationwide Cohort of 3,178 Patients with Newly Diagnosed Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Comorbidity risk is remarkably increased in patients with Systemic Lupus Erythematosus (SLE) compared with the general population. A better understanding of comorbidity development in SLE is needed to improve the prognosis in SLE patients. We assessed the accrual of comorbidity utilizing the Charlson Comorbidity Index (CCI) in a large nationwide cohort of patients with SLE compared with matched population controls.

Methods: We assembled a cohort of adult patients with incident SLE using ICD diagnosis codes registered in the Danish National Patient Register (DNPR) from January 1996 to July 2018 (n=3,178). The date of the first SLE registration in the DNPR was considered the baseline. SLE patients were age, - and sex-matched to 60,090 population controls randomly selected from the Danish Civil Registration System. Comorbidities (during outpatient and inpatient care) were identified using DNPR. We estimated the CCI score, number of CCI comorbidities and cumulative prevalence (%) of CCI comorbidities, stratified by sex, at baseline (SLE diagnosis) and at the end of follow-up (FU) (death, emigration or July 2018) in patients with SLE and controls.

Results: 84% of SLE patients and non-SLE controls were female; mean age at baseline was 47 years. *Mean CCI scores* were 2.3 times higher in SLE patients vs controls at baseline (0.7 vs 0.3) and 1.9 times higher at the end of FU (1.7 vs 0.9). Similarly, the CCI scores were about 2-3 times higher in SLE patients than controls in the 1-2, 3-4 and ≥ 5 *score categories*, both at baseline and the end of FU (Table 1). Males had higher scores than females in all the above categories.

Table 1. Baseline (SLE diagnosis) and end-of-follow-up CCI scores, stratified by sex, in patients with incident SLE compared with matched general population controls, followed during January 1996 - July 2018

CCI score*	SLE n= 3178		PC n= 60090	
	Baseline n (%)	End of follow-up n (%)	Baseline n (%)	End of follow-up n (%)
1-2				
All	807 (25.4)	1088 (34.2)	8239 (13.7)	13371 (22.3)
Females	637 (23.8)	913 (34.1)	6534 (12.9)	10939 (21.6)
Males	170 (34.0)	175 (35.0)	1705 (18.0)	2432 (25.7)
3-4				
All	180 (5.7)	474 (14.9)	1339 (2.2)	3950 (6.6)
Females	134 (5.0)	362 (13.5)	963 (1.9)	2925 (5.8)
Males	46 (9.2)	112 (22.4)	376 (4.0)	1025 (10.8)
≥ 5				
All	58 (1.82)	304 (9.57)	569 (0.95)	2910 (4.84)
Females	39 (1.46)	222 (8.29)	396 (0.78)	2108 (4.16)
Males	19 (3.8)	82 (16.4)	173 (1.83)	802 (8.46)

CCI: Charlson Comorbidity Index; PC: population control.

*The original version of the CCI contains 19 comorbidities (we excluded the rheumatologic disease category). The CCI score is calculated by summing the assigned weights for each comorbidity, e.g., assigned weight is 1 for cerebrovascular disease, 2 for moderate or severe renal disease, 3 for moderate or severe liver disease, and 6 for metastatic solid tumor (Charlson ME et al., 1987).

Table 2. Number of CCI comorbidities at baseline (SLE diagnosis) and at the end of follow-up, stratified by sex, in patients with incident SLE compared with matched general population controls, followed during January 1996 - July 2018

Number of CCI Comorbidities*	SLE n= 3178		PC n= 60090	
	Baseline n (%)	End of follow-up n (%)	Baseline n (%)	End of follow-up n (%)
0				
All	2133 (67.1)	1312 (41.3)	49943 (83.1)	39859 (66.3)
Females	1868 (69.8)	1181 (44.1)	42722 (84.4)	34643 (68.4)
Males	265 (53.0)	131 (26.2)	7221 (76.2)	5216 (55.1)
1				
All	707 (22.3)	909 (28.6)	7506 (12.5)	11625 (19.4)
Females	560 (20.9)	761 (28.4)	6017 (11.9)	9590 (19.0)
Males	147 (29.4)	148 (29.6)	1489 (15.7)	2035 (21.5)
2				
All	224 (7.1)	486 (15.3)	1809 (3.0)	4840 (8.1)
Females	176 (6.6)	400 (14.9)	1345 (2.7)	3747 (7.4)
Males	48 (9.6)	86 (17.2)	464 (4.9)	1093 (11.5)
3				
All	76 (2.4)	226 (7.1)	553 (0.9)	2170 (3.6)
Females	52 (1.9)	169 (6.3)	362 (0.7)	1587 (3.1)
Males	24 (4.8)	57 (11.4)	191 (2.0)	583 (6.2)
≥ 4				
All	38 (1.2)	245 (7.7)	279 (0.5)	1596 (2.7)
Females	22 (0.8)	167 (6.2)	169 (0.3)	1048 (1.7)
Males	16 (3.2)	78 (15.6)	110 (1.2)	548 (5.8)

CCI: Charlson Comorbidity Index; PC: population control.

* The original CCI version contains 19 comorbidities (Charlson ME et al., 1987). The Rheumatologic disease category is excluded; "Any tumor without metastasis" is combined with "Leukemia and lymphoma".

Number of CCI comorbidities

Fewer SLE patients than controls had no CCI comorbidities at baseline: 67% vs 83%, and at the end of FU: 41% vs 66% (Table 2). Two out of ten SLE patients had at least one CCI comorbidity at baseline vs one out of ten controls. Moreover, compared with controls, patients with SLE were 2-3 times more likely to have 2, 3 and 4 CCI comorbidities, at baseline and the end of FU.

Cumulative prevalence of CCI comorbidities

The cumulative prevalence of myocardial infarction, congestive heart failure, and peripheral vascular, cerebrovascular, chronic pulmonary and liver diseases was 2-4 times higher in patients with SLE than controls, at baseline and the end of FU (Table 3). Of note, in SLE patients, the cumulative prevalence of all the above comorbidities, as well as diabetes and peptic ulcer, doubled by the end of FU compared with baseline. Relative to controls, renal disease was the most prevalent comorbidity in SLE, with baseline and end-of-FU prevalence 8.6 and 6.5 times higher in SLE patients vs controls. Baseline and end-of-FU prevalence of malignancy was similar in SLE and controls. Most CCI comorbidities were more prevalent in males than females.

Table 3. Cumulative prevalence of CCI comorbidities at baseline (SLE diagnosis) and at the end of follow-up in patients with incident SLE compared with matched general population controls, followed during January 1996 - July 2018

CCI comorbidity*	SLE n= 3178		PC n=60090	
	Baseline n, %	End of FU n, %	Baseline n, %	End of FU n, %
Myocardial infarction	92 (2.9)	186 (5.9)	850 (1.4)	1872 (3.1)
Congestive heart failure	74 (2.3)	222 (7.0)	528 (0.9)	1843 (3.1)
Peripheral vascular disease	185 (5.9)	366 (11.5)	853 (1.4)	2243 (3.7)
Cerebrovascular disease	228 (7.2)	501 (15.8)	1622 (2.7)	4326 (7.2)
Chronic pulmonary disease	274 (8.6)	588 (18.5)	2877 (4.8)	5755 (9.6)
Renal disease	218 (6.9)	518 (16.3)	487 (0.8)	1485 (2.5)
Diabetes without chronic complications	89 (2.8)	213 (6.7)	1361 (2.3)	3054 (5.1)
Diabetes with chronic complications	42 (1.3)	107 (3.4)	538 (0.9)	1337 (2.2)
Liver disease, mild	64 (2.0)	142 (4.5)	410 (0.7)	863 (1.4)
Liver disease, moderate/severe	9 (0.3)	33 (1.0)	81 (0.1)	291 (0.5)
Peptic ulcer disease	85 (2.7)	174 (5.5)	1009 (1.7)	1851 (3.1)
Hemiplegia/ paraplegia	10 (0.3)	21 (0.7)	92 (0.2)	179 (0.3)
Dementia	13 (0.4)	60 (1.9)	204 (0.3)	1059 (1.8)
Malignancy without metastases*	168 (5.3)	478 (15.0)	2856 (4.8)	7632 (12.7)
Metastatic solid tumor	11 (0.4)	89 (2.8)	257 (0.4)	1431 (2.4)
AIDS	0	0	29 (0.1)	41 (0.1)

CCI: Charlson Comorbidity Index; PC: population control; FU: follow-up; AIDS: Acquired Immunodeficiency Syndrome.
* The original CCI version contains 19 comorbidities (Charlson ME et al., 1987). The Rheumatologic disease category is excluded; "Any tumor without metastasis" is combined with "Leukemia and lymphoma" into "Malignancy without metastases".

Conclusion: The baseline and end-of-follow-up cumulative prevalence of myocardial infarction, congestive heart failure, and renal, peripheral vascular, cerebrovascular, chronic pulmonary and liver diseases was substantially increased in patients with SLE compared with matched general population controls. The CCI scores and the number of CCI comorbidities were about 2-3 times higher in SLE patients than controls, at baseline and at the end of follow-up.

Disclosure: R. Baronaite Hansen: None.

Abstract Number: 0560

Genetic Determinants of Lupus Nephritis and Kidney Function in Systemic Lupus Erythematosus

Magdalena Riedl Khursigara[1], Nicholas Gold[2], Thai-Son Tang[3], Daniela Dominguez[2], Marisa Klein-Gitelman[4], Dafna Gladman[5], Daniel Goldman[6], Elizabeth Harvey[2], Mariko Ishimori[7], Caroline Jefferies[7], Diane L. Kamen[8], Sylvia Kamphuis[9], Andrea Knight[2], Chia-Chi Lee[7], Deborah Levy[2], Damien Noone[2], Karen Onel[10], Christine Peschken[11], Michelle Petri[6], Janet Pope[12], Eleanor Pullenayegum[2], Earl Silverman[13], Zahi Touma[1], Murray Urowitz[14], Daniel Wallace[7], Joan Wither[15] and **Linda Hiraki**[2], [1]University of Toronto, Toronto, ON, Canada, [2]The Hospital for Sick Children, Toronto, ON, Canada, [3]University of Toronto, Mississauga, ON, Canada, [4]Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, [5]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Department of Medicine, University of Toronto, Toronto, ON, Canada, [6]Department of Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Timonium, MD, [7]Cedars-Sinai Medical Center, Los Angeles, CA, [8]Medical University of South Carolina, Charleston, SC, [9]Sophia Children's Hospital, Rotterdam, Netherlands, [10]Hospital for Special Surgery, New York, NY, [11]University of Manitoba, Winnipeg, MB, Canada, [12]University of Western Ontario, London, ON, Canada, [13]Silverman, Toronto, ON, Canada, [14]Schroeder Arthritis Institute, Krembil Research Institute; University of Toronto Lupus Clinic; Division of Rheumatology, Toronto, ON, Canada, [15]University Health Network, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I

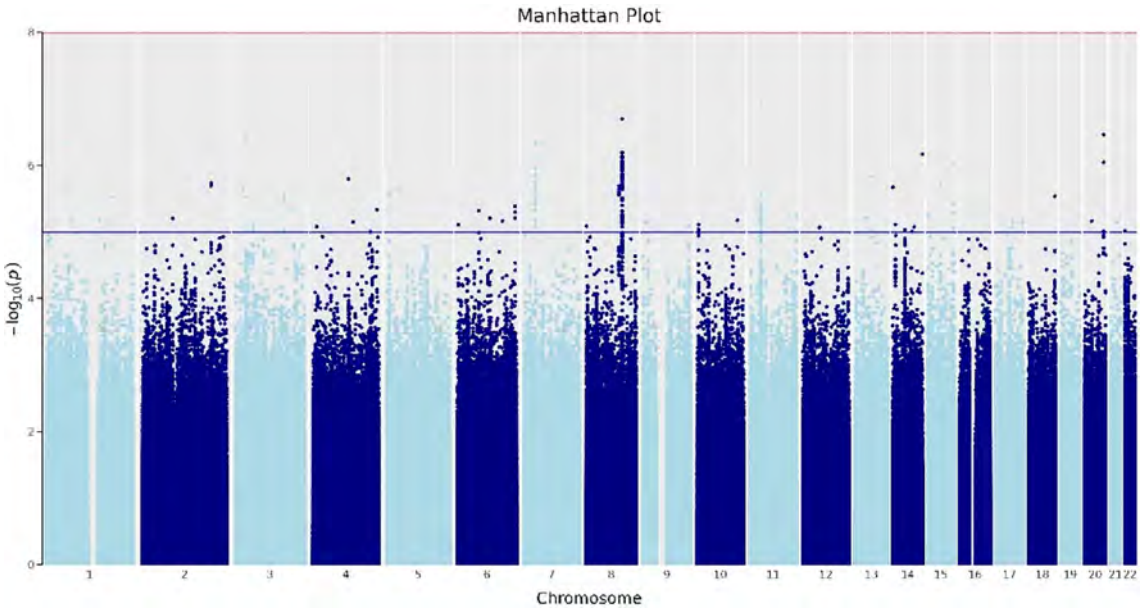
Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis (LN) is one of the most common and severe manifestation of SLE. Risk factors for lupus nephritis and renal function decline are not well understood. We completed a genome wide association study (GWAS) of LN in a multi-ethnic cohort of children and adults with SLE.

Methods: We included SLE patients from dedicated Lupus clinics and the SLICC cohort. All patients met ACR and/or SLICC SLE classification criteria and were genotyped on a multi-ethnic Illumina array. Ungenotyped SNPs were imputed to TopMed, and principal components for ancestral estimation were generated using both 1000 Genomes and GRAF-pop. LN was defined by SLE criteria and confirmed on kidney biopsy in 75%. Kidney function (estimated glomerular filtration rate, eGFR) was calculated using the Schwartz Bedside formula for measures < 18 years and CKD-EPI (without race) for >18 years of age and collected longitudinally over time. Wilcoxon rank sum or Chi-square tests were used to compare characteristics between LN and Non-LN patients. We completed GWAS of LN in marginal and multivariable adjusted regression models with principal components for ancestry, sex and cohort site.

Results: The study included 2981 patients with SLE, 88% female, 46% of European ancestry and 27% childhood-onset SLE. LN was present in 45%. People with LN were younger at diagnosis, and more likely of African American or East Asian ancestry than those without LN. People with LN had significantly lower within-person mean eGFR, greater eGFR variability



Manhattan Plot for LN, adjusted for PC, sex and site

Table: Characteristics of LN and Non-LN patients

Patient Characteristics	All SLE Patients (n=2981)	LN SLE Patients (n=1351)	Non-LN SLE Patients (n=1630)	P-value
Sex, Female	2628 (88.2)	1138 (84.2)	1490 (91.4)	$1.6e^{-09}$
Age at SLE diagnosis (years)	25.6 [16.4, 37.8]	22.6 [15.7, 33.0]	28.3 [17.3, 41.3]	$2.2e^{-16}$
cSLE diagnosis	814 (27.3)	484 (35.8)	440 (27.0)	$2.1e^{-07}$
Inferred Ancestry				$2.2e^{-16}$
European	1367 (45.9)	493 (36.5)	874 (53.6)	
East Asian	459 (15.4)	252 (18.6)	207 (12.7)	
African	555 (18.6)	316 (23.3)	239 (14.7)	
American	151 (5.1)	80 (5.9)	71 (4.4)	
South Asian	131 (4.4)	68 (5.0)	63 (3.9)	
Admixed	317 (10.6)	141 (10.4)	176 (10.8)	
Hypertension*	1017 (37.1)	659 (52.6)	358 (23.8)	$2.2e^{-16}$
Kidney failure (chronic dialysis or transplant)*	25 (0.9)	25 (2.0)	0 (0.0)	$3.0e^{-08}$
Time from diagnosis to 1st eGFR (years)*	0.6 [0.06, 3.4]	0.6 [0.08, 3.8]	0.5 [0.04, 3.0]	$3.3e^{-01}$
Time from 1st eGFR measurement to last (years)*	8.9 [4.1, 14.8]	10.0 [5.1, 16.1]	7.8 [3.4, 13.7]	$4.4e^{-13}$
Within-Person No. eGFR Measures*	16 [8, 35]	21 [10, 45]	13 [6, 29]	$2.2e^{-16}$
Within-Person Mean*	100.8 [86.0, 113.1]	100.2 [81.3, 113.4]	101.2 [88.6, 112.7]	$7.7e^{-02}$
Within-Person eGFR Variance*	106.6 [51.4, 198.7]	137.2 [69.6, 268.6]	87.2 [43.1, 156.4]	$2.2e^{-16}$
eGFR slope ml/min/1.73m^2/y*	-0.53 [-2.00, 0.48]	-0.67 [-2.26, 0.36]	-0.53 [-1.83, 0.67]	$2.3e^{-02}$

* data available for N= 2740

and slope over time compared to those without LN (Table). GWAS of LN demonstrated a peak on chromosome 8, intronic to *ATP6V1C1*, yet did not reach a genome-wide significance ($p < 5x10^{-8}$).

Conclusion: A GWAS of LN in a multiethnic cohort of children and adults with SLE, did not identify a significant locus. The top signal was on chromosome 8, intronic to *ATP6V1C1*. We will complete GWAS of repeated eGFR measures, as it is a more informative outcome that we expect will improve power for detecting genetic loci for LN.

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Abstract Number: 0561

Frequency of Anti-Ro Antibodies in Systemic Lupus Erythematosus Patients: Insights from Multicenter and National Registry

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I

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Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-Ro antibodies can be detected in 40% of patients with systemic lupus erythematosus (SLE) and have been associated with various clinical manifestations of the disease as well as maternal-fetal complications. The aim of this study was to describe the frequency of anti-Ro antibodies in SLE patients and to assess their association with disease characteristics, maternal-fetal complications, treatment, morbidity and mortality.

Methods: Retrospective observational study. Data from SLE patients of the National Registry of the Argentine Society of Rheumatology (RELESSAR) were used. Sociodemographic data, comorbidities, disease characteristics, maternal-fetal complications, SLE morbidity and mortality, activity and damage scores were recorded.

Statistical analysis: Descriptive statistics. Appropriate tests (Chi2, Fisher, Student's t-test or Wilcoxon), and univariate/multivariate logistic regression analyses were conducted to identify factors associated with presence of anti-Ro antibodies.

Table 1. Patient characteristics (N=1513)

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Age in years, mean (SD)	39.2 (13.4)
Female, n (%)	1389 (91.8)
Ethnicity, n (%)	
- Mestizo	685 (45.3)
- Caucasian	664 (43.9)
- Amerindian	124 (8.20)
- Afro-Latin American	17 (1.12)
- Other	23 (1.52)
Most common comorbidities, n (%)	
-Arterial hypertension	341 (23.2)
-Dyslipidemia	269 (20.1)
-Chronic thyroiditis	239 (17.1)
SLE duration in months, mean (SD)	102 (96.4)
Secondary Sjögren's syndrome, n (%)	105 (7.21)
Immunological laboratory, n (%)	
-Anti-dsDNA	1000 (67.4)
-Anti-Sm	864 (66.6)
-APLAs	425 (39.4)
-Anti-Ro	552 (36.5)
-Anti-La	247 (18.8)
-Anti-RNP	325 (25.1)
-Hypocomplementemia	1228 (84.3)
SLEDAI, median (IQR)	2 (0 - 4)
SLICC, median (IQR)	1 (0 - 1)
Pregnancies, n (%)	891 (25.1)
-Fetal death, n (%)	138 (15.8)
-Premature births, n (%)	79 (9.10)
-Miscarriages, n (%)	28 (3.2)
SLE morbidity and mortality	
-Hospitalizations, n (%)	772 (52)
-Number of hospitalizations, mean (SD)	1.75 (1.3)
-Severe infections, n (%)	202 (14)
-Number of serious infections, mean (SD)	1.4 (1)
-Death, n (%)	40 (2.7)
SLE treatment, n (%)	
-Corticosteroids	1358 (96.2)
-Antimalarials	1370 (97.5)
-Methotrexate	1107 (78.9)
-Azathioprine	486 (34.8)

SD = Standard Deviation; **SLE** = Systemic Lupus Erythematosus; **Anti-dsDNA** = Double-stranded anti-DNA antibodies; **Anti-Sm** = Anti-Smith antibodies; **APLAs** =Antiphospholipid antibodies; **Anti-RNP** = Anti-ribonucleoprotein antibodies; **IQR** = Interquartile range; **SLEDAI** = Systemic Lupus Erythematosus Disease Activity Index; **SLICC** = Systemic Lupus International Collaborating Clinics Damage Index.

Table 2. Characteristics of patients with positive and negative anti-Ro antibodies

Table 2. Characteristics of patients with positive and negative anti-Ro antibodies

Characteristics	Anti-Ro + (N=552)	Anti-Ro - (N=779)	p-value
Age in years, mean (SD)	39 (13)	39 (13)	0.986
Female, n (%)	514 (93)	717 (92)	0.530
Mestizo, n (%)	246 (45)	362 (46.5%)	0.336
SLE duration in months, mean (SD)	98.7 (94)	362 (46.5%)	0.194
Most common comorbidities, n (%)			
-Arterial hypertension	183 (24.1)	116 (21.4)	0.279
-Dyslipidemia	89 (17.9)	146 (21)	0.215
-Chronic thyroiditis	107 (20.5)	116 (16.1)	**0.050**
Pregnancy related, n (%)			
-Fetal death	52 (9.9)	73 (9.7)	0.190
-Premature births	25 (4.8)	46 (6.1)	0.37
-Miscarriages	15 (2.9)	12 (1.6)	0.186
Most frequent clinical manifestations, n (%)			
-Photosensitivity	397 (72)	362 (46.5)	0.320
-Inflammatory rash	361 (66)	487 (63.3)	0.241
-Alopecia	304 (55)	430 (56.2)	0.722
-Mucosal ulcers	298 (54)	410 (53.1)	0.075
-Leukopenia	281 (51)	370 (48)	0.333
-Raynaud's phenomenon	232 (42)	258 (33.1)	**0.004**
-Lupus nephritis	215 (39)	327 (42)	0.418
-Pleurisy	154 (28)	185 (24)	0.160
-Pericarditis	132 (24)	133 (17.2)	**0.005**
-Interstitial pneumonitis	31 (5.7)	23 (2.98)	**0.022**
Secondary Sjögren's syndrome, n (%)	79 (7)	26 (3.4)	**<0.001**
Immunological laboratory, n (%)			
-Anti-dsDNA	380 (69)	494 (64.3)	0.127
-Anti-Sm	297 (58)	197 (27.6)	**0.001**
-APLAs	169 (40)	215 (38)	0.464
-Anti-La	235 (44)	11 (1.4)	**0.001**
-Anti-RNP	173 (32)	141 (19)	**0.001**
-Hypocomplementemia	461 (85)	632 (82.5)	**0.05**
SLE morbidity and mortality			
-Hospitalizations, n (%)	290 (53.1)	383 (50)	0.291
-Number of hospitalizations, mean (SD)	1.8 (1.4)	1.7 (1.3)	0.162
-Severe infections, n (%)	80 (14.9)	94 (12.8)	0.307
-Number of serious infections, mean (SD)	1.3 (1)	1.5 (0.83)	**0.014**
-Death, n (%)	18 (3.3)	14 (1.8)	0.126
SLEDAI, median (IQR)	2 (0 - 4)	2 (0 - 4)	0.874
SLICC, median (IQR)	1 (0 - 1)	1 (0 - 1)	0.959
SLE treatment, n (%)	18 (3.3)	14 (1.8)	0.126
-Corticosteroids	692 (95.1)	507 (97.5)	**0.041**
-Antimalarials	504 (97.5)	709 (97.9)	0.746
-Methotrexate	124 (24.1)	139 (19.2)	**0.042**
-Azathioprine	189 (36.8)	241 (33.5)	0.262

SD = Standard Deviation; **Anti-dsDNA** = Double-stranded anti-DNA antibodies; **Anti-Sm** = Anti-Smith antibodies; **APLAs** =Antiphospholipid antibodies; **Anti-RNP** = Anti-ribonucleoprotein antibodies; **IQR** = Interquartile range; **SLEDAI** = Systemic Lupus Erythematosus Disease Activity Index; **SLICC** = Systemic Lupus International Collaborating Clinics Damage Index.

Table 3. Univariate analysis in patients with Anti-Ro determination (N=1331)

Characteristics	OR	CI 95%	p-value
Chronic thyroiditis	1.35	1-1.8	**0.04**
Anti-Sm antibodies	1.88	1.5-2.39	**<0.001**
Anti-La antibodies	53.6	30.3-106	**<0.001**
Anti-RNP antibodies	2.05	1.6-2.7	**<0.001**
Interstitial pneumonitis	1.96	1.13-3.43	**0.017**
Corticosteroids	0.49	0.25-0.92	**0.032**
Methotrexate	0.75	0.6-1	**0.036**

OR = Odds Ratio; **CI 95%**= Confidence Interval 95%; **Anti-Sm** = Anti-Smith antibodies; **Anti-RNP** = Anti-ribonucleoprotein antibodies.

Results: A total of 1513 patients were included. Patient characteristics are shown in **Table 1**. Anti-Ro antibodies were requested in 88% (n=1331), of which 41% (n=552) were positive. Characteristics of patients with positive and negative Anti-Ro antibodies can be observed in**Table 2.** Anti-Ro antibodies were associated with hypocomplementemia (p< 0.05), anti-La antibodies (< 0.001), anti-Sm antibodies (p< 0.001), anti-RNP antibodies (p< 0.001) and Sjogren's syndrome (p< 0.001). Also were associated with Raynaud's phenomenon (p< 0.004), pericarditis (p< 0.005) and interstitial pneumonitis (p< 0.02). More infections (p< 0.01) and a greater use of corticosteroids (p< 0.04) and methotrexate (p< 0.04) were observed. Univariate analysis in patients with Anti-Ro determination is shown in **table 3**. In the multivariate model, the independent variables were anti-Sm antibodies (OR 1.9, 95% CI 1.4-2.5), anti-La antibodies (OR 48, 95%CI 26-99), chronic thyroiditis (OR 1.9, 95%CI 1.3-2.7) and the use of methotrexate (OR 0.66, 95%CI 0.5-0.9).

Conclusion: In this SLE patients, anti-Ro positivity was associated with the presence of other antibodies, chronic thyroiditis and methotrexate use, but not with any specific clinical profile, maternal-fetal complications or SLE-related morbidity and mortality.

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Abstract Number: 0562

HDL-Cholesterol Efflux and the Complement System Are Linked in Systemic Lupus Erythematosus

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SESSION INFORMATION

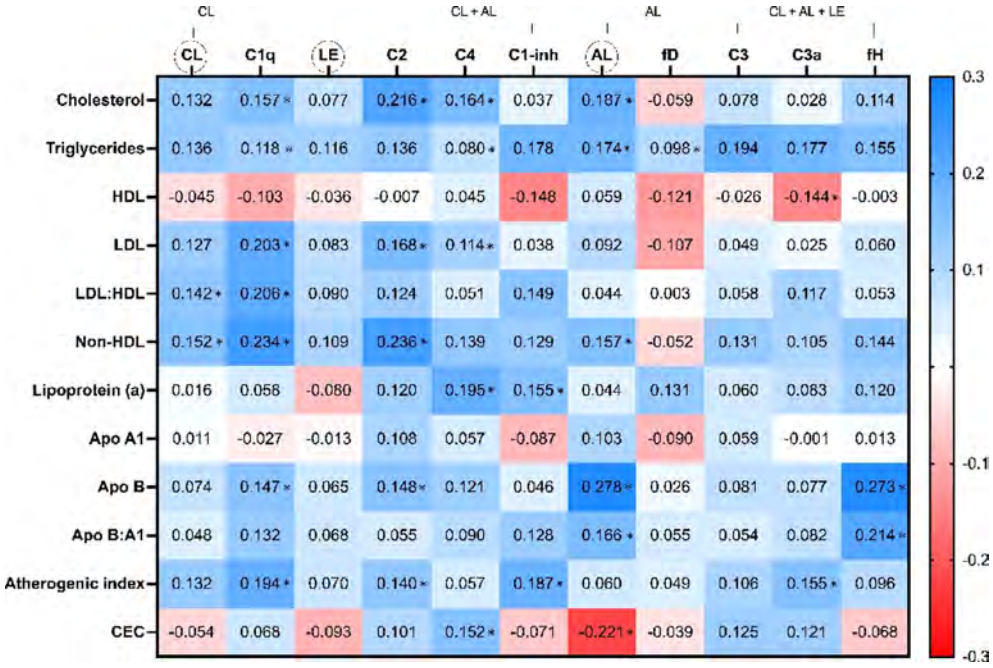
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Cholesterol efflux capacity (CEC), the ability of high-density lipoprotein (HDL) cholesterol to accept cholesterol from macrophages, has been linked to cardiovascular events. Systemic lupus erythematosus (SLE) is characterized by the consumption of complement (C) proteins, and has been associated with an increased risk of cardiovascular disease. CEC is reduced in SLE patients compared to controls. In the present work, our objective was to analyze whether the disruption of C influences CEC in patients with SLE.

Methods: New generation functional assays of the three pathways of the C system were performed in 207 patients with SLE. Additionally, serum levels of inactive (C1q, C2, C3, C4, factor D) and activated (C3a) molecules, and regulators (C1-inhibitor and factor H) of C system were measured. CEC, using an in vitro assay, and lipoprotein serum concentrations were assessed. Multivariable linear regression analysis was performed to assess the relationship between C system and CEC.

Results: Overall, no associations were found between disease characteristics or comorbidity and CEC. Only the use of methotrexate showed a significant relationship to CEC (beta coef. 3 [95%CI 0.8-4], p=0.005). Besides, the presence of hypertension and Katz index showed a trend to be associated with CEC, although, in these cases, statistical significance was not reached.

The univariable association of these lipid pattern related molecules with the cascades and individual components of the C system is exposed as Spearman's Rho correlation coefficients in **Figure 1**. In this sense, many associations were found in the univariable analysis. Most of them turned out to be positive (blue in the heatmap). The strongest, with a coefficient greater than 0.2, were found between C1q (classical pathway) and the serum levels of LDL, LDL:HDL ratio, and non-HDL cholesterol; between C2 (classical and alternative pathway) and total cholesterol and non-HDL cholesterol; and between the



Heat map of the relationship of lipid profile molecules and complement pathways and individual elements. CL: classical, AL: alternative, LE: lectin, HDL: high density lipoprotein cholesterol, LDL: low density lipoprotein cholesterol, Apo: apolipoprotein, CEC: cholesterol efflux capacity, fH: factor H, fD: factor D. Cell numbers represent Spearman's Rho correlation coefficients. Significant correlations (p inferior to 0.05) are marked with an asterisk.

Multivariable analysis of the relationship of complement system pathways and components to cholesterol efflux capacity.

	Beta coef. (95%CI), p			
	CEC, %			
	Univariable		Multivariable	
Functional complement assays, %				
Classical pathway	-0.007 (-0.02-0.009)	0.39		
Alternative pathway	**-0.03 (-0.04- -0.01)**	**0.001**	**-0.02 (-0.04- -0.002)**	**0.030**
Lectin pathway	-0.008 (-0.02-0.007)	0.28		
Individual complement components				
Classical pathway				
C1q, mg/dl	0.004 (-0.02-0.08)	0.26		
Alternative pathway				
Factor D, ng/ml	0.0001 (-0.0006-0.0003)	0.55		
Classical and alternative pathway				
C2, mg/dl	**0.5 (0.02-1)**	**0.043**	**0.5 (0.005-1)**	**0.048**
C4, mg/dl	0.04 (-0.01-0.09)	0.15	0.05 (-0.01-0.1)	0.11
C1 inhibitor, mg/dl	-0.02 (-0.08-0.05)	0.59		
Common pathway				
C3, mg/dl	0.01 (-0.0009-0.03)	0.065	**0.02 (0.005-0.04)**	**0.009**
C3a, mg/dl	0.03 (-0.03-0.09)	0.28		
Factor H, ng/ml x10e-3	-0.0002 (-0.0009-0.0004)	0.45		

Complement routes and elements are considered the independent variable.
Multivariable analysis is adjusted for hypertension, Katz index, methotrexate, azathioprine, statins intake and total cholesterol, HDL, lipoprotein (a), triglycerides and apolipoproteins A1 and B serum levels.

Multivariable analysis of the relationship of complement system pathways and components to cholesterol efflux capacity

functional test of the alternative pathway and apolipoprotein B and CEC. The molecules most associated with the activation of the three pathways were apolipoprotein B and the Apo B:ApoA1 ratio. CEC was significantly and positively associated with C4, but negatively with the alternative pathway functional assay. However, the functional test of the lectin pathway showed no association with any of the lipid pattern molecules.

The association of C functional assays and individual C elements with CEC is represented in **Table 1**. We performed a multivariable analysis controlling for hypertension, Katz index, methotrexate, azathioprine (disease related data that had a p value inferior to 0.20 in relation to CEC), statins intake, and all lipids profile molecules that were not derived from a formula (to avoid collinearity). After this adjustment, the functional assay of the alternative route showed a significant and negative relationship with CEC (beta coef. -0.02 [95%CI -0.04- -0.002], p=0.030). This was also de case for C2 and C3, in which the associations were found to be positive and statistically significant (**Table 1**).

Conclusion: C system and CEC are interconnected in patients with SLE.

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Abstract Number: 0563

Urinary Neutrophil Gelatinase-associated Lipocalin (NGAL) as a Mediator of the Association Between Particulate Matter Exposure and Disease Activity in Systemic Lupus Erythematosus

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SESSION INFORMATION
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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
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Background/Purpose: Neutrophil gelatinase-associated lipocalin (NGAL) is an acute-phase glycoprotein increased by inflammatory stimuli, oxidative stress, and tissue injury. Although NGAL is associated with global and renal disease activity in systemic lupus erythematosus (SLE), it is not known whether particulate matter (PM) affects NGAL levels and lupus activity in these patients. Thus, we investigated the mediating role of NGAL in the association between PM_{10} and $PM_{2.5}$ exposure and lupus activity in a prospective, longitudinal cohort.

Methods: The study enrolled 386 patients from three metropolitan regions in Korea. The daily average PM_{10} and $PM_{2.5}$ concentrations were measured using portable air quality monitors and based on data from the National Ambient Air Monitoring System. Urinary NGAL (uNGAL) was measured at the time of enrollment and at 12 months, and disease activity was evaluated using the SLE Disease Activity Index 2000 (SLEDAI-2K) every 3 months for 1 year. Mixed Cox proportional hazard regression was performed to evaluate the associations of PM_{10} and $PM_{2.5}$ with uNGAL and SLE disease activity.

Results: Changes in PM_{10} and $PM_{2.5}$ were associated with changes in uNGAL ($\beta = 1.038$, 95% confidence interval [CI]: 1.017–1.059, $p < 0.001$; $\beta = 1.030$, 95% CI: 1.001–1.045, $p = 0.013$, respectively), and with changes of SLEDAI-2K scores of > 8 over 1 year in SLE patients ($\beta = 0.097$, 95% CI: 0.048–0.146, $p < 0.001$; $\beta = 0.100$, 95% CI: 0.054–0.146, $p < 0.001$, respectively). In addition, changes in uNGAL were significantly associated with changes in SLEDAI-2K scores of > 8 ($\beta = 1.000$, 95% CI: 1.000–1.002, $p = 0.043$).

Conclusion: The association between PM exposure and SLE disease activity may be partially explained by uNGAL levels.

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Abstract Number: 0564

Risk Factors for Immune Thrombocytopenia in Systemic Lupus Erythematosus and Generation of a Predictive Model to Assess Its Risk of Development

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease with a wide variety of manifestations including immune thrombocytopenia (ITP), which has been described in 7-40% of SLE patients.

The aims of our study are to determine the prevalence of ITP in the cohort of patients with SLE from Hospital del Mar, to identify those risk factors associated with its development, and to build a predictive model capable of evaluating the risk of suffering ITP in these patients.

Methods: A case-control study was conducted in which 407 medical records of patients with SLE were reviewed. 34 had developed ITP (cases) and were matched by sex and age with 2 controls with SLE without ITP.

To build the model, the cases whose ITP was posterior to SLE diagnosis and their controls were selected. The model consists of a Random Forest run on a cohort of 66 patients. The variables used were those that showed the greatest disparity in frequency of appearance between both groups. The model was trained with 70% of the cohort and tested with the remaining 30%. The scores obtained were calculated by means of the average of the results obtained after 1000 executions.

Results: Table 1 describes the characteristics and differences between cases and controls and Figure 1 the characteristics used to build the model. The prevalence of ITP in our cohort was 8.35% and it was diagnosed at an age of 43.14 ± 17.11 years. No significant differences were found in demographic variables between groups. At the diagnosis of SLE, controls presented a higher prevalence of arthritis (p-val = 0.02), while cases presented a higher proportion of hemolytic anemia (p-val = 0.04). Throughout the disease, cases presented a greater presence of lupus anticoagulant (p-val = 0.01), anticardiolipin (p-val = 0.044) and anti-β2-glycoprotein 1 antibodies (anti-β2GP1) (p-val = 0.003). In turn, cases had a significantly higher SLICC than controls (p-val = 0.02). Regarding treatment, cases received mycophenolic acid (MPA) (p-val = 0.02) and azathioprine (AZA) (p-val = 0.045) more frequently.

The variables that showed the most disparity and importance for the model were hemolytic anemia, low C4, low C50, anticardiolipin and anti-β2GP1, which were more frequent in cases, and oral ulcers, arthritis and Raynaud's phenomenon (RP) in controls.

The model presented a sensitivity of 87.53%, a positive predictive value of 81.92%, a specificity of 80.50%, an area under the curve (AUC) of 83.92% (Figure 2), and an accuracy of 83.68%.

Conclusion: Patients with SLE who develop ITP seem to have a different phenotype than those who do not, presenting with less arthritis and more hemolytic anemia at diagnosis, as well as higher positivity for antiphospholipid syndrome antibodies throughout the disease. Having developed ITP was associated with higher SLICC and receiving treatment more frequently with MPA and AZA, probably indicating a more severe disease.

We have created a predictive model capable of evaluating the risk of developing ITP in patients with SLE. By combining 8 variables (hemolytic anemia, low C4, low C50, anticardiolipin, anti-β2GP1, oral ulcers, arthritis, and RP), the model correctly predicts 87.53% of patients with SLE who will develop ITP with an accuracy of 83.68%.

Table 1: Characteristics of cases and controls. * Indicates statistically significant differences between cases and controls (95% confidence level). a Indicates mean ± standard deviation. b SLEDAI-1 point. ITP: immune thrombocytopenia. APS: antiphospholipid syndrome. Anti-β2GP1: anti-β2-Glycoprotein 1 antibodies. ACA: anticardiolipin antibodies. SLEDAI: systemic lupus erythematosus disease activity index. SLICC: systemic lupus international collaborating clinics damage index.

Variables	Cases (34)	Controls (68)	P-value
Sex			1.00
Man	4/34 (11.76%)	8/68 (11.76%)	
Women	30/34 (88.24%)	60/68 (88.24%)	
Age at SLE diagnosis	43.14±17.11	43.32±17.06	0.77
Ethnicity			1.00
Caucasian	29/34 (85.29%)	57/68 (83.82%)	
Others	5/34 (14.71%)	11/68 (16.18%)	
Body mass indexa	26.01±4.87	26.23±4.54	0.82
Smoker			0.95
Yeah	9/34 (26.47%)	18/68 (26.47%)	
No	20/34 (58.82%)	42/68 (61.76%)	
Former smoker	5/34 (14.71%)	8/68 (11.76%)	
Family history of connective tissue disease	5/34 (14.71%)	14/68 (20.59%)	0.59
Clinical and biochemical parameters at diagnosis of SLE			
Photosensitivity	13/34 (38.24%)	37/68 (54.44%)	0.14
Oral ulcers	6/34 (17.64%)	18/68 (26.47%)	0.45
Arthritis	17/34 (50.00%)	50/68 (73.53%)	0.02*
Pericarditis	2/34 (5.71%)	2/68 (2.94%)	0.59
Pleuritis	3/34 (8.82%)	3/68 (4.41%)	0.39
Proteinuria	7/34 (20.59%)	10/68 (14.71%)	0.57
Nephritis	5/34 (14.71%)	6/68 (8.82%)	0.49
Hemolytic anemia	4/34 (11.76%)	1/68 (1.47%)	0.04*
Leukopenia	9/34 (26.47%)	18/67 (26.87%)	1.00
Lymphopenia	17/34 (50.00%)	35/67 (52.24%)	1.00
Raynaud's phenomenon	1/34 (2.94%)	10/68 (14.93%)	0.09
Complement			
C3 Low	14/33 (42.42%)	14/64 (21.88%)	0.06
C4 Low	8/32 (25%)	6/64 (9.38%)	0.06
CH50 Low	6/32 (18.75%)	4/61 (6.56%)	0.09
Clinical and immunological parameters throughout SLE			
Antibodies			
Antinuclear Antibodies	34/34 (100%)	68/68 (100%)	1.00
anti-dsDNA	20/34 (58.82%)	41/68 (60.29%)	1.00
anti-Sm	3/33 (9.09%)	11/67 (16.18%)	0.38
Anti Ro	10/33 (30.03%)	25/67 (37.31%)	0.51
Anti-Ro52	8/33 (24.24%)	19/66 (28.79%)	0.81
Anti-Ro60	12/33 (36.36%)	29/66 (43.94%)	0.52
Anti- La	5/33 (15.15%)	14/68 (20.59%)	0.60
Anti-RNP	5/33 (15.15%)	20/67 (29.85%)	0.14
DNA-Crithidia	8/33 (24.24%)	16/62 (25.81%)	0.49
SAF antibodies			
Anticardiolipin	15/33 (45.45%)	17/68 (25.00%)	0.04*
ACA IgG	9/33 (27.27%)	7/68 (10.29%)	0.04*
ACA IgM	9/33 (27.27%)	8/68 (11.76%)	0.09
Anti-β2GP1	13/33 (39.39%)	8/66 (12.12%)	0.003*
β2GP1-IgG	10/33 (30.03%)	6/66 (9.09%)	0.01*
β2GP1-IgM	7/33 (21.21%)	5/66 (7.56%)	0.10
Lupus anticoagulant	10/33 (30.03%)	6/66 (9.09%)	0.01*
Clinical APS	6/34 (17.65%)	6/66 (9.09%)	0.33
Other connective tissue disease	8/34 (23.53%)	23/68% (33.82%)	0.36
Current SLEDAI[a,b]	2.12±2.58	1.75±2.45	0.20
Current SLICC	1.12±1.72	0.41±0.79	0.02*
Treatments along the SLE			
Corticosteroids	23/34 (67.65%)	48/68 (70.59%)	0.82
Antimalarials	29/34 (85.29%)	57/68 (83.82%)	1.00
Mycophenolic acid	14/34 (41.18%)	12/68 (17.65%)	0.02*
Azathioprine	9/34 (26.47%)	7/68 (10.29%)	0.045*
Leflunomide	3/33 (9.09%)	8/68 (11.76%)	1.00
Methotrexate	4/34 (11.76%)	16/68 (23.53%)	0.19
Belimumab	2/34 (5.88%)	3/68 (4.41%)	1.00
Rituximab	6/34 (17.65%)	3/68 (4.41%)	0.06

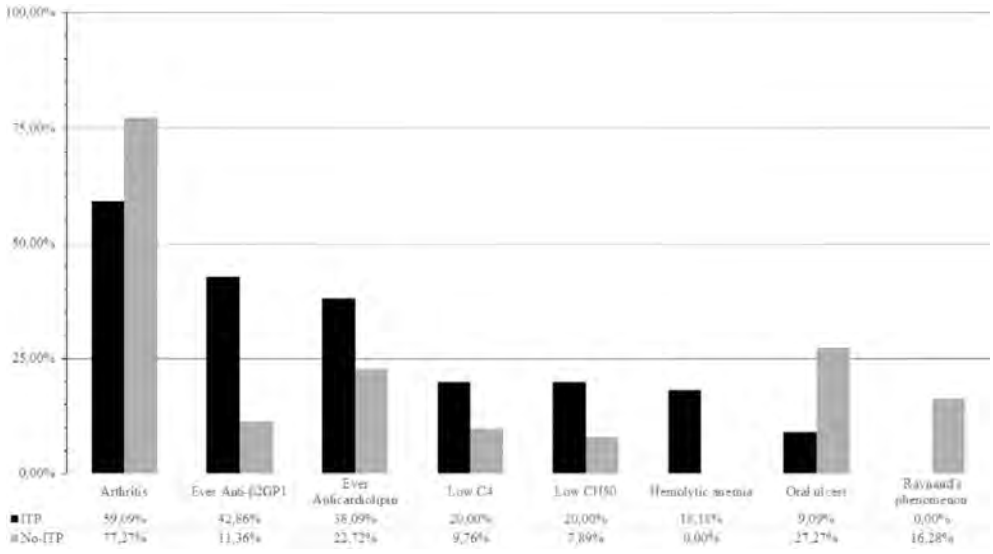

Figure 1: Variables used in the predictive model and their different prevalences in cases in controls. Ever anti-β2GP1: positivity for anti-β2-Glycoprotein 1 antibodies at any point during SLE progression. Ever anticardiolipin: positivity for anticardiolipin antibodies at any point during SLE progression.

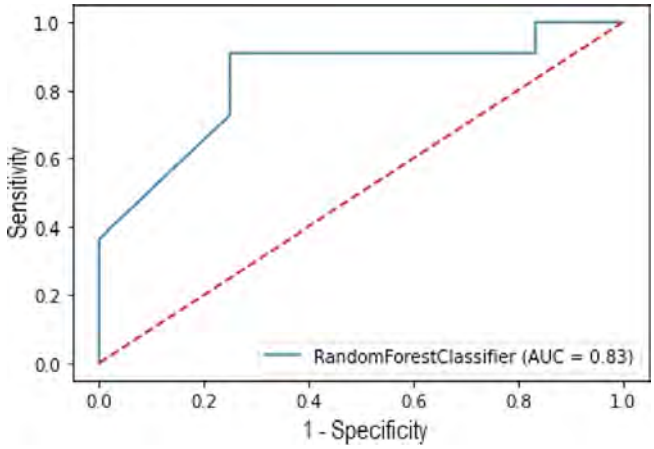

Figure 2: Area under the curve. Relationship between sensitivity and 1-specificity.

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Abstract Number: 0565

Insulin Resistance and the Complement System Are Linked in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) patients more commonly have insulin resistance (IR) than control subjects. Recent studies have revealed that the complement (C) system is not only a mediator of the immune system but is also related to the pathogenesis of atherosclerosis in the general population. Given that the C alteration is a characteristic of SLE, in the present work we set out to analyze if there is a relationship between the C system and IR in patients with SLE.

Methods: New generation functional assays of the three pathways of the C system were performed in 225 non-diabetic patients with SLE. In addition, the serum levels of inactive (C1q, C2, C3, C4, factor D), activated (C3a) and regulators (C1 inhibitor and factor H) molecules of the C system were evaluated. Insulin and C-peptide serum levels were measured, and insulin resistance and indices of beta cell function were calculated using the homeostatic model assessment –HOMA–. Metabolic syndrome criteria fulfillments were applied. Multivariable linear regression analysis was performed to assess the relationship between C system and IR indices and the presence of metabolic syndrome.

Results: C system pathways functional tests and individual elements showed significant relationships with IR indices in the univariable and multivariable analysis (Table 1). In this regard, after multivariable analysis that included age, hypertension, dyslipidemia, BMI and the use of statins and prednisone, serum C3a and factor H values were associated with higher HOMA2-IR levels. In contrast, after adjusting for covariates, no relationship was found between system C and the HOMA2-B% index expressing β-cell function.

Seventy-five (33%) patients fulfilled the definition of metabolic syndrome using the NCEP ATP III criteria. As expected, patients with metabolic syndrome were significantly older, used statins and antihypertensive treatment more frequently, suffered more commonly obesity and dyslipidemia, and had higher values of BMI and abdominal circumference. Regarding disease-related data, in the univariable analysis, patients with metabolic syndrome had more accrual damage measured through the SDI score, and less frequently were taking hydroxychloroquine when the study was performed.

Table 1. Relationship of complement system to insulin resistance and beta cell function indices.

Table 1. Relationship of complement system to insulin resistance and beta cell function indices.

	HOMA2-IR x 100				HOMA2-B%-C-peptide			
	Beta coef. (95%), p							
	Univariable		Multivariable		Univariable		Multivariable	
Classical pathway								
Functional test, %	0.3 (-0.05-0.6)	0.094	0.1 (-0.2-0.5)	0.36	0.08 (-0.2-0.4)	0.61	-0.03 (-0.3-0.3)	0.83
C1q, mg/dl	0.05 (-0.8-2)	0.45	0.03 (-1-1)	0.96	**1 (0.2-2)**	**0.023**	0.9 (-0.2-2)	0.099
Lectin pathway								
Functional test, %	0.1 (-0.2-0.4)	0.46	0.07 (-0.2-0.4)	0.66	-0.09 (-0.4-0.2)	0.53	-0.1 (-0.4-0.1)	0.35
Common elements of the classical and lectin pathways								
C2, mg/dl	-4 (-15-8)	0.52	-8 (-20-3)	0.13	8 (-2-18)	0.13	5 (-5-15)	0.31
C4, mg/dl	0.6 (-0.6-2)	0.34	0.4 (-0.9-2)	0.56	0.5 (-0.5-2)	0.33	0.4 (-0.6-1)	0.99
C1 inhibitor, mg/dl	2 (0.06-4)	0.043	0.8 (-1-3)	0.44	**2 (0.03-3)**	**0.018**	1 (-0.6-3)	0.22
Alternative pathway								
Functional test, %	**0.4 (0.03-0.8)**	**0.032**	0.3 (-0.04-0.7)	0.082	-0.07 (-0.4-0.3)	0.68	-0.1 (-0.5-0.2)	0.37
Factor D, ng/ml	0.003 (-0.006-0.01)	0.57	-0.0003 (-0.009-0.009)	0.94	-0.0005 (-0.008-0.007)	0.90	-0.0005 (-0.008-0.007)	0.90
Common elements of the three pathways								
C3, mg/dl	0.4 (-0.05-0.7)	0.083	0.2 (-0.3-0.6)	0.48	0.1 (-0.2-0.5)	0.41	0.06 (-0.3-0.4)	0.73
C3a, mg/dl	**3 (1-4)**	**<0.001**	**2 (0.2-3)**	**0.030**	**2 (0.7-3)**	**0.003**	1 (-0.1-2)	0.081
Factor H, ng/ml x10e-3	**0.02 (0.002-0.04)**	**0.033**	**0.02 (0.003-0.04)**	**0.019**	0.005 (-0.01-0.02)	0.51	0.006 (-0.008-0.02)	0.39

Beta coefficients are expressed using HOMA2-IR and HOMA2-B% as the dependent variables.
Linear regression analysis is adjusted for age, hypertension, dyslipidemia, body mass index and the use of statins and prednisone.
HOMA2-IR is calculated using insulin and glucose serum levels; HOMA2-B% is calculated with circulating C peptide and glucose.
Significant p values are depicted in bold.

Table 2. Differences of C system pathways between patients with and without metabolic syndrome.

Table 2. Differences of C system pathways between patients with and without metabolic syndrome.

	Metabolic syndrome						
				Univariable		Multivariable	
	No=148	Yes=75	p	Odds ratio, 95%(CI)	p	Odds ratio, 95%(CI)	p
Classical pathway							
Functional test, %	**85 ± 41**	**98 ± 36**	**0.036**	**1.01 (1.00-1.02)**	**0.038**	1.00 (0.99-1.01)	0.26
C1q, mg/dl	**32 ± 9**	**37 ± 13**	**0.004**	**1.04 (1.01-1.07)**	**0.005**	**1.04 (1.01-1.07)**	**0.011**
Lectin pathway							
Functional test, %	8 (1-41)	9 (1-39)	0.76	1.00 (0.99-1.01)	0.76	-	
Common elements of the classical and lectin pathways							
C2, mg/dl	2.3 ± 1.1	2.6 ± 1.3	0.060	1.26 (0.99-1.60)	0.062	1.28 (0.98-1.66)	0.070
C4, mg/dl	20 ± 11	22 ± 13	0.14	1.02 (0.99-1.04)	0.15	1.01 (0.99-1.04)	0.36
C1 inhibitor, mg/dl	**31 ± 9**	**34 ± 7**	**0.047**	1.04 (1.00-1.08)	0.050	1.02 (0.98-1.07)	0.31
Alternative pathway							
Functional test, %	35 (6-67)	42 (10-80)	0.13	1.01 (1.00-1.01)	0.13	1.01 (0.99-1.02)	0.19
Factor D, ng/ml	**2238 ± 1617**	**3055 ± 2041**	**0.004**	**1.00 (1.00-1.00)**	**0.010**	1.00 (0.99-1.00)	0.064
Common elements of the three pathways							
C3, mg/dl	**122 ± 30**	**141 ± 42**	**<0.001**	**1.02 (1.01-1.03)**	**0.000**	**1.02 (1.01-1.03)**	**0.001**
C3a, mg/dl	**37 ± 8**	**40 ± 12**	**0.033**	**1.03 (1.00-1.06)**	**0.036**	1.03 (0.99-1.06)	0.12
Factor H, ng/ml x10e-3	385 (284-550)	389 (291-614)	0.51	1 (0.99-1)	0.52	-	

According to the NCEP ATP III definition, metabolic syndrome is present if three or more of the following five criteria are met: waist circumference over 102 cm (men) or 88 cm (women), blood pressure over 130/85 mmHg, fasting triglyceride (TG) level over 150 mg/dl, fasting high-density lipoprotein (HDL) cholesterol level less than 40 mg/dl (men) or 50 mg/dl (women) and fasting blood sugar over 100 mg/dl. Metabolic syndrome is considered the dependent variable in this analysis. NCEP ATP III criteria for metabolic syndrome could not be calculated in 2 of 225 patients. Multivariable analysis is adjusted for age, prednisone and hydroxychloroquine intake. Significant p values are depicted in bold.

Besides, SLE patients with metabolic syndrome had some differences in C system routes functional assays and inactive and active individual C elements. With respect to this, in the univariable analysis, patients with metabolic syndrome exhibited higher serum levels of C1q, factor D, C3, C3a and C1-inh (Table 2). Besides, in the multivariable analysis, after adjustment for covariates, serum levels of C1q and C3 were associated with a higher odds ratio for the presence of metabolic syndrome (Table 2).

Conclusion: IR and metabolic syndrome are positively and independently related to higher serum levels of some serum C elements in patients with SLE with a predominant role of the alternative pathway elements.

Disclosure: J. Viotti-Serra: None; **M. García-González**: None; **F. Gómez-Bernal**: None; **J. Quevedo-Abeledo**: AbbVie/Abbott, 6; **Y. Fernández-Cladera**: None; **A. González-Rivero**: None; **M. Gonzalez-Gay**: AbbVie/Abbott, 5, 6, Amgen, 5, 6, Pfizer, 5, 6; **I. Ferraz Amaro**: AbbVie/Abbott, 5, 6, Amgen, 5, 6, Bristol-Myers Squibb(BMS), 6.

Abstract Number: 0566

Characterization of Disease Activity Using a Novel Physiologic Biomarker in Pediatric SLE

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex inflammatory disease involving many organ systems. To better understand and treat SLE, two phenotypes have been proposed. Type 1 is defined by signs of autoreactivity and inflammation such as nephritis, arthritis, and rash. The Type 2 state is thought to result from cytokine mediated

peripheral and central (nociplastic) changes causing fatigue, sleep disturbance, and widespread pain, which often overlap with the manifestations of fibromyalgia (FM). While the grouping of patients based on symptoms and the clinical/serological components of disease is an established practice in the field, the application of this approach is limited by the tools available to assess and measure patient disease activity.

Methods: We performed phenotype testing on 12 patients (ages 13-21y) diagnosed with SLE being seen at the Children's National Multidisciplinary Lupus Clinic. All patients met the ACR diagnostic criteria for SLE. This approach employs a novel medical device invented at Children's National Hospital. This device is a novel integration of non-invasive and innocuous neuroselective electrical stimulation with infrared pupillometry (nPRD) to activate specific sensory nerve fiber types and allows for an objective quantified characterization of sensory nerve fiber activity. This technology measures the impact of

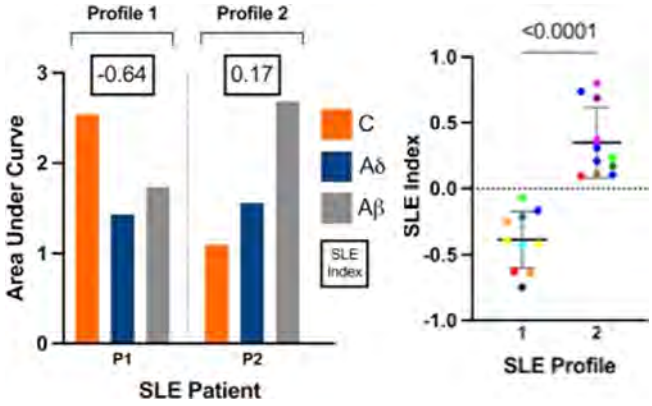

Figure 1. Distinct nociceptive profiles detected in SLE cohort by nPRD. (left) Showing nPRD-derived AUC measures of C, Ad, and Ab fibers and SLE Index scores of patients with SLE. Patients are categorized into "Profile 1" and "Profile 2" as indicated. (right) Showing the SLE Index measures for Profile 1 and Profile 2. Statistics: unpaired t-test, significance is as indicated.

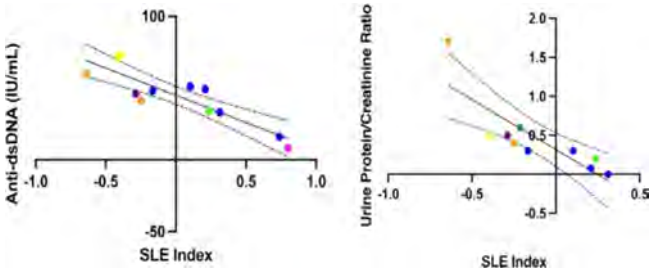

Figure 2. Anti-dsDNA antibodies and urine protein/creatinine ratio correlate with SLE Index. Plot showing line of best-fit and 95% confidence band of simple linear regression of the SLE Index with anti-dsDNA antibody (n=10) and the urine protein/creatinine ratio (n=7).

Table 1. Summary of correlation coefficients and significance of SLE Index with correlates. Statistical significance and strength indicated by *.

Correlate	r	r^2	P value
Anti-dsDNA	-0.8925	0.7965	0.0005 ***
Urine Protein/Creatinine Ratio	-0.8284	0.6863	0.0213 *
C-Reactive Protein (CRP)	0.6465	0.4180	0.0231 *
Urine Creatinine	-0.6909	0.4774	0.0269 *
C4	0.5520	0.3047	0.0505
C3	0.3987	0.1589	0.1772
Composite SLEDAI-2K	-0.4329	0.1874	0.1598

SLE-associated inflammation on sensory nerve fiber activity. The relationship of the nPRD-derived AUC for each of the three sensory fibers (Aβ, C and Aδ) at a given time are compared using a ratio (e.g., $[AUC_{A\delta}\text{-}AUC_C]/AUC_{A\beta}$) to derive a quantitative index, which is the primary measurement endpoint. This index is used as the clinical output to contextualize the type and intensity of nociceptive processing. The data were analyzed using student's t-tests and Pearson's Correlation.

Results: Using our novel technology and method we observed two overarching and significantly different SLE physiologic phenotypes ($p< 0.001$, Figure 1). P1 has relatively increased C fiber sensitivity and decreased Aδ fiber sensitivity, which has been designated "profile 1". P2 has a dominating Aβ fiber with less pronounced C and Aδ measures, which has been designated "profile 2".Nociceptive profile 1 aligns with SLE Type 1 (active disease) whereas, nociceptive profile 2 aligns with SLE Type 2 (FM and/or nociplastic).

We then correlated our SLE Index to the SLEDAI-2K composite score and specific serological components, which are shown in **Figure 2** and summarized in **Table 1**. These data demonstrate a statistically significant correlation to four parameters expected to be elevated or decreased in the SLE Type 1 active state.

Conclusion: Our preliminary data support the potential of our novel, objective, physiologic measure to characterize and quantify SLE disease activity. These findings will be verified in future studies.

Disclosure: S. Sule: None; **O. Lamanna**: None; **K. Jackson**: AlgometRx, Inc., 3, 4, 8; **S. Ahn**: None; **T. Ahmed**: None; **J. Finkel**: AlgometRx, 4, 10.

Abstract Number: 0567

N-Terminal Pro-Brain Natriuretic Peptide Correlates Strongly with Cardiovascular Damage in Systemic Lupus Erythematous (SLE): A Cross-sectional Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular (CV) disease represents the leading cause of death in SLE. Traditional risk factors are less accurate at identifying cardiovascular risk in SLE than in the general population. N-Terminal pro-Brain Natriuretic Peptide (NT-proBNP) is a key biomarker to detect heart disease and predict cardiac outcomes, in non-lupus populations. We assessed NT-proBNP in a large cross-sectional sample of unselected SLE patients and investigated associations with CV damage.

Methods: Adults meeting ACR SLE classification have been consecutively enrolled in our Lupus Clinic cohort. Patients were followed yearly with evaluations of drugs, SLICC Damage Index (SDI), SLEDAI-2K, and other measures including cardiovascular risk factors. NT-proBNP (pg/mL) levels were measured in serum collected at annual research visits between March

2022 and April 2023. The main outcome was CV damage defined as any CV SDI events. Cross-sectional associations between NT-proBNP and this outcome were evaluated using multivariable logistic regression model.

Results: Overall, 270 SLE patients (91% female 91%, median age of 50.7 [1st quartile- 3rd quartile: 39.6-62.1] years) from the MUHC cohort were included. At NT-proBNP assessment, median disease duration was 17.7 years [11.6-27.2] and median SLEDAI-2K and SDI scores were 2 [0-4] and 1 [0-3] respectively. Characteristics of patients are given in Table 1. Thirty-three (12%) patients had CV damage including coronary artery disease (n=14), cerebral vascular accident (n=12), chronic pericarditis (n=6), valvular diseases (n=5), cardiomyopathy (n=3) and peripheral artery disease (n=1). The median [1stquartile- 3rd quartile] NT-proBNP serum level was 95 [54-185] pg/mL. NT-proBNP levels were higher in patients with CV damage (281 [140-856] versus 84 [50-147] pg/mL in those without CV damage, P< 0.001) and were especially high in patients with more than one CV damage item (989 pg/mL [734–1725] versus 194 [122-327] pg/mL in those with one CV damage item only, P< 0.0001). The ROC curve for NT-proBNP demonstrated strong associations with CV damage (AUC 0.78, 95% CI 0.69-0.87). The threshold providing the best discrimination for those with/without CVD was 133 pg/mL, with a sensitivity of 79% (95% CI 64-91) and a specificity of 70% (95% CI 64-76). In multivariate analyses, hypertension (OR 3.3, 95% C 1.2-9.0), dyslipidemia (OR 3.6, 95% CI 1.3-9.6) and NT-proBNP >133 pg/mL (OR 7.0, 95% CI, 2.6-19.1) were strongly associated with CV damage. CV damage was less frequent in SLE patients on hydroxychloroquine (OR 0.3, 95% CI 0.1-0.8). Increased NT-proBNP levels were themselves associated with age (OR 4.2, 95% CI 2.2-8.3), smoking (OR 1.9, 95% CI 1.0-3.5), reduced eGFR (4.1, 95% CI 1.3-13.1), prior pericarditis/pleuritis (OR 2.5, 95% CI 1.4-4.5) and aPL antibodies (OR 2.6, 95% CI 1.4-4.9)

Conclusion: Serum NT-proBNP levels correlate with CV damage in SLE. Future evaluations are needed to identify the usefulness of NT-proBNP in tailoring treatments to prevent CV burden in SLE. The novel associations of NT-proBNP levels with pericarditis/pleuritis and aPL antibodies suggest new avenues for research to better understand what drives CV risk in SLE.

Table 1 Characteristics of SLE patients

	n=270
Age, years	50.7 [39.6-62.1]
Male sex, n (%)	24 (8.9)
SLE features, n (%)	
Mucocutaneous	210 (77.8)
Arthritis	216 (80)
Pericarditis/Pleuritis	113 (41.8)
Renal	112 (41.5
aPL antibodies	106 (39.3)
Cardiovascular risk factors, n (%)	
Smoker ever*	117 (43.3)
Hypertension**	78 (28.9)
BMI>25kg/m2**	151 (53.9)
Dyslipidemia**	52 (19.2)
Diabetes**	12 (4.4)
eGFR<50%	19 (7.0)
Treatment at study time, n (%)	
Steroids	25 (9.3)
Hydroxychloroquine	216 (80.0)
Immunosuppressive drugs	124 (45.9)
Belimumab	20 (7.4)

*data available for *269 and **268 patients only

Disclosure: K. Sacre: None; **E. Vinet**: None; **C. Pineau**: None; **A. Mendel**: None; **F. Kalache**: None; **L. Grenier**: None; **T. Huynh**: None; **S. Bernatsky**: None.

Abstract Number: 0568

Comparison of Plasma Protein Profiles and Endothelial Function in Patients with Pediatric-Onset Systemic Lupus Erythematosus and Healthy Controls

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with pediatric-onset systemic lupus erythematosus (pSLE) have elevated cardiovascular (CV) risk associated with accelerated atherosclerosis that begins in childhood. Endothelial dysfunction may be one of the earliest atherosclerotic precursors, but the role of endothelial function assessment for CV risk stratification in pSLE is unclear. We compared non-invasive endothelial function testing and plasma protein profiles between patients with pSLE and controls and evaluated associations between protein expression and endothelial dysfunction.

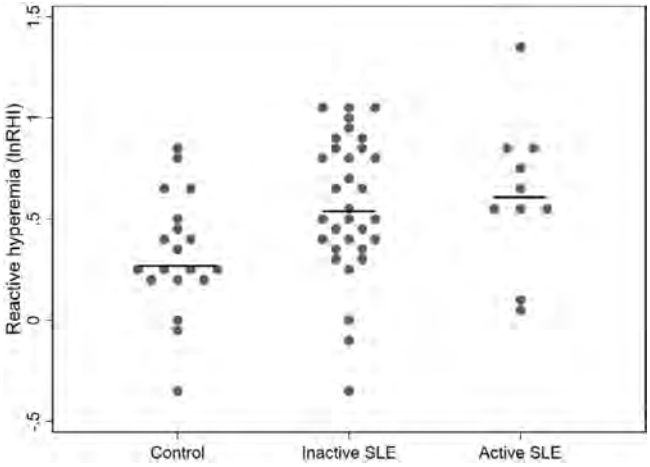
Methods: Forty-four pSLE subjects, aged 9–21 years without active Raynaud's, were recruited from pediatric rheumatology clinics at two tertiary centers. We recruited 24 age and sex-matched controls without chronic conditions from siblings of rheumatology patients, dermatology clinic or primary care network. Demographic data, traditional CV risk factors and clinical disease activity scores were collected. Endothelial function, quantified as the log-transformed reactive hyperemia index (LnRHI), was measured by peripheral arterial tonometry (EndoPAT, Itamar Medical). We measured plasma markers of neutrophil (myeloperoxidase (MPO)-DNA, neutrophil elastase-DNA, and calprotectin) and endothelial activation (ICAM-1, VCAM-1) hypothesized to induce endothelial injury, as well as a 96-target proteomic proximity extension assay (CVD-II panel, Olink[â]). We used linear regression models and Mann-Whitney U tests to evaluate differences in LnRHI and plasma biomarkers, respectively. Spearman rank correlation coefficients (r) were used to evaluate clinical factors and biomarkers associated with LnRHI in pSLE subjects.

Results: Compared to controls, pSLE subjects were more likely to report Black race, lower parental education and lower household income (Table 1). pSLE subjects also had more CV risk factors, including family history of CVD, higher body mass index and triglyceride levels, lower high-density lipoprotein (HDL), and lower physical activity scores compared to controls. Of note, 75% of the pSLE cohort had low or inactive disease (SLEDAI-2K score≤ 4).Endothelial function testing revealed higher (better) average lnRHI in pSLE subjects vs. controls (b 0.26, p< 0.01), regardless of disease activity (Fig 1), and with adjustment for body surface area (BSA) (for finger size) and HDL (b 0.30, p< 0.01). There was no significant increase in neutrophil/endothelial activation markers or CVD-related proteins in subjects vs. controls. Conversely, median MPO-DNA and VCAM-1 levels were higher in controls (Fig 2). Only BSA and diastolic blood pressure were significantly associated with lnRHI (r 0.32, p=0.03, and r-0.32, p=0.04, respectively).

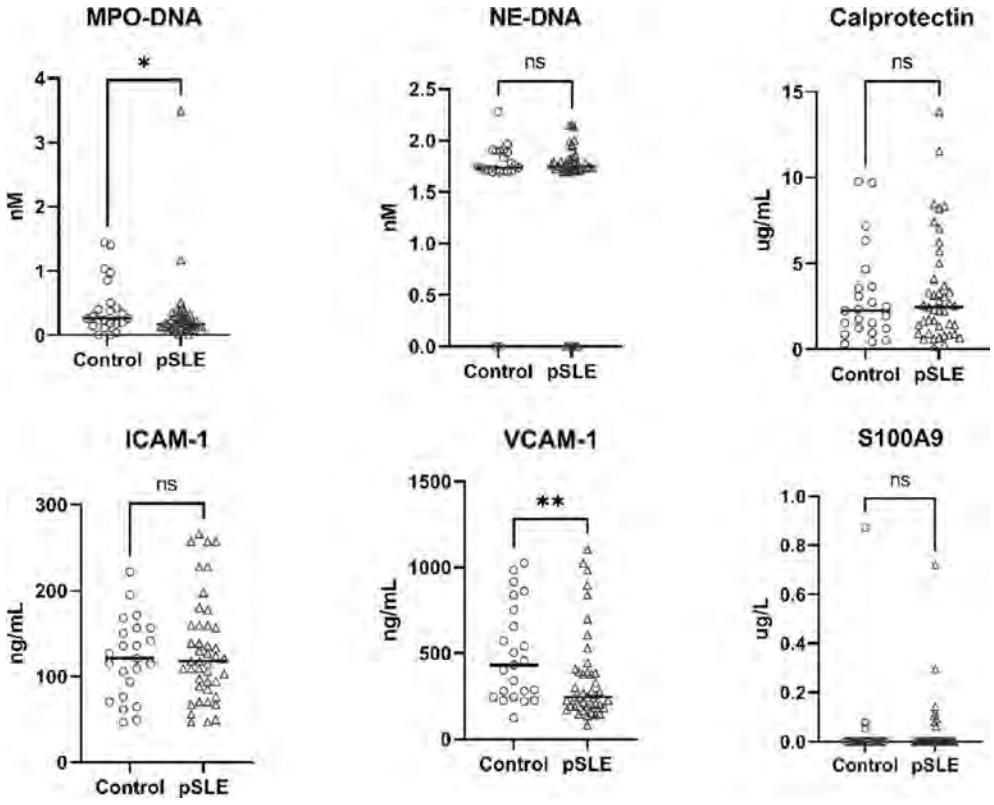
Table 1. Baseline Characteristics by SLE vs. Controls			
	Control N = 24	SLE N = 44	p-value
Demographic characteristics			
Age Visit: median (IQR)	16.5 (12.0 - 19.6)	17.0 (15.9 - 18.5)	0.69
Female Sex: n (%)	20 (83)	38 (86)	0.74
BSA: median (IQR)	1.6 (1.5- 1.7)	1.7 (1.6 - 1.9)	0.06
Self-Reported Race: n (%)			
American Indian/Native American	0 (0)	2 (5)	0.03
Asian	3 (13)	7 (16)	
Black	2 (8)	17 (39)	
Other	1 (4)	2 (5)	
White	18 (75)	16 (36)	
Self-Reported Hispanic Ethnicity: n (%)	1 (4)	11 (25)	0.05
Parental Education: n (%)			
Did not complete high school	0 (0)	5 (12)	<0.01
High school or other general education degree	2 (8)	19 (45)	
Bachelor's degree or above	22 (92)	18 (43)	
Household Income: n (%)			
< $25,000 per year	1 (5)	9 (21)	<0.01
$25,000 - $49,999 per year	1 (5)	11 (26)	
$50,000 - $74,999 per year	1 (5)	10 (24)	
$75,000 - $149,999 per year	5 (23)	7 (17)	
> $ 150,000 per year	14 (64)	5 (12)	
Traditional cardiovascular risk factors			
Family history of cardiovascular disease: n (%)	1 (4)	11 (25)	0.03
BMI percentile for age and sex: median (IQR) ^	42.5 (24.5 - 61.6)	78.6 (44.0 - 90.5)	0.02
Obesity: n (%) *	3 (13%)	6 (14%)	1.00
Low-density lipoprotein (mg/dl): median (IQR)	85.0 (73.0 - 101.0)	83.0 (70.0 - 95.0)	0.50
High-density lipoprotein (mg/dl): median (IQR)	58.0 (48.0 - 66.0)	49.0 (43.0 - 57.0)	0.01
Triglyceride (mg/dl): median IQR)	62.0 (49.0 - 76.0)	75.0 (66.0 - 95.0)	0.02
Preceding hypertension: n (%)	3 (13)	11(25)	0.56
Physical Activity Questionnaire: median (IQR)	2.4 (2.0 - 2.9)	1.9 (1.4 - 2.3)	<0.01
Disease characteristics			
Disease duration (years), mean (SD)		3 (± 2.1)	
SLEDAI-2K score at enrollment: median (IQR) †		2.0 (0.0 - 4.5)	
SLEDAI-2K score above 4: n (%)		11 (25%)	
Cumulative disease activity (AUC): median (IQR) #		18.9 (10.7 - 32.4)	
Current medication use			
Glucocorticoids: n (%)		14 (32)	
Hydroxychloroquine: n (%)		44 (100)	
DMARD: n (%) ‡		36 (82)	
Rituximab within last 6 months: n (%)		8 (18)	
Cyclophosphamide within the last month: n (%)		0 (0)	

Fisher's exact or Mann-Whitney U tests were used to compare clinical characteristics between pSLE subjects and controls. ^ BMI-for-age-and-sex percentiles are used for ages 2-19 years. * Obesity defined by BMI 95th percentile for subjects 2-19 years old, or BMI >30 kg/m2 in subjects 20 years or older. †SLEDAI <5, low disease activity; 6–10, moderate; 11–19, high; maximum, 105 #The area under the curve (AUC) was calculated as a measure of long-term burden. ‡ Disease-modifying anti-rheumatic drugs (DMARDs) include mycophenolate mofetil, methotrexate, tacrolimus, and azathioprine.

Conclusion: Our results unexpectedly demonstrated better endothelial function and lower MPO-DNA levels in children with pSLE compared to controls despite greater CV risk factors. This might be attributed to low SLE disease activity and/or effects of treatment. Further studies to understand how disease activity and immunomodulatory medications modify endothelial health in children with pSLE may provide insight into potential mechanisms of endothelial dysfunction and ideal disease activity targets.



Mean differences in baseline reactive hyperemia (LnRHI) between 42 pSLE subjects and 19 controls with evaluable peripheral arterial tonometry tracings. Both subjects with low/inactive SLE (SLEDAI-2K≤ 4) and active SLE (SLEDAI-2K> 4) had statistically significant higher average LnRHI values compared to controls (p=0.01 and p< 0.01, respectively).



Selected plasma biomarkers of neutrophil extracellular traps (myeloperoxidase [MPO]-DNA complexes, neutrophil elastase [NE]-DNA, neutrophil activation (calprotectin, S100A9), or endothelial activation (VCAM-1, ICAM-1) in 43 pSLE subjects at enrollment compared to 23 controls with evaluable samples, using Mann-Whitney U tests. * p<0.05; ** p<0.01

Disclosure: L. Kim: None; **G. Alonzi**: None; **M. Barguil Macedo**: None; **P. Weiss**: Eli Lilly, 2, Novartis, 2, Pfizer, 2; **J. Newburger**: None; **K. Costenbader**: Amgen, 2, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Eli Lilly, 2, Exagen Diagnostics, 5, Gilead, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5; **C. Lood**: Amytryx, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Citryll, 2, Eli Lilly, 5, Gilead, 5, Horizon Therapeutics, 5, Pfizer, 5, Redd Pharma, 5, 11; **J. Chang**: None.

Abstract Number: 0569

Serum S100A8 and S100A9 Are Useful Biomarker Indicated IFN Associated Organ Involvements in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: S100, a damage-related molecular pattern factor, was reported to be a biomarker associated with disease activity in SLE. Additional hydroxychloroquine, which could regulate IFN signature, was found to modulate serum S100 in patients with SLE. However, what SLE pathophysiology S100 reflects remains unclear. The study aimed to determine the usefulness of S100 as a biomarker of SLE pathogenesis.

Table 1. Characteristics of patients with SLE enrolled in this study #Nonparametric distributions are represented as median (interquartile range [IQR]).

Table 1. Characteristics of patients with SLE enrolled in this study

Characteristics	All (N = 120)
Female, no. (%)	111 (92.5)
Age, years, mean (SD)	40.5 (12.9)
Disease duration, months, mean[#]	70 (14–226.3)
History of lupus nephritis, no. (%)	53 (44.2)
History of cutaneous lesion, no (%)	98 (81.7)
Prednisone, no. (%)	104 (86.7)
Median dosage, mg/day[#]	5 (3.0–15.0)
Disease activity	
Cutaneous lesion, no (%)	69 (57.5)
Joint lesion, no. (%)	36 (30.0)
Fever, no. (%)	12 (10)
Malaise, no. (%)	11 (9.2)
Cytopenia, no. (%)	23 (19.2)
Serositis	5 (4.2)
Active LN	20 (16.7)
Active NPSLE	8 (6.7)
CLASI activity score[#]	1 (0–2.8)
SLEDAI score[#]	4 (3–8)
SLE-DAS score[#]	4.3 (1.3–7.6)
LLDAS, no. (%)	31 (25.8)
CR, no. (%)	3(2.5)
Anti-dsDNA antibodies, IU/mL[#]	7.7 (5.0–22.7)
Anti-dsDNA antibodies positive, no. (%)	48 (40)
C3, mg/dL[#]	72 (56.3–92.8)
C4, mg/dL[#]	13 (8–18)
CH50, U/mL[#]	32.6 (23.0–38.7)
Low complement, no. (%)	71 (59.1)
White blood cells, /μL[#]	5020 (3910–6735)
Neutrophils, /μL[#]	3449 (2285.8–5104.8)
Lymphocytes, /μL[#]	1025 (645.3–1561)
Platelets, ×10⁴/μL[#]	21.8 (16.6–27.7)

Methods: This single-center, retrospective, observational study enrolled patients with SLE admitted to our hospital between January 2016 and December 2021. The SELENA-SLEDAI, SLE-DAS, and lupus low disease activity state scale were used to measure disease activity. Serum cytokines reported to associated with SLE activity (TNF-α, IL-8, monocyte

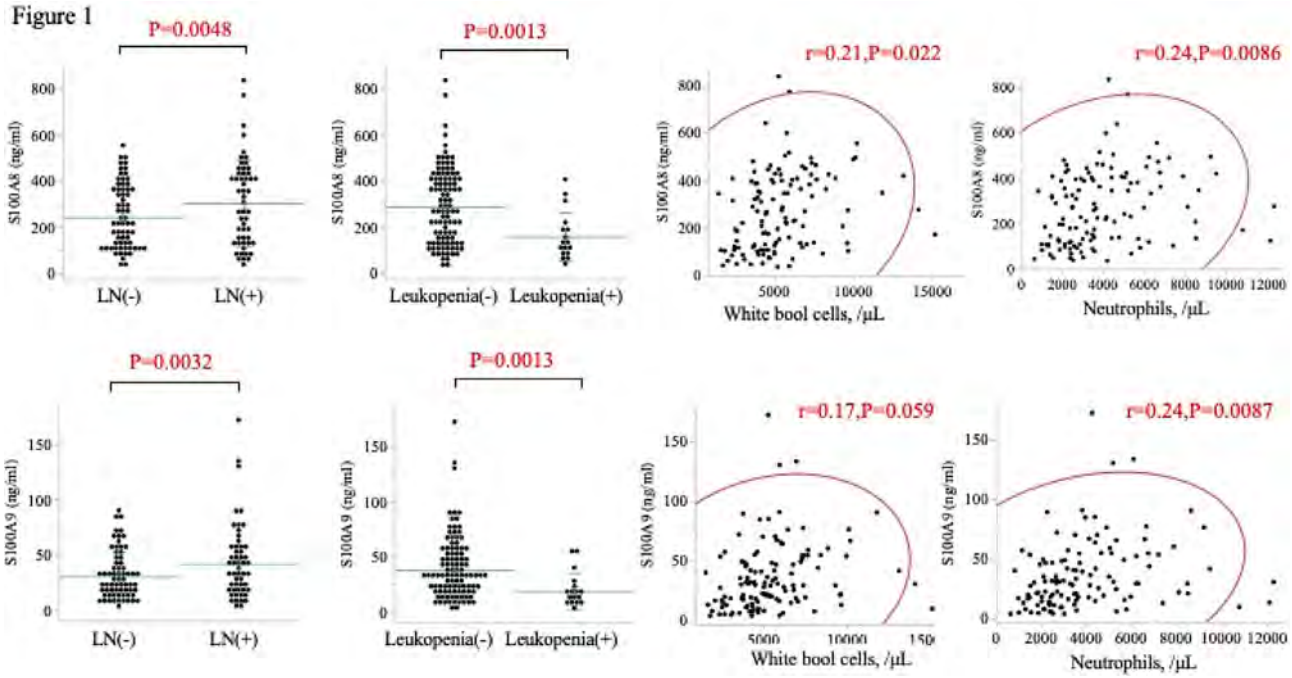

Figure 1. Association of serum S100 protein levels with lupus nephritis, immunological biomarkers, and leukopenia P-values were determined using the Mann–Whitney U test or Pearson's correlation coefficient (r).

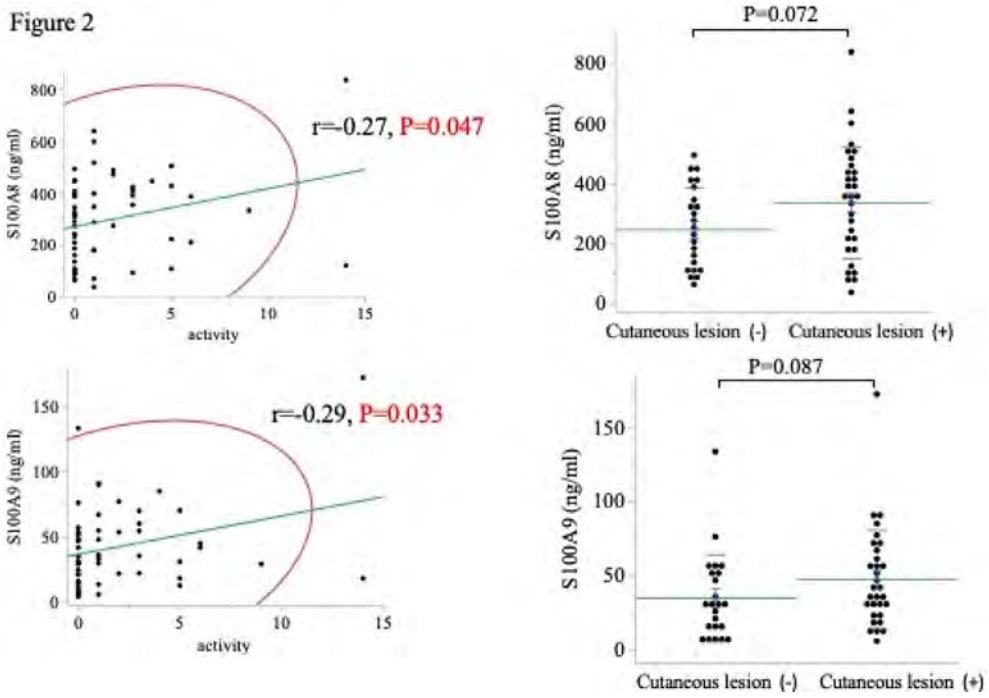

Figure 2. Association of serum S100 protein levels with cutaneous lesions in patients with SLEDAI scores of 1–4 (n = 54) For statistical analysis, the Mann–Whitney U test was used for the presence of lesions, and Pearson's correlation coefficient (r) was used for the association with CLASI activity.

chemoattractant protein-1, IL-1ra) were measured by multiplex Luminex assay, and serum S100A8 and S100A9 by ELISA. The correlation between these biomarkers and organ involvements was analyzed.

Results: Overall, 120 patients (9 men and 111 women; mean age, 40.5 years) were included. Table 1 shows the patient's characteristics when measuring serum S100A8, S100A9, and cytokines. The level of TNF-α, IL-8, monocyte chemoattractant protein-1, and IL-1ra were not associated with type of organ involvements. Renal involvement was related to the level of S100 A8 and A9 (Figure 1). S100A8 and A9 levels correlated with leukocyte and neutrophil counts positively and were significantly lower in patients with leukopenia (Figure 1). The SLEDAI score showed a slightly negative correlation with S100A8 levels, but not with S100A9 levels, whereas S100A9 levels showed a slightly positive correlation with the CLASI activity score ($r = 0.19$, $P = 0.039$). S100A8 levels positively correlated with IL-1ra levels ($r = 0.19$, $P = 0.039$) and S100A9 with IL-8 and IL-1ra levels (IL-8; $r = 0.30$, $P = 0.022$ and $r = 0.53$, $P < 0.0001$). Regarding SLEDAI scores of 1–4 ($n = 54$), patients with higher S100A8 and S100A9 levels tended to have higher SLE-DAS scores. S100A8 and S100A9 levels were higher in patients with cutaneous lesions, which correlated with the CLASI activity score (S100A8, $r = 0.27$, $P = 0.047$; S100A9, $r = 0.29$, $P = 0.033$; Figure 2).

Conclusion: Serum TNF-α, IL-8, monocyte chemoattractant protein-1, and IL-1ra were not associated with organ lesions. However, S100 was significantly associated with renal and skin lesions, which are strongly suggested to be associated with IFN.

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Abstract Number: 0570

BLyS Levels Are Elevated in Systemic Lupus Erythematosus Patients with Neuropsychiatric Manifestations

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoantibodies and auto reactive B cells participate on the pathogenesis of systemic lupus erythematosus (SLE), affecting various organs and tissues, including the nervous system, referred as neuropsychiatric SLE (NPSLE). The B-lymphocyte stimulator (BLyS) cytokine, which induces B cell proliferation and survival, may play an important role in NPSLE manifestations. In this study, we examine BLyS levels in SLE patients with well-defined NPSLE symptoms as compared to SLE patients without NPSLE and individuals with depression and cognitive impairment and healthy controls.

Methods: We included 75 SLE patients from the Rheumatology outpatient unit and 53 age and sex matched controls (20 with primary depression, 14 with mild cognitive impairment and 9 healthy controls). SLE patients were selected based on the presence of depression (N=25), cognitive impairment (N=25) or absence of neuropsychiatric (NP) manifestations

(N=25). SLE patients that have been prescribed belimumab or rituximab were excluded. SLE patients and controls had similar age and sex distribution. A complete clinical, laboratory and neurological evaluation was performed in all subjects. Mood disorders were determined through Beck Depression (BDI)). Cognitive evaluation was evaluated by Automated Neuropsychological Assessment Metrics (ANAM), *Montreal Cognitive Assessment* (*MoCA*) and formal cognitive testing. BLyS concentrations were evaluated in serum samples with Quantikine Elisa (R&D Systems, USA), following the manufacturer's instructions and with minimum detectable levels of2.68 pg/mL. All measurements were made on a single occasion. Data were analysed using the Mann-Whitney U test, with a p value < 0.05 considered significant.

Results: Active disease was observed in 23 (30.7%) SLE patients. Seventy (93%) were on immunosuppressant medication [Prednisone with doses ≥7.5 mg/day in 55 (73%), hydroxychloroquine in 57 (76%), azathioprine in 30 (40%), mycophenolate in 20 (26%). BLyS serum concentrations were significantly increased in SLE patients when compared to controls (p=0.005). BLyS serum concentration from 25 individuals with SLE and depression were significantly increased when compared to 25 SLE without NP manifestations (p=0.042), and the 20 healthy individuals with primary depression (p=0.017). No significant difference between primary depression and healthy controls was observed. BLyS serum concentration from 25 individuals with SLE and cognitive impairment were significantly increased when compared to 25 SLE without NP manifestations (p=0.003), and the 14 healthy controls with mild cognitive impairment (p=0.016). No significant difference between mild cognitive impairment controls and healthy controls was observed.

Conclusion: SLE patients with depression and cognitive impairment had higher BLyS levels when compared to SLE patients without NP manifestations and healthy controls with NP diagnoses. BLyS may play a role in NPSLE pathogenesis.

Disclosure: A. Alencar: None; **T. Mazzola**: None; **S. Sepresse**: None; **B. Aquino**: None; **I. Teixeira**: None; **I. Ribeiro**: None; **L. Rizzi**: None; **Í. Aventurato**: None; **M. Da Silva**: None; **M. Balthazar**: None; **L. Costallat**: None; **R. Marini**: None; **L. Silva**: None; **C. Yasuda**: None; **F. Cendes**: None; **T. Niewold**: AstraZeneca, 6, Progentec, 1, S3 Connected Health, 2, Zenas, 5; **S. Appenzeller**: None.

Abstract Number: 0571

A Polygenic Risk Score for Systemic Lupus Erythematosus (SLE) Discriminates Between Patients with Lupus and Individuals Without Lupus and a Positive Antinuclear Antibody Test

Gul Karakoc[1], Ge Liu[1], Jacy Zanussi[2], Cecilia Chung[2], Jorge Gamboa[1], Jonathan Mosley[1], Nancy Cox[1], C. Michael Stein[1] and **Vivian Kawai**[1], [1]Vanderbilt University Medical Center, Nashville, TN, [2]University of Miami, Miami, FL

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: A positive ANA (ANA-POS) test is present in almost all patients with SLE and is also frequently present in other autoimmune (AI) diseases and in the general population. Genetic factors play an important role in the risk for SLE and a polygenic risk score for SLE (PRS_{SLE}) is significantly different in patients with SLE compared to controls. However, several studies have reported immunologic findings or clinical features of incomplete lupus in ANA-POS patients without SLE, raising concern for increased genetic risk of SLE in these patients. Thus, a clinically important question is whether a PRS_{SLE} differs among patients with SLE and individuals without SLE who have a positive ANA test.

Methods: We built a PRS_{SLE} using a Bayesian framework with continuous shrinkage using summary data from the largest SLE genome-wide association analysis (GWAS) in individuals of European ancestry. Then, we calculated the PRS_{SLE} in individuals who were tested for ANA as part of their clinical care and had genome-wide interrogation in BioVU - a biobank that links de-identified genetic and electronic health record data at Vanderbilt. We defined 5 different groups: patients with SLE (SLE), patients with other AI diseases who had a positive (AI-ANA-POS) or a negative (AI-ANA-NEG) ANA test, and individuals without an AI disease who had a positive (ANA-POS) or a negative (ANA-NEG) ANA test. A positive ANA was defined as a titer of 1:80 or higher. The PRS_{SLE} was standardized and compared between patients with SLE and the other 4 groups. A P-value ≤ 0.0125 (0.05/ 4 comparisons) was considered significant. To test the ability of the PRS_{SLE} to discriminate patients with SLE among those with a positive ANA test, we selected individuals (n=4,086) with a positive ANA (SLE, ANA-POS and AI-ANA-POS), and trained two predictive models (PRS_{SLE} alone, and PRS_{SLE}, sex, and age) using a 70% of the sample as training set. Then, we calculated the area under the curve (AUC) of the Receiver Operating Characteristic (ROC) curve in the remaining sample (testing set). Continuous variables were analyzed using Wilcoxon rank-sum test.

Results: We studied 10,032 individuals of European ancestry with ANA results. Patients with SLE had a higher proportion of female patients and were younger compared to the other groups (all P< 0.0125) (Table). The PRS_{SLE} was higher is the SLE group compared to all other groups: AI-ANA-POS (P=1.8E-11), ANA-POS (P=3.7E-20), AI-ANA-NEG (P=1.5E-21), and

Table: Demographic characteristics and distribution of the polygenic risk score for SLE (PRS_{SLE}) in BioVU individuals tested for antinuclear antibodies

	SLE	AI ANA POS	ANA-POS	AI ANA NEG	ANA-NEG
Total count	662	1341	2083	1587	4359
Female (%)	578 (87.3%)	1002 (74.7%) P=1.2E-10	1428 (68.6%) P=4.2E-21	998 (62.9%) P=1.7E-30	2453 (56.3%) P=5.7E-52
Age (years)	48.7 [36.7, 59.8]	55.1 [40.7, 65.0] P=8.9E-08	56.2 [43.4, 66.7] P=5.4E-15	53.7 [41.0, 63.4] P=5.0E-06	53.6 [41.4, 63.9] P=3.9E-08
PRS_{SLE}	0.23 [-0.35, 0.99]	-0.10 [-0.61, 0.62] P=1.8E-11	-0.15 [-0.71, 0.47] P=3.7E-20	-0.22[-0.74, 0.49] P=1.5E-21	-0.23 [-0.72, 0.43] P=1.2E-28

SLE: systemic lupus erythematosus, AI-ANA-POS: individuals with an autoimmune disease with a positive ANA test, ANA-POS: individuals without an autoimmune disease with a positive ANA test, AI-ANA-NEG: individuals with an autoimmune disease with a negative ANA test, ANA-NEG: individuals without an autoimmune disease with a negative ANA test. PRS_{SLE} are shown as z-scores distributions. P-values represent the comparison between the SLE group and each of the other groups for a specific variable. Data are shown as counts (percentage) and median [interquartile range]

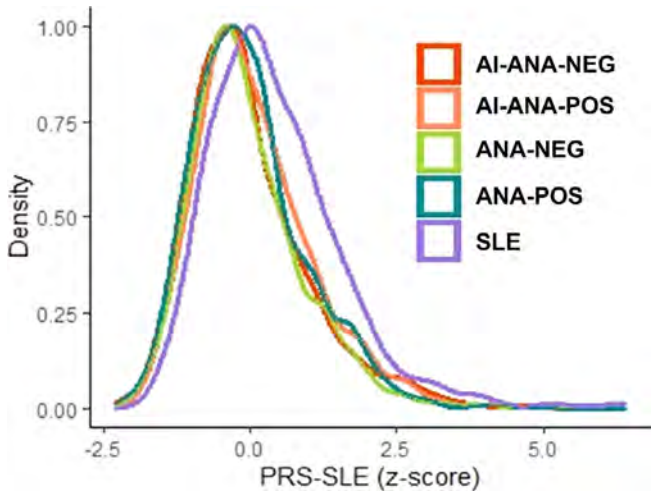

Figure 1: Distribution of the standardized Polygenic Risk Score for SLE (PRS SLE) in individuals who had an ANA test performed as part of their clinical care in BioVU.

ANA-NEG (P=1.2E-28). (Figure and Table). The PRS_{SLE} discriminated patients with SLE from those with a positive ANA test (AUC = 0.61, 95%CI [0.57, 0.66]) and the inclusion of age and sex resulted in a higher AUC (0.66, 95%CI [0.62, 0.70]) (P=0.02)

Conclusion: Patients with SLE have a higher PRS_{SLE} compared to individuals with a positive ANA test. The PRS_{SLE} had a modest discriminative ability to distinguish patients with SLE among those with a positive ANA result, and this increased when age and sex were also included in the model.

Disclosure: G. Karakoc: None; **G. Liu**: None; **J. Zanussi**: None; **C. Chung**: None; **J. Gamboa**: None; **J. Mosley**: None; **N. Cox**: None; **C. Stein**: None; **V. Kawai**: None.

Abstract Number: 0572

Serum/ Urine Levels and Expression of CD163 in Lupus Nephritis

Erdem Gurel[1], Suzan Cinar[2], Ozge Hurdogan[3], Yasemin Ozluk[3], Isin Kilicaslan[4], Sibel Varelci[1], Safak Mirioglu[5], Yasemin Yalcinkaya[6], Ahmet Gul[6], Lale Ocal[1], Murat Inanc[6] and Bahar Artim-Esen[6], [1]Division of Rheumatology, Istanbul University Istanbul School of Medicine, Istanbul, Turkey, [2]Department of Immunology, Aziz Sancar Institute of Experimental Medicine, Istanbul University, Istanbul, Turkey, [3]Department of Pathology, Istanbul University Istanbul School of Medicine, Istanbul, Turkey, [4]Department of Pathology, Istanbul University Istanbul School of Medicine, Istanbıl, Turkey, [5]Division of Nephrology, Bezmialem Vakif University School of Medicine, Istanbul, Turkey, [6]Division of Rheumatology, Department of Internal Medicine, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: CD163 is a glycosylated membrane protein expressed in monocytes and macrophages that phagocytize the hemoglobin/haptoglobin complex. As a result of proinflammatory stimuli, CD163 is shedded from the cell membrane and becomes soluble CD163. Therefore, it has been shown that serum (s) and urine (u) levels of soluble CD163 increase in acute or chronic inflammatory diseases. sCD163 and uCD163 are considered as potential biomarkers

Table 1. Serum and urine levels of CD163 across study groups

Table 1 Serum and urine levels of CD163 across study groups

Biomarker	Active LN (n=20)	Inactive LN (n=10)	P	Extrarenal active SLE (n=15)	P	Healthy control (n=20)	P
Serum CD163 % binding (mean+SD)	26,7±17,6	22,8±18,8	0,54	22,06±9,6	0,3	17,03±15,6	0,4
Serum CD163 positivity n (%)	%75	%50	0,2	%73	0,9	%40	0,05
Urine CD163 % binding (mean+SD)	3,9±2,4	2,6±0,04	0,02	2,5±0,1	0,023	2,6±0,5	0,03
Urine CD163 positivity n (%)	%90	%40	0,007	%33	0,001	%12	<0,001

LN lupus nephritis, SLE systemic lupus erythematosus, SD standard deviation

Figure 1. Serum and urine levels of CD163 after treatment

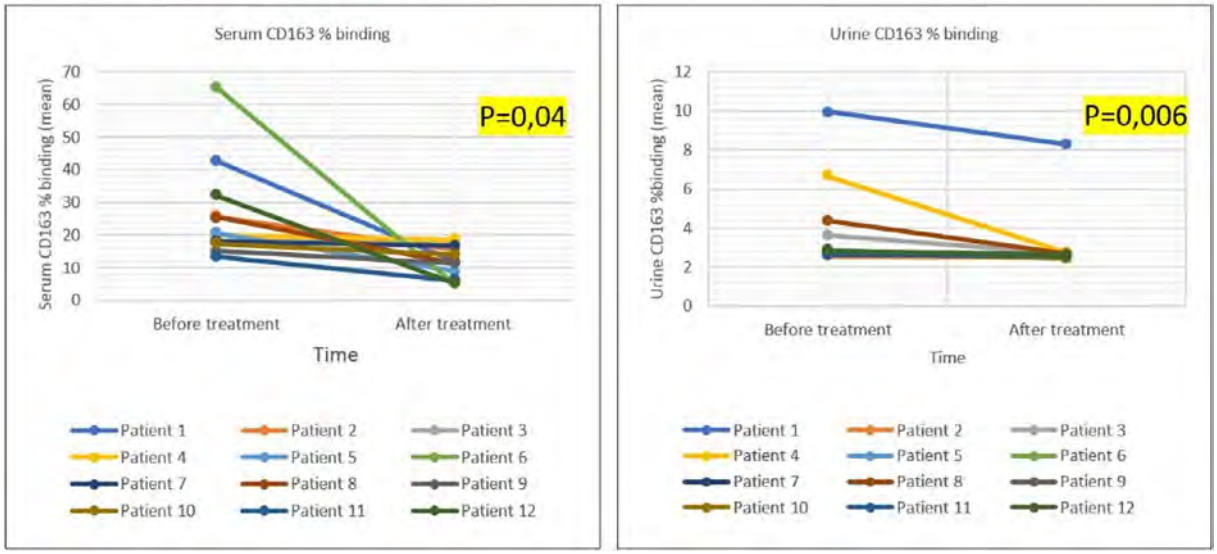

Figure 1. Serum and urine levels of CD163 after treatment

reflecting disease activity in patients with systemic lupus erythematosus (SLE).We aimed to investigate the association of serum and urine soluble CD163 levels and renal CD163 expression with disease activity in patients with lupus nephritis (LN).

Methods: Serum and urine levels of CD163 of 45 SLE patients (active renal 20, active non-renal 15, inactive 10) and 20 healthy volunteers were tested by ELISA. Control samples were taken from 12 active renal patients after six months of treatment and 30 renal biopsy specimens were examined for CD163 expression.

Results: Of 45 participants, 37 (82.2%) were female, with a median disease duration of 113 (1-436) months and a mean age of 38,9±13 (18-68) years. Both the frequency of uCD163 positivity and its levels were significantly higher in the active LN group compared to the inactive LN (p=0,007 and 0.02 respectively) and active non-renal SLE (p=0,001 and 0.023 respectively) groups (Table 1). sCD163 and uCD163 levels of 12 patients with active LN were significantly reduced after treatment (p=0,04 and p=0,006) (Figure 1). CD163+ macrophage expression in kidney biopsies of patients with active LN correlated with sCD163 (r= 0.597 and p=0.01) and uCD163 (r=0.507 and p=0.045) levels.

Conclusion: uCD163 is a promising biomarker that can differentiate active LN from inactive LN and active extrarenal SLE changing in line with treatment response. Correlation of both s and uCD163 with CD163+ macrophage expression in biopsies suggests that it may be used as an activity parameter in patients with lupus nephritis histopathologically. Further studies are awaited to confirm these results.

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Abstract Number: 0573

Presence of Mediterranean Fever Gene Variants Provides Protection from the Development of Lupus Nephritis in Patients with Systemic Lupus Erythematosus

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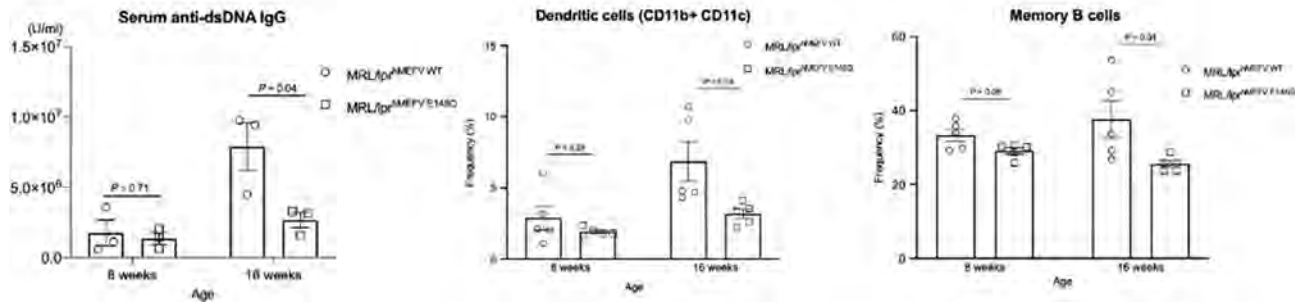
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies showed that the prevalence of variants in *Mediterranean Fever* (*MEFV*) genes was lower in adult patients with SLE compared to healthy population and thatlow prevalence of coexistence of FMF and SLE was observed in several large FMF cohorts, suggesting that a potential protective effect of the presence of *MEFV* variants and/or FMF from SLE. Also, existence of *MEFV* variants have been suggested to modify clinical phenotypes of SLE. In particular, the presence of the E148Q variant in the exon 2 of *MEFV* gene may be protective for the development of lupus nephritis among adult patients with SLE. However, all these reports showing a relationship between SLE and *MEFV* gene are limited to those in the Mediterranean region, where *MEFV* exon 10 variants are relatively common.

Methods: We conducted a retrospective analysis of 55 Japanese SLE patients between January 2008 and April 2020 at Nagasaki University Hospital. We examined whether they have *MEFV* variants by next-generation sequencing in the whole region of *MEFV*. and compared clinical characteristics of the patients based on the presence or absence of *MEFV* variants. We introduced a partial segment of human exon 2 of the MEFV gene with or without E148Q variant, which is common variant in MEFV gene, into MRL/lpr mice and compared those phenotypes between MRL/lpr mice expressing the wild-type MEFV gene (MRL/lpr$^{hMEFV\ WT}$) and those expressing the E148Q variant (MRL/lpr$^{hMEFV\ E148Q}$).

Factors associated with the development of lupus nephritis in SLE patients in multiple regression analysis

End point	Variables		Odds rate (95% CI)	P-value
Lupus nephritis	Age at onset	1 increase	1.013 (0.963 to 1.065)	0.63
	Male gender	Presence	0.754 (0.053 to 10.741)	0.84
	Low CH50	Presence	4.758 (0.869 to 26.052)	0.07
	Anti-dsDNA Ab positive	Presence	5.159 (0.761 to 34.950)	0.09
	Total count number of *MEFV* variants	1 increase	0.359 (0.137 to 0.942)	0.04



Results: A total of 33 out of 55 patients with SLE had one or more variants in exon 1–5 of *MEFV*, whereas none of the patients had a mutation in exon 10. Patients with *MEFV* variants exhibited significant lower presence of lupus nephritis than those without *MEFV* variants (P=0.007). We counted the total number of *MEFV* variants exhibited in each patient. The total number of *MEFV* variants in patients with lupus nephritis was significantly lower than those without lupus nephritis (P=0.006). Among the factors analyzed including age at onset, male gender, low CH50, anti-dsDNA Ab positive, and the total count number of *MEFV* variants, only the total count of MEFV gene variants were significantly associated with the presence of lupus nephritis (odds ratio [OR] 0.359, $p< 0.05$). Consistent with the data from patients with SLE, *MRL/lpr*$^{hMEFV\ E148Q}$ showed the tendency of less severality in lupus nephritis (not statistically significant) and showed significantly less autoantibody production ($p< 0.05$). These observed differences in disease phenotypes were suggested to be attributed by reduced induction of dendritic cells ($p< 0.05$) followed by a decrease in memory B cells ($p< 0.05$).

Conclusion: Presence of *MEFV* variant can modify clinical type of SLE and be a protective factor against the development of lupus nephritis.

Disclosure: Y. Endo: None; **T. Koga**: None; **A. Kawakami**: None.

Abstract Number: 0574

Type I IFN-associated Regulation of Immune Checkpoint Genes in Patients with SLE

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Aberrant activation of type I IFN, and subsequent adverse clinical implications, have been widely discussed in relation to SLE. With the lack of consistent data to support an association between disease activity and type I interferon, we hereby explore an alternative role of type I interferon in SLE pathogenesis. Continuous exposure to type I IFN is implicated in regulating immune checkpoint genes *in vitro* and in the context of a viral infection. Based on these findings, we investigated whether IFN exposure also regulates immune checkpoint genes in SLE, using bulk RNA-seq analysis.

Methods: We measured whole blood RNA-seq in 34 patients fulfilling the 2019 EULAR/ACR classification criteria for SLE and 15 age- and gender-matched healthy controls (HC). SLE disease activity was determined according to the SLE Disease Activity Index 2000 (SLEDAI-2K) score[1]. Whole blood samples were collected in PAXgene blood tubes (Qiagen) and analyzed for mRNA expression levels of 24 immune checkpoint genes and 12 type I IFN-stimulated genes using NanoString nCounter Technology. All expressions levels were represented as $\log_2$ fold change relative to HC. A compound type I IFN gene expression score (IGS) was calculated based on the median $\log_2$ fold change of type I IFN-stimulated gene expression and patients were grouped according to low or high IGS (IGS >1). Statistical analyses were performed using R version 3.6.1. and SPSS version 25.

Table 1. Demographics, laboratory, and clinical characteristics of SLE patients SLEDAI-2K: SLE Disease Activity Index 2000; ANA: anti-nuclear antibodies; dsDNA: double-stranded DNA; Sm: Smith. *: Azathioprine, mycophenolate mofetil, cyclophosphamide, rituximab, and/or methotrexate.

	All patients with SLE (n = 34)	SLE with high IGS (n = 24)	SLE with low IGS (n = 10)
Demographic characteristics			
Females, n (%)	34 (100)	24 (100)	10 (100)
Mean age, years (SD)	52.5 (12.5)	52.0 (13.4)	53.8 (9.8)
Ethnicity, European n (%)	34 (100)	24 (100)	10 (100)
SLE characteristics			
Disease duration in years, mean (SD)	22.4 (8.2)	21.7 (9.0)	23.9 (5.7)
Nephritis ever, n (%)	24 (71)	19 (80)	5 (50)
24 hrs. proteinuria > 0.5 g, n (%)	12 (35)	11 (46)	1 (10)
SLEDAI-2K score, median (range)	3.0 (0-10)	4 (0 - 12)	2 (0 - 4)
Medication, n (%)			
Hydroxychloroquine	4 (12)	3 (13)	1 (10)
Glucocorticoids	6 (18)	6 (25)	0 (0)
Glucocorticoids > 7.5 mg	1 (3)	0 (0)	1 (10)
Immunosuppressants*	18 (53)	14 (17)	4(40)
Autoantibodies, n (%)			
ANA	34 (100)	24 (100)	10 (100)
Anti-dsDNA	32 (94)	23 (96)	9 (90)
Anti-Sm	5 (15)	2 (8)	3 (30)
Anti-Phospholipid	15 (44)	10 (42)	5 (50)
Anti-SSA(Ro)/SSB(La)	9 (26)	8 (33)	1 (10)

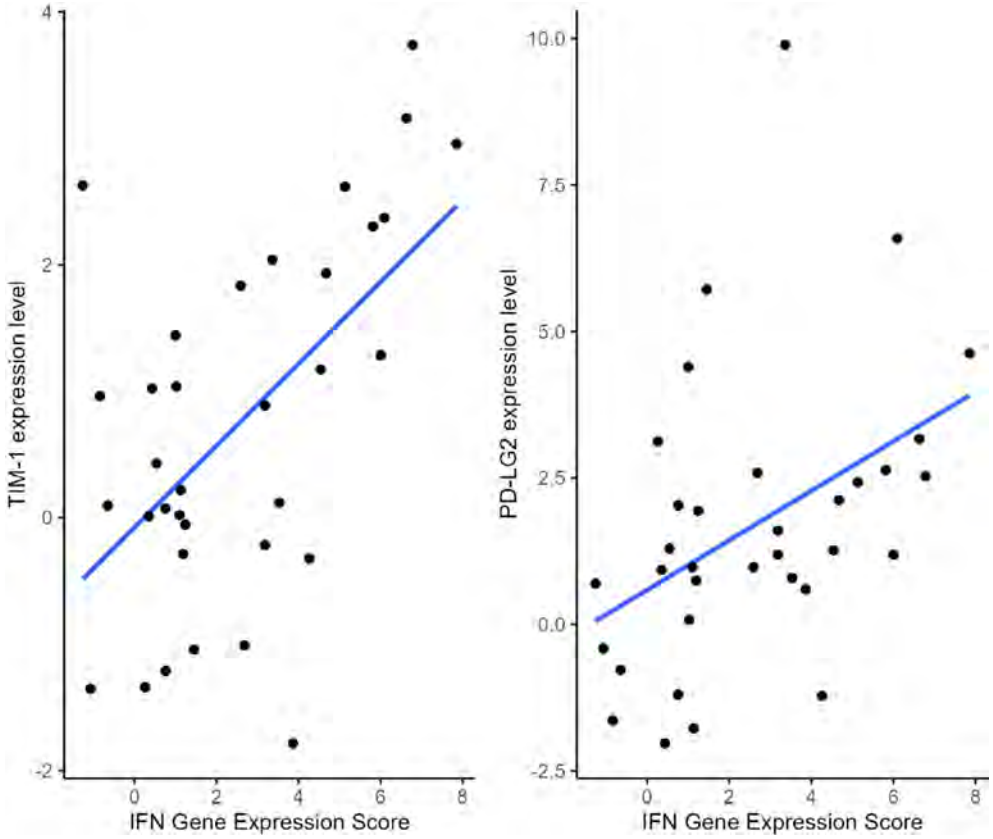

Figure 1. Whole blood gene expression in SLE patients. Scatterplot showing association between mRNA expression of immune checkpoint genes TIM-1 (left) and PD-LG2 (right). Regression lines were determined by a generalised linear model analysis.

Results: Demographic and clinical characteristics of SLE patients are detailed in **Table 1**. Twenty-four SLE patients (70%) had a high IGS. We found that genes coding for the immune checkpoints TIM-3 and PD-LG2 were upregulated in SLE patients with a high IFN score compared with HC; $\log_2$ fold changes were 0.36 and 0.89 and P-values were 0.0046, 0.0042 for TIM-3 and PD-LG2 respectively. Expression of the immune checkpoint genes paralleled the expression of the IGS but only for those patients who had a high expression of type I IFN stimulated genes (**Figure 1**). This was confirmed by a generalized linear model analysis showing a significant positive association between the IGS and expression of TIM-3 and PD-LG2 in SLE patients (P= 0.0001 and 0.006, respectively).

The median (range) SLEDAI-2K scores were 4.0 (0–10) and 2.0 (0–5) for the high and low IGS SLE patients, respectively. A generalized linear model analysis showed that SLEDAI-2K scores did not associate with the expression of TIM-3 and PD-LG2, arguing against the notion that differential expression of immune checkpoint genes in high IGS SLE patients may be related to disease activity.

Conclusion: This study revealed differential mRNA expression of immune checkpoint genes TIM-1 and PD-LG2 in a type I IFN-associated manner, which did not associate with disease activity. These results are in line with previous observations that type I IFN activity does not necessarily reflect SLE disease activity. With this, we suggest that persistent type I IFN activation perhaps regulates inhibition of immune cells in SLE patients and other rheumatic diseases characterized by such type I IFN activation.

Disclosure: K. Siddiqi: None; **A. Zinglersen**: None; **K. Iversen**: None; **S. Jacobsen**: Bristol-Myers Squibb(BMS), 5.

Abstract Number: 0575

The Real-World Utility of a Lupus Activity Monitoring Panel in the United States Community Rheumatologist Practice

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SESSION INFORMATION
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Session Type: Poster Session A
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Background/Purpose: Patients with active SLE have periods of uncontrolled disease activity that are associated with a greater risk for developing irreversible organ damage. Current standard of care (SoC) testing does not adequately monitor disease activity, and there is a lack of widespread real-world application of these tests, making it difficult to provide individualized care. To help address this, the lupus activity monitoring panel, comprising a blood test, is designed to assess SLE disease activity by measuring SLE-related biomarkers more comprehensively than SoC tests (see **Table 1** footnote). This observational, retrospective cohort study (GSK Study 217538) describes patient and provider characteristics of those who received the lupus activity monitoring panel test and those who received SoC tests.

Methods: Adults with an SLE diagnosis who received at least two lupus activity monitoring panel tests (cases) or at least one set of SoC tests (C3/C4 and anti-dsDNA; controls) between July 1, 2016, and December 31, 2021, were identified in the United Rheumatology-Normal Integrated Community Evidence repository (cases may have also received SoC tests). Eligible

patients were linked to administrative medical and pharmacy claims data from Medicare, managed Medicaid and commercial plans. Patients had continuous enrollment for 6 months pre-index (index=first recorded panel/SoC test) and 6 months post index. For cases and controls, patient and provider characteristics were assessed descriptively as mean and standard deviations (SD) for continuous variables and frequencies and proportions for categorical variables.

Results: The mean (SD) age for cases (N=75) and controls (N=616) was 57.5 (15.7) and 61.0 (15.1) years, 61% and 54% were white, and 71% and 78% had Medicare or Medicaid insurance, respectively; ≥90% of patients were female (**Table 1**). Both groups had mean baseline Deyo-Charlson Comorbidity Index scores of 2.4; the most common comorbidities were hypertension (cases, 53%; controls, 59%) and depression (cases, 27%; controls, 20%; **Table 2**). Approximately half of patients had moderate SLE, and most received ≥1 SLE therapy (cases, 60%; controls, 65%) with antimalarials most commonly prescribed. The lupus activity monitoring panel or SoC index test was ordered at a clinic with only 1 provider for 42% of cases compared with 15% of controls (**Table 3)**. The lupus activity monitoring panel was most frequently used by providers seeing 50 to < 75 patients with SLE/index year, whereas SoC testing was most common in larger practices (**Table 3**).

Table 1. Demographic characteristics measured on index date among patients with at least 6 months of continuous enrollment post index. *The lupus activity monitoring panel consists of six specialized biomarkers including: erythrocyte-bound C4d, anti-dsDNA by chemiluminescent immunoassay, complement C3 and C4, platelet-bound C4d, and the anti-C1q biomarker. NR, not reportable.

Measure	Cases* N=75	Controls N=616
Age at index date (years), mean (SD)	57.5 (15.7)	61.0 (15.1)
Age group, n (%)		
18–39 years	14 (19)	63 (10)
40–64 years	24 (32)	229 (37)
65–69 years	19 (25)	120 (19)
>70 years	18 (24)	204 (33)
Sex, n (%)		
Female	NR (>90)	NR (90)
Payer, n (%)		
Commercial	22 (29)	135 (22)
Medicare or Medicaid	53 (71)	481 (78)
Race, n (%)		
White	46 (61)	332 (54)
Length of follow-up (months), mean (SD)	31.1 (14.6)	31.6 (15.3)

Table 2. Baseline characteristics measured during the 6-month pre-index period among patients with at least 6 months of continuous enrollment post index. *As defined by Garris et al. 2013, J Med Econ 16:5;667–77 during the pre-period. **Measured using all available data prior to index date. DCCI, Deyo-Charlson Comorbidity Index.

Measure	Cases N=75	Controls N=616
DCCI score, mean (SD)	2.4 (2.0)	2.4 (1.9)
Common comorbidities, n (%)		
Depression	20 (27)	122 (20)
Diabetes	15 (20)	118 (19)
Hypertension	40 (53)	366 (59)
Neuropathy	11 (15)	49 (8)
Any SLE treatment, n (%)	45 (60)	398 (65)
Most common treatments		
Antimalarial medication	29 (39)	242 (39)
Corticosteroids	16 (21)	134 (22)
Immunosuppressant or biologic	12 (16)	164 (27)
Disease severity*, n (%)		
Mild	19 (25)	157 (25)
Moderate	42 (56)	351 (57)
Severe	14 (19)	108 (18)
Outpatient rheumatologist visits, mean (SD)	1.6 (2.1)	1.6 (1.9)
Length of time on biologic and/or immunosuppressant prior to index date (months), mean (SD)**	32.1 (27.9)	32.7 (21.9)

Table 3. Provider characteristics among patients with at least 6 months of continuous enrollment post index.

Measure	Cases	Controls
Number of provider(s) at site where index lupus activity monitoring panel or SoC test was ordered, n (%)	**52 (100)**	**367 (100)**
1 provider	22 (42)	56 (15)
>1 provider	30 (58)	311 (85)
Index visit provider SLE patient volume/index year, n (%)	**46 (100)**	**367 (100)**
<50 patients/index year	12 (26)	77 (21)
50 to <75 patients/index year	19 (41)	100 (27)
≥75 patients/index year	15 (33)	190 (52)

Conclusion: This is the first real-world study to describe use of the lupus activity monitoring panel by community-based rheumatologists and offers initial insights into the heterogeneity of this population. There is a need to further understand the lupus activity monitoring panel use in the context of SLE care management and to educate providers on appropriate use of the unique tests included in the lupus activity monitoring panel.

Funding: GSK

Disclosure: A. Concoff: Exagen, Inc, 3, Pacira, 2, United Rheumatology, 4; **L. Moore-Schiltz**: GSK, 2, Inovalon, 3; **V. Nadipelli**: GSK, 3, 11; **T. O'Malley**: Exagen, 3, 11, 12, Shareholder; **K. Worley**: GSK, 3, 11; **A. Petrilla**: GSK, 2, Inovalon, 3; **D. Zach**: Exagen, 3, 11; **S. Robinson**: GSK, 2, Inovalon, 3; **S. Taiyari**: GSK, 3, 11; **B. Jones**: GSK, 2, Inovalon, 3; **B. Rubin**: GSK, 3, 11.

Abstract Number: 0576

Enhancing Systemic Lupus Erythematosus Diagnosis: Comparative Performance Characteristics of TC4d and Anti-T-Cell Antibodies with Conventional Biomarkers

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SESSION INFORMATION
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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic, systemic autoimmune disease, affecting multiple organ systems with varying severity among patients. SLE presents a diagnostic challenge due to its protean clinical manifestations. Current standard of care biomarkers such as anti-dsDNA, anti-Smith, and complement proteins C3/C4 have limited discriminatory power characterized by poor sensitivity in incipient cases of SLE. This study aims to compare the clinimetric performance of T-cell bound complement split product C4d (TC4d) and anti-T-cell antibodies IgG (TIgG) and IgM (TIgM) with conventional biomarkers in differentiating Systemic Lupus Erythematosus (SLE) from clinically relevant controls (CRCs).

Methods: A total of 230 patients were included in the analysis (SLE = 80; CRC = 150) (Table 1). SLE patients were required to meet either the 1997 ACR, 2012 SLICC, or 2019 ACR/EULAR classification criteria for SLE; CRCs were required to have a clinical diagnosis with an associated ICD-9/ICD-10 code to confirm clinical diagnosis as enumerated in the Table 1 caption. A comprehensive machine learning pipeline integrating feature selection, multiple model architectures training, and cross-validation (CV) techniques was employed to compare the relative diagnostic performances of TIgG, TIgM, and TC4d to conventional SLE biomarkers. The robustness and generalizability of the pipeline were validated through permutational hold-out (HO) predictions, mitigating the risk of overfitting the models developed.

Results: The SLE cohort had a higher proportion of females (96.3% vs. 77.3%), younger age (mean [SD]: 47.1 [13.9] vs. 53.6 [14.3] years), and fewer Caucasians (65.0% vs. 82.7%) as compared to the CRC group (Table 1). Cumulative ROC analysis derived from multiple 10-fold CV models showed the diagnostic performances of TC4d (AUC = 0.86), TIgG (AUC = 0.81), and TIgM (AUC = 0.78) outperformed C3 (AUC = 0.77), anti-dsDNA (AUC = 0.76), anti-Smith (AUC = 0.72), and C4 (AUC = 0.70) (Figure 1, A). While the specificity of TIgG, TIgM, TC4d compared to conventional biomarkers were

Table 1: Cohort Demographics

	Total (N=230)	CRC (N=150)	SLE (N=80)
Gender			
Female	192 (83.8%)	116 (77.3%)	77 (96.3%)
Male	37 (16.2%)	34 (22.7%)	3 (3.7%)
Ethnicity			
Caucasian	176 (76.5%)	124 (82.7%)	52 (65%)
African	24 (10.4%)	12 (8.0%)	12 (15%)
Hispanic	23 (10.0%)	11 (7.3%)	12 (15%)
Asian	5 (2.2%)	1 (0.7%)	4 (5%)
Other	2 (0.9%)	2 (1.3%)	0
Age (years)			
Mean (SD)	51.3 (14.5)	53.6 (14.3)	47.1 (13.9)
Median [Min, Max]	54.0 [21.0, 80.0]	56.0 [21.0, 80.0]	46.0 [26.0, 76.0]
ANA by IFA or ELISA			
Negative	62 (27.0%)	51 (34.7%)	10 (12.5%)
Positive	168 (73.0%)	98 (65.3%)	70 (87.5%)
Anti-Smith			
Negative	223 (97.0%)	150 (100%)	73 (91.3%)
Positive	7 (3.0%)	0 (0%)	7 (8.8%)
anti-dsDNA			
Negative	199 (86.5%)	147 (98.0%)	52 (65.0%)
Positive	31 (13.5%)	3 (2.0%)	28 (35.0%)
Anti-T-Cell-IgG			
Mean (SD)	20.9 (90.0)	10.1 (51.3)	41.2 (133)
Median [Min, Max]	3.93 [0, 1110]	2.97 [0, 587]	7.88 [0.230, 1110]
Anti-T-Cell-IgM			
Mean (SD)	10.0 (26.7)	4.9 (14.3)	19.3 (39.3)
Median [Min, Max]	1.85 [0, 209]	1.25 [0, 115]	4.73 [0, 209]
T-Cell bound C4d			
Mean (SD)	117 (361)	56.5 (287)	229 (449)
Median [Min, Max]	27.8 [0, 3480]	22.1 [0, 3480]	85.7 [0, 3240]

CRC [N=150] consists of the following: Rheumatoid Arthritis [N=42]; primary Sjögrens syndrome [N=31]; chronic localized pain [N=15]; osteoarthritis [N=11]; fibromyalgia syndrome [N=10]; psoriatic arthritis [N=7]; spondyloarthritis [N=6]; UCTD [N=5]; inflammatory arthritis [N=3]; polymyalgia rheumatica [N=3]; Stills disease [N=2]; systemic sclerosis (limited) [N=2]; ANCA-associated vasculitis [N=2]; gout [N=2]; dermatomyositis [N=1]; Crohns [N=1]; enteropathic arthritis [N=1]; juvenile idiopathic arthritis [N=1]; MCTD [N=1]; cutaneous lupus [N=1]; polymyositis [N=1]; sarcoidosis [N=1]; autoimmune thyroiditis [N=1]

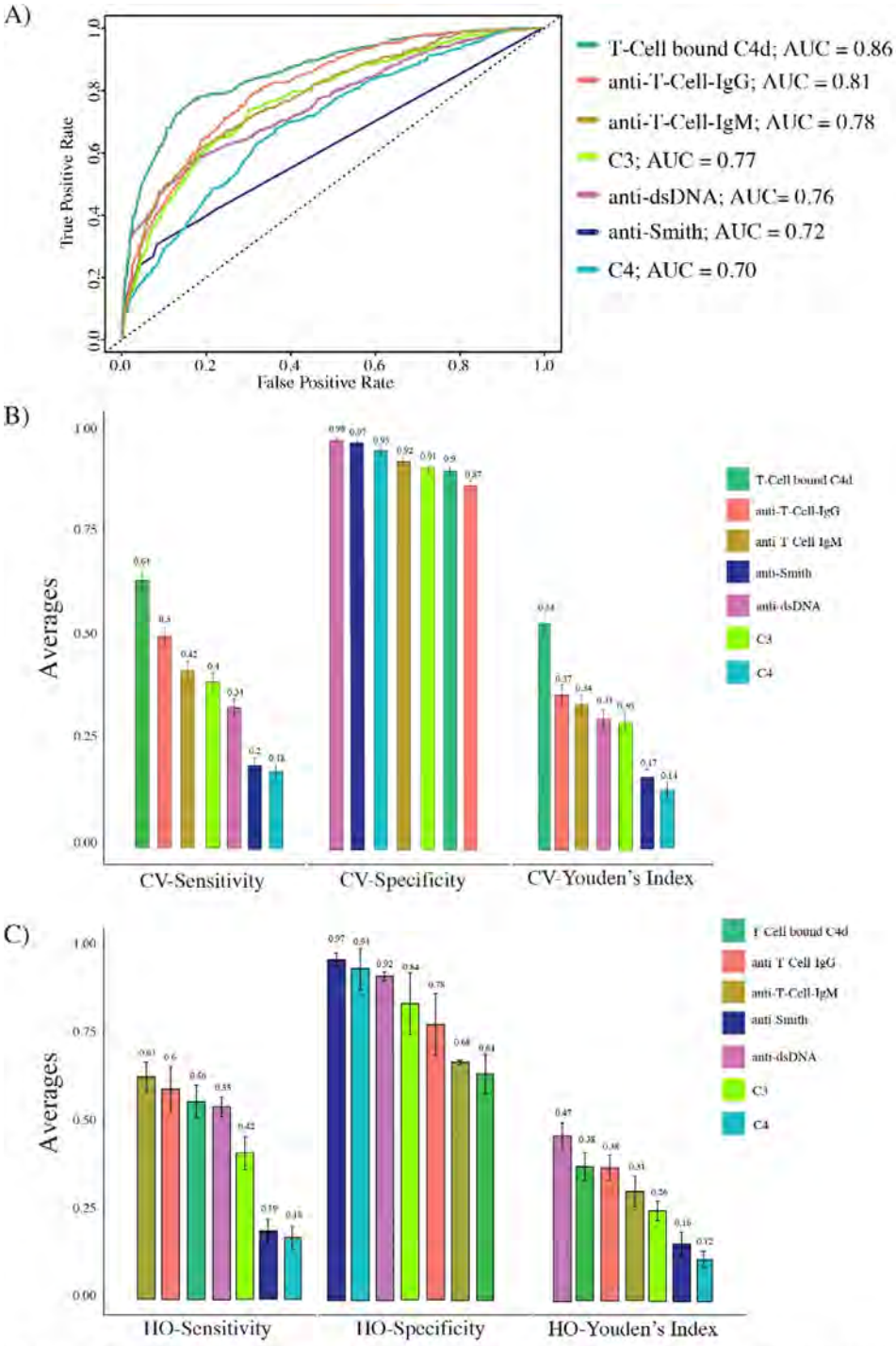

Figure 1. Comparative Performance Characteristics of TC4d and, Anti-T-Cell Antibodies, and conventional biomarkers predicting SLE from CRC samples. A) Cumulative ROC curves depicting top 10-CV models per marker. Individual biomarker AUCs are reported in the legend representing average performances of the 10-CV models in cross validation. B) Average Sensitivity, Specificity and Youden's Index (Sensitivity + Specificity -1) during cross-validation for the individual as well as combined biomarker performances at thresholds maximizing F-1 scores (the harmonic mean of Precision and Recall which aims to balance the two with maximum benefits). Average performance results are reported on top of individual bar charts per biomarker respectively. C) Average Sensitivity, Specificity and Youden's Index (Sensitivity + Specificity -1) of the hold-out data (unseen data) for the individual biomarker performances at thresholds maximizing F-1 scores. Average performance results are reported on top of individual bar charts per biomarker respectively.

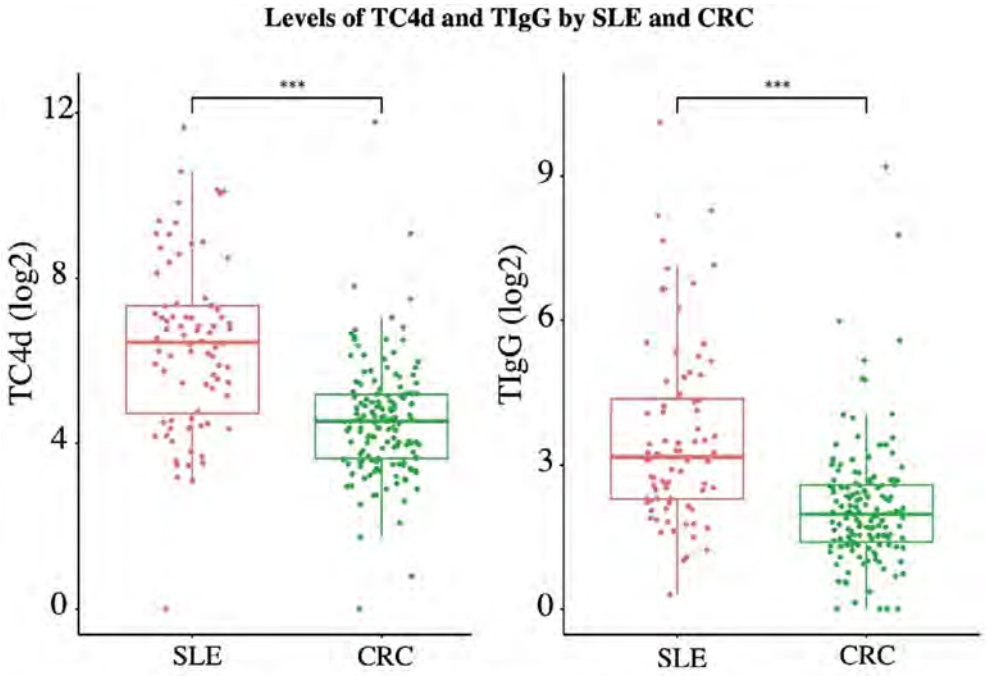

Figure 2. Blood level comparisons of TC4d and TIgG between SLE and ORD samples. The figure presents the log2 blood levels of TC4d and TIgG in SLE and ORD samples. Whisker plots depict the interquartile range, median, minimum, and maximum for each group. Outliers, where present, are represented as individual points beyond the whiskers. A significant difference between groups is indicated by ***$P<$ 0.0001 (Wilcoxon test).

similar in CV models, the sensitivity for SLE in both 10-CV and HO partitions were significantly higher for TIgG, TIgM, and TC4d compared to conventional biomarkers (Figure 1 B, C). Comparing median blood levels of TC4d and TIgG confirmed a statistically significant difference between SLE and CRC ($P<$ 0.0001) (Figure 2), further highlighting their intrinsic discriminatory power.

Conclusion: The study demonstrates the potential of TIgG, TIgM, and TC4d as sensitive and specific biomarkers for the diagnosis of SLE with improved diagnostic performance relative to conventional biomarkers. These findings suggest an opportunity for improved diagnostic accuracy that could yield timely treatment initiation and improved patient outcomes in SLE. However, further studies are needed to validate the results among larger, more diverse patient cohorts and to determine how T cell antibodies and TC4d biomarkers may improve upon existing integrated diagnostic biomarker solutions. Future efforts will explore the potential of T-Cell biomarkers to predict disease progression and as surrogates of treatment response.

Disclosure: A. Concoff: Exagen, 3, 4, 12, Shareholder, Pacira Biosciences, Inc., 2, United Rheumatology, 4; **V. Kyttaris**: AbbVie/Abbott, 5, AstraZeneca, 2, Aurinia, 1, EMD Serono, 5, Exagen, 2, 5, Fresenius Kabi, 1, Horizon Pharmaceuticals, 1, Novartis, 5, Scipher, 1, Takeda, 5, Vertex, 2; **V. Sandhu**: Exagen, 2, 5; **T. O'Malley**: Exagen, 3, 11, 12, Shareholder; **G. Casaburi**: Exagen Inc., 3; **S. Kumar**: Exagen, Inc., 3; **C. Liu**: Exagen Diagnostics, 9, 10; **S. Manzi**: AbbVie, 5, Allegheny Singer Research Institute, 10, AstraZeneca, 2, 5, Exagen Diagnostics, Inc, 2, 9, 10, GSK, 2, 5, Lilly, 2, Lupus Foundation of America, 4, Novartis, 2, UCB Advisory Board, 2, Univiersity of Pittsburgh, 10; **J. Ahearn**: Exagen Inc, 5, 6, 10.

Abstract Number: 0577

Analysis of Intracytoplasmic Toll - Like Receptors (TLRs) and MyD88 Expression in B Cell Subsets in Patients with Lupus Nephritis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1.

Variable	Active SLE without LN n=5 (31.3%) Median (interquartile range).	Active LN n=11 (68.7%) Median (interquartile range).
Demographic features		
Age, years	34.8 (21 – 39)	32 (23 – 37.5)
Female, %	5 (100)	10 (90.9)
SLE time since diagnosis, months	6 (2 – 7)	84 (36 – 108)
Clinical features		
SLEDAI – 2K	13.8 (12 – 16)	12 (8 – 14)
Articular, %	4 (80)	3 (27.3)
Constitutional, %	1 (20)	1 (9.1)
Hematological, %	2 (40)	4 (36.4)
Mucocutaneous, %	2 (40)	2 (18.2)
Neuropsychiatric, %	2 (40)	2 (18.2)
Renal, %	0 (0)	11 (100)
Serositis, %	1 (20)	0 (0)
Laboratory features		
Hemoglobin, g/dL	10 (9.8 – 11.4)	12.8 (11.5 – 13.5)
Leucocytes, X 10^3/µL	5.5 (5.5 – 6.8)	6.0 (5.55 – 7.05)
Neutrophils, X 10^3/µL	3.63 (3.58 – 5.17)	5.01 (4.24 – 6.27)
Lymphocyte, X 10^3/µL	1.43 (1.18 – 1.66)	0.69 (0.63 – 1.14)
Platelets, X 10^3/µL	218 (122 – 296)	244 (204 - 372)
Creatinine, mg/dL	0.43 (0.42 – 0.52)	0.76 (0.65 – 1-14)
Glomerular filtration rate, ml/min/1.73m^2	127 (107 – 144)	92 (67.5 - 115)
Urine protein/creatinine ratio, g/24hrs	0.338 (0.252 – 0.418)	4.45 (3.46 – 6.35)
C – reactive protein, mg/dL	0.99 (0.36 – 1.45)	0.32 (0.13 – 0.83)
Globulins, g/dL	3.2 (3.12 – 3.63)	2.52 (2.43 – 2.73)
Anti – Sm	112.3 (6.6 – 114.5)	222.1 (118.6 – 325.6)
Anti – DNAdc, UI/mL	848.4 (24.5 – 1187.3)	43.6 (15..8 – 600.2)
Anti – nucleosomes, U/mL	1703 (290.1 – 1606.2)	464.8 (64.45 – 707.25)
C 3, mg/dL	82 (35 – 89)	76 (55.5 – 103.5)
C 4, mg/dL	8 (8 – 15)	10 (8 – 30.5)
Histologic features		
Renal biopsy	0 (0)	9 (81.2)
LN class III	-	2/9 (22.2)
LN class IV	-	2/9 (22.2)
LN class III + V	-	1/9 (11.1)
LN class IV + V	-	4/9 (44.4)
Activity index	-	2 (2 – 3)
Chronicity index	-	6 (5 – 7)

Demographic, clinical, laboratory and histologic features. Data are expressed as number (percentage) or median (interquartile range).

Background/Purpose: Intrinsic signaling of intracytoplasmic TLRs (7 and 9) and MyD88 in B cells (BC) plays an important role in the development and pathogenesis of Systemic Lupus Erythematosus (SLE). Different genetic polymorphisms of TLR7 and TLR9 have been associated with the development of lupus nephritis (LN). In patients with SLE there is a higher expression of TLRs 7, 9 and MyD88 in their peripheral blood mononuclear cells (PBMCs) compared to healthy subjects. There is scarce information about the expression of TLR7, 9 and MyD88 in B cell subsets in patients with LN.

We aimed to analyze the expression of intracytoplasmic TLRs (7 and 9) and MyD88 in different subsets of BC from patients with lupus nephritis.

Methods: We included adult patients who fulfilled the ACR/SLICC 2012 classification criteria for SLE. They were stratified in 2 groups: those who had active LN (cases) proven by renal biopsy (LN class III/IV +/- V) or laboratory parameters (decreased filtration rate, proteinuria >500mg/24 hours or active urinary sediment) and those with active SLE (SLEDAI 2K: ^{3}6) but without renal involvement for the last 5 years (controls). Exclusion criteria included prior treatment with anti CD20 drugs.

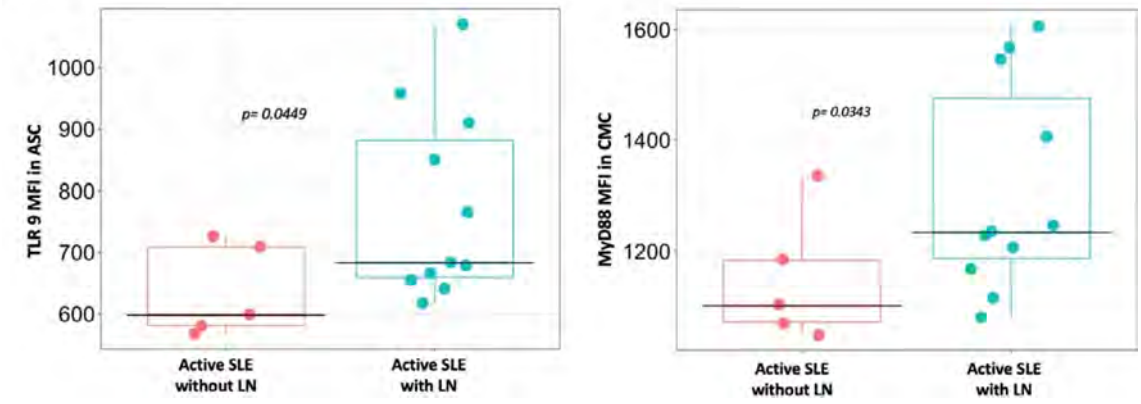
Using multiparametric flow cytometry we measured the expression of TLRs 7, 9 and MyD88 in BC subsets from a peripheral blood sample. The BC subsets evaluated were: age-associated B cells (ABC) [$CD19^{pos}CD21^{neg/lo}$ $CD11c^{hi}$ Tbet ^{pos}], antibody-secreting cells (ASC) [$CD19^{pos}$ $CD27^{hi}$ $CD38^{hi}$], classic memory cells (CMC) [$CD19^{pos}$ $CD27^{pos}$ IgD $^{pos/neg}$], double negative cells (DNC) [$CD27^{neg}$ IgD ^{neg}], naive cells (NC), non classic memory cells (NCMC) [CD27 ^{neg}] and transitional cells (TrC) [CD21 $^{neg/lo}$]. All samples were acquired in a BD LSR Fortessa flow cytometer and data were analyzed by support of the flow jo software.

Table 2.

Variable	Active SLE without LN n=5 (31.3%)	Active LN n=11 (68.7%)	P – value
TLR 9 MFI in ABC, A.U	2317 (2022 – 2344)	1948 (1288 – 2108)	0.0562
MyD88 MFI in ABC, A.U	1208 (1082 –1365)	1312 (1244 – 1654)	0.0902
TLR 9 MFI in ASC, A.U	**598 (581 – 709)**	**683 (660 – 880.5)**	**0.0449**
MyD88 % in ASC, %	0.57 (0.15 – 0.58)	1.33 (0.34 – 1.99)	0.0902
MyD88 MFI in ASC, A.U	1166 (1154 – 1383)	1341 (1256 – 1578)	0.0726
MyD88 MFI in CMC, A.U	**1101 (1071 – 1183)**	**1234 (1186 – 1476)**	**0.0343**
MyD88 MFI in NC, A.U	1091 (1053 – 1094)	1116 (1083 – 1349)	0.0902
TLR 7 % in NCMC, %	1.68 (1.11 – 5.98)	0.66 (0.44 – 1.74)	0.0562
MyD 88 MFI in TrC, A.U	939 (897 – 943)	1061.5 (948.8 – 1281.2)	0.0646

ABC: Age-associated B cells. ASC: Antibody-secreting cells. A.U: Arbitrary units. CMC: Classic memory cells. MFI: Mean fluorescence intensity. NC: Naive cells. TrC: Transitional cells. %: percentage. Data are expressed as median (interquartile range).

Figure 1.



MFI expressed in A.U. Only statistically significant (p=<0.05) data shown.

Absolute cell numbers and percentage of cells positive for TLR7, 9 and MyD88 expression was measured as well as mean fluorescence intensity (MFI) for each molecule in each of the B cell subset assessed. Comparisons were made between groups by using the Mann–Whitney U test.

Results: A total of 16 patients with active SLE were included. Eleven of them (68.7%) were assigned as cases (with LN) and 5 of them (31.3%) as controls (without LN). The majority (93.8%) were women. Their main demographic, clinical and laboratory features are depicted in Table 1.

In general, we observed increased expression of TLR 9 and MyD88 in BC subsets from patients with lupus nephritis than those without renal involvement (Table 2). Particularly, we found enhanced TLR 9 expression (MFI) in antibody-secreting cells (ASC) [active SLE with LN: 683 A.U (660 – 880.5), active SLE without LN: 598 A.U (581 – 709); p=0.0449], as well as higher MyD88 expression (MFI) in classic memory cells (CMC) [active SLE with LN: 1234 A.U (1186 – 1476), active SLE without LN: 1101 A.U (1071 – 1183); p=0.0343]. This information is reflected on the box-plots below (Figure 1).

Conclusion: Our preliminary data suggests that patients with lupus nephritis are characterized by enhanced expression of TLR 9 and MyD88 in specific B cell subsets, particularly of the effector humoral compartment, which might be involved in the pathogenesis of renal damage in SLE.

Disclosure: M. Loeza-Uribe: None; **M. Espinoza-Carranza**: None; **Y. Reyna-Juárez**: None; **B. Alcalá-Carmona**: None; **N. Mejía-Domínguez**: None; **G. Juárez-Vega**: None; **J. Maravillas-Montero**: None; **K. Santana-de Anda**: None; **J. Torres-Ruiz**: None; **D. Gómez-Martín**: None.

Abstract Number: 0578

Prospective Observational Study of Microvascular C5b-9 Deposition in Non-lesional Skin in Systemic Lupus Erythematosus Patients and Its Correlation with Active Lupus Nephritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Tissue damage in LN is mediated by immune complex activation of the classic complement pathway (PMID 23929771). In a study of LN, renal C5b-9 deposition was more frequent in nonresponders (45.5%) than responders (13%) (PMID 34996855). Additionally, complement mediated upregulation of endothelial cell adhesion molecules is seen in the dermal blood vessels of nonlesional skin (NLS) from patients with active SLE (PMID 9336415). In diseases with systemic complement activation (SCA), such as atypical hemolytic uremic syndrome, extensive C5b-9 deposition is seen in NLS (PMID 25893747). This supports hypothesis that NLS C5b-9 deposition is a biomarker for disease activity and evidence of SCA in LN

Figure 1. Positive Immunohistochemical C5b-9 staining in non-lesional skin biopsy of patient with active LN.

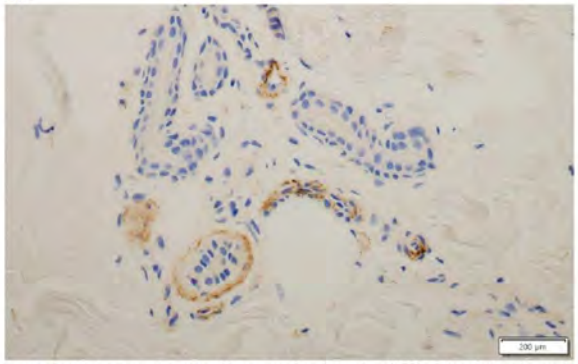

Image demonstrates extensive fine granular deposits of C5b-9 involving the endoluminal aspect of the microvasculature, specifically capillaries and venules Evidence of systemic complement pathway activation is based on counting the number of microvessels encompassing capillaries, venules, arterioles and small arteries showing endothelial and subendothelial deposition of C5b-9.

Table 1. Patient demographics and disease characteristics.

	C5b-9 positive (n=6)	C5b-9 negative (n=10)	P-value
Female	4(66.7)	8 (80)	0.60
Age, Year	32.8(9.2)	40.5(11.9)	0.15
White	0	2(20)	0.50
Black	0	4 (40)	0.23
Hispanic	3 (50)	2(20)	0.30
Asian	2(33)	0	0.50
Other	1(16.7)	2(20)	0.30
ISN/RPS LN Class *a*			0.58
III	3 (50)	2(20)	
IV	2(33)	2(20)	
III/V	0	1(10)	
IV/V	1(16.7)	2(20)	
V	0	2(20)	
Disease Duration, year	4.83(3.31)	14.66(12.56)	0.82
SELENA SLEDAI	12.6(6.6)	7.1(7.68)	0.16
Serologically Active	6 (100)	7 (70)	0.25
Hypocomplementemia	3 (50)	6(60)	0.59
dsDNA elevated	6 (100)	6(60)	0.20
Active LN	5 (83)	3(30)	0.04
NIH Activity Index *b*	7.83(2.71)	8.14 (5.98)	0.91
NIH Chronicity Index *b*	3.33(2.4)	3.29(1.97)	0.97
IFTA (%) *b*	20.41(11.22)	18.57(14.35)	0.80
Tubular reticular inclusions *c*	2 (33)	5(50)	0.77
Laboratory Tests			
Albumin g/dL	2.87(0.89)	3.46(0.8)	0.19
eGFR ml/min/1.73m^2	82.3(35.15)	82.3(37.2)	0.997
adjusted dsDNA*	6.38(3.74)	9.225(18.58)	0.72
C3, mg/dL	79.67(34.98)	78.8(33.2)	0.96
C4, mg/dL	18.3(9.8)	17.2(7.3)	0.81
Urine Studies *d*			
wbc >5/hpf	4 (66.7)	6(60)	0.79
rbc>5/hpf	4 (66.7)	3(30)	0.30
uPCR	4.92(3.33)	1.189(1.07)	0.007

Data are mean (SD) or n (%).
P values are evaluated using SPSS with t tests or Chi Square tests of independence. IFTA=Interstitial fibrosis tubular atrophy. ISN/RPS=International Society of Nephrology and Renal Pathology Society. NIH=National Institute of Health. SELENA SLEDAI=Safety of Estrogens in Systemic Lupus Erythematous National Assessment SLE Disease Activity Index. *Adjusted dsDNA calculated by dividing value by reference upper limit of normal. *a* one person LN Class missing. *b* 3 people without light microscopy details available. *c* 5 people with electron microscopy not available. *d* one person unable to provide urine due to being anuric.

Table 2. Sensitivity and specificity of significant microvascular C5b-9(i.e. 10 or more positive staining vessels) in nonlesional skin biopsy for active LN compared to traditional biomarkers of LN disease activity.

	Sensitivity (%)	Specificity (%)
Significant levels of microvascular C5b-9 Deposition(i.e. 10 or more positive vessels)	62.5	87.5
Elevated dsDNA	100	42.8
Hypocomplementemia	75	57.1
Pyuria	87.5	62.5
Hematuria	87.5	100
uPCR >0.5	100	57.1

Hematuria greater than 5 rbc/hpf. Pyuria greater than 5 wbc/hpf. Hypocomplementemia and dsDNA determined by testing laboratory's reference values.

Methods: Sixteen LN patients without TMHA consented to 4 mm NLS deltoid biopsies, were ≥18 years of age, met ACR SLE classification criteria, and a history of biopsy proven LN or undergoing first clinically indicated renal biopsy. In those undergoing renal biopsy, skin biopsy was performed within 7 days. Formalin fixed paraffin imbedded skin samples were stained for C5b-9 via diaminobenzidine technique and reviewed by dermatopathologist experienced in assessing microvascular C5b-9(PMID 33058948); she was blinded to clinical history. Classification as active LN required an activity index (AI) of ≥1 on biopsy or urine protein creatinine ratio (uPCR) $\geq$ 0.7 and albumin $\leq$ 3.7 g/dL. Inactive LN required AI of 0 or a uPCR ≤0.7, albumin ≥3.7 g/dL and no escalation of care by treating physician. Clinical, demographic, and lab parameters were compared between individuals based on presence of evidence of SCA as determined by demonstrating ≥ 10 blood vessels with endothelial or subendothelial C5b-9 deposition in NLS(PMID 33058948)

Results: Sixteen patients included: 12 females, mean age 37 years, 4 Black, 2 White, 2 Asian, 5 Hispanic and 3 other with clinical characteristics in Table 1. Of the 16 patients, 8 had active LN and 6(37.5%) were positive for endothelial C5b-9 deposition (Figure 1). Of those with SCA compatible C5b-9 deposition, 5 of 6 (83%) had active LN. Of those without significant C5b-9 deposition, 3 of 10 had active LN. Five of 8 active LN patients and 1 of 8 inactive LN patients demonstrated SCA compatible C5b-9 (p= 0.04). These findings demonstrate that SCA is present in LN and is significantly more common in active disease. Cutaneous evidence of SCA as demonstrated by quantitative C5b-9 assessment in microvessels has greater specificity, 87.5%, for active LN than pyuria, low complements, elevated dsDNA, and proteinuria (Table 2). uPCR was significantly higher in LN patients with C5b-9 deposition (4.92 vs 1.19; p =0.007). C5b-9 deposition was not associated with a higher AI, interstitial fibrosis, dsDNA, or lower complements (Table 2)

Conclusion: This is the first study to demonstrate evidence in NLS of levels of microvascular C5b-9 indicative of SCA in LN. C5b-9 deposition indicative of SCA is statistically more common and demonstrated greater specificity than historical biomarkers in active LN. Findings support a potential role for microvascular C5b-9 assessment in NLS as biomarker for LN activity. Long term follow up needed to assess if NLS evidence of SCA associates with less treatment response or poor outcomes in active LN

Disclosure: M. Anderson: None; **C. Magro**: None; **H. Belmont**: Alexion, 6, Aurinia, 6.

Abstract Number: 0579

Sub-types of Ischemic Stroke in Systemic Lupus Erythematosus,- associations with *STAT4* and *HLA-DRB1* Risk Genotypes

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Ischemic stroke is 2-3 times more common in patients with SLE as compared to the general population, and genetic susceptibility in the *STAT4* and *HLA-DRB1* genes have been reported to contribute to stroke in SLE. But few studies have investigated the distribution of stroke sub-types in SLE, and to our knowledge, none if they are associated with known susceptibility genes. We therefore investigated the distribution of ischemic stroke sub-types, classified according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) system(1), among patients with systemic lupus erythematosus (SLE).

Methods: Among 665 SLE patients fulfilling ACR -97 criteria for SLE, we identified 69 patients with ischemic stroke. Medical charts were retrieved and brain, cardiac and vascular imaging at the time of the first stroke were examined. Classification was performed according to TOAST: large-artery atherosclerosis (LAA), cardioembolism (CE), small-artery occlusion (SAO), stroke of other determined etiology (OC) and stroke of undetermined etiology (UE). Occurrence of the anti-phospholipid syndrome/antibodies (APS/aPL) were documented. Evaluators were blinded to genotypes. General population controls (N=658) and SLE patients free from previous cerebrovascular disease (N= 517) were used as comparators. Genetic susceptibility in the signal transducer and activator of transcription factor 4 (*STAT4*) gene, defined by the single nucleotide polymorphism (SNP) rs10181656(G), and the Human Leukocyte antigen (HLA)-DRB1 alleles were explored.

Table 1

Distribution of ischemic stroke subtypes in patients with SLE according to TOAST classification

Ischemic stroke subtypes	N (%)	Age in years at first event (median, range)
Any ischemic stroke	56 (100%)	52 (17-84)
Large artery artherosclerosis (LAA)	7 (12%)	55 (34-67)
Small arterial occlucion (SAO)	9 (16%)	63 (51-84)
Cardioembolic stroke (CE)	12 (21%)	57 (23-70)
Other determined etiology (OE), all APS	19 (33%)	42 (18-74)**
Undetermined etiology (UE)	9 (16%)	56 (25-73)

**Patients with OE/APS strokes were younger, as compared to all other stroke subtypes, p=0.003

Results: 56/69 patients with ischemic stroke had charts with sufficient information for TOAST classification. Median age was 52 (17-84) years, 91% were female. TOAST classification and age at first stroke is presented in Table 1. All strokes classified as OC were attributed to APS/aPL. Strokes of OE/APS and CE origin were associated with the *STAT4* risk genotype as presented in Table 2 and Figure 1. HLA-DRB1 alleles were not associated with stroke sub-types (data not shown).

Conclusion: The majority (54%) of ischemic strokes among 56 SLE patients were of APS/aPL or CE origin. These two subtypes were associated with genetic susceptibility in the *STAT4* gene. We also noted that patients with APS/aPL associated strokes were younger than other sub-types, median 42 years. *STAT4* genotype could, in addition to antiphospholipid antibodies and echocardiography, add information about stroke risk and help identify patients who will benefit from prophylactic anticoagulation treatment.

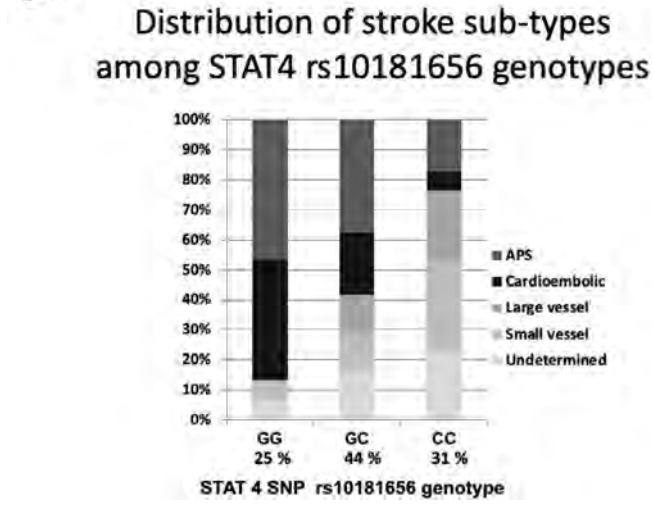
Table 2

Associations of the risk allele, STAT4 single nucleotide polymorphism (SNP) rs10181656 (G), in SLE patients with ischemic stroke overall and stroke subtypes, specified according to the TOAST classification

Stroke type	MAF %	OR (95% CI) vs. Controls N=658 RAF 22.1 %	p-value vs. Controls	OR (95% CI) vs. Non-stroke SLE, N=517 RAF 31.9 %	p-value vs. Non-Stroke SLE
Any ischemic stroke N=56	**33.7**	**3.3 (2.2-4.9)**	**<0.0001**	**2.0 (1.3-2.9)**	**0.0005**
Small artery occlusion N=9	27.8	1.4 (0.5-3.8)	0.57	0.8 (0.3-2.3)	0.71
Large artery occlusion N=7	21.4	1.0 (0.3-3.5)	1.00	0.6 (0.2-2.1)	0.56
Cardioembolic stroke N=12	**70.8**	**8.6 (3.5-20.8)**	**$1.8x10^{-8}$**	**5.1 (2.1-12.5)**	**$6.7x10^{-5}$**
Other determined etiology (all APS) N=19	**60.5**	**5.4 (2.8-10.5)**	**$3.2x10^{-8}$**	**3.2(1.7-6.3)**	**0.0003**
Undetermined etiology N= 9	33.3	1.8 (0.7-4.7)	0.28	1.1 (0.4-2.8)	0.92

RAF = risk allele frequency, N= number of patients, OR= Odds Ratio, CI = Confidence interval

Figure 1



1. Adams HP, Jr., Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke. 1993;24(1):35-41.

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Abstract Number: 0580

Performance of Conventional Cardiovascular Risk Scores in Identifying Subclinical Atherosclerosis in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I
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Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular disease (CVD) is a major cause of mortality in systemic lupus erythematosus (SLE). Role of conventional risk scores which predict cardiovascular events, to detect subclinical atherosclerosis in SLE is not established. In this study we assessed the performance of QRESEARCH database risk score-3 (QRISK3), Systemic COronary Risk Evaluation (SCORE), WHO (World Health Organization), Framingham (FRS) and modified Framingham(mFRS) CVD scores in subclinical atherosclerosis and determine clinical associations of the same

Methods: In this single centre cross-sectional analytical study, we enrolled 108 female SLE patients (without CVD) aged 40-60 years and 108 age matched healthy controls. Demography, disease activity, autoantibodies, steroid dose were noted. Subclinical atherosclerosis was defined by presence of either carotid plaque or abnormal carotid intima media thickness (cIMT) on ultrasound. CVD risk scores (QRISK3, SCORE, WHO, FRS and mFRS) were assessed. Agreement between scores was determined using kappa coefficient

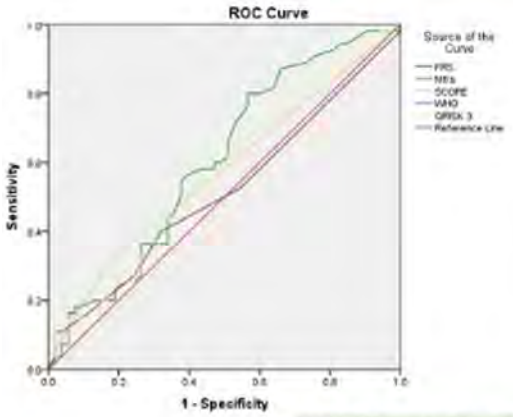
Table 1: Comparison of disease parameters between SLE patients with and without subclinical atherosclerosis

Variable	SLE with subclinical atherosclerosis (n=55)	SLE without subclinical atherosclerosis (n=53)	p value
Age in years (mean± SD)	46.8± 6.6	45±5.2	0.39
Body mass index, (mean± SD)	26.5±5.1	26.3 ±4.7	0.59
Diabetes, n (%)	12(21.8)	10(18.9)	0.7
Hypertension, n (%)	14(25.5)	14(26.4)	0.9
Age at onset of first SLE symptoms, (mean± SD)	39± 9.45	37.9± 7.3	0.32
Disease duration in months (median, IQR)	84(81)	84(72)	0.88
Treatment duration in months (median, IQR)	72(93)	72(78)	0.65
Clinical SLEDAI (median, IQR)	0(0-8)	0(0-8)	0.59
SLEDAI>6, n (%)	5(9.1)	3(5.7)	0.5
SLICC-ACR damage index (median, IQR)	0(0-3)	0(0-2)	0.37
Renal involvement ever, n (%)	**24(43.6)**	**37(69.8)**	**0.006**
CNS involvement ever, n (%)	9(16.4)	5(9.4)	0.28
Any thrombotic manifestation, n (%)	3(5.5)	2(3.8)	0.67
Cumulative steroid dose mg (mean± SD)	14273± 11088	13360 ±10330	0.8
Anticardiolipin IgG antibody, n (%)	8(14.5)	3(5.7)	0.13
Anticardiolipin IgM antibody, n (%)	2(3.6)	5(9.4)	0.2
Anti Beta2 GPI IgG antibody, n (%)	7(12.7)	8(15.1)	0.69
Anti Beta2 GPI IgM antibody, n (%)	7(12.7)	5(9.4)	0.6
Lupus anticoagulant, n (%)	8(14.5)	5(9.4)	0.46
Any antiphospholipid antibodies (aPL) positive n (%)	22(40)	16(30.2)	0.28
Triple positive aPLs, n (%)	**3(5.5)**	**0**	**0.04**

Results: Mean age of patients was 46±6 years, median duration of SLE was 72(93)months, median SLEDAI 0(0-8) and SLICC-ACR damage index was 0 (0-3) (Table 1).Subclinical atherosclerosis was present in 55 (51%) SLE [abnormal cIMT-44(41%) and plaque- 17(16%)] and in 52 (48%) controls [abnormal cIMT-46(42%) and plaque 12(11%)].Mean cIMT was comparable (0.62 ±0.2 cm) in cases and controls. All CVD risk scores had low sensitivity but good specificity to identify subclinical atherosclerosis in patients and controls (Table 2). Area under the curve (AUC) of the receiver operating characteristic curve (ROC), with subclinical atherosclerosis as outcome, showed that all scores had poor discriminatory capacity (Fig 1). In SLE, WHO and FRS had moderate agreement (kappa coefficient k 0.53), QRISK3 and mFRS had substantial agreement (k 0.65) with subclinical atherosclerosis, whereas in controls with FRS and QRISK3, and SCORE and WHO had substantial agreement (k 0.66 and 0.7 respectively) (Table 3). Proportion of patients having triple positive antiphospholipid antibodies were significantly higher in SLE with subclinical atherosclerosis than without (5.5% vs 0, p=0.04). Renal involvement was significantly less in SLE with subclinical atherosclerosis than without (43.6% vs 69.8%, p=0.006)

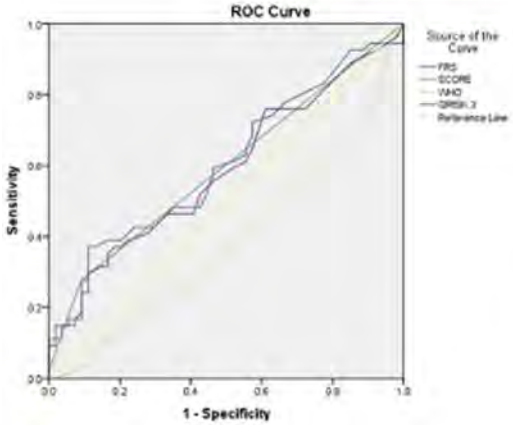
Conclusion: Prevalence of subclinical atherosclerosis was comparable in SLE and controls (51% vs 48%), though carotid plaques were significantly more prevalent in SLE (17% vs 11%). Sensitivity of conventional CVD scores in detecting subclinical atherosclerosis in SLE was poor. Hence, until further scores are validated, screening for subclinical atherosclerosis using carotid ultrasound should remain gold standard

ROC Curves for CVD scores in cases



Area Under the Curve					
				Asymptotic 95% Confidence Interval	
Test Result Variable(s)	Area	Std. Error	Asymptotic Sig.	Lower Bound	Upper Bound
FRS	.604	.055	.063	.496	.711
Mfrs	.604	.055	.063	.496	.711
SCORE	.571	.055	.201	.463	.679
WHO	.514	.056	.808	.404	.623
QRISK 3	.567	.055	.231	.459	.675

ROC Curves for CVD scores in controls



Area Under the Curve					
				Asymptotic 95% Confidence Interval	
Test Result Variable(s)	Area	Std. Error	Asymptotic Sig.	Lower Bound	Upper Bound
FRS	.603	.055	.064	.496	.710
SCORE	.594	.055	.093	.486	.701
WHO	.384	.054	.038	.278	.490
QRISK 3	.586	.055	.122	.478	.694

Figure 1: ROC curves for CVD scores in SLE cases and controls

Table 2: Sensitivity, Specificity, Positive predicitve value, and Negative predictive value of CVD risk scores in identifying subclinical atherosclerosis in SLE and controls Table 3: Agreement between the CVD risk scores measured with the Kappa coefficient

Table 2:

CVD Risk Scores	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Kappa coefficient*
	Systemic Lupus erythematosus				
SCORE	0	100	0	49	0
WHO	3	98	67	51	0.17
QRISK 3	33	74	56	51	0.06
FRS	9	94	63	50	0.03
mFRS	36	74	59	53	0.1
	Controls				
SCORE	1	100	100	52	0.017
WHO	3	100	100	53	0.03
QRISK3	3	98	83	54	0.07
FRS	15	96	80	55	0.1

*Agreement with presence of subclinical atherosclerosis

Table 3:

CVD Risk Scores	Systemic Lupus Erythematosus	Controls
SCORE AND WHO	0	0.66
SCORE AND QRISK3	0	0.3
QRISK 3 AND WHO	0.14	0.55
QRISK 3 AND FRS	0.32	0.7
SCORE AND FRS	0	0.2
WHO AND FRS	0.53	0.36
QRISK 3 AND mFRS	0.65	-
SCORE AND mFRS	0	-
WHO AND mFRS	0.12	-

Disclosure: G. MS: None; **A. Gopal**: None; **M. Mary Thabah**: None; **C. Mariaselvam**: None; **j. Singh**: None; **C. Kavadichanda**: None.

Abstract Number: 0581

Performance Characteristics of a Novel, Fully Automated Multiplexed Immunoassay Microarray Prototype for the Serological Detection of Eleven IgG Autoantibodies Commonly Found in Connective Tissue Diseases

Daphne Bijlsma, Ewa Lukasik, Michael Hausmann, **Gerber Gomez**, Christine Ginocchio and Emmanuel Moreau, Quotient Suisse SA, Eysins, Switzerland

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Detection of autoantibodies is key for the identification and prognosis of patients with connective tissue diseases (CTD); however, some current testing methods are manual, time-consuming, and fragmented, highlighting the need for the development of new fully automated diagnostic tools. We report the performance characteristics of MosaiQ Aiplex CTD prototype, (Quotient Suisse, Eysins, CH), a new planar microarray (MA) immunoassay designed for use with the fully automated, continuous random access, high throughput MosaiQ system for qualitative serological detection of eleven IgG autoantibodies commonly found in CTD (dsDNA, SS-A 60, TRIM21, SS-B, Sm, Sm/RNP, U1RNP, Jo-1, Scl-70, Centromere B, Ribosomal P).

Methods: Each MA consists of two wells, each enclosing an epoxy-silane functionalized glass chip, framed in a plastic chassis (Figure 1). Antigens probes were printed in duplicate, except in triplicate for dsDNA. One side of the MA was printed, leaving the other side available for future addition of antigens. MA were assembled into magazines and loaded in the MosaiQ 125 instrument and read by the on-board Radio Frequency Identification (RFID) antenna. Key information (i.e., number of MA, lot number, expiry date) is transmitted to the instrument which evaluates the adequacy of resources to execute the selected test order and alerts user when any replacement of reagents is required. MAs are released from the magazine and automatically processed in the system where they undergo sample/buffer/reagent addition and removal to generate a final spot signal for interpretation by the instrument.

Results: A cohort of 123 individual serum samples, of which 20 were obtained from blood donations and the rest from a CTD sample bank, were tested in 6-8 replicates with the investigational device, across 3 instruments and 3 MA lots (except for U1RNP which was tested on two lots) and compared with the results obtained with a CE-marked device. Table 1 shows that across analytes the total positive, negative, and overall percent agreement (PPA, NPA and OPA) respectively, were 82.5% (95% CI 80.7-84.2), 94.6% (95% CI 93.9-95.1), and 91.6% (95% CI 91.1-92.4). Rates of indeterminate and invalid results were 0.3% and 2.1%, respectively.

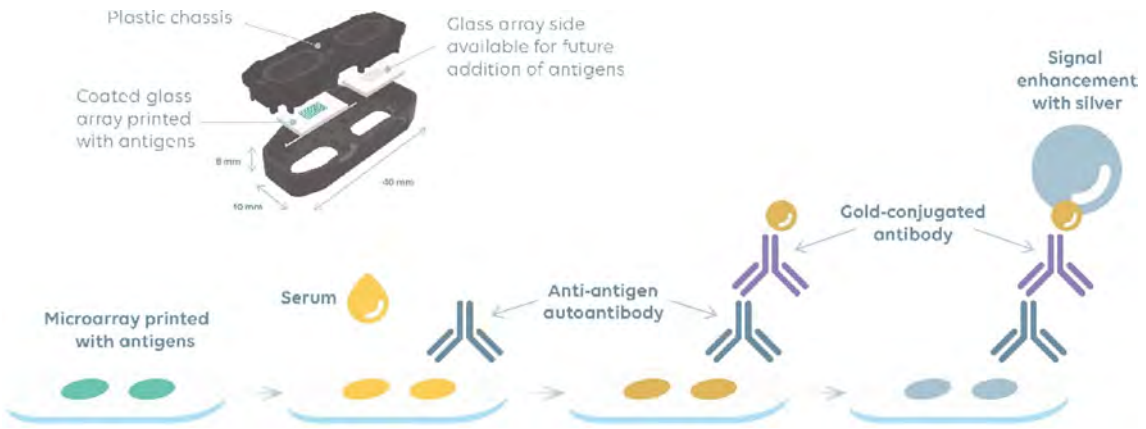


Figure 1. Microarray and assay's reactions

Table 1

Performance of MosaiQ Aiplex CTD Microarray Prototype

Concordant results n	Discordant results n	True Positive n	True Negative n	False Positive n	False Negative n	Indeterminate n (%)	Invalid n (%)	PPA % (95% CI)	NPA % (95% CI)	OPA % (95% CI)
6,608	592	1,506	5,280	304	320	36 (0.3)	158 (2.1)	82.5 (80.7-84.2)	94.6 (93.9-95.1)	91.6 (91.1-92.4)

PPA: positive percent agreement, NPA: negative percent agreement, OPA: overall percent agreement, CI: confidence interval

Conclusion: These preliminary results support the performance of the MosaiQ MA technology platform and Aiplex CTD prototype device for the serological qualitative detection of IgG autoantibodies commonly found in CTD. Clinical studies to further evaluate the performance of the investigational device are ongoing. Future versions of the MA are planned to expand the number of analytes included. The MosaiQ System has the potential to advance CTD testing by increasing laboratory efficiency and productivity by automatically analyzing multiple autoantibodies simultaneously and processing large number of samples per day.

Disclosure: D. Bijlsma: Quotient Suisse SA, 3; **E. Lukasik**: Quotient Suisse SA, 3; **M. Hausmann**: Quotient Suisse SA, 3; **G. Gomez**: Quotient Suisse SA, 3; **C. Ginocchio**: Quotient Suisse SA, 3; **E. Moreau**: Quotient Suisse SA, 3.

Abstract Number: 0582

Evaluation of Anifrolumab Treatment Responses by the Short Form 36 Health Survey Version 2 in SLE: A Post Hoc Analysis of the Placebo-Controlled Phase 3 Long-Term Extension Trial

Vibeke Strand[1], Kenneth Kalunian[2], Barnabas Desta[3], Caroline Seo[4], Gabriel Abreu[5], Raj Tummala[3], Catharina Lindholm[5] and Hussein Al-Mossawi[6], [1]Stanford University, Palo Alto, CA, [2]University of California San Diego, La Jolla, CA, [3]BioPharmaceuticals R&D, AstraZeneca, Gaithersburg, MD, [4]BioPharmaceuticals Medical Evidence, AstraZeneca, Gaithersburg, MD, [5]BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden, [6]BioPharmaceuticals R&D, AstraZeneca, Cambridge, United Kingdom

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is a chronic disease that progressively reduces patients' health-related quality of life.[1] In a post hoc analysis of the TULIP trials, patients with SLE reported improvements in patient-reported outcome measures over 52 weeks.[2] Here, we evaluated the long-term impact of anifrolumab treatment on the Short Form 36 Health Survey version 2 (SF-36v2) in patients receiving standard therapy from the placebo-controlled, phase 3 long-term extension (LTE) trial.[3]

Methods: Adult patients with moderate to severe SLE (1997 ACR criteria) who completed a 52-week TULIP-1 or TULIP-2 trial could enroll in the 3-year LTE study (NCT02794285). Patients included in this analysis were randomized to intravenous anifrolumab 300 mg or placebo every 4 weeks in TULIP-1/-2 and continued in the same treatment group in the LTE, in addition to standard therapy. Proportions of patients classified as responders (defined by positive changes in responses from baseline greater than or equal to the minimum clinically important differences [MCIDs]) in Physical and Mental Component Scores (PCS/MCS) and SF-36v2 individual domains (acute recall) were analyzed for each treatment group using a Cochran–Mantel–Haenszel approach from Weeks 52 to 208. MCIDs were defined as changes from baseline ≥2.5 for PCS and MCS scores and ≥5 for all SF-36v2 domains.[2]Patients with baseline PCS ≤73.01 and MCS ≤67.15 scores and those with each baseline SF-36v2 domain score ≤95 were included in each respective analysis. Domain scores were non-normalized and scaled from worst to best (0–100).

Results: The proportion of PCS responders treated with anifrolumab (n=257; **Figure A**) increased over time from 51% at Week 52 to 56% at Week 208, whereas the proportion of responders decreased in the placebo group (n=112; **Figure B**) from 45% to 38%. The proportion of MCS responders was sustained for patients on anifrolumab with a 1% increase over 3 years, but decreased by 10% for patients on placebo. Proportions of SF-36v2 responders treated with anifrolumab were

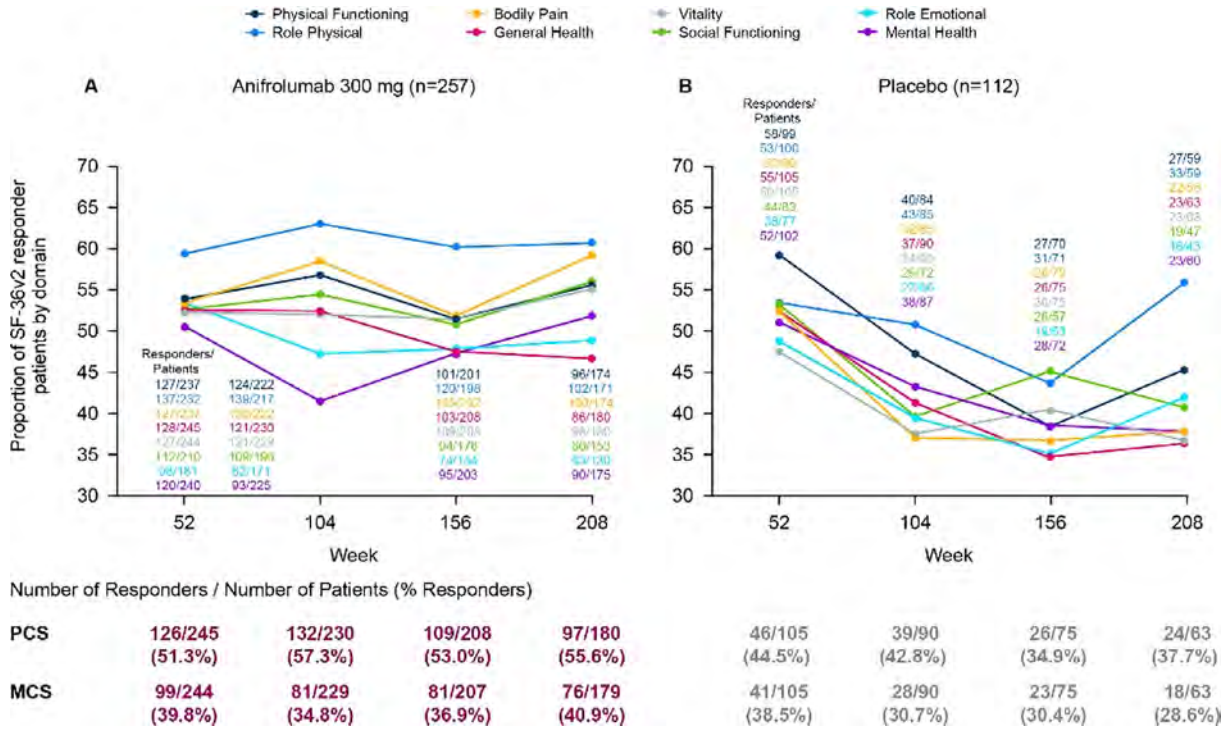


Figure. The Proportions of PCS, MCS and SF-36v2 by Domain Responder Patients by Treatment Group Throughout the TULIP-LTE Study. A) Anifrolumab 300 mg; B) Placebo. CMH, Cochran–Mantel–Haenszel; GC, glucocorticoids; IFN, interferon; LTE, long-term extension; MCS, Mental Component Score; PCS, Physical Component Score; SF-36v2, Short Form 36 Health Survey version 2; TULIP, Treatment of Uncontrolled Lupus via the Interferon Pathway. Percentages of responders were calculated using a stratified CMH approach (stratification factors: SLEDAI-2K score at screening [<10 points vs ≥10 points], Week 0 GC dose [<10 mg/day vs ≥10 mg/day] and type I IFN gene signature test result at screening [high vs low]). Responders were defined as positive changes in responses from baseline greater than or equal to the minimum clinically important differences.

generally maintained throughout the 3-year LTE period, with 47%–61% of patients reporting improved domain scores at Week 208. In all SF-36v2 domains except for General Health and Role Emotional, similar or higher proportions of anifrolumab-treated patients were responders at Week 208 compared with Week 52. In contrast, the proportions of responders receiving placebo decreased over time in all domains except Role Physical, ranging from 36%–56% at Week 208.

Conclusion: Patients with SLE treated with anifrolumab had sustained improvements in PCS, MCS, and most SF-36v2 individual domains over the 3-year LTE period. This was not observed in patients on standard therapy alone, despite the higher dropout rates and survivor bias observed in the placebo group.[3] These results support the long-term benefit of anifrolumab on self-reported, clinically important, health status outcomes across multiple domains.

References:

1. Kaul A, et al. *Nat Rev Dis Primers*.2016;2:16039.
2. Strand V, et al. *Lancet Rheumatol*. 2022;4:e198–e207.
3. Kalunian KC, et al. *Arthritis Rheumatol*. 2023;75:253–65.

Disclosure: V. Strand: AbbVie, 2, Alpine Immune Sciences, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, Bayer, 2, Bioventus, 2, Blackrock, 2, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, Celltrion, 2, Citryll, 2, Ermium, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon, 2, Inmedix, 2, Janssen, 2, Kiniksa, 2, Lilly, 2, Merck, 2, MiMedx, 2, Novartis, 2, Omeros, 2, Pfizer, 2, RAPT, 2, Regeneron, 2, R-Pharm, 2, Samsung, 2, Sandoz, 2, Sanofi, 2, Scipher,

2, Setpoint, 2, Sorrento, 2, Spherix, 2, Urica, 2, 4; **K. Kalunian**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Biogen, 2, Bristol-Myers Squibb, 2, Eli Lilly, 2, Genentech/Roche, 2, GlaxoSmithKline, 2, Janssen, 2, Pfizer, 2; **B. Desta**: AstraZeneca, 3; **C. Seo**: AstraZeneca, 3; **G. Abreu**: AstraZeneca, 3; **R. Tummala**: AstraZeneca, 3; **C. Lindholm**: AstraZeneca, 3; **H. Al-Mossawi**: AstraZeneca, 3.

Abstract Number: 0583

Therapeutic Potential of Imvotamab, a CD20-Targeted Bispecific IgM T Cell Engager, for the Treatment of Refractory Autoimmune Disease Patients

Racquel Domingo-Gonzalez[1], Isabelle Baribaud[2], Miho Oyasu[1], Sivani Pandey[1], Maya Leabman[1], Genevive Hernandez[1], Albert Candia[1], Stephen Carroll[1], Bruce Keyt[1], Maya Kotturi[1], Carrie Brodmerkel[2] and Mary Beth Harler[2], [1]IGM Biosciences, Inc., Mountain View, CA, [2]IGM Biosciences, Inc., Doylestown, PA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: B cell depletion therapy (BCDT) with conventional IgG antibodies (e.g.rituximab) has been used to treat autoimmune (AI) disease for several decades. However, many patients do not achieve long term disease control or remission. Failure of these therapies to fully deplete tissue-resident B cells may result in persistent reservoirs of pathogenic clones that contribute to the ongoing generation of autoantibodies and disease activity. Bispecific IgM antibody T cell engagers (TCEs) are exciting drug candidates with the potential to deplete tissue-resident target cells more effectively through T cell-dependent cellular cytotoxicity (TDCC) and complement-dependent cytotoxicity compared to conventional BCDT mechanisms of action. Imvotamab (IGM-2323) is an engineered high-affinity, high avidity bispecific anti-CD20 IgM antibody TCE that has been evaluated for the treatment of non-Hodgkin's lymphoma (NHL). Given the preliminary clinical profile of imvotamab in NHL, which shows durable response rates and a favorable safety profile, we evaluated its potential to deplete peripheral and tissue-resident B cells in preclinical models of AI disease.

Methods: The ability of imvotamab, rituximab (anti-CD20 IgG1) and a bispecific CD20xCD3 IgG TCE to deplete B cells in the context of AI disease was assessed using an ex vivo TDCC assay. Human peripheral blood mononuclear cells (PBMCs) from healthy donors and patients with AI disease, including SLE, RA, and multiple sclerosis (MS)were utilized. B cell killing, T cell activation status, and cytokine release were assessed. The in vivo activity of a surrogate cynomolgus monkey cross-reactive CD20xCD3 IgM bispecific TCE, IGM-2324, was evaluated for depletion of B cells in peripheral blood and tissues of cynomolgus monkeys. B cell depletion in blood was measured by flow cytometry and in tissues by immunohistochemistry (IHC).

Results: Imvotamab induced killing of B cells in PBMCs from both AI patients and healthy donors. The maximum killing of B cells and half maximal effective concentration (EC50) were comparable between imvotamab, rituximab, and the bispecific CD20xCD3 IgG TCE. Importantly, no hyper-active responses were noted for T cell activation and cytokine release following treatment of PBMCs with imvotamab or the bispecific IgG TCE from healthy volunteers and AI patients. Evaluation of tissue-resident B cells in cynomolgus monkeys following treatment with IGM-2324 resulted in significant reductions in peripheral and tissue-resident B cells. IGM-2324 treatment led to the depletion of not only high and moderate tissue-resident CD20-expressing B cells, but also B cells that expressed low levels of CD20.

Conclusion: Our preclinical data suggests that imvotamab can effectively target and kill peripheral B cells from AI patients. Moreover, a CD20xCD3 IgM bispecific TCE can penetrate tissues and mediate direct killing of CD20-expressing target cells in vivo. Clinical studies with imvotamab in patients with autoimmune diseases, including RA and SLE, are planned to evaluate the therapeutic benefit of this mechanism.

Disclosure: R. Domingo-Gonzalez: IGM Biosciences, 3, 11; **I. Baribaud**: Janssen, 3; **M. Oyasu**: IGM Biosciences, 3, 11, 12, own stocks of IGM Biosciences; **S. Pandey**: IGM Biosciences, 3, 11; **M. Leabman**: IGM Biosciences, 3; **G. Hernandez**: Genentech, 3; **A. Candia**: None; **S. Carroll**: IGM Biosciences, Inc., 3, 8, 11; **B. Keyt**: IGM Biosciences, 3, 4, 8, 10, 11; **M. Kotturi**: IGM Biosciences, Inc., 3, 10, 11; **C. Brodmerkel**: IGM Biosciences, 3, 11; **M. Harler**: IGM Biosciences, 3.

Abstract Number: 0584

Targeting Key Components of SLE Pathogenesis with the Multifaceted Immunomodulatory Properties of Cenerimod, a Selective S1P1 Receptor Modulator

Thomas Hoyler[1], Daniel Strasser[1], Ouali Berkani[2], Peter Cornelisse[1], Mark Murphy[1] and **Marianne Martinic**[1], [1]Idorsia Pharmaceuticals Ltd., Allschwil, Switzerland, [2]IDORSIA, Allschwil, Switzerland

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In SLE, aberrant lymphocyte activation and autoantibody production result in deposition of immune complexes and contribute to tissue damage. Cenerimod, a highly selective $S1P_1$ receptor modulator with a biased signaling, shows potential therapeutic effect in SLE through its immunomodulatory effects on lymphocyte trafficking, inflammation, and autoantigen transport. Preclinical and clinical data suggest that cenerimod may halt the vicious circle of autoimmunity, ultimately preventing organ damage in SLE.

Methods: A murine model of SLE (MRL/lpr mice) and a proof-of-mechanism murine model for antigen transportation were used to evaluate the effects of cenerimod on leukocyte distribution, autoantibody titers, inflammation, and antigen transport, using flow cytometry, ELISA, and histology.[1-3] Leukocytes, autoantibodies, and inflammation biomarkers were further assessed in two phase 2 clinical studies of once-daily cenerimod (0.5, 1, 2, or 4 mg) versus placebo in patients with SLE (NCT02472795 and NCT03742037 [CARE]).[3-5] In the first phase 2 study, patients were treated for 12 weeks. In the CARE study, treatment was for 12 months; patients assigned to cenerimod 4 mg were re-randomized to placebo or cenerimod 2 mg at Month 6.

Results: In rodent disease models, cenerimod reduced the migration of dendritic cells to the draining lymph node, which was accompanied by reduced T cell proliferation and pro-inflammatory cytokine secretion. Furthermore, in the MRL/lpr lupus mouse model, treatment with cenerimod led to significant disease amelioration, evidenced by a reduction of tissue-infiltrating lymphocytes, lower titers of autoantibodies, and reduced levels of inflammatory cytokines. This was associated with reduced signs of pathology in the kidneys, improved kidney function, and increased survival.

In the 12-week phase 2 clinical trial, treatment with cenerimod decreased circulating T and B lymphocytes, decreased autoantibody levels, and reduced secretion of pro-inflammatory IFN-a. These findings were supported in the CARE study, which showed that cenerimod 4 mg improved clinical indices of disease activity and reduced pro-inflammatory cytokines.

Conclusion: Both preclinical and clinical research provide evidence that cenerimod is a promising immunomodulatory drug candidate that addresses three critical aspects of SLE pathogenesis: migration of autoreactive lymphocytes, release of pro-inflammatory cytokines and chemokines, and continuous autoimmune priming. The $S1P_1$ receptor modulator cenerimod may effectively interrupt this pathogenic circle of SLE autoimmunity. The ongoing OPUS Phase 3 program (NCT05648500, NCT05672576) is designed to further investigate the safety and efficacy of cenerimod at a dose of 4 mg for the treatment of SLE in adults.

References

1. Hoyler T et al. Abstract LO-016. LUPUS KCR meeting 2023.
2. Gerossier E et al. Arthritis Res Ther 2021;23(1):289.
3. Strasser DS et al. RMD Open 2020;6(2):e001261.
4. Hermann V et al. Lupus Sci Med 2019;6(1):e000354.
5. Askanase A et al. Arthritis Rheumatol 2022;74(suppl 9):3293–7.

Disclosure: T. Hoyler: Idorsia Pharmaceuticals Ltd, 3, 11; **D. Strasser**: Idorsia Pharmaceuticals Ltd, 3, 11; **O. Berkani**: Idorsia Pharmaceuticals Ltd, 3, 11; **P. Cornelisse**: Idorsia Pharmaceuticals Ltd, 3, 11; **M. Murphy**: Idorsia Pharmaceuticals Ltd, 3, 11; **M. Martinic**: Idorsia Pharmaceuticals Ltd., 3, 11.

Abstract Number: 0585

The Impact of Impaired Vagus Nerve Activity and Transcutaneous Vagus Nerve Stimulation (tVNS) on Arterial Stiffness in Systemic Lupus Erythematosus (SLE)

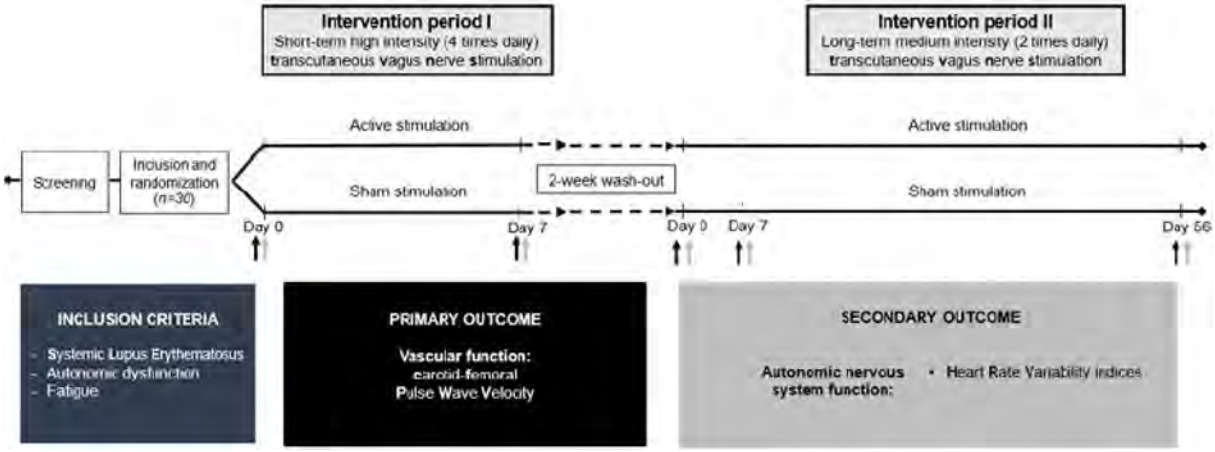
Tobias Schmidt[1], Christina Brock[2], Jesper Fleischer[3], Søren Jacobsen[1] and Amanda Hempel Zinglersen[1], [1]Copenhagen Research Center for Autoimmune Connective Tissue Diseases, Center for Rheumatology and Spine Diseases, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark, [2]Department of Gastroenterology and Hepatology, Aalborg University Hospital and Clinical Institute, Aalborg, Denmark, [3]Steno Diabetes Center Aarhus, Aarhus University Hospital, Aarhus, Denmark

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

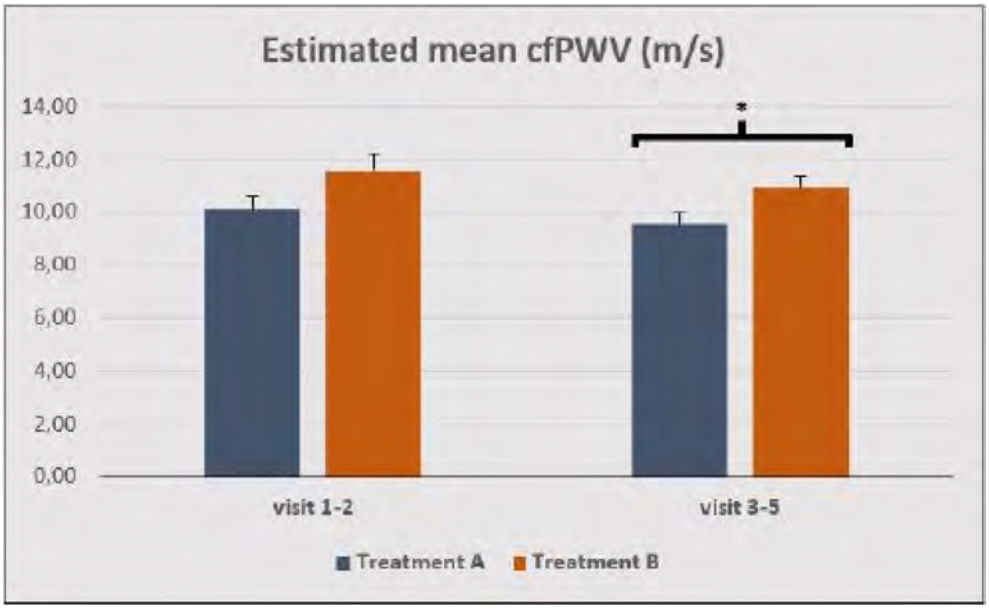
Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic inflammatory autoimmune disease with an increased risk of atherosclerosis. The development of atherosclerosis in SLE cannot be fully explained by traditional risk factors but may be partially due to chronic inflammation. SLE is associated with abnormal autonomic function i.e., decreased parasympathetic vagus nerve activity. Impaired vagal activity may impact disease severity through an impaired vagally mediated inflammatory reflex, which may lead to increased inflammation, and possibly to stiffening of conduit arteries

i.e., increased arterial stiffness. In SLE patients, we aim to determine whether impaired vagus nerve activity is associated with arterial stiffness and whether the latter can be diminished by increasing vagal activity through transcutaneous vagus nerve stimulation (tVNS).

Methods: This is a blinded sub-study (n=30) of an ongoing double-blinded, randomized, sham-controlled study investigating the effects of tVNS on SLE (n=58). In the first intervention period, patients were randomized to self-administration of either active or sham bilateral tVNS at the cervical vagus nerve for 120 seconds 4 times daily for seven days. After a stimulation-free two-week wash-out period, tVNS was self-administered for 120 seconds 2 times daily for eight weeks in the second intervention period. Pulse wave velocity (PWV), which is a gold standard method for non-invasive arterial stiffness assessment, pulse wave velocity (PWV), was recorded at two arterial sites, i.e., carotid-femoral PWV (cfPWV). Autonomic function was assessed using a VagusTM device that measured 5-min resting heart rate variability. Data was analyzed using a linear mixed model in SPSS.



Overview of the systemic lupus erythematosus (SLE)-vagus nerve stimulation (VNS) study.



Estimated mean (±SE in error bars) carotid-femoral pulse wave velocity (cfPWV) between groups during visits 1-2 and visits 3-5 (n=30). The mean difference in cfPWV between groups is based on estimated means. The groups displayed a mean difference in cfPWV during visits 3-5 (p=0.04).

Pairwise comparisons of differences between groups at visit 3-5 (n = 30)

Group	Variable	Mean diff.	[95% CI]	P-value
A vs. **B**	*cfPWV, m/s*	-1,38	[-2,72 ; -0,05]	0,04 *
	HRV indices			
A vs. **B**	*SDNN, ms*	13,33	[4,59 ; 22,06]	0,003 **
A vs. **B**	*RMSSD, ms*	13,21	[4,71 ; 21,72]	0,003 **
A vs. **B**	*LF, ms²*	83,67	[-123,98 ; 291,32]	0,4
A vs. **B**	*HF, ms²*	153,22	[56,35 ; 250,09]	0,002 **
A vs. **B**	*TP, ms²*	364,05	[19,91 ; 708,20]	0,04 *
A vs. **B**	*LF/HF ratio*	0,07	[-1,53 ; 1,39]	0,9

Mean difference (Mean diff.) between groups is based on estimated marginal means.
Mean diff. is illustrated with a negative value if overall mean of A is smaller than B.
** Mean diff. values between groups are considered significant (p<0.05).*
*** Mean diff. values between groups are considered significant (p<0.01).*

Pairwise comparisons of mean differences between groups during visits 3-5 (n=30): cfPWV, carotid-femoral pulse wave velocity; HF, high-frequency power; HRV, heart rate variability; LF, low-frequency power; RMSSD, root mean square of successive differences between normal heartbeats; SDNN, SD of all NN intervals; TP, total power.

Results: The groups were divided into A or B. However, the main study was still blinded at the time of this thesis, thus Group A was selected as the active treatment group for purpose of a meaningful discussion. Group-A (n=17) and group-B (n=13) were similar in age (51.6±14.1, 46.6±17.6 years), sex (94.1%, 86.4% females), and in the prevalence of hypertension and hypercholesterolemia. In unadjusted analyses, higher baseline cfPWV correlated with lower degrees of autonomic function in all but one measure ($p< 0.05$). During the second and longer intervention period (8 weeks), Group-A displayed a lower cfPWV, i.e., less stiff arteries, than Group B (mean difference 1.38 m/s, p=0.04).

Conclusion: In SLE, autonomic dysfunction was associated with arterial stiffness at baseline. Arterial stiffness was reduced with Treatment A, indicating a reduced the risk of vascular disease with vagus nerve stimulation in SLE. However, this needs to be verified after unblinding the main study.

Disclosure: T. Schmidt: None; **C. Brock**: None; **J. Fleischer**: None; **S. Jacobsen**: Bristol-Myers Squibb(BMS), 5; **A. Zinglersen**: None.

Abstract Number: 0586

Therapeutic Drug Monitoring of Azathioprine and Tacrolimus in SLE Pregnancies: Preliminary Results from the LEGACY Cohort

Reem Farhat[1], Arielle Mendel[2], Isabelle Malhamé[3], Joo Young (Esther) Lee[4], Luisa Ciofani[5], Sasha Bernatsky[6] and Evelyne Vinet[2], [1]McGill University, Montréal, QC, Canada, [2]McGill University Health Centre, Montréal, QC, Canada, [3]McGill University Health Centre, Montreal, QC, Canada, [4]McGill University, Montreal, QC, Canada, [5]McGill University Health Center, Montreal, QC, Canada, [6]Research Institute of the McGill University Health Centre, Montreal, QC, Canada

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Pregnant SLE women still face an unacceptably high risk of maternal and fetal morbidity, particularly when their disease is active. How to personalize SLE therapies to optimize pregnancy outcomes remains unknown. Though guidelines strongly recommend azathioprine (AZA) and tacrolimus (TAC) in specific SLE pregnancy scenarios, evidence to guide drug monitoring in this context is non-existent. Our aim is to evaluate the characteristics of SLE pregnancies according to the levels of AZA metabolites and TAC trough levels at the first pregnancy (baseline) visit.

Methods: LEGACY is a prospective cohort enrolling unselected SLE pregnancies ≤16 6/7 gestational weeks at 7 Systemic Lupus International Collaborating Clinics. We record demographics, disease activity, and drugs. In addition, whole blood samples are collected at baseline to determine AZA metabolites (e.g., erythrocyte-free 6-thioguanine, 6-TG) and trough TAC levels if applicable. The present study included Montreal LEGACY participants prescribed either AZA or TAC ≥3 months prior to their first pregnancy visit. We characterized AZA metabolite and TAC levels as continuous and categorical variables (i.e., non-adherent, sub-therapeutic, therapeutic, and supra-therapeutic, using established cut-offs in nonpregnant populations). We defined patients as non-adherent if they had undetectable or barely detectable levels despite appropriate dosing.

Results: Of 70 LEGACY pregnancies enrolled in Montreal, 23 (33%) and 6 (9%) were prescribed AZA and TAC, respectively. Among those prescribed AZA, only 9% had therapeutic levels, while 91% were subtherapeutic or non-adherent (Table 1). Compared to those with therapeutic levels, pregnancies with subtherapeutic or non-adherent AZA levels were more likely to occur in women of non-Caucasian ethnicity/race, on steroids, with longer SLE duration, and with prior lupus nephritis (Table 2). Among those prescribed TAC, 50% (3/6) had therapeutic levels, while 33% (2/6) and 17% (1/6) were subtherapeutic and supra-therapeutic, respectively. No patients on TAC were identified as non-adherent. Less than half (43%) of pregnancies non-adherent to AZA were in Lupus Low Disease Activity State (LLDAS) at baseline. Of the pregnancies with subtherapeutic TAC levels, 50% (1/2) were not in LLDAS, while all (4/4) pregnancies with therapeutic or supra-therapeutic TAC levels were in LLDAS at baseline.

Table 1. Number of pregnancies and mean drug dose at baseline visit according to AZA metabolite (6-TG) and TAC trough levels

		Non-adherent	Sub-therapeutic	Therapeutic	Supra- therapeutic
AZA (n=23)	**Pregnancies**, n (%)	7 (30)	14 (61)	2 (9)	-
	AZA dose in mg/kg, mean ± SD	2.5 ± 0.5	1.9 ± 0.5	2.0 ± 0.2	-
TAC (n=6)	**Pregnancies**, n (%)	-	2 (33)	3 (50)	1 (17)
	TAC dose in mg/kg, mean ± SD	-	0.04 ± 0.02	0.04 ± 0.02	0.03 ± 0

Table 2. Baseline maternal characteristics stratified according to AZA metabolite (6-TG) and TAC trough levels

		AZA (n=23)			TAC (n=6)		
		Non-adherent (n=7)	Sub-therapeutic (n=14)	Therapeutic (n=2)	Sub-therapeutic (n=2)	Therapeutic (n=3)	Supra-therapeutic (n=1)
Age in years, mean ± SD		34.0 ± 4.1	33.8 ± 3.9	29.0 ± 0.7	30.3 ± 3.3	31.3 ± 4.1	32.4 ± 0
Race/ Ethnicity, n (%)	Caucasian	1 (14)	4 (29)	2 (100)	2 (100)	2 (67)	1 (100)
	Hispanic	-	-	-	-	1 (33)	-
	Black	2 (29)	3 (21)	-	-	-	-
	Asian	2 (29)	5 (36)	-	-	-	-
	Arabic	1 (14)	-	-	-	-	-
Education in years, mean ± SD		15.7 ± 3.5	16.7 ± 3.1	17.0 ± 1.4	19.0 ± 1.4	14.3 ± 1.5	16.0 ± 0
Disease duration in years, mean ± SD		10.3 ± 6.5	10 ± 6.9	5.3 ± 0.7	9.3 ± 0	4.2 ± 1.1	3.8 ± 0
LLDAS, n (%)		3 (43)	10 (71)	-	1 (50)	3 (100)	1 (100)
Prior or current lupus nephritis, n (%)		5 (71)	5 (36)	-	2 (100)	1 (33)	-
Steroid use, n (%)		2 (29)	1 (7)	-	-	-	-

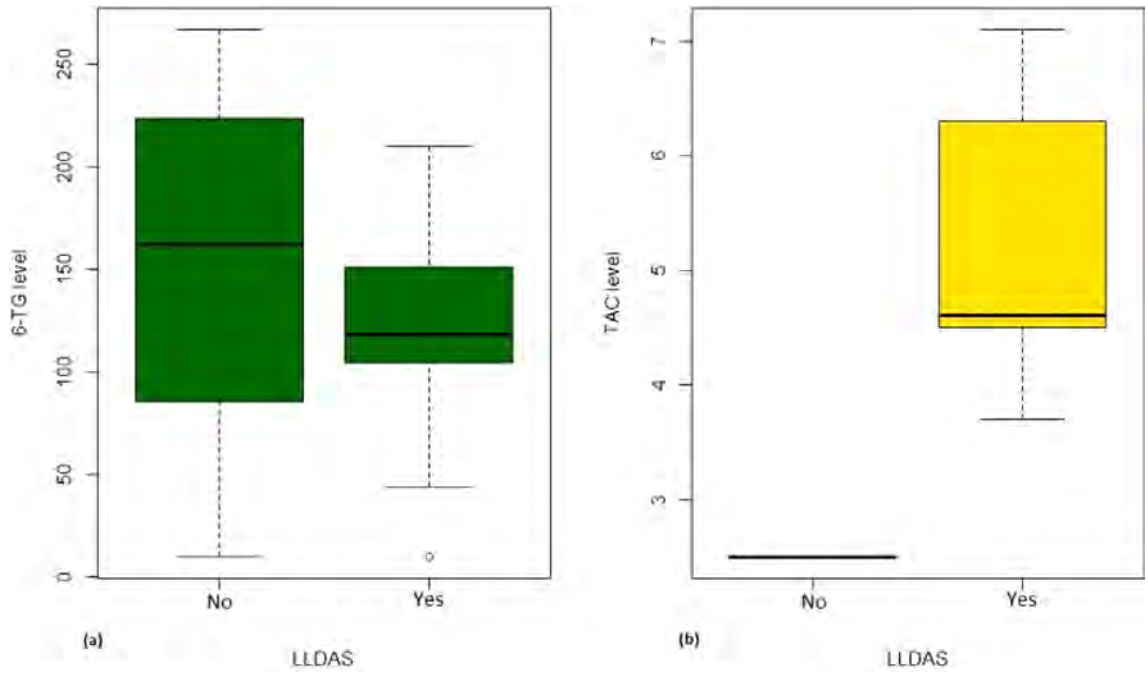


Figure 1. Boxplot of 6-TG levels [pmol/8×108 RBC] (a) and TAC trough levels [ng/ml] (b) according to LLDAS

Conclusion: We observed that most SLE pregnancies prescribed AZA had sub-therapeutic levels, with nearly a third identified as non-adherent. Pregnancies with lower AZA and TAC levels may be less likely to achieve LLDAS. Despite low numbers, our preliminary results suggest the value of personalized drug monitoring as a novel approach to precision medicine in pregnant SLE women, that might improve efficacy, safety, and adherence in a high-risk population.

Disclosure: R. Farhat: None; **A. Mendel**: None; **I. Malhamé**: None; **J. Lee**: None; **L. Ciofani**: None; **S. Bernatsky**: None; **E. Vinet**: None.

Abstract Number: 0587

Impact of up to 24 Months Intravenous (IV) Belimumab (BEL) Treatment on Steroid Use and Disease Activity in Patients with SLE in Clinical Practice: Additional Post Hoc Pooled Analysis of Multicountry OBSErve Cohort Data

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The clinical effectiveness of 6-month IV BEL use in SLE has previously been described in a post hoc pooled analysis from six OBSErve cohort studies.[1] Here we present expanded post hoc analysis of eight pooled OBSErve studies investigating the long-term effectiveness of BEL on reducing oral CS (OCS) use and achieving low disease activity (LDA) and remission, which are important treatment targets for SLE to minimize irreversible organ damage.[2,3]

Methods: This was a post hoc pooled analysis (GSK Study 219649) of data from eight OBSErve studies in Argentina, Canada, Germany, USA, Russia, Saudi Arabia, Spain, and Switzerland. Clinician-reported data were captured for adults with SLE at IV BEL initiation (index) and at 6–24 months after index. All studies captured 6 months of data after index, with Argentina and USA data extending up to 24 months after index. Enrollment was 6 months post index for all studies except Argentina and n=284/501 USA patients (pts) who enrolled 12 months after index. The primary objective was to describe the proportion of pts achieving a daily OCS dose ≤10 mg, ≤7.5 mg, ≤5 mg, or 0 mg at 6, 12, 18, or 24 months after index. Secondary objectives included: the proportion of pts who maintained their 6-month post index daily OCS dose threshold over time; and the proportion of pts achieving LDA (modified Lupus Low Disease Activity State; SLEDAI score ≤4 with no worsening of clinical manifestations and OCS dose ≤7.5 mg/day[4]) or remission (modified Definition Of Remission In SLE; SLEDAI score=0 and OCS dose ≤5 mg/day[5]) at 24 months after index.

Results: Data from 959 pts were included. Most pts were from the USA (52.2%), Germany (10.6%), and Argentina (8.4%). At enrollment, the mean age was 41.5 years, 89.5% were female, 64.6% were White (N=878 only); 55.2% had SLE for ≥5 years before enrollment.

At index, median (interquartile range) OCS dose was 10.0 (5.0, 20.0) mg/day; 14.5% were receiving an OCS dose of >20 mg/day and 41.0% >10 mg/day. The proportion of pts receiving OCS dose ≤7.5 mg/day increased from 38.5% at index to 69.4% at 6 months, 80.0% at 12 months, 83.7% at 18 months, and 92.1% at 24 months (data after 6 months for pooled Argentina/USA only; **Figure 1A**). A similar trend was seen among those who were receiving >10 mg/day at index (**-Figure 1B**). Over 87% of pts maintained the same OCS low dose threshold at 12, 18, and 24 months as at 6 months after index (**Figure 2**). At index (N=447), 0.4% of pts were in LDA state and 0.2% in remission. At 24 months, 18.2% and 12.9% achieved LDA and remission, respectively (**Table**).

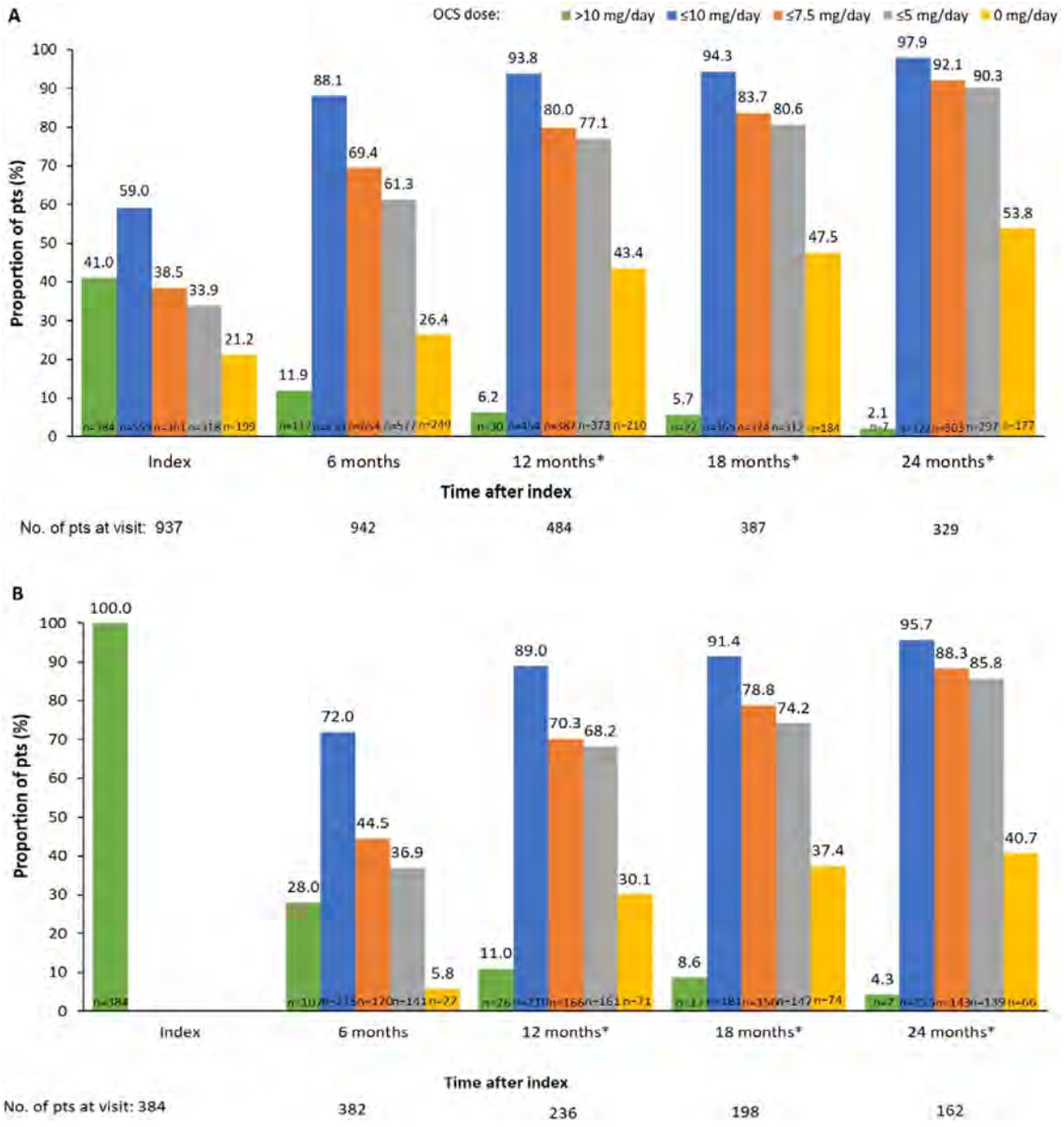

Figure 1. Summary of OCS use at index and 6, 12, 18, and 24 months after index among all pts (A) and patients receiving OCS >10 mg/day at index (B). OCS dose=prednisone equivalent. *Among pooled pts in Argentina and the USA where data were captured beyond 6 months post index.

Conclusion: These data demonstrate a steroid-sparing effect of long-term BEL use, which was evident from 6 months and maintained over 24 months, as well as an improvement of disease activity indices in pts with SLE, further supporting the effectiveness of IV BEL in real-world SLE clinical management.

Funding: GSK **References:**

1 Collins CE et al. Rheumatol Ther 2020;7:949–65
2 Fanouriakis A et al. Ann Rheum Dis 2019;78:736–45
3 Golder V et al. Rheumatol 2020;59:(Suppl5)v19–v28
4 Franklyn K et al. Ann Rheum Dis 2016;75:1615–21
5 van Vollenhoven et al. Lupus Sci Med 2021;8:e000538

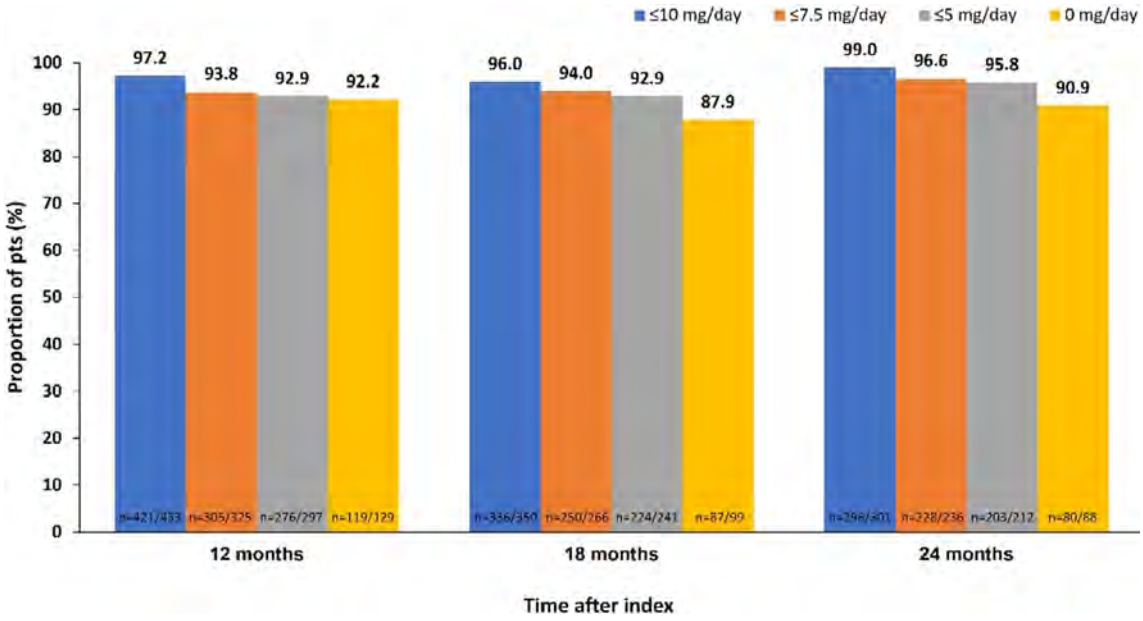

Figure 2. Proportion of pts* maintaining the same threshold of daily OCS dose (≤10 mg, ≤7.5 mg, ≤5 mg, 0 mg) from 6 months after index to 12, 18, and 24 months after index. OCS dose=prednisone equivalent. *Among pooled pts in Argentina and the USA where data were captured beyond 6 months post index.

Table. Proportion of pts with LDA or remission at index and at 24 months after index.

Pts with activity state, n/N (%)	Index	24 months post index
	All countries	*Argentina/USA*
LDA	2/447 (0.4)	18/99 (18.2)
Remission	1/447 (0.2)	13/101 (12.9)

Disclosure: D. Moldaver: GSK, 3, 11; **S. Anderson**: GSK, 3, 11; **M. Bracher**: GSK, 3, 11; **R. Levy**: GSK, 3, 11; **H. Quasny**: GSK, 3, 11; **R. Wood**: Adelphi Real World, 3, GSK, 5; **R. Wild**: Adelphi Real World, 3, GSK, 5; **A. Cusmano**: Adelphi Real World, 3, GSK, 5; **E. Rottier**: Adelphi Real World, 3, GSK, 3, 5.

Abstract Number: 0588

Long Term Safety and Predictors of Serious Infections Among Patients with Systemic Lupus Erythematosus Treated with Rituximab: Audit from a Single Center Biologic Registry

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: SLE – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Rituximab (RTX) is increasingly being employed to treat refractory systemic lupus erythematosus(SLE). Though the drug is effective there is a high risk of adverse events including infections. Most studies have focused on short term(< 1 year) safety, whereas long term follow-up data is sparse. This study was designed to look at the frequency and predictors of infections in patients with SLE receiving RTX who are on long term follow up.

Table 1: Baseline demographic and clinical details of the cohort and comparison of patient groups with and without serious infection

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Variable	Frequency (%) / Median (IQR)			P value
	Overall cohort (n=76)	Major infection (n=16)	No Major infection (n=60)	
Demographic characteristics				
Age (years)	29.0 (23.0 – 36.0)	26.5 (17.25 – 31.0)	29 (24.0 -38.5)	**0.044**
Juvenile onset patients	15 (19.7%)	7 (43.8)	8 (13.3)	**0.012**
Female sex	63 (82.9)	10 (62.5)	53 (88.3)	**0.024**
Socioeconomic status: Lower class Upper class	 43 (56.6) 33 (43.4)	 9 (56.3) 7 (43.8)	 34 (56.7) 26 (43.3)	0.976
Comorbidities				
Diabetes and/or Hypertension	24(31.6)	6 (37.5)	18 (30)	0.629
Hypothyroidism	16(21.1)	3 (18.9)	13 (21.7)	1.000
Chronic kidney disease	2(2.6)	2 (12.5)	0 (0)	**0.041**
Chronic liver disease	1(1.3)	1 (6.3)	0 (0)	0.208
Chronic lung disease	2(2.6)	0 (0)	2 (3.3)	1.000
Cardiac disease	5(6.6)	1 (6.3)	4 (6.7)	1.000
Disease activity and damage indices				
SLEDAI 2K at diagnosis	12(8.0-16.0)	12.5 (8.25 – 15.5)	12.0 (8.0 – 16.0)	0.970
SLEDAI 2K at RTX induction	10.0(7.0-14.0)	11.0 (10.0 – 14.7)	10.0 (6.0 -14.0)	0.116
SLICC ACR DI at RTX induction	1.0(0.0-1.0)	1.0 (1.0– 2.0)	1.0 (0 -1.0)	0.071
Damage present prior to RTX	45(59.2)	13 (81.3)	32 (53.3)	**0.049**
≥ 2 severe flares prior to RTX induction	53(69.7)	10 (62.5)	43 (71.7)	0.539
Prior Immunosuppression				
Standardized steroid dose	290.3 (246.2 – 345.1)	300.1 (259.9 – 374.4)	274.5 (243.4 – 343.0)	0.309
Received 2 or more pulse MPS	21(27.6)	2(12.5)	19(31.7)	0.208
2 or more induction treatments prior to RTX	59(77.6)	14(87.5)	45 (75)	0.896
Cyclophosphamide	63(82.9)	16 (100)	47 (78.3)	**0.034**
Cumulative Cyclophosphamide dose (grams)	6.0 (3.0 – 9.0)	7.2 (6.0 – 9.6)	6.0 (2.5 – 9.0)	**0.049**
Number of IS prior to RTX	3.0 (2.0 – 3.0)	2.5 (2.0 – 3.0)	3.0 (2.0 – 3.0)	0.356
RTX therapy				
Indication for RTX: Lupus nephritis	 52 (68.4)	 14 (87.5)	 38 (63.3)	**0.05**
Total number of RTX (1 gram) infusions	2.0 (2.0 – 4.0)	2.0 (2.0 – 3.5)	3.0 (2.0 -4.0)	0.150
Concurrent treatment with MMF	48(63.2)	13 (81.3)	35(58.3)	0.100
Occurrence of major Infection prior to RTX induction	26(34.2)	8 (50)	18 (30)	0.123
≥ 2 major infections prior to RTX induction	9(11.8)	3 (18.8)	6 (10)	0.383
Vaccination done (Pneumococcal and Influenza)	69(90.8)	13 (81.3)	56 (93.3)	0.152
Cotrimoxazole prophylaxis	72(94.7)	14 (87.5)	58(96.7)	0.189
Low pre-RTX globulin	27(35.5)	5 (31.3)	22(36.7)	0.633
Persistently low or post RTX low globulin	43(56.6)	9 (56.3)	34 (56.7)	0.577
Lymphopenia pre-RTX	26(34.2)	9 (56.3)	17 (28.3)	**0.046**
Persistently low or Post RTX Lymphopenia	14(18.4)	3 (18.8)	11(18.3)	0.934
Non-infectious outcomes				
Major infusion reaction	1(1.3)	1(6.3)	0 (0)	0.208
Minor infusion reaction	2(2.6)	0 (0)	2 (3.3)	1.000
MACE	1(1.3)	0 (0)	1 (1.6)	1.000
Mortality	8(10.5)	7(43.8)	1 (1.7)	0.000

Abbreviations: RTX-Rituximab, MPS-Methyl prednisolone, IS-Immunosuppressants, MMF-Mycophenolate mofetil, MACE-Major adverse cardiac event

Methods: This was a single-centre retrospective observational study. Data of SLE patients who received at least 1 gram of RTX were abstracted from the case record forms of the department's biologic registry. Patients were followed up at 3-6 monthly intervals and disease activity, infectious and non-infectious adverse events during or after RTX induction were documented. For those patients who did not have follow up for ≥ 1 year, the last available date of follow-up was considered for this study. Demographic, baseline organ involvement, laboratory data, treatment details were collected. Glucocorticoid

Table 2: Infectious complications and outcomes of patients with SLE who received RTX

Table 2: Infectious complications and outcomes of patients with SLE who received RTX

Infection related outcomes	**n=76 (%)**
Occurrence of serious infections	16 (21.05)
Occurrence of non-serious infections	33 (38.8)
Number of patients with two or more serious infections	6 (7.89)
Median time to first serious infection after induction dose [months (IQR)]	13 (5.0-16.5)
Serious infection occurring within the first year after RTX (n=16)	7 of 16 (43.75)
Site of infections	**n=59 (%)**
Respiratory tract	18 (30.5)
Skin and soft tissue	12 (20.3)
Musculoskeletal (septic arthritis, tubercular arthritis)	05 (08.4)
Cardiovascular/ Infective endocarditis	01 (01.6)
Central nervous system	04 (06.7)
Gastrointestinal tract	03 (05.0)
Urinary tract	08 (13.5)
Sepsis without focus	08 (13.5)
Pathogenic organism implicated	**n=37 (%)**
Herpes Zoster	4 (10.81)
SARS CoV2 (COVID-19)	4 (10.81)
Escherichia Coli	4 (10.81)
Klebsiella pneumonia	3 (8.10)
Herpes Simplex	2 (5.40)
Enterococcus Faecalis	2 (5.40)
Streptococcus pneumoniae	2 (5.40)
Mycobacterium Tuberculosis	2 (5.40)
Chromoblastomycosis	1 (2.70)
Disseminated Scabies	1 (2.70)
Enterococcus faecium	1 (2.70)
Methicillin sensitive *Staphylococcus aureus* (MSSA)	1 (2.70)
Methicillin resistant *Staphylococcus aureus* (MRSA)	1 (2.70)
Aspergillus Niger	1 (2.70)
Burkholderia cenocepacia	1 (2.70)
Stenotrophomonas maltophila	1 (2.70)
Providencia stuartii	1 (2.70)
Coagulase negative Staphylococcus	1 (2.70)
Corynebacterium striatum	1 (2.70)
H1N1 Influenza	1 (2.70)
Acinetobacter baumanii	1 (2.70)
Ascaris lumbricoides	1 (2.70)
Mortality	**n=76 (%)**
Overall mortality	8 (9.4)
Mortality due to infection	7 (9.2)

Table 3: Binary logistic regression analysis for predictors of serious infection

Table 3: Binary logistic regression analysis for predictors of serious infection

Binary logistic regression	Univariate analysis			Multivariate analysis		
Variable	**OR**	**95% CI**	**P value**	**OR**	**95% CI**	**P value**
Age	**0.926**	**0.861-0.996**	**0.038**	**0.878**	**0.783-0.984**	**0.025**
Male Sex	4.629	1.284-16.686	**0.019**	1.787	0.346-9.247	0.489
Disease Damage present	3.677	0.951-14.220	0.059	**12.694**	**1.995-80.793**	**0.007**
Lymphopenia prior to RTX infusion	3.071	0.992-9.514	0.052	3.789	0.814-17.632	0.089
Refractory Lupus Nephritis	0.236	0.049-1.134	0.071	0.408	0.065-2.544	0.337
Concurrent Therapy with MMF	0.332	0.086-1.288	0.111	1.066	0.462-12.913	0.553
Cumulative dose of Cyclophosphamide	1.178	1.000-1.386	0.050	2.443	0.862-1.319	0.293

Lymphopenia, total leukocyte count <1000/mm^3; RTX, rituximab; MMF, mycophenolate mofetil

exposure was assessed in terms of cumulative steroid (prednisolone) dose, standardized steroid dose (glucocorticoid intake per month of exposure) and number of times the patient received pulse IV methylprednisolone. A 'serious adverse event' was defined according to guidelines by International Council on Harmonisation (ICH) 1994. The primary outcome was the occurrence of a serious infection. Secondary outcomes included mortality, time to first serious infection, minor infections and other adverse events.

Results: A total of 76 SLE patients (median age 29 years, 83% females) were included. The median follow-up duration was 27.0 (10-49) months amounting to 177.33 person-years of follow-up. Baseline data of the patients is represented in table 1. Forty-five patients (59.2%) had at least one adverse event. Among these, non-infectious events occurred in 4 (5.26%). Infusion reactions occurred 3 (3.9%), one requiring discontinuation of therapy. One patient had worsening of pre-existing pulmonary artery hypertension. There were 43 (56.6%) patients who had infectious events, 16 of 76 (21.05%) were serious infections amounting to 9.02 infections per 100 person-years of follow-up. Majority(53%) of infections occurred after 1 year of RTX infusion. Site of infections and microrganisms implicated are detailed in table 2. There were total 8 deaths resulting in a mortality rate of 4.5 per 100 person-years of follow-up. All deaths except one were due to serious infection. Male sex, younger patients, CKD**,** previous cyclophosphamide use, higher cumulative dose of cyclophosphamide, refractory lupus nephritis, higher SLICC ACR damage index at baseline was associated with serious infections (table 1). On binary logistic regression younger age(B 95% CI) and presence of disease damage(B 95% CI) emerged as significant predictors of serious infections (table 3).

Conclusion: Serious infections following RTX are common and result in mortality in SLE. More than 50% of them occur after 1 year of RTX administration. Infections arise from common and rare opportunistic organisms. Juvenile lupus and presence of damage at baseline predispose to infections.

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Abstract Number: 0589

A Comparative Evaluation of IgA2 Anti-dsDNA Antibodies and Clinical Outcome in Two Clinical Trials of Belimumab After Rituximab in SLE

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: We have shown that serum IgA2 anti-dsDNA antibody levels is a biomarker of response to belimumab after rituximab in SLE (BEAT-lupus trial) (1). We sought to confirm these findings in the CALIBRATE trial where 43 patients with lupus nephritis refractory to conventional therapy were randomised to receive either rituximab, cyclophosphamide, and then belimumab (RCB) for 48 weeks, or rituximab and cyclophosphamide (RC) (2).

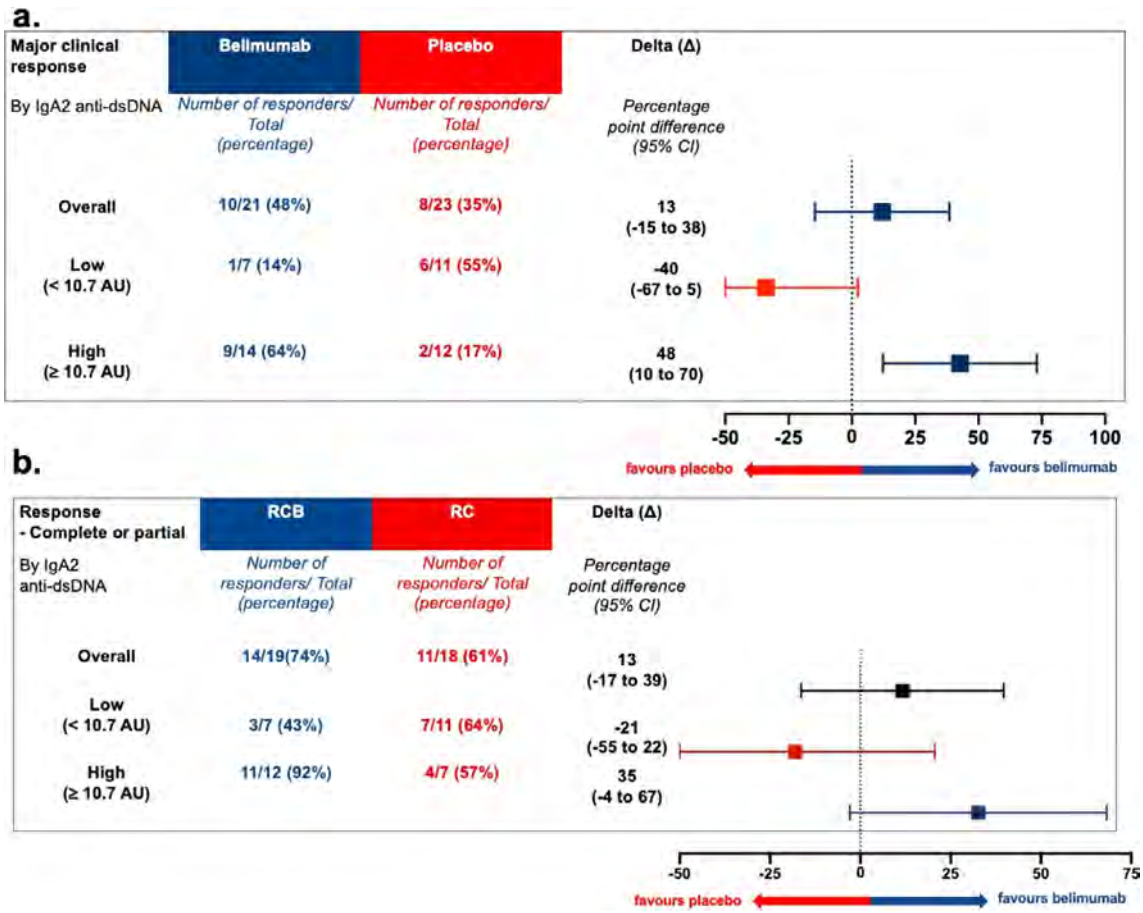

Figure 1a-b - Patients with high baseline serum IgA2 anti-dsDNA antibody levels were more likely to respond at 1 year to belimumab after rituximab compared to rituximab therapy: (a) BEAT-LUPUS and (b) CALIBRATE trial. Baseline serum IgA2 anti-dsDNA antibody levels were categorised into high or low levels (the optimal cut-point was derived from the Area under the Receiver operator characteristic (ROC) curve (AUROC) analysis (= 10.7 arbitrary units/AUs). RCB = belimumab after rituximab and cyclophosphamide, RC = rituximab and cyclophosphamide

Methods: All patients met the ACR classification criteria for SLE. Serum IgG, IgA1 and IgA2 anti-DNA antibodies were assayed by ELISA. We performed a post-hoc modified intention to treat analysis of the CALIBRATE trial so that the clinical outcome data could be matched with the BEAT-lupus trial.

Results: The intention-to-treat analysis of both the BEAT-lupus and CALIBRATE trials revealed a 13% difference in outcome at 1 year favouring belimumab after rituximab compared to rituximab. This difference increased to 35% in those patients in the CALIBRATE trial with elevated serum levels of IgA2 anti-dsDNA antibodies, the corresponding value in the BEAT-lupus trial was a 48% difference (1) (Figure 1a-b).

Matching previously published data from the BEAT-LUPUS trial (1), serum IgA2, but not IgA1, anti-dsDNA antibodylevels decreased at 48 weeks only in patients who received belimumab (p=0.002) (Figure 2a-b). Serum IgA2 anti-dsDNA antibodies increased after cessation of belimumab therapy. There was no significant difference in serum IgG anti-DNA antibody levels between the two arms of the CALIBRATE trial (Figure 2c). Serum IgA1 anti-dsDNA antibody levels in the CALIBRATE

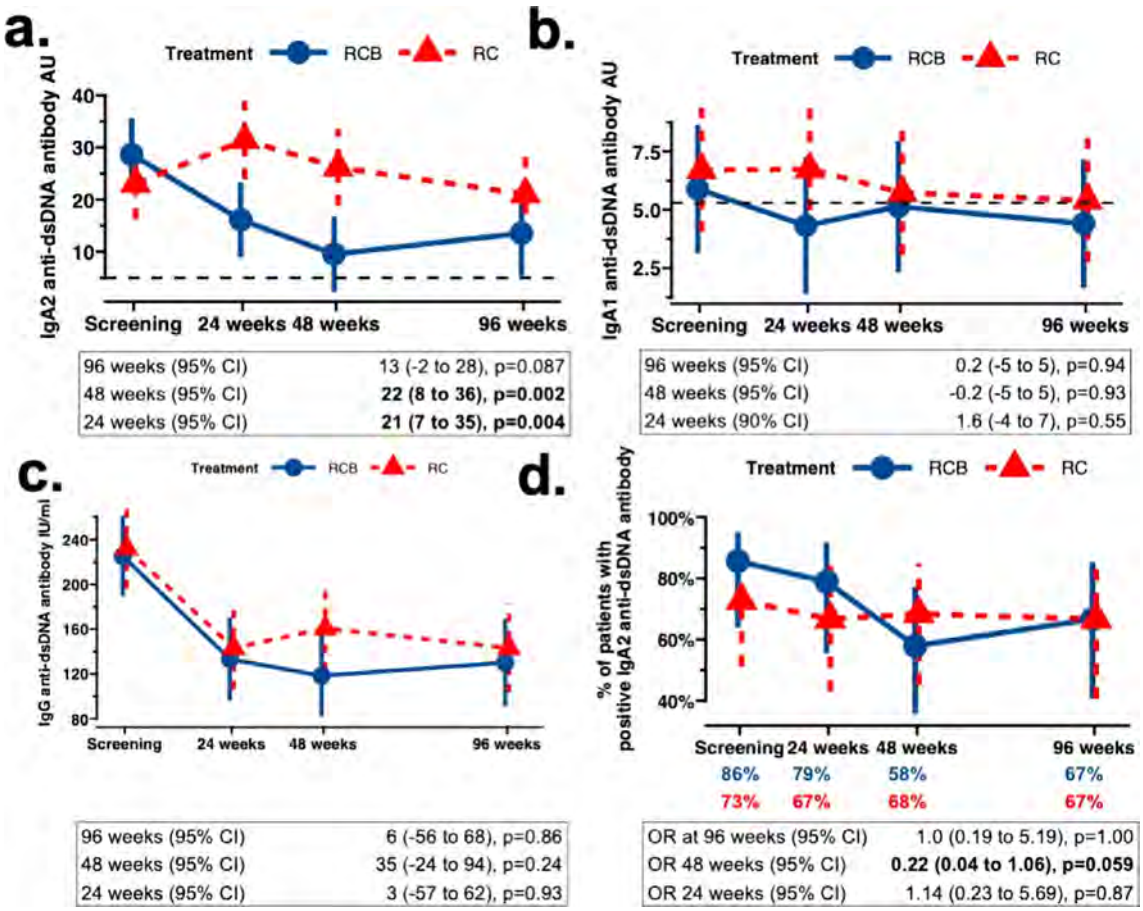

Figure 2a-d - Belimumab after rituximab decreased serum IgA2 anti-dsDNA antibody levels compared to rituximab therapy (CALIBRATE trial). Longitudinal change of (a) serum IgA2 anti-dsDNA antibodies, (b) serum IgA1 anti-dsDNA antibodies, and (c) serum IgG anti-dsDNA antibodies stratified by treatment i.e., RCB = belimumab after rituximab and cyclophosphamide versus RC = no belimumab after rituximab and cyclophosphamide. A generalised longitudinal linear mixed-effect model was fitted with random patient effect to account for clustering by patients and fixed effect of treatment group intercepting with trial times and adjusted for screening IgA2 anti-dsDNA antibody values, age, gender, and concomitant prednisolone (yes or no) to calculate expected difference at 24, 48, and 96 weeks. Estimated mean with 95% confidence intervals (95%CIs) are shown; p values are provided. The horizontal black dotted lines where shown indicate upper limit of normal (3 standard deviation above the mean of healthy control samples). (d) Proportion of patients who were positive† for IgA2 anti-dsDNA antibodies at each time point. Odds ratio (OR) of seronegative reversion for IgA2 anti-dsDNA antibodies at each time points with RCB (if positive for IgA2 anti-dsDNA antibodies at baseline) compared to RC group. †Positivity of IgA2 anti-dsDNA antibody was defined as 3 standard deviations above the mean values of healthy control samples (=5.4 arbitrary units).

trial were less than IgA2 anti-DNA antibody levels and remained close to healthy control values, consistent with our previous observation that the former is low in lupus nephritis (1).

At baseline, 18/21 patients (86%) in the RCB group and 16/22 patients (73%) in the RC group were positive for serum IgA2 anti-dsDNA antibodies. The percentage of patients with positive IgA2 anti-dsDNA antibodies reduced to 58% in the RCB group at 48 weeks (Figure 2d). The odds ratio of reversion to seronegativity in belimumab treated patients with positive IgA2 anti-dsDNA antibodies was 0.22 at 48 weeks (95% CI 0.04–1.06; p=0.059); a similar sero-reversion rate was noted in the belimumab arm of the BEAT-LUPUS trial (1).

The overall response rate in the CALIBRATE trial (74% - RCB arm, 61% - RC arm) was higher than the BEAT-LUPUS trial (48% - belimumab arm, 35% - placebo arm). Patients in the CALIBRATE trial received almost twice as much prednisolone in the first 48 weeks compared to the BEAT-LUPUS trial (Figure 3) which could reflect the slightly different patient populations (CALIBRATE- refractory lupus nephritis; BEAT-lupus – refractory lupus: 20/52 patients had lupus nephritis) and explain the difference in outcome.

Conclusion: Data from two independent trials confirm IgA2 anti-dsDNA antibody levels as a predictive biomarker of response to belimumab after rituximab in SLE. Cessation of belimumab therapy after rituximab led to a rise in IgA2 anti-dsDNA antibody levels providing a mechanistic rationale for continuation of therapy.

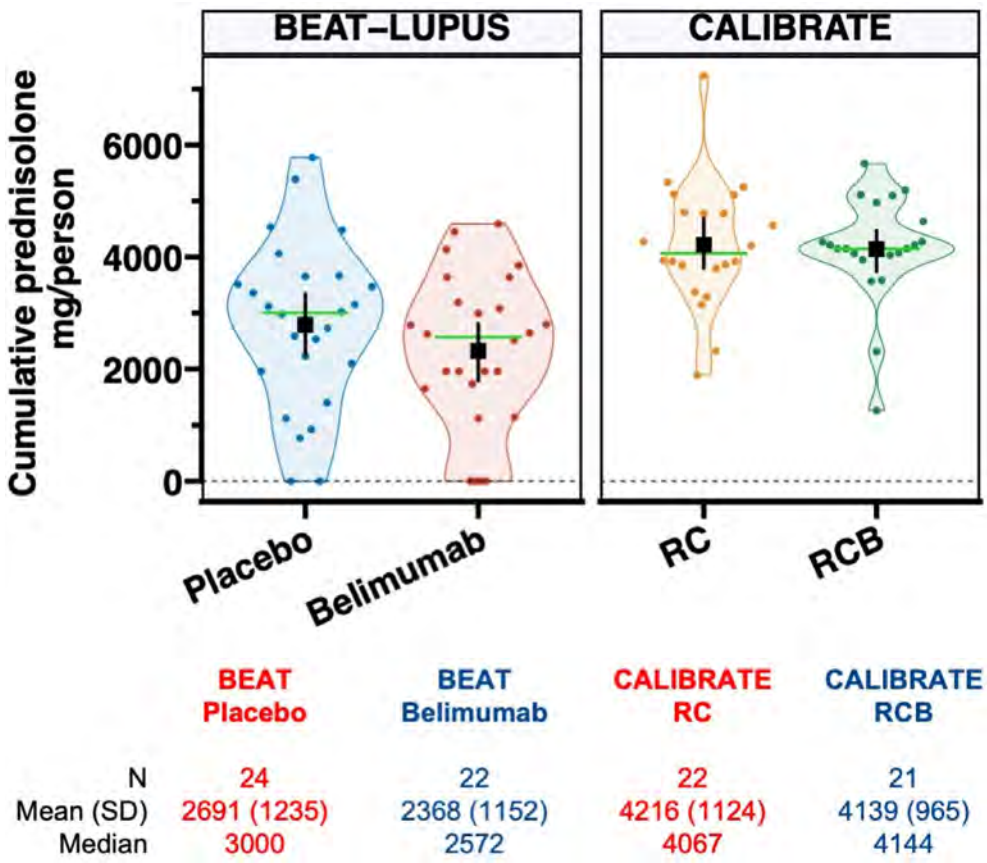

Figure 3 – Cumulative dose of prednisolone in the CALIBRATE and BEAT-lupus trials. Cumulative dose of prednisolone in the treatment arms in the BEAT-LUPUS and CALIBRATE trials over 52 and 48 weeks, respectfully. The black boxes and lines indicate mean values with 95% confidence interval, green horizontal lines indicate median values. RCB = belimumab after rituximab and cyclophosphamide. RC = no belimumab after rituximab and cyclophosphamide.

Reference

1. Shipa, M. et al. The Lancet rheumatology.2022;5: e24
2. Atisha-Fregoso, Y et al. Arthritis Rheumatol. 2021; 73:121

Disclosure: M. Shipa: None; **D. McCluskey**: None; **L. Cooney**: None; **M. Ehrenstein**: GlaxoSmithKlein(GSK), 2.

Abstract Number: 0590

Comparing Safety and Efficacy of Sodium-Glucose Co-Transporter 2 Inhibitors versus Dipeptidyl Peptidase 4 Inhibitors in Patients with Systemic Lupus Erythematosus and Comorbid Type 2 Diabetes Mellitus

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Sodium-glucose co-transporter 2 inhibitors (SGLT2i), originally approved as oral hypoglycemic agents for type 2 diabetes (T2D), have been shown to reduce progression to end-stage renal disease (ESRD), as well as heart failure and overall mortality. Those with systemic lupus erythematosus (SLE) were excluded from trials and thus the potential benefits for these patients are unknown. We conducted a simulated clinical trial comparing renal, cardiovascular, infectious, and mortality outcomes among patients with both SLE and T2D starting SGLT2i vs. dipeptidyl peptidase 4 inhibitors (DPP4i) in a large real-world administrative dataset.

Methods: We identified a cohort of patients with both SLE and T2D, age ≥ 18 years within administrative data from 92 hospitals across the United States (TriNetX) using billing claim algorithms. All patients initiated either an SGLT2i or DPP4i between 2014 and 2023. SGLT2i recipients were 1:1 propensity score (PS) matched to DPP4i recipients on demographic and clinical factors, also identified by billing codes. Cox models estimated hazard ratios (HRs) and 95% confidence intervals (CIs) for the endpoints: 1) acute kidney injury (AKI), chronic kidney disease (CKD), end-stage renal disease (ESRD), 2) heart failure, myocardial infarction, stroke, 3) infections, specifically urinary tract and genital infections, severe sepsis, 4) emergency visits, hospitalizations and all-cause mortality.

Results: **Table 1** shows the SLE/T2D populations before and after PS-matching. Of the 3,749 PS-matched patients starting SGLT2i and 3,749 starting DPP4i, mean age was 58.3 (±11.2) years; 86.9% were females. In follow-up over 7.95 (±14.5) mean years, SGLT2i vs DPP4i recipients had significantly reduced risks of developing AKI (HR 0.65; 0.56-0.75), CKD (HR 0.74; 0.66-0.82), ESRD (HR 0.40; 0.27-0.59), and heart failure (HR 0.80; 0.71-0.90) (**Table 2**). SGLT2i use was also associated with decreased future emergency visits (HR 0.82; 0.77-0.88) and hospitalization (HR 0.68; 0.53-0.89). Risk of genital infection was elevated (HR 1.29, 1.12-1.49), but urinary tract infections (HR 0.90; 0.75-0.91) and severe sepsis (HR 0.61; 0.45-0.84) were reduced. We found no significant differences in all-cause mortality, diabetic ketoacidosis, or lower limb amputation between SGLT2i versus DPP4i use (**Table 2**).

Conclusion: In this real-world head-to-head simulated randomized trial in a large population of patients with SLE and T2D from 2014-2023, SGLT2i use compared to DPP4i use was associated with significantly reduced risks of developing AKI, CKD, ESRD, hospitalization, and heart failure. Genital infection risk was elevated, but risks of emergency visits, hospitalizations, urinary tract infections, and severe sepsis were also reduced for SGLT2i users. Overall mortality was not different.

	Before propensity score matching			After propensity score matching		
	SGLT2i (4,006)	DPP4i (6,551)	Std diff.	SGLT2i (3,749)	DPP4i (3,749)	Std diff.
Age, Mean ± SD	57.8 ± 10.8	62.0 ± 12.2	0.362	58.4 ± 10.6	58.2 ± 11.7	0.02
Female n (%)	3,474 (86.7)	5,666 (86.5)	0.007	3,255 (86.8)	3,262 (87.0)	0.006
Comorbidities, n (%)						
Acute Kidney Injury	344 (8.6)	1,027 (15.7)	0.218	338 (9)	316 (8.4)	0.021
Chronic Kidney Disease	622 (15.5)	1,819 (27.8)	0.301	614 (16.4)	570 (15.2)	0.032
Heart Failure	585 (14.6)	1,309 (20)	0.143	565 (15.1)	540 (14.4)	0.019
Myocardial Infarction	181 (4.5)	317 (4.8)	0.015	162 (4.3)	160 (4.3)	0.003
Cerebrovascular Diseases	710 (17.7)	1,375 (21)	0.083	682 (18.2)	665 (17.7)	0.012
Hypertensive Diseases	3,443 (85.9)	5,699 (87)	0.031	3,227 (86.1)	3,204 (85.5)	0.018
Procedure, n (%)						
Emergency Department Services	2,437 (60.8)	3,893 (59.4)	0.029	2,277 (60.7)	2,259 (60.3)	0.010
Medications, n (%)						
Glucocorticoids	2,928 (73.1)	4,390 (67)	0.133	2,703 (72.1)	2,693 (71.8)	0.006
Ibuprofen	1,141 (28.5)	1,330 (20.3)	0.191	1,019 (27.2)	987 (26.3)	0.019
Naproxen	752 (18.8)	979 (14.9)	0.102	684 (18.2)	681 (18.2)	0.002
Hydroxychloroquine	1,360 (33.9)	1,936 (29.6)	0.095	1,242 (33.1)	1,239 (33)	0.002
Azathioprine	233 (5.8)	309 (4.7)	0.049	210 (5.6)	211 (5.6)	0.001
Cyclophosphamide	11 (0.3)	17 (0.3)	0.003	10 (0.3)	10 (0.3)	<0.001
Mycophenolate mofetil	162 (4)	340 (5.2)	0.055	152 (4.1)	161 (4.3)	0.012
Rituximab	20 (0.5)	49 (0.7)	0.032	20 (0.5)	18 (0.5)	0.008
Laboratory, Mean ± SD						
HbA1c (mmol/mol)	8.1 ± 1.8	7.7 ± 1.7	0.129	8.1 ± 1.8	7.7 ± 1.7	0.197
Creatinine (mg/dL)	1.4 ± 6.2	2.3 ± 10.2	0.240	1.2 ± 5.0	2.2 ± 10.4	0.115
Albumin (g/dL)	4.1 ± 0.4	4.0 ± 0.5	0.097	4.1 ± 0.4	4.0 ± 0.5	0.119
ESR (mm/h)	26.4 ± 21.1	33.5 ± 26.5	0.082	26.2 ± 21.5	31.0 ± 25.0	0.206

Baseline Characteristics of Patients with Systemic Lupus Erythematosus and Type 2 Diabetes Started on either SGLT2i (n=3,749) or DPP4i (n=3,749) before and after PS-Matching

Outcomes	HR (95% CI)
Acute Kidney Injury	0.65 (0.56, 0.75)
Chronic Kidney Disease	0.74 (0.66, 0.82)
End-Stage Renal Disease	0.40 (0.27, 0.59)
Heart Failure	0.80 (0.71, 0.90)
Myocardial Infarction	0.95 (0.74, 1.21)
Stroke	0.97 (0.80, 1.18)
Urinary Tract Infection	0.83 (0.75, 0.91)
Genital Infection	1.29 (1.12, 1.49)
Sepsis	0.61 (0.45, 0.84)
Diabetic Ketoacidosis	1.05 (0.67, 1.64)
Emergency Department Visit	0.82 (0.77, 0.88)
Hospitalization	0.68 (0.53, 0.89)
All-cause Mortality	0.84 (0.67, 1.04)

Hazard Ratios (with 95% Confidence Intervals) for Outcomes after PS-Matching among Patients with Both Systemic Lupus Erythematosus and Type 2 Diabetes Started on SGLT2i (n=3,749) versus DPP4i (n= 3,749) and Followed for a Mean of 7.95 (±14.5) Years

Thus, SGLT2i appear safe and effective for those with SLE and T2D. Given high risks of cardiovascular and renal disease in patients with SLE, further trials and studies should investigate whether SGLT2i should be used for patients with SLE without T2D.

Disclosure: J. Lo: None; **P. Huang**: None; **G. Tsokos**: None; **V. Kyttaris**: AbbVie/Abbott, 5, AstraZeneca, 2, Aurinia, 1, EMD Serono, 5, Exagen, 2, 5, Fresenius Kabi, 1, Horizon Pharmaceuticals, 1, Novartis, 5, Scipher, 1, Takeda, 5, Vertex, 2; **K. Costenbader**: Amgen, 2, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Eli Lilly, 2, Exagen Diagnostics, 5, Gilead, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5; **K. Ma**: None.

Abstract Number: 0591

Despite Dramatic Expansion of Approved Biologics in SLE, Unmet Needs Remain

Ryan Rex, Maxine Yarnall and Sawyer May, Spherix Global Insights, Exton, PA

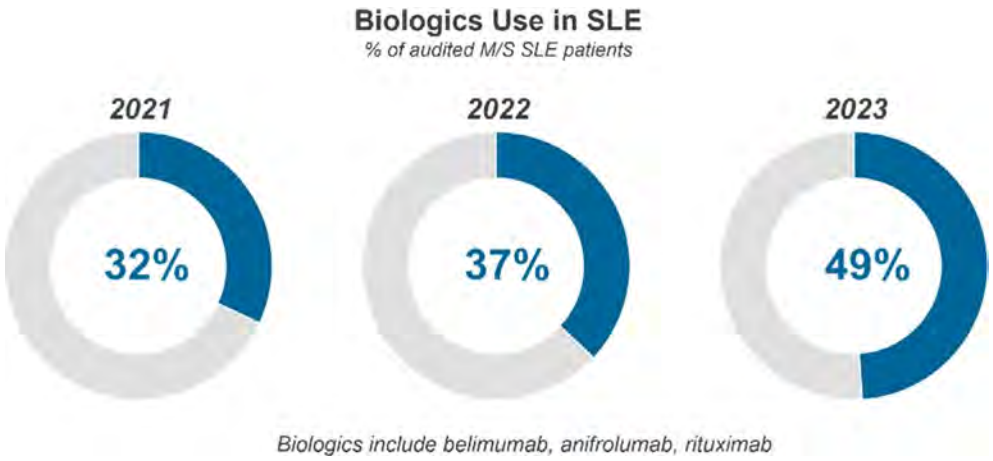
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: This study was conducted to uncover real-world treatment patterns among moderate to severely active systemic lupus erythematosus (SLE) patients in the US.

Methods: 1,011 records from SLE patients with moderate and severely active disease were collected in collaboration with 297 US rheumatologists via an online survey platform from March 31 through May 5, 2023.

Results: Study results reveal that the use of biologics in SLE has substantially increased over the past three years – marking a dramatic expansion of biologic use in moderate-to-severe SLE in a relatively short period of time.

37% of audited patients are currently on FDA-approved biologic belimumab for their moderate-to-severe SLE, substantially up from levels observed in 2022 (28%) and 2021 (21%) and increasingly driven by the drug's anticipated efficacy, steroid-sparing ability, safety profile, and recent lupus nephritis (LN) indication. 8% of audited moderate-to-severe patients are



currently on FDA-approved biologic anifrolumab compared to 3% noted in the 2022 audit.* Like belimumab, rheumatologists were most compelled to prescribe anifrolumab due to its perceived efficacy, steroid-sparing effect, and safety profile.

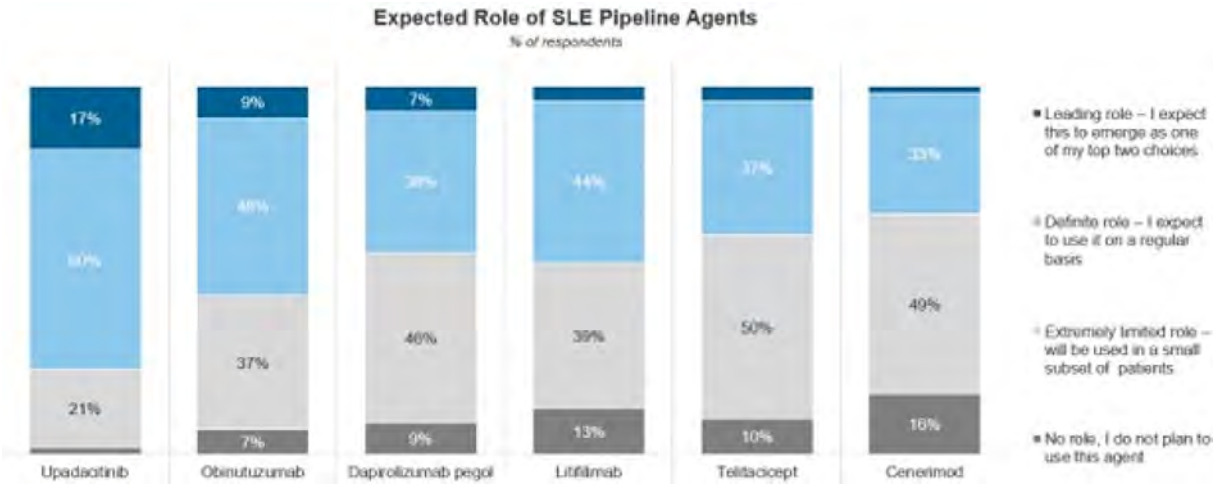
Commonly used "off label" biologic rituximab, on the other hand, is seeing a year-over-year decline in patient share with rheumatologists (4% of moderate-to-severe patients in 2023, 6% in 2022 and 11% in 2021) and physicians are considering fewer of their patients as potential candidates for the drug.

Notably, rheumatologists have also been using fewer other off-label agents in SLE over the same period, likely due to the availability of recently approved SLE agents along with safety concerns associated with the Janus kinase (JAK) inhibitor class, which has shown a steep decline in off-label use for SLE since 2021.

While the majority of rheumatologists express satisfaction with patients' response to approved biologics belimumab and anifrolumab, it is notable that only 18% of rheumatologists agree with the statement "*I am satisfied with the treatment options available to me in SLE*," underscoring the remaining unmet need for new pharmacologic treatment options.

The robust SLE pipeline – which consists of over 40 drugs in development – provides promising future treatment options for SLE. Of the SLE pipeline agents in or entering Phase III, rheumatologists expect upadacitinib to play the most important role if approved with 77% of rheumatologists saying the drug will play a leading or definite role.

While rheumatologists have been lessening their use of off-label JAK inhibitors in SLE, upadacitinib is a drug rheumatologists have experience using in a host of other rheumatic conditions, which could revitalize use of JAKs in SLE if approved.



Conclusion: Rheumatologists are increasingly using approved biologics in their moderate-to-severe SLE patients, however an unmet need for new pharmacological treatments remains. Despite the lessening of off label use of the JAK class many rheumatologists believe upadacitinib could provide significant value to their treatment armamentarium if approved.

Disclosure: R. Rex: None; **M. Yarnall**: None; **S. May**: None.

Abstract Number: 0592

Real-World Treatment Patterns in Patients with Systemic Lupus Erythematosus: An Analysis of the SLE Prospective Observational Cohort Study (SPOCS)

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: SLE – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The international SLE Prospective Observational Cohort Study (SPOCS) collected data on patients with moderate to severe SLE disease activity from June 2017 through November 2022. A unique aim of SPOCS is to evaluate relationships between various aspects of SLE and type I IFN gene signature (IFNGS) status.

Objectives: To assess medication use among SPOCS patients over 36 months.

Methods: Patients enrolled in SPOCS were ≥18 years old with moderate to severe active SLE (SLEDAI ≥6 or clinical SLEDAI ≥4) and received standard therapy with ≥6 months of systemic SLE treatment beyond non-steroidal anti-inflammatory drugs and analgesics. All patients met ACR or Systemic Lupus International Collaborating Clinics (SLICC) SLE classification criteria. Medication use data were collected over 36 months during patients' biannual clinic visits. In this analysis, we report the proportions of patients receiving antimalarials, immunosuppressants (IS), biologics (belimumab or rituximab), or glucocorticoids (GCs), as well as daily oral GC dosage (mg/day) and proportions of patients receiving low (>0 to ≤7.5 mg/day) or high (>7.5 mg/day) oral GC dosages. Medication use was also stratified by baseline IFNGS (high vs low).

Results: At baseline, most patients (n=826; IFNGS-high [70.8%], low [29.2%]) were receiving antimalarials (81.1%), 21.2% were receiving biologics, and 54.8% were receiving IS (Table). From baseline to 36 months, the proportions of patients taking antimalarials remained stable while the use of biologics and IS moderately increased. At baseline, 65.0% of patients were taking GCs and the proportion was largely stable over time. However, the proportion administered oral GC >7.5 mg/day increased from 26.0% at baseline to 44.3% at 6 months and 45.7% at 12 months, and then declined with time but did not reach the baseline level. The mean (SD) dose of oral GC increased from 6 (7.1) mg/day at baseline to 10 (8.7) mg/day at 6 months and then was stable over time. Across the study period, IS, biologics, and GCs were generally administered

Table. Medication use among SPOCS patients from baseline through 36 months. GC, glucocorticoid; SD, standard deviation. aGC use current or since previous visit. bOral GC daily dose derived from cumulative dose over treatment interval. cGroup sizes differ because oral GC use could be reported without dose information.

n (%)	Baseline n=826	6 months n=663	12 months n=542	18 months n=479	24 months n=426	30 months n=441	36 months n=409
Antimalarials	670 (81.1)	537 (81.0)	447 (82.5)	398 (83.1)	351 (82.4)	362 (82.1)	341 (83.4)
Immunosuppressants	453 (54.8)	385 (58.1)	318 (58.7)	290 (60.5)	266 (62.4)	258 (58.5)	251 (61.4)
Biologics (belimumab or rituximab)	175 (21.2)	178 (26.8)	142 (26.2)	119 (24.8)	107 (25.1)	113 (25.6)	106 (25.9)
GC[a]	537 (65.0)	437 (65.9)	351 (64.8)	316 (66.0)	279 (65.5)	281 (63.7)	253 (61.9)
IFNGS high	531 (70.8)	392 (69.9)	277 (65.8)	236 (67.4)	201 (66.1)	206 (66.9)	190 (65.1)
IFNGS low	219 (29.2)	169 (30.1)	144 (34.2)	114 (32.6)	103 (33.9)	102 (33.1)	102 (34.9)
Mean (SD) oral GC dosage (mg/day)[b]	6.0 (7.1)	9.8 (8.7)	10.3 (9.4)	10.7 (10.4)	8.8 (7.6)	9.2 (8.5)	9.8 (17.4)
Dosage group among oral GC users[c]	**n=457**	**n=377**	**n=258**	**n=201**	**n=166**	**n=155**	**n=154**
Oral GC >0 to ≤7.5 mg/day	338 (74.0)	210 (55.7)	140 (54.3)	116 (57.7)	104 (62.7)	97 (62.6)	103 (66.9)
Oral GC >7.5 mg/day	119 (26.0)	167 (44.3)	118 (45.7)	85 (42.3)	62 (37.3)	58 (37.4)	51 (33.1)

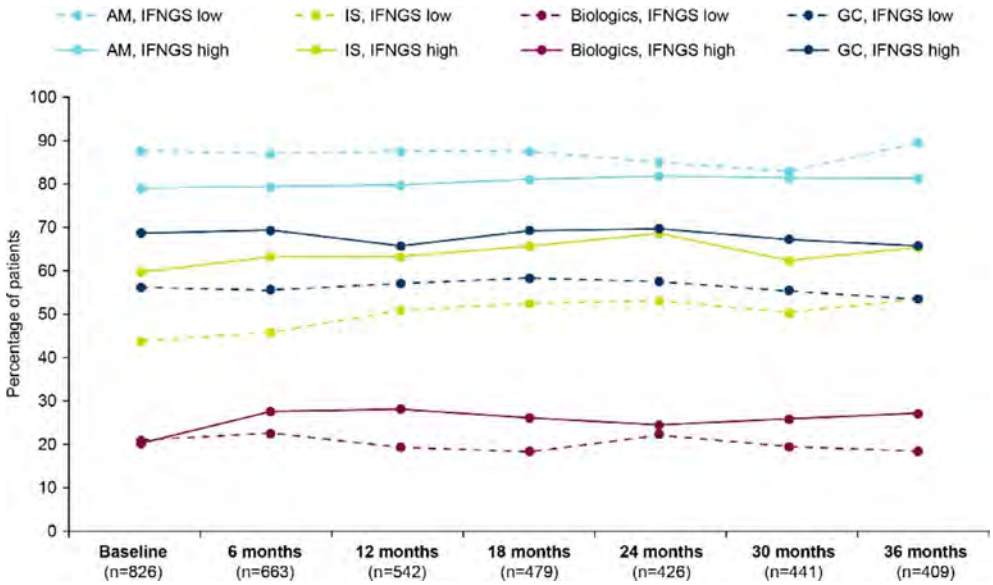

Figure. Medication use by IFNGS status from baseline through 36 months. AM, antimalarials; IFNGS, type I interferon gene signature; IS, immunosuppressants; GC, glucocorticoid.

to greater proportions of IFNGS-high than low patients (Figure). Mean oral GC daily doses were similar between IFNGS-high and low groups throughout the study period except at the final visit. At 36 months, IFNGS-low patients received a lower mean (SD) oral GC daily dose compared with IFNGS-high patients (7 [4.9] vs 11 [20.6] mg/day).

Conclusion: Overall, the increase in oral mean daily GC dose in the first 6 months was maintained through 36 months despite standard therapy, stable antimalarial use, and moderate increases in use of biologics and IS. Although the proportion of GC use was largely stable over time, those on oral GC >7.5 mg/day increased initially and then declined but did not return to the baseline level. In addition, IFNGS-high status was associated with more immunomodulatory therapy compared with those with IFNGS-low status. Together, these data indicate that additional therapies are needed to avoid high-dose GC use among patients with SLE. SPOCS will provide opportunities to increase our understanding of real-world treatment and to identify educational needs within the lupus community.

Disclosure: M. Aringer: AbbVie/Abbott, 1, 6, AstraZeneca, 1, 6, Boehringer-Ingelheim, 1, 6, Bristol-Myers Squibb(BMS), 1, 6, Chugai Pharma GmbH, 1, 6, Eli Lilly, 1, 6, Galapagos, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Merck/MSD, 1, 6, Mylan, 1, 6, Novartis, 1, 6, Pfizer, 1, 6, Roche, 1, 6, Sanofi, 1, 6, UCB, 1, 6; **L. Arnaud**: AbbVie, 6, Alexion, 6, Alpine, 2, 6, Amgen, 6, AstraZeneca, 1, 2, 6, Biogen, 6, Boehringer Ingelheim, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 1, 2, 6, Grifols, 6, Janssen, 6, Kezar Life Sciences, 2, 6, LFB, 6, Medac, 6, Novartis, 2, 6, Pfizer, 6, Roche-Chugaï, 6, UCB, 6; **R. Furie**: AstraZeneca, 2, 5, 6; **E. Morand**: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 2, 5, 6, Biogen, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, EMD Serono, 2, 5, Galapagos, 2, Genentech, 2, 5, GlaxoSmithKline, 2, 5, IgM, 2, Janssen, 2, 5, Novartis, 2, Servier, 2, Takeda, 2, UCB, 5; **C. Peschken**: AstraZeneca, 2, 5, GSK, 2, 5, Roche, 1, 2; **B. Desta**: AstraZeneca, 3; **E. Rapsomaniki**: AstraZeneca UK, 3; **J. Hedberg**: AstraZeneca, 3, 11; **T. Grünfeld Eén**: AstraZeneca, 3, 11; **A. Sorrentino**: AbbVie/Abbott, 12, Own stocks, AstraZeneca, 3, Galapagos, 12, Own stocks, Gilead, 12, Own stocks, Moderna, 12, Own stocks; **C. Ghia**: AstraZeneca, 3; **S. Chen**: AstraZeneca, 3, 11; **B. Ding**: AstraZeneca, 3.

Abstract Number: 0593

Lupus Nephritis of the Spanish National Registry of Belimumab in Patients with Systemic Lupus Erythematosus

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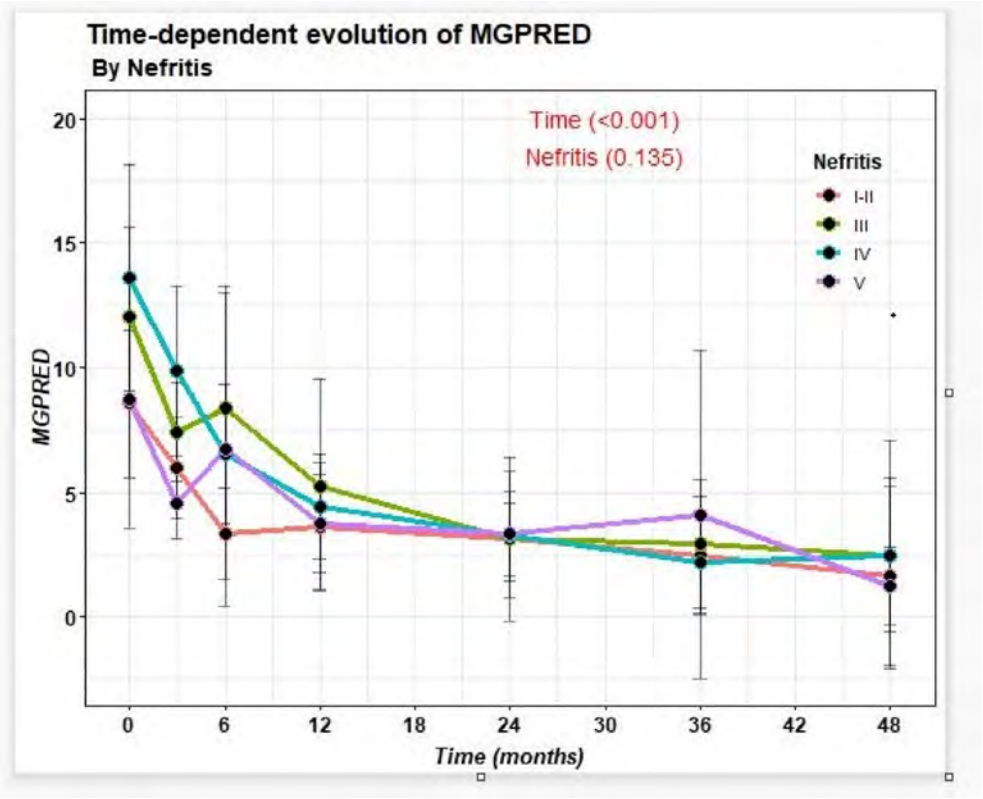
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Belimumab (BLM) is a B-cell stimulating factor (BlyS) monoclonal antibody, approved in 2022 for the treatment of lupus nephritis (NL) and since 2011 for systemic lupus erythematosus (SLE).

Objectives. To describe the demographic characteristics, efficacy and safety of BLM in real clinical practice in patients with lupus nephritis.

Age at SLE diagnosis (years)* *	26.9 (20.2-35.5)
Age at BLM starts (years)* *	37.7 (30.4-47.8)
Gender (female) n, (%)	88 (81.5)
Time from diagnosis until BLM start (years)**	8.6 (5-15.5)
ANA positive, n (%)	102 (94.4)
DNA positive, n (%)	76 (75.2)
Antiphospholipidic syndrome, n (%)	16 (14.8)
Articular involvement, n (%)	84 (77.8)
Hematologic involvement, n (%)	53 (51)
Skin involvement, n (%)	52 (48.6)
Cyclophosphamide, n (%)	59 (11.3)
bDMARD, n (%)	22 (20.4)
cDMARD pre BLM, n (%)	108 (100)
- Hydroxychloroquine	99 (91.7)
- Azathioprine	39 (36.1)
- Mycophenolate mofetil/mycophenolic acid	71 (65.7)
- Tacrolimus/cyclosporine	13 (12)

** Median (IQR).



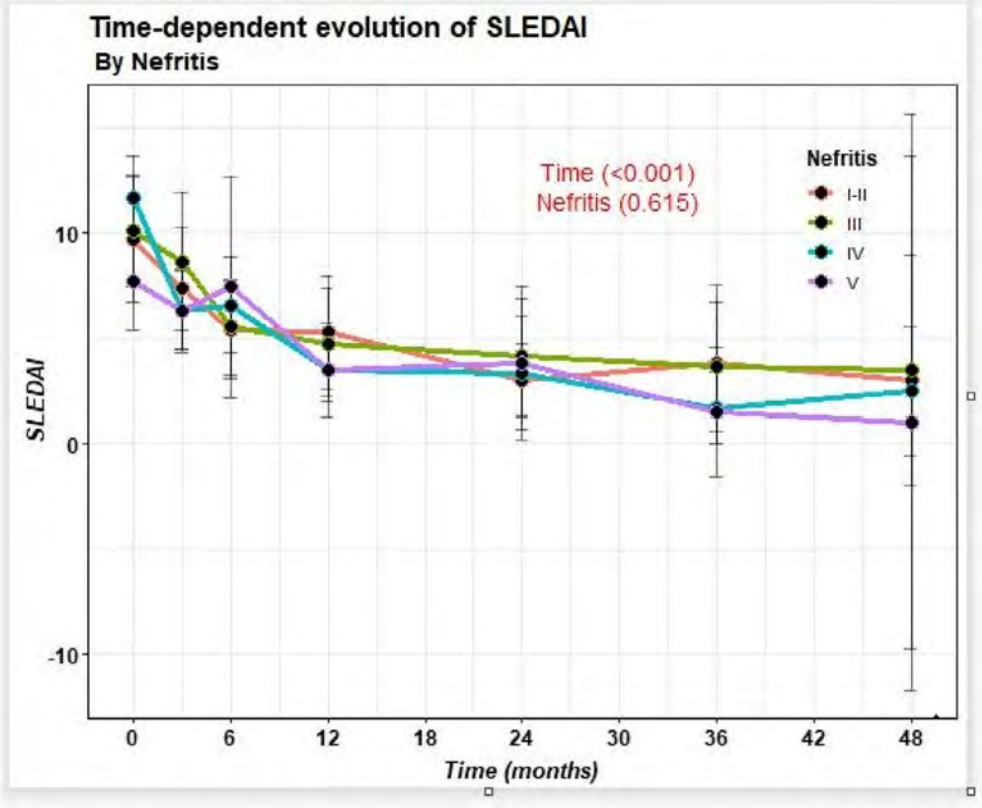
Methods: A descriptive, retrospective study of patients with lupus nephritis confirmed by biopsy from the Spanish multicenter registry of patients treated with BLM. Demographic, analytical and previous and concomitant treatment with belimumab were collected. To assess efficacy, analytical variables (anti-DNA, C3, C4), Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) scale, and steroid doses at baseline and throughout follow-up were analyzed. Renal improvement was considered when a 24-hour proteinuria of less than 0.5 grams was reached. Safety profile of BLM was analyzed.

Results: We included 108 patients, 81.5% women, with a mean age at diagnosis of SLE of 26.9 years (20.2-35.5).The most frequent nephritis class was IV (47 patients, 43.5%), followed by class III (23 patients, 21.3%), V (19 patients, 17.6%) and I-II (19 patients, 17.6%). The time of evolution of the disease until the onset of BLM was 8.6 years (5-15.5).62 patients (57.4%) started BLM subcutaneously (SC), 33 patients (30.6%) intravenously (IV) and 13 patients (12%) change from IV to SC route. Baseline characteristics are summarized in Table 1

The median proteinuria in 24 hours was 1.0 (0.5 to 2.5). The median number of pre-BLM cDMARD uses was 2.0 (2.0-3.0), with antimalarials being the most commonly used (91.7%). 39 and 22 patients received cyclophosphamide and bDMARD prior to BLM respectively, being Rituximab (RTX) the most commonly bDMARD used. 107 patients received prednisone at the time of starting BLM with a median dose of 7.5 (5-1.5) mg.

74.4% of patients improved after BLM in terms of reduction of proteinuria, with last 24-hour proteinuria of 0.2 (0.1-0.9) grams. A decrease in prednisone dose and SLEDAI improvement (Figure 1) was observed from baseline to last follow-up. On the other hand, a decrease in anti-DNA and an increase in C3 and C4 were observed.

21 patients (19.4%) discontinued treatment mainly due to ineffectiveness; 4 patients stopped BLM because of nephritis improvement. The median time on treatment for patients who had to discontinue BLM was 9 (6-24) months. In terms of safety, 28 patients had infections, most of them mild, being urine infection the most reported. One patient died due to meningitis. There were no tumors.



Conclusion: In this cohort of LN treated with BLM in real world settings, we observed an improvement of 24-hour proteinuria, SLEDAI, decrease of anti-DNA and increase of complement, despite of the administration route. No new safety alarms were reported.

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Abstract Number: 0594

Baseline Innate Immunity Transcriptional Signatures Act as Predictors of Response to Immunosuppressive and Biologic Treatments in Systemic Lupus Erythematosus While Disturbances Linked to p53-signaling Define ‘‘Resistant’’ Disease

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite recent advances, the current state of SLE therapeutics remains largely empirical with existing immunosuppressive treatments failing to induce remission in over 40% of patients. There is currently a paucity of tools that would predict response to treatment and guide therapeutic choices.

Methods: Whole blood transcriptome samples were obtained from 95 patients with moderate to severe SLE at baseline, 1 month and 6 months after initiation of treatment with cytotoxic agents (cyclophosphamide, mycophenolate mofetil), mycophenolate mofetil/anti-CD40 antibody, rituximab or belimumab. Disease activity was assessed using the SLEDAI-2K. Response to treatment was defined as achievement of Low Disease Activity State (LLDAS) or remission at 6 months. Differentially expressed genes (DEGs) were identified using the DEseq2. Weighted correlation network analysis (WGCNA) was applied to detect modules of co-expressed transcripts. Abundances of cell types were assessed by CIBERSORTx.

Results: Out of 95 patients the majority were women (93.7%) with a mean [SD] age at SLE diagnosis of 42.9 [13.6] years and a mean disease duration [SD] at sampling of 5.1 [7.2] years. At baseline, mean SLEDAI [SD] was 9.4 [5.7] and active lupus nephritis (LN) was the most common treatment indication (24%), followed by active neuropsychiatric SLE (NPSLE)

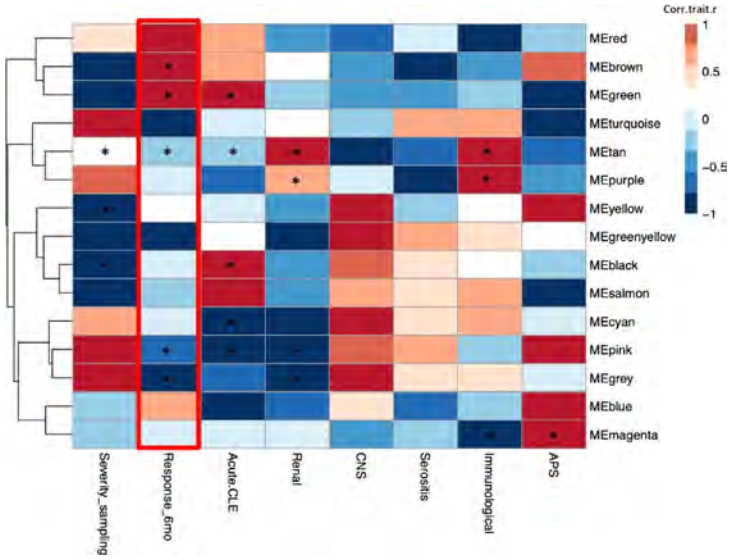

Figure 1. WGCNA module eigengene (ME) correlations to clinical features uncover the brown and green gene modules which are associated with 6 month-response to treatment. Severity_sampling: Presence of moderate or severe disease at sampling timepoint as defined by BILAG Glossary Definition combined with expert physician judgement (DB, GB); Response_6mo: Response to treatment 6 months after treatment initiation; Acute.CLE: Presence of acute cutaneous SLE at any time during the disease course; Renal: Presence of renal manifestations, as defined in the EULAR/ACR SLE classification criteria, at any time during the course of the disease; CNS: Presence of neurological features, as defined in the EULAR/ACR SLE classification criteria, at any time during the course of the disease; Serositis: Presence of polyserositis, as defined in the EULAR/ACR SLE classification criteria, at any time during the course of the disease; Immunological: Presence of immunological disturbances, as defined in the EULAR/ACR SLE classification criteria, at any time during the course of the disease; APS: Antiphospholipid Syndrome. * p-value < 0.05.

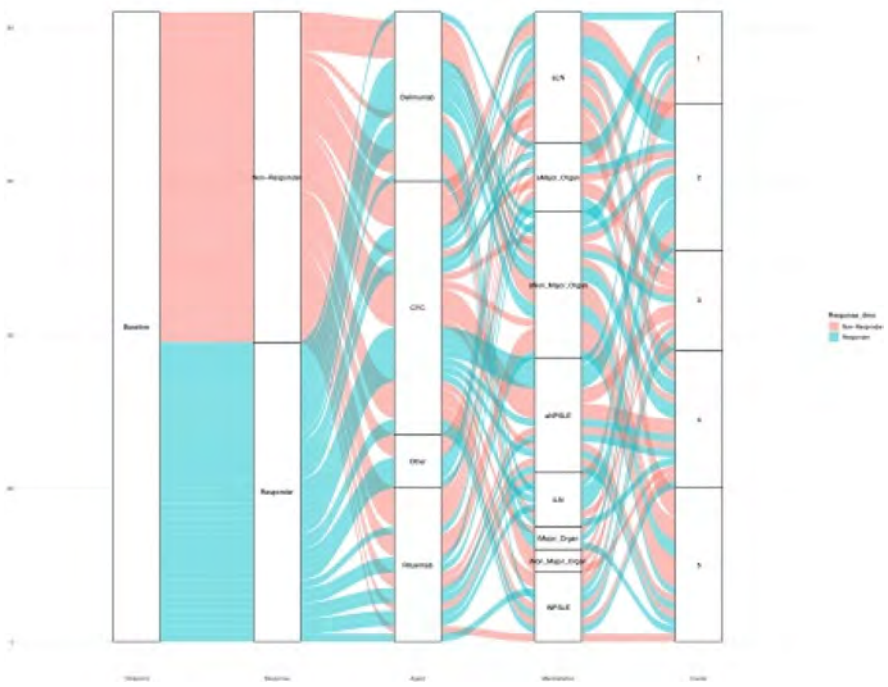

Figure 2. K-means clustering of the baseline samples based on module eigengene (ME) defined the cluster 2, enriched for responders. aLN: Active LN; aMajor_Organ: Active major organ involvement other than LN or NPSLE; aNon_Major_Organ: Active non-major organ involvement; aNPSLE: Active NPSLE; iLN: Inactive LN; iMajor_Organ: Inactive major organ involvement other than LN or NPSLE; iNon_Major_Organ: Inactive non-major orgen involvement; iNPSLE: Inactive NPSLE.

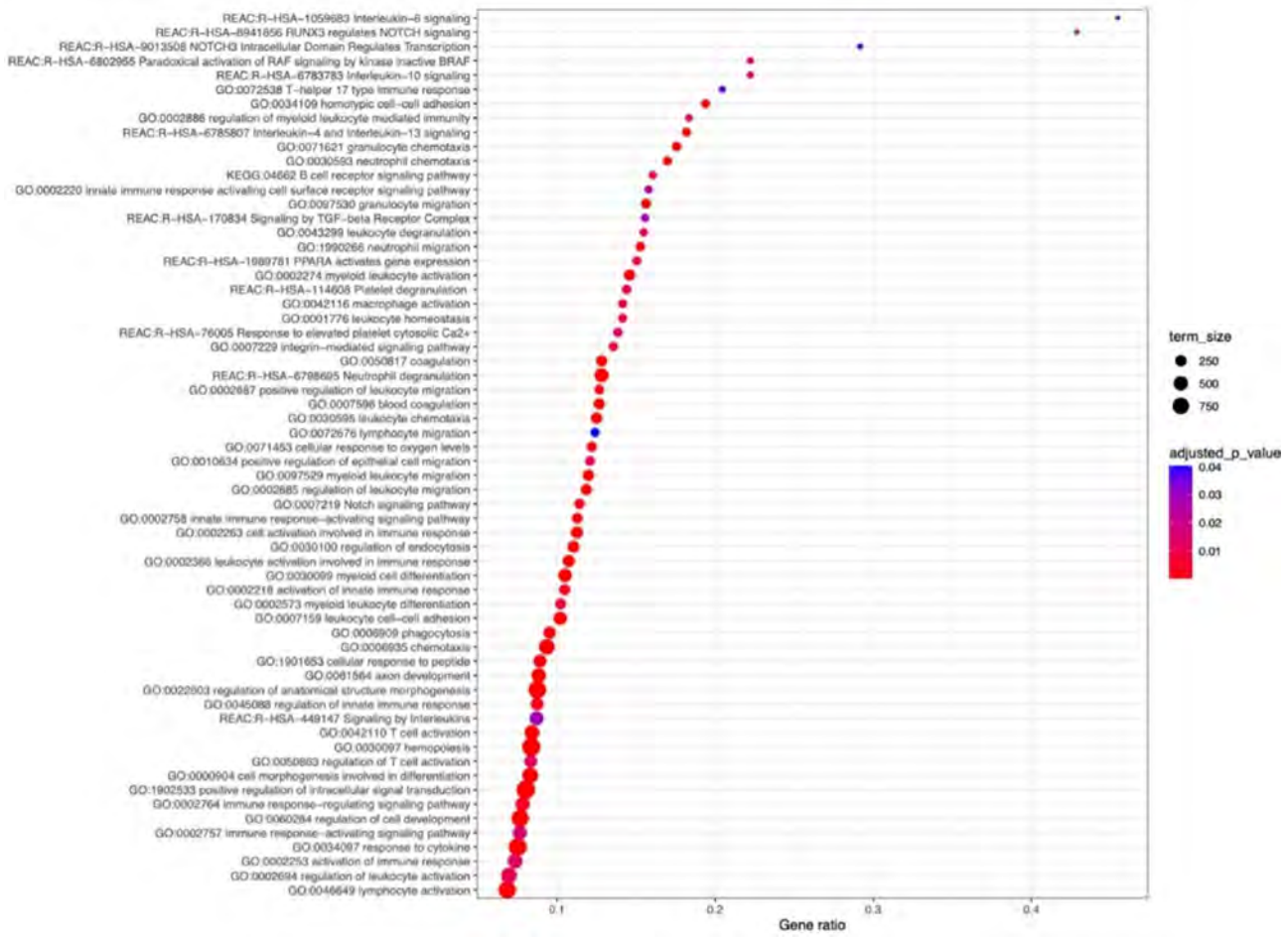

Figure 3. Functional enrichment analysis of the upregulated DEGs resulting from the comparison of responders versus non-responders 1 month after treatment initiation.

(20%). Cyclophosphamide was the most frequently used immunosuppressive agent (n=46), followed by belimumab (n=24) and rituximab (n=21). Forty-three patients responded to treatment. WGCNA-generated modules (Figure 1.) that positively correlated with response to treatment at 6 months ($p = 0.005$, $p = 0.04$) were enriched in biological processes that included type I interferon, pattern recognition receptor signaling, and neutrophil degranulation. Unsupervised clustering of the baseline samples, based on the module eigengene, revealed a respondent rich patient subset (Cluster 2), which was characterized by high prevalence of active LN (Figure 2.). The transcriptional landscape of "resistant" disease was dominated by disturbances related to p53-signaling pathway. Upregulation of pathways linked to neutrophil degranulation, Th17 responses, IL6 mediated responses, TGF-beta, PPARA, and NOTCH signaling differentiated the one-month-transcriptional profile of responders compared to non-responders (Figure 3.).

Conclusion: Baseline molecular fingerprints related to innate immunity correlated with 6-month response to treatment in SLE. Aberrances linked to p53-signaling decisively shaped the transcriptional signature of "resistant" disease.

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Abstract Number: 0595

Renal Involvement in Patients with Systemic Lupus Erythematosus Treated with Anifrolumab Compared with Placebo over a 4-Year Period

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In patients with SLE, nephritis is present in 50%–60% during the first 10 years of disease.[1] Renal involvement is associated with poor clinical outcomes including increased morbidity and mortality.[1,2] Anifrolumab is a human mAb to the type I IFN receptor that is approved for the treatment of SLE.[3] In this post hoc analysis of the phase 3 TULIP long-term extension (LTE) trial of anifrolumab, we assessed renal outcomes in patients with SLE with or without evidence of SLEDAI-2K renal involvement at baseline.[4]

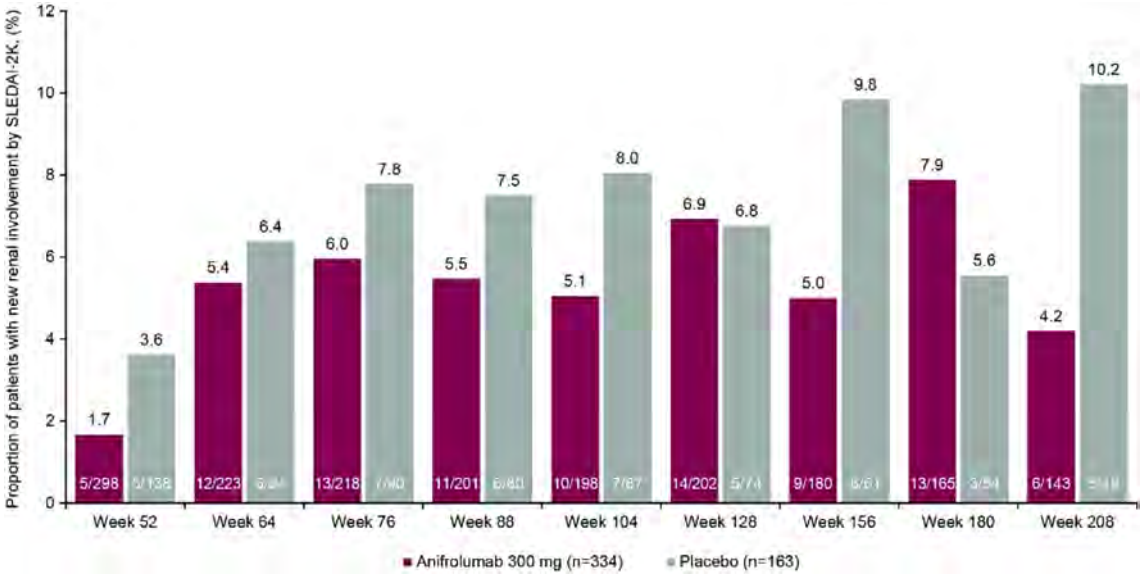


Figure. New Renal Involvement During the LTE Period Among Patients With No Renal Involvement at TULIP Baseline. No renal involvement was defined as renal SLEDAI-2K score =0. New renal involvement was defined as renal SLEDAI-2K score >0. For measuring no renal involvement, percentages are based upon all patients in the full analysis set. For measuring new renal involvement, percentages are based upon all patients in the full analysis set with no involvement at baseline and according to the number assessed at each timepoint thereafter; patients are missing due to either discontinuation, withdrawal, or missing data. Baseline means baseline of the phase 3 feeder studies, ie, the last non-missing measurement prior to dose administration on Day 1.

Methods: Adults with moderate to severe SLE (1997 ACR criteria) despite standard therapy who completed the 52-week, multicenter phase 3 TULIP-1 (NCT02446912) or TULIP-2 (NCT02446899) trials could reconsent to participate in the randomized, placebo-controlled, double-blind, 3-year extension (NCT02794285). The TULIP-1 and TULIP-2 trials excluded patients with active, severe lupus nephritis, serum creatinine >2 mg/dL, or urine protein/creatinine ratio >2 mg/mg. We identified patients with renal involvement below the threshold for exclusion at baseline, or patients without renal involvement, who were randomized to receive intravenous anifrolumab 300 mg or placebo across the TULIP-1/-2 and LTE periods (or would have continued the same treatment in the LTE if not discontinued during TULIP-1/-2). SLEDAI-2K renal domain involvement was assessed from baseline through Week 208.

Results: At TULIP baseline, the proportions of patients with SLEDAI-2K renal involvement were balanced between treatment groups (anifrolumab 6.7% [24/358] vs placebo 8.4% [15/178]). Of patients with baseline renal involvement and available data, a greater proportion of patients achieved renal improvement at LTE study entry (Week 52) with anifrolumab vs placebo (70.6% [12/17] vs 50.0% [6/12]). A greater proportion of patients with baseline renal involvement continued treatment to Week 208 with anifrolumab vs placebo (33.3% [8/24] vs 6.7% [1/15]), and renal improvement at Week 208 was achieved by more patients who received anifrolumab (90.0% [9/10]) vs placebo (0% [0 patients with available data at this timepoint]). Of all patients included in this analysis, ≤1/358 in the anifrolumab group and ≤3/178 in the placebo group experienced new renal activity greater than the baseline score at any timepoint during the study period. In patients with no baseline renal involvement, lower proportions of patients had new renal activity with anifrolumab vs placebo at all timepoints up to Week 208, except for Weeks 128 and 180 (**Figure**).

Conclusion: In the small subgroup of patients with renal involvement at baseline, more

patients treated with anifrolumab remained in the study and achieved SLEDAI-2K renal improvement compared with placebo over the 4-year TULIP-LTE trial. Of patients with no renal involvement at baseline, fewer patients had new renal activity with anifrolumab compared with placebo.

References:

1. Hahn BH, et al. *Arthritis Care Res (Hoboken)*. 2012;64:797–808.
2. Hanly JG, et al. *Rheumatology (Oxford)*. 2016;55:252–62.
3. SAPHNELO Prescribing Information, Wilmington, DE: AstraZeneca.
4. Kalunian KC, et al. *Arthritis Rheumatol*. 2023;75:253–65.

Disclosure: R. Furie: AstraZeneca, 2, 5, 6; **K. Kalunian**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Biogen, 2, Bristol-Myers Squibb, 2, Eli Lilly, 2, Genentech/Roche, 2, GlaxoSmithKline, 2, Janssen, 2, Pfizer, 2; **E. Morand**: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 2, 5, 6, Biogen, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, EMD Serono, 2, 5, Galapagos, 2, Genentech, 2, 5, GlaxoSmithKline, 2, 5, IgM, 2, Janssen, 2, 5, Novartis, 2, Servier, 2, Takeda, 2, UCB, 5; **I. Bruce**: AstraZeneca, 1, 2, 5, 6, Aurinia, 2, GSK, 1, 2, 5, 6, Janssen, 5, 6, Lilly, 1, UCB, 6; **S. Manzi**: AbbVie, 5, Allegheny Singer Research Institute, 10, AstraZeneca, 2, 5, Exagen Diagnostics, Inc, 2, 9, 10, GSK, 2, 5, Lilly, 2, Lupus Foundation of America, 4, Novartis, 2, UCB Advisory Board, 2, Univiersity of Pittsburgh, 10; **G. Atefi**: AstraZeneca, 3; **G. Bryant**: AstraZeneca, 3; **M. Hultquist**: AstraZeneca, 3, 11; **R. Tummala**: AstraZeneca, 3; **G. Abreu**: AstraZeneca, 3; **C. Lindholm**: AstraZeneca, 3; **H. Al-Mossawi**: AstraZeneca, 3.

Abstract Number: 0596

Deucravacitinib, an Oral, Selective, Allosteric Tyrosine Kinase 2 Inhibitor, in a Phase 2 Trial in Systemic Lupus Erythematosus (SLE): Achievement of Sustained SRI(4), BICLA and Dual Responses over 48 Weeks

Richard Furie[1], Cristina Arriens[2], Kenneth Kalunian[3], Marilyn Pike[4], Ronald van Vollenhoven[5], Coburn Hobar[6], Ayanbola Elegbe[6], Samantha Pomponi[6], Subhashis Banerjee[6], Shalabh Singhal[6], Thomas Wegman[7] and Eric Morand[8], [1]Northwell Health, Manhasset, NY, [2]Oklahoma Medical Research Foundation and University of Oklahoma Health Sciences Center, Department of Arthritis & Clinical Immunology, Oklahoma City, OK, [3]University of California San Diego, La Jolla, CA, [4]MedPharm consulting, Inc., Raleigh, NC, [5]Amsterdam University Medical Centers, Amsterdam, Netherlands, [6]Bristol Myers Squibb, Princeton, NJ, [7]Bristol Myers Squibb, Beaver Falls, PA, [8]Monash University, Centre for Inflammatory Diseases, Melbourne, Australia

SESSION INFORMATION

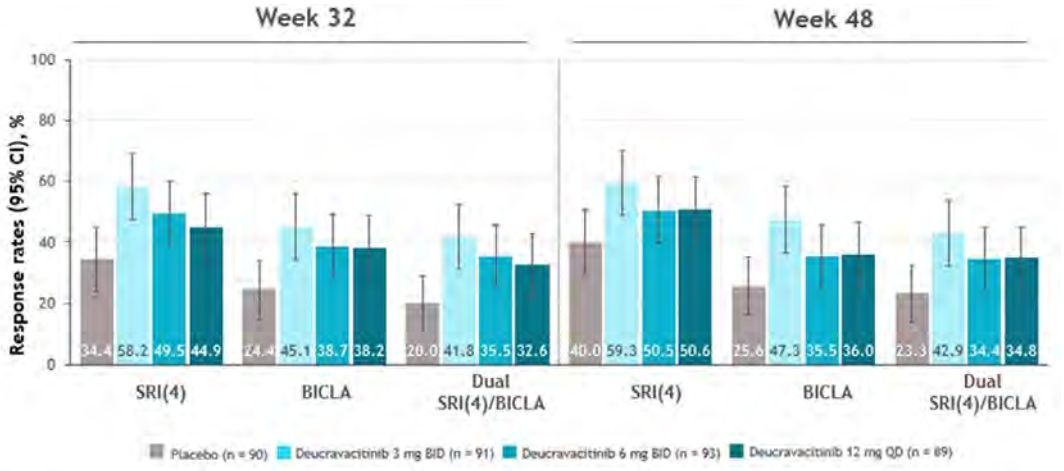
Session Date: Sunday, November 12, 2023

Session Title: SLE – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Deucravacitinib is a first-in-class, oral, selective, allosteric tyrosine kinase 2 inhibitor approved in multiple countries for the treatment of adults with plaque psoriasis. In a phase 2 trial (NCT03252587) in patients with SLE receiving standard background therapy, deucravacitinib demonstrated efficacy vs placebo across multiple endpoints, including Systemic Lupus Erythematosus Responder Index-4 (SRI[4]) responses at week 32 (primary endpoint) and week 48 (secondary endpoint) as well as British Isles Lupus Assessment Group–based Composite Lupus Assessment (BICLA) responses at week 48 (secondary endpoint).[1] Given that discordance between SRI(4) and BICLA responses has been reported with other agents,[2] this post hoc analysis further evaluated efficacy, time to response, and sustained responses with deucravacitinib vs placebo for SRI(4) and BICLA in the phase 2 trial.



BICLA, British Isles Lupus Assessment Group–based Composite Lupus Assessment; BID, twice daily; QD, once daily; SRI(4), Systemic Lupus Erythematosus Responder Index-4.

Figure 1. SRI(4), BICLA, and dual SRI(4)/BICLA response rates at weeks 32 and 48

Methods: This 48-week, double-blind trial randomized 363 patients with active SLE 1:1:1:1 to placebo or deucravacitinib 3 mg twice daily (BID), 6 mg BID, or 12 mg once daily. Endpoints included the proportions of patients achieving SRI(4), BICLA, or simultaneous (dual) SRI(4)/BICLA responses at weeks 32 and 48, time to onset of responses, and proportions of patients with sustained responses through week 48 (responder at every visit from weeks 32 through 48). BICLA response, and therefore dual response, was measurable at the first visit after steroid taper completion (week 24 [day 168]). Analyses were descriptive.

Results: At weeks 32 and 48, SRI(4), BICLA, and dual response rates were numerically higher with deucravacitinib vs placebo **(Figure 1)**. Median time to onset of SRI(4), BICLA, and dual responses were shorter with deucravacitinib vs placebo, such that median times to onset of dual response were 196 to 282 days with deucravacitinib but was not reached for placebo **(Table)**. Patients treated with deucravacitinib had a numerically higher likelihood of attaining SRI(4), BICLA, or dual SRI(4)/BICLA responses versus placebo at week 32, week 48, or sustained responses from week 32 through week 48 **(Figure 2)**.

Conclusion: Deucravacitinib elicited higher response rates and faster time to SRI(4), BICLA, and dual responses vs placebo. Patients were more likely to sustain their treatment responses from weeks 32 through 48 with deucravacitinib vs placebo. Furthermore, there was consistency between SRI(4) and BICLA responses for patients treated with deucravacitinib. These data support the robust efficacy of deucravacitinib across multiple SLE response indices.

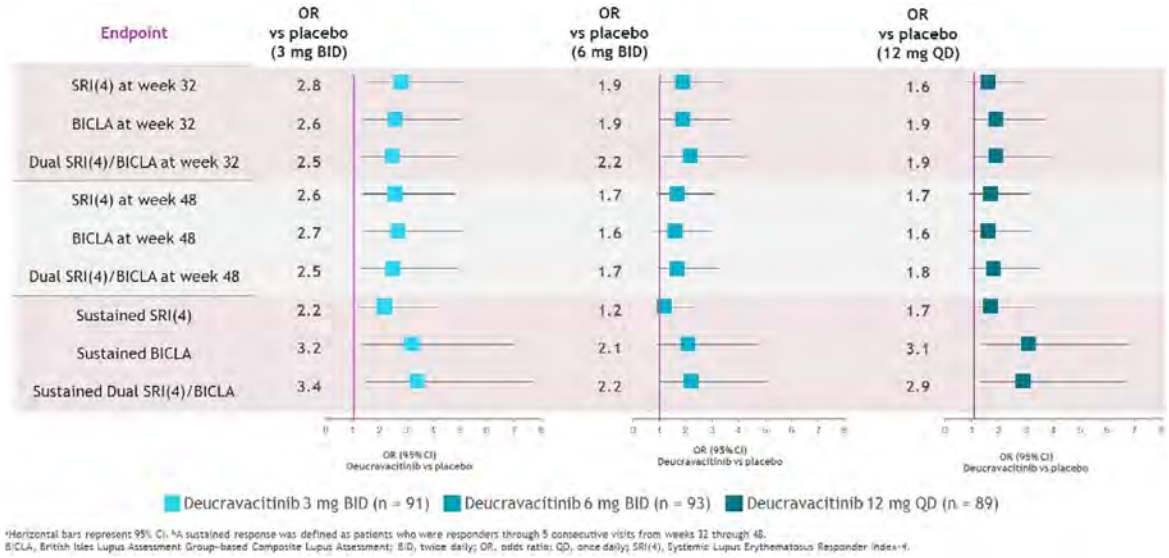


Figure 2. ORs versus placebo (a) for SRI(4), BICLA, and dual SRI(4)/BICLA at week 32, week 48, and sustained responses (b)

Table. Median time to first response for SRI(4), BICLA, and dual SRI(4)/BICLA

Outcome	Placebo (n = 90)	Deucravacitinib 3 mg BID (n = 91)	Deucravacitinib 6 mg BID (n = 93)	Deucravacitinib 12 mg QD (n = 89)
SRI(4)	116 (112, 144)	85 (85, 113)	92 (85, 138)	111 (85, 115)
BICLA	284 (176, NE*)	172 (170, 198)	224 (176, 286)	194 (170, 259)
SRI(4)/BICLA dual response	NE* (250, NE*)	196 (170, 225)	282 (198, NE*)	196 (171, NE*)

*Some points were deemed "not estimable" because they exceeded the time period of the study (48 weeks/336 days).
BICLA, British Isles Lupus Assessment Group–based Composite Lupus Assessment; BID, twice daily; NE, not estimable; QD, once daily; SRI(4), Systemic Lupus Erythematosus Responder Index-4.

References

1. Morand E, et al. *Arthritis Rheumatol*. 2023;75(2):242-252.
2. Aguirre A, et al. *Arthritis Rheumatol*. 2022; 74 (suppl 9).

Disclosure: R. Furie: Biogen, 2, 5; **C. Arriens**: AstraZeneca, 1, 5, 6, Aurinia, 6, Bristol-Myers Squibb, 1, 5, Cabaletta, 1, GSK, 1, Kezar, 1, UCB, 1; **K. Kalunian**: AbbVie/Abbott, 2, Amgen, 5, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EquilliumBio, 2, Genentech, 2, Gilead, 2, Janssen, 2, KezarBio, 1, Merck/MSD, 2, Novartis, 2, Pfizer, 2, Remegene, 2, Roche, 2, UCB, 5; **M. Pike**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, Pfizer, 2, UCB, 2; **R. van Vollenhoven**: AbbVie, 2, 6, AstraZeneca, 2, 5, 6, Biogen, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Galapagos, 2, 5, 6, GlaxoSmithKline, 6, Janssen, 2, 6, MSD/Merck Sharp and Dohme, 5, Novartis, 5, Pfizer, 2, 5, 6, RemeGen, 2, Roche, 5, Sanofi, 5, UCB, 2, 5, 6; **C. Hobar**: Bristol-Myers Squibb(BMS), 3; **A. Elegbe**: Bristol-Myers Squibb(BMS), 3; **S. Pomponi**: Bristol-Myers Squibb(BMS), 3; **S. Banerjee**: Bristol-Myers Squibb(BMS), 3, 11; **S. Singhal**: Bristol-Myers Squibb(BMS), 3; **T. Wegman**: Bristol-Myers Squibb(BMS), 3, 12, Shareholder; **E. Morand**: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 2, 5, 6, Biogen, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, EMD Serono, 2, 5, Galapagos, 2, Genentech, 2, 5, GlaxoSmithKline, 2, 5, IgM, 2, Janssen, 2, 5, Novartis, 2, Servier, 2, Takeda, 2, UCB, 5.

Abstract Number: 0597

Efficacy of Anifrolumab in Systemic Lupus Erythematosus by Overall and Organ-Specific SLEDAI-2K Improvements: Results from the Randomized, Placebo-Controlled Phase 3 Long-Term Extension Study

Richard A. Furie[1], Kenneth Kalunian[2], Eric Morand[3], Ian Bruce[4], Susan Manzi[5], Yoshiya Tanaka[6], Kevin Withrop[7], Ihor Hupka[8], Micki Hultquist[9], Raj Tummala[9], Gabriel Abreu[10], Catharina Lindholm[10] and Hussein Al-Mossawi[11], [1]Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY, [2]University of California San Diego, La Jolla, CA, [3]Monash University, Centre for Inflammatory Diseases, Melbourne, Australia, [4]University of Manchester, Manchester, United Kingdom, [5]Lupus Center of Excellence, Autoimmunity Institute, Allegheny Health Network, Pittsburgh, PA, [6]University of Occupational and Environmental Health, Kitakyushu, Japan, [7]Oregon Health & Science University, Schools of Medicine and Public Health, Portland, OR, [8]BioPharmaceuticals R&D, AstraZeneca, Warsaw, Poland, [9]BioPharmaceuticals R&D, AstraZeneca, Gaithersburg, MD, [10]BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden, [11]BioPharmaceuticals R&D, AstraZeneca, Cambridge, United Kingdom

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is a systemic autoimmune disease requiring long-term treatment. In this placebo-controlled phase 3 TULIP long-term extension (LTE) study,[1] the impact of anifrolumab in addition to standard therapy on total and organ-specific disease activity was assessed over 4 years in patients with moderate to severe SLE.

Methods: TULIP-LTE (NCT02794285) was the first randomized, placebo-controlled, double-blind, 3-year extension study in SLE. Patients with SLE (1997 ACR criteria) on standard therapy who completed a TULIP trial through the 52-week treatment period could enroll in the LTE. Treatment groups used in this analysis were patients randomized to receive intravenous anifrolumab 300 mg or placebo every 4 weeks in TULIP-1/-2 who continued the same treatment (or would have continued if not discontinued during TULIP-1/-2) in the LTE (anifrolumab 300 mg: n=358; placebo: n=178). Proportions of patients with a ≥4-point reduction in total SLEDAI-2K score from Week 0 (baseline) to Week 208 were compared between treatment groups using summary statistics. Proportions of patients with a SLEDAI-2K improvement (patients with improvement [n_1] /

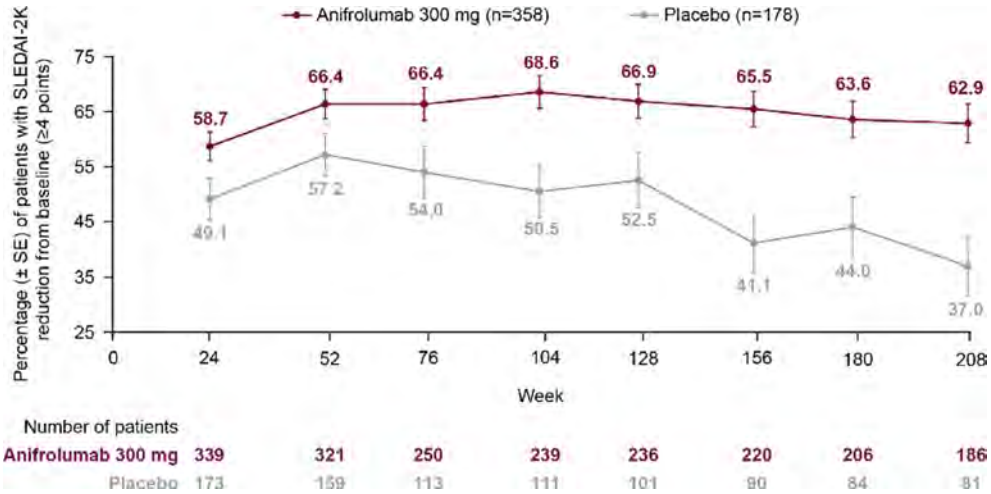


Figure. Percentage (± SE) of Patients With a SLEDAI-2K ≥4-point Reduction From Baseline* During the TULIP and LTE Period. LTE, long-term extension; SE, standard error; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE Disease Activity Index 2000. *Analysis includes patients with a SLEDAI-2K score ≥4 at TULIP baseline (Week 0) and data with discontinuation due to worsening/lack of efficacy non-improvement imputation.

patients with baseline involvement and available data at the timepoint [n_2]) were further analyzed by organ domain (mucocutaneous, musculoskeletal, immunological, hematological/fever) during the TULIP and LTE periods; SLEDAI-2K improvement was defined as a lower organ domain score than at baseline.

Results: The proportion of patients who achieved a ≥4-point reduction in SLEDAI-2K score from baseline was greater with anifrolumab vs placebo from Week 52 (66.4%, [95% confidence interval: 60.9–71.5] vs 57.2% [49.2–65.0]) to Week 208 (62.9% [55.5–69.9] vs 37.0% [26.6–48.5]), and the difference between the treatment groups increased over time (**Figure**). Baseline organ involvement was similar between treatment groups in the mucocutaneous and musculoskeletal domains (anifrolumab 300 mg vs placebo: 96.6% vs 95.5% and 93.0% vs 93.8%, respectively). Immunological and hematological/fever baseline involvement were higher in the anifrolumab group compared with placebo (65.6% vs 58.4% and 15.4 vs 9.0%, respectively). Mucocutaneous, musculoskeletal, immunological, and hematological/fever SLEDAI-2K improvements generally occurred more frequently in the anifrolumab group compared with placebo from Week 52 (73.5% [n_1/n_2: 227/309] vs 60.9% [92/151]; 67.9% [201/296] vs 64.9% [96/148]; 28.8% [61/212] vs 17.2% [16/93]; and 81.6% [40/49] vs 80.0% [12/15]) up to Week 208 (79.8% [142/178] vs 58.7% [44/75]; 71.8% [122/170] vs 56.0% [42/75]; 32.1% [36/112] vs 14.6% [6/41]; and 72.4% [21/29] vs 42.9% [3/7]). By the end of the LTE period, many patients had missing data in the placebo group, due to lack of organ involvement and/or no available data at the timepoint.

Conclusion: Compared with placebo, anifrolumab was associated with long-term, sustained ≥4-point reductions in SLEDAI-2K over the 4-year TULIP and LTE period and, despite the higher drop-out rates in the placebo group, greater improvements were seen in disease activity for individual organ domains.

References: 1. Kalunian KC, et al. *Arthritis Rheumatol*. 2023;75:253–65.

Disclosure: R. Furie: AstraZeneca, 2, 5, 6; **K. Kalunian**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Biogen, 2, Bristol-Myers Squibb, 2, Eli Lilly, 2, Genentech/Roche, 2, GlaxoSmithKline, 2, Janssen, 2, Pfizer, 2; **E. Morand**: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 2, 5, 6, Biogen, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, EMD Serono, 2, 5, Galapagos, 2, Genentech, 2, 5, GlaxoSmithKline, 2, 5, IgM, 2, Janssen, 2, 5, Novartis, 2, Servier, 2, Takeda, 2, UCB, 5; **I. Bruce**: AstraZeneca, 1, 2, 5, 6, Aurinia, 2, GSK, 1, 2, 5, 6, Janssen, 5, 6, Lilly, 1, UCB, 6; **S. Manzi**: AbbVie, 5, Allegheny Singer Research Institute, 10, AstraZeneca, 2, 5, Exagen Diagnostics, Inc, 2, 9, 10, GSK, 2, 5, Lilly, 2, Lupus Foundation of America, 4, Novartis, 2, UCB Advisory Board, 2, Univiersity of Pittsburgh, 10; **Y. Tanaka**: AbbVie, 6, AstraZeneca,

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Abstract Number: 0598

Litifilimab Modulates Type I IFN Biomarkers in Patients with SLE or CLE in the Phase 2 LILAC Study

Richard Furie[1], Victoria Werth[2], Eric Milliman[3], Kyle Ferber[3], Fergal Casey[3], Roland Brown[3], Denitza Raitcheva[3], Jad Zoghbi[3], Danielle Graham[3], George Kong[3], Youmna Lahoud[3], Nathalie Franchimont[4] and Catherine Barbey[5], [1]Northwell Health, Manhasset, NY, [2]University of Pennsylvania and Corporal Michael J. Crescenz VAMC, Philadelphia, PA, [3]Biogen, Cambridge, MA, [4]Former employee of Biogen, Cambridge, MA, [5]Biogen, Baar, Switzerland

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Litifilimab is a humanized IgG1 mAb targeting BDCA2, a receptor expressed on plasmacytoid dendritic cells (pDCs), that negatively regulates the production of Type I IFN and proinflammatory chemokines and cytokines.[1,2] In the Phase 2 LILAC study of litifilimab (NCT02847598), Part A (participants with SLE, active arthritis and rash) and Part B (participants with active CLE, with or without SLE) met their primary endpoints at Weeks (W) 24 and 16, respectively.[1,2] We evaluated the effects of litifilimab on IFN gene signature (IFNGS) scores from whole blood samples, serum IFNα concentrations, and other serum cytokine concentrations in LILAC participants.[3,4]

Methods: Expression of 22-gene panel IFNGS scores and concentrations of IFNα and other cytokines were examined over time in the modified intent-to-treat population (Part A N=120, Part B N=132) with available data at baseline (BL) and ≥1 post-BL visit. Treatment effects were estimated using a mixed model repeated measures approach. In Part A, IFNα concentration changes over time were compared with W24 total active joint counts and CLASI-A scores (Spearman rank correlations) and SLE Responder Index (SRI-4) status. In Part B, Pearson correlations between percent changes in CLASI-A score and IFNGS score were estimated and the dose-response relationship was estimated using a previously described MCP-Mod method.[2]

Results: As too few participants were IFNGS-low at BL, only data for the IFNGS-high subgroups are described. Litifilimab induced rapid, substantial, and sustained reductions in 22-gene IFNGS scores and IFNα concentrations that were greater (nominal $P< 0.05$) vs placebo (PBO) with litifilimab 150 mg (Part B) and 450 mg (Parts A and B) (**Table 1** and **Figure 1**). In Part A, TNFα and IL-10 concentrations were reduced (nominal $P< 0.05$) with litifilimab 450 mg at W24 (**Table 1**); no strong evidence of this was seen in Part B. Change in IFNα concentration and change in total active joint count with litifilimab 450 mg in Part A were correlated (Spearman correlation estimates: PBO –0.15 [95% CI: –0.41, 0.16]; 450 mg 0.34 [0.07, 0.55]), as were changes in IFNα concentration and CLASI-A score (PBO –0.01 [–0.34, 0.31]; 450 mg 0.35 [0.10, 0.58]) at W24. A trend of greater median IFNα concentration reduction in W24 SRI-4 responders relative to non-responders was seen with litifilimab 450 mg. Confirmation of these findings in larger sample sizes is warranted. In Part B, the dose-response relationship was similar to that observed with the clinical responses (**Figure 2**) and percent change in CLASI-A score was correlated with percent change in IFNGS score in all treatment groups.

Table 1. Primary efficacy endpoints and changes from BL in 22-gene panel IFNGS score and IFNα concentration for the IFNGS-high subgroup (modified intent-to-treat population). Data are LS means unless otherwise specified. Variations in n within each group at any timepoint are the result of missing samples and/or different analysis populations. *Assessed in participants who met the joint count inclusion criterion for Part A: ≥4 tender joints and ≥4 swollen joints according to a 28-joint assessment (≥4 swollen joints must have been in PIP, MCP, or wrist joints; participants were not required to have coexistent swelling and tenderness of individual joints);1 †total active joint count is the sum of the tender joint count and the swollen joint count; ‡ratio between the GM fold change from BL in the litifilimab arm and the GM fold change from BL in the placebo arm; values <1 favor litifilimab. BL, baseline; CI, confidence interval; CLASI-A, Cutaneous Lupus Erythematosus Disease Area and Severity Index–Activity; GM, geometric mean; GMR, geometric mean ratio; IFNGS, interferon gene signature; LS, least squares; PBO, placebo

Part A	PBO	450 mg
n*	35	42
Primary endpoint: Change in number of active joints† at Week 24, n	−11	−15
n	45	49
Change in IFNGS score, %		
Week 1	−6	−37
Week 24	−5	−38
IFNGS GMR‡ vs PBO at Week 24 (95% CI)		0.66 (0.48, 0.89) P=0.0072
n	41	48
Change in IFNα concentration, %		
Week 1	5	−77
Week 24	17	−74
IFNα GMR‡ vs PBO at Week 24 (95% CI)		0.22 (0.11, 0.44) P<0.0001
n	40	47
Change in TNFα concentration, %		
Week 1	−1	−1
Week 24	9	−18
TNFα GMR‡ vs PBO at Week 24 (95% CI)		0.74 (0.59, 0.95) P=0.0164
n	40	47
Change in IL-10 concentration, %		
Week 1	6	14
Week 24	8	−23
IL-10 GMR‡ vs PBO at Week 24 (95% CI)		0.72 (0.54, 0.95) P=0.0228

Part B	PBO	50 mg	150 mg	450 mg
n*	29	24	23	40
Primary endpoint: Change in CLASI-A score at Week 16, %	−11	−41	−50	−44
n	29	24	23	39
Change in IFNGS score, %				
Week 2	−18	−36	−50	−42
Week 16	−12	−40	−65	−55
IFNGS GMR‡ vs PBO at Week 16 (95% CI)		0.69 (0.45, 1.05) P=0.0805	0.40 (0.26, 0.61) P<0.0001	0.51 (0.35, 0.75) P=0.0006
n	28	24	23	40
Change in IFNα levels, %				
Week 1	−14	−64	−75	−64
Week 16	−31	−63	−82	−73
IFNα GMR‡ vs PBO at Week 16 (95% CI)		0.54 (0.25, 1.18) P=0.1225	0.26 (0.12, 0.58) P=0.0012	0.40 (0.20, 0.79) P=0.0088

Conclusion: Litifilimab induced a rapid, substantial, and sustained reduction in 22-gene IFNGS scores and IFNα concentrations, and reductions in some biomarkers correlated with clinical responses. These results further support the mechanism of action for litifilimab and the role of Type I IFN and pDCs in SLE and CLE.[5,6]

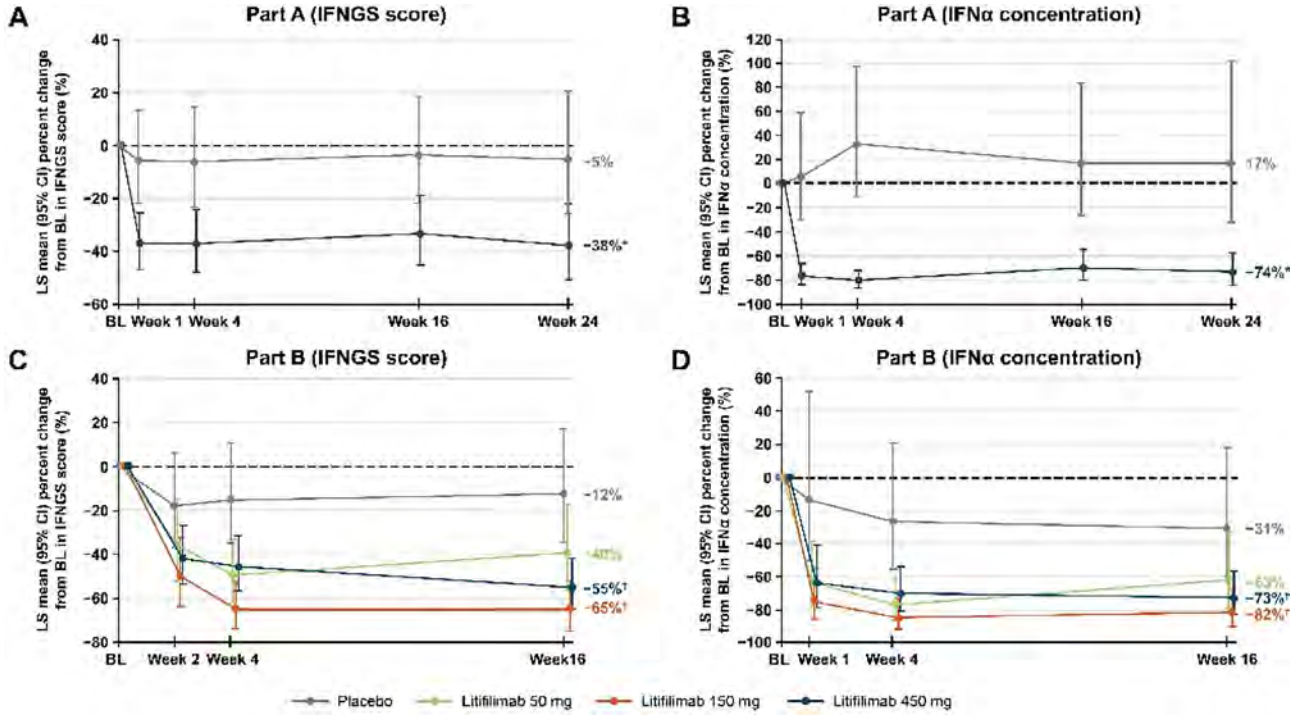

Figure 1. Change in IFNGS score and IFNα concentration over time in Part A (A and B) and Part B (C and D) of the Phase 2 LILAC study for the IFNGS-high subgroup. *At Week 24 (Part A), nominally significant (P<0.05) changes from BL in 22-gene panel IFNGS score and IFNα concentration were demonstrated for the litifilimab 450-mg group relative to placebo using GMRs; †at Week 16 (Part B), changes in IFNGS score and IFNα concentration were nominally significant (P<0.05) for the litifilimab 150- and 450-mg groups relative to placebo using GMRs. BL, baseline; CI, confidence interval; GMR, geometric mean ratio; IFNGS, interferon gene signature; LS, least squares

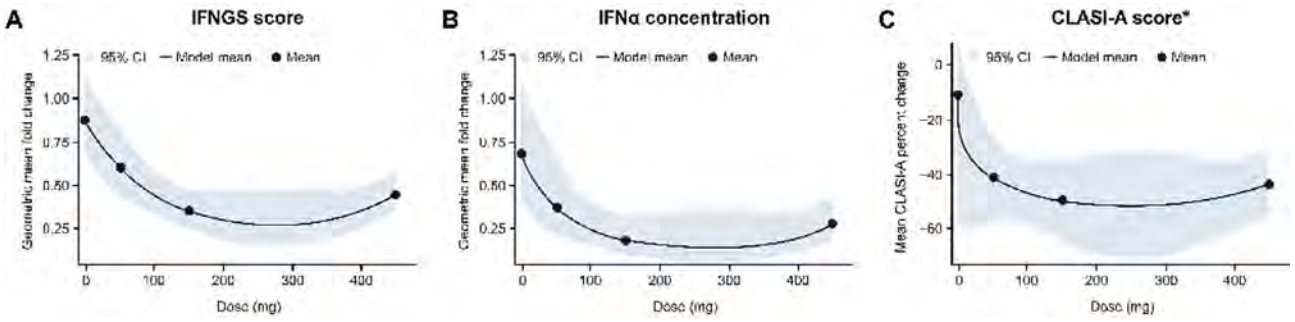

Figure 2. MCP-Mod analysis from Part B of the Phase 2 LILAC study for fold change in IFNGS score (A), fold change in IFNα concentration (B), and percent change in CLASI-A score (clinical response; C) at Week 16 for the IFNGS-high subgroup. Dose-response relationships are based on the MCP-Mod method. The MCP-Mod method uses a two-step process: a multiple comparison step to test for the presence of a significant dose-response relationship, in which placebo serves as a dose of 0 mg, and a modeling step to fit the best dose-response curve. Further details can be found in Werth VP, et al (2022).2 *CLASI-A data include participants with missing baseline biomarkers data. CI, confidence interval; CLASI-A, Cutaneous Lupus Erythematosus Disease Area and Severity Index–Activity; IFNGS, interferon gene signature; MCP-Mod, multiple comparison procedure–modeling

[1]Furie R et al. N Engl J Med 2022;387:894–904
[2]Werth V et al. N Engl J Med 2022;387:321–331
[3]Werth V et al. J Invest Dermatol 2023;143(5 Supp):S101
[4]Furie R et al. Ann Rheum Dis 2023;82(1 Supp):1453–1454
[5]Fetter T et al. Front Med (Lausanne) 2022;9:915828
[6]Rönnblom L, Leonard D. Lupus Sci Med 2019;6:e000270

Disclosure: R. Furie: Biogen, 2, 5; **V. Werth**: Abbvie, 2, Amgen, 2, 5, AnaptysBio, 2, Argenx, 5, AstraZeneca, 2, Biogen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Corbus, 5, CSL Behring, 2, 5, EMD Serono, 2, Galderma, 2, Genentech/Roche PI, 5, Gilead, 2, 5, GSK, 2, Horizon Therapeutics, 5, Janssen, 2, Kyowa Kirin, 2, Lilly, 2, Merck, 2, Nektar, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Regeneron, 5, Rome Therapeutics, 2, 5, Sanofi, 2, Ventus, 5, Viela, 2, 5, Xencor, 2; **E. Milliman**: Biogen, 3, 11; **K. Ferber**: Biogen, 3, 11; **F. Casey**: Biogen, 3, 11; **R. Brown**: Biogen, 3, 11; **D. Raitcheva**: Biogen, 3, 10, 11, Novartis, 3, 11; **J. Zoghbi**: Biogen, 3, 11; **D. Graham**: Biogen, 3, 11; **G. Kong**: Biogen, 3, 11; **Y. Lahoud**: Biogen, 3, 11; **N. Franchimont**: Alexion/AstraZeneca, 3, 11, Biogen, 3, 11, Nimbus Therapeutics, 3, 11, OMass Therapeutics, 4, 11; **C. Barbey**: Biogen, 3, 11.

Abstract Number: 0599

Targeted Inhibition of Cathepsins Limits the Intracellular Complement Activation in Lupus Nephritis Podocytes

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease that leads to damage to several tissues and organs. Inflammation of the kidney is one of the most severe manifestattions of SLE that leads to lupus nephritis (LN). Podocytes are critical for the maintenance of the glomerular filtration barrier and are injured in many kidney diseases including LN. The pathogenesis of LN involves the activation of the complement system and deposition of immune complexes. While the established pathways of complement activation are well-known, recent studies have revealed that complement component C3 can undergo activation within the cell. Specifically, proteases belonging to the cathepsin family have been shown to cleave C3 and C5, thereby introducing a novel pathway for complement activation. In this study, we investigated the production and activation of complement within the podocytes in LN, focusing on the role of cathepsin inhibition as a potential therapeutic tool to reduce intracellular complement activation

Methods: Human immortalized podocytes were cultured on engineered cell-derived decellularized matrix (DCM) coated plates (Adv. Funct. Mater. 2020, 30(44):1908752*)*. Podocytes were then exposed to IgG from patients with LN or to hypoxia. Cathepsin was inhibited *in vitro* and *in vivo* using nanoparticles (NP) loaded with E64d, a cathepsin inhibitor, and tagged with a nephrin antibody. MRL*lpr,* lupus-prone mice, and MRL*MpJ* control mice, received E64d or empty NP intravenously weekly starting at ages between weeks 8 and 12, followed by tissue harvesting at week 19. Differences at the levels of specific proteins, including C3, C3d, C5b9, and IgG, between E64d-treated and empty NP groups were analyzed. Due to non-normality of residuals, the Wilcoxon-Mann-Whitney test was used for statistical comparison. A p-value < 0.05 was considered significant.

Results: Human podocytes exposed to LN IgG or to hypoxia displayed increased production of C3, C4, C5b9, and C3 activation products. In parallel, podocytes produced cathepsins, and cathepsin inhibition using E64d NP curbed the intracellular C3 activation. There were no significant differences observed in C3 deposition between E64d-treated *vs* empty NP-treated mice, in either MRL*lpr* or MRL*MpJ* mice. The production though of C3d and the deposition of IgG were significantly decreased in the MRL*lpr* and MRL*MpJ* mice treated with E64d NP ($p< 0.05$).

Conclusion: Targeted inhibition of cathepsins in podocytes using E64d-loaded and nephrin antibody-tagged NP effectively reduced intracellular C3 activation in human podocytes exposed to LN IgG or hypoxia, as well as in MRL*lpr* and MRL*MpJ* mice. Furthermore, E64d-loaded NP treatment showed a significant decrease in IgG deposition in the mice. This study sheds light on the production of complement components by podocytes and their cathepsin-dependent intracellular activation. More importantly, our experiments indicate that targeted inhibition of complement activation in podocytes averts the deposition of IgG.Our findings have implications for the development of novel treatment strategies for LN and related autoimmune kidney diseases.

Disclosure: A. Kunzler: None; **M. Jha**: None; **M. Umeda**: None; **R. Bhargava**: None; **M. Tsokos**: None; **G. Tsokos**: None; **A. Satyam**: None.

Abstract Number: 0600

Identification of Subsets of SLE Patients Responsive to Baricitinib by Transcriptomic Analysis at Baseline

Prathyusha Bachali[1], Amrie Grammer[2] and Peter Lipsky[2], [1]AMPEL BioSolutions, Redmond, WA, [2]AMPEL BioSolutions, Charlottesville, VA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Baricitinib is an inhibitor of Jak1 approved for treatment of rheumatoid arthritis, atopic dermatitis, alopecia areata and Covid-19. A phase 2 trial showed success in treating SLE (NCT02708095), but it did not meet its primary endpoint in phase 3 trials(NCT03616964, NCT03616912). To understand the possible dichotomy between these trial results and identify patients with SLE potentially responsive to baricitinib, baseline transcriptomic analysis was carried out in patients enrolled in the phase 2 trial. The goals of this study were to identify the transcriptomic profile of SLE patients who were responsive to baricitinib and the impact of the agent on gene expression abnormalities.

Methods: Baseline whole blood samples from 272 SLE patients from the phase 2 baricitinib trial were utilized for this analysis. These patients had active disease determined by SLEDAI-2K >/=6 and involvement of skin and joints. Patients were randomized to placebo, or one of two doses of baicitinib (2 of 4 mg once daily). Clinical response was determined by perectage of patients resolving skin or joint involvement at 24 weeks using the SLEDAI-2K instrument. RNAseq was performed and analyzed by Gene Set Variation Analysis (GSVA) using 32 informative gene modules and a machine learning (ML) model tested and validated on 3,166 lupus patients from 17 datasets.

Results: ML analysis of GSVA scores from baseline samples of 272 patients yielded 8 subsets (Figure 1). Subset A had the fewest molecular abnormalities, whereas Subset H had the most disturbances in immune function, including enrichments in the IGS, immunoproteasome, IL-1/ inflammasome pathway, and neutrophil/granulocyte genes and lymphopenia. Clusters B-G had intermediate degrees of abnormal enrichment in specific gene modules. No significant differences in baseline demographic characteristics were noted between the subsets. There were significant but modest differences between subsets in baseline anti-DNA and complement C3 and C4, but no differences in SLEDAI-2K scores. Significant clinical responses to baricitinib were confined to subsets D and G (Figure 2). Effect sizes of responses in these groups were > 30%. Other subsets had higher placebo responses and no additional response to baricitinib. Treatment with baricitinib

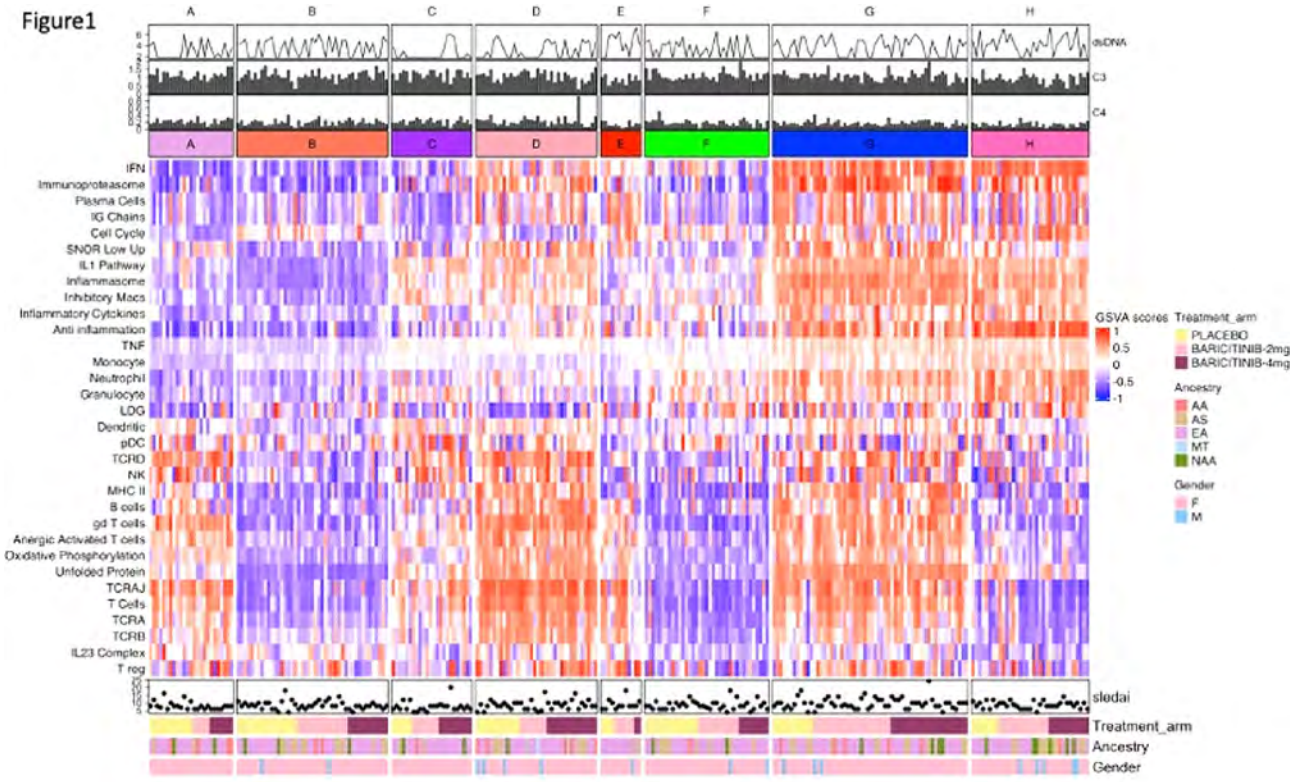

Figure1: Random Forest classifier revealed 8 SLE subsets in 272 baseline lupus samples.
Model weights from random forest (ML) model built on 3166 lupus samples[2183-train,983-test] using 32 gene informative signatures were used to classify the 272 baseline samples into 8 lupus subsets [A-H] ordered by "the least abnormal" to "the most abnormal" immunologic activity. The 8 lupus subsets are visualized by ComplexHeatmap in R.

resulted in significant decreases in the interferon, immunoproteasome, inflammasome, monocyte, granulocye and inflammatory cytokine signatures among others, with improvement observed within 4 weeks of treatment onset. (Figure 3).Notably, gene modules downstream of JAK1, JAK2 and TyK2 were significantly decreased by baricitinib, but not placebo treatment.

Figure2

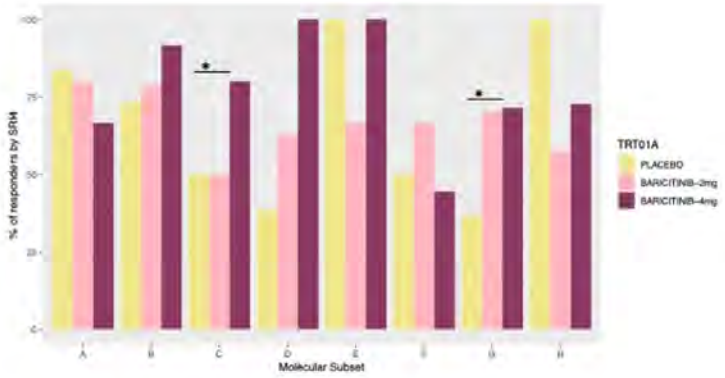

Figure2: Clinical response of lupus patients in lupus subsets by SRI4 reveals a significant response to the Baricitinib 4mg in subset D & G. Statistical differences between samples received Placebo and two doses (2mg,4mg) of Baricitinib is calculated by Chi-square test (* pval < 0.05)

Figure3

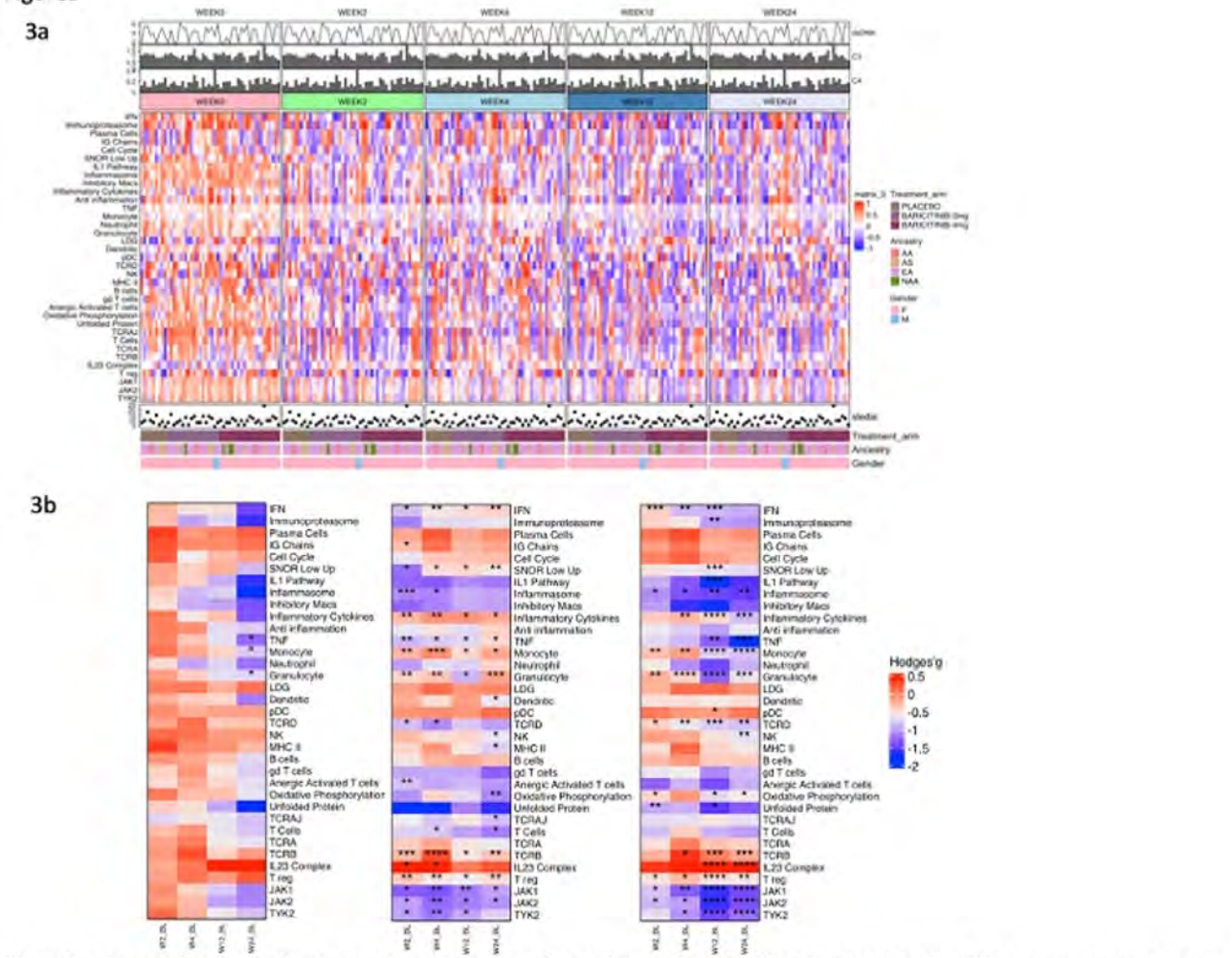

Figure3. Timeseries analysis of samples in lupus subset G explains significant decrease in IFN, Immunoproteasome, Inflammasome, Monocyte, Inflammatory cytokines, TNF, JAK1, JAK2, and TYK2 signatures. 3a)GSVA scores of samples from subset G across week0, week4, week12, week24 were visualized using ComplexHeatmap in R. 3b) Hedges' g effect sizes of cellular and process gene modules for week4, week12, and week24 compared to week0 in pateints treated with Placebo, and two doses of Baricitinib were calculated. The heatmap visualizes the increased gene expression (> 0) in red and decreased gene expression (< 0) in blue. Welch's t-test p values are referred by * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$

Conclusion: Transcriptomic analysis of of baseline samples using GSVA scores from informative gene modules and ML successfully clustered patients into subsets that exhibited differences in response to baricitinib treatment. Treatment with baricitinib altered gene expression profiles in a manner consistent with the known action of the agent. Gene expression based subsetting may be useful to enrich trials for responsive patients and monitor the impact of therapy.

Disclosure: P. Bachali: None; **A. Grammer**: None; **P. Lipsky**: None.

Abstract Number: 0601

Selective Disposition of Voclosporin, Cyclosporine, and Tacrolimus in Renal Tissue

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The calcineurin inhibitors (CNI) cyclosporine (CSA) and tacrolimus (TAC) were revolutionary when first introduced for solid organ transplant. Voclosporin (VCS), a novel CNI, is the first oral therapy approved for the treatment of active lupus nephritis. Unlike CSA and TAC, VCS has demonstrated consistent pharmacokinetics and pharmacodynamics, eliminating the need for therapeutic drug monitoring. Further, VCS is associated with a more favorable metabolic profile and has not been associated with electrolyte disturbances.

Emerging evidence indicates small molecule therapies display differential disposition within organ tissues. This suggests that CNIs may be differentially distributed and retained in the kidney, potentially explaining differences in their efficacy and safety. Here we assessed in mice and humans the disposition of each CNI in the kidney relative to its systemic drug exposure.

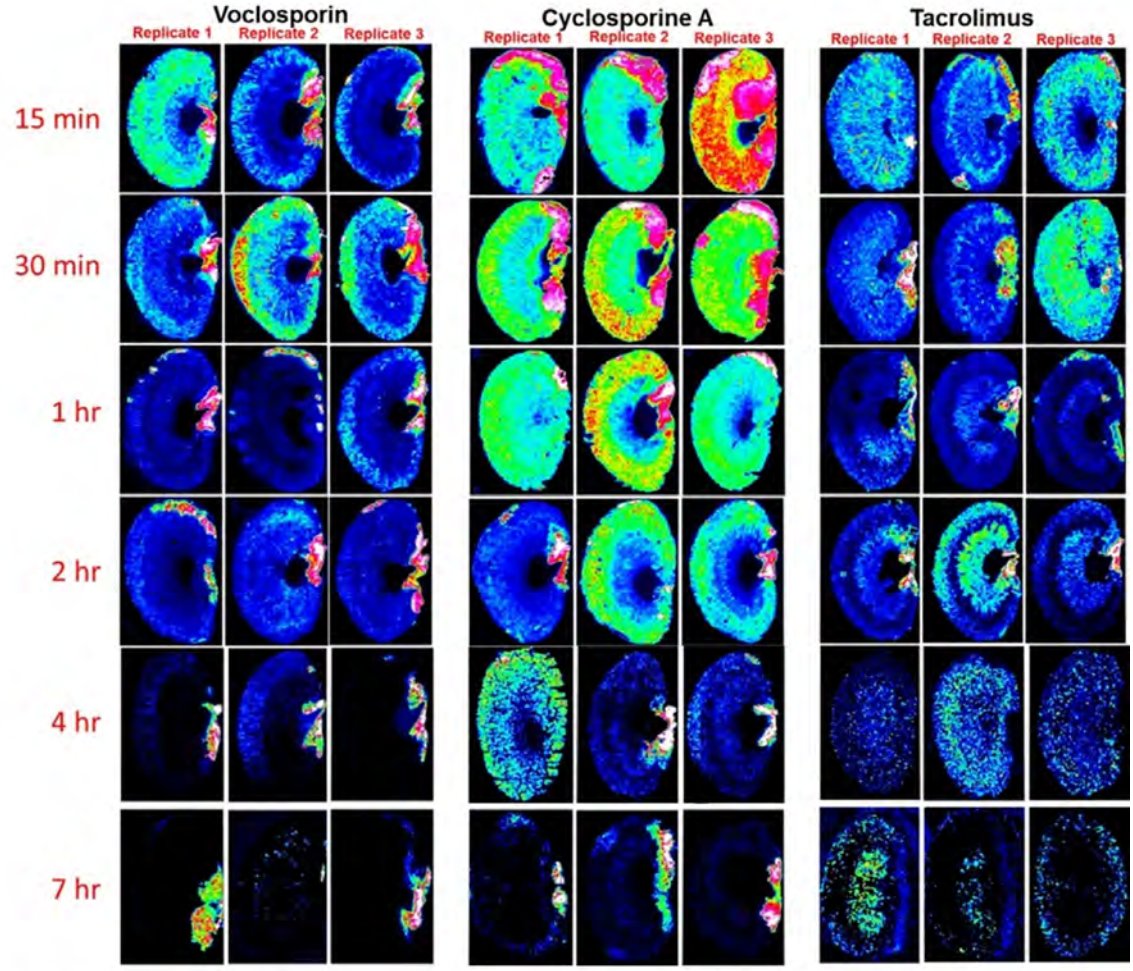
Methods: Single 30 mg/kg doses of CSA, TAC and VCS were administered intravenously (IV) to mice. Following IV administration, kidneys were collected at various time points, flash frozen in liquid nitrogen, and stored at -20 ^{0}C. Sections of kidney tissue were mounted on indium tin oxide coated glass slides. Matrix of 10 mg/mL α-Cyano-4-hydroxycinnamic acid in 85% acetonitrile/13% ethanol + 2% water + 0.1% trifluoroacetic acid was sprayed on the tissue, dried for 10 minutes, and subjected to Matrix-assisted Laser Desorption and Ionization Mass Spectrometry Imaging (MALDI-MSI). The systemic and renal clearance (CLr) in humans of CSA and TAC were obtained from literature; pharmacokinetic data on VCS was obtained from data on file. Renal secretion of each drug was compared to its expected passive filtration based on glomerular filtration rate (GFR), fraction unbound in plasma (fu), and respective systemic drug exposure.

Results: MALDI-MSI demonstrated significantly higher concentrations of drug and more diffuse tissue disposition of CSA in mouse kidney compared to VCS (Figure 1). CSA was retained up to 2 hrs post-administration. Higher concentrations and more diffuse disposition of TAC was also noted compared to VCS at 15 and 30 min; TAC was distinctively retained in the cortex and medulla. VCS had moderate distribution in the cortex and was rapidly excreted with low levels present in the kidney after 1 hr.

According to published data, CSA has a measured renal CLr of 1.48 mL/min in humans, representing approximately 10% of expected passive filtration of 12.5 mL/min (Table 1). TAC has a CLr of 0.014 mL/min representing < 2% of expected passive filtration of 1.25 mL/min. VCS has a CLr of 7.82 mL/min representing approximately 200% of its expected passive filtration rate of 3.75 mL/min.

Conclusion: MALDI-MSI revealed differential retention and distribution of CSA, TAC and VCS in mice, consistent with their CLr in humans. Higher drug exposure and >90% renal reabsorption was observed for CSA and TAC, whereas renal handling of VCS suggested significant tubular secretion. The higher rate of secretion and lower overall renal exposure to VCS

Figure 1. MALDI-MSI of voclosporin, cyclosporine, and tacrolimus in mouse kidney over time



CSA, cyclosporine; K, potassium; Tac, tacrolimus; VSP, voclosporin.

Table 1. Published pharmacokinetic data in humans

	CL	CL/F	fu	Expected CLr (GFR*fu)	CLr
Cyclosporine A	210-240 mL/min	500-600 mL/min	10%	12.5 mL/min	1.48 mL/min
Tacrolimus	37.5 mL/min	NA	1%	1.25 mL/min	0.014mL/min
Voclosporin	NA	1060 mL/min	3%	3.75 mL/min	7.82 mL/min

1. Ptachcinski R et al. Clin Pharmacokinet. 1986;11(2):107-32. 2. Moller A et al. Drug Metab Dispos. 1999;27(6):633-6. 3. Mayo PR et al. J Clin Pharmacol. 2013;53(8):819-26.

CL, clearance; CLr, renal clearance; CSA, cyclosporine A; F, bioavailability; fu, fraction unbound in plasma; GFR, glomerular filtration rate; NA, not applicable; TAC, tacrolimus.

may be associated with improved safety when compared to the more diffuse distribution and greater renal retention of CSA and TAC.

Disclosure: S. Zhou: Aurinia Pharmaceuticals Inc., 3, 11; **K. Kumari Rajanayake**: None; **M. He**: None; **B. Wen**: None; **A. Lkhagva**: Aurinia Pharmaceuticals Inc., 5; **E. Yap**: Aurinia Pharmaceuticals, 3, 11; **D. Sun**: Aurinia Pharmaceuticals, 5, 7; **J. Cross**: Aurinia Pharmaceuticals Inc., 3; **K. Engelke**: Aurinia Pharmaceuticals, 3; **R. Huizinga**: Aurinia Pharmaceuticals, 2, 9, 10.

Abstract Number: 0602

Dual Blockade of ICOS and CD28 with Acazicolcept (ALPN-101) Reveals Non-Redundant Roles of T Cell Co-Stimulation Pathways in Systemic Lupus Erythematosus

Elizabeth Repash, Tiffany Blair, Amanda Enstrom, Lawrence Evans, Susan Debrot, Katherine Lewis, Armand Bankhead, Stanford Peng and Stacey Dillon, Alpine Immune Sciences, Inc., Seattle, WA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: CD28 and inducible T cell costimulator (ICOS) play nonredundant roles in T cell activation and inhibiting these pathways can ameliorate an (auto)immune response. Systemic lupus erythematosus (SLE) is characterized by the dysregulation of T and B cell activation. Transcriptional analyses have revealed upregulation of CD28 and ICOS ligand/receptor genes in SLE[1], but single pathway inhibition has not proven clinically effective in SLE and related diseases.[2,3] Acazicolcept is an Fc fusion protein of a human variant ICOS-ligand (ICOSL) domain designed to block CD28 and ICOS simultaneously. We conducted *in vitro* assays with healthy donor (HD) and SLE patient PBMCs to analyze acazicolcept or comparators to suppress inflammatory mediators that promote disease pathogenesis. Additionally, acazicolcept was evaluated in a SLE mouse model.

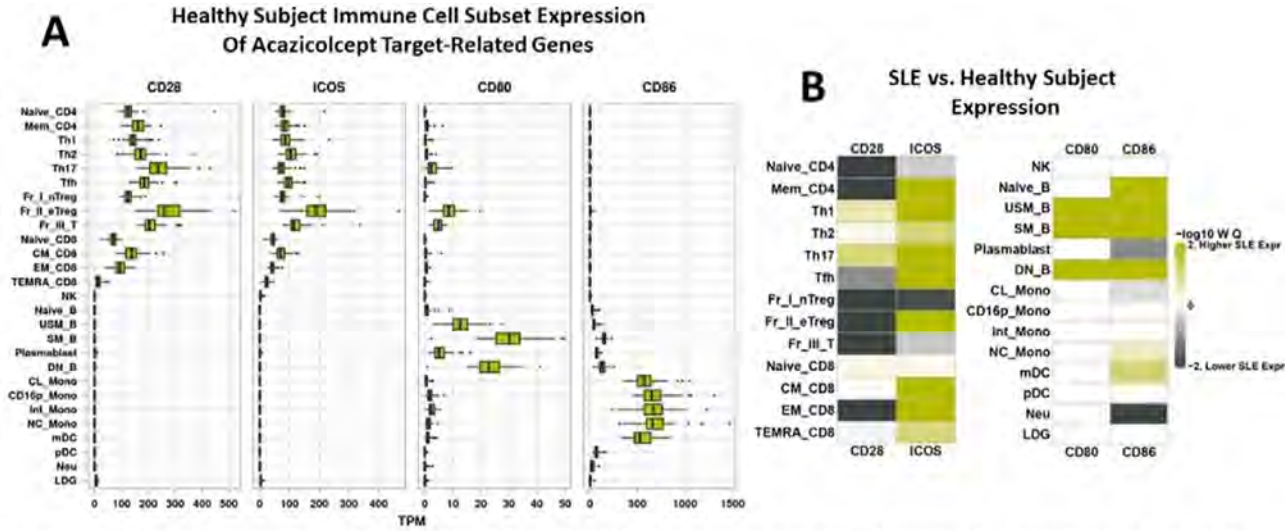


Figure 1: RNA-Seq expression of acazicolcept target-related genes in sorted PBMC subsets reported by Ota *et al.* **A** Transcripts per million (TPM) expression values for healthy sample immune cell subsets. **B** TPM values were $\log_2$ transformed and converted to z-scores for SLE vs. healthy donor comparison. Heat map colors represent negative $\log_{10}$ q-values from Wilcoxon tests between ~60 SLE and ~70 healthy subjects with positive (*green*) values representing higher SLE patient expression and negative (*black*) values representing lower SLE patient expression. White heat map values indicate either non-significance (q-values ≈1) or low expression (healthy subject median expression ≤ 10). TPM values displayed were upper quartile normalized.

Methods: HD or SLE PBMCs were stimulated with artificial antigen presenting cells expressing CD80, CD86, ICOSL and anti-CD3 (OKT3) for 48h with 100 nM of Fc control protein, acazicolcept, or comparators directed against CD28 (abatacept, [CTLA-4-Ig]) or ICOS (prezalumab [anti-ICOSL mAb]) or combined abatacept/prezalumab. Supernatants and cells were analyzed for cytokine production and gene expression. Acazicolcept was compared *in vivo* to abatacept (CTLA4-Ig) in a bm12 induced mouse model of lupus[4]. C57BL/6 recipient mice were treated 2x/wk with acazicolcept or abatacept (N=12), from Days 0-93. Serum anti-double stranded (ds) DNA antibody concentrations were measured, and frozen kidney sections collected on Day 100 wereanalyzed for IgG deposition.

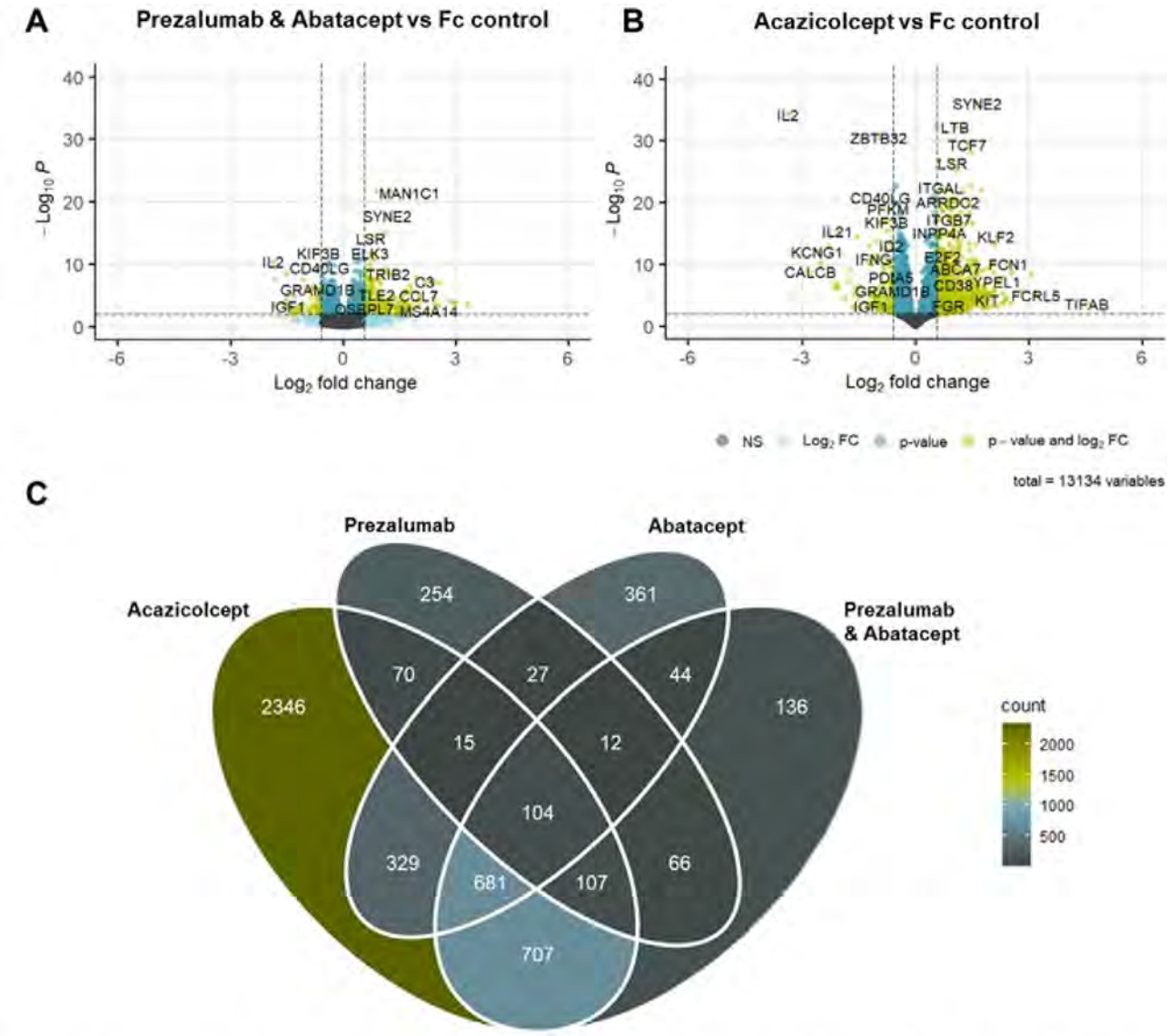


Figure 2: Acazicolcept potently downregulates genes associated with T cell activation in SLE donor PBMC stimulated with K562 cells expressing anti-CD3 (OKT3), CD80, CD86 and ICOSL. Volcano plots display differentially expressed genes from the following comparisons: **A** prezalumab and abatacept vs Fc control and **B** acazicolcept vs Fc control. Green dots represent differentially expressed genes that pass significance threshold with a p value < 0.001 and a $\log_2$ fold change cutoff with an absolute value greater than 0.58. Light blue dots pass the p value cutoff but not the fold change threshold, dark blue dots pass a fold change cutoff but not the p value threshold, and gray dots are not significant. **C** Venn diagram featuring differentially expressed genes (threshold $\log_2$ fold change > 0.58 or < -0.58 with a p value < 0.001) derived from the individual comparisons of acazicolcept, prezalumab, abatacept, or prezalumab & abatacept versus Fc control.

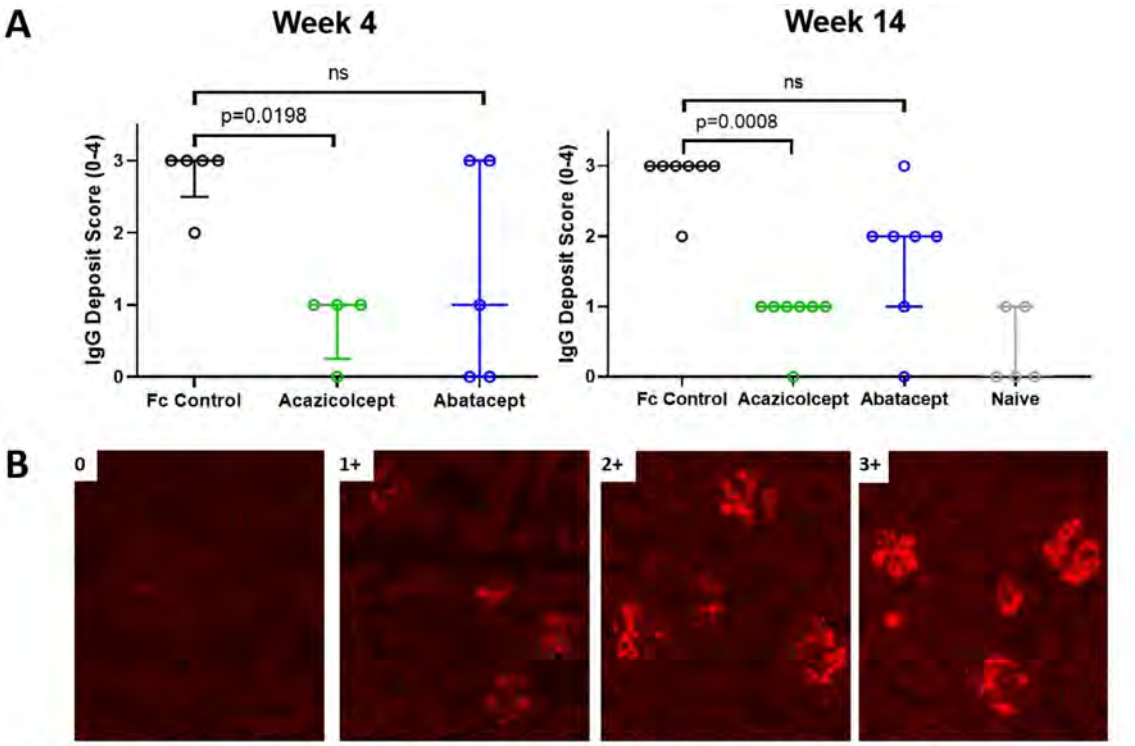


Figure 3: Acazicolcept significantly reduces glomerular IgG deposition in the bm12 induced mouse model of lupus. At termination (week 4 and week 14), kidneys were harvested from each mouse and frozen, sectioned, and stained with anti-mouse IgG antibody. The extent of mouse IgG staining indicating immune complex deposition was semi-quantitatively scored; the glomerular IgG deposit scores for each kidney collected for each treatment group at week 4 (left)and week 14 (right) are plotted in **A**. Representative sections (original magnification, 10X) for each score are shown in **B**. Data shown in **A** are from individual mice; horizontal bars and vertical error bars represent the group median ± interquartile range, respectively. Statistically significant differences between treatment groups were assessed via Kruskal-Wallis test with uncorrected Dunn's test; p values <0.05 were considered statistically significant.

Results: Acazicolcept more potently suppressed expression of genes associated with T cell activation than the abatacept or prezalumab comparators, alone or combined. Gene expression analyses revealed distinct transcriptional profiles between PBMC from HD vs. SLE patients (**Fig 1**), in agreement with previously published findings. Furthermore, acazicolcept suppressed pro-inflammatory cytokine production and inhibited pathways associated with immune activation including Th1 and Th2 activation and IL-17 signaling (**Fig 2**). In the bm12 model, acazicolcept significantly reduced serum titers of anti-dsDNA autoantibodies compared to Fc control on Weeks 2 and 6. IgG deposition scores in the kidneys of acazicolcept-treated mice were significantly lower than the Fc control group at Weeks 4 (p=0.0198) and 14 (p=0.0008), while these scores in the abatacept-treated mice were not significantly different than the Fc control group (**Fig 3**).

Conclusion: Taken together, these and previous findings indicate that simultaneously inhibiting ICOS and CD28 pathways may result in significant disease amelioration in lupus-related inflammation/autoimmunity, with activity superior to agents targeting only one of these pathways. These observations provide further support for the clinical evaluation of acazicolcept for treatment of SLE; a Phase 2 trial of acazicolcept in SLE is ongoing (NCT04835441/Synergy).

1 Ota, M, et al. 2021. Cell. 184(11): 3006-21.
2 Cheng LE, et al. 2018. Arthritis Rheumatol. 70(7): 1071-6.
3 Pontarini, E, et al. 2020. Clin Exp Rheumatol. 38 Suppl 126(4): 222-7.
4 Klarquist, J., et al., 2015. J Vis Exp. (105): e53319.

Disclosure: E. Repash: Alpine immune Sciences, Inc., 3, 11; **T. Blair**: Alpine Immune Sciences, Inc., 3, 11; **A. Enstrom**: Actym Therapeutics, 3, Alpine Immune Sciences, Inc., 3, 11, Tempest Therapeutics, 3, 11; **L. Evans**: Alpine Immune Sciences, Inc., 3, 11; **S. Debrot**: Alpine Immune Sciences, Inc., 3, 11; **K. Lewis**: Alpine Immune Sciences, Inc., 2, 11; **A. Bankhead**: Alpine Immune Sciences, Inc., 3, 11; **S. Peng**: Alpine Immune Sciences, Inc., 3, 11; **S. Dillon**: Alpine Immune Sciences, Inc., 3, 10, 11.

Abstract Number: 0603

Antiphospholipid Antibodies as Potential Predictors of Disease Severity and Poor Prognosis in Systemic Lupus Erythematosus Associated Thrombocytopeinia

Mehret Birru Talabi[1], Bonnie Bermas[2], Irene Blanco[3], Ashira Blazer[4], Megan Clowse[5], Cuoghi Edens[6], Leslie Pierce[7], Catherine Wright[1] and Rosalind Ramsey-Goldman[3], [1]University of Pittsburgh, Pittsburgh, PA, [2]UT Southwestern, Dallas, TX, [3]Northwestern University, Chicago, IL, [4]Hospital for Special Surgery, New York, NY, [5]Duke University, Chapel Hill, NC, [6]University of Chicago, Chicago, IL, [7]University of Pittsburgh, Raleigh, NC

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: SLE – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Thrombocytopenia (TP) is a common hematologic abnormality in systemic lupus erythematosus (SLE). Severe thrombocytopenia is correlated with disease activity and a worse prognosis of SLE associated thrombocytopenia (SLE-TP). Antiphospholipid antibodies (aPLs)have been proven to cause low platelet count through various mechanisms. However, the impact of aPLs on SLE-TP remains a matter of debate. In this multicenter prospective study, we aim to investigate the role of aPLs on disease severity and prognosis of SLE-TP.

Methods: All SLE patients fulfilled the 2019 the American College of Rheumatology (ACR) / the European League Against Rheumatism(EUALR) classification criteria for SLE. Antiphospholipid syndrome (APS) was diagnosed according to the revised 2006 Sapporo APS classification criteria. TP was defined as a platelet count<100×10^9/L, and patients with TP due to other causes were excluded. aPLs were tested following international guidelines (anticardiolipin, anti-β2 glycoprotein I antibodies and lupus anticoagulant). Demographic characteristics, platelet count, clinical manifestations, disease activity, and autoantibody profiles were collected at baseline. Severity of thrombocytopenia was categorized into mild, moderate, and severe group. Relapse was defined as the loss of remission. Bone marrow punctures indicated impairment of megakaryocyte maturation.

Results: A total of 371 SLE-TP patients with complete follow-up data were enrolled, out of which 199 (53.6%) were aPLs positive and 48 (24.1%) were complicated with APS. Baseline comparison showed that SLE-TP with aPLs had lower baseline platelet counts (62.0×10^9/L *vs*. 76.0×10^9/L, *P*=0.003), and a higher proportion of moderate to severe cases (17.1% *vs*. 9.9%; 23.6% *vs*. 13.4%, *P*=0.002). SLE-TP patients with aPLs had lower platelet counts at their lowest point (37.0×10^9/L *vs*. 55.0×10^9/L, *P*=0.002).In addition, the increasing number of aPLs types was associated with the decrease of baseline and minimum values of platelets (*P* < 0.001; *P*=0.001). SLE-TP carrying aPLs had a lower prevalence of arthritis (39.7% *vs*. 45.3%, *P*=0.019) and serositis (14.6% *vs*. 25.0%, *P*=0.011).Among aPLs carriers, there was a higher positivity rate for ANuA (18.1% *vs*. 10.5%, *P*=0.038), whereas it was lower for anti-RNP antibody (33.7% *vs*. 51.2%, *P*=0.001). During a median 5.47-year follow-up of 326 SLE-TP patients with complete treatment data (181 aPLspositive, 55.5%), SLE-TP carrying aPLs hada higher relapse rate(58.6% *vs*.45.5%, *P*=0.019) and lower complete response (CR) rate (85.6% *vs*.87.6%).

Table 1. Baseline characteristics, profile of autoantibodies, and clinical manifestations of 371 SLE-TP patients.

	aPLs+ (n=199)	aPLs- (n=172)	*P*
Female, n (%)	173(86.9)	157(91.3)	0.183
Age at diagnosis (years), mean±S.D.	35.2±12.2	36.3±12.7	0.304
Disease duration (years), mean±S.D.	11.0±7.1	11.7±6.1	0.308
SLEDAI, mean±S.D.	5.9±7.4	5.4±6.7	0.450
Baseline platelet count($\times10^9$/L), median (25%-75%)	62 (33-87)	76 (51.5-90)	**0.003**
Severe(<20×10^9/L), n (%)	34 (17.1)	17 (9.9)	**0.002**
Moderate(20-50$\times10^9$/L), n (%)	47 (23.6)	23 (13.4)	
Mild(50-100$\times10^9$/L), n (%)	118 (59.3)	132 (76.7)	
Skin and mucous membranes, n (%)	79 (39.7)	78 (45.3)	0.272
Arthritis, n (%)	60 (30.2)	72 (41.9)	**0.019**
Serositis, n (%)	29 (14.6)	43 (25.0)	**0.011**
Neurological involvement, n (%)	36 (18.1)	25 (14.5)	0.357
Nephropathy, n (%)	75 (37.7)	75 (43.6)	0.347
HGB($\times10^{12}$/L), median (25%-75%)	119 (101-136)	119 (103-131.8)	0.751
Anti-double stranded DNA (anti-dsDNA) antibody, n (%)	47 (23.6)	59 (34.3)	**0.023**
Anti-Sm antibody, n (%)	42 (21.1)	51 (29.7)	0.058
Anti-RNP antibody, n (%)	67 (33.7)	88 (51.2)	**0.001**
Anti-SSA antibody, n (%)	108 (54.3)	109 (63.4)	0.076
Anti-SSB antibody, n (%)	25 (12.6)	31 (18.0)	0.143
Anti-ribosomal P protein (anti-RibP) antibody, n (%)	48 (24.1)	36 (20.9)	0.464
Anti-nucleosome antibody (ANuA), n (%)	36 (18.1)	18 (10.5)	**0.038**
Anti-histone antibody (AHA), n (%)	38 (19.1)	25 (14.5)	0.243

Furthermore, the analysis of 61 SLE-TP with qualified bone marrow reports found that there was no significant difference in ratio of granulocytes to red blood cells (G/E), the total number of megakaryocyte and categories (granulosa, naked nuclear, and plate producing cells).

Table 2. The minimum PLT value during follow-up and the treatment response of 326 SLE-TP patients with different aPLs.

	aPLs+(n=181)				aPLs-(n=145)	*P*
	1 aPL+ (n=69, 38.1%)	2 aPLs+ (n=46, 25.4%)	3 aPLs+ (n=66, 36.4%)	aPLs+ total		
Minimum PLT count($\times10^9$/L), median (25%-75%)	45 (23-73.5)	29.5 (8.75-69.5)	31.5 (13.5-50)	37 (15-63.5)	55 (25.5-76)	**0.002**
Severe(<20×10^9/L), n (%)	14 (20.3)	18 (39.1)	21 (31.8)	53 (29.3)	28 (19.3)	
Moderate(20-50$\times10^9$/L), n (%)	25 (36.2)	12 (26.1)	27 (40.9)	64 (35.4)	42 (29.0)	**0.01**
Mild(50-100$\times10^9$/L), n (%)	30 (43.5)	16 (34.8)	18 (27.3)	64 (35.4)	75 (51.7)	
Latest PLT count($\times10^9$/L), median (25%-75%)	122 (84.5-210)	133.5 (85.75-218.75)	100.5 (63.75-166.75)	117 (77-204.5)	136 (82-206)	0.312
CR, n (%)	63 (91.3)	38 (82.6)	54 (81.8)	155 (85.6)	127 (87.6)	
R, n (%)	1 (1.4)	2 (4.3)	7 (10.6)	10 (5.5)	1(0.7)	**0.01**
NR, n (%)	5 (7.2)	6 (13.0)	5 (7.6)	16 (8.8)	17 (11.7)	
Loss of CR or R, n (%)	38 (55.1)	25 (54.3)	43 (65.2)	106 (58.6)	66 (45.5)	**0.019**

Note: CR, complete response,is defined as any platelet count of at least 100×10^9/L. R, response, is defined as any platelet count between 30 and 100×10^9/L and at least doubling of the baseline count. NR, nonresponse,is defined as any platelet count lower than 30×10^9/L or less than doubling of the baseline count. Loss of CR or R, platelet count below 100×10^9/L or bleeding (from CR) or below 30×10^9/L or less than 2-fold increase of baseline platelet count or bleeding (from R) 1 aPL+, single aPL positive. 2 aPLs+, double aPLs positive. 3 aPLs+, triple aPLs positive.

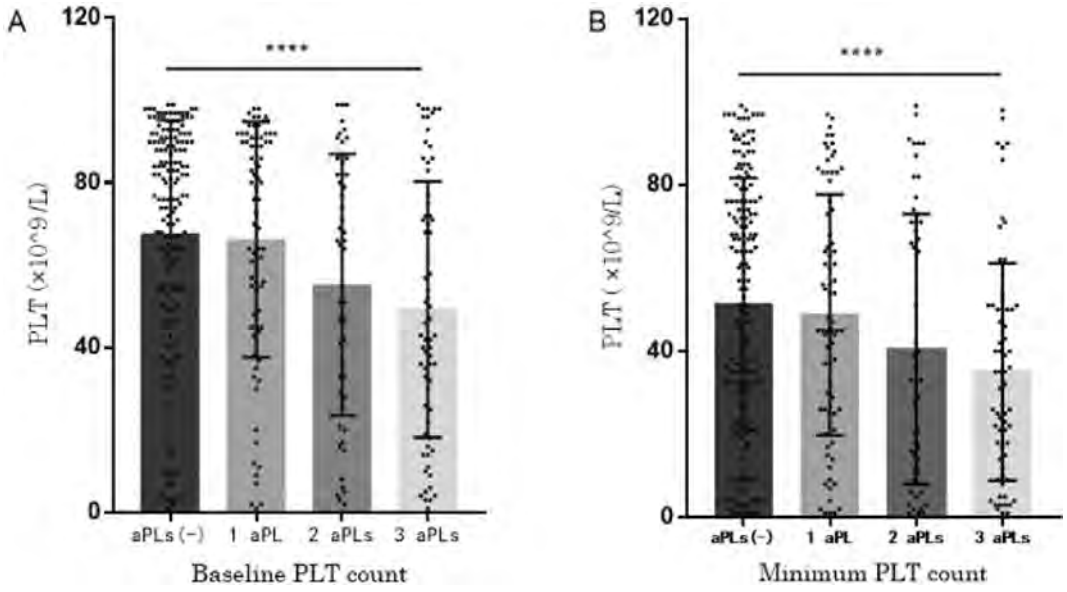


Figure. (A). Baseline platelet count of SLE-TP with different aPLs. (B) Minimum platelet count of SLE-TP with different aPLs.

Conclusion: SLE-TP with positive aPLs had more severe disease condition and a higher recurrence rate, which suggests that we should implement more proactive management strategies and maintain vigilance towards relapse in SLE-TP patients with positive aPLs.

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Abstract Number: 0604

Is Belimumab Dose Optimization Possible in Patients with Systemic Lupus Erythematosus?: Analysis of This Therapeutic Strategy in a Large Multicenter Cohort of Patients from Spanish Rheumatology Departments

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Belimumab (BLM) is an IgG-1l anti-BAFF monoclonal antibody effective in patients with systemic lupus erythematosus (SLE), being used increasingly. However, there are no published data on dose optimization in responder patients.

Aim: to assess the prevalence of dose optimization in patients with SLE treated with BLM in our country, its modalities and its impact on disease activity control.

Methods: Retrospective longitudinal and multicenter study of SLE patients, treated with

BLM in Spanish rheumatology departments. Demographic and clinical features, activity (SLEDAI), treatments and outcomes (remission (DORIS -2021) and low disease activity (LLDAS) were collected at baseline (pre-optimization) (VB), at 6 (V6M) and at 12 months (V12M) post-optimization. A comparative analysis was performed pre- and post-optimization.

Table. BLM optimization

Table 1: Differences pre and post belimumab dosage optimization

	VB (pre)	V6M (post)	V12M (post)
SLEDAI, median (p25-p75)	0 (0-2)	2 (0-49)	0 (0-2)
PGA (0-3), median (p25-p75)	0,33 (0-0,5)	0,28 (0-0.48)	0,2 (0-0.4)
DORIS remission, n/total (%)	15/26 (57.7%)	14/22 (63.6%)	12/19 (63.2%)
LLDAS, n/total (%)	23/26 (88.5%)	20/22 (90.9%)	17/19 (89.5%)
CRP, median (p25-p75)	1.65 (0.4-5.5)	1.63 (0.46-4.14)	0.7 (0.25-3.9)
C3 or C4 low, n/total (%)	5/26 (19.2%)	11/25 (44%) #	7/20 (35%) #
Anti-DNA positive, n/total (%)	5/26 (19.2%)	2/24 (8.3%)	0/20 (0%)
Active serology, n/total (%)	8/29 (27.6%)	13/24 (54.2%)	7/20 (35%)
DAMARD, n/total (%)	17/26 (65.4%)	14/25 (56%)	10/20 (50%)
Glucocorticoids (GC), n/total (%)	15/26 (57.7%)	12/24 (50%)	8/20 (40%) #
GC dose, median (p25-p75)	2.5 (0-5)	2,5 (0-5) #	5 (0.62-8.75)

VB (pre): basal visit (pre-optimization); V6M: visit at 6 months post-optimization; V12M: visit at 12 months post-optimization.
p significant
DORIS: Definition of Remission in SLE. PGA: Physician Global Assessment. LLDAS: Lupus Low Disease Activity State. CRP: C Reactive Protein. DMARD: Disease Modifying Antirheumatic Drugs.

Results: 324 patients with SLE (98%, ACR-97 or SLICC-12 criteria) treated with BLM were included; 91% women; mean age (±DS): 42.4 (±12.9) years. Median follow-up follow-up: 3.2 years (p25-p75) (1.4-5.9). A total of 29 patients (8.9%) were optimized. Median time to optimization 2.7 (1.77-4.48) years. Mean time on optimization: 11.36 (±2.5) months. Optimization modalities: increase of the interval in 9 patients with subcutaneous BLM (from 7 days to 10-21 days of interval between doses) and in 6 patients with intravenous (ivBLM) (from a 4-week to a 5- 6-weeks). Dose reduction per administration (all ivBLM) in 16 patients (from 10mg/kg to 5-9 mg/kg).

Pre-optimization status (VB): 15/26 (57.7%) in DORIS-21 remission and 23/26 (88.5%) in LLDAS. LLDAS. Only 1 patient had lupus nephritis. Detailed description of other baseline characteristics are displayed in Table 1. After optimization, 2/24 (8.3%) and 3/22(13.6%) patients lost remission-DORIS in V6M and V12M, respectively, but with no statistically significant differences with respect to VB; regarding to LLDAS, 2/23(8.7%) and 2/21(9.5%) did so in V6M and V12M, respectively, but also without statistically significant differences with respect to VB. Out of 11/23(47.8%) and 9/21(42.9%) moved from SLEDAI 0 to SLEDAI >0 in V6M and V12M, respectively. In terms of disease activity, no significant differences were found pre- and post-optimization in any of the measures, except for hypocomplementemia ($p = 0.0276$) (Table 1). Changes in activity did not lead to relevant changes in treatment, thus only one patient returned to the baseline dose of BLM and only one patient started DMARD. Significantly fewer patients received GC in V12M, even though the median dose of GC was higher in V12M (5 (0.62-8.75) vs. 2.5 (0-5) in VB) (Table 1).

Conclusion: It is possible to optimize doses of BLM without relevant changes in disease activity, at least in the short term, in a significant percentage of patients, and the most of them maintain the optimized dose. However, the increased clinical or serologic activity is possible in some patients. This makes a tighter post-optimization follow-up advisable.

More studies, with a larger number of patients and longer follow-up time, will be required to confirm these results and to analyse more robust outcomes.

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Abstract Number: 0605

Determining the ECG Cut-off Point in Systemic Lupus Erythematosus Patients Undergoing Hydroxychloroquine Therapy

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) is a widely used drug in Systemic Lupus Erythematosus (SLE) that can cause cardiac alterations such as arrhythmic events in the short-term and dose-dependent cardiomyopathy in the medium to long-term. The cardiological implications of HCQ accumulation in these patients in the medium to long-term is unknown.

Methods: Single university hospital observational study of all consecutive SLE patients who had an electrocardiogram (ECG) at baseline and at least one ECG at follow-up. New conduction disturbances were assessed by ECG, defined as atrio-ventricular block, bundle branch block or QT interval prolongation. ECGs were extracted from the medical record and interpreted at baseline and for 15.2 years (95%CI 13.24-17.16) of follow-up. We defined cumulative HCQ (cHCQ) as the total grams of HCQ that had been administered. A ROC curve analysis was performed to determine the optimal cut-off point for sensitivity and specificity.

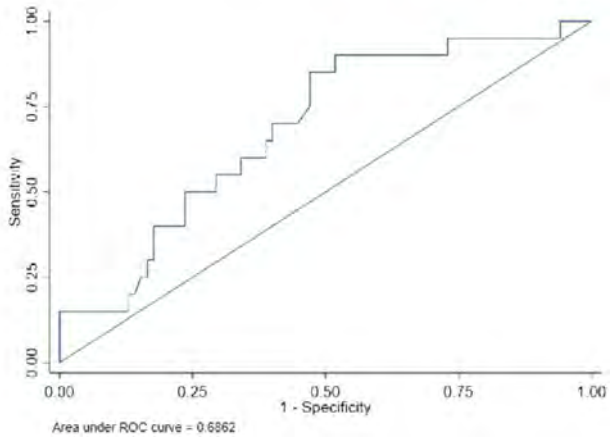
Results: We studied 105 (93 female/12 male) SLE patients with a mean (±SD) age of 61.8±14.9 years. The mean daily dose of HCQ in our sample was 256 mg per day **(Table)**. The ROC curve showed a moderate diagnostic ability for new conduction disturbances with an area under the curve of 0.69 (95% CI 0.59 - 0.77) **(Figure).** The highest efficacy cut-off point was cHCQ: 4097g (Sensitivity 15%; Specificity 100%) and the optimal cut-off point was cHCQ: 901g (Sensitivity 85%; Specificity 52.9%). This cut-off point was reached with a mean HCQ treatment in our sample of 9.7 years. High grade atrio-ventricular block was found in 5 patients. In all of them the cHCQ dose was over 901g.

Conclusion: According to our study, 901g of cumulative HCQ dose is a good cut-off point for performing a protocolized ECG to rule out cardiac conduction disturbances in patients with SLE and chronic HCQ treatment. This is equivalent to 9.7 years of treatment with the mean HCQ dose use in our sample.

Table 1. Clinical characteristics of systemic lupus erythematosus patients.

General characteristics	Global (N=105)
Current age (mean ± SD)	61.8 ± 14.9
Years of SLE evolution (mean ± SD)	16.3 ± 10.3
Sex, n (%)	93 (88.6)
Diabetes Mellitus, n (%)	15 (14.4)
Hypertension, n (%)	58 (55.2)
Dyslipidaemia, n (%)	47 (45.2)
Chronic renal failure, n (%)	10 (9.6)
Obesity, n (%)	8 (7.8)
Alcohol consumption, n (%)	3 (2.9)
Smoking history, n (%)	41 (39.0)
SLE treatment	
HCQ dose in mg/day (mean ± SD)	256 ± 87.2
Time in HCQ in months (mean ± SD)	149.8 ± 111.9
Cumulative HCQ dose in grams (mean ± SD)	1154.94 ± 946.10
Cumulative HCQ dose in grams, median (IQR)	913.1 (474, 1473)
Prednisone, n (%)	30 (28.6)
Prednisone dose in mg/day (mean ± SD)	17.3 ± 16.8
Other immunosuppressant, n (%)	14 (13.3)

Figure 1. ROC curve on cumulative hydroxychloroquine dose and new conduction disturbances.



Disclosure: C. Lasa: None; **A. Herrero-Morant**: None; **J. Zubiaur**: None; **A. Margarida**: None; **R. Pérez**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6.

Abstract Number: 0606

Risk of Damage Progression with Belimumab versus Oral Immunosuppressant Use in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

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Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Belimumab was approved for the treatment of non-renal SLE in 2011 and has been previously associated with a lower risk of damage progression when compared with prior 'usual care.' We sought to determine the risk of damage progression with belimumab versus alternative SLE immunosuppressants in a contemporary real world setting.

Methods: We identified all adults with SLE (defined by ≥2 ICD codes >30 days and < 2 years apart) in a United States multicenter electronic health record (EHR) database, TriNetX. We identified all patients who initiated belimumab, azathioprine (AZA), methotrexate (MTX), or mycophenolate (MMF) between 3/2011 and 8/2021. We designed and emulated a pragmatic target trial to compare the risk of damage progression with initiation of belimumab vs. AZA, belimumab vs. MTX, and belimumab vs MMF. For each comparison, eligible patients had never used the direct comparator but could have used other immunosuppressants and did not have lupus nephritis prior to the index date of treatment initiation. To emulate randomization, we used propensity score overlap weighting to balance baseline covariates, including demographics, geographic region, treatment initiation year, comorbidities including CKD, congestive heart failure, obesity, cardiovascular disease, the Charlson comorbidity index, tobacco use, SLE severity index (Garris C. *J Med Econ* 2013), SLE disease duration, baseline SLICC damage index score (categorized as 0, 1, or ≥2), medication use including glucocorticoids, hydroxychloroquine, and other immunosuppressants, and healthcare utilization. We assessed the outcome of damage progression defined by an increase

in the SLICC damage index (SDI), which was adapted to administrative data using ICD codes. We conducted an intention-to-treat analysis and a per-protocol analysis using pooled logistic regression where we adjusted for adherence to assigned treatment with inverse probability of treatment weighting. We also assessed the mean change in the SDI at three years among patients with ≥3 years of follow-up using linear regression.

Results: We compared 2,434 and 5,644 initiators of belimumab and AZA, (**Table 1**), 2,163 and 7,224 initiators of belimumab and MTX, and 2,431 and 6,350 initiators of belimumab and MMF, respectively. In each comparison, covariates were balanced after propensity score overlap weighting. 95% were female; the mean age was 44 years. 53% had a baseline SDI of zero. After

Table 1. Baseline Characteristics of Belimumab and Azathioprine Initiators with Non-Renal Systemic Lupus Erythematosus

	Before overlap weighting			After overlap weighting		
	Belimumab (n=2434)	AZA (n=5644)	Std. Diff.	Belimumab	AZA	Std. Diff.
Age, years, mean (SD)	44.2 (12.6)	44.7 (14.6)	0.0377	44.3	44.3	<0.001
Female, n (%)	2322 (95.4)	5218 (92.5)	0.1236	94.8	94.8	<0.001
Race/Ethnicity, n (%)			0.2828			<0.001
White	1438 (59.1)	2603 (46.1)		54.5	54.5	
Black	587 (24.1)	1869 (33.1)		27.0	27.0	
Asian	51 (2.1)	139 (2.5)		2.3	2.3	
Hispanic	169 (6.9)	593 (10.5)		8.2	8.2	
Geographic Region, n (%)			0.4104			<0.001
East	808 (33.2)	969 (17.2)		25.4	25.4	
Midwest	300 (12.3)	1011 (17.9)		14.7	14.7	
South	915 (37.6)	2827 (50.1)		42.4	42.4	
West	411 (16.9)	837 (14.8)		17.4	17.4	
Treatment initiation year, median	2018	2017	0.4990	2018	2018	<0.001
CKD stage ≥3	228 (9.4)	468 (8.3)	0.0379	8.5	8.5	<0.001
Tobacco use, n (%)	107 (4.4)	393 (7.0)	0.1111	5.1	5.1	<0.001
Charlson Comorbidity Index, mean (SD)	1.0 (0.8)	1.0 (0.9)	0.0375	1.0	1.0	<0.001
SLE Severity Index, n (%)			0.0930			<0.001
Mild	1360 (55.9)	3123 (55.3)		56.2	56.2	
Moderate	802 (32.9)	1772 (31.4)		32.2	32.2	
Severe	272 (11.2)	749 (13.3)		11.7	11.7	
SLE disease duration, n (%)			0.2354			<0.001
≤ 2 years	1435 (59.0)	3938 (69.8)		62.1	62.1	
2-4 years	472 (19.4)	830 (14.7)		18.2	18.2	
≥4 years	527 (21.7)	876 (15.5)		19.7	19.7	
Baseline SDI, n (%)			0.0985			<0.001
SDI = 0	1328 (54.6)	2856 (50.6)		53.3	53.3	
SDI = 1	564 (23.2)	1293 (22.9)		23.1	23.1	
SDI ≥ 2	542 (22.3)	1495 (26.5)		23.6	23.6	
Medication Use, n (%)						
Glucocorticoids	1561 (64.1)	3189 (56.5)	0.1564	61.2	61.2	<0.001
Hydroxychloroquine	1503 (61.8)	2875 (50.9)	0.2193	57.2	57.2	<0.001
Methotrexate	584 (24.0)	628 (11.1)	0.3431	18.0	18.0	<0.001
Mycophenolate	419 (17.2)	477 (8.5)	0.2643	13.5	13.5	<0.001
Healthcare Utilization						
Outpatient visits, median (IQR)	5 (9)	4 (10)	0.0751	5	4	<0.001
ER/Inpatient visits, n (%)	602 (24.7)	1699 (30.1)	0.1206	27.0	27.0	<0.001

Covariates assessed within the 12 months prior to the index date. Non-renal lupus defined by meeting SLE definition (≥2 SLE ICD codes ≥2 months and ≤2 years apart) and not meeting lupus nephritis definition (defined by ≥1 LN code (ICD-10 M32.14) or ≥2 nephritis codes (e.g., ICD-9 580-586, 791.0 or ICD-10 N00, N04-5, N17-18, R80.9) prior to the index date.
CKD, chronic kidney disease. CVD, cardiovascular disease; SDI, SLICC Damage Index; ER, emergency room. SLE Severity Index is adapted from Garris algorithm for administrative data, based on ICD codes and not including medication dosing.

Table 2. Risk of SLICC Damage Index Progression Over 5-Years of Use, Per-Protocol Analysis

Comparisons	Events	5-year cumulative incidence	Adjusted* Hazard Ratio (95% CI)
Intention-to-treat Analysis			
Belimumab vs. Azathioprine	2619	58.13	1.00 (ref)
Azathioprine	851	55.94	0.94 (0.87-1.02)
Belimumab			
Belimumab vs. Methotrexate	2936	54.16	1.00 (ref)
Methotrexate	809	57.50	1.10 (1.01-1.19)
Belimumab			
Belimumab vs. Mycophenolate	3262	62.38	1.00 (ref)
Mycophenolate	801	54.34	0.80 (0.74-0.87)
Belimumab			
Per-Protocol Analysis			
Belimumab vs. Azathioprine			
Azathioprine	1808	47.30	1.00(ref)
Belimumab	622	44.96	0.92 (0.82-1.03)
Belimumab vs. Methotrexate			
Methotrexate	1949	41.40	1.00(ref)
Belimumab	591	45.19	1.15 (1.03-1.29)
Belimumab vs. Mycophenolate			
Mycophenolate	2312	53.63	1.00(ref)
Belimumab	575	45.05	0.74 (0.67-0.83)

*Adjusted for adherence to treatment using inverse probability of treatment weighting.

Table 3. Change in SLICC Damage Index at Three Years of Use, Per-Protocol Analysis

Comparisons	Number of Initiators with ≥ 3 Years Follow-up	Change in SDI at 3 Years (95% CI)	Difference (95% CI)	P value
Intention-to-treat Analysis				
Belimumab vs. Azathioprine	3250	1.00 (0.94, 1.05)	Ref	<0.01
Azathioprine	1040	0.87 (0.79, 0.94)	-0.13 (-0.21, -0.05)	
Belimumab				
Belimumab vs. Methotrexate	4081	0.85 (0.81, 0.89)	Ref	0.21
Methotrexate	962	0.90 (0.82, 0.98)	0.05 (-0.03, 0.12)	
Belimumab				
Belimumab vs. Mycophenolate	3602	1.10 (1.05, 1.16)	Ref	<0.01
Mycophenolate	982	0.85 (0.77, 0.93)	-0.25 (-0.34 -0.17)	
Belimumab				
Per-Protocol Analysis				
Azathioprine	662	0.94 (0.84, 1.05)	Ref	0.31
Belimumab	326	0.86 (0.72, 0.99)	-0.09 (-0.26, 0.08)	
Belimumab vs. Methotrexate				
Methotrexate	927	0.77 (0.69, 0.85)	Ref	0.26
Belimumab	309	0.85 (0.72, 0.98)	0.08 (-0.06, 0.22)	
Belimumab vs. Mycophenolate				
Mycophenolate	857	1.31 (1.19, 1.43)	Ref	<0.01
Belimumab	301	0.85 (0.70, 0.99)	-0.47 (-0.64,-0.29)	

5 years, over 41% in each treatment group developed ≥1 new damage item on the SDI. The risk of damage progression was lower with belimumab than mycophenolate (HR 0.74 [95% CI 0.67-0.83]; **Table 2**), but there was no difference in the risk of damage progression between belimumab and AZA or belimumab and MTX. Similarly, belimumab was associated with a lower 3-year change in SDI when compared with MMF, but there was no difference when compared with AZA and MTX (**Table 3**).

Conclusion: In this real world EHR-based SLE cohort, after accounting for baseline covariates associated with the risk of organ damage, belimumab was associated with a lower risk of damage progression than MMF but not AZA or MTX use. Limitations include the use of administrative claims to identify components of the SDI.

Disclosure: A. Jorge: None; **B. Zhou**: None; **Y. Zhang**: None; **H. Choi**: Ani, 2, Horizon, 2, 5, LG, 2, Protalix, 2, Shanton, 2.

Abstract Number: 0607

CAR T Cell Therapy Leads to Long-term Abrogation of Autoimmunity in SLE Patients While Vaccination Responses Are Maintained

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: SLE – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: We have previously shown that CD19 CAR T cell therapy leads to stable drug-free remission of treatment-resistant SLE (1,2). Based on these findings we addressed the question whether disease-specific autoimmunity resolves in a sustainable way in CD19 CAR T cell- treated SLE patients. We also asked the question whether CD19 CAR T cell therapy affects long-term vaccination responses

Methods: Patients with treatment-resistant SLE received a single infusion of 1 million CD19 CAR T cells per kilogram body weight. CAR T cells were manufactured from autologous T cells and transfected with the lentiviral vector MB-CART19.1 (Miltenyi) encoding the CD19 CAR. Immunosuppressive treatment was stopped before CAR T cell infusion. Standard conditioning treatment (1g/m2 cyclophosphamide, 75 mg fludarabine) was done before CAR T cell infusion. SLE disease activity was sequentially monitored over at least one year with a maximum of up to two years. Autoantibodies (reactivities against double stranded (ds) DNA, single stranded (ss) DNA, nucleosomes, secondary necrotic cells, Smith antigen and Ro60 antigen) were measured at baseline, 3 months after CAR T cell therapy and at last follow-up (1-2 years after CAR T cell therapy). In addition, vaccination responses against measles, mumps, rubella, varicella zoster virus (VZV), Epstein Barr virus (EBV), tetanus and pneumococcus (PC) were assessed. All the antibody measurements were done by commercial ELISA. Anti-dsDNA antibodies were additionally measured by radioimmunoassay (RIA).

Results: Between March 2021 June 2023 8 SLE patients received treatment with CD19 CAR T cell therapy. Five patients had a follow up of more than one year post CAR T cell infusion. All 8 patients fulfilled DORIS remission criteria at time of writing the abstract (June 2023), had a SLEDAI-2K equal to zero and were off glucocorticoid therapy and any other

Figure 1 A

	dsDNA RIA	dsDNA	ssRNA	NUC	SNEC	Sm	Ro60
Before CAR T cells	479 [4; 5600]	91 [0; 317]	91 [0; 273]	188 [41;333]	0.18 [0; 0.69]	22.1 [0; 50.8]	0 [0; 177]
Follow Up (1-2 years)	0 [0; 0]	0 [0; 0]	0 [0; 0]	0 [0; 257]	0 [0; 0]	0 [0; 0]	0 [0; 84]

Figure 1 B

	Measles	Mumps	Rubella	Tetanus	VZV	EBV	PC
Before CAR T cells	636 [168; 1278]	196 [83; 980]	11 [8; 49]	0.97 [0.07; 1.38]	1367 [306; 2000]	32.4 [0; 49.1]	11.8 [3.5; 31.6]
Follow Up (1-2 years)	461 [50; 827]	67 [46; 255]	10 [6; 30]	1.33 [0.07; 1.96]	770 [290; 1214]	33.7 [0; 46.7]	13.1 [8.4; 105]

immunosuppressive medication. Autoantibodies against dsDNA (4/5), ssDNA (4/5), nucleosomes (5/5), secondary necrotic cells (4/5) and Smith antigen (3/5) disappeared after CD19 CAR T cell therapy with the exception of nucleosome antibody response in one patient and remained negative until the last follow-up (12-24 months after treatment) (Table 1A). Also RIA-based detection of anti-dsDNA antibodies showed sustained seroconversion. Ro60 activity, which was found in one patient, remained stable throughout the observation period but did apparently no impact disease activity. In contrast to autoantibodies, antibody reactivities against measles, mumps, rubella, VZV, EBV, tetanus and PC remained stable 12-24 months after treatment (Table 1B).

Conclusion: CD19 CAR T cells therapy lead to a sustained disappearance of autoantibodies in SLE patients, while vaccination responses remained stable. This observation suggests that the main cellular source of autoantibodies in SLE are CD19+ plasmablasts, which are depleted by CD19 CAR T cells, while antibodies related to vaccination responses appear to predominantly stem from CD19-negative plasma cells. The selective and sustained abrogation of disease specific autoimmunity without affecting vaccination responses provides a favorable combination for the safety and efficacy of CD19 CAR T cell therapy in SLE.

Disclosure: G. Schett: None; **L. Munoz**: None; **J. Taubmann**: None; **M. Aigner**: Kosmas Therapuetics, 8, Kyverna, 5, Miltenyi Biomedicine, 2, 7, Miltenyi Biotec, 6; **C. Bergmann**: Boehringer-Ingelheim, 2, 5, Janssen, 2; **J. Knitza**: None; **G. Kroenke**: None; **D. Werner**: None; **F. Müller**: AbbVie, 6, AstraZeneca, 1, 5, 6, Bristol Myers Squibb, 1, 6, Janssen, 6, KITE, 1, 6, Miltenyi Biomedicine, 1, 6, Novartis, 1, 6, Sobi, 6; **A. Mackensen**: BioNTech, 1, Bristol-Myers Squibb(BMS), 1, KITE/Gilead, 1, 6, Kyverna, 5, Miltenyi Biotech, 5.

Abstract Number: 0608

Efficacy of Cenerimod in Patients with High IFN-1 Gene Expression Signature and High Anti-dsDNA Antibody Levels: Post-hoc Analysis from a Phase 2 Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: SLE – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Cenerimod is an orally active, selective sphingosine 1-phosphate (S1P) 1 receptor modulator under investigation for the treatment of systemic lupus erythematosus (SLE). In the Phase 2 CARE study (NCT03742037), patients treated with cenerimod 4 mg showed reduced disease activity versus placebo after 6 months.[1]

Type-1 interferon (IFN-1) activation is a robust biomarker of SLE disease activity, and an elevated IFN-1 signature associates with autoantibodies and more active disease. Cenerimod reduces plasma levels of IFN-α and leads to decreased circulating B and T cells in patients with SLE, suggesting effects on innate and acquired immune responses.

Table 1. Resolution of alopecia and arthritis (assessed by SLEDAI) at Month 6 by baseline IFN-1 gene expression signature. IFN-1, interferon 1. Overall population refers to all randomized patients.

		IFN-1 gene expression signature		Overall
	Treatment group	High	Low	population
Alopecia	Cenerimod 4 mg, n (%)	10/26 (38.5)	8/31 (25.8)	19/60 (31.7)
	Placebo, n (%)	4/28 (14.3)	2/30 (6.7)	7/62 (11.3)
Arthritis	Cenerimod 4 mg, n (%)	20/35 (57.1)	12/43 (27.9)	33/83 (39.8)
	Placebo, n (%)	15/40 (37.5)	16/38 (42.1)	32/84 (38.1)

Here the efficacy of cenerimod in patients with high IFN-1 gene expression signature and high anti-dsDNA antibody levels is presented, as reported at EULAR 2023.[2]

Methods: CARE randomized 427 patients with SLE to once-daily cenerimod (0.5, 1, 2, 4 mg) or placebo. At month (M) 6, patients on 4 mg cenerimod were re-randomized to placebo or cenerimod 2 mg for the remaining 6 months; other groups continued their initially assigned treatment to M12. The primary endpoint was change from baseline to M6 in SLEDAI-2K score modified to exclude leukopenia (mSLEDAI-2K) due to the mechanism of action of cenerimod.

Subgroup analyses were performed in patients with high IFN-1 gene expression signature (based on expression of *IFI27*, *RSAD2*, *HERC5*, and *IFIT1*) or anti-dsDNA levels ≥30 IU/mL.

Results:

At baseline, 207/408 patients (51%) in CARE had high IFN-1 gene expression signature [including 36 (45%) and 40 (50%) on cenerimod 4 mg and placebo, respectively], and 86/426 (20%) had anti-dsDNA antibody levels ≥30 IU/mL [21 (25%) and 15 (17%) for cenerimod 4 mg and placebo, respectively]. There was an association between high IFN-1 gene expression signature and high anti-dsDNA levels, with more than 75% of patients with anti-dsDNA levels ≥30 IU/mL having high IFN-1 gene expression signature.

Cenerimod 4 mg resulted in decreased levels of anti-dsDNA antibodies and IFN-a protein at M6 versus baseline. In patients with high IFN-1 gene expression signature or high anti-dsDNA, 4 mg cenerimod led to greater reductions of disease activity versus placebo, as measured by mSLEDAI and SRI-4 at M6.

More patients with high IFN-1 gene expression signature at baseline had resolution of arthritis and alopecia at M6 in the treatment arm versus patients with the low IFN-1 gene expression signature (Table 1).

Conclusion: Treatment with cenerimod 4 mg resulted in greater reduction of disease activity versus placebo at M6 in patients with baseline high IFN-1 gene expression signature or high anti-dsDNA antibody levels. Cenerimod treatment also reduced levels of IFN-α protein and anti-dsDNA antibodies in these patients. Two Phase 3 studies designed to evaluate the treatment effect of cenerimod 4 mg in SLE are underway.

References

1. Askanase A et al. Arthritis Rheumatol 2022;74(Suppl 9):3293–7.
2. Adapted by permission from BMJ Publishing Group Limited. Askanase A et al. DOI: 10.1136/annrheumdis-2023-eular.3823.

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Disclosure: A. Askanase: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb, 2, Celgene, 2, Eli Lilly, 2, Genentech, 2, GSK, 2, Idorsia, 2, Janssen, 2, Mallinckrodt, 2, Pfizer, 2, UCB Pharma, 2; **D. D'Cruz**: GlaxoSmithKlein(GSK), 1, 2, Idorsia Pharmaceuticals Ltd, 1, 2, UCB, 1, 2, Vifor, 1, 2; **K. Kalunian**: AbbVie/Abbott, 2, Amgen, 5, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EquilliumBio, 2, Genentech, 2, Gilead, 2, Janssen, 2, KezarBio, 1, Merck/MSD, 2, Novartis, 2, Pfizer, 2, Remegene, 2, Roche, 2, UCB, 5; **J. Merrill**: AbbVie, 2, Alexion, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, Bristol Myers Squibb, 2, 5, EMD Serono, 2, Genentech, 2, Gilead, 2, GlaxoSmithKline, 2, 5, Lilly, 2, Merck, 2, Pfizer, 2, Provention, 2, Remegen, 2, Sanofi, 2, UCB Pharma, 2, Zenas, 2; **S. Navarra**: Astellas, 6, AstraZeneca, 6, Biogen, 2, Boehringer-Ingelheim, 2, GSK, 6, Novartis, 6, Pfizer, 6; **C. Cahuzac**: Idorsia Pharmaceuticals Ltd, 3, 11; **P. Cornelisse**: Idorsia Pharmaceuticals Ltd, 3, 11; **D. Strasser**: Idorsia Pharmaceuticals Ltd, 3, 11; **L. Trokan**: Idorsia Pharmaceuticals Ltd, 3, 11; **O. Berkani**: Idorsia Pharmaceuticals Ltd, 3, 11.

Abstract Number: 0609

Mortality After Autologous Hematopoietic Stem Cell Transplant for Autoimmune Disease: Do Scleroderma Patients Fare Worse?

Marina Birck[1], Autumn Neville[1], Jan Storek[2], Harry Atkins[3], **Marie Hudson**[4], Ines Colmegna[5], Jessie R. Lavoie[6], Jun Gao[7] and Sasha Bernatsky[1], [1]Research Institute of the McGill University Health Centre, Montreal, QC, Canada, [2]University of Calgary, Calgary, AB, Canada, [3]Ottawa Hospital Research Institute, Ottawa, ON, Canada, [4]McGill University, Montréal, QC, Canada, [5]The Research Institute of the McGill University Health Centre, Montréal, QC, Canada, [6]Health Canada, Centre for Oncology, Radiopharmaceuticals and Research, Biologic and Radiopharmaceutical Drugs Directorate, Ottawa, ON, Canada, [7]Health Canada, Centre for Regulatory Excellence, Statistics and Trials, Biologic and Radiopharmaceutical Drugs Directorate, Ottawa, ON, Canada

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Autologous hematopoietic stem cell transplantation (HSCT) has benefitted some patients with autoimmune disease (AD) but is associated with toxicity and treatment-related mortality. Autologous HSCT is an option, particularly in scleroderma, a disease associated with high mortality. We aimed to describe individuals undergoing autologous HSCT for AD, including scleroderma, and to evaluate mortality post-HSCT.

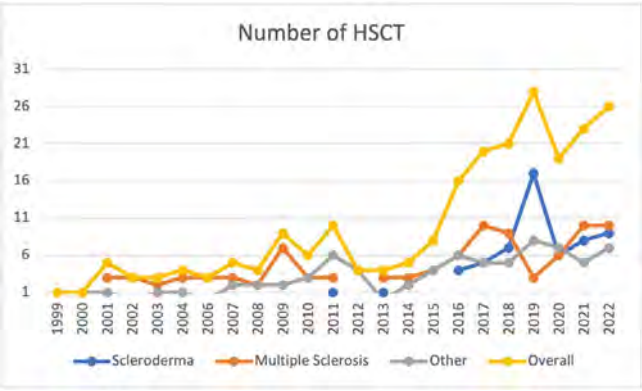

Figure 1. Number of HSCT performed at two Canadian tertiary care centers, per year, overall and stratified by indication.

Methods: CAN-AIM is a team funded to do high-priority research projects for Health Canada and other stakeholders. We employed chart review to analyze data from blood and marrow transplant programs at two Canadian tertiary care centres. We included consecutive adults (18+) who underwent autologous peripheral blood HSCT for AD from 1999-2022. Patient characteristics were summarized using median/interquartile range (IQR) or frequency/percentage. We calculated the mortality rate per 1,000 person-years (PY), calculated from index date (HSCT) to death, loss to follow-up, or end of study. Overall survival was calculated for 2 and 5 years after transplant. To compare mortality in scleroderma versus other AD, we calculated adjusted hazard ratios (aHR) with 95% confidence intervals (CI), adjusting for age at transplant, sex, time from AD diagnosis to HSCT, and calendar year.

Results: We studied 228 individuals who underwent HSCT, most commonly for multiple sclerosis (42%) and scleroderma (26%). Over half of the sample (54%) were women. The median age at HSCT was 40 (IQR 33-49), with a median time between AD diagnosis and HSCT of 4.7 years (IQR 2.4-9.1). The frequency of HSCT for AD increased across the years, and although numbers sharply decreased in 2020 (due to COVID), it is on the rise again (Figure 1). Over a median follow-up of 3.9 years (IQR 1.7-6.5), 28 of 228 patients died (23 deaths/1,000 PY). Less than a third (27%) of deaths were due to AD progression/relapse (5.7 per 1,000 PY). 35% were due to HSCT complications (defined as occurring within the first 100 days, including respiratory complications, n=3; multi-organ failure, n=2 and infections, n=2), and 38% were due to late events that occurred beyond the 100 days post-HSCT (sudden death, infection, organ failure, and cancer) including late HSCT toxicity. We observed similar results for males versus females (Figure 2). Survival at 2 years post-HSCT was 94% and 89% at 5 years, and slightly lower for scleroderma (Table 1). There was a trend in univariate analyses (HR 0.45, 95% CI 0.18-1.09) for worse survival in scleroderma (half of the deaths were due to disease relapse), which disappeared after controlling for sex, age, time since diagnosis, and calendar year (adjusted HR 0.98, 95%CI 0.32-2.95).

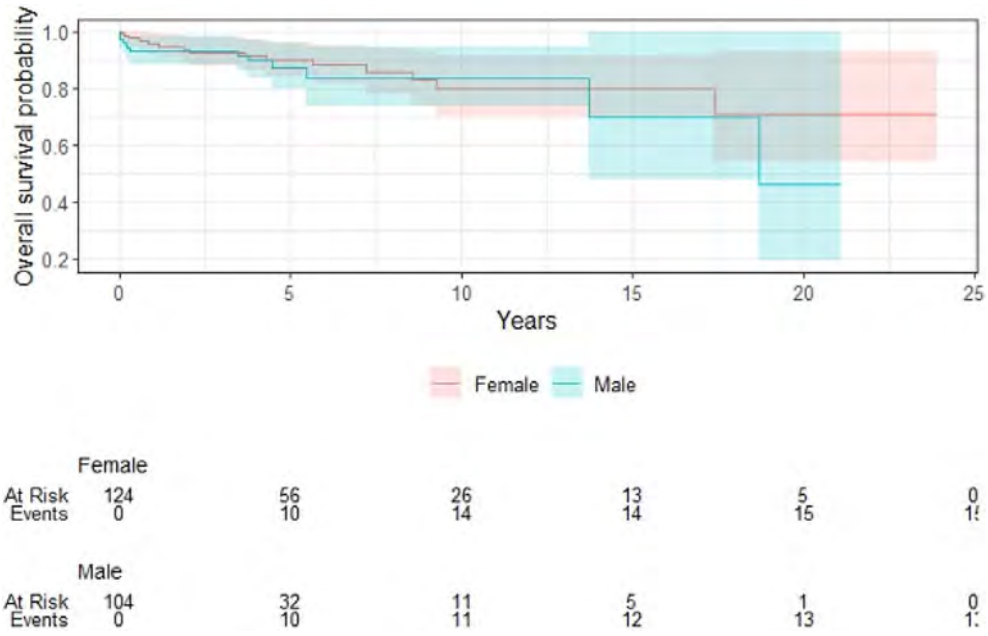

Figure 2. Kaplan-Meier curve estimating survival time between date of transplant and death or last follow-up (censor) from the transplant program, stratified by biological sex.

Table 1. Overall survival (95%CI) at 2 and 5 years after HSCT, stratified by sex at birth and restricted to scleroderma patients.

	Overall	Male	Female	Scleroderma
100 days	96.0% (93.5%-98.6%)	94.2% (89.9%-98.8%)	97.6% (94.9%-1.00%)	98.3% (95.1%-1.00%)
2 years	93.6% (90.4%-96.9%)	93.2% (88.5%-98.2%)	93.8% (89.4%-98.4%)	92.2% (85.0%-99.9%)
5 years	88.9% (84.3%-93.9%)	87.4% (79.7%-95.7%)	89.9% (84.0%-96.2%)	68.6% (49.0%-96.1%)

Conclusion: Adults undergoing HSCT for AD have a high survival rate of up to 5 years. A trend to worse outcomes in scleroderma may be due to differences in demographics (i.e. age distribution), time trends, and/or other factors.

Disclosure: M. Birck: None; **A. Neville**: None; **J. Storek**: None; **H. Atkins**: None; **M. Hudson**: AstraZeneca, 6, Boehringer-Ingelheim, 1, 5, 6, Bristol-Myers Squibb(BMS), 5, Merck, 6, UCB, 5; **I. Colmegna**: None; **J. Lavoie**: None; **J. Gao**: None; **S. Bernatsky**: None.

Abstract Number: 0610

Nailfold Capillaroscopy for Prediction of Novel Severe Organ Involvement in Systemic Sclerosis

Cristiana Sieiro Santos[1], Rúben Rego Salgueiro[2], Clara Moriano Morales[3], Carolina Álvarez Castro[3] and Elvira Díez Álvarez[3], [1]Complejo Asistencial Universitario de León, León, Spain, [2]ULS Guarda, Guarda, Portugal, [3]CAULE, León, Spain

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Nailfold capillaroscopy (NFC) has been suggested as a potential biomarker of disease severity in systemic sclerosis (SSc). Several studies report the association between capillary loss and disease severity however, the association of NFC abnormalities with novel severe organ involvement/progression in SSc has not been evaluated. We aim to evaluate the association of nailfold capillaroscopy (NFC) with novel major organ involvement/progression in SSc.

Methods: Follow-up data from patients with SSc registered between 2000 and 2022 were analysed. Patients underwent NFC at baseline. Novel severe organ involvement/progression was defined as new or progressive involvement of peripheral vasculature, lungs, heart, skin, gastrointestinal, kidney, musculoskeletal at 12 and 24 months of follow-up. The following NFC parameters were evaluated: capillary density, haemorrhages, enlarged and giant capillaries, avascular areas, organization of capillary architecture and scleroderma pattern (early/active/late). Logistic regression modelling was run to assess associations between NFC parameters and the occurrence of novel severe organ involvement and/or progression and risk factors.

Results: 113 patients with SSc were included, 70 patients (61%) developed novel overall severe organ involvement/progression: 39 patients (56%) during the first 12 months and 31 patients (44%) from 12 to24 months of follow-up. 11% of patients developed novel peripheral vascular involvement, 21% developed novel interstitial lung disease (ILD), 11% had progression of known ILD, 6% had novel pulmonary hypertension, 11% had skin progression, 10% had novel heart involvement, 10% had novel gastrointestinal involvement, 6% had scleroderma renal crisis and 13% had novel musculoskeletal involvement. Table 1 summarizes the associations between NFC and novel severe organ involvement/progression during follow-up. Loss of capillary density was associated with overall severe organ involvement (p 0.002), peripheral vascular involvement (p 0.03), new ILD (p 0.04) and skin progression (p 0.01); avascular areas were associated with overall severe organ involvement (p 0.03), new ILD (p 0.03) and progression of ILD (p 0.02) and scleroderma pattern was associated with overall severe organ involvement (p 0.03), peripheral vascular involvement (OR p 0.04), new ILD (p 0.004), progression of ILD (p 0.03) and skin progression (p 0.04).

Novel severe involvement or progression	Loss of capillary density	P value	Haemorrhages	P value	Enlarged capillaries	P value	Avascular areas	P value	Scleroderma pattern	P value
Overall future organ involvement	**3.21 (1.02-5.45)**	**0.002**	1.82 (0.82-4.52)	0.82	1.09 (0.52-3.23)	0.72	**2.1 (1.34-6.23)**	**0.03**	**1.82 (1.12-4.25)**	**0.03**
Peripheral vascular involvement	**1.7 (1.10-3.19)**	**0.03**	1.72 (0.82-2.72)	0.62	1.92 (0.64-4.2)	0.52	2.62 (0.72-3.2)	0.72	**1.82 (1.2-3.9)**	**0.04**
New ILD	**2.45 (1.32-4.23)**	**0.04**	1.2 (0.52-3.21)	0.75	1.32 (0.72-4.21)	0.82	**1.82 (1.12-3.42)**	**0.03**	**1.98 (1.32-3.42)**	**0.004**
Progression of ILD	0.98 (0.23-2.14)	0.32	0.45 (0.14-1.98)	0.45	0.78 (0.21-2.34)	0.72	**1.32 (1.10-3.52)**	**0.02**	**1.45 (1.12-3.82)**	**0.03**
New PAH	0.72 (0.14-1.98)	0.42	0.32 (0.15-1.67)	0.62	0.34 (0.21-1.52)	0.65	0.89 (0.62-2.14)	0.73	0.92 (0.52-1.45)	0.62
Skin progression	**1.42 (1.12-3.29)**	**0.01**	1.32 (0.62-2.81)	0.34	0.72 (0.32-1.30)	0.39	1.19 (0.63-3.62)	0.06	**2.3 (1.45-3.14)**	**0.04**
Novel heart involvement	0.78 (0.42-1.42)	0.14	0.62 (0.32-1.32)	0.29	0.42 (0.29-1.82)	0.75	0.35 (0.13-1.51)	0.66	1.82 (0.42-2.37)	0.78
Novel GI involvement	1.62 (0.24-1.34)	0.24	1.54 (0.32-1.54)	0.43	0.48 (0.26-1.31)	0.32	0.42 (0.24-1.23)	0.39	1.83 (0.52-3.37)	0.40
Novel SRC	0.72 (0.34-1.32)	0.52	0.86 (0.42-1.52)	0.64	0.94 (0.52-2.02)	0.76	0.66 (0.23-1.87)	0.43	0.65 (0.44-1.32)	0.32
Novel musculoskeletal involvement	0.23 (0.10-0.42)	0.24	0.18 (0.09-0.39)	0.19	0.28 (0.14-0.54)	0.34	0.25 (0.11-0.43)	0.29	0.87 (0.50-1.42)	0.29

Table 1. Associations between NFC and novel severe organ involvement/progression during follow-up

Conclusion: NFC may be a potential biomarker in SSc for predicting novel severe organ involvement and/or progression. Abnormal capillary density, avascular areas and scleroderma pattern are predictors of overall severe organ involvement, peripheral vascular involvement, novel and progression of ILD and skin progression.

Disclosure: C. Sieiro Santos: None; **R. Rego Salgueiro**: None; **C. Moriano Morales**: None; **C. Álvarez Castro**: None; **E. Díez Álvarez**: None.

Abstract Number: 0611

Demographics and Clinical Features Associated with Small Bowel Hypomotility in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The gastrointestinal (GI) tract is the second most commonly affected organ in patients with systemic sclerosis (SSc). It is estimated that the small bowel is involved in up to 50% of SSc patients at tertiary referral centers. Although some patients have mild disease, some have severe complications and may require total parenteral nutrition (TPN) to sustain life. Our aim was to identify demographic and clinical features associated with SSc patients who have delayed small bowel transit to better characterize patients at risk for this complication.

Methods: SSc patients with GI symptoms were prospectively enrolled in our study and underwent a scintigraphy-based whole gut transit (WGT) study. A cross-sectional analysis was then performed comparing demographic and clinical features between patients with and without objective small bowel transit delay by WGT. We also compared UCLA GIT 2.0 symptoms between these patient groups. Univariate logistic regression models were used to examine clinical features associated with delayed small bowel transit and a multivariable model was created using significant variables from our cross-sectional analysis and known confounders to further evaluate these associations.

Results: Of 131 patients enrolled in this study, 24 (18%) had delayed small bowel transit (defined at < 49% emptying at 6 hours). Patients with delayed small bowel transit were less likely to be female [79%, (19/118) vs. 93% (99/118); p=0.05], to be white [67%, (16/105) vs. 84% (89/105); p=0.05], and to have sicca symptoms [68% (15/107) vs. 89% (92/107);

Multivariable model evaluating the association between SSc clinical features and delayed small bowel transit after adjusting for sex and race

Covariate	Univariate model; OR (95% CI)	Multivariate model; OR (95% CI)
Maximum MRSS	1.05 (1.00, 1.11)†	1.05 (0.99, 1.11)
Myopathy	2.47 (0.91, 6.72)	2.53 (0.89, 7.22)
Cardiac involvement (≥2)	3.54 (1.00, 12.52)†	2.54 (0.64, 10.07)
Tendon friction rub	3.53 (0.90, 13.85)	2.76 (0.66, 11.58)
Sicca symptoms	0.26 (0.09, 0.76)†	0.29 (0.10, 0.90)†
Dead	3.76 (1.19, 11.94)†	
Pulmonary fibrosis	0.96 (0.35, 2.62)	0.84 (0.30, 2.42)
Pulmonary function parameters		
DLCO % predicted	0.97 (0.95, 1.00)†	0.97 (0.95, 1.00)
Anti-RNA polymerase III	7.00 (0.88, 55.41)	3.79 (0.33, 43.25)

†Statistically significant

SSc = Systemic sclerosis; WGT= whole-gut transit scintigraphy study; MRSS = modified Rodnan Skin Score; Cardiac involvement = maximum Medsger cardiac severity score ≥ 2; Normal DLCO = diffusing capacity of carbon monoxide >60%

p=0.01]. Those with delayed small bowel transit were more likely to have low (worse) mean DLCO (51% vs. 68%, p=0.03) and were more likely to die [26% (6/15) vs. 9% (9/15); p=0.02]. In the univariate analyses, we determined that a higher modified Rodnan skin score [Odd's ratio (OR)=1.05, confidence interval (CI) 1.00-1.11, p=0.05], more cardiac involvement (OR=3.54, CI 1.00-12.52, p=0.05), less sicca symptoms (OR=0.26, CI 0.09-0.76, p=0.02), and lower DLCO (OR=0.97, CI 0.95-1.00, p=0.03) were associated with delayed small bowel transit. In the multivariable model, sicca symptoms (OR=0.29, CI 0.10-0.90, p=0.03) remained negatively associated with delayed small bowel transit.

Conclusion: These findings suggest delayed small bowel transit in SSc is associated with a high mortality and a specific clinical phenotype. Recognizing patients at risk for delayed small bowel transit is important for clinical care and in the design of future studies evaluating this high-risk group.

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Abstract Number: 0612

COVID Vaccinations and Infections Among Individuals with Systemic Sclerosis: A Scleroderma Patient-centered Intervention Network (SPIN) Cohort Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: We previously surveyed individuals with systemic sclerosis (SSc) enrolled in Scleroderma Patient-centered Intervention Network (SPIN) Cohort between April-May 2021 to determine COVID-19 vaccination rates, adverse reactions, and vaccine hesitancy. The purpose of the present study was to extend analyses through June-July 2022 and assess (1) COVID vaccination rates, including boosters; (2) vaccine-related adverse events from primary series and booster vaccine doses; (3) peri-vaccination immunosuppressive (IS) medication management; (4) vaccine hesitancy and perceptions; and (5) rate and severity of self-reported COVID-19 in SSc.

Methods: Participants were adults with SSc enrolled in the SPIN Cohort, which includes 47 centers from seven countries. Participants from the SPIN Cohort, including those who did and did not complete the 2021 survey, were invited to complete the second survey from June 1 to July 4, 2022. The survey included items related to COVID-19 history, COVID-19 vaccinations, and perceptions related to COVID-19 vaccines. Participants were considered "fully vaccinated" if they had completed a primary vaccine series and received at least one booster dose.

Results: 544 participants answered the 2021 survey only, 101 answered the 2022 survey only, and 388 answered both. Participant characteristics are shown in Table 1. 437 of 489 (89%) participants who completed the 2022 survey received a booster dose. 18 of 31 (58%) participants who were vaccine hesitant in 2021 were vaccinated by the 2022 survey. Adverse events following primary vaccine and booster doses are shown in Table 2. SSc symptom worsening was reported after the first and second vaccine dose in 6% (53 of 960 and 39 of 657, respectively) and after the booster dose in 4% (17 of 437) (Table 2). Of 157 patients taking methotrexate (MTX) or mycophenolate (MMF), 129 (82%) held those at the time of booster vaccination. Of 58 individuals not fully vaccinated, 29 (50%) were worried that the vaccine would cause an SSc flare; 19 (33%) indicated that they did not have enough information to decide about vaccination. 172 of 489 (35%) from the 2022 survey reported a history of COVID-19 (Table 3), 114 (66%) of which occurred after completing a primary vaccine series. 9 (5%) were asymptomatic, 66 (44%) had mild symptoms, 82 (48%) had moderate symptoms, and 15 (9%) required hospitalization. Of those 15 hospitalized individuals, 9 (60%) were taking at least one IS medication, 11 were fully vaccinated, 3 were partially vaccinated, and 1 was unvaccinated at the time of hospitalization.

Conclusion: Most participants were fully vaccinated, and a majority held their MTX or MMF post-booster vaccination, which is aligned with recent American College of Rheumatology Guidance. Most vaccine-hesitant participants were concerned regarding risk of SSc flare; however, few vaccinated participants reported an SSc flare following primary (6%) or booster

Table 1. Participant Characteristics

Variable	Total N=1033	Survey 1 only participant N=544	Survey 1 and survey 2 participant N=388	Survey 2 only participant N=101
Age, years, mean (SD)	61 (12)[a]	61 (12)	62 (12)[b]	60 (12)
Female, N (%)	921 (89)	486 (89)	344 (89)	91 (90)
Race/ethnicity, N (%)				
White	866	448 (82)	346 (89)	72 (71)
Black	52	35 (6)	10 (3)	7 (7)
Other	94	51 (9)	28 (7)	15 (15)
Not reported	21	10 (2)	4 (1)	7 (7)
Country, N (%)		-	-	
United States	305	161 (30)	114 (29)	30 (30)
France	316	179 (33)	102 (26)	35 (35)
Canada	290	144 (27)	121 (31)	25 (25)
United Kingdom	96	48 (9)	38 (10)	10 (10)
Australia	24	11 (2)	12 (3)	1 (1)
Mexico	1	0 (0)	1 (0)	0 (0)
Not reported	1	1 (0)	0 (0)	0 (0)
Disease subtype, N (%)				
Limited	610	319 (59)	234 (60)	57 (56)
Diffuse	377	197 (36)	137 (35)	43 (43)
Sine	37	23 (4)	13 (3)	1 (1)
Not reported	9	5 (1)	4 (1)	0 (0)
Years since first non-Raynaud's symptoms, mean (SD)	16 (9)[c]	16 (9)[d]	17 (10)[e]	14 (12)[f]
Current immunosuppressive, N (%)	482	261 (48)	173 (45)	48 (48)
Corticosteroids[g]	219	114 (21)	87 (22)	18 (18)
Mycophenolate	225	110 (20)	93 (24)	22 (22)
Hydroxychloroquine[h]	81	81 (15)	--	--
Methotrexate	99	52 (10)	32 (8)	15 (15)
Rituximab	38	18 (3)	11 (3)	9 (9)
Tocilizumab	22	12 (2)	7 (2)	3 (3)
Azathioprine	28	9 (2)	13 (3)	6 (6)
Cyclophosphamide	14	8 (1)	6 (2)	0 (0)
Abatacept	9	6 (1)	2 (1)	1 (1)
Tofacitinib	6	3 (1)	2 (1)	1 (1)
Stem cell transplant	24	18 (3)	6 (2)	--
Interstitial lung disease, N (%)	251	133 (24)	118 (30)	--
Pulmonary hypertension, N (%)	143	79 (15)	64 (17)	--
Current smoker, N (%)	44	27 (5)	17 (4)	--

Survey 1 was conducted in 2021; Survey 2 was conducted in 2022. "–" indicates that data are missing.

Table 2. Self-reported adverse events following a COVID vaccine among 1033 individuals with systemic sclerosis enrolled in the SPIN Cohort who received at least one dose

Adverse reaction, N (%)	First Dose (N=960)	Second Dose (N=657)	Booster (N=437)
No adverse reaction	630 (66%)	343 (52%)	290 (64%)
At least one adverse reaction[a]	330 (34%)	314 (48%)	147 (34%)
Sore arm	257 (27%)	244 (37%)	110 (25%)
Fatigue	197 (21%)	218 (33%)	100 (23%)
Muscle ache	86 (9%)	129 (20%)	57 (13%)
Joint pain	55 (6%)	65 (10%)	26 (6%)
Flu-like symptoms	56 (6%)	86 (13%)	45 (10%)
Fever	57 (6%)	86 (13%)	45 (10%)
Chills	63 (7%)	95 (14%)	42 (10%)
Shortness of breath	20 (2%)	16 (2%)	11 (3%)
Rash	15 (2%)	12 (2%)	3 (1%)
Severe allergy	0 (0%)	0 (0%)	0 (0%)
Hives	0 (0%)	3 (0%)	0 (0%)
At least one systemic sclerosis symptom worsening	53[b] (6%)	39[c] (6%)	17[d] (4%)

[a]Participants could report > 1 adverse reaction; [b]Most common systemic sclerosis symptoms worsening (first dose): fatigue (n=32), muscle weakness (n=18), Raynaud's (n=19), shortness of breath (n=18), arthritis (n=13); [c]Most common SSc symptoms worsening (second dose): fatigue (n=26), muscle weakness (n=16), Raynaud's (n=15), gastrointestinal symptoms (n=14), arthritis (n=14), shortness of breath (n=12); [d]Most common SSc symptoms worsening (second dose): fatigue (n=11), muscle weakness (n=7), gastrointestinal symptoms (n=6), arthritis (n=6), Raynaud's (n=6), shortness of breath (n=3).

doses (4%). In a highly vaccinated cohort, 35% reported a history of COVID-19, of whom 9% required hospital care. This is the largest, longitudinal study to-date of COVID-19 focused upon SSc. These data may be used to counsel patients regarding vaccine safety and COVID-19 outcomes.

Table 3. COVID-19 history among individuals with systemic sclerosis who completed the 2022 survey

Variable	Total N=489	History of COVID-19[a] N=172	No history of COVID-19 N=317
Vaccination, n (%)[b]			
Fully vaccinated	437	140 (32%)	297 (68%)
Partially vaccinated	39	25 (64%)	14 (36%)
Unvaccinated	13	7 (54%)	6 (46%)
Sex, n (%)			
Female	435	155 (36%)	280 (64%)
Male	54	17 (32%)	37 (68%)
Age[c]	61 (12)	59 (11)	62 (12)
Race/ethnicity, n (%)			
White	418	143 (34%)	275 (66%)
Black	17	10 (59%)	7 (41%)
Other	43	15 (35%)	28 (65%)
Not reported	11	4 (36%)	7 (64%)
Country, n (%)			
United States	144	41 (29%)	103 (71%)
France	137	64 (47%)	73 (53%)
Canada	146	37 (25%)	109 (75%)
United Kingdom	48	29 (60%)	19 (40%)
Australia	13	1 (8%)	12 (92%)
Mexico	1	0 (0%)	1 (100%)
Disease subtype, n (%)			
Limited	291	101 (35%)	190 (65%)
Diffuse	180	67 (37%)	113 (63%)
Sine	14	4 (29%)	10 (71%)
Not reported	4	0 (0%)	4 (100%)
Years since first non-Raynaud's symptoms, mean (SD)[d]	16 (10)	15 (9)	17 (10)
Immunosuppressive medication, any, n (%)	221	84 (38%)	137 (62%)
Corticosteroids[e]	105	41 (39%)	64 (61%)
Methotrexate	47	23 (49%)	24 (51%)
Azathioprine	19	9 (47%)	10 (53%)
Mycophenolate	115	40 (35%)	75 (65%)
Tocilizumab	10	1 (10%)	9 (90%)
Abatacept	3	2 (67%)	1 (33%)
Tofacitinib	3	0 (0%)	3 (100%)
Cyclophosphamide	6	1 (17%)	5 (83%)
Rituximab	20	8 (40%)	12 (60%)
Stem cell transplant, n (%)[f]	6	3 (50%)	3 (50%)
Interstitial lung disease, n (%)	118	39 (33%)	79 (69%)
Pulmonary hypertension, n (%)	64	21 (34%)	43 (66%)
Current smoker, n (%)	17	4 (24%)	13 (76%)

a. Indicates at least one COVID infection. 11 participants had two infections, and 1 participant had three infections; b. Fully vaccinated indicates the participant completed a primary vaccine series and had received at least one booster dose. c. N = 488. For the group of no history of COVID, N = 316. d. N=453, for the group with history of COVID, N = 155, and for the group of no history of COVID, N = 298; e. Includes prednisone and/or methylprednisolone or prednisolone; f. The following four variables were not available among the Survey 2 only participants, so N = 388.

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Abstract Number: 0613

Quantification of Skin Hardness of Patients with Systemic Sclerosis Using SOFTGRAM

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: No quantitative and objective methods for measuring skin hardness have been established. Japanese technology leads the world in the tactile sensor field, and SOFTGRAM has received an award from the Going-Global Innovations Competition 2019.This study aimed to verify whether SOFTGRAM, a device that can measure elastic modulus using the Hertz elastic contact theory, could be used to evaluate skin hardness in systemic sclerosis (SSc). As a far-reaching effect, this study might be one of the triggers to progress a diagnosis with medical artificial intelligence systems for various diseases.

Methods: Skin score according to the modified Rodnan's total skin thickness score and elastic modulus of the skin using SOFTGRAM were measured for 20 patients with SSc and 20 healthy controls on 8 parts, both of the cheeks, forearms, fingers, and hands (Figure 1). Five observers shared to measure skin score 320 times (40 participants × 8 parts). Elastic modulus was measured 1600 times (40 participants × 8 parts × 5 times each). As an additional examination to compare differences among observers, the skin score of another healthy control was measured 40 times (5 observers × 8 parts). Elastic modulus was measured 200 times (5 observers × 8 parts × 5 times each).

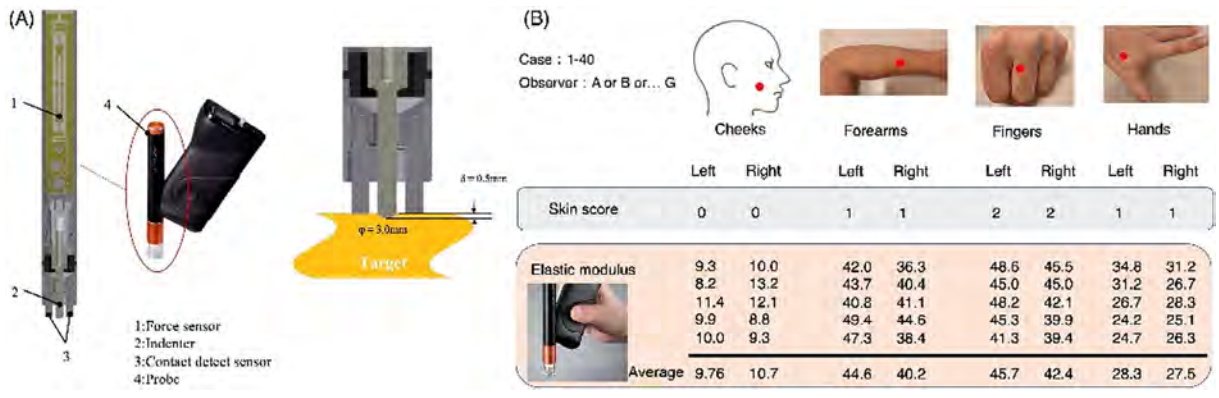

Figure 1. (A) Sensing device. (B) Measurement points and an example.

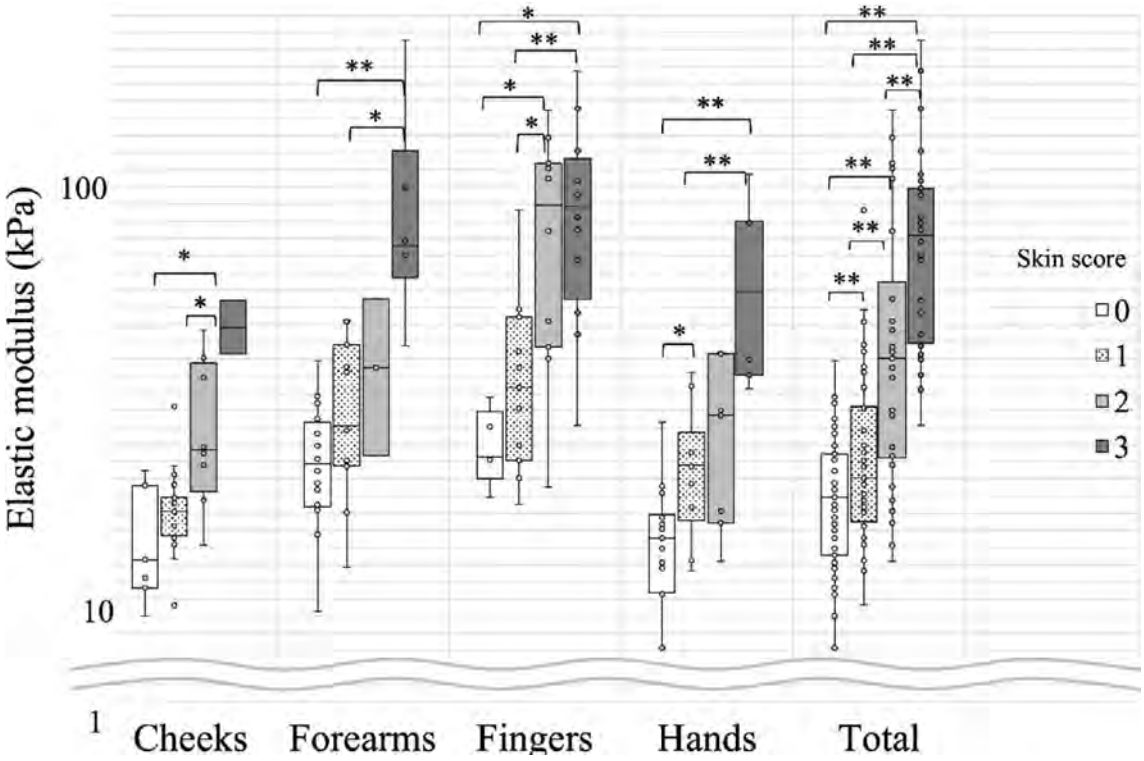

Figure 2. Correlation between elastic modulus (logarithmic scale) with SOFTGRAM and skin score of 40 participants (*p<0.05, **p<0.01).

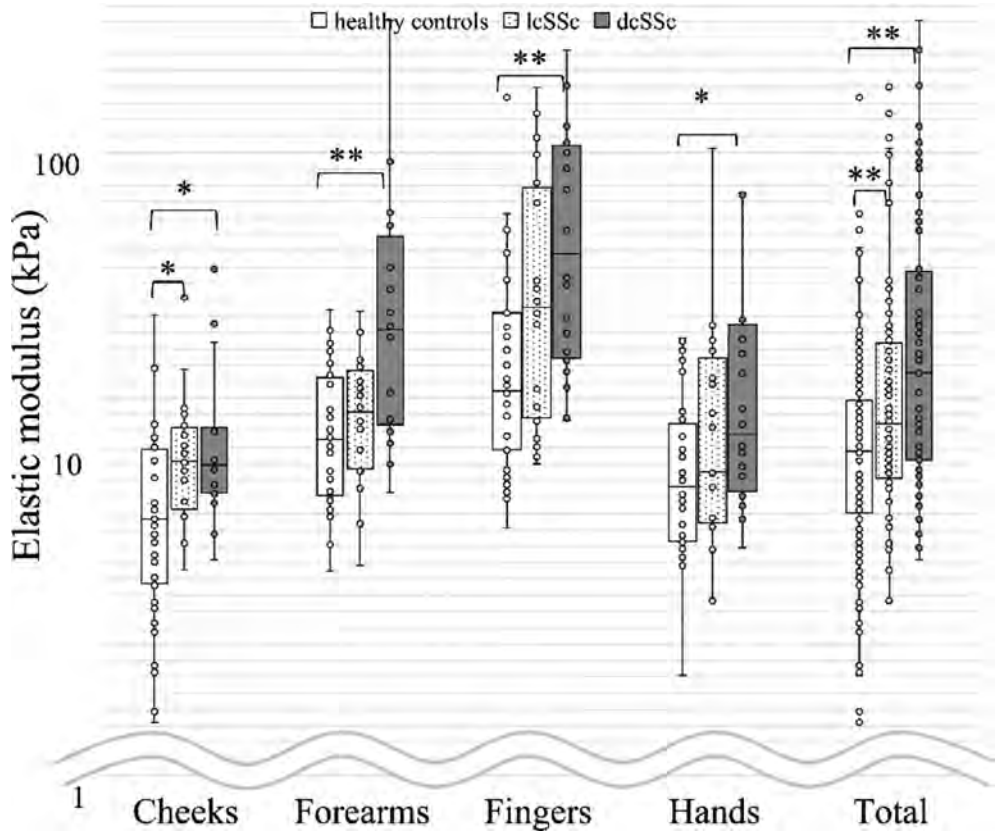

Figure 3. Elastic modulus of healthy controls, lcSSc, and dcSSc patients (*p<0.05, **p<0.01).

Results: Data were collected from 20 healthy Japanese controls (1 male and 19 females; 63.2±12.3 years old), 10 lcSSc patients (10 females; 65.9±6.3 years old), and 10 dcSSc patients (1 male and 9 females; 58.8±14.9 years old).Our findings reveal a significant correlation between elastic modulus and skin score (correlation coefficient=0.67, $p< 0.001$; Figure 2). Furthermore, we observed significant differences in elastic modulus among healthy controls, limited cutaneous SSc, and diffuse cutaneous SSc (22.6±15.7 vs. 32.0±27.7 vs. 44.8±39.8, $p< 0.001$; Figure 3). Intraobserver reliabilities were sufficient in 6 of 7 observers; however, interobserver was less satisfactory.It would be because elastic modulus depended on the skin position and the power and speed to push by SOFTGRAM. Regarding the skin position, bone hyperreflection might affect elastic modulus. If SOFTGRAM is improved to measure only the more shallow parts, the effect of bone hyperreflection might be minimal.

Conclusion: SOFTGRAM has many advantages compared to previous methods. This study showed the practicality of SOFTGRAM as an accurate measurement method of skin hardness but also revealed points to be improved. SOFTGRAM will have further improvements, and sensing devices will be able to useful especially for clinical trials and research.

Disclosure: H. Kokubu: ISHIDA MEDICAL CO.,LTD., 5; **Y. Ikuno**: ISHIDA MEDICAL CO.,LTD., 5; **K. Uchiyama**: ISHIDA MEDICAL CO.,LTD., 5; **M. Kato**: ISHIDA MEDICAL CO.,LTD., 5; **M. Yamamoto**: ISHIDA MEDICAL CO.,LTD., 5; **H. Asada**: ISHIDA MEDICAL CO.,LTD., 5; **S. Rikitake**: ISHIDA MEDICAL CO.,LTD., 5; **Y. Kobayashi**: ISHIDA MEDICAL CO.,LTD., 5; **T. Koike**: ISHIDA MEDICAL CO.,LTD., 5; **S. Sugiura**: ISHIDA MEDICAL CO.,LTD., 5; **T. Hayami**: ISHIDA MEDICAL CO.,LTD., 5; **K. Yoneta**: ISHIDA MEDICAL CO.,LTD., 5; **T. Takahashi**: ISHIDA MEDICAL CO.,LTD., 5; **B. Yamamoto**: ISHIDA MEDICAL CO.,LTD., 5; **T. Kato**: ISHIDA MEDICAL CO.,LTD., 5; **Y. Kunisaki**: ISHIDA MEDICAL CO.,LTD., 3; **M. Nakatani**: ISHIDA MEDICAL CO.,LTD., 3; **K. Okamoto**: ISHIDA MEDICAL CO.,LTD., 3; **N. Fujimoto**: ISHIDA MEDICAL CO.,LTD., 5.

Abstract Number: 0614

Self-Reported Sexual Dysfunction and Perceptions of Rheumatologist Engagement on This Issue in Patients with Systemic Sclerosis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Few studies have investigated the prevalence and risk factors of sexual dysfunction among individuals with systemic sclerosis (SSc). The purpose of this study is to define, among individuals with SSc, (1) the prevalence and risk factors associated with sexual dysfunction, (2) the frequency of discussions regarding this subject, and (3) patient-perceived barriers to those discussions.

Methods: We developed the Sexual Function in SSc Questionnaire (SFSScQ) to anonymously survey individuals with self-reported SSc regarding their sexual function and sexual health discussions with their MD rheumatologist. Participants were asked to complete the SSFSScQ and to complete the Female Sexual Function Index (FSFI) or the International Index of Erectile Function (IIEF) Questionnaire based on self-reported sex. Participant characteristics between those with vs. without self-reported sexual dysfunction were compared using Fisher's Exact test. Agreement to statements regarding potential barriers to sexual function conversations were compared between those who reported feeling satisfied vs. not satisfied with sexual

Table 1. Bivariate comparison between participants with systemic sclerosis who self-reported sexual dysfunction and participants who did not by characteristics and demographics.

Variable	Total, n. (wt%)	Self-Reported Sexual Dysfunction		*P* value
		Not present, n. (wt%)	Present, n. (wt%)	
	N = 41	N = 15 (37%)	N = 26 (63%)	
Scleroderma Subtype				0.518
Limited Cutaneous	11 (26.8%)	5 (33.3%)	6 (23.1%)	
Diffuse Cutaneous	15 (36.6%)	5 (33.3%)	10 (38.5%)	
Systemic Sclerosis Sine	7 (17.1%)	1 (6.7%)	6 (23.1%)	
I am not sure	8 (19.5%)	4 (26.7%)	4 (15.4%)	
SSc Disease Duration				0.448
Mean (SD)	10.0 (8.3)	7.3 (7.2)	11.6 (8.5)	
Age (years)				0.102
18-40	5 (12.2%)	4 (26.7%)	1 (3.9%)	
41-60	25 (61.0%	7 (46.7%)	18 (69.2%)	
61+	11 (26.8%)	4 (26.7%)	7 (26.9%)	
Sex at Birth				0.064
Female	31 (75.6%)	14 (93.3%)	17 (65.4%)	
Male	10 (24.4%)	1 (6.7%)	9 (34.6%)	
Ethnicity				0.387
Hispanic or Latino	7 (17.5%)	1 (7.1%)	6 (23.1%)	
Non-Hispanic or Non-Latino	33 (82.5%)	13 (92.9%)	20 (76.9%)	
Race*				0.390
Asian	3 (7.3%)	2 (13.3%)	1 (3.9%)	
Black or African American	4 (9.8%)	2 (13.3%)	2 (7.7%)	
White	34 (82.9%	11 (73.3%)	23 (88.5%)	
Preferred Language*				0.366
English	40 (97.6%)	14 (93.3%)	26 (100.0%)	
Spanish	1 (2.4%)	1 (6.7%)	0 (0.0%)	
Insurance*				0.478
Private	23 (56.1%)	8 (53.3%)	15 (57.7%)	
Medicaid only	4 (9.8%)	0 (0.0%)	4 (15.4%)	
Medicare	2 (4.9%)	1 (6.7%)	1 (3.9%)	
Medicare/Medicaid	2 (4.9%)	1 (6.7%)	1 (3.9%)	
Medicare/Private	9 (22.0%)	4 (26.7%)	5 (19.2%)	
Other	1 (2.4%)	1 (6.7%)	0 (0.0%)	
Education*				0.435
High School Diploma or Equivalent	5 (12.2%)	1 (6.7%)	4 (15.4%)	
Associate Degree	10 (24.4%)	2 (13.3%)	8 (30.8%)	
Bachelor's Degree	14 (34.2%)	7 (46.7%)	7 (26.9%)	
Graduate Degree	12 (29.3%)	5 (33.3%)	7 (26.9%)	
Employment*				0.113
Employed, Part-time	6 (14.6%)	1 (6.7%)	5 (19.2%)	
Employed, Full-time	16 (39.0%)	6 (40.0%)	10 (38.5%)	
Not Employed, Unable to work	5 (12.2%)	0 (0.0%)	5 (19.2%)	
Retired	13 (31.7%)	7 (46.7%)	6 (23.1%)	
Student	1 (2.4%)	1 (6.7%)	0 (0.0%)	
Religion				0.070
Atheism	5 (12.2%)	1 (6.7%)	4 (15.4%)	
Christianity	15 (36.6%)	3 (20.0%)	12 (46.2%)	
Islam	1 (2.4%)	1 (6.7%)	0 (0.0%)	
Judaism	5 (12.2%)	2 (13.3%)	3 (11.5%)	
Other	6 (14.6%)	5 (33.3%)	1 (3.9%)	
Prefer Not to Say	9 (22.0%)	3 (20.0%)	6 (23.1%)	
Sexual Orientation*				1
Asexual	3 (7.3%)	1 (6.7%)	2 (7.7%)	
Bisexual	2 (4.9%)	1 (6.7%)	1 (3.9%)	
Heterosexual	35 (85.4%)	13 (86.67%)	22 (84.6%)	
Homosexual	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Other**	1 (2.4%)	0 (0.0%)	1 (3.9%)	
Relationship Status*				0.256
Divorced	5 (12.2%)	3 (20.0%)	2 (7.7%)	
Married	27 (65.9%)	8 (53.3%)	19 (73.1%)	
Single	5 (12.2%)	1 (6.7%)	4 (15.4%)	
Current Relationship (Not Married)	3 (7.3%)	2 (13.3%)	1 (3.9%)	
Widowed	1 (2.4%)	1 (6.7%)	0 (0.0%)	
Prefer Not to Say	0 (0.0%)	0 (0.0%)	0 (0.0%)	

*Categories that no participants reported or identified as were removed from the table

**1 participant reported identifying as parsexual

Variable	Total, n. (wt%)	Self-Reported Sexual Dysfunction		*P* value
		Not present, n. (wt%)	Present, n. (wt%)	
	n = 30	n= 10 (33.3%)	n = 20 (66.7%)	
Sexual Dysfunction (as defined by FSFI and IIEF Questionnaire)				0.431
Present	21 (70.0%)	6 (60.0%)	15 (75.0%)	
Not Present	9 (30.0%)	4 (40.0%)	5 (25.0%)	

Variable	Total, n (%)	Satisfaction with conversation with rheumatologist regarding sexual health		*P* value
		Satisfied, n (%)	Not Satisfied, n (%)	
	n = 41	n = 8 (19.5%)	n = 33 (80.5%)	
"I am comfortable discussing my sexual function with my rheumatologist."				**0.012***
Agree[1]	14 (34.2%)	6 (75.0%)	8 (24.2%)	
Does not agree[2]	27 (65.9%	2 (25.0%)	25 (75.8%)	
"My rheumatologist makes time to listen to and answer all my questions and concerns about my sexual function."				**0.003****
Agree[1]	8 (19.5%)	5 (62.5%)	3 (9.1%)	
Does not agree[2]	33 (80.5%)	3 (37.5%)	30 (90.9%)	
"My rheumatologist has been helpful when addressing sexual function."				**0.002****
Agree[1]	5 (12.5%)	4 (57.1%)	1 (3.0%)	
Does not agree[2]	35 (87.5%)	3 (42.9%)	32 (97.0%)	
"I think it is important to discuss my sexual function with my rheumatologist."				0.436
Agree[1]	19 (46.3%)	5 (62.5%)	14 (42.4%)	
Does not agree[2]	22 (53.7%)	3 (37.5%)	19 (57.6%)	
"It is my rheumatologist's job to start the conversation about sexual function."				0.172
Agree[1]	8 (19.5%)	3 (37.5%)	5 (15.2%)	
Does not agree[2]	33 (80.5%)	5 (62.5%)	28 (85.9%)	
"I wish my rheumatologist would bring up my sexual function more often."				0.079
Agree[1]	12 (29.3%)	0 (0.0%)	12 (36.4%)	
Does not agree[2]	29 (70.7%)	8 (100.0%)	21 (63.6%)	
Self-Reported Sexual Dysfunction				1
Present	26 (63.4%)	5 (62.5%)	21 (63.6%)	
Not present	15 (36.6%)	3 (37.5%)	12 (36.4%)	

[1] 'Agree' includes participants who reported 'Agree' and 'Strongly Agree'

[2]'Does not agree' includes participants who reported 'Strongly disagree', 'Disagree', 'Does not apply', and 'Neutral'

* significant at $p < 0.05$ ** significant at $p < 0.005$

health discussions using Fisher's Exact test. Univariable and multivariable logistic regression were performed to assess factors associated with sexual dysfunction.

Results: 41 participants completed the SFSScQ; 30 (73%) also completed the FSFI or IIEF. 26 (63%) participants reported sexual dysfunction. Clinical characteristics of those with vs. without self-reported sexual dysfunction are shown in Table 1. In both unadjusted and adjusted regression models, age, sex, race, SSc subtype, and time since SSc diagnosis were not predictors of sexual dysfunction. Self-reported sexual dysfunction was not associated with the presence of sexual dysfunction on the scored questionnaires (p=0.431); 25% of individuals who self-reported sexual dysfunction did not meet scored questionnaire criteria (Table 2). 36 (88%) of 41 participants had never discussed sexual health with their rheumatologist, of whom 23 (64%) self-reported sexual dysfunction. 19 (46.3%) participants agreed that having conversations with their rheumatologist regarding sexual function was important. Most (33 (81%)) were not satisfied with the sexual health discussions they have had to-date (Table 3). Patients who were satisfied (vs. not satisfied) with their sexual health discussions more often felt comfortable discussing sexual function with their rheumatologist (p=0.012), believed their rheumatologist makes time to discuss sexual function (p=0.003), and felt that their rheumatologist has been helpful regarding sexual function (p=0.002) (Table 3).

Conclusion: A majority of participants with self-reported SSc indicated that they experience sexual dysfunction but have never discussed sexual health with their rheumatologist. No patient-level factors were identified as independent predictors of sexual dysfunction; however, our sample size is small. Self-reported sexual dysfunction was not associated with sexual dysfunction determined by scored questionnaires, suggesting that SSc sexual dysfunction may encapsulate disease specific complaints not captured by surveys designed for other populations.

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Abstract Number: 0615

Prevalence of Barrett's Esophagus in Patients with Systemic Sclerosis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Gastrointestinal manifestations of systemic sclerosis are common and include luminal dysmotility. Esophageal aperistalsis (scleroderma esophagus) presents with dysphagia and reflux; and can predispose patients to esophagitis, theoretically increasing the risk for Barrett's esophagus, which is a known risk factor of esophageal adenocarcinoma. However, no current data is available in literature regarding the risk of Barrett's esophagus or esophageal adenocarcinoma in patients with SS.

Methods: A retrospective cohort study was conducted using the multi-institutional research network TriNetX. All patients with systemic sclerosis (age 16 and above) were identified. Prevalence and incidence proportion of Barrett's esophagus were calculated for the year 2022.

Table 1: Baseline characteristics of patients with Systemic Sclerosis and Barrett's Esophagus before and after propensity score matching.

Variables	Before the propensity score match			After the propensity score match		
	SS cohort Mean±SD or Number (%)	Control cohort Mean±SD or Number (%)	SMD	SS cohort Mean±SD or Number (%)	Control cohort Mean±SD or Number (%)	SMD
Age at index	10808(56.6 ± 15.3)	1969047(53.3 ± 19.2)	0.1878	10808(56.6 ± 15.3)	10808(56.6 ± 15.3)	<0.0001
Sex, n (%), *Female*	8939(82.7)	1114772(56.6)	0.5919	8939(82.7)	8938(82.7)	0.0002
Male	1869(17.3)	854086(43.4)	0.5917	1869(17.3)	1869(17.3)	<0.0001
Ethnicity, n (%),						
Hispanic or Latino	1171(10.8)	156878(7.9)	0.0984	1172(10.8)	773(7.2)	0.1290
Non Hispanic or Latino	7978(73.8)	1409554(71.6)	0.0501	7978(73.8)	8127(75.2)	0.0316
Race, n (%),						
White	7487(69.3)	1401534(71.2)	0.0417	7487(69.3)	7487(69.3)	<0.0001
Black or African Americans	1658(15.3)	246634(12.5)	0.0814	1658(15.3)	1658(15.3)	<0.0001
BMI	6831(27.3±7.03)	959433(28.4±7.26)	0.1592	6831(27.3±7.03)	6830(29.4±7.41)	0.2946
Personal history of Nicotine use	2460(22.8)	279610(14.2)	0.2219	2460(22.8)	2460(22.8)	<0.0001
GERD	8271(76.5)	934434(47.5)	0.6277	8271(76.5)	8271(76.5)	<0.0001
Esophagitis	2319(21.5)	221866(11.3)	0.2781	2319(21.5)	1350(12.5)	0.2405
Omeprazole	5213(48.2)	563621(28.6)	0.4116	5213(48.2)	4022(37.2)	0.2242
Pantoprazole	4595(42.5)	578571(29.4)	0.2763	4595(42.5)	3779(34.5)	0.1554
Esomeprazole	2471(22.9)	198097(10)	0.3505	2471(22.9)	1445(13.4)	0.2484
Lansoprazole	1068(9.9)	98892(5)	0.1858	1068(9.9)	659(6.1)	0.1399
Dexlansoprazole	501(4.6)	21500(1.1)	0.2137	501(4.6)	178(1.6)	0.1720
Rabeprazole	256(2.4)	18170(0.9)	0.1138	256(2.4)	143(1.3)	0.0777

Baseline characteristics of patients with Systemic Sclerosis and Barrett's Esophagus before and after propensity score matching

Propensity matched analysis was then performed, utilizing age, gender, race, presence of GERD, and history of smoking as covariates, to compare rates of BE diagnosis at index endoscopy in patients with and without SS who underwent EGD during the study time period.

Results: A total of 60,907 patients with SS were identified in the research network. The prevalence and incidence proportion of Barrett's esophagus in patients with SS during 2022 were calculated to be 3.96% and 0.39% respectively. Incidence rate of BE diagnosis in the cohort was 0.000014 cases/ person day. The prevalence and incidence rate of Barrett's esophagus in patients without SS during the same period was 0.54% and 0.074% respectively.

Patients with SS who underwent EGD examinations were identified and 1:1 propensity score matching was performed to identify a control cohort of patients without SS who underwent index EGD during the study period (10,808 patients in each cohort). In PSM analysis, the risk of Barrett's esophagus diagnosis at index esophagogastroduodenoscopy (EGD) was not different between patients with systemic sclerosis compared to patients without SS who underwent EGD for any indication [3.67% vs 3.37 %, RR: 1.09 (0.95 – 1.25)]. However, the risk of BE esophagus diagnosis at any time during follow up was higher in patients with SS [8.11% vs 6.17%, RR: 1.32 (1.19-1.45)]. No difference was noted in rates of esophageal cancer diagnosis in the two cohorts [0.86% vs 0.96%, RR: 0.89 (0.68-1.18)].

Conclusion: The prevalence and incidence rate of BE diagnosis in patients with SS is high. Provider vigilance is advised, and EGD screening and proton pump inhibitor therapy should be considered in patients with SS with upper GI symptoms.

Disclosure: F. Rida Ul Jannat: None; **D. Verma**: None; **L. Sakkal**: None.

Abstract Number: 0616

Does Systemic Sclerosis Affect the Interpretation of Mammograms? A Retrospective Cohort Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Sclerosis is an autoimmune disorder marked by thickened and hardened skin. Cutaneous cutis, the deposition of insoluble calcium salts in the skin and subcutaneous tissues, occurs frequently in patients with systemic sclerosis. Breast mammography is a screening tool used to detect breast cancer. Approximately 10% of all patients have abnormal mammograms with areas of calcification, which may be a sign of malignancy. There has been no formal study to date evaluating the mammograms of patients with systemic sclerosis. This study compared the mammograms and breast biopsies of systemic sclerosis patients with that of age matched controls.

Methods: Patients diagnosed with systemic sclerosis and with mammograms done at Mount Sinai Hospital between 01/01/2017 and 01/11/2022 were identified using the Reports function in Epic. The results of these mammograms and subsequent breast biopsy results were analyzed. Participants' race/ethnicity, serologic markers, clinical features, use of immunosuppressive medications, and duration of systemic sclerosis diagnosis were determined by chart review. These results were compared to age matched controls with abnormal mammograms and breast biopsies. The primary outcome was the frequency of false positive abnormal mammography findings. Sub-analysis was performed among the patients with systemic sclerosis comparing patients with malignancy found on breast biopsy to those with benign findings. Chi Square analysis and Independent Sample T test were used to check for statistical significance.

Results: Of the patients with systemic sclerosis, more than a third of these patients (36%) were found to have had calcifications on their mammograms. 29/152 (19%) were found to have abnormal breast mammograms and were referred for breast biopsy. Of these patients, 34.5% were diagnosed with a malignancy after completing their breast biopsy. 65.5% of the scleroderma patients were found to have false positive screening mammograms versus 67% of the age-matched control group. Sub-analysis within the scleroderma cohort found no statistically significant differences in serologic markers or clinical features amongst patients with breast cancer compared to those without breast cancer. Of the systemic sclerosis patients found to have had true malignancies, only 1 (10%) was taking hydroxychloroquine, while 10 (52.6%) of patients with false positive mammograms were taking hydroxychloroquine. There were no other statistically-significant differences in terms of medication usage.

Conclusion: Approximately 1/5th of patients with systemic sclerosis were found to have abnormal breast mammograms. There were no significant differences in the rate of false positive mammograms in patients with systemic sclerosis and healthy controls.

Disclosure: L. Meir: None; **T. Sandhu**: None; **W. Chi**: None; **G. Santiago**: None.

Abstract Number: 0617

Pulmonary Rehabilitation in Connective Tissue Disease-Related Interstitial Lung Diseases

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a common manifestation of connective tissue disease (CTD)[1]. Pulmonary rehabilitation (PR) can be utilized to improve dyspnea and quality of life in patients with chronic lung conditions, including both obstructive and restrictive lung diseases[2]. This study aims to determine if PR can be a useful therapy to improve dyspnea and hall walk in CTD-ILD.

Methods: Patients at a tertiary center who were referred to PR rheumatology as the standard of care were enrolled in this study. To determine the outcomes of patients who underwent PR, pulmonary function tests (PFTs), 6-minute walk test (6MWT), and patient-reported outcomes (PROs) including PROMIS Dyspnea, St George Respiratory Questionnaire

Table 1: Baseline Demographics. *Three subjects did not fall into the CTD types above. One patient had high titer anti-CCP, one had Sjogren's and Polymyositis, one had Undifferentiated CTD.

Variable	Statistics (n=21)
Age (year), Mean (Standard Deviation)	65.5 (8.0)
Type of CTD, n (%)	
Systemic Sclerosis	16 (76.2%)
Rheumatoid Arthritis	2 (9.5%)
Other*	3(14.3%)
Sex, n (%)	
Female	13 (61.9%)
Race, n (%)	
Caucasian/White	18 (85.7%)
Ethnicity, n (%)	
Non-Hispanic/Non-Latino	20 (95.2%)
FVC % Predicted, Mean (Standard Deviation), n=19	
Baseline	64.8 (20.4)
DLCO % Predicted, Mean (Standard Deviation), n=18	
Baseline	45.3 (12.6)

Table 2: Average 6MWD and PROMIS dyspnea scores were recorded at baseline and 8 weeks after starting PR. Mean (Standard Deviation) is reported in table above.

Primary Outcome Measures	Baseline	Week 8	Difference	p-value
6MWD (meters), n=18	402.3 (114.3)	447.3 (94.8)	45.1 (63.0)	**0.007**
PROMIS Dyspnea				
Characteristics, n=21	17.2 (11.7)	15.5 (9.2)	-1.7 (7.7)	0.26
Severity, n=21	52.3 (7.5)	51.6 (6.3)	-0.6 (4.5)	0.59
Functional Limitation, n=21	54.3 (7.4)	52.4 (9.2)	-1.9 (4.9)	0.09
Secondary Outcome Measures				
LCQ, n=21	16.2 (3.7)	17.2 (3.6)	0.9 (1.8)	**0.03**
Physical, n=21	5.4 (1.0)	5.8 (0.9)	0.4 (0.6)	**0.01**
Psychological, n=21	5.4 (1.4)	5.7 (1.4)	0.3 (0.7)	0.06
Social, n=21	5.5 (1.4)	5.7 (1.4)	0.2 (0.6)	0.17
SGRQ, n=19	41.2 (17.7)	39.3 (15.9)	-1.9 (10.5)	0.23
Symptom, n=19	51.7 (18.1)	42.2 (15.8)	-9.6 (14.4)	**0.01**
Activity, n=20	29.5 (15.1)	29.4 (14.3)	-0.04 (11.4)	0.49
Impact, n=20	12.5 (8.2)	11.4 (7.8)	-1.1 (4.3)	0.28

(SGRQ), and Leicester Cough Questionnaire (LCQ) were collected before and at 8 weeks after PR. 21 patients were included in the data analysis. P< 0.05 was considered statistically significant.

Results: The baseline characteristics are shown in Table 1. Following PR, there was a statistically significant improvement in 6MWT (Table 2). Improvement in scores was observed in LCQ and the symptom domain of the SGRQ. Trends were noted in PROMIS Dyspnea scores.

Conclusion: In CTD-ILD patients, an 8-week course of PR led to improvements in functional capacity (6MWT) and certain quality of life domains (LCQ and symptom domain of SGRQ). Future studies are required to determine the longer-term benefit of PR in CTD-ILD patients and if these improvements are sustained.

References:

1. Wallace B, Vummidi D, Khanna D. Management of connective tissue diseases associated interstitial lung disease: a review of the published literature. Curr Opin Rheumatol. 2016 May;28(3):236-45. doi: 10.1097/BOR.0000000000000270. PMID: 27027811; PMCID: PMC4826478.
2. Nolan CM, Polgar O, Schofield SJ, Patel S, Barker RE, Walsh JA, Ingram KA, George PM, Molyneaux PL, Maher TM, Man WD. Pulmonary Rehabilitation in Idiopathic Pulmonary Fibrosis and COPD: A Propensity-Matched Real-World Study. Chest. 2022 Mar;161(3):728-737. doi: 10.1016/j.chest.2021.10.021. Epub 2021 Oct 23. PMID: 34699771; PMCID: PMC8941605.

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Abstract Number: 0618

Incident versus Prevalent Interstitial Lung Disease in Systemic Sclerosis in the EUSTAR Database: Different Disease Phenotypes and Prognosis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
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Background/Purpose: Although 50% of patients with systemic sclerosis (SSc) present with interstitial lung disease (ILD) at baseline, new onset of ILD can also occur later in the disease. We aimed to compare the phenotypes and prognostic outcome between incident and prevalent ILD in SSc.

Table 1. Baseline characteristics of SSc patients according to the ILD status

	ILD prevalent group (n=5042)	ILD incident group (n=1080)	ILD negative group (n=5359)	P value between 3 groups	P value ILD prevalent vs ILD incident
Age, years, mean±SD	57 ± 13	57 ± 14	54 ± 14	**<0.01**	0.39
Sex female, n (%)	4054 (80)	876 (81)	4624 (86)	**<0.01**	0.77
Disease duration, years, mean±SD	9 ± 8	11 ± 8	7 ± 7	**<0.01**	**<0.01**
Caucasian, n (%)	4661 (92)	1012 (94)	5123 (96)	**<0.01**	**<0.01**
Smoking ever, n (%)	660 (17)	303 (28)	558 (10)	**<0.01**	**<0.01**
BMI, mean±SD	25±4	24±4	25±4	0.48	0.79
Diffuse cutaneous SSc, n (%)	2493 (49)	495 (46)	1235 (23)	**<0.01**	0.11
Modified Rodnan Skin score, median (IQR)	9 (0-51)	8 (0-47)	7 (0-50)	**<0.01**	**<0.01**
Digital ulcers ever, n (%)	1552 (31)	519 (48)	811(15)	**<0.01**	**<0.01**
Pitting scars on fingertips, n (%)	1995 (40)	512 (47)	1500 (28)	**<0.01**	**<0.01**
Arthritis ever, n (%)	584 (12)	250 (23)	173 (3)	**<0.01**	**<0.01**
Tendon friction rubs, n (%)	383 (8)	56 (5)	221 (4)	**<0.01**	**0.02**
Muscle weakness, n (%)	832 (17)	136 (13)	601 (11)	**<0.01**	**<0.01**
Esophageal symptoms, n (%)	3302 (65)	693 (64)	3126 (58)	**<0.01**	0.22
Dyspnea NYHA stage≥2, n (%)	2675 (53)	513 (47)	1589 (30)	**<0.01**	**<0.01**
Pericardial effusion, n (%)	285 (6)	53 (5)	152 (3)	**<0.01**	0.32
Diastolic function abnormal, n (%)	1019 (20)	204 (19)	641(12)	**<0.01**	0.31
Left ventricular ejection fraction, %, mean±SD	62±6	62±5	62±5	**<0.01**	0.75
DLCO/SB, % predicted, mean±SD	61±18	65±17	75±17	**<0.01**	**<0.01**
FVC, % predicted, mean±SD	86±21	91±20	99±18	**<0.01**	**<0.01**
Systolic PAP on ECHO, mmHg, mean±SD	31±9	31±8	29±7	**<0.01**	**0.03**
Anti-centromere/ Anti-Topoisomerase I/ Anti-RNA polymerase III/ Anti- Pm/Scl, none of above or other, n (%)	936 (19) / 2689 (53)/ 167 (3) / 103 (2) / 1147 (23)	312 (29) / 525 (49) / 29 (3) / 13 (1) / 202 (19)	3060 (57) / 976 (18) / 220 (4) / 50 (1) / 1053 (20)	**<0.01**	**<0.01**
Increased inflammatory markers, n (%)	1230 (23)	210 (19)	667 (12)	**<0.01**	**0.02**
Immunosuppressants ever, n (%)	1436/1890 (76)	432/ 577 (75)	796 (65)	**<0.01**	0.36

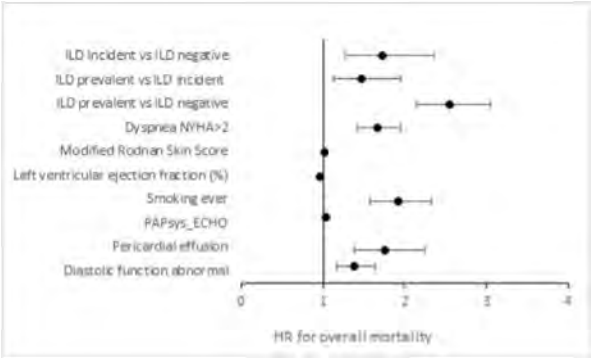

Figure 1. Multivariate prediction model of mortality in the ILD incident and ILD prevalent groups.

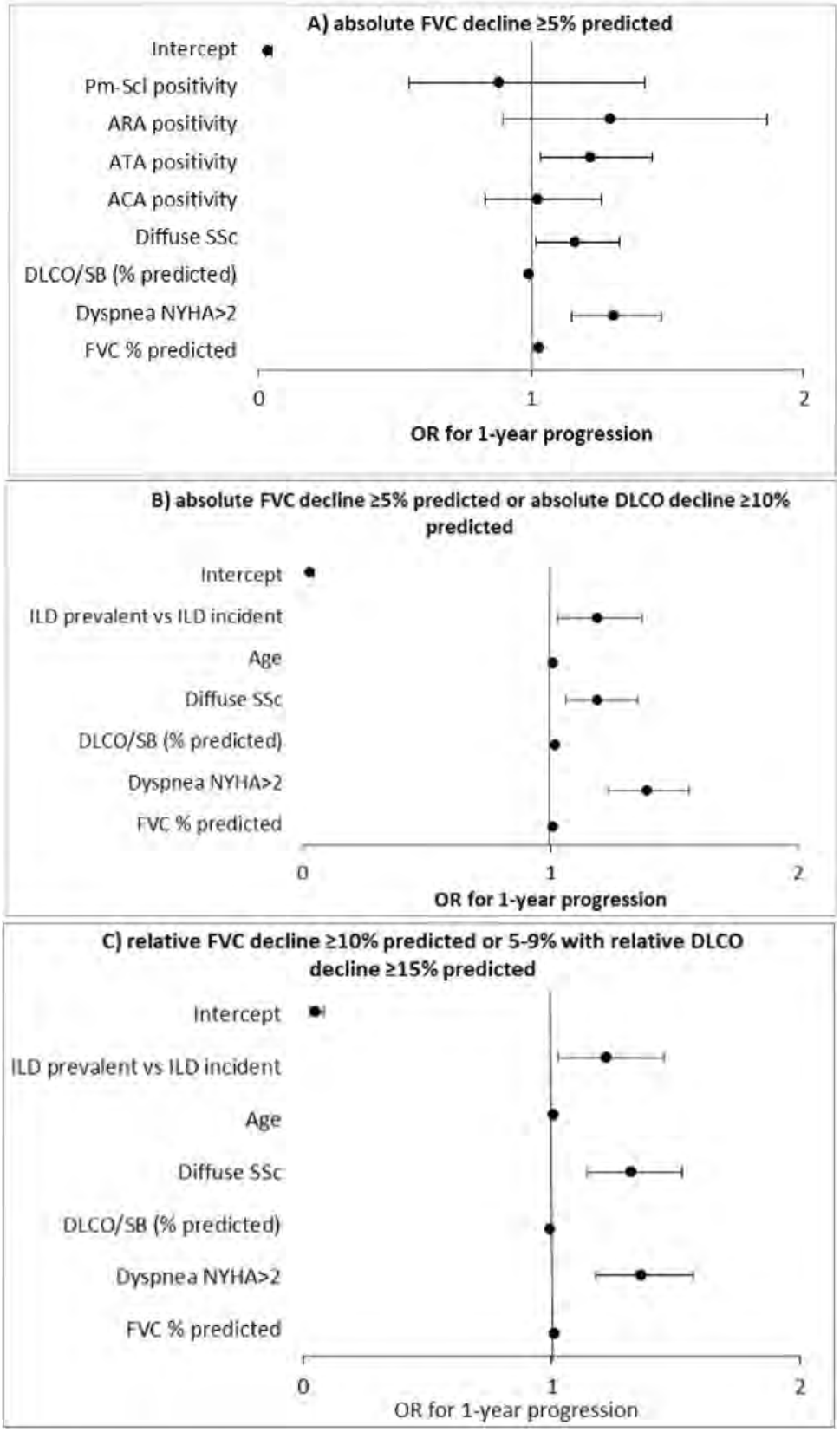

Figure 2. Multivariate prediction models of functional progression of SSc-ILD according to three definitions used.

Methods: SSc patients from the EUSTAR database were eligible if classified according to the 2013 ACR/EULAR criteria, with available information for ILD on high-resolution computed tomography (HRCT) at baseline and follow-up visits. Patients with pulmonary arterial hypertension on right heart catheterization were excluded.

Based on HRCTs, our population was divided in 3 groups: patients with ILD at baseline (ILD prevalent), patients with new onset of ILD during the follow-up (ILD incident) and patients who remained ILD negative (ILD negative). Disease features were compared between these groups.

ILD groups were tested as a predictor of mortality using multivariable Cox regression with backward selection.

Functional progression of ILD at 12±3 months intervals represented the secondary endpoint. Three different definitions of progression were applied: (A) absolute FVC decline ≥5% predicted, (B) absolute FVC decline ≥5% predicted or absolute DLCO decline ≥10% predicted and (C) relative FVC decline ≥10% predicted or 5-9% with relative DLCO decline ≥15% predicted. Logistic regression with backward selection was used to identify independent predictors, comparing prevalent vs incident ILD.

Known predictors of SSc-ILD progression and mortality were chosen as covariates from the literature and based on expert opinion.

Results: We analyzed 11481 SSc patients, including 5042 (44%) ILD prevalent, 1080 (9%) ILD incident and 5359 (47%) ILD negative patients. In comparison to the prevalent group, the ILD incident group was characterized by a milder functional impairment, higher prevalence of peripheral vascular manifestations, arthritis and smoking ever (Table 1).

During median 3.8 (IQR 1.8-7.3) years follow-up, 753/10157 deaths were recorded, more frequent in the ILD prevalent (67%) compared to ILD incident (22%) or ILD negative (11%)groups ($p < 0.01$ by Log-rank test).

In the Cox regression model adjusted for covariates (Fig.1), the ILD prevalent group showed higher risk of mortality in comparison to both ILD incident (HR 1.47, 95% CI 1.12-1.95) and ILD negative (HR 2.55, 95% CI 2.14-3.05) groups. Notably, the ILD incident had higher risk of mortality than the ILD negative group (HR 1.73, 95% CI 1.27-2.35).

ILD progression was variably observed among 7337 follow-ups of 2803 SSc-ILD patients (in 25% vs 35% vs 19% observations, according to the respective abovementioned definitions).

In comparison to the ILD incident group, the ILD prevalent group showed a higher risk of ILD progression evaluated by definition B (OR 1.18, 95% CI 1.03-1.37) and C (OR 1.21, 95% CI 1.02-1.45) after adjustment for covariates, but it was not confirmed for definition A (Fig.2).

Conclusion: Incident ILD carries a higher risk of mortality compared to ILD negative cases, despite representing a milder phenotype compared to prevalent ILD. Therefore, screening for SSc-ILD should be continued during the follow-up after a negative baseline.

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Abstract Number: 0619

Different Definitions of Disease Severity, Progression and Outcomes in Systemic Sclerosis Associated Interstitial Lung Disease: A Systematic Literature Review

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: There is no established consensus on defining the clinical course and the outcomes of systemic sclerosis-associated interstitial lung disease (SSc-ILD), both among experts and in the literature. Most proposed definitions of progression or severity of SSc-ILD are based on research data from idiopathic pulmonary fibrosis and are not fully validated for SSc-ILD. The aim of our study is to collect the available evidence about definitions of severity, progression and outcomes in SSc-ILD.

Methods: A systematic search of the literature was performed according to the PRISMA guidelines, to identify all papers including definitions of SSc-ILD severity, progression and outcome (PROSPERO registration CRD42022379254). Medline, Embase and Web of Science databases were searched up to December 31st, 2021.Randomized clinical trials, cross sectional or longitudinal studies were included if they focused on SSc or on cohorts in which data on SSc patients could be extracted, considered ILD as primary target (representing at least one of population, exposure, outcome) and included at least 10 adult patients. Exclusion criteria were papers not in English, non-human non-clinical studies, ILD onset as an outcome, literature reviews and no full-text availability.

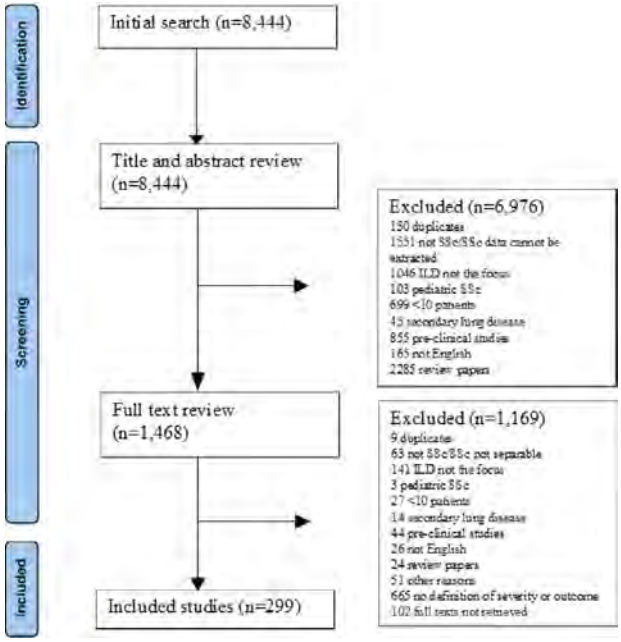

Figure 1. PRISMA flow diagram of studies selection. ILD, interstitial lung disease; SSc, systemic sclerosis.

Results: Out of 8,444 papers identified by the primary literature search (Fig. 1), 299 original research manuscripts including 35'463 patients with SSc-ILD were finally selected. Mean age was 52 years (range from 32 to 66 years), 72.5 % were females. The mean disease duration ranged from 2 to 10 years.

A definition of SSc-ILD severity was included in 138 (46%) papers (Fig. 2). Most papers (52%) used the extent of ILD on high resolution computed tomography (HRCT) to assess severity, mostly through visual quantification, either alone or in combination with pulmonary function tests (PFTs) data. The second most frequently used tool for severity was PFTs, based on forced vital capacity (FVC) in 30 (22%), on combination of FVC and diffusion of the lung for carbon oxide (DLCO) in 15 (11%) and on DLCO in 11 (8%) papers.

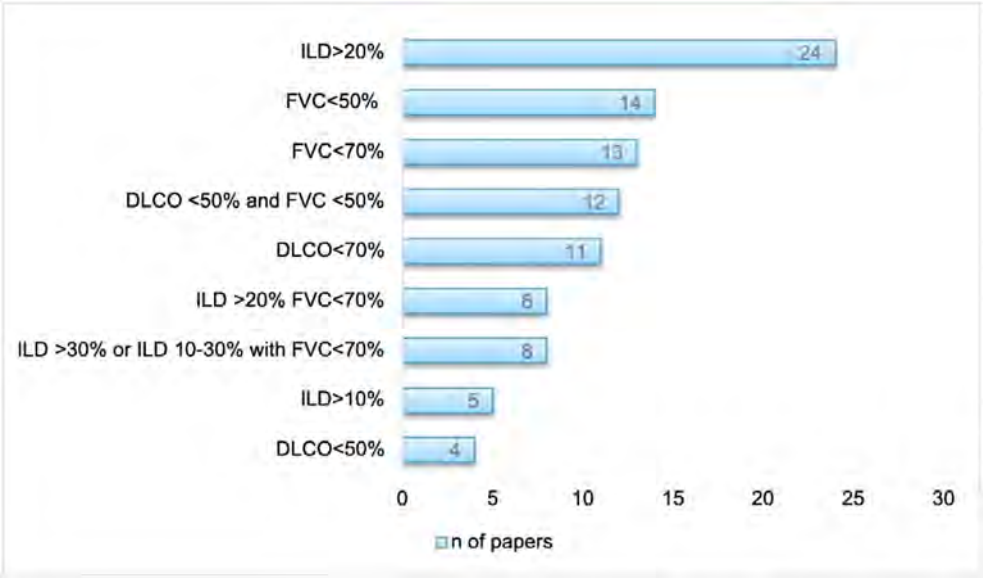

Figure 2. Number of studies stratified by the core of most commonly used definition of SSc-ILD severity.

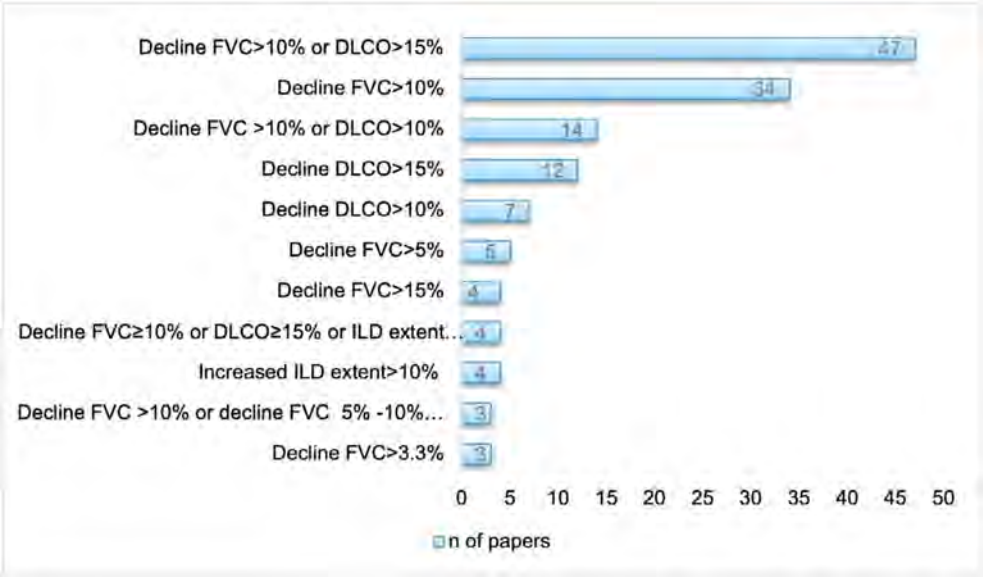

Figure 3. Top candidate definitions of SSc-ILD progression.

Sixty-four of 181 studies (35%) provided a definition of SSc-ILD progression referred to changes in FVC and DLCO, 51 (28%) in FVC, 23 (13%) in DLCO, 19 (10%) in ILD extent on HRCT, 7 (4%) to combination of PFTs and HRCT changes, 5 (3%) to combination of PFTs, clinical signs and HRCT data, 12 (7%) to other aspects (Fig.3). The timing to evaluate for SSc-ILD progression was also heterogeneous, including the re-assessment at 6 (5.5% papers), 12 (32.6 %), 24 (16.6%), 36 (10.5%), 60 (3.3%), or more than 60 months (7.2%).

The long-term outcomes recorded included mortality (131 papers, both ILD and non ILD-related), hospitalization (4 papers), end-stage ILD (5 papers), lung transplantation (2 papers) and infections (1 paper). Non-primarily ILD-related outcomes, such as malignancy, were also identified (4 papers).

Conclusion: our study showed large heterogeneity in definitions of SSc-ILD progression, severity, and outcome. This emphasizes the need to develop a standardized, consensus definition of severe SSc-ILD, to link a disease specific definition of progression as a surrogate outcome for clinical trials and clinical practice.

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Abstract Number: 0620

Physical and Mental Health in Early Systemic Sclerosis: Baseline Results for Patient-Reported Outcomes Measurement Information System-29 from the Collaborative National Quality and Efficacy Registry

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Patient-Reported Outcomes Measurement Information System-29 version 2.0 (PROMIS-29v2) is a patient-centered questionnaire used to assess health-related quality of life (HRQoL). PROMIS-29v2 has shown validity and responsiveness to change in patients with systemic sclerosis (SSc) but has not yet been described specifically in early SSc. This study's aim was to describe PROMIS-29v2 outcomes and clinical associations in the Collaborative National Quality and Efficacy Registry (CONQUER), which is a multi-center US-based registry of patients with early limited cutaneous (lc) and diffuse cutaneous (dc) SSc.

Methods: Patients enrolled in CONQUER meet 2013 ACR-EULAR Classification criteria for SSc and have a disease duration of less than 5 years from their first non-Raynaud SSc symptom. Baseline results of the PROMIS-29v2 domains of physical function (PF), ability to participate in social roles/activities or social function (SF), pain interference, fatigue, anxiety/fear, sleep disturbance, and depression were described for the entire CONQUER cohort and compared between patients with lcSSc and dcSSc using two-sample t-tests. Pearson's correlation assessed the relationship between patient clinical characteristics and PROMIS-29v2 domain scores.

Results: Baseline data were available for 536 participants. Of these, 368 (68.7%) had dcSSc (Table 1). Disease duration from first non-Raynaud's symptom was 2.6 [1.3, 3.8] years for the whole group and was not significantly different between lcSSc and dcSSc. Individuals with dcSSc had worse PF, SF and pain interference, but significant differences were not seen for fatigue, anxiety/fear, sleep disturbance and depression (Table 1). Female participants had significantly higher anxiety/fear, 54.1 (95% CI 40.3, 60.3) versus 44.1 (40.3, 57.5) for males, p=0.001 (Table 2). PF score was worse (lower) in participants with digital ulcers, restrictive lung disease (RLD, defined as FVC < 70% or TLC < 80%) and pulmonary hypertension. The presence of digital ulcers correlated with worse scores in multiple domains, including PF, SF, pain interference and

depression/sadness. RLD correlated with worse PF and SF. Higher mRSS was weakly correlated with PF, r = -0.38 (95% CI -0.45, -0.3) and SF, r = -0.27 (-0.35, -0.19) in the whole group and in the dcSSc group (Table 3). Statistically significant correlations of variable strengths were seen with the UCLA SCTC GIT 2.0 score in all domains (Table 3). The strongest correlations for GIT were seen with fatigue, r = 0.53 (0.46, 0.59); pain interference, r = 0.46 (0.39, 0.52), and SF, r = -0.42 (-0.48, -0.34). Musculoskeletal manifestations including the presence of large or small joint contractures, tendon friction rubs, proximal muscle weakness, calcinosis and the use of ambulatory aids were associated with worse scores in multiple domains (data not shown).

Table 1

Table 1: Demographics and Baseline Characteristics of Patients that Completed the PROMIS-29v2 at Baseline.

	Overall (N = 536)	Limited cutaneous[1] (N = 168)	Diffuse cutaneous[1] (N = 368)	P-value
Age (years)	53.7 [42.7, 63.5]	54.6 [42.1, 65.9]	53.5 [42.9, 62.3]	0.228[3]
Female	438 (81.7%)	145 (86.3%)	293 (79.6%)	0.063[4]
Race/ethnicity				0.017[4]
Hispanic	58 (10.8%)	11 (6.5%)	47 (12.8%)	
Non-Hispanic White	373 (69.7%)	134 (79.8%)	239 (65.1%)	
Non-Hispanic Black or African American	58 (10.8%)	12 (7.1%)	46 (12.5%)	
Non-Hispanic Asian	36 (6.7%)	9 (5.4%)	27 (7.4%)	
Non-Hispanic Other	10 (1.9%)	2 (1.2%)	8 (2.2%)	
Disease duration from date of first Raynaud's symptom (years)	3.1 [1.4, 4.7]	3.8 [2.4, 6.2]	2.8 [1.3, 4.2]	<.001[3]
Disease duration from date of first non-Raynaud's symptom to baseline visit (years)	2.6 [1.3, 3.8]	2.9 [1.4, 3.9]	2.5 [1.2, 3.7]	0.244[3]
BMI	25.8 [22.0, 29.5]	26.8 [22.9, 30.2]	25.0 [21.6, 29.1]	0.011[3]
mRSS	10.0 [4.0, 19.0]	3.0 [2.0, 5.0]	15.0 [8.0, 24.0]	<.001[3]
Tobacco use				0.795[4]
Never	360 (67.2%)	115 (68.5%)	245 (66.6%)	
Former	156 (29.1%)	48 (28.6%)	108 (29.3%)	
Current	20 (3.7%)	5 (3.0%)	15 (4.1%)	
Employment status				0.012[4]
Full-time	265 (50.8%)	88 (53.7%)	177 (49.4%)	
Part-time	39 (7.5%)	12 (7.3%)	27 (7.5%)	
Retired	107 (20.5%)	42 (25.6%)	65 (18.2%)	
Disabled	60 (11.5%)	8 (4.9%)	52 (14.5%)	
Other	51 (9.8%)	14 (8.5%)	37 (10.3%)	
Presence of digital ulcers	41 (7.6%)	2 (1.2%)	39 (10.6%)	<.001[4]
SSc-restrictive lung disease	201 (41.7%)	53 (36.6%)	148 (43.9%)	0.133[4]
FVC % predicted	86.7 [74.6, 98.4]	89.9 [78.2, 102.5]	84.8 [73.8, 97.2]	0.008[3]
Pulmonary hypertension[2]	24 (4.5%)	7 (4.2%)	17 (4.6%)	0.814[4]
Renal crisis	22 (4.1%)	2 (1.2%)	20 (5.5%)	0.022[4]
UCLA SCTC GIT total score	0.3 [0.1, 0.6]	0.3 [0.1, 0.6]	0.3 [0.1, 0.6]	0.564[3]
Musculoskeletal severity				
Large joint contracture	70 (13.5%)	3 (1.8%)	67 (18.9%)	<.001[4]
Small joint contracture	226 (43.5%)	25 (15.2%)	201 (56.5%)	<.001[4]
Tendon friction rubs	63 (12.1%)	2 (1.2%)	61 (17.0%)	<.001[4]
Proximal weakness	83 (16.0%)	31 (18.7%)	52 (14.7%)	0.247[4]
Calcinosis	30 (5.7%)	6 (3.6%)	24 (6.6%)	0.165[4]
Acro-osteolysis	16 (3.1%)	3 (1.8%)	13 (3.7%)	0.254[4]
Use of ambulatory aids	19 (3.5%)	6 (3.6%)	13 (3.5%)	0.982[4]
PROMIS-29v2				
Physical function	43.3 [38.3, 57.0]	47.8 [41.0, 57.0]	42.0 [37.2, 47.8]	<.001[3]
Ability to participate in social roles/activities	50.1 [44.0, 58.3]	51.8 [44.2, 64.2]	48.3 [41.5, 56.8]	<.001[3]
Pain interference	55.7 [41.6, 61.3]	52.6 [41.6, 60.0]	55.7 [41.6, 61.3]	0.002[3]
Sleep disturbance	55.5 [53.3, 57.6]	55.5 [53.7, 57.5]	55.5 [53.3, 57.6]	0.632[3]
Fatigue	55.2 [48.6, 62.7]	53.2 [46.0, 60.7]	55.2 [48.6, 62.7]	0.075[3]
Anxiety/fear	53.8 [40.3, 59.6]	51.8 [40.3, 59.6]	53.8 [40.3, 59.6]	0.726[3]
Depression/sadness	48.9 [41.0, 56.0]	48.9 [41.0, 55.9]	48.9 [41.0, 57.3]	0.063[3]

Unless otherwise specified, all variables are as recorded at baseline.
[1] SSc subtype is defined as whether the patient has ever been diagnosed as having diffuse SSc. Otherwise, the patient is assumed to have limited SSc.
[2] Pulmonary hypertension is diagnosed using a right heart catheterization in patients who were symptomatic.
[3] Two-sample t-test
[4] Chi-square test of independence

Table 2

Table 2: Outcomes of PROMIS-29v2 Domains in Patients with Systemic Sclerosis by Clinical Characteristics.

	Gender			Presence of digital ulcers			Restrictive lung disease			Pulmonary hypertension*			Renal crisis			FVC % Predicted		
	Male (N = 99)	Female (N = 536)	P value	Yes (N = 131)	No (N = 492)	P value	Yes (N = 207)	No (N = 291)	P value	Yes (N = 25)	No (N = 512)	P value	Yes (N = 22)	No (N = 509)	P value	<80% (N = 175)	≥80% (N = 331)	P value
Physical function	44.4 [37.2, 57.0]	45.3 [38.8, 48.7]	0.587	38.8 [32.1, 46.7]	48.7 [38.8, 57.0]	0.002	41.4 [36.3, 47.8]	48.1 [40.4, 57.0]	<.001	38.4 [33.2, 42.3]	45.7 [38.8, 57.0]	<.001	39.2 [35.5, 44.6]	45.4 [38.8, 57.0]	0.021	40.2 [35.8, 45.1]	45.1 [40.7, 57.0]	<.001
Ability to participate in social roles/activities	51.8 [42.4, 64.2]	50.1 [44.0, 58.3]	0.836	39.6 [37.1, 51.8]	50.1 [44.2, 58.5]	<.001	46.8 [40.2, 57.1]	51.8 [44.2, 58.5]	0.002	44.2 [37.3, 49.3]	50.1 [44.2, 58.5]	0.002	46.1 [37.2, 53.6]	50.1 [44.2, 58.5]	0.074	46.8 [39.6, 53.6]	51.8 [44.2, 64.2]	<.001
Pain interference	54.4 [51.8, 60.0]	55.7 [51.8, 61.3]	0.293	64.0 [53.9, 66.7]	55.7 [51.8, 61.3]	<.001	55.7 [51.8, 62.3]	55.7 [51.8, 63.9]	0.149	55.7 [51.8, 63.3]	55.7 [51.8, 61.3]	0.559	55.7 [51.7, 66.7]	55.7 [51.8, 61.3]	0.191	55.7 [51.8, 62.8]	55.7 [51.8, 63.9]	0.037
Sleep disturbance	55.6 [54.2, 57.4]	50.6 [53.3, 57.6]	0.269	50.6 [54.2, 56.9]	55.5 [53.3, 57.5]	0.042	55.8 [54.4, 58.6]	54.8 [53.3, 57.5]	0.099	55.4 [54.4, 59.9]	50.6 [53.3, 57.6]	0.268	54.4 [52.5, 60.6]	55.5 [53.6, 57.7]	0.329	56.2 [54.4, 58.7]	54.7 [53.2, 57.4]	0.002
Fatigue	53.2 [48.0, 60.6]	55.2 [49.8, 62.7]	0.091	60.6 [49.8, 64.7]	55.0 [49.6, 61.8]	0.010	55.3 [49.6, 62.7]	55.0 [49.6, 63.6]	0.059	59.1 [54.2, 64.7]	55.2 [49.8, 62.6]	0.029	60.7 [53.1, 69.0]	55.2 [49.6, 62.7]	0.042	57.1 [49.6, 64.7]	53.4 [49.0, 60.2]	<.001
Anxiety/fear	44.1 [40.3, 57.6]	54.1 [43.3, 60.3]	0.031	56.0 [43.3, 63.6]	53.1 [40.3, 58.6]	0.125	54.1 [40.3, 60.6]	51.8 [40.3, 59.3]	0.251	52.8 [40.3, 57.7]	53.8 [43.3, 59.6]	0.716	56.7 [43.3, 63.6]	53.8 [40.3, 58.6]	0.228	55.2 [40.3, 61.4]	51.8 [40.3, 59.3]	0.191
Depression/sadness	51.0 [41.0, 55.9]	48.9 [41.0, 56.1]	0.185	55.9 [41.0, 63.2]	48.9 [41.0, 55.9]	0.002	49.5 [41.0, 57.4]	48.9 [41.0, 55.9]	0.221	48.9 [41.0, 56.2]	48.9 [41.0, 56.0]	0.588	52.8 [41.0, 60.6]	48.9 [41.0, 55.9]	0.134	51.2 [41.0, 57.5]	48.9 [41.0, 55.9]	0.150

PROMIS-29v2 is a standardized questionnaire that assesses health related quality of life related to seven domains: physical function, social role, pain interference, sleep disturbance, fatigue, anxiety, and depression. Each question is scored on a scale from 1 to 5. The scores for each domain are averaged to produce a T-score, which has a mean of 50 and a standard deviation of 10 for the general population. For physical function and social role, a score higher than 50 is a better outcome. For pain interference, sleep disturbance, fatigue, anxiety, depression, a higher score is a worse outcome.
PROMIS-29v2 domain scores are compared between each subgroup using a two-sample t-test.

Table 3

Table 3: Correlation of PROMIS-29 Domain Scores with Patient Characteristics in Systemic Sclerosis.

	Physical function	Ability to participate in social roles/ activities	Pain interference	Sleep disturbance	Fatigue	Anxiety/fear	Depression/ sadness
Disease duration since date of first non-Raynaud's symptom to baseline (years)	0.14 (0.06, 0.22)	0.16 (0.07, 0.24)	-0.17 (-0.25, -0.09)	-0.06 (-0.14, 0.03)	-0.08 (-0.17, 0)	-0.09 (-0.18, -0.01)	-0.09 (-0.17, -0.01)
Age at baseline (years)	-0.12 (-0.2, -0.03)	-0.02 (-0.11, 0.06)	-0.02 (-0.1, 0.07)	0.01 (-0.07, 0.09)	-0.07 (-0.16, 0.01)	-0.14 (-0.22, -0.06)	0 (-0.08, 0.09)
mRSS at baseline	-0.38 (-0.45, -0.3)	-0.27 (-0.35, -0.19)	0.28 (0.2, 0.36)	0.08 (-0.01, 0.16)	0.16 (0.08, 0.25)	0.06 (-0.03, 0.14)	0.17 (0.08, 0.25)
FVC % predicted at baseline	0.28 (0.2, 0.36)	0.2 (0.12, 0.28)	-0.09 (-0.18, -0.01)	-0.1 (-0.18, -0.02)	-0.13 (-0.21, -0.05)	-0.08 (-0.16, 0.01)	-0.04 (-0.13, 0.04)
UCLA SCTC GIT 2.0 score Overall at baseline	-0.39 (-0.46, -0.32)	-0.42 (-0.48, -0.34)	0.46 (0.39, 0.52)	0.12 (0.04, 0.2)	0.53 (0.46, 0.59)	0.34 (0.26, 0.41)	0.39 (0.31, 0.46)

Summary statistics are Pearson Correlation (95% Confidence Interval).

Conclusion: We describe the use of PROMIS-29v2 to assess quality of life in an early US-based SSc cohort. Diffuse disease, higher mRSS, musculoskeletal manifestations, presence of digital ulcers, RLD and UCLA SCTC GIT scores were associated with reduced HRQoL as measured by PROMIS-29v2. Multivariable analysis and assessment of longitudinal change are underway.

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Boehringer-Ingelheim, 2, 5, 6, CSL Behring, 2, GlaxoSmithKline, 2, Horizon, 5, Prometheus, 5, Roche, 2; **J. Gordon**: Cumberland Pharmaceuticals, 5, Prometheus Pharmaceuticals, 5.

Abstract Number: 0621

Scleroderma Renal Crisis: A Large Single-center Experience

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Scleroderma renal crisis (SRC) is a life-threatening vascular manifestation of systemic sclerosis (SSc) occurring in up to 5% of SSc patients. This condition continues to have significant morbidity and mortality despite the advent of angiotensin converting enzyme (ACE) inhibitors. We identified risk factors associated with SRC in addition to evaluating its management and outcomes in consecutively diagnosed patients in a large Australian tertiary referral hospital [St Vincent's Hospital Melbourne (SVHM)].

Methods: 17 incident SRC cases were diagnosed at SVHM between 2012-2022. Patient demographics, SSc disease manifestations, and SRC treatments were determined using data prospectively collected in the Australian Scleroderma Cohort Study supplemented by chart review. Differences between those with SRC (n=17) and those without SRC (n=466) were assessed using logistic regression analyses to determine the risk factors associated with SRC.

Results: There were 483 SSc patients included in this study, their demographics and disease characteristics are presented in Table 1. 17 (3.5%) of the cohort experienced SRC during our 10 year study period.

The median SSc disease duration at SRC onset was 2.5 (IQR 1-4) years. At SRC presentation, 16 patients (94.12%) presented with a systolic blood pressure (SBP) >140mmHg (median SBP = 169 (IQR 153-182)mmHg) and a median creatinine of 120 (IQR 80-156) µmol/L. Peak creatinine occurred at a median of 11 (IQR 5-14) days post SRC diagnosis, with SBP

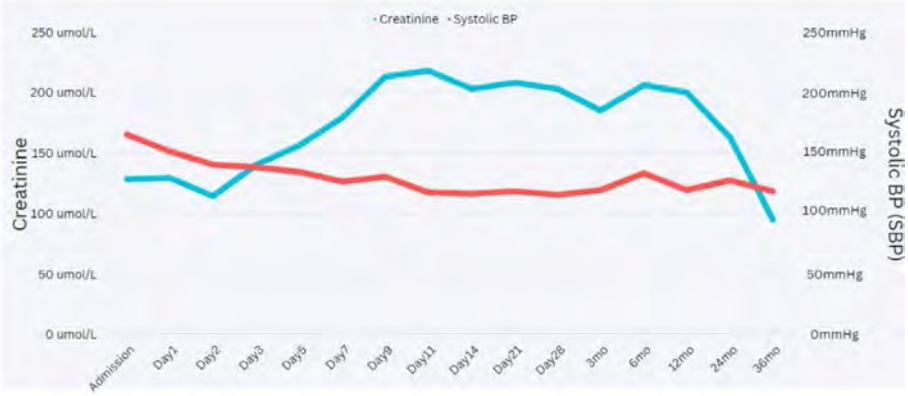

Figure 1: Mean systolic blood pressure and creatinine post SRC onset

Table 1: Demographics and disease characteristics of SSc patients at SVHM

	SVHM SRC patients (n=17)	SVHM SSc patients (n=466)
Male	10 (58.82%)	59 (12.80%)
Diffuse subclass	11 (88.24%)	114 (24.46%)
Centromere positive	0 (0%)	231 (49.57%)
ANA – nucleolar	7 (41.18%)	116 (24.89%)
Scl70 positive	7 (41.18%)	80 (17.17%)
RNAP III positive	8 (47.06%)	59 (14.71%)*
ANCA positive	1 (5.88%)	22 (4.72%)
Myocardial involvement	2 (11.76%)	27 (5.79%)
ILD	6 (35.29%)	134 (28.76%)
Raynauds phenomenon	15 (88.24%)	462 (99.14%)
Digital ulcers	11 (64.71%)	225 (48.28%)
Telangiectasia	3 (17.65%)	440 (94.42%)
Calcinosis	3 (17.65%)	199 (42.70%)
PAH	3 (17.65%)	76 (16.31%)

*401/466 patients had RNA polymerase III Ab tested

peaking at onset of SRC. Nine (52.94%) SRC patients had evidence of acute neurologic and cardiac complications including retinopathy (n=2), encephalopathy (n=6), and acute cardiac failure (n=3).

In terms of SRC management, all patients received ACE inhibitors, with a median of 3 anti-hypertensive agents required to manage hypertension. Adjuvant anti-hypertensive agents used included calcium channel blockers (most commonly amlodipine), moxonidine, and prazosin.

Complications of SRC included acute hemofiltration required in 3 (17.65%) patients, while 3 (17.65%) patients (including 2 patients that needed acute hemofiltration) required ongoing renal replacement therapy. During our observation period, 7 (41.18%) SRC patients died at a median of 2.75 (IQR 0.74-7.25) years after SRC onset, with at least 2 deaths attributable directly to complications of SRC.

Patients with SRC were more likely to be male (OR 9.73, 95% CI 3.57-26.56), have diffuse disease (OR 23.16, 95% CI 5.22-102.80), and have antibodies to Scl70 (OR 3.34, 95% CI 1.24-9.04) or RNA polymerase III (RNAP III) (OR 5.15, 95% CI 1.91-13.89).

Conclusion: In our case series, peak serum creatinine was most likely to occur 11 days after peak SBP. Refractory hypertension was a near universal feature, with adequate SBP control often requiring multiple anti hypertensives and often taking more than 7 days to achieve.

Over half of the cases of SRC in our series were negative for RNAP III, highlighting the importance of remaining vigilant for SRC, particularly in patients with diffuse disease subtype and Scl-70 antibodies.

The frequency of patients requiring renal replacement therapy (18%) in our cohort is lower than 25-81% reported in other Western countries.

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Abstract Number: 0622

The Effectiveness of Breath-holding Test to Predict Pulmonary Function in Systemic Sclerosis Patients Using Machine Learning Model

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Pulmonary involvement is major causes of mortality in patients with systemic sclerosis (SSc). The breath-holding test (BHT), rapid bedside test, is a useful surrogate marker of pulmonary capacity in SSc patients. This study aimed to develop a machine learning (ML) model to predict pulmonary parameters, using real-time data of oxygen saturation (SpO2) and pulse rates obtained during the BHT in SSc patients.

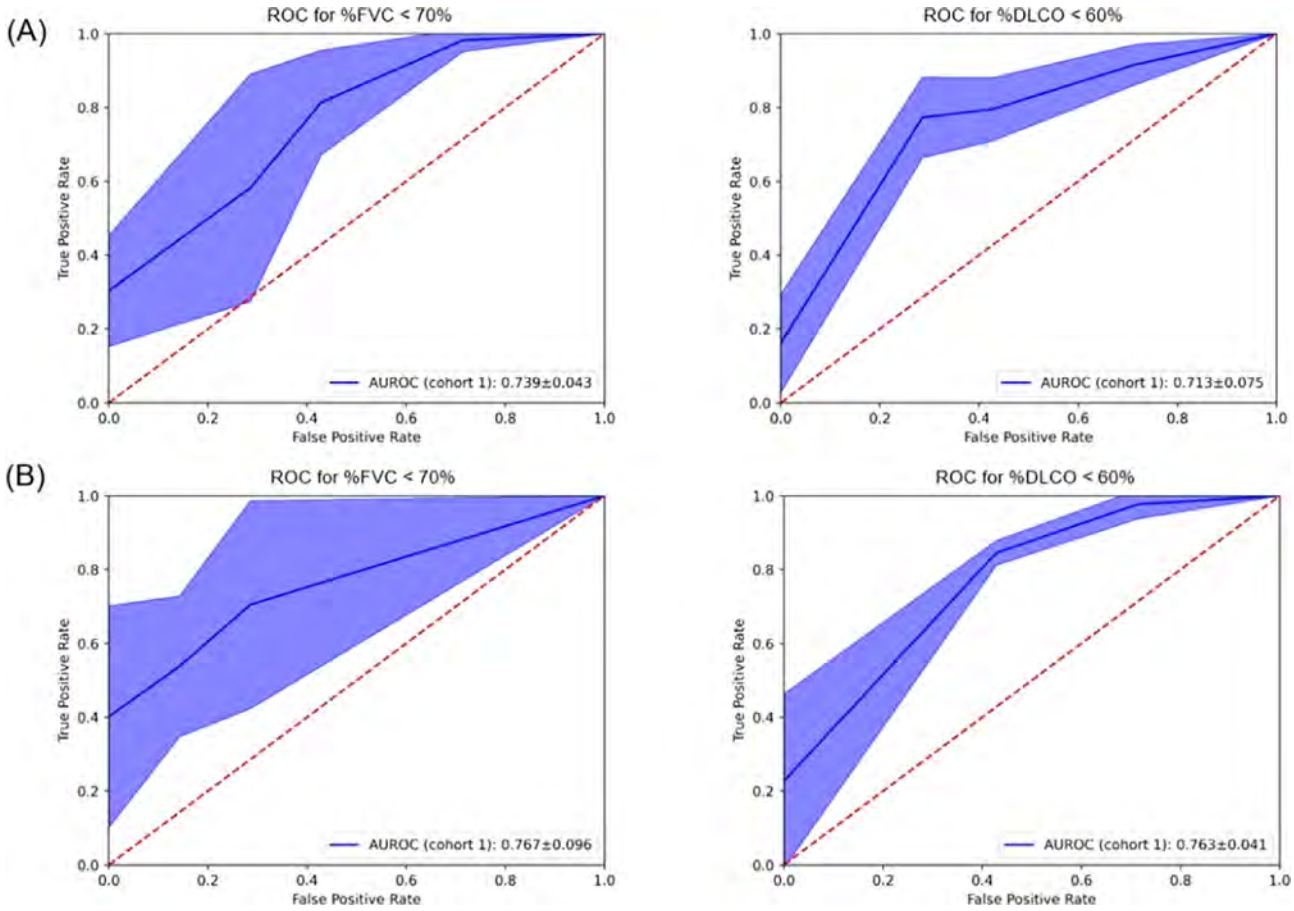

Figure 1. Receiver Operating Characteristic curves of the machine learning algorithm in the internal 4-fold cross validation using data from SpO2 and pulse rates (A) and only SpO2 (B) in breath-holding test.

Methods: Two prospective SSc cohorts were recruited for the study. Cohort 1 (n = 72) was for training a ML model and collected from August 2020 to February 2021, while Cohort 2 (n = 84) was for external validation of the established model and collected from April 2022 to September 2022. Real-time values of SpO2 and pulse rates were obtained during the BHTs and 6-min walking tests (6MWT) in Cohort 1, while the same data were collected during BHT in Cohort 2. The random forest classifier was applied to predict pulmonary functions (Forced vital capacity, FVC; diffusion capacity of carbon monoxide, DLCO), using data on SpO2 and pulse rates. In addition, demographic information such as age, gender, and body mass index, modified Rodnan skin score was also concatenated to the input feature. The validity of the ML model was evaluated using the Receiver Operating Characteristic (ROC) curve and the Area Under the ROC Curve (AUROC).

Results: A total of 72 subjects were enrolled in Cohort 1 and 84 subjects in Cohort 2, respectively. There was an overlap of 36 subjects between Cohort 1 and 2. In 4-fold cross-validation evaluation from Cohort 1, the ML algorithm using data from BHT showed AUROC of 0.739 ± 0.043 for %FVC < 70%, and 0.713 ± 0.075 for %DLCO < 60%, respectively (Figure 1A). A model using only SpO2 during BHT values showed a comparable AUROC to predict FVC and DLCO (AUROC for %FVC; 0.767 ± 0.096, and %DLCO; 0.763 ± 0.041, respectively) (Figure 1B). The ML model using data from 6MWT showed similar performance compared with BHT (AUROC for %FVC; 0.780 ± 0.040 and %DLCO; 0.754 ± 0.099, respectively). Cohort 2, an external validation cohort, showed similar AUROC (For %FVC, 0.686; for %DLCO, 0.669).

Conclusion: Our ML models showed the potential to discriminate decreased pulmonary function in SSc patients using data from SpO2 and pulse rates during the BHT and 6MWT. Our results suggest that BHT, when combined with SpO2 monitoring, can be useful to detect impaired lung capacity in SSc patient in whom a pulmonary function test is difficult to perform. (NCT04484948)

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Abstract Number: 0623

Nailfold Capillaroscopy in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD) Treated with Nintedanib

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SESSION INFORMATION
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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Microvascular damage is part of the pathogenesis of systemic sclerosis and is associated with internal organ involvement. Nintedanib is a tyrosine kinase inhibitor approved for the treatment of SSc-ILD. The SENSCIS trial was a placebo-controlled trial of nintedanib in patients with SSc-ILD. We assessed absolute changes in nailfold videocapillaroscopy (NVC) measures in a sub-study of the SENSCIS trial.

Methods: The SENSCIS trial enrolled patients with SSc with first non-Raynaud symptom in the prior ≤7 years and an extent of fibrotic ILD on high-resolution computed tomography ≥10%. Patients were randomized to receive nintedanib or placebo. In a sub-study, NVC was performed at baseline and weeks 12, 24, 36 and 52 [Smith et al. Autoimmun Rev

2020;19:102458]. Images from all 8 fingers were assessed by a central reader. Data were summarized by patient for mean capillary density (number of capillaries/mm), mean number of giant capillaries, mean number of abnormal shapes, and the percentage of fingers with microhemorrhages. These data are presented descriptively as the mean (SD) across patients.

Results: Of 576 patients in the SENSCIS trial, 120 participated in the NVC sub-study. At baseline, among the patients in the sub-study, mean (SD) age was 53.2 (11.9) years, 73.3% were female, median time since first non-Raynaud symptomwas 3.4 years, 50.0% had diffuse cutaneous SSc, mean (SD) modified Rodnan skin score was 11.4 (8.8), 59.2% were taking mycophenolate. Mean (SD) capillary density was 5.4 (1.8) capillaries/mm. The mean (SD) number of giant capillaries was

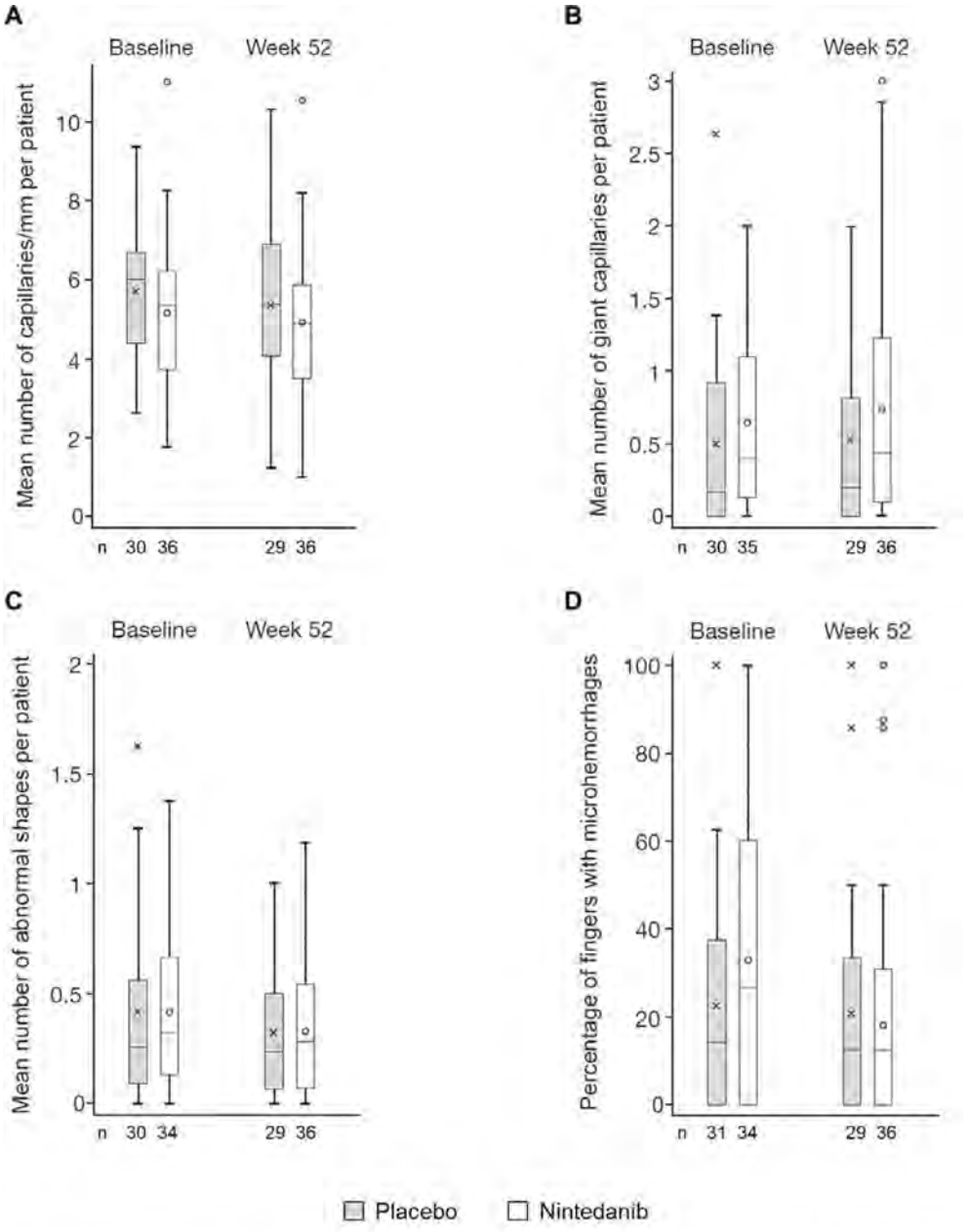

Figure. (A) Mean capillary density per patient, (B) mean number of giant capillaries per patient, (C) mean number of abnormal shapes per patient and (D) percentage of fingers with microhemorrhages at baseline and week 52 in the placebo and nintedanib groups.

0.6 (0.6) and the mean (SD) number of abnormal shapes was 0.4 (0.4). The mean (SD) percentage of fingers with microhemorrhages was 28.0 (30.4). There were no notable changes in mean capillary density, the mean number of giant capillaries, the mean number of abnormal shapes, or the percentage of fingers with microhemorrhages over 52 weeks in either the placebo or nintedanib groups (Figure).

Conclusion: In a sub-study of the SENSCIS trial in patients with SSc-ILD, NVC showed no notable changes in the mean number of microvascular abnormalities over 52 weeks in either the placebo or nintedanib groups. These analyses were limited by the small number of patients providing data at baseline and week 52. Further evaluation is needed to assess whether there were differences in capillaroscopic characteristics in patients whose disease did or did not progress, as has been observed in previous studies [Avouac et al. Semin Arthritis Rheum 2017;47:86-94; Vanahecke et al. Rheumatology (Oxford) 2022:61:4384-96].

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Abstract Number: 0624

Outcomes in Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD) Based on Serological Profiles: Focus on Anti-Centromere Antibody (ACA) and Anti-RNA Polymerase III (ARA) Antibodies

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Autoantibody profiles are associated with organ involvement and outcomes in patients with SSc. Anti-topoisomerase I antibody (ATA) positivity has been associated with a greater risk of developing SSc-ILD, while positivity for ACA or ARA has been associated with a lower risk. No prior studies have assessed the rate of progression of SSc-ILD in subgroups by ACA or ARA status in the context of a clinical trial. The purpose of this post-hoc analysis of the SENSCIS trial was to determine whether participants with ACA or ARA experience progression of SSc-ILD.

Methods: The SENSCIS trial enrolled participants with SSc with first non-Raynaud symptom in the prior ≤7 years and an extent of fibrotic ILD on high-resolution computed tomography (HRCT) ≥10%. Participants were randomized to receive nintedanib or placebo, stratified by ATA status. We analyzed the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks in subgroups by ACA status and ARA status (based on central laboratory data) at baseline. Exploratory interaction

p-values were calculated to assess potential heterogeneity in the effect of nintedanib versus placebo between the subgroups. We also analyzed the rate of decline in FVC (mL/year) over 52 weeks in participants who were negative for ATA, ACA and ARA.

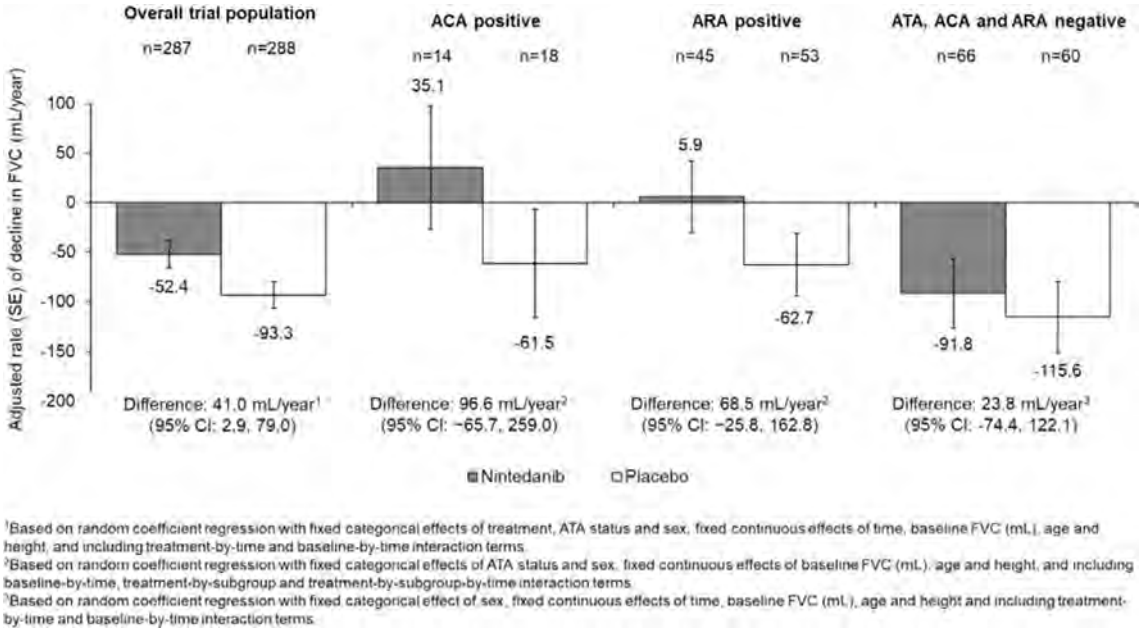
Results: Among 549 participants with available data, 5.8% were ACA positive. Compared with ACA negative participants, ACA positive participants were older, had a lower mean modified Rodnan skin score (mRSS), and a lower proportion had diffuse cutaneous SSc (Table). Among 528 participants with available data, 18.6% were ARA positive. Compared with ARA negative participants, a greater proportion of ARA positive participants had diffuse cutaneous SSc (Table). In the placebo arm, the adjusted rate (SE) of decline in FVC (mL/year) over 52 weeks was numerically greater in participants who were ACA negative than positive (-94.8 [14.3] vs -61.5 [54.5]) and numerically greater in those who were ARA negative than positive (-99.1 [15.9] vs -62.7 [31.6]). The effect of nintedanib versus placebo on reducing the rate of FVC decline was numerically more pronounced in participants who were ACA positive than negative (difference 96.6 mL/year [95% CI –65.7, 259.0] vs 34.8 [-5.1, 74.6]) or ARA positive than negative (difference 68.5 mL/year [95% CI –25.8, 162.8] vs 26.9 [-16.8, 70.7]), but the interaction p-values (>0.05) did not indicate heterogeneity in the effect of nintedanib between these subgroups. In the placebo arm, the rate of decline in FVC (mL/year) over 52 weeks, and the effect of nintedanib versus placebo in reducing the rate of FVC decline, were similar between the subset of patients who were negative for ATA, ACA and ARA and the overall trial population (Figure).

Conclusion: While the results of these post-hoc analyses should be interpreted with caution given the small number of participants who were ACA positive, the results suggest that patients who are ACA positive or ARA positive can experience SSc-ILD progression and should be monitored closely. The effect of nintedanib on slowing FVC decline was numerically more pronounced in participants with SSc-ILD who were ACA positive or ARA positive.

Table. Baseline characteristics by autoantibody status in the SENSCIS trial.

	Overall trial population (n=576)	ACA positive (n=32)	ACA negative (n=517)	ARA positive (n=98)	ARA negative (n=430)	ATA, ACA and ARA negative (n=127)
Age, years	54.0±12.2	62.3±11.8	53.5±12.1	54.2±12.2	54.2±12.2	55.4±12.2
Female	75.2	87.5	74.7	71.4	75.6	68.5
Body mass index, kg/m^2	25.9±5.0	26.7±5.3	25.7±4.9	25.6±5.2	25.9±5.0	25.4±4.4
Years since first non-Raynaud symptom	3.5±1.7	3.6±1.7	3.5±1.7	3.6±1.8	3.5±1.7	3.2±1.6
Years since diagnosis of SSc-ILD	2.6±1.7	2.5±1.8	2.6±1.7	2.7±1.8	2.6±1.7	2.3±1.6
Diffuse cutaneous SSc	51.9	21.9	54.4	60.2	51.6	38.6
ATA positive	60.8	25.0	63.1	39.8	66.0	0
Modified Rodnan skin score	11.1±9.0	7.8±8.4	11.3±8.9	13.6±10.6	10.7±8.3	9.0±7.6
Extent of fibrotic ILD on HRCT, %*	36.0±21.3	36.3±23.2	35.6±21.2	36.0±20.4	35.9±21.5	36.2±21.2
FVC % predicted	72.5±16.7	76.8±20.3	72.4±16.5	71.8±17.8	72.7±16.5	74.6±16.3
DLco % predicted†	53.0±15.1	52.8±14.9	53.3±15.0	53.5±15.5	53.2±15.1	53.4±14.9
Taking mycophenolate	48.4	43.8	48.4	53.1	48.6	46.5

Data are mean±SD or % of participants. *Assessed in whole lung to nearest 5% by central review. Pure (non-fibrotic) ground glass opacity was not included. †Corrected for hemoglobin. ATA, anti-topoisomerase I antibody; DL_{CO}, diffusing capacity of the lungs for carbon monoxide; FVC, forced vital capacity; HRCT, high-resolution computed tomography.



[1]Based on random coefficient regression with fixed categorical effects of treatment, ATA status and sex, fixed continuous effects of time, baseline FVC (mL), age and height, and including treatment-by-time and baseline-by-time interaction terms.
[2]Based on random coefficient regression with fixed categorical effects of ATA status and sex, fixed continuous effects of baseline FVC (mL), age and height, and including baseline-by-time, treatment-by-subgroup and treatment-by-subgroup-by-time interaction terms.
[3]Based on random coefficient regression with fixed categorical effect of sex, fixed continuous effects of time, baseline FVC (mL), age and height and including treatment-by-time and baseline-by-time interaction terms.

Figure. Rate of decline in FVC (mL/year) over 52 weeks in patients who were ACA positive, ARA positive, or ATA, ACA and ARA negative in the SENSCIS trial.

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Abstract Number: 0625

Use of Heated Gloves for Raynaud's Phenomenon in Systemic Sclerosis

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SESSION INFORMATION
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Background/Purpose: RP and its ischaemic complications are a major cause of morbidity in SSc. Non-pharmacological measures to minimise cold exposure can play a vital role in managing RP. This study sought to compare the efficacy of heated gloves compared with routine practice in SSc.

Table 1. Baseline characteristics of participants with SSc (n=26).

Characteristic	Value
Age, years, mean (SD)	62.5 (10.0)
Female, n (%)	23 (88.5)
SSc subtype	
- dcSSc	6 (23.1)
- lcSSc	20 (76.9)
Duration of SSc, years, median (IQR)	16.5 (11.8, 28.8)
Duration of RP, years, median (IQR)	18.5 (13.0, 34)
Digital ulcers (current), n (%)	8 (30.8)
Pitting scars, n (%)	14 (53.8)
Pharmacological treatment for RP, n (%)	13 (50.0)
Active smoker, n (%)	1 (3.8)
Baseline RCS score (1-10), mean (SD)	5.1 (2.2)

RCS: Raynaud Condition Score; RP: Raynaud's phenomenon; dcSSc: diffuse cutaneous systemic sclerosis; lcSSc: limited cutaneous systemic sclerosis

Table 2. Descriptive statistics and linear mixed model analyses comparing routine practice and heated glove use.

Outcomes	Mean (SD)	Median (IQR)	Min, Max	Linear Mixed Model Results			
				Est (95% CI)	P-value	Adjust period effect Est (95%CI)	Adjust period effect P-Value
Primary							
Mean RCS (1-10)							
Routine practice	4.43 (2.2)	4.34 (2.7, 5.7)	1.2, 8.7				
Heated gloves	2.9 (2.0)	2.4 (1.2, 3.7)	1.0, 8.5				
Routine practice vs Heated gloves				-1.57 (-2.50, -0.65)	0.001	-1.51 (-2.28, -0.75)	<0.001
Secondary							
Mean number of attacks (n/day)							
Routine practice	2.44 (1.4)	2.14 (1.3, 3.3)	0.4, 6.4				
Heated gloves	1.79 (1.2)	1.71 (1.0, 2.8)	0.0, 4.1				
Routine practice vs Heated gloves				-0.65 (-1.09, -0.21)	0.005	-0.64 (-1.09, -0.19)	0.007
Mean attack duration (mins)							
Routine practice	100.76 (98.3)	86.82 (31.0, 109.8)	12.5, 389.7				
Heated gloves	63.71 (76.0)	31.96 (14.9, 71.0)	1.1, 253.9				
Routine practice vs Heated gloves				-37.05 (-67.82, -6.29)	0.020	-36.01 (-67.05, -4.97)	0.025
CFHS (0-90)							
Routine practice	12.81 (18.0)	5.50 (2.0, 10.8)	0.0, 67.0				
Heated gloves	12.73 (16.9)	6.00 (1.0, 14.0)	0.0, 52.0				
Routine practice vs Heated gloves				-0.08 (-2.26, 2.11)	0.945	-0.04 (-2.14, 2.05)	0.970
HAQ-DI (0-3)							
Routine practice	0.71 (0.6)	0.50 (0.3, 0.8)	0.0, 2.4				
Heated gloves	0.68 (0.6)	0.50 (0.3, 0.8)	0.0, 2.3				
Routine practice vs Heated gloves				-0.03 (-0.13, 0.08)	0.587	-0.03 (-0.13, 0.08)	0.609

RCS: Raynaud Condition Score, CFHS: Cochin Hand Function Scale, HAQ-DI: Health Assessment Questionnaire-Disability Index

Methods: A single centre, randomized crossover trial was undertaken in patients with SSc according to 2013 ACR/EULAR classification criteria. The study was conducted during winter and participants were randomized into two groups. Group GR (Gloves/Routine practice) commenced treatment with heated gloves for 28 days followed by 28 days of usual practice (which could include use of non-heated gloves). There was a one week washout between heated gloves and routine care. Group RG (Routine practice/Gloves) followed the same protocol in reverse order. Patients were advised to continue their pharmacotherapy. Data was collected via patient diary and included a daily Raynaud's Condition Score (RCS), hours gloves worn, RP attack details, and adherence to pharmacotherapy. Cochin Hand Function Scale (CHFS) and HAQ-Disability Index (HAQ-DI) score were collected at baseline and at each period end. The primary outcome measure was RCS, averaged over 28 days for each participant for heated glove use versus routine practice. Power calculation indicated a sample size of 22 required to achieve 90% power for detecting a minimal clinically important difference of 1.4 in RCS determined by Khanna *et al*. at a significance criterion of $\alpha = 0.05$. To determine if the timing of active treatment influenced response between

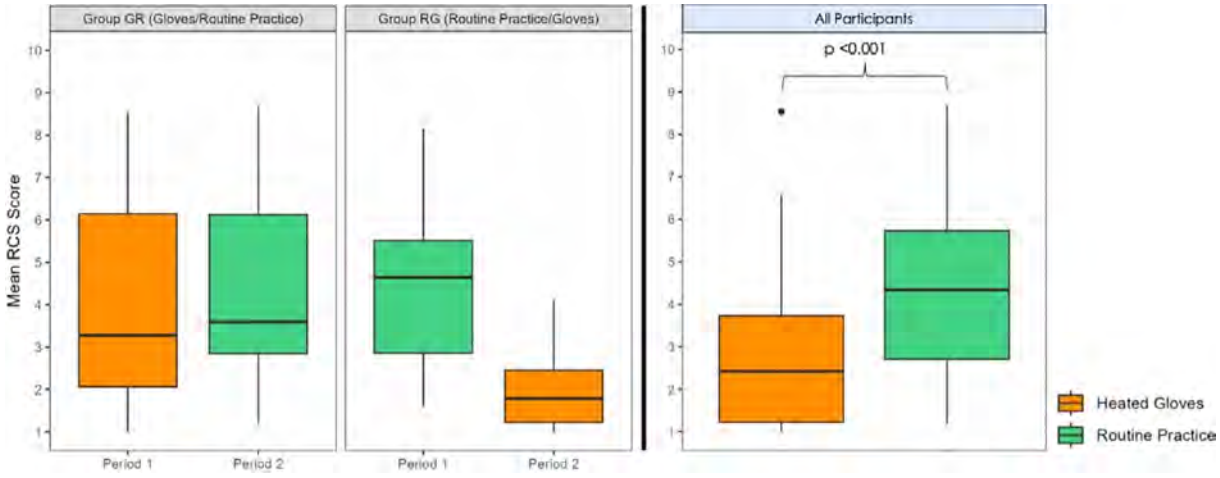

Figure 1. Boxplots of participant mean (SD) RCS score by intervention for crossover groups and all participants combined. P-value shown for linear mixed model results comparing mean RCS for heated gloves and routine practice.

groups, a linear mixed effects model was fitted to the average RCS and adjusted for period effect. The model was repeated for secondary outcomes including mean number and duration of RP attacks, CHFS and HAQ-DI score. RCS, CHFS and HAQ-DI analyses were baseline adjusted.

Results: Twenty-six participants completed the trial (Table 1). Two participants were withdrawn due to insufficient data, one following baseline visit and one from the GR group at washout. Mean hours of glove wearing per day was 4.77 in the GR group and 2.68 in the RG group. From the period and baseline adjusted model, the combined heated gloves groups had a 1.51 unit lower mean RCS score compared to routine practice (95%CI (-2.28, -0.75), P< 0.001) (Table 2, Figure 1). From the period-adjusted model, the heated gloves group had a 0.64 reduction in mean number of attacks (95%CI (-1.09, -0.19), P=0.007). For the mean duration of attacks, there was no significant period effect (0.377) but there was interaction between period and treatment (P=0.027). From the period adjusted model, the heated gloves group had 37.05 minutes lower mean attack duration compared to the control group (95% CI (-67.05, -4.97), P=0.025). There was no difference in CHFS score (95%CI (-2.14, 2.05), P=0.970) or HAQ-DI score (95%CI (-0.13, 0.08), P=0.609) between treatment periods. Reported side effects included skin dryness (2 participants) and intolerance to glove heat (2 participants).

Conclusion: Heated gloves resulted in a statistically and clinically significant reduction in daily RCS. Heated gloves are an effective and safe intervention for reducing RP symptoms in SSc and may be a useful alternative/adjunct to current practice.

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Abstract Number: 0626

Clinical Features of Anti-hUBF Antibodies-positive Patients: A Single-center Retrospective Study

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SESSION INFORMATION
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Background/Purpose: Anti-human upstream-binding factor (hUBF) antibodies (Abs) have been reported predominantly in patients with connective tissue diseases (CTDs) but have also been reported in non-CTDs such as hepatocellular carcinoma. Because of the low frequency of expression and few case reports on this Abs, there is no consensus on the clinical significance of this Abs. Thus, we aimed to examine the clinical features of patients with anti-hUBF Abs.

Methods: Serum samples were collected from 1042 patients clinically suspected of CTDs. The presence of anti-hUBF Ab was screened by Immunoprecipitation (IP) assays. AutoAbs associated with various CTDs were identified by specific indirect immunofluorescence staining, enzyme-linked immunosorbent assay, or IP assay. Clinical characteristics of systemic sclerosis (SSc) patients were first analyzed among patients positive for anti-hUBF Abs or negative for this Abs. We next compared the clinical features among three subgroups: Anti-hUBF Abs, anti-centromere Abs (ACA), and anti-topoisomerase I (topo I) Abs. Statistical analyses were performed at a 0.05 significance level using SPSS version 27 (IBM, Tokyo, Japan).

Results: Of 1042 patients, 19 (1.82%) were positive for anti-hUBF Abs. Of the 19 patients, 10 were diagnosed with undifferentiated connective tissue disease (UCTD), 6 were SSc, and 3 were others. Of the 10 patients with UCTD, 5 were referred to our hospital suspected of SSc. All 5 patients did not fulfill the 2013 American College of Rheumatology/European League Against Rheumatism classification criteria, but 3 of them got 7 points which was a relatively high score. Of the 6 patients with SSc, anti-hUBF-positive patients had a significantly lower modified Rodnan total skin thickness score (mRSS) than those with anti-hUBF-negative patients (2[0-2] vs 7[0-49], $p< 0.01$). Compared with anti-topo I Abs, anti-hUBF-positive patients had a significantly lower mRSS (2[0-2] vs 13[0-42], $p< 0.01$) and lower incidence of scleroderma renal crisis (0/6 vs 8/184, $p< 0.01$). Whereas compared with ACA, anti-hUBF-positive patients had a higher incidence of interstitial lung disease (ILD) but there was no significant difference (4/6 vs 19/239).

Conclusion: Anti-hUBF Abs were positive predominantly in CTDs and UCTD. In CTDs, SSc had a high ratio and they seemed to have lower mRSS and higher incidence of ILD. In UCTD, they should be followed up carefully because they might be CTDs in the future.

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Clinical Significance of Anti-Ro/SSA Antibodies in Patients with Systemic Sclerosis: A Study from the EUSTAR Database

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SESSION INFORMATION

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Background/Purpose: Despite the progress in understanding the patient heterogeneity in systemic sclerosis (SSc) based on SSc-specific antibodies, better risk stratification is needed. SSc non-specific antibodies might represent surrogate markers to improve the stratification of SSc patients. Here, we aim to evaluate the prevalence of anti-Ro/SSA antibodies in the largest available cohort of established SSc patients and study their association with disease phenotype and clinical outcomes, focusing on lung involvement.

Methods: Patients from the EUSTAR database fulfilling the ACR 2013 classification criteria for SSc with available data on anti-Ro/SSA antibodies were included. Clinical characteristics of patients with or without anti-Ro/SSA antibodies were compared at baseline using t-test and chi-squared according to the distribution of the variable. The progression of lung fibrosis was defined (i) in patients with lung fibrosis (FVC%decline from baseline of ≥ 10% or an FVC%decline of 5-9% in association with aDLCO% decline of ≥15%)or (ii) by a decline of FVC >5% in patients with lung fibrosisor (iii) by the development of lung fibrosis de novo (on HRCT scan). Prognostic factors for lung fibrosis progression and death during the follow-up were tested by multivariate Cox proportional hazards regression. Covariates were selected according to literature evidence. Multiple imputation was used to impute missing data in these models.

Results: Among the 4.421 patients fulfilling the inclusion criteria, 661 (15.2%) had positive anti-Ro/SSA antibodies. Anti-Ro/SSA antibodies were more frequently observed among Asians and Africans and less prevalent in Caucasians (Table 1). Anti-Ro/SSA antibodies were positively associated ($p<0.001$) with anti-SSB, anti-U1RNP antibodies, and rheumatoid factor. Patients with anti-Ro/SSA antibodies more frequently presented with muscular involvement (18% vs 12.5%, $p<0.001$), PAPs >45 mmHg on echocardiography (9.2% vs. 6.5%, $p=0.058$) and lung fibrosis on HRCT (56.2% vs 47.8%, $p=0.001$). Specifically, the percentage predicted of DLCO in patients with lung fibrosis was significantly lower in patients with anti-SSA antibodies (59.0±18.6% vs. 61.9±20.2, $p=0.041$). Over a median follow-up of 2.4 years [95CI: 2.2-2.9], anti-SSA antibodies did not predict lung fibrosis progression ((i) HR: 1.03 [0.8-1.33], (ii) HR: 1.05 [0.83-1.31] and (iii) HR: 0.98 [0.72-1.32] or death (HR: 1.27 [0.8-2]).

Conclusion: In the large EUSTAR cohort, anti-SSA antibodies are detected in 15% of SSc-patients and are associated with more severe lung involvement. These data support the inclusion of anti-SSA antibodies in clinical practice for better SSc-patient risk stratification.

Table1: Comparison of SSc-patients with and without anti-Ro/SSA antibodies

	Patients with anti-Ro/SSA antibodies (n=641)	Patients without anti-Ro/SSA antibodies (n=3580)	P value
Age	56.4±13.9	55.2±13.9	0.056
Sex	556 (86.7%)	2996 (83.7%)	0.059
Disease duration	7.0±7.4	7.5±8.5	0.233
Ethnicity:			**0.002**
Asian	58 (9.5%)	193 (6.0%)	
Africans	11 (1.8%)	30 (0.9%)	
Caucasians	523 (85.9%)	2920 (90.0%)	
Ever smoker	193 (33.7%)	1198 (37.3%)	0.112
Extent of skin involvement			0.834
Sine scleroderma	24 (11.7%)	126 (10.3%)	
Diffuse cutaneous form	56 (27.2%)	329 (27.0%)	
Limited cutaneous form	126 (61.2%)	765 (62.7%)	
Anti-La/SSB antibodies	104 (17.4%)	17 (0.5%)	**<0.001**
Anticentromere antibodies	245 (39.6%)	1459 (42.1%)	0.267
Anti-topoisomerase 1 antibodies	224 (35.7%)	1354 (38.0%)	0.277
Anti-RNA polymerase III antibodies	39 (7.7%)	255 (8.9%)	0.446
Isolated ANA (without SSc specific Ab)	113 (17.6%)	514 (14.4%)	**0.037**
anti-U1RNP antibodies	61 (10.7%)	138 (4.2%)	**<0.001**
Rheumatoid factor	143 (28.2%)	409 (14.1%)	**<0.001**
Tendon friction rubs	25 (4.1%)	169 (4.9%)	0.456
Joint synovitis	84 (13.7%)	440 (12.6%)	0.514
Joint contractures	90 (14.7%)	635 (18.4%)	**0.034**
Muscular involvement	103 (18.0%)	414 (12.5%)	**<0.001**
CRP >10 mg/L	24 (4.6%)	117 (4.1%)	0.64
Digital Ulcers			0.888
Current	91 (15.5%)	489 (14.8%)	
Previously	133 (22.7%)	760 (22.9%)	
Never	362 (61.8%)	2066 (62.3%)	
Dyspnea NYHA			0.892
I	117 (57.6%)	730 (59.8%)	
II	67 (33.0%)	393 (32.2%)	
III	14 (6.9%)	65 (5.3%)	
IV	1 (0.5%)	8 (0.7%)	
Scleroderma pattern on capillaroscopy	357 (89.2%)	2020 (88.0%)	0.521
Upper gastrointestinal involvement	378 (60.6%)	2107 (60.4%)	0.965
Scleroderma renal crisis	10 (1.6%)	61 (1.7%)	0.949
LVEF<50%	12 (2.5%)	59 (2.3%)	0.937
PAPsys > 45 mmHg	38 (9.2%)	147 (6.5%)	0.058
Lung.fibrosis on HRCT	286 (56.2%)	1260 (47.8%)	**0.001**
FVC in patients with lung fibrosis	85.2±22.0	85.2±22.0	0.992

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Abstract Number: 0628

Interstitial Lung Disease in Very Early Systemic Sclerosis

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Background/Purpose: Interstitial lung disease (ILD) affects around 50% of patients with systemic sclerosis (SSc) and is the main cause of mortality. Preliminary data from small cohorts suggest ILD may occur even in very early SSc (veSSc, prescleroderma). The main aim of this study is to assess the prevalence and the characteristics of ILD in veSSc and to identify possible predictors of ILD development during follow-up.

Methods: This is a longitudinal cohort study of a single EUSTAR center. We included patients with veSSc, defined as Raynaud's phenomenon and/or at least one of puffy fingers, antinuclear antibodies (ANA), abnormal capillaroscopy, not fulfilling the 2013 ACR/EULAR classification criteria for SSc at baseline. ILD was diagnosed by expert radiologists on high-resolution computer tomography of the chest, which was performed yearly. We analyzed the clinical and spirometry parameters of ILD cases at baseline and during follow-up. Standardized mean difference (SMD) was used to compare patient groups with and without ILD. Cox regression analysis was used to identify risk factors for development of ILD in veSSc. Covariates were chosen according to previous literature and expert opinion.[1]

Results: In our cohort of 737 patients, we identified 159 patients with veSSc. Among these, 25 (15.7%) patients had ILD (Table 1). There were 9 ILD cases (5.7%) at baseline and 16 cases were first detected at follow-up. All of these patients fulfilled the classification criteria during the follow-up period, 10/16 at the visit when ILD was diagnosed. The groups with- and without ILD were imbalanced as measured by SMD: patients with ILD were older, had a longer disease duration (measured

since the first occurrence of Raynaud phenomenon) and more often elevated inflammatory markers, especially ESR (Table 1). There was a significant association between ILD at baseline and a reduced diffusing capacity for carbon monoxide (defined as DLCO < 70% of predicted) (p=0.007, Fisher's test). However, we neither found an association between ILD at baseline and a low forced vital capacity (FVC< 80% of predicted), nor with specific antibodies (anti-centromere, anti-Scl70

Table 1. Characteristics of the patients with- and without ILD during the follow-up period.

	Overall	No ILD	ILD	SMD
n	159	109	25	
Age (median [IQR])	48.00 [35.00, 60.00]	46.00 [34.00, 57.00]	61.00 [53.00, 71.00]	1.116
Male gender (%)	17 (10.7)	11 (10.1)	3 (12.0)	0.061
Baseline visit only (%)	51 (32.1)	38 (34.9)	5 (20.0)	0.338
Disease duration (years) (median [IQR])	3.33 [1.23, 9.92]	3.25 [1.31, 10.42]	9.17 [7.67, 31.00]	0.819
Fulfilled criteria during follow-up (%)	27 (18.9)	20 (18.3)	1 (11.1)	0.205
Raynaud phenomenon (%)	143 (89.9)	100 (91.7)	20 (80.0)	0.342
ANA (%)	153 (96.2)	104 (95.4)	24 (96.0)	0.029
Anti-centromere Ab (%)	82 (53.6)	55 (52.9)	9 (37.5)	0.313
Anti-Scl70 Ab(%)	13 (8.6)	8 (7.7)	4 (16.0)	0.259
Anti-RNA-Polymerase III Ab (%)	12 (8.8)	10 (10.4)	2 (8.0)	0.084
Specific Ab positive* (%)	106 (66.7)	73 (67.0)	14 (56.0)	0.227
Elevated CRP (>5 mg/l) (%)	19 (12.5)	13 (12.4)	5 (20.0)	0.208
Elevated ESR (>25mm/h) (%)	17 (11.9)	8 (7.6)	8 (33.3)	0.672
FVC < 80% (%)	15 (10.4)	10 (9.6)	4 (16.0)	0.192
DLCO <70% (%)	25 (16.8)	14 (13.7)	10 (40.0)	0.621
Dyspnea NYHA I or II (%)	137 (94.5)	100 (98.0)	17 (73.9)	0.741
Dyspnea NYHA III or IV (%)	8 (5.5)	2 (2.0)	6 (26.1)	0.741
6-MWT (distance in m) (median [IQR])	585.00 [513.25, 670.50]	602.50 [524.25, 679.25]	515.50 [406.75, 571.75]	0.743
Desaturation ≥4% in the 6-MWT (%)	11 (10.4)	5 (6.4)	6 (25.0)	0.528
Lung involvement HRCT > 20%	2 (8.7)	0 (NaN)	2 (8.7)	NaN
Abnormal diastolic function (%)	18 (13.4)	12 (12.8)	6 (33.3)	0.504
Esophageal symptoms (%)	50 (31.6)	35 (32.4)	9 (36.0)	0.076
Cigarette smoking ever (%)	36 (51.4)	27 (57.4)	6 (31.6)	0.539

*Specific antibodies were considered: anti-centromere, anti Scl-70 and anti-RNA Polymerase III antibodies

ILD interstitial lung disease; SMD standardized mean difference; n number; ANA anti-nuclear antibodies; Ab antibodies; CRP C-reactive protein; ESR erythrocyte sedimentation rate; FVC forced vital capacity; DLCO diffusing capacity of the lungs for carbon monoxide; NYHA New York Heart Association; 6-MWT 6-minutes walking test; HRCT high resolution computer tomography;

	HR	95% CI	P-Value
DLCO < 70%	2.761	1.056 to 7.216	0.038
Esophageal symptoms (reflux)	1.925	0.844 to 4.390	0.120

DLCO diffusing capacity of the lungs for carbon monoxide; ILD interstitial lung disease; HR hazard ratio

Figure 1. A reduced DLCO (<70%) predicts development of ILD (Cox regression model with the outcome ILD at follow-up).

or anti-RNA polymerase III), presence of puffy fingers or a short disease duration. Only a DLCO< 70% at baseline was a predictor for developing ILD during the follow-up period (HR 2.761, 95% CI 1.056 to 7.216, p=0.038), whereas the presence of reflux symptoms was not significant in the regression model with these two covariates (Figure 1).

Conclusion: After a first analysis of ILD in veSSc, we observed that ILD occurs even in these very mild cases. Therefore, screening for ILD is important even in veSSc. A reduced DLCO < 70% at baseline was not only associated with ILD at baseline, but also predicted the development of ILD at follow-up.

References

1. Hoffmann-Vold AM et all Progressive interstitial lung disease in patients with systemic sclerosis-associated interstitial lung disease in the EUSTAR database. Ann Rheum Dis. 2021 Feb;80(2):219-227.

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Abstract Number: 0629

Negative Affect, Anxiety and Fatigue Moderate the Association Between Pain Intensity and Physical Function in People with Systemic Sclerosis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Pain is a common symptom of systemic sclerosis (SSc), affecting over 80% of those living with the condition, with over a third experiencing pain of moderate or severe intensity. Pain intensity is strongly associated with physical functioning in SSc, however psychosocial moderators of this association are understudied. If modifiable psychosocial factors decouple the pain intensity-physical functioning association, addressing them may help diminish physical limitations attributable to SSc-related pain. Accordingly, this study examined psychosocial factors as potential moderators of the pain intensity-physical function association in SSc.

Methods: This cross-sectional observational study used baseline data from a trial examining the effectiveness of a web- and app-based intervention for fatigue management for people with SSc (ClinicalTrials.gov identifier NCT04908943). Participants were $\geq$18 years old with any SSc subtype, with a mean score $\geq$4 on the Fatigue Severity Scale. A questionnaire battery captured information about demographic, clinical and psychosocial factors. Pain intensity was assessed using the PROMIS Global Pain item (average pain past 7 days; 0-10 Numeric Rating Scale); physical function was assessed with the PROMIS short-form v2.0 Physical Function 4a. Psychosocial factors examined as potential moderators were positive and negative affect (Positive and Negative Affect Schedule), resilience (Connor-Davidson Resilience Scale), and PROMIS measures of anxiety, depression, fatigue, sleep disturbances, and self-efficacy. Linear regression was used to quantify the association between pain intensity and physical function, with interaction terms added for each moderator in separate models, adjusted for age, SSc subtype, and disease duration.

Results: Of 174 people recruited to the trial, 173 were randomized and included. 93% were female, sample mean age 54.5 (standard deviation (SD) 11.7). Most were white (83%), non-Hispanic/non-Latino (87%), and married (65%). 47% had diffuse cutaneous SSc, 35% limited,13% overlap, and 5% other/unsure. Mean (SD) pain intensity was 4.9 (2.3) and mean physical function T-score was 38.5 (1.2 SD below the general US population). There was a linear association between pain intensity and physical function, with pain intensity explaining 31% of variability in physical functioning, adjusted for age, SSc subtype, and disease duration. Statistically significant interaction effects were identified for level of negative affect, anxiety, and fatigue. In all cases, higher psychosocial symptom levels were associated with a stronger, negative association between pain intensity and physical functioning.

Conclusion: Negative affect, anxiety and fatigue moderated the association between pain intensity and physical functioning. Compared to those with lower levels of these psychosocial symptoms, those with higher levels experienced poorer physical functioning at higher pain intensities. If replicated, these findings would support longitudinal studies to examine whether addressing high levels of negative affect, anxiety and fatigue improve physical functioning of people with SSc-related pain.

Disclosure: D. Whibley: None; **Y. Chen**: None; **A. Kratz**: American Psychological Association, 12, Editor, Happify/Twill, 2; **D. Khanna**: AbbVie, 12, DSMB, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb, 2, 5, CSL Behring, 2, Genentech, 2, Horizon Therapeutics, 2, 5, Janssen, 2, 6, Pfizer, 5, Prometheus, 2; **S. Murphy**: None.

Abstract Number: 0630

Prevalence and Risk Factors for Systemic Sclerosis Digital Ischemic Complications in the Collaborative National Quality and Efficacy Registry

Marissa Savoie[1], Monica Harding[2], Jessica Alvey[2], John VanBuren[2], Shervin Assassi[3], Elana Bernstein[4], Lorinda Chung[5], Luke Evnin[6], Tracy Frech[7], Jessica Gordon[8], Faye Hant[9], Laura Hummers[10], Dinesh Khanna[11], Kimberly Lakin[8], Dorota Lebiedz-Odrobina[12], Yiming Luo[13], Ashima Makol[14], Jerry Molitor[15], Duncan Moore[16], Carrie Richardson[17], Nora Sandorfi[18], Ami Shah[19], Ankoor Shah[20], Brian Skaug[21], Virginia Steen[22], Elizabeth Volkmann[23] and Flavia Castelino[1], [1]Massachusetts General Hospital, Boston, MA, [2]University of Utah, Salt Lake City, UT, [3]University of Texas McGovern Medical School at Houston, Houston, TX, [4]Division of Rheumatology, Department of Medicine, Vagelos College of Physicians and Surgeons, Columbia University Irving Medical Center, New York, NY, [5]Department of Medicine, Division

of Immunology and Rheumatology, Stanford University School of Medicine, Woodside, CA, [6]Scleroderma Research Foundation, Brisbane, CA, [7]Vanderbilt University Medical Center, Nashville, TN, [8]Hospital for Special Surgery, New York, NY, [9]Medical University of South Carolina, Charleston, SC, [10]Johns Hopkins University, Baltimore, MD, [11]University of Michigan, Ann Arbor, MI, [12]University of Utah, Cottonwood Heights, UT, [13]Division of Rheumatology, Department of Medicine, Columbia University Irving Medical Center, New York, NY, [14]Mayo Clinic, Rochester, MN, Rochester, MN, [15]University of Minnesota, Minneapolis, MN, [16]Northwestern University, Department of Rheumatology, Chicago, IL, [17]Northwestern University, Chicago, IL, [18]University of Pennsylvania, Philadelphia, PA, [19]Department of Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Ellicott City, MD, [20]Duke University, Durham, NC, [21]Division of Rheumatology, University of Texas McGovern Medical School, Houston, TX, [22]Georgetown University School of Medicine, Washington, DC, [23]University of California Los Angeles, Los Angeles, CA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Digital ischemic ulcers (DIU) develop in 36-44% of patients with systemic sclerosis (SSc).[1,2]Prior international observational studies have evaluated characteristics of digital pitting and ulcers in their SSc patient populations; however, these studies do not necessarily reflect the US SSc patient population. We examined the prevalence of digital ischemic complications in a US-based longitudinal registry and evaluated clinical factors and patient reported outcomes associated with current digital pitting scars (DPS) and DIU.

Methods: We conducted a cross-sectional study utilizing the Collaborative National Quality and Efficacy Registry (CONQUER), a US-based, prospective, multi-center cohort of adults with SSc who meet 2013 ACR/EULAR Classification Criteria, with a disease duration ≤ 5 years from first non-Raynaud's symptom at enrollment. At study enrollment, clinicians recorded the presence of DPS and DIU, and demographic, clinical, laboratory variables, and patient reported outcomes were collected. Multivariable-adjusted logistic regression models were designed using directed acyclic graphs.

Results: Among 772 eligible CONQUER participants, 166 (22%) had at least one DPS and 47 (6%) had active DIU at enrollment (Tables 1 and 2). Half of the participants with DPS were prescribed calcium channel blockers. Participants with DPS had worse PROMIS-29 v2.0 social function and pain scores, and participants with DIU had worse physical function, depression, social function, and pain scores. In our multivariable logistic regression model, younger age and male sex were associated with DPS (OR for female sex 0.50, 95% CI: 0.30 to 0.84 and OR for increased age by 5-year increments 0.90, 95% CI: 0.83 to 0.98, Figure). Race, tobacco use, abnormal nailfold capillaries, presence of telangiectasias, mRSS, disease subtype, disease duration, hypertension, and autoantibody status were not associated with DPS.

Conclusion: Digital ischemic complications were associated with impaired quality of life among patients with SSc, specifically in the domains of social function and pain. Younger age and male sex were associated with presence of digital pitting scars.

References

1. Khimdas S, Harding S, Bonner A, et al. Associations with digital ulcers in a large cohort of systemic sclerosis: results from the Canadian Scleroderma Research Group registry. Arthritis Care Res (Hoboken) 2011;63(1):142–149.
2. Meier FMP, Frommer KW, Dinser R, et al. Update on the profile of the EUSTAR cohort: an analysis of the EULAR Scleroderma Trials and Research group database. Ann Rheum Dis 2012;71(8):1355–1360.

Table 1: Demographics and baseline characteristics by digital pitting status

		Digital pitting scars				
	Overall	None	1	2-3	> 3	P-value
All participants	772	606 (78.5%)	51 (6.6%)	82 (10.6%)	33 (4.3%)	
Age at baseline visit (years)	52 (13.7)	53 (13.7)	51 (11.8)	47 (13.5)	45 (12.5)	<0.001[1]
Sex: Female	631 (81.7%)	509 (84.0%)	38 (74.5%)	63 (76.8%)	21 (63.6%)	0.007[2]
Race/ethnicity						0.03[2]
Hispanic	85 (11.1%)	66 (10.9%)	6 (11.8%)	10 (12.3%)	3 (9.4%)	
Non-Hispanic White	528 (68.8%)	429 (71.0%)	32 (62.7%)	47 (58.0%)	20 (62.5%)	
Non-Hispanic Black or African American	89 (11.6%)	55 (9.1%)	10 (19.6%)	19 (23.5%)	5 (15.6%)	
Non-Hispanic Asian	49 (6.4%)	41 (6.8%)	2 (3.9%)	4 (4.9%)	2 (6.3%)	
Non-Hispanic Other	17 (2.2%)	13 (2.2%)	1 (2.0%)	1 (1.2%)	2 (6.3%)	
Disease duration from date of first Raynaud's symptom to baseline visit (years)	5 (6.9)	5 (7.2)	5 (7.1)	5 (6.5)	3 (2.3)	0.05[1]
Disease duration from date of first non-Raynaud's symptom to baseline visit (years)	3 (1.4)	2 (1.4)	3 (1.4)	3 (1.4)	3 (1.4)	0.10[1]
SSc subtype						0.10[2]
Limited cutaneous	287 (37.4%)	234 (38.9%)	18 (35.3%)	29 (35.4%)	6 (18.2%)	
Diffuse cutaneous	481 (62.6%)	368 (61.1%)	33 (64.7%)	53 (64.6%)	27 (81.8%)	
Modified Rodnan Skin Score (mRSS)	13 (10.8)	12 (10.8)	13 (10.8)	14 (10.5)	16 (9.5)	0.01[1]
Abnormal nailfold capillaries	639 (82.9%)	503 (83.0%)	43 (84.3%)	70 (86.4%)	23 (69.7%)	0.21[2]
Telangiectasias of face or lips	352 (46.5%)	268 (45.3%)	27 (52.9%)	37 (45.7%)	20 (60.6%)	0.27[2]
Telangiectasias of hands	189 (25.0%)	143 (24.2%)	10 (19.6%)	20 (24.7%)	16 (48.5%)	0.02[2]
UCLA SCTC GIT 2.0 score Overall	0 (0.4)	0 (0.4)	0 (0.4)	1 (0.5)	0 (0.4)	0.29[1]
ILD (ever)	343 (63.6%)	264 (63.5%)	25 (65.8%)	40 (65.6%)	14 (58.3%)	0.92[2]
History of renal crisis[3]	31 (4.1%)	27 (4.5%)	3 (6.1%)	1 (1.3%)	0 (0.0%)	0.31[2]
ANA/Autoantibody classification[4]						
ANA negative	26 (4.0%)	23 (4.5%)	2 (4.4%)	1 (1.5%)	0 (0.0%)	
ANA positive	625 (96.0%)	492 (95.5%)	43 (95.6%)	65 (98.5%)	25 (100.0%)	0.69[2]
Centromere	120 (18.4%)	98 (19.0%)	9 (20.0%)	10 (15.2%)	3 (12.0%)	
Scl 70	188 (28.9%)	138 (26.8%)	8 (17.8%)	30 (45.5%)	12 (48.0%)	
RNA polymerase III	162 (24.9%)	142 (27.6%)	11 (24.4%)	7 (10.6%)	2 (8.0%)	
Other	155 (23.8%)	114 (22.1%)	15 (33.3%)	18 (27.3%)	8 (32.0%)	
Smoking status						0.06[2]
Never	515 (66.8%)	404 (66.7%)	37 (74.0%)	53 (64.6%)	21 (63.6%)	
Former	225 (29.2%)	183 (30.2%)	9 (18.0%)	25 (30.5%)	8 (24.2%)	
Current	31 (4.0%)	19 (3.1%)	4 (8.0%)	4 (4.9%)	4 (12.1%)	
Hypertension (SBP > 130 mmHg)	196 (25.7%)	158 (26.4%)	13 (26.0%)	19 (23.5%)	6 (18.8%)	0.80[2]
Pulmonary hypertension[5]	31 (4.0%)	21 (3.5%)	5 (9.8%)	4 (4.9%)	1 (3.0%)	0.16[2]
Medications						
Calcium channel blocker (CCB)	289 (37.4%)	206 (34.0%)	25 (49.0%)	39 (47.6%)	19 (57.6%)	0.002[2]
Statin	111 (14.4%)	91 (15.0%)	6 (11.8%)	11 (13.4%)	3 (9.1%)	0.82[2]
PDE-5 inhibitor	99 (12.8%)	58 (9.6%)	12 (23.5%)	19 (23.2%)	10 (30.3%)	<0.001[2]
Anti-platelet	99 (12.8%)	69 (11.4%)	8 (15.7%)	14 (17.1%)	8 (24.2%)	0.07[2]
Anti-coagulant	24 (3.1%)	18 (3.0%)	3 (5.9%)	2 (2.4%)	1 (3.0%)	0.60[2]
HAQ Score	1 (0.8)	1 (0.8)	1 (0.8)	1 (0.9)	1 (0.7)	0.64[1]
Physician Global Assessment: Overall Health	3 (2.0)	3 (2.1)	3 (2.0)	4 (1.8)	4 (1.7)	0.05[1]
Physician Global Assessment: Scleroderma Activity	4 (2.1)	3 (2.1)	3 (1.9)	4 (2.0)	4 (1.9)	0.009[1]
Physician Global Assessment: Scleroderma Damage	3 (2.1)	3 (2.1)	3 (1.9)	4 (2.1)	4 (2.0)	0.005[1]
Participant Global Assessment Score	4 (2.5)	4 (2.6)	4 (2.3)	5 (2.3)	4 (2.9)	0.38[1]
Scleroderma Health Assessment Questionnaire						
Intestinal	2 (2.6)	2 (2.6)	2 (2.6)	3 (3.1)	3 (2.7)	0.10[1]
Breathing	2 (2.5)	2 (2.5)	2 (2.3)	2 (2.1)	3 (3.4)	0.52[1]
Raynaud's	3 (2.9)	3 (2.9)	3 (2.4)	4 (3.3)	4 (2.8)	0.04[1]
Finger ulcers	1 (2.3)	1 (1.9)	1 (2.5)	3 (3.2)	3 (3.1)	<0.001[1]
Severity	4 (2.6)	3 (2.6)	4 (2.5)	4 (2.9)	4 (2.8)	0.03[1]
PROMIS-29 Profile v2.0						
Physical function	45 (8.9)	45 (8.8)	44 (9.5)	43 (8.9)	43 (9.4)	0.24[1]
Anxiety	52 (10.0)	52 (10.1)	53 (8.3)	53 (10.8)	54 (9.0)	0.73[1]
Depression	50 (8.9)	49 (8.8)	52 (7.4)	51 (9.7)	51 (10.0)	0.22[1]
Fatigue	54 (10.7)	54 (10.6)	54 (11.3)	56 (11.6)	56 (10.1)	0.41[1]
Sleep	56 (3.8)	56 (3.9)	56 (3.0)	55 (3.9)	56 (3.0)	0.76[1]
Social function	50 (10.2)	50 (10.2)	52 (10.0)	47 (10.4)	48 (9.7)	0.05[1]
Pain	54 (9.8)	54 (9.9)	54 (8.7)	58 (10.3)	58 (7.3)	0.01[1]

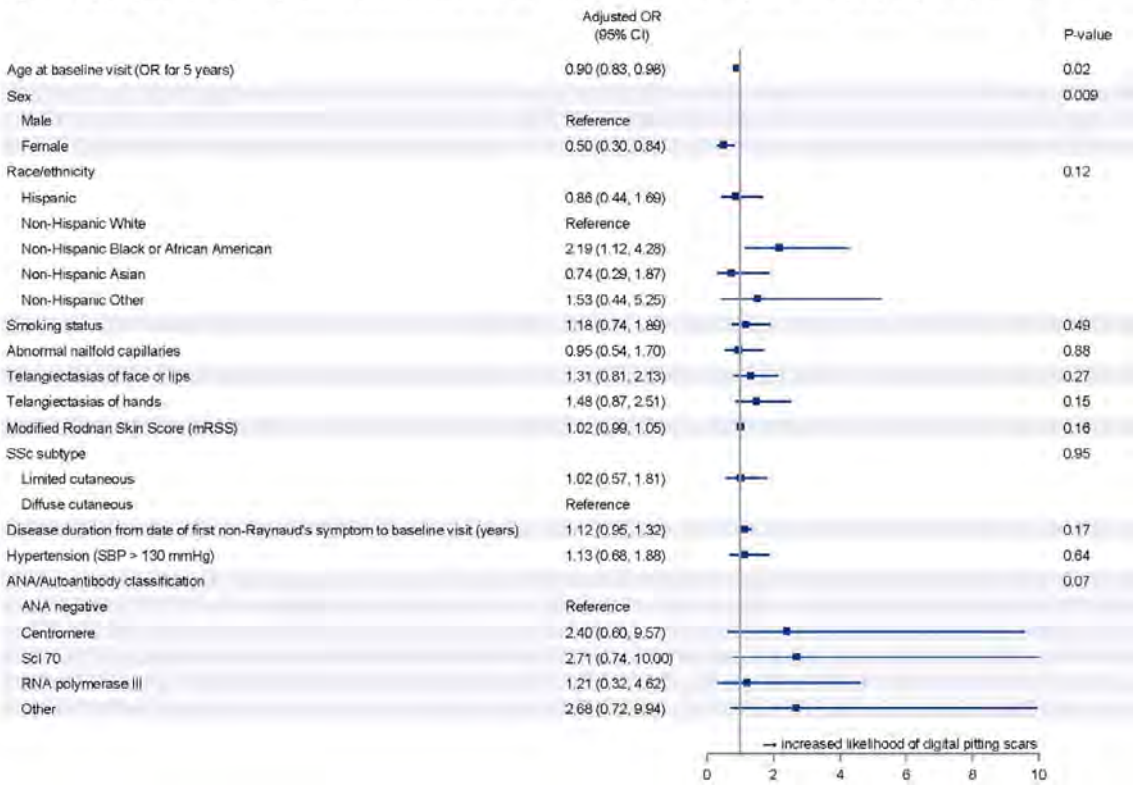
Continuous variables are summarized as Mean (SD).
Missing data indicated if >3% missing data. UCLA SCTC GIT data missing for 95 participants, ILD (ever) data missing for 233 participants, ANA/autoantibody data missing for 121 participants; HAQ data missing for 87 participants, Participant Global Assessment Score data missing for 91 participants; Scleroderma Health Assessment Questionnaire (SHAQ) data missing for between 95 and 119 participants, PROMIS data missing for 239 participants.
[1] Fishers Exact test with Monte Carlo approximation
[2] Kruskal-Wallis test.
[3] Defined as systolic blood pressure (SBP) > 140, diastolic blood pressure (DBP) > 90, rise in SBP > 30, or rise in DBP > 20
[4] Other includes two subserologies: U1 RNP, U3 RNP, Th/To, PM SCL. KU, Isolated Nucleolar, ANA only (no subserology)
[5] Pulmonary hypertension is diagnosed using a right heart catheterization. If pulmonary hypertension is missing, it was assumed that the patient was not diagnosed with pulmonary hypertension.

Table 2: Demographics and baseline characteristics by presence of digital ischemic ulcers

		Digital ischemic ulcers		
	Overall	No	Yes	P-value
All participants	772	725 (93.9%)	47 (6.1%)	
Age at baseline visit (years)	52 (13.7)	52 (13.4)	47 (17.0)	0.04[1]
Sex, Female	631 (81.7%)	597 (82.3%)	34 (72.3%)	0.12[2]
Race/ethnicity				0.50[2]
Hispanic	85 (11.1%)	79 (10.9%)	6 (13.0%)	
Non-Hispanic White	528 (68.8%)	498 (69.0%)	30 (65.2%)	
Non-Hispanic Black or African American	89 (11.6%)	81 (11.2%)	8 (17.4%)	
Non-Hispanic Asian	49 (6.4%)	48 (6.6%)	1 (2.2%)	
Non-Hispanic Other	17 (2.2%)	16 (2.2%)	1 (2.2%)	
Disease duration from date of first Raynaud's symptom to baseline visit (years)	5 (6.9)	5 (7.0)	4 (5.0)	>0.99[1]
Disease duration from date of first non-Raynaud's symptom to baseline visit (years)	3 (1.4)	3 (1.4)	2 (1.4)	0.16[1]
SSc subtype				0.76[2]
Limited cutaneous	287 (37.4%)	271 (37.6%)	16 (34.0%)	
Diffuse cutaneous	481 (62.6%)	450 (62.4%)	31 (66.0%)	
Modified Rodnan Skin Score (mRSS)	13 (10.8)	12 (10.6)	16 (12.9)	0.09[1]
Abnormal nailfold capillaries	639 (82.9%)	605 (83.6%)	34 (72.3%)	0.07[2]
Telangiectasias of face or lips	352 (46.5%)	337 (47.5%)	15 (31.9%)	0.05[2]
Telangiectasias of hands	189 (25.0%)	179 (25.3%)	10 (21.3%)	0.61[2]
UCLA SCTC GIT 2.0 score Overall	0 (0.4)	0 (0.4)	0 (0.5)	0.71[1]
ILD (ever)	343 (63.6%)	324 (63.8%)	19 (61.3%)	0.85[2]
History of renal crisis[3]	31 (4.1%)	29 (4.1%)	2 (4.3%)	0.71[2]
ANA/Autoantibody classification[4]				
ANA negative	26 (4.0%)	25 (4.1%)	1 (2.4%)	
ANA positive	625 (96.0%)	585 (95.9%)	40 (97.6%)	>0.99[2]
Centromere	120 (18.4%)	109 (17.9%)	11 (26.8%)	
Scl 70	188 (28.9%)	175 (28.7%)	13 (31.7%)	
RNA polymerase III	162 (24.9%)	157 (25.7%)	5 (12.2%)	
Other	155 (23.8%)	144 (23.6%)	11 (26.8%)	
Smoking status				0.61[2]
Never	515 (66.8%)	484 (66.9%)	31 (66.0%)	
Former	225 (29.2%)	212 (29.3%)	13 (27.7%)	
Current	31 (4.0%)	28 (3.9%)	3 (6.4%)	
Hypertension (SBP > 130 mmHg)	196 (25.7%)	181 (25.2%)	15 (33.3%)	0.22[2]
Pulmonary hypertension[5]	31 (4.0%)	28 (3.9%)	3 (6.4%)	0.43[2]
Medications				
Calcium channel blocker (CCB)	289 (37.4%)	261 (36.0%)	28 (59.6%)	0.002[2]
Statin	111 (14.4%)	106 (14.6%)	5 (10.6%)	0.67[2]
PDE-5 Inhibitor	99 (12.8%)	91 (12.6%)	8 (17.0%)	0.37[2]
Anti-platelet	99 (12.8%)	94 (13.0%)	5 (10.6%)	0.82[2]
Anti-coagulant	24 (3.1%)	23 (3.2%)	1 (2.1%)	>0.99[2]
HAQ Score	1 (0.8)	1 (0.8)	1 (1.0)	0.17[1]
Physician Global Assessment: Overall Health	3 (2.0)	3 (2.0)	4 (1.9)	<0.001[1]
Physician Global Assessment: Scleroderma Activity	4 (2.1)	3 (2.0)	5 (2.3)	<0.001[1]
Physician Global Assessment: Scleroderma Damage	3 (2.1)	3 (2.0)	4 (2.4)	0.006[1]
Participant Global Assessment Score	4 (2.5)	4 (2.6)	5 (2.1)	0.05[1]
Scleroderma Health Assessment Questionnaire				
Intestinal	2 (2.6)	2 (2.6)	2 (3.3)	0.92[1]
Breathing	2 (2.5)	2 (2.5)	2 (2.7)	0.26[1]
Raynaud's	3 (2.9)	3 (2.9)	4 (3.0)	0.02[1]
Finger ulcers	1 (2.3)	1 (2.0)	5 (3.6)	<0.001[1]
Severity	4 (2.6)	4 (2.6)	5 (2.6)	<0.001[1]
PROMIS-29 Profile v2.0				
Physical function	45 (8.9)	45 (8.8)	41 (8.5)	0.007[1]
Anxiety	52 (10.0)	52 (10.0)	54 (10.1)	0.21[1]
Depression	50 (8.9)	49 (8.8)	55 (9.1)	<0.001[1]
Fatigue	54 (10.7)	54 (10.6)	56 (12.2)	0.34[1]
Sleep	56 (3.8)	56 (3.8)	57 (3.8)	0.32[1]
Social function	50 (10.2)	50 (10.1)	45 (11.0)	0.006[1]
Pain	54 (9.8)	54 (9.8)	60 (9.6)	<0.001[1]

Continuous variables are summarized as Mean (SD).
Missing data indicated if >3% missing data. UCLA SCTC GIT data missing for 95 participants, ILD (ever) data missing for 233 participants, ANA/autoantibody data missing for 121 participants; HAQ data missing for 87 participants. Participant Global Assessment Score data missing for 91 participants; Scleroderma Health Assessment Questionnaire (SHAQ) data missing for between 95 and 119 participants. PROMIS data missing for 239 participants.
[1] Fishers Exact test.
[2] Wilcoxon rank-sum test.
[3] Defined as systolic blood pressure (SBP) > 140, diastolic blood pressure (DBP) > 90, rise in SBP > 30, or rise in DBP > 20.
[4] Other includes two subserologies: U1 RNP, U3 RNP, Th/To, PM SCL. KU, Isolated Nucleolar, ANA only (no subserology)
[5] Pulmonary hypertension is diagnosed using a right heart catheterization. If pulmonary hypertension is missing, it was assumed that the patient was not diagnosed with pulmonary hypertension.

Figure: Multiple logistic regression of systemic sclerosis characteristics and vascular risk factors with the presence of digital pitting scars at baseline



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Abstract Number: 0631

Safety of Radiotherapy for Malignancy in Systemic Sclerosis. a Systematic Review

Aos Aboabat[1], Mohammed AlDohan[2], Patrick Cheung[2], Ani Orchanian-Cheff[3] and Sindhu Johnson[4], [1]University of Toronto, Toronto, ON, Canada, [2]Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada, [3]Library and Information Services, University Health Network, Toronto, ON, Canada, [4]Division of Rheumatology, Department of Medicine, Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western and Mount Sinai Hospitals; Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a chronic autoimmune disorder with higher risks of malignancies. Concerns regarding offering radiotherapy (RT) to SSc patients stem from the potential to worsen SSc manifestations and RT-specific toxicity. Through systematic review of the literature, we evaluated the effect of RT on SSc-manifestations and RT-specific adverse

Methods: MEDLINE, Embase, Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials were searched using subject headings and text words for systemic sclerosis and RT. Inclusion criteria were a physician-based diagnosis of SSc, development of cancer after SSc diagnosis, and exposure to RT. The outcomes were SSc manifestations (cutaneous thickening by mRSS or physicians' clinical assessment, pulmonary fibrosis, flare of SSc) and RT-related toxicity (acute and late).

Results: The search yielded 25 articles, comprising 12 case reports, 3 case series, 5 retrospective cohort studies, and 5 case-control studies. A total of 121 SSc patients who received RT were included, with a mean age of 54.9 years, and 73.6% were female. Indications for RT were breast (N = 46), intrathoracic (N = 7), head and neck (N = 4), genitourinary (N = 3), colorectal (N = 3), and central nervous system (N = 1) cancers. The intent of RT was curative (88.7%) and (11.3% palliative. Post-RT 36/39 (92.3%) did not develop worsening skin thickening, 1/39 (2.6%) had minimal worsening of skin thickening and 2/39 (5.1%) had progressive skin thickening beyond the radiation port. Following RT, 36/39 (92.3%) did not develop SSc-related pulmonary complications, 1/39 (2.6%) developed pulmonary fibrosis, and 1/39 (2.6%) diffuse alveolar hemorrhage. Acute RT adverse effects were reported in 57 patients, with severe acute adverse events observed in a minority. Late non-severe RT adverse effects (Grade 1 and 2 toxicities) included seromas and telangiectasias, whereas late severe adverse effects (Grade 3- 5) included dysphagia, laryngeal edema, radiation pneumonitis, esophageal stricture and small-bowel obstruction. The frequency of grade 3-5 toxicity in cohort studies ranged between 15%-24%.

Conclusion: The majority of SSc patients did not develop worsening SSc-related manifestations following RT, suggesting that RT can be safely administered. A minority experienced acute severe RT-related adverse effects. However, the risk of severe late RT-related adverse effects may be high, underlining the need for close follow-up during and after RT. A larger prospective controlled study is needed to confirm these findings and to identify potential risk factors for adverse outcomes in SSc patients undergoing RT.

Disclosure: A. Aboabat: None; **M. AlDohan**: None; **P. Cheung**: None; **A. Orchanian-Cheff**: None; **S. Johnson**: None.

Abstract Number: 0632

A Longitudinal Analysis of Mouth Opening in 1101 Systemic Sclerosis Patients from the French National Cohort Study

Benjamin Chaigne[1], Alexandre Bense[2], Christian AGARD[3], Yannick ALLANORE[4], Gregory Pugnet[5], Eric Hachulla[6], Jérôme Avouac[7], Boris Bienvenu[8], Sylvain Palat[9], Claire Grange[10], Sabine Berthier[11], Emmanuel Chatelus[12], sebastien riviere[11], Marie-Elise Truchetet[13], Jean-Emmanuel Kahn[14], Francois Maurier[15], elisabeth diot[16], Alice Berezne[11] and Luc Mouthon[17], [1]Paris Cité University, Paris, France, [2]APHP, Paris, France, [3]Internal medicine, Nantes University Hospital, Nantes, France, [4]Université Paris Cité, Paris, France, [5]CHU Toulouse Rangueil Service de Medecine Interne et Immunologie Clinique, Toulouse, France, [6]University of Lille, Lille, France, [7]Service de Rhumatologie, Hôpital Cochin, AP-HP.Centre – Université Paris Cité, Paris, France, [8]Saint Joseph Hospital, Marseille, France, [9]...., Paris, France, [10]..., Paris, France, [11]Internal Medicine - Cochin University Hospital, Paris, France, [12]Internal Medicine - Cochin University Hospital, Strasbourg, France, [13]Bordeaux University Hospital, Bordeaux, France, [14]AP-HP, Suresnes Cedex, France, [15]Hôpitaux privés de Metz, Vaux / Frankreich, France, [16]Internal Medicine - Cochin University Hospital, Tours, France, [17]Hopital Cochin - Paris University, Paris, France

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Background/Purpose: Few studies have evaluated mouth opening (MO) in systemic sclerosis (SSc). None have studied MO trajectories.

Methods: We performed a multicentre study patients enrolled in the French national SSc cohort with at least one MO assessment, described patients based on MO baseline measure, modelized MO trajectories, and associated MO measures with SSc prognosis.

Results: 1101 patients were included in the study. Baseline MO was associated with disease severity. Kaplan Meier analysis showed that MO < 30mm was associated with a worse 30-year-survival ($p< 0.01$) and higher risk of pulmonary arterial hypertension occurrence ($p< 0.05$). Individual MO trajectories were heterogenous between patients. The best model of MO trajectories using latent process mixed models showed that 88.8% patients had a stable MO trajectory, and clustered patients into 3 groups which were predictive of SSc survival ($p< 0.05$). and interstitial lung disease (ILD) ($p< 0.05$). It highlighted a cluster of 9.5% patients with diffuse SSc (dcSSc) ($p< 0.05$) and a high but decreasing MO over one year ($p< 0.0001$) at higher risk of a poor survival and ILD occurrence.

Conclusion: MO, which is a simple and reliable measure, is predictive of disease severity and survival in SSc. Although it remains stable in most SSc patients, dcSSc patients with high but decreasing MO are at risk of poor survival and ILD occurrence.

Disclosure: B. Chaigne: None; **A. Bense**: None; **C. AGARD**: None; **Y. ALLANORE**: AbbVie/Abbott, 2, Alpine Immunoscience, 5, AstraZeneca, 2, Bayer, 2, Boehringer-Ingelheim, 2, Janssen, 2, Medsenic, 2, 5, Mylan, 2, OSE Immunotherapeutics, 5, Prometeus, 2, Roche, 2, Sanofi, 2; **G. Pugnet**: None; **E. Hachulla**: Bayer, 2, CSL Behring, 5, GlaxoSmithKlein(GSK), 2, 5, 6, johnson&Johnson, 2, 5, 6, Novartis, 2, 5, Otsuka, 6, Roche-Chugai, 2, 5, 6, sanofi-genzyme, 2, 5, Sobi, 5; **J. Avouac**: AbbVie, 6, AstraZeneca, 6, Biogen, 6, BMS, 5, 6, Fresenius Kabi, 5, 6, Galapagos, 5, 6, Janssen, 6, Lilly, 6, Medac, 6, MSD, 6, Nordic Pharma, 6, Novartis, 6, Novartis (Dreamer), 5, Pfizer, 6, Pfizer (Passerelle), 5, Roche-Chugai, 6, Sandoz, 6, Sanofi, 6; **B. Bienvenu**: None; **S. Palat**: None; **C. Grange**: None;

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Abstract Number: 0633

Prediction of Progressive Fibrosing Interstitial Lung Disease in Systemic Sclerosis Patients: Insight from the CRDC Cohort Study

Min Hui[1], Xinwang Duan[2], Jiaxin Zhou[3], Mengtao Li[3], Qian Wang[4], Jiuliang Zhao[1], Yong Hou[1], Dong Xu[5] and xiaofeng Zeng[4], [1]Department of Rheumatology, Peking Union Medical College Hospital, Beijing, China, [2]Department of Rheumatology, The Second Affiliated Hospital of Nanchang University, Beijing, China, [3]Peking Union Medical College Hospital, Beijing, China, [4]Department of Rheumatology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China, [5]Department of Rheumatology, Peking Union Medical College, Beijing, China

SESSION INFORMATION

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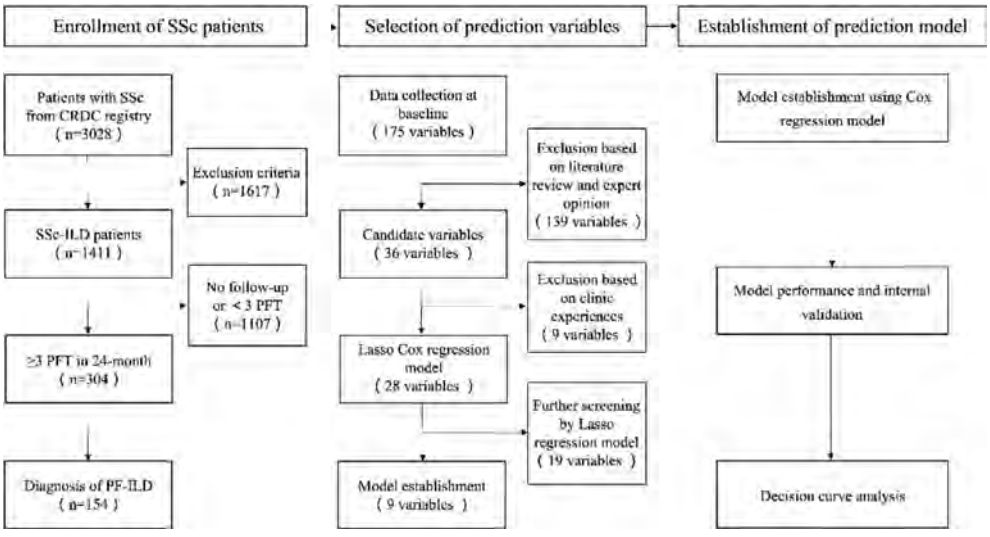
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) patients can develop progressive fibrosing interstitial lung disease (PF-ILD), linked to a poor outcome. This study aims to establish a reliable prediction model of PF-ILD in SSc-ILD patients, to achieve early risk stratification, and to help better preventing disease progression.

Methods: Three hundred and four SSc-ILD patients registered on Chinese Rheumatism Data Center (CRDC) database since January 2008, with no less than three pulmonary function tests within 6-24 months, were included. The major outcome was development of PF-ILD, which was defined as an absolute annualized forced vital capacity (FVC) decline ≥5% predicted. We collected data at baseline and compared differences between SSc patients with PF-ILD (SSc PF-ILD) group and SSc patients without PF-ILD (SSc non-PF-ILD) group. Lasso regularization regression was performed for further screening. Multivariable Cox regression were used to construct the prediction model, which were presented as nomogram and forest plot.

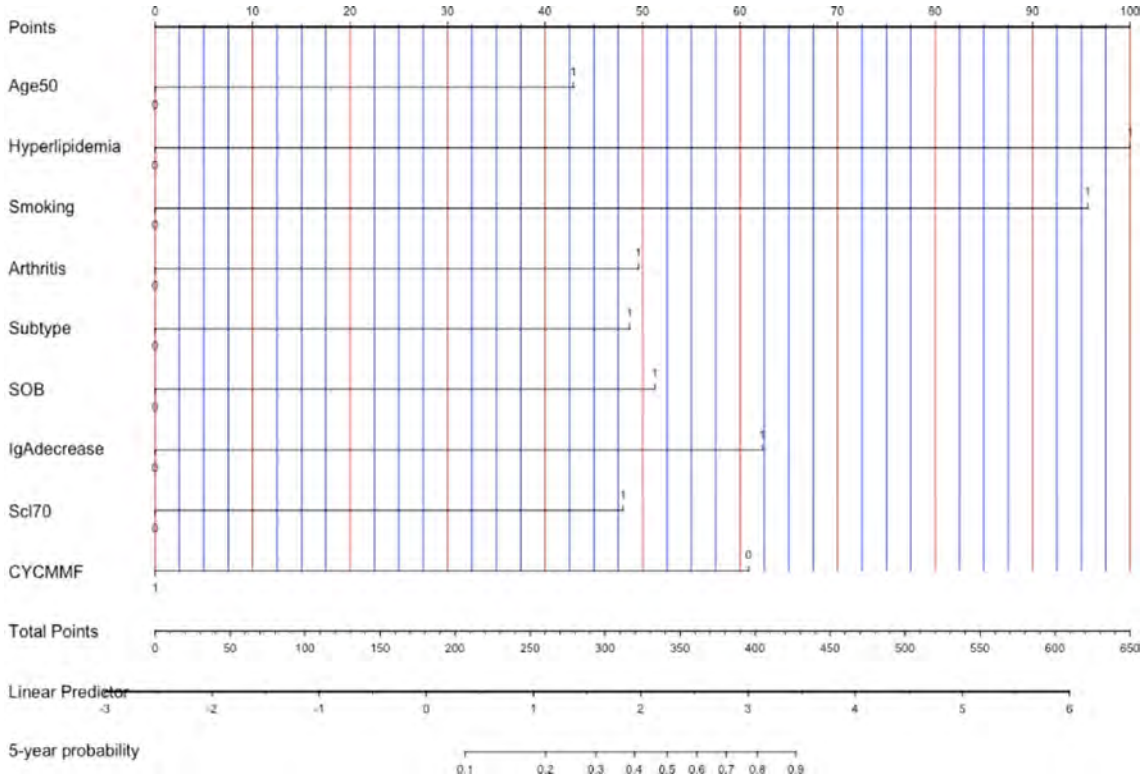


Flow chart showing the study design

Results: SSc-ILD patients were divided into SSc PF-ILD group (n=154) and SSc non-PF-ILD group (n=150). Compared with SSc non-PF-ILD group patients at baseline, SSc PF-ILD patients were at older age (48.5±11.9 years vs 44.9 ±11.3 years, p< 0.001), had more male patients (9.7% vs 6.0%, p=0.012), more diffused SSc (dcSSc) subtype (58.4% vs 32.7%, p< 0.001), and a significant higher incidence of hyperlipidemia (31.2% vs 8.7%, p< 0.001), smoking history (18.2% vs 5.3%, p< 0.001), arthritis (38.3% vs 24.7%, p< 0.001), shortness of breath (84.4% vs 80.0%, p< 0.001) and anti Scl-70 antibody positivity (53.2% vs 40.0%, p< 0.001), as well as more serum IgA deficiency (11.0% vs 5.3%, p< 0.001). The use of cyclophosphamide (CYC) and/or mycophenolate mofetil (MMF) were less common in SSc PF-ILD group compared with SSc non-PF-ILD group (58.4% vs 68.7%, p< 0.001). Based on the results of univariable Cox analysis and Lasso regularization regression, a 9-variable prediction model was constructed, including age≥50 years, hyperlipidemia, smoking history, dcSSc subtype, arthritis, shortness of breath, serum IgA deficiency, positive anti-Scl70 antibody and usage of CYC/MMF. C-index for the model was 0.874, while the Brier scores were 0.144 after bootstrap resampling internal validation.

	SSc PF-ILD (n=154)	SSc Non-PF-ILD (n=150)	HR (95%CI)	p
Demographic characteristics				
Age, y	48.5±11.9	44.9±11.3	1.023 (1.008-1.038)	0.003
Age≥50 years, n (%)	79 (51.3)	60 (40.0)	3.694 (2.579-5.290)	<0.001
Male, n (%)	15 (9.7)	9 (6.0)	1.993 (1.163-3.416)	0.012
Duration of SSc from diagnosis, m	37.9 (0.1, 417.6)	44.7 (0.3, 408.8)	0.999 (0.996-1.001)	0.314
Duration≥60m, , n (%)	39 (25.3)	27 (18.0)	1.007 (0.697-1.455)	0.970
BMI>24kg/m^2	44/151 (29.1)	39/147 (26.5)	1.002 (0.972-1.075)	0.390
Comorbidities				
Hypertension, n (%)	21/151 (13.9)	19/143 (13.3)	1.192 (0.583-2.437)	0.631
Hyperlipidemia, n (%)	48 (31.2)	13 (8.7)	3.564 (2.511-5.059)	<0.001
Malignancy, n (%)	7 (4.5)	3 (2.0)	1.319 (0.617-2.818)	0.475
Family history of rheumatism, n (%)	30 (19.5)	29 (19.3)	1.057 (0.702-1.592)	0.790
Smoking history, n (%)	28 (18.2)	8 (5.3)	6.202 (4.033-9.538)	<0.001
Allergic history, n (%)	13 (8.4)	9 (6.0)	1.509 (0.853-2.670)	0.157
Clinical features				
DcSSc subtype, n (%)	90 (58.4)	49 (32.7)	2.363 (1.707-3.270)	<0.001
Proximal skin sclerosis, n (%)	126 (81.8)	112 (74.7)	1.267 (0.840-1.911)	0.260
Digital ulcers, n (%)	44/139 (31.7)	36/130 (27.7)	1.079 (0.753-1.546)	0.677
Arthritis, n (%)	59 (38.3)	37 (24.7)	3.868 (2.716-5.510)	<0.001
PAH, n (%)	23/137 (16.8)	24/123 (19.5)	0.659 (0.414-1.049)	0.079
GERD, n (%)	73 (47.4)	71 (47.3)	1.008 (0.732-1.387)	0.961
6MWD, m	471.2±83.6	480.0±90.4	1.000 (0.997-1.003)	0.880
6MWD < 500m, n (%)	88 (57.1)	81 (54.0)	1.144 (0.830-1.577)	0.412
SOB, n (%)	130 (84.4)	120 (80.0)	3.375 (2.136-5.334)	<0.001
ESR elevation, n (%)	68 (44.2)	61 (40.7)	1.067 (0.772-1.475)	0.693
Decreased serum IgA level, n (%)	17 (11.0)	8 (5.3)	2.665 (1.563-4.544)	<0.001
Autoantibody				
ANA, n (%)	142/152 (93.4)	142/149 (95.3)	0.793 (0.414-1.517)	0.484
Anti-Scl-70, n (%)	82 (53.2)	60 (40.0)	5.997 (3.869-9.296)	<0.001
ACA, n (%)	16 (10.4)	22 (14.7)	0.985 (0.585-1.657)	0.954
Anti-RNP, n (%)	37/148 (25.0)	47/147 (32.0)	0.792 (0.543-1.154)	0.224
Treatment				
Glucocorticoids≥15mg/d, n (%)	78 (50.6)	81 (54.0)	0.843 (0.613-1.159)	0.294
CYC/MMF, n (%)	90 (58.4)	103 (68.7)	0.168 (0.114-0.248)	<0.001

Baseline demographic and clinical characteristics of the SSc-ILD patients analyzed for PF-ILD risk in univariate Cox proportional hazards regression analysis



Nomogram predicting the probability that a systemic sclerosis patient with interstitial lung disease (ILD) will develop PF-ILD

Conclusion: This study developed the first prediction model for PF-ILD in SSc-ILD patients based on data from CRDC database, and internal validation showed favorable accuracy and stability of the model.

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Abstract Number: 0634

Prevalence and Associations of Anaemia in Systemic Sclerosis Patients in a National Observational Cohort; Results from the Australian Scleroderma Cohort Study

Raychel Barallon[1], Gene-Siew Ngian[1], Diane Apostolopoulos[1], Dylan Hansen[2], Kathleen Morrisroe[3], Wendy Stevens[4], Susanna Proudman[5], Mandana Nikpour[6] and Joanne Sahhar[1], [1]Monash Health and Monash University, Clayton, Australia, [2]Department of Rheumatology, St Vincent's Hospital Melbourne, Fitzroy, Australia, [3]The University of Melbourne at St Vincent's Hospital Melbourne, Fitzroy, Australia, [4]Department of Rheumatology, St Vincent's Hospital Melbourne, Fitzroy, Australia, [5]Royal Adelaide Hospital and University of Adelaide, Adelaide, Australia, [6]The University of Melbourne at St. Vincent's Hospital Melbourne, Departments of Medicine and Rheumatology, Melbourne, Australia

SESSION INFORMATION

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Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Anaemia in systemic sclerosis (SSc) is under-studied and under-characterised. Its prevalence amongst SSc patients is not well described, nor are its effects on outcomes and survival. The aim of this study was to report the prevalence and nature of anaemia in a large national SSc cohort, and the associations with SSc disease manifestations, malignancy, hospitalisations, and mortality.

Methods: Data prospectively collected between 2007 and 2019 as part of the Australian Scleroderma Cohort Study (ASCS) were used. All ASCS patients meeting 2013 SSc ACR/EULAR criteria were included. The prevalence of anaemia (defined as ever having a haemoglobin < 120 g/L for females and < 130 g/L for males) and severe anaemia (defined as ever having a haemoglobin < 80 g/L) were calculated. The median lowest haemoglobin ever was calculated, as was the median time to anaemia diagnosis from SSc disease onset. Anaemia status by sex and disease subclass was also assessed. Proportions of anaemic patients who experienced gastric antral vascular ectasia (GAVE), interstitial lung disease (ILD), pulmonary arterial hypertension (PAH), angina/acute myocardial infraction (AMI), malignancy, hospitalisation, and death were calculated. P-values were generated by chi square test for categorical variables, and by Wilcoxon rank-sum test for continuous variables. Survival analysis was performed using Kaplan-Meier survival estimates.

Table 1. Prevalence of anaemia in the whole cohort, and by sex and disease subclass. Values are expressed as number (%). Abbreviations: SSc – systemic sclerosis.

	Anaemia	No anaemia	*p-value*
Overall (n=1,929)	741 (38.4%)	1,188 (61.6%)	
Female (n=1,648)	619 (37.6%)	1029 (62.4%)	0.036
Male (n=276)	122 (44.2%)	154 (55.8%)	
Limited SSc (n=1,367)	487 (35.6%)	880 (64.4%)	<0.001
Diffuse SSc (n=460)	221 (48%)	239 (52%)	

Table 2. Proportions within the whole cohort, and by anaemia status, of patients who also experienced other systemic sclerosis manifestations/ comorbidities ever, were hospitalised at least once for reasons other than DU, and died within the follow up period. Values are expressed as number (%). Abbreviations: GAVE - gastric antral vascular ectasia, PAH - pulmonary arterial hypertension, ILD – interstitial lung disease, AMI – acute myocardial infraction, DU – digital ulcers.

	Whole cohort n = 1,929	Anaemia n=741	No anaemia n=1,188	*p-value*
GAVE ever	212 (11%)	124 (16.7%)	88 (7.4%)	<0.001
PAH ever	184 (9.5%)	116 (15.7%)	68 (5.7%)	<0.001
ILD ever	526 (27.3%)	251 (33.9%)	275 (23.1%)	<0.001
Angina/AMI ever	220 (11.6%)	126 (17.3%)	94 (8.0%)	<0.001
Malignancy ever	436 (22.6%)	195 (26.3%)	241 (20.3%)	0.002
Ever hospitalised (for reasons other than DU)	1048 (55.2%)	519 (70.8%)	529 (45.4%)	<0.001
Death within the follow up period	338 (17.6%)	219 (29.6%)	119 (10.1%)	<0.001

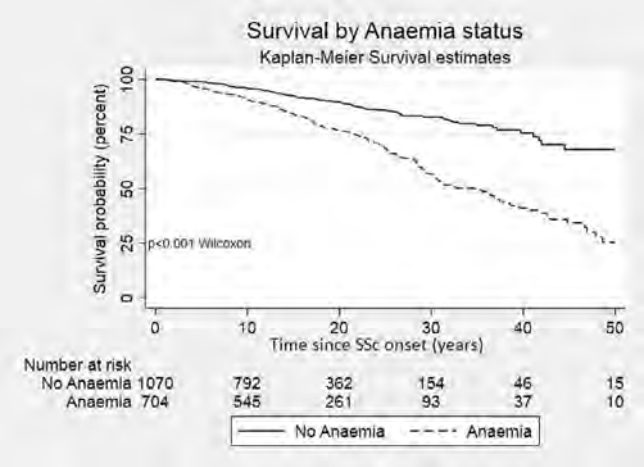

Figure 1. Survival from the first non-Raynaud's symptom onset to death according to anaemia status. Abbreviations: SSc - systemic sclerosis.

Results: Of 1,929 patients, 38.4% experienced anaemia (Table 1) and 1.3% experienced severe anaemia. Anaemia affected 44.2% of males and 37.6% of females (p= 0.036). The proportion of patients with diffuse SSc who had anaemia was 48%, compared to 35.6% of those with limited SSc (p< 0.001). The median lowest ever haemoglobin recorded was 125 g/L (interquartile range (IQR): 114 -133) amongst the whole cohort, and 110 g/L (IQR: 101-116) amongst the anaemic group (p< 0.001). The median time to anaemia diagnosis from SSc disease onset was 10.49 years (IQR: 3.91-19.46). More anaemic patients experienced GAVE compared to non-anaemic patients (16.7% vs. 7.4%, p< 0.001) (Table 2). Similarly, PAH occurred more often in anaemic patients (15.7% vs. 5.7%, p< 0.001), as did ILD (33.9% vs. 23.1%, p< 0.001), angina/AMI (17.3% vs. 8%, p< 0.001), and malignancy (26.3% vs. 20.3%, p= 0.002). More anaemic patients were hospitalised ≥ 1 time (for reasons other than digital ulcers) compared to non-anaemic patients (70.8% vs. 45.4%, p< 0.001). Death within the follow up period occurred more often in the anaemic group (29.6% vs. 10.1%, p< 0.001). Survival was significantly worse in those with anaemia (p< 0.001, Figure 1).

Conclusion: To our knowledge, this is the first study to report prevalence of all-cause anaemia in a large SSc cohort. The prevalence of anaemia in the ASCS was substantial at 38.4%. Severe anaemia was rare. A greater prevalence of anaemia was seen in male patients and in those with diffuse disease. Frequencies of GAVE, cardiopulmonary disease, and malignancy, were higher in anaemic patients, as were hospital admissions and mortality. These findings may guide clinical practice, prompting clinicians to be vigilant for concomitant anaemia in SSc, and to monitor more closely for these associations.

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Abstract Number: 0635

Clinical Characteristics and Longitudinal Outcomes of Patients with Childhood-Onset Systemic Sclerosis at a Tertiary Center

Jessica Nguyen[1], Andrea Ramirez[2], Maria Pereira[2], Eyal Muscal[3], Manuel Silva-Carmona[2] and Marietta De Guzman[2], [1]Baylor College of Medicine, Manvel, TX, [2]Baylor College of Medicine, Houston, TX, [3]Division of Rheumatology, Department of Pediatrics, Baylor College of Medicine, Houston, TX

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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Childhood-onset systemic sclerosis (SSc) is a rare autoimmune multisystemic condition with immune, fibrotic, and vascular manifestations. Although progress has been made in recognizing this condition in children, pediatric outcomes are not well described. We report on clinical characteristics and long-term outcomes of pediatric patients diagnosed with SSc at our center.

Table 1: Demographics and Clinical Characteristics of Patients with Systemic Sclerosis at a Large Tertiary Center

	Systemic Sclerosis (n=15)	Systemic Sclerosis Overlap Syndrome (n=7)	Total (n=22)
Female (%)	14 (93)	7	21 (95)
Race/Ethnicity (%)			
Hispanic or Latino	6 (40)	2 (29)	8 (36)
White	5 (33)	1 (14)	6 (27)
Black	3 (20)	2 (29)	5 (22)
Arabic	1 (7)	0	1 (5)
Ethiopian	0	1 (14)	1 (5)
Mixed Black/White	0	1 (14)	1 (5)
Age at Diagnosis, years (SD)	12 (3.6)	13 (4.6)	12.4 (3.8)
Duration of Symptoms prior to Diagnosis, months (IQR)	12 (6-37)	12 (8-31)	12 (7.5-32.5)
Length of Follow-Up, years (IQR)	8 (4-10)	3 (1-6)	6 (1.75-8.25)
Fulfilled 2013 ACR/EULAR classification criteria for SSc (%)	15	5 (71)	20 (91)
Fullfilled 2007 PRES/ACR/EULAR provisional classification criteria for juvenile SSc (%)	13 (87)	5 (71)	18 (82)
Autoantibodies and Other Immunologic Features (%)			
ANA	12 (80)	6 (86)	18 (82)
Scl-70	5 (33)	2 (29)	7 (32)
RNP	4 (27)	0	4 (18)
U3-RNP	0	3 (43)	3 (14)
U1-RNP	0	1 (14)	1 (5)
PM/Scl-100	1 (7)	1 (14)	2 (9)
RNA-Pol 3	0	0	0
Centromere	0	0	0
SSA	2 (13)	3 (43)	5 (23)
SSB	0	2 (29)	2 (9)
dsDNA	0	1 (14)	1 (5)
Sm	0	2 (29)	2 (9)
Low C3 and C4	0	3 (43)	3 (14)
C1q	0	1 (14)	1 (5)
MDA5	0	2 (29)	2 (9)
KU	1 (7)	0	1 (5)
EJ	1 (7)	0	1 (5)
PL-12	0	1 (14)	1 (5)
Clinical Features at Presentation (%):			
Cutaneous	15	5 (71)	20 (91)
Vascular	15	6 (86)	21 (95)
Musculoskeletal	15	7	22
Major Organ Involvement During Clinical Course (%):			
Pulmonary	9 (60)	6 (86)	15 (68)
ILD	8 (53)	5 (71)	13 (59)
Pulmonary Hypertension	3 (20)	2 (29)	5 (23)
Gastrointestinal	13 (87)	5 (71)	18 (82)
Cardiac	3 (20)	0	3 (14)
Renal	0	0	0

Methods: Under IRB approval, we retrospectively reviewed patients with SSc between 2005 to 2023; 91% of patients fulfilled the 2013 EULAR/ACR classification criteria. Patients with SSc overlap syndrome who also fulfilled the 2017 EULAR/ACR juvenile dermatomyositis (JDM) classification criteria or 2012 SLICC criteria for lupus (SLE) were included. Demographics, clinical features, diagnostic findings, and outcomes were collected.

Results: A total of 22 patients were diagnosed with SSc: 15 (68%) classified as SSc between 2005-2022 and 7 (32%) classified as SSc overlap syndrome between 2015-2023 (n=4 with JDM overlap, n=1 with SLE, n=1 with Sjogren's, and n=1 patient with both JDM and SLE features). Table 1 summarizes patient's demographics and clinical characteristics. Six patients (27%) were diagnosed more than 24 months after symptom onset.

ANA was positive in 82% of patients, and 32% had Scl-70 antibody. No patients had anti-centromere or Pol III antibodies. U1-RNP or U3-RNP antibodies and hypocomplementemia were noted in overlap syndrome. Most patients had typical cutaneous, vascular, and musculoskeletal features at presentation. Pulmonary involvement was seen in 68% of patients, and 3 (all non-overlap) had worsening of their disease at their last visit. Gastrointestinal (GI) involvement was seen in 82% of patients; GERD and esophageal dysmotility being most common. Eleven patients (50%) had active or worsening GI disease at their last visit. Three patients developed cardiomyopathy with heart failure, and 2 required ICD placement. No patients developed renal disease throughout their course.

Patients received a range of immunomodulatory therapies (Figure 1); 20 (91%) received corticosteroids with 13 (59%) remaining on corticosteroids at their last visit. No patient with overlap syndrome received cyclophosphamide, however these patients were more likely to be on a biologic agent.

Figure 1: Percentage of Patients by Treatment

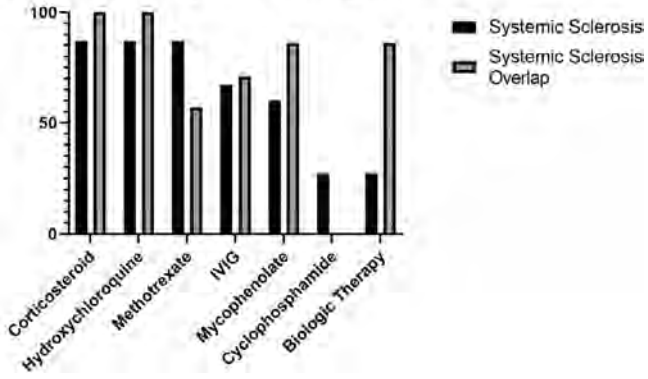

Figure 1: The most common biologic therapy includes rituximab (6 patients total) and tocilizumab (4 patients total).

Table 2: Adverse Events in Patients with Systemic Sclerosis at a Large Tertiary Center

	Systemic Sclerosis (n=15)	Systemic Sclerosis Overlap Syndrome (n=7)	Total (n=22)
Infections (%)			
Cellulitis	3 (20)	1 (14)	4 (18)
UTI	3 (20)	3 (43)	6 (27)
STI	1 (7)	1 (14)	2 (9)
Pneumocystis jirovecii pneumonia	0	1 (14)	1 (5)
Bacteremia	1 (7)	1 (14)	2 (9)
Concern for Mood Disorder (%)	4 (27)	2 (29)	6 (27)
Suicidal Ideation	2 (13)	1 (14)	3 (14)
Pregnancy (%)	1 (7)	0	1 (5)
Death (%)	1 (7)	1 (14)	2 (9)

Three patients had interruptions in care due to insurance or financial reasons. Other adverse events are shown in Table 2. Out of 12 eligible patients, 5 were successfully transitioned to an adult scleroderma center of excellence, 3 to other adult rheumatologists, and 4 did not have any transition records available at the time of the study.

Conclusion: Childhood-onset SSc and SSc overlap syndrome are rare and potentially life-threatening autoimmune conditions, and this cohort addresses a gap in knowledge about long-term outcomes. Cardiopulmonary and GI involvement remained a significant source of morbidity despite multimodal therapy. Treatment including corticosteroids was well tolerated. Defining the differences in clinical course and prognosis between juvenile SSc and SSc overlap syndrome are limited by the nature of the study, the small cohort, and variability in available treatments at the time of caring for the patient.

Disclosure: J. Nguyen: None; **A. Ramirez**: None; **M. Pereira**: None; **E. Muscal**: Sobi, 1, 11; **M. Silva-Carmona**: None; **M. De Guzman**: None.

Abstract Number: 0636

Chasing Pain: Investigating Somatosensory Profiles in Patients with Rheumatological Diseases Using Quantitative Sensory Testing

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Pain is a prominent symptom in numerous rheumatological diseases. In order to allow for a standardized quantification and the assessment of nociceptive and non-nociceptive submodalities of various afferent nerve fiber groups and central pathways, and to identify sensitive plus or minus signs like hyperalgesia or hypesthesia, the "Quantitative Sensory Testing" (QST) protocol was developed. This tool, established by the German Neuropathic Pain Research Network

Small fiber mediated stimuli		Large fiber mediated stimuli	
CDT[1]	A δ-Fibers	VDT[12]	Aβ-Fibers
WDT[2]	C-Fibers	MDT[13]	Aβ-Fibers
TSL[3], PHS[4]	A δ-Fibers, C-Fibers	ALL[11]	Aβ-Fibers
CPT[5], HPT[6]	A δ-Fibers, C-Fibers		
MPT[7]	A δ-Fibers, C-Fibers		
MPS[8]	A δ-Fibers, C-Fibers		
WUR[9]	A δ-Fibers, C-Fibers		
PPT[10]	A δ-Fibers, C-Fibers		
ALL[11]	A δ-Fibers, C-Fibers		

Fig. 1 QST-Testing categories with their associated nerve fibers (1) Cold detection threshold, (2) Warm detection threshold, (3) Thermal sensory limen, (4) Paradoxical heat sensations, (5) Cold pain threshold, (6) Heat pain threshold, (7) Mechanical pain threshold, (8) Mechanical pain sensitivity, (9) Wind-up-Ratio, (10) Pain pressure threshold, (11) Allodynia, (12) Vibration detection threshold, (13) Mechanical detection threshold

Mechanical Detection Threshold (Log (MDT))				Vibration Detection Threshold (VDT)			
	Estimates	95 %CI	p		Estimates	95 %CI	p
Intercept	-0.75	-1.30 – -0.20	**0.009**	Intercept	8.00	7.85 – 8.15	**<0.001**
SCC	0.86	0.08 – 1.65	**0.030**	SCC	-0.17	-0.38 – 0.05	0.126
RA	0.90	0.12 – 1.68	**0.025**	RA	-0.33	-0.55 –-0.12	**0.003**
PsA	1.30	0.52 – 2.09	**0.001**	PsA	-0.23	-0.45 –-0.02	**0.033**
SpA	0.80	0.02 – 1.58	**0.045**	SpA	-0.30	-0.51 – -0.09	**0.006**

Fig. 2 Results of the linear modelling for Mechanical Detection Threshold (MDT) and Vibration Detection Threshold (VDT)

(DFNS), generates somatosensory profiles [1]that can serve as a valuable tool for guiding targeted pain management strategies. This study investigates variations in somatosensory profiles between healthy individuals and patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), axial spondyloarthritis (SpA), systemic sclerosis (SSc).

Methods: Twenty patients of each disease group (RA, PsA, SpA and SSc) and 20 healthy individuals were enrolled in this monocentric five-armed study, which received ethical approval under Institutional Review Board #065/20. Each of the 100 participants underwent the standardized QST procedure for the creation of a somatosensory profile. QST included both small fiber mediated stimuli and large fiber mediated stimuli incorporating all categories depicted in figure 1. Additional clinical data (including laboratory values, joint manifestations, and pain and disease activity assessments) was collected via standardized questionnaires (BASDAI, PASDAS, CDAI and mRSS). Data was analyzed by using linear modelling and standardized z-scores.

Results: A preliminary data analysis of all 100 study participants was performed. As shown in figure 2, all patient groups presented with increased mechanical detection thresholds ($p \leq 0.045$ for RA, PsA, SpA and SSc). Furthermore, RA, PsA and SpA patients showed diminished vibration perception ($p \leq 0.033$ for RA, PsA and SpA). A higher prevalence of allodynia was seen in all patient groups, as in 5% of patients with SSc, 15% of RA, 25% of PsA, and 15% of all SpA patients, compared with 0% in the control group.

Additionally, the study showed that people with systemic sclerosis notice cold and cold pain stimuli much earlier than healthy individuals ($p=0.023$).

Conclusion: Allodynia, mechanical detection and vibration are perceived through A β-fibers. Considering that all these three modalities showed deviations within the somatosensory profiles, A β-fibers seem to be most severely affected from rheumatological diseases. Accordingly, further research on the role of A β-fibers, particularly in allodynia, is thought to be supportive in the improvement of targeted and personalized pain management. Systemic sclerosis patients' particular susceptibility to cold stimuli is explained given the presence of Raynaud's syndrome.

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Abstract Number: 0637

Comparison of Four Risk Stratification Models for Prediction of Mortality in Systemic Sclerosis-associated Pulmonary Arterial Hypertension in the EUSTAR Cohort

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The 2022 ESC/ERS Guidelines recommend comprehensive risk stratification at diagnosis of pulmonary arterial hypertension (PAH) to guide optimized management.[1]Several risk stratification tools have been developed with data derived mainly from patients with idiopathic PAH. However, patients with systemic sclerosis (SSc)-associated PAH have a worse prognosis. We aimed to assess the performance of current risk stratification tools to predict mortality in SSc-PAH by adding variables specific to SSc.

Methods: We included SSc patients from the EUSTAR database who were diagnosed with PAH by right heart catheterization (RHC) between 2001-2021 (Project Number: CP122). PAH was defined as a mean pulmonary arterial pressure >20 mmHg, pulmonary artery wedge pressure ≤15 mmHg and pulmonary vascular resistance >2 WU. We excluded patients with previous PAH-specific treatment and meaningful interstitial lung disease (ILD), defined as an extent of ILD >20% on HRCT or FVC < 70% in patients with missing quantification. We applied four different approaches:

(I) **2022 ESC/ERS 3-strata:** Three risk groups based on the mean of up to 17 risk parameters from the guidelines graded 1-3 representing low-high risk

(II) **2022 ESC/ERS 4-strata:** Equals no. (I), but divides the intermediate-risk group into two groups

(III) **COMPERA 2.0:** Four risk groups based on the mean of WHO-functional class (FC) and/or six-minute walk distance (6MWD) and NT-proBNP graded 1-4 representing low-high risk.[2]

(IV) **REVEAL Lite 2:**Three risk groups based on six weighted variables (WHO-FC, systolic blood pressure, heart rate, 6MWD, NT-pro-BNP, and eGFR)[3]

We performed Cox regression adjusted for general and SSc-specific factors associated with worse outcome based on expert opinion and published literature (age, male sex, anti-centromere antibodies, digital ulcers, DLCO and limited ILD). Harrell's C-index and ROC analysis with area under the curve (AUC) were applied to compare the performance and discriminating ability of the models with >0.7 defined as acceptable.

Results: Of 890 patients who had RHC, 367 were eligible. Among these, 87% were females, mean age was 66 years, and 83% had limited cutaneous SSc.

In univariable analysis, only COMPERA 2.0 and REVEAL Lite 2 had acceptable predictive value with a C-index >0.7 (table). Adjusted for general and SSc-specific variables, all models were acceptable (table, fig. 1).Numerically, COMPERA 2.0 and REVEAL Lite 2 were the most accurate to predict mortality (table, fig. 1). Hazard ratios increased with higher risk scores (fig. 2). However, COMPERA 2.0 and REVEAL Lite 2 did not significantly discriminate the lower risk groups (fig. 2).

Conclusion: In SSc-PAH, we suggest that risk stratification at time of PAH diagnosis should take general and SSc-specific variables into account. The COMPERA 2.0 and REVEAL Lite 2 risk stratification models perform best when used as stand-alone tools. Neither requires invasive measurements, making them easily applicable in clinical practice. Importantly, these models identify patients in the high-risk group where aggressive upfront treatment is recommended.

Table: Harrell's C-index and AUC in the four approaches

	Univariable analysis		Multivariable analysis	
	C-index	AUC (p=0.04)	C-index	AUC (p=0.27)
ESC/ERS 3-strata	0.64	0.64	0.71	0.71
ESC/ERS 4-strata	0.66	0.67	0.72	0.72
COMPERA 2.0	0.72	0.72	0.76	0.75
REVEAL Lite 2	0.73	0.72	0.78	0.73

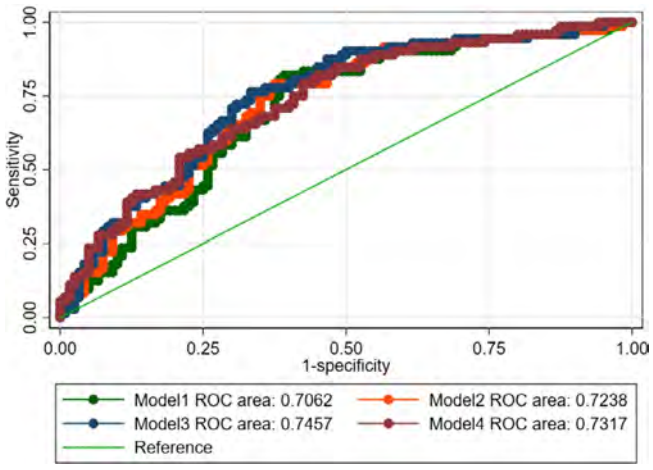

Figure 1: ROC curve with AUC in the four multivariable Cox regression models

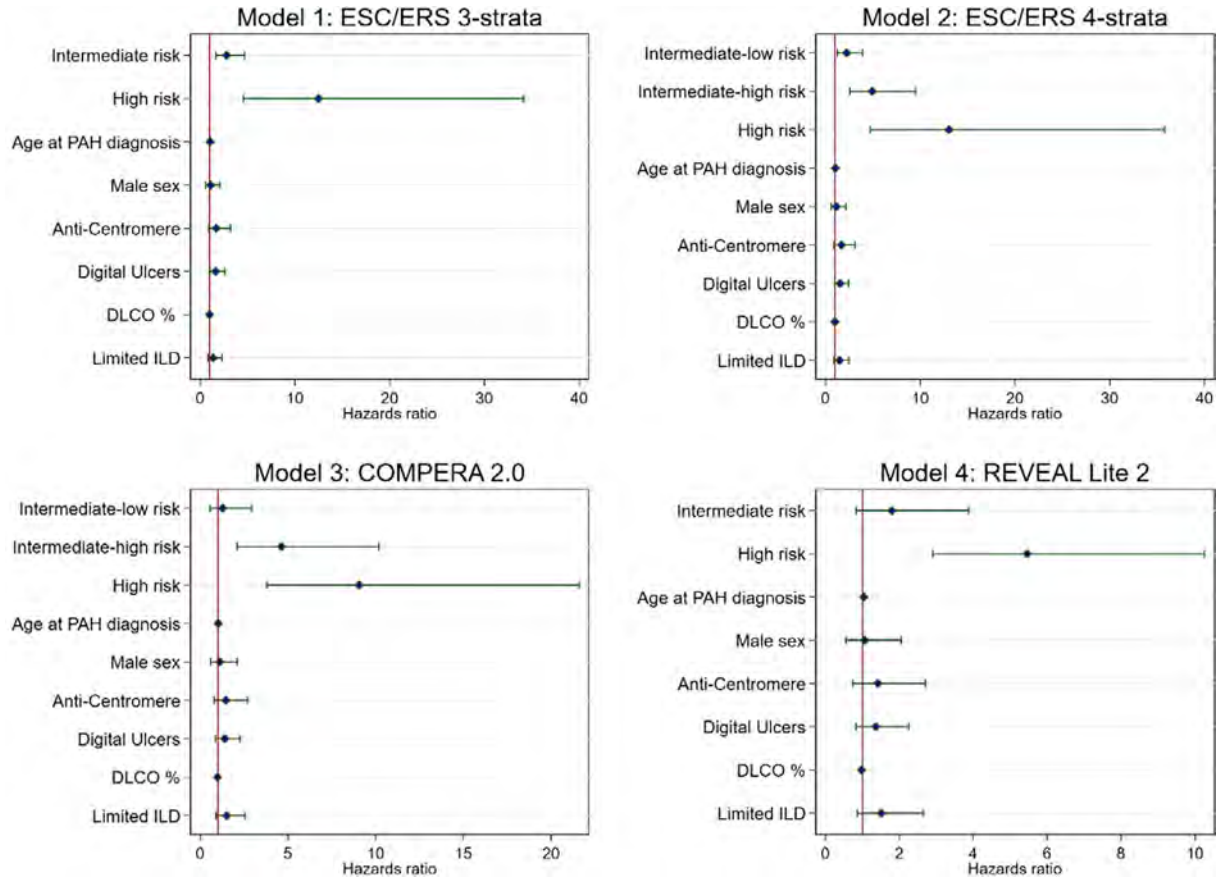

Figure 2: Forest plots of the multivariable cox regression models

References:

[1]Humbert, Eur Heart J, 2022
[2]Hoeper, Eur Respir J, 2022
[3]Benza, Chest, 2021

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Mitsubishi, 2, 6, Pfizer, 2, 6, regeneron, 2, 6, Roche, 2, 6, samsung, 2, 6; **I. Castellvi**: None; **E. Siegert**: None; **E. Hachulla**: Bayer, 2, CSL Behring, 5, GlaxoSmithKlein(GSK), 2, 5, 6, johnson&Johnson, 2, 5, 6, Novartis, 2, 5, Otsuka, 6, Roche-Chugai, 2, 5, 6, sanofi-genzyme, 2, 5, Sobi, 5; **O. Distler**: 4P-Pharma, 2, 5, 6, AbbVie, 2, 5, 6, Acceleron, 2, 5, 6, Alcimed, 2, 5, 6, Altavant Sciences, 2, 5, 6, Amgen, 2, 5, 6, AnaMar, 2, 5, 6, Arxx, 2, 5, 6, AstraZeneca, 2, 5, 6, Bayer, 2, 5, 6, Blade Therapeutics, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Citus AG, 12, Co-Founder, Corbus Pharmaceuticals, 2, 5, 6, CSL Behring, 2, 5, 6, Galapagos, 2, 5, 6, Galderma, 2, 5, 6, Glenmark, 2, 5, 6, Gossamer, 2, 5, 6, Horizon Therapeutics, 2, 5, 6, Janssen, 2, 5, 6, Kymera, 2, 5, 6, Lupin, 2, 5, 6, Medscape, 2, 5, 6, Miltenyi Biotec, 2, 5, 6, Mitsubishi Tanabe, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143), 10, Prometheus Biosciences, 2, 5, 6, Redx Pharma, 2, 5, 6, Roivant, 2, 5, 6, Topadur, 2, 5, 6; **A. Hoffmann-Vold**: Arxx Therapeutics, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Support for travel, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, 12, Support for travel, Roche, 2, 6, 12, Support for travel.

Abstract Number: 0638

Application of the 2022 European Society of Cardiology (ESC) Risk Assessment Model in Australian and Singaporean Systemic Sclerosis Patients with Newly Diagnosed Pulmonary Arterial Hypertension (PAH)

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Pulmonary arterial hypertension (PAH) patients can be stratified as low, intermediate, or high risk of 1-year mortality based on clinical, biochemical and haemodynamic prognostic variables measured at diagnosis. In 2022, the European Society of Cardiology (ESC) and European Respiratory Society (ERS) updated their risk assessment method which is intended to guide therapeutic strategy over time.(1)

Methods: We evaluated incident systemic sclerosis-associated PAH (SSc-PAH) in a large combined cohort of Singaporean and Australian patients. We applied the 2022 ESC 3- and 4-strata risk assessment at baseline and first follow up (within 2 years), respectively. Kaplan-Meier survival analyses and Cox proportional hazards regression models were used to evaluate survival according to risk score.

Results: At baseline (n = 200), the majority of SSc-PAH (72.2%) were intermediate risk according to the 2022 ESC 3-strata risk assessment, based on ten variables. At follow-up, according to the 4-strata risk assessment (based on three variables: WHO functional class, serum N-terminal pro-brain type natriuretic peptide and six-minute walk distance), half (53.5%) of the

cohort were classified as low or intermediate-low risk (Figure 2). The 2022 4-strata risk model at follow up demonstrated statistically significant differences in survival between risk groups with low risk having better survival, and a change in risk category from high or intermediate risk to low or lower risk was associated with an improvement in survival (Figure 1). All three individual parameters were significantly associated with mortality at baseline and/or follow up and included WHO functional class, serum N-terminal pro-brain type natriuretic peptide and six-minute walk distance (Table 1).

Conclusion: The 2022 ESC risk assessment strategy at baseline and follow up accurately predicts survival in SSc-PAH and is sensitive to change. Treatment decisions for SSc-PAH should include risk assessments, aiming to achieve low risk status according to the 2022 ESC guidelines as this is associated with improved outcome.

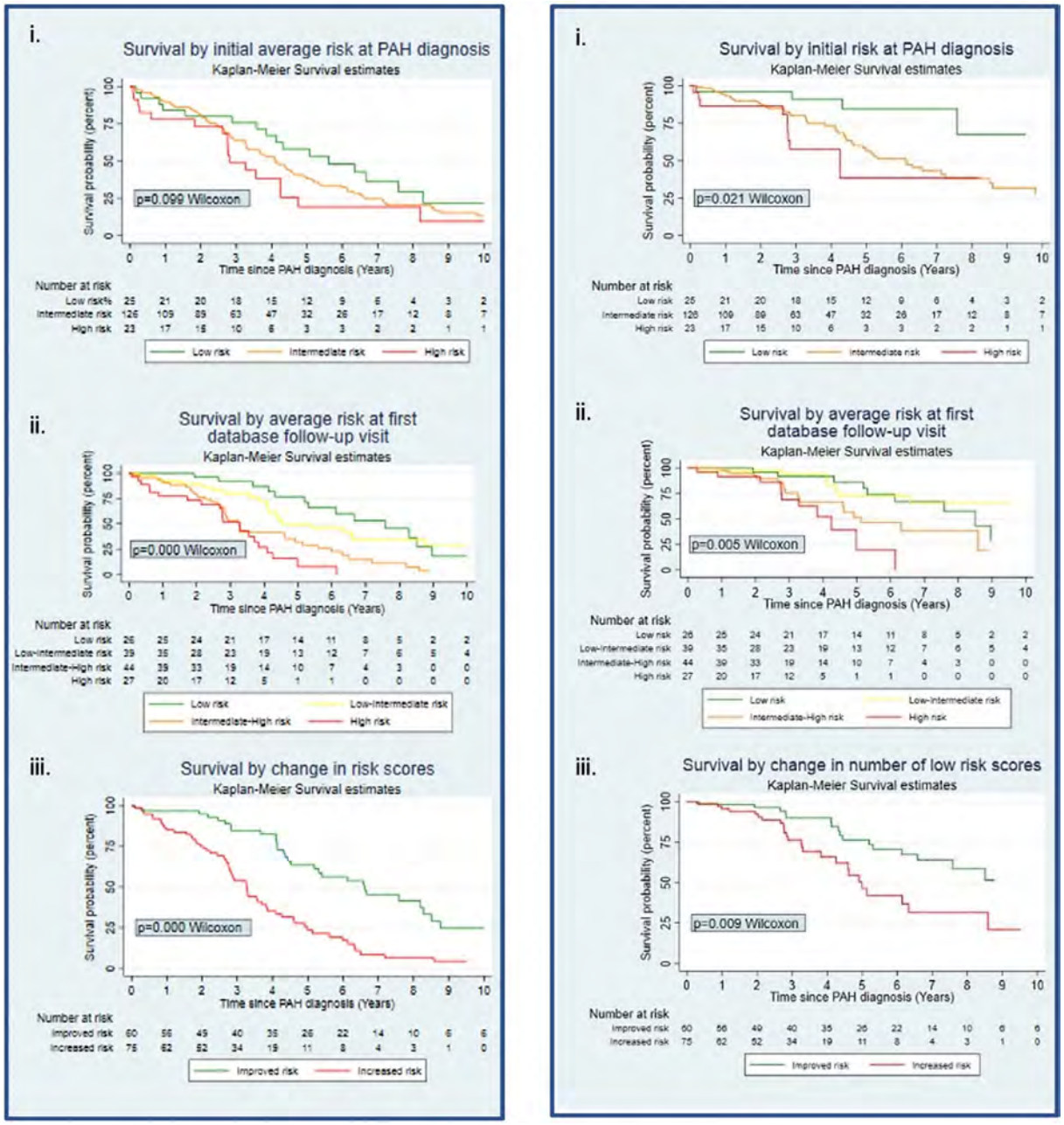

Figure 1. Kaplan-Meier survival curve according to 2022 ESC risk score from PAH diagnosis to mortality applied at i. PAH diagnosis, ii. First follow up and iii. Change in risk score: a.) All-cause mortality b.) PAH-related mortality

Table 1. Hazard ratios for all-cause and cardiac-cause mortality according to individual risk variables in combined ASCS and SCORE cohort

Table 1. Hazard ratios for all-cause and cardiac-cause mortality according to individual risk variables in combined ASCS and SCORE cohort

Variable	Value	PAH diagnosis to all-cause mortality				PAH diagnosis to cardiac-cause mortality			
		n	HR	95% CI	P value	n	HR	95% CI	P value
WHO FC									
Baseline	Low Risk	37	1.00	-	-	37	1.00	-	-
	Intermediate Risk	98	0.87	0.55 – 1.38	0.557	98	3.72	1.34 – 10.38	0.012
	High Risk	18	2.11	1.10 – 4.02	0.024	18	10.29	3.24 – 32.68	<0.001
Follow-up	Low Risk	42	1.00	-	-	42	1.00	-	-
	Intermediate Risk	52	1.37	0.81 – 2.33	0.240	52	2.20	0.98 – 4.92	0.055
	High Risk	14	3.88	1.89 – 7.96	<0.001	14	8.30	3.14 – 21.94	<0.001
Change	Improved maintained low	42	1.00	-	-	42	1.00	-	-
	Increased or maintained high	60	1.47	0.90 – 2.41	0.128	60	2.47	1.18 – 5.20	0.017
6MWD									
Baseline	Low Risk	16	1.00	-	-	16	1.00	-	-
	Intermediate Risk	92	1.69	0.85 – 3.38	0.137	92	3.27	1.15 – 9.34	0.027
	High Risk	13	1.77	0.67 – 4.72	0.250	13	4.29	1.18 – 15.59	0.027
Follow-up	Low Risk	22	1.00	-	-	22	1.00	-	-
	Intermediate Risk	63	1.85	0.94 – 3.61	0.073	63	2.63	1.06 – 6.50	0.037
	High Risk	6	9.01	2.97 – 27.29	<0.001	6	13.68	3.28 – 57.10	<0.001
Change	Improved or maintained low	25	1.00	-	-	25	1.00	-	-
	Increased or maintained high	57	1.64	0.85 – 3.15	0.138	57	2.18	0.93 – 5.12	0.074
Serum NT-proBNP									
Baseline	Low Risk	20	1.00	-	-	20	1.00	-	-
	Intermediate Risk	32	1.71	0.72 – 4.06	0.221	32	1.36	0.38 – 4.86	0.634
	High Risk	34	2.90	1.32 – 6.39	0.008	34	1.53	0.43 – 5.51	0.513
Follow-up	Low Risk	16	1.00	-	-	16	1.00	-	-
	Intermediate Risk	27	1.97	0.88 – 4.41	0.098	27	0.77	0.21 – 2.81	0.690
	High Risk	20	1.69	0.72 – 3.96	0.229	20	1.43	0.44 – 4.64	0.552
Change	Improved or maintained low	17	1.00	-	-	17	1.00	-	-
	Increased or maintained high	29	1.20	0.57 – 2.53	0.625	29	0.77	0.22 – 2.71	0.679

n, number; HR, Hazard Ratio, 95% CI, 95% confidence interval; WHO FC, World Health Organisation Functional Class; 6MWD, six-minute walk distance; NT-proBNP, N-terminal pro-brain type natriuretic peptide

*2022 ESC cut-offs: WHO FC, low risk FC I, II; intermediate risk FC III; high risk FC IV; 6WMD, low risk >440m; intermediate risk 165 – 440m; high risk <165m; NT-proBNP, low risk <300ng/L; intermediate risk 300 – 1100ng/L; high risk >1100ng/L.(1)

Reference

1. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. European Respiratory Journal. 2022:2200879.

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Abstract Number: 0639

Evaluating Esophageal Dysmotility by Scintigraphy in Systemic Sclerosis: Subsets and Phenotypes

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Gastrointestinal (GI) dysmotility affects most patients with systemic sclerosis (SSc), and the esophagus is the most commonly affected region. While most SSc patients are negatively impacted by esophageal dysmotility, significant heterogeneity exists (i.e., absent contractility, ineffective esophageal motility). Importantly prior studies demonstrate that esophageal manometry is useful for risk stratification. For example, absent contractility associates with a more severe extraintestinal clinical phenotype of SSc, (e.g., diffuse cutaneous disease, lower diffusing capacity of the lungs for carbon monoxide (DLCO) values and more severe Raynaud's) while ineffective esophageal motility associates with a milder SSc clinical phenotype. However, manometry can be difficult to obtain due to poor access to the study, and its invasive nature limits tolerability among patient subgroups (i.e., cardiopulmonary complications). Scintigraphy offers a non-invasive alternative to manometry in characterizing motility. We therefore sought to determine (1) whether distinct SSc clinical features associate with decreased esophageal transit on scintigraphy; and (2) how such features compare to the previously described extraintestinal clinical phenotypes described in patients with absent contractility and ineffective esophageal motility on manometry.

Methods: Clinical and demographic features and patient reported outcomes were compared between patients with and without delayed esophageal transit on scintigraphy. Patients were part of a prospective cohort of patients who had clinical data and blood samples collected every 6 months during clinical visits. Scintigraphy-based whole gut transit was used to measure transit time and the percent emptying in each part of the gut from the esophagus to the colon. Medsger scores were used to evaluate SSc disease activity, UCLA-GIT scores were used to evaluate GI symptoms, and the COMPASS-31 survey was used to evaluate symptoms of dysautonomia.

Results: Among 131 patients in our cohort, 79 (60%) had delayed esophageal transit and 52 (40%) did not. Patients with delayed esophageal transit were more likely to have diffuse scleroderma [24 (32%) vs. 11 (22%); p=0.024]. Esophageal transit time negatively correlated with DLCO values (correlation coefficient: -0.317; p=0.014) and % esophageal emptying at 10 seconds was positively correlated with DLCO values (correlation coefficient: 0.339; p=0.0173). Secretomotor symptoms were negatively associated with esophageal transit time (correlation coefficient -0.223; p=0.041). Interestingly, patients with delayed esophageal transit had a higher median (IQR) diarrhea GIT score [0.5 (0-1) vs. 0 (0-1); p=0.050].

Conclusion: Our results suggest that esophageal scintigraphy is a useful tool that can identify patients with a more severe SSc phenotype. Furthermore, patients with delayed esophageal transit on scintigraphy have similar clinical characteristics to SSc patients with absent contractility diagnosed on manometry. Further studies are needed to determine whether esophageal scintigraphy may serve as non-invasive tool to identify SSc patients who may have specific GI and extraintestinal complications.

Table 1. Clinical, demographic, and antibody data of our cohort separated by presence of esophageal transit delay.

Clinical and demographic features	Total (n)	Delayed esophageal transit (n=79)	No delay in esophageal transit (n=52)	P-value
Sex (female), n (%)	131	70 (88.61)	48 (92.31)	0.488
Age at time of WGT, mean (± SD)	131	57.02 (12.5)	55.67 (12.8)	0.552
Race (white), n (%)	130	60 (76.92)	44 (84.62)	0.283
Disease duration in years‡, mean (± SD)	123	11.31 (8.9)	10.94 (9.2)	0.824
SSc Type (diffuse), n (%)	126	24 (31.58)	11 (22)	**0.024†**
Severe Raynaud's phenomenon, n (%)	125	36 (47.37)	15 (30.61)	0.063
Severe Lung involvement, n (%)	90	22 (40.74)	7 (19.44)	**0.034†**
Severe Cardiac involvement, n (%)	96	12 (20.34)	4 (10.81)	0.271
Severe GI involvement, n (%)	126	18 (23.38)	5 (10.2)	0.062
Severe Muscle involvement, n (%)	117	9 (12.5)	3 (6.67)	0.366
Arthralgia, n (%)	114	43 (59.72)	18 (42.86)	0.082
History of cancer, n (%)	131	16 (20.25)	19 (36.54)	**0.039†**
Pulmonary Fibrosis, n (%)	112	29 (40.85)	18 (43.9)	0.752
Calcinosis, n (%)	124	21 (27.63)	13 (27.08)	0.947
Telangiectasias, n (%)	118	62 (83.78)	33 (75)	0.244
Baseline MRSS, median (25th, 75th)	122	3 (2, 9)	2 (0, 6)	0.069
Sicca symptoms, n (%)	125	64 (83.12)	42 (87.5)	0.507
Max RVSP, mean ± SD	68	32.61 (9.2)	32.2 (10.4)	0.866
Pulmonary function tests				
FVC, median (IQR)	114	90 (69.8, 102)	92 (79, 106)	0.221
DLCO*, median (IQR)	61	62.9 (40.5, 84.1)	76.7 (57.8, 96.4)	0.064
Antibodies				
CENP, n (%)	85	20 (37.04)	13 (41.94)	0.656
Scl-70, n (%)	85	9 (16.67)	5 (16.13)	0.949
RNA pol3, n (%)	84	3 (5.56)	1 (3.33)	1.00
ThTo, n (%)	83	0 (0)	1 (3.33)	0.361
U3RNP/Fibrillarin, n (%)	85	1 (1.85)	1 (3.23)	1.00
Ku, n (%)	85	2 (3.7)	1 (3.23)	1.00
Ro-52, n (%)	85	12 (22)	4 (12.9)	0.391

WGT=whole gut transit, SSc=systemic sclerosis, GI=gastrointestinal, MRSS= modified Rodnan skin score, RVSP=right ventricular systolic pressure measured by transthoracic echocardiogram, DLCO=diffusing capacity of the lungs for carbon monoxide, FVC=forced vital capacity. † denotes p-values that are statistically significant. ‡ disease duration was taken from time from first non-Raynaud's phenomenon symptom to the time of the WGT study. Severe Raynaud's phenomenon was defined as patients having Medsger scores of 2 or greater. Severe lung involvement was defined as patients having Medsger scores of 3 or greater. Severe cardiac involvement was defined as patients having Medsger scores of 2 or greater. Severe GI involvement was defined as patients having Medsger scores of 3 or greater.

Clinical, demographic, and antibody data of our cohort separated by presence of esophageal transit delay.

Disclosure: A. Salas: None; **L. Yanek**: None; **Z. McMahan**: Boehringer-Ingelheim, 12, medical writing support for a different manuscript.

Abstract Number: 0640

Multidisciplinary and Multiparametric Evaluation of Sarcopenia in Patients with Systemic Sclerosis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a chronic autoimmune disease with a heterogeneous clinical expression that heavily affects the functionality and quality of life of patients. Sarcopenia is an insidious complication of SSc, often poorly recognized and underdiagnosed, but difficult to manage and with important prognostic repercussions. The aim of this study was to evaluate the prevalence of sarcopenia in subjects with SSc, trying to obtain a characterization as complete as possible through a multidisciplinary approach.

Methods: Consecutive adult SSc patients were evaluated by a multidisciplinary team of rheumatologists, nutritionists and physiotherapists to identify the presence of sarcopenia according to the diagnostic algorithm proposed by the EWGSOP2 consensus in 2019. After completing the SARC-F questionnaire, generally used for the case finding, the patients' muscle strength was measured with the hand grip test and the 5-times sit to stand test (5STS). Subsequently, the confirmation of a possible sarcopenia was obtained by measuring the appendicular skeletal muscle mass (ASSM) by bioimpedance vector analysis (BIVA), a method also used to identify subjects with a state of malnutrition. Finally, the severity of sarcopenia was assessed using the following physical performance tests: short performance physical battery (SPPB - composite score of balance tests, 4m linear walk and 5STS), time up and go (TUG - static balance and dynamic) and gait speed.

Results: Thirty-three SSc patients (87.8% female, mean age 61.2 ± 12 years) were evaluated. The SARC-F questionnaire resulted pathological in 9 of them, whereas for the evaluation of muscle strength pathological values were observed in 42.4% and in 45.4% of the hand grip and 5STS tests, respectively. The ASSM/height ratio was used for the evaluation of muscle mass and was found pathologically reduced in 37.2% of patients. Finally, physical performance tests had pathological results in 27.2% of SPPB, 9% of TUG and 15.1% of gait speed tests. According to the definitions proposed by the EWGSOP2, in our cohort sarcopenia was found in 13 (39.4%) SSc patients, of which 5 (15.1%) presented a severe form. In addition, BIVA found malnutrition in 12 patients and this happened in combination with a sarcopenic state in 75% of cases. Malnourished subjects had significantly lower hand grip strength values (p=0.007), worse SPPB scores (p=0.03), and longer TUG times (p=0.05).

Conclusion: Sarcopenia emerges as a relatively frequent complication in SSc, with important repercussions on the physical-dynamic sphere and a profound interrelationship with nutritional status. A multidisciplinary approach is essential for an accurate diagnosis of sarcopenia in potentially high-risk individuals such as those with SSc.

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Abstract Number: 0641

The Evaluation of Lower Extremities Arterial Disease in Systemic Sclerosis Patients Through Rheumatologist-Vascular Surgeon Multidisciplinary Management: Preliminary Data from an Italian Single Center Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The occurrence of lower limbs macrovascular complications configuring lower extremities arterial disease (LEAD) has been reported in Systemic Sclerosis (SSc) patients. Recently, digital ulcers (DUs), pulmonary arterial hypertension (PAH), steroid use and active smoking/having stopped ≤3 years were identified as factors associated with lower limbs amputation in a single-centre SSc cohort[1]. Our aim was the estimation of LEAD prevalence in: (i) the overall SSc cohort and (ii) at-risk patients according to the above-mentioned features.

Methods: Consecutive SSc patients attending our centre for scheduled visits between October 2022 and April 2023 were included. Patients without known LEAD with ≥1 feature associated to lower limb amputation, as described above[1] were referred for lower extremities arterial Doppler ultrasonography (DUS) performed by a single expert vascular surgeon.

Results: Among 192 SSc patients evaluated (93% females, 81% limited cutaneous involvement, 45% anti-centromere), 18 (9%) were previously diagnosed with LEAD, requiring revascularization interventions in 8 (44%) and amputations in 5 (28%). As compared to the remaining 174, they were older (median[1st-3rd quartile]: 75[69-79] vs 62[51-70] years; p< 0.001), had a longer disease duration (20[15-27] vs 12[6-19] years; p:0.004), higher frequency of DUs (90% vs 54%; p:0.001), especially at lower limbs (67% vs 12%; p< 0.001), more comorbidities (Charlson Comorbidity Index: 6[5-7] vs 3 [2-5]; p< 0.001), and were more frequently treated with prostanoids (67% vs 31%; p:0.002) and steroids (61% vs 31%; p:0.010).

At least 1 LEAD risk factor was identified in 124/174 patients (71%) (DUs (77%); steroid use (40%); smoking (26%); PAH (5%)). Among 41 patients so far evaluated by DUS, LEAD was detected in 13 (32%) (**Table 1**): 10 were asymptomatic (stage I), 2 reported mild claudication (stage IIa), 1 reported pain also at rest (stage III). 10/13 were already on treatment with anti-

Table 1. Characterization of LEAD findings on DUS in 13 patients. Variables are expressed as n (%).

	Occlusion	Stenosis	Intimal thickening	Calcifications
Proximal arteries	0 (0)	5 (39)	6 (46)	6 (46)
Femoral arteries	0 (0)	5 (39)	5 (39)	6 (46)
Popliteal arteries	0 (0)	1 (8)	6 (46)	3 (23)
Distal arteries	8 (62)	1 (8)	2 (15)	5 (39)
Anterior tibial arteries	1 (8)	1 (8)	1 (8)	4 (31)
Posterior tibial arteries	6 (46)	0 (0)	2 (15)	2 (15)
Peroneal arteries	2 (15)	0 (0)	0 (0)	2 (15)

Table 2. Comparison of demographic, clinical-therapeutic features and CV risk factors in patients with LEAD on DUS vs patients with normal DUS. Categorical variables are expressed as n (%) and compared with Chi Squared/Fisher exact test; continuous variables are expressed as median (1st-3rd quartile) and compared with Mann Whitney test. Abbreviations: BMI= Body Mass Index, CV= cardiovascular, PDE5= phosphodiesterase 5.

	Normal DUS (n=28)	LEAD on DUS (n=13)	p value
Female sex	27/28 (96.4)	10/13 (76.9)	0.086
Age, years	59.0 (55.0-71.5)	67.0 (61.0-75.0)	0.287
Disease duration, years	10.5 (6.0-16.5)	13.0 (8.0-18.0)	0.546
Anti-centromere+	15/28 (53.6)	8/13 (61.5)	0.632
Anti-topoisomerase 1+	8/28 (28.6)	4/13 (30.8)	1.000
Antiphospholipid antibodies+	5/23 (21.7)	2/9 (22.2)	1.000
Never smokers	13/28 (46.4)	3/13 (23.1)	0.154
Arterial hypertension	6/28 (21.4)	5/13 (38.5)	0.280
Diabetes	4/28 (14.2)	1/13 (7.7)	1.000
Dyslipidemia	7/28 (25.0)	5/13 (38.5)	0.469
BMI, Kg/m^2	22.4 (20.8-25.9)	22.3 (20.5-22.9)	0.445
≥1 CV risk factor	22/28 (78.6)	11/13 (84.6)	1.000
Limited cutaneous involvement	22/28 (78.6)	8/13 (61.5)	0.252
Digital ulcers (ever)	22/28 (78.6)	12/13 (92.3)	0.399
Pulmonary arterial hypertension	2/28 (7.1)	0/13 (0.0)	1.000
Scleroderma renal crisis	1/28 (3.6)	1/13 (7.7)	0.539
Interstitial lung disease	7/17 (41.2)	3/7 (42.9)	1.000
Calcium channel blockers	17/28 (60.7)	5/13 (38.5)	0.184
Anti-platelets	23/28 (82.1)	8/13 (61.5)	0.241
Prostanoids	15/28 (53.6)	9/13 (69.2)	0.499
Endothelin-antagonists	6/28 (21.4)	3/13 (23.1)	1.000
PDE5-inhibitors	3/28 (10.7)	0/13 (0.0)	0.539
Selexipag	1/28 (3.6)	0/13 (0.0)	1.000
Steroids	9/28 (32.1)	4/13 (30.8)	1.000
Immunosuppressive therapy	7/28 (25.0)	4/13 (30.8)	0.719
Statins	4/28 (14.3)	5/13 (38.5)	0.113
Anticoagulants	2/28 (7.1)	2/13 (15.4)	0.579

platelets/anti-coagulants, in the remaining 3 patients low dose aspirin was added; the patient with LEAD stage III was referred to angiographic study. As compared to 28 patients with a normal DUS, no differences were observed in clinical-demographic features (**Table 2**).

Conclusion: Based on these preliminary data, in our SSc cohort the prevalence of diagnosed LEAD stands at 9%. However, by selecting at-risk SSc patients (DUs, PAH, steroid use and smoking), LEAD signs on DUS were detected in 32% of them, mostly free from lower limb symptoms and traditional CV risk-factors. This underlines the need to implement the diagnostic/therapeutic work-up of SSc patients by performing lower extremities arterial DUS and including vascular surgeons in the multidisciplinary team dedicated to SSc patients.

References. [1]Bertolino et al. JSRD. 2020

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Clinical Characteristics of Systemic Sclerosis, Systemic Sclerosis Overlap Syndromes and Systemic Sclerosis-mixed Connective Tissue Disease in an Asia-Pacific Cohort- an APLAR Scleroderma Special Interest Group Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) patients with clinical features of another connective tissue disease (CTD) may have different clinical characteristics from patients with SSc alone. Our aim was to compare the clinical characteristics and survival of patients with SSc, SSc-overlap and SSc-mixed connective tissue disease (MCTD).

Table 1: Demographics and clinical characteristics

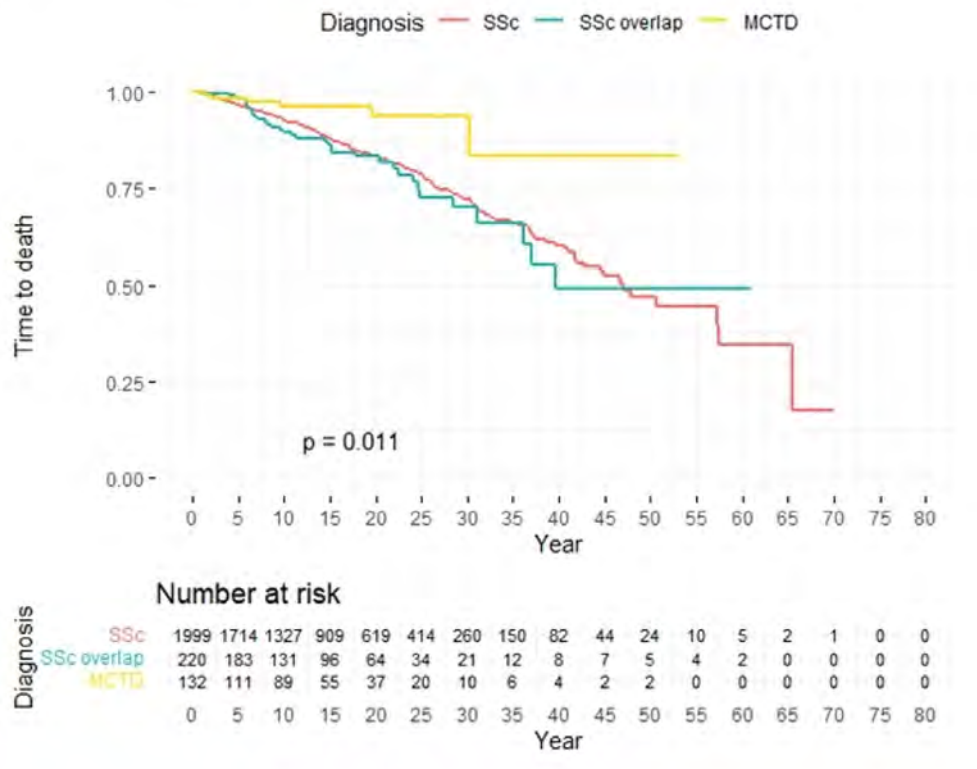
Table 1: Demographics and clinical characteristics

	SSc (n=2131)	SSc-overlap (n=250)	SSc-MCTD (n=164)	P value
Diffuse SSc, n (%)	666 (31.3)	45 (18.5)	21 (20.2)	<0.001
Female, n (%)	1786 (84.9)	220 (89.4)	151 (92.1)	0.008
Modified Rodnan skin score	11.2 ± 9.8	9.0 ± 9.0	6.5 ± 7.2	<0.001
Raynaud's phenomenon, n (%)	1944 (92.6)	224 (91.4)	160 (98.2)	0.019
Digital ulcer, n (%)	969 (45.9)	98 (39.8)	49 (30.1)	<0.001
Arthritis, n (%)	752 (35.8)	150 (61.2)	100 (61.0)	<0.001
Myositis, n (%)	110 (5.2)	69 (27.7)	35 (21.3)	<0.001
Interstitial lung disease on HRCT, n (%)	617 (56.0)	87 (58.8)	66 (66.7)	0.112
Forced vital capacity, mean ± SD	89.0 ± 22.8	84.6 ± 23.5	80.1 ± 19.9	<0.001
Pulmonary arterial hypertension, n (%)	144 (6.8)	10 (4.0)	8 (4.9)	0.325
Upper Gastrointestinal involvement, n (%)	1927 (90.6)	211 (84.7)	127 (77.9)	<0.001
Lower Gastrointestinal involvement, n (%)	1186 (81.8)	130 (67.4)	66 (50.8)	<0.001
Autoantibodies, n (%)				
Anti-centromere	854 (43.4)	70 (30.8)	7 (4.4)	<0.001
Anti-Topo I	441 (23.0)	62 (28.8)	15 (10.6)	<0.001
Anti-PM/Scl	28 (1.7)	9 (5.4)	3 (2.9)	0.007
Anti- ribonucleoprotein	74 (3.9)	25 (11.6)	162 (100)	<0.001
Double-stranded DNA	109 (6.7)	44 (21.3)	42 (29.0)	<0.001
Anti-Ro	163 (8.7)	66 (31.0)	59 (38.3)	<0.001
Anti-La	44 (2.4)	15 (7.1)	19 (12.3)	<0.001
Jo-1	9 (0.5)	7 (3.3)	4 (2.6)	<0.001
Anti-cyclic citrullinated peptide	20 (3.3)	15 (14.6)	5 (8.5)	<0.001
Rheumatoid factor	129 (20.0)	35 (33.0)	33 (47.1)	<0.001
Immunomodulators, n (%)	1236 (59.7)	216 (88.2)	145 (89.5)	<0.001

Methods: This retrospective cohort study included SSc, SSc-overlap and SSc-MCTD patients from Australia, Hong Kong, Malaysia, Singapore, and Thailand. SSc patients fulfilled the 2013 ACR-EULAR SSc classification criteria; SSc-overlap patients also fulfilled the criteria for another CTD which included rheumatoid arthritis, systemic lupus erythematosus, or inflammatory myositis; SSc-MCTD patients had anti-RNP antibody positivity and at least 3 of the following features (per Alargon-Sergovia criteria): swollen hands, synovitis, myositis, Raynaud phenomenon (RP) and acrosclerosis/sclerodactyly. Univariate comparison of clinical characteristics among groups was performed by analysis of variance or chi-square testing. Survival analysis was performed using Kaplan-Meier curves.

Results: Among 2545 patients (11.3% from Singapore, 5.3% from Malaysia, 3.8% from Thailand, 3.3% from Hong Kong and 76.3% from Australia), 250 (9.8%) had SSc-overlap syndrome, 164 (6.4%) had SSc-MCTD and 2131 (83.7%) had SSc. SSc-overlap and SSc-MCTD, respectively, occurred more frequently in the Asian (SSc-overlap: 13.2%-17.9%; MCTD: 8.3%-31.8%) vs Australian (SSc-overlap: 8.2%; MCTD: 3.7%) cohorts. SSc patients were more likely to have diffuse cutaneous SSc, significantly higher modified Rodnan skin score (11.2 ± 9.8 in SSc vs 9.0 ± 9.0 in SSc-overlap vs 6.5 ± 7.2 in SSc-MCTD, p< 0.001), gastrointestinal involvement, higher % predicted forced vital capacity (89.0 ± 22.8 in SSc vs 84.6 ± 23.5 in SSc-overlap vs 80.1 ± 19.9 in SSc-MCTD, p< 0.001) and digital ulcerations as compared to SSc-overlap and SSc-MCTD patients. Arthritis and myositis were significantly more prevalent in SSc-overlap and SSc–MCTD than in SSc

Figure 1: Survival by diagnosis group



Comparison	KM analysis	Univariate Cox regression		
	Log-rank test p value*	HR (95% CI)	P value	Omnibus P value
SSc vs SSc overlap	0.6082	0.903 (0.640, 1.273)	0.5586	0.0220
SSc vs MCTD	0.0053	2.886 (1.326, 6.282)	0.0076	
SSc overlap vs MCTD	0.0053	3.198 (1.386, 7.379)	0.0064	

* adjusted for multiple comparison (BH method)

Figure 1: Survival by diagnosis group

patients. RP was more frequent in SSc-MCTD than in SSc and SSc-overlap patients. At baseline, more patients with SSc (27.7%) and SSc-overlap (21.2%) were in NYHA III/IV than MCTD (15.3%; p< 0.001). There was no significant difference in the frequency of interstitial lung disease and pulmonary arterial hypertension in the 3 groups. Anti-centromere antibody was more frequently seen in SSc patients, and anti-topoisomerase I antibody in SSc-overlap and SSc patients; other antibodies including anti-PM/Scl, double-stranded DNA, rheumatoid factor, anti-Ro, anti-La and Jo-1 were significantly less frequent in the SSc group compared to the SSc-overlap and SSc-MCTD groups. SSc-MCTD and SSc-overlap patients were also more likely to receive immunomodulators than SSc patients (Table 1). Overall survival was better in SSc-MCTD than SSc or SSc-overlap (p=0.011) (Figure 1).

Conclusion: Our study showed significant differences in the clinical characteristics and survival outcomes in patients with SSc, SSc-overlap and SSc-MCTD.

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Abstract Number: 0643

Progression of Interstitial Lung Disease in Systemic Sclerosis Does Not Predict Further Progression

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: In clinical practice, we often wait for progression of interstitial lung disease (ILD) in systemic sclerosis (SSc) to initiate or escalate therapy. Similarly, progressive SSc-ILD patients are recruited into trials to enrich for further progression. These strategies assume that patients with recent ILD progression have a higher risk for further progression. Here, we assessed whether ILD progression predicts subsequent progression using four definitions of progressive disease.

Methods: We included all SSc patients from two expert SSc centers who had ILD on HRCT and consecutive annual forced vital capacity (FVC) measurements. For the primary analysis, ILD progression was defined as absolute FVC decline ≥5% over 12 months. Patients were grouped into progressors (FVC ≥5% decline) and non-progressors (all others). At the next annual

follow up visit, all patients were again assessed for ILD progression. In secondary analyses, we applied other definitions of progression such as:

1. 2022 ATS/ERS/JRS/ALAT PPF guideline criteria with (1) worsening of respiratory symptoms; (2) absolute decline in FVC ≥5% or in DLCO ≥10% and (3) disease progression on HRCT over 12 months
2. INBUILD PF-ILD criteria with (1) FVC decline ≥10%, (2) FVC decline >5%-< 10% and worsening of respiratory symptoms or an increased extent of fibrosis on HRCT, or (3) worsening of respiratory symptoms and an increased extent of fibrosis within 24 months
3. Composite criteria with decline in FVC ≥10%; or FVC ≥5%-9% and DLCO >15%.

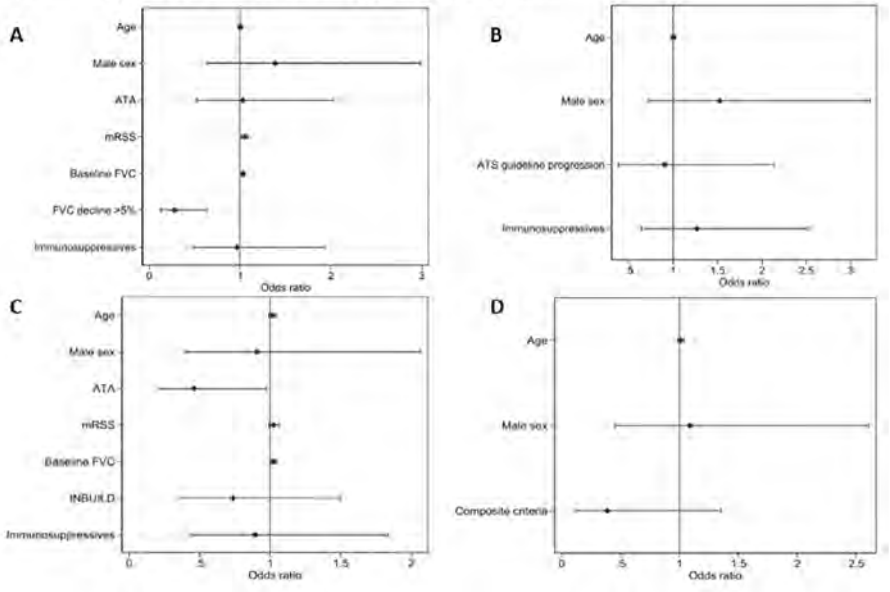
Multivariable logistic regression was applied, adjusting for known risk factors of ILD progression, including treatment.

Results: In total, 231 SSc-ILD patients were included (Table 1). At 12 months, 71 (30.7%) showed FVC decline >5% and were classified as progressors. In multivariable logistic regression ILD progression was significantly protective for further progression at the next annual follow-up (Odds Ratio 0.28, 95%CI 0.12-0.63, p=0.002, Figure1a). When other definitions of

Table1: Baseline characteristics and death of patients fulfilling different definitions for ILD progression

	FVC decline>5% N=71	PPF N=39	PF ILD N=89
Male sex, n (%)	20 (28)	11 (28)	27 (30)
Age at onset, y (SD)	49 (14.8)	49 (13.5)	48 (13.0)
Disease duration<3y, n (%)	9.4 (11.2)	7.8 (8.8)	7.9 (8.9)
dcSSc, n (%)	36 (51)	22 (56)	46 (52)
ATA, n (%)	33 (47)	20 (51)	38 (43)
CRP↑, n (%)	7 (14)	2 (9)	7 (11)
FVC, % (SD)	93 (19.6)	88 (18.9)	89 (20.4)
DLCO, % (SD)	66 (16.3)	61 (16.4)	65 (17.7)
Functional class 3&4, n (%)	9 (19)	5 (18)	11 (18)
ILD>20%, n (%)	17 (26)	15 (44)	27 (34)
Ground glass, n (%)	28 (42)	22 (59)	44 (51)
O_2 desaturation, n (%)	6 (14)	6 (30)	9 (16)
Immunosuppressives, n (%)	20 (28)	18 (46)	38 (44)
Death, n (%)	32 (45)	18 (46)	39 (44)

Figure 1: Multivariable logistic regression for ILD progression using definitions of ILD progression (A) FVC decline >5%, (B) Guideline criteria; (C) INBUILD criteria and (D) composite criteria



ATA: anti-topoisomerase I antibody; mRSS: modified Rodnan skin score; FVC: forced vital capacity

progression were applied, similar results were obtained: 39 (19%) fulfilled the PPF guideline criteria, 89 (39%) the PF-ILD criteria and 33 (14%) the composite criteria. Multivariable regression analysis adjusted for age, sex and treatment (PPF), for age and sex (composite) and for age, sex, anti-Topoisomerase I antibody (ATA), modified Rodnan skin Score (mRSS), baseline FVC and treatment (PF-ILD) showed the same direction as the primary analysis (Figure1b-d).

Conclusion: SSc-ILD progression does not predict further progression using any definition of ILD progression. These results challenge current treatment practice, since waiting for progression to initiate or escalate treatment does not seem to be the adequate strategy.

Disclosure: A. Hoffmann-Vold: Arxx Therapeutics, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Support for travel, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, 12, Support for travel, Roche, 2, 6, 12, Support for travel; **L. Petelytska**: None; **H. Fretheim**: actelion, 5, bayer, 2, Boehringer-Ingelheim, 6, GlaxoSmithKlein(GSK), 5; **T. Aaløkken**: Boehringer-Ingelheim, 6; **M. Becker**: Amgen, 6, Bayer, 6, GSK, 6, Mepha, 6, MSD, 6, Novartis, 6, Vifor, 6; **H. Jenssen Bjørkekjær**: Janssen, 5; **C. Brunborg**: None; **C. Bruni**: AbbVie/Abbott, 5, Boehringer-Ingelheim, 2, 12, Travel Support, Eli Lilly, 6; **C. Clarenbach**: AstraZeneca, 1, 6, Boehringer-Ingelheim, 1, 6, CSL Behring, 1, 6, Daiichi Sankyo, 1, GlaxoSmithKlein(-GSK), 1, 6, Grifols, 1, 6, Merck/MSD, 1, OM Pharma, 1, 6, Sanofi, 1, 6, Vifor, 1, 6; **P. Diep**: Boehringer-Ingelheim, 6, Roche, 6; **R. Dobrota**: Actelion, 5, 6, Amgen, 5, Articulum Fellowship, sponsored by Pfizer, 5, Boehringer-Ingelheim, 6; **M. Durheim**: Boehringer-Ingelheim, 2, 5, 6, Roche, 6; **M. Elhai**: AstraZeneca, 12, Travel to Congress support, Janssen, 12, Congress support; **T. Frauenfelder**: Boehringer-Ingelheim, 6; **S. Jordan**: None; **E. Langballe**: None; **O. Midtvedt**: None; **C. Mihai**: Boehringer-Ingelheim, 2, 5, 6, Janssen, 2, MED Talks Switzerland, 2, Mepha, 2, PlayToKnow AG, 2; **O. Molberg**: None; **O. Distler**: 4P-Pharma, 2, 5, 6, AbbVie, 2, 5, 6, Acceleron, 2, 5, 6, Alcimed, 2, 5, 6, Altavant Sciences, 2, 5, 6, Amgen, 2, 5, 6, AnaMar, 2, 5, 6, Arxx, 2, 5, 6, AstraZeneca, 2, 5, 6, Bayer, 2, 5, 6, Blade Therapeutics, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Citus AG, 12, Co-Founder, Corbus Pharmaceuticals, 2, 5, 6, CSL Behring, 2, 5, 6, Galapagos, 2, 5, 6, Galderma, 2, 5, 6, Glenmark, 2, 5, 6, Gossamer, 2, 5, 6, Horizon Therapeutics, 2, 5, 6, Janssen, 2, 5, 6, Kymera, 2, 5, 6, Lupin, 2, 5, 6, Medscape, 2, 5, 6, Miltenyi Biotec, 2, 5, 6, Mitsubishi Tanabe, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143), 10, Prometheus Biosciences, 2, 5, 6, Redx Pharma, 2, 5, 6, Roivant, 2, 5, 6, Topadur, 2, 5, 6.

Abstract Number: 0644

Prediction of Stable SSc-ILD Depends on Definition of ILD Progression

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Progression of interstitial lung disease (ILD) reduces long-term survival in patients with systemic sclerosis (SSc), and aggressive treatment and tight monitoring should be considered. Conversely, identifying stable SSc-ILD patients over time is important in clinical practice to avoid overtreatment and facilitate inclusion into clinical trials. The objective was to determine predictive factors for stable ILD in SSc.

Methods: We included all SSc patients who had ILD on HRCT from two expert SSc centers with well characterized SSc cohorts. Consecutive annual lung function tests including forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DLCO), and comprehensive serial clinical and imaging assessments were evaluated. Patients were defined as long-term stable ILD if no progression was observed over three years, using the following definitions for ILD progression:

(A) FVC decline ≥5% over 12 months

	All N=231	Stable ILD using		
		No FVC decline>5% N=75	No PPF N=133	No PF-ILD N=105
Male sex, n (%)	55 (24)	19 (25)	27 (20)	22 (21)
Age at onset, y (SD)	48 (14.6)	47 (13.8)	48 (15.5)	48 (15.4)
Disease duration<3y, n (%)	67 (31)	19 (28)	28 (23)	20 (21)
dcSSc, n (%)	94 (41)	24 (33)	42 (32)	31 (30)
Anti-topoisomerase I Ab, n (%)	83 (37)	24 (33)	46 (36)	34 (34)
CRP↑, n (%)	28 (18)	10 (20)	18 (26)	13 (18)
Reflux disease, n (%)	142 (63)	43 (59)	74 (58)	60 (59)
Arthritis, n (%)	18 (17)	3 (11)	6 (11)	5 (12)
Tendon friction rub, n (%)	14 (7)	1 (2)	4 (4)	3 (4)
FVC, % (SD)	89 (19.9)	83 (18.1)	90 (18.7)	89 (18.3)
DLCO, % (SD)	65 (18.7)	65 (19.5)	68 (17.0)	67 (18.0)
Functional class 3&4, n (%)	35 (19)	8 (13)	17 (17)	10 (12)
ILD>20%, n (%)	59 (27)	20 (27)	24 (19)	20 (20)
Ground glass, n (%)	89 (42)	30 (46)	36 (30)	30 (34)
O_2 desaturation at 6 min walking test, n (%)	19 (13)	5 (11)	9 (11)	8 (12)
Immunosuppressives, n (%)	109 (48)	37 (50)	52 (39)	41 (39)

Disease characteristics of stable patients not fulfilling the different definitions for ILD progression over an observation period of 3 years

Table 2: Variables predicting significantly (red) or numerically (orange) stable ILD using the competing definitions for ILD progression assessed with univariable logistic regression

	Stable ILD defined by		
	No FVC<5% decline	No PPF	No PF-ILD
Age			
Male Sex			
Disease duration			1.02 (0.99-1.05)
Anti-topoisomerase I Ab			
Anti-centromere Ab			
dcSSc	0.60 (0.33-1.08)	0.42 (0.24-0.72)	0.43 (0.25-0.74)
mRSS		0.98 (0.93-0.99)	0.98 (0.94-0.99)
Arthritis		0.39 (0.13-1.13)	
Tendon friction rub	0.17 (0.02-1.32)	0.30 (0.09-0.99)	0.35 (0.09-1.29)
Reflux disease		0.60 (0.35-0.99)	
CRP			
Lung paramteres			
FVC	0.98 (0.96-0.99)		
DLCO		1.01 (0.99-1.03)	
Lung fibrosis >20%		0.34 (0.18-0.63)	0.48 (0.26-0.90)
Ground glass		0.32 (0.18-0.58)	0.54 (0.31-0.96)
Honey combing			
Functional class >2	0.52 (0.22-1.23)		0.39 (0.17-0.87)
Six minute walking distance	1.00 (0.99-1.00)		
Desaturation at six min walking test			

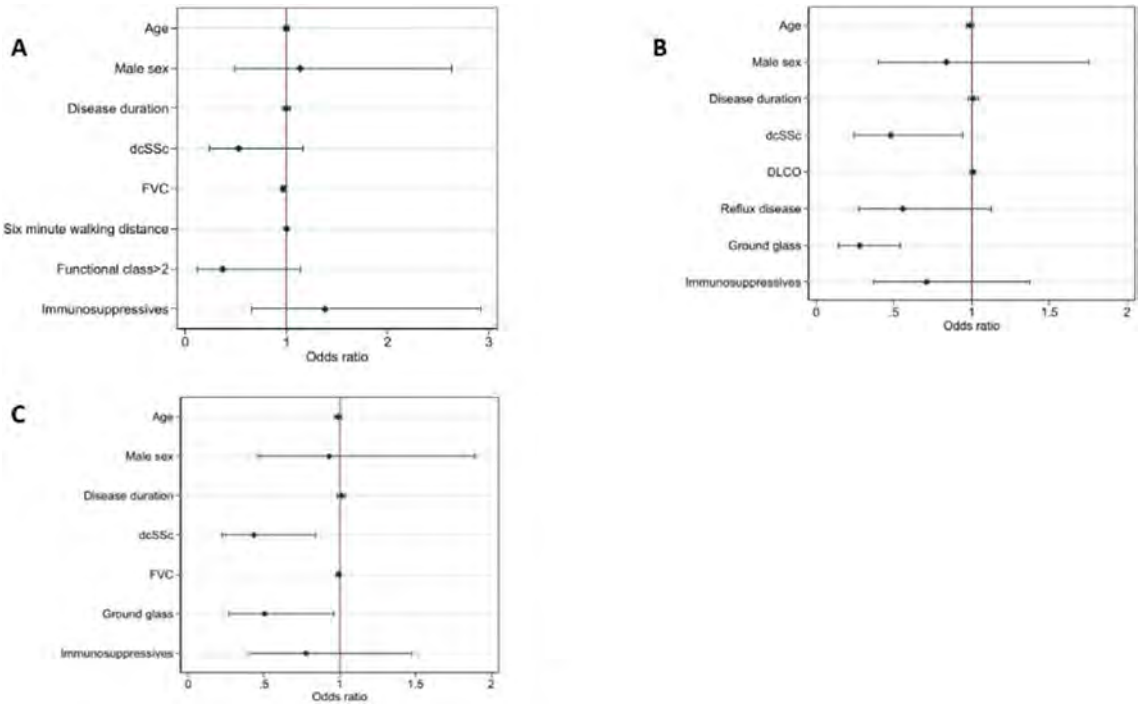

Figure 1: Variables predicting stable ILD using (A) FVC ≥5% decline, (B) PPF and (C) PF-ILD assessed with multivariable logistic regression

(B) 2022 ATS/ERS/JRS/ALAT guideline progressive pulmonary fibrosis (PPF) criteria with (1) worsening of respiratory symptoms; (2) absolute decline in FVC ≥5% or in DLCO≥10% and (3) disease progression on HRCT over 12 months

(C) INBUILD progressive fibrosing ILD (PF-ILD) criteria with (1) relative FVC decline ≥10%, (2) relative FVC decline ≥5-< 10% and worsening of respiratory symptoms or an increased extent of fibrosis on HRCT, or (3) worsening of respiratory symptoms and an increased extent of fibrosis within 24 months.

Multivariable logistic regression was applied, adjusting for known risk factors for ILD progression, including treatment, to identify predictors of stable ILD.

Results: In total, 231 SSc-ILD patients were included (Table 1). We identified 75 (32%) patients with stable ILD over mean three years defined by no FVC decline≥5%, 133 (58%) defined by no PPF guideline criteria and 105 (45%) by no INBUILD PF-ILD criteria. Factors predicting long-term stable ILD varied in univariable logistic regression depending on which definition was applied and no consistent factors could be identified (Table 2). Multivariable logistic regression models also varied based on the applied definition. Stable ILD as defined by no FVC >5% decline was predicted by lower baseline FVC (Figure 1A). Stable ILD defined by no PPF criteria and no PF-ILD criteria was significantly predicted by the absence of dcSSc and of ground glass opacities on HRCT (Figure 1B and C).

Conclusion: Long-term stable ILD in SSc occurs but varies based on which definition is applied. Prediction of stability is challenging, highlighting the necessity of comprehensive disease assessment and monitoring.

Disclosure: A. Hoffmann-Vold: Arxx Therapeutics, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Support for travel, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, 12, Support for travel, Roche, 2, 6, 12, Support for travel; **L. Petelytska**: None; **H. Fretheim**: actelion, 5, bayer, 2, Boehringer-Ingelheim, 6, GlaxoSmithKlein(GSK), 5; **T. Aaløkken**: Boehringer-Ingelheim, 6; **M. Becker**: Amgen, 6, Bayer, 6, GSK, 6, Mepha, 6, MSD, 6, Novartis, 6, Vifor, 6; **C. Brunborg**: None;

C. Bruni: AbbVie/Abbott, 5, Boehringer-Ingelheim, 2, 12, Travel Support, Eli Lilly, 6; **C. Clarenbach**: AstraZeneca, 1, 6, Boehringer-Ingelheim, 1, 6, CSL Behring, 1, 6, Daiichi Sankyo, 1, GlaxoSmithKlein(GSK), 1, 6, Grifols, 1, 6, Merck/MSD, 1, OM Pharma, 1, 6, Sanofi, 1, 6, Vifor, 1, 6; **P. Diep**: Boehringer-Ingelheim, 6, Roche, 6; **R. Dobrota**: Actelion, 5, 6, Amgen, 5, Articulum Fellowship, sponsored by Pfizer, 5, Boehringer-Ingelheim, 6; **M. Durheim**: Boehringer-Ingelheim, 2, 5, 6, Roche, 6; **M. Elhai**: AstraZeneca, 12, Travel to Congress support, Janssen, 12, Congress support; **T. Frauenfelder**: Boehringer-Ingelheim, 6; **S. Jordan**: None; **E. Langballe**: None; **C. Mihai**: Boehringer-Ingelheim, 2, 5, 6, Janssen, 2, MED Talks Switzerland, 2, Mepha, 2, PlayToKnow AG, 2; **O. Midtvedt**: None; **O. Molberg**: None; **O. Distler**: 4P-Pharma, 2, 5, 6, AbbVie, 2, 5, 6, Acceleron, 2, 5, 6, Alcimed, 2, 5, 6, Altavant Sciences, 2, 5, 6, Amgen, 2, 5, 6, AnaMar, 2, 5, 6, Arxx, 2, 5, 6, AstraZeneca, 2, 5, 6, Bayer, 2, 5, 6, Blade Therapeutics, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Citus AG, 12, Co-Founder, Corbus Pharmaceuticals, 2, 5, 6, CSL Behring, 2, 5, 6, Galapagos, 2, 5, 6, Galderma, 2, 5, 6, Glenmark, 2, 5, 6, Gossamer, 2, 5, 6, Horizon Therapeutics, 2, 5, 6, Janssen, 2, 5, 6, Kymera, 2, 5, 6, Lupin, 2, 5, 6, Medscape, 2, 5, 6, Miltenyi Biotec, 2, 5, 6, Mitsubishi Tanabe, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143), 10, Prometheus Biosciences, 2, 5, 6, Redx Pharma, 2, 5, 6, Roivant, 2, 5, 6, Topadur, 2, 5, 6.

Abstract Number: 0645

Continuous Progressive ILD in Systemic Sclerosis Is Associated with Mortality

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

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Background/Purpose: We have previously shown that short term progression of interstitial lung disease (ILD) in systemic sclerosis (SSc) is associated with mortality. However, it is less clear how multiple progressive ILD events over years affect mortality. The objective was to determine the number of progressive SSc-ILD events over three years and assess its impact on mortality.

Methods: We included all SSc patients from two expert SSc centers with well characterized SSc cohorts who had ILD on HRCT, consecutive annual lung functions including forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DLCO) and comprehensive serial clinical and imaging assessments available. ILD progressive events were observed over a follow-up period of 3 years segregated in no, 1 or >1 progressive event using:

(A) FVC ≥5% decline over 12 months

(B) 2022 ATS/ERS/JRS/ALAT guideline progressive pulmonary fibrosis (PPF) criteria with (1) worsening of respiratory symptoms; (2) absolute decline in FVC ≥5% or in DLCO ≥10% and (3) disease progression on HRCT over 12 months

(C) INBUILD progressive fibrosing ILD (PF-ILD) criteria with (1) relative FVC decline ≥10%, (2) relative FVC decline ≥5-< 10% and worsening of respiratory symptoms or an increased extent of fibrosis on HRCT, or (3) worsening of respiratory symptoms and an increased extent of fibrosis within 24 months

(D) Composite decline with FVC ≥10% decline; or FVC ≥5%-9% and DLCO ≥15% over 12 months

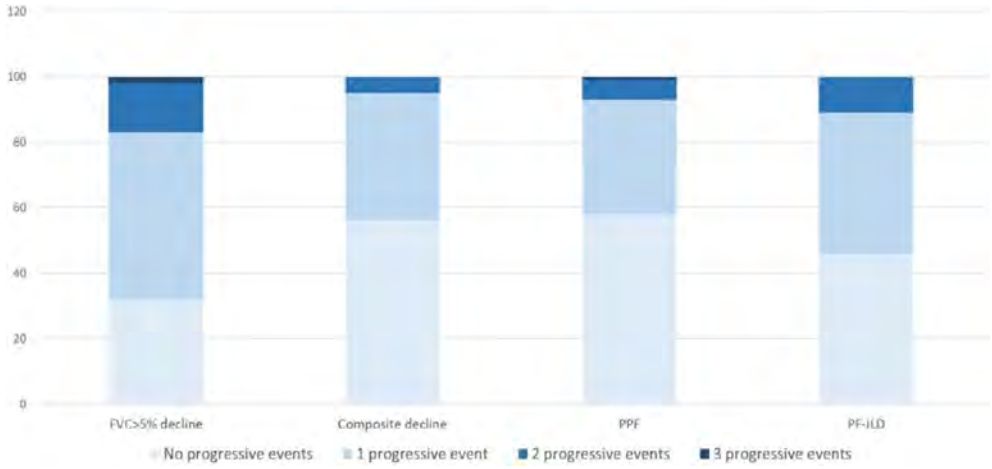

Figure 1: Prevalence of number of progressive events applying different definitions of progressive ILD

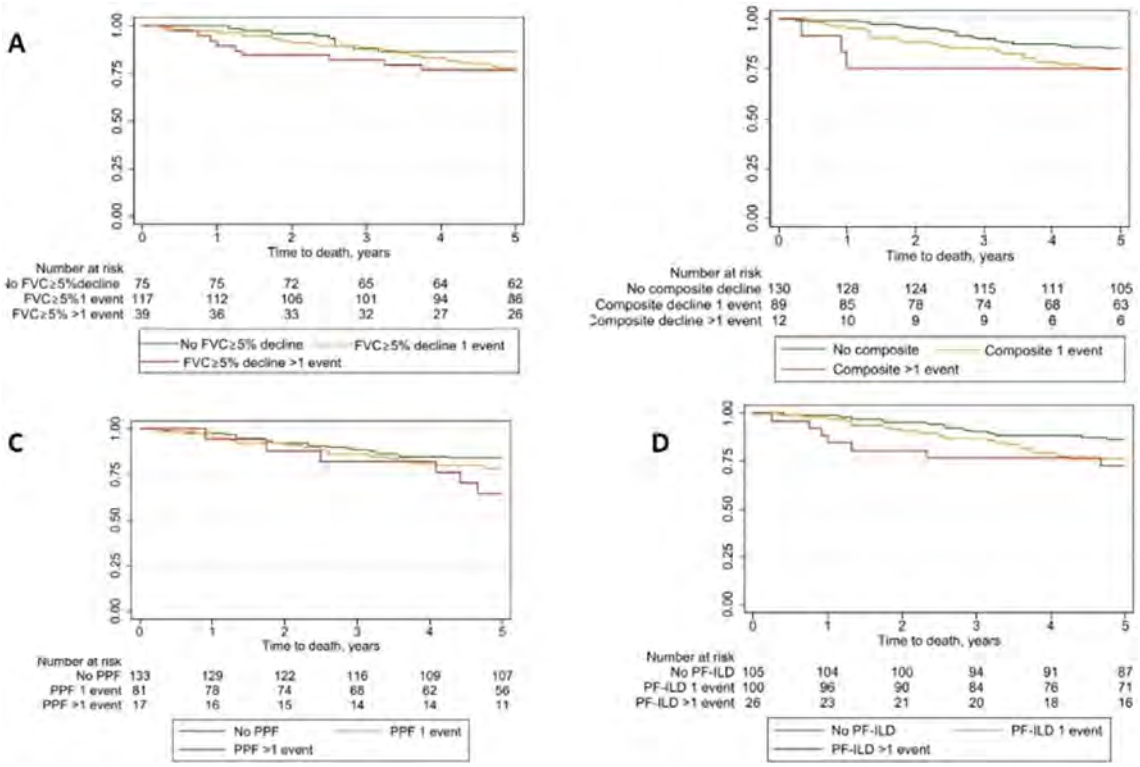

Figure 2: Survival estimates segregated by number of progressive events using FVC ≥5% decline (p=0.008); (B) composite decline (p=0.015), (C) PPF (p=0.169) and (D) PF-ILD (p<0.001)

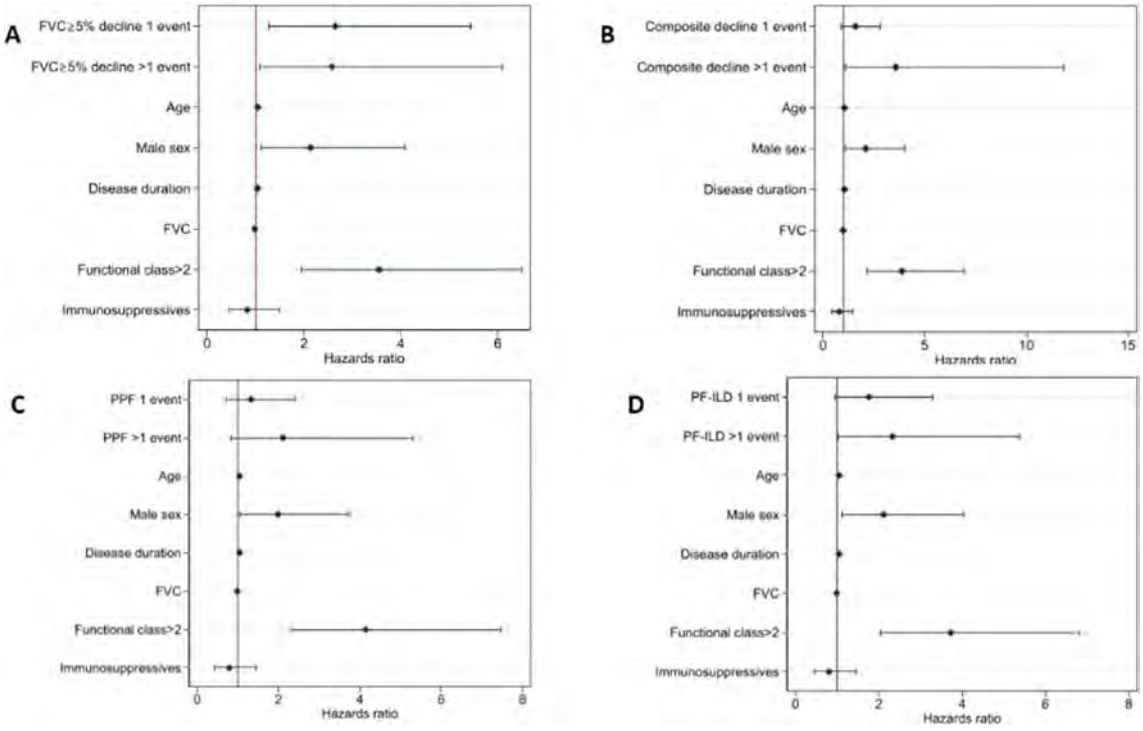

Figure 3: The impact of number of progressive ILD events using (A) FVC ≥5% decline; (B) Composite decline; (C) PPF and (D) PF-ILD on mortality compared to no even

Survival was assessed with Kaplan-Meier survival estimates. Multivariable Cox regression was applied, adjusting for known risk factors including treatment to identify the impact of multiple progressive ILD events on mortality.

Results: In total, 231 SSc-ILD patients were included. The number of progressive events varied depending on the applied definition, with FVC ≥5% decline showing >1 event over 3 years in 17%, compared to 5% using composite decline, 7% using PPF and 11% using the PF-ILD criteria (Figure 1). Over the observation period of 7.7 (SD3.9) years, 81 (35%) died. When assessing the impact of number of events on survival by Kaplan Meier estimates, we found significant difference for FVC ≥5% decline, composite decline, PF-ILD but not PPF (Figure 2).When assessing the impact of number of progressive events on mortality compared to no progression adjusted for other known risk factors, we identified that >1 events of PF-ILD and composite decline were associated with increased mortality (Figure 3).

Conclusion: ILD progression has a major impact on long-term outcome with even one event of FVC≥5% decline reducing long-term survival, but with multiple events further reducing survival. It is therefore of high importance to prevent progression in SSc-ILD to improve survival.

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Abstract Number: 0646

Racial Variability in Immune Responses Only Partially Explains Differential Systemic Sclerosis Disease Severity

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Individuals with self-identified Black race have a higher incidence of systemic sclerosis (SSc), develop SSc at a younger age, and have a more severe clinical phenotype than their White counterparts. To understand the roles autoantibodies may play in driving racial variation in disease severity, we compared autoantibody distribution and associated phenotypes between cohorts of Black and White individuals from the US multicenter Genome Research in African American Scleroderma Patients (GRASP) cohort and the Johns Hopkins Scleroderma Center cohort, respectively.

Methods: 803 Black and 2178 White patients with SSc had systematic autoantibody testing for anti-centromere (ACA), anti-RNA-polymerase III (POLR3), anti-Scl70, anti-PMSCL, anti-NOR90, anti-ThTo, anti-Ku, anti-U3RNP, and anti-Ro52 using the Euroimmun platform and anti-U1RNP using a commercial ELISA assay. 93.7% and 94.2% of individuals in the Black and White cohorts met 2013 ACR/EULAR criteria for SSc. Autoantibody frequency was compared between the two groups. To assess the effect of autoantibodies on the association between race and clinical outcomes, odds ratio coefficients for race from multivariable models including and excluding autoantibodies were compared. Multivariable logistic regression analyses were performed to assess the association between each autoantibody and clinical outcomes. Clinical outcomes included common manifestations of SSc, and organ-specific disease severity.

Figure 1: Comparison of Autoantibody Distributions between Black and White Individuals with SSc

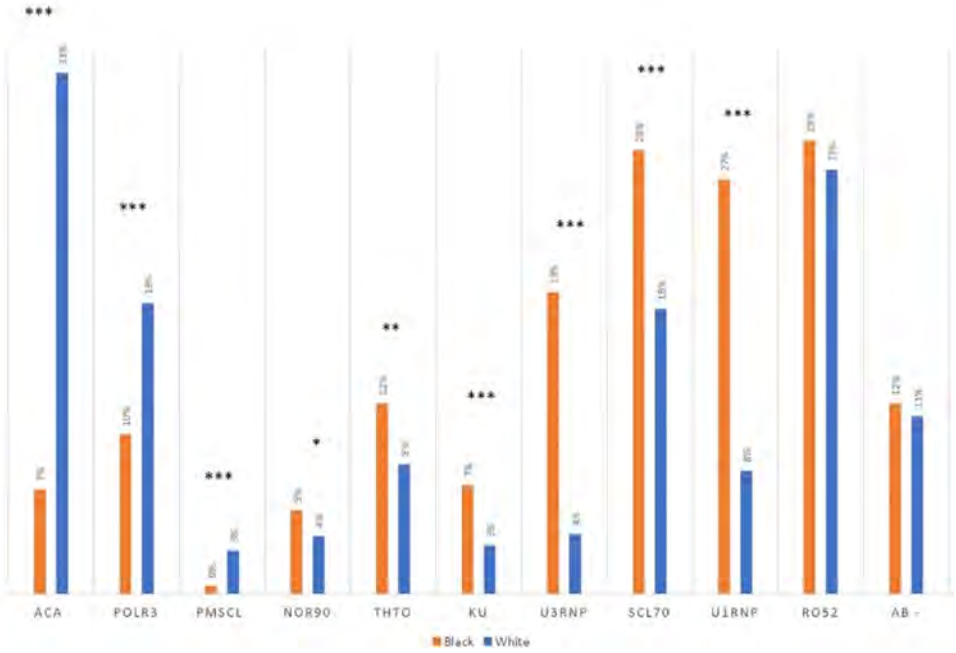

Figure 1: Distribution of autoantibodies among individuals in Black and White cohorts who underwent autoantibody testing. Numbers do not add up to 100% due to autoantibody overlap. ACA=anti-centromere antibody, POLR3=anti-RNA polymerase III, anti-Scl70=anti-topoisomerase, Ab negative refers to a group that underwent Euroimmun testing and testing for U1RNP but was not positive for any detectable antibodies. Comparison of autoantibody frequency using Chi-squared testing and Fisher's exact testing was done as appropriate. * $p<0.05$, ** $p<0.005$, *** $p<0.0005$.

Results: Comparing these self-reported racial groups, the Black cohort had a higher mean modified Rodnan skin score and higher rates of pulmonary fibrosis; Black individuals had higher rates of severe Raynaud's phenomenon, skin, gastrointestinal and lung disease. Statistically significant differences were seen in autoantibody distribution between the Black and White cohorts (Figure 1). Among the Black cohort, anti-Scl70 (28%), anti-U1RNP (27%), and anti-U3RNP (19%) were most common while the White cohort was enriched for ACA (33%) and anti-POLR3 (19%). In multivariable models, anti-Scl70 was associated with diffuse skin disease, severe cutaneous disease, pulmonary fibrosis and severe lung disease (Table 1). Anti-U3RNP was associated with diffuse skin disease, telangiectasias, calcinosis, and severe Raynaud's phenomenon. Anti-POLR3 was associated with severe skin and renal disease. Adjusting for autoantibodies decreased the effect of race on clinical outcome by 17%, 10% and 10% for FVC< 70%, severe lung and heart disease respectively; it increased the effect of race by 18% for severe skin and 44% for severe kidney disease (Table 2).

Conclusion: This study is the largest systematic analysis of autoantibody responses and associated clinical phenotypes in a geographically diverse population of Black individuals with SSc. Black and White individuals with SSc had distinct autoantibody distributions. Antibodies common in the Black cohort (anti-Scl70, anti-U1RNP, anti-U3RNP, anti-ThTo) commonly associate with severe skin disease and interstitial lung disease. However, differences in autoantibody distributions explain only a small fraction of the racial effects on clinical outcomes for FVC< 70%, severe lung and heart disease.

Table 1a and 1b: Multivariable regressions assessing association between autoantibodies and clinical outcomes were conducted. These models controlled for the covariates of sex, age of symptom onset, disease duration, race and diffuse skin disease (for non-cutaneous outcomes). Pulmonary, cardiac and vascular analyses also controlled for history of smoking. Autoantibodies included ACA, POLR3, PMSCL, Ku, ThTo, Nor90, U1RNP, U3RNP, Ro52. Statistically significant associations were seen for ACA, POLR3, U3RNP, Scl-70 and PMSCL, the data for which is included in this table. Conversely, no statistically significant associations were seen for Ku, ThTo, Nor90, U1RNP, and Ro52. Analyses in Table 1a assess the associations between autoantibodies and common clinical outcomes in SSc. Analyses in Table 1b evaluate the association between autoantibodies and organ specific disease severity as defined by a Medsger severity score of 3 or 4. * p<0.05, ** p<0.005, *** p<0.0005 † Covariate of smoking status (ever versus never smoked cigarettes was included in the multivariate analysis)

Table 1a: Association between autoantibodies and clinical outcomes in combined Black and White cohorts

	Diffuse	Telangiectasias	Calcinosis	Pulmonary Fibrosis†	FVC%<70†	Pulmonary Hypertension†	SRC
ACA	0.27 (0.17-0.42)***	1.57 (0.92-2.69)	1.38 (0.96-1.98)	0.29 (0.19-0.46)***	0.31 (0.22-0.43)***	1.08 (0.75-1.54)	0.40 (0.13-1.23)
POLR3	4.77 (3.26-6.99)***	0.80 (0.51-1.25)	1.29 (0.88-1.90)	0.86 (0.60-1.24)	0.73 (0.52-1.03)	0.94 (0.63-1.39)	3.93 (2.16-7.17)***
U3RNP	2.02 (1.37-2.99)***	2.58 (1.69-3.94)***	1.66 (1.08-2.54)*	0.47 (0.31-0.70)***	0.80 (0.44-1.16)	0.77 (0.50-1.17)	1.32 (0.62-2.81)
Scl-70	1.82 (1.36-2.44)***	1.21 (0.86-1.70)	1.47 (1.06-2.03)*	2.36 (1.68-3.32)***	1.37 (1.02-1.84)*	0.98 (0.71-1.35)	0.43 (0.19-0.97)*
PMSCL	1.04 (0.34-3.22)	2.34 (0.40-13.70)	5.60 (1.79-17.50)**	1.09 (0.37-3.19)	0.84 (0.30-2.39)	1.01 (0.27-3.81)	3.86 (0.77-19.37)

1b: Association between autoantibodies and organ specific disease severity in combined Black and White cohorts

	Skin	Raynaud's†	Lung†	Heart†	Muscle	GI	Renal
ACA	0.74 (0.46-1.22)	2.10 (1.48-2.99)***	0.57 (0.41-0.90)**	0.94 (0.64-1.38)	0.54 (0.13-2.20)	1.03 (0.65-1.65)	0.30 (0.08-1.08)
POLR3	3.88 (2.69-5.59)***	0.89 (0.60-1.30)	0.63 (0.44-0.90)*	0.67 (0.43-1.05)	0.33 (0.09-1.25)	0.44 (0.26-0.74)**	4.41 (2.16-9.01)***
U3RNP	0.93 (0.59-1.69)	1.49 (1.01-2.20)*	0.67 (0.46-0.99)	0.85 (0.50-1.44)	2.06 (0.82-5.18)	1.27 (0.79-2.06)	0.31 (0.07-1.38)
Scl-70	1.47 (1.05-2.07)*	2.29 (1.69-3.09)***	1.44 (1.07-1.93)*	0.87 (0.59-1.27)	0.53 (0.19-1.42)	0.76 (0.51-1.14)	0.48 (0.19-1.23)
PMSCL	0.39 (0.05-3.07)	0.76 (0.20-2.87)	2.19 (0.58-8.36)	0.46 (0.10-2.20)	--	0.46 (0.06-3.63)	4.10 (0.80-21.12)

Table 2: Ratio of odds: Multivariable regressions were done. Model A refers to a multivariable regression assessing association between race and clinical outcomes controlling for the covariates of sex, age of symptom onset, disease duration, and diffuse skin disease. Pulmonary, cardiac and vascular outcomes controlled for history of smoking. Model B refers to multivariable regression assessing association between race and clinical outcomes, controlling for the previous covariates, as well as the tested antibodies (ACA, POLR3, PMSCL, Ku, ThTo, Nor90, U1RNP, U3RNP Ro52). Ratio of odds refers to the ratio between the coefficient for race in Model B and the coefficient for race in Model A. Upper and lower bounds of the ratio of odds are calculated based on 5000 random samples of the data. * statistical significance

Table 2: Comparison of association between race and clinical outcomes in multivariable models with and without autoantibodies

	Model A: Black (Odds ratio)	*p value*	*Model B: Black (Odds Ratio)*	*p value*	*Ratio of odds [Model B/Model A] (95% CI)*
Clinical outcomes					
Diffuse disease	1.12	0.36	1.1	0.52	0.98 (0.85-1.12)
Calcinosis	0.53	<0.0001	0.54	<0.0001	1.02 (0.91-1.13)
Telangiectasias	0.1	<0.0001	0.09	<0.0001	0.91 (0.78-1.02)
Pulmonary fibrosis	2.64	<0.0001	2.66	<0.0001	1.01 (0.89-1.16)
FVC<70%	1.3	0.04	1.07	0.6	0.83 (0.74-0.92)*
Pulmonary hypertension	0.53	<0.0001	0.53	<0.0001	1.0 (0.90-1.09)
Renal crisis	0.64	0.1	0.82	0.50	1.29 (1.0-1.67)
Disease severity					
Skin	0.84	0.25	0.98	0.93	1.18 (1.04-1.35)*
RP	1.15	0.31	1.1	0.51	0.96 (0.86-1.06)
Lung	0.73	0.02	0.66	0.003	0.90 (0.81-1.0)*
Heart	0.52	<0.0001	0.47	<0.0001	0.90 (0.79-0.99)*
Muscle	1.04	0.92	0.79	0.59	0.76 (0.52-1.08)
GI	1	0.99	0.9	0.6	0.90 (0.79-1.04)
Kidney	0.4	0.006	0.57	0.1	1.44 (1.11-1.88)*

Disclosure: K. Kuchinad: None; **J. Kim**: None; **A. Woods**: None; **G. Leatherman**: None; **L. Gutierrez**: None; **M. Mayes**: Boehringer Ingelheim, 1, 5, British Medical Journal, 9, Corbus, 5, EICOS, 1, 5, Horizon Pharma, 5, Medtelligence, 6, Mitsubishi Tanabe, 1, 5, Oxford University Press, 9, Prometheus, 5, Springer International Publishing, 9; **R. Domsic**: Aisa Pharma, Inc., 2, CSL Behring, 1; **P. Ramos**: None; **R. Silver**: None; **J. Varga**: None; **L. Saketkoo**: None; **S. Kafaja**: Acceleron, 5, Bayer, 5, Biogen, 2, 5, Boehringer-Ingelheim, 2, Corbus Pharmaceuticals, 2, CSL Behring, 5, Cumberland Pharmaceuticals, 5, Eicos Sciences, 2, 5, Galapagos, 5, Genentech, 2, 5, GlaxoSmithKlein(GSK), 5, Horizon Pharmaceuticals, 5, Mitsubishi Tanabe, 5, Novartis, 5; **V. Shanmugam**: None; **J. Gordon**: Cumberland Pharmaceuticals, 5, Prometheus Pharmaceuticals, 5; **L. Chung**: Eicos Science, 1, 2, Eli Lilly, 1, 2, Genentech, 1, 2, IgM biosciences, 1, 2, Janssen, 1, 2, Kyverna, 1, 2, Mitsubishi Tanabe, 1, 2; **E. Bernstein**: None; **P. Gourh**: None; **F. Boin**: None; **D. Kastner**: None; **S. Zeger**: None; **L. Casciola-Rosen**: None; **F. Wigley**: None; **A. Shah**: Arena Pharmaceuticals, 5, Eicos Sciences, 5, Kadmon Corporation, 5, Medpace LLC, 5.

Abstract Number: 0647

Prevalence and Risk Factors of Left Ventricular Diastolic Dysfunction in Systemic Sclerosis: Insights from New Echocardiographic Parameters

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a rare autoimmune connective tissue disease that can affect multiple organs including the heart. Primary heart involvement in SSc refers to the presence of cardiac fibrosis, inflammation, and dysfunction in the absence of pulmonary hypertension (PH). Although PH is usually considered one of the major risk factors for death in SSc patients, diastolic dysfunction (DD) has been proposed as an independent predictor of mortality, which may

Table 1: Difference in variables between patients with left ventricle diastolic dysfunction and not. Bold indicates p-value<0.05. LVDD: left ventricle diastolic dysfunction; TAPSE: tricuspid annular plane systolic excursion, LVEF: left ventricle ejection fraction; RV: right ventricle; LA: left atrium; RA: right atrium; CVRF: cardiovascular risk factors; AGEs: advanced glycation end products; ATA: anti-topoisomerase antibodies; ACA: anticentromere antibodies; NT-proBNP: aminoterminal pro B-type natriuretic peptide.

	LVDD No	LVDD Yes	p-value
Age	56.9 (12.4)	70.1 (10.8)	**<0.001**
Body Mass Index	24.0 [20.8;27.8]	27.4 [23.3;31.5]	**0.008**
TAPSE	21.1 (2.38)	20.5 (2.23)	0.257
LVEF	64.0 [62.0;66.0]	63.0 [60.8;64.7]	0.239
LV Strain	-21.40 (3.03)	-21.06 (2.26)	0.625
RV Free Wall Strain	-26.89 (2.71)	-23.88 (3.74)	**0.039**
LA Strain	39.5 (13.3)	27.7 (9.49)	**0.001**
RA Strain	45.7 (10.6)	39.1 (13.8)	0.148
Smoker	11 (22.9%)	4 (14.8%)	0.588
Obesity	8 (16.7%)	11 (40.7%)	**0.043**
Arterial Hypertension	9 (18.8%)	15 (55.6%)	**0.003**
Diabetes	1 (2.08%)	4 (14.8%)	0.056
Number of CVRF	1.00 [0.00;2.00]	2.00 [1.00;2.00]	**0.020**
AGEs	2.59 (0.50)	3.02 (0.53)	**0.001**
ATA	8 (17.0%)	1 (3.70%)	0.144
ACA	29 (61.7%)	21 (77.8%)	0.244
NT-ProBNP	78.4 [42.9;156]	138 [73.3;310]	**0.012**

be more robust than PH. Early identification and management of heart complications in SSc patients are crucial to prevent further deterioration and improve treatment outcomes. However, myocardial damage caused by SSc is often poorly understood, and the long-term effects and prognosis remain unknown.

Our purpose is to study the prevalence and factors associated with left ventricular DD (LVDD) in a cohort of patients with SSc.

Methods: Cross-sectional study of 75 patients with SSc evaluated between Feb/2022 and Feb/2023. We classified patients as having LVDD as recommended by the 2016 American Society of Echocardiography/European Association of Cardiovascular Imaging (ASE/EACVI) guidelines. We compared the presence of factors associated with LVDD by performing first a bivariate analysis and lately a logistic regression adjusting by confounders (age, arterial hypertension (AH) and body mass index (BMI)).

Results: Of the 75 patients, 27 (36%) had LVDD and 48 (64%) had normal diastolic function. Table 1 shows compared characteristics of both groups. Older age, AH, BMI, the total number of cardiovascular risk factors (CVRF), advanced glycation end products (AGEs), NT-proBNP levels, impairment of the right ventricular (RV) free wall strain, and lower left atrial (LA) strain reservoir function were significantly associated with having LVDD (Table 1), while classical parameters of ventricular function, such as left ventricular ejection fraction or tricuspid annular plane systolic excursion were not. After adjusting for confounding factors in the logistic regression, the presence of anticentromere antibodies (ACA) conferred a risk 32 times higher (OR 32.15 95%CI [1.3;775.86], p=0.03) for presenting LVDD than having anti-topoisomerase antibodies. An increase in 1 unit of AGEs also augmented the risk of LVDD almost 5 times (OR 4.9 95%CI [1.3;18.43], p=0.018).

Conclusion: LVDD is highly prevalent in SSc, particularly in elderly patients with a higher BMI, AH and more CVRF. LVDD is associated with higher levels of NT-proBNP and findings in less classical echocardiographic parameters like the RV free wall strain impairment and lower LA strain function. ACA and higher level of AGEs were associated with a significant increased risk of LVDD after adjusting for confounders. These findings highlight the importance of regular cardiovascular monitoring in SSc patients and the potential value of using new echocardiographic parameters to identify those at risk for LVDD.

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Abstract Number: 0648

Incidence and Prevalence of Malnutrition and Its Impact on Mortality in the Multicentre Singapore Systemic Sclerosis Cohort

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Table 1. Baseline disease characteristics of SSc patients in SCORE cohort

Demographic variables	
Mean (SD) age, years	51.8 (13.6)
Female, n (%)	307 (89.0)
Race, n (%)	
Chinese	257 (74.5)
Malay	41 (11.9)
Indian	20 (5.8)
Mean disease duration*, years	6.3 (12.4)
SSc subtype, n (%)	
Diffuse	108 (31.3)
Limited	138 (40.0)
SSc-overlap	78 (22.6)
Anti-centromere positive	66 (19.1)
Anti-Scl70 positive	130 (37.7)
Mean (SD) body mass index	22.5 (4.4)
Fulfil GLIM phenotype criterion, n (%)	78 (22.6)
Fulfil GLIM etiologic criterion, n(%)	179 (51.9)
Fulfil GLIM malnourished criteria, n(%)	50 (14.5)

GLIM = Global Leadership Initiative on Malnutrition;
*disease duration from onset of first non-Raynaud's symptom or SSc diagnosis

Background/Purpose: Gastrointestinal (GI) involvement is common in patients with systemic sclerosis (SSc), and may lead to malnutrition that adversely affects quality of life, morbidity and mortality. The Global Leadership Initiative on Malnutrition (GLIM) criteria is a new criterion reported to have better sensitivity in detecting malnutrition than the Malnutrition Universal Screening Tool.

Aim: To determine 1) the incidence and prevalence of malnutrition using GLIM criteria 2) the impact of malnutrition on mortality.

Methods: From 1st of January 2008 to 31st of December 2020, patients fulfilling the SSc ACR/EULAR 2013 criteria were recruited from 3 tertiary rheumatology centres into the Systemic Sclerosis Cohort Singapore (SCORE) cohort. Baseline demographics, disease characteristics, medications and mortality were recorded. Patients with < 6 months followup were excluded from analysis. To fulfil malnutrition with GLIM criteria, at least 1 phenotypic and 1 etiologic criteria are required. For phenotypic criterion, we used BMI < 18.5 (< 70 years old) or BMI < 20 (>70 years old); for etiologic criterion, we used presence of any one of severe vasculopathy, modified Rodnan skin score > 15, pulmonary hypertension, forced vital capacity < 70%, cardiac involvement, renal crisis, total gastrointestinal tract score > 1.00. Univariate analysis using chi-square test was performed, with p-values < 0.05 considered statistically significant.

Results: Of 345 SSc patients, mean age at baseline visit was 51.8 years, with mean disease duration of 6.3 years. More patients were positive for anti-Scl70 (37.7%) than anti-centromere antibody (19.1%). Mean body mass index was 22.5 (Table 1). Prevalence of malnutrition at baseline visit was 14.5%. Cumulative incidence of malnutrition was 2% at 2 years and 6.4% across the follow-up period (median 47 months). Presence of malnutrition at baseline visit was not associated with mortality, although ever presence of malnutrition during the follow up period was associated with an increased risk of mortality [OR 4.47 (95%CI 3.67-5.26), p-value 0.0008].

Conclusion: This study highlights the burden of malnutrition in SSc patients. Among patients with malnutrition, majority fulfilled GLIM criteria for malnutrition at first visit. The persistence or development of malnutrition throughout the follow-up period was significantly associated with mortality.

References:

1. Santosa A, et al. Lung and Gastrointestinal Complications are Leading Causes of Death in SCORE, a Multi-Ethnic Singapore Systemic Sclerosis Cohort. Scand J Rheumatol 2016; 45:499-506
2. Cederholm T et al. J Cachexia Sarco Muscle 2019;10:207-217

Disclosure: B. Jiang: None; **E. Salazar**: None; **S. Saffari**: None; **G. Teng**: None; **X. Lim**: None; **S. Ng**: None; **A. Santosa**: None; **C. Hong**: None; **A. Low**: Boehringer-Ingelheim, 6, Janssen, 6.

Abstract Number: 0649

Early Systemic Sclerosis Definitions: Time to Rethink 'Early' in SSc Disease?

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a chronic autoimmune fibrotic disease with highly variable type and severity of organ involvement. Pathological changes in the skin, lungs, gastrointestinal tract, kidneys and heart determine clinical outcomes, with cardiopulmonary complications being the main cause of mortality, and musculokeletal changes and loss of hand function driving morbidity and disability. Early identification of the disease has been targeted in clinical trials in order to identify windows of opportunities for intervention, before organ damage becomes irreversible. Here we review how early SSc is defined in the literature and propose a paradigm shift in definition.

Table 1: Clinical diagnosis criteria for early SSc

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Reference	Country of origin	Summary of classification criteria
VEDOSS criteria	Europe	(1) Raynaud's phenomenon (2) puffy fingers (3) antinuclear antibodies and (4) capillaroscopy or (5) SSc-specific antibodies
ACR EULAR 2013	International (US and Europe)	Nine items including skin thickening of the fingers of both hands extending proximal to the metacarpophalangeal joints, skin thickening of the fingers, fingertip lesions, and abnormal nailfold capillaries
LeRoy and Medsger, 2001	US	• Limited SSc (lSSc) (1) Raynaud's phenomenon and (2) abnormal wide-field nailfold capillaroscopy or (3) SSc selective autoantibodies • Limited cutaneous (lcSSc): criteria for lSSc and cutaneous changes distal to the elbow, knees and clavicles • Diffuse cutaneous (dcSSc): criteria for lSSc and cutaneous involvement of the arms, chest, abdomen, back, or thighs
ARA criteria, 1980	US	• One major criterion: proximal scleroderma defined as tightening, thickening and non-pitting induration proximal to the metacarpophalangeal or metatarsophalangeal joints; • or ≥2 minor criteria: (1) sclerodactyly (2) digital pitting scars of the fingertips or loss of the substance of the distal pad (3) bilateral basilar pulmonary fibrosis
Koening et al., 2008	Canada	Raynaud's phenomenon plus either SSc marker autoantibodies and/or megacapillaries or avascular areas and no manifestation other than puffy fingers and/or arthritis

Table 2: Definitions of early SSc in the literature

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Definition	Early SSc classification criteria	Additional criteria	Number of publications
Very early SSc	VEDOSS	–	22
	Independent classification	–	1
Early SSc	ACR/EULAR 2013	–	20
		Additional clinical criteria	2
		Disease duration criteria (range 2 – 5 years)	11
	LeRoy and Medsger	–	8
		And ACR/EULAR 2013	1
		Disease duration criteria (range 0 – 3 years)	3
	ARA 1980	–	1
		And LeRoy and Medsger	1
		Additional clinical criteria	2
		Disease duration criteria (range 2 – 5 years)	13
	Koening, 2008	–	1
		And LeRoy and Medsger	5
	Independent classification	–	14

Methods: Structured, targeted searches were conducted by two reviewers in PubMed, Google Scholar, Google, and ClinicalTrials.gov in November 2021 and updated in March 2023. Search terms included 'early systemic sclerosis', 'early systemic sclerosis criteria', 'patients with early systemic sclerosis', 'opportunities in early systemic sclerosis', 'early scleroderma criteria' and 'early systemic sclerosis definition' to identify publications, treatment guidelines and clinical trial records.

Results: Published evidence defining early SSc included 103 publications, three clinical guidelines and 16 clinical trial records. Early SSc is commonly defined by one of four classification criteria (ARA, 1980; LeRoy and Medsger; Koening, 2008; or ACR/EULAR, 2013) (Table 1), often alongside a time from first non-Raynaud's symptom (Table 2). However, there was no universal consensus on what this duration should be (generally ranging from 2 to 5 years). The key finding was the significant heterogeneity in definitions used across the literature (Table 2); however, there was consensus that Raynaud's phenomenon is usually the first sign. Some publications even used their own variations of the classification criteria. The aim of each of the main definitions was to improve the early identification of patients, with studies adding additional criteria to provide further clarity and/or to aid treatment decisions to avoid early disease damage and burden.

Conclusion: There is no clear consensus on the optimal clinical classification criteria or disease onset duration that should be used to define early SSc. This is likely due to the differing rationale behind existing research. A common drive for a definition of 'early', aligned with 'potentially reversible', may be true at different times across different organs. Since the goal to treat early SSc patients is to prevent irreversible organ damage, we would suggest that early is not considered as a factor of time, but of severity of organ involvement, and would recommend a consensus statement exercise to align on an appropriate definition.

Disclosure: F. Del Galdo: AbbVie/Abbott, 5, arxx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, capella, 2, Chemomab, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Mitsubishi-Tanabe, 2, 5; **M. Woods**: None; **M. Ehlers**: Boehringer Ingelheim, 3; **S. Di Donato**: None.

Abstract Number: 0650

Understanding the Employment Landscape in People with Systemic Sclerosis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a systemic rheumatic disease that restricts participation in various life roles, including in the workplace. Our objectives were to identify the job sectors where people with SSc work, and comparatively evaluate health factors, work factors and workplace accommodations between those who are employed and not employed.

Methods: A cross-sectional survey was conducted of employed and unemployed individuals with SSc. Demographics, sector of employment, health factors, non-disease related variables, frequency of disease flares, and the need, availability and use of various workplace supports were collected.

Results: We report 140 participants (108 (77.1%) women, 32 (22.9%) men) where 110 (78.6%) were employed and 30 (21.4%) not employed. Sectors in which the participants worked were Education/Health/Sciences/Arts (n=51 (36.4%), Sales/Retail (n=23, 16.5%), Banking/Insurance/Business/Technology (n=22, 15.7%), Government (n=15, 10.7%), Construction/Utilities (n=10, 7.1%), and Manufacturing/Agriculture/Mining/ Logging (n=10, 7.1%), with no difference in employment across job sectors (p=0.69). The employed have a significantly lower mean age (48.4 versus 54.3 years), higher level of education (77.3% post-secondary education versus 22.7% without post-secondary education), and higher income (44.8% income >$100,000, 32.3% income $60,000-$100,000, 22.9% income of $10,000-$59,999). Those who had no flares had the highest employment rate (41.7%), compared to those who had 1-2 flares (35.2%) and ≥3 flares (23.1%). The *availability* of workplace accommodations differed significantly between the employed and unemployed: flexible hours (75.2% versus 41.4%, p=0.005), more rest periods (81.8% versus 46.7%, p=0.0001), special equipment (87.5% versus 50%, p< 0.0001), and alternative work-schedule flexibility (70.2% versus 38.8%, p=0.003).

Conclusion: Health factors alone do not differentiate those who are employed and not employed. This study lays the groundwork for where SSc-specific efforts in workplace policies and practices should be directed.

Disclosure: H. Jazayeri: None; **Z. Ahmad**: None; **M. Gignac**: None; **S. Johnson**: None.

Abstract Number: 0651

Abnormal Nailfold Video-capillaroscopy Is Independently Associated with non-UIP Radiographic Patterns in Autoimmune ILD: A Multicenter Study from the NEREA Registry

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SESSION INFORMATION

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Background/Purpose: The aim of this study is to describe the nailfold video-capillaroscopy (NVC) findings in patients with interstitial lung disease associated to connective tissue diseases (CTD-ILD), interstitial pneumonia with autoimmune features (IPAF) or undifferentiated autoimmune interstitial pneumonia (uAIP), and to assess the association of ILD features with abnormal NVC findings.

Methods: This is a cross-sectional study from a multicenter prospective registry (NEREA) of patients with a clinical diagnosis of ILD in the context of an autoimmune disease including CTD-ILD, IPAF or uAIP, from 10 hospitals in Madrid. All patients with available data on NVC were included. NVC studies were performed according to standardized definitions from the EULAR study group on capillaroscopy. Main outcome: abnormal NVC pattern (including systemic sclerosis [SSc] pattern and non-SSc pattern).Independent variables: radiographic patterns grouped as UIP (usual interstitial pneumonia), NSIP (non-specific interstitial pneumonia) and others. Covariates: demographics, clinical diagnosis. Statistics: For bivariate associations, Student's t-test, Mann-Whitney test or Kruskal-Wallis test were used for the analysis of continuous variables while categorical variables were analyzed with Chi-square or the Fisher test. A logistic regression multivariate model was also run (Odds ratio (OR) and 95% Confidence Interval [CI]).

Results: Seventy six patients with a mean age of 61.4 ± 13.3 years (66% women) were included (Table 1). Main clinical groups were IPAF (33 patients, 43.4%) and SSc (16 patients, 21.1%). NVC was classified as normal/minimal changes in 36 (47.4%), SSc-pattern in 19 (15%) and non-SSc pattern in 21 (27.6%) patients, respectively. Abnormal NVC was associated with younger age (p=0.016), Raynaud's phenomenon (p=0.003), and a non-UIP pattern on CT (p=0.001). There were statistically significant differences among clinical subgroups (p< 0.001), with a higher number of abnormal NVC in SSc and IIM groups. With regards to antibody status, an abnormal NVC pattern was associated with positive ANA (p=0.002) and SSc-specific antibodies (p=0.002). Although abnormal NVC was associated with Raynaud's phenomenon, in our cohort we also found abnormal NVC in 14 out of 40 patients (35%) without this manifestation. NVC features are detailed in table 2.

In the multivariate analysis, non-UIP patterns (NSIP and others), CTD and Raynaud's phenomenon were independently associated with abnormal NVC (table 3).

Conclusion: NVC may be a useful tool in the assessment of patients with autoimmune ILD. Besides the acknowledged association of NVC lesions with SSc and IIM, our findings support that performance of NVC may help identify an underlying autoimmune disease in patients with ILD and a non-UIP radiographic pattern.

Table 1. Patients characteristics. SSc=systemic sclerosis, IIM=idiopathic inflammatory myopathy, IPAF=interstitial pneumonia with autoimmune features, uAIP=undefined autoimmune interstitial pneumonia, CT=computerized tomography, UIP=usual interstitial pneumonia, NSIP=non-specific interstitial pneumonia, PFT=pulmonary function tests, FVC=forced vital capacity, DLCO= Diffusing capacity for carbon monoxide.

	All patients (n=76)	Normal/minimal changes (n=36)	Abnormal (n=40)	p
Demographic data				
Age (years), mean +/-SD	61.4±13.3	65.3±12.3	57.9±13.4	0.016
Sex (women), n (%)	50 (65.8)	24 (66.7)	26 (65)	ns
Smoking, n (%) • Active • Former • Never	 6 (8.9) 36 (47.4) 34 (44.7)	 3 (8.3) 16 (44.4) 17 (47.3)	 3 (7.5) 20 (50) 17 (42.5)	ns
BMI, mean +/-SD	26.84±4.2	27.02 ±4.3	26.7 (4.2)	ns
Disease (CTD) duration • Incident (lag time from baseline visit±12months) (n=52) • Prevalent (n=24), median [p25-75]	4.2[2.5-9.7]	4.8[2.8-9.7]	3.3 [2.5-8.8]	ns
Rheumatologic diagnosis, n (%)				
• SSc • IIM • Other CTD • IPAF • uAIP	16 (21.1) 9 (11.8) 11 (14.5) 33 (43.4) 7 (9.2)	0 (0) 2 (5.6) 8 (22.2) 21 (58.3) 5 (13.9)	16 (40) 7 (17.5) 3 (7.5) 12(30) 2(5)	<0.001
Clinical characteristics, n (%)				
Raynaud's phenomenon + (n=66)	26 (39.4)	6 (18.7)	20 (58.8)	0.003
ILD characteristics, n (%)				
CT pattern • UIP/probable UIP • NSIP • Others	 26 (34.2) 24 (31.6) 26 (34.2)	 19 (52.8) 5 (13.9) 12 (33.3)	 7 (17.5) 19 (47.5) 14 (35)	0.001
PFT at the time of NVC • FVC% • DLCO% (n=49)	 79.24± 17.43 65.63 ±21.8	 88.5±17.5 60.7±24.0	 78.2±17.4 69.8±19.1	 ns 0.1

Table 2. NVC features according to clinical diagnosis. SSc=systemic sclerosis, IIM=idiopathic inflammatory myopathy, IPAF=interstitial pneumonia with autoimmune features, uAIP=undifferentiated autoimmune interstitial pneumonia

	SSc (n=16)	IIM (n=9)	IPAF (n=33)	uAIP (n=7)	Other CTD (n=11)
NVC pattern					
- Normal/minimal changes	0	2 (22.2)	21 (63.6)	5 (71.4)	8 (72.7)
- Abnormal (SSc)	13 (81.2)	2 (22.2)	2 (6.1)	0	2 (18.2)
- Abnormal (non-SSc)	3 (18.7)	5 (55.6)	10 (30.3)	2 (28.6)	1 (9.1)
Capillary dimension					
- Normal	0	4 (44.4)	18 (56.2)	6 (85.7)	35 (47.3)
- Dilated capillaries	5 (31.2)	4 (44.4)	12 (37.5)	1 (14.3)	23 (31.1)
- Giant capillaries	11 (68.7)	1 (11.1)	2 (6.2)	0	16 (21.6)
Capillary morphology					
- Normal	4 (26.7)	2 (22.2)	17 (53.1)	3 (52.9)	6 (60)
- Abnormal shapes	11 (73.3)	7 (77.8)	15 (46.9)	4 (57.1)	4 (40)
* Tortuous shape	5 (33.3)	5 (55.5)	11 (34.4)	4 (57.1)	3 (30)
Haemorrhages	8 (53.3)	3 (33.3)	9 (26.1)	1 (14.3)	2 (20)
Capillary density					
- Normal	2 (18.7)	2 (22.2)	22 (71.9)	2 (71.4)	6 (60)
- Low density	9 (56.3)	4 (44.4)	8 (25)	2 (28.6)	2 (30)
- Avascular areas	4 (25)	3 (33.3)	1 (3.1)	0	1 (10)
Telangiectasias	4 (28.6)	0	4 (12.5)	0	0
Subpapillary plexus					
- Normal	12 (85.7)	7 (77.8)	24 (75)	5 (71.4)	10 (100)
- Prominent	2 (14.3)	2 (22.2)	8 (25)	2 (28.6)	0

Table 3. Abnormal NVC associations (multivariate analysis). CT=computerized tomography, UIP=usual interstitial pneumonia, NSIP=non-specific interstitial pneumonia, CTD=connective tissue disease, IPAF=interstitial pneumonia with autoimmune features, uAIP= undifferentiated autoimmune interstitial pneumonia, RA=rheumatoid arthritis *Other patterns= organising pneumonia, lymphocytic interstitial pneumonia, micronodular/peribronchovascular abnormalities. **CTD=connective tissue disease (systemic sclerosis, idiopathic inflammatory myopathy, mixed connective tissue disease, Sjögren's syndrome, systemic vasculitis).

Variable	OR	CI [95%]	p
Sex (female)	2.49	0.69-8.96	0.163
Age (in years)	0.99	0.94-1.04	0.694
Raynaud's phenomenon	11.85	1.87-74.86	0.009
CT pattern			
• **UIP/probable UIP**	1		
• **NSIP**	18.3	2.7-120.72	0.003
• **Other patterns***	11.22	1.7-73.8	0.012
Diagnosis (CTD vs IPAF/uAIP/RA)**	4.78	1.18-19.4	0.028

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Abstract Number: 0652

Ethnic Variations in Systemic Sclerosis Associated Interstitial Lung Disease

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a multisystem fibrosing autoimmune disease with a high mortality rate. Ethnicity can influence prevalence and disease characteristics in SSc. Less is known about SSc-associated interstitial lung disease (SSc-ILD), an important subgroup with even higher mortality rate. We investigate whether there are ethnic variations in people with SSc-ILD.

Methods: We conducted a retrospective cohort study of the Toronto Scleroderma Program – a network of academic and community clinics (1970-2023). Ethnicity was self-reported and categorized as Caucasian, Black, East-Asian, South Asian, or First Nations. We evaluated differences in demographics, disease manifestations, comorbidities, and survival in people with SSc-ILD. Kaplan-Meier survival curves were used to determine median survival and survival at 1-5, 10, 15, and 20 years. A Cox proportional hazards model estimated survival, adjusting for age, age of diagnosis, disease duration, and comorbidities.

Results: 405 people with SSc-ILD were included with n=234 (58%) Caucasian, n=57 (14%) South-Asian, n=49 (12%) East-Asian, n=28 (7%) Black, n=16 (4%) First Nation and n=22 (5%) Other. The median age at SSc diagnosis was significantly younger for First Nations ethnicity compared to Caucasian (38.4 years versus 52.0 years, $p< 0.01$). More Caucasians, South-Asians, and East-Asians had limited disease (53.2%, 51.8%, 53.1%), while more Black and First Nation had diffuse disease (57.1%, 62.5% respectively). Esophageal dysmotility was more common in Black and First Nations (96.4%, 93.8% respectively) than Caucasians, South Asians, and East Asians (88.5%, 80.7%, 71.4% respectively, p=0.01). Coronary artery disease occurred more frequently in First Nations (18.8%) than Caucasians, South Asians and East Asians (11.5%, 3.5%, 6.1%, p=0.04). East Asians had significantly better 10-year survival 93.2% (95%CI 85%, 100%) than Caucasians 78.3% (95%CI 72.1%, 85.1%). People of First Nations ethnicity appeared to have worse 10-year survival of 65.9% (95%CI 42.9%, 100%) but this was not statistically significant. In the adjusted survival analysis, age at diagnosis ($p< 0.001$) was an independent risk factor mortality, whereas ethnicity was not associated with mortality.

Conclusion: Ethnic variations in demographics, disease manifestations and comorbidities exist in SSc-ILD yet this does not result in significant differences in survival across ethnicities.

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Abstract Number: 0653

Association Between Systemic Sclerosis and Increased Risk of Ischemic Stroke: A Meta-Analysis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
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Background/Purpose: Systemic Sclerosis (SSc) is an autoimmune rheumatic disease characterized by significant vascular abnormalities due to microvascular damage and intimal proliferation in the small arterioles. Additionally, SSc has been associated with macrovascular complications, including cardiovascular disease (CVDs) and peripheral vascular disease. Cerebrovascular accident, also known as stroke, is a macrovascular condition that can occur among patients with SSc. In this study, we conducted a meta-analysis to corroborate previous studies on the risk of ischemic stroke in SSc patients.

Methods: Two investigators searched published articles on Medline database using two subject heading (MeSH) terms. Term A was "SSc OR Systemic Sclerosis OR Scleroderma OR CREST syndrome". Term B was "Stroke OR cerebrovascular accident OR cerebrovascular event". Inclusion criteria were studies describing the association between SSc and ischemic and/or hemorrhagic stroke. Statistical calculation of pooled proportions was conducted in R language. The outcome of interest was the proportion of patients with SSc that developed stroke. The heterogeneity between studies was assessed by the I2 test.

Results: Four studies (4 cohort studies) were met our criteria with 7871 patients with SSc. Our analysis demonstrated a statistically significant higher risk of ischemic stroke in patients with SSc compared with controls yielding a pooled risk estimate of 1.36 (95% CI, 1.16 to 1.61). The level of statistical heterogeneity was moderately low with an I2 of 39.9%. As shown in the respective forest plot, no significant asymmetry was observed between the included studies (Figure).

Conclusion: To our knowledge, this meta-analysis includes the largest number of SSc patients and provides robust evidence supporting an increased risk of ischemic stroke in SSc patients. These results underscore the importance of recognizing SSc as a potential risk factor for cerebrovascular complications and highlight the need for prevention and close monitoring in this patient population.

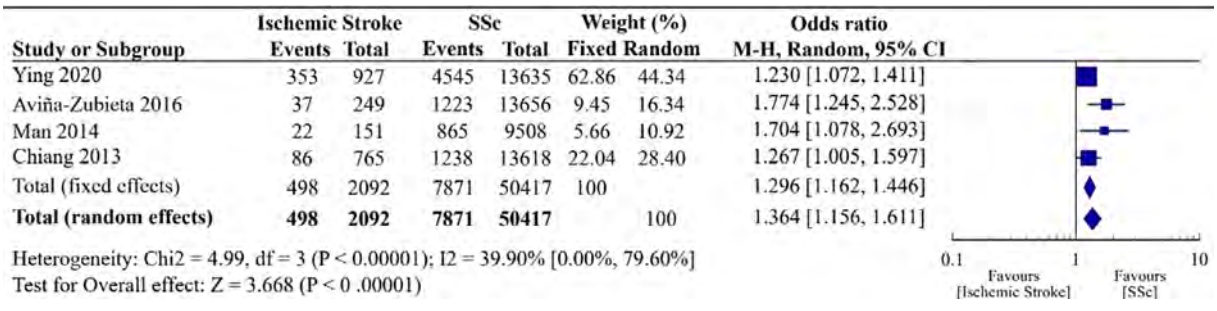

Figure: Forest plot illustrating the risk of ischemic stroke in patients with systemic sclerosis

Disclosure: C. Flourou: None; **A. Liampas**: None; **K. Parperis**: None.

Abstract Number: 0654

Comparison of Cardiovascular Risk in Patients with Systemic Sclerosis and the General Population

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Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic sclerosis (SSc) may be burdened by increased cardiovascular (CV) risk due to accelerated atherosclerosis (ATS) due to systemic inflammation, and vascular impairment. This study aimed to evaluate CV risk in SSc patients SSc compared to healthy controls (HC) and to assess its association with disease-specific features.

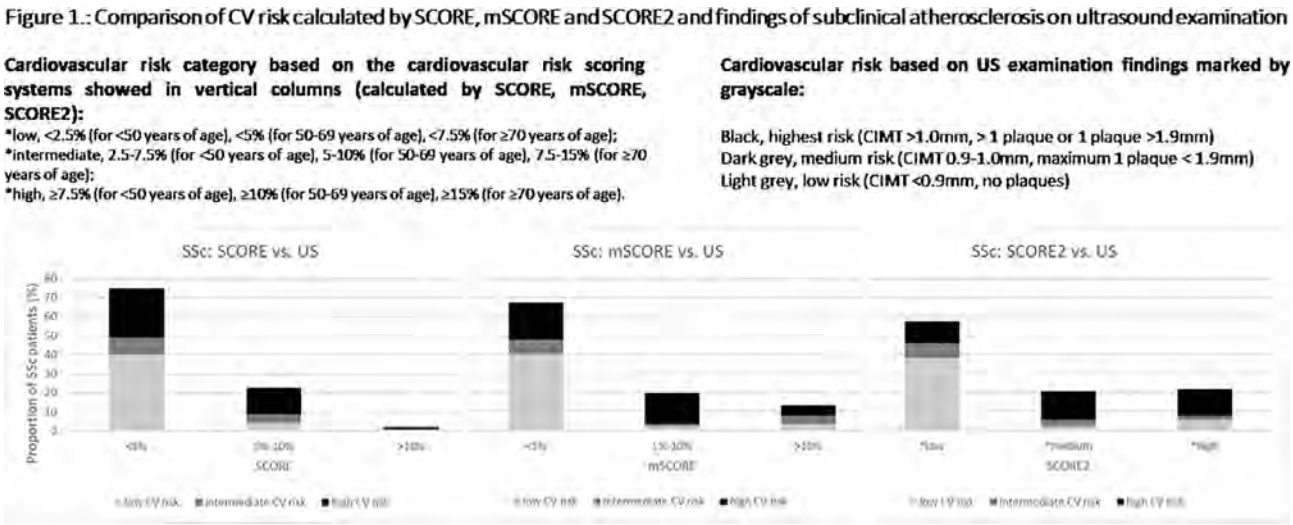

Figure 1.: Comparison of CV risk calculated by SCORE, mSCORE and SCORE2 and findings of subclinical atherosclerosis on ultrasound examination

Methods: 92 patients with SSc (81 females; mean age 52; mean disease duration 6.8 years; diffuse cutaneous (dc)SSc: n=28, limited cutaneous (lc)SSc: n=64) and 197 HC (147 females, mean age 56.7) were included, all with no history of CV disease (angina pectoris, myocardial infarction, cerebrovascular, and peripheral arterial vascular events). Comorbidities and current treatment were recorded. Disease activity and organ involvement were evaluated in SSc, including lung function tests and skin involvement (by mRSS). All participants underwent examinations of carotid intima-media thickness (CIMT), pulse wave velocity (PWV), ankle-brachial index (ABI), and body composition (by densitometry (DXA) and bioelectrical impedance analysis (BIA)). The risk of fatal CV events was evaluated by the Systematic COronary Risk Evaluation (SCORE, charts for the European population) and its modifications: SCORE multiplied by the coefficient 1.5 (mSCORE), and SCORE2.

Results: SSc patients had a trend to higher prevalence of dyslipidemia (p=0.063) and significantly more often prediabetes (p< 0.001) than HC, but a comparable prevalence of arterial hypertension, diabetes mellitus, and current smoking to HC. Nevertheless, SSc had significantly more frequent use of antihypertensive treatment compared to HC (p< 0.001), including calcium channel blockers (indicated for Raynaud's phenomenon).

The prevalence of carotid artery disease was significantly increased in SSc compared to HC. SSc had significantly more unfavorable CIMT and ABI (p< 0.05 for both). There was only a trend to lower SCORE and overall CV risk based on SCORE in SSc compared to HC, but no significant difference in SCORE2. On the contrary, the overall CV risk based on US examination showed significantly higher CV risk in SSc. A comparison of CV risk with the findings of subclinical ATS on US examination showed that none of the CV risk scoring systems in SSc was exact in estimating the CV risk (Figure 1). Nevertheless, SCORE2 underestimated the real CV risk significantly less than SCORE (p=0.043), while SCORE2 vs. mSCORE and SCORE vs. mSCORE were comparable. In SSc, the CV risk and markers of subclinical ATS were associated especially with age, HbA1c, disease duration, and mean arterial pressure (p< 0.05 for all).

Conclusion: This cross-sectional case-control study in SSc patients demonstrated a significantly increased risk of subclinical ATS in SSc compared to HC, although there was an opposite trend in CV risk estimated by calculated SCORE. The CV risk in SSc was associated especially with age, disease duration, and HbA1c levels, among others. Scoring systems underestimated the CV risk (when compared to ultrasound findings), while SCORE2 was significantly more accurate than SCORE.

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Disclosure: S. Oreska: None; **H. Storkanova**: None; **J. Kudlicka**: None; **V. Tuka**: None; **O. Mikes**: None; **Z. Krupickova**: None; **M. Satny**: None; **E. Chytilova**: None; **J. Kvasnicka**: None; **M. Spiritovic**: None; **B. Hermankova**: None; **P. Cesak**: None; **M. Rybar**: None; **K. Pavelka**: Abbvie, 2, 6, Amgen, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Egis, 2, 6, MSD, 2, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 6; **L. Senolt**: None; **R. Becvar**: Boehringer-Ingelheim, 2, GlaxoSmithKlein(GSK), 2; **J. Vencovsky**: Argenx, 2, Eli Lilly, 6, Galapagos, 2, Horizon, 2, Merck, 2; **M. Vrablik**: None; **M. Tomcik**: None.

Abstract Number: 0655

A Novel Association Between Lipodermatosclerosis and Key Vascular Outcomes in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Lipodermatosclerosis (LDS) is a progressive manifestation of chronic venous insufficiency characterized by distinctive lower extremity changes, including an "inverted champagne bottle" appearance, skin hyperpigmentation, and occasionally, non-healing ulcers. (see Figure 1) While LDS is not extensively studied in the context of connective tissue diseases, it shares similar pathogenic pathways with systemic sclerosis (SSc), where vasculopathy leads to tissue hypoxia, inflammation, and subsequent fibrosis of the skin and subcutaneous tissues. This study estimated the prevalence of LDS in SSc, examined the demographic and SSc-related characteristics of patients with LDS, and estimated the association between LDS and major vascular outcomes in patients with SSc.

Methods: We performed a retrospective cohort analysis of adult patients who had prospectively enrolled in our Autoimmune Skin Disease Registry between 2004-2023 and met ACR/EULAR 2013 classification criteria for SSc. Descriptive statistics were used to summarize data, and chi-square/Fisher's exact test and t-test/Mann-Whitney U test were employed to compare categorical and continuous variables, respectively. Logistic regression estimated prevalence odds ratios (pOR) and 95% confidence intervals of the association between LDS and a composite macrovascular outcome measure, including digital gangrene and/or renal crisis and/or pulmonary hypertension, adjusted for age and follow-up time. A. sensitivity analysis was conducted for the outcome of pulmonary hypertension (PH).

Results: Among 586 SSc patients, 4% (N=25) had LDS. Baseline demographic and disease features were similar between patients with and without LDS (Tables 1 and 2) with the exception that patients with LDS had higher frequencies of cardiac arrhythmias, heart failure, and PH. Among patients with LDS, 36% were either discharged to hospice or died during a median follow-up time of 7.5 (IQR- 3.9, 11.4) years, compared to 20.5% of patients without LDS followed for 5.6 (IQR- 1.5, 9.8) years. LDS was associated with the composite vascular outcome in adjusted analysis with pOR=2.36 [1.02-5.45], but this was primarily driven by the association with PH. Sensitivity analysis confirmed an elevated pOR between LDS and pulmonary hypertension, with an adjusted pOR of 3.20 [1.37-7.49].

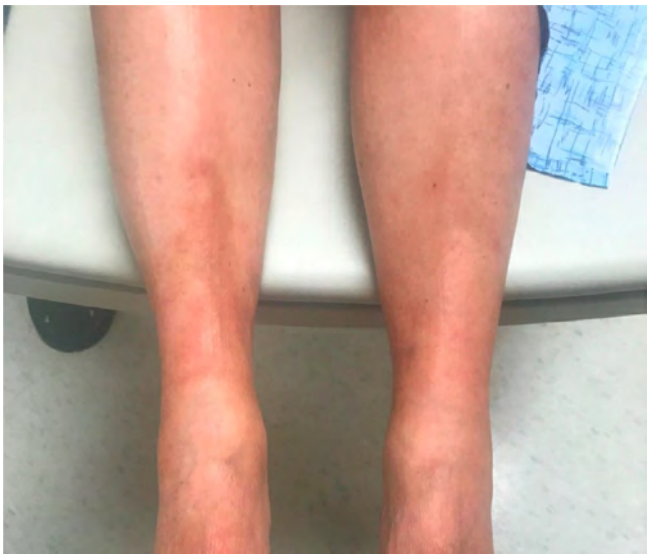


Figure 1 A 66-year-old female with SSc having lipodermatosclerosis of bilateral lower extremities

Conclusion: LDS was diagnosed in 4% of SSc patients evaluated at a multi-disciplinary Rheumatologic Dermatology Clinic. Patients with LDS have more than two-fold higher prevalence of a composite macrovascular outcome and more than three-fold higher prevalence of pulmonary hypertension. We conclude that LDS could portend severe vasculopathic manifestations in SSc, however, temporality could not be determined by our analyses. Clinicians should recognize the clinical features of LDS in SSc patients and closely monitor these patients for PH and other macrovascular complications.

Table 1- Comparison of demographic and SSc disease features between patients with and without LDS

Characteristic		SSc with LDS (N= 25)	SSc without LDS (N= 561)	p-value
Age (mean+/-SD)		52.3 (14.1)	53.5 (14.4)	0.69
Female biological sex		23 (92)	489 (87.2)	0.78
Race*	White	14 (58.3)	344 (65.4)	0.78
	Asian	5 (20.8)	95 (18.1)	
	Black	1 (4.2)	23 (4.4)	
	Others	4(16.7)	64 (12.2)	
Hispanic ethnicity*		5 (20)	66 (12.3)	0.23
Current or past smoking		9 (36.0)	187 (33.3)	0.78
Limited subtype		15 (60)	329 (58.7)	0.89
Diffuse		10 (40)	232 (41.4)	
ANA>1:80 *		22 (95.7)	474 (87.0)	0.34
Anti Scl-70*		7 (31.8)	116 (22.1)	
Anti-centromere*		6 (31.6)	171 (35.2)	
Anti RNA polymerase III*		3 (21.4)	80 (27.1)	
U1-RNP*		8 (34.8)	45 (9.5)	
Pm-Scl*		0 (0)	19 (16.8)	
SS-A*		6 (28.6)	78 (17.5)	
SS-B*		0 (0)	12 (2.8)	
Anti-cardiolipin*		4 (18.2)	66 (14.4)	
Lupus anticoagulant*		2 (10.0)	7 (1.6)	
Anti-beta glycoprotein*		2 (10.0)	37 (9.3)	
Raynaud's duration (median (IQR)) *		5.3 (1.3, 10.6)	5.4 (1.2, 14.9)	0.70
Disease duration$ (median (IQR))		4.9 (1.3, 8.4)	3.2 (1.1, 10.1)	0.64
Follow-up time (median (IQR))		7.5 (3.9, 11.4)	5.6 (1.5, 9.8)	0.05
Death or Comfort Care		9 (36.0)	115 (20.5)	0.06

Abbreviations: LDS- Lipodermatosclerosis SSc- Systemic sclerosis, ANA- anti-nuclear antibody, SD- Standard Deviation, IQR- interquartile range with 25th and 75th percentiles. $- From onset of 1st non-Raynaud's symptom.

*- Missing data: Variable (LDS count/non-LDS count): Race (1/35), Ethnicity (0/25), Raynaud's(0/25), ANA(2/16), anti-Scl-70(3/35), Anti-centromere(6/75), RNA polymerase III(11/266), U1-RNP(2/88), Pm-Scl(20/448), SS-A(4/116), SS-B(4/125), Anti-cardiolipin(3/103)), Lupus anti-coagulant(5/125), anti-beta glycoprotein(5/164)

Table 2- Comparison of the scleroderma complications among those with and without LDS.

Complication	With LDS (N=25) N (%)	Without LDS (N=561) N (%)	p-value$
Digital ulcers or digital pitting scars*	16 (64.0)	297 (53.1)	0.31
Abnormal nailfold capillaries*	18 (81.8)	405 (79.9)	1.00$$
Cutaneous telangiectasias*	23 (92.0)	430 (79.0)	0.12
Inflammatory arthritis*	15 (60.0)	301 (54.0)	0.56
Myositis*	3 (12.0)	100 (18.0)	0.60$$
Calcinosis*	10 (40.0)	193 (34.8)	0.60
Cardiac arrhythmias*	11 (45.8)	147 (26.7)	0.04
Heart failure *	7 (28.0)	57 (10.3)	0.01$$
Interstitial lung disease*	10 (40.0)	273 (49.7)	0.34
GERD*	24 (96)	529 (94.6)	1.00$$
Gastric Antral Vascular Ectasia*	1 (4.2)	36 (6.7)	1.00$$
Small Intestinal Bacterial Overgrowth*	7 (28.0)	118 (21.6)	0.45
Scleroderma renal crisis*	0 (0)	37 (6.6)	0.39$$
Pulmonary hypertension*	12 (48.0)	137(24.8)	0.009
Digital gangrene *	4 (16.0)	69 (12.7)	0.55$$

Abbreviations: LDS- Lipodermatosclerosis GERD- gastroesophageal reflux disease

$- p-value was calculated using Chi-square analysis except for $$- Fishers exact test.

*-Missing (LDS/non-LDS): Digital ulcer (0/2), Abnormal nailfold capillaries (3/54), telangiectasias (0/17), inflammatory arthritis (0/4), myositis (0/5), calcinosis (0/7), arrhythmias (1/10), heart failure (0/6), ILD (0/12), GERD (0/2), GAVE (1/21), SIBO (0/15), SRC (0/1), PAH (0/9), Digital gangrene (0/17)

Disclosure: S. Davuluri: None; **P. Kapoor**: None; **S. Nandyala**: None; **D. Fiorentino**: Acelyrin, 2, Amgen, 2, Argenyx, 2, 12, Contracted research, Biogen, 2, Bristol-Myers Squibb(BMS), 2, EMD Serono, 12, Contracted research, Gilead, 2, Janssen, 2, Merck, 2, Pfizer, 2, 12, Contracted research, UCB, 2; **J. Simard**: None; **L. Chung**: Eicos Science, 1, 2, Eli Lilly, 1, 2, Genentech, 1, 2, IgM biosciences, 1, 2, Janssen, 1, 2, Kyverna, 1, 2, Mitsubishi Tanabe, 1, 2.

Abstract Number: 0656

Concordance and Prognostic Relevance of Different Definitions of Systemic Sclerosis Interstitial Lung Disease Progression

enrico De Lorenzis[1], Francesco Del Galdo[2], gerlando Natalello[1], Stefano Di Donato[2], lucrezia verardi[1], Vishal Kakkar[2], pier giacomo Cerasuolo[1], Francesco Varone[3], Luca Richeldi[3], Maria Antonietta D'Agostino[1] and Silvia Bosello[1], [1]Division of Rheumatology - Catholic University of the Sacred Heart, Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy, [2]University of Leeds - Leeds Institute of Rheumatic and Muskuloskeletal Medicine, Leeds, United Kingdom, [3]Division of Pulmonology - Catholic University of the Sacred Heart, Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy

SESSION INFORMATION

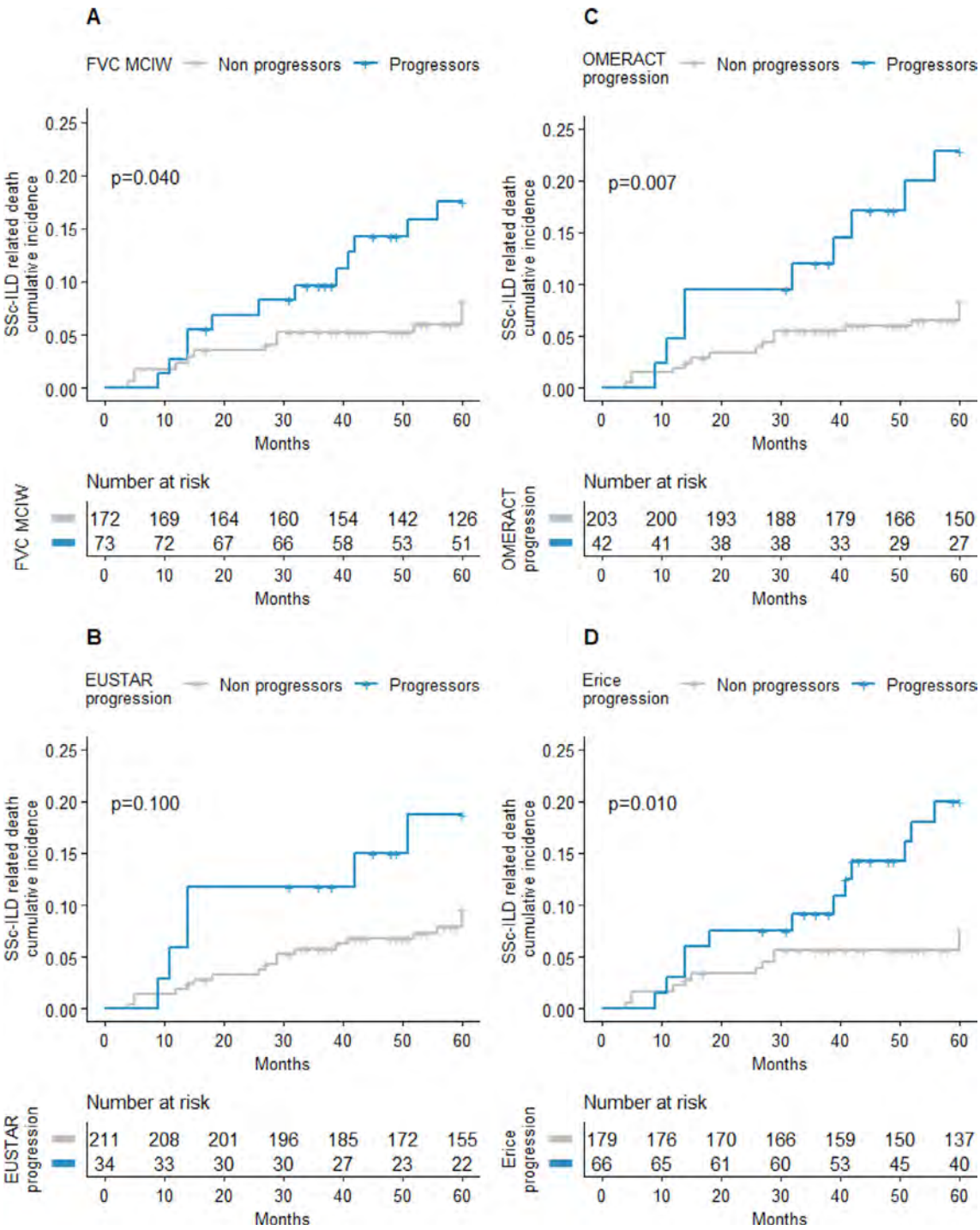
Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial Lung Disease (ILD) in systemic sclerosis (SSc) is a common complication that has varied progression rate and prognosis. Different progression definitions include minimal clinically important worsening of forced vital capacity (FVC MCIW), EUropean Scleroderma Trials and Research group (EUSTAR) progression, Outcome Measures



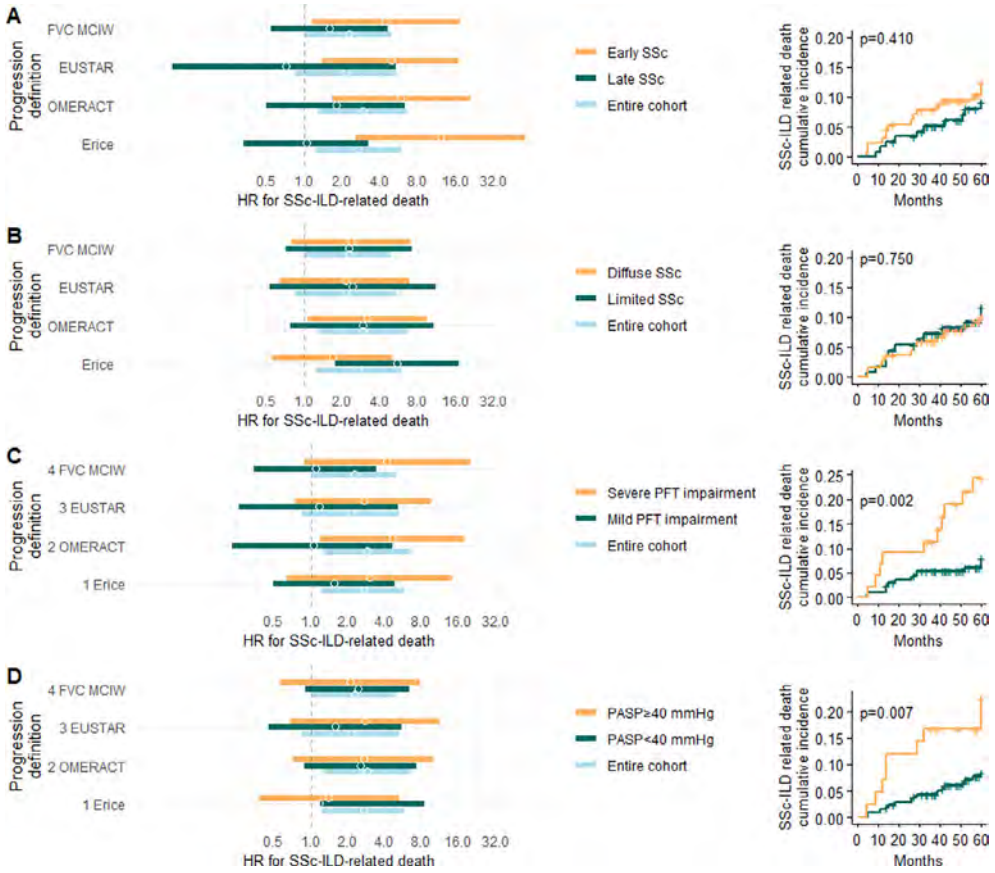
Comparisons of SSc-ILD survival of progressors and non-progressors according to different definitions. Four main definitions are compared: A) FVC MCIW, B) OMERACT definition, C) EUSTAR definition D) Erice definition. Abbreviations: EUSTAR EUropean Scleroderma Trials and Research group; FVC MCIW minimal clinical important worsening of forced vital capacity, OMERACT Outcome Measures in Rheumatology Clinical Trials, SSc-ILD scleroderma-related interstitial lung disease.

in Rheumatology Clinical Trials (OMERACT) progression, and INBUILD/ Erice ILD working group progression. The aim of the study was to assess the concordance and prognostic value of these different definitions in SSc-ILD patients overall and specific clinical subsets.

Methods: Progression status in consecutive SSc-ILD patients was assessed over 24 months, comparing SSc-ILD-related mortality between progressors and non-progressors according to different definitions over the following 60 months. The prediction performances of different progression definitions were investigated with Cox Regression analysis and compared using Akaike information criterion (AIC) with a difference greater than 2 considered as evidence in favor of the model with the smaller AIC.

Results: The 245 SSc-ILD patients enrolled had a mean age of 54.6± 3.2 years and a median disease duration of 4 (IQR 2-8) years from the first non-Raynaud symptoms. Among these patients, 18.8% were males, and 54.7% had the diffuse LeRoy cutaneous variant, 59.2% had anti-Scl70 positivity, and 14.3% anti-centromere antibody positivity.

Twenty-six deaths were reported, and mortality was linked to progression per FVC MCIW (HR 2.27, 95% CI 1.03 - 4.97, p=0.041), OMERACT (HR 2.90, 95% CI 1.28 - 6.57, p=0.011), and INBUILD/Erice trial definitions (HR 11.02, 95% CI 2.38 - 51.08, p=0.002). Prognostic prediction using these four definitions was challenging in patients with longer disease duration, mild pulmonary function impairment, and pulmonary artery systolic pressure (PASP)≥40 mmHg. Erice criteria were



Risk of SSc-ILD-related death in progressor patients across key clinical subsets The patients were divided according to A) disease duration, B) LeRoy cutaneous variant, C) severity of baseline functional lung impairment and D) PASP values on echocardiography. The average risks of the whole population are also reported as comparators. The corresponding survival curves of the considered subgroup are displayed and compared on the right. Abbreviations: EUSTAR EUropean Scleroderma Trials and Research group; FVC MCIW minimal clinical important worsening of forced vital capacity, HR hazard ratio, OMERACT Outcome Measures in Rheumatology Clinical Trials, PASP pulmonary artery systolic pressure, PFT pulmonary function test, SSc-ILD scleroderma-related interstitial lung disease.

superior in patients with disease duration >3 years, limited cutaneous variant, and PASP< 40 mmHg (ΔAIC >2). OMERACT criteria performed better in diffuse cutaneous variant patients with severe baseline functional impairment (ΔAIC >2).

Conclusion: The proposed SSc-ILD progression definitions are not interchangeable, risking potential misdiagnosis in up to a third of progressors. Regardless of criteria, progressors frequently showed diffuse skin disease variant, shorter disease duration, and worse functional impairment.

Disclosure: e. De Lorenzis: None; **F. Del Galdo**: AbbVie/Abbott, 5, arxx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, capella, 2, Chemomab, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Mitsubishi-Tanabe, 2, 5; **g. Natalello**: None; **S. Di Donato**: None; **I. verardi**: None; **V. Kakkar**: None; **p. Cerasuolo**: None; **F. Varone**: None; **L. Richeldi**: None; **M. D'Agostino**: AbbVie/Abbott, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **S. Bosello**: None.

Abstract Number: 0657

The Value of the Six-Minute Walk Test in Detecting Cardiopulmonary Involvement in Patients with Systemic Sclerosis

Saad Ahmed, Sophie Liem, Jeska de Vries-Bouwstra and Thomas Huizinga, Leiden University Medical Center, Leiden, Netherlands

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiopulmonary involvement (CPI) in systemic sclerosis (SSc) is associated with significant morbidity and mortality. Early detection and timely treatment is warranted. The Six-minute walk test (6-MWT) is a non-invasive exercise test that evaluates the distance a patient can walk in 6 minutes (6-MWD), pre- and post-test heart rate and oxygen saturation. There is ongoing debate about the sensitivity and specificity of the 6-MWT as a screening tool for CPI in SSc. Therefore, this study aimed to assess the course of the 6-MWT parameters over time, its main determinants and the diagnostic value to detect new onset CPI in a large cohort of SSc patients.

Table 1: Disease characteristics impacting the 6MWT at baseline.

	6-MWD				Desaturation at 6 minutes		
	Univariable β (95% CI)	Adjusted for BMI, sex and age β (95% CI)	Multivariable model β (95% CI)	VIF	Univariable OR [95% CI]	Adjusted for BMI, sex and age OR [95% CI]	Multivariable model OR [95% CI]
CPI	-47,5 [-68,5, -26,6]	-40 [-59, -21]	-25,8 [-46,1, -5,5]	1,08	6,5 [3,8, 10,9]	5,8 [3,4, 9,9]	6,7 [3,6, 12,4]
DcSSc	-36,3 [-61.8, -10.8]	-61 [-84,5, -37,8]	-39,7 [-64,7, -14,8]	1,15	1,6 [0,9, 2,7]	1,5 [0.8, 2,6]	1,3 [0,7, 2,4]
Myositis	-52,2 [-134,5, 30]	-67,7 [-142,2, 6,7]	-42 [-114,2, 30,2]	1,05	1,6 [0,3, 7,7]	1,1 [0,2, 5,7]	1 [0,2, 5,7]
Renal crisis	-78,1 [-145,4, -10,8]	-81,5 [-141,6, -21]	-62,9 [-123,9, -2]	1,04	0,5 [0,06, 3,7]	0,4 [0,05, 3,4]	0,5 [0,06, 4]
Arthritis	-56 [-86.7, -25.2]	-55,9 [-84,2, -27]	-47,8 [-76,1, -19,5]	1,01	0,7 [0,3, 1,6]	0,7 [0,3, 1,6]	0,6 [0,3, 1,5]
Hemoglobin	36,1 [24,6, 47,6]	30,8 [19,6, 42]	19,6 [7,6, 31,6]	1,19	1,2 [0,9, 1,6]	1,2 [0,9, 1,6]	1,4 [0,99, 2]

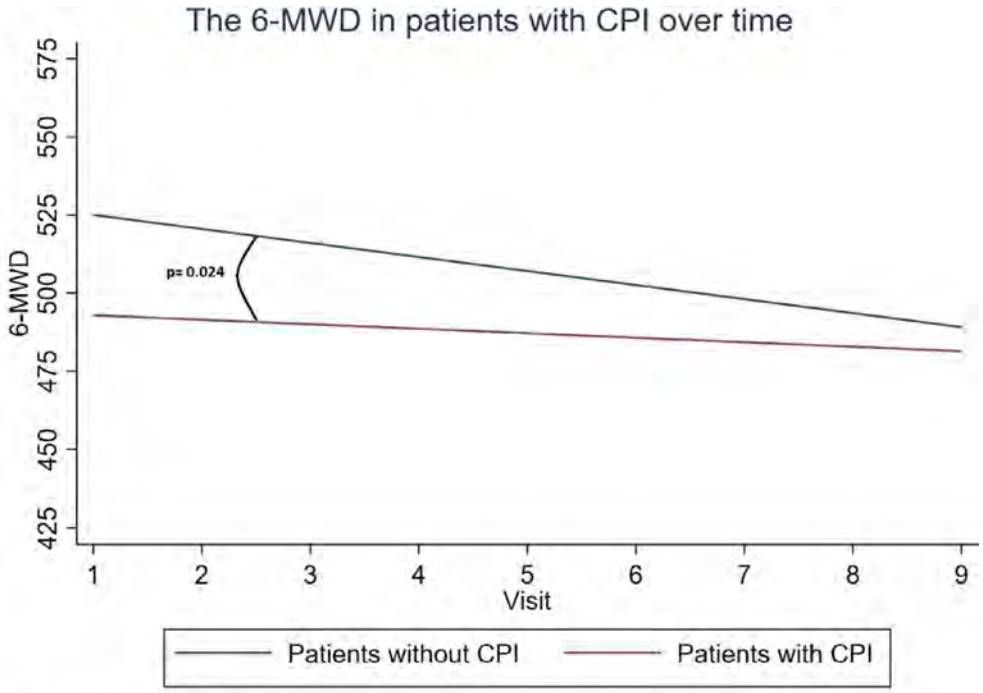
6-MWD: Six-minute walk distance; **CPI:** Cardiopulmonary involvement; **DcSSc:** Diffuse cutaneous systemic sclerosis.

Example: Presence of CPI results in an Odds ratio of 6.5, when correcting for Age, sex and BMI this becomes 5.8, when taking into account the other disease characteristics we find an odds ratio of 6.7. This is also statistically significant and informs us that patients with CPI have higher odds at having a desaturation after the test than patients without, corrected for BMI, sex, age, hemoglobin level and the presence of DcSSc, myositis, renal crisis, arthritis.

Methods: All SSc-patients from the Leiden Combined Care in SSc (CCISS)-cohort, who fulfilled ACR/EULAR 2013 criteria and performed ≥1 6-MWT, were included. CPI included presence of interstitial lung disease (ILD), pulmonary arterial hypertension (PAH) and/or myocardial involvement. Differences in 6-MWT parameters were assessed cross-sectionally at baseline between patients with and without CPI using multivariable linear regression. Course of 6-MWT parameters over time and its main associates were assessed using linear mixed models. Sensitivity and specificity of a decline in 6-MWD distance using a decline of ≥ 33 as cut-off to detect newly developed CPI was determined.

Results: 685 patients were included, with median follow-up duration of 5.4 years and in total 2769 6MWTs available (median 6 [IQR 4-8] 6MWTs per patient). 267 (39%) patients had CPI at baseline, 75 (11%) patients developed CPI during follow-up, 343 (50%) patients did not develop CPI at all. At baseline, 6 Minute walking distance (6-MWD) was significantly associated with sex, age, BMI, CPI, diffuse skin involvement, hemoglobin level, renal crisis and arthritis (see table 1). Patients with CPI also were more likely to develop a desaturation at 6 minutes (OR [95% CI]: 6,7 [3,6, 12,4]) at baseline (see table 1). Over time, CPI was independently associated with a lower 6-MWD (β [95% CI]: 27 [-42, -12]) and a higher occurrence of desaturation at 6 minutes (OR [95% CI]: 8.9 [1.1, 13]). Strikingly, over time, patients without CPI experienced a steeper decline in their 6-MWD in comparison to patients with CPI (See figure 1). A decline in 6-MWD did not accurately identify patients with new CPI (sensitivity 22%, specificity 80%).

Conclusion: This study shows that functional capability of SSc patients as evaluated by 6-MWT is importantly and strongly impacted by cardiopulmonary involvement at baseline and over time. Patients without CPI experienced a faster decline of the 6-WMD, which may be due to a survivor bias. Unfortunately change in 6-MWT parameters over time are not sensitive nor specific enough to identify SSc patients at risk for newly developed CPI. Based on these observations we conclude that



Dropout rates and death rates by presence of CPI

Visit		1	2	3	4	5	6	7	8	9
No CPI	Patients (N)	343	263	203	147	112	87	60	39	22
	Dropout (N)	31	20	13	4	1	2	1	0	0
	Death (N)	7	3	1	0	0	0	0	0	0
CPI	Patients (N)	342	274	225	178	137	115	86	59	41
	Dropout (N)	40	21	16	16	3	5	4	2	3
	Death (N)	22	11	11	10	3	2	3	1	2

we can apply 6-MWT to capture a general idea of functional capability of SSc patients but that for diagnostic screening of new CPI this test should be used in combination with other tests like PFT and laboratory testing.

Disclosure: S. Ahmed: Janssen, 5; **S. Liem**: None; **J. de Vries-Bouwstra**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, galapagos, 5, Janssen, 2, 6, Janssen-Cilag, 5, Roche, 5; **T. Huizinga**: None.

Abstract Number: 0658

Evaluating the Associations Between Autonomic Dysfunction, Clinical Phenotype and Gastrointestinal Transit in Patients with Systemic Sclerosis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

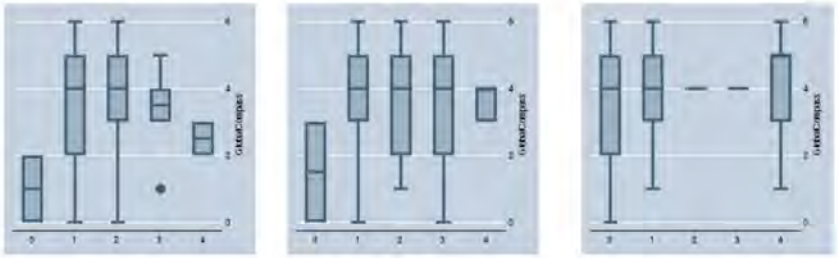
Background/Purpose: The gastrointestinal (GI) tract is the second most commonly impacted organ in systemic sclerosis (SSc). However, the pathogenesis and clinical expression of GI involvement in SSc are heterogeneous. Although it is well-established that a subset of patients with SSc have co-existing dysautonomia, the type(s) of GI dysmotility seen among these patients, and the clinical and serologic features that distinguish such patients from the rest of the SSc population are unknown. Therefore, we sought to determine whether patients with SSc have a high burden of autonomic symptoms, a distinct clinical and serologic phenotype, and specific GI transit abnormalities.

Methods: Patients were part of a prospectively enrolled cohort of SSc patients with GI disease who were evaluated at the Johns Hopkins Scleroderma Center, and demographic and clinical data for all study participants were obtained every 6 months at routine clinic visits. Autonomic symptoms were identified using the maximum obtained values of the validated Composite Autonomic Symptom Score (COMPASS)-31 questionnaire. GI transit was measured by Whole-gut transit (WGT) scintigraphy, which captures the percent emptying of the esophagus, stomach, small bowel, and colon at defined time points. The presence and severity of organ involvement were assessed using the maximum Medsger severity scores. We then sought to define the clinical and demographic features associated with significant dysautonomia in SSc. Clinical and demographic variables were compared between patients with global autonomic dysfunction [(GAD); ≥5 positive

Table 1. Total scores of each 6 subdomains of the COMPASS-31 questionnaire in our GAP cohort.

COMPASS-31 Subdomain	SSc GAP cohort, mean score (SD)
Orthostatic	3.6 (2.4)
Vasomotor	3.5 (1.6)
Secretomotor	3.2 (1.8)
Gastrointestinal	9.7 (4.1)
Urinary	1.1 (1.4)
Pupillomotor	6.1 (3.6)
Total COMPASS-31	36.7 (14.2)

*Medsger GI 0: Normal. 1: GERD Meds or abnormal small bowel series. 2: High-dose GERD meds or antibiotics for bacterial overgrowth. 3: Malabsorption syndrome or episodes of pseudo-obstruction. 4: Total parental nutrition required. *Medsger RP 0 No RP.1: RP with/without vasodilator required. 2: Digital pitting scars. 3: Digital tip ulcerations. 4: Digital gangrene. *Medsger muscle 0: Full strength. 1: Power 4/5 in upper extremities (UE) or lower extremities (LE). 2 Power 3/5 in UE or LE.3 Power <3/5 in UE or LE.4 Requires ambulation aids.



Medsger GI Medsger RP Medsger muscle

Figure 1. Evaluation of associations between Medsger severity scores and global COMPASS-31 scores.

Table 2. Demographic and clinical characteristics between patients with global and limited autonomic dysfunction.

*Global autonomic dysfunction (GAD): patients with ≥ 5 positive subdomains (positive subdomain score >0) and limited autonomic dysfunction (LAD): patients with <5 positive subdomains.

Demographic and disease characteristics	COMPASS-31 GAD n = 27	COMPASS-31 LAD n = 61	p value
Age, yrs, mean (SD)	55 (12)	57 (13)	0.555
Sex, n (%)			
Female	27 (100)	52 (85)	*0.052*
Race, n (%)			
White	23 (85)	50 (82)	1.000
African American	4 (15)	11 (18)	
Ever smoker	30 (7/23)	35 (17/49)	0.794
Disease duration, yrs			
From any 1st symptom, median (IQR)	13 (6, 20)	11 (7, 22)	0.992
SSc type, n (%)			
Limited	22 (85)	40 (68)	0.122
Antibodies n (%)			
Topoisomerase I	1 (6)	7 (17)	0.417
Centromere	8 (47)	20 (48)	1.000
RNA polymerase III	1 (6)	1 (2)	0.497
ThTo	0 (0)	0 (0)	n/a
U3 RNP	0 (0)	1 (2)	1.000
Ku	0 (0)	1 (2)	1.000
PMSCI	1 (6)	3 (7)	1.000
Clinical features			
Modified Rodnan skin score, median (IQR)	4 (1, 6)	4 (2, 12)	0.120
Significant GI disease, n (%) (Medsger score ≥2)	24 (89)	48 (83)	0.538
Significant cardiac disease, n (%) (Medsger score ≥2)	0 (0)	12 (26)	**0.014**
Significant lung disease, n (%) (Medsger score ≥2)	7 (37)	27 (63)	*0.058*
Significant Raynaud's phenomenon (Medsger score ≥2)	11 (41)	23 (40)	1.000
Significant Muscle weakness (Medsger score ≥2)	11 (44)	15 (27)	0.139
Myopathy	6 (22)	11 (19)	0.755
Arthralgia	25 (93)	50 (91)	1.000
Sicca	27 (100)	48 (83)	**0.027**

COMPASS-31 subdomains] and those with limited autonomic dysfunction [(LAD); < 5 positive subdomains] as previously defined. Differences in GI transit in across different regions of the gut were also compared between the GAD and LAD groups.

Results: The study included 99 patients with SSc and GI involvement. The mean age was 58 years (IQR 49-67), 90% were female, 74% had limited cutaneous disease, and 49% had anticentromere proteins antibodies. 83% had significant GI disease (Medsger score ≥2), and 88% had Sicca syndrome. The mean COMPASS-31 score across the cohort was 36.7 ± 14.2 (SD), which was higher overall than COMPASS-31 scores in another SSc cohort and healthy control cohorts in the published literature. We found that 31% of patients had GAD, and 69% had LAD. Patients with GAD were significantly more likely to have Sicca symptoms (100% vs. 83%; p=0.027) and less likely to have severe heart disease (0% vs. 23%; p=0.014). Patients with more severe upper GI involvement (Medsger scores 1 or 2) had higher autonomic symptom scores. All patients with Raynaud´s phenomenon (RP) and patients with severe myopathy were more likely to have higher autonomic symptoms. Patients with GAD had a higher percentage of gastric emptying of solids at 4 hours than LAD patients (97% vs 94%, respectively, p =0.023).

Conclusion: Global dysautonomia is common among patients with SSc and GI dysmotility and associated with a distinct clinical features. Identifying these clinical characteristics may help support patient risk stratification and aid in choosing the right patient population who may benefit from the evolving array of autonomic nervous system modulating therapies.

Disclosure: M. Alvarez Hernandez: None; **B. Adler**: None; **J. Perin**: None; **M. Hughes**: Certa, 1, Eli Lilly, 6, Janssen, 5, 6, Pfizer, 6; **Z. McMahan**: Boehringer-Ingelheim, 12, medical writing support for a different manuscript.

Abstract Number: 0659

Cigarette Exposure in Systemic Sclerosis: Impact on Autoantibody Expression and Disease Manifestations: Analysis of the EUSTAR Cohort

Jacopo Ciaffi[1], Sophie Liem[2], Saad Ahmed[2], Eva Hoekstra[2], Piotr Wiland[3], Tatsuya Atsuma[4], Gabriella Szucs[5], Alexandra Balbir-Gurman[6], Laszlo Czirjak[7], Elisabetta Zanatta[8], Ina Koetter[9], Joerg Henes[10], marco Matucci Cerinic[11], Paolo Airò[12], Francesco Ursini[13], Thomas Huizinga[2] and Jeska de Vries-Bouwstra[2], [1]IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy, [2]Leiden University Medical Center, Leiden, Netherlands, [3]Wroclaw University of Medicine, Wroclaw, Poland, [4]Hokkaido University, Department of Rheumatology, Endocrinology and Nephrology, Sapporo, Japan, [5]University of Debrecen, Department of Rheumatology, Debrecen, Hungary, [6]Rheumatology Institute, Rambam Health Care Campus and Rappaport Faculty of |Medicine, Technion, Haifa, Israel, [7]Dept. Rheumatol Immunol, Medical School, university of Pecs, Pecs, Hungary, [8]Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Padova, Padua, Italy, [9]University Hospital Eppendorf, Prisdorf, Germany, [10]University Hospital Tuebingen, Tuebingen, Germany, [11]Unit of Immunology, Rheumatology, Allergy and Rare diseases, IRCCS San Raffaele Hospital, Milan, Milan, Italy, [12]Spedali Civili di Brescia, Scleroderma UNIT, UOC Reumatologia ed Immunologia Clinica, Piazzale Spedali Civili 1, 25123, Brescia, Italy, [13]IRCCS Istituto Ortopedico Rizzoli, Bologna, Netherlands

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In rheumatoid arthritis, cigarette smoking confers a risk for anti-CCP positive disease and the risk further increases in smokers carrying specific HLA DRB1-variants. These observations have fuelled the hypothesis that, in susceptible individuals, chronic exposure to specific antigens, (for example in the lungs) can trigger a targeted chronic autoimmune response. With this in mind, the lower frequency of anti-topoisomerase antibodies (ATA) observed among never-

smokers in systemic sclerosis (SSc) is intriguing. We evaluated in the EUSTAR database the effect of smoking on ATA expression, both for the total cohort and also for males and females separately. We evaluated how sex, smoking and ATA/anticentromere (ACA) expression interact and impact on disease progression.

Methods: All SSc patients with complete information about smoking status available were included and categorised as "never-smokers" or "ever-smokers". Chi-square test and logistic regression were used to evaluate differences in ATA and ACA expression between ever-smokers and never-smokers. A possible dose-response effect was evaluated using logistic regression with pack/years or smoking duration as predictors. We evaluated the association between disease progression,

Table 1. Baseline characteristics of USTAR cohort patients included in the analysis. Legend: DLCO: diffusing capacity of the lungs for carbon monoxide; FVC: forced vital capacity; IQR: interquartile range; SD: standard deviation. Disease duration was defined since the date of onset of Raynaud's phenomenon.

Demographic and clinical variables		Number of patients with data
Male sex, n (%)	1921 (16)	12314
Ever-smokers, n (%)	4271 (35)	12314
Pack/years, median (IQR)	15 (6 - 30)	2112
Smoking duration, mean ± SD	23.7 ± 13.2	1686
Age, mean ± SD, years	55.5 ± 13.8	12314
Disease duration, median (IQR)	7.6 (3.0 - 16.0)	8773
Extent of skin involvement		8649
no skin involvement, n (%)	584 (7)	
only sclerodactyly, n (%)	831 (10)	
limited cutaneous involvement, n (%)	4751(56)	
diffuse cutaneous involvement, n (%)	2483 (29)	
Modified Rodnan Skin Score, median (IQR)	7 (4 -13)	1822
Digital ulcers, n (%)	3266 (40)	8266
Pulmonary hypertension, n (%)	644 (21)	3039
Anti-centromere antibodies, n (%)	4637 (38)	12314
Anti-topoisomerase I antibodies, n (%)	3919 (32)	12314
Interstitial lung disease, n (%)	4472 (44)	10173
DLCO % predicted, mean ± SD	69.9 ± 20.8	9012
FVC % predicted, mean ± SD	94.9 ± 22.0	8677
Gastrointestinal symptoms, n (%)	8189 (67)	12198

Table 2. Positivity of anti-centromere (ACA) and anti-topoisomerase I (ATA) antibodies in the whole EUSTAR cohort, in men and in women according to the smoking status.

	Ever-smokers	Never-smokers	p-value
	All patients (12314)		
n	4271	8043	
Autoantibodies			
ATA, n (%)	1136 (27%)	2783 (35%)	**<0.001**
ACA, n (%)	1632 (38%)	3005 (37%)	0.354
	Men (1921)		
n	1222	699	
Autoantibodies			
ATA, n (%)	492 (40%)	296 (42%)	0.372
ACA, n (%)	232 (19%)	130 (19%)	0.835
	Women (10393)		
n	3049	7344	
Autoantibodies			
ATA, n (%)	644 (21%)	2487 (34%)	**<0.001**
ACA, n (%)	1400 (46%)	2875 (39%)	**<0.001**

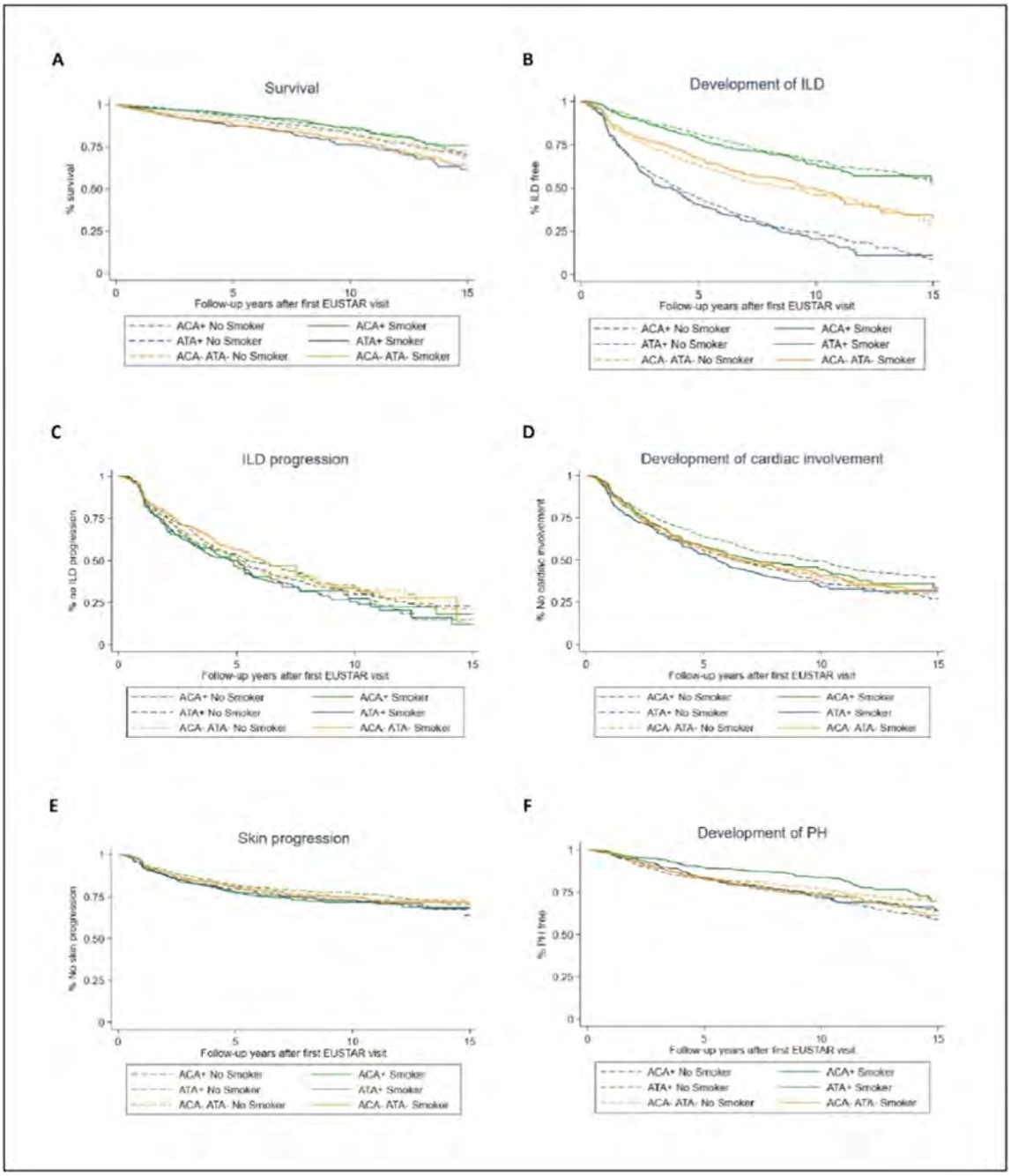


Figure 1: Kaplan–Meier curves of ever-smokers and never-smokers showing survival rate (panel A), development of interstitial lung disease (ILD) (panel B), ILD progression (panel C), development of cardiac involvement (panel D), skin progression (panel E) and development of pulmonary hypertension (panel F) in the EUSTAR patients stratified by positivity of anti-centromere antibodies (ACA+), positivity of anti-topoisomerase I antibodies (ATA+), or negativity for both antibodies (ACA- ATA-).

smoking and antibody expression using Kaplan-Meier curves and multivariate Cox regression models corrected for age and sex and with stratification for ACA/ATA status.

Results: In total 12314 patients were included (Table 1). In women 34% of never-smokers were ATA+ compared to 21% of ever-smokers ($p < 0.001$; Table 2).Ever-smoking females had lower risk of ATA+ [OR 0.523 (95% CI 0.473 – 0.578), $p < 0.001$] and higher exposure further decreased the risk of being ATA+ [OR number of pack/years 0.988 (95% CI 0.978 – 0.997), $p= 0.009$; OR years smoking duration 0.963 (95% CI 0.952 – 0.975), $p < 0.001$]. Ever-smoking females had

increased risk to be ACA+ [OR 1.320 (95% CI 1.212 – 1.437),p< 0.001] and a higher number of pack/years further increased risk of ACA expression [OR 1.012(95% CI 1.002 – 1.021), p= 0.014].In men, the proportion of ATA+ was comparable between non-smokers and ever-smokers, but higher exposure decreased the risk of ATA expression (OR 0.989 (95% CI 0.979 – 0.999), p= 0.032]. We observed different associations with disease progression depending on antibody status: in ACA+ patients, smoking was associated with mortality (HR 1.3, 95%CI 1.0–1.6), cardiac involvement (HR 1.2, 95%CI 1.1–1.4) and lower risk of pulmonary hypertension (HR 0.8, 95%CI 0.6–1.0), while in ATA+ patients, smoking was a risk factor for mortality (HR 1.4, 95%CI 1.1–1.8) and digital ulcers (HR 1.2, 95%CI 1.0–1.3) (Figure 1).

Conclusion: In this large EUSTAR cohort we observe a clear association between smoking exposure and ATA expression in SSc, particularly in females. For the first time, we describe a negative dose-response relationship between cumulative cigarette exposure and ATA expression, pointing at a possible etiopathogenetic link between smoking and ATA expression. Intruigingly, smoking exposure had different impact on disease manifestations depending on ATA/ ACA status.

Disclosure: J. Ciaffi: AbbVie/Abbott, 6, Amgen, 6, Boehringer-Ingelheim, 2, Janssen, 1, Novartis, 6; **S. Liem**: None; **S. Ahmed**: Janssen, 5; **E. Hoekstra**: None; **P. Wiland**: None; **T. Atsuma**: AbbVie, 5, 6, Alexion, 5, 6, Astellas, 5, 6, Boehringer-Ingelheim, 2, Bristol-Myers Squibb, 6, Chugai, 5, 6, Daiichi Sankyo, 5, 6, Eisai, 5, 6, Eli Lilly, 5, 6, Gilead, 5, 6, GSK, 2, 5, Merck Sharp & Dohme, 2, 6, Mitsubishi Tanabe Pharma, 5, 6, Otsuka, 5, 6, Pfizer, 5, 6, Sanofi/Genzyme, 2, 6, Takeda, 5, 6, UCB, 5, 6; **G. Szucs**: None; **A. Balbir-Gurman**: None; **L. Czirjak**: Abbvie, AstraZeneca, Boehringer Ingelheim, MSD, 6, Roche, 6; **E. Zanatta**: None; **I. Koetter**: None; **J. Henes**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, GlaxoSmithKlein(GSK), 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **m. Matucci Cerinic**: accelerong, 2, 6, actelion, 2, 6, bayer, 2, 6, biogen, 2, 6, Boehringer-Ingelheim, 2, 6, Chemomab, 2, 6, corbus, 2, 6, CSL Behring, 2, 6, Eli Lilly, 2, 6, galapagos, 2, 6, Inventiva, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 6, Mitsubishi, 2, 6, Pfizer, 2, 6, regeneron, 2, 6, Roche, 2, 6, samsung, 2, 6; **P. Airò**: Boehringer-Ingelheim, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, CSL Behring, 2, 5, 6, Janssen-Cilag, 2, 5, 6, Novartis, 2, 5, 6, Roche, 2, 5, 6; **F. Ursini**: AbbVie/Abbott, 6, Gilead, 6, Pfizer, 6; **T. Huizinga**: None; **J. de Vries-Bouwstra**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, galapagos, 5, Janssen, 2, 6, Janssen-Cilag, 5, Roche, 5.

Abstract Number: 0660

Cigarette Smoking Increases the Risk of All-Cause Mortality in Male Patients with Systemic Sclerosis: An Analysis of the EUSTAR Cohort

Jacopo Ciaffi[1], Sophie Liem[2], Saad Ahmed[2], Eva Hoekstra[2], Piotr Wiland[3], Tatsuya Atsuma[4], Gabriella Szucs[5], Alexandra Balbir-Gurman[6], Laszlo Czirjak[7], Elisabetta Zanatta[8], Ina Koetter[9], Joerg Henes[10], marco Matucci Cerinic[11], Paolo Airò[12], Francesco Ursini[13], Thomas Huizinga[2] and Jeska de Vries-Bouwstra[2], [1]IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy, [2]Leiden University Medical Center, Leiden, Netherlands, [3]Wroclaw University of Medicine, Wroclaw, Poland, [4]Hokkaido University, Department of Rheumatology, Endocrinology and Nephrology, Sapporo, Japan, [5]University of Debrecen, Department of Rheumatology, Debrecen, Hungary, [6]Rheumatology Institute, Rambam Health Care Campus and Rappaport Faculty of |Medicine, Technion, Haifa, Israel, [7]Dept. Rheumatol Immunol, Medical School, university of Pecs, Pecs, Hungary, [8]Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Padova, Padua, Italy, [9]University Hospital Eppendorf, Prisdorf, Germany, [10]University Hospital Tuebingen, Tuebingen, Germany, [11]Unit of Immunology, Rheumatology, Allergy and Rare diseases, IRCCS San Raffaele Hospital, Milan, Milan, Italy, [12]Spedali Civili di Brescia, Scleroderma UNIT, UOC Reumatologia ed Immunologia Clinica, Piazzale Spedali Civili 1, 25123, Brescia, Italy, [13]IRCCS Istituto Ortopedico Rizzoli, Bologna, Netherlands

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Cigarette smoking is an established risk factor for mortality in the general population but, in systemic sclerosis (SSc), evidence about the role of smoking in the evolution of the disease is lacking. In this study, we aim to determine whether smoking is a risk factor for reduced survival in SSc and whether smoking can contribute to the excess mortality observed in male patients compared with females.

Methods: The multinational EUSTAR database was analysed. Individuals with missing or inconsistent information about smoking status were excluded. The included patients were categorised as "never-smokers" or "ever-smokers" at the baseline visit. After stratification for sex, Kaplan–Meier estimates of time until death in ever-smokers and never-smokers were compared using a log-rank test. Follow-up time was censored at 15 years. Cox proportional hazards models adjusted for age were used to assess the risk of mortality in men and women, expressed as hazard ratios (HR) and 95% confidence

Table 1. Baseline characteristics of EUSTAR cohort patients included in the analysis. Legend: DLCO: diffusing capacity of the lungs for carbon monoxide; FVC: forced vital capacity; IQR: interquartile range; SD: standard deviation. Disease duration was defined since the date of onset of Raynaud's phenomenon.

Demographic and clinical variables		**Number of patients with data**
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Gastrointestinal symptoms, n (%)	8189 (67)	12198

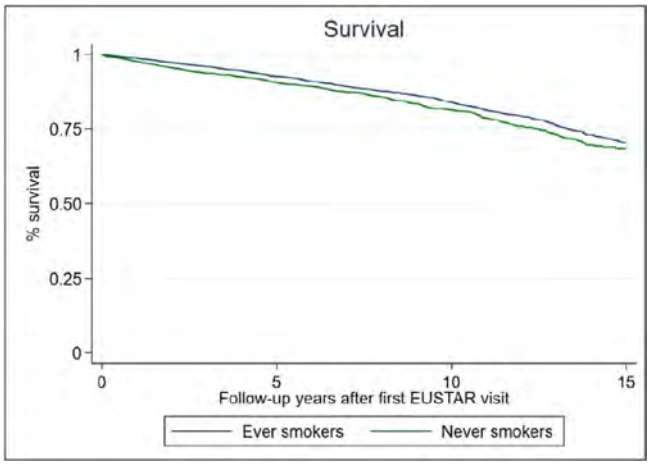

Figure 2. Kaplan–Meier curves showing survival rate of ever-smokers and never-smokers in the whole EUSTAR cohort.

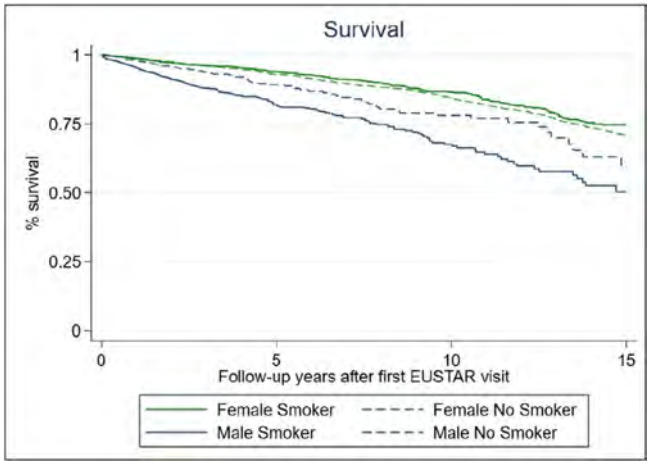

Figure 2. Kaplan–Meier curves of ever-smokers and never-smokers showing survival rate in male and female SSc patients.

intervals (95% CI). Incidence rates of mortality and 95% CI were calculated in men and women according to their smoking habit, considering never-smoking women as the reference category to determine the relative risk (RR) of death.

Results: Of the 12314 included patients (Table 1), 10393 were females (84%) and 1921 were males (16%). Overall, 807 deaths were observed during 47162 patient-years of follow-up in females and 241 deaths were observed in males over 6878 patient-years of follow-up, accounting for a mortality rate of, respectively, 28% and 46%. Survival was significantly lower in ever-smokers compared to never-smokers (68% vs 70%, p= 0.001, Figure 1). This difference was accounted for by the males: survival was 50% in ever-smoking males compared to 60% in never-smoking males ($p < 0.001$) (Figure 2). No difference was found in ever-smoking and never-smoking female patients (survival rate 75% vs 71%, p= 0.207). In Cox regression analysis adjusted for age, smoking was associated with increased risk of mortality (HR 1.63, 95% CI 1.23 – 2.16, p= 0.001) in male patients and no association emerged in women (HR 1.13, 95% CI 0.96 – 1.32, p= 0.148). Incidence rate for mortality was 1.77/100 patient-years in never-smoking women (reference category), 1.56/100 patient-years in ever-smoking women (RR= 0.88), 2.53/100 person-years in never-smoking men (RR= 1.43), 4.10/100 person-years in ever-smoking men (RR= 2.32).

Conclusion: Using he largest available real-life registry of longitudinally collected data on SSc, we demonstrated for the first time that smoking increases the risk for mortality in male SSc patients, but not in female SSc patients. Our results indicate that smoking partially explains the excess mortality observed in male SSc patients.

Disclosure: J. Ciaffi: AbbVie/Abbott, 6, Amgen, 6, Boehringer-Ingelheim, 2, Janssen, 1, Novartis, 6; **S. Liem**: None; **S. Ahmed**: Janssen, 5; **E. Hoekstra**: None; **P. Wiland**: None; **T. Atsuma**: AbbVie, 5, 6, Alexion, 5, 6, Astellas, 5, 6, Boehringer-Ingelheim, 2, Bristol-Myers Squibb, 6, Chugai, 5, 6, Daiichi Sankyo, 5, 6, Eisai, 5, 6, Eli Lilly, 5, 6, Gilead, 5, 6, GSK, 2, 5, Merck Sharp & Dohme, 2, 6, Mitsubishi Tanabe Pharma, 5, 6, Otsuka, 5, 6, Pfizer, 5, 6, Sanofi/Genzyme, 2, 6, Takeda, 5, 6, UCB, 5, 6; **G. Szucs**: None; **A. Balbir-Gurman**: None; **L. Czirjak**: Abbvie, AstraZeneca, Boehringer Ingelheim, MSD, 6, Roche, 6; **E. Zanatta**: None; **I. Koetter**: None; **J. Henes**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, GlaxoSmithKlein(GSK), 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **m. Matucci Cerinic**: accelerong, 2, 6, actelion, 2, 6, bayer, 2, 6, biogen, 2, 6, Boehringer-Ingelheim, 2, 6, Chemomab, 2, 6, corbus, 2, 6, CSL Behring, 2, 6, Eli Lilly, 2, 6, galapagos, 2, 6, Inventiva, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 6, Mitsubishi, 2, 6, Pfizer, 2, 6, regeneron, 2, 6, Roche, 2, 6, samsung, 2, 6; **P. Airò**: Boehringer-Ingelheim, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, CSL Behring, 2, 5, 6, Janssen-Cilag, 2, 5, 6, Novartis, 2, 5, 6, Roche, 2, 5, 6; **F. Ursini**: AbbVie/Abbott, 6, Gilead, 6, Pfizer, 6; **T. Huizinga**: None; **J. de Vries-Bouwstra**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, galapagos, 5, Janssen, 2, 6, Janssen-Cilag, 5, Roche, 5.

Abstract Number: 0661

Assessment of Systemic Sclerosis-Associated Myocarditis: A Single Center Case Series Study

Nafsika Gerolymatou[1], NIck Koletsos[1], Aliki Venetsanopoulou[2], Anastasia Giantsouli[3], Sophie Mavrogeni[4] and PARASKEVI VOULGARI[5], [1]Rheumatology Clinic, Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece, [2]Medical School of Ioannina, Ioannina, Greece, [3]Radiology Department, University Hospital of Ioannina, Ioannina, Greece, [4]Department of Cardiology, Onassis Cardiac Surgery Center, Athens, Greece, [5]Rheumatology Clinic, Department of Internal Medicine, University of Ioannina, Ioannina, Greece

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Myocardial involvement is a significant contributor to mortality in patients with Systemic Sclerosis (SSc). The objective of this study was to analyze the clinical characteristics of SSc patients with myocardial involvement (MI) and assess their outcomes after treatment modifications.

Methods: We conducted a retrospective study involving patients who met the ACR/EULAR 2013 Scleroderma criteria and were diagnosed with non-ischemic myocarditis. The study period spanned from July 2010 to May 2023. Cardiac MRI (CMR) scans were primarily conducted to evaluate cardiovascular symptoms, as well as to investigate abnormal findings in echocardiography and/or Holter monitoring.

Results: Our study included a total of 18 female SSc patients, diagnosed with non-ischemic myocarditis following CMR. The mean age at diagnosis was 50.6 years (SD 14.3), with a mean disease duration of 9.7 years (SD 7.3). The follow-up period since MI diagnosis was 3.6 years (SD 3). Notably, half of the patients (9/18) had early-stage disease, diagnosed within three years from the onset of SSc. No significant differences were found in the clinical characteristics between the two MI groups (early vs. established SSc), except for a slightly higher occurrence of gastrointestinal involvement noted in the early SSc group (p=0.058).Echocardiography performed at the time of MI diagnosis, revealed a slightly lower ejection fraction in patients with established SSc compared to those with early SSc (EF=55.6, SD 9.7 vs EF=60.6, SD 5.3), but this difference did not reach statistical significance. Diastolic dysfunction was identified in only three patients. Conversely, abnormal findings on 24-hour Holter monitoring were observed in 9 out of 18 patients (5/9 patients with early SSc). Regarding treatment modifications, 5 patients received cyclophosphamide as the initial treatment regimen for SSc myocarditis, while 10 patients were treated with rituximab. Concomitant use of corticosteroids was observed in 11 patients. In 6 out of the 18 patients, a second CMR was performed. The interval between the initial and second MRI varied, with a one-year interval in 4 patients, a 5-year interval in 1 patient, and a 10-year interval in 1 patient. Among these patients, myocarditis had resolved in 2 cases, both of whom were receiving a combination of Rituximab and corticosteroids. Improvement in T2-weighted parameters (T2 ratio), reflecting decrease of myocardial oedema, was observed in other 2 cases, undergoing combination therapy with rituximab and mycophenolate mofetil. Surprisingly, the remaining 2 patients who had initially received cyclophosphamide as the treatment for myocardial involvement showed no change in the cardiac MRI parameters.

Conclusion: The results of our study align with the theory that myocardial involvement in SSc can occur in both early and long-standing disease. The findings highlight the significance of early detection of SSc patients with myocarditis, as there is evidence suggesting that some patients may experience resolution of myocardial lesions. However, further studies are needed to determine the most appropriate treatment regimen and to investigate the potential use of cardiac MRI as a monitoring tool for treatment response.

Disclosure: N. Gerolymatou: None; **N. Koletsos**: None; **A. Venetsanopoulou**: None; **A. Giantsouli**: None; **S. Mavrogeni**: None; **P. VOULGARI**: None.

Abstract Number: 0662

Changes in Treatment Patterns and Their Influence on the Outcome of Systemic Sclerosis-interstitial Lung Disease (SSc-ILD) Patients: An EUSTAR Analysis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

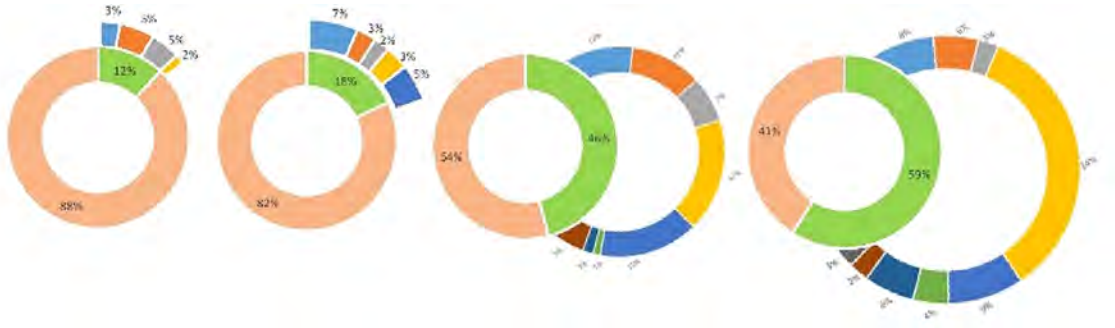
Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The treatment armamentarium with immunosuppressive treatments (ISTs) for interstitial lung disease (ILD) in systemic sclerosis (SSc) has greatly expanded. It is to date unclear to which degree and its impact on ILD progression, which is of importance for the management of patients and clinical trials. Here, we assess treatment regimens and its impact on ILD progression and mortality in SSc-ILD.

Methods: SSc patients registered in the EUSTAR database with presence of ILD on imaging, available FVC%, DLCO% predicted and treatments at baseline and at 12 ± 3 months were included. ILD progression was defined as absolute FVC≥5% or DLCO≥10% decline. We segregated treatment regimens into four periods based on patients first assessment: 1) ≤ 2006; 2) 2007-2011; 3) 2012-2016; 4) ≥ 2017 and assessed clinical characteristics and type of IST. Next, we evaluated the impact of ISTs across the periods on ILD progression and a combined morbidity-mortality endpoint (progression and 3-year death). Lastly, we assessed the impact of ISTs on these endpoints in patients with positive anti-topoisomerase I (ATA) and short disease duration (≤60 months since first non-Raynaud's symptom) in a subgroup analysis. Non-parametric tests were used for multiple group comparisons.

Results: We included 1408 SSc–ILD patients with 122 (8.7%) in period 1; 376 (26.7%) in period 2; 459 (32.6%) in period 3 and 451 (32.0%) in period 4. We did not identify major differences in clinical characteristics across the periods (Table 1); whereas the ISTs changed significantly from 12 % treated with IST in period 1 to 59% in period 4 (Figure 1). When assessing the impact of ISTs across the periods on our endpoints, we did not identify significant impact on ILD progression or the morbidity-mortality (Figure 2). In the subgroup analysis, enriching for progressive patients with short disease duration and ATA, we included 324 (23%) SSc-ILD patients across the 4 periods (4, 32, 120 and 168 in period 1-4). In this analysis, excluding those from period 1 due to low numbers, we identified significantly less ILD progression with 59.4%, 37.5% and



Treatment	≤2006	2007-2011	2012-2016	≥2017	P-value
IST, n(%)	15 (12.3)	67 (17.8)	213 (46.4)	265 (58.8)	<0.001
Azathioprine, n(%)	4 (26.7)	25 (37.3)	47 (22.1)	35 (13.2)	0.047
Steroids ≥ 10 mg/d, n(%)	7 (46.7)	10 (14.9)	43 (20.2)	24 (9.0)	<0.001
Cyclophosphamide, n(%)	6 (40)	8 (11.9)	27 (12.7)	12 (4.5)	0.016
Mycophenolate,n (%)	2 (13.3)	12 (17.9)	68 (31.9)	149 (56.2)	<0.001
Methotrexate, n(%)	0	19 (28.4)	60 (28.2)	41 (15.4)	<0.001
Tocilizumab, n(%)	0	1 (1.4)	4 (1.9)	19 (7.1)	<0.001
Rituximab, n(%)	0	0	7 (3.2)	26 (9.8)	<0.001
Abatacept, n(%)	0	0	2 (0.9)	1 (0.4)	0.832
Nintedanib, n(%)	0	0	0	14 (5.3)	<0.001
Pirfenidone, n(%)	0	0	0	1 (0.4)	0.674
No IST (%)	88%	82%	54%	41%	<0.001

Figure 1. Immunosuppressive therapies across the four periods

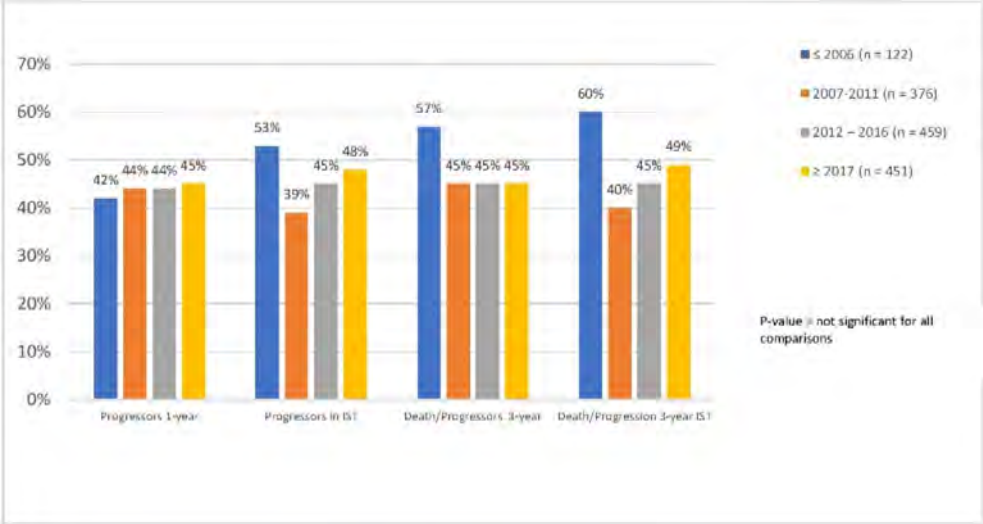


Figure 2. Outcomes of SSc-ILD patients at first-time assessment across the four periods.

Table 1. Clinical and treatment features of SSc-ILD patients at first-time assessment across the four periods

Time Period	≤ 2006 (n = 122)	2007-2011 (n = 376)	2012 – 2016 (n = 459)	≥ 2017 (n = 451)	p-value
Age (SD)	54.8 (13.3)	55.7 (11.0)	55.0 (12.8)	55.5 (13.4)	0.670
Male (%)	26 (21.3)	77 (20.5)	91 (19.8)	91 (20.2)	0.981
Disease Duration (months)	100.4 (88.0)	97.8 (99.1)	98.0 (98.2)	95.8 (89.7)	0.876
%pDLCO (SD)	61.4 (18.7)	61.3 (21.7)	60.3 (20.2)	59.9 (19.3)	0.825
%pFVC (SD)	86.3 (19.9)	85.2 (22.3)	85.6 (20.0)	83.9 (21.2)	0.599
Skin involvement, n	120	354	453	443	
Sine, n(%)	3 (2.4)	14 (4.0)	16 (3.5)	10 (2.3)	0.637
Limited cutaneous, n(%)	66 (53.2)	183 (51.7)	235 (51.9)	211 (47.6)	0.794
Diffuse cutaneous, n(%)	55 (44.4)	157 (44.4)	202 (44.6)	222 (50.1)	0.885
Antibodies, n	116	350	432	421	
Anti-centromere, n(%)	25 (18.4)	61 (15.6)	85 (16.9)	75 (15.3)	0.780
Anti-topoisomerase, n(%)	66 (47.8)	222 (55.4)	268 (52.0)	282 (56.3)	0.235
Anti-RNA-polymeraseIII, n(%)	7 (9.7)	11 (5.2)	16 (5.8)	15 (5.7)	0.537

35.1%, respectively (p =0.037) and morbidity-mortality endpoint with 62.5%, 38.3% and 38.7%, respectively (p=0.036).

Conclusion: We show that treatment with immunosuppressives has increased significantly over the past decade, with currently 60% of SSc-ILD patients on IST. This is important knowledge for the design and inclusion of patients into clinical trials. We do not identify an impact on ILD progression in the total cohort but in an enriched population, showing the importance of treatment, specifically of patients at risk for progression.

Disclosure: C. Campochiaro: Boehringer Ingelheim, 1, 6, Janssen, 1, 6, Novartis, 1, 6; **M. Truchetet**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Gilead, 5, 6, Merck/MSD, 6, UCB, 6, 12, support for conferences; **M. Vonk**: Boehringer Ingelheim, 5, 6, Corbus, 1, EUSTAR, 4, Ferrer, 5, Galapagos, 5, Janssen, 5, 6, MSD, 6, Systemic Sclerosis ERN ReCONNET, 4; **G. Cuomo**: None; **L. Ananieva**: None; **E. Hachulla**: Bayer, 2, CSL Behring, 5, GlaxoSmithKlein(GSK), 2, 5, 6, johnson&Johnson, 2, 5, 6, Novartis, 2, 5, Otsuka, 6, Roche-Chugai, 2, 5, 6, sanofi-genzyme, 2, 5, Sobi, 5; **V. Smith**: Boehringer Ingelheim, 2, 5, 6, 12, Support for travel, Galapagos, 6, Janssen-Cilag, 1, 2, 5, 6; **A. Gheorghiu**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Ewopharma, 2, 6, Sandoz, 2, 6; **R. Becvar**: Boehringer-Ingelheim, 2, GlaxoSmithKlein(GSK), 2; **N. Hunzelmann**: None; **D. Furst**: Amgen, 2, 5, Corbus, 2, 5, CSL Behring, 5, Galapagos, 2, 5, Gilead, 5, GSK, 5, Horizon, 5, Novartis, 5, Pfizer, 5, Roche, 5; **V. Ortiz-Santamaria**: None; **P. Carreira**: None; **F. Del Galdo**: AbbVie/Abbott, 5, arxx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, capella, 2, Chemomab, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Mitsubishi-Tanabe, 2, 5; **m. Matucci Cerinic**: acceleron, 2, 6, actelion, 2, 6, bayer, 2, 6, biogen, 2, 6, Boehringer-Ingelheim, 2, 6, Chemomab, 2, 6, corbus, 2, 6, CSL Behring, 2, 6, Eli Lilly, 2, 6, galapagos, 2, 6, Inventiva, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 6, Mitsubishi, 2, 6, Pfizer, 2, 6, regeneron, 2, 6, Roche, 2, 6, samsung, 2, 6; **A. Hoffmann-Vold**: Arxx Therapeutics, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Support for travel, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, 12, Support for travel, Roche, 2, 6, 12, Support for travel.

Abstract Number: 0663

Vaccine-Preventable Diseases in Hospitalized Patients with Systemic Sclerosis: A Nationwide Cohort Analysis

Saman Tanveer, Chun Pan and Faria Sami, John H. Stroger Jr. Hospital of Cook County, Chicago, IL

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Connective tissue disorders, including systemic sclerosis (SSc), are associated with an increased risk of infections. Infections are the most common diagnosis during hospitalizations and the leading cause of in-hospital deaths for SSc patients. A significant number of these infections are preventable through vaccination. In our study, we have measured the frequency and demographics of patients with SSc who were hospitalized with a vaccine-preventable disease (VPD) compared to patients without SSc.

Methods: We conducted a population-based descriptive cohort study using the US National Inpatient Sample (NIS) from 2016 to 2020. International classification disease (ICD-10) was used to identify cohorts. We measured the frequency of patients with SSc who were admitted to the hospital with a vaccine-preventable disease (VPD). Frequencies and demographics were determined and compared between patients with SSc and patients without SSc.

Table 1 - Adjusted Odds Ratio for incidence of vaccine preventable diseases in hospitalized patients with SSc as compared to hospitalized patients without SSc

VPD	Adjusted Odds Ratio (95% CI)	P value
Herpes Zoster Virus	1.65 (1.39-1.97)	<0.001
Meningococcal meningitis	2.77 (0.68-11.20)	0.15
Influenza	0.75 (0.64-0.89)	<0.001
Pneumococcal pneumonia	0.92 (0.69-1.22)	0.55
Hepatitis A	0.59 (0.32-1.08)	0.18

Table 2 - Hospitalization characteristics of SSc patients admitted with vaccine preventable diseases (LOS: Length of stay)

	Herpes zoster	Meningococcal Meningitis	Influenza	Pneumococcal Pneumonia	Hepatitis A
Total Hospitalizations (n)	1,065	10	1,785	305	55
Mean Age (years)	63.38±1.06	52.50±5.30	62.52±0.74	61.19±1.80	57.00±3.53
Mortality %	2.35%	0%	5.32%	9.84%	0%
Mean LOS (days)	6.82±0.46	9	6.82±0.47	11.85±1.42	5.99±0.98
Mean total charge ($)	72293.22±7189	110949.3±7513	78411.86±7544	173183.6±48903	67013.28±15746.69
Total hospitalization charge ($)	75900000±9471316	1109467± 788102	138000000±1.53e+07	52000000±1.61e+07	3685726±1408948

Results: We identified 1,834,149 hospitalizations with a principal diagnosis of a VPD (including influenza, Herpes Zoster Virus (HZV), pneumococcal pneumonia, hepatitis A virus, and meningococcal meningitis). Among these, 3,179 had concomitant secondary diagnosis of SSc. The most common VPDs among patients with SSc were influenza (56.1%), herpes zoster virus (HZV) (33.5%) and pneumococcal pneumonia (9.5%). Hepatitis A virus (1.7%) and meningococcal meningitis (0.3%) were less common. Patients with SSc were more likely to have HZV when compared to non-SSc patients (odds ratios [OR] = 1.65, 95% Confidence Interval [CI] = 1.39–1.97, $P < 0.001$). Interestingly, patients with SSc were less likely to develop influenza infection when compared to non-SSc patients (OR = 0.75, 95% CI = 0.64–0.89], $P < 0.001$). There was no significant difference in frequency of other VPDs between the two groups.

Conclusion: There was a significantly higher frequency of HZV infections in SSc hospitalizations compared to non-SSc admissions. This finding is pertinent as it could signify a possible low rate of vaccination versus vaccination failure in a potentially immunocompromised population, increasing the risk of infection. Most common infection in SSc patients was influenza, but observed to be less frequent than in the non-SSc group. These findings can help clinicians introduce and improve HZV vaccination programs for SSc patients.

Disclosure: S. Tanveer: None; **C. Pan**: None; **F. Sami**: None.

Abstract Number: 0664

Quantitative Hand Held Dynamometry to Assess Muscle Strength in Scleroderma Associated Myopathy

Julie Paik[1], Christopher Mecoli[2], Anshula Nallapati[1], Ami Shah[3], Fred Wigley[4], Zsuzsanna McMahan[5] and Laura Hummers[1], [1]Johns Hopkins University, Baltimore, MD, [2]Johns Hopkins University School of Medicine, Baltimore, MD, [3]Department of Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Ellicott City, MD, [4]Department of Rheumatology, Johns Hopkins Medicine, Baltimore, MD, [5]Johns Hopkins Rheumatology, Lutherville, MD

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Manual muscle strength testing can be challenging in SSc associated myopathy (SSc-AM) due to contractures or skin tightening. Since there is currently no validated strength assessment in SSc, the purpose of this study is to investigate the reliability and validity of hand held dynamometry (HHD) in SSc-AM.

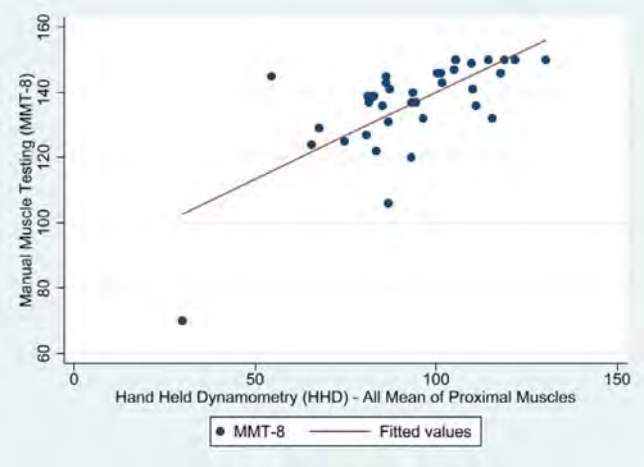
Methods: This was a prospective, cross-sectional study of 36 patients with SSc-AM enrolled at a single-center from August 2021 to May 2022. Inclusion criteria required patients to fulfill the 2013 ACR/EULAR criteria for SSc, and have skeletal myopathy as defined by a history of proximal weakness and/or elevated creatine kinase (CK) with at least one abnormal objective test result such as myopathic findings on EMG, muscle edema on muscle MRI, or inflammation, necrosis, or fibrosis on muscle biopsy.

Quantitative muscle strength testing of 3 proximal muscle groups [neck flexors, iliopsoas (bilateral hip flexors), and deltoid (bilateral arm abductors)], was assessed using a Micro-FET2 HHD and compared to the validated Manual Muscle Testing of 8 muscles (MMT-8). Each patient underwent 3 serial measurements for each of the three proximal muscle groups. A second blinded investigator performed the same assessments on 7 patients to assess inter-rater reliability. Both investigators had prior training using HHD and MMT-8.

The final HHD score was an average of each proximal muscle group (with or without neck flexors). Intra-rater reliability was assessed with a Pearson correlation and the intraclass correlation coefficient (ICC). Inter-rater reliability was also assessed with ICC. To determine how well the HHD score correlated with MMT-8, Pearson correlation was used to quantify the magnitude of correlation.

Results: Thirty-six patients with SSc-AM were enrolled. The average age at enrollment was 52.5 ± 11.1 years and at SSc diagnosis was 44.2 ± 11.9 years. 75% (27 of 36) were female and 44% (16 of 36) were Black while 37% (17 of 36) were Caucasian. 63.8% had diffuse SSc with a maximum modified Rodnan skin score (mRSS) of 13.7 ± 10.1. Maximum CK was 311 ± 425 U/L and aldolase was 12.6 ± 8.9 U/L . Closest CK at time of enrollment was 165 ± 166 U/L. Available commercial autoantibody testing and Euroimmun SSc profile demonstrated that 15% were anti-Scl-70 positive, 15% anti-PM-Scl positive, 6.25% anti-centromere B positive, 15% anti-RNA Poly III positive, 22% anti-U3RNP positive, 5.5% positive for U1RNP.

HHD strongly correlated with MMT-8 with neck flexors ($r=0.70$, $p< 0.00001$) and without neck flexors ($r=0.68$, $p< 0.00001$) (See Figure 1). Intra-rater reliability of HHD for the three consecutive assessments was also strong for the neck flexors and arm abductors with ICC of 0.96 (CI 0.94, 0.98) and hip flexors was ICC of 0.87 (CI 0.79,0.93), $p=0.001$. The inter-rater



reliability of HHD between two examiners was good for the neck flexors [ICC of 0.87 (CI 0.23-0.97), p=0.01], arm abductors [ICC of 0.88 (CI 0.39-0.98), p=0.006] and hip flexors with [ICC of 0.73 (CI -0.56-0.95, p=0.07)].

Conclusion: HHD highly correlates with the validated MMT-8 in SSc-AM and demonstrates good intra-rater and inter-rater reliability, thereby making it a feasible alternative to quantify and measure muscle strength in scleroderma.

Disclosure: J. Paik: None; **C. Mecoli**: None; **A. Nallapati**: None; **A. Shah**: Arena Pharmaceuticals, 5, Eicos Sciences, 5, Kadmon Corporation, 5, Medpace LLC, 5; **F. Wigley**: None; **Z. McMahan**: Boehringer-Ingelheim, 12, medical writing support for a different manuscript; **L. Hummers**: AbbVie/Abbott, 1, Biotest, 2, Boehringer-Ingelheim, 1, 5, CSL Behring, 1, Cumberland Pharmaceuticals, 5, GlaxoSmithKlein(GSK), 5, Kadmon Corporation, 5, Medpace, 5, Mitsubishi Tanabe, 5, Prometheus, 5.

Abstract Number: 0665

A Descriptive Study of Disease Characterisics of SSc Patients with the U2RNP Autoantibody

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: U2RNP is a spliceosome-associated autoantibody that has in prior case reports presented with scleroderma with myositis (SSc/PM)and SLE overlap. Autoantibodies are growing in prognostic importance in rheumatology and our center has performed immunoprecipitation for decades. There are few existing publications on U2RNP-associated disease features. This study aims to characterize disease phenotypes of U2RNP-positive patients.

We hypothesized based on limited available literature that patients positive for the anti-U2RNP autoantibody would display SSc features along with SLE or myositis characteristics compared to controls such as oral ulcers, thrombotic events, or cutaneous features.

Methods: This case-control study used our longstanding, prospectively followed SSc dataset. U2RNP patients initially seen in clinic between 1982 and 2015 were captured. Controls were the next two individuals seen without U2RNP (U2RNP-) Two-sided t-tests for continuous and Chi-squared tests for categorical variables were performed at a 95% confidence level.

Table 1: Baseline Characteristics

Table 1: Baseline Characteristics

	Positive U2-RNP autoantibody (n=79[+])	**Controls (negative U2-RNP antibody) (n=158[+])**	**p-value**
DEMOGRAPHICS			
Biological Sex (F/M)	61 (77.2%)/18 (22.8%)	122 (77.2%)/36(22.8%)	NS
Ethnic Origin (Non-White/White)	11 (13.9%)/68 (86.1%)	18 (11.4%)/140 (88.6%)	0.73
Mean age (+/- SD)) at first SSc symptom in years	40.88 +/- 14.68	45.08 +/- 14.91	**0.04***
Diffuse Skin (%)	45 (56.96%)/34 (43.04%)	85 (53.80%)/73 (46.20%)	0.64
DISEASE CHARACTERISTICS			
Median (IQR) Disease Duration (years) **Mean (SD)** **Median, [25-75%ile IQR]**	 3.8,(5.61) 1.48, [.67, 18.17],	 4.94 (6.63) 1.75 [0.58,6.67]	0.17
Diffuse Skin (%)	45 (56.96%)/34 (43.04%)	85 (53.80%)/73 (46.20%)	0.64
Maximum total skin score **Mean (SD)** **Median, [25-75%ile IQR]** **Min, Max**	 13.48, (12.67) 11, [3, 23] 0, 45	 15.25, (14.73) 9, [3, 25] 0, 51	0.18
Pulmonary fibrosis at first visit on chest imaging [+]database is missing values for 3 controls which are excluded from analysis	43 (54.4%)	63 (39.9%)	0.06
Gottron's sign at first visit [+]database is missing values for 52 cases and 99 controls which are excluded from analysis	25 (31.6%)	58 (36.7%)	0.48
Pericarditis at first visit [+]database is missing values for 7 controls which are excluded from analysis	13 (16.5%)	27 (17.1%)	0.9302

NS= not significant, *statistically significant at a 5% significance level **statistically significant at a 1% significance level

Table 2: Follow up disease characteristics and comorbidities

Table 2: Follow-up disease characteristics and comorbidities

	Cases (n=79*)	Controls (n=158[‡])	Total (n= 237[‡])	P-value
Aneurysm†: n (%)	5 (6.3%)	3 (1.9%)	8 (3.38%)	0.1619
Calcinosis: n (%) *database is missing values for 31 cases and 52 controls which are excluded from analysis	8 (10.1%)	23 (14.6%)	31 (13.1%)	0.614
Abnormal nailfold capillary microscopy†: n (%)	8 (10.1%)	28 (17.7%)	36 (15.2%)	0.125
Vascular event - CVA: n (%) *database is missing values for 3 controls which are excluded from analysis	0 (0%)	2 (1.27%)	2 (0.844%)	0.7925
Diastolic dysfunction: n (%) *database is missing values for 2 controls which are excluded from analysis	9 (11.4%)	15 (9.49%)	24 (10.1%)	0.85
Digital ulcerations: n (%) *database is missing values for 1 control which is excluded from analysis	33 (41.8%)	57 (36.1%)	90 (38%)	0.50
Digital scars: n (%) *database is missing values for 1 control which is excluded from analysis	40 (50.6%)	67 (42.4%)	107 (45.1%)	0.31
Unspecified DM-like rash†: n (%)	0 (0%)	1 (0.063%)	1 (0.42%)	0.48
Pulmonary fibrosis: n (%) *database is missing values for 3 controls which are excluded from analysis	45 (57%)	70 (44.3%)	115 (48.5%)	0.12
Gottron's papules/sign†: n (%)	3 (3.8%)	4 (2.53%)	7 (2.95%)	0.587
Gottron's papules: n (%) *database is missing values for 51 cases and 100 controls which are excluded from analysis	1 (1.27%)	1 (0.633%)	2 (0.844%)	0.594
Gottron's sign: n (%)	3 (3.8%)	2 (1.27%)	5 (2.11%)	0.369
Heliotrope rash†: n (%)	0 (0%)	1 (0.63%)	1 (0.42%)	0.479
Livedo Reticularis: n (%)	4 (5.06%)	5 (3.16%)	9 (3.8%)	0.714
[‡]database is missing values for 35 cases and 70 controls which are excluded from analysis				
Livedo Reticularis†: n (%)	4 (5.06%)	10 (6.33%)	14 (5.91%)	0.697
Unspecified SLE-like rash†: n (%)	4 (5.06%)	3 (1.9%)	7 (2.95%)	0.342
Mechanic's Hands: n (%) *database is missing values for 50 cases and 97 controls which are excluded from analysis	0 (0%)	3 (1.9%)	3 (1.27%)	0.5576
MI†: n (%)	1 (1.27%)	21 (13.3%)	22 (9.28%)	**0.005****
Myositis: n (%) *database is missing values for 32 cases and 65 controls which are excluded from analysis	9 (11.4%)	15 (9.49%)	24 (10.1%)	0.83
Nephritis†: n (%)	0 (0%)	4 (2.53%)	4 (1.69%)	0.3727
Oral ulcers†: n (%)	3 (3.8%)	21 (13.3%)	24 (10.1%)	**0.022****
Panniculitis: n (%) *database is missing values for 54 cases and 94 controls which are excluded from analysis	25 (31.6%)	63 (39.9%)	88 (37.1%)	0.530
Clinical pericarditis: n (%)	13 (16.5%)	27 (17.1%)	40 (16.9%)	0.9128
No (#, frequency)	66 (83.5%)	123 (77.8%)	189 (79.7%)	
Yes (#, frequency)	13 (16.5%)	27 (17.1%)	40 (16.9%)	
Missing (unknown per EMR review and SSc database- excluded from analysis)	0 (0%)	8 (5.06%)	8 (3.38%)	
Pericarditis†: n (%)				
Yes (#, frequency)	13 (16.5%)	28 (17.72%)	41 (17.30%)	0.808
Pericardial effusion *database is missing values for 32 cases and 63 controls which are excluded from analysis	9 (11.4%)	21 (13.3%)	30 (12.7%)	0.8511
Periorbital rash†	4 (5.06%)	8 (5.06%)	12 (5.06%)	NS
Pulmonary hypertension†	16 (20.25%)	49 (31.01%)	65 (27.43%)	0.080
Pulmonary hypertension subtype				0.5327
*database is missing values for 10 cases and 20 controls which are excluded from analysis				
None	55 (69.6%)	107 (67.7%)	162 (68.4%)	
Primary (clinically or after right heart catheterization)	4 (5.06%)	16 (10.1%)	20 (8.44%)	
Secondary to pulmonary fibrosis	9 (11.4%)	13 (8.23%)	22 (9.28%)	
Secondary to cardiac scleroderma	1 (1.27%)	2 (1.27%)	3 (1.27%)	
Pleurisy†: n (%)	2 (2.53%)	17 (10.8%)	19 (8.02%)	**0.05***
Serositis†: n (%)	15 (19%)	41 (25.9%)	56 (23.6%)	0.3043
Sicca syndrome *database is missing values for 45 cases and 84 controls which are excluded from analysis	16 (20.3%)	27 (17.1%)	43 (18.1%)	0.4061
Telangiectasias†: n (%)	21 (26.92%)	112 (70.89%)	133 (56.36%)	**<0.001*****
Thrombus: n (%)	4 (5.06%)	45 (28.5%)	49 (20.7%)	**0.0001*****
Thrombus type (arterial/venous/unknown/none) at any visit				**0.005****
Arterial: n (%)	2 (2.53%)	27 (17.09%)	29 (12.24%)	
Both: n (%)	0 (0%)	1 (0.63%)	1 (0.42%)	
Venous: n (%)	14 (5.91%)	11 (6.96%)	14 (5.91%)	
None: n (%)	74 (93.67%)	116 (73.42%)	190 (80.17%)	
Unknown: n (%)	0 (0%)	3 (1.90%)	3 (1.27%)	
Unspecified rash†: n (%)	12 (15.2%)	7 (4.43%)	19 (8.02%)	**0.0087****

†Obtained from retrospective chart review *significant at 5% significance level, ** significant at 1% significance level, ***significant at .01% significance level, * Sample size may vary from group as some missing data was excluded from analysis

Results: 79 U2RNP+ and 158 U2RNP- patients were identified. There was no significant difference in proportion of non-white patients between groups. Mean age of symptom onset was earlier for U2RNP+ patients (mean 40.9, SD 14.7) than controls (mean 45, SD 14.9) with a p-value of 0.05 (Table 1).

Amongst U2RNP+ patients, 43% had diffuse skin thickening, similar to U2RNP- patients. We did not find a difference in rates of myositis between groups. Surprisingly, U2RNP- controls had a higher incidence of SLE-like features such as oral ulcers, thrombi, and pleurisy (Table 2). Only unspecified rashes differed significantly between groups (15.2% in U2RNP+ vs. 4.43% in U2RNP-, $p = 0.0087$). There was no difference in vascular comorbidities other than higher rate of MI in the U2RNP- group.

For SSc features, less U2RNP+ patients (26.92%) had telangiectasias than U2RNP- (70.9%; $p < 0.0001$). A larger percentage of individuals in the U2RNP+ group developed pulmonary fibrosis (57% vs. 44%, $p = 0.12$) in follow-up, and had pulmonary fibrosis at their first visit (54.4% vs. 39.9%, $p = 0.06$), though both findings related to fibrosis were not statistically significant. There was no difference in development and subtypes of pulmonary hypertension (Table 2).

Conclusion: This is the first large case-control study of patients with the anti-U2RNP antibody. Unlike U1RNP, U2RNP+ did not present with typical SLE or myositis features, aside from unspecified rash. Approximately 43% of U2RNP+ patients had diffuse skin thickening, but with less telangiectasias (27%). Though not statistically significant, there is a greater percentage of pulmonary fibrosis over the long-term and at initial visit in the U2RNP+ group. This finding may be further elucidated in further studies that match for age, biological sex, and other environmental factors that may influence fibrosis and perhaps guide screening recommendations for individuals who test positive for the autoantibody through serologies. The primary weakness is that this is a single-center study.

Disclosure: M. Dilip: None; **M. Laffoon**: None; **Y. Park**: None; **R. Lafyatis**: Advarra/GSK, 1, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, 5, Certa Therapeutics, 2, Corbus, 2, 5, EMD Serono, 2, Formation, 2, 5, Genentech, 1, 2, Merck/MSD, 2, Moderna, 5, Morphic, 2, Pfizer, 2, 5, Regeneron, 5, Third Rock Venture, 2, Thirona Bio, 2, 4, 11, Zag Bio, 2; **T. Medsger**: None; **V. Steen**: None; **L. Freno**: None; **R. Domsic**: Aisa Pharma, Inc., 2, CSL Behring, 1.

Abstract Number: 0666

Troponin I Levels in Systemic Sclerosis Patients with Myocardial Involvement

Eva Hoekstra[1], Sophie Liem[1], Nivine Levarht[1], Cynthia Fehres[1], Saad Ahmed[1], Nina Ajmone Marsan[2], Thomas Huizinga[1] and Jeska de Vries-Bouwstra[1], [1]Leiden University Medical Center, Leiden, Netherlands, [2]Department of Cardiology, Heart Lung Centre, Leiden University Medical Centre, Leiden, Netherlands

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: As primary myocardial involvement in systemic sclerosis (SSc) is associated with worse prognosis, research on diagnostic tools for recognition is essential. Troponin I was suggested as a more specific biomarker for myocardial involvement in SSc than the frequently used troponin T. The aim of this study is to evaluate the association between troponin I levels and primary myocardial involvement in SSc patients, and to evaluate the presence of subclinical myocardial involvement by comparing troponin I levels between SSc patients and healthy controls.

Methods: A cross-sectional observational study was performed, including four groups of each 20 SSc patients, fulfilling ACR/EULAR 2013 criteria, selected from the Leiden Combined Care in Systemic Sclerosis cohort: (1) patients with primary myocardial involvement, (2) patients with myositis, (3) patients with elevated troponin T and CK levels but without organ involvement, and (4) patients without any suggestions of organ involvement. Primary myocardial involvement was assessed independently by an experienced rheumatologist and an experienced cardiologist. Troponin I levels were measured in patient sera and 20 additional healthy donors using ELISA. Troponin I levels were compared between the different groups using Mann-Whitney U and Kruskal-Wallis tests.

Results: The mean age of the 80 included patients was 56.2 ± 12.7 years, 61% of the study population was female. Troponin I levels were comparable between patients with and without myocardial involvement (2.7 [0.5 – 15.3] vs. 1.2 [0.1 – 6.6] ng/L; p = 0.117). Within the group of patients without myocardial involvement, SSc patients with myositis, SSc patients with elevated troponin T levels without organ involvement and SSc patients with normal troponin T levels without organ involvement, had median troponin I levels of 0.4 (0.0 – 4.7) ng/L, 2.2 (0.0 – 9.9) ng/L, and 1.2 (0.2 – 7.2) ng/L, respectively. No significant differences were found in median troponin I levels between the four different subgroups (p=0.131) (Figure 1). SSc patients (without myocardial involvement) were more often positive for troponin I than healthy controls (30.0% vs. 65.0%, p = 0.006) (Figure 2).

Conclusion: Elevated troponin T and I levels were identified in SSc patients without myocardial involvement possibly indicating subclinical myocardial involvement in the majority of patients. However, these elevated levels were not of additive value to identify SSc patients with clinical myocardial involvement.

Table 1. Patient characteristics of included patients with systemic sclerosis.

	SSc patients (n=80)	SSc patients with myocardial involvement (n=20)	SSc patients without myocardial involvement (n=60)
Age (years)	56.2 ± 12.7	52.4 ± 14.0	57.5 ± 12.1
Female sex, *n (%)*	49 (61.3)	13 (65.0)	36 (60.0)
Smoking (at time of study visit), *n (%)*	10 (12.5)	1 (5.0)	9 (15.0)
Comorbidity:			
- Cardiovascular disease, *n (%)*	14 (17.4)	7 (35.0)	7 (11.7)
- Diabetes mellitus, *n (%)*	5 (6.3)	1 (5.3)	4 (6.7)
Disease duration^ (months)	23.0 (7.3-80.8)	38.0 (11.5-145.8)	19.5 (6.0-72.3)
Diffuse SSc, *n (%)*	36 (45.0)	16 (80.0)	20 (33.3)
ANA, *n (%)*	78 (97.5)	18 (90.0)	60 (100)
- Anti-topoisomerase I, *n (%)*	20 (25.0)	8 (40.0)	12 (20.0)
- Anti-centromere, *n (%)*	21 (26.3)	0 (0)	21 (35.0)
Troponin T (ng/L)~	23.0 (8.0-56.0)	26.0 (10.5-108.3)	22.0 (8.0-49.5)
Creatinine (µmol/L)	76.5 (63.5-97.3)	80.0 (58.0-86.0)	75.0 (66.0-100.0)
CK (U/L)	109.0 (71.8-197.8)	103.0 (72.0-283.0)	115.0 (71.0-187.0)
ILD#, *n (%)*	12 (15.0)	4 (20.0)	8 (13.3)
PAH, *n (%)*	2 (2.5)	1 (5.0)	1 (1.7)
Use of any immunosuppressives ever*, *n (%)*	55 (68.8)	13 (65.0)	42 (70.0)

Parametric data are reported as mean ± SD, non-parametric data as median (IQR).
^ Since first non-Raynaud symptom.
* Includes methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil, corticosteroids, biologicals.
~ Note that 40 out of 80 patients were selected partially based on elevated or normal troponin T levels.
# Defined as ILD on CT combined with FVC < 80%.
Abbreviations. ANA: anti-nuclear antibodies; ATA: anti-topoisomerase antibodies; ACA: anti-centromere antibodies; CK: creatinine kinase; ILD: interstitial lung disease; PAH: pulmonal arterial hypertension.

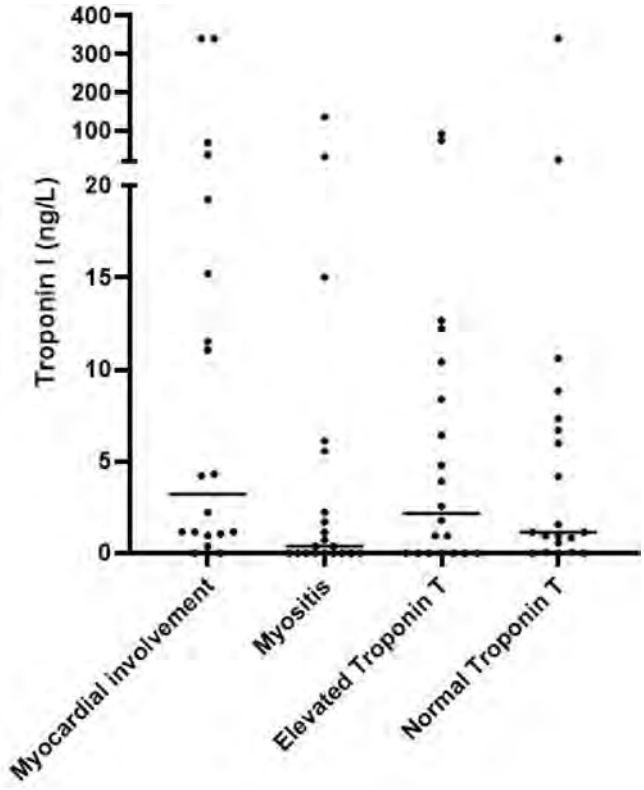


Figure 1. Troponin I levels in SSc patients.

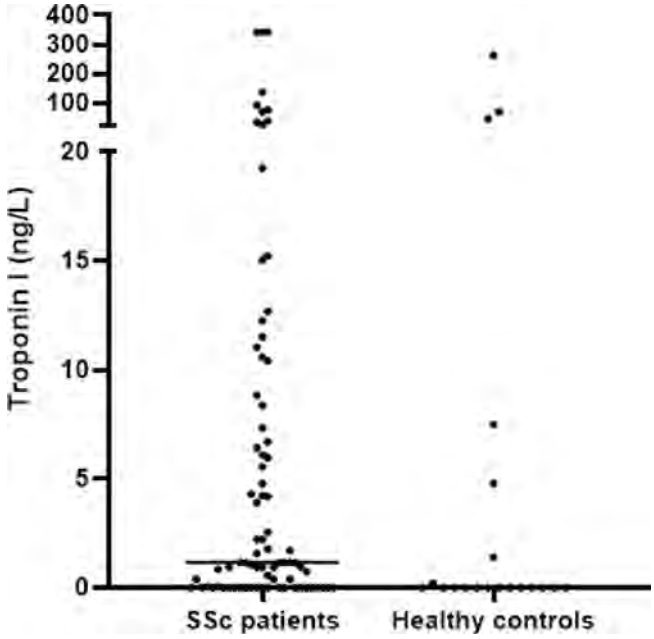


Figure 2. Troponin I levels in SSc patients and healthy controls.

Disclosure: E. Hoekstra: None; **S. Liem**: None; **N. Levarht**: None; **C. Fehres**: None; **S. Ahmed**: Janssen, 5; **N. Ajmone Marsan**: None; **T. Huizinga**: None; **J. de Vries-Bouwstra**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, galapagos, 5, Janssen, 2, 6, Janssen-Cilag, 5, Roche, 5.

Abstract Number: 0667

The Risk of Stroke and Myocardial Infarction in Systemic Sclerosis: A Population-based Study

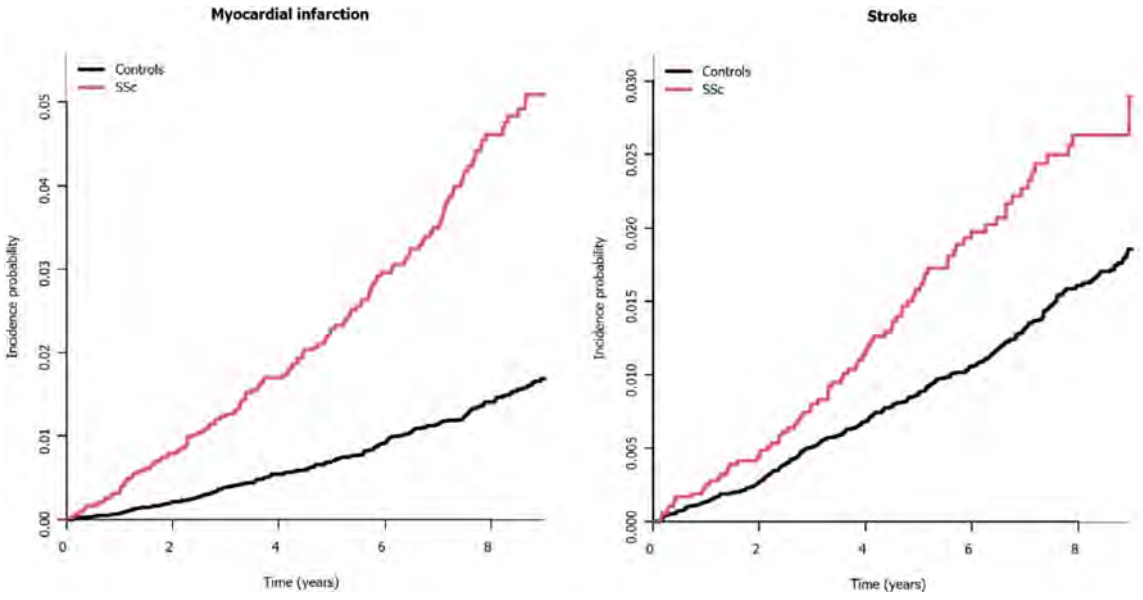
Jiwon Hwang[1], Yeonghee Eun[2], Kyungdo Han[3] and Joong Kyong Ahn[2], [1]Samsung Changwon Hospital, Sungkyunkwan University School of Medicine, Changwon, South Korea, [2]Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea, [3]Department of Statistics and Actuarial Science, Soongsil University, Seoul, South Korea

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies have suggested a link between systemic sclerosis (SSc) and cardiovascular disease, but large-scale data are still lacking due to the nature of rare autoimmune diseases. We aimed to compare the incidence of myocardial infarction (MI) and stroke in patients with SSc and age- and sex-matched controls in a nationwide population-based cohort in Korea.

Methods: We included patients with SSc defined by the ICD-10 code (M34) and rare and intractable disease code (V138) and 1:5 age- and sex-matched controls using the Korean National Health Insurance Database. The outcomes of the study were MI and stroke. Cox proportional hazard analysis and Kaplan-Meier curve were used to compare the incidence of outcomes between patients with SSc and controls.

Results: A total of 4700 patients with SSc and 23500 controls were included in the study. The mean follow-up period was 5.6 ± 2.8 years. At baseline, patients with SSc had higher prevalent rates of comorbidities such as hypertension, hyperlipidemia, and congestive heart failure than controls. Patients with SSc had a 3-fold higher risk of MI (adjusted hazard ratio [aHR] 3.01, 95% confidence interval [CI] 2.41–3.76) and a 1.7-fold higher risk of stroke (aHR 1.65, 95% CI 1.28–2.14) compared to controls. There were no differences in the association between SSc and MI or stroke by age, sex, or comorbidities.



Cumulative incidence of myocardial infarction and stroke

Conclusion: This nationwide population-based cohort study revealed an association between SSc and increased risk of MI and stroke. Therefore, careful monitoring and preventive measure for the cardiovascular diseases in patients with SSc are required.

Disclosure: J. Hwang: None; **Y. Eun**: None; **K. Han**: None; **J. Ahn**: None.

Abstract Number: 0668

Increased Risk of Cancer in Patients with Systemic Sclerosis: A Population-based Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies have shown an association between systemic sclerosis and cancer. However, because the disease is rare, large-scale studies are lacking, especially in Asians. We aimed to compare the incidence of cancer in patients with SSc and age- and sex-matched controls in a nationwide population-based cohort in Korea.

Methods: We included patients with SSc defined by the ICD-10 code (M34) and rare and intractable disease code (V138) and 1:5 age- and sex-matched controls using the Korean National Health Insurance Database. The outcomes of the study were incidence of cancer. Cox proportional hazard analysis and Kaplan-Meier curve were used to compare the incidence of cancer between patients with SSc and controls.

Results: A total of 5,145 patients with systemic sclerosis and 25,725 controls were included in the study. During the study period, the overall cancer incidence rate was 11.07 per 1,000 person-years in patients with systemic sclerosis and 7.59 per 1,000 person-years in controls. Overall cancer risk was 1.5 times higher in patients with systemic sclerosis (adjusted hazard ratio 1.46, 95% confidence interval 1.28–1.67). Lung cancer and lymphoma had a high risk in both male and female patients with systemic sclerosis, and colorectal cancer had a high risk only in male patients with systemic sclerosis. The risk of biliary cancer, skin cancer, and cervical cancer was high in female systemic sclerosis patients.

Conclusion: This nationwide cohort study showed that patients with systemic sclerosis were associated with increased cancer risk. Clinicians should be aware of cancers that may increase the risk in patients with systemic sclerosis and apply appropriate screening measures.

Disclosure: J. Hwang: None; **Y. Eun**: None; **K. Han**: None; **J. Ahn**: None.

Abstract Number: 0669

Optical Coherence Tomography Angiography in Systemic Sclerosis: Correlations with Morphological and Functional Peripheral Microvascular Status

Carlo Alberto Cutolo[1], Elvis Hysa[2], Andrea Cere[3], Paola Toma[1], Tommaso Cannavacciuolo[1], Chiara Toma[1], Serena Balito[4], Veronica Gerli[4], Alberto Sulli[3], Vanessa Smith[5], Carlo Enrico Traverso[1], Massimo Nicolò[1] and **Maurizio Cutolo**[6], [1]Ophthalmology Clinic DiNOGMI, IRCCS Ophthalmology Unit San Martino Polyclinic, University of Genoa, Genoa, Italy, [2]Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS San Martino Polyclinic Hospital, Genova, Italy, [3]Laboratory of Experimental Rheumatology and Academic Division of Rheumatology, Department of Internal Medicine, University of Genoa, IRCCS San Martino Polyclinic Hospital, Genoa, Italy, [4]Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genoa, Italy - IRCCS San Martino Polyclinic, Genoa, Italy, [5]Ghent University Hospital, Gent, Belgium, [6]Laboratory of Experimental Rheumatology, Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS San Martino Polyclinic, Genova, Italy

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a rare and complex autoimmune disease featured by a progressive microvascular damage. The involvement of the ocular microvasculature has been reported in SSc but correlations with nail-fold capillaroscopy (NVC) and laser speckle contrast analysis (LASCA) have been scarcely investigated [1].

We aimed to compare Optical Coherence Tomography Angiography (OCTA) variables in SSc patients vs age- and sex-matched healthy controls (HCs). The morphological peripheral microvascular status, assessed by NVC, and the functional perfusion, analysed by LASCA, were correlated with the OCTA data among the SSc cohort.

Methods: The enrolment included 35 SSc patients (mean age 61.1 ± 13.4 years, mean disease duration 9.5 ± 6 years) and 28 HCs in a single centre from March to October 2022.

Table 1. Comparisons of ocular features and OCTA data between SSc and HCs. Abbreviations. SSc: systemic sclerosis; HCs: healthy controls; lcSSc: localized cutaneous systemic sclerosis; dcSSc: diffuse cutaneous systemic sclerosis; RNFL= retinal nerve fiber layer.

Variable	SSc (n=32)			HCs (n=27)	p-value
Intraocular pressure, (mmHg)	13.6 ± 2.3			11.9 ± 2.2	**0.006**
Scan quality	61±6			63±5	0.315
Superficial capillary plexus, (% of perfusion)	39.4±2.4			40.8±2.7	**0.040**
Deep capillary plexus, (% of perfusion)	39.6±2.7			41.3±3.0	**0.026**
Choriocapillaris, (% of perfusion)	51.1±2.7			52.9±1.5	**0.003**
	lcSSc (n = 22)	**dcSSc (n = 10)**	**p- value**		
	51.8±1.5	49.8±3.6	**0.03**		
Choroidal thickness, (µm)	212±90			220±68	0.725
	lcSSc (n = 22)	**dcSSc (n = 10)**	**p- value**		
	176±79	304±57	**p < 0.0001**		
Retinal thickness, (µm)	267±28			275±15	0.181
RNFL, (µm)	101 ± 11			102 ± 10	0.707

The patients were classified according to the ACR/EULAR 2013 criteria, and multiple assessments were performed, at the same day, including ophthalmological examinations, OCTA, NVC and LASCA.

The clinical, laboratory and instrumental data of SSc patients were analysed and correlated with the OCTA data.

Patients were under standard treatment for SSc and those requiring endovenous prostanoids were evaluated for the study assessment at least one month after the last infusion.

Results: Among the ocular features, the intraocular pressure (IOP) was significantly higher in SSc than in HCs (p=0.006).

Despite the structural features in OCTA being similar, a significant difference was detected in all the perfusion variables, including the superficial vascular plexus (SVP), deep vascular plexus (DVP), and choriocapillaris (CC) **(Table 1**).

When patients were stratified according to the clinical extension of skin involvement, diffuse cutaneous SSc (dcSSc) patients showed a significantly reduced CC perfusion compared to limited cutaneous SSc (lcSSc) patients. Interestingly, the choroidal thickness (CT) in dcSSc was nearly twice that of lcSSc ($p < 0.0001$). The age and disease duration did not significantly differ among the two subgroups (respectively, $p = 0.18$ and $p = 0.37$).

In addition, the mean number of capillaries per linear mm at NVC and the mean peripheral perfusion assessed by LASCA at the level of 2^{nd} to 5^{th} fingertip were negatively correlated with the IOP ($r = -0.30$ and $r = -0.36$, both $p < 0.01$).

Finally, the mean capillary number at NVC was also positively correlated with the perfusion values of the SVP and DVP at OCTA ($r = 0.3$, $p = 0.01$ and $r = 0.28$, $p = 0.01$) and the mean peripheral perfusion detected by LASCA positively correlated with the DVP and CC perfusion ($r = 0.29$ and $r = 0.28$, both $p = 0.01$).

Conclusion: The higher IOP in all SSc patients might be in line with reported vascular abnormalities occurring in the optic nerve head [2].

The reduced capillary density and perfusion of the retina and choriocapillaris suggest an ocular microvascular impairment similarly to what is observed at the nailfold and fingertips in SSc patients.

The increased CT limited to dcSSc might be related to attempts of ocular microvascular reactivity and deposition of subendothelial extracellular matrix in agreement with the fibrotic process observed in other tissues in such patients.

References: [1] Kreps et al. Semin Arthr Rheum 2019. [2] Hysa et al. Aut Rev 2021

Disclosure: C. Cutolo: None; **E. Hysa**: None; **A. Cere**: None; **P. Toma**: None; **T. Cannavacciuolo**: None; **C. Toma**: None; **S. Balito**: None; **V. Gerli**: None; **A. Sulli**: None; **V. Smith**: Boehringer Ingelheim, 2, 5, 6, 12, Support for travel, Galapagos, 6, Janssen-Cilag, 1, 2, 5, 6; **C. Traverso**: None; **M. Nicolò**: None; **M. Cutolo**: Amgen, 5, Boehringer Ingelheim, 5, Bristol-Myers Squibb, 5, Lab.Baldacci, 5.

Abstract Number: 0670

Title: Patient Characteristics and Outcomes of Scleroderma Renal Crisis versus Hypertensive Emergencies: A Nationwide Comparative Study

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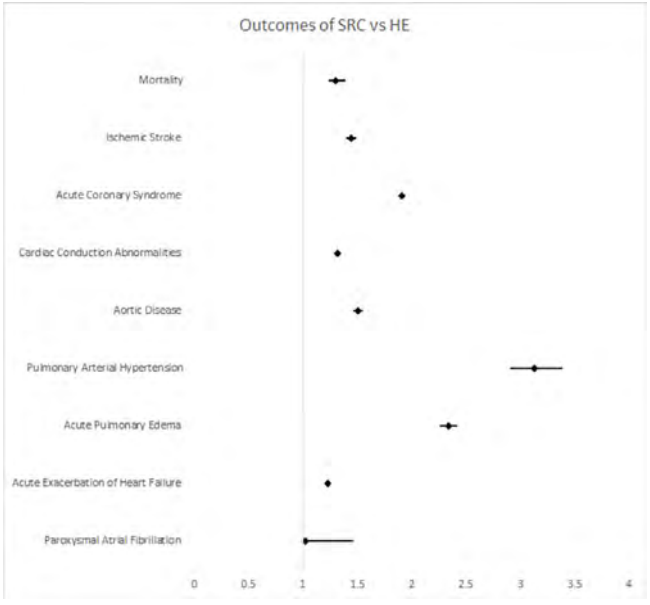
SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Scleroderma renal crisis (SRC) is a life-threatening complication of systemic sclerosis. It presents with sudden onset of severe hypertension, a rise in serum creatinine levels with oliguria, and/or thrombotic microangiopathy. We aimed to identify the differences in outcomes and comorbidities in patients with this SRC in comparison to patients presenting with hypertensive emergency without SRC (HE).

Methods: The 2016-2020 National Inpatient Sample database (NIS) was analyzed to identify adult hospitalizations with SRC, using International Classification of Diseases – 10 Clinical Modification (ICD-10-CM) codes. The studied primary outcome was to assess SRC versus HE inpatient mortality and inpatient morbidities. A multivariate logistic regression, and linear regression analyses were used to adjust for possible confounders.

Results: Logistic and linear regression analyses showed that patients with SRC had a higher odds of mortality (adjusted Odds Ratio [aOR] of 1.3, 95% Confidence Interval [CI] 1.24-1.39), ischemic stroke (aOR: 1.44, CI: 1.40-1.49), acute coronary syndrome (aOR: 1.91, CI: 1.87-1.95), cardiac conduction abnormalities (aOR: 1.32, CI: 1.30-1.35), aortic disease (aOR: 1.51, CI: 1.46-1.55), pulmonary arterial hypertension (aOR: 3.13, CI: 2.9-3.39), acute pulmonary edema (aOR: 2.34, CI: 2.26-2.42), acute exacerbation of heart failure (aOR: 1.23, CI: 1.21-1.25), and paroxysmal atrial fibrillation (aOR: 1.02,



Outcomes in patients with SRC versus patients with Hypertensive disease only

CI: 1.008-1.046) in comparison to HE. Figure 1 shows the Forrest plot for multivariate analysis of in hospital morbidities when adjusted for patient demographics, comorbidities, and hospital characteristics.

Conclusion: In conclusion, our study underscores the notable distinctions between patients with scleroderma renal crisis and those presenting with hypertensive emergencies without scleroderma. Our findings demonstrate that patients with scleroderma renal crisis face significantly elevated risks of mortality, ischemic stroke, acute coronary syndrome, cardiac conduction abnormalities, aortic disease, pulmonary arterial hypertension, acute pulmonary edema, and acute exacerbation of heart disease. These results highlight the imperative for healthcare providers to exercise heightened caution and tailored management strategies when dealing with scleroderma renal crisis patients due to their heightened susceptibility to complications.

Disclosure: H. el Sharu: None; **S. Singh**: None; **O. Alwahadneh**: None; **M. Alqaisieh**: None.

Abstract Number: 0671

Decreased Odds of Malignancy with Mycophenolate Use in a Single-Center Scleroderma Cohort

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Prior studies have shown an increased risk of malignancy in patients with systemic sclerosis (SSc). The reasons for this increased risk may be multifactorial, including effects of chronic inflammation, genetics, shared environmental risk factors, use of immunosuppressive medications, among others. The aim of this study is to identify and characterize malignancy risk factors in a diverse SSc cohort.

Methods: A retrospective cohort was assembled of all patients with SSc followed within a large, urban, tertiary care center. Validated ICD codes were used to identify cases. Descriptive statistics were used to study the cross-sectional distribution of patient characteristics, including age, sex, ethnicity, health insurance status, smoking status, scleroderma subtype, mycophenolate (MMF) use and other immunosuppressant use. Student t-test was performed to compare variations in age. Chi-square test and Fisher exact test were used to examine the difference in other categorical characteristics of patients with and without malignancy. The prevalence of specific types of cancers was calculated. Odds ratios (OR) of cancer diagnosis with respect to patient characteristics were calculated with multivariable logistic regression.

Results: A total of 625 patients met inclusion criteria. The distribution of participant characteristics was calculated and stratified by cancer diagnosis (Table 1). 93 (14.9%) patients were found to have a history of cancer. Breast cancer (N=32, 5.1%) was the most prevalent cancer in our cohort; distribution of each specific malignancy is outlined in Figure 1. Patients with a malignancy history were older than those without malignancy (median age 69 vs 61 $P < 0.01$). Lack of medical insurance was associated with increased odds of malignancy (OR 2.13, 95% CI 1.07-4.24, $P = 0.03$). Participants taking MMF were significantly less likely to be diagnosed with malignancy (OR 0.58, 95% CI 0.36-0.94, $P = 0.03$), whereas other

Table 1. Characteristics of patients with systemic sclerosis with and without history of malignancy (N = 625)

		History of malignancy (N=93)	No history of malignancy (N=532)	P-value
Median age, years		69	61	<0.01
		N (%)	*N (%)*	
Female Sex		79 (85.0%)	438 (82.3%)	0.54
Ethnicity	White	47 (50.5%)	225 (42.5%)	0.31
	Black	18 (19.4%)	86 (16.2%)	
	Asian	1 (1.1%)	18 (3.4%)	
	Hispanic	5 (5.4%)	48 (9.0%)	
	Other	22 (23.7%)	155 (29.1%)	
Health Insurance	Private	25 (26.9%)	203 (38.2%)	0.07
	Public	52 (55.9%)	268 (50.4%)	
	None	16 (17.2%)	61 (11.5%)	
Scleroderma Subtype	Limited	59 (63.4%)	349 (65.6%)	0.69
	Diffuse	34 (36.6%)	183 (34.4%)	
Smoking history		4 (4.3%)	29 (5.5%)	0.80
Mycophenolate use		28 (30.1%)	226 (42.5%)	0.03
Other Immunosuppressant Use		62 (66.7%)	256 (48.1%)	<0.01

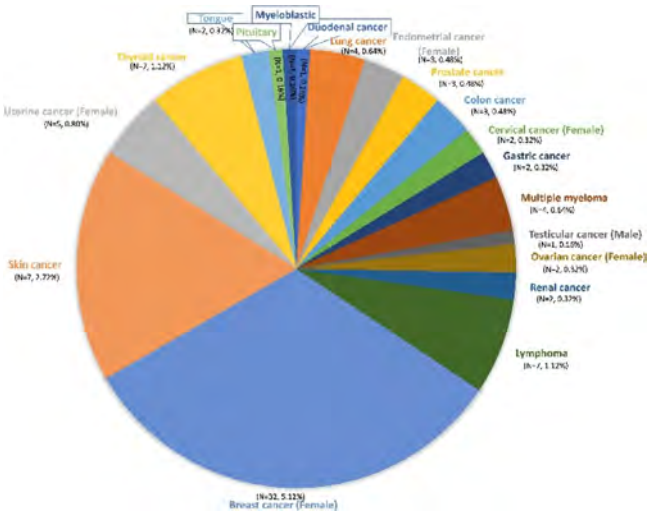

Figure 1. Prevalence of specific malignancies in patients with scleroderma, distributed in a pie chart

immunosuppressant use was associated with higher prevalence of malignancy (OR 2.16, 95% CI 1.36-3.43, P = 0.001) (Figure 2). The multivariable logistic regression showed cancer had statistically significant associations with public insurance (P = 0.01), lack of insurance(P = 0.01), MMF (P< 0.01), and other immunosuppressants (P< 0.01), but not with SSc's time of diagnosis, SSc subtypes, or smoking.

Conclusion: While MMF has been associated with increased malignancy risk in prior studies, this analysis showed a reduced odds of malignancy in participants with SSc treated with mycophenolate. The reason for this unexpected finding is unclear and further studies are warranted to determine if a relationship exists beyond correlation. Lack of health insurance, increasing age and non-MMF immunosuppressant use are associated with increased malignancy risk in this urban, single-center multiethnic SSc cohort. The cancer prevalence in our cohort is similar to prior SSc studies, and higher than the general population.

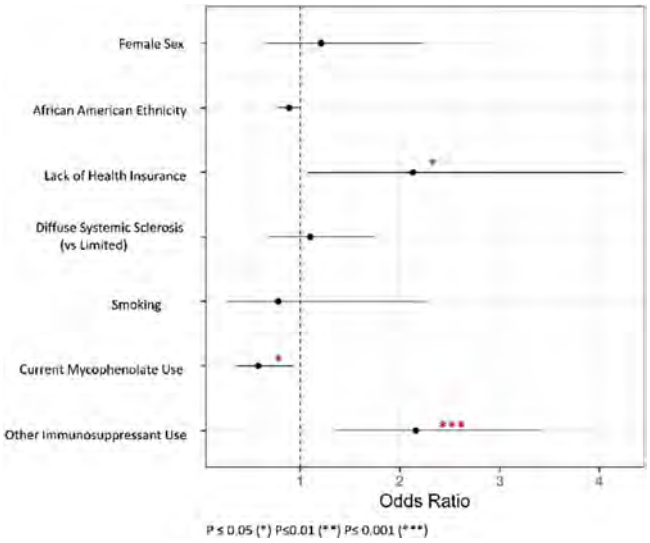

Figure 2. Adjusted odds ratios for patient characteristics vs malignancy

Disclosure: J. Feng: None; **C. Dobrowolski**: None; **C. He**: None; **H. Verma**: None; **R. Vasoya**: None; **D. Qian**: None; **E. olumuyide**: None; **A. Leong**: None; **J. Menand**: None; **M. Bastos Silva**: None; **V. Courant**: None; **S. Lutgen**: None.

Abstract Number: 0672

Risk of New-onset Depression in Patients with Systemic Sclerosis : A Nationwide Population-based Study

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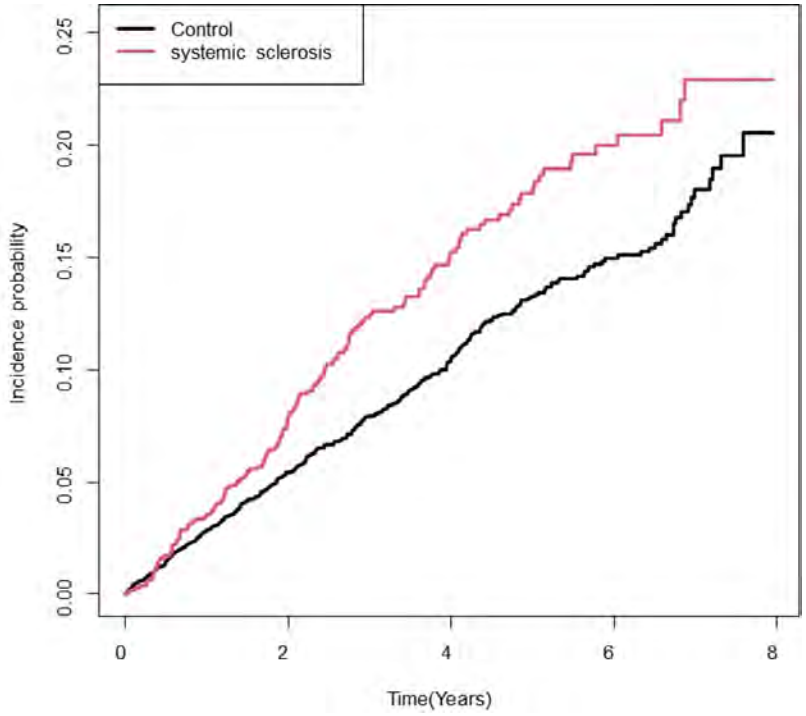
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I: Research
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a rare chronic inflammatory disease characterized by vasculopathy, autoimmunity and progressive fibrosis in various organs. The patients with SSc are suffered from dyspnea, cough, and gradual skin and joint contracture, resulting in significant physical and psychological burden. Psychological symptoms in SSc patients include pain, depression, and concerns about appearance disfigurement. Previous studies have reported that depression is common in SSc patients, ranging from 36% to 65%. However, no study has unveiled the risk of new-onset depression in SSc patients.

The present study was conducted to determine whether SSc is an indeed risk factor for the development of new-onset depression. To determine whether the incidence rate (IR) of new- onset depression in SSc patients is higher than in normal subjects, we used data from a nationwide health care database.

Methods: We selected subjects from National Health Insurance System database who were diagnosed with SSc between 2010 and 2016. Subjects who did not get a general health checkup in the previous 2 years, who were diagnosed with depression before their SSc diagnosis, who were less than 20 years old, or who had missing data were excluded. To minimize the possibility of reverse causality, an analysis with a 1-year lag was performed. Kaplan-Meier analysis was conducted



Incidence of new-onset depression in SSc patients.

to assess the incidence of new-onset depression, and Cox proportional hazards regression was used to calculate adjusted and unadjusted hazard ratio (HR) and 95% CIs. HR for new-onset depression was adjusted for age, sex, smoking, drinking, physical activity, body mass index (BMI), income, diabetes, hypertension, and dyslipidemia.

Results: A total of 1,063 SSc patients (female 82.4 %) and 3,189 age-, sex-matched non-SSc controls with mean (SD) age of 53.1 (10.6) years were included in the analysis. During follow-up periods after 1 year of lag time, the cumulative incidence of new-onset depression was significantly higher in patients with SSc vs controls (38.7 vs. 27.7 IR per 1000 person-years). After adjusting for covariates (age, sex, smoking, drinking, physical activity, BMI, income, diabetes, hypertension, and dyslipidemia), the presence of SSc was associated with 38.1 % increased risk of new-onset depression (HR 1.381; 95% CI, 1.128-1.691), compared with controls. SSc disease itself was determined as an independent risk factor for new-onset depression in subjects with younger age (age < 65 years; HR 1.41; 95% CI 1.122-1.773), female gender (HR 1.415; 95% CI 1.139-1.759), and absence of regular exercise (HR 1.433; 95% CI 1.143-1.795), after adjusting for covariates. Interestingly, the risk of new-onset depression after SSc diagnosis was found to be relatively higher in the low-income group (HR 1.667; 95% CI 1.121-2.479 vs HR 1.303; 95% CI 1.028-1.650).

Conclusion: The present study suggests that the SSc diagnosis is associated with a significantly increased cumulative incidence and risk of new-onset depression. This association is more pronounced in female gender, younger age group, and those who do not exercise regularly. Regular assessment of the occurrence of depressive symptoms should be more emphasized in the patients with SSc after diagnosis.

Subgroup	systemic sclerosis	n	depression	follow-up duration	Incidenc rate per 1000 PY	Model	p for interaction
Age 65							
Age < 65	No	2775	270	11008.56	24.5264	1(Ref.)	0.9706
	Yes	925	120	3463.06	34.6515	1.41(1.122,1.773)	
Age ≥ 65	No	414	77	1508	51.0611	1(Ref.)	
	Yes	138	31	430.27	72.0476	1.263(0.815,1.958)	
SEX							
Male	No	561	45	2298.6	19.5771	1(Ref.)	0.8762
	Yes	187	19	715.68	26.5483	1.222(0.686,2.175)	
Female	No	2628	302	10217.96	29.5558	1(Ref.)	
	Yes	876	132	3177.65	41.5401	1.415(1.139,1.759)	
Low income							
No	No	2466	266	9569.7	27.7961	1(Ref.)	0.2825
	Yes	814	110	3005.93	36.5943	1.303(1.028,1.65)	
Yes	No	723	81	2946.86	27.4869	1(Ref.)	
	Yes	249	41	887.4	46.2025	1.667(1.121,2.479)	
Diabetes							
No	No	2872	306	11331.98	27.0032	1(Ref.)	0.8985
	Yes	967	137	3555.68	38.5298	1.39(1.121,1.723)	
Yes	No	317	41	1184.58	34.6115	1(Ref.)	
	Yes	96	14	337.64	41.4638	1.629(0.867,3.06)	
Hypertension							
No	No	2278	217	8977.04	24.1728	1(Ref.)	0.8475
	Yes	423	51	1504.22	33.9046	1.433(1.055,1.946)	
Yes	No	911	130	3539.52	36.7281	1(Ref.)	
	Yes	640	100	2389.11	41.8566	1.358(1.033,1.785)	
Dyslipidemia							
No	No	2329	242	9368.92	25.8301	1(Ref.)	0.934
	Yes	797	109	2984.89	36.5173	1.38(1.084,1.756)	
Yes	No	860	105	3147.64	33.3583	1(Ref.)	
	Yes	266	42	908.44	46.233	1.418(0.975,2.061)	
Regular Exercise							
No	No	2534	268	9939.82	26.9622	1(Ref.)	0.6179
	Yes	874	124	3179.34	39.0018	1.433(1.143,1.795)	
Yes	No	655	79	2576.74	30.6589	1(Ref.)	
	Yes	189	27	713.99	37.8159	1.219(0.767,1.937)	
CKD							
No	No	3059	326	12014.5	27.1339	1(Ref.)	0.774
	Yes	1003	136	3659.34	37.1652	1.368(1.107,1.69)	
Yes	No	130	21	502.06	41.8276	1(Ref.)	
	Yes	60	15	233.99	64.1056	1.327(0.617,2.854)	
Current smoker							
No	No	2931	326	11447.78	28.4771	1(Ref.)	0.3408
	Yes	981	140	3605.49	38.8297	1.355(1.099,1.671)	
Yes	No	258	21	1068.78	19.6486	1(Ref.)	
	Yes	82	11	287.84	38.2155	2.125(0.943,4.79)	
Drinking							
No	No	2201	254	8578.68	29.6083	1(Ref.)	0.9144
	Yes	753	113	2726.39	41.4467	1.36(1.077,1.718)	
Yes	No	988	93	3937.88	23.6168	1(Ref.)	
	Yes	310	38	1166.93	32.564	1.488(0.993,2.231)	

Incidence rates and hazard ratios for new-onset depression according to covariates in SSc patients.

Disclosure: H. Son: None; **S. Moon**: None.

Abstract Number: 0673

Reporting of Race, Ethnicity, Sex, Gender, Socioeconomic Status and Representativeness of Race and Ethnicity in ANCA-associated Vasculitis Randomized Trials

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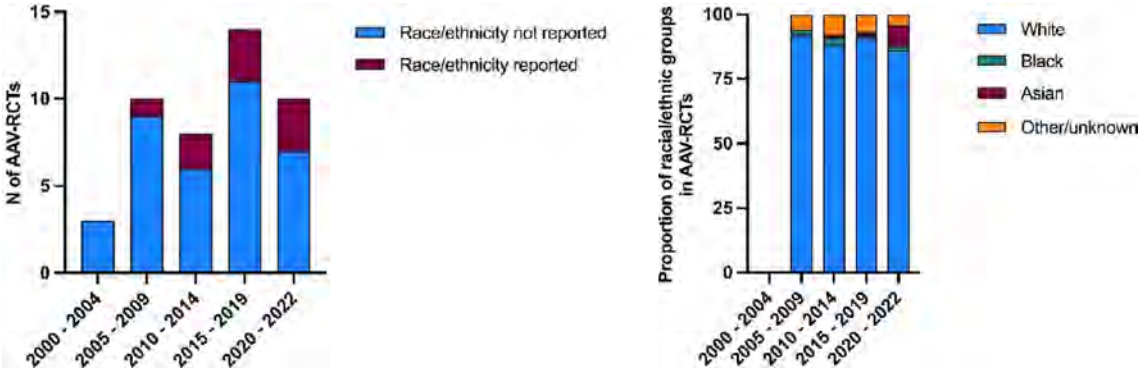
SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: To assess how and to what extent race, ethnicity, sex, gender and socioeconomic status of participants are reported in ANCA-associated vasculitis (AAV) randomized controlled trials (RCTs), and to estimate the representativeness of different ethnic/racial groups in AAV-RCTs.

Methods: We searched all published AAV-RCTs indexed in PubMed and Embase since 2000. We retrieved information on main features of RCTs published from 2000 to 2022 and recorded for each study whether participant race/ethnicity, socioeconomic status (SES) and sex/gender were reported; how ethnicity/race was defined and assigned; the number of patients included for each racial/ethnic group. Descriptive statistics was used to summarize the main study results.

Results: We included 45 studies enrolling a total of 5053 patients (42% recruiting in more than one country), mostly published between 2011 - 2022 (62%), including patients with mainly granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) (68%), and mainly investigating pharmacologic interventions (98%). Information on race/ethnicity was available in 9 (20%) studies, 7 of which published ≥ 2011, including a total of 1445 (28%) patients. Figure 1 (left panel) shows the number of studies reporting race/ethnicity over time. Sex and/or gender of participants was reported in all but one study, but in 33 (73%) studies the authors clearly specified whether they reported the sex or the gender. In univariate analysis, we found a better reporting of race/ethnicity for larger studies including patients from different continents, funded by industry, and being published in higher impact factor journals. In studies where race/ethnicity was reported, White patients were the most represented (90%), followed by Asian (3%) and African American (2%). Figure 1 (right panel)presents temporal trends in the proportion of included participants across racial/ethnic groups in the overall sample of studies. Studies never reported



the reasons for collecting race/ethnicity or subgroup analyses focusing on race/ethnicity. Only one study provided the definitions used to identify different patient's origin. Only one paper reported patient SES.

Conclusion: Reporting of race/ethnicity and socioeconomic status deserves to be improved in AAV-RCTs. The non-White patients are underrepresented in AAV-RCTs reporting race/ethnicity of participants.

Disclosure: M. Iudici: Boehringer-Ingelheim, 1; **J. Rueda**: None; **X. Puéchal**: None.

Abstract Number: 0674

Efficacy and Safety of Mepolizumab During Maintenance Therapy in Patients with Eosinophilic Granulomatosis with Polyangiitis

Daiki Sakai[1], Kaichi Kaneko[1], Karin Furukawa[2], Mai Kawazoe[2], Yasuo Matsuzawa[3] and Toshihiro Nanki[2], [1]Division of Rheumatology, Department of Internal Medicine, Toho University Sakura Medical Center, Sakura, Japan, [2]Division of Rheumatology, Department of Internal Medicine, Toho University School of Medicine, Ota-ku, Japan, [3]Division of Respiratory Medicine, Department of Internal Medicine, Toho University Sakura Medical Center, Sakura, Japan

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA) is a small-vessel vasculitis characterized by asthma, hyper-eosinophilia, and progressive multiorgan organ involvement. Mepolizumab (MPZ) is a humanized monoclonal anti-interleukin-5 antibody that can reduce peripheral blood eosinophil. Previous studies demonstrated the efficacy and safety of MPZ for induction of remission in patients with relapsing or refractory EGPA, but the efficacy of MPZ during maintenance therapy in patients with EGPA remains unclear. This study is to clarify the efficacy and safety of MPZ during maintenance therapy compared with standard therapy for improving disease activity, preventing relapse, and reducing glucocorticoid (GC) dose.

Methods: This was a retrospective observational study. This study was approved by the Ethics Committees at Toho University School of Medicine (approval number; A22065). Patients, diagnosed with EGPA and treated at Toho University Sakura or Omori Medical Center between January 2016 and June 2022, were included if they met all of the following criteria:

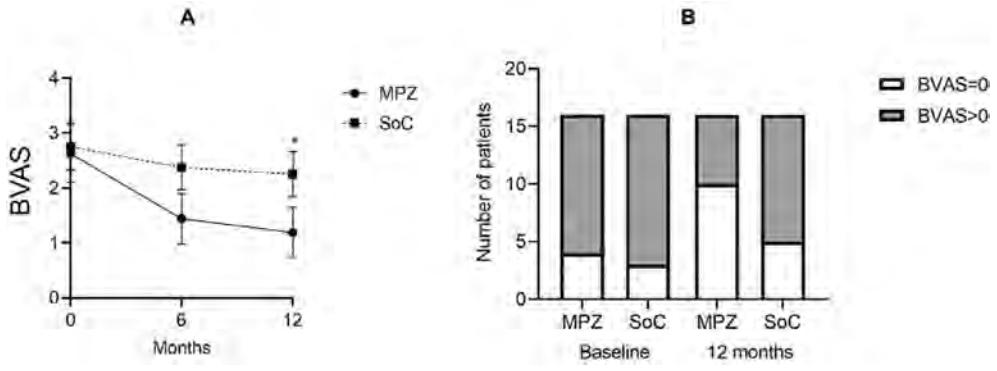


Figure1. Comparison of changes of BVAS between 12 months period in MPZ and SoC groups. A Changes in BVAS over 12 months, B Percentage of patients achieving BVAS = 0 at baseline and 12 months. BVAS; Birmingham Vasculitis Activity Score, MPZ; Mepolizumab, SoC; standard-of-care

prednisolone ≤ 20 mg/day, Birmingham Vasculitis Activity Score (BVAS) < 10 and administration of MPZ or immunosuppressants after 6 months or more from the onset of EGPA. Participants comprised patients with EGPA on MPZ (MPZ group: n = 16) and those on immunosuppressants (standard-of-care [SoC] group: n= 16). Disease activity was evaluated by BVAS as an index of disease activity and a predictor of the prognosis and outcome in patients with EGPA. GC toxicity was evaluated by GC toxicity index (GTI). We investigated BVAS, MPZ retention rate, absolute eosinophil count, cumulative GC dose and GTI after 12 months of MPZ or other immunosuppressant treatment in patients with EGPA.

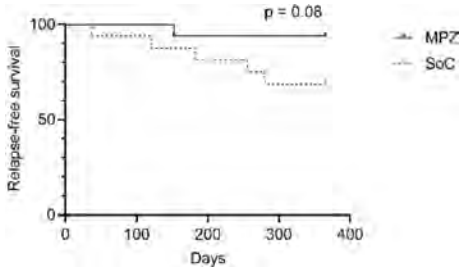


Figure 2. Relapse-free survival in MPZ and SoC groups. MPZ; Mepolizumab, SoC; standard-of-care

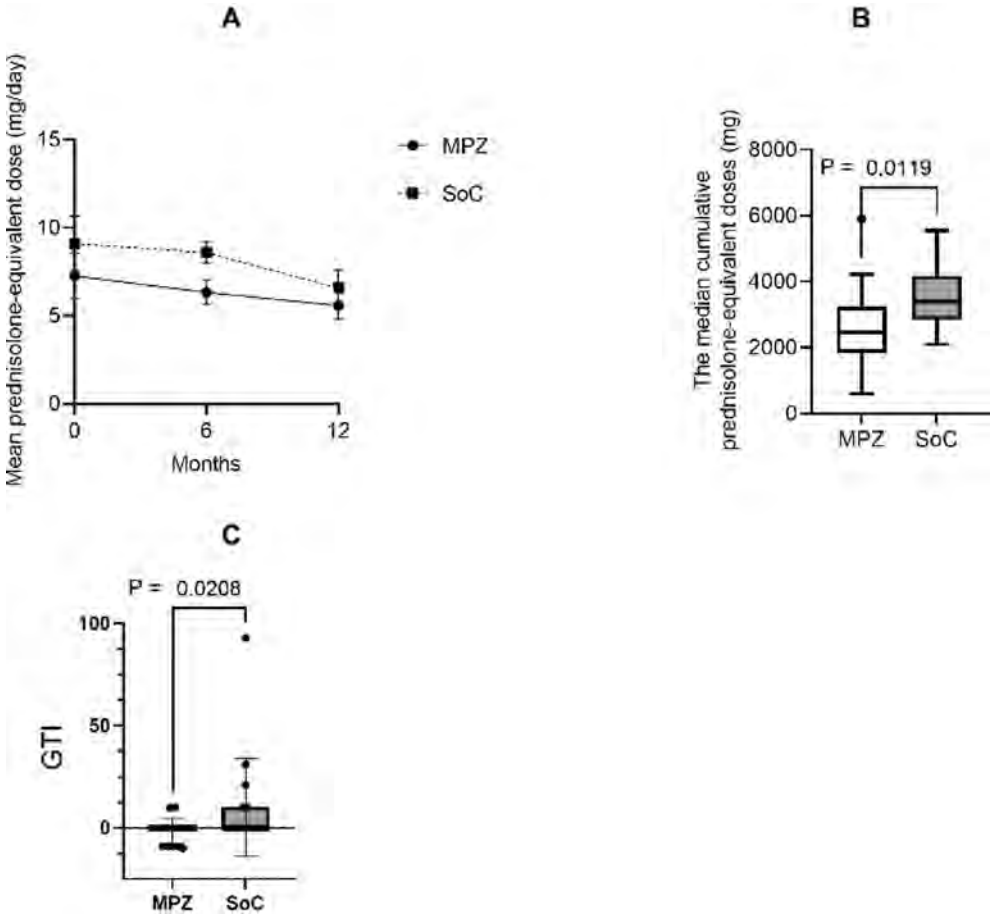


Figure3. Comparison of changes in glucocorticoid dose and GTI over 12 months period in MPZ and SoC groups. A. Changes in glucocorticoid dose over 12 months, B. Cumulative glucocorticoid dose at 12 months, C. GTI at 12 months. GTI; Glucocorticoid toxicity index, MPZ; Mepolizumab, SoC; standard-of-care

Results: There were no statistically significant differences in age, BMI, CRP, MPO-ANCA, IgE and CRP and BVAS between two groups at baseline. The median disease duration of MPZ group was significantly longer than that of SoC group [46.5 (22.5-122.8) months, 11.0 (3.2-29.0) months, P = 0.001]. The median absolute eosinophil count in MPZ group was significantly higher than that in SoC group [596.0 (114.5-784.2) /μL, 134.6 (2.0-262.1) /μL, P = 0.0034]. No significant differences were observed in the concomitant GC dose or the rate of concomitant immunosuppressant use between the groups. The BVAS at 12 months after treatment was significantly lower in MPZ group than in SoC group (P = 0.0367) (Figure 1). Percentage of patients achieving BVAS = 0 at 12 months tended to be higher in MPZ group than in SoC group. Relapse rates tended to be lower in the MPZ group (1 patient) than in the SoC group (6 patients) (P = 0.08) (Figure 2). Cumulative GC dose at 12 months were significantly decreased in the MPZ group than in the SoC group [2452 (1825-3256) mg, 3384 (2840-4179) mg, P = 0.0356] (Figure 3). The GTI at 52 weeks was significantly lower in the MPZ group than in the SoC group [0.0 (-9.0-0.0), 0.0 (0.0-10.0), P = 0.0208].

Conclusion: Our study demonstrated that administration of MPZ to EGPA during maintenance therapy reduced disease activity and relapse rates. MPZ in EGPA maintenance therapy may also have the potential to reduce cumulative GC dosage and GC toxicity.

Disclosure: D. Sakai: None; **K. Kaneko**: AbbVie/Abbott, 6, AstraZeneca, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, Gilead, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, Novartis, 6, Pfizer, 6, UCB, 6; **K. Furukawa**: None; **M. Kawazoe**: Asahi Kasei Pharma Corp, 6, AstraZeneca, 6, Ayumi Pharmaceutical Corporation, 6, GlaxoSmithKlein(GSK), 6; **Y. Matsuzawa**: AstraZeneca, 6, Boehringer-Ingelheim, 6, Eli Lilly, 6, GlaxoSmithKlein(-GSK), 6, Janssen, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6; **T. Nanki**: AbbVie GK, 5, 6, Asahikasei Pharma Corp., 5, 6, Astellas Pharma Inc., 6, AstraZeneca K.K., 6, Ayumi Pharmaceutical Co., 5, 6, Bristol-Myers Squibb K.K., 5, Chugai Pharmaceutical Co., 2, 5, 6, Eisai Co.,Ltd., 5, 6, Eli Lilly Japan K.K., 5, 6, GlaxoSmithKline plc., 6, Janssen Pharmaceutical K.K., 6, Mitsubishi-Tanabe Pharma Co., 5, 6, Mochida Pharmaceutical Co., Ltd., 5, 6, Nippon Boehringer Ingelheim Co., Ltd., 5, 6, Nippon Kayaku Co., Ltd., 5, Ono Pharmaceutical Co., Ltd., 5, 6, Pfizer Japan Inc., 6, Shionogi & Co., Ltd., 5, Taisho Pharmaceutical Co.,Ltd., 5, Takeda Pharmaceutical Co., Ltd., 6, Teijin Pharma Ltd., 5, UCB Japan Co. Ltd., 1, 6.

Abstract Number: 0675

Investigating the Impact of anti-IL5 Therapy in the Management of Relapsing and Refractory Eosinophilic Granulomatosis with Polyangiitis (EGPA); A Three Year Longitudinal Perspective and Beyond

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In the randomized, placebo-controlled MIRRA trial for relapsing and refractory eosinophilic granulomatosis with polyangiitis (EGPA), adjuvant therapy with 300mg anti-IL5 mAB Mepolizumab [MEPO] for 12 months (M), accrued longer times in remission, reduced steroid exposure and reduced relapse rates[2]. The aim of this study is to analyze

the outcome of 100mg MEPO monthly s/c for a minimum of 36 months. Changes to adjuvant immunosuppression and indications for anti-IL5 class switch from MEPO 100mg s/c to Benralizumab (BRZ) or Reslizumab (Res) were assessed.

Methods: In this observational study, 20 EGPA patients received anti-IL5 therapy for a minimum of 36M (range 49-68M). All commenced on 100mg s/c MEPO every four weeks. Anti-IL5 therapy switched to BRZ or Res due to partial response or intolerance. Assessment time points included MEPO commencement, 6, 12, 18, 24 and 36 months.

Results: Overall, there was a 50% reduction in steroid usage by 12 months. This continued to reduce to 24M, by which time 2 were off steroids and further 10 on weaning dose ≤ 5mg. Mean steroid dosage continued to decreased to 36 months. The number on adjuvant conventional immunosuppressants (ACIS), reduced over time from 10 at M0 to 4 by M24. Clinical benefits included ANCA serology normalized in all four positive patients by 12 months. Mean eosinophil count reduced from 0.42mg ±0.33 $X10^9$/L at M0 to 0.04±0.03 $X10^9$/L at 12 and 24M. BVAS reduced from median 5 [3-7], to 0 [0-1] by 24M. The change in mean FEV1 over 12 months was from (M0) 2.11±0.66 to (M12) 2.39±0.62 and FVC (M0) 3.42±0.87 to (M12) 3.67±0.93/105.60±20.47 respectively.

All 20 EGPA patients receiving anti -IL5 therapy, ranging from 49-68M remain on therapy. At 36M, 9 have remained on 100mg s/c MEPO. 10 (50%) have switched to an altenative anti-IL5 agent - 10 switched to benralizumab, 1 initially on benralizumab to reslizumab. 9/10 had achieved partial response prior to switch (reduction in steroids / relapse rate), 1/10 had no response. During the duration of the study,3 patients had a break of therapy, but all resumed anti-IL5 treatment with good response. Hence, all 20 remain on anti-IL5 beyond 24M. After 36M, one patient required cyclophosphamide along with anti-IL5 therapy for myocarditis. A further patient had Rituximab for EGPA/ Rheumatoid arthritis overlap between anti-IL5 agents.

Conclusion: In this study, there was a 50% reduction in steroid dosage by 12 months and steroid requirements continue to decrease to 36M. By 24 months 2 are steroid free and a further 10 on weaning dose ≤ 5mg. Furthermore, the number on adjuvant conventional immunosuppression reduced over the 24M (n=4 at 24M). This study demonstrates that anti-IL5 therapy serves as a favorable model for steroid and conventional immunosuppressant minimization in EGPA. Clinical benefits of reduction in BVAS, improved pulmonary function tests and reduced serum eosinophilia were recorded. The relapsing nature of EGPA places a dependency of therapy on steroids and this study demonstrated sustained and ongoing improvement annually with continued anti-IL5 therapy. Some participants required a switch in anti-IL5 agent.

Disclosure: a. egan: AstraZeneca, 1; **P. Sivasothy**: None; **D. Jayne**: AstraZeneca, 2, Aurinia, 4, Boehringer Ingelheim, 2, Chinook, 2, CSL Vifor, 2, Roche, 2.

Abstract Number: 0676

Mepolizumab Can Achieve Glucocorticoid Discontinuation in Eosinophilic Granulomatosis with Polyangiitis Patients Regardless of IgE Levels: A Retrospective Study at a Single Center

Takashi Yamane[1] and Akira Hashiramoto[2], [1]Kakogawa Central City Hospital, Kakogawa, Japan, [2]Kobe University Graduate School of Health Sciences, Kobe, Japan

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes
Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA) is a systemic vasculitis associated with eosinophil infiltration and Anti-neutrophil cytoplasmic antibody (ANCA) production. Mepolizumab (MPZ), an anti-IL-5 monoclonal antibody, facilitates good disease control, but the evidence for glucocorticoid (GC) discontinuation is still insufficient. In daily clinical practice, IgE levels along with peripheral blood eosinophil counts, ESR and CRP levels are used to evaluate disease activity, but they are limited in their ability to predict disease recurrence. In this study, we investigated the significance of IgE levels in the process of reducing or discontinuing GC in patients with EGPA.

Methods: Patients with EGPA at Kakogawa Central City Hospital as of January 2023 were classified into two groups: IgE high (>232IU/ml) and IgE low (≤232IU/ml) at the start of MPZ. The diagnosis of EGPA was based on the 1990 American College of Rheumatology criteria. The differences in patient backgrounds were examined by IgE, eosinophil count, Birmingham Vasculitis Activity Score (BVAS), daily prednisolone (PSL) dose and Vascular Damage Index (VDI). The rate of GC discontinuation and disease relapse were also examined. Statistical analysis was performed using SPSS version 26 (IBM Corp, Armonk, NY, USA), and P< 0.05 was considered significant.

Results: 27 patients had received MPZ for median 34 months. Patient background at the initiation of MPZ was median 59 years and 11 female (41%), disease duration was median 3 years (Table1). The eosinophil count was median 432/μl, CRP 0.06mg/dl, IgE 128 IU/mL, and 11 patients (41%) were in IgE high group. When compared the IgE levels at the initiation of MPZ, patients with high IgE were significantly younger. In addition, eosinophil counts were significantly higher in patients

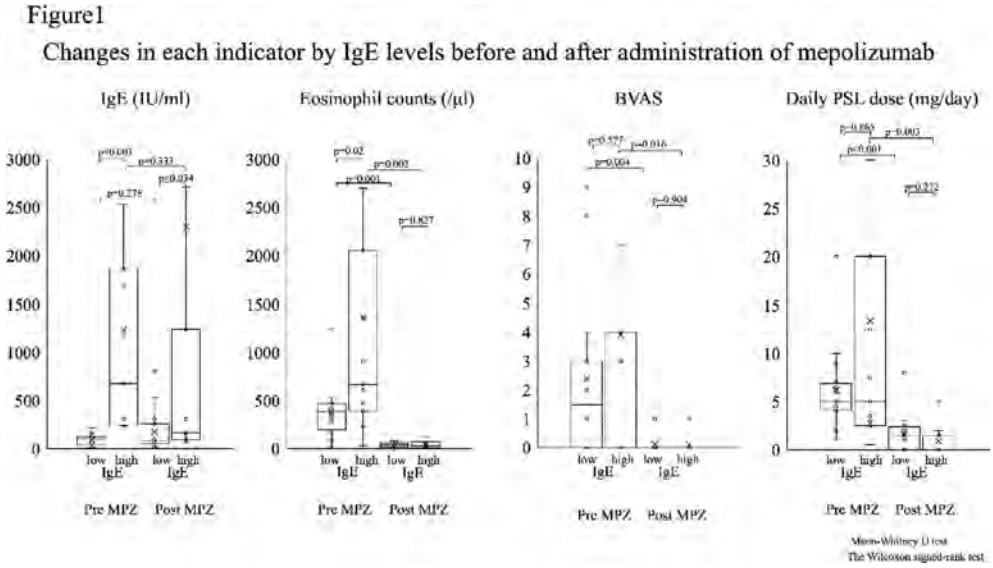
Table1 Patient background at the time of mepolizumab initiation

	N=27
Age (years), median (IQR)	59 (5-70)
Female sex, n (%)	12 (41)
Disease duration (years), median (IQR)	3 (2-6.5)
ANCA positive status, n (%)	10 (37) ((MPO-ANCA9 (33), PR3-ANCA1 (4))
Absolute eosinophil counts (/μl), median (IQR)	431 (332-670)
CRP (mg/dL), median (IQR)	0.06 (0.02-0.16)
IgE (IU/mL), median (IQR)	128 (95-306)
FFS (score), median (IQR)	1 (1-1)
0, n (%)	6 (22)
1, n (%)	16 (59)
2, n (%)	5 (19)
BVAS, median (IQR)	7 (5-8.5)
Daily prednisolone dosage (mg), median (IQR)	5 (3.1-7.5)
Concomitant immunosuppressive maintenance therapy, n (%)	18 (67)
Azathioprine, n (%)	8 (44)
Mycophenolate mofetil, n (%)	5 (28)
History of GC pulse therapy, n (%)	13 (48)
History of Immunosuppressive induction therapy, n (%)	12 (44)
History of relapses, n (%)	8 (28)

Table2 Patient background by IgE level at the time of mepolizumab initiation

	IgE >232IU/ml N=11	IgE ≤232IU/ml N=16	*P*-value
Age (years), median (IQR)	50 (28-56)	62.5 (53.4-66.0)	0.013
Female sex, n (%)	4 (36)	7 (44)	0.701
Absolute eosinophil counts (/μl), median (IQR)	670 (434-1709)	388 (245-457)	0.020
CRP (mg/dL), median (IQR)	0.09 (0.04-0.25)	0.04 (0.02-0.09)	0.251
IgE (IU/mL), median (IQR)	675 (256-1774)	100 (38-123)	<0.001
ANCA positive status, n (%)	3 (27)	7 (44)	0.384
Disease duration (years), median (IQR)	12 (2.4-66)	12 (12-42)	0.790
Daily prednisolone dosage (mg), median (IQR)	5 (2.8-16.2)	5 (4.4-6.6)	0.865
Concomitant immunosuppressive maintenance therapy, n (%)	5 (45)	15 (94)	0.009
Azathioprine, n (%)	1 (9)	7 (44)	0.090
Mycofenolate mofetil, n (%)	1 (9)	5 (31)	0.350
History of GC pulse therpy, n (%)	6 (55)	7 (44)	0.581
History of Immunosuppressive induction therapy, n (%)	7 (64)	8 (50)	0.484
History of relapses, n (%)	1 (9)	6 (38)	0.183

Mann-Whitney U test Fisher's exact test Pearson's chi-test



without concomitant immunosuppressive drugs (Table 2). After MPZ initiation, eosinophil counts, BVAS and the daily PSL dose were significantly reduced in both groups while IgE levels did not change at all (Figure 1). Significant improvement in VDI was observed in patients with low IgE. GC discontinuation was achieved in 7 patients (64%) in the high IgE group and 6 (38%) in the low IgE group (p=0.182), and patients who achieved GC discontinuation had no disease relapse during a median follow-up of 19 months.1 patient with low IgE experienced a disease flare-up, which subsequently went into remission with continued administration of MPZ.

Conclusion: Although there is a limitation of single center retrospective data, more than half of the EGPA patients were able to discontinue GCs after approximately 3 years of treatment with MPZ. Notably, IgE levels did not appear to affect the reduction in GC or the achievement of GC discontinuation.

Disclosure: T. Yamane: GlaxoSmithKlein(GSK), 6; **A. Hashiramoto**: Eli Lilly, 5.

Abstract Number: 0677

Analysis of Clinical Outcomes in Eosinophilic Granulomatosis with Polyangiitis (EGPA) Treated with Mepolizumab over 2 Years for Remission Induction or Maintenance: A Single Center Experience in Japan

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Contrary to Western countries, MPO-ANCA-associated vasculitis (MPO-AAV) is dominant in Japan or Asian countries. It is possible that therapeutic responses to EGPA with mepolizumab (MPZ) are different in Asian countries. In addition, there have been few reports on the course of long-term treatment of EGPA with MPZ. We conducted a

retrospective analysis of the clinical database of the 25 patients of EGPA treated with MPZ in our hospital for remission induction or remission maintenance.

Methods: Twenty-five EGPA patients [19 females and 6 males. 11 MPO-ANCA positive and 14 MPO-negative.] have been treated with MPZ and followed for at least two years since 2018 in the department of Nephrology and Rheumatology in Kyorin University Hospital. They were analysed for clinical courses, including dose of administered corticosteroids (GC) and rates of flare-up. Remission was defined as Birmingham Vasculitis Activity Score (BVAS) was 0. Disease flare-up was defined as a state the disease activity increased and required intensification of immunosuppressive therapy.

They were divided into patients who were administered MPZ within 3 months of onset (early administration group) and who were started administration of MPZ during maintenance therapy at least 3 months after onset (during maintenance group).

Results: Of the 25 patients administered MPZ, 6 patients were categorized as the early administration group (1 male and 5 females; 4 patients were ANCA-positive and 2 patients were ANCA-negative) and the other 19 patients were categorized as the during maintenance group (5 males and 14 females; 7 patients were ANCA-positive and 12 patients were ANCA-negative). Mean ages at onset of groups of the early administration and the during maintenance were 52.2 and 55.0 years old, respectively.

In addition to GC and MPZ, cyclophosphamide (CY) was used in 17% (1/6) of the early group and in 53% (10/19) of the maintenance group.

After two years of therapy, mean doses of GC of each group were 1.7±2.1mg/day and 3.6±2.7mg/day, respectively. The achievement rates of GC dose below 5mg/day after two years treatment of the early group and the maintenance group were 100% and 47% (9/19), respectively. While no flare-up was observed in the early group, 26% (5/19) of the maintenance group developed flare-up after the start of MPZ therapy. These results were similar regardless of ANCA positivity. The incidence of serious infections requiring hospitalization and death after starting MPZ were 0 in both groups.

Conclusion: These results showed that long-term use of MPZ was effective and had an acceptable safety profile in EGPA patients. The use of MPZ from early stage might be recommended because the start of MPZ within 3 months of onset might reduce the dose of GCs after two years of therapy and the flare-up rate.

Disclosure: S. KAWASHIMA: None; **Y. Komagata**: None; **M. Kishimoto**: AbbVie, 2, 6, Amgen, 2, 6, Asahi-Kasei Pharma, 2, 6, Astellas, 2, 6, Ayumi Pharma, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Chugai, 2, 6, Daiichi-Sankyo, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Ono Pharma, 2, 6, Pfizer, 2, 6, Tanabe-Mitsubishi, 2, 6, UCB, 2, 6; **S. Kaname**: None.

Abstract Number: 0678

Benralizumab in Eosinophilic Granulomatosis with Polyangiitis

Adrien Cottu[1], Matthieu Groh[2], Charlène Desaintjean[3], Sylvain Marchand-Adam[4], Loic Guillevin[5], Xavier Puéchal[6], Estibaliz Lazaro[7], Maxime Samson[8], Camille Taillé[9], Cécile-Audrey Durel[10], Elisabeth Diot[11], Sarah Nicolas[11], Laurent Guilleminault[12], Mikael Ebbo[13], Pascal Cathébras[14], Clairelyne Dupin[9], Halil Yildiz[15], Nabil Belfeki[16], Gregory Pugnet[17], Pierre Chauvin[18], Stephane Jouneau[19], François Lifermann[20], Jean-Philippe Martellosio[21], Vincent Cottin[22] and Benjamin Terrier[23], [1]Department of Internal Medicine, Hôpital Cochin, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France, [2]National Referral Center for Hypereosinophilic Syndrome (CEREO), Hôpital Foch, Suresnes, France, [3]Department of Respiratory Diseases, Hôpital Louis Pradel, Lyon, France, [4]CHRU Tours, service de pneumologie et d'explorations fonctionnelles respiratoires, Tours, France, [5]University Paris Descartes, Paris, France, [6]National Referral Center for Rare Systemic Autoimmune Diseases, Paris, France, [7]Bordeaux Hospital University, Pessac, France,

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

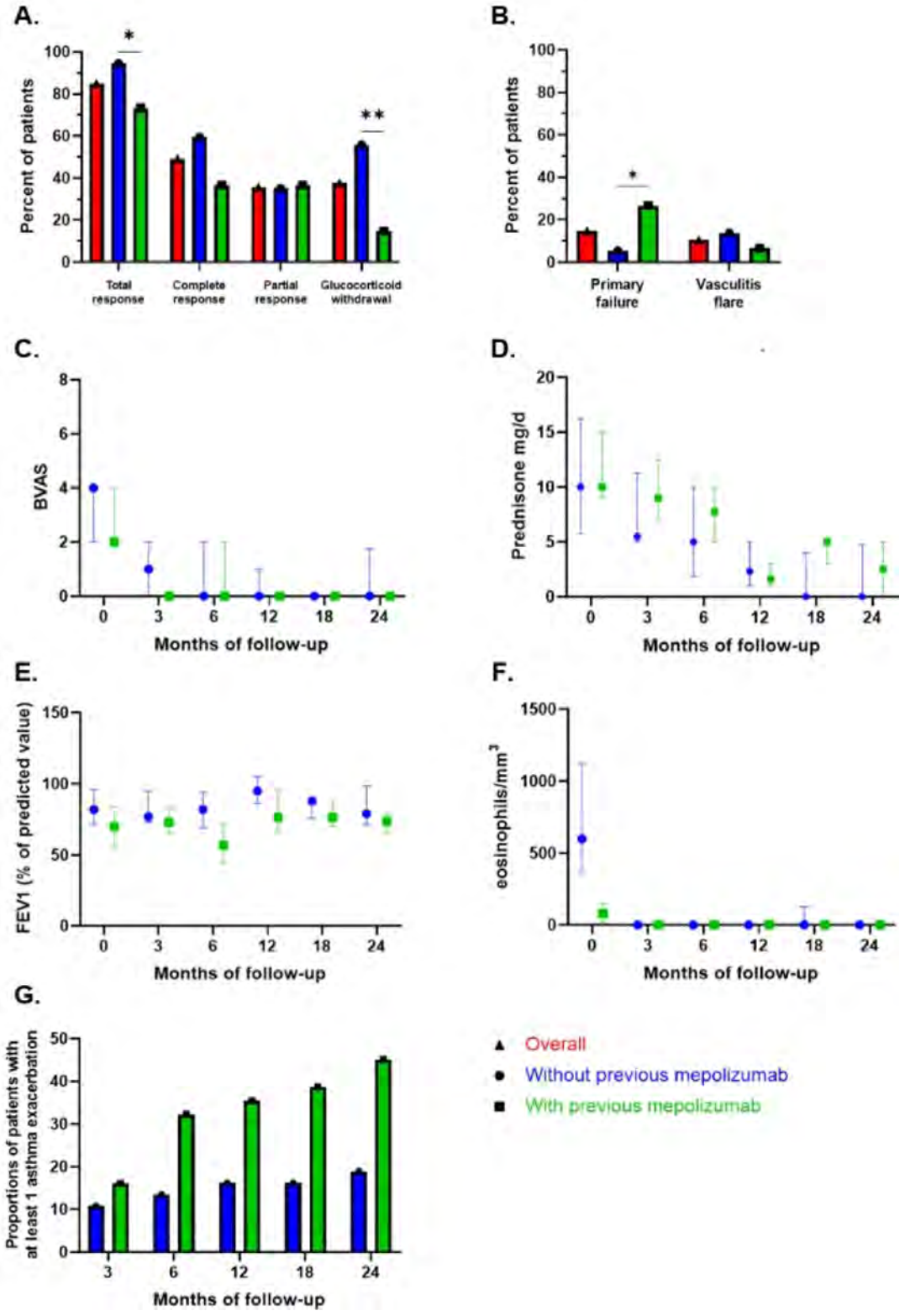
Background/Purpose: Gucocorticoid (GC)-dependant asthma and ENT exacerbations may persist in more than 80% of eosinophilic granulomatosis with polyangiitis (EGPA). The MIRRA trial demonstrated the efficacy of mepolizumab, a monoclonal antibody targeting interleukin-5 (IL-5), in treating these manifestations. However, roughly 70% of patients still required more than 4 mg per day of prednisone at the end of follow-up or relapsed. Benralizumab, a monoclonal-antibody targeting IL-5 receptor, causes profound eosinophil depletion in plasma, sputum, and tissues. However, its efficacy in GC-dependent manifestations remains to be determined in EGPA. We aimed to describe the use and efficacy of benralizumab in patients with refractory manifestations of EGPA.

Methods: We conducted a multicentre, retrospective study of patients with EGPA according to ACR/EULAR 2022 criteria and treated with benralizumab between February 2019 and February 2023. Complete response was defined as no disease activity (BVAS=0) and a prednisone dose ≤4 mg/day. Partial response was defined as no disease activity and a prednisone dose ≥4 mg/day. Total response was defined by either complete or partial response. Comparisons between patients with and without prior mepolizumab therapy were made using the Fisher exact test and the Mann Whitney test. Comparisons of responses or time to vasculitis flares were made with log-rank test.

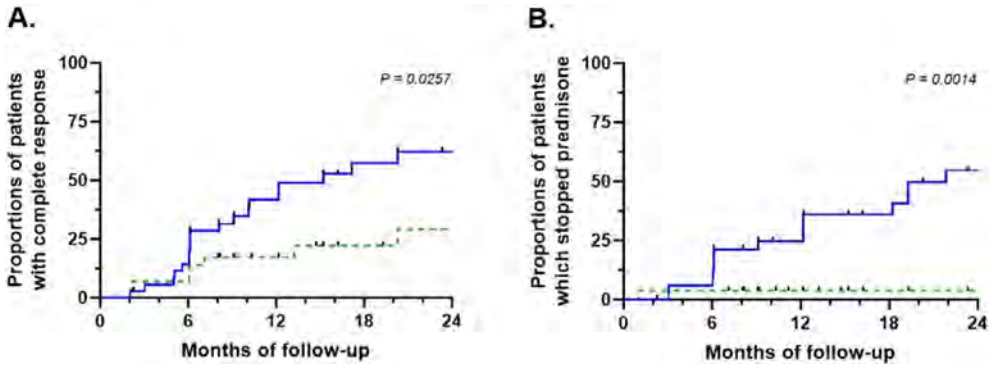
Results: Sixty-eight patients were included. The median age was 50 (IQR 39-63) years. ANCA were positive in 20 (29%) patients at EGPA diagnosis. Thirty-one patients (46%) had previously received mepolizumab, at a dose of 100 mg/month in 18/26 (69%) and 300 mg/month in 8/26 (31%). Primary or secondary failure of mepolizumab accounted for 16 patients (52%) and 15 patients (48%). The use of benralizumab was justified by uncontrolled asthma in 54 (81%), uncontrolled ENT manifestations in 27 (40%) and persistent glucocorticoid use in 48 (74%) patients. The asthma regimen (30 mg/month 3 times then every 2 months) was used in 63/66 patients (95%). Sixteen patients (24%) were concomitantly treated with another immunosuppressant.

Median follow-up after initiation of benralizumab was 23 months (IQR 9-34). Thirty-three patients (49%) had a complete response, 24 (36%) had a partial response and 10 (15%) failed to respond (response assessed in 67 patients). Of 57 patients with at least a partial initial response, 10 (18%) experienced secondary failure. GCs were discontinued in 23 patients (38%). Prior mepolizumab use was associated with more primary failure (p=0.034) and less GC discontinuation (p=0.001).

Vasculitis flares occurred in 7 patients (11%) and were associated with histological evidence of vasculitis and/or ANCA positivity at benralizumab initiation (p=0.010). Six infections requiring specific treatments were reported during follow-up.



Response to benralizumab (A) and failure to benralizumab (B) among patients with eosinophilic granulomatosis with polyangiitis, according to previous treatment by mepolizumab. Variation in disease activity using the Birmingham Vasculitis Activity Score (BVAS) (C), daily dose of prednisone (D), variation in the forced expiratory volume in 1 second (FEV1) (E) and eosinophils count (F) among patients with eosinophilic granulomatosis with polyangiitis treated with benralizumab, according to previous treatment by mepolizumab. Accumulated proportions of patient with at least one asthma exacerbations during follow-up (G). Values in C, D, E, and F are the median and interquartile range. IS = immunosuppressant; * = $P < 0.05$; ** = $P < 0.01$ (Fisher exact test).



Kaplan-Meier survival curve of complete response (A) and withdrawal of glucocorticoids (B) among patients with eosinophilic granulomatosis with polyangiitis treated with benralizumab, according to previous treatment by mepolizumab. Blue full line = without previous mepolizumab; green dotted line = with previous mepolizumab. (Logrank test)

Conclusion: Benralizumab appears to be an effective treatment for refractory asthma or ENT manifestations in EGPA and allows glucocorticoid withdrawal. However, its efficacy was lower after prior mepolizumab failure.

Disclosure: A. Cottu: None; **M. Groh**: AstraZeneca, 6, GSK, 6, Sanofi, 6; **C. Desaintjean**: None; **S. Marchand-Adam**: None; **L. Guillevin**: None; **X. Puéchal**: None; **E. Lazaro**: None; **M. Samson**: ARGENX, 2, Boehringer-Ingelheim, 2, CHUGAI, 2, CSL Vifor, 2, GlaxoSmithKlein(GSK), 2, NOVARTIS, 2, 5; **C. Taillé**: AstraZeneca, 6, Chiesi, 5, 6, GSK, 5, 6, Novartis, 5, 6, Sanofi, 6; **C. Durel**: None; **E. Diot**: None; **S. Nicolas**: None; **L. Guilleminault**: None; **M. Ebbo**: None; **P. Cathébras**: None; **C. Dupin**: AstraZeneca, 6, GSK, 6; **H. Yildiz**: GSK, 6; **N. Belfeki**: None; **G. Pugnet**: None; **P. Chauvin**: None; **S. Jouneau**: None; **F. Lifermann**: None; **J. Martellosio**: None; **V. Cottin**: Boehringer Ingelheim, 2, 5, 6, 12, Support for attending meetings, Celgene/BMS, 1, 2, CSL Behring, 2, Ferrer, 2, 6, 12, Support for attending meetings, FibroGen, 1, Galapagos, 1, 2, Galecto, 1, GlaxoSmithKline, 2, Pliant, 2, Pure Tech, 2, Redx, 2, Roche, 1, 2, 6, 12, Support for attending meetings, Sanofi, 2, Shionogi, 2; **B. Terrier**: AstraZeneca, 5, CSL Vifor, 2, GlaxoSmithKlein(GSK), 2.

Abstract Number: 0679

Long-term Safety of Rituximab (Mabthera) in Granulomatosis with Polyangiitis (GPA) or Microscopic Polyangiitis (MPA): Rituximab Surveillance Study in VASculitis (RIVAS)

Lisa Uchida[1], Dr Rachel Jones[2], Rona Smith[1], Claudia Loechel[3], Maria King[3], Marianna Nodale[4], Simon Bond[4], Raashid Luqmani[5], David Gray[5], Joe Barrett[5] and David Jayne[6], [1]Department of Medicine, University of Cambridge, Cambridge, United Kingdom, [2]Vasculitis and Lupus Clinic, Addenbrooke's Hospital, Cambridge, United Kingdom, [3]Vasculitis and Lupus Clinic, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom, [4]Cambridge Clinical Trials Unit, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom, [5]Nuffield Department of Orthopedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom, [6]University of Cambridge, Cambridge, United Kingdom

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Rituximab is a first-line treatment for remission induction and the prevention of relapse in ANCA-associated vasculitis (AAV). There is a paucity of real-world data on the long-term safety of rituximab in patients with AAV. This study aimed to estimate the incidence of safety events and to compare time to first SAE between a rituximab cohort and a cohort treated with non-rituximab therapy up to 15 years from first exposure.

Methods: RIVAS was a single-center, retrospective observational study including patients with GPA/MPA who had received rituximab (MabThera) or other treatments between 2003 and 2017 at Addenbrooke's hospital, Cambridge, UK followed up until 30 September 2018. Time 0 was defined as either initiation of MabThera treatment for the rituximab cohort or time of first disease flare/diagnosis for the control cohort. The primary endpoint was time to first SAE. Key secondary endpoints were time to first pre-categorized SAE including serious infection and cardiovascular disorder. Time to second SAE was an exploratory endpoint.

Results: 392 GPA/MPA patients were enrolled: 247 in the rituximab and 145 in the control cohort with a total of 2,217 person-years (mean study duration 5.7 years). Mean age was 61 years (SD 16.3), 52% were female, 77% had GPA and 23% MPA. The median disease duration at baseline was 25.0 months (range: 0-393.7) in the rituximab and 1.6 months (range: 0-272.6) in the control arm. There were differences in the baseline characteristics between groups reflecting the predominant use of rituximab for relapsing or refractory disease. Three hundred and eighty-six SAEs occurred in 134 patients (54%) in the rituximab and 114 in 58 patients (40%) in the control groups (Table 1). Sixty-five patients (26%) in the rituximab group and 18 (12%) in the control group experienced serious infections. Twenty-one patients (9%) in the rituximab group developed severe hypogammaglobulinemia (IgG < 3 g/L) requiring change of treatment and 19 (8%) received immunoglobulin replacement for hypogammaglobulinemia compared to 3 (2%) and 1 (0.7%) of patients in the control group. There were no differences in incidence rates for malignancy, cardiovascular events or renal insufficiency between groups. Time to first SAE was shorter in the rituximab group than in the control group (HR 1.55, 95%CI 1.07-2.26, p=0.022) (Figure 1). Time to first serious infection was shorter in the rituximab group (HR 2.34, 95%CI 1.079-5.07, p=0.031), while no between-group differences were found for other SAE categories. Also, a shorter time to second SAE was observed in the rituximab group. Predictors of first SAE were higher vasculitis damage scores and chronic pulmonary or kidney disease. The relative risk of serious infection and additional safety events was higher in the rituximab group (unadjusted relative risk (RR) 2.12, 95%CI 1.31-3.43; RR 1.86, 95%CI 1.30-2.65, respectively).

Conclusion: Over 40% of patients with GPA/MPA experienced at least one SAE in their disease course. Although the risk of first and second SAE was higher in the rituximab group, baseline imbalances, particularly in disease duration and prior immunosuppressive use, due to the study design were a cause of bias and results should be interpreted with caution.

Table 1. Serious adverse events (SAEs) by event category for rituximab and control groups

Event type	Events (n)/ Patients (n (%)) Rituximab	Events (n)/ Patients (n (%)) Control
All SAEs	386/ 134 (54%)	114/ 58 (40%)
Serious infection	121/ 65 (26%)	28/ 18 (12%)
Cardiovascular disorder	28/ 23 (9%)	17/ 15 (10%)
Hematological events	9/ 8 (3%)	2/ 2 (1%)
Malignant events	11/ 11 (4%)	8/ 8 (6%)
Renal Insufficiency	19/ 14 (6%)	19/ 15 (10%)
PML	1/ 1 (0.4%)	0/ 0 (0%)
Additional safety events*	197/ 95 (38%)	40/ 30 (21%)

*This category includes 'Any other SAEs of unclear categorization (most common)', 'Hypogammaglobulinemia (IgG<3g/L) requiring change of treatment', 'Hypogammaglobulinemia requiring immunoglobulin replacement', 'Serious disease flares', 'Serious infusion-related reaction' and 'Vaccination failure'.
n, number; PML, progressive multifocal leukoencephalopathy.

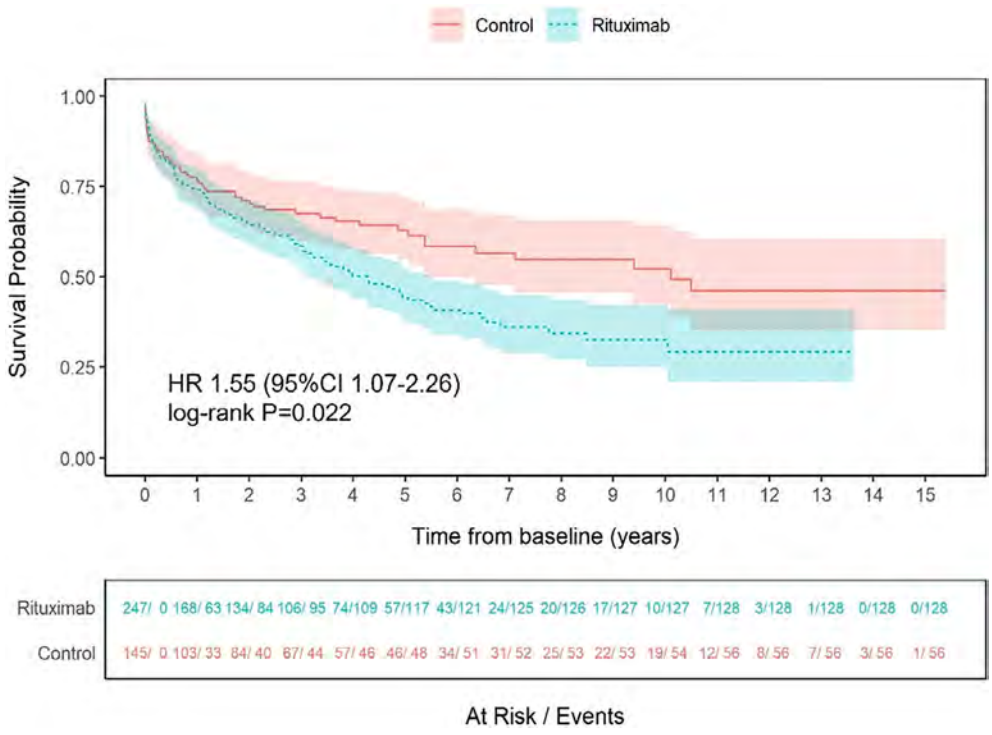


Figure 1. Time to first SAE for the rituximab and the control group

Disclosure: L. Uchida: None; **D. Jones**: CSL Vifor, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Roche, 5, 6; **R. Smith**: GSK, 5, Union Therapeutics, 5; **C. Loechel**: None; **M. King**: None; **M. Nodale**: None; **S. Bond**: None; **R. Luqmani**: Roche, 5; **D. Gray**: None; **J. Barrett**: None; **D. Jayne**: AstraZeneca, 2, Aurinia, 4, Boehringer Ingelheim, 2, Chinook, 2, CSL Vifor, 2, Roche, 2.

Abstract Number: 0680

Risk Factors for Hypogammaglobulinemia and Association with Relapse and Severe Infections in ANCA-Associated Vasculitis: A Retrospective Single-Centre Cohort Study

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SESSION INFORMATION
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Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes
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Session Time: 9:00AM–11:00AM

Background/Purpose: B-cell depletion induced by rituximab (RTX) in ANCA-associated vasculitis (AAV) is a risk factor for hypogammaglobulinemia. Aggregating data on the kinetics of gammaglobulin levels during RTX and its association with the risk of relapse and serious infection is of interest.

Methods: We conducted a retrospective single-centre cohort study including patients with granulomatosis with polyangiitis and microscopic polyangiitis who received RTX maintenance therapy between January 2010 and November 2022. Gammaglobulin levels were measured before induction therapy (month -6), at initiation of RTX maintenance therapy (month 0) and every 6 months during maintenance therapy. Patients were categorized into several groups: (1) patients with gammaglobulin levels < 6 g/L at initiation month 0; (2) patients with gammaglobulin decline between induction and initiation of maintenance therapy >25%; and finally (3) patients responding to both criteria simultaneously. Our primary objective was to assess the impact of gammaglobulin decline on the risk of vasculitis relapse and serious infections.

Results: We included 98 patients, all of whom fulfilled the ACR/EULAR classification criteria of AAV. The median gammaglobulin level at initiation of induction therapy was 10.4 g/L (IQR 8.4–12.9) and it significantly decreased to 7.5 g/L (5.9-8.8) at initiation of maintenance therapy with a median decrease of -25% (IQR -13.8 – -42.4). Gammaglobulin levels remained stable throughout follow-up **(Figure 1).** Factors associated with gammaglobulin level decline >25% and gammaglobulin level < 6 g/L after induction were age > 60 years (OR 4.1; 95%CI 1.2–14.7), baseline gammaglobulin levels < 10 g/L (OR 5.9; 95%CI 1.7–25.4) and use of pulses of methylprednisolone at induction (OR 4.7; 95%CI 1.4–2). Gammaglobulin decline was not associated with the risk of relapse. In contrast, serious infection-free survival was significantly poorer in patients with both gammaglobulin < 6 g/L and gammaglobulin decline >25% (adjusted HR 2.3; 95%CI 1.0–5.1) **(Figure 2)** and in those who received pulses of methylprednisolone (HR 5.6; 95%CI 2.3–13.4) **(Table 1).**

Table 1. Odds ratios (95% CI) for the risk of severe infection (N=98)

			Risk of severe infection	
	Overall (N=98)	**N events (%)**	**Univariate OR (95%CI)**	**Multivariate OR (95%CI)**
Gammaglobulin <6 g/L at month 0	26 (26.5)	4 (15.4)	2.6 (1.2-5.6)	
Gammaglobulin decline >25% between induction and month 0	49 (50)	6 (12.2)	4.4 (1.8-10.9)	
Gammaglobulin <6 g/L AND decline >25%	19 (19.4)	4 (21.1)	3.2 (1.5-7.0)	2.3 (1.0-5.1)
Pulses of methylprednisolone at induction	31 (31.6)	31 (31.6)	6.8 (2.9-15.9)	5.6 (2.3-13.4)

HR=Hazard ratios; 95% CI = 95% confidence interval.

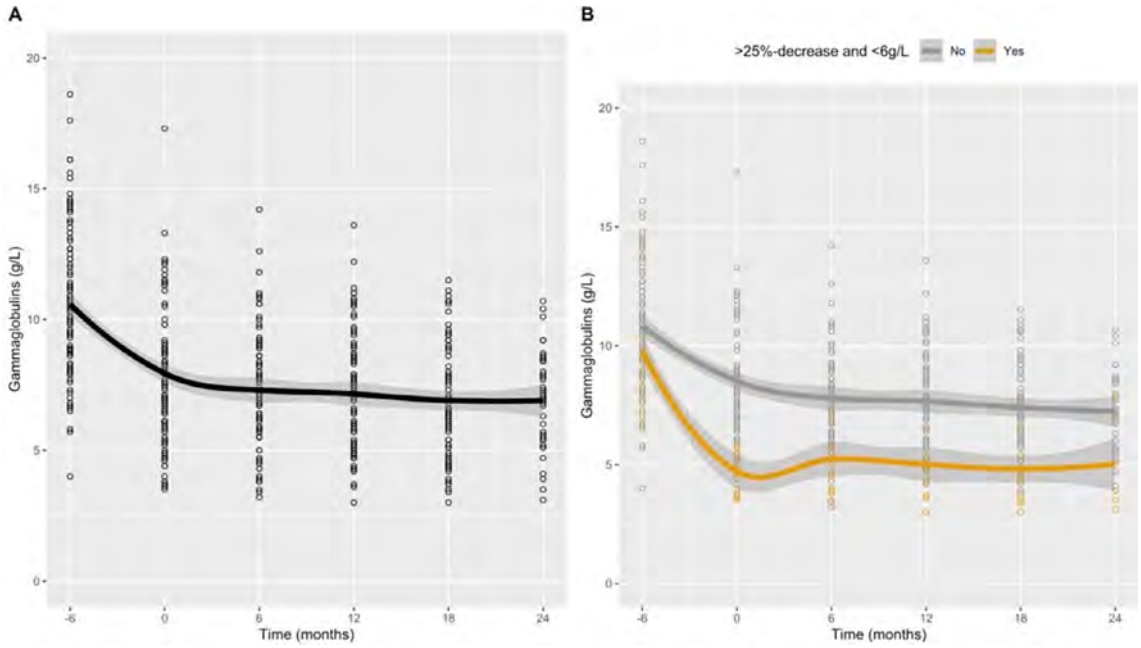


Figure 1. Evolution of gammaglobulin levels after induction and maintenance therapy with RTX. Panel A shows the evolution of gammaglobulin levels after induction and maintenance therapy for the whole population (N=98). Panel B shows the evolution of gammaglobulin levels after induction and maintenance therapy comparing the group with or without both gammaglobulin decrease >25% and gammaglobulin level <6 g/L.

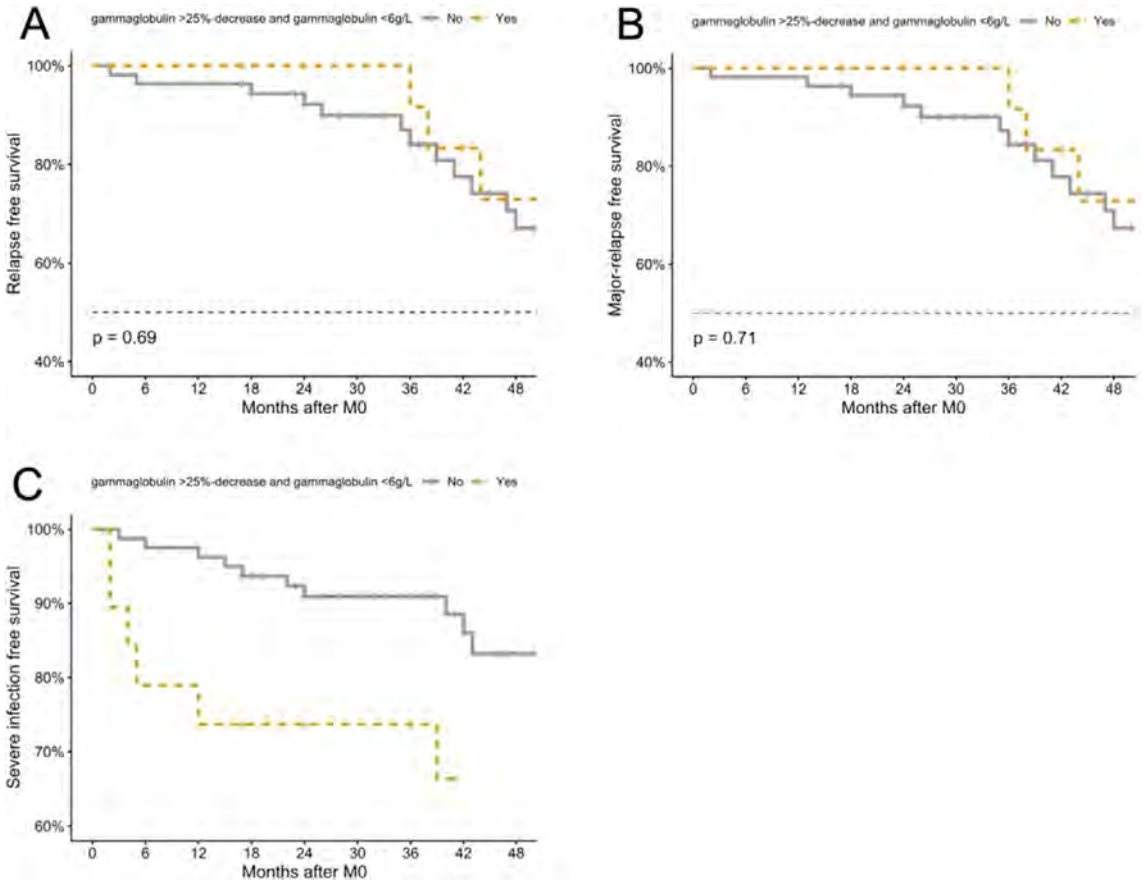


Figure 2. Kaplan–Meier plots of the risk of vasculitis relapse, major relapse and severe infections. Panel A shows the time to the first relapse according to gammaglobulin decline and gammaglobulin level at month 0. Panel B shows the time to the first major relapse according to gammaglobulin decline and gammaglobulin level at month 0. Panel C shows the time to the first severe infection according to gammaglobulins decline and gammaglobulin level at month 0.

Conclusion: Older age, low gammaglobulin levels and pulses of methylprednisolone at induction are associated with greater gammaglobulin decline after induction. Although it is not associated with a lower risk of vasculitis relapse, gammaglobulin decline is associated with an increased risk of serious infections.

Disclosure: J. LIBERATORE: None; **Y. Nguyen**: None; **J. HADJADJ**: None; **P. Cohen**: None; **L. Mouthon**: None; **X. Puéchal**: None; **L. Guillevin**: None; **B. Terrier**: AstraZeneca, 5, CSL Vifor, 2, GlaxoSmithKlein(GSK), 2.

Abstract Number: 0681

Real-World Outcomes for Remission Induction in Working-Age Adults with Severe Anti-Neutrophil Cytoplasmic Antibody-associated Vasculitis

Itay Marmor[1], Katelin Nickel[2], Matthew Keller[2], Guy Hazan[3], Kevin Baszis[4], Anthony French[5] and Mary Hartman[2], [1]Dana-Dwek Children's Hospital, Hod Hasharon, Israel, [2]Washington University in St. Louis, St. Louis, MO, [3]Soroka University Medical Center, Beer Sheva, Israel, [4]Washington Univ in St. Louis School of Medicine, St. Louis, MO, [5]Washington University School of Medicine, St. Louis, MO

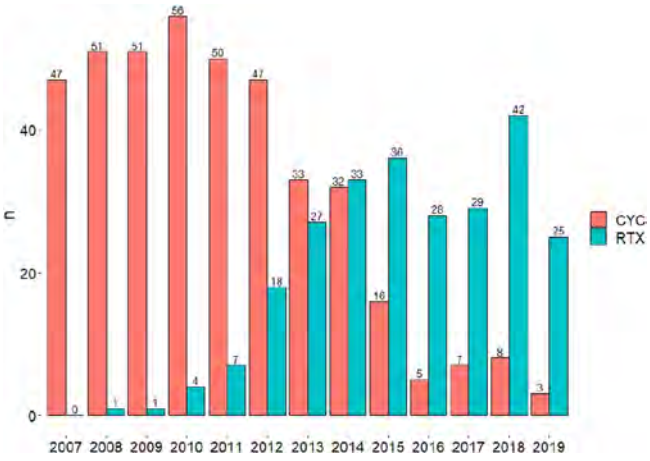
SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

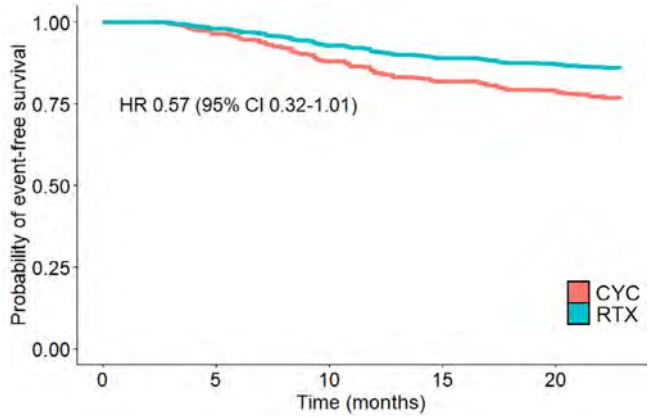
Background/Purpose: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), including Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA), often manifests with life-threatening complications. Cyclophosphamide (CYC) and rituximab (RTX) are the mainstay of remission induction treatment in severe AAV, but their safety and efficacy have not been comprehensively compared in "real-world" settings.

Methods: We conducted a retrospective cohort study using administrative data from the

2006–2019 IBM® MarketScan® Commercial Database. We identified working-age adults (age 18-64 years) with a new diagnosis of GPA/MPA, using the International Classification of Diseases (ICD) version 9 or 10 codes, who received induction treatment with CYC or RTX. We used propensity score matching and a Cox proportional hazard model to estimate hazard ratios (HRs) for the first major disease relapse and severe infection.



Absolute number of patients treated with each induction medication, by year. The data clearly shows a shift in practice over time, with RTX gradually becoming the medication of choice. CYC, cyclophosphamide; RTX, rituximab



Adjusted event-free survival for the primary outcomes, in the first 24 months following induction, by induction medication. 3A: Major relapse; 3B: Severe infection. Curves were plotted using multivariate Cox proportional hazards model, conducted following propensity score matching. CYC, cyclophosphamide; RTX, rituximab; HR, hazard ratio; CI, confidence interval

Variable	First Major Relapse HR (95% CI)	p [a]	First Severe Infection HR (95% CI)	p [a]
Full cohort (N = 657)				
Induction with RTX	0.63 (0.38-1.04)	0.073	0.63 (0.40-0.99)	**0.044**
Age	1.00 (0.98-1.02)	0.842	1.01 (0.98-1.03)	0.575
Female sex	1.13 (0.78-1.64)	0.521	1.07 (0.72-1.57)	0.74
Elixhauser comorbidity score	1.02 (0.97-1.06)	0.45	1.07 (1.02-1.12)	**0.004**
GPA diagnosis	1.05 (0.67-1.64)	0.835	1.02 (0.63-1.65)	0.93
Major BVAS score at baseline	1.04 (1.02-1.06)	**<0.001**	1.04 (1.02-1.06)	**<0.001**
Additional exposure to CYC [b]	0.59 (0.27-1.32)	0.2	1.65 (0.70-3.89)	0.25
Additional exposure to RTX [b]	0.75 (0.38-1.47)	0.4	0.78 (0.33-1.86)	0.57
Exposure to DMARDs [b]	0.63 (0.38-1.02)	0.063	1.38 (0.81-2.36)	0.23
Propensity score matching cohort (N = 454)				
Induction with RTX	0.57 (0.32-1.01)	0.052	0.63 (0.39-1.02)	0.059
Age	1.00 (0.98-1.03)	0.69	1.01 (0.98-1.03)	0.61
Female sex	1.06 (0.67-1.68)	0.81	0.97 (0.59-1.60)	0.92
Elixhauser comorbidity score	1.02 (0.97-1.08)	0.48	1.02 (0.95-1.08)	0.62
GPA diagnosis	0.97 (0.55-1.73)	0.92	0.74 (0.42-1.33)	0.32
Major BVAS score at baseline	1.05 (1.03-1.08)	**<0.001**	1.06 (1.03-1.08)	**<0.001**
Additional exposure to CYC [b]	0.80 (0.28-2.30)	0.68	1.68 (0.54-5.22)	0.37
Additional exposure to RTX [b]	0.80 (0.36-1.78)	0.59	0.66 (0.22-1.99)	0.46
Exposure to DMARDs [b]	0.66 (0.34-1.26)	0.2	1.75 (0.93-3.29)	0.081

[a] Using Cox proportional hazard model, $\alpha < 0.05$

[b] Time-dependent covariates: exposure to medication at the time of the event
For CYC/RTX: exposure more than 180 days after the induction date
For DMARDs: exposure at any time

HR, hazard ratio; CI, confidence interval; RTX, rituximab; GPA, granulomatosis with polyangiitis; BVAS, Birmingham Vasculitis Activity Score; DMARDs, disease ,modifying anti-rheumatic drugs

Multivariable-adjusted risk factors a for the primary outcomes in the first 24 months following induction

Results: We identified 657 patients, 406 (61.8%) of whom were treated with CYC and 251 (38.2%) with RTX. Patients in the CYC group had worse disease severity scores at baseline.

In the 24 months after induction, 146 (22.2%) patients experienced a major disease relapse and 129 patients (19.6%) had severe infection. Multivariate analysis with propensity score matching showed no significant differences between RTX and CYC in the likelihood of experiencing major relapse (HR 0.57, 95% CI 0.32-1.01) or severe infection (HR 0.63, 95% CI 0.30-1.02).

Conclusion: In a nationally representative sample of working-age adults, RTX was found to be comparable to CYC for remission induction treatment in severe AAV.

Disclosure: I. Marmor: None; **K. Nickel**: None; **M. Keller**: None; **G. Hazan**: None; **K. Baszis**: None; **A. French**: None; **M. Hartman**: None.

Abstract Number: 0682

Avacopan in ANCA-associated Vasculitis Received Intensified Induction Therapy with Cyclophosphamide Plus Rituximab – Retrospective Case Serial of 12 Patients

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The orally administered C5a receptor inhibitor avacopan is approved for the therapy of ANCA-associated vasculitis (AAV) in combination with rituximab or cyclophosphamide and shows significant steroid sparing effect as recently published [1]. In severe disease manifestations, preferentially with multiple organ involvement, combined immunochemotherapy of cyclophosphamide plus rituximab can be considered using protocols analogous to the RITUXIVAS

Table 1. Characteristics of ANCA-associated vasculitis patients (n=12)

AAV patients	
Diagnosis GPA/MPA (n)	10/12
ANCA status PR3/MPO (n)	11/1
vasculitis/ with granuloma (n)	12/2
gender female/male (n)	3/9
age (year median, min-max)	51 (19-79)
Manifestations	
kidney with any glomerulonephritis (n)*	12
lung (n)	12
periphereal nerve (n)	3
ZNS (n)	2
HNO (n)	8
eye (n)	5
arthritis (n)	5
GIT (n)	1
treatment	
cyclophosphamide (g, kumulativ, mean)	6.5
Regime RITUXIVAS (n)	6
Regime CycLowVas (n)	6
RTX maint. 500mg (n)#	8
Avacopan 60mg (treatment in weeks, mean)	44.1

*histologically proven by biopsy
#Rituximab maintenance after 4-to 6 months
ANCA=anti-neutrophile cytoplasm antibody; GIT=gastrointestinal tract

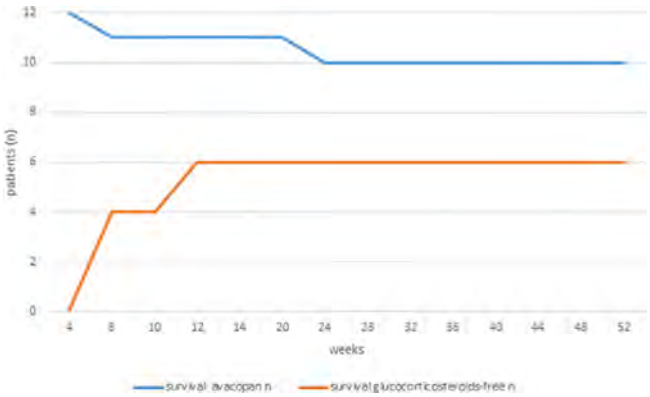

Figure 1: Survival of avacopan treatment and corresponding glucocorticosteroid free in ANCA-associated vasculitis patients (n=12) over 52 weeks

study [2] as well as to CycLowVas study [3]. However, there is no experience with the implementation of avacopan in this therapeutic setting.

Methods: Here we present the case serial of 12 patients with AAV, all of whom had severe renal and pulmonary involvement and received induction therapy with high-dose glucocorticoids and cyclophosphamide in combination with rituximab. In addition, patients received avacopan for rapid steroid reduction/slowing down later in the course (from week 2-6), following the above mentioned study [1] in which up to 20mg prednisolone equivalent was given in addition to avacopan as needed. Patients` characteristics are shown in Table 1.All patients were suffering from kidney and lung manifestations and additionally at least one more organ involvement of nervous system, HNO tract, eye, joints or gastrointestinal tract. Three of them had previous courses of cyclophosphamide due to relapsing disease. All patients were treated between February 2022 and June 2023 in the University Hospital Minden (n=10), University Clinic department of Goettingen (n=1), and the Hospital of Holstein-University in Luebeck; the mean observation time was 44.1 weeks (8-72); supportive treatment including anti-infective prophylaxis were administered according to standard treatment regimes.

Results: Avacopan were stopped in 2 patients, one due to relapsing disease in week 24, and one due to infectious complication in week 4; the remaining 10 patients on avacopan achieved stable remission of AVV, in 6 cases even with successful discontinuation of glucocorticosteroids on average after 11.8 weeks (from 6 to 20; figure 1). 4-6 months after induction therapy, patients received rituximab maintenance therapy in accordance with guidelines (n=8).

Conclusion: Avacopan appears to favor steroid tapering in severe courses of AAV on combined therapy with cyclophosphamide plus rituximab. However, due to the small number of cases and the retrospective evaluation, the results have to be confirmed by studies with larger number of cases.

[References: [1] Jayne DRW et al, NEJM, 2021. [2] Jones RB et al, NEJM, 2010. [3] McAdoo SP et al, Nephrol Dial Transplant, 2018]

Disclosure: G. Assmann: AbbVie/Abbott, 2, 5, 6, AstraZeneca, 2, Boehringer-Ingelheim, 2, 6, Novartis, 5, UCB, 1; **C. Rittich**: None; **F. Neumann**: None; **U. Kellner**: None; **R. Turkiewicz**: None; **J. Radermacher**: None; **P. Lamprecht**: AstraZeneca, 2, GlaxoSmithKlein(GSK), 2, 5, Novartis, 2, Vifor, 2, 5; **B. Tampe**: Vifor, 6.

Abstract Number: 0683

Remission, Glucocorticoid Toxicity, Health-Related Quality of Life, and Safety Outcomes in Patients with Renal Involvement in the Phase 3 Trial of Avacopan for the Treatment of ANCA-Associated Vasculitis

Duvuru Geetha[1], Frank Cortazar[2], Annette Bruchfeld[3], alexandre Karras[4], **Peter Merkel**[5] and David Jayne[6], [1]Johns Hopkins University, Baltimore, MD, [2]New York Nephrology, Watervliet, NY, [3]Karolinska Institutet, Stockholm, Sweden, [4]HEGP - APHP, Paris, France, [5]University of Pennsylvania, Philadelphia, PA, [6]University of Cambridge, Cambridge, United Kingdom

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: In the Phase 3 ADVOCATE trial comparing avacopan to a prednisone taper, 81% of patients with ANCA-associated vasculitis (AAV) had renal involvement based on the Birmingham Vasculitis Activity Score. This renal subgroup had a baseline mean estimated glomerular filtration rate of 45.1 mL/min/1.73 m^2.

Methods: This post hoc analysis evaluated remission, glucocorticoid (GC) use, GC toxicity index (GTI), health-related quality of life (HRQoL by SF-36), and safety in patients with baseline renal involvement for those treated with avacopan (N=134) versus a prednisone taper (N=134).

Table 1: Baseline Characteristics, Remission Rates, Glucocorticoid Toxicity, Health-Related Quality of Life, and Safety for Patients with ANCA-Associated Vasculitis with Renal Involvement in the ADVOCATE Trial

	Avacopan (N=134)	**Prednisone taper** (N=134)
Baseline characteristics		
Age (years), mean ± SD	60.9 ± 14.6	62.2 ± 13.9
Male / Female	84 (63%) / 50 (37%)	76 (57%) / 58 (43%)
Newly diagnosed / Relapsed, n (%)	98 (73%) / 36 (27%)	100 (75%) / 34 (25%)
Proteinase 3+ / Myeloperoxidase+, n (%)	53 (40%) / 81 (60%)	47 (35%) / 87 (65%)
GPA / MPA, n (%)	65 (49%) / 69 (51%)	63 (47%) / 71 (53%)
Rituximab / Cyclophosphamide, n (%)	81 (60%) / 53 (40%)	82 (61%) / 52 (39%)
eGFR (mL/min/1.73 m^2), mean ± SD	44.6 ± 27.7	45.6 ± 27.3
Key Results		
Disease remission week 26, n (%)	99 (73.9%)	95 (70.9%)
Sustained disease remission week 52, n (%)	91 (67.9%)	76 (56.7%)
Total all-source glucocorticoid dose during 52-week period, mg (mean / median)	1589 / 575	3801 / 3028
GTI-CWS at weeks 13 / 26, LSM ± SEM	24.1 ± 3.9 / 38.9 ± 3.9	37.7 ± 4.0 / 58.5 ± 4.0
GTI-AIS at weeks 13 / 26, LSM ± SEM	8.5 ± 3.9 / 11.2 ± 4.0	24.3 ± 4.0 / 24.3 ± 4.0
SF-36 PCS Score, Change from baseline at weeks 26 / 52, LSM ± SEM	4.8 ± 0.8 / 4.9 ± 0.8	1.9 ± 0.8 / 3.1 ± 0.8
SF-36 MCS Score, Change from baseline at weeks 26 / 52, LSM ± SEM	5.2 ± 0.9 / 6.6 ± 1.0	3.5 ± 1.0 / 5.1 ± 1.0
Serious Adverse Events, n patients (%), n events	61 (45.5%) 104 events	65 (48.5%) 148 events
Deaths, n (%)	2 (1.5%)	3 (2.2%)

AIS, aggregate improvement score; CWS, cumulative worsening score; eGFR, estimated glomerular filtration rate; GTI, glucocorticoid toxicity index; GPA, granulomatosis with polyangiitis; LSM, least squares mean; MCS, mental component summary; MPA, microscopic polyangiitis; PCS, physical component summary; SEM, standard error of the mean; SF-36, Short Form-36.

Results: Compared to the overall study population, for this subgroup the mean age was similar (62 vs 61 years), but there was a slightly higher proportion of patients with newly diagnosed AAV (74% vs 69%), myeloperoxidase+ ANCA (63% vs 57%), microscopic polyangiitis (52% vs 45%), and use of cyclophosphamide (39% vs 35%). The avacopan group achieved a higher sustained remission rate at week 52 (67.9% vs 56.7%) while receiving a (mean/median) 2.4-/5.3-fold less total GC dose than the prednisone taper group (**Table 1**). The GTI cumulative worsening and aggregate improvement scores were lower at weeks 13 and 26 in the avacopan group compared to the prednisone group. At weeks 26 and 52 the avacopan group reported a greater improvement in SF-36 physical and mental component summary scores. Serious adverse events occurred in 46% (2 deaths) and 49% (3 deaths) of patients in the avacopan and prednisone groups, respectively.

Conclusion: In the ADVOCATE trial, patients with AAV with baseline renal involvement treated with avacopan achieved higher sustained remission rates while receiving less GCs, experiencing less GC-related toxicity, and reporting greater improvements in HRQoL versus those treated with a prednisone taper.

Disclosure: D. Geetha: Amgen, 2, Aurinia, 2, calliditas, 2, chemocentryx, 2, GlaxoSmithKlein(GSK), 2; **F. Cortazar**: Amgen, 2, 6, Aurinia, 2, 6, Calliditas, 6, Travere, 2, Valenza Bio, 2; **A. Bruchfeld**: Amgen, 2, AstraZeneca, 2, 12, Investigator fees, Bayer, 2, ChemoCentryx, 1, 12, Investigator fees, CSL Vifor, 2, 12, Investigator fees, Fresenius, 2, 12, Investigator fees, Merck/MSD, 2, 12, Investigator fees; **a. Karras**: AstraZeneca, 6, GlaxoSmithKlein(GSK), 4, Novartis, 2, Pfizer, 6; **P. Merkel**: AbbVie/Abbott, 5, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos, 5, Electra, 5, Genentech, 5, GlaxoSmithKlein(-GSK), 2, 5, HiBio, 2, InflaRx, 2, 5, Janssen, 2, Jubilant, 2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, Takeda, 2, 5, UpToDate, 9, Visterra, 2; **D. Jayne**: AstraZeneca, 2, Aurinia, 4, Boehringer Ingelheim, 2, Chinook, 2, CSL Vifor, 2, Roche, 2.

Abstract Number: 0684

Report on Twelve Patients with Diffuse Alveolar Hemorrhage in the Phase 3 Trial of Avacopan for the Treatment of ANCA-Associated Vasculitis

Ulrich Specks[1], David Jayne[2] and **Peter Merkel**[3], [1]Mayo Clinic, Rochester, MN, [2]University of Cambridge, Cambridge, United Kingdom, [3]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Although respiratory tract involvement in ANCA-associated vasculitis (AAV) is frequent and associated with increased mortality, studies focusing on diffuse alveolar hemorrhage (DAH) in AAV are uncommon. DAH can progress rapidly and is often life-threatening. The 330-patient ADVOCATE trial was an active-controlled, randomized, Phase 3 study that compared avacopan to a prednisone-tapering regimen and enrolled 12 patients with DAH.

Methods: This post hoc analysis focuses on outcomes of the 12 patients with DAH at baseline on the basis of BVAS. Patients requiring invasive pulmonary ventilation support at screening were excluded from enrollment. Remission at Week 4 was defined as BVAS=0. Remission at Week 26 was defined as BVAS=0 and no glucocorticoid (GC) use in the previous 4 weeks. Sustained remission at Week 52 was defined as BVAS=0 and no GC use in the previous 4 weeks, remission at

Table 1: Baseline Characteristics, Glucocorticoid Dose, Pulmonary Manifestations, Remission, and Relapses for Patients with Diffuse Alveolar Hemorrhage at Baseline in the ADVOCATE trial of Avacopan for ANCA-Associated Vasculitis

Case	Study Treatment/ Background Therapy	Age, Sex, Type of AAV, Race, ANCA status, AAV disease status	Cumulative GC Dose (mg)		Pulmonary Manifestations of AAV			Remission (weeks 4 and 26) Sustained remission (week 52)			Relapse
			Days -1 to -14	Days 1 to 29	Baseline	Week 4	Week 26	Week 4	Week 26	Week 52	
1	Avacopan/ Rituximab	54, M, White, GPA, PR3+, Newly diagnosed	1758	763	DAH	None	None	Yes	Yes	Yes	No
2	Avacopan/ Rituximab	68, M, White, GPA, PR3+, Newly diagnosed	140	625	DAH	None	None	Yes	Yes	Yes	No
3	Avacopan/ Rituximab	50, M, White, GPA, PR3+, Relapsed	0	500	DAH, Wheeze, Nodules/Cavities	None	None	Yes	Yes	Yes	No
4	Avacopan/ Rituximab	57, M, White, GPA, PR3+, Newly diagnosed	300	0	DAH, Respiratory failure	Nodules/ Cavities	None	No	No	No	No
5	Avacopan/ Rituximab	81, F, Asian, GPA, MPO+, Relapsed	728	650	DAH, Infiltrate, Nodules/ Cavities	None	None	Yes	Yes	Yes	No
6	Prednisone/ Rituximab	35, F, Black, GPA, PR3+, Newly diagnosed	2377	3010	DAH, Infiltrate, Wheeze	None	None	Yes	Yes	Yes	No
7	Prednisone/ Rituximab	88, M, White, GPA, MPO+, Relapsed	60	1627	DAH	None	None	Yes	Yes	Yes	No
8	Prednisone/ Rituximab	61, F, White, GPA, MPO+, Relapsed	240	1779	DAH	None	None	Yes	Yes	Yes	No
9	Prednisone/ Rituximab	81, F, White, MPA, MPO+, Newly diagnosed	4465	2112	DAH	None	None	Yes	No	No	No
10	Prednisone/ Rituximab	55, M, White, GPA, PR3+, Relapsed	0	1558	DAH, Infiltrate	None	None	No	Yes	No	Yes
11	Prednisone/IV Cyclophosphamide	57, M, White, GPA, PR3+, Newly diagnosed	1945	1368	DAH, Infiltrate	None	None	Yes	Yes	Yes	No
12	Prednisone/IV Cyclophosphamide	48, M, White, GPA, PR3+, Relapsed	2225	1597	DAH, Infiltrate, Endobronchial disease	Infiltrate, Endobronchial disease	None	No	No	No	Yes

AAV, ANCA-associated vasculitis; DAH, diffuse alveolar hemorrhage; GPA, granulomatosis with polyangiitis; IV, intravenous; MPA, microscopic polyangiitis; MPO, myeloperoxidase; PR3, proteinase 3

Week 26, and no relapse between Week 26 and Week 52. Relapse was defined as a return of vasculitis activity on BVAS with ≥1 major item, ≥3 minor items, or 1 or 2 minor items for at least two consecutive trial visits.

Results: Five patients in the avacopan group and 7 in the prednisone taper group had DAH at baseline. Of the 12 patients, 11 (92%) had granulomatosis with polyangiitis, 10 (83%) received rituximab background therapy, 8 (67%) were male, 8 (67%) had PR3-ANCA, and 6 (50%) were newly diagnosed (**Table 1**). BVAS was 19.5±5.4 (mean±SD) at baseline. The total dose of GCs (median / mean) from all sources for the avacopan and prednisone taper groups, respectively, were 300 / 585 mg vs 1945 / 1616 mg during the screening period (day -14 to -1) and 625 / 508 mg vs 1627 / 1866 mg during day 1 to 29. DAH was no longer active by Week 4 for all patients (**Table 1**). Remission rates in the avacopan and prednisone taper groups, respectively, were 80.0% (4/5) and 71.4% (5/7) at Week 4, 80.0% (4/5) and 71.4% (5/7) at Week 26, and 80.0% (4/5) and 57.1% (4/7) at Week 52. No patients in the avacopan group and 2 in the prednisone taper group relapsed during the treatment period. One patient in the avacopan group (case 3) was hospitalized twice for pneumonia. Two in the prednisone taper group had hospitalizations, twice for one patient (case 9) due to hepatocellular injury andherpes keratitis and once for the other patient (case 12) for worsening of AAV. Prednisone taper treatment was not completed in case 9 due to a serious adverse event of lymphopenia (day 33). None of the patients required mechanical ventilation during the study.

Conclusion: In the ADVOCATE trial of patients with AAV, the outcomes of patients with DAH were similar for those treated with avacopan versus with a prednisone taper. None of the patients with DAH in the avacopan group progressed to respiratory failure, despite receiving a minimal dose of GCs. In this report on a small number of patients, overall remission rates were higher in the avacopan group than the prednisone taper group at Weeks 4, 26, and 52, although all pulmonary manifestations of AAV were resolved in all patients by Week 26. These data provide support for the treatment of DAH in AAV using avacopan with a lower dose of GCs.

Disclosure: U. Specks: Amgen, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 5, ChemoCentryx, 2, Genentech, 5, GlaxoSmithKlein(GSK), 5; **D. Jayne**: AstraZeneca, 2, Aurinia, 4, Boehringer Ingelheim, 2, Chinook, 2, CSL Vifor, 2, Roche, 2; **P. Merkel**: AbbVie/Abbott, 5, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos, 5, Electra, 5, Genentech,

5, GlaxoSmithKlein(GSK), 2, 5, HiBio, 2, InflaRx, 2, 5, Janssen, 2, Jubilant, 2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, Takeda, 2, 5, UpToDate, 9, Visterra, 2.

Abstract Number: 0685

Efficacy and Safety of Avacopan in Patients with ANCA-Associated Vasculitis Receiving Rituximab in a Phase 3 Trial

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The randomized, double-blind, double-dummy, controlled Phase 3 ADVOCATE trial tested whether avacopan, an oral selective C5a receptor inhibitor approved for the treatment of ANCA-associated vasculitis (AAV), could replace a glucocorticoid (GC)-tapering regimen. Randomization was stratified according to vasculitis disease status (newly diagnosed or relapsing), ANCA status (anti-proteinase 3 (PR3) positive or anti-myeloperoxidase positive), and immunosuppressive treatment (cyclophosphamide (CYC) or rituximab (RTX)). American College of Rheumatology/Vasculitis Foundation guidelines recommend induction treatment with RTX over CYC (Chung SA et al, *Arthritis Care Res* (*Hoboken)* 2021). For relapsing disease, EULAR guidelines recommend RTX (Hellmich B et al,*Ann Rheum Dis* 2023). The objective of this study was to evaluate the efficacy and safety of avacopan in patients in the RTX stratum of the ADVOCATE trial.

Methods: Primary efficacy endpoints were the proportion of patients achieving disease remission at week 26 and sustained remission at week 52 (Birmingham Vasculitis Activity Score (BVAS) of 0 and no GC use for AAV 4 weeks before measurement). RTX was administered intravenously 375 mg/m^2 once weekly for 4 weeks beginning on Day 1. The protocol did not include repeat dosing of RTX, according to its approved labeled regimen at the time.

Results: A total 214 of 330 patients (64.8%) comprised the RTX stratum. At baseline, patients were 60 years old (mean), ~76% had renal vasculitis (based on BVAS), ~46% were PR3-ANCA positive, and ~58% were newly diagnosed. Men constituted 57.0% of the avacopan group and 48.6% of the prednisone group. Baseline estimated glomerular filtration rate

Table 1: Efficacy and Safety for Patients with ANCA-Associated Vasculitis in the Rituximab Stratum in the ADVOCATE Trial

	Avacopan Group (N=107)	Prednisone Group (N=107)
Remission at Week 26, n (%)	83 (77.6%)	81 (75.7%)
Sustained remission at Week 52, n (%)	76 (71.0%)	60 (56.1%)
Relapse rate, n (%)	9 (8.7%)	21 (20.2%)
eGFR change at Week 52, mL/min/1.73 m^2, mean ± SEM	5.9 ± 1.56	3.2 ± 1.56
UACR percent change at Week 4, geometric mean	-43.4%	8.3%
GTI-CWS at Week 26, mean ± SEM	36.8 ± 3.62	52.9 ± 4.92
GTI-AIS at Week 26, mean ± SEM	11.7 ± 3.42	19.8 ± 4.31
Any Serious Treatment Emergent Adverse Event; patient experiencing events, n (%), number of events (n)	37 (34.6%), 62 events	42 (39.3%), 91 events

eGFR=estimated glomerular filtration rate; UACR=urinary albumin:creatinine ratio; GTI-CWS=Glucocorticoid Toxicity Index Cumulative Worsening Score; GTI-AIS=Glucocorticoid Toxicity Index Aggregate Improvement Score

(eGFR) was 57.1±32.2 and 56.0±33.4 mL/min/1.73 m^2 (mean±SD), for the avacopan and prednisone groups, respectively. Remission at week 26 was 77.6% in the avacopan group and 75.7% in the prednisone group (**Table 1**). Sustained remission at week 52 was 71.0% in the avacopan group and 56.1% in the prednisone group (**Table 1**), estimated common difference, 16.5 percentage points; 95% confidence interval, 4.3 to 28.6. Additionally, there were numerical improvements in relapse rate, albuminuria, and lower GC-associated toxicity in the avacopan group versus the prednisone group. The proportion of patients experiencing a serious treatment emergent adverse event (TEAE) was 34.6% (n = 37) with 62 events in the avacopan group compared to 39.3% (n = 42) with 91 events in the prednisone group (**Table 1**).

Conclusion: This analysis from the ADVOCATE trial of patients with AAV receiving RTX showed a significantly increased sustained remission rate at week 52 in the avacopan group compared to the prednisone group. Compared to the prednisone group, patients in the avacopan group had numerical improvements in remission at week 26, relapse rate, eGFR, albuminuria, and less GC toxicity. There was no increase in serious TEAEs in patients treated with avacopan. These results demonstrate the efficacy of avacopan for achieving and sustaining remission in patients with AAV treated with RTX.

Disclosure: D. Geetha: Amgen, 2, Aurinia, 2, calliditas, 2, chemocentryx, 2, GlaxoSmithKlein(GSK), 2; **A. Dua**: AbbVie/Abbott, 2, Amgen, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2, sanofi, 2; **H. Yue**: Amgen, 3, 11, ChemoCentryx, 3, 11; **C. Salvarani**: CSL Vifor, 1, 2, 6, Eli Lilly, 1, 2, 6; **D. Jayne**: AstraZeneca, 2, Aurinia, 4, Boehringer Ingelheim, 2, Chinook, 2, CSL Vifor, 2, Roche, 2; **P. Merkel**: AbbVie/Abbott, 5, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos, 5, Electra, 5, Genentech, 5, GlaxoSmithKlein(GSK), 2, 5, HiBio, 2, InflaRx, 2, 5, Janssen, 2, Jubilant, 2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, Takeda, 2, 5, UpToDate, 9, Visterra, 2.

Abstract Number: 0686

Safety and Efficacy of Avacopan in Patients 65 Years and Older with ANCA-Associated Vasculitis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Older adults are at increased risk of glucocorticoid (GC)-related toxicity; minimization of GCs is a major focus for treatment of patients with ANCA-associated vasculitis (AAV). Although AAV especially affects older adults, many studies have excluded patients >75 years (y). In the Phase 3 ADVOCATE trial of avacopan, there was no exclusion criterion for maximum participant age.

Methods: This post hoc analysis reports safety and efficacy of avacopan compared to a prednisone taper in the subgroups of patients 65-74y (N=109) and ≥75y (N=51).

Results: In both studied age and treatment groups, a similar proportion of patients (69.4-73.1%) achieved remission at week 26 (**Table 1**). In the 65-74y age group, sustained remission rates at week 52 were 55.1% in the prednisone arm and 65.0% in the avacopan arm. Relapse rates were 18.8% in the prednisone arm and 12.3% in the avacopan arm. The total

Table 1: Safety and Efficacy Outcomes in Patients with ANCA-Associated Vasculitis Aged 65 to 74 Years and 75 Years and Older in the ADVOCATE Trial of Avacopan

Outcome	Age 65-74 (N=109)		Age ≥75 (N=51)	
	Prednisone taper (n=49)	Avacopan (n=60)	Prednisone taper (n=25)	Avacopan (n=26)
Remission at Week 26, n (%)	34 (69.4)	43 (71.7)	18 (72.0)	19 (73.1)
Sustained remission at Week 52, n (%)	27 (55.1)	39 (65.0)	14 (56.0)	17 (65.4)
Relapse rate[§], n (%)	9 (18.8)	7 (12.3)	5 (20.8)	1 (3.8)
eGFR change at Week 52[†], LSM ± SEM	5.4 ± 1.6	4.6 ± 1.5	7.8 ± 1.7	10.7 ± 1.7
UACR percent change at Week 4[‡], LSM ± SEM	-19 ± 1.2	-34 ± 1.2	-8 ± 1.2	-33 ± 1.3
SF-36 PCS change at Week 52, LSM ± SEM	1.3 ± 1.3	3.0 ± 1.2	0.7 ± 2.5	3.2 ± 2.2
SF-36 MCS change at Week 52, LSM ± SEM	5.4 ± 1.6	6.9 ± 1.4	7.4 ± 3.0	7.0 ± 2.6
EQ-5D-5L VAS change at Week 52, LSM ± SEM	6.0 ± 2.5	13.0 ± 2.2	2.4 ± 5.5	13.7 ± 4.7
EQ-5D-5L Index change at Week 52, LSM ± SEM	0.020 ± 0.03	0.032 ± 0.02	0.021 ± 0.06	0.040 ± 0.05
GTI-CWS at Week 26, LSM ± SEM	53.6 ± 7.2	43.4 ± 6.3	51.4 ± 10.1	33.1 ± 8.8
GTI-AIS at Week 26, LSM ± SEM	15.1 ± 6.8	13.6 ± 5.9	15.1 ± 9.7	0.4 ± 8.5
Total all-source GC dose, mg (mean / median)	3579 / 3055	1410 / 575	3382 / 2840	1718 / 588
Total AEs, n (%) patients, n events	48 (98.0) 681 events	59 (98.3) 623 events	25 (100.0) 318 events	26 (100.0) 273 events
AEs of Infections, n (%) patients, n events	38 (77.6) 88 events	40 (66.7) 86 events	20 (80.0) 40 events	20 (76.9) 42 events
AEs possibly related to GCs, n (%) patients	41 (83.7)	30 (50.0)	20 (80.0)	24 (92.3)
Total SAEs, n patients, %	22 (44.9) 51 events	25 (41.7) 43 events	14 (56.0) 34 events	17 (65.4) 22 events
SAEs of Infections, n (%) patients, n events	5 (10.2) 6 events	11 (18.3) 13 events	6 (24.0) 8 events	4 (15.4) 4 events
SAEs possibly related to GCs, n patients, %	4 (8.2)	7 (11.7)	7 (28.0)	5 (19.2)
Deaths, n (%)	2 (4.1)	2 (3.3)	0 (0.0)	0 (0.0)

[§] Relapse rates are based on the number of patients who achieved a Birmingham Vasculitis Activity Score (BVAS) of 0 during the 52-week treatment period

[†] eGFR assessed only in patients with renal involvement (based on BVAS) at baseline

[‡] UACR assessed only in patients with renal involvement (based on BVAS) at baseline and baseline UACR≥10 mg/g creatinine

AE, adverse events; AIS, aggregate improvement score; CWS, cumulative worsening score; eGFR, estimated glomerular filtration rate; GC, glucocorticoid; GTI, glucocorticoid toxicity index; LSM, least squares mean; MCS, mental component summary; PCS, physical component summary; SAE, serious adverse event; SEM, standard error of the mean; SF-36, Short Form-36; UACR, urine albumin:creatinine ratio; VAS, visual analogue scale.

all-source median GC dose was 5.3x higher in the prednisone vs avacopan arm. Serious adverse events (SAEs) occurred in 22/49 patients (45%) in the prednisone arm (2 deaths) and 25/60 patients (42%) in the avacopan arm (2 deaths). In the ≥75y age group, sustained remission rates at week 52 were 56.0% in the prednisone arm and 65.4% in the avacopan arm. Relapse rates were 20.8% in the prednisone arm and 3.8% in the avacopan arm. Median GC dose was 4.8x higher in the prednisone vs avacopan arm. SAEs occurred in 14/25 patients (56%) in the prednisone arm and 17/26 patients (65%) in the avacopan arm. Other results including renal and quality of life outcomes are in **Table 1**.

Conclusion: A subgroup analysis of patients ≥65y demonstrated similar trends of efficacy and safety of avacopan as in the overall ADVOCATE trial, including reductions in GC-related toxicities, supporting a role for avacopan in the treatment of older adults with AAV.

Disclosure: D. Jayne: AstraZeneca, 2, Aurinia, 4, Boehringer Ingelheim, 2, Chinook, 2, CSL Vifor, 2, Roche, 2; **D. Geetha**: Amgen, 2, Aurinia, 2, calliditas, 2, chemocentryx, 2, GlaxoSmithKlein(GSK), 2; **C. Pagnoux**: AstraZeneca, 1, 2, 6, GlaxoSmithKlein(GSK), 1, 6, Otsuka, 1, 2, 5, 6, Pfizer, 5, Roche, 2; **S. Sattui**: AstraZeneca, 5, Bristol Myers Squibb Foundation, 5, Rheumatology Research Foundation, 5, Sanofi, 2, 5; **P. Merkel**: AbbVie/Abbott, 5, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos, 5, Electra, 5, Genentech, 5, GlaxoSmithKlein(GSK), 2, 5, HiBio, 2, InflaRx, 2, 5, Janssen, 2, Jubilant,

2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, Takeda, 2, 5, UpToDate, 9, Visterra, 2.

Abstract Number: 0687

Avacopan for the Treatment of ANCA-associated Vasculitis. Real World Experience in Spain

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: ANCA-associated vasculitis are chronic and relapsing diseases. Relapses are frequently associated with organ damage accrual as a consequence of disease activity or treatment-related side effects. Avacopan, a selective antagonist of C5a receptor, has been approved for the treatment of adult patients with severe and active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) in combination with rituximab (RTX) or cyclophosphamide (CF). We describe our initial experience with avacopan as part of an Early Access program in Spain.

Methods: The study population consisted of all patients diagnosed with GPA/PAM who initiated treatment with avacopan between June 2022 and March 2023 as part of the program. Patients (newly diagnosed or relapsing) were locally selected by participating investigators based on impaired renal function or long glucocorticoid exposure and toxicities. Descriptive statistics (mean and SD or median and IQR for continuous variables, and percentages for categorical variables) are presented.

Results: 24 patients were included: age 58,5±15 years, 60% women, 50% newly diagnosed and 71% ANCA- MPO+. 88% (21/24) had kidney involvement with an eGFR of 26±15 ml/min/1.73m^2 (n=17). Extrarenal manifestations were present in 42% (10/24), the most common was pulmonary involvement (6/24).

In 75% of patients avacopan was initiated because of presence/risk of glucocorticoid (GC)-related adverse events (AEs) (diabetes, hypertension, osteoporosis, previous infection, frailty, cardiovascular risk and previous GC exposure). 30% had previous GC-derived AEs and 8% were on chronic GC use. In 30% of patients, avacopan was added for refractory disease and in 46% of patients for potential recovery of kidney function.

RTX was used for induction in 100% of patients and was combined with CF in 54% of cases. Moreover, 67% received methyl-prednisolone pulses, 96% oral prednisone and 25% plasma exchange. Median follow-up under avacopan treatment was 5,4 months (IQR 2,55-9,25). Remission was achieved by 79% of patients with no relapses during follow. eGFR increased 6.1±12.5 ml/min/1.73m2

Prednisone was completely discontinued in 33% of patients (after 11,3±5,9 weeks). At the time of this analysis, 40% were tapering GC. Three AEs were reported (diarrhea, urinary tract infection and neutropenia). Avacopan was discontinued in 1 patient.

Conclusion: Combination of avacopan and standard remission induction therapy had a good safety profile in real world clinical practice. Although in the presence of efficient induction therapy, short follow up and lack of comparator no conclusions can be drawn about efficacy, our patients tolerated lower GC exposure than previously adviced.

Disclosure: G. Espigol-Frigole: CSL Vifor, 1, GlaxoSmithKlein(GSK), 1; **M. Cid**: AbbVie/Abbott, 1, 2, 6, AstraZeneca, 1, GSK, 1, 2, 6, Kininksa Pharmaceutical, 5, SCL-Vifor, 2, 6; **J. Bordignon Draibe**: CSL Vifor, 1; **M. Prados**: Alexion, 2, CSL VIFOR, 2, GlaxoSmithKlein(GSK), 6; **E. Guillen**: CSL Vifor, 1; **A. Huerta**: Alexion, 2, 6, AstraZeneca, 6, CSL Vifor, 2, GlaxoSmithKlein(GSK), 6, Sanofi, 6; **J. Villacorta**: Fresenius, 2, Vifor, 2; **C. Vega**: CSL Vifor, 1; **J. Martins**: CSL Vifor, 1; **B. Gracia**: Boehringer-Ingelheim, 6, GlaxoSmithKlein(GSK), 6, Roche, 6; **E. Morales**: Alexion, 6, CSL Vifor, 2, 6, GlaxoSmithKlein(GSK), 2, 6, Otsuka, 6.

Abstract Number: 0688

Efficacy and Safety Experience with Avacopan Beyond 52 Weeks in the Early Access Program (EAP)

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Avacopan, a selective C5aR1 inhibitor, has demonstrated efficacy and safety over 52 weeks in patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis. However, efficacy and safety data on avacopan beyond 52 weeks are limited. Here, we describe the experience with avacopan beyond 52 weeks from the EAP.

Methods: Safety data in patients with severe, active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) within the EAP were recorded in a global safety database from Feb 2019 – Apr 2023. Adverse events (AE) included a lack of effect and other events (i.e., relapse or worsening of disease).

Results: A total of 19 patients were treated with avacopan beyond 52 weeks within the EAP. Average age was 47 years, with 13 patients (68%) diagnosed with GPA and 6 (32%) with MPA. The median duration of therapy was 17 months (range 12–45). A total of 9 AEs were recorded in 2 patients (10.6%) (Table 1). One vasculitis flare was recorded 6 months after avacopan initiation and coincided with an unintended dose reduction to 20 mg BID, due to a product supply issue during COVID. The event was well-managed with rituximab, with no additional use of glucocorticoids, and avacopan 30 mg BID was reinstated. No further cases of a lack of effect, worsening of disease, or disease relapse were reported. Data regarding concomitant medications did not indicate a decline in the patients' status during treatment. No treatment discontinuations due to AEs were recorded.

Conclusion: These results suggest that continuation of avacopan beyond 52 weeks is generally well-tolerated in patients with GPA and MPA and may be effective in terms of disease control. Limitations of this program include low patient number, potential underreporting, and incomplete data.

Table 1. Overview of Safety Events Reported in 2 of 19 Patients Receiving Avacopan Beyond 52 Weeks in the Early Access Program

System Organ Class (*Preferred term*)	No. of events
Patient 1	
General disorders and administration site conditions *Malaise*	1
Infections and infestations *COVID-19*	1
Injury, poisoning, and procedural complications *Product dose omission issue*	1
Product issues *Product supply issue*	1
Patient 2	
General disorders and administration site conditions *Pain*	1
Musculoskeletal and connective tissue disorders *Psoriatic arthropathy* *Arthritis*	2
Surgical and medical procedures *Therapy interrupted*	1
Vascular disorders *Vasculitis*	1
Total	9

Disclosure: F. Alberici: AstraZeneca, 1, 2, 6, CSL Vifor, 1, 2, 6; **C. Salvarani**: CSL Vifor, 1, 2, 6, Eli Lilly, 1, 2, 6; **C. Chan**: CSL Vifor, 3; **A. Obergfell**: CSL Vifor, 3; **T. Popov**: CSL Vifor, 3.

Abstract Number: 0689

Use of Avacopan in Patients with ANCA-associated Vasculitis and Estimated Glomerular Filtration Rate < 15 mL/min/1.73m^2

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Glomerulonephritis represents a severe manifestation of anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV) and is associated with substantial morbidity and mortality. Therefore, maximal recovery of kidney function is imperative to improve long-term survival and quality of life. Patients who require kidney replacement therapy (KRT) have the worst long-term outcomes with kidney function following six months of therapy being predictive of future requirement of KRT. Despite advances in induction therapy, there remains a substantial reliance on glucocorticoids, resulting in significant treatment-associated morbidity. Avacopan, a small molecule C5a receptor antagonist, was recently demonstrated to be superior to prednisone with respect to sustained remission at 52 weeks and reduced glucocorticoid toxicity. Avacopan has also been shown to improve estimated glomerular filtration rate (eGFR) compared to prednisone, particularly in the subset of patients with eGFR < 20 mL/min/1.73m^2. However, patients with eGFR < 15 mL/min/1.73m^2 were excluded from the clinical trials. Our objective was to describe the experience of patients at our centre with AAV who presented with eGFR < 15 mL/min/1.73m^2.

Table 1: Characteristics and outcomes of patients treated with avacopan

Table 1: Characteristics and outcomes of patients treated with avacopan

	Patient 1	Patient 2	Patient 3	Patient 4
Age	76	59	80	63
Sex	F	F	F	M
Follow up (mo)	6	3	4	8
ANCA type	MPO	PR3	MPO	MPO
Berden Class	Mixed	Mixed	Focal	Mixed
Brix Score	9	3	3	11
Creatinine[1]	420	402	465	882
eGFR[2]	8	10	7	5
Urine PCR[3]	128.8	103	N/A	114
ANCA titer (AI)	>800	561	48.1	4.3
Hematuria at time zero (/hpf)	>30	>30	150	21-30
Induction therapy	CYC	CYC/RTX	CYC	RTX
PLEX (Y/N)	N	N	N	N
Day avacopan initiated	19	14	21	28
Remission	Yes	Yes	Yes	Yes
Creatinine at follow up[1]	218	136	134	N/A (HD)
eGFR at follow up[2]	18	37	32	N/A (HD)
Urine PCR at follow up[3]	48.8	25	N/A	40
ANCA titer at follow up (AI)	196.8	28	N/A	4.3
Hematuria at follow up (/hpf)	0-2	0-2	20	0-2
Cumulative oral GC	1720	1055	1260	1190

ANCA, anti-neutrophil cytoplasmic antibody; MPO, myeloperoxidase; PR#, proteinase 3; eGFR, estimated glomerular filtration rate, PCR, protein-to-creatinine ratio; hpf, high-power field; CYC, cyclophosphamide; RTX, rituximab; PLEX, plasma exchange; GC, glucocorticoid
[1]units are μmol/L
[2]units are mL/min/1.73m^2
[3]units are mg/mmol

Methods: This was a retrospective case series of four patients with AAV and an eGFR < 15 mL/min/1.73m^2, treated with avacopan at the University of Calgary, Calgary, Canada between November 2022 and May 2023.

Results: Four patients with AAV presenting with an eGFR < 15 mL/min/1.73m^2 were treated at our centre. Their clinical characteristics, management and outcomes are detailed in Table 1. The patients ranged in age from 59-80. Two patients had GPA and one was PR3 positive. All four had an eGFR < 15 (range 5-10 mL/min/1.73m^2) at presentation and a renal biopsy documenting glomerulonephritis. Two received cyclophosphamide as induction, one a combination of rituximab and cyclophosphamide and one rituximab. All four patients were in remission at last follow-up with one patient dialysis dependent. For the patient dialysis dependent, avacopan was stopped at three months. Cumulative steroid exposure ranged from 1 to 1.7 grams of prednisone or prednisone equivalent. There were no treatment related adverse events or serious infections.

Conclusion: In conclusion, we present four cases describing the use of avacopan in individuals with AAV and eGFR < 15 mL/min/1.73m^2 at presentation. Avacopan appeared to be safe, with reduced glucocorticoid exposure in all patients, and resulted in substantial eGFR recovery in three individuals. More study is required to understand the short- and long-term impacts of avacopan on kidney function in this subgroup of AAV patients.

Disclosure: B. Barr: Otsuka, 1; **K. Cheema**: Alexion, 1, 6, Novartis, 1, Otsuka, 6; **A. Fifi-Mah**: Bristol-Myers Squibb(BMS), 5, Celltrion, 1, Frenesius-Kabi, 6, Novartis, 1, Otsuka, 1, Pfizer, 5, Sanofi, 1; **S. Garner**: Abbvie, 1, JAMP, 1, Janssen, 1, Novartis, 1, Otsuka, 1, 6, UCB, 1, 5; **L. Girard**: Chemocentryx, 1, CIHR, 5, Otsuka, 2, 6; **J. Ma**: Alexion, 1.

Abstract Number: 0690

Treating Patients with ANCA-Associated Vasculitis and Very Severe Renal Injury with an Intensified B Cell Depletion Therapy: Comparison with a Control Cohort Receiving a Conventional Therapy

Dario Roccatello[1], Savino Sciascia[2], SILVIA GRAZIETTA FODDAI[3], gIACOMO QUATTROCCHIO[4], MASSIMO RADIN[3], IRENE CECCHI[3], ALICE BARINOTTI[3], ELENA RUBINI[3], MICHELA FERRO[4], EMANUELE DE SIMONE[4], carla naretto[4], ANTONELLA BARRECA[5], ANDREA SAMMARTINO[4], DANIELA ROSSI[4] and ROBERTA FENOGLIO[4], [1]University of Torino, Torino, Italy, [2]University of Turin, Torino, Italy, [3]University Center of Excellence on Nephrologic, Rheumatologic and Rare Diseases (ERK-Net, ERN-Reconnect and RITA-ERN Member) with Nephrology and Dialysis Unit and Center of Immuno-Rheumatology and Rare Diseases (CMID), Coordinating Center of the Interregional Network for Rare Diseases of Piedmont and Aosta Valley, Department of Clinical and Biological Sciences, University of Turin, Turin, Italy, [4]University Center of Excellence on Nephrologic, Rheumatologic and Rare Diseases (ERK-net, ERN-Reconnect and RITA-ERN Member) with Nephrology and Dialysis Unit and Center of Immuno-Rheumatology and Rare Diseases (CMID), Coordinating Center of the Interregional Network for Rare Diseases of Piedmont and Aosta Valley, San Giovanni Bosco Hub Hospital, Turin, Italy, [5]Pathology Unit, Città della Salute e della Scienza, Turin, Italy

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – ANCA-Associated Poster I: Treatment Outcomes

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Rituximab (RTX), an anti-CD20 monoclonal antibody, has shown to be an effective induction treatment for small-vessel vasculitides associated with antineutrophil cytoplasm antibodies (AAV) in both newly diagnosed and relapsing patients. However, the role of RTX in the management of the most severe cases of AAV remains to be fully elucidated. Objective of the study

to assess both safety and efficacy of an intensified B-cell depletion therapy (IBCDT) protocol, including RTX, cyclophosphamide (CYC), and methylprednisolone pulses without additional maintenance immunosuppressive therapy compared to conventional therapy regimen based on oral CYC and steroids and prolonged maintenance therapy with azathioprine (AZA) in patients with AAV and severe renal injury.

Methods: A cohort of 15 AAV patients with the most severe features of AVV renal involvement (as < 15 ml/min GFR and histological findings of paucimmune necrotizing glomerulonephritis with more than 50% crescents of non-sclerotic glomeruli at the renal biopsy) was treated IBCDT and compared to compared toa control group of 10 patients with AAV treated with a conventional therapy regimen based on oral CYC and steroids and prolonged maintenance therapy with azathioprine (AZA). Independently on the pharmacologic regimen, plasma exchange (7 procedures with 1-1.5 plasma volume replacement) was performed in the presence of 1. alveolar haemorrhage, and 2.more than 50% florid crescents in the nonsclerotic glomeruli, or 3. dialysis dependence.

Results: Complete clinical remission (BVAS 0) was observed at 6 months in 14 of 15 patients (93%). All cases treated with IBCDT who achieved a complete clinical remission experienced a depletion of peripheral blood B cells at the end of therapy. Of the 10 dialysis dependent patients at onset, 6 subjects (60%) experienced a functional recovery allowing the suspension of dialysis treatment. When compared to the control group, no statistically significant difference was observed in patients treated with IBCDT in terms of overall survival, 6-month therapeutic response rate, and 6-, and 12-month functional renal recovery. The cumulative total dose of CYC in the case group was on average 1 g/patient while in the control group on average 8.5 g / patient ($p = 0.00008$). Plasmapheresis sessions were performed at part of the induction therapy among 13 patients (87%) in the case group and 8 (80%) in the control group.

Conclusion: The results of this study showed that IBCDT appeared to be safe and has the same efficacy profile when compared to conventional therapy with CYC plus AZA in the management of the most severe patients with AAV. Additionally, this avoids the need of prolonged maintenance therapy for long, and limits the exposure to CYC with consequent reduced toxicity and drug-related side effect rates.

Disclosure: D. Roccatello: None; **S. Sciascia**: None; **S. FODDAI**: None; **g. QUATTROCCHIO**: None; **M. RADIN**: None; **I. CECCHI**: None; **A. BARINOTTI**: None; **E. RUBINI**: None; **M. FERRO**: None; **E. DE SIMONE**: None; **c. naretto**: None; **A. BARRECA**: None; **A. SAMMARTINO**: None; **D. ROSSI**: None; **R. FENOGLIO**: None.

Abstract Number: 0691

Recognizing the New Disorder "Idiopathic Hypocryoglobulinaemia" in Patients with Previously Unidentified Clinical Conditions

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: A considerable number of patients with high clinical suspicion for cryoglobulinaemic vasculitis either show negative results for the detection of cryoglobulins or show only trace amounts which cannot be characterized for composition.We aimed at establishing whether the failure to detect or the detection of trace amounts of cryoglobulin with conventional methods either identifies a peculiar subset of low level cryoglobulinaemia (from now on *hypocryoglobulinaemia*) or represents a separate entity.

Methods: The present cohort includes 237 patients, median age 60.8, range 22–97 years, 100 males and 137 females, having trace amounts of cryoglobulins (< 0.5% cryocrit) detected in the Laboratory of CMID, San Giovanni Bosco Hub Hospital and University of Turin between 2008 and 2021. Patients presenting with high clinical suspicion of autoimmune systemic conditions yet negative for the detection of cryoglobulinemia with the standard technique were tested for hypocryoglobulins.All patients with urinary abnormalities underwent kidney biopsy.

Results: Using a modified precipitation technique in hypo-ionic medium, we prospectively identified between 2008 and 2021 237 patients (median age 60.8 years [22–97], 137 females) having < 0.5% cryocrit and clinical suspicion of autoimmune disorder. Of these 237 patients, only 54 (22.7%) had a history of HCV infection. One hundred and sixty-nine out of 237 patients (71%) had an established underlying disease, while 68 patients (28.6%) (median age 62.9 years [29–93], 35 females) did not show either laboratory markers or clinical symptoms consonant with an underlying aetiology. These 68 cases with only trace amounts of cryoglobulins were defined as having a *putatively idiopathic* hypocryoglobulinaemia. Nineteen of these 68 patients (27.9%) had a history of HCV infection. Twenty-four patients out of 68 (35.3%) were positive for rheumatoid factor (RF), while 25 (36.7%) patients had signs of complement consumption (i.e., C4 < 15 mg/dl and/or C3 < 80 mg/dl), and 36 (52.9%) had increased inflammatory indexes. Seven patients only had arthralgia and constitutional symptoms while 61 out of 68 (89.7%) presented with at least one of the three cardinal signs of cryoglobulinaemic vasculitis including skin lesions, peripheral nerve involvement, and glomerulonephritis. Seventy-five percent of the subjects had type III hypocryoglobulins. In patients with hypocryoglobulinaemia the histologic features of glomerulonephritis (also examined by electron microscopy) resembled those of mixed cryoglobulinaemia-associated glomerulonephritis.

Conclusion: In conclusion, hypocryoglobulins are often polyclonal and are mainly unrelated to HCV infection. Patients who present high clinical suspicion for vasculitis, especially glomerulonephritis and yet test negative for cryoglobulinaemia detected by standard techniques, could require deeper investigation even in the absence of HCV infection, RF activity or signs of complement consumption.

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Abstract Number: 0692

Behçet's Disease-Associated TCR in the Eye Points to HLA Class I-Restricted Autoimmunity

Johannes Nowatzky[1], Ziyan Lin[2], Yesim Ozguler[3], Alireza Khodadadi-Jamayran[2], Didar Ucar[4], Aristotelis Tsirigos[5], Gulen Hatemi[6] and Olivier Manches[7], [1]NYU Grossman School of Medicine, Department of Medicine, Department of Pathology, Division of Rheumatology, NYU Behçet's Disease Program, NYU Ocular Rheumatology Program, New York, NY, [2]NYU Grossman School of Medicine, Applied Bioinformatics Laboratories, New York, NY, [3]NYU Grossman School of Medicine, Department of Medicine, Division of Rheumatology and Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Department of Internal Medicine, Division of Rheumatology, New York, NY, [4]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Department of Ophthalmology, Istanbul, Turkey, [5]NYU Grossman School of Medicine, Department of Pathology, Department of Medicine, Institute for Computational Medicine, New York, NY, [6]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, [7]EFS, Recherche et Développement, Department of Pulmonology and Physiology, CHU Grenoble-Alpes, Université Grenoble-Alpes, INSERM U1209, CNRS UMR, Institute for Advanced Biosciences, Grenoble, France

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Behçet's disease (BD) is an HLA class I-associated disorder, given its strong link to *HLA-B*51*. However, evidence of HLA class I restriction is lacking, and candidate antigens are elusive. Here, we hypothesized that clonal CD8 T cell expansions are present in BD at tissue sites during active disease aiming to provide evidence of HLA class I restriction by identifying their disease-related CD8 TCR.

Methods: We performed scRNAseq with TCR V(D)J analyses in PBMC from a Turkish cohort of 37 untreated subjects (14 HD, 23 BD) with ocular and vascular BD. In a separate set of experiments, we obtained anterior chamber fluid cells from two additional *HLA-B*51*$^+$ Behçet's uveitis (BU) subjects from an independent cohort, as well as time-matched autologous peripheral blood, assessed TCR sequences, clonotype- and T cell phenotype distribution between peripheral blood and the eye, and clonotype sharing across study subjects in both cohorts.

Results: Anterior chamber fluid cells in BU showed substantial oligoclonal CD8 T cell expansions. Highly expanded ocular clonotypes overlapped with autologous peripheral blood exhibiting an intraclonotype shift towards a more cytotoxic (Granzyme B$^+$) phenotype in the eye over peripheral blood. An identical disease-related CD8 a/bTCR, determined in the eye-blood paired sample experiments, was re-identified in *HLA-B*51*$^+$ active uveitis peripheral blood in the Turkish cohort but not in HDs or BD subjects without uveitis. We identified additional clonotypes which showed high CDR3 sequence similarity to our experimentally determined TCR computationally, using TCRdist. Again, we re-located those in *HLA-B*51*$^+$ subjects with active uveitis but not in HD, BD without uveitis, or *HLA-B*51*$^-$ subjects.

Conclusion: We demonstrate the presence of highly expanded CD8 T cells in BU eyes and autologous peripheral blood and identify disease-associated TCR across independent cohorts of affected *HLA-B*51*-carrying subjects but not HDs. Our findings suggest that an HLA class I-restricted process drives BD in a subset of clinically distinct patients and will facilitate antigen discovery by enabling the identification of cognate peptides in an *HLA-B*51* restriction context.

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Abstract Number: 0693

Comparison of the Cardiovascular Risk in Patients with Vasculitis and Diabetes Mellitus

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular disease (CVD) has been reported as the most common cause of death in ANCA-associated vasculitis (AAV)[1,2]. Systemic inflammation, in addition to traditional risk factors such as diabetes mellitus (DM), has been suggested as the main contributor to cardiovascular (CV) events in vasculitis, as there is a well-known association between chronic inflammation and atherosclerosis[3].

Table 1. Baseline Characteristics

Table 1. Baseline Characteristics

NIS 2016-2019	Vasculitis 109,410		DM 32,491,290		P-value
	N	%	N	%	
Age	67.8 (67.5-68.0)		65.6 (65.6-65.7)		
Female	69,540	63.6	16,047,385	49.4	<0.001
Hypertension	77,915	71.2	27,107,773	83.4	<0.001
Obesity	12,285	11.2	8,535,218	26.3	<0.001
CKD	40,200	36.7	11,078,998	34.1	<0.001
Ischemic Heart Disease	24,300	22.2	11,504,328	35.4	<0.001
Prior CVA/ TIA	12,100	11	4,278,029	13.2	<0.001
Congestive Heart Failure	27,350	25	10,377,878	31.9	<0.001
Hyperlipidemia	39,650	36.2	17,882,467	55	<0.001
Anemia	9,170	8.4	2,025,205	6.2	<0.001
Smoker	29,720	27.2	8,621,158	26.5	0.049
Prior MI	6,105	5.6	3,097,365	9.5	<0.001
Prior PCI	5,550	5.1	2,897,505	8.9	<0.001
Prior CABG	4,060	3.7	2,781,449	8.6	<0.001
Presence of pacemaker	3,500	3.2	1,210,350	3.7	<0.001
Drug abuse	4,205	3.8	1,443,715	4.4	<0.001
Alcohol abuse	2,735	2.5	1,342,555	4.1	<0.001
Long term history of steroid use	24,805	22.7	548,175	1.7	<0.001
Personal history of steroid use	55	0.1	1,485	0.01	<0.001
Primary payer					**<0.001**
Medicare	75,315	68.8	20,699,983	63.7	
Medicaid	9,135	8.3	4,188,059	12.9	
Private	21,040	19.2	5,739,379	17.7	
Self-pay	1,955	1.8	980,505	3	
Income quartiles					**<0.001**
<25th	23,940	21.9	10,947,531	33.7	
26-50th	27,205	24.9	8,591,337	26.4	
51-75th	28,325	25.9	7,243,358	22.3	
76-100th	28,300	25.9	5,159,044	15.9	

The aim of this study is to assess the CV risk in patients with vasculitis and DM, and understand whether the risk of CVD in patients with vasculitis is as high as in those with DM.

Methods: In this retrospective cohort study, we identified patients with different types of vasculitis without DM based on ICD-10 codes, including large vessel vasculitis (LVV), ANCA-associated vasculitis (AAV), and other vasculitis such as Bechet disease (BD), polyarteritis nodosa (PAN) and cryoglobulinemia. We used the Nationwide Inpatient Sample database (NIS) from 2016 to 2019. We included all-cause mortality, acute coronary syndrome (ACS), cerebrovascular accident (CVA), transient ischemic attack (TIA), and deep venous thrombosis (DVT) or pulmonary embolism (PE) as our primary outcomes. Atrial

Table 2. Primary and Secondary Outcomes

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Primary Outcomes	**Vasculitis 109,410**		**DM 32,491,290**		**P-value**
	N	**%**	**N**	**%**	
Mortality	3,640	3.3	848,635	2.6	<0.001
ACS	1,965	1.8	1,348,340	4.1	<0.001
HF	4,030	3.7	2,359,579	7.3	<0.001
CVA	2,730	2.5	959,955	3	<0.001
TIA	510	0.5	149,785	0.5	0.91
DVT/PE	1,000	0.9	160,760	0.5	<0.001
Secondary Outcomes					
	N	**%**	**N**	**%**	**P-value**
Afib/ AF	25,730	23.5	6,707,233	20.6	<0.001
Metabolic Syndrome	80	0.07	117,210	0.4	<0.001
PVD	6,785	6.2	1,179,654	3.6	<0.001

Table 3. Comparison of mortality and CV outcomes in patients with vasculitis vs DM

Table 3. Comparison of mortality and CV outcomes in patients with vasculitis vs DM				
Primary Outcomes	**OR**	**95% CI**		**P-value**
Mortality	1.38	1.28	1.49	<0.001
ACS	1.64	1.480	1.82	<0.001
HF	0.69	0.64	0.75	<0.001
CVA	1.62	1.07	1.27	<0.001
TIA	1.08	0.89	1.32	0.41
DVT/PE	2.33	2.02	2.69	<0.001
Secondary Outcomes	**OR**	**95% CI**		**P-value**
Afib/ AF	1.73	1.66	1.80	<0.001
Metabolic Syndrome	0.33	0.19	0.56	<0.001
PVD	2.56	2.4	2.73	<0.001

fibrillation (Afib), atrial flutter (AF), peripheral vascular disease (PVD), and metabolic syndrome were our secondary outcomes. We implemented logistic regression analysis in the univariable and multivariable models. In the multivariable model, we adjusted all outcomes for potential confounders, including age, sex, ethnicity, obesity, anemia, hypertension, renal failure, history of smoking or alcohol abuse, prior history of MI, primary coronary intervention, or coronary artery bypass grafting, coagulopathy, ischemic cardiomyopathy, Elixhauser comorbidity index, hypothyroidism, history of defibrillator or pacemaker, and long-term use of steroids, insurance status and income quartiles. The analysis was done using the STATA software, version 17.0 (MP).

Results: We identified 32,491,290 patients with DM and 109,410 patients with vasculitis without DM, of whom 50,265 (46%) had LVV, 41,220 (37.7%) had AAV, and 13,635 had other vasculitides (12.5%). Our results showed that patients with vasculitis had a higher mortality (OR: 1.38; 95%-CI 1.28-1.49; p-value < 0.001), and increased risk of developing ACS (OR: 1.64; 95%-CI 1.48-1.82; p-value < 0.001), CVA (OR: 1.62; 95%-CI 1.07-1.27; p-value < 0.001), DVT/PE (OR: 2.33; 95%-CI 2.02-2.69; p-value < 0.001), Afib/AF (OR: 1.73; 95%-CI 1.66-1.80; p-value < 0.001), and PVD (OR: 2.56; 95%-CI 2.4-2.73; p-value < 0.001) when compared to patients with DM even after adjusting for potential confounders.

Conclusion: Patients with vasculitis had a higher risk of cardiovascular disease and venous thromboembolism. Our study confirms the high CV risk in patients with vasculitis as highlighted in previous studies, and suggests an even higher risk when compared to patients with DM.

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Abstract Number: 0694

Off-label Use of Biologics in Urticarial Vasculitis: A European Cohort Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Urticarial vasculitis (UV) is characterized by atypical urticarial lesions and leukocytoclastic vasculitis, sometimes with extra-cutaneous manifestations. First-line treatment is often based on colchicine, hydroxychloroquine, dapsone or low-dose glucocorticoids. In refractory forms, the use of biologics has been anecdotally described as potentially effective. We aimed to describe the efficacy and safety of biologics in patients with UV.

Methods: We conducted a retrospective European multicentre study including patients with hypocomplementemic (HUV) or normocomplementemic (NUV) UV who received at least one biologic, including anti-CD20, anti-IgE and/or anti-IL-1. We analyzed the clinical and biological characteristics as well as the efficacy and safety of the biologics.

Results: Forty-one patients were analyzed, including 24 patients with HUV and 17 with NUV.Fifty-two therapeutic sequences were recorded, including rituximab in 23, anti-IL1 in 16 and anti-IgE in 13 cases. Extra-cutaneous manifestations were present in 90%. The most common manifestations were arthralgia in 66%, arthritis in 27%, ocular inflammation in 24%, gastrointestinal involvement in 15%, renal involvement in 15% and pulmonary involvement in 12%.

The median number of treatments before biologic was 4 (IQR 3-6). A higher proportion of HUV was observed in patients treated with anti-CD20 (83%), while a higher proportion of NUV was observed in patients treated with anti-IL-1 (62%) and omalizumab (77%). All patients with renal involvement were treated with anti-CD20.

Biologics were used in combination with glucocorticoids in 75% of patients, with a median prednisone dose of 18 mg/day (IQR 10-39), hydroxychloroquine in 25%, dapsone in 6% and azathioprine in 8%.

After a median follow-up of 25 (IQR 12-43) months, the cutaneous response was complete in 40%, partial in 37% and considered inadequate in 23%. Extracutaneous response was similar to cutaneous response in 84%. Prednisone dose reduction to < 10 mg/day was achieved in 72% of patients, including discontinuation of glucocorticoids in 34%. Despite different disease profiles for each biologic, cutaneous and global clinical response rates were broadly comparable across all biologics.

Severe adverse events, mainly serious infectious, were observed in 7 patients (17%), including 4 patients treated with rituximab and 3 patients treated with anakinra.

Conclusion: Rituximab, anti-IL-1 and omalizumab are an effective and well-tolerated treatment option for UV that are refractory to conventional therapies. Rituximab was mainly used for HUV while anakinra and omalizumab were mainly used for NUV.

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Abstract Number: 0695

Impact and Cardiovascular Outcomes of Large Vessel Vasculitis in Atrial Fibrillation Hospitalization: A Nationwide Inpatient Database Study

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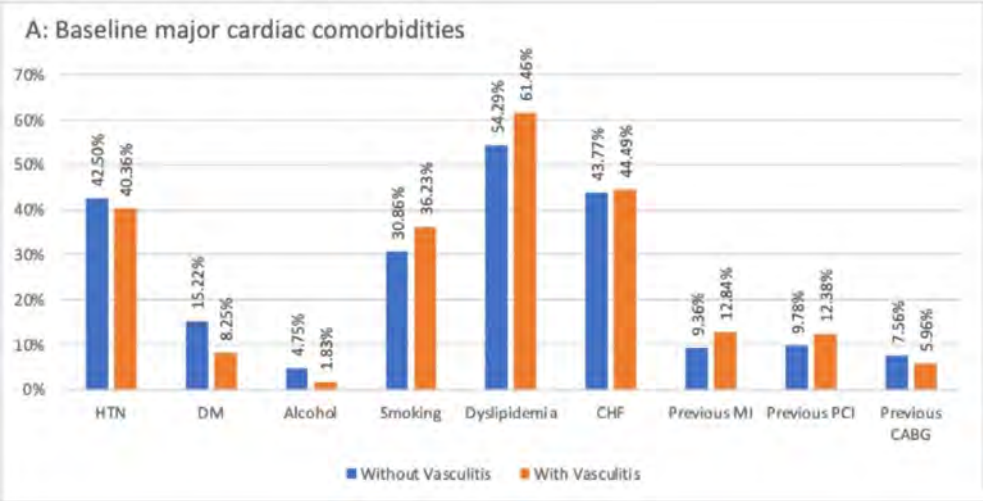
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Atrial fibrillation is the most commonly treated cardiac arrhythmia, associated with significant morbidity and mortality. Recent research is suggestive that autoimmunity and inflammation might have a role in the pathophysiology of atrial fibrillation (AF). While several autoimmune conditions are associated with AF, autoimmune vasculitis confers a worse survival in patients with AF. Current literature is limited in determining the impact of large vessel vasculitis (LVV) in AF patients. We present a study discussing the cardiovascular outcomes in patients with LVV and atrial fibrillation.



Baseline major co-morbidities

			Unadjusted		Adjusted	
	Without vasculitis, (%)	With vasculitis, (%)	OR(95% CI)	P-value	aOR(95% CI)	P-value
MACCE	3.9%	7.79%	2.05(1.25-3.37)	<0.001	1.72(1.02-2.89)	0.04
In-hospital mortality	0.73%	1.37%	1.90 (0.61-5.94)	0.27	1.42 (0.43-4.68)	0.56
AMI	2.85%	6.42%	2.34(1.36-4.02)		1.99(1.13-3.51)	0.017
AKI	0.09%	0.92%	9.77(2.42-39.41)	<0.001	9.73(2.33-40.68)	0.002
stroke	0.53%	0.46%	0.86(0.12-6.13)	0.88	0.75(0.10-5.35)	0.77
Cardiac Arrest	0.30%	0.46%	1.52(0.21-10.89)	0.674	1.48 (0.21-10.68)	0.698
Shock	0.61%	0.92%	1.50(0.37-6.02)	0.567	1.60(0.38-6.77)	0.52
NAE	8.04%	7.34%	0.906(0.54-1.50)	0.703	0.85(0.50-1.42)	0.53
Bleeding	0.62%	0.91%	1.46(0.36-5.92)	0.59	1.27(0.31-5.20)	0.73
PCI	0.40%	0.45%	0.81 (0.11-5.84)		0.925(0.12-6.58)	0.93
HF	28.19%	23.8%	0.79(0.58-1.09)	0.156	0.60(0.42-0.78)	0.008
Length of stay (days)	3.38 ± 3.73	4.44 ± 4.23				<0.001
Total charges ($)	46643.05 ± 65421.51	46549.59 ± 63771.15				0.98

In-hospital outcomes and resource utilization in patients with Atrial Fibrillation with and without vasculitis

Methods: We queried the National Inpatient Sample database in the period between 2016 - 2019. Primary AF hospitalizations were identified and subsequently we stratified the cohort based on the presence of LVV. The adjusted odds ratios (aOR) of in-hospital outcomes and resource utilization were calculated using chi-square statistics in software STATA v.17.

Results: Of 1,041,670 AF hospitalizations between 2016-2019; 1,090 had LVV (Giant cell arteritis: 1050 and Takayasu arteritis: 40). Afib with LVV patients were older (78.33 vs. 71.04, p< 0.001) and predominantly female (71.55 vs. 51.39, p< 0.001). On adjusted analysis, compared to non-LVV patients, LVV patients had significantly higher MACCE (aOR 1.72, 95% CI 1.02-2.89), AMI (aOR 1.99, 95% CI 1.13-3.51), AKI (aOR 9.73, 95% CI 2.33-40.68) with longer length of stay (3.38±3.73 vs. 4.44±4.23). Interestingly, there seemed to be a reduced risk of heart failure in AF patients with vs without vasculitis (aOR 0.60, 95% CI 0.42-0.78). On the contrary, there was no difference in in-hospital mortality, stroke, bleeding, need for PCI and total charge of hospitalization between the two groups.

Conclusion: The clinical outcomes in patients with concurrent LVV and AF are significantly worse, as evidenced by increased risk of MACCE, AMI and AKI compared to patients with only AF but not LVV. This study provides evidence that patients with large vessel vasculitis and AF need to be managed more aggressively as clinical outcomes are notably worse. However, we do not have enough data to suggest whether patients with LVV need to be screened for AF. Further prospective trials are needed to answer these queries.

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Abstract Number: 0696

Association of Large-vessel Vasculitis with Inflammatory Bowel Diseases: A European Case-control Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The association of large vessel vasculitis (LVV), whether Takayasu arteritis (TA) or giant cell arteritis (GCA), with inflammatory bowel disease (IBD) is a rare and challenging condition. The prevalence of LVV in IBD cohorts is less than 1%, but the prevalence of IBD can be as high as 15.4% in TA cohorts, and population-based studies confirmed this association. We aimed to describe the characteristics and outcome of LVV-IBD patients, with a focus on the therapeutic management.

Methods: We performed an observational, multicenter, retrospective case-control study in Western Europe countries (France, Italy, Spain, Germany, Belgium). Cases were adults or children with both LVV and IBD (LVV-IBD), whereas controls had isolated TA (iTA) or GCA (iGCA).

Results: Fifty-one LVV-IBD patients were included, including 39 TA-IBD and 12 GCA-IBD patients, and compared with 93 iTA and 52 iGCA. LVV-IBD patients were mostly females (75% in TA-IBD and 72% in GCA-IBD). Crohn's disease was more common in TA-IBD (67%), while ulcerative colitis was more common in GCA-IBD (58%). LVV occurred after IBD in most cases (56% in TA-IBD and 75% in GCA-IBD), with a median interval of 1 year in TA-IBD and 8.6 years in GCA-IBD, and were diagnosed concomitantly in 16%. Location, behaviour and complications of IBD were similar to previously reported IBD cohorts.

Compared to iTA patients, TA-IBD patients were significantly younger at TA diagnosis (27 vs. 37 years, $p < 0.001$) and had more upper limb claudication (36 vs 12%, p=0.006). The number of affected arterial segments was lower in TA-IBD (3 vs. 4 segments, p=0.015) and carotid artery involvement was less common in TA-IBD patients than in iTA patients (50 vs. 75% respectively, p=0.005).

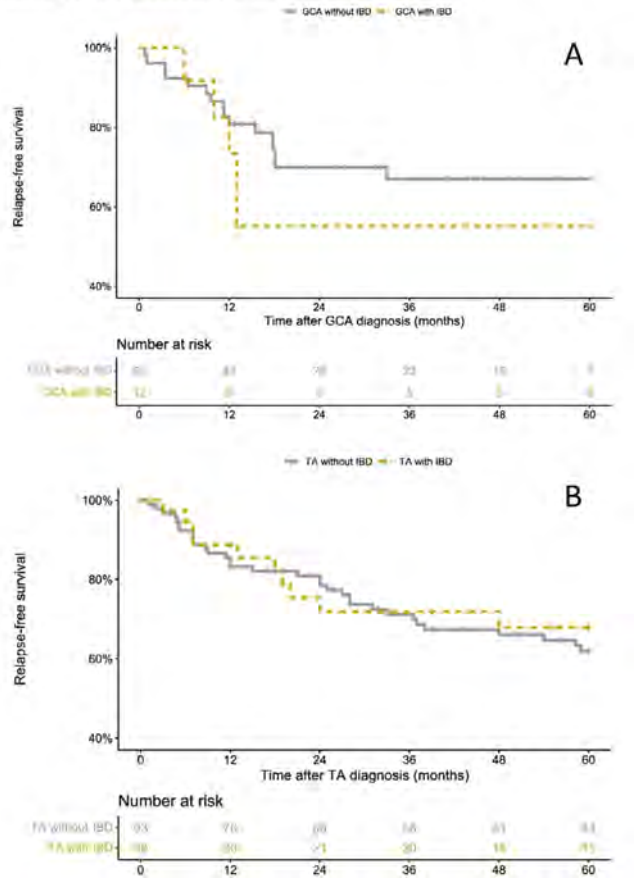
Compared to iGCA patients, GCA-IBD patients had more arthralgia (50 vs 15%, p=0.017) and vascular murmur (25 vs 0%, p=0.016). GCA-IBD patients had more arterial thickening or stenosis than controls (75 vs. 30% respectively, p=0.044).

Table 1. Comparisons between GCA and TA patients with and without IBD (N=196)

Feature	N	Overall (N = 196)	GCA-IBD (N = 12)	iGCA (N = 52)	p	TA-IBD (N = 39)	iTA (N = 93)	p
Demography								
Gender = female	196	154/196 (79%)	9/12 (75%)	41/52 (79%)	0.72[1]	29/39 (72%)	76/93 (82%)	0.29
Age at LVV diagnosis	196	44 (26-66)	68 (65-72)	72 (67-78)	0.066[2]	27 (22-36)	37 (26-48)	<0.001[2]
Symptoms								
General symptoms	196	130/166 (88%)	8/12 (67%)	11/52 (79%)	0.5[3]	37/39 (88%)	54/93 (88%)	0.2[3]
Musculoskeletal symptoms	195	71/196 (36%)	7/12 (58%)	25/52 (48%)	0.5[3]	12/39 (31%)	27/92 (29%)	0.9[3]
Polymyalgia rheumatica	187	29/187 (15%)	4/12 (33%)	23/52 (44%)	0.5[3]	-	-	-
Arthralgia	196	49/196 (25.1%)	6/12 (50%)	8/52 (15%)	0.017[3]	8/39 (21%)	27/92 (29.3%)	0.3[3]
Ocular symptoms	195	30/195 (15%)	1/12 (8.3%)	15/52 (29%)	0.3[3]	2/39 (5.1%)	12/92 (13%)	0.2[3]
Cranial symptoms	196	73/196 (37%)	7/12 (58%)	44/52 (85%)	0.056[3]	3/39 (7.7%)	13/92 (21%)	0.070[3]
Neurologic symptoms	195	12/169 (8.7%)	2/12 (0%)	2/52 (3.8%)	>0.9[3]	2/39 (5.1%)	13/92 (14%)	0.2[3]
Skin symptoms	194	55/194 (7.7%)	1/12 (8.3%)	0/51 (0%)	0.3[3]	1/39 (2.6%)	13/92 (14%)	0.064[3]
Gastrointestinal symptoms	193	50/193 (26%)	3/11 (27%)	1/51 (2.0%)	0.016[3]	15/39 (38%)	31/92 (34%)	0.6[3]
Cardiac symptoms	194	28/194 (14%)	3/12 (0%)	2/51 (3.9%)	>0.9[3]	7/39 (18%)	16/92 (17%)	0.7[3]
Vascular involvement	172	166/172 (96%)	8/12 (67%)	21/29 (72%)	0.7[3]	39/39 (100%)	91/92 (99%)	>0.9[3]
Upper limb claudication	188	22/186 (14%)	1/8 (12%)	0/52 (0%)	0.15[3]	10/39 (56%)	7/87 (12%)	0.006[3]
Lower limb claudication	188	12/186 (7.7%)	1/8 (12%)	2/52 (3.8%)	0.4[3]	3/39 (7.7%)	6/87 (11%)	0.7[3]
Cerebralgia	188	17/186 (11%)	0/8 (0%)	0/52 (0%)	>0.9[3]	3/39 (7.7%)	9/87 (10%)	0.6[3]
Vascular murmur	186	68/186 (38%)	2/8 (25%)	0/52 (0%)	0.016[3]	21/39 (54%)	45/91 (49%)	0.6[3]
Inflammatory syndrome at LVV diagnosis								
Present	171	142/171 (83%)	8/8 (100%)	44/46 (96%)	>0.9[3]	28/31 (90%)	61/85 (72%)	0.056[3]
C-reactive protein, mg/L	144	60 (27-118)	75 (66-147)	74 (50-138)	0.6[2]	70 (21-120)	38 (16-104)	0.4[2]
Imaging characteristics								
Number of arteries involved	168	4.00 (3.00-5.00)	4.50 (1.50-5.75)[4]	4.00 (1.00-5.00)	0.9[2]	3.00 (2.25-4.75)	4.00 (3.00-6.00)	0.015[2]
Stenosis/Parietal thickening	168	134/168 (85%)	8/8 (75%)	6/20 (30%)	0.044[3]	39/39 (100%)	87/91 (96%)	0.44
Dilation/Aneurysm	168	30/168 (18%)	2/8 (25%)	1/20 (5.0%)	0.2[3]	7/39 (18%)	22/91 (24%)	0.62
Arteries involved								
Ascendent aorta	170	99/170 (58%)	8/10 (80%)	18/28 (57%)	0.3[3]	18/39 (46%)	54/93 (58%)	0.2[3]
Descendent thoracic aorta	169	97/169 (57%)	7/10 (70%)	17/28 (61%)	0.7[3]	17/38 (45%)	56/93 (60%)	0.11[3]
Abdominal aorta	168	65/166 (39%)	5/10 (50%)	12/27 (44%)	>0.9[3]	12/39 (34%)	35/93 (38%)	0.7[3]
Iliac/coxal arteries	166	51/166 (33%)	2/10 (20%)	0/28 (0%)	0.054[3]	14/38 (37%)	35/93 (38%)	>0.9[3]
Upper limb arteries	170	124/170 (73%)	4/10 (40%)	15/29 (52%)	0.3[3]	28/39 (74%)	74/93 (80%)	0.5[3]
Carotid	168	107/160 (63%)	6/10 (60%)	12/28 (43%)	0.5[3]	13/39 (50%)	70/93 (75%)	0.005[3]
Vertebral artery	166	34/160 (23%)	0/10 (0%)	2/26 (7.7%)	>0.9[3]	5/38 (13%)	27/93 (29%)	0.055[3]
Lower limb arteries	170	44/170 (28%)	1/10 (40%)	10/29 (34%)	>0.9[3]	7/39 (18%)	23/93 (25%)	0.6[3]
Renal arteries	166	31/169 (18%)	1/10 (10%)	2/28 (7.1%)	>0.9[3]	9/38 (24%)	19/93 (20%)	0.7[3]
LVV treatments								
LVV treatments received: ever								
Systemic glucocorticoids	196	179/196 (91%)	12/12 (100%)	39/52 (100%)	>0.9[3]	35/39 (90%)	93/93 (100%)	0.6[3]
Methotrexate	194	84/194 (43%)	5/12 (42%)	16/52 (31%)	0.5[3]	11/39 (28%)	52/93 (57%)	0.002[3]
Azathioprine	193	32/193 (17%)	1/12 (8.3%)	0/52 (0%)	0.2[3]	17/39 (44%)	14/90 (16%)	<0.001[3]
Mycophenolate mofetil	192	47/89 (2.1%)	3/12 (0%)	0/52 (0%)	>0.9[3]	1/39 (2.6%)	3/90 (3.3%)	>0.9[3]
Cyclophosphamide	188	6/188 (3.2%)	2/12 (17%)	0/52 (0%)	0.053[3]	0/39 (0%)	4/86 (4.7%)	0.3[3]
Biotherapy	196	48/196 (24%)	2/12 (17%)	2/52 (3.8%)	0.2[3]	17/39 (44%)	27/93 (29%)	0.11[3]
TNF-α blockers	193	34/193 (18%)	1/12 (8.3%)	0/52 (0%)	0.3[3]	13/39 (33%)	20/90 (22%)	0.2[3]
Tocilizumab	191	20/191 (10%)	1/12 (8.3%)	2/52 (3.8%)	0.3[3]	6/38 (16%)	11/88 (12%)	0.7[3]
Other	196	8/196 (4.1%)	2/12 (0%)	1/52 (1.9%)	>0.9[3]	3/39 (7.7%)	4/93 (4.3%)	0.4[3]
Endovascular or surgical treatment	196	49/196 (25%)	1/12 (8.3%)	0/52 (0%)	0.2[3]	15/39 (38%)	33/93 (35%)	0.7[3]
Follow-up								
Follow-up of LVV (months)	193	84 (41-160)	167 (86-231)	44 (24-68)	0.002[2]	184 (82-317)	113 (56-160)	0.068[2]
Death	196	7/196 (3.6%)	2/12 (17%)	0/52 (0%)	0.033[3]	2/39 (5.1%)	3/93 (3.2%)	0.6[3]
At least 1 LVV relapse during FU	196	80/196 (41%)	8/12 (50%)	17/52 (33%)	0.2[3]	11/39 (28%)	44/93 (48%)	0.024[3]
Number of LVV relapses, if any	80	1.00 (1.00-3.00)	1.00 (1.00-1.25)	1.00 (1.00-2.00)	0.6[4]	1.00 (1.00-3.00)	1.00 (1.00-3.00)	0.8[4]
LVV status at last FU visit					0.6[3]			0.021[3]
Remission under treatment	165	100/165 (61%)	8/12 (50%)	28/52 (56%)		27/39 (71%)	36/83 (46%)	
Remission without treatment	165	79/165 (42%)	8/12 (50%)	23/52 (44%)		9/39 (24%)	40/89 (46%)	
Active	165	7/165 (4.6%)	2/12 (17%)	0/52 (0%)		2/39 (5.2%)	5/83 (6.0%)	

n/N (%); Median (IQR); [1]Pearson's Chi-squared test; [2]Welch Two Sample t-test; [3]Fisher's exact test; [4]Wilcoxon rank sum test

Figure 1. Kaplan Meier curves for the risk of (A) GCA and (B) Takayasu Arteritis relapses depending on the association with IBD



LVV occurred in IBD patients while on therapy in 77% (86% for TA-IBD and 56% for GCA-IBD), including oral glucocorticoids (GCs) in 36%, azathioprine (AZA) in 25%, or TNF-a blockers in 33% of TA-IBD.

LVV-IBD were treated with GCs in 91%, methotrexate in 43%, AZA in 17% or cyclophosphamide in 3.2%. Biologics were used in 24%, including mainly TNF-a blockers in TA-IBD patients (33%). AZA was used more frequently in TA-IBD patients than in iTA, with the latter mainly receiving methotrexate.

The presence of IBD did not influence the vasculitis relapse rate (OR 1.40 [0.39-5.10] for GCA and OR 0.72 [0.34-1.51] for TA). Aortic insufficiency in GCA patients (OR 8.36, 95% CI 1.35-51.66), and ascendent aorta involvement (OR 2.35, 95% CI 1.20-4.60) and the presence of general symptoms (HR 2.02, 95% CI 1.01-4.03) in TA patients were identified as independent vasculitis relapse risk factors.

Conclusion: This large case-control study identifies new clinical, imaging and outcome features in LVV-IBD. Vascular involvement seems to be less severe in TA-IBD than in iTA, while it seems to be the opposite in GCA-IBD. LVV-IBD occurred despite ongoing treatment in 77%, including AZA and/or TNF-a blockers in almost half of the cases.

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GSK, 6; **O. Fain**: None; **M. Samson**: ARGENX, 2, Boehringer-Ingelheim, 2, CHUGAI, 2, CSL Vifor, 2, GlaxoSmithKlein(-GSK), 2, NOVARTIS, 2, 5; **G. Gondran**: None; **V. Abitbol**: None; **B. Terrier**: AstraZeneca, 5, CSL Vifor, 2, GlaxoSmithKlein(GSK), 2.

Abstract Number: 0697

Alterations in Composition and Function of Gut Microbiota in Patients with Large-Vessel Vasculitis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The gut microbiome has a critical role in immune homeostasis and there is growing interest in understanding the relationship between the microbiome and autoimmunity. There are epidemiologic and genetic associations between large-vessel vasculitis (LVV) and inflammatory bowel disease, an autoimmune disease where intestinal dysbiosis is common. This study evaluated the relationship between composition and function of gut microbiota and disease activity in patients with LVV.

Methods: In this longitudinal, prospective cohort study, stool samples and clinical data were collected from patients with giant cell arteritis (GCA) and Takayasu arteritis (TAK) every 6 months at a single center. Diagnosis and disease activity of LVV were determined by the investigator and informed by the 1990 ACR classification criteria and BVAS, respectively. Healthy control patients without autoimmune disease were also recruited and supplemented by existing healthy control stool microbiome data from a separate convenience cohort. The fecal microbiome was profiled using shotgun metagenomic sequencing. Comparisons to healthy controls were conducted using samples from the first visit at which: 1) LVV was inactive, and 2) LVV was active. The relative abundance of microbial taxa in the stool was estimated using Kraken2, and the relative abundance of microbial gene orthologs was determined by alignment to the Kyoto Encyclopedia of Genes and Genomes (KEGG). Community-level differences in taxonomic (beta diversity) and gene function composition in the microbiome were assessed using Bray-Curtis distances between samples in principle coordinate analysis (PCoA) plots. The relative abundance of the 10 most common functional pathways, determined by the abundance of constituent genes, was

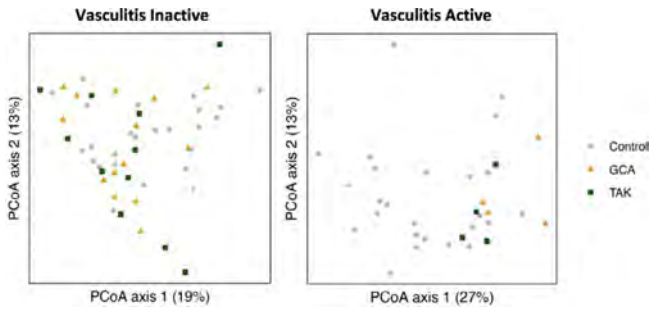

Figure 1. Bacterial composition in large-vessel vasculitis (inactive and active) vs controls. Principal coordinate analysis (PCoA) plots compare beta diversity between controls vs inactive vasculitis (left panel) and active vasculitis (right panel) using Bray-Curtis distances. Beta diversity did not significantly differ when comparing inactive LVV to controls ($p=0.21$) but did between active vasculitis and controls ($p<0.01$).

compared using heatmaps and linear models. P-values were adjusted to control for a false discovery rate of 5% when multiple comparisons were made.

Results: 27 patients with LVV, which included 16 with GCA and 11 with TAK, and 23 healthy controls were included in the study with a total of 76 stool samples obtained. GCA patients were 75% female with mean age 70.4 years (SD 6.5) while TAK patients were all female with mean age 37.2 years (SD 13.8). Eight patients with LVV experienced a flare with the most common symptoms in GCA being constitutional symptoms (75%) and headache (50%) and in TAK chest pain/dyspnea (50%) and lower limb claudication (25%). Composition of fecal microbiota, measured by beta diversity, was significantly different in active LVV samples but not inactive LVV when compared to controls (**Figure 1**). In our analysis of microbial gene ortholog abundance, functional genes of bacteria were significantly different in both active and inactive LVV patients

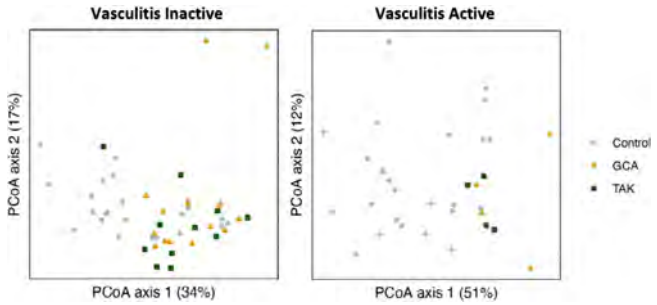

Figure 2. Bacterial functional analysis in large-vessel vasculitis (inactive and active) vs controls. PCoA plots compare microbial metagenomic functional composition in inactive vasculitis (left panel) and active vasculitis (right panel) compared to controls using Bray-Curtis distances. These distributions significantly differed between controls and vasculitis subgroups both during inactive disease ($p<0.01$) and active disease ($p<0.01$).

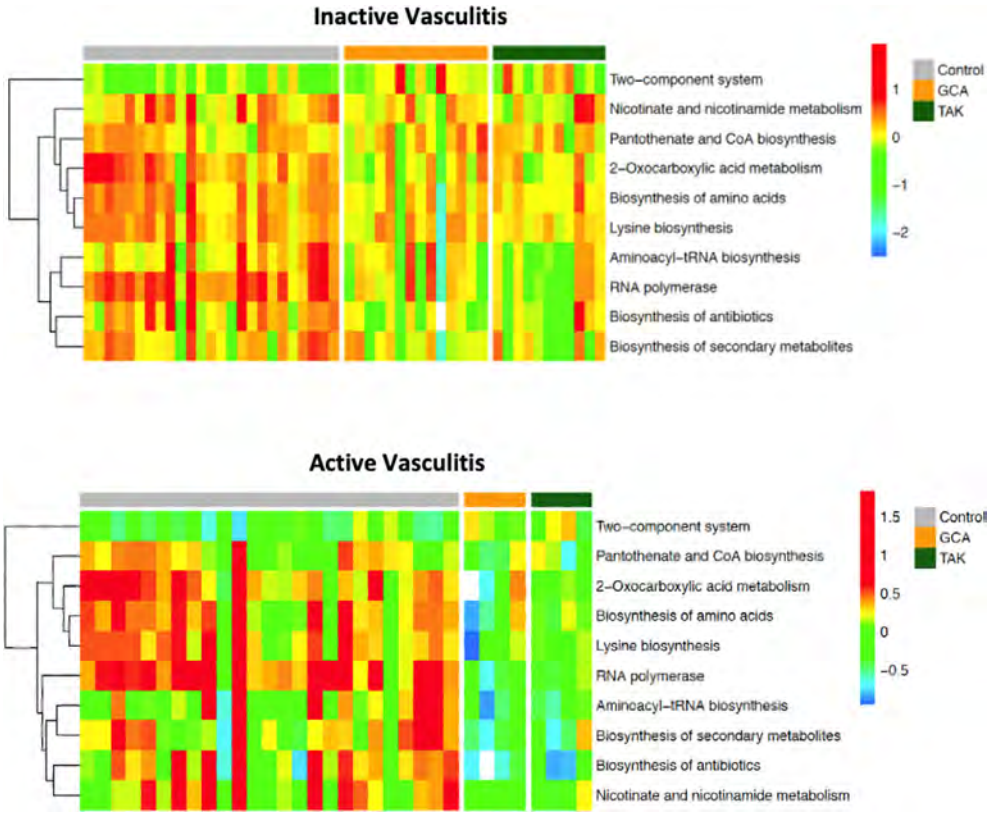

Figure 3. Functional pathways of gut microbiota in large-vessel vasculitis vs controls. Heatmaps representing relative abundance of functional pathways between control patients, patients with giant cell arteritis, and patients with Takayasu arteritis. While few pathways significantly differed between groups during inactive vasculitis (top), more significant differences were observed from samples during active vasculitis (bottom).

compared to controls (**Figure 2**). Several microbial gene pathways were identified to distinguish patients with active LVV from controls, but few emerged in our comparison of inactive LVV and controls (**Figure 3**).

Conclusion: Patients with LVV, particularly those with active disease, have altered composition, functional genes and pathways of gut microbiota compared to healthy controls. The possibility of shared mechanisms driving the altered microbiome in GCA and TAK warrants further investigation.

Disclosure: A. Mayer: None; **W. Hu**: None; **K. Bittinger**: None; **R. Liang**: None; **N. Amudala**: None; **S. Banerjee**: None; **P. Merkel**: AbbVie/Abbott, 5, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos, 5, Electra, 5, Genentech, 5, GlaxoSmithKlein(GSK), 2, 5, HiBio, 2, InflaRx, 2, 5, Janssen, 2, Jubilant, 2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, Takeda, 2, 5, UpToDate, 9, Visterra, 2; **R. Rhee**: None.

Abstract Number: 0698

Differentiating Large Vessel Vasculitis from Vasculitis Mimickers in a Real World Setting: Clinical Presentation, Laboratory Tests and Radiographic Findings

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: As the resolution of Computed Tomography Angiography (CTA) has improved, rheumatologists have faced an increased volume of consults to evaluate patients for the presence of radiographic abdominal vasculitis (RAV). Biopsy is often not possible due to the nature of the lesion. In our experience, a large portion of these patients are ultimately not found to have vasculitis after a thorough evaluation. In this study we sought to identify the most predictive symptoms, laboratory, and imaging findings of having RAV at the first point of contact with the rheumatology consult service.

Methods: Patients with billing codes for vasculitis or non-inflammatory arteriopathies (NIA) evaluated by the rheumatology service between January 1, 2016 and December 31, 2021 were considered for inclusion in this study. Of these, only patients with question of vasculitis by imaging of the renal arteries, abdominal aorta, or mesenteric arteries and their branches (celiac, inferior and superior mesenteric arteries) with >1 year of follow up were included in the final analysis. Biographic data, presenting symptoms, laboratory data, and imaging reports were extracted. Patients were classified by their final diagnosis at the 1-year time point as either having vasculitis or NIA as determined by the treating physician based on their clinical course and response to treatment. Statistical analysis was conducted using STATA software.

Results: Of 683 candidate patients, 63 were seen by rheumatology for the question of RAV. 27 were excluded for insufficient data, 1 was excluded for question of vasculitis surrounding a stent, and 35 were included in the final analysis. Of these, 17 were ultimately determined to have vasculitis, and 18 were determined to not have vasculitis. Baseline patient characteristics are available in table 1. Notably 2 patients ultimately found to not have vasculitis received treatment for vasculitis in the follow up period, and 1 patient ultimately found to have vasculitis was managed as non-vasculitis with observation before

Table 1: Demographics and clinical characteristics of patients at baseline diagnosed with vasculitis vs non-vasculitis after consultation for question of RAV. AID denotes autoimmune disease, HTN smoking, HLD hyperlipidemia, and CAD coronary artery disease.

Characteristics	*Vasculitis (N=17)*	*Non-vasculitis (N=18)*	*Total (N=35)*
Age			
Mean years *(SD)*	53.3+/- 14.1	59.2+/-16.2	59.2+/-15.1
Sex - no. (%)			
Female	9 (53)	9 (50)	18 (51.5)
Male	8 (47)	9 (50)	17(48.5)
Race - no. (%)			
White	15 (88.2)	12 (66.6)	27 (77.1)
African American	2 (11.8)	1 (5.5)	3 (8.6)
Asian	0	3 (16.6)	3 (8.6)
Hispanic	0	2 (11.1)	2 (5.7)
History of Smoking - no. (%)	6 (35)	11 (61)	17 (48.6)
History of Diabetes - no. (%)	0	4 (22)	4 (11.4)
History of AID* - no. (%)	4 (23.5)	5 (27.8)	9 (25.7)
History of HTN - no. (%)	7 (41)	6 (33)	13 (37.1)
History of HLD - no. (%)	3 (18)	8 (44)	11 (31.4)
History of CAD - no. (%)	2 (12)	2 (11)	4 (11.4)

Table 2: Sensitivity, specificity, and positive/negative likelihood ratios (+LR/-LR) of presenting symptoms and CTA findings of patients with and without vasculitis.

Variable	*Sensitivity*	*Specificity*	*+LR*	*-LR*
Imaging Findings (%)				
Wall Thickening	59%	83%	3.53	0.49
Fat Stranding	41%	67%	1.24	0.88
Stenosis	29%	44%	0.53	1.59
Aneurysm	6%	89%	0.53	1.06
Pseudoaneurysm	6%	83%	0.35	1.13
Enhancement	18%	94%	3.18	0.87
Soft tissue encasement	18%	83%	1.06	0.99
Presenting Symptoms (%)				
Fatigue	29%	83%	1.76	0.84
Weight loss	29%	78%	1.32	0.91
Headache	24%	89%	2.11	0.86
Abdominal Pain	41%	17%	0.49	3.52
Nausea/vomiting	18%	44%	0.31	1.85
Diarrhea	12%	78%	0.52	1.13
Numbness/weakness	12%	94%	2.11	0.93
Fevers	29%	89%	2.65	0.79

treatment was initiated. Analysis of the predictive value of imaging findings and presenting symptoms are reported in table 2. Notably, wall thickening of the relevant vessels was found to be the most helpful finding with a specificity of 83% and positive likelihood ratio (+LR) of 3.53. Interestingly fat stranding was found to be less helpful with a specificity of 67% and +LR of 1.2. Wall enhancement was rarely seen but was highly specific for vasculitis with a specificity of 94% and +LR of 3.18. None of the presenting symptoms were found to be especially predictive of vasculitis. Analysis of laboratory findings on presentation revealed initial white blood cell count (WBC) and platelet count (Plt) were significantly higher in patients with vasculitis (Table 3).

Conclusion: Our study identified wall thickening, wall enhancement, and elevations in WBC and Plt as being predictive of having abdominal vasculitis. While commonly reported, fat stranding was non-specific. Interestingly the tested presenting symptoms were not successful in delineating which patients were ultimately determined to have vasculitis. Confirmation of these findings with larger prospective studies is warranted.

Table 3: Comparison of baseline laboratory values ($P < 0.05$ is statistically significant). CRP denotes C-reactive protein, WBC white blood cell count, Plt platelets, AST aspartate aminotransferase, ALT alanine aminotransferase, ALP alkaline phosphatase, and IQR interquartile range. CRP is in mg/L. AST, ALT, and ALP are in mg/dL. WBC and Plt are in K/μL.

Baseline Labs	*Vasculitis (N=17)*	*Non-vasculitis (N=18)*	*p Value*
CRP – median (IQR)	43.6 (11, 112.8)	16.95 (4.8, 37.3)	0.24
WBC – median (IQR)	9.7 (7.6, 13)	7.15 (6.1, 8.3)	0.006
Plt – median (IQR)	375 (266, 398)	218.5 (176, 272)	<0.001
AST – median (IQR)	20 (18, 24)	19 (13, 41)	0.88
ALT – median (IQR)	21 (14, 27.5)	20 (18, 39)	0.79
ALP – median (IQR)	100 (77, 116)	82 (67, 104)	0.070

Disclosure: J. haigney: None; **L. Fandino**: None; **V. Kyttaris**: AbbVie/Abbott, 5, AstraZeneca, 2, Aurinia, 1, EMD Serono, 5, Exagen, 2, 5, Fresenius Kabi, 1, Horizon Pharmaceuticals, 1, Novartis, 5, Scipher, 1, Takeda, 5, Vertex, 2.

Abstract Number: 0699

T Cell Subset Analysis in Patients with Large-Vessel Vasculitis

Rebecca Kuan[1], Christopher Redmond[1], McKella Sylvester[2], Mary Maclean[1], Francoise Meylan[1], Marcela Ferrada[1], Kaitlin Quinn[1] and Peter Grayson[3], [1]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [2]Colgate University, Bethesda, MD, [3]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Chevy Chase, MD

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Large-vessel vasculitis (LVV) is characterized by granulomatous inflammation of the aorta and its major branches. The two major forms are giant cell arteritis (GCA) and Takayasu's arteritis (TAK). Clinical manifestations and angiographic patterns of diseases can be similar between these diseases; however, GCA exclusively affects older people while TAK is frequently a disease of the young. Few studies directly compare circulating immune cell subsets between TAK and GCA. Some studies have independently shown involvement of Treg, Th1, and Th17 subsets in GCA and TAK. The study objectives were to profile human peripheral blood mononuclear cells (PBMCs) using spectral flow cytometry and directly compare $CD4^+$ T helper (Th) and $CD8^+$ cytotoxic T cell (Tc) subsets between patients with GCA and TAK.

Methods: Cryopreserved PBMCs, collected during active disease from patients with LVV enrolled in an observational cohort study and from healthy controls (HC), were profiled. A 30-color panel for spectral flow cytometry was designed. Each antibody was titrated to determine its optimal volume and then adjusted until the staining pattern was comparable between multicolor and single-color staining. The two conditions tested involved 4-6 h PBMC incubation with PMA, ionomycin, and Brefeldin A (stimulated) and in media alone (unstimulated). Treg, Th1, Th2, Th9, Th17, Tc1, Tc2, Tc9, and Tc17 subsets were defined as the proportion of CD4 or CD8 T cells expressing a key transcription factor or cytokine. Kruskal-Wallis tests were conducted to compare between groups. Spearman correlation was reported for comparisons of subset abundance and age within HC.

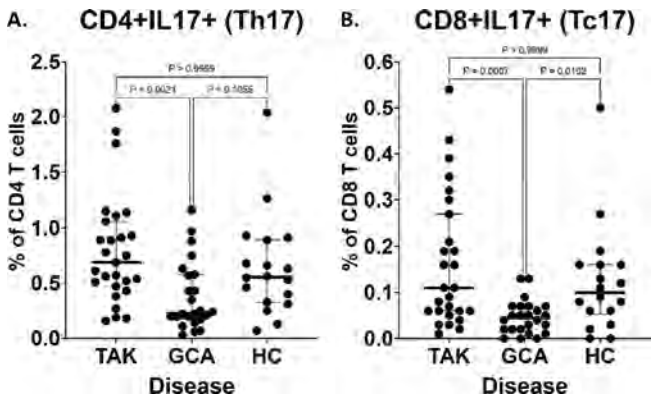

Figure 1: Expression of (A) Th17 and (B) Tc17 subsets in PBMCs from patients with Takayasu's arteritis (TAK), patients with giant cell arteritis (GCA), and healthy controls (HC)

Results: Patients with active GCA (N=24, ages 54-88), patients with active TAK (N=27, ages 15-54), and HC (N=18, ages 14-74) were included. Statistically significant differences between TAK and GCA were only observed in Th17 and Tc17 subsets. TAK patients (median 0.69%) showed significantly higher Th17 (CD4+IL17+) compared to GCA patients (0.23%, p=0.002) but not HC (0.56%, p >0.999) (Figure 1). GCA patients (0.05%) had significantly lower Tc17 (CD8+IL17+) levels than TAK (0.11%, p=0.001) and HC (0.10%, p=0.033) (Figure 1). Neither of Th17 nor Tc17 correlated with age within the HC group (r=-0.194 and r=-0.1741 respectively). There were no significant differences between TAK and GCA for Th1 and Tc1 populations. TAK patients (31.7%) did have lower Tc1 (CD8+IFNg+) than HC (56.1%, p=0.028). The only significantly difference observed in Tregs (CD4+FOXP3+) was lower expression in GCA patients (4.99%) than HC (7.06%, p=0.004).

Conclusion: Abundance of Th17 and Tc17 subsets were greater in TAK compared to GCA with no differences in Treg, Th1, or Tc1 subsets. Differences in IL17-producing T lymphocytes may be a fundamental immunologic difference between GCA and TAK and may inform novel therapeutic strategies in these conditions. A lack of strong differences in circulating immune cell populations between TAK, GCA, and HC suggests that profiling peripheral blood may not be as informative as direct study of affected arterial tissue in these conditions.

Disclosure: R. Kuan: Colgate-Palmolive Company, 5; **C. Redmond**: None; **M. Sylvester**: None; **M. Maclean**: None; **F. Meylan**: None; **M. Ferrada**: None; **K. Quinn**: None; **P. Grayson**: None.

Abstract Number: 0700

A Population-Based Study of Vasculitis Among Farmers and Urban Residents in Alberta

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic vasculitis encompasses a group of autoimmune diseases involving inflammation of blood vessels. Although a rare disease, vasculitis can present with life-threatening symptoms which pose a significant burden on patients as well as the health care system. Newer studies have demonstrated some association with environmental factors and geographic location. In this study, we compare the epidemiology of vasculitis of farmers to other populations in Alberta in a province-wide study.

Type of Vasculitis	Urban (n =103,112)		Rural (non-farm) (n= 96,667)		Rural (farm) (n= 102,310)	
PMR	678	44.20%	687	43.05%	1220	51.74%
Large vessel	142	9.26%	151	9.46%	219	9.29%
Medium vessel	37	2.41%	46	2.88%	69	2.93%
Small vessel	289	18.84%	272	17.04%	393	16.67%
Arteritis unspecified	253	16.49%	277	17.36%	307	13.02%
Single organ	122	7.95%	153	9.59%	144	6.11%
Variable vessel	13	0.85%	10	0.63%	6	0.25%

Methods: An Alberta intergovernmental data linkage identified all farm families in 1999.Two comparison groups were chosen: a random sample of rural residents and a random sample of urban residents. Vasculitis cases across these groups were determined using linked administrative health data from physician claims and hospital episodes. Data was retrieved from Alberta Health Services, a unifying healthcare provider for all residents of Alberta. This data includes all residents covered under the Canadian universal healthcare system. Descriptive statistics were generated comparing incident cases of vasculitis. Data were collected between April 1, 2000, and March 31, 2021.

Results: A total of 5488 vasculitis cases were found across all populations. Incidence rates varied across the 3 populations with farmers having the highest at 110.6/100,000 person-years followed by rural non-farmers (94.3) and urbanites (71.7).Age adjustment narrowed the variation between the incidence rates, but they remained in the same order: 90.1 farmers, 83.8 rural non-farmers, and 70.7 urbanites. In most cases, ∼60% were initially identified by physician claims. Polymyalgia rheumatica accounted for 47% of cases followed by Arteritis Unspecified (15%) and small-vessel vasculitis (14%) with the remainder being distributed among 9 other sub-categories. More males were observed having vasculitis in the farm population (50%) versus rural non-farmers and urbanites (41% and 40% respectively). Age at diagnosis was also higher in the farmer population (66.2 years) compared to rural non-farmers (64.5 years) and urbanites (63.9 years). Urban dwellers with vasculitis used fewer hospital-based health services than farmers and other rural residents.

Conclusion: In this large data set, the farm population in Alberta faces a greater burden of vasculitis compared to others in terms of rates of diagnosis and number of hospital admissions. This study lays the cornerstone for subsequent studies on assessing environmental exposures and the distribution of healthcare resources. Understanding the incidence of disease and relating to health care service intervention is important for access to care and management with vasculitis patients.

Disclosure: E. Yacyshyn: None; **S. Gulati**: None; **W. Hung**: None; **D. Voaklander**: None; **A. Jones**: None.

Abstract Number: 0701

Incidence of Neurobehçet Disease in Northern Spain 1999-2019. a Population-based Study

Fabricio Benavides[1], Alba Herrero-Morant[2], Jose Luis Martin-Varillas[3], Carmen Alvarez Reguera[1], Lara Sanchez-Bilbao[4], David Martinez-Lopez[5], Raul Fernandez[1], Ivan Ferraz Amaro[6], Jose Luis Hernandez[1] and Ricardo Blanco[7], [1]Hospital Universitario Marqués de Valdecilla, Santander, Spain, [2]Hospital Universitario Marqués de Valdecilla, Ontinyent, Spain, [3]Hospital de Laredo, Laredo, Spain, [4]Hospital Universitario Marques de Valdecilla, Santander, Spain, [5]Hospital de Sierrallana, Santander, Spain, [6]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [7]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Behçet's Disease (BD) incidence varies widely worldwide. Neurobehcet's disease (NBD) is one of the most severe manifestations of BD**.** Data on NBD incidence is scarce and contradictory.

Our Objective was to estimate NBD incidence in Northern Spain.

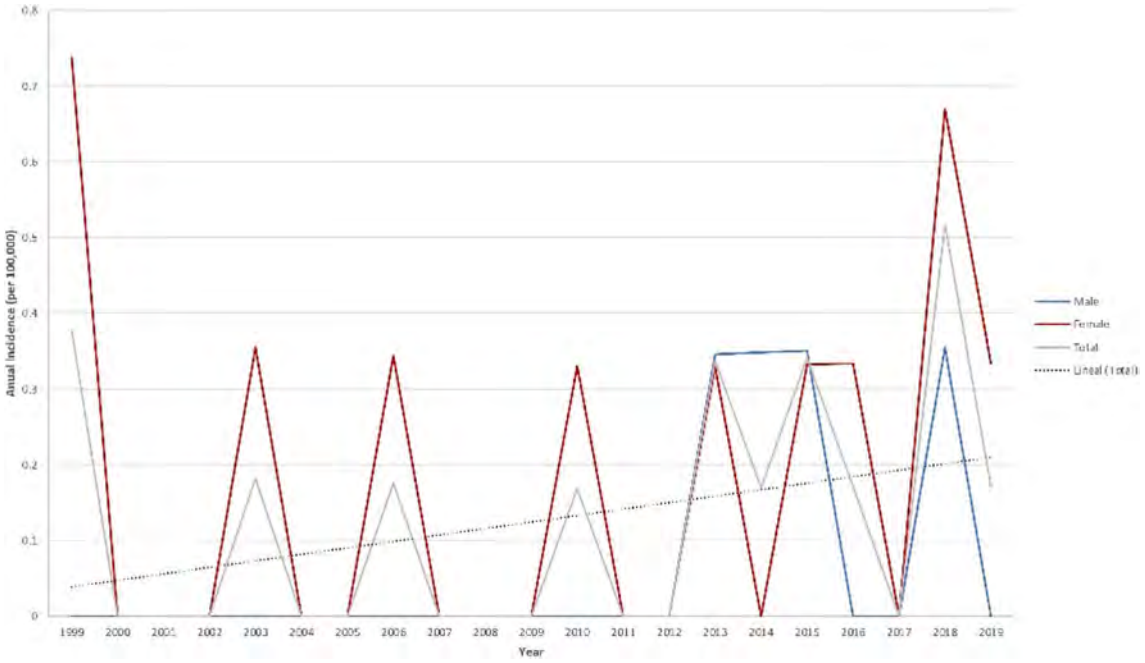

FIGURE. Incidence of neurobehçet's disease in residents in Northern Spain, in 1999-2019 according to gender.

Table. Main clinical features of neurobehçet's disease in different geographical areas. Abbreviations: BD: Behçet's disease, NBD: Neurobehçet's disease, ND: Non data

Author, year	Country	cases			Male n (%)		Age at onset years mean ± SD		HLAB51+ n (%)	
		BD	NBD	%	BD	NBD	BD	NBD	BD	NBD
Ideguchi et al.,2010	Japan	412	54	13	33 (61)	33 (75)	36.9±11.9	35.8±10.3	123 (50)	16 (55)
E. Bolek et al., 2020	Turkey	419	26	6.2	225 (53.7)	39 (56.5)	29.2±9.0	27.4±9.2	104 (69.3)	13 (65)
Akman-Demir et al.,1999	Turkey	ND	200	ND	ND	155 (77.5)	ND±ND	31.5±ND	ND	ND
Houman et al.,2013	Tunis	430	121	28.1	295 (68.6)	78 (64.5)	29.17±ND	29.02±ND	84 (19.5)	14 (33.3)
Al-Araji et al., 2003	Iraq	140	20	14.3	105 (75)	14 (70)	34.2±ND	34.1±ND	ND	ND
Riera-Maestra et. al., 2010	Spain	360	20	5.6	ND	13 (ND)	34±ND	36.3±ND	ND	ND
Talarico et al., 2012	Italy	117	13	38	72 (61.5)	36 (50)	25±4.0	25±4.0	77 (66)	ND
Domingos et al., 2015	Portugal	138	25	18,1	45 (32.6)	10 (40)	35.8±9.2	37.5±9.4	59 (42.9)	10 (41.1)
Sbai A et al., 2003	France	ND	109	ND	ND	78 (65.1)	ND±ND	31±ND	ND	ND
Present study, 2022	Spain	92	23	25	58 (60.4)	8 (34.8)	38±13.9	44±13.9	43 (48.3)	5 (38.4)

Methods: Population-based cohort study of 120 patients diagnosed with BD in Northern Spain, between January 1, 1999, to December 31, 2019. Finally, 92 were included according to the 2013 International Criteria for BD**(2).** NBD was diagnosed according to the International Consensus Recommendation criteria **(3).** The incidence of NBD between 1999-2019 was estimated by gender, age, and year of diagnosis. Annual incidence is expressed as cases per 100,000 people.

Results: NBD was diagnosed in 23 of 92 (25%) patients (15 women/8 men) (mean±SD age: 44±13.9 years). Ten (43.5%) patients had parenchymatous NBD, 10 (43.5%) had non-parenchymatous NBD and 3 (13%) cases had mixed NBD. Annual incidence of NBD in Northern Spain in the 1999-2019 period was 0.13 per 100,000 people [95% CI: 0.11-0.26] (0.14 [0.04-0.23] in men, 0.24 [0.12-0.37] in women). There were variations in annual incidences, with a minimum value of 0.08 in 2009-2010 and a maximum of 0.26 in 2017-2018 (**Figure**).

The highest incidence rate was observed in men in the 20-29 years group (0.03 per 100,000 people) and in women in the 30-39 years group (0.07per 100,000 people). On the other hand, the lowest incidence rate was observed in the 10-19 years group and 80-89 years group (0.008per 100,000 people). When analyzed the incidence rate stratified by age, there were no statistical differences according to gender. The annual incidence studied by year showed an annual peak incidence over the last 20 years. A comparison between different geographical areas was made (**Table**). NBD frequency ranges from 5.6 to 38%. It is usually more frequent in male young adults.

Conclusion: NBD frequency varies widely. The epidemiological characteristics of NBD in our series are similar to other except for gender predominance. Like in other immune mediated diseases this cyclic pattern in annual incidence could possibly be related to infectious environmental factors.

Disclosure: F. Benavides: None; **A. Herrero-Morant**: None; **J. Martin-Varillas**: None; **C. Alvarez Reguera**: None; **L. Sanchez-Bilbao**: None; **D. Martinez-Lopez**: None; **R. Fernandez**: None; **I. Ferraz Amaro**: AbbVie/Abbott, 5, 6, Amgen, 5, 6, Bristol-Myers Squibb(BMS), 6; **J. Hernandez**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6.

Abstract Number: 0702

Large Vessel Vasculitis Increases Risk of Acute Myocardial Infarction in Patients Admitted for Congestive Heart Failure : A Nationwide Inpatient Database Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiac disease has been known to be a major morbidity and mortality cause in vasculitis. Large vessel vasculitis is mostly associated with pericarditis, myocarditis and valvular disease. The impact of association between LVV and CHF is less studied. 15-50% of Takayasu arteritis patients have aortic insufficiency and cases have been reported where patients present with acute congestive heart failure secondary to aortic insufficiency as their presenting symptom. On the other hand, the incidence of cardiac involvement in Giant Cell arteritis is less compared to Takayasu. Generally, there is a

paucity of data due to the rarity of cases. Our study attempted to determine the association of CHF and LVV in one of the largest datasets available in the country.

Methods: National inpatient sample database from 2016-2019 was queried to identify patients with a primary diagnosis of CHF and stratified based on the presence of LVV. The adjusted odds ratios (aOR) of in-hospital outcomes were calculated using chi-square statistics in software STATA v.17.

Results: Of 1,276,429 patients with CHF, 669 had LVV (Giant cell arteritis: 619 and Takayasu arteritis: 50). CHF with LVV patients were older (78.32 vs 70.72, p-value 0.00) and predominantly female (71.6% vs 48%, p-value 0.00). On adjusted analysis, compared to non-LVV patients, LVV patients had significantly higher acute myocardial infarction (AMI) (aOR 2.2,

Table 1. Baseline characteristics of CHF hospitalizations with and without Vasculitis

	Without Vasculitis (n= 1,275,760)	Without Vasculitis (%)	With Vasculitis (n= 669)	With Vasculitis (%)	P-value
Age (years)	70.72		78.32		0.00
Female		48		71.6	0.00
Comorbidities					
Smoking	381,824	29.93	190	28.35	0.68
Previous MI	175,265	13.73	95	14.17	0.87
Previous PCI	135,025	10.58	40	5.97	0.08
Previous CABG	174,970	13.71	95	14.17	0.87
Alcohol	56,330	4.41	5	0.74	0.03
Dyslipidemia	564,899	44.27	270	40.29	0.35
DM	262,265	20.55	85	12.68	0.02
AIDS/HIV	695	100	0	0	0.37
HTN	393,370	30.83	165	24.62	0.13
Hypothyroidism	220,145	17.25	170	25.37	0.01
Pulmonary disease	426,895	33.46	195	29.10	0.27
Obesity	286,790	22.47	150	22.38	0.97
Renal failure	503,684	39.48	330	49,25	0.021

Table 2. In-hospital outcomes and resource utilization among patients with CHF with and without LVV

			Unadjusted		Adjusted*	
	Without LVV, n(%)	With LVV, n(%)	OR(95% CI)	P-value	aOR(95% CI)	P-value
MACCE**	6.92%	9.70%	1.44 (0.83-2.53)	0.20	1.31 (0.75-2.30)	0.342
In-hospital mortality	3.11%	0.75%	0.23 (0.033-1.68)	0.15	0.25 (0.028-1.40)	0.102
Acute myocardial infarction	3.77%	8.21%	2.2 (1.25-4.17)	<0.001	2.2 (1.19-3.93)	0.012
Acute stroke	0.42%	1.49%	3.52 (0.87-14.30)	0.08	3.97 (0.97-16.21)	0.054
Cardiogenic shock	2.86%	1.49%	0.52 (0.13-2.09)	0.35	0.69 (0.16-2.94)	0.620
Net adverse events	7.82%	5.97%	0.75 (0.34-1.63)	0.466	0.77 (0.36-1.66)	0.504
Length of stay (days)	5.35	6.17				0.148
Total charges ($)	52,447.9±135,101.1	43,794.35±64,506.53				0.124

*Adjusted for age, sex, race, median household income, elixhauser co-morbidities summary index, hospital region, teaching hospital status, hospital size, ESRD, hyperlipidemia, obesity, smoking status, history of prior myocardial infarction, alcohol, prior PCI, prior CABG, obstructive sleep apnea, pulmonary disease, immunocompromised status, hypothyroidism, liver disease, gout, peripheral artery disease, valvular heart disease, hypertension, coagulopathy

**Major adverse cardiac and cerebrovascular events

95%CI 1.19-3.93). There was no difference in major adverse cardiac and cerebrovascular events (aOR 1.31, 95%CI 0.75-2.30), in-hospital mortality (aOR 0.25, 95% CI 0.028-1.40), stroke (aOR 3.97, 95% CI 0.97-16.21), or cardiogenic shock (aOR 0.69, 95%CI 0.16-2.94) between the two groups.

Conclusion: Large vessel vasculitis has no effect on in-hospital outcomes in CHF patients, except for a significant increase in risk for AMI.

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Abstract Number: 0703

Cardiovascular Disease-Related Mortality in Primary Systemic Vasculitis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular disease (CVD) is the leading cause of death in patients with the most common subtypes of primary systemic vasculitides. We aimed to estimate the scope of cardiovascular-related death in patients with primary systemic vasculitis in the United States in recent years.

Methods: We used the CDC Wonder Multiple Causes of Death database and its query system. All deaths related to cardiovascular disease (CVD) as the UCD, and primary systemic vasculitides as CCDs were included from January 1, 1999, to December 31, 2020. We used the ICD-10 code I00-I99 (Diseases of the circulatory system) as the UCD, and the ICD-10 codes of the different subtypes of the primary systemic vasculitides were grouped as CCDs. Diseases of the circulatory system and all grouped vasculitides were initially queried separately, and the 2 disorders were also queried together to find out the mortality rates of CVD as UCD and vasculitis as CCD. We also performed the analysis by vasculitis subtypes. We obtained mortality rates by year, gender, race, and state. To obtain age-adjusted mortality rates we used the year 2000 U.S. standard population. We show mortality rates as the number of deaths per 100,000 for CVD, and per million for vasculitis. We applied a linear regression model to evaluate trends over time.

Results: During the 22-year period, CVD was the UCD of death of 18,783,791 patients. The age-adjusted mortality rate was 254.38 per 100,000 (95% CI: 254.27-254.50). For vasculitis as CCD, there were 29,229 deaths, and the age-adjusted mortality rate was 4.02 per 1,000,000 (95% CI: 3.97-4.07). When CVD as UCD and vasculitis as CCD were combined, there were 6,042 deaths, with an age-adjusted rate of 0.82 per 1,000,000 (95% CI: 0.80-0.84). Since 1999, there has been a significant trend to the decrease ($p < 0.0001$) (Figure 1). The age-adjusted mortality rate was higher in females than in males (0.88 vs. 0.71 per million). The percentage of females was 64.5%. The age-adjusted mortality rate was higher in Whites (0.90, 0.87-0.92) than in Blacks (0.39, 0.34-0.44) (Table 1). The percentage of Whites was 93.4%. M31.6 (Other giant cell arteritis) accounted for 58% of all vasculitis deaths. There was differential geographic distribution in the mortality rates by state. The states with the highest age-adjusted mortality rates were Maine, Vermont, Oregon, Iowa, and Minnesota (Table 2). The states with the lowest rates were Louisiana, Nevada, Mississippi, Florida, and Georgia.

Conclusion: There has been a progressive decrease in mortality rates in recent years. Contrary to what is found in the general population, in our study, the age-adjusted mortality rates were higher in females and in Whites. This can be explained, at least in part, by the fact that vasculitides are more frequent in Whites, and GCA, which is the subtype of vasculitis associated with the highest mortality rate in our study, is more frequent in white females. Mortality rates of vasculitis are more frequent in northern states. Investigation of the reasons for the geographic disparities is warranted. Our findings should be taken with caution until quality studies to determine the reliability of the data about these rare diseases available in national databases are performed.

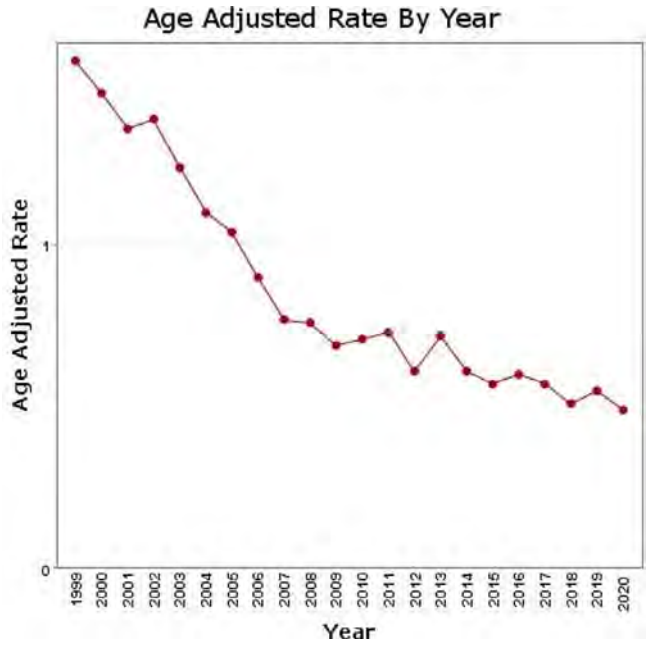

Figure 1. Age-adjusted mortality rate for cardiovascular as the underlying cause of death and with vasculitis as contributing cause of death, by year.

Table 1. Age-adjusted mortality rate per million for cardiovascular disease as underlying cause of death and vasculitis as contributing cause of death, by race and gender.

Race	Gender	Deaths	Population	Age-adjusted Rate (95% CI)	% of Total Deaths
White	Female	3,646	2,712,095,815	0.96 (0.93-0.99)	60.34
	Male	1,996	2,654,949,252	0.77 (0.73-0.80)	33.04
	Total	5,642	5,367,045,067	0.90 (0.87-0.92)	93.38
Black or African American	Female	172	479,588,642	0.41 (0.34-0.47)	2.85
	Male	98	439,446,295	0.31 (0.25-0.39)	1.62
	Total	270	919,034,937	0.39 (0.34-0.44)	4.47
Asian or Pacific Islander	Female	65	193,229,411	0.41 (0.31-0.52)	1.08
	Male	44	178,684,640	0.29 (0.20-0.40)	0.73
	Total	109	371,914,051	0.38 (0.31-0.46)	1.80
American Indian or Alaska Native	Female	11	44,089,936	Unreliable (0.18-0.67)	0.18
	Male	10	44,272,656	Unreliable (0.16-0.75)	0.17
	Total	21	88,362,592	0.37 (0.22-0.57)	0.35

Table 2. The 12 states with the highest mortality due to cardiovascular disease as underlying cause of death and vasculitis as contributing cause of death, with age-adjusted rates and 95% confidence interval.

	Deaths	Population	Age-Adjusted Rate per 1,000,000 (95% CI)
Maine	65	29,046,732	1.77 (1.36-2.27)
Vermont	28	13,674,812	1.70 (1.13-2,46)
Oregon	158	83,915,155	1.62 (1.36-1.87)
Iowa	130	66,861,208	1.48 (1,23-1.74)
Minnesota	190	116,354.336	1.46 (1.25-1.67)
Washington	206	147,569,534	1.35 (1.16-1.54)
North Dakota	25	15,194,827	1.26 (0.81-1.88)
Idaho	40	33,894,011	1.20 (0.86-1.63)
Montana	30	21,654,987	1.15 (0.77-1.64)
Wisconsin	162	124,026,036	1.12 (0.95-1.30)

Disclosure: A. Rodriguez-Pla: None.

Abstract Number: 0704

Clinical Characteristics and Outcomes in Patients Found to Have Clinically Isolated Aortitis After Aortic Aneurysm Repair: A Single-Center Experience

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Clinically isolated aortitis (CIA), or aortitis in the absence of identifiable systemic vasculitis, is typically discovered histopathologically after aortic aneurysm repair. The approach to caring for CIA patients as a rheumatologist remains uncertain, including the role of immunosuppression (IS) and the risk of developing systemic rheumatologic disease. To add to the limited literature on this topic[1,2],we conducted a study using the Cardiovascular Health Improvement Project (CHIP) database at Michigan Medicine, which is enriched for patients with surgical aortic disease. Our aim was to identify and describe CIA patients in CHIP and provide insights into the clinical characteristics and outcomes.

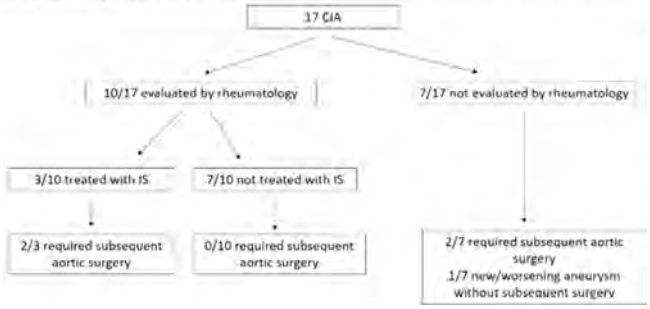
Methods: We queried CHIP to identify patients with diagnosis codes or keywords in the electronic medical record (EMR) related to aortitis from 8/1/2013-3/31/2022. CIA cases were independently verified with chart review by two physicians. Patients without any follow-up in the EMR after diagnosis of aortitis were excluded. Clinical data was recorded at time of CIA diagnosis until date of last follow-up in EMR, including subsequent aortic events (subsequent aortic surgery, new or worsening aneurysm, new stenosis, or dissection).

Table 1. Characteristics at time of CIA diagnosis (N=17).

Age, median (IQR) years	69 (63, 74)
Female	8 (47)
Caucasian	16 (94)
BMI, median (IQR) kg/m^2	27.8 (26.4, 32)
Comorbidities	
Hypertension	12 (71)
Hyperlipidemia	6 (35)
Type 2 diabetes mellitus	3 (18)
Coronary artery disease	0 (0)
Ever-smoker	14 (82)
Smoking, median (IQR) pack-years	15 (1, 30)
Histopathologic pattern of aortitis	
Lymphoplasmacytic	8 (47)
Giant cell/granulomatous aortitis	6 (35)
Nonspecific aortitis	3 (18)
ESR Post-operative, median (IQR) mm/hr*	15 (12.5, 26.5)
CRP Post-operative, median (IQR) mg/dl*	0.5 (0.15, 0.55)

Values are number (%) unless indicated otherwise. CIA=clinically isolated aortitis, BMI=body mass index, ESR= erythrocyte sedimentation rate, CRP= C-reactive protein.
*ESR and CRP checked 2-6 months post-operatively were available for n=7. No pre-operative ESR/CRP were available.

Figure 1. Flow diagram of outcomes among patients found to have clinically isolated aortitis (CIA) after aortic aneurysm repair. IS= immunosuppression.



Results: 17 patients with CIA were identified with 7.1 (IQR 2.9, 10.0) years of follow-up, all of whom had undergone ascending aortic aneurysm repair. Clinical characteristics at CIA diagnosis are presented in **Table 1**. Rheumatology was engaged post-operatively in 10 cases (59%); only 3 patients (18%) were treated with IS (steroids ± tocilizumab) at any point during follow-up. One patient was diagnosed with systemic rheumatologic disease (rheumatoid arthritis) 6.6 years after CIA diagnosis. Subsequent aortic events occurred in 5 patients (29%) at median 3.7 (IQR 1.5, 6.2) years of follow-up (**Figure 1**). One patient passed due to unrelated reasons 16.4 years after CIA diagnosis.

Conclusion: In this single-center cohort of 17 patients with CIA aortic aneurysm repair, there was a high prevalence of hypertension and ever-smoking, and post-operative inflammatory markers (when available) tended to be normal. Interestingly, evolution into systemic rheumatologic disease was uncommon. A third of patients had subsequent aortic events after CIA diagnosis, highlighting the need for continued clinical surveillance of patients with CIA; no conclusions could be drawn regarding the impact of IS on preventing subsequent aortic events.

References:

1. Mayer A, Sperry A, Quimson L, Rhee R. Long-term clinical and radiographic outcomes in patients with clinically isolated aortitis. ACR Open 2022 Dec;4(12):1013-1020.

2. Clifford A, Arafat A, Idrees J et al. Outcomes among 196 patients with noninfectious proximal aortitis. Arth Rheum 2019 71(12):2112:2120.

Disclosure: O. Gewurz-Singer: None; **J. Ford**: None; **T. Aung**: None; **L. Humphrey-Stark**: None.

Abstract Number: 0705

Sleep Disturbances in Patients with Vasculitis: Results of the Vasculitis Patient-Powered Research Network Sleep Study (SleepVasc)

Misa Tanaka[1], Saverio Stranges[1], Kathy Speechley[1], Osvaldo Espin Garcia[1], Molly Mason[2], Renee Borchin[3], Cristina Burroughs[3], Christine Yeung[4], Indira Gurubhagavatula[4], Christian Pagnoux[5], Peter Merkel[4] and **Lillian Barra**[1], [1]Western University, London, ON, Canada, [2]Vasculitis Patient Powered Research Network, Philadelphia, PA, [3]University of South Florida, Tampa, FL, [4]University of Pennsylvania, Philadelphia, PA, [5]Mount Sinai Hospital, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Sleep deprivation and sleep disorders can impair health-related quality of life and increase the risk of chronic diseases, such as cardiovascular disease, and mental illness. In patients with vasculitis, several factors could contribute to a higher risk of disordered sleep, including glucocorticoid use and upper airway involvement. This study aimed to describe sleep disturbances in patients with vasculitis.

Methods: In this cross-sectional study, we conducted an online survey of patients registered with the Vasculitis Patient-Powered Research Network (VPPRN). The questionnaire included these validated measures: Epworth Sleepiness Scale (ESS, range 0-24, < 10 normal), Functional Outcomes of Sleep Questionnaire-10 (FOSQ-10, range 5-20, higher scores indicate better function), and the Multivariable Apnea Prediction Index (MVAP, range 0-1, 1 indicates highest risk for obstructive sleep apnea (OSA)). Patients were also asked about previously diagnosed sleep disorders, characteristics of their vasculitis, medication use, and demographics. Responses were collected from February 1 to April 1, 2023.

Table 1: Characteristics of the study population

	Total	Female	Male
Sample size, n (%)	1104	821 (74.4)	280 (25.4)
Type of vasculitis, n (%)			
Giant cell arteritis	60 (5.4)	60 (7.3)	0 (0.0)
Takayasu's arteritis	72 (6.5)	61 (7.4)	11 (3.9)
Microscopic polyangiitis	111 (10.1)	85 (10.4)	26 (9.3)
Granulomatosis with polyangiitis	479 (43.4)	334 (40.7)	144 (51.4)
Eosinophilic granulomatosis with polyangiitis	147 (13.3)	92 (11.2)	10 (3.6)
Other types of vasculitis[a]	235 (21.3)	189 (23.0)	89 (31.8)
Body mass index, kg/m^2, mean (SD)	28.2 (7.9)	28.5 (8.4)	27.2 (6.3)
Age, mean (SD)	59.5 (13.6)	58.5 (13.8)	62.7 (12.5)
Race, White, n (%)	1005 (91.0)	756 (92.1)	249 (88.9)
Treatments received at survey completion, n (%)			
Glucocorticoids	386 (35.0)	281(34.2)	102(36.4)
Prednisone-equivalent glucocorticoid dose			
0- 10 mg/day	316 (28.6)	225(27.4)	88 (31.4)
11-39 mg/day	57 (5.2)	43 (5.2)	14 (5.0)
≥ 40 mg/day	10 (0.9)	10 (1.2)	0 (0.0)
Rituximab	200 (18.1)	145(17.1)	53 (18.9)
Azathioprine	92 (8.3)	71 (8.6)	21 (7.5)
Methotrexate	86 (7.8)	64 (7.8)	22 (7.9)
Mycophenolate	79 (7.1)	58 (7.1)	20 (7.1)
Other immunosuppressive drugs[b]	120 (10.9)	98 (11.9)	22 (7.9)
Pain at time of survey, 0=no pain, 10=worst pain; median VAS (IQR)	3.0 (4.0)	3.0 (4.0)	2.0 (3.0)
Symptoms of vasculitis at the time of survey, 0=no symptoms, 10=severe symptoms; median VAS (IQR)	4.0 (4.0)	4.0 (4.0)	2.0 (5.0)

SD: standard deviation; IQR: inter-quartile range

[a]Includes polyarteritis nodosa, IgA vasculitis, cryoglobulinemic vasculitis, hypocomplementemic urticarial vasculitis, Behçet's disease, central nervous system vasculitis

[b]Includes biologic therapies other than rituximab and Janus kinase inhibitors

Results: Of the 1,104 patients with vasculitis recruited, 1,037 completed the questionnaire in full. Participants included 479 with granulomatosis with polyangiitis, 147 with eosinophilic granulomatosis with polyangiitis, 111 with microscopic polyangiitis, 60 with Takayasu arteritis, 72 with giant cell arteritis, and 235 with other types of vasculitis. The study population was 74.4% female. The mean (SD) age and disease duration were 59.5 (13.6) and 9.7 (8.4) years, respectively. Use of glucocorticoids and immunosuppressants were common at the time of the survey (**Table 1**). At least 1 sleep disturbance was reported by 82% of patients with vasculitis. Excessive daytime sleepiness occurred in 26%, impaired daily function in 77%, and 19% were at high risk for obstructive sleep apnea (OSA). Previously diagnosed OSA, insomnia, and restless legs syndrome were reported by 20%, 14%, and 11% of patients, respectively (**Table 2**). Prevalence of OSA among this sample was higher than what is reported for the general population (6-17%). Similar to the general population, the risk of OSA was higher in males. Other sleep disorders, excessive daytime sleepiness, and daily functional impairment were more common in females (**Table 2**). Sleep disturbances were more prevalent in those taking higher doses of glucocorticoids (**Table 3**).

Table 2: Sleep disturbances among patients with systemic vasculitis

	Total	Female	Male	p-value
Epworth sleep scale				
Median (IQR)	7.0 (7.0)	7.0 (7.0)	6.0 (6.0)	0.007
≥ 11, n (%); Excessive daytime sleepiness	274 (24.8)	215 (26.2)	57 (20.4)	0.032
Functional outcomes of sleep questionnaire				
Median (IQR)	14.7 (6.3)	14.3 (6.0)	16.2 (6.0)	<.001
< 18, n (%); Significant impairment in daily function	841 (76.2)	655 (79.8)	183 (65.4)	<.001
Multivariable apnea prediction index				
Median (IQR)	0.29 (0.4)	0.20 (0.3)	0.51 (0.3)	<.001
≥ 0.6, n (%); High risk for obstructive sleep apnea	183 (16.6)	82 (10.0)	101 (36.1)	<.001
Previously diagnosed sleep disorders[a], n (%)				
Obstructive sleep apnea	218 (19.7)	144 (17.5)	73 (26.1)	0.004
Insomnia	158 (14.3)	132 (16.1)	26 (9.3)	0.004
Restless leg syndrome	124 (11.2)	95 (11.6)	29 (10.4)	0.500
Narcolepsy	9 (0.8)	7 (0.9)	2 (0.7)	0.802
Any sleep disturbance[b], n (%)	908 (82.2)	688 (83.8)	217(77.5)	<.001
Use of a sleep aid in the past month[c], n (%)	1046 (94.7)	772 (94.0)	271 (96.8)	0.404
Sleep satisfaction, n (%)				
Dissatisfaction	521 (47.2)	400 (48.7)	118 (42.1)	0.022
Neutral	272 (24.6)	200 (24.4)	72 (25.7)	
Satisfaction	252 (22.8)	172 (21.0)	80 (28.6)	
Sleep satisfaction at time of survey compared to prior to the diagnosis of vasculitis, n (%)				
Worse	623 (56.4)	481 (58.6)	140 (50.0)	0.003
Same	297 (26.9)	199 (24.2)	98 (35.0)	
Better	125 (11.3)	92 (11.2)	32 (11.4)	

[a]based on self-report of a sleep disorder diagnosed by a health professional
[b]defined as having ESS ≥ 11 or FOSQ-10 < 18 or MVAP ≥ 0.6 or a prior diagnosis of any sleep disorder by a health professional
[c]includes prescription medications, over the counter medications, and non-pharmacologic interventions (exercise, meditation, etc.)

Table 3:Sleep disturbances among patients with systemic vasculitis by prednisone-equivalent glucocorticoid doses

	Prednisone-equivalent glucocorticoid dose in mg/day, n (%)				
	0	0 to 10	11 to 39	≥ 40	p-value
	658 (59.6)	316 (28.6)	57 (5.2)	10 (0.9)	
Epworth sleep scale[a]					
median (IQR)	7 (6.0)	7 (7.0)	9 (6.0)	13.5 (7.0)	<.001
≥ 11, n (%)	153 (23.3)	82 (25.9)	23 (40.4)	7 (70.0)	0.001
Functional outcomes of sleep questionnaire[b]					
median (IQR)	15.2 (6.0)	14.3 (6.3)	10.5 (6.8)	10.3 (5.3)	<.001
< 18, n (%)	490 (74.5)	256 (81.0)	51 (89.5)	10 (100)	0.007
Multivariable apnea prediction index[c]					
median (IQR)	0.26 (0.37)	0.33 (0.45)	0.32 (0.49)	0.26 (0.18)	0.163
≥ 0.6, n (%)	97 (14.7)	70 (22.2)	15 (26.3)	1 (10.0)	0.011
Previously diagnosed sleep disorder, n (%)					
Obstructive sleep apnea	134 (20.4)	67 (21.2)	14 (24.6)	1 (10.0)	0.811
Insomnia	92 (14.0)	48 (15.2)	14 (24.6)	4 (40.0)	0.025
Restless leg syndrome	70 (10.6)	40 (12.7)	11 (19.3)	2 (20.0)	0.267
Narcolepsy	6 (0.9)	2 (0.6)	1 (1.8)	0 (0.0)	0.931

[a] ≥ 11 on the Epworth sleep scale indicates excessive daytime sleepiness.
[b] <18 on the Functional outcomes of sleep questionnaire indicates significant impairment in daily function
[c] ≥ 0.6 on the Multivariable apnea prediction index indicates high risk for OSA

Conclusion: Sleep disturbances are common in patients with vasculitis and significantly impact daily function. Use and dose of glucocorticoids may increase the risk of sleep disturbances in patients with vasculitis.

Disclosure: M. Tanaka: None; **S. Stranges**: None; **K. Speechley**: None; **O. Espin Garcia**: None; **M. Mason**: None; **R. Borchin**: None; **C. Burroughs**: None; **C. Yeung**: None; **I. Gurubhagavatula**: None; **C. Pagnoux**: AstraZeneca, 1, 2, 6, GlaxoSmithKlein(GSK), 1, 6, Otsuka, 1, 2, 5, 6, Pfizer, 5, Roche, 2; **P. Merkel**: AbbVie/Abbott, 5, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos, 5, Electra, 5, Genentech, 5, GlaxoSmithKlein(GSK), 2, 5, HiBio, 2, InflaRx, 2, 5, Janssen, 2, Jubilant, 2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, Takeda, 2, 5, UpToDate, 9, Visterra, 2; **L. Barra**: AstraZeneca, 1, GlaxoSmithKlein(GSK), 1, 6, Otsuka, 1, 5, 6, Pfizer, 1, 5, 6.

Abstract Number: 0706

Aortitis and Periaortitis Spectrum in 135 Patients from a Single Referral Centre

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Aortitis is the inflammation of the aortic wall, and can be idiopathic or associated with a cluster of infectious and non-infectious diseases **(1-3)**. Periaortitis, is an inflammatory process arising from the adventicia of the aortic wall and extending into the surrounding periaortic space. The aim of this study is to assess the causes and the main features of patients with aortitis and/or periaortitis.

Methods: Observational study of patients with aortitis or periaortitis from a large-vessel vasculitis monographic consultation at a referral hospital from June 2022 to April 2023. Aortitis and periaortitis were diagnosed by imaging techniques.

Results: We include 135 patients (87 female/ 48 male) (mean±SD age; 57.3±7.6 years). The different subtypes of aortitis/ periaortitis were: Giant-cell arteritis (GCA) (n=102), Takayasu arteritis (n=6), other immune mediated diseases (n=13), IgG4-related disease (IgG4-RD) (n=6), infectious (n=3), retroperitoneal idiopathic fibrosis (n=2), malignancy (n=1), drugs (n=1), and isolated aortitis (n=1). The imaging techniques used for the diagnosis of aortitis were: PET/TAC (n=134), TAC (n=44), and RMN (n=33). The main features of the patients with non-infectious aortitis/periaortitis are summarized in **Table**. Aortitis was most frequent in women. High blood pressure and dyslipidaemia was present in 52% and 48% respectively. Polymyalgia rheumatica and general symptoms were the more frequent manifestations. The underlying diseases in the group of aortitis related to other immune mediated diseases were: Sjögren syndrome (n=2), sarcoidosis (n=2), rheumatoid arthritis (n=2), axial spondyloarthritis (n=2), inflammatory bowel disease (n=1), primary biliary cirrhosis (n=1), lung fibrosis (n=1), recurrent pericarditis (n=1), and polyarteritis nodosa (n=1). The ascending thoracic aorta was the most frequently involved segment **(Figure)**.

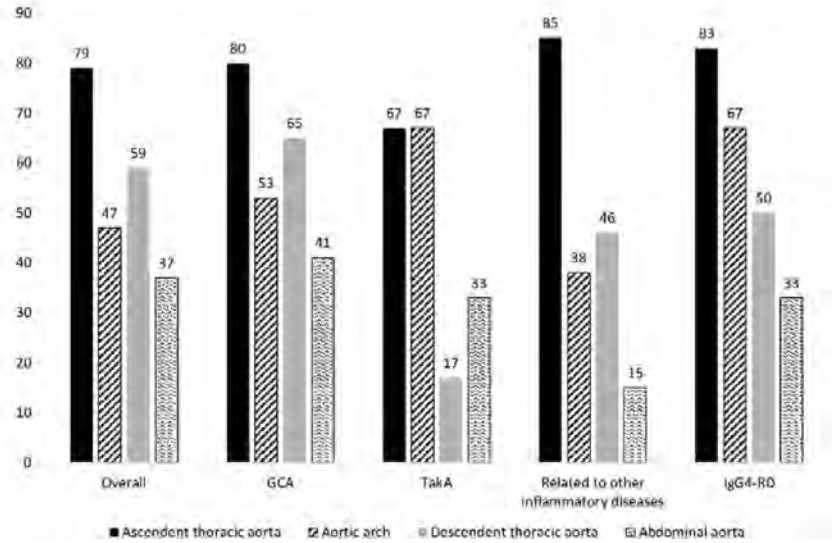
TABLE. Main features of the patients with non-infectious aortitis/periaortitis.

FEATURES	OVERALL (n=132)	GCA (n=102)	TA (n=6)	OTHER INFLAMMATORY DISEASES (n=13)	IgG4-RD (n=6)	Idiopathic retroperitoneal fibrosis (n=2)	Malignancy (n=1)	Drugs (n=1)	Isolated aortitis (n=1)
General features									
Age (years), mean±SD	68.0±8.2	67.9±9.9	41.8±14.1	57.8±20.1	56.3±11.1	63.5±3.5	62	48	48
Female/Male (% female)	87/45 (66)	65/37 (64)	6/0 (100)	10/3 (77)	3/3 (50)	2/0 (100)	0/1 (0)	1/0 (100)	0/1 (0)
Cardiovascular risk factors									
High blood pressure, n (%)	68 (52)	54 (53)	4 (67)	8 (61)	3 (50)	0 (0)	0 (0)	0 (0)	0 (0)
Dyslipidaemia, n (%)	63 (48)	48 (47)	4 (67)	6 (46)	2 (33)	1 (50)	0 (0)	1 (100)	1 (100)
Diabetes mellitus, n (%)	17 (13)	14 (14)	0 (0)	1 (8)	0 (0)	0 (0)	1 (100)	1 (100)	0 (0)
Active smoker or ex-smoker, n (%)	37 (28)	23 (23)	5 (83)	6 (46)	1 (17)	1 (50)	0 (0)	0 (0)	1 (100)
Systemic manifestations									
General symptoms	73 (55)	53 (52)	4 (67)	8 (61)	4 (67)	1 (50)	1 (100)	1 (100)	1 (100)
PmR, n (%)	70 (53)	63 (63)	0 (0)	3 (23)	3 (50)	0 (0)	1 (100)	0 (0)	0 (0)
Fever, n (%)	23 (17)	18 (18)	1 (17)	4 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cranial ischaemic manifestations									
Headache, n (%)	43 (33)	40 (39)	2 (33)	0 (0)	1 (17)	0 (0)	0 (0)	0 (0)	0 (0)
Visual symptoms, n (%)	20 (15)	17 (17)	1 (17)	1 (8)	1 (17)	0 (0)	0 (0)	0 (0)	0 (0)
Jaw claudication, n (%)	12 (9)	12 (12)	0(0)	0 (0)	0 (0)	(0)	0 (0)	0 (0)	0 (0)
Other manifestations									
Limb claudication, n (%)	35 (26)	26 (25)	4 (67)	3 (23)	1 (17)	0 (0)	1 (100)	0 (0)	0 (0)
Abdominal pain, n (%)	8 (6)	3 (3)	1 (17)	2 (15)	1 (17)	1 (50)	0 (0)	0 (0)	0 (0)
Inflammatory back pain, n (%)	34 (26)	29 (28)	0 (0)	2 (15)	3 (50)	0 (0)	0 (0)	0 (0)	0 (0)
Laboratory									
CRP (mg/dL), median [IQR]	0.5 [0.4-4]	0.6 [0.4-3.2]	0.4 [0.2-2.0]	0.4 [0.3-3.6]	4 [0.1-4.3]	0.4	1.1	0.5	0.4
ESR (mm/1h), median [IQR]	43.5 [6-50]	26.5 [7-54]	16.5 [3.5-32.5]	36 [6-47]	9 [7.5-59]	-	50	29	12.5 [10-15]

Abbreviations: CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, GCA: giant cell arteritis, IgG4-RD: IgG4-related disease, PmR: polymyalgia rheumatica, TA: Takayasu arteritis

Main features of the patients with non-infectious aortitis/periaortitis.

Figure. Segments of the aorta affected. All data are in %.



Segments of the aorta affected. All data are in %.

Conclusion: Aortitis can be isolated or secondary to infectious and more frequently to non-infectious processes. GCA is the most frequent cause, being common the presence of PmR and constitutional symptoms. The thoracic aorta, specially ascending, seems to be the most frequently involved segment.

References:

1. Loricera J, et al. Rev Esp Med Nucl Imagen Mol. 2015. PMID: 26272121
2. Prieto-Peña D, et al. Ther Adv Musculoskelet Dis. 2021. PMID: 34211589
3. Loricera J, et al. Clin Exp Rheumatol. 2018. PMID: 29799390

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Abstract Number: 0707

Prevalence and Distribution of Vascular Calcifications at CT Scan in Patients with Large Vessel Vasculitis and Patients with Lymphoma: A Matched Cross-sectional Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Arterial wall calcifications are a hallmark of atherosclerosis and represent an important cardiovascular risk factor. Accelerated atherosclerosis and vascular calcifications have been reported in large vessel vasculitis (LVV), but data are scarce about the amount and localizations. The aim of this study was to compare the prevalence, entity, and local distribution of arterial wall calcifications evaluated on CT scans in patients with LVV and lymphoma.

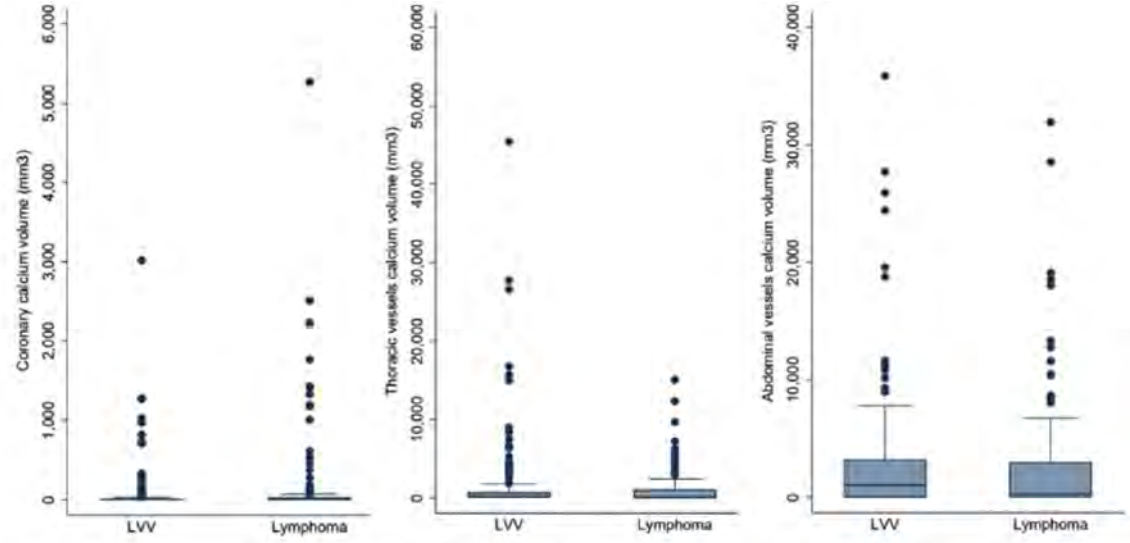

Figure: Distribution of the volume of calcifications in coronary, thoracic, and abdominal vessels in the LVV group (including non-matched patients) and lymphoma group.

Distribution of the volume of calcifications in coronary, thoracic, and abdominal vessels in the LVV group (including non-matched patients) and lymphoma group.

Table: Association of LVV group with the presence of calcification in different locations

	LVV Group Prevalence of calcification	Lymphoma Group Prevalence of calcification	*OR (95%CI) of calcification in LVV vs. Lymphoma group*	*P value*
Coronary Calcification	35/129 (27.1%)	38/129 (29.5%)	0.79 [0.35 – 1.78]	0.575
Thoracic Calcification	93/129 (72.1%)	71/129 (55.0%)	4.13 [1.35 – 12.66]	0.013
Abdominal Calcification	93/129 (72.1%)	86/129 (66.7%)	2.05 [0.48 – 8.71]	0.328

*Conditional logistic regression analyses on matched patients (n=129 for each group). OR, Odds Ratio; CI, confidence interval.

Association of LVV group with the presence of calcification in different locations

Methods: All consecutive patients diagnosed with LVVs with available baseline PET-CT scan performed between 2007 and 2019 were included; lymphoma patients were matched by age (+/-5 years), sex, and year of baseline PET-CT (≤2013; >2013). CT images derived from baseline PET-CT scans of both patient groups were retrospectively reviewed by a single radiologist who, after setting a threshold of minimum 130 HU, semi-automatically computed vascular calcifications in three separate locations (coronaries, thoracic and abdominal arteries), quantified as Agatston and volume scores.

Results: A total of 266 patients were included (129 for each group and 8 non-matched LVV patients). Thoracic artery calcifications were more represented in LVV patients, when compared with lymphoma patients (mean volume 2026 in LVVs vs 1014 in lymphomas, p=0.054), coronary calcifications were higher in lymphoma patients (mean volume 104 in LVVs and 198 in lymphomas, p=0.13), whereas abdominal artery calcifications were equally distributed (mean volume 3220 in LVVs and 2712 in lymphomas) (Figure). Being in the LVVs group was associated with the presence of thoracic calcifications after adjusting by age and year of diagnosis (OR=4.13, 95%CI=1.35-12.66; p=0.013). Similarly, LVVs group was significantly associated with the volume score in the thoracic arteries (p=0.048) (Table).In patients >50 years old, calcifications in the coronaries were more extended in lymphoma patients (p=0.027 for volume).

Conclusion: When compared with lymphoma patients, LVVs patients have higher volumes of calcifications in the thoracic arteries, but not in coronary and abdominal arteries.

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Abstract Number: 0708

NFKB1 and *NFKBIA:* Relevant Players in the Pathogenesis of IgA Vasculitis?

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Immunoglobulin A Vasculitis (IgAV) is a B-cell-mediated inflammatory disease. NF-kappa B (NF-kB) plays a key role in autoimmunity and inflammation[1]. In this regard, the development of B-cells is described as dependent on the activation of NF-kB[2]. In addition, *NFKB1* (gene encoding NF-kB) is described as a shared risk *locus* for several immune-mediated diseases[3]. Specifically, *NFKB1* is crucial in the pathogenesis of IgA nephropathy[4,5], a disease that shares molecular mechanisms with IgAV. Accordingly, we aimed to determine whether *NFKB1* and *NFKBIA* (gene encoding the NF-kB Inhibitor Alpha) represent novel genetic risk factors for IgAV.

Methods: 410 patients with IgAV, the largest series of Caucasian patients with IgAV ever assessed for genetic studies, and 764 healthy ethnically matched controls, were recruited for this study. Six tag single nucleotide polymorphisms (SNPs) within *NFKB1* (rs77830930, rs1598856, rs7340881, rs4648055, rs4648090 and rs230547) and 7 *NFKBIA* tag SNPs (rs3138055, rs696, rs1022714, rs2233419, rs2233415, rs1050851 and rs1957106) were genotyped using TaqMan Probes. P-values were corrected with the FDR method for multiple testing.

Results: A statistically significant decrease of *NFKB1* rs4648055 A allele was disclosed in patients with IgAV when compared to controls (p=0.013 OR=0.78 [0.64 - 0.95], Tables 1 and 2). Additionally, a statistically significant decrease in the *NFKB1* GGCAGC haplotype was observed in IgAV patients compared to controls (p=0.007, Table 3). These results were

Table 1: *NFKB1* and *NFKBIA* genotype and allele frequencies in IgAV patients and healthy controls.

Locus	SNP	Change 1/2	Sample Set	Genotypes, %(n) 1/1	1/2	2/2	Alleles, %(n) 1	2
NFKB1	rs77830930	G/A	IgAV	49.9 (192)	46.2 (178)	3.9 (15)	72.9 (562)	27 (208)
			Controls	52.4 (393)	39.5 (296)	8.1 (61)	72.1 (1082)	27.87 (418)
	rs1598856	G/A	IgAV	26.1 (104)	49.3 (196)	24.6 (98)	50.7(404)	49.3 (392)
			Controls	27 (203)	49.8 (375)	23.2 (175)	51.9 (781)	48.1 (725)
	rs7340881	C/T	IgAV	70.6 (281)	27.6 (110)	1.8 (7)	84.4 (672)	15.6 (124)
			Controls	75.1 (567)	23.1 (174)	1.8 (14)	86.6 (1308)	13.4 (202)
	rs4648055	G/A	IgAV	58.2 (231)	36.3 (144)	5.5 (22)	76.3 (606)	23.7 (188)
			Controls	51.9 (389)	39.1 (293)	9 (67)	71.5 (1071)	28.5 (427)
	rs4648090	G/A	IgAV	69.2 (276)	28.3 (113)	2.5 (10)	83.3 (665)	16.7 (133)
			Controls	72.3 (546)	25.3 (191)	2.4 (18)	85 (1283)	15 (227)
	rs230547	C/T	IgAV	80.5 (310)	17.9 (69)	1.6 (6)	89.5 (689)	10.5 (81)
			Controls	82.5 (619)	16.3 (122)	1.2 (9)	90.7 (1360)	9.7 (140)
NFKBIA	rs3138055	T/C	IgAV	49.3 (188)	42 (160)	8.7 (33)	70.3 (536)	29.7 (226)
			Controls	52.9 (397)	41.4 (311)	5.73 (43)	73.6 (1105)	26.4 (397)
	rs696	C/T	IgAV	38.2 (151)	47.9 (189)	13.9 (55)	62.2 (491)	37.8 (299)
			Controls	37.5 (283)	48.4 (365)	14.1 (106)	66.2 (931)	33.8 (475)
	rs1022714	G/A	IgAV	59.3 (214)	36.8 (133)	3.9 (14)	77.7 (561)	22.3 (161)
			Controls	60.2 (456)	35.4 (268)	4.4 (33)	77.9 (1180)	22.1 (334)
	rs2233419	G/A	IgAV	67.94(267)	28 (110)	4 (16)	81.9 (644)	18.1 (142)
			Controls	66.1 (500)	31.3 (237)	2.6 (20)	81.7 (1237)	18.3 (277)
	rs2233415	G/A	IgAV	43.5 (164)	47.8 (180)	8.8 (33)	67.4 (508)	32.6 (246)
			Controls	47.8 (361)	42.3 (320)	9.9 (75)	68.9 (1042)	31.1 (470)
	rs1050851	G/A	IgAV	60 (237)	33.2 (131)	6.8 (33)	75.4 (605)	25.6 (197)
			Controls	57.9 (434)	38 (285)	4.1 (31)	76.9 (1153)	23.1 (347)
	rs1957106	G/A	IgAV	56.1 (211)	38.6 (145)	5.3 (20)	75.4 (567)	24.6 (185)
			Controls	54.7 (414)	38.6 (292)	6.7 (51)	74 (1120)	26 (394)

IgAV: IgA Vasculitis; SNP: single nucleotide polymorphism; OR: Odds Ratio; CI: Confidence Interval.

Table 2. Genotype and allele analysis in IgAV patients and healthy controls.

Locus	SNP		IgAV Patients *vs* Healthy Controls	
			P	OR [95% CI]
NFKB1	rs77830930	GG	-	-
		GA	0.11	1.23 [0.95 - 1.59]
		AA	0.02	0.50 [0.28 - 0.91]
		G	-	-
		A	0.67	0.96 [0.79 - 1.16]
	rs1598856	GG	-	-
		GA	0.89	1.02 [0.76 - 1.37]
		AA	0.61	1.1 [0.77 – 1.54]
		G	-	-
		A	0.61	1.05 [0.88 - 1.24]
	rs7340881	CC	-	-
		CT	0.08	1.3 [0.96 -1.68]
		TT	0.98	1.00 [0.40 – 2.53]
		C	-	-
		T	0.15	1.19 [0.94 - 1.52]
	rs4648055	GG	-	-
		GA	0.15	0.82 [0.64 -1.07]
		AA	0.021	0.55 [0.33 – 0.92]
		G	-	-
		A	0.013	0.78 [0.64 - 0.95]
	rs4648090	GG	-	-
		GA	0.26	1.17 [0.89 – 1.54]
		AA	0.81	1.1 [0.50 – 2.41]
		G	-	-
		A	0.30	1.13 [0.89 - 1.43]
	rs230547	CC	-	-
		CT	0.46	1.13 [0.81 – 1.56]
		TT	0.59	1.33 [0.47 – 3.77]
		C	-	-
		T	0.37	1.14 [0.86 - 1.52]
NFKBIA	rs3138055	TT	-	-
		TC	0.53	1.08 [0.84 – 1.40]
		CC	0.05	1.62 [0.99 – 2.64]
		T	-	-
		C	0.10	1.17 [0.97 - 1.42]
	rs696	CC	-	-
		CT	0.82	0.97 [0.74 – 1.26]
		TT	0.88	0.97 [0.66 – 1.42]
		C	-	-
		T	0.85	0.98 [0.82 - 1.17]
	rs1022714	GG	-	-
		GA	0.68	1.06 [0.81 – 1.38]
		AA	0.76	0.90 [0.47 – 1.72]
		G	-	-
		A	0.90	1.01 [0.82 - 1.25]
	rs2233419	GG	-	-
		GA	0.31	0.87 [0.66 – 1.14]
		AA	0.24	1.49 [0.76 – 2.94]
		G	-	--
		A	0.89	0.98 [0.79 - 1.23]
	rs2233415	GG	-	-
		GA	0.11	1.24 [0.95 – 1.60]
		AA	0.89	0.97 [0.62 – 1.52]
		G	-	-
		A	0.46	1.07 [0.89 - 1.29]
	rs1050851	GG	-	-
		GA	0.19	0.84 [0.65 – 1.09]
		AA	0.08	1.59 [0.93 – 2.74]
		G	-	-
		A	0.88	1.02 [0.83 - 1.25]
	rs1957106	GG	-	-
		GA	0.84	0.97 [0.74 – 1.27]
		AA	0.34	0.77 [0.44 – 1.35]
		G	-	-
		A	0.46	0.93 [0.76 - 1.13]

IgAV: IgA Vasculitis; SNP: single nucleotide polymorphism; OR: Odds Ratio; CI: Confidence Interval.

Table 3. Haplotype analysis in IgAV patients and healthy controls.

Locus	Haplotype[1]	IgAV Patients, %	Healthy controls, %	Chi[2]	P
NFKB1	AACGGC	26.6	27.7	0.35	0.55
	GGCAGC	22.9	28.1	7.25	0.007
	GACGGC	12.9	11.1	1.48	0.22
	GACGGT	8.9	8.3	0.26	0.61
	GGTGAC	8.5	8.1	0.12	0.73
	GGCGAC	7.3	6.0	1.42	0.23
	GGTGGC	6.0	4.5	2.74	0.09
NFKBIA	AGGGGTT	17.7	17.4	0.03	0.86
	GGAGACC	18.5	16.6	1.33	0.25
	GAGAGCT	16.1	15.5	0.15	0.69
	GGAGGTT	10.6	11.0	0.08	0.78
	GGGGGCT	7.3	8.6	1.21	0.27
	GGGGGTT	6.1	5.5	0.37	0.54
	AGGGGCT	4.3	6.0	3.07	0.08

IgAV: IgA Vasculitis. The table shows the *NFKB1* and *NFKBIA* haplotypes with a frequency greater than 5%. [1]Haplotypes are arranged in the following order: *NFKB1* (rs77830930, rs1598856, rs7340881, rs4648055, rs4648090, and rs230547) and *NFKBIA* (rs1957106, rs1050851, rs2233415, rs2233419, rs1022714, rs696, rs3138055).

not significant after FDR correction. No other statistically significant results were found in *NFKB1* and *NFKBIA* genotype, allele, or haplotype frequencies between patients with IgAV and controls (Tables 1-3), nor when IgAV patients were stratified according to the age at disease onset or the presence/absence of gastrointestinal or renal manifestations (data not shown).

Conclusion: Our results suggest that *NFKB1* and *NFKBIA* do not seem to be involved in the pathogenesis of IgAV.

References:[1] *N Engl J Med 1997;336:1066-71;* [2] *Nat Immunol 2003;4:274-9*; [3] *Hum Mol Genet 2004;13:35-45*; [4] *Front Immunol 2019;10:815*.; [5] *Cell Biosci 2015;5:63*.

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Abstract Number: 0709

Survival of Adults with IgA Vasculitis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Data on survival of adults with IgA vasculitis (IgAV) are scarce. The aim of our study was to estimate for the first time the survival of IgAV patients in our country.

Methods: Our cohort consisted of adult patients diagnosed with IgAV between January 2010 and July 2022 and followed at our secondary/tertiary rheumatology center. To study the survival/mortality the censor date of 22, December 2022 was set, and time until death or the censor date, whichever came first, was recorded. Kaplan–Meier analysis and standardized mortality ratio (SMR) were plotted using survival data from age and sex matched Slovenian population as a reference. Cox proportional hazards regression analysis was used to study prognostic factors for mortality in IgAV.

Results: Of 265 IgAV patients (156 (58.9%) males, median (IQR) age at diagnosis 61 (44; 74) years; median (IQR) follow up time 62 (27; 93) months), 48 (18.1%) patients died. Five-year survival in our cohort was 78% (95% CI 74%; 83%); in adults < 51 years 100% survival, and in adults aged ≥51 years 68% survival (the difference was significant, p=0.01). Ten-year survival in our patients was 65% (95%CI 59%; 72%). We found no sex related differences in the survival (p=0.37). The comparison of mortality between the IgAV cohort and age and sex matched general Slovenian population showed a significantly higher overall mortality in IgAV cohort, with an overall SMR of 1.4 (95%CI 1.14-1.71). The Kaplan-Meier survival curves of IgAV patients and matched general population as a comparator are shown in Figure 1. Excess deaths occurred mainly during the first two years of follow-up (Table 1). As risk factors associated with increased mortality in IgAV emerged patient age (HR 1.09 (95%CI 1.06; 1.13)), purpura above waistline (HR 2.14 (95% CI 1.13; 4.06)) and pre-existent heart failure (HR 7.37 (95%CI 3.74; 14.54)).

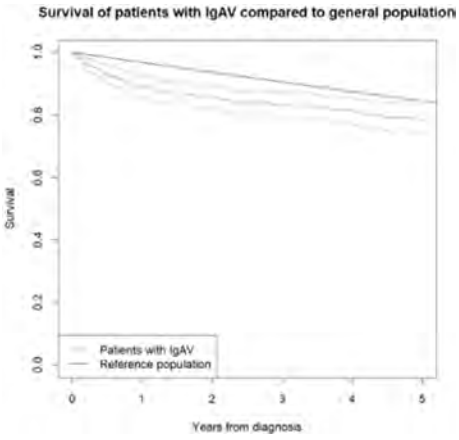

Figure 1. Survival curve of IgAV patients according to Kaplan–Meier analysis compared to sex and age matched general Slovenian population

Table 1. The standardized mortality ratio of adults with IgAV . Legend: SMR standardized mortality ratio

Follow-up	SMR (95% CI)	P value
1 year	3.79 (2.68 – 5.20)	<0.001
2 years	2.75 (2.05 – 3.62)	<0.001
3 years	2.18 (1.66 – 2.82)	<0.001
4 years	1.84 (1.41 – 2.35)	<0.001
5 years	1.70 (1.33 – 2.15)	<0.001
6 years	1.60 (1.26 – 1.99)	<0.001
7 years	1.53 (1.22 – 1.90)	<0.001
8 years	1.46 (1.17 – 1.80)	<0.001
9 years	1.42 (1.14 – 1.75)	0.001
10 years	1.39 (1.12 – 1.70)	0.002

Cardiovascular diseases, cancer and infections represented the most frequent causes of death in our patients, recorded in 16 (33.3%), 6 (12.5%) and 6 (12.5%) patients, respectively, followed by hepatobiliary disease (3 cases), respiratory failure (2 cases), trauma/bleeding (3 cases) and dementia (3 cases). In one patient death was related to IgAV relapse, and in 8 (16.7%) patients the cause of death was unknown.

Conclusion: Survival of adults with IgAV was worse compared to matched general population in our country. Nevetheless, IgAV per se was an infrequent cause of death during follow up in our population.

Disclosure: A. Hocevar: None; **J. OSTROVRŠNIK**: None; **v. JURČIĆ**: None; **M. Tomšič**: None; **Z. Rotar**: None.

Abstract Number: 0710

The Association of IgA Vasculitis and Malignancy in Adults: A Systematic Review

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
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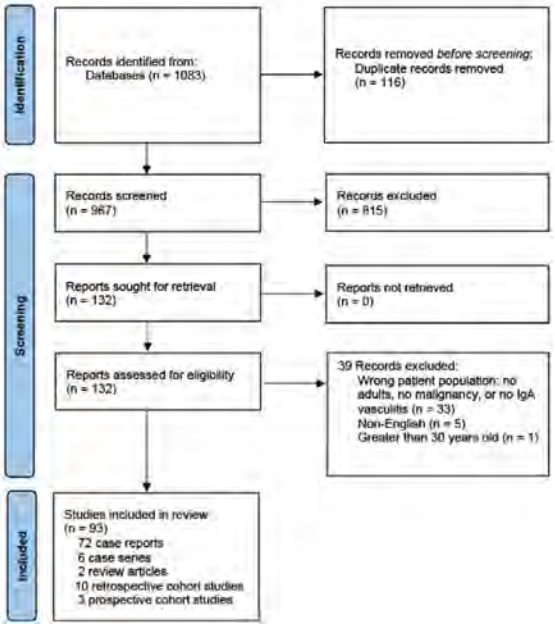
Background/Purpose: IgA vasculitis (IgAV) is associated with malignancy in adult patients [1,2]. The clinical characteristics, temporal relationship, and underlying mechanisms of malignancy-associated IgAV are not well understood. Currently, there are no evidence-based screening guidelines for occult malignancies in adults presenting with IgAV.

Methods: We performed a systematic literature review of five major databases: Cochrane Library, Embase.com, PubMed.gov, Google Scholar, and Web of Science Core Collection using the Preferred Reporting Items for Systematic Reviews and MetaAnalyses (PRISMA) guidelines. A combination of multiple synonyms, controlled vocabulary search terms (MeSH in PubMed and Emtree in Embase), and exhaustive text words were used to search the databases. Two independent reviewers selected studies, extracted data, and determined study quality. A third reviewer adjudicated the article if there was a discrepancy between the 2 reviewers. The articles met inclusion criteria if they contained information regarding IgAV and malignancy in adults older than 18 years-old. Non-English articles and articles older than 30 years-old were excluded.

Figure 1. PRISMA Flowchart illustrating article selection and inclusion process



Flowchart illustrating article selection and inclusion process.

Table 1. Demographic and clinical information by malignancy type

		Solid Malignancy	Hematologic Malignancy	Total
		N = 73 (67.7%)	N = 35 (32.4%)	N = 108 (100%)
Age				
	Mean (years)	61.7 ± 12.1	57.4 ±14.3	60.3 ± 12.9
	Range (years)	25 - 84	28 - 84	25 - 84
Sex		*N (%)*	*N (%)*	*N (%)*
	Male	47 (64.4)	24 (68.6)	71 (65.7)
	Female	19 (26.0)	7 (20.0)	26 (24.1)
	Not reported	7 (9.6)	4 (11.4)	11 (10.2)
Race/ Ethnicity				
	White	14 (19.2)	6 (17.1)	20 (18.5)
	Black	1 (1.4)	0 (0)	1 (0.9)
	Asian	9 (12.3)	4 (11.4)	13 (12.0)
	Hispanic	1 (1.4)	0 (0)	1 (0.9)
	Not reported	48 (65.7)	25 (71.4)	73 (67.6)
Relative timing				
	Before IgAV	35 (47.9)	8 (22.9)	43 (39.8)
	Synchronous	23 (31.5)	11 (31.4)	34 (31.5)
	After IgAV	7 (9.6)	11 (31.4)	18 (16.7)
	Median time difference (days)	61 (IQR 0-365)	91 (IQR 0-912.5)	61 (IQR 0-411)
Systemic involvement				
	Renal	52 (71.2)	21 (60.0)	73 (67.6)
	Gastrointestinal	34 (46.6)	15 (42.9)	49 (45.4)
	Joint	34 (46.6)	12 (34.3)	46 (42.6)
Pathology/serology				
	IgA on skin DIF	35 (70.0)*	17 (73.9)**	52 (71.2)***
	IgA on renal bx	24 (88.9)+	15 (100)++	39 (92.9)+++
	Elevated serum IgA	14 (63.6)~	12 (75.0)~~	26 (68.4)~~~
Outcomes				
	Remission	28 (49.1)°	19 (63.3)•	47 (54.0)•
	Mortality	22 (38.6)°	5 (16.7)•	27 (31.0)•

Footnote: *N=50; **N=23; ***N=73; +N=27; ++N=15; +++N=42; ~N=22; ~~N=16 ; ~~~N=38; °N=57; •N=30; •N=87

Summary of sample demographic information, including age, sex, and race/ethnicity, and clinical information, including relative timing, systemic involvement, pathology, serology , and outcomes, by malignancy type.

Results: We screened 967 studies and 93 articles were included, comprising of 108 individual patient cases (Figure 1). The mean age of patients was 60.3±12.9 years, and the majority (n=71, 65.7%) were male (Table 1). Solid malignancy was more commonly associated with IgAV than hematologic malignancy (67.7% vs 32.4%). Malignancy preceded IgAV for most patients with solid cancer, whereas for most with hematological cancer, IgAV preceded malignancy or was diagnosed synchronously. Patients with IgAV and solid malignancies had a significantly higher mortality rate compared to patients with IgAV and hematological malignancies (38.6% vs. 16.7%, $p \leq 0.05$). Patients with solid malignancies were also more likely to exhibit systemic involvement of IgAV, including renal, gastrointestinal, joint, and cutaneous symptoms, although the differences were not significant. The majority of patients with skin biopsy had IgA on DIF (71.2%), and of the patients that reported serum IgA levels, 26 (68.2%) had elevated serum IgA.

Conclusion: To our knowledge, this is the largest systematic review of IgAV associated with malignancy. Based on our findings, screening older patients with new-onset or recurring IgAV for malignancy, particularly solid organ cancer, should be considered. Serum IgA levels might serve as a useful, non-invasive screening test since elevated IgA may correlate with underlying malignancy, though further studies are needed to validate these findings.

References

1. Mitsui H, Shibagaki N, Kawamura T, Matsue H, Shimada S. A clinical study of Henoch-Schönlein Purpura associated with malignancy. Journal of the European Academy of Dermatology and Venereology 2009;23:394-401.
2. Hankard A, Michot J-M, Terrier B, et al. New insights on IgA vasculitis with underlying solid tumor: a nationwide French study of 30 patients. Clinical Rheumatology 2021;40:1933-40.

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Abstract Number: 0711

IgA Vasculitis in a Diverse Adult Patient Population

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SESSION INFORMATION
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Background/Purpose: Immunoglobulin-A (IgA) Vasculitis (IgAV) is a small-vessel vasculitis that is primarily diagnosed based on the European League Against Rheumatism (EULAR) criteria. There is limited knowledge about the IgAV phenotype in a racially and ethnically diverse population. We aimed to describe the clinicopathologic characteristics of IgAV in our adult skin of color (SOC) patients.

Methods: We retrospectively reviewed adult patients (>18 years) from the dermatopathology database with leukocytoclastic vasculitis (LCV) at Montefiore Medical Center between January 2012–December 2022 (Figure 1). We collected demographic, clinical, laboratory, and histopathological data from the electronic medical record to identify individuals with SOC who met EULAR criteria. We defined SOC as any non-White race/ethnicity. Descriptive statistics and Fisher's exact test were used to analyze the SOC cohort.

Results: We identified 65 patients with LCV, 52 patients met EULAR criteria for IgAV, of which 42 (81%) were SOC. In our SOC cohort of 42 patients, 32 (76%) identified themselves as Spanish/Hispanic/Latino, 7 (17%) identified themselves as Black, and 3 (7%) identified themselves as Asian. The mean (±SD) age was 56 (±16) years and 29 (69%) were females. The median (IQR) number of affected body sites was 3 (2-5). Renal involvement was present in 36 (86%) patients (Table 1). Gastrointestinal (GI) involvement was present in 16 (38%) and joint involvement was present in 5 (12%). Elevated neutrophil/lymphocyte ratio (NLR) was present in 22 (52%). Elevated serum IgA levels were present in 13 (62%) of the 21 patients with measured serum IgA. Skin biopsy direct immunofluorescence (DIF) was performed in 28 (67%) patients and showed IgA and C3 in 11 (39%) and 19 (64%), respectively. Remission was achieved in 34 (81%) patients and 8 (19%) experienced relapse.

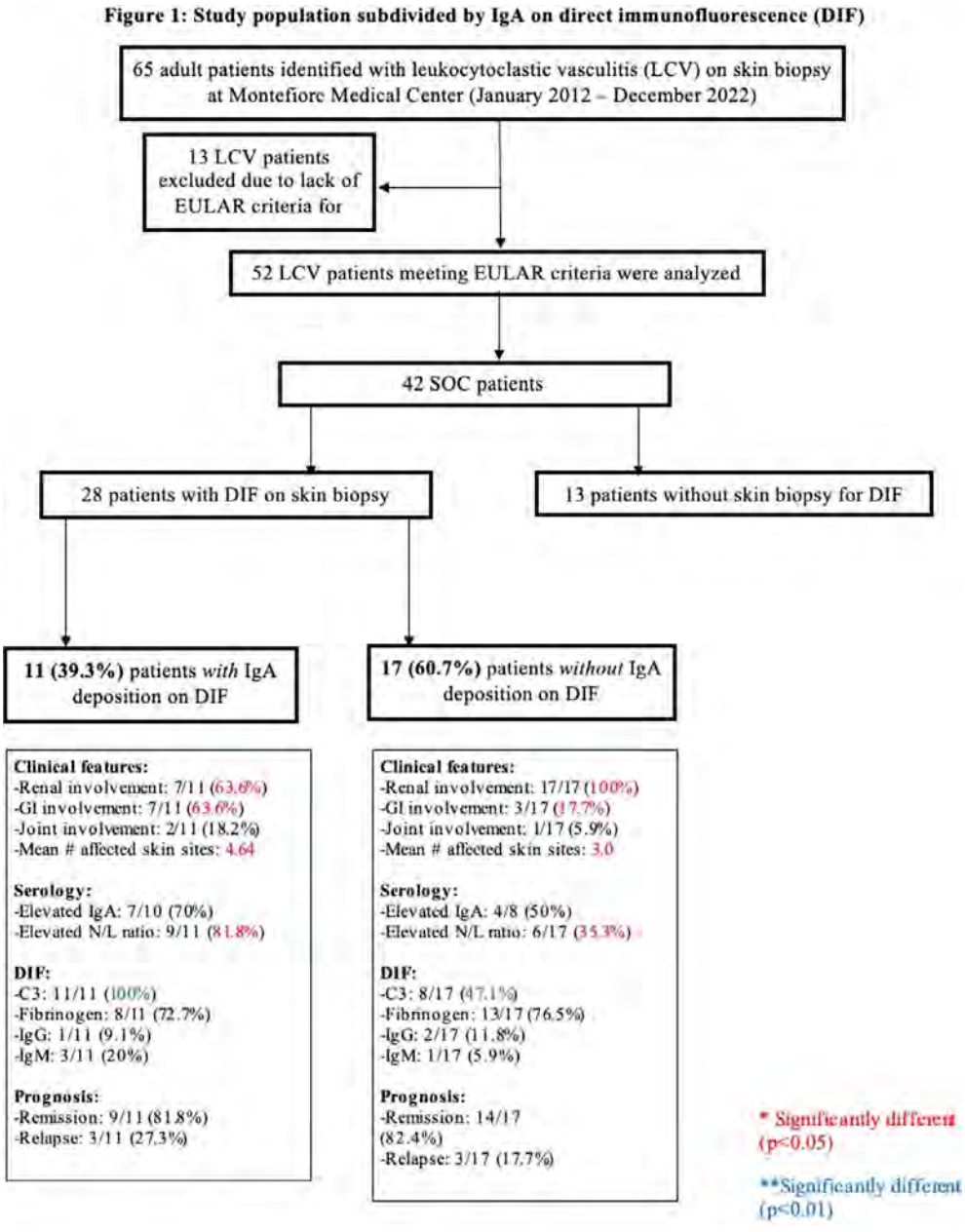

Figure 1: Study population subdivided by IgA on direct immunofluorescence (DIF)

Table 1: Disease characteristics of IgA vasculitis

Table 1: Disease characteristics of IgA vasculitis

		Mean ± SD, median (IQR), or N (%)
Clinical Information		N = 42
	Number affected skin sites	3 (2-5)
	Lesions above waist	26 (61.9%)
	Renal involvement	36 (85.7%)
	GI involvement	16 (38.1%)
	Abdominal pain	16 (38.1%)
	Diarrhea	8 (19.0 %)
	Nausea/vomiting	3 (7.1%)
	Hematochezia	5 (11.9%)
	Positive Stool occult blood	5 (11.9%)
	Joint involvement	5 (11.9%)
	Ocular involvement	0 (0.0%)
Laboratory Analysis		N = 42
	IgA	489 (346.5-805)[*]
	Elevated IgA	13 (61.9%)[*]
	C3	127.8 ± 44.9[#]
	Low C3	5 (13.9%)[#]
	C4	25.8 ± 11.9[^]
	Low C4	9 (24.3%)[^]
	CH50	117. 3 ± 87.1[v]
	Elevated CH50	9 (75%)[v]
	NLR	3.6 (1.6-6.6)
	Elevated NLR	22 (52.4%)
	Cr at dx	1 (0.7-1.82)[+]
	Cr increase of ≥0.3	13 (35.1%)[+]
	Cr at 1-year f/u	1 (0.7-1.7)[•]
	Cr increase of ≥0.3	6 (19.4%)[•]
	Cr at 2-year f/u	0.8 (0.7-1.4)[•]
	Cr increase of ≥0.3	5 (31.3%)[•]
	Proteinuria at dx	29 (69.0%)
	Proteinuria at 1-year f/u	20 (47.6%)
	Proteinuria at 2-year f/u	7 (16.7%)
	Hematuria at dx	23 (54.8%)
	Hematuria at 1-year f/u	16 (38.1%)
	Hematuria at 2-year f/u	7 (16.7%)
Skin Biopsy – DIF		N = 28
	IgA	11 (39.3%)
	C3	19 (67.9%)
	Fibrinogen	21 (75.0%)
	IgG	3 (10.7%)
	IgM	4 (14.3%)
Treatment and Outcomes		N = 42
	Topical tx	33 (78.6%)
	Systemic tx	16 (38.1%)
	Remission	34 (81.0%)
	Relapse	8 (19.0%)
	Death (all-cause)	4 (9.5%)

Footnote: SD = standard deviation, IQR = interquartile range, NLR = neutrophil-to-lymphocyte ratio, Cr = creatinine, dx = diagnosis, f/u = follow-up, DIF = direct immunofluorescence, tx = treatment, [*]N = 21, [#]N = 36, [^]N = 37, [v]N = 12, [+]N = 37, [•]N = 31, [•]N = 16

We further analyzed the 28 patients who had skin biopsy with DIF and compared those with and without IgA deposition (Figure 1). The IgA^+ group had significantly lower prevalence of renal involvement (p=0.0161), higher prevalence of GI involvement (p=0.0204), high NLR (p=0.0238), and C3 deposition on DIF (p=0.0039), and greater number of affected body sites (p=0.0206). Lesions above waistline and elevated serum IgA were not associated with systemic symptoms, including renal involvement, or positive DIF. Elevated NLR was associated with IgA deposition (p=0.0209).

Conclusion: In contrast to previous studies, the majority of our adult SOC patients had renal or GI involvement with IgA^+ DIF being associated with lower prevalence of renal involvement. Additionally, our SOC patients with IgA^+ DIF had more widely distributed lesions. Cutaneous involvement above the waist was not associated with renal complications. Prior studies showing the predictive value of skin biopsy and lesion location in predominantly White populations may not apply to SOC patients.

Disclosure: M. Toker: None; **U. Khanna**: None; **R. Nazarian**: None; **A. Mehta**: None; **B. Ayesha**: None; **A. Kumthekar**: None; **B. Wu**: None.

Abstract Number: 0712

Clinical and Histologic Prognostic Factors of Renal Progression in Adults with IgA Vasculitis

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: IgA Vasculitis (IgAV) is a systemic small vessel vasculitis that affects the skin, joints, gastrointestinal tract, and kidneys. While most common in children, it is rare in adults and associated with worse prognosis. IgAV has a variable course with many patients spontaneously entering remission, making it difficult to know which patients need treatment.

A few retrospective trials have shown that adult IgAV patients with greater proteinuria, kidney insufficiency at time of biopsy, and hypertension have worse overall prognosis, often developing progressive kidney disease. Retrospective studies in European and Asian populations have also considered the MEST-C renal biopsy score components as predictive tools in IgAV.

The goal of this study is to expand on existing studies and identify clinical factors that predict poor outcome in IgAV adults. We also aim to identify histologic prognostic factors using the MEST-C score components. Identifying prognostic factors will improve patient treatment plans while informing future therapeutic studies.

Methods: We conducted a retrospective analysis of 31 IgAV adult patients. A Cohort Discovery Tool was built to identify eligible patients. The primary outcome was progressive kidney disease, defined as nephrotic range proteinuria (> 3.5g/d) or > 30% creatinine elevation within 1 year of kidney biopsy.

We included patients age > 18, with at least one symptom of IgA Vasculitis (cutaneous palpable purpura, arthritis, bowel angina), and kidney biopsy consistent with IgAV.

We collected data on patient's kidney function at time of diagnosis, and at 3, 6, and 12 month intervals. For preliminary analyses, we assessed Pearson correlation of clinical factors and MEST-C components with the primary outcome.

Results: Baseline creatinine was shown to have significant correlation with renal progression at 1 year**,** yielding a Pearson coefficient of .887 (2-tailed significance < .001, n = 21). Age, systolic blood pressure, and degree of proteinuria did not have significant Pearson coefficients at 3, 6, or 12 month intervals.

The "E" component in MEST-C, which stands for Endocapillary Hypercellularity, also showed significant correlation with renal progression at 1 year, with a Pearson coefficient of .776 (2-tailed significance < .001, n = 26). Other components of the MEST-C score did not yield significant correlations

Conclusion: Similar to existing studies, renal insufficiency at baseline is a prognostic indicator of poor outcomes in IgA Vasculitis patients. Age, initial proteinuria, and hypertension were not correlated with kidney progression in our study, which diverges from prior literature. Regarding histologic predictive factors, the "E" in MEST-C (Endocapillary Hypercellularity) is predictive of renal progression in prior studies, and we were able to validate this finding. Next steps in our study include expanding our cohort, as well as correlating treatment regimens with renal progression at 1 year.

Disclosure: M. Vanka: None; **T. Kim**: None.

Abstract Number: 0713

IgG4-Related Disease as a Potencial Etiology of Idiopathic Constrictive Pericarditis

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Background/Purpose: Constrictive pericarditis (CP) is a type of diastolic heart failure characterized by impaired cardiac filling due to the presence of an inelastic pericardium. Histologically, the pericardium exhibits fibrotic and thickened features. While tuberculosis remains the primary cause of CP in developing countries, idiopathic CP predominates in North America and Europe. The extent to which idiopathic CP patients may belong to the spectrum of IgG4-related disease remains unknown. Therefore, our objective was to determine the number of idiopathic CP patients meeting histopathological criteria for IgG4-RD.

Methods: Clinical records of patients with CP attended between 1987-2020 were reviewed. Those without a biopsy or with a known etiology of CP were excluded. Pericardial biopsies were analyzed in search of dense lymphoplasmacytic infiltrate, storiform fibrosis, and obliterative phlebitis. Immunohistochemistry for IgG and IgG4 was performed. The number of IgG+ and IgG4+ plasma cells and the IgG4/IgG ratio were determined according to the International Consensus on Pathology (ICP) of IgG4-RD. According to the ICP, cases were classified as highly suggestive, probable histopathological

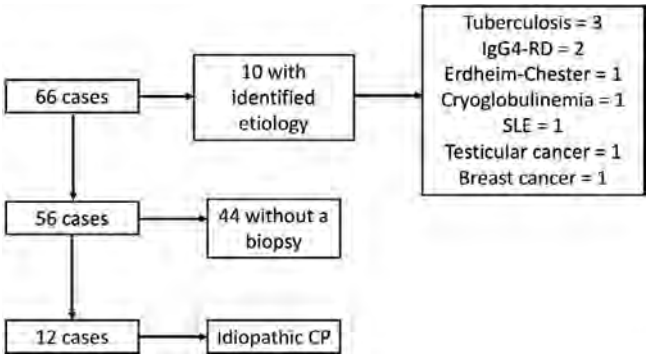

Figure 1. Flowchart illustrating the inclusion criteria.

Table 1. Electrocardiographic and cardiac imaging findings.

Table 1.	N=12 n (%)
Electrocardiogram	
Low QRS voltage	3 (25)
Increased heart rate	3 (25)
Echocardiogram	
Pericardial thickening	5 (41.7)
Pericardial effusion	4 (33)
Atrial enlargement	4 (33)
Hypokinesia	3 (25)
Cardiac magnetic resonance imaging	
Pericardial thickening	5/9 (55.5)
Pleural effusion	2/9 (22.2)
Pericardial effusion	1/9 (11.1)
Cardiac computed tomography	
Pleural effusion	4/6 (66.6)
Pericardial effusion	3/6 (50)
Pericardial thickening	2/6 (33.3)

characteristics, or insufficient histopathological evidence. The Comprehensive Diagnostic Criteria for IgG4-RD (CDCI) and the 2019 ACR/EULAR classification criteria (AECC) were also applied. Clinical characteristics were extracted from the patients' medical records.

Results: Sixty-six cases were reviewed, of which 10 had an identified etiology. Of the remaining 56, only 12 had a pericardial biopsy. All had been classified as idiopathic (Figure 1). Mean age of 43.5 ± 14.4 years; 9 were men. Regarding clinical behavior, all patients presented with signs and symptoms of heart failure. Six (50%) patients presented with effusive CP and 10 (83.3%) with chronic CP (non-mutually exclusive). Findings on electrocardiogram, echocardiogram, cardiac magnetic resonance imaging and cardiac computed tomography are summarized in Table 1. All patients underwent pericardiectomy, with glucocorticoid treatment administered to only one patient. At last follow-up, 3 (25%) patients had died.

Lymphoplasmacytic infiltrate was found in all, fibrosis in eight, and storiform fibrosis in only one case. Obliterative phlebitis was not found. In 2 cases the IgG stains were not assessable, so the IgG4/IgG ratio was calculated in 10 cases. The median number of IgG4+ plasma cells/HPF was 30.5 (IQR 16.5-41). The median IgG4/IgG ratio was 59.5% (IQR 27-66). All cases had >10 IgG4+ plasma cells/HPF while 7/10 (70%) had an IgG4/IgG ratio >40%. According to the ICP, 1 (8.3%) case was highly suggestive, 6 (50%) had probable histological characteristics, and 5 (41.6%) showed insufficient histopathological evidence. Seven (58.3%) were diagnosed as probable IgG4-RD according to the CDCI, but only one patient met 2019 AECC for atypical IgG4-RD.

Conclusion: A significant proportion of pericardial biopsies from patients with idiopathic CP display findings indicative of IgG4-RD and meet at least one set of diagnostic or classification criteria. Considering the implications for treatment, IgG4-RD should be considered when evaluating patients with CP.

Disclosure: E. Cortez-Domínguez: None; **G. Hernandez-Molina**: None; **N. Uribe-Uribe**: None; **M. Lizardo-Thiebaud**: None; **E. Martin-Nares**: None.

Abstract Number: 0714

Single Center Experience of Rituximab Treatment for IgG4-RD Disease in a Large Multi-ethnic Cohort

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SESSION INFORMATION
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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: IgG4-related disease (IgG4-RD) is a systemic fibro-inflammatory disorder that can affect almost any organ system. Response to corticosteroids(CS) is typically prompt although adverse effects are commonplace and relapses frequently occur during withdrawal. There is evidence to suggest that rituximab (RTX) may be an effective alternative however as yet, the optimal RTX treatment regimen for IgG4RDremains unclear. In this retrospective study, we report the use of a RTX treatment protocol for multi-system IgG4RD in a large single tertiary center cohort.

Methods: Patients were selected from an IgG4RD multi-disciplinary service receiving referrals from the catchment of North West London. Patients diagnosed with IgG4-RD received RTX according to local protocol guided by B cell repopulation (to a level of > 10 cells/uL) for a target period of two years. The electronic patient records were reviewed to record presentation and outcome data over the course of their RTX therapy.

Results: In total, 45 patients received treatment with RTX. 1 patient was excluded from analysis due to insufficient follow up data. The median age was 62 and 66% were male. Multiple ethnic backgrounds were represented; 20% black, 20% white and 60% Asian. The average number of organs affected was 2.9 (range 1-7) and the average IgG4-RD Responder Index (RI) prior to treatment was 10.02. 8/44 (18%) were on another conventional immunosuppressant at the time of RTX induction and 27/44 (61%) had concurrent treatment with CS. The proportions of the 27 patients remaining on CS at 9, 12 and 24 months were 66%, 54% and 19% (average dose at 2 years 3.8mg). All patients demonstrated reduced disease activity post RTX with an average IgG4-RI of 2.4 at most recent review (76% reduction). 34 patients had follow-up imaging and all had a degree (100%) of disease response; 2/34 (6%) stable; 21/34 (62%) partial response; 11/34 (33%) had a complete response. Intercurrent flares did occur in 9 patients, 7 of whom had concurrent B cell repopulation (78%). All 7/7 (100%) patients treated with further RTX responded positively. 15 patients completed two years of consistent RTX-induced B cell depletion with no subsequent flares (average follow up 15 months, median 10 months, range 1-51 months). The only 2 patients requiring >2 years maintenance RTX therapy had isolated pituitary disease. 12/45 (27%) of the entire cohort experienced an adverse event including infection requiring admission (4), hypogammaglobinaemia (2), infusion reaction (1) and death (5; 11%; average age 81).

Conclusion: In this cohort of patients treated with RTX for IgG4-RD, all patients demonstrated improved disease activity according to IgG4-RD RI and available imaging. Flares did occur but most often in the presence of measurable B cell repletion and all patients re-treated with further RTX responded. In those who discontinued treatment after >2 years of B cell depletion therapy, there were no further flares over an average follow-up duration of almost 15 months. This retrospective study indicates that protocolled management of IgG4RD with RTX is an effective treatment option for IgG4-RD. Patient selection is important to minimize the risk of complications.

Disclosure: M. Colquhoun: Pfizer, 6; **T. Youngstein**: None; **J. Tomlinson**: AstraZeneca, 6.

Abstract Number: 0715

Glucocorticoid Toxicity in Patients with IgG4-Related Disease Within the First Year of Treatment

Ana Mora-Rosas, Gabriela Hernandez-Molina, Edwin Ulises Cortez-Domínguez and Eduardo Martin-Nares, Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with IgG4-related disease (IgG4-RD) often require long-term glucocorticoid therapy. The prevalence, types, and underlying factors of glucocorticoid toxicity in IgG4-RD patients remain unknown. We aimed to describe the prevalence, types, and associated factors of glucocorticoid toxicity in our IgG4-RD cohort.

Methods: We retrospectively included patients diagnosed with IgG4-related disease (IgG4-RD) based on the Comprehensive Diagnostic Criteria and/or the 2019 ACR/EULAR classification criteria who had received glucocorticoid treatment for a minimum of one month and were followed up for at least one year. We categorized them into clinical phenotypes: pancreatobiliary (group 1), retroperitoneal/aortic (group 2), head and neck limited (group 3), Mikulicz/systemic (group 4), and undefined (group 5). From the medical records, we collected demographic, clinical, and treatment variables. We focused on prednisone usa during the first year of treatment, including the mean daily dose of prednisone, accumulated prednisone

Table 1. Frequency of glucocorticoid-related toxicity in IgG4-related disease patients.

Table 1.	Glucocorticoid-induced toxicity N (%)
Endocrinologic/metabolic	36 (63.3)
Weight gain	26 (45.6)
Newly diagnosed overweight status	15 (25.3)
Newly diagnosed obesity	7 (12.3)
Newly diagnosed diabetes	6 (10.5)
Change in diabetes treatment	14 (24.6)
Cushing's syndrome	3 (5.3)
Newly diagnosed hypertension	8 (14)
Increased in LDL cholesterol	3 (5.3)
Dermatologic	8 (14)
Moon facies	4 (7)
Capillary fragility	2 (3.5)
Acneiform rash	3 (5.3)
Delayed scarring	1 (1.8)
Musculoskeletal/osseus	7 (12.3)
Osteoporosis	3 (5.3)
Osteopenia	3 (5.3)
Myopathy	1 (1.8)
Neuropsychiatric	7 (12.3)
Insomnia	4 (7)
Depression	3 (5.3)
Anxiety	1 (1.8)
Cognitive decline	1 (1.8)
Gastrointestinal	6 (10.5)
Gastritis	6 (10.5)
Gastroesophageal reflux	4 (7)
Infections	3 (5.3)
Herpes zoster	2 (3.6)
Pneumonia	1 (1.8)

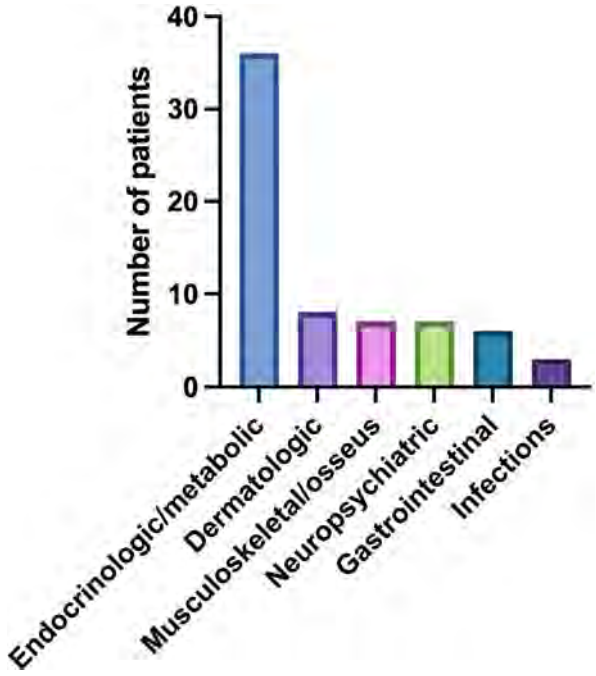

Figure 1. Frequency of glucocorticoid-related toxicity in IgG4-related disease patients.

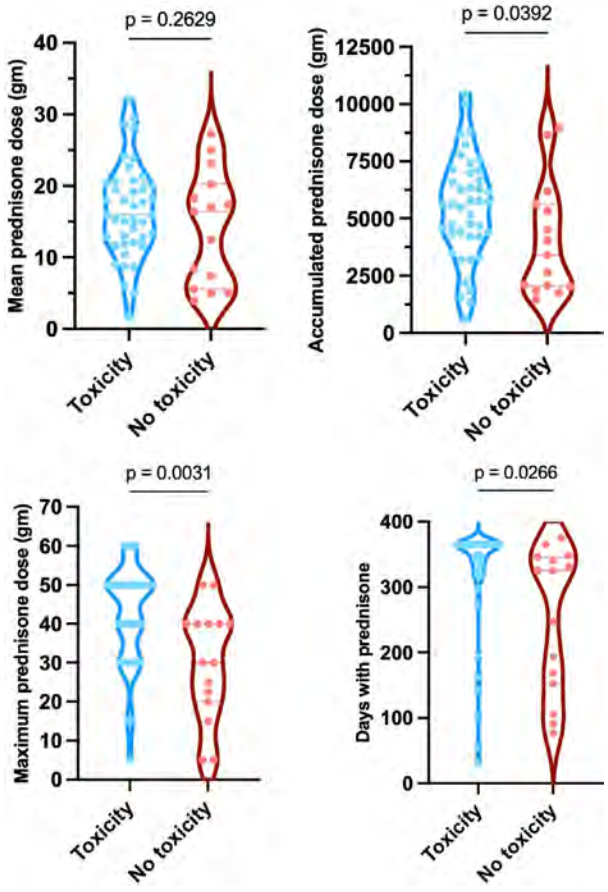

Figure 2. Prednisone use in patients who experienced toxicity vs. those who did not.

dose, maximum prednisone dose, and duration of prednisone treatment. To assess glucocorticoid toxicity, we employed the definitions proposed in the Glucocorticoid Toxicity Index, along with its domains and appendixes.

Results: Fifty-seven patients were included with a mean age of 53±15.8 years, of whom 34 (59.6%) were male. Fifteen (26.3%) belong to group 1, six (10.5%) to group 2, 13 (22.8%) to group 3, 19 (33.3%) to group 4 and 4 (7%) to group 5. The mean prednisone daily dose was 15.9±6.9 grm the median accumulated prednisone dose was 4,967.5 (IQR 3,195-6,670) gm, the mean maximum dose of prednisone was 39.3±14.2 gm, while the median number of days under prednisone treatment was 303.2 ± 103.9 days.

Forty-two (73.7%) patients developed one or more toxicities. The first toxicity was documented at a median of 64 (IQR 34.5-132) days. The median number of toxicities was 3 (IQR 1-4). The frequency and types of toxicities reported during the study period (non-mutually exclusive) are summarized in Figure and Table 1.

There were no differences in daily, accumulated, and maximum prednisone dose, or days with prednisone treatment, development of toxicities, days to first toxicity or number of toxicities according to sex or clinical phenotypes. Patients in group 3 and 4 presented more endocrinologic/metabolic toxicities compared to the other groups.

Patients who experienced toxicities had a higher accumulated prednisone dose (5,605 [IQR 4.215-7,015] vs. 3,400 gm [IQR 2,025-5,638], p=0.03), maximum prednisone dose (42.5±12.8 vs. 30.2±14.5 gm, p=0.003) and days of prednisone treatment (321.3±96.7 vs. 252.6±110, p=0.02) than patients without toxicities (Figure 2). Patients that used immunosuppressors did not present lower accumulated prednisone doses (5,335 [IQR 4,132-6,314] vs. 4,272.5 gm [IQR 2,100-7,427], p=0.41) or a lower incidence of toxicities (29 [74.4%] vs. 13 [72.2%], p=0.23).

Conclusion: Our findings highlight the high prevalence of glucocorticoid toxicity in patients with IgG4-RD undergoing glucocorticoid therapy, even within a relatively brief timeframe of one year. The presence of glucocorticoid toxicity was associated with higher doses and a longer use of prednisone.

Disclosure: A. Mora-Rosas: None; **G. Hernandez-Molina**: None; **E. Cortez-Domínguez**: None; **E. Martin-Nares**: None.

Abstract Number: 0716

Efficacy of Immunosuppressants for Disease Relapse in Patients with IgG4-related Disease at Our Institution

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Most patients with IgG4-related disease (IgG4-RD) have a good response to glucocorticoid (GC) therapy, however, disease relapses sometimes occur during GC tapering. Therefore, the immunosuppressants are considered in these cases. On the other hand, the predictors of disease relapse and the efficacy of immunosuppressants have not been fully clarified.

Therefore, we retrospectively analyzed the current treatment status of patients with IgG4-RD to identify the efficacy of immunosuppressants for disease relapse.

Methods: We used the data of patients with IgG4-RD diagnosed by May 2023 based on the 2020 revised comprehensive diagnostic criteria for IgG4-RD, and extracted those who had undergone therapeutic intervention. We retrospectively evaluated the organ involved, immunological findings including serum IgG4 levels, treatment agents, especially in GC dose and concomitant use of immunosuppressants, and the presence of relapse within 2 years after the start of treatment.

Results: 95 patients were diagnosed according to the 2020 revised comprehensive diagnostic criteria for IgG4-RD. Of these, 59 patients underwent therapeutic intervention, and all cases were initially treated with GC at a mean dose of 0.54 mg/kg body weight. Immunosuppressants were used concomitantly in 30 patients (50.8%), mostly azathioprine. In 17 of these cases, immunosuppressants were started either at the time of initial therapy or GC dose reduction. There was no significant difference between the 17 patients who received these immunosuppressants and the other patients (Table 1), however, the rate of definite cases tended to be higher in the cases who received immunosuppressants (P=0.06). 15 patients (25.4%) relapsed during GC reduction, and the mean time to disease relapse from the start of treatment was 33.2

Table 1. Patients' characteristics at diagnosis with or without immunosuppressant use

	IS(+) (n=17)	IS(-) (n=42)	P value
Age (years old)[#]	63.7 ± 13.4	67.6 ± 9.5	0.44
Sex (male:female)[†‡]	11:6	31:11	0.53
Definite/probable/possible (n (%))[‡§]	13 (76.5)/1 (5.9)/3 (17.7)	18 (42.9)/5 (11.9)/19 (45.2)	0.06
FDG-PET findings			
The number of organ involvement[#]	3.0 ± 1.9	3.0 ± 1.4	0.98
SUV max[#]	9.0 ± 6.2	7.8 ± 3.4	1.00
Laboratory findings			
IgG4 (mg/dL)[#]	685.4 ± 810.8	664.4 ± 817.4	0.93
IgG (mg/dL)[#]	2487.5 ± 1504.4	2528.6 ± 1204.9	0.49
C3 (mg/dL)[#]	94.8 ± 47.6	88.9 ± 32.9	0.82
C4 (mg/dL)[#]	19.0 ± 12.6	18.2 ± 10.4	0.85
CH50 (mg/dL)[#]	39.7 ± 16.0	39.2 ± 14.4	0.86
CRP (mg/dL)[#]	1.6 ± 3.9	1.1 ± 2.0	0.41
sIL-2R (IU/dL)[#]	1172.5 ± 901.0	1231.9 ± 1038.2	0.83
Treatment			
Initial GC dose per body weight (mg/kg)[#]	0.54 ± 0.1	0.54 ± 0.1	0.41

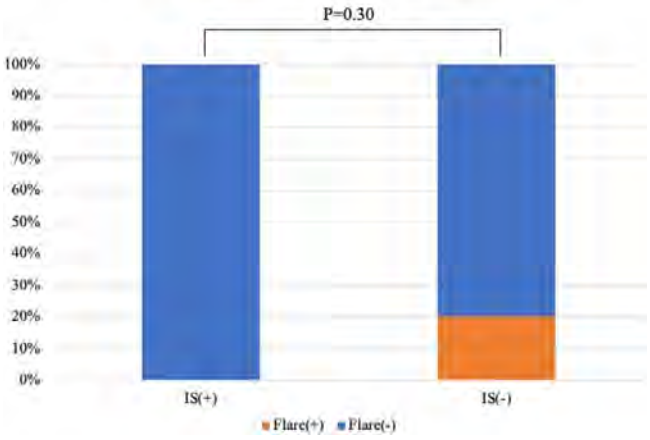
Values are presented as mean ± standard deviation or number (%). [#]Wilcoxon rank sum test; [‡]Fisher's exact test. IS; immunosuppressant.

Table 2. Patients' characteristics at diagnosis with or without flare during two years

	Flare(+) (n=6)	Flare(-) (n=33)	P value
Age (years old)[a]	67.8 ± 10.1	64.7 ± 12.1	0.66
Sex (male:female)[a]	6:0	22:11	0.16
Definite/probable/possible (n (%))[a]	2 (33.3)/2 (33.3)/2 (33.3)	18 (54.6)/3 (9.1)/12 (36.4)	0.25
FDG-PET findings			
The number of organ involvement[a]	3.7 ± 1.5	3.0 ± 1.6	0.29
SUV max[a]	6.4 ± 3.1	7.9 ± 3.4	0.17
Laboratory findings			
IgG4 (mg/dL)[a]	797.8 ± 556.2	567.7 ± 628.9	0.13
IgG (mg/dL)[a]	2986.2 ± 1239.2	2570.2 ± 1357.2	0.40
C3 (mg/dL)[a]	93.0 ± 19.6	90.5 ± 40.0	0.95
C4 (mg/dL)[a]	19.2 ± 7.8	18.2 ± 11.4	0.85
CH50 (mg/dL)[a]	40.9 ± 6.3	38.5 ± 16.0	0.88
CRP (mg/dL)[a]	2.3 ± 3.4	1.4 ± 3.2	0.31
sIL-2R (IU/dL)[a]	1387.0 ± 556.2	1232.9 ± 1140.7	0.22
Treatment			
Initial GC dose per body weight (mg/kg)[a]	0.54 ± 0.1	0.54 ± 0.1	0.95
Immunosuppressant use (n (%))[a]	0 (0)	9 (27.3)	0.30

Values are presented as mean ± standard deviation or number (%). [a]Wilcoxon rank sum test; [b]Fisher's exact test.

Figure. The rate of flare within 2 years after initial treatment with and without immunosuppressants



±32.0 months. Most of the disease relapsed cases were treated with GC monotherapy, and after relapse, immunosuppressants were administered in addition to increased doses of GC. Additionally, 39 patients who continued treatment for 2 years were analyzed separately according to whether they relapsed or not (Table 2). There were no significant differences in age at diagnosis, gender, number of lesions, immunological findings including serum IgG4 levels, or GC dose at the start of treatment. However, all patients who had received immunosuppressants either at the time of initial treatment or GC dose reduction did not relapse during the 2-year period (Figure). Their GC dose at 2 years after the start of treatment was 4.1 ± 2.1 mg/day. In contrast, the GC dose at relapse in the 6 patients relapsing within 2 years was 7.8 ± 1.4 mg/day.

Conclusion: No relapses were observed in patients treated with immunosuppressants during the first 2 years of treatment. Early concomitant use of immunosuppressants is a useful therapeutic strategy for IgG4-RD, but further studies are needed to determine which patients should be considered for concomitant use.

Disclosure: K. Chujo: None; **H. Shimada**: None; **H. Ozaki**: None; **R. Wakiya**: None; **S. Nakashima**: None; **t. miyagi**: None; **Y. Ushio**: None; **K. Sugihara**: None; **M. Mizusaki**: None; **R. Mino**: None; **R. Kagawa**: None; **H. Yamaguchi**: None; **T. Kameda**: None; **H. Dobashi**: None.

Abstract Number: 0717

Mitochondria-mediated Platelet Activation in Polymyalgia Rheumatica

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Platelets have been suggested to be involved in polymyalgia rheumatica (PMR) pathogenesis with elevated platelet activation observed in early stages of the disease. Upon platelet activation, mitochondria are expelled into the extracellular space. Extracellular mitochondria, due to their prokaryotic origin, are immunogenic and promote inflammation, as well as serve as a source of autoantigens leading to formation of anti-mitochondrial antibodies (AMAs). The purpose of this study was to explore whether patients with PMR have elevated plasma levels of thrombospondin-1 (TSP-1)—an alpha granule protein of human platelets, presence of the extracellular mitochondrial component N-formyl methionine peptide (fMET) in plasma, and autoantibodies directed towards specific mitochondrial antigens. We also sought to explore whether extracellular mitochondria could be mediators of platelet activation in patients with PMR.

Methods: Levels of TSP-1, fMET, and anti-mitofusin 1 IgG (anti-MFN1) were measured by ELISA in the plasma of healthy controls (HC, n=30) and PMR patients before (n=54) and after (n=60) treatment with glucocorticoids. Ultrapure mitochondria isolated from HepG2 cells were opsonized with patient (n=56) or healthy control (n=10) plasma and, upon washing, incubated with platelets isolated from a healthy donor in the presence of the fibrin polymerization inhibitor, GPRP. Mitochondria-mediated platelet activation was assessed by measurement of the platelet cell surface marker P-selectin via flow cytometry.

Results: Plasma levels of anti-MFN1 IgG, fMET, and TSP-1 were elevated in patients with PMR before glucocorticoid therapy compared to HC ($p< 0.001$, Table 1). Levels of anti-MFN1 IgG, fMET, and TSP-1 significantly decreased after treatment with glucocorticoids ($p< 0.001$, $p< 0.001$, and $p=0.016$ respectively, Table 2). Mitochondria opsonized with plasma factors

Table 1. Median concentration of mitochondrial biomarkers and thrombospondin-1 (TSP-1) in patients with active PMR before glucocorticoid therapy compared to healthy controls.

Biomarker	Patients with PMR Median (Q1-Q3)	Healthy Control Median (Q1-Q3)	MW P-value
Before cortisone	N=54	N=30	
Anti-MFN1	0.46 (0.28-0.83)	0.22 (0.15-0.25)	p<0.001
fMET	18.32 (16.59-19.81)	11.31 (7.14-16.26)	p<0.001
TSP-1	26.9 (17.9-33.15)	8.93 (4.8-11.6)	p<0.001

P-values calculated with Mann Whitney (MW) U test. Anti-MFN1: anti-mitofusin 1, fMET: N-formyl methionine peptide

Table 2. Median concentration of mitochondrial biomarkers and thrombospondin-1 (TSP-1) before and after glucocorticoid therapy in patients with PMR.

Biomarker	Before glucocorticoids Median (Q1-Q3)	After glucocorticoids Median (Q1-Q3)	Wilcoxon P-value
	N=54	N=60	
Anti-MFN1	0.46 (0.29-0.83)	0.35 (0.23-0.51)	p<0.001
fMET	18.32 (16.59-19.81)	13.85 (8.76-16.47)	p<0.001
TSP-1	26.9 (17.9-33.15)	23.7 (16.5-29.5)	p=0.016

P-values calculated with Wilcoxon signed rank test. Anti-MFN1: anti-mitofusin 1, fMET: N-formyl methionine peptide

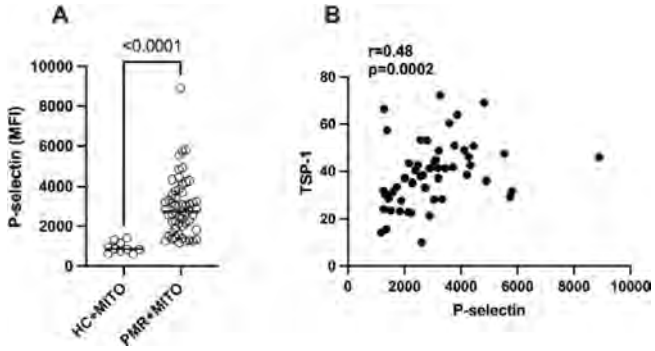

Figure 1. Mitochondrial-induced platelet activation in patients with PMR. A. Platelet rich plasma (PRP) from a healthy individual was exposed to mitochondria (mito) opsonized with plasma of patients with PMR (n=56) or HC (n=10. B. Plasma levels of TSP-1 were related to levels of mitochondrial-induced P-selectin in patients with PMR. Results are shown as the mean fluorescence intensity (MFI). Statistical analyses were done using the Mann-Whitney U-test and Spearman's correlation test. Each circle represents an individual sample, with the bar representing the median of the group.

from PMR patients showed markedly higher platelet activation than mitochondria opsonized with plasma factors from healthy individuals ($p< 0.0001$) (Figure 1A). Further, the extent of platelet activation (P-selectin level) by opsonized mitochondria correlated with plasma levels of TSP-1 in patients with PMR ($r=0.48$, $p=0.0002$, Figure 1B). TSP-1 levels were also associated with levels of immune complexes (IC) before glucocorticoid therapy. ($r=0.32$, $p< 0.05$).

Conclusion: Our results indicate increased platelet activation, the presence of mitochondrial damage-associated molecular patterns (DAMPs), and AMAs in the circulation of patients with PMR, associated with active disease. These results suggest a pathogenic involvement of mitochondrial antigens and autoantibodies in PMR. Blocking mitochondrial-mediated platelet activation may reduce inflammation in patients with PMR, with potential therapeutic implications.

Disclosure: D. Michailidou: Chemocentryx, 1; **L. Johansson**: None; **J. Armando Gonzalez-Chapa**: None; **T. Wang**: None; **J. Chen**: None; **J. López**: None; **S. Rantapää-Dahlqvist**: None; **C. Lood**: Amytryx, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, CityrII, 2, Eli Lilly, 5, Gilead, 5, Horizon Therapeutics, 5, Pfizer, 5, Redd Pharma, 5, 11.

Abstract Number: 0718

Clinical and Economic Burden of Polymyalgia Rheumatica in Patients with an Inadequate Response to Glucocorticoids in a Real-World Setting

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The burden of continuing glucocorticoids (GCs) in patients with polymyalgia rheumatica (PMR) who have an inadequate response (IR)to GCs has not been evaluated.

Methods: An inception cohort of adult patients with a new diagnosis of PMR was created using fee-for-service Medicare claims data from 2016 to 2020. Patients with PMR were included if they were aged≥50 and had 1)≥1 inpatient or ≥2 outpatient claims with ICD-10-CM M35.3 ≥30 days apart, 2) a prescription for GC 7.5–25 mg/day <30 days from the 1stinpatient code or between 1stoutpatient code to 30 days after the 2ndcodewith cumulative use of≥200 mg over ≥120 days, and 3) continuous enrollment ≥1 year prior (baseline) to index date, with no evidence for PMR. The index date was the later of the 2nd outpatient PMR diagnosis, or the inpatient PMR diagnosis; and the date that GC dose/use criteria was met; and had to fall between 10/1/2016 to 12/31/2019. Exclusion criteria included baseline diagnosis of seropositive rheumatoid arthritis, other systemic rheumatic disease (including giant cell arteritis),organ transplant, multiple sclerosis, or active treatment of malignancy or who had any prescription for conventional immunomodulatory therapy or an interleukin-6 receptor inhibition

Table 1: Rates* of selected GC-AEs and all-cause HCRU costs stratified by GC-IR status

	Time since index date				
	Months 6–12	Months 12–18	Months 18–24	Months 24–30	Months 30–36
New event or health condition cohorts and outcomes					
Hospitalized infection (1st event)					
GC-IR	**13.47 (12.10–14.95)**	**9.99 (8.76–11.34)**	8.17 (6.92–9.58)	6.53 (5.25–8.03)	5.84 (4.40–7.60)
Non-GC-IR	**6.05 (4.02–8.74)**	**4.47 (2.14–8.22)**	4.86 (1.95–10.02)	4.21 (1.15–10.78)	5.46 (1.13–15.96)
Hospitalized infection (all)					
GC-IR	**24.50 (22.66–26.45)**	**21.34 (19.55–23.25)**	**20.51 (18.52–22.66)**	**20.39 (18.10–22.88)**	15.83 (13.43–18.54)
Non-GC-IR	**6.26 (4.20–9.00)**	**4.91 (2.45–8.79)**	**4.86 (1.95–10.02)**	**4.21 (1.15–10.78)**	5.46 (1.13–15.96)
New onset diabetes					
GC-IR	5.07 (4.04–6.28)	2.76 (2.00–3.72)	2.88 (2.00–4.00)	3.28 (2.21–4.68)	2.37 (1.33–3.91)
Non-GC-IR	2.38 (1.14–4.38)	2.46 (0.80–5.73)	2.29 (0.47–6.69)	2.30 (0.28–8.30)	1.99 (0.05–11.09)
MACE					
GC-IR	**2.77 (2.08–3.61)**	1.83 (1.26–2.56)	1.85 (1.21–2.71)	2.35 (1.52–3.46)	2.47 (1.46–3.90)
Non-GC-IR	**0.53 (0.06–1.93)**	1.08 (0.13–3.92)	0.86 (0.02–4.81)	0.00 (0.00–4.88)	0.00 (0.00–8.06)
Osteoporosis Dx or Tx					
GC-IR	7.32 (6.04–8.80)	6.17 (4.96–7.58)	5.20 (3.96–6.71)	4.70 (3.36–6.40)	6.27 (4.39–8.68)
Non-GC-IR	8.91 (6.20–12.39)	7.70 (4.31–12.70)	4.68 (1.72–10.18)	0.00 (0.00–4.32)	3.96 (0.48–14.30)
Fracture (1st event)					
GC-IR	4.50 (3.73–5.38)	**4.01 (3.25–4.89)**	**4.55 (3.63–5.62)**	3.94 (2.96–5.12)	2.61 (1.69–3.85)
Non-GC-IR	2.16 (1.04–3.97)	**0.89 (0.11–3.23)**	**0.69 (0.02–3.87)**	2.10 (0.25–7.60)	1.82 (0.05–10.14)
Fracture (all)					
GC-IR	**7.52 (6.51–8.63)**	**7.11 (6.10–8.25)**	**7.93 (6.71–9.31)**	7.27 (5.93–8.81)	7.40 (5.79–9.32)
Non-GC-IR	**2.16 (1.04–3.97)**	**0.89 (0.11–3.23)**	**0.69 (0.02–3.87)**	3.16 (0.65–9.23)	1.82 (0.05–10.14)
Osteonecrosis					
GC-IR	0.19 (0.06–0.44)	0.21 (0.07–0.48)	0.32 (0.12–0.69)	0.14 (0.02–0.51)	0.00 (0.00–0.38)
Non-GC-IR	0.00 (0.00–0.80)	0.00 (0.00–1.65)	0.00 (0.00–2.56)	0.00 (0.00–3.88)	0.00 (0.00–6.71)
Glaucoma					
GC-IR	2.22 (1.69–2.86)	1.15 (0.76–1.66)	1.44 (0.95–2.09)	1.56 (0.98–2.36)	0.41 (0.11–1.06)
Non-GC-IR	1.51 (0.61–3.12)	1.34 (0.28–3.92)	0.69 (0.02–3.87)	0.00 (0.00–3.88)	1.82 (0.05–10.14)
Steroid myopathy					
GC-IR	2.32 (1.77–2.99)	1.86 (1.35–2.49)	1.36 (0.88–2.01)	1.59 (1.00–2.41)	1.37 (0.73–2.34)
Non-GC-IR	1.53 (0.62–3.16)	0.91 (0.11–3.29)	0.00 (0.00–2.61)	0.00 (0.00–3.95)	0.00 (0.00–6.81)
GI perforation, bleed, ulcer					
GC-IR	0.42 (0.21–0.75)	0.59 (0.32–0.98)	0.70 (0.37–1.20)	0.58 (0.25–1.14)	0.31 (0.06–0.92)
Non-GC-IR	0.22 (0.01–1.22)	0.00 (0.00–1.67)	0.00 (0.00–2.58)	0.00 (0.00–3.90)	0.00 (0.00–6.79)
Heart failure					
GC-IR	6.56 (5.52–7.73)	5.41 (4.44–6.52)	4.90 (3.87–6.12)	5.38 (4.14–6.86)	4.75 (3.37–6.49)
Non-GC-IR	3.64 (2.04–6.01)	3.55 (1.43–7.30)	2.37 (0.49–6.93)	3.56 (0.73–10.40)	2.01 (0.05–11.21)
All-cause HCRU cost, $**					
GC-IR Mean (SD) Median (IQR)	13181.11 (29622.82) 2788.72 (754.70–12503.79)	11666.51 (32324.14) 1955.27 (526.74–9453.96)	11288.32 (26538.31) 1835.50 (501.62–9466.90)	11724.20 (29982.46) 1925.97 (471.64–8854.89)	9739.41 (25496.29) 1437.96 (411.41–7125.10)
Non-GC-IR Mean (SD) Median (IQR)	7581.74 (26675.06) 915.66 (269.30–3599.75)	6285.15 (23742.48) 698.06 (184.89–2605.66)	5321.67 (17420.96) 653.44 (144.81–2462.79)	5840.72 (20589.23) 699.37 (162.66–2442.98)	5921.46 (21405.66) 497.46 (136.76–2784.86)
Mean difference (95% CI), $	**5599.40 (3665.20–7533.50)**	**5381.40 (2589.60–8173.10)**	**5966.70 (3158.30–8775.00)**	**5883.50 (1915.20–9851.80)**	**3817.90 (440.00–8075.90)**

*Events/100 patient-years (95% CI).

**Mean costs associated with inpatient hospitalization, outpatient visits, ER visits and prescriptions per person in each 6-month period.

Cells in bold denote statistical significance based on non-overlapping 95% CI, and a p value < 0.05.

CI, confidence interval; Dx, diagnosis; ER, emergency room; GC-AE, glucocorticoid-associated adverse event; GC-IR, glucocorticoid inadequate responder; GI, gastrointestinal; HCRU, healthcare resource utilization; IQR, interquartile range; MACE, major adverse cardiac event; SD, standard deviation; Tx, treatment.

Table 2: Event rates* for AEs and cost by steroid dose quartile among GC-IRs in the 6–12-month interval after the index date

	Overall	Quartile 1	Quartile 2	Quartile 3	Quartile 4
Hospitalized infection (1st event)	13.47 (12.10–14.95)	12.18 (9.42–15.49)	13.18 (10.43–16.42)	11.49 (9.09–14.35)	16.24 (13.56–19.28)
New onset diabetes	5.07 (4.04–6.28)	4.99 (2.85–8.11)	2.94 (1.47–5.26)	4.81 (2.98–7.36)	6.85 (4.80–9.48)
MACE	2.77 (2.08–3.61)	1.78 (0.72–3.67)	3.55 (2.03–5.77)	3.24 (1.85–5.27)	2.44 (1.36–4.02)
Osteoporosis Dx or Tx	7.32 (6.04–8.80)	6.71 (4.16–10.26)	4.98 (2.90–7.97)	8.21 (5.65–11.54)	8.58 (6.21–11.56)
Fracture (1st event)	4.50 (3.73–5.38)	3.12 (1.82–4.99)	4.00 (2.56–5.95)	3.97 (2.62–5.78)	6.23 (4.64–8.19)
Osteonecrosis	0.19 (0.06–0.44)	0.00 (0.00–0.68)	0.33 (0.04–1.20)	0.29 (0.04–1.06)	0.12 (0.00–0.67)
Steroid myopathy	4.28 (3.35–5.39)	2.23 (0.96–4.40)	3.99 (2.28–6.48)	2.73 (1.41–4.76)	7.45 (5.22–10.32)
Glaucoma	2.22 (1.69–2.86)	1.83 (0.88–3.37)	2.31 (1.26–3.87)	2.63 (1.56–4.16)	2.06 (1.20–3.30)
Heart failure	6.56 (5.52–7.73)	4.57 (2.79–7.05)	5.73 (3.84–8.23)	5.91 (4.09–8.26)	9.14 (6.95–11.78)
Total all-cause HCRU cost**, $	13,181.11 (29622.82)	12902.25 (30757.37)	12677.44 (35306.56)	11271.88 (23684.90)	15600.14 (27896.09)

*Events/100 patient-years (95% CI).
**Sum of cost associated with inpatient hospitalization, outpatient visits, ER visits and prescriptions; data shown as mean (SD).
AE, adverse event; CI, confidence interval; Dx, diagnosis; ER, emergency room; GC-IR, glucocorticoid inadequate responder; HCRU, healthcare resource utilization; MACE, major adverse cardiac event; SD, standard deviation; Tx, treatment.

at baseline. Patients were classified as GC inadequate responders (GC–IRs), defined as use of ≥7.5 mg/day at 6 months (i.e., presumed flare), continued use of GCs >12 months, or relapse (re-initiation of GC after >60-day gap discontinuation) or non-GC–IR.

All-cause healthcare resource utilization cost and event rate of pre-specified, GC-associated adverse events (GC-AEs) that were defined by ICD-10-CM diagnosis codes, medication use, and/or Healthcare Common Procedure Coding System medical procedures beginning 6 months after the index date and updated in 6-month intervals were reported. Adverse events (AEs) were identified using claims-based algorithms that have been previously used or reported in the literature. For GC-AEs, with the exception of hospitalized infections and fractures, only the 1stevent was counted. Event rates and 95% confidence intervals were estimated using Exact Poisson methods. A subgroup analysis of the GC–IR cohort was performed, estimating outcomes by cumulative steroid dose quartiles received; dose quartiles were updated at 6 months.

Results: A total of 6,054 patients with PMR met eligibility criteria:mean age 77.0 years, 65.4% women, 96.1% White, and 3.0% Hispanic. The rate of GC-AEs and medical cost were consistently higher in the GC–IR versus non-GC–IR through 18 months, except for osteoporosis (Table 1). In the GC–IR cohort, cost and most GC-AEs suggested a decrease over time, likely due to GC discontinuation or lower doses of GC, and/or for AE-related censoring (i.e., depletion of at-risk patients). Further, most outcomes showed a dose-response relationship between cumulative GC dose and outcomes (Table 2).

Conclusion: There is a substantial clinical and economic burden of continuing GCs in PMR patients with IR. Some GC-AEs and associated costs may be enduring. These data provide insight into the potential benefit of minimizing long-term GCuse and need for more effective GC-sparing therapies.

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Abstract Number: 0719

Polymyalgia Rheumatica Following SarsCOV-2 Vaccination: A Single Center Cohort Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Polymyalgia rheumatica (PMR) incidence peaks in individuals between 70 and 80 years of age; this same group is also at increased risk of complications and mortality related to COVID-19 infection. Vaccination against SARS-CoV2 is an essential tool in combatting COVID-19. There have been several case reports of PMR following vaccination with mRNA SARS-CoV2 vaccines.

The aim of this study was to identify patients with temporal association between mRNA SARS-CoV2 vaccination and PMR onset and to compare characteristics and disease course to those with new onset PMR without temporal association with SARS CoV2 vaccine exposure.

TABLE 1

	Entire Cohort	PMR without temporal association to vaccine	PMR within 6 weeks of vaccine	p-value
N	80	60	20	
Age , median (IQR)	74.5 (71, 80)	75.5 (71, 80)	73.5 (69, 79.5)	0.43
Sex				0.80
Male	40 (50%)	29 (48%)	11 (55%)	
Female	40 (50%)	31 (52%)	9 (45%)	
Vaccine Type				1.00
Moderna	38 (48%)	29 (48%)	9 (45%)	
Pfizer	42 (53%)	31 (52%)	11 (55%)	
Baseline ESR (mm/hr), median (IQR)	44 (24, 65)	42 (24, 63)	44.5 (23, 65)	0.89
CRP at baseline (mg/L), median (IQR)	20 (7.55, 48.5)	20 (9, 42)	14.2 (7, 60.2)	0.77
Initial steroid dose, median (IQR)	20 (15, 30)	20 (15, 24)	20 (15, 37.5)	0.96
Additional vaccine received?				0.55
No	22 (28%)	15 (25%)	7 (35%)	
Yes	43 (54%)	33 (55%)	10 (50%)	
missing	15 (19%)	12 (20%)	3 (15%)	
ESR at 6 months (mm/hr), median (IQR)	16 (5, 24)	16 (5, 30)	9.5 (4, 21.5)	0.27
Steroid dose at 6 months (mg), median (IQR)	5 (4, 8)	5 (4, 9.5)	6 (2, 8)	0.74
Relapse at 6 months				0.74
No	51 (64%)	36 (60%)	15 (75%)	
Yes	15 (19%)	12 (20%)	3 (15%)	
missing	14 (18%)	12 (20%)	2 (10%)	
ESR at 12 months (mm/hr), median (IQR)	14 (4, 29)	14 (4, 34)	13.5 (3, 24)	0.81
CRP at 12 months (mg/L), median (IQR)	7 (4, 7.5)	7 (5, 9)	7 (3, 7)	0.51
Steroid dose at 12 months (mg), median (IQR)	3 (0, 6)	3 (1.25, 6)	0 (0, 4)	0.11
Relapse at 12 months				0.65
No	27 (34%)	22 (37%)	5 (25%)	
Yes	8 (10%)	6 (10%)	2 (10%)	

Methods: We conducted a retrospective chart review of all newly diagnosed PMR patients in a single center. Using ICD-10 codes, our EMR was queried to identify patients with newly diagnosed PMR beginning in December 2020, when the first SARS-CoV-2 vaccines were available in the US. Charts were reviewed for demographic information, disease characteristics and vaccination details. Patients who developed onset of PMR symptoms within 6 weeks after vaccination were compared to those whose PMR symptoms occurred without temporal association to vaccination. When available data at 6 and 12 months following diagnosis was collected.

Results: Eighty patients with newly diagnosed PMR between 12/1/2020 and 12/31/2021 were identified. There were 60 patients with new PMR without a temporal association to vaccination who were compared to 20 patients who developed PMR symptoms within 6 weeks of vaccination. Baseline demographics did not differ between the two groups. In the 20 cases with PMR onset after vaccination, symptoms developed a mean 38 days (IQR 19.5-48) after first dose of vaccine and 11.5 days (IQR 1-22) after second dose. There were no differences in baseline demographics, glucocorticoid dosages or relapse rates at 6 and 12 months following diagnosis. There was no association between vaccine manufacturer and PMR onset after vaccination (TABLE 1)

Conclusion: In this cohort, patients with onset of PMR within 6 weeks following mRNA vaccination against SARSCoV2 were similar to patients with de novo PMR at diagnosis, with no significant differences in disease course over the first 12 months. This does not support the notion that PMR following vaccination is a unique disease entity. The recognition of new PMR onset following SARS CoV2 vaccine may be coincidental in this common inflammatory disorder in a population with high rates of vaccine exposure.

Disclosure: L. Lally: Amgen, 2, 6; **A. Bloostein**: None; **D. Jannat-Khan**: None; **R. Spiera**: AbbVie/Abbott, 2, 5, Amgen, 2, AstraZeneca, 5, chemocentryx, 5, corbus, 5, Formation Biologics, 5, GSK, 2, 5, Inflarx, 5, Kadmon, 5, Novartis, 2, 5, Principia, 5, Sanofi, 2.

Abstract Number: 0720

Cognitive Function and Its Associated Factors in Polymyalgia Rheumatica

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Over the past decade our understanding of the prevalence, and indeed impact of cognitive impairment in rheumatic diseases has increased. Intact cognitive function is imperative not only for quality of life and maintenance of one's functional capacity, but also for the successful therapeutic management of disease, namely the adherence to treatment regimens. The prevalence of cognitive impairment in community dwelling older adults has been estimated at 13%.[1]To date the prevalence of cognitive impairment in Polymyalgia Rheumatica (PMR) has not been studied. The aim of this research is therefore to explore the prevalence and potential associated factors of cognitive impairment in those with PMR.

Methods: Patients with a diagnosis of PMR (fulfilling the 2012 EULAR/ACR Classification Criteria) who were in clinical remission and on active treatment with glucocorticoids were recruited from two centres. Patients were ≥3 months and ≤12 months from diagnosis. Cognitive function was evaluated using the Montreal Cognitive Assessment (MoCA) test which

was conducted by two trained interviewers. Cognitive impairment was defined by the previously validated MoCA cut-off score of < 26.Demographics, clinical and laboratory data, in addition to patient reported outcomes (PRO's) were collected. PRO's including anxiety, using the Generalised Anxiety Disorder Assessment (GAD-7), mood using the Patient Health Questionnaire (PHQ-9), fatigue using the Functional Assessment of Chronic Illness Therapy - Fatigue Scale (FACIT-F), pain using the visual analogue scale (VAS) and overall health related quality of life using the Health Assessment Questionnaire-Disability Index (HAQ-DI).The associations between categorical variables were compared using the chi-squared or Fishers exact test as appropriate. The association between continuous variables and categorical variables were assessed using the Kruskal-Wallis test. Correlations were calculated using Pearson's r. All analyses were conducted using R (R Core Team, 2022). A p-value of < 0.05 was considered as statistically significant.

Results: 51 consecutive patients with PMR were recruited, of which 56.9% (n=29) were female. 70.6% (n=36) of patients were cognitively impaired, with visual-spatial, delayed recall and abstraction the most commonly affected cognitive domains. Interestingly, those with cognitive impairment had a younger age, versus those without (p=0.514). Although not statistically significant, median BMI, anxiety, depression and pain scores were all higher in those who were cognitively impaired. Moreover, median fatigue scores were also worse in the cognitively impaired group. No statistically significant difference in serum markers was observed.

Characteristic	Impaired cognitive function (n=33)	Normal Cognitive function (n=14)	p-value
Sex, female, n(%)	23 (63.9)	6 (40)	0.135
Age, median (IQR)	70 (65-74)	72 (68-74.5)	0.514
Body Mass Index, median (IQR)	27.2 (24.5- 31.9)	25.4 (23.5-29)	0.169
Rheumatic disease comorbidity index (RDCI), median (IQR)	2.0 (0.8-3)	2.0 (1.0-2.5)	0.916
GAD-7 score, median (IQR)	1.5 (0-4.2)	0 (0-1.5)	0.209
PHQ-9 score, median (IQR)	2.5 (0-7.2)	2 (0-3)	0.168
HAQ-DI score, median (IQR)	0 (0-0)	0 (0-0.1)	0.282
VAS pain score, median (IQR)	2 (0-4)	0 (0-1)	0.082
FACIT-F score, median (IQR)	44.5 (38-50)	47 (42.5-49.5)	0.443
C-reactive protein (mg/L), median (IQR)	3.8 (1.2-6.1)	3.4 (1.1-5.5)	0.835
Erythrocyte sedimentation rate (mm/hr), median (IQR)	10 (4-25)	8 (5.5-21)	0.915
Serum interleukin-6 levels (pg/ml) median (IQR)	6.8 (3.1-10.1)	6.7 (4.6-13.2)	0.539
Haptoglobin level (g/L), median (IQR)	1.7 (1.3-2.6)	1.7 (1-2.1)	0.414
Hemoglobin (g/dL), median (IQR)	13.2 (12.6-13.7)	13.7 (13.4-14.1)	0.234

Baseline Characteristics stratified by cognition status.

Conclusion: This study demonstrates the burden of cognitive impairment in PMR is significant and is markedly higher than that observed usually at population level. This has a potential profound impact on disease management, including treatment compliance, and thus disease outcomes. Future studies exploring this, in addition to specific etiologic contributors of cognitive impairment are needed.

Disclosure: P. Harkins: Janssen, 5; **S. Cowley**: None; **D. Kane**: None; **R. Conway**: AbbVie/Abbott, 5, 6, Celltrion, 5, Fresenius Kabi, 6, Galapagos, 6, Janssen, 5, 6, Nordic Pharma, 5, Novartis, 5, UCB, 6, Viatris, 6.

Abstract Number: 0721

Characterization of Numeric Rating Scales for Symptom Assessment in Polymyalgia Rheumatica

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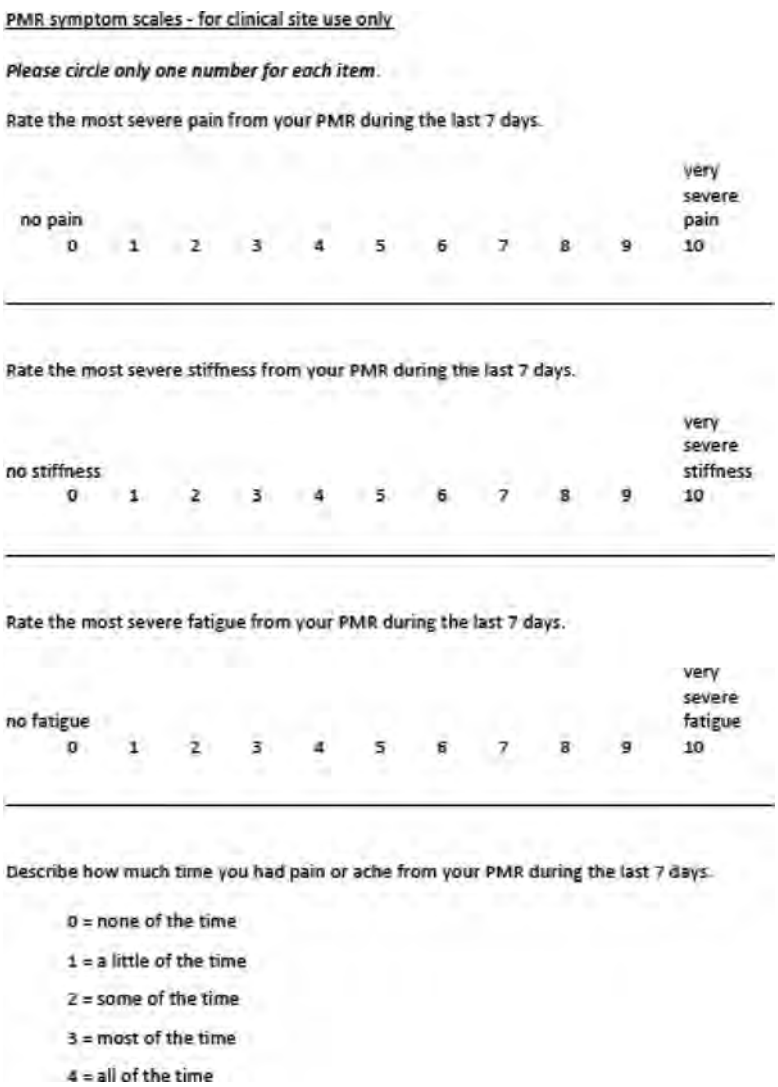
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Pain, stiffness, and fatigue have been defined as core assessment domains in polymyalgia rheumatica (PMR) by the OMERACT PMR Working Group (PMRWG). Patient partners have expressed a preference for numeric rating scales (NRS) over visual analogue scales to measure these symptoms. Numerous NRS forms have been used in different PMR clinical trials, yet evidence to support their use is lacking. We propose a standardized NRS form and provide initial results of some measurement properties.

Methods: PMRWG clinicians, methodologists, and patient partners rated two different NRS stems and anchors and provided free-text feedback. The preferred set was modified according to patient partner input. Clinical trial participants with PMR, no or low disease activity, and who received prednisolone 10 mg for ≥ 1 week prior to entry were treated with prednisolone 10 mg for 4 weeks and received each of SPI-62 and matching placebo as adjunctive therapy for 2 weeks. They completed individual NRS for pain, stiffness, and fatigue intensity, and pain chronicity, each at fortnightly trial visits with a 7-day look-back and daily at home with a 1-day look-back. Compliance at home, test-retest reliability, and correlation between the on-site and at-home versions were assessed using placebo period data from the inception trial cohort (N=12).

Results: The standardized items are shown (Figure). At-home compliance was 97%; 7/12 had 100% compliance. There were no missing items, only occasional days that participants did not respond at all. Weighted k comparing responses 2 weeks apart for on-site pain, stiffness, and fatigue intensity were 0.52, 0.45, and 0.67, and for pain chronicity was 0.54. Intraclass correlation coefficients, with intra-individual as the variance of interest, for at-home pain, stiffness, and fatigue intensity were 0.62, 0.70, and 0.84, and for pain chronicity was 0.72. Weighted k between the on-site response for 7-day look-back and the maximum at-home response for 1-day look back during any of the 7 prior days were 0.53, 0.82, and 0.80 for the intensity items and 0.55 for pain chronicity. When the on-site response was compared instead to the at-home response on the same day, weighted k were 0.51, 0.68, 0.76, and 0.64. Confidence intervals for all statistics were wide due to the limited number of participants.



PMR symptom scales - for clinical site use only

Please circle only one number for each item.

Rate the most severe pain from your PMR during the last 7 days.

no pain 0 1 2 3 4 5 6 7 8 9 very severe pain 10

Rate the most severe stiffness from your PMR during the last 7 days.

no stiffness 0 1 2 3 4 5 6 7 8 9 very severe stiffness 10

Rate the most severe fatigue from your PMR during the last 7 days.

no fatigue 0 1 2 3 4 5 6 7 8 9 very severe fatigue 10

Describe how much time you had pain or ache from your PMR during the last 7 days.

0 = none of the time

1 = a little of the time

2 = some of the time

3 = most of the time

4 = all of the time

Standardized clinical site items. Patient diary items replace '7 days' with '24 hours'.

Conclusion: The results provide necessary initial evidence to encourage further examination of these NRS' psychometrics. They suggest high patient compliance for daily symptom report and moderate test-retest reliability. Patient ability to recall accurately their most severe symptoms during 7 days prior to a trial visit was strong for stiffness and fatigue, whilst moderate for pain. Symptom recall did not appear to be particularly biased by symptoms of the most recent 24 hours. The reported measurement properties point favorably toward validated symptom assessment for PMR clinical trials, lack of which currently limits conduct of patient-centric research. More data are needed to confirm these results on reliability, and to support other measurement properties such as thresholds of meaning.

Disclosure: T. Marmon: Sparrow Pharmaceuticals, 2; **J. Cole**: Sparrow Pharmaceuticals, 2; **C. Owen**: AbbVie/Abbott, 1, 6, Janssen, 6, Novartis, 6; **S. Mackie**: AbbVie/Abbott, 2, AstraZeneca, 2, GlaxoSmithKlein(GSK), 3, 12, Investigator, National Institute for Health and Care Research, 5, 12, investigator on STERLING-PMR trial, funded by NIHR; patron of the charity PMRGCAuk, Pfizer, 2, 6, Roche, 2, 6, 12, Support from Roche/Chugai to attend EULAR2019 in person, Sanofi, 2, 12, Investigator, Sparrow, 12, Investigator, UCB and Novartis, 6, Vifor, 6; **D. Katz**: Sparrow Pharmaceuticals, 3, 4, 8.

Abstract Number: 0722

Acute Cardiovascular Events in Autoimmune Rheumatic Disease Pregnancies

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Plenary I
Session Type: Plenary Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Cardiovascular diseases (CVDs) complicate 1-4% of pregnancies. Autoimmune rheumatic diseases (ARDs) are associated with a 1.5 to 3-fold higher CVD risk. Similarly, antiphospholipid syndrome (APS) is associated with increased risks of thromboembolism, pregnancy loss, and CVDs. However, research on the impact of ARDs and APS on maternal cardiovascular health is limited. In this study, we aim to compare the rates of acute CVEs in pregnant women with ARDs and primary APS as compared to a general population of pregnant women with neither condition, using a large population-based birth cohort in California.

Methods: We retrospectively analyzed pregnant individuals who delivered singleton liveborn infants in California between 2005-2020. Birth certificates were linked by the California Study of Outcomes in Mothers and Infants (SOMI) to maternal hospital discharge, emergency department and ambulatory surgery records. We identified ARDs, APS, and acute CVEs during pregnancy and up to 6 weeks postpartum using ICD codes. We used logistic regression to calculate adjusted relative risks (RRs) and 95% confidence intervals (CI) of association between acute CVEs and ARDs and APS, for each specific category of ARDs, and for CVEs by timing in relation to delivery. We performed mediation analysis to investigate if pregnancy complications such as gestational diabetes mellitus (GDM) and pre-eclampsia mediated the association between ARDs and CVEs.

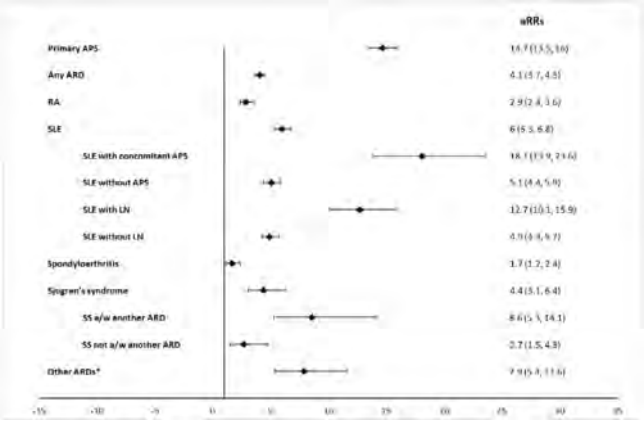

Figure 1. Comparison of risks of acute cardiovascular events during pregnancy or within 6 weeks post-partum for autoimmune rheumatic diseases (ARDs) and primary antiphospholipid syndrome (APS) as compared to the comparison group with neither condition, 2005 – 2020 #Adjusted relative risks (aRRs) adjusted for baseline covariates that occurred before pregnancy (maternal age at delivery, race/ethnicity, payer for delivery, maternal education, maternal pre-pregnancy body mass index, preexisting hypertension, preexisting diabetes, hyperlipidemia, smoking, alcohol use, drug use, and depression). * APS: antiphospholipid syndrome, ARD: autoimmune rheumatic disease, RA: rheumatoid arthritis, SLE: systemic lupus erythematosus, LN: lupus nephritis, SS: Sjogren's syndrome, * Other ARDs (Systemic sclerosis, myositis, vasculitis)

Table 2. Rates of acute cardiovascular events by timing in relation to delivery for autoimmune rheumatic diseases (ARDs) and primary antiphospholipid syndrome (APS) as compared to the comparison group with neither condition, 2005 – 2020 *ARD: autoimmune rheumatic disease, APS: antiphospholipid syndrome, CVE: cardiovascular event, ED: emergency department

	No ARD or APS	Any ARD	Primary APS
	n (%)	n (%)	n (%)
	RR (95% CI)	RR (95% CI)	RR (95% CI)
	aRR (95% CI)	aRR (95% CI)	aRR (95% CI)
Sample	7,004,334	19,340	7,758
Any CV event	21,385 (0.4)	388 (2.0)	538 (6.9)
Antepartum			
Any antepartum CVE	9,948 (0.1)	143 (0.8)	294 (3.8)
	Ref	5.3 (4.5, 6.2)	26.7 (23.8, 30.0)
	Ref	**3.6 (3.1, 4.3)**	**19.9 (17.7, 22.4)**
Birth admission			
Any birth admission CVE	8,609 (0.1)	157 (0.8)	229 (3.0)
	Ref	6.6 (5.6, 7.7)	24.1 (21.1, 27.8)
	Ref	**4.5 (3.9, 5.4)**	**18.1 (15.9, 20.7)**
Postpartum			
Any postpartum CVE	6,536 (0.1)	118 (0.6)	131 (1.9)
	Ref	6.6 (5.5, 7.9)	19.6 (16.0, 22.6)
	Ref	**4.5 (3.8, 5.5)**	**12.7 (10.7, 15.1)**
Postpartum CVE on ED records	3,567 (0.1)	38 (0.2)	40 (0.5)
	Ref	4.3 (3.1, 5.8)	13.4 (8.4, 15.6)
	Ref	**3.1 (2.2, 4.2)**	**7.9 (5.8, 10.8)**
Postpartum CVE on readmission record	3,484 (0.1)	85 (0.4)	105 (1.4)
	Ref	8.9 (7.2, 11.1)	28.7 (23.7, 34.9)
	Ref	**5.8 (4.6, 7.2)**	**18.6 (15.3, 22.6)**

Results: CVEs occurred in 2.0% of 19,340 pregnant women with ARDs, 6.9% of 7,758 women with primary APS, and 0.4% of 7,004,334 women with neither. The risks of acute CVEs were significantly higher for pregnant women with ARDs (aRR 4.1, 95% CI 3.7, 4.5) and primary APS (aRR 14.7, 95% CI 13.5,16.0) than for the comparison group. Systemic lupus erythematosus (SLE) was associated with a 6-fold increased risk for CVE, which was further elevated with concomitant APS or nephritis (aRRs 18.1 and 12.7, respectively). (**Figure 1**). Only 12% of the excess association of acute CVEs with an ARD was mediated by preeclampsia and < 1% by GDM. About 25-30% of the CVEs occurred postpartum as documented in readmission records. This represented a 6-fold greater risk than in the comparison group (**Table 2).**

Conclusion: Pregnant women with ARDs and primary APS have significantly higher risks for acute CVEs compared to pregnant women without these conditions, with the highest risks among those with SLE with concomitant APS, followed by primary APS and SLE with nephritis. Furthermore, about 25-30% of CVEs occurred during the postpartum period, highlighting the importance of close monitoring of cardiovascular risks and events in women with ARDs or APS both during pregnancy and postpartum.

Disclosure: R. Dhital: None; **R. Baer**: None; **M. Guma**: None; **K. Kalunian**: AbbVie/Abbott, 2, Amgen, 5, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EquilliumBio, 2, Genentech, 2, Gilead, 2, Janssen, 2, KezarBio, 1, Merck/MSD, 2, Novartis, 2, Pfizer, 2, Remegene, 2, Roche, 2, UCB, 5; **A. RA SLE Network**: None; **C. Chambers**: Amgen, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Genzyme Sanofi-Aventis, 5, Gerber Foundation, 5, Gilead, 5, GlaxoSmithKline, 5, Hoffman La-Roche-Genentech, 5, Janssen Pharmaceuticals, 5, Leo Pharma, 5, Novartis, 5, Pfizer, Inc., 5, Regeneron, 5, Sanofi, 5, Sun Pharma Global FZE, 5, Takeda Pharmaceutical Company Limited, 5, UCB Pharma, USA, 5.

Abstract Number: 0723

Investigating the Effects and Molecular Mechanisms of TRAF5 on the Pathogenesis of SLE Associated Pulmonary Arterial Hypertension

Xiaoyue Deng[1], Junyan Qian[1], Ranran Wang[2], JIULIANG ZHAO[3], Qian Wang[4], Tianyi Yuan[2], MENGTAO LI[1] and Xiaofeng Zeng[5], [1]Peking Union Medical College Hospital, Beijing, China, [2]Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China, [3]Beijing Union Medical College Hospital, Beijing, China, [4]Peking Union Medical College, Beijing, China, [5]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Plenary I
Session Type: Plenary Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Pulmonary arterial hypertension (PAH) is a serious complication in SLE patients, with rapid progression and poor prognosis. In China, approximately 3% of the over one million SLE patients suffer from PAH. PAH is believed to result from inflammation and genetic abnormalities leading to dysfunction of pulmonary arterial endothelial cells (PAEC), followed by cellular proliferation and progressive pulmonary vascular remodeling. Considering the high morbidity and mortality rates, our research aims to investigate the pathogenesis of SLE-PAH and identify new biomarkers.

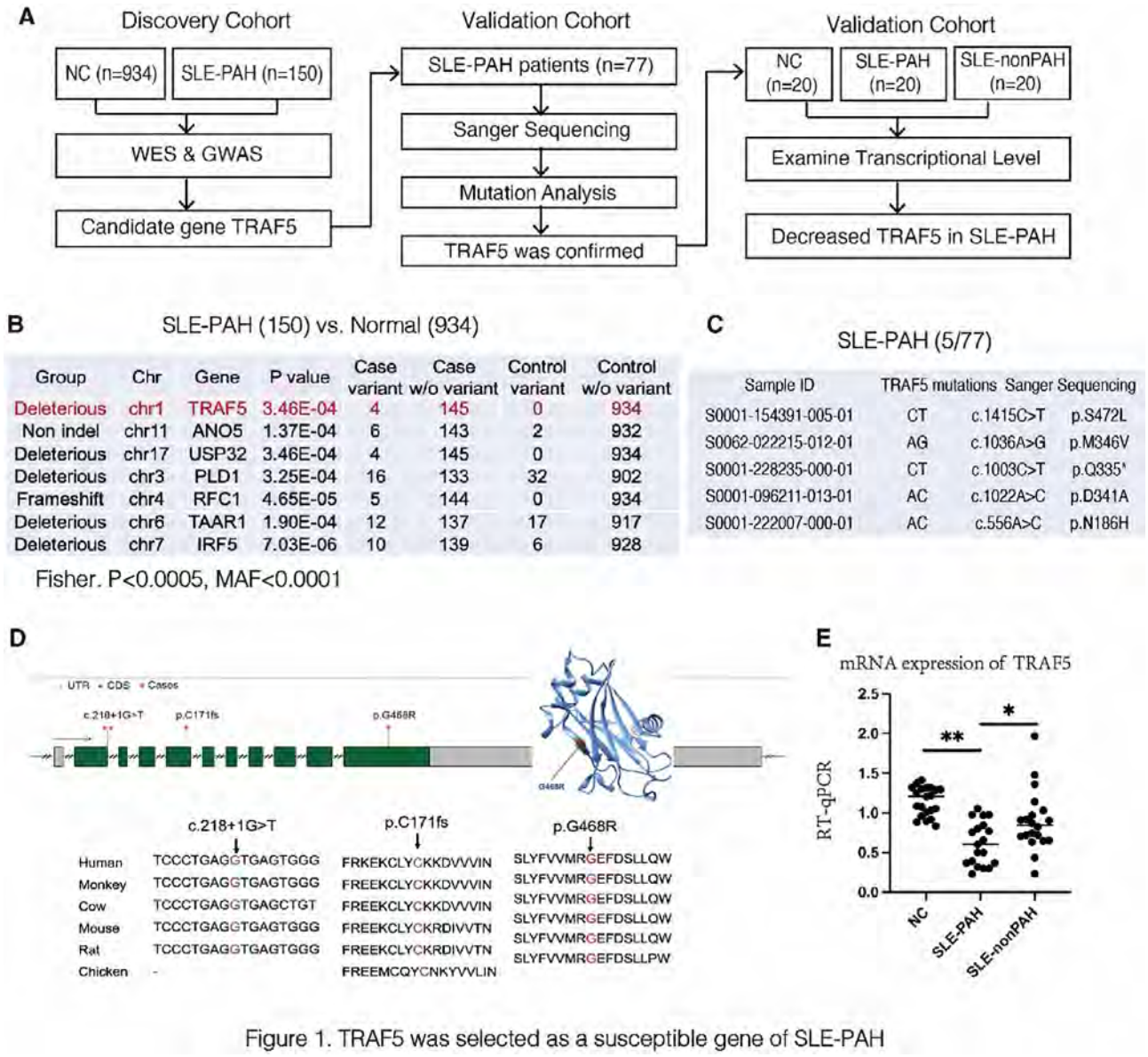

Figure 1. TRAF5 was selected as a susceptible gene of SLE-PAH

Figure1 Identification of TRAF5 as a Susceptible Gene in SLE-PAH. A) Workflow of selecting susceptible genes of SLE-PAH; B) and C) Results of GWAS and Sanger sequencing; D) Genomic and protein structure of TRAF5. p.G468R mutation causes dysfunction of protein. E) TRAF5 mRNA expression levels in peripheral blood .

Methods: To investigate the pathogenesis of SLE-PAH, we employed various approaches. First, we performed whole-exome sequencing (WES) on peripheral blood samples from 150 SLE-PAH patients and conducted a genome-wide association study (GWAS) by comparing them with samples from 934 healthy controls. Subsequently, we validated mutations of candidate gene in 77 patients using Sanger sequencing. Additionally, we assessed the transcriptional expression levels of the identified genes in peripheral blood using RT-qPCR. In vitro intervention experiments were performed on human PAEC to elucidate the potential pathogenesis. RNA-seq and gene ontology analysis were employed to identify downstream pathways. Furthermore, we established SLE-PAH mouse models through pristane injection and hypoxia induction and measured pulmonary arterial pressure (PAP) using right heart catheterization. We also examined the effects of tail-intravenous injection of therapeutic vectors based on candidate gene. Lastly, we examined expression of candidate genes on monocrotaline (MCT) induced rat model of PAH.

Results: 1. Based on WES and GWAS, we identified the tumor necrosis factor receptor-associated factor 5 (TRAF5) as a susceptible gene in SLE-PAH. Transcriptional analysis revealed a significant reduction in TRAF5 expression in the peripheral blood of SLE-PAH patients, indicating its potential clinical diagnostic value. 2. Knockdown of TRAF5 in PAEC demonstrated notable effects on early apoptosis and the pathogenesis of PAH through distinct pathways. Flow cytometry analysis showed

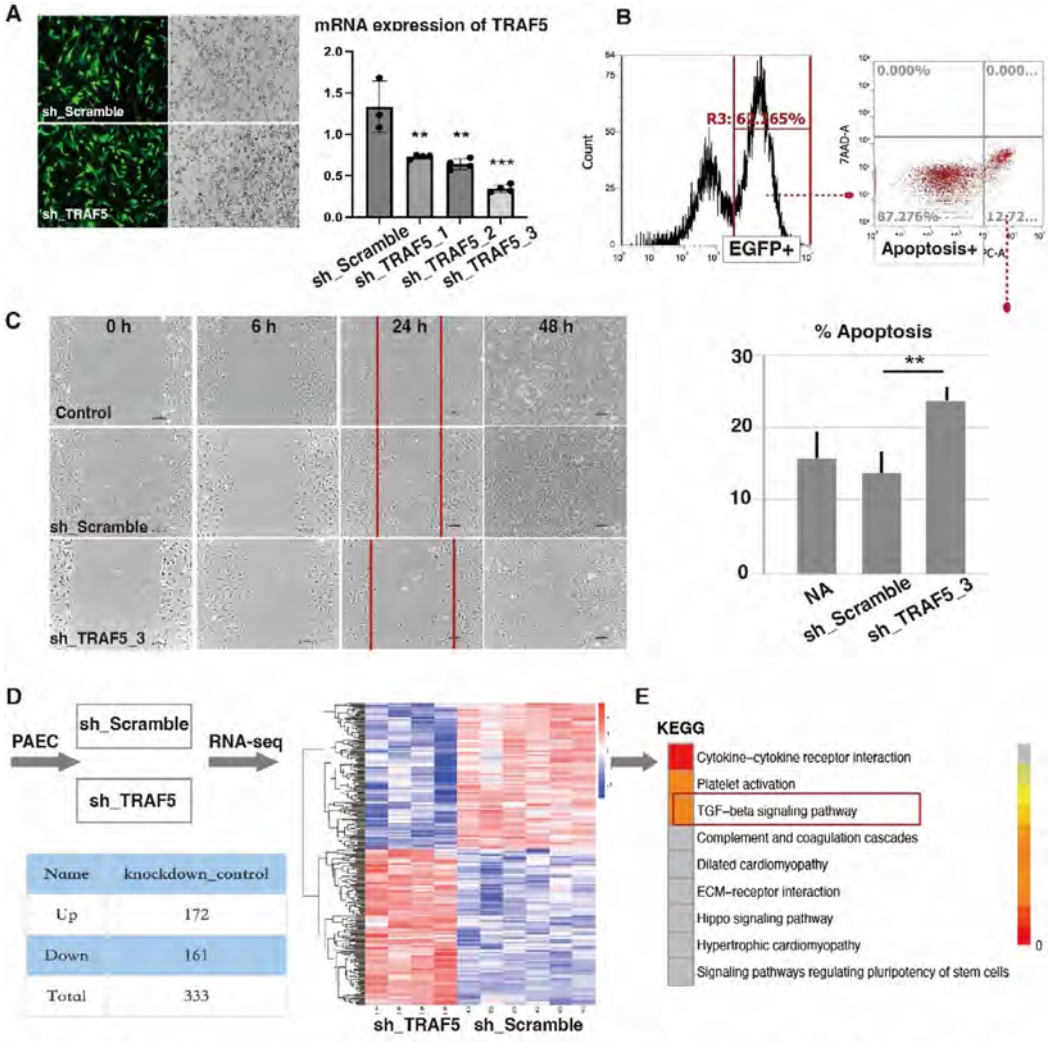

Figure 2. Knockdown of TRAF5 significantly increased early apoptosis of PAEC through distinct pathway.

Figure2 Knockdown of TRAF5 Affected the Functions of PAEC. A) shTRAF5 transfected human PAEC (EGFP positive); B) FACS was performed to detect early apoptotic cells labeled with Annexin V-APC (Apoptosis Detection Kit); C) Wound healing experiments were performed in different groups; D) and E) TGF-β pathway was identified as downstream targets of TRAF5 using RNA-seq and KEGG analysis.

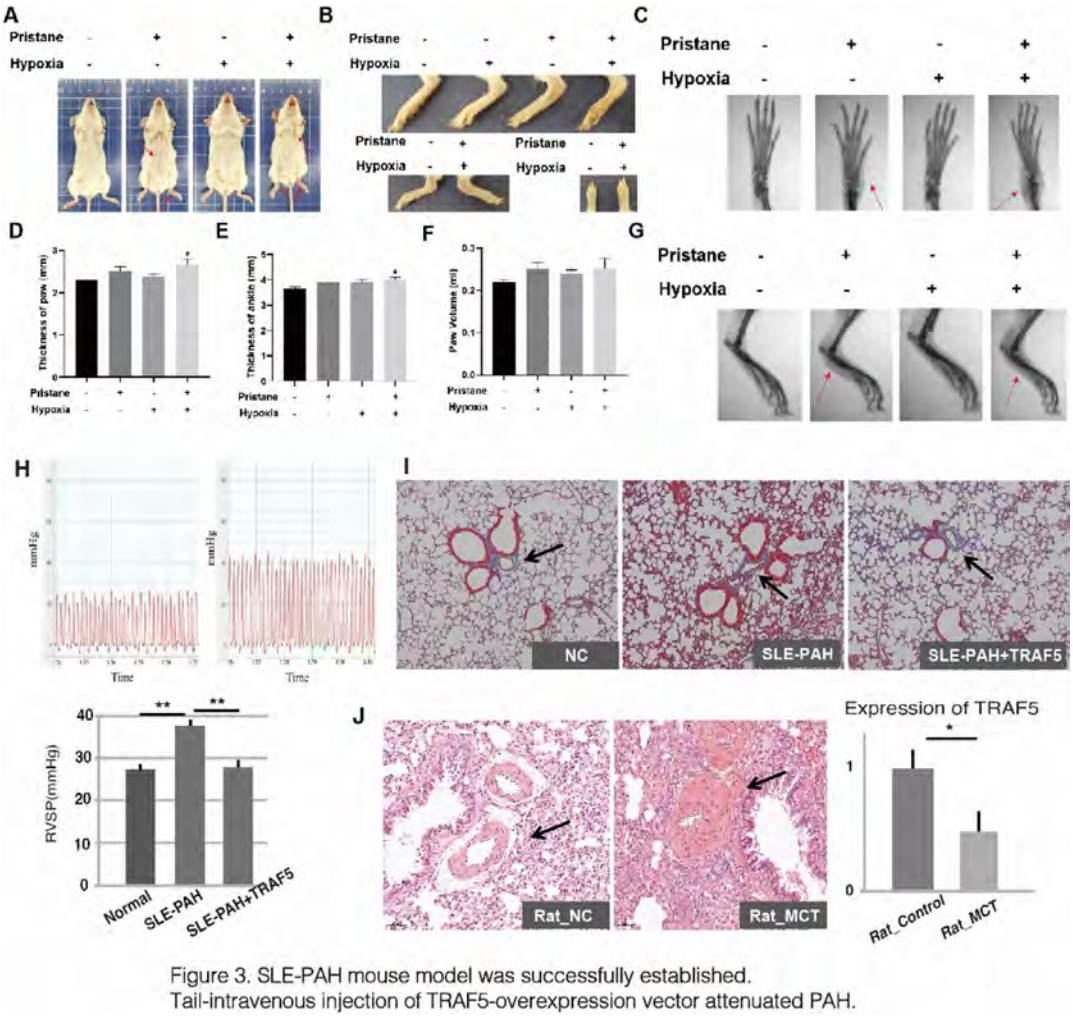

Figure 3. SLE-PAH mouse model was successfully established.
Tail-intravenous injection of TRAF5-overexpression vector attenuated PAH.

Figure 3 SLE-PAH Mouse Model was Successfully Established. A-G) SLE phenotypes were observed after pristane induction; H-I) mPAP was elevated in model mouse, and tail-intravenous infection of TRAF5-overexpression vector attenuated PAH; J) Expression of TRAF5 was decreased significantly in MCT induced rats.

a significant increase in early apoptotic cells, and wound healing experiments demonstrated the loss of migratory ability in PAEC following TRAF5 knockdown. RNA-seq and KEGG pathway analysis identified TRAF5's regulatory role in the TGF-beta pathway. 3. Our SLE-PAH mouse model successfully exhibited lupus phenotypes and increased mean PAP levels. Tail-intravenous injection of a TRAF5-overexpression vector attenuated PAH symptoms. Additionally, TRAF5 expression was significantly decreased in lung tissue of the MCT-induced PAH model rats.

Conclusion: In conclusion, lack of TRAF5 triggers the pathogenesis of PAH in SLE patients by inducing dysfunction of PAEC, which highlights the significance of TRAF5 as a susceptible gene in SLE-PAH and underscores its potential as a candidate biomarker for the diagnosis and therapy of SLE-PAH. Therefore, further research on TRAF5 and its involvement in the pathogenesis of SLE-PAH may provide valuable insights for the identification of novel therapeutic targets and improved management strategies for this condition.

Disclosure: X. Deng: None; **J. Qian**: None; **R. Wang**: None; **J. ZHAO**: None; **Q. Wang**: None; **T. Yuan**: None; **M. LI**: None; **X. Zeng**: None.

Abstract Number: 0724

Synovial Macrophage Subsets Defined by ScRNAseq Demonstrate Sexually Dimorphic Gene Expression in RA and a Mouse Inflammatory Arthritis Model

Richard Bell, Ewurama Cann, Chao Yang, Accelerating Medicine Partnership Rheumatoid Arthritis, Amit Lakhanpal, Laura Donlin and Lionel Ivashkiv, Hospital for Special Surgery, New York, NY

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Plenary I
Session Type: Plenary Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Macrophages (MΦ) play a key pathogenic role in Rheumatoid Arthritis (RA), a disease that exhibits female sex bias. Recent work using scRNAseq has defined putative pathogenic synovial MΦ subtypes in RA. It is not known whether these MΦ subtypes exhibit sexually dimorphic gene expression that can contribute to female sex bias. Additionally,

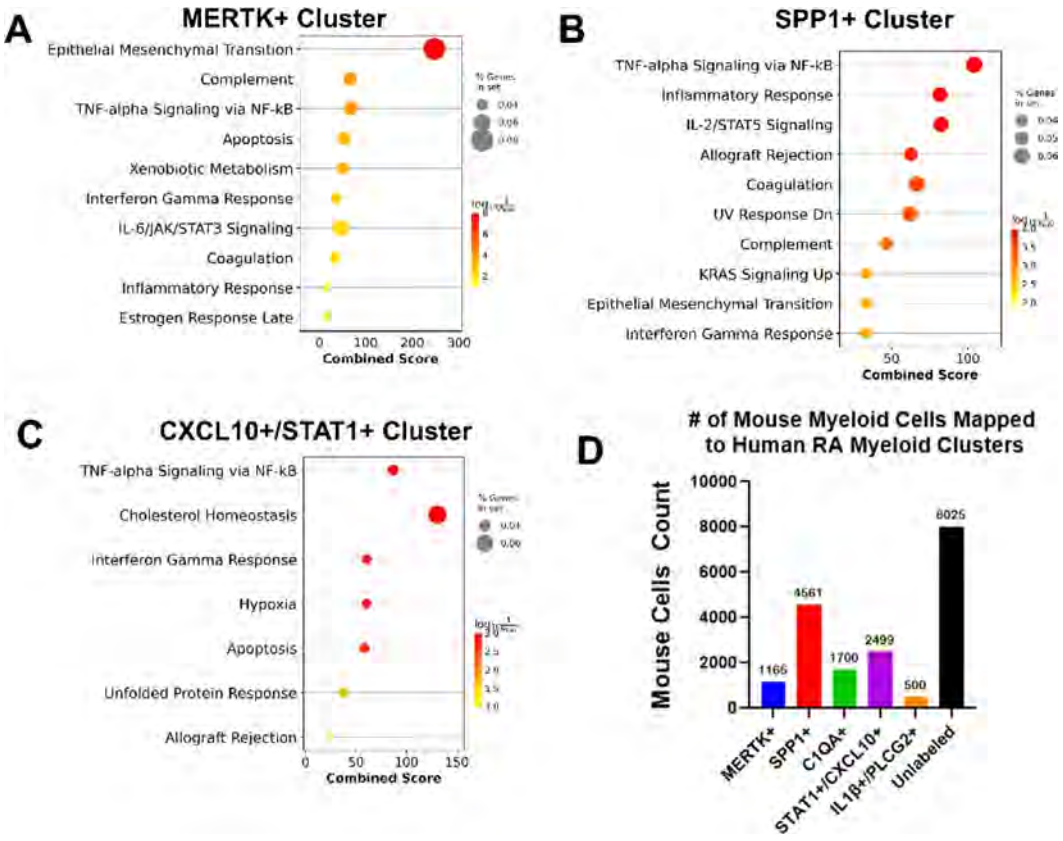

Figure 1. Human RA Female macrophages subsets are enriched with inflammatory and IFN gene signature. We performed DEG and GSEA analysis between male and female subjects within each putative pathogenic MΦ cluster. In 3 clusters (SPP1+, CXCL10+/STAT1+, and MERTK+ clusters), female cells were enriched with IFN related pathways (IFN-γ Response, EMT, Allograft Rejection) and other inflammatory pathways (TNF signaling, Inflammatory Response, A-C). To validate our mouse model, we built a mouse-to-human transfer learning model (a five-fold cross validated gradient boosted decision tree) to classify the human cell types (MERTK+; SPP1+, C1QA; STAT1+/CXCL10; IL1β/PLCG2). The model produced high quality predictions with an overall F1 score of 0.76 ± 0.1. This model was then transferred to the mouse dataset via mouse-to-human gene mapping and used to predict which human cluster each mouse cell is in. This analysis reveals that mouse ZIA synovium map to relevant sexually dimorphic human cell clusters (D).

the causal role of RA MΦ subsets in inflammatory arthritis is difficult to ascertain in the absence of a disease model that recapitulates these cells' phenotype and gene expression. We tested the hypothesis that pathogenic MΦ subsets express higher levels of inflammatory genes in females, and developed a mouse model that recapitulates select RA MΦ subsets and the sexually dimorphic gene expression pattern.

Methods: We analyzed the myeloid scRNAseq data from the Accelerating Medicines Partnership-RA (AMP-RA) consortium[1] comprised of ~76K cells from human synovial biopsies with RA clustered into 5 MΦ subsets (MERTK+, SPP1+, C1QA+, CXCL10+/STAT1+ and IL1β+/PLCG2+). We performed differential gene expression (DEG) and GSEA between female (n=55) and male (n=20) RA subjects. Zymosan induced arthritis (ZIA) was induced via intra-articular injection of 180 ug of zymosan in female and male, WT and Tg8 (transgenic for human TLR8) mice.scRNAseq of synovial tissue CD45+ cells depleted of neutrophils at peak ZIA disease, D7 and DEG with GSEA between female and male mice was performed. We also performed qPCR analysis of FACS-sorted immune cells at D2 of disease and histologic analysis at D28. To assess the similarity between human RA and ZIA, we performed scRNAseq mouse-to-human (M2H) transfer learning to map mouse cells to human defined clusters. Appropriate t-test and two-ANOVA's with Tukey's post-hoc tests were used for all statistical analysis.

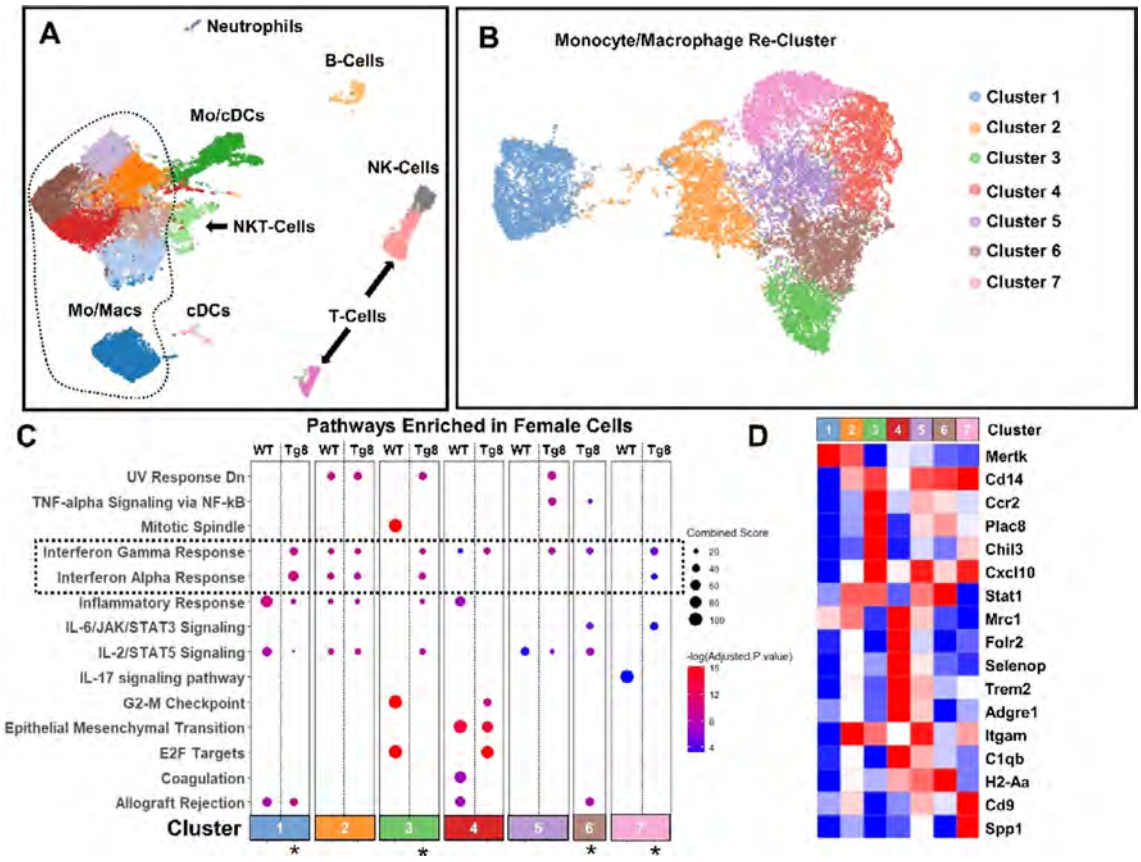

Figure 2. scRNAseq reveals Tg8 Female specific monocyte/macrophage sub-clusters that are enriched with IFN genes. scRNAseq of synovial CD45+ cells depleted of neutrophils on day 7 of ZIA show distinct clusters of immune cells, and sub clusters of monocyte/macrophages in UMAP space (A&B). Differential gene expression comparing male WT to female WT and male Tg8 to female Tg8 with subsequent gene set enrichment shows clusters 1, 3, 6 & 7 (Asterisks) are enriched in IFN related genes (Dotted Box) in female Tg8 cells (D). Mean expression of marker genes per cluster demonstrate that cluster 1 and 2 are proliferating tissue resident macrophages (Ccr2-, Cd14-, Mrc1+, MerTK+), Cluster 3, 5, and 6 are inflammatory monocytes (CD14+, Ccr2+ Chil3+, Plac8+, and Ly6c2+) with cluster 6 being MHCII+, cluster 4 are other tissue resident M2-like macrophages (Mrc+, Trem2+, Adgre1+) and cluster 7 is a monocyte derived inflammatory macrophages (CD14+, CD9+, Spp1+). Analysis: R, Orchestrating Single Cell Experiments, deSeq2, EnrichR, Two-way ANOVA with Tukey's post-hoc tests. scRNAseq: 4 mice pooled per group; Mo/cDC: Monocyte Derived or Conventional Dendritic Cells; Mo/Macs: Monocyte or Macrophages; NK: Natural Killer.

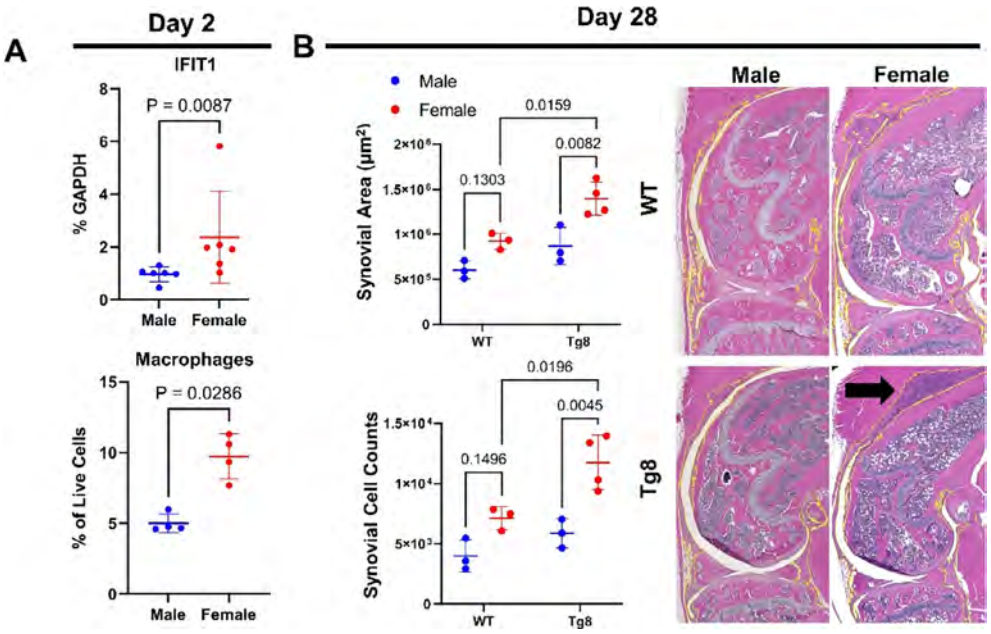

Figure 3. Early increase in IFIT1 in female macrophages with a concomitant increase macrophage abundance in female synovium that leads to increased synovitis at Day 28. On Day 2 after ZIA, FACS sorted F4-80+, CD11b+ macrophages show an increase of ISG expression, one example shown here IFIT1, in female cells. Macrophage numbers are also increased in female mice (A). Histologic analysis at Day 28 indicates that Female Tg8 mice develop increased synovial area and cell counts (B). H&E representative images are presented in the right panel with the synovium outlined in Yellow, note the large synovial reaction still present in the Tg8 female only (Arrow).

Results: GSEA demonstrated that the MERTK+, SPP1+ and CXCL10+/STAT1+ RA myeloid synovial cell clusters showed significant female bias in IFN and other inflammatory pathways (**Fig 1A-C,** FDR < 0.05, LFC >1). The M2H model produced high quality predictions with an overall F1 score of 0.76 ± 0.1 and revealed that ~60% of cells in the mouse ZIA synovium map to human RA synovial myeloid cell subsets (**Fig 1D**) validating our approach. After sub-setting the myeloid cells in ZIA synovium (**Fig 2A**) and re-clustering (**Fig 2B**), 4 of 7 clusters (C1, C3, C6 and C7) were enriched in IFN pathways in Tg8 female cells (FDR< 0.05, logFC > 1, **Fig 2C,** marked with *). These cell clusters represent tissue resident MΦ (C1: *Ccr2*-, *MerTK*+); inflammatory monocytes (C3 & C6: *Ccr2*+, *Chil3*+); and inflammatory MΦ (C7: *Cd14*+, *Cd9*+, *Spp1*+, **Fig 2D**). In addition, qPCR confirmed female specific increase of ISGs in MΦ with concomitant increase in CD11b+ cell abundance by flow cytometry on D2 (**Fig 3A**). This Tg8 female specific gene signature translates into histologic differences at D28 (**Fig 3B**).

Conclusion: This is the first demostration of sexually dimporhic myeloid gene signatures in human RA. We also validate the ZIA mouse model by mapping to human RA and demostrate that it is sexually dimorphic. We are currently exploring mechanistics studies to determine the roles of sex dependent factors, like steroid hormone signaling and X-inactivation, and their specific interactions with the IFN signaling axis.

Disclosure: R. Bell: None; **E. Cann**: None; **C. Yang**: None; **A. Rheumatoid Arthritis**: None; **A. Lakhanpal**: None; **L. Donlin**: Bristol-Myers Squibb(BMS), 2, Stryker, 2; **L. Ivashkiv**: None.

Abstract Number: 0725

Real-life Use of the PEXIVAS Reduced-dose Glucocorticoid Regimen in Granulomatosis with Polyangiitis and Microscopic Polyangiitis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Plenary I

Session Type: Plenary Session

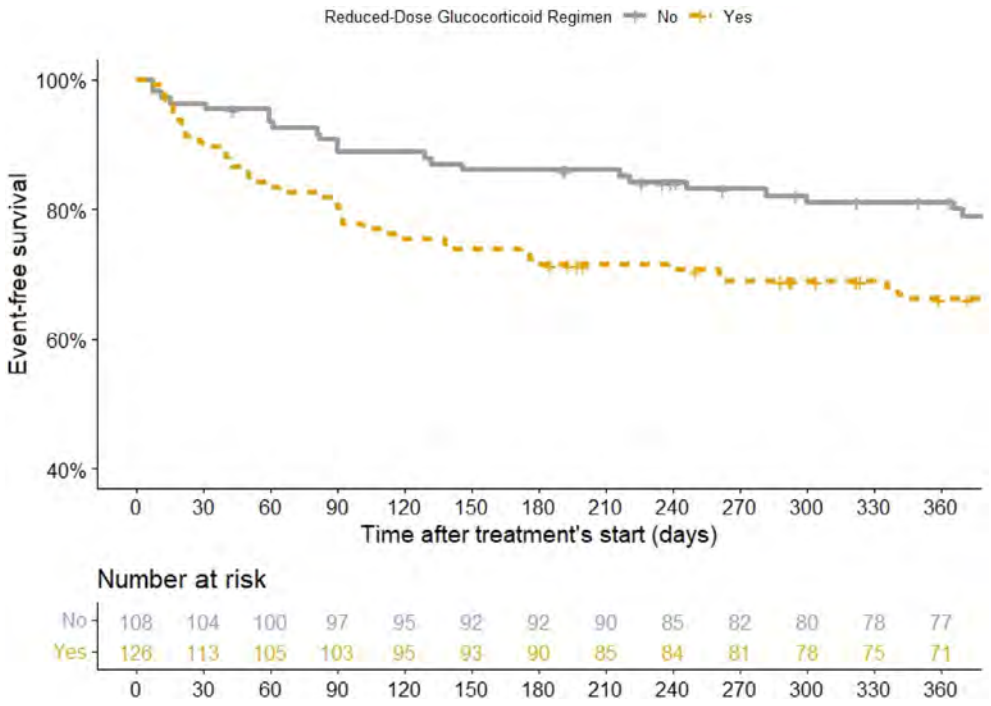
Session Time: 11:00AM–12:30PM

Background/Purpose: Glucocorticoids (GCs) in combination with rituximab (RTX) or cyclophosphamide are the cornerstone of treatment for patients with severe granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA). GCs are associated with adverse effects, including serious infections. The PEXIVAS trial demonstrated non-inferiority of reduced-dose GC regimen compared to standard dose for the incidence of death or end-stage kidney disease (ESKD), with a significant reduction in serious infections at one year. However, the primary endpoint did not include disease progression or relapse, the majority of patients received cyclophosphamide as induction therapy, and subgroup analysis showed a trend towards an increased risk of death or ESKD in RTX-treated patients. We aimed to evaluate the efficacy and safety of the reduced-dose GC regimen in a real-world setting.

Methods: We conducted a retrospective, multicentre study comparing the PEXIVAS reduced-dose GC regimen with a standard regimen in patients with severe GPA or PAM flare between January 2018 and April 2022. The primary composite endpoint included the occurrence of death, ESKD, progression before remission requiring treatment modification or relapse, whichever occurred first. Factors associated with the occurrence of the primary endpoint and of death or ESKD (i.e. the PEXIVAS endpoint) were estimated using univariate and multivariate Cox models. In a sensitivity analysis, patients treated with reduced-dose and standard-dose GCs were compared after matching on a propensity score.

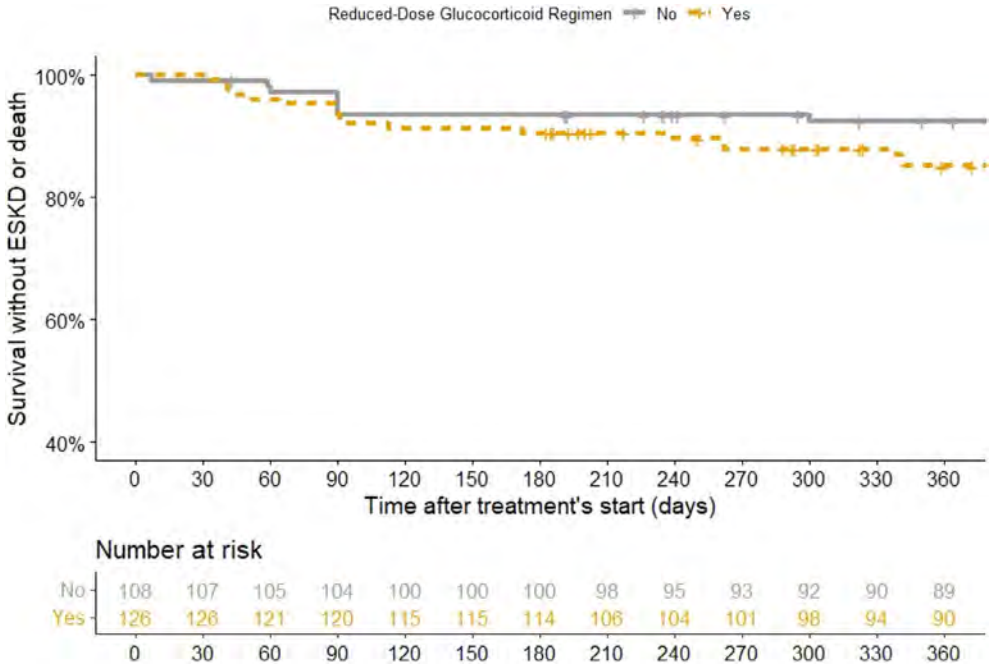
Results: Of the 234 patients enrolled (93 MPA and 148 GPA), 126 (53.8%) received a reduced GC regimen and 108 (46.2%) received a standard regimen. The primary endpoint occurred in 62/234 (26.5%) of patients during the first year of follow-up: 33.3% of patients on the reduced dose versus 18.5% on the standard dose (p=0.016).

In multivariate analysis, a reduced GC regimen was significantly associated with the occurrence of the endpoint compared to a standard regimen (HR 1.72; 95%CI 1.08-2.74) (Figure 1), but was not associated with an increased risk of death or ESKD (HR 1.62; 95%CI 0.82-3.19) (Figure 2). There was no significant difference in serious infections at 1 year (20.6% vs 15.7%, p=0.427).

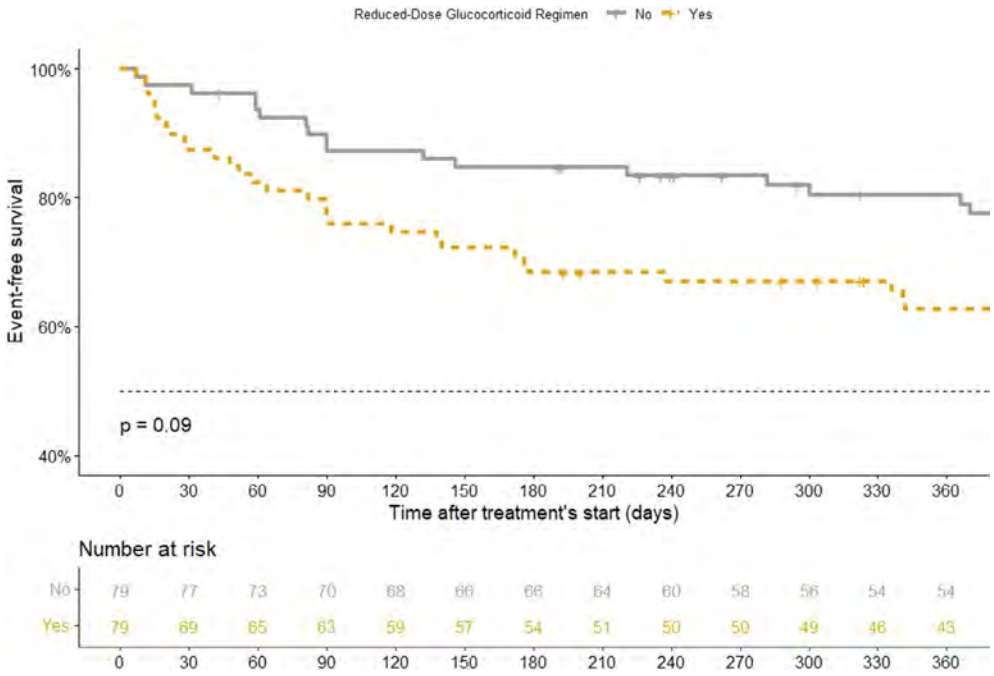


Kaplan-Meier survival curve comparing occurence of primary endpoint at 12 months between patients treated with reduced-dose GC regimen (Yes: orange) and patients treated with standard-dose regimen (No: grey) during the first year of follow-up

After propensity score matching, the reduced-dose GC regimen tended to be more likely to meet the primary endpoint than the standard regimen (HR 1.57; 95%CI 0.93-2.64) (Figure 3). In the subgroup of patients treated with the reduced-dose GC regimen, patients with creatinine levels above 300 µmol/L were more likely to meet the primary endpoint (RR 2.14; 95% CI 1.14-4.03). Similarly, in the subgroup of patients treated with RTX, the reduced-dose GC regimen tended to be more likely



Kaplan-Meier survival curve comparing occurence of death or ESKD at 12 months between patients treated with reduced-dose GC regimen (Yes: orange) and patients treated with standard-dose regimen (No: grey) during the first year of follow-up



Kaplan-Meier survival curve comparing occurence of primary endpoint at 12 months between patients treated with reduced-dose GC regimen (Yes: orange) and patients treated with standard-dose regimen (No: grey) during the first year of follow-up, after matching with a propensity score

to achieve the primary endpoint (HR 1.61; 95% CI 0.94-2.77) and was more likely to meet death or ESKD (HR 2.42; 95%CI 1.04-5.66).

Conclusion: In patients with severe GPA or MPA, the reduced-dose GC regimen was associated with an increased risk of death, ESKD, progression before remission requiring treatment modification or relapse. This risk was even greater in patients with creatinine levels above 300 μmol/L and in those treated with RTX as induction therapy.

Disclosure: S. Nagle: None; **Y. Nguyen**: None; **X. Puéchal**: None; **D. Titeca-Beauport**: None; **T. Crépin**: None; **R. Mesbah**: None; **I. Boudhabhay**: None; **G. Pugnet**: None; **J. Woessner**: None; **R. Outh**: None; **C. Lebas**: None; **A. Néel**: None; **a. Karras**: AstraZeneca, 6, GlaxoSmithKlein(GSK), 4, Novartis, 2, Pfizer, 6; **E. Hachulla**: None; **B. Subran**: None; **P. Kerschen**: None; **M. Gerfaud-Valentin**: None; **S. Vinzio**: None; **T. Goulenok**: None; **R. Borie**: None; **S. Humbert**: None; **Y. Uzunhan**: None; **S. Melboucy-Belkhir**: None; **J. Gouin**: None; **M. Guerry**: None; **B. Terrier**: AstraZeneca, 5, CSL Vifor, 2, GlaxoSmithKlein(GSK), 2.

Abstract Number: 0726

Expert Consensus Recommendations for Musculoskeletal Ultrasound Education in Canadian Rheumatology Residency Training Programs

Maria Powell[1], Steven Thomson[1], Sibel Aydin[2], Mohammad Bardi[3], Susan Barr[1], Lihi Eder[4], Gurjit S Kaeley[5], Sahil Koppikar[6], Shirley Lake[7], Christopher Lyddell[8], Chris Penney[1], Michael Stein[9], Pooneh Akhavan[10], Minna Kohler[11], Maggie Larche[12], Samar Aboulenain[13], Dana Jerome[6], Adam Kovacs-Litman[13], Ashley Yip[14], Janeve Desy[1], Kevin McLaughlin[1] and Irene W Y Ma[1], [1]University of Calgary, Calgary, AB, Canada, [2]Department of Medicine, Ottawa Hospital Riverside Campus, Ottawa, ON, Canada, [3]Dr. M Bardi Inc, Vancouver, BC, Canada, [4]Women's College Research Institute, Division of Rheumatology, University of Toronto, Toronto, ON, Canada, [5]University of Florida College of Medicine – Jacksonville, Ponte Vedra Beach, FL, [6]Women's College Hospital & University of Toronto, Toronto, ON, Canada, [7]Sunny Brook Hospital & University of Toronto, North York, ON, Canada, [8]Self, Edmonton, AB, Canada, [9]McGill University,

Montréal, QC, Canada, [10]self-employed, Toronto, ON, Canada, [11]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [12]McMaster University, Hamilton, ON, Canada, [13]University of Toronto, Toronto, ON, Canada, [14]University of Alberta, Edmonton, AB, Canada

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Plenary I
Session Type: Plenary Session
Session Time: 11:00AM–12:30PM

Background/Purpose: The Royal College of Physicians and Surgeons of Canada has recently incorporated musculoskeletal ultrasound (MSUS) education into Canadian rheumatology residency programs as an optional training experience. Many Canadian rheumatology programs offer MSUS training for residents, but there is currently no national ultrasound curriculum in Canada outside of externally available courses. The objective of this study was to establish expert consensus on the MSUS competencies that can be incorporated into Canadian rheumatology residency training programs.

Methods: We used a 3-stage consensus design to identify MSUS competencies for Canadian rheumatology residents. We defined consensus a priori as agreement of 70% or higher. We identified all study participants using non-probability sampling and snowball technique. In stage 1, we invited 13 MSUS experts to participate in an online meeting using a modified nominal group technique (NGT) to identify a prioritized list of MSUS competencies. In stage 2, we invited 18 individuals including MSUS experts, rheumatology residents with MSUS experience, and rheumatology program directors with exposure to MSUS in their residency program to participate in a MSUS working group. We invited members of the MSUS working group to complete 3 rounds of online surveys using a modified Delphi technique to establish consensus on the items that should be included for each of the prioritized MSUS competencies identified during the modified NGT. Items not reaching consensus were re-addressed in a maximum of two subsequent rounds. In Stage 3, we invited MSUS experts to attend a structured online focus group to review the final list of competencies.

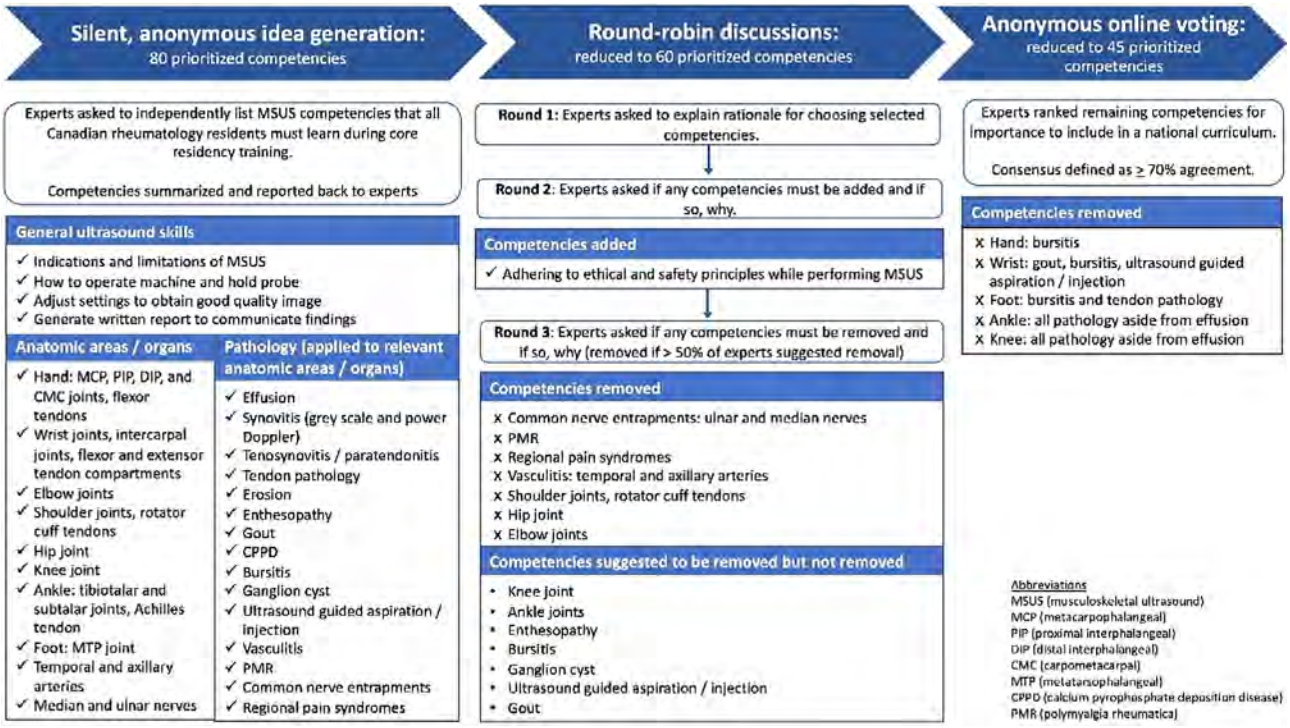


Figure 1: Summary of the modified nominal group technique (NGT) process used to identify prioritized musculoskeletal ultrasound (MSUS) competencies for Canadian rheumatology residents.

Results: Ten of the 13 invited MSUS experts attended the online meeting using a modified NGT, in which experts reached consensus on a prioritized list of 45 competencies (Figure 1). In stage 2, members of the MSUS working group included individuals from 7/12 (58%) Canadian rheumatology programs (English stream) and two MSUS experts from the United States. There was a 100% response rate for all 3 rounds of surveys in the modified Delphi technique. The first round of surveys addressed 86 items derived from the prioritized competencies identified during the modified NGT. The second round of surveys addressed 51 items, and the third round addressed 10 items. After 3 rounds of surveys, the MSUS working group reached consensus on all but 5 items, recommending 42 items be mandatory and 39 be optional. Members of the MSUS working group recommended that it is mandatory for all Canadian rheumatology residents to learn basic ultrasound skills;

Table 1: Summary of final recommended musculoskeletal ultrasound (MSUS) competencies for Canadian rheumatology residents after 3 rounds of surveys using a modified Delphi technique.

Consensus: Mandatory Competencies

Basic ultrasound Skills

Prior to the scan

1. Understand the basic physics of ultrasound including frequency, wavelength, amplitude, etc.
2. Know the indications and limitations of the MSUS exam being performed.
3. Select appropriate probe based on structure being imaged, recognizing how frequency relates to resolution and penetration.

During the scan

1. Maneuver the probe appropriately to define structural characteristics (sufficient gel and pressure).
2. Ensure proper patient positioning for image optimization.
3. Adjust gain and depth to obtain the best image possible.
4. Adjust focal zone to area of interest.
5. Understand basic sonographic characteristics of tissues including bone, tendon, nerve, blood vessel, fat, fluid, etc.
6. Recognize relevant MSUS artifacts such as anisotropy, acoustic shadow, reverberation, and mirror image.
7. Obtain an acceptable image in at least two views (orthogonal planes).
8. Observe the As Low As Reasonable Achievable (ALARA) principle when possible.
9. Perform a MSUS exam in an ergonomic fashion.
10. Save and archive image if desired.

After the scan

1. Properly clean / sanitize the machine and transducers after the exam.
2. Ensure all MSUS exams adhere to ethical principles and patient safety guidelines.
3. Document MSUS findings in the medical record.
4. Integrate relevant MSUS findings into patient management.

Hand: focused ultrasound exam for features of inflammatory arthritis

1. Effusion: MCP and PIP joints
2. Synovitis (grey scale): MCP and PIP joints
3. Synovitis (power Doppler): MCP and PIP joints
4. Bone erosion vs osteophyte: MCP and PIP joints
5. Tenosynovitis: flexor tendon (finger level)

Wrist: focused ultrasound exam for features of inflammatory arthritis

1. Effusion: radio-carpal joint
2. Synovitis (grey scale): radio-carpal joint
3. Synovitis (power Doppler): radio-carpal joint
4. Tenosynovitis: 6th extensor compartment
5. Select carpal bones: lunate, capitate

Foot: focused ultrasound exam for features of inflammatory arthritis

1. Effusion: MTP joint
2. Synovitis (grey scale): MTP joint
3. Synovitis (power Doppler): MTP joint
4. Bone erosion vs osteophyte: MTP joint
5. Double contour sign: MTP joint

Knee: limited ultrasound exam to identify a joint effusion

1. Effusion: suprapatellar and parapatellar recesses of the knee joint

Ankle: limited ultrasound exam to identify a joint effusion

1. Effusion: anterior recess of the tibiotalar joint

Consensus: Optional Competencies

Hand

1. Pathology: gouty tophi, crystal deposition, tendon tear, calcific tendinopathy, ganglion cyst, cartilage degradation
2. Anatomic areas: DIP joint, CMC joint, extensor tendon (finger level)

Wrist

1. Pathology: bone erosion, tendon tear, calcific tendinopathy, ganglion cyst
2. Anatomic areas: radio-ulnar joint, ulno-carpal joint, flexor tendons at the level of the carpal tunnel

Foot

1. Pathology: tenosynovitis, crystal deposition
2. Anatomic areas: IP joint, Lisfranc joint

Knee: limited ultrasound exam to identify a joint effusion

1. Infrapatellar, medial, lateral, and posterior views of the knee

Ankle: limited ultrasound exam to identify a joint effusion

1. Posterior view of ankle
2. Subtalar joint
3. Talonavicular joint

No Consensus

Hand

1. Double contour sign: MCP and PIP joints

Wrist

1. Tenosynovitis: 1st extensor tendon compartment
2. Tenosynovitis: 2-5th extensor tendon compartment
3. Synovitis: lunate-capitate joint (only addressed in 2 rounds)

Foot

1. Gouty tophi: MTP joint

Abbreviations
MSUS (musculoskeletal ultrasound)
MCP (metacarpophalangeal)
PIP (proximal interphalangeal)
DIP (distal interphalangeal)
MTP (metatarsophalangeal)
IP (interphalangeal joint)
CMC (carpometacarpal)

how to perform a focused MSUS exam of the hands, wrists, and feet for features of inflammatory arthritis including effusion, synovitis (grey scale and power Doppler), bone erosion versus osteophyte, and tenosynovitis; and a limited MSUS exam of the knee and ankle to identify a joint effusion (Table 1).

Conclusion: This study reports the expert consensus recommendations for MSUS in Canadian rheumatology residency training programs. These recommendations can be used to help guide programs as they develop MSUS curricula.

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Abstract Number: 0727

A Novel Active Pemphigus Vulgaris Mouse Model Induced by Immunization with TLR Ligand Adjuvanted Recombinant Desmoglein 3 Protein Vaccine

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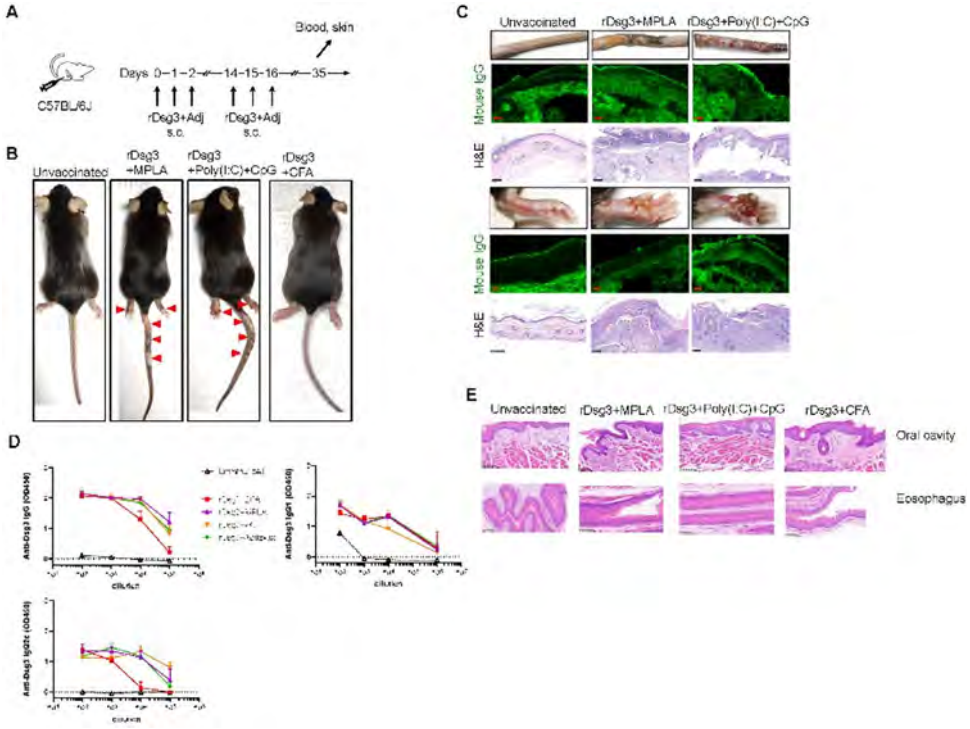
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Pemphigus vulgaris (PV) is an autoimmune bullous skin disease mediated by desmoglein-3 (Dsg3) specific auto-antibody present in skin and mucosae. The binding of pathogenic antibody to Dsg3, which are cell-cell adhesion molecules found in desmosome, induces loss of adhesion between keratinocyte in epidermis and blister formation, resulting in painful erosion in PV patient and are even fatal when severe. Animal model plays vital role in developing safe and effective therapies for PV. However, the PV adult animal model is quite limited, with the adoptive transfer mouse model being the most widely-used, which requires both *Dsg3* knock-out mice and immune-deficient mice as donor and recipient mice, respectively. In this study, we aimed to develop a novel active adult PV model to overcome some of the limitations of current animal models.

Methods: The recombinant Dsg3 (rDsg3) protein vaccines were prepared by mixing rDsg3 and different candidate immune adjuvants for induction of active PV model. Wild-type C57BL/6J mouse was immunized by subcutaneous injection in the footpad through a prime/boost regime. The gross phenotype was monitored and plasma was prepared periodically post immunization. Enzyme-linked immunosorbent assay (ELISA) was conducted for measurement of anti-Dsg3 antibody levels. Passive neonatal mouse model was used to determine the pathogenicity of plasma from PV model mouse. Skin tissues were harvest and formalin-fixed, paraffin-embedded for histological examination, or snap-frozen in liquid nitrogen and embedded in OCT for direct immunofluorescence (IF) to detect the deposition of auto-antibodies.



Direct immunization induced PV symptoms in wild-type mice. (A) A scheme showing the treatment of mice. Mice were vaccinated with rDsg3 and different adjuvants as indicated by a prime-boost regime. 35 days after first vaccination, plasma or serum was prepared from peripheral blood and skin or mucosal tissues were harvested for histological analysis. (B) Gross phenotype of mice. Red arrowhead indicated the sites with skin erosion. (C) Skin tissues from tail and footpad were harvested for H&E staining or direct IF. (D) Dsg3 specific IgG, IgG1 and IgG2c were measured by ELISA. OD values at serial dilution read at 450nm was shown. (E) Histological examination of mucosal tissues from oral cavity and esophagus. Scale bar: 100μm. Results represented are from three-four independent experiments with similar results and shown as mean ± SD.

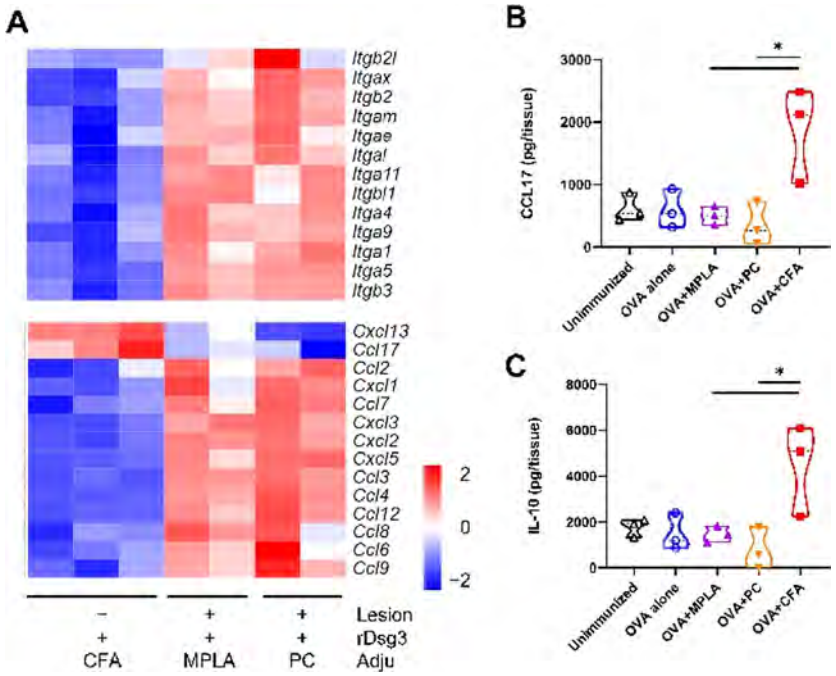


Fig. 2. CCL17 was down-regulated by TLR ligands. (A) Skin lesion of PV model mice was harvested and homogenized for RNA-seq. Transcriptome was analyzed. (B) Mice were vaccinated with OVA and different adjuvants as indicated. 7 days after immunization, draining lymph node was harvested and homogenized for quantification of cytokines by ELISA. Results are representative of three independent experiments and shown as mean ± SD. *p<0.05 indicate a significant difference between.

Results: We found that immunization with rDsg3 adjuvanted with single or a combination of TLR ligands could induce blister formation, skin erosion and hemorrhage in the footpad and tail. H&E staining indicated suprabasilar blister with acantholysis in skin tissues. Direct IF showed deposition of IgG between keratinocyte in the epidermis of PV model mice. A significant elevation of anti-Dsg3 level was observed in plasma of PV model mice as compared with unvaccinated mice measured by ELISA. We also found that completeFreund's adjuvant could not facilitate the breach of tolerance against self-desmoglein 3, as indicated by gross phenotype and histological examination. Bulk RNA-seq suggested Treg-attractant chemokine *Ccl17* was down-regulated by TLR ligand, which was confirmed by ELISA at the protein level, indicating the reduced recruitment of regulatory T cell into the skin lesion and uncontrolled autoimmunity against Dsg3 when TLR ligands was applied.

Conclusion: A novel active pemphigus vulgaris mouse model was established by immunization wild-type C57BL/6J mouse with adjuvanted recombinant desmoglein 3 protein vaccine, which closely mimic clinical symptoms of mucocutaneous type of PV patients. This model could compensate for current PV models with no need of either *Dsg3* knock-out mice or immune-deficient mice, and greatly promote the development of antigen-specific therapies for PV.

Disclosure: C. Gao: None; **Z. Wang**: None; **Q. Lu**: None.

Abstract Number: 0728

Systemic Lupus Erythematosus B Lymphocyte Responsiveness to Type I and Type III Interferon Is Determined by Donor IFN Status and B Cell Phenotype

Diana Alzamareh, Mary O'Connell, Jennifer Anolik and **Jennifer Barnas**, University of Rochester Medical Center, Rochester, NY

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Systemic lupus erythematous (SLE) is a heterogenous autoimmune disorder characterized by pathogenic antinuclear antibodies. An interferon (IFN) gene signature and B cell aberrations are found in subsets of SLE patients. Type I IFN is involved in immune cell activation, correlates with disease activity, and promotes plasma cell (PC) development. Anifrolumab is a monoclonal type I IFN receptor neutralizing antibody approved for SLE treatment. Anifrolumab reduces PC numbers differentiated from B cells *in vitro*.CD11c+ T-Bet+ autoimmune-associated B cells (ABC) are expanded in SLE and thought to be precursors to autoreactive antibody-producing PCs. We hypothesized that B cell IFN responsiveness is determined by phenotype and past *in vivo* IFN exposure. Here, we characterized the IFN response of IgD- CD27- double negative (DN) B cells, a subset enriched in CD11c+ T-Bet+ ABCs in SLE.

Methods: We screened our biorepository of SLE peripheral blood mononuclear cells (PBMC) for IFI27 expression, an IFN stimulated gene, by quantitative RT-qPCR. Serum IFN-α levels were measured by ELISA. Age, sex, and race matched IFI27-low and high SLE PBMCs were stimulated with IFN-α2 or IFN-λ1 then immunostained for flow cytometry (n=9 pairs plus n=5 matched healthy donor, HD). STAT1 phosphorylation after IFN stimulation was measured by median fluorescent intensity. We measured IFNLR1 expression (type III IFN receptor subunit) in HD B cells by RT-qPCR after TLR and IFN stimulation. Flow cytometry immunophenotyping of PBMC from SLE patients starting anifrolumab prior to first infusion and after second infusion was used to identify DN1 (CD11c- T-Bet- IgD- CD27-) and DN2 (CD11c+ T-Bet+ IgD- CD27-) B cells.

Results: SLE PBMC with high IFI27 had significantly higher level serum IFN-α compared to PBMC from SLE with low IFI27 or HD. Baseline pSTAT1 was not statistically different between low versus high SLE IFI27 donors for ABC/DN2 or DN1.However, ABC/DN2 had higher baseline pSTAT1 when compared to DN1 from the same donor in all groups (HD p=0.02, IFI27 low 0.0001, IFI27 high,0.0008; Wilcoxon matched pairs signed rank test with FDR). DN1 responsiveness to IFN-α was markedly reduced when cells were derived from a high IFI27 patient (p=0.001 for Δstim-unstim pSTAT1) while ABC/DN2 response was unchanged. Despite higher baseline pSTAT1, Δstim-unstim pSTAT1 was higher (p=0.001) after IFN-λ1 stimulation when ABC/DN2 came from a high IFI27 donor. IFN-α2, IFN-λ1, and IFN-γ did not change total B cell IFNLR1 expression. However, TLR7 agonist R848 was able to increase IFNLR1. One month of anifrolumab therapy did not alter percentages of ABC/DN2 in our preliminary phenotyping analyses for ABC/DN2.

Conclusion: Our data demonstrate that type I and type III IFN have differential effects on B cells subsets in both SLE and HD. When cells are derived high IFN environments in SLE, responsiveness of ABC/DN2 to type III IFN is increased while DN1 remain minimally responsive to type III IFN and have reduced type I responses as compared to DN B cells derived from low IFN patients. The role of type III IFN in the setting of type I IFN blockade such as anifrolumab requires further exploration given its potential to stimulate ABC/DN2, a B cell subset target of interest.

Disclosure: D. Alzamareh: None; **M. O'Connell**: None; **J. Anolik**: None; **J. Barnas**: None.

Abstract Number: 0729

ROCK1 Orchestrates B-cell Differentiation Under Stress

Juan Rivera-Correa[1], Sanjay Gupta[1], Edd Ricker[2], Danny Flores-Castro[1], Daniel Jenkins[1], Stephen Vulcano[1], Tania Pannellini[1], Matthew Miele[3], Zhuoning Li[3], Nahuel Zamponi[4], Young-Bum Kim[5], Evgenia Giannopoulou[1], Leandro Cerchietti[4] and **Alessandra Pernis**[1], [1]Hospital for Special Surgery, New York, NY, [2]Columbia University, New York, NY, [3]Memorial Sloan Kettering Cancer Center, New York, NY, [4]Weill Cornell Medicine, New York, NY, [5]Beth Israel Deaconess Medical Center, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: The mechanisms utilized by B cells to execute their differentiation programs when exposed to damaging and stressful environments, which often accompany severe infections and inflammatory disorders, are poorly understood. RhoA GTPases are molecular switches, which signal by binding to key downstream effectors. In particular, RhoA signaling activates two crucial serine-threonine kinases, ROCK1 and ROCK2. In B cells, ROCK2 is known to regulate the positioning and cholesterol biosynthesis of germinal center B cells and to control plasma cell (PC) differentiation. Although ROCK1 and ROCK2 share a highly homologous kinase domain, they exhibit a lower degree of similarity in the remainder of the molecule suggesting the existence of isoform-specific functions. The precise role of ROCK1 in B cells has, however, not been studied. Here, we have investigated the contribution of ROCK1 to B cell differentiation in complex inflammatory settings by employing a malaria infection model and *in vitro* studies.

Methods: Mice with B cell-specific deletion of ROCK1 (CD23-Cre.Rock1$^{flox/flox}$) were subjected to *Plasmodium yoelii 17XNL (P. yoelii),* a non-lethal malaria infection model characterized by severe transient anemia. Rock1$^{flox/flox}$ mice were employed as controls. Immune responses were monitored by FACS at various timepoints and histopathological analyses. Antibody responses and cytokine production were assessed by ELISA. The molecular mechanisms employed by ROCK1 to regulate

B cell differentiation were examined by FACS-sorting B cell populations from spleens followed by RNA-sequencing analyses and *in vitro* experiments coupled with transcriptomic, phospho-proteomic, and biochemical strategies.

Results: *In vivo* and *in vitro* studies demonstrate that the serine-threonine kinase ROCK1 helps B cells execute their differentiation programs upon exposure to pathogen-associated stressors, like TLR9 ligands and high levels of heme. ROCK1 restrains premature plasma cell differentiation by phosphorylating the heme-regulated transcription factor Bach2. As B cells differentiate, furthermore, ROCK1 limits the proinflammatory potential of B cells, and fine-tunes mTORC1 activity and stress responses. ROCK1 orchestrates these processes by regulating the assembly of p62 complexes containing mTORC1, TBK1, RhIM-domain proteins, and molecules involved in RNA metabolism and proteostasis.

Conclusion: These studies indicate that ROCK1 is a critical "stress" sensor, which helps B cells execute their differentiation programs upon exposure to potentially damaging conditions by coordinating the activity and localization of a key core of molecules that mediate cell-fate decisions, proinflammatory functions, and RNA and protein homeostasis. These ROCK1-dependent mechanisms may be widely employed by B cells to cope with intense environmental stresses and these findings may be relevant not only for infections, but also for vaccinations, and autoimmune diseases.

Disclosure: J. Rivera-Correa: None; **S. Gupta**: None; **E. Ricker**: None; **D. Flores-Castro**: None; **D. Jenkins**: None; **S. Vulcano**: None; **T. Pannellini**: None; **M. Miele**: None; **Z. Li**: None; **N. Zamponi**: None; **Y. Kim**: None; **E. Giannopoulou**: None; **L. Cerchietti**: None; **A. Pernis**: None.

Abstract Number: 0730

NF-κB Signaling Is Critically Important for Functional Responses of ACPA-producing B Cell Clones from Patients with Rheumatoid Arthritis

Giulia Frazzei[1], Jan Piet van Hamburg[2], Ronald van Vollenhoven[2] and **Sander Tas**[3], [1]Amsterdam University Medical Center, location AMC, Amsterdam, Netherlands, [2]Amsterdam University Medical Centers, Amsterdam, Netherlands, [3]Amsterdam UMC, locatie AMC, Utrecht, Netherlands

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Anti-citrullinated protein antibodies (ACPA) play a role in rheumatoid arthritis (RA) pathogenesis, and their presence is associated with disease severity. Consequently, detailed analysis of ACPA^{pos} B cells is required to disentangle the role of these cells in RA. Multiple intracellular signaling pathways are involved in functional B cell responses. NF-κB signaling is one of the prime regulators of B cell proliferation, differentiation and (auto)antibody production. Moreover, NF-κB activation leads to pro-inflammatory cytokine and chemokine production. JAK-STAT signaling is induced after activation of the B cell receptor (BCR) and is also involved in B cell proliferation and maturation. Targeting NF-κB or JAK-STAT signaling may advance our understanding of the mechanisms involved in the activation of ACPA-producing B cells. We make use of ACPA^{pos} B cell clones, since peripheral ACPA^{pos} cells are present at low frequencies in the peripheral blood.

We aimed to identify whether NF-κB or JAK-STAT signaling inhibition using small molecule inhibitors (SMIs) is effective in targeting functional responses of ACPA^{pos} B cell clones from RA patients.

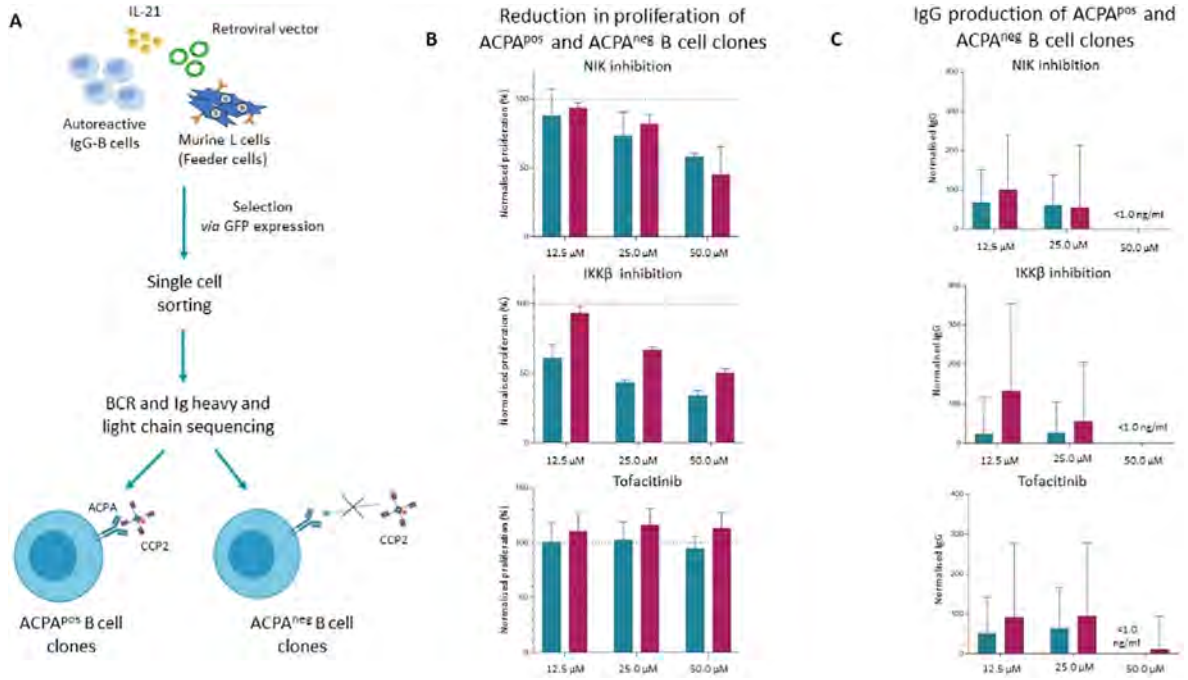


Fig. 1 - ACPApos and ACPAneg B cell clone generation (A). Effects of small molecule inhibition of intracellular signaling pathways on B cell proliferation (B, data normalized on DMSO) and IgG production (C). Legend: ACPApos B cell clones in blue, ACPAneg B cell clones in red.

Methods: Previously generated ACPA^{pos} and ACPA^{neg} B cell clones (Fig. 1A) were expanded and cultured with anti-CD40 and IL-21. Canonical and non-canonical NF-κB signaling were targeted by validated SMIs of Inhibitor of κB kinase β (IKKβi, canonical NF-κB signaling) and NF-κB inducing kinase (NIKi, non-canonical NF-κB signaling), respectively. Tofacitinib (a JAK1/JAK3 specific SMI) was used to target JAK-STAT signaling. Cell viability, proliferation and differentiation were evaluated by flow cytometry. Antibody production was measured by ELISA.

Results: We observed a dose-dependent reduction in proliferation in ACPA^{pos} B cell clones treated with either IKKβi (12.5 μM IKKβi: 39.12±9.86% decrease, 25 μM IKKβi: 56.55±1.84% decrease, 50 μM IKKβi: 65.65±3.1% decrease) or NIKi (12.5 μM NIKi: 12.13±19.42% decrease, 25 μM NIKi: 26.63±17.37% decrease, 50 μM NIKi: 41.69±2.00% decrease) upon stimulation with 2.25 μg/ml anti-CD40 and 1.0 ng/ml IL-21 (Fig. 1B). Similarly, we observed a dose-dependent reduction in IgG production (Fig. 1C). IKKβi treatment seemed to have a stronger effect than NIKi treatment on ACPA^{pos} B cell clones.

We did not observe a clear difference between IKKβi and NIKi in ACPA^{neg} B cells (12.5 μM IKKβi: 6.90±5.38% decrease, 25 μM IKKβi: 33.32±2.15% decrease, 50 μM IKKβi: 50.11±3.15% decrease; 12.5 μM NIKi: 6.09±3.61% decrease, 25 μM NIKi: 17.83±6.53% decrease, 50 μM NIKi: 54.67±20.37% decrease). Cell viability was not affected by IKKβi or NIKi treatment. In contrast to IKKβi and NIKi treatment, tofacitinib only had limited effects on ACPA^{pos} and ACPA^{neg} B cell proliferation and IgG production. At present these results are being corroborated in freshly isolated ACPA^{pos} B lineage cells of RA patients.

Conclusion: Our data point towards a critical role of the NF-κB signaling pathways in the functional responses of ACPA-producing B cells, whereas a limited role of JAK-STAT signaling was observed. Consequently, targeting NF-κB signaling may have beneficial effects in limiting (autoreactive) B cell responses in RA.

Disclosure: G. Frazzei: None; **J. van Hamburg**: None; **R. van Vollenhoven**: AbbVie, 2, 6, AstraZeneca, 2, 5, 6, Biogen, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Galapagos, 2, 5, 6, GlaxoSmithKline, 6, Janssen, 2, 6, MSD/Merck Sharp and Dohme, 5, Novartis, 5, Pfizer, 2, 5, 6, RemeGen, 2, Roche, 5, Sanofi, 5, UCB, 2, 5, 6; **S. Tas**: None.

Abstract Number: 0731

ZEB2 Acts as a Crucial Transcriptional Regulator Governing Age-Associated B Cell Formation and Pathogenicity in Systemic Lupus Erythematosus

Dai Dai[1], Shuangshuang Gu[1], Xiaxia Han[1], Huihua Ding[2], Yang Jiang[1], Sheng Chen[1] and **Nan Shen**[2], [1]Shanghai Institute of Rheumatology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University (SJTUSM), Shanghai, China, [2]Shanghai Jiao Tong University School of Medicine, Shanghai, China

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Age-associated B cells (ABCs) accumulate and contribute to the pathogenesis of systemic autoimmune diseases like lupus. Despite recent insights into the ontogeny and function of ABCs, the key transcriptional regulators of ABCs differentiation remain ill-defined. Addressing this gap in knowledge will reveal targets to enable the prevention or reduction of ABCs in disease therapy.

Methods: We employed single-cell RNA sequencing to identify transcription factors (TFs) that were differentially expressed in age-associated B cells (ABCs) from both lupus patients and lupus-prone mice. An arrayed CRISPR screen of these regulatory TFs was conducted under in-vitro conditions that induce ABC formation. In our cohort, we included patients diagnosed with Mowat-Wilson Syndrome (MWS), a condition attributed to ZEB2 haploinsufficiency. We constructed B-cell-specific Zeb2 knockout mice and subjected them to TLR7-driving and Bm12-transfer lupus models, enabling us to study Zeb2's regulatory role in ABC formation and associated autoimmunity. The detection of autoantibodies was achieved using an autoantigen microarray. To investigate Zeb2's direct targets, we performed ATAC-seq, Cut & Tag, and Cut & Run sequencing, and integrated these regulome findings with transcriptome data obtained from RNA sequencing. We employed trans-well and PHrodo staining techniques to study the distinct migratory and phagocytic features of ABCs. The induced lupus models were used to evaluate the potential of the JAK1/3 inhibitor tofacitinib in intervening with ABC formation and associated autoimmunity.

Results: We carried out a screening process and identified that Zeb2 is required for in-vitro differentiation of ABCs in both humans and mice. We observed a reduction in ABCs in individuals with ZEB2 haploinsufficiency and in mice devoid of Zeb2 in B-cells. By utilizing mice that selectively lack Zeb2 in B cells, we demonstrated the essential role of Zeb2 in facilitating autoimmune pathology relevant to ABCs, including autoantibody formation, production of proinflammatory cytokines and chemokines, migration to end-organ tissues, and induction of tissue damage in a lupus model. Zeb2 binds to the +20kb intronic enhancer of Mef2b, thereby repressing Mef2b-mediated germinal center B-cell differentiation and instead promoting ABC formation. Zeb2 also targets genes crucial for ABC specification and function, including Itgax. Furthermore, Zeb2 regulates the distinct cellular characteristics of ABCs, including their migration and phagocytic abilities. The differentiation of ABCs driven by Zeb2 necessitates Jak-Stat signaling. Notably, we found that the use of tofacitinib, an approved JAK1/3 inhibitor, effectively reduces the accumulation of ABCs in autoimmune mice and patients.

Conclusion: Our study reveals that ABCs, a unique B cell subset, rely on Zeb2 expression and regulation. Zeb2 affects germinal center B cell development and dictates ABC identity. Modulating Zeb2-mediated Jak-Stat signaling could effectively curb ABC accumulation and related autoimmunity, presenting a potential therapy for autoimmune diseases.

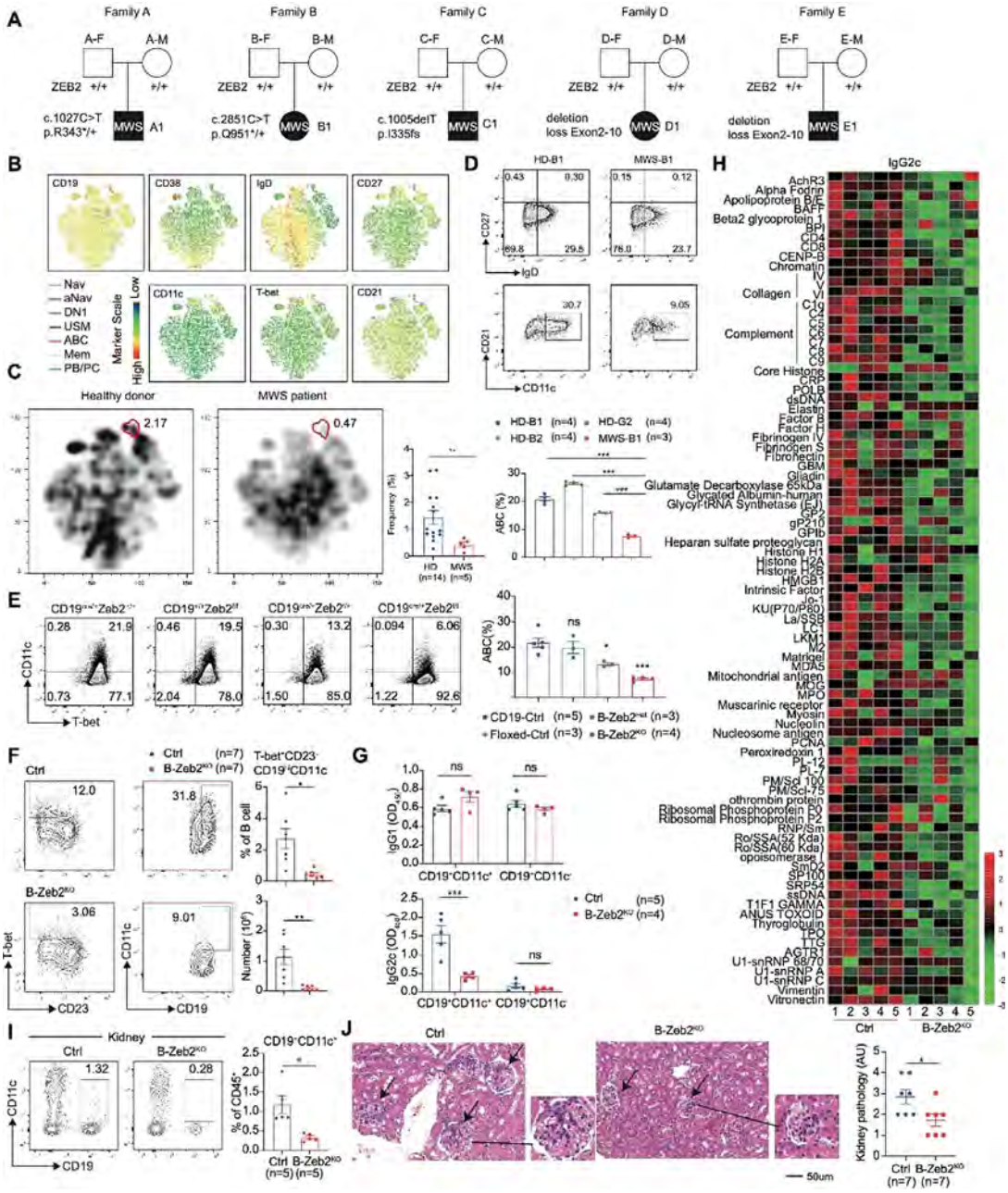


Fig 1. Zeb2 is required for ABC formation and pathogenicity in autoimmunity. (A) Family pedigrees showing de novo heterozygous mutations of ZEB2 in Mowat-Wilson syndrome (MWS) patients. (B) Comprised t-SNE plots of peripheral B cell clusters for all donors. Eight B cell clusters were identified based on lineage marker expression as naïve B cell (Nav), activate naïve B cell (aNav), CXCR5+ double negative B cells (DN1), unswitch memory B cells (USM), age-associated B cells (ABC), memory B cell (Mem), plasma blast (PB) and plasma cells (PC). (C) Separated t-SNE plots for two representative HD (left) and MWS (right) samples. Statistical analysis of ABC in PBMC for HD versus MWS group. (D) Primary B cells were isolated from HDs and a MWS patient and cultured with an ABC-skewing cocktail for 3 days. Representative plots and frequency of ABCs (CD19+CD38-CD27-IgD-CD11c+CD21-). (E) Splenic B cells were isolated from CD19Cre/+ (CD19-Ctrl), Zeb2f/f (Floxed-Ctrl), Zeb2f/+CD19cre/+(B-Zeb2Het), Zeb2f/f CD19cre/+(B-Zeb2KO) mice and cultured with ABC-skewing cocktail for 3 days. Representative plots and frequency of ABCs (CD19+CD11c+T-bet+). (F) B-Zeb2KO and CD19Cre/+ (Ctrl) mice were induced by imiquimod (IMQ) for 6 weeks. Flow cytometry plots and statistical analysis of splenic ABCs (CD19+CD23-CD11c+T-bet+) (G) Splenic CD19+CD21-CD11c+ and CD19+CD21+CD11c- B cells sorted by flow cytometry from mice described in (F) were stimulated with anti-IgM, anti-CD40, R848, IL-21 for one day and then the supernatants were collected to detect IgG1 and IgG2c antibodies. (H) Autoantigen microarray was used to detect IgG2c autoantibodies in the serum of mice described in (F) by OmicsArray. (I) Representative plots and frequency of renal ABCs (CD19+CD11c+) from mice described in (F). (J) H&E staining (left) analysis of kidneys from mice described in (F). Bars indicate mean ± SEM values. Statistical significance determined by Student's t-test.*p<0.05, **P<0.01, ***P<0.001, ns, not significant.

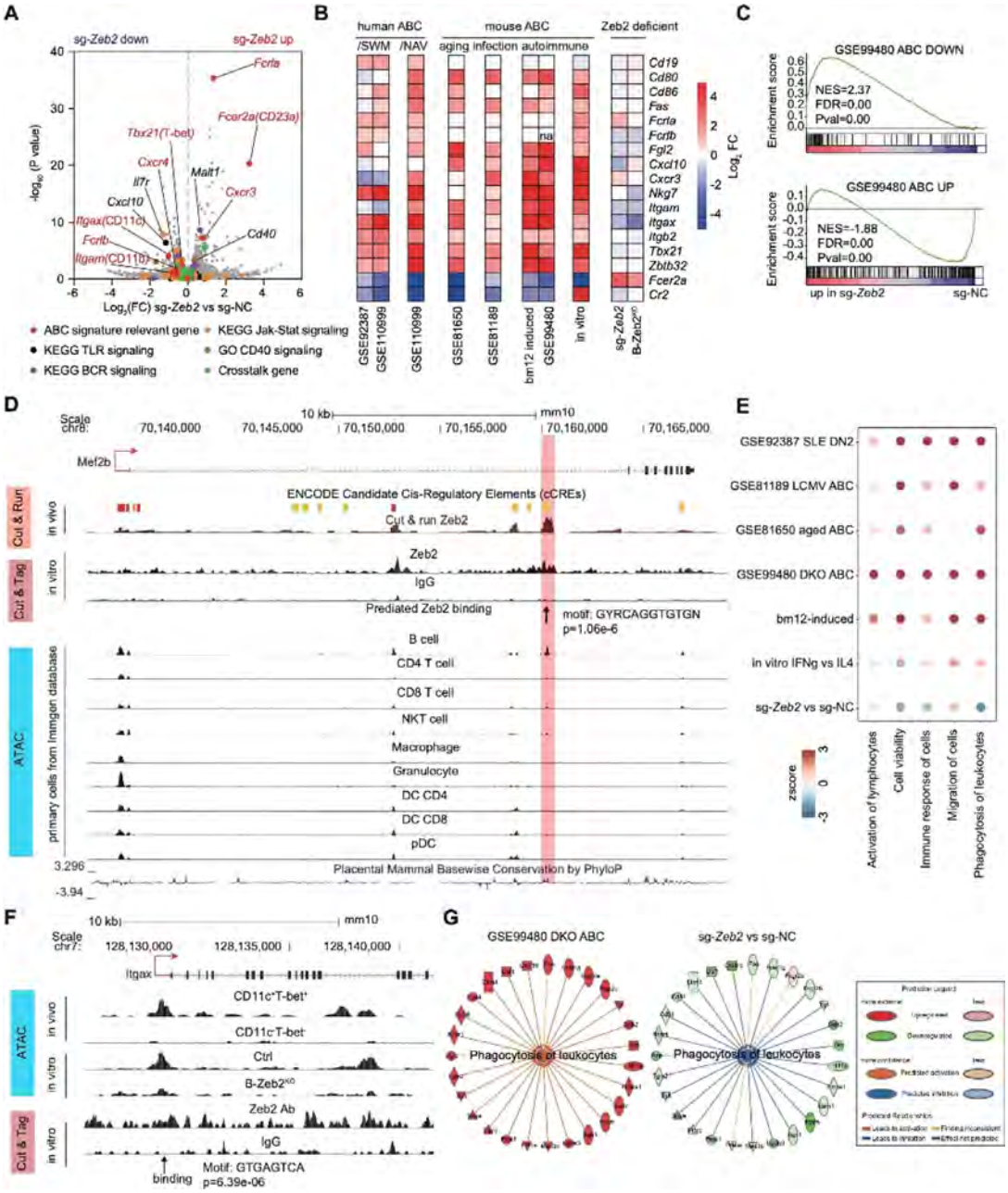


Fig 2. Zeb2 regulates specification and cellular identity of ABCs. (A) Volcano graph showing the transcriptional profiles in mouse B cells edited by sg-NC and sg-Zeb2 under in vitro ABC induction for 3 days. ABC signature relevant genes, genes of BCR, TLR, Jak-Stat signaling, CD40 signaling and crosstalk genes were labeled with colored dots. (B) Heatmap showing expression of representative ABC signature genes in publicly available RNA-seq datasets: GSE92387, GSE110999, GSE81650, GSE81189, GSE99480 and our own RNA-seq datasets: bm12-induced (Splenic CD11c+T-bet+CD21- and CD11c-T-bet-CD21+ B cells were sorted by flow cytometry from T-bet-tdTOMATO reporter mice immunized with bm12 T cells), in vitro (mouse B cells were cultured with ABC-skewing cocktail for 3 days), sg-Zeb2 (described in (A)), B-Zeb2KO (B cells from B-Zeb2KO and Ctrl mice were cultured with ABC-skewing cocktail for 3 days). (C) GSEA showing the enrichment of the ABC-down geneset and ABC-up geneset from DKO mice (GSE99480) in sg-Zeb2 versus sg-NC ABCs. (D) CUT & RUN, CUT & Tag, and ATAC-seq tracks display Zeb2 binding around the Mef2b locus in indicated immune cells, visualized with the UCSC genome browser. The chromatin accessibility of Mef2b in mouse primary immune cell subsets from Immgene database. (E) Chromatin accessibility by ATAC-seq and Zeb2-binding by CUT & Tag in the promoter site of mouse Itgax. ATAC-seq was performed in ex-vivo sorted ABC (CD11c+T-bet+) and non-ABC (CD11c-T-bet-) from bm12-induced mice and in-vitro derived Zeb2-deficient and ctrl B cell cultured for 3 day under ABC skewing condition. (F) Dot plot showing the activation Z-score for IPA-predicated biological function of ABCs including activation, cell viability, immune response, migration and phagocytosis from RNA-seq datasets described as in (B). (G) Network diagram representing phagocytosis pathway in sg-Zeb2 versus sg-NC ABCs by IPA. The color of each node indicates change in the expression: red (upregulated) and green (downregulated). The edges indicate the predicted relationship between nodes and biological function: orange representing activation, blue representing inhibition, gray representing effect not predicted.

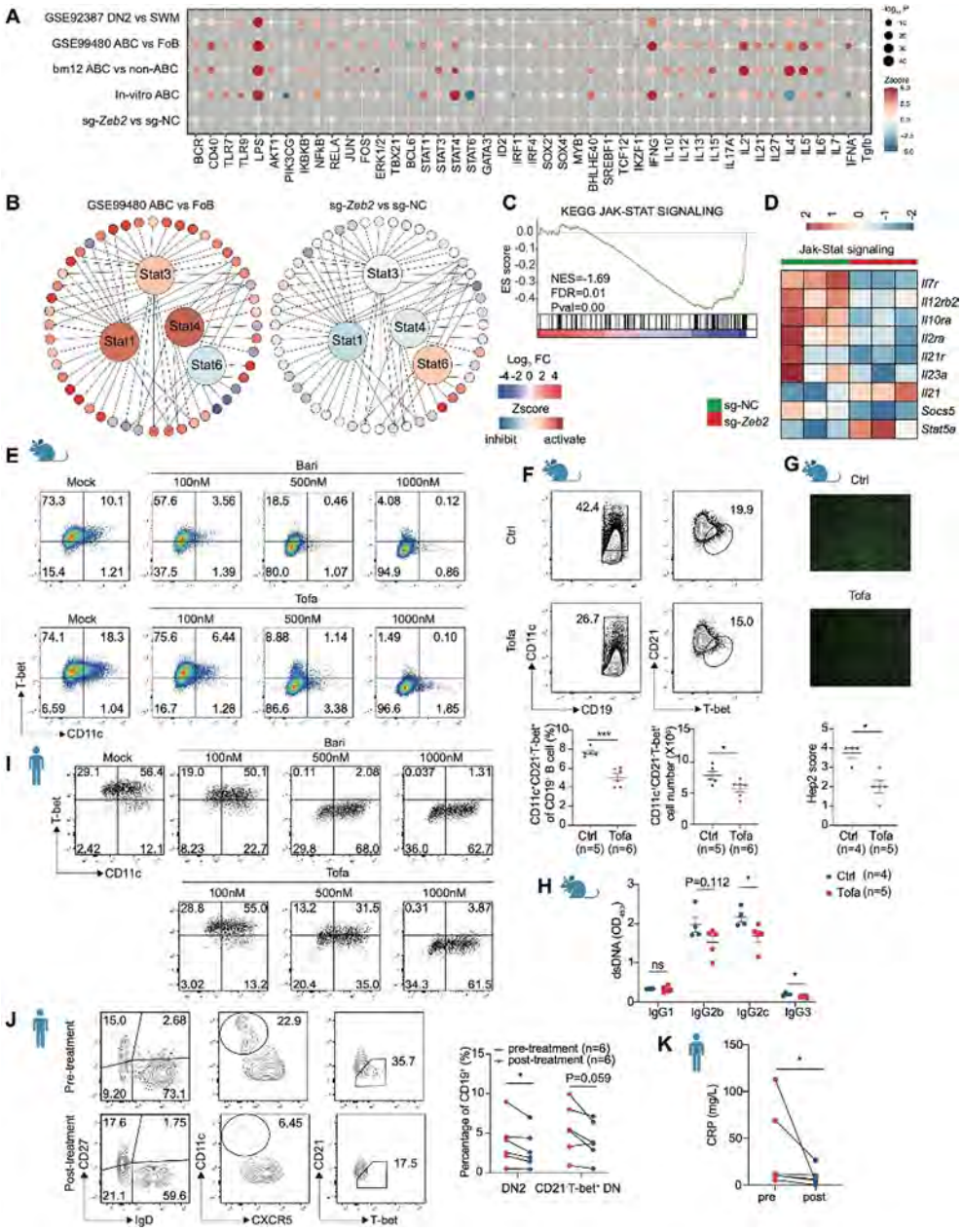


Fig 3. Zeb2-Jak-Stat axis controls ABC differentiation and JAK inhibitor ameliorates ABC formation and autoimmunity. (A) Activation Z-score heatmap for IPA-predicted upstream regulators in indicated datasets mainly described in Fig 2B. P-values were log-normalized and presented by the size of the plot. The color of the plot indicates the activated (orange) or inhibited (blue) regulation of the predicted regulators. (B) Upstream regulator analysis showing Stat1, Stat3, Stat4 activated and Stat6 inhibited in ABCs (DKO, GSE99480), while the opposite effects were observed in sg-Zeb2 vs sg-NC dataset. The color of the surrounding circles indicates the change in the expression: red (upregulated) and blue (downregulated). The color of the center circles indicates predicted regulators: orange (activated) and blue (inhibited). (C) GSEA showing impaired Jak-Stat pathway in sg-Zeb2+ B cells compared with sg-NC. (D) Heatmap showing expression of selected Jak-Stat signaling genes in sg-NC+ and sg-Zeb2+ B cells. (E) Flow cytometry plots of in vitro induced mouse ABCs (CD11c+T-bet+) with different concentrations of baricitinib (Bari) or tofacitinib (Tofa). (F-H) C57 mice were immunized with bm12 T cells for 2 weeks and treated with tofacitinib (Tofa) or dissolved solution (Ctrl) by oral gavage once a day to analyze splenic ABCs (CD19+CD11C+T-bet+CD21-, F), ANA (G) and anti-dsDNA Ig (H) in serum. (I) Flow cytometry plots of in vitro induced human ABCs (CD11c+T-bet+) with different concentration of baricitinib or tofacitinib. (J) Flow cytometry plots of human ABCs (DN2, CD19+CD27-IgD-CD11c+CXCR5-) or (CD21-T-bet+ DN, CD19+CD27-IgD-CD21-T-bet+) in PBMCs from patients with rheumatoid arthritis before and after Jak-Stat inhibitor tofacitinib treatment for 4 weeks. (K) CRP level in RA patients described in (J). n represents distinct samples (biological repeats). Data are representative of 2-3 independent experiments. Data are mean ± SEM values. *p<0.05, **P<0.01, ***P<0.001, ns, not significant, unpaired t-test (F, H), Mann-Whitney test (G), paired t-test (J) and paired Wilcoxon test (K).

Disclosure: D. Dai: None; **S. Gu**: None; **X. Han**: None; **H. Ding**: None; **Y. Jiang**: None; **S. Chen**: None; **N. Shen**: None.

Abstract Number: 0732

Should Complete B-cell Depletion Be Maintained in Patients Treated Long-term with Rituximab for Rheumatoid Arthritis?

Roba Ghossan[1], Omar AL TABAA[2], Alice Combier[3], Alexia STEELANDT[3], Marion THOMAS[3], Olivier Fogel[3], Corinne MICELI[4], Anna Molto[3] and Jérôme Avouac[5], [1]COCHIN HOSPITAL, Paris, France, [2]APHP / Cochin Hospital, Paris, France, [3]HOPITAL COCHIN AP-HP, Service de Rhumatologie, Paris, France, [4]Université de Paris Cité, HOPITAL COCHIN AP-HP, Service de Rhumatologie, Paris, France, [5]Service de Rhumatologie, Hôpital Cochin, AP-HP.Centre – Université Paris Cité, Paris, France

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Complete peripheral B cell depletion has been considered as a relevant indicator of short-term response to rituximab (RTX) in rheumatoid arthritis (RA). The purpose of our study was to determine whether sustained complete B cell (BC) depletion is associated with a better clinical response in RA patients long-term treated with RTX.

Methods: Retrospective routine care study conducted in the Rheumatology department of Cochin hospital. We included consecutive patients fulfilling the ACR/EULAR 2010 classification criteria for RA hospitalized in 2021 for a new RTX infusion. All recruited patients had received at least 3 prior RTX infusions and had disease activity assessment (DAS28 and DAS28-CRP) and CD19 counts (Aquios, Beckman Coulter) available during each of the 4 last infusion visits. The primary endpoint was the evaluation of the disease activity (mean DAS28 and DAS28-CRP) calculated the day of the last 4 infusion

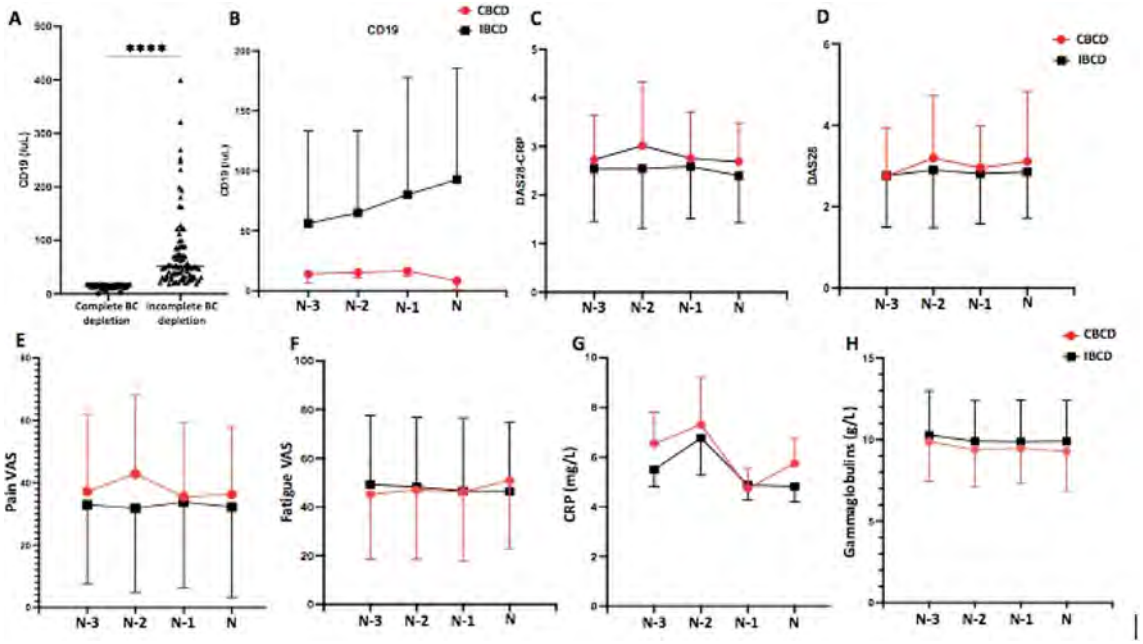


Figure 1: Course of mean (SD) CD19, DAS28, DAS28-CRP, pain and fatigue VAS, CRP and gammaglobulins at the last 4 RTX infusion visits according to sustained complete or incomplete B cell depletion (CBCD and IBCD respectively).

Table 1: Patient and disease characteristics at inclusion according to sustained complete or incomplete B cell depletion.

	Total (n=126)	Complete BC depletion (n=43)	Incomplete BC depletion (n=83)	p-value
Age (years), mean±SD	64±12	63±14	64±11	0.87
Females, n (%)	105 (83)	36 (84)	69 (83)	0.89
Disease duration (years), mean±SD	22±5	21±9	22±11	0.67
Rheumatoid factor, n (%)	110 (87)	34 (77)	76 (92)	0.018
ACPA, n (%)	101 (80)	31 (72)	70 (84)	0.11
Radiographic damage, n (%)	98 (78)	34 (79)	64 (77)	0.80
DAS 28, mean±SD	2.9±1.3	3.1±1.7	2.9±1.1	0.42
DAS28-CRP, mean±SD	2.5±0.9	2.7±0.8	2.4±0.9	0.10
Concomitant treatment, n (%)				
• Methotrexate	67 (53)	19 (45)	48 (58)	0.44
• Corticosteroids	63 (50)	25 (58)	38 (46)	0.20
Previous lines of targeted therapies prior to RTX, n (%)				
0	38 (30)	9 (21)	29 (35)	0.11
1	33 (26)	8 (19)	25 (30)	0.19
2	37 (29)	16 (37)	21 (25)	0.16
>2	18 (14)	10 (23)	8 (10)	0.049
Median duration of RTX exposure (months), mean±SD	76±52	69±47	99±57	0.003
Number of infusions, mean±SD	14±7	12±6	14±7	0.037
Cumulative RTX dose (g), mean±SD	9±6	8±5	10±6	0.010
Median retreatment interval (months), mean±SD	7.5±2	6±1	8±3	0.001

visits, according to the persistence of complete BC depletion (mean CD19 counts of the last 4 visits < 18/mL) or incomplete BC depletion (mean CD19 counts of the last 4 visits ≥18/mL). Secondary endpoints were the frequency of end-of-dose effect and patient self-reported RA flares at each infusion visit, the course of pain/fatigue VAS, CRP and gammaglobulin levels

Results: We included 126 patients with a mean age of 64±12 years and a mean disease duration of 22± 5 years. Only 43 patients (34%) had maintained complete BC depletion during the last 4 infusions (mean CD19 counts 13±4/mL) (Figure 1A-B). Patients with incomplete BC depletion (n=83, mean CD19 counts: 77±73/mL, p< 0.001) did not differ from those who maintained complete BC depletion in terms of age, gender, disease duration, structural damages and concomitant treatment. Patients with incomplete BC depletion had received RTX for a longer period (99±57 months vs. 69 ±47 months, p=0.003), with significantly higher number of infusions (14±7 vs. 12±6 infusions, p=0.037) and increased cumulative dose (10±6 g vs. 8±5 g, p=0.10) compared to patients with sustained complete BC depletion. On the other hand, their interval between 2 infusions was significantly longer (8±3 months vs. 6±1 months, p< 0.001). The course of DAS28 and DAS28-CRP during the last 4 infusions was not different between the 2 groups (Figures 1C-D). The mean DAS28 and DAS28-CRP calculated at the time of last 4 infusion visits did not differ between patients with incomplete or sustained complete BC depletion (DAS28: 2.71±1.06 vs. 3.01±1.10, p=0.33 and DAS28-CRP: 2.53±0.88 vs. 2.88±0.84, p=0.095). Secondary outcomes were similar between the 2 groups (Figures 1E-H).

Conclusion: While it is associated with a better response to RTX at the start of treatment, the persistence of complete BC depletion is not associated with better efficacy of RTX in RA patients receiving this treatment over the long term. There is a limited benefit of monitoring CD19 in RA patients long term treated with RTX and having achieved low disease activity/remission. During the COVID-19 pandemic, this data is all the more important as the humoral anti-SARS-CoV-2 vaccine response is preferentially obtained in patients with incomplete BC depletion.

Disclosure: R. Ghossan: None; **O. AL TABAA**: None; **A. Combier**: None; **A. STEELANDT**: None; **M. THOMAS**: None; **O. Fogel**: None; **C. MICELI**: None; **A. Molto**: None; **J. Avouac**: AbbVie, 6, AstraZeneca, 6, Biogen, 6, BMS, 5, 6, Fresenius Kabi, 5, 6, Galapagos, 5, 6, Janssen, 6, Lilly, 6, Medac, 6, MSD, 6, Nordic Pharma, 6, Novartis, 6, Novartis (Dreamer), 5, Pfizer, 6, Pfizer (Passerelle), 5, Roche-Chugai, 6, Sandoz, 6, Sanofi, 6.

Abstract Number: 0733

Global Identification of Lupus Genetic Risk Variants Facilitating the Type I Interferon Pathway Through CRISPR-based Genomic Screening

Guojun Hou[1], Xinyi Zhu[1], Yutong Zhang[1], Zhaorui Cheng[1] and **Nan Shen**[2], [1]Shanghai Institute of Rheumatology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University (SJTUSM), Shanghai, China, [2]Shanghai Jiao Tong University School of Medicine, Shanghai, China

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Genetics, Genomics & Proteomics
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Genome-Wide Association Studies (GWAS) have unveiled over 1000 risk variants for lupus, predominantly situated in non-coding genomic regions. Their functional roles, especially their potential impacts on the dysregulated type I interferon pathway inherent in lupus, remain largely uncharted. To bridge this knowledge gap, our study employs CRISPR/Cas9 technology, enabling a deeper exploration into the functional implications of these risk loci.

Methods: Our novel strategy entailed CRISPR-based screening for functional variants that regulate the type I interferon pathway. We collected all known SLE-associated SNPs and expanded them through linkage disequilibrium in the population where the SNP was reported. We designed an sgRNA library covering these SLE-associated SNPs and developed a

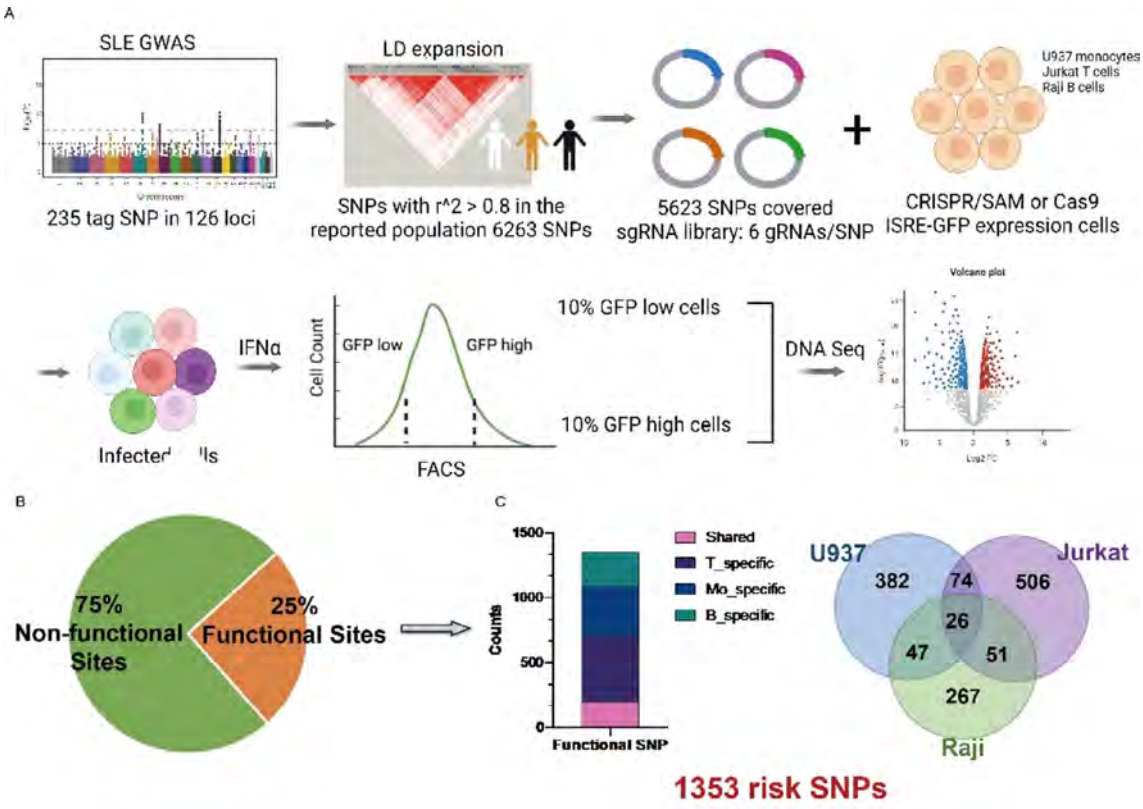


Figure 1. Functional Variant Screening for Regulation of Type I Interferon Pathway Activation Using CRISPR/SAM and CRISPR/Cas9 Across Various Immune Cells. (A) A depiction of the CRISPR screening workflow. (B) Representation of the proportion of functional regions implicated in the modulation of the type I interferon pathway. (C) Evaluation of functional variant regions that are common or specific to individual cell types.

cellular model using U-937, Jurkat, and Raji cells that stably express the CRISPR/Cas9-ISRE-GFP and CRISPR/SAM-ISRE-GFP systems. Post-transduction with the sgRNA lentiviral library, we sorted cells based on GFP intensity and extracted and sequenced DNA from these sorted cells. The functional variants were identified and characterized using multi-omics analysis (eQTL data, HiC data, RNA-sequencing data). We validated the function of the rs11152966-located region and identified PRDM1 as the target gene of rs11152966 through integration of advanced technologies like capture-HiC, CRISPR-SAM, and prime editing technology.

Results: We've characterized the comprehensive landscape of functional SNPs related to lupus that regulate the Type I interferon pathway. Notably, we discovered that the majority of these functional variant regions are cell type-specific .Utilizing the CRISPR/Cas9 and CRISPR/SAM systems effectively, we found these tools to have complementary benefits in the identification of these functional variants. Furthermore, these functional variant regions were found to be associated with the expression of critical regulators within the JAK-STAT pathway and interferon-stimulated genes (ISGs). Importantly, we observed a correlation between the expression of transcription factors disrupted by these functional variants and the expression of ISGs in SLE patients. One standout finding was the negative regulatory effect on the Type I interferon pathway upon activation of the region

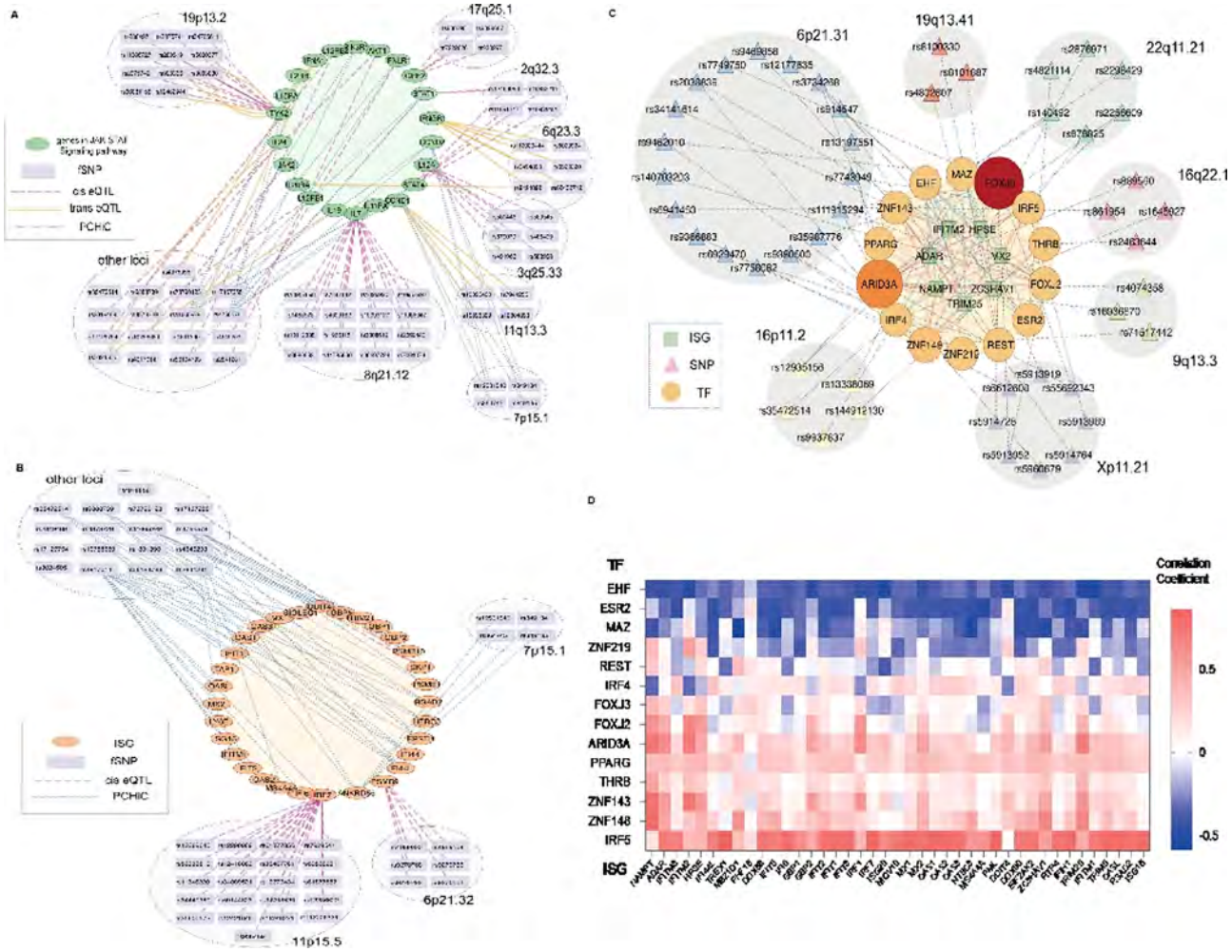


Figure 2. Annotation of SNP-Target Gene-TF Interaction Network and Their Role in the Interferon (IFN) Pathway (A-B) Illustrates the interconnection of functional SNPs and associated genes in the JAK-STAT signaling pathway and ISGs, with lines denoting eQTL signals or 3D genomic interactions. Gene size and color correspond to differential expression results in SLE patients. (C) Shows a network of functional SNPs, disrupted TFs due to SNP, and ISGs with significant correlation to these TFs. Gray lines suggest disruption of TF binding motifs by SNPs. Blue and red lines indicate negative and positive correlations between ISGs and TFs, respectively. TF size and color display its degree or interaction count, as determined by Cytoscape. (D) Demonstrates Spearman correlation analysis between transcription factors and ISGs expression levels (RPKMs) in whole blood samples from SLE patients.

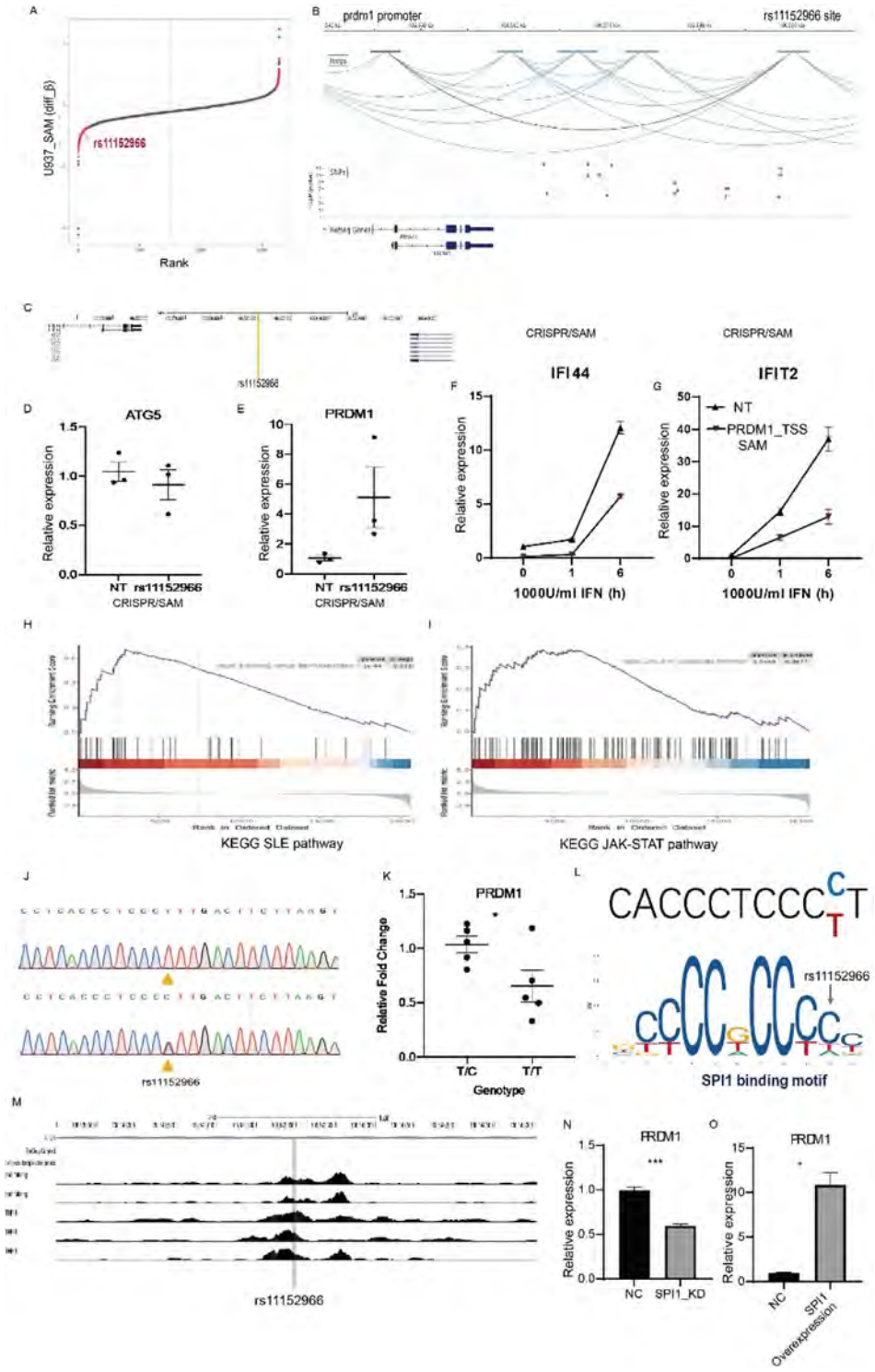


Figure 3. PRDM1 expression is regulated by rs11152966, contributing to the modulation of the type I interferon pathway. (A) A region containing rs11152966, revealed by CRISPR screening, inhibits the activation of the type I interferon pathway. (B) Gene loop between the rs11152966 location and PRDM1 promoter, as evidenced by HiC data. (C-E) CRISPR/SAM targeting the area containing rs11152966 boosts PRDM1 expression, but not the adjacent gene ATG5. (F-G) Targeting of the PRDM1 TSS region by CRISPR/SAM results in reduced ISGs expression. (H-I) Analysis by GSEA of JAK-STAT and SLE pathways in PRDM1 KO U-937 cells post-IFNα stimulation for 1 hour. (J) Genotype of rs11152966 in cell clones established by prime editing technology. (K) The T risk allele of rs11152966 results in diminished PRDM1 expression compared to the C non-risk allele. (L) SPI1 has a preference for binding to the non-risk C allele of rs11152966. (M) ChIP-seq data indicate SPI1 binding within the rs11152966 region. (N-O) PRDM1 expression following SPI1 overexpression or knockdown.

containing the SNP rs11152966. This region, inclusive of the SNP, forms a gene loop with the PRDM1 promoter, thereby managing PRDM1 expression. Additionally, we provided evidence that PRDM1 acts as a novel negative regulator of the Type I interferon pathway. Lastly, our research revealed a link between the presence of the risk allele T and a reduction in PRDM1 expression. This reduced expression appears to be due to the allele T's effect on the binding of the transcription factor SPI1.

Conclusion: Our study leveraged advanced gene-editing tools to elucidate the landscape of functional SNPs in lupus, revealing their cell type-specific regulation of the Type I interferon pathway and their influence on key genes in the JAK-STAT pathway. Notably, we highlighted the significant role of SNP rs11152966 and its target gene PRDM1 in regulating the interferon pathway in lupus.

Disclosure: G. Hou: None; **X. Zhu**: None; **Y. Zhang**: None; **Z. Cheng**: None; **N. Shen**: None.

Abstract Number: 0734

Immune Isoform Atlas: Landscape of Alternative Splicing in Human Immune Cells and Involvement of Dysregulated Alternative Splicing in Autoimmune Diseases

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Genetics, Genomics & Proteomics
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Alternative splicing events play a critical role in the immune system[1,2] and one of major causal mechanisms for complex traits including immune-mediated diseases (IMDs), but they have been understudied due to the limitation of the short-read sequencing technology[3,4]. With the emergence of long-read sequencing, large-scale projects have aimed to reconstruct full-length transcripts; however, existing studies focusing on whole blood cells or lymphoblastoid cell lines[5,6]. The profiling of isoforms by cell types will help elucidate complicated immune system networks and unknown pathogenesis of IMDs.

Methods: We isolated 29 immune cell subsets from the peripheral blood cells of a healthy donor (42 years-old female) (Figure 1A). cDNA libraries were made from the poly(A) mRNA, PCR amplified, and subjected to long-read sequencing using the MinION. After mapping raw reads and quality control steps, we generated the atlas containing the full-length of isoforms.

Results: Our atlas (Immune Isoform Atlas) contained a total of 159,369 isoforms transcribed from 17,496 genomic loci. We discovered novel isoforms such as a read-through transcript from the TOMM40-APOE locus, known as the Alzheimer's disease locus (Figure 1B). Further, we identified disease-associated isoforms by remapping short-read RNA-seq datasets from

SLE[7], RA[8] individuals and relevant controls to the Immune Isoform Atlas (isoform switch analysis). For SLE, we identified 84 genes whose isoform fractions were significantly switched between SLE and healthy individuals (false discovery rate < 0.05). For example, the expression of the known isoform of IRAK1 (ENST 00000393687.6) with a protein kinase domain

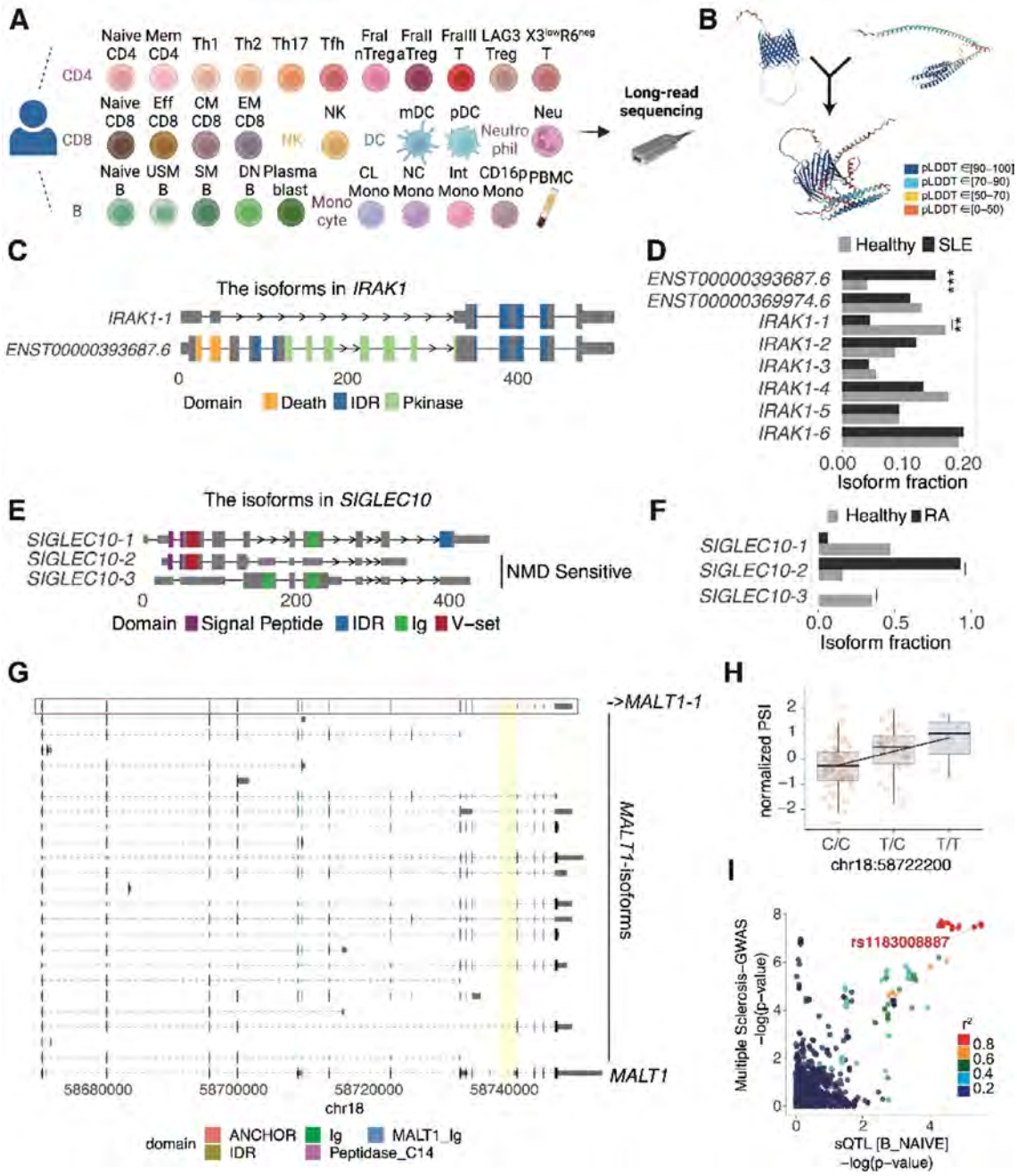

Figure 1. Overview of the Immune Isoform Atlas. (A) Summary of the cell subsets included in long-read RNA sequencing in our study. (B) Protein 3D structures of TOMM40 (left), APOE (right), and the read-though isoform (bottom) predicted using AlphaFold2. pLDDT is a per-residue estimate of its confidence on a scale from 0 - 100. Regions with pLDDT > 90, between 70 and 90, between 50 and 70, and < 50 are expected to be high accuracy, well (a generally good backbone prediction), low confidence, and a reasonably strong predictor of disorder, respectively. (C) Structures of isoforms transcribed from the IRAK1 locus. The x-axis shows distance from the TSS. (D) Isoform fractions in IRAK1 in SLE and healthy individuals. The significance of comparison is as follows: ***, p<0.001; **, p<0.01; *, p<0.05. (E) Structures of isoforms transcribed from the SIGLEC10 locus. (F) Isoform fractions in SIGLEC10 in RA and healthy individuals. (G) Structures of isoforms transcribed from MALT1. The collapsed gene structure registered in GENCODE is shown at the bottom. (H) sQTL plot of normalized PSI of the unique junction (chr18:58739121-58741865, highlighted in yellow in Figure 1G) in the related isoform (MALT1-1, highlighted in red in Figure 1G) in naïve B cells. (I) Colocalization plot of sQTL and GWAS of multiple sclerosis.

increased in SLE individuals compared to controls, while the novel IRAK1-1 without this domain decreased (Figure 1C-D). As to RA, we found that one of the novel isoforms in SIGLEC10 being sensitive to nonsense-mediated mRNA decay was more highly expressed in RA compared to controls (Figure 1E-F). Finally, to investigate disease-causal isoforms, we evaluated the colocalization between loci identified by Genome-Wide Association Studies (GWAS) for autoimmune diseases and splicing quantitative trait loci (sQTL) signals using coloc[9]. Among them, an SNP in MALT1 (rs11873030), which was associated with multiple sclerosis[10], had an sQTL effect for a junction read unique to MALT1-1; this isoform decreased with the risk allele for the disease (Figure 1G-I).

Conclusion: Our atlas, obtained by long-read RNA sequencing of 29 immune cell subsets, provided a comprehensive full-length isoform profiling in the human primary immune cells. Our atlas will help reveal unknown pathogenic mechanisms via alternative splicing.

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Deep Immunophenotyping Reveals Circulating Activated Lymphocytes in Individuals at Risk for Rheumatoid Arthritis

Jun Inamo[1], Joshua Keegan[2], Alec Griffith[2], Tusharkanti Ghosh[3], Alice Horisberger[2], Kaitlyn Howard[2], John Pulford[2], Ekaterina Murzin[2], Brandon Hancock[2], Jennifer Seifert[4], Marie Feser[4], Jill Norri[5], Anna Helena Jonsson[6], Ye Cao[7], William Apruzzese[8], S. Louis Bridges[9], Vivian Bykerk[10], Susan Goodman[9], Laura Donlin[9], Gary S Firestein[11], Harris Perlman[12], Joan Bathon[13], Laura Hughes[14], Darren Tabechian[15], Andrew Filer[16], Costantino Pitzalis[17], Jennifer Anolik[15], Larry Moreland[18], Joel Guthridge[19], Judith James[19], Michael Brenner[2], Soumya Raychaudhuri[6], Jeffrey Sparks[20], The Accelerating Medicines Partnership RA/SLE Network[21], Michael Holer[4], kevin Deane[4], James Lederer[2], Deepak Rao[6] and Fan Zhang[22], [1]University of Colorado School of Medicine, Aurora, CO, [2]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [3]School of Public Health, University of Colorado, Anschutz Medical Campus, Aurora, CO, [4]University of Colorado Anschutz Medical Campus, Aurora, CO, [5]Colorado School of Public Health, Denver, CO, [6]Brigham and Women's Hospital, Boston, MA, [7]Brigham and Women's Hospital, Boston, MA, [8]Accelerating Medicines Partnership® Program: Rheumatoid Arthritis and Systemic Lupus Erythematosus (AMP® RA/SLE) Network, Boston, MA, [9]Hospital for Special Surgery, New York, NY, [10]Department of Rheumatology, Hospital for Special Surgery, New York, NY, [11]Department of Medicine, University of California San Diego, La Jolla, CA, [12]Northwestern University, Chicago, IL, [13]Columbia University, New York, NY, [14]University of Alabama at Birmingham Medicine, Birmingham, AL, [15]University of Rochester Medical Center, Rochester, NY, [16]University of Birmingham, Birmingham, United Kingdom, [17]Queen Mary University of London, London, United Kingdom, [18]University of Colorado, Denver, CO, [19]Oklahoma Medical Research Foundation, Oklahoma City, OK, [20]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [21]The Accelerating Medicines Partnership RA/SLE Network, [22]University of Colorado, Aurora, CO

SESSION INFORMATION

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Session Title: Abstracts: Genetics, Genomics & Proteomics

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a systemic autoimmune disease with currently no effective prevention strategies. Single-cell technologies have been used to investigate established RA heterogeneity (1), but it is unknown if the immune populations identified from RA tissues play important roles in blood during the preclinical phase of disease. Thus, identifying pathogenic immune phenotypes in individuals who are at risk for future RA, designated "At-Risk RA", is crucial to establishing prevention strategies.

Methods: We applied mass cytometry to deeply characterize immunophenotypes in PBMCs (peripheral blood mononuclear cells) from At-Risk individuals based on the presence of antibodies to citrullinated protein antigens (ACPA) and/or first-degree relative (FDR) status (n=52), established RA (n=67), and healthy controls (n=48) (Figure 1). We performed co-varying neighborhood analysis to characterize immunophenotypes in At-Risk individuals and identify phenotypical changes between At-Risk subpopulations accounting for batch effect, age, sex, and inter-individual variation. We further developed an "RA immunophenotype score" for cross-phenotype classification using mixed-effect modeling and logistic regression.

Results: We quantified the immune populations and uncovered significant cell expansions in At-Risk individuals compared with controls (p = 6e-3), including CCR2+CD4+ effector memory T cells (TEM) (OR = 1.47), T peripheral helper cells (Tph) (OR = 1.30), type 1 T helper cells (OR = 1.31), and CXCR5+CD8+ T cells (OR = 3.33) (Figure 2A-B). We further confirmed the expansions of these T cell phenotypes in the At-Risk individuals using our validation cohort with 57 At-Risk and 23 healthy individuals. In addition, we found that CD15+ classical monocytes were especially expanded in ACPA-negative At-Risk individuals who had FDR (p = 1e-3, OR = 1.30), and an activated PAX5low naïve B cell population expanded in ACPA-positive individuals who also had an FDR with RA (p = 9e-3, OR = 1.35). Further, we demonstrated that our "RA immunophenotype score" classification method built based on the degree of enrichment and the abundance of cell states relative to established RA (adjusted p < 0.05) (Figure 3A) is able to significantly distinguish At-Risk individuals from the control (p = 0.039, AUC >0.6) (Figure 3B-C).

Conclusion: We systematically characterized altered circulating immune phenotypes in At-Risk individuals, along with immunophenotypical differences among ACPA+ and FDR At-Risk subpopulations. Our classification model may provide a promising approach for understanding the pathogenesis of preclinical RA with the goal to develop preventive strategies and novel therapeutic targets.

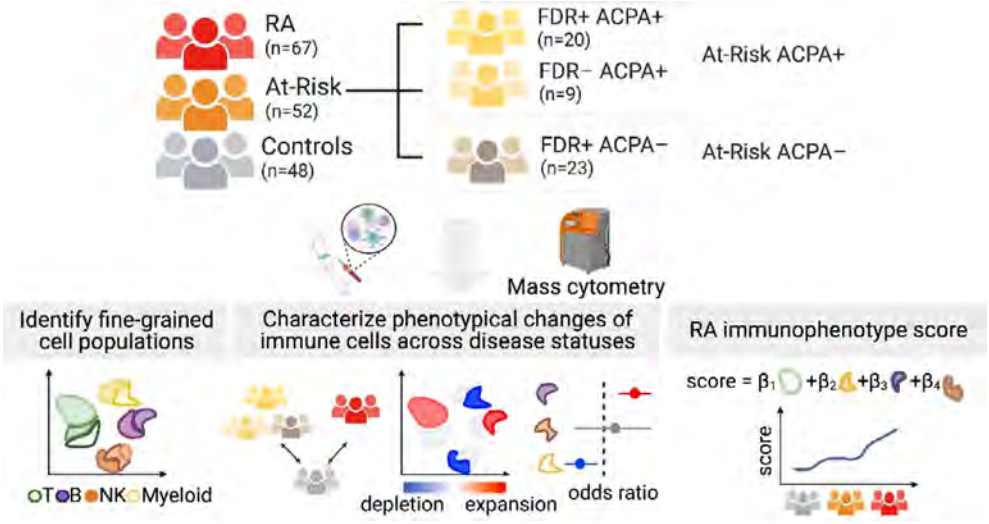

Fig.1: Overview of mass cytometry analytical strategy, clustering, and classifications for At-Risk RA and established RA individuals.

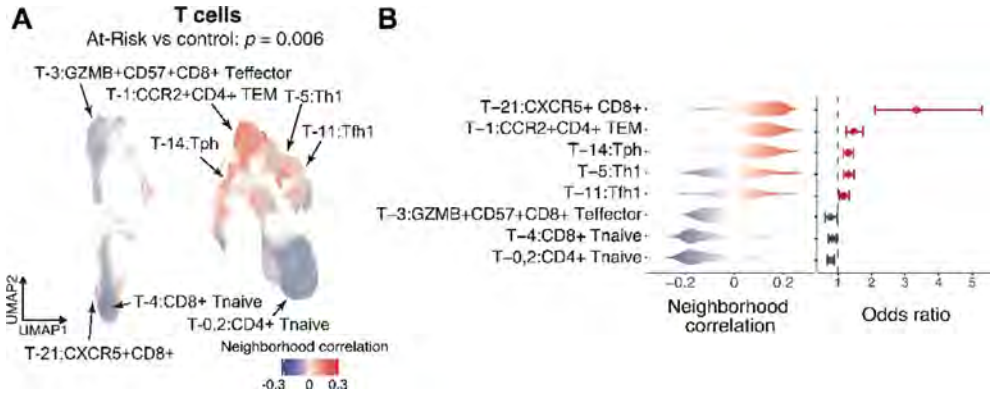

Fig.2: Identifications of specific T cell populations that were associated with At-Risk. A. Cells in UMAP are colored in red (expansion) or blue (depletion) and p-value is shown as well. B. Distributions of cell neighborhood correlations and odds ratio. Error bars represent 95% confidence intervals.

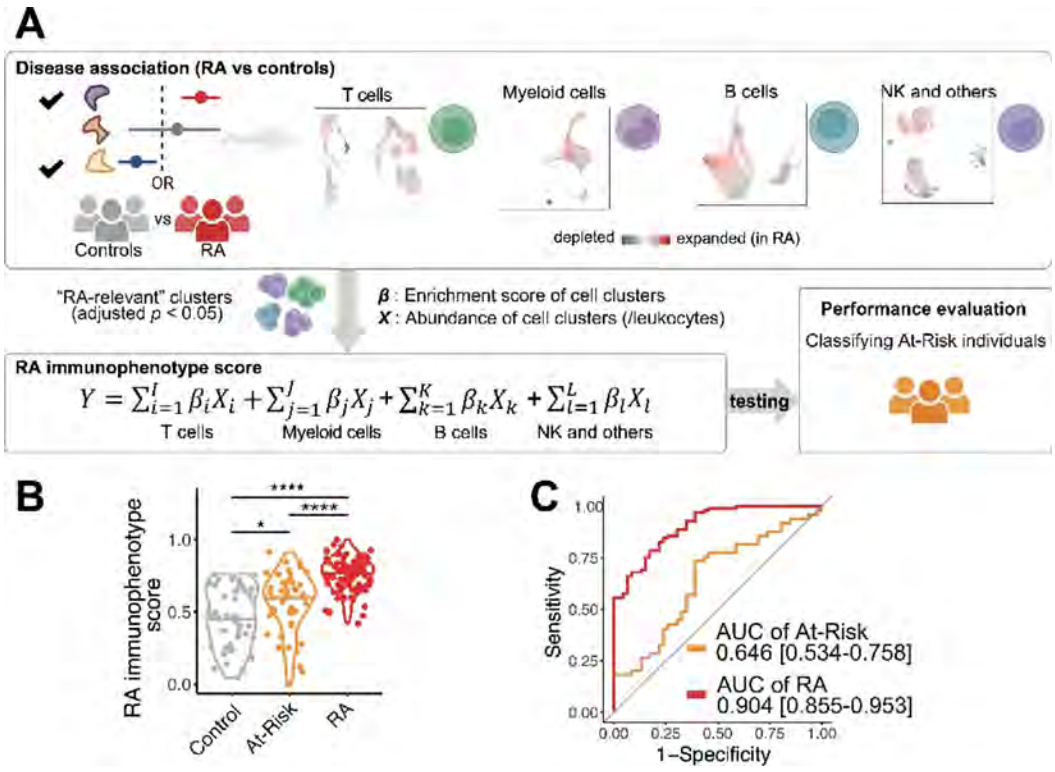

Fig.3: Classifications for At-Risk individuals and established RA individuals. A. RA immunophenotype score utilizing RA-specific cell type abundances to quantify and distinguish At-Risk individuals from control. For each cell type, all p-values from the covarying neighborhood analysis test were p = 1e-3. We incorporated clusters that are significantly associated with RA (adjusted $p < 0.05$) to model the RA immunophenotype score. We calculated RA immunophenotype score based on cell type abundances multiplied by corresponding major cell type proportions and enrichment scores for each cell type, B. Distribution of RA immunophenotype score across individual samples from RA, At-Risk, and controls; **** $p < 0.0001$, * $p < 0.05$, C. Receiver operating characteristic (ROC) analysis to evaluate the classification performance of RA immunophenotype score in distinguishing At-Risk from control. Areas under the curve (AUC) with 95% confidence intervals were described. All the analyses are adjusted for age and sex.

References:

1. Zhang, F. et al. Cellular deconstruction of inflamed synovium defines diverse inflammatory phenotypes in rheumatoid arthritis. bioRxiv (2022) doi: https://doi.org/10.1101/2022.02.25.481990

Disclosure: J. Inamo: None; **J. Keegan**: None; **A. Griffith**: None; **T. Ghosh**: None; **A. Horisberger**: None; **K. Howard**: None; **J. Pulford**: None; **E. Murzin**: None; **B. Hancock**: None; **J. Seifert**: None; **M. Feser**: None; **J. Norri**: None; **A. Jonsson**: None; **Y. Cao**: None; **W. Apruzzese**: Pfizer, 3; **S. Bridges**: None; **V. Bykerk**: AbbVie, 2, Bristol Myers Squibb, 1, 2, 5, Pfizer, 1, 2; **S. Goodman**: NIH, 5, Novartis, 5; **L. Donlin**: Bristol-Myers Squibb(BMS), 2, Stryker, 2; **G. Firestein**: Eli Lilly, 5; **H. Perlman**: None; **J. Bathon**: None; **L. Hughes**: None; **D. Tabechian**: amgen, 12, share holder; **A. Filer**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 5, Janssen, 5, Nascient, 5, Sonoma Biotherapeutics, 2; **C. Pitzalis**: None; **J. Anolik**: None; **L. Moreland**: Boehringer-Ingelheim, 12, member of independent Data Safety Monitoring Board, Celltrion, 12, member of independent Data Safety Monitoring Board; **J. Guthridge**: None; **J. James**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 2, Novartis, 2, Progentec Biosciences, 5; **M. Brenner**: 4FO Ventures, 2, GlaxoSmithKlein(GSK), 2, Mestag Therapeutics, 2, 8, Third Rock Ventures, 2; **S. Raychaudhuri**: AbbVie, 6, Janssen, 1, Mestag, Inc, 2, 8, Pfizer, 1, Sanofi, 1, Sonoma, 1, 8; **J. Sparks**: AbbVie, 2, Amgen, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, 5, Gilead, 2, Inova Diagnostics, 2, Janssen, 2, Optum, 2, Pfizer, 2, ReCor, 2; **T. RA/SLE Network**: None; **M. Holer**: None; **k. Deane**: Bristol-Myers Squibb(BMS), 1, Gilead, 5, Janssen, 5, Werfen, 1, 12, Biomarker kits; **J. Lederer**: None; **D. Rao**: AstraZeneca, 2, Bristol-Myers Squibb, 2, 5, GlaxoSmithKlein(GSK), 2, Hifibio, 2, Janssen, 5, Merck, 5, Scipher Medicine, 2; **F. Zhang**: None.

Abstract Number: 0736

Deciphering Complement System-dependent Cellular Pathways in Human Rheumatoid Arthritis Synovial Tissue Using Large Single-cell Computational Omics

Juan Vargas[1], Ian Mantel[2], Nirmal Banda[1], Anna Helena Jonsson[3], Kevin Wei[4], Deepak Rao[3], Susan Goodman[5], kevin Deane[1], Jennifer Seifert[1], Jennifer Anolik[6], Michael Brenner[4], Soumya Raychaudhuri[3], Accelerating Medicines Partnership (AMP) RA/SLE Network[7], Michael Holer[1], Laura Donlin[5] and **Fan Zhang**[8], [1]University of Colorado Anschutz Medical Campus, Aurora, CO, [2]Weill Cornell Medicine, New York, NY, [3]Brigham and Women's Hospital, Boston, MA, [4]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [5]Hospital for Special Surgery, New York, NY, [6]University of Rochester Medical Center, Rochester, NY, [7]the Accelerating Medicines Partnership (AMP) RA/SLE Network, Boston, MA, [8]University of Colorado, Aurora, CO

SESSION INFORMATION

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Session Title: Abstracts: Genetics, Genomics & Proteomics

Session Type: Abstract Session

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Background/Purpose: The complement system is a major component of innate immunity and plays a vital role in autoimmune disease pathogenesis. In patients with rheumatoid arthritis (RA), complement activation proteins generated in the synovium can interact with macrophages and other cell types. However, it remains to be determined how complement components directly modulate cell-type functions in the RA synovium to influence phagocytosis and inflammation resolution.

Methods: We have classified the spectrum of RA biopsies into six tissue phenotypes called CTAPs (Cell Type Abundance Phenotypes) using a comprehensive synovial single-cell multimodal atlas (>314,000 cells, 28 treatment naïve, 27 Methotrexate and 15 TNF inadequate responders) generated from the AMP RA/SLE (1). In this current study, we linked single-cell transcriptomics of complement activation pathway components and receptors with cell-type heterogeneity and tested significant associations with different tissue phenotypes using unsupervised clustering and network analysis. Next, we characterized myeloid cell differentiation using single-cell trajectory analysis and aligned complement gene expression to myeloid functional states. Furthermore, we utilized cell-type interactome analysis to explore whether complement-dependent receptor-ligand pairs are likely to contribute to tissue pathology.

Results: We generated a complement cellular graph characterizing interactions between complement components and cell-type patterns in RA synovium. The complement components present unexpected distinct transcriptomic expression across cell types (**Figure 1A**). We next systematically captured the relationship between tissue phenotypes with specific complement gene expression (**Figure 1B**). Within myeloid cells, we identified a myeloid cell differentiation axis revealing that functional macrophage modules align with complement pathways; in particular, complement *FCN1* and *CFP* co-vary with the *IL1B*+ pro-inflammatory macrophages (p < 2e-16; R=0.48), while complement *C1QA-C* and *C3AR1* co-vary with the *MERTK*+ phagocytic macrophages (p < 2e-16; R=0.7) (**Figure 2**). Intriguingly, we revealed that the abundance of complement-dependent receptor-ligand (C3AR1-C3 and C5AR2-C5) are correlated across patients (**Figure 3A**), and interactome analysis further suggests a potential interaction between the *C3AR1* highly expressed *MERTK*+ macrophages and *C3* highly expressed sublining fibroblasts in a particular RA synovial phenotype that relatively lacks lymphocytes (**Figure 3B**).

Conclusion: Through systematically aligning complement pathways with synovial heterogeneity, we generated a graph describing how complement components can modulate functional cells, especially macrophage phenotypes, in stratified RA patients. This approach of analyzing high-resolution single-cell data in human synovium brings insights into complement pathway-based targets and mechanisms to evaluate in patients with RA, and provides a roadmap for other complex pathways in tissues.

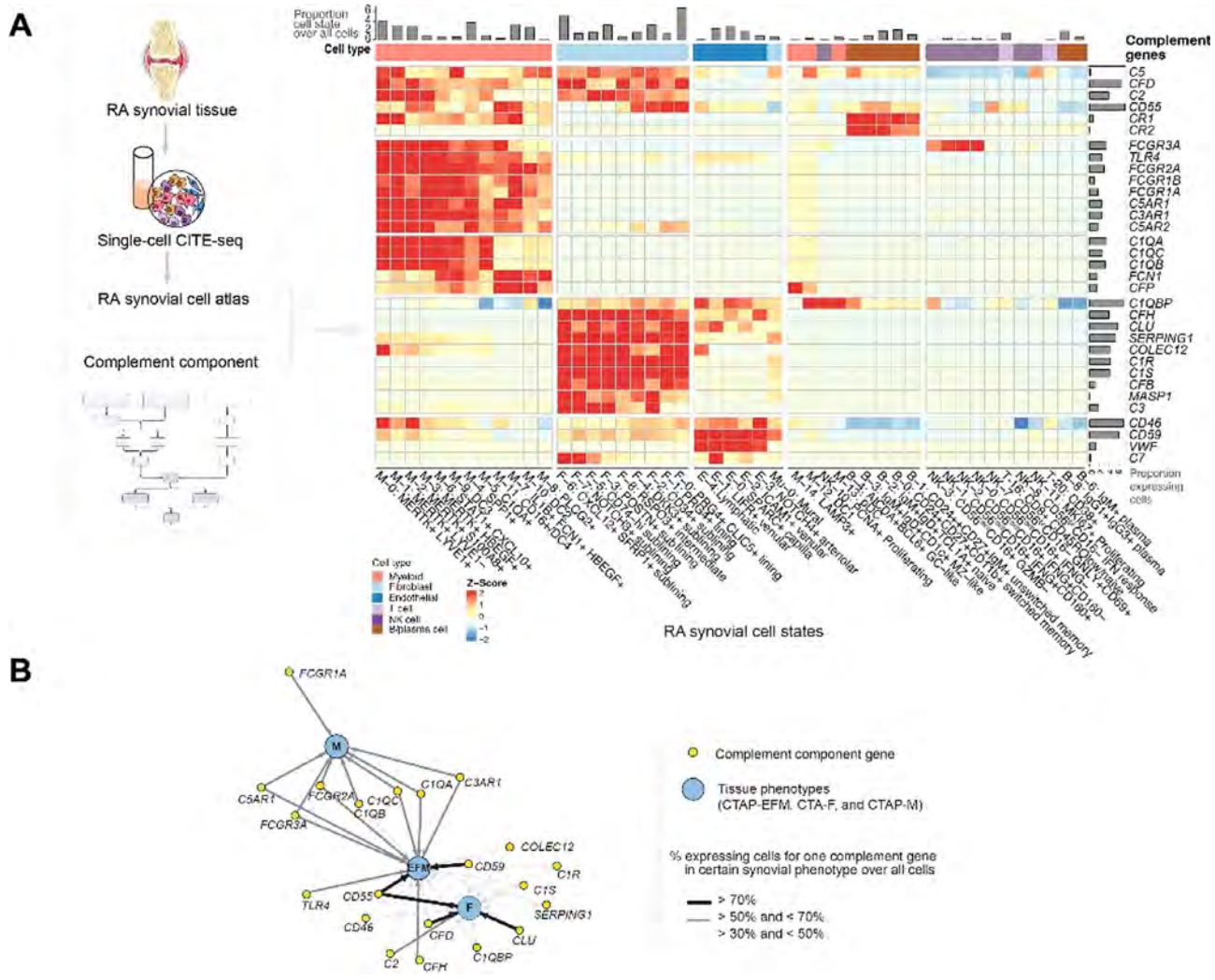

Fig. 1. Single-cell expression distributions of complement components across cell types in rheumatoid arthritis synovial tissues (A). Different myeloid, fibroblast and endothelial cell states express different complement components. Relationship between complement components and RA synovial tissue phenotypes (B).

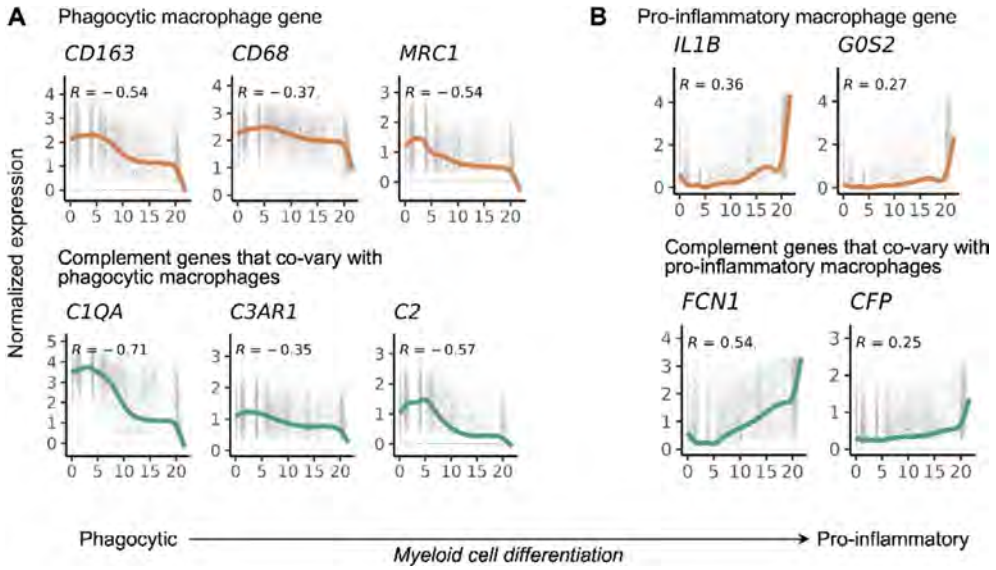

Fig. 2. Myeloid-specific single-cell trajectory analysis revealed a myeloid cell differentiation trajectory from phagocytic to pro-inflammatory lineage. Complement components C1QA-B, C3AR1, and C2 expressions correlated with anti-inflammatory/phagocytic functions (A); complement components FCN1 and CFP expressions correlated with pro-inflammatory function (B). Spearman correlation R and p-value are shown.

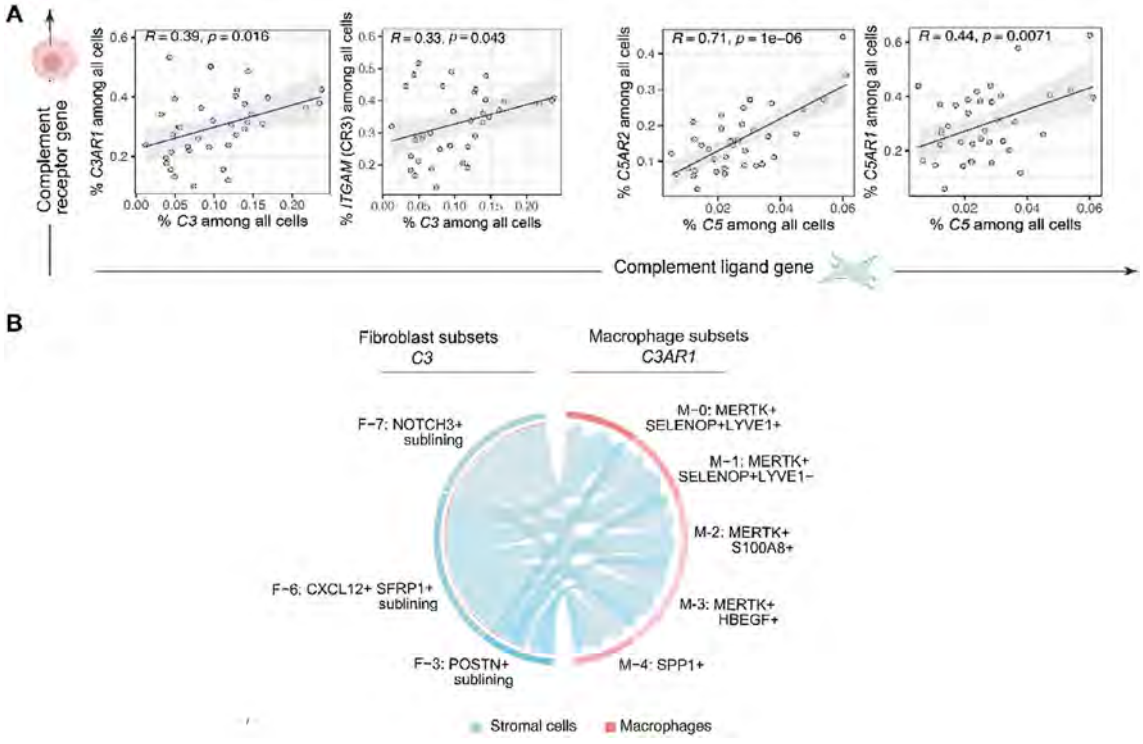

Fig. 3. Across cell type analyses revealed complement-development receptor-ligand correlations (A) and potential complement pathway-dependent C3+ sublininig fibroblasts and MERTK+ tissue macrophages interacting patterns in stratified RA tissues (B). Spearman correlation and p-value are shown.

References.

1. Zhang, F. *et al*. Cellular deconstruction of inflamed synovium defines diverse inflammatory phenotypes in rheumatoid arthritis. *bioRxiv* 2022 doi:10.1101/2022.02.25.481990.

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Abstract Number: 0737

Unraveling Pathophysiology and Hematopoiesis of VEXAS Syndrome by Multi-omics Analysis and Targeted Gene Editing

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SESSION INFORMATION

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Background/Purpose: VEXAS syndrome is an adult-onset, X-linked, life-threatening, autoinflammatory and hematological disease caused by somatic mutation in *UBA1* gene. To understand its pathophysiology, we aimed to achieve a molecular and phenotypic characterization of hematopoiesis of VEXAS patients and to develop cellular and humanized mouse models by gene editing.

Methods: Six VEXAS patients (p.Met41 >Thr; p.Met41 >Val; p.Met41 >Leu; c.118-1 G >C) were recruited from our Unit. Variant allele frequency (VAF) of *UBA1* mutant cells was quantified by targeted sequencing in isolated hematopoietic lineages and hematopoietic stem/progenitor cells (HSPCs). Multiparametric immunophenotypic analysis was performed on peripheral blood and bone marrow (BM), focusing on HSPCs. Circulating monocytes were analyzed by whole RNA-seq and metabolome analysis. Healthy age and sex-matched controls were included. To introduce UBA1 mutations and develop VEXAS models, cutting-edge gene editing technologies were adopted in healthy human HSPCs.

Results: Targeted sequencing in VEXAS patients showed >0.8 VAF in HSPCs. Conversely, VAF largely differed across mature cells, averaging 0.81 in neutrophils, 0.64 in monocytes, 0.42 in NK, 0.07 in T cells, and 0.09 in B cells, supporting a myeloid skewing of mutant HSPCs. Multiparametric immunophenotypic analyses showed unbalanced composition of HSPCs in the BM, with 2-to-3-fold reduction of primitive stem cells, multipotent and lymphoid progenitors, and 2-fold increase of myeloid progenitors, compared to matched healthy individuals. HSPCs, myeloid-biased HSPCs and immature myeloid cells were increased by 3-to-4 fold in the circulation ($p< 0.03$). Gene expression analysis of circulating monocytes

displayed upregulation of inflammatory pathways and metabolic rewiring (Fig. 1, panels A-B). Metabolomic analyses confirmed hyperactivation of the glycolytic pathway and specific lipid metabolism (Fig. 1, C-D). Models of VEXAS generated by gene editing recapitulated patients' hematopoiesis and pathophysiology *in vitro* and *in vivo*. UBA1 mutations were installed at VAF >0.9 in HSPCs and generated a myeloid bias *in vitro*. Transplantation of edited HSPCs in immunodeficient mice resulted in a 100-fold reduction in circulating B cells, while NK and myeloid compartments were preserved. Human BM HSPCs were 5-fold lower than control mice, largely myeloid-biased and presented abnormal vacuolar morphology. Concordantly, VAF was >0.8 in myeloid cells and HSPCs and < 0.3 in B cells.

Figure 1

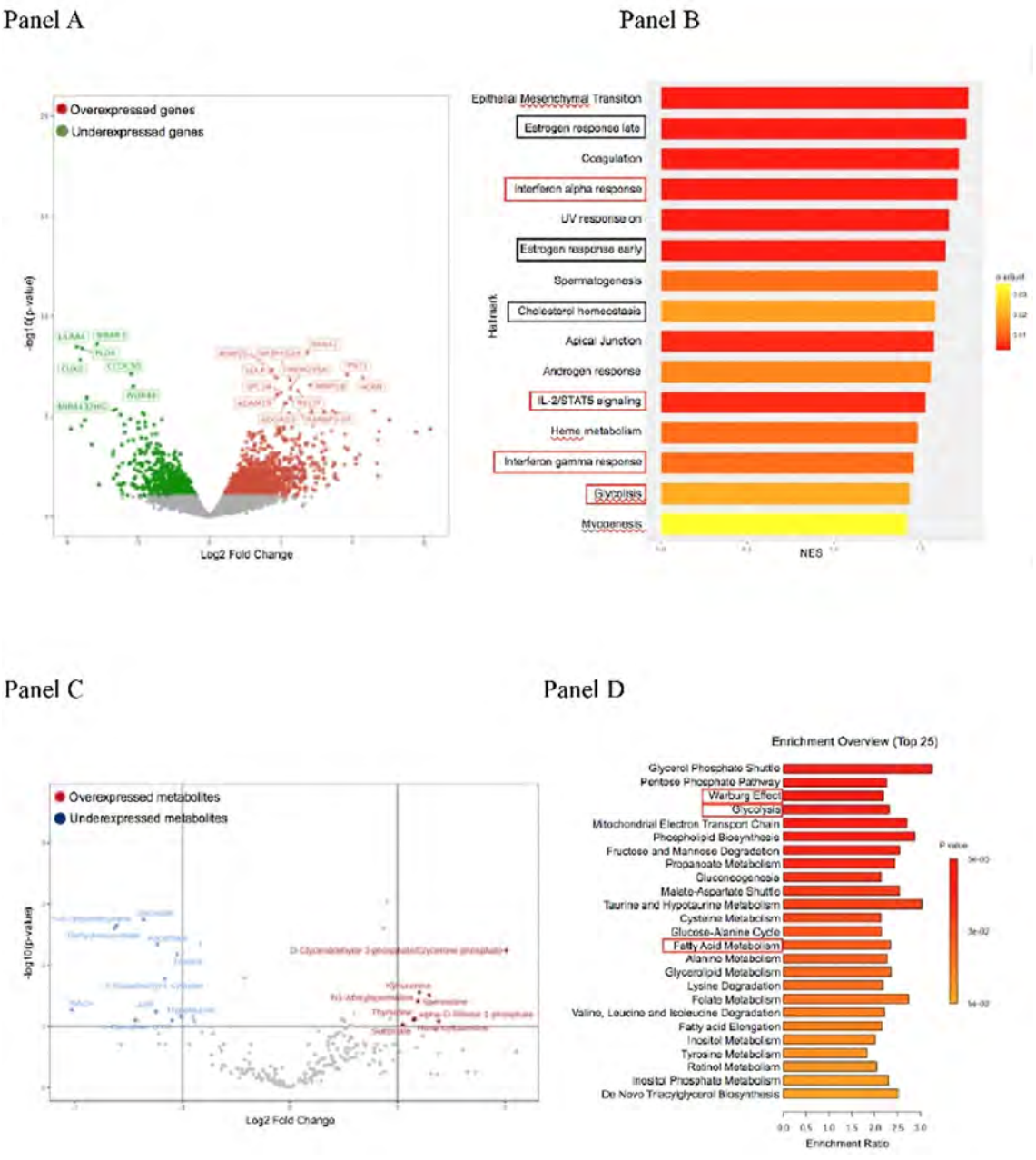

Figure 1. Panel A. Gene expression analysis of peripheral monocytes in VEXAS patients compared to controls. Panel B. Gene-enrichmed pathway analysis in VEXAS patients compared to controls. Panel C. Metabolic analysis in VEXAS patients compared to controls. Panel D. Metabolic-enriched pathway analysis in VEXAS patients compared to controls.

Conclusion: Mutations in UBA1 drive expansion of HSPCs and enhance myelopoiesis-guided accumulation of myeloid precursors. Mutant lymphoid cells are negatively selected and their myeloid counterpart in peripheral blood displays upregulation of transcriptomic signatures and metabolic pathways indicative of inflammatory activation. Gene editing-based models hold promise to enable preclinical testing and validation of novel therapeutics to treat VEXAS syndrome.

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Abstract Number: 0738

A Genome-wide Association Study Suggests New Susceptibility Loci for Primary Antiphospholipid Syndrome

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Genetics, Genomics & Proteomics

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Primary antiphospholipid syndrome (PAPS) is a rare autoimmune disease characterized by the presence of antiphospholipid antibodies and the occurrence of thrombotic events and pregnancy complications. Although the etiology of PAPS is incompletely understood, previous studies have suggested a role for genetic susceptibility in this disease. The goal of our study was to identify novel susceptibility loci associated with PAPS by performing a large genome-wide association study across five different populations of European ancestry.

Methods: A total of 482 patients with PAPS and 5,006 controls from five independent populations were included. Genotyping was performed using the Illumina Infinium ImmunoArray, Global Screening Array, and the Infinium Human Core platforms. PLINK software was used for quality control and association analyses adjusting for population structure. Genotype imputation was performed in each independent cohort using the TOPMed Imputation Server and the TOPMed version R2

as reference panel. Summary statistics from each population were meta-analyzed and further *in silico* functional analyses were performed. A weighted polygenic risk score was calculated and compared between populations. Hierarchical clustering and Mahalanobis distance analyses were used to assess genetic similarities between PAPS and other immune-mediated diseases.

Results: The meta-analysis of 7 million variants revealed two significant loci (p-value< $5x10^{-8}$) and 43 suggestive loci (p-value< $1x10^{-5}$) associated with PAPS. Significant signals are located near *STAT4* (rs11889341, OR [95% CI]=0.61 [0.52-0.71], p-value=$1.39x10^{-9}$) and *HLA-DRA* (rs9269041, OR [95% CI]=0.63 [0.54-0.74], p-value=$2.07x10^{-8}$). Biological process enrichment analysis revealed association of PAPS susceptibility loci with pathways related to the nervous system (p-value=$1.91x10^{-5}$) and the immune response (p-value=$3.39x10^{-3}$). Our data suggest a higher genetic risk for PAPS in East Asian compared to European populations. Genetic similarity analysis showed that PAPS is genetically most closely related to neuromyelitis optica, systemic sclerosis, and Sjögren's syndrome.

Conclusion: Our results provide new insights into the genetic basis of PAPS across multiple populations. Genetic similarities of PAPS with other immune-mediated diseases characterized by neurological and vascular involvement might provide additional insights into the etiology and pathogenesis of antiphospholipid syndrome.

Disclosure: D. Casares: None; **M. Martínez-Bueno**: None; **M. Borghi**: None; **G. Pons-Estel**: GlaxoSmithKlein(GSK), 1, 5, 6, Janssen, 1, 5, 6, Novartis, 1, 6, Pfizer, 5, 6, Werfen/Inova, 5, 6; **P. Clinical Consortium**: None; **Y. Zuo**: None; **G. Espinosa**: None; **A. Zhernakova**: None; **C. Wijmenga**: None; **T. Radstake**: AbbVie/Abbott, 3; **L. van den Hoogen**: None; **G. Reales**: None; **C. Wallace**: None; **J. Guthridge**: None; **J. James**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 2, Novartis, 2, Progentec Biosciences, 5; **R. Cervera**: None; **P. Meroni**: None; **J. Martin**: None; **J. Knight**: Jazz Pharmaceuticals, 2; **M. Alarcon-Riquelme**: None; **A. Sawalha**: None.

Abstract Number: 0739

Major Adverse Cardiovascular Event and Venous Thromboembolism Risk Comparing Advanced Therapies Among Individuals with Axial Spondylarthritis and Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Epidemiology & Public Health I
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Individuals with axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) have increased cardiovascular risk compared to the general population, which is partly explained by systemic inflammation. While emerging evidence suggests tumor necrosis factor inhibitors (TNFi) may be cardioprotective, there are safety concerns for Janus kinase inhibitors (JAKibs) in regard to major adverse cardiovascular events (MACE) and venous thromboembolism (VTE). We aimed to assess the risk of MACE and VTE in axSpA and PsA comparing users of JAKibs versus TNFi.

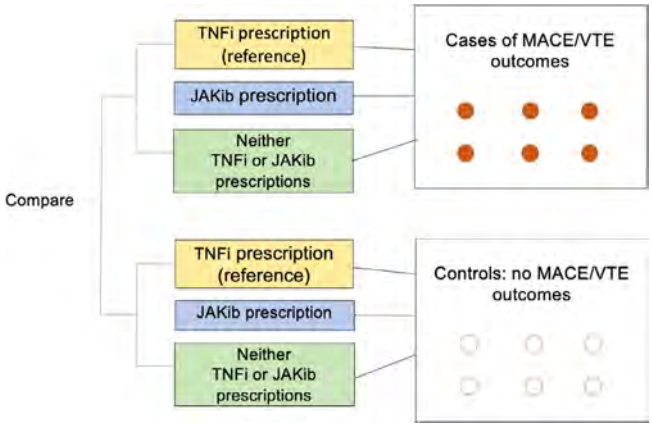

Figure 1. Study design for nested case-control study with cases and controls identified by outcome status and 3-level medication exposure status assessed in 6 months prior to outcome (index date).

Table 1. Baseline demographics and clinical characteristics of study subjects for each case-control sample stratified by MACE and VTE outcomes.

	MACE outcomes		VTE outcomes	
	Cases N=1065	Controls N=4260	Cases N=1554	Controls N=6216
Age (mean, years)	55.5	55.1	52.9	52.8
Female (%)	47.2	47.2	53.3	53.3
Obesity (%)	47.3	36.2	53.9	35.8
Tobacco Use (%)	20.8	10.1	16.9	10.2
Chronic kidney disease (%)	19.0	6.9	15.8	6.3
Cardiovascular disease history* (%)	52.5	20.9	60.5	18.7
Diabetes (%)	37.3	23.1	31.0	21.2
Hypertension (%)	78.7	59.0	73.2	55.7
Hyperlipidemia (%)	67.0	59.5	62.2	54.5
Malignancy$^{\Delta}$ (%)	8.1	5.3	12.2	4.6
Antihypertensives/Antianginal meds (%)	60.5	45.2	55.0	42.4
Anti-arrhythmic meds (%)	3.0	1.2	2.4	1.0
Aspirin/Antiplatelets/Anticoagulants (%)	19.2	6.9	39.8	5.5
Lipid lowering meds (%)	38.2	31.9	32.1	28.9
Oral DMARDs# (%)	30.4	33.1	36.9	33.5
Glucocorticoids (%)	42.2	31.7	50.1	32.8
Non-TNF Biologics+ (%)	14.8	12.5	13.6	13.9
NSAIDs (%)	38.9	39.7	37.3	40.9

* Includes history of atrial fibrillation/flutter, heart failure and non-ischemic heart disease, cerebrovascular accident/TIA, ischemic heart disease, peripheral vascular disease or acute myocardial infarction, venous thromboembolism

$^{\Delta}$ Includes breast, colorectal, endometrial, lung, prostate and urologic (kidney, renal pelvis and ureter) cancers; and leukemias/lymphomas

Includes apremilast, auranofin, azathioprine, chloroquine, cyclophosphamide, cyclosporine, hydroxychloroquine, leflunomide, methotrexate, mycophenolate, sulfasalazine and thiomalate

+ Includes abatacept, Tocilizumab, sarilumab, ustekinumab, guselkumab, Risankizumab, secukinumab, ixekizumab, rituximab, rilonacept, canakinumab and anakinra.

Table 2. Association of each drug treatment category with major cardiovascular event and venous thromboembolism outcomes, among individuals with axial spondyloarthritis and psoriatic arthritis

Medication use	Cases, N		Controls, N		Crude Odds Ratio (95% CI)		*Adjusted Odds Ratio (95% CI)	
	MACE	VTE	MACE	VTE	MACE	VTE	MACE	VTE
TNFi (ref)	273	452	1348	2055	ref	ref	ref	ref
JAKib	8	26	39	70	1.01 (0.46-2.20)	1.71 (1.07-2.72)	0.86 (0.37-1.99)	1.39 (0.79-2.44)
Non-users	784	1076	2873	4091	1.36 (1.16-1.58)	1.20 (1.06-1.36)	1.27 (1.08-1.50)	1.12 (0.96-1.29)

*Adjusted for age, cardiovascular disease history, diabetes, hypertension, hyperlipidemia, use of aspirin, antiplatelets, and/or anticoagulants, obesity and tobacco use

Abbreviations: TNFi: tumor-necrosis alpha inhibitors; etanercept, adalimumab, golimumab, certolizumab and infliximab. JAKib: Janus kinase inhibitors; tofacitinib, upadacitinib, baricitinib and abrocitinib

Methods: We conducted two nested case-control studies (**Figure 1**) using 2006-2021 data from the MarketScan Commercial Claims and Encounters (Merative) Database, which includes de-identified, patient-specific data of reimbursed healthcare claims. We included adults aged 18-65 years with ≥1 inpatient or 2 outpatient axSpA or PsA ICD-9/-10 diagnosis codes separated by ≥7 days.

For the first case control study, MACE was defined as the first inpatient claim for myocardial infarction or stroke/transient ischemic attack; for the second case control study, VTE was defined using the first inpatient/outpatient claim. The index date was the date of the MACE or VTE outcome among cases; or matching the case's outcome date among controls. Cases and controls were matched 1:4 by age, gender and axSpA/PsA diagnosis date using risk-set sampling. We evaluated drug exposure (TNFi or JAKib use or neither) using pharmacy claims and CPT codes within 6 months prior to the index date.

We assessed the association of drug exposure (referent: TNFi use) with the outcomes of MACE and VTE in separate models, using conditional logistic regression with adjustment for potential confounders (age, cardiovascular disease history, comorbidities, and tobacco use) to calculate odds ratios (OR) and 95% confidence intervals (CI).

Results: We identified 1065 MACE cases among 5325 adults with AxSpA or PSA and 1554 VTE cases among 7770 axSpA/PsA subjects. Demographics and clinical characteristics are shown in **Table 1**. Comorbidities including cardiovascular disease history, obesity, diabetes and hypertension were more commonly seen in cases versus controls.

In the MACE nested case control study, 47 (0.9%) were JAKib users, 1621 (30.4%) were TNFi users and 3657 (68.7%) were non-users of JAKib and TNFi. In the VTE sample, 96 (1.2%) were JAKib users, 2507 (32.3%) were TNFi users and 5167 (66.5%) were non-users.

Non-users of TNFi and JAKibs had 1.3 times the odds of MACE relative to TNFi users (95% CI 1.08-1.50; **Table 2**). In JAKib users versus TNFi users, the odds of MACE was not increased (OR 0.86, 95% CI 0.37-1.99). The odds ratio for VTE was 1.39 among JAKib users however, this was not statistically significant after confounder adjustment (95% CI 0.79-2.44).

Conclusion: Using a large US insurance claims database, we did not find a statistically significant association between JAKib use and risk of MACE or VTE, compared with TNFi use among individuals with axSpA and PsA, although there was a trend toward increased VTE events among JAKib users. The accrual of further data is needed to better study the comparative safety of JAKibs versus TNFi in this study population.

Disclosure: S. Merjanah: None; **D. Driscoll**: None; **C. Peloquin**: None; **J. liew**: None; **M. Dubreuil**: Amgen, 2, Pfizer, 5, UCB Pharma, 2.

Abstract Number: 0740

Renal Arteriosclerosis in Index Lupus Nephritis Biopsies Predicts Future Cardiovascular Disease

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
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Background/Purpose: Patients < 40 years old with lupus nephritis (LN) face 42-fold higher risk of cardiovascular disease (CVD) compared to peers. Traditional CVD risk calculators fail to accurately predict future CVD risk in young LN patients, making decisions to prescribe empiric CVD prevention wrought with uncertainty. While a kidney biopsy is routinely performed to diagnose LN, renal arteriosclerosis (ASCL) is not routinely reported. Renal arteriosclerosis (ASCL) in kidney biopsies at LN diagnosis might represent changes in systemic arteries and could guide CVD risk stratification when most probably don't take this into account. Thus, in this study we systematically graded renal arteriosclerosis in kidney biopsies at LN diagnosis and examined its role as an early predictor of future incident CVD events.

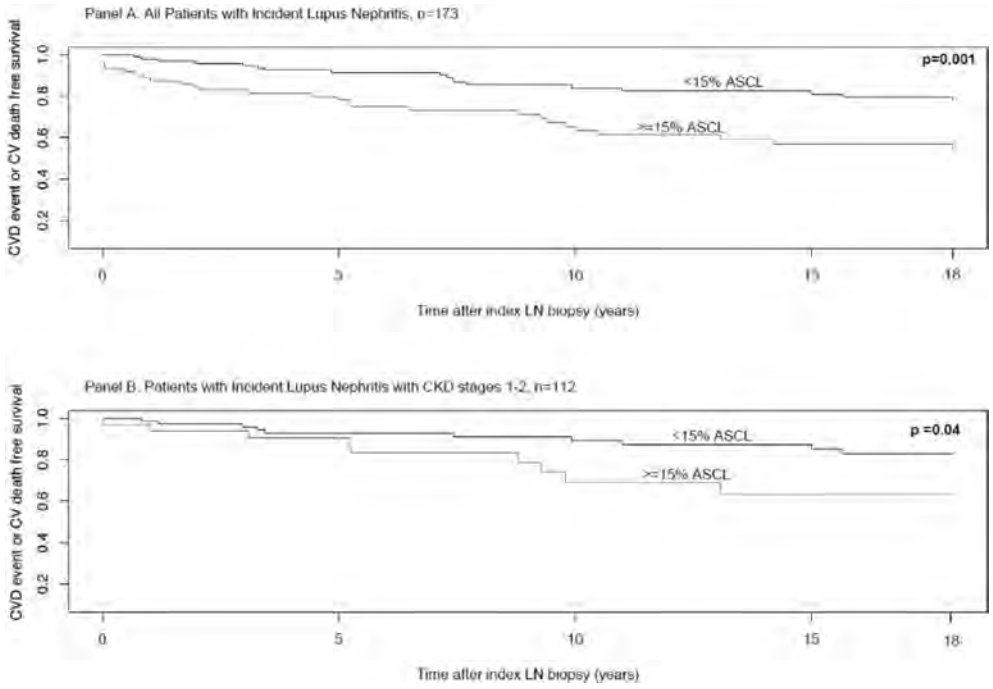

Figure 1. Survival curves showing CVD event or CVD related death free survival over 18-year follow-up period by 15% or more luminal narrowing of renal arteries (ASCL) in diagnostic LN biopsies in all patients with LN (Panel A.) and in patients with LN with preserved kidney function defined as CKD stages 1-2 (Panel B)

Methods: Data were abstracted from adult LN patients who underwent diagnostic kidney biopsy between 1994-2021, including socio-demographics, traditional CVD risk factors, and pathology reports. Incident CVD-related deaths and non-fatal CVD events (ischemic heart disease, cerebrovascular accident, transient ischemic attack, and peripheral vascular disease) were adjudicated using published guidelines. Index standard of care kidney biopsies performed to diagnose LN were re-read by a pathologist to grade renal arteriosclerosis (ASCL) by calculating percent luminal narrowing of renal arteries using

Table 1. Multivariable Cox model showing risk factors at lupus nephritis (LN) diagnosis for incident cardiovascular disease (CVD) events or CVD related deaths in: A) All LN patients; B) LN patients with preserved kidney function (CKD stages 1-2)

Table 1. Multivariable Cox model showing risk factors at lupus nephritis (LN) diagnosis for incident cardiovascular disease (CVD) events or CV deaths in: A) All LN patients; B) LN patients with preserved kidney function (Chronic kidney disease (CKD) stages 1-2)

A. All patients with LN, n=173

Variables at LN Diagnosis	Adjusted HR (CIs)	p	Adjusted HR (CIs)	p	Adjusted HR (CIs)	p	Adjusted HR (CIs)	p
Age per 10 years	1.02 (0.99, 1.05)	0.10	1.02 (0.99, 1.05)	0.053	1.02 (1.0, 1.05)	0.09	1.01 (0.99, 1.04)	0.4
Female	0.81 (0.35, 1.7)	0.57	0.70 (0.36, 1.4)	0.31	0.77 (0.39, 1.5)	0.47	1.04 (0.51, 2.1)	0.9
Black/Other Race or Hispanic Ethnicity	1.1 (0.58, 2.2)	0.72	1.2 (0.60, 2.3)	0.63	1.1 (0.54, 2.1)	0.87	0.95 (0.48, 1.9)	0.88
GFR per 10 ml/min/m² decrease	**1.13 (1.01, 1.2)**	**0.007**	**1.1 (1.04, 1.2)**	**0.01**	**1.1 (1.03, 1.2)**	**0.01**	**1.1 (1.01, 1.2)**	**0.03**
Hypertension	0.61 (0.31, 1.2)	0.15	0.60 (0.31, 1.2)	0.14	0.58 (0.30, 1.1)	0.11	0.74 (0.38, 1.4)	0.38
LN Chronicity index per 1 point increase	0.98 (0.82, 1.2)	0.80	1.0 (0.84, 1.2)	0.93	0.97 (0.82, 1.2)	0.76	1.01 (0.85, 1.2)	0.93
Renal ASCL per 10% increase	1.13 (1.0, 1.3)	0.06*						
Renal ASCL Threshold								
≥15%			**2.2 (1.02, 4.1)**	**0.03**				
≥25%					**2.8 (1.3, 5.8)**	**0.007**		
≥50%							**2.3 (1.02, 5.0)**	**0.046**

B. Patients with LN with preserved kidney function (CKD stages 1-2), n=112

Variables at LN Diagnosis	Adjusted HR (CIs)	p	Adjusted HR (CIs)	p	Adjusted HR (CIs)	p	Adjusted HR (CIs)	p
Age per 10 years	1.02 (0.98, 1.1)	0.39	1.02 (1.0, 1.05)	0.07	1.02 (0.99, 1.04)	0.12	1.02 (0.98, 1.1)	0.34
Female	0.84 (0.28, 2.5)	0.76	0.70 (0.35, 1.4)	0.31	0.78 (0.39, 1.6)	0.48	0.80 (0.27, 2.4)	0.69
Black/Other Race or Hispanic Ethnicity	1.1 (0.38, 3.3)	0.85	1.1 (0.59, 2.2)	0.68	1.1 (0.55, 2.1)	0.84	1.04 (0.36, 3.0)	0.95
GFR per 10 ml/min/m² decrease	1.01 (0.99, 1.03)	0.31	**1.02 (1.01, 1.03)**	**0.004**	**1.02 (1.01, 1.03)**	**0.01**	1.01 (0.99, 1.03)	0.28
Hypertension	0.68 (0.22, 2.1)	0.72	0.59 (0.30, 2.2)	0.12	0.59 (0.30, 1.2)	0.12	0.67 (0.21, 2.1)	0.50
LN Chronicity index	1.1 (0.78, 1.4)	0.72	0.98 (0.83, 1.2)	0.85	0.98 (0.83, 1.2)	0.83	0.99 (0.73, 1.3)	0.94
Renal ASCL per 10% increase	**1.2 (1.04, 1.5)**	**0.02**						
Renal ASCL Threshold								
≥15%			**2.2 (1.1, 4.3)**	**0.03**				
≥25%					**2.4 (1.1, 5.0)**	**0.02**		
≥50%							2.8 (0.9, 9.0)	0.07*

*Bold font indicates significant values (p-value ≤0.5). CVD=Cardiovascular Disease. *Trend towards significance. ASCL=Arteriosclerosis; GFR=Glomerular Filtration Rate*

Table 2. Predictive values, sensitivity, and specificity of traditional cardiovascular disease (CVD) risk factors, luminal renal arterial narrowing (renal arteriosclerosis (ASCL)) thresholds, and combined traditional risk factors and renal ASCL thresholds.

Table 2. Predictive values, sensitivity, and specificity of traditional cardiovascular disease (CVD) risk factors, luminal renal arterial narrowing (renal arteriosclerosis (ASCL)) thresholds, and combined traditional risk factors and renal ASCL thresholds.

A. All patients with LN, n=173

Variables at LN Diagnosis	n	CVD events, n	PPV	NPV	Sensitivity	Specificity
Traditional CVD Risk Factors						
CKD Stage ≥3	60	25	42%	82%	56%	68%
Hypertension (HTN)	57	15	26%	70%	33%	54%
CKD Stage ≥3 & HTN	23	8	35%	73%	18%	73%
Renal Arteriosclerosis (ASCL) Thresholds						
≥10%	86	28	33%	80%	62%	54%
≥15%	75	27	36%	**81%**	60%	**61%**
≥20%	64	26	41%	**82%**	58%	**70%**
≥25%	63	25	41%	**82%**	58%	**70%**
≥30%	54	23	43%	**81%**	51%	**75%**
≥40%	48	20	42%	**80%**	44%	**77%**
≥50%	42	19	45%	**80%**	42%	**81%**
Combined CVD Risk Factors (Renal ASCL & Traditional Risk Factors)						
CKD Stage ≥3 & ASCL ≥15%	37	18	49%	**80%**	40%	**82%**
CKD stage ≥3, HTN, & ASCL ≥15%,	29	12	41%	**77%**	27%	**83%**

B. Patients with LN with preserved kidney function (CKD stages 1-2), n=112

Variables	n	CVD events, n	PPV	NPV	Sensitivity	Specificity
Traditional CVD Risk Factors						
Hypertension	32	7	22%	82%	37%	62%
Renal Arteriosclerosis (ASCL) Thresholds						
≥10%	42	9	21%	**84%**	47%	**62%**
≥15%	35	9	26%	**86%**	47%	**69%**
≥20%	26	8	31%	**86%**	42%	**78%**
≥25%	22	8	36%	**87%**	42%	**83%**
≥30%	22	8	36%	**87%**	42%	**83%**
≥40%	19	7	37%	**86%**	37%	**85%**
≥50%	16	6	38%	**85%**	32%	**87%**
Combined CVD Risk Factors (Renal ASCL & Traditional Risk Factors)						
ASCL ≥15% & HTN	13	4	31%	85%	21%	52%

Bold font indicates that better predictive values and specificity of renal ASCL and combined risk factors vs. traditional CVD risk factors. CVD=Cardiovascular Disease; PPV=Positive Predictive Value; NPV=Negative Predictive Value; ASCL=Arteriosclerosis; HTN=Hypertension; CKD=Chronic Kidney Disease

the Banff criteria. We examined the role of renal ASCL in diagnostic LN biopsies as an early predictor of future CVD using a Cox proportional hazards model in: a) all LN patients; b) those with preserved kidney function defined as chronic kidney disease stages 1-2.

Results: Among 173 adult patients with incident LN, 75% were female and 35% were of Black race or Hispanic ethnicity, and mean age at diagnosis was 38±17 years. Mean eGFR was 79±38 ml/min/1.73m^2; 65% of patients had preserved kidney function. We noted 47% and 32% of patients had renal ASCL ≥15% and 25%.

A total of 45 CVD-related deaths and events were observed during up to 18 years of follow-up after LN diagnosis. Mild renal ASCL changes (15% and 25% luminal narrowing) were associated with 2-3-fold higher risk of future CVD (Adjusted HR 2.2 & HR 2.8; Table 1A). The Cox proportional hazard model highlighted accelerated CVD events in patients with renal ASCL ≥15% compared to those without renal ASCL (Fig. 1A). Renal ASCL had higher specificity compared to traditional CV risk factors (Table 2A).

In those with persevered kidney function (n=112), mild renal ASCL predicted 2-fold higher risk of CVD (Adjusted HR 2.2 & HR 2.4; Table 1B). Again, patients with renal ASCL had accelerated CVD events even in this low-risk group (Fig. 1B). Renal ASCL was an early independent risk factor of future CVD with higher specificity than traditional CV risk factors in this low-risk group (Table 2B).

Conclusion: Renal arteriosclerosis found in kidney biopsy at LN diagnosis was a strong, early, and independent risk factor for future CVD events, outperforming traditional CVD risk factors. This observation held consistent even in LN patients with preserved kidney function. This suggests systematic grading of renal ASCL in LN biopsies may help to identify patients who could benefit from aggressive CVD prevention.

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Abstract Number: 0741

Adverse Events Among Patients with and Without Autoimmune Rheumatic Disease Prescribed SGLT2 Inhibitors

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
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Background/Purpose: Sodium glucose cotransporter 2 inhibitors (SGLT2i) are oral hypoglycemic agents for Type II diabetes mellitus (T2D) now prescribed for renal and cardiovascular indications. Patients with autoimmune rheumatic diseases (ARD) have been excluded from SGLT2i clinical trials due to theoretical increased infection risk in the immunosuppressed. We compared adverse events associated with SGLT2i prescription in patients with vs. without ARD.

Methods: Using a large data repository, we identified patients with ≥2 ICD10 diagnostic codes for ARD who were prescribed dapagliflozin, canagliflozin, or empagliflozin from 1/1/2016 to 12/10/2021. Each ARD patient was matched by age, sex, and race to a patient without ARD prescribed the same SGLT2i. Baseline demographic and clinical data, prescription dates, and adverse events were collected from electronic health records for all subjects and compared in univariable analyses. Multivariable Cox models, adjusting for clinical and demographic variables, calculated hazard ratios (HR) for adverse events, following from prescription date (index) and censoring at 1st adverse event, discontinuation/last day prescription, death, or study period end. Models were then stratified by sex.

Table 1. Baseline Characteristics of Patients with and without Autoimmune Rheumatic Disease at Date of SGLT2 Prescription in the Mass General Brigham Healthcare System, 2016-2021

	Patients with ARD (n = 466)	Patients without ARD (n = 427)	p
Age, mean (SD)*	64.09 (11.33)	63.64 (11.21)	0.54
Female, n (%)*	277 (59.4)	270 (63.2)	0.25
Race, n (%)*			0.46
White	332 (71.2)	299 (70.0)	
Black	60 (12.9)	62 (14.5)	
Asian	16 (3.4)	18 (4.2)	
Hispanic	14 (3.0)	10 (2.3)	
Other	44 (9.4)	38 (8.9)	
Smoking status, n (%)			**0.004**
Never	216 (46.4)	230 (53.9)	
Past	213 (45.7)	153 (35.8)	
Current	37 (7.9)	44 (10.3)	
Body mass index, kg/m2, mean (SD)	32.64 (7.25)	32.54 (7.01)	0.84
Prescribed SGLT2 Inhibitor, n (%)			0.64
Dapagliflozin	45 (9.7)	49 (11.5)	
Empagliflozin	365 (78.3)	335 (78.5)	
Canagliflozin	56 (12.0)	43 (10.1)	
Indication for Prescription, n (%)			
Diabetes Mellitus/Hyperglycemia	401 (86.1)	368 (86.2)	0.95
Chronic Kidney disease	20 (4.3)	17 (4.0)	0.82
Heart Failure	62 (13.3)	67 (15.7)	0.31
Weight Loss	24 (5.2)	9 (2.1)	**0.02**
Atherosclerosis prevention	9 (1.9)	12 (2.8)	0.39
Concurrent therapies, n (%)			
Glucocorticoids**	172 (36.9)	88 (20.6)	**<0.0001**
Hydroxychloroquine	79 (17.0)	2 (0.5)	**<0.0001**
csDMARDs***	132 (28.3)	6 (1.4)	**<0.0001**
bDMARDs****	105 (22.5)	1 (0.2)	**<0.0001**
tsDMARDs*****	15 (3.2)	0	**<0.0001**
Autoimmune/Rheumatic Disease (≥2 ICD Codes), n (%)			
Rheumatoid Arthritis	251 (53.9)		
Psoriatic Arthritis	105 (22.5)		
Systemic Lupus Erythematosus	39 (8.4)		
Sjogren's syndrome	26 (5.6)		
Inflammatory Myositis	43 (9.2)		
Scleroderma	20 (4.3)		
MCTD/Overlap syndrome	7 (1.5)		
Medical Insurance Type			0.13
Federal	251 (53.9)	207 (48.5)	
Private	211 (45.3)	217 (50.8)	
Uninsured	4 (0.9)	3 (0.7)	

*Matching factor **Glucocorticoids: prednisone, prednisolone or medrol, solumedrol ***csDMARDs (conventional synthetic disease-modifying antirheumatic drugs): methotrexate, sulfasalazine, azathioprine, leflunomide ****bDMARDs (biologic disease-modifying antirheumatic drugs): etanercept, adalimumab, golimumab, certolizumab, infliximab, abatacept, tocilizumab, rituximab, belimumab, golimumab, ustekinumab *****tsDMARDs (targeted synthetic disease-modifying antirheumatic drugs): tofacitinib, upadacitinib, baricitinib; ARD=autoimmune rheumatic diseases, MCTD=mixed connective tissue disorder

Results: We matched 519 patients with ARD to 519 patients without ARD prescribed SGLT2i: 466 and 427 in the two groups started the prescription and were studied **(Table 1)**. The two groups were comparable (mean age 64 years; 61% female), except for past smoking, more common in patients with ARD. Empagliflozin accounted for 78% of prescriptions and T2D was the most common indication (86%). Mean hemoglobin A1c in T2D patients at index date was comparable between groups (8.08 vs 8.10 mg/dL)**.** We identified 12 categories of adverse events and reasons for discontinuation **(Table 2)**. Yeast infections (9.9% vs 6.1%; p 0.04) and muscular symptoms (e.g., myalgias and weakness; 3.4% vs 0.9%, p 0.01) were more frequent in ARD patients. Other adverse event categories were numerically more common in ARD patients. ARD patients also had significantly shorter SGLT2i use duration (8.7 vs 12.6 months; p< 0.0001) and time to adverse event (0.62 vs 0.96 years; p< 0.0001). We found a significant increased risk in adverse events in those with ARDs (HR 1.74 [95% CI 1.33, 2.29]), persisting upon adjustment for glucocorticoid and DMARD use (HR 1.80 [95%CI 1.34, 2.40]). Kaplan Meier curves showed separation of event-free survival over time (all log-rank p < 0.001; **Figure 1**). Significantly more adverse events occurred among females than males (p< 0.00001). Adverse event risk was also higher in women with ARD vs without ARD, even upon adjustment for glucocorticoid and immunosuppressant use (HR 2.05 [95% CI 1.47, 2.85]).

Conclusion: This observational study identified significant increased adverse event risk in patients with vs. without ARDs using SGLT2i. Both ARD and non-ARD female patients were more likely to have adverse events than males, with female ARD patients most affected. To our knowledge, this is the first study to consider SGLT2i adverse events in ARD vs. non-ARD patients. Further rigorous testing of safety and efficacy of SGLT2i among patients with ARDs is warranted.

Table 2. Adverse Events Following SGLT2i Usage in Patients with and matched Patients without Autoimmune Rheumatic Disease (ARD) in the Mass General Brigham Healthcare system, 2016-2021

Adverse Events, n (%)	Patients with ARD (n = 466)	Patients without ARD (n = 427)	p
Yeast infection	46 (9.9)	26 (6.1)	**0.04**
Urinary tract infection	26 (5.6)	14 (3.3)	0.10
Gastrointestinal intolerance	22 (4.7)	20 (4.7)	0.98
Rash	9 (1.9)	4 (0.9)	0.22
Diabetic ketoacidosis	4 (0.9)	4 (0.9)	0.90
Syncope/lightheadedness/dizziness/hypotension	19 (4.1)	18 (4.2)	0.92
Decline in kidney function/renal failure	10 (2.2)	9 (2.1)	0.97
Vaginal itching/irritation/vaginitis	14 (3.0)	5 (1.2)	0.056
Myalgias/muscle weakness	16 (3.4)	4 (0.9)	**0.01**
Urinary symptoms, non-infectious	7 (1.5)	3 (0.7)	0.26
Other infection	6 (1.3)	8 (1.9)	0.48
Other	17 (3.7)	10 (2.3)	0.25
Any adverse event	130 (27.9)	101 (23.7)	0.15
Any adverse event among females (n=547)	103 (37.2)	80 (29.6)	0.06
Any adverse event among males (n=346)	27 (14.3)	21 (13.4)	0.81

ARD=autoimmune rheumatic disease

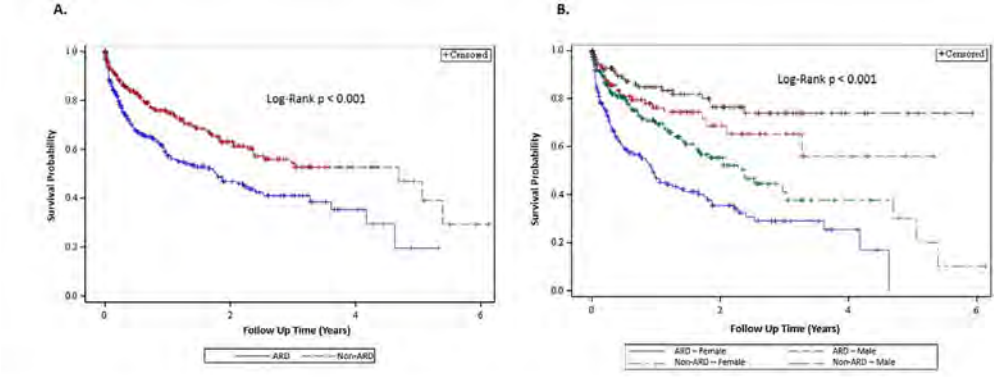

Figure 1. Kaplan Meier Curves showing Probability of Survival without Adverse Event from SGLT2i Prescription (Index date) in Patients with vs. without Autoimmune Rheumatic Disease (ARD) **(A)**, and stratified by sex **(B)**, censoring at adverse event, discontinuation, death, or end of follow-up period.

Disclosure: E. Oakes: None; **J. Ellrodt**: None; **M. Choi**: AbbVie/Abbott, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 6, Mallinckrodt, 2, Merck/MSD, 2, MitogenDx, 2, Organon, 6, Pfizer, 2, 6, Roche, 2, Werfen, 2; **J. Yee**: None; **H. Guan**: None; **K. Costenbader**: Amgen, 2, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Eli Lilly, 2, Exagen Diagnostics, 5, Gilead, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5.

Abstract Number: 0742

Risk of Incident Gout Associated with Initiation of Sodium-glucose cotransporter-2 Inhibitors versus Other Second-line Agents Among Metformin Users with Type 2 Diabetes

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Epidemiology & Public Health I
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Sodium-glucose cotransporter-2 inhibitors (SGLT2i) are a revolutionary second-line treatment for type 2 diabetes associated with lower risk of cardiovascular and all-cause mortality, heart failure, and chronic kidney disease progression. Many trials have also found SGLT2i lower serum urate levels. However, data on gout risk are limited and the few available prior studies were not specific to those using metformin, the primary target populations of recent landmark trials like GRADE [GRADE Study Research Group, NEJM 2022;387:1075-88].

Our objective was to emulate recent clinical trials and compare incident gout risk among metformin-treated patients with type 2 diabetes initiating SGLT2i versus other second-line type 2 diabetes treatments (dipeptidyl peptidase 4 inhibitors [DPP-4i], glucagon-like peptide-1 receptor agonists [GLP1-RA], or sulfonylureas).

Methods: We performed a new user, active comparator, population-based cohort study using administrative health data for nearly all residents of British Columbia, Canada from Jan 2014 to June 2022, including all dispensed prescriptions, regardless of funder. A cohort of adults with type 2 diabetes using metformin (first-line therapy) was identified from ICD codes and dispensing data. Primary outcome was incident gout, defined as inpatient or outpatient diagnosis of gout plus dispensing of a gout medication (colchicine, corticosteroids, or NSAIDs) within 7 days, and no prior recorded gout diagnosis. We also stratified by sex, age, and baseline diuretic use.

Cox proportional hazards models were used with propensity score overlap weighting, stratified by calendar year of initiation. We also assessed for risk of genital infection (for which we expected SGLT2i would have a positive association), and for the risk of any osteoarthritis encounter, a negative control outcome for which we expected a null association.

Results: We included 27,791 type 2 diabetes patients in the SGLT2i vs. DPP-4i cohort (58% male, mean age 61), 19,875in the SGLT2i vs. GLP1-RA cohort (44% male, mean age 57), and 71,625in the SGLT2i vs. sulfonylurea cohort (60% male, mean age 59).Baseline characteristics, including diabetes duration and presence of complications, were well balanced between SGLT2i and comparators after overlap weighting (SMD < 0.1) (**Table 1**).Weighted hazard ratio (wHR) for incident gout associated with SGLT2i initiation was 0.54 (95% CI: 0.39, 0.74) vs. DPP-4i initiation, 0.39 (0.24, 0.62) for SGLT2i

vs. GLP1-RA, and 0.61 (0.46, 0.80) for SGLT2i vs. sulfonylureas (**Table 2**).Results were consistent regardless of sex or age or baseline diuretic use.

For control outcomes, SGLT2i initiators had higher risk of genital infection than initiators of each comparator, as expected, while there was no difference in risk of osteoarthritis (**Table 2**).

Table 1. Selected baseline characteristics among metformin-treated type 2 diabetes patients initiating SGLT2i vs. DPP-4i, GLP1-RA, or sulfonylureas, before and after propensity score overlap weighting. * difference < 0.1 indicates negligible differences. n, number; y, years; SD, standard deviation; SGLT2i, sodium glucose cotransporter-2 inhibitors; DPP-4i, dipeptidyl peptidase 4 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists.

Table 1. Selected baseline characteristics among metformin-treated type 2 diabetes patients initiating SGLT2i vs. DPP-4i, GLP1-RA, or sulfonylureas, before and after propensity score overlap weighting

	SGLT2i vs. DPP-4i			SGLT2i vs. GLP1-RA			SGLT2i vs. Sulfonylureas		
	SGLT2i	DPP-4i	Standardized Mean Difference (SMD)*	SGLT2i	GLP1-RA	Standardized Mean Difference (SMD)*	SGLT2i	Sulfonylureas	Standardized Mean Difference (SMD)*
Age, y, mean (SD)	61 (7.2)	61 (8.7)	<0.001	57 (5.3)	57 (9.0)	<0.001	59 (10.1)	59 (5.8)	<0.001
Male, %	58	58	<0.001	44	44	<0.001	60	60	0.006
N Hospitalisations, mean (SD)	0.32 (0.47)	0.22 (0.56)	<0.001	0.29 (0.31)	0.29 (0.53)	<0.001	0.28 (0.58)	0.29 (0.32)	<0.001
N Outpatient encounters, mean (SD)	18.1 (7.9)	18.1 (9.8)	<0.001	19.6 (6.3)	19.6 (9.7)	<0.001	17.3 (10.1)	17.3 (5.9)	<0.001
Diabetes duration, y, mean (SD)	10.2 (4.3)	10.2 (4.7)	<0.001	9.3 (3.0)	9.3 (5.4)	<0.001	8.9 (5.8)	9.8 (3.1)	0.001
Diabetes complications, %									
Nephropathy	3.2	3.2	<0.001	2.7	2.7	<0.001	2.3	2.2	0.005
Retinopathy	46.3	46.3	<0.001	10.8	10.8	<0.001	13.1	18.3	0.007
Neuropathy	11.7	11.7	<0.001	14.8	14.8	<0.001	11.8	11.8	<0.001
Other comorbidities, %									
Obesity	9	9	<0.001	24.2	24.2	<0.001	9.4	9.5	0.006
Hypertension	71.2	71.2	<0.001	71.3	71.3	<0.001	65.1	65.1	0.001
Chronic kidney disease	8.1	8.1	<0.001	7.6	7.6	<0.001	6.6	6.8	0.006

* difference < 0.1 indicates negligible differences. n, number; y, years; SD, standard deviation; SGLT2i, sodium glucose cotransporter-2 inhibitors; DPP-4i, dipeptidyl peptidase 4 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists.

Table 2. Risk of incident gout and control outcomes among patients with type 2 diabetes treated with metformin, after propensity-score overlap weighting. SGLT2i, sodium glucose cotransporter-2 inhibitor; DPP-4i, dipeptidyl peptidase 4 inhibitor; GLP1-RA, glucagon-like peptide-1 receptor agonist

Table 2. Risk of incident gout and control outcomes among patients with type 2 diabetes treated with metformin, after propensity-score overlap weighting

	SGLT2i compared with DPP-4i [Reference]	SGLT2i compared with GLP1-RA [Reference]	SGLT2i compared with Sulfonylureas [Reference]
Incident Gout	**Weighted Hazard Ratio (95% CI)**		
Overall (Primary Outcome)	0.54 (0.39, 0.74)	0.39 (0.24, 0.62)	0.61 (0.46, 0.80)
Subgroups			
Sex			
Men	0.57 (0.37, 0.86)	0.29 (0.16, 0.49)	0.58 (0.41, 0.81)
Women	0.49 (0.29, 0.82)	0.59 (0.28, 1.27)	0.66 (0.42, 1.05)
Age			
≤ 65 years	0.61 (0.39, 0.95)	0.39 (0.21, 0.70)	0.63 (0.43, 0.91)
> 65 years	0.49 (0.30, 0.82)	0.39 (0.19, 0.83)	0.63 (0.41, 0.95)
Baseline diuretic use			
Yes	0.54 (0.35, 0.84)	0.40 (0.21, 0.75)	0.73 (0.51, 1.06)
No	0.55 (0.34, 0.90)	0.37 (0.18, 0.75)	0.51 (0.34, 0.78)
Control Outcomes	**Weighted Hazard Ratio (95% CI)**		
Genital infection (POSITIVE CONTROL)	2.35 (1.85, 2.99)	3.50 (2.43, 5.04)	1.69 (1.46, 1.95)
Osteoarthritis (NEGATIVE CONTROL)	1.06 (0.86, 1.30)	0.91 (0.65, 1.27)	1.12 (0.95, 1.30)

SGLT2i, sodium glucose cotransporter-2 inhibitor; DPP-4i, dipeptidyl peptidase 4 inhibitor; GLP1-RA, glucagon-like peptide-1 receptor agonist

Conclusion: SGLT2i initiation among metformin-treated patients with type 2 diabetes was associated with substantially lower risk of incident gout (i.e., primary prevention), compared with any other second-line option. Along with its known urate-lowering effects, as well as cardiovascular and survival benefits, SGLT2i could substantially reduce risk of incident gout for patients needing a second-line agent after metformin.

Disclosure: N. McCormick: None; **C. Yokose**: None; **N. Lu**: None; **H. Choi**: Ani, 2, Horizon, 2, 5, LG, 2, Protalix, 2, Shanton, 2.

Abstract Number: 0743

Risk and Temporal Trends of Heart Failure Subtypes in Rheumatoid Arthritis: A National Veterans Affairs Matched Cohort Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Epidemiology & Public Health I
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: There has been limited study of the risk of heart failure (HF) subtypes in RA at a population level, given the requirement for left ventricular ejection fraction (LVEF) from unstructured echocardiographic data to define HF with preserved (HFpEF) or reduced (HFrEF) ejection fraction. As the underlying pathophysiology differs, understanding the burden of HF subtypes in RA and whether advances in RA management have impacted their development is critical. Thus, we examined the risk and temporal trends of HFrEF and HFpEF in RA, leveraging LVEF values derived from natural language processing (NLP) in national Veteran's Health Administration (VA) data.

Methods: We conducted a retrospective, matched cohort study of RA patients (≥2 RA ICD codes, rheumatologist diagnosis, and positive autoantibody or DMARD fill) matched up to 10 comparators (no RA ICD codes) on age, sex, and VA enrollment year. Patients with prevalent HF (≥1 ICD code prior to index) were excluded. Incident HF events were defined as a primary hospital discharge diagnosis or HF-related death, linking VA, Medicare, and National Death Index data. Echocardiogram-derived LVEF values were extracted from clinical notes using a validated NLP tool. HFrEF (EF < 50%)

Table 1. Risk of HF subtypes in RA compared to matched non-RA controls in the Veteran's Health Administration

Table 1. Risk of HF subtypes in RA compared to matched non-RA controls in the Veteran's Health Administration

	RA (N=67,850)		Non-RA (N=570,933)			
HF Subtype	**N events**	**IR per 1000 PY (95% CI)**	**N events**	**IR per 1000 PY (95% CI)**	**Unadjusted HR***	**Adjusted HR***
HFrEF (EF <50%)	2,451	4.47 (4.30-4.65)	13,772	2.69 (2.65-2.73)	**1.72 (1.65-1.79)**	**1.40 (1.33-1.48)**
HFpEF (EF ≥50%)	2,241	4.10 (3.92-4.26)	11,299	2.21 (2.17-2.24)	**1.94 (1.86-2.03)**	**1.58 (1.49-1.68)**

*Estimated using Cox regression, stratified by case-control pairs matched on age, sex, and calendar year of enrollment into the VA. Multivariable models further adjusted for race/ethnicity, body mass index, smoking status, comorbidity burden as assessed by the Rheumatic Disease Comorbidity Index, and healthcare utilization as assessed by the number of hospitalizations in the year prior to index.

Abbreviations: CI, confidence interval; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; IR, incidence rate; PY, person years; RA, rheumatoid arthritis;

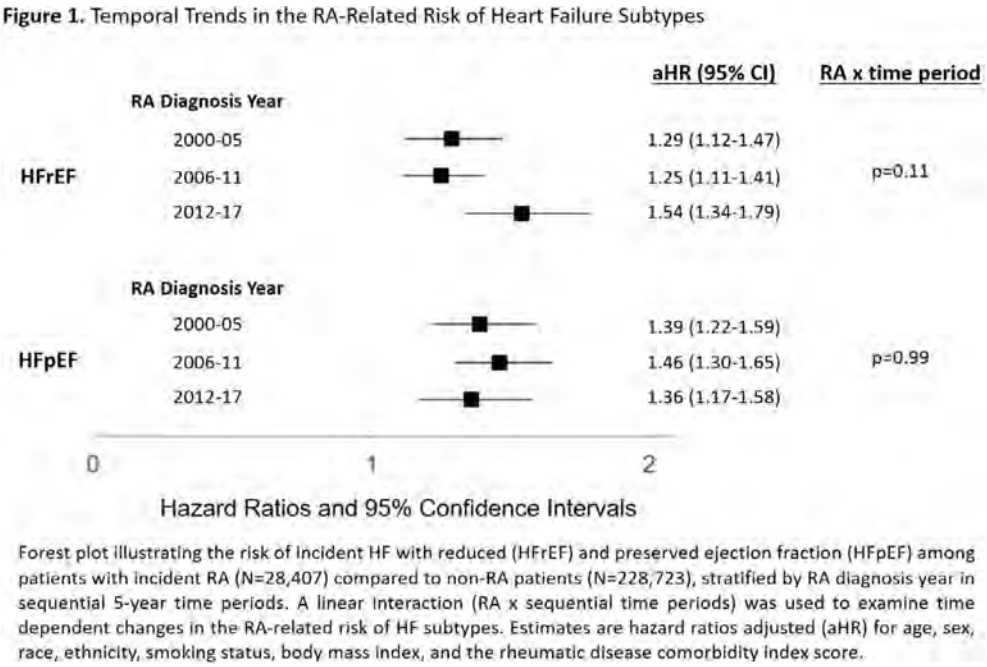

Figure 1. Temporal Trends in the RA-related Risk of Heart Failure Subtypes

and HFpEF (EF ≥50%) were defined using the most proximate LVEF within 1 year prior to a HF event, or if missing, < 30 days following the event. We examined the association of RA with incident HFrEF and HFpEF separately in multivariable Cox regression models, stratified on matched pairs and censoring patients if they developed HF with no available LVEF, the alternative HF subtype, death, or reached end of study period (01/2020). Models were adjusted for demographics, smoking status, BMI, comorbidity burden, and healthcare utilization (number of hospitalizations in the year prior to index). Temporal trends were evaluated in an incident RA subcohort (no RA diagnostic codes or medication for >365 days following VA enrollment) by testing the interaction of RA status and sequential time periods in a linear manner, then stratifying analyses on RA diagnosis year (2000-2005, 2006-2011, 2012-2017).

Results: We matched 67,850 RA patients (mean 62 years, 87% male) to 570,933 patients without RA. Over a mean follow up of 8.9 years (5,663,152 person-years), we observed 5,983 incident HF events in RA (10.9 per 1000 PY) vs. 40,283 events in non-RA (7.9 per 1000 PY) **(Table 1)**. LVEF values were identified in 82% of RA vs. 68% of non-RA patients who developed incident HF. After multivariable adjustment, RA patients were at an increased risk of HFpEF (adjusted HR [aHR] 1.58, 95% CI 1.49-1.68) and HFrEF (aHR 1.40, 1.33-1.48). Among the incident RA subcohort (N=28,407 RA; 228,723 non-RA), we observed no improvement in the RA-related risk of HFpEF (range aHR 1.36-1.46) or HFrEF (range aHR 1.25-1.54) over time **(Figure 1).**

Conclusion: In this large, matched cohort study, patients with RA experienced a 58% increased risk of HFpEF compared to a 40% increased risk of HFrEF. No significant change was observed in the RA-related risk of either HF subtype over time. These findings suggest that RA-related HF risk persists despite major RA treatment advances and highlights the need to elucidate the factors contributing to the ongoing heightened risk of HF in RA.

Disclosure: T. Johnson: None; **Y. Yang**: None; **P. Roul**: None; **J. Baker**: CorEvitas, 2, Cumberland Pharma, 2, Horizon Pharmaceuticals, 5; **B. Sauer**: None; **G. Cannon**: None; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **B. England**: Boehringer-Ingelheim, 2, 5.

Abstract Number: 0744

Personalizing Cardiovascular Risk Prediction for Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Epidemiology & Public Health I
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Cardiovascular disease (CVD) risk is elevated in patients with SLE but underestimated by current general population prediction algorithms that do not include SLE-related variables. We aimed to develop a novel SLE-specific prediction tool, SLECRISK, to estimate CVD risk more accurately in SLE.

Methods: We studied patients in the Brigham and Women's Hospital SLE cohort. We collected 1-year baseline data on traditional CVD risk factors, demographic and SLE-related clinical features from the electronic medical records at cohort enrollment. Ten-year follow-up for 1stmajor adverse cardiovascular event (MACE, non-fatal myocardial infarction [MI], non-fatal stroke, and cardiac death) began at day +1 after baseline period (index date). ICD-9/10 codes identified MACE, adjudicated by medical record review by board-certified cardiologists. Least absolute shrinkage and selection operator (LASSO) regression selected SLE-related variables to add to the American College of Cardiology (ACC)/American Heart Association (AHA) Pooled Cohort Risk Equations 10-year risk Cox regression model. Model fit statistics and performance for predicting moderate- and high-risk (≥10%) of MACE were assessed and compared to ACC/AHA alone, Framingham risk score (FRS), and modified FRS (FRS multiplied by 2, mFRS). Optimism adjustment was performed using bootstrapping with 300 samples.

Results: We included 1,243 patients with 90 MACEs (46 MIs, 36 strokes, 19 cardiac deaths) over 8,946.5 person-years follow-up (**Table 1**).

Our best **SLECRISK 10-Year CVD Risk equation** was: 1-0.92*exp(βx-1.84), whereby βx = 5.44*Base ACC/AHA Risk Score + 0.31*disease activity (remission/mild vs. moderate/severe) + 0.04*disease duration (years) + 0.17*Creatinine (mg/dL) + 0.35*Anti-dsDNA + 0.22*Anti-RNP + 0.47*Lupus anticoagulant + 0.31*Anti-Ro + 0.49*low C4.

Sensitivity for detecting moderate/high-risk (≥10%) of MACE (0.64) and c-statistic for model discrimination (0.76) were improved vs. traditional models (**Table 2**). The AIC estimate of model fit improved (1190.5 to 1162.2) and Hosmer-Lemeshow goodness-of-fit tests yielded favorable results (P 0.02 in base ACC/AHA model and P 0.77 in SLECRISK), indicating good model calibration. SLECRISK identified >3-fold more high-risk patients, particularly more young women with few traditional risk factors, but more severe SLE, including lupus nephritis, higher creatinine, more autoantibodies, including antiphospholipid antibodies, hypocomplementemia, and more taking azathioprine (**Fig 1**).

Conclusion: We derived and internally validated a novel SLE-specific CVD risk tool based on the ACC/AHA score and SLE-related factors. SLECRISK was more sensitive and accurate than the traditional CVD generic tools for predicting moderate- and high-risk for MACE over 10 years of follow-up. If externally validated, SLECRISK may be incorporated into SLE management guidelines to help guide decision-making in the primary prevention of CVD in clinical practice.

Table 1. Baseline demographic, cardiovascular, and clinical features among 1,243 patients with SLE in the Brigham and Women's Hospital Lupus Cohort with vs. without Major Adverse Cardiovascular Event (MACE)[1] in follow-up, according to Definite (Adjudicated[2]) and Probable MACE definitions.

	CVD Event (n=90)	No CVD Event (n=1153)
Demographics, mean (SD)		
Age	50.19 (14.04)	40.95 (13.07)
Female, n (%)	1074 (93.15)	82 (91.11)
White, n (%)	60 (66.67)	717 (62.19)
CVD Traditional Risk Factors		
Total Cholesterol, mg/dL, mean (SD)	189.53 (38.05)	182.17 (60.17)
HDL, mg/dL, mean (SD)	56.4 (18.68)	55.68 (20.00)
LDL, mg/dL, mean (SD)	110.54 (35.71)	99.21 (39.93)
SBP, mg/dL, mean (SD)	131.91 (28.23)	121.54 (16.48)
DBP, mg/dL, mean (SD)	81.09 (16.69)	75.28 (10.95)
Anti-hypertensive, n (%)	48 (53.33)	363 (31.48)
Current Smoker, n (%)	18 (20.00)	136 (11.8)
Body Mass Index, kg/m^2, mean (SD)	27.79 (6.12)	29.59 (39.99)
Diabetes, n (%)	15 (16.67)	71 (6.16)
SLE Clinical Features		
Creatinine, mg/dL, mean (SD)	1.42 (1.47)	0.96 (0.98)
SLE Duration, mg/dL, mean (SD)	15.44 (11.64)	10.31 (8.68)
Lupus nephritis, n (%)	35 (38.89)	359 (31.14)
Physician Global Assessment most recent, n (%)		
Remission/Mild	74 (82.22)	1022 (88.64)
Moderate	9 (10)	88 (7.63)
Severe	7 (7.78)	43 (3.73)
Physician Global Assessment over the past year, n (%)		
Remission/Mild	70 (77.78)	933 (80.92)
Moderate	11 (12.22)	100 (8.67)
Severe	9 (10)	120 (10.41)
Positive Serologies and Low Complement Levels, n (%)		
Antinuclear antibody	87 (96.67)	1127 (97.75)
Anti-dsDNA	72 (80)	782 (67.82)
Anti-RNP	41 (45.56)	444 (38.51)
Anti-Sm	30 (33.33)	365 (31.66)
Anti-Ro	52 (57.78)	542 (47.01)
Anti-SSB/La	30 (33.33)	321 (27.84)
Lupus anticoagulant, n (%)	15 (16.67)	117 (10.15)
Anti-cardiolipin IgG, n (%)	22 (24.44)	236 (20.47)
Anti-cardiolipin IgM, n (%)	11 (12.22)	163 (14.14)
Anti-β2GP1 IgG, n (%)	6 (6.67)	74 (6.42)
Anti-β2GP1 IgM, n (%)	0 (0)	33 (2.86)
Any positive antiphospholipid, n (%)	24 (26.67)	270 (23.42)
Low C3, n (%)	44 (48.89)	526 (45.62)
Low C4, n (%)	41 (45.56)	369 (32.00)
Current Medications, n (%)		
Glucocorticoids[3]	57 (63.33)	650 (56.37)
Hydroxychloroquine	47 (52.22)	702 (60.88)
Mycophenolate mofetil	12 (13.33)	167 (14.48)
Cyclophosphamide	3 (3.33)	46 (3.99)
Azathioprine	12 (13.33)	151 (13.10)
Rituximab	1 (1.11)	21 (1.82)
Cyclosporin	1 (1.11)	10 (0.87)
Leflunomide	3 (3.33)	15 (1.3)
Methotrexate	2 (2.22)	91 (7.89)
Tacrolimus	1 (1.11)	18 (1.56)
IV IgG Immunoglobulin	1 (1.11)	25 (2.17)
Belimumab	0 (0)	16 (1.39)
Aspirin	20 (22.22)	147 (12.75)
Statin	24 (26.67)	119 (10.32)
Warfarin	13 (17.57)	72 (6.16)
Angiotensin-converting enzyme (ACE) inhibitors	24 (26.67)	202 (17.52)
Angiotensin receptor blockers (ARBs)	14 (15.56)	46 (3.99)
Calcium channel blockers	26 (28.89)	136 (11.80)
Beta-blockers	32 (35.56)	141 (12.23)
Diuretics	5 (5.56)	65 (5.64)

1. Major adverse cardiovascular event includes non-fatal myocardial infarction, non-fatal stroke, and cardiac death
2. Adjudicated by board-certified cardiologists
3. Includes oral and intravenous glucocorticoids

Abbreviations: β2GP1CVD, Beta2 glycoprotein 1; C3, complement 3; C4, complement 4; cardiovascular disease; DBP, diastolic blood pressure; dsDNA, anti-double stranded DNA; HDL, high density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; SD, standard deviation; SLE, systemic lupus erythematosus

Table 2. Novel SLECRISK, American College of Cardiology/American Heart Association (ACC/AHA), Framingham Risk Score (FRS), Modified Framingham Risk Score (mFRS) Model Performances for Prediction of <10% (low risk) vs. ≥10% (moderate/high risk) One and Ten-Year Risks of Definite and Probable MACE among 1,243 Patients with SLE at Baseline

	SLECRISK	ACC/AHA	FRS	mFRS
Low Risk (<10%), n (%)	864 (69.5)	1010 (81.3)	1009 (81.2)	990 (79.7)
Moderate Risk (10-20%), n (%)	265 (21.3)	200 (16.1)	171 (13.8)	116 (9.3)
High Risk (>20%), n (%)	114 (9.2)	33 (2.7)	63 (5.1)	137 (11.0)
Sensitivity*	0.64	0.41	0.42	0.47
Specificity*	0.72	0.83	0.83	0.82
Positive Predictive Value*	0.15	0.16	0.16	0.17
Negative Predictive Value*	0.96	0.95	0.95	0.95
Harrell's c-statistic*	0.76	0.70	0.71	0.71
Optimism-Corrected c-statistic*	0.73	-	-	-
Integrated Time-Dependent AUC*	0.77	0.71	0.71	0.71
Year 1 AUC*	0.68	0.60	0.62	0.69
Year 10 AUC*	0.69	0.65	0.68	0.75
AIC	1162.16	1190.50	1175.89	1171.82
Hosmer-Lemeshow goodness-of-fit	0.77	0.02	0.10	0.10

*Performance assessed using the using cut-off <10% (low risk) vs. ≥10% (moderate/high risk)
Abbreviations: AIC, Akaike's information criterion; AUC, area under the curve; ACC/AHA American College of Cardiology/American Heart Association; FRS, Framingham Risk Score; mFRS, modified Framingham Risk Score.

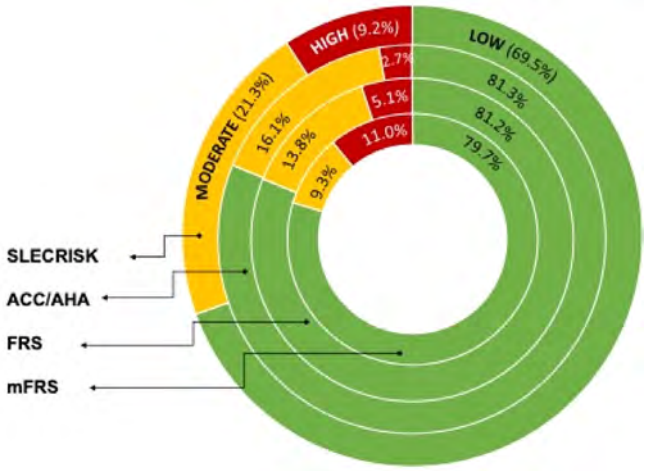

Figure 1. Risk Classification (%) by Cardiovascular Risk Prediction Models as Low (<10%), Moderate (10-20%), and High (>20%) Ten-year MACE Risk of Definite and Probable MACE among 1,243 Patients with SLE at Baseline. Abbreviations: ACC/AHA, American College of Cardiology/ American Heart Association; mFRS, FRS Framingham risk score; modified Framingham risk score

Disclosure: M. Choi: AbbVie/Abbott, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 6, Mallinckrodt, 2, Merck/MSD, 2, MitogenDx, 2, Organon, 6, Pfizer, 2, 6, Roche, 2, Werfen, 2; **H. Guan**: None; **K. Yoshida**: Takeda, 3; **B. Kargere**: None; **J. Ellrodt**: None; **E. Stevens**: None; **T. Cai**: None; **B. Everett**: None; **B. Weber**: Bristol-Myers Squibb(BMS), 1, Horizon Therapeutics, 1, Kiniksa, 1, Novo Nordisk, 1; **K. Costenbader**: Amgen, 2, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Eli Lilly, 2, Exagen Diagnostics, 5, Gilead, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5.

Abstract Number: 0745

Artificial Intelligence Models for Computer-Assisted Joint Detection and Sharp-van Der Heijde Score Prediction in Hand Radiographs from Patients with Rheumatoid Arthritis

Carol Hitchon[1], Saqib Al Islam[1], Daryl LX Fung[1], Qian Liu[1], Leann Lac[1], Susan Bartlett[2], Louis Bessette[3], Gilles Boire[4], Vivian Bykerk[5], Glen Hazlewood[6], Edward Keystone[7], Janet Pope[8], Orit Schieir[9], Carter Thorne[10], Diane Tin[11], Marie-France Valois[12], Désirée van der Heijde[13], Canadian Early Arthritis Cohort (CATCH) Investigators[14], Liam O'Neil[1] and Pingzhao Hu[15], [1]University of Manitoba, Winnipeg, MB, Canada, [2]McGill University, Montreal, QC, Canada, [3]Centre de l'Ostéoporose et de Rhumatologie de Québec, Quebec City, QC, Canada, [4]Université de Sherbrooke, Sherbrooke, QC, Canada, [5]Hospital for Special Surgery, New York, NY, [6]University of Calgary, Calgary, AB, Canada, [7]Keystone Consulting Enterprises Inc., Toronto, ON, Canada, [8]University of Western Ontario, London, ON, Canada, [9]McGill University, Montréal, QC, Canada, [10]Southlake Regional Health Centre, Newmarket, ON, Canada, [11]The Arthritis Program Research Group, Newmarket, ON, Canada, [12]McGill University, Pointe-Claire, QC, Canada, [13]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [14]CATCH, Winnipeg, MB, Canada, [15]Western University, London, ON, Canada

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Imaging of Rheumatic Diseases

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Radiographs are used to detect and monitor joint damage due to rheumatoid arthritis (RA).Scoring methods such as the Sharp van der Heijde tool (SVH) quantify joint space narrowing (JSN) and erosions. Obtaining SVH scores is time-consuming and requires expertise not always available. We aimed to develop and validate a deep learning system for automated detection and prediction of SVH scores in hand radiographs of patients with RA**.**

Methods: We used a convolutional neural network (CNN) based algorithm (You Only Look Once (YOLO)v5l6) trained on an object detection model (COCO-Common Objects in Context) to detect joints in 240 training and 89 test pediatric hand radiographs from the Radiologic Society of North America database. Radiographs were annotated by boxing and labeling the joints of interest: proximal interphalangeal, metacarpophalangeal, wrist, distal radius, distal ulna. Images were augmented using mix-up (mixing features of different images into one), mosaic (combining 4 training images into 1 image), rotation, translation, scaling, and shearing. The joint detection model was validated with 54 clinician-annotated radiographs from 4 adult RA patients followed for 9-13 years (10-12 images per patient) (joint detection gold standard). We applied a supervised vision transformer model (VTM) to predict each joint's SVH erosion and JSN score. The VTM was validated using 2249 hand radiographs with clinician-assigned SVH scores from 381 RA patients from the Canadian Early Arthritis Cohort

Table: Accuracy of model for joint detection

	RSNA radiographs pre-trained on COCO						
	Images	Number targets	F1 score	Mean precision	Mean recall	map0.1	map
All	89	1157	0.991	0.998	0.983	0.993	0.854
PIP	89	445	0.994	1	0.987	0.994	0.772
MCP	89	445	0.991	0.993	0.989	0.994	0.624
Wrist	89	89	0.993	1	0.986	0.994	0.958
Radius	89	89	0.998	1	0.976	0.994	0.983
Ulna	89	89	0.987	0.997	0.978	0.988	0.933
	Adult Rheumatoid Arthritis radiographs pre-trained on COCO						
All	54	1354	0.812	0.923	0.725	0.871	0.627
PIP	54	518	0.880	0.893	0.869	0.823	0.615
MCP	54	521	0.860	0.939	0.794	0.814	0.601
Wrist	54	102	0.883	0.965	0.814	0.886	0.876
Radius	54	109	0.821	0.909	0.750	0.828	0.661

(SVH score gold standard). We applied techniques used to train highly class-imbalanced datasets including weighted sampling, stratified data-split, data augmentation and transfer learning (TL). As the joint detection model was trained to detect the whole wrist and we had clinician-assigned SVH scores for individual wrist joints, we trained a separate multi-task model to predict wrist joint scores from whole wrist images. The performance of the VTM to predict joint scores was compared to CNN-based EfficientNetV2 and MobileNetV3. Model accuracy for joint detection is reported as the F1-score (reflecting model precision and model recall) and mean absolute precision (mAP) for a range of Intersection-over-Union (IoU) measures

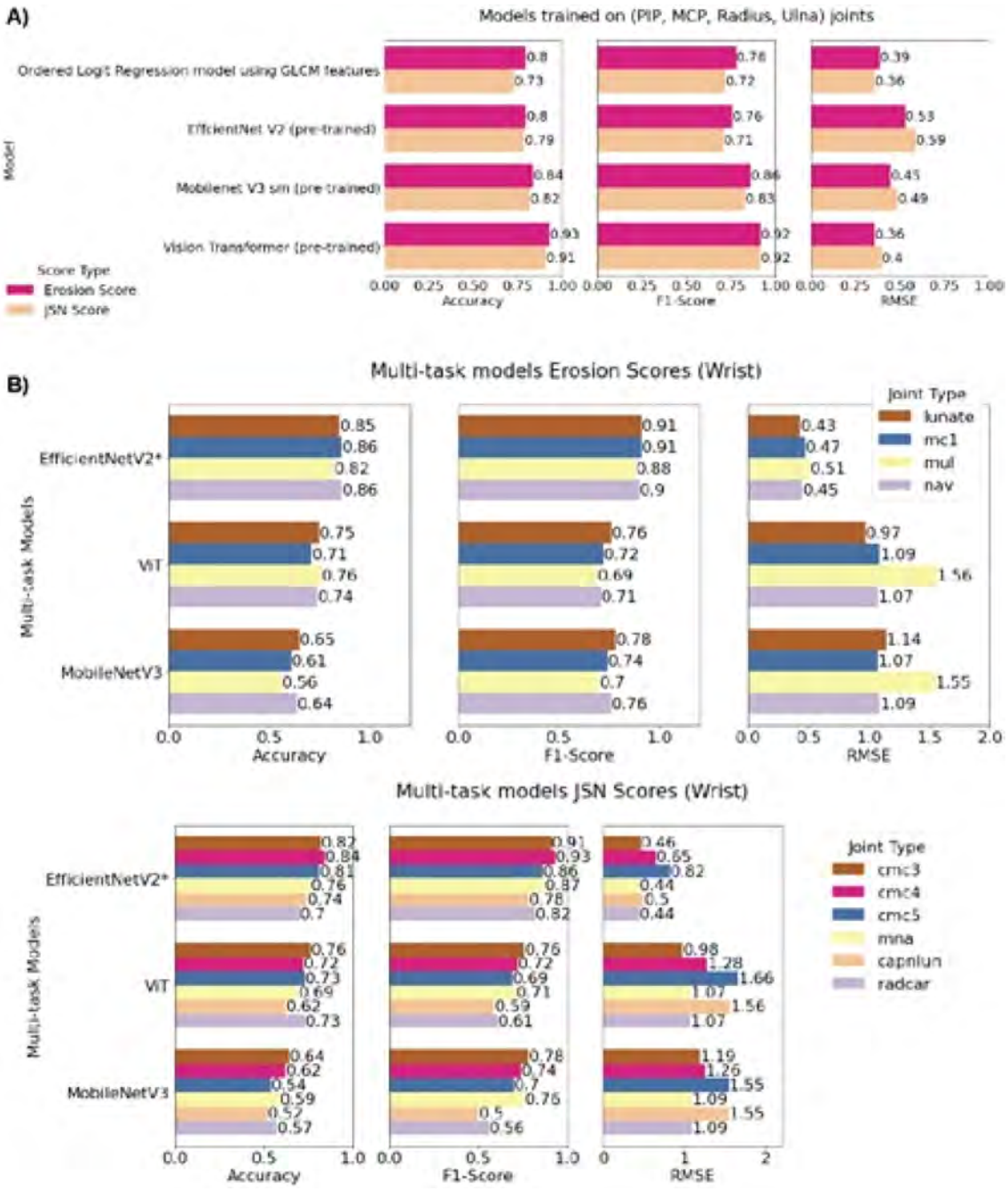

Figure: Joint damage score prediction models. A) Models trained on all joints except wrist. The metrics reported were balanced accuracy, F1-Score and Root Mean Square Error (RMSE) predicting Joint Space Narrowing (JSN) and Erosion scores. B) Models were trained on wrist joints. Separate models trained to detect the erosion score and JSN scores. PIP=proximal interphalangeal, MCP=metacarpophalangeal, JSN= joint space narrowing, Vit= Vision Transformer, mc = metacarpal, nav = navicular, cmc = carpometacarpal

reflecting the overlap between clinician and model assigned bounding boxes of detected joints. Accuracy for SVH score prediction is reported as root mean squared error (RMSE) and balanced accuracy.

Results: The joint detection model accurately identified target joints (pediatric data FI-score = 0.991, map0.1 = 0.993 with an IoU threshold of 0.1 ; adult data F1-score = 0.812, map0.1 = 0.871 (n=54) (Table 1). Applying TL improved the joint detection model's mean precision by 0.05 over the COCO model. The VTM predicted JSN and erosion SVH scores with high accuracy (RMSE JSN 0.91, erosion 0.93). The multi-task models predicted SVH erosion and JSN scores of wrist joints with moderately high accuracy (0.6-0.91). EfficientNetV3 performed better for wrist joints (VTM vs EfficientNetV3 average difference 0.10) (Figure 1).

Conclusion: Automated deep learning systems accurately identify and predict joint damage in hand radiographs from patients with rheumatoid arthritis and may aid in monitoring joint damage.

Disclosure: C. Hitchon: Astra Zeneca, 1, Pfizer, 5; **S. Al Islam**: None; **D. Fung**: None; **Q. Liu**: None; **L. Lac**: None; **S. Bartlett**: Janssen, 6, Merck/MSD, 2, 6, Novartis, 2, Organon, 1, 6, PROMIS Health Organization, 4, Sandoz, 2, 6; **L. Bessette**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol Myers Squibb, 2, 5, 6, Eli Lilly, 2, 5, 6, Fresenius Kabi, 2, 6, Gilead, 2, 5, 6, JAMP Pharma, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Organon, 2, 6, Pfizer, 2, 5, 6, Sandoz, 2, 6, Sanofi, 2, 5, 6, Teva, 2, 6, UCB, 2, 5, 6, UCBA, 5; **G. Boire**: Eli Lilly, 1, Janssen, 6, Organon, 1, Orimed Pharma, 1, 6, Otsuka, 1, Pfizer, 1, 5, Sandoz, 1, Teva, 1, Viatris, 1, 6; **V. Bykerk**: Abbvie, 2, BMS, 2, Pfizer, 2; **G. Hazlewood**: None; **E. Keystone**: AbbVie/Abbott, 2, 6, Amgen, 2, 6, celltrion, 2, 6, Eli Lilly, 2, 6, Fresenius Kabi, 2, 6, Pfizer, 2, 6, Samsung Bioepsis, 2, sandoz, 2, 6; **J. Pope**: AbbVie, 1, 2; **O. Schieir**: None; **C. Thorne**: Abbvie, 1, Biogen, 2, Nordic Pharma, 1, Pfizer, 1, 5, Roche, 1, Sandoz, 1, 2; **D. Tin**: None; **M. Valois**: None; **D. van der Heijde**: AbbVie, 2, Bayer, 2, BMS, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GSK, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; **C. (CATCH) Investigators**: AbbVie Corporation, 5, Amgen Canada, 5, Hoffman La Roche Limited, 5, Medexus Pharmaceuticals, 5, Organon Canada, 5, Pfizer Canada, 5, Sandoz Biopharmaceuticals Canada, 5; **L. O'Neil**: None; **P. Hu**: None.

Abstract Number: 0746

The Association Between Sonographic Imaging Phenotype and Response to Treatment in Patients with Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Imaging of Rheumatic Diseases
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Ultrasound (US) may improve characterization of psoriatic arthritis (PsA) phenotypes and help predict disease outcomes. We aimed to assess whether US phenotypes are associated with clinical features and treatment outcomes in patients with active PsA.

Methods: We conducted a prospective cohort study of patients with active PsA prior to initiation of systemic therapy. Disease activity in various PsA domains was clinically assessed.

Baseline US assessment of inflammatory and structural lesions was conducted for the following features: synovitis, peritenonitis, tenosynovitis, new bone formation (NBF), bone erosion, and enthesitis for inflammatory (inflm) and structural (str) lesions. The following treatment outcomes were analyzed: drug persistence, Disease Activity in PsA (DAPSA) change, and DAPSA low disease activity (LDA) at 3-6 months.

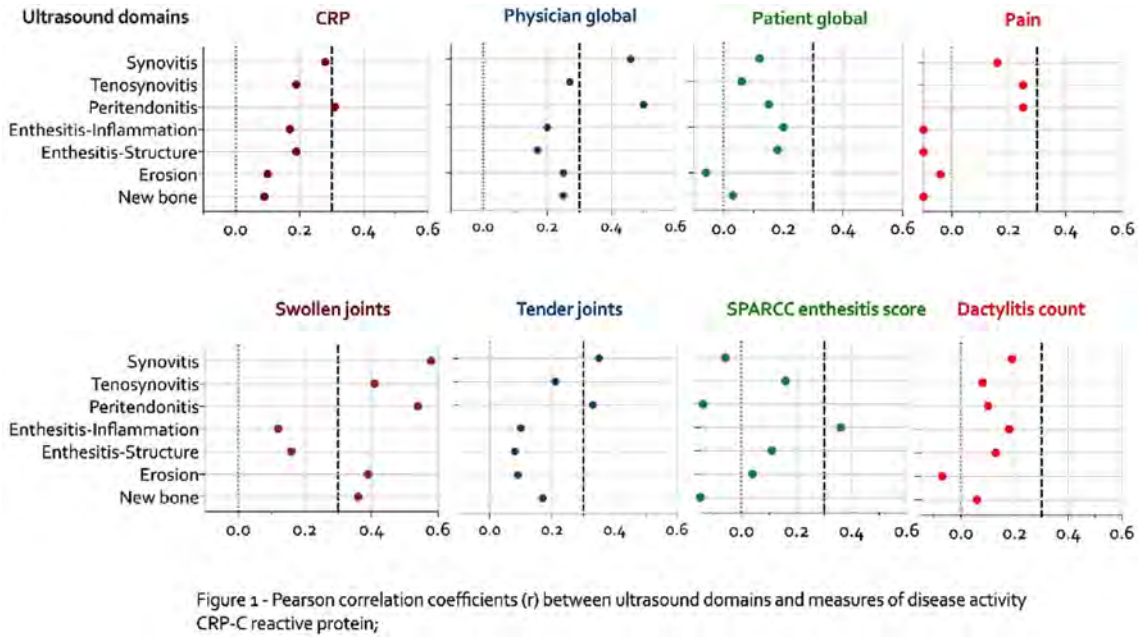

Figure 1 - Pearson correlation coefficients (r) between ultrasound domains and measures of disease activity
CRP-C reactive protein;

Figure 1 - Pearson correlation coefficients (r) between ultrasound domains and measures of disease activity

Table 1 - The association between baseline ultrasound scores and change in DAPSA score from baseline to follow up visit at 3-6 months - GEE linear regression model

Table 1 - The association between baseline ultrasound scores and change in DAPSA score from baseline to follow up visit at 3-6 months - GEE linear regression model

	Multivariate model All patients (N=87)		Multivariate model Patients on TNF inhibitors (N=41)	
	β (95% CI)	P value	β (95% CI)	P value
Total synovitis score	**-3.89 (-7.09, -0.68)**	**0.02**	**-5.26 (-8.84, -1.68)**	**0.004**
Total PTI score	**-3.93 (-7.01, -0.84)**	**0.01**	**-6.11 (-9.85, -2.38)**	**0.001**
Total erosion score	-0.86 (-3.79, 2.07)	0.56	-1.68 (-3.56, 0.20)	0.08
Total NBF score	1.20 (-2.83, 5.22)	0.56	-0.79 (-6.08, 4.51)	0.77
Total tenosynovitis	-4.21 (-8.62, 0.21)	0.06	**-5.18 (-8.73, -1.64)**	**0.004**
Total enthesitis-inflammation	-2.28 (-5.15, 0.57)	0.12	-1.32 (-4.68, 2.04)	0.44
Total enthesitis-structure	**-2.91 (-5.75, -0.06)**	**0.045**	**-3.21 (-6.37, -0.07)**	**0.045**

**Models are adjusted for medication class (targeted DMARD vs. conventional DMARD) and prior exposure to tDMARDs*
CI – confidence intervals; NBF- new bone formation; PTI- peritenon inflammation
Ultrasound scores are standardized.

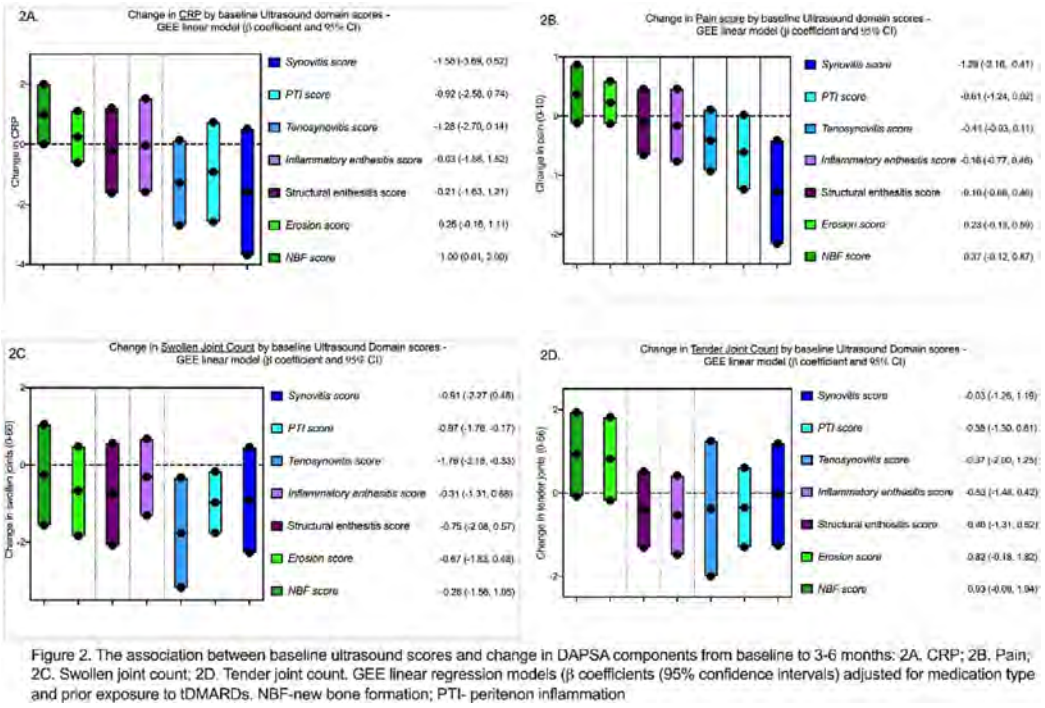

Figure 2. The association between baseline ultrasound scores and change in DAPSA components from baseline to 3-6 months: 2A. CRP; 2B. Pain; 2C. Swollen joint count; 2D. Tender joint count. GEE linear regression models (β coefficients (95% confidence intervals) adjusted for medication type and prior exposure to tDMARDs. NBF-new bone formation; PTI- peritenon inflammation

Figure 2 - The association between baseline ultrasound scores and change in DAPSA components from baseline to 3-6 months: 2A. CRP; 2B. Pain; 2C. Swollen joint count; 2D. Tender joint count. GEE linear models adjusted for medication type and exposure to tDMARDs

The correlation between various baseline clinical and US features was assessed (r >0.3 was considered moderate correlation). The association between baseline US features and treatment outcomes were assessed using Cox proportional hazards models (for drug persistence), linear models via GEE (for DAPSA change) and logistic GEE models (for DAPSA-LDA). Models were adjusted for type of drug (targeted (t) vs. conventional DMARDs) and prior exposure to tDMARDs.

Results: A total of 135 treatment periods (107 patients) with PsA (49% females) were analyzed. The mean age and disease duration were 47.7 (SD=13.7) and 4.7 (SD=6.8) years, respectively.

Highest correlations were found for US synovitis and peritonitis with physician global assessment (PhyGA) and swollen joints (Figure 1). PhyGA correlation with other US features was low. Synovitis and peritenonitis US scores correlated moderately with CRP and tender joints. Tenosynovitis and enthesitis-inflm showed moderate correlation with swollen joints and enthesitis score, respectively.

Drug persistence was analyzed in 105 treatment periods (40% drug discontinuation). The only US feature associated with drug discontinuation was US erosion score (adjusted Hazards Ratio 1.28, 95% confidence interval 1.03, 1.61).

87 treatment periods were analyzed for DAPSA response at 3-6 months (54% achieved DAPSA-LDA). No association was found between any US feature and DAPSA-LDA. Greater reduction in DAPSA scores was associated with higher baseline synovitis, peritenonitis and enthesitis-str scores (Table 1). Restriction of the analysis to users of TNFi (N=41) resulted in numerically higher effect sizes for several US features.

A multivariable analysis was performed to assess which components of DAPSA are influenced by US features (Figure 2). We found significant associations between US synovitis and reduction in pain (b= -1.28), US NBF and increase in CRP (b= 1.00), US tenosynovitis (b= -1.76) and peritenonitis (b= -0.97) and reduction in swollen joint count. None of the US features were associated with changes in tender joint count.

Conclusion: Discordance between imaging and clinical features of PsA exists. Sonographic synovitis, peritenonitis and tenosynovitis correlate more strongly with clinical features of disease activity and response outcomes.

Disclosure: J. Gutierrez Manjarrez: None; **S. Thib**: None; **R. Cook**: None; **L. Eder**: AbbVie, 2, 5, Eli Lilly, 2, 5, Fresenius Kabi, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Sandoz, 5, UCB, 2, 5.

Abstract Number: 0747

Clinical Phenotype of Patients with Subclinical Giant Cell Arteritis in Polymyalgia Rheumatica

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Imaging of Rheumatic Diseases
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: It has been reported that more than a quarter of patients with polymyalgia rheumatica (PMR) have subclinical giant cell arteritis (GCA). It remains unclear if all PMR patients should have ultrasound assessment for subclinical GCA or if there are certain phenotypes of patients that are more at risk of having subclinical GCA.

Methods: Newly diagnosed PMR patients who met a clinical diagnosis for PMR, verified by two rheumatologists were examined with vascular ultrasound (US) of their temporal and axillary arteries. US of all 6 branches of the superficial temporal and both axillary arteries was performed using a GE P9 device. Sonographic abnormalities considered indicative of vasculitis in the temporal arteries included the halo sign and non-compressible arteries with a thickened intima-media complex. An intima-media thickness of 0.42mm for the common superficial temporal branch, 0.34mm for the frontal branch, and 0.29mm for the parietal branch was considered positive. In the axillary arteries, a halo sign, and an intima-media thickness of >1.0mm was considered positive. Clinical and laboratory characteristics were recorded. Halo scores were calculated for positive cases. Ultrasound findings were compared to a cohort of GCA patients.

Results: 91 patients with newly diagnosed PMR and 57 patients with newly diagnosed GCA were included. ACR/EULAR classification criteria were met in 67 of those with PMR (primarily due to prior corticosteroid use in primary care resulting in normal ESR/CRP) and all of those with GCA. Of the 91 patients with PMR, 16 were identified as having subclinical GCA on ultrasound (17.5%).

	PMR (75)	PMR with subclinical GCA (16)	GCA (47)
Age (mean and range)	69 (51-89)	70 (53-84)	74 (56-92)
Female	48	4	24
Male	27	12	33
Mean BMI	28.2	28.1	27.8
Mean ESR at baseline	38mm/hr	49mm/hr	58mm/hr
Mean CRP at baseline	29mg/l	39.9mg/l	66mg/l
Mean halo count	0	4.33	4.36
Mean temporal artery halo score	0	4.68	13.17
Mean axillary artery halo score	0	9.75	13.28

Figure 1: Results

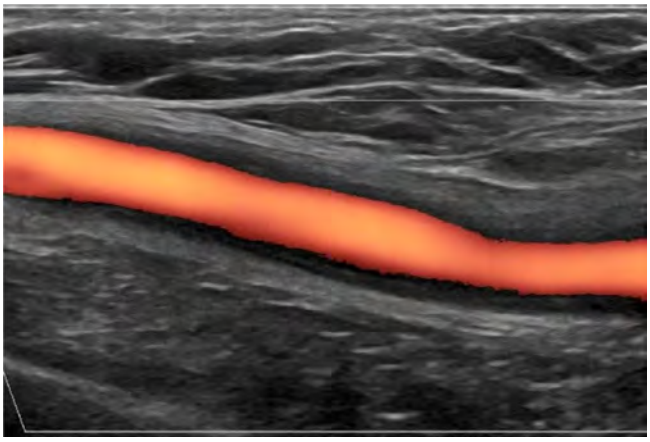

Figure 2: Axillary artery with halo sign

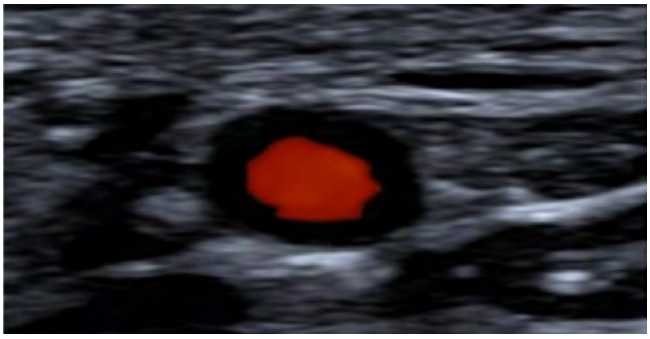

Figure 3: Temporal artery with halo sign

The mean age at time of diagnosis was 69 years for those with PMR, 70 years for those with subclinical GCA in PMR and 74 years for those with GCA. Males were more likely to have subclinical GCA in PMR, accounting for 12 (75%) of the subclinical GCA group compared to 27 (36%) of the pure PMR group (p=0.045). The mean ESR at baseline for those with subclinical GCA in PMR was higher than those with isolated PMR; 49mm/hr compared to 38mm/hr (p=0.18).

The extent of involvement of the temporal and axillary arteries of the 16 patients in the subclinical GCA group was compared to a cohort of 57 GCA patients. The total halo count was similar for both subclinical GCA in PMR and classic GCA patients at 4.33 and 4.36 respectively. However, GCA patients had higher halo scores in both temporal and axillary vessels of 13.17 and 13.28 respectively, compared to those with subclinical GCA with halo scores of 4.68 and 9.75. This suggests that patients with subclinical GCA in PMR have less vessel wall oedema than those with GCA. The subclinical GCA group had higher halo scores in the axillary arteries versus the temporal arteries, (p=0.0074) suggesting a predilection for the axillary vessels.

Conclusion: Patients with subclinical GCA had higher halo scores in the axillary arteries compared to the temporal arteries suggesting an extracranial phenotype. Male gender and a higher ESR at the time of PMR diagnosis appear to be risk markers for subclinical GCA though this requires analysis in larger cohorts of patients.

Disclosure: S. Cowley: None; **C. Kirby**: None; **P. Harkins**: Janssen, 5; **R. Conway**: AbbVie/Abbott, 5, 6, Celltrion, 5, Fresenius Kabi, 6, Galapagos, 6, Janssen, 5, 6, Nordic Pharma, 5, Novartis, 5, UCB, 6, Viatris, 6; **D. Kane**: None.

Abstract Number: 0748

Assessment of Myositis-related Interstitial Lung Disease by ^{68} Ga-DATA. SA.FAPi PET/CT

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Imaging of Rheumatic Diseases

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Background/Purpose: Interstitial lung disease (ILD) is a common manifestation of idiopathic inflammatory myopathies (IIM) ranging up to 78% in IIM and is a key contributor to hospitalization, excess morbidity and mortality. In-vivo visualization evidence of ongoing tissue remodeling in IIM-ILD is scarce. In this study, we aimed to quantify and compare fibroblast activation in the lungs of IIM-patients and control subjects using ^{68}Ga-labelled inhibitor of Fibroblast-Activation-Protein based (^{68}Ga-DATA.SA.FAPI) positron emission tomography combined with computed tomography (FAPI PET/CT) imaging.

Methods: Patients with IIM recruited prospectively from the rheumatology outpatient clinic, and control subjects without rheumatic conditions or ILD recruited from the cardiology outpatient clinic underwent FAPI PET-CT imaging. Pulmonary FAPI accumulation was assessed by measuring the maximal standardized uptake (SUV) value (SUVmax) and mean SUV (SUVmean) over the whole lung (wl) using the liver as internal reference, respectively. Values of SUV were compared across IIM patients with and without ILD and controls using analysis of variance test and displayed as mean ± standard deviation (SD). Standard-of-care procedures such as high-resolution computed tomography (hr-CT) and pulmonary function testing (PFT) were performed in all IIM-patients at baseline and in patients with ILD at follow-up.

Results: The clinical characteristics of patients with IIM (14 patients with ILD confirmed by hr-CT and 5 non-ILD patients with primary muscular affection) and control subjects (n=19) are displayed in Table 1. Three (n=3) patients in the control group were excluded from analysis due to pulmonary disease or cardiac decompensation. In individuals with IIM-related ILD, whole-lung ^{68}Ga-DATA.SA.FAPI uptake assessed by wlSUVmax (Figure 1A) and wlSUVmean (Figure 1B) corrected for the liver was significantly increased as compared to both non-ILD IIM patients and the control group. No differences of wlSUVmax or wlSUVmean were observed between non-ILD IIM patients and the control group. FAPI uptake in the lungs correlated significantly with pulmonary function tests, severity of dyspnea and serum concentration of acute phase reactants at baseline. Moreover, IIM-patients with progressive ILD (defined as worsening in pulmonary function tests at 1-year follow up and/or need for intensification of immunosuppressive therapy) had significantly increased pulmonary FAPI uptake at baseline (Figure 2).

Conclusion: Our study demonstrates higher FAPI uptake in patients with IIM-ILD. Intensity of pulmonary FAPI accumulation was associated with progression of ILD. Thus, ^{68} Ga-DATA.SA.FAPi PET/CT may serve as a useful non-invasive tool for risk stratification of lung disease in IIM.

Table 1: Demographic and clinical characteristics of participants at baseline. Abbreviations: DLCO, diffusion capacity of the lungs for carbon monoxide; FVC, forced vital capacity; IIM: idiopathic inflammatory myopathy; ILD: interstitial lung disease; No./n, number; NSIP, nonspecific interstitial pneumonia; OP, organizing pneumonia; SD, standard deviation; UIP, usual interstitial pneumonia

		IIM patients	Controls
No. (n)		19	19
Sex (female)		11 (57.9%)	14 (73.7%)
Mean age (years ± SD)		52.6 ± 15.3	79.0 ± 3.8
Ethnicity (Caucasian)		18 (94.7%)	19 (100%)
Disease subtype			
	Antisynthetase syndrome	11 (57.9%)	-
	Dermatomyositis	3 (15.8%)	-
	Overlap myositis	3 (15.8%)	-
	Immune-mediated necrotizing myopathy	2 (10.5%)	-
ILD (presence/absence)			
	Yes	14 (73.7%)	-
ILD-Subtype			
	NSIP	8 (53.3%)	-
	UIP	1 (6.7%)	-
	OP	3 (20%)	-
	NSIP and OP	3 (20%)	-
Autoantibodies			
	Aminoacyl-tRNA synthetase	11 (57.9%)	-
	Ro-52	3 (15.8%)	-
	MDA5	2 (10.5%)	-
	Mi-2	1 (5.3%)	-
	Seronegative	2 (10.5%)	-
Pulmonary function tests			
FVC % (mean ±SD)		82.3 ± 21.6	-
DLCO % (mean ±SD)		66.2 ± 21.2	-

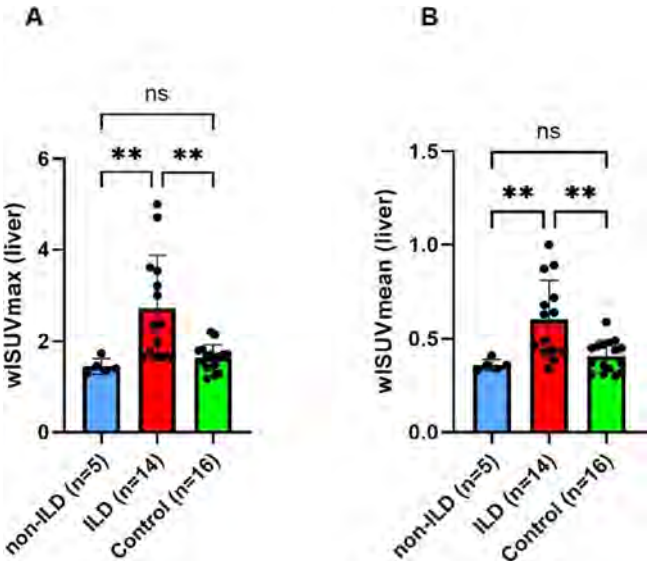

Figure 1: ^{68}Ga-FAPI uptake in the lungs of IIM-patients and controls. A) Whole-lung maximal standardized uptake value; B) whole-lung mean standardized uptake value in myositis patients with or without interstitial lung disease and control subjects. Abbreviations: wlSUVmax (liver), whole-lung maximal standardized uptake value in relation to liver; wlSUVmean (liver), whole-lung mean standardized uptake value in relation to liver; ILD, interstitial lung disease, ns, not significant.

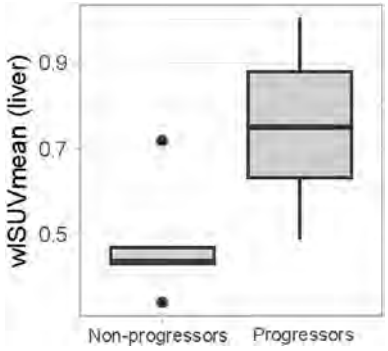

Figure 2: Baseline pulmonary ^{68}Ga-FAPI accumulation and ILD progression. Boxplot demonstrating FAPI uptake determined by whole-lung mean standardized uptake value (wlSUVmean) in relation to liver. IIM-patients with progressive ILD (Progressors) were defined as worsening in pulmonary function tests at 1-year follow up and/or need for intensification of immunosuppressive therapy. Non-progressors were defined as patients with myositis-related ILD with forced vital capacity reduction of less than 5%, diffusion capacity of carbon monoxide reduction of less than 10%, and stable respiratory symptoms. Abbreviations: wlSUVmean (liver), whole-lung mean standardized uptake value in relation to liver.

Disclosure: K. Kastrati: None; **T. Nakuz**: None; **O. Kulterer**: None; **S. Blüml**: None; **M. Bonelli**: Eli Lilly, 12, personal fees, Galapagos, 5, GlaxoSmithKlein(GSK), 5; **I. Gessl**: None; **H. Kiener**: None; **W. Langsteger**: None; **D. Mrak**: None; **F. Prayer**: None; **H. Prosch**: AstraZeneca, 5, 6, Boehringer-Ingelheim, 1, 5, 6, 12, Travel grants, Bristol-Myers Squibb(BMS), 1, 6, EU Commission (EU4Health, Horizon Europe Health), 5, Janssen, 6, Merck/MSD, 1, 6, Novartis, 6, Roche, 1, 6, Sanofi, 1, 6, Siemens Healthcare, 5, 6, Takeda, 6; **E. Simader**: None; **T. Traub-Weidinger**: None; **D. Aletaha**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Janssen, 2, 6, Lilly, 2, 5, 6, Merck, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6, Sandoz, 2, 6, Sanofi, 5, Sobi, 5; **H. Radner**: None; **M. Hacker**: None; **P. Mandl**: AbbVie/Abbott, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Celgene, 5, 6, Eli Lilly, 5, 6, Janssen, 5, 6, Merck/MSD, 5, 6, Novartis, 5, 6, Roche, 5, 6, UCB, 5, 6.

Abstract Number: 0749

Impact of Sprifermin on Denuded Areas of Subchondral Bone (dABs): A Post Hoc Analysis of the FORWARD Study

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SESSION INFORMATION
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Session Title: Abstracts: Imaging of Rheumatic Diseases
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Background/Purpose: Sprifermin, recombinant human fibroblast growth factor 18 (rhFGF-18), is being investigated as a potential disease-modifying osteoarthritis drug. The Phase 2 FORWARD study demonstrated that intra-articular (IA) sprifermin significantly and dose-dependently improved cartilage thickness in knee OA (KOA).Cartilage defects, the most severe of which present as dABs, are known to increase in size with KOA progression and be associated with KOA pain and incident knee replacement. This analysis investigates the impact of sprifermin treatment on dABs in KOA.

Methods: In FORWARD, participants (pts) were randomized 1:1:1:1:1 to 3 weekly IA injections (1 cycle) of either PBO or sprifermin 30 μg or 100 μg every 6 or 12 months (Q6M, Q12M) for 18 months, then followed through year 5. The modified (with baseline [BL] and ≥1 post-BL MRI) intent-to-treat (mITT) and subgroup at risk (mSAR, enriched for more severe KOA [BL WOMAC Pain ≥40, minimum medial or lateral joint space width {mJSW} 1.5-3.5 mm]) populations were analyzed. dABs, derived from manual, quality-controlled cartilage and subchondral bone segmentations, were computed as the percentage (%) of the total area of subchondral bone not covered by cartilage of femorotibial joint (FTJ) regions. Measurements were analyzed at BL and Week 104 (W104) for the a) 30 and 100 μg arms individually, b) 30 and 100 μg arms combined, and c) pts with BL dAB. No imputation was performed for missing data; only descriptive data are provided.

Table 1. Baseline Characteristics and Week 104 Change from Baseline in TFTC Cartilage Thickness by dAB Status – mITT

Baseline Characteristic (unless otherwise stated)		Placebo (n=96)		Sprifermin			
				30 μg combined (n=198)		100 μg combined (n=200)	
		No dAB FTJ n=48	dAB FTJ n=48	No dAB FTJ (n=94)	dAB FTJ (n=104)	No dAB FTJ (n=97)	dAB FTJ (n=103)
Mean age, years (SD)		64.3 (8.6)	63.1 (8.7)	63.3 (9.1)	65.1 (8.1)	64.0 (8.1)	65.6 (8.0)
Female, n (%)		36 (75.0)	30 (62.5)	65 (69.1)	74 (71.2)	72 (74.2)	66 (64.1)
Asian race, n (%)		10 (20.8)	11 (22.9)	20 (21.3)	23 (22.1)	18 (18.6)	24 (23.3)
White race, n (%)		38 (79.2)	37 (77.1)	74 (78.7)	81 (77.9)	79 (81.4)	79 (76.7)
Hispanic/Latino, n (%)		1 (2.1)	0	0	1 (1.0)	0	0
Mean BMI (kg/m^2) (SD)		29.8 (6.4)	29.3 (5.3)	28.7 (5.0)	29.4 (5.6)	29.3 (5.7)	28.9 (4.8)
≥30, n (%)		21 (45.7)	18 (37.5)	37 (41.1)	42 (41.2)	39 (41.1)	35 (35.4)
KL Grade 3, n (%)		11 (22.9)	20 (41.7)	15 (16.0)	48 (46.2)	16 (16.5)	45 (43.7)
Mean medial mJSW, mm (SD)		3.8 (1.03)	3.7 (1.31)	3.9 (0.87)	3.6 (1.16)	3.9 (0.91)	3.7 (1.28)
TFTC Cartilage thickness, mm (SD)	Baseline	1.82 (0.25) n=47	1.79 (0.30) n=48	1.86 (0.26) n=92	1.76 (0.25) n=104	1.84 (0.27) n=95	1.78 (0.26) n=103
	Δ at W104	-0.01 (0.04) n=37	-0.03 (0.09) n=46	0.00 (0.06) n=77	-0.02 (0.08) n=101	0.03 (0.08) n=80	0.02 (0.07) n=100

Δ=change; BMI=body mass index; dAB=denuded area of bone; FTJ=femorotibial joint; KL=Kellgren Lawrence; KR=knee replacement; mITT=modified intent-to-treat; mJSW=minimum joint space width; N=total sample size; n=sample evaluated; SD=standard deviation; TFTC=total femorotibial compartment; W104=Week 104.

Table 2. %Denuded Area of Bone (DAB) and Week 104 Change from Baseline in %DAB – mITT and mSAR

Mean Absolute % Denuded Area of Bone		Placebo	Sprifermin				
			30 μg x 2	30 μg x 4	100 μg x 2	100 μg x 4	100 μg combined
mITT, n analyzed		84 of 96	95 of 99	90 of 99	92 of 99	94 of 101	186 of 200
MT (SD)	Baseline	0.93 (3.04)	0.83 (3.78)	0.74 (1.93)	0.94 (2.95)	1.49 (6.52)	1.22 (5.07)
	Δ at W104	1.04 (7.44)	0.65 (2.92)	0.31 (1.66)	0.68 (2.84)	0.09 (0.51)	0.38 (2.05)
cMF (SD)	Baseline	3.08 (5.86)	4.00 (9.04)	1.74 (4.13)	4.75 (9.82)	3.46 (9.04)	4.10 (9.43)
	Δ at W104	1.22 (9.07)	0.85 (3.34)	0.71 (5.91)	1.26 (5.49)	0.32 (1.64)	0.79 (4.05)
MFTC (SD)	Baseline	1.62 (3.19)	1.89 (5.28)	1.08 (2.42)	2.18 (4.23)	2.13 (6.97)	2.15 (5.76)
	Δ at W104	1.11 (8.00)	0.72 (2.84)	0.44 (3.10)	0.87 (3.53)	0.17 (0.68)	0.51 (2.55)
LT (SD)	Baseline	1.95 (6.69)	2.26 (4.51)	1.72 (4.08)	1.86 (5.81)	1.75 (4.00)	1.80 (4.97)
	Δ at W104	0.13 (0.57)	0.09 (1.18)	0.38 (1.74)	0.06 (0.73)	0.23 (0.78)	0.15 (0.76)
cLF (SD)	Baseline	2.20 (4.70)	3.17 (6.17)	2.00 (4.57)	1.85 (3.60)	2.67 (5.17)	2.26 (4.47)
	Δ at W104	0.35 (1.18)	0.27 (1.71)	0.17 (1.27)	-0.01 (0.99)	0.18 (0.95)	0.08 (0.97)
LFTC (SD)	Baseline	2.08 (5.52)	2.64 (4.56)	1.84 (3.85)	1.88 (4.41)	2.11 (3.82)	2.00 (4.11)
	Δ at W104	0.21 (0.56)	0.16 (1.29)	0.30 (1.45)	0.04 (0.74)	0.22 (0.67)	0.13 (0.71)
mSAR, n analyzed		27 of 34	30 of 36	25 of 27	27 of 31	30 of 33	57 of 64
MT (SD)	Baseline	2.51 (4.75)	2.12 (6.51)	1.11 (2.81)	1.78 (4.62)	2.04 (9.68)	1.92 (7.65)
	Δ at W104	2.99 (13.05)	1.60 (4.74)	0.45 (1.24)	1.11 (3.71)	0.09 (0.32)	0.57 (2.59)
cMF (SD)	Baseline	2.75 (5.90)	6.17 (13.65)	3.05 (6.25)	6.73 (11.70)	3.03 (8.93)	4.78 (10.41)
	Δ at W104	3.56 (15.90)	1.30 (3.62)	0.60 (2.53)	1.36 (4.47)	0.70 (2.60)	1.01 (3.59)
MFTC (SD)	Baseline	2.55 (4.19)	3.48 (8.77)	1.77 (3.81)	3.31 (5.44)	2.34 (9.25)	2.80 (7.63)
	Δ at W104	3.23 (14.03)	1.50 (4.30)	0.50 (1.61)	1.20 (3.85)	0.29 (0.86)	0.72 (2.73)
LT (SD)	Baseline	4.86 (10.86)	2.75 (5.96)	2.02 (4.00)	0.99 (1.89)	3.04 (5.67)	2.06 (4.40)
	Δ at W104	0.32 (0.94)	0.41 (1.98)	0.29 (0.74)	0.04 (0.28)	0.42 (1.13)	0.24 (0.86)
cLF (SD)	Baseline	4.19 (6.92)	2.63 (4.94)	1.86 (2.81)	1.56 (3.24)	2.53 (4.24)	2.07 (3.80)
	Δ at W104	0.58 (1.61)	0.49 (2.31)	0.29 (1.00)	0.02 (0.47)	0.31 (0.88)	0.18 (0.72)
LFTC (SD)	Baseline	4.71 (8.77)	2.73 (4.91)	1.97 (2.90)	1.22 (1.90)	2.83 (4.34)	2.07 (3.48)
	Δ at W104	0.41 (0.78)	0.45 (2.09)	0.29 (0.76)	0.03 (0.28)	0.38 (0.87)	0.22 (0.68)

x 2=cycle every 12 months; x 4=cycle every 6 months; Δ=change; cLF=central lateral femur; cMF=central medial femur; LFTC=lateral femorotibial compartment; LT=lateral tibia; MFTC=medial femorotibial compartment; mITT=modified intent-to-treat; MT=medial tibia; mSAR=modified subgroup at risk; N=total sample size; n=sample evaluated; SD=standard deviation; W104=Week 104.

Results: Characteristics at BL showed 52% (n=255/494) of the mITT population had some FTJ dAB (Table 1); in the SAR, 61% (n=98/161). Those with FTJ dAB at BL had more severe radiographic disease by Kellgren-Lawrence (KL) grade (44.3% vs 17.6% KL3) and medial mJSW (3.6 mm vs 3.9 mm).Baseline dABs were associated with more structural progression by quantitative cartilage thickness measures, independent of treatment arm (Table 1). Table 2 presents the %dAB and absolute change from BL (CFB) in %dAB data for the 6 FTJ regions analyzed. Of these, the weight-bearing (central) medial femur (cMF) showed the greatest %dAB (range 1.74-4.75) in the different treatment arms at BL in the mITT (Table 2). In the medial compartment, the absolute %dAB CFB at W104 also tended to be greater (worse) in the PBO- (range 1.04-1.22) vs the sprifermin-treated arms (eg, range 0.38-0.79 for sprifermin 100 μg combined), with the cMF showing the greatest differentiation. The degree of the differences in longitudinal changes between treatment arms in the medial compartment was more pronounced in the mSAR than mITT population, eg, W104 CFB of cMF %dAB mSAR 3.56 vs 1.01 and mITT 1.22 vs 0.79 in the PBO vs sprifermin 100 μg combined group. Yet, little difference was seen in the longitudinal changes in %dAB between the sprifermin- and PBO-treated arms in the lateral compartment.

Conclusion: The presence of dAB appears to be associated with more severe radiographic OA and structural progression of KOA. Sprifermin treatment, particularly at the highest dose, appears to slow the increase (worsening) of dAB compared to PBO, especially in the medial compartment. Further evaluation of these findings and the relationship of dAB with symptomatic outcomes is warranted, including in prospective clinical trials.

Disclosure: F. Eckstein: 4P Moving, 2, Kolon Tissue Gene, 2, Merck, 2, Novartis, 2, TrialSpark, 2; **W. Wirth**: Chondrometrics GmbH, 3, 11, TrialSpark, 2; **P. Conaghan**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, Genascense, 2, GlaxoSmithKlein(GSK), 2, Grunenthal, 2, Janssen, 2, Levicept, 2, Merck/MSD, 2, Moebius Medical, 2, Novartis, 2, 6, Stryker, 2, Takeda, 2, TrialSpark, 2; **M. Hochberg**: TrialSpark, 2; **A. Guermazi**: BICL, LLC, 11, ICM, Coval, TrialSpark, TissueGene, Medipost, 2, Novartis, 2, Pfizer, 2; **J. Andrade**: TrialSpark, 3, 11; **L. Zhao**: TrialSpark, 3, 11; **N. Goel**: TrialSpark, 3, 11.

Abstract Number: 0750

Multispectral Optoacoustic Tomography of the Entheses Reveals Common Metabolic and Architectural Tissue Patterns in Psoriasis and Psoriatic Arthritis Independent of Inflammation

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SESSION INFORMATION

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Background/Purpose: Multispectral optoacoustic tomography (MSOT) is a novel imaging platform that combines ultrasound (US) with optoacoustic imaging to allow non-invasive in vivo quantification of key metabolites of inflammation such as hemoglobin (Hb), oxygen saturation (SO2), and collagen and lipid levels by analyzing the wavelength spectra of the target tissues when exposed to near-infrared laser light (Regensburger AP, Biomedicines (2021)). MSOT has already proven capable of identifying arthritis and enthesitis in patients with PsA and RA (Tascilar K, Rheumatology (2023)). In our study, we aimed to assess metabolic and inflammatory changes at the entheses in patients with psoriasis (PsO), PsA, and healthy controls (HC) using MSOT in order to identify new potential imaging biomarkers for enthesitis.

Methods: A cross-sectional study in bDMARD-naïve PsA and PsO patients and HC was performed. Participants underwent sequential clinical, US and MSOT examination of six entheses (lateral humeral epicondyle, distal patellar tendon attachment, Achilles). MSOT wavelength spectra were determined and the corresponding values of Hb, SO2, collagen, and lipid were quantified. Mean differences between groups were calculated using linear mixed effects models. MSOT-measured analytes were compared between tender and non-tender entheses and between entheses with and without OMERACT-defined US anomalies. The study was approved by the Ethics Committee of the University of Erlangen-Nuremberg (464_18 B; 7) and was registered as a clinical trial (DRKS00024360).

Table 1 – Clinical and demographic characteristics

Table 1 – Clinical and demographic characteristics

Characteristics		Overall	PsA	PsO	Healthy
Participants, *n*		90	30	30	30
Age, mean (S.D.)		49,7 ±13,48	54,0 ±10,3	42,7 ±14,1	52,4 ±13,2
Sex, *n* (%)	Male	36	7	19	10
	Female	54	23	11	20
Skin disease duration, years, median (IQR)		12,0 (5,8-31,0)	11,0 (6,0-31,0)	13,0 (6,0-31,0)	–
Musculoskeletal disease duration, years, median (IQR)		–	2,0 (1,0-6,8)	–	–
DAPSA, median (IQR)		–	7,0 (?,5-15,3)	–	–
MDA achievement, *n* (%)		–	9 (32,9%)	–	–
CRP in mg/dL, mean (SD)		–	8,0 ± 5,9	–	–
Tender entheses, median (IQR)		0 (0-1)	0 (0-4)	0 (0-1)	0 (0-0)
Current therapy, *n* (%)	None		15 (50%)	26 (8,7%)	30 (100.0%)
	NSAIDs	–	1 (3,3%)	–	–
	Corticosteroids	–	1 (3,3%)	–	–
	Leflunomide	–	2 (6,7%)	–	–
	Methotrexate	–	13 (43,3%)	1 (3,3%)	–
	Fumarate	–	–	3 (10,0%)	–

Table 2 – Mean overall measurements of MSOT-measured metabolite levels across all examination sites by study group and mean difference from healthy controls

Table 2 – Mean overall measurements of MSOT-measured metabolite levels across all examination sites by study group and mean difference from healthy controls

Wavelength, nm	Group	Difference from HC	p value
Hb-total	PsA	0.02 (0.00 to 0.04)	0.057
	Pso	0.01 (-0.01 to 0.03)	0.328
	HC	-	-
Hb-deoxy	PsA	-0.01 (0.02 to 0.01)	0.370
	Pso	-0.01 (-0.02 to 0.00)	0.223
	HC	-	-
Hb-oxy	PsA	0.03 (0.01 to 0.04)	0.005*
	Pso	0.02 (0.00 to 0.04)	0.044*
	HC	-	-
SO2	PsA	0.05 (0.02 to 0.07)	<0.001*
	Pso	0.04 (0.02 to 0.06)	0.001*
	HC	-	-
Collagen	PsA	-850.55 (-1323.23 to -377.87)	<0.001*
	Pso	-830.98 (-1309.27 to -352.70)	<0.001*
	HC	-	-
Lipid	PsA	27.28 (-268.74 to 323.31)	0.855
	Pso	-38.85 (-337.84 to 260.13)	0.797
	HC	-	-

Figure 1 MSOT wavelength spectra for psoriasis, psoriatic arthritis and healthy controls stratified by examination site.

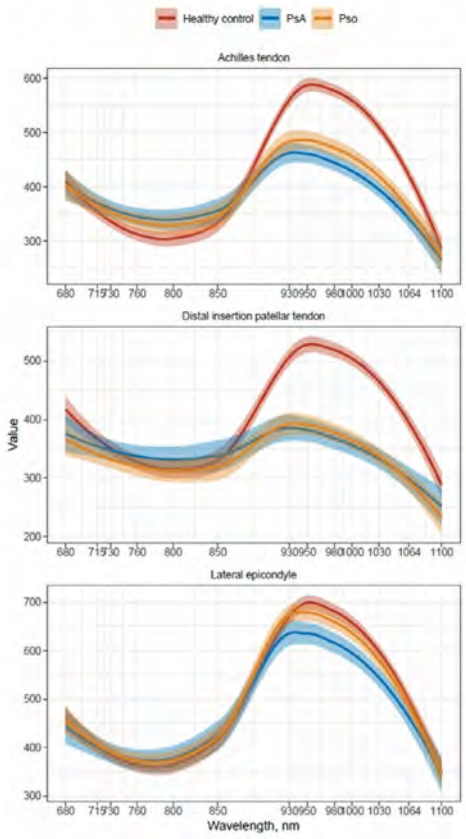

Figure 1 – MSOT wavelength spectra for psoriasis, psoriatic arthritis and healthy controls stratified by examination site.

Results: Ninety participants were included (30 PsO, 30 PsA, 30 HC). Clinical and demographic characteristics are shown in table 1.540 entheses were clinically assessed, 540 US and 830 MSOT scans were obtained. Comparing MSOT wavelength spectra, significant differences from HC emerged for PsA between 800 nm and 1064 nm, and for PsO between 930 nm and 1100 nm (Figure 1). The corresponding metabolites distribution was obtained. Both PsA and PsO patients showed significantly increased oxygenated Hb (PsA: p=0.005; PsO: p=0.001) and SO2 (PsA: p< 0.001; PsO, p=0.001) levels and decreased collagen signals (PsA: p< 0.001; PsO: < 0.001) compared to HC, with more pronounced changes in the PsA group (Table 2). Significantly lower collagen levels (p=0.01) and increased signal for lipids (p=0.02) were recorded in tender entheses compared with non-tender ones. The presence of at least one US anomaly was associated with a significant positive difference in SO2 (p=0.003).

Conclusion: PsO and PsA patients show a distinct entheseal metabolic profile that is common to all psoriatic patients independently from clinical and US-detected signs of inflammation, thereby supporting the notion of a psoriatic disease spectrum characterized by varying degrees of musculoskeletal inflammation. Furthermore, MSOT can detect differences between inflamed and uninflamed entheses that are more pronounced in PsA than in those with skin psoriasis alone. Research efforts should now focus on defining MSOT cutoff values for enthesitis and longitudinal analyses should be conducted to assess the utility of MSOT as a risk stratification tool for the risk of progression to PsA in at-risk patients.

Disclosure: F. Fagni: Eli Lilly, 6, Galapagos, 6, Novartis, 6; **K. Tascilar**: None; **R. Noversa de Sousa**: None; **S. Bayat**: El Lilly, 5; **L. Sollfrank**: None; **A. Kleyer**: None; **M. Sticherling**: El Lilly, 5, El Lilly, 6, Janssen, 5, 6, Novartis, 5, 6; **A. Regensburger**: None; **F. Knieling**: None; **G. Schett**: None; **M. Waldner**: None; **D. Simon**: Janssen, 5.

Abstract Number: 0751

Recombinant Zoster Vaccination Among U.S. Veterans Receiving Immunosuppressive Medications 2017-2023

Sharon Abada[1], Jing Li[1], Gary Tarasovsky[2], Cherish Wilson[3], Jinoos Yazdany[1], Mary Whooley[1] and Gabriela Schmajuk[3], [1]University of California San Francisco, San Francisco, CA, [2]San Francisco VA, San Francisco, CA, [3]UCSF / SFVA, San Francisco, CA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Measures & Measurement of Healthcare Quality
Session Type: Abstract Session
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Background/Purpose: Patients receiving immunosuppressive therapies are known to have a higher risk of herpes zoster and subsequent complications compared to the general population. The recombinant zoster vaccine (Shingrix, hereafter referred to as "RZV") has been shown to be both safe and efficacious among such patients. In 2021, the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) updated their recommendations and approval for the administration of RZV to include all immunosuppressed adults (any age). We assessed patient characteristics associated with RZV vaccination rates among U.S. veterans.

Methods: We performed a cross-sectional observational study using national Veterans Affairs (VA) data from the VA Corporate Data Warehouse. The study population included all VA patients aged ≥ 18 who were prescribed at least one immunosuppressive medication (including conventional synthetic (cs) DMARDs, biologics, and targeted synthetic (ts) DMARDs) for ≥ 90 days between 2017 and 2023. We identified patients with one or more doses of RZV documented. We examined whether demographic and clinical characteristics (age, sex, race, ethnicity, rurality of residence, medication type, rheumatology specialty care) were associated with receiving RZV using multivariate logistic regression, accounting for clustering by facility and report the predicted marginal proportions of patients vaccinated.

Results: We identified 142,336 veterans across 130 facilities as prevalent users of csDMARDs, biologics, or tsDMARDs between 2017 and 2023 (Table 1). Most patients were male (85.8%), white (73.6%), non-Hispanic (89.2%), and lived in urban areas (64.0%). Mean age (SD) was 66.5 (14.0) years. Of these patients, 34.8% had received at least two doses of RZV (fully immunized), 7.7% had received 1 dose of RZV, and 57.4% had not received any doses of RZV. Multivariate logistic regression revealed the largest differences in vaccination rates were for patients < 50 years vs ≥ 50 years (11.2% vs 47.8%, $p < 0.05$), African American vs white patients (36.9% vs 43.8%, $p < 0.05$), and those without a recent visit with a rheumatologist vs those with at least one rheumatology visit since 2018 (38.8% vs 46.0%, $p < 0.05$; Table 2). Patients receiving tsDMARDs (vs receiving neither a biologic nor tsDMARD) were more likely to receive at least 1 dose of RZV (48.6% vs 41.8%, $p < 0.05$).

Conclusion: Among adult U.S. veterans receiving immunosuppressive medications, less than half have received at least one dose of RZV. Patients under 50 years old were least likely to have received RZV, likely reflecting a lag in implementing updated CDC guidance for this group. Quality improvement efforts should specifically focus on younger patients and African American patients. Future work should explore the development of population-health management tools (such as clinical dashboards in electronic medical records) to support quality improvement in RZV administration rates for immunosuppressed patients.

Table 1. Demographic characteristics of patients on immunosuppressive medications, with or without at least one dose of recombinant zoster vaccination (RZV)

	All patients (N = 142,336) n (%)	WITH at least 1 dose of RZV (N = 60,670) n (%)	WITHOUT any doses of RZV (N = 81,666) n (%)	p-value
Age				<0.001
mean (SD)	66.5 (14.0)	70.0 (10.6)	63.9 (15.5)	
<50	19,997 (14.0)	2,288 (3.8)	17,709 (21.7)	
≥50	122,339 (86.0)	58,382 (96.2)	63,957 (78.3)	
Sex				<0.001
Female	20,203 (14.2)	8,052 (13.3)	12,151 (14.9)	
Male	122,133 (85.8)	52,618 (86.7)	69,515 (85.1)	
Race				<0.001
White	104,736 (73.6)	46,215 (76.2)	58,521 (71.7)	
African American	24,119 (16.9)	8,932 (14.7)	15,187 (18.6)	
Asian	1,612 (1.1)	688 (1.1)	924 (1.1)	
Other	2,712 (1.9)	1,141 (1.9)	1,571 (1.9)	
Unknown	9,157 (6.4)	3,694 (6.1)	5,463 (6.7)	
Ethnicity				<0.001
Hispanic	8,847 (6.2)	3,562 (5.9)	5,285 (6.5)	
Not Hispanic	126,941 (89.2)	54,628 (90)	72,313 (88.5)	
Unknown	6,548 (4.6)	2,480 (4.1)	4,068 (5)	
Facility region				<0.001
Continental	25,488 (17.9)	9,764 (16.1)	15,724 (19.3)	
Midwest	33,398 (23.5)	16,061 (26.5)	17,304 (21.2)	
North Atlantic	31,389 (22.1)	13,959 (23)	17,430 (21.3)	
Pacific	24,311 (17.1)	10,764 (17.7)	13,547 (16.6)	
Southeast	27,750 (19.5)	10,089 (16.6)	17,661 (21.6)	
Rurality of residence				<0.001
Urban	91,163 (64.0)	38,680 (63.8)	52,483 (64.3)	
Rural	50,825 (35.7)	21,884 (36.1)	28,941 (35.4)	
Unknown	348 (0.2)	106 (0.2)	242 (0.3)	
≥ 1 rheum visit since 2018	75,495 (53.0)	34,798 (57.4)	40,697 (49.8)	<0.001
Medication type*				
csDMARD	98,758 (69.4)	43,283 (71.3)	55,475 (67.9)	<0.001
b/tsDMARD				<0.001
Biologics only	69,826 (49.1)	28,749 (47.4)	41,077 (50.3)	
tsDMARD only	6,562 (4.6)	3,320 (5.5)	3,242 (4.0)	
Not on b/tsDMARD	65,948 (46.3)	28,601 (47.1)	37,347 (45.7)	

p-values were determined by t-test for continuous variables and chi-square for categorical variables.
*Patients may be on multiple immunosuppressive medications.

Table 2. Predictive margins from un-adjusted and adjusted multivariate logistic regression models, clustered by facility

	Un-adjusted Predictive margins (95% CI)	Adjusted Predictive margins (95% CI)
Age		
<50	11.4 (11.0 - 11.9)	11.2 (10.2 - 12.2)
≥50	47.7 (47.4 - 48.0)	47.8 (46.0 - 49.7)
Gender		
Female	39.9 (39.2 - 40.5)	45.2 (43.4 - 46.9)
Male	43.1 (42.8 - 43.4)	42.3 (40.5 - 44)
Race		
White	44.1 (43.8 - 44.4)	43.8 (42.0 - 45.6)
African American	37.0 (36.4 - 37.6)	36.9 (34.9 - 38.8)
Asian	42.7 (40.3 - 45.1)	50.7 (46.5 - 54.9)
Other	42.1 (40.2 - 43.9)	43.7 (40.6 - 46.7)
Unknown	40.3 (39.3 - 41.3)	42.4 (40.4 - 44.3)
Ethnicity		
Hispanic	40.3 (39.2 - 41.3)	43.0 (39.7 - 46.3)
Not Hispanic	43.0 (42.8 - 43.3)	42.7 (41.0 - 44.4)
Unknown	37.9 (36.7 - 39.0)	41.1 (39 - 43.3)
Rurality of residence		
Urban	42.4 (42.1 - 42.8)	43.2 (41.6 - 44.9)
Rural	43.1 (42.6 - 43.5)	41.7 (39.6 - 43.8)
Unknown	30.5 (25.6 - 35.3)	30.0 (19.8 - 40.3)
≥ 1 rheumatology visit since 2018		
No	38.7 (38.3 - 39.1)	38.8 (37.2 - 40.4)
Yes	46.1 (45.7 - 46.4)	46.0 (44.1 - 48.0)
On csDMARD		
No	39.9 (39.4 - 40.4)	42.0 (40.2 - 43.7)
Yes	43.8 (43.5 - 44.1)	42.9 (41.2 - 44.6)
On b/tsDMARD		
No b/tsDMARD	43.4 (43.0 - 43.7)	41.8 (40.0 - 43.6)
Biologics	41.2 (40.8 - 41.5)	42.9 (41.1 - 44.6)
tsDMARD	50.6 (49.4 - 51.8)	48.6 (46.3 - 50.8)

Model adjusted for all variables shown in the table.

Disclosure: S. Abada: None; **J. Li**: None; **G. Tarasovsky**: None; **C. Wilson**: None; **J. Yazdany**: Astra Zeneca, 2, 5, Aurinia, 5, Gilead, 5, Pfizer, 2; **M. Whooley**: None; **G. Schmajuk**: None.

Abstract Number: 0752

Tuberculosis Screening Among New Users of a Biologic or Targeted Synthetic DMARD: Gaps in Coverage Overall and Among JAKi Initiators

Eric Roberts[1], Gabriela Schmajuk[2] and Jinoos Yazdany[1], [1]University of California San Francisco, San Francisco, CA, [2]UCSF / SFVA, San Francisco, CA

SESSION INFORMATION

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Session Type: Abstract Session

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Background/Purpose: Screening for latent tuberculosis (TB) is recommended prior to starting biologics or targeted synthetic DMARDs (b/tsDMARDs). With a growing number of these drugs available in rheumatology, it is important to investigate whether TB screening practices have kept pace with recommendations. Using national data, we aim to describe the proportion of new users of a b/tsDMARD who were screened for TB, and evaluate potential gaps in testing by drug type, patient characteristics and practice.

Methods: Data come from RISE, an electronic health record-based registry of US rheumatology practices with linkage to Medicare Parts A, B, and D claims. Individuals in RISE with continuous Medicare enrollment in 2017 and 2018 who were new users of a qualifying b/tsDMARD in 2018 in Medicare were included. New users were defined as those with a prescription for a b/tsDMARD in 2018 but no prescription (in Medicare or RISE) in the year prior. Use of b/tsDMARDs, information on TB testing (IGRA, TST or medical exception), and patient demographics were extracted from Medicare and RISE, to gather the most comprehensive data on b/tsDMARD use and TB testing. We calculated the proportion of patients tested in either

Table 1. Percent of new b/tsDMARD users screened for TB within 1 year and 3 years with a 30 day grace period overall and by TB screening method.

	New users of Biologics or tsDMARDs (n=2821)	
	1-year lookback	3-year lookback with 30-day grace period
Any screening	65.19	72.78
Screened with IGRA	61.75	69.20
Screened with TST	4.71	6.88
Documented medical exception	3.44	5.10

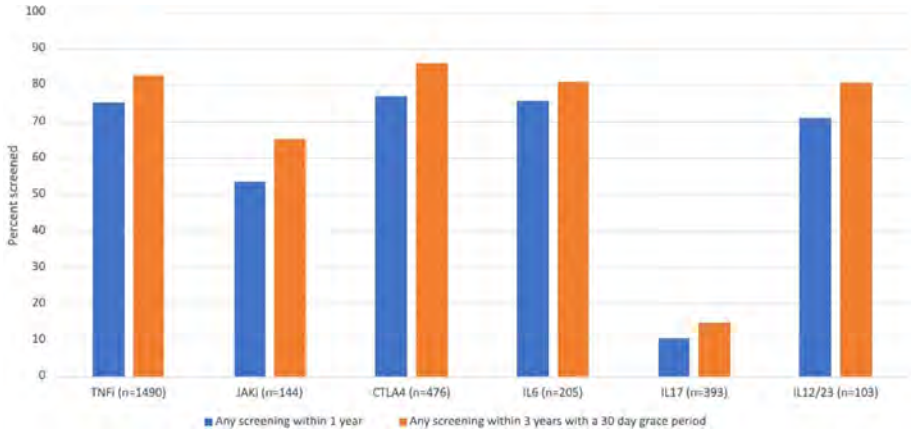

Figure 1. Proportion of new b/tsDMARD users screened for TB by DMARD type.

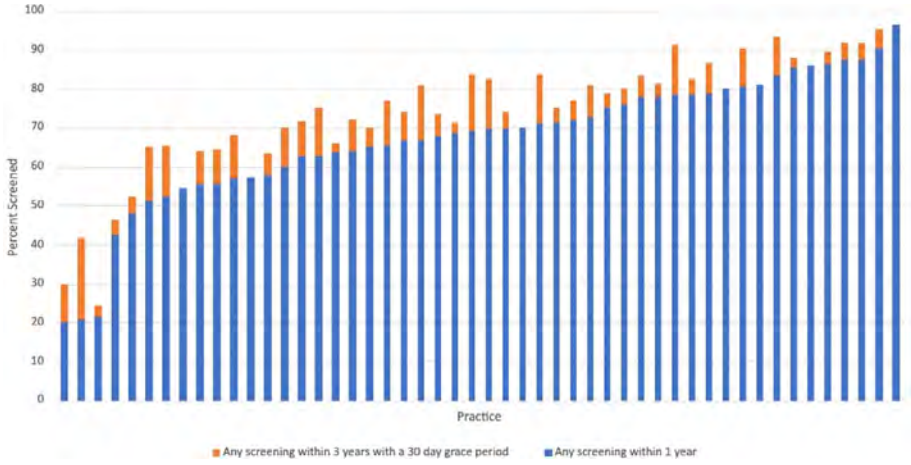

Figure 2. Proportion of new b/tsDMARD users screened for TB by practice among practices with at least 20 patients.

RISE or Medicare claims in the year prior to the new b/tsDMARD, consistent with the Quality Payment Program measure. In a sensitivity analysis we permitted TB screening in the 3 years before up to 30 days after the patient's start date. We computed screening rates by b/tsDMARD type. Using logistic regression we tested for differences in screening by age, sex, race-ethnicity, insurance and socioeconomic status (using the area deprivation index). We calculated the proportion of patients screened among practices with at least 20 new users.

Results: Among 2821 new b/tsDMARD users, mean age was 73±8.6 years, 72% female, 73% non-Hispanic White, 6.8% Black, 4.7% Hispanic and 1.2% Asian. In the year prior to drug starts, 65.2% of patients had any TB screening documented, including 61.8% with an IGRA, 4.7% with a TST, and 3.4% with a documented medical exception. In our sensitivity analysis, 77.9% had any TB screening (Table 1). Rates of screening within 1 year by drug type were greater or equal to the overall screening rate for most drugs with the exception of JAKi (53.5%) and IL17i (10.4%) (Figure 1). In a fully adjusted logistic regression, patients in the highest quartile of SES had significantly lower odds (OR=0.64; 95%CI 0.48-0.87) of being screened within 1 year compared to the lowest quartile. 50 practices had at least 20 patients; screening rates ranged from 20-96.3% of patients (Figure 2).

Conclusion: Using a comprehensive data source that includes both registry data and Medicare claims, we found that just over 1 in 3 new users of a b/tsDMARD did not receive TB screening within the recommended time window. When the screening window was expanded, performance only slightly improved with approximately 1 in 4 new users not receiving screening. Although lower TB screening rates for IL-17i may reflect greater uncertainty about TB risk with this drug mechanism, emerging evidence suggests that TB risk for JAKi is significant. Filling these gaps in care are important areas for quality improvement.

Disclosure: E. Roberts: None; **G. Schmajuk**: None; **J. Yazdany**: Astra Zeneca, 2, 5, Aurinia, 5, Gilead, 5, Pfizer, 2.

Abstract Number: 0753

Facility Variation in HLA-B*58:01 Allele Testing for Asian and Black Patients Receiving Allopurinol in the Veterans Affairs Healthcare System

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Measures & Measurement of Healthcare Quality
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Background/Purpose: New guidelines published in 2020 conditionally recommend HLA-B*58:01 allele testing for South Asian and Black patients receiving allopurinol to reduce the risk of severe cutaneous adverse events. However, no data exists on population-wide genetic testing rates. We investigated HLA-B*58:01 testing among allopurinol users in the Veterans Health Administration (VHA) Healthcare System.

Methods: Using data from the VHA Corporate Data Warehouse (CDW), we identified facilities with structured fields available for capturing HLA-B*58:01 test results. From these facilities, we identified all patients with a current, active prescription for allopurinol as of December 2022. We assessed the proportion of patients with a documented HLA-B*58:01 test at any time

within the CDW, by race or ethnicity. We repeated this analysis among incident users of allopurinol (defined as users with a prescription in 2022 and no allopurinol use in the preceding 3 years). Finally, we examined variation in HLA-B*58:01 testing among self-identified Asian or Black patients by VHA facility, among facilities with ≥ 20 eligible patients. We contacted the top performing facility to learn about local workflows for obtaining genetic testing for allopurinol users.

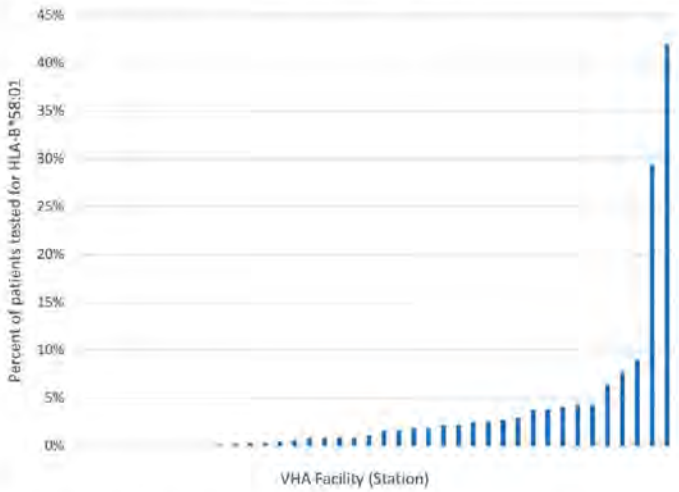
Results: Only 40 out of 130 facilities had a structured field available for capturing HLA-B*58:01 test results. We identified 79,361 users of allopurinol at these facilities; 98% of them were male, and mean age was 70 years (SD 12). Among prevalent users, 13.8% of Asian and 2.4% of Black patients were ever tested for the HLA-B*58:01 allele (**Table**). Among incident users, testing was documented among 10.1% of Asian and 3.0% of Black patients. We observed wide variation in HLA-B*58:01 testing across facilities (range 0% - 42.0%; **Figure**). The top-performing facility (proportion tested 42.0%) relayed that they had developed an allopurinol order set and pharmacy workflow that prevented allopurinol prescribing prior to completion of genetic testing.

Table. Percent of allopurinol users with HLA-B*58:01 testing documented in the VHA electronic health record, stratified by race or ethnicity, among facilities with a structured field available for HLA-B*58:01 results (N facilities = 40)

	Prevalent Allopurinol Users		Incident Allopurinol Users†	
	N	% with HLA-B*58:01 testing	N	% with HLA-B*58:01 testing
Overall	79,361	1.57%	7,925	1.70%
Race or Ethnicity‡				
American Indian or Alaska native	532	0.94%	58	1.72%
Asian	3,123	13.83%	356	10.11%
Black or African American	18,117	2.44%	1,844	2.98%
Hispanic	2,703	1.70%	292	2.74%
Native Hawaiian or other Pacific Islander	1,766	3.96%	196	4.59%
Non-Hispanic White	48,069	0.35%	4,472	0.42%
Multiple	267	4.49%	24	0.00%
Unknown	4,784	1.57%	683	1.02%

† Incident users defined as patients with a current prescription and no allopurinol use in the preceding 3 years
‡ Race or ethnicity were self-reported. Patients reporting one or more race or ethnicity categories were grouped into the "Multiple" category

Figure. Percent of self-identified Asian or Black prevalent users of allopurinol who were tested for the HLA-B*58:01 allele, by VHA facility (N facilities = 36)*



*Facilities without a structured field for HLA-B*58:01 results and with fewer than 20 self-identified Asian or Black patients were excluded.

Conclusion: Across the VHA Healthcare System, testing for HLA-B*58:01 in high-risk groups was very low, and variation across facilities was high. Most facilities lack a structured field for HLA-B*58:01 results, which hinders measurement of quality gaps. In order to improve testing rates, facilities should consider implementing order sets or pharmacy "hard stops" that require HLA-B*58:01 testing for high-risk groups.

Disclosure: J. Sullivan: None; **A. Ware**: None; **G. Tarasovsky**: None; **C. Wilson**: None; **M. Whooley**: None; **J. Singh**: Other, 2, 6, 11, 11, 12, Adaptimmune Therapeutics, GeoVax Labs, Pieris Pharmaceuticals, Enzolytics Inc., Seres Therapeutics, Tonix, Charlotte's Web, 12, Atai life sciences, kintara therapeutics, Intelligent Biosolutions, Acumen pharmaceutical, TPT Global Tech, Vaxart pharmaceuticals, Atyu biopharma, 12, speaker's bureau of Simply Speaking, other, 12, received institutional research support from Zimmer Biomet Holdings. JAS received food and beverage payments from Intuitive Surgical Inc./Philips Elec, Other, 12, Schipher, Crealta/Horizon, Medisys, Fidia, PK Med, Two labs Inc., Adept Field Solutions, Clinical Care options, Clearview healthcare partners, Putnam; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, Gilead, 5, Pfizer, 2; **G. Schmajuk**: None.

Abstract Number: 0754

Towards a Guide for Evidence-based Remote Monitoring: Sensitivity of Patient Reported Outcomes to Change in Disease Activity Status in Early and Established Rheumatoid Arthritis

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Background/Purpose: In the treatment and follow-up of rheumatoid arthritis (RA) patients, it has become more desirable to detect changes in disease activity through remote monitoring. Patient reported outcomes(PROs) might be useful for this purpose. So far associations between PROs and changes in disease activity have been mostly investigated on a continuous scale. However, in daily practice, and in line with the current recommendations, treatment decisions are mainly based on the patient's disease activity status. Earlier literature has shown that functionality, morning stiffness, health-related quality of life (HRQoL), general health (GH), joint pain and fatigue change with the development and resolution of a disease flare.

Therefore, our aim is to determine if PROs that cover functionality, joint pain, morning stiffness, HRQoL, GH and fatigue are sensitive to disease activity status alterations in patients with early and established RA.

Methods: Early RA patients from the tREACH trial and established RA patients from the TARA trial were included. Both studies are multicentre, single-blinded trials with a treat-to-target approach. Treatment alterations were based on the disease activity score (DAS44) and PROs were collected at 3-montly intervals. The following PROs were studied: (1) the Health Assessment Questionnaire-Disability Index(HAQ-DI), (2) morning stiffness severity (numeric rating scale, NRS 0-10), (3) the 3-level EQ-5D(EQ-5D-3L) (4) GH (visual analogue scale, VAS 0-100mm), (5) joint pain (NRS 0-10) and (6) fatigue (VAS 0-100mm).

Disease activity status were defined as: (1) active disease (DAS≥2.4), (2) low disease activity (LDA, DAS< 2.4 and ≥1.6), and (3) remission (DAS< 1.6). Differences in disease activity status between two consecutive visits were compared to changes in PROs. Mean changes in PROs per disease activity status alteration were compared to stable disease activity status using linear mixed models.

Results: A total of 587 early and 189 established RA patients were included. The median symptom duration (interquartile range, IQR) was 0.4 (0.2-0.6) and 6.2 (4.1-8.9) years respectively. The mean DAS (95% confidence interval, CI) at baseline was 3.0 (3.0-3.2) in the early and 1.0 (0.9-1.1) in the established RA group.

Figure 1 mean changes in patient reported outcome after disease activity status alteration

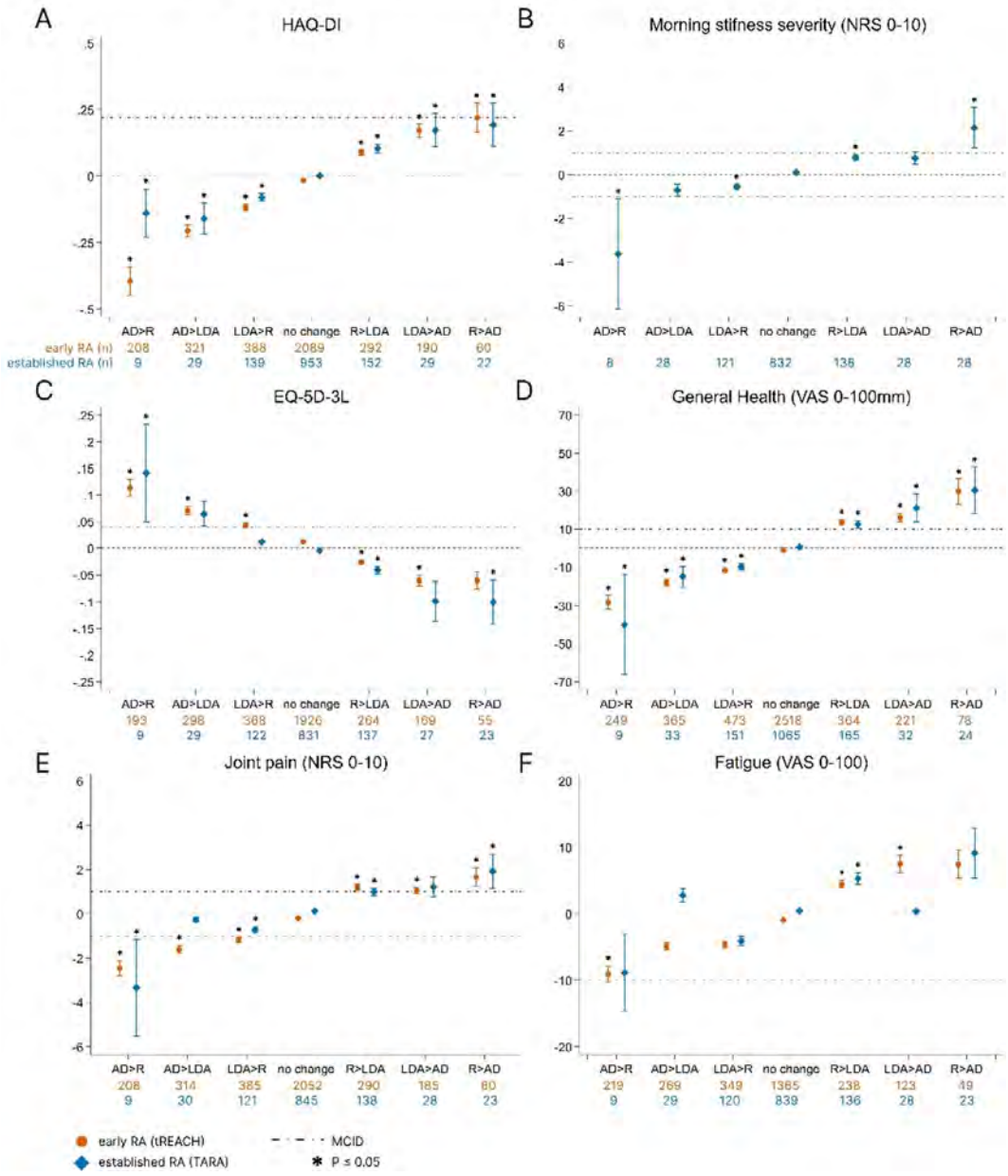

Figure 1A-F show the mean change (95%CI) in PRO after disease activity status alteration for early and established RA patients. * indicates that change in PRO is significantly (p<0.05) different compared to stable disease activity status. Abbreviations: AD, active disease; EQ-5D-3L, 3-level EQ-5D; HAQ-DI, health assessment questionnaire-disability index; LDA, low disease activity; NRS, numeric rating scale; R, remission; VAS, visual analogue scale.

Figure 1 shows the mean change in PROs per change in disease activity status(with 95%CI and significance). Changes in HAQ-DI, morning stiffness severity, EQ-5D-3L, GH, joint pain and fatigue (in early RA) were in concordance with improvement or worsening of the disease activity status. Changes from remission or LDA to active disease and vice versa had a bigger impact on the change in PRO compared to changes between LDA and remission.

Conclusion: HAQ-DI, morning stiffness, EQ-5D-3L, GH and joint pain are sensitive to changes in disease activity status. These results suggest that aforementioned PROs may be helpful in remote monitoring of RA.

Disclosure: A. Loiojen: None; **E. van Mulligen**: None; **A. van der Helm-van Mil**: None; **P. de Jong**: None.

Abstract Number: 0755

Changes in Rheumatology Providers' Perceptions of Telehealth Appropriateness from 2021 to 2022

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Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Telehealth in rheumatology rapidly expanded in the wake of the COVID-19 pandemic, however it remains unknown how provider perceptions of telehealth changed as the pandemic evolved and providers gained additional experience with telehealth. In this project, we describe rheumatology providers' perceptions of telehealth appropriateness from 2021 - 2022, along with the clinical and demographic factors that align with telehealth appropriateness.

Methods: Providers at a single academic rheumatology practice in the U.S. documented their perception of telehealth appropriateness by recording the Encounter Appropriateness Score for You (EASY) in their progress notes immediately following each in-person or telehealth encounter. The EASY score asks providers, "Which of the following encounter types would have been most appropriate for TODAY'S visit? (Irrespective of the pandemic)." Response options include: (1) Either in-person or telehealth acceptable; (2) In-person preferred; (3) Telehealth preferred. For this analysis, EASY scores 1 and 3 were consolidated into a single variable, "telehealth acceptable." We analyzed changes in EASY scores and encounter modality from 1/1/2021 – 10/30/2022. In addition, we analyzed the distribution of EASY scores according to patient demographic and clinical variables. This analysis was limited to return encounters.

Results: Over the study period, 27 providers documented EASY scores for 21,670 return encounters. Of these, 6,551 (30.2%) were rated as telehealth acceptable and 15,119 (69.8%) in-person preferred. The proportion of EASY scores rated as telehealth acceptable declined over time, from approximately 47% in January 2021 to 25% from August 2021 - October 2022 (**Figure 1**). The proportion of visits that occurred by telehealth also declined from 33% in January 2021 to approximately 15% in 2022. The proportion of EASY scores matching the actual encounter type (indicating the appropriate type of visit actually occurred) increased for all encounters from 69% in January 2021 to approximately 80% throughout 2022

(**Figure 2**). Among the 27 providers, there was substantial variability in the proportion of visits each provider rated as telehealth acceptable (median 35%, IQR 12-43%, full range 3-72%). Patient characteristics, including demographics, diagnoses, and patient-reported symptom severity (RAPID3), were related to telehealth appropriateness (**Figure 3)**, with the most telehealth acceptance among patients with RAPID3 scores indicating remission (45%) and the least acceptance with high disease activity (22%).

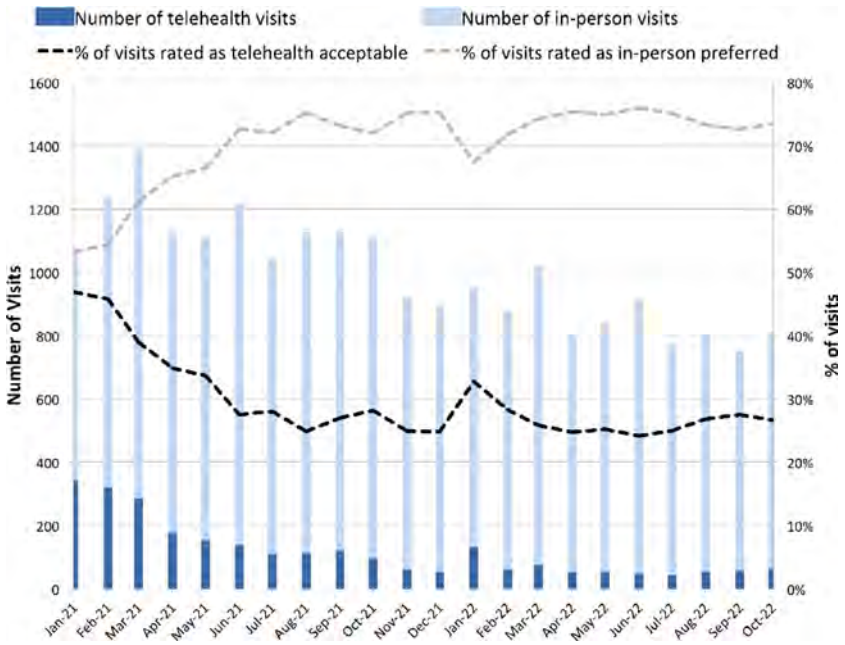


Figure 1. Provider ratings of telehealth appropriateness according to EASY scores (dotted lines) and actual visit modalities (bars) for all return encounters with a documented EASY score, January 2021 through October 2022.

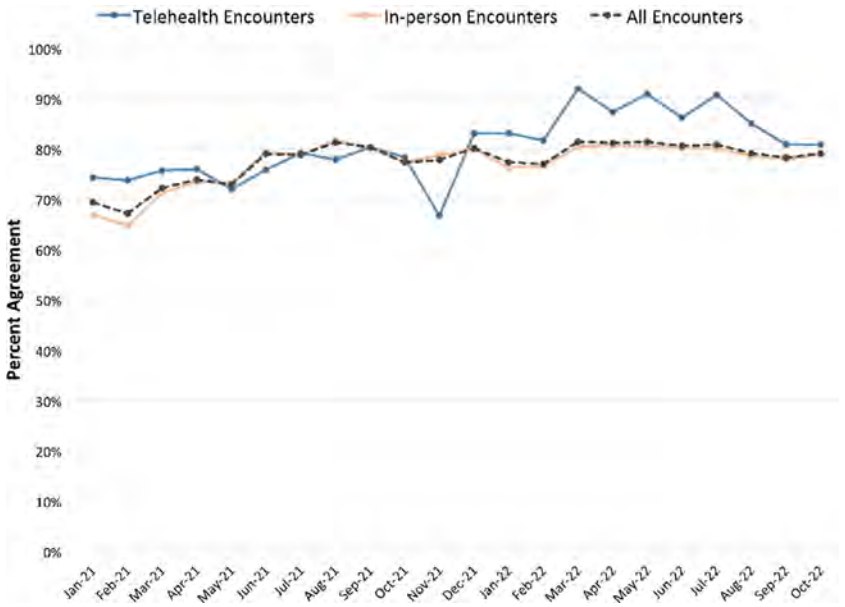


Figure 2. Percent of encounters where the provider EASY score and encounter modality matched per month for telehealth encounters (blue), in-person encounters (orange), and all encounters (black).

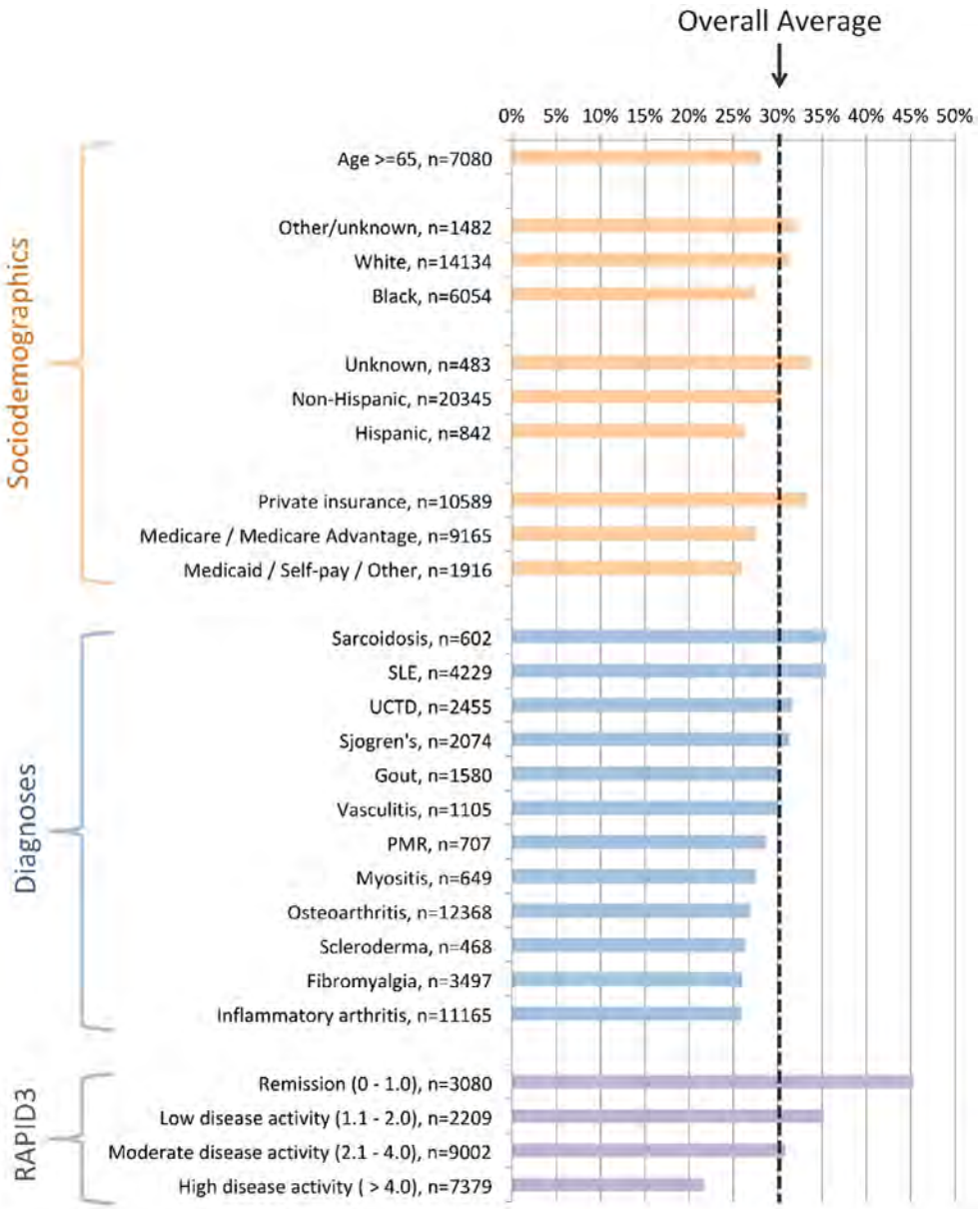


Figure 3. Proportion of return encounters where EASY score indicated telehealth acceptable (EASY = 1 or 3), according to sociodemographics, diagnoses, and RAPID3 scores from January 2021 – October 2022. Diagnoses are grouped using ICD-10 codes. Inflammatory arthritis includes patients with rheumatoid arthritis, psoriatic arthritis, spondyloarthritis, and juvenile idiopathic arthritis. Abbreviations: PMR = polymyalgia rheumatica; SLE = systemic lupus erythematosus; UCTD = undifferentiated connective tissue disease.

Conclusion: Providers became progressively less likely to consider a visit appropriate for telehealth over the first half of 2021, but then stabilized estimating approximately 25% of all return visits telehealth-appropriate. Frequency of telehealth visits followed a similar pattern, though generally telehealth visits accounted for fewer than 25% of visits in 2022, suggesting that telehealth is under-utilized. For example, providers report telehealth as appropriate in over 35% of encounters when the patient reports low symptom severity, suggesting that this sub-population of patients could be a good target for increased telehealth use.

Disclosure: D. Leverenz: Pfizer, 5, Rheumatology Research Foundation, 5, Sanofi, 2; **M. Solomon**: None; **R. Henao**: None; **I. Smith**: None; **C. Howe**: None; **N. Economou-Zavlanos**: None; **B. Adagarla**: None; **T. Coles**: Merck/MSD, 5, Pfizer, 5, Regenxbio, 2; **A. Overton**: None; **J. Doss**: None; **M. Clowse**: Exagen, 5, GlaxoSmithKlein(GSK), 2, 5, Immunovant, 5, UCB, 2, 5.

Abstract Number: 0756

Validation of Quantitative Effusion-synovitis Volume Measured by Deep-learning: Data from the Osteoarthritis Initiative

Banafshe Felfeliyan[1], Stephanie Wichuk[2], Abhilash Hareendranathan[3], Janet Ronsky[4] and Jacob Jaremko[2], [1]University of Alberta, Calgary, AB, Canada, [2]University of Alberta, Edmonton, AB, Canada, [3]Radiology and Diagnostic Imaging, Edmonton, AB, Canada, [4]University of Calgary, Calgary, AB, Canada

SESSION INFORMATION

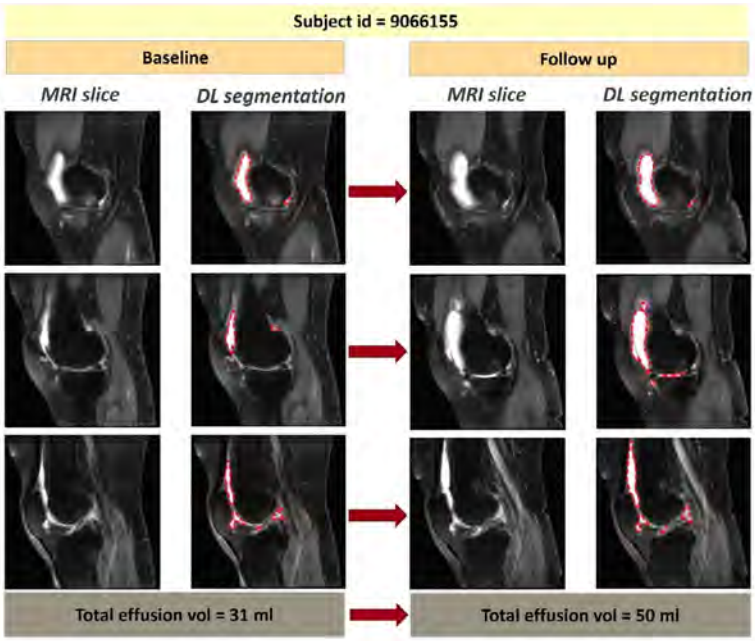
Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Measures & Measurement of Healthcare Quality

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Knee effusion-synovitis (ES) is an attractive target for therapeutic interventions in arthritis, since it is associated with stiffness, pain, and disease progression to arthroplasty. Rapid, objective methods to assess ES on MRI are desirable. Currently, ES is assessed by global user impression or semi-quantitative tools such MRI OA Knee Score (MOAKS); these approaches have high inter-user variability, are insensitive for change if categories are broad, or are time-



Deep learning effusion segmentation result for one subject at baseline and follow-up

	All cases (n=656)	Kellgren-Lawrence Grade at Baseline			
		1 (n=221)	2 (n=240)	3 (n=195)	p-value
Baseline DL Extracted Effusion-Synovitis Volume Median (IQR)	19.8 (15.6-26.2)	17.3 (13.7-21.2) *	19.9 (15.8-26.0) *	24.1 (18.4-31.9) *	<0.00001
1 year change in DL Extracted Effusion-Synovitis Volume Median (IQR)	1.3 (-2.1-5.3)	1.2 (-2.0-4.2)	1.3 (-2.0-5.6)	1.8 (-3.7-5.6)	0.605

* Significantly different from all other K-L grades

Deep learning effusion segmentation result for one subject at baseline and follow-up

consuming if scoring is detailed. To address these limitations, we have developed a novel deep learning (DL) approach to automatically measure ES volume (DL-ES), with high inter-rater reliability ICC=0.96 vs. human expert readers [1].

Here, we automatically generated ES volumes in a from a large subset of **Osteoarthritis Initiative (OAI)** dataset and assessed validity vs. other imaging scoring systems and clinical findings.

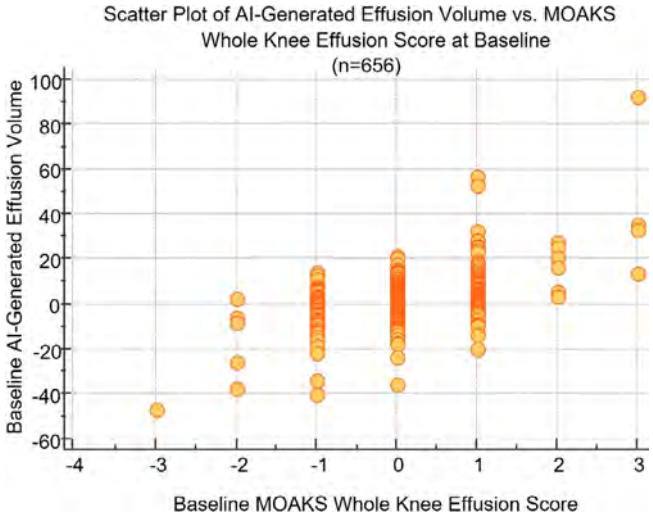
Methods: Total of 4659 MRIs from 1165 individuals with baseline (BL) and 1-year follow-up MOAKS and WOMAC scores were available from the OAI dataset. Scans were processed using a custom IMaskRCNN DL model, previously trained on 700 MRI slices with gold-standard effusion labels from an expert radiologist.

Cases with follow-up time≥11 months, total WOMAC score >0, and KL grades < 4 were analyzed(n=656). Criterion validity of DL-ES was assessed through comparison of BL and 1-year change(Δ) in volume with MOAKS whole knee effusion and WOMAC scores via Kendall's tau and Spearman rank correlation. Differences in DL-ES volumes between KL grades were evaluated via Kruskal-Wallis test.

Results: DL-EF calculation took 35 seconds/scan (Fig1). Median (IQR) baseline DL-ES volume was 19.8 (15.6-26.2) mL, with median (IQR) 1-year Δ of 1.3 (-2.1-5.3) mL. Median (IQR) DL-ES volume at BL increased significantly with BL KL Grade [17.3 (13.7-21.2) mL, 19.9 (15.8-26.0) mL, and 24.1 (18.4-31.9) mL for KL grades 1,2, and 3, respectively, p< 0.0001]. There was no significant difference in 1-year Δ in DL-ES between BL KL grades.

	All cases (n=656)	Kellgren-Lawrence Grade at Baseline			
		1 (n=221)	2 (n=240)	3 (n=195)	p-value
Baseline DL Extracted Effusion-Synovitis Volume Median (IQR)	19.8 (15.6-26.2)	17.3 (13.7-21.2) *	19.9 (15.8-26.0) *	24.1 (18.4-31.9) *	<0.00001
1 year change in DL Extracted Effusion-Synovitis Volume Median (IQR)	1.3 (-2.1-5.3)	1.2 (-2.0-4.2)	1.3 (-2.0-5.6)	1.8 (-3.7-5.6)	0.605
* Significantly different from all other K-L grades					

Deep-Learning Extracted Effusion-Synovitis Volume in cases with Kellgren-Lawrence Grades 1,2, and 3.



Kendall's tau=0.30 (95% C 0.24-0.36, p<0.0001)

There was significant moderate positive correlation between DL-ES and MOAKS effusion BL and Δ scores [Kendall's tau=0.27 (95% CI 0.21-0.32, p< 0.0001) and 0.30 (95% C 0.24-0.36, p< 0.0001), respectively].

DL-ES volumes showed a small significant positive correlation with WOMAC pain [Spearman's rho=0.11 (95% CI 0.033-0.18, p=0.005) and 0.1 (95% CI 0.03-0.18, p=0.007) for BL and Δ, respectively], and WOMAC stiffness [Spearman's rho= 0.08 (95% CI 0.01-0.16, p=0.03) and 0.11 (95% CI 0.04-0.19, p=0.004 for BL and Δ, respectively].

Conclusion: ES volume measured automatically using DL shows promising correlations to manual semiquantitative effusion scoring (MOAKS) and clinical features of knee arthritis (pain and stiffness). As others have found when measuring ES in other ways, we found higher (KL) grades (e.g., 3-4) were associated significantly with larger effusions. These results demonstrate validity of the proposed method for fully automated knee effusion quantification, which may ultimately prove useful in clinical care and clinical trials. [1] Felfeliyan et al., Improved-Mask R-CNN: Towards an accurate generic MSK MRI instance segmentation platform, CMIG 2022

Disclosure: B. Felfeliyan: None; **S. Wichuk**: None; **A. Hareendranathan**: None; **J. Ronsky**: None; **J. Jaremko**: None.

Abstract Number: 0757

Identification of 23 Novel *COPA* Rare Exonic Non-Synonymous Variants and Their Associated Autoimmune and Inflammatory Clinical Phenotypes Among 53,364 Individuals

Pierre-Antoine Juge[1], Gregory McDermott[2], Keigo Hayashi[2], Jing Cui[3], Clémence David-Gabarre[4], Marie-Louis Frémond[4], Holly Wobma[5], Soumya Raychaudhuri[2], Elizabeth Karlson[2], Philippe Dieudé[6] and Jeffrey Sparks[7], [1]Division of Rheumatology, Inflammation, and Immunity Brigham & Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital, Boston, MA, [3]Brigham and Women's Hospital, Boston, MA, [4]Imagine, Paris, France, [5]Division of Immunology, Boston Children's Hospital, Boston, MA, [6]Assistance Publique-Hôpitaux de Paris, Bichat-Claude Bernard University Hospital, INSERM UMR1152, University de Paris Cité, Department of Rheumatology, Paris, France, [7]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases I
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: COPA syndrome is a rare, severe monogenic autoinflammatory/autoimmune disorder with variable penetrance, most commonly affecting the lungs and joints. It is caused by dominant negative mutations located in a specific hot spot (from the 7th to the 10th exons) of the *COPA* gene on chromosome 1, encoding the α subunit of the COP1 complex involved in protein transport from the Golgi apparatus to the endoplasmic reticulum. COPA syndrome is associated with autoimmunity and upregulation of both the type 1 interferon pathway and T helper-17 cells. Clinical manifestations usually start during childhood, but late-onset diseases have been described with up to 30% of asymptomatic carriers. We aimed to identify additional novel non-synonymous variants (NSV) in *COPA* and to describe their associated phenotypes.

Methods: All individuals from a large institutional biobank of adults with available whole-exome sequencing (WES) data were included in this study. All NSV from the 7th to the 10th exons of *COPA* were identified and annotated according to allele frequency reported in an online database (gnomAD) and functional predictive tools (SIFT, POLYPHEN-2, and CADD score).

Table 1. List of the identified non-synonymous variants in the COPA hot spot. *CADD score: Combined Annotation Dependent Depletion score, variants with scores over 20 are predicted to be the 1% most deleterious possible substitutions in the human genome. MAF: minor allele frequency, SNP: single nucleotide polymorphisms.

POSITION GRCh38	Nucleotide change	Amino acid change	SNP/previous description	MAF (GnomAD)	SIFT Score	POLYPHEN-2	CADD Score*	Patients with history of inflammatory or autoimmune disease / number of carriers
160313133	c.877C>T	p.R293C	rs1253097568	$3.98x10^{-5}$	Deleterious	Deleterious	35	0/1
160313142	c.868G>A	p.D290N	novel	-	Deleterious	Probably deleterious	26.5	0/1
160313147	c.863G>A	p.R288H	rs781647709	$2.39x10^{-5}$	Deleterious	Deleterious	35	1/1
160313990	c.842G>A	p.R281Q	Reported in COPA syndrome	-	Deleterious	Deleterious	35	1/1
160314045	c.787T>G	p.L263V	novel	-	Deleterious	Probably deleterious	22.5	1/1
160314053	c.779G>T	p.R260L	novel	-	Deleterious	Deleterious	35	1/1
160314053	c.779G>A	p.R260H	rs1381216320	$7.97x10^{-6}$	Tolerated	Deleterious	23.9	0/1
160314054	c.778C>T	p.R260C	rs773838802	$1.99x10^{-5}$	Deleterious	Deleterious	35	0/3
160314066	c.766G>A	p.V256I	rs143714109	$4.25x10^{-5}$	Tolerated	Benign	23.2	4/7
160314066	c.766G>T	p.V256F	rs143714109	-	Deleterious	Probably deleterious	26.3	1/1
160314069	c.763G>A	p.A255T	rs138359166	$1.99x10^{-5}$	Tolerated	Probably deleterious	23.6	4/11
160323437	c.700A>G	p.M234V	novel	-	Deleterious	Probably deleterious	23.2	0/1
160323484	c.653C>T	p.P218L	rs967646112	-	Deleterious	Deleterious	33	0/1
160323484	c.653C>A	p.P218H	rs967646112	$8.01x10^{-6}$	Deleterious	Deleterious	30	1/1
160323488	c.649A>G	p.M217V	novel	-	Deleterious	Benign	23.1	2/2
160323494	c.643C>G	p.P215A	rs758218973	$4.00x10^{-5}$	Deleterious	Deleterious	26.7	0/1
160323503	c.634G>A	p.A212T	novel	-	Tolerated	Benign	23.7	0/1
160323505	c.632C>T	p.A211V	rs141575695	$1.60x10^{-5}$	Tolerated	Benign	23.3	2/5
160323526	c.611A>C	p.H204P	novel	-	Deleterious	Deleterious	28.2	0/1
160325620	c.529G>A	p.V177M	novel	-	Tolerated	Probably deleterious	16.9	0/1
160325622	c.527C>T	p.A176V	rs375484084	$3.98x10^{-6}$	Deleterious	Probably deleterious	23.9	1/1
160325640	c.509A>G	p.K170R	rs750784548	$1.06x10^{-5}$	Deleterious	Deleterious	26.7	1/1
160325644	c.505A>G	p.K169E	rs1242581995	$3.98x10^{-5}$	Deleterious	Deleterious	24	0/2
160325652	c.497G>T	p.G166V	rs1424434292	$3.98x10^{-5}$	Deleterious	Deleterious	24.2	1/1

Medical record review was performed for all NSV-carrying individuals to collect personal and family medical history as well as results of autoantibody testing and chest imaging obtained through routine clinical care.

Results: Among the 53,364 adults with available WES data, 24 unique NSV in the *COPA* hot spot were identified in a total of 48 individuals (prevalence 0.09%, **Table 1**); 33 were women (69%), median age at medical record review was 51.7 years (IQR 39.6, 64.5). Only one NSV (p.R281Q) had been previously reported as a mutation in a COPA syndrome. This patient developed seronegative RA at age 18 and autoimmune hepatitis at age 35 without clinically diagnosed COPA syndrome. All other identified NSV were novel to COPA syndrome: 15 with a frequency < 0.0001 and 8 never previously identified so unable to estimate known frequency. Deleterious impact was predicted by both SIFT and POLYPHEN-2 for 12 variants (50%). Autoimmune or inflammatory disease was reported for 21 of the 48 carriers (44%); median age at disease onset was 42.9 years (IQR 28.2, 56.0; **Table 2**). 19/21 (91%) had adult-onset of these diseases. Inflammatory arthritis occurred in 6 patients, 4 diagnosed as rheumatoid arthritis (RA). Interstitial lung disease was observed in 5 patients. Five patients had psoriasis and/or Crohn's disease. Antinuclear antibodies, anti-CCP, and rheumatoid factor were positive for 9/15, 3/8 and 4/9 patients, respectively. A family history of autoimmune/inflammatory disease was reported in 9 patients. Two individuals died, both from acute on chronic heart failure, at ages 64 and 79.

Conclusion: In this first investigation of *COPA* in a large adult biobank, we identified 23 novel NSV beyond the known causal mutations and described associations with inflammatory and autoimmune diseases among nearly half of SNV, most of which were adult-onset. If functional impact of the newly identified NSV is proven, rare exonic NSV in *COPA* could contribute to the genetic architecture of several common autoimmune and inflammatory phenotypes.

Table 2. Characteristics of patients identified to be COPA hotspot NSV carriers. ANA: anti-nuclear antibodies, anti-CCP: anti-citrullinated peptides, CT: computed tomography, CTD: connective-tissue diseases; ILD: interstitial lung disease; JIA: juvenile idiopathic arthritis, PANDAS: Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infections, PsA: psoriatic arthritis, RA: rheumatoid arthritis, RF: rheumatoid factor, UCTD: undifferentiated connective tissue disease

	n=48
Median age at medical record review, years (IQR)	51.7 (39.6, 64.5)
Median age at inflammatory and/or autoimmune disease onset, years, (IQR) Min - Max	42.9 (28.2, 56.0) 3.5 – 63.9
Onset ≥18 years among those inflammatory and/or autoimmune disease, n (%)	19/21 (91)
Female sex, n (%)	33 (69)
Race/ethnicity	
- Non-Hispanic White	30 (63)
- Black	12 (25)
- Asian	3 (6)
- Hispanic	3 (6)
History of inflammatory and/or autoimmune disease, n (%)	21 (44)
- Inflammatory arthritis	6 (13)
o RA	4 (8)
o PsA	1 (2)
o JIA	1 (2)
- Other systemic autoimmune rheumatic diseases	3 (6)
o UCTD	1 (2)
o Antisynthetase syndrome	1 (2)
o Primary Sjogren's disease	1 (2)
- Crohn's disease	3 (6)
- Psoriasis	3 (6)
- Autoimmune liver disease	2 (4)
- Acute idiopathic myocarditis or pericarditis	2 (4)
- Hashimoto thyroiditis	2 (4)
- Neuromyelitis optica	1 (2)
- Multiple sclerosis	1 (2)
- Severe idiopathic scleritis	1 (2)
- Giant cell arteritis	1 (2)
History of chest CT scan-proven ILD	5 (10)
Family history of inflammatory and/or autoimmune disease	9 (19)
- RA	2 (4)
- Multiple sclerosis	2 (4)
- Dermatomyositis with ILD	1 (2)
- Systemic lupus erythematosus	1 (2)
- PsA	1 (2)
- Hashimoto thyroiditis	1 (2)
- PANDAS syndrome	1 (2)
Autoantibodies:	
- ANA positive/total tested	9/15
- Anti-CCP positive/total tested	3/8
- RF positive/tested	4/9

Disclosure: P. Juge: None; **G. McDermott**: None; **K. Hayashi**: None; **J. Cui**: None; **C. David-Gabarre**: None; **M. Frémond**: None; **H. Wobma**: None; **S. Raychaudhuri**: AbbVie, 6, Janssen, 1, Mestag, Inc, 2, 8, Pfizer, 1, Sanofi, 1, Sonoma, 1, 8; **E. Karlson**: None; **P. Dieudé**: AbbVie, 2, 6, Boehringer Ingelheim, 1, 2, 6, Bristol-Myers Squibb, 1, 2, 5, 6, Chugai, 5, Galapagos, 5, 6, Janssen, 2, 6, Novartis, 2, Pfizer, 1, 2, 5, 6; **J. Sparks**: AbbVie, 2, Amgen, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, 5, Gilead, 2, Inova Diagnostics, 2, Janssen, 2, Optum, 2, Pfizer, 2, ReCor, 2.

Abstract Number: 0758

Clinical and Biological Characteristics of Children and Adults Affected with Still's Disease: A Systematic Review and Meta-analysis Informing the 2023 EULAR/PReS Recommendations for the Diagnosis and Management of Systemic Juvenile Idiopathic Arthritis and Adult-onset Still's Disease

STEPHANE MITROVIC[1], Arianna De Matteis[2], Sara Bindoli[3], Fabrizio De Benedetti[4], Bruno Fautrel[5], Loreto Carmona[6] and On Behalf Of The Eular/PreS QoC011 Task Force Member[7], [1]Pitie Salpetriere Hospital, Sorbonne University, APHP, Paris, France, [2]IRCCS Ospedale Pediatrico Bambino Gesu', Rome, Italy, [3]Rheumatology Unit, Dept of Medicine, University of Padova, Padova, Italy, [4]Bambino Gesu Children's Hospital, Division of Rheumatology, Rome, Italy, [5]Sorbonne Université APHP, Paris, France, [6]Instituto de Salud Musculoesquelética (InMusc), Madrid, Spain, [7]EULAR/PReS QoC011 Task Force members are: Jordi Anton, Alexandre Belot, Claudia Bracaglia, Tamas Constantin, Lorenzo Dagna, Alessandro De Bartolo, Eugen Feist, Dirk Foell, Marco Gattorno, Sophie Georgin-Lavialle, Roberto Giacomelli, Alexei Grom, Yvan Jamilloux, Katarina Laskari, Calin Lazar, Francesca Minoia, Peter Nigrovic, Filipa Oliveira Ramos, Seza Ozen, Pierre Quartier-dit-Maire, Piero Ruscitti, Erdal Sag, Sinisa Savic, Marie-Elise Truchetet, Bas Vastert, Tanita Wilhelmer, Carine Wouters., Paris, France

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases I

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Systemic juvenile idiopathic arthritis (sJIA) and adult-onset Still's disease (AOSD) are part of the non-familial (sporadic) systemic inflammatory disorders and are frequently mentioned as being the same disease occurring at different ages. However, they are studied disconnectedly leading to lost opportunities in therapeutic innovation and variability in clinical management. In this context, the European Alliance of Associations for Rheumatology (EULAR) and the Paediatric Rheumatology European Society (PReS) established a Task Force to issue the first recommendations for the diagnosis and management of sJIA and AOSD, acknowledging they are the same disease. The following work was undertaken to inform the Task Force. The objective was to analyze the prevalence of clinical manifestations (including complications) and laboratory findings in sJIA and AOSD.

Methods: Two systematic reviews (SRs) were performed. The first SR included cohort studies comparing sJIA vs AOSD with a description of clinical and biological manifestations (including complications) and with more than 20 patients per group ("prevalence SR"); the second SR identified studies in which biomarkers were tested in both diseases and their diagnostic performance evaluated ("diagnostic SR"). Medline (via PubMed), Embase, and Cochrane Library were systematically searched. The risk of bias was assessed with an adapted form of the Hoy scale for prevalence studies in prevalence SR and with the QUADAS in the diagnostic SR. We performed meta-analyses of proportions for the different qualitative descriptors using the Stata command *metaprop*.

Results: Eight studies were included in the prevalence SR (n= 1005 participants) and 33 in the diagnostic biomarker SR. There was no difference in the pooled estimated prevalence of clinical manifestations between sJIA and AOSD, except for myalgia, sore throat, and weight loss, which were more frequently reported in AOSD, as they are likely ascertained incompletely in sJIA, especially in young children (Figure 1). Except for AA amyloidosis, more frequent in sJIA, there was no statistical difference between sJIA and AOSD in terms of complication prevalence (Figure 2). Likewise, biological findings did not differ between groups (Figure 3). Ferritin, S100 proteins and interleukin-18 were the most frequently used diagnostic biomarkers, and showed overlapping diagnostic performance parameters in sJIA and AOSD.

Conclusion: All these similarities argue for a continuum between sJIA and AOSD. We postulate that a common name is warranted, as well as a novel common set of classification criteria and disease activity score.

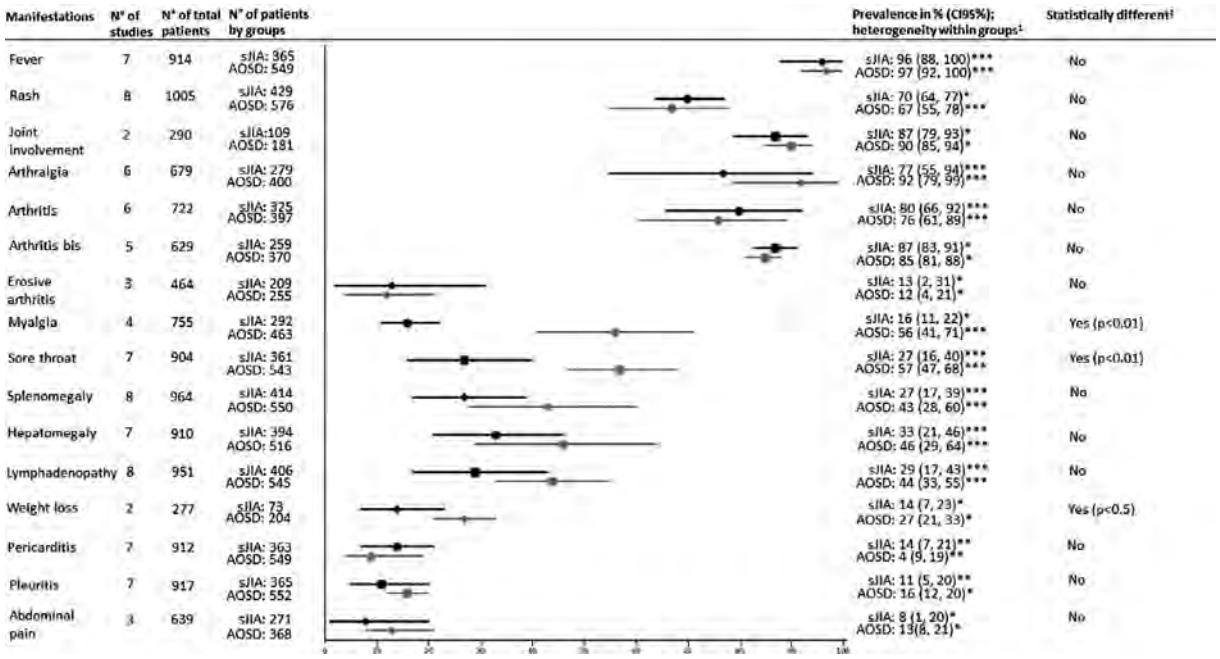


Figure 1. Prevalence (pooled estimates) of clinical manifestations in sJIA and AOSD. Values are pooled estimates of prevalence (95% CI). For each parameter, prevalence is represented in black for sJIA and in grey for AOSD. 1Heterogenity is summarised visually by asterisks: *, low heterogeneity (I2 <50%); **, moderate heterogeneity (50 < I2< 75%); ***, high heterogeneity (I2 > 75%). 2This line gives the arthritis pooled estimate prevalence without one study by Inoue 2016, because it had a very low rate of arthritis in both age groups, accounting for the large part of variability when taken into account. CI, confidence interval.

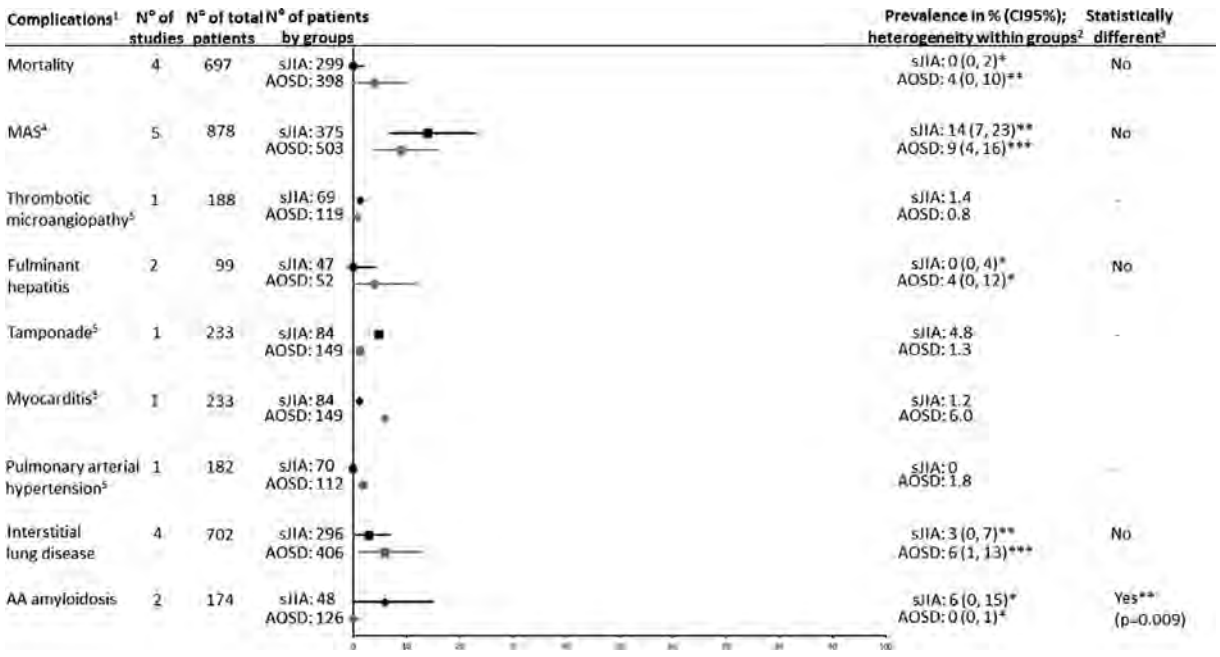


Figure 2. Prevalence (pooled estimates) of complications in sJIA and AOSD. Values are pooled estimates of prevalence (CI95%). For each parameter, prevalence is represented in black for sJIA and in grey for AOSD. 1In Neau 2022, the details of MAS, thrombotic microangiopathy, tamponade, myocarditis and interstitial lung disease for each group (sJIA and AOSD) have been obtained directly from the authors (not published data). 2Heterogenity is summarised visually by asterisks: *, low heterogeneity (I2 <50%); **, moderate heterogeneity (50 < I2< 75%); ***, high heterogeneity (I2> 75%). 3Heterogeneity between groups is statistically different if p<0.05. 4Note that for Neau 2022, the authors reported a total n=26 in the published data, but in their Excel file n=24 (12 in sJIA group, 12 in AOSD group), so we considered n=24 for our meta-analysis. 5 Only one study (Neau 2022) reported on the frequency of thrombotic microangiopathy, tamponade, myocarditis or pulmonary hypertension, and so meta-analysis was not performed for these complications.

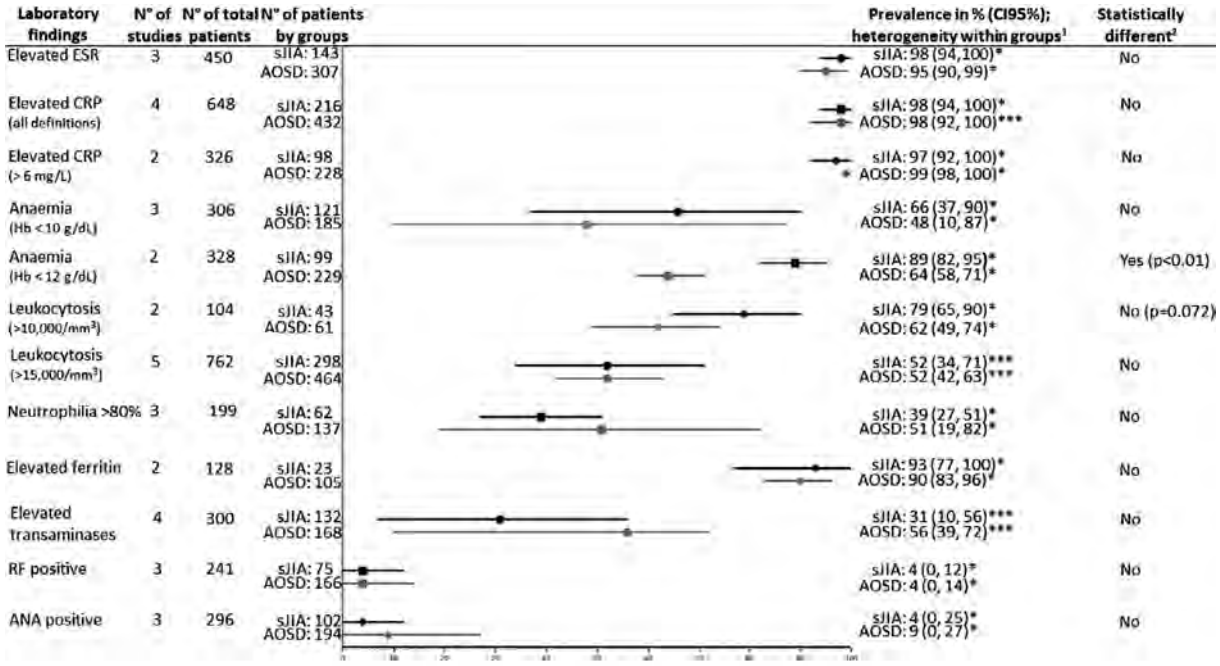


Figure 3. Prevalence (pooled estimates) of modified biological features in sJIA and AOSD Values are pooled estimates of prevalence (CI95%). For each parameter, prevalence is represented in black for sJIA and in grey for AOSD. 1Heterogenity is summarised visually by asterisks: *, low heterogeneity (I2 <50%); **, moderate heterogeneity (50 < I2< 75%); ***, high heterogeneity (I2 > 75%). For details of the I^2s and p-values of each group, please refer to the supplementary material. 2Heterogeneity between groups is statistically different if p<0.05. For details of p-values, please refer to the supplementary material. ANA, antinuclear antibody – CI, confidence interval – Hb, haemoglobin – RF, rheumatoid factor.

Disclosure: S. MITROVIC: Eli Lilly, Pfitzer, BMS, SOBI, 2; **A. De Matteis**: None; **S. Bindoli**: None; **F. De Benedetti**: Abbvie, Novimmune, Novartis, Roche, Sanofi-Aventis, Sobi, Regeneron, Elixiron and Zydus, 5; **B. Fautrel**: AbbVie, 2, BMS, 2, Chugai, 2, Fresenius Kabi, 2, Galapagos, 2, Lilly, 2, Medac, 2, Nordic Pharma, 2, Novartis, 2, Pfizer, 2, Sobi, 2, UCB, 2; **L. Carmona**: Amgen, Fresenius Kabi Espana, Galapagos, Gilead, Pfizer, Lilly, Meda Pharma, MSD, Novartis, Roche, Sanofi Aventis, Upjohn, BMS, Novo Nordisk, and Sand, 5; **O. Task Force Member**: None.

Abstract Number: 0759

Derivation and Validation of Four Patient Clusters in Still's Disease, Results from GIRRCS AOSD-study Group and AIDA Network Still Disease Registry

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases I

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Still's disease is a rare inflammatory disorder, these patients have a highly heterogeneous disease according to age of onset, clinical presentation, presence of life-threatening complications, and outcomes. Thus, we aimed at deriving and validating disease clusters in a multicentre, observational, prospective study to stratify these patients.

Methods: Patients included in GIRRCS AOSD-study group and AIDA Network Still Disease Registry were selected to be assessed in this analysis if clinical variables selected for cluster analysis were available [i.e., age, systemic score, erythrocyte sedimentation rate (ESR), C reactive protein (CRP), and ferritin]. A cluster analysis was performed to devise deeper levels of categorization. The k-means algorithm with Euclidean metric was performed, setting 100 random assignments to the cluster seeds. Z-scores were also provided to account for the different units of the selected variables. The Elbow plot was used to devise an adequate number of clusters, avoiding too large choice which could underwent to overfitting. Besides the cluster plot enabled the view of the separation among clusters using the first two principal components. After that a descriptive assessment of the clusters was performed.

Results: By combining clinical selected variables, the K-means clustering assessment provided 4 clusters based on means standardized according to z-scores on 349 patients. The "within" and "between" separation properties were also derived. Within cluster sum of squares (SS) by cluster was estimated: i. cluster 1: 251.69; ii. cluster 2: 283.22; iii. cluster 3: 159.98; iv. cluster 4: 323.76. $SS_{between}/SS_{total}$ was derived to be 41.5%. The latter is not particularly high, but not affected by overfitting phenomena. In fact, the derived clusters showed reasonable "within" and "between" variability properties. After that, randomly sampling 50% of the original records, the same number of clusters was provided by the elbow plot with a similar $SS_{between}/SS_{total}$ of 42.6%.

All clusters mainly presented fever, skin rash, and joint involvement but each one of these has some different clinical features from others. Cluster 1 ("Juvenile/Transitional") was composed by 115 patients distinguished by the lowest value of age and characterized by skin rash myalgia, sore throat, and splenomegaly. Cluster 2 ("Common") included 128 patients identified by the lowest levels of ESR, ferritin, and systemic score; multiorgan manifestations were less frequently observed. Cluster 3 ("Hyperferritinemic") comprised 31 patients categorised by the highest levels of CRP and ferritin, they were characterized by fever and joint involvement. Cluster 4 ("Catastrophic") contained 75 patients derived by the highest values of age and systemic score. Myalgia, sore throat, liver involvement, and life-threatening complications, leading to a high mortality rate, were observed in these patients.

Conclusion: Four patient clusters in Still's disease may be recognized by a multidimensional characterization. Each one of these has some different clinical features from others; cluster 4 was burdened by an increased rate of life-threatening complications and mortality, suggesting a more severe patient group.

Disclosure: P. Ruscitti: None; **A. Vitale**: None; **I. Di Cola**: None; **R. giacomelli**: None; **L. Cantarini**: None.

Abstract Number: 0760

Treatment Patterns and Outcomes in Patients with Macrophage Activation Syndrome Secondary to Still's Disease Treated with Emapalumab: The REAL-HLH Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
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Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Macrophage activating syndrome (MAS) is a rare, potentially fatal complication of systemic juvenile idiopathic arthritis (sJIA) and adult-onset Still's disease (AOSD). MAS (a form of secondary HLH) is associated with overproduction of proinflammatory cytokines, such as interferon gamma (IFNγ). The REAL-HLH study assessed the real-world utilization of emapalumab, an anti-IFNγ antibody, among patients in the US. Treatment patterns and outcomes in patients with MAS secondary to Still's disease and treated with emapalumab are presented.

Methods: A retrospective medical chart review conducted across 33 US hospitals identified patients treated with≥1 dose of emapalumab between November 20, 2018 and October 31, 2021. Data extracted on the subset of patients with MAS secondary to Still's disease from the time of emapalumab initiation to end of data availability, death, or study end (December 31, 2021) were analyzed.

Results: Of the 105 patients identified, 10 had Still's disease (sJIA, n=9; AOSD, n=1). Most patients were female (8/10; 80%) and white (6/10; 60.0%). At diagnosis, mean (SD) age was 5.6 (6.4) years, and 70% (7/10) of patients met the 2016 ACR MAS diagnostic criteria. At diagnosis, the patient with AOSD was 22 years of age. At time of emapalumab initiation, all patients had received or were receiving other HLH-related therapies, including corticosteriods and anakinra; 60% of patients were in the intensive care unit. Emapalumab was mainly initiated to treat refractory (4/10; 40%), recurrent (3/10; 30%), or progressive (2/10; 20%) disease. Median (range) time from diagnosis to emapalumab initiation was 13.0 (1, 101) days, and median (range) treatment duration was 65.5 (25, 367) days. Emapalumab treatment doses are shown in the Table. Median (range) number of emapalumab doses was 15.5 (2, 35). The majority of patients achieved normal levels of ferritin (5/10; 50%), fibrinogen (6/10; 60%), platelets (8/10; 80%), alanine transaminase (8/10; 80%), absolute neutrophil count (9/10; 90%), and absolute lymphocyte count (9/10; 90%) during treatment. Median time to first normalization of these laboratory parameters ranged from 7 to 46 days. Overall survival and 12-month survival probability following emapalumab initiation was 90% (9/10) for patients with Still's disease. One patient died due to uncontrolled viremia, which was deemed by the investigator to be unrelated to the clinical condition for which emapalumab was used.

Conclusion: This is the first study to report real-world treatment patterns and outcomes among patients with MAS secondary to Still's disease treated with emapalumab. A phase 3 clinical trial of emapalumab in patients with sHLH/MAS and underlying rheumatologic disease is ongoing (NCT05001737).

Table. Emapalumab Treatment Doses in Patients With Still's Disease

	Median (range), mg/kg
Starting dose	3.7 (0.9-5.9)
Maximum single dose	5.8 (0.9-6.6)
Cumulative administered dose	53.2 (6.7-171.3)

Disclosure: C. Allen: Sobi, Inc, 1, 2; **S. Chandrakasan**: Sobi, Inc, 1, 2; **M. Jordan**: Sobi, Inc, 1, 2; **J. Leiding**: Sobi, Inc, 1, 2; **A. Oladapo**: Sobi, 3; **P. Pednekar**: Sobi, Inc, 2; **K. Walkovich**: Sobi, Inc, 1, 2; **J. Yee**: Sobi Inc., 3.

Abstract Number: 0761

EULAR / PreS Recommendations for the Diagnosis and Management of Systemic Juvenile Idiopathic Arthritis (sJIA) and Adult Onset Still's Disease (AOSD)

Bruno Fautrel[1], STEPHANE MITROVIC[2], Arianna De Matteis[3], Sara Bindoli[4], Jordi Anton[5], Alexandre Belot[6], Claudia Bracaglia[3], Tamas Constantin[7], Lorenzo Dagna[8], Alessandro de Bartolo[9], Eugen Feist[10], Dirk Foell[11], Marco Gattorno[12], Sophie Georgin-Lavialle[13], Roberto Giacomelli[14], Alexei Grom[15], Yvan Jamilloux[16], Katerina Laskari[17], Calin Lazar[18], Francesca Minoia[19], Peter Nigrovic[20], Filipa Oliveira Ramos[21], Seza Ozen[22], Pierre Quartier Dit Maire[23], Piero Ruscitti[24], Erdal Sag[25], Sinisa Savic[26], Marie-Elise Truchetet[27], Sebastiaan Vastert[28], Tanita Wilhelmer[29], Carine Wouters[30], Loreto Carmona[31] and Fabrizio De Benedetti[32], [1]Sorbonne Université APHP, Paris, France, [2]Pitie Salpetriere Hospital, Sorbonne University, APHP, Paris, France, [3]IRCCS Ospedale Pediatrico Bambino Gesu', Rome, Italy, [4]Rheumatology Unit, department of Medicine,University of Padova, Padova, Italy, [5]Hospital Sant Joan de Déu, Pediatric Rheumatology Department, Universitat de Barcelona, Barcelona, Spain, [6]Hospices Civils de Lyon, Collonges au mont d'or, France, [7]Semmelweis University, Budapest, Hungary, [8]Ospedale San Raffaele, Milano, Italy, [9]PReS Patient Research Partner, Milan, Italy, [10]Helios Department of Rheumatology and Clinical Immunology, Vogelsang-Gommern, Germany, [11]University Hospital Münster, Münster, Germany, [12]UOC Reumatologia e Malattie Autoinfiammatorie, Genoa, Italy, [13]AP-HP, Tenon hospital, Paris, France, [14]Policlinico Universitario Campus Bio-Medico, Roma, Italy, [15]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [16]Hospices Civils de Lyon, Lyon, France, [17]Athens University Medical School, Athens, Greece, [18]University of Medicine and Pharmacy, Cluj-Napoca, Romania, [19]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy, [20]Boston Children's Hospital, Boston, MA, [21]Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal, [22]Hacettepe University Medical Faculty, Ankara, Turkey, [23]Necker Hospital, Paris Cedex 15, France, [24]University of L'Aquila, L'Aquila, Italy, [25]Department of Pediatric Rheumatology, Hacettepe University, Ankara, Turkey, [26]Leeds University, Leeds, United Kingdom, [27]Bordeaux University Hospital, Bordeaux, France, [28]University Medical Center Utrecht, Utrecht, Netherlands, [29]EULAR Patient Research Partner, Bludenz, Austria, [30]Leuven University, Leuven, Belgium, [31]Instituto de Salud Musculoesquelética (InMusc), Madrid, Spain, [32]Bambino Gesu Children's Hospital, Division of Rheumatology, Rome, Italy

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases I

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Systemic juvenile idiopathic arthritis (sJIA) and adult-onset Still's disease (AOSD) are supposed to be age counterparts of the same disease, but no consensus has been reached yet on a common approach to diagnosis and management across ages.

Methods: In May 2022, EULAR (European Alliance of Associations of Rheumatology) and PReS (Pediatric Rheumatology European Society) endorsed a proposal for a joint task force (TF) to develop recommendations for the diagnosis and management of sJIA and AOSD. The TF included 2 convenors (BF, FdB), a methodologist (LC), three fellows (SM, AdM, SB), 25 medical experts and 2 patient research partners (AdB, TW). The TF agreed during a first meeting in September 2022 to cover four main topics: similarity between sJIA and AOSD, novel diagnostic biomarkers, therapeutic targets and strategies, and complications including macrophage activation syndrome (MAS). Four systematic reviews (SRs) were conducted accordingly. Their results were presented to the TF members during a second meeting in March 2023, which enabled the production of overarching principles (OP), recommendations (R) or items for research agenda (RA).

Results: The TF based their recommendation on three OPs (Table): 1) SJIA and AOSD one disease and should be designated by one name, Still's disease, 2) A treat-to-target approach and a shared decision making should be implemented, with the final goal of reaching drug-free remission, and 3) although several innovative therapies are available, MAS should remain a concern for the physician throughout disease evolution.

Table: Overarching principles (OP) and recommendations (R) for the diagnosis and management of children and adults living with Still's disease (formerly called sJIA/AOSD)

		LoE	Strength	A	LoA
OP1	sJIA and AOSD are the same disease, that should be designated by the same unique name, Still's disease (formerly called sJIA / AOSD)	2a	B	100%	9.7
OP2	The treatment targets and the therapeutic strategy should be based on shared decision making between the parents/patients and the treating team. Treatment to Target (T2T) by regularly assessing disease activity and adapting therapy accordingly is important. The ultimate goal is drug-free remission.	2b	C	96%	9.9
OP3	MAS should be detected promptly and treated rapidly.	2b	D	100%	10
R1	To facilitate rapid diagnosis and initiate early treatment, operational definitions should be used to identify patients with Still's disease, - Fever is typically spiking with temperature ≥ 39°C (102.2°F) for at least 7 days, - Rash is transient and coinciding with fever spikes, preferentially involving the trunk. It is typically erythematous (salmon pink), but other rashes (e.g., urticarial) may be consistent with the diagnosis, - Musculoskeletal involvement is usually present with arthralgia / myalgia. Overt arthritis is supportive but not necessary for diagnosis and may appear later, - High levels of inflammation are typically identified by neutrophilic leukocytosis, increased serum CRP and ferritin.	2a	B	94%	9.6
R2	Marked elevation of IL-18 and/or S100 proteins (e.g. calprotectin) strongly supports the diagnosis, and therefore should be measured if available	4	C	90%	8.9
R3	Alternative diagnoses such as malignancies, infectious diseases, other immune-mediated inflammatory diseases and monogenic autoinflammatory disorders should be carefully considered	5	D	83%	9.8
R4	Clinically inactive disease (CID) is defined as absence of Still's disease-related symptoms and normal ESR or CRP. Remission is defined as a period of at least 6 months with clinically inactive disease	5	D	85%	9.4
R5	In order to achieve the ultimate goal (drug-free remission), the following intermediate targets are recommended: - At day 7, resolution of fever and reduction of CRP by > 50%, - At week 4, no fever, reduction of active (or swollen) joint count by > 50%, normal CRP and physician and patient/parent global assessment less than 20 on a 0-100 VAS, - At month 3, clinical inactive disease with glucocorticoids less than 0.1 or 0.2 mg/kg/day, - At month 6, clinical inactive disease without glucocorticoids.	5	D	86%	9.0
R6	NSAIDs are symptomatic treatments and can be used as bridging therapy during the time of investigations. GCs are efficacious; however, long-term use of systemic GCs to achieve and maintain the target must be avoided. The efficacy of IL-1 and IL-6 inhibitors is supported by a high level of evidence and therefore their use should be prioritized.	1b	A	96%	9.8
R7	An IL-1 or an IL-6 inhibitor should be initiated as early as possible when the diagnosis is established.	2b	B	96%	9.4
R8	Maintenance of CID for 3 to 6 months without glucocorticoids should be achieved before initiating bDMARD tapering	5	D	96%	9.2
R9	Severe / life-threatening complications, including macrophage activation syndrome or lung disease, may develop at any point during the disease course. Patients should be actively screened and monitored.	2a	B	100%	9.9
R10	MAS should be considered in patients with persistent fever, splenomegaly, elevated or rising serum ferritin, inappropriately low cell counts, abnormal LFT, intravascular activation of coagulation, elevated or rising serum triglycerides. To facilitate MAS diagnosis, scores (M- or H-score) or classification criteria (MAS 2016 criteria) could be used.	2a	B	100%	9.9
R11	MAS treatment must include high dose glucocorticoid. In addition, treatments including anakinra, ciclosporin and/or IFNγ inhibitors should be considered as part of initial therapy.	2b	B	100%	9.8
R12	Lung disease should be actively screened by search for clinical symptoms (e.g., clubbing, persistent cough, shortness of breath) and pulmonary function tests (pulse oxygenometry, DLCO measurement). High resolution CT-scan should be performed in any patients with clinical concerns.	2b	B	98%	9.7
R13	There is insufficient evidence to withhold first line IL-1 or IL-6 inhibitors in pts with new onset Still's disease and LD risk factors. There is insufficient evidence to withdraw IL-1 or IL-6 inhibitors in pts developing Still's-LD. Based on the current understanding of the pathogenesis, a T cell directed therapy may be considered in patients developing Still's-LD.	2b	B	96%	9.4
R14	Difficult-to-treat patients, those with severe MAS and those with LD should be managed in collaboration with Still's disease expert centers.	5	D	96%	9.9

LoE: Level of Evidence – A: Agreement among the TF experts – LoA: Level of Agreement

Fourteen specific recommendations were issued and are detailed in the Table. Two therapeutic targets were defined: clinically inactive disease (CID) and remission, i.e., CID maintained for at least 6 months. The optimal therapeutic strategy relies on glucocorticoids (GCs) for a maximal duration of 6 months with prioritization of IL-1 or IL-6 inhibitors initiated as early as possible after diagnosis. Life-threatening complications can occur any time during disease course, i.e., at diagnosis, under targeted therapies, and after CID achievement. MAS treatment should rely on high-dose GCs, IL-1 inhibitors, cyclosporin and IFNγ inhibitors. A specific concern rose recently with cases of severe lung disease in children with Still's disease. The

main characteristics are the following: initially mild clinical symptoms including erythematous clubbing, dry cough or shortness of breath; subpleural and septal thickening on CT-scan; interstitial lymphocytic expansion, evidence of T cell activation and features of alveolar proteinosis on biopsy. Risk factors include eosinophilia, increased serum IL-18, history of MAS, exposure to IL-1 or IL-6 inhibitors, and presence of HLA DRB1*15 allele. Adding T-cell directed immunosuppressant seems to be the most appropriate treatment option. Finally, the recommendations emphasized the key role of expert centers, notably those of the RITA European Reference Centers.

Conclusion: These recommendations are the first recommendation for the diagnosis and management of children and adults affected with Still's disease. All OPs and recommendations were agreed by over 80% of the TF experts with a high level of agreement (9 or more).

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Abstract Number: 0762

Liver Disease Is a Common Feature of HA20 That Causes Significant Morbidity Associated with Interferon Induction

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases I

Session Type: Abstract Session

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Background/Purpose: Heterozygous loss-of-function *TNFAIP3* mutations cause A20 haploinsufficiency (HA20), an early-onset immune dysregulatory disease[1]. While HA20 was initially described as an inherited form of Behcet's syndrome, it is now known to cause wider range of phenotypes including psoriasis, lymphoproliferation, membranous nephropathy, and liver injury.[2] Prior work suggests that liver disease is seen in only 8% of HA20 patients.[3-7] Contrary to this paradigm, we noted a high prevalence of liver injury when evaluating a cross-section of 41 HA20 patients by virtual consultation. We therefore systematically assessed our cohort of 25 HA20 patients, finding an unexpectedly high prevalence of liver disease with significant morbidity.

Methods: 41 HA20 patients from 5 countries were referred for virtual consultation. 24 of these patents were evaluated at the NIH Clinical Center or at UPMC; 1 subject was deceased at time of assessment but had been evaluated at the referring institution. Clinical laboratory and imaging data were obtained via chart review. Interferon stimulated genes (ISGs) were measured in whole blood (Nanostring) from 15 patients. Fisher's t-test with multiple comparison adjustment (Benjamini-Hochberg) was used to compare patients with vs. without liver disease.

Results: Liver disease was described in 19 virtual consultation patients (44%). 12 (29.3%) were diagnosed with autoimmune hepatitis, 2 of whom (4.9%) died from complications of HA20. Serial laboratory results were available for all 25 retrospectively evaluated patients, abdominal imaging was available for 14, and liver biopsies had been done in 6. 12 patients (48%) had liver disease: 8 (29.2%) were diagnosed clinically, and 4 occult cases were found on abdominal imaging.

Mean age of onset was 11.2. Mutations involved various domains of A20; the entire coding sequence was deleted in 4 patients from 2 families (**Figure 1**). 6 patients were diagnosed with autoimmune hepatitis, 1 had recurrent transaminase elevation (>3x upper limit of normal), 2 had hepatic steatosis, and 3 had isolated hepatomegaly (**Table 1**). Fibroscan scores ranged from 2.7–22.7 kPa. 6 patients had biopsy-proven fibrosis: 4 had cirrhosis and 3 had portal hypertension. ISGs were checked in 9 patients and elevated in 8 (88.8%). 4 patients (33.3%) complete or partial prior response to azathioprine (AZA); 6 (50%) patients had complete or partial prior response to JAK inhibitors (JAKi). Compared with the rest of the cohort (n = 13), patients with liver disease had significantly more cytopenias (**Table 2**). There was a trend towards more immunodeficiency, more autoimmunity, more ISG induction, and fewer Behcet's-like features.

Conclusion: Hepatitis is highly prevalent in HA20 and has a substantial morbidity and mortality. Occult steatosis and hepatomegaly are common; longitudinal studies are needed to determine the significance of these features. We recommend screening all HA20 patients periodically (hepatic panel, ultrasound) and referring patients with abnormal findings to hepatology. In HA20 patients with liver disease, we recommend AZA as a reasonable first-line treatment. JAK inhibitors may be effective in patients with incomplete responses to AZA.

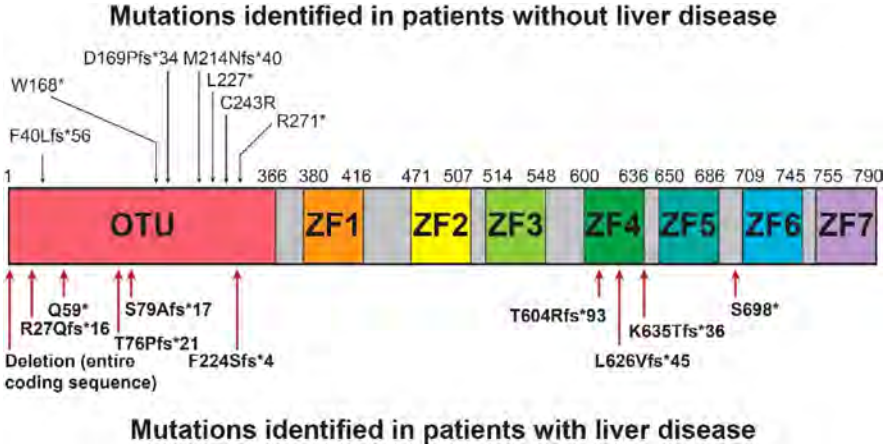

Figure 1. TNFAIP3 mutations in patients with and without liver injury. Liver disease associated mutations involve multiple domains of HA20, including deletion of the entire coding sequence

Table 1. Features of HA20 patients with liver disease. AIH: autoimmune hepatitis, CS: corticosteroids; AZA: azathioprine, ISG: interferon stimulated genes, ITP: Immune thrombocytopenic purpura, JAKi: Janus Kinase Inhibitor, N/A: not applicable, N/C: not checked

Patient	Mutation	Diagnosis	Fibrosis	Associated Features	Current Treatment	Prior Effective Treatments	ISG elevation	Outcome
1	Deletion of entire coding sequence	AIH	Y (cirrhosis)	ITP	AZA, JAKi, CS	AZA, CS	Y	Medical management, stable
2	Deletion of entire coding sequence	AIH	Y (mild)	ITP, oral and nasal ulcers, arthritis	AZA, JAKi, CS	AZA, CS	Y	Medical management, stable
3	Deletion of entire coding sequence	AIH	Y (moderate)	oral ulcers, diabetes, neutropenia, immunodeficiency	None	IVIG, CS	N/C	Medical management, stable
4	Leu626Val fsX45	AIH	Y (moderate)	ITP, autoimmune thyroid disease	AZA, JAKi, CS	JAKi, CS	Y	Medical management, stable
5	Gln59*	AIH	Y (cirrhosis)	ITP, immunodeficiency, arthritis, ocular involvement	N/A	SCIG	N/C	Death
6	Arg27Glufs*16	AIH	Y (cirrhosis)	lipoatrophic panniculitis, diabetes, livedo, oral ulcers, arthritis, fevers, lymphadenopathy	AZA, CS	AZA, CS	N	Medical management, stable
7	Phe224Serfs*4	Steatosis	N	Neuroinflammation, ITP, orogenital ulcers, rash, arthritis, fevers	Colchicine, CS	AZA, anakinra, IVIG, JAKi, CS	Y	Failed escalating medical therapy; underwent HSCT.
8	Phe224Serfs*4	Steatosis	N	Class V lupus nephritis, orogenital ulcers, arthritis, rash, fevers	JAKi	anakinra, JAKi, CS	Y	Medical management, stable
9	Thr604Argfs*93	Hepatomegaly	N	orogenital ulcers, GI ulcers, arthritis	JAKi	JAKi, CS	Y	Medical management, stable
10	Phe224Serfs*4	Hepatomegaly	N	orogenital ulcers, rash, arthritis, immunodeficiency	JAKi	anakinra, JAKi, CS	Y	Medical management, stable
11	Lys635Thrfs*36	Hepatomegaly	N	Lupus nephritis (end-stage renal disease), serositis, cytopenias, vaginal ulcers	MMF, tacrolimus, CS	MMF, tacrolimus, CS	N/C	Medical management, stable
12	Deletion of entire coding sequence	Transaminase elevation	N	orogenital ulcers, arthritis, neuropathy	JAKi	JAKi, CS	Y	Medical Management, stable

AIH: autoimmune hepatitis, CS: corticosteroids; AZA: azathioprine, ISG: interferon stimulated genes, ITP: Immune thrombocytopenic purpura, JAKi: Janus kinase inhibitor, N/A: not applicable, N/C: not checked

Table 2. Clinical and Immunologic phenotypes in HA20 patients with vs. without liver disease. ISG: interferon stimulated genes, GI: gastrointestinal

	% (n)	% (n)	
Symptoms	*Patients with liver disease (n = 12)*	*Patients without liver disease (n = 13)*	*Adjusted p-value (Benjamini-Hochberg)*
Liver Involvement	100% (12)	0% (0)	N/A
Cytopenias	58.33% (7)	0% (0)	0.0256
ISG elevation (n = 9; n = 6)	88.89% (8 of 9)	28.57% (2 of 7)	0.1292
Immunodeficiency	33.33% (4)	7.69 (1)	0.5126
Autoimmune Endocrinopathy	25% (3)	0% (0)	0.4428
Renal Involvement	16.67% (2)	0% (0)	0.5170
Neurologic Involvement	25% (3)	7.69% (1)	0.6434
Fevers	41.67% (5)	76.92% (10)	0.4428
Aphthous Ulcers	66.67% (8)	100% (13)	0.3128
Genital Ulcers	50% (6)	76.92% (10)	0.5170
Lymphadenopathy	25% (3)	23.08% (3)	1
Luminal GI Involvement	33.33% (4)	38.46% (5)	1
Lung/airway involvement	8.33%(1)	7.69%(1)	1
Vascular Involvement	16.67% (2)	7.69% (1)	1
Serositis	25% (3)	15.38% (2)	1
Skin Disease	41.67% (5)	46.15% (6)	1
Eye Disease	16.67% (2)	15.38% (2)	1
Arthritis	66.67% (8)	61.54% (8)	1

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Abstract Number: 0763

Sticking the Landing: A 3-Year Qualitative Longitudinal Study on Navigating Transitions in Pediatric Rheumatology Fellowship

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Professional Education
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Transitions present many challenges for medical trainees, and a lack of preparedness for these transitions is associated with negative outcomes, including higher rates of burnout (Westerman et al., 2013). Fellowship program directors are tasked with guiding trainees as they transition from residency to fellowship and from earlier to later years of fellowship. Yet little is known about what facilitates successful transitions. A longitudinal study is well-poised to explore transitions and to arm program directors with the knowledge to support fellows through these vulnerable periods.

Methods: We conducted a qualitative longitudinal study of 6 pediatric rheumatology fellows, each at a different institution in the United States that varied by size, geography, and hospital setting. Consistent with qualitative longitudinal research methodology (Balmer et al. 2021), we completed in-depth, recursive interviews of the fellows annually during their three years of training. We created inductive codes from patterns in the data and clustered codes into more abstract themes. We organized the findings into an explanatory model analogized to a Rubik's cube, drawing from multiple and multidimensional transitions (MMT) theory (Jindal-Snape & Hannah, 2014), which posits that individuals inhabit multiple, non-static domains (for

Figure 1. The search for a faculty position ("job search") represents the culmination and merging of each theme that influenced the fellows' transitions into and through fellowship.

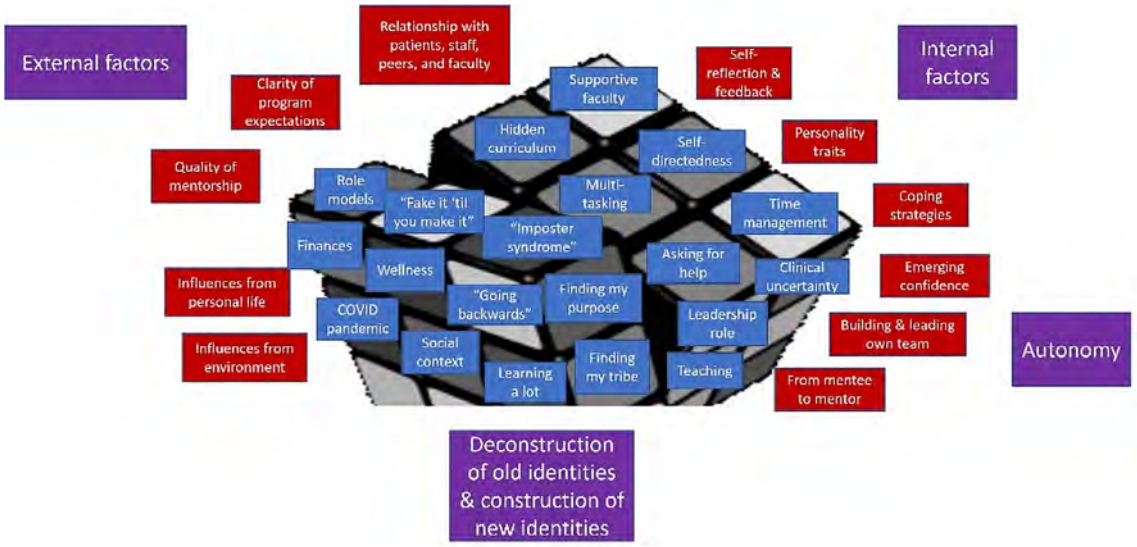

Figure 2. Explanatory model of the factors influencing the successful transitions of pediatric rheumatology fellows, based on multiple and multidimensional transitions (MMT) theory. The blue items are examples of codes; the red items are sub-themes; and the purple items are themes. A transition related to any one domain (code, sub-theme, or theme) prompts additional transitions in other domains.

example, distinct and evolving roles at work and at home) and that a transition in one domain triggers transitions in other domains.

Results: The successful transitions of pediatric rheumatology fellows were facilitated by: (1) deconstructing old identities and constructing new ones, (2) navigating internal and external factors, and (3) acting with increasing autonomy. Fellows who were initially plagued by imposter syndrome later expressed excitement about their integration into the rheumatology community. Internal factors included personality traits; coping strategies; and self-reflection and feedback. External factors included influences from personal life, professional life, and the environment; close relationships (with patients, peers, staff, and superiors), clarity of program expectations, and quality of mentorship all play roles. For fellows, recognizing their emerging confidence, building and leading their own teams, and shifting from mentees to mentors allowed for the development of graded autonomy. Ultimately, the search for a faculty position ("job search") in the final year of fellowship requires the assembling of new identities, navigation of internal and external factors, and autonomous actions (Figure 1).

Conclusion: Our qualitative longitudinal study closes a gap in the literature by elucidating successful transitions for pediatric rheumatology fellows. MMT theory provides a theoretical framework to explain the interplay of the many factors facilitating these transitions (Figure 2). Program directors can guide fellows through transitions and "stick the landing" in the job search by directly managing external factors related to professional life, aiding in the development of autonomy and of skills that mediate the impact of internal factors, and supporting fellows through challenges in their personal lives.

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Abstract Number: 0764

An Atypical ClassRheum: RheumMadness, a Collaborative Rheumatology Competition Building Knowledge and Community

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SESSION INFORMATION
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Background/Purpose: To evaluate the evolving impact of RheumMadness, an online educational tournament of competing rheumatology concepts, over three years by describing changes in participant engagement, learner experience via the Community of Inquiry (CoI) framework, and incorporation of RheumMadness into local programs.

Methods: RheumMadness 2021, 2022, and 2023 presented single-elimination brackets of 16, 16, and 22 concepts, respectively, represented by scouting reports written by volunteer groups. During the 2021 and 2022 seasons the RheumMadness leadership team selected the concepts, whereas in 2023, authors selected the concepts. Participants submitted brackets predicting matchup outcomes, listened to the RheumMadness podcast, and discussed concepts on social media.

Table 1: Direct and self-reported participant characteristics and engagement with each curricular element in RheumMadness. Direct metrics (left columns) are derived from bracket and scouting report submissions, Google Analytics, Buzzsprout.com, and Keyhole as indicated. Self-reported data are derived from a survey distributed via social media, newsletter, and email. * Direct metrics of participant training level and country of residence are not available for 2021. † Data from Google Analytics from the time the reports were posted until tournament completion each year of the tournament. Scouting report views are not available in 2022 as the reports were hosted on an external website. ‡ Data from Buzzsprout.com hosting service from July through April each season. § Data from Keyhole.co, measuring engagement (primarily on Twitter) with the hashtag #RheumMadness from January through April of each tournament year.

	2021		2022		2023	
	Direct	Self-reported	Direct	Self-reported	Direct	Self-reported
Participant characteristics, n (%)						
Total participants	105	58	128	63	142	56
Training level, n (%)						
Attending	*	31 (53%)	46 (36%)	26 (41%)	63 (44%)	28 (50%)
Fellow	*	19 (33%)	36 (28%)	21 (33%)	37 (26%)	19 (34%)
Resident	*	4 (7%)	27 (21%)	10 (16%)	18 (13%)	6 (11%)
Medical student	*	1 (2%)	3 (2%)	3 (5%)	7 (5%)	2 (4%)
Other / not reported	*	1 (2%)	16 (13%)	3 (5%)	17 (12%)	1 (1%)
Country of residence, n (%)						
USA	*	50 (86%)	84 (65%)	58 (92%)	91 (64%)	50 (89%)
Non-U.S.A.	*	8 (14%)	15 (12%)	5 (8%)	20 (14%)	6 (11%)
Not reported	*	-	29 (23%)	-	31 (22%)	-
Engagement characteristics						
Scouting report engagement						
Number of scouting reports	16	-	16	-	22	-
Total contributors, n (%)	52	14 (24%)	70	20 (32%)	123	21 (38%)
Total page views (average per report) †	1,472 (92)	-	†	-	2,853 (130)	-
Number of participants reading at least half of the scouting reports, n (%)	-	36 (62%)	-	40 (63%)	-	42 (75%)
Podcast engagement						
Podcast episodes per season	15	-	9	-	8	-
Total downloads (average per episode) ‡	2,449 (163)	-	2,206 (245)	-	1,838 (230)	-
Participants listening to at half of the podcast episodes, n (%)	-	22 (38%)	-	24 (38%)	-	19 (34%)
Social media engagement§						
Users	137	-	134	-	179	-
Posts	570	-	556	-	959	-
Engagements	2,392	-	1,930	-	3,335	-
Participants reading related social media at least once per week, n (%)	-	42 (72%)	-	45 (71%)	-	37 (66%)
Participants posting related social media at least once per week, n (%)	-	23 (40%)	-	21 (33%)	-	15 (27%)
Newsletter subscribers	-	-	106	38 (60%)	167	35 (63%)

Web-based analytics tracked engagement. A Qualtrics survey was distributed each year to assess self-reported engagement and CoI presences. The 2023 survey asked additional questions about incorporation of RheumMadness content into local programs. Prism v.9.3.1 was used to analyze normalized and non-normalized data with one-way ANOVA and the Kruskal-Wallis test by ranks, respectively.

Results: Participation increased annually from 105 bracket submissions in 2021 to 142 in 2023 (**Table 1**). Similarly, the number of authors contributing to a scouting report grew from 52 in 2021 to 123 in 2023. Scouting report views grew from 92 per report in 2021 to 130 per report in 2023, and over 60% of participants reported reading at least half of the scouting reports all three years. Despite an increase in direct metrics of social media engagement (users, posts, and engagements) from 2021 to 2023, there was a non-significant decrease in self-reported reading (p= 0.7531) or posting (p= 0.2560) related content on social media. Across all three years, over half of respondents agreed or strongly agreed with CoI prompts related to each cognitive, social, and teaching subdomain (**Figure 1**). Within the cognitive presence, there was a significant increase in knowledge integration in 2023 versus prior years (p= 0.04). Other subdomains did not change significantly over time. In 2023, 26/56 (46%) of respondents reported that their local training program incorporated RheumMadness content in some way, primarily by creating a scouting report. Some programs also reviewed RheumMadness content in a didactic session, hosted a journal club, or created quizzes (**Figure 2**). Further curricular integration at the undergraduate and graduate medical education may be warranted, as RheumMadness increased interest in rheumatology for 23/26 (88%) medical student and resident respondents.

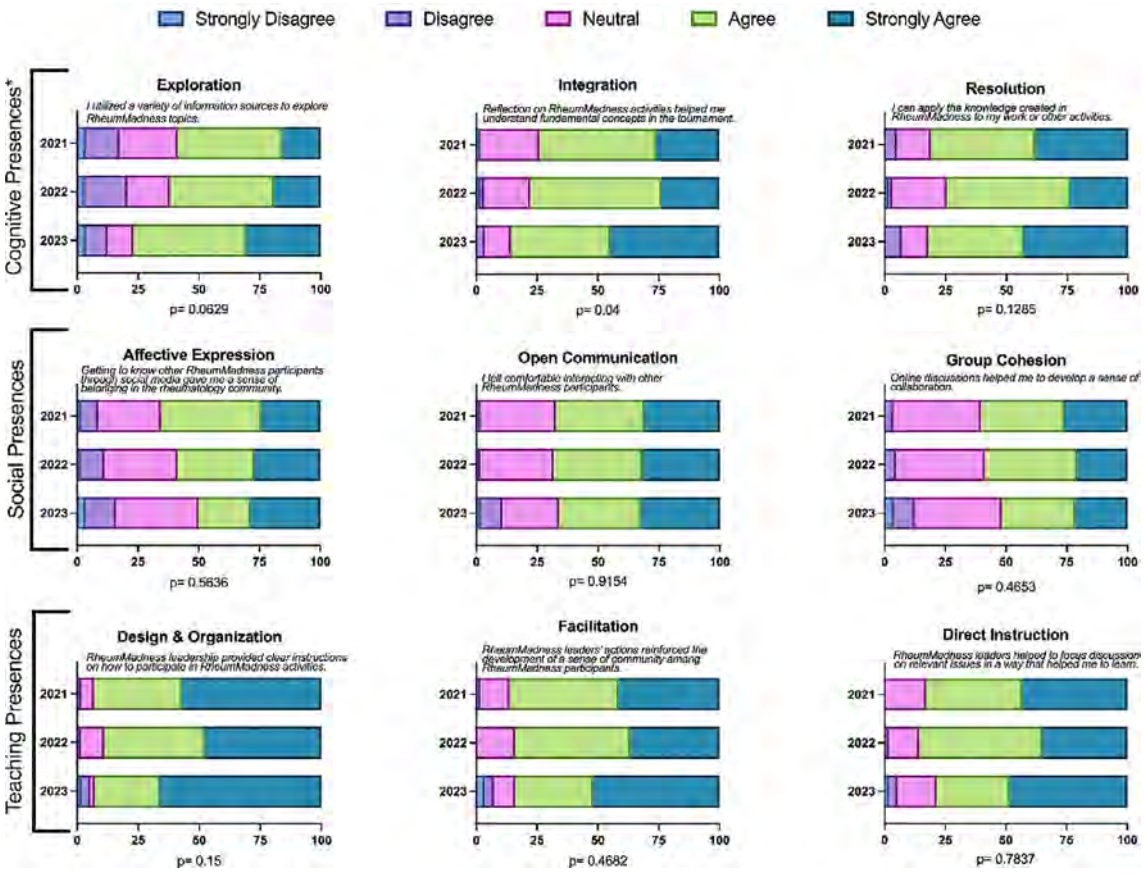

Figure 1: Changes in agreement with Community of Inquiry (CoI) presences across time. Participant responses to four* cognitive, three social, and three teaching presences (written in italics) on a 1-5 point Likert scale during the 2021, 2022, and 2023 seasons. The proportion of respondents selecting a given level of agreement are represented by size of colored bar. Group averages by year were compared using one-way ANOVA or the Kruskal-Wallis test by ranks for normalized or non-normalized data, respectively, with p values represented below corresponding graph. *The triggering presence (I can apply the knowledge created in RheumMadness to my work or other activities) was omitted from representation of cognitive presences due to space; participants demonstrated stable (p= 0.7075) agreement.

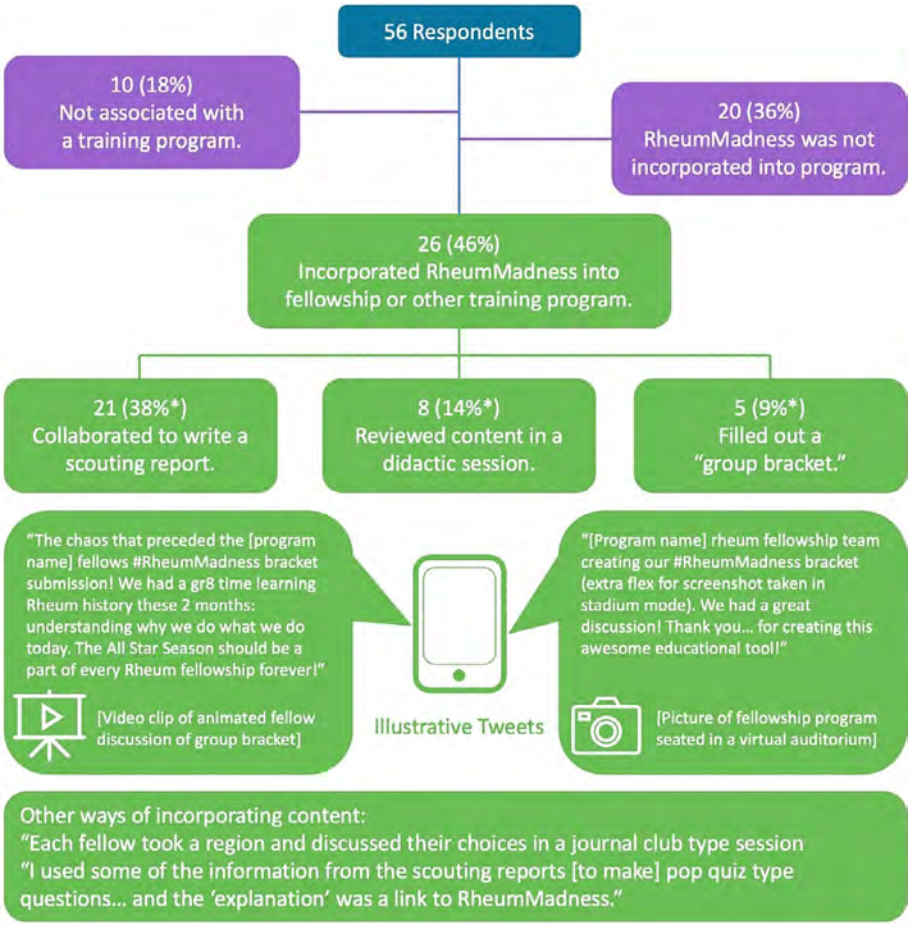

Figure 2. Incorporation of RheumMadness into fellowship or other training program amongst 56 survey respondents in 2023. Respondents could select more than one response option. Illustrative tweets demonstrating incorporation of #RheumMadness were selected by the leadership team. *Percent reflects the proportion of all respondents (n= 56) selecting a response.

Conclusion: Growth in engagement metrics and stable positive self-reported CoI experience suggests that RheumMadness continues to foster an online rheumatology community of learning. Enhanced knowledge integration in 2023 suggests effective improvement efforts, such as team selection by scouting report authors. Incorporation of RheumMadness content into rheumatology training programs and positive impact on early trainees indicates utility as an educational and recruitment tool, with opportunity for expansion as a novel curricular element for graduate and continuing medical education alike.

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Abstract Number: 0765

RheumMadness and TheMednet: The Impact of a Collaboration Between Independent Educational Initiatives

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SESSION INFORMATION
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Session Title: Abstracts: Professional Education
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Background/Purpose: RheumMadness is an online tournament of rheumatology concepts that has been shown to engage learners using the Community of Inquiry (CoI) framework. theMednet is another online educational platform in which physician users submit clinical questions that are answered by experts in the field in an interactive question and answer forum. We sought to evaluate the educational impact of integrating content and engagement between these two independent learning platforms.

Methods: The 2023 RheumMadness tournament consisted of 22 teams of competing concepts that were presented as scouting reports written by trainees and rheumatologists. On the day that scouting reports were published, 7 clinically-focused questions relating to specific RheumMadness teams (6 curated by theMednet team, 1 user-submitted) were posted on theMednet along with expert responses. Leadership teams from both RheumMadness and theMednet publicized updates about each other's initiatives on their respective platforms. At the conclusion of the tournament, all participants, excluding leadership team members, were invited to complete a voluntary survey that assessed engagement in RheumMadness and theMednet as well as educational impact using the CoI framework. Surveys used Likert scores (1=very dissatisfied/strongly disagree, 5=very satisfied/strongly agree). Engagement in RheumMadness content on theMednet was examined and compared to that of its 5 most recent comparable educational programs. Statistical analyses were performed using Chi-square tests and unpaired T tests as appropriate.

Table 1. Questions associated with RheumMadness teams on theMednet. DMARD: disease-modifying antirheumatic drug; ANA: antinuclear antibody; ANCA: antineutrophil cytoplasmic antibody; ULT: urate-lowering therapy; SLE: systemic lupus erythematosus; HCQ: hydroxychloroquine; RA: rheumatoid arthritis; HAQ: Health Assessment Questionnaire; CPPD: calcium pyrophosphate deposition disease; NSAIDs: nonsteroidal anti-inflammatory drugs; MSU: monosodium urate.

theMednet Question	Associated RheumMadness Team	Views	Poll Voters
Do you use conventional DMARDs aside from methotrexate to prevent anti-drug antibody development for patients on infliximab?	Etanercept + MTX	521	77
How do you approach follow up in pts with isolated +ANA, but no current clinical signs or sx of SLE?	Abs before SLE	624	N/A
Is there a role for monitoring serum ANCAs to assess ANCA associated vasculitis disease activity?	Pathogenic ANCA	469	80
Are there patients in whom you would avoid initiating of ULT during acute gout flare?	ULT During Flare	278	N/A
Do you ever consider discontinuing hydroxychloroquine SLE patients in longstanding remission except in cases of overt toxicity?	HCQ Withdrawal	627	64
What target do you utilize in clinical practice for defining disease remission in RA?	HAQ	244	73
Do you use IL-1 inhibitors to prevent flares of gout or CPPD in patients who experience flares despite prophylaxis with colchicine, NSAIDs, and/or low-dose prednisone?	MSU & NLRP3	451	53

Results: RheumMadness-related questions posted on theMednet and associated engagement are shown in **Table 1**; views per question ranged from 244 to 627, and number of poll voters per question from 53 to 80. When compared with the 5 most recent comparable educational programs on theMednet (**Table 2**), RheumMadness questions reached more users and institutions, and RheumMadness questions had significantly more views than questions from other educational programs (mean 459 vs. 249 views/question, respectively). Among RheumMadness participants, demographics and engagement with other RheumMadness curricular elements were similar between participants who engaged with theMednet content (n=24) and non-engagers (n=34), but CoI engagement was significantly higher in the overall cognitive presence and 3 of its components as well as the overall social presence among theMednet engagers (**Table 3**). Participants who engaged with theMednet Q&A reported that it contributed positively to the educational experience of RheumMadness (mean Likert score 4.25).

Conclusion: Establishing a collaboration between RheumMadness and theMednet strengthened learning in both programs. In addition to an effect of the collaboration, engagement with RheumMadness-related questions compared with previous educational programs on theMednet may have also been enhanced by the growing overall number of users over time and more varied nature of the topics presented in RheumMadness compared with previous programs. Collaborations

Table 2. Engagement with RheumMadness questions compared with the five other most recent educational programs on theMednet. *Values for five educational programs combined and reported as mean (SD) unless noted otherwise. Other educational programs were journal clubs consisting of questions relating to recent landmark publications with answers from manuscript authors and other experts.

	RheumMadness	Other Education Programs*	P value
Number of questions	7	3.8 (0.84)	N/A
Total views in program	3214	948 (508)	N/A
Users reached	600	278 (103)	N/A
Institutions reached	141	123 (29)	N/A
Views per question, mean (SD)	459 (151)	249 (92)	**0.0002**

Table 3. Educational impact of RheumMadness in theMednet engagers and non-engagers. All values reported as mean (SD) Likert scores (1=very dissatisfied/strongly disagree, 5=very satisfied/strongly agree) unless noted otherwise.

Characteristic	theMednet Engagers	theMednet Non-Engagers	P value
N	24	34	N/A
Demographics, n (%)			
Attending	10 (42)	20 (59)	0.37
Fellow	10 (42)	10 (29)	0.43
Resident/medical student	4 (17)	3 (9)	0.40
Other	0 (0)	1 (3)	0.40
Engagement, n (%)			
Read at least half of scouting reports	18 (75)	24 (71)	0.85
Listened to at least half of podcast episodes	7 (29)	12 (35)	0.69
Read social media posts at least weekly	18 (75)	24 (71)	0.85
Posted on social media at least weekly	8 (33)	6 (18)	0.23
Overall satisfaction	4.67 (0.56)	4.39 (0.75)	0.139
Community of Inquiry (CoI)			
Triggering	4.71 (0.46)	4.36 (0.78)	0.060
Exploration	4.29 (0.91)	3.58 (1.03)	**0.009**
Integration	4.54 (0.51)	4.00 (0.91)	**0.011**
Resolution	4.50 (0.51)	3.88 (1.02)	**0.008**
Overall cognitive presence	4.51 (0.63)	3.95 (0.97)	**<0.001**
Affective expression	3.79 (0.88)	3.36 (1.25)	0.156
Open communication	3.92 (0.83)	3.73 (1.15)	0.496
Group cohesion	3.83 (0.87)	3.30 (1.07)	0.052
Overall social presence	3.85 (0.85)	3.46 (1.16)	**0.019**
Design/organization	4.58 (0.72)	4.42 (0.97)	0.500
Facilitation	4.42 (0.58)	4.09 (1.23)	0.236
Direct instruction	4.38 (0.77)	4.03 (1.07)	0.186
Overall teaching presence	4.46 (0.69)	4.18 (1.10)	0.062
theMednet contributed positively to educational experience of RheumMadness	4.25 (0.85)	N/A	N/A

between educational programs should be encouraged, as this may allow programs to reach broader audiences and accomplish more effective learning.

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Abstract Number: 0766

The OMERACT GCA Phantom Project: Validation of 3D Printed Ultrasound Training Models for Giant Cell Arteritis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Professional Education

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Ultrasonography has been validated as a diagnostic tool for giant cell arteritis (GCA). There is a need to develop training resources, because the glucocorticoid responsiveness of abnormalities of affected vessels and the uun-predictability and relative scarcity of presentation makes it challenging to predictably use real patients for educational

purposes. To address this, we have developed cost-effective ultrasound phantoms using high-resolution 3D printing techniques [1]. The aim of this study is to validate these models within the subgroup on large vessel vasculitis of the Outcome Measures in Rheumatology (OMERACT) ultrasound working group.

Methods: Normal and pathological phantoms of the axillary (AA) and temporal artery (TA) were developed and printed using a Formlabs SLA 3D printer. The phantoms were then embedded in a special gelatine as eight sets of three (AA) or two (TA). Participants from twelve European countries were provided with eight sets of both AA and TA phantoms. The phantoms were evaluated individually in a blinded fashion using a predefined protocol and the OMERACT definitions of abnormalities in GCA [2], [3]. The artificial intima-media thickness (IMT) of each vessel phantom was measured at most prominent site in mm, preferably on the distal wall [4]. The phantoms were classified by each investigators normal (AA&TA), acute (AA&TA), chronic (AA only), or none of the above (AA&TA). Descriptive parameters and interrater-reliability were calculated. Furthermore, we conducted a one-way analysis of variance.

Results: The phantoms were correctly classified in 87% of cases resulting in a Fleiss' kappa of 0.80 (95%CI 0.78-0.82). The published cut-off values for normal and pathological IMT were met, with the exception of the parietal branch of the TA [5]. Excellent agreement among participants was demonstrated for IMT measurements, with an intraclass correlation coefficient (ICC 1.1) of 0.98 (95% CI 0.98-0.99). The results of IMT measurements are shown in Table 1. A one-way analysis of variance (ANOVA) revealed a significant difference in average IMT between pathological and healthy phantoms for both AA and TA. Detailed results of the ANOVA, divided by the different arteries, are presented in Table 2.

Table 1 – Results of the IMT measurements and Interrater-reliability Notice, that there are no chronic phantoms of temporal arteries (SD: standard deviation; ICC: intra-class correlation coefficient; CI: confidence interval)

Vessel	Measurements	Mean (SD) Normal	Mean (SD) Acute	Mean (SD) Chronic	ICC 1.1 (95%CI)	Fleiss Kappa (95%CI)
Common superficial temporal arteries	416	0,35 (0,10)	0,72 (0,14)	-	0,99 (0,98-0,99)	0,70 (0,68-0,73)
Frontal rami	416	0,32 (0,09)	0,63 (0,11)	-	0,99 (0,98-0,99)	0,82 (0,79-0,85)
Parietal rami	416	0,35 (0,10)	0,66 (0,08)	-	0,98 (0,97-0,99)	0,85 (0,82-0,87)
Axillary arteries	558	0,66 (0,14)	1,26 (0,19)	1,19 (0,27)	0,96 (0,93-0,98)	0,75 (0,73-0,77)

Table 2 – Results of the analysis of variance The table shows the results of the analysis of variance along with their significance (p-value) and their effect size (η2) (p-value: probability value; η2: partial eta square; df: degrees of freedom; CI: confidence interval)

Vessel	F-value	df1, df2	p-value	η^2 (95%CI)
Common superficial temporal arteries	501,812	2; 413	<0,001	0,71 (0,67-0,74)
Frontal rami	526,936	2, 413	<0,001	0,71 (0,66-0,74)
Parietal rami	599,231	2, 413	<0,001	0,78 (0,74-0,81)
Axillary arteries	37,499	3, 518	<0,001	0,62 (0,57-0,66)

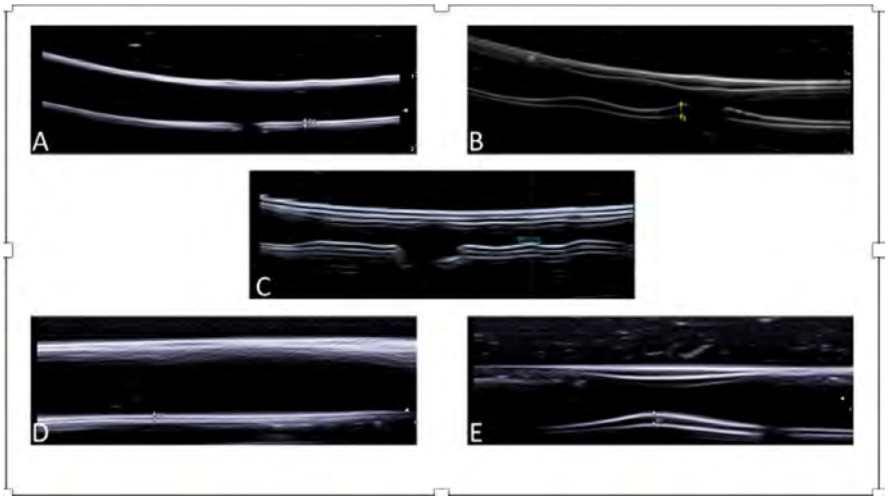

Figure 1 – Ultrasound of the phantoms A=Normal axillary artery; B=Axillary artery with acute GCA pathology; C=Axillary artery with GCA chronic pathology; D=Normal temporal artery; E=Temporal artery with acute GCA pathology

Conclusion: Our novel ultrasound models accurately represent the normal state and pathology of GCA adhering to the OMERACT definitions and cut-off values for IMT. There was a high agreement among investigators to correctly classify the models and good reliability with measurement of artificial IMT. This is also a first step in the evaluation of the phantom for educational purposes.

Disclosure: V. Schäfer: None; **T. Schremmer**: None; **F. Recker**: None; **W. Hartung**: None; **C. Duftner**: None; **S. Monti**: CSL Vifor, 6; **A. Hocevar**: None; **R. Karalilova**: None; **A. Iagnocco**: None; **P. MACCHIONI**: None; **G. Germano**: None; **M. Naredo Sanchez**: None; **E. De Miguel**: None; **L. Seitz**: None; **T. Daikeler**: None; **M. Aschwanden**: None; **D. Boumans**: None; **C. Mukhtyar**: None; **s. kate**: None; **R. Wakefield**: None; **A. Diamantopoulos**: None; **S. Chrysidis**: None; **B. Nielsen**: None; **K. Keller**: None; **U. Dohn**: None; **L. Terslev**: Eli Lilly, 1, Janssen, 1, 6, Novartis, 6, UCB, 1; **M. Milchert**: None; **A. Juche**: None; **W. Schmidt**: AbbVie/Abbott, 1, 5, 6, Amgen, 1, 6, Bristol-Myers Squibb(BMS), 6, Chugai, 6, GlaxoSmithKlein(GSK), 1, 5, 6, Janssen, 6, Medac, 6, Novartis, 1, 5, 6, Roche, 6, UCB, 6; **G. Bruyn**: None; **C. Dejaco**: AbbVie/Abbott, 2, 5, 6, Amgen, 6, Eli Lilly, 2, 6, Galapagos Pharma, 2, 6, Janssen, 1, Novartis, 2, 5, 6, Pfizer, 6, Sparrow, 2.

Abstract Number: 0767

Current Musculoskeletal Ultrasound Practices of 12 Years of past Participants of a 10-Months Rheumatology Ultrasound Training Program (Ultrasound School of North American Rheumatologists)

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Professional Education

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Musculoskeletal ultrasound (MSKUS) is an integral part of rheumatology training. The Ultrasound School of North American Rheumatologists (USSONAR) has been a leader in rheumatology MSKUS training for fellows (Fundamentals in Musculoskeletal Ultrasound (FMU) track) and practitioners (Train the Trainer (TTT) track). Limited data exits regarding the practices of rheumatology US professionals trained through USSONAR. The survey aimed to determine the current use of MSKUS for diagnostic and/or procedural MSKUS among past participants of USSONAR's training program and explore barriers to successful implementation.

Methods: A 28 question survey was sent in September 2022 to 482 participants of the USSONAR FMU/TTT courses who completed a final examination (2009-2020). Each respondent was given a unique identifier matched to their exam scores and total number of practice studies submitted in their training year.

Results: After removing 108 non-deliverable emails, the survey received a response rate of 105/374 (28%). Participant track influenced survey participation, 31.5% in the TTT versus 19.5% in the FMU, (p=0.006). Analyses using background variables such as FMU vs. TTT status, year of graduation, number of studies submitted or exam scores did not show evidence of nonresponse bias.

The median years practicing MSKUS was 6, with 70.9% practicing in academic medical centers. 71% of the respondents held a MSKUS certification. 81.9% and 19.8% were adult and pediatric rheumatologists respectively. 86.7% performed and/or interpreted diagnositc MSKUS themselves and 81% performed their own procedures (Figure1). 58.8% billed for at least 50% of diagnostic studies and 78.8% of procedural studies.

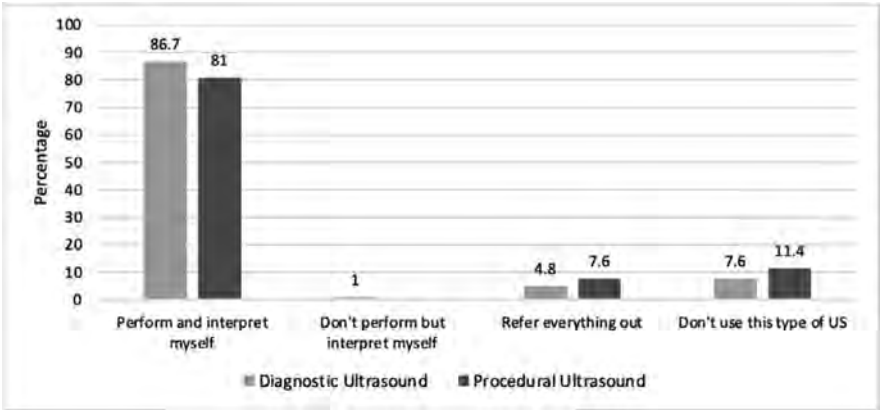

Figure 1: Performing Diagnostic or Procedural Ultrasound (n=105)

Table 1: Reasons for Not Billing or Billing Less than 50% of the Time for Diagnostic or Procedural Ultrasound (multiple selections possible)

Reasons	Diagnostic Ultrasound (n=37)	Procedural Ultrasound (n=18)
	% (n)	
Lack of time to document my study	43.2 (16)	44.4 (8)
Lack of certification	24.3 (9)	22.2 (4)
Poor reimbursement for the amount of effort	35.1 (13)	38.9 (7)
Concern over legal liability	32.4 (12)	22.2 (4)
Other	32.4 (12)	22.2 (4)

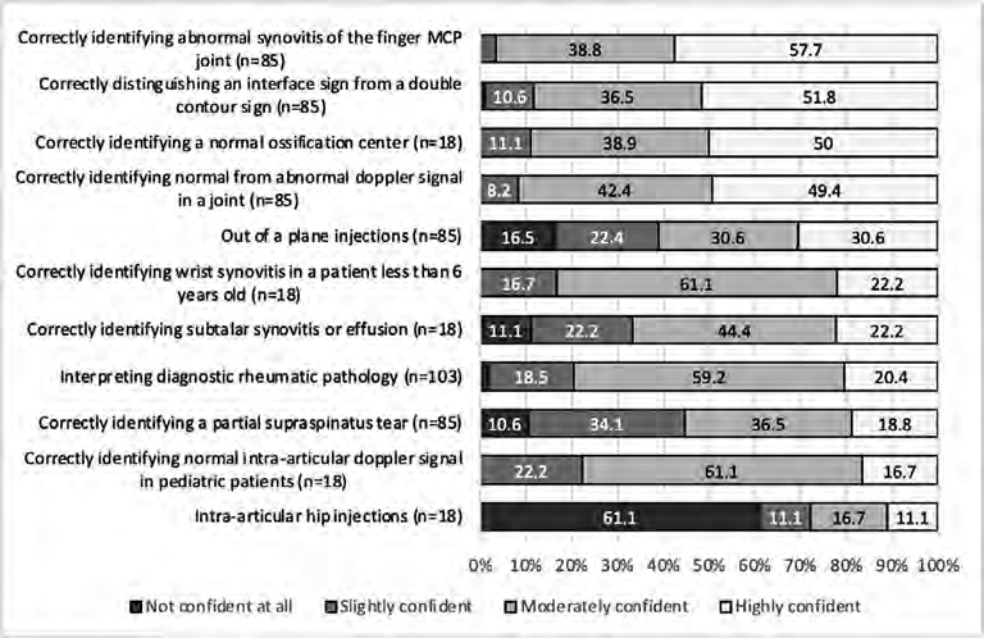

Figure 2: Confidence of adult providers and pediatric providers overall and in scenarios 2 years after participation in the USSONAR FMU/TTT Course

The leading reason for not personally doing diagnostic US was lack of administrative support.

The leading reason for not personally doing procedural MSKUS was lack of time (Table 1).

When asked to rate their confidence in a set of MSKUS skills 2 years after their USSONAR course, the majority of adult rheumatologists felt moderately to highly confident in their skills, similarly the vast majority of pediatric rheumatologists felt moderately confident in a set of pediatric MSKUS skills (Figure 2). Adult clinicians were least confident about performing out of plane injection and identifying partial supraspinatus tendon tears, while pediatric clinicians were least confident performing intra-articular hip injection.

Conclusion: USSONAR training provided the majority of FMU and TTT participants the knowledge and skills to use and bill for MSKUS in practice. Participants had confidence in performing diagnostic and procedural studies and also passed a certification exam in MSKUS. Most participants agreed that USSONAR training made them a better rheumatologist.

Disclosure: M. Nishio: None; **F. Aslam**: None; **S. Ziniel**: None; **E. Kissin**: None.

Abstract Number: 0768

Using Participatory Design-Thinking Process to Create a More Applicant-Centered Rheumatology Fellowship Interview Experience

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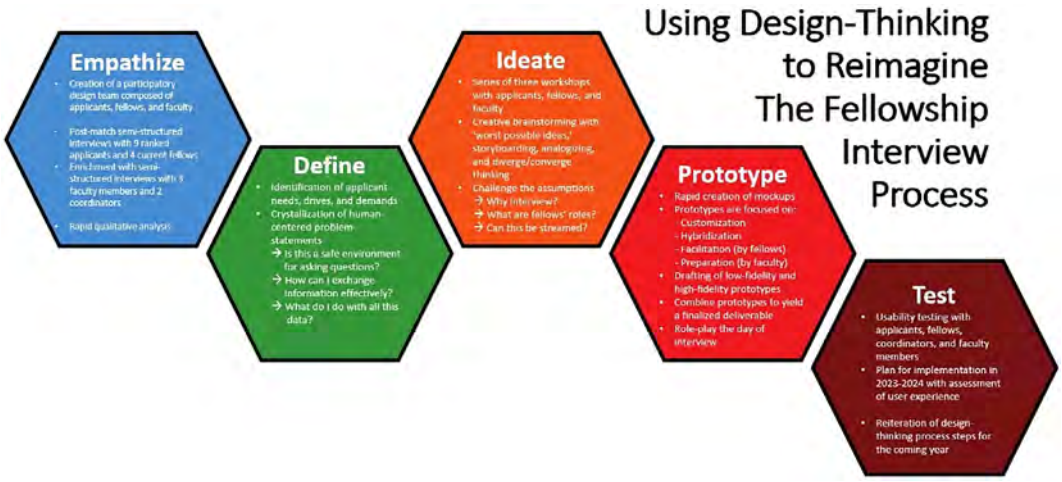
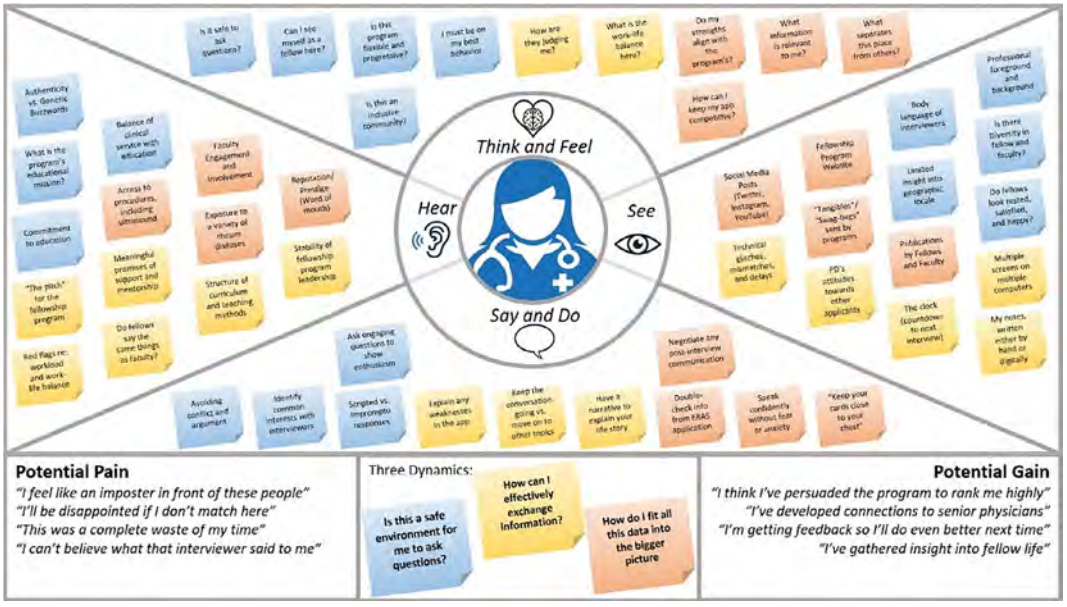
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Professional Education
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

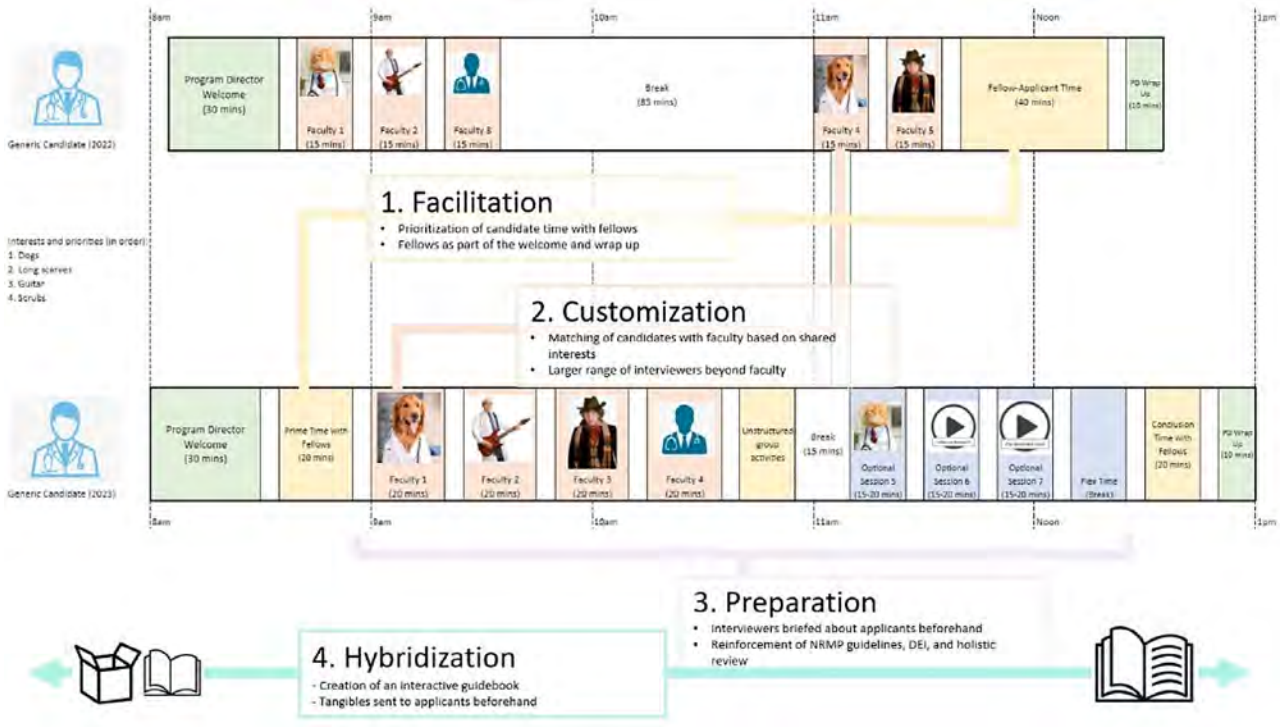
Background/Purpose: Design-thinking is a creative problem-solving process used to better understand users' needs and experiences so that a product or service can be improved. Its emphasis on empathy, iterative prototyping, and participatory collaboration make it an ideal methodology for innovation in medical education. We apply this framework to refine the virtual rheumatology fellowship interview process, a relatively new and ad hoc development emerging as a necessity during the COVID pandemic, so that virtual interviews can become more applicant-centered.



Design-Thinking Principles were employed in an iterative fashion through the five steps in order to create a final set of prototypes for testing



Interviews with 9 fellowship candidates revealed a variety of perceptions and observations that were organized into this empathy map. Three major themes predominated: (1) Is this a safe environment for me to ask questions? (2) How can I effectively exchange information? and (3) How do I fit all this data into the bigger picture?



As a result of the design-thinking process, four prototypes were conceived emphasizing (1) Facilitation, (2) Customization, (3) Preparation, and (4) Hybridization.

Methods: This educational quality improvement project uses a design-thinking framework to identify opportunities and challenges for rheumatology fellowship applicants. The investigators use the 5-step process (Empathize, Define, Ideate, Prototype, Test) and incorporate rapid qualitative analysis of semi-structured interviews to innovate the interview experience. The iterative and collaborative nature of this process has empowered participants to co-design an applicant-centered interview experience.

Results: Interviews with fellowship applicants (n=9), fellow physicians (n=4), and faculty members (n=3) identified three major dynamics of the interview process: (1) Is it a safe environment to ask questions? (2) how do I exchange information effectively? and (3) how do I fit all this data into the bigger picture? Creative brainstorming techniques at a series of 3 workshops yielded 4 prototypes emphasizing customization, hybridization, facilitation, and preparation. A finalized applicant-centered interview template was devised in preparation for the 2023-2024 application season.

Conclusion: Design-thinking has yielded insights into three important dynamics that drive applicant experiences. These insights allow for a redesign of processes so that virtual interviews can be more applicant-centered. This framework allows for further iterations and modifications as the needs of applicants and programs evolve over time.

Disclosure: A. Feng: None; **A. Iftekhar**: None; **R. Ni**: None; **G. Gheriani**: None; **B. Kumar**: None.

Abstract Number: 0769

Development and Validation of a Combined Clinical and Genetic Risk Score for Interstitial Lung Disease in a Large, Multicenter, Prospective Rheumatoid Arthritis Cohort

Austin Wheeler[1], Joshua Baker[2], Yangyuna Yang[1], Punyasha Roul[1], K Wysham[3], Grant Cannon[4], Gary Kunkel[5], Gail Kerr[6], Dana Ascherman[7], Paul Monach[8], Andreas Reimold[9], Jill Poole[1], Tony Merriman[10], Ted R Mikuls[11] and Bryant England[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Pennsylvania, Philadelphia, PA, [3]VA Puget Sound/University of Washington, Seattle, WA, [4]University of Utah and Salt Lake City VA, Salt Lake City, UT, [5]University of Utah, Salt Lake City, UT, [6]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [7]University of Pittsburgh, Pittsburgh, PA, [8]VA Boston Healthcare System, Boston, MA, [9]University of Texas Southwestern Medical Center, Dallas, TX, [10]University of Alabama at Birmingham, Birmingham, AL, [11]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes I: RA-ILD

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Rheumatoid arthritis-associated interstitial lung disease (RA-ILD) is an extra-articular manifestation of RA that causes substantial morbidity and mortality. Although some clinical and genetic risk factors (predominantly *MUC5B* rs35705950) have been identified, there are no routinely used tools for risk stratification. We sought to develop a risk model for ILD in a large, multicenter RA cohort.

Methods: Participants were enrollees in the Veterans Affairs Rheumatoid Arthritis (VARA) registry, a multicenter prospective cohort of U.S. Veterans with RA. Participants were genotyped for single nucleotide polymorphisms (SNPs) associated with idiopathic pulmonary fibrosis, including *MUC5B* rs35705950 and 11 other SNPs. ILD was validated through systematic medical record review of provider diagnosis, imaging, and biopsy findings. A meta-analytic odds ratio for ILD was calculated for each SNP by pooling results from VARA (N=2386; N=224 ILD) and Juge et al. (N=514; N=272 ILD) (**Table 1**). A genetic risk score (GRS) was computed from variant alleles weighted by their effect size with ILD, using backwards predictor selection. The GRS was combined with established clinical risk factors (age, sex, smoking history, DAS28-CRP, and RF positivity)

Table 1. Genotype frequencies for each allele and pooled odds ratio (OR) for associations with interstitial lung disease (ILD).

	ILD (%)	no-ILD (%)	VARA OR (95% CI) N=2386	Juge et al. OR (95% CI) N=514	Pooled OR (95% CI)
***MUC5B* rs35705950 (G>T)**					
GG	151 (7.8)	1782 (92.2)			
GT, TT	73 (16.1)	413 (83.9)	2.27 (1.68, 3.06)	3.63 (2.54, 5.31)	2·37 (1·72, 3·03)
***LRRC34* rs6793295 (T>C)**					
TT	94 (7.9)	1096 (92.1)			
TC, CC	130 (10.9)	1066 (89.1)	1.42 (1.08, 1.88)	0.89 (0.68, 1.15)	1·40 (1·01, 1·79)
***OBFC1* rs11191865 (A>G)**					
AA	57 (8.2)	635 (91.8)			
AG, GG	167 (9.9)	1527 (90.1)	1.22 (0.89, 1.67)	0.81 (0.62, 1.05)	1·21 (0·83, 1·59)
***DSP* rs2076295 (T>G)**					
TT	42 (6.4)	617 (93.6)			
GT, GG	182 (10.5)	1545 (89.5)	1.73 (1.22, 2.45)	1.01 (0.80, 1.28)	1·68 (1·10, 2·26)
***FAM13A* rs2609255 (G>T)**					
TT	18 (14.4)	107 (85.6)			
GT, GG	206 (9.1)	2055 (90.9)	0.60 (0.35, 1.00)	0.89 (0.67, 1.16)	0·61 (0·30, 0·91)

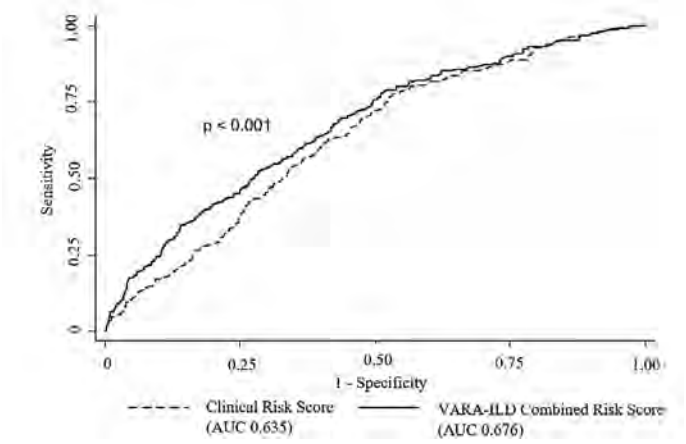
Abbreviations: ILD (interstitial lung disease), no-ILD (no interstitial lung disease), VARA (Veterans Affairs Rheumatoid Arthritis registry), OR (odds ratio) Pooled OR obtained by meta-analysis of OR from VARA and Juge et al. 2018, calculated via fixed-effects model.

Table 2. VARA-ILD Combined Risk Score Model.

Variable	Odds Ratio (95% CI)	P Value	Beta Coefficient
VARA-ILD GRS	2.64 (1.92, 3.62)	<0.001	0.9706451
Age, per 1-yr increase over age 69.5 years	1.03 (1.01, 1.04)	0.001	0.0253936
Male sex	1.37 (0.75, 2.50)	0.31	0.3115712
Smoking history (ever)	1.50 (1.00, 2.23)	0.05	0.4026723
DAS28-CRP (mean)	1.27 (1.12, 1.44)	<0.001	0.2362551
RF positive (≥15 IU/mL)	1.84 (1.23, 2.75)	0.003	0.6091225
Model constant			-4.240544

Abbreviations: interstitial lung disease (ILD), RA (rheumatoid arthritis), CI (confidence interval), DAS-28-CRP (disease activity score with 28 joints and c-reactive protein), RF (rheumatoid factor), single nucleotide polymorphism (SNP)

Figure 1. Comparison of ROC curves for clinical risk factors and VARA-ILD Combined Risk Score model for presence of RA-ILD.



Abbreviations: ROC (receiver operating characteristic), ILD (interstitial lung disease), AUC (area under the curve), P value calculated via nested likelihood ratio test.

using logistic regression to generate the VARA-ILD Combined Risk Score. Internal validation and calibration were completed using bootstrapping techniques to address over-fitting and determine a shrinkage-corrected performance. Model performance was assessed using the area under the receiver operating curve (AUC), and models were compared via nested likelihood ratio tests as well as Akaike and Bayesian information criterion (AIC, BIC).

Results: Of 2,386 participants (89% male, mean age 69.5 years), 9.4% had ILD. VARA-ILD Combined Risk Score containing the GRS (based on 5 SNPs) and clinical factors (**Table 2**) outperformed clinical risk factors alone in discriminating ILD (AUC 0.686 vs. 0.635, p< 0.001; **Figure 1**). Following internal validation and bootstrapping, the shrinkage-corrected performance for combined and clinical-only models was 0.675 (95% CI 0.635, 0.709) and 0.623 (95% CI 0.584, 0.651). VARA-ILD Combined Risk Score also outperformed a model including clinical factors and the *MUC5B* rs35705950 promoter variant alone (AUC 0.648 [95% CI 0.612, 0.681]) based on AIC (1408 vs. 1429) and BIC (1448 vs. 1469). Demonstrating its potential role in ILD screening, utilizing a risk score cut-point of 0.05 (sensitivity 90%) would eliminate 25% (N=582) of participants from undergoing low-yield ILD diagnostic testing.

Conclusion: The VARA-ILD Combined Risk Score, including multiple genetic risk variants, discriminated ILD in a large, multicenter RA cohort better than established clinical risk factors alone. These results demonstrate the potential utility of genetic risk scores in RA-ILD identification and will support further investigation into individualized risk stratification and screening.

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Abstract Number: 0770

Plasma Matrix Metalloproteinases in Rheumatoid Arthritis-Interstitial Lung Disease: Associations with Disease Presence, Severity, and Subtypes

Brent Luedders[1], Austin Wheeler[1], Dana Ascherman[2], Joshua Baker[3], Michael Duryee[1], Yangyuna Yang[1], Punyasha Roul[1], K Wysham[4], Paul Monach[5], Andreas Reimold[6], Gail Kerr[7], Gary Kunkel[8], Grant Cannon[9], Jill Poole[1], Geoffrey Thiele[1], Ted R Mikuls[10] and Bryant England[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Pittsburgh, Pittsburgh, PA, [3]University of Pennsylvania, Philadelphia, PA, [4]VA Puget Sound/University of Washington, Seattle, WA, [5]VA Boston Healthcare System, Boston, MA, [6]University of Texas Southwestern Medical Center, Dallas, TX, [7]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [8]University of Utah, Salt Lake City, UT, [9]University of Utah and Salt Lake City VA, Salt Lake City, UT, [10]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

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Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Matrix metalloproteinases (MMPs) are enzymes involved in extracellular matrix remodeling that have been implicated in the pathogenesis and progression of rheumatoid arthritis (RA) and interstitial lung diseases (ILD). We aimed to assess the associations of plasma MMPs with the presence and severity of RA-ILD, as well as RA-ILD sub-groups defined by imaging and genetic risk.

Methods: We performed a cross-sectional study of participants with/without ILD in the Veterans Affairs Rheumatoid Arthritis registry, a multicenter prospective cohort of U.S. Veterans with RA. Participants who developed ILD after registry enrollment were excluded. Prevalent ILD diagnoses were systematically validated through medical record review of clinical diagnoses, imaging findings, and biopsy reports. Imaging pattern was classified as usual interstitial pneumonia (UIP) when documented in the clinical read or if honeycombing was present vs. non-UIP for all others. Plasma MMP-1, -3, -7, and -9 concentrations (MesoScale Discovery platform) and the *MUC5B* rs35705950 promoter variant (Illumina Infinium Global Screening Array) were measured on plasma and DNA samples, respectively, collected at enrollment. MMP values were log-transformed, standardized, and categorized into quartiles. The most proximate forced vital capacity (FVC) result within three years of registry enrollment was collected from the electronic health record. Associations of MMPs with prevalent RA-ILD were assessed with logistic regression models adjusted for age, sex, race, smoking status, anti-CCP positivity, and RA disease activity. Associations of MMP values with FVC were assessed with Pearson's correlation coefficient. MMP values were compared across *MUC5B* genotypes (positive vs. negative) and ILD patterns using Kruskal-Wallis tests. In sensitivity analyses, we included RA-ILD cases developing within one year after enrollment given disease latency.

Results: Among 2,189 participants (89% male, mean age 64 years), RA-ILD was present in 93 at the time of registry enrollment (point prevalence 4.2%). Higher plasma concentrations of MMP-7 (OR 1.64 [95% CI 1.31, 2.05] per standardized unit) and MMP-9 (OR 1.27 [1.01, 1.59]) were significantly associated with prevalent RA-ILD, but MMP-1 and -3 were not. Participants with the highest quartile of MMP-7 had over 3 times the odds of prevalent RA-ILD (OR 3.63 [1.80, 7.34], **Figure 1**) compared to the lowest quartile. The highest quartile of MMP-9 was also associated with >2-fold higher odds of RA-ILD.

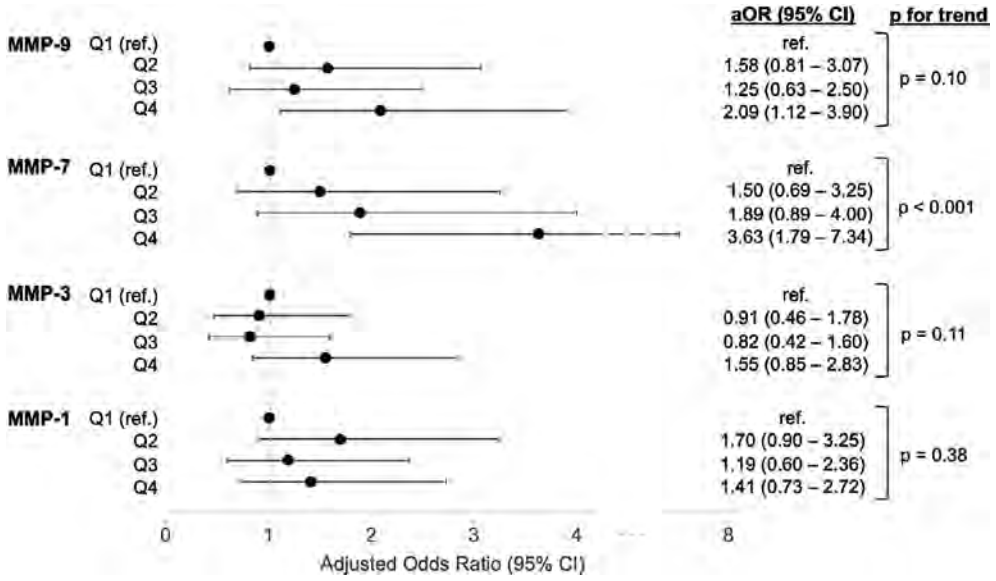

Figure 1. Forest plot illustrating the associations of plasma MMP concentrations in quartiles with prevalent ILD in patients with RA. Odds ratio adjusted for age, sex, race, smoking status, anti-citrullinated peptide antibody status, and rheumatoid arthritis disease activity in logistic regression model. Quartile 1 (referent) was the lowest values. Abbreviations: MMP = matrix metalloproteinase, ILD = interstitial lung disease, RA = rheumatoid arthritis, aOR = adjusted odds ratio, ref. = referent.

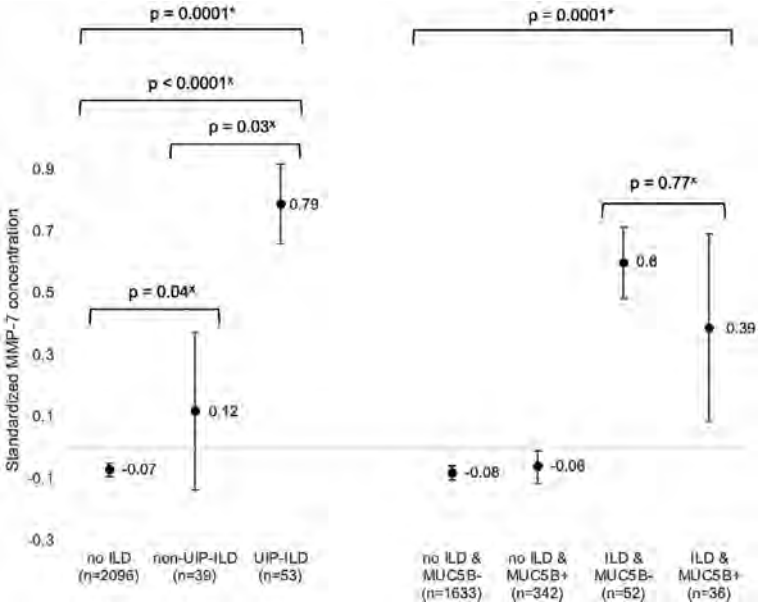

Figure 2. Mean plasma MMP-7 concentrations (per 1 SD) by ILD pattern and MUC5B rs35705950 promoter variant. Standardized values of log-transformed MMP-7 concentrations were calculated by subtracting the sample mean value and dividing by the standard deviation. Error bars indicate standard error of the mean. *across entire sample by Kruskal-Wallis test x pairwise comparison by post hoc Dunn test Abbreviations: MMP = matrix metalloproteinase, ILD = interstitial lung disease, UIP = usual interstitial pneumonia

MMP-9 concentrations, but not other MMPs, were weakly negatively correlated with FVC (r = -0.28, p = 0.015) among those with ILD. MMP-7 was higher among participants with a UIP vs. non-UIP pattern (**Figure 2**). MMP concentrations did not differ by the presence of the *MUC5B* promoter variant (MMP-7 shown in **Figure 2**). Similar results were observed in sensitivity analyses (data not shown).

Conclusion: Plasma concentrations of MMP-7/9 were strongly associated with prevalent RA-ILD, which was largely driven by patients with a UIP pattern of ILD. MMP-9, but not MMP-7, was weakly correlated with RA-ILD severity by FVC. These findings add to a growing body of literature suggesting MMPs may have a potential pathogenic role in RA-ILD.

Disclosure: B. Luedders: None; **A. Wheeler**: None; **D. Ascherman**: None; **J. Baker**: CorEvitas, 2, Cumberland Pharma, 2, Horizon Pharmaceuticals, 5; **M. Duryee**: None; **Y. Yang**: None; **P. Roul**: None; **K. Wysham**: None; **P. Monach**: Genentech, 12, Lecture with honorarium, HI-Bio, 2; **A. Reimold**: None; **G. Kerr**: AstraZeneca, 2, Aurinia, 6, Horizon, 2, Janssen, 2, Pfizer, 1, Sanofi, 2; **G. Kunkel**: None; **G. Cannon**: None; **J. Poole**: AstraZeneca, 12, I have received no monies. I received anti-IL-33 monoclonal antibody from AstraZeneca for animal research sutdies.; **G. Thiele**: None; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **B. England**: Boehringer-Ingelheim, 2, 5.

Abstract Number: 0771

A Modified Idiopathic Pulmonary Fibrosis-Derived Composite Biomarker Score Is Associated with Interstitial Lung Disease Among U.S. Veterans with Rheumatoid Arthritis

Brent Luedders[1], Dana Ascherman[2], Daniel Kass[3], Joshua Baker[4], Michael Duryee[1], Yangyuna Yang[1], Punyasha Roul[1], K Wysham[5], Paul Monach[6], Andreas Reimold[7], Gail Kerr[8], Gary Kunkel[9], Grant Cannon[10], Jill Poole[1], Geoffrey Thiele[1], Ted R Mikuls[11] and Bryant England[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Pittsburgh, Pittsburgh, PA, [3]University of Pittsburgh School of Medicine, Pittsburgh, PA, [4]University of Pennsylvania, Philadelphia, PA, [5]VA Puget Sound/University of Washington, Seattle, WA, [6]VA Boston Healthcare System, Boston, MA, [7]University of Texas Southwestern Medical Center, Dallas, TX, [8]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [9]University of Utah, Salt Lake City, UT, [10]University of Utah and Salt Lake City VA, Salt Lake City, UT, [11]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes I: RA-ILD
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Based on the overlap in peripheral blood biomarkers associated with rheumatoid arthritis interstitial lung disease (RA-ILD) and idiopathic pulmonary fibrosis (IPF), a composite biomarker score based on IPF-molecular profiles was previously derived that correlated with RA-ILD disease stage (Kass et al. *Arth Rheum*, 2022; 74(suppl 9)). In this study, we aimed to externally validate the predictive value of a modified version of this biomarker score with prevalent and incident ILD in a large, multicenter RA cohort.

Methods: We performed cross-sectional and longitudinal analyses of participants in the Veterans Affairs Rheumatoid Arthritis registry, a prospective cohort of U.S. veterans with RA. RA-ILD diagnoses were validated by medical record review, with prevalent and incident ILD defined pre- and post-enrollment, respectively. Concentrations of 7 of 8 previously proposed IPF mediators (matrix metalloproteinase [MMP]-7, MMP-9, eotaxin, macrophage-derived chemokine [MDC], monocyte

chemoattractant protein-1 [MCP-1], Fms-like tyrosine kinase 3 ligand [Flt3L] and interleukin-8 [IL-8]; MMP-2 unavailable and not included) were measured from serum/plasma at enrollment (MesoScale Discovery platform). Log-transformed and standardized values (per cohort mean and standard deviation for each analyte) were summed to compute a composite biomarker score. Associations of the biomarker score (continuous and quartile) with prevalent and incident RA-ILD were assessed in multivariable regression models (logistic and Cox), adjusted for age, sex, race, smoking status, anti-CCP positivity, and RA disease activity. Discrimination of prevalent RA-ILD was evaluated with receiver operating characteristic (ROC) curves, initially using the aforementioned clinical predictors alone and subsequently with the addition of the biomarker score.

Results: Among 2,092 participants (89% male, mean age 64 years), prevalent RA-ILD was identified in 86 and incident RA-ILD developed in 116 participants during a mean follow-up of 7.7 years. Mean composite biomarker scores were significantly lower in participants without RA-ILD than in those with prevalent ILD or incident RA-ILD (-0.35 vs. 0.89 and 0.54, respectively, both $p < 0.02$). Higher biomarker scores were significantly associated with prevalent (aOR 1.08 [1.01, 1.15]) and incident (aHR 1.06 [1.01, 1.12] per 1 point increase) RA-ILD. Participants with biomarker scores in the highest quartile had over 2-fold higher odds of prevalent RA-ILD (**Figure 1**) and risk of incident RA-ILD (**Figure 2**). The addition of the biomarker score to clinical predictors did not significantly improve prevalent RA-ILD discrimination (AUC 0.653 [0.595, 0.711] clinical vs. 0.669 [0.613, 0.725] clinical and biomarker score, $p = 0.30$).

Conclusion: A modified composite biomarker score based on IPF molecular profiles was associated with prevalent and incident ILD in a large, multicenter RA cohort. While externally validating prior findings by Kass et al. and implicating IPF mediators in RA-ILD pathogenesis, the IPF-derived composite biomarker score had modest discriminative performance. Further

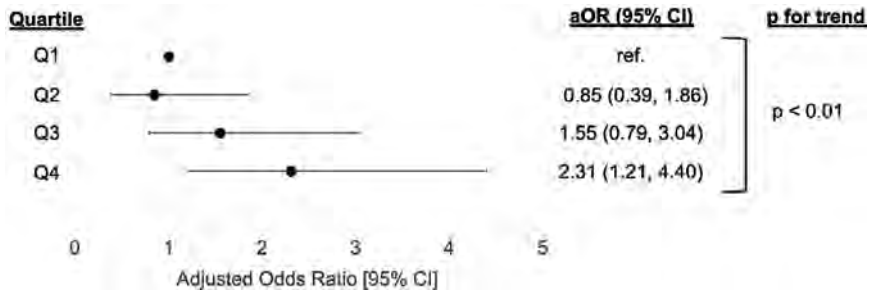

Figure 1. Forest plot illustrating the associations of an IPF-derived composite biomarker score (quartiles) with prevalent ILD in a multicenter RA cohort. Models adjusted for age, sex, race, smoking status, anti-citrullinated peptide antibody status, and rheumatoid arthritis disease activity (28-joint disease activity score [DAS28]). Abbreviations: ILD = interstitial lung disease, RA = rheumatoid arthritis, aOR = adjusted odds ratio, ref. = referent

work is needed to evaluate the clinical utility of this, and other, RA-ILD risk scores.

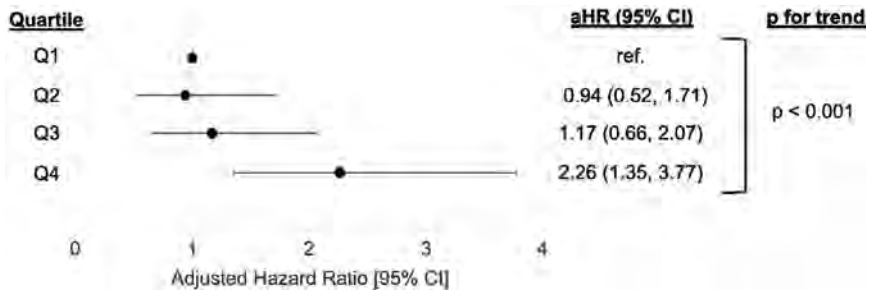

Figure 2. Forest plot illustrating the associations of an IPF-derived composite biomarker score (quartiles) with incident ILD in a multicenter RA cohort. Models adjusted for age, sex, race, smoking status, anti-citrullinated peptide antibody status, and rheumatoid arthritis disease activity (28-joint disease activity score [DAS28]). Abbreviations: ILD = interstitial lung disease, RA = rheumatoid arthritis, aHR = adjusted hazard ratio, ref. = referent

Disclosure: B. Luedders: None; **D. Ascherman**: None; **D. Kass**: None; **J. Baker**: CorEvitas, 2, Cumberland Pharma, 2, Horizon Pharmaceuticals, 5; **M. Duryee**: None; **Y. Yang**: None; **P. Roul**: None; **K. Wysham**: None; **P. Monach**: Genentech, 12, Lecture with honorarium, HI-Bio, 2; **A. Reimold**: None; **G. Kerr**: AstraZeneca, 2, Aurinia, 6, Horizon, 2, Janssen, 2, Pfizer, 1, Sanofi, 2; **G. Kunkel**: None; **G. Cannon**: None; **J. Poole**: AstraZeneca, 12, I have received no monies. I received anti-IL-33 monoclonal antibody from AstraZeneca for animal research sutdies.; **G. Thiele**: None; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **B. England**: Boehringer-Ingelheim, 2, 5.

Abstract Number: 0772

MUC5B Promoter Variant and Survival in Rheumatoid Arthritis-Associated Interstitial Lung Disease

Jacob Klein[1], Austin Wheeler[1], Joshua Baker[2], Yangyuna Yang[1], Punyasha Roul[1], K Wysham[3], Gail Kerr[4], Andreas Reimold[5], Dana Ascherman[6], Gary Kunkel[7], Grant Cannon[8], Paul Monach[9], Jill Poole[1], Geoffrey Thiele[1], Ted R Mikuls[10] and Bryant England[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Pennsylvania, Philadelphia, PA, [3]VA Puget Sound/University of Washington, Seattle, WA, [4]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [5]University of Texas Southwestern Medical Center, Dallas, TX, [6]University of Pittsburgh, Pittsburgh, PA, [7]University of Utah, Salt Lake City, UT, [8]University of Utah and Salt Lake City VA, Salt Lake City, UT, [9]VA Boston Healthcare System, Boston, MA, [10]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes I: RA-ILD

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: The gain of function *MUC5B* rs35705950 promoter variant is the strongest genetic risk factor for the development of RA-ILD (specific to a usual interstitial pneumonia (UIP) pattern) and idiopathic pulmonary fibrosis (IPF). Since it remains uncertain whether the variant also impacts disease prognosis in RA-ILD or IPF, we examined the association of the *MUC5B* promoter variant with survival in a multicenter cohort of U.S. Veterans with RA-ILD.

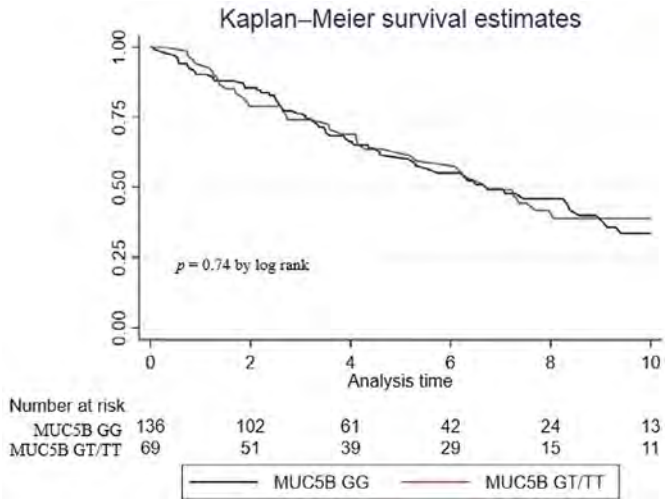

Figure 1. Kaplan-Meier survival curve with log-rank test by MUC5B promoter variant status in RA-ILD.

Table 1. Associations of MUC5B promoter variant status with survival in RA-ILD

	Deaths / PY	Unadjusted HR (95% CI)	Adjusted* aHR (95% CI)
Overall (n=205)			
MUC5B (GG)	62 / 625.79	Ref	Ref
MUC5B (GT/TT)	34 / 365.07	0.93 (0.61, 1.42)	0.75 (0.45, 1.24)
Incident RA-ILD (n=113)			
MUC5B (GG)	37 / 332.98	Ref	Ref
MUC5B (GT/TT)	16 / 155.93	0.90 (0.50, 1.62)	0.84 (0.38, 1.87)

Adjusted for: age, sex, smoking history, baseline DAS28, baseline FVC % predicted, and ILD duration (overall only).
*Adjusted models with n=158 overall, and n=86 incident.
Abbreviations: aHR, adjusted hazard ratio; CI, confidence interval; HR, hazard ratio; PY, person years;

Methods: We studied participants in the Veteran Affairs Rheumatoid Arthritis (VARA) registry with validated ILD diagnoses based on standardized medical record review requiring a provider diagnosis of RA-ILD and either imaging or biopsy findings consistent with ILD. Participants were followed from the latest of either VARA enrollment or ILD diagnosis (index date; to prevent immortal time bias) until death or the end of the study period (12/31/2019). The *MUC5B* rs35705950 promoter variant was measured via the Infinium Global Screening Array-24 v2.0 (Illumina, Inc; San Diego, CA). The major allele was the guanine (G) nucleotide while the minor allele was the thymine (T) nucleotide. An autosomal dominant inheritance pattern was assumed. Survival was determined from Veterans Affairs death records and linkage with the National Death Index. Kaplan-Meier curves were generated and stratified by the *MUC5B* variant. Associations of the *MUC5B* promoter variant with survival were tested in unadjusted and adjusted Cox regression models adjusting for age, sex, smoking history, baseline DAS28, baseline FVC % predicted, and ILD duration. To explore potential survival bias among prevalent ILD cases, a subgroup analysis was completed examining *MUC5B* status and survival among only incident RA-ILD cases. A sensitivity analysis was also performed restricting to participants with UIP or honeycombing on chest computed tomography (CT) reports.

Results: We studied 205 participants with RA-ILD (mean age 69 years, 94% male, 73% white). A smoking history was present in 85%, and the mean ILD duration at index date was 1.7 years. The *MUC5B* promoter variant was detected in 33.7%. Over 990 patient-years of follow-up, 96 deaths occurred. Mortality rate was similar between those with (9.3/100PY [6.7, 13.0]) and without (9.9/100PY [7.7, 12.7]) the variant (**Figure 1**; p = 0.74 by log rank test). In the overall RA-ILD cohort, *MUC5B* status was not significantly associated with survival in unadjusted or adjusted (aHR 0.75 [0.45, 1.24]) models **(Table 1).** Restricting RA-ILD to incident cases produced similar results, with no significant association between the *MUC5B* promoter variant and survival in unadjusted or adjusted (aHR 0.84 [0.38, 1.87]) models (**Table 1**). Findings were similar when restricting to participants with UIP or honeycombing on chest CT (data not shown).

Conclusion: While associated with RA-ILD risk, the *MUC5B* gain of function promoter variant was not predictive of survival in this multicenter RA-ILD cohort. Further studies are needed to identify and evaluate other potential genetic and non-genetic prognostic factors in RA-ILD to inform disease prognostication and management.

Disclosure: J. Klein: None; **A. Wheeler**: None; **J. Baker**: Bristol-Myers Squibb(BMS), 2, Burns-White, LLC, 2, CorEvitas, LLC, 2, Pfizer, 2; **Y. Yang**: None; **P. Roul**: None; **K. Wysham**: None; **G. Kerr**: AstraZeneca, 2, Aurinia, 6, Horizon, 2, Janssen, 2, Pfizer, 1, Sanofi, 2; **A. Reimold**: None; **D. Ascherman**: None; **G. Kunkel**: None; **G. Cannon**: None; **P. Monach**: Genentech, 12, Lecture with honorarium, HI-Bio, 2; **J. Poole**: AstraZeneca, 12, I have received no monies. I received anti-IL-33 monoclonal antibody from AstraZeneca for animal research sutdies.; **G. Thiele**: None; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **B. England**: Boehringer-Ingelheim, 2, 5.

Abstract Number: 0773

Sputum *Lautropia* Abundance Is Decreased in Rheumatoid Arthritis-Associated Pulmonary Fibrosis and Correlates with Lung Disease Severity

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes I: RA-ILD

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Rheumatoid arthritis-associated interstitial lung disease (RA-ILD) develops in 5-10% of RA patients and more often manifests as the fibrotic subtype of ILD known as usual interstitial pneumonia (UIP). Fibrotic ILD can also be detected early in patients with RA before meeting criteria for UIP or becoming clinically apparent. RA-UIP contributes significantly to morbidity and mortality, yet the pathophysiology remains poorly understood. In idiopathic pulmonary fibrosis (IPF), which shares significant clinical and pathophysiologic overlap with RA-UIP, lung microbial dysbiosis has been associated with lung disease progression, exacerbations of the underlying ILD and mortality. We evaluated the lung microbiome using induced sputum in RA patients with pulmonary fibrosis (RA-PF) compared to RA patients without pulmonary fibrosis (RA-no-PF) to establish lung microbial relationships with RA-PF and lung disease severity.

Table 1. Patient demographics and clinical characteristics

	RA-no-PF	RA-PF	P-value
n	32	33	
Age	50.9 (14.6)	64.5 (10.8)	<0.001
Sex (Female)	92%	57%	0.001
Smoking status			
Former/Current smokers	32%	51%	0.157
Pack-years	15.6 (16.4)	24.2 (21.9)	0.271
Serum autoantibodies			
RF+	79%	82%	1.0
CCP +	81%	78%	1.0
Lung disease parameters			
% pred FVC	104.9 (14.9)	88.3 (18.0)	<0.001
% pred DLCO	94.6 (20.9)	76.9 (18.6)	0.001
% DTA fibrosis	N/A	7.8 (11.6)	N/A
Radiographic fibrosis	N/A	51%	N/A
RA-ILD (UIP)	N/A	49%	N/A

Methods: We included 33 patients with RA-PF and 32 patients with RA-no-PF. Presence or absence of PF was determined by high resolution computed tomography (HRCT) read by two chest radiologists blinded to patient characteristics. The RA-PF group included 1) patients with HRCT evidence of early fibrosis but no clinical diagnosis of ILD and 2) patients with established ILD in a radiographic pattern of UIP. Patients with other forms of ILD (e.g., nonspecific interstitial pneumonia) were excluded. Induced sputum was collected from all participants and underwent 16s rRNA microbiome sequencing (MiSeq). Sputum was also tested for levels of pro-inflammatory cytokines (multiplex immunoassay, Meso Scale Discovery). Pulmonary function tests and HRCT were performed within 3 months of sputum collection. Lung fibrosis was quantified by HRCT using the data-driven textural analysis (DTA) computer method. Linear discriminant effect size analysis (LEfSe) was used to identify differences in relative abundance of genus-level taxa between groups.

Results: Demographics and clinical data are shown in Table 1. There were no differences in alpha or beta diversity between groups. In the LEfSe analysis, we found a significantly lower abundance of *Lautropia, Bergeyella, and Haemophilus* in RA-PF compared to RA-no-PF (Figure 1). Of these taxa, lower abundance of *Lautropia* significantly correlated with reduced % predicted forced vital capacity (%FVC; r=0.364, p=0.004) and increased extent of lung fibrosis (r=-0.414, p=0.032) (Figure 2). Additionally, decreased abundance of all three taxa were significantly associated with increased levels of various inflammatory cytokines within sputum, including MCP-1, TNF-α, IL-1β, IL-6, and IL-8 (Figure 2).

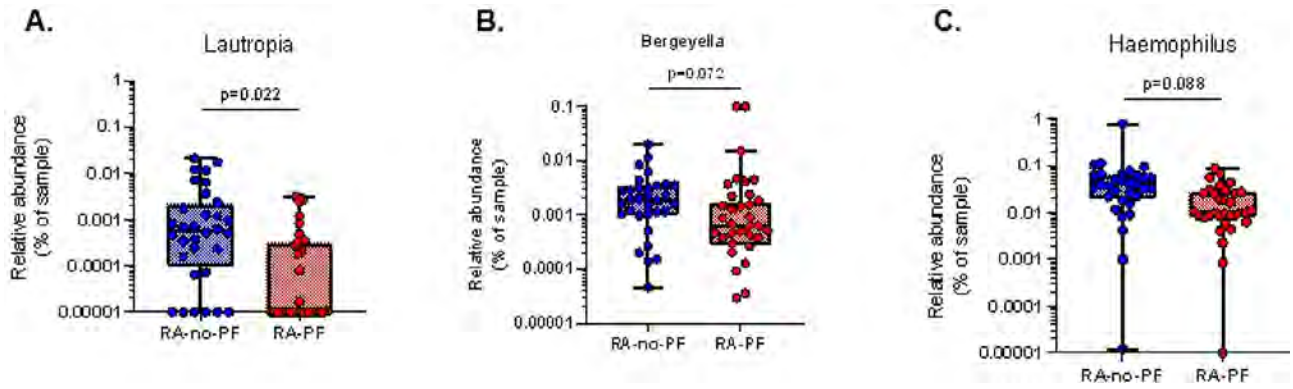

Figure 1. Significant taxa differences at genus level in RA-PF compared to RA-no-PF (A. Lautropia; B. Bergeyella; C. Haemophilus). Read count data was filtered with a minimum read count cutoff of 4 and prevalence in samples of 20%, and a feature low variance cutoff of 10% based on inter-quartile range (IQR). Read counts were rarefied to the minimum library size and scaled using the cumulative sum scaling (CSS) method. Significant differences determined using a linear discriminant effect size analysis (LEfSe) and false discovery rate (FDR) adjusted p-value <0.1.

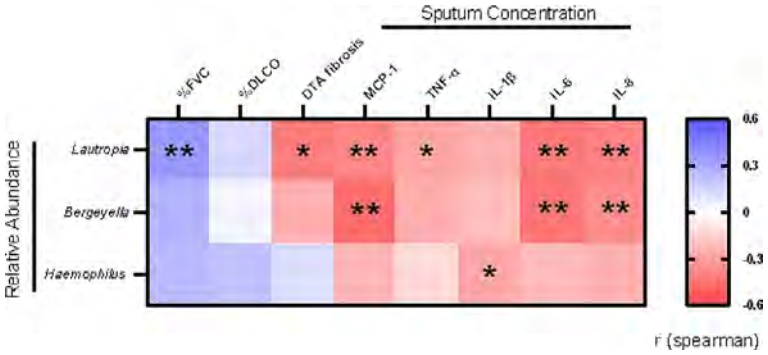

Figure 2. Heatmap of spearman correlation analysis of taxa abundance with markers of lung disease severity and sputum cytokine levels. %FVC = % pre-dicted forced vital capacity, %DLCO = %predicted diffusion capacity carbon monoxide, DTA fibrosis = data drive textural analysis HRCT fibrosis score, MCP-1 = monocyte chemoattractant protein 1, TNF-α = tumor necrosis factor alpha, IL-1β = interleukin 1 beta, IL-6 = interleukin 6, IL-8 = interleukin 8. P-value based on spearman correlation, <0.05 = *, <0.01 = **.

Conclusion: We found taxonomic level differences in the lung microbiome of RA patients with pulmonary fibrosis. Of particular interest, *Lautropia* was lower in RA-PF and lower abundance significantly correlated with impaired lung physiology, higher lung fibrosis and higher levels of local inflammatory cytokines. Future studies are needed to investigate the role of *Lautropia* and other respiratory microbes in driving fibrotic, or perhaps anti-fibrotic, changes within the lungs of RA patients.

Disclosure: T. Wilson: None; **B. Allen**: None; **j. harris**: None; **S. Humphries**: None; **k. Kuhn**: pfizer, 5, ucb, 2; **k. Deane**: Bristol-Myers Squibb(BMS), 1, Gilead, 5, Janssen, 5, Werfen, 1, 12, Biomarker kits; **j. Lee**: Blade, 2, Boehringer-Ingelheim, 1, 5, Eleven P15, 2, Pliant, 5, United Therapeutics, 1; **j. Solomon**: None; **K. Demoruelle**: Boehringer-Ingelheim, 5, Gilead, 5, Pfizer, 5.

Abstract Number: 0774

Deciphering Rheumatoid Arthritis-associated Interstitial Lung Disease Phenotypes Using Unsupervised Hierarchical Clustering Analysis: Results from a Large Collaborative International Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes I: RA-ILD

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: RA-associated interstitial lung disease (ILD) is not a single entity as illustrated by different HRCT patterns, different risk factors and prognoses suggesting heterogenous phenotypes. Our objective was to identify definite subphenotypes among a large RA-ILD dataset performing unsupervised clustering analysis.

Table 1. Distribution of active variables within the clusters among patients with RA-ILD (n=1696). Data are numbers (percentages) for categorical variables or means (Standard Deviation) for continuous variables. 95% confidence interval for clustering analysis are indicated in the brackets for each variable. Normalized ACPA and RF represents fold above upper limit normal. ACPA: anti-citrullinated peptides antibodies; DLCO: diffusion capacity of the lung for carbon monoxide; HRCT: high-resolution computed tomography; ILD: interstitial lung disease; LIP: lymphocytic interstitial pneumonia; NSIP: non-specific interstitial pneumonia; OP: organizing pneumonia; RF: rheumatoid factor; UIP: usual interstitial pneumonia

Active variable	Cluster 1 n=1015	Cluster 2 n=681	p-value
Male	462 (45.5)	261 (38.3)	**0.003**
Duration between RA and ILD (years)	8.4 (10.3)	8.1 (11.2)	0.531
Age at RA onset (years)	56.9 (13.3)	53.8 (14.5)	**<0.001**
Age at ILD onset (years)	65.5 (10.1)	61.9 (12.3)	**<0.001**
Ethnicity (self-reported) - European - Turk - Hispanic - Black - Asian - Other	 872 (85.9) 137 (13.5) 2 (0.2) 4 (0.4) 0 (0) 0 (0)	 465 (68.3) 4 (0.6) 102 (14.5) 50 (7.3) 12 (1.8) 48 (7.1)	**<0.001**
Pulmonary symptoms at ILD onset	867 (85.4)	519 (76.2)	**<0.001**
Sjogren syndrome	110 (10.8)	140 (20.6)	**<0.001**
ACPA positive	921 (90.7)	477 (70.0)	**<0.001**
Normalized ACPA titers	27.7 (32.8)	32.0 (162.2)	0.494
RF positive	972 (95.8)	459 (67.4)	**<0.001**
Normalized RF titers	16.1 (25.4)	18.7 (44.7)	0.170
Ever smoker at RA onset	651 (64.1)	373 (54.8)	**<0.001**
Current smoker at RA onset	233 (23.0)	126 (18.5) [15.6-21.4]	**0.025**
Pack-year at RA onset	17.6 (21.5)	14.4 (21.8)	**0.002**
Ever smoker at ILD onset	652 (64.2)	379 (55.7)	**<0.001**
Current smoker at ILD onset	176 (17.3)	100 (14.7)	0.141
Pack-year at ILD onset	19.4 (23.1)	15.1 (21.1)	**<0.001**
HRCT pattern - UIP - Indeterminate for UIP - NSIP - OP - LIP - Other	 736 (72.5) 0 (0) 227 (27.3) 0 (0) 1 (0.1) 1 (0.1)	 210 (30.8) 189 (27.8) 117 (17.2) 39 (5.7) 10 (1.5) 116 (17.0)	**<0.001**
Forced vital capacity (%)	86.2 (21.7)	84.2 (23.8)	0.069
DLCO (%)	58.51 (19.6)	59.8 (21.3)	0.192

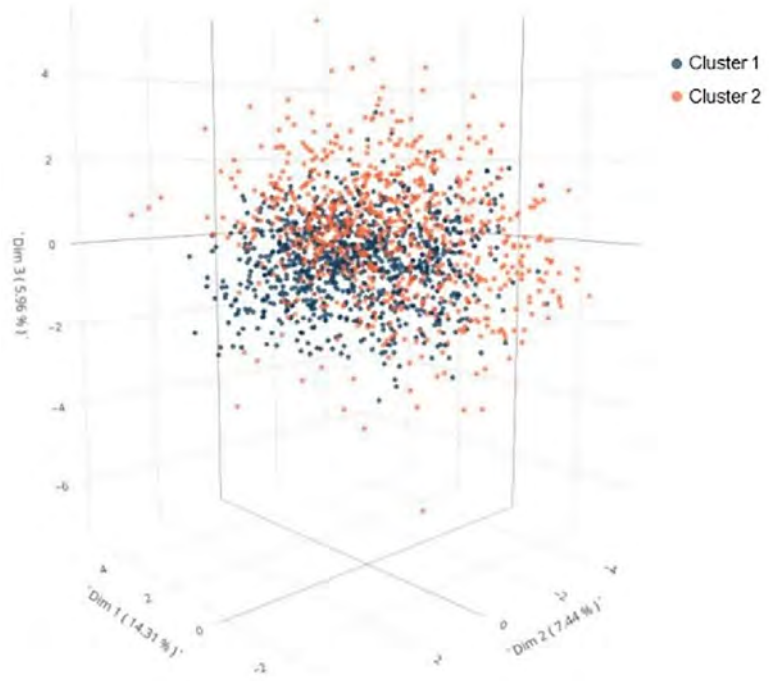

Figure 1. Clusters representation on the first three dimensions of Multiple Correspondence Analysis (MCA) The map is a 3D representation of patients and their clusters (n = 1696). A point represents a patient, and its color represents the cluster assigned to this patient (cluster 1 in blue and cluster 2 in orange). The first three dimensions of MCA together explain 27.7% of the total variance.

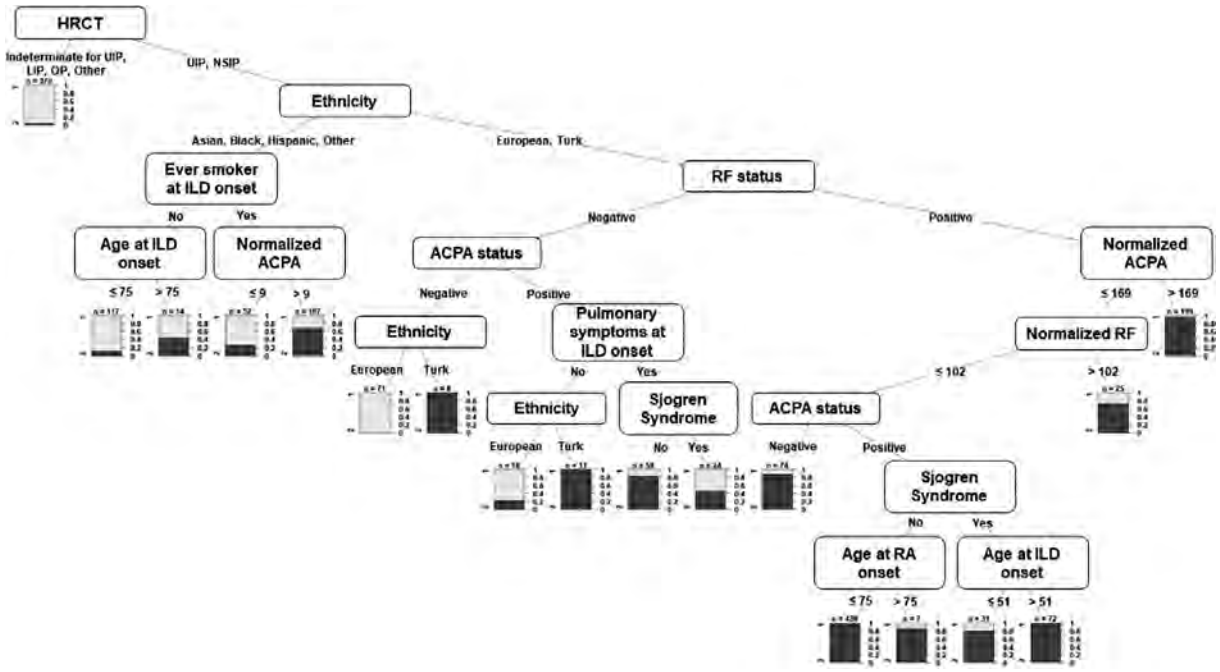

Figure 2. Decision tree to predict a cluster for a new patient with RA-ILD The tree is a set of paths. Each path is a sequence of conditions that lead to a decision (cluster 1 or cluster 2). The nodes present active variables that are important in the decision-making and the edges present conditions to be checked by a patient in order to classify him in one of the two clusters. The barplot (final node of each path) presents the two clusters (cluster 1 and cluster 2) on the left and the probability to be in cluster 1 on the right. ACPA: anti-citrullinated peptides antibodies; HRCT: high-resolution computed tomography; ILD: interstitial lung disease; LIP: lymphocytic interstitial pneumonia; NSIP: non-specific interstitial pneumonia; OP: organizing pneumonia; RF: rheumatoid factor; UIP: usual interstitial pneumonia

Methods: In this international collaborative study (22 centers from 13 countries), we included patients with RA (ACR/EULAR 2010 classification criteria) having ILD defined by high-resolution computed tomography (HRCT) chest scan. Clinical, biological, imaging, and functional data were retrospectively collected from extensive chart review. Missing data were handled using multiple imputation with chained equations. A multiple correspondence analysis was performed on each sample to reduce dimensions and a non-parametric Bayesian algorithm was used to attribute a cluster to each patient. The clusters were aggregated over the multiple imputations using weighted Non-negative Matrix Factorization.*MUC5B* rs35705950 T risk allele distribution in the identified clusters was investigate for patients with available genotype. A surrogate decision tree was conducted using the non-imputed dataset to predict a cluster for each patient. The prediction error rate of the tree was estimated using cross-validation.

Results: A total of 1696 patients with RA-ILD were included in the cluster analysis; **Table 1**. Among the 37 collected variables, 20 active variables were used to construct clusters. The non-parametric Bayesian clustering algorithm detected 2 definite clusters: cluster 1 (n=1015) and cluster 2 (n=681); **Table1, Figure 1**. Compared to cluster 2, patients from cluster 1 were more frequently male (45.5% vs 38.3%, p=0.003), older at RA onset (56.9 ± 13.3 vs 53.8 ± 14.5, p< 0.001) and at ILD onset (65.5 ± 10.1 vs 61.9 ± 12.3, p< 0.001), more frequently with European ethnicity (85.9% vs 68.3%, p< 0.001), more frequently ever smokers at ILD onset (64.2% vs 55.7%, p< 0.001) and had less Sjogren syndrome (10.8% vs 20.6%, p< 0.001). They were more frequently positive for anti-citrullinated peptides antibodies (90.7% vs 70.0%, p< 0.001) and for rheumatoid factor (95.8% vs 67.4%, p< 0.001). UIP HRCT pattern was predominant in cluster 1 (72.5%) whereas various patterns were observed in cluster 2 (UIP = 30.8%, NSIP = 17.2%), p< 0.001. There was no difference in lung function at ILD onset between the 2 clusters. *MUC5B* rs35705950 genotype was available for 444 patient (26.2%) with a higher minor allele frequency (MAF) in cluster 1 (33% compared to 18%, p< 0.001). **Figure 2** shows the decision tree that can be used to predict the cluster for a new patient with a prediction error rate of 9.8%.

Conclusion: Our results provide evidence that RA-ILD is a heterogeneous disease and allow the identification of at least two distinct subsets. This heterogeneity is illustrated by a contribution of the *MUC5B* promoter variant restricted to cluster 1, promoting the identification of specific risk scores for each RA-ILD subset. This heterogeneity underlies distinct physio pathological mechanisms which could influence not only the prognosis of patients with RA-ILD but also their therapeutic management.

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Abstract Number: 0775

Effectiveness of Dose Reduction and Withdrawal Strategies of TNF Inhibitors in Psoriatic Arthritis and Axial Spondyloarthritis: Long Term Extension of the DRESS-PS Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment I: PsA
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Tumor Necrosis Factor inhibitors (TNFi) are effective in PsA and axial SpA, but are associated with increased infections risk, patient burden and high costs. The DRESS-PS study[1] was the first study to show that a Treat-To-Target (T2T) tapering strategy in PsA and axSpA patients is non-inferior compared to T2T without tapering regarding Low Disease Activity (LDA) status at 12 months, with a considerable reduction of TNFi use. If these effects can be maintained up to 2 years is unknown.

The aim of this study was to describe effectiveness of disease activity guided dose optimization of TNFi up to 24 months follow-up in patients with PsA and axSpA who participated in the DRESS-PS study.

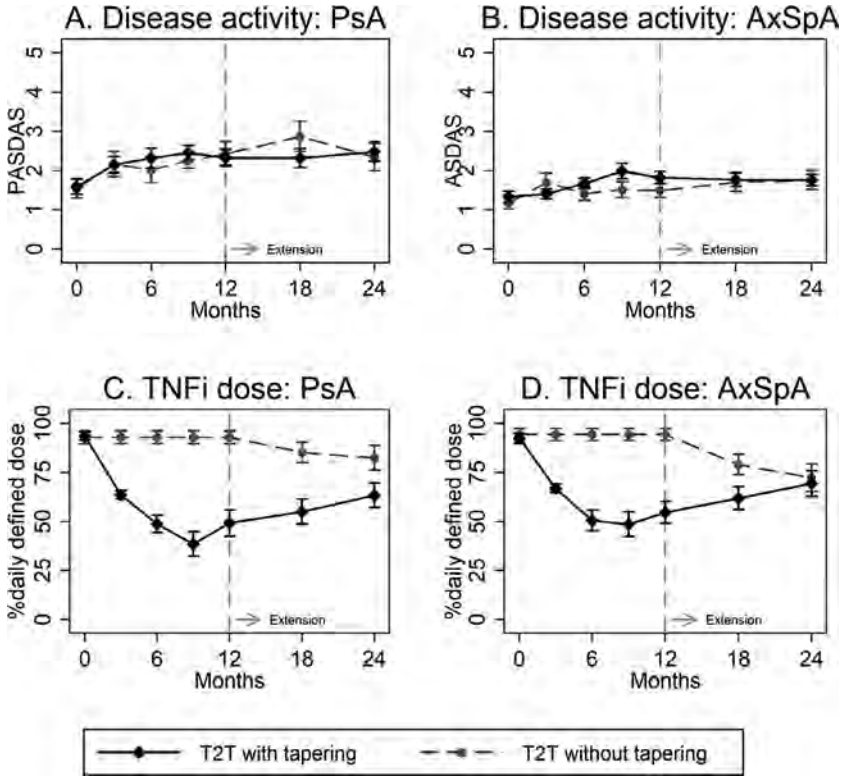

Figure 1: Mean disease activity presented as PASDAS in patients with PsA (A) and ASDAS in patients with AxSpA (B) and mean TNFi dose presented as percentage of daily defined dose in patients with PsA (C) and patients with AxSpA (D), between T2T with tapering and T2T without tapering.

Methods: This study is a 12-month observational extension of the DRESS-PS study. In the DRESS-PS study, patients were allocated to protocolized T2T tapering (intervention) or to T2T without tapering (control). During the extended follow-up, treatment decisions were according to usual care and T2T tapering was allowed for all patients. Patients visited the outpatient clinic bi-annually.

Primary outcomes were disease activity (presented as proportion in LDA and mean disease activity), and TNFi use (presented as percentage of the current daily dose to the defined daily dose (DDD)). Secondarily, functioning measured with HAQ-DI and BASFI and quality of life measured with EQ5D, SF12 and ASAS-HI at 24 months are reported.

We also compared effects of protocolized tapering to routine care tapering, by comparing the intervention group at 12 months to the control group at 24 months.

Results: 114 patients (of 122) were included in the extension study (table 1). The proportion in LDA state at 24 months was 67% (45 of 67) in patients originally allocated in the intervention group and 72% (23 of 32) in patients originally allocated in the control group (difference 4.7% (95%CI: -15% to 24%)). Mean disease activity remained stable during the extension period (Figure 1A and 1B).

Table 1. Baseline characteristics of patients with PsA or axSpA treated with a T2T strategy with tapering attempt (intervention) or a T2T strategy without tapering attempt (control)

Characteristics	Intervention (n=79)	Control (n=35)
Diagnosis, n (%)		
PsA	40 (51)	18 (51)
axSpA	39 (49)	17 (49)
Female, n (%)	28 (35)	16 (46)
Age in years at inclusion, mean (sd)	49 (14)	52 (16)
Disease duration at inclusion, years, median (IQR)	11 (5 to 21)	11 (5 to 25)
CASPAR criteria, n (%)	32 (80)	15 (83)
ASAS criteria, n (%)	35 (90)	15 (88)
Disease activity, mean (SD)		
PASDAS	1.60 (1.25)	1.54 (1.00)
ASDAS	1.33 (0.89)	1.18 (0.64)
Duration of current bDMARD use, years, median (IQR)	2 (1 to 6)	3 (2 to 9)

Baseline ASDAS was missing for 1 SpA patient
PsA, Psoriatic Arthritis; axSpA, axial SpondyloArthritis; CASPAR, Classification Criteria for Psoriatic Arthritis; ASAS, Assessment of SpondyloArthritis; PASDAS, Psoriatic Arthritis Disease Activity; ASDAS, Ankylosing Spondylitis Disease Activity Score

Table 2. Results of questionnaires on Quality of life and functioning in patients with PsA and axSpA in a T2T tapering strategy (intervention) and T2T strategy without tapering (control) at 24 months

Quality of life (24 months)	Intervention Median (iqr)	Control Median (iqr)
EQ-5D-3L	0.84 (0.78 to 0.93)	0.84 (0.78 to 0.93)
SF-12 PCS	44.4 (38.5 to 49.6)	44.0 (36.6 to 46.4)
SF-12 MCS	55.0 (46.6 to 59.4)	56.1 (48.2 to 59.3)
ASAS-HI	5 (2 to 7)	4 (2 to 8)
Functioning (24 months)	**Intervention Median (iqr)**	**Control Median (iqr)**
HAQ-DI	0.25 (0 to 0.63)	0.31 (0.13 to 0.81)
BASFI	1.95 (1.15 to 3.45)	1.70 (0.80 to 3.60)

Results are presented as median with interquartile range. EuroQol five-dimension scale with three levels (EQ-5D-3L), ranges from 0 to 1, with higher scores indicating better quality of life. Short Form Health Survey 12 (SF-12), ranges from 0 to 100, consists of a physical and mental component score, higher scores indicate better quality of life. Assessment of SpondyloArthritis International Society-Health Index (ASAS-HI), ranges from 0 to 17, this questionnaire was only fulfilled by patients with axSpA , with higher scores indicating worse quality of life. Health Assessment Questionnaire-Disability Index (HAQ-DI), ranges from 0 to 3, higher scores indicate lower functioning. Bath Ankylosing Spondylitis Functional Index (BASFI), ranges from 0 to 10, this questionnaire was only fulfilled by patients with axSpA, with higher scores indicating lower functioning. Not all patients fulfilled all questionnaires.

101/114 (89%) patients attempted tapering during follow up (100% intervention vs 63% control). TNFi %DDD at 24 months was 66% (95%CI: 57% to 75%) in the original intervention group and 77%% (95%CI: 68% to 87%) in the original control group (Figure 1C and D). Functioning and quality of life at 24 months was similar between patients originally randomized to intervention and control (table 2).

The comparison between protocolized tapering and routine care tapering showed no difference in patients in LDA state 12 months after start of tapering: 70% vs 72%% (difference 2.3% (95%CI: -16% to 21%)). However, there was a significant difference in TNFi use: %DDD 52% in the intervention group at 12 months and 77% in the control group at 24 months (difference 26% (95%CI: -13% to 38%)).

Conclusion: T2T tapering of TNFi remains effective and safe regarding disease control up to two years. However, the % DDD seems to increase somewhat in the intervention group, and is higher compared to studies in RA, and tapering in usual care seems less frequent. Whether this is by chance, or caused by a disease-specific need for higher dosing or more subjective disease activity measures, remains a topic for further research.

References

1. Michielsens CA et al. Ann Rheum Dis. 2022 Oct;81(10):1392-1399.

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Abstract Number: 0776

Efficacy and Safety of Intravenous Secukinumab for the Treatment of Active Psoriatic Arthritis: 16- and 52-Week Results from a Randomized, Double-Blind, Phase 3 Study

Alan Kivitz[1], Liliana Sedova[2], Melvin Churchill[3], Roshan Kotha[4], Atul Singhal[5], Alexander Torres[6], Guillermo Valenzuela[7], Sarah Whelan[8], Thomas Dumortier[9], Xuan Zhu[10], Ruvie Martin[10] and Luminita Pricop[10], [1]Altoona Center for Clinical Research, Duncansville, PA, [2]Institute of Rheumatology, Prague, Czech Republic, [3]Arthritis Center of Nebraska, Lincoln, NE, [4]Sharp Community Medical Group, La Mesa, CA, [5]Southwest Arthritis Research Group, Mesquite, TX, [6]Highlands Advanced Rheumatology and Arthritis Center, Avon Park, FL, [7]Integral Rheumatology & Immunology Specialists, Plantation, FL, [8]Novartis Ireland Ltd, Dublin, Ireland, [9]Novartis Pharma AG, Basel, Switzerland, [10]Novartis Pharmaceuticals Corporation, East Hanover, NJ

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment I: PsA
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: To investigate the long-term efficacy, safety, and tolerability of intravenous (IV) secukinumab (SEC) in patients with active psoriatic arthritis (PsA) through 52 weeks.

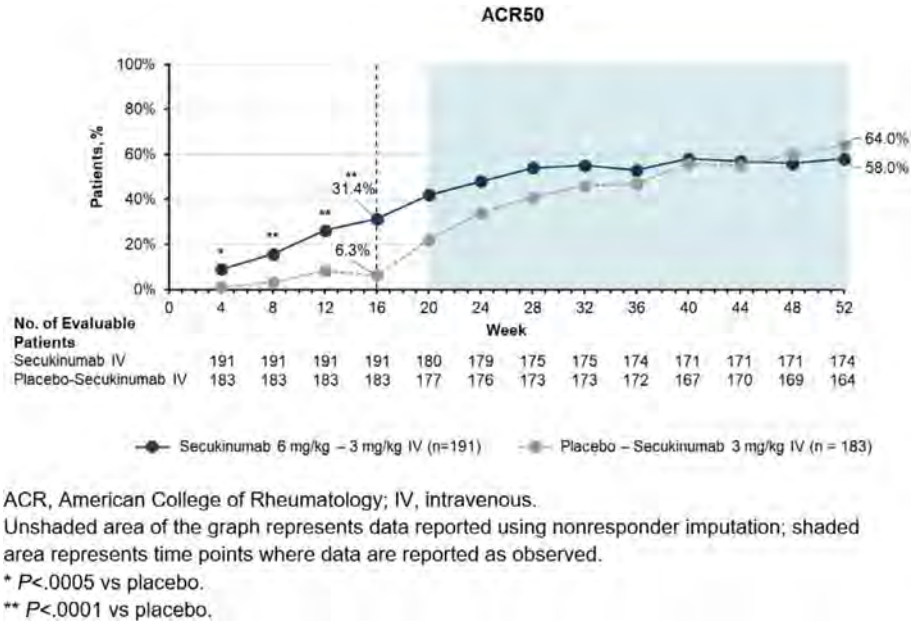
Methods: INVIGORATE-2 (NCT04209205) is a randomized, double blind, placebo (PBO)-controlled, parallel group, phase 3 study. All patients met the CASPAR criteria for active PsA, had symptoms for ≥6 months, and had a Tender Joint Count of 78 joints (TJC78) ≥3 and a Swollen Joint Count of 76 Joints (SJC76) ≥3 at baseline. Patients were randomized 1:1 to receive IV SEC (6 mg/kg at baseline followed by 3 mg/kg q4w) or PBO. At Week 16, patients randomized to SEC continued

receiving SEC and patients randomized to PBO were switched to IV SEC (3 mg/kg q4w) through Week 52. The primary efficacy endpoint was American College of Rheumatology (ACR) 50 response rate at Week 16 versus PBO. Secondary efficacy outcomes included achievement of ACR20, minimal disease activity, PASI90, dactylitis resolution, and enthesitis resolution. All efficacy outcomes were assessed through Week 52, and safety was evaluated through Week 60. Data through week 16 are reported using nonresponder imputation; data from Week 20 through Week 52 are reported as observed.

Table 1. Patient demographics and baseline disease characteristics

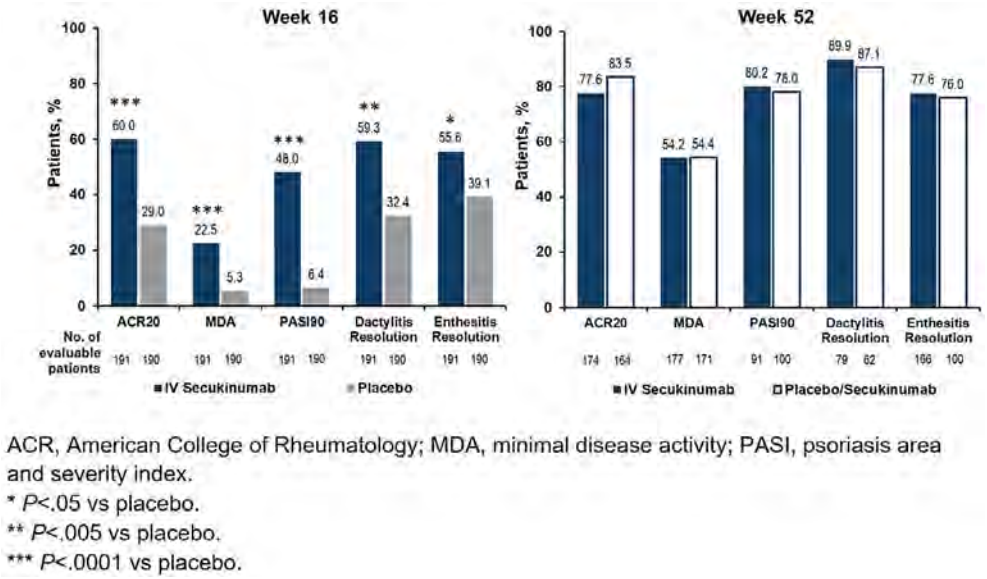
Characteristic	Secukinumab (n=191)	Placebo/Secukinumab (n=190)
Age, mean (SD), years	47.5 (13.5)	48.1 (13.7)
Sex, n (%)		
Male	87 (45.5)	85 (44.7)
Female	104 (54.5)	105 (55.3)
Weight, mean (SD), kg	84.6 (22.9)	85.1 (22.7)
Previous TNFi exposure, n (%)		
Naive	165 (86.4)	162 (85.3)
Inadequate responder	26 (13.6)	28 (14.7)
Enthesitis (LEI), n (%)	126 (66.0)	110 (57.9)
Dactylitis, n (%)	81 (42.4)	71 (37.4)
Nail psoriasis, n (%)	130 (68.1)	121 (63.7)
Psoriasis ≥3% of BSA, n (%)	102 (53.4)	109 (57.4)

BSA, body surface area; LEI, Leeds Enthesitis Index; TNFi, tumor necrosis factor inhibitor



ACR, American College of Rheumatology; IV, intravenous.
Unshaded area of the graph represents data reported using nonresponder imputation; shaded area represents time points where data are reported as observed.
* $P<.0005$ vs placebo.
** $P<.0001$ vs placebo.

Figure 1. Proportion of patients with PsA who achieved ACR50 through Week 16 (nonresponder imputation) and through Week 52 (observed data)



ACR, American College of Rheumatology; MDA, minimal disease activity; PASI, psoriasis area and severity index.
* P<.05 vs placebo.
** P<.005 vs placebo.
*** P<.0001 vs placebo.

Figure 2. Proportions of patients with PsA who achieved binary secondary efficacy outcomes at Week 16 (nonresponder imputation) and Week 52 (observed data)

Results: Demographics and baseline characteristics were balanced across treatment groups (**Table 1**). Among patients randomized to IV SEC (n=191) and IV PBO/SEC (n=190), similar proportions of patients completed the entire study period (90.6% and 87.9%, respectively). A higher proportion of patients receiving SEC than PBO achieved ACR50 at Week 16 using nonresponder imputation (60/191 [31.4%] vs 12/190 [6.3%]; P< .0001; **Figure 1**). An increase in ACR50 response was observed by Week 20 among patients initially randomized to PBO who were switched to SEC at Week 16. Both groups had similar ACR50 response rates by Week 52 based on observed data (SEC, 58.0%; PBO/SEC, 64.0%). Patients receiving SEC had greater improvements in secondary efficacy outcomes compared with PBO at Week 16, and both SEC and PBO/SEC groups had comparable efficacy outcomes by Week 52 (**Figure 2**). Through Week 16, the incidences of adverse events (AEs; 37.7% vs 38.4%), serious AEs (1.6% vs 2.1%), and AEs leading to treatment discontinuation (0.5% vs 1.6%) were similar for patients receiving SEC or PBO. Among patients receiving any SEC through the entire study period, 63.4%, 5.9%, and 1.9% reported any AE, serious AEs, and AEs leading to treatment discontinuation, respectively. One death was reported in the PBO group prior to Week 16. No new safety signals were observed with IV SEC.

Conclusion: IV SEC (6 mg/kg at baseline followed by 3 mg/kg q4w) was safe and effective for the long-term treatment of active PsA. Treatment responses were maintained up to Week 52 for patients randomized to IV SEC. For patients originally randomized to PBO who switched to receive IV SEC at Week 16, an increase in efficacy responses comparable to those in patients randomized to IV SEC was observed up to Week 52. Safety was consistent with the known safety profile of subcutaneous SEC, and no new safety signals were observed.

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G. Valenzuela: AbbVie, 2, Bristol-Myers Squibb, 12, Investigator, Celgene, 2, Eli Lilly, 2, Genentech, 2, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, Merck, 2, MLKCDT, 12, Investigator, Novartis, 2, Pfizer, 2, Regeneron, 2, Sanofi, 2, UCB, 2; **S. Whelan**: Novartis, 3, 11; **T. Dumortier**: Novartis, 3, 11; **X. Zhu**: Novartis, 3, 11; **R. Martin**: Novartis, 3, 11; **L. Pricop**: Novartis, 3, 11.

Abstract Number: 0777

Characteristics of Difficult-To-Treat Psoriatic Arthritis: A Comparative Analysis

Cecile PHILIPPOTEAUX[1], Anne Marty-Ane[1], Emeline Cailliau[1], Peggy Philippe[1], Bernard Cortet[1], Julien Paccou[1], Rene-Marc Flipo[1] and Jean-Guillaume Letarouilly[2], [1]University Hospital Center of Lille, Lille, France, [2]CHU Lille, Lille, France

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment I: PsA
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: The EULAR task force recently published the difficult-to-treat RA (D2T RA) definition [1], however, a definition of D2T PsA is still lacking. To date, we have little data concerning D2T PsA, especially in real-world. One of the limitations of the D2T RA EULAR definition is the absence of a temporal criterion. The primary endpoint of this work was to study the characteristics of D2T PsA patients using the EULAR definition. The second objective was to study a sub-group of patients with a predefined more stringent definition including a temporal criterion.

Methods: A retrospective study was performed in a tertiary center. PsA patients 18 years old or older starting a b/tsDMARDs with at least two-year follow-up were included. D2T PsA was defined as failure of ≥ 2 b/tsDMARDs with different mechanism of action among TNF inhibitors, anti-IL 17, anti-IL 23 and JAK inhibitors. Very D2T PsA was defined as failure of ≥ 2 b/tsDMARDs in less than 2 years of follow-up. D2T and Very D2T PsA patient's characteristics were compared between with non-D2T (nD2T) patients using statistical tests. The significant factors at the level of 0.10 were introduced into a multivariable multinomial logistic regression model.

Results: 150 PsA patients were included: 49 D2T PsA (32.7%) and 101 non-D2T (nD2T) PsA (67.3%). Results showed a significant difference in clinical PsA features at baseline including axial involvement, with a proportion of 43.8% in the D2T group vs. 26.0% in the nD2T group (p=0.03) (**Table 1**). Structural damage at baseline (axial and/or peripheral) concerned 76.2% of the D2T patients and 51.0% of the nD2T patients (p=0.006). In multivariate analysis, structural damage was found to be a predictive factor for D2T PsA with an OR of 2.49 (1.05 to 5.89; p=0.038) (**Table 2**).

There was no significant difference regarding comorbidities such as obesity, smoking status, fibromyalgia or depression. The median delay to first b/tsDMARD in the D2T group was 42 (12 to 120) months vs. 36 (14,5 to 108) months in the nD2T group (p=0,95). Treatment trajectory of D2T PsA patients were reported from 1st to 5th line (**-Figure 1**). There was at least one therapeutic switch for dermatological ineffectiveness in 40.4% of patients in the D2T group vs 18.8% in the nD2T group (p=0.005). In multivariate analysis, bDMARD discontinuation due to poor dermatological control was found to be more frequent in the D2T population with an OR of 2.75 (1.23 to 6.14; p=0.013) (**Table 2**).

17 patients (11.3%) were categorized as Very D2T. When compared to the nD2T group, proportion of obesity was higher (p=0.015) and axial involvement at baseline was more prevalent in the Very D2T group (p=0.020).

Table 1 – Baseline characteristics of D2T PsA and nD2T PsA patients

Parameters	N	D2T PsA n = 49	N	nD2T PsA n = 101	p value
Men	49	29 (59.2)	101	52 (51.5)	0.37
Age (years), mean ± SD	49	54.3 ± 11.9	101	53.7 ± 14.2	0.82
BMI, mean ± SD	46	29.6 ± 7.2	96	27.7 ± 5.7	0.093
PsA duration (years), median (IQR)	49	17 (8 to 20)	99	11 (6 to 21)	0.22
Active smoking status	49	16 (32.7)	101	33 (32.7)	1.00
Clinical PsA characteristics at baseline					
Axial involvement	48	21 (43.8)	100	26 (26.0)	0.030
Peripheral involvement	49	49 (100.0)	101	99 (98.0)	NA
Monoarthritic	48	3 (6.3)	101	11 (10.9)	-
Oligoarthritic	48	22 (45.8)	101	51 (50.5)	-
Polyarthritic	48	23 (47.9)	101	37 (36.6)	-
Dactylitis	45	10 (22.2)	101	32 (31.7)	0.24
Uveitis	49	1 (2.0)	101	2 (2.0)	NA
Psoriasis at baseline	49	43 (87.8)	101	89 (88.1)	0.95
Structural damage at baseline (axial and/or peripheral)	42	32 (76.2)	96	49 (51.0)	0.006
IBD at baseline	49	0 (0.0)	101	3 (3.0)	NA
Positive HLA B27 status	24	10 (41.7)	51	18 (35.3)	0.59
Baseline CRP (mg/L), median (IQR)	40	13.6 (6.0 to 31.5)	86	8.1 (3.0 to 20.0)	0.11
BASDAI Baseline, mean ± SD	8	65.1 ± 16.6	22	58.5 ± 11.7	0.23
Main comorbidities					
Diabetes mellitus	49	6 (12.2)	101	15 (14.9)	0.67
Fibromyalgia	49	2 (4.1)	101	0 (0)	NA
Depression	49	7 (14.3)	101	9 (8.9)	0.32
HBP	49	16 (32.7)	101	25 (24.8)	0.31
Dyslipidaemia	49	8 (16.3)	101	17 (16.8)	0.94
Treatments received					
Infliximab		9 (18.4)		12 (11.9)	0.28
Etanercept		26 (53.1)		42 (41.6)	0.19
Adalimumab		30 (61.2)		46 (45.5)	0.072
Golimumab		30 (61.2)		46 (45.5)	0.57
Certolizumab		30 (61.2)		46 (45.5)	0.18
Secukinumab		30 (61.2)		46 (45.5)	0.81
Ustekinumab		13 (26.5)		22 (21.8)	0.52
Guselkumab		0 (0.0)		2 (2.0)	NA
Ixekizumab		0 (0.0)		2 (2.0)	NA
JAKi		0 (0.0)		1 (1.0)	NA
bDMARD discontinuation due to poor dermatological control	47	19 (40.4)	101	19 (18.8)	0.005

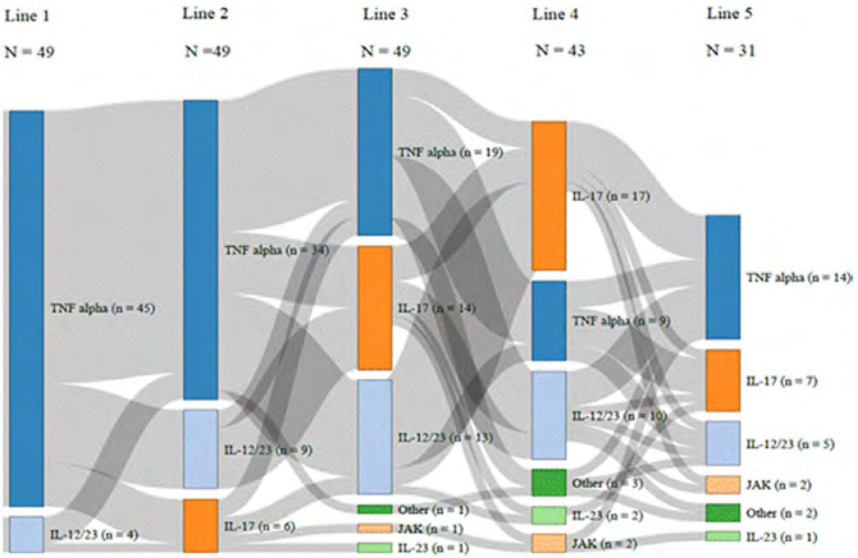
Values are expressed as number (%) unless otherwise stated. BASDAI: Bath Ankylosing Spondylitis Disease Activity; bDMARD: biological disease modifying antirheumatic drug; BMI: body mass index; CRP: C-reactive protein; (n)D2T: (non) difficult-to-treat; HBP: High blood pressure; HLA: human leukocyte antigen IBD: inflammatory bowel disease; IQR: interquartile range; N: number of available observations; NA: not applicable; PsA: psoriatic arthritis; SD: standard deviation.

Conclusion: D2T PsA was associated with a higher prevalence of axial involvement, structural damage and therapeutic discontinuation due to poor dermatological control. Very D2T PsA patients were more likely obese with axial involvement. Very D2T PsA represent a minim proportion of patients when applying a more stringent definition. Pending the PsA D2T definition by the European and American societies, this study highlights some characteristics that may help practitioners better identify D2T patients.

Table 2 - Multivariate analysis for D2T PsA predictive factors

	Odds-ratio (95%CI)	p-value
BMI	1.26 (0.92 to 1.71)[1]	0.14
Axial involvement at baseline	1.80 (0.82 to 3.93)	0.14
Structural damage at baseline (axial and peripheral)	2.49 (1.05 to 5.89)	**0.038**
bDMARD discontinuation due to poor dermatological control	2.75 (1.23 to 6.14)	**0.013**
Previous treatment with Adalimumab	1.69 (0.80 to 3.56)	0.17

Abbreviations: BMI=body mass index; CI=confidence interval.[1]Expressed for an increase of 5 units.



Abbreviations: JAK: JAK inhibitors (tofacitinib, upadacitinib); IL 12/23: IL 12/23 inhibitors (ustekinumab, guselkumab); IL 17: IL 17 inhibitors (secukinumab, ixekinumab) Other: abatacept, rituximab. TNF alpha: TNF alpha inhibitors (infliximab, certolizumab, golimumab, adalimumab, etanercept).

Figure 1 – Treatment trajectory for D2T PsA patients from first to fifth line

[1] Nagy G *et al*. EULAR definition of difficult-to-treat rheumatoid arthritis. *Ann Rheum Dis* 2021;80:31–5.

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Abstract Number: 0778

The Effect of Probiotic Modulation of Enteral Dysbiosis on Disease Activity in Patients with Psoriatic Arthritis - A Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
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Session Type: Abstract Session
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Background/Purpose: Psoriatic Arthritis (PsA) is a painful disease of the joints and spine. Recent studies have described enteric dysbiosis as a possible pathological mechanism in PsA and hence could be a target for therapy. In an open label pilot study, probiotic supplementation ameliorated enteric dysbiosis and reduced disease activity of PsA patients. The aim of this

study was to test the effect of probiotic supplementation on disease activity in PsA in a larger randomized controlled trial (RCT).

Methods: The study was designed as a single center, double-blind, RCT (NCT04588623) on consecutive patients with PsA in Moderate Disease Activity (MoDA) (Psoriatic ArthritiS Disease Activity Score [PASDAS] >3.2 - < 5.4) under stable treatment. Patients were randomized to either placebo or probiotic containing Bifidobacterium and Lactobacillus strains (OMNi-BiOTiC® STRESS Repair, Institut Allergosan, Graz, Austria) for 12 weeks. After week 12 (W12) patients received probiotics, irrespective of the initial grouping and were followed up again at week 24 (W24). The patients enrolled were given a full clinical assessment and samples (stool, serum, and PBMCs) were collected at baseline (BSL), W12, W24. Immune cell composition in the peripheral blood was analyzed using flow cytometry. Stool microbiome was analyzed via 16s rRNA sequencing and levels of Zonulin, Calprotectin and Anti-Trypsin were assayed through ELISA as a measure of gut permeability and intestinal inflammation. The primary end point of the study was the reduction of disease activity to low DA or remission (PASDAS < 3.2) at W12.

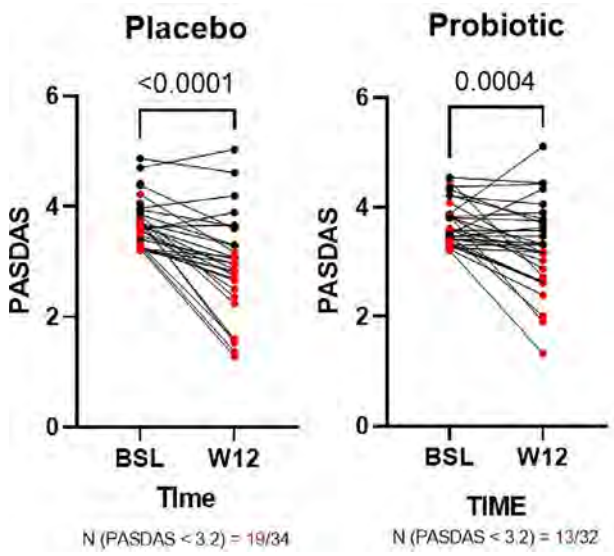

Fig1 Changes in PASDAS score in patients grouped by probiotic intervention. Samples in red denote specifically the patients that achieved low DA or remission (PASDAS < 3.2).

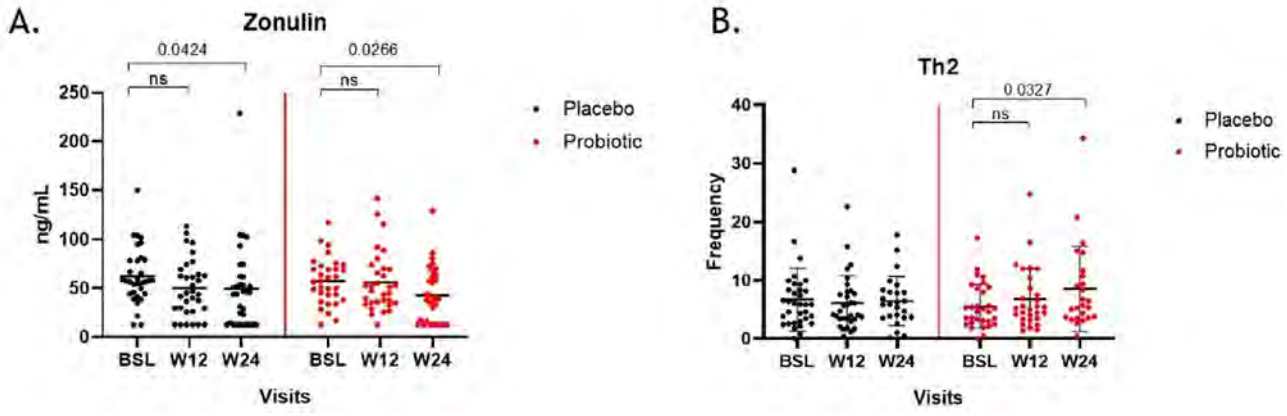

Fig2. A. Changes in concentration of zonulin in stool samples at different time points as measured by ELISA (ng/ML). B. Frequency of Th2 cells at different time points in both intervention groups as a frequency of the parent population. In both graphs black dots denote placebo group and red denotes probiotic group.

Results: A total of 65 patients were recruited and off these 32 patients were randomized into the probiotic group and 34 patients into the placebo group. A significant reduction in disease activity was observed as measured by the PASDAS score in both groups irrespective of probiotic intervention (Fig1). The proportion of patients reaching low DA or remission was not different between probiotic and placebo (55.8% vs 40.63%). A significant reduction in zonulin levels was observed in the probiotic group at W24 compared to BSL, whereas only a slightly weaker effect was seen in the placebo group (Fig2A). Results from immune cell phenotyping, revealed a significant increase in the frequency of Th2 cells in the probiotic group at W24 (Fig2B). No significant differences were observed in the frequencies of other lymphocyte subsets like Th1, Th17 and Tregs.

Conclusion: In this double-blind RCT, supplementation of probiotics in PsA patients showed limited effects on the dysbiosis of the gut measured by marker Zonulin and also had minor effects on the T-cell composition. However, no difference was seen in the amelioration of disease activity compared to placebo treatment, which could be due to the small samples size and the short recording period of the trial.

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Abstract Number: 0779

Influence of Sex on the Persistence of Different Classes of Targeted Therapies for Psoriatic Arthritis: A Cohort Study of 14,778 Patients from the French Health Insurance Database (SNDS)

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SESSION INFORMATION
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Session Type: Abstract Session
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Background/Purpose: Psoriatic arthritis (PsA) is a heterogeneous condition and sex differences in phenotypic presentation, disease trajectory, and treatment response have been reported. Nevertheless, it remains unclear whether classes of targeted therapies differentially impact men and women with PsA.

Our objective was to assess the influence of sex on the long-term persistence of each class of targeted therapies in a national healthcare database.

Methods: This nationwide cohort study involved the administrative healthcare database of the French health insurance scheme linked to the hospital discharge database (SNDS). We included all adults with PsA, new users of targeted therapies (not in the year before the index date) during 2015-2021, and studied each different treatment line during the study. Persistence was defined as the time from treatment initiation to discontinuation and was estimated by the Kaplan-Meier method. Comparison of persistence by sex involved using multivariate frailty model and adjusting on csDMARDs and prednisone as time-dependant variables. Similar analyses were performed in patients receiving first-line targeted therapy only. To control the risk of type 1 error, a Bonferroni adjustment was applied: a $p \leq 0.01$ was considered significant, and 99% confidence intervals (CI) were calculated.

Table: Comparison of targeted therapies persistence by sex and therapeutic classes

	Women vs. Man	
	HR_a (99%CI)	p-value
All lines		
TNFi n = 15,654	**1.39 (1.32-1.47)**	**<10^{-4}**
IL17i n = 6,195	**1.18 (1.08-1.29)**	**<10^{-4}**
IL12/23i n = 2,809	1.14 (0.97-1.33)	0.03
IL23i n = 798	1.07 (0.75-1.52)	0.64
JAKi n = 863	1.21 (0.89-1.63)	0.11
First line		
TNFi n = 10,407	**1.48 (1.38-1.58)**	**<10^{-4}**
IL17i n = 2,310	**1.40 (1.18-1.65)**	**<10^{-4}**
IL12/23i n = 1,541	1.17 (0.97-1.41)	0.03
IL23i n = 287	1.57 (0.74-3.32)	0.12
JAKi n = 233	1.00 (0.51-1.83)	0.95

Adjusted for age, morbid or complicated obesity, smoking (proxy), alcohol (proxy), Charlson comorbidity index, hospitalization for psoriatic arthritis within 2 years, consultations with a rheumatologist within 2 years, csDMARDs at index date, NSAIDs at index date, prednisone at index date, csDMARDs within 2 years, NSAIDs within 2 years, and prednisone within 2 years, and then on prednisone and csDMARDs as time-dependent variables. Values in bold correspond to significant results: the p value is considered significant if <0.01 (Bonferroni correction). *TNFi: tumor necrosis factor inhibitor; ILi: interleukin inhibitor; JAKi: Janus Kinase inhibitor; HR_a: adjusted hazard ratio; 99%CI: 99% confidence interval.*

Results: We included 14,778 patients with PsA new users of targeted therapies: 8,475 (57%) women (mean age 50 ±13 years), 6,303 (43%) men (51±13 years). The number of lines of therapy were: within women, 9,462 (60%) TNF inhibitors (TNFi), 3,762 (24%) IL17i, 1,639 (10%) IL12/23i, 392 (2%) IL23i, 576 (4%) JAKi, and within men 6,192 (59%) TNFi, 2,433 (23%) IL17i, 1,170 (11%) IL12/23i, 406 (4%) IL23i and 287 (3%) JAKi. Overall, 1-year persistence rates were 52% for women and 62% for men. Persistence decreased markedly over time in both sexes to 27% and 39% respectively at the end of the third year, although in varying proportions by therapeutic class. After adjustments, persistence was statistically lower in women than in men for TNFi (adjusted hazard ratio (HR_a) 1.4, 99%CI 1.3-1.5) and IL17i (HR_a 1.2, 99%CI 1.1-1.3), but not for IL12/23i (HR_a 1.1, 99%CI 0.9-1.3), IL23i (HR_a 1.1, 99%CI 0.7-1.5) and JAKi (HR_a 1.2, 99%CI 0.9-1.6). Results were similar for patients receiving first-line therapy (*Table*).

Conclusion: Treatment persistence is lower in women than in men for TNFi and IL17i, but no longer significant for IL12/23i, IL23i and JAKi. This may be due to differences in rheumatic phenotype, disease activity/severity or immunogenicity, but also to disparities in healthcare-seeking behavior due to gender norms. This highlights the need for sex- and gender-based studies to better understand the underlying mechanisms, but also for face-to-face studies with sex-stratified analyses to optimize the management of PsA patients and achieve the ambitious goal of personalized medicine in the coming years.

Disclosure: L. PINA VEGAS: None; **L. Penso**: None; **E. Sbidian**: None; **p. claudepierre**: AbbVie/Abbott, 2, Amgen, 2, Biogen, 6, Bristol-Myers Squibb(BMS), 2, 4, Celltrion, 6, Eli Lilly, 2, Galapagos, 2, Janssen, 2, Merck/MSD, 2, 4, Novartis, 2, 4, Pfizer, 2, 4, Roche, 2, 4, UCB, 2.

Abstract Number: 0780

Assessing Differential Effects of DMARDs on Psoriasis Area and Severity Index and Patient Global Assessment in Subgroups of Patients with Active PsA Treated over 52-weeks with Secukinumab in a Non-Interventional Trial (AQUILA) Using a Multistage Clustering Approach

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment I: PsA

Session Type: Abstract Session

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Background/Purpose: Individualized treatment strategies are of high importance in the treatment of patients with active psoriatic arthritis (PsA), a heterogeneous immune-mediated disease. IL-17 inhibition has demonstrated efficacy in all domains of PsA. Nevertheless, approx. 30% of patients will not achieve remission after initiation of therapy. Therefore, the identification of patient characteristics with a high impact on treatment response is important to guide treatment choice and its adjustments in clinical routine care to promote an improved outcome. An adapted machine learning approach (cluster analysis) was used to analyze baseline (BL) patient characteristics to detect clinical patterns of disease activity in PsA patients treated in a non-interventional trial with secukinumab (SEC).

Methods: Data from 1257 patients from the German non-interventional study AQUILA with active PsA whose first SEC treatment occurred no more than 4 weeks prior to BL was analyzed. All patients were included irrespective of treatment response. We identified patient groups by applying an extended version of the machine learning method of hierarchical density-based clustering to the BL data, where features included patient and disease characteristics variables as well as standardized patient-reported outcomes (Table 1). Feature groups with high numbers of missing values were initially excluded, and subsequent clustering was performed to achieve stepwise integration of all features. At each step, an additional feature group was included in a re-clustering using a complete subset of subjects. This led to a further split of some of the original clusters. For every final cluster, disease activity over the course of the study was visualized including patient and physician-derived assessments.

Results: The machine learning approach resulted in the categorization of 14 different clusters of patients and outliers (n=391, cluster -1) (Fig. 1). The focus is directed towards two medically relevant clusters that differ primarily in their pretreatments prior to SEC. Cluster 1 included PsA patients with predominantly bDMARD pretreatment incl. IL-23-inhibitors, while cluster 2 primarily received csDMARD pretreatments including apremilast (Fig. 2). Cluster 1, showed a greater reduction in disease activity than cluster 2 as measured by PASI and PGA (mean reduction: PASI: cluster 1: 8.0, cluster 2: 5.6; PGA: cluster 1: 2.8, cluster 2: 2.4) by week 52 (Fig. 2). However, these comparisons did not reach statistical significance for this sample.

Conclusion: We present a machine-learning approach to exploring the association between BL features of patients treated with SEC and their disease activity scores in the large PsA cohort of the AQUILA trial. The cluster analysis revealed that pretreatment with bDMARDs did not affect the efficacy of SEC compared to the predominantly csDMARD patient cohort

Table 1: Overview of dataset characteristics of 1,257 PsA patients at baseline, across all 14 clusters. *Total n can differ from 1,257 in table, due to missing values, ** stroke, chronic heart failure or coronary heart disease, *** for enthesitis patients only

Baseline Criteria	Total n =1,257 *
Age, [years] (median) (n=1,257)	47.9
BMI, [kg/m²] (median) (n=1,225)	28.4
Active Smokers (n=1,158)	321
Ex Smokers (n=1,158)	218
bDMARD -naïve	572
Previous TNF	647
Previous Abatacept	22
Previous Ixekizumab	7
Previous IL-23	135
Previous JAKi	3
Previous csDMARDs	931
Previous Apremilast	137
Glucocorticoids Concomitant	344
csDMARDs Concomitant	377
MTX Concomitant	350
Depression (n=1,195)	209
Uveitis (n=1,223)	21
Cardiovascular**	117
Enthesitis (n=422)	98
LEI (median)*** (n= 422)	2.0
PhGA (median) (n=1,160)	5.9
PGA (median) (n=870)	6.0
PsAID-12 (median) (n=1,184)	5.0
CRP [mg/dl] (median) (n=646)	3.8
PASI (median) (n= 474)	3.0
Tender joint count 68 (median) (n= 844)	5.0
Swollen joint count 66 (median) (n= 845)	2.0

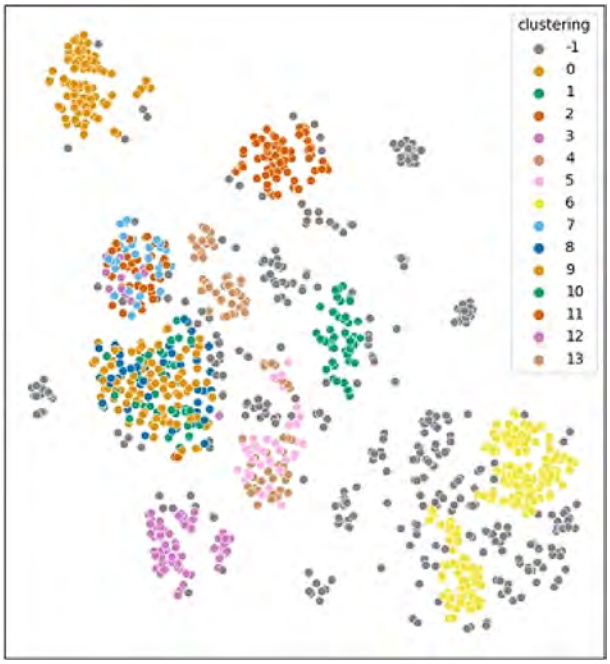

Figure 1: Result of multistage clustering of BL characteristics of 1,257 active PSA patients. The clustering reveals 14 clusters and outliers (cluster –1). Important cluster characteristics: Cluster 1, pretreatment with bDMARDs (including IL-23i); Cluster 2, pretreatment with csDMARDs (including apremilast). The scatterplot of the patient characteristics is created by the dimension reduction TSNE to 2 dimensions and thus has, resulting in arbitrary units on the axes.

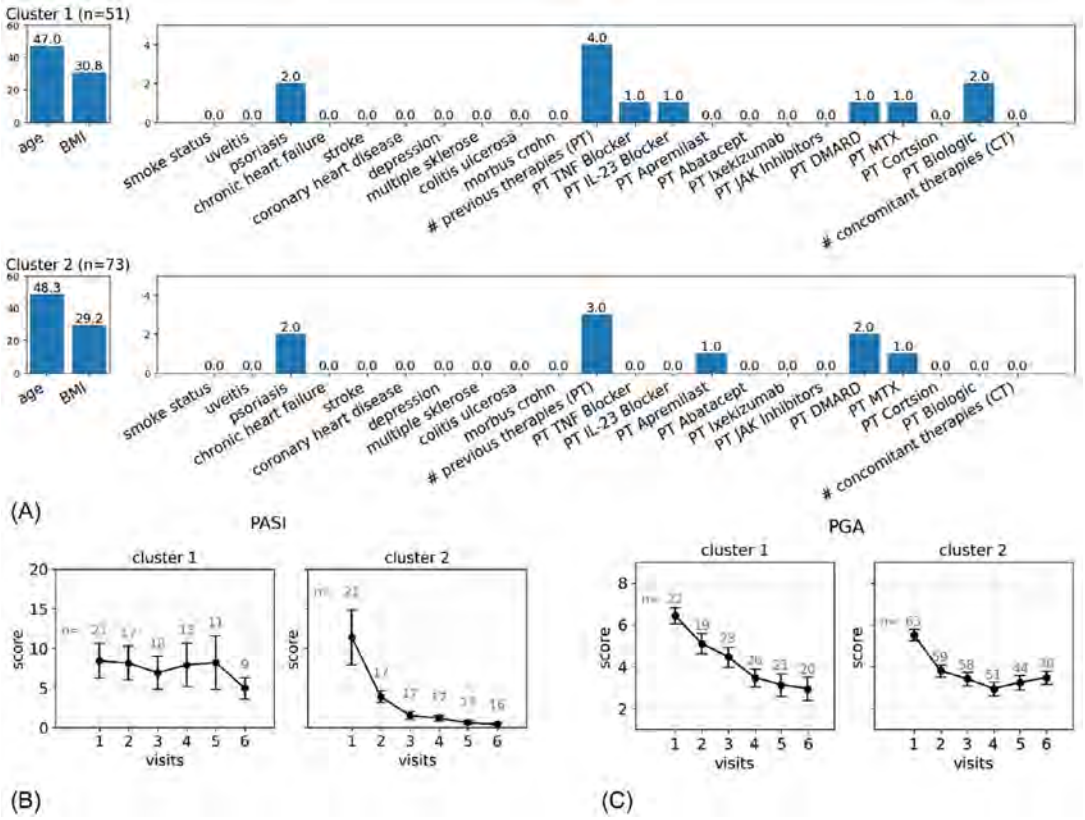

Figure 2 (A) Median BL characteristics of patients of cluster 1 and cluster 2 (B) Mean PASI with standard error of patients of cluster 1 and cluster

(predominantly bDMARD naïve). PASI and PGA tend to have a stronger improvement in patients pretreated with bDMARDs than in patients pretreated with csDMARDs including apremilast after 52 weeks of treatment with SEC.

Disclosure: M. Koehm: Janssen, 2, 5, 6, Novartis GmbH, 2, 5, 6; **M. Klippstein**: Novartis GmbH, 5; **S. Kugler**: Novartis GmbH, 5; **S. Mackay**: Novartis GmbH, 5; **D. Schulz**: Novartis GmbH, 5; **A. Vodencarevic**: Novartis, 3; **G. Wendt**: Novartis GmbH, 3; **D. Peterlik**: Novartis, 3; **U. Kiltz**: AbbVie, 2, 5, 6, Amgen, 5, Biocad, 2, 6, Biogen, 5, Bristol-Myers Squibb(BMS), 2, 5, Chugai, 2, 6, Eli Lilly, 2, 6, Fresenius, 5, Gilead, 2, 5, GlaxoSmithKline (GSK), 5, Grünenthal, 2, 6, Hexal, 5, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, onkowiessen.de, 2, 5, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Viatris, 2, 5; **J. Brandt-Juergens**: AbbVie/Abbott, 2, 6, Affibody, 2, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Gilead, 2, Janssen, 2, 6, Medac, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **F. Behrens**: AbbVie/Abbott, 2, 5, 6, Affibody, 2, Amgen, 2, 5, 6, Bionorica, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Chugai Pharma GmbH, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Genzyme, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Iron4u, 2, 5, 6, Leo, 2, 5, 6, Merck/MSD, 2, 5, 6, Moon-Lake, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sandoz, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0781

Low vs. High Initial Oral Glucocorticoid Dose for Lupus Nephritis Induction Treatment: A Pooled Analysis of Randomized Controlled Clinical Trials

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: SLE – Treatment I: Renal

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Traditional induction treatment regimens for proliferative or membranous lupus nephritis (LN) have utilized oral glucocorticoids (GC) in initial doses up to 1.0 mg/kg/day prednisone equivalent with or without a preceding intravenous (IV) methylprednisolone pulse. More recent management guidelines have recommended lower starting oral GC doses following a short IV steroid course, with several clinical trials suggesting this protocol may yield similar results to those using higher GC doses. As there have been no large studies directly comparing responses in patients receiving low vs. high initial oral GC doses for LN treatment, this pooled analysis of randomized controlled trials (RCTs) aims to evaluate differences in efficacy and safety among these groups.

Table 1. Demographics and Outcomes in Standard of Care Arm of Lupus Nephritis RCTs Using Low Initial Oral Glucocorticoid Doses

	Voclosporin Phase II[a]	Voclosporin Phase III[a]	Obinituzumab Phase II[b]	Anifrolumab Phase II[c]	Total
Year Published	2019	2021	2022	2022	
Inclusion Criteria LN Class	III/IV (+/- V) or pure V	III/IV (+/- V) or pure V	III/IV (+/- V)	III/IV (+/- V)	
Inclusion Criteria UPCR	>1.5 mg/mg (>2.0 mg/g pure V)	>1.5 mg/mg (>2.0 mg/g pure V)	>1.0 mg/mg	>1.0 mg/mg	
Mandatory Initial IV Methylpred	500-1000 mg (physician discretion)	500-1000 mg (physician discretion)	1000-3000 mg (physician discretion)	500 mg	
Starting Oral Prednisone Dose	20-25 mg (based on weight)	20-25 mg (based on weight)	0.5 mg/kg/day	0.5 mg/kg/day	
Mandatory Prednisone Taper	≤2.5 mg/d by week 16	≤2.5 mg/d by week 16	≤7.5 mg/d by week 12	≤7.5 mg/d by week 12	
Background Med and Target Dose	MMF 2.0 g	MMF 2.0 g	MMF 2.0-2.5 g (physician discretion)	MMF 2.0 g	
Final Week of Study	48	52	104	52	
N (Standard of Care Arm)	88	178	62	49	377
White Race	42 (47.7%)	61 (34.3%)	26 (41.9%)	24 (49.0%)	153 (40.6%)
Hispanic Ethnicity	13 (14.8%)	59 (33.1%)	49 (79.0%)	20 (40.8%)	141 (37.4%)
Baseline UPCR, mean (SD)	4.4 (3.6)	3.9 (2.4)	2.9 (2.5)	3.7 (3.2)	
Baseline UPCR >3.0 mg/mg	N/A	N/A	20 (32.2%)	23 (46.9%)	43/111 (38.7%)
ACE-I/ARB at Baseline	53 (60.2%)	120 (67.4%)	N/A	33 (67.3%)	206/315 (65.4%)
CRR with UPCR <0.5 mg/mg	22 (25.0%)	40 (22.5%)	14 (22.6%)	12/45 (26.7%)	88/373 (23.6%)
UPCR <0.5 mg/mg	24 (27.3%)	41 (23.0%)	23 (37.1%)	N/A	88/328 (26.7%)
CRR or PRR	42 (47.7%)	92 (51.7%)	18 (29.0%)	N/A	152/328 (46.3%)
Serious Adverse Event	14 (15.9%)	38 (21.3%)	18 (29.0%)	8 (16.3%)	78 (20.7%)
Infection SAE	7 (8.0%)	20 (11.2%)	11 (17.7%)	N/A	38/328 (11.6%)

RCT: Randomized Controlled Trial; LN: Lupus Nephritis; UPCR: Urine protein/creatinine ratio; IV: Intravenous; MMF: Mycophenolate mofetil; SD: Standard deviation; N/A: Not available; ACE-I: Ace Inhibitor; ARB: Angiotensin II Receptor Blocker; CRR: Complete renal response; PRR: Partial renal response; SAE: Serious adverse event; ULN: Upper limit of normal; RBC: Red blood cell; HPF: High powered field

a) CRR: UPCR ≤0.5 mg/mg, eGFR ≥60 mL/min/1.73 m^2 or no confirmed eGFR decrease >20% from baseline, no rescue medication, and ≤10 mg prednisone equivalent per day for ≥3 consecutive days or for ≥7 days in total during weeks 44 through 52
PRR: ≥50% reduction from baseline UPCR

b) CRR: UPCR <0.5 mg/mg, normal renal function (serum creatinine ≤ULN) without worsening of baseline serum creatinine by >15%, and inactive urinary sediment (<10 RBC/HPF without RBC casts)
PRR: ≥50% reduction in UPCR from baseline to a value <1 mg/mg (to <3 mg/mg if baseline UPCR was ≥3 mg/mg), serum creatinine not increased >15% from baseline and urinary RBCs <10/HPF or ≤50% increase over baseline value

c) CRR: 24-hour UPCR <0.5 mg/mg, eGFR ≥60 mL/min/1.73 m^2 or no decrease ≥20% from baseline, no investigational product discontinuation and no use of restricted medications

Table 2. Demographics and Outcomes in Standard of Care Arm of Lupus Nephritis RCTs Using High Initial Oral Glucocorticoid Doses

	Rituximab Phase III [a]	Ocrelizumab Phase III [b]	Abatacept Phase II [c]	Abatacept Phase II/III [d]	Belimumab Phase III [e]	Total
Year Published	2012	2013	2014	2014	2020	
Inclusion Criteria LN Class	III/IV (+/- V)	III/IV (+/- V)	III/IV (+/- V)	III/IV (+/- V)	III/IV (+/- V) or pure V	
Inclusion Criteria UPCR	>1.0 mg/mg	≥0.44 mg/mg (with active sediment)	>1.0 mg/mg	>1.0 mg/mg	>1.0 mg/mg	
Mandatory Initial IV Methylpred	2000 mg	None	None	None	None	
Starting Oral Prednisone Dose	0.75 mg/kg/day	0.5-0.75 mg/kg/day	60 mg	0.8 mg/kg/day	0.5-1.0 mg/kg/day	
Mandatory Prednisone Taper	≤10 mg/d by week 16	≤10 mg/d by week 10	≤10 mg/d by week 10	N/A	≤10 mg/d by week 24	
Background Med and Target Dose	MMF 3.0 g	MMF 3.0 g or Euro Lupus CYC + aza 2.0 mg/kg	Euro Lupus CYC + aza 2.0 mg/kg	MMF 1.5 g in China MMF 2.0 g in White MMF 3.0 g in AA	MMF 3.0 g or Euro Lupus CYC + aza 2.0 mg/kg	
Final Week of Study	52	48	24	52	104	
N (Standard of Care Arm)	72	126	68	100	223	589
White Race	26 (36.1%)	58 (46.0%)	33 (48.5%)	38 (38.0%)	75 (33.6%)	230 (39.0%)
Hispanic Ethnicity	23 (31.9%)	51 (40.5%)	28 (79.0%)	20 (41.2%)	N/A	102/268 (38.3%)
Baseline UPCR, mean (SD)	4.2 (3.2)	N/A	4.1 (3.4)	3.6 (2.9)	3.5 (3.6)	
Baseline UPCR >3.0 mg/mg	42 (58.3%)	58 (46.0%)	31 (45.6%)	45 (45.0%)	92 (41.3%)	268 (45.5%)
ACE-I/ARB at Baseline	N/A	N/A	N/A	49 (49.0%)	150 (67.2%)	199/333 (59.8%)
CRR with UPCR <0.5 mg/mg	22 (30.6%)	26/75 (34.7%)	21 (30.9%)	20 (20%)	44 (19.7%)	133/538 (24.7%)
UPCR <0.5 mg/mg	N/A	28/75 (37.3%)	N/A	N/A	64 (28.7%)	92/298 (30.9%)
CRR or PRR	33 (45.8%)	41/75 (54.7%)	40 (58.8%)	34 (34.0%)	82 (36.8%)	230/538 (42.8%)
Serious Adverse Event	29 (40.6%)	34/125 (27.2%)	20 (29.4%)	31 (31.0%)	67 (30.0%)	181 (30.7%)
Infection SAE	14 (19.7%)	18/125 (14.4%)	N/A	17 (17.0%)	N/A	49/298 (16.4%)

ACT: Rituximab Controlled Trial; LN: Lupus Nephritis; UPCR: Urine protein/creatinine ratio; IV: Intravenous; N/A: Not available; MMF: Mycophenolate mofetil; CYC: Cyclophosphamide; Aza: Azathioprine; AA: African American; SD: Standard deviation; ACE-I: Ace inhibitor; ARB: Angiotensin II Receptor Blocker; CRR: Complete renal response; PRR: Partial renal response; SAE: Serious adverse event; ULN: Upper limit of normal; RBC: Red blood cells; HPF: High powered field

a) CRR: Normal serum creatinine level if abnormal at baseline, or a serum creatinine level of ≤115% of baseline if normal at baseline, inactive urinary sediment (<5 RBCs/HPF and absence of RBC casts), and UPCR <0.5 mg/mg
PRR: serum creatinine level ≤115% of baseline, RBCs/HPF ≤50% above baseline and no RBC casts and at least a 50% decrease in the UPCR to <1.0 mg/mg (if baseline UPCR ≥1.0 mg/mg) or to ≤1.0 (if baseline UPCR <1.0 mg/mg)

b) CRR: Normal serum creatinine (≤25% increase from baseline) and improvement in UPCR to <0.5 mg/mg
PRR: Serum creatinine ≤25% above baseline, and 50% improvement in UPCR, and if baseline ratio >3.0 mg/mg, then UPCR <3.0 mg/mg

c) CRR: UPCR <0.5 based on 24-hour urine collection, serum creatinine ≤1.2 mg/dL or ≤125% of baseline, and adherence to the prednisone taper to 10 mg/d by week 12
PRR: 50% reduction of UPCR based on a 24-hour urine collection, serum creatinine ≤1.3 mg/dl, or ≤104% of baseline, adherence to the prednisone taper to 10 mg/d by week 12

d) CRR: UPCR <0.5 mg/mg and inactive urinary sediment
PRR: Serum creatinine level normal or ≤125% of baseline; UPCR <50% of baseline and <3.0 mg/mg if nephrotic, or <1.0 mg/mg if non-nephrotic; urinary sediment inactive or >50% reduction in RBC/HPF from baseline

e) CRR: UCR% <2.5 mg/mg, eGFR that is ≤15% below the pre-flare value or at least 60 ml/min/1.73 m^2, and no rescue therapy
PRR: eGFR ≤10% below baseline value or within normal range and ≥50% decrease in the ratio of UPCR with one of the following: UPCR <1.0 mg/mg if the baseline ratio was ≥3.0 mg/mg, or a UPCR <3.0 mg/mg if the baseline ratio was >3.0 mg/mg; no treatment failure; not a complete renal response.

Methods: Published data was analyzed from RCTs that assessed variable doses of GC and an experimental LN treatment with standard of care (SOC) compared to GC and SOC alone. SOC regimens consisted of either mycophenolate mofetil or Euro-Lupus cyclophosphamide followed by azathioprine. Patients from SOC arms receiving a starting prednisone dose of up to 0.5 mg/kg/day (low dose) were compared to those receiving up to 1.0 mg/kg/day (high dose). Complete renal response 0.5 (CRR 0.5) was defined as patients with urine protein/creatinine ratio (UPCR) < 0.5 mg/mg at study completion, along with other parameters that varied between studies (Tables 1, 2). CRR 0.5, serious adverse events (SAE), and where available, isolated UPCR < 0.5 mg/mg, partial renal response (PRR, defined in Tables 1, 2) and SAE due to infections were compared between groups using Fischer's exact tests.

Results: 377 patients from the SOC arms of 4 studies were exposed to low dose initial GC while 589 patients from 5 studies were treated with high dose GC. LN class and UPCR required for inclusion were generally similar across studies, as were baseline characteristics including white race and, where reported, Hispanic ethnicity, UPCR and percentages on ACE-I/ARB medications (Tables 1, 2). All low dose oral GC studies required an IV steroid pulse compared to only one high dose study. In patients receiving initial low dose oral GC, 23.6% achieved CRR 0.5 at the end of study compared to 24.7% in high dose patients (p=0.75). In reports with available data, similar percentages were seen between groups for isolated UPCR < 0.5 mg/mg (26.7% low dose vs. 30.9% high dose, p=0.29) and CRR or PRR (46.3% low dose vs. 42.8% high dose, p=0.32). SAEs were less common in patients receiving lose dose GC, present in 20.7% compared to 30.7% in high dose patients, p=0.0006. In studies reporting SAE due to infection, low dose GC patients had less frequent events (11.6% vs. 16.4%, p=0.08).

Conclusion: Based on data pooled from multiple published trials utilizing SOC treatment for LN, there is no significant difference in renal responses between patients receiving IV steroid followed by low dose prednisone compared to those receiving high prednisone doses as initial oral GC during induction. Serious adverse events were less frequent in patients receiving low

dose initial GC, although other study-specific considerations may factor in that association. These findings support the use of lower oral GC doses in LN treatment.

Disclosure: A. Saxena: AbbVie, 1, AstraZeneca, 1, GSK, 1; **P. Izmirly**: None; **J. Law**: None; **C. Sorrento**: None; **H. Belmont**: Alexion, 6, Aurinia, 6; **J. Buyon**: Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, Related Sciences, 1.

Abstract Number: 0782

Comparison of Dual-immunosuppressive Therapy with a Voclosporin-based, Triple-immunosuppressive Regimen for Lupus Nephritis in the ALMS and AURORA 1 Studies

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Abstracts: SLE – Treatment I: Renal
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Dual-immunosuppressive regimens consisting of high-dose glucocorticoids and higher doses (>2 g/day) of mycophenolate mofetil (MMF) are still frequently used for the initial management of active lupus nephritis (LN) despite the known serious and dose-dependent safety risks associated with both of these agents.

To understand the safety and efficacy of a voclosporin-based, MMF and glucocorticoid-sparing, triple immunosuppressive regimen as an initial approach to treatment in active LN compared to more conventional regimens, we compared and analyzed safety and efficacy data in propensity-matched patients from the ALMS and AURORA 1. We hypothesized that a

Table 1 Key Baseline Disease Characteristics

Parameter	ALMS N=96	AURORA 1 N=96
Duration of SLE, years		
Mean (SD)	5.33 (5.5)	5.18 (6.2)
Albumin, g/dL		
Mean (SD)	2.9 (0.6)	2.8 (0.7)
UPCR, g/g		
Mean (SD)	4.2 (4.5)	4.3 (2.9)
C3, mg/dL		
Mean (SD)	76.8 (29.53)	79.1 (34.3)
Low <90 mg/dL, n (%)	66 (68.8)	59 (61.5)
C4, mg/dL		
Mean (SD)	15.6 (12.3)	15.8 (10.0)
Low <10 mg/dL, n (%)	37 (38.5)	31 (32.3)
anti-dsDNA, IU/mL		
Mean (SD)	117.9 (93.2)	118.3 (133.6)
High >10 IU/mL, n (%)	94 (97.9)	77 (80.2)

Propensity score methodology was used to generate two groups of matched patients (n=96) from the ALMS and AURORA 1 studies based on the following parameters: age, duration of lupus nephritis, duration of SLE, albumin, C3, C4, creatinine, anti-dsDNA, eGFR, UPCR, biopsy class, sex, and geographical region.
Anti-dsDNA, anti-double strand deoxyribonucleic acid; C3, complement 3; C4, complement 4; SLE, systemic lupus erythematosus; SD, standard deviation.

voclosporin-based, triple immunotherapy approach would reduce patient exposure to the toxicities associated with glucocorticoids and MMF, resulting in an improved safety profile without compromising efficacy.

Methods: Both studies enrolled patients with active LN. In ALMS, MMF was dosed to a target of 3 g/day with oral glucocorticoids initiated at a maximum dose of 60 mg/day and tapered every 2 weeks to 10 mg/day. In AURORA 1, patients received voclosporin 23.7 mg BID in combination with MMF (target dose 2 g/day) and oral glucocorticoids (starting dose of 25 mg/day tapered to 2.5 mg/day by Week 16). Propensity score matching was used to generate two groups of matched patients based on a set of demographic and disease characteristics. Safety and efficacy outcomes were assessed at 3 and 6 months.

Results: Propensity matching identified 96 pairs of patients with similar demographics and baseline disease characteristics (Table 1). At 3 and 6 months, MMF and glucocorticoid exposure was more than two-fold higher in ALMS than AURORA 1. Overall, fewer adverse events were observed in AURORA 1 across the majority of organ systems, including gastrointestinal, skin and subcutaneous tissues, endocrine, and psychiatric disorders, although more patients in AURORA 1 were reported to experience GFR decrease (Table 2). The incidence of serious adverse events was similar in both groups at 3 and 6 months. In the first 3 months, significantly more patients in AURORA 1 achieved >25% UPCR reduction from

Table 2. Treatment Exposure and Safety Outcomes

	3 Months		6 Months	
	ALMS N=96	AURORA 1 N=96	ALMS N=96	AURORA 1 N=96
Glucocorticoid and MMF Exposure				
Glucocorticoid daily dose, mg Mean (SD)	21.81 (5.8)	6.13 (3.7)	10.12 (2.8)	5.08 (11.2)
Cumulative glucocorticoid exposure, mg Mean (SD)	2849.8 (544.6)	1104.9 (142.8)	3818.5 (777.5)	1502.3 (410.0)
MMF daily dose, mg Mean (SD)	2.8 (0.55)	1.9 (0.5)	2.8 (0.4)	1.9 (0.6)
Cumulative MMF exposure, mg Mean (SD)	209.8 (45.2)	161.8 (33.5)	414.3 (117.9)	322.0 (74.3)
Adverse Events (AE), n (%)				
Any AE	89 (92.7)	81 (84.4)	92 (95.8)	88 (91.7)
Serious AE (SAE)	18 (18.8)	13 (13.5)	22 (22.9)	18 (18.8)
Treatment-related SAE	9 (9.4)	4 (4.2)	11 (11.5)	6 (6.3)
Disease-related AE	55 (57.3)	35 (36.5)	63 (65.6)	44 (45.8)
AE leading to study drug discontinuation	7 (7.3)	4 (4.2)	10 (10.4)	7 (7.3)
Fatal AE	3 (3.1)	0 (0.0)	3 (3.1)	0 (0.0)
Select AEs by System Organ Class, n (%)				
Infections and infestations	57 (59.4)	45 (46.9)	69 (71.9)	60 (62.5)
Serious infections and infestations	9 (9.4)	7 (7.3)	12 (12.5)	8 (8.3)
Gastrointestinal disorders	49 (51.0)	30 (31.3)	57 (59.4)	38 (39.6)
Musculoskeletal/connective tissue disorders	38 (39.6)	17 (17.7)	45 (46.9)	22 (22.9)
Skin and subcutaneous disorders	30 (31.3)	17 (17.7)	41 (42.7)	22 (22.9)
Renal/urinary disorders	6 (6.3)	8 (8.3)	11 (11.5)	11 (11.5)
Psychiatric disorders	16 (16.7)	2 (2.1)	16 (16.7)	4 (4.2)
Select AEs by Preferred Term, n (%)				
GFR decreased	0	16 (16.7)	0	20 (20.8)
Hypertension	11 (11.5)	14 (14.6)	14 (14.6)	16 (16.7)
Hyperglycemia	5 (5.2)	0	5 (5.2)	0
Cushingoid/Cushing's syndrome	8 (8.3)	0	8 (8.3)	0

Based on data from 96 patients from ALMS and AURORA 1 matched using propensity scoring. Adverse events occurred on or after the first dose of study drug up to either 3 or 6 months of treatment. Adverse events are coded using MedDRA v 9.1 (ALMS) and v20.0 (AURORA 1). MMF, mycophenolate mofetil; SD, standard deviation.

Table 3. Efficacy Outcomes at 3 and 6 Months

	ALMS N=96	AURORA 1 N=96
At 3 Months		
UPCR reduction >25%, n (%)	63 (65.6)	78 (81.3)
OR (95% CI) vs ALMS, p-value	2.50 (1.23, 5.08) 0.0110	
At 6 Months		
UPCR ≤0.5 g/g, n (%)	25 (26.0)	36 (37.5)
OR (95% CI) vs ALMS, p-value	1.85 (0.94, 3.65) 0.0752	
UPCR reduction >50%, n (%)	61 (63.5)	69 (71.9)
OR (95% CI) vs ALMS, p-value	1.54 (0.8, 2.95) 0.1956	

Based on data from 96 patients from ALMS and AURORA 1 matched using propensity scoring. CI, confidence interval; MMF, mycophenolate mofetil; OR, odds ratio; UPCR, urine protein creatinine ratio.

baseline (p=0.011; Table 3); the proportions of patients achieving UPCR ≤0.5 g/g and >50% UPCR reduction from baseline were numerically greater in the voclosporin arm; the differences were not statistically significant.

Conclusion: Patients treated with voclosporin in combination with low-dose glucocorticoids and lower-dose MMF demonstrated an improved safety profile and earlier reductions in proteinuria compared to patients treated with high-dose glucocorticoids and higher doses of MMF. These findings affirm the KDIGO 2023 recommendation that a voclosporin-based, triple-immunotherapy regimen should be considered as an initial therapy in patients with active LN.

Disclosure: M. Dall'Era: Annexon Biosciences, 2, 5, AstraZeneca, 2, Aurinia, 2, Biogen, 2, GlaxoSmithKlein, 2, 5, Pfizer, 2; **E. Yap**: Aurinia Pharmaceuticals, 3, 11; **M. Truman**: Aurinia Pharmaceuticals, 2; **L. Hodge**: Aurinia, 3, 11; **N. Solomons**: Aurinia, 2, 3, 11.

Abstract Number: 0783

Tolerability of CAR T Cell Therapy in Autoimmune Disease

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Abstracts: SLE – Treatment I: Renal
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: We have previously shown that CD19 CAR T cell therapy can lead to improvement of severe forms of B cell mediated autoimmune disease including SLE (1,2), idiopathic inflammatory myopathy (IIM) (3) and systemic sclerosis (SSc) (4). In hematologic malignancies, CD19 CAR T cell therapy is often associated with side effects such as cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). We therefore addressed

the incidence, severity and reversibility of CRS and ICANS in patients with autoimmune disease receiving CD19 CAR T cell therapy.

Methods: Patients with active and treatment-refractory SLE, IIM and SSc received a single infusion of 1 million CD19 CAR T cells manufactured from autologous T cells and transfected with the lentiviral vector MB-CART19.1 (Miltenyi) encoding the CD19 CAR. Immunosuppressive treatment was stopped before CAR T cell infusion. Standard conditioning treatment (1g/m2 cyclophosphamide, 75 mg fludarabine) was administered before CAR T cell infusion. Incidence, severity and reversibility of CRS and ICANS were monitored during the first 14 days after infusion. CRS was graded as 1 (fever), 2 (hypotension), 3 (one vasopressor, high-ventilation) and 4 (multiple vasopressors, positive airway pressure). ICANS was graded as 1 (dizziness, fatigue), 2 (somnolence, delirium), 3 (spoor, seizures) and 4 (coma). In addition, reversibility of CRS and ICANS in response to anti-pyretic drugs and/or tocilizumab was documented.

Results: Between March 2021 and June 2023 15 patients (mean ± SD age: 35,7± 11,2 years) received treatment with CD19 CAR T cell therapy (8 SLE, 3 IIM and 4 SSc). SLE patients were younger (28.0 ± 7.2) than IIM (43.0 ± 1.0) and SSc patients (45.7 ± 11.1 years). CRS was observed in 60% (9/15) and was graded mild (grade 1) in 8/9 cases (4 SLE, 2 IIM and 2 SSc) and moderate (grade 2) in 1/9 cases (1 IIM). The moderate CRS was based on pre-existing dyspnea based on interstitial lung disease, which worsened during the fever bout and required oxygen treatment for one day. CRS events happened between day 1 and day 4 after CAR T cell therapy. CRS resolved fast after using anti-pyretic drugs. Tocilizumab was given in 40% (6/15) of the patients, mostly as single infusion, which lead to immediate resolution of CRS. Only one patient received three tocilizumab infusions. Mild ICANS (1IIM) was observed in one patient, presenting with dizziness 7 days after infusion. The patient received a short course of glucocorticoids, which led to resolution of ICANS. The cases of CRS grade 2, ICANS grade 1 and repeated tocilizumab treatment occurred in different patients.

Conclusion: Overall safety of CD19 CAR T cells therapy in autoimmune disease appears to be high. Low-grade CRS is frequent but can be managed well. Higher grade CRS was not found and seems to be infrequent. Also ICANS appears to be infrequent in patients with autoimmune disease. Tolerability of CD19 CAR T cell therapy seems to be similar in SLE, IIM and SSc and no influence of age was observed.

1. Mougiakakos D, et al. N Engl J Med. 2021; 385:567-9.
2. Mackensen A, et al. Nat Med. 2022; 28:2124-32.
3. Müller F, et al. Lancet 2023;401: 815-818.
4. Bergmann C et al., Ann Rheum Dis 2023, May 5;ard-2023-223952.

Disclosure: J. Taubmann: None; **F. Müller**: AbbVie, 6, AstraZeneca, 1, 5, 6, Bristol Myers Squibb, 1, 6, Janssen, 6, KITE, 1, 6, Miltenyi Biomedicine, 1, 6, Novartis, 1, 6, Sobi, 6; **M. Aigner**: Kosmas Therapuetics, 8, Kyverna, 5, Miltenyi Biomedicine, 2, 7, Miltenyi Biotec, 6; **I. Minopoulou**: AbbVie/Abbott, 6; **J. Knitza**: None; **D. Werner**: None; **C. Bergmann**: Boehringer-Ingelheim, 2, 5, Janssen, 2; **G. Kroenke**: None; **A. Mackensen**: BioNTech, 1, Bristol-Myers Squibb(BMS), 1, KITE/Gilead, 1, 6, Kyverna, 5, Miltenyi Biotech, 5; **G. Schett**: None.

Abstract Number: 0784

Kidney-Related Outcomes and Steroid-Sparing Effects in Patients with Active Lupus Nephritis Treated with Obinutuzumab: A Post Hoc Analysis of a Phase 2 Trial

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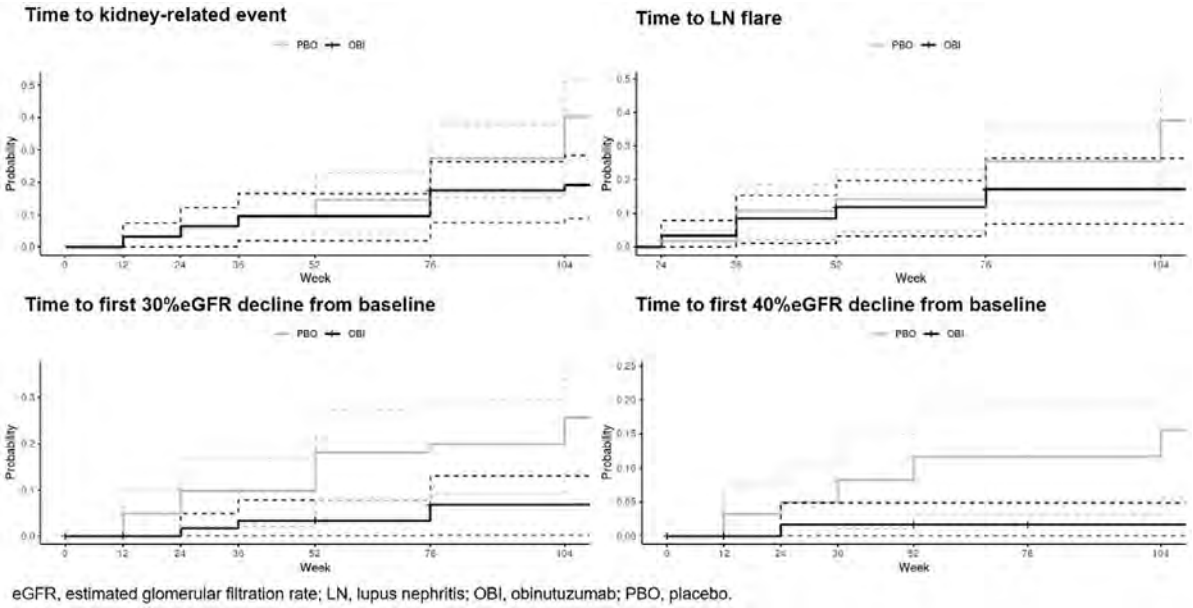
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: SLE – Treatment I: Renal
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Preservation of long-term kidney function and sustained reduction of glucocorticoid use are major therapeutic goals in lupus nephritis (LN). In the randomized, double-blind, placebo-controlled, Phase 2 NOBILITY trial (NCT02550652), patients with proliferative LN receiving obinutuzumab with standard-of-care therapy showed clinically meaningful improvement in complete and overall renal responses (CRR and ORR) at Weeks 52, 76 and 104 compared with those receiving placebo and standard-of-care therapy.[1] We conducted a post hoc analysis of NOBILITY to assess kidney-related outcomes and steroid-sparing effects.

Methods: Cox regression analysis was conducted for the time to first kidney-related event (death, doubling of serum creatinine and treatment failure), LN flare and first 30% and 40% eGFR decline from baseline. The eGFR slope was assessed in a linear mixed-effects model. Assessment of a steroid-sparing effect of ≤7.5 mg/day of prednisone while achieving CRR at Weeks 76 and 104 without use of >7.5 mg/day of prednisone between Weeks 64 and 76 and Weeks 92 and 104, respectively, was calculated by the Cochran–Mantel–Haenszel test stratified for race (Afro-Caribbean/African American vs others) and country (US vs non-US). Glucocorticoid dose was imputed by the LOCF method for patients who discontinued the study and/or for missing data. All patients met ACR classification criteria for systemic lupus erythematosus and had biopsy-proven proliferative LN.

Results: Obinutuzumab significantly reduced the risk of kidney-related events or death (HR, 0.40; 95% CI, 0.20 to 0.80), LN flare (HR, 0.43; 95% CI, 0.20 to 0.95) and time to first eGFR decline of 30% (HR, 0.20; 95% CI, 0.06 to 0.61) and 40% (HR, 0.09; 95% CI, 0.01 to 0.73) (**Figure**). Risk of sustained eGFR decline of 30% and 40% was numerically lower, and a significant difference in attenuation of eGFR slope decline was observed between patients receiving obinutuzumab and standard-of-care therapy and those receiving placebo and standard-of-care therapy (annual slope difference, 4.10 mL/min/year; 95% CI, 0.14 to 8.08). Patients receiving obinutuzumab and standard-of-care therapy were significantly more likely to achieve



eGFR, estimated glomerular filtration rate; LN, lupus nephritis; OBI, obinutuzumab; PBO, placebo.

CRR at Week 76 without receiving >7.5 mg/day of prednisone from Week 64 through 76 than those receiving placebo and standard-of-care therapy (24 of 63 patients [38.1%] vs 10 of 62 [16.1%], respectively; $P< 0.01$). A similar trend was observed at Week 104 without receiving >7.5 mg/day of prednisone from Week 92 through 104, but this did not reach statistical significance.

Conclusion: Obinutuzumab, in addition to increasing the possibility of achieving CRR, significantly reduced the risk of kidney-related events, eGFR decline, time to LN flare and eGFR slope decline in a post hoc analysis, suggesting that obinutuzumab in combination with standard-of-care therapy may positively impact kidney-related outcomes. In addition, a significant steroid-sparing effect was observed at Week 76. Obinutuzumab is being evaluated in patients with active proliferative LN in the global registrational Phase 3 REGENCY trial (NCT04221477).

Reference

1. Furie RA, et al. *Ann Rheum Dis*. 2022;81:100-107.

Disclosure: B. Rovin: AstraZeneca, 2, 5, Aurinia, 2, 5, Biogen, 2, F. Hoffmann-La Roche Ltd, 2, Genentech, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **J. Ross Terres**: F. Hoffmann-La Roche Ltd, 11, Genentech, Inc., 3; **S. Giang**: F. Hoffmann-La Roche Ltd, 11, Genentech, Inc., 3; **T. Schindler**: F. Hoffmann-La Roche Ltd, 3, 11; **A. Turchetta**: F. Hoffmann-La Roche Ltd, 3, 11; **J. Garg**: F. Hoffmann-La Roche Ltd, 11, Genentech, Inc., 3; **R. Furie**: Biogen, 2, 5; **W. Pendergraft III**: F. Hoffmann-La Roche Ltd, 11, Genentech, Inc., 3; **A. Malvar**: F. Hoffmann-La Roche Ltd, 2, Genentech, Inc., 2.

Abstract Number: 0785

Therapeutic Range of Hydroxychloroquine Blood Levels May Reduce Odds of High Lupus Disease Activity

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: SLE – Treatment I: Renal
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Hydroxychloroquine (HCQ) is the cornerstone of lupus (or SLE) treatment. Yet the optimal dosing of HCQ in SLE is unknown. Reducing HCQ dose to 5 mg/kg to limit toxicity per American Academy of Ophthalmologists (AAO) guidelines, increases lupus flare risk by 6-fold. Therefore, establishing effective reference ranges of HCQ blood levels with upper and lower bounds for efficacy may inform individualizing HCQ dosing to maximize efficacy and limit toxicity. While studies suggest various thresholds for therapeutic HCQ blood levels, none have offered a therapeutic range with upper and lower bounds for HCQ levels that predict minimum and maximum efficacy. Moreover, clinical interpretation of a threshold is difficult as it may not account for changes in patient-level factors such as weight and kidney function and fluctuations in HCQ blood levels over time. Thus, the objectives of this study were to: 1) examine the association between HCQ blood levels and high lupus disease activity (HDA) in a prospective SLE cohort; 2) define therapeutic thresholds of HCQ blood levels with upper and lower bounds for HCQ blood levels that predict maximum and minimum efficacy.

Methods: This study measured HCQ blood levels in unique SLE visits using liquid chromatography-tandem mass spectrometry. HCQ blood levels and SLE disease activity index (SLEDAI) scores were measured on the day of the visit for each patient. High lupus disease activity (HDA) was defined as SLEDAI scores of ≥6. We performed nonparametric spline regression analysis to identify HCQ blood levels cut-points associated with reduction in the odds of HDA. To identify an effective therapeutic range with lower and upper limits of HCQ blood levels that are associated with lower odds of HDA, we examined associations between HDA and every 50-100 ng/ml increase in HCQ blood levels starting at 100 ng/ml through 1500 ng/ml using univariable and multivariable logistic regression models. Factors that can affect HCQ levels, such as kidney function, HCQ dose and timing, were included in analyses.

Results: Among 158 SLE patients in whom HCQ blood levels were measured, 92% were women and 32% were of Black race or Hispanic ethnicity. HDA was noted in 18% of patients.

Using nonparametric spline regression models, we noted that HCQ blood levels, 750 and 1100 ng/ml, significantly reduced the odds of HDA (Figure 1A). HCQ blood levels < 700 & >1150 did not reduce the odds of HDA (Figure 1B & Table 1). Levels of 750 ng/ml lowered the lower odds of HDA by 76% (OR 0.24, p=0.016, Fig 1B & Table 1). A sustained reduction in the odds of HDA with HCQ blood levels was noted through 1000 ng/ml. Peak effects were noted at levels of 1100 ng/ml with a 90% reduction in the odds of HDA (Figure 1B. & Table 1). Figure 2. illustrates how these findings could guide clinicians to individualize HCQ dosing to achieve therapeutic blood levels to maximize efficacy, while balancing safety.

Conclusion: An effective therapeutic range of HCQ levels, 750-1100 ng/ml, significantly reduced the odds of high lupus disease activity by 76-90%. These findings could be guide clinicians to individualize HCQ dosing to maximize efficacy during routine lupus visits.

Table 1. Factors associated with high lupus disease activity (HDA defined as SLEDAI ≥6) using multivariable logistic regression, n=158

Variables	Adjusted OR (95% CIs)	p	Adjusted OR (95% CIs)	p	Adjusted OR (95% CIs)	p
Age, per 10 years increase	0.99 (0.95, 1.02)	0.48	0.99 (0.96, 1.03)	0.77	0.99 (0.96, 1.02)	0.46
Female	**0.13 (0.02, 0.84)**	**0.03**	**0.18 (0.03, 1.1)**	**0.064**	**0.08 (0.01, 0.56)**	**0.015**
Black race & Hispanic ethnicity	0.69 (0.23, 1.9)	0.69	0.61 (0.0.2, 1.7)	0.36	0.77 (0.26, 2.1)	0.62
Weight, per 5 kg increase	0.97 (0.93-1.01)	0.17	0.98 (0.97, 1.02)	0.34	0.97 (0.93-1.01)	0.17
GFR, per 10 ml/min/m^2 increase	0.97 (0.96, 1.02)	0.99	0.99 (0.97, 1.02)	0.68	0.97 (0.99, 1.02)	0.49
HCQ total dose						
200 mg/day	ref		ref		ref	
300 mg/day	3.1 (0.71, 15)	0.14	2.3 (0.57, 10)	0.24	1.7 (0.41, 7.1)	0.48
400 mg/day	3.7 (0.67, 24)	0.15	2.7 (0.49, 17)	0.26	2.0 (0.39, 12)	0.42
AAO-Guideline based dose, ≤5 mg/kg/day	1.2 (0.2, 12)	0.83	1.3 (0.21, 10)	0.77	1.3 (0.20, 11)	0.77
Patient-reported adherence ≥80%	1.47 (0.37, 6.3)	0.59	0.80 (0.23, 2.9)	0.73	0.58 (0.86, 1.9)	0.36
Social Determinants of Health, Present	1.6 (0.56, 4.6)	0.39	1.3 (0.48, 3.6)	0.58	1.3 (0.45, 3.6)	0.64
HCQ dose timing, Per 2 hours	0.77 (0.54, 1.1)	0.15	0.81 (0.57, 1.1)	0.22	0.71 (0.49, 1.01)	0.063
HCQ levels, per 100 ng/ml increase	**0.78 (0.65, 0.91)**	**0.003**				
Levels ≥750 ng/ml			**0.24 (0.07, 0.75)**	**0.016**		
Levels ≥1100 ng/ml					**0.1 (0.01, 0.39)**	**0.02**

Significant findings in bold font. AAO=American Academy of Ophthalmologists; HCQ=Hydroxychloroquine

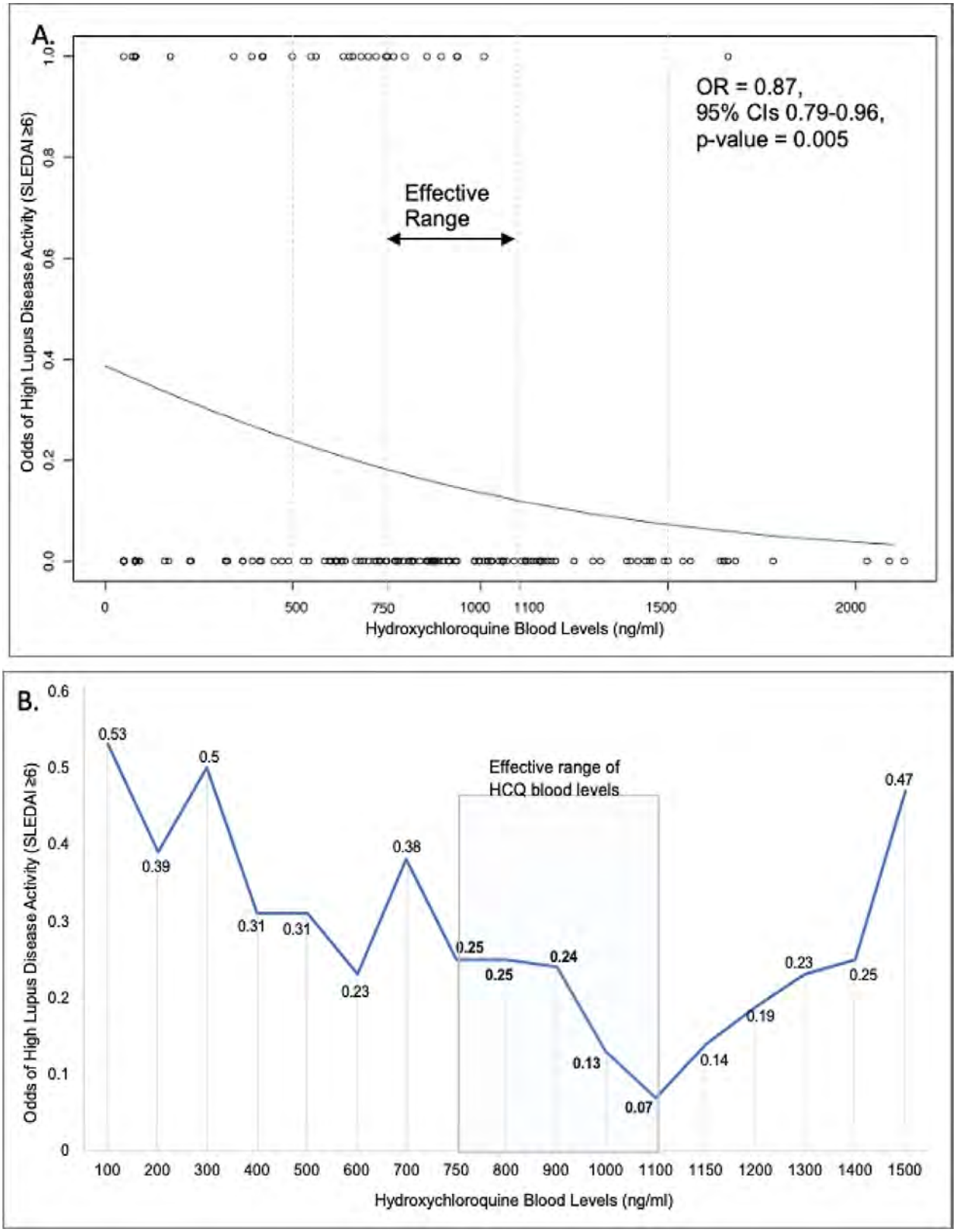

Figure 1. Effective range of HCQ levels associated with lower odds of high lupus disease activity (HDA) using: A) spline and B) logistic regression analysis

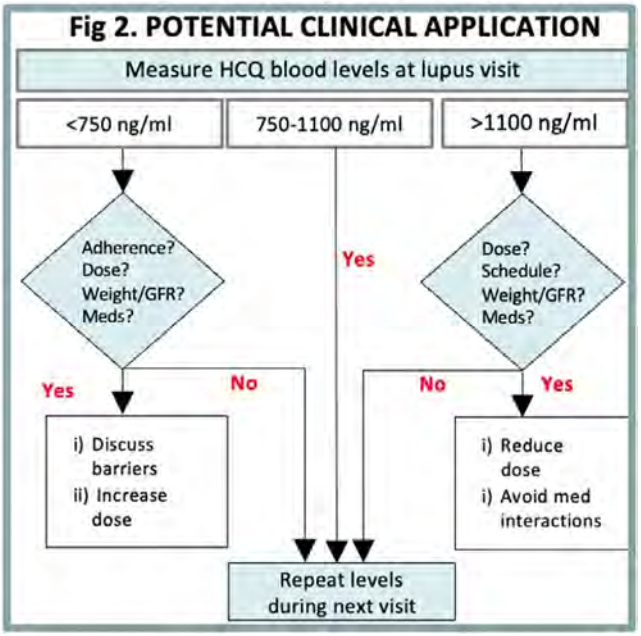

Figure 2. Potential clinical application of therapeutic hydroxychloroquine blood level monitoring during routine clinic visits

Disclosure: S. Garg: None; **B. Chewning**: None; **B. Astor**: None; **C. Bartels**: Pfizer, 5.

Abstract Number: 0786

A Retrospective Analysis of the Efficacy of the Euro-Lupus Nephritis Cyclophosphamide Regimen versus NIH Regimen in a South Carolina Lupus Nephritis Cohort

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: SLE – Treatment I: Renal
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Manifestations of systemic lupus erythematous (SLE) vary in severity and presentation; lupus nephritis (LN) affects up to half of SLE patients and confers a high risk of morbidity and mortality. Since the early 1990s, the standard regimen for SLE patients with glomerulonephritis was high-dose IV cyclophosphamide (CTX) given once monthly for 6 months with 2 additional quarterly doses. This was widely accepted until the Euro-Lupus Nephritis Trial (ELNT) results were published in 2002 and demonstrated non-inferiority. It is now accepted to give a fixed dose of 500mg IV CTX every two weeks for 12 weeks (6 doses). However, the trial population in ELNT differs significantly than the population of SLE patients treated in the United States and more specifically, South Carolina, where African Americans represent 26.7% of the population. African Americans have a higher prevalence of LN and often more severe disease which may suggest the need for more aggressive therapy. Additionally, renal damage progressing to ESRD is still more common in African Americans. We hypothesized that the two regimens may not have equivalent efficacies in multiethnic patient cohorts.

Methods: We undertook a retrospective analysis to compare the Euro-Lupus Nephritis regimen to the NIH regimen in patients with lupus nephritis treated at the Medical University of South Carolina. Data was collected from patients with LN age 18-90 years old treated with CTX at MUSC from 2012 to 2022. There were no exclusion criteria. Data includes demographics, dates of visits and treatments, renal histological parameters, clinical laboratory values of lupus disease activity and renal status, medications, and dosing data.

Results: Eighty-five patients fit the inclusion criteria. Of these, 40 received ELNT, and 45 received the NIH protocol. There are 80 females and 5 males. Of the 85 subjects, 73 are African American (85.9%). In the ELNT cohort, 33 are African American (82.5%). There are 40 African Americans in the NIH group (88.9%). Demographics are provided in Table 1. Baseline and

Table 1: Enrollment Demographics

	Total	ELNT	NIH
Enrolled	85	40	45
Average Age at Treatment (Years)	30	32	29
Gender			
Male	5 (6%)	2 (5%)	3 (6.7%)
Female	80 (94%)	38 (95%)	42 (93.3%)
Race			
African American	**73 (85.9%)**	**33 (82.5%)**	**40 (88.9%)**
White	4 (4.7%)	3 (7.5%)	1 (2.2%)
Asian	3 (3.5%)	2 (5%)	1 (2.2%
Hispanic	4 (4.7%)	2 (5%)	2 (4.4%)
Other	1 (1.2%)	0	1 (2.2%)

Table 2: Laboratory value averages with standard deviations at baseline and 1 year from last treatment.

	Baseline Laboratory Values		1 Year from Treatment End	
	ELNT	NIH	ELNT	NIH
Serum Creatinine	1.65 (±1.15)	1.84 (±1.69)	2.60 (±2.99)	1.77 (±2.40)
eGFR	47.44 (±35.99)	38.38 (±33.79)	43.38 (±36.58)	53.23 (±38.83)
C3	62.94 (±33.44)	64.15 (±35.18)	97.77 (±33.35)	117.68 (±34.38)
C4	14.99 (±11.48)	13.25 (±0.58)	30.04 (±23.74)	26.43 (±13.44)
dsDNA	78.53 (±75.02)	63.4 (±71.71)	43.66 (±52.30)	24.45 (±33.16)

Table 3: Average change of serum creatinine in patients between 1 year and baseline laboratory values. The increase in ELNT was 0.91 while NIH improved by an average of 0.13.

	Average Change Between Patients	
	ELNT	NIH
Serum Creatinine	0.91 (±3.02)	-0.13 (±2.83)

one year laboratory averages with standard deviations are provided in Table 2. Table 3 shows the average change in serum Cr amongst patients in each treatment group. In the ELNT group, the average change showed an increase in creatinine by 0.91 (±3.02). The serum creatinine in the NIH cohort decreased by 0.13 (±2.83). Findings from this ongoing analysis suggest that at the one-year mark, patients in the ELNT group on average have an increase in serum creatinine, with 10 patients (25%) needing to be put on hemodialysis versus only 4 patients (8.8%) in the NIH cohort (p=0.0468).

Conclusion: No known prior studies have evaluated the efficacy of the ELNT protocol in a predominantly African American cohort. This project is currently ongoing. Preliminary results indicate that patients receiving the ELNT protocol at MUSC have increased serum creatinine at 1 year, possibly suggesting that the therapy is not aggressive enough. This is also shown in the proportion of patients requiring hemodialysis within 1 year. Additional research is needed to identify the optimal choice for cyclophosphamide regimen in different populations of patients with lupus nephritis.

Disclosure: A. Arar: None; **D. Kamen**: None; **P. Nietert**: None; **M. Cunningham**: Aurinia, 2.

Abstract Number: 0787

Understanding Distinct Resident and Migratory Fibroblast Populations in Systemic Sclerosis Skin Through Single-cell RNAseq and Immunohistochemistry

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Systemic Sclerosis & Related Disorders I: Translational
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: We previously described distinct migratory and resident fibroblast populations from lesional skin biopsies in SSc patients. Both populations are profibrotic compared with those from healthy control (HC) skin, however migratory SSc fibroblasts display increased expression of αSMA, greater gel contraction, and faster migration in the scratch-wound assay. The two SSc populations differ by bulk RNAseq expression, with resident fibroblasts overexpressing CCL2, CXCL8 and ICAM1, whereas migratory fibroblasts overexpress genes such as COMP, TRIP3. Here we describe the use of scRNAseq of whole skin to define the functional differences between these two fibroblasts subsets

Methods: scRNAseq was performed on 12 SSc whole skin biopsies and 3 HC, using the 10X genomics platform. The markers identified in bulk RNAseq for each fibroblast populations were used to identify corresponding clusters in scRNAseq. Candidate gene sets to identify the resident and migratory fibroblast populations were developed, and KEGG gene set enrichment pathways (GSEA) identified.

We explored differences in relative frequency of resident and migratory fibroblasts populations in whole skin by stage and subset between ATA (anti-topoisomerase) and ARA (anti-RNA pol III), as well as late and early-stage disease.

Finally, we utilised CellDive® multiplex imaging to localize the two fibroblast populations within the dermis of skin biopsies

Results: Bulk RNAseq revealed 739 genes significantly overexpressed genes in the migratory fibroblast population, whereas 745 genes were significantly upregulated in the resident fibroblasts (Table 1).

10 clusters of fibroblasts were identified on scRNAseq. Cluster 0 and 4 showed gene expression similar to migratory fibroblasts, whereas the resident fibroblasts gene expressions paralleled clusters 3 and 6 (Figure 1).

Interrogating the scRNAseq clusters, revealed the migratory fibroblasts are the most abundant cell population. Subgrouping by autoantibody identified migratory fibroblasts as most abundant in the ATA subgroup, whereas resident fibroblasts are most abundant in the ARA subgroup, suggesting autoantibody status tracks distinct fibroblast subsets (Figure 2).

GSEA of KEGG pathways confirmed concordance between migratory and resident fibroblast clusters in bulk and scRNAseq analysis. Resident fibroblasts showed upregulation of complement and coagulation genes, and JAK/STAT signalling pathway. There was upregulation of glycolysis gluconeogenesis, and PPAR signalling in migratory fibroblasts.

Table 1: Table showing top 20 statistically significant differentially expressed genes between SSc migratory and SSc resident fibroblasts by fold change (FC).

Resident Fibroblasts	FC		Migratory Fibroblasts	FC
CCL2	12.61		INHBE	4.21
ANGPTL4	11.29		GPR1	3.46
CXCL8	9.15		ANKRD33B	3.12
LIF	9.05		PPME1	2.99
HBEGF	7.59		COL10A1	2.83
PTGS2	7.19		KIF20A	2.77
ICAM1	6.65		CENPF	2.75
MX1	6.64		STC2	2.69
EGR1	6.59		MATN3	2.65
GPR68	6.36		DYSF	2.60
EGR2	5.84		ASPM	2.56
IFI44L	5.44		CTH	2.56
CXCL6	5.43		TRIB3	2.43
HERC6	5.38		VLDLR	2.42
KCNK9	5.37		PLEKHA2	2.42
OAS2	5.36		NEK2	2.39
IFI6	5.17		DLGAP5	2.37
PDGFD	4.98		DDIT4	2.36
OAS1	4.95		COL11A1	2.13
CLDN11	4.80		IL21R	2.03

Using CellDive® multiplexed technology, and markers of resident and migratory fibroblasts, the fibroblast populations localise to different areas of the dermis, with migratory fibroblasts being more perivascular, and resident being scattered throughout the dermis

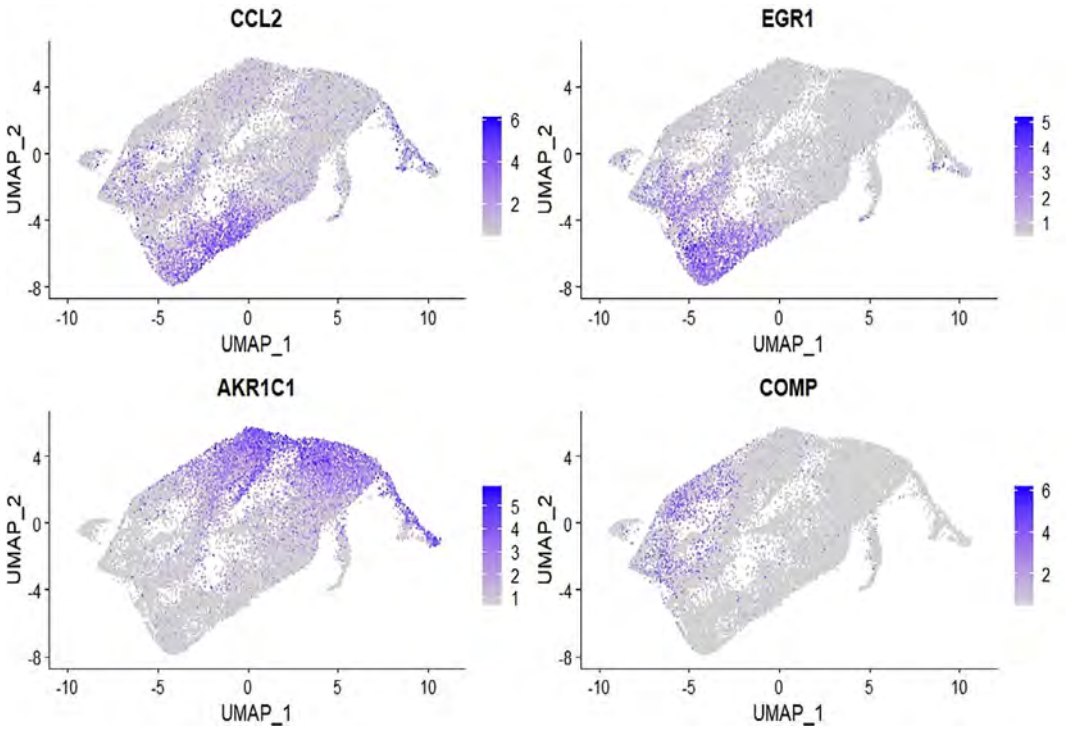

Figure 1: Identifying resident and migratory fibroblasts in scRNAseq. Migratory fibroblasts were identified with COMP and AKR1C1, whereas CCL2 and EGR1 were more specific for resident fibroblasts.

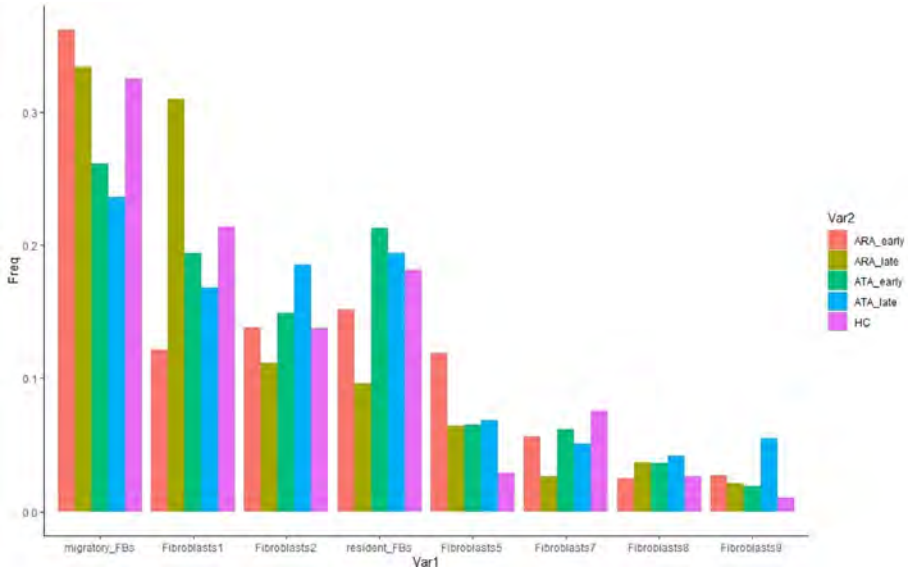

Figure 2: Abundance of fibroblast populations by antibody and stage. Migratory fibroblasts first column and resident fibroblasts 4th column

Conclusion: We extended our understanding of two fibroblast populations in SS and describe a molecular basis for their functional differences and location within the dermis. Understanding their different functions, and appreciating their tight association with auto antibody subset, begins to explain the differences in clinical phenotype and response to therapeutics linked to disease stage and subset of SSc.

Disclosure: K. Clark: None; **S. Xu**: None; **V. Ong**: None; **C. Buckley**: Bristol-Myers Squibb(BMS), 5, Mestag, 11; **C. Denton**: AbbVie, 2, Acceleron, 2, Arxx Therapeutics, 5, Bayer, 2, Boehringer-Ingelheim, 2, 6, Corbus, 2, 6, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Horizon Therapeutics, 2, Inventiva, 2, 5, Janssen, 6, Roche, 2, Sanofi, 2, Servier, 5.

Abstract Number: 0788

Whole Exome Sequencing and Evolutionary Action Missense Mutation Analysis Identifies *MICB* as a New SSc Susceptibility Locus and the Interferon Pathway as Contributors to SSc Pathogenesis

Shamika Ketkar[1], Hongzheng Dai[1], Brian Dawson[1], Lindsay Burrage[1], David Murdock[1], Jennifer Asmussen[1], Kevin Wilhelm[1], Olivier Lichtarge[1], Martin Kerick[2], Javier Martin[3], Shervin Assassi[4], Brendan Lee[1] and **Maureen Mayes**[5], [1]Baylor College of Medicine, Houston, TX, [2]Spanish National Research Council, Granada, Spain, [3]Instituto de Parasitologia y Biomedicina Lopez-Neyra - CSIC, Granada, Spain, [4]University of Texas McGovern Medical School at Houston, Houston, TX, [5]Division of Rheumatology, University of Texas McGovern Medical School, Houston, TX

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Systemic Sclerosis & Related Disorders I: Translational
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Systemic Sclerosis (SSc) is characterized by fibrosis of the skin and internal organs associated with vasculopathy and autoantibodies and exhibiting wide clinical heterogeneity. Contributors to pathogenesis include genetic variants and currently unidentified external triggers. Several genome-wide association studies (GWASs) have shed light on the genetic component and estimated that it contributes 30% to the risk of developing SSc. We used Whole Exome Sequencing (WES) data to identify novel SSc susceptibility loci, and to identify putative causative pathways.

Methods: Exome sequencing (ES) was performed by Regeneron in an academic-industry partnership. ES data was provided to the study team and all analyses were performed by the authors independently of Regeneron. We first performed GWAS analysis of 2,865 Caucasian cases and 1,043 controls from samples in the SSc Registry and DNA Repository. Genotype imputation was performed with the 1000 Genome Project Phase 3 panel which yielded 5,522,961 variants. Case-control association analysis was performed using PLINK v1.9 logistic regression model of additive effects, including gender and the first two principal components (PCs) as covariates. Replication testing was performed in an independent case-control set of European ancestry (949 SSc patients, 998 controls from collaborators Kerick and Martin).

The **evolutionary action method** estimates the functional and clinical impact (mutational harm) of missense protein coding variations.

Results: We identified a novel susceptibility locus at *MICB* (rs2516497, $P = 8.42 \times 10^{-15}$) within the HLA region. *MICB* (MHC class I chain-related gene B) is a protein coding gene in the MHC region whose gene product is a stress-inducible cell surface molecule that labels malfunctioning cells for targeting by cytotoxic lymphocytes such as natural killer cells.

Additionally, we confirmed and firmly established the role of *HLA-DQA1* (rs1048372, $P = 2.95 \times 10^{-21}$) and *HLA-DQB1* (rs2647032, $P = 1.32\times 10^{-16}$) gene regions as SSc genetic risk factors. Replication testing in an independent case-control set of European ancestry confirmed association of this *MICB* SNP (rs2516497, $P = 7.17 \times 10^{-9}$) to SSc. In addition, the replication cohort also confirmed that the association of this *MICB* SNP is an independent event, i.e., it is not in linkage disequilibrium with other HLA class genes.

Next, we applied the evolutionary action method to investigate genes and pathways associated with SSc. Evolutionary action predicts the impact of missense variants on protein function. Using the *de novo* missense variants from the ES data, this method corroborated genes associated with SSc and identified additional genes in the interferon pathway among others. *IFI44L* and *IFIT5* are interferon genes and are shown to be dysregulated in SSc blood and skin.

Conclusion: Using a GWAS analysis applied to WES data, we identified *MICB* as a novel SSc susceptibility locus independent of other HLA class genes. Additionally, by application of the evolutionary action analysis method to this dataset, we identified missense mutations in the interferon pathway that may contribute to SSc pathogenesis.

Disclosure: S. Ketkar: None; **H. Dai**: None; **B. Dawson**: None; **L. Burrage**: None; **D. Murdock**: None; **J. Asmussen**: None; **K. Wilhelm**: None; **O. Lichtarge**: None; **M. Kerick**: None; **J. Martin**: None; **S. Assassi**: AstraZeneca, 2, aTyr, 2, Boehringer Ingelheim, 2, 5, CSL Behring, 2, Janssen, 5, Merck, 2, Momenta, 5, TeneoFour, 2; **B. Lee**: None; **M. Mayes**: Boehringer Ingelheim, 1, 5, British Medical Journal, 9, Corbus, 5, EICOS, 1, 5, Horizon Pharma, 5, Medtelligence, 6, Mitsubishi Tanabe, 1, 5, Oxford University Press, 9, Prometheus, 5, Springer International Publishing, 9.

Abstract Number: 0789

Telomere Length of Peripheral Blood Cells Predicts More Severe Pulmonary Disease and Worse Survival in Systemic Sclerosis

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SESSION INFORMATION
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Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Peripheral blood leukocyte telomere length (PBL-TL) has been associated with disease and organ specific morbidity and mortality in conditions associated with pulmonary fibrosis including connective tissue disorders. TL shortening has been implicated in SSc-related interstitial lung disease (ILD), but its association with other organ involvement, disease severity, and overall survival remains unknown. The goal of this study was to define the relationship of PBL-TL with SSc-specific disease manifestations and clinical outcomes including mortality.

Methods: A retrospective longitudinal cohort study was performed using a large, well characterized cohort of SSc patients fulfilling the ACR/EULAR 2013 classification criteria and healthy controls (HC). PBL-TL was measured by quantitative PCR from DNA isolated from the blood. Age adjusted TL was calculated using linear regression of TL from HC. Multivariate modeling was utilized to assess the association of PBL-TL with SSc disease presence and severity of skin thickening, ILD, pulmonary arterial hypertension (PAH), peripheral vascular disease (PVD), and event free survival (lung transplantation and/or death) from disease onset and time of TL measurement. To assess concordance of findings between blood and SSc target

Table 1: Demographic and clinical characteristics of SSc patients and healthy controls

		SSc		
	Control (N=314)	Limited (N=161)	Diffuse (N=83)	All SSc (N=244)
Age (years)				
Mean (SD)	52.2 (12.8)	55.8 (13.0)	52.5 (12.6)	54.7 (12.9)
Median [Min, Max]	53.0 [21.0, 82.0]	57.0 [19.0, 85.0]	54.0 [23.0, 79.0]	56.0 [19.0, 85.0]
Sex				
Male	10 (3.2%)	21 (13.0%)	14 (16.9%)	35 (14.3%)
Female	304 (96.8%)	140 (87.0%)	69 (83.1%)	209 (85.7%)
Race				
White	246 (78.3%)	98 (60.9%)	47 (56.6%)	145 (59.4%)
Hispanic	19 (6.1%)	13 (8.1%)	5 (6.0%)	18 (7.4%)
Black	7 (2.2%)	17 (10.6%)	8 (9.6%)	25 (10.2%)
Asian	42 (13.4%)	19 (11.8%)	13 (15.7%)	32 (13.1%)
Other	0 (0%)	14 (8.7%)	10 (12.0%)	24 (9.8%)
Telomere length (bp)				
Mean (SD)	7340 (691)	6270 (528)	6450 (506)	6330 (526)
Median [Min, Max]	7380 [5580, 9140]	6330 [4670, 7700]	6500 [4990, 7670]	6370 [4670, 7700]
Disease Duration (years)				
Mean (SD)		11.4 (8.67)	9.68 (7.68)	10.8 (8.38)
Median [Min, Max]		9.77 [0.310, 41.3]	8.28 [0.360, 30.9]	9.27 [0.310, 41.3]
mRSS				
Mean (SD)		3.14 (1.73)	11.6 (9.28)	6.02 (6.87)
Median [Min, Max]		3.00 [0, 13.0]	10.0 [0, 46.0]	3.00 [0, 46.0]
ILD present (%)		87 (54.0%)	52 (62.7%)	139 (57.0%)
pHTN present (%)		35 (21.7%)	26 (31.3%)	61 (25.0%)
Severe RP present (%)		10 (6.2%)	6 (7.2%)	16 (6.6%)

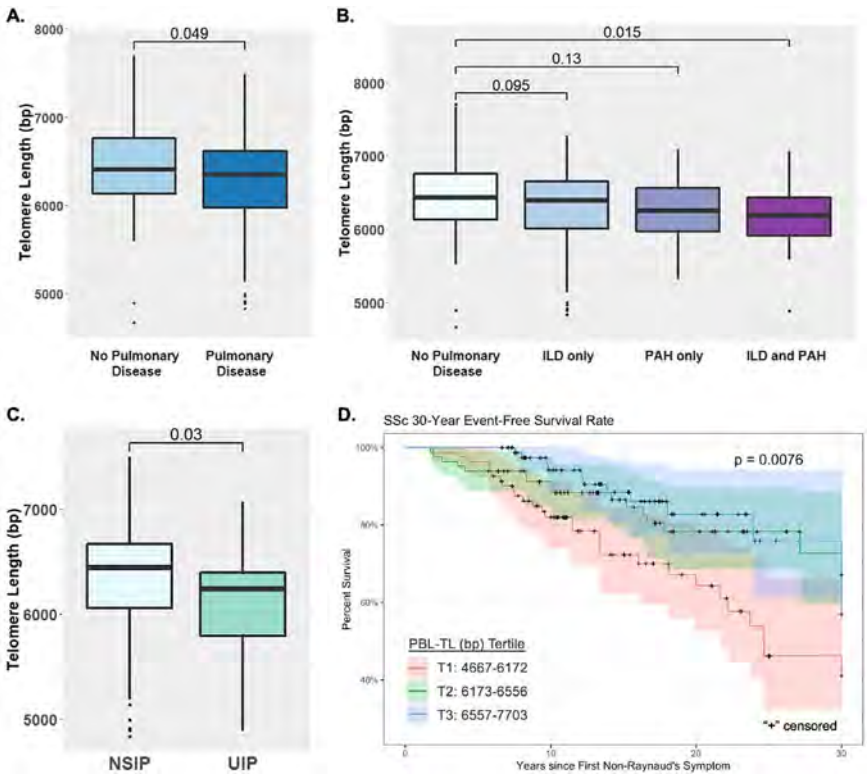

Figure 1: PBL-TL was significantly shorter in patients with pulmonary involvement (A), especially in those with concurrent ILD and PAH (B) and with UIP pattern of ILD on chest CT (C). PBL-TL associates with survival as patients with shortest TL (Tertile 1) had significantly worse 30 year survival (D).

tissues, TL was measured in skin and lung tissue by telomere fluorescence in situ hybridization (Telo-FISH) in SSc and HC, and compared using Wilcoxon rank-sum test.

Results: 558 participants (244 SSc and 314 controls) were included in this study (Table 1). PBL-TL was significantly shorter in SSc than healthy controls. In multivariate modeling, controlling for age, sex, race, smoking, disease duration and autoantibody status, shortened TL was significantly associated with presence of SSc related pulmonary involvement (OR 1.98 per 1000bp shortening, p=0.03) (Fig1A). PBL-TL was not associated with SSc skin disease (p=0.21) or PVD (p=0.20). Within pulmonary disease, TL shortening was strongly associated with ILD presence (OR 2.21, p =0.009). The shortest PBL-TL was found in subjects with concurrent ILD and PAH (Fig 1B). Shortened TL was also associated with lung disease severity including lower DLCO% (p=0.006) and UIP pattern by chest CT compared to NSIP (p=0.03, Fig 1c). Patients requiring hospitalization for respiratory or right ventricular failure had shorter TL (6169 ±434 vs. 6350±535, p=0.02) and TL shortening was associated with worse event free survival among all SSc patients from both time of TL measurement (p=0.03) and disease onset (p=0.008) (Figure 1D). TL was shorter in type II alveolar cells in lung tissues from SSc-ILD patients compared to healthy controls (p=0.014). In contrast, no difference was found in TL in epidermal cells (KRT5+) of skin (p=0.82).

Conclusion: This cohort study found a strong association between TL measured in the peripheral blood of SSc patients and more severe pulmonary involvement, particularly with concurrent ILD/PAH, and worse clinical outcomes including increased hospitalization due to respiratory failure as well as worse survival. This study provides rationale to further investigate the role of telomere dysfunction in SSc-ILD pathogenesis and to validate TL as a potentially useful biomarker in SSc.

Disclosure: M. Yang: None; **S. Liu**: None; **S. Lee**: None; **S. French**: None; **P. Wolters**: None; **F. Boin**: None.

Abstract Number: 0790

Transcriptomic Analyses of Lung Tissues Reveals Potential Key Genes Associated with Progression of Systemic Sclerosis-Interstitial Lung Disease (SSc-ILD)

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SESSION INFORMATION
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Background/Purpose: SSc-ILD is the leading cause of death in SSc affecting around 50% of the patients. Lung tissue of patients with early-stage SSc-ILD is characterized by a predominant inflammatory response with inconspicuous fibrosis, which can progress to honeycombing fibrosis. Although several biomarkers and drug targets have been proposed to monitor and halt SSc-ILD progression, none has reached clinical application. A better understanding of the molecular mechanisms underpinning SSc-ILD pathogenesis is needed to improve treatment options and progression prediction. This transcriptomic study aims to reveal the differential gene expression between healthy control (ctrl) lung sections and regions of interest (ROIs) within SSc-ILD lung tissue.

Methods: The nanoString (nS) nCounter Human Fibrosis Panel containing 770 genes related to all stages of fibrosis was used to analyze gene expression in formalin-fixed and paraffin-embedded lung tissues with varying stages of SSc-ILD (n=18) and control lung tissue (n=6). The SSc-ILD tissues were stratified by an experienced lung pathologist into three ROIs, inflammatory (inf), prefibrotic (prefib), or fibrotic (fib). Every group comprised 6 samples. This stratification aimed to define a longitudinal simulation of early to late phases of SSc-ILD: ctrl à inflammation à prefibrosis à fibrosis. nSolver and Rosalind software were used for data and statistical analysis. The immunohistochemistry was performed using specific antibodies in the same tissues used for nS analysis to confirm protein expression.

Results: To validate our simulation model, we performed subgroup analysis that showed an incremental increase in pathway scores related to the severity of fibrosis including, among others, ECM and collagen 1 biosynthesis, PDGF signalling, and myofibroblast regulation (Fig.1). Ctrl vs SSc-ILD comparison demonstrated 24 differentially expressed genes, two of which had the most pronounced *p*-values. Cyclin-Dependent Kinase Inhibitor 2C (CDKN2C) was significantlyoverexpressed ($p = 0.00052$) in SSc-ILD compared to ctrl, while expression of Pellino E3 ubiquitin-protein ligase 1 (PELI1) showed lower expression significantly ($p = 0.0012$). Additionally, the expression of CDKN2C and PELI1 showed an incremental increase and decrease in the four groups, respectively (Fig.2). Immunohistochemistry of CDKN2C and PELI1 showed consistent results with the nS analysis with incremental increase and decrease of positive staining in the 4 groups, respectively.

Conclusion: Expression of CDKN2C and PELI1 was associated with more severe stages of SSc-ILD on histologic assessment. PELI1 decrease is probably due to loss of bronchial tissue during the fibrosis processes and thus secondary to the already existing pathology. We report the potential of the cell cycle inhibitor, CDKN2C to predict fibrosis progression. Further

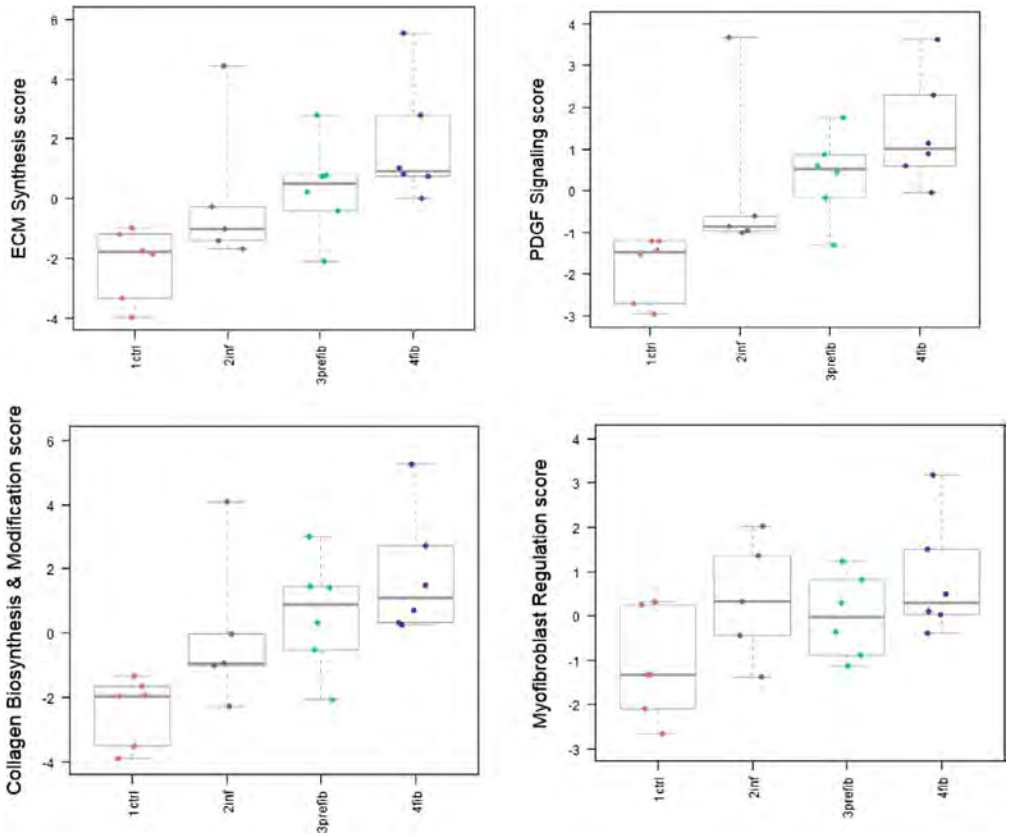

Figure 1: Pathway score analysis. Four pathways related to fibrosis and tissue remodeling are shown. Control (Ctrl) samples scored lowest while fibrotic samples scored highest. Among others, these pathways were the most differentially elevated in 51 annotated pathways within the fibrosis panel. ECM, Extracellular matrix; PDGF, Platelet-derived growth factor; Inf, inflammatory; prefib, prefibrotic; fib, fibrotic.

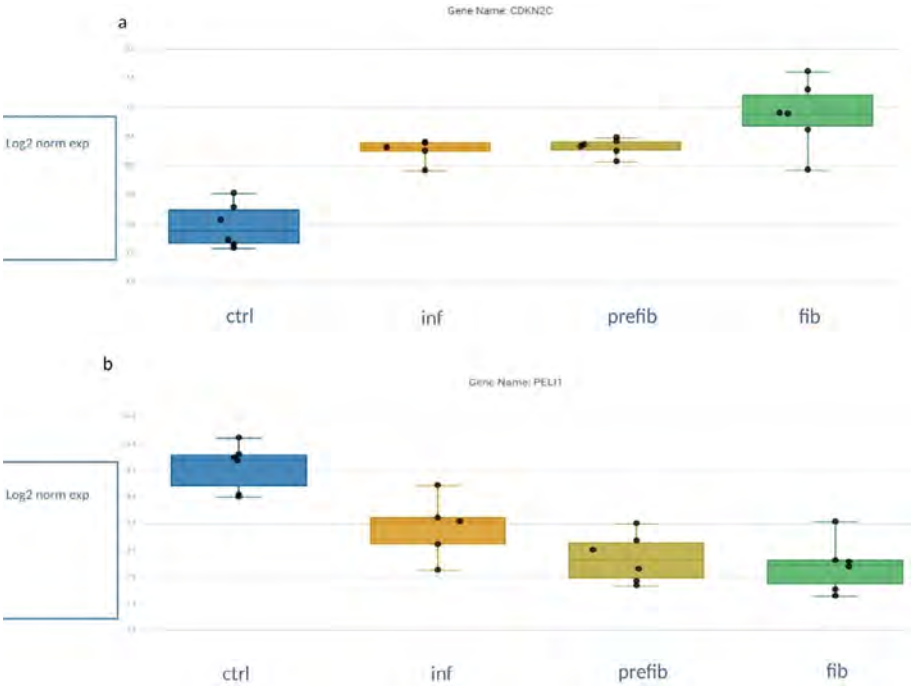

Figure 2: CDKN2C and PELI1 gene expression change between the four groups shown as (Log2) fold-change. (a) CDKN2C expression increases from the ctrl group up until the fibrotic group incrementally through inflammatory and prefibrotic groups. (b) PELI1 gene expression decreases from the ctrl group up until the fibrotic group incrementally through inflammatory and prefibrotic groups.

research is required to validate these findings and correlate additional cell cycle regulation and/or senescence markers with CDKN2C. determine the potentiality of CDKN2C as a putative progression marker candidate.

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Abstract Number: 0791

Expression of TL1A, Inflammatory, and Fibrotic Pathways in Patients with Diffuse Systemic Sclerosis

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SESSION INFORMATION
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Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Systemic sclerosis (SSc) is a multiorgan disease characterized by systemic vascular injury, inflammation, and fibrosis. While SSc mainly affects the skin, pulmonary manifestations such as interstitial lung disease (ILD) are the leading cause of morbidity and mortality. Tumor necrosis factor–like cytokine 1A (TL1A) is a membrane costimulatory

protein and cytokine that drives multiple inflammatory and fibrotic pathways implicated in SSc. TL1A can induce lung fibrosis and tissue remodeling in mice and can stimulate cellular proliferation and extracellular matrix protein production in human lung fibroblasts. The present study evaluated the expression of TL1A and related pathways in serum, skin, and lung tissue in patients with SSc. An anti-TL1A monoclonal blocking antibody, PRA023, is currently in phase 2 trial for SSc-ILD.

Methods: Soluble TL1A was measured in serum samples from early diffuse (< 2yr; n=58) and late diffuse (>5yr; n=57) SSc and matched healthy control sera (n=60) (University of Texas cohort). Bulk and single-cell transcriptomic public data from SSc lung and skin were analyzed for gene expression. Gene expression and chromatin accessibility from the same cell were profiled in skin biopsies and peripheral blood mononuclear cells (PBMCs) from patients with SSc with (n=4) and without (n=4) ILD and healthy controls (n=4) using 10X Genomics Chromium Single Cell Multiome technology (University of Michigan cohort). TL1A and its receptor, DR3, proteins were detected in SSc skin (n=15), SSc-ILD (n=5), and healthy control lung tissue (n=5) by immunohistochemistry in both cohorts.

Results: TL1A levels were elevated in late diffuse SSc compared with early diffuse and healthy control sera ($p< 0.05$). In bulk transcriptomic SSc skin public datasets, Th1, Th2, Th17, and TL1A-induced T cell and fibrosis gene signatures were increased. In the skin, single-cell gene expression and chromatin accessibility analysis showed that TL1A was expressed in myeloid and epithelial cells, while DR3 was expressed on T cells. Differential gene expression analysis between SSc and control skin revealed several genes upregulated in fibroblasts (eg, *COL16A1, ELN, PRRX1*; $p< 0.05$) and in myeloid cells (eg, *HLA-DRB1, NRP1, SRGN*; $p< 0.05$). TL1A-induced genes were upregulated in myeloid cells and fibroblasts of SSc skin compared with controls ($p< 0.001$). In donor-matched PBMCs, single-cell gene expression and chromatin accessibility data indicated TL1A expression in myeloid cells, a cell population expanded in SSc, and DR3 expression in T cells. In lung tissue bulk RNA, TL1A gene expression was increased in SSc-ILD compared to healthy controls. In single-cell RNAseq SSc-ILD lung data, TL1A was expressed by myeloid and epithelial cells, while DR3 was expressed by T cells and epithelial and endothelial cells. Although SSc skin showed relatively low levels of TL1A and DR3 protein expression, TL1A and DR3 proteins were relatively abundant in SSc-ILD compared with healthy control lung tissues.

Conclusion: TL1A expression and pathway activity analyses suggest that TL1A may modulate immune and fibrotic pathways in SSc skin and the lung, with higher activity of the pathway in lung tissue compared with the skin.

Disclosure: H. Llewellyn: Prometheus Biosciences, 3; **L. Tsoi**: Galderma, 5, Janssen, 5, Novartis, 5; **M. Wu**: Boehringer-Ingelheim, 5, Janssen, 5, Prometheus Biosciences, 5; **K. Grigaityte**: Prometheus Biosciences, 3; **T. Wang**: Prometheus Biosciences, 3; **J. Seibold**: Prometheus Biosciences, 3; **E. Muñoz-Elias**: Prometheus Biosciences, 3; **D. Khanna**: AbbVie, 12, DSMB, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb, 2, 5, CSL Behring, 2, Genentech, 2, Horizon Therapeutics, 2, 5, Janssen, 2, 6, Pfizer, 5, Prometheus, 2; **J. Gudjonsson**: Abbvie, 2, 5, Almirall, 2, 5, AnaptysBio, 2, Boehringer Ingelheim, 2, Celgene/BMS, 2, 5, Eli Lilly, 2, 5, Galderma, 2, Janssen, 2, 5, Kyowa Kirin, 5, MiRagen, 2, Novartis, 2, Prometheus Biosciences, 5, Sanofi, 2, SunPharma, 5, TimberPharma, 5.

Abstract Number: 0792

Single Cell RNA-seq of Myeloid Cells from Systemic Sclerosis Patients Identifies Circulating Monocyte Population with Interferon Signature Associated with Interstitial Lung Disease

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Systemic Sclerosis & Related Disorders I: Translational
Session Type: Abstract Session
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Background/Purpose: Growing evidence supports a critical role for innate immunity in systemic sclerosis (SSc) pathogenesis. Altered myeloid cell numbers and functions have been implicated in the initiation and progression of SSc, but their functional characterization and relationship with specify disease manifestations such as interstitial lung disease (ILD) remain

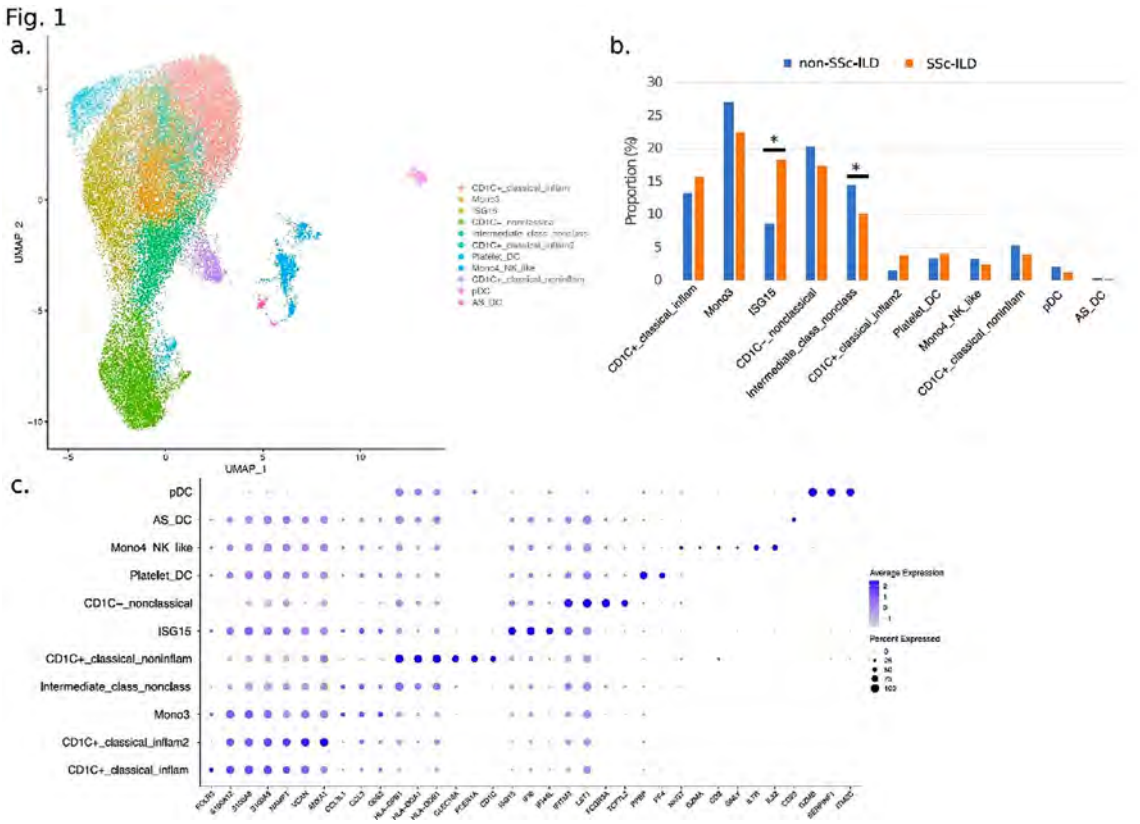

Fig. 1. a. UMAP of myeloid cells split into 11 clusters. b. Frequency barplot for each cell-type split by ILD status. c. Bubble plot of selected marker genes.

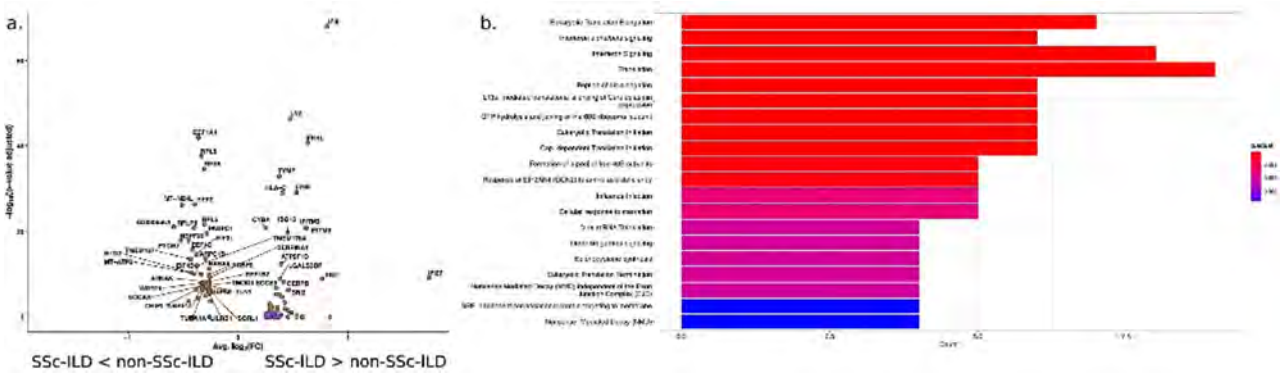

Fig. 2. a. Volcano plot for ISG15 monocytes ILD vs non-ILD. b. Pathways for 33 differentially expressed genes.

poorly understood. We sought to characterize specific myeloid populations associated with SSc-ILD and investigate how disease severity affects the transcriptional regimen.

Methods: Single cell RNA-seq was performed on peripheral blood obtained from 60 SSc patients meeting 2013 ACR/EULAR criteria. Unsupervised clustering identified dendritic/monocyte populations which were then selected for further sub-clustering analysis and annotation. Differential expression analysis and sub-type frequency analysis was conducted between 40 patients with SSc-ILD and 20 patients without (non-SSc-ILD). Using the worst recorded forced vital capacity (fvc) value (%-predicted), correlation analysis against pseudo-bulk expression was performed for an unbiased genome-wide assessment of SSc-ILD severity associations.

Results: Clustering and annotation of 39,582 dendritic/monocyte cells identified 11 myeloid cell types (Fig.1a). Comparison of relative cell type proportions between SSc-ILD and non-SSc-ILD (Fig.1b) revealed a 2.1-fold increase (p-value=1.7x10-2) in a "ISG15-hi" monocyte population expressing high levels of interferon (IFN)-inducible markers (i.e. IFI6 and IFI44L, Fig.1c). Concomitantly, an "Intermediate" monocyte population (expressing classical NAMPT and non-classical IFITM3, Fig.1c) showed a significantly decreased frequency (1.4-fold, p-value=2.8x10-2) in SSc-ILD subjects, and a strong negative correlation with ISG15hi subset counts (Pearson r=-0.70; p-value=2.45x10-7). Differential expression analysis identified 33 genes (1.2-fold, FDR < 2x10-2) between SSc-ILD and non-SSc-ILD in ISG15-hi monocytes (Fig.2a), with robust enrichment in the "Interferon signaling" pathway (FDR=1.5x10-10) (Fig.2b). For the Intermediate monocyte population, 61 genes had a significant negative correlation (-0.50 < Pearson r< -0.31; p-value < 0.05) associated with SSc-ILD severity and were enriched in pathways including "Cytokine signaling in immune system" (FDR=3.27x10-5) and "Innate immune system" (FDR=8.07x10-3). Of note, 18/61 genes were found to be significantly differentially expressed in SSc-ILD patients with the highest ILD severity (fvc < 55%), including the innate immunity gene FPR1 (Pearson r =-0.48, p-value=1.15x10-3).

Conclusion: Using single cell analysis, we identified a novel cluster of circulating monocytes expressing high levels of type I IFN-inducible markers that exhibits a significant association with presence and severity of SSc-ILD. Our findings suggest that these ISG15-hi monocytes may be cellular effectors critically involved in the dysregulated type I IFN activation driving SSc pathogenesis and identify them as promising targets for disease-specific therapeutic intervention.

Disclosure: R. Ainsworth: None; **K. Taylor**: None; **Y. Cao**: None; **T. Sasaki**: None; **D. Rao**: AstraZeneca, 2, Bristol-Myers Squibb, 2, 5, GlaxoSmithKlein(GSK), 2, Hifibio, 2, Janssen, 5, Merck, 5, Scipher Medicine, 2; **N. Bottini**: Thirona Bio, 2; **F. Boin**: None.

Abstract Number: 0793

The Dual Specificity Phosphatase 6 (DUSP6) Regulates Arthritis Severity and IL10 Production

Teresina Laragione, Carolyn Harris, Natasha Rice and Percio Gulko, Icahn school of Medicine at Mount Sinai, New York, NY

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: RA – Animal Models
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

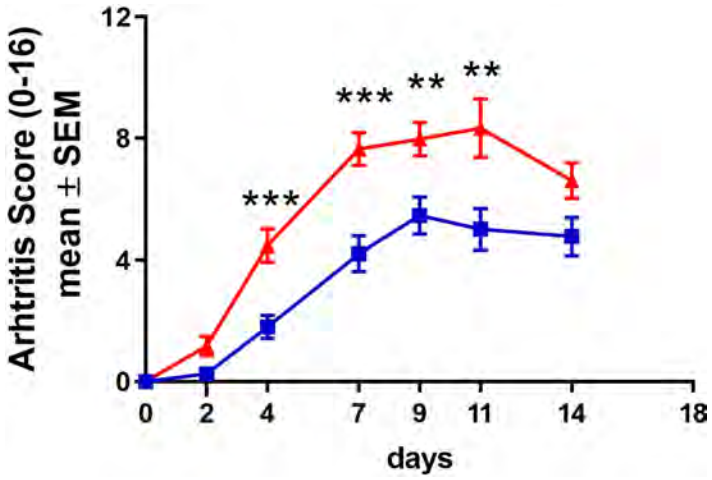

Figure 1. DUSP6 KO mice (BLUE line) were significantly protected in KSIA, compared with DUSP6 wild-type (RED line). (**P<0.001; ***P<0.0007).

Background/Purpose: We have previously identified the Huntingtin-interacting protein-1 (HIP1) as a new gene implicated in the regulation of the rheumatoid arthritis (RA) fibroblast-like synoviocyte (FLS) invasiveness induced by receptor tyrosine kinases, and in arthritis severity. Following that observation we examined genes and proteins regulated by HIP1 as those might generate important understanding of disease pathogenesis, and potentially new targets for treatment.

Methods: We used a combination of siRNA knockdown, gene expression and invasion assays in RAFLS, followed by immunoprecipitation and western blots. DUSP6 knockout (KO) mice were studied in the KRN serum induced arthritis (KSIA) model.

Results: In RA FLS knockdown for HIP1 we detected increased mRNA levels of the dual specificity phosphatase 6 (DUSP6). We confirmed protein expression of DUSP6 in RA FLS cell lines and binding of DUSP6 to HIP1 by immunoprecipitation in RA FLS cell extracts, followed by western blotting. We hypothesized that, like HIP1, DUSP6 might also be involved in FLS invasiveness. Knockdown of DUSP6 with siRNA significantly decreased RA FLS invasiveness by more than 50% ($P< 0.001$). In the arthritis model of KSIA, both male and female DUSP6 KO mice were significantly protected compared with wild-type mice, developing a significantly milder disease (maximum disease reduction of nearly 50% at day seven; figure). DUSP6 KO mice also had increased numbers of $CD4^+CD45^-CD49b^+LAG3^+IL10^+$ Tr1 regulatory T cells ($P< 0.01$) in the spleen, increased serum levels of IL10, and lower serum levels of IL6 ($P< 0.01$). RNA sequencing analyses revealed significantly increased representation of ERK and MAPK pathways and genes in the spleens of DUSP6 KO mice, compared with DUSP6 wild-type. DUSP6 is known to inactivate MAPK pathway proteins and therefore the RNA sequencing finding were consistent with decreased DUSP6 activity.

Conclusion: We identified a new HIP1-binding protein, DUSP6, and demonstrated that like HIP1, DUSP6 regulates arthritis severity and joint damage. Our findings suggest that DUSP6 interferes with disease severity by modulating FLS invasiveness and regulating IL10 production by Tr1 cells and suppression of IL6. This new discovery has the potential to become the basis for the development of new treatments for RA and possibly other autoimmune and inflammatory diseases.

Disclosure: T. Laragione: None; **C. Harris**: None; **N. Rice**: None; **P. Gulko**: None.

Abstract Number: 0794

Microbiota-dependent Indole Production Is Required for the Development of Collagen-induced Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: RA – Animal Models
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: While alterations in tryptophan (Trp) metabolism have been broadly implicated across autoimmune diseases (including RA, SpA, SLE, and MS), the specific role(s) of Trp metabolites in the development of disease are not well characterized. We previously identified significant alterations in tryptophan metabolism in mice with collagen-induced arthritis (CIA) that occurred in a microbiome-dependent manner, including significantly elevated indole. As indole is exclusively produced via microbial Trp metabolism, we modulated indole production through either antibiotic-mediated microbiome depletion or reduction of dietary Trp to dissect the effects of tryptophan, indole, and the microbiome on the development of CIA.

Methods: To regulate dietary Trp, 6wk-old male DBA/1J mice were maintained on either a Trp-sufficient (TS, 0.18% Trp) or Trp-low (TL, 0.05% Trp) diet. For the microbiome depletion studies, mice were treated with broad-spectrum antibiotics (ampicillin, neomycin, metronidazole, and vancomycin) in the setting of a Trp-sufficient diet. CIA was induced by immunization of bovine type II collagen (CII) emulsified in CFA at days 0 and 21. Indole or vehicle were added back either in drinking water or by oral gavage. CIA severity was assessed clinically and histologically. On day 35, serum and tissues were analyzed by flow cytometry, ELISA, and immunohistochemistry.

Results: Depletion of either the microbiome or dietary Trp protected mice from developing CIA. Adding back indole in either setting rescued CIA severity, suggesting that indole is sufficient to incite disease. These findings were confirmed further by amelioration of disease in mice colonized with tryptophanase-deficient bacteria, which are unable to produce indole. Indole supplementation in the TL setting lead to significant increases in RA-relevant serum cytokines (IL-6, TNF, IL-1β) and IL-17-producing, CII-reactive Th17 cells. Indole supplementation also resulted in increased activation of complement by CII-specific antibodies, C3 deposition in the joints, CII-specific IgG2b, and antibody galactosylation compared to the Trp-sufficient group.

Conclusion: Altogether, our data suggest that the presence of either the microbiota or dietary Trp alone are insufficient to induce disease, and that microbial metabolism of Trp into indole is essential for CIA development. Indole supplementation induces a pro-inflammatory, Th17-skewed immune signature. As IgG2b and galactosylation are thought to promote complement binding and activation, our findings suggest that indole supplementation may enhance pathogenic autoantibody function, which is consistent with the observed increase in complement activation and C3 deposition in the joints. While the cellular target(s) of indole are yet to be identified, this data provides a novel mechanism through which altered tryptophan metabolism promotes disease development in the CIA model. Furthermore, these findings identify microbiome-mediated modulation of Trp metabolism as a potential pathway to block or treat disease.

Disclosure: B. Seymour: None; **B. Trent**: None; **B. Allen**: None; **S. Liu**: None; **S. Sneed**: None; **R. Anthony**: None; **k. Kuhn**: pfizer, 5, ucb, 2.

Abstract Number: 0795

The Focal Adhesion Protein Lasp1 Links the Arp2/3 Complex to Cell-to-cell Contact Formation in Arthritic Fibroblast-like Synoviocytes

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SESSION INFORMATION
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Session Title: Abstracts: RA – Animal Models
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Session Time: 4:00PM–5:30PM

Background/Purpose: In rheumatoid arthritis (RA), fibroblast-like synoviocytes (FLS) undergo a stable transformation leading to an aggressive phenotype that mediates cartilage damage through increased levels of adhesion molecules. In this context, Lasp1 and the Arp2/3 complex are of interest as they modulate actin organization and turnover of focal adhesions. Therefore, we investigated the effects of Arp2/3 on cadherin-11 mediated cell-to-cell contact formation using the arthritic hTNFtg mouse model.

Methods: The expression levels of Lasp1 and Arp2/3 protein complex were examined in synovial tissue of wild type (wt) and hTNFtg hind paws by using Western blot analysis and their subcellular distribution was investigated by immunofluorescence stainings. In addition, *lasp1*$^{-/-}$ mice were crossed with hTNFtg animals, and offspring were examined for disease progression and joint destruction. Primary FLS were isolated from wt, *lasp1*$^{-/-}$, hTNFtg and *lasp1*$^{-/-}$hTNFtg mice, and co-immunoprecipitation experiments with cell lysates using G-labelled Dynabeads were performed. Furthermore, the effects of the Arp2/3 inhibitor CK666 on the formation of cadherin-11 mediated cell-to-cell contacts in FLS from hTNFtg and *lasp1*$^{-/-}$hTNFtg mice were analyzed by immunofluorescence stainings. To determine the functional effects of CK666 on FLS migration, all genotypes were examined in a modified scratch assay, to also assess the effects on pathway activation, cells were stimulated with the growth factor PDGF.

Results: Elevated levels of Lasp1 were detected in synovial tissue and FLS of hTNFtg compared to wt mice. Assays showed that Arp2/3 is part of the adherens junction (AJ) machinery in wt and hTNFtg FLS, although Arp2/3 expression levels were not altered between genotypes. *In vivo*, assessment of *lasp1*$^{-/-}$hTNFtg mice revealed a milder arthritis score, less cartilage degradation and reduced FLS attachment to articular cartilage compared with hTNFtg mice.*In vitro*, β-catenin expression was found mainly at adhesion sites between adjacent cells, but the loss of Lasp1 resulted in an altered β-catenin pattern and marked changes in AJ arrangement. In hTNFtg FLS, these structures were characterized by a zipper-like pattern. In contrast, these structures were interrupted in *lasp1*$^{-/-}$hTNFtg FLS. Interestingly, CK666 induced zipper-like structures in hTNFtg FLS comparable to the pattern were found in *lasp1*$^{-/-}$hTNFtg cells. Quantification of scratch assay data revealed a significantly reduced migration rate of *lasp1*$^{-/-}$hTNFtg FLS compared to hTNFtg FLS (-75.2.%, $p< 0.05$) and even more prominently in the presence of CK666 the hTNFtg FLS showed a reduction in migration compared to controls (-42.7%, $p< 0.05$). Furthermore,*lasp1*$^{-/-}$hTNFtg FLS showed decreased Src phosphorylation following PDGF stimulation compared with hTNFtg FLS. Interestingly, the presence of CK666 also blocked the phosphorylation of Src in hTNFtg FLS.

Conclusion: Lasp1 represents an interesting target involved in RA-related joint destruction, as its loss leads to significantly reduced cartilage destruction and altered FLS contacts mediated by Arp2/3.

Disclosure: D. Beckmann: None; **A. Krause**: None; **U. Hansen**: None; **H. Kiener**: None; **J. Kremerskothen**: None; **H. Pavenstädt**: None; **A. Korb-Pap**: Galapagos, 5; **T. Pap**: AbbVie/Abbott, 2, Galapagos, 5, UCB, 2.

Abstract Number: 0796

Role of Group 2 Innate Lymphoid Cells in the Pathogenesis of Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: RA – Animal Models
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Immune-cell mediated activation of joint-lining fibroblast-like synoviocytes (FLS) play a key role in joint inflammation and destruction during Rheumatoid arthritis (RA). Thus, identifying factors that promote aggressive and joint-destructive FLS behavior is viewed as a high priority in the development of novel anti-RA therapies. Innate Lymphoid Cells (ILC) are a family of tissue resident innate immune cells that are the innate counterparts to T cells. A major function of ILCs is to interact with local tissue stromal cells in order maintain tissue homeostasis. Although ILCs have been identified in the synovium of RA patients, their role in disease pathogenesis and their potential interaction with FLS remains largely unknown. Here, we identified a novel pathogenic role for ILC2 in arthritis that is mediated through their production of the fibroblast-activating growth factor amphiregulin (AREG).

Methods: Subsets of synovial ILC were assessed in the active K/BxN model and the K/BxN serum transfer-inducing arthritis (STIA) model. Role of ILCs in arthritis was determined by subjecting Rag2-deficient ($Rag2^{-/-}$) and ILC-deficient ($Rag2^{-/-}IL2rg^{-}$) mice to STIA. Role of AREG in the STIA model was evaluated using AREG-KO mice and mice with a conditional deletion of AREG in ILC2 ($Rag2^{-/-}$ IL5-Cre Areg-floxed). Clinical scoring of arthritis was followed by histological assessment. Effect of ILC-derived cytokines on FLS migration was evaluated in vitro. Mann-Whitney or un-paired T tests were used for statistical differences.

Results: Assessment of ILC subsets revealed that ILC2 is the predominant ILC population in the arthritic synovium of mice with active K/BxN arthritis and STIA (*P=0.05* vs. non-arthritic control). ILC-deficient mice ($Rag2^{-/-}IL2rg^{-}$) showed reduced development of STIA (*P=0.0072* vs. $Rag2^{-/-}$ mice), indicating that ILCs promote arthritis development. Assessment of ILC signature cytokines identified the ILC2-derived growth factor AREG to be significantly increased in arthritic joints (*P=0.0001* vs. non-arthritic control). A pathogenic role for AREG in arthritis development was supported by a significant alleviation in disease severity in AREG-KO mice subjected to STIA (*P=0.05* vs. control littermate mice). We identified ILC2 as the

major source of synovial AREG during arthritis and conditional deletion of AREG in ILC2 resulted in reduced arthritis development (*P=0.0044* vs. WT littermate controls). Mechanistically, we found that AREG promotes activation and migration of FLS (*P=0.0001* vs control).

Conclusion: We find that ILC2 is the predominant ILC subset in arthritic joints of mice with K/BxN arthritis. Furthermore, ILC2-derived AREG enhances development of arthritis in mice and promotes FLS activation and migration. We propose that the AREG signaling pathway may provide a novel therapeutic option for the treatment of RA.

Disclosure: A. Nguyen: None; **A. Lastowska**: None; **M. Bollmann**: None; **S. Kourmoulakis**: None; **C. van der Plas**: None; **A. Hultgård Ekwall**: AbbVie/Abbott, 1, 2, Boehringer-Ingelheim, 6, Pfizer, 1; **D. Zaiss**: None; **G. Firestein**: Eli Lilly, 5; **M. Svensson**: None.

Abstract Number: 0797

Innate Lymphoid Cells Enhance Development of CD4+ T-cell Driven Autoimmune Arthritis

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SESSION INFORMATION
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Session Title: Abstracts: RA – Animal Models
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Innate Lymphoid cells (ILCs) are innate counterparts to T-cells that, based on their functional phenotype, can be divided into three subpopulations called Group 1 (ILC1), Group 2 (ILC2) and Group 3 (ILC3). ILC subsets in autoimmune and chronic inflammatory diseases have been shown to display altered distribution and function, indicating subset-specific involvement. Although these tissue resident immune cells have been identified in the synovium of patients with rheumatoid arthritis (RA), their role in disease pathogenesis still remains largely unknown. SKG mice, which carry the Zap70W163C point mutation, develop autoimmune arthritis due to a defective negative selection of CD4+ T-cells in thymus. Here, we use the SKG mouse model to further assess the role of ILCs in arthritis development and find that ILCs have an important role in aggravating disease progression.

Methods: Arthritogenic CD4+ SKG T-cells were transferred to T and B cell deficient Rag2-knock out (Rag2-/-) mice to induce development of SKG arthritis. ILC subsets were evaluated in arthritic joints of mice with either spontaneous or mannan- induced SKG arthritis by flow cytometry. The role of ILCs in SKG arthritis was evaluated by transferring CD4+ SKG T-cells to ILC-deficient Rag2 and IL2rg double knockout (Rag2-/-IL2rg-) mice. Additionally, ILCs were isolated by flow cytometry, expanded in vitro and adoptively transferred in combination with CD4+ SKG T-cells into ILC-deficient (Rag2-/-IL2rg-) mice. Development of arthritis was monitored by clinical scoring. Mann-Whitney or un-paired T tests were used for statistical differences.

Results: Phenotypic characterization of ILC subsets in arthritic ankles revealed that ILC2 is the dominant synovial ILC population in joints of mice in both mannan-induced and spontaneous arthritis. ILC1 expanded in joint of mice during both mannan-induced and spontaneous arthritis. However, a synovial presence of ILC3 could only be observed in mice with mannan-induced arthritis. Surprisingly, there was no significant difference in severity between mannan-induced and

spontaneous arthritis in Rag2$^{-/-}$ mice after transfer of CD4^{+} SKG T cells. The role of ILC in SKG arthritis was supported by an alleviated arthritis development in ILC-deficient mice (P=0.041) after transfer with CD4+ SKG T cells. Finally, reconstitution of ILC-deficient mice with ILCs aggravated arthritis development after transfer with CD4+ SKG T cells (P=0.027).

Conclusion: Here we identify that ILC2 is the dominant ILC population in joints of mice with SKG arthritis. In addition, the aggravated development of arthritis in ILC-deficient mice after reconstitution of ILCs demonstrates the pathological effect of ILCs in SKG arthritis. Furthermore, the mannan-specific expansion of ILC3 in arthritic joints, suggest that synovial ILC3 are either directly or indirectly activated by inflammatory signals induced via the lectin pathway. Together, our results show that ILCs play a key role in promoting development of SKG arthritis and that different inflammatory triggers (e.g. mannan) induce unique synovial ILC distribution, which could result in specific synovial pathotypes.

Disclosure: A. Lastowska: None; **C. van der Plas**: None; **A. Nguyen**: None; **S. Kourmoulakis**: None; **M. Bollmann**: None; **M. Svensson**: None.

Abstract Number: 0798

A Novel 3D Model of Rheumatoid Arthritis Synovial Tissue Incorporating Fibroblasts, Endothelial Cells and Macrophages

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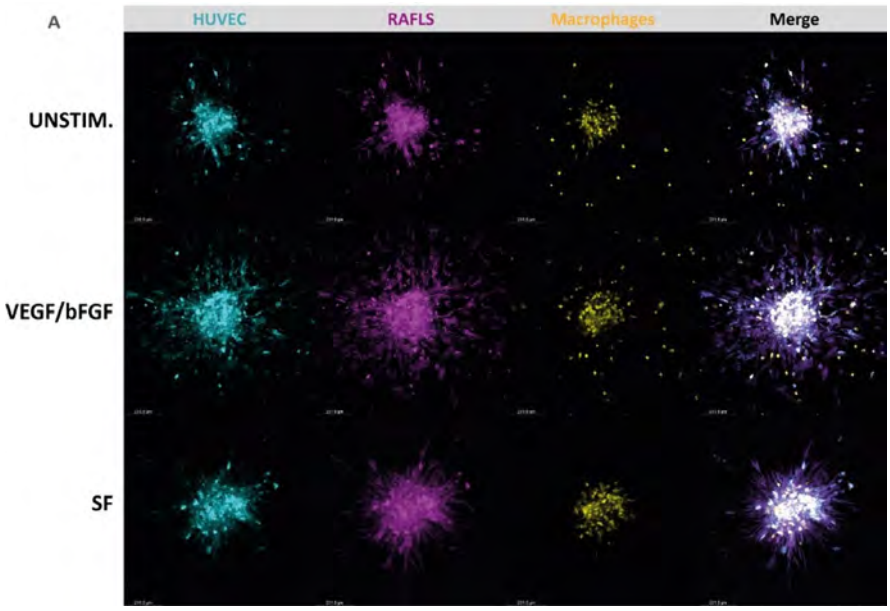
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: RA – Animal Models
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Rheumatoid Arthritis (RA) is a progressive and systemic autoimmune disorder associated with chronic and destructive inflammation of the joints. The hallmarks of RA are synovial cell proliferation, extensive neoangiogenesis and infiltration of numerous immune cells into the synovial tissue. *In vitro* approaches simulating RA synovial tissue are crucial in preclinical and translational research to expand our knowledge on RA human pathophysiology and to test new diagnostic and therapeutic applications. Here, we present the engineering of a spheroid-based model of RA synovial tissue which mimics the close interaction between cells and key pro-inflammatory mediators present in the inflamed synovium.

Methods: Monocyte-derived macrophages were cultured at different concentrations with RA fibroblast-like-synoviocytes (RAFLS) and endothelial cells (ECs) for 24 hours to allow for spheroid formation. Then, the spheroids were placed in a collagen-based matrix for 40 hours to study spheroid outgrowth in 3 dimensions. The spheroids were left unstimulated, or cultured in the presence of growth factors VEGF/bFGF or RA synovial fluid (SF). Spheroid outgrowth and cell migration were quantified for all conditions using confocal microscopy and a new quantification approach by machine learning (QuPath).

Results: Addition of macrophages to the previously established 3D model of RA angiogenesis consisting of ECs and RAFLS resulted in close interaction of macrophages with RAFLS and ECs within the spheroid structure. The number of macrophages that migrated out from the core increased with the initial macrophage input while slightly promoting spheroid outgrowth. The optimal ratio between RA-FLS, ECs and macrophages in our system was established accordingly as 1:2:0.8.



Representative confocal Z-stack projection pictures of the 3D model containing 3.75x10^4 RAFLS (magenta), 7.5x10^4 EC (cyan) and 3.0x10^4 macrophages (yellow). Spheroids were left either unstimulated (UNSTIM.), stimulated with VEGF/bFGF (10 ng/ml) or SF (20%). VEGF/bFGF induces spheroid outgrowth in the new 3D model containing macrophages, whereas RASF enhances macrophage containment and compaction.

Addition of growth factors (VEGF/bFGF) significantly promoted spheroid outgrowth compared to the unstimulated condition in the new model *($p< 0.05$)*. The presence of SF significantly enhanced cell containment of the ECs and macrophages within the core ($p< 0.05$).

Conclusion: We present a novel 3D-spheroid based model consisting of RA-FLS, ECs and macrophages that mimics the RA synovial tissue microenvironment. This model is useful to dissect the role of specific cell types in inflammatory responses in RA, to study specific signaling pathways involved in the disease pathogenesis and examine the potential of novel diagnostic (molecular imaging) and therapeutic compounds, including small molecule inhibitors and biologics.

Disclosure: E. Philippon: None; **L. van Rooijen**: None; **J. van Hamburg**: None; **F. Khodadust**: None; **C. Van der Laken**: None; **S. Tas**: None.

Abstract Number: 0799

Human Chimeric Antigen Receptor (CAR)-Tregs Targeting OX40L for Treatment of Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: T Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Chimeric Antigen Receptor Regulatory T cells (CAR-Tregs) are an emerging strategy to restore immune tolerance during auto- or allo-immune conditions. However, most autoimmune diseases do not have a single or consistent pathogenic antigen to target. OX40L is a co-stimulatory protein expressed on activated antigen presenting cells (APCs). Polymorphisms in OX40L that lead to increased expression are associated with systemic lupus erythematosus (SLE), and the frequency of OX40L+ APCs tracks with disease activity in SLE patients. OX40L may thus serve as an ideal CAR-Treg target in SLE.

Methods: We engineered a CAR construct containing a single chain variable fragment of anti-OX40L IgG (αOX40L scFv CAR) under transcriptional control of the *FOXP3* promoter to constrain CAR expression to canonical Treg. CAR-Tregs were compared with polyclonal Control-Tregs, transduced with a Neon Green reporter-encoding construct, for key features, including expression of immune regulatory proteins, suppression of T cell activation, and inhibition of APC functions *in vitro*.

Results: αOX40L scFv CAR expression was stable and selectively expressed in FOXP3+ Tregs during *in vitro* expansion over three weeks. CAR-Tregs were strongly activated by OX40L+ K562 cells **(Figure 1)**, which, relative to wild type K562 cells, drove expression of Treg-associated immune regulatory proteins LAG3 (5.6-fold), CTLA4 (14.8-fold), GARP (6.9-fold), and LAP (5.5-fold) without induction of pro-inflammatory cytokines (IL-2, TNFα, IL-17A, IFNγ). CAR-Tregs more potently

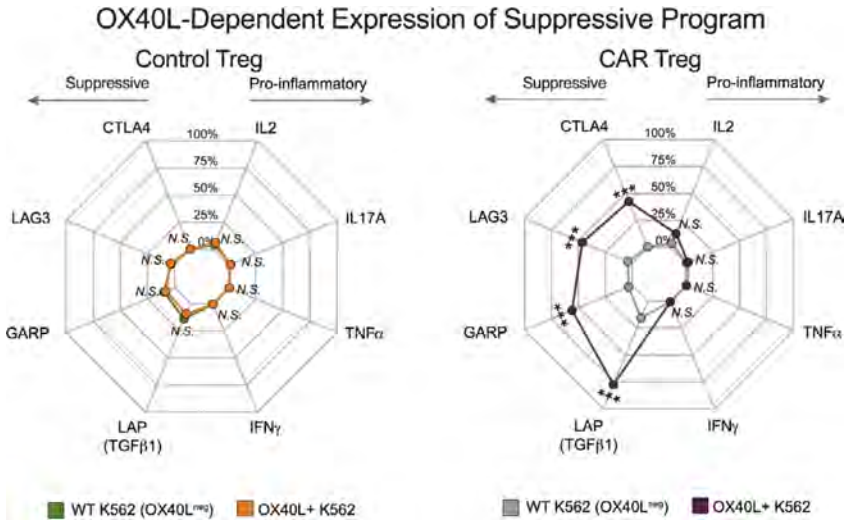

Figure 1: Activation of Treg suppressive program in OX40L-exposed CAR-Tregs. OX40L+ K562 cells led to a suppressive program in CAR-Tregs that was not seen in Control Tregs or when wild type (WT) K562 cells were used as stimulators. Expression of suppressive and inflammatory markers was measured by flow cytometry with the average values shown on radar plots.

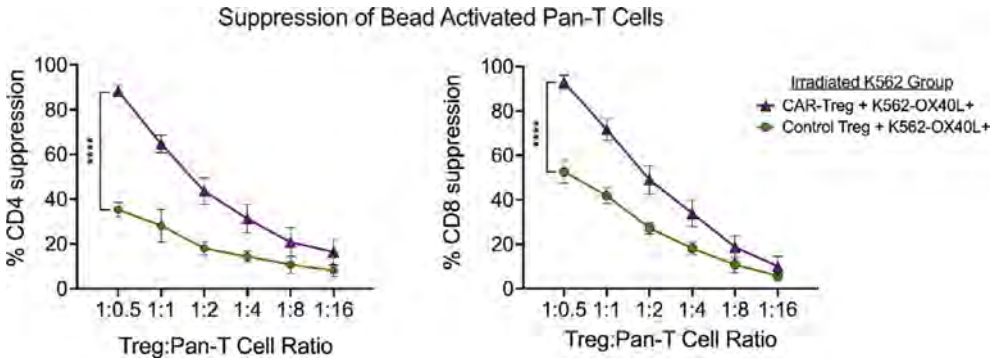

Figure 2: Superior T cell suppression by CAR-Tregs. CAR-Tregs exhibited a superior in vitro capability to suppress anti-CD3/CD28 mAb (bead) mediated CD4+ (left) and CD8+ (right) T cell proliferation. Tregs were co-cultured with irradiated OX40L+ K562 cells for one day prior to assay. Percent suppression was calculated based on cell division, comparing the 'with Treg' to the 'no Treg' conditions.

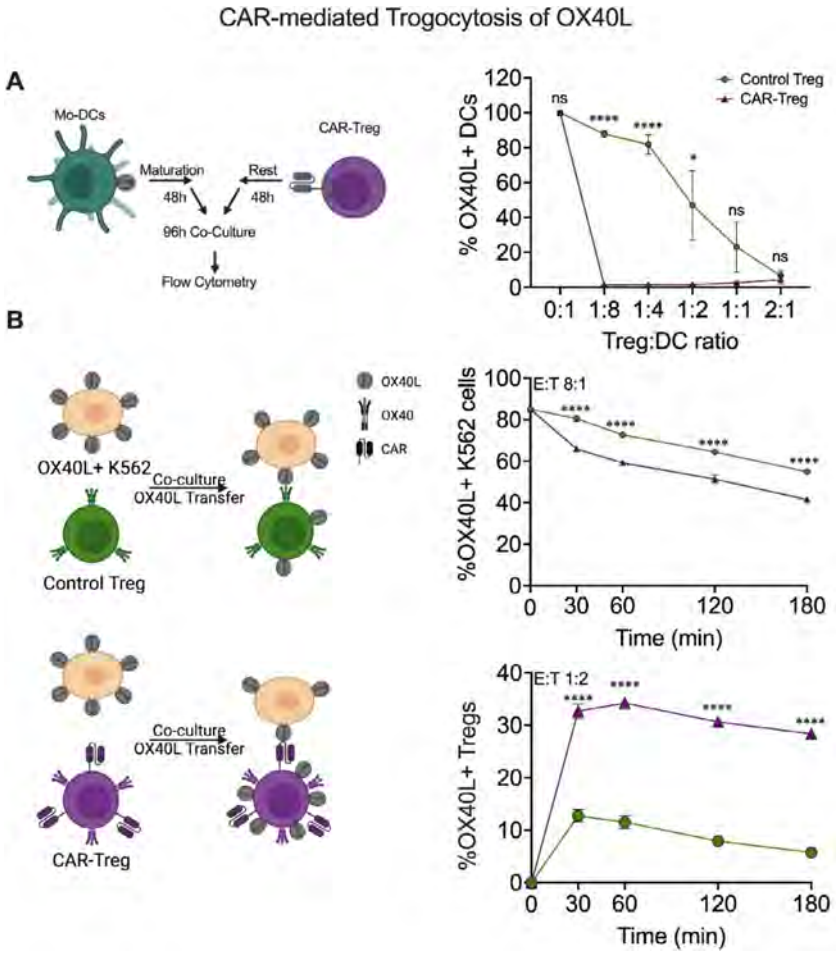

Figure 3. Superior trogocytosis of OX40L by CAR-Tregs. A. %OX40L+ cells gated on CD83+CD14+CD4- mo-DCs after co-culture with either Control- or CAR-Tregs for four days. B. Time-course assay showing rapid loss of OX40L from OX40L+ K562 cells (top) and gain on Control- or CAR-Tregs (bottom) upon co-culture. E:T indicates effector (Treg) to target (K562) cell ratio.

suppressed anti-CD3/CD28 mAb mediated CD4+ and CD8+ T cell proliferation than Control-Tregs (maximum suppression at a 2:1 Treg:T-cell responder ratio: 88.5%±3.7% vs.35.3±4.6% for CD4+ responders, $p < 0.0001$) **(Figure 2)**. CAR-Tregs also led to a greater reduction of OX40L on the surface of monocyte-derived dendritic cells (mo-DCs) relative to Control-Tregs as a result of enhanced OX40L trogocytosis – findings confirmed using OX40L+ K562 cells **(Figure 3)**.

Conclusion: We designed a novel CAR-Treg stimulated by OX40L on activated APCs. The αOX40L scFv CAR was selectively expressed in Tregs due to control by a *FOXP3* promoter, and CAR-Tregs preserved their anti-inflammatory expression profile. CAR-Tregs had superior *in vitro* suppression of both activated T cells and dendritic cells relative to Control-Tregs. This may be due to universal and potent activation of CAR-Tregs vs. polyclonal Control-Tregs but also from CAR mediated trogocytosis of OX40L on APCs making it unavailable for T-cell co-stimulation. Future work will be aimed at designing a mouse OX40L targeted CAR-Treg to assess in traditional murine SLE models. Overall, we demonstrate a unique approach to CAR-Treg design for treating autoimmune disorders by directing CAR-Treg against activated, disease-associated APCs.

Disclosure: H. Wobma: None; **X. Rui**: None; **F. Alvarez-Calderon**: None; **U. Gerdemann**: allovir, 9, 11, Pfizer, 3, Tessara Therapeutics, 5; **C. McGuckin**: None; **B. Blazar**: None; **V. Tkachev**: None; **L. Kean**: Bristol-Myers Squibb(BMS), 5, 9, Hifibio, 1, Mammoth bio, 1, Merck/MSD, 5, Novartis, 5, tessera, 5, vertex, 2.

Abstract Number: 0800

CD4$^+$ CD96$^+$ T Cells Are Pathogenic Effector Cells in Giant Cell Arteritis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

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Background/Purpose: In Giant Cell Arteritis (GCA), granulomatous infiltrates occupy the vessel wall and elicit maladaptive vascular remodeling with intimal hyperplasia. The major cell types of the granulomatous lesions are CD4$^+$ T cells and macrophages, some of which differentiate into multinucleated giant cells. Lesional CD4$^+$ T cells undergo clonal expansion and vasculitic arteries contain mRNA and protein of multiple T cell effector cytokines, but it is unclear whether GCA patients possess specialized T cell subsets that promote macrophage multinucleation and granuloma formation in the vessel wall.

Methods: Patients with a positive temporal artery biopsy or unequivocal evidence for GCA aortitis were enrolled into the study. Patients with granulomatosis with polyangiitis served as disease controls and age-matched healthy controls were recruited through the Biobank. Tissue lesions were analyzed by immunofluorescence staining of temporal artery sections. T cell phenotyping relied on multiparametric flow cytometry and T cell reactivity was tested against anti-CD3-loaded antigen-presenting cells. The functional relevance of CD4$^+$ T cell subsets was examined in immunodeficient mice engrafted with human arteries and immuno-reconstituted with immune cell populations from GCA patients (human artery-SCID chimeric mice).

Results: Memory CD4$^+$ T cells isolated from GCA patients and age-matched controls fell into 10 clusters based on the combinatorial expression of 8 immunoreceptors (CD45RA, CCR7, PD1, LAG3, CD226, CD96, TIGIT, TIM3). GCA patients selectively expanded CD4$^+$CD96$^+$ memory T cells (10.9% control, 16.9% GCA), while CD4$^+$TIGIT^{high} populations were reduced (24.5% control, 17.4% GCA). CD4$^+$CD96^{low} T cells, generated by siRNA transfection, induced vascular inflammation in artery-SCID chimeric mice (p=0.0044), indicating that CD96 delivers a negative signal and opposes T cell activation. The expansion of CD4$^+$CD96$^+$ T cells was dependent on interaction of CD96 with its ligand CD155 on the surface of antigen-presenting cells. Maldifferentiation of CD4$^+$ T cells in GCA patients was associated with the excessive production of three effector cytokines: IL-9 (p=0.02), IL-21 (p=0.028), and IFN-γ (p=0.03). In vivo testing identified IL-9 as a strong driver of vascular inflammation, associated with marked damage of the vessel wall smooth muscle cell layer. Anti-IL-9 treatment efficiently suppressed vascular inflammation (p=0.0025). In single cell RNA sequencing from tissue derived T cells, CD96 expression mapped to the T follicular helper cell population.

Conclusion: In GCA patients, the differentiation of CD4$^+$ memory T cells is abnormal, leading to the selective expansion of immature and multifunctional T cells, while the transition into effector T cells is decelerated. The underlying defect lies in antigen-presenting cells that withdraw opposing signals as T cells progress through their differentiation cycle. Resulting CD4$^+$ memory T cells hyperproduce IL-9, IL-21, and IFN-γ. Blocking T cell effector functions in GCA will therefore require targeting an array of cytokines.

Disclosure: S. Ohtsuki: None; **J. Morales**: None; **Y. Sato**: None; **C. Wang**: None; **M. Koster**: None; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Chemocentryx, 1, 6, Eli Lilly, 5, kiniksa, 5; **G. Berry**: None; **J. Goronzy**: AbbVie/Abbott, 1, Bristol-Myers Squibb(BMS), 1, Gilead, 1; **C. Weyand**: AbbVie/Abbott, 1, Bristol-Myers Squibb(BMS), 1, Gilead, 1.

Abstract Number: 0801

LncRNA PIGL-217 Regulates Th17 Differentiation by Targeting miR-5008-5p and Suppressing FoxO1 in Behçet's Disease

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: T Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Dysregulated Th17 cells are implicated in Behçet's disease (BD). However, the underlying mechanism remains unclear. Here we aim to elucidate the mechanism of forkhead box O1 (FoxO1) and its regulating long non-coding RNA (lncRNA) in modulating Th17 cells in BD.

Methods: Th17 cells in peripheral blood mononuclear cells (PBMCs) from BD and healthy controls (HCs) were analyzed by flow cytometry. Naïve $CD4^+$T cells from both groups were isolated for further experiments. Microarray analysis was performed on naïve $CD4^+$T cells of six BD patients and six gender- and age-matched HCs to gain insight into their respective gene expression profiles, which was validated by qRT-PCR analyses. To investigate the role of lncRNA in Th17 differentiation, naïve $CD4^+$T cells were transfected using siRNA, overexpression plasmids or miRNA mimics as required, and were incubated under Th17-polarizing condition for 5 days. A dual-luciferase reporter assay was used to confirm the target of miRNA.

Results: Circulating Th17 cells were elevated in active BD patients ($p< 0.0001$), which were positively correlated with BDCAF. BD naïve $CD4^+$T cells showed enhanced Th17 cell differentiation capacity compared to HC cells ($p< 0.001$) (Fig. 1). Microarray analysis revealed that Th17-related FoxO signaling pathway was inhibited in BD naïve $CD4^+$T cells, along with downregulation of FoxO1 and its related lncRNA PIGL-217 (Fig. 2A-B), which was confirmed in vitro ($p< 0.0001$ and $p< 0.001$, respectively). We further demonstrated that PIGL-217 silencing in naïve $CD4^+$T cells decreased FoxO1

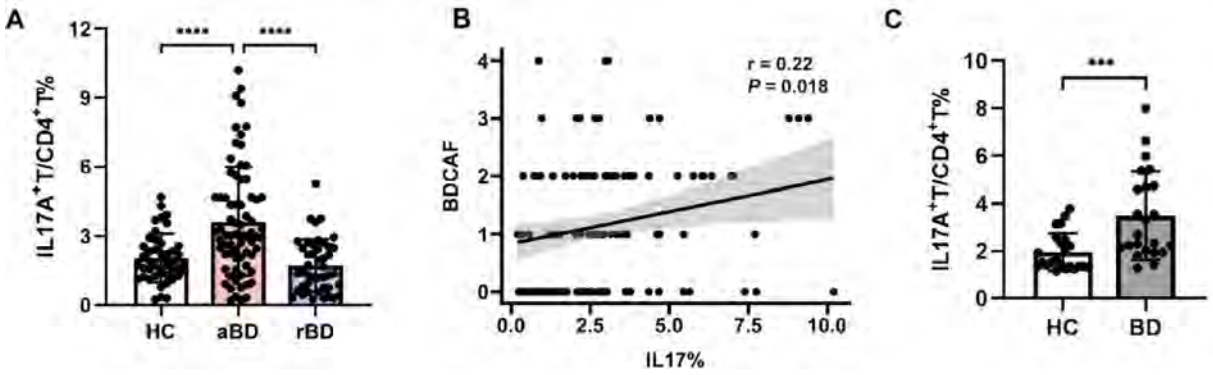

Fig. 1 Aberrant Th17 cells in BD patients. (A) Level of IL-17A+T cells in peripheral CD4+T cells of HC (n=43), active (n=71) and inactive (n=44) BD patients. (B) Pearson correlation of BDCAF with frequency of circulating IL-17A+T cells. (C) Level of IL-17A+T cells induced from HC (n=23) and BD (n=23) naïve CD4+T cells under Th17-polarizing condition for 5 days. ***p < 0.001, ****p < 0.0001.

expression ($p< 0.05$) and enhanced Th17 differentiation ($p< 0.05$), which was attenuated by FoxO1 overexpression ($p< 0.01$) (Fig. 2C). Using competing endogenous RNA (ceRNA) prediction, we identified miR-5008-5p as a candidate gene (Fig. 3A), with increased expression in BD naïve $CD4^+$T cells ($p< 0.0001$). Dual-Luciferase reporter assay confirmed FoxO1 and PIGL-217 were targeted by miR-5008-5p (Fig. 3B), the expression of which was significantly increased after PIGL-217 knockdown ($p< 0.05$). Finally, miR-5008-5p mimics significantly down-regulated FoxO1 expression ($p< 0.001$) and promoted Th17 differentiation ($p< 0.01$), which was reversed by PIGL-217 overexpression ($p< 0.001$) (Fig. 3C).

Conclusion: Our data suggest that Th17 cell differentiation is enhanced and plays a role in BD. We identify PIGL-217 as a novel lncRNA regulating Th17 differentiation, which acts as a sponge for miR-5008-5p to regulate FoxO1 expression via the ceRNA mechanism.

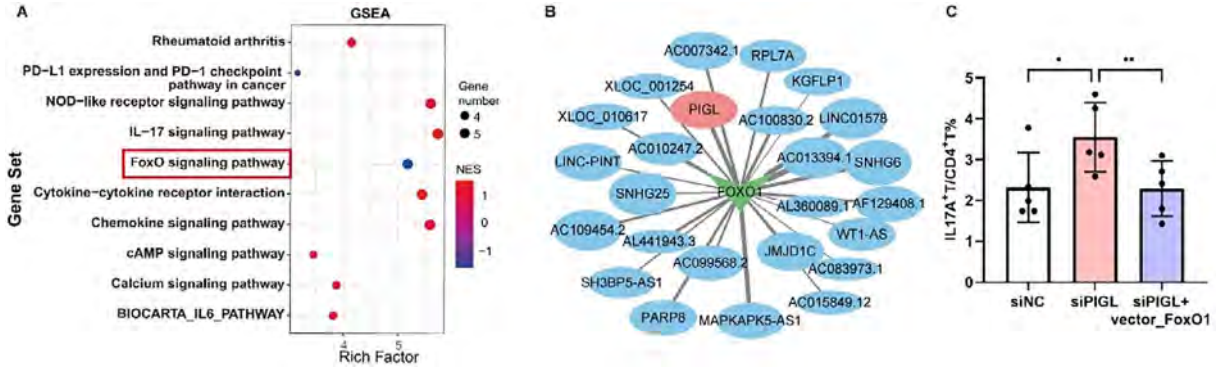

Fig. 2 Dysregulated PIGL-217 and FoxO1 in BD naïve CD4+T cells. (A) GSEA pathway analysis for differentially expressed mRNAs of BD naïve CD4+T cells. (B) Co-expression network of FoxO1 with associated 25 lncRNAs. (C) Level of Th17 differentiation with PIGL knockdown and FoxO1 overexpression. *p < 0.05, **p < 0.01.

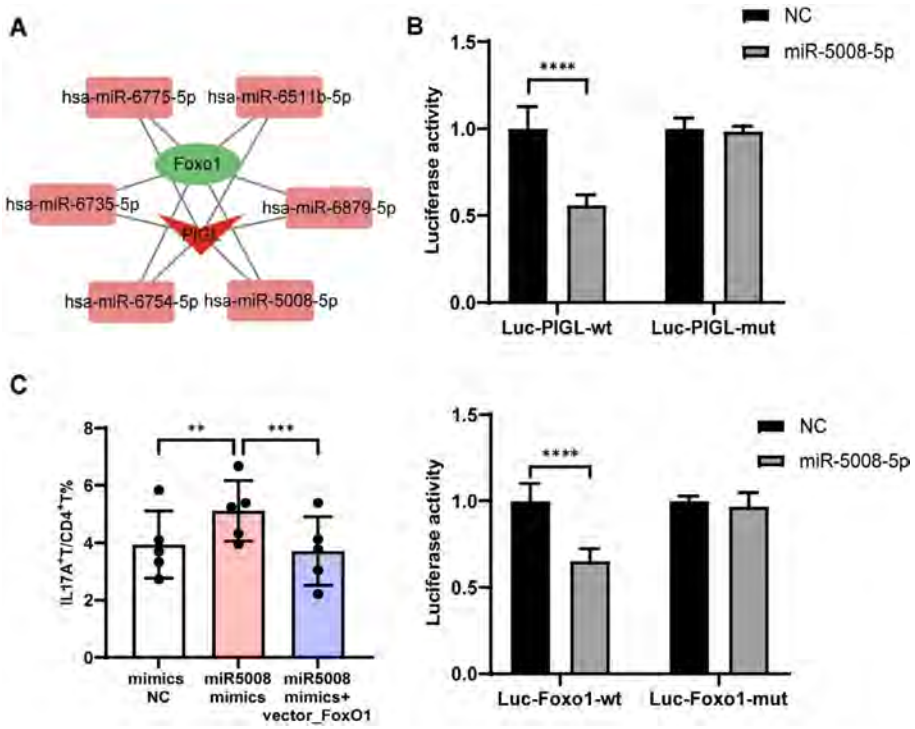

Fig. 3 PIGL-miR-5008-5p-FoxO1 ceRNA network. (A) Co-expression network of FoxO1 and PIGL-217 with associated 6 miRNAs. (B) Luciferase reporter activity of PIGL-217 (up) and FoxO1-3′UTR (down) in HEK-293T cells co-transfected with miR-5008-5p mimics or mimics NC. (C) Level of Th17 differentiation transfected with miR-5008-5p mimics alone or co-transfected with FoxO1 overexpression vector. **p < 0.01, ***p < 0.001, ****p < 0.0001.

Disclosure: Z. Wang: None; **X. Yu**: None; **H. Chen**: None; **W. Zheng**: None.

Abstract Number: 0802

Targeting Fibroblasts in Inflammatory Disease Using Engineered T Cells

Samuel Kemble[1], Christopher Mahony[2], Charlotte Smith[2], Joel Rurik[3], Haig Aghajanian[3], Jonathan Epstein[3], Mark Coles[4] and Adam Croft[2], [1]University Birmingham, Rugeley, United Kingdom, [2]University of Birmingham, Birmingham, United Kingdom, [3]University of Pennsylvania, Philadelphia, PA, [4]University of Oxford, Oxford, United Kingdom

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: T Cell Biology & Targets in Autoimmune & Inflammatory Disease

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

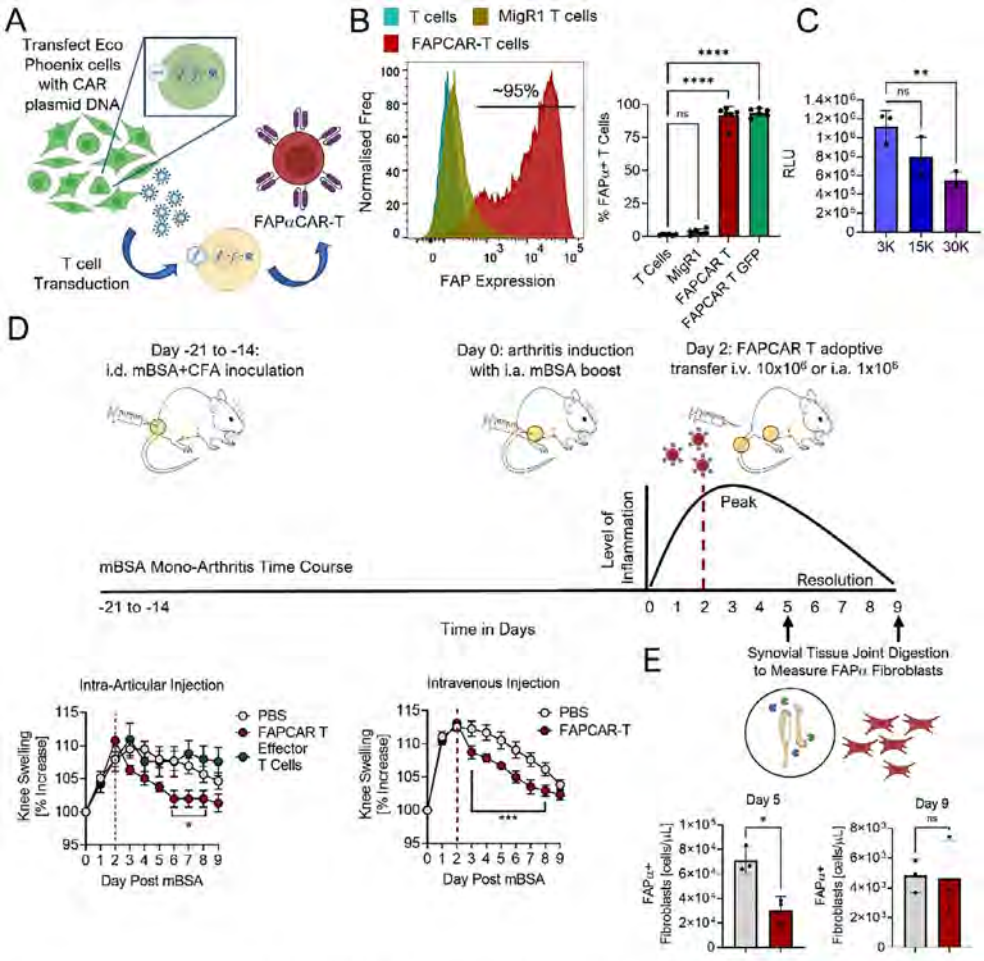

Figure 1: A) A schematic of FAPCAR-T cell generation. B) FAPCAR-T cell FAP expression measured by flow cytometry compared to non-transduced T cells and MigR1 (vector only) transduced T cells. C) In vitro killing assay: FAPCAR-T cells ($3x10^3$-$30x10^3$) were cultured for 24h with FAPα+luciferase HEK293T cells. After culture the remaining HEK293T cells were lysed and luciferase was measured by luminometer to determine cell targeting (the greater the cell death the lower the luciferase signal). D) The mBSA mono-arthritis model of inflammatory arthritis time course. Following induction of arthritis in a single knee joint (day 0), mice were administered FAPCAR-T cells i.v. ($10x10^6$) or i.a. ($1x10^6$) prior to peak of inflammation (day 2) and joint swelling was measured using callipers. E) At day 5 and day 9, synovial tissue from PBS and FAPCAR-T treated mice was enzymatically digested and the number of FAP expressing synovial fibroblasts was measured by flow cytometry.

Background/Purpose: Fibroblast activation protein alpha (FAPa) expressing fibroblasts orchestrate tissue inflammation and damage in rheumatoid arthritis (RA) as well as tissue immunity in primary Sjögren's syndrome (PSS) through the formation of tertiary lymphoid structures (TLS; Croft et al., Nature 2019 & Nayar et al., PNAS 2019). As a result, therapeutic targeting of these resident cells has the potential to reset the inflammatory tissue microenvironment, in favour of resolution. Our aim was to determine the therapeutic efficacy of FAPa-targeted chimeric T (FAPCAR-T) cell immunotherapy in inflammatory disease.

Methods: FAPCAR-T cells were generated and functionally tested as previously described (Aghajanian et al., Nature 2019) and were administered systemically and/or locally prior to peak of inflammation in murine models of inflammatory arthritis, or an inducible salivary gland inflammation model. Arthritis severity was determined by clinical scores and caliper measurements of swollen joints and changes in fibroblast activation states using 3′ single cell RNA profiling of CD45- sort-purified, CAR-treated synovial tissue. TLS characterization was determined by immunohistochemistry. FAPCAR-T-GFP, Fibroblast FAPa expression and leukocyte infiltration in enzymatically digested synovial or salivary gland tissue was measured by flow cytometry to determine CAR-T homing, FAPa targeting and inflammation, respectively.

Results: In arthritis, targeted deletion of FAPa fibroblasts was achieved through the adoptive transfer of FAPCAR-T cells that homed to the site of inflammation upon systemic administration and resulted in significant FAPa fibroblast cell depletion in the inflamed tissue. In both mono-articular and polyarticular arthritis models the intravenous or direct intra-articular administration of FAPCAR-Tcells prior to peak of inflammation suppressed disease severity by significantly attenuating joint inflammation. Single cell RNA profiling of CD45- sort-purified, FAPCAR-T treated synovial tissue identified a global defect in the stromal cell landscape. Systemic administration of FAPCAR-T cells in the salivary gland model significantly decreased the proportion of T and B cells and influenced TLS formation and maturity.

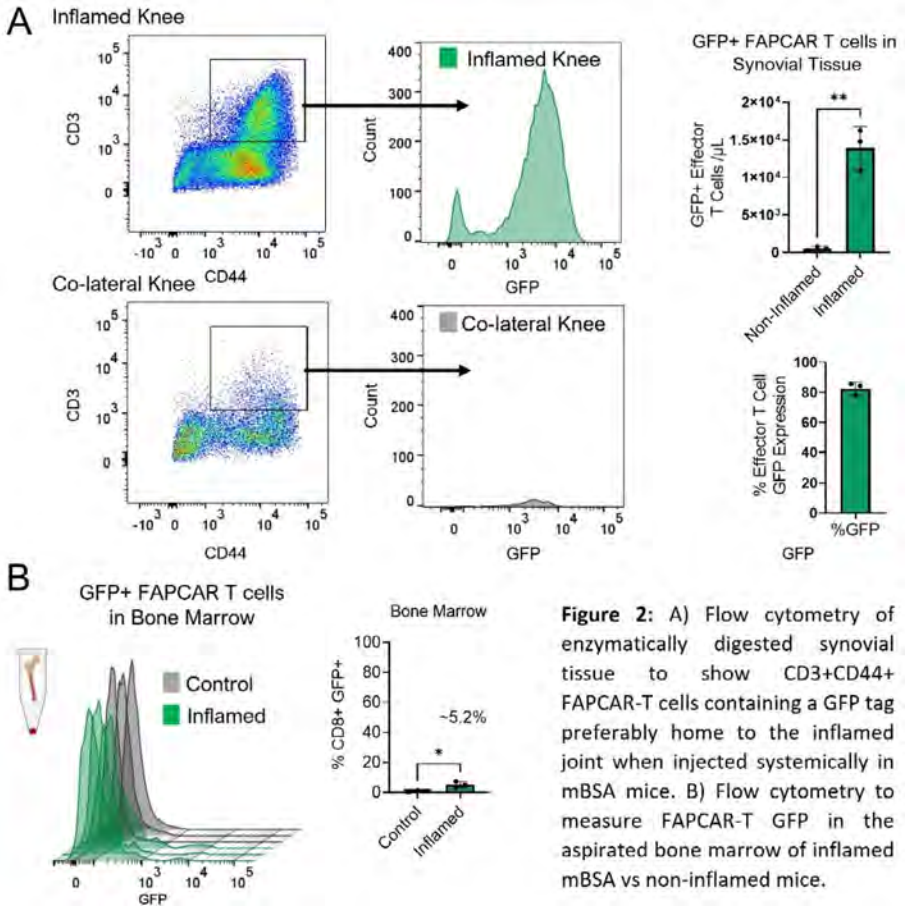

Figure 2: A) Flow cytometry of enzymatically digested synovial tissue to show CD3+CD44+ FAPCAR-T cells containing a GFP tag preferably home to the inflamed joint when injected systemically in mBSA mice. B) Flow cytometry to measure FAPCAR-T GFP in the aspirated bone marrow of inflamed mBSA vs non-inflamed mice.

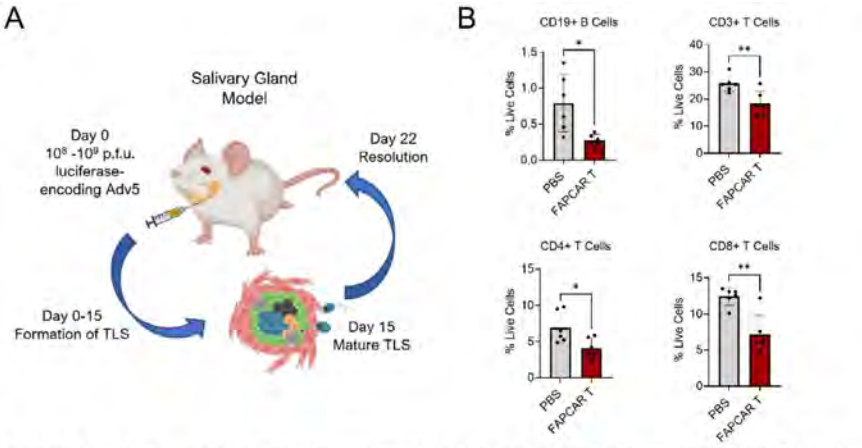

Figure 3: A) A schematic of the salivary gland PSS model. B) Mice were systemically administered 10x10^6 FAPCAR-T cells or PBS on day 10 and the % live T and B cells were measured by flow cytometry on day 15 (when mature, fully developed TLS are normally present).

Conclusion: FAPα is an attractive, therapeutically targetable biomarker of pathogenic fibroblasts. This study demonstrates potential therapeutic efficacy of fibroblast-targeted immunotherapy as a novel treatment in inflammatory disease.

Disclosure: S. Kemble: None; **C. Mahony**: None; **C. Smith**: None; **J. Rurik**: None; **H. Aghajanian**: Capstan Therapeutics, 1, 3, 8, 10, 11; **J. Epstein**: AstraZeneca, 2, Calico Laboratories, 5, Capstan Therapeutics, 2, 5, 8, 10; **M. Coles**: None; **A. Croft**: None.

Abstract Number: 0803

IL10 Inhibits Toll-like Receptor-9-induced T Cell Receptor-mediated T Cell Activation in Macrophage Activation Syndrome

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Abstracts: T Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Macrophage activation syndrome (MAS) is a potentially fatal complication of systemic juvenile idiopathic arthritis (sJIA). Gene expression pathway analyses have identified altered Toll-like receptor (TLR) signaling in sJIA and MAS. Repeated administration of CpG, a TLR-9 agonist, induces an MAS-like phenotype in mice; fulminant disease is induced with co-administration of intereukin-10 receptor blocking antibody (αIL10R). IL10 is an anti-inflammatory cytokine that induces T cell immune tolerance. Deficient production of IL10 by antigen presenting cells drives pathology in sJIA patients and animal models of the disease. Polymorphisms in the IL10 gene family confer susceptibility to sJIA. We hypothesized that IL10 inhibits T cell activation (TCA) in TLR-9-induced inflammation, and that TCA contributes to hypercytokinemia in TLR-9-induced inflammation.

Methods: Five experimental groups of C57Bl6 mice were studied: 1) untreated, negative controls; 2) MAS: treated with CpG 50 μg intraperitoneally (ip) every other day for 5 doses days -8 – 0; 3) CpGHi: treated with CpG 500 μg ip on day 0; 4) CpGHi+αIL10R: treated with CpG 500 μg plus αIL10R 1000 μg (both ip) on day 0; 5) αCD3ε (positive controls): treated intravenously with 50 μg of anti-CD3ε stimulating antibody on day 0. On day 1 following completion of treatment animals were sacrificed. Spleens were harvested and digested, and leukocytes were isolated. Cells were cultured in brefeldin A to entrap expressed products intracellularly or were stained directly post-isolation. Stained cells were analyzed with flow cytometry. Cytokine-driven-TCA was quantified by CD69 staining on flow cytometry. T cell receptor-mediated- (TCR-) TCA was quantified by Nur77 staining on flow cytometry. Data were analyzed using one-way Analysis of Variance with Šídák post-hoc tests.

Results: MAS exposure did not affect cytokine-driven-TCA. CpGHi-exposure increased cytokine-driven-TCA in CD4+ T cells compared to MAS-exposed mice and untreated controls (Fig. 1, $p < 0.05$). CpGHi+αIL10R exposure increased cytokine-driven-TCA compared to MAS- and CpGHi-exposed mice, and untreated controls (Fig. 1, $p < 0.05$). MAS exposure did not affect TCR-TCA. CpGHi exposure increased TCR-TCA compared to MAS-exposed mice and untreated controls (Fig. 2, $p < 0.05$). CpGHi+αIL10R exposure increased TCR-TCA compared to MAS- and CpGHi-exposed mice, and untreated controls (Fig. 2, $p < 0.05$). CpGHi+αIL10R exposure increased the proportion of CD8+ T cells expressing TNFα compared to untreated controls and CpGHi-exposed mice (Fig. 3B, $p < 0.05$), but not MAS-exposed mice. CpGHi+αIL10R exposure increased serum concentrations of TNFα, IL6, and IL12 compared to MAS- and CpGHi-exposed mice, and

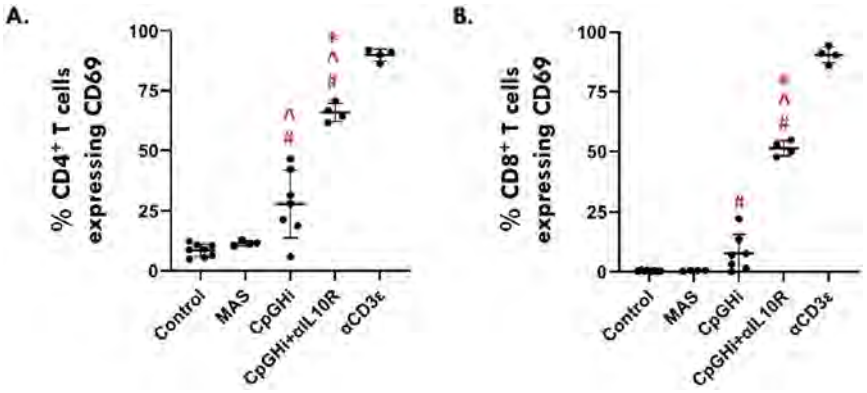

Figure 1. Flow cytometric data showing the relative proportions of CD69+ splenic (A) CD4+ and (B) CD8+ T cells. Data are pooled from three experiments of 12, 7 and 8 10-12-week-old mice. Gates defining T cell populations were unique to individual experiments. αCD3ε-exposed mice served as positive controls for individual experiments (%CD69+ CD4+ and CD8+ T cells set at 90%). Data were analyzed using one-way Analysis of Variance with Šídák post-hoc tests. # vs Control; ^ vs MAS; * vs CpGHi; $p < 0.05$.

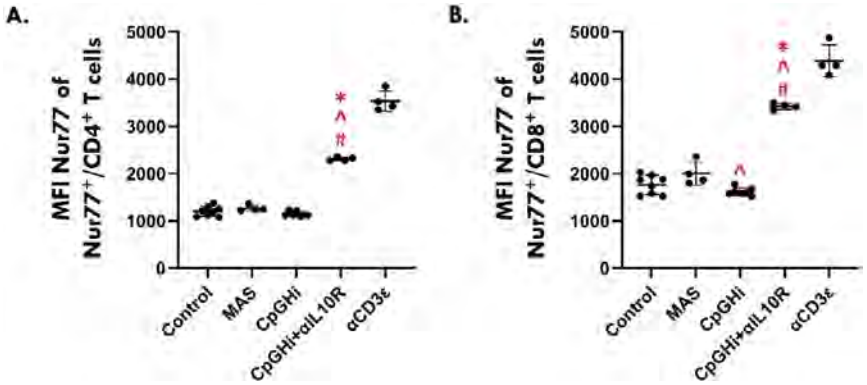

Figure 2. Flow cytometric data showing the median fluorescence intensities (MFIs) of Nur77+ splenic (A) CD4+ and (B) CD8+ T cells. Data are pooled from three experiments of 12, 7 and 8 10-12-week-old mice. Gates defining T cell populations were unique to individual experiments. αCD3ε-exposed mice served as positive controls for individual experiments (%Nur77+ CD4+ and CD8+ T cells set at 90%). Data were analyzed using one-way Analysis of Variance with Šídák post-hoc tests. # vs Control; ^ vs MAS; * vs CpGHi; $p < 0.05$.

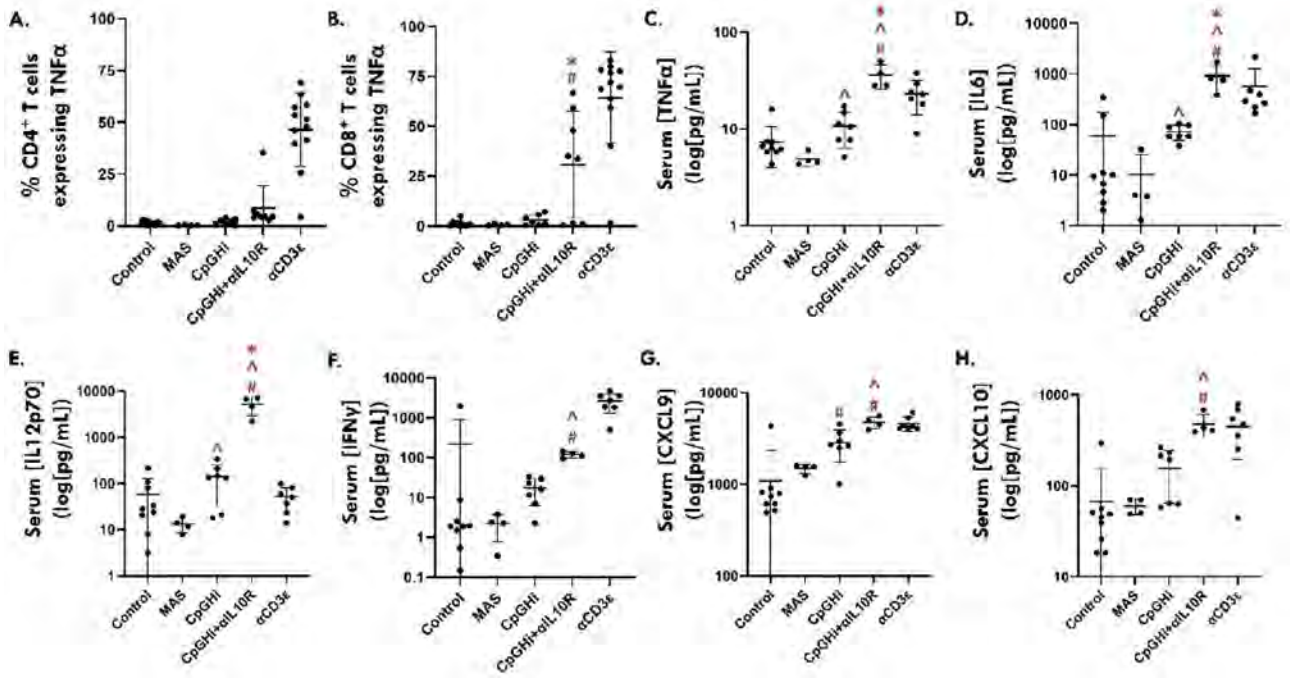

Figure 3. Flow cytometric data showing the relative proportions of TNFα+ splenic (A) CD4+ and (B) CD8+ T cells. Data are pooled from four experiments of 12, 11, 8 and 12 10-12-week-old mice. (C-H) Serum cytokine levels obtained via submandibular cheek bleed. Data are pooled from three experiments of 12, 11, and 8 and 10-12-week-old mice. (C-H) Statistical analyses were performed following log transformation of the data owing to failure of tests for normality. Data were analyzed using one-way Analysis of Variance with Šídák post-hoc tests. # vs Control; ^ vs MAS; * vs CpGHi; $p < 0.05$.

untreated controls (Fig. 3C-E, $p < 0.05$). CpGHi+αIL10R exposure increased serum concentrations of IFNγ, CXC-motif chemokine ligand 9 (CXCL9), and CXCL10 compared to MAS-exposed mice and untreated controls (Fig. 3F-H, $p < 0.05$).

Conclusion: IL10 prevents TLR-9-induced TCA. TCA contributes to TLR-9-induced hypercytokinemia. The established, non-infectious model of MAS with repeated administration of low-dose CpG does not adequately capture the contribution of T cells to the development of fulminant disease.

Disclosure: M. Eremita: None; **O. Geier**: None; **J. Hui-Yuen**: None; **M. Taylor**: None.

Abstract Number: 0804

Mutated NOD2 Controls IL-2 Production in Blau Syndrome Patients and Mice

Leah M. Huey[1], Emily Vance[1], Holly L. Rosenzweig[2], Bryce Binstadt[3] and Ruth J. Napier[2], [1]Oregon Health & Science University, Portland, OR, [2]Oregon Health & Science University, VA Portland Health Care System, Portland, OR, [3]University of Minnesota, Minneapolis, MN

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: T Cell Biology & Targets in Autoimmune & Inflammatory Disease

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Microbial sensing molecule nucleotide-binding oligomerization-domain containing protein 2 (NOD2) is expressed by CD4+ T cells and plays a novel T cell-intrinsic role within CD4+ T cells in protecting against Th17-mediated experimental uveitis and arthritis. It is known that CD4+ T cells from Nod2-deficient (*Nod2*$^{-/-}$) mice have increased IL-17A responses and decreased IL-2 compared to WT mice. However, it is unknown how *NOD2* mutations that cause the rheumatic disease Blau Syndrome affect T cell function. Here, we investigated how mutated *NOD2* controls T cell activation and cytokine production in Blau patients and Blau knock-in mice (*Nod2*^{R314Q}).

Methods: Peripheral blood mononuclear cells from Blau patients or healthy controls were treated with T cell receptor (TCR) activator, anti-CD3, and co-stimulatory agent, anti-CD28, either overnight or for 5 days followed by a 4-hour incubation with anti-CD28 or phorbol myristate acetate (PMA) and ionomycin. After incubation, cytokine expression was quantified by ELISA and flow cytometry in supernatants and cells, respectively. Patient plasma IL-2 was quantified by ELISA. Splenocytes from wildtype (WT) naïve mice or Blau knock-in mice expressing *Nod2*^{R314Q}, a mutation in *Nod2* known to cause Blau in humans, were stimulated with T cell activators and analyzed for cytokine production by ELISA and flow cytometry. Data were analyzed by unpaired two-sided student T test, and $p < 0.05$ were considered significant.

Results: Blau patients had decreased plasma IL-2 compared to control subjects (29 pg/mL vs. 320 pg/mL). TCR-activation of Blau patients' CD4+ T cells resulted in lower production of IL-2 after 5 days, supporting of a role for mutated NOD2 in controlling T cell function. Conversely, Blau patient T cell incubation with PMA and ionymin, a T cell stimulant which bypasses the TCR, resulted in similar levels of IL-2, indicating NOD2 plays a role directly downstream of the TCR. In corroboration, TCR-activation of T cells from naïve Blau *Nod2*^{R314Q} mice resulted in decreased IL-2 production compared to WT mice. Mechanistically, freshly isolated and overnight stimulated CD4+ T cells from naïve Blau *Nod2*^{R314Q} mice had increased expression of Nur77 (T cell activation molecule directly proportional to the strength of TCR engagement) and Ki67 (indicator of proliferation) compared to WT T cells, yet similar levels of CD69 (early TCR-activation molecule) and CD25 (IL-2 receptor alpha). Cumulatively, these data suggest that *NOD2*^{R314Q} expression results in dysregulated T cell responses downstream of TCR-specific activation including enhanced TCR-signaling strength, increased proliferation, and reduced IL-2 production.

Conclusion: Our data suggest that defective IL-2 signaling is driving aspects of systemic inflammation in Blau patients as similar patients with loss-of-function mutations in IL-2 signaling have unchecked CD4+ T cell proliferation and develop systemic autoimmunity. Additionally, our data indicate that *Nod2*^{R314Q} expression may be altering TCR signaling strength, resulting in a dysregulation of T cell activation. Thus, further studies investigating how NOD2 is controlling TCR signaling will contribute to novel T cell-targeted therapeutics for Blau patients.

Disclosure: L. Huey: None; **E. Vance**: None; **H. Rosenzweig**: None; **B. Binstadt**: Sobi, Inc., 5; **R. Napier**: None.

Abstract Number: 0805

De-escalation of Anti-TNFs in Older Adults with Rheumatoid Arthritis

Jiha Lee[1], Navasuja Kumar[1], Mohammed Kabeto[1], Andrzej Galecki[1], Chiang-Hua Chang[1], Namrata Singh[2], Raymond Yung[3], Una Makris[4] and Julie Bynum[1], [1]University of Michigan, Ann Arbor, MI, [2]University of Washington, Bellevue, WA, [3]Michigan Medicine, Ann Arbor, MI, [4]UT Southwestern Medical Center and Dallas VA, Dallas, TX

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Health Services Research I
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Biologic disease modifying anti-rheumatic drugs (bDMARDs) such as anti-tumor necrosis factors(anti-TNFs) improve clinical and radiographic outcomes in rheumatoid arthritis (RA). However, their use is associated with dose- and age-dependent adverse effects including increased risk of serious infections. In recent years, de-escalation (or deprescribing or tapering/discontinuing) has been proposed as an approach to reduce polypharmacy and optimize medication use in older adults more prone to the negative, often additive, adverse effects of medications. Current clinical practice guidelines recommend de-escalating bDMARDs in RA patients with low disease activity or in remission. We evaluated the prevalence of and factors associated with anti-TNF de-escalation among Medicare beneficiaries with RA in usual care.

Methods: We identified adults ≥66 years of age with RA, on anti-TNF therapy within 6-months of RA diagnosis with at least 6-7 months duration (proxy for stable use), using 20% Medicare data from 2009-2017. Patient demographic and clinical characteristics including concomitant use of glucocorticoid (GC) and conventional synthetic DMARDs (csDMARDs) were collected. Anti-TNF use was categorized as either de-escalation, identified by dose reduction, dosing interval increase or cessation of use, or continuation. We used (1) prospective cohort design with Cox regression models to analyze the association between patient characteristics and time to de-escalation event and, (2) case-control design with propensity score

Table 1: Compare characteristics by patterns of TNF inhibitor use among Medicare beneficiaries with RA

Variables	Continuation N=4528	De-escalation N=1192
Age, mean (SD) median (Q1, Q3)	74.2 (6.0) 72.8 (69.2, 78.2)	73.5 (5.2) 72.3 (69.3, 77.0)
Female n (%)	3504 (77.4)	935 (78.4)
Race/Ethnicity n (%)		
White	3756 (83.0)	1013 (85.0)
Black	258 (5.7)	59 (5.0)
Hispanic	313 (6.9)	85 (7.1)
Other	201 (4.4)	35 (2.9)
Dual eligibility (any), yes/no, n (%)	883 (19.5)	175 (14.7)
Low Income Subsidy (any), n(%)	1259 (27.8)	245 (20.6)
12 months interval before index date		
Comorbidities mean (SD) median (q1, q3)	2.2 (2.0) 2.0 (1.0, 3.0)	1.9 (1.7) 2.0 (1.0, 3.0)
Concomitant csDMARD use (any), n(%)	2560 (56.5)	714 (59.9)
Concomitant Methotrexate use (any), n(%)	2250 (49.7)	652 (54.7)
Concomitant oral GC use (any), n(%)	2259 (49.9)	556 (46.6)
Concomitant long-term GC, >90 days, n(%)	1399 (30.9%)	317 (26.6)

Table 2: Patient characteristics associated with de-escalation of anti-TNF among Medicare beneficiaries with RA

Variables	HR (95% CI) N=5720			
	Unadjusted (Univariable)	P-value	Adjusted	P-value
Age at index	0.99 (0.98, 1.00)	0.16	0.99 (0.98, 1.00)	0.16
Female	1.01 (0.88, 1.16)	0.91	1.06 (0.92, 1.22)	0.42
Race				
White (ref)	-		-	
Black	0.90 (0.69, 1.17)	0.43	1.02 (0.78, 1.33)	0.90
Hispanic	1.00 (0.80, 1.25)	0.99	1.23 (0.97, 1.57)	0.086
Other	0.66 (0.47, 0.92)	0.014	0.75 (0.53, 1.05)	0.092
Low Income Subsidy	0.73 (0.63, 0.83)†	<0.0001	0.70 (0.60, 0.82)†	<0.0001
Comorbidities (baseline)	0.99 (0.97, 1.03)	0.89	1.01 (0.98, 1.05)	0.48

† statistically significant with p<0.05

Table 3: Propensity score matched odds for de-escalation by clinical condition or concomitant medication use

Exposure	Unadjusted OR	P-value	Propensity score* adjusted OR	P-value
Clinical Condition				
Serious Infection	0.51 (0.40, 0.65)	<0.0001	0.54 (0.42, 0.69)†	<0.0001
New Cancer	0.41 (0.20, 0.86)	0.0178	0.37 (0.18, 0.78)†	0.0085
New Heart Failure	0.58 (0.38, 0.87)	0.0095	0.67 (0.44, 1.03)	0.0670
Concomitant Medication Use				
Any csDMARD	1.23 (1.08, 1.39)	0.0020	1.14 (0.99, 1.30)	0.0514
Methotrexate	1.34 (1.18, 1.53)	<0.0001	1.19 (1.04, 1.36)†	0.0094
Long-term glucocorticoids	0.83 (0.72, 0.96)	0.0094	0.80 (0.70, 0.93)†	0.0031

† statistically significant with p<0.05
*Propensity score calculated based on age and comorbidity at event, gender, race, low-income subsidy status and year of index date.

adjusted logistic regression to retrospectively assess the association of de-escalation with different clinical conditions and concomitant medication use.

Results: We identified 5720 Medicare beneficiaries with RA on anti-TNF. Average age at index was 74.0 (SD 5.8), 78% were female, 83% were non-Hispanic white, 26% had low income subsidy (LIS), and average Elixhauser comorbidity score was 2.2 (SD 1.9). One in five (21%) met criteria for de-escalation, of whom 61% either reduced dose or increased dosing interval and 39% ceased use. De-escalation was less likely in those with LIS status (HR 0.70, 95% CI 0.60-0.82), adjusting for patient age, sex, race/ethnicity, and comorbidity. Lower odds of de-escalation was associated with serious infection (OR 0.54, 95% CI 0.42-0.69), new cancer diagnosis (OR 0.37, 95% CI 0.18-0.78), and long-term GC use (OR 0.80, 95% CI 0.70-0.93), whereas higher odds was associated with concomitant methotrexate use (OR 1.19, 95% CI 1.04-1.36).

Conclusion: Although older adults with greater burden of polypharmacy and multimorbidity are more likely to benefit from de-escalation, anti-TNFs are de-escalated in 21% of older adults with RA in usual care. This in comparison to clinical trials showing 30-50% of younger adults with RA can de-escalate bDMARDs without significant disease progression. Further study to understand sub-groups of older adults with RA most likely to benefit from and the impact of de-escalation can help optimize the use of anti-TNFs in this population.

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Abstract Number: 0806

Effectiveness of a Technology-enabled Self-monitoring and Physical Therapist Counselling Program for Improving Self-management Ability in People with Rheumatoid Arthritis: A Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Health Services Research I
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: To achieve optimal health outcomes, people with rheumatoid arthritis (RA) need to know their symptom patterns and be able to practice self-care activities. With patient partners, we co-developed a Fitbit®-compatible app (OPERAS) for monitoring symptoms, disease activity, physical activity, and self-care goals. This study assessed a remote physical therapist (PT) counselling intervention using self-monitoring tools for enhancing self-management ability, physical activity participation, and health outcomes.

Methods: Eligible participants had a physician-confirmed diagnosis of RA. After baseline assessment (T0) and randomization, the *ImmediateGroup (IG)* received group education (2 hours), a Fitbit®, the app, and phone calls from a PT at weeks 2, 4, 6, 8, 13 and 26 to review their symptoms, treatment use, physical activity, and self-care goals. The *Delay Group (DG)* received a monthly e-newsletter unrelated to RA management until week 26, and then the intervention. Participants were assessed again at 27 weeks (T1) and 53 weeks (T2). Primary Outcome: Self-management ability assessed with the Patient Activation Measure (PAM-13). Secondary Outcomes: 1) RA Disease Activity Index (RADAI), 2) McGill Pain Questionnaire, 3) Fatigue Severity Scale, 4) Patient Health Questionnaire-9 (PHQ-9), 5) Self-Reported Habit Index for sitting/walking,6) daily time in moderate/vigorous physical activity and sedentary activity, and step count(SenseWear®).

Table 1: Participant outcomes

	Immediate Group (SD*)			Delay Group (SD)		
	Baseline (T0)	27 weeks (T1)	53 weeks (T2)	Baseline (T0)	27 weeks (T1)	53 weeks (T2)
	n = 66	*n = 59*	*n = 55*	*n = 66*	*n = 62*	*n = 55*
Patient Activation Measure (0-100; higher = better)	65.1 (13.6)	69.9 (17.0)	67.3 (15.1)	68.3 (13.9)	67.1 (13.5)	72.2 (17.5)
Rheumatoid Arthritis Disease Activity Index (0-10; lower = better)	3.6 (1.9)	3.0 (2.0)	2.8 (2.0)	3.7 (1.9)	3.6 (1.8)	2.8 (1.8)
McGill Pain Questionnaire (0-45; lower = better)	10.9 (8.3)	9.3 (8.1)	9.2 (7.9)	10.2 (7.5)	10.0 (7.1)	9.5 (8.5)
Fatigue Severity Scale (1-7; lower = better)	4.6 (1.4)	4.3 (1.5)	4.5 (1.5)	4.6 (1.3)	4.6 (1.3)	4.4 (1.5)
Patient Health Questionnaire-9 (0-27; lower = better)	7.6 (5.6)	5.0 (3.8)	4.8 (4.0)	7.0 (4.9)	6.3 (5.3)	5.4 (5.0)
Self-Reported Habit Index (1-7; higher = stronger habit)						
Sitting at Work subscale	4.6 (1.4)	4.6 (1.4)	4.5 (1.6)	4.7 (1.7)	4.6 (1.6)	4.6 (1.8)
Sitting at Leisure subscale	4.5 (1.3)	4.5 (1.1)	4.4 (1.3)	4.6 (1.3)	4.7 (1.5)	4.6 (1.6)
Walking subscale	4.5 (1.6)	4.6 (1.7)	4.8 (1.6)	4.5 (1.8)	4.3 (1.9)	4.7 (1.7)
	n = 59	*n = 50*	*n = 43*	*n = 60*	*n = 51*	*n = 46*
Daily steps	5,703.4 (2,827.6)	6,362.0 (3,291.3)	6,522.1 (3,537.7)	5,631.4 (2,498.7)	5,863.9 (2,832.6)	6,209.5 (2,720.3)
Time in MVPA† [mins]	36.8 (35.9)	42.0 (41.0)	42.4 (44.0)	38.4 (38.6)	45.5 (54.5)	47.8 (55.8)
Time in purposeful activity†† [mins]	14.7 (21.3)	15.8 (20.7)	19.9 (28.0)	12.2 (17.4)	18.4 (40.3)	17.9 (32.1)
Sedentary time‡ [mins]	514.5 (174.6)	538.9 (185.1)	546.7 (163.2)	467.8 (175.2)	504.2 (184.4)	504.0 (164.2)

*SD = Standard deviation
† MVPA (moderate/vigorous physical activity) was performed at ≥3 MET and in bouts ≥10 minutes with allowance for 2-minute interruptions
†† Purposeful activity was performed at ≥4 MET and in bouts ≥10 minutes with allowance for 2-minute interruptions
‡Sedentary behaviours were performed at ≤1.5 MET in bouts ≥20 minutes

Table 2: Intervention effect estimates using general linear mixed-effects models

	Adjusted Group effect Immediate vs. Delay Coefficient (95% CI)		
	Contrast 1	Contrast 2	Contrast 3
Patient Activation Measure	5.4 (0.9, 9.9)*	5.1 (1.1, 9.2)*	5.3 (2.0, 8.7)*
Rheumatoid Arthritis Disease Activity Index	-0.5 (-1.0, 0.0)	-0.8 (-1.3, -0.2)*	-0.6 (-1.1, -0.2)*
McGill Pain Questionnaire	-0.8 (-2.7, 1.1)	-0.4 (-2.0, 1.1)	-0.6 (-2.0, 0.7)
Fatigue Severity Scale	-0.3 (-0.7, -0.1)*	-0.3 (-0.5, 0.0)*	-0.3 (-0.5, -0.1)*
Patient Health Questionnaire-9	-1.6 (-2.9, -0.3)*	-0.8 (-1.9, 0.4)	-1.3 (-2.3, -0.3)*
Self-Reported Habit Index			
Sitting at Work subscale	0.0 (-0.4, 0.4)	0.0 (-0.4, 0.3)	0.0 (-0.3, 0.3)
Sitting at Leisure subscale	-0.2 (-0.6, 0.1)	-0.1 (-0.5, 0.2)	-0.2 (-0.5, 0.1)
Walking subscale	0.3 (-0.1, 0.8)	0.4 (0.1, 0.8)*	0.4 (0.0, 0.7)*
Daily steps	624.4 (-274.9, 1,523.7)	331.6 (-345.6, 1,008.9)	502.9 (-134.8, 1,140.6)
Time in MVPA†	2.3 (-9.7, 14.3)	6.1 (-7.3, 19.4)	4.1 (-4.5, 12.7)
Time in purposeful activity††	2.1 (-3.7, 7.8)	2.1 (-4.7, 8.9)	2.1 (-2.1, 7.3)
Sedentary time‡	-37.8 (-92.3, 16.7)	2.8 (-30.0, 35.6)	-13.1 (-46.1, 20.0)

Contrast 1: Immediate Group T1–T0 vs. Delay Group T1–T0
Contrast 2: Delay Group T2–T1 vs. Delay Group T1–T0
Contrast 3: Average of Contrast 1 and Contrast 2

* $P < 0.05$
† MVPA (moderate/vigorous physical activity) was performed at ≥3 MET and in bouts ≥10 minutes with allowance for 2-minute interruptions
†† Purposeful activity was performed at ≥4 MET and in bouts ≥10 minutes with allowance for 2-minute interruptions
‡ Sedentary behaviours were performed at ≤1.5 MET in bouts ≥20 minutes

We conducted intention-to-treat analysis using Generalized Linear Mixed-effect Models, adjusting forage and sex. The dependent variable was the change in outcome variable between two assessment time points. Three contrasts were assessed: 1) between-group difference (*DG* vs. *IG*) in the outcome change at T1 from T0 (T1-T0); 2) within-group difference (*DG* only): T2-T1 vs. T1-T0; and 3) average of contrasts 1 and 2. Contrast 3 was the primary contrast as it combined the between-group intervention effect and the within-group intervention effect.

Results: We recruited 132 participants (*IG*: n=66, 92.4% women; *DG*: n=66, 90.9% women). Both groups were similar in age [*IG:* 55.1 years (SD 13.3); *DG*: 56.9 years (SD 13.2)]. 80.3% completed the study during the COVID-19 pandemic. The adjusted mean difference in PAM-13 was 5.4 (95% CI: 0.9, 9.9). Contrast 3 was statistically significant for PAM-13 (Contrast coefficient: 5.3, 95% CI: 2.0, 8.7; $p = 0.002$).Examination of Contrasts 1 and 2 revealed that the effect on PAM-13 was underpinned by both the between group difference at T0-T1 and the within group change in the *DG* from T0-T1 (no-intervention period) to T1-T2 (intervention period) (**Tables 1 & 2**). Intervention effects were also found in RADAI (Contrast 3: -0.6, 95% CI: -1.1, -0.2), Fatigue Severity Scale (Contrast 3: -0.3, 95% CI: -0.5, -0.1), PHQ-9 (Contrast 3: -1.3, 95% CI: -2.3, -0.3), and Self-Reported Habit Index - walking subscale (Contrast 3: 0.4, 95% CI: 0.0, 0.7).

Conclusion: Remote PT counselling paired with use of self-monitoring tools improved self-management ability in people with RA. We also found significant effects in disease activity, fatigue, depression, and perceived walking habit at 26 weeks, suggesting the intervention had a positive effect on symptom management.

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Abstract Number: 0807

Inferring Disease Activity Scores and Low Disease Activity at Registry Visits Based on Structured and Narrative Data from Electronic Health Records

David Cheng[1], Dana Weisenfeld[2], Kumar Dahal[2], Qing Liu[2], Vidul Ayakulangara Panickan[3], Mary Jeffway[2], Thany Seyok[2], Gregory McDermott[2], Michael Weinblatt[4], Nancy Shadick[5], Tianxi Cai[6] and Katherine Liao[2], [1]Massachusetts General Hospital, Boston, MA, [2]Brigham and Women's Hospital, Boston, MA, [3]Harvard Medical School, Boston, MA, [4]Harvard Medical School, Waban, MA, [5]Brigham and Women's Hospital, Boston, MA, [6]Harvard T.H. Chan School of Public Health, Boston, MA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

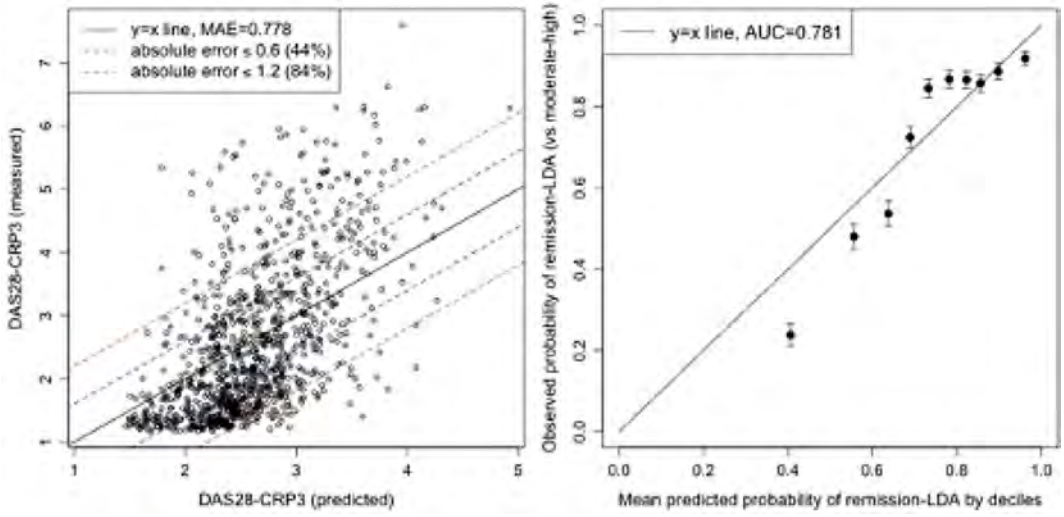
Session Title: Abstracts: Health Services Research I

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Real-world data including electronic health records (EHRs) are a promising resource for learning to optimize treatment strategies for rheumatoid arthritis (RA). A major challenge in leveraging real-world data in rheumatology is the lack of standardized collection of disease activity measures. Previous studies had limited success inferring disease activity with administrative claims and EHR data. This study aimed to assess the accuracy of inferring disease activity as measured by the Disease Activity Score in 28 joints with CRP (DAS28-CRP) using both structured and narrative EHR data extracted from notes with natural language processing (NLP).

Methods: We studied RA patients from a single center registry linked with EHR data. The structured data included RA-related diagnosis and procedure codes, medication prescriptions, and laboratory test encounters and values. The NLP data included mentions of RA and disease activity concepts. Models were trained on DAS28-CRP obtained during in-person study visits from the registry. For each visit, structured and NLP data were extracted from EHR encounters within 24 weeks. In 80% of the visits, we fit separate random forest models to predict the continuous DAS28-CRP value and the binary



Observed vs. predicted DAS28-CRP values among the validation set based on structured + NLP features (left). Calibration plot (right) shows observed probability of LDA and corresponding 95% confidence intervals vs. mean predicted probability of LDA by deciles of predicted probability based on structured + NLP features.

Features	Performance Metrics
DAS28-CRP values	
Structured (diagnosis codes, procedure codes, medications, lab encounters and values)	MAE=0.843 (79% ≤1.2, 44% ≤0.6)
Structured + NLP concepts from notes	MAE=0.778 (84% ≤1.2, 44% ≤0.6)
Disease activity status (remission-LDA vs moderate-high by DAS28-CRP ≤ 3.2)	
Structured (diagnosis codes, procedure codes, medications, lab encounters and values)	AUC=0.677
Structured + NLP concepts from notes	AUC=0.781
Manual chart review (in 67 visits)	Sensitivity=73.3%, Specificity=45.5%, AUC=0.705

Performance of phenotyping models with and without RA-related NLP concepts from notes and relative to manual chart review. MAE: mean absolute error, AUC: area under the curve, NLP: natural language processing.

disease activity status categorized into remission/low (LDA; DAS28≤3.2) vs moderate/high disease activity (DAS28 >3.2). We validated the predictions in the remaining 20%. To assess the accuracy of predicting DAS28-CRP values, we estimated the mean absolute error (MAE; lower values indicate lower error), percentage of predictions within 0.6 (reported measurement error for DAS28-CRP), and 1.2 (minimal clinically important difference (MCID)) of the observed values. For LDA status, we calculated the area under the curve (AUC). Observed values and probabilities were plotted against predicted values and mean predicted probabilities in deciles to further assess prediction performance. We identified influential EHR features for predictions using Gini impurity. These analyses were repeated with and without including NLP data. We benchmarked against manual chart-review for inferring LDA, using LDA defined by DAS28-CRP as reference, in a sample of 67 visits.

Results: We identified 4,883 visits among 1,059 patients with a DAS28-CRP score. The mean age at first visit was 60.5 years old, with 83.6% of patients being female and 89.4% White. The MAE for DAS28-CRP values was 0.778, with 84% and 44% of absolute errors within 1.2 (MCID) and 0.6 (measurement error). The AUC for LDA was 0.781 (Figure 1). Incorporating NLP data consistently improved prediction performance (Table 1). Features with the highest importance included CRP and ESR values, age, receiving a CRP test, and NLP mentions of disease activity and glucocorticoids. The model incorporating NLP data achieved a higher AUC over manual chart review.

Conclusion: Inferring disease activity with EHR data collected from routine care, particularly with the addition of data from narrative notes, achieved moderate accuracy against prospectively collected DAS28-CRP measures. Further work is needed to validate whether these inferred disease activity measures can be applied to reliably assess response to treatment in observational data.

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Abstract Number: 0808

Real-World Disease Monitoring Patterns in Rheumatoid Arthritis-Associated Interstitial Lung Disease in the Veterans Affairs Health Care System

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

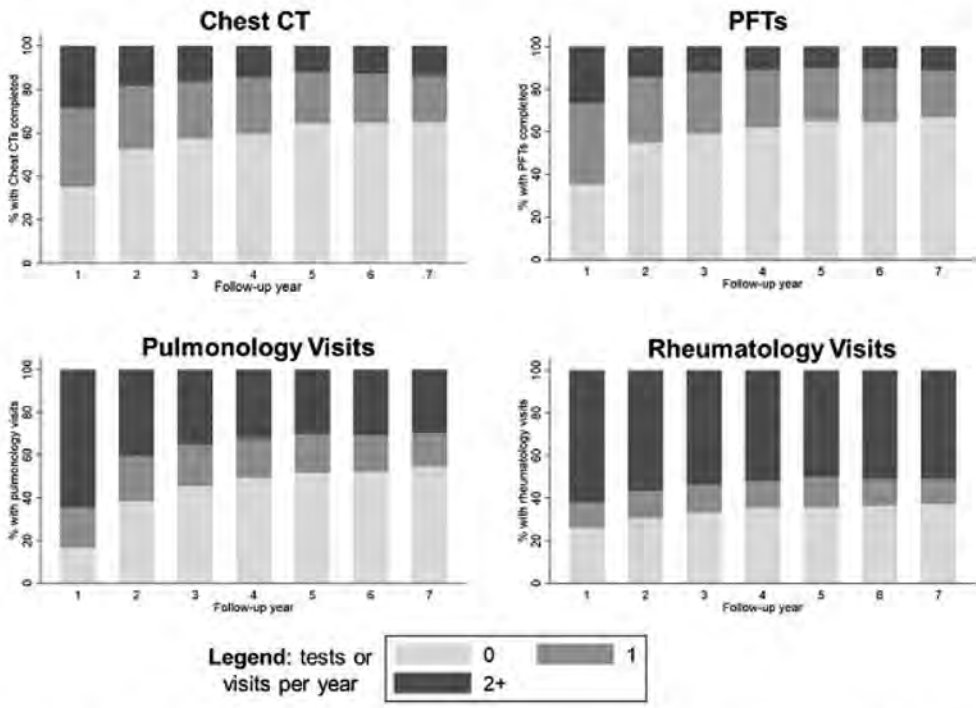
Session Title: Abstracts: Health Services Research I

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: There are currently no clinical practice guidelines for monitoring RA-associated interstitial lung disease (RA-ILD). Pulmonary function tests (PFTs) and chest computed tomography (CT) imaging are among the most common tests utilized for RA-ILD surveillance, but the frequency of these tests in real-world settings is unclear. We examined real-world disease monitoring patterns in RA-ILD within the Veterans Affairs (VA) Health Care System, the largest integrated health care system in the U.S., from 1999-2021.

Figure 1. RA-ILD Disease Monitoring During the Disease Course.



Figures show the percent of patients with 0, 1, or 2+ tests/visits during each 1-year interval after the index date (date fulfilling RA-ILD algorithm).

Abbreviations: CT, computed tomography; PFTs, pulmonary function tests

Figure 1. RA-ILD Monitoring During the Disease Course

Methods: We performed a cohort study within national VA data warehouses, identifying individuals with RA-ILD (prevalent and incident) using validated algorithms that required multiple RA and ILD diagnostic codes (PPV >70%). The index date was the date patients fulfilled RA-ILD algorithm, and patients were followed for up to 7-years post-index date (reflecting the median survival in RA-ILD), censoring for death. Over the entire follow-up period and by sequential one-year intervals following the index date, we assessed completion of PFTs, chest CT imaging (any type), and outpatient visit frequency to rheumatology and pulmonology. PFTs, chest CTs, and outpatient visits (rheumatology and pulmonology) were obtained from VA administrative data and linked Centers for Medicare Services data. Vital status was determined from VA death records. Descriptive statistics were used to summarize RA-ILD monitoring patterns.

Results: We identified n=6,232 patients with RA-ILD (92.6% male, mean age 69.1 years). During follow-up, RA-ILD patients underwent monitoring with PFTs every 1.4 years (median [IQR] 0.5 [0.2, 1.0] tests/year) and chest CT imaging every 1.1 years (median 0.7 [0.3, 1.2] tests/year). PFT and CT monitoring frequency steadily decreased over the duration of disease, with PFTs or chest CTs being obtained in fewer than 50% of RA-ILD patients each year after the first year of follow-up (**Figure 1**). Among RA-ILD patients who did undergo PFTs or chest CTs during each 1-year interval, the majority had a single PFT or chest CT test during that year. Rheumatology visits (median 1.8 [0.6, 2.9]) per year) occurred more frequently than pulmonology visits (median 1.3 [0.5, 2.4]] per year) throughout the follow-up period. However, pulmonary visit frequency more closely correlated with PFT ($r=0.51$, $p < 0.001$) and chest CT ($r=0.35$, $p < 0.001$) testing frequency than rheumatology visits (PFT $r=0.20$, $p < 0.001$; chest CT $r=0.09$, $p < 0.001$). Baseline forced vital capacity negatively correlated with PFT ($r=-0.13$, $p< 0.001$) and CT ($r=-0.04$, $p=0.01$) testing rate.

Conclusion: RA-ILD monitoring is highly variable and appears to be sub-optimal (relative to idiopathic pulmonary fibrosis guidelines; Raghu et al. AJRCCM, 2022) in real-world settings. Sources of this variability could include the heterogeneity of the disease and prognosis, involvement of multiple medical specialties, a lack of evidence-based guidance for disease monitoring, and patient preferences, among others. These findings highlight the need for clinical practice guidelines on RA-ILD monitoring to inform rheumatologist and pulmonologist engagement in RA-ILD surveillance, particularly with the emergence of additional therapeutic options in RA-ILD.

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Abstract Number: 0809

Underserved by Rehabilitation: Characteristics Among Adults with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Health Services Research I

Session Type: Abstract Session

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Background/Purpose: Adults with rheumatoid arthritis (RA) often experience functional limitations (e.g., difficulty walking, dressing oneself), even with low disease activity and good pharmaceutical management. Rehabilitation services (i.e. physical therapy and occupational therapy) improve function, yet rehabilitation service use is low among adults with RA. Taken together, this suggests that many adults with RA are underserved by rehabilitation, conservatively defined as high functional burden (moderate-severe functional limitation) with no prior use of rehabilitation for RA. To better understand the gaps in care, we must understand rehabilitation use among those with functional needs and identify characteristics associated with being underserved. The purpose of this study was to examine the associations of demographic and clinical characteristics with being underserved by rehabilitation among adults with RA.

Methods: Data were cross-sectionally collected from online surveys from patients with RA who received care at UNC Health rheumatology clinics in 2020 and 2021. The primary outcome was being underserved by rehabilitation, which was defined as reporting moderate-severe functional limitation (PROMIS PF10a score < 40) and never previously using rehabilitation services related to RA (self-reported use yes vs. no). The demographics and clinical exposure variables were race and ethnicity (non-Hispanic Black, non-Hispanic White, Hispanic of any race), gender (women, men), health insurance (private, Medicare, Medicaid, none), income (higher [exceeding basic needs], lower [not exceeding basic needs]), education status (higher [at least some college], lower [no college]), work status (disabled, other), and BMI (normal, overweight, obese). We calculated the proportion of the sample with moderate-severe functional limitation, no prior rehabilitation use for RA, and underserved by rehabilitation. We examined associations of the exposure variables with being underserved using logistic

Table 1: Associations of Exposure Variables with being Underserved by Rehabilitation

Characteristic	n	Proportion with moderate-severe functional limitation % (n)	Proportion with no prior rehabilitation use for RA % (n)	Proportion who are underserved by rehabilitation % (n)	Odds of being underserved by rehabilitation *Adj. OR (95% CI)
Overall Sample	294	45% (133)	64% (189)	25% (72)	-
Race/Ethnicity					
Non-Hispanic White	192	39% (75)	63% (121)	20% (38)	REF
Non-Hispanic Black	57	56% (32)	63% (36)	30% (17)	1.78 (0.90, 3.53)
Hispanic	34	59% (20)	71% (24)	38% (13)	**2.41 (1.04, 5.55)**
Gender					
Women	241	49% (119)	63%	26% (63)	REF
Men	51	24% (12)	73%	16% (8)	0.44 (0.19, 1.06)
Insurance Status					
Private	149	26% (38)	68% (101)	13% (20)	REF
Medicare	88	65% (57)	60% (5)	34% (30)	**4.90 (2.36, 10.2)**
Medicaid	15	80% (12)	53% (8)	40% (6)	**3.92 (1.24, 12.4)**
None	30	67% (20)	73% (22)	47% (14)	**4.68 (1.94, 11.3)**
Income Status					
Higher Income (exceeds basic needs)	191	29% (56)	64% (122)	13% (25)	REF
Lower Income (does not exceed basic needs)	102	75% (76)	65% (66)	45% (46)	**5.60 (3.07, 10.2)**
Education Status					
Higher Education (at least some college)	219	40% (88)	59% (130)	18% (40)	REF
Lower Education (no college)	74	60% (44)	78% (58)	42% (31)	**3.16 (1.75, 5.69)**
Disabled Work Status					
No	236	36% (84)	60% (34)	18% (43)	REF
Yes	57	84% (48)	65% (154)	49% (28)	**4.79 (2.53, 9.08)**
BMI Category					
Normal	81	28% (23)	64% (52)	17% (14)	REF
Overweight	86	34% (29)	65% (56)	16% (14)	1.04 (0.45, 2.42)
Obese	122	65% (79)	64% (78)	35% (43)	**2.63 (1.29, 5.37)**

*Adjusted for age, disease duration, and prior joint replacement

regression models adjusted for self-reported age, disease duration, and joint replacement. Odds ratios and 95% confidence intervals were presented.

Results: Of 294 adults with RA who participated (age 56.3±14.2 years, disease duration 10.1±10.7 years), 45% reported moderate-severe functional limitation, 64% never used rehabilitation services related to RA, and 25% were underserved by rehabilitation. The following characteristics were strongly associated (adjusted OR range 2.4-5.6) with being underserved by rehabilitation: Hispanic ethnicity (compared to Non-Hispanic White), Medicare, Medicaid, or no health insurance (compared to private insurance), lower income (compared to higher), lower education (compared to higher), disabled work status (compared to other work status), and obesity (compared to normal weight), as detailed in Table 1.

Conclusion: Strikingly, at least one in four adults with RA were underserved by rehabilitation using a conservative definition. There is a clear unmet need for rehabilitation, particularly in historically marginalized groups. Future work must develop strategies for facilitating rehabilitation referral and use for those with functional needs.

Disclosure: C. Lane: None; **L. Mihalek**: None; **K. Allen**: None; **B. Jonas**: None; **P. Katz**: None; **L. Thoma**: None.

Abstract Number: 0810

Telehealth Utilization and Satisfaction Among Patients with Rheumatic Diseases: Trends Since the Onset of the COVID-19 Pandemic

Kristin Wipfler[1] and Kaleb Michaud[2], [1]FORWARD, The National Databank for Rheumatic Diseases, Omaha, NE, [2]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Health Services Research I
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: The COVID-19 pandemic prompted a rapid transition to increased telehealth utilization, with many rheumatology providers replacing in-person clinical visits with telehealth visits or expanding their telehealth offerings. Understanding trends in telehealth utilization and satisfaction among people with rheumatic diseases (RDs) is crucial as telehealth options continue to be offered and used even as COVID-19 safety measures are scaled down. We investigated trends in telehealth utilization and satisfaction among individuals with RDs from the onset of the pandemic to the present.

Methods: The study population included participants in the FORWARD Databank who completed semiannual questionnaires from June 2020 to April 2023 with items related to their telehealth utilization in 6-month time periods from January 2020 through December 2022. In each of the questionnaires offered, participants were asked if they had any telehealth appointments and if so, they were asked to rate their satisfaction on a Likert scale. Descriptive statistics were calculated for participant characteristics, and comparisons were made by telehealth vs no telehealth and by satisfied vs not satisfied with telehealth. Multivariable logistic regression models (adjusted for age, sex, race, education, rural/urban residence, smoking history, BMI, autoimmune diagnosis, Rheumatic Disease Comorbidity Index, glucocorticoid use, opioid use, and Patient Activity Scale-II) were used to identify factors associated with telehealth utilization and satisfaction over time.

Table 1. Characteristics of FORWARD participants by telehealth utilization and telehealth satisfaction. Data were collected from 2020 to 2023 (six semiannual questionnaires). For participants who reported any telehealth utilization between January 2020 and December 2022, the observation included here was the first report of telehealth use. For participants who reported no telehealth utilization during that time period, the observation included here was the first observation.

	No Telehealth n=1,441	Telehealth n=3,846	p	Not Satisfied n=1,330	Satisfied n=2,446	p
Demographics						
Age, years	68.7 (11.6)	66.4 (11.8)	<0.001	67.6 (11.8)	65.5 (11.7)	<0.001
Female, %	79.7	85.2	<0.001	82.6	86.7	<0.01
Caucasian, %	93.3	91.1	0.01	91.9	90.8	0.30
Education, years	14.6 (2.2)	15.0 (2.2)	<0.001	14.6 (2.4)	15.2 (2.2)	<0.001
Rural residence, %	34.8	21.3	<0.001	23.7	20.2	0.02
History of smoking, %	44.6	43.8	0.62	45.6	42.4	0.06
BMI, kg/m2	28.5 (6.9)	29.2 (7.3)	<0.01	29.0 (6.8)	29.3 (7.6)	0.35
Primary Diagnosis, %						
Rheumatoid arthritis	58.9	62.9		64.7	61.9	
Osteoarthritis	17.5	14.3		13.7	14.5	
Fibromyalgia	5.0	5.1		4.4	5.5	
Lupus	4.7	6.2	<0.01	6.0	6.4	0.44
Psoriatic arthritis	3.8	3.3		3.0	3.5	
Ankylosing spondylitis	1.5	1.1		1.4	0.9	
Other	8.7	7.1		6.8	7.2	
Comorbidities, %						
Hx pulmonary disorder	40.7	51.4	<0.001	50.2	52.1	0.26
Hx cardiac disorder	38.5	47.3	<0.001	47.4	47.1	0.86
Hx fracture	29.8	36.6	<0.001	36.3	36.6	0.84
Hx depression	45.6	58.6	<0.001	57.9	58.9	0.54
Hx diabetes	22.4	26.9	<0.01	27.3	26.4	0.58
Hx cancer	31.2	35.5	<0.01	35.8	35.1	0.63
Hx GI disorder	63.3	74.5	<0.001	74.4	74.3	0.96
Medications, %						
csDMARD	47.4	50.9	0.03	52.4	50.4	0.24
TNFi bDMARD	20.4	20.5	0.91	20.7	20.3	0.80
nTNFi bDMARD	9.9	14.2	<0.001	13.5	15.0	0.25
JAKi	4.7	5.7	0.14	5.4	5.9	0.48
Glucocorticoid	13.3	20.4	<0.001	20.3	20.6	0.83
Nonopioid analgesic	44.4	43.3	0.52	44.2	42.9	0.45
Opioid	15.0	21.8	<0.001	21.8	21.9	0.96
Healthcare visits, %						
0-2 visits	54.4	31.4		31.1	31.1	
3-5 visits	29.6	33.9	<0.001	34.0	34.1	0.80
6-8 visits	10.5	15.8		14.6	16.2	
9 or more visits	5.6	19.0		20.3	18.6	
PROs						
Fatigue, 0-10	3.5 (2.9)	4.4 (3.1)	<0.001	4.5 (3.0)	4.4 (3.1)	0.61
Pain, 0-10	3.3 (2.7)	3.9 (2.8)	<0.001	4.0 (2.7)	3.9 (2.9)	0.33
Global severity, 0-10	3.1 (2.5)	3.9 (2.5)	<0.001	4.0 (2.5)	3.8 (2.6)	<0.01
HAQ-II, 0-3	0.7 (0.6)	0.9 (0.7)	<0.001	0.9 (0.7)	0.9 (0.7)	0.10
PAS-II, 0-10	3.0 (2.1)	3.6 (2.2)	<0.001	3.7 (2.1)	3.5 (2.2)	0.03

Respondents who selected "somewhat satisfied" or "very satisfied" on the Likert scale were included in the "Satisfied" group. Respondents who selected "neutral," "somewhat dissatisfied," or "very dissatisfied" were included in the "Not Satisfied" group. Healthcare visits included general practice, rheumatologist, other specialist, nurse, and other health worker visits within the previous six month time period, both in person and telehealth. BMI=Body Mass Index; DMARD=disease-modifying antirheumatic drug; csDMARD=conventional synthetic DMARD; TNFi=tumor necrosis factor inhibitor; bDMARD=biologic DMARD; nTNFi=non-TNFi; JAKi=Janus kinase inhibitor; PRO=patient-reported outcome; HAQ-II=Health Assessment Questionnaire II; PAS-II=Patient Activity Scale II.

Results: Of 5,287 unique respondents, 3,846 (73%) reported telehealth utilization between January 2020 and December 2022. Respondent characteristics are presented in Table 1, and temporal trends are presented in Figure 1. Telehealth utilization peaked at 61% in the second half of 2020 and stabilized at approximately 40% throughout 2022. Higher education, younger age, urban residence, greater comorbidity burden, and worse disease activity were consistently associated with telehealth use throughout the pandemic thus far. Telehealth users earlier in the pandemic had significantly higher odds of having an autoimmune diagnosis, but since July 2021 this was not statistically significant. Telehealth satisfaction demonstrated a steady increase over time, rising from 63% to 73%. Higher education and younger age were consistently associated with greater telehealth satisfaction.

A

	Jan-June 2020	July-Dec 2020	Jan-June 2021	July-Dec 2021	Jan-June 2022	July-Dec 2022
Higher education	●	●	●	●	●	●
Younger age	●	●	●	●	●	●
Urban residence	●	●	●	●	●	●
Greater comorbidity burden	●	●	●	●	●	●
Higher disease activity	●	●	●	●	●	●
Autoimmune diagnosis	●	●	●			
Glucocorticoid use	●	●			●	
Opioid use	●					●
Female sex		●				
History of smoking				●		
n:	3,384	3,919	3,573	3,670	2,966	1,434
Telehealth utilization:	58%	61%	52%	48%	41%	42%

B

	Jan-June 2020	July-Dec 2020	Jan-June 2021	July-Dec 2021	Jan-June 2022	July-Dec 2022
Higher education	●	●	●	●	●	●
Younger age	●	●	●	●	●	
Female sex	●					
Greater comorbidity burden	●					
Lower disease activity	●			●		
Non-white race		●				
Non-autoimmune diagnosis		●				
Urban residence			●		●	
No opioid use					●	
n:	1,926	2,372	1,843	1,748	1,205	595
Telehealth satisfaction:	63%	67%	65%	68%	71%	73%

Figure 1. Factors associated with (A) telehealth utilization and (B) telehealth satisfaction over time. Multivariable logistic regression models were generated at each time point for each of the two outcomes. All models were adjusted for age, sex, race, education, rural/urban residence, smoking history, BMI, autoimmune diagnosis, Rheumatic Disease Comorbidity Index (comorbidity burden), and Patient-Activity Scale-II (disease activity). Significant covariates from each model are marked with a filled circle.

Conclusion: Rates of telehealth utilization among individuals with RDs has remained substantial throughout the COVID-19 pandemic, although rates have decreased since 2020. Improved telehealth infrastructure and growing familiarity with the technology may have contributed to increased satisfaction over time, but individuals who are younger and more highly educated continue to have higher odds of telehealth satisfaction. Those with greater comorbidity burdens and higher disease activity have very consistently been the most likely to utilize telehealth services. Ensuring quality of care for these higher risk populations remains essential as telehealth continues to become a more integral part of rheumatology practice.

Disclosure: K. Wipfler: None; **K. Michaud**: None.

Abstract Number: 0811

Comparative Effectiveness of Sodium-glucose cotransporter-2 Inhibitors for Recurrent Gout Flares and Gout-primary Emergency Department Visits and Hospitalizations: A General Population Cohort Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Sodium-glucose cotransporter-2 inhibitors (SGLT2i) lower serum urate (primary prevention); however, whether this translates into preventing recurrent flares among gout patients (secondary prevention) and gout-primary emergency department visits or hospitalizations remains unknown. Furthermore, their potential role on cardiovascular risk has not been studied.Our objective was to compare gout flares and cardiovascular (CV) events among gout patients initiating SGLT2i versus dipeptidyl peptidase 4 inhibitors (DPP-4i), another second-line glucose-lowering agent not associated with serum urate lowering or CV risk.

Methods: This new-user, active comparator cohort study used administrative health data covering nearly all residents of British Columbia, Canada from Jan 2014 to June 2022, including all dispensed prescriptions, regardless of funder. Primary outcome was recurrent gout flare counts, ascertained by emergency department (ED), hospitalization, outpatient, and medication dispensing records (PPV 95% for ≥ 1 flare over a similar period). We also specifically investigated flares requiring hospitalization or ED visit, and stratified by sex, age, diuretic and urate-lowering therapy (ULT) use, and gout intensity (presence of ≥1 gout-coded encounter or colchicine dispensing over the past year). Myocardial infarction and stroke were secondary outcomes. We also assessed genital infection as positive control and osteoarthritis encounter as negative control. Poisson and Cox proportional hazards regressions were used with 1:1 propensity-score matching (primary analysis) and overlap weighting (sensitivity analysis).

Results: We included 8150 gout patients with type 2 diabetes whose characteristics, including baseline flare rate and gout medication use, were well balanced after propensity matching (standardized mean difference< 0.1) (**Table 1**). During follow-up, flare rate was lower among SGLT2i initiators than DPP4i initiators (52.4 and 79.7 events per 1000 person-years, respectively), with rate ratio (RR) for SGLT2i initiation 0.66 (95% CI: 0.57, 0.75) and rate difference (RD) of -27.4 (-36.0, -18.7) fewer flares per 1000 person-years (**Table 2**).RR and RD for flares requiring hospitalization or ED visit were 0.52 (0.32, 0.84) and -3.4 (-5.8, -0.9), respectively. Findings were similar during the first year of SGLT2i initiation (among those without prior ULT use), suggesting no apparent paradoxical flares (**Table 2**). Results were consistent across subgroups, though absolute RD was higher in patients with greater gout intensity: -71.6 [-111.1, -32.1] vs. 20.8 [-28.8, -12.7] per 1000 person-years, respectively (**Table 2**). Hazard ratio (HR) and RD for myocardial infarction were 0.69 (0.54, 0.88) and -7.6 (-12.4, -2.8) per

Table 1. Selected baseline characteristics among gout patients with type 2 diabetes initiating SGLT2i vs. DPP-4i, before and after 1:1 Propensity Matching. *SMD, standardized mean difference, difference < 0.1 indicates negligible differences. ‡Frequency during the past 1 year. n, number; y, years; SD, standard deviation; SGLT2i, sodium glucose cotransporter-2 inhibitors; DPP-4i, dipeptidyl peptidase 4 inhibitors; NSAIDs, non-steroidal anti-inflammatory drugs; PPIs, proton pump inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists.

	Before matching			After matching		
Variable list	**SGLT2i (n=8,318)**	**DPP-4i (n=6,749)**	**SMD***	**SGLT2i (n=4,075)**	**DPP-4i (n=4,075)**	**SMD***
Demographics						
Age, mean (SD), y	64.11 (11.26)	68.71 (12.32)	0.39	66.04 (10.79)	66.03 (12.08)	< 0.01
Male (%)	6100 (73.3)	4542 (67.3)	0.13	2913 (71.5)	2900 (71.2)	0.01
Type 2 diabetes duration, mean (SD), y						
	12.5 (7.34)	13.5 (7.19)	0.15	12.8 (7.12)	12.8 (7.24)	< 0.01
Gout duration, mean (SD), y	11.5 (7.93)	11.4 (7.80)	0.01	11.5 (7.87)	11.5 (7.88)	< 0.01
Gout flares, mean (SD)	0.12 (0.48)	0.15 (0.58)	0.04	0.12 (0.49)	0.12 (0.47)	< 0.01
Comorbidity (%)						
Obesity	1346 (16.2)	812 (12.0)	0.12	559 (13.7)	536 (13.2)	0.02
Hypertension	7434 (89.4)	6178 (91.5)	0.07	3676 (90.2)	3643 (89.4)	0.03
Myocardial infarction	1573 (18.9)	1323 (19.6)	0.02	719 (17.6)	719 (17.6)	< 0.01
Stroke	1402 (16.9)	1506 (22.3)	0.14	778 (19.1)	740 (18.2)	0.02
Heart failure	1966 (23.6)	1890 (28.0)	0.10	937 (23.0)	945 (23.2)	0.01
Ischaemic heart disease	4956 (59.6)	4187 (62.0)	0.05	2445 (60.0)	2390 (58.7)	0.03
Peripheral vascular disease	1450 (17.4)	1374 (20.4)	0.08	698 (17.1)	718 (17.6)	0.01
Chronic kidney disease	1870 (22.5)	2418 (35.8)	0.30	1038 (25.5)	1003 (24.6)	0.02
Diabetes complications (%)						
Nephropathy	772 (9.3)	1388 (20.6)	0.32	515 (12.6)	504 (12.4)	0.01
Retinopathy	1611 (19.4)	1568 (23.2)	0.10	819 (20.1)	820 (20.1)	< 0.01
Neuropathy	1603 (19.3)	1211 (17.9)	0.03	719 (17.6)	717 (17.6)	< 0.01
Medication‡ (%)						
Other diabetes medication						
Metformin	6777 (81.5)	5288 (78.4)	0.08	3320 (81.5)	3335 (81.8)	0.01
Sulfonylureas	3461 (41.6)	3511 (52.0)	0.21	1886 (46.3)	1904 (46.7)	0.01
GLP1-RA	592 (7.1)	110 (1.6)	0.27	119 (2.9)	108 (2.7)	0.02
Insulin	1706 (20.5)	989 (14.7)	0.15	653 (16.0)	641 (15.7)	0.01
Gout medication						
Urate-lowering therapy	2516 (30.2)	2174 (32.2)	0.04	1207 (29.6)	1199 (29.4)	< 0.01
Colchicine	1048 (12.6)	851 (12.6)	< 0.01	467 (11.5)	458 (11.2)	0.01
Corticosteroid	787 (9.5)	826 (12.2)	0.09	429 (10.5)	426 (10.5)	< 0.01
NSAIDs	1298 (15.6)	1024 (15.2)	0.01	671 (16.5)	663 (16.3)	0.01
Aspirin	269 (3.2)	410 (6.1)	0.14	166 (4.1)	163 (4.0)	< 0.01
Statins	748 (9.0)	732 (10.8)	0.06	399 (9.8)	402 (9.9)	< 0.01
Thiazide diuretics	2171 (26.1)	1745 (25.9)	0.01	1057 (25.9)	1060 (26.0)	< 0.01
Loop diuretics	1139 (13.7)	1291 (19.1)	0.15	566 (13.9)	565 (13.9)	< 0.01
Healthcare utilization, mean (SD)‡						
Hospitalizations and ED visits for diabetes	0.34 (0.80)	0.53 (1.14)	0.19	0.38 (0.86)	0.38 (0.87)	0.01
Total outpatient encounters	24.05 (16.61)	29.49 (24.72)	0.26	25.05 (17.91)	24.83 (19.27)	0.01
Rheumatology encounters	0.13 (0.72)	0.13 (0.82)	< 0.01	0.11 (0.65)	0.11 (0.67)	< 0.01
Endocrinology encounters	0.46 (1.44)	0.46 (1.64)	< 0.01	0.40 (1.33)	0.38 (1.51)	0.02

1000 person-years; HR, 0.81 (0.62, 1.05) for stroke. For control outcomes, SGLT2i initiators showed higher risk of genital infection, as expected, and no altered risk of osteoarthritis encounter (**Table 3**).Results were similar when applying propensity-score overlap weighting.

Conclusion: Among gout patients, SGLT2i may reduce recurrent flares and gout-primary ED visits/hospitalizations, along with cardiovascular benefits, without apparent paradoxical flares.

Table 2. Recurrent gout flare count among gout patients with type 2 diabetes initiating SGLT2i vs. DPP-4i, after propensity-score matching, overall and sensitivity and subgroup analyses. SGLT2i, sodium glucose cotransporter-2; RR, rate ratio; RD, rate difference; 95% CI, 95% confidence interval; IR, incidence rate; DPP-4i, dipeptidyl peptidase 4 inhibitors; ED, emergency department; ULT, urate-lowering therapy. *Higher gout intensity defined as ≥ 1 gout-coded healthcare encounter or dispensing of colchicine within the year prior to index date; lower gout intensity defined as no gout-coded healthcare encounter or dispensing of colchicine within the year prior to index date.

Primary Outcome		
Gout Flare Counts	**SGLT2i**	**DPP-4i**
IR, per 1000 person-years	52.4	79.7
RR (95% CI)	0.66 (0.57, 0.75)	1.0 (ref)
RD (95% CI)	-27.4 (-36.0, -18.7)	Ref
Sensitivity Analyses		
Flares Requiring ED Visits or Hospitalizations	**SGLT2i**	**DPP-4i**
IR, per 1000 person-years	3.6	7.0
RR (95% CI)	0.52 (0.32, 0.84)	1.0 (ref)
RD (95% CI)	-3.4 (-5.8, -0.9)	Ref
Up to 1 Year of Follow-Up, No Prior ULT Use	**SGLT2i**	**DPP-4i**
IR, per 1000 person-years	73.1	103.8
RR (95% CI)	0.70 (0.59, 0.84)	1.0 (ref)
RD (95% CI)	-30.1 (-46.3, -15.1)	Ref
Subgroup Analyses		
Baseline Diuretic Use	**SGLT2i**	**DPP-4i**
IR, per 1000 person-years	76.6	101.4
RR (95% CI)	0.75 (0.62, 0.92)	1.0 (ref)
RD (95% CI)	-24.8 (-42.1, -7.5)	Ref
No Baseline Diuretic Use	**SGLT2i**	**DPP-4i**
IR, per 1000 person-years	41.4	65.5
RR (95% CI)	0.63 (0.52, 0.77)	1.0 (ref)
RD (95% CI)	-24.1 (-34.2, -14.1)	Ref
Baseline ULT Use	**SGLT2i**	**DPP-4i**
IR, per 1000 person-years	48.4	73.6
RR (95% CI)	0.66 (0.50, 0.87)	1.0 (ref)
RD (95% CI)	-25.2 (-41.8, -8.6)	Reference
No Baseline ULT Use	**SGLT2i**	**DPP-4i**
IR, per 1000 person-years	50.4	89.9
RR (95% CI)	0.56 (0.48, 0.66)	1.0 (ref)
RD (95% CI)	-39.5 (-50.4, -28.7)	Reference
Higher Intensity Gout*	**SGLT2i**	**DPP-4i**
IR, per 1000 person-years	134.7	206.3
RR (95% CI)	0.65 (0.51, 0.82)	1.0 (ref)
RD (95% CI)	-71.6 (-111.1, -32.1)	Ref
Lower Intensity Gout	**SGLT2i**	**DPP-4i**
IR, per 1000 person-years	36.2	57.0
RR (95% CI)	0.64 (0.53, 0.76)	1.0 (ref)
RD (95% CI)	-20.8 (-28.8, -12.7)	Ref

SGLT2i, sodium glucose cotransporter-2; RR, rate ratio; RD, rate difference; 95% CI, 95% confidence interval; IR, incidence rate; DPP-4i, dipeptidyl peptidase 4 inhibitors; ED, emergency department; ULT, urate-lowering therapy.

*Higher gout intensity defined as ≥ 1 gout-coded healthcare encounter or dispensing of colchicine within the year prior to index date; lower gout intensity defined as no gout-coded healthcare encounter or dispensing of colchicine within the year prior to index date.

Table 3. Cardiovascular and control outcomes among patients with gout and type 2 diabetes initiating SGLT2i vs. DPP-4i. SGLT2i, sodium glucose cotransporter-2 inhibitors; IR, incidence rate; HR, hazard ratio; RD, risk difference; DPP-4i, dipeptidyl peptidase 4 inhibitors; 95% CI, 95% confidence interval.

	SGLT2i (n=4,075)	DPP-4i (n=4,075)
CARDIOVASCULAR ENDPOINTS		
Myocardial Infarction		
Event, number.	108	153
Mean follow-up (years)	1.66	1.53
IR, per 1000 person-years	16.0	23.6
HR (95% CI)	0.69 (0.54, 0.88)	1.0 (ref)
RD (95% CI)	-7.6 (-12.4, -2.8)	Reference
Stroke		
Event, number.	99	121
Mean follow-up (years)	1.66	1.60
IR, per 1000 person-years	14.6	18.5
HR (95% CI)	0.81 (0.62, 1.05)	1.0 (ref)
RD (95% CI)	-3.9 (-8.3, 0.4)	Reference
CONTROL OUTCOMES		
Genital Infections **(POSITIVE CONTROL OUTCOME)**		
Event, number.	65	30
Mean follow-up (years)	1.67	1.63
IR, per 1000 person-years	9.6	4.5
HR (95% CI)	2.15 (1.39, 3.30)	1.0 (ref)
RD (95% CI)	5.0 (2.2, 7.9)	Reference
Any Osteoarthritis Encounter **(NEGATIVE CONTROL OUTCOME)**		
Event, number.	580	534
Mean follow-up (years)	1.45	1.40
IR, per 1000 person-years	98.1	93.7
HR (95% CI)	1.07 (0.95, 1.20)	1.0 (ref)
RD (95% CI)	4.4 (-6.8, 15.7)	Reference

SGLT2i, sodium glucose cotransporter-2 inhibitors; IR, incidence rate; HR, hazard ratio; RD, risk difference; DPP-4i, dipeptidyl peptidase 4 inhibitors; 95% CI, 95% confidence interval.

Disclosure: N. McCormick: None; **C. Yokose**: None; **J. Wei**: None; **N. Lu**: None; **D. Wexler**: None; **M. De Vera**: None; **J. Avina-Zubieta**: None; **Y. Zhang**: None; **H. Choi**: Ani, 2, Horizon, 2, 5, LG, 2, Protalix, 2, Shanton, 2.

Abstract Number: 0812

Length of Synovial Fluid Monosodium Urate Crystals According to Sonographic Articular Deposits: Advancing in the Crystallization Process

Elena Sansano[1], Mª Carmen López-González[2], Cristina Rodríguez-Alvear[3], Irene Calabuig-Sais[3], Agustín Martínez-Sanchís[3], Eliseo Pascual[3] and **Mariano Andrés**[3], [1]Miguel Hernandez University, Alicante, Spain, [2]General University Hospital Dr. Balmis, Alacante, Spain, [3]Dr Balmis Alicante General University Hospital-ISABIAL, Alicante, Spain

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science

Session Type: Abstract Session

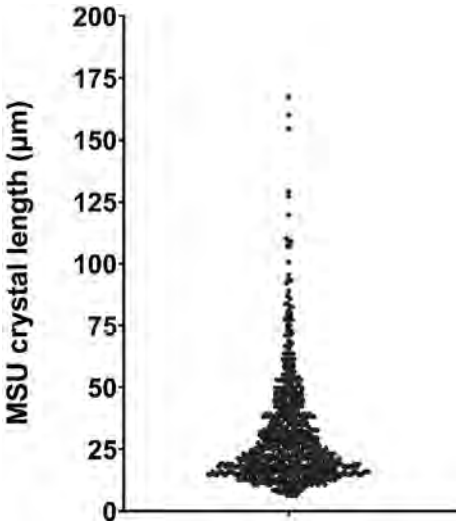
Session Time: 4:00PM–5:30PM

Background/Purpose: We described bands of fibers having deposited orderly arrayed monosodium urate (MSU) crystals suggesting the need for protein templates to start crystallization [PMID 9709185]. However, tophi sections demonstrate the presence of longer crystals, highly arranged in a fan display, likely formed after other crystals [PMID 26369610]. Hence, a double mechanism of crystallization may exist in the joint. Here, we aimed to assess whether synovial fluid MSU crystals found in joints with organized sonographic deposits (likely, many crystals deriving from them) are longer than when deposits are absent or not visible.

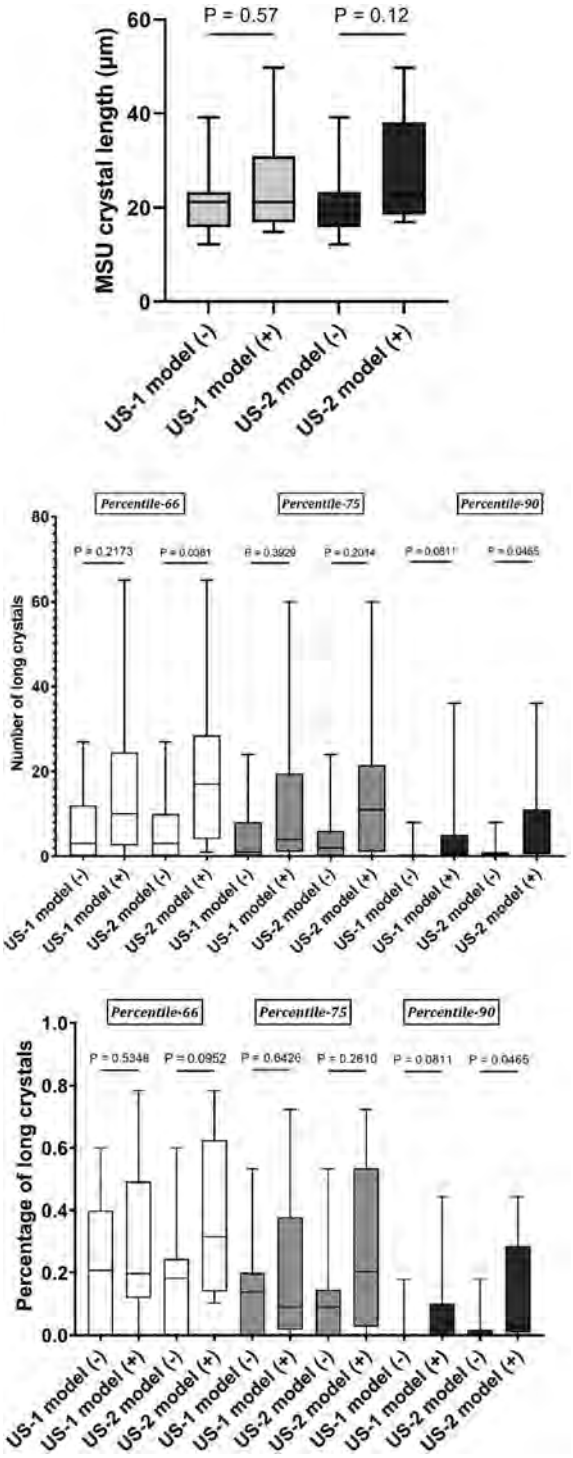
Methods: We recruited patients with crystal-proven gout during a flare. Ultrasound of the target joint was performed to detect elementary gout lesions [OMERACT 2021]: double-contour (DC) sign, tophi, and aggregates. Two sonographic models were assessed: *US-1 model*, grade 2-3 of any deposit (DC sign, tophi, or aggregates), and *US-2 model*, limited to grade 2-3 DC sign or tophi. Later, synovial fluid was aspirated. The length of MSU crystals was measured by a blinded observer using a calibrated polarized light microscope. The distribution of MSU crystal length (in μm) and the presence of long crystals (defined according to percentiles 66, 75, or 90) were tested with each sonographic model using Mann-Whitney U's test. Quantitative variables are shown as median (p25-75).

Results: We analyzed 742 crystals from 20 joints in 17 patients (three with an oligo-polyarticular flare), median aged 62.5 years (55-73), and 30% with subcutaneous tophi. The 2-year median serum urate was 7.5mg/dL (7.1-8.2), with current urate-lowering therapy in 35% of patients. The median length of MSU crystals was 21.2μm (95%CI 17.7-26.5), where crystals mostly gathered [Figure 1]. Applying the *US-1* model (fulfilled by 13 joints, 65%), no difference in crystal lengths was noted (21.2μm in those with deposits vs. 21.2μm in those without deposits; p=0.588) [Figure 2, top], with a similar distribution of long crystals (P66, P75 or P90) [Figure 2, middle and bottom]. However, those with deposits according to *US-2* model (n=9, 45%) showed a numerically greater crystal length (22.8μm vs. 18.5μm; p=0.112) [Figure 2, top] and more presence of long crystals [Figure 2, middle and bottom] compared to patients without deposits. Crystal lengths and the presence of long crystals showed no association with gout characteristics or serum urate levels.

Conclusion: Our synovial fluid analysis from different individuals with gout suggests two different mechanisms of MSU crystallization, one of reduced length shared by most crystals and the other with longer crystals better identified by the presence of sonographic deposits (but not aggregates), which resembles what is seen in tophi pathological sections. This exploratory finding adds evidence to the hypothesis that a secondary formation using as templates previously formed crystals occurs in the process of MSU crystallization.



Distribution of monosodium urate crystals length in the whole sample.



Comparisons between ultrasound models in crystal length (top), number of long crystals - according to percentiles 66, 75, or 90 - (middle), and percentage of long crystals - according to percentiles 66, 75, or 90 (bottom).

Disclosure: E. Sansano: None; **M. López-González**: None; **C. Rodríguez-Alvear**: None; **I. Calabuig-Sais**: None; **A. Martínez-Sanchís**: None; **E. Pascual**: None; **M. Andrés**: None.

Abstract Number: 0813

Sonographic Crystal Deposits and Power-Doppler Signal in Patients with Gout Fulfilling Remission Criteria: A Multicenter Study Enrolling 115 Participants

Mariano Andrés[1], Nalia Domínguez-Lirón[2], Enrique Calvo-Aranda[3], Esther Vicente Rabaneda[4], Agustín Martínez-Sanchís[1], Francisca Sivera[5], Diana Peiteado[6], Alejandro Prada[7], Blanca Garcia[8], Basilio Rodríguez[9], BORIS ANTHONY BLANCO CACERES[10], José Antonio Bernal[11], Santos Castañeda[12], Laura Barrio[7], Sonia Minguez[9], Mónica Vázquez Díaz[13], José Miguel Senabre[11], Cristina Bohorquez[14], Silvia Gómez-Sabater[15], Rocío Caño-Alameda[15] and Eugenio De Miguel[16], [1]Dr Balmis Alicante General University Hospital-ISABIAL, Alicante, Spain, [2]Miguel Hernández University, Alicante, Spain, [3]Hospital Universitario Infanta Leonor, Madrid, Spain, [4]Rheumatology, Hospital Universitario de La Princesa, Madrid, Spain, [5]Elda General University Hospital, Elda, Spain, [6]Hospital La Paz, Madrid, Spain, [7]Hospital Universitario de Torrejón, Madrid, Spain, [8]Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain, [9]Fundació Althaia, Manresa, Spain, [10]Hospital Universitario Ramon y Cajal, Madrid, Spain, [11]Hospital Marina Baixa, Villajoyosa, Spain, [12]Hospital Universitario de la Princesa, Madrid, Spain, [13]Hospital Ramon y Cajal, Madrid, Spain, [14]Rheumatology Unit, Hospital Universitario Príncipe de Asturias, Alcalá de Henares, Spain, [15]Rheumatology Department, Dr. Balmis University General Hospital, Alicante. Institute for Health and Biomedical Research (ISABIAL), Alicante, Spain, [16]Hospital Universitario La Paz, Madrid, Spain

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: The prevalence of sonographic monosodium urate (MSU) crystal deposition and inflammation in patients with gout in remission is unknown. In 2022, we reported a preliminary estimation of 88.7% of patients with persistent deposits, while one out of three had a positive power-Doppler (PD) signal [1]. This abstract communicates the sonographic evaluation of our initial 115 patients with gout in remission.

Methods: Observational cross-sectional multicenter study. Consecutive patients with gout (ACR/EULAR classification criteria +/- MSU crystal-proven) who met preliminary remission criteria [2] were recruited at eleven Spanish rheumatology units. They underwent a sonographic scanning of the first metatarsophalangeal and second metacarpophalangeal joints, knees, talar cartilages, and patellar and Achilles tendons. The sonographers were blinded to participants' clinical and laboratory data. We determined the prevalence (with 95% confidence interval -CI) of sonographic MSU crystal deposits (tophi,

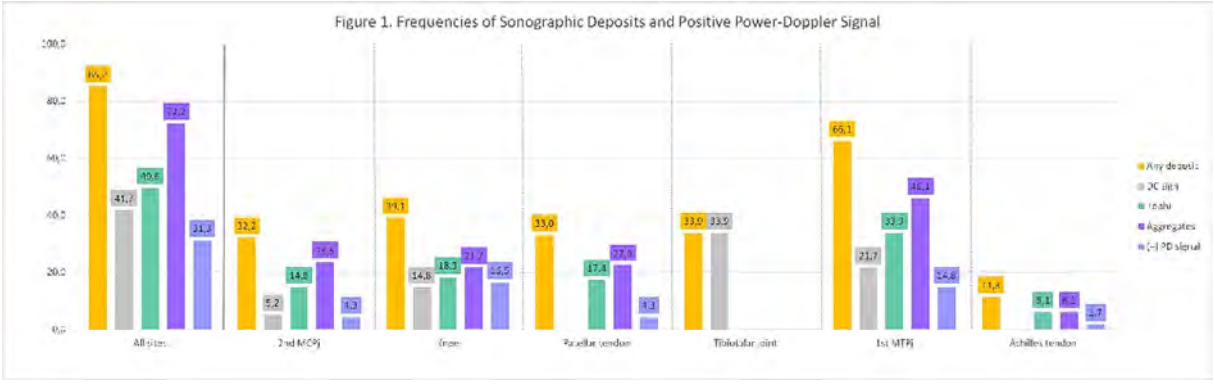


Figure 1.

aggregates, and double contour sign) and inflammation by power Doppler [PD] signal (graded as 0-3, positive if ≥1). Associations between deposits and PD signal and clinical and laboratory variables were also analyzed by chi-2 and logistic regression.

Results: The sample includes 115 participants, mean age of 65.2 years (SD 9.7), 93.9% males. The mean gout duration was 13.9 years (SD 10.9), and the disease was tophaceous at baseline in 15.7%. The mean serum urate level in the preceding year was 4.5 mg/dl (SD 0.9), with a mean duration of urate-lowering therapy of 55.8 months (SD 34.7). The prevalence of deposits in at least one location was 85.2% (95%CI 77.6-90.6%), with a median of 3 locations with deposits (range 0-9). Articular deposits (80.0%) were more common than tendinous deposits (39.1%), and aggregates were the most frequent sonographic finding (83.0%) [Figure 1]. If aggregates are not considered, prevalent deposits dropped to 73.0% (95%CI 64.3-80.3%). A positive PD signal was present in 31.3% of participants (95%CI 23.6-40.3%), mainly at joints (27.8%). Rates of deposits and positive PD signals were mildly lowered when restricted to four locations (82.6% and 27.8%, respectively) and any site except 1MTP joints (77.4% and 22.6%). A significant association between deposits and positive PD signal was confirmed at joints (p=0.005) and tendons (p=0.033). No secondary variable was associated with deposits or positive PD signal.

Conclusion: Our updated multicenter dataset confirms that most patients with gout fulfilling remission criteria still show sonographic MSU crystal deposits and one third, sonographic inflammation. The relevance of persistent deposits and inflammation in this setting needs further clarification.

References: [1] *Domínguez-Lirón N. Arthritis Rheumatol 2022;74(suppl 9)*. [2] *de Lautour H. Arthritis Care Res 2016;68(5):667*.

Disclosure: M. Andrés: None; **N. Domínguez-Lirón**: None; **E. Calvo-Aranda**: None; **E. Vicente Rabaneda**: None; **A. Martínez-Sanchís**: None; **F. Sivera**: AbbVie/Abbott, 1, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 5, GlaxoSmithKlein(GSK), 6, Novartis, 5, 6, Pfizer, 1, Roche, 5, UCB, 6; **D. Peiteado**: None; **A. Prada**: None; **B. Garcia**: None; **B. Rodríguez**: None; **B. BLANCO CACERES**: None; **J. Bernal**: None; **S. Castañeda**: None; **L. Barrio**: None; **S. Minguez**: None; **M. Vázquez Díaz**: None; **J. Senabre**: None; **C. Bohorquez**: None; **S. Gómez-Sabater**: None; **R. Caño-Alameda**: None; **E. De Miguel**: None.

Abstract Number: 0814

Treat-to-target Urate-lowering Therapy Reduces Gout Flare Burden: Post-hoc Analysis of a Multicenter, Randomized, Double-blind, Non-inferiority Trial

Joshua Qu[1], Lindsay Helget[1], Maria Androsenko[2], Hongsheng Wu[3], Bridget Kramer[1], Jefferey Newcomb[4], Mary Brophy[3], Anne Davis-Karim[5], Bryant England[1], Ryan Ferguson[3], Michael Pillinger[6], Tuhina Neogi[7], Paul Palevsky[8], James O'Dell[1] and Ted R Mikuls[9], [1]University of Nebraska Medical Center, Omaha, NE, [2]Department of VA, Newton, MA, [3]Boston VA, Boston, MA, [4]University of Nebraska, Omaha, NE, [5]Albuquerque VA, Albuquerque, NM, [6]New York University Grossman School of Medicine, New York, NY, [7]Boston University School of Medicine, Boston, MA, [8]University of Pittsburgh, Pittsburgh, PA, [9]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: To optimally manage gout, the ACR recommends a treat-to-target (T2T) strategy, which entailsthe titration of urate-lowering therapy (ULT) to achieve and maintain a serum urate (SU) level of <6.0 mg/dL.Current data indicates that T2T using conventional ULT may be required for up to 2 years to reduce gout flare frequency compared to usual care (Doherty et al, Lancet 2018). Using data from the STOP Gout Study (O'Dell JR et al. NEJM Evidence 2022), a recently completed multicenter, randomized, double-blind, non-inferiority trial, we examined whether achievement of SU goalat 48 weeks reduces gout flare burdenas early as 48-72 weeks after T2T initiation.

Methods: Trial participants with gout and SU concentration ≥6.8 mg/dL were randomized 1:1 to receive allopurinol or febuxostat. ULT was titrated during weeks 0-24 (Phase 1) and maintained during weeks 25-48 (Phase 2), with escalation as necessary to reach goal SU of <6.0 mg/dl (<5 mg/dl if tophi) or until maximum dosing achieved. Participants were then observed on stable ULT with a primary study outcome of at least 1 flare occurring during weeks 49-72 (Phase 3).SU goal achievement was assessed at 48 weeks. For this analysis, the association of SU goal achievement at the end of Phase 2 with flare during Phase 3 was assessed in a multivariable logistic regression model, adjusting for covariates significantly associated with flare in univariate analysis. Covariates assessed included baseline age, sex, race, education, comorbidities, body mass index (BMI), quality of life (EQ5D score), and gout-related factors (baseline SU, tophi, gout duration, diuretic use, prior allopurinol use).

Results: Of the 940 trial participants (mean age 62 years, 98% male, mean [SD] baseline SU 8.5 [1.4] mg/dl), 749 had flare data available during Phase 3 and were included in this analysis. The most common reasons for early termination were either participant decision (n=99) or loss to follow-up (n=41). Of the 749 with flare data, 449 (60%) remained flare-free between week 49 and week 72. Patients achieving SU goal at 48 weeks were more likely than those not achieving SU goal to remain flare-free during Phase 3 (62% vs. 49%; p = 0.004 by chi-square). In unadjusted analyses, other baseline factors associated

Table 1: Baseline characteristics of trial participants based on occurrence of flare between 49 and 72 weeks

Characteristic	Flare-free	≥ 1 Flare
	N=449	N=300
GOUT RELATED FACTORS		
sUA mg/dL, Mean (SD)	8.5 (1.4)	8.6 (1.3)
Duration of gout, years, Mean (SD)	8.9 (11.1)	11.0 (10.5)
Presence of tophi, %	11.1	22.3
Prior Allopurinol use, %	36.7	37.3
Diuretic use, %	42.1	31.7
DEMOGRAPHICS		
Age, year, Mean (SD)	62.4 (12.0)	62.0 (12.5)
Male, %	97.6	99.3
Race, %		
White/Caucasian	70.6	68.0
Black/African American	21.2	19.0
Other	8.2	13.0
CORMOBIDITY & HEALTH FACTORS		
Chronic kidney disease – Stage III, %	37.9	35.7
Hypertension, %	78.8	73.3
Diabetes, %	34.5	31.0
Cardiovascular disease, %	25.8	25.7
Overweight or obese by BMI (>25 kg/m^2), %	68.6	63.3
EQ-5D-3L index, Mean (SD)	0.7 (0.2)	0.7 (0.2)

**Significant differences ($p < 0.05$) observed for gout duration, tophi, and diuretic use; all other differences non-significant; education status not shown*

Table 2. Multivariable associations of SU response at week 48 and baseline covariates with remaining flare-free between weeks 49 and 72 (n = 749)

	Odds Ratio (95% CI)	P-value
Responders (sUA <6 mg/dl or <5 if tophi present) at week 48	1.60 (1.09, 2.36)	0.018
Presence of tophi at baseline	0.48 (0.31, 0.72)	<0.001
Duration of gout (per year)	0.99 (0.97, 1.00)	0.084
Diuretic use	1.62 (1.18, 2.22)	0.003

with flare during Phase 3 included longer duration of gout (p = 0.009) and presence of tophi (p-value < 0.001), while baseline diuretic use was associated with a lower risk (p = 0.004) (Table 1). After adjusting for tophi, disease duration, and diuretic use, SU goal achievement at 48 weeks was associated with remaining flare-free in Phase 3(OR 1.60; 95% CI 1.09-2.36, p = 0.018; Table 2).

Conclusion: In this post-hoc analysis from a large, randomized double-blind, non-inferiority trial, we found that SU achievement following a T2T strategy was associated with a 60% greater odds of remaining flare-free between 49 and 72 weeks of follow-up. These results support ACR guidelines that endorse a T2T strategy in gout management and demonstrate that benefits in flare prevention may begin to occur as early as 12 to 18 months.

Disclosure: J. Qu: None; **L. Helget**: None; **M. Androsenko**: None; **H. Wu**: None; **B. Kramer**: None; **J. Newcomb**: None; **M. Brophy**: None; **A. Davis-Karim**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **R. Ferguson**: None; **M. Pillinger**: Federation Bio, 2, Fortress Biotech, 2, Hikma, 5, Horizon Therapeutics, 2, 5, Scilex, 2, Sobi, 2; **T. Neogi**: None; **P. Palevsky**: None; **J. O'Dell**: None; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9.

Abstract Number: 0815

Intermittent Fasting Reduces Crystal-induced Inflammation

Nghia Pham[1], Twinu Wilson Chirayath[2], Florence Castelli[3], François Fenaille[3], Anvi-Laetitia Nguyen[3], François Brial[4], Augustin Latourte[4], Frédéric Lioté[4], Pascal Richette[5], Thomas Bardin[6] and Hang Korng EA[7], [1]INSERM 1132, BIOSCAR, Lariboisière hospital, Paris, France, [2]INSERM, Paris, France, [3]Laboratoire d'études du métabolisme des médicaments UMS 28, CEA Saclay, Gif-sur-Yvette, France, [4]INSERM 1132, BIOSCAR, Paris, France, [5]Lariboisière Hospital, Paris, France, [6]Université de Paris Cité, Paris, France, [7]INSERM-BIOSCAR, Paris, France

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Inflammation induced by monosodium urate (MSU) and calcium pyrophosphate (CPP) crystals depends on interleukin (IL)-1β activated by the NLRP3 inflammasome. The inflammatory response can be modulated by diet, fasting, and caloric restriction.

Ojective: To determine whether intermittent fasting reduces MSU and CPP crystal-induced inflammation.

Methods: Crystal-induced inflammation was assessed using both types of crystals in vivo in the air pouch model in 8-week-old wild-type male mice fed either with a normal ad libitum diet or intermittent fasting (IF) (every over day fast, 2 days during 1 week). Inflammatory cytokine production (IL1β and CXCL-1) was assessed in the pouch lavages and the cellular infiltrate analyzed by histology (H&E staining). Metabolomic analyses were performed by high-performance liquid chromatography coupled to high-resolution mass spectrometry (LC-HRMS) on air pouch membrane, serum, and liver samples.

In vitro, human monocytes THP-1 were stimulated by sterile synthetic crystals of MSU and CPP while the production of inflammatory cytokines was quantified by ELISA.

To assess the role of glutamine/glutamate metabolism pathway related to IF in microcrystalline disease, the concentrations of glutamine/glutamate in synovial fluids (SF) from patients with gout, CPP-related disease and osteoarthritis (OA) were quantified by ultra-performance liquid chromatography coupled to tandem mass spectrometry (UPLC-MS/MS).

Results: Inflammation induced by MSU and CPP crystals was drastically decreased by IF compared with normal diet: IL-1β (MSU 0.0 vs. 30.0 pg/ml; CPP 0.0 vs. 47.5 pg/ml $p< 0.0001$); CXCL-1 (MSU 67.5 vs. 186.8 pg/ml, CPP 156.1 vs. 549.5 pg/ml, $p< 0.005$); as were cell infiltration assessed by number of cells in the air pouch lavages (MSU 0.2 x 106 vs. 1.1 x 106 ; CPP 0.4 x 106 vs 2.9 x 106; $p< 0.0001$) and membrane histology semi-quantitative score (MSU 0.6 vs 3.0; CPP 0.8 vs 2.7; $p< 0.0001$).

Reduction of inflammation by IF was associated with significant changes in membrane, serum and liver metabolites. Many metabolic pathways were altered by IF such as galactose, starch, sucrose, aspartate, glutamate, alanine and arginine metabolism. Interestingly, the glutamine and glutamate metabolic pathway was enriched in serum, membrane and liver compartments.

Glutamine/glutamate involvement in microcrystal-induced inflammation was evidenced in SFs. The glutamine/glutamate ratio was decreased in synovial fluids of crystal-related diseases compared to OA (gout 1.4 and CPP 6.1 vs OA 9.4, $p< 0.0001$ and $p< 0.05$ respectively).

In vitro, crystal-induced inflammatory cytokine production was decreased by overnight serum deprivation (IL-1β: MSU 1446 vs 5464 pg/ml; CPP 3670 vs 7797 pg/ml, $p< 0.005$; TNF-α: MSU 7.0 vs 47.0 pg/ml; CPP 15.6 vs 89.3 pg/ml, $p< 0.05$; IL-8: MSU 2896 vs 9781 pg/ml; CPP 3984 vs 6820 pg/ml, $p< 0.01$).

Conclusion: Intermittent fasting alleviates crystal-induced inflammation by altering many metabolic pathways, particularly those associated with glutamine and glutamate. Further studies are needed to determine how crystals modulate metabolism and potential anti-inflammatory effects.

Disclosure: N. Pham: None; **T. Wilson Chirayath**: None; **F. Castelli**: None; **F. Fenaille**: None; **A. Nguyen**: None; **F. Brial**: None; **A. Latourte**: None; **F. Lioté**: None; **P. Richette**: None; **T. Bardin**: None; **H. EA**: None.

Abstract Number: 0816

Additive Association of *ABCG2* rs4148155 and *SLC22A12* rs75786299 Polymorphisms with Hyperuricemia, Gout and Nephrolithiasis, a Hospital-Based, Case-Control Study

Ching-Tsai Lin[1], I-Chieh Chen[2], Wen-Nan Huang[1], Yi-Hsing Chen[1], Ching-Heng Lin[2] and Yi-Ming Chen[1], [1]Taichung Veterans General Hospital, Taichung, Taiwan, [2]Department of Medical Research, Taichung Veterans General Hospital, Taichung, Taiwan

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: This study aimed to investigate the interaction between the *ABCG2* rs4148155 and *SLC22A12* rs75786299 variants and their association with incident gout and nephrolithiasis in the Taiwanese population to better understand the genetic loci regulating hyperuricemia and their contribution to nephrolithiasis development.

Table 1. Demographics, comorbidities and ABCG2 rs4148155 , SLC22A12 rs75786299 genetic variations of the study subjects by the presence of gout

Variables	With Gout (n=7056)		Without Gout (n=28,224)		p-value
	n	(%)	n	(%)	
Age, years[a](mean±SD)	64.40±14.62		62.37±14.72		<.0001
Gender					0.009
female	1857	26.3	7868	27.9	
male	5199	73.7	20356	72.1	
Overweight (BMI≧24 kg/m^2)[a]					<.0001
No	2017	30.5	10026	40.1	
Yes	4592	69.5	14978	59.9	
Smoking[b]					0.37
Never	5605	79.5	22358	79.9	
Ever or current	1450	20.6	5616	20.1	
Alcohol consumption[b]					0.76
Former drinker	3297	92.1	12019	92.2	
Current drinker	284	7.9	1013	7.8	
Regular physical exercise[b]					0.0001
No	89	66.4	736	80.9	
Yes	45	33.6	174	19.1	
Hyperlipidemia[b]					<.0001
No	2516	35.7	18499	65.5	
Yes	4540	64.3	9725	34.5	
Hypertension[b]					<.0001
No	2198	31.2	17257	61.1	
Yes	4858	68.9	10967	38.9	
Diabetes mellitus[b]					<.0001
No	3938	55.8	19530	69.2	
Yes	3118	44.2	8694	30.8	
ABCG2_rs4148155[b](miss:15)					<.0001
AA	2595	36.8	13634	48.3	
AG	3379	47.9	11969	42.4	
GG	1081	15.3	2607	9.2	
SLC22A12_rs75786299[b](miss 89)					
GG	6775	96.3	27569	97.9	<.0001
GA	264	3.8	583	2.1	
AA	0	0.0	0	0.0	
rs4148155+rs75786299[b]					
non_carrier	2501	35.5	13307	47.3	<.0001
1_carrier	4361	62.0	14541	51.7	
both_carrier	176	2.5	291	1.0	
non_carrier	2501	35.5	13307	47.3	<.0001
carrier	4537	64.5	14832	52.7	

[a]Continuous variables were expressed as mean ± standard deviation (SD) and were analyzed using Student's t-test for normal data distributions.

[b]Categorical variables were expressed as numbers (percent) and analyzed using the Chi-square test.

BMI: body mass index.

Table 2. Association of ABCG2 rs4148155 , SLC22A12 rs75786299 alleles, hyperuricemia gout and nephrolithiasis with sex stratification

Variables	Female					Female				Female			
	With HUA (n=1857)		Without HUA (n=7868)		p-value	Risk of Gout			p-value	Risk of nephrolithiasis			p-value
	n	(%)	n	(%)		OR	95% CI			OR	95% CI		
rs4148155+rs75786299					<.0001								
non_carrier	736	39.7	3697	47.1		1	-	-		1	-	-	
one_carrier	1077	58.1	4066	51.8		1.33	1.20	1.48	<.0001	1.04	0.91	1.20	0.06
both_carrier	40	2.2	87	1.1		2.31	1.58	3.39	<.0001	1.81	1.11	2.94	0.02
Variables	Male					Male				Male			
	With HUA (n=5199)		Without HUA (n=20356)		p-value	Risk of Gout			p-value	Risk of nephrolithiasis			p-value
	n	(%)	n	(%)		OR	95% CI			OR	95% CI		
rs4148155+rs75786299					<.0001								
non_carrier	1765	34.0	9610	47.4		1	-	-		1	-	-	
one_carrier	3284	63.3	10475	51.6		1.71	1.60	1.82	<.0001	1.18	1.09	1.27	0.44
both_carrier	136	2.6	204	1.0		3.63	2.91	4.54	<.0001	1.57	1.18	2.10	0.01

Data are expressed as number (percentage).

The relationship between categorical variables was ascertained by the chi-square test.

Odds ratio (OR) adjusted for all variables (age, diabetes mellitus, hypertension and hyperlipidemia); CI: confidence intervals

HUA, Hyperuricemia.

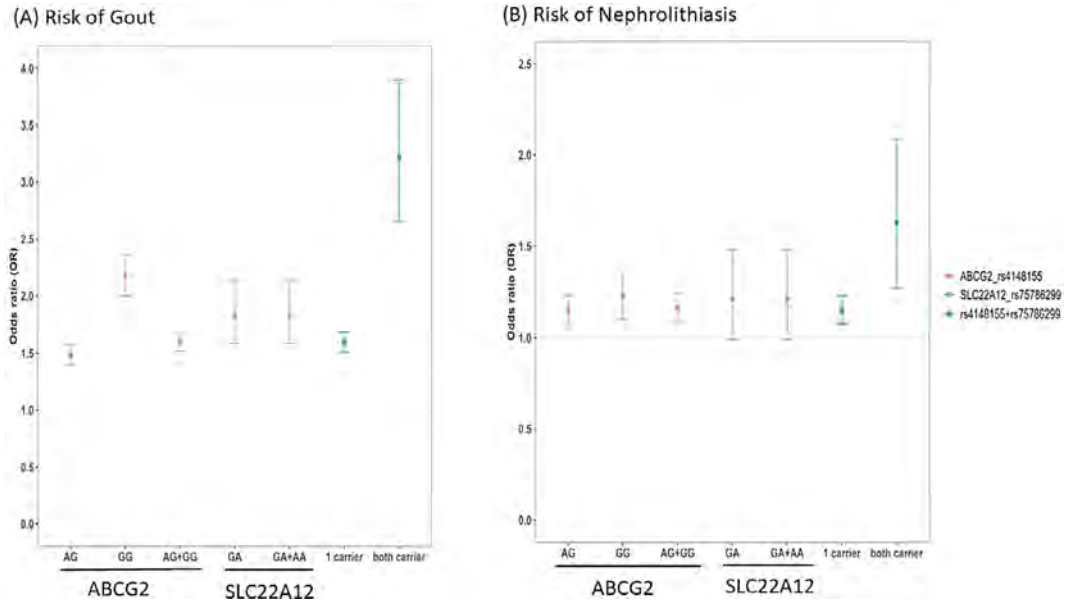


Figure 1 Risk of gout (A) and nephrolithiasis (B) among the carriers of ABCG2 rs4148155, SLC22A12 rs75786299 genotypic variants. Error bars represent the 95% confidence intervals (CI) of the odds ratios (ORs). (A) The univariable ORs (95% confidence intervals [CI] and p-values) for ABCG2 rs4148155 GG, AG, and AG+GG compared to the AA genotype were 2.18 (2.00-2.36, p<0.0001), 1.48, (1.4-1.57, p<0.0001), 1.61, (1.52-1.70, p<0.0001) and for SLC22A12 rs75786299 GA was 1.84 (1.59-2.14, p<0.0001) polymorphisms which were significantly associated with gout risk, respectively. Furthermore, under an additive model of inheritance, one and two carriers of ABCG2 rs4148155 (G) and SLC22A12 rs75786299 (A) remained independently associated with gout (OR = 1.60, 95% CI 1.51-1.69, p<0.0001; and OR = 3.22, 95% CI 2.66-3.90, p<0.0001, respectively). (B). The univariable ORs for the rs4148155 AG, GG, and AG+GG genotypes compared to the AA genotype were 1.15 (1.07–1.23, p=0.0001), 1.23 (1.10–1.37, p=0.0002), and 1.16 (1.06–1.24, p<0.0001), which were significantly associated with risk of nephrolithiasis respectively. In addition, the ORs for incident nephrolithiasis in individuals carrying one and two copies of the ABCG2 rs4148155(G) and SLC22A12 rs75786299(A) genotypic variants were 1.15 (1.08–1.23, p<0.0001) and 1.63 (1.27–2.09, p=0.0001).

Methods: This retrospective case-control study involved 35,280 adults from the Taiwan Precise Medicine Initiative (TPMI) database. We examined the prevalence of gout and ultrasound confirmed nephrolithiasis as the primary and secondary outcome. Univariable and multivariable logistic regression models were used to explore the associations between genetic variants, serum uric acid levels, incident gout, and nephrolithiasis.

Results: The frequencies of the rs4148155 G allele and the rs75786299 A allele was 33% and 2.4%, respectively. Among participants, 7,056 were gout, and 4,110 had nephrolithiasis. Multivariable odds ratios (ORs) for gout were 1.65 (1.56-1.75) and 3.59 (2.92-4.41) among one and two carriers, respectively (p=0.01 and p< 0.001). For nephrolithiasis, the multivariable ORs were 1.09 (1.02-1.17) and 1.40 (1.09-1.81) for one and two carriers, respectively (p=0.01 and p=0.009). Sex-stratified analysis revealed an additive risk of gout and nephrolithiasis among carriers of these genetic variants, regardless of gender. Independent risk factors for nephrolithiasis included higher age, male gender, and the presence of gout, hypertension, and hyperlipidemia.

Conclusion: The study highlights a significant association between the rs4148155 (G) and rs75786299 (A) alleles and the development of gout and nephrolithiasis, indicating an additive risk among carriers. These findings support precision healthcare approaches for individuals with these genetic variants to target hyperuricemia, gout, and systemic comorbidities, ultimately preventing nephrolithiasis.

Disclosure: C. Lin: None; **I. Chen**: None; **W. Huang**: None; **Y. Chen**: None; **C. Lin**: None; **Y. Chen**: None.

Abstract Number: 0817

Comparative Effectiveness of Yoga and Strengthening Exercise for Treating Knee OsteoArthritis: A Randomised Controlled Trial (YOGA Trial)

Bedru Abafita[1], Ambrish Singh[1], Dawn Aitken[1], Steffany Moonaz[2], Andrew J Palmer[1], Leigh Blizzard[1], Changhai Ding[1], Stan Drummen[1], Graeme Jones[3], Kim Bennell[4] and Benny Samuel Antony[1], [1]Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia, [2]Department of Clinical and Health Services Research, Southern California University of Health Sciences, Whittier, CA, [3]Menzies Institute for Medical Research, University of Tasmania, Melbourne, Australia, [4]University of Melbourne, Melbourne, Australia

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Osteoarthritis I: Clinical Trials
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: There is uncertainty about the best type of exercise to optimise outcomes for people with knee osteoarthritis (OA). Strengthening exercise is commonly recommended. However, yoga may have greater effects than strengthening given its focus on the mind and body with purposed benefits on flexibility, muscle strength, balance, fitness, while addressing the psychosocial sequelae. This study compared the effectiveness of a 24-week yoga program to strengthening exercise for knee OA.

Methods: The YOGA trial is an assessor-blinded (for non-patient-reported outcomes) randomised, active controlled superiority trial that included pre-specified non-inferiority outcomes. We recruited eligible symptomatic knee OA participants aged ≥40 years who fulfilled ACR clinical criteria with knee pain ≥40mm on 100mm visual analog scale (VAS). Participants were randomly assigned to a 24-week yoga program or strengthening exercise program (two supervised sessions and one home-based session per week for 12 weeks + three home-based sessions per week from 13-24 weeks). The primary outcome was change

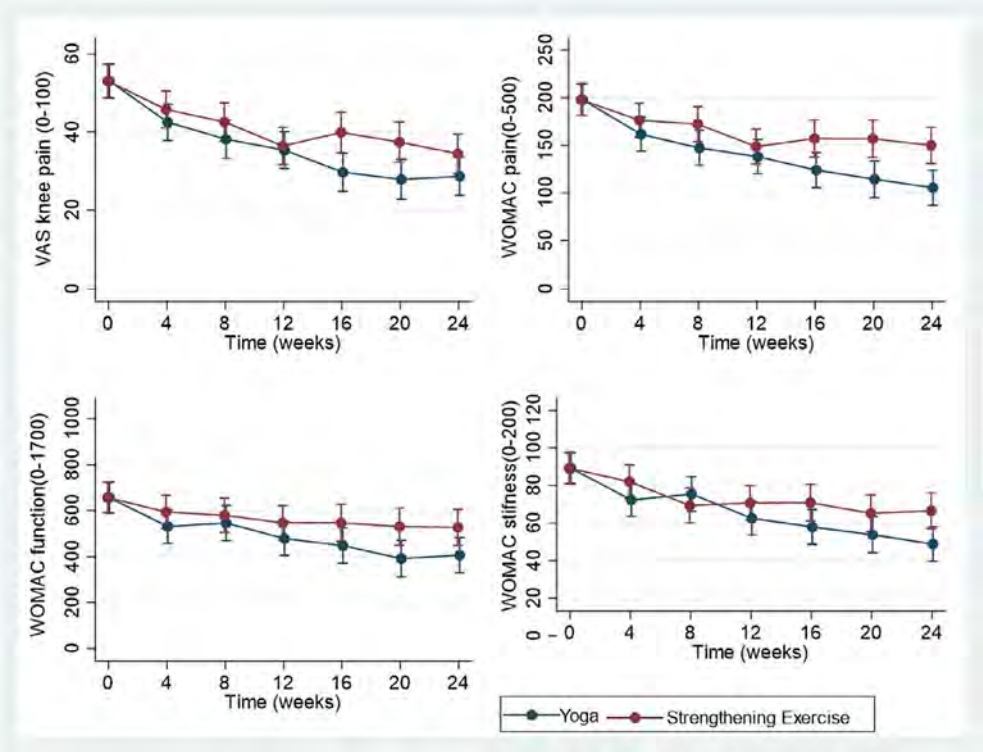


Figure 1. Mean visual analog scale (VAS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) subscale scores (95%CI) in the yoga and strengthening exercise groups during 24 weeks of intervention.

in knee pain over 12 weeks, assessed on a 100mm VAS. Secondary outcomes included, WOMAC scores, patient global assessment, physical performance measures, quality of life, depression, and neuropathic pain over 12 and 24 weeks.

Results: We screened 213 participants for eligibility between June 2021 and June 2022 and randomly assigned 117 participants to a yoga program (n=58) or a strengthening exercise program (n=59). Baseline characteristics of the participants between the groups were similar, with a mean (SD) age of 62.5(8.3) years, and 72.6% were female. Over 12 weeks, VAS knee pain score did not differ significantly between yoga and strengthening exercise groups with a between-group difference of -1.1mm [95%CI:-7.8,5.7]. Similarly, the VAS knee pain over 24 weeks was not significantly different (-5.8 mm [95%CI:-12.8,1.2]). The yoga group showed significantly greater improvements than the strengthening exercise group over 24 weeks (between-group difference) for WOMAC pain (-44.5mm [95%CI:-70.7,-18.3]), WOMAC function (-139mm [95% CI:-228.3,–49.7]), WOMAC stiffness (-17.6mm [95%CI:-30.9,-4.3]) and patient global assessment (-7.6mm [95%CI:-15.1,-0.2]). Additionally, yoga group had a significantly greater improvement than the strengthening exercise in depression (-1.1 [95%CI:-1.9,-0.2]) over 12 weeks and quality of life (0.04 unit [95%CI:0.0,0.07]) over 24 weeks. No serious adverse events were reported. There were 31 non-serious adverse events in 22(39%) participants in the yoga group and 23 in 16 (28%) participants in the strengthening exercise group over 24 weeks, mostly not related to the interventions.

Conclusion: A 24-week yoga program did not significantly reduce knee pain more than a strengthening exercise program over 12 weeks in participants with knee OA. However, the yoga program was non-inferior to strengthening exercise, as per the predetermined non-inferiority margin. Secondary outcomes indicated that the yoga program resulted in modestly greater improvements in knee symptoms, depression, and quality of life over 24 weeks compared to strengthening exercise.

Disclosure: B. Abafita: None; **A. Singh**: None; **D. Aitken**: None; **S. Moonaz**: None; **A. Palmer**: None; **L. Blizzard**: None; **C. Ding**: None; **S. Drummen**: None; **G. Jones**: None; **K. Bennell**: None; **B. Antony**: None.

Abstract Number: 0818

Efficacy of XT-150, a Novel Non-Viral Gene Therapy Delivering IL-10v, on Moderate to Severe Pain Due to Osteoarthritis of the Knee: Results of a Phase 2 Trial

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Osteoarthritis I: Clinical Trials

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Interleukin (IL)-10 is a regulator of cytokine activity and has the potential to restore homeostasis in osteoarthritis (OA) of the knee. Unfortunately, relatively short half-life has limited the therapeutic potential of native IL-10 protein.[1] The primary objective of this study (NCT04124042) was to establish the safety and tolerability of a single intra-articular (IA) dose of XT-150, a non-viral gene therapy designed to transiently express a proprietary version of the anti-inflammatory cytokine IL-10. The secondary objective was to establish the analgesic efficacy of a single IA dose of XT-150. Exploratory analyses evaluated effects on pain and function following single and repeat doses.

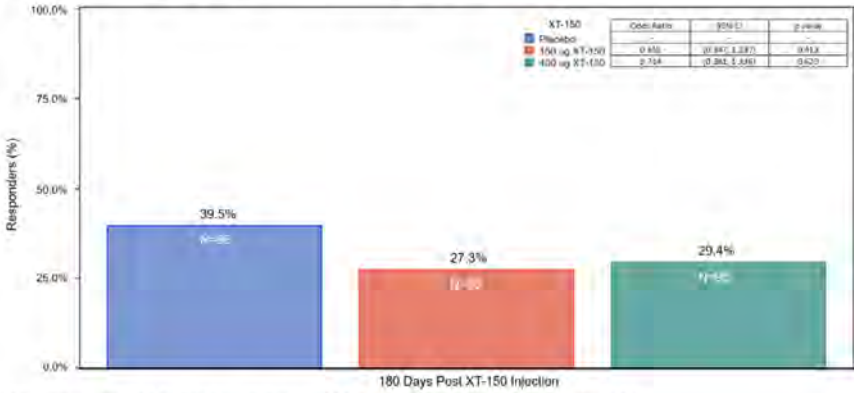
Methods: This was a two-stage double-blind Phase 2 study. Stage A compared 2 active doses of XT-150 to a placebo control arm. Stage B was a 6-month follow-up with the option to randomly receive a single injection of XT-150 at one of two doses (0.15 or 0.45 mg) between Day 180 and Day 330. The dose range was chosen from supportive evidence in previous clinical (XT-150-1-0201 & XT-150-1-0202) and preclinical studies. Participants 45-85 years of age with symptomatic knee

Table 1: Summary of Participant Demographic Data

Demographic Parameter	Sub-group	Treatment Sequence/Dose (mg) Sequence					
		XT-150 – XT-150				Placebo – XT-150	
		0.15 – 0.15 (N=49)	0.15 – 0.45 (N=47)	0.45 – 0.15 (N=47)	0.45 – 0.45 (N=47)	0 – 0.15 (N=48)	0 – 0.45 (N=48)
Age (years), Mean (SD)		62.1 (8.15)	62.0 (6.68)	64.9 (7.09)	62.6 (7.82)	62.9 (7.35)	65.3 (9.52)
Gender, n (%)	Female	20 (40.8)	20 (42.6)	22 (46.8)	33 (70.2)	27 (56.3)	33 (68.8)
	Male	29 (59.2)	27 (57.4)	25 (53.2)	14 (29.8)	21 (43.8)	15 (31.3)
Race, n (%)	White	35 (71.4)	41 (87.2)	39 (83.0)	38 (80.9)	31 (64.6)	39 (81.3)
	American Indian or Alaska Native	1 (2.0)	-	-	-	-	-
	Asian	-	-	1 (2.1)	2 (4.3)	-	3 (6.3)
	Black or African American	10 (20.4)	6 (12.8)	5 (10.6)	5 (10.6)	11 (22.9)	4 (8.3)
	Native Hawaiian or Other Pacific Islander	-	-	-	-	1 (2.1)	-
	Multiple	3 (6.1)	-	2 (4.3)	1 (2.1)	3 (6.3)	2 (4.2)
	Other	-	-	-	1 (2.1)	-	-
	Unknown	-	-	-	-	2 (4.2)	-
Ethnicity n (%)	Hispanic or Latino	7 (14.3)	4 (8.5)	-	-	1 (2.1)	2 (4.2)
	Not Hispanic or Latino	42 (85.7)	43 (91.5)	47 (100.0)	47 (100.0)	47 (97.9)	46 (95.8)
Weight (kg), Mean (SD)		96.26 (25.34)	94.67 (22.31)	91.73 (24.56)	94.94 (25.17)	95.69 (19.35)	88.25 (23.30)
Height (cm), Mean (SD)		171.78 (12.34)	172.57 (10.76)	171.88 (10.20)	168.56 (10.74)	170.78 (9.48)	166.47 (10.63)
BMI (kg/m^2), Mean (SD)		32.48 (7.40)	31.82 (7.09)	31.10 (7.19)	33.40 (8.19)	32.41 (5.23)	31.66 (7.24)

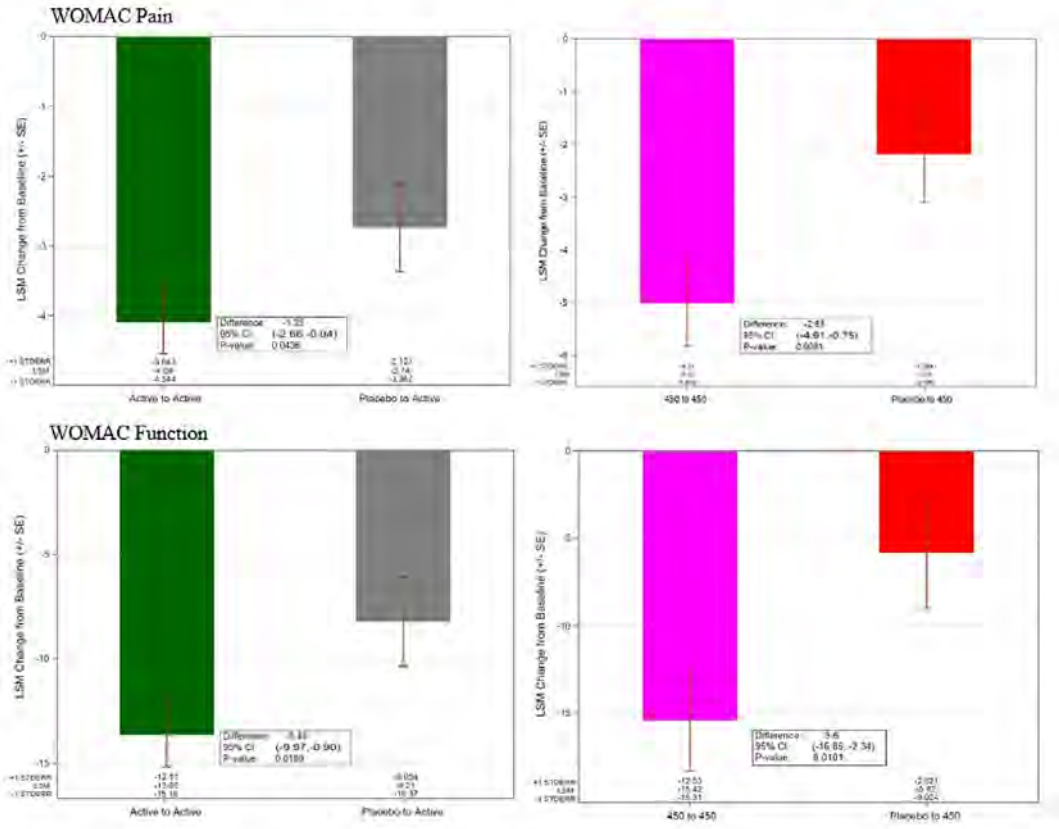
Abbreviations: BMI=body mass index; SD=standard deviation.

Figure 1: Stage A: Responders Reaching 30% Threshold (WOMAC Pain)



Abbreviation: WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index

Figure 2: Stage B: Post Hoc Analyses (mITT Population)



Abbreviation: WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index
Active to active=2-doses XT-150 (pooled active followed by active [0.15 mg to 0.15 mg; 0.15 mg to 0.45 mg; 0.45 mg to 0.15 mg; 0.45 mg to 0.45 mg XT-150]); placebo to active=1-dose XT-150 (pooled placebo followed by active [placebo to 0.15 mg XT-150; placebo to 0.45 mg XT-150]); 450 to 450=2 doses 0.45 mg XT-150 (0.45 mg to 0.45 mg); placebo to 450=1 dose 0.45 mg XT-150 (placebo to 0.45 mg)
Least squares mean (LSM), standard error (SE), LSM difference and 95% confidence interval (CI) of LSM difference by mixed-model analyses. Note difference in scale between left and right panels.

OA (defined as a WOMAC Pain score of ≥8 at screening and Kellgren-Lawrence grade 2 or 3) were randomized on Day 0 to one of 6 treatment sequences. Injections were completed under imaging guidance to confirm positioning within the joint prior to injection. Screening evaluation took place up to 30 days before enrollment. Efficacy measures were evaluated at baseline and at follow-up visits on Day 7, 30, and monthly thereafter. In Stage A, 286 participants received at least one dose of XT-150 or placebo (phosphate buffered saline) as a single IA injection into the knee. In Stage B, 244 received a second injection, all with XT-150. Separate analyses were conducted for Stages A and B. Stage A analyses included the primary intent to treat (ITT) population to assess the efficacy of XT-150. The primary efficacy outcome measure was at least 30% improvement from Baseline in WOMAC Pain score (obtained from KOOS questionnaire) at Day 180. Stage B analyses included a post hoc modified ITT (mITT) population with a baseline WOMAC Pain score of 9-20. Post hoc analyses in the ITT and mITT populations compared single active doses with repeat active doses.

Results: Demographic data are summarized in **Table 1**. There was no statistically significant difference in patients achieving at least 30% improvement in WOMAC Pain score between either dose (0.15 mg or 0.45 mg) of XT-150 vs placebo when given as a single dose by Day 180 **(Figure 1)**. Statistically significant changes from baseline WOMAC Pain scores were observed at Day 360 comparing 2 doses of 0.45 mg XT-150 vs 1 dose of placebo followed by 1 dose of 0.45 mg XT-150 in post hoc analyses (p=0.0081, **Figure 2**). The two-dose regimen of 0.45 mg XT-150 also showed a statistically significant reduction in WOMAC function score at Day 360 vs the single-dose regimen of 0.45 mg XT-150 (p=0.0101).

Conclusion: These data suggest improvement in pain and function with two doses vs one dose of XT-150 and support the future development of repeat doses of XT-150 for the potential treatment of pain from moderate-to-severe knee OA.

1. Kwilasz AJ, et al. Neuropharmacology. 2015;96(Pt A):55-69.

Disclosure: E. Grigsby: Eli Lilly, 5, Jointstem, 5, Kolon Tissuegene, 5, Medtronic, 2, 5, Neuros, 5, Sollis Therapeutics, 2, Tenex Health Inc., 2, Xalud Therapeutics, 2; **S. Collins**: Xalud Therapeutics, Inc., 1, 4, 8, 11; **L. Kapural**: Avanos, 1, 5, Gimer, 1, Nalu, 5, Neuralace, 5, Neuros, 1, Nevro, 1, 5, PainTeq, 1, Presidio, 1, Saluda, 5; **M. McBride**: None; **J. Rieger**: Xalud Therapeutics, 4, 8, 10; **M. Stokes**: Xalud Therapeutics, 3; **H. Rutman**: Xalud Therapeutics, 3, 11; **F. Cicuttini**: Xalud Therapeutics, Inc., 5.

Abstract Number: 0819

Regression to the Mean for Physical Function and Quality of Life in Trials for Symptomatic Knee Osteoarthritis

Martin Englund and Aleksandra Turkiewicz, Lund University, Lund, Sweden

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Osteoarthritis I: Clinical Trials
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Improvement in pain reported in clinical trials for osteoarthritis (OA) is typically strongly depending on the regression-to-the-mean phenomenon. Regression to the mean has been estimated to explain about 1 NRS point (0-10 scale) of the absolute improvement since baseline. However, the potential effects of regression to the mean on typical secondary outcomes in trials for knee OA are unknown. Thus, our purpose was to estimate the absolute size of improvement in knee physical function and knee-related quality of life (QOL) explained by regression to the mean in a typical trial for symptomatic knee OA.

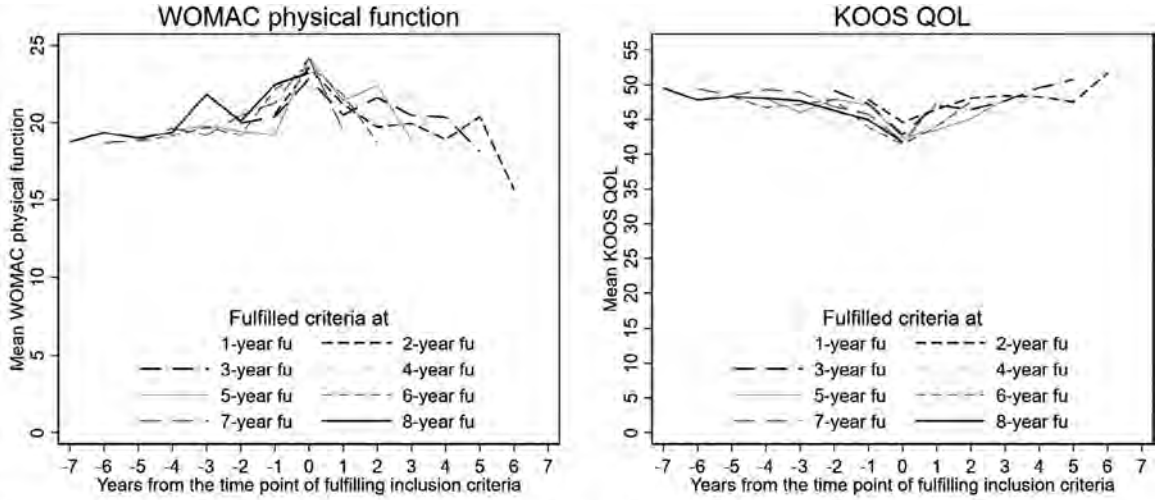


Figure. Mean levels of physical knee function and knee-related quality of life (QOL) among 547 persons fulfilling criteria for inclusion in a hypothetical knee osteoarthritis trial, illustrating the occurrence of regression to the mean when conditioning on knee pain at inclusion. Time 0 means the moment when fulfilling the criteria. Each line represents a cohort of subjects fulfilling criteria at one follow-up occasion (between year 1 and year 8 post baseline).

Methods: We included participants of Osteoarthritis Initiative who fulfilled inclusion criteria typically required for enrolment in a clinical trial (Hochberg *et al*. JAMA 2019). These included: age 40-79 years, symptomatic knee OA, Kellgren-Lawrence grade 2-3, use of pain medication more than half the days of a month in past 12 months, numerical rating scale (NRS) pain of 4 to 9 in the target knee. We studied observed changes in the mean levels of WOMAC physical function (scale 0 to 68; higher score = worse function) and KOOS QOL (scale 0 to 100; higher score = better QOL) with respect to conditioning on current knee pain. To account for the fact, that a person could fulfil the criteria at more than one time point and the longitudinal measurements, we used linear mixed models for estimation of means and differences over the follow-up time.

Results: We identified 547 subjects who fulfilled inclusion criteria on at least one annual follow-up between year 1 and year 8. The mean level of WOMAC knee physical function and KOOS QOL at each follow-up time point was similar, about 18, and 52 respectively. However, at the time of fulfilling the inclusion criteria (theoretical inclusion in a trial), the mean level of physical function and QOL in the same subjects were about 23 and 43, respectively. The mean improvement in WOMAC physical function between the theoretical point of inclusion in a trial and one and two years later, was -2.5 (95% CI to -3.2 to -1.7) and -3.1 (95% CI to -3.8 to -2.3), respectively. The corresponding improvement in KOOS QOL was 2.7 (95% CI ,1.7 to 3.7) and 4.2 (95% CI, 3.1 to 5.3) (figure).

Conclusion: Regression to the mean in typical trials for knee OA is not only likely to explain substantial improvement in pain, but also albeit to a lesser extent, improvement in knee function and QOL. Regression to the mean is a phenomenon that often misleads the investigators to exagerate effectiveness as the phenomenon neither represents improvement from the intervention nor placebo response from the intervention and its context.

Disclosure: M. Englund: Cellcolabs AB, 2; **A. Turkiewicz**: None.

Abstract Number: 0820

Radiographic and Pain Outcomes from a Phase 3 Extension Study Evaluating the Safety and Efficacy of Lorecivivint in Subjects with Severe Osteoarthritis of the Knee (OA-07): 36 Month Single Blind and Placebo Crossover Phase Results

Yusuf Yazici[1], Christopher Swearingen[2], Victor Lopez[3], Jon Britt[4], Sarah Kennedy[5], Jeyanesh Tambiah[2] and Timothy McAlindon[6], [1]NYU Grossman School of Medicine, La Jolla, CA, [2]Biosplice Therapeutics, Inc., San Diego, CA, [3]Biosplice Therapeutics, Inc., Santa Clarita, CA, [4]Biosplice Therapeutics, Inc., Los Angeles, CA, [5]Biosplice Therapeutics, Inc., Superior, CO, [6]Tufts Medical Center, Arlington, MA

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Osteoarthritis I: Clinical Trials

Session Type: Abstract Session

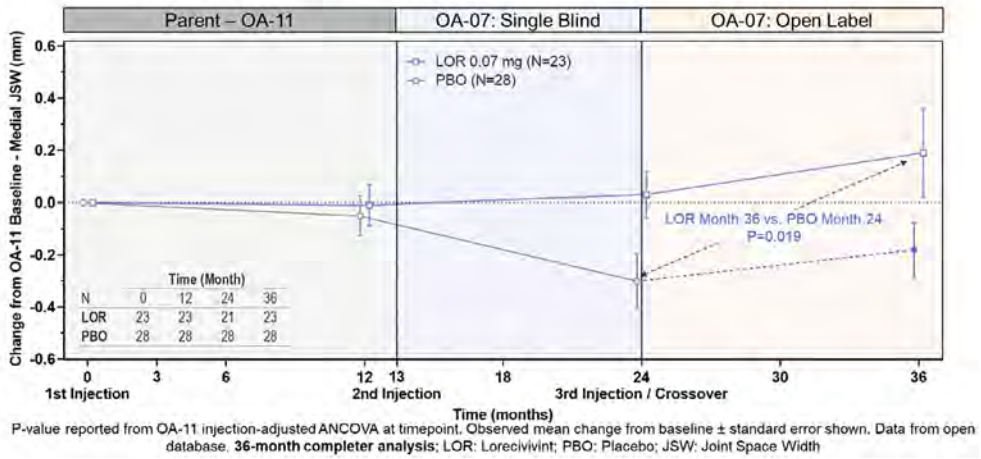
Session Time: 4:00PM–5:30PM

Background/Purpose: Knee osteoarthritis (OA) has unmet need for safe, efficacious symptom and disease-modifying treatments. Lorecivivint (LOR), an intra-articular (IA) CLK/DYRK inhibitor thought to modulate Wnt and inflammatory pathways has previously appeared safe, demonstrated patient-reported outcome (PRO) improvements compared with placebo (PBO), and maintenance of radiographic medial joint space width (JSW). A Phase 3 extension study, OA-07 (NCT04520607), evaluated LOR safety and efficacy with outcomes of medial JSW (mm), Pain Numerical Rating Scale (NRS [0-10]), WOMAC Pain [0-100], and WOMAC Function [0-100].

Methods: Participants had structurally advanced knee OA (medial JSW 1.5-4 mm) and completed the parent Phase 3 trial. A repeat injection according to original randomization (LOR / PBO) was given at the beginning of the single-blind (participants and investigators) extension Year 1. In Year 2 of the extension, all participants received open-label 0.07 mg LOR, while still blind to original treatment assigments. Baseline-adjusted ANCOVA was used to estimate differences between LOR and PBO outcomes using the OA-07 baseline. Treatment effect at Month 36 was estimated using marginal comparison from baseline-adjusted ANCOVA to last PBO observation prior to crossover for LOR only. Concordance between OA-07 baseline-adjusted medial JSW change and pain response was conducted for 36 month completers using logistic regression. Final data are expected Q4 2023.

Figure 1: Change in Medial Joint Space Width in OA-07 from OA-11 Baseline

FAS 36-month completer analysis



P-value reported from OA-11 injection-adjusted ANCOVA at timepoint. Observed mean change from baseline ± standard error shown. Data from open database. **36-month completer analysis**; LOR: Lorecivivint; PBO: Placebo; JSW: Joint Space Width

Results: 277 participants (mean age 61.0 ± 8.2 years, BMI 31.8 ± 4.9 kg/m^2, female 62.8%, KL3 45.5%, medial JSW 2.63 ± 0.69 mm, 67.1% bilaterally symptomatic, 68.6% medial JSW < 3 mm) were enrolled. LOR appeared safe and well-tolerated. At 24 months, LOR showed numerically reduced medial JSW loss compared to placebo: LOR -0.11 (± 0.05) mm (n=111) vs. PBO -0.20 (± 0.05) mm (n=119) (Δ=0.09 mm, 95% CI [-0.06, 0.23], *P*=0.246). At 36 months, LOR completers (n=23) medial JSW change was +0.19 (± 0.14) mm, difference -0.49 mm (*P*=0.019) LOR compared to last PBO measure before crossover at 24 months (Figure 1).

Average change from extension baseline to 24 months in Pain NRS was LOR -0.25 (± 0.19, n=121) compared to PBO 0.09 (± 0.19, n=130) (Δ=-0.34, 95% CI [-0.87, 0.19], *P*=0.207). Similar trends were seen for LOR treatment effect over PBO at 24 months for WOMAC Function Δ=-4.90 (95% CI [-9.92, 0.13], *P*=0.056) and WOMAC Pain Δ=-5.18 (95% CI [-10.28, -0.08], *P*=0.047). Additional improvements were seen at 36 months in LOR (n=35) Pain NRS with change from OA-07 baseline of -0.91 (±0.34) and cross-over from PBO to LOR (n=45) improving -0.43 (±0.30). Good concordance was shown between change in medial JSW and at least a 20% improvement in Pain NRS at 36 months (n=20, AUC=0.719).

Figure 2: **Change in WOMAC Pain in OA-07 from OA-07 Baseline**

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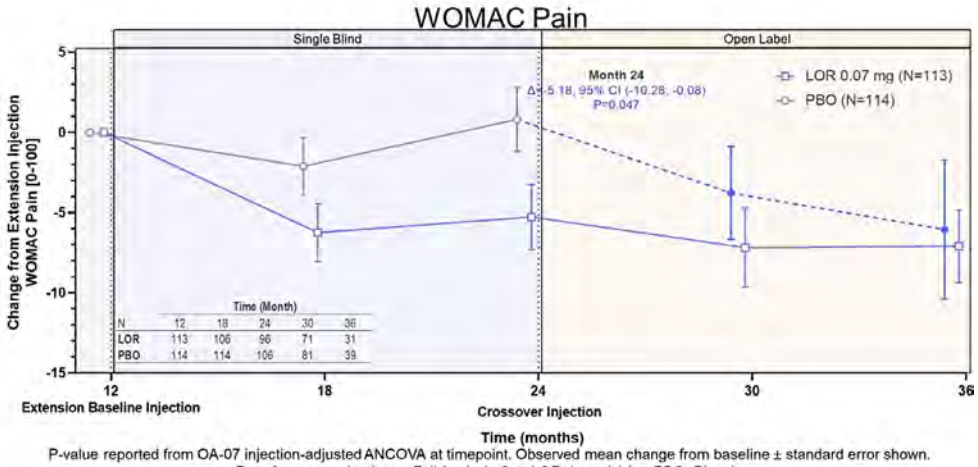

P-value reported from OA-07 injection-adjusted ANCOVA at timepoint. Observed mean change from baseline ± standard error shown.
Data from open database. Full Analysis Set; LOR: Lorecivivint; PBO: Placebo

Figure 3: **Change in WOMAC Function in OA-07 from OA-07 Baseline**

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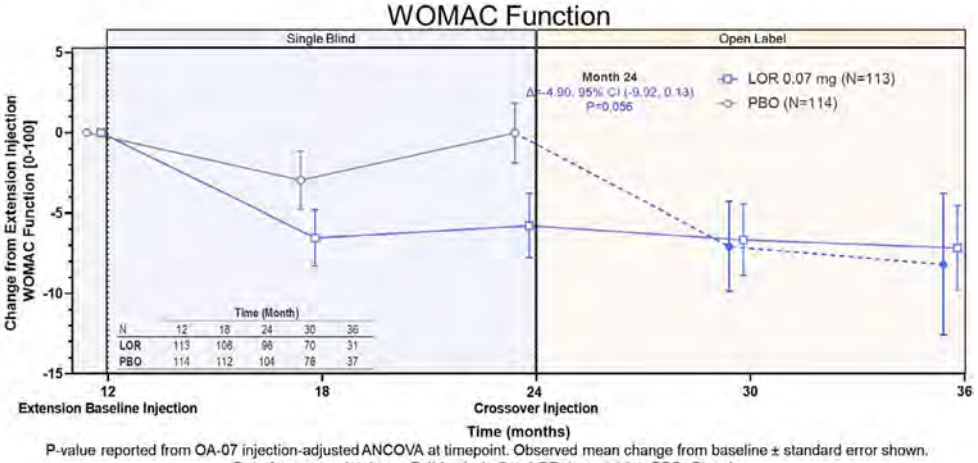

P-value reported from OA-07 injection-adjusted ANCOVA at timepoint. Observed mean change from baseline ± standard error shown.
Data from open database. Full Analysis Set; LOR: Lorecivivint; PBO: Placebo

Conclusion: LOR continued to appear safe and well tolerated. A potential benefit of LOR 0.07 mg compared with PBO in medial JSW was observed 12 months after the extension baseline (second) injection, which persisted in those who completed an additional 12 months (total 36 months, 3 injections) and in PBO participants who crossed to LOR treatment. Potential LOR benefit compared to PBO is also seen across PROs with preliminary good concordance between medial JSW and pain improvement.

Disclosure: Y. Yazici: Biosplice Therapeutics, Inc, 3, 4, 8; **C. Swearingen**: Biosplice Therapeutics, Inc, 3; **V. Lopez**: Biosplice Therapeutics, Inc, 3, 8; **J. Britt**: Biosplice Therapeutics, 3; **S. Kennedy**: Biosplice Therapeutics, Inc, 3, 8; **J. Tambiah**: Biosplice, 3, 11; **T. McAlindon**: None.

Abstract Number: 0821

Effects of Sprifermin on a Novel Outcome of Osteoarthritis Symptom Progression: Post Hoc Analysis of the FORWARD Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Osteoarthritis I: Clinical Trials
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: People with knee OA (KOA) desire therapies which delay or reverse disease progression supporting the need for disease-modifying OA drugs (DMOADs). Sprifermin, truncated recombinant human fibroblast growth factor-18, demonstrated dose-dependent increased cartilage thickness in KOA in the Phase 2 FORWARD study. Improvement from baseline (BL) in WOMAC Pain and Function occurred in all sprifermin study arms with a lack of differentiation from placebo (PBO), potentially due to including participants (pts) not at risk of KOA progression. Minimum clinically meaningful changes (improvement or worsening) in WOMAC Pain and Function have been defined as ~10 points (0-100 scale). A post hoc analysis of FORWARD identified a subgroup at risk (SAR) enriched for disease progression, in which improvement in WOMAC Pain ≥10 points for sprifermin over PBO was seen by Year (Y) 3. Worsening WOMAC Pain ≥10 points has been predictive of worsening function, structural progression, and knee replacement in KOA natural history studies. This post hoc analysis of the FORWARD study evaluates the effect of sprifermin on the symptomatic progression of KOA.

Methods: Pts were randomized 1:1:1:1:1 to intra-articular PBO or sprifermin 30 μg or 100 μg every 6 or 12 months (Q6M or Q12M) for 18 months and followed through Y5. WOMAC was collected Q3M and MRI Q6M through Y2 and then Q6M and Q12M, respectively. In this Kaplan-Meier analysis, time to symptomatic progression (ie, first occurrence of worsening [increase] of WOMAC Pain of ≥10 points with no improvement [≤9 point decrease] in WOMAC Function) was evaluated through Y3. All treatment arms of the intent-to-treat population (ITT) and SAR (ie, BL WOMAC Pain 40-90, minimum joint space width 1.5-3.5 mm) were analyzed, as well as the sprifermin 100 μg groups combined for additional power. Time to symptomatic progression was also analyzed by changes in cartilage thickness (decrease or no change/increase) for those with evaluable MRIs at BL and ≥1 post-BL timepoint, ie, modified (m) ITT and mSAR.

Results: Baseline characteristics were comparable across the FORWARD ITT and SAR treatment arms (Table). Sprifermin showed dose-dependent benefits in the time to symptomatic progression compared to PBO, with clinically meaningful and statistically significant separation from PBO for the sprifermin 100 µg groups combined (nominal logrank p-value ITT < 0.05, SAR < 0.01; HR [95% CI] ITT 0.59 [0.37, 0.95], SAR 0.35 [0.16, 0.81]) (Figure); separation from PBO was more pronounced in the SAR compared to the ITT. The sprifermin 100 µg combined group also demonstrated less symptomatic progression than PBO regardless of an increase or no change/decrease in cartilage thickness in the mSAR and mITT.

Conclusion: These post hoc results support that sprifermin may prevent symptomatic progression of KOA, with benefits seen in both ITT and SAR populations for the sprifermin 100 µg combined group. Further study is needed to confirm the symptomatic and structural benefits of sprifermin. As differences between the sprifermin- and PBO-treated groups were detectable in a 3-year time frame, time to symptomatic progression of KOA could be a meaningful endpoint for a DMOAD trial.

Figure: Time to Symptomatic Progression in FORWARD

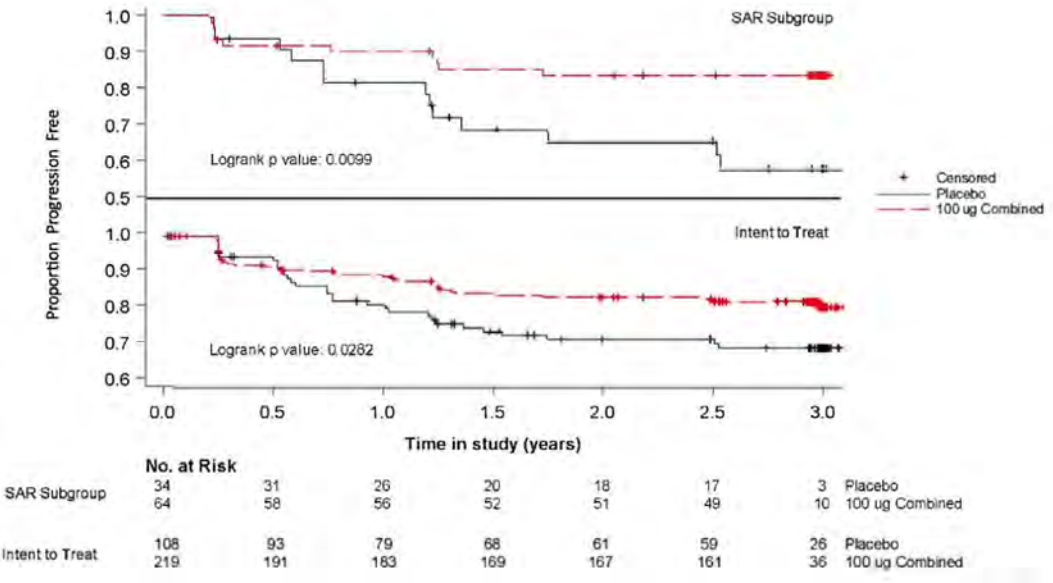

Table. Baseline Characteristics by Treatment Arm – FORWARD Study – ITT and SAR

Characteristic	ITT (N=549)					SAR (N=161)				
	Placebo	Sprifermin (n=441)				Placebo	Sprifermin (n=127)			
	n=108	30 µg×2 n=110	30 µg×4 n=111	100 µg×2 n=110	100 µg×4 n=110	n=34	30 µg×2 n=36	30 µg×4 n=27	100 µg×2 n=31	100 µg×4 n=33
Mean age, years (SD)	63.5 (8.5)	65.2 (8.4)	63.2 (8.4)	63.4 (9.1)	65.2 (8.0)	62.2 (7.7)	65.3 (8.1)	65.9 (6.1)	66.0 (7.9)	66.8 (7.0)
Female, n (%)	76 (70.4)	73 (66.4)	80 (72.1)	77 (70.0)	73 (66.4)	24 (70.6)	27 (75.0)	22 (81.5)	26 (83.9)	28 (84.8)
Asian race, n (%)	21 (19.4)	22 (20.0)	23 (20.7)	23 (20.9)	21 (19.1)	7 (20.6)	6 (16.7)	6 (22.2)	10 (32.3)	5 (15.2)
White race, n (%)	87 (80.6)	88 (80.0)	88 (79.3)	87 (79.1)	89 (80.9)	27 (79.4)	30 (83.3)	21 (77.8)	21 (67.7)	28 (84.8)
Hispanic/Latino, n (%)	1 (0.9)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mean BMI (kg/m²) (SD)	30.1 (6.1)	29.5 (5.3)	28.9 (5.5)	28.5 (5.2)	29.6 (5.1)	31.1 (6.8)	30.9 (6.5)	30.1 (6.3)	29.3 (5.4)	31.3 (5.0)
≥30, n (%)	48 (45.7)	46 (43.0)	41 (38.0)	38 (35.8)	45 (42.1)	15 (44.1)	19 (54.3)	10 (37.0)	12 (38.7)	19 (57.6)
KL Grade 2, n (%)	74 (68.5)	73 (66.4)	77 (69.4)	77 (70.0)	78 (70.9)	14 (41.2)	17 (47.2)	12 (44.4)	14 (45.2)	19 (57.6)
Mean medial mJSW, mm (SD)	4.20 (1.30)	4.11 (1.14)	4.23 (1.28)	4.33 (1.23)	4.23 (1.07)	3.57 (1.35)	3.32 (0.86)	3.49 (0.82)	3.40 (0.77)	3.51 (0.74)
Mean WOMAC A1 score, 0-10 (SD)	5.6 (1.4)	5.6 (1.4)	5.6 (1.4)	5.5 (1.2)	5.8 (1.4)	6.2 (1.4)	6.0 (1.4)	6.1 (1.3)	6.2 (1.2)	6.4 (1.0)

×2=every 12 months for 2 cycles; ×4=every 6 months for 4 cycles; BMI=body mass index; ITT=intent-to-treat; KL=Kellgren-Lawrence; mJSW=minimum joint space width; N=number in entire analysis set; n=number in sample; SAR=subgroup at risk; SD=standard deviation; WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index.

Disclosure: P. Conaghan: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, Genascense, 2, GlaxoSmithKlein(GSK), 2, Grunenthal, 2, Janssen, 2, Levicept, 2, Merck/MSD, 2, Moebius Medical, 2, Novartis, 2, 6, Stryker, 2, Takeda, 2, TrialSpark, 2; **N. Katz**: TrialSpark, 2; **d. Hunter**: None; **M. Hochberg**: TrialSpark, 2; **A. Guermazi**: BICL, LLC, 11, ICM, Coval, TrialSpark, TissueGene, Medipost, 2, Novartis, 2, Pfizer, 2; **K. Somberg**: TrialSpark, 1, 11; **J. Clive**: TrialSpark, 2; **M. Johnson**: Trialspark, 2; **N. Goel**: TrialSpark, 3, 11.

Abstract Number: 0822

From Biomarkers to Endotypes: Data-driven Identification of Knee Osteoarthritis Patients Subtypes

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Osteoarthritis I: Clinical Trials
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Osteoarthritis (OA) is a diverse and multifaceted condition. Despite its widespread incidence, the core mechanisms of the disease remain elusive, and therapeutic interventions are restricted. The complexity of OA is compounded by the absence of well-defined subgroups or "endotypes" that could elucidate specific triggers and guide towards more personalized treatments. Recent studies propose that molecular biomarkers could distinguish various OA endotypes. For instance, certain biomarkers might show elevated levels in OA patients experiencing inflammation, while others might increase in those with advanced cartilage deterioration.

This study aimed to uncover OA endotypes via soluble biomarkers of tissue turnover, using unsupervised machine learning methodologies.

Methods: The study measured biomarkers of cartilage alteration (CTX-II, C2M, T2CM, PRO-C2), bone modification (N-MID, UCTX-I, SCTX-I), and tissue inflammation (CRPM, VICM, C1M, C3M) were measured at baseline in phase III clinical trials SMC01 (n=1176) and SMC02 (n=1030) which tested the effectiveness and safety of oral salmon calcitonin in knee OA patients.

Table 1 – A summarization of the dispersion of subjects within each cluster, i.e., endotype and the change of clinical parameters as an indicator of patients in the placebo-groups natural OA progression. For each cluster age, BMI and relevant clinical parameters are reported in terms of median and IRQ (Q1,Q3). KL proportions are proportions of subjects with a change in KL score.

Endotype	Cluster 1 Low tissue turnover	Cluster 2 Systemic inflammation	Cluster 3 Structural damage	P-value KW-test
Subject	***Median (Q1, Q3)***	***Median (Q1, Q3)***	***Median (Q1, Q3)***	
sAge	n = 160	n = 197	n = 171	
BMI	63.95 (60.68, 67.95) 29.3 (26.18, 32.76)	64.60 (60.50, 69.60) 28.50 (25.50, 31.30)	64.90 (60.40, 69) 27.10 (24.45, 29.70)	
JSW	***Median (Q1, Q3)***	***Median (Q1, Q3)***	***Median (Q1, Q3)***	
	n = 160 -0.28 (-0.77, 0.04)	n = 197 -0.16 (-0.47, 0.13)	n = 171 -0.32 (-0.67, 0.12)	0.0488
WOMAC	***Median (Q1, Q3)***	***Median (Q1, Q3)***	***Median (Q1, Q3)***	
Pain	n = 159 -108 (-174.50, -42)	n = 197 -114 (-174, -36)	n = 171 -115 (-179.50, -47)	0.7928
Stiffness	n = 159 -36 (-46, -8.5)	n = 197 -36 (-62, 4)	n = 171 -42 (-77, -5.5)	0.2315
Functionality	n = 157 -287 (-174.50, -42)	n = 195 -308 (-549.50, -51)	n = 169 -323 (-589, -54)	0.7380
VAS	***Median (Q1, Q3)***	***Median (Q1, Q3)***	***Median (Q1, Q3)***	
	n = 160 -25.50 (-41.25, -5.75)	n = 197 -25 (-40, -6)	n = 171 -25 (-40, -3.50)	0.9365
KL	***Proportion (%)***	***Proportion (%)***	***Proportion (%)***	χ^2
	n = 160	n = 197	n = 171	0.7506
-1	0	1.01	1.17	
0	88.75	89.85	88.89	
1	11.25	9.14	9.94	

The study included only placebo group patients who had more than 5 biomarkers available (n=528). About 4% of data was missing and was imputed using Random Forest. K-Means clustering was employed on UMAP dimensionality-reduced data. Associations between the changes in symptomatic and radiographic parameters over two years with the identified clusters were compared using the Kruskal Wallis test for numerical variables and chi-square test for categorical variables.

Results: The K-Means clustering resulted in three unique clusters; 1) a low tissue turnover endotype, 2) a systemic inflammation endotype and 3) a structural damage endotype (figure 1). The structural damage endotype showed elevated levels of bone remodeling markers CTX-I, N-MID, and the cartilage degradation marker CTX-II. The systemic inflammation endotype was characterized by higher levels of C1M, C2M, C3M, CRPM, and VICM associated with tissue inflammation. Conversely, the low tissue turnover endotype displayed generally lower levels of both tissue-related and inflammatory markers. A difference in JSW change over two years was noted among the three groups (Cluster 1: -0.28 mm, Cluster 2: -0.16 mm, Cluster 3: -0.32 mm; p=0.049), but the difference was not statistically significant in the adjusted analysis. Broadly, the three endotypes showed similar progression.

Conclusion: These findings indicate the presence of unique biomarker-based endotypes in OA, underlining the fact that several mechanistic pathways may result in joint degradation. Identifying these endotypes could facilitate the development of more precise treatments that are designed to address specific causes of OA in distinct patient subgroups.

Disclosure: M. Hannani: None; **Z. Lisowska-Petersen**: None; **M. Karsdal**: Nordic Bioscience, 3, 11; **C. Bager**: Nordic Bioscience, 3, 11; **A. Bay-Jensen**: Nordic Bioscience, 3, 3, 8, 9; **C. Thudium**: Nordic Bioscience, 3, 11.

Abstract Number: 0823

Sleep Disturbance Predicts Pain Interference in Patients with Early Rheumatoid Arthritis in a Prospective Real-World Cohort

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes I: Assessment Tools

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Despite taking strong immunosuppressive medications to control inflammation, many patients with rheumatoid arthritis (RA) continue to experience moderate to severe pain that does not correlate with laboratory or clinical findings. Sleep disturbances are extensively reported among patients with RA and could influence pain perception. Prior investigations have demonstrated that one night of partial sleep loss is associated with increases in next day pain in patients with RA. However, there is a knowledge gap regarding the impact of sleep disturbances on long-term pain outcomes. The

objective of the present study was to determine whether sleep disturbances early in the disease are associated with future pain interference.

Methods: Data were from adults with early RA (joint symptoms ≤12 months) enrolled in the Canadian Early Arthritis Cohort between 2016-2023 who completed PROMIS (Patient-Reported Outcomes Measurement Information System) measures at 0, 6-, 12-, 18-, and 24-months to assess sleep disturbance (primary predictor) and pain interference (primary outcome). PROMIS sleep disturbance assesses perceptions of sleep quality, depth, and restoration. PROMIS pain interference measures the extent to which pain interferes with physical, mental, and social functioning. To estimate longitudinal associations between sleep disturbance and pain interference, the dataset was lagged so that repeat measures of sleep disturbance at 0, 6, 12 and 18 months were specified to predicted pain interference 6-months later at 6-,12-, 18- and 24-months follow up. Linear mixed effects regression was used to estimate crude and adjusted effects of sleep disturbance on pain interference over the 24-month study period adjusted for age, sex, body mass index (BMI), education, income, smoking status, comorbidity index, steroid use, and treatment.

Results: The sample included 502 patients with early RA. At baseline, the sample was 68% female, 81% Caucasian, 73% seropositive (RF/ACPA), and 77% met the 1987 ARA Classification Criteria for RA or the 2010 ACR/EULAR RA Classification Criteria; with a mean (SD) age of 56 (14) years, BMI of 28.4 (6.7) kg/m^2,and disease duration of 5.4 (2.9) months (Table 1). The mean (SD) T-score for PROMIS pain interference was 60.4 (8.6) and PROMIS sleep disturbance was 53.5

Table 1. Baseline demographic and clinical characteristics of sample (N = 502).

Characteristic	Value
Demographic	
Age (years), mean (SD)	56 (14)
Female, freq (%)	341 (68)
Caucasian (White or European), freq (%)	405 (81)
BMI ever ≥ 30 kg/m^2, freq (%)[§]	153 (32)
Post-secondary education, freq (%)	308 (61)
Income ≤ $50,000, freq (%)[§]	125 (37)
Current smoker, freq (%)	73 (15)
Number of comorbidities (RDCI), mean (SD)	1.4 (1.4)
RA disease characteristics	
Disease duration (months), mean (SD)	5.4 (2.9)
Meet 1987 ARA Classification Criteria for RA or 2010 ACR/EULAR RA Classification Criteria, freq (%)	389 (77)
Seropositivity (RF/ACPA), freq (%)[§]	349 (73)
TJC28, median (IQR)	7 (3 to 12)
SJC28, median (IQR)	6 (3 to 10)
CRP, median (IQR)	6.9 (2.9 to 18.5)
Treatment, frequency (%)	
Oral Steroids	156 (31)
MTX	384 (76)
Non-MTX DMARDs	281 (56)
Advanced therapy	2 (0)
TNFi	2 (0)
JAKs	0 (0)
Other MOA	0 (0)
PROMIS T-score, mean (SD)	
Sleep disturbance	53.5 (8.8)
Pain interference	60.4 (8.6)

Note. [§] % of non-missing
Abbreviations: BMI, body mass index. RDCI, rheumatic disease comorbidity index. TJC, tender joint count. SJC, swollen joint count.

Table 2. Mean change and 95% CI in PROMIS Pain Interference T-score from univariate and multivariable mixed effects models with 6-month time lag (sleep disturbance predicting pain interference 6 months later).

	Univariate (unadjusted)			Multivariable (adjusted[B])		
Predictor	Mean Change	95% CI	N (visits)	Mean Change	95% CI	N (visits)
Sleep disturbance, *T-score*[A]	0.74	0.47, 1.01	1,153	0.77	0.44, 1.09	844

Note. [A]Per 5-unit increase in PROMIS sleep disturbance T-score. [B]Model includes covariates: age, sex, BMI, education, income, current smoking status, comobidity index, SJC28, CRP, lagged treatment from previous visit (MTX, oral steroids, and advanced therapy).

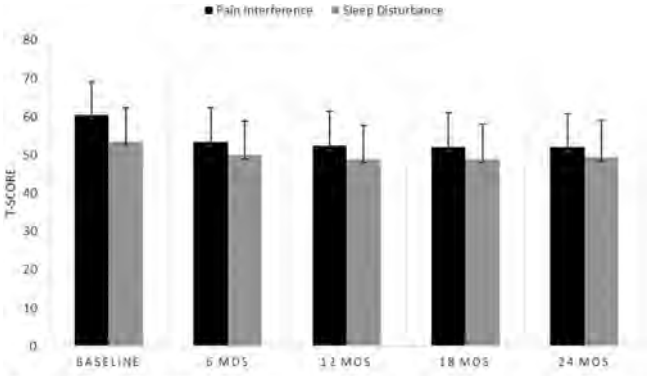

Figure 1. Mean PROMIS pain interference and sleep disturbance T-scores at 6-month intervals from baseline to 24 months (error bars indicate SD). Higher T-score indicates more of the concept being measured with a score of 50 (10) representing the general population mean (SD).

(8.5) at baseline (Figure 1). The unadjusted and adjusted linear mixed effects regression models revealed a significant association between sleep disturbance and pain interference scores, indicating that better sleep 6-months prior was associated with less pain interference at the following 6-month evaluation (Table 2).

Conclusion: In this cohort of patients with early RA, more disturbed sleep predicted greater pain interference 6 months later. These findings underscore the importance of addressing sleep disturbances as part of pain management strategies. Identifying and targeting problematic sleep disturbances early on may help improve long-term pain outcomes. Further work is needed to explore the underlying mechanisms and to investigate potential interventions targeting sleep to alleviate pain in RA.

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Abstract Number: 0824

Defining Poor Global Functioning and Health in Axial Spondyloarthritis, Using the EQ-5D-3L Questionnaire, When the ASAS-Health Index Is Not Available Is Feasible. an Analysis of 2651 Patients from the PERSPA Study

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SESSION INFORMATION

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Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes I: Assessment Tools

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: In axial Spondyloarthritis (axSpA) it is recommended to assess global functioning and health, a concept close to health-related quality of life (HR-QoL), using the ASAS Health Index (ASAS-HI), a patient-reported outcome measure [1]. Impairment status of poor global health (GH) has been defined as an ASAS-HI score of ≥ 12/17 [1]. However, the ASAS-HI is a recent outcome measure and is not always available in existing datasets. Our objective was to explore the link between ASAS-HI and a frequently used measure of GH and utility, the EuroQol-5D-3L (EQ-5D) and to explore the possibility of defining a cut-off value for EQ-5D, corresponding to the ASAS-HI cut-off of 12 points.

Methods: This was a reanalysis of a cross-sectional observational study: PERSPA, analyzing the subgroup of patients fulfilling ASAS criteria for axSpA, and with available EQ-5D and ASAS-HI scores [2]. The ASAS-HI is a specific composite measure for GH in axSpA, scored 0-17, with a validated cut-off of ≥ 12/17 for poor health status [1]. The EQ-5D is a generic score for utility and HR-QoL, with an index value between 1 (perfect health) and 0 or negative (health state equivalent to death or worse) [3] – here we reversed the scores to align with better health being lower scores (as for the ASAS-HI). Distributions of EQ-5D and ASAS-HI were visually compared with assessment of normality by Shapiro-Wilk test. The correlation between ASAS-HI and EQ-5D (Spearman) was computed. Patients were grouped into deciles based on EQ-5D and ASAS-HI scores, and weighted kappa was calculated. Then, to determine a cut-off for EQ-5D corresponding to an ASAS-HI ≥ 12, a ROC curve of EQ-5D according to ASAS-HI category was obtained; the Youden index for EQ-5D that maximizes sensitivity and specificity was then determined.

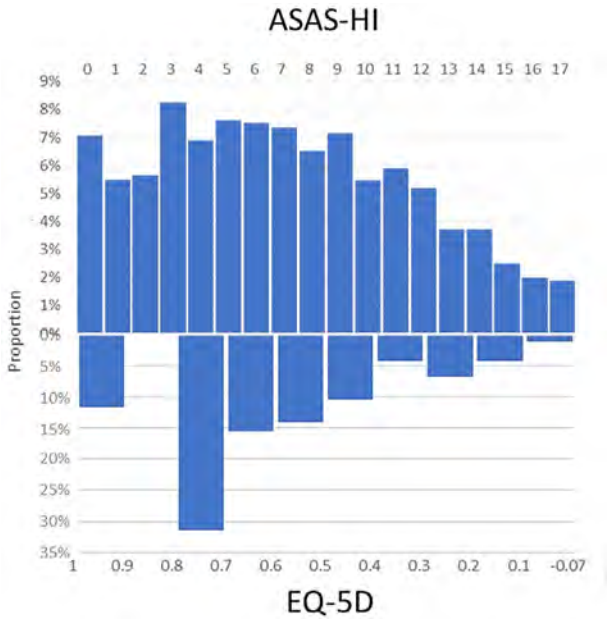

Figure 1 Distributions of EQ-5D and ASAS-HI in 2651 axSpA patients (The axis for EQ-5D is reversed to present best results on the left for both scores)

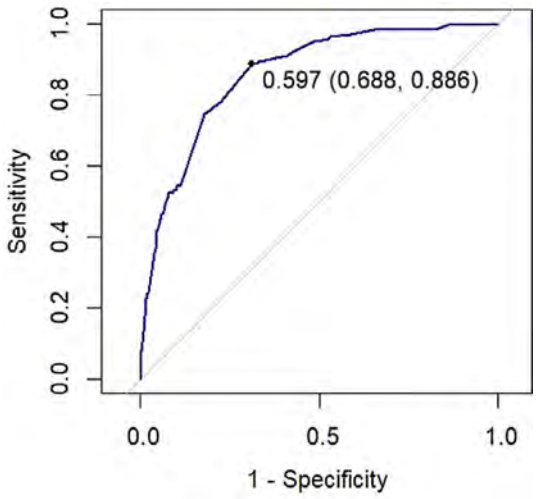

Figure 2: ROC curve of EQ-5D according to ASAS-HI category

Results: In 2651 patients (mean age 42.0 years, 66.5% men), GH was generally moderate to good using both the ASAS-HI and EQ-5D: mean ASAS-HI was 7.05 (SD 4.49) (median 7.00) and mean EQ-5D was 0.63 (SD 0.23) (median 0.65). The distributions appeared similar overall though neither distribution was normal (Shapiro-Wilk $p< 0.001$) **(Figure 1).** ASAS-HI had a high negative correlation with EQ-5D ($r = -0.71$, $p < 0.001$), however the agreement between deciles was moderate (weighted kappa = 0.51)**.** Using the published cutoff of 12 for ASAS-HI, we established that 448 (16.9%) patients had severe impairment of GH. The ROC curve showed a satisfactory link between the 2 scores: area under the curve was 0.86 (**-Figure 2).** The threshold of 0.597 for EQ-5D maximized both sensitivity (0.89) and specificity (0.69) against the ASAS-HI cut-off of 12.

Conclusion: The EQ-5D, a widely validated, widely-available generic score to assess utility, can be used to assess overall GH in axSpA, which is usually assessed through the ASAS-HI. In a large group of patients, we have shown that the two outcome measures are linked, with a high correlation but no full overlap. Furthermore, we propose an EQ-5D threshold corresponding to the published ASAS-HI threshold for severe impairment in GH. These results may be useful for comparing GH when only one of the outcome measures is available.

(1) Kiltz U, et al., Ann Rheum Dis 2018 ;77 :1311-7
(2) López-Medina C, et al., RMD Open 2021;7:e001728.
(3) https://euroqol.org

Disclosure: J. Drouet: None; **C. López Medina**: AbbVie, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 6, MSD, 6, Novartis, 2, 5, 6, UCB Pharma, 2, 5, 6; **A. Molto**: None; **B. Granger**: Bristol-Myers Squibb(BMS), 2; **B. Fautrel**: AbbVie, 2, BMS, 2, Chugai, 2, Fresenius Kabi, 2, Galapagos, 2, Lilly, 2, Medac, 2, Nordic Pharma, 2, Novartis, 2, Pfizer, 2, Sobi, 2, UCB, 2; **C. Gaujoux Viala**: AbbVie/Abbott, 2, Amgen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, Janssen, 2, Medac, 2, Merck-Serono, 2, Mylan, 2, Nordic Pharma, 2, Novartis, 2, Pfizer, 2, Roche-Chugai, 2, Sandoz, 2, Sanofi, 2, UCB Pharma, 2; **U. Kiltz**: AbbVie, 2, 5, 6, Amgen, 5, Biocad, 2, 6, Biogen, 5, Bristol-Myers Squibb(BMS), 2, 5, Chugai, 2, 6, Eli Lilly, 2, 6, Fresenius, 5, Gilead, 2, 5, GlaxoSmithKline (GSK), 5, Grünenthal, 2, 6, Hexal, 5, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, onkowiessen.de, 2, 5, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Viatris, 2, 5; **M. Dougados**: AbbVie, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Roche, 2, 5, UCB, 2, 5; **L. Gossec**: AbbVie, 2, 12, Personal fees, Amgen, 2, Biogen, 5, BMS, 12, Personal fees, Celltrion, 12, Personal fees, Eli Lilly, 5, 12, Personal fees, Galapagos, 12, Personal fees, Janssen, 12, Personal fees, MSD, 12, Personal fees, Novartis, 5, 12, Personal fees, Pfizer, 12, Personal fees, Sandoz, 5, 12, Personal fees, UCB Pharma, 5, 12, Personal fees.

Abstract Number: 0825

A Revised Outcome Measure for Dermatomyositis Clinical Trials: The Dermatomyositis Outcomes for Muscle and Skin (DMOMS)

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes I: Assessment Tools

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Current clinical trials in dermatomyositis (DM) are largely focused on muscle improvement, and use the Total Improvement Score (TIS) as the primary efficacy measure. The TIS consists of Patient Global Assessment (PtGA), Physician Global Assessment (PGA), Extramuscular Global Assessment (EMGA), Manual Muscle Testing (MMT), serum muscle enzymes, and Health Assessment Questionnaire (HAQ). TIS may contain redundant measures and lacks a skin-specific measure. Skin is a defining feature of DM that should be directly measured in the primary endpoint. This study evaluated a new composite outcome measure, the Dermatomyositis Outcomes for Muscle and Skin (DMOMS), which includes components of TIS and a skin-specific measure. DMOMS consists of improvement from baseline in MMT, PGA, and PtGA, all scored as in TIS with the exception of a 50% increase in weight for PtGA. It also includes the Cutaneous Dermatomyositis Disease Area and Severity Index-Activity (CDASI-A) score, weighted equally to the MMT score.

Methods: Data was collected from the lenabasum phase 3 trial in DM. All components of TIS and CDASI-A scores were collected at Baseline and at Week 52. Pearson's correlation on TIS components tested for redundancy ($r > 0.8$). Additionally, patients that had at least a 10-point improvement in MMT scores or 11-point improvement in CDASI-A scores at Week 52 compared to Baseline were considered to be responders. To assess efficacy of TIS and DMOMS scores in capturing skin and muscle disease improvement, a Student's t-test ($p < 0.05$) was used to compare mean percent improvement in scores for both responders (R) and non-responders (NR).

Results: Ninety-six DM patients were included in the analysis, with a majority of the patients being female (77%) and self-identifying as Caucasian (87%). Their mean (SD) age was 53 (11) years. Pearson's correlation on TIS components showed that PGA and EMGA were redundant measures (r=0.827).CDASI-A R (n = 36) vs NR had a mean improvement in TISof 47.2% vs 29.8% ($p < 0.001$) and a mean improvement in DMOMS of 63.6% vs 28.8% ($p < 0.001$). MMT R (n = 27) vs NR had a mean improvement in TIS of 49.4% vs 31.2% ($p < 0.001$) and a mean improvement in DMOMS of 65.7% vs 32.5% ($p < 0.001$).

Conclusion: Compared to TIS, DMOMS is a simpler composite score, with four versus six component measures, and does not contain the redundant measure of EMGA. DMOMS also contains a skin-specific measure scored equally to a muscle-specific measure and assigns greater weight to PtGAto reflect clinical benefit as assessed by patients. It provides about twice the treatment effect for R vs NR in both muscle and skin response, without any increase in score in NR. DMOMS is a more sensitive outcome measure to reflect improvement from baseline in DM and may be better suited to determine treatment effect in future DM clinical trials.

Disclosure: R. Pandya: None; **J. Dan**: None; **J. Kleitsch**: None; **D. Lim**: None; **B. White**: Corbus Pharmaceuticals, 12, Own stock; **V. Werth**: AbbVie, 2, Amgen, 2, 5, Anaptysbio, 2, Argenx, 5, AstraZeneca, 2, Biogen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Corbus, 5, CSL Behring, 2, 5, EMD Serono, 2, Galderma, 2, Genentech, 5, Gilead, 2, 5, GlaxoSmithKline, 2, Horizon Therapeutics, 5, Idera, 2, Incyte, 2, Janssen, 2, Kyowa Kirin, 2, Lilly, 2, MedImmune, 2, Medscape, 2, Merck, 2, Nektar, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Principia, 2, Regeneron, 5, Resolve, 2, 2, Rome Therapeutics, 2, 5, Sanofi, 2, Ventus, 5, Viela, 2, 5, Xencor, 2.

Abstract Number: 0826

Development of a Decision Aid for Clinical Trial Participation in Systemic Lupus Erythematosus

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SESSION INFORMATION
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Session Time: 4:00PM–5:30PM

Background/Purpose: Standard of care therapy for SLE relies heavily on broad-spectrum immune suppressants. Therapeutic drug development is critical to the approval of targeted therapies; however, patient recruitment in lupus clinical trials faces many challenges that include patient, provider, and community barriers, as well as clinical trial design constraints. Here we describe the development of a decision aid (DA) for participation in clinical trials, outlining the choice to continue with standard of care (SOC) vs. enroll in the clinical trial for the treatment of moderate to severe SLE disease activity or flares.

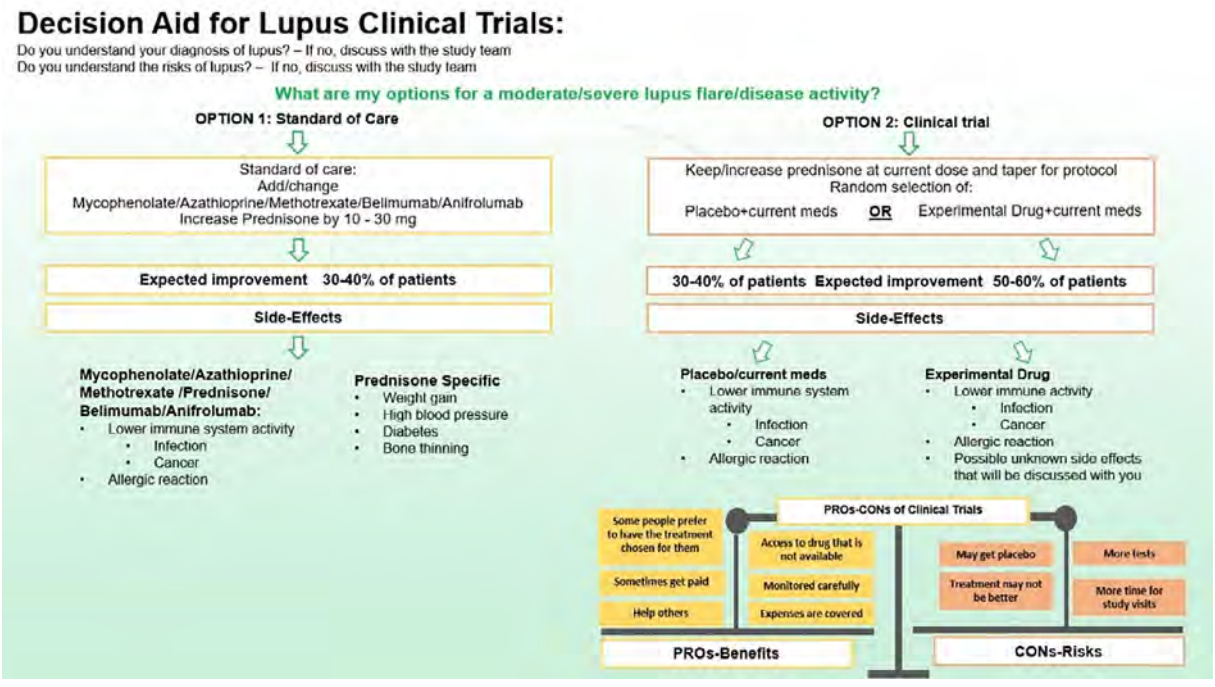

Figure 1. Decision Aid for Lupus Clinical Trials

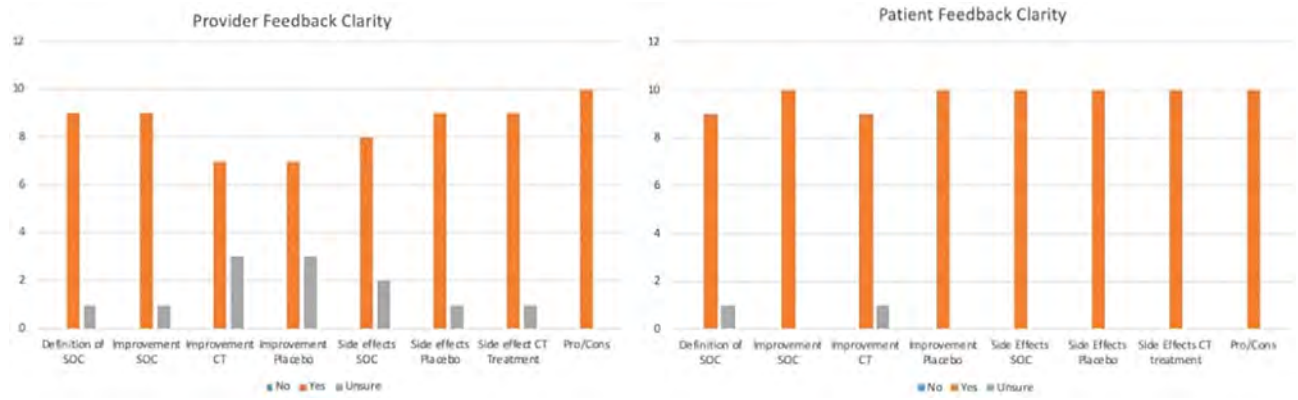

Figure 2. Decision Aid Feedback

Methods: The DA was developed using a collaborative, iterative process. The development working group included lupus clinical trialists, clinicians, methodologists, and patients. The initial draft based on the International Patient Decision Aid Standards (IPDAS) guidelines was evaluated and refined in semi-structured focused interviews with 10 lupus providers and 10 patients and working version of the decision aid was finalized, see Figure 1. Patients and providers were asked if the components of the DA, including definitions of treatments, expected improvement were clear (yes, no, unsure) and helpful (on a scale of 0-5). Interviews were conducted until thematic saturation was achieved. Responses on usefulness were accumulated, and mean usefulness scores were calculated.

Results: The 10 providers (9 physicians and one advanced practice provider) that participated in the focus group were well versed in the care of patients with lupus and had a mean of 8.1 years of practice. All 10 patients met the 2019 ACR/EULAR criteria for SLE and had been involved in clinical trials, clinical research, and advocacy work in the past. Their mean disease duration was 9 years. Findings of the semi structured interviews are summarized in Figure 2: 90% of providers and patients reported that the definition of SOC treatment was accurate. Additionally, the expected improvement for SOC (90% of providers, 100% of patients), clinical trial drug (70%, 90%), and placebo were clear (70%,100%). Side effects of SOC (80%,100%), placebo (90%, 100%), and clinical trial drug treatment (90%,100%) were also noted to be clear. 100% of providers and patients thought that the figure outlining pros/cons of participating in clinical trials was appropriate. The overall mean usefulness scores were 4.45/5 for providers and 4.72/5 for patients.

Conclusion: We developed a lupus clinical trial DA for patient-provider shared decision-making outlining the choice to continue with SOC vs. enroll in a clinical trial for the treatment of moderate to severe SLE as required by the majority of SLE clinical trials. More data on the usability and performance of the DA is needed to fully understand its role in clinical trial participation.

Disclosure: L. Khalili: None; **R. Kukafka**: None; **L. Geraldino-Pardilla**: None; **N. Schmidt**: None; **S. Inzerillo**: None; **J. Weiner**: None; **W. Tang**: None; **A. Askanase**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb, 2, Celgene, 2, Eli Lilly, 2, Genentech, 2, GSK, 2, Idorsia, 2, Janssen, 2, Mallinckrodt, 2, Pfizer, 2, UCB Pharma, 2.

Abstract Number: 0827

Development and Initial Validation of a Brief Measure of Uncertainty in Rheumatic Disease

Caleb Bolden[1], Claire Cook[1], Lucy Finkelstein-Fox[1], Xiaoqing Fu[1], Flavia Castelino[1], Hyon K. Choi[2], Cory Perugino[1], John Stone[3], Elyse Park[1], **Zachary Wallace**[4] and Daniel Hall[1], [1]Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital and Harvard Medical School, Lexington, MA, [3]Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Concord, MA, [4]Massachusetts General Hospital, Newton, MA

SESSION INFORMATION

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Session Type: Abstract Session

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Background/Purpose: Patients with systemic autoimmune rheumatic disease (SARD) are often tasked with monitoring ambiguous and unpredictable physical symptoms on their own. Higher levels of uncertainty in rheumatic disease (URD) are associated with increased anxiety, depression, and sickness impact (J Rheum 2022;49:1059). Existing measures to evaluate URD are adapted from longer instruments (e.g., 22 items), limiting the ability to implement routine assessment in clinical practice. We aimed to develop a brief measure of URD and perform an initial validation of this brief measure.

Methods: Patients with antineutrophil cytoplasmic antibody-associated vasculitis (AAV), IgG4-related disease (IgG4-RD), and systemic sclerosis (SSc) seen at a rheumatology clinic at a large academic hospital completed a cross-sectional survey assessing URD (rheumatology-adapted version of the Mishel Uncertainty in Illness Scale, Survivor Version; MUIS-S), anxiety (GAD-7), depression (PHQ-8), and sickness impact (SIP). First, we performed an exploratory factor analysis of the previously adapted rheumatology-specific 22-item MUIS-S to identify the amount of variance loaded across each item following the established convention of 0.6 (stopping rule of 75% variance explained per factor) to select the final items. Second, we tested the brief URD measure for internal consistency (Cronbach's alpha) and convergent validity. Third, we performed a series of hierarchal regression models assessing variance explained, controlling for age and sex.

Table 1: Demographics of Survey Respondents

	Total	AAV	IgG4-RD	SSc
N %	132	41 (31%)	61 (46%)	30 (23%)
Age (Mean, SD)	64.7, 11.3	64.7, 10.3	64.5, 12.0	64.9, 11.8
Race/Ethnicity n (%)				
American Indian or Alaskan Native	1 (0.8)	0(0.0)	1 (1.6)	0 (0.0)
Asian	13 (9.8)	2 (4.9)	9 (14.8)	2 (6.7)
Black or African American	1 (0.8)	0 (0.0)	1 (1.6)	0(0.0)
Hispanic or Latino	6 (4.5)	1 (2.4)	3 (4.9)	2 (6.7)
Native Hawaiian or Other Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
White	110 (83.3)	38 (92.7)	46 (75.4)	26 (86.7)
Other	4 (3.0)	1 (2.4)	3 (4.9)	0 (0.0)
Sex n (%)				
Female	69 (52.3)	23 (56.1)	17 (27.9)	29 (96.7)
Relationship status n (%)				
Single, never married	12 (9.1)	7 (17.1)	2 (3.3)	3 (10.0)
Married/Living with partner	101 (76.5)	28 (68.3)	54 (88.5)	19 (63.3)
Widowed/Divorced	16 (12.1)	5 (12.2)	4 (6.6)	7 (23.3)
Other	2 (1.5)	1 (2.4)	0 (0.0)	1 (3.3)
Comorbidities n (%)				
Cardiovascular disease (i.e. heart disease, stroke, high blood pressure, high cholesterol)	59 (44.7)	16 (39.0)	27 (44.3)	16 (53.3)
Diabetes	15 (11.4)	3 (7.3)	11 (18.0)	1 (3.3)
Kidney disease	17 (12.9)	4 (9.8)	11 (18.0)	2 (6.7)
Liver disease	3 (2.3)	0 (0.0)	3 (4.9)	0 (0.0)
Lung disease (e.g., asthma, COPD, sleep apnea)	43 (32.6)	20 (48.8)	16 (26.2)	7 (23.3)
Overweight/obesity	26 (19.7)	9 (22.0)	12 (19.7)	5 (16.7)
Underweight	2 (1.5)	0 (0.0)	0 (0.0)	2 (6.7)
Other	31 (23.5)	11 (26.8)	13 (21.3)	7 (23.3)
Self-Reported Disease activity n (%)				
In remission	56 (42.4)	21 (51.2)	32 (52.5)	3 (10.0)
Not in remission	42 (31.8)	13 (31.7)	13 (21.3)	16 (53.3)
I do not know	34 (25.8)	7 (17.1)	16 (26.2)	11 (36.7)

Results: We included 132 patients: 41 (31%) with AAV, 61(46%) with IgG4-RD, and 30 (23%) with SSc (**Table 1**). The mean age was 64.7 years, the majority were White (83%) and female (52%). The exploratory factor analysis of the 22-item MUIS-S identified 9 items to retain (**Table 2**). In further factor analysis of these 9 items, 7 were retained and captured 2 factors: ambiguity and unpredictability (**Table 3**). There was high internal consistency for the overall composite 7-item URD measure (alpha=.85) and its subscales: ambiguity (alpha=.79) and unpredictability (alpha=.81). Convergent validity was found between the 7-item measure with anxiety (r=0.417, p< .001), depression (r=0.473, p< .001), and sickness impact (r=0.335, p< .001). URD, as measured using the 7-item measure, explained a significant amount of variance: 14.2% in anxiety (r^2 = 0.142, F(2,113) = 11.25, p< .001), 23.2% in depression (r^2 = 0.232, F(2,113) = 19.685, p< .001), and 14.8% in sickness impact (r^2 = 0.148, F(2,113) = 10.177, p< .001) after controlling for age and sex.

Conclusion: We developed a brief, 7-item measure of URD with high internal consistency and convergent validity with measures of anxiety, depression, and sickness impact. Given the burden of anxiety, depression, and other mental health comorbidities in these conditions, this instrument can be useful for tailoring screening and referral pathways for healthcare services and consultation visits (e.g., specialists, supportive care). This measure may also be useful as part of research studies developing interventions aimed at improving resiliency in the face of URD. Additional validation is needed.

Table 2: Factor Analysis of the Original 22 Item Rheumatology Adapted MUIS

	Items	Factors				
		1	2	3	4	5
1	The purpose of each rheumatology treatment is clear to me	0.03	0.026	-0.026	0.504	-0.033
2	When I have pain, I know what this means about my rheumatology condition	0.09	0.187	-0.068	0.583	0.117
3	**I understand everything explained to me by my rheumatology providers**	0.25	-0.046	0.206	**0.601**	-0.1
4	I can predict how long my rheumatology condition will last	0.063	0.057	0.102	0.372	0.114
5	I usually know if I am going to have a good or bad day	-0.08	-0.007	0.104	0.359	0.217
6	I do not know what is wrong with me	0.478	0.305	0.03	-0.001	0.214
7	**I have a lot of questions without answers**	**0.621**	0.321	0.212	0.18	0.227
8	I am unsure if my rheumatology condition is getting better or worse	0.487	0.313	0.065	0.26	0.583
9	It is unclear how bad my symptoms will be	0.348	0.232	0.243	0.229	0.538
10	**The explanations that my rheumatology providers give about my condition seem unclear to me**	**0.734**	0.331	0.131	0.092	0.121
11	I do not know when to expect things like lab tests, biopsies, x-rays, or other tests will be done to me	0.593	0.046	0.385	0.037	0.176
12	**The symptoms of my rheumatology condition continue to change unpredictably**	0.341	0.215	**0.71**	0.005	0.2
13	**My rheumatology providers say things to me that could mean many things**	**0.601**	0.171	0.352	0.169	-0.017
14	My rheumatology treatment is too complicated to figure out	0.403	0.366	0.285	0.208	0.199
15	It is difficult to know if the rheumatology treatments I am getting are helping	0.253	0.572	0.18	0.088	0.286
16	**I see so many different types of providers; it is unclear who is responsible for what**	0.335	**0.65**	0.118	0.09	-0.082
17	**Because of the unpredictability of my rheumatology condition, I cannot plan for the future**	0.189	**0.633**	0.357	0.061	0.164
18	**The course of my rheumatology condition keeps changing. I have good and bad days.**	0.215	0.348	**0.67**	0.061	0.067
19	It is unclear to me how I will manage my rheumatology condition after I leave appointments with my rheumatology providers	0.596	0.453	0.351	0.085	-0.013
20	I have been given many differing opinions about what is wrong with me	0.233	0.414	0.231	0.047	0.218
21	It is not clear what is going to happen to me in the future because of my rheumatology condition	0.157	0.51	0.23	0.097	0.45
22	**The results of my rheumatology tests are always changing**	0.173	0.199	**0.636**	0.211	0.088

Table 3: Factor Analysis of the 7 Item MUIS Factor Analysis

	Factors	
	Ambiguity	Unpredictability
The symptoms of my rheumatology condition continue to change unpredictably	0.35	**0.727**
I see so many different types of providers; it is unclear who is responsible for what	**0.484**	0.31
The course of my rheumatology condition keeps changing. I have good and bad days.	0.27	**0.784**
I have a lot of questions without answers	**0.778**	0.266
The results of my rheumatology tests are always changing	0.232	**0.645**
The explanations that my rheumatology providers give about my condition seem unclear to me	**0.804**	0.208
My rheumatology providers say things to me that could mean many things	**0.559**	0.366

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Abstract Number: 0828

Item Reduction and Validation of the Cutaneous Lupus Erythematosus Quality of Life Questionnaire

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SESSION INFORMATION
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Session Type: Abstract Session
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Background/Purpose: Cutaneous lupus erythematosus (CLE) symptoms often require patient-reported outcome measures (PROMs) to monitor disease progression. The CLE quality of life (CLEQoL) instrument was devised as a disease-specific PROM. However, its 37-item length can be time-consuming. Creating a brief version could reduce respondent burden and increase clinical utility. Thus, we sought to develop a brief version of the CLEQoL, while maintaining clinical relevance and psychometric properties including internal consistency, structural and convergent validity.

Methods: This retrospective cohort study analyzed data from CLE patients recruited in outpatient dermatology clinics at University of Texas Southwestern Medical Center and Parkland Health from June 2016 to November 2022. Patients completed the CLEQoL, Short-Form-36 (SF-36), and a visual analogue scale (VAS). Item reduction was conducted by evaluating each item's response distribution and local dependency with other items. Internal consistency of the reduced scale was

Table 1. Patient Characteristics

Characteristics	N = 185
Age (Mean ± SD)	49.14 ± 16.25
Sex	
Female	153 (82.7%)
Race and Ethnicity	
Black	90 (48.6%)
White, Non-Hispanic	55 (29.7%)
White, Hispanic	25 (13.5%)
Asian	7 (3.8%)
Mixed Race, Non-Hispanic	5 (2.7%)
Mixed Race, Hispanic	2 (1.1%)
Native American/Alaskan Native	1 (0.5%)
Age at CLE Diagnoses (Mean ± SD)	41.09 ± 15.71
Age at SLE Diagnosis (Mean ± SD)	33.56 ± 12.51
SLE	82 (44%)
Predominant CLE Subtype	
Acute CLE	7 (3.8%)
Subacute CLE	32 (17.3%)
Chronic CLE	146 (78.9%)
DLE	122 (65.9%)
LE Panniculitis	4 (2.2%)
LE Tumidus	20 (10.8%)
CLASI Activity Score Mean ± SD	7.02 ± 7.7
CLASI Damage Score Mean ± SD	7.52 ± 7.19

Abbreviations: CLASI – cutaneous lupus erythematosus disease area and severity index; CLE – cutaneous lupus erythematosus; DLE – discoid lupus erythematosus; SLE – systemic lupus erythematosus;

Table 2. Factor Eigenvalues and Item Loading Values after a Varimax Rotation

Items		Factor 1	Factor 2	Factor 3
Factor 1: Emotions and Social Interactions (% of variance = 49.21, eigenvalue = 11.81)				
i.	I worry that my skin condition may be serious	**0.529**	0.498	0.176
ii.	My skin condition effects my social life	**0.727**	0.357	0.235
iii.	My skin condition makes me feel depressed	**0.796**	0.339	0.225
iv.	I am ashamed of my skin condition	**0.788**	0.245	0.177
v.	I worry my skin condition may get worse	**0.682**	0.242	0.309
vi.	I am angry about my skin condition	**0.773**	0.237	0.129
vii.	My skin condition affects my interactions with others	**0.77**	0.217	0.198
viii.	I am frustrated by my skin condition	**0.732**	0.321	0.256
ix.	I am annoyed by my skin condition	**0.666**	0.164	0.397
x.	When talking to someone else, I worry about what they may be thinking of me	**0.72**	0.175	0.196
Factor 2: Symptoms and Functioning (% of variance = 7.61, eigenvalue = 1.83)				
xi.	My skin hurts	0.126	**0.856**	0.104
xii.	My skin affects how well I sleep	0.141	**0.815**	0.215
xiii.	My skin condition makes it hard to work or do hobbies	0.406	**0.698**	0.164
xiv.	My skin condition burns or stings	0.325	**0.76**	0.196
xv.	I worry about getting scars from my skin condition	0.452	**0.474**	0.281
xvi.	My skin itches	0.469	**0.524**	0.215
xvii.	My skin is irritated	0.331	**0.706**	0.139
xviii.	My skin is sensitive	0.263	**0.561**	0.359
Factor 3: Lupus Specific (% of variance = 6.97, eigenvalue = 1.67)				
xix.	I worry about going outside because the sun might flare my disease	0.188	0.23	**0.811**
xx.	I am worried about hair loss	0.339	0.058	**0.593**
xxi.	My skin disease prevents me from doing outdoor activities	0.349	0.294	**0.669**
xxii.	My skin condition affects the clothes I wear	0.207	0.314	**0.576**
xxiii.	My skin condition affects my grooming practices	0.455	0.215	**0.485**
xxiv.	My skin condition affects my sun protection habits during recreation	0.094	0.103	**0.843**

assessed using Cronbach's alpha. Structural validity was examined via exploratory factor analysis with principal component analysis and varimax rotation. Convergent validity was determined via Spearman correlations between CLEQoL, SF-36, VAS, and Cutaneous Lupus Erythematosus Disease Area and Severity (CLASI) scores. Data were analyzed using SPSS version 29.0 and significance was set at $p< 0.05$.

Results: 185 patients completed the CLEQoL (Table 1). Thirteen items were removed, resulting in a 24-item scale (Figure 1). Internal consistency was satisfactory (Cronbach's alpha: 0.842-0.939). Exploratory factor analysis identified three domains (each with and eigenvalue greater than 1): *"Emotions and Social Interactions," "Symptoms and Functioning," and "Lupus Specific Questions"*– each factor had an eigenvalue greater than 1 and contributed more than 5% unique variability (Table 2). The brief CLEQoL demonstrated convergent validity with relevant domains of the SF-36 (*r* range: -0.243 to -0.172) and VAS (0.348 – 0.671). However, it did not demonstrate convergent validity with CLASI activity or damage scores. The limited convergent validity between the scale and CLASI scores may be attributed to the small range of observed CLASI activity scores (median 5, IQR 1.25-10).

Conclusion: The brief 24-item CLEQoL was found to be a valid and reliable PROM for assessing CLE patients' quality of life, and establishing its psychometric properties is crucial for its use in outpatient clinics and clinical trials. The nonconvergence between the brief CLEQoL and CLASI can be attributed to their measurement of different constructs. The brief CLEQoL captures subjective patient experiences such as social functioning, and emotional well-being. In contrast, the CLASI relies on clinical observations to assess disease severity. Integrating information from both measures allows for a more comprehensive and holistic assessment of the patient's condition. Future plans involve prospectively administering the brief CLEQoL to a larger and more heterogeneous CLE patient cohort to further evaluate its psychometric properties.

Brief CLE-specific quality of life measure (CLEQoL)

These questions concern your feelings over the past 4 weeks about the skin condition that has bothered you the most. **Check the answer that comes closest to the way you have been feeling.**	**NEVER**	**RARELY**	**SOMETIMES**	**OFTEN**	**ALL THE TIME**
1. My skin hurts	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
2. My skin affects how well I sleep	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
3. I worry that my skin condition may be serious	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
4. My skin condition makes it hard to work or do hobbies	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
5. My skin condition effects my social life	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
6. My skin condition makes me feel depressed	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
7. My skin condition burns or stings	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
8. I worry about getting scars from my skin condition	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
9. My skin itches	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
10. I am ashamed of my skin condition	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
11. I worry my skin condition may get worse	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
12. I am angry about my skin condition	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
13. My skin is irritated	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
14. I am frustrated by my skin condition	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
15. My skin is sensitive	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
16. I am annoyed by my skin condition	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
17. My skin condition affects my interactions with others	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
18. I worry about going outside because the sun might flare my disease	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
19. I am worried about hair loss	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
20. My skin disease prevents me from doing outdoor activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
21. When talking to someone else, I worry about what they may be thinking of me	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
22. My skin condition affects the clothes I wear	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
23. My skin condition affects my grooming practices	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
24. My skin condition affects my sun protection habits during recreation	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

The final brief CLE-Qol questionnaire. The original CLEQoL was reduced from 37 items to a single page, 24-item scale.

Disclosure: M. Adams: None; **L. Hynan**: None; **M. Ogunsanya**: MAPI Research Trust, 2, 10; **B. Chong**: Biogen Inc, 1, 2, 12, Site PI for Clinical Trial, Bristol-Myers Squibb(BMS), 2, EMD Serono, 2, Horizon Therapeutics, 2.

Abstract Number: 0829

Decreased History of Breastfeeding During Infancy in Juvenile Spondyloarthritis: A Case-Control Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Pediatric Rheumatology – Clinical I: JIA
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: The pathogenesis of juvenile spondyloarthritis (JSpA) is multifactorial, and includes a genetic predisposition of the HLA-B27 allele, and environmental exposures such as the microbiome. Breastfeeding during infancy is the most robust source of microbiome colonization and differs markedly from the microbiota offered through formula feeding. Early breastfeeding practices are associated with the development of various autoimmune conditions, though this was yet to be investigated in JSpA. This study aims to evaluate 1) differences in parent-reported infant feeding type and duration between children with JSpA and matched controls and 2) if an association exists between early nutrition practices and JSpA disease severity at presentation.

Methods: This retrospective case-control study included 195 children with JSpA and 195 age- and sex-matched healthy controls. Demographics and early nutrition practices of cases and controls were parent-reported via electronic questionnaires. The type and duration of feeding was limited to the first 6 months of life and included the options of breastmilk only, breast and formula, formula only, breast and cereal or other food, or "other". Between-group comparisons were made using the Pearson's χ^2 or Fisher's exact test. JSpA disease activity was quantified by the modified JSpA disease activity-6 (JSpADA-6) index, a validated tool consisting of patient- and physician-reported measures (score range 0-6). Components of the JSpADA-6 index were collected as part of a JSpA registry. Linear regression was used to assess the association of JSpA disease activity at the index visit and infant feeding type and duration. Index visit was defined as the first visit in the JSpA registry that occurred within 6 months of diagnosis or prior to the initiation of disease-modifying antirheumatic drugs or biologic therapy.

Table 1. Characteristics of children with JSpA versus healthy controls

Characteristic	All	Controls	JSpA	p-value
No. of subjects	390	195	195	
Age, mean ± SD	13.03 ± 0.24	13.03 ± 0.24	13.03 ± 0.24	
Female, n (%)	186 (47.69%)	93 (47.69%)	93 (47.69%)	
Race, n (%)				0.54
African American	25 (6.41%)	11 (5.64%)	14 (7.18%)	
American Indian/Alaskan Native	1 (0.26%)	1 (0.51%)	0	
Asian American	18 (4.62%)	8 (4.10%)	10 (5.13%)	
Multiracial	26 (6.67%)	10 (5.13%)	16 (8.21%)	
Native Hawaiian or Other Pacific Islander	1 (0.26%)	1 (0.51%)	0	
White	306 (78.46%)	159 (81.54%)	147 (75.38%)	
Other/Unknown	13 (3.33%)	5 (2.56%)	8 (4.10%)	
Form of delivery, n (%)				0.51
Vaginal delivery	268 (68.72%)	131 (67.18%)	137 (70.26%)	
Cesarean delivery	122 (31.28%)	64 (32.82%)	58 (29.74%)	

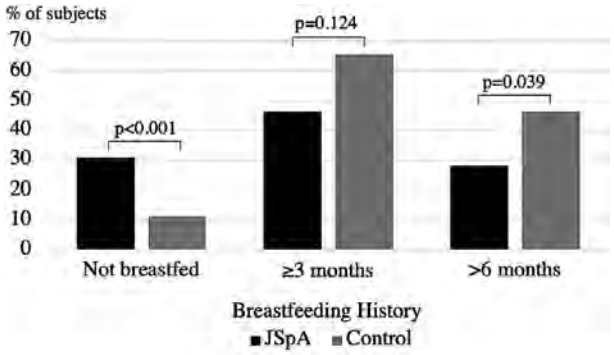

Figure 1. For the 173 controls and 135 patients with JSpA who were exposed to breastfeeding, the % that were breastfed exclusively for ≥3 or >6 months are shown above. The ≥3 and >6-month groups are not mutually exclusive.

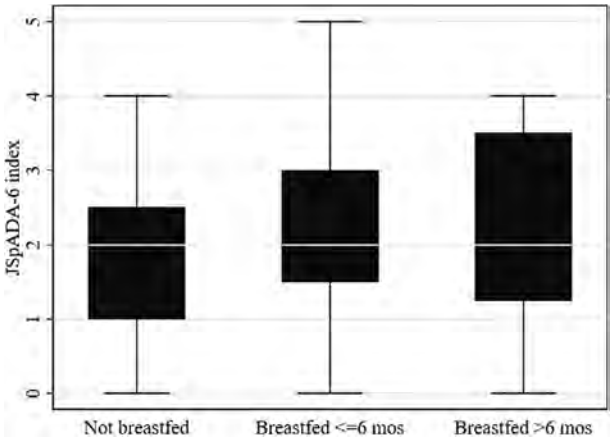

Figure 2. The JSpADA-6 index and parent-reported infant feeding type was available for 103 JSpA patients at the index registry visit, a median of 0.3 months after diagnosis and prior to the initiation of disease-modifying antirheumatic drugs or biologic therapy (IQR 0-10.5). The above groups are mutually exclusive.

Results: For each group of 195 controls and 195 cases, the mean age was 13.03 ± 0.24 years and 47.69% were female (Table 1). Of the healthy controls and children with JSpA, 88.72% and 69.23% were exposed to breastfeeding of any duration, respectively (p< 0.001).The frequency of exclusive breastfeeding for longer than 6 months was significantly lower in children with JSpA than in healthy controls (28.36% of children with JSpA vs 46.47% of healthy controls; p=0.039; figure 1). There was no significant difference in form of delivery, vaginal or cesarean delivery, between children with JSpA and healthy controls. The JSpADA-6 index and parent-reported breastfeeding duration was available for 103 JSpA patients at the index registry visit, a median of 0.3 months after diagnosis (IQR 0-9.4). The median JSpADA-6 index was 2 (IQR: 1.5-3; range: 0-5) and was not significantly different in children with a history of no breastfeeding and exclusive breastfeeding for ≤6 months (β=0.13, 95% CI: -0.39-0.66) or exclusive breastfeeding for >6 months (β=0.21, 95% CI: -0.41-0.84).

Conclusion: This study suggests a potential association of early breastfeeding practices and the occurrence of JSpA. A shorter duration of exclusive breastfeeding or absence of breastfeeding was higher in cases with JSpA than controls. Breastfeeding for >6 months was not associated with JSpA disease severity at diagnosis.

Disclosure: K. Baggett: None; **T. Brandon**: None; **R. Xiao**: None; **P. Weiss**: Eli Lilly, 2, Novartis, 2, Pfizer, 2.

Abstract Number: 0830

The Upregulation of MAP Kinase Pathway Genes Is Associated with Poor Treatment Response to Tofacitinib in Polyarticular Course Juvenile Idiopathic Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Pediatric Rheumatology – Clinical I: JIA

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Despite significant progress in understanding the pathophysiology of Juvenile Idiopathic Arthritis (JIA), the availability of tools to accurately predict treatment response remains limited. Our objective was to identify gene expression patterns that may predict treatment response to tofacitnib in patients with polyarticular course JIA.

Methods: Whole blood samples were collected from JIA patients using PAXgene tubes prior to starting tofacitinib treatment as part of the clinical trial NCT02592434. Patients were categorized as treatment responders (TR) if they achieved a JIA-ACR70 response or higher at week 18, while those with a JIA-ACR response of 30 or less were considered poor responders (PR). Bulk RNA sequencing was performed using Illumina Nova-seq, generating 50 million reads per sample. Gene expression levels were measured at baseline. Differential gene expression analyses were conducted using the dream method from variance Partition. Gene ontology overrepresentation analyses were subsequently performed using the dseqr adaptation of the goana function from the limma R package.

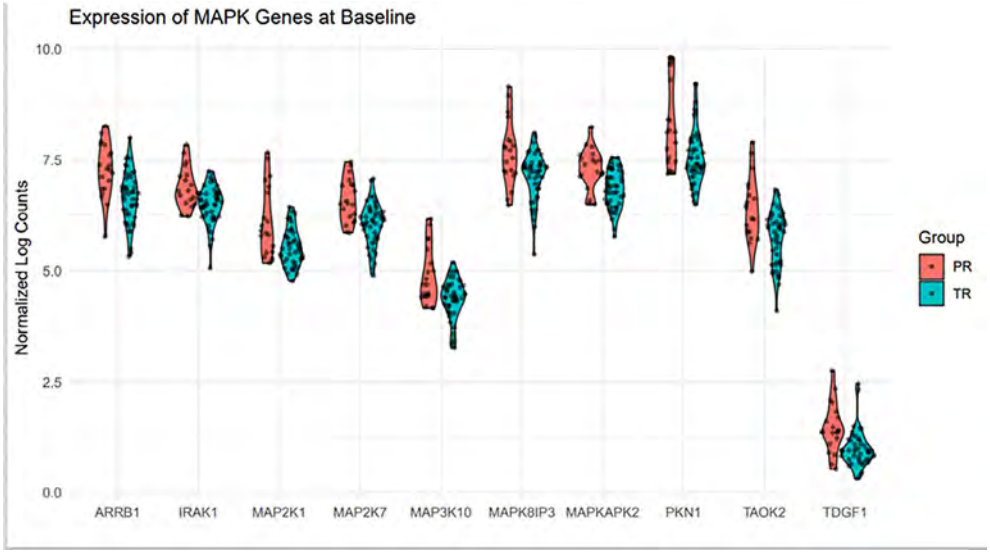

Figure 1.a: Expression of MAPK genes at baseline in treatment responders versus poor responders after covariate modeling

Results: 663 of 31,799 genes assayed were identified as differentially expressed in PR as compared to TR (FDR< 0.05) from samples acquired prior to treatment initiation. Gene ontology analysis revealed a significant upregulation of genes associated with MAP kinase pathway activation in PR (p=9.40E-05) (Figure 1.a &1.b). Other ontologies that were upregulated in PR included myeloid stem cell development (p=8.13E-05), activation of GTPase activity (p=0.00015), and organelle transport along microtubule (p= 0.00021) (Table 1).

Conclusion: Assessment of MAP kinase pathway gene expression prior to treatment may aid in identification of polyarticular course JIA patients that could exhibit poor response to tofacitinib. If confirmed, this finding could be used to personalize treatment of JIA patients for whom tofacitinib treatment is considered.

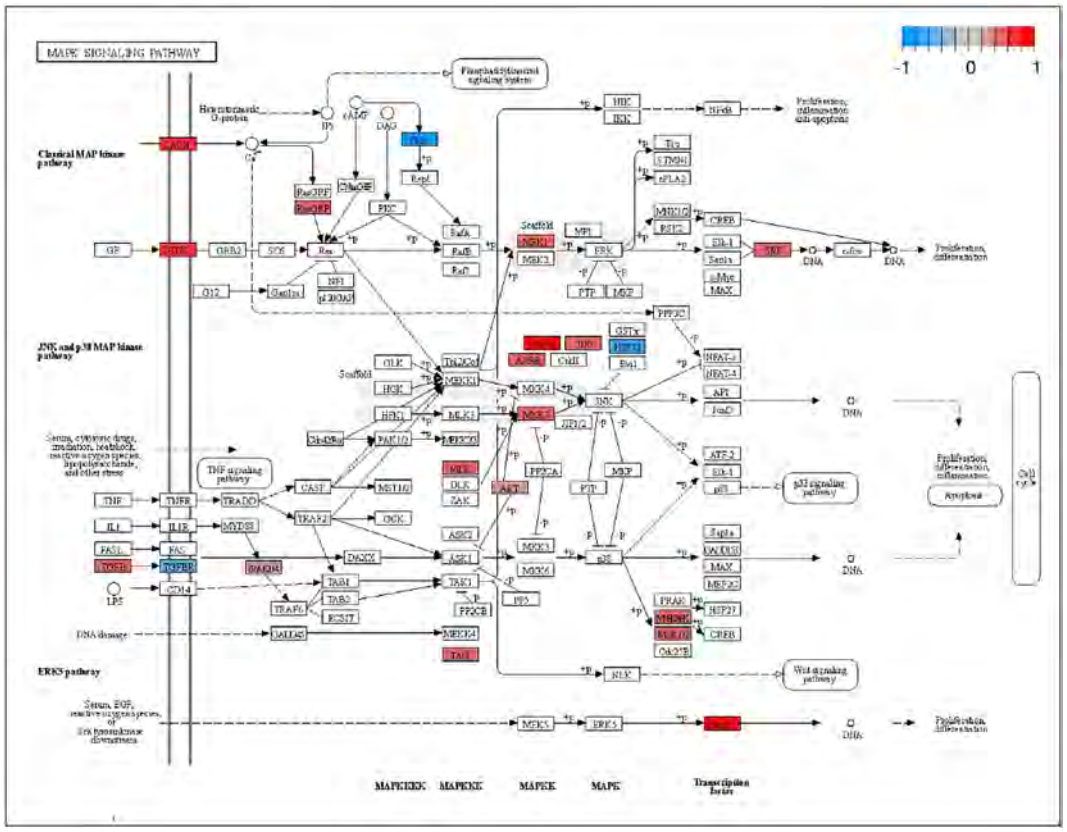

Figure 1.b: Visualization of the MAPK pathway using the KEGG database

	Term	On	N	U	Do	P.Value	FDR	Genes
GO:0061	myeloid cell development	BP	72	7	1	8.13E-05	0.00	ERCC2, SRF, SH2B3, TRIM58, ZBTB7A, PAFAH1B1, FAM20C
GO:0048	* -- erythrocyte development	BP	35	5	0	0.000139	0.00	ERCC2, SRF, SH2B3, TRIM58, ZBTB7A
GO:0000	activation of MAPK activity	BP	15	10	4	9.40E-05	0.00	ARRB1, IRAK1, MAP3K10, PKN1, MAP2K1, MAP2K7, TDGF1,
GO:0090	activation of GTPase activity	BP	10	8	1	0.000154	0.00	ABR, AKT2, RANGAP1, SCRIB, ARHGAP45, TBC1D10B, EVI5L,
GO:0072	organelle transport along microtubule	BP	84	7	0	0.000215	0.00	CLN3, PAFAH1B1, STK11, AP3D1, TRAK1, SUN2, TRIM58
GO:0010	* -- transport along microtubule	BP	16	9	3	0.000549	0.01	CLN3, PAFAH1B1, STK11, AP3D1, TRAK1, MAPK8IP3, SUN2,
GO:0047	* -- vesicle transport along microtubule	BP	49	5	0	0.000693	0.01	CLN3, PAFAH1B1, STK11, AP3D1, TRAK1
GO:0099	microtubule-based transport	BP	18	10	4	0.000444	0.01	CLN3, PAFAH1B1, STK11, AP3D1, TRAK1, MAPK8IP3, SUN2,
GO:0030	* -- cytoskeleton-dependent intracellular transport	BP	19	10	5	0.000665	0.01	CLN3, PAFAH1B1, STK11, AP3D1, TRAK1, MAPK8IP3, SUN2,
GO:0001	regulation of cytokine-mediated signaling pathway	BP	16	9	1	0.000549	0.01	IRAK1, IRF3, PAFAH1B1, ADIPOQ, IKBKE, SH2B3, SPPL2B, MAVS,
GO:0060	* -- regulation of response to cytokine stimulus	BP	17	9	2	0.000884	0.01	IRAK1, IRF3, PAFAH1B1, ADIPOQ, IKBKE, SH2B3, SPPL2B, MAVS,
GO:0010	positive regulation of cell morphogenesis involved in	BP	15	9	2	0.000457	0.01	ARHGDIA, FLNA, P4HB, PAFAH1B1, MAP2K1, SRF, STK11,
GO:0043	receptor metabolic process	BP	19	10	1	0.000545	0.01	GRK2, ARRB1, AP2S1, CLTA, TGFB1, ADIPOQ, HDAC6, SCRIB,
GO:0046	protein autophosphorylation	BP	23	11	1	0.000703	0.01	CSF1R, IRAK1, MAP3K10, STK11, MAPKAPK2, TAOK2, ADIPOQ,
GO:0034	plasma lipoprotein particle clearance	BP	52	5	0	0.000911	0.01	APOC2, AP2S1, CLTA, ADIPOQ, APOBR
GO:0097	* -- regulation of plasma lipoprotein particle levels	BP	87	6	1	0.001647	0.02	APOC2, AP2S1, CLTA, ADIPOQ, APOBR, P4HB
GO:0007	lysosomal transport	BP	11	7	2	0.001102	0.01	CLN3, GAK, AP3D1, TRAK1, ATP13A2, NAGPA, CACNG8
GO:0007	* -- vacuolar transport	BP	14	8	3	0.001492	0.02	CLN3, GAK, AP3D1, TRAK1, ATP13A2, NAGPA, CACNG8,

Disclosure: E. Eloseily: None; **A. Pickering**: None; **S. Dhakal**: None; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb (BMS), 2, 5, Celgene, 2, Eli Lilly, 2, 5, EMD Serono, 2, F-Hoffman La Roche, 2, 5, GlaxoSmithKlein (GSK), 2, 5, 6, Horizon, 2, 2, Janssen, 5, Merck, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6; **S. Thornton**: None; **A. Grom**: Novartis, 2, 5, Sobi, 2, 5.

Abstract Number: 0831

Two- and Three-Year Outcomes from the Childhood Arthritis and Rheumatology Research Alliance Start Time Optimization of Biologic Therapy in Polyarticular JIA (STOP-JIA) Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Pediatric Rheumatology – Clinical I: JIA

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: The STOP-JIA study was designed to compare the effectiveness of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Consensus Treatment Plans (CTPs) for untreated polyarticular JIA (pJIA) in achieving ACR clinically inactive disease (CID) at 1 year. The CTPs differ in the timing of initiation of biologic disease modifying anti-rheumatic drug therapy (bDMARD). The objective of this study was to measure the impact of CARRA STOP-JIA CTPs on clinical outcomes at 2 and 3 years.

Table 1: Patient characteristics at enrollment for participants with 2- and/or 3- year data

Characteristic	Follow-up at 2-3 Years (n=325)	No Follow-up (n=75)	SMD
Age - years (mean (SD))	10.2 (4.8)	11.4 (5.5)	0.235
Male (%)	90 (27.7)	16 (21.3)	0.148
Race (%)			0.340
White	237 (72.9)	54 (72.0)	
Black	19 (5.8)	11 (14.7)	
Other	69 (21.2)	10 (13.3)	
Months Since Diagnosis (median [IQR])	0 [0, 0.80]	0 [0, 0.93]	0.234
JIA Category - n (%)			0.414
Poly (RF-)	193 (59.4)	49 (65.3)	
Poly (RF+)	64 (19.7)	14 (18.7)	
Enthesitis related	25 (7.7)	8 (10.7)	
Psoriatic	19 (5.8)	4 (5.3)	
Extended oligoarticular	14 (4.3)	0 (0)	
Undifferentiated	10 (3.1)	0 (0.0)	
Physician Global - mean (SD)	5.5 (2.2)	5.6 (1.9)	0.070
Parent Global - mean (SD)	4.3 (2.7)	4.3 (2.6)	0.019
cJADAS-10 - mean (SD)	18.1 (4.7)	17.9 (4.5)	0.058
Active Joint Count - median [IQR]	10 [6, 17]	9 [6, 16.5]	0.124
CHAQ - median [IQR]	0.87 [0.25, 1.47]	0.75 [0.25, 1.12]	0.171

Abbreviations: SMD: standardized mean difference; IQR: interquartile range; RF=rheumatoid factor; MD Global=Physician Global Assessment of Disease Activity; cJADAS10=clinical Juvenile Arthritis Disease Activity Score based on 10 joints; CHAQ: Childhood Health Assessment Questionnaire.

Methods: STOP-JIA compared 3 CARRA CTPs in 400 children with pJIA: 1) Step-Up (SU) – starting conventional, synthetic DMARD monotherapy (csDMARD), adding bDMARD if needed after 3 months; 2) Early Combination (EC) – starting csDMARD and bDMARD within the first 3 months; and 3)Biologic First (BF) – starting bDMARD monotherapy and adding csDMARD if needed after 3 months. There was no randomization. Patients with 2 to 3 years of follow-up were included. The primary outcome was the percentage of children achieving CID off glucocorticoids at 2 and/or 3 years. Propensity score (PS) weighting was used to balance baseline differences in potential confounders between CTPs. Secondary outcomes included comparison of proportions of patients with clinical Juvenile Arthritis Disease Activity Score based on 10 joints inactive disease (cJADAS10-ID £ 2.5), clinical remission on medications (CRM; consecutive visits with CID ^{3} 6 months), and proportion of time spent in CID or cJADAS10-ID.

Table 2: Propensity Score-adjusted difference between CTP groups in estimates of CID at 24 months, CRM at any time up to 24 months, and percentages of time spent in CID and JADAS10-ID over 24 months

24-Month Outcomes			
		Difference Between CTPs	
CTP	Estimate % [upper, lower 95%CI)	vs. Biologic First	vs. Step Up
Percentage of patients in CID at 24 months			
Early Combination	57.7 [45.5, 70.0]	5.3 [-19.6, 30.4; p=0.68]	15.9 [1.2, 30.5; p=0.03]
Biologic First	52.4 [30.7, 74.0]	-	10.6 [-12.6, 33.7; p=0.37]
Step Up	41.8 [34.4, 49.3]	-	-
Percentage of patients with CR at any time over 24 months			
Early Combination	46.3 (32.9, 59.7)	16.1 [-8.8, 41.1; p=0.21]	17.6 [2.5, 32.6; p=0.02]
Biologic First	30.2 (9.2, 51.2)	-	1.4 [-20.7, 23.5; p=0.9]
Step Up	28.8 [22.3, 35.2]	-	-
Mean percentage of time in CID over 24 months			
Early Combination	32.4 [25.4, 39.4]	6.4 [-9.5, 18.8; p=0.52]	6.4 [-1.6, 14.4; p=0.12]
Biologic First	27.7 [15.3, 40.2]	-	1.7 [-11.3,14.8; p=0.79]
Step Up	26.0 [22.4, 29.6]	-	-
Mean percentage of time in cJADAS10 inactive disease over 24 months			
Early Combination	43.9 [36.2, 51.5]	8.2 [-6.6, 22.9; p=0.28]	8.4 [-0.3, 17.2; p=0.06]
Biologic First	35.7 [23.0, 48.5]	-	0.3 [-13.3, 13.8; p=0.97]
Step Up	35.4 [31.4, 39.5]	-	-

Abbreviations: PS: propensity score; CTP: Consensus Treatment Plan; cJADAS10=clinical Juvenile Arthritis Disease Activity Score based on 10 joints; CI: Confidence interval.

Table 3: Propensity Score-adjusted difference between CTP groups in estimates of CID at 36 months, CRM at any time up to 36 months, and percentages of time spent in CID and JADAS10-ID over 36 months

36-Month Outcomes			
		Difference Between CTPs	
CTP	Estimate % [upper, lower 95%CI)	vs. Biologic First	vs. Step Up
Percentage of patients in CID at 36 months			
Early Combination	34.7 [20.8, 48.5]	-7.5 [-33.3, 18.3; p=0.57]	-0.7 [-16.9, 15.5; p=0.93]
Biologic First	42.2 [20.1, 64.2]		6.8 [-16.9, 30.5; p=0.58]
Step Up	35.4 [27.4, 43.4		
Percentage of patients with CR at any time over 36 months			
Early Combination	66.1 [54.4, 77.8]	25.6 [1.6, 49.6; p=0.04]	26.0 [11.6, 40.4; p<0.001]
Biologic First	40.5 [18.5, 62.5]	-	0.4 [-23.4, 24.1; p=0.97]
Step Up	40.1 [31.9, 48.3]	-	-
Mean percentage of time in CID over 36 months			
Early Combination	42.8 [36.4, 49.2]	8.8 [-5.5, 23.1; p=0.23]	14.1 [6.3, 21.8; p<0.001]
Biologic First	34.0 [20.7, 47.3]	-	5.3 [-8.8, 19.3; p=0.46]
Step Up	28.8 [24.6, 32.9]	-	-
Mean percentage of time in cJADAS10 inactive disease over 36 months			
Early Combination	52.5 [45.0, 600]	11.4 [-3.8, 26.6; p=0.14]	13.1 [4.6, 21.6; p=0.003]
Biologic First	41.1 [27.7, 54.5]	-	1.7 [-12.5, 15.9; p=0.82]
Step Up	39.4 [35.3, 43.5]	-	-

Abbreviations: PS: propensity score; CTP: Consensus Treatment Plan; cJADAS10=clinical Juvenile Arthritis Disease Activity Score based on 10 joints; CI: Confidence interval.

Results: 325 participants had a 2- and/or 3-year visit (n=210 SU, 83 EC, 32 BF; Table 1). Percentage of patients in CID at 2 years was 42% for SU, 58% EC, and 52% BF (p=0.03 for SU versus EC; Table 2). CID differences were not statistically significant at 3 years. Likewise, there was no significant difference between CTPs for JADAS10-ID at 2 or 3 years. However, there were significant percentage differences in CRM, which were higher for EC compared to SU over 2 years (46.3% versus 28.8% [p=0.02]) and 3 years (66.1% versus 40.1% [p< 0.01]), and for percentages of time spent in CID (42.8% versus 28.8% [p< 0.01]) and cJADAS10-ID (52.5% versus 39.4% [p< 0.01]) at 3 years.

Conclusion: These data support improved effectiveness of EC versus SU and BF at 2 and 3 years for most outcomes, but did not reach statistical significance for all comparisons. There were significant differences favoring EC versus SU in outcomes that reflected duration of time spent with less disease activity at 2 and 3 years, which may be most important in limiting disease burden. More research is needed to improve understanding of which pJIA patients will respond to a particular CTP in order to optimize individual outcomes.

Disclosure: S. Ringold: Janssen Research & Development, LLC, 3; **G. Tomlinson**: Editas Medicine Inc, 1, Spectral Medical Inc, 7; **L. Schanberg**: Bristol-Myers Squibb(BMS), 5, Sanofi, 12, DSMB, UCB, 12, DSMB; **v. del gaizo**: None; **K. Murphy**: None; **B. Feldman**: AB2Bio, 2, Janssen, 2, Novo Nordisk, 2, Pfizer, 2; **M. Ong**: Pfizer, 5; **M. Natter**: None; **Y. Kimura**: None; **F. The CARRA Registry Investgators**: None.

Abstract Number: 0832

Cumulative Social Disadvantage Is Associated with Disease Activity and Functional Disability in Juvenile Idiopathic Arthritis: An Analysis of the CARRA Registry

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Pediatric Rheumatology – Clinical I: JIA
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: The impact of race and social determinants of health (SDoH) on health outcomes in juvenile idiopathic arthritis (JIA) remains poorly understood. Prior disparities research in JIA has largely analyzed these complex, intertwined social variables as independent risk factors and have reported inconsistent results of their impact on clinical outcomes, such as joint damage, pain, and disability. These inconsistencies may result from a failure to investigate interrelationships between social variables. A recent analysis demonstrated an association between cumulative social disadvantage and childhood arthritis using a combined score. In this analysis of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry, we used a similar method to investigate the effect of cumulative social disadvantage on disease activity and functional disability in JIA.

Methods: This is a cohort study of subjects with JIA enrolled in the CARRA Registry between July 2015-January 2022 with at least one Registry visit including all components of the clinical Juvenile Arthritis Disease Activity Score (cJADAS) and Child Health Assessment Questionnaire (CHAQ) score. A cumulative social disadvantage score was created, with a score of 1 given for each of the following: income (household income < $50,000/year), guardian education (high school or less), insurance (public insurance or none), and non-White race. Any missing components were given a score of 0.Univariate and

multivariable logistic regression models, adjusted for age at enrollment, sex, JIA category, and any use of a conventional (cs-), biologic (bs-) DMARD, or small molecule, were used to estimate the odds of persistent disease activity (oligoarticular JIA – cJADAS ≥1.1; all other categories >2.5) and functional disability (CHAQ score > 0).Random effect was included in the regression models to account for repeated measures.

Results: 9,672 subjects with JIA were identified (Table 1).Oligoarticular and RF- polyarticular JIA were the most common JIA subtypes reported. The majority of cohort required DMARD treatment (68.7%).48.9% of the cohort had exposure to at least one variable associated with the combined score.47.9% of patients were classified as having high cJADAS, and 56.8% had a high CHAQ score. In both unadjusted and adjusted analysis, cumulative social disadvantage with higher odds of active

Table 1: Demographic and clinical characteristics of pediatric patients with juvenile idiopathic arthritis (JIA) in the CARRA Registry.

	N (%)
Total N	9672
Median age at enrollment in years (IQR)	11.7 (7.3, 15.1)
Sex	
Female	6720 (69.9)
Male	2892 (30.1)
JIA Category	
Oligoarticular JIA	3417 (35.7)
RF+ polyarticular JIA	611 (6.4)
RF- polyarticular JIA	2830 (29.6)
Systemic JIA	745 (7.8)
Enthesitis-related arthritis	1012 (10.6)
Psoriatic arthritis	703 (7.4)
Undifferentiated arthritis	244 (2.6)
Median Area Deprivation Index (IQR)	37.0 (20.0, 60.0)
Ever use of a csDMARD, bsDMARD, or small molecule*	6643 (68.7)
Components of cumulative social disadvantage score	
Non-white race	2236 (23.1)
Household income <$50,000/year	1842 (19.0)
Guardian education of high school or less	1587 (16.4)
Publicly insured or no insurance	2546 (26.3)
Cumulative social disadvantage score	
0	4938 (51.1)
1	2458 (25.4)
2	1299 (13.4)
3	753 (7.8)
4	224 (2.3)
Components of the cJADAS[†]	
Median Physical Global Assessment	1.0 (0.0, 3.0)
Median Parent/patient Global Assessment	2.0 (0.0, 4.0)
Active Joint Count	1.0 (0.0, 3.0)
Median cJADAS (IQR)	2.0 (0.0, 6.0)
High cJADAS[†]	4633 (47.9)
Median CHAQ[¥] (IQR)	0.1 (0.0, 0.6)
High CHAQ[‡]	5029 (56.8)

*Conventional synthetic DMARD, biologic DMARD
[†]Clinical Juvenile Arthritis Disease Activity Score
[†]Defined in subjects with oligoarticular JIA as cJADAS ≥1.1 and in all other JIA categories as >2.5
[¥]Child Health Assessment Questionnaire
[‡]Defined as a CHAQ score of >0.

Table 2: Mixed effects model to estimate the effect of cumulative social disadvantage on persistent disease activity in children with JIA in the CARRA Registry

Cumulative Social Disadvantage Score	Unadjusted OR (95% CI), p-value	Adjusted[†] OR (95% CI), p-value
0	—	—
1	1.32 (1.19, 1.46), <0.001	1.34 (1.21, 1.48), <0.001
2	1.70 (1.50, 1.94), <0.001	1.82 (1.61, 2.07), <0.001
3	2.09 (1.77, 2.46), <0.001	2.31 (1.97, 2.71), <0.001
4	1.92 (1.45, 2.54), <0.001	2.18 (1.65, 2.86), <0.001

[†]Model adjusted for age at enrollment, sex, JIA category, and any use of a cs- or bDMARD or small molecule

Table 3: Mixed effects model to estimate the effect of cumulative social disadvantage on persistent functional disability in children with JIA in the CARRA Registry

Cumulative Social Disadvantage Score	Unadjusted OR (95% CI), p-value	Adjusted[†] OR (95% CI), p-value
0	—	—
1	1.62 (1.41, 1.87), <0.001	1.64 (1.42, 1.88), <0.001
2	3.61 (3.02, 4.31), <0.001	3.49 (2.92, 4.17), <0.001
3	3.89 (3.11, 4.89), <0.001	3.94, (3.15, 4.93), <0.001
4	3.81 (2.59, 5.59), <0.001	3.91 (2.67, 5.74), <0.001

[†]Model adjusted for age at enrollment, sex, JIA category, and any use of a cs- or bDMARD or small molecule

disease, highest for a score of 3 (Table 2 - adjusted odds ratio [aOR] 2.31, 95% CI: 1.97-2.71), and functional disability, also highest for a score of 3 (Table 3 - aOR 3.94, 95% CI: 3.15-4.93).

Conclusion: Cumulative social disadvantage was associated with higher odds of active disease and functional disability compared to those not experiencing these exposures among JIA subjects in the CARRA Registry. Exposure to multiple variables associated with social disadvantage confers higher risk of poor outcomes in JIA. To mitigate these disparities, targeted social risk screening adopted within pediatric rheumatology clinics should be studied as a potential intervention to identify at-risk patients who may benefit from social network support or other programming, such as patient navigation services.

Disclosure: W. Soulsby: None; **E. Lawson**: Pfizer, 5; **J. Boscardin**: None; **E. von scheven**: None.

Abstract Number: 0833

Machine Learning Detected Healthcare Encounter Patterns Leading to Diagnosis of Juvenile Arthritis in a Population-Based Canadian Cohort

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Pediatric Rheumatology – Clinical I: JIA
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Increases in health care visits precede the first diagnosis code for inflammatory arthritis (IA) by an average of 5 years in adults, but it is unknown if this occurs in children. Reports of symptoms before juvenile arthritis (JA) are usually < 6 months but could be longer for some. We hypothesized that patterns of visits that precede JA diagnosis differ from those in non-JA controls. We aimed to discover visit patterns preceding JA diagnosis in health administrative databases (HAD).

Methods: ***Populations:*** JA patients diagnosed from 1983-2012 in the only paediatric rheumatology centre in Manitoba, Canada were linked to provincial population-based HAD. Controls were matched 5:1 to JA patients by age ± 1 year, sex, health regions, JA diagnosis dates (index dates for controls) and did not have an IA code ≤ 18 years old in HAD. Visits since birth or immigration until diagnosis/ index dates were used for analysis (1980-2018). ***Data preprocessing:*** Diagnosis codes (International Classification of Diseases versions 9-CM and 10-CA) from all inpatient and outpatient visits were clustered into clinically-relevant categories using open-source Clinical Classification Software. Visits were examined in 6-month intervals

Table: Top 10 discriminating patterns of JA

Pattern Number	Patterns	Percent of JA patients	Percent of controls	Odds ratio of JA vs controls (95% confidence intervals)
1	Joint Disorders @6-0 months	65.80	1.40	135.62 (87.85, 209.37)
2	Joint Disorders @6-0 months , Joint disorders @6-0 months	37.82	0.21	292.91 (107.5, 798.09)
3	Other musculoskeletal @6-0 months	32.12	3.47	13.16 (9.52, 18.20)
4	Upper Respiratory Infections @12-6 months, Joint Disorders @6-0 months	23.83	0.52	60.08 (30.93, 116.72)
5	Upper Respiratory Infections @24-18 months, Joint Disorders @6-0 months	23.32	0.52	192.48 (60.52, 612.16)
6	Upper Respiratory Infections @18-6 months, Joint Disorders @6-0 months	23.06	0.16	58.38 (30.03, 113.48)
7	Upper Respiratory Infections @30-24 months, JD @6-0 months	21.50	0.00	Not applicable
8	Skin disorders @6-0 months	24.87	4.15	7.66 (5.55, 10.56)
9	Upper Respiratory Infections @36-30 months, Joint Disorders @6-0 months	19.95	0.00	Not applicable
10	Joint Disorders @6-0 months , Joint Disorders @6-0M, Joint Disorders @6-0 months	18.91	0.05	449.89 (62.3, 3248.64)

Top 10 Most Common Healthcare Encounter Patterns Preceding Juvenile Arthritis Diagnosis and Odds Ratio (95% Confidence Intervals Compared to Controls

from birth until diagnosis/index date. ***Analysis:****Prefixspan*, a sequential pattern mining (SPM) machine learning algorithm was applied to visits of JA cases and controls to detect ***patterns (temporal sequence of events)*** preceding diagnosis/ index dates. We modified the algorithm to assign lower weights to encounters that were more remote to diagnosis than those closer in time to diagnosis (time fading). JA and control patterns were compared by relative percentages (of patterns) and odds ratios (of JA compared to controls) thresholds. Patterns were screened and evaluated for face validity by the clinical team.

Results: 386 JA patients (65% females) were matched to 1930 controls. Median age of JA patients at diagnosis was 8 years. JA subgroups: oligoarticular 42%, polyarticular 28%, spondyloarthropathy 13%, others 17%. We studied 98649 visits: 20946 JA, 77703 controls. JA patients had more visits compared to controls, respectively with median (25-75thpercentile) of 19.5 (7.0-38.5) versus 15 (5-31) general practitioner visits, and 15 (4.5-35) versus 8 (1-23) specialist visits. ICD codes were classified into 101 chronic diseases, 116 acute diseases/ poisoning/trauma categories. We detected 544 discriminating patterns. Patterns of JA were detectable ≤3 years pre-JA diagnosis. The most common 10 patterns that discriminated between JA patients and non-JA controls, before diagnosis are presented (Table).

Conclusion: Machine learning methods detected healthcare encounter patterns more likely associated with JA relative to controls in a population-based cohort, ≤ 3 years before diagnosis. Visits preceded IA codes, providing an insight into heterogeneity in JA presentations and potential associated events before JA. Once validated, our method may be used to: i) identify potential JA patients for earlier management, ii) define disease cohorts for outcome studies at a population level in HAD.

Disclosure: L. Lim: Pfizer, 6; **C. Hryhoruk**: None; **R. Marrie**: None; **C. Peschken**: AstraZeneca, 2, 5, GSK, 2, 5, Roche, 1, 2; **C. Leung**: None; **L. Lix**: None.

Abstract Number: 0834

Characterization of the Youngest Cohort with Non-Systemic Juvenile Idiopathic Arthritis: Demographics and Medication Use of Patients ≤2 Years of Age in the Childhood Arthritis and Rheumatology Research Alliance Registry

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Pediatric Rheumatology – Clinical I: JIA

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children. Tumor necrosis factor inhibitors (TNFi) have demonstrated efficacy and safety in older JIA patients and are approved for use in children over age 2 years. However, use of these therapies in children ≤2 years is not well described despite frequent use in clinical practice. Children ≤2 yo who would benefit from these medications may have delays in treatment due to the lack of FDA approval, resulting in increased morbidity. Our aim was to describe the demographics, medication use, and changes in medication use over time in the cohort of children diagnosed with non-SJIA ≤2 yo enrolled in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) registry.

Methods: The CARRA registry is a national multicenter observational database for children with rheumatic diseases in the United States. Demographics, disease phenotype, and medication use of patients diagnosed with non-SJIA before the age of 2 years enrolled in the CARRA Registry were analyzed using descriptive statistics. Those who started a TNFi ≤2 yo, >2 yo, and those who never used TNFi were analyzed; summary statistics are presented using median with interquartile range (IQR) for continuous variables and count with frequency for categorical variables. Group comparisons were completed using Welch's ANOVA for continuous variables and Chi Square test for categorical variables with a significance level of 0.05.

Results: 1,458 patients diagnosed with non-SJIA ≤2 yo were enrolled in the CARRA registry between 2015 and 2021. Consistent with known demographics of JIA subtypes, there were fewer enthesitis related arthritis and RF + polyarticular JIA patients diagnosed before the age of 2. Of these, 259 (18%) started a TNFi before the age of 2. Patients started on TNFi after their 2nd birthday tended to have a longer disease duration at time of registry enrollment as compared to those that started before age 2 ($p < 0.01$). Early initiation of TNFi did not vary based on race or average income. Half of patients with RF - polyarticular JIA were started on TNFi ≤2 yo, and joint counts of ≥5 had higher rates of early TNFi initiation (Table 1). DMARD and TNFi use before age 2 increased over time but decreased from 2018-2021 (figure 1). Less than 1% of our cohort was started on a non-TNFi biologic at ≤2yo.

Conclusion: Our findings demonstrate that despite the lack of FDA approval, TNFi medications are being utilized in 18% of patients under the age of 2, with higher early utilization rates when olig-JIA patients are removed from the analysis. Possible explanation for decreased use from 2018-2021 could be due to early concerns regarding immunosuppresion in COVID19; future data will clarify. Overall, TNFi medications are an accepted treatment amongst pediatric rheumatologists in early-onset JIA. Future analysis will look at patients diagnosed ≤2yo enrolled in the registry near time of diagnosis, and assess the relationship between disease activity and TNFi initiation, efficacy, and adverse events in this population.

Table 1: Demographics and Medication use of Patients with Non-Systemic JIA Diagnosed at ≤2yo

	Total diagnosed with JIA at < or =2yo (n = 1,458)	Started TNFi ≤ 2 yo (n = 259)	Never started TNFi (n = 569)	Did not start TNFi <2 yo but started TNF after age 2 (n = 630)	p-value
Age (month), median (IQR)	22 (19 - 26)	21 (18 - 24)	22 (19 - 26)	23 (19 - 26)	<0.01
Disease duration at time of enrollment (month), median (IQR)	43 (5 - 100)	13 (2 - 58)	19 (2 - 68)	75 (33 - 130)	<0.01
Race / Ethnicity, n (%)					0.14
Asian	40 (2.7)	11 (4.3)	17 (3.0)	12 (1.9)	
Black	17 (1.2)	3 (1.2)	10 (1.8)	4 (0.6)	
Hispanic	92 (6.3)	16 (6.2)	37 (6.5)	39 (6.2)	
Multiracial	74 (5.1)	13 (5.0)	37 (6.5)	24 (3.8)	
White	1,169 (80.2)	208 (80.3)	443 (78.0)	518 (82.2)	
Other	41 (2.8)	3 (1.2)	18 (3.2)	20 (3.2)	
Unknown	24 (1.6)	5 (1.9)	6 (1.1)	13 (2.1)	
Gender, n (%)					
Female	1,238 (84.9)	216 (83.4)	468 (82.3)	554 (87.9)	0.02
JIA classification (n, %)					<0.01
Enthesitis related arthritis	18 (1.2)	2 (0.8)	5 (0.9)	11 (1.8)	
Oligoarthritis	831 (57.0)	87 (33.6)	414 (72.8)	330 (52.4)	
Polyarthritis (RF -)	480 (32.9)	132 (51.0)	119 (20.9)	229 (36.4)	
Polyarthritis (RF +)	20 (1.4)	5 (1.9)	7 (1.2)	8 (1.3)	
Psoriatic arthritis	87 (6.0)	30 (11.6)	16 (2.8)	41 (6.5)	
Undifferentiated arthritis	22 (1.5)	3 (1.2)	8 (1.4)	11 (1.8)	
Joint count, n (%)					<0.01
< 5	708 (48.6)	91 (35.1)	382 (67.1)	235 (37.3)	
≥ 5	717 (50.6)	167 (64.5)	182 (32.0)	388 (61.6)	
Other medications, n (%)					<0.01
Anti-IL1	9 (0.2)	3 (0.4)	0 (0.0)	6 (0.2)	
Anti-IL6	211 (4.6)	59 (7.6)	32 (2.6)	120 (4.6)	
JAK-inhibitor	27 (0.6)	7 (0.9)	2 (0.2)	18 (0.7)	
Methotrexate	3,923 (84.8)	643 (82.7)	1,101 (89.4)	2,179 (83.2)	
Other biologic	182 (3.9)	35 (4.5)	32 (2.6)	115 (4.4)	
Other non-biologic	276 (6.0)	31 (4.0)	65 (5.3)	180 (6.9)	
Total	4,628	778	1,232	2,618	
Household income, n (%)					0.52
<25,000	105 (7.2)	17 (6.6)	50 (8.8)	38 (6.0)	
25K - 49,999	161 (11.0)	31 (12.0)	51 (9.0)	79 (12.5)	
50K - 74,999	179 (12.3)	35 (13.5)	62 (10.9)	82 (13.0)	

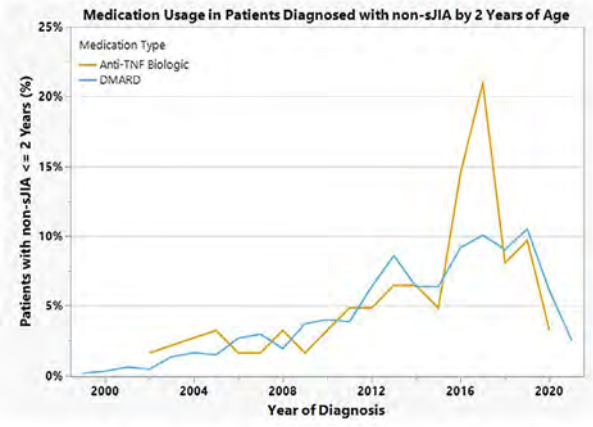

Figure 1: Medication Usage in Children Diagnosed with non-SJIA at ≤2yo Over Time

Disclosure: C. Gulla: None; **T. Lozy**: None; **D. Choi**: None; **G. Janow**: None; **F. The CARRA Registry Investgators**: None.

Abstract Number: 0835

Abatacept in Individuals at Risk of Developing Rheumatoid Arthritis: Results from the Arthritis Prevention in the Pre-clinical Phase of RA with Abatacept (APIPPRA) Trial

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: RA – Treatments I: Novel RA Treatments & Mechanisms of Action

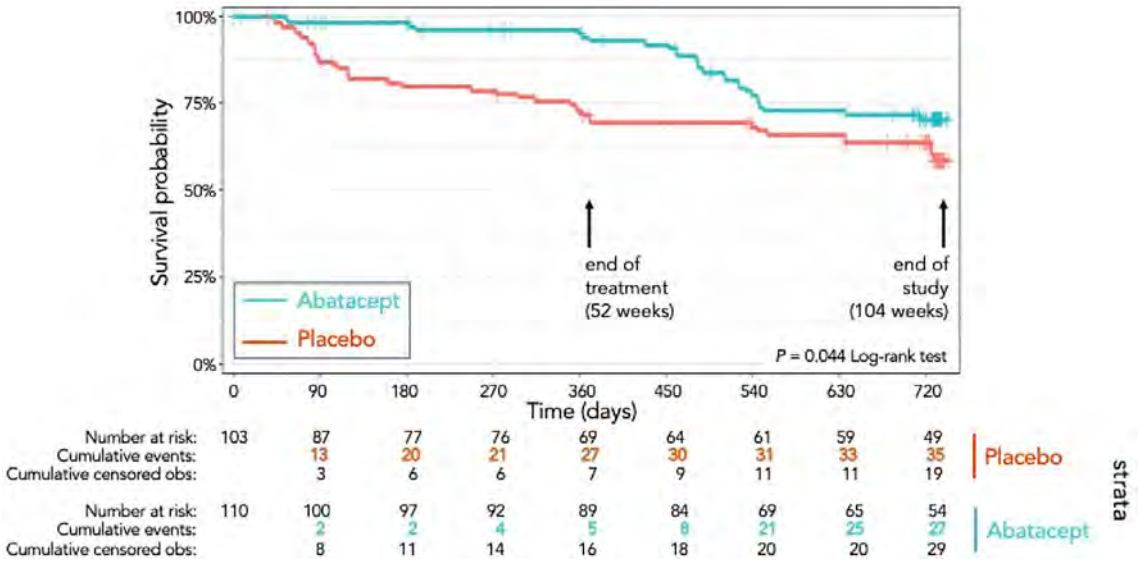
Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: The definition of higher risk states for rheumatoid arthritis (RA) has been refined in more recent years through inclusion of serum autoantibodies and symptom complexes, such as inflammatory joint pain. Data from at risk cohorts have reported rates of progression to RA in excess of 50% over 24 months. These combined features have provided a framework for the design of interception studies, aimed at delaying or preventing RA. We set out to evaluate the feasibility, efficacy and acceptability of T-cell co-stimulation modulation with abatacept in individuals at risk of developing RA in the Arthritis Prevention In the Pre-clinical Phase of RA with Abatacept (APIPPRA) study.

Methods: APIPPRA is a Phase IIB randomised, double blind, placebo-controlled trial recruiting $ACPA^{+}RF^{+}$ or $ACPA^{hi}RF^{-}$ individuals with arthralgia. Consenting participants were randomised to receive 52 weekly subcutaneous injections of placebo or 125mg abatacept, and followed up for a further 52 weeks. Exclusion criteria included previous episodes of clinical synovitis, prior corticosteroids or DMARDs. The primary endpoint was the time to development of either clinical synovitis in 3 or more joints, or RA according to ACR/EULAR 2010 criteria, whichever was met first. Joint synovitis was confirmed by ultrasonography. Secondary endpoints included multiple disease activity assessments, including ultrasound scores, as well as safety data.

Results: Between December 2014 and January 2019, 280 individuals were evaluated for eligibility across 31 study sites, 28 in the UK and 3 in the Netherlands. Two hundred and thirteen were randomised, 103 to placebo and 110 to abatacept. Mean age was 49 and 77% were female. Ninety-three percent of individuals were $ACPA^{hi}$. Ultrasonography at baseline



suggested modest levels of active sub-clinical synovitis (73% of participants with power Doppler score of 0). In total, there were 65 primary outcome events. At 52 weeks there were 30 events (29%) in the placebo arm and 7 (6%) in the abatacept arm. By the end of the study there were 38 (37%) and 27 (25%) events, respectively, resulting in differences in mean arthritis-free survival time between arms of 99.2 days (95% CI 37.5 – 160.9; *p*-value=0.002), in favour of abatacept. The respective log-rank test for difference in the survival distribution was *p*=0.044, reflecting a large effect in the first year and convergence over the second year (see Figure 1). The per protocol analysis showed similar results. Pre-specified exploratory analysis revealed that individuals with high levels of ACPA or who had an extended autoantibody profile at baseline were more likely to remain arthritis-free following abatacept therapy. Those treated with abatacept had lower HAQ-DI and pain scores, and higher EQ-5DL scores during the treatment period, when compared to placebo. There were 4 serious adverse events in the abatacept group and 10 in the placebo group, including two deaths, one in each arm, none deemed attributable to study drug.

Conclusion: Therapeutic intervention during the RA at risk phase is feasible, with acceptable safety profiles. T cell co-stimulation modulation with abatacept for 52 weeks showed a reduction in the development of RA over two years. There were no new safety signals.

Disclosure: A. Cope: Bristol-Myers Squibb(BMS), 2, 5, 6; **M. Jasenecova**: Bristol-Myers Squibb(BMS), 5; **J. Vasconcelos**: Bristol-Myers Squibb(BMS), 5; **A. Filer**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 5, Janssen, 5, Nascient, 5, Sonoma Biotherapeutics, 2; **K. Raza**: Bristol-Myers Squibb(BMS), 5; **S. Qureshi**: Bristol-Myers Squibb(BMS), 5; **M. D'Agostino**: AbbVie/Abbott, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **I. McInnes**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Bristol Myers Squibb, 2, 5, Cabaletta, 2, 11, Causeway Therapeutics, 2, 11, Celgene, 2, 5, Compugen, 2, 11, Dextera, 11, Eli Lilly, 2, EveloBio, 1, 2, 4, 11, Gilead, 2, Janssen, 2, 5, Moonlake, 2, NHS GGC, 4, Novartis, 2, 5, Pfizer, 2, Sanofi, 2, UCB, 2, 5, Versus Arthritis, 12, Trustee Status; **J. Isaacs**: Bristol-Myers Squibb(BMS), 5; **A. Pratt**: Bristol-Myers Squibb(BMS), 5; **B. A Fisher**: Bristol-Myers Squibb(BMS), 2, Celgene, 5, Galapagos, 2, 5, Janssen, 2, 5, Novartis, 2, Roche, 2, Sanofi, 2, Servier, 2, 5, UCB, 2; **C. Buckley**: Bristol-Myers Squibb(BMS), 5, Mestag, 11; **P. Emery**: Boehringer Ingelheim, 2, Eli Lilly, 2, Novartis, 2; **P. Ho**: Bristol-Myers Squibb(BMS), 5; **M. Buch**: AbbVie, 2, 6, 12, All paid to host institution, Boehringer Ingelheim, 2, 6, 12, Paid to host institution, Galapagos, 2, 6, 12, Paid to host institution, Gilead, 2, 5, 6, 12, Paid to host institution, Lilly, 2, 6, 12, All paid to host institution, National Insitute for Health and Care Research (NIHR), 3, 12, Maya H Buch is a National Institute for

Health and Care Research (NIHR) Senior Investigator. The views expressed are those of the authors and not nece, Pfizer, 2, 12, Paid to host institution; **C. Ciurtin**: Bristol-Myers Squibb(BMS), 5; **R. Toes**: Bristol-Myers Squibb(BMS), 5; **T. Huizinga**: None; **D. van Schaardenburg**: None; **C. Caroline**: Bristol-Myers Squibb(BMS), 5; **T. Prevost**: Bristol-Myers Squibb(BMS), 5.

Abstract Number: 0836

Vagotomy and Subsequent Risk of Rheumatoid Arthritis and Osteoarthritis: A Danish Register-Based Cohort Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: RA – Treatments I: Novel RA Treatments & Mechanisms of Action
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Vagus nerve stimulation (VNS) is an emerging potential therapy for rheumatoid arthritis (RA). Given preliminary benefit observed with VNS in RA, we hypothesized that vagotomy might increase the risk of developing RA, without impacting the risk of developing osteoarthritis (OA). Historically, patients underwent vagotomy to treat refractory peptic ulcer disease by one of three methods: 1) full truncal vagotomy, 2) selective vagotomy (in which the celiac branch remains intact), and 3) superselective vagotomy (in which only the direct vagal inputs to the stomach are affected). The aim of this study was to examine the risk of developing RA or OA after various methods of vagotomy.

Methods: We performed a population-based cohort study in Denmark utilizing the Danish National Patient Registry and Danish Civil Registration System (CRS) from January 1, 1977 to December 31, 1995. We identified individuals who underwent vagotomy using International Classification of Diseases (ICD)-8 codes. A comparison cohort of patients who had not undergone vagotomy was randomly selected from the general population and matched on year of birth, sex, and date of vagotomy (index date). We excluded patients who were not registered in the CRS at least two years before the index date and those with prior diagnoses of OA or RA at any time before the index date. We examined the incidence of RA or OA based on two or more diagnosis codes for RA or OA 7-365 days apart, as well as OA with joint replacement based on a diagnosis of OA and a procedure code for knee or hip arthroplasty. Incidence of RA and OA was calculated using cumulative incidence function and treating death as a competing event. We used Cox proportional hazards regression models to compute hazard ratios (HRs) adjusted for age, sex, and comorbidities and corresponding 95% CIs, comparing patients with truncal vagotomy versus a matched general population comparison cohort and superselective vagotomy versus a matched comparison cohort.

Results: We identified 2,260 patients who underwent truncal vagotomy, matched with 22,610 comparators (Table), as well as 3,810 superselective vagotomy patients matched with 38,090 comparators (Table). The cumulative incidence estimates for truncal vagotomy are shown in Figure 1 and for superselective vagotomy in Figure 2. After adjusting for confounders, the HR for developing RA was 2.62 (95% CI 1.47-4.67) among patients who underwent truncal vagotomy compared with matched pairs. The HR for OA was 1.23 (95% CI 0.86-1.78), and for OA with joint replacement it was 0.73 (95%CI 0.36-1.50). For superselective vagotomy patients compared with a general population comparison cohort, the HR for developing RA was 1.05 (95% CI 0.51-2.17), for OA it was 1.01 (95% CI 0.70-1.45), and for OA with joint replacement it was 0.73 (95% CI 0.36-1.50).

Table. Characteristics of vagotomy and matched comparison cohorts.

Table. Characteristics of vagotomy and matched comparison cohorts.

	Truncal Vagotomy Cohort (*n* = 2260)	Truncal Vagotomy Comparison Cohort (*n* = 22610)	Superselective Vagotomy Cohort (*n* = 3810)	Superselective Vagotomy Comparison Cohort (*n* = 38090)
Age group, years, n (%)				
18-40	210 (9.0)	2070 (9.2)	920 (24.0)	9170 (24.1)
41-50	380 (17.0)	3840 (17.0)	1120 (29.3)	11170 (29.3)
51-60	500 (22.0)	5020 (22.2)	990 (26.1)	9940 (26.1)
61-70	540 (23.8)	5380 (23.8)	610 (16.0)	6110 (16.0)
71+	630 (27.8)	6300 (27.9)	170 (4.5)	1700 (4.5)
Sex, n (%)				
Female	940 (41.4)	9420 (41.6)	1250 (32.7)	12470 (32.7)
Male	1320 (58.2)	13190 (58.3)	2560 (67.2)	25620 (67.2)
Calendar year, n (%)				
1977-1981	500 (21.8)	4960 (21.9)	1540 (40.3)	15360 (40.3)
1982-1986	660 (29.1)	6600 (29.2)	1270 (33.3)	12720 (33.4)
1987-1991	760 (33.7)	7640 (33.8)	730 (19.2)	7280 (19.1)
1992-1995	340 (15.0)	3410 (15.1)	270 (7.2)	2730 (7.2)
Charlson comorbidity score, n (%)				
0	1780 (77.5)	20260 (89.6)	3570 (93.7)	36450 (95.7)
1-2	410 (18.3)	2080 (9.2)	210 (5.6)	1520 (4.0)
≧ 3	90 (3.7)	270 (1.2)	30 (0.7)	120 (0.3)

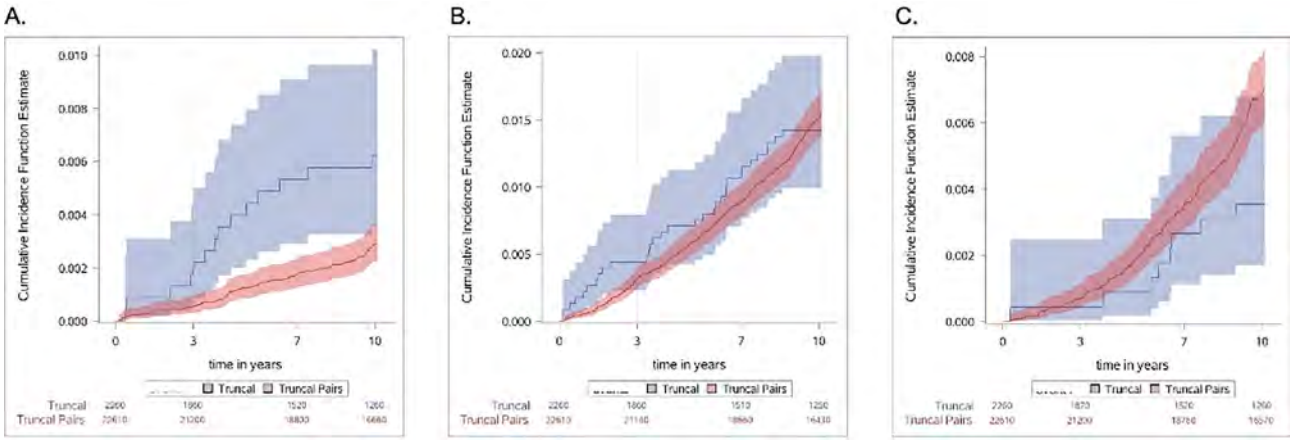

Figure 1. Cumulative incidence estimates for A. rheumatoid arthritis, B. osteoarthritis, and C. osteoarthritis with joint replacement, in subjects who underwent truncal vagotomy compared with a general population comparison cohort.

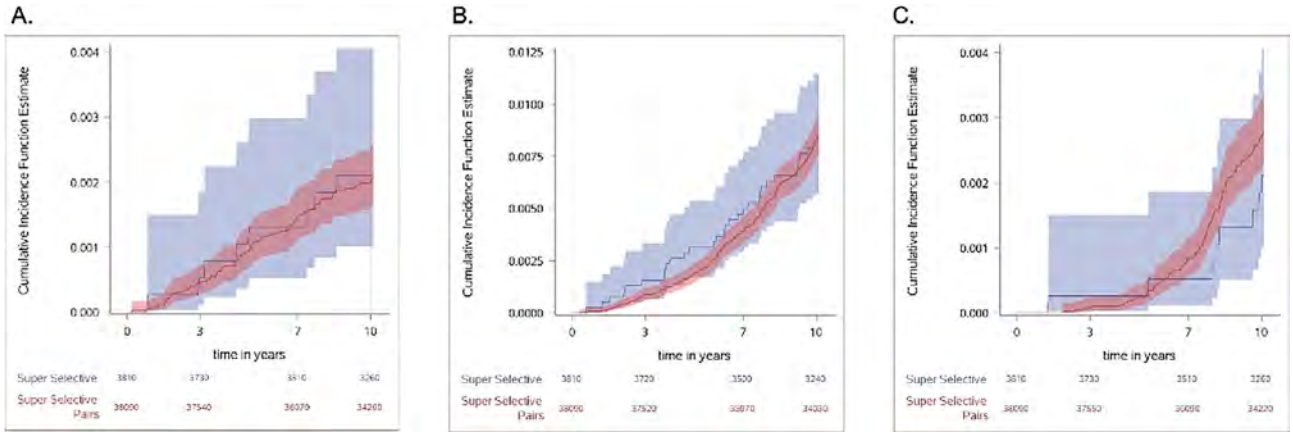

Figure 2. Cumulative incidence estimates for A. rheumatoid arthritis, B. osteoarthritis, and C. osteoarthritis with joint replacement, in subjects who underwent superselective vagotomy compared with a general population comparison cohort.

Conclusion: Truncal vagotomy was associated with an increased risk of developing RA. No difference in the risk of RA was seen in the superselective vagotomy group. Neither truncal nor superselective vagotomy were associated with an increased risk of developing OA. These results support the hypothesis that disruption of vagus nerve signaling may contribute to the development of RA.

Disclosure: M. Baker: Mobility Bio, 8, Nēsos, 2; **D. Nagy**: None; **S. Tamang**: None; **E. Horváth-Puhó**: None; **H. Toft Sørensen**: None.

Abstract Number: 0837

A Randomized, Double-Blind, Sham-Controlled, Clinical Trial of Auricular Vagus Nerve Stimulation for the Treatment of Active Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: RA – Treatments I: Novel RA Treatments & Mechanisms of Action
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Session Time: 4:00PM–5:30PM

Background/Purpose: Vagus nerve stimulation (VNS) has emerged in recent decades as a potential therapy for RA.We have previously shown that auricular VNS produced an average reduction of 1.4 in the disease activity score of 28 joints with C-reactive protein (DAS28-CRP) and significant improvements in the American College of Rheumatology (ACR) responses in an open-label study of 30 patients with active RA. Similarly, studies with an implantable cervical vagus nerve stimulator have shown reduced signs and symptoms of RA. However, studies to date have been relatively small and/or uncontrolled. The purpose of this study was to investigate the safety and efficacy of auricular vagus nerve stimulation for the treatment of RA in a randomized, double-blind, sham-controlled study.

Methods: This randomized, double-blind, sham-controlled trial enrolled patients aged 18-75 years with active RA who had failed or were intolerant of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and were naïve to biologic and/or targeted synthetic DMARDs. All patients received an auricular vagus nerve stimulator and were randomized 1:1 to active stimulation or sham. The primary endpoint was the proportion of patients achieving 20% improvement in American College of Rheumatology criteria (ACR20) at week 12. Secondary endpoints included mean changes in disease activity score of 28 joints with C-reactive protein (DAS28-CRP) and Health Assessment Questionnaire-Disability Index (HAQ-DI).

Results: A total of 113 patients received study therapy, and 101 patients (89.4%) completed the study visits through week 12. Baseline characteristics are shown in Table 1.

ACR20 responses at week 12 were not significantly different in patients receiving active unilateral stimulation versus sham: 25.0% for active stimulation vs 26.9% for sham (difference vs sham: -1.9% [-18.8% to 14.9%]; p=0.823) (Table 2 and Figure). The LS mean (SE) changes in DAS28-CRP from baseline to week 12 were –0.95 (0.16) for active unilateral stimulation and –0.66 (0.16) for sham, with a difference in LS means (SE) vs sham of –0.29 (0.23) (p=0.201) (Figure). The LS mean

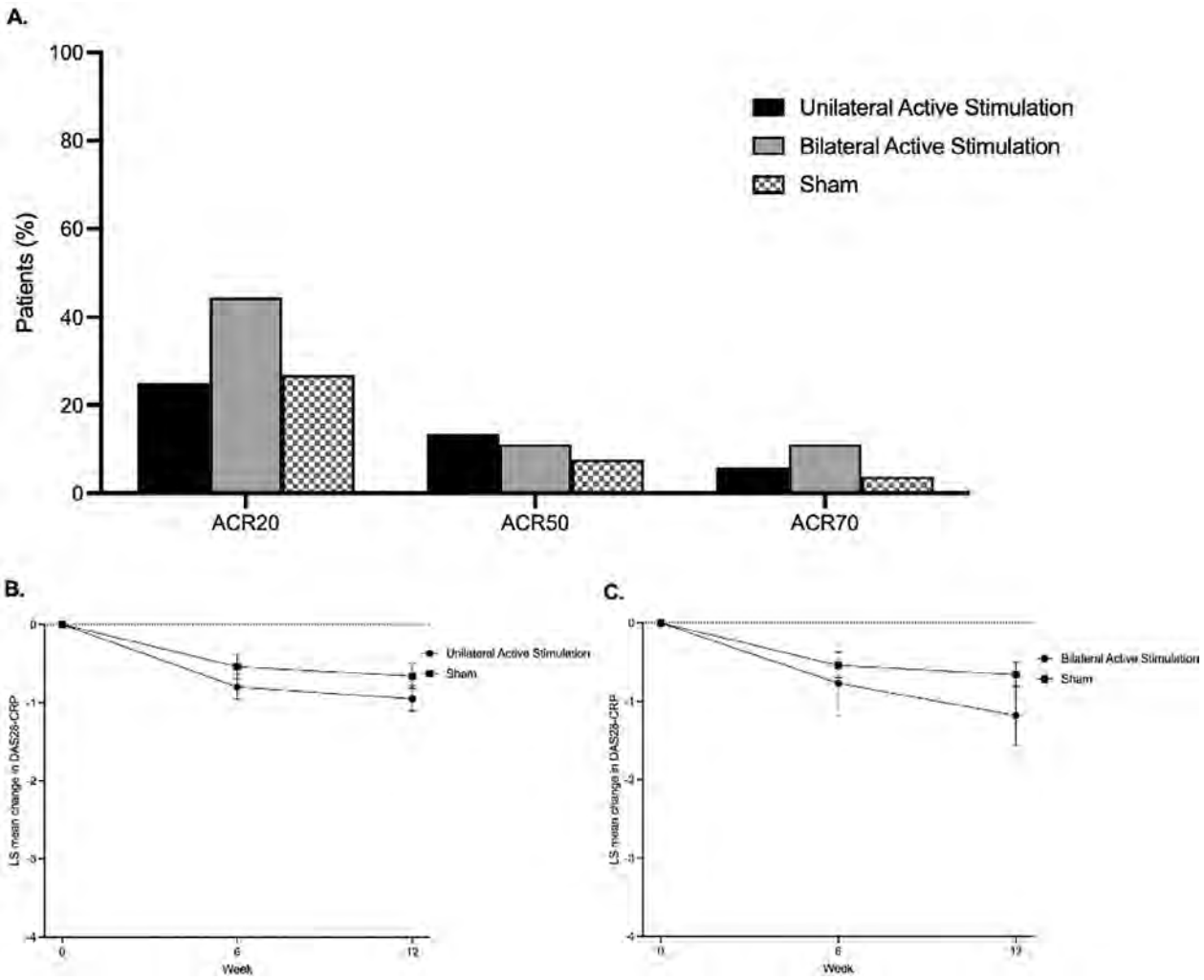

Figure. Primary and secondary efficacy end points. Panel A shows the percentage of patients who had 20% improvement in American College of Rheumatology response criteria (ACR20), 50% improvement (ACR50), and 70% improvement (ACR70) at week 12, respectively, with non-responder imputation. Panels B and C show the least square mean change from baseline in the 28-joint disease activity score based on the level of disease activity score in 28 joints using C-reactive protein (DAS28-CRP). For Panels B-C, a mixed-effects model with repeated measures was used to evaluate treatment effect on change from baseline with fixed effects for treatment, visit, and treatment-by-visit interaction and baseline value as a covariate. Comparison of bilateral active stimulation vs sham is a post-hoc analysis.

(SE) changes in HAQ-DI from baseline to week 12 were –0.19 (0.06) for active unilateral stimulation and –0.02 (0.06) for sham, with a difference in LS means (SE) vs sham of –0.17 (0.08) (p=0.044). No significant differences were seen in DAS28-CRP of 2.6 or less, ACR50, ACR70, CDAI, or SDAI between the unilateral active stimulation and sham groups (Table 2, Figure).

Treatment-emergent AEs were reported in 10 patients (18.9%) receiving unilateral active stimulation, 2 patients (22.2%) receiving bilateral active stimulation, and 5 patients (9.8%) receiving sham. No AEs were grade 3 or greater in severity by Common Terminology Criteria for Adverse Events, and no serious adverse events (SAEs) or deaths occurred.

Conclusion: Auricular VNS was safe and well tolerated, but it did not meaningfully improve RA disease activity. More large, controlled studies of VNS for the treatment of RA are needed to better understand its potential future role.

Table 1. Baseline characteristics of rheumatoid arthritis patients included in a trial of auricular vagus nerve stimulation.

Characteristic, No. (%)	Total Cohort (n = 113)	Unilateral Active Stimulation (n = 52)	Bilateral Active Stimulation (n = 9)	Sham (n = 52)	SMD[a]
Age, mean (SD), y	54.4 (12.5)	55.9 (12.2)	49.7 (10.4)	53.8 (13.2)	0.165
< 40	14 (12.4)	6 (11.5)	1 (11.1)	7 (13.5)	0.097
≥ 40 to < 65	70 (61.9)	30 (57.7)	8 (88.9)	32 (61.5)	0.088
≥ 65	29 (25.7)	16 (30.8)	0	13 (25.0)	0.159
Gender					0.050
Female	93 (82.3)	43 (82.7)	8 (88.9)	42 (80.8)	
Male	20 (17.7)	9 (17.3)	1 (11.1)	10 (19.2)	
Race					0.166
American Indian/Alaska Native	1 (0.9)	0	0	1 (1.9)	
Asian	5 (4.4)	3 (5.8)	1 (11.1)	1 (1.9)	
Black	14 (12.4)	8 (15.4)	0	6 (11.5)	
Hispanic	25 (22.1)	13 (25.0)	2 (22.2)	10 (19.2)	
White	67 (59.3)	27 (51.9)	6 (66.7)	34 (65.4)	
Other	1 (0.9)	1 (1.9)	0	0	
Body Mass Index, mean (SD), kg/m^2	29.8 (7.8)	29.9 (6.9)	26.9 (3.7)	30.1 (9.0)	0.025
Concomitant medications					
Methotrexate	80 (70.8)	38 (73.1)	4 (44.4)	38 (73.1)	0
Leflunomide	9 (8.0)	5 (9.6)	0	4 (7.7)	0.135
Sulfasalazine	9 (8.0)	3 (5.8)	2 (22.2)	4 (7.7)	0.170
Hydroxychloroquine	36 (31.9)	18 (34.6)	3 (33.3)	15 (28.8)	0.147
Prednisone	22 (19.4)	11 (21.2)	2 (22.2)	9 (17.3)	0.137
Duration of RA, mean (SD), y	6.8 (7.6)	7.1 (7.2)	5.9 (6.5)	6.7 (8.2)	0.052
Rheumatoid factor positive	102 (90.3)	47 (90.4)	8 (88.9)	47 (90.4)	0
Anti-CCP antibody positive	98 (86.7)	46 (88.5)	6 (66.7)	46 (88.5)	0
CRP, mean (SD), mg/L	13.9 (27.8)	15.2 (31.6)	8.6 (13.6)	13.5 (25.9)	0.058
DAS28-CRP, mean (SD)	5.0 (1.0)	5.0 (1.1)	4.8 (1.0)	5.0 (1.0)	0
TJC (68 assessed), mean (SD)	19.1 (11.9)	18.8 (12.3)	17.3 (8.2)	19.7 (12.1)	0.074
SJC (66 assessed), mean (SD)	11.1 (7.9)	11.3 (7.9)	8.4 (5.1)	11.4 (8.3)	0.012
TJC (28 assessed), mean (SD)	12.5 (7.0)	12.3 (7.3)	12.6 (6.8)	12.7 (6.7)	0.057
SJC (28 assessed), mean (SD)	8.9 (5.4)	9.0 (5.7)	7.6 (5.5)	9.1 (5.2)	0.018
HAQ-DI score, mean (SD)	1.1 (0.6)	1.1 (0.7)	1.2 (0.6)	1.1 (0.6)	0
CDAI score, mean (SD)	30.8 (12.9)	30.9 (13.8)	29.0 (12.6)	30.9 (12.2)	0
SDAI score, mean (SD)	32.1 (13.3)	32.4 (14.1)	29.8 (12.7)	32.2 (12.8)	0.015
Physician's global assessment of disease activity, mean (SD)	50.6 (18.3)	52.5 (18.8)	46.1 (17.8)	49.4 (17.9)	0.169
Patient's global assessment of disease activity, mean (SD)	43.0 (26.1)	43.6 (27.1)	42.3 (26.8)	42.6 (25.5)	0.038
Patient's assessment of pain, mean (SD)	52.3 (25.8)	52.6 (26.3)	50.3 (24.4)	52.3 (25.9)	0.012
FACIT-F, mean (SD)	32.4 (12.2)	35.3 (12.3)	32.6 (9.8)	29.4 (11.9)	0.488

SD = standard deviation; y = year; kg = kilogram; m = meter; RA = rheumatoid arthritis; CCP = cyclic citrullinated peptide; CRP = C-reactive protein; DAS28 = disease activity score in 28 joints; TJC = tender joint count; SJC = swollen joint count; HAQ-DI = Health Assessment Questionnaire-Disability Index; SDAI = Simple Disease Activity Index; CDAI = Clinical Disease Activity Index; FACIT-F = Functional Assessment of Chronic Illness Therapy–Fatigue.

[a]SMD = standardized mean difference for Unilateral Active Stimulation vs Sham Stimulation.

Table 2. Efficacy results in the intent-to-treat population after 12 weeks of treatment.

	Active Stimulation			Difference vs Sham		*P* Value for Active Stimulation	
Endpoint	Unilateral (*n* = 52)	Bilateral (*n* = 9)	Sham (*n* = 52)	Unilateral (*n* = 52)	Bilateral (*n* = 9)	Unilateral (*n* = 52)	Bilateral (*n* = 9)
ACR20, No. (%)	13 (25.0)	4 (44.4)	14 (26.9)	-1.9 (-18.8 to 14.9)[a]	17.5 (-18.06 to 51.38)[a]	0.823	0.429
ACR50, No. (%)	7 (13.5)	1 (11.1)	4 (7.7)	5.8 (-14.3 to 25.5)[a]	3.4 (-18.4 to 25.2)[a]	0.526	0.730
ACR70, No. (%)	3 (5.8)	1 (11.1)	2 (3.8)	1.9 (-18.1 to 21.8)[a]	7.3 (-13.9 to 28.5)[a]	>0.999	0.352
DAS28-CRP							
Mean (SD)	4.00 (1.28)	3.73 (1.20)	4.20 (1.25)				
LS mean change from baseline (SE)	-0.95 (0.16)	-1.18 (0.38)	-0.66 (0.16)	-0.29 (0.23)[b]	-0.52 (0.41)[b]	0.201	0.207
DAS28-CRP < 2.6, No. (%)	6 (11.5)	1 (11.1)	4 (7.7)	3.8 (-16.2 to 23.7)[a]	3.4 (-18.4 to 25.2)[a]	0.741	0.730
CDAI							
Mean (SD)	19.75 (13.09)	16.39 (13.96)	21.20 (13.40)				
LS mean change from baseline (SE)	-10.11 (1.70)	-13.66 (4.06)	-8.02 (1.67)	-2.09 (2.38)[b]	-5.64 (4.39)[b]	0.381	0.202
SDAI							
Mean (SD)	20.86 (13.51)	17.27 (13.97)	23.18 (15.96)				
LS mean change from baseline (SE)	-10.77 (1.85)	-13.86 (4.38)	-7.01 (1.81)	-3.76 (2.58)[b]	-6.85 (4.74)[b]	0.149	0.152
HAQ-DI							
Mean (SD)	0.92 (0.62)	0.92 (0.53)	1.07 (0.67)				
LS mean change from baseline (SE)	-0.19 (0.06)	-0.22 (0.14)	-0.02 (0.06)	-0.17 (0.08)[b]	-0.21 (0.15)[b]	0.044	0.174
TJC68							
Mean (SD)	14.16 (15.68)	8.88 (7.24)	13.48 (14.80)				
LS mean change from baseline (SE)	-4.50 (1.71)	-9.22 (4.08)	-4.00 (1.68)	-0.49 (2.40)[b]	-5.22 (4.42)[b]	0.839	0.240
SJC66							
Mean (SD)	5.18 (6.37)	5.63 (7.21)	7.09 (6.83)				
LS mean change from baseline (SE)	-4.60 (0.82)	-3.79 (1.95)	-3.30 (0.80)	-1.30 (1.14)[b]	-0.50 (2.11)[b]	0.256	0.815
Physician's GADA, mm							
Mean (SD)	38.56 (24.36)	28.00 (18.02)	36.75 (24.64)				
LS mean change from baseline (SE)	-13.73 (3.24)	-22.82 (7.56)	-12.42 (3.20)	-1.32 (4.56)[b]	-10.40 (8.21)[b]	0.774	0.208
Patient's GADA, mm							
Mean (SD)	33.63 (27.73)	25.88 (18.72)	38.18 (21.24)				
LS mean change from baseline (SE)	-9.45 (3.09)	-18.91 (7.21)	-4.01 (3.05)	-5.44 (4.34)[b]	-14.90 (7.83)[b]	0.213	0.060
Patient's pain assessment, mm							
Mean (SD)	36.58 (28.30)	35.13 (21.38)	43.95 (25.51)				
LS mean change from baseline (SE)	-16.67 (3.85)	-18.06 (8.99)	-8.33 (3.80)	-8.34 (5.41)[b]	-9.73 (9.76)[b]	0.126	0.321
CRP, mg/L							
Mean (SD)	9.57 (10.81)	8.79 (7.90)	19.80 (59.89)				
LS mean change from baseline (SE)	-4.14 (6.23)	-4.57 (14.69)	7.35 (6.12)	-11.49 (8.73)[b]	-11.92 (15.91)[b]	0.192	0.456

ACR = American College of Rheumatology; DAS28 = disease activity score in 28 joints; CRP = C-reactive protein; SD = standard deviation; LS = least squares; SE = standard error; CDAI = Clinical Disease Activity Index; SDAI = Simple Disease Activity Index; HAQ-DI = Health Assessment Questionnaire-Disability Index; TJC = tender joint count; SJC = swollen joint count; GADA = global assessment of disease activity.
[a]Percentage difference (95% CI).
[b]LS mean difference (SE).
For ACR20/50/70 and DAS28-CRP < 2.6, non-responder imputation was used. For all other endpoints, the analysis was based on a mixed model for repeated measures with fixed effects for treatment, visit, and treatment-by-visit interaction and baseline value as a covariate with no imputation for missing data.

Disclosure: M. Baker: Mobility Bio, 8, Nēsos, 2; **S. Kavanagh**: Karuna Therapeutics, 2, Nēsos, 7, PharPoint Research, 2, UCB, 2, Worldwide Clinical Trials, 2; **S. Cohen**: AbbVie, 2, 5, Aclaris, 2, Amgen, 5, Astellas, 5, Bristol-Myers Squibb (BMS), 2, 5, Eli Lilly, 2, 5, Galvani, 2, Genentech, 5, Gilead, 2, 5, Janssen, 5, Novartis, 5, Pfizer, 2, 5, Roche, 5, Sandoz, 5, Sonoma Therapeutics, 2, UCB, 2; **A. Matsumoto**: AbbVie, 5, Amgen, 5, Bristol-Myers Squibb (BMS), 5, Eli Lilly, 5, Gilead, 5, GlaxoSmithKlein (GSK), 5, Horizon, 5, Janssen, 5, Nēsos, 5, Novartis, 5, Pfizer, 5, Scipher, 2, UCB, 5; **A. Dikranian**: AbbVie, 2, 6, Amgen, 6, Exagen, 2, Mallinckrodt, 6, Pfizer, 6, Sanofi-Genzyme, 6, Scipher, 2; **J. Tesser**: AbbVie, 2, 5, 6, Alpine, 5, Amgen, 2, 5, 6, Anthrosi Therapeutics, 5, AstraZeneca, 2, 6, Aurinia, 2, 6, Bendcare, 5, Biogen, 5, Boehringer Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, 6, Celgene, 5, Corevitas, 5, CSL Behring, 5, DRL, 5, Eli Lilly, 2, 5, 6, Emerald, 5, Exagen, 5, Genentech, 5, 6, Gilead, 5, GlaxoSmithKlein (GSK), 2, 6, Global Health Living Foundation, 5, Horizon, 5, Janssen, 2, 5, 6, Kolon TissueGene, 5, Mitsubishi, 5, Nēsos, 5, Novartis, 2, Organogenesis, 5, Pfizer, 2, 5, 6, Sanofi-Genzyme, 2, 6, Sanumen/Biosplice, 2, 5, Selecta, 5, Setpoint, 5, Sun Pharma, 5, Takeda, 5, UCB, 2; **A. Kivitz**: AbbVie, 6, Amgen, 6, 11, Chemocentryx, 1, Eli Lilly, 6, Fresenius Kabi, 2, Genzyme, 2, Gilead, 2, 11, GlaxoSmithKlein (GSK), 2, 6, 11, Grunenthal, 2, Horizon, 1, 2, Janssen, 1, 2, Novartis, 4, 11, Pfizer, 2, 6, 11, Selecta, 2, Synact, 2, Takeda, 2, UCB, 1, 6; **K. Alataris**: Nēsos, 3, 11; **M. Genovese**: Gilead, 3, 11, Nēsos, 2, 11, Setpoint, 2, 5.

Abstract Number: 0838

Infusion of Etanercept into the Peripheral Lymphatics Significantly Reduces Disease Activity in Rheumatoid Arthritis Patients with Inadequate Response to Subcutaneous Injections

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: RA – Treatments I: Novel RA Treatments & Mechanisms of Action

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: The lymphatic system serves as a conduit for transporting immune cells and inflammatory molecules present in arthritic joints to lymph nodes (LN), playing a critical role in the pathology of RA[1], yet all bDMARDs are dosed systemically potentially limiting the delivery to the target site of action. Therefore, targeting bDMARDs, like etanercept, to joint draining lymphatics could increase neutralization of inflammatory molecules and reduce unwanted immune cell activation that propagates the inflammatory cascade in RA. Nanotopography-microneedles (NTM) have previously been shown to increase the infusion of etanercept into the peripheral lymphatics and draining LNs in collagen-induced arthritic rats[2]. Here we report results from a 10-patient Phase 1b clinical trial in RA patients with an inadequate response to 50 mg etanercept SC injections who were switched to 25 mg peripheral lymphatic infusions of etanercept via the NTM device. All patients had been on SC injections of etanercept for more than 3 months prior to the study.

Methods: The NTM device was applied to the dorsal forearm and 25 mg of etanercept was infused for 1.25 hours. Once weekly dosing was performed for the first 12 weeks, followed by biweekly and monthly dosing to explore reduced dose frequency in responding patients for a total of 36 weeks. The device was alternated between the left and right dorsal forearm every other dose. Lymphatic imaging was conducted using Near-Infrared Fluorescence with indocyanine green dye[2]to measure lymphatic pump rates before and after etanercept lymphatic infusions.

Results: Switching patients from weekly 50 mg SC injections to 25 mg NTM infusions significantly reduced global disease activity without drug delivery-related immune responses. DAS28(CRP) scores were reduced from 5.40 ± 0.16 to 3.55 ± 0.21 and Patient Global Assessment of Disease Activity and Pain decreased by 66% and 77%, respectively, in the first 12 weeks and remained stable as dosing frequency was reduced to biweekly and monthly dosing (Figure 1). SJC and TJC were concomitantly decreased and remained stable (Figure 1). Lymphatic pumping rates increased from 1.0 ± 0.2 to 2.9 ± 0.3 pumps/minute after 12 weeks and TNFα levels initially increased and were significantly reduced by week 36 (Figure 2). No SAEs were reported, and primary AEs consisted of mild erythema at the NTM infusion site.

Conclusion: The NTM device effectively infused etanercept into the peripheral lymphatics that drain to the LN. The NTM device was well accepted by all patients with an application pain rating of 3.8 ± 3.6 mm on a 100 mm VAS scale. DAS28(CRP) scores, 28TJC and 28SJC, and Global Disease Activity and Pain were improved in all patients infused with the NTM device at half the SC injection dose administered weekly, biweekly, and monthly. These results suggest that administering TNFα inhibitors to arthritic joint draining LN may reduce dose frequency and improve both TNFα neutralization and impaired lymphatic function, and reduce unwanted immune cell activation that contributes to the inflammatory cascade in RA.

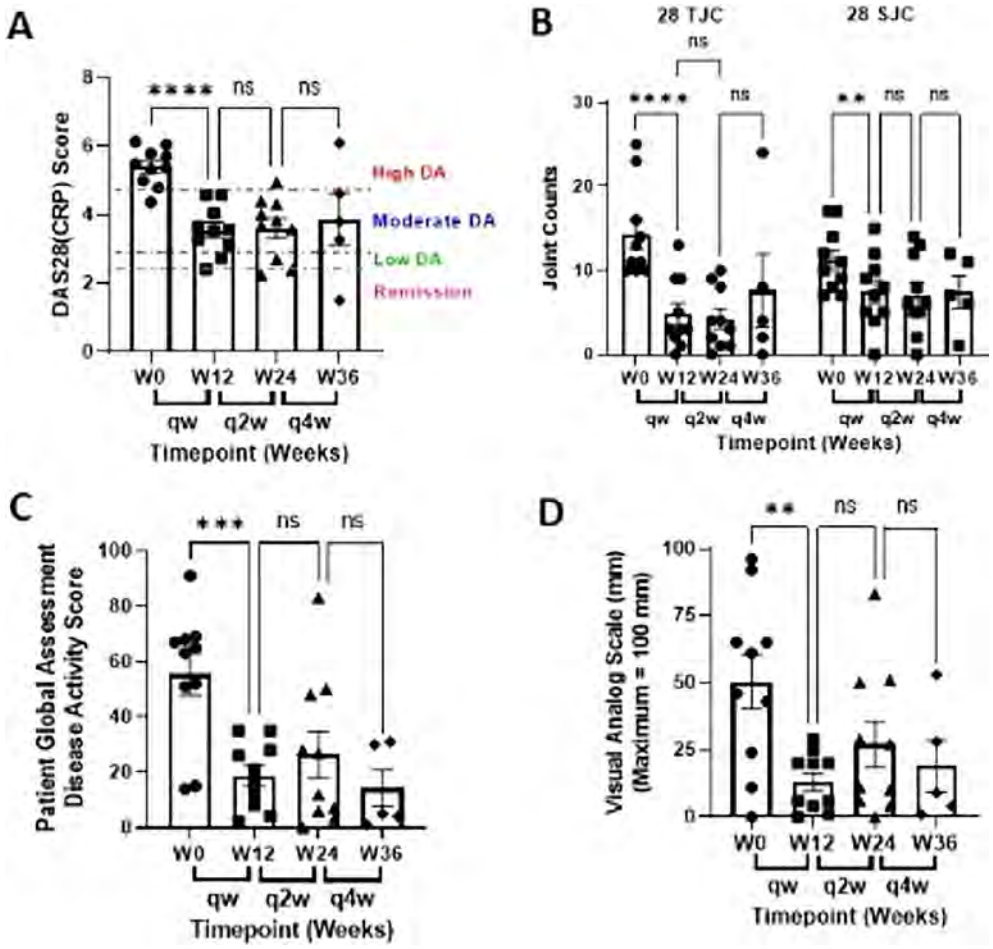

Figure 1: Disease Activity Scoring and Assessments in patients treated using lymphatic infusion of etanercept. A) DAS28(CRP) levels at W0 (baseline), W12, W24, and W36. W0 to W12 was weekly dosing (qw), W12 to W24 was bi-weekly dosing (q2w), and W24 to W36 was monthly dosing (q4w). B) 28 Tender Joint Counts (28 TJC) and 28 Swollen Joint Counts (28 SJC). C) Patient Global Assessment of Disease Activity, and D) Patient Assessment of Pain. Data represent mean ± SEM and *p<0.0332, **p<0.0021, ***p<0.0002, ****p<0.0001, ns denotes no significance.

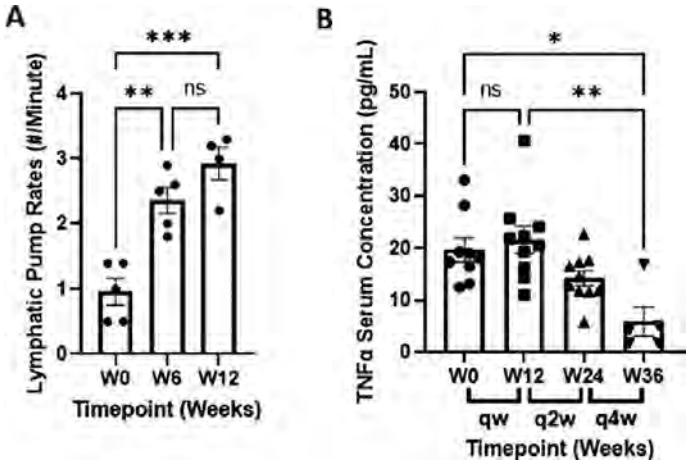

Figure 2. Lymphatic pumping rates and TNFα serum concentrations in patients treated using lymphatic infusion of etanercept. A) Lymphatic pump rates were measured by delivering ICG via the NTM device and performing visual inspection of lymphatic vessels and pumping at W0, W6, and W12. B) TNFα concentrations were measured at W0, W12, W24, and W36. W0 to W12 was weekly dosing (qw), W12 to W24 was bi-weekly dosing (q2w), and W24 to W36 was monthly dosing (q4w). Data represent mean ± SEM and *p<0.0332, **p<0.0021, ***p<0.0002, ****p<0.0001, ns denotes no significance.

1.Yousef, M et al.: J Pharm Pharm Sci 2021; 24: 533-47
2. Aldrich, MB et al.: Arth Res Ther 2017; 19:1–13

Disclosure: R. Ross: Sorrento Therapeutics, 3; **V. Strand**: Abbvie, 2, Alpine Immune Sciences, 2, Amgen, 2, Arena, 2, AstraZeneca, 2, Bayer, 2, Biosplice, 2, Bioventus, 2, Blackrock, 2, 2, BMS, 2, Boehringer Ingelheim, 2, Celltrion, 2, Chemocentryx, 2, EMD Serono, 2, Equillium, 2, Ermium, 2, Eupraxia Pharmaceuticals, 2, Flexion, 2, Galapagos, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon, 2, Ichnos, 2, Inmedix, 2, Janssen, 2, Kiniksa, 2, 2, Kypha, 2, Lilly, 2, Merck, 2, MiMedx, 2, Novartis, 2, Omeros, 2, Pfizer, 2, Regeneron, 2, Rheos, 2, R-Pharm, 2, Samsung, 2, Sandoz, 2, Sanofi, 2, Scipher, 2, Setpoint, 2, Sorrento, 2, Spherix, 2, Tonix, 2, UCB, 2, Urica, 2; **R. Querubin**: Sorrento Therapeutics, 12, Principal Investigator; **J. Goldman**: Sorrento Therapeutics, 2; **R. Leff**: Kezar Life Sciences, 2, 8, 11, Sorrento Therapeutics, 7; **A. Melson**: Sorrento Therapeutics, 3; **P. Roerig**: Sorrento Therapeutics, 7; **A. Smith**: Sorrento Therapeutics, 7.

Abstract Number: 0839

Efficacy and Safety of Nipocalimab in Patients with Moderate to Severe Active Rheumatoid Arthritis (RA): The Multicenter, Randomized, Double-blinded, Placebo-controlled Phase 2a IRIS-RA Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Abstracts: RA – Treatments I: Novel RA Treatments & Mechanisms of Action
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: RA is a chronic inflammatory disease associated with autoantibodies. Despite the use of targeted therapies, up to half of patients fail to achieve remission or low disease activity (LDA). Anti-citrullinated protein antibodies (ACPAs), key autoantibodies that predict progression of joint destruction in RA, are largely an immunoglobulin G (IgG)

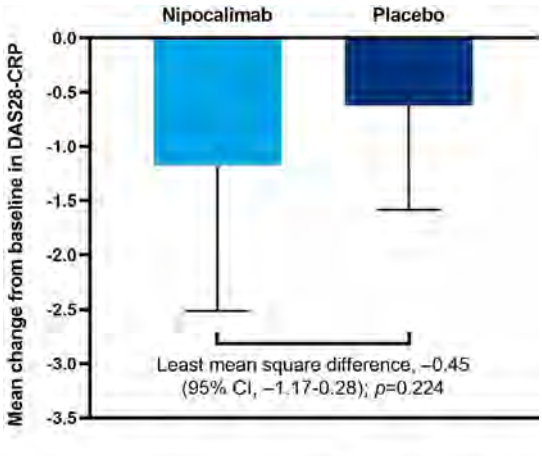

Figure 1. Change from Baseline in DAS28 (CRP) Score after 12 Weeks

isotype. Nipocalimab is a high affinity, fully human, IgG1 monoclonal antibody that is designed to selectively block the neonatal Fc receptor (FcRn), preventing recirculation and thereby lowering IgG levels, potentially including ACPAs and other pathogenic antibodies. In this phase 2a proof-of-concept study (IRIS-RA; NCT04991753), we report the efficacy and safety of nipocalimab in patients with moderate to severe, active RA.

Methods: Eligible adult patients with moderate to severe RA (≥6 swollen/tender joints), positive for ACPA or rheumatoid factor, and ≥1 advanced therapies, were randomized 3:2 to receive intravenous 15 mg/kg nipocalimab or placebo every 2 weeks for 10 weeks. The primary endpoint was the change from baseline in the Disease Activity Score 28 using C-reactive protein (DAS28-CRP) at Week 12. Secondary endpoints included the proportion of patients who achieved ACR20, ACR50, ACR70, and ACR90 responses, DAS28-CRP remission, and change from baseline in Health Assessment Questionnaire – Disability Index (HAQ-DI) at Week 12.

Table 1. Number of Patients Who Achieved ACR20, ACR50, ACR70, and ACR90 Responses at Week 12 Using CMH

Response, n (%)	Nipocalimab (n = 33)	Placebo (n = 20)	Treatment difference[a], % (95% CI)	*P* value
ACR20	15 (45.5)	4 (20.0)	27.0 (3.2-50.9)	0.055
ACR50	5 (15.2)	1 (5.0)	8.6 (–6.7-23.8)	0.390[b]
ACR70	4 (12.1)	0	11.6 (0.9-22.3)	0.285[b]
ACR90	2 (6.1)	0	5.8 (–2.0-13.6)	0.521[b]

[a]The treatment difference between nipocalimab versus placebo and the CIs was based on the Wald statistic with the CMH weight.
[b]The *p* value was based on the CMH chi-square test, stratified by random stratification factor; baseline MTX use. The Mantel Fleiss criterion was not satisfied with the indicated *p* values and was therefore based on the Fisher's exact test.
ACR, American College of Rheumatology; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; MTX, methotrexate.

Table 2. Overall Summary of TEAEs

Patients, n (%)	Nipocalimab (n = 33)	Placebo (n = 20)
Patients with ≥1 TEAE	27 (81.8)	12 (60.0)
Related TEAEs[a]	12 (36.4)	3 (15.0)
Most common (≥10%) TEAEs		
Rheumatoid arthritis	9 (27.3)	6 (30.0)
Headache	4 (12.1)	1 (5.0)
COVID-19	4 (12.1)	0
Serious TEAEs	3 (9.1)	0
Related serious TEAEs	1 (3.0)	0
Burn infection	1 (3.0)	0
Infusion-related reaction	1 (3.0)	0
Deep vein thrombosis	1 (3.0)	0
TEAEs leading to treatment discontinuation	6 (18.2)	6 (30.0)
Related TEAEs leading to treatment discontinuation[a]	1 (3.0)	1 (5.0)
Infections and infestations	13 (39.4)	5 (25.0)
Related infections[a,b]	0	0
Burn infections[b]	1 (3.0)	0
Infusion reactions[c]	4 (12.1)	1 (5.0)
Infusion site reactions[b]	2 (6.1)	1 (5.0)
Hypersensitivity	3 (9.1)	0
Hypoalbuminemia (<20 g/L)	0	0
Markedly abnormal cholesterol	6 (18.2)	3 (15)

[a]Assessed by the investigator as related to study treatment.
[b]Assessed by the investigator.
[c]Temporally associated with infusion (during or within 1 hour of infusion).
TEAE, treatment-emergent adverse event.

Results: In total, 53 patients were enrolled (nipocalimab, n=33; placebo, n=20). Most patients were female (67.9%) and white (90.6%) with a median age of 59 (range, 26-74) years. Demographic and baseline disease characteristics were comparable between groups except higher CRP in placebo. At Week 12, patients treated with nipocalimab showed a numerically greater mean (standard deviation [SD]) change in DAS28-CRP score compared to the placebo group (–1.17 [1.34] vs –0.62 [0.96]; mean difference [95% confidence interval], –0.45 [–1.17-0.28]; p=0.224); **Figure 1**). A numerically higher proportion of patients achieved ACR20, ACR50, ACR70, and ACR90 responses compared to placebo (**Table 1**). In the nipocalimab group, 7 (21.2%) patients achieved DAS28-CRP remission compared to 2 (10.0%) patients in the placebo group (treatment difference, 9.9% [–9.5-29.3%]; p=0.456). Similarly, patients in the nipocalimab group had a numerically greater mean (SD) improvement in HAQ-DI score (–0.27 [0.55] vs –0.11 [0.36], respectively). Median post-dose serum nipocalimab concentrations ranged from 411.0-426.0 μg/mL across Weeks 0, 2, and 8. The proportion of patients with treatment-emergent adverse events (TEAEs) were 81.8% vs 60.0% in the nipocalimab vs placebo groups (**Table 2**). In the nipocalimab group, 3 serious TEAEs were reported, including burn infection, infusion-related reaction, and deep-vein thrombosis. There were no TEAEs that led to death.

Conclusion: Treatment with nipocalimab resulted in consistent and numerically higher improvements across ACR20, ACR50, ACR70, and ACR90 responses, as well as DAS28-CRP, DAS28-CRP remission, and HAQ-DI, with acceptable safety profile. Nipocalimab showed activity in patients with moderate to severe RA and warrants further investigation to understand the predictors of nipocalimab response.

Disclosure: P. Taylor: AbbVie, 2, Biogen, 2, Eli Lilly, 2, Fresenius, 2, Galapagos, 2, 5, Gilead Sciences, 2, GSK, 2, Janssen, 2, Nordic Pharma, 2, Pfizer Inc, 2, Sanofi, 2, UCB, 2; **G. Schett**: None; **F. Ibrahim**: Janssen, 3, Johnson & Johnson, 11; **B. Zhou**: Janssen, 3, Johnson & Johnson, 11; **J. Leu**: Janssen, 3, Johnson & Johnson, 11; **S. Liva**: Janssen, 3, Johnson & Johnson, 11; **Q. Wang**: Janssen, 3, Johnson & Johnson, 11; **R. Cella**: Janssen, 3, Johnson & Johnson, 11; **C. Karyekar**: Janssen, 3, Johnson & Johnson, 11; **K. Fei**: Janssen, 3, Johnson & Johnson, 11.

Abstract Number: 0840

Head-to-Head Comparison of TLL-018 and Tofacitinib in Patients with Active Rheumatoid Arthritis: Final Results from a Phase IIa Study

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: RA – Treatments I: Novel RA Treatments & Mechanisms of Action

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: None of the currently approved treatments for rheumatoid arthritis (RA) can achieve ACR50 in >50% of the patients, and 5 – 20% of the RA patients are considered "difficult to treat", failing ≥2 targeted therapies. TLL-018 is a highly selective dual JAK1/TYK2 inhibitor. Its TYK2 activity might contribute to efficacy in RA patients. The objective is to compare efficacy of TLL-018 with tofacitinib in RA patients.

Methods: 101 patients with moderate-to-severe active RA who had inadequate response or were intolerant to methotrexate were randomized (1:1:1:1 ratio) to receive twice-daily oral TLL-018 10mg, 20mg, 30mg or tofacitinib 5mg. After 12-weeks of treatment, patients who achieved ACR50 continue the same treatment, and those who didn't change treatment as follows: patients on tofacitinib and TLL-018 10mg change to TLL-018 20mg; patients on 20mg and 30mg change to or continue 30mg TLL-018 (Figure 1). The Primary endpoint is the proportion of patients achieving ACR50 at Week 12. Secondary endpoints include the proportion of patients achieving DAS28-CRP < 2.6, ACR20, ACR70 at all scheduled time points, ACR50 at scheduled time points exclude week 12, CDAI and other parameters at 12 week. Safety was assessed via adverse event (AE) and laboratory examinations.

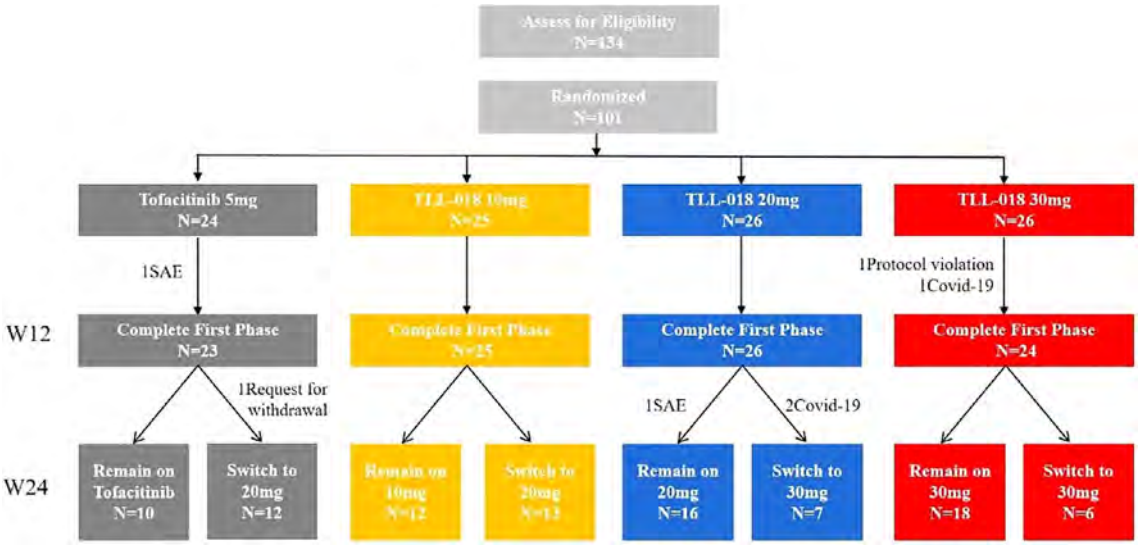

Figure 1: Trial design.

Table 1: Efficacy, number (%) of patients who achieved ACR50.

Cohort		Tofacitinib		TLL-018		TLL-018		TLL-018	
	Dose	5mg BID		10mg BID		20mg BID		30mg BID	
	Baseline	(N=24)		(N=25)		(N=26)		(N=26)	
Week 4	n (nmiss)	24 (0)		25 (0)		25 (1)		21 (5)	
	ACR50	5 (20.8)		2 (8.0)		4 (16.0)		5 (23.8)	
Week 8	n (nmiss)	24 (0)		25 (0)		25 (1)		24 (2)	
	ACR50	7 (29.2)		8 (32.0)		9 (36.0)		9 (37.5)	
Week 12	n (nmiss)	24 (0)		25 (0)		26 (0)		25 (1)	
	ACR50	10 (41.7)		12 (48.0)		17 (65.4)		18 (72.0)	
		Remain on Tofa (N=10)	Switch to 20mg (N=13)	Remain on 10mg (N=12)	Switch to 20mg (N=13)	Remain on 20mg (N=17)	Switch to 30mg (N=9)	Remain on 30mg (N=18)	Remain on 30mg (N=6)
Week 16	n (nmiss)	10 (0)	12 (1)	11 (1)	13 (0)	15 (2)	7 (0)	17 (1)	3 (3)
	ACR50	10 (100.0)	5 (41.7)	10 (90.9)	4 (30.8)	12 (80.0)	4 (57.1)	17 (100.0)	3 (100.0)
Week 20	n (nmiss)	10 (0)	12 (1)	12 (0)	13 (0)	14 (3)	7 (0)	17 (1)	5 (1)
	ACR50	9 (90.0)	9 (75.0)	11 (91.7)	4 (30.8)	11 (78.6)	2 (28.6)	16 (94.1)	3 (60.0)
Week 24	n (nmiss)	10 (0)	12 (1)	12 (0)	13 (0)	15 (2)	7 (0)	18 (0)	6 (0)
	ACR50	8 (80.0)	10 (83.3)	11 (91.7)	5 (38.5)	12 (80.0)	3 (42.9)	18 (100.0)	4 (66.7)

Table 2: Safety, AEs of interest.

	Tofacitinib 5mg BID (N=24)	TLL-018 10mg BID (N=25)	TLL-018 20mg BID (N=26)	TLL-018 30mg BID (N=26)
ADR n (%)	19 (79.2)	16 (64.0)	23 (88.5)	20 (76.9)
Lipids abnormalities	10 (41.7)	10 (40.0)	13 (50.0)	12 (46.2)
Upper respiratory tract infection	2 (8.3)	3 (12.0)	3 (11.5)	3 (11.5)
Urinary tract infection	0	3 (12.0)	2 (7.7)	0
Herpes zoster	0	0	2 (7.7)	0
GI system	4 (16.7)	0	2 (7.7)	3 (11.5)
Peripheral edema	1 (4.2)	1 (4.0)	1 (3.8)	2 (7.7)
Anemia	1 (4.2)	0	3 (11.5)	1 (3.8)

Results: 101 patients were randomized, ~50% of them also had prior bDMARDs and ~30% had prior JAK inhibitors, but the responses to those treatments were unknown. Demographics and baseline disease characteristics were balanced across treatment arms. At week 12, ACR50 response rates in TLL-018 treated groups (10mg, 20mg and 30mg, 48.0%, 65.4%, 72.0%, respectively) were higher than that for tofacitinib (41.7%) (Table 1). TLL-018 20 and 30mg were statistically superior to tofacitinib ($p < 0.05$). Proportions of patients achieving clinical remission (DAS28-CRP< 2.6) at week 12 were 39.1%, 37.5%, 57.2% and 17.4% at week 12 for the 10, 20, 30mg TLL-018 and tofacitinib, respectively. TLL-018 20mg dramatically improved responses in patients who didn't achieve ACR50 on tofacitinib at week 12.

The most frequently reported treatment-emergent AEs were hyperlipidemia and respiratory infection in TLL-018 or tofacitinib-treated patients(Table 2). There were one case of malignancy in tofacitinib treatment group, and two cases of herpes zoster in the 20mg group. No death, venous thromboembolism or major adverse cardiovascular event was observed in the study.

Conclusion: TLL-018 20 and 30mg demonstrated superior efficacy over tofacitinib in RA patients, suggesting that inhibition of TYK2, in addition to JAK1, enhances efficacy. TLL-018 was well tolerated with most AEs being Grade 1 or 2 as expected from this class of compounds. No unexpected safety concerns were observed in the study. TLL-018 20 and/or 30mg BID warrants further studies in "difficult to treat" RA patients.

Disclosure: X. Zeng: None; **c. wu**: None; **J. Hu**: None; **S. LIU**: None; **Z. Jiang**: None; **J. Li**: None; **X. Wang**: None; **J. Liu**: None; **C. Yuan**: Hangzhou Highlightll Pharmaceutical Co., Ltd, 3; **G. Yang**: Hangzhou Highlightll Pharmaceutical Co., Ltd, 3; **C. Liang**: Hangzhou Highlightll Pharmaceutical Co., Ltd, 4.

Abstract Number: 0841

Spondyloarthritis Research and Treatment Network (SPARTAN) Draft Referral Recommendations for Axial Spondyloarthritis

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SESSION INFORMATION

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Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: In the United States (US), the diagnosis of axial spondyloarthritis (axSpA) continues to be delayed by an average of 10 years from symptom onset. This diagnostic delay prevents effective management that controls disease activity, and maintains mobility, function, and quality of life. We developed the first SPARTAN recommendations for the referral of adults with chronic back pain to a rheumatologist for evaluation of axSpA by convening a multidisciplinary group comprised of clinicians that manage patients with back pain and conditions related to axSpA, expert rheumatologists and axSpA patient partners.

Methods: A systematic literature review (SLR) was conducted including studies through March 2022 to address individual clinical, laboratory, and imaging features associated with diagnosis or classification of axSpA. Sensitivity, specificity, positive likelihood ratios (LR+), and positive predictive values for each axSpA feature were calculated. At the 2022 SPARTAN annual meeting, members were asked the minimal probability of axSpA diagnosis that was appropriate for an adult with chronic back pain to be referred to a rheumatologist. In a Delphi exercise, members were asked to review test characteristics for each axSpA feature and to vote whether to include or exclude that feature in draft referral recommendations. Features gaining 70% consensus for inclusion were carried forward while those with consensus to exclude were omitted. Features that did not gain consensus for inclusion/exclusion were evaluated using discrete choice experiments (DCE). LR+ of individual axSpA features were used to calculate the probability of axSpA for combinations of features to develop draft referral recommendation for expert and stakeholder consideration. Draft recommendations in the form of a 'major and minor criteria', and a 'points-based' system were discussed and put to vote by SPARTAN members at the 2023 annual SPARTAN meeting.

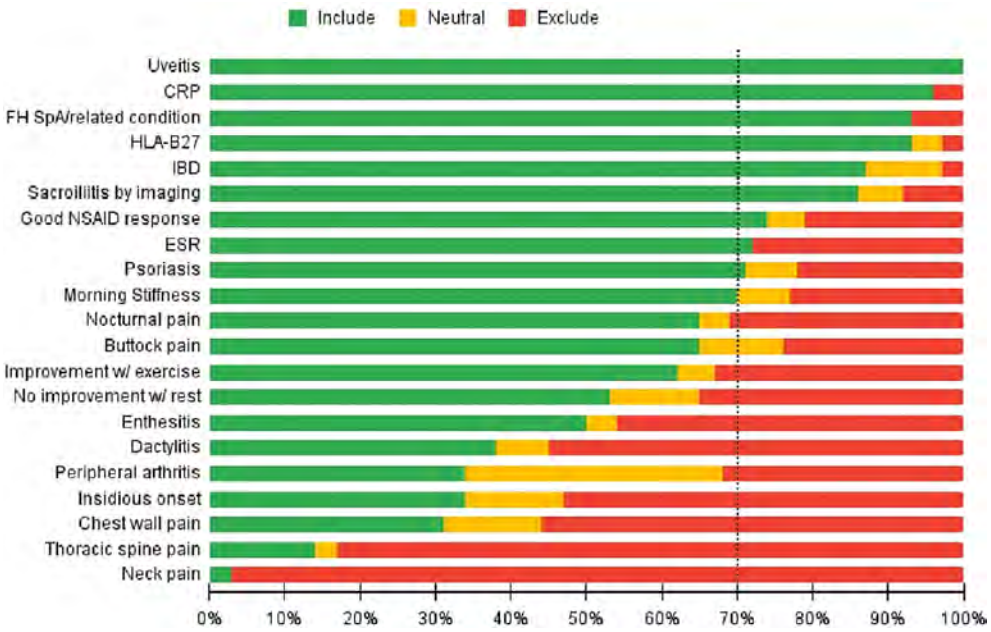

Figure 1. Delphi exercise results: AxSpA experts' votes for inclusion or exclusion of features in referral recommendations. Consensus was considered present if >70% voted to include or exclude.

Refer adults with chronic (>3 months) back/hip/buttock pain with onset before age 45 and a score of 3 or more	Points
X ray or MRI sacroiliitis	3
Elevated ESR or CRP	2
HLA-B27+	2
Uveitis	2
Inflammatory bowel disease	1
Psoriasis	1
Back pain has a good response to NSAIDs	1
Back pain improvement with exercise and not with rest	1
Alternating buttock pain	1
Family history of axial spondyloarthritis, uveitis, psoriasis or inflammatory bowel disease	1
Total	**Refer if score of 3 or more**

Figure 2. SPARTAN Draft Referral Recommendations for Axial Spondyloarthritis

Results: SLR uncovered 28 features associated with axSpA. LR+ ranged from 0.5 to 10. A probability of 33% or higher was considered adequate for referral by 90% of SPARTAN members. The Delphi process resulted in consensus to include: uveitis, elevated ESR or CRP, family history of SpA or a related condition, HLA-B27 positivity, inflammatory bowel disease (IBD), sacroiliitis by imaging, good response to NSAIDs and psoriasis (Figure 1). There was consensus to exclude neck pain and thoracic spine pain. DCE-derived relative importance values of several features were approximately half as important as uveitis. Eighty-six percent of SPARTAN members preferred a point-based referral strategy and 89% voted in favor of its adoption (Figure 2).

Conclusion: SPARTAN members and a diverse stakeholder group used a data-driven process to develop the first draft SPARTAN recommendations for referral of adults with chronic back pain to a rheumatologist for evaluation of axSpA. Validation is needed to determine if application of these recommendations leads to approximately 33% probability of axSpA among those referred, and ultimately whether diagnostic delay of axSpA is reduced through their implementation.

Disclosure: M. Dubreuil: Amgen, 2, Pfizer, 5, UCB Pharma, 2; **A. Danve**: Abbvie, 2, Amgen, 2, Janssen, 2, Lilly, 5, Medscape, 6, Novartis, 2, 5, Spondylitis Association of America, 5, Spondyloarthritis Research and Treatment Network, 5, UCB, 1; **S. Alexander**: None; **M. Bittar**: None; **L. Fraenkel**: None; **A. Grimshaw**: None; **A. Kumthekar**: None; **M. LaValley**: None; **J. liew**: None; **M. Magrey**: AbbVie, 2, Bristol Myers Squibb, 2, Eli Lilly, 2, Novartis, 2, Pfizer Inc, 2, UCB, 5; **V. Majithia**: AbbVie/Abbott, 2, Novartis, 2, UCB, 2; **S. Merjanah**: None; **H. Norton**: AbbVie/Abbott, 1, 5, 6, Amgen, 1, AstraZeneca, 1, Eli Lilly, 1, 5, 6, Horizon, 5, Janssen, 1, 6, Novartis, 1, 5, Pfizer, 1, 6, UCB, 1, 6; **J. Walsh**: AbbVie, 5, Amgen, 2, Eli Lilly, 2, Janssen, 2, Merck, 5, Novartis, 2, Pfizer, 2, 5, UCB Pharma, 2; **A. Deodhar**: AbbVie, 2, 5, Amgen, 2, Aurinia, 2, Bristol Myers Squibb, 2, 5, Celgene, 5, Eli Lilly, 2, 5, Janssen, 2, 6, MoonLake, 2, 5, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5.

Abstract Number: 0842

Low Rate of Switching from Nr-axSpA to r-axSpA After 10 Years of Follow up in Early Axialspondyloarthritis. Data from DESIR Cohort

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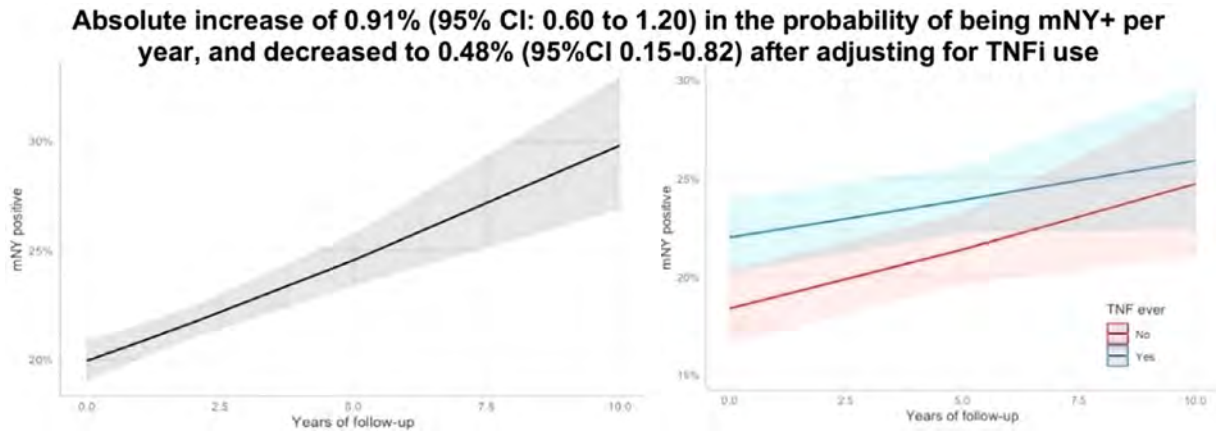
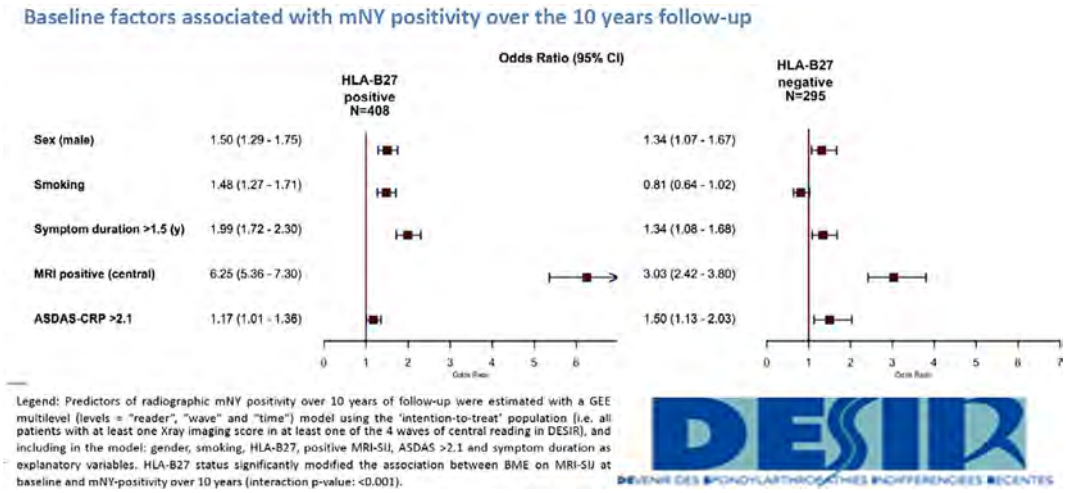
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes I: AxSpA
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: The objective of this analysis was to evaluate the proportion of patients switching from non-radiographic axSpA (nr-axSpA) toradiographic axSpA (r-axSpA) after 10 years of follow-up and whether BME on MRI-SIJ at baseline is associated with the r-axSpA status over time.

Methods: Patients with ≤3 years axSpA onset from the DESIR cohort were included. The radiographic status of the patients (r-axSpA versus nr-axSpA) was based on the mNY criteria (i.e. at least a bilateral grade 2 or a unilateral grade 3 on pelvic radiographs according to 2 out of 3 central readers). BME on MRI-SIJ was defined as positive ASAS definition according to 2 out 3 central readers at baseline. Information on mNY criteria was obtained in four reading waves (0 to 10y). Images were scored by 3 trained central readers, all of them unaware of the chronology of the images and the results of the other modality. A "progressor" was defined as a patient switching from nr-axSpA to r-axSpA. A "regressor" was defined as a patient switching from r-axSpA to nr-axSpA. The % of mNY net progressors (i.e. number of "progressors" minus number of "regressors" divided by the total number of patients) was assessed in "completers" (i.e., with pelvic radiographs available at BL and 10y in wave 4). A sensitivity analysis was conducted using a multilevel GEE model ('integrated analysis') that included all waves from all patients with at least one available mNY score from at least one reader available ("intention-to-follow" population). From this model, we estimated the absolute change per year in the percentage of mNY positive cases with and without adjusting for the use of anti-TNF drugs. Finally, the effect of BME on MRI-SIJ at baseline on mNY positivity over 10 years, adjusting for potential confounders (Figure) were evaluated in a multivariable GEE model in the "intention-to-follow" population.

Results: Completers included 299 patients (mean age 34.5Y and 48.2% males), while the intention-to-follow population included 704 participants (mean age 33.7Y and 46.2% males). In the completers, the net % of progressors (switch from nr-axSpA to r-axSpA) was 5.7%. In the intention-to-follow population, there was a 0.91% (95%CI 0.60-1.20) increase per year in the probability of being mNY-positive (i.e. a progression of 9.1% after 10Y). After adjusting for anti-TNF use, this percentage decreased to 0.48% (95%CI 0.15-0.82) per year. The HLA-B27 status modified the association between BME on MRI-SIJ at baseline and mNY-positivity over 10 years (interaction pvalue: < 0.001). BME on MRI-SIJ was associated with being mNY positive over time in both HLA-B27 positive (OR 6.25 (95%CI 5.36-7.30)) and HLA-B27 negative patients (OR 3.03 (95%CI





2.42-3.80)), but the association was stronger in the former (Figure). In addition, male sex, symptom duration >1.5Y, ASDAS >2.1 (in HLA-B27 negatives) and smoking (in HLA-B27 positives) were also associated with being mNY-positive over 10 years.

Conclusion: Patients with early axSpA have a low likelihood of changing from nr-axSpA to r-axSpA over 10 years, especially when considering the use of anti-TNF. Local inflammation on MRI-SIJ is strongly associated damage accrual in the SIJ over time, in particular in patients who are HLA-B27 positive.

Disclosure: A. Molto: None; **C. López Medina**: AbbVie, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 6, MSD, 6, Novartis, 2, 5, 6, UCB Pharma, 2, 5, 6; **M. de Hooge**: UCB, 6; **M. Van Lunteren**: None; **A. Sepriano**: None; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, Galapagos, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, UCB Pharma, 2, 5; **M. Dougados**: AbbVie, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Roche, 2, 5, UCB, 2, 5.

Abstract Number: 0843

Predictive Validity of Data-driven Definitions for Active and Structural Lesions in the SI Joints Typical for Axial SpA: A 2-year Follow-up in the SPondyloArthritis Caught Early Cohort

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes I: AxSpA

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: The Assessment of Spondyloarthritis international Society MRI (ASAS MRI) group has proposed definitions for active and structural lesions typical for axial SpA (axSpA) on SI joint MRI (MRI-SIJ), based on high specificity and positive predictive values (PPV; ≥95%) for the rheumatologist's diagnosis of axSpA (Maksymowych et al., 2021). These

cut-offs have not been validated in other cohorts nor assessed in early disease. Here, we analyze the predictive validity of the proposed cut-offs for active and structural MRI-SIJ lesions in early axSpA after 2 years follow-up.

Methods: Patients with chronic back pain (unknown origin; ≥3 months; ≤2 years; onset < 45 years) from the SpA Caught Early (SPACE) inception cohort were followed-up and diagnosed (axSpA/no axSpA) by a rheumatologist after 2 years (Marques et al., 2023). Three central readers scored baseline MRI-SIJ for bone marrow edema (BME), erosion, fat lesions, and sclerosis. Patients with a certain (level of confidence about the diagnosis ≥7) or very probable (level of confidence < 7 and a consistent diagnosis in the last 2 available visits) diagnosis were included for analysis. When data were available for ≥2 readers, the MRI SIJ were analyzed for consensus between ≥2 readers on scored lesions and each individual reader. The lesions were assessed for quadrants, consecutive slices, or combinations between different lesions (Table 1 & 2). We calculated sensitivity, specificity, PPV and negative predictive values (NPV) for each cut-off. Based on consensus, a combination of specificity ≥95% and PPV ≥95% was required for a cut-off to be considered validated. For the individual readers, a PPV of ≥94% in ≥2 readers was accepted.

Results: We analyzed 447 patients (age 30 (SD 8) years; 45% males; 66% axSpA). BME in ≥1 quadrant, or ≥2 consecutive slices met the threshold based on consensus (Table 1). BME in ≥2 quadrants or ≥2 consecutive slices met the threshold in ≥2 individual readers (Table 1 & 2). Erosions in ≥2 quadrants or ≥4 consecutive slices, and fat in ≥1 quadrant or ≥2 consecutive slices met the threshold based on consensus. Erosion in ≥3 consecutive slices met the threshold in ≥2 individual readers, and fat in ≥2 quadrants or ≥3 consecutive slices met the threshold in all individual readers. All combinations of BME-fat met the threshold based on consensus (Table 1). Combinations of BME-erosions and fat-erosion in ≥1 quadrants,

Table 1. Predictive validity of the consensus between readers for singular active and structural lesions typical in axSpA, by assessing each definition against the rheumatologist's diagnosis at 2-year follow-up.

Baseline MRI data	Total % +	axSpA at follow-up (yes/no)				Threshold consensus	Threshold 2/3 individual readers	Validated consensus & individual readers for ASAS MRI
		Sensitivity	Specificity	PPV	NPV			
BME score in ≥1 SIJ quadrants	30	44.3	97.4	97.0	47.1	✓		
BME score in ≥2 SIJ quadrants	22	32.4	99.3	99.0	42.9	✓	✓	
BME score in ≥3 SIJ quadrants	15	23.0	99.3	98.6	39.7	✓	✓	
BME score in ≥4 SIJ quadrants	10	15.2	100.0	100.0	37.6	✓	✓	✓
BME in ≥2 consecutive slices	27	39.9	98.0	97.5	45.4	✓	✓	
BME in ≥3 consecutive slices	22	32.8	98.7	98.0	42.8	✓	✓	✓
BME in ≥4 consecutive slices	18	27.7	100.0	100.0	41.4	✓	✓	
Erosion score in ≥1 SIJ quadrants	20	27.4	95.4	92.0	40.1			
Erosion score in ≥2 SIJ quadrants	9	13.2	99.3	97.5	36.9	✓	✓	
Erosion score in ≥3 SIJ quadrants	5	6.8	99.3	95.2	35.2	✓	✓	✓
Erosion score in ≥4 SIJ quadrants	2	3.4	100.0	100.0	34.6	✓	✓	
Erosion in ≥2 consecutive slices	13	17.2	96.7	91.1	37.3			✗
Erosion in ≥3 consecutive slices	7	9.8	98.7	93.5	35.8		✓	
Erosion in ≥4 consecutive slices	3	4.4	100.0	100.0	34.8	✓	✓	!
Fat lesion in ≥1 SIJ quadrants	18	25.7	97.4	95.0	40.1	✓		
Fat lesion in ≥2 SIJ quadrants	13	18.6	99.3	98.2	38.4	✓	✓	
Fat lesion in ≥3 SIJ quadrants	9	12.8	99.3	97.4	36.8	✓	✓	
Fat lesion in ≥4 SIJ quadrants	2	7.8	100.0	100.0	35.6	✓	✓	
Fat lesion in ≥5 SIJ quadrants	3	3.7	100.0	100.0	34.6	✓	✓	✓
Fat lesion in ≥2 consecutive slices	15	22.0	98.0	95.6	39.1	✓		
Fat lesion in ≥3 consecutive slices	11	15.5	99.3	97.9	37.5	✓	✓	✓
Fat lesion in ≥4 consecutive slices	7	10.5	99.3	96.9	36.1	✓	✓	
BME score ≥1 and erosion score ≥1	13	19.9	99.3	98.3	38.8	✓		
BME score ≥2 and/or erosion score ≥1	31	43.9	95.4	94.9	46.5			
BME score ≥2 and/or erosion score ≥2	25	37.8	99.3	99.1	44.9	✓		
BME score ≥3 and/or erosion score ≥1	27	37.8	95.4	94.1	43.9			
BME score ≥3 and/or erosion score ≥2	20	29.4	99.3	98.9	41.8	✓		
BME score ≥1 and fat lesion score ≥1	11	15.9	99.3	97.9	37.6	✓	✓	
BME score ≥2 and/or fat lesion score ≥1	32	46.3	96.7	96.5	47.9	✓		
BME score ≥2 and/or fat lesion score ≥2	29	42.6	98.7	98.4	46.7	✓	✓	
BME score ≥3 and/or fat lesion score ≥1	27	39.5	96.7	95.9	44.9	✓		
BME score ≥3 and/or fat lesion score ≥2	24	35.1	98.7	98.1	43.7	✓	✓	
Fat lesion score ≥1 and erosion score ≥1	11	16.2	100.0	100.0	37.8	✓		
Fat lesion score ≥2 and/or erosion score ≥1	23	32.4	94.7	92.3	41.7			
Fat lesion score ≥2 and/or erosion score ≥2	15	22.6	98.7	97.1	39.4	✓		
Fat lesion score ≥3 and/or erosion score ≥1	22	31.1	94.7	92.0	41.2			
Fat lesion score ≥3 and/or erosion score ≥2	13	19.3	98.7	96.6	38.4	✓		

N=447; $N_{axial\ SpA}$=296; $N_{no\ axial\ SpA}$=151. ✓ indicates that cut-off has the required specificity and positive predictive value. In de last column the symbol indicates that the consensus and individual reader assessment have validated the ASAS MRI definition (Maksymowych et al., 2021). ✗ indicates that the consensus and individual reader assessment have not validated the ASAS MRI definition (Maksymowych et al., 2021). ! indicates that we propose this cut-off instead of a cut-off proposed by the ASAS MRI group (Maksymowych et al., 2021). The yellow color indicates a definition was proposed by the ASAS MRI group (Maksymowych et al., 2021). The green color emphasizes validated cut-offs. AxSpA: axial spondyloarthritis; BME: bone marrow edema; NPV: negative predictive value; PPV: positive predictive value.

Table 2. Predictive validity of the consensus between readers for combinations of active and structural lesions typical in axSpA. by assessing each definition against the rheumatologist's diagnosis at 2-year follow-up.

Baseline MRI data	Specificity			PPV			Threshold 2/3 individual readers
	Reader 1	Reader 2	Reader 3	Reader 1	Reader 2	Reader 3	
BME score in ≥1 SIJ quadrants	95.4	89.4	92.7	95.1	90.1	92.9	
BME score in ≥2 SIJ quadrants	99.3	98.7	98.7	98.9	98.2	98.3	✓
BME score in ≥3 SIJ quadrants	99.3	99.3	99.3	98.6	98.8	98.6	✓
BME score in ≥4 SIJ quadrants	100.0	100.0	100.0	100.0	100.0	100.0	✓
BME in ≥2 consecutive slices	98.0	95.4	94.7	97.3	95.0	94.3	✓
BME in ≥3 consecutive slices	98.7	97.4	98.7	97.8	96.7	98.1	✓
BME in ≥4 consecutive slices	100.0	99.3	100.0	100.0	98.9	100.0	✓
Erosion score in ≥1 SIJ quadrants	87.4	79.5	93.4	82.4	82.1	91.0	
Erosion score in ≥2 SIJ quadrants	99.3	90.7	98.0	96.9	87.4	95.2	✓
Erosion score in ≥3 SIJ quadrants	99.3	97.4	98.7	94.1	92.7	94.7	✓
Erosion score in ≥4 SIJ quadrants	100.0	99.3	99.3	100.0	96.4	95.5	✓
Erosion in ≥2 consecutive slices	95.4	87.4	94.7	85.4	86.4	90.8	
Erosion in ≥3 consecutive slices	99.3	96.7	96.0	95.7	94.1	87.8	✓
Erosion in ≥4 consecutive slices	100.0	98.7	99.3	100.0	96.3	94.7	✓
Fat lesion in ≥1 SIJ quadrants	92.7	92.7	95.4	89.1	90.4	90.4	
Fat lesion in ≥2 SIJ quadrants	98.0	97.4	98.0	94.7	95.2	95.0	✓
Fat lesion in ≥3 SIJ quadrants	100.0	98.7	98.7	100.0	96.6	95.2	✓
Fat lesion in ≥4 SIJ quadrants	100.0	99.3	100.0	100.0	97.4	100.0	✓
Fat lesion in ≥5 SIJ quadrants	100.0	100.0	100.0	100.0	100.0	100.0	✓
Fat lesion in ≥2 consecutive slices	95.4	94.0	96.7	90.9	91.0	92.5	
Fat lesion in ≥3 consecutive slices	98.0	96.0	98.7	94.4	92.1	96.1	✓
Fat lesion in ≥4 consecutive slices	99.3	98.7	99.3	96.4	96.3	96.3	✓

N=380; $N_{axial\ SpA}$=296; $N_{no\ axial\ SpA}$=151. The yellow color indicates a definition was proposed by the ASAS MRI group (Maksymowych et al., 2021). ✓ indicates that in ≥2 readers the cut-off has a specificity of ≥95% and positive predictive value of ≥94%. If definitions met the threshold in ≥2 readers, the readers' values are presented in blue. AxSpA: axial Spondyloarthritis; BME: bone marrow edema; PPV: positive predictive value.

each and/or one of both ≥2 quadrants, or ≥3 quadrants with fat lesions and/or ≥2 quadrants with erosion met the threshold based on consensus. Combined lesions did not outperform single item lesions.

Conclusion: In early axSpA, the proposed ASAS MRI cut-offs for active SIJ lesions have been validated in consensus and individual reading. For structural SIJ lesions, the proposed cut-offs for fat in quadrants and consecutive slices as well for erosions in quadrants have been confirmed. However, we propose a higher cut-off of ≥4 consecutive slices for erosions. All these cut-offs have now shown a high specificity and PPV in both early and established axSpA.

Disclosure: L. de Bruin: None; **M. marques**: None; **M. Van Lunteren**: None; **M. de Hooge**: UCB, 6; **S. Exarchou**: Amgen, 2, Janssen, 2, Novartis, 2, UCB Pharma, 2; **F. Van Gaalen**: AbbVie, 12, Personal fees, BMS, 12, Personal fees, Eli Lilly, 12, Personal fees, Jacobus Stichting, 5, MSD, 12, Personal fees, Novartis, 5, 12, Fees, Stichting ASAS, 5, Stichting Vrienden van Sole Mio, 5, UCB Pharma, 5; **D. van der Heijde**: AbbVie, 2, Bayer, 2, BMS, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GSK, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, Galapagos, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, UCB Pharma, 2, 5.

Abstract Number: 0844

Facet Joint Inflammation Is Rare, but When Present It Is Associated with Facet Joint Ankylosis in Radiographic Axial Spondyloarthritis Patients from the SIAS Cohort

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes I: AxSpA

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: To assess whether posterior element (PE) inflammation, in particular in the facet joints (FJ), is associated with new facet joint ankylosis on MRI one year later, in patients with radiographic axial spondyloarthritis (r-axSpA).

Methods: Patients with an r-axSpA diagnosis recruited from Germany (Herne) and the Netherlands (Leiden) were included in the Sensitive Imaging in Ankylosing Spondylitis (SIAS) observational cohort when all following criteria were met: 1) presenting with ≥1 inflammatory lesion on MRI-spine according to SPondyloArthritis Research Consortium of Canada score, 2) presenting with 1-18 syndesmophytes (assessed with modified Stoke Ankylosing Spondylitis Spinal Score), and 3) fulfilling the modified New York criteria. Spinal MRIs were performed at baseline, after 1 year and after 2 years. PE inflammatory lesions and facet joint ankylosis were assessed on MRI, per vertebral unit level (VU) by 3 readers independently. FJ inflammation in the cervical spine was not assessed. With conditional probability tables the probability of developing facet joint ankylosis after one year was described. Multilevel time-lagged auto-regressive GEE was used for the association between PE (or FJ) inflammation and the development of facet joint ankylosis one year later, taking the reader and VU levels into account.

Results: In 58 patients MRI data of at least 2 readers was available. Their average age was 49±10 years and 85% was male. Inflammation in the PE or FJ at baseline was seen in 34 (58.6%) and 14 (24.1%) patients respectively. PE inflammation was distributed throughout the whole spine but emphatically more prevalent in the lower part of the thoracic spine (8.6%-15.5%). FJ inflammation was infrequently present, it was more often reported in the higher thoracic segment of the spine (1.7%-5.2%) (heatmap). Facet joint ankylosis was reported in 15 patients (25.9%) at baseline and in 17 patients (29.3%) with follow up visits. Facet joint ankylosis was mainly present in the upper half of the spine (heatmap). In 19 patients (32.8%) the development of new facet joint ankylosis over 1 or 2 years was seen by at least 1 reader.

	Baseline			1 year vitis			2 years vitis			
VU	Posterior element inflammation	Facet joint inflammation	Facet joint ankylosis	Posterior element inflammation	Facet joint inflammation	Facet joint ankylosis	Posterior element inflammation	Facet joint inflammation	Facet joint ankylosis	VU
1	0	Not assessed	1	0	Not assessed	2	0	Not assessed	2	1
2	0	Not assessed	5	1	Not assessed	6	1	Not assessed	5	2
3	0	Not assessed	6	1	Not assessed	7	1	Not assessed	7	3
4	0	Not assessed	5	1	Not assessed	6	1	Not assessed	6	4
5	1	Not assessed	6	1	Not assessed	6	1	Not assessed	6	5
6	2	0	6	2	0	6	2	1	7	6
7	3	2	11	1	0	11	3	1	11	7
8	2	2	10	4	0	10	5	3	12	8
9	6	1	8	5	1	7	6	0	8	9
10	5	2	6	6	3	8	9	1	8	10
11	4	1	6	8	2	7	4	0	10	11
12	9	2	6	8	0	5	4	1	7	12
13	9	1	5	7	0	6	6	3	6	13
14	5	0	6	5	0	6	5	0	6	14
15	9	0	3	7	1	4	5	0	4	15
16	9	0	1	8	1	1	7	0	1	16
17	9	1	2	3	0	3	5	0	3	17
18	2	0	2	2	2	1	2	1	1	18
19	2	0	0	0	0	0	2	0	1	19
20	2	1	0	1	0	0	3	0	2	20
21	2	0	1	3	1	1	4	3	2	21
22	3	0	0	3	1	0	4	0	1	22
23	0	0	0	1	0	0	2	0	1	23

The extent of posterior element lesions on MRI across the 23 vertebral units (VU) in radiographic axial spondyloarthritis patients with 2 years follow-up.

Table. Probability of developing facet joint ankylosis with and without posterior element inflammation present one year before, in r-axSpA patients from the SIAS cohort. PE; posterior elements, *; number of VU levels with inflammation in at least 1 part of the posterior elements (pedicle, facet joint, processes spinosi, soft tissue), #; number of facet joints, FJ; facet joint, P; probability

Inflammation in any part of the posterior elements			
PE inflammation	New facet joint ankylosis after one year	N*	P (FJ ankylosis/ PE inflammation)
0	0	7195	P (FJ ankylosis/0) = 43/7238 = 0.0059
0	1	43	
1	0	511	P (FJ ankylosis/1) =2/511 = 0.0039
1	1	2	
Inflammation only in the facet joint			
Facet joint inflammation	New facet joint ankylosis after one year	N#	P (FJ ankylosis/ FJ inflammation)
0	0	5934	P (FJ ankylosis/0) = 38/5972 = 0.0064
0	1	38	
1	0	93	P (FJ ankylosis/1) =1/94 = 0.0106
1	1	1	

Of the VU levels with PE or FJ inflammation only very few showed new facet joint ankylosis after one year; 2 and 1 VU levels, respectively (table). There was no association between PE inflammation and the development of new facet joint ankylosis in the same level after one year (OR=1.15, 95%CI 0.55-2.42). However, FJ inflammation was associated with the development new facet joint ankylosis one year later (OR=3.79, 95%CI 1.47-9.75).

Conclusion: PE inflammation and facet joint ankylosis on MRI were uncommonly present in r-axSpA patients. No association was found between inflammation in the PE and the development of facet joint ankylosis. However, when inflammation in the FJ is present the likelihood of developing facet joint ankylosis after 1 year is over 3 times higher compared to FJ without inflammation. This finding adds to the pathophysiological relationship between inflammation and damage at the same anatomical location.

Disclosure: M. de Hooge: UCB, 6; **R. Stal**: None; **A. Sepriano**: None; **X. Baraliakos**: AbbVie, 2, 6, BMS, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, 6, UCB, 2, 6; **M. Reijnierse**: None; **J. Braun**: None; **D. van der Heijde**: AbbVie, 2, Bayer, 2, BMS, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GSK, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; **F. Van Gaalen**: AbbVie, 12, Personal fees, BMS, 12, Personal fees, Eli Lilly, 12, Personal fees, Jacobus Stichting, 5, MSD, 12, Personal fees, Novartis, 5, 12, Fees, Stichting ASAS, 5, Stichting Vrienden van Sole Mio, 5, UCB Pharma, 5; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, Galapagos, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, UCB Pharma, 2, 5.

Abstract Number: 0845

The Yield of Repeated Assessments in Chronic Back Pain Patients Suspected of Early Axial Spondyloarthritis: Two-year Data from the SPondyloArthritis Caught Early (SPACE) Cohort

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Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway, [7]Groene Hart Ziekenhuis, Gouda, Netherlands, [8]Lund University, Åkarp, Sweden, [9]University of Padova, Department of Rheumatology, Padova, Italy

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes I: AxSpA
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: We have shown in the SPACE cohort that a diagnosis of early axial Spondyloarthritis (axSpA) can be reliably made in patients with chronic back pain (CBP) of less than two years (2y). However, diagnostic uncertainty can be an obstacle to initiating appropriate treatment. The value of repeated assessments of SpA features for a definite diagnosis is yet to be determined. Here we aimed to assess the yield of repeated assessments of SpA features over 2y to make a *definite axSpA* diagnosis in patients with recent onset CBP referred to the rheumatologist, and to describe the characteristics of patients who change to *definiteaxSpA* over time.

Methods: We used the 2y data from the SPACE cohort, a European multicentre inception cohort of patients (< 45y) with CBP of recent onset (≥3 months, ≤2y) included from 2008 to 2016. The diagnostic work-up consisted of patient history, physical exam, acute phase reactants (APR) and HLA-B27 testing, radiographs, and MRI of the sacroiliac joints (SI-CR and SI-MRI) and of the spine (not shown). In patients with ≥1 major or ≥2 minor prespecified SpA features, clinical assessments, APR, and imaging were repeated at 3 months, 1y and 2y visits. At each visit, the rheumatologist reported a clinical diagnosis of *axSpA* or *no axSpA* with level of confidence (LoC; numeric rating scale from 0 (*not confident at all*) to 10 (*very confident*)). Herein, we categorized patients by diagnosis likelihood (baseline and 2y definitions in ***Figure 1***). The ASAS classification criteria were applied using local reading. We explored the diagnostic course over 2y. In patients with a new diagnosis of *definite axSpA* at 2y, SpA features were investigated over time.

Results: We included 552 patients. *Definite axSpA* was attributed to 175 (32%) patients at BL and 165 (30%) at 2y (***Figure 2***), 155/175 (89%) and 145/165 (87%) fulfilled ASAS classification criteria, respectively. Of the 175 patients with *definite axSpA* at BL, 133 (76%) retained the diagnosis, and only 11 (6%) changed to *no axSpA* at 2y. Although still considered as axSpA by the rheumatologist, 31/175 (17%) *definite axSpA* patients at baseline were no longer *definite axSpA* at 2y, due to a decrease in LoC < 7 (n=14/31) or incomplete follow-up (n=17/31). Overall, the diagnosis changed to definite axSpA over 2y in 32 patients (BL: 16 uncertain axSpA, 11 uncertain no axSpA, and 5 definite no axSpA); on average, 3 to 4 SpA features were already present at BL and 1 new SpA feature developed over 2y (***Table 1***), with response to NSAIDs (9/24 patients) and MRI sacroiliitis (8/24 patients) being the most frequently developed over time. Of the 8 patients with new MRI sacroiliitis over time, 7 (88%) were HLA-B27+ and 5 (63%) were male.

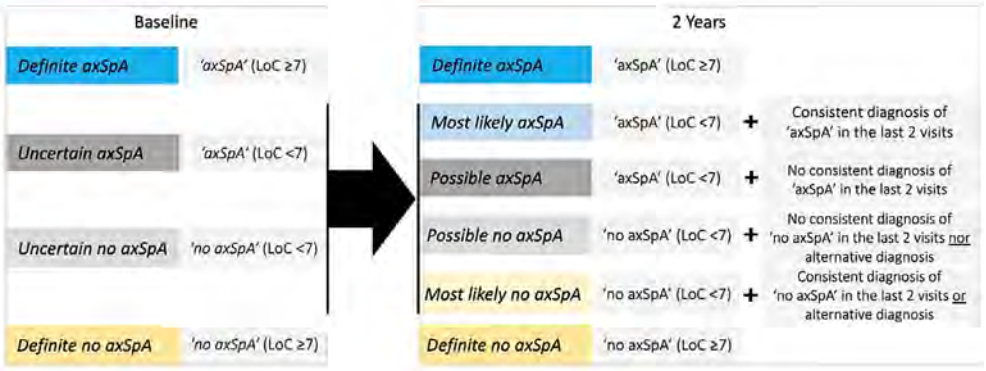

Figure 1. Definitions for diagnostic categories at baseline and at two years. If two-year visit data was missing, a last observation carried forward approach was used. axSpA – axial Spondyloarthritis; LoC – level of confidence.

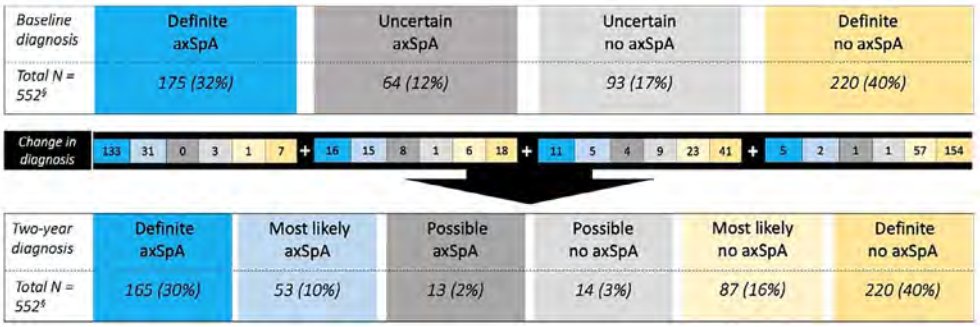

Figure 2. Course of diagnosis from baseline to two years in patients with recent onset chronic back pain of unknown origin. axSpA – axial Spondyloarthritis.

Table 1. Characteristics of 32 patients changing to definite axSpA with newly developed SpA features over 2 years Data presented as mean (SD), % or n of patients. §Local readings. ^including HLA-B27 positivity and sacroiliitis on imaging. $Of the 32 patients, 24 (75%) developed new SpA features over time. #Cumulative numbers over the two-year follow-up. BL – baseline; MRI – magnetic resonance imaging.

Baseline diagnosis	Uncertain axSpA at BL N=16		Uncertain no axSpA at BL N=12		Definite no axSpA at BL N=5	
	BL	2Y#	BL	2Y#	BL	2Y#
Age at inclusion, years	30.3 (8.6)	-	35.1 (7.9)	-	25.8 (6.1)	-
Male	50%	-	73%	-	40%	-
Symptom duration, months	12.7 (6.8)	-	12.5 (6.8)	-	12.0 (4.7)	-
HLA-B27 +	81%	-	55%	-	80%	-
Family history of SpA	8	9	3	4	3	4
Inflammatory back pain	14	15	6	7	5	5
Good response to NSAIDs	4	10	5	7	3	4
Peripheral manifestations	4	8	1	3	1	2
Extra-musculoskeletal manifestations	4	6	3	4	0	1
Increased acute phase reactants	4	4	1	3	2	2
Sacroiliitis on radiographs§	0	0	1	2	0	1
Sacroiliitis on MRI§	3	8	3	5	0	1
Total nr of SpA features^	3.4 (1.1)	4.6 (1.4)	2.6 (1.0)	3.7 (1.3)	3.6 (0.5)	4.8 (0.8)
Nr of new SpA-features over follow-up^§	-	1.3 (1.0)	-	1.1 (0.9)	-	1.2 (0.8)
ASAS classification criteria	-	81%	-	58%	-	80%

Conclusion: The yield of repeated assessments of SpA features in patients with CBP suspected of axSpA was modest for the increase of new *definite axSpA* diagnosis at 2y. Most SpA features were already present at BL, with sacroiliitis on MRI and response to NSAIDs being the two most frequently incident SpA features potentially adding to a *definite axSpA* diagnosis over time. Usefulness of repeating MRI in terms of diagnostic yield is low but can be considered in HLA-B27+ patients, especially if male.

Disclosure: M. marques: None; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, Galapagos, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, UCB Pharma, 2, 5; **M. Van Lunteren**: None; **R. Stal**: None; **R. Landewé**: AbbVie, 2, 5, AstraZeneca, 2, BMS, 2, Eli Lilly, 2, Novartis, 2, 5, Pfizer, 2, 5, Rheumatology Consultancy BV, 12, Owner, UCB Pharma, 2, 5; **M. van de Sande**: AbbVie, 2, Eli Lilly, 5, Janssen, 6, Novartis, 2, 5, 6, UCB Pharma, 2, 5, 6; **K. Minde Fagerli**: None; **I. Jorid Berg**: None; **M. van oosterhout**: None; **S. Exarchou**: Amgen, 2, Janssen, 2, Novartis, 2, UCB Pharma, 2; **R. Ramonda**: None; **D. van der Heijde**: AbbVie, 2, Bayer, 2, BMS, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GSK, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; **F. Van Gaalen**: AbbVie, 12, Personal fees, BMS, 12, Personal fees, Eli Lilly, 12, Personal fees, Jacobus Stichting, 5, MSD, 12, Personal fees, Novartis, 5, 12, Fees, Stichting ASAS, 5, Stichting Vrienden van Sole Mio, 5, UCB Pharma, 5.

Abstract Number: 0846

Preosteoclast Plays a Pathogenic Role in Syndesmophyte Formation of Ankylosing Spondylitis Through the Secreted PDGFB - GRB2/ERK/RUNX2 Pathway

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes I: AxSpA

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

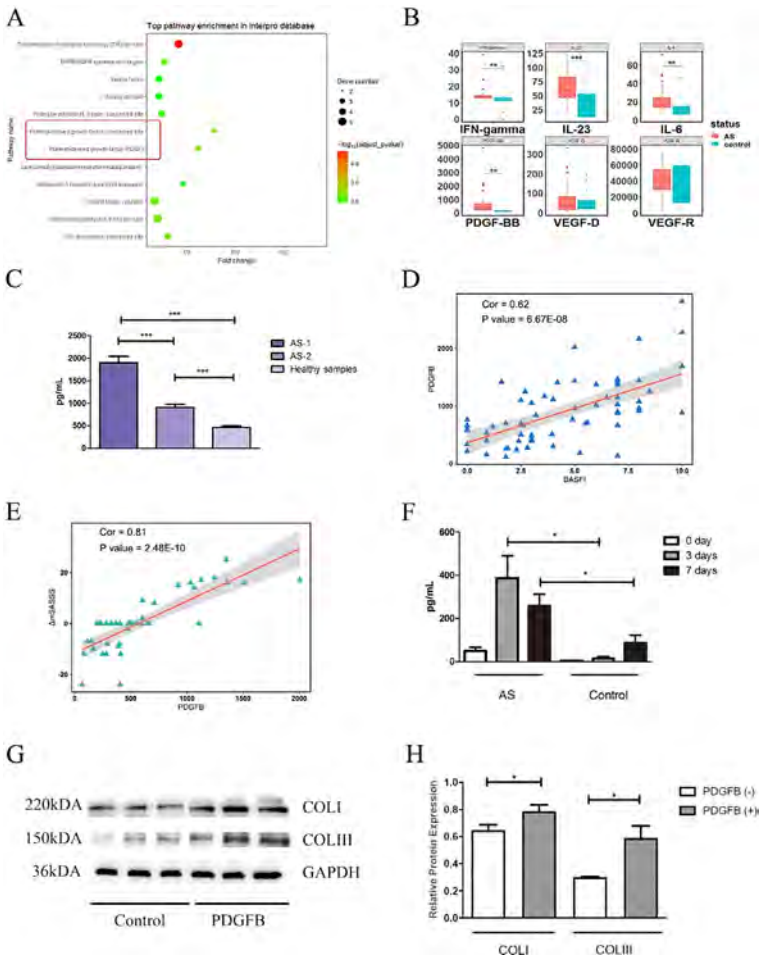

Figure 1 A, Top pathway enrichment according to the InterPro database. B, Differential expression of six cytokines in AS and healthy controls in validation I stage. C, Differential expression of PDGFB in Chinese AS patients and healthy controls in the validation II stage. AS-1 represents the 40 AS patients at baseline in the validation II stage, and AS-2 represents the 60 late-stage AS patients who have had a disease duration longer than 5 years. D, Correlation between PDGFB and BASFI. E, Correlation between PDGFB and ΔmSASSS in Chinese AS patients in validation II-40. F, Expression level of PDGFB secreted from monocytes after stimulation with M-CSF and RANKL for 7 days, which were analysed by ELISA. G, Collagen expression of FOB1.19 in the two groups (PDGF-, PDGF+). H, Relative protein level of collagen expression in FOB1.19 in the two groups (PDGF-, PDGF+). The expression levels of cytokines and the relative protein levels were compared by unpaired sample t-tests. *** $P < 0.005$, ** $P < 0.01$.

Background/Purpose: Ankylosing spondylitis (AS) is a chronic inflammatory disease that mainly affects the sacroiliac joint and spine. However, the real mechanisms of immune cells acting on syndesmophyte formation in AS are not well identified. We aimed to find the key AS-associated cytokine and assess its pathogenic role in AS.

Methods: A protein array with 1000 cytokines was performed in five AS patients with the first diagnosis and five age- and gender-matched healthy controls to discover the differentially expressed cytokines. The candidate differentially expressed cytokines were further quantified by multiplex protein quantitation (3 AS-associated cytokines and 3 PDGF-pathway

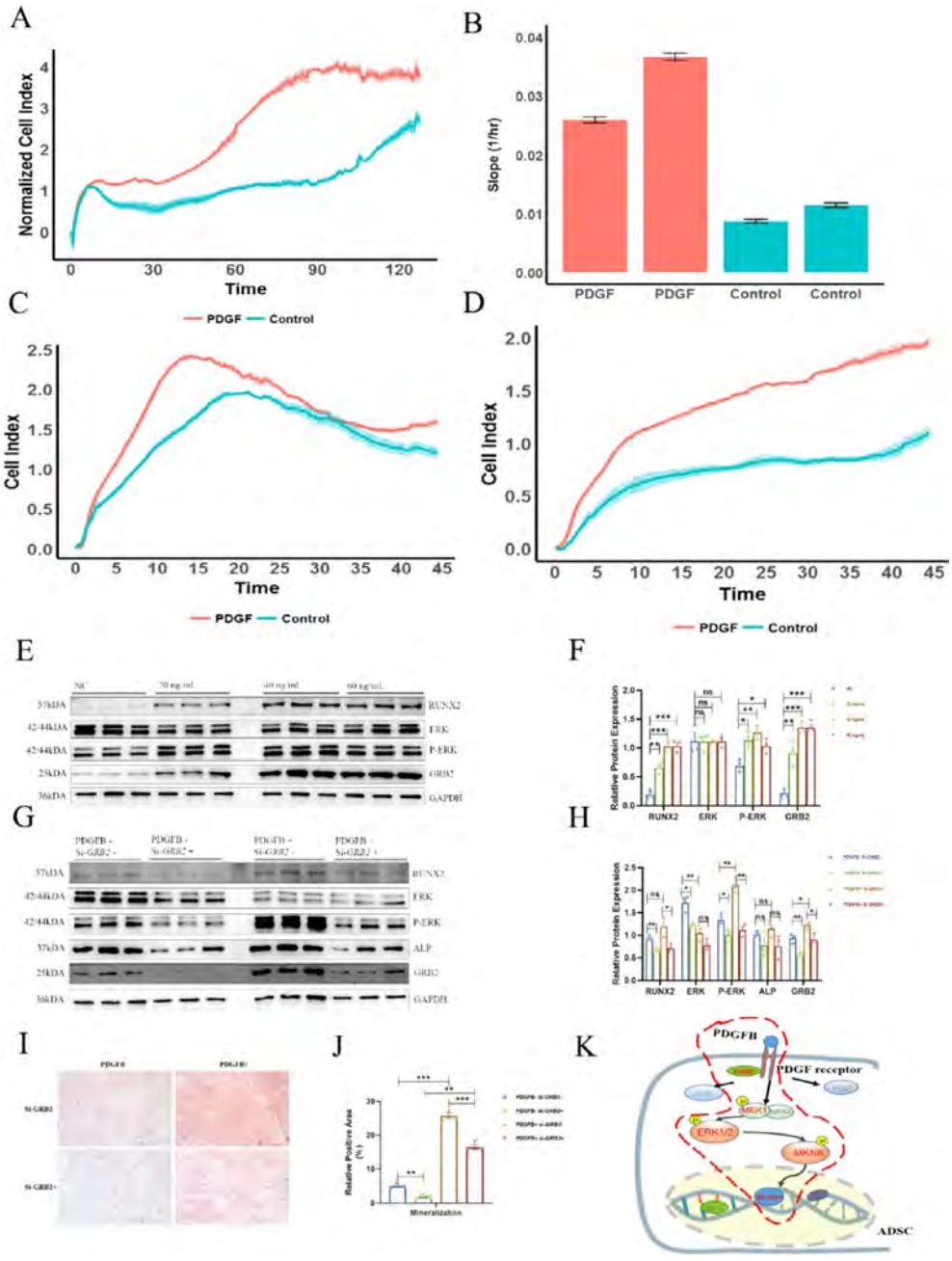

Figure 2 Effects of PDGFB on ADSCs. A, Proliferation in the two groups. B, Slope of proliferation in the two groups. C, Chemotaxis in the two groups. D, Migration results for the two groups. E-F, PDGFB activated the GRB2-pERK-RUNX2 axis in a dose-dependent manner. G-H, Western blot of several key molecules in the GRB2-pERK-RUNX2 axis with/without the treatments of PDGFB and si-GRB2. I-J, The mineralization ability of ADSCs with/without the treatments of PDGFB and si-GRB2, examined by Alizarin red S staining. K, Differential enrichment of phosphopeptides in ADSCs. MEK1, ERK1/2 and MKNK were identified as differentially phosphorylated in the MAPK pathway. The gene and protein levels were compared by unpaired sample t-tests. *** $P < 0.005$, ** $P < 0.01$, * $P < 0.05$.

cytokines) and ELISA (PDGFB) in independent samples (a total of 140 AS patients vs 140 healthy controls). The effects of PDGFB, the candidate cytokine, were examined by using adipose-derived stem cells (ADSCs) and human fetal osteoblast cell line (hFOB1.19) as *in vitro* mesenchymal cell and preosteoblast models, respectively. Furthermore, whole-transcriptome sequencing and enrichment of phosphorylated peptides were performed by using cell models to explore the underlying mechanisms of PDGFB. The xCELLigence system was applied to examine the proliferation, chemotaxis, and migration abilities of PDGFB-stimulated or -unstimulated cells.

Results: The PDGF pathway was observed to have abnormal expression in the protein array, and PDGFB expression was further found to be up-regulated in 140 Chinese AS patients (Figures 1A-C). Importantly, PDGFB expression was significantly correlated with BASFI (Pearson coefficient/p value = 0.62/6.70E-8) and with the variance of the mSASSS score ($mSASSS_{\text{two years} - \text{baseline}}$, Pearson coefficient/p value = 0.76/8.75E-10) (Figures 1D-E). In AS patients, preosteoclasts secreted more PDGFB than the healthy controls (p value = 1.16E-2) (Figure 1F), which could promote ADSCs osteogenesis and enhance collagen synthesis (COLI and COLIII) of osteoblasts (hFOB 1.19) (Figures 1G-H). In addition, PDGFB promoted the proliferation, chemotaxis and migration of ADSCs (Figures 2A-D). Mechanismly, in ADSCs, PDGFB stimulated ERK phosphorylation by upregulating GRB2 expression, and then increased the expression of RUNX2 to promote osteoblastogenesis of ADSCs (Figures 2E-K).

Conclusion: PDGFB stimulates the GRB2/ERK/RUNX2 pathway in ADSCs, promotes osteoblastogenesis of ADSCs, and enhances the extracellular matrix of osteoblasts, which may contribute to pathological bone formation in AS.

Disclosure: Y. Tang: None; **Q. Liu**: None; **K. Tang**: None; **C. Geng**: None; **J. Xie**: None; **J. Wang**: None; **Q. Zhu**: None; **J. Liu**: None.

Abstract Number: 0847

Development of an IFN 5-Gene Signature Score to Identify IFN-high and IFN-low Subsets and as a Pharmacodynamic Biomarker for Deucravacitinib Treatment in a Phase 2 Trial in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes I: Biomarkers
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Elevated IFN activity is observed in a subset of lupus subjects suggesting that those with higher levels of IRGs may benefit from interferon targeted therapies, however, to date responses by this dichotomization have been inconsistent. Tyrosine kinase 2 (TYK2) mediates cytokine pathways (eg, type I IFN, IL-12 and IL-23) linked with SLE pathogenesis. Deucravacitinib is a first-in-class, oral, selective, allosteric TYK2 inhibitor and was found to be efficacious in a phase

2 SLE trial.[1] We developed a customized IFN 5-gene signature score, assessed the pharmacodynamic effects of deucravacitinib on the IFN score, and evaluated the score's association with SLE disease activity and clinical response in the phase 2 trial (NCT03252587).

Methods: Patients were randomized equally to placebo or deucravacitinib (3 mg twice daily [BID], 6 mg BID, or 12 mg once daily [QD]). DxTerity chemical ligation-dependent probe amplification was used to measure 51 immune system–related genes from whole blood. IFN genes were selected based on distribution, correlations, hierarchical clustering, and consistency of k-means clusters. Serum proteins, blood cell subsets, and antibodies were measured by immunoassays and flow cytometry. Systemic Lupus Erythematosus Responder Index-4 (SRI[4]) and British Isles Assessment Group–based Composite Lupus Assessment (BICLA) were measured at weeks 32 and 48.

Results: An IFN 5-gene (*MX1*, *HERC5*, *IFIT1*, *RSAD2*, and *EIF2AK2*) signature score was identified and used to classify patients into IFN-high or IFN-low subgroups (Figure 1). Higher baseline score was associated with higher baseline SLEDAI and Cutaneous Lupus Erythematosus Disease Area and Severity Index scores, higher IFN activity biomarker (eg, IFNα, IFNλ, B-cell activating factor, C-X-C motif chemokine ligand 10) and anti–double-stranded DNA levels, and lower complement and lymphocyte counts. Deucravacitinib reduced the IFN score from weeks 4 through 44 by > 50%. Patients with high IFN

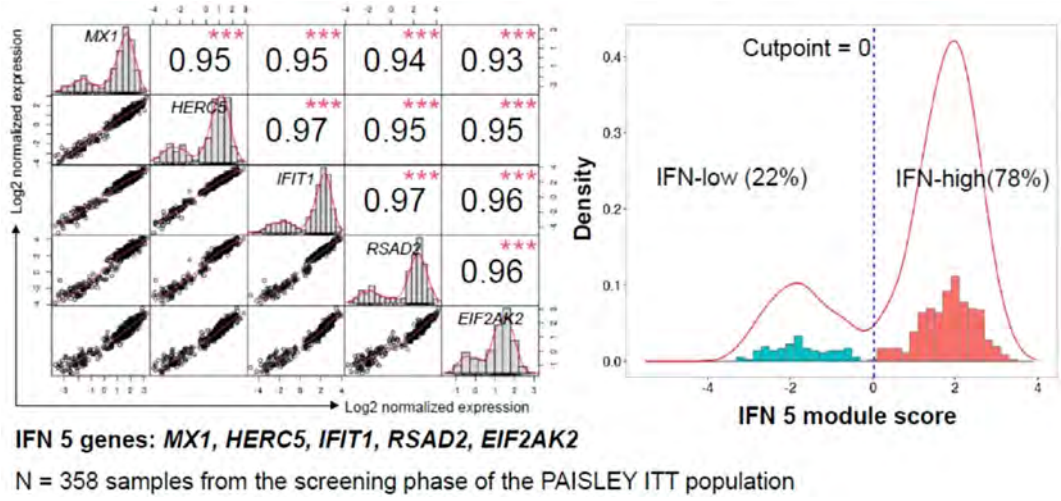

Figure 1. IFN 5-gene signature score with k-means clustering–derived cut point in the PAISLEY trial

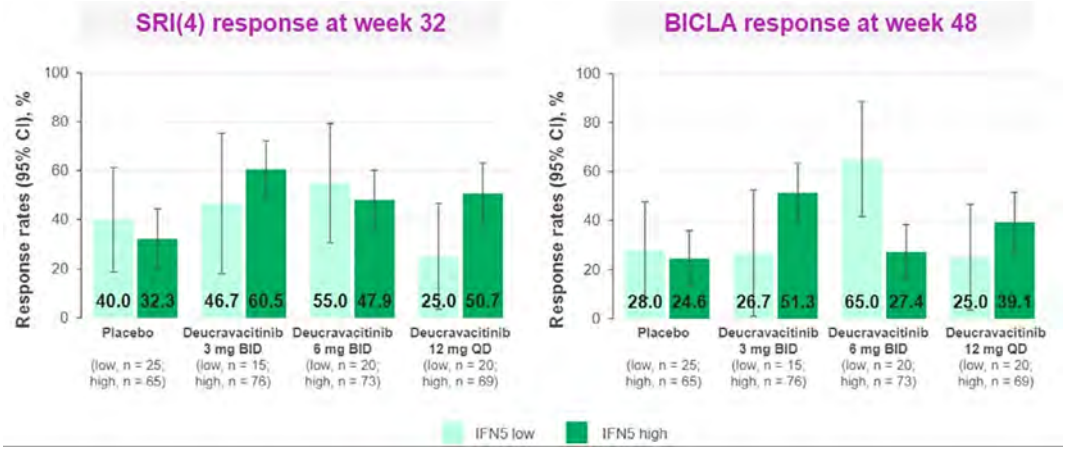

Figure 2. Clinical response by IFN 5-gene score subgroup

scores had numerically higher SRI(4) response rates at week 32 and BICLA response rates at week 48 in the 3-mg BID and 12-mg QD dose groups, but not in the 6-mg BID group, compared with patients with low IFN score (Figure 2).

Conclusion: These data support the IFN 5-gene signature score as a biomarker to classify patients with SLE into IFN-high or IFN-low subgroups; however, clinical response by IFN score was inconsistently improved. IFN-regulated gene expression performs well as a pharmacodynamic biomarker to confirm deucravacitinib mechanism of action and to aid in phase 3 dose selection.

Reference:

1. Morand E, et al. *Arthritis Rheumatol* 2023;75:242–252.

Disclosure: C. Wu: Bristol Myers Squibb, 3; **Y. Hu**: BMS, 3, 12, BMS stock holder; **M. Crow**: AMPEL BioSolutions, 2, AstraZeneca, 2, Bristol Myers Squibb, 2, Eli Lilly, 2, Gilead Sciences, 5, GlaxoSmithKlein(GSK), 2; **A. Saxena**: AbbVie/Abbott, 1, AstraZeneca, 1, GlaxoSmithKlein(GSK), 1; **C. Arriens**: AstraZeneca, 1, 5, 6, Aurinia, 6, Bristol-Myers Squibb, 1, 5, Cabaletta, 1, GSK, 1, Kezar, 1, UCB, 1; **C. Hobar**: Bristol-Myers Squibb(BMS), 3; **A. Coles**: Bristol-Myers Squibb(BMS), 3; **I. Catlett**: Bristol Myers Squibb, 3, 8.

Abstract Number: 0848

Performance of Serum MRP8/14, sCD14, IL-6 and Neutrophil CD64 in Isolation and in Combination for Differentiating Flare from Bacterial Infection in Febrile SLE Patients

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes I: Biomarkers
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Disease flare and infections are the major causes of fever in a patient with SLE. It is vital to differentiate between these two as escalation of immunosuppressive treatment can be disastrous in a patient with infection. A low-cost calculator was recently described for differentiation (*Lupus. 2022;31:1254-1262*). Newer biomarkers are being explored and data on sepsis markers like MRP8/14, IL-6, sCD14 and neutrophil CD64 is limited in SLE. Thus, we evaluated these 4 markers in febrile SLE patients for their utility as well as their ability to improve performance of this low-cost calculator.

Methods: Patients with SLE who had fever of more than 2 days, but less than 2 weeks duration were included in the study. Patients were evaluated in detail for infection and fever episode was classified as infection, disease activity or combination of both. Complete blood counts, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), procalcitonin, complement C3 and C4, anti-dsDNA antibodies were measured. In addition, soluble CD14 (sCD14), Myeloid related protein (MRP) 8/14 and interleukin (IL)-6 were measured by ELISA. neutrophil CD64 expression was measured by flowcytometry and is expressed as % of neutrophil expressing CD64.

Among patients with infection episode and disease flare the variables were analyzed using Mann Whitney-U test for continuous and chi-square for categorical variables respectively, ROC curve analysis was used for test performance.

Results: 156 episodes of fever were studied. The mean age of the patients was 26.8 years while the mean duration of disease was 3.5 years. Among 156 episodes, 52 were because of infection while 65 were related to disease flare and 38 were due to combination of two and 1 due to malignancy.

Among 52 patients with infection, 46 had bacterial infection, 4 had tuberculosis and 1 each had fungal and viral infection. Among patients with bacterial infection, the site of infection was lower respiratory tract in 17, urinary tract infection in 14, skin and soft tissue in 3, meningitis in 2 and gastrointestinal in 4 and others in 6.

Patients with infection had higher CRP, procalcitonin, neutrophil to lymphocyte ratio while patients with disease activity had lower C3, C4 and higher anti-dsDNA antibodies and SLEDAI2K (Table 1).

Table 1: Comparison between bacterial infection and disease flare group

	Infection (n=46)	Disease flare (n=65)	p
Age(mean) (years)	29.26±12.21	24.62±8.54	0.02
Gender Female	39	61	0.11
Duration of disease(months)	51.54±67.57	36.86±46.51	0.17
Clinical manifestation at baseline n(%)			
Musculoskeletal			
Renal	40(87%)	50(83.3%)	0.18
Serositis	16(35%)	28(43%)	0.37
CNS	9(19.5%)	12((18.5%)	0.79
Mucocutaneous	19(41%)	19(29.2%)	0.13
APS	29(63%)	43(65.1%)	0.97
Hematological	3(6.5%)	0	0.07
	19(41%)	28(43%)	0.85
Prednisolone >7.5 mg	28	39	0.93
Current prednisolone dose (mg)			
<7.5	18	26	
7.5 -15	17	11	
16-30	7	20	0.06
>30	4	8	
MPS pulse in Last 3 weeks	4	10	
Steroid sparing agent use (n)	33	35	0.056
Mean fever duration (days)	7±2.87	9.8±4.6	0.0003
TLC (per mm^3)	10094±9695	6336±3389	0.004
Neutrophil Lymphocyte Ratio	8.08±9.59	5.35±4.52	0.045
Erythrocyte sedimentation rate (mm)	97.89±43.9	84.40±38.28	0.08
C Reactive Protein (mg/L)	75.0±94.1	28.9±40.6	0.0006
ESR/CRP ratio (Median)	6.37	1.67	0.005
Anti DSDNA (IU/ml)	146±174.4	324.9±266.3	<0.0001
<20	12	1	
21-50	10	6	<0.0001
51- 100	5	7	
>100	19	51	
Procalcitonin(ng/ml)	10.8±27.46	0.79±2.20	0.0067
C3 (mg/dl)	94.30±42.25	60.5±31.60	0.0001
C4 (mg/dl)	23.23±14.76	14.21±9.65	0.0002
Number with low C3 or C4	22	52	0.0009
SLEDAI 2K	5.58±6.27	14.14±9.31	<0.0001
SLEDAI2KG	8.58±7.46	7.61±10.29	<0.0001
MRP8/14(µg/ml)	19.87±22.28	49.31±109.60	0.15
Soluble CD14(µg/ml)	6.84±4.72	5.37±2.67	0.04
IL-6 (pg/ml)	53.33±79.62	56.98±136.5	0.87
Neutrophils expressing CD64 (%)	73.84±38.02	66.93±36.14	0.38

SLEDAI 2K- Systemic Lupus Erythematosus Disease Activity Index 2000.

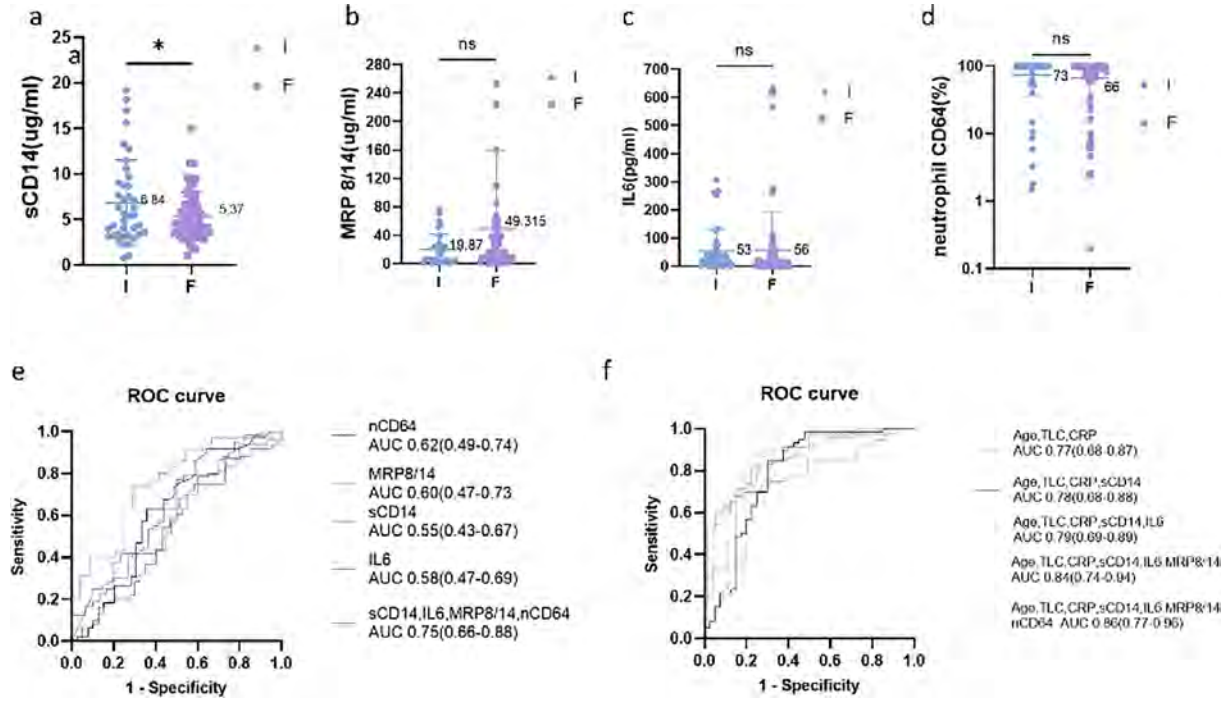

Figure 1: Scatter plot showing differences in level of a) sCD14 b) MRP8/14 c) IL-6 and d) neutrophil CD64 between patients with infection and flare. Panel e depicts the ROC curve for the 4 markers and their combination. Panel f shows the ROC curve for addition sCD14 alone and in combination with other new biomarkers to low cost biomarker panel.

The levels of sCD14 were higher in patients with infection whereas the level of IL-6 and MRP8/14 were no different between the two groups. Neutrophil CD64 expression was also not different between the two groups. (Figure 1a-d).

On ROC curve analysis the new biomarkers had AUC between 0.55 to 0.62 and in combination they had an AUC of 0.75. (Figure 1e). When three or all of the newer biomarkers were added to a recently described calculator comprising of age, TLC, and CRP, it improved its performance from AUC of 0.77 to 0.86. (Figure 1f)

Conclusion: Newer biomarkers of sepsis like MRP8/14, IL-6, sCD14 and neutrophil CD64 expression in combination have modest performance to differentiate flare from infection. Addition of these biomarkers in combination improved the accuracy of recently described calculator.

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Abstract Number: 0849

Multiplex Profiling and Machine Learning Reveal Distinct Signatures of Circulating Cytokines Associated with Autoantibody Profiles and Disease Severity in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes I: Biomarkers
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: SLE is one of the leading causes of death in young females suffering from autoimmune disorders. Nephritis, afflicts 60-70% of patients which contribute significantly to morbidity and mortality despite therapeutic advances. Disrupted cytokine networks and autoantibodies play an important role in disease pathogenesis. However, conflicting reports and non-reproducibility have hindered progress with regards to translational potential of cytokines. This study attempts to address the existing knowledge gap using a multiplex cytokine assay and machine learning algorithms.

Methods: 69 SLE patients fulfilling SLICC criteria were recruited. Baseline characteristics along with disease activity was recorded for all patients. Cytokines were measured by a commercially available multiplex cytokine kit (Millipore). Fluorescence values were logarithmically transformed before analysis. To visualize relationships between cytokines, Network graphs were constructed based on Spearman correlation values. For stratifying individuals based on cytokine profiles, we used Sparse Partial Least Squares Discriminant Analysis (sPLS-DA) followed by factor loadings plots to assess which cytokines contribute most to the observed differences between groups. Patterns of co-occurrence of autoantibodies within the SLE patients were identified by the K-Modes algorithm and the patients were visualized on a dimensionally reduced plot obtained by constructing a 2-dimensional representation by multiple correspondence analysis (MCA).

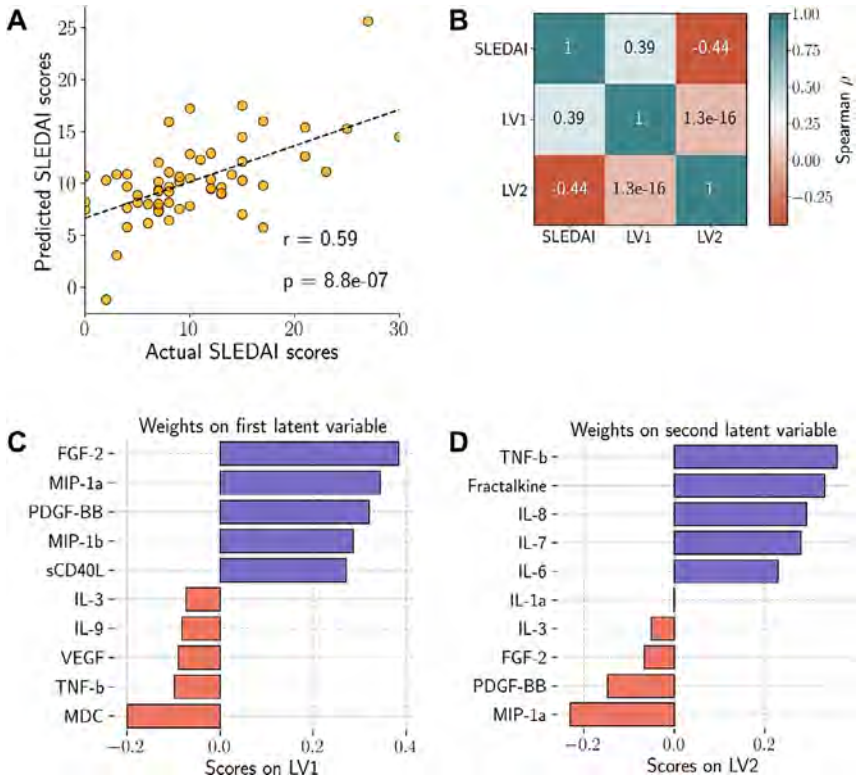

Figure 1: Combined cytokine response in SLE is predictive of disease severity. (A) Correlation between observed vs. predicted SLEDAI scores in patients with SLE. The SLEDAI scores were predicted from a PLSR model with cytokines. (B) Correlation of SLEDAI scores with the first two components of the PLSR model. (C) Cytokine contributions towards the first PLSR component (LV1: Latent variable 1). (D) Cytokine contributions towards the second PLSR component (LV2: Latent variable 2).

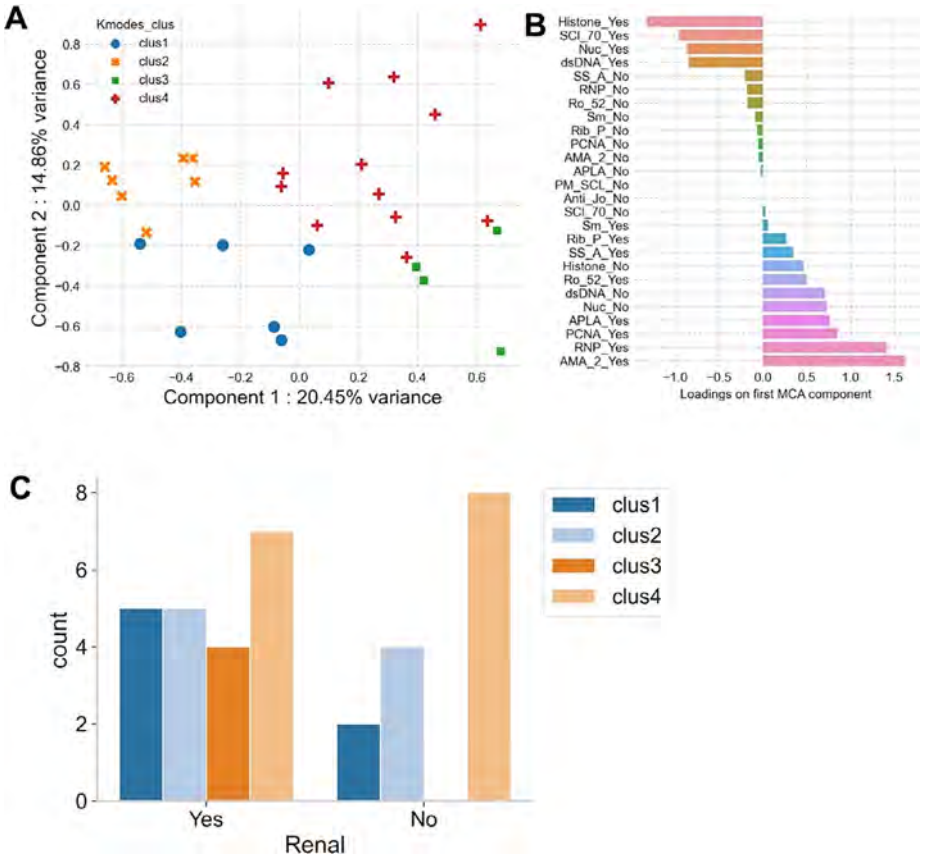

Figure 2: SLE patients have distinct combinations of autoantibody profiles that associate with lupus nephritis. (A) K Modes clustering algorithm identifies 4 distinct clusters of patients based on combined autoantibody profiles. The patients are then visualized on a 2D representation of the multidimensional data by multiple correspondence analysis (MCA). (B) Factor loadings plot demonstrating the relative contributions of the individual autoantibodies to the separation observed in (A). (C) Counts of patients presenting with or without lupus nephritis with the corresponding autoantibody clusters.

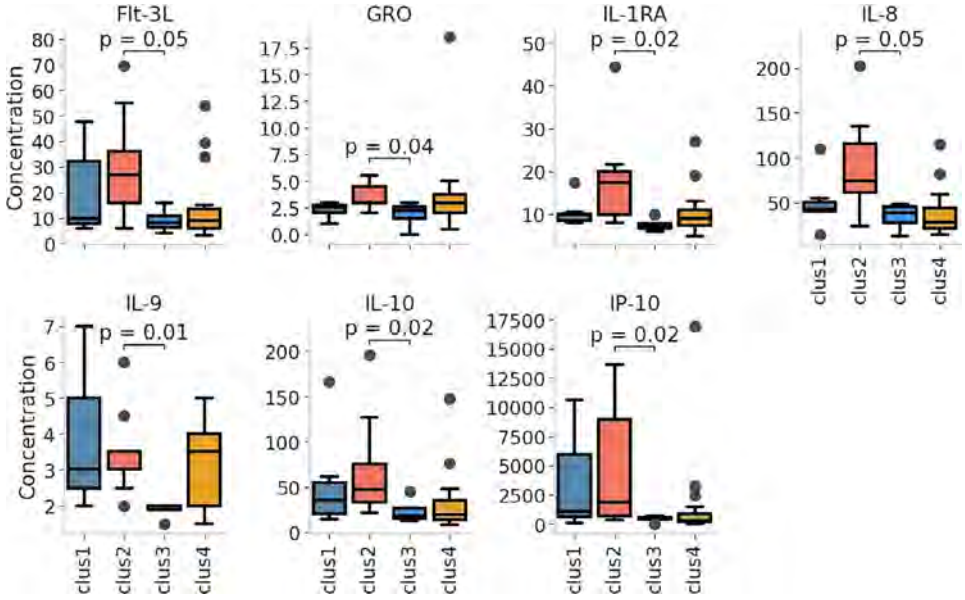

Figure 3: Cytokine profiles associated with autoantibody clusters. Comparison of cytokine levels between Clusters 2 and 3 was done by a Mann-Whitney U test, corrected for multiple tests by the Bonferroni method.

Results: We observed a positive association between actual disease activity scores (SLEDAI) and predicted scores from a partial least squares regression (PLSR) analysis of multivariate cytokine response data (Figure 1a). A study of the first two PLSR components revealed the SLEDAI scores to be positively associated with the first component (LV1) and negatively associated with the second component (LV2) (Figure 1b). Analysis of cytokine contributing towards the first two PLSR components revealed MIP-1α to have a strong positive influence towards component 1 and a negative influence on component 2, indicating a strong association with increased disease severity (Figure 1c and d). K-Modes clustering analysis identified 4 distinct clusters of patients with specific autoantibodies (Figure 2a and b), with clusters 2 and 3 being the most well-separated. Furthermore, we also observed striking differences in distributions of lupus nephritis between the clusters, with all patients in cluster 3 presenting with nephritis (Figure 2c). Finally, our results also demonstrate unique cytokine signatures associated with autoantibody profiles, with patients in cluster 3 showing significantly lower levels of cytokines responsible for modulating inflammation and maintaining cellular homeostasis (Figure 3), an observation that is in line with the clinical feature of nephritis.

Conclusion: Cytokine response can predict disease activity. Nephritis is associated with specific autoantibody profiles and cytokine signatures.

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Abstract Number: 0850

Persistence of Urinary Biomarkers of Intrarenal Inflammation Precedes Loss of Kidney Function in Lupus Nephritis

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes I: Biomarkers
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: One third of lupus nephritis (LN) patients develop irreversible kidney damage despite achieving a clinical response based on resolution of proteinuria. Furthermore, per protocol kidney biopsies in patients with proteinuria < 0.5 g/g showed clinically significant histological activity in 50% despite the minimal proteinuria. We hypothesized that persistence of intrarenal inflammation (=LN histological activity) after treatment leads to accrual of kidney damage. We have previously identified several urinary biomarkers that correlate with the NIH Activity Index (histological activity). Here, we tested whether the elevation of these candidate biomarkers of LN immunological activity at 6 and 12 months from the diagnostic kidney biopsy predict loss of kidney function at 3 years.

Methods: We quantified 1200 biomarkers (Kiloplex, RayBiotech) in urine samples collected on the day of (73%) or within 3 weeks (27%) of kidney biopsy and week 12, 24, or 52 in LN patients (ISN class III, IV, V, or mixed) with proteinuria > 1 g/d. Glomerular filtration rate (GFR) was estimated using the CKD-EPI equation. Significant GFR loss was defined as a decline of >15 ml/min below 90 ml/min at 3 years from biopsy or end-stage kidney disease (ESKD) by year 3 requiring dialysis or transplant.

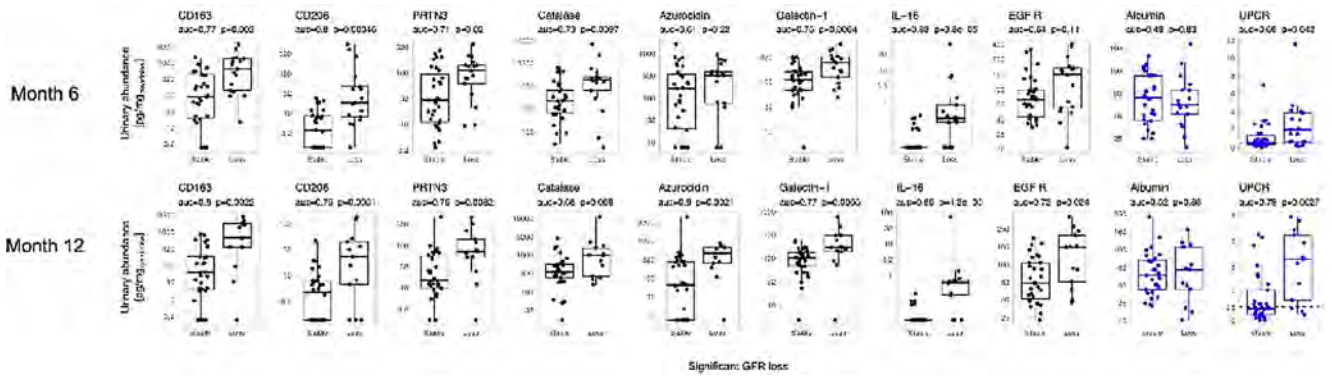

Figure 1. Association of candidate urinary biomarkers of histological activity with significant GFR loss. Urinary abundance (pg/mgcreatinine) of urinary biomarkers selected a priori based on their correlation with histological activity (NIH Activity Index) in a matching kidney biopsy of LN according to GFR loss at 3 years. Urine protein and albumin to creatinine ratios are reported for reference as clinically used biomarkers.

Results: We included 73 patients: 85% female, 46% identified as Black, 40% as White, 10% as Asian, and 4% as Other. ISN classification included 25% pure proliferative (III or IV), 40% pure membranous (V), and 35% mixed (III or IV + V). Mean GFR at biopsy was 85 (SD 34.7) ml/min. There were 32/73 (44%) patients who developed significant GFR loss. **Figure 1** shows the associations of candidate urinary biomarkers at 6 and 12 months with significant GFR loss at 3 years. Most urinary biomarkers of histological activity were higher at 6 and 12 months in patients who ultimately lost GFR at 3 years. For example, IL-16 outperformed UPCR both at 6 and 12 months (**Figure 1**) and was independent of proteinuria (not shown). UPCR at 12 months predicted 3-year GFR loss with AUC 0.79, but albuminuria did not. In a multivariable model, the combination of CD163 (macrophage activation), PRTN3 (degranulation), and IL-16 (cellular inflammation in LN) urinary levels at 12 months predicted GFR loss at 3 years with an AUC of 0.96.

Conclusion: Elevation of urinary biomarkers of histological activity after 6 or 12 months of treatment predict GFR loss at 3 years better than proteinuria, especially IL-16. These findings suggest that insufficient immunosuppression results in persistent intrarenal immunological activity in LN that increases the risk of kidney function loss. The ultimate treatment goal in LN is long term preservation of kidney function. Therefore, clinical trial endpoints should include response definitions that best associate with GFR preservation. Because noninvasive urinary biomarkers of immunological activity parallel intrarenal inflammation and predict future GFR, they could be used to 1) monitor treatment response/failure, 2) allow early treatment changes, and 3) serve as surrogate endpoints in clinical trials.

Disclosure: A. Fava: Annexon Biosciences, 2, Sanofi, 1; **M. Atta**: Bayer, 5, Dimerix, 5, horizon therapeutics, 1, Morphosys AG, 5, Novartis, 5, REATA, 5, Vertex, 5; **J. Monroy-Trujillo**: None; **D. Fine**: None; **D. Goldman**: None; **I. peter**: None; **H. Belmont**: Alexion, 6, Aurinia, 6; **t. Accelerating Medicines Partnership in RA/SLE**: None; **J. Buyon**: Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, Related Sciences, 1; **M. Petri**: Alexion, 1, Amgen, 1, AnaptysBio, 1, Annexon Bio, 1, Argenx, 1, Arhros-Focus Med/Ed, 6, AstraZeneca, 1, 5, Aurinia, 1, 5, 6, Axdev, 1, Biogen, 1, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CVS Health, 1, Eli Lilly, 1, 5, Emergent Biosolutions, 1, Exagen, 5, Exo Therapeutics, 2, Gilead Biosciences, 2, GlaxoSmithKlein(GSK), 1, 5, 6, Horizon Therapeutics, 2, Idorsia Pharmaceuticals, 2, IQVIA, 1, Janssen, 1, 5, Kira Pharmaceuticals, 2, MedShr, 6, Merck/EMD Serono, 1, Momenta Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Proviant, 2, Sanofi, 2, Sinomab Biosciences, 2, Thermofisher, 5, UCB, 2.

Abstract Number: 0851

Lupus Nephritis Flares Linked to Platelet Activation During Gut Pathobiont Blooms

Abhimanyu Amarnani[1], Doua Azzouz[2], MacIntosh Cornwell[3], David Mieles[3], Peter Izmirly[4], Jill Buyon[5], Kelly Ruggles[6] and Gregg Silverman[5], [1]NYU Langone Medical Center, New York, NY, [2]NYU Langone Health (School of medicine), New York, NY, [3]New York University, New York, NY, [4]New York University School of Medicine, New York, NY, [5]NYU Grossman School of Medicine, New York, NY, [6]NYU Langone, New York, NY

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes I: Biomarkers

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is associated with gut microbiota dysbiosis, and community imbalance can coincide with flares of Lupus nephritis (LN). Herein, we sought to understand the blood cell gene expression patterns and antibody responses to a gut pathobiont in longitudinal assessments of SLE patients with LN and concurrent gut colonization blooms of *Blautia (Ruminococcus) gnavus* (RG).

Methods: In a well-characterized SLE cohort, we performed bulk RNA-seq from whole-blood PAXGene tubes. Our cohort consisted of 24 female subjects (8 controls, 8 with non-renal SLE, 4 LN without RG blooms, and 4 LN concurrent with RG blooms) with longitudinal assessment of whole-blood RNA sequencing, lupus activity, and serum anti-RG lipoglycan antibody levels. After quality control and filtering, gene expression profiles were analyzed. Serum levels of the platelet factors, P-selectin and platelet factor 4 (PF4), were assessed by ELISA.

Results: Differential expression and unsupervised clustering analysis revealed distinct gene expression patterns between LN patient without and with RG gut blooms (372 differentially expressed genes; p< 0.01. Gene set enrichment analysis of the differentially expressed genes revealed significant enrichment for "platelet activation", "platelet alpha granule" and "platelet degranulation" pathways (Figure 1A, FDR < 0.001). Gene expression levels in SLE samples were compared to

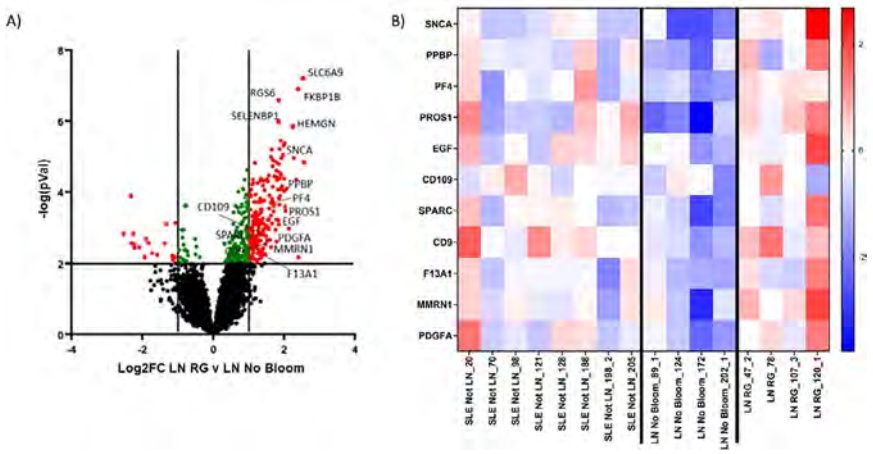

Figure 1. LN patients with RG gut blooms overexpress genes, including for platelet activation. (A) Volcano plot of genes differentially expressed in LN patients with (LN RG) and without RG bloom (LN No Bloom) (Red indicates p<0.01 and log2FC>1 or <-1, and green p<0.01 with Log2FC <1 or >-1). (B) Heatmap illustrates differential gene expression in patients with non-renal SLE (SLE Not LN), LN (LN No Bloom), and RG blooms (LN RG), compared to control samples, for 11 genes that intersect with the "Platelet Activation" pathway.

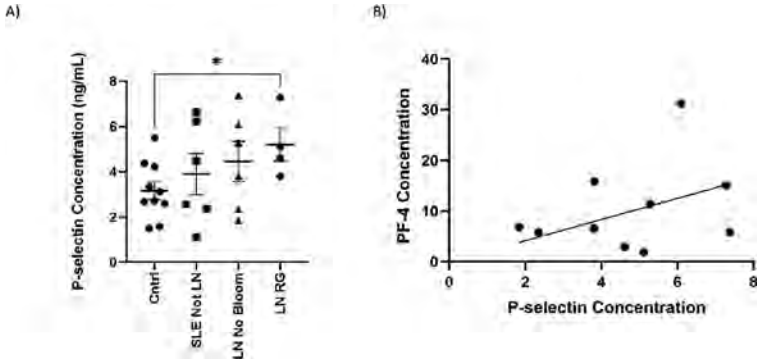

Figure 2. P-selectin levels are increased in patients with LN and RG bloom. (A) P-selectin/CD62-P levels in SLE patients and (B) correlation of P-selectin and PF-4 s in sera of patients with LN and levels of serum RG anti-LG antibodies above level in healthy individuals (p=0.003). *indicates p<0.05, non-parametric Mann-Whitney U analysis of LN RG vs. Control. Based on commercial ELISA of serum (P-selectin 1:400, PF4 1:20, ng/mL).

controls (Figure 1B). As platelet degranulation was found to be upregulated in a subset of LN patients with RG blooms, we interrogated serum levels of P-selectin/CD62P, a protein produced by activated platelets affecting leukocyte activation/migration. We found that P-selectin was increased in LN patients with RG blooms. No significant difference was observed in LN patient without RG blooms or non-renal SLE patients (Figure 2A). The gene expression of PF4, a chemokine protein primary secreted by platelets upon activation was found to be higher in LN RG, compared to controls (Figure 1A). Serum P-selectin directly correlated with PF4 levels (p=0.003)(Figure 2B).

Conclusion: Patients with LN and RG gut blooms displayed upregulated expression of genes for platelet activation and degranulation. Gut blooms with the pathobiont RG, known to cause gut leakiness from the gut and induce high serum anti-RG lipoglycan antibodies, are herein associated with increased platelet activation and raised serum P-selectin and PF4. Taken together, our data point to a potential role for platelet activation and thrombo-inflammation in LN pathogenesis.

Disclosure: A. Amarnani: None; **D. Azzouz**: None; **M. Cornwell**: None; **D. Mieles**: None; **P. Izmirly**: None; **J. Buyon**: Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, Related Sciences, 1; **K. Ruggles**: None; **G. Silverman**: None.

Abstract Number: 0852

Screening for Specific Antinuclear Antibodies Using an Artificial Intelligence-enabled Antinuclear Antibody HEp-2 Substrate by Indirect Immunofluorescence Assay

Patrick Vanderboom, Surendra Dasari, Anne Tebo, Melissa Snyder and **Ali Duarte-Garcia**, Mayo Clinic, Rochester, MN

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes I: Biomarkers
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Antinuclear antibodies (ANA) are key biomarkers in the diagnostic evaluation of systemic autoimmune diseases and are widely used in clinical practice. The most accepted ANA screening is ANA by immunofluorescence (IFA) on HEp-2 cells, which allows the detection of antibody binding to specific intracellular targets, resulting in diverse

Table. Performance characteristics of the convolutional neural network (CNN) image analysis models and traditional immunofluorescence staining patterns for predicting specific autoantibody positivity among patients with a positive ANA.
*p<0.001 AUC in CCN model vs. traditional pattern

Performance characteristics. AUC (95 CI)	Anti-Smith*	Centromere antibodies*	Anti-SSB/La*	Anti-dsDNA*	Anti-SSA/Ro*	Anti-U1 RNP*
CNN Image Analysis Models	0.88 (0.82-0.94)	0.87 (0.82-0.93)	0.84 (0.79-0.89)	0.8 (0.75-0.85)	0.8 (0.77-0.83)	0.68 (0.63-0.72)
Homogeneous pattern	-	-	-	0.68 (0.63-0.73)	-	-
Speckled pattern	0.65 (0.57-0.73)	-	0.64 (0.59-0.70)	-	0.59 (0.56-0.63)	0.58 (0.54-0.62)
Centromere pattern	-	0.83 (0.78-0.89)	-	-	-	-

AUC, area under the curve; CI, confidence intervals

Performance characteristics of the convolutional neural network (CNN) image analysis models and traditional immunofluorescence staining patterns for predicting specific autoantibody positivity among patients with a positive ANA.

staining patterns. While a HEp-2 IFA pattern(s) can guide confirmatory testing and may be useful for elucidating a specific clinical diagnosis or prognosis, pattern recognition is observer-dependent and subjective. We tested the hypothesis that applying artificial intelligence (AI) to Hep2 IFA could identify specific autoantibodies associated with systemic autoimmune diseases.

Methods: Using paired ANA by Hep-2 images and autoantibody testing data, we trained a convolutional neural network (CNN) to identify patients with positivity for anti-dsDNA, Smith, U1RNP (recombinant human antigens for RNP68 or RNPA), SS-A/Ro (combined for Ro52 and ro60), SS-B/La, and Centromere B antibodies. We included patients with at least one digital image of an ANA by Hep-2 between 12-12-2016 and 6-2-2022 who also were tested for the indicated autoantibodies ≤ 90 days of the ANA by Hep2. If a patient had multiple ANA by Hep2, only the first result was included. We allocated the positive ANA images (those with a titer of ≥ 1:80) to the training, internal validation, and testing datasets on an 80:10:10 ratio. The validation dataset was used to monitor the training process for each autoantibody model. The performance of each model was then evaluated in a separate holdout testing data set by performing receiver operator characteristic analysis to determine the area under the curve from (AUC). For reference, the predictive performance of each image analysis model was compared to the IFA staining patterns classically associated with each respective autoantibody.

Results: In total, 410,075 patients tested for ANA by HEp-2 IFA were included in the dataset. Of these, 136,156 had a positive ANA, and 47,093 also had specific autoantibody serology testing within 90 (mean age = 55.0 ± 17.7 years, % female = 78.6%). The results are detailed in the table. All models, except anti-RNP, had an AUC ≥ 0.80. The CNN image models had a superior predictive performance in all cases than the traditional staining patterns ($P < 0.001$), except centromere antibody, where the performance was similar ($P=0.135$).

Conclusion: The application of AI to the widely used ANA by HEp-2 IFA permits the identification of specific autoantibody detection without relying on stain patterns. This model requires further refinement and external validation. However, it holds promise as a revolutionary way to screen for autoantibodies, eliminating concerns about technical staff expertise and inter-rater reliability, increasing access to care, information obtained from the ANA by HEp-2 IFA, and decreasing costs.

Disclosure: P. Vanderboom: None; **S. Dasari**: None; **A. Tebo**: None; **M. Snyder**: None; **A. Duarte-Garcia**: None.

Abstract Number: 0853

Early Experience with Avacopan for ANCA-Associated Vasculitis in a Large Integrated Healthcare System

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Vasculitis – ANCA-Associated I
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: ANCA-associated vasculitis (AAV) is a small-to-medium vessel vasculitis associated with substantial morbidity and mortality, in part due to glucocorticoid exposure. Avacopan, an oral C5a inhibitor, is non-inferior to a standard glucocorticoid regimen, as part of usual remission induction treatment for AAV. Avacopan is increasingly used but little is known about real-world experience with this drug.

Methods: We identified all prescriptions for avacopan in a large integrated healthcare system in the US that includes 12 hospitals, including their primary care practices, community health centers, specialty clinics, and inpatient settings. The study period was from the date of FDA approval of avacopan (October 8, 2021) through March 30, 2023. Patients were followed through May 15, 2023. Details extracted from the medical record included: date of initiation, reason for non-initiation (if applicable), ANCA type, BVAS/GPA, glucocorticoid use, duration of avacopan use, flares, and concomitant immunosuppression. We used the Kaplan-Meier method to estimate the time to treatment without glucocorticoids after avacopan initiation.

Table 1: Demographic features and concomitant treatments in patients prescribed avacopan

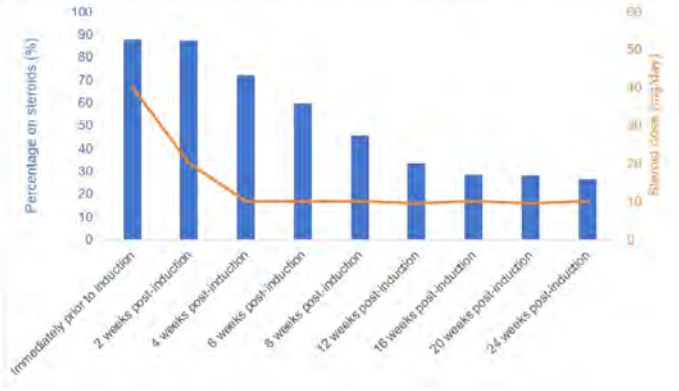
N	66
Age at Diagnosis (mean, SD)	56.8 (17.0)
Age at Time of Prescription (mean, SD)	60.0 (16.7)
Female (n, %)	45 (68.2%)
ANCA Type	
MPO-ANCA+	38 (57.6%)
PR3-ANCA+	22 (33.3%)
Dual	1 (1.5%)
ANCA-negative (n, %)	5 (7.6%)
AAV Status	
New diagnosis	46 (69.7%)
Relapse	20 (30.3%)
Setting of Avacopan Prescription	
Inpatient	19 (28.8%)
Outpatient	47 (71.2%)
Features Among those who Initiated Avacopan After Prescription	
AAV Features (Among Those Initiating)	
Baseline BVAS/WG (median, IQR)	4 (2, 6)
Renal Involvement	27 (46%)
Baseline eGFR (median, IQR)	61.5 (28.8, 83.3)
eGFR < 15ml/min	9 (16%)
Pulmonary Hemorrhage	12 (21%)
Concurrent Treatment at Avacopan Initiation	
Rituximab	26 (46.4%)
Rituximab with short oral bridging course of cyclophosphamide	26 (46.4%)
Cyclophosphamide	2 (3.6%)
Azathioprine	2 (3.6%)
Treatment 6 Months After Avacopan Initiation *(among those reaching month 6)*	27
Rituximab	24 (88.9%)
Cyclophosphamide	1 (3.7%)
Other	2 (7.4%)

Table 2: Characteristics and management of flares in avacopan users

Number with a Flare During Follow-Up	10 (18%)
Major Relapse*	4 (40%)
Minor Relapse	6 (60%)
Flare on Prednisone Treatment	5 (50%)
Prednisone Dose Range at Flare	2.5mg/d-12mg/d
Prednisone Dose Range for Treatment	12.5mg/d-40mg/d
Flare Off of Prednisone Treatment	5 (50%)
Prednisone Dose Range for Treatment	5mg/d-40mg/d
Time from induction to flare (mean, median)	100.3, 77

*Major relapse was defined as a relapse involving at least one major item on the BVAS/WG. Other relapses were defined as minor.

Figure: Steroid tapering trends among avacopan users in a large healthcare system.



Results: Avacopan has been prescribed to 66 patients (**Table 1**). The mean age was 66 years; the majority were female (68.2%), MPO-ANCA+ (57.6%), and newly diagnosed (69.7%). Most initial prescriptions were in the outpatient setting (71.5%). Of the 66 patients, 56 (84.9%) began avacopan; 10 (15.1%) never initiated avacopan because of insurance-related barriers (n=5), intubation (n=2), and patient preference (n=1). The median time from prescription to initiation was 14.5 days. The most common induction regimens were rituximab (46.4%) or rituximab with a short oral course of cyclophosphamide (46.4%). Of the 56 patients who began avacopan, 49 (87.5%) were also treated with steroids. The median time to discontinuing steroid was 56 (28-168) days (**Figure**). At 8 weeks, 45.7% remained on prednisone (median dose 10mg/d). At 24 weeks, 26.5% were on prednisone (median dose 10mg/d). The median time on avacopan was 159 days (total exposure of 9,184 days). Avacopan was discontinued by 19 (33.9%), most often because of completion of the intended course (n=10; at 6 months in n=8). Avacopan was discontinued by 5 (8.9%, 0.05/100 person days) because of an adverse event (e.g., transaminitis, paresthesia, pruritis). Ten (18%) patients had a disease flare; 6 were minor and the median time to flare was 77 days (**Table 2**). Five patients were on steroids at the time of flare and increased their dose; the other five started prednisone. One patient who initiated avacopan died during their initial presentation because of hypoxemic respiratory failure attributed to infection.

Conclusion: This is among the first reports of real-world experience with avacopan. Avacopan users quickly tapered prednisone doses but low-to-moderate doses of prednisone were commonly used for prolonged periods. Nearly one-in-five patients experienced a flare. We identified insurance-related barriers to access. Studies are needed to determine the optimal use of steroids with avacopan and factors associated with relapse.

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Abstract Number: 0854

Long-term Efficacy of Remission-induction Regimens for Eosinophilic Granulomatosis with Polyangiitis

Martin Dutertre[1], Gregory Pugnet[2], Claire De Moreuil[3], Bernard Bonnotte[4], YGAL BENHAMOU[5], Dominique Chauveau[6], Elisabeth Diot[7], Pierre Duffau[8], Nicolas Limal[9], Antoine Néel[10], GEOFFREY URBANSKI[11], Noémie Jourde-Chiche[12], Nicolas MARTIN SILVA[13], Francois Maurier[14], Arsène Mekinian[15], Nicolas Schleinitz[16], Felix ackermann[17], Anne-Laure Fauchais[18], Antoine Froissart[19], Thomas Le Gallou[20], Yurdagul Uzunhan[21], Jean-Francois Viallard[22], Alice Berezne[23], laurent chiche[24], Bruno Crestani[25], Guillaume Direz[26], Cecile-Audrey DUREL[27], Pascal Godmer[28], Jean-Emmanuel Kahn[29], Marc Lambert[30], Mathilde de Menthon[1], Thomas Quemeneur[31], Jacques Cadranel[1], Pierre Charles[32], Antoine Dossier[1], Loic Guillevin[33], Xavier Puéchal[34] and Benjamin Terrier[35], [1]AP-HP, Paris, France, [2]CHU Toulouse Rangueil Service de Medecine Interne et Immunologie Clinique, Toulouse, France, [3]CHU de Brest, Brest, France, [4]Department of Internal Medicine and Clinical Immunology, Dijon University Hospital, Dijon, France, [5]rouen university hospital, Rouen, France, [6]Hôpital Le Tripode, Bordeaux, France, [7]Service de médecine interne et immunologie clinique, CHU Tours, Tours, France, [8]CHU Bordeaux, Bordeaux, France, [9]AP-HP, Créteil, France, [10]CHU de Nantes, Nantes, France, [11]CHU Angers, Angers, France, [12]AP-HM, Marseille, France, [13]CHU Caen, Caen, France, [14]Hôpitaux privés de Metz, Vaux / Frankreich, France, [15]Department of Internal Medicine, Hôpital Saint-Antoine, AP-HP, Paris, France, [16]Aix Marseille university, AP-HM, Marseille, France, [17]Hôpital Foch, Suresnes, France, [18]Dupuytren Hospital, Limoges, France, [19]CHI Créteil, Créteil, France, [20]CHU Rennes, Rennes, France, [21]AP-HP, Bobigny, France, [22]CHU de Bordeaux, Hôpital Haut-Lévêque, Pessac, France, [23]CH Annecy, Annecy, France, [24]Hopital Europeen, Marseille, France, [25]Hopital Bichat, Paris University, Paris, France, [26]CH Le Mans, Le Mans, France, [27]Hospices Civils de Lyon, Lyon, France, [28]CH Bretagne Atlantique, Vannes, France, [29]AP-HP, Suresnes Cedex, France, [30]CHRU Lille, Lille, France, [31]CH Valenciennes, Valenciennes, France, [32]Institut Mutualiste Montsouris, Service de Médecine Interne, Paris, France, [33]University Paris Descartes, Paris, France, [34]National Referral Center for Rare Systemic Autoimmune Diseases, Paris, France, [35]Department of Internal Medicine, Hôpital Cochin, AP-HP, Paris, France

SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Vasculitis – ANCA-Associated I

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: The Rituximab in Eosinophilic Granulomatosis With Polyangiitis (REOVAS) trial compared rituximab (RTX) infusions to conventional strategy for remission-induction in eosinophilic granulomatosis with polyangiitis (EGPA). This trial failed to show a superiority of RTX over the conventional strategy to induce remission at 180 days. However, the long-term efficacy and safety of RTX as compared with conventional strategy in EGPA remains unknown. We report here the long-term results of the REOVAS trial.

Methods: After completion of the 12-month REOVAS trial, patients were followed prospectively, with data on disease activity, medications and adverse events collected by the patients' physicians every 6 months until the last follow-up. The primary endpoint was the minor and major relapse-free survival. Secondary endpoints were major relapses and asthma and ENT exacerbations were also assessed.

Results: Among 105 enrolled patients, only one was lost to follow-up. The median follow-up was 45 months (IQR 34-53).

At month 45 (median follow-up), for the RTX and conventional strategy arms, respectively, the minor and major relapse-free survival rates were 63.5% (95%CI 49.9%-75.2%) and 50.9% (95%CI 37.9%-63.9%) (p=0.24) ; major relapse-free survival rates were 90.4% (95%CI 79.4%-95.8%) and 79.2% (95%CI 66.5%-88.0%) (p=0.17); asthma and/or ENT exacerbation-free survival rates were 42.3% (95%CI 29.9%-55.8%) and 34.0% (95%CI 22.7%-47.4%) (p=0.42) ; and overall EGPA-related event-free survival rates were 32.7% (95%CI 21.5%-46.2%) and 22.6% (95%CI 13.5%-35.5%) (p=0.28). We then

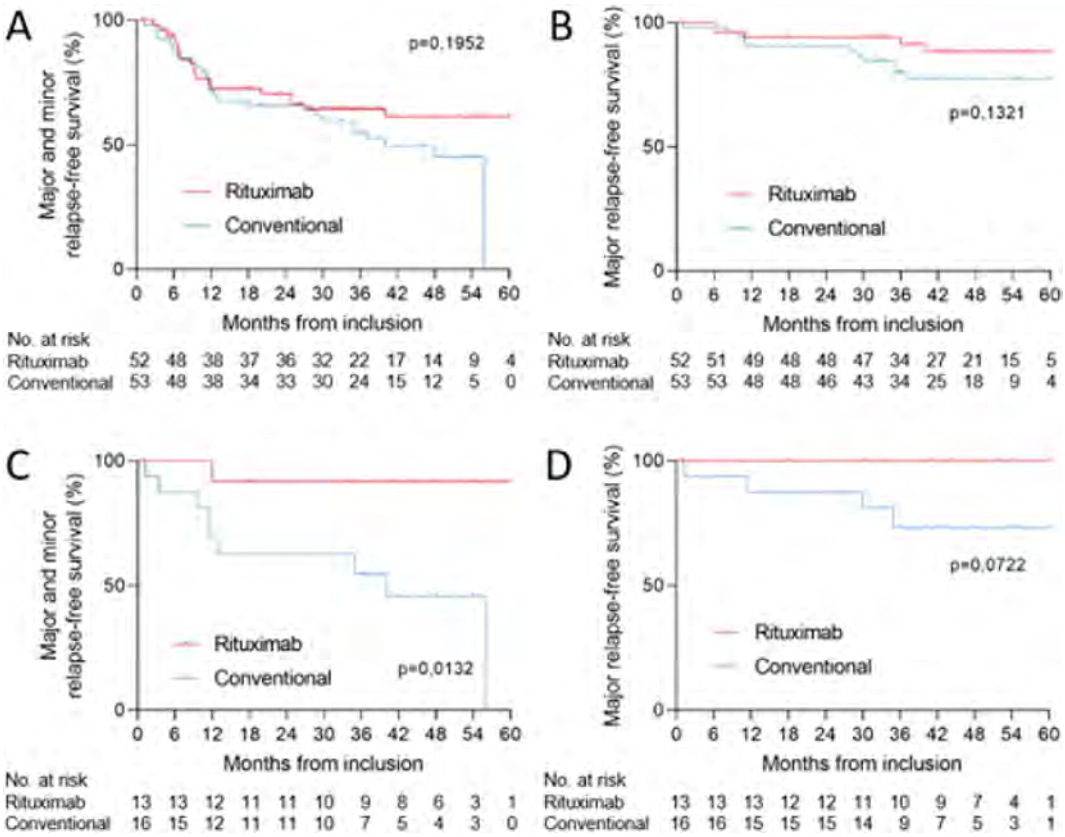

Figure 1. Kaplan-Meier curves of the risk of all (major and minor) relapse (A), major relapse (B) in all patients; all relapse (C) and major relapse (D) in MPO-ANCA-positive patients, according to treatment group. Patients were randomly assigned to receive remission induction therapy with rituximab strategy or conventional strategy, stratified according to disease-flare category, ANCA positivity and the Five Factor score

Table 1. Baseline characteristics of the patients included in the REOVAS study

	Rituximab n=52	Conventional n=53	Total n=105
Age - yr	57 (48 - 69)	64 (51 - 70)	61 (49 - 70)
Female sex, n (%)	27 (51.9%)	28 (52.8%)	55 (52.4%)
Patient status			
New diagnosis, n (%)	37 (71.2%)	37 (69.8%)	74 (70.5%)
Relapsing EGPA, n (%)	15 (28.8%)	16 (30.2%)	31 (29.5%)
ANCA positivity, n (%)	24 (46.2%)	22 (41.5%)	46 (43.8%)
MPO-positive patients, n (%)	13 (25%)	16 (30.2%)	29 (27.6%)
Severity of disease			
FFS = 0, n (%)	31 (59.6%)	32 (60.4%)	63 (60%)
FFS ≥ 1, n (%)	21 (40.4%)	21 (39.6%)	42 (40%)
Cardiac involvement, n (%)	14 (26.9%)	18 (34.0%)	32 (30.5%)
BVAS	13.5 (9 - 16)	16.0 (12 - 20)	14.0 (10 - 18)
Eosinophils count - /mm3	3800 (1255 - 9645)	4915 (1148-7082)	4400 (1310 - 8810)

ANCA : antineutrophil cytoplasmic antibodies, BVAS : Birmingham activity score, EGPA : Eosinophilic Granulomatosis with Polyangiitis, FFS : Five-Factor Score, MPO : myeloperoxidase.

Table 2. Numbers of patients with SAE according to treatment group

	Rituximab n=52	Conventional n=53
Severe infection	16	14
Bronchopulmonary (excluding SARS-Cov2)	5	5
SARS-CoV-2	2	4
Cardiovascular event	6	5
Cancer	5	3
Liver disorder	2	1
Hematologic disorder	2	1
Pulmonary embolism	2	0
Bronchospasm	0	1

SAE: severe adverse event.

focused our analysis on patients with MPO-ANCA and showed that the minor and major relapse-free survival rates were 92.3% (95% CI 66.7% - 99.6%) and 50% (95% CI 58% - 72%) for the RTX and conventional arms, respectively (p=0.02).

As 39 patients were enrolled during follow-up in the double-blind MAINRITSEG trial evaluating RTX versus azathioprine for maintenance in EGPA, we focused our analysis on the 66 patients (63%) who were not enrolled in MAINRITSEG. At month 45, the minor and major relapse-free survival rates for the RTX (n=30) and conventional strategy (n=36) arms were 60.0% (95%CI 42.3%-75.4%) and 38.9% (95%CI 24.8%-55.2%), respectively (p=0.14), and the major relapse-free survival rates were 90.0% (95%CI 73.6%-97.3%) and 72.2% (95%CI 55.9%-84.3%), respectively (p=0.12). When analyzing only ANCA-positive patients (14 in the RTX and 14 in the conventional arms), the minor and major relapse-free survival rates were 78.6% (95%CI 51.7%-93.2%) and 35.7% (95%CI 16.2%-61.4%), respectively (p=0.054). Similar results were found when analyzing only MPO-ANCA positive patients (6 in the RTX and 9 in the conventional arms), showing that minor and major relapse-free survival rates were 100.0% (95%CI 55.7%-100.0%) and 22.22% (95%CI 5.3%-55.7%), respectively (p=0.007).

Conclusion: Among EGPA patients with active disease, long-term follow-up supports that RTX and the conventional strategy have similar efficacy in inducing and maintaining remission. However, in ANCA-positive patients, RTX was associated with a better relapse-free survival compared to the conventional strategy.

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Abstract Number: 0855

Real-world Experience with Avacopan in ANCA Vasculitis: A Multi-center Retrospective Cohort Analysis

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SESSION INFORMATION

Session Date: Sunday, November 12, 2023

Session Title: Abstracts: Vasculitis – ANCA-Associated I

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Avacopan (AVP) is a recently approved adjunct therapy for remission induction of ANCA-associated vasculitis (AAV). Data on real-world use of AVP in AAV are lacking. The objective of this study was to describe the current practice in the use of AVP for the treatment of AAV and associated outcomes.

Methods: We performed a multi-center retrospective cohort study of 80 adult patients with new and relapsing AAV treated with AVP. Follow-up time was up to 52 weeks from diagnosis. The primary outcome measure was clinical remission, as determined by the investigator. Secondary outcome measures included Birmingham Vasculitis Activity Score (BVAS) 3, cumulative glucocorticoid dose, estimated glomerular filtration rate (eGFR) (mL/min/1.73m^2), proteinuria (g/g), hematuria, disease relapses, hospitalizations, end-stage kidney disease (ESKD), infections, and death. Data are presented as mean (±SD), median (IQR), or number (percent).

Results: Mean age was 59 years (±17), 65% were female, 59 (74%) had MPO ANCA, and 76 (95%) had kidney involvement. At diagnosis, 19 patients (24%) had eGFR < 15 mL/min/1.73m^{2,} and 8 (10%) were dialysis-dependent. Rituximab plus cyclophosphamide was the most common induction regimen (49%), followed by rituximab only (46%). AVP was started 8.8 weeks (SD ± 19.6) after glucocorticoid initiation with 58 patients (73%) discontinuing prednisone 7.5 weeks (±18) after

Table 1. Outcomes of patients with AAV treated with avacopan AVP = avacopan, BVAS = Birmingham Vasculitis Activity Score, uPCR = urine proteine creatinine ratio, eGFR = estimated glomerular filtration rate

	Time points			
	At diagnosis	At AVP initiation	Follow-up	
Outcomes	T = 0 weeks n = 80	T = 8.8 weeks (20) n = 80	T = 26 weeks n = 59	T = 52 weeks n = 32
BVAS, median (IQR)	13 (10 – 19)	6 (3 – 12)	0 (0 – 0)	0 (0 – 0)
eGFR, mL/min/1.73m^2, mean (SD)	47 (34)	42 (32)	59 (34)	62 (38)
Change in eGFR from baseline, mL/min/1.73m^2, mean (SD)	-	-4.4 (19)	+8.3 (28)	+14 (29)
uPCR, g/g, median (IQR)	1.5 (0.3 – 2.7)	1.3 (0.3 – 2.3)	0.4 (0.2 – 1.1)	0.3 (0.1 – 0.7)
Hematuria, n (%)	60 (75%)	37 (46%)	11 of 30 (37%)	3 of 10 (30%)
Clinical remission, n (%)	-	-	54 (92%)	29 (91%)

AVP = avacopan, BVAS = Birmingham Vasculitis Activity Score, uPCR = urine protein creatinine ratio, eGFR = estimated glomerular filtration rate

starting AVP. Outcomes are summarized in **Table 1**. Among the 60 patients (75%) with hematuria at diagnosis, 70% had resolution of hematuria 14 weeks (±14) after AVP initiation. Nadir proteinuria of 0.3 g/g (0.1 – 0.7) was achieved 10 weeks (±21) after AVP initiation. The cumulative dose of IV methylprednisolone was 2.4 g (±1.4), and 12-week oral prednisone was 1.8 g (±1.1). At week 26, 5 of 59 patients (8%) remained on prednisone. Of the 80 patients, 60 were started on remission maintenance therapy with rituximab (n = 56), azathioprine (n = 3), and intravenous immunoglobulin (n = 1).

AVP was stopped in 25 patients (31%): 11 (14%) after completing 52 weeks of treatment, and 14 (18%) before 52 weeks due to adverse events, including 4 patients with transaminitis. At a mean follow-up time of 8 months (±6), 5 (6%) had a disease relapse, 7 (9%) had infections requiring hospitalization, 3 (4%) progressed to end-stage kidney disease, and 3 (4%) patients died.

Conclusion: Patients with AAV treated with AVP in conjunction to standard remission-induction therapy have a high rate of clinical remission at weeks 26 and 52 and demonstrate a sustained improvement in eGFR. There was variability in the time till initiation of AVP and glucocorticoid discontinuation. AVP was discontinued in a group of patients due to adverse events or after 1-year of continuous treatment. Further data on the longer-term use of AVP is needed.

Disclosure: S. Sattui: AstraZeneca, 5, Bristol Myers Squibb Foundation, 5, Rheumatology Research Foundation, 5, Sanofi, 2, 5; **C. Diffie**: ChemoCentryx, 6; **A. Shaikh**: None; **J. Ford**: None; **D. Bulbin**: AbbVie/Abbott, 2, 6, Alexion, 2, 6, Amgen, 2, 6, Novartis, 2, Sanofi Genzyme, 6; **O. Gewurz-Singer**: None; **F. Aqeel**: None; **R. Zonozi**: None; **A. Sassine Geara**: Amgen, 5, Chinook, 5, GlaxoSmithKlein(GSK), 2, Novartis, 2, Travere, 2, 5, Vera, 5; **D. Le**: None; **G. Sauvage**: None; **M. Chung**: None; **I. Ayoub**: Aurinia, 1; **F. Cortazar**: Amgen, 2, 6, Aurinia, 2, 6, Calliditas, 6, Travere, 2, Valenza Bio, 2; **A. Bomback**: Amgen, 2; **K. Guaman**: None; **J. George**: None; **J. Niles**: Amgen, 1, 12, planning participation is a phase IV trial; **D. Geetha**: Amgen, 2, Aurinia, 2, calliditas, 2, chemocentryx, 2, GlaxoSmithKlein(GSK), 2.

Abstract Number: 0856

Dupilumab for Relapsing or Refractory Eosinophilic Granulomatosis with Polyangiitis: A European Retrospective Study

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SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Vasculitis – ANCA-Associated I
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA) is an ANCA-associated vasculitides characterized by asthma, blood and tissue eosinophilia and systemic manifestations. Glucocorticoids (GCs)-dependent asthma and/or disabling ear, nose and throat (ENT) symptoms may persist in half of the patients. Mepolizumab represent an important strategy in these situations. Nevertheless, some patients may show poor or dissociated response between asthma and ENT involvement, requiring alternative options. Dupilumab, a monoclonal antibody directed against the IL-4/IL-13 receptor, has been approved for the treatment of eosinophilic asthma and chronic rhinosinusitis with nasal polyposis, raising the question of its efficacy and its tolerance in EGPA. We aimed to describe the safety and efficacy of the off-label use of dupilumab to treat relapsing and/or refractory EGPA.

Methods: We conducted a European multicenter retrospective study including patients with EGPA fulfilling 2022 ACR/EULAR classification criteria and treated with dupilumab. We collected safety and efficacy data. Response was defined as complete by BVAS=0 and prednisone dose ≤4 mg/day, and partial by BVAS=0 and prednisone dose >4 mg/d

Results: Fifty patients were included, with a median age of 52 years (IQR, 45-57), 29 were women (58%). Dupilumab was initiated for disabling ENT manifestations in 41 (82%) cases, GCs-dependency in 28 (56%) and/or poorly controlled asthma in 27 (54%). Dupilumab was associated with methotrexate in 5, azathioprine in 3, and mycophenolate in 1. Median follow-up after dupilumab initiation was 13.2 (5.4-17.8) months.

Twenty-one patients (42%) achieved a complete response and 12 (24%) a partial response. Median BVAS was 2 (1-4) at dupilumab initiation and dropped to 0 (0-1.5) at 12 months (p=0.01). Baseline prednisone dose was 8 mg/d (5-13.8) and decreased to 2.5 mg/d (0-5) at 12 months (p=0.04).

Seventeen (34%) patients reported adverse events (AE). Main AE were mild-to-moderate and included headache (n=4), injection-site reaction (n=3), myalgia (n=3), arthralgia (n=3). Two patients experienced non-fatal anaphylactic shock. Dupilumab-induced eosinophilia was reported in 33 patients (66%), with a median peak eosinophil count of 1980/mm3 (IQR 560-9800) occurring 13 weeks (IQR 5-18) after starting dupilumab. This dupilumab-induced eosinophilia remained asymptomatic in 42% cases.

Fifteen (30%) patients presented a EGPA flarewhich was associated with blood eosinophilia in 13/15 (87%) cases leading to dupilumab discontinuation in 11 cases (73%), including systemic flares in 7 cases, asthma exacerbation in 6 cases, ENT relapse in 1 and inflammatory arthralgia in 1.

In total, 21 (42%) patients discontinued dupilumab: vasculitis flare (n=11), dupilumab-induced eosinophilia (n=7), anaphylactic shock (n=2), cancer (n=1). No deaths were reported.

Conclusion: These results suggest that dupilumab may be effective in relapsing and/or refractory EGPA, particularly in ENT manifestations. However, dupilumab-induced eosinophilia is common and may remain asymptomatic or be associated with relapse, so caution is warranted.

Disclosure: B. Molina: None; **R. Padoan**: GlaxoSmithKlein(GSK), 6; **M. Urban**: None; **P. Novikov**: None; **M. Caminati**: None; **C. Taillé**: AstraZeneca, 6, Chiesi, 5, 6, GSK, 5, 6, Novartis, 5, 6, Sanofi, 6; **A. Néel**: None; **L. Bouillet**: None; **P. Fraticelli**: None; **N. Schleinitz**: CSL behring, 1, Eusapharma, 6, GSK, 6; **C. Christides**: None; **L. Moi**: None;

B. Godeau: None; **A. Knight**: None; **J. Schroeder**: None; **S. Marchand-Adam**: None; **H. Gil**: None; **V. Cottin**: Boehringer Ingelheim, 2, 5, 6, 12, Support for attending meetings, Celgene/BMS, 1, 2, CSL Behring, 2, Ferrer, 2, 6, 12, Support for attending meetings, FibroGen, 1, Galapagos, 1, 2, Galecto, 1, GlaxoSmithKline, 2, Pliant, 2, Pure Tech, 2, Redx, 2, Roche, 1, 2, 6, 12, Support for attending meetings, Sanofi, 2, Shionogi, 2; **C. Durel**: None; **E. Gelain**: None; **B. Lerais**: None; **M. Ruivard**: None; **M. Groh**: AstraZeneca, 6, GSK, 6, Sanofi, 6; **M. Samson**: ARGENX, 2, Boehringer-Ingelheim, 2, CHUGAI, 2, CSL Vifor, 2, GlaxoSmithKlein(GSK), 2, NOVARTIS, 2, 5; **L. Moroni**: None; **J. Thiel**: None; **A. Kernder**: None; **J. Tervaert**: None; **G. Costanzo**: None; **M. Folci**: None; **S. Rizzello**: None; **P. Cohen**: None; **G. Emmi**: AstraZeneca, 2, Boehringer-Ingelheim, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2, Sanofi, 2, Sobi, 2; **B. Terrier**: AstraZeneca, 5, CSL Vifor, 2, GlaxoSmithKlein(GSK), 2.

Abstract Number: 0857

Change in Albuminuria in Patients with ANCA-Associated Vasculitis Treated with Avacopan

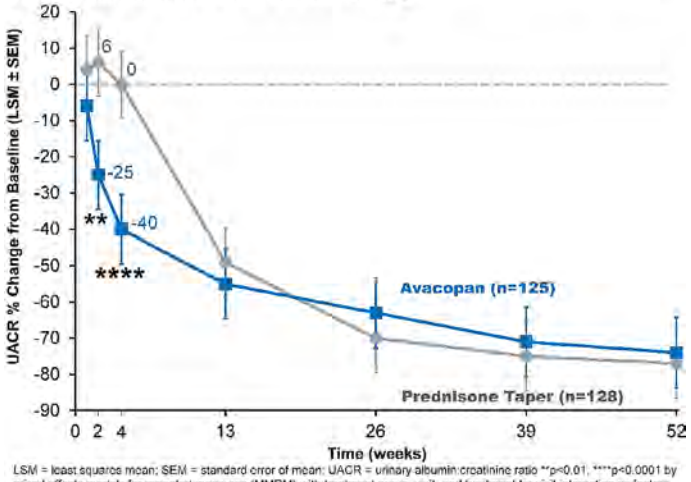
Duvuru Geetha[1], Frank Cortazar[2], alexandre Karras[3], Annette Bruchfeld[4], Huibin Yue[5], Peter Merkel[6] and **David Jayne**[7], [1]Johns Hopkins University, Baltimore, MD, [2]New York Nephrology, Watervliet, NY, [3]HEGP - APHP, Paris, France, [4]Karolinska Institutet, Stockholm, Sweden, [5]Amgen, Inc., Thousand Oaks, CA, [6]University of Pennsylvania, Philadelphia, PA, [7]University of Cambridge, Cambridge, United Kingdom

SESSION INFORMATION

Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Vasculitis – ANCA-Associated I
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

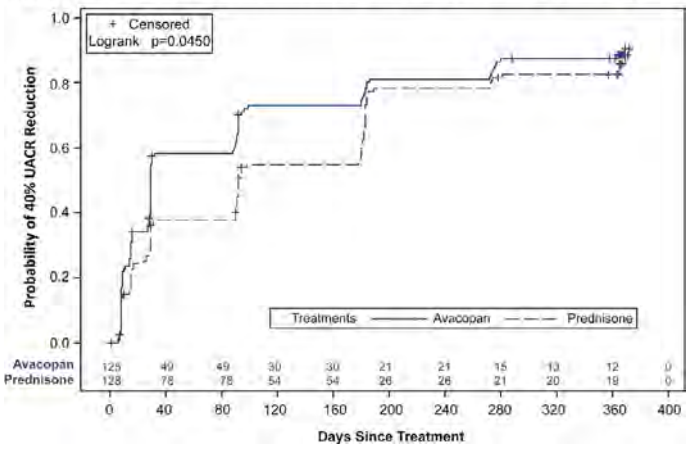
Background/Purpose: Urinary albumin:creatinine ratio (UACR) is an important biomarker of active glomerulonephritis, a common complication of antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV). In most glomerular diseases, high UACR levels and low estimated glomerular filtration rate are associated with the long-term risk of end-stage kidney disease, cardiovascular disease, and death (Levey AS et al, *N Engl J Med* 2022).In the double-dummy, double-blind, controlled ADVOCATE Phase 3 trial (Jayne DRW et al, *N Engl J Med* 2021), patients were randomized to receive avacopan, an oral C5a receptor (C5aR) antagonist that blocks C5a-mediated neutrophil activation and migration, or a prednisone taper. All patients received background immunosuppression with either cyclophosphamide followed by azathioprine, or

Figure 1. Percent Change in UACR from Baseline in the Avacopan vs Prednisone Taper Groups in Patients with Kidney Involvement and UACR≥10 mg/g



LSM = least squares mean; SEM = standard error of mean; UACR = urinary albumin:creatinine ratio **p<0.01, ****p<0.0001 by mixed effects models for repeated measures (MMRM) with treatment group, visit, and treatment-by-visit interaction as factors and baseline as covariate. Percent changes from baseline are based on ratios of geometric means of visit over baseline.

Figure 2. Time to 40% UACR Reduction in the Avacopan vs Prednisone Taper Groups



rituximab. Primary endpoints were remission at week 26 and sustained remission at week 52. Prespecified secondary endpoints included the evaluation of kidney function. The effect of avacopan on UACR in patients with AAV is described.

Methods: This post hoc analysis compared the time to achieve the maximum mean difference in percent change in UACR from baseline between the avacopan and prednisone taper groups using Kaplan-Meier survival analysis. Change in UACR from baseline was a prespecified secondary endpoint but was not adjusted for multiplicity. This analysis included patients from the ADVOCATE trial with kidney involvement (based on the Birmingham Vasculitis Activity Score) and a UACR of at least 10 mg/g at baseline.

Results: The baseline geometric mean UACR mg/g (range) in the avacopan group (n=125) and the prednisone taper group (n=128) was 433 (20 to 6461) and 312 (11 to 5367), respectively. A statistically significant UACR reduction (based on least-square means) in the avacopan group compared to the prednisone taper group occurred as early as week 2 (-25% vs. 6%, p=0.0068, difference between groups: -29%, 95% confidence interval (CI) [-45%, -9%]). UACR continued to decrease at week 4 to the maximum difference between the two groups (-40% vs. 0%, p< 0.0001, difference between groups: -40%, 95% CI [-53%, -22%]) (**Figure 1**). UACR was comparable between the two groups by week 13 (-55% vs. -49%, p=0.3028, difference between groups: -12%, 95% CI [-32%, 13%]). During the 52-week treatment period, 84% (105/125) of patients in the avacopan group achieved a 40% UACR reduction from baseline within a median time of 29 days (95% CI [29, 88]), compared to 83% (106/128) of patients in the prednisone taper group within a median time of 92 days (95% CI [91, 180]) (logrank p=0.0450) (**Figure 2**). There was an overall mean improvement in estimated glomerular filtration rate (eGFR) of 7.6 mL/min/1.73 m^2 in the avacopan group and 4.6 mL/min/1.73 m^2 in the prednisone taper group at week 52.

Conclusion: In the ADVOCATE trial, UACR, an important early indicator of improving kidney function, improved three times faster in the avacopan group compared to the prednisone taper group. The rapid reduction in UACR seen in patients with AAV receiving avacopan suggests more rapid control of glomerular inflammation which may have contributed to the observed subsequent improvement in eGFR.

Disclosure: D. Geetha: Amgen, 2, Aurinia, 2, calliditas, 2, chemocentryx, 2, GlaxoSmithKlein(GSK), 2; **F. Cortazar**: Amgen, 2, 6, Aurinia, 2, 6, Calliditas, 6, Travere, 2, Valenza Bio, 2; **a. Karras**: AstraZeneca, 6, GlaxoSmithKlein(GSK), 4, Novartis, 2, Pfizer, 6; **A. Bruchfeld**: Amgen, 2, AstraZeneca, 2, 12, Investigator fees, Bayer, 2, ChemoCentryx, 1, 12, Investigator fees, CSL Vifor, 2, 12, Investigator fees, Fresenius, 2, 12, Investigator fees, Merck/MSD, 2, 12, Investigator fees; **H. Yue**: Amgen, 3, 11, ChemoCentryx, 3, 11; **P. Merkel**: AbbVie/Abbott, 5, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos,

5, Electra, 5, Genentech, 5, GlaxoSmithKlein(GSK), 2, 5, HiBio, 2, InflaRx, 2, 5, Janssen, 2, Jubilant, 2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, Takeda, 2, 5, UpToDate, 9, Visterra, 2; **D. Jayne**: AstraZeneca, 2, Aurinia, 4, Boehringer Ingelheim, 2, Chinook, 2, CSL Vifor, 2, Roche, 2.

Abstract Number: 0858

Randomized, Controlled, Double-Blind Trial on the Impact of Rosuvastatin on Sublinical Markers of Atherosclerosis in Patients with ANCA-Associated Vasculitis

Benjamin Terrier[1], Gregory Pugnet[2], Marie-Emmanuelle Sirieix[3], Thomas Quemeneur[4], Xavier Puéchal[5], Francois Maurier[6], Antoine Néel[7], YGAL BENHAMOU[8], Bernard Bonnotte[9], Jean Schmidt[10], Adrien Michon[3], Antoine Baudet[11], Pierre Charles[12], Fleur Cohen[13], Claire De Moreuil[14], Emanuelle Dernis[15], Pauline Belenotti[16], Marc Ruivard[17], Olivier Aumaitre[18], Olivier Fain[19], Raphaele Seror[20], Cécile-Audrey Durel[21], Noémie Jourde-Chiche[22], Estibaliz Lazaro[23], Gilles Chironi[24], Guillaume Armengol[25], Jeremy Bellien[25], Philippe Ravaud[26], Gabriel Baron[26] and Loic Guillevin[27], [1]Department of Internal Medicine, Hôpital Cochin, AP-HP, Paris, France, [2]CHU Toulouse Rangueil Service de Medecine Interne et Immunologie Clinique, Toulouse, France, [3]HEGP, Paris, France, [4]CH Valenciennes, Valenciennes, France, [5]National Referral Center for Rare Systemic Autoimmune Diseases, Paris, France, [6]Hôpitaux privés de Metz, Vaux / Frankreich, France, [7]CHU Nantes, Nantes, France, [8]rouen university hospital, Rouen, France, [9]Department of Internal Medicine and Clinical Immunology, Dijon University Hospital, Dijon, France, [10]CHU Amiens, Amiens, France, [11]CH Annecy, Annecy, France, [12]Institut Mutualiste Montsouris, Service de Médecine Interne, Paris, France, [13]Sorbonne Université, Paris, France, [14]CHU de Brest, Brest, France, [15]CH Le Mans, Le Mans, France, [16]CHU Marseille, Marseille, France, [17]CHU Clermont Ferrand, Clermont Ferrand, France, [18]CHU Saint Antoine, Paris, France, [19]Hopital SAINT ANTOINE APHP, Paris, France, [20]University Hospital Paris Saclay, Le Kremlin-Bicêtre, France, [21]CHU Lyon, Lyon, France, [22]AP-HM, Marseille, France, [23]Bordeaux Hospital University, Pessac, France, [24]Monaco, Monaco, Monaco, [25]CHU Rouen, Rouen, France, [26]Paris Cité University, Paris, France, [27]University Paris Descartes, Paris, France

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Abstracts: Vasculitis – ANCA-Associated I
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Despite more effective therapeutic strategies in ANCA-associated vasculitis (AAV), there is still a significant risk of morbidity and mortality, mainly due to infection, and cardiovascular disease. Carotid intima-media thickness (cIMT) is a marker of subclinical atherosclerosis associated with cardiovascular risk factors and is predictive of major cardiovascular events (MACE). We hypothesized that patients with AAV might benefit from statin treatment in primary prevention to reduce subclinical markers of atherosclerosis and the incidence of major cardiovascular events.

Methods: This phase 3, multicentre, randomized, controlled, double-blind, superiority study compared rosuvastatin with placebo in reducing the progression of subclinical markers of atherosclerosis. Patients with AAV in remission after a first flare or relapse were randomized 1:1 to receive the experimental strategy based on the use of rosuvastatin 20 mg/day or placebo for 24 months. The primary endpoint was the mean change in mean cIMT (distal wall of primary carotid arteries) at 24 months.

Results: A total of 111 participants underwent randomization (55% male, mean age 54.8 (13.3) years, 63.1% GPA, 28.8% EGPA, 8.1% MPA), with 54 participants assigned to receive rosuvastatin and 57 to placebo.

The primary endpoint was not met. The mean change in cIMT at month 24 was not different between the two study groups (difference -0.002 [-0.034 ; 0.030], p=0.89) (**Figure 1**). The annualized rate of change in mean cIMT was 0.0110 (0.0617) mm/year in the rosuvastatin group and 0.0189 (0.0556) mm/year in the placebo group (difference -0.0062 [-0.0318 ;

0.0193], p=0.61). Similar results were found for the mean change in the number of plaques in the carotid and femoral arteries and abdominal aorta (difference 0.01 [-0.39 ; 0.42], p=0.94).

Mean LDL-cholesterol levels were significantly different between the two study groups at all time points evaluated (P< 0.001, P< 0.001, and P< 0.001 for reductions between the rosuvastatin and the placebo groups at months 6, 12 and 24, respectively) (**Figure 2**). Also, high-sensitivity CRP levels were significantly different between the two study groups at month 24 (difference -3.16 [-5.58 ; 0.74], p=0.011 for reductions between the rosuvastatin and the placebo groups).

There was only one MACE in the rosuvastatin group. Vasculitis relapse-free survival did not differ between the two groups (HR 1.59, 95%IC = [0.81 ; 3.09], p=0.18).

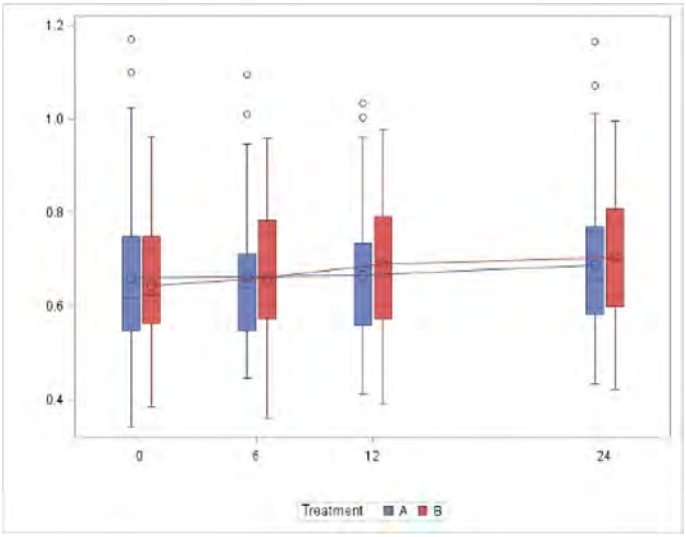


Figure 1. Evolution of mean carotid intima-media thickness (in mm) during the study period in the two groups. Rosuvastatin arm is group A and placebo arm is group B.

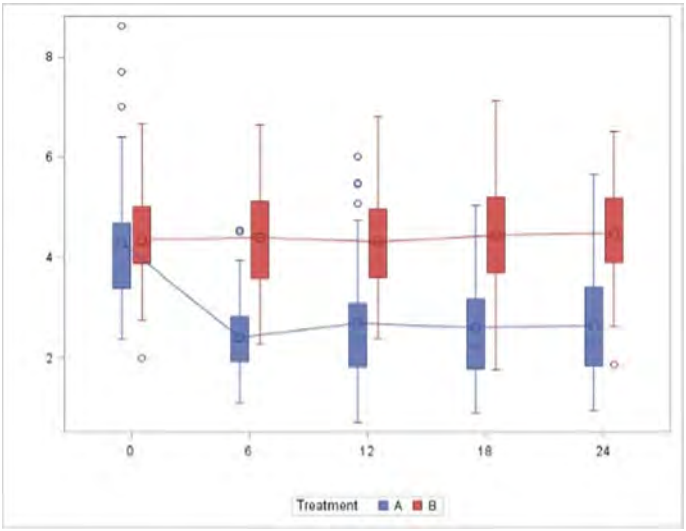


Figure 2. Evolution of mean LDL-cholesterol (in mmol/L) during the study period in the two groups. Rosuvastatin arm is group A and placebo arm is group B.

Eleven and seventeen patients discontinued intervention in the rosuvastatin and the placebo groups, respectively. The incidence of serious adverse events was similar in the two groups: 27.8% in the rosuvastatin group and 22.8% in the placebo group.

Conclusion: Among patients with ANCA-associated vasculitis, 24 months of rosuvastatin reduced LDL-cholesterol but did not reduce the progression of subclinical markers of atherosclerosis (Funded by the French Ministry of Health; STATVAS ClinicalTrials.gov number, NCT02117453).

Disclosure: B. Terrier: AstraZeneca, 5, CSL Vifor, 2, GlaxoSmithKlein(GSK), 2; **G. Pugnet**: None; **M. Sirieix**: None; **T. Quemeneur**: None; **X. Puéchal**: None; **F. Maurier**: None; **A. Néel**: None; **Y. BENHAMOU**: None; **B. Bonnotte**: None; **J. Schmidt**: None; **A. Michon**: None; **A. Baudet**: None; **P. Charles**: None; **F. Cohen**: None; **C. De Moreuil**: None; **E. Dernis**: AbbVie/Abbott, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, Janssen, 2, MSD, 2, Nordic Pharma, 2, Novartis, 2, Pfizer, 2, Roche, 2, Roche-Chugai, 2, Sandoz, 2, Sanofi, 2, UCB Pharma, 2; **P. Belenotti**: None; **M. Ruivard**: None; **O. Aumaitre**: None; **O. Fain**: None; **R. Seror**: None; **C. Durel**: None; **N. Jourde-Chiche**: None; **E. Lazaro**: None; **G. Chironi**: None; **G. Armengol**: None; **J. Bellien**: None; **P. Ravaud**: None; **G. Baron**: None; **L. Guillevin**: None.

Abstract Number: 0859

Single Injection AAV2-hFGF18 Demonstrates Superior Safety and Efficacy over Repeat rhFGF18 Protein Injections in a Model of Induced Osteoarthritis

Alex Goraltchouk[1], Judith Hollander[2], Francesco Luppino[3], Li Zeng[2] and Alexey Seregin[3], [1]Remedium Bio, Inc, Needham, MA, [2]Tufts University, Boston, MA, [3]Remedium Bio, Inc., Needham, MA

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is the largest unmet need in rheumatology, affecting 1 in 7 adults, with no approved disease modifying treatments. A recent placebo-controlled clinical study of rhFGF18 demonstrated, for the first time, the ability to reverse cartilage loss in OA - with the highest dose/frequency arresting progression to joint replacement.

Figure 1

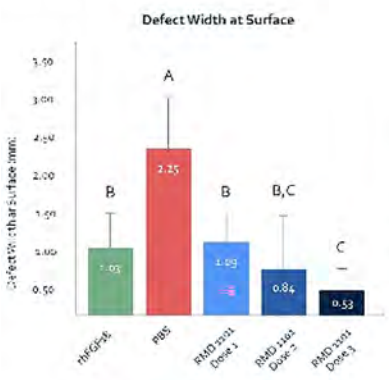


Figure 2

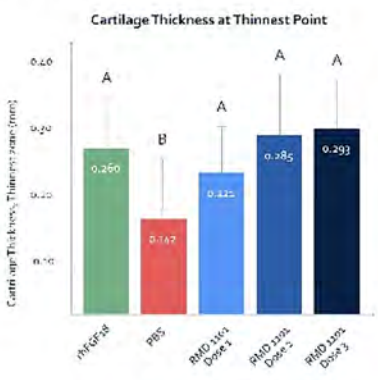
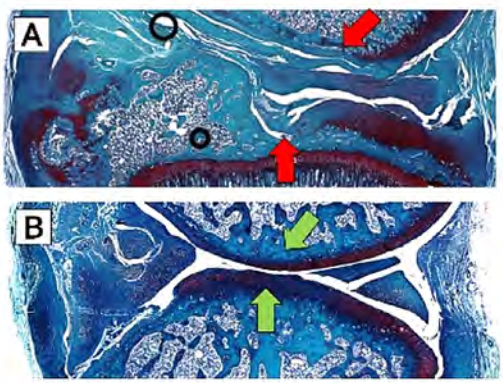


Figure 3



While promising, the safety and efficacy of this approach is limited by the required frequency of intra-articular injections, due to synovial joint pharmacokinetics. In this study, we compared the effects of repeated rhFGF18 protein injections and a single injection AAV2-hFGF18 on cartilage anabolism in healthy and arthritic joints.

Methods: Chondrogenic properties of AAV2-hFGF18 were compared to rhFGF18 protein, AAV2-GFP, and PBS. Cytocompatibility was assessed by cellular viability over 168h in culture. Gene expression was analyzed by RNA-seq on primary human chondrocytes. In vivo durability of gene expression was confirmed using bioluminescence imaging. Cartilage anabolism was evaluated by measuring thickness of the tibial plateau in 300-375g healthy and OA male Sprague-Dawley rats, with OA induced by destabilization of the medial meniscus. Effect on disease progression was assessed by measuring cartilage defect width and depth following administration of AAV2-hFGF18, rhFGF18 protein, and PBS.

Results: At multiplicities of infection (MOIs) of 0.1k and 1k, AAV2-hFGF18 induced proliferative increases of 36 and 84%, respectively, which was in line with rhFGF18 protein dosed at 1-10k ng/ml (38-110%), and statistically above PBS (8%). At the same time, AAV2 demonstrated cytocompatibility through MOIs up to 50k. RNA-seq revealed rhFGF18- and AAV2-hFGF18-induced upregulation of hyaline cartilage-associated HAS2 and COL2A1, and downregulation of fibrocartilage-associated COL1A1. AAV2-hFGF18, but not rhFGF18, upregulated SOX9, a chondrocyte differentiation marker, and PRG4, an articular cartilage lubricating protein, while downregulating the aggrecan-targeting protease ADAMTS15. Compared to healthy cartilage, a significantly more pronounced chondrogenic effect was observed in arthritic joints. Defect widths were reduced in the gene therapy-treated knees by 51.6 – 76.4% relative to PBS, with the highest dose achieving statistical significance over rhFGF18 (54.2% reduction) (Fig 1). Similarly, cartilage thickness at the thinnest point increased in the gene therapy treated joints, reaching 2.06x of PBS (Fig 2). Severe OA pathology was observed in the placebo-treated knees (Fig 3A), including significant cartilage loss, subchondral bone collapse, and formation of bone voids; in contrast, such phenotypes were not observed in the high-dose gene therapy group (Fig 3B). Finally, repeat injections of rhFGF18, while chondroprotective, induced synovitis-mediated joint swelling even in healthy joints, that remained unresolved through 2-months post treatment.

Conclusion: Our findings suggest that a single injection of AAV2-hFGF18 demonstrates superior safety and efficacy over a multi-injection rhFGF18 protein treatment regimen in a model of Osteoarthritis.

Disclosure: A. Goraltchouk: Remedium Bio, Inc., 3, 4, 8, 11; **J. Hollander**: None; **F. Luppino**: Remedium Bio, Inc., 3, 4, 8; **L. Zeng**: Remedium, 2; **A. Seregin**: None.

Abstract Number: 0860

Vagus Nerve Stimulation Enhances Bone Morphology in a Rodent Model of Central Nervous System Inflammation

Chandramohan Natarajan[1], Julia Lucchino[1], David Chenoff[2] and **Yaakov Levine**[1], [1]SetPoint Medical, Valencia, CA, [2]SetPoint Medical, Sausalito, CA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Electrical stimulation of the vagus nerve activates the inflammatory reflex to inhibit cytokines and decrease clinical signs and symptoms of chronic inflammatory disease such as rheumatoid arthritis (RA)[1]. Joint preservation (cartilage and bone) was reported in rat collagen induced arthritis and derosions were observed by MRI in early human clinical

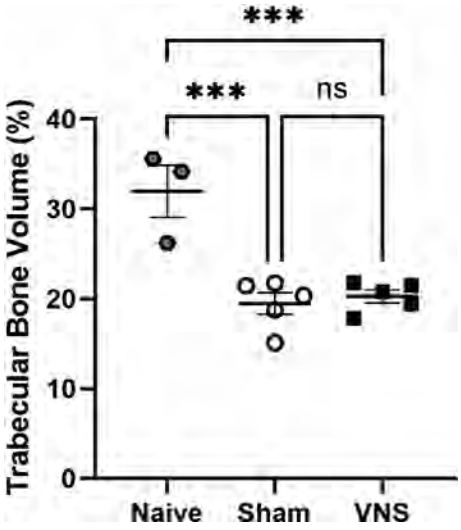


Figure 1.

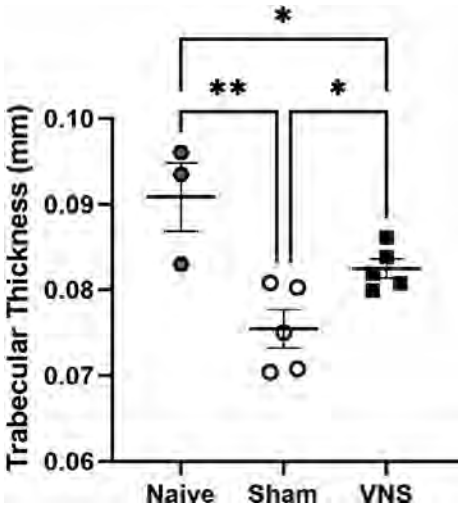


Figure 2.

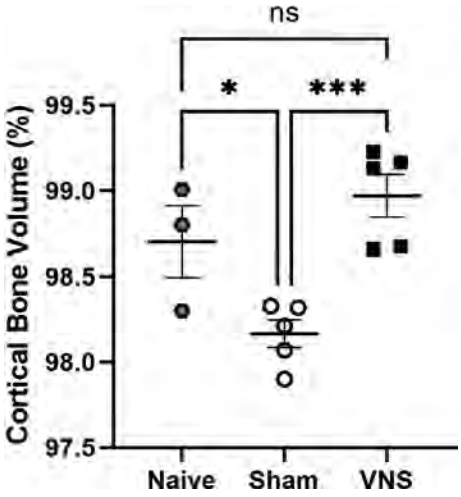


Figure 3.

studies for treatment-resistant RA[1,2]. It is currently unclear whether the beneficial effects of vagus nerve stimulation on bone in RA are specific to bone remodeling, or are simply secondary to a decreased synovial inflammatory milieu. To separate the bone turnover-related effects from the amelioration of joint-specific inflammation, we stimulated the vagus nerve of rats with experimental autoimmune encephalomyelitis (EAE), a CNS-specific disease model with bone resorption as a known comorbidity.

Methods: Vagus nerve stimulation devices (SetPoint Medical, CA) were implanted in 6-week-old female Lewis rats. Following recovery, EAE was induced with myelin basic protein (0.1 mg/rat) and complete Freund's adjuvant (Hooke Laboratories, CT). Conscious rats (n=5/group) were treated with active or sham stimulation from 7 days post-induction (DPI), the day prior to the typical onset of clinical neurologic symptoms, through 21 DPI. Cortical and trabecular bone parameters were calculated through μCT analysis of the proximal femurs and difference in means compared by ANOVA.

Results: On 21 DPI, both active and sham stimulated rats had a significant decrease in trabecular bone mineral density vs. naïve (Fig 1). Trabecular thickness was significantly higher in actively stimulated rats vs. sham (Fig 2). Cortical bone mineral density was numerically reduced in the sham, but not in the active stimulation group. There was a significant reduction in cortical bone volume in the sham, but not in the active stimulation group (Fig 3). *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

Conclusion: The data show that subacute vagus nerve stimulation enhances trabecular thickness and cortical bone volume in the femurs of rats with EAE. This is an important indicator of a bone-specific protective effect of vagus nerve stimulation, in addition to, and independent of, amelioration of joint-specific inflammation. Studies to further understand of the mechanisms of action are underway.

1 Genovese et al, Lancet Rheumatology S2665-9913(20)30172-7 (2020)
2 Levine et al, PLoS One 2014; 9(8):e104530

Disclosure: C. Natarajan: SetPoint Medical, 3, 10, 11; **J. Lucchino**: SetPoint Medical, 3; **D. Chenoff**: SetPoint Medical, 3, 10, 11; **Y. Levine**: SetPoint Medical, 3, 10, 11.

Abstract Number: 0861

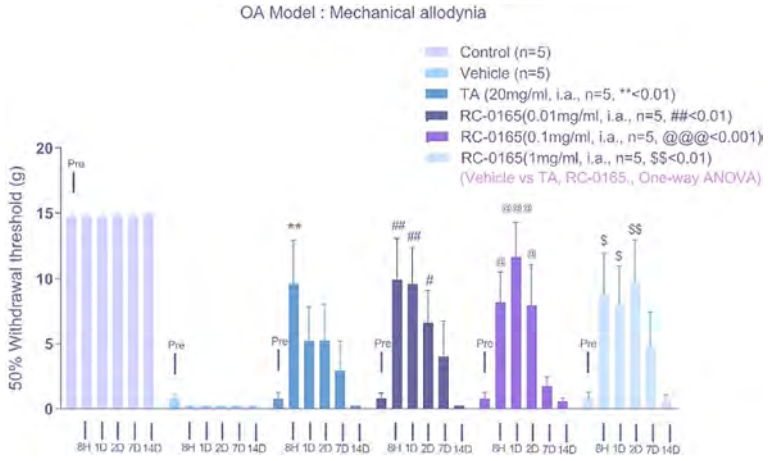
The Analgesic Effect of RC-0165, a TRPV1 Antagonist, for Osteoarthritis Pain

Donghui kim, Juil park, Minjung kim and Yongho kim, RudaCure, Seoul, South Korea

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA), the most common form of arthritis, arises from the deterioration of cartilage within joint bones, resulting in pain and functional disability with limited range of motion. Despite many studies that aimed to find a new target to treat OA pain or regenerate cartilage, OA remains an area of high unmet need due to the lack of effective analgesics and disease-modifying drugs.

The Transient Receptor Potential Vanilloid 1 (TRPV1) cation channel is a member of the Transient Receptor Potential (TRP) channels that acts as a molecular detector of noxious signals in primary sensory neurons. Many companies have attempted to develop TRPV1 antagonists to treat OA pain, however due to TRPV1's role in thermoregulation, most have been halted from side effects such as hyperthermia.



effects of RCI002 compare to TA for OA

RC-0165 is a potent and selective peptide TRPV1 antagonist that potently blocks capsaicin activation of the TRPV1 channel with negligible influence on pH or heat activation modes. We found that when injected intraarticularly, RC-0165 attenuates neuropathic and OA pain without causing any effect on body temperature in both primates (marmosets) and non-primates (rat&mouse).

In this study, calcium imaging was used to assess the effects of RC-0165 on HEK293T cells expressing TRPV1. We also evaluated the efficacy of RC-0165 through pain-related behavioral test using a Monosodium iodoacetate (MIA)-induced OA rat model.

Methods: In vitro, the level of calcium influx after TRPV1 antagonism by RC-0165 in TRPV1-expressing human embryonic kidney (HEK) 293T cells were measured via calcium imaging experiments. In vivo, pain-related behavioral effects were compared to RC-0165 and triamcinolone acetonide (TA)as positive control in a MIA-induced OA rat model, which was assessed using Von Frey, Hargreaves, open field, and rotarod tests.

Results: We confirmed that RC-0165, a novel peptide TRPV1 antagonist, diminishes calcium influx in cells related to pain signals through TRPV1 inhibition. Analgesic efficacy was also investigated in-vivo studies by injecting RC-0165 intraarticularly in MIA-induced OA rat model. In the Von Frey test, which measures the pain in response to mechanical stimulation, the RC-0165(0.01, 0.1 and 1mg/ml) group showed a significant increase in pain threshold compared to TA group and its efficient pain-reducing effect lasted for 3 days. In the open field and rotarod tests, the RC-0165 group showed meaningful increase in exercise capacity and promising results of improvement in OA pain.

Conclusion: The results of our study suggest that RC-0165 may be a promising approach to significantly reduce OA pain compared to TA by suppressing pain signals mediated by TRPV1

Disclosure: D. kim: None; **J. park**: None; **M. kim**: None; **Y. kim**: None.

Abstract Number: 0862

Role of CRTAC1 as a Biomarker of Osteoarthritis

Aneta Pekacova[1], Jiri Baloun[2], Adela Navratilova[3], Lucia Ondrejcakova[4], Jana Zborovjanova[4], Petr Fulin[5], Rastislav Ballay[6], Michal Tomcik[7] and Ladislav Senolt[8], [1]First faculty of medicine, Charles University, Prague, Czech Republic, [2]Institute of Rheumatology, Prague, Czech Republic, [3]Institute of Rheumatology and Department of Rheumatology, First

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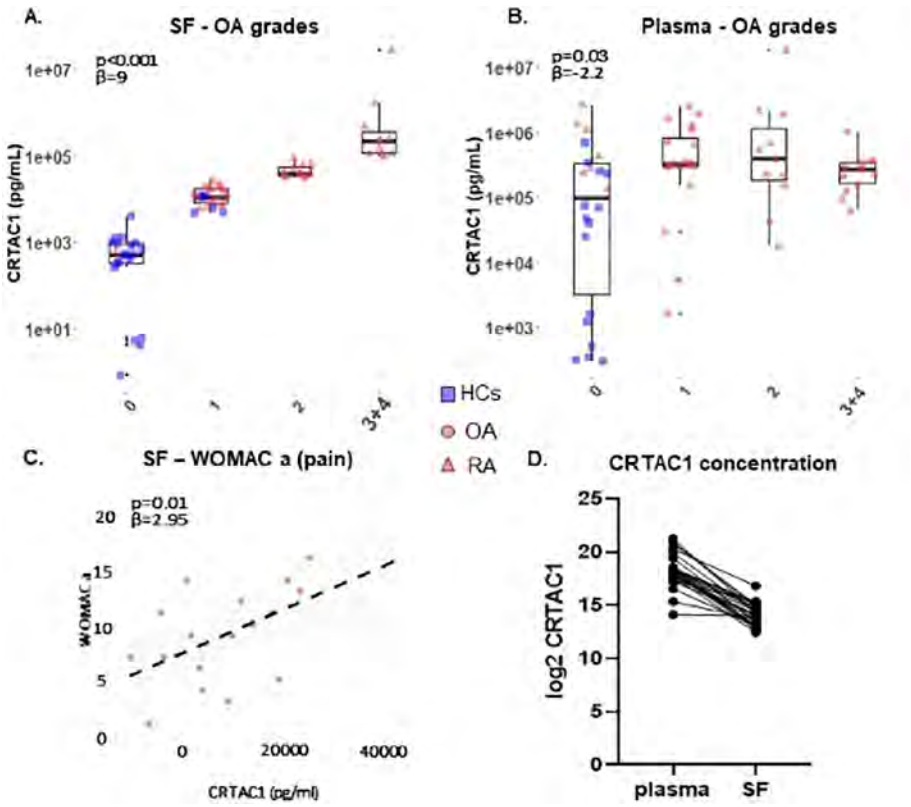
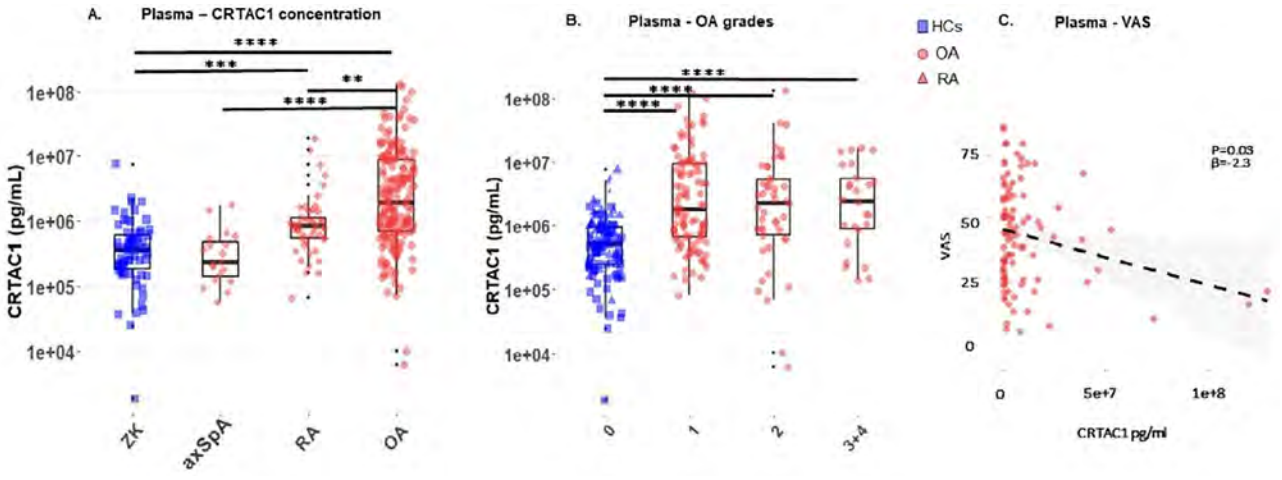
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Cartilage acidic protein-1 (CRTAC1) has been recently considered a promising biomarker of osteoarthritis (OA) progression (1,2). The aim of this study is to compare CRTAC1 levels in paired synovial fluid (SF) and plasma samples from patients with knee OA and rheumatoid arthritis (RA) with unpaired samples from healthy controls (HCs). Secondly, to compare plasma CRTAC1 levels in patients with OA and patients with other inflammatory musculoskeletal diseases. Thirdly, to evaluate the association between CRTAC1 levels and OA severity.

Methods: Paired plasma and synovial fluid (SF) samples were obtained from patients with knee OA (n=26) and from RA patients who had knee effusion (n=19) and underwent therapeutic arthrocentesis. Control samples were obtained from HCs with post-traumatic knee effusion (n=25). Plasma samples were obtained from 67 HCs, 130 patients with OA (including knee, hip, and hand OA), 49 patients with RA, and 20 patients with axial spondyloarthritis (axSpA). CRTAC1 levels were



A. CRTAC1 levels in SF of patients with different OA severity. B. CRTAC1 levels in paired plasma samples of patients with different OA severity. The p-values show the statistical significance of linear regression, including healthy individuals (blue, square), OA patients (red, circle) and RA patients (red, triangle). C. Association of CRTAC1 and WOMAC a (pain) in SF of OA patients, computed via linear modelling. D. Comparison of CRTAC1 concentration in paired SF and plasma samples.



A. CRTAC1 levels in a wider cohort of plasma samples in HCs and patients with axSpA, RA and OA. B. CRTAC1 levels in plasma samples of patients with different OA severity. The p-values show statistical significance between healthy individuals (blue, square), axSpA (red, rhombus), OA patients (red, circle) and RA patients (red, triangle) and were computed using ANOVA. Linear modelling did not reveal the association between CRTAC1 levels and OA severity. C. Association of CRTAC1 and VAS in the wider cohort in plasma samples, computed via linear modelling.

measured using the CRTAC1 ELISA (Bio-Rad). Knee radiographs were evaluated by a blinded assessor using the Kellgren-Lawrence grading scale. Patients were examined by experienced rheumatologists and filled out the Visual Analog Scale (VAS) pain, the Western Ontario and McMaster Universities Arthritis Index (WOMAC), the AUStralian CANadian Osteoarthritis Hand Index (AUSCAN), and the Health Assessment Questionnaire (HAQ).

Results: CRTAC1 levels in SF and plasma were significantly higher in patients with OA compared to HCs ($p< 0.001$). Regression analysis showed a positive relationship between CRTAC1 levels in SF and OA severity ($p< 0.001$; $\beta=9$); however, systemic CRTAC1 levels showed the opposite trend ($p=0.03$, $\beta=-2.2$). We found a positive association between SF levels of CRTAC1 and WOMAC-A ($p=0.01$, $\beta=2.95$).In wider cohort, plasma CRTAC1 levels were higher in patients with OA compared to patients with RA, axSpA, and HCs (all $p< 0.01$). We found a negative association between systemic CRTAC1 levels and VAS pain ($p=0.03$, $\beta=-2.3$) in OA. There were no significant differences in CRTAC1 levels among OA subtypes.

Conclusion: This study provides the first evidence of a distinct local and systemic profile of CRTAC1 in patients with knee OA. CRTAC1 levels in synovial fluid may better reflect pain and severity of joint involvement compared to its plasma counterparts, which likely reflect other physiological and pathophysiological processes.

Acknowledgement: Supported by GAUK-266523, MHCR 023728

Reference: (1) Styrkarsdottir U, et al. The CRTAC1 Protein in Plasma Is Associated With Osteoarthritis and Predicts Progression to Joint Replacement: A Large-Scale Proteomics Scan in Iceland. *Arthritis Rheumatol*. 2021;73(11):2025-2034. doi:10.1002/art.41793 (2) Szilagyi IA, et al. Plasma proteomics identifies CRTAC1 as a biomarker for osteoarthritis severity and progression. *Rheumatology (Oxford)*. 2023;62(3):1286-1295. doi:10.1093/rheumatology/keac415

Disclosure: A. Pekacova: None; **J. Baloun**: None; **A. Navratilova**: None; **L. Ondrejcakova**: None; **J. Zborovjanova**: None; **P. Fulin**: None; **R. Ballay**: None; **M. Tomcik**: None; **L. Senolt**: None.

Abstract Number: 0863

Phenotype and Energy Metabolism Differ Between Osteoarthritic Chondrocytes from Male Compared to Female Patients

Lekha Jain, Caitlin Jardim, Richard Yulo, Scott Bolam, A Paul Monk, Jacob Munro, Rocco Pitto, Jade Tamatea, Nicola Dalbeth and **Raewyn Poulsen**, University of Auckland, Auckland, New Zealand

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Changes in chondrocyte phenotype and energy metabolism occur in osteoarthritis (OA). The prevalence of OA is higher in females compared to males however whether there are sex differences in OA chondrocytes is unknown. The purpose of this study was to compare phenotype and energy metabolism in OA chondrocytes from male and female patients.

Methods: OA chondrocytes were isolated from male and female patients undergoing knee arthroplasty for end-stage primary OA (Kellgren-Lawrence Grade 4). Phenotype was determined by polymerase chain reaction, western blot and enzyme-linked immunoassays. Energy metabolism was determined by measuring glucose/fat consumption, lactate production, oxygen consumption rate and extracellular acidification rate.

Results: Protein levels of SOX9, a transcriptional regulator of *COL2A1* and *ACAN* as well as a promoter of glycolysis, were higher in OA chondrocytes from male compared to female patients (Figure 1). OA chondrocytes from males secreted higher amounts of type II collagen, had higher protein levels of the GLUT1 glucose transporter, higher glucose consumption, higher lactate production and higher glycolytic rate than OA chondrocytes from females. Knockdown of SOX9 reduced expression of *ACAN* and the glycolytic gene *PGK1,* in chondrocytes from male but not female patients. SOX9 knockdown reduced *COL2A1* expression in chondrocytes from both males and females, however the magnitude of effect was greater for males. OA chondrocytes from female patients consumed higher amounts of fat and had a higher oxygen consumption rate than OA chondrocytes from males indicating greater usage of oxidative energy metabolism.PGC1α protein levels (which promotes mitochondrial oxidative energy metabolism and potentiates SOX9-mediated collagen synthesis) were also higher in OA chondrocytes from females (Figure 1). Knockdown of PGC1α reduced *COL2A1* expression in OA chondrocytes from female but not male patients.

Conclusion: SOX9 and PGC1α are differentially expressed in OA chondrocytes from male compared to female patients resulting in differences in energy metabolism pathway usage and the transcriptional control of *COL2A1*. OA chondrocytes from male patients synthesise higher amounts of type II collagen compared to OA chondrocytes from females. This may render females more susceptible to rapid cartilage loss in OA. Differences in chondrocyte biology between male and female

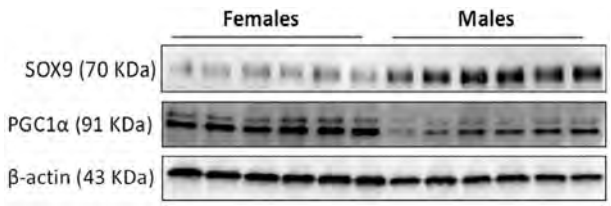


Figure 1 Protein levels of SOX9 and PGC1α (as measured by western blotting) in osteoarthritic chondrocytes isolated from male versus female patients.

patients raise the possibility that the mechanisms involved in OA development may also differ between the two highlighting the importance of considering gender and sex when studying OA pathogenesis and evaluating the efficacy of candidate OA treatments.

Disclosure: L. Jain: None; **C. Jardim**: None; **R. Yulo**: None; **S. Bolam**: None; **A. Monk**: None; **J. Munro**: Corin, 6, Zimmer Biomet, 6; **R. Pitto**: None; **J. Tamatea**: None; **N. Dalbeth**: Arthrosi, 2, AstraZeneca, 2, Dyve Biosciences, 2, Hikma, 6, Horizon, 2, JW Pharmaceutical Corporation, 2, LG, 2, Novartis, 6, Novotech, 5, PK Med, 2, Protalix, 2, PTC Therapeutics, 2, Selecta, 2, Unlocked Labs, 2; **R. Poulsen**: None.

Abstract Number: 0864

Proteomic Analysis of Circulating Neutrophils from Osteoarthritis Patients Shows Metabolic Dysregulation That Is Associated with Decreased Physiologic Apoptosis

Jennifer Amsler[1], Morgane Le Gall[2], Camille Daste[3], François Rannou[3] and Véronique Witko-Sarsat[2], [1]Institut Cochin, Bern, Switzerland, [2]Institut Cochin, Paris, France, [3]Hôpital Cochin, Paris, France

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) has long been thought to be only of local mechanical origin. However, it has been shown recently that there is a phenotype of OA with inflammatory properties. Here, we hypothesize that circulating neutrophils could be involved in disease pathogenesis suggesting a systemic involvement in this "local" disease.

Methods: We investigated the cytosolic proteome of blood neutrophils from four OA patients with an inflammatory knee osteoarthritis and compared it to the cytosolic proteome of blood neutrophils from three healthy controls (HC) of similar age. Functional analysis was generated through the use of the software Ingenuity Pathway Analysis (IPA). We further investigated in vitro the physiological apoptosis of isolated circulating neutrophils from OA patients compared to neutrophils from HC and measured the glycogen content in neutrophil cytosol.

Results: Based on the differentially regulated proteins, IPA predicts a downregulation of the glycogen degradation pathway as the most important difference between blood neutrophils from OA patients and those from HC, suggesting a disturbance in glycogen storage or use in OA neutrophils. Further, IPA predicts an inhibition of cell death of immune cells and an activation of senescence of cells. One of the differentially regulated proteins involved in survival is PCNA, which is found to be increased in neutrophils from OA patients. When measuring the glycogen content in blood neutrophils from OA patients compared with that from HC, we found no difference in glycogen content. However, we found a significant difference in the content of glycogen between neutrophils at a basal state and apoptotic neutrophils in both groups, suggesting that neutrophils use glycogen during their apoptosis. There was no correlation between the basal glycogen concentration of the cells and the percentage of apoptosis in neutrophils from both HC and OA, suggesting that the initial glycogen concentration has not a direct impact on the process of apoptosis of neutrophils. Preliminary results of Annexin-V labeling showed that neutrophils from OA patients have a significant delayed apoptosis compared with HC.

Conclusion: Our findings uncover for the first time a dysregulation in circulating neutrophils in OA that could have an impact on the disease pathogenesis and demonstrate a systemic involvement in OA. We provide evidence that cytosolic proteins of circulating neutrophils of OA patients are disturbed in terms of glycogen metabolism and apoptosis, which might result in a higher survival rate. Molecular mechanisms underlying these disturbances remain to be elucidated.

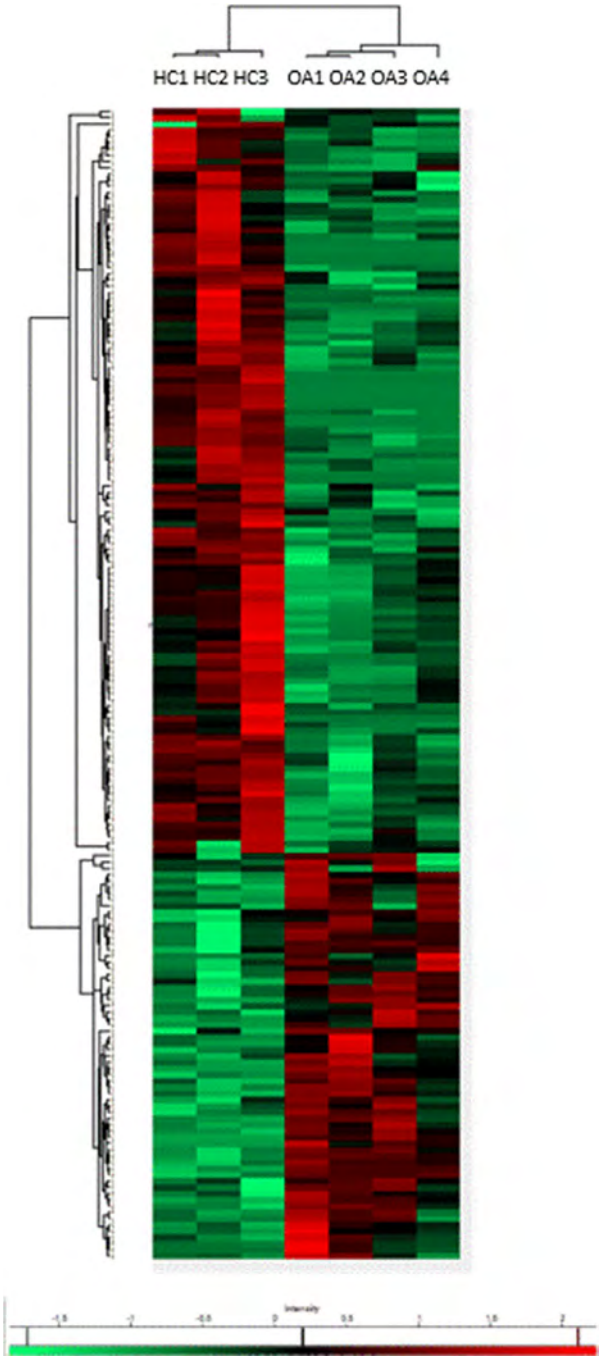


Figure 1: Heat map of differentially expressed proteins between neutrophil cytosol from blood of healthy control (HC) and osteoarthritis patients (OA). The proteins (rows) and samples (columns) are hierarchically clustered using Pearson correlation and average linkage on z-score quantification intensities. Each number indicates one patient. Color depicts the z-score changes in protein intensities respective to baseline expression levels, red: overexpression and green: underexpression.

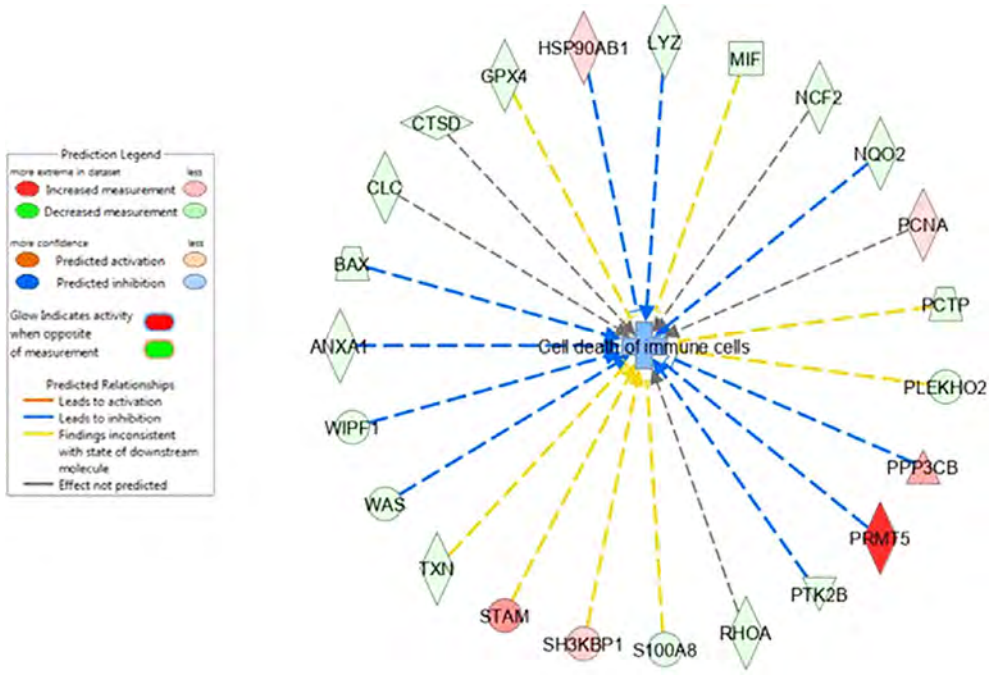


Figure 2: Specific network of cell death pathway shows differentially expressed proteins in the cytosol of blood neutrophils from OA patients and HC. Red indicates increased measurement of proteins, green indicates decreased measurements of proteins in neutrophils from OA patients compared to HC. Blue and orange indicate predicted inhibition and activation as shown in the colored legend.

Disclosure: J. Amsler: None; **M. Le Gall**: CHUGAI ROCHE, 6; **C. Daste**: None; **F. Rannou**: Eli Lilly, 6, Fidia, 6, Ipsen, 6, Thuasne, 5, 6; **V. Witko-Sarsat**: None.

Abstract Number: 0865

Reactive Oxygen Species-scavenging Nanoparticles Target Macrophage Polarization for Osteoarthritis Therapy

Caifeng Deng[1], Yongbing Xiao[2], Xuan Zhao[1], Hui Li[2], Yuxiao Chen[1], Chao Zeng[2] and Guanghua Lei[2], [1]Xiangya Hospital, Changsha, China, [2]Department of Orthopaedics, Xiangya Hospital, Central South University, Changsha, China

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Unbalanced M1/M2 polarization of synovial macrophages plays vital roles in the symptomatic and structural progression of osteoarthritis (OA). The accumulation of intracellular reactive oxygen species (ROS) and the inflammation response cooperatively regulate the phenotype of M1macrophages.The compensatory pathwaysbetween ROS and inflammation in M1macrophages limited the efficacy of treatment regimen modulating a single element (oxidative stress or inflammation). Therefore, we developed a ROS-scavengingand anti-inflammatory agent (licofelone, LCF)-loaded nanoplatform (termed LCF-CSBN) for simultaneously down-regulating inflammatory response and reducing ROS in M1macrophages. The purpose of this study was to investigate the phenotypic reprogramming effect of LCF-CSBN on M1 macrophages and evaluate the efficiency and safety of intraarticular (IA) injection of LCF-CSBN in dealing with OA rat models.

Methods: Cell internalization of LCF-CSBN in M1macrophages was examined by flow cytometry analysis and colocalization study. Scavenging of intracellular ROS were detected by ROS assay kit. RNA sequencing analysis, immunofluorescence (IF) staining, and enzyme-linked immunosorbent assay were performed to measure the mRNA and protein expressions of pathogenic mediators and macrophage polarization markers inM1macrophages treated with LCFand LCF-CSBN. The intra-articular retention time and biodistribution of LCF-CSBN in vivo were evaluated by vivo imaging system and IF staining. Furthermore, LCF-CSBN was injected intra-articularly into the osteoarthritic knee of rats at 3 days after monosodium iodoacetate (MIA) injection and at 5 weeks and 8 weeks after anterior cruciate ligament transection combined with partial medial meniscectomy surgery. Pain behavior assessments, histological analysis, immunohistochemical staining, micro-computerized tomography analysis, and serum enzyme analysis were performed to evaluate the therapeutic effect and safety of IA injection of LCF-CSBN.

Results: Results of RNA sequencing revealed that LCF-CSBN significantly down-regulated the expression of inflammation related genes and reprogrammed the phenotype of M1macrophages. LCF-CSBN was demonstrated to successfully transform M1 macrophages into the M2 phenotype by eliminating cellular ROS and inhibiting expression of inflammatory factors. Additionally, LCF-CSBN was retained in the joint for up to 28 days and selectively distributed into synovial macrophages. In both MIA induced and surgically induced OA rat models, LCF-CSBN effectively and safely relieved pain and suppressed synovial inflammation, as well as alleviated cartilage degradation.

Conclusion: LCF-CSBN has an extended joint-retention time and good capacity of reprogramming the phenotype of synovial M1 macrophages, which exhibits satisfying effect on relieving OA pain and delaying OA progression.Taken together, LCF-CSBN is a promising nanomedicine for OA therapy.

Disclosure: C. Deng: None; **Y. Xiao**: None; **X. Zhao**: None; **H. Li**: None; **Y. Chen**: None; **C. Zeng**: None; **G. Lei**: None.

Abstract Number: 0866

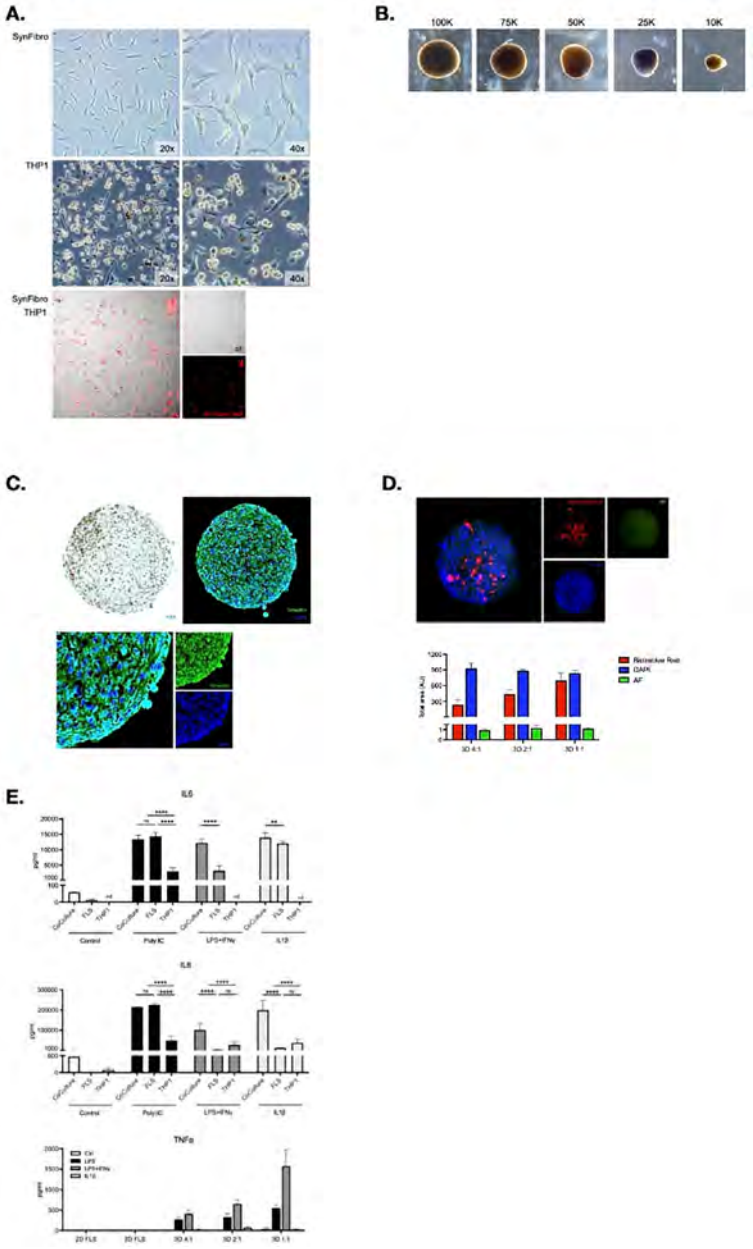
A Novel 3D-Synovium-Immune Microenvironment Mimics Macrophage-Synovial Fibroblast Interactions in Inflammatory Arthropathies

André Tiaden[1], Simone Häner Massimi[1], Ulrich Walker[2], Diego Kyburz[3] and **Stavros Giaglis**[1], [1]Laboratory for Experimental Rheumatology, Department of Biomedicine, University of Basel, Basel, Switzerland, [2]Basel University Hospital, Basel, Switzerland, [3]University Hospital Basel, Basel, Switzerland

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmunity, trauma, or infection lead to devastating arthropathies, within enormous socioeconomic impact due to its high frequency and chronicity. The development of novel treatments remains a significant challenge. Moreover, disease a etiology, sequence and drug responsiveness are exceptionally patient-specific, underscoring the need for personalized therapeutic strategies. Invitro cultures and animal models have been helpful in identifying and describing the pathological processes in arthritis; still, they cannot predict individual responses to treatment due to the complexity of the synovium. In the present study we sought to establish a reproducible organoid model that emulates the complex biological interactions within the human synovium, mimicking pathological conditions of the inflamed joint.

Figure 1



Methods: For the establishment of 2D and 3D cell cultures, native synovial fibroblasts and THP1 macrophages were utilized. Patient sample collection and biobank storage at the Rheumatology Department and Orthopedics Department USB was approved by the ethics review board EKNZ (2019-01391). Organoids were assembled by adding biocompatible magnetic nanoshuttles and subsequent bioprinting (m3D, Greiner BioOne), allowing self-assembly of cells into 3D structures by building autologous extracellular matrix. This highly scalable, reproducible, independent of artificial scaffolds approach, supports a native microenvironment preserving endogenous tissue phenotypes. Optimal setup parameters - growth status, cell number, size and culture conditions - organoid maturation, and medium formulation were tested, and inflammatory responses were assessed in the presence of RA-relevant stimuli by measuring the secretion of cytokines (ELISA) and the expression of cellular phenotypes (IHC).

Results: Biological material from 6 OA patients, including synovial tissue, plasma, serum, and synovial fluid was collected and stored. 2D and 3D synovial fibroblast and THP1 macrophage cultures (Figure 1A), cocultures (Figure 1B) and organoids (Figure 1C) were established. Macrophage incorporation in the synovial organoids was confirmed in different coculture

schemes (Figure 1D). Data from a restricted set of RA-relevant markers displayed a synergistic effect of the coculture setting on proinflammatory cytokine secretion after stimulation; moreover, initial assessments comparing the 2D cultures and 3D organoids upon inflammatory stimulation showed that macrophages are the main source of TNFα (Figure 1E).

Conclusion: The establishment of an engineered human 3D synovial tissue model, emulating the human synovium by utilizing targeted tissue material, serves to functionally test essential aspects of synovial inflammation. The ability to induce inflammatory responses in the organoids provides a proof of concept for cytokine-driven inflammation in autoimmunity. This may serve as an important tool in drug development and personalized medicine, and tackle the limited predictive value of existing in vitro and in vivo animal models.

(A.) Representative bright-field microphotographs of 2D cultures of synovial fibroblasts (upper panel), THP1 macrophages (middle panel) in two different magnifications, and respective cocultures (lower panel); THP1 derived macrophages are stained with BioTracker Red (magnification: 10x). (B.) Representative bright-field microphotographs of organoids depicting the process of optimization of the synovial fibroblast number (10.000-100.000) used in the 3D organoid cultures. (C.) Representative bright-field microphotograph depicting a synovial fibroblast-derived organoid with gold-iron oxide polylysine magnetic nanoparticles (upper left panel). A similar culture setup was confirmed by fluorescent IHC of the synovial fibroblast marker vimentin (upper right panel); a detail of vimentin spatial distribution is provided in the lower panel. (D.) Successful incorporation of the THP1 macrophages in the synovial organoid was confirmed by Biotracker Red cellular stainings (left panel), in different proportional schemes of cocultruring -1:1, 1:2, 1:4 (right panel). (E.) Protein secretion of IL6 (upper panel) and IL8 (middle panel) in supernatants of single culture and cocultures of synovial fibroblasts and THP1 cells. Macrophages appear to be the main producers of TNFα in the 3D organoids, as assessed by ELISA (lower panel).

Disclosure: A. Tiaden: None; **S. Häner Massimi**: None; **U. Walker**: None; **D. Kyburz**: Abbvie, 1, 5, Eli Lilly, 1, 6, Janssen, 1, 6, Novartis, 1, 6, Pfizer, 1; **S. Giaglis**: None.

Abstract Number: 0867

Pentosan Polysulfate Sodium, a Glycosaminoglycan Mimetic Demonstrates Durable Effects on Pain, Function and Joint Structure in Canine Naturally Occurring Osteoarthritis

Ravi Krishnan[1], Catherine Stapledon[2], Christian Reiter[2], Stewart Ryan[3], Sebastien Bauquier[3] and Thierry Beths[3], [1]Paradigm Biopharmaceuticals, Adelaide, Australia, [2]Paradigm Biopharmaceuticals, Melbourne, Australia, [3]U-Vet Werribee Animal Hospital, University of Melbourne, Melbourne, Australia

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Pentosan Polysulfate sodium (PPS) is a semi-synthetic polysaccharide and a glycosaminoglycan mimetic. The multiple actions of PPS involve anti-inflammatory effects via inhibition of NF-κB; analgesia by normalising the pain mediator, NGF; and chondroprotection by inhibiting ADAMTS-5 degradation of aggrecan in cartilage. The study objectives were to evaluate the durability of effect of PPS therapy in companion dogs with naturally occurring osteoarthritis (OA) at six months (26 weeks) and to evaluate the effects of PPS for disease modifying potential.

*Effect size (ES) of PPS Treatment Compared to Placebo demonstrate durability of favourable outcome measures in pain, function, joint structure, and serum biomarker: Hedges' g analysis at week 8 and 26 from baseline

Outcome Measures	8 Weeks (ES)	26 Weeks (ES)
HCPI	0.39#	1.79##
TPI%	0.55	0.5
Cartilage Volume	1.06	0.73
CTX-1	1.15	1.6
HA	0.58	1.19
TIMP-1	0.96	1.27

*Effect Size Ranges: Small (0.2 – 0.49); Medium (0.5 – 0.79); Large (>0.8)
% change from week 6
% change from week 8

Methods: In a double-blinded study, twenty dogs (12 males and 8 females; mean weight: 26.05 kg, (SD 4.5); mean age: 9.9 years, (SD 2.0)) with OA were randomised to subcutaneous PPS injections (3 mg/kg; human equivalent dose of 1.7 mg/kg) or placebo weekly for 6 weeks in a 2:1 ratio, respectively. At baseline, week 8 and week 26, the index stifle or elbow were analysed by the Helsinki Chronic Pain Index (HCPI) for pain; gait analysis by Total Pressure Index % (TPI%) for joint function; and total cartilage volume by MRI for joint structural changes. Validated ELISAs for serum biomarkers of joint degeneration (CTX-I, Hyaluronic acid (HA), TIMP-1) were assayed. The mean percentage change from baseline (%CFB) at weeks 8 and 26 were used to determine the effect size (ES) of PPS treatment compared to placebo using the Hedges' *g* test.

Results: PPS treatment showed meaningful ES improvement in pain at week 26 compared to placebo with a reduction in mean percentage change from the previous follow-up at week 8 in HCPI (ES 1.79). The improvement in pain was reflected by a larger effect size at the later time of 26 weeks relative to week 8 (ES 0.39) suggesting durability of PPS effects on pain. Long-term functional improvements in gait were demonstrated by an increase in mean %CFB in TPI% and sustained by ES of 0.55 and 0.5 at weeks 8 and 26, respectively. Furthermore, the mean %CFB in TPI% for PPS treatment at weeks 8 and 26 was 7.3% and 8.2%, respectively, whereas clinically meaningful increases reported at 5% were not met by placebo. There were larger reductions in cartilage volume in the placebo group compared to PPS treatment at 8 and 26 weeks with a large PPS ES of 1.06 and 0.73, respectively suggesting reduction in structural degeneration of the articular cartilage. PPS favourably affected serum levels of CTX-1, HA and TIMP-1 supporting the in vivo mechanisms of drug action.

Conclusion: Compared to placebo, the long-term effect of PPS therapy results in the improvement of pain, function, cartilage volume and serum biomarkers at 26 weeks from baseline suggesting that PPS stabilises disease progression in canine OA and may translate to disease modification in humans. PPS was well tolerated during treatment and follow up.

Disclosure: R. Krishnan: Paradigm Biopharmaceuticals, 3, 11; **C. Stapledon**: Paradigm Biopharmaceuticals, 3, 11; **C. Reiter**: Paradigm Biopharmaceuticals, 3, 11; **S. Ryan**: None; **S. Bauquier**: None; **T. Beths**: None.

Abstract Number: 0868

Enhancing Oxidative Phosphorylation Through PDK2 Depletion Alleviates Cartilage Degradation in Surgically Induced Osteoarthritis

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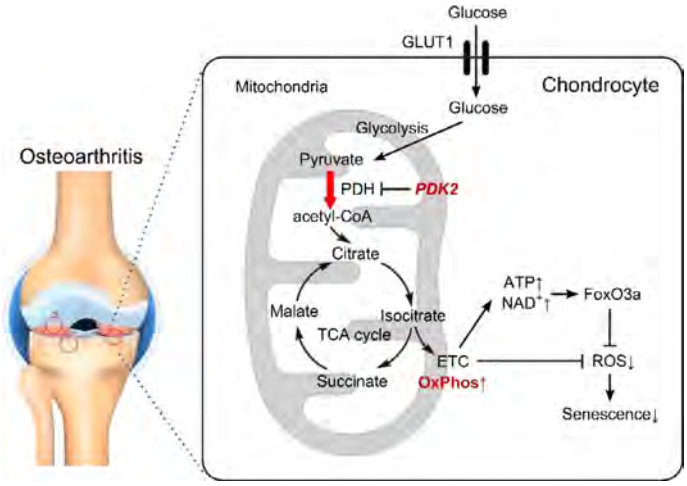
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Although chondrocytes rely primarily on glycolysis to meet their cellular energy needs, they have the metabolic flexibility to shift toward oxidative phosphorylation (OxPhos) in the early stage of osteoarthritis (OA). As the disease progresses, however, this metabolic adaptation of OA cartilage reaches its limit and eventually fails, resulting in mitochondrial dysfunction and oxidative stress which are hallmarks of OA. The objective of this study was to determine whether the modulation of OxPhos through pyruvate dehydrogenase kinase (PDK)-2 affects metabolic flexibility of chondrocytes, and cartilage degeneration in surgical model of OA.

Methods: Primary chondrocytes were obtained from E15.5 C57BL/6J long bones of PDK2 KO mice and their WT littermates. Interleukin (IL)-1β (10 ng/mL) was applied to recapitulate the catabolic stress mimicking OA conditions. Surgical OA was induced in 12-week-old male WT (C57BL/6J) and PDK2 KO mice by destabilization of the medial meniscus (DMM). Metabolic shift by PDK2 deficiency was analyzed with XF96 Extracellular Flux Analyzer.

Results: Among PDK isoforms (PDK1-4), only PDK2 expression was increased by IL-1β at both RNA and protein levels in vitro, and in the articular cartilage of the DMM OA model in vivo. PDK2-deficient mice exhibited significant protection from DMM-induced cartilage destruction, which was accompanied by a decrease in oxidative stress and pain-related behaviors. PDK2 deficiency partially restored oxidative phosphorylation and decreased glycolysis in IL-1β-treated chondrocytes, which led to an increase in ATP concentration, and the NAD+/NADH ratio. PDK2 deficiency significantly increased the phosphorylation of pyruvate dehydrogenase (PDH), the inactive form, which was accompanied by a decrease in reactive oxygen species (ROS) and chondrocyte senescence, as well as the expression of MMP-13 and IL-6 induced by IL-1β treatment. At the signaling level, PDK2 deficiency enhanced FoxO3a and decreased p38 signaling, but did not affect AMPK, mTOR, and NF-kB pathways upon IL-1β stimulation. FoxO3a knockdown masked the reduction of ROS and senescence brought about by PDK2 deficiency, implying that PDK2 effects are FoxO3a-dependent.

Conclusion: Our study provides the proof-of-concept of PDK2-mediated metabolic reprogramming of chondrocytes towards OxPhos as a new therapeutic strategy for OA.



PDK2 is predominantly expressed under catabolic conditions, and its deficiency promotes oxidative phosphorylation and ATP production in chondrocytes. It induces FoxO3a activation, subsequently leading to the reduction of oxidative stress and cellular senescence.

Disclosure: S. Han: None; **J. Han**: None; **Y. kim**: None; **Y. Kim**: None; **D. Park**: None.

Abstract Number: 0869

Clinical Impact of PTEN as a Marker for Diabetes-Associated Osteoarthritis

Irene Lorenzo Gomez[1], Uxía nogueira Recalde[2], Christian García Domínguez[1], Natividad Oreiro Villar[3], Jose Antonio Pinto Tasende[3], Mohit Kapoor[4], Francisco J. Blanco[3] and Beatriz Carames[1], [1]Unidad de Biología del Cartílago, Grupo de Reumatología, Instituto de Investigación Biomédica de A Coruña (iNIBIC), A Coruña, Spain, [2]Unidad de Biología del Cartílago, Grupo de Reumatología, Instituto de Investigación Biomedica de A Coruña (iNIBIC), A Coruña, Spain, [3]Rheumatology department, Complexo Hospitalario Universitario A Coruña (CHUAC). Instituto de Investigación Biomédica A Coruña (INIBIC), A Coruña, Spain, [4]Division of Orthopaedics, Osteoarthritis Research Program, Schroeder Arthritis Institute, and Krembil Research Institute, University Health Network, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Defects in homeostatic mechanisms, such as autophagy, contribute to joint aging and Osteoarthritis (OA) and precede joint damage (1). OA is a complex and multifactorial disease where systemic metabolic status plays a key role. Hence, patients with Type 2 Diabetes (T2D) present more prevalent and severe OA, so it has been recognized as an independent clinical phenotype of OA. However, mechanisms underlying this comorbidity are poorly understood. Previous results from our group showed that diabetic conditions compromise autophagy in chondrocytes, and this facilitates OA development and progression, suggesting that impaired autophagy can be one of the mechanisms involved in OA-T2D interaction (2). Moreover, pharmacological activation of autophagy was sufficient to protect against diabetes-induced joint destruction (3). These observations support studies exploring autophagy markers at systemic and tissue levels to identify key mechanisms of OA-T2D interactions.

Methods: To address this objective a comparative analysis of 35 autophagy genes was performed using an autophagy expression gene array from blood of non-OA subjects (n=18) and Knee OA subjects (n=18, OA grade III-IV) from the Prospective Cohort of OA of A Coruñ a (PROCOAC) and then validated in a second set of subjects (Non-OA and Knee-OA subjects (n=30) by qPCR. Differentially regulated candidate genes were analyzed by qPCR in blood from Knee OA-T2D subjects (n=30, OA grade III-IV) and cartilage from Knee OA and OA-T2D subjects (n=12, OA grade III-IV). Contribution of candidate marker to chondrocyte homeostasis was explored by using a model of diabetes exposing human chondrocytes to high glucose and insulin (3).

Results: The gene expression array and the validation studies confirmed a significant downregulation of *PTEN*, *HSP90AA1* and *MAP1LC3B* in blood from knee OA subjects compared to non-OA subjects. Then, these candidate genes were analyzed in a subgroup of subjects from the PROCOAC cohort with knee OA-T2D. The results confirmed a significant downregulation of *HSP90AA1* in knee OA-T2D subjects ($p < 0.01$) and no significant differences were found for *MAP1LC3B* (4). Interestingly, *PTEN,* a potent tumor suppressor gene that inhibits the PI3K/Akt signaling pathway and governs basic celular metabolic processes, was significantly upregulated in blood and cartilage from subjects with knee OA-T2D compared to knee OA subjects ($p < 0.01$). In addition, the regression analysis showed that upregulation of *PTEN* is associated with a risk incidence for knee OA-T2D. Preliminary data from in vitro model of diabetes in human chondrocytes reveals that PTEN is increased upon high glucose and insulin exposure. Moreover, this increase was correlated with defective autophagy flux and increased chondrocyte senescence.

Conclusion: These results suggest that PTEN is a promising candidate marker for Knee OA-T2D subjects. Further studies of this homeostasis mechanism in OA associated to diabetes might elucidate its relevance in the progression of disease.

1. Caramés et al. doi: 10.1002/art.39073. 2. Ribeiro et al. doi: 10.1016/j.joca.2015.10.017. 3. Ribeiro et al. doi: 10.1016/j.joca.2016.06.019. 4. Lorenzo-Gómez et al. doi: 10.1016/j.joca.2023.02.076

Disclosure: I. Lorenzo Gomez: None; **U. nogueira Recalde**: None; **C. García Domínguez**: None; **N. Oreiro Villar**: None; **J. Pinto Tasende**: None; **M. Kapoor**: None; **F. Blanco**: None; **B. Carames**: None.

Abstract Number: 0870

Targeting Peroxisome Proliferator-Activated Receptor α Is a Disease-Modifying Therapy for Osteoarthritis

Uxía nogueira Recalde[1], Patricia Díaz rodríguez[2], Francisco J. Blanco[3], Eduardo Dominguez Medina[4] and **Beatriz Carames**[5], [1]Unidad de Biología del Cartílago, Grupo de Reumatología, Instituto de Investigación Biomedica de A Coruña (iNIBIC), A Coruña, Spain, [2]Department of Pharmacology, Pharmacy and Pharmaceutical Technology, Pharmacy School, Santiago de Compostela, Spain, [3]Rheumatology department, Complexo Hospitalario Universitario A Coruña (CHUAC). Instituto de Investigación Biomédica A Coruña (INIBIC), A Coruña, Spain, [4]Center for Research in Molecular Medicine and Chronic Diseases, Santiago de Compostela, Spain, [5]Unidad de Biología del Cartílago, Grupo de Reumatología, Instituto de Investigación Biomédica de A Coruña (INIBIC), A Coruña, Spain

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Disease-modifying therapeutic agents to prevent progression of Osteoarthritis (OA) are an urgent clinical need. Targeting senescence and autophagy in chondrocytes with small molecules is a useful strategy to prevent against chondrocyte death, cartilage aging and OA. Fenofibrate (FN), a peroxisome proliferator activated receptor α (PPARα) agonist employed as a therapy for dyslipidemiaswas identified as a senolytic and pro-autophagy molecule showing chondroprotective properties. Here, we evaluated the efficacy of FN in preclinical models as a disease modifying therapy targeting lipid metabolism for OA. To test the effect of this mechanism, FN was administered by both oral route and intra-articular delivery in surgical models of OA.

Methods: Surgical OA was performed by transection of the medial meniscotibial ligament and the medial collateral ligament in the right knee of 4 months-old C57BL/6 male mice. Left knee was employed as a Sham knee. Mice were randomized according to body weight in two groups for oral administration of FN (O-FN) [Vehicle group (DMSO), N=8 and Treated group (100 mg/kg body weight/day, daily, N=8). An intra-articular drug delivery by extended-release of FN in microspheres for 3 months (IA-FN) was developed to 1) to extend the delivery of FN, which is insoluble in water 2) to provide direct access to the joint enhancing the bioavailability in damaged tissue, and 3) to diminish the effects of systemic administration. Mice were divided into three groups for IA-FN efficacy study [Vehicle group (empty microspheres), N=8, Treated group 1 (1 μg FN) and Treated group 2 (10 μg FN). Determination of pain was performed by using the incapacitance test to measure pain by assessing the dynamic weight bearing of spontaneous postural changes. Pain was evaluated every two weeks until euthanasia. Histopathological changes in articular cartilage and synovium were evaluated. The target engagement studies were performed by immunohistochemistry.

Results: In a preclinical model of OA in mice, the treatment with O-FN did not induce changes in body weight and no liver toxicity occurred after the treatment. The histopathological changes in joint cartilage were significantly reduced in the FN treated group ($P < 0.05$). In addition, the histological evaluation showed a significant decrease in synovitis after O-FN (*P*

< *0.05*). This protective effect was correlated with increased expression of PPARα in mouse knee joints after O-FN treatment (*P < 0.001*). The IA-FN was prepared and comprehensively characterized. IA-FN comprises a PLGA matrix in an optimized ratio, adequate size, appropriate molecular weight, and exhibits a 3-month extended-release profile in human synovial fluid. The preclinical results showed a reduction of joint pain after intra-articular injection of FN (*P < 0.01*). Moreover, IA-FN improved joint function (*P < 0.01*) compared to vehicle condition, suggesting that IA-FN is a disease-modifying therapy for OA.

Conclusion: These findings support further non-clinical regulatory studies to develop IA-FN formulation as a candidate therapy for OA. A GMP manufactured formulation could be used to test the safety of this treatment in patients with OA of the Knee in a Phase 1 clinical trial.

Disclosure: U. nogueira Recalde: None; **P. Díaz rodríguez**: None; **F. Blanco**: None; **E. Dominguez Medina**: None; **B. Carames**: None.

Abstract Number: 0871

Mitochondrial Transfer Functionally Restores the Human Osteoarthritis (OA) Chondrocyte, Is Protective Against Oxidative Stress and Improves OA in a Clinical Model of Disease

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthrosis (OA) is a leading cause of pain, disability and early mortality, with no disease modifying treatments. Mitochondrial dysfunction is a known driver of disease. Mesenchymal stromal cells (MSCs) -widely tested in OA- transfer their mitochondria (MT) to damaged tissues in response to stress. **Aim**: To characterize the functional impact of MT transfer (MitoT) from umbilical cord-derived MSC (MSCs) to the human OA chondrocyte (OA-Ch) and clinical effect of MSC-derived MT in a murine model of OA.

Methods: Primary chondrocytes from OA patient surgery were tested for MitoT using *in vitro* co-culture with MSCs. MitoT was evidenced by flow cytometry and confocal microscopy of MitoTracker stained and YPF-tagged MT protein. To single out effects of MitoT on target cells, we employed direct transfer of MSC-derived MT to OA-Chs (Mitoception). The response of target cells was gauged by ATP production, oxygen consumption (OCR), extracellular acidification (ECAR) rates, levels of reactive oxygen species (ROS) superoxide dismutase (SOD), MT network fussion/fission and OA-Ch viability by TUNEL assays. Intra-articular injection of MSC-derived MT was tested in a collagenase induced murine model of OA.

Results: Dose-dependent cell-to-cell MitoT from MSCs to cultured OA-Chs was detected starting at 4 hours of co-culture, with increasing (3.2x) MT-fluorescence levels at higher MSC:Ch ratios. PCR analysis confirmed the presence of exogenous MSC-MT within MitoT$^+$ OA-Chs up to 9 days post Mitoception. Metabolic analysis showed a 2x increase ($p< 0.001$) in ATP and a higher OXPHOS/Glycolysis ratio ($p=0.0213$) in target OA-Chs revealing a switch towards an activated energy state of chondrocytes after MitoT. Increased SOD2 mRNA transcripts ($p< 0.05$), protein levels (1.8-fold), MT-SOD activity (2.9-fold)

and reduced ROS levels (p=0.039) were coincident with enhanced resistance of OA-Chs to apoptosis, indicating this effect of MitoT is related to the control of ROS. In parallel, the change in mRNA transcripts and proteins that control the fusion/fission state of the MT network, showed increased expression of MFN2 ($p< 0.01$) and decreased p-DRP1 ($p< 0.05$) that promote a predominantly fused MT network, that contributes to chondrocyte preservation. In the preclinical OA model, intra-articular treatment with MSC-derived MT improved histologic scores ($p< 0.001$) and MicroCT imaging of the diseased joints ($p< 0.01$).

Conclusion: MSC-derived MT transferred to the OA-Ch convey significant changes in energy balance, MT dynamics, resistance to oxidative stress and OA-Ch apoptosis. Intra-articular MT treatment improved disease in a murine model of OA. These findings might represent a new strategy in the treatment of this disease.

Disclosure: F. Figueroa: None; **A. Court**: None; **P. Luz Crawford**: None; **A. Vega Letter**: Innovacell, 3; **F. Velarde**: None; **C. Garcia**: None; **M. Khoury**: Cells for Cells SA, 4, 5, 10.

Abstract Number: 0872

Synovial 5-LOX-Derived Oxylipins Define a B Cell-Enriched Synovium

Jessica Murillo-Saich[1], Roxana Coras[2], Felipe Julio Ramirez Garcia[3], Estefania Quesada-Masachs[4], Marta Sala Climent[5], Katharina Eschelbach[4], Christopher Mahony[6], Raquel Celis[7], Aaron Armando[8], Oswald Quehenberger[8], Adam Croft[6], Arthur Kavanaugh[9], Eric Chang[5], Juan D Canete[10], Abha Singh[1] and Monica Guma[11], [1]Department of Medicine, University of California San Diego, La Jolla, CA, [2]Cedars-Sinai Medical Center, Los Angeles, CA, [3]Hospital Clínic, Barcelona, Spain, [4]La Jolla Institute for Immunology, La Jolla, CA, [5]University of California San Diego, San Diego, CA, [6]University of Birmingham, Birmingham, United Kingdom, [7]Arthritis Unit, Rheumatology Department, Hospital Clinic and IDIBAPS, Barcelona, Spain, [8]Department of Pharmacology, University of California San Diego, La Jolla, CA, [9]University of California San Diego, School of Medicine, Riverside, CA, [10]Hospital Clinic an IDIBAPS, Barcelona, Spain, [11]San Diego VA Healthcare Service, La Jolla, CA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session B

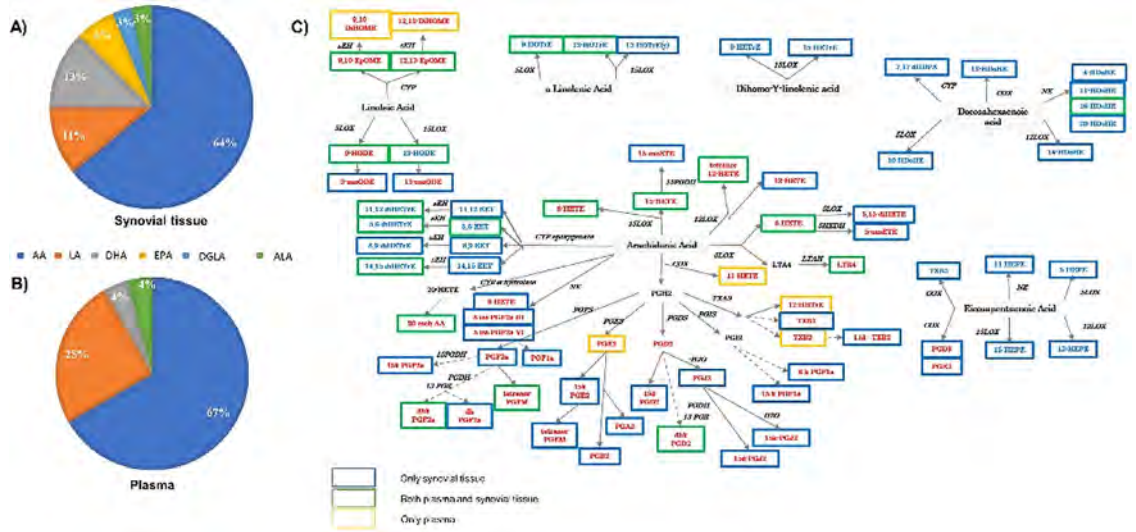
Session Time: 9:00AM–11:00AM

Background/Purpose: Oxylipins are bioactive lipids derived from polyunsaturated fatty acids (PUFAs) that modulate inflammation and may remain overexpressed in refractory synovitis. These mediators in plasma could also be biomarkers of synovial pathology. The aim of this study is to determine synovial oxylipins in active inflamed joints and their correlation with plasma oxylipins.

Methods: Patients with established rheumatoid or psoriatic arthritis with active disease despite treatment were recruited and paired synovial tissue (ST) and plasma were collected. Oxylipins were determined by liquid chromatography with tandem mass spectrometry and were classified into groups according to their PUFA precursor and enzyme. The expression of CD20, CD68, CD3 and CD138 were obtained to describe synovial histology. Cell specific expressions of oxylipin-related genes were identified by examining available synovial scRNA-seq data.

Results: We included a total of 32 ST and 26 paired-plasma samples. A total of 64 oxylipins were identified in ST but only 28 were identified in plasma (**Figure 1**). Only levels of 11,12-di-HETrE, 15-HETE, 16-HDoHE and tetranor-PGFM had a statistically significant positive correlation between plasma and ST. Multivariate approaches were conducted to capture the global picture of oxylipins disturbances according to the histological classification. Although PLS-DA with the identified

Figure 1. Oxylipin profile in tissue and plasma. A-B) Pie chart representing the percentage of oxylipins grouped by precursors in tissue A) and B) plasma. C) Scheme showing the panel of oxylipins found in both tissue and plasma in a green box. The oxylipins found only in plasma are highlighted in yellow, and the oxylipins found only in synovial tissue are highlighted in blue. Pro-inflammatory oxylipins are marked in red and oxylipins associated with resolution of inflammation are marked in blue. AA: arachidonic acid; LA: linoleic acid; DHA: docosahexaenoic acid; EPA: eicosapentaenoic acid; DGLA: dihomo gamma linolenic acid; ALA: alpha-linolenic acid. The abbreviations list for oxylipin names can be found in Supplementary Table 1. COX – cyclooxygenase; LOX – lipoxygenase; CYP – cytochrome P450; NE – non-enzymatic; PGFS – prostaglandin F synthase; PGES – prostaglandin E synthase; PGDS – prostaglandin D synthase; PGIS – prostaglandin I synthase; TXAS – thromboxane A2 synthase; LTAH – leukotriene A4 hydrolase; MDB – membrane dipeptidase; HEDH - hydroxyeicosanoid dehydrogenase; PGDH - hydroxyprostaglandin dehydrogenase; 13-PGR – 15-ketoprostaglandinΔ13 reductase; sEH – soluble epoxide hydrolase.



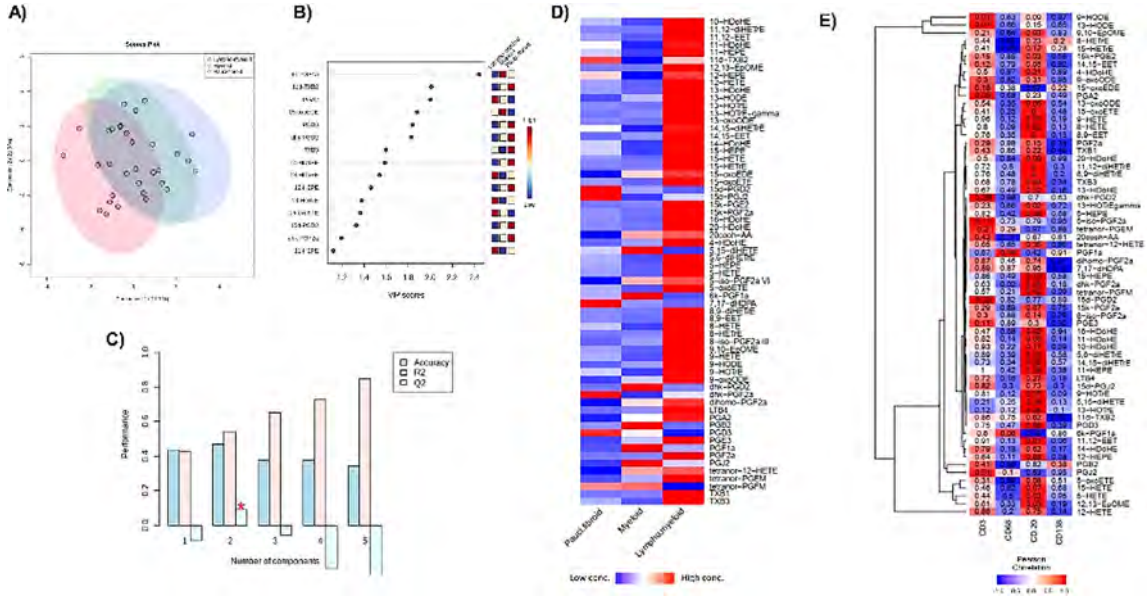


Figure 2. Discrimination between pauci-fibroid, myeloid and lympho-myeloid phenotypes in tissue. A) PLS-DA considering all samples of tissue (n=32) where is observed an overlap within the 3 phenotypes and B) VIP score obtained from the second component of PLS-DA analysis. C) Cross validation analysis using a maximum of 5 components to search and leave-one-out cross validation. Component 2 showed positive predictive ability to separate the three phenotypes with an accuracy= 0.47, R2= 0.54 and Q2= 0.09. D) Heatmap of mean concentrations of oxylipins by histological phenotypes where red is high concentration and blue shows low concentration. E) Pearson correlation adjusted by age and BMI between histological markers semi quantification and concentration of oxylipins in tissue using Euclidean distance and ward clustering algorithms where red color indicates positive strength of association while blue indicates negative correlation. P value is stated on each cell.

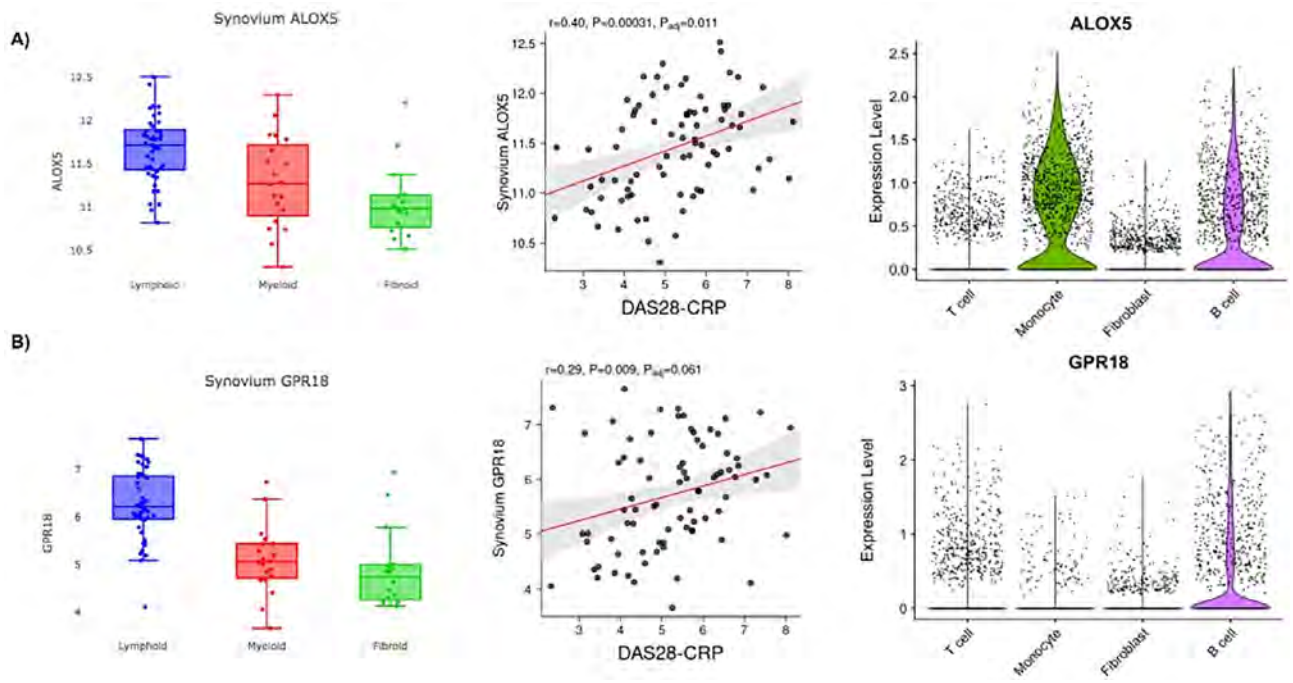


Figure 3. Synovial 5-LOX-derived oxylipins define the synovial lympho-myeloid phenotype. RNA-seq expression of 5-LOX (A) and GPR18 (B) in the different histologic phenotypes and correlation with disease activity from PEAC "gene view", and violin plots from scRNA-seq data2. Boxplots of ALOX5 showed a higher expression in lymphoid group compared to myeloid (p= 0.009) and pauci-fibroid (p< 0.001) phenotypes and positive correlation with disease activity (r=0.40, p=0.01). In violin-plot is observed that ALOX5 was highly expressed in monocytes and B cells. GPR18 shows in boxplot higher expressed in the lymphoid group compared to myeloid (p <0.001) and pauci-fibrotic (p= <0.001), showing a tendency with a positive correlation with disease activity (r= 0.29, p= 0.06), and highly expressed in B cells observed in violin plot.

metabolites in the tissue showed some overlap between the 3 groups (**Figure 2A**),6k-PGF1a, 11d-TXB2 and PGA2 were the most important metabolites in component 2 to discriminate between the three groups with a VIP score >2 (**Figure 2B).** This component showed a positive predictive ability to separate the three phenotypes with an accuracy= 0.47, R2= 0.54 and Q2= 0.09 (**Figure 2C)**. We found higher concentration of several oxylipins in the lymphoid-myeloid phenotype (**-Figure 2D**) which a positive correlation with CD3 and CD20 semiquantification (**Figure 2E**). Several oxylipins and oxylipin-related genes were differentially expressed among synovial phenotypes. Specifically, several 5-LOX-derived oxylipins were statistically elevated in lympho-myeloid phenotype and associated with B cells expression (**Figure 3**).

Conclusion: The lack of correlation between synovial tissue and plasma oxylipins suggests that synovial lipid profiling better characterizes active pathways in treated joints. Synovial 5-LOX-derived oxylipins were more highly expressed in B cell-enriched synovium, thus combination therapy with 5-LOX inhibitors to improve refractory inflammation may be needed in patients with this histological group.

Disclosure: J. Murillo-Saich: None; **R. Coras**: None; **F. Ramirez Garcia**: AbbVie/Abbott, 2, 6, Amgen, 6, Eli Lilly, 6, Janssen, 6, 12, Paid Instructor, Novartis, 2, 6, 12, Paid Instructor, Pfizer, 5, 6, UCB, 2, 6; **E. Quesada-Masachs**: None; **M. Sala Climent**: None; **K. Eschelbach**: None; **C. Mahony**: None; **R. Celis**: None; **A. Armando**: None; **O. Quehenberger**: None; **A. Croft**: None; **A. Kavanaugh**: AbbVie, 1, 2, Amgen, 1, 2, BMS, 1, 2, Eli Lilly, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, UCB, 1, 2; **E. Chang**: None; **J. Canete**: None; **A. Singh**: None; **M. Guma**: Genentech, 5, Gilead, 5, Novartis, 5, Pfizer, 5.

Abstract Number: 0873

FOXO Activators as Drugs for Osteoarthritis

Ichiro Kurakazu, Merissa Olmer, Kevin Myers and Martin K Lotz, Scripps Research Institute, La Jolla, CA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Forkhead box O (FOXO) proteins are a family of transcription factors involved in lifespan, aging, and autophagy. FOXO are essential for maintaining cartilage homeostasis as reduced expression of FOXO1 and FOXO3 with aging, results in osteoarthritis (OA) due to reduction in the expression of autophagy-related genes. FOXO activity is strictly regulated by nuclear-cytoplasmic shuttling. Drugs that promote nuclear FOXO and activity could be promising therapeutics for OA. Here, we discovered candidates of FOXO activators and evaluated their effects on chondrocytes.

Methods: We performed in silico drug prioritization of small molecules that enhance nuclear accumulation of FOXO1 or FOXO3 and selected 5 drug candidates, selinexor, dactolisib, cyproheptadine, LOM612, and psammaplysene-A from previously identified FOXO activators and confirmed their effects on FOXO nuclear translocation in human chondrocytes. Next, chondrocytes were treated with FOXO activators to evaluate their effects on the expression of autophagy-related genes, and the induction of catabolic factors after IL1β stimulation by qRT-PCR. RNA-sequencing of chondrocytes treated with cyproheptadine with or without IL1β stimulation was performed to clarify the target genes and mechanisms.

Results: Selinexor induced the nuclear accumulation both of FOXO1 and FOXO3, dactolisib and cyproheptadine induced FOXO3 nuclear accumulation, whereas LOM612 and psammaplysene A did not change FOXO translocation in chondrocytes. Among the 3 drugs which induced FOXO nuclear accumulation, cyproheptadine most effectively upregulated the expressions of autophagy-related genes (*MAP1LC3B*, *GABALAPL1*, *ATG14*) and inhibited the induction of catabolic factors (*IL6* and *MMP13*) under IL1β stimulation (Figure 1). Enrichment analysis with the upregulated genes in RNA-seq showed that 'Cholesterol metabolism' was the most highly enriched pathway, suggesting that cyproheptadine modulates cholesterol

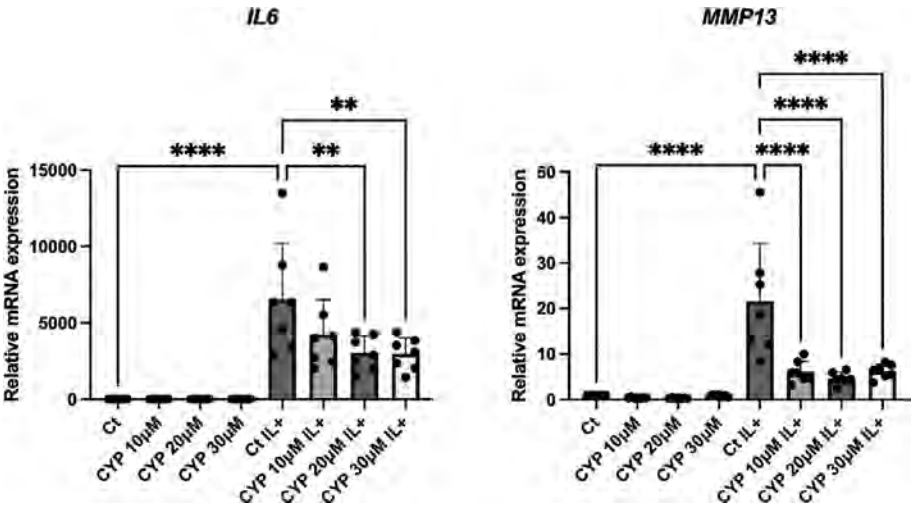


Figure.1: Gene expression of IL6 and MMP13 in human primary chondrocytes with or without IL1β stimulation (1ng/mL) for 6 hours after pretreatment with cyproheptadine (CYP) for 24 hours. **P<0.01, ****P<0.0001 (One-way ANOVA with the Tukey-Kramer post hoc test).

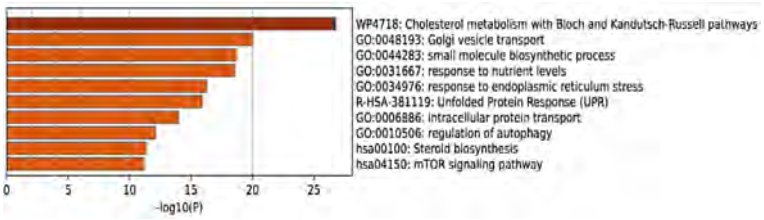


Figure.2: Enrichment analysis with the upregulated genes in RNA-seq of human primary chondrocytes treated with cyproheptadine (30μM) for 24 hours.

levels in chondrocytes (Figure 2). Cyproheptadine also regulated 'Autophagy'. In the presence of IL1β, the enrichment analysis with the downregulated genes showed cyproheptadine inhibited 'Cytokine signaling' via NFκB pathway.

Conclusion: Cyproheptadine induced FOXO3 nuclear accumulation and autophagy-related genes expression and inhibited catabolic factors. In addition, cyproheptadine showed a potential as a modulator of cellular cholesterol biosynthesis, which is associated with age-related diseases including OA. Further experiments in vitro and in vivo are ongoing to clarify the detailed effects of cyproheptadine as a candidate for drug-repurposing in OA.

Disclosure: I. Kurakazu: None; **M. Olmer**: None; **K. Myers**: None; **M. Lotz**: None.

Abstract Number: 0874

RNA-Binding Proteins That Are Highly Expressed and Enriched in Healthy Cartilage but Suppressed in Osteoarthritis

Hannah Swahn, Merissa Olmer and Martin K Lotz, Scripps Research Institute, La Jolla, CA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: RNA-binding proteins (RBPs) have diverse and essential biological functions, but their role in cartilage health and disease is largely unknown. The objectives of this study were (i) map the global landscape of RBPs expressed and enriched in heathy cartilage and dysregulated in osteoarthritis (OA); (ii) prioritize RBPs for their potential role in cartilage and in OA pathogenesis and as therapeutic targets.

Methods: Our published bulk RNA-sequencing (RNA-seq) data of healthy and OA human cartilage, and a census of 1,542 RBPs were utilized to identify RBPs that are expressed in healthy cartilage and differentially expressed (DE) in OA. Next, our comparison of healthy cartilage RNA-seq data to 37 transcriptomes in the Genotype-Tissue Expression (GTEx) database was used to determine RBPs that are enriched in cartilage. Finally, expression of RBPs was analyzed in our single cell RNA-sequencing (scRNA-seq) data from healthy and OA human cartilage.

Results: We first investigated in an RNA-seq dataset of healthy human knee cartilage the expression patterns of genes encoding RBPs. Expression of RBPs was higher than nonRBPs, transcription factors (TFs) and long non-coding RNAs (lncRNAs) in healthy cartilage. We next asked which RBPs were specifically enriched in cartilage compared to 37 other issues in GTEx. This analysis revealed 313 cartilage-enriched genes, 11 of which were RBPs (Figure 1). In OA cartilage,

188 RBPs were DE, with a greater proportion downregulated (Figure 2). After identifying the DE RBPs, we investigated their protein associations using STRING. The 188 DE RBPs formed a highly dense protein-protein interaction network. We next investigated both the gene ontology programs and biological pathways associated with the up- and downregulated RBPs. Ribosome biogenesis was enriched in the upregulated RBPs, while splicing and transport were enriched in the downregulated. ChIP-X Enrichment Analysis 3 (ChEA3) was used to identify potential TFs that regulate the DE RBPs. Of the top

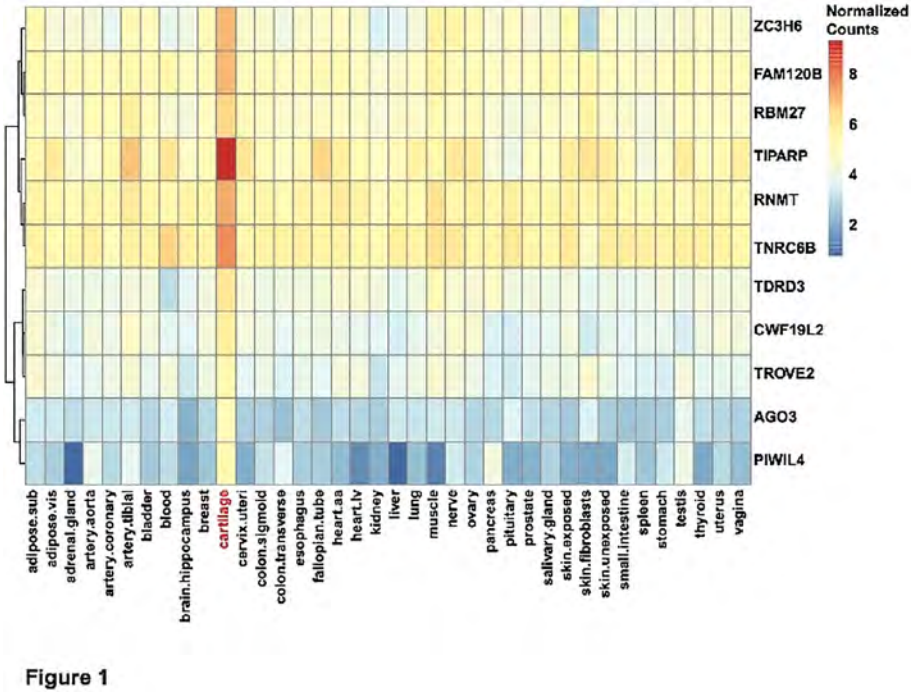


Figure 1. Heatmap showing average normalized counts of cartilage-enriched RBPs compared to all other GTEx tissues.

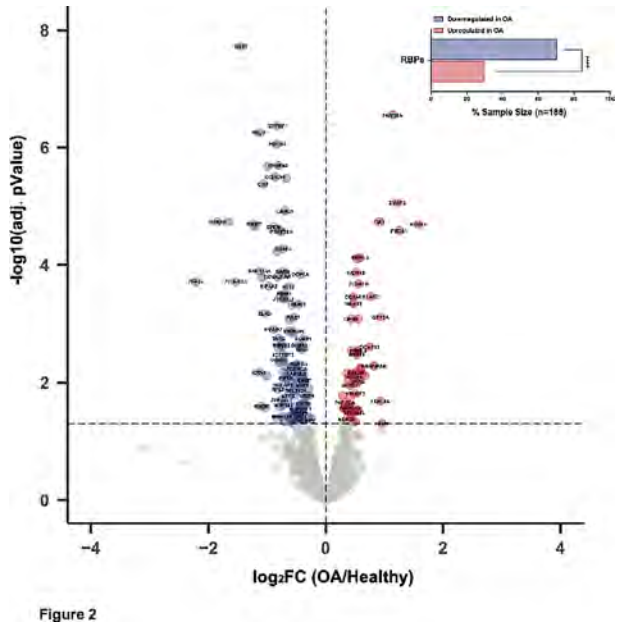


Figure 2. Volcano plot showing 188 DE RBPs. Blue indicates downregulation in OA cartilage compared to healthy, and red indicates upregulation. Gray indicates no significance. Bar chart showing proportion of downregulated (blue) vs upregulated (red) RBPs in OA cartilage. ****p<0.0001 by comparison of proportions test.

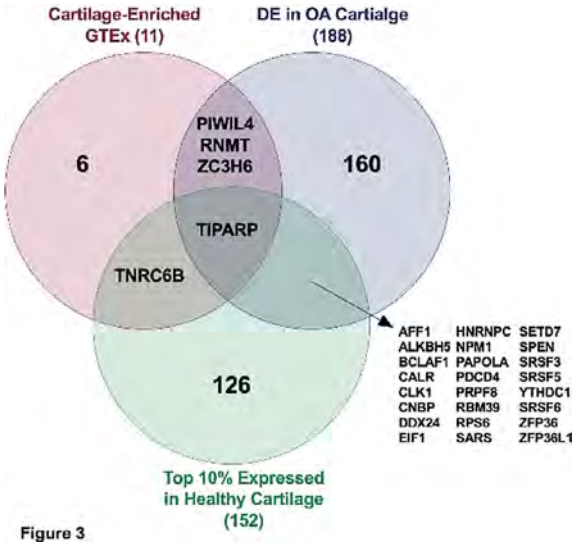


Figure 3. Venn diagram showing intersection of highly expressed (top 10%) RBPs in healthy cartilage, GTEx cartilage-enriched RBPs and DE RBPs in OA cartilage.

20 TFs, the MYC proto-oncogene (MYC) was predicted to regulate the largest number of upregulated RBPs at 42. Of the top 20 TFs, Activating Transcription Factor 1 (ATF1) was predicted to regulate the largest number of downregulated RBPs at 58. To identify a candidate RBP for further studies and as potential therapeutic targets, we investigated other parameters in addition to differential expression including: (i) the top 10% expressed RBPs in healthy cartilage and (ii) those that were cartilage-enriched according to GTEx. Intersecting these three criteria, we identified Tetrachlorodibenzodioxin (TCDD) Inducible Poly(ADP-Ribose) Polymerase (TIPARP) as a candidate RBP (Figure 3). TIPARP was downregulated in OA at both the gene expression and protein levels. scRNA-seq data revealed TIPARP was most significantly downregulated in the 'pathogenic cluster' as well as other fibrocytic clusters, suggesting a context-specific effect for TIPARP in chondrocyte function, which was not evident in the bulk RNA-seq data alone.

Conclusion: Our global analyses reveal expression patterns of RBPs in healthy and OA cartilage. We also identified TIPARP and other RBPs as novel mediators in OA pathogenesis and as potential therapeutic targets.

Disclosure: H. Swahn: None; **M. Olmer**: None; **M. Lotz**: None.

Abstract Number: 0875

INV-1498, a Promising Caspase Inhibitor, Exhibits Dose-dependent Therapeutic Efficacy in a Canine Model of Osteoarthritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis poses a substantial medical challenge, as the available treatments primarily target symptom relief and fail to effectively halt the progressive cartilage deterioration that ultimately leads to joint replacement. Addressing this therapeutic gap, the development of interventions capable of preventing or slowing down the progression of osteoarthritis is imperative. This study unveils INV-1498 as an advanced late pre-clinical candidate that exhibits noteworthy, dose-dependent effects on joint structure, function, and pain, offering a promising avenue for addressing osteoarthritis.

Methods: A total of thirty-five purpose-bred dogs were selected for this study. Prior to surgery, the knees of each animal were shaved and the animals were anesthetized. Anterior cruciate ligament resection and excision of the medial meniscus were performed, followed by wound closure. Antibiotics and analgesics were administered for 7 days post-surgery. One week after surgery, the animals underwent artificial exercise for 14 days, with daily sessions lasting 30 minutes. The experimental groups received different doses of the study product (10 mg, 1 mg, or 1 mg in a 1 mL volume) every 5 weeks, while one group received a single 10 mg dose. Triamcinolone 12.5 mg was administered intra-articularly every 5 weeks as an active comparator. After 14 weeks, a CT scan of the knee joint was performed. Pain assessment was conducted throughout the study using the LAMNESS GRADE scale (0-4). At 15 weeks post-osteoarthritis (OA) induction, the dogs were euthanized, and a comprehensive macroscopic evaluation of the operated knee joint was conducted. Tissue sections were prepared and stained with H&E and Safranin O for blinded OARSI histologic scoring.

Results: In the gait assessment, all doses of INV-1498, including the highest dose (10 mg, p=0.0009), exhibited significant improvements, indicating reduced pain. Although there was no statistical significance between doses, a dose-dependent trend of improvement was observed (Figure 1). Analysis of joint structure by CT scan revealed significant improvement only in the highest dose group (10 mg, p=0.0135). Histopathologic evaluation, using the OARSI histopathology method, demonstrated that the highest dose of INV-1498 (10 mg, p=0.0021) significantly reduced proteoglycans, chondrocytes (p=0.0109), and femur-layer lining cells (10 mg, p=0.025). Although not statistically significant, synovial membrane hyperplasia and inflammation tended to be reduced in the INV-1498 group compared to the control group (Figure 2).

Conclusion: Taken together, these data provide compelling evidence of the efficacy of INV-1498 in controlling osteoarthritis progression and symptoms. We found that even a dosing scheme of every 5 weeks prevented the most important pathophysiological changes that promote osteoarthritis progression. These findings position INV-1498 as a highly promising candidate for clinical development as a disease-modifying therapy for osteoarthritis, offering the additional benefit of pain reduction.

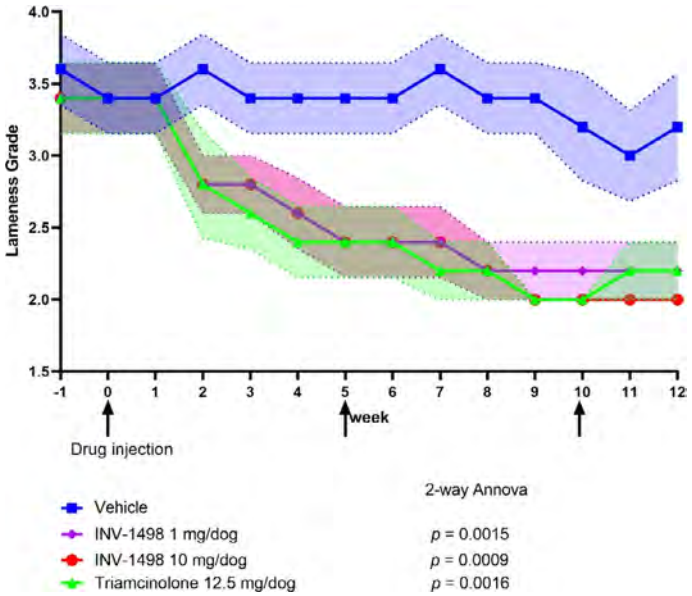

Figure 1. Evaluation of pain relief using gait assessment in a beagle dog meniscectomy model. The line and bar graphs represent mean ± SEM (n = 5).

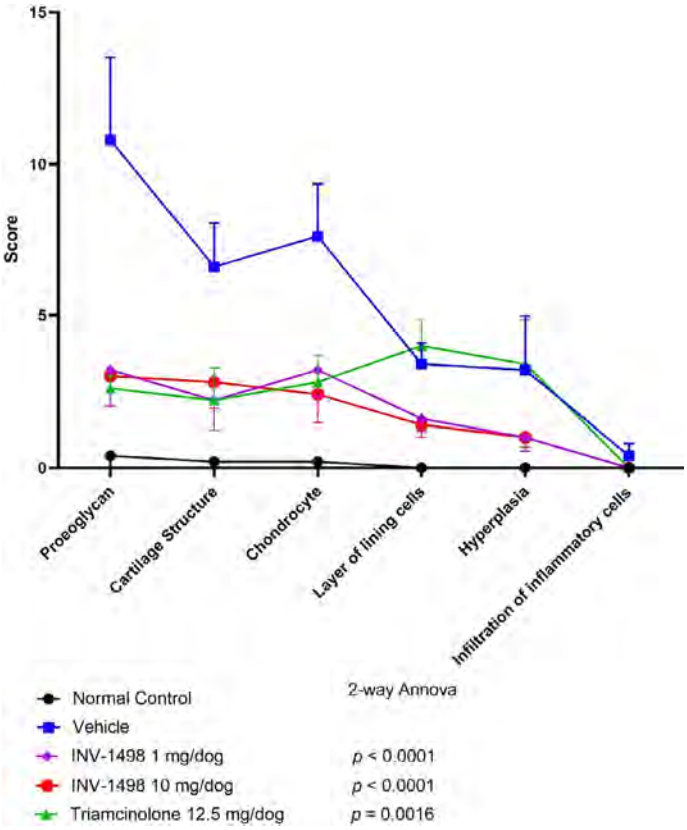

Figure 2. Histopathologic evaluation of the femoral cartilage layer and synovium in a beagle dog meniscectomy model. The Bars represent the mean ± SEM (n = 5).

Disclosure: J. Park: None; **Y. Lee**: None; **J. Park**: None; **m. Kim**: None.

Abstract Number: 0876

Metabolomic Analysis Reveals Associations Between Calcium Crystals and Metabolites in Osteoarthritic Synovial Tissue

Nathan Argel[1], Sina Stücker[2], Adnan Cutuk[3], Robert Meyer[3], Nancy Lane[4], Jessica Bertrand[2], Monica Guma[3] and Jessica Murillo-Saich[1], [1]Department of Medicine, University of California San Diego, La Jolla, CA, [2]Department of Orthopaedic Surgery, Otto-von-Guericke-University Magdeburg, Magdeburg, Germany, [3]San Diego VA Healthcare Service, La Jolla, CA, [4]University of California, Hillsborough, CA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Emerging research suggests that synovial inflammation and metabolic alterations are involved in the progression of osteoarthritis (OA). Additionally, the presence of calcium-containing crystals (CC), such as basic calcium phosphate (BCP) and calcium pyrophosphates (CPP) crystals, has been implicated in the development of OA, potentially contributing to inflammatory responses and pain. However, our understanding of the impact of CC on synovial tissue

(ST) in OA remains limited. Therefore, the aim of this study is to investigate the relationship between synovial CC, histological composition, pain as well as the synovial metabolic profile in OA.

Methods: A total of 28 ST samples were collected from patients diagnosed with OA during total joint replacement surgeries. The ST samples were either fixed in formalin for subsequent histological analysis, or snap-frozen for metabolomic analysis. The histological assessment of ST samples was performed using the Krenn histopathological synovitis score, which categorized the samples into two groups: inflammation grade 0-I and inflammation grade II-III. Synovial CD68 positive cells and synovial area containing CC (%Ca++) were assessed by immunohistochemistry and Von Kossa staining respectively, and semi-quantified using Image J. The severity of OA disease was evaluated using the Western Ontario and McMaster

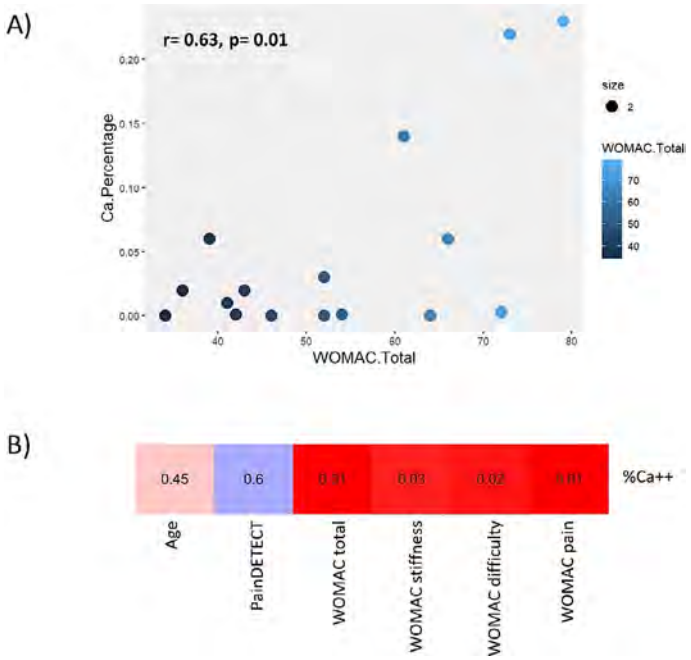

Figure 1. A) Scatter plot showing Pearson correlation between %Ca++ in synovial tissue and total WOMAC. B) Pearson correlation between the % Ca++ in synovial tissue and age, painDETECT and WOMAC scores.

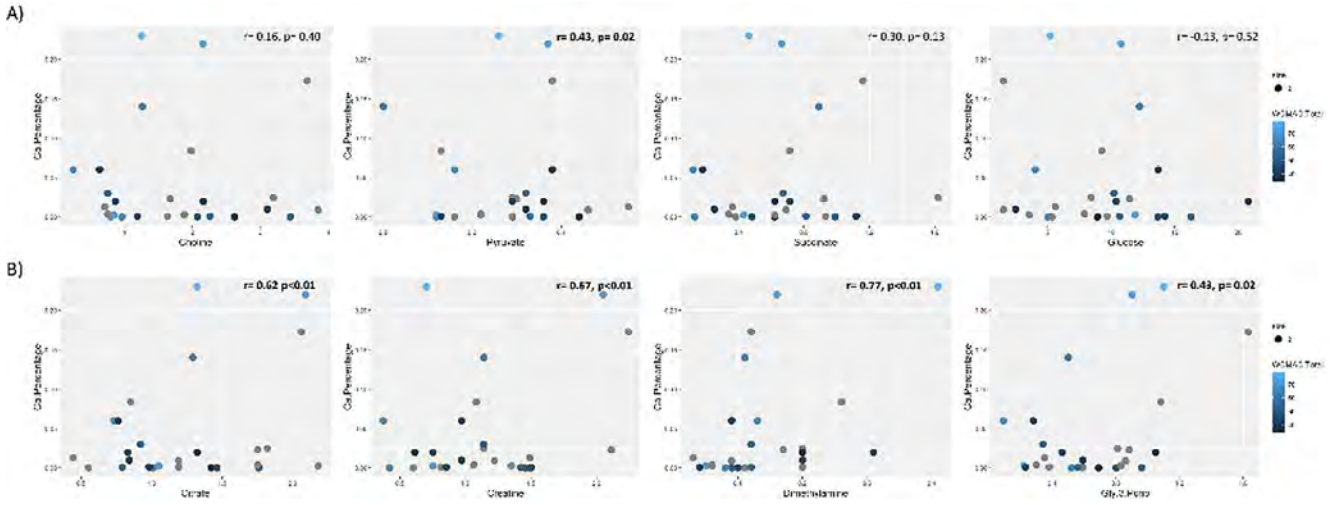

Figure 2. Scatter plot showing Pearson correlation between %Ca++ in synovial tissue and A) metabolites associated to inflammation and B) other metabolites statistically significant.

Universities Arthritis Index (WOMAC). Nuclear Magnetic Resonance (NMR) spectra of the ST samples were acquired using a 600 MHz Bruker Avance III spectrometer with 1H-NMR. The Chenomx NMR Suite 8.5 professional software was employed for metabolite identification and quantification(μM). For statistical analysis, MetaboAnalyst 5.0, SPSS v26, and R Studio software were utilized.

Results: 13 samples with inflammation grade 0-I and 15 samples with inflammation grade II-III samples were included. There were no significant differences observed in the synovial area containing CC (%Ca++) between the two inflammation groups (p=0.48). Furthermore, no correlation was found between %Ca++ and CD68 expression (p=0.84). However, WOMAC scores showed a positive correlation with %Ca++ (**Figure 1A-B**). Regarding metabolites associated with %Ca++, we observed a positive association between pyruvate and %Ca++ (r=0.43, p=0.02) and a tendency for a positive correlation between succinate and %Ca++ (r=0.30, p=0.13). However, metabolites such as choline and glucose did not show any correlation with %Ca++ in ST (**Figure 2A**). Interestingly, we also found positive correlations between %Ca++ and citrate (r=0.62, p< 0.01), creatinine (r=0.67, p< 0.01), dimethylamine (r=0.77, p< 0.01), and sn-glycero-3-phosphocholine (r=0.43, p=0.02) (**Figure 2B**).

Conclusion: Our findings provide evidence supporting the association between synovial CC and the pain phenotype in OA. Although no direct correlation between inflammation and %Ca++ was observed, our results suggest that these crystals may contribute to metabolic alterations in the ST. Further investigations are warranted to elucidate whether the presence of CC in OA triggers pain and to identify the underlying metabolic pathways.

Disclosure: N. Argel: None; **S. Stücker**: None; **A. Cutuk**: None; **R. Meyer**: None; **N. Lane**: None; **J. Bertrand**: None; **M. Guma**: Genentech, 5, Gilead, 5, Novartis, 5, Pfizer, 5; **J. Murillo-Saich**: None.

Abstract Number: 0877

Loss of Transient Receptor Potential Channel 1 (TRPC1) Links Regulation of Intracellular Calcium to Cellular Senescence and Leads to Development of Osteoarthritis

Meike Sambale[1], starlee lively[2], Osvaldo Espin-Garcia[2], Pratibha Potla[2], Chiara Pastrello[3], Alexandra Schaefer[1], Jessica Bertrand[4], Mohit Kapoor[5], Thomas Pap[1] and **Joanna Sherwood**[1], [1]University Hospital Münster, Münster, Germany, [2]University Health Network, Toronto, ON, Canada, [3]Osteoarthritis Research Program, Division of Orthopaedic Surgery, Schroeder Arthritis Institute and Data Science Discovery Centre for Chronic diseases, Krembil Research Institute, Toronto, ON, Canada, [4]Department of Orthopaedic Surgery, Otto-von-Guericke-University Magdeburg, Magdeburg, Germany, [5]Division of Orthopaedics, Osteoarthritis Research Program, Schroeder Arthritis Institute, and Krembil Research Institute, University Health Network, Toronto, ON, Canada

SESSION INFORMATION

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Session Title: Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Transient receptor potential channel 1 (TRPC1) is a widely expressed mechanosensitive ion channel located within the endoplasmic reticulum membrane. It is crucial for the refilling of depleted internal calcium stores as part of calcium-dependent signaling. Considering the impact of calcium signaling regulation on both homeostatic and inflammatory signaling in chondrocytes, we aimed to examine the role of TRPC1 within cartilage homeostasis and osteoarthritis by monitoring expression during human and murine osteoarthritis (OA) and by assessing the impact of TRPC1 deficiency on OA development and chondrocyte phenotypic stability.

Methods: 10-week old male WT and *Trpc1*$^{-/-}$ mice were subjected to destabilization of the medial meniscus (DMM) and were analyzed by microCT, RNA sequencing, histology and immunofluorescence staining at either 2 weeks or 8 weeks post-surgery for OA severity, TRPC1 expression and phenotypic marker expression. TRPC1 protein expression was evaluated in human OA cartilage samples by immunohistochemistry. *In vitro*, the phenotype of knee articular chondrocytes obtained from 4 day old mice was compared by QPCR, Western blot, SA-b-Gal staining and immunofluorescence. Intracellular calcium mobilization was measured by fluo-4 calcium influx assay.

Results: TRPC1 was found to be depleted from chondrocytes during both human and murine OA development. *Trpc1*$^{-/-}$ mice subjected to DMM developed a more severe OA-like phenotype than wild type (WT) controls. Analysis 2 weeks post-DMM revealed an increased rate of chondrocyte survival in *Trpc1*$^{-/-}$ cartilage, with remaining cells expressing less SOX9 and increased levels of MMP13 and the senescence marker p16^{INK4a}. RNA sequencing followed by GO analysis of articular cartilage from *Trpc1*-/- and WT mice identified a set of differentially expressed genes related to cell number, apoptosis and extracellular matrix organization biological processes.*In vitro*, stimulation of WT chondrocytes with bFGF, ionomycin or thapsigargin all led to an increase in intracellular calcium, however these effects were significantly reduced in *Trpc1*$^{-/-}$chondrocytes. Although *Trpc1*$^{-/-}$ chondrocytes expressed similar levels of chondrocyte differentiation markers at basal level as WT controls, *Trpc1*$^{-/-}$ chondrocytes lost expression of type II collagen and increased type I collagen expression significantly faster than WT during serial passage. Replicative senescence and p16^{INK4a} expression was found to be significantly higher in *Trpc1*$^{-/-}$, both during passage and following IL1 stimulation.

Conclusion: *Trpc1*$^{-/-}$ chondrocytes were less able to maintain a stable chondrocyte phenotype *in vitro* than WT, indicating that TRPC1 activity is required for chondrocyte phenotypic stability. TRPC1 loss was associated with early stages of OA development, while *Trpc1*$^{-/-}$ mice developed a more severe OA-like phenotype following DMM surgery. Both *in vivo* following DMM, and*in vitro* during passage and following IL1 stimulation, *Trpc1*$^{-/-}$ chondrocytes demonstrated an increased susceptibility to cellular senescence. These findings suggest that TRPC1 is a protective factor required for cartilage homeostasis during conditions of physiological challenge.

Disclosure: M. Sambale: None; **s. lively**: None; **O. Espin-Garcia**: None; **P. Potla**: None; **C. Pastrello**: None; **A. Schaefer**: None; **J. Bertrand**: None; **M. Kapoor**: None; **T. Pap**: AbbVie/Abbott, 2, Galapagos, 5, UCB, 2; **J. Sherwood**: None.

Abstract Number: 0878

Synovial Fibroblasts Undergo a Phenotypic Shift from Early- to Late-stage Knee Osteoarthritis

Kabriya Thavaratnam[1], Eric Gracey[2], Anusha Ratneswaran[1], Jason Rockel[1], Shabana Vohra[1], Chiara Pastrello[3], Igor Jurisica[4], starlee lively[5], Sam Dupont[6], Raja Rampersaud[1], Nizar Mahomed[7], Rajiv Gandhi[8], Dirk Elewaut[9] and **Mohit Kapoor**[10], [1]Schroeder Arthritis Institute, Toronto, ON, Canada, [2]Ghent University Hospital, Gent, Belgium, [3]Osteoarthritis Research Program, Division of Orthopaedic Surgery, Schroeder Arthritis Institute and Data Science Discovery Centre for Chronic diseases, Krembil Research Institute, Toronto, ON, Canada, [4]Schroeder Arthritis Institute, Krembil Research Institute and Departments of Medical Biophysics and Computer Science and Faculty of Dentistry, University of Toronto and Institute of Neuroimmunology, Slovak Academy of Sciences, Bratislava, Slovakia, [5]University Health Network, Toronto, ON, Canada, [6]Ghent University Hospital, Ghent, Belgium, [7]Division of Orthopaedics, Osteoarthritis Research Program, Schroeder Arthritis Institute, Krembil Research Institute, and Toronto Western Hospital, University Health Network, Toronto, ON, Canada, [8]Schroeder Arthritis Institute, Krembil Research Institute, University Health Network and Division of Orthopaedics, Department of Surgery, University of Toronto, Toronto, ON, Canada, [9]Ghent University and VIB Center for Inflammation Research, Ghent, Belgium, [10]Schroeder Arthritis Institute, University Health Network and Department of Surgery, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Monday, November 13, 2023
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Session Time: 9:00AM–11:00AM

Background/Purpose: The synovium is a connective tissue that lines the joint capsule and is emerging as a key contributor to joint destruction during osteoarthritis (OA). During knee (K)OA pathogenesis, the synovium undergoes substantial changes including inflammation, cellular proliferation and fibrosis. However, the contributions of distinct synovial cell types, particularly fibroblasts (major synovial cells), to synovial pathologies in early and late-stages of KOA are unknown. To identify if distinct cell subtypes and their transcriptomic profiles exist in the synovium during distinct stages of OA disease severity, we used synovium from early (KL1) and late stages (KL3/4) of radiographic KOA and from a knee OA mouse model and subjected these samples to high throughput transcriptomic technologies such as single nucleus RNA sequencing (snRNAseq), bulk RNA sequencing, advanced bioinformatics and functional assays.

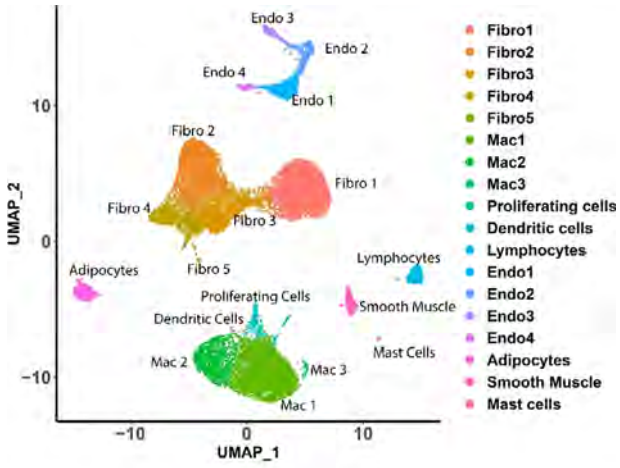

Figure 1: Clustering analyses illustrating all cell types found in KL1 & KL3/4 human radiographic knee OA synovium.

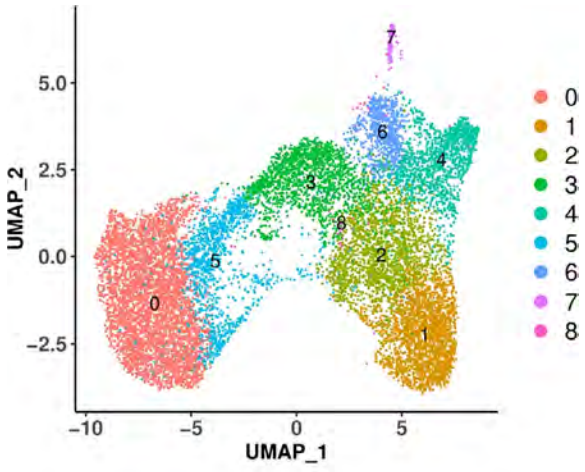

Figure 2: Fibroblast cell clustering analyses identifying 9 fibroblast subtypes.

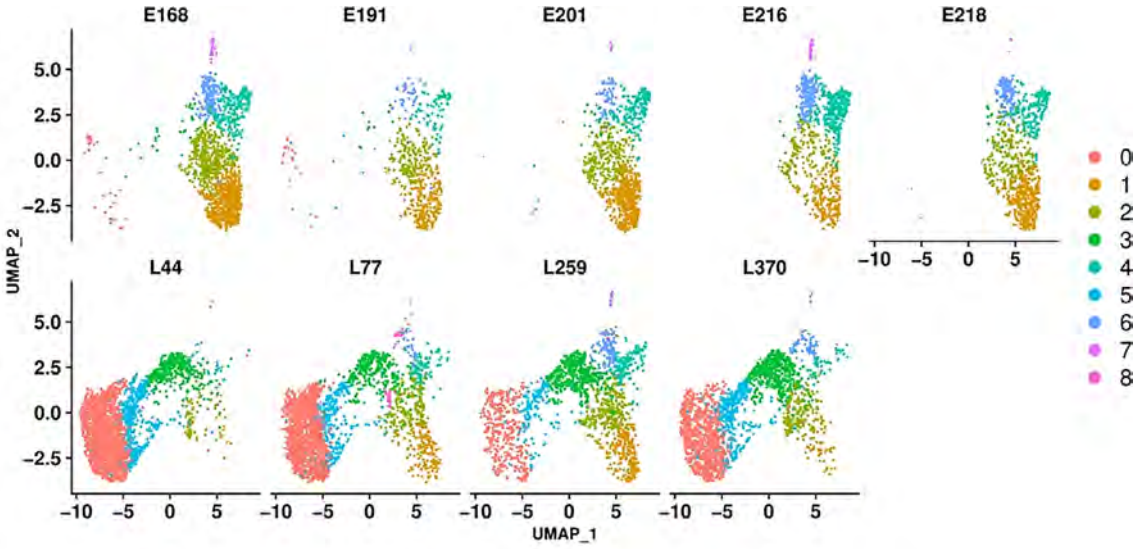

Figure 3: Individual patient fibroblast cell subtype clustering analyses illustrating differences in presence of subclusters between KL1 and KL3/4 radiographic knee OA patients.

Methods: Synovia from early- (n=5; KL=1) and late-stage (n=4; KL=3/4) radiographic KOA patients were subjected to single nucleus (sn)RNAseq. Bulk RNA sequencing was performed in the synovium of n=6 early and n=8 late-stage radiographic KOA patients. Knee synovia isolated from naïve (control mice; n=4), 2 weeks (n=3) and 10 weeks (n=4) post-DMM surgery were also subjected to snRNAseq. Sequencing data was subjected to clustering analysis, differential expression analysis (to identify transcriptomic profiles), pathway analysis and upstream transcriptional regulator analyses.

Results: Up to 50% of the cells from early and late-stage KOA human synovium were of fibroblast origin (Fig 1). Clustering analysis identified 8 distinct fibroblast subclusters in the KOA synovium (Fig 2). A phenotypic shift in fibroblast subsets was observed from early to late stages of KOA (fibroblast clusters 1, 2, 4 and 6 were predominantly associated with early-stage while fibroblast clusters 0, 3 and 5 were predominantly associated with late-stage OA) (Fig 3). Unique transcriptomic profiles were identified for each fibroblast subset, some being cell surface markers that were confirmed by immunohistochemistry to be differentially expressed in the synovium of early or late-stage KOA in vivo. Furthermore, pathway analyses suggest that the two major fibroblast subclusters, clusters 1 (early) and cluster 0 (late), may play crucial roles in ECM/fibrosis related pathways. Computational analysis has also identified putative upstream transcriptional regulators that may play key roles in ECM regulation and fibrosis. snRNAseq data of mouse synovium also identified some overlapping fibroblast clusters in human and mouse synovium. Specifically, late-stage cluster 0 identified in human snRNAseq analysis showed expansion in mouse synovium 10 weeks post DMM surgery compared to 2 week-DMM and naïve (control) synovium. Current efforts are focussed on targeting select transcription factor(s) using in vitro and in vivo gain and loss of function studies to identify their role in OA synovial pathology.

Conclusion: snRNAseq analysis has led us to identify distinct synovial fibroblast subsets with unique transcriptomic profiles in early and late-stages of KOA that may play a key role in driving OA synovial pathology.

Disclosure: K. Thavaratnam: None; **E. Gracey**: None; **A. Ratneswaran**: None; **J. Rockel**: None; **S. Vohra**: None; **C. Pastrello**: None; **I. Jurisica**: None; **s. lively**: None; **S. Dupont**: None; **R. Rampersaud**: None; **N. Mahomed**: AIC, 4, ARTHUR HEALTH CORP, 3; **R. Gandhi**: None; **D. Elewaut**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 2, galapagos, 5, Janssen, 6; **M. Kapoor**: None.

Abstract Number: 0879

Recommendations for a Standardized Approach to Histopathologic Evaluation of Synovial Membrane in Murine Models of Experimental Osteoarthritis

Alia Obeidat[1], Sung Yeon Kim[2], Baofeng Hu[3], Jun Li[1], Shingo Ishihara[1], Rui Xiao[4], Rachel Miller[1], Anne-Marie Malfait[1] and Carla Scanzello[5], [1]Rush University Medical Center, Chicago, IL, [2]University of Pennsylvania School of Engineering and Applied Sciences, Philadelphia, PA, [3]University of Pennsylvania, Wynnewood, PA, [4]Department of Biostatistics, Epidemiology and Informatics, Perelman School of Medicine, University of Pennsylvania,Department of Pediatrics Division of Biostatistics, Children's Hospital of Philadelphia, Philadelphia, PA, [5]Translational Musculoskeletal Research Center, Corp. Michael J Crescenz VA Medical Center,4Division of Rheumatology, Perelman School of Medicine University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

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Session Title: Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Synovial pathology is an active component of osteoarthritis (OA) that has been linked to disease progression and pain in patients. Macroscopic and microscopic grading systems for synovial pathology in human OA have been extensively described. However, a comprehensive histologic scoring system for murine models of OA is lacking. Thus, we sought to develop a reproducible approach and set of recommendations for evaluation of synovial changes in murine models of OA.

Methods: Coronal sections from murine knee joints as part of other studies were used as follows: 1. Hematoxylin and Eosin (H&E) or Toluidine Blue (T-Blue) stained sections from mice 6 weeks after destabilization of medial meniscus (DMM) or sham surgery and age matched naïve controls (n=5/group), 2. Safranin O (Saf-O) sections from mice 16 weeks after DMM or sham surgery (n=5-6/group), 3. T-Blue sections from mice 16 weeks after DMM or sham surgery (n=10/group), 4. T-Blue sections from 12 weeks after partial meniscectomy (PMX) or sham surgery (n=10/group), 5. H&E sections from 12 weeks after PMX or sham surgery (n=5/group). Four blinded readers graded four pathological features (hyperplasia, cellularity, inflammation, and fibrosis) at four anatomic locations (lateral and medial femoral gutters, and lateral and medial tibial gutters) using midjoint sections. Inter-reader reliability tests (IRR) (Kendall's coefficient of concordance (W) for hyperplasia, inflammation, and cellularity; Fleiss Kappa test (κ) for fibrosis) were performed to assess agreement between readers.

PMX	Toluidine Blue				H&E			
	Cellularity	Inflammation	Hyperplasia	Fibrosis	Cellularity	Inflammation	Hyperplasia	Fibrosis
W	0.745	0.665	0.727	-	0.830	0.525	0.888	-
κ	-	-	-	0.736	-	-	-	0.687

DMM	Toluidine Blue				Safranin O/Fast Green			
	Cellularity	Inflammation	Hyperplasia	Fibrosis	Cellularity	Inflammation	Hyperplasia	Fibrosis
W	0.607	0.526	0.723	-	0.431	0.737	0.607	-
κ	-	-	-	0.736	-	-	-	0.687

Table 3: Inter-reader reliability scores of murine knee joints 12 weeks after PMX or sham surgery and 16 weeks after DMM or sham surgery. Kendall's coefficient of concordance (W), for the variables graded from 0-3, and Fleiss Kappa tests (κ) for fibrosis which was simply graded 0 or 1

Results: IRR measures (Table 1) demonstrate that there was acceptable to very good agreement between raters. Inflammation scores were excluded because of poorer concordance between readers and overlap with the cellularity assessment. Increased hyperplasia and cellularity and a trend of increased fibrosis were observed in the medial tibial and medial femoral gutters compared to controls 6wks after DMM (Fig 1A-C). At 16-weeks post-DMM, significant increase in cellularity and fibrosis were observed in the medial side with no significant hyperplasia (Fig 1D-F). No significant lateral changes were observed in any of DMM groups. At 12 weeks after PMX, a significant increase in hyperplasia, cellularity and fibrosis were observed in the medial gutters compared to sham mice (Fig 1G-I). Increased cellularity and hyperplasia were evident in the lateral gutters of PMX mice. Additionally, we assessed 4 sections/knee from PMX mice and found that synovial changes were consistent from section to section (Fig 2). Finally, we assessed the effect of different stains on IRR (Table 1). Higher reliability was observed using H&E and T-blue stains.

Conclusion: Based on our findings, we suggest evaluating 3 pathological features at 4 anatomic areas of the joint to assess synovial pathology in murine models of OA. A minimum of 3 readers are recommended, for which the IRR should be determined. A single midjoint section is likely sufficient for analysis, and a careful choice of stain should be considered. It is important to note that these recommendations are considered an initial step to allow comparison across labs and models, and to be used to guide more detailed subsequent analyses.

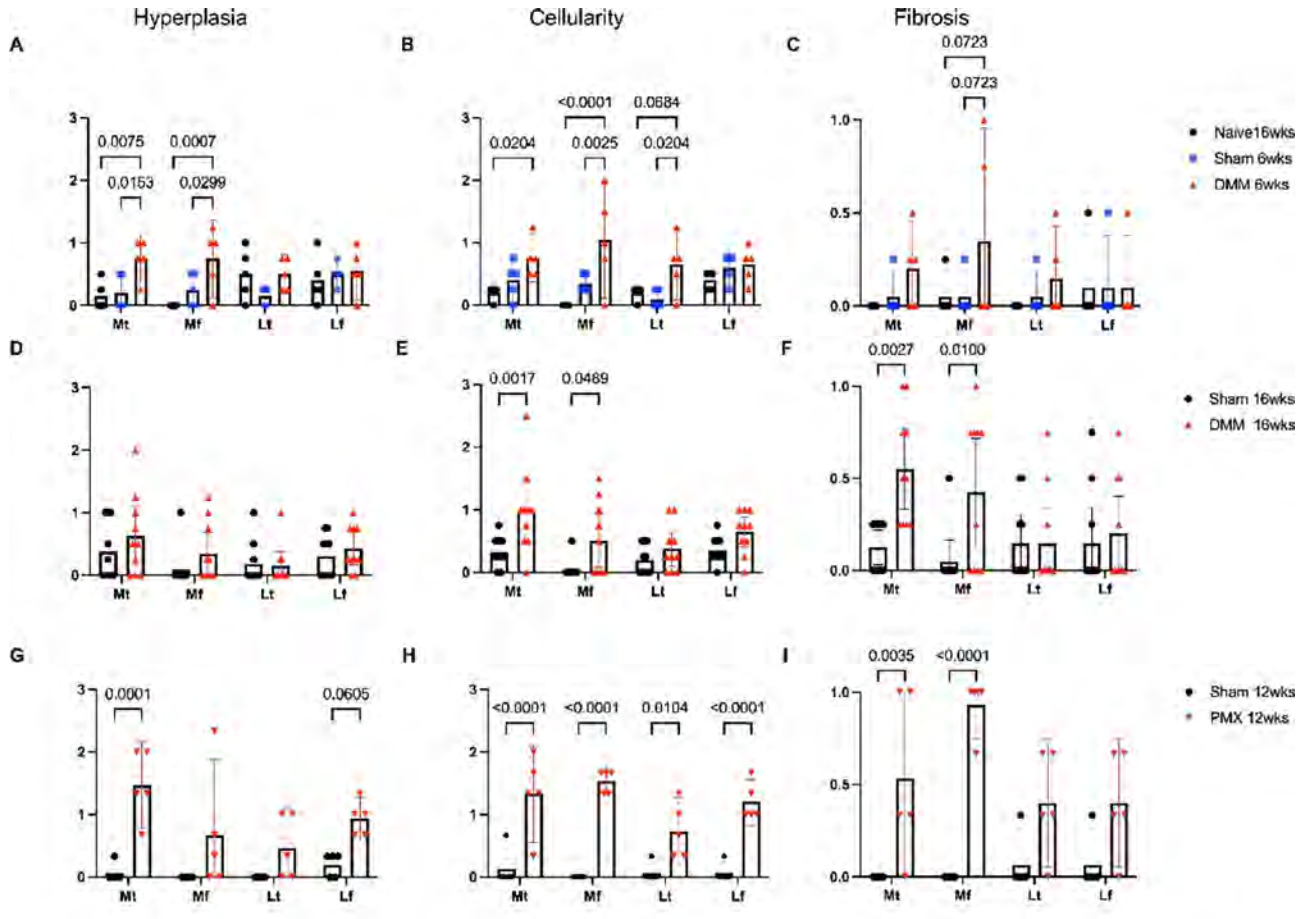

Figure 1: (A-I) Histopathologic scoring of synovial hyperplasia, cellularity and fibrosis for medial tibial (mt), medial femoral (mf), lateral tibial (lt) and lateral femoral (lf) areas in 16-week old naïve mice and mice 6 weeks after sham or DMM surgery (n=5/group) in (A-C); mice 16-week after sham or DMM surgery (n=10/group) in (D-F), and mice 12 weeks after PMX or sham surgery (n=5/group) in (G-I). Each score represents the average score of 4 blinded scorers. 2way ANOVA with Tukey's multiple comparisons test. Mean ± 95% CI.

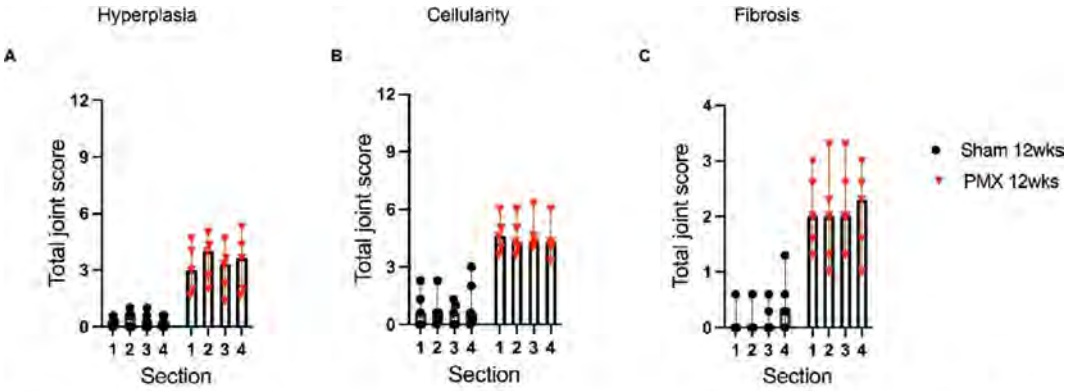

Figure 2: (A-C) Histopathologic scores of synovial hyperplasia, cellularity and fibrosis respectively summed for 4 joint areas in mice 12-week after sham and PMX surgery (n=5/group). 4 mid-joint sections per mouse were used to evaluate synovial changes, sections were H&E stained. 4 sets of data are shown in x-axis, each set represents one section per mouse for n=5 mice/group. 2way ANOVA with Tukey's multiple comparisons test. Mean ± 95% CI.

Disclosure: A. Obeidat: None; **S. Kim**: None; **B. Hu**: None; **J. Li**: None; **S. Ishihara**: None; **R. Xiao**: None; **R. Miller**: None; **A. Malfait**: None; **C. Scanzello**: None.

Abstract Number: 0880

CD14 Inhibition as a Potential Therapeutic in Post Traumatic OA

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is the most common joint disorder, and growing evidence has identified inflammation to be a major driver of disease progression. During disease, the synovium is identified as a reservoir of inflammatory mediators and immune cells, primarily consisting of monocyte/macrophages.[1] CD14, a co-receptor of inflammatory toll-like receptor signaling and a macrophage-activation-related protein, has been identified within synovial fluid and positively associated with joint space narrowing and knee pain.[2] We previously reported that global genetic CD14 deficiency in mice protects against OA-associated bone-remodeling and pain-related joint dysfunction.[3] Thus, **we hypothesize an anti-CD14 therapeutic will mediate inflammatory activation in the synovium during OA, and mitigate disease progression and pain.**

Methods: *OA model (n=12-14):* We performed destabilization of the medial meniscus (DMM) surgery to induce OA in skeletally mature (10-12 wk old) C57BL/6 mice.[3] *Intervention:* Mice were treated intra-articularly with either an anti-CD14 monoclonal antibody (mAb, clone biG53) or an IgG2a control (both 0.5mg/kg), two dosing strategies were tested: 1) *Prevention strategy:*mice received anti-CD14 or IgG control weekly x 3 doses, starting 48 hrs post DMM. 2) *Treatment strategy:* mice received 3 weekly injections beginning 4 wks post DMM. *Behavioral analysis*: Evaluation of spontaneous cage behaviors was performed via the laboratory animal behavior observation registration and analysis system (LABORAS, Metris).[3] Paw weight bearing analysis was performed via the advanced dynamic weight bearing (ADWB, Bioseb) system.[4]

Immunohistochemistry (n=3): In a separate early dosing 4-wk study, whole knee joints were fixed, decalcified, paraffin embedded, and sectioned. Sagittal sections underwent antigen retrieval and overnight incubation with primary antibodies (monocyte: Ly6C/D, macrophage: CD64), followed by incubation with fluorescent secondary antibodies, and lastly cover-slipped with mounting medium containing DAPI nuclear dye and imaged.

[1]Sanchez 2012 [2]Lieberthal 2015 [3]Sambamurthy 2018 [4]Krug 2019

Results: Prevention strategy: Early CD14 blockade increased total distance traveled and rearing time at 4- and 8-wks post DMM, compared to control mice ($p < 0.05$) (**Fig. 1**). Front to rear paw weight ratio 8-wks post DMM had a strong decreasing trend ($p=0.057$) in CD14 inhibitor treated mice compared to controls (**Fig. 1**). Treatment strategy: When treatment was delayed (4 wks post-DMM), no significant behavior or weight bearing changes were observed between groups (**Fig. 2**). Evaluating inflammation, early CD14 blocked increased the presence of Ly6C/G+ cells within the synovial lining layer compared to control at 4-wks post DMM (**Fig. 3**). Few CD64+ cells were observed (**Fig. 3**).

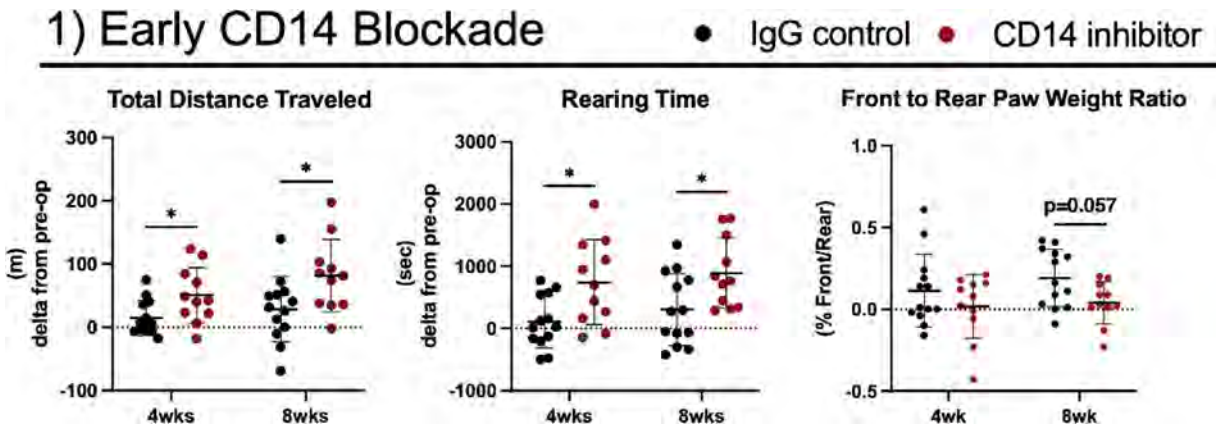


Figure 1: Spontaneous behavioral testing results from the early CD14 blockade groups. LABORAS behavioral analysis of the change from pre-op in total distance traveled (m) and time spent rearing (s). ADWB weight bearing analysis of the change from pre-op of front to rear paw & weight % ratio. *p<0.05 Student's T-test.

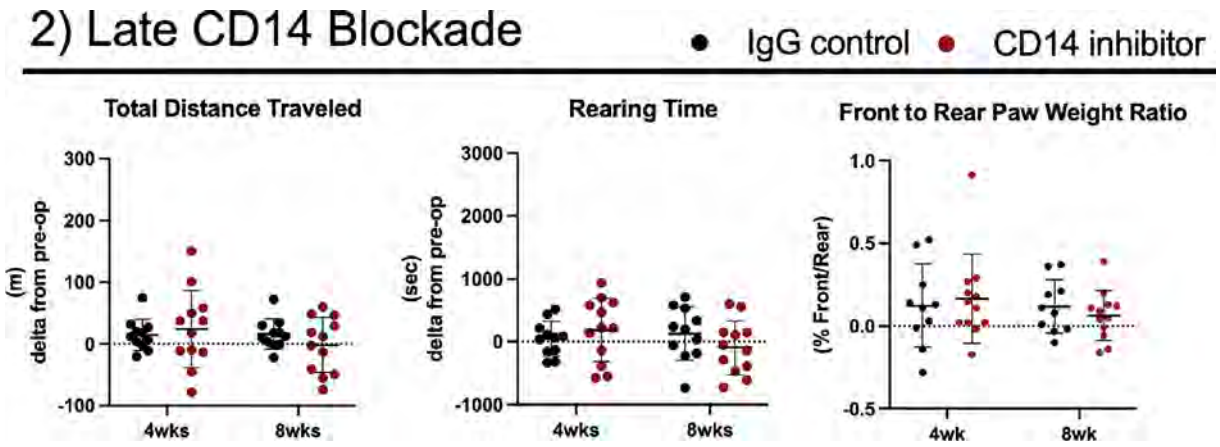


Figure 2: Spontaneous behavioral testing results from the late CD14 blockade groups. LABORAS behavioral analysis of the change from pre-op in total distance traveled (m) and time spent rearing (s). ADWB weight bearing analysis of the change from pre-op of front to rear paw & weight % ratio. *p<0.05 Student's T-test.

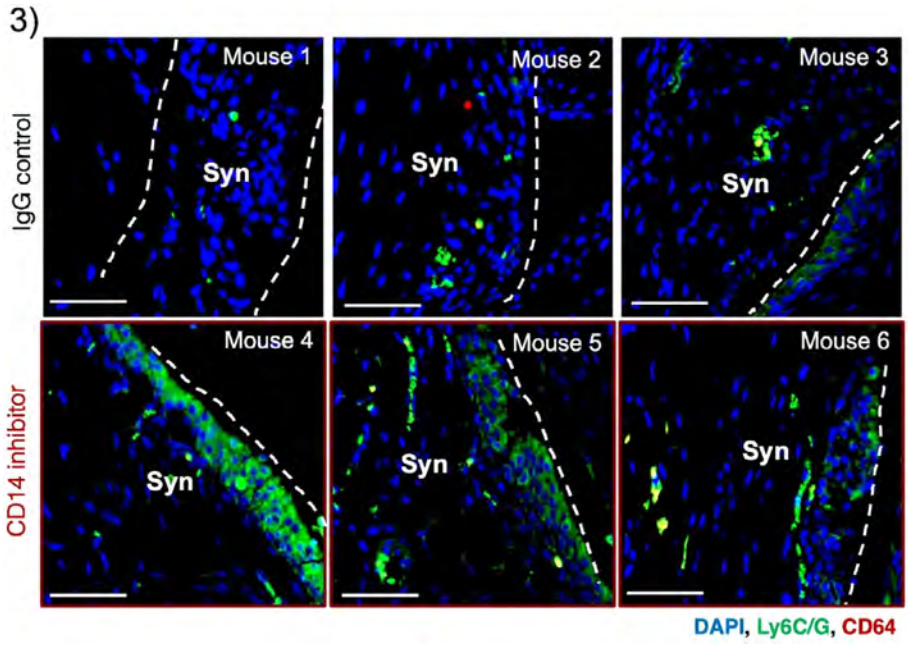


Figure 3: Immune cell presence following DMM. Fluorescent images of mice from IgG control and CD14 blockade treated mice (n=3) at 4 wks post DMM, stained for a general myeloid cell marker (Ly6C/G) and mature macrophage marker (CD64). Synovium (syn) is labeled with the lining layer indicated (white dashed line). Scale bar = 50μm.

Conclusion: Results revealed early delivery of a CD14 blocking mAb after DMM injury was more effective at improving mobility, compared to delayed dosing. Immunostaining suggests that anti-CD14 treatment may be modulating myeloid cell activation, clearance, or differentiation within the synovium during OA progression. **Results provide significant support for further evaluation of CD14 as a therapeutic for painful OA.**

Disclosure: K. Burt: None; **V. Nguyen**: None; **L. Murphy**: None; **D. Herbert**: None; **R. Mauck**: None; **C. Scanzello**: None.

Abstract Number: 0881

Deficiency of the Pattern-recognition Receptor CD14 Protects Against LPS-induced Inhibition of Osteoclastogenesis *in Vitro*

Lance Murphy[1], Kevin Burt[2], Baofeng Hu[3], Vu Nguyen[2], Robert Mauck[2] and Carla Scanzello[2], [1]University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, [2]University of Pennsylvania, Philadelphia, PA, [3]University of Pennsylvania, Wynnewood, PA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis is associated with bone changes such as subchondral sclerosis, bone marrow lesions, and osteophyte formation (Donel S, 2019). Prior work has demonstrated that CD14-deficient mice show significantly less OA-associated subchondral bone (Sambamurthy N, 2018). CD14 is a GPI-anchored surface protein and co-

receptor for several inflammatory TLRs, and is highly expressed in myeloid cells including osteoclast precursors (Zanoni, I 2013; Xue, J 2020). TLR activation can both activate and inhibit osteoclastogenic potential. Therefore, using a CD14-deficient mouse model we **hypothesized that inhibitory effects of TLR-stimuli on RANKL-mediated osteoclast differentiation would be ameliorated in CD14 deficient cells.**

Methods: *Cell isolation and culture (n=3-5):* Bone Marrow was isolated from femurs and tibiae of skeletally mature (10-12 wk old) C57BL/6 (WT) and CD14-deficient mice. Following 24 hr suspension culture, cells were cultured in complete DMEM with 30 ng/mL M-CSF, for 5 days to expand osteoclast precursors (macrophages). Cells were passaged on day 6 and cultured (24 well plate, 50,000 cells/well) in the presence or absence of RANKL (100 ng/mL). In a separate study, cells were stimulated with a TLR4-stimulus (LPS, 1 ng/mL), soluble CD14 (1 μg/mL), and a TLR4-inhibitor (CLI-095, 1 μg/mL).

Osteoclast staining and image analysis: Cells were stained for Tartrate-resistant acid phosphatase (TRAP) on days 3 and 4 after addition of RANKL. Cells were imaged at 10x (3 images/well over 4 wells per timepoint) and quantified (% area covered) using ImageJ (NIH) and CellProfiler. Number of osteoclasts (cells with >3 nuclei) per 10X field was also quantitated. Multiple unpaired t-test were performed with Holm-Sidak correction.

Results: CD14-deficient cells showed more rapid differentiation than WT cells at baseline (**Fig. 1**). Numbers of osteoclasts (**Fig. 1E**) and area of the plate covered by osteoclasts (**Fig. 1F**) were higher in CD14-deficient cells on day 3 and day 4 ($p < 0.001$ and $p < 0.05$, respectively). TLR4-stimuli: With LPS stimulation, CD14-deficient cells differentiated more quickly compared to WT at day 3 ($p < 0.001$) (**Fig. 3G**). LPS stimulation led to a 77% decrease of osteoclastogenesis in the WT cells, but only a 7.5% decrease in osteoclastogenesis on the CD14-deficient cells **(Figure 2G, 3G)** Addition of CLI-095 mitigated

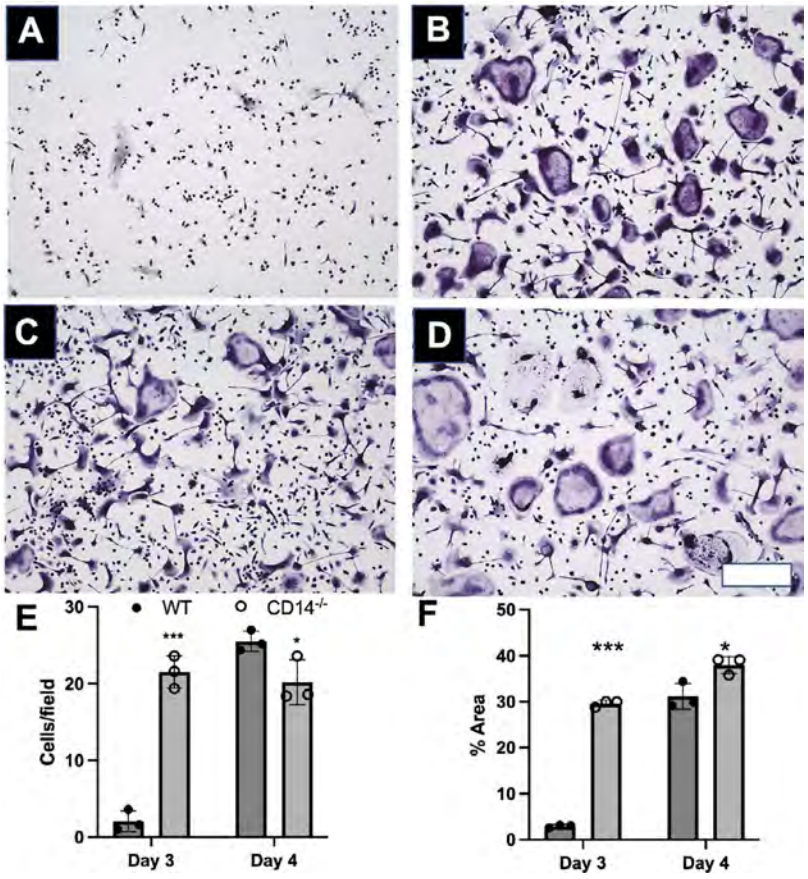


Figure 1: TRAP staining and quantification of osteoclasts at baseline: WT osteoclasts on days 3 and 4 (A,C) and CD14-/- (B,D) . Quantification of osteoclasts/field (E), % Area of frame of osteoclasts (F) *p<.05, ***p<.001 compared to WT. Scale bar 100 μM

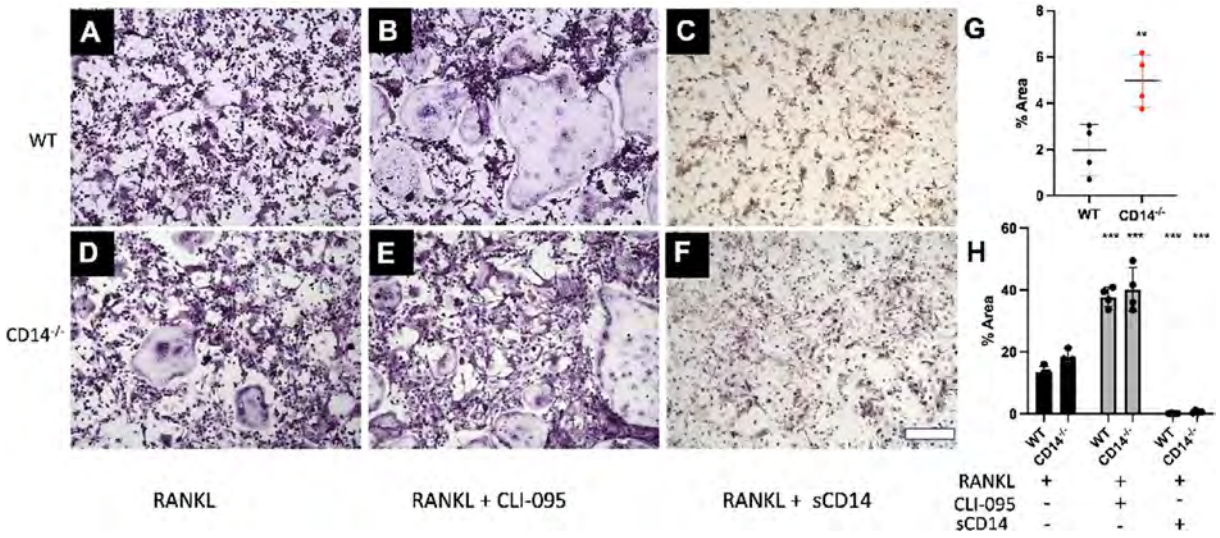


Figure 2: TRAP staining of Osteoclasts treated with TLR4 inhibitor and soluble CD14: Osteoclasts derived from WT (A,B,C) and CD14-deficient precursors (D,E,F) treated with RANKL, RANKL + CLI-095, and RANKL+ sCD14, respectively. Quantification of RANKL treatment at day 3 (G) and all treatments at day 4 (H).**p < .01 compared to WT, ***p < .001 compared to RANKL within mouse strain. Scale bar 100 μM

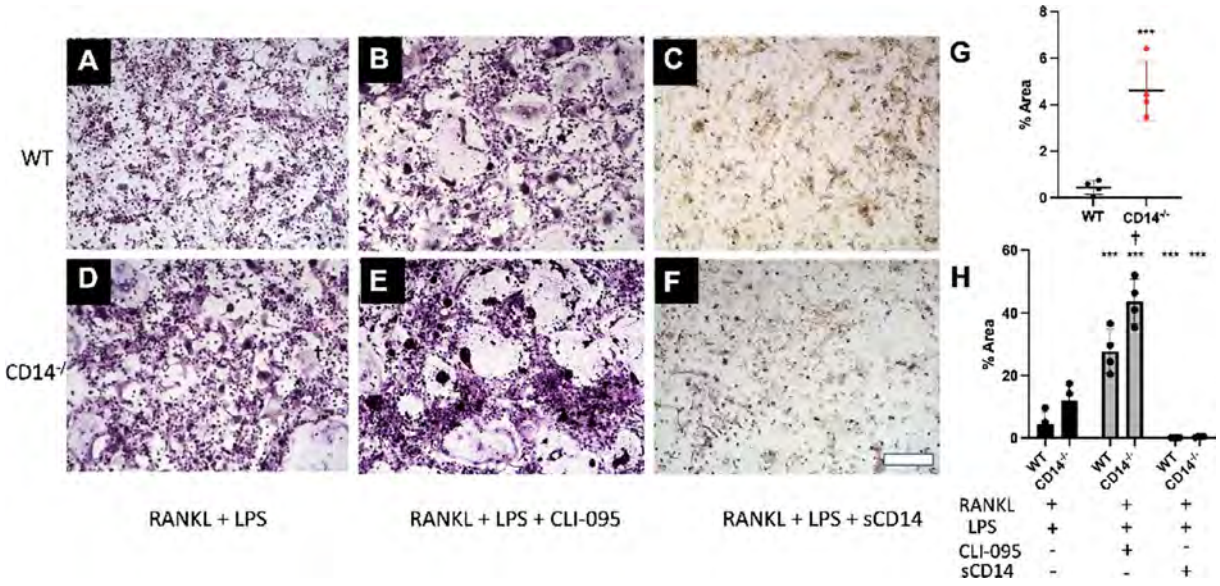


Figure 3: TRAP staining of osteoclasts treated with LPS: Osteoclasts derived from WT (A,B,C) and CD14-deficient cells (D,E,F) treated with RANKL + LPS, RANKL + LPS + CLI-095, and RANKL + LPS + sCD14, respectively. Quantification of RANKL + LPS treatment at day 3 (G, *** p < .001 compared to WT) and all treatments at day 4 (H). ***p < .001 compared to RANKL + LPS within mouse strain. † p<.001 compared to WT within treatment. Scale bar is 100 μM.

some inhibitory effects of LPS in WT, but had a synergistic effect on CD14-deficient cells (Fig 3H). The addition of sCD14 inhibited osteoclastogenesis in the CD14-deficient group, both with and without LPS.

Conclusion: Our results show that at baseline, CD14-deficient osteoclasts precursors differentiate more quickly than WT cells. **Further, during TLR4 stimulation studies, CD14-deficient cells were protected from LPS-TLR4 mediated inhibition of osteoclastogenesis, compared to WT cells.** Though mechanism of early differentiation remains unclear, with possible intervention of TLR-ligand production during differentiation, further work will investigate this production, and further effects of OA-relevant TLR ligands on osteoclastogenesis in the setting of CD14 deficiency or blockade.

Disclosure: L. Murphy: None; **K. Burt**: None; **B. Hu**: None; **V. Nguyen**: None; **R. Mauck**: None; **C. Scanzello**: N/A, 10.

Abstract Number: 0882

Activation of Ovarian Cancer G-Protein Coupled Receptor (OGR1) Attenuates Chondrocytes Inflammation via ERK1/2 Signaling Pathways in an in Vitro Model of Osteoarthritis

Omar Syed, Bhakti Patel, William Martin, Martha Diaz-Hernandez, Hicham Drissi and Mohd Nazir Khan, Emory University, Atlanta, GA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is the most prevalent joint disease, accounting for 50% of the musculoskeletal burden. Inflammation plays a crucial role in the development of OA and is often accompanied by synovial fluid acidosis and an acidic extracellular environment.As OA progresses, chondrocytes experience changes in osmolarity and acidity in their surrounding environment. However, the mechanism by which chondrocytes detect and respond to acidic stress is currently unknown. Recently, there has been growing interest in the role of proton-sensing GPCRs such as Ovarian Cancer G-Protein Coupled Receptor (OGR1 or GPR68) in musculoskeletal tissues. Nevertheless, the expression and function of OGR1 in cartilage during OA remain unexplored. This study aims to examine whether the OGR1 contributes to the regulation of inflammation during OA progression.

Methods: High throughput RNA-Seq data (GSE114007) in healthy donors and OA cartilage was analyzed to determine the role of proton-sensing orphan GPCRs during OA pathogenesis. Primary human OA chondrocytes were obtained from discarded cartilage of patients undergoing arthroplasty. siRNA mediated OGR1 knockdown was used to determine its role in inflammatory signaling in human chondrocytes. Activation of OGR1 was done by treating chondrocytes with Ogerin and activity was measured using Ca+ release and fluorescent based biosensor assay. Western immunoblotting was performed to analyze the expression at protein level. Statistical analyses were performed using one-way analysis of variation (ANOVA) with Tukey's post-hoc tests.

Results: Differential gene expression analysis of RNA-seq data identified OGR1 was highly expressed in human OA cartilage. Immunohistochemistry and qPCR further confirmed the expression of OGR1 in human OA cartilage and in chondrocytes treated with IL1β. Low density array analysis of OGR1 knockdown showed that silencing of OGR1 significantly induced the expression of various inflammatory cytokines and chemokines including IL6, NOS2, CSF2, CXCL6, CCL3, CXCL2. Interestingly, Ogerin mediated OGR1 activation in chondrocytes repressed the expression of these inflammatory genes suggesting the role of GPR68 in the regulation of inflammatory gene expression. Furthermore, MAPK inhibitors studies showed that inhibition of ERK and P38 MAPK pathways significantly reverse the effect of OGR1 knockdown on the induction of IL6 gene expression in IL1β stimulated OA chondrocytes. These data suggest the involvement of ERK1/2 and P38 MAPK signaling in OGR1 mediated regulation of inflammatory genes in chondrocytes during OA pathogenic conditions.

Conclusion: Our data suggest that OGR1 is highly expressed in human OA cartilage and regulates inflammatory gene expression via MAPK activation. Our results showed the involvement of OGR1 in the inflammatory pathways and highlights its potential as a therapeutic target for OA treatment. Exploring the mechanisms through which OGR1 influences the development of OA could offer novel perspectives and lead to the development of novel therapies that can modify the course of the disease for individuals with OA.

Disclosure: O. Syed: None; **B. Patel**: None; **W. Martin**: None; **M. Diaz-Hernandez**: None; **H. Drissi**: None; **M. Khan**: None.

Abstract Number: 0883

The Role of Plasmin and Fibrinolysis Pathways in Osteoarthritis

Qian Wang, heidi Wong, Audrey Bai, Zelda Love, Constance Chu and William Robinson, Stanford School of Medicine, Stanford, CA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is the major cause of joint failure. Increasing evidence suggests that activation of fibrinolysis is involved in the pathogenesis of OA. Here we used gene expression, proteomic, in vitro assays, and mouse models to further define the role of fibrinolysis in OA.

Methods: Gene expression in synovial membranes from individuals with early- or end-stage OA and healthy individuals were analyzed, and ELISA and immunohistochemistry on human OA synovium and cartilage samples performed. Genetic and pharmacologic studies were performed targeting plasmin, tPA, uPA in an OA mouse model. We performed MicroPET/CT imaging studies on mouse OA model to further define the role of uPA in OA pathogenesis.

Results: We identified dysregulated expression of plasmin and the plasmin activators tPA, uPA and uPA receptor uPAR in human OA joints. Pharmacologic blockade of plasmin attenuated the progression of OA in DMM mice, while genetic deficiency in plasmin activator inhibitor PAI-1 or injection of plasmin protein exacerbated OA in DMM mice. We detected increased uptake of uPA/uPAR in mouse OA joints by microPET/CT imaging. Further *in vitro* studies identified that plasmin

Figure 1. Key molecules in fibrinolysis pathways are dysregulated in human OA joints (A) Unsupervised hierarchical clustering of uPA and uPAR expression in microarray dataset on synovial membranes from healthy individuals (n=7) or those with early- (n=10) or end-stage OA (n=9). Scale bar indicates z score. (B) ELISA analysis of plasmin levels in knee joint synovial fluids from individuals with OA (n=6), ACL tear (n=8), DMT (n=3) and in the plasma from healthy individuals (n=8). (C, D) ELISA analysis of activated uPA (C) or uPAR (D) levels in synovial fluid of knee joints and serum from individuals with confirmed OA (n=10). (E) Representative images from immunohistochemical staining of tPA, uPA, uPAR, and isotype control in damaged knee cartilage (left) and synovium (right) of OA from individuals underwent total knee replacement. The arrowhead indicates positive staining for tPA, uPA, and uPAR. For panels B-D, data are the mean ± SEM of duplicates or triplicates and are representative of ≥2 independent experiments. *P < 0.05, **P < 0.01, and ***P < 0.001 by t test or one-way ANOVA. For panel E, scale bar, 200μm; cartilage and synovial tissues from n = 5 individuals were analyzed and the representative images were shown.

Figure 2. Genetic deficiency or pharmacological blockade of plasmin attenuates OA in mice (A) Representative cartilage degeneration in Safranin-O–stained sections of the medial region of stifle joints from plg+/+ (n=10) and plg-/- (n=5) male mice 20 weeks after DMM, and quantification of the cartilage degeneration. (B) Representative cartilage degeneration in Safranin-O–stained sections of the medial region of stifle joints from C57B/6J mice treated for 12 weeks with intra-articular injected plasmin (n=10) or PBS (n=10), and quantification of the cartilage degeneration. (C, D) Representative cartilage degeneration in Safranin-O–stained sections of the medial region of stifle joints from C57B/6J mice subjected to DMM and treated with intra-articular injection of anti-plasmin antibody (n=10), α2-macroglobulin (n=10), or PBS (n=10) (C), or with i.p. injection of tranexamic acid (n=6) or PBS (n=6) (D) for 12 weeks, and quantification of the cartilage degeneration. Arrowheads indicate areas of cartilage degeneration. Scale bars, 200μm. All data are the mean ± SEM of triplicates and are representative of three independent experiments. *P ≤ 0.05, **P ≤ 0.01 by t test or one-way ANOVA.

Figure 5. Another key fibrinolysis molecule uPA and its receptor uPAR also play critical roles in the pathogenesis of OA (A, B) Representative cartilage degeneration in Safranin-O–stained sections of the medial region of stifle joints from plau+/+ (n=10) and plau-/- (n=9) (A), and plaur+/+ (n=9) and plaur-/- (n=9) mice (B) 20 weeks after DMM, and quantification of the cartilage degeneration. Arrowheads indicate areas of cartilage degeneration. Scale bar, 200μm. (C, D) MicroPET/CT imaging of mouse knee joints 20 weeks after DMM or sham surgery, and quantification of relative 68Ga uptake levels in these joints (n=7). Mice were i.v. injected with 68Ga-NODAGA-AE105 (C), or 68Ga-NODAGA-AE105 plus unlabeled AE105 (D). (E, F) qPCR analysis of relative mRNA expression levels of OA-related inflammatory, degradative mediators as well as VEGFα in synovial tissues from plau+/+ (n=5) and plau-/- (n=5) mice (E) or plaur+/+ (n=5) and plaur-/- (n=5) mice (F) 20 weeks after DMM. Data are the mean ± SEM of duplicates or triplicates and are representative of ≥2 independent experiments. NS P > 0.05, *P ≤ 0.05, ** P ≤ 0.01, and *** P ≤ 0.001 by t test.

promotes OA development through multiple mechanisms including the degradation of lubricin and cartilage proteoglycans, activation of matrix metalloproteinases (pro-MMPs), and induction of inflammatory and degradative enzymes.

Conclusion: Our results demonstrate that fibrinolysis contributes to the development of OA through multiple mechanisms. We demonstrated that uPA and uPAR contribute to OA by activating the PI3K, PDK1, AKT, and ERK signaling cascades which mediate the production of inflammatory and degradative enzymes. Together, our results suggest that therapeutic targeting of the fibrinolysis pathways provides the potential to reduce development of OA.

Disclosure: Q. Wang: None; **h. Wong**: None; **A. Bai**: None; **Z. Love**: None; **C. Chu**: None; **W. Robinson**: None.

Abstract Number: 0884

Identification of a Mast Cell-high Synovial Pathotype of Osteoarthritis

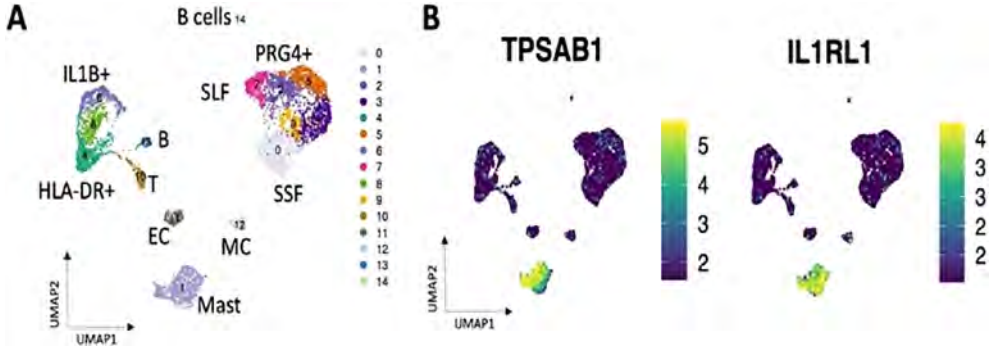
Shady Younis, Audrey Bai, heidi Wong, Zelda Love, Qian Wang and William Robinson, Stanford School of Medicine, Stanford, CA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Mast cells in the osteoarthritis (OA) synovium correlate with disease severity. This study aimed to further elucidate the role of mast cells in OA by RNA-Seq analysis and pharmacological blockade of the activity of histamine, a key mast cell mediator, in murine OA.

Methods: WeexaminedOA synovial tissues and fluids by flow cytometry, immunostaining, single-cell and bulk RNA-Seq, qPCR, and ELISA.Cetirizine,a histamine H1 receptor (H_1R) antagonist, was used to treat the destabilization of the medial meniscus (DMM) mouse model of OA.

Results: Flow cytometry and immunohistology analysis of OA synovial cells detected the frequencies of KIT^+ $Fc\varepsilon RI^+$ and $TPSAB1^+$ mast cells. Single-cell RNA-Seq of OA synovial cells identified the expression of prototypical mast cell markers *KIT, TPSAB1, CPA3* and *HDC*, as well as distinctive markers *HPGD, CAVIN2,IL1RL1*, *PRG2*, and *CKLF*, confirmed by bulk



Single cell RN-seq of OA synovial tissues. (A) Detection of major cell types present in OA synovial tissues including mast cells, synovial lining fibroblasts (SLF), synovial sub-lining fibroblasts (SSF), endothelial cells (EC) , muscle cells (MC), T B cells. (B) Mast cells expressing high level of TPSAB1 and IL1RL1 genes.

RNA-Seq and qPCR.A mast cell prototypical marker expression score classified 40 OA patients into three synovial pathotypes: mast cell-high, -medium, and -low. Additionally, we detected mast cell mediators including histamine, tryptase AB1, CPA3, PRG2, CAVIN2, and CKLF in OA synovial fluids. Elevated H_1R expression was detected in human OA synovium, and treatment of mice with the H_1 receptor antagonist cetirizine reduced the severity and OA-related mediators in DMM.

Conclusion: Based on differential expression of prototypical and distinct mast cell markers, human OA joints can be stratified into mast cell-high, -medium, and -low synovial tissue pathotypes. We further show that pharmacologic blockade of histamine activity reduces development of OA in mice, suggesting that targeting of the mast cell mediator histamine has the potential to provide benefit in subsets of OA in which mast cells contribute to pathogenesis.

Disclosure: S. Younis: None; **A. Bai**: None; **h. Wong**: None; **Z. Love**: None; **Q. Wang**: None; **W. Robinson**: None.

Abstract Number: 0885

Mice Fed a Well-formulated Ketogenic Diet After OA Induction Develop Worse OA Outcomes and Increased Pain Sensitivity

Montana Barrett[1], Gabby Dyson[2], Meeshal Khan[3], Nicholas Hanebutt[2], Cindy Miranda[2], Leoni Schlupp[2], Emmaline Holmlund[2] and **Matlock Jeffries**[2], [1]Oklahoma State University, Guthrie, OK, [2]Oklahoma Medical Research Foundation, Oklahoma City, OK, [3]University of Oklahoma Health Sciences Center, Oklahoma City, OK

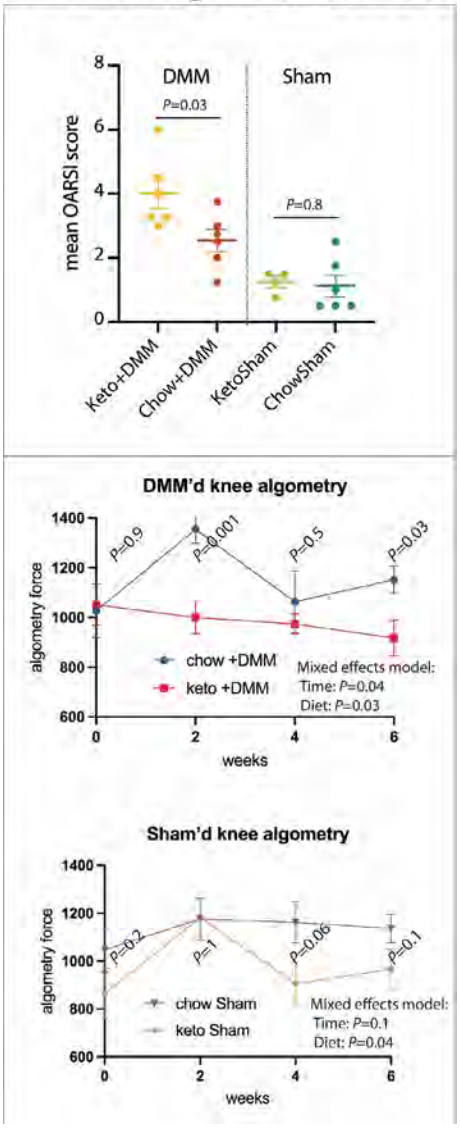
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: A ketogenic diet (KD) has beneficial effects in preclinical models of a variety of systemic autoimmune diseases. In this study, we set out to evaluate whether KD would alter OA outcomes in a commonly-used mouse model.

Methods: Adult male B6 mice (n=6 per group) had disruption of the medial meniscus (DMM) surgery performed on a unilateral knee joint, then were placed in clean cages and fed a standard chow diet or KD (carbohydrates replaced by plant-based oils including medium-chain triglycerides). A second set of mice were fed KD or chow and had sham DMM surgery performed. Pain sensitivity around the operated knee was tested by a handheld algometer at baseline, 2, 4, and 6 weeks after DMM and analyzed with a mixed-effects model. Eight weeks after DMM, mice were sacrificed, knee joints fixed, paraffin-embedded, stained with Safranin-O and histologically graded for OARSI score. Serum cytokines were evaluated with a Bioplex-pro 23 assay. Serum lipopolysaccharide (LPS) was determined by chromogenic assay. Gut microbiome analysis was performed via 16S sequencing.

Results: KD mice had worse histologic OA compared to chow diet mice (Figure 1) (OARSI score 4.0±1.8 mean±SEM vs. 2.5±0.4, P=0.03) despite losing weight on KD (final weight chow: 31±0.7 vs. 25±0.7g, P=2E-4). OARSI scoring was no different in sham mice (1.25±0.2 vs. 1.13±0.3, P=0.8); sham mice lost a similar amount of weight on KD (chow: 33 ±0.6 vs. 29±0.8, P=0.002). Pain sensitivity was similar at baseline in DMM mice (P=0.9) and sham mice (P=0.2); however, KD mice demonstrated increased pain sensitivity, evidenced by reduced algometry force-at-paw-withdrawal, in both DMM (mixed effects model P=0.03) and sham (mixed effects model P=0.04) (Figure 1). LPS was reduced in KD-DMM mice vs. to chow-DMM mice (P=0.04), but no different in KD-Sham mice vs. chow-Sham mice (P=0.1). Microbiome analysis demonstrated several significantly different clades between KD and chow diet. *Lactobacillus*, *Blautia*, and *Clostridium* were all

Figure 1: Histologic and pain sensitivity OA outcomes in ketogenic diet and chow diet



correlated with better histology and pain outcomes, whereas *Bacillales* and *Oscillospira* were correlated with worse histology and pain outcomes.

Conclusion: Initiation of a KD immediately after DMM induction in mice is associated with worse histologic and pain outcomes, findings which correlate with disruption of particular gut microbiome clades. Further research is needed to evaluate the effects of KD initiation prior to OA induction, as well as pathophysiological investigations into this observed phenotype.

Disclosure: M. Barrett: None; **G. Dyson**: None; **M. Khan**: None; **N. Hanebutt**: None; **C. Miranda**: None; **L. Schlupp**: None; **E. Holmlund**: None; **M. Jeffries**: None.

Abstract Number: 0886

Neonatal Roseolovirus Infection Predisposes to Development of Lupus-like Disease After TLR7 Stimulation

Tarin Bigley[1], Eden Xue[1], Lifei Zhu[1], Li-ping Yang[1] and wayne Yokoyama[2], [1]Washington University in St. Louis, St. Louis, MO, [2]Washington University School of Medicine, St. Louis, MO

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Viral infections have been implicated as major factors in autoimmune disease but demonstrating causality is often challenging. We found that neonatal infection with a roseolovirus (murine roseolovirus, MRV) resulted in transient thymic atrophy, CD4+ T cell depletion, and disruption of central tolerance. Although mice recovered from infection, we observed durable immune dysregulation manifested as autoimmune gastritis and a broad repertoire of autoantibodies. In these studies, we found that additional immune stimulation resulted in systemic autoimmunity.

Methods: We developed a mouse model in which neonatally infected C57BL/6 mice were treated with a toll-like receptor 7 (TLR7) agonist as adults to induce a lupus-like phenotype. Histology, immunofluorescence, ELISA, transcription analysis as well as flow cytometry were used to characterize disease and evaluate immune dysregulation. We used depletion and adoptive transfer experiments to identify the contribution of specific cell types to disease.

Results: We found that MRV replication during the first seven days of life induced a loss of central tolerance and development of autoimmune gastritis and autoantibodies, including those typically associated with autoimmune connective tissue disease. Interestingly, treatment with a TLR7 agonist induced a systemic autoimmune disease with characteristics observed in systemic lupus erythematosus, including splenomegaly, cytopenia, positive ANA, and multi-organ system inflammation in mice. In C57BL/6 mice, this lupus-like disease was only observed after neonatal MRV infection. Although a feature of MRV-induced lupus-like disease was significant thymic disruption, we did not observe MRV reactivation after TLR7 stimulation. We also observed major changes in the phenotype of T and B cells in the blood and spleen, suggesting a shift in the number and activation of different subsets. Moreover, we found that T and B cells play different roles in development of disease.

Conclusion: We have shown that MRV induces autoimmune after neonatal infection in a murine system. Moreover, our data suggest that neonatal MRV infection not only induces mild, organ-specific autoimmunity, but also results in durable immune dysregulation and predisposition to severe systemic autoimmunity after additional immune stimulation.

Disclosure: T. Bigley: None; **E. Xue**: None; **L. Zhu**: None; **L. Yang**: None; **w. Yokoyama**: None.

Abstract Number: 0887

Dapagliflozin Modulates Inflammation and Germinal Centers in Lupus by Increasing Regulatory T Cells

Javier Rangel-Moreno[1], Maria de la Luz Garcia-Hernandez[2], Mary O'Connell[3], Daria Krenitsky[4], Maria Fernanda Ossa-Echeverri[1], Mark Lusco[5], John Looney[6] and Jennifer Anolik[3], [1]University of Rochester, Rochester, NY, [2]University of Rochester, West Henrietta, NY, [3]University of Rochester Medical Center, Rochester, NY, [4]Division of Allergy, Immunology

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Nephritis is one of the most severe manifestations of lupus, affecting 40-70% of patients. Though immune-targeted therapies have improved, a significant number of patients experience renal damage and even progression to end-stage renal disease (ESRD). Recently, sodium and glucose cotransporter 2 inhibitors (SGLT2i) have proven efficacious in preventing adverse renal outcomes in patients with a variety of chronic diseases. The mechanisms of protection by SGLT2i include their capacity to modulate hypoxia and fibrosis. Other literature supports the role of local hypoxia in the lupus nephritis (LN) kidney in driving pathogenic immune cell function, including in CD8 T cells. Here, we hypothesized that by alleviating hypoxia, SGLT2i will modulate local inflammation and fibrosis in LN.

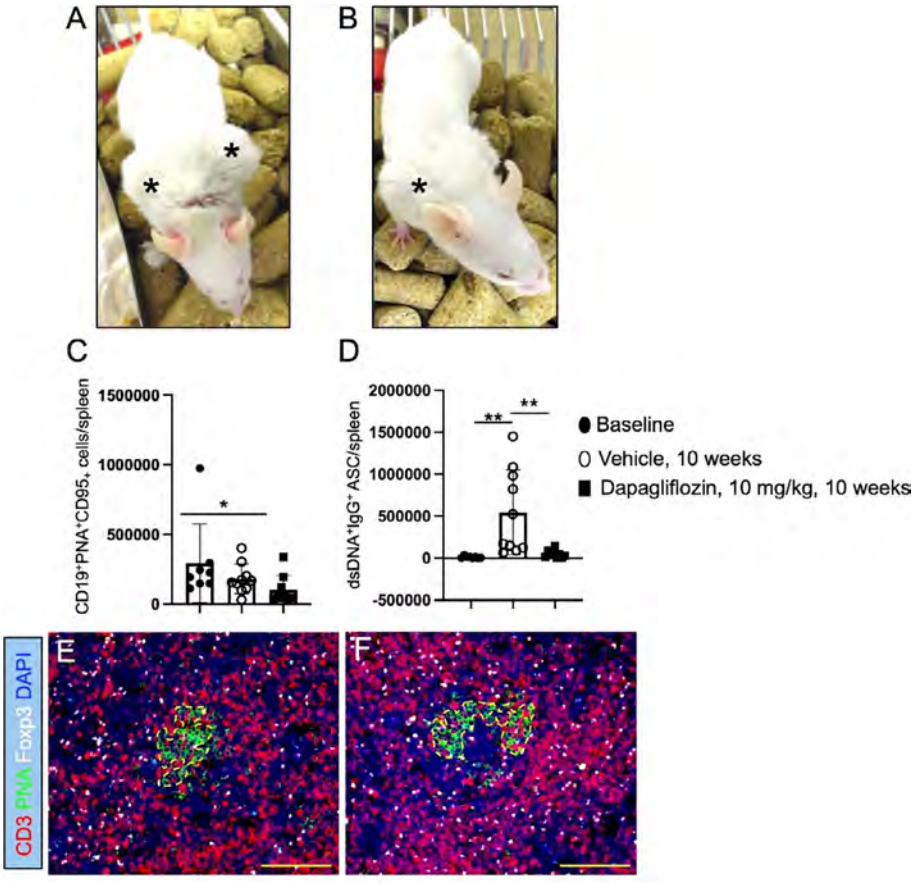

Figure 1. Immunomodulatory effects of dapagliflozin on lupus prone mice. 10 weeks old MRL/lpr female mice were daily treated for 10 weeks with dapagliflozin at 10 mg/kg by gavage or received same volume of vehicle. A) MRL/lpr female mice receiving vehicle show increased inflammation in peripheral lymph nodes, compared to B) aged matched MRL/lpr mice treated with dapagliflozin. Asterix point to inflamed peripheral lymph nodes (LNs). C) Germinal center B cells were decreased in the spleen of MRL/lpr female mice treated with dapagliflozin for 11 weeks. D) Production of autoreactive dsDNA antibody-secreting cells (ASC) in the spleen was significantly reduced by dapagliflozin therapy. E) T follicular regulatory T cells (TFHregs) were less numerous in the germinal centers (GCs) and contiguous areas in the LNs of control mice, compared to F) the significant accumulation of TFHregs in GCs of dapagliflozin-treated mice. 200x magnification pictures. Scale bars = 100 μm. n = 8-10 mice/group. Unpaired t test, Mann Whitney test: *, $p \leq 0.05$, **, $p \leq 0.005$.

Methods: Ten weeks old MRL/lpr female mice were treated daily with dapagliflozin at 10 mg/kg or vehicle by gavage for 11 weeks. Sera was collected to measure autoantibodies and creatinine by ELISA. Immune cells and Sodium and Glucose Co-Transporter 2 (SGLT2) expression were quantitated in the spleen, lymph nodes (LNs) and kidneys by flow cytometry and immunofluorescence. Inflammation, fibrosis, and infiltration by CD8 T cells or regulatory T cells were assessed in the kidneys of MRL/lpr mice at baseline and 11 weeks after starting SGLT2i therapy.

Results: Consistent with a slow induction of SGLT2i therapeutic effect in humans and despite the efficient targeting of SGLT2 in MRL/lpr mice, proteinuria was not affected after 11 weeks of daily SGLT2i administration. Unexpectedly SGLT2i therapy had a remarkable impact on the formation of germinal centers (GCs) (vehicle vs. dapagliflozin: *, $p = 0.0205$) and the production of autoreactive plasma cells in the spleen (vehicle vs. dapagliflozin: **, $p = 0.009$). In line with the induction of regulatory T cells by SGLT2i in diabetic kidney disease, T follicular helper cells with a regulatory phenotype significantly increased in the GCs of mice treated with dapagliflozin (vehicle vs. dapagliflozin: **, $p = 0.003$). In addition, skin and lymph node inflammation were attenuated by SGLT2i. However, inflammatory cell infiltration in the kidney was not affected by SGLT2i.

Conclusion: Despite modest effects on kidney inflammation, SGLT2i surprisingly modulated splenic autoreactive GCs via significant accumulation of T follicular regulatory T cells, impairing the production of autoreactive plasma cells. One of the potential explanations for the modest kidney effects is the rapid disease progression in MRL/lpr mice and the slow therapeutic induction with SGLT2i. Thus, future studies are planned in NZB/NZW mice treated for longer periods of time and with combined immune suppressive therapy.

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Abstract Number: 0888

Functionally Selective Immunomodulator Shows Robust Efficacy in Spontaneous Lupus Mouse Model

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex, heterogeneous autoimmune disease. There is still a high unmet need to improve current treatment options. Type 1 interferon (IFN) has recently been validated as clinical target for SLE.

CXCR4 antagonist IT1t has shown to selectively induce an immunomodulating profile through downmodulation of IFN-α release by plasmacytoid dendritic cells (pDCs)[1]. Functionally selective immunomodulators derived from IT1t, with low/no CXCR4 antagonism and increased immunomodulating activity, not limited to the control of type 1 IFN, have been discovered and may represent a novel therapeutic approach for interferonopathies, like SLE.

In vivo efficacy of one representative compound, ER000145 was evaluated in (NZB x NZW) F1 mice. This spontaneous lupus mouse model is sharing several pathophysiological features of human SLE, with clear kidney development starting around 22 weeks of age.

Methods: As of 24 weeks of age female (NZB x NZW) F1 mice received daily intraperitoneal (ip) administrations of ER000145 at either 3, 10 or 30 mg/kg for 16 weeks. Cyclophosphamide was administered once a week at 50 mg/kg ip as positive control. Body weight was recorded twice per week and proteinuria were measured weekly up to week 40 of age. At week 40 of age, kidney function readouts were performed by assessing the levels of blood urea nitrogen (BUN) and creatinine. At week 24, 34 and 40 of age, anti-dsDNA antibody titers were evaluated by ELISA. After 16 weeks of treatment, mice were sacrificed and cytokine levels were determined in serum using ELISA. Furthermore, kidneys were prepared for histopathological scoring using hematoxylin and eosin (H&E) staining for assessment of nephritis. In addition, spleen and bone pathology was performed to assess potential for immunosuppression using haematological and histological endpoints.

Results: Daily treatment of mice for 16 weeks with ER000145 did not show compound-induced body weight loss. Significant dose-dependent decreases in proteinuria, BUN levels and anti-ds DNA antibody titers were shown at week 40 of age for the 10 mg/kg and 30 mg/kg ER000145 treatment groups versus the vehicle control group. Despite overall low systemic cytokine levels, a reduction of serum TNF-α and IL-6 was observed for mice treated with ER000145. Histopathological analysis of the kidney confirmed a significant dose-dependent reduction of glomerular and tubular scores upon ER000145 treatment versus the vehicle control group at week 40 of age, confirming the inhibition of nephritis development. Haematology and histopathology of lymphoid organs showed no overt cell atypia nor cell depletion, a histological profile consistent with an absence of immunosuppression as opposed to the cyclophosphamide-treated group.

Conclusion: ER000145 showed robust and dose-dependent efficacy upon once daily ip treatment for 16 weeks in (NZB x NZW) F1 lupus-prone mice. No signs of immunosuppression were detected.

Based on these promising efficacy data obtained in vivo with ER000145, orally available functionally selective immunomodulators are currently being developed as a potentially novel and innovative treatment option for SLE.

1 Smith et al. Sci Adv. 2019 ;5(7)eaav9019

Disclosure: H. ASNAGLI: Ermium Therapeutics, 3; **S. TESSIER**: Ermium Therapeutics, 3; **M. FOSTER**: Citryll BV, 2, Ermium Therapeutics, 2; **S. DENIES**: Ermium Therapeutics, 2; **E. HOEBEN**: Ermium Therapeutics, 2; **J. CROUZET**: Ermium Therapeutics, 4; **A. VAN DER AA**: Ermium Therapeutics, 4.

Abstract Number: 0889

Axl Receptor Tyrosine Kinase Ameliorates Pristane Induced Diffuse Alveolar Hemorrhage in Mice by Regulating Macrophage Polarization

Wenwen Pei[1], Ranran Yao[1], Ziye Wang[2], Ruyu Liang[3], Renge Liang[2], Xiaolin Sun[4] and Yin Su[2], [1]Peking University, Beijing, China, [2]Peking University People's Hospital, Beijing, China, [3]Peking University, XiCheng, China, [4]Peking University People's Hospital, Beijing, China

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Diffusealveolar hemorrhage (DAH) is an infrequent but life-threatening complication in patients with systemic lupus erythematosus (SLE). Cells of the monocyte/macrophage lineage are essential to the pathogenesis of lung hemorrhage.An increasing number of research proved that Axl receptor tyrosine kinase(AxlTK)was especially highly expressed in macrophages. In this study, we explore whether AxlTK affects pathogenesis in DAH mice model by regulating macrophage polarization.

Methods: Bone marrow cells were obtained from femurs and tibias of Axl KO and WT Mice. Bone marrow-derived macrophages (BMDMs) were stimulated with 50ng/ml LPS and 20 ng/ml IFN-γ to promote M1 polarization, or 50ng/ml IL-4 to induce M2 polarization, respectively. Then, macrophages were examined by flow cytometry (FCM). At 8-10 weeks of age, wild type (WT) and Axl KO mice received a single intraperitoneal injection of 1 ml of pristane. After 14 daysof incubation, lung tissues were harvested and stained with H&E. And single-cell suspensions from lungs tissues were stained with the corresponding Ab mixtures for marking M1 and M2 macrophages. Cells were analyzed using a flow cytometry system.

Results: The expression of iNOS(M1 marker)and CD206(M2 marker) on BMDMs were significantly decreased in Axl KO compared to WT mice, respectivety. Significantly, lungs tissues from Axl KO mice with no or partial or complete hemorrhage, whereas those from WT mice showedpartial or complete hemorrhage in pristane-induced DAH micemodel. Mechanically, the expression of iNOS on macrophges in lungs tissues of Axl KO mice also showed a significantly decreased, while the expression of CD206 were slightly increased as compared to WT mice.

Conclusion: AxlTK may promotes macrophage polarization towards M1 and M2and ameliorates pristane induced diffuse alveolar hemorrhage in mice.

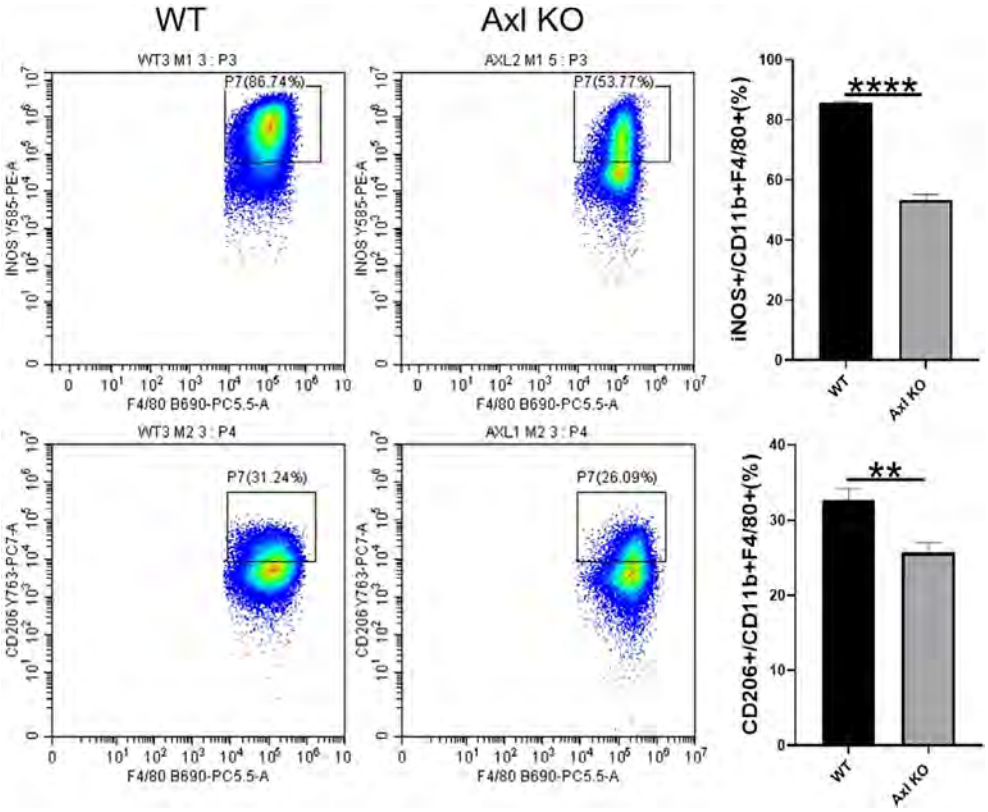


Figure1 BMDMs from WT and Axl KO mice were induced M1 and M2

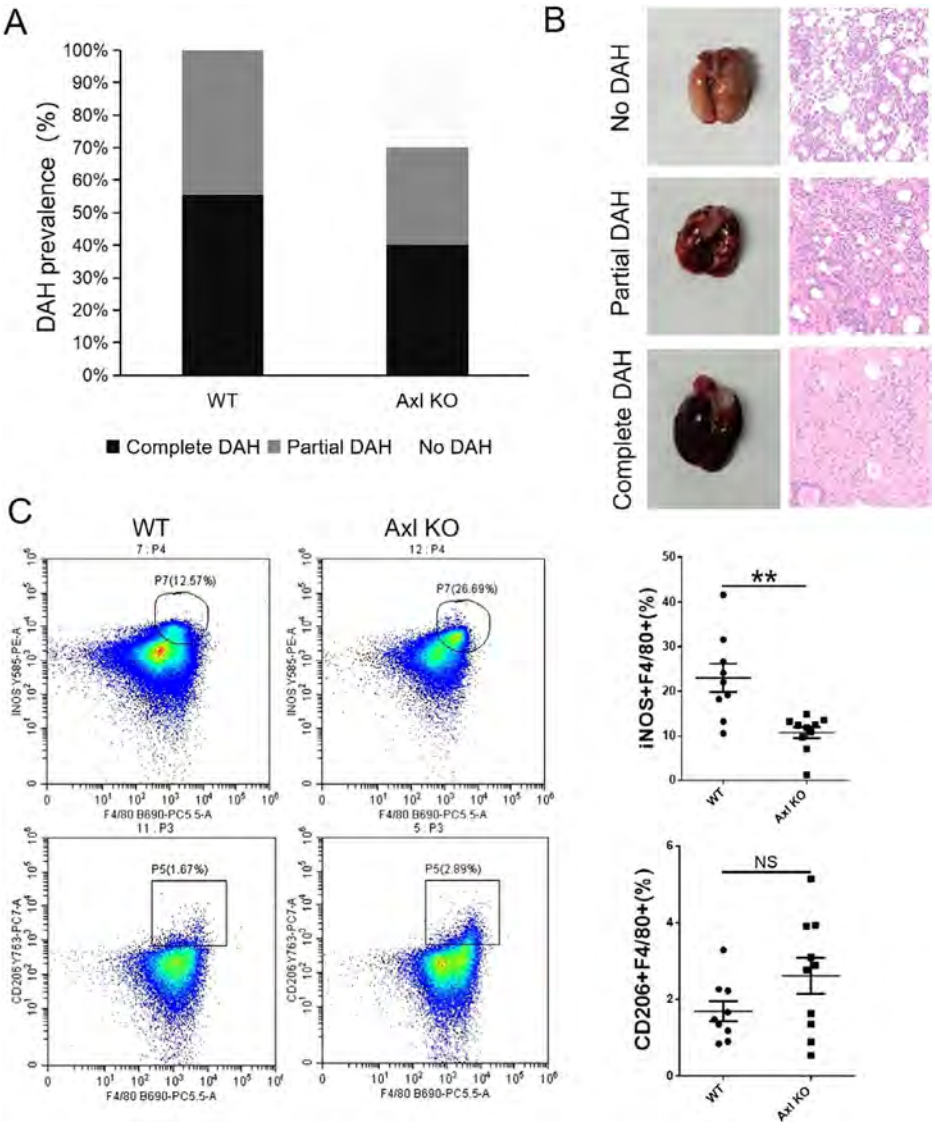


Figure2 Axl KO mice were prevented pristane induced diffuse alveolar hemorrage

Disclosure: W. Pei: None; **R. Yao**: None; **Z. Wang**: None; **R. Liang**: None; **R. Liang**: None; **X. Sun**: None; **Y. Su**: None.

Abstract Number: 0890

Specificity of Brain-Intrinsic and Hematopoietic-Derived Mechanisms in Mediating Neuropsychiatric Symptoms of Systemic Lupus Erythematosus

Hadijat Makinde, Yidan Wang, Stumpf Cecilia and **Carla Cuda**, Northwestern University, Chicago, IL

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disease that affects multiple end organs including the brain. Despite a prevalence of over 50% in SLE patients depending on the attribution model, neuropsychiatric symptoms of SLE (NPSLE) are among the least understood complications. Notwithstanding the paucity of data examining underlying mechanisms, accumulating evidence points to microglia, a brain-resident innate immune cell population, as a driver of disease. Our group was the first to show that microglial expression of disease-associated genes correlates with the severity of behavioral deficits in a NPSLE model prior to overt systemic disease. Previous data suggest NPSLE-like disease persists in bone marrow (BM) chimeric $MRL^{lpr/lpr}$ mice (MRL BM $MRL^{lpr/lpr}$) despite mitigation of systemic disease, suggesting a brain-intrinsic mechanism. However, these findings do not negate the contribution of circulating mediators of SLE-like disease at subclinical levels (antibodies, proteins, immune cells) to brain dysfunction. Indeed, the reciprocal chimera ($MRL^{lpr/lpr}$ BM MRL) was not evaluated. Further, radiation impacts microglial function and recipient mice from this study were not head-shielded.

Methods: Young female CD45.1 (Jackson 033076) and SLE-prone B6.*Sle1Sle2Sle3* (B6.TC; Jackson 007228) mice were used to generate head-shielded reciprocal BM chimeric mice with busulfan treatment to clear remaining BM (CD45.1 BM CD45.1; B6.TC BM CD45.1; CD45.1 BM B6.TC; B6.TC BM B6.TC). Mice underwent a behavioral tasks and PET imaging of activated microglia 10 weeks post-transfer. Perfused brains were extracted, meninges were removed and live $CD45^+$ cells were FACSorted from pooled cell suspensions (n=3/group to account for biological variability) for cellular indexing of transcriptomes and epitopes by sequencing (CITE-seq; 10X Genomics 3' v3.1).

Results: Introduction of B6.TC BM into CD45.1 hosts yields 95% reconstitution and induces systemic inflammation indicative of SLE-like disease. Conversely, B6.TC hosts receiving CD45.1 BM showed a trend towards dampened SLE-like disease resulting from only 50% reconstitution. Optimization (increased busulfan, transfer of double CD45.1 BM cells) was unsuccessful following head-shielded irradiation of B6.TC mice, suggesting that the minor fraction of B6.TC host-derived progenitors remaining will still outcompete CD45.1 donor progenitors. Similar to NPSLE patients, B6.TC mice exhibit heightened anxiety. Anxiety persists in chimeric mice of B6.TC, but not CD45.1, host origin, suggesting that brain-intrinsic defects in B6.TC mice are required for this behavior. However, impaired motor learning in B6.TC mice is recapitulated by both brain-intrinsic and hematopoietic-derived defects in B6.TC mice. Analysis of PET tracer uptake and CITE-seq data are pending and will provide critical insight into the activation status of microglia and other immune cell subsets.

Conclusion: We find that NPSLE manifestations diverge in mechanistic origin within the same organism. Further understanding this specificity of brain-intrinsic and/or hematopoietic-derived mechanisms mediating NPSLE will be critical for developing treatment strategies.

Disclosure: H. Makinde: None; **Y. Wang**: None; **S. Cecilia**: None; **C. Cuda**: None.

Abstract Number: 0891

Selective and Potent Inhibition of Cyclic GMP-AMP Synthase (cGAS) Fully Normalizes Autoinflammation Across Tissues in a Trex1-/- Mouse Model for Type I Interferonopathies

Arnaud Bourin[1], Zuzana Hořejší[2], Isabelle Cambré[1], Juraj Dobiaš[2], Mikhail Klychnikov[2], Radek Liboska[2], Maroš Smolíček[2], Zdeněk Vavřina[2], Wanda Haeck[1], Hugo Klaassen[1], Marnik Nijs[1], Kristine Metzger[1], Sandro Boland[1], Dries De Clercq[1], Sara Allasia[1], Gunter Carlens[1], Patrick Chaltin[3], Arnaud Marchand[1], Ondřej Páv[2], **Matthias Versele**[1] and Gabriel Birkuš[2], [1]Centre for Drug Design and Discovery (CD3) - Cistim, Leuven, Belgium, [2]Institute of Organic Chemistry and Biochemistry, Prague, Czech Republic, [3]Centre for Drug Design and Discovery (CD3) - KU Leuven, Leuven, Belgium

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The cGAS enzyme is a sensor of cytosolic double-strand (ds) DNA. It serves to detect viruses and elicits an acute, transient cGAMP-STING mediated type I interferon (IFN) response as part of anti-viral immunity. Recently, evidence has accumulated pointing to chronic stimulation of cGAS through endogenous (self) cytosolic dsDNA in the context of a wide variety diseases associated with a type I IFN signature. Clear examples of such auto-inflammatory diseases include Aicardi-Goutières Syndrome (AGS) and Systemic Lupus Erythematosus (SLE), which can harbour loss-of-function mutations in the gene encoding a 3' repair exonuclease, TREX1, which functions to prevent accumulation of cytosolic dsDNA. Indeed, mice deficient for Trex1 exhibit severe chronic systemic inflammation, which can be completely reversed by concomitant deletion of cGAS or STING. Other diseases associated with strong activation of cGAS include, among others, dermatomyositis, age-related macular degeneration, and Parkinson's disease (PD).

Methods: We report on the discovery and optimization of a novel series of small-molecule inhibitors of cGAS. The molecular binding mode is supported by crystallography, direct binding assays and multiple enzymatic assay formats. Compounds are assessed across different cellular contexts (including monocytes, microglia and retinal epithelial cells) using distinct sources of dsDNA as a stimulus. Lead compounds are prioritized based on DMPK (Drug Metabolism and Pharmacokinetics) properties, including distribution to the brain in mice. Mouse models have been used to prioritize compounds based on the ability to suppress acute HSV-mediated cGAS activation and chronic systemic autoimmunity (in Trex1-/- mice).

Results: Best compounds in the series have low nM potency in enzymatic assays using either mouse or human cGAS. No cross-reactivity with other enzymes that also use ATP or GTP as substrates were detected. Unlike many previously reported cGAS inhibitors, our compounds exhibit potent inhibition of cGAMP production and IFN response in cells, either stimulated with an exogenous source of dsDNA or mimicking a pathologic chronic stimulation of the pathway (e.g. using TREX1 deficient monocytes). Likewise, examples of the series display potent inhibition of microglia activation using alpha synuclein fibrils. The orally bioavailable lead compound, which displayed robust brain distribution, showed dose-dependent inhibition of autoimmunity across tissue types (PBMCs, kidney, lungs, heart and brain) in Trex1-/- mice and was significantly superior to the previously reported STING inhibitor, H151. In most cases, inflammation markers were restored to levels of WT mice within 2 weeks of dosing our cGAS inhibitor to Trex1-/- mice.

Conclusion: We discovered novel cGAS inhibitors and demonstrated their potential in preclinical models as therapeutics to treat peripheral auto-immune diseases such as AGS and SLE, and neurodegenerative diseases associated with a strong neuro-inflammation component such as PD.

Disclosure: A. Bourin: None; **Z. Hořejší**: None; **I. Cambré**: None; **J. Dobiaš**: None; **M. Klychnikov**: None; **R. Liboska**: None; **M. Smolíček**: None; **Z. Vavřina**: None; **W. Haeck**: None; **H. Klaassen**: None; **M. Nijs**: None; **K. Metzger**: None; **S. Boland**: None; **D. De Clercq**: None; **S. Allasia**: None; **G. Carlens**: None; **P. Chaltin**: None; **A. Marchand**: None; **O. Páv**: None; **M. Versele**: None; **G. Birkuš**: None.

Abstract Number: 0892

Single-Cell RNA Sequencing Reveals Keratinocytes and Fibroblasts Drive Hippo and TGFb Dysregulation and Fibrosis in Epidermal Overexpression of VGLL3 in Cutaneous Lupus

Mehrnaz Gharaee-Kermani[1], Allison Billi[1], Jacob Martens[1], Marisa Hildebrandt[1], Amanda Victory[1], Mitra Maz[2], Shannon Loftus[1], J. Michelle Kahlenberg[1] and Johann E. Gudjonsson[1], [1]University of Michigan, Ann Arbor, MI, [2]University of Michigan Medical School, Ann Arbor, MI

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Fibrosis is characterized by collagen deposition, fibro/myofibroblast (MYOFB) accumulation, and extracellular matrix remodeling. In some subtypes of cutaneous lupus erythematosus (CLE), particularly discoid lupus erythematosus (DLE) scarring alopecia and fibrotic lesional resolution may be widespread with no effective treatment. However, mechanisms of scar formation in CLE are not understood. We have shown that epidermal-directed overexpression of murine Vgll3 causes fibrotic-appearing skin lesions suggestive of CLE, and thus, we aimed to explore the role of Vgll3 in cutaneous fibrosis.

Methods: 2–3-month-old male and female transgenic (TG) mice overexpressing *Vgll3* in the epidermis under the K5 promoter were compared to wildtype (WT) C57Bl/6 mice (n=3-5 per group). Fibrotic biomarkers of human DLE and scleroderma were compared via immunohistochemistry. In addition, single-cell-RNA-sequencing (scRNA-seq) via 10x platform of lesional and nonlesional skin was completed to investigate the transcriptomes of the potential cellular fibrotic players. Several subclusters of fibroblasts (FBs), MYOFBs, and T cells were identified and fibrotic markers for each FBs subcluster were analyzed in lesional and non-lesional skin.

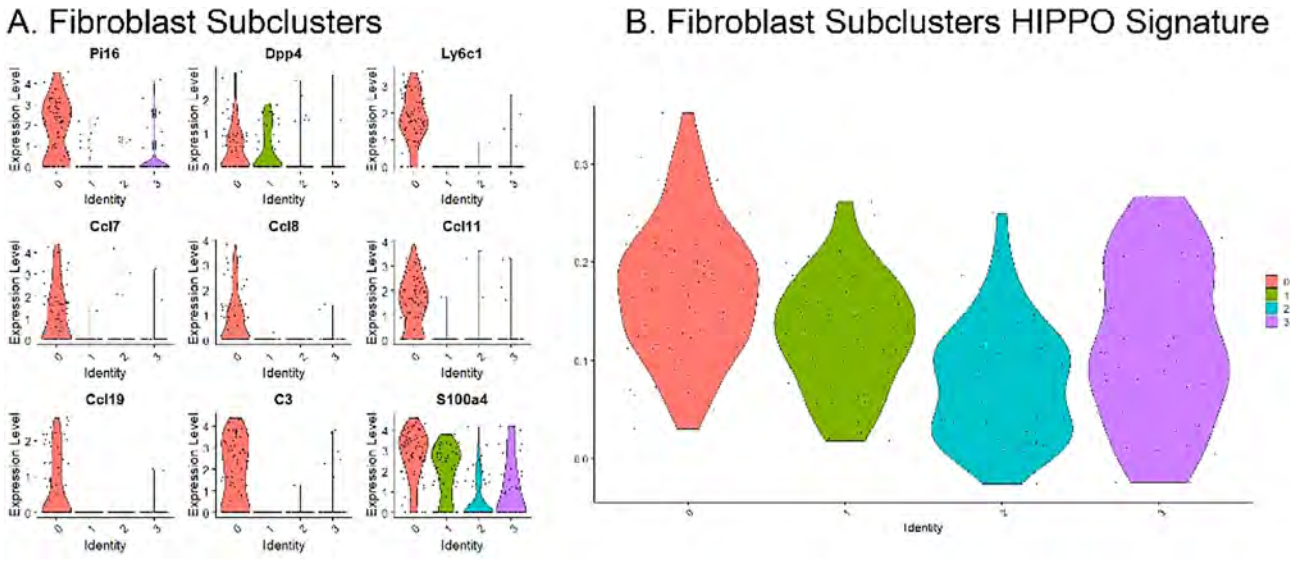


Fig. 1 Single-cell RNA-sequencing identified a fibroblast subcluster and Hippo signature. A) Lesional Vgll3 TG specific-fibroblasts (FB) subcluster (subcluster 0) express Pi16+ adventitial FB phenotype and express chemokines uniquely. This subcluster Pi16+ adventitial FB (disease FB) is unique to lesional Vgll3 TG skin which express chemokines (CCL7, CCL8, CCL11, CCL19) and exhibit higher MHC class I pathway genes. B) Cluster 0 has highest HIPPO Signature.

Results: 2–3-month-old male and female transgenic (TG) K5-Vgll3 exhibit cutaneous inflammation and fibrosis as evidenced by trichrome staining. TG lesional skin demonstrated a significant increase in fibrotic markers (*Acta2, Col1a1, Col1a2, Tgfb1, Ctgf)* and pro-fibrotic cytokines (*Il4, Il13*) also found in human DLE and scleroderma lesions compared to non-lesional skin. ScRNA-seq of lesional and nonlesional skin from TG vs WT skin showed increased inflammatory infiltrate in lesional TG greater than nonlesional TG, and nonlesional TG, higher than WT skin, which was verified by immunohistochemistry. Increased myeloid cells in lesional TG was higher than nonlesional TG and WT skin. Increased inflammatory gene expression (*Nfkb1, Cxcr4, Cxcl2, Il1b, Tnf, Cd14*), and CD4+ T cells in lesional TG skin exhibited greater *Foxp3, Gata3,* and *Tgfb1* expression than nonlesional TG and WT skin**.** Additionally, lesional TG skin exhibited higher expression of *Tgfb1,Col1a1,* and *Col1a2* compared to nonlesional TG and WT mouse skin (transcript and protein). Further, we identified a FB subcluster unique to lesional TG skin representing adventitial Pi16+ FB which expressed chemokines (*Ccl7, Ccl8, Ccl11, Ccl19*) and exhibited higher MHC class I pathway genes **(Fig.1.A)** and a higher Hippo signature **(Fig.1.B).** Finally,

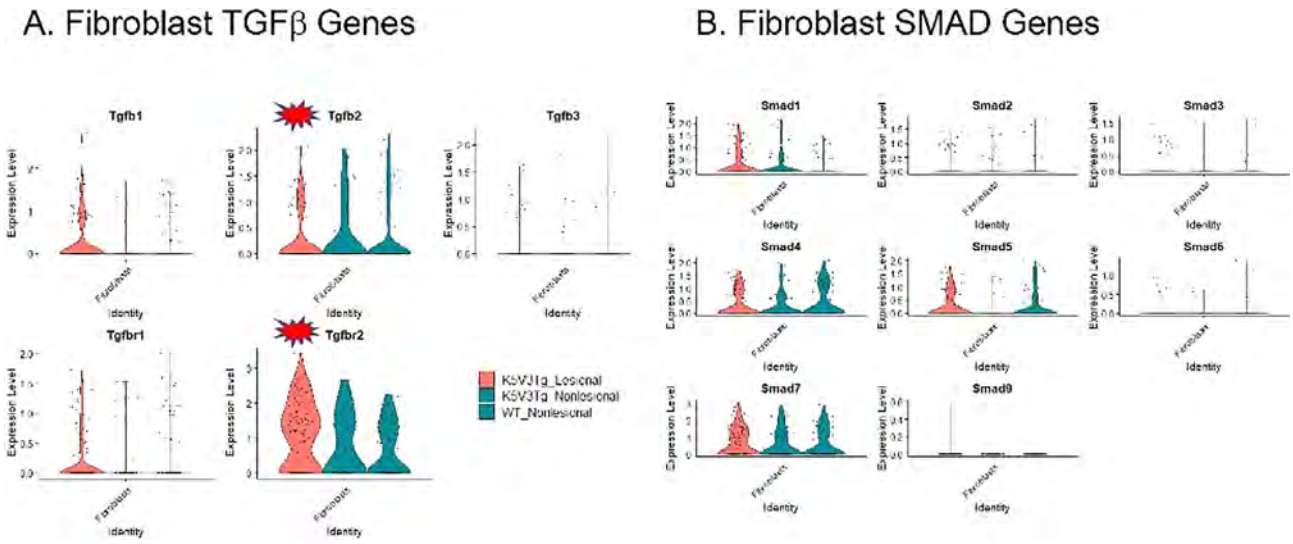


Fig.2 Single-cell RNA sequencing shows Tgfb gene expression and Smad gene expression in fibroblasts. A) Lesional Vgll3 TG Fibroblast have higher Tgfb2 and Tgfbr2 expression compared to nonlesional or wild type (WT). B) Lesional Vgll3 TG fibroblasts have higher Smads 1, 3, 4, and 5 gene expression compared to nonlesional or wild type (WT).

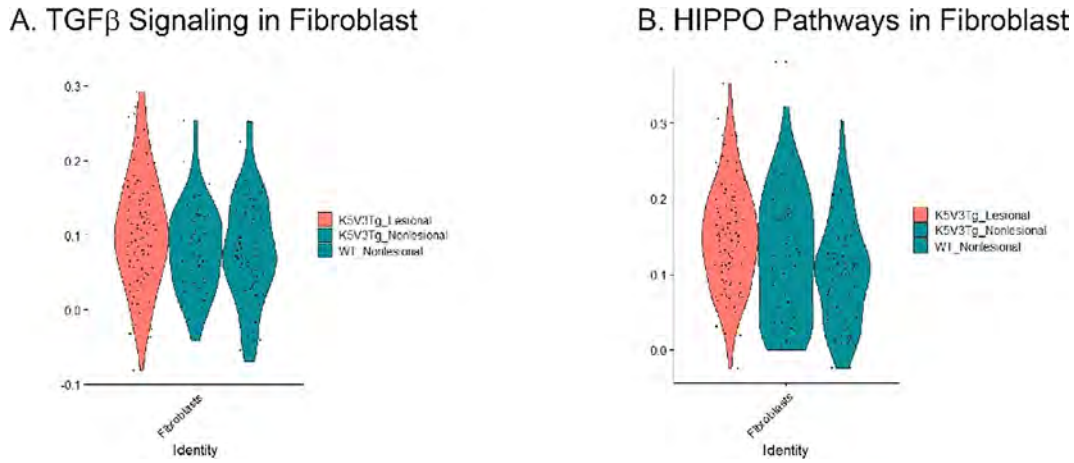


Fig.3 Single-cell RNA sequencing shows Hippo and Tgfb signaling in fibroblasts. A) Lesional Vgll3 TG fibroblasts have higher TGFb signaling score compared to nonlesional. B) Lesional Vgll3 TG fibroblast have higher HIPPO pathways score compared to nonlesional.

increased expression of Hippo and TGFβ pathway-regulated genes in FBs **(Figs.2-3),** and keratinocytes from lesional and nonlesional TG skin was seen, suggesting Hippo target dysregulation is an early event in fibrosis driven by epidermal Vgll3 that may drive pathologic myofibroblasts differentiation.

Conclusion: Overall, we have linked Vgll3-driven dysregulation of the Hippo and TGFβ pathways to fibrotic phenotypes, which may provide a critical novel target for the alleviation of disfiguring fibrosis in CLE.

Disclosure: M. Gharaee-Kermani: Rome Therapeutics, 5; **A. Billi**: None; **J. Martens**: None; **M. Hildebrandt**: None; **A. Victory**: None; **M. Maz**: None; **S. Loftus**: None; **J. Kahlenberg**: AstraZeneca, 1, Bristol-Myers Squibb(BMS), 2, 5, EMD Serano, 2, exo therapeutics, 2, Gilead, 2, GlaxoSmithKlein(GSK), 1, horizon Therapeutics, 2, Janssen, 5, Pfizer, 2, ROME Therapeutics, 2, 5, Rome Therapeutics, 5, Ventus Therapeutics, 2, 5; **J. Gudjonsson**: Abbvie, 2, 5, Almirall, 2, 5, AnaptysBio, 2, Boehringer Ingelheim, 2, Celgene/BMS, 2, 5, Eli Lilly, 2, 5, Galderma, 2, Janssen, 2, 5, Kyowa Kirin, 5, MiRagen, 2, Novartis, 2, Prometheus Biosciences, 5, Sanofi, 2, SunPharma, 5, TimberPharma, 5.

Abstract Number: 0893

Involvement of Type I Interferon-responsive Myeloid Cells in Renal Inflammation in a Lupus Mouse Model

Trine Jorgensen and **Lindsey Han**, Lerner Research Institute, Cleveland Clinic Foundation, Cleveland, OH

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is an autoimmune disease that can cause damage to multiple organs, including the kidneys in Lupus Nephritis (LN). Current treatments for SLE are limited to conventional disease-modifying anti-rheumatic drugs, while treatments for LN are limited to corticosteroid therapy, as well as Calcineurin inhibitors or Leflunomide, both of which have been studied mainly in Asian populations and are lacking in data. A more targeted therapy is necessary to address the underlying pathogenesis of the disease. Type I interferon (IFN-I) and its receptor (IFNAR) are known to play a significant role in the progression of SLE/LN, making them a major focus of research and therapy. The exact mechanism by which IFNAR expression on myeloid cells affects SLE/LN activity remains unclear.

Methods: Female mice were used to investigate whether deficiency of IFNAR on myeloid cells will drive or reduce disease progression of SLE/LN in B6.Nba2 lupus-prone mice. Study mice were: B6.Nba2.LysMcre/cre.IFNARflx/flx (n=16) (cKO), and control mice were: B6.Nba2 (WT) lupus-prone mice (n=18) and B6 (C57Bl/6) healthy mice (n=4). The tests performed included flow cytometry of kidney cells from 9 month old mice, and ELISA of urine biomarkers S100a8, VCAM-1, and PF4, a novel methodology scarcely done in LN mouse-model studies to analyze LN-related kidney damage without invasive biopsy.

Results: Kidney 9mo flow data revealed elevated neutrophil and decreased monocytic infiltration in the WT, but normalized levels in cKO, as well as specifically reduced levels of B cells in cKO. Furthermore, we found that CD4+ T cells were reduced, CD8+ T cells were elevated, and Double positive (DP) T cells were normalized in 9mo cKO kidneys as compared to WT mice. We observed nephromegaly in cKO mice at 9 mo of age, but the urinary biomarkers S100a8 and PF4 were decreased in 9mo cKO mice compared to WT mice.

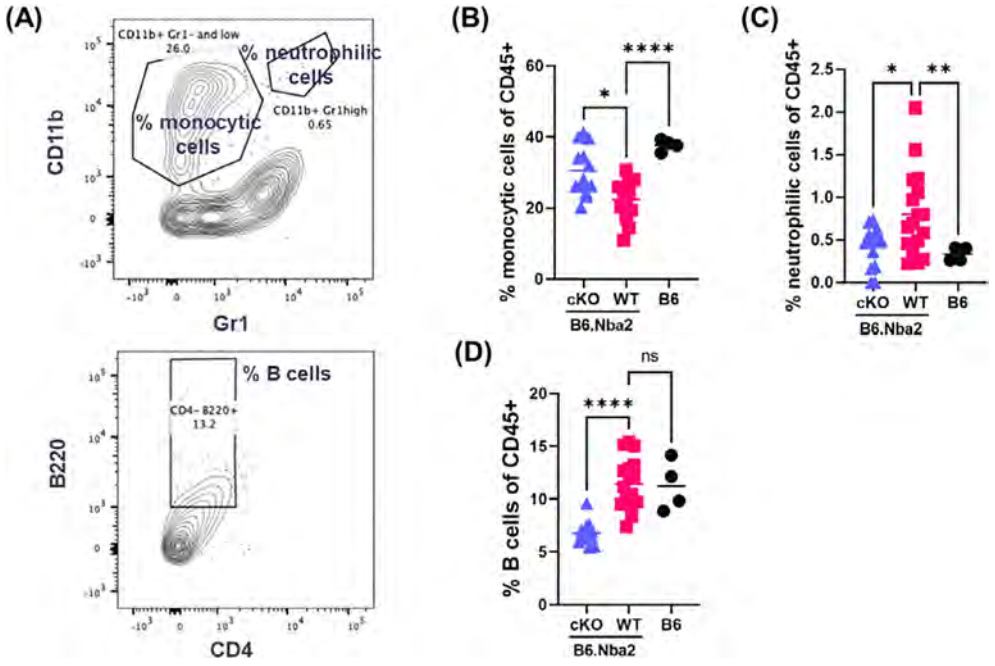


Figure 1: Kidney infiltrating myeloid cells approach levels seen in B6 mice, while B cells are specifically reduced in cKO mice. Myeloid inflammatory cell subsets were analyzed in 9-month-old female B6.Nba2 cKO, B6.Nba2, and B6 control mice. (A) Gating strategy: All cells were gated as CD45+. (B-C) The proportion of monocytic and neutrophilic cells in myeloid-cell specific B6.Nba2 cKO mice were closer to the B6 non-autoimmune controls. (D) In B6.Nba2.IFNAR cKO, B cells were specifically and significantly reduced compared to both B6.Nba2 and B6. Each symbol represents one mouse. * p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001

Conclusion: In summary, we observed that reduced levels of neutrophilic cells, B cells, CD4+ T cells and DP T cells were associated with reduced levels of urinary biomarkers S100a8 and PF4 in cKO mice, suggesting that neutrophils infiltrate the kidney in a type I interferon-dependent manner, which subsequently results in the secretion of urinary markers previously found to be associated with nephritis in both pediatric and adult SLE-LN patients. Thus, we suggest that in response to type I interferons neutrophilic cells are recruited to the kidney, leading to the release of chemokines and the further recruitment of inflammatory lymphocytes, ultimately resulting in renal cell damage and the development of LN.

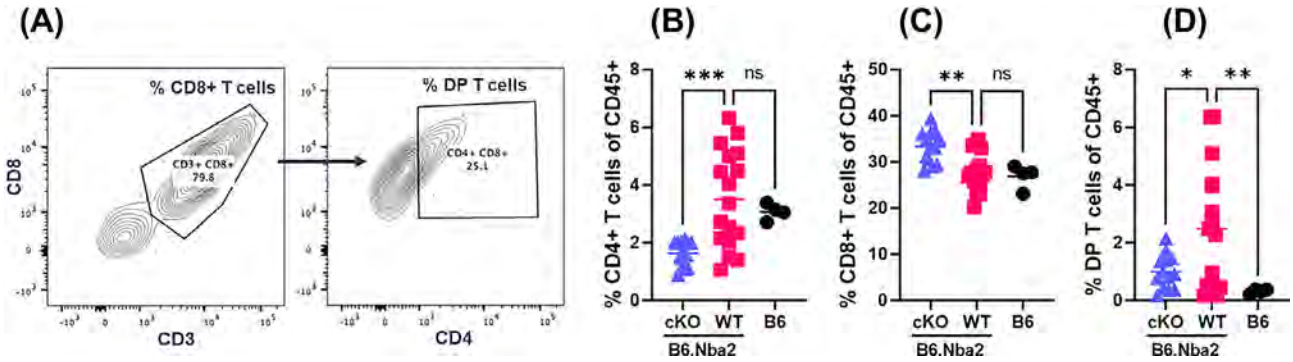


Figure 2: Lack of IFNAR on myeloid cells affect the type of T cells infiltrating kidneys of cKO mice. T cells were detected in 9-month-old female B6.Nba2 cKO, B6.Nba2, and B6 control mice. (A) Gating strategy. All cells were gated as CD45+. (B) In CD4+ Helper T cells, WT and B6 were unaltered, while the cKO mice were specifically reduced. (C) In CD8+ T cells, WT and B6 were also unaltered, while the cKO mice were specifically increased. Further studies to determine if elevated population is representative of CD8+ Tregs. (D) In double positive T cells, cKO mice were closer to levels of B6 healthy mice compared to the WT. Each symbol represents one mouse. ** p<0.01, *** p<0.001, **** p<0.0001

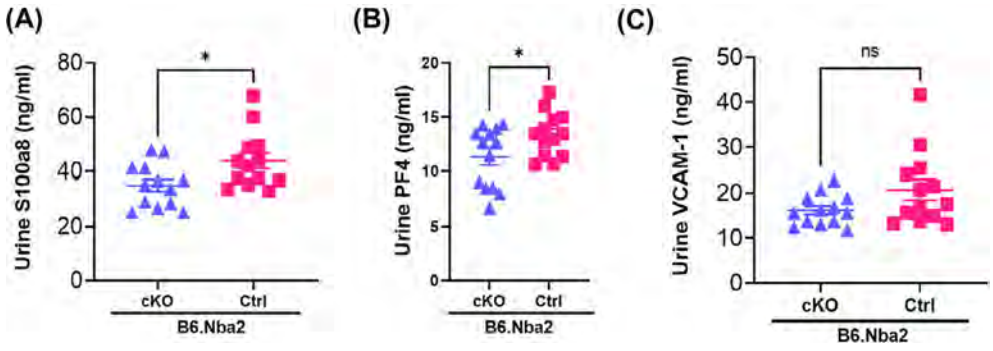


Figure 3: Decreased concentrations of urinary biomarkers suggest reduced LN disease activity in cKO mice. Concentrations of urinary biomarkers were analyzed in 9-month-old female B6.Nba2 cKO, B6.Nba2, and B6 control mice. (A) Concentration of S100a8 (Saliva 100 calcium-binding protein a8) was significantly reduced in cKO mice. (B) Concentration of PF4 (Platelet Factor 4) or CXCL4 (CX Chemokine ligand 4) was significantly reduced in cKO mice. (C) Concentration of VCAM-1 (Vascular cell adhesion molecule 1) was reduced in cKO mice. Each symbol represents one mouse. * p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001

Disclosure: T. Jorgensen: None; **L. Han**: None.

Abstract Number: 0894

The Cellular and Spatial Type I Interferon Response Following Skin Exposure to Ultraviolet Light

Jie An[1], Xizhang Sun[1], Rayan Najjar[1], Connie Zhao[1], Paul Kong[2], Stephanie Weaver[2], Amanda Koehne[2], Matt Fitzgibbon[2] and Keith Elkon[1], [1]University of Washington, Seattle, WA, [2]Fred Hutchinson Cancer Center, Seattle, WA

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE patients characteristically have a prominent type I interferon (IFN-I) signature in lesional and non-lesional skin. We recently demonstrated that, following a single exposure to ultraviolet light (UVB), UVB induces an IFN signature not only in the skin but also in the blood and kidneys of wild type mice. We asked three questions: which cells (skin or immune) are responsible for IFN-I production? 2) which subset of immune cells or which part of the skin are responsible for IFN-I production after UV? And 3) What are the different Type I IFNs (IFN-a, IFN-b, IFN-k) being made after UV exposure?

Methods: Shaved mouse skin received a single exposure of 500 mJ/cm^2 UVB and biopsies taken at time 0 and then 6, 12 and 24 hours after UVB exposure (n=3 per groups). Single cell nuclear RNA sequencing (snRNAseq) used Illumina Nextseq protocols with bioinformatics utilizing Monocle and Seurat pipelines. In situ hybridization (ISH) was performed with IFN-alpha consensus (IFNac), beta (b) and kappa (k) probes with HALO software for quantification. For spatial transcriptomics analysis, fixed tissue was first stained with antibodies to CD45 and to cytokeratin (CK) to mark immune cells and keratinocytes respectively. 7 regions of interest were selected and processed on the GeoMx digital spatial profiler. We used the mouse whole transcriptome probe set for next generation sequence analysis and results processed on the nanoString software Suite 2.5.1.145. Pathway analysis was determined by Gene Set Enrichment Analysis using the curated mouse gene set collection from MSigDB (2626 gene set).

Figure 1:

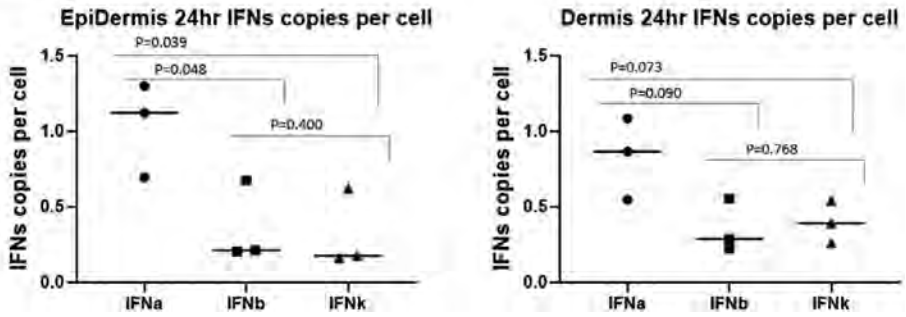


Figure 1. Average copy number of interferon alpha (consensus), beta and kappa in the epidermis (left) and dermis (right) at 24 hrs following skin exposure to UV light.

Results: SnRNAseq revealed that ISGs such as Ifit1, Isg15 and Isg20 were significantly increased at 24 hr post UV (p adj $< 10^{-5}$) relative to baseline. When ISG expression was clustered by cell type, the highest Isg15 and Isg20 expression was seen in two epidermal clusters (p adj $< 10^{-5}$ and 10^{-10} respectively). Utilized the ISH approach, we observed the highest signals in the epidermal region for IFN-ac (> 1 copy/ cell) versus IFN-b and IFN-k (< 1 copy/ cell). Whole transcriptome spatial analysis confirmed highest Isg15 and 20 expression in the cytokeratin positive cells. When the top 20 pathways activated by UV at 6 hr in the epidermis and dermis were compared, statistically significant differences (p adj < 0.01) in the cytokeratin positive cells included apoptosis, epigenetic (H3K27ME3), and NFkb targets whereas in the CD45 cell population, differences in GVHD, innate immune system, platelet activation and brown myeloid cell development were observed. At 24 hr post UV, significant changes were observed in multiple RNA processing reactomes in both cytokeratin and CD45+ cells. In the dermis, an increase in several lipid and fatty acid reactomes occurred.

Conclusion: We have identified the spatial locations of different IFN-I species in the skin following UV light injury. Copy number was highest in the epidermis for IFN-ac. Spatial transcriptomics also illuminates differences in inflammatory versus metabolic programs that are activated in immune (CD45) versus epidermal (cytokeratin positive) and dermal locations. These studies will lead to better understanding of how UV inflammation provokes lupus in susceptible individuals.

Disclosure: J. An: None; **X. Sun**: None; **R. Najjar**: None; **C. Zhao**: None; **P. Kong**: None; **S. Weaver**: None; **A. Koehne**: None; **M. Fitzgibbon**: None; **K. Elkon**: None.

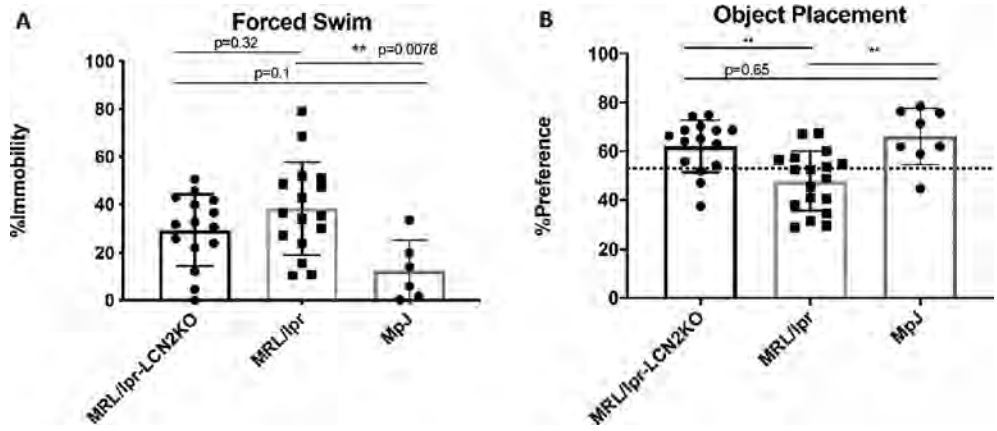
Abstract Number: 0895

Lipocalin-2 Promotes Cutaneous and Neuropsychiatric Disease in Murine Lupus

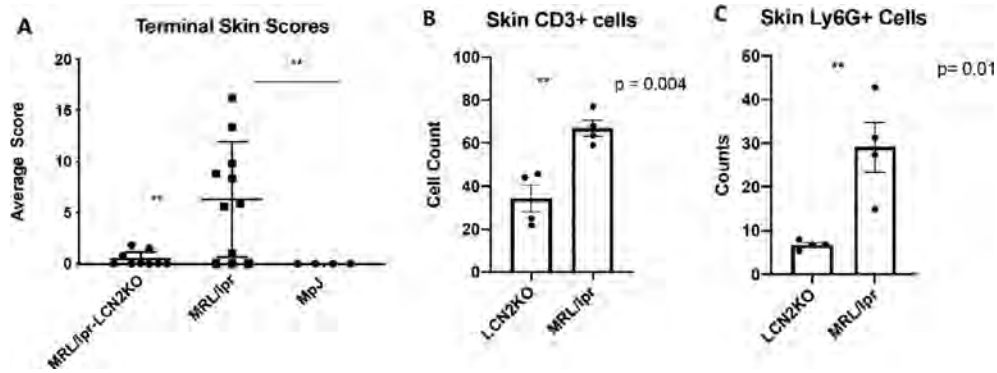
Chaim Putterman[1], Elise Mike[2] and **Sayra Garcia**[1], [1]Albert Einstein College of Medicine, Bronx, NY, [2]Johns Hopkins, Bronx, NY

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM



LCN2 deficient MRL/lpr mice (n=15) showed a significant improvement in the Porsolt swim test, which evaluates depression like behavior (A) and the object placement test, which evaluates spatial memory (B) compared to MRL/lpr wild type mice.



Macroscopic lesion scores in LCN2 deficient MRL/lpr mice were significantly improved compared to the MRL/lpr wildtype lesions (A). Lesional skin taken from LCN2-deficient MRL/lpr mice had a reduction of infiltrating CD3+ T cell (B) and Ly6G+ neutrophil (C) counts compared to the MRL/lpr wildtype mice as determined by immunofluorescent staining.

Background/Purpose: One central mechanism believed to contribute to the pathogenesis of neuropsychiatric systemic lupus erythematosus (NPSLE) is temporary disruption of the blood brain barrier (BBB). Astrocytes are abundant glial cells in the brain that work with endothelial cells to regulate tight junctions, which maintain BBB integrity. Astrocyte end-feet localized along the BBB can sense and detect inflammatory cytokines and cells in the periphery; thus, the systemic inflammatory milieu present in SLE can lead to the activation of astrocytes, temporarily breaching the BBB and compromising the brain's immune privilege. BBB dysfunction can also lead to the migration of immune cells into the brain and further activation of astrocytes and microglia, resulting in neuronal damage and subsequent cognitive defects. The MRL/lpr mouse is the most widely used spontaneous murine model of NPSLE. MRL/lpr mice show behavioral abnormalities such as cognitive deficits in the form of impaired memory (spatial recognition) as well as depressive-like behavior. Lipocalin-2 (LCN2) is an acute phase protein implicated in immune-mediated and neuroinflammatory diseases, including multiple sclerosis and traumatic brain injury. To examine a possible role of LCN2 in the pathogenesis of SLE we generated aMRL/lprLCN2 knockout (KO) mouse strain, and evaluated end organ disease, including neuropsychiatric, skin, and kidney disease. Furthermore, we focused on uncovering specific mechanisms by which LCN2 improves disease in lupus target organs.

Methods: Seventeen week old MRL/lpr-LCN2KO (n=15)and MRL/lprLCN2 wild type (n=16) mice underwent standardized behavioral testing, and were subsequently bled and sacrificed. Skin lesions were scored using a validated scoring protocol. Serum was tested for anti-dsDNA antibodies and IgG levels via ELISA. Skin and brain tissues were processed for

immunofluorescent staining for T cells, B cells, macrophages, and neutrophils. Brain tissue was stained for NeuN (a neuronal marker) and glial fibrillary acidic protein (GFAP, an astrocyte activation marker).

Results: We found that MRL/lpr-LCN2KO mice had significantly improved cognitive performance on spatial recognition memory and tests of behavioral despair, but unchanged levels of serum IgG and anti-dsDNA antibodies, compared to MRL/lpr mice. Additionally, we found that skin scores (macroscopic) in LCN2KO mice were significantly improved, together with a reduction in infiltrating T-cell and neutrophil counts. In the brain, we found diminished GFAP expression in MRL/lpr-LCN2KO mice, indicating reduced astrocyte activation. Moreover, NeuN expression was decreased inMRL/lprLCN2KO-derived hippocampal neurons, consistent with improved hippocampal neuron viability in LCN2 deficient mice.

Conclusion: LCN2 deficiency improves skin and neuropsychiatric disease in MRL/lpr lupus prone mice. While investigation of additional mechanisms is in progress, we found that skin disease is improved through reduction of infiltrating immune cells known to contribute to the severity of cutaneous lesions, while in the brain LCN2 deficiency reduces astrocyte activation and improves hippocampal neuron damage.

Disclosure: C. Putterman: Equillium, 2, KidneyCure, 1, Progentec, 2; **E. Mike**: None; **S. Garcia**: None.

Abstract Number: 0896

Targeting Toll-Like Receptor 7 with DS-7011a, a Promising Novel Antagonistic Antibody for the Treatment of Systemic Lupus Erythematosus

Atsushi Manno[1], Tomohiro Honda[1], Chiharu Kuwata[2], Shiho Ito[2], Michinori Kadokura[1], Reiko Mizutani[3], Shinnosuke Yamada[1] and Yoshiaki Tomimori[1], [1]Daiichi Sankyo Co., Ltd., Shinagawa-ku, Japan, [2]Daiichi Sankyo Co., Ltd., Edogawa-ku, Japan, [3]Daiichi Sankyo RD Novare Co., Ltd., Edogawa-ku, Japan

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The centrality of Toll-like receptor 7 (TLR7) to the pathogenesis of systemic lupus erythematosus (SLE) was recently underscored by a report that high TLR7 gene expression drives autoantibody production in SLE (Wang et al., 2019)and reaffirmed by a report that TLR7 gain-of-function mutations confer susceptibility to SLE (Brown et al., 2022). It was also reported that an antagonistic anti-mouse TLR7 monoclonal antibody (mAb) improves survival and inhibits autoantibody production in NZBWF1 mice, which spontaneously develop lupus (Murakami et al., 2021). We have identified DS-7011a, an antagonistic anti-human TLR7 mAb, and examined its preclinical pharmacological activity and safety. We have also examined the expression of the TLR7 gene signature (GS) as an indicator of target engagement in NZBWF1 mice.

Methods: The species cross-activity and the binding specificity of DS-7011a were evaluated using Lenti-X 293 T cells over-expressing either TLR7 ortholog proteins of several animal species or human TLR family proteins. To evaluate the modulation of cytokine and antibody production by anti-TLR7 antagonistic antibodies, human or mouse peripheral blood mononuclear cells (PBMCs) were stimulated with CL264 or ssRNA9.2s, which are TLR7 agonists. A surrogate antagonistic anti-mouse TLR7 mAb was administered to NZBWF1 mice intraperitoneally at 0.2 mg/mouse once a week from Week 21 to Week 30 of age to study the impact on the lupus model along with the modulation of TLR7 GS. TLR7 GS was defined using

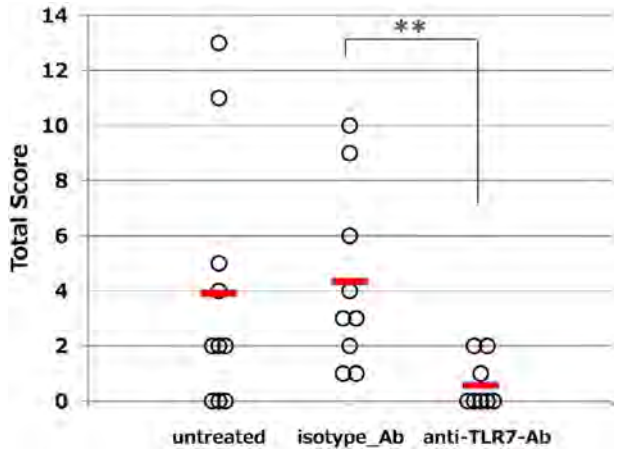


Figure 1. Renal histological scores in untreated, isotype antibody-treated, and anti-TLR7 antibody-treated mice (**: $p < 0.01$ by Wilcoxon rank sum test)

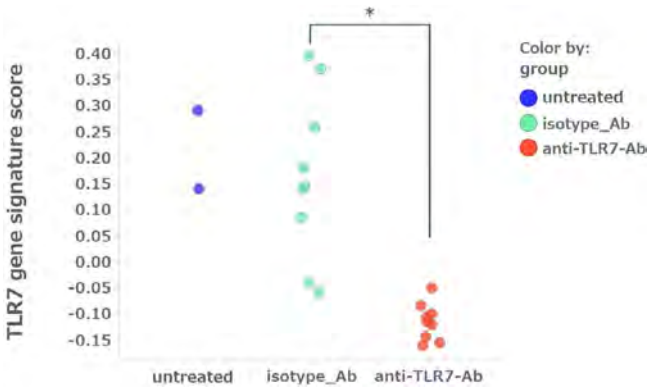


Figure 2. TLR7 gene signature scores in untreated, isotype antibody-treated, and anti-TLR7 antibody-treated mice (*: $p < 0.001$ by Welch two sample t-test)

public microarray data of mouse macrophages treated with R848, a TLR7 agonist. TLR7 GS scores were calculated using blood gene expression data from NZBWF1 mice treated with anti-TLR7 mAb or isotype control antibody or left untreated. To evaluate safety, DS-7011a was administered intravenously once every 2 weeks for 3 months to cynomolgus monkeys at doses up to 400 mg/kg.

Results: DS-7011a bound to both human and cynomolgus monkey TLR7 but not to mouse or rat TLR7. DS-7011a bound to human TLR7 but not to other human TLR family proteins. DS-7011a suppressed the TLR7-stimulated production of IL-6 and IFN-alpha by human PBMCs. The surrogate anti-mouse TLR7 mAb suppressed the TLR7-stimulated IL-6 production by mouse PBMCs and it reduced kidney tissue damage (Figure 1), inhibited autoantibody production, and suppressed TLR7 GS expression in NZBWF1 mice (Figure 2). There were no toxicity findings in monkeys treated for 3 months at doses up to 400 mg/kg.

Conclusion: DS-7011a shows the ability to inhibit the TLR7-stimulated production of inflammatory cytokines and shows no toxicity in monkeys after 3-month treatment up to and including the maximum administered dose. An anti-mouse TLR7 mAb ameliorated manifestations of a mouse lupus model, suppressing the expression of TLR7 GS. These findings indicate that, by targeting TLR7, DS-7011a is a promising therapeutic option for the treatment of SLE.

Disclosure: A. Manno: Daiichi Sankyo Co., Ltd., 3, 3; **T. Honda**: Daiichi Sankyo Co., Ltd., 3; **C. Kuwata**: Daiichi Sankyo Co., Ltd., 3; **S. Ito**: Daiichi Sankyo Co., Ltd., 3; **M. Kadokura**: Daiichi Sankyo Co., Ltd., 3; **R. Mizutani**: Daiichi Sankyo RD Novare Co., Ltd., 3; **S. Yamada**: Daiichi Sankyo Co., Ltd., 3; **Y. Tomimori**: Daiichi Sankyo, 3.

Abstract Number: 0897

Steroid-sparing Effects of Afimetoran (BMS-986256), an Equipotent Toll-like Receptor (TLR)7 and TLR8 Antagonist, in a Lupus Mouse Model

Shailesh Dudhgaonkar[1], Puneet Chopra[2], Anjuman Rudra[2], Siva Subramani[2], Sourabha Palachandra[2], Nikita Bhatt[2], Veeresh Pabbala[2], Sourabh Ranade[2], Durga Siva Prasad Ega[2], Alaric Dyckman[3] and Qihong Zhao[3], [1]Bristol Myers Squibb, Bangalore, India, [2]Biocon Bristol Myers Squibb Research Center, Bangalore, India, [3]Bristol Myers Squibb, Lawrenceville, NJ

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Animal Models Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with extensive phenotypic heterogeneity due to the underlying molecular diversity of dysregulated pathways. Patients with SLE receive glucocorticoids as part of standard-of-care treatment but can develop resistance over time, making steroid resistance an important unmet need. Furthermore, side effects make long-term use undesirable. Toll-like receptor (TLR)7 and TLR8, endosomal receptors that play a key role in innate immunity, are expressed in immune cells, where they recognize single-stranded RNA and initiate downstream signaling via the nuclear factor kappa B (NFκB) and interferon regulatory factor pathways. NFκB signaling activation via TLR7 and TLR8 pathways could be a driving factor in steroid resistance. We evaluated the steroid-sparing potential of afimetoran, an equipotent, dual TLR7 and TLR8 antagonist, currently in clinical development for SLE and cutaneous lupus erythematosus.

Methods: NZB/W mice with moderate disease (proteinuria, 60–100 mg/dL) were treated therapeutically once daily with vehicle or selected doses of afimetoran and/or prednisolone. Survival, kidney injury, splenomegaly, age-associated B cells (ABCs), serum auto-antibody titers (anti-double-stranded DNA antibodies, anti-nuclear antibodies), and interleukin-12p40 (IL-12p40) were assessed in all treatment groups. To assess the impact of afimetoran on TLR7 activation–mediated steroid resistance in vitro, C57 wild-type (WT) mouse bone marrow cells (BMCs) were challenged with the TLR7 agonist gardiquimod and treated with prednisolone alone or in combination with afimetoran. B-cell and plasmacytoid dendritic cell (pDC) apoptosis was evaluated by annexin V staining using flow cytometry in C57 WT BMCs treated in vitro and NZB/W BMCs from mice dosed orally.

Results: Afimetoran alone and in combination with prednisolone improved survival in the NZB/W mouse model. Significant, dose-dependent suppression of kidney injury markers such as proteinuria, neutrophil gelatinase-associated lipocalin (NGAL), or tissue inhibitor of metalloproteinases 1 (TIMP1) was observed. Splenomegaly was improved, particularly when afimetoran was combined with prednisolone; suppression of ABCs was also improved with this combination. Significant, dose-dependent suppression of plasma IL-12p40 and serum auto-antibody titers was also observed, demonstrating the potential of afimetoran in this mouse model of SLE. An improved steroid response was seen with afimetoran in vitro in gardiquimod-stimulated C57BL/6 mouse BMCs, which showed a significant increase in prednisolone-induced apoptosis of pDCs and B cells compared with baseline control or prednisolone alone. A similar trend was seen in vivo for BMCs collected from NZB/W mice dosed with combinations of afimetoran and prednisolone.

Conclusion: Afimetoran, alone or in combination with low-dose (1mg/kg) prednisolone, showed robust efficacy in NZB/W mice with moderate disease. Bone marrow pDCs and B cells showed afimetoran-induced reversal of resistance to prednisolone-induced apoptosis. These data confirm that afimetoran has the clinical potential to be steroid sparing.

Disclosure: S. Dudhgaonkar: Bristol-Myers Squibb(BMS), 3, 11; **P. Chopra**: Bristol-Myers Squibb(BMS), 3; **A. Rudra**: Bristol-Myers Squibb(BMS), 3; **S. Subramani**: Bristol-Myers Squibb(BMS), 3; **S. Palachandra**: Bristol-Myers Squibb(BMS), 3; **N. Bhatt**: Bristol-Myers Squibb(BMS), 3; **V. Pabbala**: Bristol-Myers Squibb(BMS), 3; **S. Ranade**: Bristol-Myers Squibb(BMS), 3; **D. Prasad Ega**: Bristol-Myers Squibb(BMS), 3; **A. Dyckman**: Bristol-Myers Squibb(BMS), 3; **Q. Zhao**: Bristol-Myers Squibb(BMS), 3, 11.

Abstract Number: 0898

The Role of the Endothelin System in the Development of TLR7-accelerated Lupus-Associated Cardiac Dysfunction

Kennedy Hawkins, Marice McCrorey, C. Alex Colvert, Kristine DeLeon-Pennell, Melissa Cunningham and Justin Van Beusecum, Medical University of South Carolina, Charleston, SC

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by autoantibody formation and immune complex deposition in target organs. While it is known that plasma endothelin-1 (ET-1) is elevated in patients with lupus and is associated with high rates of hypertension, renal injury, and cardiovascular disease, the underlying mechanisms contributing to cardiac complications associated with lupus are still unknown. Herein, we hypothesized that disease acceleration with the toll-like receptor 7/8 agonist, Resiquimod, would promote higher incidence of cardiac pathology and dysregulation of the ET system in a preclinical lupus murine model.

Methods: Female B6.Nba2 lupus prone mice aged 10-14 weeks were treated topically with either 30 uL of acetone or Resiquimod (R848;100μg/30μl) twice weekly for 4 weeks. Echocardiograms were performed every 4 weeks for 16 weeks to evaluate ejection fraction (EF), left ventricular wall thickening, and end-systolic and diastolic volumes. At 16 weeks, hearts and spleens were harvested, weighed and frozen or fixed for histological analysis. ET-1, endothelin receptor A (ET_A), and endothelin receptor B (ET_B) were analyzed by real-time PCR (RT-PCR), immunoblotting, and immunohistochemical analysis.

Results: Cardiac imaging showed R848-treated mice had increased left ventricular wall thickness at 4 weeks compared to acetone treatment ($p< 0.01$). After 16 weeks, mice previously treated with R848 for 4 weeks had profound cardiac dysfunction indicated by decreased EF ($p< 0.001$) and increased end-systolic volume ($p< 0.01$) compared to acetone treatment. R848-treated mice also exhibited profound cardio- (118.6 ± 1.014 vs. 187.7 ± 2.967; $p< 0.0001$) and splenomegaly (162.4 ± 33.3 vs. 658.3 ± 205.7; $p< 0.05$) at 16 weeks. Interestingly, histological analysis of the left ventricle demonstrated significantly increased perivascular fibrosis in the R848-treated mice compared to acetone ($1.174 \pm 0.1\%$ vs. $1.651 \pm 0.1\%$; $p< 0.05$). Interrogation of the cardiac ET system showed that R848-treated mice had significantly elevated ET-1 levels ($p< 0.05$), without a significant change in ET_A or ET_B receptor expression.

Conclusion: These data demonstrate that acceleration of lupus with the TLR7 agonist R848 increases cardiac dysfunction and pathological production of cardiac ET-1. Moreover, our model presents a novel avenue to better understand the role and contributions that the ET system plays in the development of lupus associated cardiac dysfunction.

Disclosure: K. Hawkins: None; **M. McCrorey**: None; **C. Colvert**: None; **K. DeLeon-Pennell**: None; **M. Cunningham**: Aurinia, 2; **J. Van Beusecum**: None.

Abstract Number: 0899

Complement Factor I (CFI) Gene Expression by Kidney Tubular Cells Is Increased in Lupus Nephritis Patients with Interstitial Fibrosis and Tubular Atrophy

Shudan Wang[1], John Greally[2], Masako Suzuki[3], Jee-Young Moon[2], Tao Wang[2], Yvonne M Saenger[2], Brad Rovin[4] and J. Michelle Kahlenberg[5], [1]Albert Einstein College of Medicine / Montefiore Medical Center, New York, NY, [2]Albert Einstein College of Medicine, Bronx, NY, [3]Texas A&M University, College Station, TX, [4]Ohio State University, Columbus, OH, [5]University of Michigan, Ann Arbor, MI

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Etiology & Pathogenesis Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Tubulointerstitial injury is a strong predictor of progression to kidney failure in lupus nephritis (LN). Prior animal studies suggest intrarenal complement activation has an important and underrecognized role in tubulointerstitial fibrosis in LN, yet this has not been shown in LN patients. This study aimed to identify complement markers of

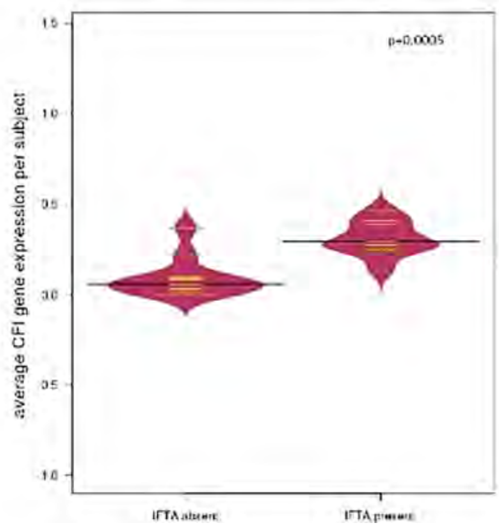
TABLE 1: Comparison of Demographics, Laboratory, Medication Use and Histopathology between Lupus Nephritis (LN) Patients with and without Interstitial Fibrosis/Tubular Atrophy (IFTA)*

	Overall n=20	LN without (<10%) IFTA n = 11	LN with (≥ 10%) IFTA n = 9	P- Value
Demographics Parameters				
Age, median (IQR), years	28 (21.5, 34)	29 (20, 38)	26 (26, 33)	0.84
Female, n (%)	18 (90.0%)	10 (90.9%)	8 (88.9%)	1.00
Non-white race[#], n (%)	8 (40.0%)	3 (27.3%)	5 (55.6%)	0.36
Hispano/Latino, n (%)	9 (45.0%)	6 (54.6%)	3 (33.3%)	0.41
Mycophenolate mofetil, n (%)	12 (60.0%)	6 (54.6%)	6 (66.7%)	0.67
Prednisone, n (%)	13 (65.0%)	7 (63.6%)	6 (66.7%)	1.00
ACEI/ARB¶, n (%)	9 (45.0%)	6 (54.6%)	3 (33.3%)	0.41
Laboratory Parameters at Kidney Biopsy				
Elevated dsDNA, n (%)	16 (80.0%)	8 (72.7%)	8 (88.9%)	0.58
Low serum C3 (<70), n (%)	13 (65.0%)	6 (54.6%)	7 (77.8%)	0.37
Low serum C4 (<14), n (%)	14 (70.0%)	7 (63.6%)	7 (77.8%)	0.64
Proteinuria (g/g), median (IQR)	2.9 (1.2, 4.3)	2.4 (1.2, 4.3)	3.4 (1.1, 3.7)	1.00
Nephrotic-range proteinuria (>3.5 g/g)	8 (40.0%)	4 (36.4%)	4 (44.4%)	1.00
Histological Parameter				
Lupus Nephritis Class				0.64
Proliferative/Mixed: III, IV, III/V, IV/V	13 (65.0%)	8 (72.7%)	5 (55.6%)	
Membranous: V, mesangial II	7 (35.0%)	3 (27.3%)	4 (44.4%)	
Activity Index, median (IQR)	3 (1.5, 6)	3 (2, 6)	4.5 (2, 7)	0.31
Chronicity Index, median (IQR)	1 (0, 3)	0 (0, 1)	3 (3, 4)	**0.0042**
Tubulointerstitial inflammation present[Δ], n (%)	6 (30.0%)	1 (9.1%)	5 (55.6%)	0.05

*All values are presented in median (IQR interquartile range). #Black or Asian race ¶Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker. ΔDefined as ≥ 10% tubulointerstitial affected

tubulointerstitial fibrosis in LN and potential therapeutic targets. Tubular complement gene expression in LN kidneys from patients with and without interstitial fibrosis/tubular atrophy (IFTA) was compared using scRNA-seq data.

Figure 1: Complement Factor I (CFI) Gene Expression by the Overall Kidney Tubular Cells in Lupus Nephritis Patients with and without IFTA.



Black line is over the median of each group. White line represents each subject.

TABLE 2: Comparison of Complement Gene Expression by the Overall Kidney Tubular Cells between LN patients with and without Interstitial Fibrosis/Tubular Atrophy (IFTA)*

	Overall n=20	LN without (<10%) IFTA, n = 11	LN with (≥10%) IFTA n = 9	P-Value
Complement Activators				
C1QA	0.004 (0, 0.338)	0.008(0, 0.245)	0(0, 0.384)	0.96
C1QB	0 (0, 0.376)	0 (0, 0.075)	0.050 (0, 0.240)	0.15
C1QC	0 (0, 0.336)	0 (0, 0.029)	0.023 (0, 0.096)	0.21
C1R	0.070 (0.003, 0.158)	0.036 (0, 0.190)	0.110 (0.028, 0.137)	0.41
C1S	0.069 (0, 0.220)	0 (0, 0.070)	0.109(0, 0.217)	0.31
C2	0 (0, 0.026)	0 (0, 0.022)	0 (0, 0.033)	0.88
C3	0.062 (0, 0.160)	0.033(0, 0.193)	0.065(0, 0.445)	0.28
C5	0 (0, 0.071)	0 (0, 0.052)	0.006 (0, 0.094)	0.57
C5AR1	0.023 (0, 0.047)	0.024 (0, 0.040)	0 (0, 0.052)	0.99
C5AR2	0.004 (0, 0.076)	0.036 (0, 0.107)	0 (0, 0.029)	0.29
C6	0 (0, 0.007)	0 (0, 0.000)	0 (0, 0.015)	0.99
C7	0.037 (0, 0.401)	0.006 (0, 0.199)	0.251(0, 0.730)	0.12
[illegible]	0 (0, 0.003)	0(0, 0.011)	0(0,0)	0.44
CFB	0.061 (0, 0.248)	0.034 (0, 0.250)	0.114 (0.060, 0.200)	0.36
CFD	0 (0, 0.051)	0 (0, 0.075)	0 (0, 0.048)	0.87
MASP1	0.005 (0, 0.060)	0.009 (0, 0.070)	0 (0, 0.000)	0.87
Complement Regulators				
CFH	0.044 (0, 0.120)	0 (0, 0.181)	0.110 (0.009, 0.110)	0.34
CFI	0.163 (0.071, 0.288)	0.059 (0.018, 0.100)	0.298 (0.258, 0.383)	**0.0005**
CD46	0.262 (0.089, 0.522)	0.409 (0.159, 0.598)	0.235(0.070, 0.406)	0.11
CD55	0.008 (0, 0.144)	0 (0, 0.122)	0.115 (0, .181)	0.37
CD59	0.532 (0.223, 0.718)	0.412 (0.115, 0.810)	0.647 (0.214, 0.973)	0.50

*Kidney tubular cells include proximal tubule, loop of Henle, distal tubule and collecting duct cells. The average gene expression per subject was calculated and compared between the groups using the Wilcoxon rank sum test.

References:

1. [illegible] applied to lupus nephritis reveal type I IFN and fibrosis relevant pathways. Nat Immunol. 2019;20(7):915-27.

2. Zhang Y, Goodfellow RX, Ghiringhelli Borsa N, Dunlop HC, Bicat SA, et al. Complement Factor I Variants in Complement-Mediated Renal Diseases. Front Immunol. 2022;13:866330.

Methods: We used data from the Accelerating Medicine Partnership/ Multi-Ethnic Translational Research Optimization Lupus cohort, which applied scRNA-seq to 20 LN kidney tissue samples [1]. Cells between 200 and 2500 detected features were included. The data was normalized, scaled, and underwent principal component analysis and clustering using Uniform Manifold Approximation and Projection plots to identify distinct cell subtypes. Specific marker genes were used to identify the kidney tubular cell subtypes: ALDOB (proximal tubules), UMOD (loop of Henle), CALB1 (distal convoluted tubules), and SLC4A1/ TMEM213 (collecting duct). Complement gene expression was compared between LN patients with and without IFTA in the overall tubular cells and in each tubular cell subtypes using two approaches: 1) subject-based analysis where the average gene expression per subject was calculated and compared between the groups using the Wilcoxon rank sum test. 2) single-cell analysis using a linear mixed effects model. IFTA was defined as ≥10% of interstitium with fibrosis and atrophy.

Results: Of the 20 LN patients, 9 had IFTA on kidney biopsy. Table 1 compares demographics, medication use, laboratory, and histopathology between LN patients with (≥ 10%) and without (< 10%) IFTA on biopsy. LN patients with IFTA had a higher proportion with tubulointerstitial inflammation as compared with those without IFTA (56% vs. 1%, p=0.05) and higher chronicity index median score 3 (IQR= 3, 4) vs 1(0,1). There was no difference in other variables. A total of 1162 kidney tubular cells were identified: 287 proximal tubular, 171 loop of Henle, 587 distal tubular and 117 collecting duct cells. LN patients with IFTA had significantly higher overall tubular expression of Complement Factor I (CFI) as compared to those without IFTA: median average expression 0.298 (0.258, 0.383) vs. 0.059 (0.019, 0.100), p=0.0005, Figure 1. No differential expression of other complement genes was found (Table 2). When evaluating each tubular cell subtype, no difference in average CFI expression was found. Single cell analysis also showed increased overall tubular expression of CFI (β=0.27, SE=0.05, p< 0.001) and C7 (β=0.31, SE=0.15, p=0.049) among LN patients with IFTA. Specifically, CFI expression was increased in the distal tubular cells (β=0.27, SE=0.06, p< 0.001) but not in the other tubular cell subtypes.

Conclusion: This study identifies CFI, a regulator of the alternative complement pathway, as a potential marker of IFTA in LN. Increased CFI has been found in other kidney diseases [2] and may overcompensate for a dysfunctional complement system.

Disclosure: S. Wang: None; **J. Greally**: None; **M. Suzuki**: None; **J. Moon**: None; **T. Wang**: None; **Y. Saenger**: None; **B. Rovin**: AstraZeneca, 2, 5, Aurinia, 2, 5, Biogen, 2, F. Hoffmann-La Roche Ltd, 2, Genentech, 2, GlaxoSmithKlein(-GSK), 2, Novartis, 2; **J. Kahlenberg**: AstraZeneca, 1, Bristol-Myers Squibb(BMS), 2, 5, EMD Serano, 2, exo therapeutics, 2, Gilead, 2, GlaxoSmithKlein(GSK), 1, horizon Therapeutics, 2, Janssen, 5, Pfizer, 2, ROME Therapeutics, 2, 5, Rome Therapeutics, 5, Ventus Therapeutics, 2, 5.

Abstract Number: 0900

Complement Deposition on Extracellular Mitochondria Induces Platelet Activation *in Vitro*

Marina Barguil Macedo and Christian Lood, University of Washington, Seattle, WA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Mitochondria are extruded upon cell death and platelet activation, being elevated in several inflammatory conditions, including systemic lupus erythematosus (SLE). Mitochondria are immunogenic, with SLE patients having anti-mitochondrial antibodies (AMA), including anti-cardiolipin antibodies, which are associated with thrombosis. However,

the role of AMAs, as well as other opsonins such as complement, in regulating mitochondrial-mediated platelet activation, has not been carefully investigated. In the current study, we set out to determine the role of AMAs and complement components in modifying the ability of extracellular mitochondria to promote platelet activation.

Methods: Ultra-pure mitochondria were isolated from HepG2 cells through Dounce homogenization and differential centrifugation. Mitochondria were pre-opsonized with isolated IgG from SLE patients or healthy controls, as well as complement C3-deficient or sufficient plasma, prior to adding the washed opsonized mitochondria to platelets from healthy individuals. Markers of platelet activation were assessed by flow cytometry (P-Selectin; CD62P) or by ELISA of the supernatant (platelet factor 4; PF-4, and thrombospondin-1; TSP-1).

Results: Extracellular mitochondria were able to induce CD62P on the platelet surface (8x increase from baseline, $p< 0.0001$, Figure 1A), even to a higher extent than ADP, a known platelet activator, used as positive control. Surprisingly, opsonization of mitochondria with SLE IgG only marginally amplified platelet activation. Mitochondria supported complement activation, with binding of both C1q and activated C3 to the outer membrane. Importantly, C3-sufficient, but not deficient, sera supported enhanced mitochondrial-mediated platelet activation as determined by CD62P, PF-4 (3x increase from baseline, $p< 0.001$) and TSP-1 levels (4x increase from baseline, $p< 0.001$, Figure 1B). Of note, EDTA, a chelator of divalent cations, $Ca2+$ and $Mg2+$ necessary for complement activation, prevented mitochondrial opsonization with C3, and prevented subsequent platelet activation.

Conclusion: Extracellular mitochondria were able to induce CD62P on the platelet surface (8x increase from baseline, $p< 0.0001$, Figure 1A), even to a higher extent than ADP, a known platelet activator, used as positive control. Surprisingly, opsonization of mitochondria with SLE IgG only marginally amplified platelet activation. Mitochondria supported complement activation, with binding of both C1q and activated C3 to the outer membrane. Importantly, C3-sufficient, but not deficient, sera supported enhanced mitochondrial-mediated platelet activation as determined by CD62P, PF-4 (3x increase from baseline, $p< 0.001$) and TSP-1 levels (4x increase from baseline, $p< 0.001$, Figure 1B). Of note, EDTA, a chelator of divalent cations, $Ca2+$ and $Mg2+$ necessary for complement activation, prevented mitochondrial opsonization with C3, and prevented subsequent platelet activation.

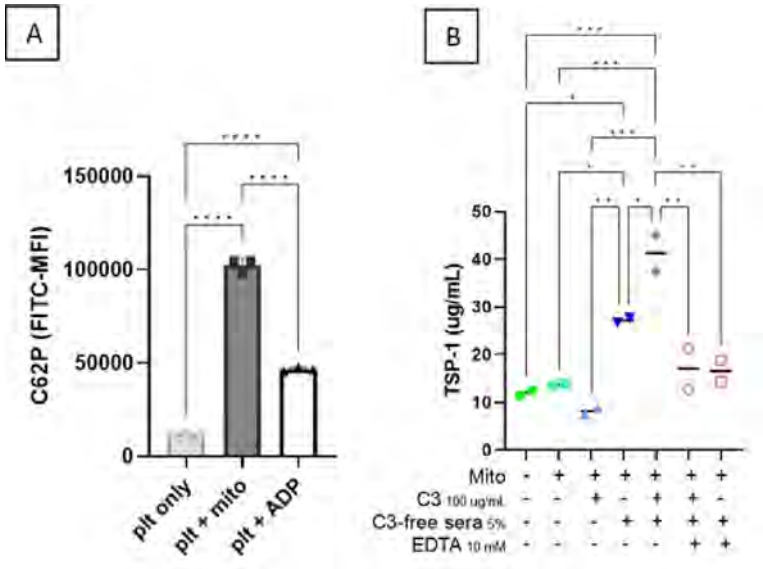


Figure 1. Mitochondrial-mediated platelet activation. A) Platelet P-selectin (CD62P) expression upon co-culture with mitochondria (mito) or ADP. B) Platelet activation (TSP-1) upon co-culture with mitochondria pre-opsonized with C3-sufficient (purple diamond) or deficient (blue down-pointing triangle) sera in presence of absence of EDTA (pink open circle).

Disclosure: M. Barguil Macedo: None; **C. Lood**: Amytryx, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Citryll, 2, Eli Lilly, 5, Gilead, 5, Horizon Therapeutics, 5, Pfizer, 5, Redd Pharma, 5, 11.

Abstract Number: 0901

Scavenging of Isolevuglandins Attenuates Neutrophil Expansion and Aortic NETosis in Systemic Lupus Erythematosus

Jaya Krishnan[1], Néstor de la Visitación[1], Jonathan Williams[1], Leslie Crofford[2] and **David Patrick**[3], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Vanderbilt University Medical Center, Melbourne, AR, [3]Department of Veterans Affairs, Nashville, TN

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Atherosclerosis and vascular inflammation are a cause of morbidity and mortality in systemic lupus erythematosus (SLE). Vascular NETosis is a driver of atherosclerosis and vascular inflammation. Isolevuglandins (IsoLGs) are lipid-aldehydes formed by peroxidation of arachidonic acid or prostaglandin-H_2. IsoLGs are efficiently scavenged by 2-hydroxybenzylamine (2-HOBA). Treatment of SLE-prone *B6.SLE123* mice with 2-HOBA attenuates systemic inflammation and reduces blood pressure. Additional studies have shown that isoLGs directly contribute to the formation of neutrophil extracellular traps (NETosis). We hypothesized that isoLGs contribute to neutrophil expansion and aortic NETosis in SLE-prone mice.

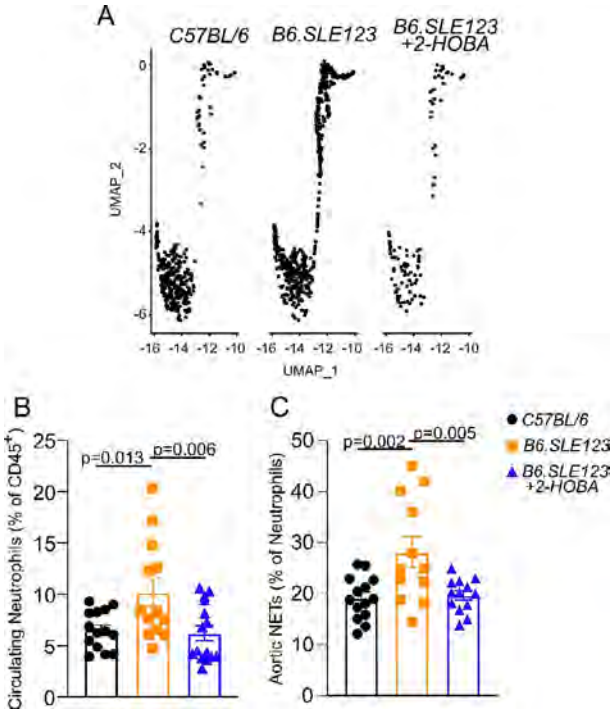


Figure 1. (A) UMAP of neutrophil clusters from cells isolated from spleens of C57BL/6, B6.SLE123, and B6.SLE123 mice treated with 2-HOBA following single cell sequencing. Significant expansion of neutrophils is present in SLE prone mice. This expansion is attenuated by 2-HOBA. (N=3) (B) Circulating neutrophils were quantified by flow cytometry. (C) NETs were quantified in aortas by flow cytometry. (N=12-14, data were compared with one-way ANOVA followed by Dunnett's multiple comparison test).

Methods: We treated 8-week-old female SLE prone *B6.SLE123* mice with 1g/L 2-HOBA in the drinking water for 4-weeks. *C57BL/6* mice were used as healthy controls. Spleens were harvested and splenocytes were submitted for single cell sequencing. Data were analyzed with Seurat v4.0.0 in R v4.0.4. NETosis in mouse tissue was measured by flow cytometry. Peripheral blood was obtained from a research subject with SLE that was recruited as part of the Memantine for the Treatment of Cognitive Impairment in Systemic Lupus Erythematosus clinical trial (IRB# 180256). To determine the role of isoLGs in NETosis, neutrophils were harvested from peripheral blood. Cells were seeded onto poly-L-lysine coated plates and incubated at 37°C for 2-hours in the presence of 200 μM ethyl-2-hydroxybenzylamine (ethy-2-HOBA), an isoLG scavenger with improved nuclear penetrance, or phosphate buffered saline as a control. Human NET formation was determined with immunofluorescence and quantified using the Imaris Cell Imaging Software (Oxford Instruments).

Results: Single cell sequencing revealed an increase in splenic neutrophils in *B6.SLE123* mice compared to *C57BL/6* controls. Treatment with 2HOBA attenuated this increase (*C57BL/6* 2.1%, B6.SLE123 3.8%, B6.SLE123+2HOBA 0.6% of total sequenced cells, N=3) (Figure 1A). Flow cytometry revealed an increase in circulating neutrophils in *B6.SLE123* mice that was attenuated with 2HOBA (*C57BL/6* 6.5 ± 1.9%, *B6.SLE123* 10.2 ± 4.8%, *B6.SLE123*+2HOBA 6.2 ± 2.8% of $CD45^+$ cells, N = 12-14)(Figure 1B). Aortic NETs were also increased in SLE prone mice which was attenuated following 2HOBA treatment (*C57BL/6* 19.2 ± 4.2%, *B6.SLE123* 28.1 ± 10.17%, *B6.SLE123*+2HOBA 19.7 ± 3.2% of neutrophils, N = 12-14)-(Figure 1C). Human SLE subject neutrophils showed a reduction in total NET area after treatment with ethyl-2-HOBA (Control 4,415 ± 1238 μm^2/field vs 2,215 ± 1372 μm^2/field, n = 5, p = 0.029).

Conclusion: In a murine model of SLE, scavenging of isoLGs reduces neutrophils in secondary lymphoid tissue and peripheral blood. Additionally, we observe a reduction in vascular NETosis. Treatment of human neutrophils with an isoLG scavenger attenuates NET formation. These findings describe a role of isoLGs in SLE-associated NETosis and resultant vascular inflammation. Moreover, these findings suggest a potential role for isoLGs in NET-driven autoinflammation and vascular disease in SLE.

Disclosure: J. Krishnan: None; **N. de la Visitación**: None; **J. Williams**: None; **L. Crofford**: None; **D. Patrick**: Metabolic Technologies, Inc., 9, 10.

Abstract Number: 0902

Neutrophils in Systemic Lupus Erythematosus Demonstrate Heterogeneity Based on Sex

William Ambler[1], Gustaf Wigerblad[1], Eduardo Patino-martinez[1], Shuichiro Nakabo[1], Norio Hanata[1], Stephen Brooks[2], Kan Jiang[2], Carmelo Carmona-Rivera[1] and Mariana Kaplan[3], [1]Systemic Autoimmunity Branch, National Institute of Arthritis and Musculoskeletal and Skins Diseases, National Institutes of Health, Bethesda, MD, [2]Biodata Mining and Discovery Section, National Institute of Arthritis and Musculoskeletal and Skins Diseases, National Institutes of Health, Bethesda, MD, [3]Lupus Clinical Trials Unit, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health (NIH); Systemic Autoimmunity Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health (NIH), Bethesda, MD

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Sex differences in the immune system may contribute to o an increased incidence of autoimmunity in women and an increased susceptibility to infection and cancer in men. Human neutrophils, which have a putative role in systemic lupus erythematosus (SLE) disease initiation, propagation and tissue injury, display sexual dimorphism. This is

characterized in healthy controls by female neutrophils exhibitingheightened type I-interferon (IFN) response and enhanced activation and NET formation compared to males, while men have less mature and activated neutrophils compared to women. SLE has a significant female bias (9:1 ratio). However, men with SLE often have very severe disease. It is not currently well understood if there are different immunological drivers in lupus between men and women and if sex differences in immune cells are present in SLE. There is a subset of neutrophils in SLE called low density granulocytes (LDGs) that have been reported to have important pathogenic roles in the disease but whether these cells exhibit sexual dimorphism is also not known. Understanding sex differences in immune cell subsets in SLE may improve understanding of disease heterogeneity and could provide insight for sex- specific treatment targets.

Methods: Age matched male and female patients with SLE were recruited from a comprehensive lupus clinic. Peripheral blood mononuclear cells (PBMC), LDGs and normal dense neutrophils (NDN) were purified and then subjected to cellular indexing of transcriptomes and epitopes by sequencing (CITE-seq) via the 10x platform. Downstream analysis was performed with Cell Ranger and the Seurat package in R. Functional assays were performed.

Results: Six patients with SLE (3 male and 3 female) have been analyzed thus far. The average age in years was 36.7 and 36.3 for males and females, respectively. Average SLEDAI was 6.7 and 4.7 male and female, respectively. All patients were on less than or equal to 15 mg of daily prednisone. There was significant heterogeneity between males and females in neutrophil analysis by CITE-Seq compared to other immune cells. Overall, females had an increased proportion of a type I IFN-stimulated gene (ISG)^{hi} LDG cluster compared to males. Female LDGs had a higher IFN-I signature score. Female NDNs were similarly enriched in the ISG^{hi} cluster and also had a higher IFN-I score compared to males. Male LDGs and NDNs were enriched in less mature neutrophil clusters. Other cell types did not display as much heterogeneity.

Conclusion: These preliminary results show sex differences in SLE by single cell transcriptomics with much of the heterogeneity arising from the neutrophils. More patients are currently being recruited to further understand neutrophil heterogeneity and functional implications in male and female lupus. This information may provide insight into SLE heterogeneity between sexes and could lead to stratified lupus treatments.

Disclosure: W. Ambler: None; **G. Wigerblad**: None; **E. Patino-martinez**: None; **S. Nakabo**: None; **N. Hanata**: None; **S. Brooks**: None; **K. Jiang**: None; **C. Carmona-Rivera**: None; **M. Kaplan**: AstraZeneca, 5, Bristol Myers Squibb, 5, Cytrill, 2, Neutrolis, 2.

Abstract Number: 0903

Effects of Hydroxychloroquine on Maternal Outcomes in Pregnant Patients with Systemic Lupus Erythematous

Yurilu Gonzalez[1] and Irene Tan[2], [1]Albert Einstein Medical Center, Wyncote, PA, [2]Einstein Medical Center Philadelphia, Bala Cynwyd, PA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease, that affects women of childbearing age. SLE is a high-risk condition in pregnant patients due to increased maternal and fetal mortality and morbidity. Hydroxychloroquine (HCQ) has demonstrated beneficial effects on pregnancy outcomes in patients with SLE based on

Table 1. Pregnancy outcomes of women with systemic lupus erythematosus grouped by Hydroxychloroquine usage

	HCQ n=9805	Non HCQ n=8869	OR (95% CI) p value
Recurrent pregnancy loss/spontaneous abortion	118	151	0.77 (0.60-0.98) p=0.03
Gestational DM	113	161	0.69 (0.54-0.88) p=0.003
Prolonged pregnancy	35	84	0.41 (0.27-0.61) p<0.0001
Fetal malpresentation	188	200	0.94 (0.76-1.15) p=0.55
Hypertensive disorders of pregnancy [a]	460	430	1.12 (0.98-1.29) p=0.08

Abbreviations: CI, confidence interval; HCQ, hydroxychloroquine; OR, odds ratio.

[a]Hypertensive disorders in pregnancy denotes any diagnosis of preeclampsia, eclampsia, chronic hypertension, preeclampsia superimposed upon chronic hypertension and gestational hypertension.

Pregnancy outcomes of women with systemic lupus erythematosus grouped by hydroxychloroquine usage

immunomodulatory, metabolic, and vasculoprotective properties. This study aims to describe the effects of HCQ use on maternal outcomes in pregnant SLE patients.

Methods: This is a nationwide, cross-sectional study. We used the global, multicenter research network (TriNetX) database from 82 large healthcare organizations across multiple countries. We included pregnant women from age 18 to 55 with diagnosis of SLE between January 1^{st,} 2010, and December 31^{st,} 2022 using International Classification of Disease-10 codes. We compared pregnant SLE patients on HCQ with pregnant-SLE patients not on HCQ, using a 1:1 propensity score matching that accounted for demographics variables (age, race, ethnicity), comorbidities [hypertension, overweight/obesity, diabetes mellitus (DM), dyslipidemias], laboratory results, including levels of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), cholesterol, triglycerides, hemoglobin A1C (HbA1c) and use of steroids (prednisone or prednisolone) at baseline. The outcomes of interest include recurrent pregnancy loss/spontaneous abortion, hypertensive disorders of pregnancy, gestational DM, prolonged pregnancy, and fetal malpresentation events. The exposure time window for outcomes was any time during the pregnancy duration. Odds ratios with 95% confidence intervals were calculated for each outcome. A two-sided p-value less than 0.05 was considered statistically significant.

Results: We identified 9,805 pregnant SLE patients on HCQ and 8,869 pregnant SLE patients not on HCQ. At baseline, patients who were not taking HCQ, had higher levels of CRP (14.1±31.4 vs 11.4±28.7 mg/L, p=0.002), cholesterol (174 ±41.3 mg/dL vs 171±44.8 mg/dL, p=0.02), triglycerides (125±113 mg/dL vs 118±85.6 mg/dL, p=0.02) and HbA1c (5.71 ±1.54% vs 5.57±1.19%, p=0.001). When compared both groups, the odds of developing recurrent pregnancy loss/spontaneous abortion (OR=0.77, CI95% 0.60-0.98, p=0.03), gestational DM (OR=0.69, CI95% 0.54-0.88, p=0.003) and prolonged pregnancy (OR=0.41, CI95% 0.27-0.61, p< 0.0001), were significantly lower among patients taking HCQ, whereas the odds of developing fetal malpresentation (OR=0.94, CI95% 0.76-1.15, p=0.55) and hypertensive disorders of pregnancy (OR=1.12, CI95% 0.98-1.29, p=0.08) was not statistically different when compared both groups.

Conclusion: Pregnant patients with SLE taking HCQ appear to have lower odds of recurrent pregnancy loss/spontaneous abortion, gestational DM, and prolonged pregnancy compared with ones not taking HCQ. Larger studies, preferably randomized and blinded, will be required to confirm these findings.

Disclosure: Y. Gonzalez: None; **I. Tan**: None.

Abstract Number: 0904

KYV-101, a Fully Human Anti-CD19 CAR T Cell Therapy, Demonstrates CAR-Mediated and CD19-Dependent Activity Against Autologous B Cells from Patients with Autoimmune Disease

Soo Park[1], Gloria Lutzny-Geier[2], Natalia Giltiay[1], Jazmin Bravo[1], Simone Sandoval[1], Joseph Cheng[1], Catherine Dong[1], Nicole Khoshnoodi[1], Ames Register[1], Daniel Anaya[1], Michael Aigner[3], Andreas Mackensen[3], Georg Schett[4], Charles Kaplan[1], Dominic Borie[1], James Chung[1] and Tom Van Blarcom[5], [1]Kyverna Therapeutics, Emeryville, CA, [2]Friedrich Alexander Universität Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany, [3]Department of Internal Medicine 5, Hematology and Oncology, Universitätsklinikum Erlangen and Friedrich-Alexander-Universität Erlangen Nürnberg, Erlangen, Germany, [4]Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany, [5]Kyverna Therapuetics, Emeryville, CA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Etiology & Pathogenesis Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: A significant unmet need remains in the treatment of relapsed and/or refractory B cell-driven autoimmune diseases, including systemic lupus erythematosus (SLE),systemic sclerosis (SSc), and idiopathic inflammatory myopathy (IIM). The presence of autoantibodies is a hallmark of such diseases and implicates dysregulated B cell function in their pathogenesis. The central role of B cells in these diseases is also supported by the presence of B cells in diseased tissues. We have recently shown that anti-CD19 chimeric antigen receptor (CAR) T cells are well tolerated and highly effective in patients with B cell-driven autoimmune diseases including SLE, IIM,and SSc (Mackensen Nat Med 2022, Muller Lancet 2023, Bergman Ann Rheum Dis 2023).KYV-101 is an autologous anti-CD19 CART cell therapy designed to deplete B cells, including autoreactive B cells. Importantly, the human anti-CD19 CAR used in KYV-101 was previously tested in B-cell lymphoma patients and demonstrated similar efficacy with an improved safety and immunogenicity profile compared to historical controls (Brudno Nat Med 2020).Since anti-CD19 CART cells target and kill a broad set of B cells in both circulation and tissues, a more complete depletion of autoreactive B cells is expected with KYV-101 leading to a greater magnitude and durability of disease control than current immunotherapies. These studies examined the CAR-mediated and CD19-dependent activity ofKYV-101 against autologous, patient-derived B cells.

Methods: Autologous CD4+ and CD8+ T cells were enriched from healthy donors (HD) or SLE, SSc, or IIMpatients.KYV-101 CAR T cells were produced following transduction with a lentiviral vector encoding a fully human second generation anti-CD19 CAR. The CAR-mediated and CD19-dependent activity of KYV-101 was monitored in vitrovia cytotoxicity, cytokine release, and proliferation studies in response to CD19+ target cell lines or autologousCD19+ B cells.

Results: Following an overnight incubation, KYV-101 generated from HDs or autoimmune patients induced greater cytotoxicity against both the human CD19+ NALM6 cell line and autologous, patient-derived primary B cells than untransduced(UNTD) control T cells. An increase in the production of cytokines such as IFNγ was also observed following co-culture. In contrast, no differences in cytotoxicity nor cytokine production were observed whenKYV-101 or UNTD control T cells were co-cultured with CD19- target cell lines. In addition, following a 96-hour incubation, KYV-101 generated from HDs or autoimmune patients proliferated when co-cultured with the NALM6 cells or autologous B cells, whereas substantially lower levels of proliferation were observed in the UNTD control T cells co-cultured with NALM6 or autologous B cells, or in KYV-101 and UNTD control T cells co-cultured with the CD19- cell lines.

Conclusion: KYV-101 generated from autoimmune disease patient lymphocytes demonstrates CAR-mediated and CD19-dependent activity against autologous B cells and thus may represent a novel therapeutic option for B cell-driven autoimmune diseases. KYV-001 is being investigated in a Phase 1 trial in adults with refractory lupus nephritis. *Soo Park and Gloria Lutzny-Geier contributed equally.

Disclosure: S. Park: Kyverna Therapeutics, 3; **G. Lutzny-Geier**: Gilead, 5, Kyverna Therapeutics, 5; **N. Giltiay**: Kyverna Therapeutics, 3; **J. Bravo**: Kyverna Therapeutics, 3; **S. Sandoval**: Kyverna Therapeutics, 3; **J. Cheng**: Kyverna Therapeutics, 3; **C. Dong**: Kyverna Therapeutics, 3; **N. Khoshnoodi**: Kite Pharma, a Gilead Company, 3, Kyverna Therapeutics, 3; **A. Register**: Genentech, 3, Kyverna Therapeutics, 3; **D. Anaya**: Daniel Anaya, 3; **M. Aigner**: Kosmas Therapuetics, 8, Kyverna, 5, Miltenyi Biomedicine, 2, 7, Miltenyi Biotec, 6; **A. Mackensen**: BioNTech, 1, Bristol-Myers Squibb(BMS), 1, KITE/Gilead, 1, 6, Kyverna, 5, Miltenyi Biotech, 5; **G. Schett**: None; **C. Kaplan**: Kyverna Therapeutics, 3; **D. Borie**: Kyverna Therapeutics, 3; **J. Chung**: Kyverna Therapeutics, 3; **T. Van Blarcom**: Allogene Therapeutics, 3, Kyverna Therapeutics, 3.

Abstract Number: 0905

Low-Density Granulocytes and Neutrophil Extracellular Traps in Incomplete Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Incomplete SLE (iSLE) defines a group of patients with symptoms typical of SLE but not meeting sufficient criteria required for the classification of SLE. Up to 55% of patients with iSLE will eventually develop SLE, but it is unclear which patients are at risk of progression.(1) Neutrophil dysfunction, among which aberrant neutrophil extracellular trap (NET) formation driven by low density granulocytes (LDGs), has been implicated in SLE pathogenesis.(2) However, the role of neutrophil dysfunction in early forms of SLE is still unclear. Therefore, the aim of this study was to investigate whether LDGs are elevated in iSLE patients, compared to healthy controls (HCs) and SLE patients with quiescent disease (SLEDAI $\leq$ 4). Next to that, we investigated presence of circulating NETs in plasma of iSLE as well as SLE patients and HCs.

Methods: Circulating plasma NETs were measured cross sectionally in 38 iSLE patients, 30 SLE patients with quiescent disease and 12 HCs while LDGs were measured in 18 iSLE patients, 13 SLE patients and 14 HCs. SLE patients were classified according to the Systemic Lupus International Collaborating Clinics (SLICC) criteria. Patients with iSLE had to meet at least one clinical and one immunological criterion but less than four SLICC criteria in total. LDGs ($CD14^{low}CD15^{+}$) were measured in freshly isolated PBMCs with flow cytometry and were expressed as percentage of total PBMCs. Circulating plasma NETs were measured with a sandwich enzyme linked immunosorbent assay using a plate coated with an anti-myeloperoxidase antibody.

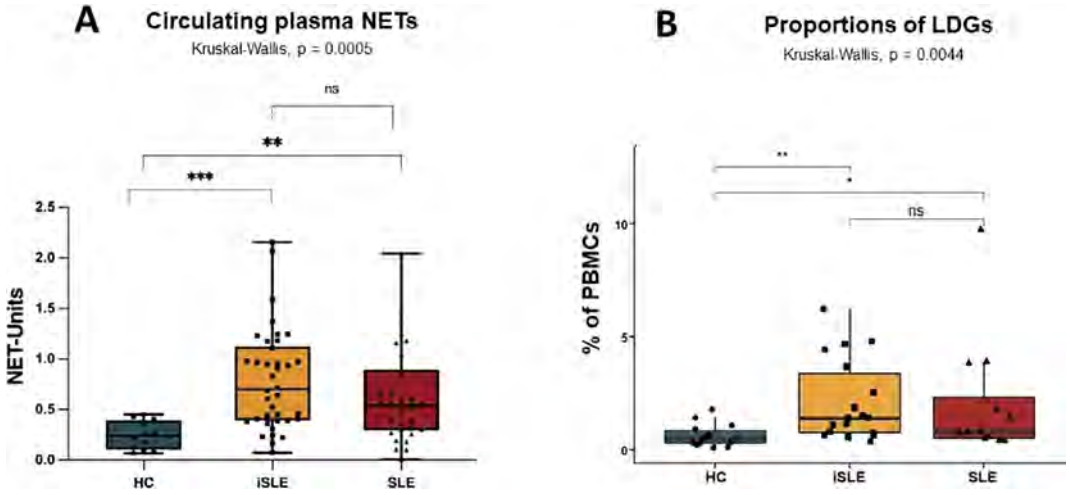

Figure 1. A: Circulating plasma NETs (neutrophil extracellular trap) per group measured with enzyme linked immunosorbent assay. B: Low density granulocytes (LDGs) measured with flow cytometry; Single data points represent individual cases. Median and interquartile range are depicted per group. Stars represent p-values for pairwise comparison calculated with Mann Whitney tests. *p <0.05, ** p<0.01, *** p<0.0001. HCs: healthy controls; iSLE: incomplete systemic lupus erythematosus, SLE: systemic lupus erythematosus.

Results: Proportions of LDGs and NET-levels were significantly increased in iSLE patients compared to HCs, as shown in Figure 1. The proportion of LDGs and circulating plasma NETs was similar between SLE and iSLE patients.

Conclusion: Our data shows significantly higher amounts of LDGs and circulating NETs in the iSLE and SLE cohort compared to healthy controls, suggesting that aberrant NET formation and clearance is present in early stages of the disease. In future studies, we aim to investigate the correlation between LDGs, circulating NETs and other immunological parameters, such as interferon signature, and anti-dsDNA levels.

(1) Lambers WM, Westra J, Bootsma H, de Leeuw K. From incomplete to complete systemic lupus erythematosus, A review of the predictive serological immune markers. Vol. 51, Seminars in Arthritis and Rheumatism. W.B. Saunders; 2021. p. 43–8.

(2) Kaplan MJ. Neutrophils in the pathogenesis and manifestations of SLE. Vol. 7, Nature Reviews Rheumatology. 2011. p. 691–9.3

Disclosure: S. Henning: None; **T. Reimers**: None; **B. Doornbos-van der Meer**: None; **B. Horvath**: None; **H. Bootsma**: None; **K. de Leeuw**: None; **J. Westra**: None.

Abstract Number: 0906

Paired Autoantibody Specificities from Serum and Immune Complexes Do Not Fully Explain the Circulating Immune Complex Load in Systemic Lupus Erythematosus: A Study on 530 Patients

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a prototypical autoimmune disease where autoantibody production and immune complex (IC) formation play a key role. Which antibodies contribute to the load of circulating C1q-binding ICs (CIC) in SLE is still unclear. We investigated whether either serum and/or IC-derived levels of typical SLE antibodies could explain the observed CIC levels of a large SLE cohort.

Methods: We studied n=530 consecutive SLE patients (≥ 4 ACR 1982 revised SLE criteria) who received care at a tertiary referral center for SLE. The control population consisted of region of residence, age and sex-matched controls (n=192) and n=200 local experimental controls. Serum was obtained at inclusion, and was stored at -80°C. To obtain IC-derived antibodies, a novel validated method was employed. Briefly, aliquots of sera were incubated with C1q-coated beads and C1q-bound ICs were then eluted through two sequential buffers, yielding disassembled IC eluates with conserved antibody specificity (Sohrabian et al. Ann Rheum Dis 2018;77:1345). Antibody levels of Anti-dsDNA, Anti-Histone, Anti-Sm, Anti-U1RNP, Anti-Ro52, Anti-Ro60, Anti-SSB were measured in IC eluates and in serum with a bead-based multiplex assay. Parallel analyses of autoantibody levels in serum and in IC eluates were performed. CIC levels were measured with a commercial ELISA according to the manufacturer's instructions. Results were reported on a standard curve; the 98th percentile of the standard curve values of control sera were set as the threshold for positivity in serum and IC respectively.

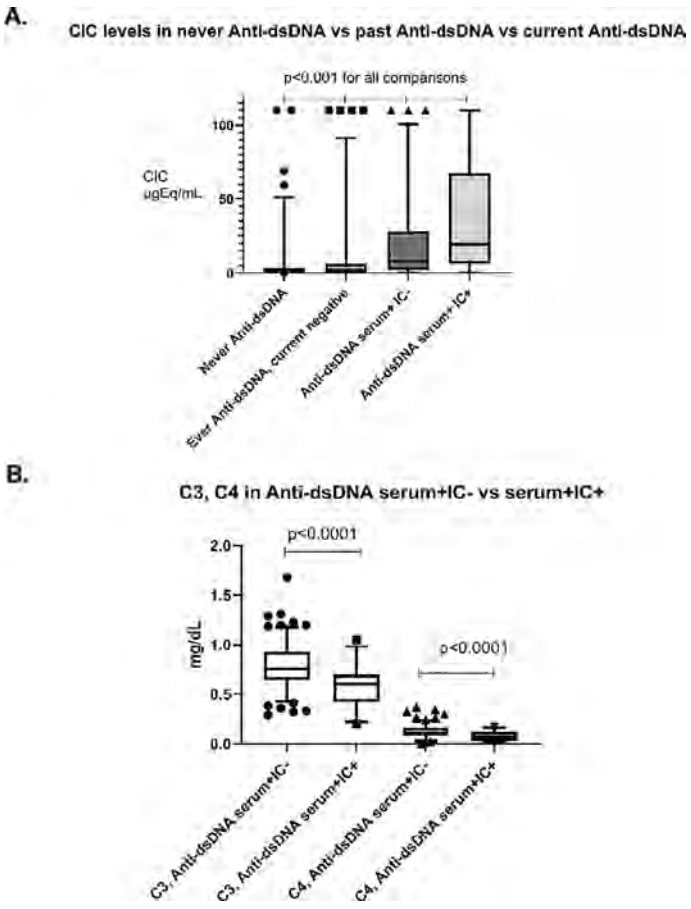

Figure 1 A. and 1 B.

Results: CIC levels were higher and with a wider variance in SLE patients than controls (p< 0.0001). A higher CIC load was associated with nephritis, arthritis and SLEDAI > 6 (p< 0.0001). Among autoantibody specificities, Anti-dsDNA in serum was independently associated with a high CIC load (OR 4.8, 95% CI 2.5-9.5, p< 0.0001, Figure 1 A). Concordance between serum and IC-eluate positivity varied strongly among autoantibody specificities, being highest for Anti-SSA/SSB, and lowest for Anti-dsDNA (Table 1). Among serum Anti-dsDNA+ patients, carriers of Anti-dsDNA from ICs displayed higher Anti-dsDNA titers, lower complement levels, and higher SLEDAI scores (p< 0.01 for all, Figure 1 B). Despite this, anti-dsDNA from ICs had a limited, although significant, explanatory power for total CIC levels (Figure 2).

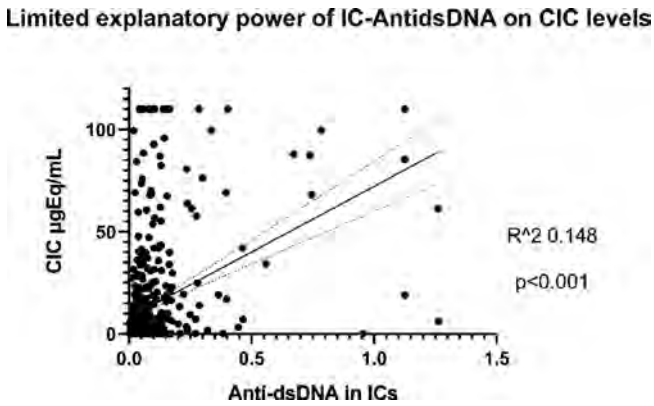

Figure 2

Table 1

	Of which Anti-Ro52 IC +, %	Of which Anti-Ro60 IC +, %	Of which Anti-SSB IC +, %	Of which Anti-Sm IC +, %	Of which Anti-U1RNP IC +, %	Of which Anti-dsDNA IC +, %	Of which Anti-Histone IC +, %
Anti-Ro52+ sera n= 139	**84.9%**	90.6%	56.8%	17.9%	23.7%	12.2%	16.5%
Anti-Ro60+ sera n= 192	62%	**94.3%**	49.5%	17.2%	22.4%	13%	17.7%
Anti-SSB+ sera n= 95	**74.7%**	90.5%	**91.6%**	13.7%	16.8%	15.8%	17.9%
Anti-Sm+ sera n= 88	39.7%	47.7%	26.1%	**45.5%**	54.5%	31.8%	32.9%
Anti-U1RNP+ sera n=99	29.3%	35.4%	17.2%	32.3%	**66.7%**	17.2%	23.2%
Anti-dsDNA+ sera n= 196	27.6%	38.8%	21.9%	16.8%	28%	**20.9%**	30.1%
Anti-Histone+ sera n=160	32.5%	42.5%	23.8%	19.4%	30.6%	21.9%	**38.1%**

Conclusion: Anti-dsDNA indicates the capacity to assemble immune complexes in SLE patients, and recoverable Anti-dsDNA antibodies from IC eluates are associated with more complement activation and disease activity. Importantly, Anti-dsDNA, either alone or in combination with common ANA specificities, has a limited explanatory power for the variation in CIC levels among different SLE patients, i.e. it is unlikely to form the majority of the observable CIC in SLE. The constituents of the circulating immune complex load in SLE remain elusive and deserve further elucidation.

Disclosure: E. Fuzzi: None; **A. Svanqvist**: None; **C. Westerberg**: None; **A. Zickert**: None; **I. Gunnarsson**: None; **J. Rönnelid**: None; **E. Svenungsson**: None.

Abstract Number: 0907

Epstein Barr Virus Reactivation May Associate with Transition from Incomplete to Systemic Lupus Erythematosus

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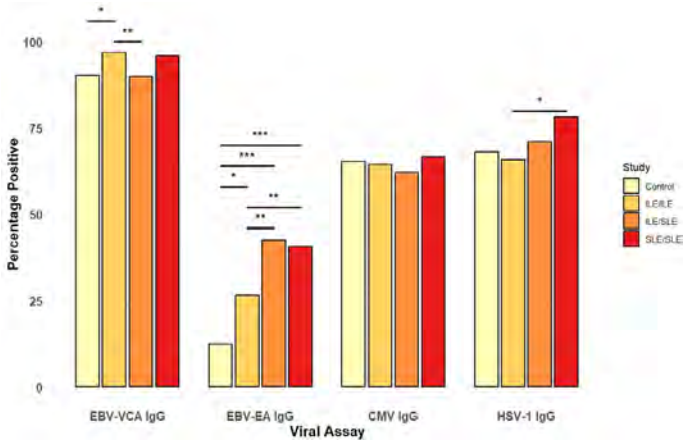
SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with incomplete lupus erythematosus (ILE) have evidence of SLE but do not fulfill SLE classification criteria. Although most ILE patients maintain a relatively mild disease course, about 20% will transition to SLE. However, the factors influencing SLE development in subsets of ILE patients are largely unknown. We previously found that serological markers of EBV reactivation, measured by antibodies against EBV-early antigen (EBV-EA), were associated with increased numbers of SLE-associated autoantibodies and eventual SLE transition in SLE relatives. In addition, EBV reactivation is associated with increased disease activity in SLE patients. Therefore, this study determined whether reduced EBV

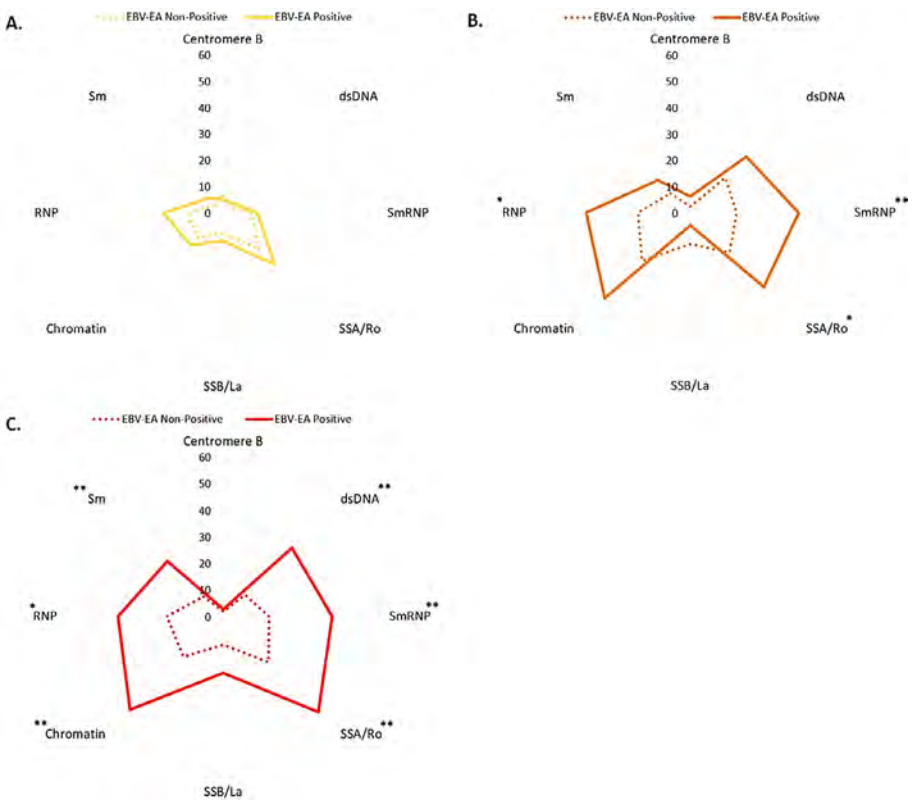


Percentage of positive viral assay results in controls (n=72), ILE/ILE (n=286), ILE/SLE (n=148), and SLE (n=173). * $p < 0.05$, **$p < 0.01$, *** $p < 0.001$ by Fisher's exact test with a Benjamini-Hochberg correction.

reactivation contributes to milder disease course in ILE and whether increased EBV reactivation may influence transition to SLE in ILE patients.

Methods: Serum samples consented for use in these studies were obtained from existing collections in the Arthritis & Clinical Immunology Biorepository at the Oklahoma Medical Research Foundation. Healthy controls (n=72) were ANA-negative with no ACR 1997 criteria. ILE/ILE subjects (n=286) met less than 4 ACR criteria and were categorized as ILE by SLICC criteria. ILE/SLE subjects (n=148) met less than 4 ACR criteria but met SLE classification by SLICC criteria. SLE subjects (n=173) were classified as SLE by both ACR and SLICC criteria. Subjects were matched by age, sex, and ancestry. Serum autoantibodies against dsDNA, chromatin, SSA/Ro, SSB/La, Sm, SmRNP, RNP, and centromere-B were determined by BioPlex 2200® ANA kit. Serum antibodies against EBV-Viral Capsid Antigen (VCA), EBV-EA, CMV, and HSV-1 were determined by ELISA.

Results: EBV-EA positivity was more prevalent in ILE/ILE, ILE/SLE, and SLE patients compared to controls (Figure 1). However, EBV-EA positivity was less prevalent in ILE/ILE compared to ILE/SLE and SLE patients (Figure 1). EBV-VCA positivity was more prevalent in ILE/ILE compared to controls or ILE/SLE, but neither ILE/SLE nor SLE significantly differed from controls, consistent with previous studies (Figure 1). In contrast, CMV and HSV-1 positivity did not differ between the groups, except for a slight increase in SLE patients compared to ILE/ILE patients (Figure 1). In ILE/ILE patients, SLE-associated autoantibodies were not associated with EBV-EA positivity (Figure 2A). However, EBV-EA positivity was associated with anti-SmRNP, -SSA/Ro, and -RNP autoantibodies in ILE/SLE patients (Figure 2B). In addition to these autoantibodies, EBV-EA positivity also associated with anti-dsDNA, -chromatin, and -Sm in SLE patients (Figure 2C).



Percentage of positive autoantibody results according to EBV-EA result in (A) ILE/ILE (n=286) (EBV-EA Positive n = 176, Non-Positive n = 210), (B) ILE/SLE (n=148) (EBV-EA Positive n = 63, Non-Positive n = 85), and (C) SLE (n=173) (EBV-EA Positive n = 71, Non-Positive n = 102). * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ by Fisher's exact test with a Benjamini-Hochberg correction.

Conclusion: Serological markers of EBV reactivation are lower in ILE/ILE patients compared to ILE/SLE and SLE patients, suggesting that reduced EBV reactivation may contribute to the milder disease course observed in ILE patients. In addition, EBV-EA positivity was associated with SLE-associated autoantibodies in ILE/SLE patients but not ILE/ILE patients. EBV-EA positivity correlated with positivity for a higher number of SLE-associated autoantibodies in SLE patients compared to those with ILE/SLE. Therefore, increased EBV reactivation may be a harbinger of disease transition in ILE patients.

Disclosure: B. Jones: None; **C. Guthridge**: None; **M. Beel**: None; **C. Wagner**: None; **S. Kamp**: None; **C. Arriens**: AstraZeneca, 1, 5, 6, Aurinia, 6, Bristol-Myers Squibb, 1, 5, Cabaletta, 1, GSK, 1, Kezar, 1, UCB, 1; **J. Merrill**: AbbVie, 2, Alexion, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, Bristol Myers Squibb, 2, 5, EMD Serono, 2, Genentech, 2, Gilead, 2, GlaxoSmithKline, 2, 5, Lilly, 2, Merck, 2, Pfizer, 2, Provention, 2, Remegen, 2, Sanofi, 2, UCB Pharma, 2, Zenas, 2; **T. Aberle**: None; **N. Redinger**: None; **R. Wood**: None; **L. Guthridge**: None; **S. Macwana**: None; **W. DeJager**: None; **J. Guthridge**: None; **J. James**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 2, Novartis, 2, Progentec Biosciences, 5.

Abstract Number: 0908

Association of Biologic Sex with Glycosphingolipids and the N-glycome in Lupus Nephritis and Renal Mesangial Cell Function

Tammy Nowling, bethany wolf, Calvin Blaschke, Richard Drake, Sandra Sanchez, Mariia Stefanenko, Mykhailo Fedoriuk, Oleg Palygin, Hongxia Bai and Jessalyn Rodgers, Medical University of South Carolina, Charleston, SC

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE primarily afflicts women and many SLE patients develop nephritis, a serious complication of lupus. Identification of biomarkers and the pathogenic mechanisms underlying LN is crucial to better understand sex bias and disease progression. Therefore, we interrogated glycosphingolipid (GSL) metabolism and the N-glycome with respect to disease and biologic sex in LN patient samples. We also evaluated response of human primary renal mesangial cells (hRMCs) with respect to disease and biologic sex.

Methods: Urine and serum were collected from 20 healthy control (HC) subjects and 20 LN patients who met the ACR criteria for active disease. Ten males and 10 females were included in each group. N-linked glycans attached to proteins (N-glycans) were measured by matrix-assisted laser desorption/ionization quadrupole time of flight (MALDI-QTOF) and the GSL lactosylceramide (LacCer) was quantified by *Supercritical fluid chromatography-tandem mass spectrometry* (SFC-MS/MS). Responses of male- and female-derived hRMCs to treatment with sera from each LN or HC subject were assessed by measuring intracellular calcium (Ca^{2+}) using fluor8 indicator, cytokine secretion by ELISA, GSLs levels by SFC-MS/MS, and N-glycans by MALDI-QTOF. Associations between N-glycans with LN status and biologic sex were evaluated using linear mixed models.P-values were adjusted using False Discover Rate with < 0.05 considered meaningful.

Results: All major LacCer species and total LacCers were significantly elevated and 72 urine N-glycans were significantly altered in LN patients compared to HCs. In particular, there was a significant increase in the N-glycans associated with pro-inflammatory IgGs and a decrease in N-glycans associated with anti-inflammatory IgGs in the urine of LN patients. The increase in urine LacCers (LN vs HC) was 2-3 fold higher in males, and three urine N-glycans differed significantly

between the sexes. Three individual N-glycans provided perfect separation of LN and HC (AUC of 1.0) when added to a model that included only total LacCers and biologic sex. In the serum, 2 of the major LacCer species and 21 N-glycans were significantly altered in LN compared to HC. *In vitro*, no differences were observed in the responses of hRMCs to female- vs male-derived sera. However, the female-derived hRMCs exhibited significantly higher Ca^{2+} flux and cytokine secretion compared to male-derived hRMCs in response to LN sera. The female-derived hRMCs expressed higher levels of GSLs than the male-derived hRMCs.

Conclusion: Urine LacCers levels and changes in the N-glycome may serve as robust biomarkers of LN and likely reflect renal disease activity. The larger increase in LacCers in LN males compared to LN females may underscore worse renal disease in males once tolerance is broken. The significantly higher levels of LacCers observed in the female-derived hRMCs may partly explain the heightened pathologic response. Thus, elevated GSL metabolism in females may poise renal cells to be more sensitive to or respond more robustly to inflammatory stimuli.

Disclosure: T. Nowling: None; **b. wolf**: None; **C. Blaschke**: None; **R. Drake**: None; **S. Sanchez**: None; **M. Stefanenko**: None; **M. Fedoriuk**: None; **O. Palygin**: None; **H. Bai**: None; **J. Rodgers**: None.

Abstract Number: 0909

Rab4A Controls the Depletion of IL-2 in CD4+ T Cells via Enhanced CD38 Expression: Potential Involvement in Proinflammatory Lineage Development in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: HRES-1/Rab4 (Rab4A) is a small GTPase that is overexpressed in SLE patient T cells[1,2], mediates the enhanced recycling of CD3 and CD4 cell surface receptors[1,2], and the activation of the mechanistic target of rapamycin (mTOR)[3]. Recently, increased expression of CD38[4], mTOR activation[5], and loss of IL-2 production[6,7] have been implicated in pro-inflammatory T cell development in SLE. In this study, we investigated the impact of Rab4A on the expression of CD38 and the secretion of IL-2 and characterized the impact of CD38 expression on the activation of mTOR in $CD4^+$ T cells.

Methods: To understand the cellular consequences of Rab4A overexpression, our lab has created unique Rab4A-mutant Jurkat cell lines, which contain GFP-expressing vector alone (control), doxycycline-inducible vectors that overexpress Rab4A ($Rab4A^{++}$) or the dominant-negative mutant $Rab4A^{S27N}$ ($Rab4A^{DN}$)[8]. We also CRISPR knocked out (KO) CD38 in these cell lines, leading to six different lines: (1) $Rab4A^{WT}$ $CD38^{WT}$, (2) $Rab4A^{WT}$ $CD38^{KO}$, (3) $Rab4A^{++}$ $CD38^{WT}$, (4) $Rab4A^{++}$ $CD38^{KO}$, (5) $Rab4A^{DN}$ $CD38^{WT}$, and (6) $Rab4A^{DN}$ $CD38^{KO}$. These cells were cultured with doxycycline and co-stimulated with anti-CD3 mAb (OKT3) and phorbol myristate acetate (PMA) to induce cytokine production[9]. Cell surface markers and cytokines were analyzed by flow cytometry and protein levels by western blot. NAD^+ levels were measured by LC-MS/MS. To understand the impact of CD38 expression on mTOR activation, we isolated peripheral blood mononuclear

cells from SLE patients (n=21) and age, sex, and race matched healthy controls (n=18). The cells were cultured for 24 hours with and without CD3/CD28 co-stimulation and were analyzed by flow cytometry.

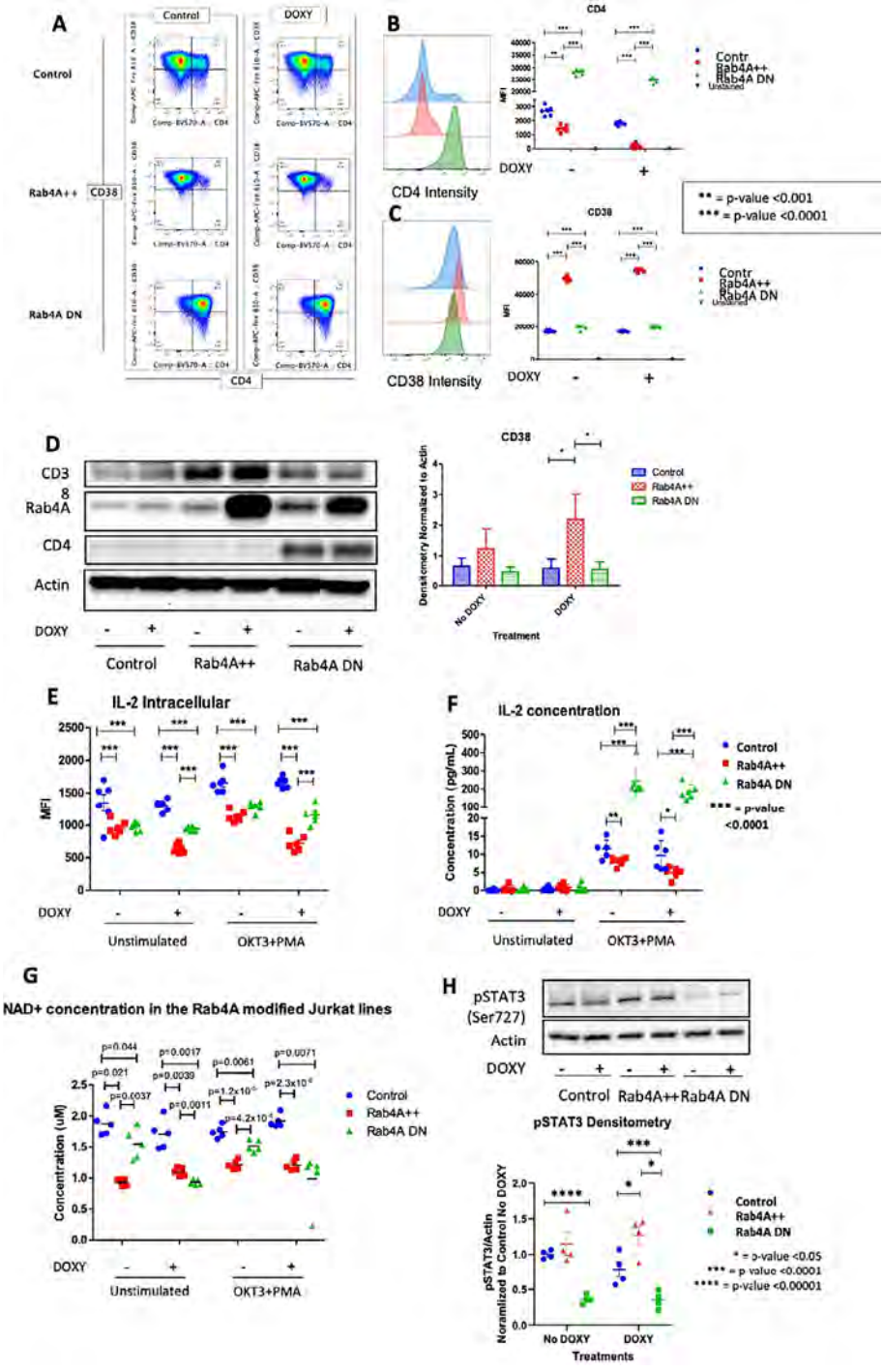


Fig. 1. Rab4A controls the surface expression of CD4 and CD38 in Jurkat cells. (A) Flow cytometry and (D) Western Blot results show that Rab4A++ cells have increased CD38 expression compared to the control and Rab4A-DN cells. Rab4A effects on CD4 expression is shown for confirmation. Quantified fluorescent intensity of (B) CD4 and (C) CD38. Rab4A controls the (E) intracellular expression and (F) production of IL-2, (G) NAD+ levels and (H) pSTAT3 (Ser727) levels in Jurkat cells. (E) Intracellular production and (F) secretion of IL-2 were significantly decreased in the Rab4A++ cells (fold change=-0.566, p=1.16x10-7 and fold change=-0.481, p=0.0401, respectively) compared to the control. In the Rab4ADN cells, IL-2 secretion was significantly increased (fold change=18.091, p=7.513x10-7, respectively). (G) LC-MS shows NAD+ is significantly decreased in in the Rab4A++ cells, compared to the control (doxycycline only: fold change=0.647, p=0.0039; doxycycline treated and stimulated: fold change=0.632, p=2.3x10-6). (H) In Rab4A++ cells, pSTAT3 is increased compared to the control (fold change=2.052, p=0.0318).

Results: In the Rab4A^{++} cells compared to the control, CD38 expression was upregulated ($p=2.49x10^{-13}$), intracellular production and secretion of IL-2 significantly decreased ($p=1.16x10^{-7}$ and $p=0.0401$, respectively), NAD^{+} concentration decreased ($p=0.0039$), while pSTAT3 levels increased ($p=0.0318$). In the Rab4A^{++} CD38^{KO} cells compared to the Rab4A^{++} CD38^{WT} cells, secretion of IL-2 significantly increased ($p=0.0145$) and pSTAT3 levels decreased. pAkt1 was increased

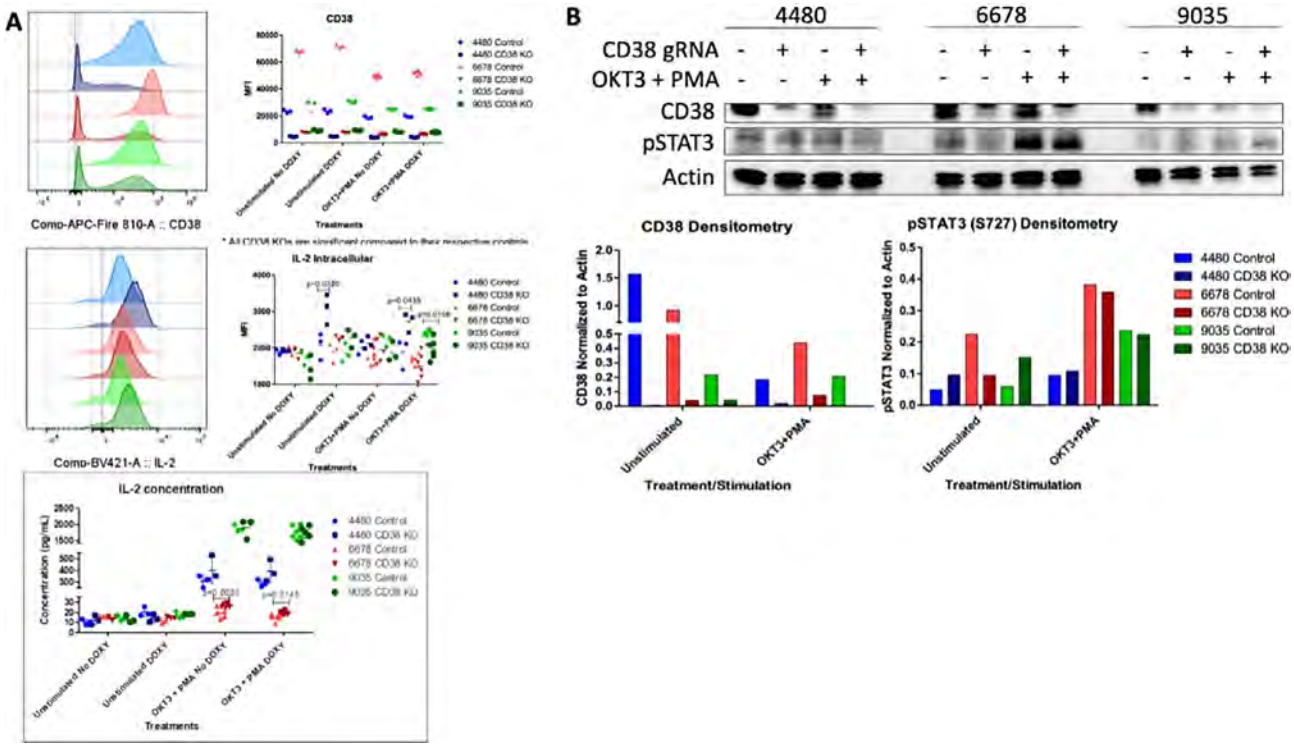


Figure 2. Knocking out CD38 in Rab4A-overexpressed Jurkat cells (A) increases IL-2 production ($p=0.0145$) and (B) decreases pSTAT3.

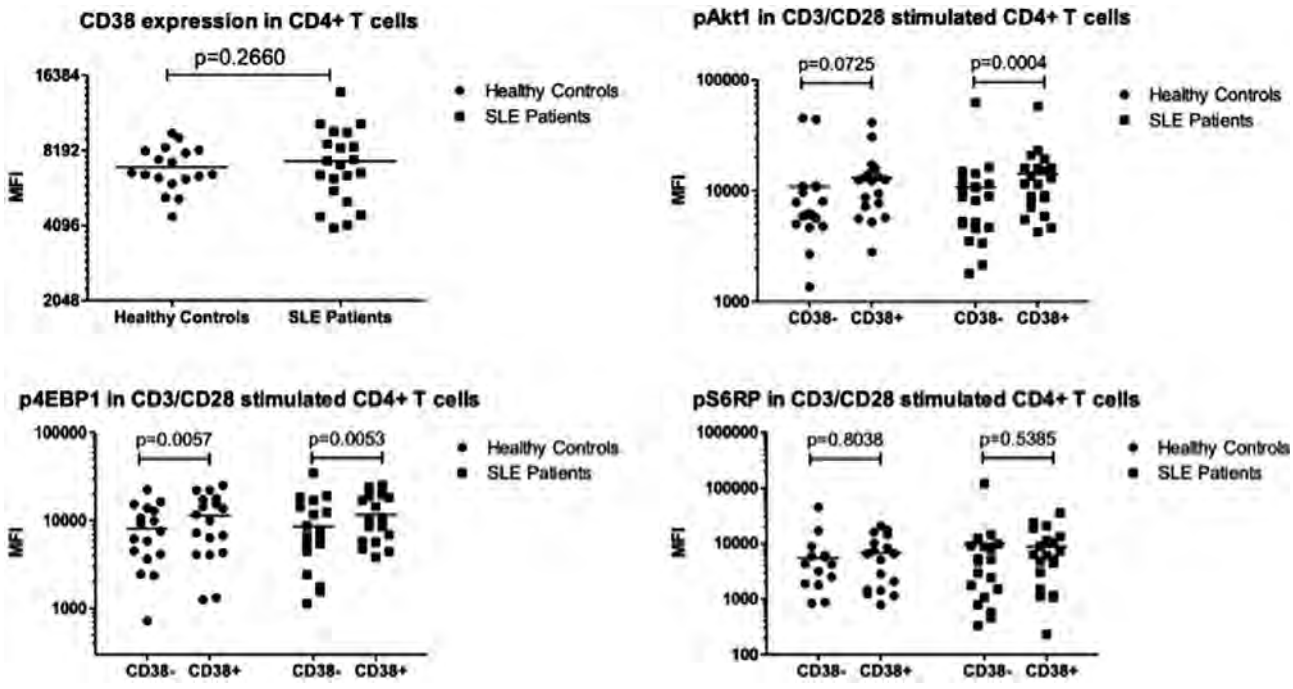


Figure 3. In SLE patients' CD38+ CD4+ T cells compared to CD38- CD4+ T cells, pAkt1 ($p=0.0004$) and p4EBP1 ($p=0.0053$) are increased.

significantly in CD38$^+$ CD4$^+$ T cells compared to CD38$^-$ CD4$^+$ T cells in only the SLE patients (p=0.0004), while p4EBP1 increased significantly in CD38$^+$ CD4$^+$ T cells compared to CD38$^-$ CD4$^+$ T cells for both the SLE patients (p=0.0053) and healthy controls (p=0.0057).

Conclusion: The increased pAkt1 and p4EBP1 in SLE patients' CD38$^+$ CD4$^+$ T cells suggests that CD38 activates mTOR via Akt, coinciding with a recent finding of CD38/PI3K/Akt/mTOR axis in cervical cancer[10]. CD38 is an NAD$^+$ hydrolase, which regulates Sirtuin-1 activity, a NAD$^+$-dependent histone deacetylase that suppresses STAT3 activity. STAT3 activation is also known to be regulated by mTOR[11–13]. Elevated pSTAT3 levels may underlie diminished IL-2 production by binding to the promoter of *FoxO1,* which inhibits IL-2 production. The overexpression of Rab4A, increased CD38, pAkt1, p4EBP1, and pSTAT3, and diminished IL-2 production reflect changes observed in SLE patients. Our results suggest that increased expression of Rab4A and CD38 may underlie the diminished secretion of IL-2 in SLE.

Disclosure: J. Park: None; **X. Wang**: None; **A. Godavarthy**: None; **A. Patel**: None; **K. Daniel**: None; **J. Nolan**: None; **J. Chilton**: None; **B. Blaker**: None; **A. Perl**: None.

Abstract Number: 0910

17β-estradiol and B-cell Intrinsic Type I Interferon Amplify Toll-like Receptor 7 Signaling Loop in B Cells of Female Lupus Prone BXD2 Mice

Kathryn Sullivan, Yong Wang, Winn Chatham, John Mountz and Hui-chen Hsu, University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: While systemic lupus erythematosus (SLE) disproportionally affects women versus men, elevation in estradiol (E2) alone is not sufficient to promote the development of autoantibody producing B cells. The objective of the present study is to determine if B-cell intrinsic mechanisms contribute to the increased TLR7 response to E2 stimulation.

Methods: Serum levels of E2 and anti-Smith (Sm), and expression of IFNb in naïve B cells were evaluated in African American (AA) SLE patients (24-41yr-old), compared to older AA (42-56yr-old) and European American SLE patients (24-66-yr-old). Similarly, serum levels of E2, anti-Smith (Sm), anti-DNA, and anti-Sm/RNP were compared between female lupus prone BXD2 mice post-puberty (12-wk-old) versus pre-puberty (4-6-wk-old). TLR7-induced expression of interferon-beta (IFNb) and CD69 in transitional stage 1 (T1: CD23$^-$IgM$^+$ CD93$^+$) B cells after stimulation with E2 with or without TLR7 agonist R848 were evaluated using female BXD2 mice, compared to male mice.

Results: We identified that there were elevated circulating levels of E2 in young African American (AA) SLE patients (24-41yr-old), compared to older AA (42-56yr-old) and European American SLE patients (24-66-yr-old). Circulating E2 levels positively correlated with the levels of anti-Smith (Sm) and the expression of IFNb in naïve B cells of SLE patients (n=39). Mouse studies were used to determine if E2 stimulates the expression of IFNb in B cells and if sex plays a role to influence B cell responses to E2.Serum levels of Sm/RNP and RNP autoAbs positively correlated with the levels of E2 in female lupus prone BXD2 mice post-puberty (12-wk-old) but not pre-puberty (4-6-wk-old).At the post-puberty stage (>12 wk-old), there were significantly elevated levels of anti-DNA and anti-Sm in female BXD2 mice, compared to male mice.This was associated with

an increased TLR7-induced expression of interferon-beta (IFNb) and CD69 in transitional stage 1 (T1: $CD23^{-}IgM^{+}$ $CD93^{+}$) B cells in female BXD2 mice, compared to male mice. Interestingly, E2 stimulation promoted intracellular levels of IFNb and TLR7 in T1 B cells from female but not male BXD2 mice.

Conclusion: Together, our results suggest that elevation of E2 in combination with an increased B-cell susceptibility to E2 induction of IFNb may play a role in the increased B cell responses to TLR7 stimulation in individuals predisposed to the development of SLE.

Disclosure: K. Sullivan: None; **Y. Wang**: None; **W. Chatham**: None; **J. Mountz**: None; **H. Hsu**: None.

Abstract Number: 0911

Spatial Transcriptomics Reveals Normal-density and Low-density Neutrophils Are More Prevalent Than Macrophages in Lupus Nephritis Glomeruli, and Urine DNA Methylation Analyses Capture Both Myeloid Populations

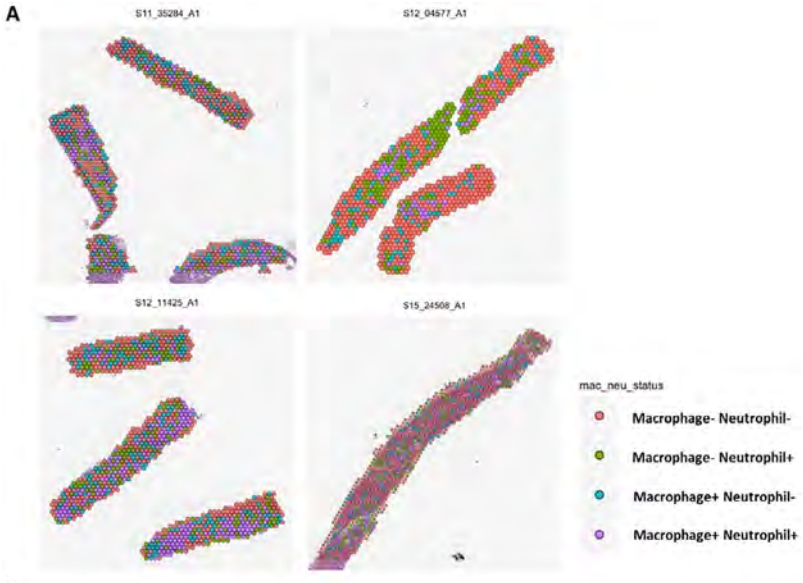
Sladjana Skopelja-Gardner[1], Joshua Skydel[2], Alecia Roy[3], Brenna Kerin[3], James Whitley[3], Fred Kolling[4], Noelle Kosarek[4], Michelle Petri[5], Andrea Fava[6], Lucas Salas[7] and Christopher Burns[3], [1]Department of Medicine, Dartmouth Hitchcock Medical Center, Geisel School of Medicine at Dartmouth, Lebanon, NH, [2]Dartmouth-Hitchcock Medical Center, Lebanon, NH, [3]Dartmouth Hitchcock Medical Center, Lebanon, NH, [4]Geisel School of Medicine at Dartmouth, Hanover, NH, [5]Department of Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Timonium, MD, [6]Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, [7]Department of Epidemiology, Geisel School of Medicine at Dartmouth, Lebanon, NH

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite compelling evidence that normal-density (NDN) and low-density neutrophils (LDN) are activated in the blood of lupus patients, their role in lupus nephritis (LN) remains elusive. This large gap in knowledge stems from the limitations in approaches to capture and profile neutrophils. Neither NDNs nor LDNs are usually captured in scRNAseq studies of LN kidneys and urine due to their loss by sample freezing, potentially skewing the conclusions that monocytes or macrophages are the dominant pathogenic myeloid cell population in LN.

Methods: Neutrophils were detected in LN kidneys by IHC staining of neutrophil elastase (NE, n = 19). Spatial transcriptomics was performed on class III/IV LN patients using Visium 10X Genomics. Differential expressed genes (DEGs) between neutrophils (NDN, LDN) and Mos were defined using publicly available RNAseq data. Spots containing NDNs, LDNs, and Mos and their glomerular vs tubular location were defined using Variance Adjusted-Mahalanobis to compute cell-specific pathway scores based on DEGs. Neutrophils and macrophages were quantified in urine cell pellets of SLE patients (+/- LN), collected at Dartmouth Hitchcock Lupus Clinic and the Johns Hopkins Lupus Center, by deconvolution of DNA methylation data (DNAm, Illumina EPIC).

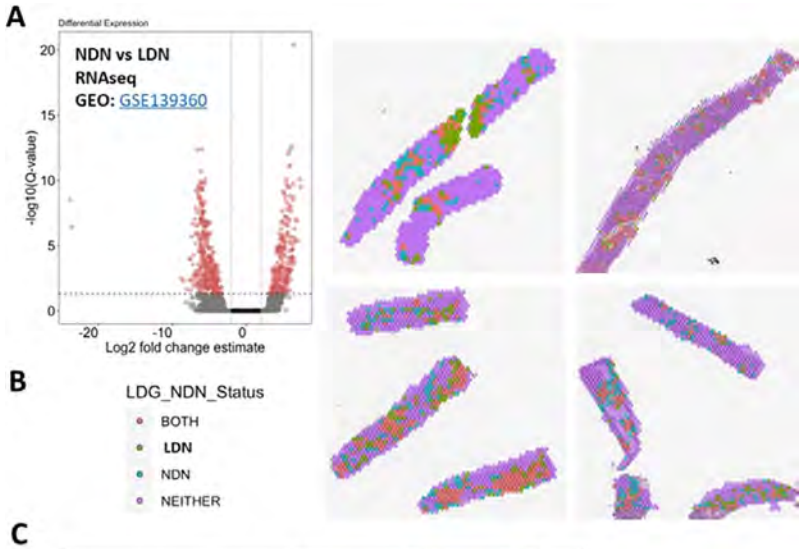
Results: Glomerular neutrophil numbers in LN kidneys (#NE+ cells/glomerulus) inversely correlated with serum C3 levels ($r = -0.671$, $^{**}p = 0.0056$), supporting a role for neutrophils in disease pathogenesis. Neutrophils were equally or more represented in LN kidneys compared to macrophages: 35% vs. 32% of all spots (**Fig. 1**). Macrophages preferentially localized



B

	Neutrophils	Macrophages
% All spots	35.1	31.9
% Tubular spots	10.1	27.6
% Glomerular Spots	88.4	40.8
% Interstitium	35.5	33.5

Fig. 1 Lupus Nephritis kidney spatial transcriptomics data reveal Macrophage and Neutrophil populations in situ. (A) Transcriptional pathways scores are defined by Variance Adjusted-Mahalanobis (VAM) method to compute cell specific pathway scores based on differentially expressed genes between neutrophils and macrophages on the 10x Visium (n = 4 LN class III/IV). (B) Percent NDN+ and LDN+ spots in LN kidney regions defined by VAM scores of unique gene signatures.



C

	NDN	LDN	Both
% Tubular spots	7.03	5.50	10.10
% Glomerular Spots	65.41	75.83	88.42
% Interstitium	26.95	19.16	35.50

Fig. 2 Both NDNs and LDNs localize to LN kidneys. (A) Differentially expressed genes between lupus NDNs and LDNs were defined using RNAseq data from the Mistry et al 2019 PNAS study (n = 6 samples per group). (B) Spots containing NDNs and LDNs were defined using Variance Adjusted-Mahalanobis (VAM) to compute cell-specific pathway scores based on differentially expressed genes in A. (C) Percent NDN+ and LDN + spots in LN kidney regions defined by VAM scores of unique gene signatures.

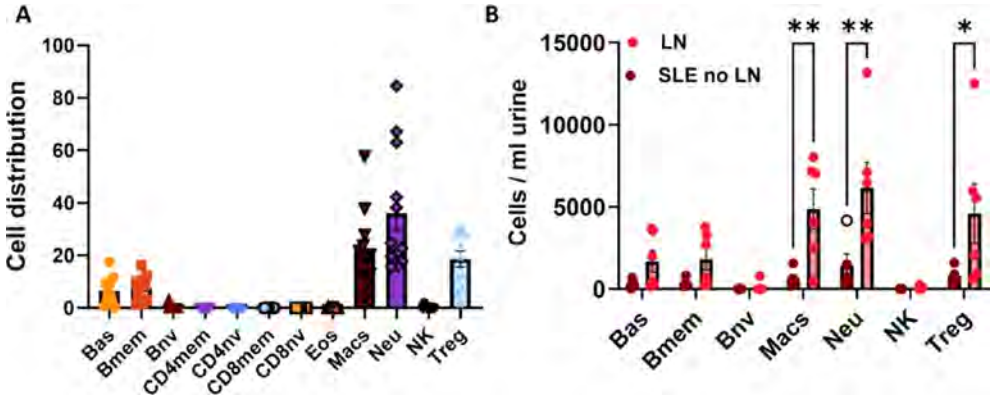


Fig. 3 Urine DNAm Deconvolution reveals (A) high Macrophage (Macs) and Neutrophil (Neu) cell distribution in lupus urine and (B) Increased Macs and Neu cells/ml urine in lupus (SLE) patients with LN vs. SLE patients without LN. One-way ANOVA, *p< 0.05, **p < 0.01

to the tubules vs. neutrophils (27% vs. 10%) but, strikingly, neutrophils localized to glomerular regions to a much greater extent (41% vs 88%). Similar interstitial distribution was found for both myeloid cell populations. Both NDNs and LDNs infiltrated LN tissues at comparable levels (**Fig. 2**). LDNs were the more predominant neutrophil population in the glomeruli: 76% LDN+ spots vs. 65% NDN+ spots. NDNs were the more predominant neutrophil population in both tubular and interstitial areas: 5% LDN+ spots vs. 7% NDN+ spots in tubules; 19% LDN+ spots vs. 27% NDN+ spots in the interstitium. The most prevalent NDN subtype in tubular regions was mature and transcriptionally quiescent neutrophils (Nh2), whereas immature and interferon+ NDNs were the prevalent subtype in glomeruli. DNAm analysis of urine cell pellets recapitulated high neutrophil and macrophage presence in LN kidneys (**Fig. 3**). Higher macrophage levels were found in urine cell pellets of SLE patients with active LN. There was a significant correlation between urine macrophage levels with UPCR (r = 0.64, **p = 0.008) and disease activity (SLEDAI >5, *p = 0.05).

Conclusion: Neutrophils, not only macrophages, are highly abundant in LN kidneys. Both NDNs and LDNs are highly prevalent myeloid cells in LN kidneys with predominantly glomerular localization. Spatial transcriptomics and urine DNA methylation approaches overcome the shortcomings of scRNAseq and are useful tools to define the pathogenic role of myeloid cells in LN.

Disclosure: S. Skopelja-Gardner: None; **J. Skydel**: None; **A. Roy**: None; **B. Kerin**: None; **J. Whitley**: None; **F. Kolling**: None; **N. Kosarek**: None; **M. Petri**: Alexion, 1, Amgen, 1, AnaptysBio, 1, Annexon Bio, 1, Argenx, 1, Arhros-Focus Med/Ed, 6, AstraZeneca, 1, 5, Aurinia, 1, 5, 6, Axdev, 1, Biogen, 1, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CVS Health, 1, Eli Lilly, 1, 5, Emergent Biosolutions, 1, Exagen, 5, Exo Therapeutics, 2, Gilead Biosciences, 2, GlaxoSmithKlein(GSK), 1, 5, 6, Horizon Therapeutics, 2, Idorsia Pharmaceuticals, 2, IQVIA, 1, Janssen, 1, 5, Kira Pharmaceuticals, 2, MedShr, 6, Merck/EMD Serono, 1, Momenta Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Proviant, 2, Sanofi, 2, Sinomab Biosciences, 2, Thermofisher, 5, UCB, 2; **A. Fava**: Annexon bio, 1, Sanofi, 1; **L. Salas**: None; **C. Burns**: None.

Abstract Number: 0912

Inadequate Screening for Antiphospholipid Syndrome with Antiphospholipid Antibodies in Patients with Systemic Lupus Erythematosus

tooba Munawar[1], Mahnoor Sherazi[2] and Andras Perl[3], [1]Upstate University Hospital, Jamesville, NY, [2]Upstate University Hospital, Syracuse, NY, [3]SUNY, Syracuse, NY

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Antiphospholipid Syndrome (APS) is classified into primary and secondary; the latter being associated with connective tissue disease. Systemic lupus erythematosus (SLE) is the most common cause of secondary APS, and the prevalence of antiphospholipid antibodies (APLAs), in patients with SLE is reported to be as high as 30% to 50% (1). The aim of our study was to determine what percentage of our SLE patients have had a complete APLA profile with or without thrombosis. We also looked at the timing these antibodies were obtained in regard to thrombotic events.

Methods: We reviewed EMR of patients with a diagnosis of SLE from 2012-2022. Data was obtained on presence or absence of antiphospholipid antibodies testing in these patients along with the timing of these tests in relation to thrombotic events. Deep vein thrombosis, Cardiovascular accidents, Pulmonary Embolism and History of Miscarriages were few of the thrombotic events included for review.

Results: A total of 5965 patient's charts were used for analysis. 5207 of these were females. Only 898 (15%) patients were found to have an entire antiphospholipid antibodies panel tested in them. 571 of SLE patients had a thrombotic event and 309 of these were without an APLA panel prior to the event. When number of SLE patients who had APLA testing done with and without thrombotic events were compared to those without APLA testing, the results were found to be statistically significant. (p value < 0.0001 ; Table 1).

Conclusion: Despite the increased risk of APS and thrombosis in patients with SLE, there is inadequate screening with antiphospholipid antibodies in these patients. Most of the times antibody testing in these patients is driven by a thrombotic event. We purpose an EMR alert to obtain antiphospholipid antibodies testing in all SLE patients who are without one to better categorize their risk of APS and thrombosis.

	SLE patients with thrombotic event	SLE patients without thrombotic event	Total
With APLA testing	262	636	898
Without APLA testing	309	4758	5067

Table 1- Number of SLE patients with APLA testing with and without thrombotic events as compared to those without it.

Two-tailed chi square p value < 0.0001

Disclosure: t. Munawar: None; **M. Sherazi**: None; **A. Perl**: None.

Abstract Number: 0913

Neutrophils in Patients with Systemic Lupus Erythematosus Show Pronounced Inflammatory Signals

Annie Law[1], Chee Jian Pua[2], Dianyang Guo[3], Chin Teck Ng[4], Julian Thumboo[1], Andrea Hsiu Ling Low[5] and **Xiubo Fan**[1], [1]Singapore General Hospital; Duke-NUS Medical School, Singapore, Singapore, [2]National Heart Centre, Singapore, Singapore, [3]Singapore General Hospital, Singapore, Singapore, [4]Singapore General Hospital; Duke-NUS Medical School, Singapore, Malaysia, [5]Department of Rheumatology and Immunology, Singapore General Hospital, Singapore, Singapore

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Etiology & Pathogenesis Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: IFN response, plasmablasts and neutrophils are three hallmarks of systemic lupus erythematosus (SLE). Studies showed that the netting neutrophils stimulated plasmacytoid dendritic cells to secret type I interferon directly and further promoted the expansion of plasmablasts indirectly, suggesting the upstream position of neutrophils in the pathogenesis of SLE. The blood transcriptomic profiling of human SLE, with a focus on lymphoid (T cells, B cells and NK cells) and partial myeloid (monocytes and dendritic cells) lineages, has been uncovered. However, due to the sample processing challenge – a rapid process of fresh blood sample for optimal cell quality, the transcriptomic profiling of neutrophils remains incomplete.

Methods: To determine cell-type specific signatures, we planned to decipher neutrophil transcriptional changes in human SLE using single cell RNA sequencing (scRNA-seq). Briefly, freshly isolated white blood cells from healthy controls (n = 3) and SLE patients (SLEDAI ≤ 4, n = 3) were collected for scRNA-sq sample preparation and sequencing with BD Rhapsody microwell-based single-cell partitioning technology. For data analysis, Scrublet was used for multiplet removal, BBKNN for batch correction, Python-based Scanpy pipeline for data pre-processing, visualization, clustering and differential expression testing and UMAP for data plotting.

Results: Neutrophils were clustered to 5 subpopulations (pre-neutrophils (PreNeu), early neutrophils (EarlyNeu), middle neutrophils (MidNeu), late neutrophils (LateNeu) and late IFN-expressing neutrophils (LateIFNNeu), according to Gustaf et al. In SLE patients (cases), the frequency of EarlyNeu in myeloid cells was markedly increased (48.7% vs 26.3%), whereas the frequencies of MidNeu (18.8% vs 25.4%), LateNeu (7.3% vs 13.3%), LateIFNNeu (10.4% vs 14.8%) were reduced compared to healthy controls. Gene set enrichment analyses were performed using hallmark gene sets to identify the possible pathophysiology of the disease. In line with our speculation, interferon (IFN-αand IFN-γ) response, inflammatory response and TNF-α/NF-κB signals were found to be enriched in cases for PreNeu, EarlyNeu and LateNeu. In addition, relative to controls, IL-6/JAK/STAT3 and apoptosis signals were enriched in cases for EarlyNeu and LateNeu; complement signal was enriched in cases for LateNeu; IL-2/STAT5 signal was enriched in cases for MidNeu and LateNeu; cell cycle (e.g., G_2M checkpoints, E2F targets and mitotic spindles) and DNA repair signals were under-represented in cases for PreNeu. Conversely, IFN-γ signal was under-represented in cases for MidNeu and LateIFNNeu.

Conclusion: In SLE patients, pronounced inflammatory signals were observed in neutrophils across different stages.

Disclosure: A. Law: None; **C. Pua**: None; **D. Guo**: None; **C. Ng**: None; **J. Thumboo**: None; **A. Low**: Boehringer-Ingelheim, 6, Janssen, 6; **X. Fan**: None.

Abstract Number: 0914

Transcription Factor RFX1 Promotes M1 Macrophage Polarization in Systemic Lupus Erythematosus via Regulating APOBEC3A

shuang Yang[1], Pei Du[1], Sujie Jia[2] and **Ming Zhao**[2], [1]Department of Dermatology, Hunan Key Laboratory of Medical Epigenomics, The Second Xiangya Hospital of Central South University, Changsha, China, [2]Institute of Dermatology, Chinese Academy of Medical Sciences and Peking Union Medical College, Nanjing, China

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Aberrant macrophage polarization is generally present in autoimmune diseases. Overwhelming M1 macrophage induces the continuous progression of inflammation, which is one of the vital reasons for the development of autoimmune diseases. However, the underlying mechanism is still unclear. This study mainly explores the role of regulation factor X1 (RFX1) on macrophage polarization in systemic lupus erythematosus (SLE), and elucidates the mechanism of RFX1 regulating abnormal macrophage polarization.

Methods: Western blot (WB) was used to detect RFX1 expression in $CD14^+$ monocyte-derived macrophage (hMDMs) and mouse peritoneal macrophages (PMAs). The conditional knockout mice-$Rfx1^{f/f}$Lyz2-Cre (CKO) was constructed to inhibit RFX1 expression specifically in macrophages. The RNA-seq was used to detect the differently expressed genes in RFX1-overexpressed or knockout PMAs. The expression levels of macrophage markers and pro-inflammatory cytokines in macrophages were detected by RT-qPCR, Flow cytometry or ELISA. The CKO and WTmice with colitis or lupus-like symptom were induced by dextran sulfate sodium (DSS) or IMQ respectively. The damage of intestinal or kidney tissue was examined by H&E staining. The infiltrations of $CD45^+$, neutrophils, macrophages, $CD4^+$ and $CD8^+$ cells in colon or kidney were detected by flow cytometry, as well as markers of M1 and M2 subtypes. ChIP-seq was used to screen the target genes regulated by RFX1.

Results: The protein expression of RFX1 was increased significantly in LPS induced M1 macrophage. Compared with control group, the expressions of M1-related genes were increased in RFX1-overexpressed PMAs, while the expressions were significantly reduced in *Rfx1*-deficient PMAs. We also found that the relative mRNA and protein expression of RFX1 in $CD14^+$ monocyte from the peripheral blood of SLE patients was significantly increased compared with healthy control (HC).

In addition, deficiency of Rfx1 protect the integrity of the intestinal structure in colitis mice and inhibited the damage to kidney from lupus-like mice. The infiltration of immune cells was obviously reduced in colon or kidney form CKO mice. The M1-related gene expression such CD86 or MHCII was decreased in macrophages from CKO mice. Besides, the concentrations of pro-inflammatory cytokines including Il-6 and Tnf-a and Il-1b were lessened significantly in serum from CKO mice.

Dual luciferase reporter and ChIP-qPCR assay indicated that APOBEC3A transcription was regulated by RFX1 directly. And the methylation of *IL6* and *TNF* promoter in macrophage was decreased by APOBEC3A or RFX1 overexpression. Besides, the methylation of *IL6* and *TNF* promoter were also decreased in monocyte and macrophage from SLE patients.

Conclusion: Both *in vitro* and *in vivo* experiments show that RFX1 promotes M1 polarization by APOBEC3A-mediated demethylation. And RFX1 may promoted the autoimmune inflammation in SLE.

Disclosure: s. Yang: None; **P. Du**: None; **S. Jia**: None; **M. Zhao**: None.

Abstract Number: 0915

IL-16+ Is Abundantly Expressed by Kidney-infiltrating Myeloid and Lymphoid Cells in Lupus Nephritis: A Spatially Resolved Multiplexed Approach

Alessandra Ida Celia[1], Xiaoping Yang[2], Hana Minsky[2], Silvia Malvica[2], Michelle Petri[3], the Accelerating Medicines Partnership in RA/SLE[4], Avi Rosenberg[5] and Andrea Fava[2], [1]John Hopkins University of Medicine, Rome, Italy, [2]Johns Hopkins University, Baltimore, MD, [3]Department of Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Timonium, MD, [4]Multiple, Multiple, [5]Department of Pathology, The Johns Hopkins University School of Medicine, Baltimore, MD

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Etiology & Pathogenesis Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: We previously discovered that IL-16 is the urinary protein most strongly correlated with histological activity in lupus nephritis (LN), followed by neutrophil degranulation products such as PR3. IL-16 is a proinflammatory chemokine that binds to CD4 and CD9 which are also expressedby myeloid cells. IL-16 is a key mediator in renal ischemia-reperfusion injury. Furthermore, IL-16 polymorphisms carry a higher risk of SLE (OR 3.3-10.4), suggesting a potential causal role. Our hypothesis is that IL-16 critically amplifies the immune response in proliferative LN, thereby attracting myeloid populations that can ultimately lead to kidney damage. The aims of our study are to investigate IL-16+ cells in LN kidney, define their immunophenotype, and to explore the presence of PR3+ cells in the same spatial area in order to gain insight on the spatial relation between the two populations.

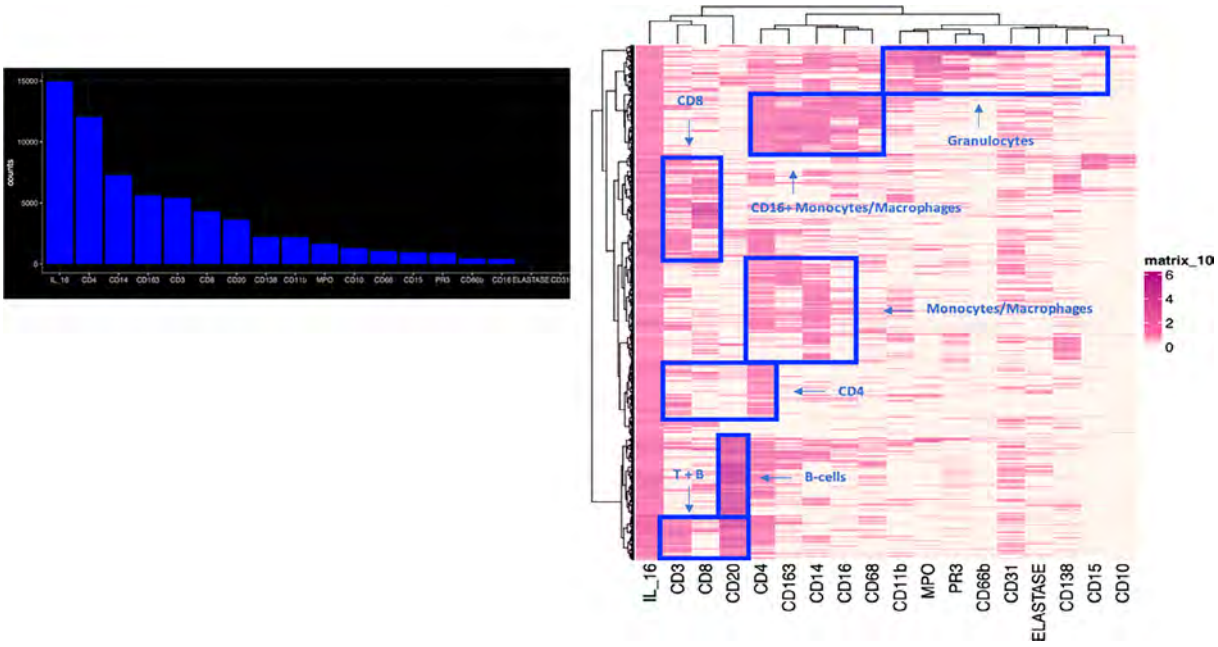


Figure1. IL-16+ cells immune phenotype (A) Coexpression of lineage markers in IL-16+ cells. Values indicate number (count) of positive cells. (B) Heatmaps displaying the heterogeneity of marker coexpression at the single cell level for IL-16+ cells (B). Data from one representative kidney biopsy (class IV lupus nephritis, NIH Activity Index 8/24, Chronicity Index 6/12).

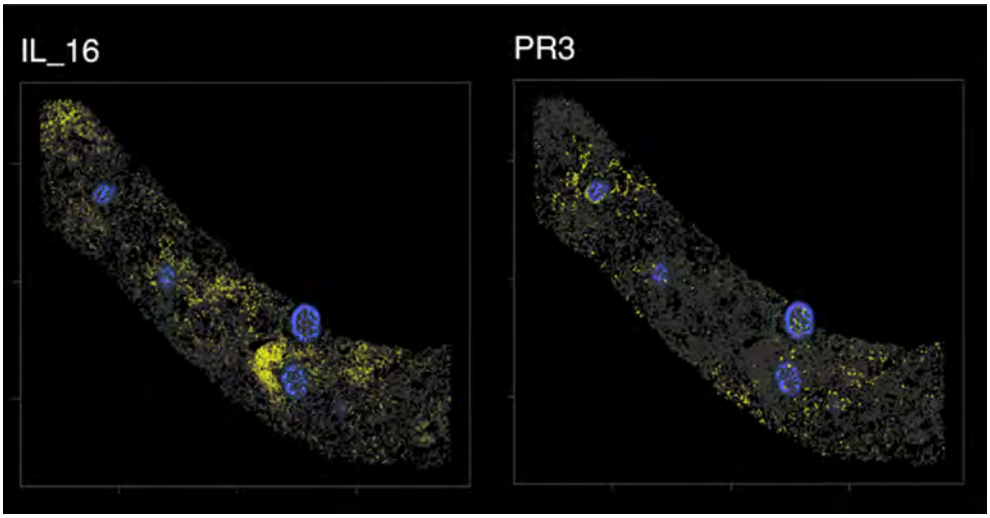


Figure2. Spatial distribution of IL-16+ and PR3+ cells Biopsy detail mapping IL-16 and PR3+ cells (in yellow); glomeruli in blue. There was no obvious spatial relation between IL16+ and PR3+ cells. Data from one representative kidney biopsy (class IV lupus nephritis, NIH Activity Index 8/24, Chronicity Index 6/12).

Methods: We performed 20-plex serial immunohistochemistry (sIHC) on one archival LN kidney biopsy (ISN/RPS class IV) to identify IL-16+ and PR3+ cells and evaluate the expression of multiple cell lineage markers. We utilized Indica HALO to perform image analysis, including deconvolution, cell segmentation, glomerular annotation, and quantitative histology.

Results: A total of 95,619 cell objects present in the sample were analyzed. We observed an abundant IL-16+ infiltrate, mostly in the tubulointerstitium. Multiple kidney-infiltrating immune cell types produced IL-16. The co-expression of lineage markers by IL-16+ cells is summarized by **Figure1A. Figure 1B**displays the heterogeneity of marker co-expression at the single cell level for IL-16+ cells. Most IL-16+ cells also expressed CD4, a ligand for IL-16. **Figure 2** illustrates the tissue distribution of IL-16 and PR3+ cells showing how IL-16 and PR3 are not spatially related.

Conclusion: IL-16+ cells abundantly infiltrate the kidney in LN. IL-16 is producedby most types of immune cells including lymphoid and myeloid cells. There was no spatial relationship between IL-16+ and PR3+ cells suggesting no obvious chemotactic activity. The release of IL-16 by multiple immune cell types may promote and amplify LN.

Disclosure: A. Celia: None; **X. Yang**: None; **H. Minsky**: None; **S. Malvica**: None; **M. Petri**: Alexion, 1, Amgen, 1, AnaptysBio, 1, Annexon Bio, 1, Argenx, 1, Arhros-Focus Med/Ed, 6, AstraZeneca, 1, 5, Aurinia, 1, 5, 6, Axdev, 1, Biogen, 1, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CVS Health, 1, Eli Lilly, 1, 5, Emergent Biosolutions, 1, Exagen, 5, Exo Therapeutics, 2, Gilead Biosciences, 2, GlaxoSmithKlein(GSK), 1, 5, 6, Horizon Therapeutics, 2, Idorsia Pharmaceuticals, 2, IQVIA, 1, Janssen, 1, 5, Kira Pharmaceuticals, 2, MedShr, 6, Merck/EMD Serono, 1, Momenta Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Proviant, 2, Sanofi, 2, Sinomab Biosciences, 2, Thermofisher, 5, UCB, 2; **t. Accelerating Medicines Partnership in RA/SLE**: None; **A. Rosenberg**: None; **A. Fava**: Annexon Biosciences, 2, Sanofi, 1.

Abstract Number: 0916

Upregulation of the M-CSF Receptor on Non-Classical Monocytes from SLE Patients as an Indicator for Premature Monocyte Aging

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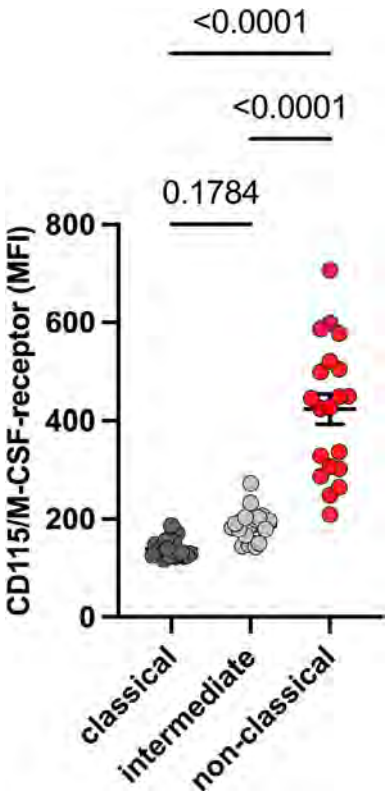
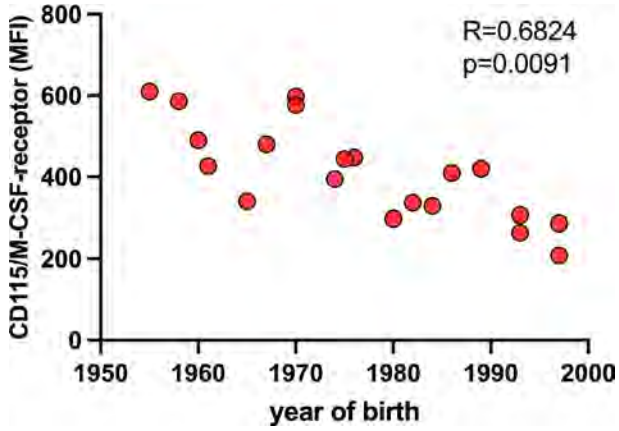
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Circulating monocytes are divided into three subsets: classical, intermediate, and non-classical monocytes. Monocytes egress from the bone marrow as classical monocytes and develop into intermediate and later non-classical monocytes. In patients with systemic lupus erythematosus (SLE), the proportion of non-classical monocytes is increased in the peripheral blood and kidneys in case of glomerulonephritis. However, the biology of non-classical monocytes in patients with SLE and their implications in the disease process are not fully characterized.

Methods: Peripheral blood mononuclear cells (PBMC) were isolated from patients with SLE (defined by the 2019 EULAR/ACR criteria; n=20), healthy controls (n=20), and patients with connective tissue diseases other than SLE (n=10). PBMC were stained for CD14, CD16, and CD115 and analyzed by flow cytometry. In additional experiments, mitochondrial



Surface expression of CD115 (MFI) on classical (CD14+CD16-), intermediate (CD14+CD16+), and non-classical monocytes (CD14dim CD16++) in healthy control donors (n=20).



Correlation of the surface expression of CD115 (MFI) on non-classical monocytes (CD14dim CD16++) and the year of birth of the respective healthy blood donor (n=20).

membrane potential and mitochondrial reactive oxygen species were measured by flow cytometry, expression of miR146a was quantified by RT-qPCR. All patients and blood donors gave written informed consent and the study was approved by the ethical review board of the University of Freiburg.

Results: Surface expression of CD115, the receptor for macrophage colony stimulating factor (M-CSF), a key survival factor for myeloid cells, is markedly upregulated on non-classical monocytes from patients with SLE. While CD115 is almost absent on the classical monocyte subset and intermediate monocytes show low levels of CD115, only non-classical monocytes exhibit a relevant surface expression of the M-CSF receptor (Figure 1). Non-classical monocytes from SLE patients increase their CD115 expression not only in comparison with healthy age-matched controls (p=0.004) but also compared to patients with connective tissue diseases other than SLE (p=0.009), identifying the upregulation of the M-CSF receptor as biological signature of non-classical monocytes in SLE. These CD115+ monocytes in SLE patients display a senescent cell phenotype with increased mitochondrial membrane potential (p=0.012), higher production of mitochondrial reactive oxygen species (p=0.021) and upregulation of the senescence marker miR146a (p=0.008). When investigating CD115 expression in different age groups in healthy individuals, CD115 receptor levels on non-classical monocytes were age-dependent with low levels on cells from young adults and significantly higher levels in individuals over 50 years of age (Figure 2). Thus, the upregulated CD115 expression of non-classical monocytes from young SLE patients was indicative for premature monocyte aging in line with the upregulation of senescence markers in those cells.

Conclusion: We identified the upregulation of the M-CSF receptor (CD115) as a biological signature of non-classical monocytes from SLE patients. CD115+ non-classical monocytes are increased only in the peripheral blood of patients with SLE and not in patients with other connective tissue diseases and display a senescent phenotype indicative of premature monocyte aging in SLE.

Disclosure: M. Zeisbrich: None; **S. Finzel**: AbbVie, 6, AstraZeneca, 2, 6, Chugai, 6, Galapagos, 2, 6, Novartis, 2, Novo Nordisk, 2, UCB, 6; **N. Venhoff**: None; **R. Voll**: None.

Abstract Number: 0917

Role of Immunoglobulin Polygenic Risk in Systemic Lupus Erythematosus

Victor Gothefors-Holm[1], Sarah Reid[1], Ahmed Sayadi[1], Maija-Leena Eloranta[1], Martina Frodlund[2], Karoline Lerang[3], Andreas Jonsen[4], Solbritt Rantapää-Dahlqvist[5], Anders Bengtsson[4], Anna Rudin[6], Oyvind Molberg[3], Christopher Sjöwall[2], Johanna Sandling[1], Lars Rönnblom[1] and Dag Leonard[1], [1]Rheumatology, Department of Medical Sciences, Uppsala University, Uppsala, Sweden, [2]Department of Biomedical and Clinical Sciences, Division of Inflammation and Infection/Rheumatology, Linköping University, Linköping, Sweden, [3]Department of Rheumatology, Oslo University Hospital, Oslo, Norway, [4]Rheumatology, Department of Clinical Sciences, Lund University, Lund, Sweden, [5]Department of Public Health and Clinical Medicine/Rheumatology, Umeå University, Umeå, Sweden, [6]Department of Rheumatology and Inflammation Research, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease partly characterized by production of autoantibodies, causing inflammation and tissue damage. In this study we investigated whether cumulative genetic risk for elevated immunoglobulin G (IgG)-levels in the general population, represented by an IgG polygenic risk score (IgG-PRS) is associated with an increased risk of SLE, clinical manifestations or autoantibody-profile.

Methods: Patients with SLE, fulfilling the ACR-82, ACR-97 or SLICC-2012 criteria (n=1532) and healthy controls (n=1947) were genotyped using Illumina's Global Screening Array. Clinical data was retrieved from medical charts. A weighted IgG-PRS was assigned to each individual including 13 single nucleotide polymorphisms (SNPs) associated with elevated IgG-levels in the general population, as reported by Jonsson *et al*. (1). Next, two sub-PRSs were developed to investigate the SLE and non-SLE genetic effect of the IgG-PRS, one including SLE-associated SNPs ($r^2 > 0.2$, n=5) and another including non-SLE associated SNPs (n=8), table 1. Multiple logistic- and linear regression analyses were performed, adjusting for sex and SLE-duration. P-value < 0.05 was considered significant.

Results: The IgG-PRS did not differ between SLE patients and healthy controls or between men and women (both p >0.05). Out of the ACR-82 criteria, high IgG-PRS was most significantly associated with increased prevalence of arthritis (OR 4.39 (1.13-17.09), p=0.033), table 2. Further, a high IgG-PRS was associated with a greater number of different types of

Table 1. Overview of the immunoglobulin-level associated SNPs in Jonsson *et al* (1)

SNP-ID	Candidate Gene	Riskallele	SLE**	MAF(%)	Beta***
rs9271324*	HLA-DQA1	G	r^2=0.26	28.0	-0.07
rs9276244*	HLA-DQA2	G	r^2=0.38	32.8	0.05
rs10065637	ANKRD55	T	r^2=0.45	22.6	-0.05
rs3184504	SH2B3	T	r^2=0.96	37.9	0.03
rs34562254	TNFSF13B	A	r^2=0.60	7.7	0.09
rs3832181*	RNF168	C	r^2<0.2	38.4	0.04
rs28720928*	PTPN7	T	r^2<0.2	11.4	0.07
rs1448187	BCL2L11	T	r^2<0.2	29.9	0.06
rs5743618	TLR1	A	r^2<0.2	34.8	-0.03
rs3815768	ELL2	T	r^2<0.2	29.3	0.04
rs2269710	HLA-E	C	r^2<0.2	35.8	0.03
rs142973694	HLA-B	A	r^2<0.2	6.6	0.06
rs3803800	TNFSF13	A	r^2<0.2	24.2	0.04

List of SNPs included in the IgG-PRS from Jonsson *et al* (1).
*Indicates a proxy SNP was used instead in the PRS.
** LD with known SLE-associated SNPs in the NHGRI-EBI GWAS Catalog.
***Beta for the SNPs association to IgG levels in Jonsson *et al*.(1) MAF=Minor allele frequency in Jonsson *et al* (1), SNP=Single nucleotide polymorphism.

Table 2. Association of clinical parameters with the IgG-PRSs

	IgG-PRS		IgG-non-SLE-PRS		IgG-SLE-PRS	
	OR(CI)	P	OR(CI)	P	OR(CI)	P
SLE/Healthy	1.75(0.85-3.61)	0.13	**0.17(0.06-0.44)**	**<0.001**	**22.2(8.06-61.30)**	**<0.001**
Sex	3.56(0.67-18.96)	0.14	3.73(0.34-41.2)	0.28	1.20(0.12-12.02)	0.88
Onset*	0.79(0.19-3.26)	0.75	0.91(0.11-7.24)	0.93	2.04(0.29-14.53)	0.48
Onset#	-7.01(-16.24-2.22)	0.14	-2.88(-16.60-10.84)	0.68	-1.08(-13.80-11.64)	0.87
ACR1-Malar rash	1.00(0.31-3.30)	1.00	0.70(0.15-3.25)	0.65	1.11(0.22-5.72)	0.90
ACR2-Discoid rash	0.47(0.12-1.88)	0.29	0.38(0.06-2.30)	0.29	1.38(0.21-9.25)	0.74
ACR3-Photosensitivity	0.36(0.11-1.21)	0.1	0.28(0.06-1.35)	0.11	0.67(0.13-3.62)	0.64
ACR4-Oral ulcers	3.27(0.91-11.83)	0.07	4.61(0.88-24.16)	0.07	1.99(0.34-11.72)	0.45
ACR5-Arthritis	**4.39(1.13-17.09)**	**0.03**	4.25(0.73-24.80)	0.11	2.81(0.43-18.37)	0.28
ACR6-Serositis	1.72(0.52-5.68)	0.37	1.24(0.26-5.80)	0.79	2.13(0.41-11.01)	0.37
ACR7-Nephritis	0.69(0.20-2.37)	0.56	0.81(0.16-4.01)	0.80	0.51(0.09-2.80)	0.44
ACR8-Neurology	3.29(0.45-23.98)	0.24	5.85(0.46-75.19)	0.18	0.78(0.05-11.8)	0.86
ACR9-Hematology	0.56(0.17-1.85)	0.34	**0.21(0.05-1.01)**	**0.05**	1.63(0.31-8.44)	0.56
ACR10-Immunology	1.30(0.37-4.61)	0.68	1.45(0.28-7.43)	0.66	0.84(0.15-4.79)	0.84
ACR-score	1.07(0.29-4.00)	0.92	0.51(0.09-2.81)	0.44	2.59(0.42-16.2)	0.31
Anti-Cardiolipin	1.51(0.43-5.33)	0.53	1.61(0.25-10.56)	0.62	0.27(0.05-1.57)	0.15
Anti-RNP	**0.19(0.04-0.85)**	**0.03**	9.73(0.94-100.48)	0.06	**0.058(0.01-0.47)**	**0.01**
Anti-SSA	1.50(0.45-4.95)	0.51	0.86(0.15-5.05)	0.87	2.71(0.52-14.19)	0.24
Anti-SSB	**4.39(1.06-18.19)**	**0.04**	2.97(0.38-23.16)	0.30	2.24(0.32-15.89)	0.42
Anti-Sm	0.52(0.06-4.27)	0.54	0.55(0.02-15.25)	0.72	**0.04(0.002-0.74)**	**0.03**
Anti-dsDNA	3.08(0.86-11.10)	0.09	1.62(0.23-11.28)	0.63	1.59(0.27-9.27)	0.61
Antibody-score**	**5.42(1.27-23.13)**	**0.02**	0.49(0.05-4.66)	0.53	4.77(0.67-33.94)	0.12
Antibody-score #	**0.96(0.13-1.78)**	**0.02**	-0.53(-1.81-0.75)	0.42	0.75(-0.37-1.87)	0.19

Logistic regression analyses adjusting for sex and disease duration. Values in bold indicate p<0.05 CI=95% confidence interval. IgG-PRS; PRS including SNPs associated with IgG-levels in Jonsson *et al.*(1) IgG-non-SLE-PRS; IgG-PRS excluding SLE-associated SNPs. IgG-SLE-PRS; IgG-PRS including SNPs in LD with known SLE-associated SNPs. OR=Odds ratio. ACR= American College of Rheumatology SLE-classification criteria.
*Age at SLE-diagnosis, ≤20 vs. >20. **Number of different types of antibodies, 0-1 vs. 2-6. #Linear regression analysis.

autoantibodies including anti-SSA, anti-SSB, anti-RNP, anti-Sm, anti-dsDNA and anti-cardiolipin antibodies (p=0.02). When investigating the autoantibodies separately, a high IgG-PRS was associated with higher prevalence of anti-SSB (OR 4.39 (1.06-18.19), p=0.04) and lower prevalence of anti-RNP (OR 0.19 (0.043-0.85), p=0.03) antibodies. In total, 38% of the SNPs included in the IgG-PRS were in linkage disequilibrium with SLE-associated SNPs (r^2 = 0.26-0.96). Separating the SLE and non-SLE genetic effect for the IgG PRS, demonstrated a positive association for the SLE associated IgG PRS, and conversely a negative association for the IgG PRS excluding SLE associated SNVs (OR 22.2(8.06-61.30), p<0.001 and OR 0.17(0.06-0.44), p <0.001, respectively), table 2.

Conclusion: The cumulative effect of genetic variants affecting IgG-levels in the general population is associated with both the type and the number of different autoantibodies in SLE. Investigating common genetic variants linked to immunological functions in the general population may provide further insight into the genetics driving SLE. References: < !1. Jonsson S, Sveinbjornsson G, de Lapuente Portilla AL *et al*.Identification of sequence variants influencing immunoglobulin levels**.** Nature Genetics 49(8):1182-1191, 2017.

Disclosure: V. Gothefors-Holm: None; **S. Reid**: None; **A. Sayadi**: None; **M. Eloranta**: None; **M. Frodlund**: None; **K. Lerang**: None; **A. Jonsen**: None; **S. Rantapää-Dahlqvist**: None; **A. Bengtsson**: None; **A. Rudin**: AstraZeneca, 12, financial support; **O. Molberg**: None; **C. Sjöwall**: None; **J. Sandling**: None; **L. Rönnblom**: None; **D. Leonard**: None.

Abstract Number: 0918

Network Analysis of Genome Sequences Identifies Important Pathways in the Pathogenesis of Childhood-onset Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Etiology & Pathogenesis Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic, systemic autoimmune disorder. The pathogenesis of SLE is not fully understood, but high twin/sibling concordance rates suggest a genetic component triggered by environmental events. Childhood-onset SLE (cSLE) patients have an extreme phenotype, therefore is an ideal population to study genetic contributors to SLE. Historically, studies have focused on unrelated individulas who share variants in individual genes. However, this approach doesn't consider that rare variants in SLE could cluster in genes participating in related biological processes. We performed genome sequencing in a diverse cohort of cSLE patients and parental controls, and describe a network-of-pathways approach to identify biological pathways enriched in genes with rare variants that may contribute to cSLE pathogenesis.

Methods: SLE patients met at least 4 of 11 revised American College of Rheumatology classification criteria, with disease onset 18 years. Whole blood samples were collected from 83 patients with cSLE and 109 unaffected parents and whole genome sequencing was performed. The genome sequences were filtered to select for rare (minor allele frequency< 0.01), nonsynonymous variants in coding exons. Selected variants had to be present only in cSLE patients or in both patients and parents, but at a significantly higher level in patients (Fisher's exact test (p0.05)).This resulted in 501 unique variants, which

Table 1. Demographic data of the cSLE cohort

	cSLE (n=83)
% female n	80% (66)
Age at diagnosis, median (range)	12 (5-17)
Ancestry	
% European	22 (18)
% African	13 (11)
% Amerindian	17 (14)
% East Asian	16 (13)
% South Asian	6 (5)
% Admixed	27(22)
Family Structure	
Trios (%) n	51 (42)
Dyads (%) n	30 (25)
Singletons (%) n	19 (16)

corresponded to 232 genes.Using the 232 genes, we performed pathway enrichment analysis based on Gene Ontology biological processes with Metascape. We generate a network of enriched pathways, weighted by enrichment values and overlap coefficients with Cytoscape. Pathway clusters in the network were manually reviewed and classified. We analyzed clinical phenotypes and CADD-Phred for each pathway cluster.

Results: Rare genetic variants in cSLE patients are enriched in biological pathways such as RNA processing and apoptosis (Figure 1). Some pathways(i.e. nucleic acid regulation) are well-established causes of monogenic SLE, while others are novel. The median CADD-Phred score for each of the 18 networks ranges from 11.5-23.6.The mitochondrial functions cluster had higher rates of lupus nephritis, and the cell adhesion cluster had higher rates of CNS SLE compared to other clusters (Figure 2).

Conclusion: Network analysis is a useful approach to identify biological pathways and specific genes that could contribute to cSLE risk. Ongoing detailed analysis of the specific variants identified in each pathway will allow us to prioritize key genes and pathways for further study. In total, this analysis may contribute to advancing the understanding of cSLE beyond a broad clinical phenotype and towards a more precise molecular diagnosis.

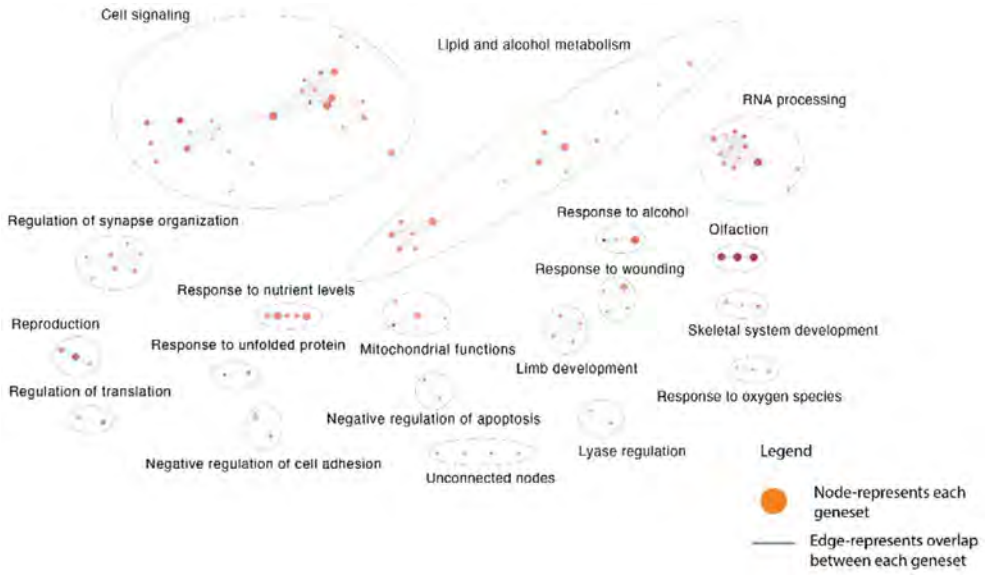

Figure 1. Biologic pathways enriched in rare coding variants in cSLE patients.

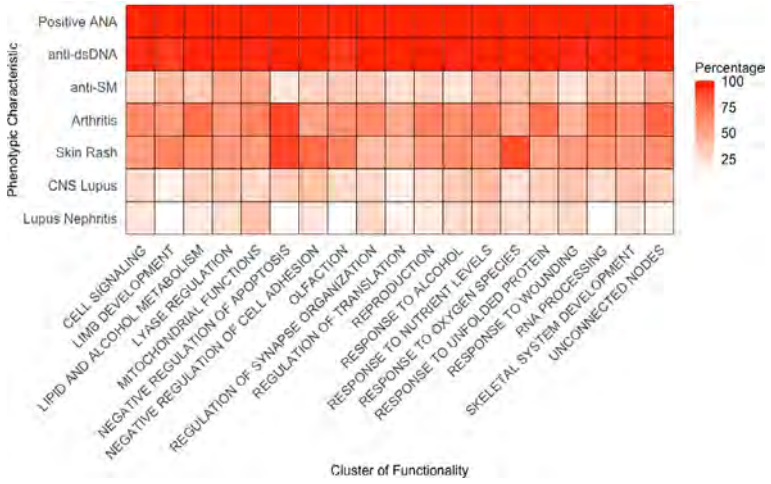

Figure 2. Key phenotypes for variants enriched in cSLE grouped by functional biologic clusters

Disclosure: K. Heitzman: None; **S. Dass**: None; **L. Hiraki**: None; **E. Silverman**: None; **C. Scott**: None; **A. Barrera-Vargas**: None; **Z. Deng**: None; **M. Kaplan**: AstraZeneca, 5, Bristol Myers Squibb, 5, Cytrill, 2, Neutrolis, 2; **L. Franco**: None; **L. Lewandowski**: None.

Abstract Number: 0919

Investigating the Role of Interferon in Promoting Flares of SLE at a Single Cell Level

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease with unpredictable flares interspersed with prolonged periods of disease quiescence. Interferon (IFN) is a hallmark of disease and has been linked to disease flares, but the precise mechanism by which this occurs remain unclear. To address this question, we examined the association between IFN and the immune changes in flaring and quiescent SLE patients at a single cell level.

Methods: A 41-marker panel was developed that enabled measurement of IFN-induced proteins (IIPs) in peripheral blood immune populations using CyTOF.Fifteen healthy controls (HCs), 26 quiescent (clinical SLEDAI-2K = 0 for one year) and 42 recently flaring (< 1 month, change in clinical SLEDAI-2K ≥ 1 requiring escalation of therapy) SLE patients were examined. Expression of individual IIPs normalized to healthy controls, as well as a composite IIP score incorporating the expression of all seven proteins was assessed.

Results: Twenty-six distinct immune populations were identified, all of which demonstrated a strong correlation between IIP levels and the IIG score in SLE (Figure 1).In all immune populations, the levels of IIPs were significantly elevated in SLE patients compared to HCs. In most cell populations, the levels of IIPs were elevated in flaring compared to quiescent SLE patients (Figure 2A) and correlated with the clinical SLEDAI-2K. Comparison of the abundance of the 26 immune populations between flaring and quiescent patients revealed that only classical monocytes, intermediate activated classical monocytes, and age-associated B cells (ABCs) were significantly elevated in flaring patients (Figure 2B). Very limited changes were seen between these 2 groups of patients for markers of cellular activation, such as CD86, TLR7, TLR9, FOXP3, HLA-DR, Ki67, and PD1. In contrast, in many relevant immune populations, elevations of these markers were associated with IIP levels suggesting that IFN, rather than disease status (i.e., flare vs quiescence), is driving this activation. In patients who were flaring at baseline, elevations of IIPs in pre-ABCs, ABCs, low density granulocytes (LDGs), and intermediate activated monocytes were associated with clinical disease activity one year later (Figure 3A).In contrast, quiescent patients that subsequently flared and were active at one year had elevations of IIPs in multiple T and B cell populations (Figure 3B).

Conclusion: The findings suggest that IFN initiates flares by promoting B and T cell activation, while sustained or recurrent disease activity appears to be more dependent upon its impact on ABCs, LDGs, and monocytes.

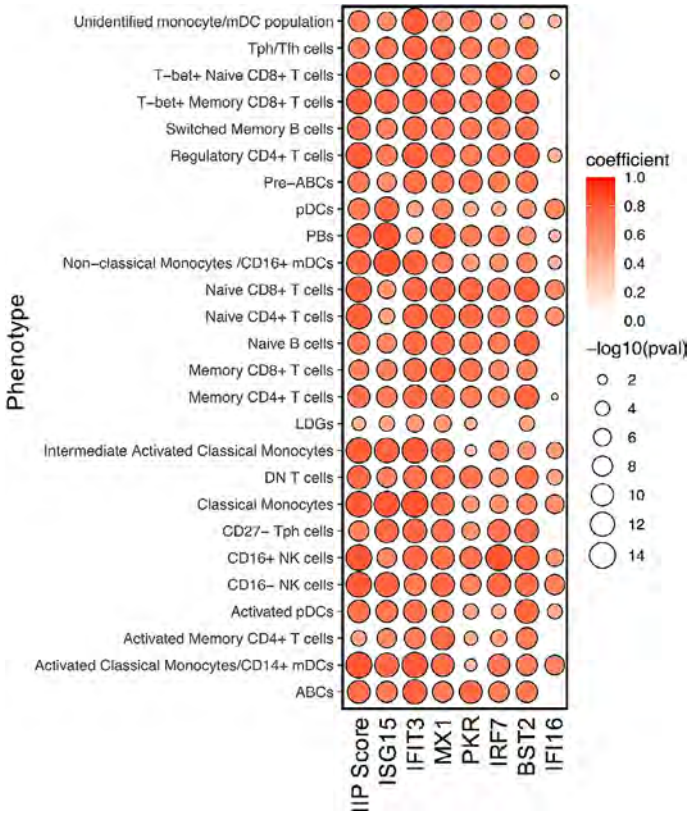

Figure 1. IFN induced protein (IIP) expression is significantly correlated with IFN induced gene (IIG) expression. Correlation between IIP expression (shown on the x axis) in individual cell populations (shown on the y axis) and IIG expression, as measured by a composite score calculated by summing the log2 transformed, normalized expression of 10 IFN-induced genes. R values are denoted by colour, and p values by the size of the dots.

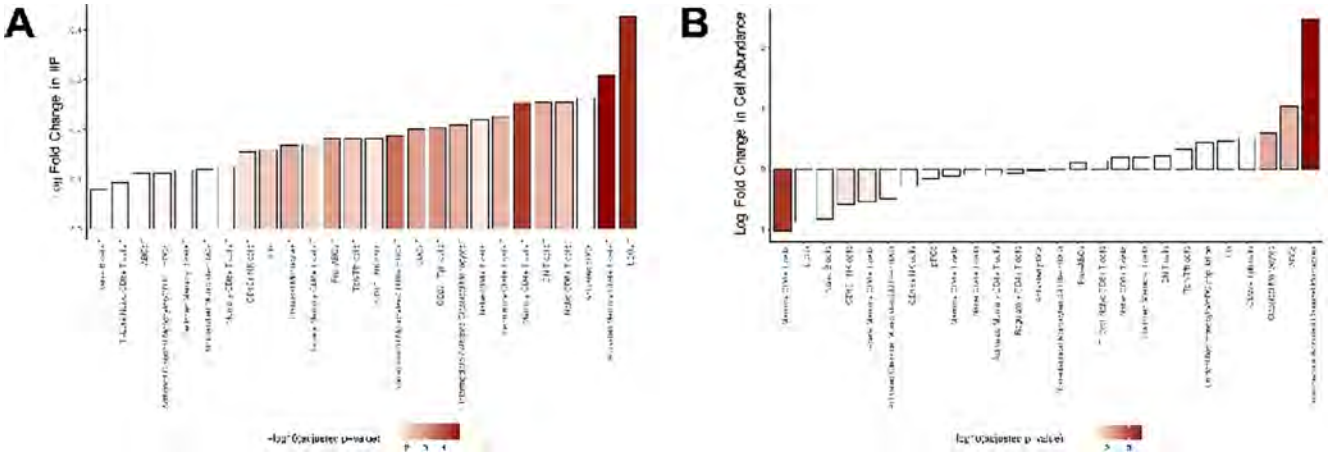

Figure 2. Immunologic differences between flaring and quiescent patients. Waterfall plots showing the fold change differences between flaring and quiescent SLE patients. Bars above the x axis are increased and below the x axis are decreased in flaring relative to quiescent patients. A) Waterfall plot of IIP scores showing that flaring patients have significantly higher levels of IIP expression in 21 out of the 26 immune populations surveyed. B) Waterfall plot of cellular abundance showing that flaring patients have significantly increases in some monocyte subsets and ABCs as compared to quiescent patients.

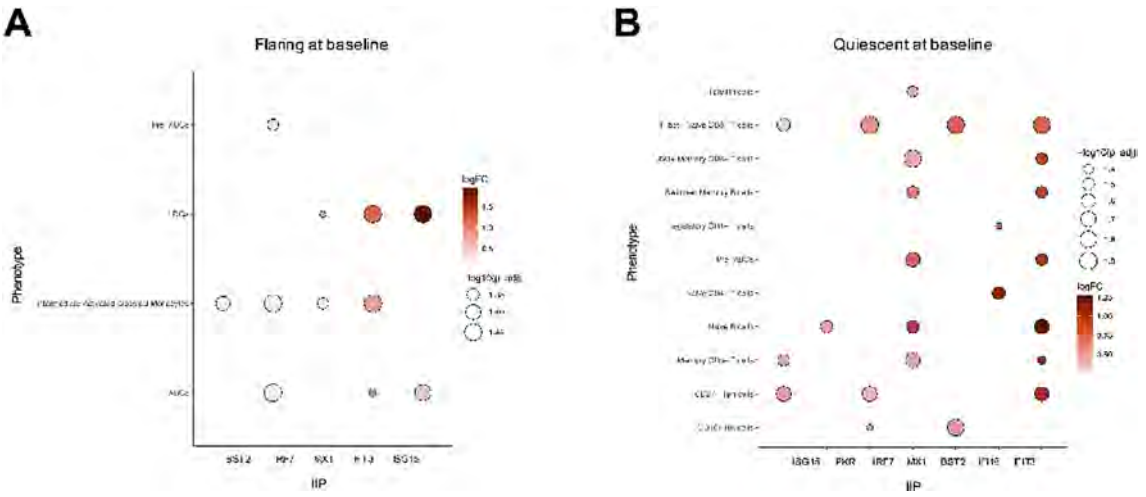

Figure 3. Interferon-induced protein (IIP) levels in distinct immune populations at baseline inform disease status at one year follow up. A) Patients who were flaring at baseline and were active at one year had significantly higher expression of IIPs in their ABCs, LDGs, and some monocyte cell subsets when compared to those who had inactive disease activity at follow up. B) Patients who were quiescent at baseline and eventually experienced an increase in disease activity at 1 year had significantly higher expression of IIPs in their B and T cell subsets than those who had sustained disease quiescence at one year follow up.

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Abstract Number: 0920

Proinflammatory Neutrophils and NETs Mediate Skin and Kidney Inflammation During Lupus Flare in Asymptomatic Lupus-prone Mice Triggered by UVB

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Ultraviolet B (UVB) exposure triggers lupus flare by worsening both skin lesions and systemic symptoms, i.e. lupus nephritis. We recently reported that UVB exposure induces skin inflammation with infiltration of neutrophils, which can form neutrophil extracellular traps (NETs) in wild-type mice. Interestingly, we recently found that UVB exposure of asymptomatic MRL-lpr lupus-prone mice induced lupus flare with not only skin inflammation, but also proteinuria. However, the underlying mechanisms remain unclear.

Methods: To study the relevant mechanisms, we investigated skin lesions, proteinuria, infiltrated neutrophils, their expression of cytokines or complement C3, and formation of NETs in both skin and kidneys of UVB-irradiated asymptomatic young female MRL-lpr lupus-prone mice.

Results: UVB exposure induced inflammatory responses in skin and kidneys with proteinuria, showing elevated skin thickness, immune cell infiltration, increased CXCR4 expression in neutrophils, and deposition of NETs, and NET-associated IFNα or C3 in both skin and kidneys. Interestingly, infiltrated cell count in skin was positively correlated with proteinuria ($r=0.57$, $p< 0.05$), indicating a link between skin infiltrates and kidney injury. In kidneys, glomerular hypercellularity ($r=0.73$, $p< 0.05$), CXCR4-positive neutrophils ($r=0.7$, $p< 0.05$), NETs ($r=0.74$, $p< 0.05$), NET-associated IFNα ($r=0.81$, $p< 0.05$) or C3 ($r=0.88$, $p< 0.01$) were correlated with proteinuria in UVB-irradiated lupus-prone mice, suggesting a role for CXCR4-positive neutrophils, NETs and their associated IFNα or C3 in kidney inflammation. To explore the origin of the pro-inflammatory neutrophils, we found that stimulation with UVB or platelet-activating factor can upregulate expression of CXCR4, IFNα or C3 *in vitro* in neutrophils from lupus-prone mice. About 20-50% of them co-expressed IFNα or C3 with CXCR4, which may mediate cross-organ communication. Given that only a portion of infiltrated neutrophils become NETotic in the skin of UVB-irradiated wildtype mice in our recent publication, we sought to explore if inhibition of CXCR4 can reduce kidney injury. Notably, intraperitoneal application of CXCR4 inhibitor IT1t significantly attenuated proteinuria, with reduced glomerular infiltration of CXCR4-positive neutrophils. Consequently, we found decreased glomerular deposition of neutrophil NETs and NET-associated IFNα (3.2% Area in UVB vs 0.43% in IT1t+UVB mice, $P< 0.01$) in kidneys of UVB-irradiated MRL/lpr mice with IT1t application as compared to those in mice without IT1t administration.

Conclusion: In conclusion, UVB-induced proinflammatory neutrophils and NETs contribute to skin and kidney inflammation during lupus flare in asymptomatic lupus-prone mice irradiated by UVB. Inhibition of CXCR4-mediated neutrophil transmigration ameliorated kidney inflammation with attenuated proteinuria in UVB-triggered lupus flare. Our results provide insights into novel therapeutics into UVB-induced lupus flare.

Disclosure: X. Lyu: None; **m. li**: None; **p. zhang**: None; **W. Wei**: None; **v. werth**: AbbVie, 2, Amgen, 2, 5, Argenx, 2, AstraZeneca, 2, 5, Beacon Bioscience, 2, Biogen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 2, 5, Corcept, 2, Crisalis, 2, CSL Behring, 2, Cugene, 2, Eli Lilly, 2, EMD Serono, 2, Genentech, 2, Gilead, 2, 5, GlaxoSmithKline, 2, Idera, 2, Incyte, 2, Janssen, 2, 5, Kirin, 2, Lupus Research Alliance, 5, MedImmune, 2, Medscape, 2, Nektar, 2, Principia, 2, Resolve, 2, UCB, 2, Viela Bio, 2, 5; **M. Liu**: None.

Abstract Number: 0921

SAP^{high} T Peripheral Helper Cells Are a Novel Subset Associated with Lupus Nephritis

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SESSION INFORMATION
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Session Title: SLE – Etiology & Pathogenesis Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Better understanding of the abnormal immune responses in lupus nephritis (LN) is fundamental to identifying new therapies. We previously reported that the adaptor protein SAP (SLAM Associated Protein) is increased in circulating T follicular helper (T_{FH}) and T peripheral helper (T_{PH}) cells of patients with SLE. SAP regulates T cell function by binding to the co-stimulatory SLAMF (signaling lymphocytic activation molecule family) receptors. SAP and SLAMF are critical for T_{FH} and T_{PH}-dependent B cell maturation into autoantibody-producing plasma cells that characterize SLE pathogenesis. In this work, we set out to evaluate the association between circulating SAP^{hi} T cells and clinical disease activity.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated using density gradient separation from whole blood. Cells were stained for cell surface markers, followed by permeabilization and staining of intracellular SAP. T_{FH} were defined as $CD3^{+}CD4^{+}CD8^{-}PD1^{hi}CXCR5^{+}$ and T_{PH} were defined as $CD3^{+}CD4^{+}CD8^{-}PD1^{hi}CXCR5^{-}$. Other markers included CXCR3, CCR4, CCR6, CD25, CD127 and HLADR. Additionally, we analyzed SAP expression from renal infiltrating LN T cells using the publicly available single-cell RNA sequencing (sc-RNA Seq) Accelerated Medicines Partnership (AMP) in SLE dataset. (*Nat Immunol* 2019; 20: 902-914.)

Results: PBMCs from 35 patients with SLE (1997 ACR criteria), including 10 patients with LN, were analyzed. The clinical characteristics are presented in Table 1. Mean age was 34±10, 83% were female. Males were more likely to have LN (p=0.03). We found an increase in total SAP-positive CD4 and CD8 T cells in SLE compared with controls (56±16 vs. 41 ±12 and 53±16 vs 39±10, respectively). In CD4 T cells, the highest SAP expression was in the T_{PH}, detectable in > 90% of T_{PH} cells in some patients. (Fig. 1A) The percent of $SAP^{hi}T_{PH}$ in circulation was associated with SLEDAI-2K (Pearson r=0.5, p=0.01) and showed a trend for inverse association with C3 and C4 levels. $SAP^{hi}T_{PH}$ cells were expanded in SLE patients presenting with flare vs. no flare. A sub-analysis revealed an association with active urine sediment, elevated anti-dsDNA, and nephrotic syndrome. SLE patients with renal disease had higher levels of circulating $SAP^{hi}T_{PH}$, and the association between $SAP^{hi}T_{PH}$ and LN remained significant after adjusting for age, sex, race, low complements, and elevated anti-dsDNA (p=0.02).(Fig. 1B)To validate these findings we used the AMP scRNA-Seq data. Using the authors' clustering analysis, we found a small but statistically significant increase in SAP levels from renal infiltrating T cells from SLE compared with control kidney biopsy samples (p=0.03). Notably, SAP expression in CD4 T cells was differentially upregulated in the T_{FH}-like vs. the T-regulatory subsets in the SLE vs. control group. (Fig. 2)

	SLE		
	no LN (n=20)	**LN (n=10)**	**p-value**
Age	35.9 ± 11.4	31.2 ± 6.9	ns
Sex (Female)	19 (95%)	6 (60%)	0.03
Race			
White	2 (10%)	1 (10%)	ns
Black	6 (30%)	2 (20%)	ns
Hispanic	12 (60%)	7 (70%)	ns
Weight (kg)	75.0 ± 21.4	83.3 ± 35	ns
Ever Smoker	2 (10%)	2 (20%)	ns
Years Disease	3[1-11]	10.5[4-15]	ns
ACR Criteria			
malar rash	11 (55%)	7 (70%)	ns
discoid rash	6 (30%)	3 (30%)	ns
photosensitivity	10 (50%)	2 (20%)	ns
mucositis	8 (40%)	5 (50%)	ns
arthritis	17 (85%)	10 (100%)	ns
serositis	9 (45%)	4 (40%)	ns
hematological	7 (35%)	6 (60%)	ns
Serologies			
ANA	20 (100%)	10 (100%)	ns
anti-dsDNA	17 (85%)	9 (90%)	ns
anti-smith	7 (35%)	5 (50%)	ns
aPL	8 (40%)	3 (33%)	ns

Patient Characteristics.

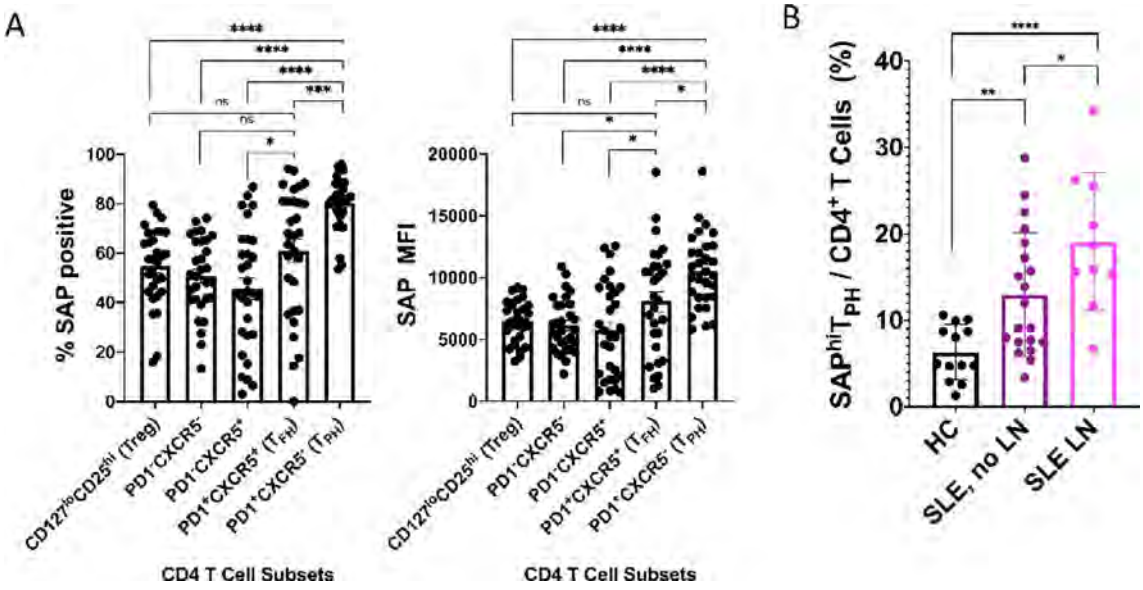

Figure 1. SAP expression in the T peripheral helper (TPH) CD4 T cells is associated with lupus nephritis. (A) SAP levels are increased in the TPH subset of CD4 T cells isolated from patients with SLE patients. (B)SAPhiTPH cells are expanded in SLE patients with LN compared to SLE patients without LN or in healthy controls (HC).

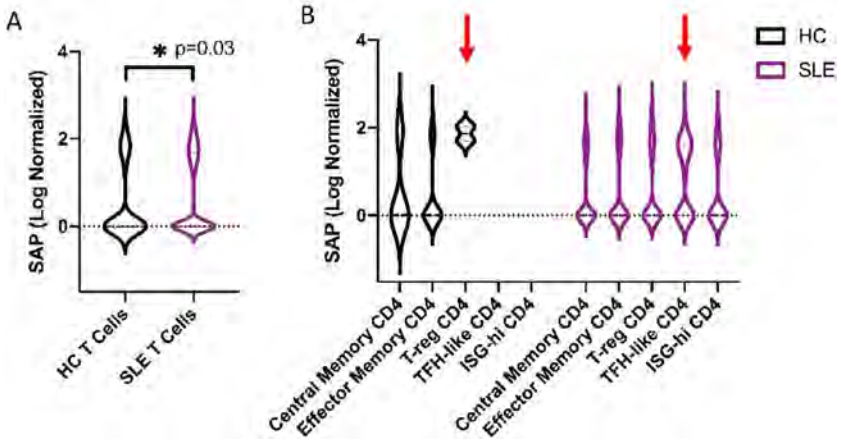

Figure 2. SAP levels are increased in the TFH-like renal infiltrating cells in LN. We analyzed the scRNA-Seq data from the publicly available Accelerated Medicines Partnership in the SLE LN dataset using the authors' original clustering algorithm. (A) SAP expression in all CD3 positive T cells. (B) Sub-analysis of SAP levels based on the authors' original T cell clustering algorithm. HC, healthy control. SLE, systemic lupus erythematosus.

Conclusion: We identified that $SAP^{hi}T_{PH}$ cells are associated with active SLE, specifically LN. Furthermore, we validated the presence of an analogous SAP^{hi} T_{FH}-like subset in the LN kidney biopsy samples, suggesting direct tissue-level infiltration by these cells. Future work to improve our understanding of SAP functions and signaling in these cells is likely to reveal novel therapeutic targets in SLE.

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Abstract Number: 0922

The Multi-Omic Landscape of Systemic Lupus Erythematosus Patients Highlights Metabolic and Immune Pathways Associated with Distinctive Clinical Profiles

Tomás Cerdó[1], Carlos Perez-Sanchez[2], Laurel Woodridge[3], Mª Angeles Aguirre[4], Rafaela Ortega Castro[5], Ismael Sánchez-Pareja[6], Laura Muñoz-Barrera[1], Pedro Segui[1], Christian Merlo[6], Pedro Ortiz Buitrago[7], Desiree Ruiz Vilchez[8], Maria del Carmen Abalos-Aguilera[8], Pilar Font Ugalde[1], Nuria Barbarroja[9], Alejandro Escudero[10], Elizabeth Jury[3] and Chary Lopez-Pedrera[11], [1]IMIBIC/Reina Sofia Hospital/University of Cordoba, Córdoba, Spain, [2]IMIBIC, Córdoba, Spain, [3]Centre for Rheumatology Research, Division of Medicine, University College London, London, United Kingdom, [4]Reina Sofía University Hospital/ Rheumatology Department, Córdoba, Spain, [5]Hospital Reina Sofía, Cordoba, Spain, [6]IMIBIC/ Reina Sofia Hospital/University of Cordoba, Rheumatology, Córdoba, Spain, [7]IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, [8]Rheumatology Department, Reina Sofia University Hospital/Maimonides Biomedical Research Institute of Cordoba (IMIBIC), Córdoba, Spain, [9]University of Cordoba, Córdoba, Spain, [10]SAS, Córdoba, Spain, [11]IMIBIC - Reina Sofia Hospital, Córdoba, Spain

SESSION INFORMATION
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Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
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Background/Purpose: Systemic lupus erythematosus (SLE) poses a significant challenge at the diagnostic and treatment levels due to its severe multisystem nature and notable heterogeneity in clinical course and therapeutic response. We investigated the serum proteomic and metabolomic profiles of SLE, to uncover new mechanisms underlying relevant clinical patterns.

Methods: Proteomic and metabolomic approaches were used to assess the serum levels of 184 inflammation and organ damage-related proteins [proximity extension immunoassay (PEA, Olink)] and 168 serum metabolites, [nuclear magnetic resonance (NMR, Nightingale)] in consecutive SLE patients (n = 135) and age-matched healthy donors (HD) (n = 27). In parallel, an extensive clinical and analytical profile was conducted. To evaluate the contribution of molecular profiles to the disease severity, unsupervised hierarchical clustering analyses were developed.

Results: Fifty-three proteins related to inflammation and organ damage, and 32 metabolites, were significantly altered (p = < 0.05, FC= 1.5, FDR) in the serum of SLE patients compared to HD. Unsupervised hierarchical clustering of proteomic data differentiated 2 patient clusters, where patients belonging to one cluster were characterized by elevated disease activity (SLEDAI >5), and increased incidence of atheroma plaques, dyslipidaemia, and hypertension. The top features driving classification were CD40, PGF, PDL1 and CSF1, with area under the curve >0.9, known to be associated with immune activation. At the molecular level, these patients showed 49 overexpressed proteins (p = < 0.05, FC= 1.5, FDR), enriched in biological pathways linked to chemotaxis and lipid metabolism.

Unsupervised hierarchical clustering of metabolomic data also identified 2 patient clusters with patients in one cluster showing a greater preponderance of lupus nephropathy (LN). The top features driving classification included short chain fatty acids, total fatty acids, total lipids and total free cholesterol, with area under the curve >0.9. Molecularly, these patients showed increased levels of 60 proatherogenic VLDL and LDL subsets (p = < 0.05, FC= 1.5, FDR) and metabolite enrichment analysis identified ketone body and butyrate pathways.

Integrating proteomic and metabolomic patient clusters identified two patient subgroups with the most (N=41) and least (N=36) severe molecular and clinical profiles. The group with more severe profiles (SLEDAI >5, prevalence of LN, and higher incidence of atheroma plaques, hypertension, and dyslipidaemia) exhibited higher levels of 56 proteins associated with

chemotaxis, inflammatory response and cytokine signalling, as well as 53 proatherogenic lipoproteins, ($p = < 0.05$, FC= 1.5, FDR) confirming the original molecular stratification.

Conclusion: The simultaneous application of proteomic and metabolomic approaches for molecular profiling in SLE patients offers valuable complementary information enabling a more accurate definition of their clinical profile, providing novel therapeutic targets and biomarkers of disease.

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Abstract Number: 0923

Identification of Lupus Nephritis Kidney Immune Populations via Hi-Resolution 20-Plex Immunohistochemistry Single-Cell Spatial Analyses

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SESSION INFORMATION

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Background/Purpose: Immunohistochemistry is the gold standard for antibody staining in microscopy. However, a lack of multiplexing limits its utility in the use of discovery. Here we demonstrate a serial Immunohistochemistry (sIHC) staining work-flow and analysis pipeline allowing for multiplexing of 18 antibodies on a single section.

Methods: 29 FFPE block were included for preliminary analyses from the 127 clinically indicated kidney biopsies recruited as part of the Lupus nephritis (LN) Accelerating Medicines Partnership (AMP) project).

Staining: 10mm sections from LN kidney biopsies in FFPE were deparaffinized, rehydrated, and antigen retrieved with boiling citrate. Slides were blocked for peroxidases, washed, and incubated with primary antibody, secondary HRP reagents, AEC-Red Chromogen, and Hematoxylin. Images were acquired at 40X magnification. Slides were decolored in 90% Ethanol and stripped in an antibody elution buffer, then cycled for all markers.

Image Stacks: Image files were imported into HALO-AI v3.5 (Indica Labs) for deconvolution, pseudo-coloring, co-registration, and alignment. Registered images were fused to create a single composite image with all 18 markers and a representative DNA and counterstain channel. Tissue regions were identified by a DenseNet V2 AI tissue classifier trained on an original co-registered IHC image and individual cell objects were identified by nuclear detection and segmented by cell distance boundaries.

Analysis: Single-cell marker expression datasets were analyzed in R. Cells located on the edge of the tissue or in regions classified as wrinkles were removed to reduce potential artifacts. Marker expression values underwent CLR-normalization and standardization within each sample and then combined and harmonized by Harmony to further minimize batch effect. PCA and UMAP were used for dimensional reduction, and KNN and SNN algorithms were applied to identify cell clusters. Clusters with CD45 expression levels > 2 standard deviations were selected as candidate immune cell clusters. Cell clusters with high keratin marker expression were removed to eliminate renal tubular epithelial cells. Remaining clusters were then re-clustered via KNN and SNN to identify distinct immune cell types with the help of heatmaps and feature plots.

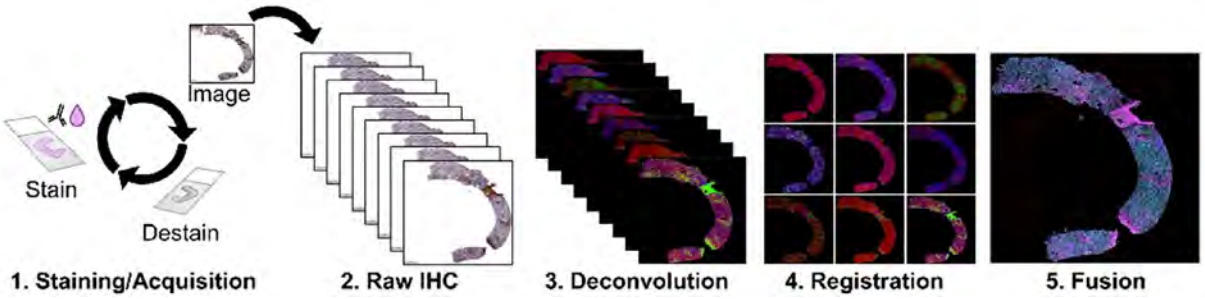

Figure 1-sIHC Staining and Image Stack Pipeline

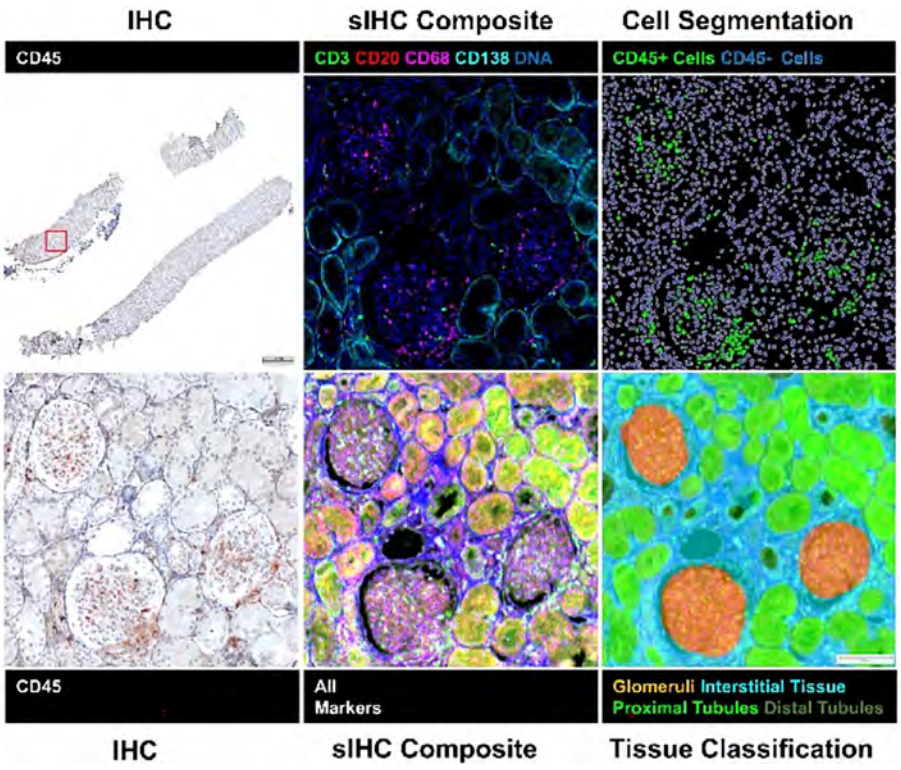

Figure 2 – sIHC Composites, Cell Segmentation, and AI-Based Tissue Classification

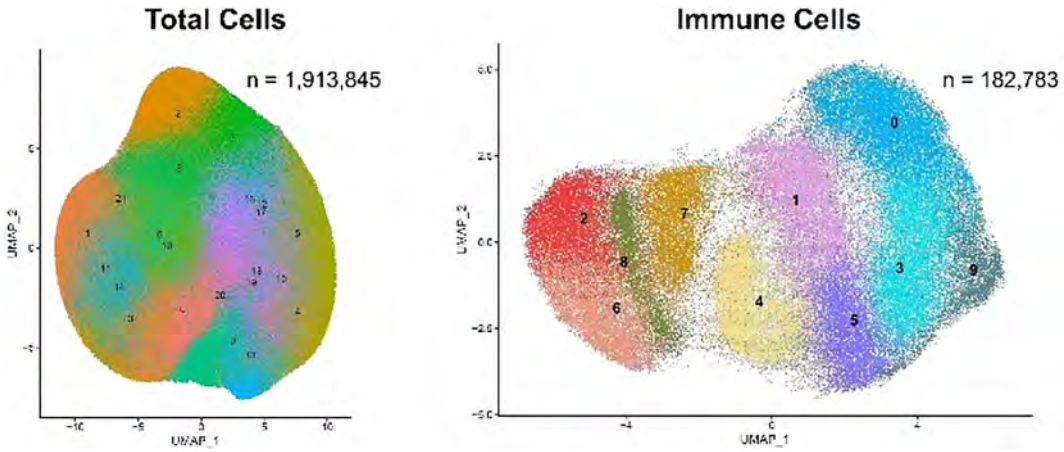

Figure 3 – Dimension Reduction and Clustering of sIHC Single-Cell Data

Results: The co-registration and fusion of images produced image stacks in which all 20 markers could be visualized within the same image. Tissue classification and single-cell segmentation allowed for clear identification of regions of the tissue and the individual cells that constituted each region. Single-cell analyses identified 1,913,845 cells and 182,783 CD45+ cells which were classified into 10 distinct immune cell phenotypes.

Conclusion: Here we demonstrate imaging and analysis of 20 markers using sIHC for the first time, while producing a large, spatially informed, clinically-relevant dataset in 29 LN Kidney Biopsies.sIHC can be successfully employed to perform multiplexed whole slide analysis harnessing both the subcellular resolution (brightfield) and the reliability of IHC.

Disclosure: C. Marlin: None; **A. Celia**: None; **R. Furie**: Biogen, 2, 5; **J. James**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 2, Novartis, 2, Progentec Biosciences, 5; **A. Fava**: Annexon Biosciences, 2, Sanofi, 1; **J. Guthridge**: None; **A. Rosenberg**: None; **T. Stephens**: None; **C. Wright**: None; **J. Hodgin**: AstraZeneca, 5, 6, Eli Lilly, 5, Gilead, 5, Janssen, 5, Moderna, 5, Novo Nordisk, 5, Regeneron, 5; **P. Izmirly**: None; **H. Belmont**: Alexion, 6, Aurinia, 6; **J. Anolik**: None; **M. Petri**: Alexion, 1, Amgen, 1, AnaptysBio, 1, Annexon Bio, 1, Argenx, 1, Arhros-Focus Med/Ed, 6, AstraZeneca, 1, 5, Aurinia, 1, 5, 6, Axdev, 1, Biogen, 1, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CVS Health, 1, Eli Lilly, 1, 5, Emergent Biosolutions, 1, Exagen, 5, Exo Therapeutics, 2, Gilead Biosciences, 2, GlaxoSmithKlein(GSK), 1, 5, 6, Horizon Therapeutics, 2, Idorsia Pharmaceuticals, 2, IQVIA, 1, Janssen, 1, 5, Kira Pharmaceuticals, 2, MedShr, 6, Merck/EMD Serono, 1, Momenta Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Proviant, 2, Sanofi, 2, Sinomab Biosciences, 2, Thermofisher, 5, UCB, 2; **J. Buyon**: Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, Related Sciences, 1; **D. Kamen**: None; **C. Putterman**: Equillium, 2, KidneyCure, 1, Progentec, 2; **A. The**: None; **C. Lee**: None; **X. Yang**: None.

Abstract Number: 0924

Distinct Cell-Bound Complement Activation Products Associate with Disease Activity and Immune Transcriptional Signatures in SLE

Gabriel Arguelles, Lynne Mitchell, Dennis Hourcade, John Atkinson, Elisha Roberson and **Alfred Kim**, Washington University School of Medicine, St. Louis, MO

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Complement plays a central role in SLE, generating an array of bioactive soluble and cell-bound complement activation products (CB-CAPs) during disease activity. Data are lacking though detailing the types, quantities, and impacts of the numerous CB-CAP on SLE immune cells, especially with respect to disease activity. We applied a mass cytometry (MC) panel that can detect over 20 CB-CAPs and complement receptors to PBMCs from paired flare and remission samples from 6 patients with classified SLE. Furthermore, we analyzed single-cell transcriptional profiles on flaring samples using antibodies to the most prevalent CB-CAPs using cellular indexing of transcriptomes and epitopes (CITE)-seq.

Methods: Adults with ACR- or SLICC-classified SLE (n=6) were consented for PBMC collection at Washington University School of Medicine. Isolated PBMCs were subjected to single cell MC and CITE-seq (n=3). MC data analysis was performed with Cytobank. CITE-seq data analyses was performed with Seuret, gProfileR, and Comprehensive Multi-omics Platform for Biological InterpretatiOn (COMPBIO).

Results: We found the highest frequency of C4d, C3d, C5, and Bb deposition on B cells compared to T cells and monocytes during SLE flares (Fig 1). During disease remission, low levels of all CB-CAPs were observed in these cells. Compared to controls, transitional B cells from flaring patients with SLE had high levels of C5 and Bb with little C4d or C3d (Fig 2). $CD11c^+$ B cells from flaring patients also had elevated Bb deposition compared to controls. CITE-seq transcriptional profiling identified Bb- and C3d-bearing $CD11c^+$ B cells possessing a type I interferon signature, with Bb-bearing B cells further possessing a TNF/NF-κB transcriptional signature.

Conclusion: A high level of CB-CAP deposition was observed in B cells obtained from flaring subjects with a SLE, which was absent during disease remission. The types of CB-CAPs found on PBMCs were not uniform between cell types, potentially opening a previously undescribed heterogeneity in SLE. Additional heterogeneity was observed in the transcriptional profiles associated with specific CB-CAPs on B cells. These pilot data demonstrate the feasibility of the MC complement

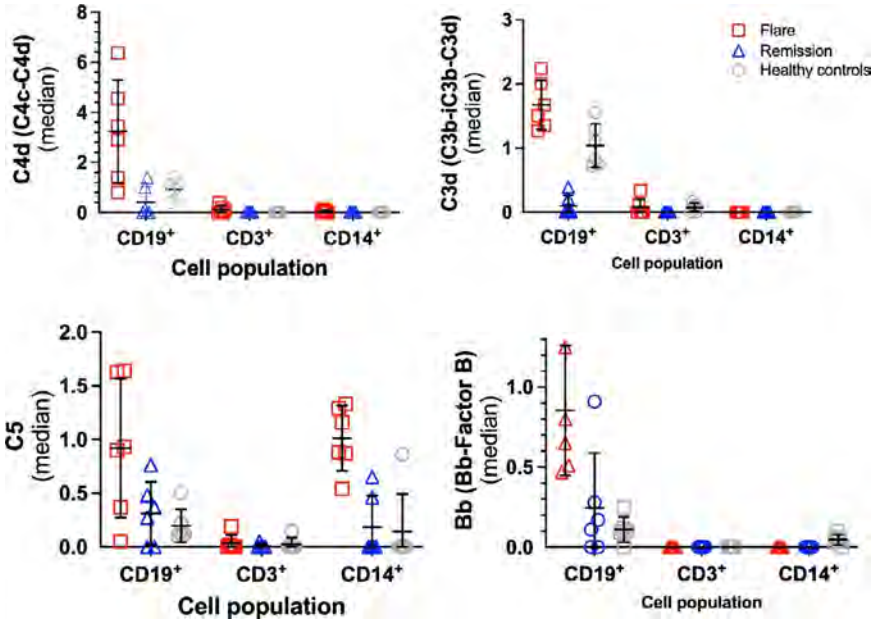

Fig 1. Mass cytometry of CB-CAP deposition on PBMCs from paired flaring and remission patients with SLE, along with matched controls.

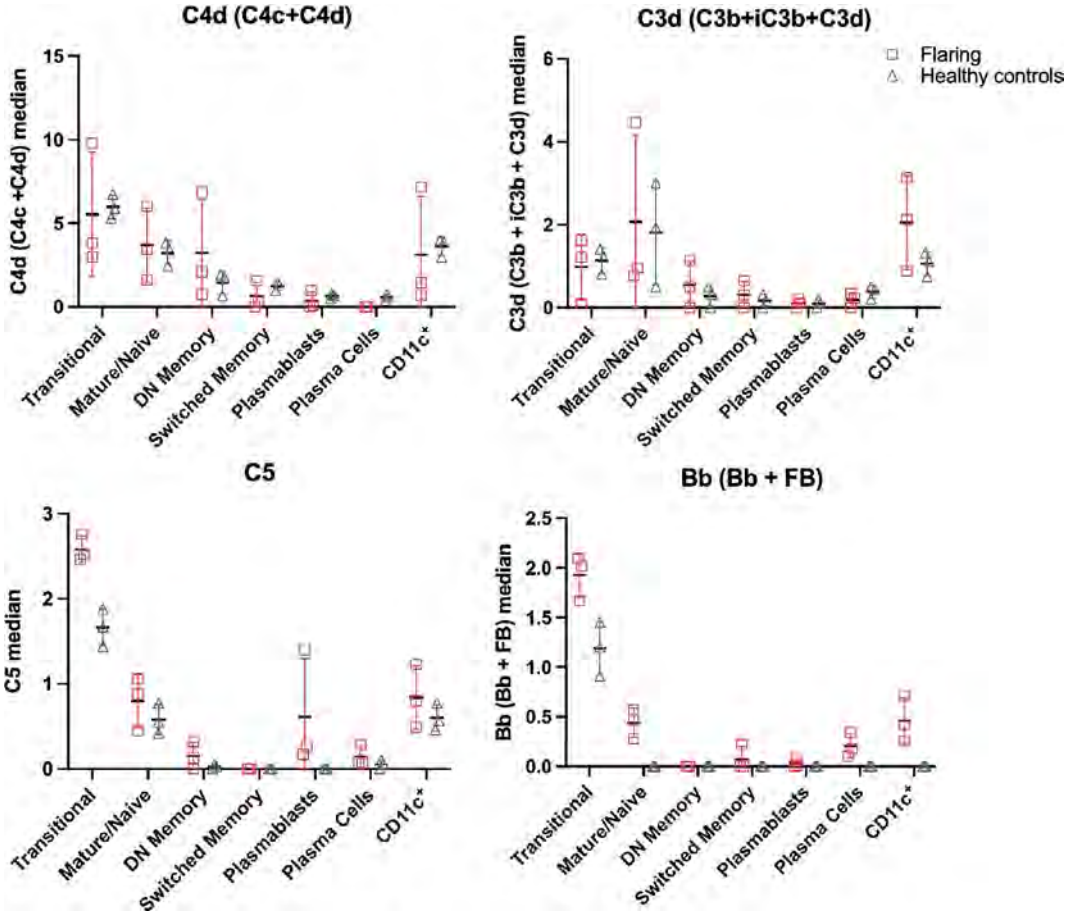

Fig 2. Mass cytometry of of CB-CAP deposition on B cell subsets from flaring patients with SLE versus matched controls.

panel on human samples, and the potential insights CITE-seq has using CB-CAPs in discovering novel mechanisms of complement activation and regulation.

Disclosure: G. Arguelles: None; **L. Mitchell**: None; **D. Hourcade**: None; **J. Atkinson**: Alexion Pharmaceuticals, 2, Alnylam Pharmaceuticals, 2, Celldex Therapeutics, 2, Genentech, 2, Idera Pharmaceuticals, 2, Kereos Inc, 2; **E. Roberson**: None; **A. Kim**: ANI Pharmaceuticals, 2, AstraZeneca, 2, 5, Aurinia Pharmaceuticals, 2, Exagen Diagnostics, 2, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Kypha Inc, 2, 10, Novartis, 5, Pfizer, 2.

Abstract Number: 0925

IL-4 Acts Through Aryl Hydrocarbon Receptor to Antagonize TLR7-induced Double Negative 2 B Cells in Lupus

Changming Lu, Hui-chen Hsu, Min Gao, Jose Rubio, Winn Chatham and **John Mountz**, University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Etiology & Pathogenesis Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: We recently showed that in SLE, IL-4 suppressed the development of interferon-beta (IFNβ) and TLR7-stimulated T-bet$^+$ double negative 2 (DN2) B cells. Here we investigate the potential DN2 B-cell suppressive effects of IL-4 through the IL-4-induced 1 (IL-4i1)-aryl-hydrocarbon receptor (AhR) pathway.

Methods: The mechanism of IL-4 in suppressing the development of DN2 B cells *in vivo* was studied using R848-treated BXD2 mice. The B-cell developmental trajectory was determined using single-cell RNA-sequencing (scRNA-seq) analysis. Adult patients whomet theACR 1997 revised criteria for SLE were recruited. The *in vitro* effects of IL-4 and two potent AhR agonistic ligands, Kynurenine (Kyn) and 6-formylindolo[3,2-b]carbazole (FICZ) in suppressing the development of DN2 B cell were determined using IFNβ plus TLR7 stimulated B cells. B-cell subsets and transcription factors (TFs) expression was measured by surface and intra-nuclear FACS analysis. AhR pathway and target genes were analyzed using qPCR. Autoantibodies were measured by ELISA.

Results: Administration of IL-4 significantly inhibited the development of anti-Smith, anti-DNA, and anti-histone autoantibodies induced by the TLR7 agonist R848 in BXD2 mice. This was associated with a decreased percentage of CD11c$^+$T-bet$^+$ IgD$^-$ B cells. Feature-barcoding single-cell RNA-sequencing analysis showed that IL-4 modulated B-cell development at the transitional stage 2 (T2) and skewed naïve B cells to develop into the CD23$^+$CD21$^-$ follicular B cells. IL-4 induced the gene encoding *Ii4i1*, an enzyme that metabolizes aromatic amino acids, and this was associated with the upregulation of AhR and downstream genes *Cyp1a1* and *Ido1*. In the absence of IL-4, both Kyn and FICZ significantly suppressed TLR7 plus IFNβ-induced T-bet$^+$ B-cell development *in vitro* in BXD2 mice. Analysis of AhR expression in healthy control (HC) and SLE subjects show a significantly lower expression of AhR in both the IgD$^-$CD27$^-$ DN and IgD$^+$CD27$^-$ naïve B-cell populations of SLE compared to HC. qPCR analysis further indicates a significantly lower expression of *CYP1A1* and *IL4I1* in SLE B cells compared to HC B cells. B cell culture with either IL-4 or Kyn significantly reduced the development of DN2 B cells stimulated by IFNβ plus TLR7. Kyn also significantly induced the expression of *CYP1A1* and promoted the expression of PD-1 in IFNβ plus TLR7-stimulated B cells.

Conclusion: Our results suggest that IL-4R acts through the IL4i1-AhR pathway to induce a B-cell regulatory response to TLR7 and type I IFN. Identifying small molecular metabolites that act directly in B cells to induce homeostasis may lead to the development of orally active druggable targets that are efficacious in treating SLE.

Disclosure: C. Lu: None; **H. Hsu**: None; **M. Gao**: None; **J. Rubio**: None; **W. Chatham**: None; **J. Mountz**: None.

Abstract Number: 0926

Single-cell Multi-Omic Evaluation of Differences in Immune Cell Populations in Progression Toward Systemic Lupus Erythematosus

Aleksandra Bylinska, Miles Smith, Samantha Slight-Webb, Carla Guthridge, Caleb Marlin, Kevin Thomas, Christian Wright, Marci Beel, Susan Macwana, Wade DeJager, Judith James and Joel Guthridge, Oklahoma Medical Research Foundation, Oklahoma City, OK

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Several groups of individuals are at higher risk for SLE, including those with African American ancestry (AA), lupus-associated autoantibodies (ANA+), or some clinical symptoms of SLE, termed incomplete lupus erythematosus (ILE). However, only a minority of ANA+ individuals develop autoimmune disease, and most ILE patients never progress

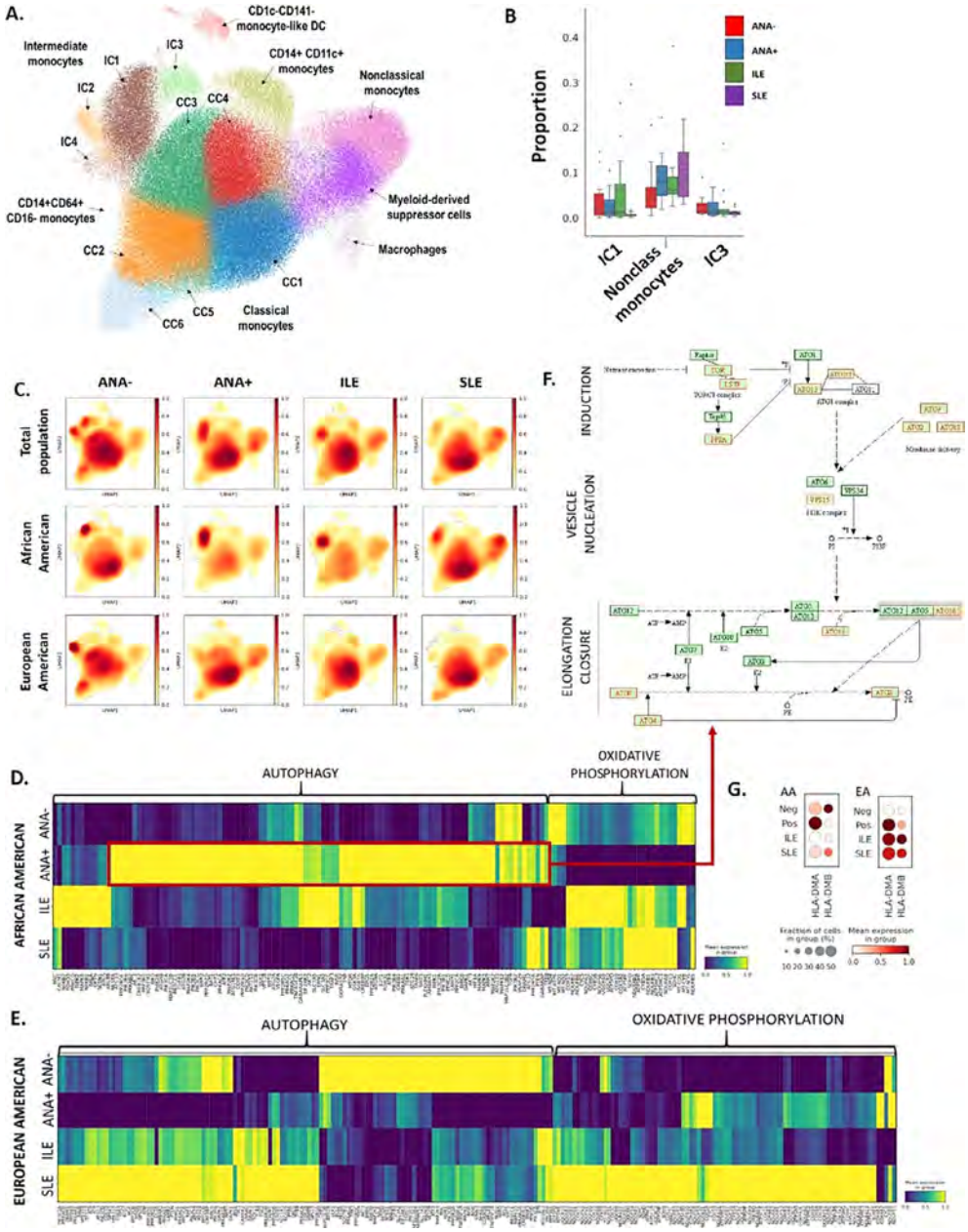

Fig.1. A. UMAP projection of distinct myeloid clusters. B. Cell fractions for distinct cluster by disease group. C. Density of myeloid cell total population and by ancestry across 4 disease groups. D, E. Expression of genes involved in autophagy and oxidative phosphorylation pathways by disease group for each ancestry. F. Autophagy pathway (genes expressed higher in AA ANA+ in red box) G. HLA-DM expression by ancestry and disease group.

to SLE. Metabolic pathways are known to be involved in myeloid cell dysregulation; however, whether they contribute to the progression of autoimmune disease remains unclear. This study determined whether alterations in myeloid and B cell population frequencies or activation of particular cellular processes are dysregulated in subjects at-risk of SLE.

Methods: PBMCs from 32 subjects from African (AA) or European ancestry (EA), divided evenly among healthy individuals (ANA-), healthy with autoantibodies (ANA+), ILE, and SLE. We performed multi-omic single-cell experiments (5' scRNA-seq/137-plex CITE-seq and BCR/TCR repertoire analysis) to assay for distinct disease-associated clusters, differential gene signatures and dysregulated pathways.

Results: We obtained profiles for 324,721 cells across all PBMCs. We identified 8 distinct myeloid (Fig 1A) and 7 B cell clusters across all subjects (Fig 2A). The proportion of cells in each cluster varied by disease group and ancestry (Fig 1B,C, 2B). The proportion of nonclassical monocytes was higher in SLE with variations between ANA+ and ILE (Fig 1B,C). Intermediate monocyte fractions were lower in SLE (Fig 1B,C). Fractions of naïve B cells were already higher in EA ANA-, while memory B cells are higher in AA ANA+ and EA ILE, EA SLE (Fig. 2B). Analysis of differentially expressed genes revealed the importance of metabolic processes in both cell types, such as autophagy and oxidative phosphorylation that varied between ancestries (Fig 1D-E, 2D-E). A discrete part of autophagy pathway is upregulated in myeloid cells of AA ANA+, while a different set of genes is upregulated in AA ILE (Fig 1D). Autophagy profile is detected earlier in EA; its progression is observed along disease transition and cell states (Fig 1E). Specific autophagy-related genes are already upregulated in EA ANA-. Oxidative phosphorylation pathway is downregulated in AA ANA+ but upregulated in AA ILE and AA SLE (Fig 1D). In EA, upregulation was mainly observed in SLE patients (Fig 1E). Involvement of antigen presentation pathways and altered expression of

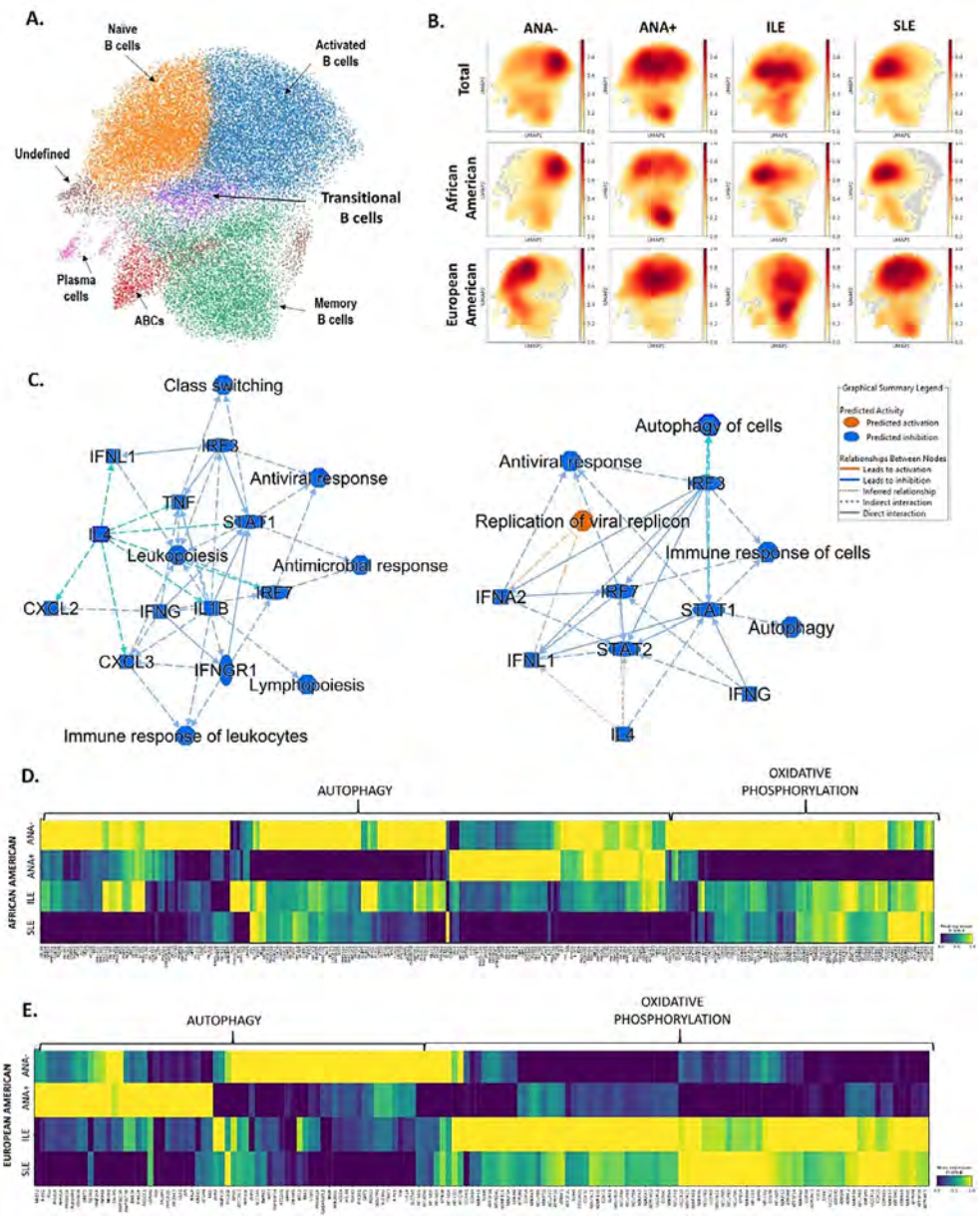

Fig.2. A. UMAP projection of distinct B cell clusters. B. Density of B cells total population and by ancestry across 4 disease groups. C. Graphical summary of pathways and transcription factors involved in B cell dysregulation. D, E. Expression of genes involved in autophagy and oxidative phosphorylation pathways by disease group for each ancestry.

HLA-DM were detected in AA, which might be related to autophagy dysregulation (Fig 1F, G). Oxidative phosphorylation pathway is upregulated in B cells of EA ILE and EA SLE (Fig. 2E), however it is downregulated in AA ANA+ (Fig. 2D). We found additional signatures in B cells suggestive of the activation of pathways related to antiviral response, class switching and lymphopoiesis, as well as the involvement of transcription factors (IFN, TNF, IL4, STAT) in SLE (Fig.2C).

Conclusion: Dysregulation of oxidative phosphorylation and autophagy pathways in both monocyte and B cell populations is suggestive of a preclinical autoimmunity development trajectory. Alterations of these processes may vary by ancestral background, reflecting the heterogeneity of SLE presentation and trajectory.

Disclosure: A. Bylinska: None; **M. Smith**: None; **S. Slight-Webb**: None; **C. Guthridge**: None; **C. Marlin**: None; **K. Thomas**: None; **C. Wright**: None; **M. Beel**: None; **S. Macwana**: None; **W. DeJager**: None; **J. James**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 2, Novartis, 2, Progentec Biosciences, 5; **J. Guthridge**: None.

Abstract Number: 0927

A Complex Interplay Among Gut *Lachnoclostidium*, HLA Haplotype DRB1*07:01, and the TNF Superfamily in Anti-Ro+ Women with a Spectrum of Preclinical and Clinical Autoimmunity Whose Children Have Neonatal Lupus

Robert Clancy[1], Caroline Izmirly[1], Miranda Marion[2], Nicola Fraser[1], Joel Guthridge[3], Timothy Howard[2], Peter Izmirly[4], Mala Masson[5], Jill Buyon[1], Judith James[3] and Carl Langefeld[6], [1]NYU Grossman School of Medicine, New York, NY, [2]Wake Forest University, Winston-Salem, NC, [3]Oklahoma Medical Research Foundation, Oklahoma City, OK, [4]New York University School of Medicine, New York, NY, [5]New York University, New York, NY, [6]Wake Forest University School of Medicine, Winston-Salem, NC

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Mothers of children with neonatal lupus (NL) are often clinically asymptomatic or have insufficient criteria for a formal rheumatologic diagnosis, despite having high titers of autoantibodies to Ro60 and 52. That some women never progress, while others transition to SLE or SS, provides a unique opportunity to identify early drivers of disease. Informed by quantifications of cytokine levels in army recruits who develop lupus, TNF superfamily factors are posited to drive progression from benign preclinical to clinical autoimmunity.While many factors have contributed to this model, the gut microbiome and its interplay with HLA haplotypes (class II, in particular) are understudied. Here, we test the specific hypothesis that levels of three cytokines (BAFF, TNFRI, TNFRII) vary as a function of gut *Lachnoclostridium* abundance and DRB1*07:01 status in anti-Ro+ NL mothers who have progressed to clinical disease.

Methods: Anti-Ro+ NL mothers (n=59) who carried the allele of interest (DRB1*03:01 at HLA, Figure, Panel A) had 16S microbiome sequencing of stool samples. Taxa relative abundances, including that of *Lachnoclostridium*, were center log ratio (CLR) transformed, hereafter referred to as relative abundance, consistent with the compositional nature of 16 S data.BAFF, TNFRI, and TNFRII were assayed using a validated multiplex bead-based (xMAP) approach in serum from NL mothers with a blood sample drawn near the time of stool specimen collection and who had HLA genotyping.

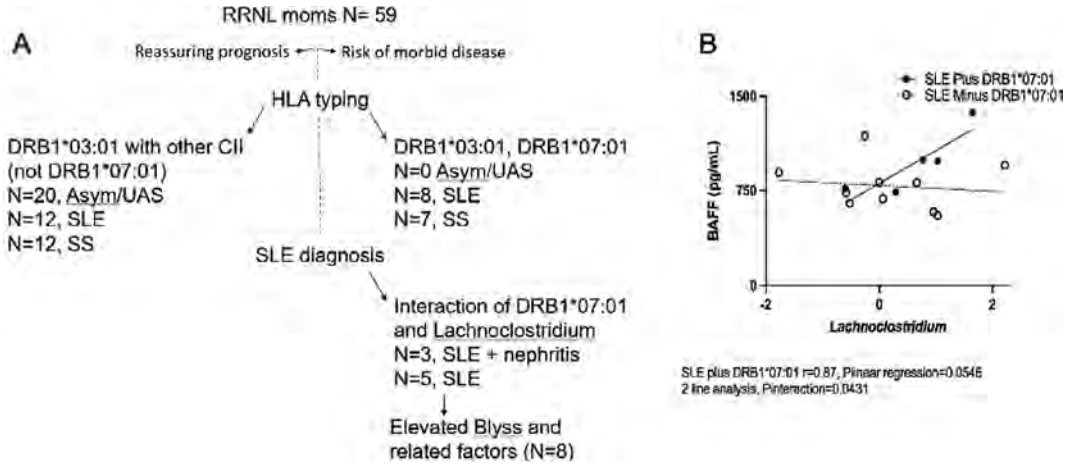

Figure. Panel A. Flow diagram of the various diseases and alleles. Panel B. Quantifications of the TNF superfamily factors (BAFF is shown, similar data with TNFRI and TNFRII) in NL mothers who develop lupus, in context of gut Lachnoclostridium and HLA haplotype.

Results: In addition to carrying DRB1*03:01, the HLA Haplotype also included DRB1*07:01, which was reported in 8/20 NL mothers with SLE and 7/19 NL mothers with SS (Figure, Panel A). Of those with SLE, 4 had lupus nephritis (LN) with 3 carrying DRB1*07:01 while only 5/16 without LN carry DRB1*07:01. In contrast to SLE and SS, DRB1*07:01 was not observed in NL mothers with preclinical disease (0 of 20; asymptomatic/undifferentiated autoimmune syndrome, Asym/UAS). Serologic levels of BAFF, TNFRI, and TNFRII were notable in the NL mothers with SLE versus subjects in the SS and Asym/UAS groups. Specifically, for TNFRI, levels (pg/mL) of 1255, 1265, and 1160 correspond to SLE, SS, and Asym/UAS, respectively.In addition there was an enrichment of SLE with DRB1*07:01 (1321 pg/mL). *Lachnoclostridium* relative abundance was positively associated with levels of BAFF, TNFRI, and TNFRII in NL mothers who carry DRB1*07:01 but not in those without DRB1*07:01 (with r values of 0.87, 0.79, 0.55, respectively, Figure, Panel B). NL mothers diagnosed with SS (N=19) did not show a parallel trend as that of those diagnosed with SLE.Specifically, those with SS had comparable TNFRI levels within groups that were stratified by DRB1*07:01 haplotype.*Lachnoclostridium* did not exhibit an association with DRB1*07:01, suggesting a dichotomy of clinical disease for NL mothers.

Conclusion: These results suggest a path to discriminate anti-Ro-positive SLE patients with a reassuring prognosis from those at risk of morbid disease based on the complex interplay between DRB1*07:01 and *Lachnoclostridium* abundance. Further, NL mothers who are DRB1*07:01 positive may trigger a higher relative abundance of *Lachnoclostridium,* leading to a cascade of events toward clinical disease.

Disclosure: R. Clancy: None; **C. Izmirly**: None; **M. Marion**: None; **N. Fraser**: None; **J. Guthridge**: None; **T. Howard**: None; **P. Izmirly**: None; **M. Masson**: None; **J. Buyon**: Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, Related Sciences, 1; **J. James**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 2, Novartis, 2, Progentec Biosciences, 5; **C. Langefeld**: None.

Abstract Number: 0928

Skewing of B Cell Receptor Repertoire in Unswitched Memory B Cells Is Associated with Disease Activity of Systemic Lupus Erythematosus and Targeted by Belimumab

Keishi Fujio[1], Mineto Ota[1], Masahiro Nakano[2], Yasuo Nagafuchi[3], Satomi Kobayashi[1], Hiroaki Hatano[2], Ryochi Yoshida[1], Yuko Akutsu[1], Takahiro Itamiya[1], Nobuhiro Ban[4], Yumi Tsuchida[1], Hirofumi Shoda[1], Kazuhiko Yamamoto[5], Kazuyoshi Ishigaki[6] and Tomohisa Okamura[7], [1]Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, [2]Laboratory for Autoimmune Diseases, RIKEN Center for Integrative Medical Sciences, Tokyo, Japan, [3]Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, Department of Functional Genomics and Immunological Diseases, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, [4]Research Division, Chugai Pharmaceutical Co., Ltd., Yokohama, Japan, [5]Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo and Laboratory for Autoimmune Diseases, Center for Integrative Medical Sciences, RIKEN, Yokohama, Japan, [6]RIKEN, Tokyo, Japan, [7]Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo and Department of Functional Genomics and Immunological Diseases, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Etiology & Pathogenesis Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Despite the involvement of B cells in the pathogenesis of immune-mediated diseases, the biological mechanisms underlying their function are poorly understood. To address this gap, we constructed and investigated a large-scale repertoire catalog of five B cell subsets from patients with immune-mediated diseases, including systemic lupus erythematosus (SLE).

Methods: We mapped B cell receptor regions from RNA sequencing data of sorted B cell subsets. Our dataset consisted of 595 donors with immune-mediated diseases and healthy individuals. We characterized the repertoire features from various aspects, including their association with immune cell transcriptomes and clinical features, as well as their response to belimumab treatment.

Results: In healthy individual, gene usage preference among 5 B cell subsets was observed. Principal component analysis (PCA) of VDJ gene usage revealed clear separation according to cell types, suggesting B cell development based on VDJ gene segments. In 136 SLE patient, VDJ gene usage was skewed, particularly in plasmablasts and unswitched-memory B cells. We developed a scoring system, repertoire naiveness (RN) score, to assess this skewing. RN scores in plasmablasts and USM B showed significant positive correlations with SLEDAI-2K. Moreover, RN score positively correlated with peripheral helper T (TPH) cell transcriptomic signatures and negatively correlated with the amount of somatic hypermutations in plasmablasts, suggesting an association with the extra-follicular pathway. Furthermore, this skewing led to increased usage of IGHV4-34 in unswitched-memory B cells, with its usage showing a significant positive correlation with disease activity in SLE. Mediation analysis indicated that over one-half of the association between RN scores in USM B and SLEDAI-2K was mediated by IGHV4-34 usage. Notably, belimumab treatment ameliorated gene usage skewing in unswitched-memory B cells, but not in the other subsets. These results were consistent with our previous functional genome analysis of ImmuNexUT dataset that indicated the association between generic risk of SLE and unswitched memory B cells (Ota M et al. Cell 2021;184:3006-3021).

Conclusion: Our multimodal repertoire analysis revealed the importance of unswitched-memory B cells in the pathogenesis of SLE.

Disclosure: K. Fujio: AbbVie/Abbott, 6, Asahi Kasei, 5, 6, Astellas, 6, AstraZeneca, 6, Ayumi, 6, Bristol-Myers Squibb(BMS), 5, 6, Chugai Pharmaceutical., 5, 6, Daiichi-Sankyo, 6, Eisai, 5, 6, Eli Lilly, 5, 6, Janssen, 6, Novartis, 6, Ono, 6, Pfizer, 6, Sanofi, 6, Tanabe Mitsubishi, 5, 6, Tsumura, 5; **M. Ota**: Chugai, 12, MO belonged to the Social Cooperation Program, Department of functional genomics and immunological diseases, supported by Chugai Pharmaceu; **M. Nakano**: None; **Y. Nagafuchi**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, 6, Chugai Pharmaceutical., 12, belong to the Social Cooperation Program, Department of Functional Genomics and Immunological Diseases, supported by Chugai Pharmaceutical., GlaxoSmithKlein(GSK), 5, Novartis, 6; **S. Kobayashi**: None; **H. Hatano**: None; **R. Yoshida**: None; **Y. Akutsu**: None; **T. Itamiya**: Chugai Pharmaceutical Co., Ltd., 5; **N. Ban**: Chugai, 3; **Y. Tsuchida**: None; **H. Shoda**: AbbVie/Abbott, 6, Asahi Kasei, 6, Astellas, 6, AstraZeneca, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Chugai Pharmaceutical., 6, Daiichi-Sankyo, 6, Eisai, 6, Eli Lilly, 6, Gilead, 6, GlaxoSmithKline, 6, Jansen, 6, Novartis, 6, Pfizer, 6, Sanofi, 6, Taisho Pharmaceutical, 6, Takeda, 6; **K. Yamamoto**: AbbVie, 6, Pfizer Japan Inc, 12, Outsourcing contract, RegCell, 1, Sun Pharmaceutical Industries Ltd, 6; **K. Ishigaki**: None; **T. Okamura**: Chugai Pharmaceutical., 12, belong to the Social Cooperation Program, Department of Functional Genomics and Immunological Diseases, supported by Chugai Pharmaceutical..

Abstract Number: 0929

Persistent Up- or Down-regulation of SOCS1 Exacerbates the Pathogenesis of Systemic Lupus Erythematosus Through Several Mechanisms

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: SOCS1 (suppressor of cytokine signaling 1) is a suppressor molecule of the JAK/STAT pathway and has been reported to be involved in the pathogenesis of SLE. T cell-specific or regulatory T cell (Treg)-specific *Socs1*-deficient mice exhibited lupus pathology with enhanced Treg plasticity, which rapidly lost the expression of Foxp3 through DNA hypermethylation of the Foxp3 promoter/enhancer and produced high levels of inflammatory cytokines (Takahashi R et al., J Immunol. 2017, Takahashi R et al., J Exp Med. 2011). In addition, loss-of-function mutant lineages of SOCS1 have recently been found to develop SLE and other diseases (Nature (2020, Nat Commun (2020)). In the present study, we examined whether the pathogenesis of SLE is suppressed in T-cell specific *Socs1* transgenic (*Socs1* Tg) mice.

Methods: Imiquimod cream was administered on the ear of age-matched 8-week-old female wild-type (WT) mice and *Socs1* Tg mice every other day for up to 8 weeks, as reported previously. Pathological and immunological analyses of the spleen, lymph nodes, and kidneys of these mice were performed. Tregs and non-Tregs ($CD4^+CD25^-$ effector cells) from *Socs1* Tg or WT mice with or without induction of lupus pathology were isolated using a cell sorter and analyzed. Peripheral blood lymphocytes of SLE patients were analyzed by gene transfer of *Socs1*.

Results: In the *Socs1* Tg mice, the lupus-like phenotype was worse than when lupus was induced in WT mice by DNA antibody measurements and pathological analysis. To analyze those mechanisms, we first analyzed Treg function and found that *in vitro*, Tregs from *Socs1* Tg mice had a more stable suppressive function than Tregs from WT mice, even under inflammatory conditions, by preventing plasticity. *In vivo*, in lupus-induced WT mice, Tregs from *Socs1* Tg mice suppressed lupus pathology more potently than those from WT mice. Furthermore, similar experiments in lupus-induced *Socs1* Tg mice

showed that lupus pathology could not be suppressed with the same amount of Tregs derived from WT or *Socs1* Tg mice as in lupus-induced WT mice, but could be suppressed by transplanting a sufficient amount of Tregs from *Socs1* Tg mice. Next, analysis of non-Tregs in *Socs1* Tg mice showed that they were activated and reduced in number in the spleen and lymph nodes, with cytokine production such as IL-17A, which was emphasized in the induction of lupus pathology. As a further cause of the reduction in non-Tregs, non-Tregs of *Socs1* Tg mice were observed to decrease IL-7 receptor expression and increase apoptosis, which was accentuated in the induction of lupus pathology. Finally, *Socs1* expression in peripheral blood lymphocytes of SLE patients did not show a characteristic relationship with lupus activity. However, transfection of *Socs1* into lymphocytes from SLE patients promoted apoptosis in some patients but was not related to the production of IFNγ or IL-17A.

Conclusion: Both sustained up- or down-regulation of SOCS1 cause changes in $CD4^+$ T cells through different mechanisms and exacerbate the pathogenesis of lupus. The importance of further exploring these pathological mechanisms to understand the dynamics of SOCS1 expression in SLE patients and to search for factors that regulate this dynamics is suggested.

Disclosure: R. Takahashi: None; **Y. Imura**: None.

Abstract Number: 0930

Genetic Risk Profiles of Patients with Lupus Nephritis to Identify Those at Risk for Kidney Deterioration and Eventual Damage

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Many genetic variants are associated with lupus nephritis (LN). Yet, the majority of associated variants have a small effect size; hence, they convey small risk. Polygenic risk scores (PRS) provide a unique opportunity to aggregate an individual's genetic risks. PRS are a weighted sum of genome-wide genetic risk load for an individual such that multiple variants, including variants that do not meet genome-wide cutoff, are included. We hypothesize that PRS constructed using multiple variants, along with demographic and clinical variables, are predictive of LN outcomes such as the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) estimated glomerular filtration rate (eGFR) and end-stage kidney disease (ESKD).

Methods: Subjects with LN were genotyped using Illumina Global Screening Array V3. Ancestry was determined using principal component analysis of the genotyped data. PRS for systemic lupus erythematosus (SLE) and CKD were constructed using multi-ancestry SLE and CKD base GWAS using the clumping and thresholding (C+T) approach. The base SLE Immunochip study included 11,590 SLE cases and 15,984 controls, and the base CKD GWAS study used eGFR as outcome and included 1,201,909 individuals. Relationships between SLE and CKD PRS with CKD-EPI eGFR and ESKD were assessed using multivariable linear and logistic regression models, adjusting for ancestry, sex, age at SLE diagnosis and history (yes/no) of hypertension, diabetes, and smoking.

Results: 653 individuals (87.3% female, 19.4% smokers, 9.8% diabetic and 55.2% hypertensive) were considered in the study. Genotyping PCA identified 46.6% African American, 27.9% European American, 13.1% Argentinian, 9.6% Mexican, and 2.9% Asian individuals. Mean (SD) age at SLE diagnosis was 26.7 (11.9) years. Mean (SD) CKD-EPI eGFR at last visit was 71.0 (41.4) mL/min/1.73m^2; 86 (16.3%) individuals developed ESKD. 529 individuals were included in the final analyses following quality control and exclusion of individuals of Asian ancestry due to small sample size. Following C+T, approximately 23K SNPs were retained for both eGFR and ESKD PRS computation using SLE base data, and 482K SNPs were retained using CKD base data.

Lower eGFR was associated with higher SLE PRS (β = -8.45; 95% CI: -12.9, -3.97), older age (β = -0.44; 95% CI: -0.77, -0.12) and history of hypertension (β = -18.9; 95% CI: -27.6, -10.1); CKD PRS and ancestry were not associated with eGFR. Similarly, increased odds of ESKD were associated with higher SLE PRS (OR: 1.59; 95% CI: 1.08, 2.38), higher CKD PRS (OR: 2.61; 95% CI: 1.39, 5.01), and history of hypertension (OR: 3.01, 95% CI: 1.37, 7.12). Additionally, African American ancestry had higher odds of ESKD relative to European American (OR: 11.3; 95% CI: 2.51, 56.0) or Argentinian ancestry (OR: 9.54; 95% CI:1.92, 55.1).

Conclusion: SLE and CKD PRS are associated with LN outcomes like eGFR and ESKD and can potentially be used to identify those at risk for kidney deterioration and eventual damage. Adding assessment of genetic risk score for disease monitoring can allow physicians to focus on patients expected to do poorly and employ targeted as well as kidney-protective therapies earlier.

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Abstract Number: 0931

Down-Regulation of Human NADH-Ubiquinone Oxidoreductase Chain 6 by N6-Methyladenosine Methylation Is Associated with Lupus CD4+ T Cell Activation

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Recently mitochondria have been recognized as a key player in the pathogenesis of systemic lupus erythematosus (SLE). Given that N6-methyladenosine (m^{6}A) modifications can regulate almost all aspects of RNA metabolism, such as splicing, stability, structure and translation, and are directly related to T cell function, in order to clarify the impact of epigenetic regulation on mitochondrial function, in this study, we focused on m^{6}A-associatedmitochondrial abnormalities and their effects on lupus CD4+ T cells.

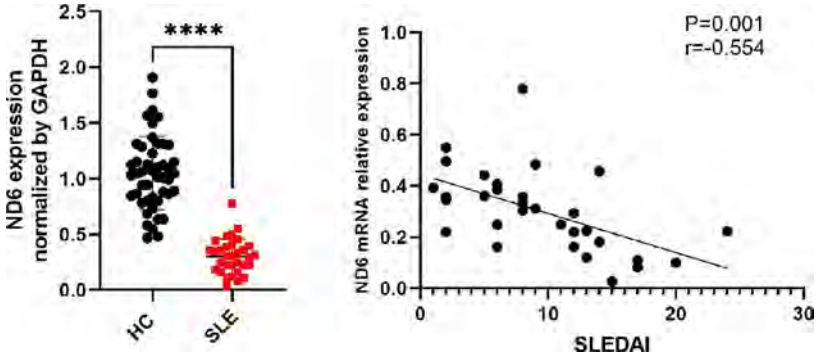

Figure.1 MT-ND6 expression decreased in PBMCs from SLE patients and was associated with SLE disease activity index score.

Methods: MethylatedRNAimmunoprecipitation sequencing (MeRIP-seq) was performed using peripheral blood mononuclear cells (PBMCs) from SLE patients and healthy controls to screen for mRNA with abnormal m6A modification and differential expression. The expression of human NADH-ubiquinone oxidoreductase chain 6(MT-ND6)in PBMCs from SLE patients and healthy controls was verified by quantitative real-time polymerase chain reaction (qPCR) and western blot, and analyzed for the correlation with clinical variables. The effects of MT-ND6 on T cell mitochondrial function were clarified by detecting reactive oxide species, mitochondrial reactive oxide species, mitochondrial membrane potential (MMP) and adenosine triphosphate (ATP). To observe the effects of MT-ND6 silencing on CD4+ T cells, small interfering RNA (siRNA) was designed and added into *in vitro* cultures.

Results: MeRIP-seq identified 370 differentially expressed genes with increased or decreased m6A methylation in lupus, including mitochondrial gene MT-ND6. Independent sample validation showed that both mRNA and protein levels of MT-ND6 in PBMCs from SLE patients were significantly lower than that of healthy controls. MT-ND6 mRNA expression was negatively correlated with SLE disease activity index score **(Figure 1)** ($r=-0.55$, $p=0.001$) and 24-hour urine protein level ($r=-0.57$, $p< 0.05$), and was lower in patients with positive anti-Sm or anti-dsDNA antibodies. The expression of MT-ND6 in CD4+ T cells from lupus patients was also significantly decreased compared to healthy controls and was accompanied by significantly increased ROS and mtROS levels, decreased mitochondrial membrane potential and insufficient ATP production. Consistently, when silencing MT-ND6 in CD4+ T cells, ROS and mtROS were significantly increased, while mitochondrial membrane potential and ATP production were reduced.After gene silencing, the levels of IFN-γ and T-bet in CD4+ T cells were significantly increased, and the levels of key inflammatory pathway factors, including STAT4, AP-1 and NF-κB, were all increased.

Conclusion: Low expression of MT-ND6 in lupus can lead to mitochondrial dysfunction, thereby activating CD4+T cells. Our result may provide new therapeutic targets for the treatment of autoimmune diseases.

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Abstract Number: 0932

The Landscape of Immune Cells in Systematic Lupus Erythematosus Patients with Epstein-Barr Virus Infection by Single-cell Sequencing

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: This study aimed to analyze the immune cell profiles, especially B cells and B-cell receptor (BCR) of systematic lupus erythematosus (SLE) patients with or without Epstein-Barr virus (EBV) infection, and to identify the differences between the two groups.

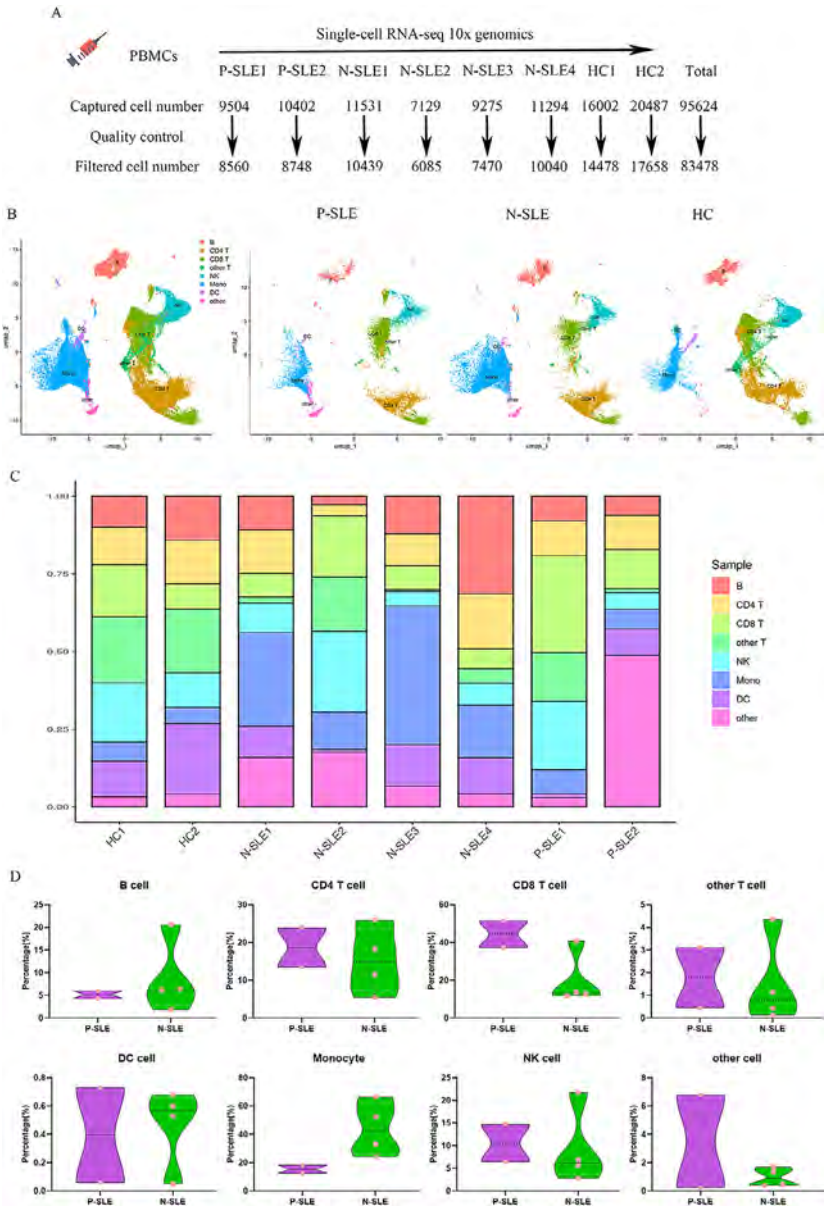

Figure 1. Study design and single-cell transcriptional profiling of PBMCs from HCs and SLE patients with or without EBV. A. The schematic shows the study design. B. Cellular populations identified from 2 P-SLE, 4 N-SLE, and 2 HC, showing the formation of 8 clusters with the respective labels. Each dot corresponds to a single cell, colored according to cell type. C. A UMAP plot representing the 8 clusters across 83478 PBMCs from 8 individuals (2 P-SLE, 4 N-SLE, and 2 HC). The cluster labels were added manually. D. Violin plots comparing the proportion of each cluster between P-SLE(n=2) and N-SLE(n=4). The results for P-SLE are shown in purple, and those for N-SLE are in green, each dot corresponds to a sample. The P values were calculated using a Wilcoxon test.

Methods: We included 2 cases of SLE patients with EBV infection (P-SLE), 4 cases of SLE patients without EBV infection (N-SLE), and 2 cases of healthy controls (HC). Using single-cell RNA sequencing (scRNA-seq) to interrogate the heterogeneity of cell populations by combining the transcriptomic profile and BCR repertoire.

Results: 83478 cells were obtained in our study and were divided into 8 major cell types or subtypes, including B cells, CD4+ T cells, CD8+ T cells, other T cells, natural killer (NK) cells, monocytes, dendritic cells (DCs) and other cells. There is no significant difference in the proportion of cell clusters between P-SLE and N-SLE. Interferon-alpha/beta pathways were upregulated in T cells, monocytes, and B cells in P-SLE compared with N-SLE. B cells were further divided into four different clusters, including naive B cells, intermediate B cells, memory B cells, and plasmablast. For V gene segments in the heavy

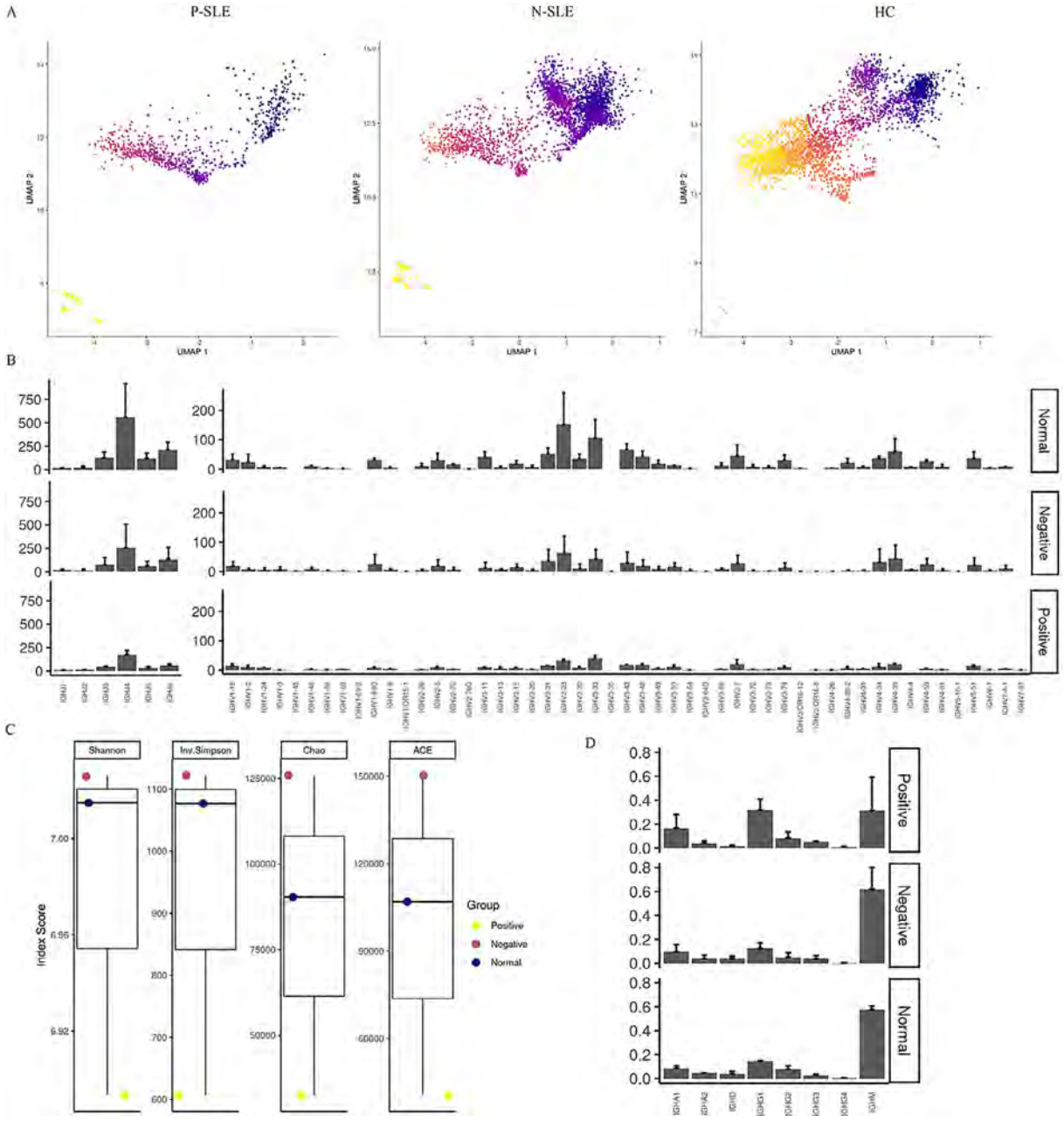

Figure 2. Comparison of B cells single-cell landscapes and BCR between P-SLE, N-SLE, and HC. A. UMAP plots representing four B cell clusters with the respective labels. B. Comparison of variable (V) and joining (J) gene usage in BCR heavy chain between three groups. C. The clonal diversity of P-SLE, N-SLE, and HC. D. Analysis of Ig isotypes in three groups.

chain, IGHV3, IGHV4, and IGHV2 gene families were frequently used in both patients and HC, especially IGHV3 and IGHV4 families. However, the frequencies of gene segments in each IGHV family were significantly different between the three groups. We also found that the BCR diversity was significantly reduced in P-SLE compared with N-SLE and HC. Moreover, IgM presents the largest proportion in all BCR repertoire, but its proportion was significantly decreased in P-SLE patients. We also observed that the proportions of IgG1, IgG3, and IgA1 were significantly increased in P-SLE than that in HC or N-SLE.

Conclusion: Our study provides a comprehensive characterization of the immune cell profiles and BCR repertoire in SLE patients with or without EBV infection, which contributes to the understanding of the mechanism for the immune response to EBV infection in SLE patients.

Disclosure: L. Hu: None; **J. Tu**: None; **J. Gui**: None; **M. Fang**: None; **X. Chen**: None; **L. Sun**: None.

Abstract Number: 0933

The 'Sweet' in Lupus - IgG Glycosylation in Lupus Nephritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis (LN) occurs in 50% of patients with systemic lupus erythematosus (SLE) for which we lack biomarkers, and an understanding of its pathogenesis. We have previously demonstrated that IgG in LN is aberrantly glycosylated and can injure podocytes.

Methods: We evaluated the IgG glycome by N-glycan profiling in a pediatric cohort of 40 children with SLE and 20 paired pre and post treatment LN samples using LS-MS Mass Spectrometry. We used enzymatic treatments to evaluate the role of glycans in podocyte injury. Data were analyzed using GEE analysis, Spearman test, t-test and regression analysis. Podocyte phenotype was evaluated by wound healing assay, cytoskeleton evaluation (F-actin) and podocyte specific proteins by RT-PCR and western blotting.

Results: We found that the overall glycosylation was reduced 6 months post treatment in patients with LN. Furthermore, those decorated with terminal galactose were increased while those with terminal sialic acid were reduced. In addition, neutral glycans were increased after treatment while negatively charged glycans were decreased. To evaluate whether these differences were due to treatment rather than LN activity, we analyzed the IgG glycome in SLE without LN, LN, LN in remission 6-month after treatment. We found that neutral glycans and negatively charged glycan chains changed with LN activity. Furthermore, the presence or absence of sialic acid and galactose correlated with parameters that influence active nephritis (renal SLEDAI, dsDNA, C3, cellular crescents and proteinuria). A switch from tri to bi -antennary complex type N-Glycans was noted in those with decling GFR. More interestingly, treatment of IgG with PNGase- F, which removes glycan chains, prevented cytoskeleton and motility changes in podocytes that were induced in LN. In addition, nephrin expression was preserved following PNG-ase treatment.

Conclusion: The IgG glycome in pediatric SLE patients is altered and is further aberrantly glycosylated in LN. The magnitude of change is associated with LN activity. More importantly, the glycans on IgG can lead to podocyte injury in LN. Our data shed light on the role of IgG glycosylation in the development of podocyte injury and propose the development of approaches using the IgG glycome to diagnose and monitor LN. Further, it highlights IgG glycosylation as an important pathogenic mechanism in LN.

Disclosure: R. Bhargava: None; **R. Upadhyay**: None; **S. Wenderfer**: AstraZeneca, 1, Novartis, 1; **J. Chen**: None; **G. Tsokos**: None.

Abstract Number: 0934

Anti-fibrotic Effects of MT-5562, a Novel Potent Selective Autotaxin Inhibitor, in Preclinical Studies: Roles of Lysophosphatidic Acid in Autoimmune Diseases and Clues to Treat Skin and Lung Fibrosis in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Targeted small-molecule therapies to autotaxin (ATX), the lysophosphatidic acid (LPA)-producing enzyme, have been shown to be potentially effective in systemic sclerosis (SSc), but the clinical benefit and safety of selective inhibition remains unclear. To explore the potential of MT-5562, a novel oral selective inhibitor of ATX, as a therapeutic agent for SSc, its efficacy and toxicity in preclinical models were evaluated. Furthermore, the levels of LPA in plasma derived from patients with autoimmune diseases including SSc were also investigated.

Methods: We examined the inhibitory effects of MT-5562 and its free form (MT-5562F) in comparison to other autotaxin inhibitors such as ziritaxestat and cudetaxestat on ATX activity using the choline assay. We also investigated the effects of MT-5562F on the production of IL-6 and connective tissue growth factor (CTGF) by human dermal and lung fibroblasts stimulated with TGF-β. The effects of MT-5562F on skin and lung fibrosis were evaluated using murine SSc models induced by bleomycin (BLM) and the plasma concentrations of MT-5562F and LPA were also determined. The plasma levels of LPA in SSc patients (n=70) were compared with those of healthy controls (n=45) or patients with other autoimmune diseases including rheumatoid arthritis (n=69), systemic lupus erythematosus (n=37) and Sjögren's syndrome (n=18).

Results: MT-5562F, ziritaxestat, and cudetaxestat inhibited the enzyme activity of human ATX with IC50s of 0.45, 49.3, and 2.77 nmol/L, respectively. MT-5562F and ziritaxestat inhibited the enzyme activity of mouse ATX with IC50s of 0.15 and 10.9 nmol/L, respectively. MT-5562F concentration-dependently inhibited production of IL-6 and CTGF by human

fibroblasts stimulated with TGF-β. MT-5562 showed minimal effects on cell viability measured by live cell counting even at the maximum dissolved concentration (60 μmol/L). On the other hand, ziritaxestat showed more cytotoxic effects than MT-5562 on cell viability in vitro. MT-5562 did not show off-target inhibition in receptor binding and kinase profiling assays. In vivo, MT-5562F and ziritaxestat (10, 30 mg/kg) dose-dependently reduced plasma LPA C18:2concentrations in mice, and MT-5562F showed more sustained effects on LPA reduction compared with ziritaxestat. Therapeutic treatment with MT-5562F (30, 60 mg/kg, b.i.d.) significantly reduced skin thickening and the numbers of myofibroblasts in the subcutaneous BLM-induced therapeutic skin fibrosis model. In addition, MT-5562F (30, 60 mg/kg, q.d.) significantly decreased the average Ashcroft score and collagen severity score in the BLM-induced lung fibrosis model in parallel with the reduction of LPA concentration. A total of 5 different LPA species were detectable in plasma derived from patients with autoimmune diseases. Most of the LPA species had significantly higher levels in the plasma of SSc patients compared to other autoimmune diseases.

Conclusion: Our results suggest that multiple LPA species are elevated in plasma of SSc patients and that MT-5562 is a selective and potent ATX inhibitor with a good preclinical safety and efficacy profile. It may offer a good option to treat lung and skin fibrosis in SSc, which has to be analyzed in clinical trials.

Disclosure: H. Matsuura: Mitsubishi Tanabe Pharma Corporation, 3; **M. Kondo**: Mitsubishi Tanabe Pharma Corporation, 3; **R. Ohno**: Mitsubishi Tanabe Pharma Corporation, 3; **A. Ishii**: Mitsubishi Tanabe Pharma Corporation, 3; **M. Piruzyan**: Mitsubishi Tanabe Pharma Corporation, 3; **K. Funayama**: Mitsubishi Tanabe Pharma Corporation, 3; **Y. Ono**: Mitsubishi Tanabe Pharma Corporation, 3; **A. Iwamura**: Mitsubishi Tanabe Pharma Corporation, 3; **T. Endo**: Mitsubishi Tanabe Pharma Corporation, 3; **T. Akashi**: Mitsubishi Tanabe Pharma Corporation, 3; **T. Tomari**: Mitsubishi Tanabe Pharma Corporation, 3; **N. Uchiyama**: Mitsubishi Tanabe Pharma Corporation, 3; **N. Seki**: Mitsubishi Tanabe Pharama Corporation, 3; **K. Chiba**: Mitsubishi Tanabe Pharma Corporation, 3; **G. Kania**: None; **P. Blyszczuk**: None; **O. Distler**: 4P-Pharma, 2, 5, 6, AbbVie, 2, 5, 6, Acceleron, 2, 5, 6, Alcimed, 2, 5, 6, Altavant Sciences, 2, 5, 6, Amgen, 2, 5, 6, AnaMar, 2, 5, 6, Arxx, 2, 5, 6, AstraZeneca, 2, 5, 6, Bayer, 2, 5, 6, Blade Therapeutics, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Citus AG, 12, Co-Founder, Corbus Pharmaceuticals, 2, 5, 6, CSL Behring, 2, 5, 6, Galapagos, 2, 5, 6, Galderma, 2, 5, 6, Glenmark, 2, 5, 6, Gossamer, 2, 5, 6, Horizon Therapeutics, 2, 5, 6, Janssen, 2, 5, 6, Kymera, 2, 5, 6, Lupin, 2, 5, 6, Medscape, 2, 5, 6, Miltenyi Biotec, 2, 5, 6, Mitsubishi Tanabe, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143), 10, Prometheus Biosciences, 2, 5, 6, Redx Pharma, 2, 5, 6, Roivant, 2, 5, 6, Topadur, 2, 5, 6; **T. Takeuchi**: AbbVie, 2, 5, 6, AYUMI, 5, Bristol-Myers Squibb, 6, Chugai, 2, 5, 6, Daiichi Sankyo, 5, Eisai, 5, 6, Eli Lilly Japan, 2, 6, Gilead, 2, 6, Janssen, 6, Mitsubishi-Tanabe, 2, 5, 6, ONO, 5, Pfizer Japan, 6, Taiho, 2; **Y. Kaneko**: AbbVie/Abbott, 1, 6, Ashai Kasei Pharma, 1, 6, Astellas Pharma, 1, 6, AstraZeneca, 1, 6, AYUMI Pharmacutia, 1, 6, Bristol-Myers Squibb(BMS), 1, 6, Chugai-Pharm, 1, 6, Eisai, 1, 6, Eli Lilly, 1, 6, Gilead Sciences Inc., 1, 6, GlaxoSmithKlein(GSK), 1, 6, Janssen Pharmaceutical KK, 1, 6, Novartis, 1, 6, Pfizer, 1, 6, Tanabe Mitsubishi Pharma, 1, 6, UCB Japan, 1, 6.

Abstract Number: 0935

Sodium Pyruvate Improves Mitochondrial Fitness in SSc Fibroblasts to Prevent Fibroblast-to-myofibroblast Transition and Fibrotic Remodeling

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systematic sclerosis (SSc) is an autoimmune disease characteristic by fibroblast transition and overproduction of extracellular matrix, yet with limited treatment. Recent studies provided evidence that aberrant fibroblast activation is at least in part due to mitochondrial dysfunction and associated metabolic changes. Sodium pyruvate is the stable form of pyruvate acid that works as a central hub in several key metabolism pathways including glycolysis, tricarboxylic acid (TCA) cycle, and fatty acid metabolism. In this study, we tested the hypothesis that supplementation with pyruvate may compensate several of the metabolic defects in SSc to improve mitochondrial fitness and that this metabolic rebalancing may dampen fibroblast activation and fibrotic tissue remodeling in SSc.

Methods: The effect of sodium pyruvate on metabolism, mitochondrial fitness, collagen synthesis and fibroblast-to-myofibroblast transition was evaluated in cultured human dermal fibroblasts from SSc patients and controls, in mice with bleomycin-induced dermal fibrosis and precision cut human skin slices. Outcomes included metabolic flux assays, real-time PCR, IF and IHC stainings, cellomics, histomorphometry, hyodroxyproline assays, RNA-seq analysis and datamining of published transcriptomic data of SSc skin.

Results: Several key regulatory components of pyruvate metabolism such as MPC1, PC and PDK2, were found to be dysregulated in the skin of SSc patients compared to matched healthy individuals in the PRESS cohort. Treatment of SSc fibroblasts with sodium pyruvate improve OXPHOS metabolism and the mitochondrial potential. Of note, these metabolic changes upon pyruvate supplementation were associated with a reduced expression of fibrotic related genes including *COL1A1* and *ACTA2*, of markers of myofibroblasts and decreased synthesis of extracellular matrix. Pyruvate supplementation also showed prominent antifibrotic effects at well tolerated doses in mice with bleomycin-induced dermal fibrosis with 55% change reduced dermal thickening, decreased hydroxyproline content of the skin and lower myofibroblast numbers. Moreover, treatment with pyruvate also reduced the expression of profibrotic genes including *COL1A1* and *ACTA2* in human skin as an *ex vivo* trial approach.

Conclusion: Sodium pyruvate, which as available as a nutrient supplementation, improves metabolic defects and improves mitochondrial fitness to inhibit fibroblast-to-myofibroblast transition and collagen in human dermal fibroblasts, in experimental murine models of fibrosis and directly in human skin. Pyruvate supplementation may thus by one of the first examples of a metabolically-directed, antifibrotic therapy and may offer potential for further evaluation in clinical studies in SSc.

Disclosure: X. Zhou: None; **T. Trinh-Minh**: None; **A. Matei**: None; **H. Zhu**: None; **H. Györfi**: Boehringer-Ingelheim, 6; **C. Tran Manh**: None; **X. Hong**: None; **J. Distler**: 4D Science and FibroCure, 8, 11, AbbVie, Active Biotech, Anamar, ARXX, AstraZeneca, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, Genentech, GSK, Inventiva, Janssen, Novarti, 2, Anamar, Argenx, ARXX, BMS, Bayer Pharma, Boehringer Ingelheim, Cantargia, Celgene, CSL Behring, Galapagos, GSK, 5, Inventiva, Kiniksa, Lassen, Sanofi-Aventis, RedX, UCB, 5.

Abstract Number: 0936

Impaired DNA Repair Responses Activate a Novel FOXO1-dependent Metabolic Remodelling in Patients with Progressive Systemic Sclerosis to Promote Fibrosis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a deadly disease characterized by immune dysregulation, vasculopathy, and fibrosis. SSc is the most lethal rheumatic disease associated with the poorest quality of life. The extent of skin fibrosis may predict internal organ involvement. The cells promoting skin fibrosis in SSc are human dermal fibroblasts (HDFs) which develop a myofibroblast (MFB)-phenotype, senescence-like-features, and resistance-to-apoptosis. We recently showed that increased genomic instability associated with double-stranded DNA breaks (DSBs) and senescence like features are present in rapidly progressive diffuse (dcSSc) HDF. In cancer, dysregulated DSBs and senescence-like-features are associated with activation of the transcription factor, forkhead box protein O (FOXO1) to promote metabolic remodelling. Therefore, we hypothesized that DSBs promotes FOXO1 activation to promote fibrosis.

Methods: Primary HDFs were generated from healthy volunteers (HC), less severe early limited (lcSSc, < 2 year disease duration), and severe dcSSc 4 mm skin biopsies (< 2 year disease duration). All our SSc patients met 2013 ACR/EULAR inclusion criteria. DSBs were quantified by measuring γ-H2AX (a DSB marker) via immunoblots (IB) and immunofluorescence/confocal microscopy (IF). Nuclear FOXO1-translocation, MFB differentiation and fibrotic markers were measured using IF, IB and qRT-PCR. HC HDFs were treated with DNA damage-inducing agents (e.g. etoposide), then nuclear FOXO1 and the MFB marker alpha-SMA were quantified using IB and IF. Pro-fibrotic signals were measured in dcSSc HDF following FOXO1 inhibition.

Results: dcSSc HDFs had the highest levels of γ-H2AX compared to HC (*p< 0.05) and lcSSc patients. They also had a substantially higher nuclear accumulation of FOXO1 which was associated with increased mRNA expression of the FOXO1 transcriptional target, pyruvate dehydrogenase kinase 4 (*p< 0.05). FOXO1 inhibition resulted in decreased fibrotic-markers and *PDK4* (*p< 0.05) in dcSSc HDF. Etoposide treatment promoted FOXO1 activation, MFB differentiation, and PDH phosphorylation.

Conclusion: DSBs are more commonly present in HDF from dcSSc patients, which may promote MFB differentiation, resistance-to-apoptosis and fibrosis. We propose that FOXO1 activation may promote a downstream metabolic remodelling and an associated senescence like signal that promotes cell survival, and propagation of acquired genomic mutations with associated downstream inflammatory signals. Our findings provide mechanistic insights that may impart a deeper understanding for the role(s) of DSB-associated FOXO1 activation in promoting fibrosis in SSc. They may also have far-reaching implications related to the development of novel therapeutic strategies in SSc.

Disclosure: L. Khan: None; **D. Redmond**: None; **M. Elezzabi**: None; **R. Gniadecki**: None; **J. Tervaert**: None; **M. Osman**: None.

Abstract Number: 0937

IL-4+ and IFN-α+ Profibrotic T Cells Aggravate Systemic Sclerosis via STIM1/STING Signaling in SKG Mice

Ji Won Yang[1], Kun Hee Lee[2], Jin Seok Woo[2], Ha Yeon Jeong[2], JeongWon Choi[2], Eui-Jong Kwon[1], Mi-La Cho[2] and Sung-Hwan Park[1], [1]Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea, [2]Rheumatism Research Center, Catholic Research Institute of Medical Science, College of Medicine, The Catholic University of Korea, Seoul, South Korea

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SS), also known as scleroderma, is a chronic autoimmune disease caused by inflammation, tissue fibrosis, and vasculopathy. Although the pathological mechanisms of SS are unclear, proinflammatory cytokines, such as IL-4 and IL-17, and the tissue microenvironment are important factors in its development. In this study, we aim to investigate whether T cells induce fibrosis in SS and assess the effect of simultaneous regulation of T cells and fibroblasts via dedicated signals.

Methods: SKG mice, T cell-mediated autoimmune murine models originated from a spontaneous point mutation in ZAP70, and BALB/c mice (control) were subcutaneously injected with bleomycin (BLM) to induce SS-like phenotypes including fibrosis. The degree of fibrosis, and expression levels of inflammatory or profibrotic cytokines were determined by histological assessments using immunohistochemistry and confocal microscopy. Potential molecular mechanisms related to T cell activation were determined in the same mice both in vitro and ex vivo. The profibrotic effects of human T cells were evaluated using a humanized murine SS model induced by peripheral blood mononuclear cells (PBMCs) from SS patients.

Results: Dermal thickness and expression of fibrosis markers in skin tissue were increased in BLM-treated SKG mice compared to control mice. Infiltration of T cells, particularly Th2 and Th17 cells and expression of related cytokines were increased in skin tissues from BLM-treated SKG mice than those from controls. In CD4+ T cells from SKG mice, the STING pathway including downstream factors such as STAT6 and IRF3 was activated, subsequently resulting in increased populations of IL-4 and IFN-α-producing CD4+ T cells. IL-4 and IFN-α directly promoted fibrosis in skin fibroblasts via the STING pathway. Increased fibrosis and infiltration of IL-4 and IFN-α-producing CD4+ T cells were replicated in humanized mice induced by PBMCs from SS patients. Lastly, pharmacological inhibitions of STING as well as STAT6 reduced fibrosis in the murine models.

Conclusion: Our findings suggest that STING-induced production of IL-4- and IFN-α by CD4+ T cells is a key factor of pathological fibrosis in SS. The STING and STAT6 signaling pathways can be potential therapeutic targets in SS.

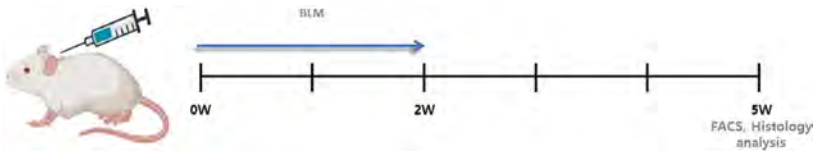

Fig 1. BALB/c and SKG mice were subcutaneously injected with BLM for 2 weeks, and euthanized 3 weeks after the final BLM treatment.

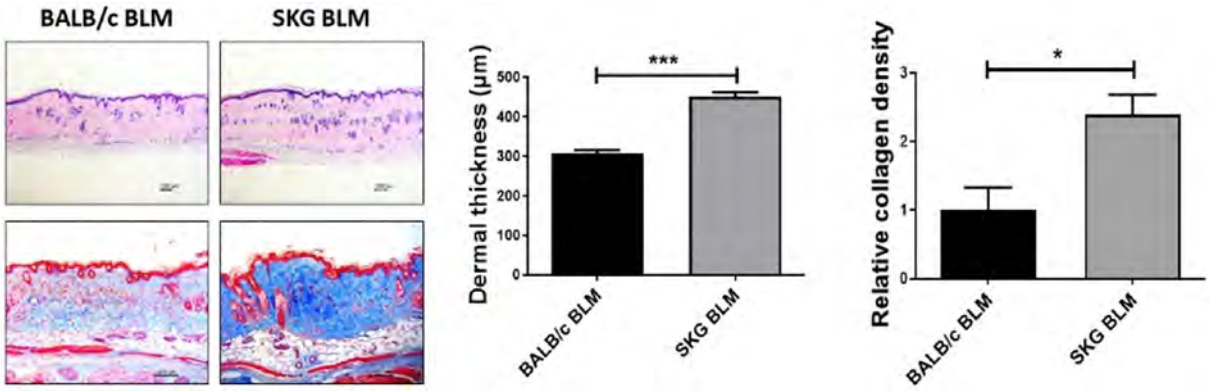

Fig 2. Skin thickness and fibrosis were increased in BLM-treated SKG mice compared to BLM-treated BALB/c mice.

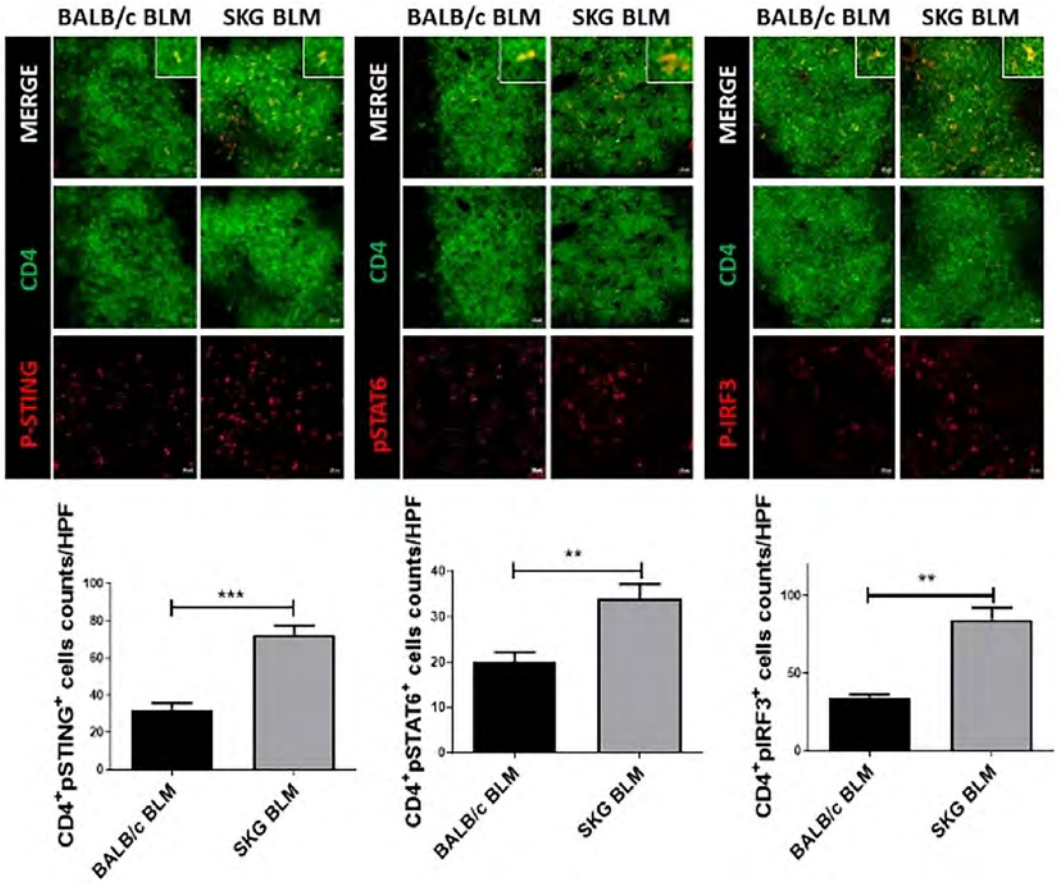

Fig 3. The STING pathway including downstream factors of CD4+ T cells in spleen tissue were activated in BLM-treated SKG mice.

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Abstract Number: 0938

Deconvolution of the Molecular Signature of Very Early Diagnosis of Systemic Sclerosis (VEDOSS) and Established Disease: A Biomarker Blueprint of Scleroderma Disease Continuum

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Background/Purpose: Systemic sclerosis (SSc) is an autoimmune disease that affects multiple organs asynchronously, leading to highly variable fibrotic damage and consequent increased morbidity and mortality. The significant heterogeneity of time, type and severity of organ involvement often challenges the robustness of short proof-of-concept (PoC) clinical studies. In this study, we integrate high-quality published skin omics datasets and new serum proteomics analysis to deconvolute molecular signatures of SSc over time and across clinical subsets.

Methods: We used the "*treat*" function from the LIMMA package to identify significantly differentially expressed genes (FDR ≤ .05) in affected early and late SSc skin (GSE130955, GSE58095, and GSE181549). These genes were further analyzed using algorithms of 1) overconnectivity, 2) causal reasoning, 3) hidden nodes, 4) interconnectivity, and 5) network propagation to identify key and significant network objectives (adjusted p ≤ .05). To identify the key affected pathways and processes, we conducted enrichment analysis using Gene Ontology and Metabase Pathway Maps and Networks. Olink Explore-1536 panel serum proteomics of patients spanning from VEDOSS (-2yrs from fulfilling Classification criteria) to late disease (>7years) allowed identification of independent and significant serum biomarkers ($p< 0.05$, $>Log_2 1$) of disease activity over time.

Results: The skin transcriptomics profiling revealed a unique set of genes (n=739 biomarkers) and network regulators (overconnected nodes with upregulated genes, n=119; causal reasoning, n=339, hidden nodes, n=89; interconnectivity, n=12; network propagation, n=208) in diffuse cutaneous SSc (dcSSc). Pathway analyses revealed significant dysregulation in inflammatory signaling (Jak-STAT, IL6, Chemotaxis, Interferon, and others) and fibroplasia (cell-matrix interaction, ECM remodeling, others) as unique for early dcSSc, whereas angiogenesis, connective tissue degradation, and blood coagulation pathways are dysregulated throughout the disease natural history and clinical subsets. Altogether, the analyses highlighted 6 biological elements as drivers and potentiators of SSc pathobiology. The analysis of the integrated VEDOSS and SSc cohort indicated that serum biomarkers of Type I IFN (STAT5, CCL5, IL10, TLR3) and inflammatory (PAI1, CCL2, IL6, vWF) signaling as well as epithelial damage (PRSS8, SFTPD, WFDC2, SFTPA1) showed continuity between patients at increased risk of progression to disease or to disease major complications over time (progressive skin and lung involvement).

Conclusion: Our comprehensive molecular profiling highlights the significance of skin and serum omics in defining a pathologic disease continuum in SSc, preceding fulfillment of classification criteria and remaining active through disease progression. The perseverance of inflammatory and epithelial damage biomarkers throughout time underlines the currently unmet therapeutic need of SSc and can be utilized to enrich patients with active disease progression and support a robust short PoC clinical study design.

Disclosure: S. Kim: AbbVie/Abbott, 3, Merck/MSD, 11; **T. Sornasse**: AbbVie, 3, 11; **V. Kakkar**: None; **R. Ross**: None; **Y. Bi**: AbbVie/Abbott, 3; **H. Hu**: AbbVie/Abbott, 3; **L. Hazelwood**: AbbVie/Abbott, 3, 11; **L. Reinke-Breen**: AbbVie/Abbott, 3, 11; **j. karman**: None; **C. Butler**: None; **J. Van Camp**: AbbVie/Abbott, 3; **F. Del Galdo**: AbbVie/Abbott, 5, arxx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, capella, 2, Chemomab, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Mitsubishi-Tanabe, 2, 5.

Abstract Number: 0939

HRCT-derived Delta Radiomic Features Classify Response to Anti-Fibrotic Treatment in Experimental and Human Fibrosing Interstitial Lung Disease

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SESSION INFORMATION

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Background/Purpose: Quantification of response to anti-fibrotic drugs in patients with fibrosing interstitial lung disease (ILD) relies on repeated pulmonary function tests (PFT) and visual evaluation of HRCT scans, which require long observation periods to achieve conclusive results. HRCT-derived radiomic features, capturing in-depth information of whole-organ properties without bias, may present a more sensitive approach for quantification of treatment response. Here, we studied if radiomic feature changes can classify response to treatment in experimental and human ILD.

Methods: Mice with bleomycin-induced ILD received nintedanib (n=10) or vehicle-only (n=13) from day 7 to 21. Lung μCT scans were acquired before and after treatment for calculation of delta radiomic features (n=1'386). Phosphoproteome profiles were measured in subsets to validate nintedanib target engagement. Whole-lung proteomics was performed in all sample for correlation with delta radiomics. Selected disease markers were measured by gene expression and immunohistochemistry analysis. Delta radiomic features classifying response in mice, as evaluated in univariate analysis, were validated in a nintedanib-treated ILD cohort (n=10), where pre- and post-treatment HRCT scans and PFT data were available. Response in patients was classified by FVC change ≤5% from baseline, resulting in a 5:5 class distribution. All statistical analyses were performed in R.

Results: Molecular readouts in mice indicated that response to nintedanib was heterogeneous, despite a clear separation on μCT-derived lung tissue density and on phosphoproteome level compared to vehicle treatment. Unsupervised hierarchical clustering of delta radiomic features in nintedanib-treated mice revealed two stable clusters. On molecular level, these clusters exhibited differences on expression of fibrosis (*Col1a1*, *Col3a1*, *Fn1*) and drug-related (*Tgfb1*, *Timp1*, *Cxcl1*) targets, in addition to different levels of α-SMA+ myofibroblast and F4/80+ macrophage infiltration. As such, these clusters indicated presence of different treatment response profiles. To define the biological basis underlying cluster separation, we performed correlation analysis of the top discriminative delta radiomic features (AUC≥0.9, n=44) with matched proteomics profiles. Reactome pathway analysis of correlated proteins ($\rho \geq 0.6$, $p < 0.05$) revealed significant enrichment for multiple

pathways involved in ILD pathophysiology, including extracellular matrix remodeling and collagen/elastic fiber formation. Validation of the predictive radiomic features in our human cohort demonstrated good performance for treatment response classification (AUC≥0.6 in *n*=24 features), with two of the best performing features (AUC≥0.8) showing a strong association with fibrotic pathway activation in mice. Our results highlight that molecular changes are paralleled on radiomics level in experimental lung fibrosis and that they are translatable to human ILD.

Conclusion: HRCT-derived delta radiomic signatures may provide a powerful measure for early and accurate classification of patients benefiting from anti-fibrotic therapy.

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Abstract Number: 0940

A Novel Therapeutic Opportunity in Systemic Sclerosis: The Fibrolytic Activities of a Specialized Macrophage Secretome

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) a complex and rare immune-mediated connective tissue disorder characterized by microvascular damage, inflammatory cell infiltration, and excessive deposition of extracellular matrix proteins (ECMs) resulting in fibrosis of the skin and internal organs. Like for many chronic inflammatory diseases dysfunctional macrophage activity is linked to the failure of initiating the resolution of inflammation programs and with that a main disease driver and a central part of disease progression in affected organs. The objective of our preclinical analysis, was to evaluate the therapeutic activity of an innovative secretome drug candidate Resolvix, which was developed from experimentally induced resolution type macrophages, in experimental models of SSc.

Methods: Two established inducible preclinical models of SSc (bleomycin (BLM) and HOCl) were used to monitor the impact of Resolvix on skin (thickness and collagen deposition), lung (leucocyte infiltration and alveolar macrophage efferocytosis) and lymphoid organs (Tregs) as well as selected plasma proteins. A single treatment at predetermined therapeutic

activity or respective controls were administrated intra-venously at 3 weeks post disease induction and mice were monitored daily and sacrificed for analysis after 3 weeks post treatment.

Results: In both models we could show a significant reduction of skin thickening and collagen deposition in skin samples after a single administration of Resolvix when compared to controls. Leucocyte infiltrates particularly evident in the HOCl model were significantly reduced by the Resolvix treatment in skin and lung tissues. Furthermore, Resolvix treatment restored the efferocytosis activity in alveolar macrophages collected from broncho-alveolar lavage (BAL) fluids that were significant reduced in these models as sign of uncontrolled ongoing chronic inflammation and recently reported in SSc patients. Efferocytosis capacities were restored to comparable levels as detected in healthy mice.

Conclusion: Collectively our preclinical data demonstrate that the pro-resolution factors harnessed from these specialized macrophages are able to durably revert skin fibrosing, control inflammatory cell infiltration and restore defective macrophage efferocytosis and function as a novel and advanced therapeutic approach in SSc. Resolvix may be considered as a next generation cell-free and disease modifying biological drug candidate for further development for the treatment of SSc.

Disclosure: F. Bonnefoy: None; **S. Behlke**: None; **S. Perruche**: None.

Abstract Number: 0941

RUNX1 Expression and Binding Site Accessibility Is Associated with Increased Disease Severity in Systemic Sclerosis

Rezvan Parvizi[1], Zhiyun Gong[1], Dillon Popovich[1], Tamar Abel[2], Helen Jarnagin[1], Madeline Morrisson[1], Tammara Wood[2], Jonathan Garlick[3], Monique Hinchcliff[4], Patricia Pioli[1] and Michael Whitfield[1], [1]Geisel School of Medicine at Dartmouth, Hanover, NH, [2]Dartmouth College, Hanover, NH, [3]Tufts University School of Dental Medicine, Boston, MA, [4]Yale School of Medicine, Westport, CT

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Runt-related transcription factor 1 (*RUNX1*) is a member of the core-binding factor family that regulates proliferation, differentiation, and cell survival in multiple cell lineages. Activation of *RUNX1* in fibroblasts has been implicated in wound healing and a network analysis of transcription factor (TF) activity suggested that it is a key regulator in diffuse cutaneous systemic sclerosis (dcSSc) skin. Here, we analyze the specific contribution and function of *RUNX1* in systemic sclerosis (SSc) dermal fibroblasts.

Methods: *RUNX1* was analyzed in gene expression data from SSc forearm skin biopsies (GSE59787) and in single-cell RNA sequencing (scRNA-seq) data from Tabib et al. 2021 (GSE138669), and in SSc and control scRNA-seq and scATAC-seq data of 3D skin-like tissues. We further generated and analyzed genome-wide DNA methylation profiles and bulk ATAC-seq data to evaluate epigenetic state and genome chromatin accessibility of *RUNX1* in dcSSc-isolated fibroblasts. Fibroblasts in 2D and 3D skin-like tissues were treated with a selective *RUNX1* inhibitor, Ro5-3335 or siRNA against *RUNX1* followed by collagen contraction, proliferation assays and qRT-PCR for select target genes.

Results: Analysis of gene expression data from a cohort of 124 individuals revealed significant over-expression of *RUNX1* in skin biopsies of SSc patients. Correlation analysis demonstrated significantly increased expression of *RUNX1* and in patients with higher modified Rodnan Skin Score (mRSS) (r^2= 0.33, *p-value* = 4.4e-10) (Fig 1A, B). Analysis of scRNA-seq data from SSc and control skin showed enrichment of *RUNX1* in PDGFRA1/COL1A1 expressing fibroblasts subpopulations (Fig 1C). Analysis of scRNA-seq and scATAC-seq of *in vitro* 3D skin-like tissues showed increase expression and *RUNX1* binding site

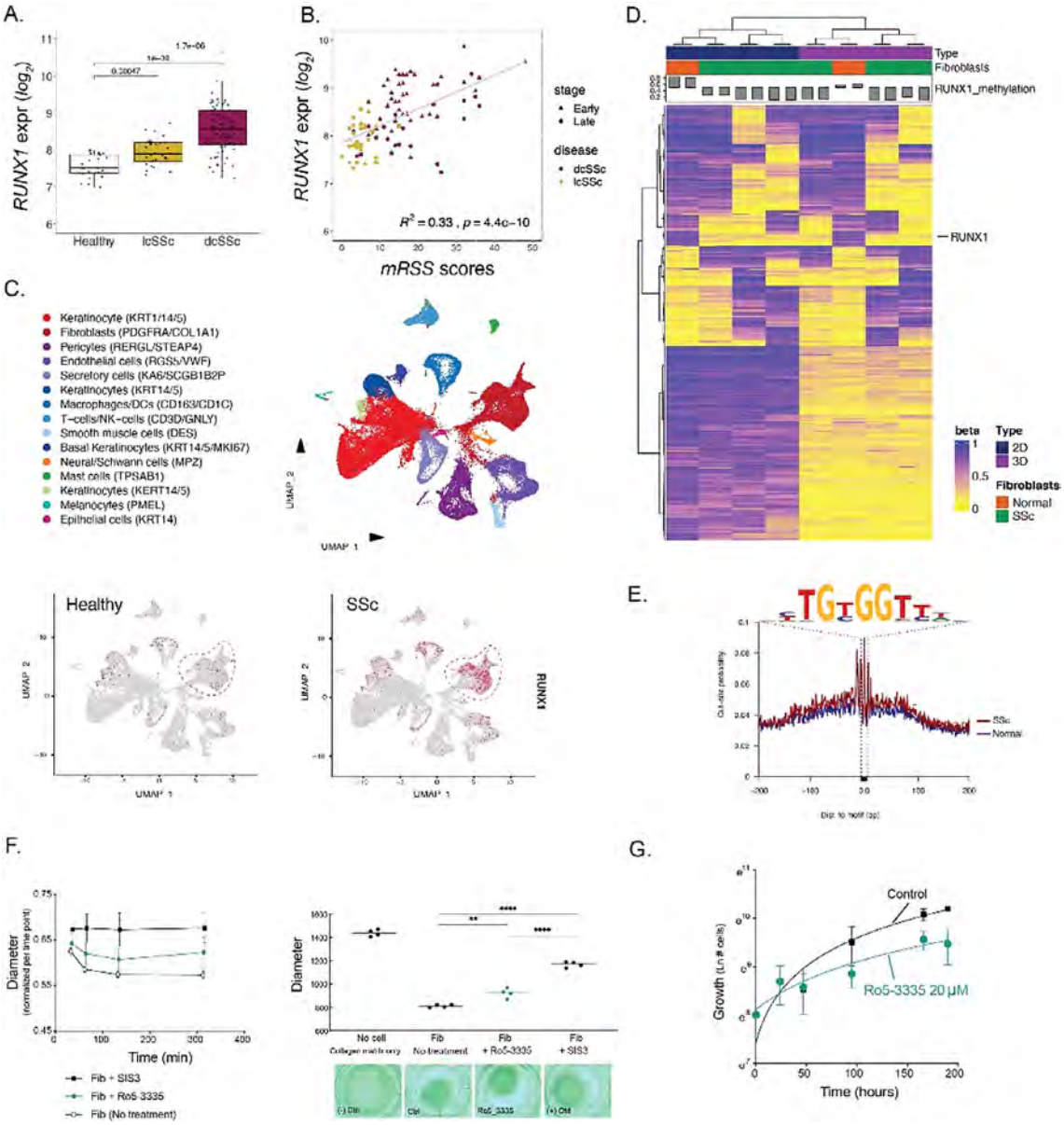

Figure 1. RUNX1 in Systemic Sclerosis Dermal Fibroblasts. A) RUNX1 expression in forearm skin biopsies of 24 healthy, 68 diffuse cutaneous systemic sclerosis (dcSSc), and 32 limited cutaneous systemic sclerosis (lcSSc) individuals. B) Pearson Correlation between RUNX1 expression and mRSS. Stage: Early, < 2 years; Late, >2 years of disease onset/diagnosis. C) UMAP projection of cell types from Tabib et al. 2021 single-cell RNA-Seq data from 10 healthy and 12 dcSSc forearm skin biopsies. Feature plots of RUNX1 is shown in heathy (left) and SSc (right) in red. Dash lines indicate fibroblast cluster. D) DNA methylation profile of 2D and 3D cultured fibroblasts that were isolated from dcSSc and healthy donors using Illumina's Infinium Methylation EPIC array. Heatmap shows top 593 methylated CpG sits with blue/yellow gradient of beta values. The bar-plot on top shows RUNX1 beta value that is labeled within the heatmap. E) Footprint profiles of RUNX1 in SSc (red) and healthy (blue) isolated fibroblasts. The consensus sequence of RUNX1 motif is shown. F) 3D collagen contraction assays, fixed (left) and floating (right) models, of normal human dermal fibroblasts treated with Ro5-3335 (RUNX1 inhibitor). SIS3 (SMAD3 inhibitor) was used as positive control and significantly eliminates the contraction ability of fibroblasts. (Student t-test P value: ** 0.001 to 0.01, **** <0.0001 in GraphPad Prism v.9). G) Normal human dermal fibroblast proliferation curve in presence and absence of Ro5-3335.

accessibility in ECM producing fibroblasts. DNA methylation profiling of isolated fibroblasts from dcSSc and healthy donors demonstrated hypomethylation of *RUNX1* in SSc fibroblasts (Fig 1D). Bulk ATAC-seq of dcSSc fibroblasts showed increased accessibility of *RUNX1* chromatin binding (Fig 1E), which facilitates TF binding. Inhibition of *RUNX1* activity by Ro5-3335 significantly reduced the ability of dermal fibroblasts to contract collagen gel matrices (Fig 1F) and reduced fibroblast proliferation rate (Fig 1G). *RUNX1* knockdown by siRNA resulted in statistically significant changes in αSMA, fibronectin (FN1) and COL1A1 expression.

Conclusion: These findings implicate *RUNX1* as a key regulator of ECM producing SSc fibroblasts. Our observations indicate a potential association between the severity of dermal fibrosis and *RUNX1* expression levels. Identifying hypomethylated CpG sites near the *RUNX1* gene suggests their potential involvement in the upregulation of *RUNX1* expression. Notably, our analysis of ATAC-seq data revealed higher accessibility of the chromatin region where *RUNX1* binding sites are located. Lastly, inhibition of *RUNX1* activity using Ro5-3335 caused a reduction in fibroblasts' contraction and proliferation rates, and the regulation of key genes implicated in SSc pathogenesis.

Disclosure: R. Parvizi: None; **Z. Gong**: None; **D. Popovich**: None; **T. Abel**: None; **H. Jarnagin**: None; **M. Morrisson**: None; **T. Wood**: None; **J. Garlick**: None; **M. Hinchcliff**: Boehringer-Ingelheim, 5, Kadmon, 5; **P. Pioli**: Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 2, 5, Celdara Medical LLC, 2, 5, Pfizer, 5; **M. Whitfield**: Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 2, 5, Celdara Medical, 2, 5, 12, Scientific Founder.

Abstract Number: 0942

G Protein-coupled Receptor Kinase 5 in Fibrotic Tissue Remodeling

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Background/Purpose: G-protein coupled receptor kinase 5, GRK5, is a central regulator of G protein-coupled receptors (GPCRs), a vast family of cell surface receptors involved in a variety of physiological activities. GRK5 acts by phosphorylating GPCRs, causing desensitization and internalization. In addition, GRK5 exerts GPCR-independent effects and can enter the nucleus to modulate the expression of target genes. GRK5 has previously been implicated in the pathophysiology of inflammation and immunological responses, migration and invasion of cancer cells, neurodegenerative diseases and post-ischemic remodeling of the heart. However, its role in rheumatologic diseases and in particular in fibrotic tissue remodeling has not been investigated so far. Here, we tested the hypothesis that GRK5 might modulate the transcription of profibrotic target genes in fibroblasts to promote fibrotic tissue remodeling.

Methods: GRK5 expression was examined in SSc patients and experimental models of SSc using real-time PCR, Western Blot and immunofluorescence staining. GRK5 expression was modulated in vitro and in vivo with knockdown and knockout techniques and adenoviral overexpression. The antifibrotic efficacy of GRK5 inactivation was investigated in

three SSc animal models: bleomycin-induced dermal and bleomycin-induced pulmonary fibrosis and fibrosis produced by overexpression of a constitutively active TGF receptor type I (TBRI^{act}). Target genes of GRK5 in fibroblasts were identified by RNA-Seq.

Results: Increased mRNA levels and nuclear accumulation of GRK5 protein were observed in fibroblasts in fibrotic skin and lung samples compared to non-fibrotic control samples. GRK5 expression was also upregulated in murine models of SSc. TGFβ, but not the other profibrotic or proinflammatory mediators such as EGF, FGF9 or IL-1, induced GRK5 overexpression. Knockdown of GRK5 in fibroblasts reduced their sensitivity to the profibrotic effects of TGFβ with impaired fibroblast-to-myofibroblast transition and decreased collagen synthesis. Similarly, fibroblast-specific knockout of GRK5 demonstrated potent antifibrotic effects in the murine models of bleomycin-induced dermal and bleomycin-induced pulmonary fibrosis. In addition, GRK5 knockout mice were also protected from TBRI^{act}-induced fibrosis. Overexpression of GRK5 in fibroblasts, on the other hand, caused fibroblast-to-myofibroblast transition and collagen release. In a mouse model of bleomycin-induced dermal fibrosis, adenoviral overexpression of GRK5 exacerbated skin fibrosis. RNA-Seq unraveled GRK5 as a novel upstream regulator of numerous profibrotic genes including *COL1A1, ACTA2, CTGF* and *PAI-1*. Mechanistically, RNA-Seq also revealed that GRK5 modulated signal transducer and activator of transcription 3 (STAT3) and histone deacetylases (HDACs) activity to induce fibroblast activation.

Conclusion: We demonstrate that GRK5 is sufficient and required for fibroblast activation in response to TGFβ and serves as an upstream regulator of multiple profibrotic signals. Inactivation of GRK5 exerts potent antifibrotic effects in various preclinical models of SSc. Inactivation of GRK5 may thus offer potential as a target for antifibrotic therapies.

Disclosure: C. Tran-Manh: None; **T. Trinh-Minh**: None; **C. Liebel**: None; **C. Chen**: None; **J. Distler**: 4D Science and FibroCure, 8, 11, AbbVie, Active Biotech, Anamar, ARXX, AstraZeneca, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, Genentech, GSK, Inventiva, Janssen, Novarti, 2, Anamar, Argenx, ARXX, BMS, Bayer Pharma, Boehringer Ingelheim, Cantargia, Celgene, CSL Behring, Galapagos, GSK, 5, Inventiva, Kiniksa, Lassen, Sanofi-Aventis, RedX, UCB, 5.

Abstract Number: 0943

Attenuation of Fibroblast Activation and Fibrosis by Adropin in a Hedgehog-Dependent Manner

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Adropin is a secretory protein encoded by the energy homeostasis - associated (*ENHO*) gene. Emerging evidence indicate its role in metabolism and energy homeostasis, which is known to be deregulated in Systemic Sclerosis (SSc). However, Adropin / *ENHO* has not been linked to the pathogenesis of fibrosis, tissue remodeling or fibroblast activation so far. The aim of the current study was to investigate the role of Adropin / *ENHO* in the pathogenesis of fibroblast activation and fibrosis in SSc.

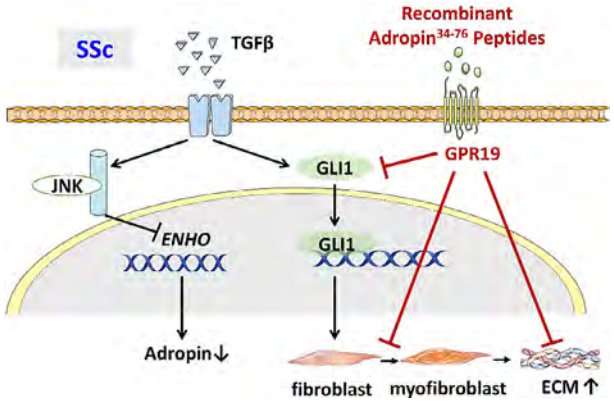

Figure 1. Proposed model of Adropin / ENHO signaling in TGFβ-stimulated fibroblasts and mode of action of Adropin34-76. The illustration was created by using images from Servier Medical Art (http://smart.servier.com/), licensed under CC BY 3.0 (https://creativecommons.org/licenses/by/3.0/).

Methods: Machine learning and bioinformatics models were used to identify candidate genes regulating fibroblast activation in SSc. The expression of Adropin / *ENHO* in skin samples of SSc patients and healthy individuals was analyzed by quantitative PCR, immunofluorescence and western blot, and validated by *in silico* data mining. The effects of Adropin were analyzed in cultured human fibroblasts, 3D skin equivalents, complimentary murine SSc models of sclerodermatous GvHD (sclGvHD) and bleomycin-induced lung fibrosis mice, and precision-cut human skin slices (PCSS). RNA sequencing (RNAseq) was performed to identify downstream regulatory pathways.

Results: Biostatistical screening of publically available datasets identified Adropin / *ENHO* as a potential molecular mediator involved in fibroblast activation with pronounced downregulation in SSc skin. We first confirmed the impaired expression of Adropin / *ENHO* in SSc patients and SSc models. TGFβ reduced Adropin / *ENHO* expression in a JNK-dependent manner. Recombinant Adropin peptides in turn inhibited TGFβ-induced fibroblast activation and subsequent fibrosis. Treatment of biologically active peptides Adropin$^{34-76}$inhibited TGFβ induced fibroblast activation and extracellular matrix (ECM) production in cultured primary dermal fibroblasts, in 3D skin equivalents, as well as in PCSS. Moreover, therapeutical administration of Adropin$^{34-76}$ in mice with preestablished fibrosis exerted potent antifibrotic effects in skin and lungs of two complimentary murine SSc models, sclGvHD and bleomycin-induced lung fibrosis mice. RNAseq demonstrated the antifibrotic effects of Adropin were functionally linked to hedgehog signaling and GLI1 deactivation, which experimentally confirmed *in vitro* and *in vivo*. Knockdown of *GPR19*, a putative receptor of Adropin, abrogated the therapeutic effect of Adropin on αSMA- and GLI1-expression in fibroblasts, indicating Adropin may regulate GLI1 signaling and fibroblast activation via GRP19.

Conclusion: We demonstrate a novel regulatory loop of Adropin / *ENHO* in TGFβ signaling: TGFβ inhibits the expression of Adropin / *ENHO*, while recombinant Adropin peptides inhibited fibroblast activation by GPR19-dependent inhibition of hedgehog / GLI1 signaling. Our findings characterize Adropin peptides as a potential approach to interfere with aberrant fibroblast activation and tissue fibrosis in SSc.

Disclosure: M. Liang: None; **J. Distler**: 4D Science and FibroCure, 8, 11, AbbVie, Active Biotech, Anamar, ARXX, AstraZeneca, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, Genentech, GSK, Inventiva, Janssen, Novarti, 2, Anamar, Argenx, ARXX, BMS, Bayer Pharma, Boehringer Ingelheim, Cantargia, Celgene, CSL Behring, Galapagos, GSK, 5, Inventiva, Kiniksa, Lassen, Sanofi-Aventis, RedX, UCB, 5.

Abstract Number: 0944

Macrophages Regulate Adipocyte Differentiation and Proliferation in Skin Fibrosis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune systemic sclerosis (SSc) is characterized by inflammation, vasculopathy, and dermal and internal organ fibrosis. A widely-reported but poorly understood aspect of SSc skin disease is the loss of hypodermal cutaneous fat or dermal white adipose tissue (DWAT), which precedes the onset of dermal fibrosis. While recent work suggests that reprogramming of adipocytic cells into activated, extracellular matrix-secreting myofibroblasts may account for the loss of DWAT and resulting fibrosis observed in SSc patient skin, the molecular mechanism that regulates this process has not been elucidated. Because we have shown that macrophages (MØs) from SSc patients secrete active TGF-β, which has been implicated in adipocyte-myofibroblast transition, we hypothesized that activated MØs in SSc modulate the differentiation and proliferation of adipocytes through release of secreted mediators, including TGF-β, leading to loss of DWAT and increased ECM deposition.

Methods: To assess the effect of MØs on DWAT deposition *in vivo*, we employed the bleomycin-induced mouse model of fibrosis and used a cellular immunotherapeutic approach to eliminate dermal MØs. To elucidate the potential mechanism by which activated MØs alter adipocyte differentiation, we developed an *in vitro* co-culture model. Adipose derived stem cells (ADSC) and bone marrow derived MØs (BMDM) were isolated from C57BL/6J mice. BMDMs were differentiated using GM-CSF, M-CSF, IL-4 and IL-13 or skin conditioned media (SCM). SCM was generated by subcutaneously implanting osmotic pumps with BLM for 7 days, harvesting the fibrotic skin, incubating the skin for 48 hours in media followed by collection of skin supernatant. ADSCs were differentiated into pre-adipocytes using media containing IBMX, dexamethasone, insulin, and rosigalitazone and co-cultured with differentiated BMDMs for 36 hours in Transwells. BMDMs and pre-adipocytes were collected for surface marker and gene expression analyses by flow cytometry and RT-qPCR. Cell supernatants were collected for analysis of secreted mediators by ELISA.

Results: Targeted elimination of dermal pro-fibrotic MØs in the bleomycin mouse model of fibrosis led to a restoration of DWAT. *In vitro* results demonstrated that expression of CD206 was increased on BMDMs differentiated with M-CSF, IL-4 and IL-13 and SCM, in contrast with GM-CSF. However, only BMDMs differentiated with SCM showed increased expression of IL-6, M-CSF, and IFNγ, which we have shown in prior studies are characteristic of SSc MØs. Furthermore, SCM-differentiated BMDMs secrete increased levels of TGF-β1 and inhibit adipogenesis.

Conclusion: Our results provide insight into a mechanism by which MØs modulate skin fibrosis through regulation of DWAT deposition. These findings suggest MØ-targeted therapies may be effective in ameliorating subcutaneous fat loss and potentially limiting excessive ECM deposition, particularly in combination with anti-fibrotic therapies.

Disclosure: C. Park: None; **H. Jarnagin**: None; **M. Whitfield**: Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 2, 5, Celdara Medical, 2, 5, 12, Scientific Founder; **P. Pioli**: Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 2, 5, Celdara Medical LLC, 2, 5, Pfizer, 5.

Abstract Number: 0945

The Nuclear Receptor TR4 Orchestrates Cytoskeletal Organization in a Gα12/ROCK-dependent Manner to Promote Myofibroblast Differentiation and Tissue Fibrosis in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Members of the superfamily of nuclear receptors have been implicated in inflammatory processes and pathologic tissue remodeling and have emerged as attractive targets for pharmaceutical intervention. However, the role of the testicular receptor 4 (TR4, also known as Nr2c2) in fibroblast activation and rheumatologic diseases has not yet been investigated.

Methods: TR4 expression in fibroblasts in the skin of systemic sclerosis (SSc) patients and in murine models of SSc were analyzed by immunofluorescence staining and Western blot. We performed bulk RNA sequencing (RNAseq) of TGFβ-stimulated fibroblasts with or without knockdown of TR4 by siRNA. The effect of TR4 on fibroblasts activation was studied using extracellular matrix staining. ROCK activity was quantified by ELISA in vitro. To confirm the findings, we applied TBRIact-, bleomycin-, cGvHD-induced dermal fibrotic as well as bleomycin-induced pulmonary fibrotic model in mice with fibroblast-specific-knockout of Tr4.

Results: Here we find that the expression of TR4 was upregulated in fibroblasts in the skin of systemic sclerosis (SSc) patients and in murine models of SSc. TGFβ stimulation induced the expression of TR4 in fibroblasts in a SMAD3-dependent manner. TR4 regulated numerous genes and functional terms associated with cytoskeletal remodeling. Knockdown of TR4 by siRNA prevented fibroblast-to-myofibroblast-transition, whereas plasmid-driven-overexpression of TR4 fostered TGFβ-induced fibroblast activation. Fibroblast-specific-knockout of Tr4 ameliorated skin fibrosis induced by overexpression of TBRIact, by bleomycin, associated with sclGvHD as well as bleomycin-induced pulmonary fibrosis. By RNA sequencing of TR4 target genes in fibroblasts and by analyzingthe functional role of ROCK and Gα12 using small molecule inhibitors and siRNA,we identified the profibrotic effects of TR4 were dependent on Gα12- and ROCK-associated cytoskeletal remodeling.

Conclusion: Our data indicate that TR4 is upregulated in SSc in a TGFβ-dependent manner to promote fibroblast activation. Inhibition of TR4 interferes with activation of ROCK, prevents cytoskeletal remodeling and fibroblast-to-myofibroblast transition and ameliorates dermal and pulmonary fibrosis. Inactivation of TR4 might thus offer therapeutic potential for the treatment of fibrosis in SSc and related diseases.

Disclosure: Y. Zhang: None; **L. Shen**: None; **y. Li**: None; **H. Györfi**: Boehringer-Ingelheim, 6; **J. Distler**: 4D Science and FibroCure, 8, 11, AbbVie, Active Biotech, Anamar, ARXX, AstraZeneca, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, Genentech, GSK, Inventiva, Janssen, Novarti, 2, Anamar, Argenx, ARXX, BMS, Bayer Pharma,

Boehringer Ingelheim, Cantargia, Celgene, CSL Behring, Galapagos, GSK, 5, Inventiva, Kiniksa, Lassen, Sanofi-Aventis, RedX, UCB, 5.

Abstract Number: 0946

Immunoglobulins G Purified from Systemic Sclerosis Patients Influence Cytoplasmic and Nuclear Proteins Profile in Dermal Fibroblasts

Aurélien Chepy[1], Marie Duhamel[2], Solange Vivier[1], Clément Chauvet[1], Lucile Guilbert[3], Eric Hachulla[4], Sylvain Dubucquoi[1], David Launay[1], Michel Salzet[2] and Vincent Sobanski[1], [1]Univ. Lille, Inserm, CHU Lille, U1286 - INFINITE - Institute for Translational Research in Inflammation, Lille, France, [2]Univ. Lille, Inserm, CHU Lille, U1192 - Protéomique Réponse Inflammatoire Spectrométrie de Masse - PRISM, Lille, France, [3]CHU Lille, Institut d'Immunologie, Lille, France, [4]CHU Lille, Département de Médecine Interne et Immunologie Clinique, Centre de Référence des Maladies Auto-immunes Systémiques Rares du Nord et Nord-Ouest de France (CeRAINO), Lille, France

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Autoantibodies (Aab) are frequent in systemic sclerosis (SSc). While recognized as potent biomarkers, their pathogenic role is unclear. Recently, we showed that immunoglobulins G (IgG) from SSc patients can modify the phenotype and secretome of fibroblasts (FB). The aim of this study was to gain a better understanding of the effect of purified IgG on FB by analyzing cytoplasmic and nuclear proteomic profiles.

Methods: Normal dermal FB (ATCC® Number: PCS-201-012 ™) were cultured in the presence of IgG from patients with diffuse cutaneous SSc (dcSSc, n=20), limited cutaneous SSc (lcSSc, n=10) or healthy controls (HC, n=10). Cytoplasmic and nuclear proteins were extracted and explored separately using mass spectrometry coupled with liquid chromatography.

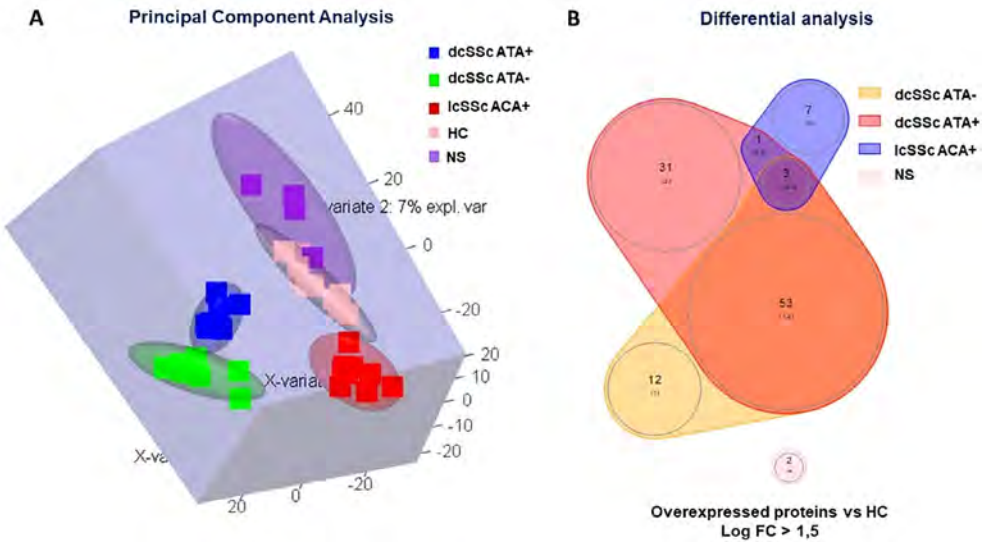

Figure 1: Cytoplasmic proteomics of FB in the presence of purified IgG from SSc patients and HC. Data visualization performed by principal component analysis (A); Venn diagram representing differential analysis vs HC (B). SSc: systemic sclerosis; dcSSc ATA+: diffuse SSc anti-topoisomerase-I positive patients; dcSSc ATA-: diffuse SSc anti-topoisomerase-I negative patients; lcSSc ACA+: limited SSc anti-centromere positive patients; HC: healthy controls; NS: non stimulated fibroblast. For differential analysis, proteins with p-value<0.05 and Log Fold Change > 1.5 were considered.

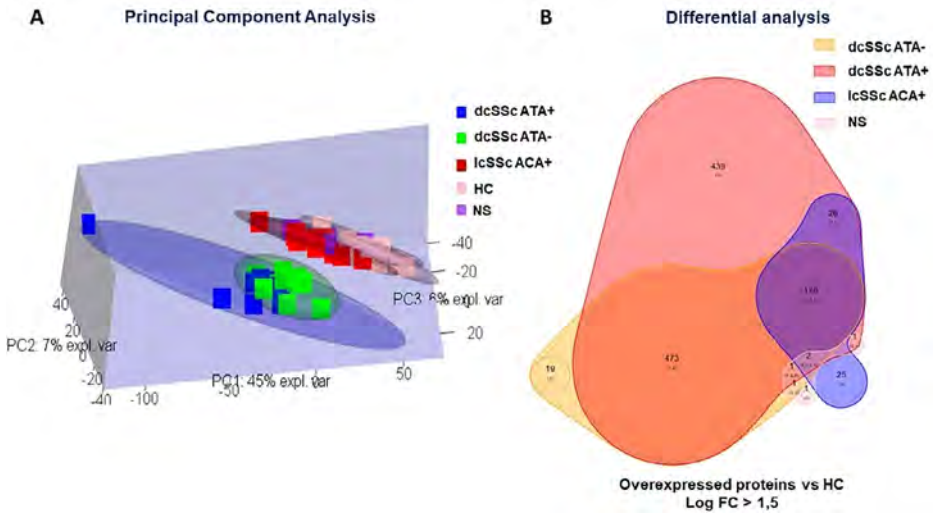

Figure 2: Nuclear proteomics of FB in the presence of purified IgG from SSc patients and HC. Data visualization performed by principal component analysis (A); Venn diagram representing differential analysis vs HC (B). SSc: systemic sclerosis; dcSSc ATA+: diffuse SSc anti-topoisomerase-I positive patients; dcSSc ATA-: diffuse SSc anti-topoisomerase-I negative patients; lcSSc ACA+: limited SSc anti-centromere positive patients; HC: healthy controls; NS: non stimulated fibroblast. For differential analysis, proteins with p-value<0.05 and Log Fold Change > 1.5 were considered.

Data were visualized using principal component analysis (PCA) and protein profile were studied by performing differential analysis and gene set enrichment analysis.

Results: Cytoplasmic proteomics identified and quantified 1,630 proteins. PCA revealed five groups of subjects according to cytoplasmic proteins expression: dcSSc anti-topoisomerase-I (ATA) positive patients (dcSSc ATA+) which appeared to be the most distinct group, dcSSc ATA negative patients (dcSSc ATA-), lcSSc anti-centromere (ACA) positive patients (lcSSc ACA+), healthy controls (HC) and non-stimulated FB (NS) (**Figure 1A**). Fifty-three proteins were commonly overexpressed in the dcSSc ATA+ and ATA- and five in all SSc subtypes. Thirty-one proteins were exclusively overexpressed in the dcSSc ATA+ condition compared to HC such as Leucine Reach Repeat Containing 15 and Tripartite Motif Containing 25 (**Figure 1B**). Nucleus proteomics identified and quantified 1593 proteins. PCA revealed two main groups of subjects according to protein expression: the first was composed of dcSSc patients and the second was composed of lcSSc ACA + patients, HC, and NS (**Figure 2A**). Four hundred and seventy-three proteins were commonly overexpressed in dcSSc conditions and 128 were commonly overexpressed in all SSc conditions compared to HC. A total of 439 proteins were exclusively overexpressed in dcSSc ATA+ such as Transgelin 2 and RuvB Like AAA ATPase 2 (**Figure 2B**).

Functional enrichment analysis revealed that cytoplasmic proteins overexpressed in the dcSSc ATA+ and dcSSc ATA- conditions were involved in protein binding. Proteins exclusively overexpressed in dcSSc ATA+ condition were involved in cell adhesion molecule binding and positive regulation of cell migration. Nuclear proteins overexpressed in dcSSc conditions were involved in protein and RNA binding.

Conclusion: IgG purified from SSc patients modified both cytoplasmic and nuclear proteins expression according to cutaneous subtype and Aab profile. The group dcSSc ATA+ induced a characteristic cytoplasmic and nuclear proteins profile. Protein binding, cell adhesion molecule binding and positive regulation of cell migration in the cytoplasm, and protein and RNA binding in the nucleus were enriched in FB co-incubated with purified IgG from dcSSc ATA+ patients.

Disclosure: A. Chepy: None; **M. Duhamel**: None; **S. Vivier**: None; **C. Chauvet**: None; **L. Guilbert**: None; **E. Hachulla**: Bayer, 6, Boehringer-Ingelheim, 6, CSL Behring, 5, GlaxoSmithKlein(GSK), 5, 6, Johnson & Johnson, 5, 6, Roche, 5, 6, Sanofi-Genzyme, 6; **S. Dubucquoi**: None; **D. Launay**: None; **M. Salzet**: None; **V. Sobanski**: None.

Abstract Number: 0947

Fcγ Receptors Define Pro-Phagocytic Macrophages and Trigger Pro-Inflammatory Responses in Patients with Systemic Sclerosis

Amela Hukara[1], Gino Andrea Bonazza[1], Tracy Tabib[2], Raphael Micheroli[1], Suzana Jordan[3], Kristina Bürki[1], Sylvie Schlitz Schönbächler[1], Adrian Ciurea[4], Oliver Distler[3], Robert Lafyatis[5], Przemyslaw Blyszczuk[1] and Gabriela Kania[1], [1]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [2]Division of Rheumatology and Clinical Immunology, Department of Medicine, University of Pittsburgh, Pittsburgh, PA, [3]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [4]University Hospital Zurich, Zürich, Switzerland, [5]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Fcy receptors (FcγR) are opsonic phagocytic receptors, requiring tight regulations to prevent uncontrolled activation of pro-inflammatory phagocytosis. SSc macrophages display an alternatively-activated profibrotic phenotype. However, a comprehensive understanding of how this distinct macrophage phenotype can contribute to SSc pathogenesis is missing. We aimed to study if alternatively-activated macrophages from SSc patients exhibit a pro-phagocytic signature.

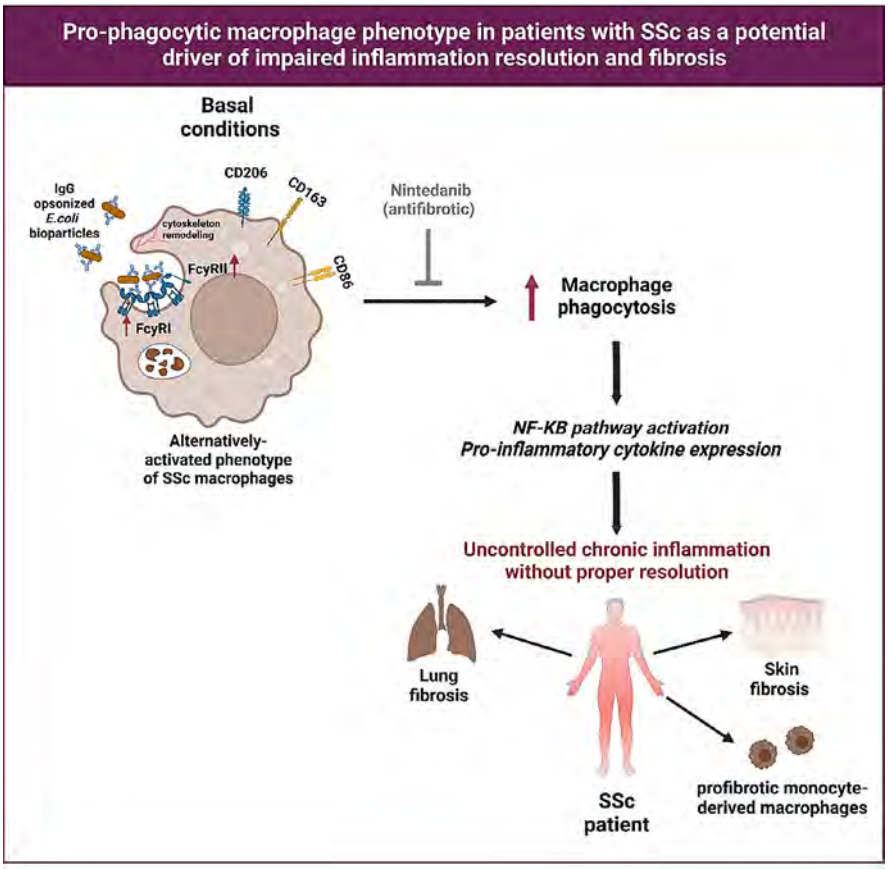

Figure 1 Proposed mechanism of impaired resolution in SSc patients leading to chronic inflammation and fibrosis driven by phagocytic FcγR. Created with BioRender.com

Methods: Publicly available single-cell RNA sequencing (scRNA-seq) datasets (GSE138669, GSE212109) on healthy control and SSc patient skin or lung macrophage populations were analyzed using Seurat v4.3.0 package. Human monocyte-derived macrophages (hMDM) were differentiated from $CD14^+$ blood-derived monocytes from healthy controls, SSc, RA, PsA and axSpA patients.For some experiments, M(0) hMDM were pre-treated for 24 hours with 0.1 μM of the antifibrotic drug Nintedanib. Phagocytic activity of M(0) hMDM was measured using pHrodo Red *E.coli* bioparticles and detected by flow cytometry. Macrophage surface markers were assessed by flow cytometry. NF-κB signalling cascade was studied on the protein level by Western Blot, and *IL6* expression was measured using RT-qPCR.

Results: scRNA-seq analysis revealed upregulated *FCGR* genes and FcγR-mediated pathways in skin macrophages from 12 dcSSc patients and in lung macrophages from 5 SSc patients with interstitial lung disease (ILD) (p.adj.≤0.05; log2FC≥0.5). We identified *FCGR3A*^{hi} macrophages in dcSSc patient skin and *FCN1*^{hi} macrophages in the lungs of SSc-ILD patients as the main phagocytic populations. Functional *in vitro* studies confirmed enhanced phagocytic activity in alternatively-activated M(0) SSc hMDM (n=57) compared to healthy control cells (n=36, p< 0.0001). Phagocytic activity was observed in M(0) hMDM from pre-early SSc (n=14, p=0.0021), lcSSc (n=38, p=0.0006) and dcSSc (n=5, p=0.0581) patients, and was therefore independent of the disease subtype. Phagocytic activity positively correlated with FcγRI (n=14, Pearson r=0.663, p=0.006) and FcγRII (n=14, Pearson r=0.5178, p=0.0478) expression. Subsequently, engulfment of pHrodo Red *E.coli* bioparticles led to NF-κB pathway activation followed by increased *IL6* expression in SSc M(0) hMDM (n=7) compared to healthy controls (n=5, p=0.0278). Pre-treatment of M(0) SSc hMDM with Nintedanib led to a reduction in phagocytic activity compared to untreated M(0) SSc hMDM (n=7, p=0.0066). In addition, we found that the pro-phagocytic phenotype of SSc M(0) hMDM is also present in other rheumatic diseases, including RA (n=10, p=0.0363) and PsA (n=11, p=0.0235), but not axSpA (n=9, p=0.4867) patients.

Conclusion: Our findings proposed enhanced FcγR expression as a novel biomarker to identify pro-phagocytic macrophages in SSc patients, which can trigger pro-inflammatory responses. Uncontrolled activation of pro-phagocytic macrophages could contribute to the aberrant resolution of inflammation followed by fibrosis in SSc patients (Figure 1). Furthermore, targeting pro-phagocytic macrophages may be an interesting approach for rheumatic diseases beyond SSc.

Disclosure: A. Hukara: None; **G. Bonazza**: None; **T. Tabib**: None; **R. Micheroli**: None; **S. Jordan**: None; **K. Bürki**: None; **S. Schlitz Schönbächler**: None; **A. Ciurea**: None; **O. Distler**: 4P-Pharma, 2, 5, 6, AbbVie, 2, 5, 6, Acceleron, 2, 5, 6, Alcimed, 2, 5, 6, Altavant Sciences, 2, 5, 6, Amgen, 2, 5, 6, AnaMar, 2, 5, 6, Arxx, 2, 5, 6, AstraZeneca, 2, 5, 6, Bayer, 2, 5, 6, Blade Therapeutics, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Citus AG, 12, Co-Founder, Corbus Pharmaceuticals, 2, 5, 6, CSL Behring, 2, 5, 6, Galapagos, 2, 5, 6, Galderma, 2, 5, 6, Glenmark, 2, 5, 6, Gossamer, 2, 5, 6, Horizon Therapeutics, 2, 5, 6, Janssen, 2, 5, 6, Kymera, 2, 5, 6, Lupin, 2, 5, 6, Medscape, 2, 5, 6, Miltenyi Biotec, 2, 5, 6, Mitsubishi Tanabe, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143), 10, Prometheus Biosciences, 2, 5, 6, Redx Pharma, 2, 5, 6, Roivant, 2, 5, 6, Topadur, 2, 5, 6; **R. Lafyatis**: Advarra/GSK, 1, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, 5, Certa Therapeutics, 2, Corbus, 2, 5, EMD Serono, 2, Formation, 2, 5, Genentech, 1, 2, Merck/MSD, 2, Moderna, 5, Morphic, 2, Pfizer, 2, 5, Regeneron, 5, Third Rock Venture, 2, Thirona Bio, 2, 4, 11, Zag Bio, 2; **P. Blyszczuk**: None; **G. Kania**: None.

Abstract Number: 0948

Nintedanib Alters Fibroblast and Macrophage Diversity in a 3D Skin Model of Systemic Sclerosis (SSc)

Noelle Kosarek[1], Tamar Abel[2], Sasha Shenk[3], Tammara Wood[2], Jonathan Garlick[4], Patricia Pioli[5] and **Michael Whitfield**[5], [1]Dartmouth Geisel School of Medicine, Lebanon, NH, [2]Dartmouth College, Hanover, NH, [3]Tufts University, Boston, MA, [4]Tufts University School of Dental Medicine, Boston, MA, [5]Geisel School of Medicine at Dartmouth, Hanover, NH

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Sclerosis (SSc) is a rare autoimmune disease characterized by fibrosis of the skin and internal organs. While the tyrosine kinase inhibitor Nintedanib is now FDA-approved to treat lung fibrosis in SSc patients, the mechanism by which this drug alters fibroblast and immune cell activation in SSc is unknown.

Methods: We constructed SSc and control 3D skin-like tissues using fibroblasts, monocytes, keratinocytes, and plasma from SSc patients or healthy donors in the presence or absence of Nintedanib. Multiple samples were pooled from each 3D skin-like tissue and processed for histology, flow cytometry, and single cell RNA-sequencing (scRNA-seq). Data were analyzed in R using Seurat, Signac, monocle3, and nichenetr packages.

Results: Analysis of the 14 SSc and 14 healthy control tissues by scRNA-seq in the absence of drug treatment identified four distinct fibroblast populations and five macrophage populations. To assess the effect of Nintedanib on fibroblast and macrophage representation in SSc skin, we exposed 6 SSc and 6 healthy control 3D skin-like tissues to Nintedanib, which reduced tissue thickness and contractility. SSc-derived saSE tissues displayed measures of increased fibrosis.SSc tissues were significantly thicker (p=0.0007) than healthy control tissues. Notably, the organization of the control tissues was clearly defined with obvious dermal and epidermal layers, while the SSc tissues had a more disorganized appearance with less well-defined layers. There was a statistically significant decrease in both tissue contractility (p=0.0002) and thickness (p=0.0008) after Nintedanib-treatment of SSc tissues; healthy control tissues showed a significant decrease in contractility but did not show a significant difference in tissue thickness. Proportional shifts were noted in two of the four fibroblast populations after Nintedanib treatment. Consistent with prior reports of elevated macrophage numbers in SSc-affected tissues, macrophages were significantly increased in SSc saSE tissues compared to healthy control saSE tissues. Macrophage numbers in SSc saSE tissues were significantly reduced by Nintedanib-treatment. Gene expression analysis of Nintedanib-treated skin demonstrated significant alterations in the expression of matrix and fibrosis-related genes, suggesting these changes underlie drug-mediated anti-fibrotic activity. This included significant reductions in the expression of ELN (p=1.42*1^-61), COL1A1 (p=0.016), TNFAIP3 (p=0.007), TNFAIP2 (p=1.75*10^-8), MMP1 (p=1.26*10^-5), and TNFAIP6 (p=8.27*10^-5).

Conclusion: Our results suggest SSc fibroblast and macrophage populations are plastic and require cell-cell, cell-matrix, and circulating factors to maintain their phenotype in culture. Nintedanib resulted in changes to fibroblasts and macrophage populations, including decreased expression of matrix and secreted factors.

Disclosure: N. Kosarek: None; **T. Abel**: None; **S. Shenk**: None; **T. Wood**: None; **J. Garlick**: None; **P. Pioli**: Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 2, 5, Celdara Medical LLC, 2, 5, Pfizer, 5; **M. Whitfield**: Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 2, 5, Celdara Medical, 2, 5, 12, Scientific Founder.

Abstract Number: 0949

Development of Interstitial Pneumonia with Autoimmune Features in Conditional Tgfb3 Deletion

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: We found that TGF-β3 regulates humoral immunity in a context-dependent manner [1]. Recent genome-wide association study reveals that TGF-β3 might be a novel target in African American systemic sclerosis (SSc) patients [2]. Since *Tgfb3*$^{-/-}$ mice die within 20 hours of birth [3], the physiological roles of TGF-β3 have not clearly elucidated. In this study, we evaluated the immunological and fibrotic roles of TGF-β3 by using mice with conditional Tgfb3 deletion.

[1] Komai T, et al. Front Immunol. 2018;9:1364., [2] Kaundal U, et al. ACR2022, Arthritis Rheumatol. 2022; 74 (suppl 9), [3] Kaartinen V, et al. Nat Genet. 1995;11(4):415-21.

Methods: TGF-β3 conditional knockout mice in CD4$^+$ T cells (*Tgfb3*$^{fl/fl}$*CD4*^{Cre}) and B cells (*Tgfb3*$^{fl/fl}$*CD19*^{Cre}) were created. Histopathology, expression of fibrosis-related genes in lung by qRT-PCR in lungs, and flow cytometric analysis of splenocytes from these mice were conducted. Also, a continuous bleomycin infusion delivered by osmotic minipumps to these mice was conducted as an induced SSc model. To evaluate the effects of overexpression of TGF-β3, either pCAGGS-Mock, pCAGGS-Tgfb3 plasmid vectors were intravenously administered to lupus prone MRL/*lpr* mice with spontaneous interstitial pneumonia, and lung pathologies were assessed.*In vitro,* normal human lung fibroblasts (NHLFs) cultured with and without TGF-β3 were evaluated.

Results: *Tgfb3*$^{fl/fl}$*CD4*^{Cre} mice developed inflammatory cell infiltration and fibrosis in lungs spontaneously (**Figure 1A**), and low-titer anti-dsDNA antibody production and increased marginal zone B cells was observed. The bleomycin-induction exacerbated interstitial pneumonia, and fibrosis-related genes of the lung tissue such as *mCol1a1*, *mCol1a2*, *mSerpine1*, and *mSpp1* were up-regulated in both *Tgfb3*$^{fl/fl}$*CD4*^{Cre} and *Tgfb3*$^{fl/fl}$*CD19*^{Cre} mice in comparison to *Tgfb3*$^{fl/fl}$mice

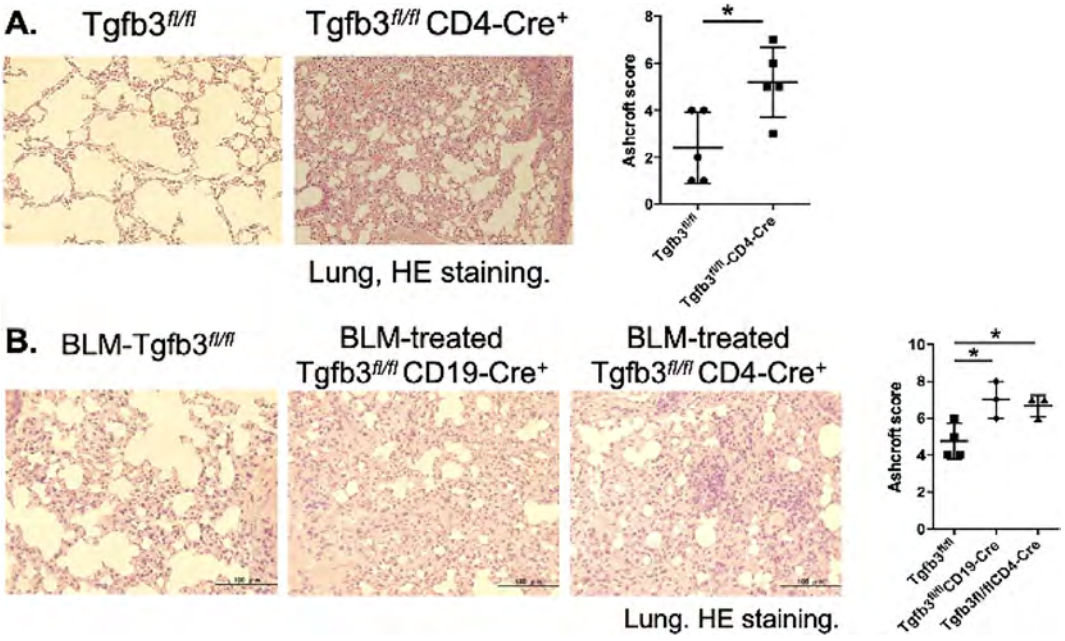

Figure 1. Exacerbation of interstitial pneumonia by conditional Tgfb3 deletion.

(**Figure 1B**). Further, the interstitial pneumonia of MRL/*lpr* mice was prone to be ameliorated by pCAGGS-Tgfb3 administration. In *in vitro* experiments, TGF-β3 inhibited the proliferation of NHLFs in a dose-dependent manner.

Conclusion: Our study suggested that TGF-β3 contributes to regulate systemic autoimmune and fibrotic responses. Anti-inflammatory and anti-fibrotic function of TGF-β3 might lead to future therapeutic target for interstitial pneumonia with autoimmune features.

Disclosure: T. Komai: Amgen, 6, Asahi Kasei, 6, Chugai, 5, 6, Daiichi-Sankyo, 6, Eisai, 6, Eli Lilly, 1, 6, GlaxoSmithKlein(GSK), 5, 6, Janssen, 6, Novartis, 6, Tanabe Mitsubishi, 6; **T. Okamura**: Chugai Pharmaceutical., 12, belong to the Social Cooperation Program, Department of Functional Genomics and Immunological Diseases, supported by Chugai Pharmaceutical.; **M. Kono**: Asahi Kasei Pharma, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6; **K. Yamamoto**: AbbVie, 6, Pfizer Japan Inc, 12, Outsourcing contract, RegCell, 1, Sun Pharmaceutical Industries Ltd, 6; **K. Fujio**: AbbVie/Abbott, 6, Asahi Kasei, 5, 6, Astellas, 6, AstraZeneca, 6, Ayumi, 6, Bristol-Myers Squibb(BMS), 5, 6, Chugai Pharmaceutical., 5, 6, Daiichi-Sankyo, 6, Eisai, 5, 6, Eli Lilly, 5, 6, Janssen, 6, Novartis, 6, Ono, 6, Pfizer, 6, Sanofi, 6, Tanabe Mitsubishi, 5, 6, Tsumura, 5.

Abstract Number: 0950

KL-6 and IL-18 Levels Are Negatively Correlated with Respiratory Function Tests and ILD Extent Assessed on HRCT in Patients with Systemic Sclerosis-related Interstitial Lung Disease (SSc-ILD)

Cristiana Sieiro Santos[1], Sara Calleja[2], Javier de la Calle Lorenzo[2], Carmen López Garay[2], Clara Moriano[2], Elena Bollo de miguel[2] and Elvira Díez Álvarez[2], [1]Complejo Asistencial Universitario de León, León, Spain, [2]CAULE, León, Spain

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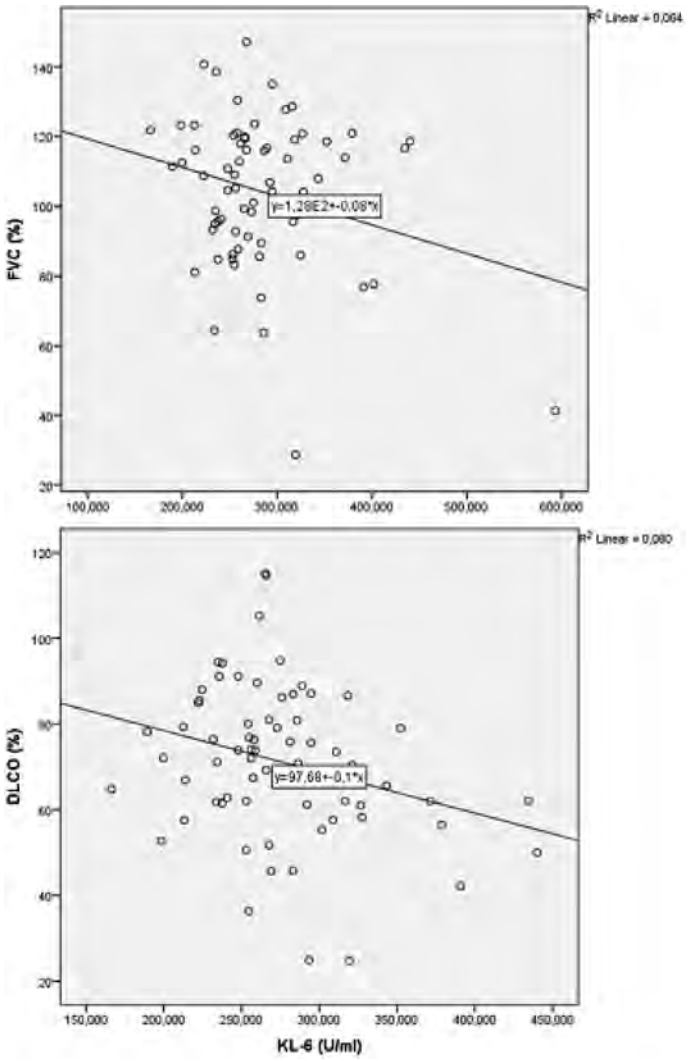
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is one of the leading causes of mortality in patients with systemic sclerosis (SSc). Serum biomarkers have been suggested as indicators for pulmonary damage with clinical value in the diagnosis and prognosis of SSc-ILD.Our objectives are to investigate the role of serum biomarkers (Krebs von den Lungen-6 KL-6, IL-18 and IL-18BP) as potential biomarkers reflecting the severity of SSc-ILD as assessed through high-resolution computed tomography (HRCT) and pulmonary function tests (PFT), including forced vital capacity (%FVC) and diffusing capacity of the lung for carbon monoxide (%DLCO).

Methods: A cross-sectional study including patients with SSc fulfilling the 2013 ACR/EULAR criteria was performed. Patients were classified according to disease duration and pulmonary involvement (presence of ILD). All SSc patients underwent chest HRCT scans and pulmonary function test at baseline. Serum concentration of KL-6, IL8 and IL18BP were determined using sandwich ELISA technique (solid phase sandwich Enzyme Linked-Immunosorbent Assay), with kits from MyBiosource for KL-6 and from Invitrogen for IL18 and IL18BP. A semiquantitative grade of ILD extent was evaluated through HRCT scan (grade 1, 0–20%; grade 2, >20%). Extensive lung disease was defined as >20% of lung involvement on HRCT, and FVC < 70% predicted and limited lung involvement as ≤20% of ILD involvement on HRCT, and an FVC ≥70% predicted.

Results: 74 patients were included, 27% were male. The mean age at diagnosis was 57.5±15 years. The mean time since diagnosis was 7.67±8 years. 28 patients had ILD (38%). 64 % of patients had < 20% of ILD extent classified through HRCT scan. SSc-ILD patients had elevated serum KL-6 and IL-18 levels compared to patients without ILD (p=0.003 and p=0.04), and those findings were preserved after adjusting for age and sex (table 1). Mean erythrocyte sedimentation rate (ESR) was higher in patients with SSc-ILD. A negative correlation between KL-6 levels and %FVC (β=-0.25, p 0.037) and %DLCO (β=-0.28, p 0.02) and between IL-18 levels and %FVC (β=-0.20, p 0.03) and %DLCO (β=-0.14, p 0.04) were found. Linear



	ILD (28)	ILD (-) (46)	P value
Mean age, years	57.3±16	57.7±28	0.97
Sex, male	6 (21%)	13 (28%)	0.51
Mean ESR (mm/h)	23±16	9±8	**0.04**
Mean CRP (mg/dL)	7.1±4.3	5.03±3.25	0.36
Serum KL-6 (U/mL)	320±68	262.5±39	**0.003**
Serum IL-18BP (U/mL)	150.46±130	123.23±90	0.21
Serum IL-18 (U/mL)	300.63±167	209.65±180	**0.03**
Pulmonary function tests			
Mean FVC %	96.2±34	111±22.3	**0.01**
Mean DLCO%	65.7±18	77.5±19.7	**0.001**

Table 1: Demographic and clinical characteristics of patients with SSc-ILD and non-SSc-ILD.

regression models representing correlation between KL-6 and PFT are represented in the scatter plot in figure 1. Serum KL-6 and IL-18 levels successfully differentiated grades 1 and 2 (p = 0.028 and p=0.021). Semiquantitative grades of ILD on the HRCT scan were significantly proportional to the KL-6 (p 0.01) and IL-18 (p=0.03). A positive correlation between extensive lung disease and KL-6 (β=0.61, p 0.007) but not with IL-18 was found.

Conclusion: Serum KL-6 levels and IL-18 were increased in patients with SSc-ILD and showed a positive correlation with ILD severity as measured using a semiquantitative HRCT grading scale and a negative correlation with PFT parameters. KL-6 is positively correlated with extensive lung disease. Serum KL-6 and IL-18 could be a clinically useful biomarker in screening and evaluating SSc-ILD.

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Abstract Number: 0951

Single Cell Analysis of Transitional B Cells in Systemic Sclerosis Highlights Defective Peripheral Tolerance

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Transitional B cells comprise a distinct population of B cells that have recently migrated to the periphery from the bone marrow. In systemic sclerosis (SSc),previous data from our laboratory has demonstrated that there are differences in the number and function of transitional B cells compared to healthy controls (HCs). In addition, we have previously isolated transitional B cells from SSc patients which are seropositive for anti-topoisomerase Iautoantibodies (ATA)demonstrating that these cells evade tolerance. To investigate why these autoreactive B cells are not tolerised in those withSSc,we performed a paired bulk and single-cell RNA sequencing study of the transitional B cell subsets in SSc and HCs.

Methods: 5000 $CD19^{+}CD24^{hi}CD38^{hi}$ transitional B cells were sorted from four HCs and four treatmentnaïveATA-positive SSc patients.Single-cell RNA-sequencing was performed on the sorted transitional B cells and the datawas analysed using Seurat in RStudio. Additionally, in a subset of this cohort paired bulk RNA-sequencing of the sorted transitional T1 ($CD19^{+}CD24^{hi}CD38^{hi}CD27^{-}IgM^{hi}IgD^{med}$) and T2($CD19^{+}CD24^{hi}CD38^{hi}CD27^{-}IgM^{hi}IgD^{hi}$) populations was carried out.

Results: As shown in Figure 1 single cell transcriptomics identified four distinct transitional B cell clusters in SSc patients and HCs. Notably, cluster 1 is diminished in the SSc group and cluster 0 is expanded in SSc compared to HCs. These clusters were characterised using relevant genes as shown in the dotplot in Figure 2. Clusters 0, 1 and 2 all share similar transcriptomic features whilst cluster 3 has upregulated expression of genes associated with commitment to the B cell lineage (EBF1). Thisindicates that cluster 3 is the earliest B cell emigrant from the bone marrow. Clusters 2, 1 and 0 can then be differentiated through expression of genes such as PLD4 and KLF2. Subsequent pathway analyses provided evidence for defective tolerance in SSc patients which may be mediated through dysregulated NF-κB signalling. In addition, differential

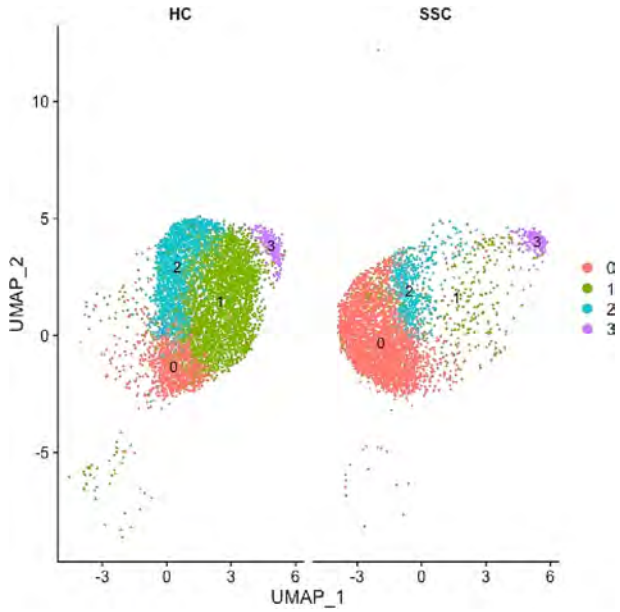

Figure 1. A UMAP plot depicting an integrated scRNA-seq analysis of transitional B cell clusters in 4 healthy controls (HC) and 4 systemic sclerosis (SSc) patients.

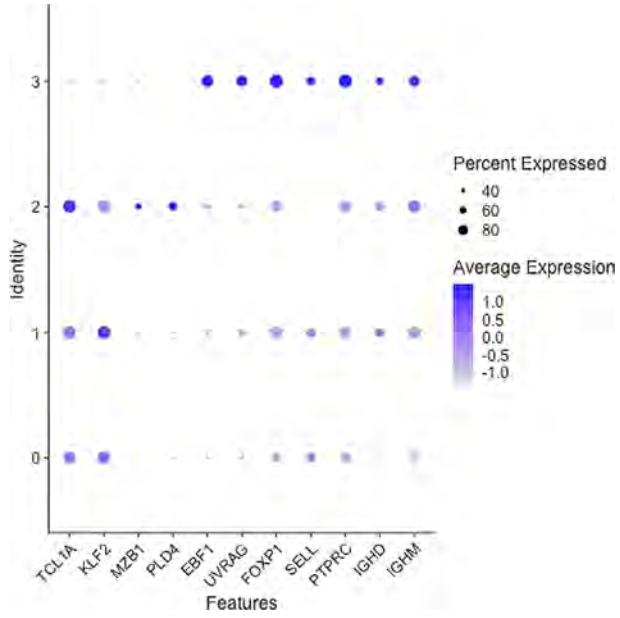

Figure 2. A dotplot of key genes used to identify transitional B cell clusters in a scRNA-seq study of 4 healthy controls (HC) and 4 systemic sclerosis (SSc) patients.

gene expression analysis using bulk RNA-sequencing of sorted T1 and T2 transitional subsets have identified five candidate gene signatures which are significantly enriched in the T2 cells compared with the T1 cells. This finding was in concordance with the single cell data and provides further evidence to support the existence of a peripheral tolerance/selection checkpoint at the transitional B cell stage.

Conclusion: Through this data we have identified four transitional B cell subsets and have characterised their transcriptomic profile. Additionally, we have found further evidence for a potential breach in tolerance in the SSc patients. Studies are ongoing to explore biological pathways through which altered gene expression impacts peripheral tolerance in SSc.

Disclosure: C. Beesley: Versus Arthritis, 5; **N. Goldman**: None; **D. Abraham**: None; **C. Denton**: AbbVie, 2, Acceleron, 2, Arxx Therapeutics, 5, Bayer, 2, Boehringer-Ingelheim, 2, 6, Corbus, 2, 6, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Horizon Therapeutics, 2, Inventiva, 2, 5, Janssen, 6, Roche, 2, Sanofi, 2, Servier, 5; **R. Mageed**: None; **V. Ong**: None.

Abstract Number: 0952

Unraveling the Role of MiR-181 in Skin Fibrosis Pathogenesis by Targeting NUDT21

Tingting Mills[1], Minghua Wu[2], Hydia Puente[3], Jerry Alonso[4], Julio charles[4], Maureen Mayes[4] and Shervin Assassi[5], [1]Biochemistry Department, University of Texas McGovern Medical School, Houston, TX, [2]Department of Internal Medicine, Division of Rheumatology, The University of Texas Health Science Center at Houston, Houston, TX, [3]UTHealth-Houston, Houston, TX, [4]Division of Rheumatology, University of Texas McGovern Medical School, Houston, TX, [5]University of Texas McGovern Medical School at Houston, Houston, TX

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Nudix Hydrolase 21 (NUDT21, also known as CFIm25) is a master regulator of alternative polyadenylation. Previous studies have revealed that NUDT21 is significantly decreased in systemic sclerosis (SSc) skin and that its downregulation in fibroblasts potentiates both skin and lung fibrosis (Weng T et al. J Clin Invest. 2019 & J Exp Med 2020). This study aims to investigate the upstream mechanisms that lead to NUDT21 repression in skin fibrosis.

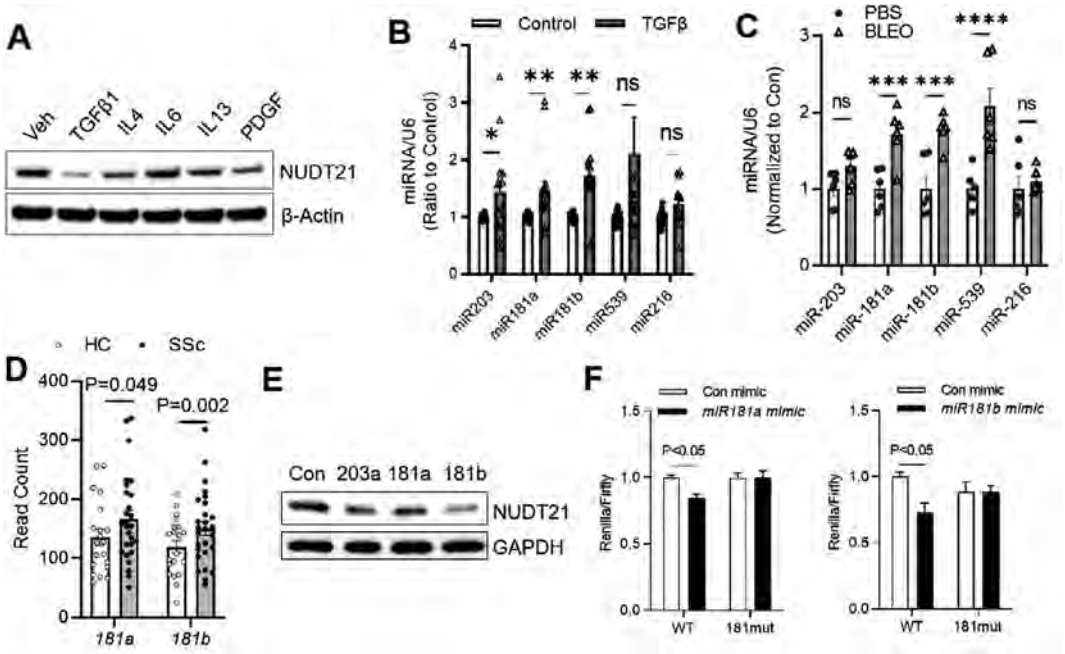

Figure 1: (A) NUDT21 levels in normal human dermal fibroblasts treated with different cytokines. Transforming growth factor β (TGFβ1) is the cytokine that most profoundly downregulates NUDT21 expression. (B-D) The levels of potential NUDT21-targeting miRNAs in (B) TGFβ treated dermal fibroblasts, (C) Day 21 mouse skin subcutaneously injected with bleomycin 5 times a week, and (D) Primary dermal fibroblasts from 20 healthy controls (HC) and 27 SSc patients. (E) NUDT21 levels in normal human dermal fibroblasts treated with MiR-203a, 181a and -181b mimics. (F) Dual-luciferase assay showing miR-181a and -181b can repress the luciferase activities of WT NUDT21 3'UTR but not the NUDT21 3'UTR that have miR-181 binding sites mutated.

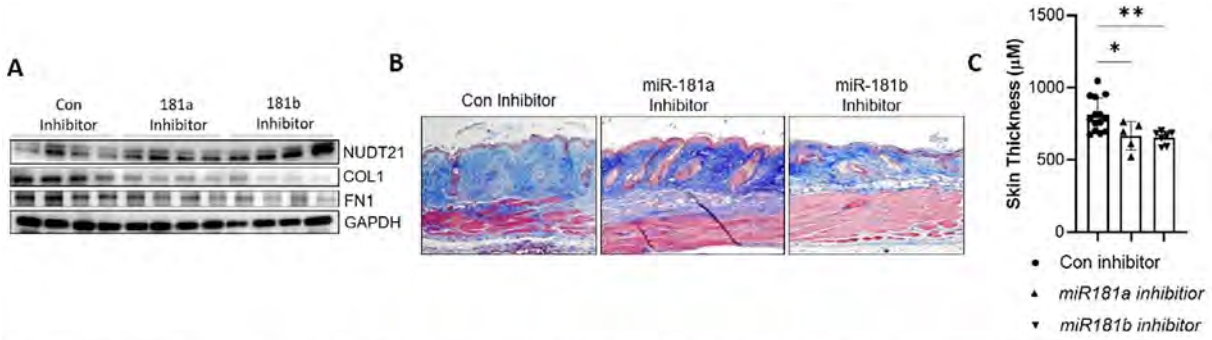

Figure 2: MiR-181a and -181b inhibitors attenuated skin fibrosis in association with increased NUDT21 protein levels. (A) Western blot demonstrates protein levels of NUDT21 and fibrotic markers. (B) Representative images of slides stained with Masson's trichrome. (C) Dermal thickness was measured in a blinded manner.

Methods: NUDT21 levels in cells treated with different cytokines were determined by western blot and RT-qPCR. Dual-luciferase assays were performed to determine the micro RNA (miRNA) regulation of NUDT21. MiR-181a and -181b mimics and inhibitors were injected subcutaneously 10 days after the initial subcutaneous bleomycin treatment to determine their effects on skin fibrosis (n≥ 5 per group).

Results: In comparison to IL4, IL6, IL13, and PDGF, transforming growth factor β (TGFβ1) led to a stronger downregulation of NUDT21 in healthy control (HC) dermal fibroblasts (Fig. 1A). Further investigation showed that TGFβ did not downregulate NUDT21 transcript until 48 hours after treatment, suggesting that it regulated NUDT21 through an indirect mechanism such as miRNA induction. Screening potential NUDT21 targeting miRNAs revealed that miR-181a and -181b were elevated in TGFβ1 treated human dermal fibroblasts and bleomycin-induced skin fibrosis in mice (Fig. 1B-C). Consistent with these findings, miR-181a and -181b were both significantly increased in primary dermal fibroblasts from 27 patients with early diffuse SSc compared to fibroblasts obtained from 20 matched HCs while the levels of other NUDT21 targeting miRNAs were not increased (Fig. 1D). Both miR-181a and -181b could directly bind NUDT21 3'UTR to repress NUDT21 expression in skin fibroblasts (Fig. 1E-F). Functional studies demonstrated that miR-181a and -181b inhibitors attenuated bleomycin-induced skin fibrosis murine models in association with decreased NUDT21 expression (Fig.2), while miR-181a and -181b mimics exaggerated bleomycin-induced skin fibrosis.

Conclusion: Taken together, these findings suggest miR-181a/b play a role in SSc pathogenesis and are potential therapeutic options for skin fibrosis.

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Abstract Number: 0953

Flavin-containing Monooxygenase (FMO3) Links the Gut and Fibrosis in Systemic Sclerosis

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Background/Purpose: Trimethylamine (TMA) generated by the gut microbiome is converted into trimethylamine N-oxide (TMAO) via the host enzyme FMO3. The TMA-FMO3-TMAO metaorganismal axis has been linked to chronic metabolic, renal, and cardiovascular diseases, and triggers myofibroblast reprogramming in mesenchymal cell types[1,2]. However, despite growing evidence implicating gut dysbiosis in SSc[3], the expression and pathogenic role in FMO3 in SSc has never been investigated.

Methods: The TMA-derived metabolite TMAO was measured in the circulation by LC tandem mass spectrometry in 200 adults with SSc, and 100 age-matched controls undergoing elective cardiac evaluation. FMO3 was evaluated in skin biopsies and fibroblasts via single cell RNA-seq (scRNA), immunohistochemistry and immunofluorescence. To investigate the pathogenic role of the TMAO-producing enzyme FMO3, C57BL/6 mice engineered with liver-specific gain-of-function of human FMO3 (hFMO3-TG)[4] were used in models of fibrosis and inflammation.

Results: Serum TMAO was elevated in SSc patients compared to controls (median 3.31 μM [IQR: 2.18, 5.23] vs. 2.70 μM [IQR: 1.74, 4.11]; p=0.016), with highest levels among obese and male SSc patients. Remarkably, while FMO3 is expressed in the liver, we also detected FMO3 in skin. SSc patient-derived biopsies and explanted fibroblasts showed elevated FMO3 protein and mRNA expression colocalizing with collagen production. scRNA-seq of the skin showed the highest expression of FMO3 localized to $CLDN1^+$ fibroblasts, a cellular subpopulation seen primarily in SSc biopsies and associated with extracellular matrix remodeling. Male mice engineered to express human FMO3 (hFMO3-TG) show a significant increase in circulating TMAO[4]. Bleomycin treatment caused significantly exaggerated fibro-inflammatory pathology in hFMO3-TG mice compared to identically treated wildtype mice.

Conclusion: Collectively, our results demonstrate that gut microbiome-derived vasculopathic/profibrotic TMAO is elevated in patients with SSc, and transgenic mice expressing human FMO3, the enzyme that generates TMAO, develop augmented fibrotic responses associated with elevated TMAO. This is the first study to identify a potential pathogenic role for FMO3 in SSc, linking gut dysbiosis to fibrosis and vasculopathy via a metaorganismal axis.

REFERENCES

1. Brown et al., 2017. Targeting of microbe-derived metabolites to improve human health: the next frontier for drug discovery. *Journal of biological chemistry*, *292*(21), pp.8560-8568.
2. Kim et al., 2022. Gut microbe-derived metabolite trimethylamine N-oxide activates PERK to drive fibrogenic mesenchymal differentiation. *Iscience*, *25*(7), p.104669.
3. Tan et al., 2023. Gut microbiome profiling in systemic sclerosis: a metagenomic approach. *Clinical and Experimental Rheumatology*.
4. Zhu et al., 2018. Flavin monooxygenase 3, the host hepatic enzyme in the metaorganismal trimethylamine N-oxide-generating pathway, modulates platelet responsiveness and thrombosis risk. Journal of Thrombosis and Haemostasis, 16(9), pp.1857-1872.

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Abstract Number: 0954

Non-canonical WNTA Promotes Cytoskeletal Rearrangement and Integrin Alpha V Clustering via JNK and ROCK to Control the Activation of Latent TGFβ

Thuong Trinh-Minh[1], Chih-Wei Chen[2], Cuong Tran Manh[1], yi-nan Li[1], Honglin Zhu[3], Debomita Chakraborty[4], Yun Zhang[1], Simon Rauber[5], Clara Dees[5], Christina Bergmann[6], Alexander Kreuter[7], Christiane Reuter[8], Florian Groeber-Becker[8], Beate Eckes[9], Oliver Distler[10], Andreas Ramming[11], Georg Schett[12] and Joerg Distler[1], [1]Clinic for Rheumatology University Hospital Düsseldorf, Medical Faculty of Heinrich Heine University, Düsseldorf, Germany; Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich Heine University, Düsseldorf, Germany, [2]3 Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany. 4 Deutsches Zentrum für Immuntherapie, Friedrich Alexander University Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany., Erlangen, Germany, [3]3 Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany. 4 Deutsches Zentrum für Immuntherapie, Friedrich Alexander University Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany. 5 Department of Rheumatology, Xiangya Hospital, Central South University, Changsha, China, [4]3 Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany. 4 Deutsches Zentrum für Immuntherapie, Friedrich Alexander University Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany, [5]3 Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany. 4 Deutsches Zentrum für Immuntherapie, Friedrich Alexander University Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany., Erlangen, Germany, [6]Department Internal Medicine, University Hospital Erlangen, Germany, Erlangen, Germany, [7]Clinic for Dermatology, Venereology and Allergology, HELIOS St. Elisabeth Clinic, Oberhausen, Germany, [8]Translational Center for Regenerative Therapies, Fraunhofer Institute for Silicate Research (ISC) Würzburg, Würzburg, Germany, [9]Translational Matrix Biology, University of Cologne, Cologne, Germany. 9 Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD), University of Cologne, Köln, Germany, [10]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [11]Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany; Deutsches Zentrum für Immuntherapie, Friedrich Alexander University Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany, [12]Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany

SESSION INFORMATION

Session Date: Monday, November 13, 2023

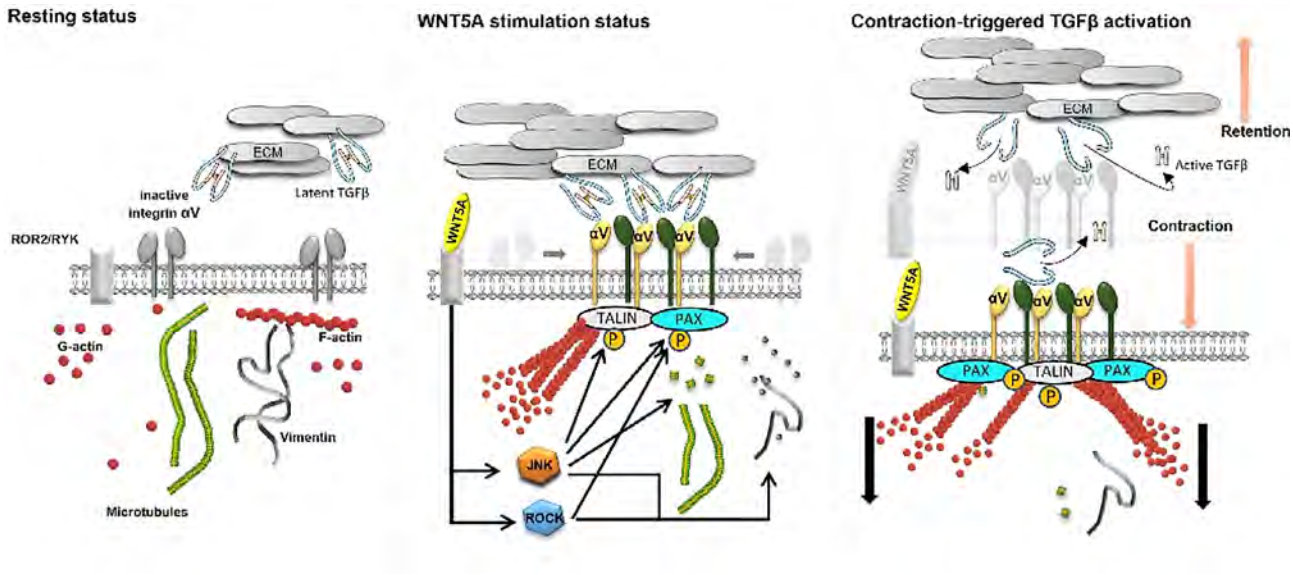
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a chronic autoimmune disorder with vasculopathy, inflammation, and fibrosis of the skin and organs. Fibrosis is caused by the abnormal activation of latent transforming growth factor beta (TGFβ) by fibroblasts, resulting in excessive extracellular matrix and tissue damage. WNT5A is a non-canonical WNT ligand which significantly expresses higher in fibrotic diseases. We aimed to investigate the role of WNT5A and its downstream intracellular signaling and gene expression in fibroblast activation in SSc and other fibrotic diseases. We also tested the effect of blocking WNT5A downstream targets on latent TGFβ activation and fibrosis.

Methods: We performed bulk RNA sequencing (RNAseq) of WNT5A-stimulated fibroblasts with or without pretreatment with inhibitors of potential downstream mediators of WNT5A (small molecule inhibitors against JNK, ROCK, integrin alpha V - ITGAV, TGFβR1 and actin polymerization). To confirm the findings, we treated WNT5A-overexpressing mice with those inhibitors. We quantified the active TGFβ level in vitro and in vivo by transformed mink lung epithelial cells assays. The



WNT5A induces JNK and ROCK to promote coordinated cytoskeletal remodeling that drives ITGAV-dependent activation of latent TGFβ in fibrotic disorders

contraction force and cellular stiffness of WNT5A-stimulated fibroblasts were analyzed by 3D microtissue assays and magnetic tweezers. Formation of focal adhesions (FAs) and cytoskeleton rearrangement were evaluated by Western blot, IF staining, and live-cell imaging.

Results: 38% of DEGs of a cohort of patients with early, diffuse-cutaneous SSc (PRESS[1]) matched the genes regulated by WNT5A in cultured fibroblasts. Ubiquitous knockout of WNT5A or fibroblast-specific knockout of WNT5A are protected from experimental fibrosis. RNAseq of fibroblasts treated with respective inhibitors revealed 75% of the WNT5A-regulated DEGs were regulated by JNK- and ROCK-dependent manner. Functional analysis of the DEGs indicated that WNT5A regulates TGFβ signaling, FAs, integrin activation and cytoskeleton organization. Indeed, WNT5A induced the formation of FAs with increased levels of p-Talin and p-Paxillin, ITGAV clustering and cytoskeletal rearrangement involving Vimentin, actin filaments, and microtubules. All of these changes were dependent on the activation of latent TGFβ, which was strongly induced by WNT5A in cultured fibroblasts. Pharmacological inhibition of JNK, ROCK, TGFβR1, ITGAV, or actin polymerization blocked the activation of latent TGFβ, reduced cellular stiffening, prevented integrin activation, and in particular reduced fibroblast-to-myofibroblast transition and collagen deposition in cultured fibroblasts. Moreover, Pharmacological inhibition of the downstream mediators also reduced the levels of active TGFβ and fibrotic remodeling of skin in mice overexpressing WNT5A.

Conclusion: We demonstrate that WNT5A/JNK/ROCK signaling axis regulates the activation of latent TGFβ by induction of cytoskeletal rearrangement, cellular tension forces and clustering of ITGAV. Blocking of WNT5A or its downstream pathways prevents the aberrant activation of latent TGFβ in experimental fibrosis, prevents fibroblast-to-myofibroblast transition and tissue fibrosis. Targeting of WNT5A may thus offer potential for novel antifibrotic therapies.

Disclosure: T. Trinh-Minh: None; **C. Chen**: None; **C. Tran Manh**: None; **y. Li**: None; **H. Zhu**: None; **D. Chakraborty**: None; **Y. Zhang**: None; **S. Rauber**: None; **C. Dees**: None; **C. Bergmann**: Boehringer-Ingelheim, 2, 5, Janssen, 2; **A. Kreuter**: None; **C. Reuter**: None; **F. Groeber-Becker**: None; **B. Eckes**: None; **O. Distler**: 4P-Pharma, 2, 5, 6, AbbVie, 2, 5, 6, Acceleron, 2, 5, 6, Alcimed, 2, 5, 6, Altavant Sciences, 2, 5, 6, Amgen, 2, 5, 6, AnaMar, 2, 5, 6, Arxx, 2, 5, 6, AstraZeneca, 2, 5, 6, Bayer, 2, 5, 6, Blade Therapeutics, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Citus AG, 12, Co-Founder, Corbus Pharmaceuticals, 2, 5, 6, CSL Behring, 2, 5, 6, Galapagos, 2, 5, 6, Galderma, 2, 5, 6, Glenmark,

2, 5, 6, Gossamer, 2, 5, 6, Horizon Therapeutics, 2, 5, 6, Janssen, 2, 5, 6, Kymera, 2, 5, 6, Lupin, 2, 5, 6, Medscape, 2, 5, 6, Miltenyi Biotec, 2, 5, 6, Mitsubishi Tanabe, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143), 10, Prometheus Biosciences, 2, 5, 6, Redx Pharma, 2, 5, 6, Roivant, 2, 5, 6, Topadur, 2, 5, 6; **A. Ramming**: None; **G. Schett**: None; **J. Distler**: 4D Science and FibroCure, 8, 11, AbbVie, Active Biotech, Anamar, ARXX, AstraZeneca, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, Genentech, GSK, Inventiva, Janssen, Novarti, 2, Anamar, Argenx, ARXX, BMS, Bayer Pharma, Boehringer Ingelheim, Cantargia, Celgene, CSL Behring, Galapagos, GSK, 5, Inventiva, Kiniksa, Lassen, Sanofi-Aventis, RedX, UCB, 5.

Abstract Number: 0955

GRB2 Serves as a Viable Target Against Skin Fibrosis in Systemic Sclerosis by Regulating Endothelial Cell Apoptosis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Sclerosis (SSc) is an autoimmune disease characterized by vascular and immune system dysfunction, along with tissue fibrosis. Vascular damage has been recognized as the pathological basis of SSc, but there are no medicines approved by FDA for SSc early vasculopathy treatment for the underlying mechanism remains elusive. Our previous study found *GRB2* was downregulated by salvianolic acid B, a small molecule drug that attenuated skin fibrosis of SSc by protecting endothelial cells from oxidative stress injury. Here we aim to investigate the role of GRB2 in the vasculopathy of SSc.

Methods: The microarray data of SSc skin biopsies in Caucasians were obtained from the Gene Expression Omnibus (GEO) database (GSE95065). The expression of *GRB2* was further detected in Chinese SSc patients (n = 20) and healthy controls (n = 20). To further explore the possible effects of Grb2 on skin fibrosis *in vivo*, Grb2 siRNA was used to lower the expression of Grb2 in the BLM-induced skin fibrosis mouse model. The apoptosis of EA.hy926 endothelial cells was induced by H_2O_2 and apoptosis ratio was measured by flow cytometric. Transcriptome and phosphoproteomic analyses in EA.hy926 cells transfected with NC and GRB2 siRNA were performed to explore the GRB2 regulated pathway.

Results: The expression of *GRB2* was significantly enhanced in SSc patient skin, 1.51-fold in Caucasians and 1.40-fold in Chinese. The immunohistochemical staining showed that there were more GRB2 positive cells in SSc patients than in normal controls, and double immunofluorescence staining showed the endothelial cells of SSc patient's skin highly expressed GRB2 (Figure 1). Then the *in vivo* study revealed that *in situ* apoptosis of endothelium increased under the treatment of BLM, while interfering Grb2 could reduce endothelial cell apoptosis, also proved by the protein expression of cleaved caspase-3 (Figure 2). The *in vitro* study showed that decreased GRB2 expression level could up-regulate tight junction related genes expression and inhibit apoptosis to protect endothelial cells from H_2O_2-induced hyperpermeability (Figure 3). Moreover, both transcriptome and phosphoproteomic analysis suggested the focal adhesion pathway was enriched in GRB2 siRNA transfected endothelial cells (Figure 3).

Conclusion: Our results demonstrated GRB2 is highly expressed in endothelial cells of SSc skin, and inhibiting GRB2 could effectively attenuate endothelial cell apoptosis and BLM-induced skin fibrosis. GRB2 may regulate focal adhesion and VEGF signaling pathways to induce apoptosis of endothelial cells. GRB2 is expected to be a new therapeutic target for SSc.

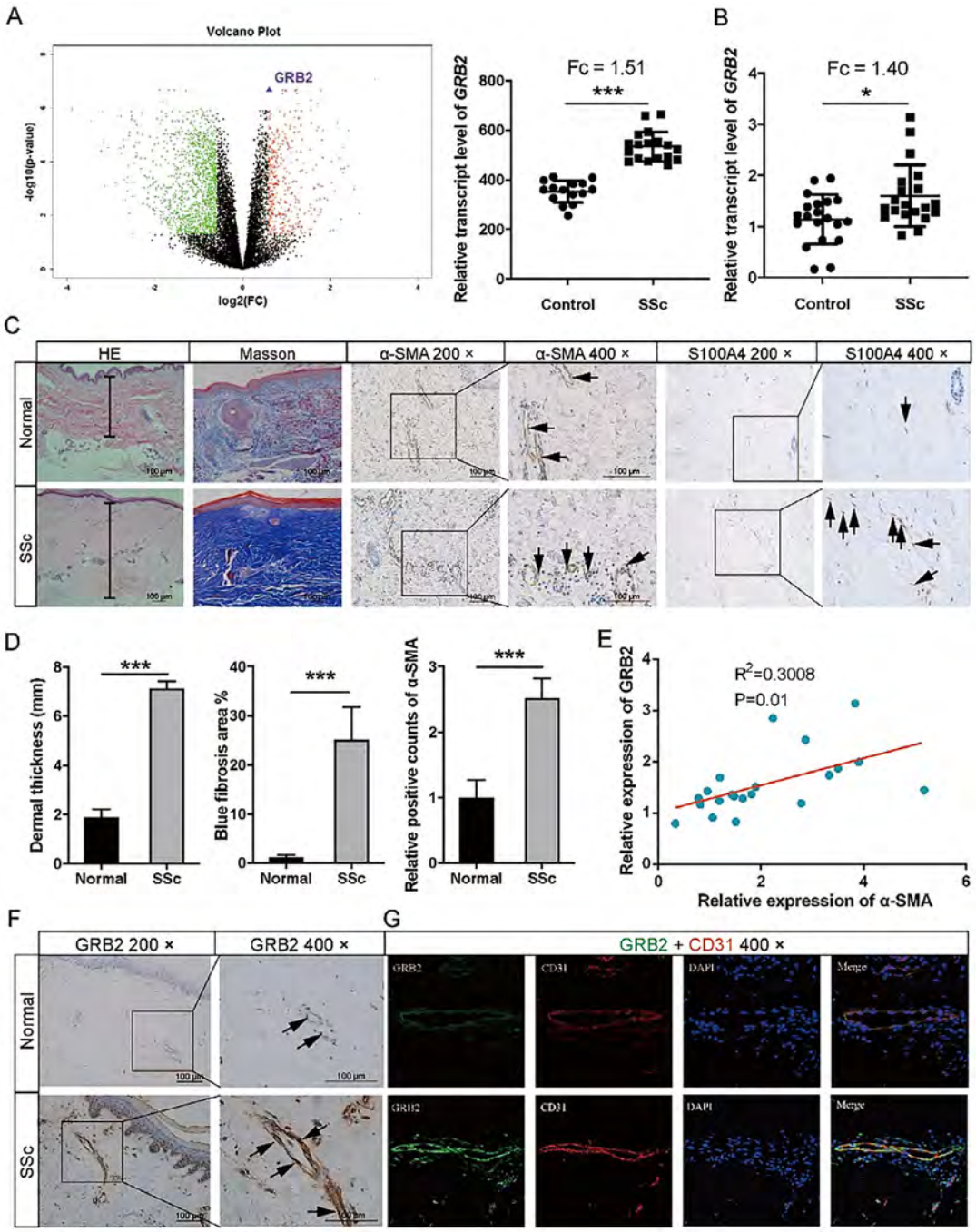


Figure 1. Expression of GRB2 was increased in the skin lesions of SSc patients. (A) Left: The volcano plot of differential expression genes between normal and SSc. Right: Relative transcription levels of GAB1 in the skin lesions from the GEO database. (B) Relative transcription levels of GAB1 in the Chinese skin lesions. (C) HE, Masson's staining, and IHC staining for healthy control and SSc patients. Black arrows indicate α-SMA/S100A4 positive staining cells. (D) The left plot shows dermal thickness calculated by measuring the distance between the dermal-epidermal junction and the dermal–subcutaneous fat junction. The middle plot shows the blue fibrosis area of Masson's staining for healthy control and SSc patients. The right plot shows the relative positive counts of α-SMA of IHC staining for healthy control and SSc patients. (E) The association of GRB2 and α-SMA expression levels were analyzed. (F) IHC staining for GRB2 in the skin of healthy control and SSc patients. Black arrows indicate GRB2 positive staining cells. (G) GRB2 and CD31 in the skin were labeled by double immunofluorescence staining, and the cell nucleus was stained with DAPI. Data are presented as mean ± SD in two groups and compared by t-test. *P < 0.05, *** P < 0.001.

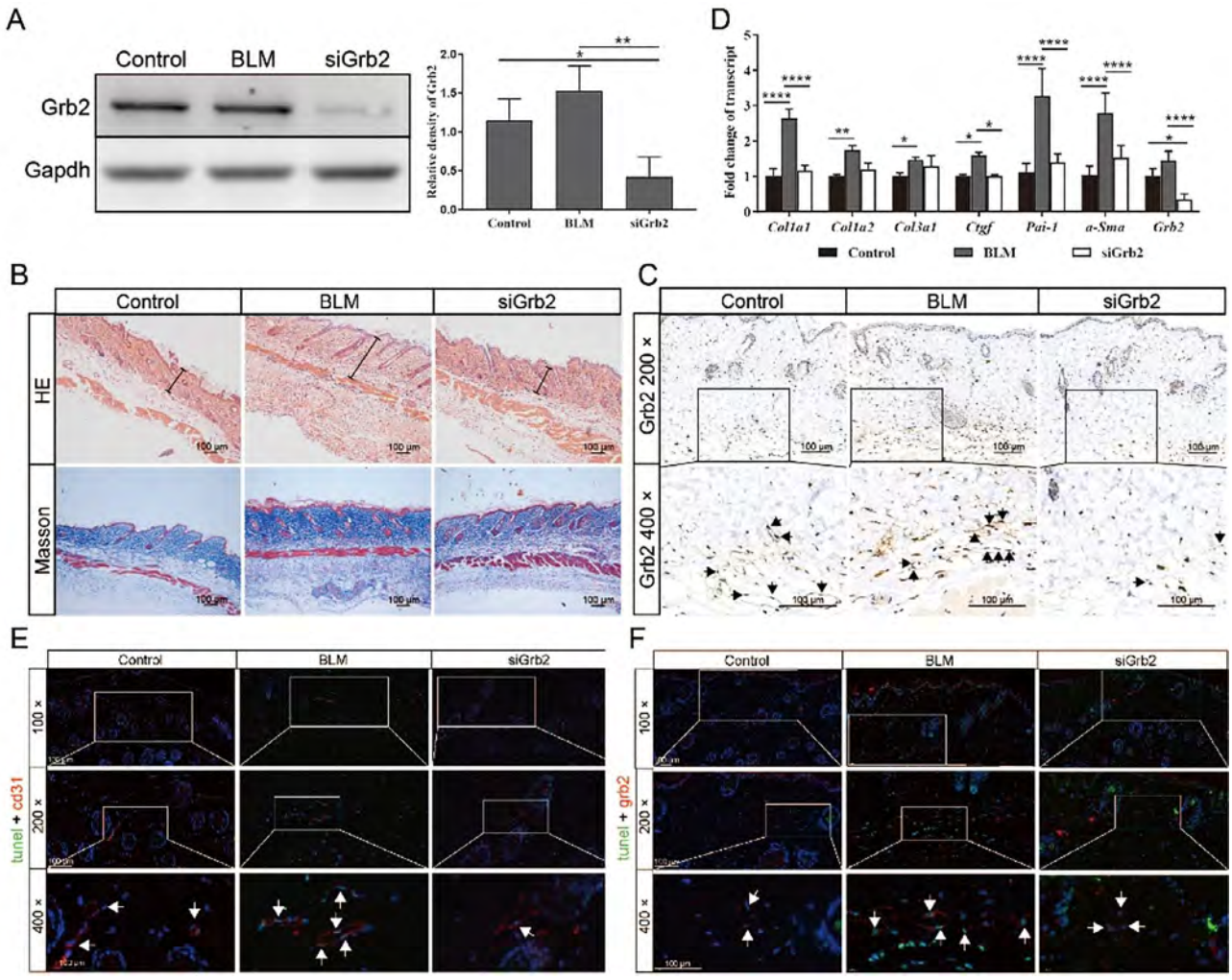


Figure 2. Grb2 knockdown alleviated skin fibrosis and endothelial apoptosis in BLM-induced SSc fibrosis model. (A) Grb2 protein expression level in the dorsal skin of mice was determined by western blot analysis and analyzed by ImageJ. (B) IHC staining for Grb2 in the mouse skin of different groups. The black arrows indicate Grb2-positive staining cells. (C) IHC staining of the dorsal skin of mice in different groups showed the relative positive number of Grb2. (D) Relative transcription levels of Grb2 and fibrotic genes in mouse skin were measured by real-time RT-PCR. (E) Double immunofluorescence staining of tunel and cd31 in normal, BLM, and siGrb2 groups. The white arrows indicate tunel-cd31-positive staining cells. (F) Double immunofluorescence staining of tunel and grb2 in different groups. Arrows indicate the positive cells. Data are presented as mean ± SD of three samples and compared with one-way ANOVA; *P < 0.05, ** P < 0.01, *** P < 0.001.

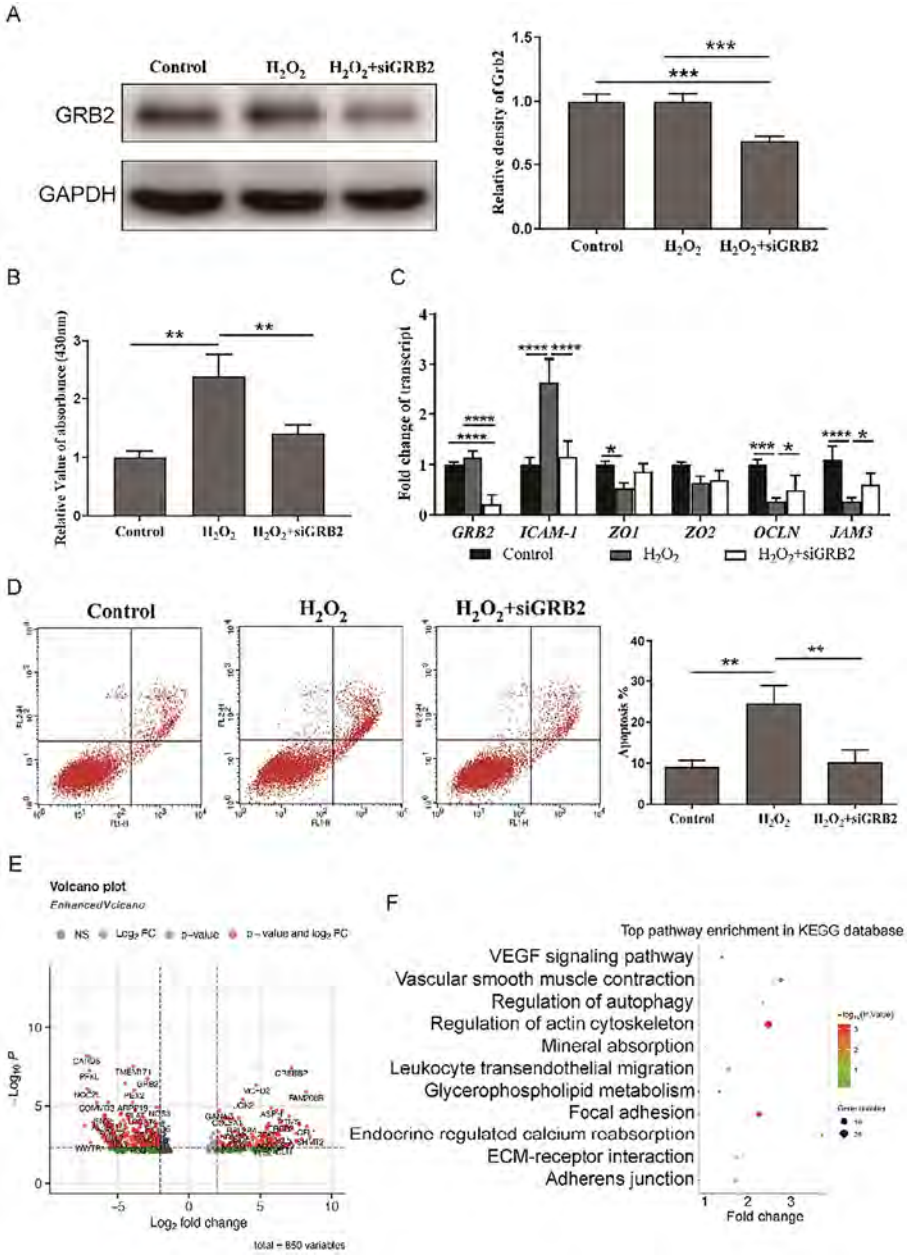


Figure 3. GRB2 siRNA transfection protected EA.hy926 endothelial cells from H2O2-induced hyperpermeability and the transcriptome analysis. (A) The protein level of GRB2 was determined by western blotting and quantified by ImageJ. (B) Effects of siGRB2 on H2O2-induced endothelial permeability in EA.hy926 cells detected by cell permeability assay. (C) The relative mRNA levels of ICAM1, ZO1, ZO2, OCLN, and JAM3 were detected by real-time RT-PCR in different groups. (D) The ratio of apoptosis detected by flow cytometry in the cells of the control, H2O2, and H2O2 + siGRB2 groups. The column plot shows the apoptosis ratio in the different groups. (E) The Volcano plot of differentially expressed genes (DEGs) in NC or GRB2 siRNA transfected EA.hy926 cells. (F) KEGG pathway analysis of DEGs. Data are presented as means ± SD of three samples and compared with one-way ANOVA; *P < 0.05, ** P < 0.01, *** P < 0.001.

Disclosure: Y. Huang: None; **H. Zhao**: None; **X. Shi**: None; **J. Liu**: None; **J. Lin**: None; **Q. Ma**: None; **S. Jiang**: None; **W. Pu**: None; **Y. Ma**: None; **J. Liu**: None; **W. Wu**: None; **J. Wang**: None; **Q. Liu**: None.

Abstract Number: 0956

Effects of B Cell Depletion by CD19-targeted CAR-T Cells in a Murine Model of Systemic Sclerosis

Jérôme Avouac[1], Anne Cauvet[2], Cindy Orvain[3], Morgane boulch[4], Philippe Bousso[4] and Yannick ALLANORE[5], [1]Service de Rhumatologie, Hôpital Cochin, AP-HP.Centre – Université Paris Cité, Paris, France, [2]INSERM U1016, Paris, France, [3]INSERM U1016, Paris, [4]Institut Pasteur, Paris, France, [5]Université Paris Cité, Paris, France

SESSION INFORMATION

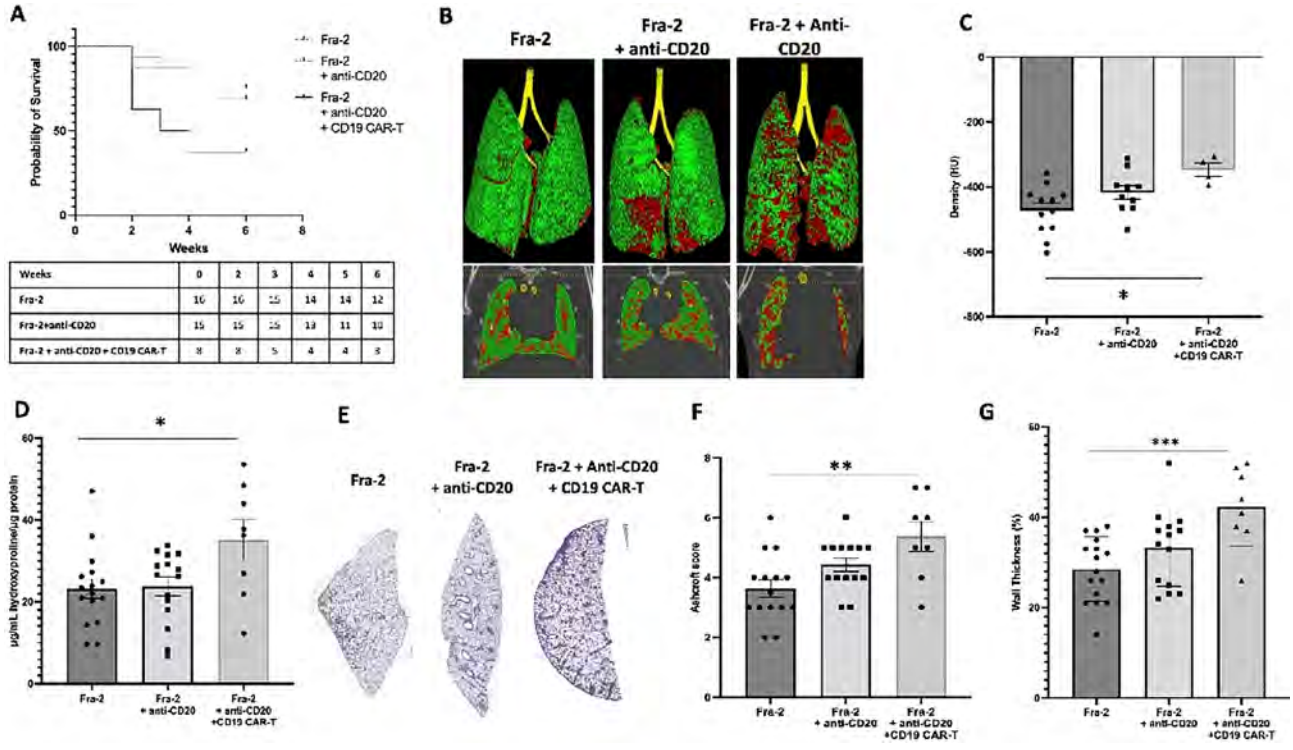
Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Chimeric antigen receptor (CAR)-T cells represent a potentially curative strategy for B cell malignancies. A first successful clinical experience has been recently reported in systemic lupus erythematosus, suggesting that CD19-targeted CAR-T cell transfer was feasible and tolerable. Since systemic sclerosis (SSc) and SLE are both severe diseases sharing B cell implication in their pathogenesis, we aimed at assessing the efficacy and tolerance of two B cell depletion strategies, including one with CD19-targeted CAR-T cells, in a preclinical model mimicking the severe lung damages observed in SSc.



Weeks	0	2	3	4	5	6
Fra-2	16	16	15	14	14	12
Fra-2+anti-CD20	15	15	15	13	11	10
Fra-2 + anti-CD20 + CD19 CAR-T	8	8	5	4	4	4

Figure 1: Effects of B cell depletion by anti-CD20 mAb in association or not with CD19-targeted CAR-T cells in Fra-2 Tg mice A, Survival curves of Fra-2 mice after anti-CD20 mAb and CD19-targeted CAR-T cell infusion. Significance was determined by log rank (Mantel-Cox; p=0.031). B, Representative pictures of micro-computed tomography. C, Y-axis shows the lung density at micro-computed tomography. D, Y-axis shows the content of collagen in a lung fragment (µg) evaluated by Sircol assay. E, Representative HES 4-µm lung sections (magnification × 8). F, Y-axis shows the Ashcroft histological score. G, Y-axis shows the right ventricular systolic pressure (RVSP). All data are shown as the mean ± SEM. * p<0.05, ** p<0.01, ***p<0.001 determined by one-way analysis of variance with Tukey's post hoc test.

Methods: B cell depletion strategies were evaluated in the Fra-2 transgenic (Tg) mouse model. We considered a first group of 16 untreated mice, a second group of 15 mice receiving a single intravenous (IV) dose (50 mg) of anti-CD20 monoclonal antibody (mAb) at day 1 and a third group of 8 mice receiving 50 mg anti-CD20 mAb IV at day 1 followed by the IV injection of $20*10^6$CD19-targeted CAR-T cells at day 3. After 6 weeks of clinical evaluation, different validated markers of inflammation, lung fibrosis and pulmonary vascular remodeling were assessed.

Results: Following treatment with anti-CD20 mAb, CD19 expression was significantly decreased in peripheral blood and lesional lungs of Fra-2 Tg mice by 59% ($p< 0.001$) and 40% ($p=0.019$), respectively, compared to control Fra-2. B cell depletion was even more pronounced in mice treated with CD19-targeted CAR-T cells: CD19 expression was decreased in peripheral blood and lungs of Fra-2 Tg mice by 92% ($p< 0.001$) and 85% ($p< 0.001$), respectively, compared to control Fra-2. CAR-T cell infusion worsened clinical score and increased mortality in Fra-2 Tg mice (**Figure 1A**). In line with the above findings, mice receiving CD19-targeted CAR-T cells displayed a significant increase in lung density (mean difference of 55 ±28 Hounsfield Units, p=0.038) (**Figure 1B-C**) and a marked reduction of functional residual capacity(mean difference of 25±9%, p=0.041) as compared to control Fra-2 when assessed by chest micro-CT imaging. CAR-T cell infusion significantly increased lung collagen content (mean difference of 11.93±4.44 mg/mL, p=0.020) (**Figure 1D**), histological fibrosis score (mean difference 1.74±0.48, p=0.002) (**Figure 1E-F**) and right ventricular systolic pressure (mean difference 8.52 ±2.70 mmHg, p=0.013) (**Figure 1G**). CAR-T cells accumulated in lesional lungs and promoted T-cell activation, with a significant increase of CD4+ effector memory T cells and the fraction of CD69 and PD1-expressing cells within the CD4+ and CD8+ subsets. Moreover, in the lung of CD19-targeted CAR-T cell-treated Fra-2 Tg mice. Moreover, the levels of inflammatory cytokines IL6, TNF-a and IFNg were markedly elevated in lesional lungs of mice treated with CAR-T cells. Treatment with anti-CD20 mAb in monotherapy had no impact on lung inflammation-driven fibrosis and pulmonary hypertension.

Conclusion: B-cell therapies failed to show efficacy in the Fra2 transgenic mice. The exacerbated Fra-2 lung inflammatory burden stimulated accumulation and expansion of activated CD19-targeted CAR-T cells, secondarily inducing T-cell activation and systemic inflammation, finally leading to disease worsening.

Disclosure: J. Avouac: AbbVie, 6, AstraZeneca, 6, Biogen, 6, BMS, 5, 6, Fresenius Kabi, 5, 6, Galapagos, 5, 6, Janssen, 6, Lilly, 6, Medac, 6, MSD, 6, Nordic Pharma, 6, Novartis, 6, Novartis (Dreamer), 5, Pfizer, 6, Pfizer (Passerelle), 5, Roche-Chugai, 6, Sandoz, 6, Sanofi, 6; **A. Cauvet**: None; **C. Orvain**: None; **M. boulch**: None; **P. Bousso**: None; **Y. ALLANORE**: AbbVie/Abbott, 2, Alpine Immunoscience, 5, AstraZeneca, 2, Bayer, 2, Boehringer-Ingelheim, 2, Janssen, 2, Medsenic, 2, 5, Mylan, 2, OSE Immunotherapeutics, 5, Prometeus, 2, Roche, 2, Sanofi, 2.

Abstract Number: 0957

Rationale for Targeting Insulin-like Growth Factor Signalling in Systemic Sclerosis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies have shown that insulin like growth factor (IGF) pathways may promote extracellular matrix deposition and be upregulated in systemic sclerosis (SSc). Teprotumumab, a monoclonal antibody targeting IGF1 receptor (IGF1-R), is approved for treatment of thyroid eye disease and is being tested as a potential therapeutic in systemic sclerosis. This study explored levels of IGF ligand and receptor in serum of well characterised SSc patients and examined effects of teprotumumab on gene and protein expression in dermal explant fibroblasts from SSc or healthy control (HC) skin biopsies.

Methods: Serum levels of IGF1, IGF2 and IGF1-R were measured in SSc (n=63) and healthy controls (n=15) using commercial ELISA and levels compared across subset and organ based complication of SSc.Dermal fibroblasts from SSc (n=3) and healthy control (n=3) forearm skin biopsies were grown by explant culture and cell layer was analysed for key profibrotic proteins (alpha-SMA and pro(I)collagen) by western blot analysis and RNA analysis by quantitative PCR for alpha-SMA and

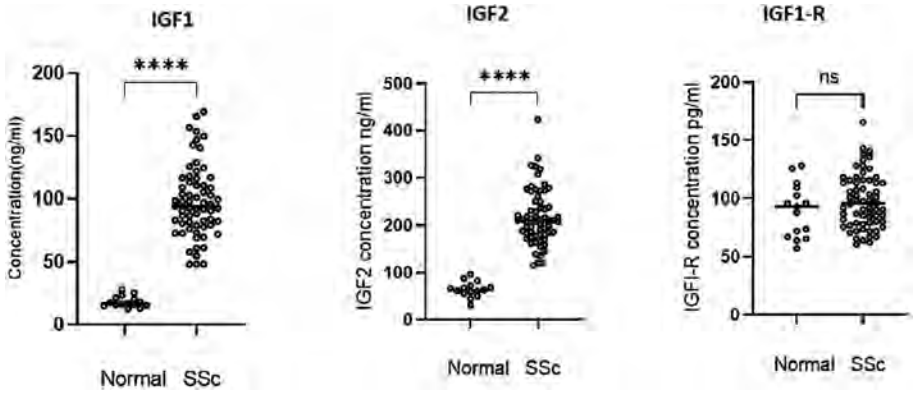


Figure 1 IGF ligand and receptor levels in SSc or control serum

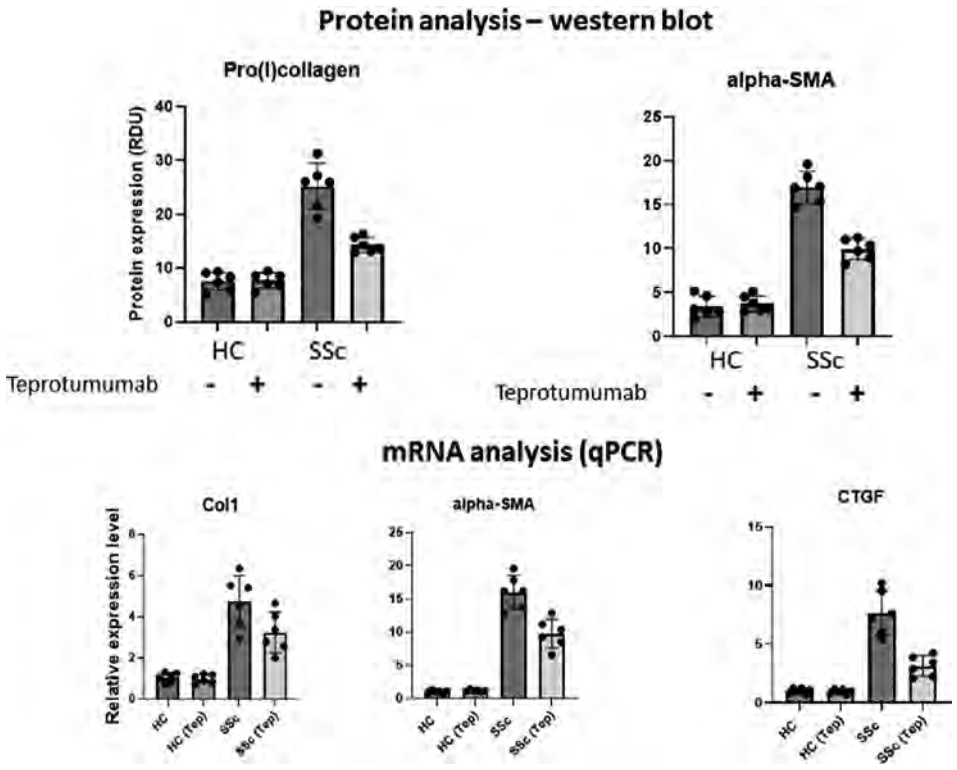


Figure 2 Effect of teprotumumab on protein and mRNA expression in SSc and HC fibroblasts

pro(I)collagen and connective tissue growth factor.For inhibition experiments, cells were pre-incubated overnight in the presence of teprotumumab (50 mg/ml).

Results: There was significant elevation in serum IGF1 in SSc compared with HC serum samples (mean[SD] ng/ml SSc 98.1 [28.4] versus HC 18.5[4.4], p< 0.0001) and IGF2 (SSc 217.6[57.9] versus HC 64.6[16.5], p< 0.0001) whereas serum IGF1-R levels were similar in both cohorts (**Figure 1**).Though elevated in SSc, no significant association was observed for major complications, including lung fibrosis and gut disease, and levels were similar for limited and diffuse skin subsets. SSc fibroblasts showed constitutive upregulation of profibrotic proteins (mean[SD] RDU Col1 SSc 25.2[4.2] vs. HC 7.6 [1.7] and alpha-SMA SSc16.9[1.8] vs. HC 3.4[1.2]) and genes compared with HC fibroblast strains (all p< 0.0001).The profibrotic phenotype in SSc fibroblasts was significantly attenuated by teprotumumab, with 43% reduction in pro(I)collagen and 41% reduction in alpha-SMA protein respectively, and similar qualitative effects on normalised mRNA levels. Teprotumumab did not significantly affect HC fibroblasts (**Figure 2**).

Conclusion: Elevated levels of IGF1 and IGF2 in SSc suggest that these proteins may be mediators or markers of pathobiology in vivo. Attenuation of hallmark profibrotic gene and protein signature in explant dermal SSc fibroblasts by teprotumumab is consistent with autocrine or paracrine activation of SSc fibroblasts by IGF1 or IGF2 via IGF1-R. Our findings are consistent with an antifibrotic effect and support clinical evaluation of teprotumumab as a possible therapy in SSc.

Disclosure: V. Ong: None; **S. Xu**: None; **L. Xue**: None; **B. Kumar**: horizon therapeutics, 3, 10; **C. Denton**: AbbVie, 2, Acceleron, 2, Arxx Therapeutics, 5, Bayer, 2, Boehringer-Ingelheim, 2, 6, Corbus, 2, 6, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Horizon Therapeutics, 2, Inventiva, 2, 5, Janssen, 6, Roche, 2, Sanofi, 2, Servier, 5.

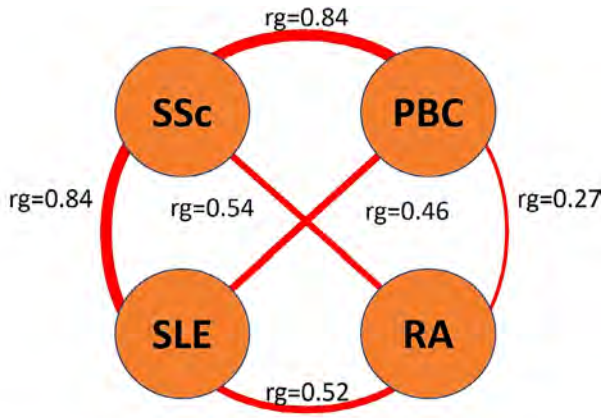
Abstract Number: 0958

Shared Genetic Susceptibility Between Systemic Sclerosis and Primary Biliary Cholangitis: Analyses from Genome-Wide Association Studies

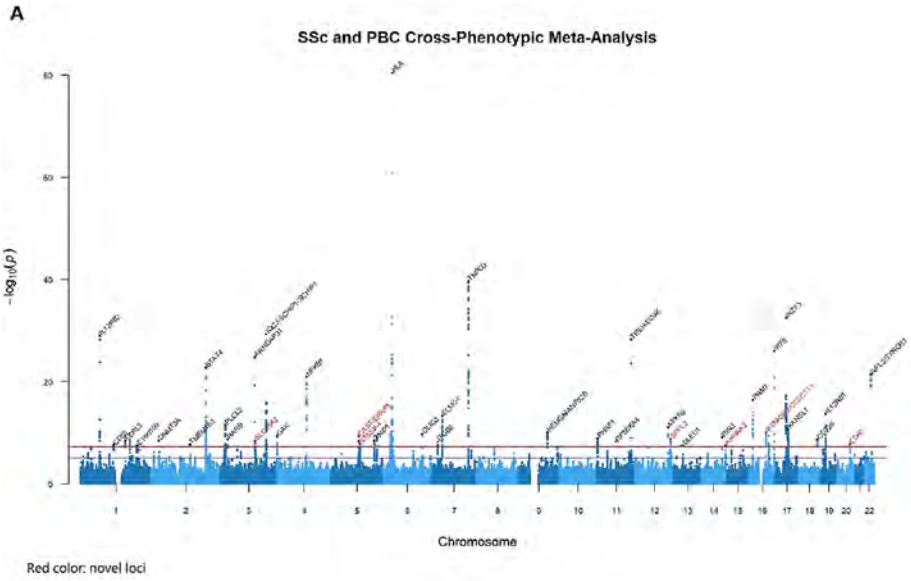
Yiming Luo[1], Atlas Khan[2], Gabriel Perreault[3], Lili Liu[2], Cue Hyunkyu Lee[4], Pravitt Gourh[5], Sydney Pomenti[3], Krzysztof Kiryluk[2] and Elana Bernstein[6], [1]Division of Rheumatology, Department of Medicine, Columbia University Irving Medical Center, New York, NY, [2]Division of Nephrology, Department of Medicine, Columbia University Irving Medical Center, New York, NY, [3]Division of Digestive and Liver Diseases, Department of Medicine, Columbia University Irving Medical Center, New York, NY, [4]Department of Biostatistics, Mailman School of Public Health, Columbia University Irving Medical Center, New York, NY, [5]National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [6]Division of Rheumatology, Department of Medicine, Vagelos College of Physicians and Surgeons, Columbia University Irving Medical Center, New York, NY

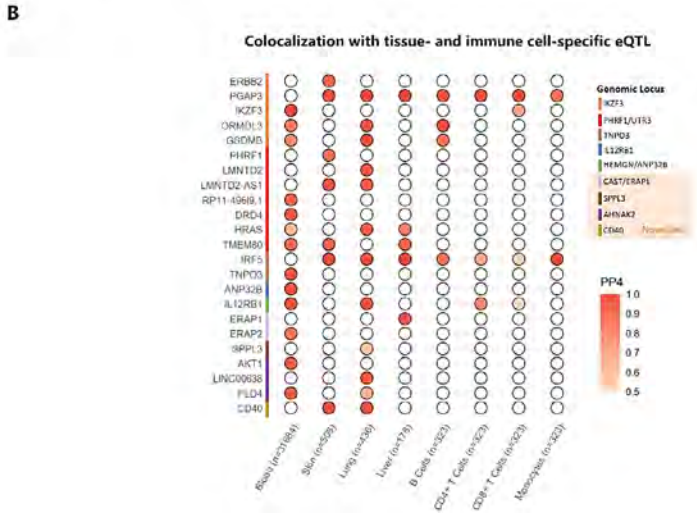
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a multi-system autoimmune disorder characterized by organ inflammation, fibrosis, and vasculopathy. Primary biliary cholangitis (PBC) is an autoimmune disorder involving inflammation and fibrosis of the intrahepatic biliary tract. An increased risk of PBC has been noted in patients with SSc. Our study aims to investigate the shared genetic susceptibility between the two disorders using data from genome-wide association studies (GWAS).

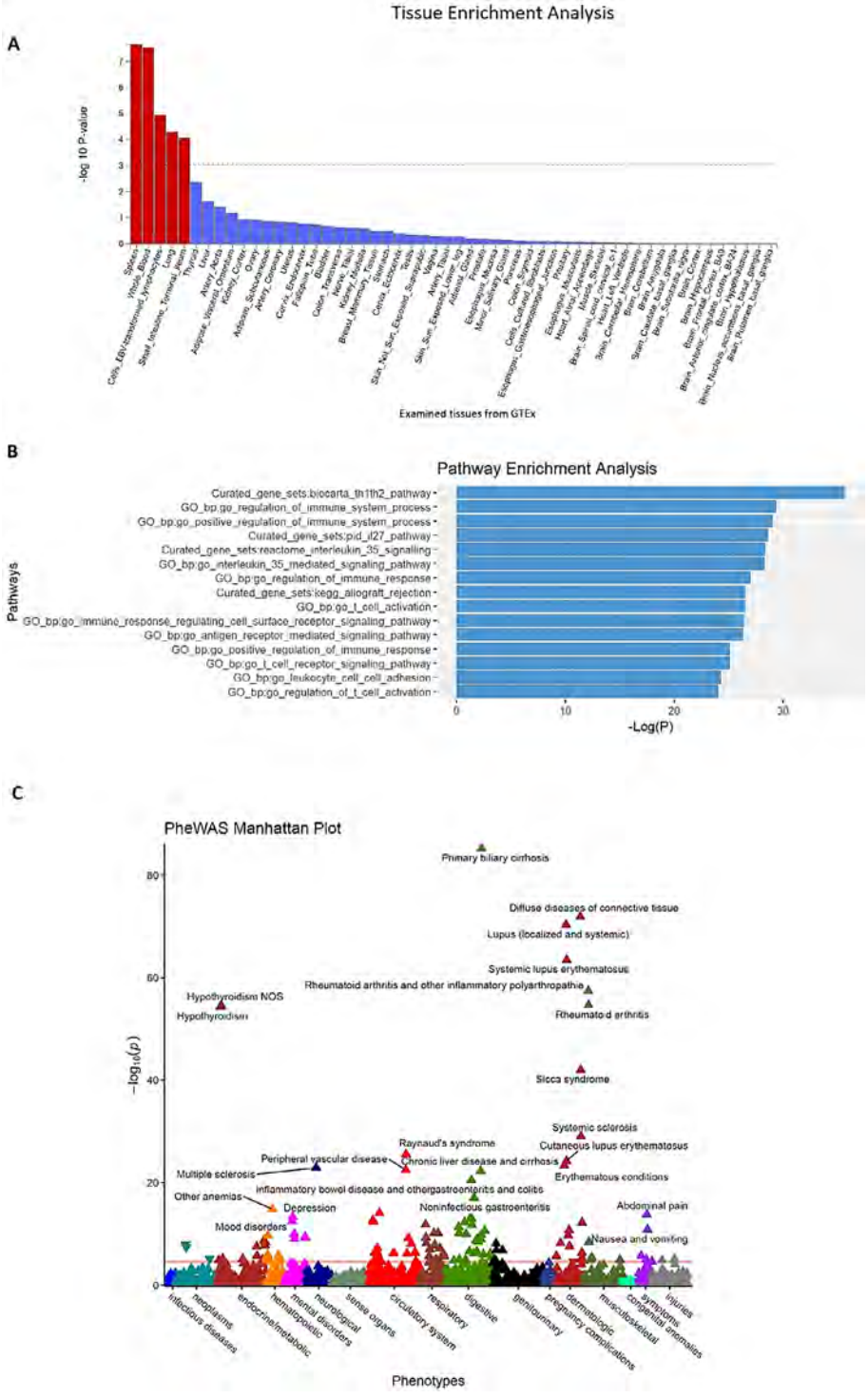


SSc: systemic sclerosis; PBC: primary biliary cholangitis; SLE: systemic lupus erythematosus; RA: rheumatoid arthritis; rg: genetic correlation





Methods: We obtained the GWAS summary statistics for SSc, PBC, rheumatoid arthritis (RA), and systemic lupus erythematosus (SLE) from the GWAS Catalog website. We performed a genetic correlation analysis using linkage disequilibrium score regression (excluding HLA region) and a cross-phenotype GWAS meta-analysis of SSc and PBC, followed by colocalization to investigate whether the pleiotropic signals were driven by shared causal variants. For genomic loci that were significant in the cross-phenotype meta-analysis and colocalized between SSc and PBC, we further performed colocalization with expression quantitative trait loci (eQTL) in relevant tissues and immune cells from the blood eQTLGen consortium, Genotype-Tissue Expression (GTEx), and Correlated Expression & Disease Association Research (CEDAR). Additionally,



we performed tissue and pathway enrichment analyses using MAGMA (Multi-marker Analysis of GenoMic Annotation) on the cross-phenotype meta-analysis statistics. Finally, we performed meta-phenome-wide association studies (meta-PheWAS) on the calculated polygenic risk score (PRS) of the SSc-PBC meta-analysis using data from the Electronic Medical Records and Genomics Network, All of Us and UK Biobank.

Results: The GWAS summary statistics included 9,095 cases and 17,584 controls for SSc and 8,021 cases and 16,489 controls for PBC. There was a strong genetic correlation between SSc and PBC (rg = 0.84, p = 1.7 x 10-6), in which the effect estimate was comparable to the genetic correlation between SSc and SLE (rg = 0.84, p = 1.6 x 10-15) (Figure 1). There were 44 non-HLA loci that reached genome-wide significance ($p < 5 \times 10\text{-}8$) in the cross-phenotype GWAS (Figure 2A). Evidence of shared causal variants between SSc and PBC was found in 13 out of the 44 significant loci in the colocalization analyses. Nine of the 13 loci showed evidence of shared causal variants with at least one expressed gene in the examined eQTL datasets. Among the 4 novel loci, eQTL colocalized transcripts included ERAP1, ERAP2, SPPL3, AKT1, PLD4, and CD40 (Figure 2B). These represented the predicted changes in gene expression resulting from the shared genomic signals between SSc and PBC. MAGMA prioritized multiple immune-related tissues and molecular pathways (Figures 3A and 3B). The meta-PheWAS revealed that the PRS calculated from the SSc-PBC meta-analysis was associated with multiple autoimmune phenotypes (Figure 3C).

Conclusion: We identified shared genetic susceptibility between SSc and PBC and prioritized several candidate genes by eQTL colocalization analyses. Our findings suggest that the genetic predisposition to SSc and PBC has pleiotropic effects across multiple autoimmune disorders.

Disclosure: Y. Luo: None; **A. Khan**: None; **G. Perreault**: None; **L. Liu**: None; **C. Lee**: None; **P. Gourh**: None; **S. Pomenti**: None; **K. Kiryluk**: None; **E. Bernstein**: Boehringer Ingelheim, 2, 5, Kadmon, 5, Pfizer, 5.

Abstract Number: 0959

Redirecting Macrophage Immunophenotype Attenuates Inflammation and Fibrotic Activation in Systemic Sclerosis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Sclerosis (SSc) is a rare autoimmune disease with multiple clinical and pathological manifestations including vascular involvement, immune activation, oxidative stress, and fibrosis. In prior work, we have shown that SSc macrophages (MØs) have a pro-fibrotic activation profile that is conferred, at least in part, by crosstalk with SSc dermal fibroblast-derived exosomes, resulting in upregulation of secreted mediators of fibrosis and inflammation. Because MØs are plastic, we hypothesized that reshaping the immunophenotype of SSc MØs would alleviate inflammation and fibrotic activation in SSc.

Methods: To redirect MØ activation, we used CDDO-methyl ester (CDDO-Me), a synthetic triterpenoid derived from oleanoic acid that targets multiple signaling pathways implicated in SSc pathogenesis, including NFkB, STAT3, and Nrf2. Initial studies were performed by incubating SSc MØs with 300 nM CDDO-Me, which we have shown in previous studies alters

MØ activation, for 24 hours.To assess effects on exosome-mediated activation, an established Transwell co-culture system was used. Dermal fibroblasts were isolated from SSc patients and healthy control (HC) donors following informed written consent and cultured in complete media supplemented with exosome-depleted fetal bovine serum (FBS) to isolate exosomes. Fibroblasts were stimulated with 5 ng/ml TGF-b for 24 hours prior to exosome harvest. Exosomes were harvested from cell-free supernatants followed by quantification and characterization by immunoblot and NanoSight NS300 tracking analysis. HC monocytes were differentiated into MØs in followed by activation with SSc fibroblast-derived exosome (SSc FB-Exo) in RPMI/exosome-depleted FBS for additional 2 days. After MØ activation, SSc fibroblasts were placed into Transwell inserts and 300 nM CDDO-Me was added to cultures. MØs and fibroblasts were evaluated using flow cytometry, qRT-PCR, and multiplex.

Results: Consistent with prior reports**,** SSc MØs upregulated expression of IL-10, IL-6, IL-1b, and CCL2 compared with HC MØs. Treatment with CDDO-Me resulted in significant attenuation of these inflammatory and fibrotic mediators.CDDO-Me induced activation of Nrf2 signaling in SSc MØs, as evidenced by increased expression of HO-1 and KEAP1. Surface expression of CD163, CD206, and HLA-DR and pro-fibrotic mediator production, including CCL2, from SSc FB-Exo activated MØs was inhibited by incubation with CDDO-Me. In Transwell experiments, SSc fibroblasts co-cultured with CDDO-Me-treated SSc FB-Exo activated MØs showed decreased expression of fibrosis-related genes, including FN1 and α-SMA.

Conclusion: In this work, we demonstrated that CDDO-Me reshapes the pro-fibrotic immunophenotype of SSc activated MØs, leading to a decrease in release of cytokines implicated in SSc pathogenesis and attenuated SSc fibroblast activation. CDDO-Me targets multiple signaling pathways including oxidative stress and inflammation. Our results suggest CDDO-Me may have therapeutic utility in the reduction of oxidative stress, inflammation, and fibrosis associated with SSc.

Disclosure: H. Yang: None; **R. Bhandari**: None; **S. Han**: None; **C. Park**: None; **C. Wang**: None; **E. Morris**: None; **M. Whitfield**: Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 2, 5, Celdara Medical, 2, 5, 12, Scientific Founder; **P. Pioli**: Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 2, 5, Celdara Medical LLC, 2, 5, Pfizer, 5.

Abstract Number: 0960

MiR-3606-3p Alleviates Skin Fibrosis by Suppressing Fibroblast Inflammation and Migration via Inhibiting GAB1 and ITGAV

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) and keloid are typical skin fibrotic diseases with unclear epigenetic mechanisms and clinical targets. As an important epigenetic regulatory factor, microRNAs play an important role in the occurrence and development of fibrosis in recent studies. This study aimed to assess the role of miR-3606-3p in skin fibrosis and the therapeutic potential.

Methods: The levels of miR-3606-3p were detected in SSc and keloid patients by qPCR and in situ hybridization. RNA-seq, in silico software and luciferase were performed to investigate the targets of miR-3606-3p. The effects of miR-3606-3p, GAB1 and ITGAV on fibroblast fibrogenesis, inflammation and migration were assessed in primary dermal fibroblasts by

qPCR, western blotting, wound healing scratch assay. Histology, immunofluorescence analysis and in vivo imaging techniques were used to evaluate the effect of miR-3606-3p on alleviating skin fibrosis in keloid-bearing mice.

Results: MiR-3606-3p was reduced in the skin tissues and fibroblasts from both SSc and keloid patients and negatively correlated with disease severity. RNA-seq analysis and in silico prediction indicated GRB2 associated binding protein 1 (*GAB1*) and integrin subunit alpha V (*ITGAV*) were potential targets of miR-3606-3p. We then found that miR-3606-3p downregulated both *GAB1* and *ITGAV* by directly targeting their 3′-UTRs, and further reduced p-AKT and p-ERK activities to inhibit collagen synthesis and NF-κB induced fibroblast inflammation. Furthermore, miR-3606-3p inhibited fibroblast migration in primary fibroblasts and keloid-bearing nude miceby wound healing scratch assay and *in vivo*imaging techniques respectively. In contrast, GAB1 and ITGAV were upregulated in SSc and keloid patients, and siRNA-mediated *GAB1* or

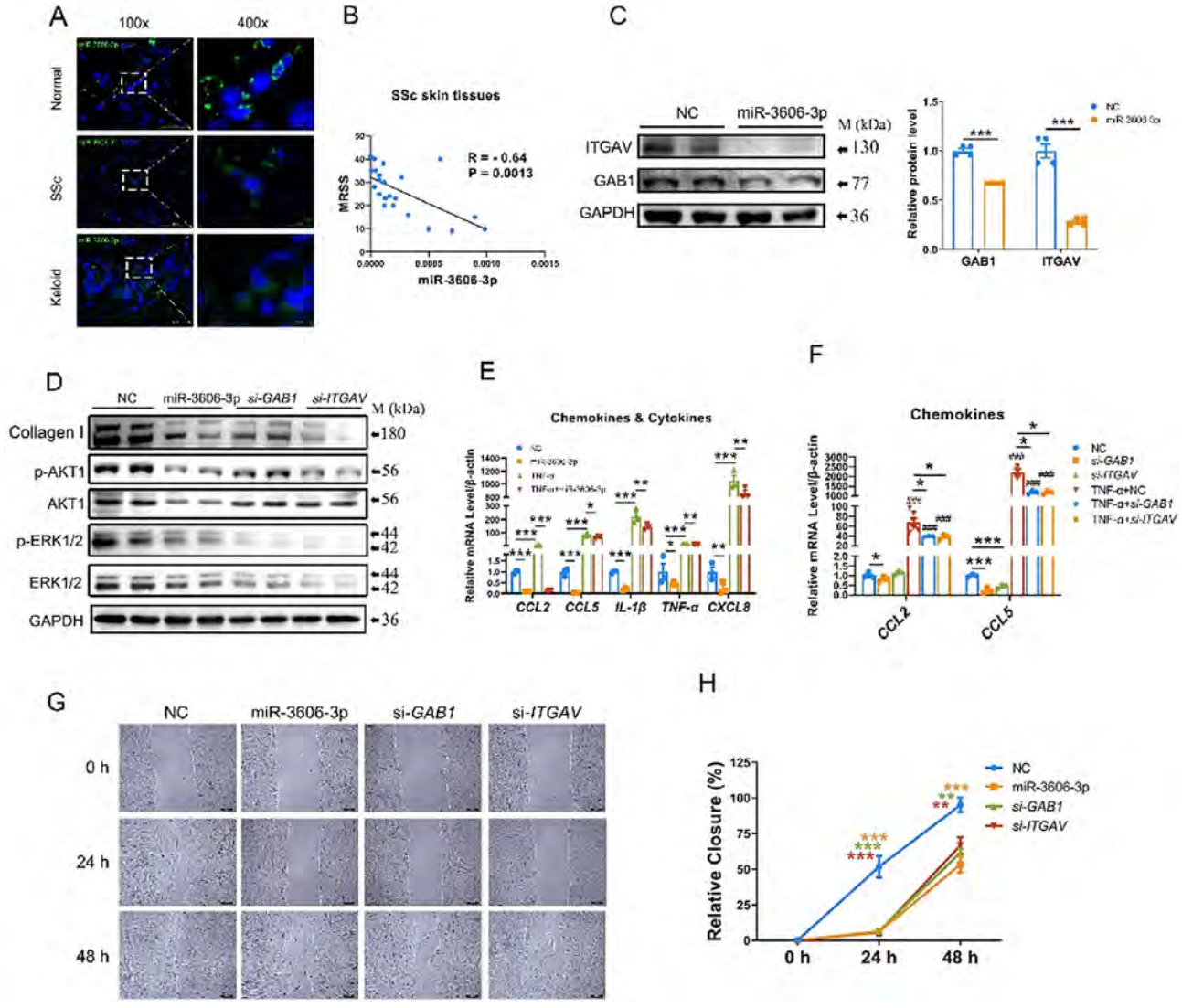


Figure 1. miR-3606-3p decreased in fibrosis skin tissue, while upregulating miR-3606-3p or inhibiting GAB1 and ITGAV supressed collagen production, inflammation and cell migration. (A) miR-3606-3p decreased in fibrosis skin tissue by in situ hybridization. (B) The relationship between MRSS and miR-3606-3p in SSc skin tissues. (C) miR-3606-3p inhibited GAB1 and ITGAV by western blotting. (D) Downregulation of type I collagen, p-AKT, AKT, p-ERK1/2, and ERK1/2 levels in SSc primary fibroblast with NC, miR-3606-3p mimics, si-GAB1 and si-ITGAV. (E) Downregulated chemokines and cytokines in miR-3606-3p overexpressing and TNF-α treated fibroblasts. (F) The effects of GAB1 siRNA and ITGAV siRNA on CCL2 and CCL5 expression in fibroblasts with or without TNF-α treatment. (G) Cell migration assay results by morphology in primary fibroblast with miR-3606-3p overexpression or GAB1 knockdown or ITGAV knockdown. N=3. (H) Relative closure distance of cell migration in fibroblasts with miR-3606-3p overexpression or GAB1 knockdown or ITGAV knockdown. N=3. *P < 0.05; **P < 0.01; ***P < 0.001.

ITGAV knockdown replicated the phenotypes observed in miR-3606-3p-overexpressing fibroblasts, including inflammation, migration and fibrogenesis (Figure 1). Finally, by constructing the humanized mouse model of transplanted keloid graft, we found that miR-3606-3p treatment inhibits GAB1 and ITGAV leading to significantly alleviate skin fibrosis (Figure 2).

Conclusion: Our results indicated miR-3606-3p inhibits ECM deposition, inflammation, and migration of fibroblasts by downregulating GAB1 and ITGAV. miR-3606-3p-enhancing strategies may have beneficial effects on skin fibrosis through lowing p-AKT/p-ERK activity.

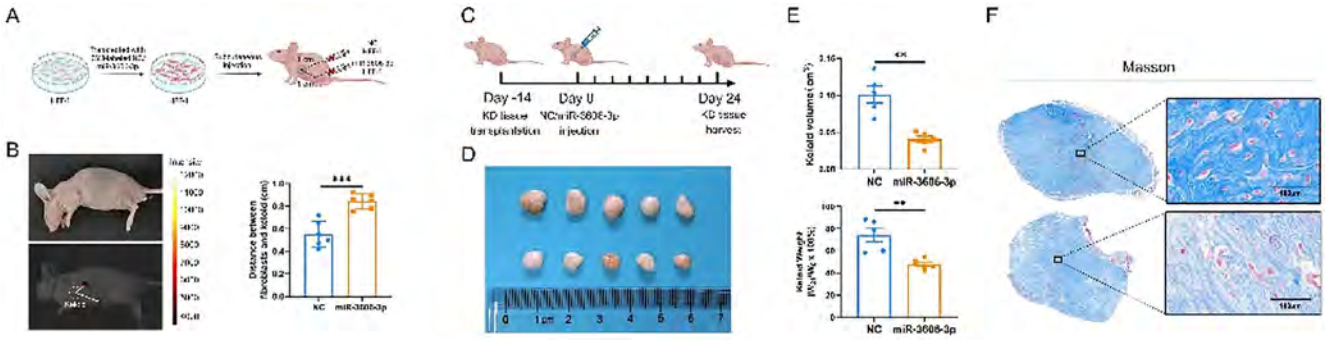
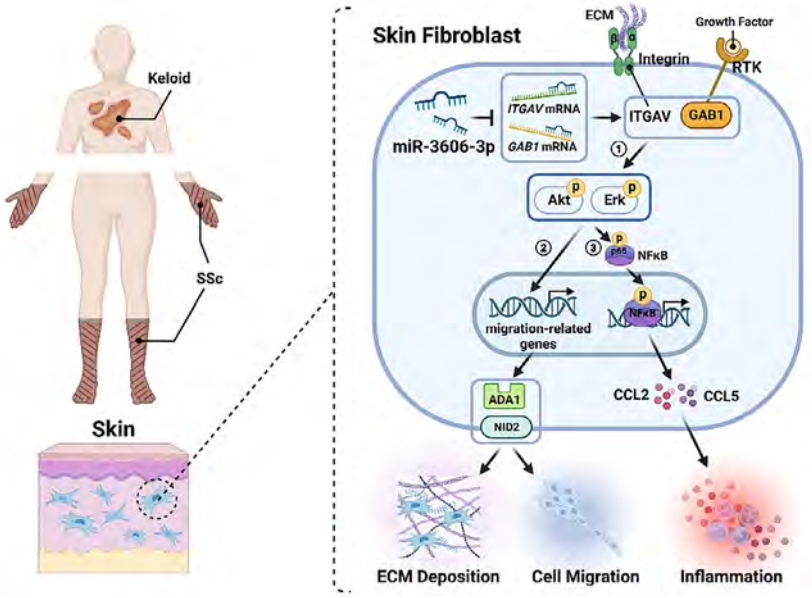


Figure 2. miR-3606-3p treatment inhibits migration of fibroblasts and alleviates skin fibrosis in keloid-bearing mice. (A) Diagram and (B) live imaging of assessing cell migration rate in vivo. N=6. (C) The construction of a keloid-bearing mouse model. (D) Morphological evaluation and (E) quantitative analysis of subcutaneous keloid grafts (5 NC vs. 5 miR-3606-3p). (F) Quantitative analysis of collagen content in Masson's staining. *P < 0.05; **P < 0.01; ***P < 0.001.



Graphical Abstract. The mechanism of miR-3606-3p on anti-inflammatory and anti-fibrotic effects. ① miR-3606-3p targeted the 3'-UTRs of GAB1 and ITGAV mRNA and subsequently inhibited their protein expression, then attenuated the phosphorylation of AKT and ERK1/2. MiR-3606-3p and knockdown of GAB1 and ITGAV exert an inhibitory effect on inflammation, migration, and collagen deposition as follows: ② Two important negative regulators of fibroblast migration, named ADA1 and NID2, were inhibited by p-AKT/ERK1/2 resulting in collagen deposition and cell migration. ③ p-AKT/ERK1/2 triggered inflammatory responses by activating p-p65 of the NF-κB signalling pathway and releasing the inflammatory factors, including CCL2 and CCL5. Collectively, miR-3606-3p repressed the expression of GAB1, and ITGAV, eventually leading to attenuation of collagen deposition, cell migration and inflammation.

Disclosure: y. chen: None; **M. shi**: None; **W. Wang**: None; **C. Shi**: None; **X. Xia**: None; **w. Wu**: None; **J. Wang**: None; **X. Shi**: None.

Abstract Number: 0961

Transcriptomic Analysis of Scleroderma Monocytes Identifies Distinct Clinically Relevant Clusters and Novel Genes Associated with Disease Complications

Mehmed Dinc[1], Fatima El Adili[2], Justin Lui[3], Giovanni Ligresti[3], Robert Lafyatis[4], Maria Trojanowska[3] and Andreea Bujor[3], [1]Boston University School of Medicine, Boston, MA, [2]Boston University School of Medicine, Revere, MA, [3]Boston University, Boston, MA, [4]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is an autoimmune disease characterized by skin and internal organ fibrosis, vascular abnormalities, and immunological disturbances. Monocytes play a critical role in SSc, but their contribution to disease pathogenesis remains unclear. A better understanding of gene expression changes in SSc monocytes and their associations with disease complications may lead to novel therapies.

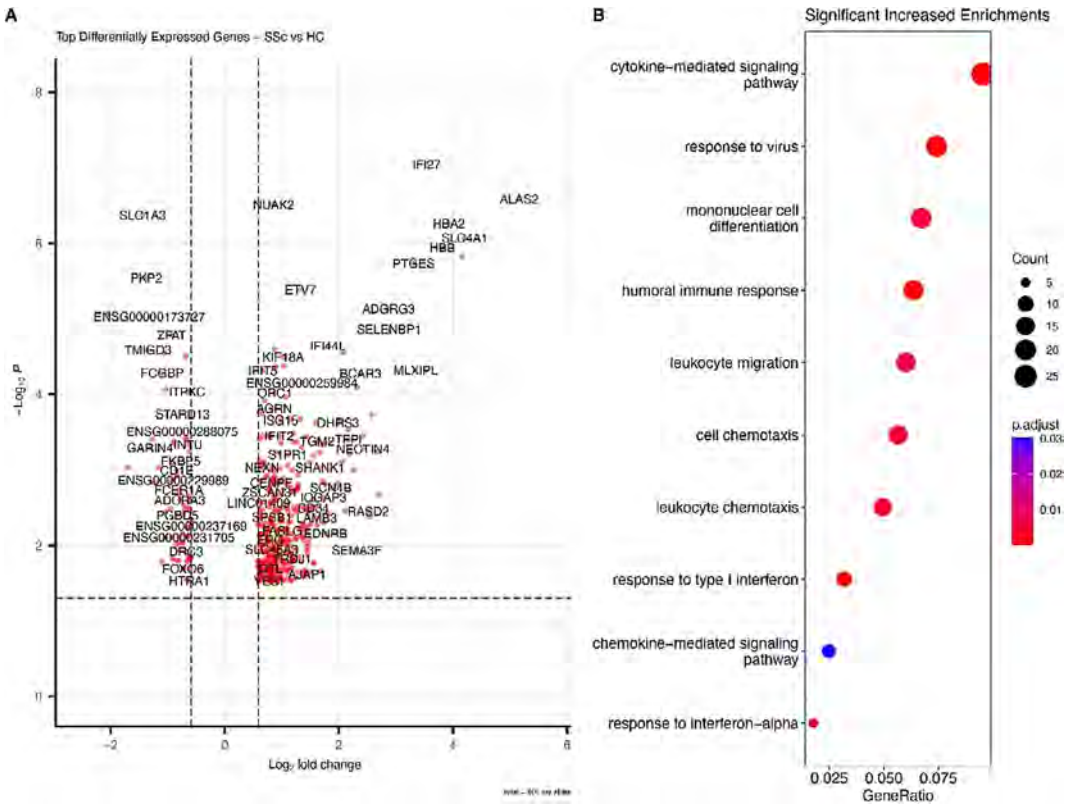


Figure 1. A. Volcano plot showing differentially expressed genes in SSc versus controls B. Pathway enrichment on differentially upregulated genes

Methods: Peripheral blood mononuclear cells were obtained from 48 SSc patients and 15 controls (HC) after informed consent and under an institutional approved IRB protocol. Magnetic bead separation was used to isolate monocytes and bulk RNA sequencing performed using the Illumina NextSeq platform. DESeq2 was used to identify differentially expressed genes between groups. We employed hierarchical clustering to group samples exhibiting similar transcriptional trends. Functional enrichment analysis was performed using ORA with the GO database to investigate the biological processes linked to each group. Pearson correlation was used for mRSS. DEG, GO and correlation analysis were conducted using R version 4.3.0. Pathways analysis for clinical features was performed using Ingenuity Pathway Analysis.

Results: 460 genes were found to be differentially regulated between SSc and HC. Interferon-related genes (IFI27, IFIT5, IFI44L, SIGLEC) were among top differentially expressed, along with genes not previously linked to SSc, including NUAK2, a TGFb induced protein kinase belonging to the AMPK family (FC 1.82, padj 0.001), and LGALS3BP, a secreted galectin-3 binding protein, that regulates cell-cell interactions and inflammation (FC 2.08, padj 0.04). Hierarchical clustering in SSc unveiled three groups. Cluster 1 ("inflammatory-like", 21 patients) predominantly displayed interferon related pathways, and included >80% of SSc patients with pulmonary hypertension (PH) from the entire SSc cohort. Cluster 2 ("T cell-like", 10 patients) exhibited enrichment in multiple pathways associated with T cell activation and contained the majority of

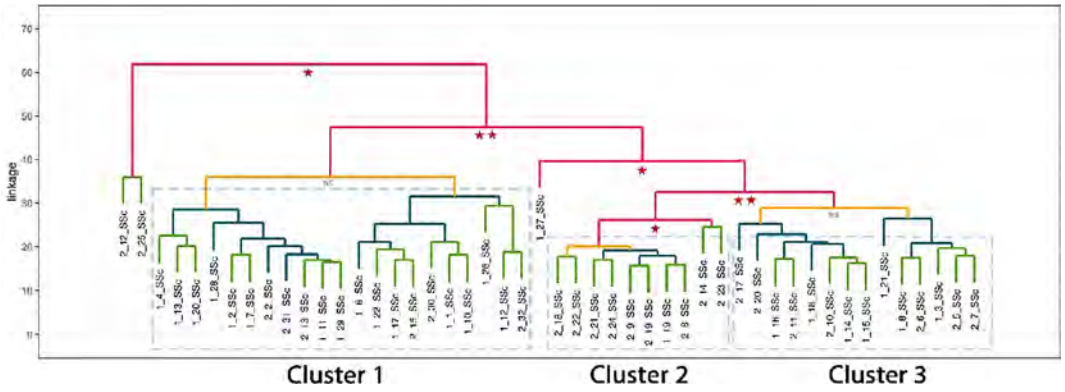


Figure 2. Hierarchical clustering analysis, revealing three significant clusters with distinct gene expression patterns.

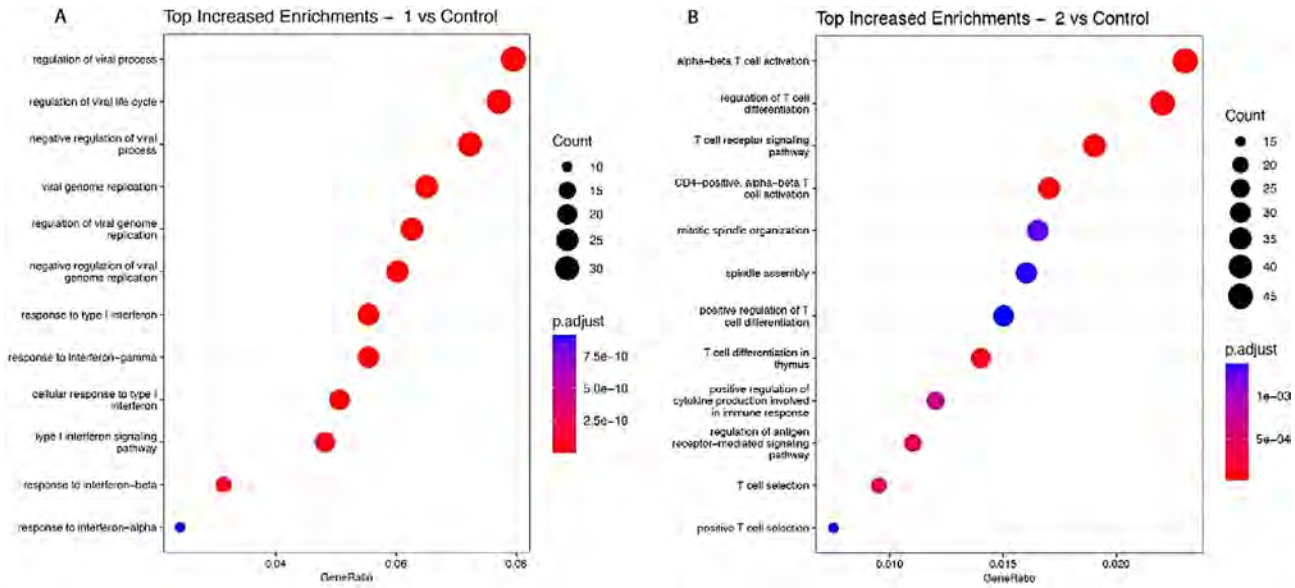


Figure 3. Pathway enrichment on differentially upregulated genes for cluster 1 (A) and 2 (B) vs controls. Cluster 3 did not reveal any significant pathways.

patients undergoing immunosuppressive therapy. Cluster 3 ("normal-like", 14) closely resembled the control group. Three patients did not belong to any clusters. There were significant associations between gene expression and clinical features. Interferon signaling pathway was the top most upregulated pathway in SSc-PH patients versus HC, but did not differentiate patients with and without PH. Cardiomyopathy patients had enhanced FAK and integrin signaling, and phagosome formation pathways. IPA analysis of SSc-ILD vs HC revealed association with pulmonary fibrosis signaling pathway with increased expression of SERPINE1 and PLAU genes. mRSS was highly correlated with XPR1, a novel gene implicated in phosphate homeostasis (r=0.72, padj 0.006).

Conclusion: Our results suggest that SSc patients can be classified into distinct groups based on transcriptomic profiles of monocytes, which correlate with specific clinical characteristics. The DEGs for clinical features revealed significant connections to the disease manifestations, potentially opening the avenue for new therapeutic targets.

Disclosure: M. Dinc: None; **F. El Adili**: None; **J. Lui**: United Therapeutics, 5; **G. Ligresti**: None; **R. Lafyatis**: Advarra/GSK, 1, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, 5, Certa Therapeutics, 2, Corbus, 2, 5, EMD Serono, 2, Formation, 2, 5, Genentech, 1, 2, Merck/MSD, 2, Moderna, 5, Morphic, 2, Pfizer, 2, 5, Regeneron, 5, Third Rock Venture, 2, Thirona Bio, 2, 4, 11, Zag Bio, 2; **M. Trojanowska**: None; **A. Bujor**: None.

Abstract Number: 0962

Topological Proteomic Differences in Fibrotic and Unaffected Skin in Scleroderma

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Scleroderma (SSc) is a chronic autoimmune and rheumatic disease characterized by varying levels of tissue fibrosis in the skin and other internal organs. It currently has no cure, with little understanding of the pathogenesis of skin fibrosis and an acute need for novel therapeutic targets. Because the skin is a complex, multi-layer organ with diverse functions, it is critical to examine the regional molecular changes throughout each distinct layer to understand the fibrotic processes that occur in the affected skin of SSc patients. To do this, we performed laser capture microdissection (LCM) to separate the epidermis, papillary dermis, and reticular dermis layers from fibrotic and unaffected skin of SSc patients for further proteomic analysis.

Methods: Skin biopsies were collected from fibrotic and unaffected skin of three patients with diffuse SSc (dSSc); subsequently, the epidermis, papillary dermis, and reticular dermis were dissected using LCM. The dissected tissue was digested and subjected to liquid chromatography with tandem mass spectrometry (LC-MS/MS) for proteomic analysis. Univariate and clustering analysis were performed using the MetaboAnalyst 5.0 package. Univariate analysis was performed using fold change analysis and t-test, and hierarchical clustering analysis was performed using Euclidean distance measurements to identify proteins significantly up or downregulated in fibrotic skin compared to unaffected skin for each skin sublayer.

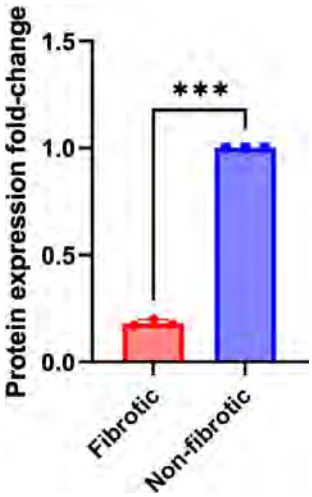


Figure 1: FAM161B is significantly downregulated in papillary dermis of fibrotic skin. Fibrotic and unaffected skin biopsies from patients with SSc (n=3) were subjected to LCM to isolate the papillary dermis, then LC-MS/MS for proteomic analysis. The graph shows fold-change for FAM161B normalized to non-fibrotic protein intensity. Statistical significance was assessed using two-tailed paired t test, ***p<0.0001

Results: All patients biopsied were female, had been diagnosed with dSSc, had early SSc (< 3 yrs from SSc diagnosis), and were being treated with mycophenolate mofetil. Univariate analysis of fibrotic versus unaffected skin revealed unique proteins that were significantly ($p< 0.05$) down or upregulated (fold-change >2) in each region. Interestingly, when comparing fibrotic and unaffected papillary dermis we identified a significant downregulation of FAM161B (fold change=-2.4573, p-value< 0.0001), a cilial protein, in all three patients. This is compelling because decreased expression of SPAG17, another cilial protein, has been correlated with increased skin fibrosis in SSc patients. Importantly, none of the differentially expressed proteins in the distinct skin layers overlapped with each other, confirming that fibrosis affects the microenvironments of the skin layers in SSc patients.

Conclusion: Through the use of LCM, we established a method for proteomic analysis of substructures from fibrotic and unaffected skin of SSc patients. This technology can be used to complement single-cell spatial transcriptomics to provide key information on in situ gene expression profiles and identify disease and substructure-specific targets for SSc skin fibrosis.

Disclosure: I. Choi: None; **C. Yu**: None; **F. Boin**: None; **E. Volkmann**: Boehringer-Ingelheim, 2, 5, 6, CSL Behring, 2, GlaxoSmithKline, 2, Horizon, 5, Prometheus, 5, Roche, 2; **S. Stanford**: None; **N. Bottini**: Thirona Bio, 2.

Abstract Number: 0963

Anti-Topoisomerase Antibody in dcSSc: Unravelling Its Intracellular Effects in Systemic Sclerosis

Maithri Aspari[1], Josephine Geertsen Keller-Socin[1], Stinne Greisen[2], Esben Naeser[3], Klaus Soendergaard[4], Birgitta R Knudsen[5], Voon Ong[6], Christopher Denton[7], David Abraham[7] and Bent Deleuran[1], [1]Aarhus University, Aarhus, Denmark, [2]Aarhus University/Aarhus University Hospital, Aarhus, Denmark, [3]Rheumatology, Aarhus University Hospital, Aarhus, Denmark, [4]Aarhus University Hospital, Aarhus, Denmark, [5]Institute for molecular Biology, Aarhus University, Aarhus, Denmark, [6]UCL Medical School Royal Free Campus, London, United Kingdom, [7]University College London, London, United Kingdom

SESSION INFORMATION

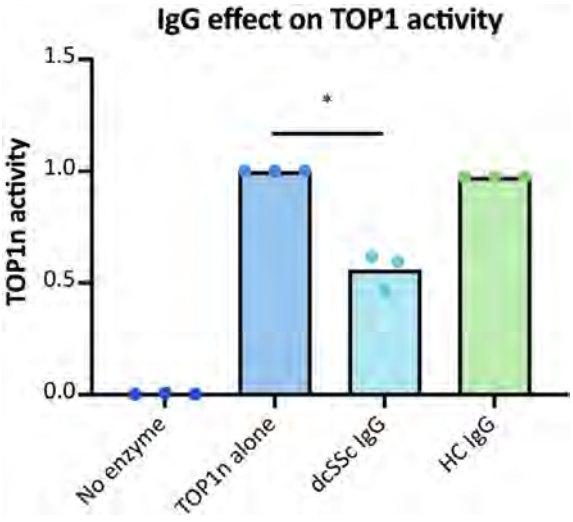
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The presence of autoantibodies, especially directed towards topoisomerase I (ATA), in diffuse cutaneous Systemic Sclerosis (dcSSc) is known to be associated with severe clinical manifestations. Though various detection methodologies are used in the clinic, less is known about the intracellular functionality of this antibody. Analysis of ATAs ability to inhibit topoisomerase 1 (TOP1) may function as a new biomarker of progressive and severe disease.

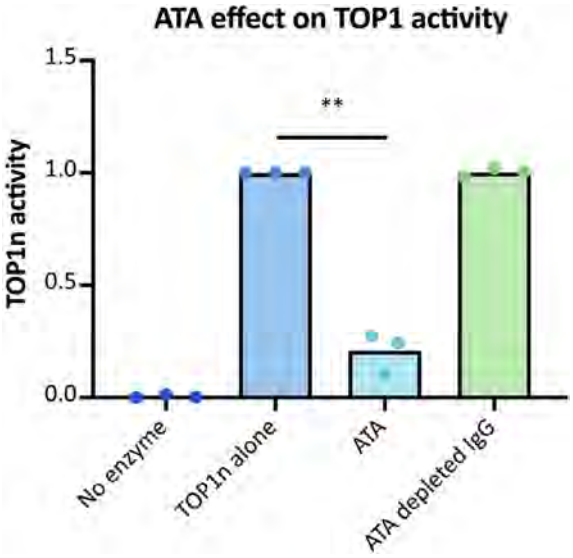
Methods: ATA was separated from serum from dcSSc patients (n=10) and healthy controls (HC, n=2). The immunoglobulin G (IgG) fraction was separated using a Protein G column (Figure A) followed by column separation towards TOP1. Sensitivity and purity were tested using western blot and biacore affinity analysis. The effect of serum, total IgG, ATA, and ATA depleted IgG from dcSSc patients and serum and IgG from HC on TOP1 catalysis were analyzed. We used a rolling circle amplification activity detection assay (REEAD) measuring the DNA cleavage-ligation activity of TOP1, as well as a nicking assay where TOP1 trapped in covalent complex with one strand of a plasmid DNA. To address the intracellular effect of ATA on TOP1 activity, dcSSc fibroblasts cultures were incubated with ATA or HC IgG mixed with lipofectamine for 6 hours, extracellular matrix protein signalling was analysed by PCR.

Results: dcSSc serum and IgG showed significant inhibition of TOP1 DNA cleavage-ligation activity when compared to HC serum and IgG, in a dose dependant manner. (Image 1). ATA separated from dSSc patients showed significant inhibition on TOP1 activity and this inhibition was abrogated when the ATA fractions were removed from the IgG pool. (Image 2). DcSSc IgG created TOP1 induced DNA nicks, suggesting that dcSSc IgG to induce accumulation of TOP1 cleavage complexes, which is a well-known inducer of DNA fragmentation in cells (Image not shown). PCR analysis of fibroblast transfected with ATA and HC IgG showed significant increase in signalling for extracellular matrix proteins such as intercellular adhesion molecule (ICAM) and Vascular cell adhesion molecule (VCAM)(Image 3).

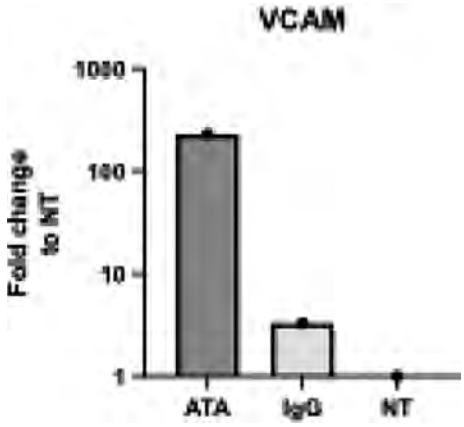
Conclusion: We have successfully separated functional ATA from dcSSc patients. These antibodies show significant effect on both nuclear and mitochondrial TOP1 activity. ATA causes DNA nicks and release free DNA into the cytosol, activating a cascade of inflammatory pathways leading to increased production of proinflammatory cytokines and extracellular matrix proteins. This study links ATA to central intracellular pathways, thus providing a better understanding of the disease pathogenesis



REEAD assay showing the inhibitory effect of dcSSc IgG on nuclear Topoisomerase activity



REEAD assay showing significant inhibitory effect of Antitopisomerase antibody(ATA) on nuclear Topoisomerase 1, this effect is lost on depleting ATA from the IgG pool



Graph representing the fold change in VCAM signalling in dcSSc fibroblasts stimulated with Antitopoisomerase antibody and normal human IgG, analysed by PCR

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Abstract Number: 0964

Systemic Sclerosis (SSc) Dermal Fibroblasts Show Shortened Primary Cilia Due to Aberrant Aurora a Kinase Activation Independently of Transforming Growth Factor β Signalling

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Sclerosis (SSc) is an autoimmune disorder characterised by abnormal activation of tissue fibroblasts, resulting in tissue and vascular fibrosis of the skin and internal organs. Aberrant activation of TGFβ signalling plays a central role in the profibrotic fibroblast phenotype. Fibroblasts cultured from SSc skin biopsies maintain their profibrotic activation in vitro. Patients with SSc do not show classic signs of primary aberrant profibrotic activation such as keloid or fibrotic responses to injury, leaving the mechanisms underlying fibroblast activation and tissue fibrosis not completely elucidated. The primary cilium (PC) is a sensory antenna-like organelle on the cell, forming a specialised signalling hub for several pathways involved in tissue homeostasis and response to the extracellular microenvironment. The aim of this study was to investigate the structure of the PC in SSc dermal fibroblasts to determine its potential contribution to SSc pathogenesis.

Methods: Dermal fibroblasts were isolated from forearm skin biopsies of healthy control (HC) and SSc patients. PC were visualised by immunofluorescence with an Acetylated-α-Tubulin antibody followed by confocal microscopy. PC length was quantified from at least 100 PC across 3 independent fields per condition. Fibroblasts were stimulated with TGFβ for 24h or a set time course with increments between 0-24h. SD208 (1μM) was used to inhibit TGFβ Receptor Kinase 1 (TGFβR1), MLN8054 (5μM) was used to inhibit Aurora A Kinase (AURKA), and Tubastatin A (1μM) was used to inhibit Histone Deacetylase 6 (HDAC6).

Results: PC length was normally distributed in both HC and SSc dermal fibroblasts. PC from SSc fibroblasts were on average 45% shorter than HC (2.5 ± 0.6 μm vs 4.6 ± 1.3 μm, respectively ($P< 0.0001$)). TGFβ treatment significantly reduced the mean PC length in both HC and SSc, reaching around 1.8 μm in both by 24 hours. Time course experiments showed a quicker response to TGFβ in SSc fibroblasts, with PC starting to shorten as soon as 2h vs 6h in HC. Inhibition of TGFβR1 prevented the ability of TGFβ to shorten PC in both, but did not 'rescue' SSc fibroblast PC length to that of HC. On the contrary, inhibition of AURKA – a kinase known to be involved in PC disassembly – did not abolish the effect of TGFβ in either cell type. However, AURKA inhibition increased PC length of SSc cells from 2.9 ± 0.4 μm to 4.4 ± 0.9 μm ($P< 0.05$), without affecting HC PC length, effectively "rescueing" the shortened PC phenotype of SSc cells, increasing PC length, indistinguishable from HC PC. The effect of AURKA was independent of its primary effector, HDAC6, as neither the difference in basal PC length nor the TGFβ effect were rescued by HDAC6 inhibition with Tubastatin A.

Conclusion: PC length is stably reduced in SSc dermal fibroblasts independently of TGFβR1 activity. Inhibition of AURKA in SSc restores "healthy" PC length via an atypical mechanism not involving its primary effector HDAC6. These observations support the notion that the profibrotic activation of dermal fibroblasts in SSc may go beyond a TGFβ-dependent mechanism. Modulation of PC length by AURKA deserves to be further explored as a contributor to profibrotic activation, and a potential therapeutic target for tissue fibrosis.

Disclosure: R. Wells: None; **R. Ross**: None; **A. Timmis**: None; **I. Georgiou**: None; **C. Johnson**: None; **N. Riobo-Del Galdo**: Dark Blue Therapeutics, 2, 5; **F. Del Galdo**: AbbVie/Abbott, 5, arxx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, capella, 2, Chemomab, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Mitsubishi-Tanabe, 2, 5.

Abstract Number: 0965

Comparing Predictors of DAPSA28, DAPSA66/68 and DAS28-CRP Remission at 6 Months in Bio-naive Patients with Psoriatic Arthritis Initiating a TNFi in Clinical Practice – Results from the EuroSpA Collaboration

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Epidemiology & Public Health Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: The Disease Activity index for PSoriatic Arthritis based on 66/68 joints (DAPSA66/68) and the Disease Activity Score in 28 joints with C-reactive protein (DAS28-CRP) are two widely used disease activity scores to monitor patients with psoriatic arthritis (PsA). A modified DAPSA based on 28 joints (DAPSA28) has been proposed and validated in patients with PsA. We aimed to identify and compare predictors of clinical remission according to DAPSA28 (≤4), DAPSA66/68 (≤4) and DAS28-CRP (< 2.6) in a broader population of European patients with PsA initiating a first tumor necrosis factor inhibitor (TNFi).

Methods: Prospectively collected real-world data from PsA patients initiating a first TNFi between 2009 and 2018 from nine countries participating in the European Spondyloarthritis (EuroSpA) Research Collaboration Network were pooled. Patients with complete data on DAPSA28, DAPSA66/68 as well as DAS28-CRP at 6-month follow-up (from 90 to 270 days after treatment start date) constituted the study cohort. Logistic regression analyses on multiple imputed baseline data (20 imputed datasets) were used to identify predictors of DAPSA28, DAPSA66/68 and DAS28-CRP remission at 6 months. Fifteen baseline (from 30 days before to 30 days after treatment start date) demographic and clinical characteristics were included as potential predictors. For each remission outcome, variable selection was performed separately in each imputed dataset. Predictors that appeared in at least half of the datasets were included in the final model.

Results: Of 10,249 PsA patients, 3,159 (30.8%) had complete assessments of DAPSA28, DAPSA66/68 and DAS28-CRP at 6 months and were included in the analyses. Baseline characteristics of included patients were similar to those not included (Table 1). Among included patients, 896 (28.4%), 861 (27.3%), and 1,866 (59.1%) were in DAPSA28, DAPSA66/68 and DAS28-CRP remission at 6 months, respectively. The same eleven predictors were identified for DAPSA28 and DAPSA66/68 remission, while nine predictors were selected for DAS28-CRP remission (Table 2). Eight predictors were common for all three remission outcomes: male gender, longer disease duration and higher CRP were positive predictors, while older age, higher body mass index, patient global score, health assessment questionnaire and 68 tender joint count reduced the odds of remission (Table 2). The same predictors were identified when substituting 66/68-joint counts with 28-joint counts in the set of potential predictors (with 28 tender joint count replacing 68 tender joint count as a predictor).

Table 1. Baseline characteristics of PsA patients starting a first TNFi among patients included and excluded from the analyses

	Patients with complete data on DAPSA28, DAPSA66/68 and DAS28-CRP at follow-up (n=3,159)		Patients without complete data on DAPSA28, DAPSA66/68 and DAS28-CRP at follow-up (n=7,090)	
	Available data, n (%)	Value	Available data, n (%)	Value
Demographics				
Age at treatment start, years	3,159 (100%)	49 (40-58)	7,090 (100%)	49 (40-58)
Time since diagnosis, years	2,548 (81%)	4 (1-9)	5,092 (72%)	3 (1-8)
Men, n (%)	3,159 (100%)	1,599 (51%)	7,090 (100%)	3,287 (46%)
BMI, kg/m^2	986 (31%)	27.7 (24.6-31.3)	1,923 (27%)	27.4 (24.2-30.8)
Current smokers, n (%)	2,872 (91%)	407 (14%)	5,875 (83%)	1,108 (19%)
Treatment				
TNFi, n (%)	3,159 (100%)		7,090 (100%)	
Infliximab		533 (17%)		1,448 (20%)
Etanercept		1,093 (35%)		2,460 (35%)
Adalimumab		900 (28%)		2,082 (29%)
Certolizumab pegol		195 (6%)		365 (5%)
Golimumab		438 (14%)		735 (10%)
TNFi start year, n (%)	3,159 (100%)		7,090 (100%)	
2009-2014		1,394 (44%)		4,110 (58%)
2015-2018		1,765 (56%)		2,980 (42%)
Concomitant csDMARD, n (%)	3,159 (100%)	2,009 (64%)	7,090 (100%)	3,770 (53%)
Patient reported outcomes				
Patient pain score (0-100 mm)	2,407 (76%)	64 (44-75)	4,355 (61%)	62 (43-76)
Patient fatigue score (0-100 mm)	1,773 (56%)	66 (45-80)	2,913 (41%)	68 (46-80)
Patient global score (0-100 mm)	2,445 (77%)	64 (46-79)	4,591 (65%)	65 (46-80)
HAQ (0-3)	2,292 (73%)	1.0 (0.5-1.4)	4,281 (60%)	0.9 (0.5-1.4)
Clinical measures				
SJC28 (0-28)	2,442 (77%)	3 (1-6)	4,566 (64%)	2 (0-5)
SJC66 (0-66)	2,069 (65%)	4 (2-8)	2,295 (32%)	4 (1-7)
TJC28 (0-28)	2,440 (77%)	4 (2-9)	4,568 (64%)	4 (1-9)
TJC68 (0-68)	2,082 (66%)	8 (4-13)	2,353 (33%)	7 (3-13)
CRP, mg/L	2,450 (78%)	7 (3-17)	4,801 (68%)	6 (2-13)
Physician global score (0-100 mm)	1,392 (44%)	50 (30-65)	2,605 (37%)	37 (20-55)
Composite scores				
DAPSA66/68, units	1,900 (60%)	26 (19-37)	1,646 (23%)	24 (17-33)
DAPSA28, units	2,241 (71%)	26 (18-39)	3,698 (52%)	25 (17-36)
DAS28-CRP, units	2,274 (72%)	4.2 (3.4-5.0)	3,913 (55%)	4.2 (3.3-4.9)

Data are as observed, median (range) or percentage. Percentages are calculated based on the number of patients with available data.

BMI: Body Mass Index; CRP: C-reactive protein; csDMARD: conventional synthetic Disease Modifying Anti-Rheumatic Drug; DAPSA28: Disease Activity index for Psoriatic Arthritis based on 28 joints; DAPSA66/68: Disease Activity index for Psoriatic Arthritis based on 66/68 joints; DAS28-CRP: disease activity score in 28 joints based on CRP; HAQ: Health Assessment Questionnaire; HLA-B27: Human Leukocyte Antigen subtypes B*2701-2759; SJC28: Swollen Joint Count based on 28-joint assessment; SJC66: Swollen Joint Count based on 66-joint assessment; TJC28: Tender Joint Count based on 28-joint assessment; TJC68: Tender Joint Count based on 68-joint assessment; TNFi: Tumor Necrosis Factor inhibitor.

Table 2. Univariable and final multivariable analyses for predicting DAPSA28, DAPSA66/68 and DAS28-CRP remission at 6 months (n=3,159)

	Prediction of DAPSA28 remission				Prediction of DAPSA66/68 remission				Prediction of DAS28-CRP remission			
Patients achieving the outcome, n (%)	896 (28.4%)				861 (27.3%)				1,866 (59.1%)			
Baseline variables	**Univariable**		**Multivariable**		**Univariable**		**Multivariable**		**Univariable**		**Multivariable**	
	OR (95% CI)				**OR (95% CI)**				**OR (95% CI)**			
Age at treatment start, years	0.98	(0.97 - 0.98)	0.98	(0.97 - 0.99)	0.98	(0.97 - 0.98)	0.98	(0.97 - 0.99)	0.97	(0.97 - 0.98)	0.98	(0.97 - 0.99)
Time since diagnosis, years	1.01	(1.00 - 1.02)	1.03	(1.01 - 1.04)	1.01	(1.00 - 1.02)	1.02	(1.01 - 1.04)	1.00	(0.99 - 1.01)	1.01	(1.00 - 1.03)
Men	2.21	(1.89 - 2.60)	1.72	(1.43 - 2.07)	2.27	(1.93 - 2.67)	1.77	(1.47 - 2.13)	2.34	(2.02 - 2.70)	1.88	(1.60 - 2.22)
BMI, kg/m²	0.93	(0.91 - 0.95)	0.95	(0.92 - 0.98)	0.94	(0.92 - 0.96)	0.95	(0.93 - 0.98)	0.95	(0.92 - 0.97)	0.97	(0.94 - 1.00)
Current smokers	0.70	(0.54 - 0.89)			0.71	(0.55 - 0.91)			0.72	(0.58 - 0.89)		
Concomitant csDMARD	1.01	(0.86 - 1.18)			1.01	(0.86 - 1.19)			0.96	(0.83 - 1.12)		
1st TNFi start, year (2015-2018)	1.08	(0.93 - 1.26)			1.05	(0.89 - 1.23)			1.23	(1.07 - 1.42)	1.28	(1.09 - 1.51)
*CRP>10 mg/l**	1.26	(1.05 - 1.50)	1.61	(1.32 - 1.97)	1.35	(1.12 - 1.61)	1.78	(1.45 - 2.19)	1.05	(0.88 - 1.24)	1.33	(1.10 - 1.62)
Patient pain score, mm	0.98	(0.97 - 0.98)			0.98	(0.97 - 0.98)			0.98	(0.98 - 0.98)		
Patient fatigue score, mm	0.98	(0.98 - 0.98)	0.99	(0.99 - 1.00)	0.98	(0.98 - 0.98)	0.99	(0.99 - 1.00)	0.98	(0.98 - 0.99)		
Patient global score, mm	0.97	(0.97 - 0.98)	0.99	(0.98 - 0.99)	0.97	(0.97 - 0.98)	0.99	(0.98 - 0.99)	0.98	(0.97 - 0.98)	0.99	(0.98 - 0.99)
Physician global score, mm	0.98	(0.98 - 0.99)	0.99	(0.98 - 1.00)	0.98	(0.98 - 0.99)	0.99	(0.98 - 1.00)	0.98	(0.98 - 0.99)		
HAQ, units	0.36	(0.31 - 0.42)	0.71	(0.56 - 0.89)	0.36	(0.30 - 0.42)	0.69	(0.55 - 0.86)	0.34	(0.29 - 0.39)	0.56	(0.46 - 0.67)
SJC66, units	0.98	(0.97 - 1.00)	1.04	(1.01 - 1.07)	0.98	(0.96 - 1.00)	1.03	(1.00 - 1.06)	0.95	(0.93 - 0.97)		
TJC68, units	0.95	(0.94 - 0.96)	0.97	(0.95 - 0.99)	0.95	(0.94 - 0.97)	0.97	(0.96 - 0.99)	0.94	(0.93 - 0.95)	0.96	(0.95 - 0.98)

Baseline variables that are common predictors across all outcomes are highlighted in italics.

Variable selection process: For each remission outcome, the selection was performed separately in each of the 20 imputed datasets. Initially, univariable logistic regression analyses were performed for all potential predictors. Variables with a p-value <0.20 in univariable analyses were included in the initial multivariable model, where a backward stepwise selection was applied. Next, potential predictors excluded in univariable analyses were introduced one at a time in the multivariable model and their significance tested. The final model included the predictors that appeared in at least half of the 20 separate models. Once the set of predictors was selected, the model was fitted to all 20 imputed datasets and the model estimates were pooled according to Rubin's rules. Likelihood ratio tests were used to assess all models.

BMI: Body Mass Index; CI: confidence interval; CRP: C-reactive protein; csDMARD: conventional synthetic Disease Modifying Anti-Rheumatic Drug; DAPSA28: Disease Activity index for Psoriatic Arthritis based on 28 joints; DAPSA66/68: Disease Activity index for Psoriatic Arthritis based on 66/68 joints; DAS28-CRP: disease activity score in 28 joints based on CRP; HAQ: Health Assessment Questionnaire; OR: odds ratio; SJC66: Swollen Joint Count based on 66-joint assessment; TJC68: Tender Joint Count based on 68-joint assessment; TNFi: Tumor Necrosis Factor Inhibitor.

*The CRP cut-off was decided based on the various detection limits used across registries.

Conclusion: Identical variables were found as predictors of both DAPSA28 and DAPSA66/68 remission in patients treated with a first TNFi. The majority of these variables also predicted DAS28-CRP remission, although DAS28-CRP remission was more commonly achieved. Our findings suggest that baseline determinants of remission according to different disease activity scores are similar and support the use of DAPSA28 in datasets where only 28-joint counts are available.

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Gilead, 2, 6, Hospira, 2, 6, Janssen, 2, 6, MEDAC, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Novo Nordisk, 2, 6, Orion, 2, 6, Pfizer, 2, 6, Regeneron, 2, 6, Roche, 2, 6, Sandoz, 2, 6, Sanofi, 2, 6, UCB, 2, 6.

Abstract Number: 0966

The Burden of Oligoarticular Psoriatic Arthritis in the United States

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with oligoarticular psoriatic arthritis (oligo PsA), defined as four or less joints involved, often do not meet criteria for entry in trials of targeted treatments. However, clinical data suggest oligo PsA impacts the patient equally as polyarticular (poly) PsA (> 4 joints) (Gladman D, et al. J Rheumatol. 2021;48:1824-1829). Limited information exists on oligo PsA burden in the United States (US). This study aimed to describe the demographic and clinical characteristics of oligo PsA patients and compare quality of life (QoL) and economic impact of this disease relative to the general population.

Methods: Retrospective, cross-sectional data from the 2019 National Health and Wellness Survey (Cerner Enviza) conducted in the US were utilized to identify adult respondents who self-reported a diagnosis of PsA and those who did not (ie, no psoriasis or PsA), representing the general US population (non psoriasis [Pso]/PsA). Within the PsA population, the oligo PsA cohort was selected if self-reported ≤ 4 affected joints and the remainder constituted the poly PsA cohort. Prevalence estimates were weighted to the US population using US census weights. Demographic and health characteristics

Table 1. Demographic characteristics

	Non Pso/PsA Cohort Unweighted N= 72,431	Oligo PsA Cohort Unweighted N= 374	p-value
Female, n (%)	41,236 (56.9)	143 (38.2)	*
Age, mean	47.5	45.3	*
Married, n (%)	35,857 (49.5)	210 (56.2)	
Ever smoked cigarettes Yes, n (%)	27,144 (37.5)	222 (59.4)	*
Alcohol consumption Yes, n (%)	48,658 (67.2)	290 (77.5)	*
College Graduate, n (%)	36,465 (50.3)	208 (55.6)	*
Completed graduate school (e.g., M.S., M.D., Ph.D.), n (%)	14,267 (19.7)	91 (24.3)	*
Employed	43,104 (59.5)	263 (70.3)	*
Household income $75K & over	29,229 (40.4)	200 (53.5)	*
Mean Body Mass Index (BMI)	27.8	28.2	
Mean number of days vigorously exercised in the past month	8.5	8.2	

*p-value significant at 0.05 significance level

Table 2. Psoriatic arthritis characteristics

	Diagnosed with PsA	Oligo PsA Cohort	Poly PsA Cohort^
Total (Unweighted), n (% of Diagnosed with PsA)	679 (100)	374 (55.1)	305 (44.9)
Physician who diagnosed arthritis, n (%)			
Primary Care Physician/GP/Internist	300 (44.2)	166 (44.4)	134 (43.9)
Nurse Practitioner/Physician Assistant	40 (5.9)	29 (7.8)	11 (3.6)
Orthopedist	43 (6.3)	29 (7.8)	14 (4.6)
Rheumatologist	210 (30.9)	86 (23.0)	124 (40.7)
Other	31 (4.6)	18 (4.8)	13 (4.3)
Treatment, n (%)			
Using Rx or OTC	541 (79.7)	287 (76.7)	254 (83.3)
Untreated	138 (20.3)	87 (23.3)	51 (16.7)
Rx only	397 (58.5)	197 (52.7)	200 (65.6)
Prescribing physician, n (%)			
Total (Unweighted)	937	374	563
Primary Care Physician/GP/Internist	363 (38.7)	141 (37.7)	222 (39.4)
Nurse Practitioner/Physician Assistant	86 (9.2)	61 (16.3)	25 (4.4)
Orthopedist	77 (8.2)	41 (11.0)	36 (6.4)
Rheumatologist	330 (35.2)	101 (27.0)	229 (40.7)
Other	81 (8.6)	30 (8.0)	51 (9.1)

^all PsA minus oligo PsA

Table 3. Health outcomes

	Non Pso/PsA Cohort Unweighted N= 72,431	Oligo PsA Cohort Unweighted N= 374	Poly PsA Cohort^ Unweighted N=201	p-values	
				Oligo PsA vs. Non PsO/PsA	Oligo PsA vs. Poly PsA
Mean Charlson Comorbidity Index Score	0.4	1.6	1.6	*	
HRQoL					
Mean Mental SF-36 Score	46.7	41.6	41.6	*	
Mean Physical SF-36 Score	50.4	43.1	37.3	*	*
Mean EQ5D Index Score	0.8	0.7	0.6	*	
Health care resource utilization					
% Visited GP in the past 6 months	48.9%	50.0%	75.6%		*
% Any HCP in the past 6 months	76.9%	93.9%	96.0%	*	
Mean # of visits in the past 6 months	3.6	6.4	8.5	*	*
WPAI					
% Employed Full Time	43.6	55.1	28.9	*	*
Mean % Absenteeism	8.9	26.6	18.9	*	
Mean % Presenteeism	22.2	54.9	45.5	*	
Mean % Work productivity loss	24.9	61.2	49.5	*	*
Activity impairment	24.8	48.3	56.7	*	*

*p-value significant at 0.05 significance level; HRQoL: health-related quality of life; WPAI, work productivity and activity impairment
^available questionnaires data

were compared across cohorts. Additional outcomes assessed included: PsA characteristics (joints affected, prescribing/diagnosing physician), health-related QoL (HRQoL), healthcare resource utilization in the prior 6 months, and work productivity and activity impairment (WPAI).

Results: A total of 374 respondents were classified as having oligo PsA (weighted count: 1.3 million); 72,431 were classified as non Pso/PsA (weighted count: 241.8 million).Individuals with oligo PsA were more likely to be younger, male, employed, smoke or consume alcohol, to have a higher annual income and to have graduated college relative to non Pso/PsA (Table 1). About 44.4% of oligo PsA patients were diagnosed by their primary care physician with 52.7% prescribed treatment (Table 2). Although the most frequently affected joints (knees, fingers, hands and feet) were similar in both oligo and poly PsA (n=305), a larger proportion of oligo PsA patients were untreated (23.3% vs. 16.7%) and a smaller proportion diagnosed by rheumatologists (23% vs. 40.7%). Respondents with oligo PsA reported higher co-morbidities, lower HRQoL, lower mental and physical functioning, higher health care provider visits and higher WPAI relative to non Pso/PsA. Additionally, while a higher proportion of individuals with oligo PsA were employed relative to poly PsA, individuals with oligo PsA reported greater work productivity losses (Table 3).

Conclusion: The oligo PsA population was active in the workforce but had significantly higher comorbidity burden and impairments in both QoL and work productivity than the general population. Furthermore, despite the perception of poly PsA as a more severe disease, the oligo PsA population had a similar QoL burden (EQ-5D) and reported greater work productivity losses than those with poly PsA. These findings suggest that the burden of oligo PsA is high in the United States and warrants further research and clinical attention.

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Abstract Number: 0967

Overall Survival in Patients with versus Without Rheumatoid Arthritis Initiating Immune Checkpoint Inhibitors for Metastatic Non Small Cell Lung Cancer

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SESSION INFORMATION
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Background/Purpose: Immune checkpoint inhibitors (ICI) increase one-year survival in metastatic non-small cell lung cancer (mNSCLC) from 49% to 69% with chemotherapy-based regimens. Patients with rheumatoid arthritis **(**RA) have a 60% higher risk of lung cancer than the general population but were not included in seminal ICI trials. The goal of this study was to compare overall survival (OS) in ICI-treated patients with mNSCLC with pre-existing RA versus without RA.

Methods: We used a curated Medicare claims dataset that consist of a 100% sample of patients with RA. ICI use was identified using Healthcare Common Procedure Coding System (HCPCS) codes. Patients with mNSCLC were defined by having two claims at least two months apart associated with an ICD-9 162.9 or ICD-10 C34.X diagnosis code for malignant neoplasm of lung and bronchus. We limited the cohort to patients who initiated ICI between 2015-2019 because ICI was only approved for mNSCLC during this period, and not for earlier stages or other types of lung cancer. RA was defined as having two claims associated with an ICD-9-CM or ICD-10-CM diagnosis code for RA. ICI-treated non-RA comparator patients were identified in the Medicare 5% sample. Descriptive statistics were calculated for each cohort and for overall survival. Kaplan Meier curves and adjusted log logistic survival models were created to measure overall survival, anchored at the time of first ICI initiation. Patients were followed through 12/31/2019 and were censored at time of death or last recorded visit in the database.

Results: A total of 10454 ICI-treated patients with mNSCLC were included in the analysis; 4,544 with RA (100% sample) and 5910 without RA (5% sample). Overall mean age was 74.3 (SD 8.22) and 85% were White and non-Hispanic (Table 1). Patients with RA were more likely to be female, White and Hispanic than non-RA patients. Median time to death

Table 1. Demographics for immune checkpoint inhibitor-treated patients with metastatic non-small cell lung cancer, with and without rheumatoid arthritis

	Total	RA	non-RA	p-value
Total	10,454	4,544	5,910	
Age, mean (SD)	74.3 (68.9 79.8)	75.0 (69.6, 80.1)	73.8 (68.5, 79.5)	<0.001
Female	5585 (53.4%)	2796 (61.5%)	2789 (47.2%)	<0.001
Race				0.004
White	8,898 (85.1%)	3,841 (84.5%)	5,057 (85.6%)	
Black	919 (8.8%)	397 (8.7%)	522 (8.8%)	
Asian	143 (1.4%)	52 (1.1%)	91 (1.5%)	
Unknown/ Other	439 (4.2%)	224 (4.9%)	215 (3.6%)	
Missing	55 (0.5%)	30 (0.7%)	25 (0.4%)	
Hispanic	221 (2.1%)	162 (3.6%)	59 (1.0%)	<0.001
First ICI				0.980
Atezolizumab	877 (8.4%)	379 (8.3%)	498 (8.4%)	
Nivolumab	4,764 (45.6%)	2,070 (45.6%)	2,694 (45.6%)	
Pembrolizumab	4,813 (46.0%)	2,095 (46.1%)	2,718 (46.0%)	
Time ICI initiation to Death or Follow Up, median (IQR)	226 (89, 472)	232 (91, 477.5)	222 (88, 468)	0.190

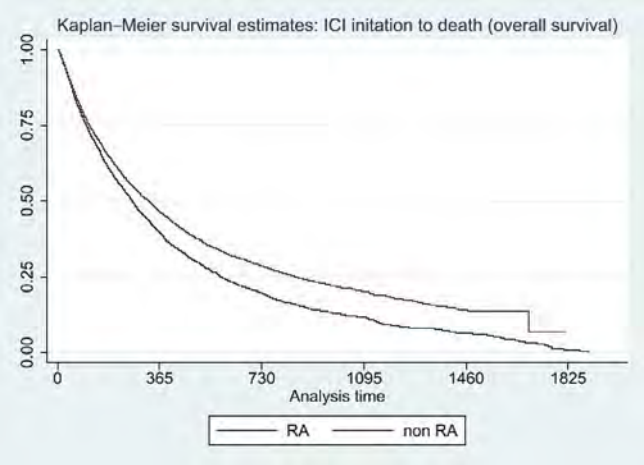

Figure 1: Overall survival in immune checkpoint inhibitor-treated metastatic non-small cell lung cancer patients with versus without rheumatoid arthritis

from first ICI initiation was 180 days (IQR 73,370) and 70% died (N=7,305). Figure 1 displays overall survival for ICI-treated mNSCLC patients with RA compared to those without RA.

Conclusion: Patients with pre-existing RA who develop lung cancer and initiate ICI for mNSCLC appear to have significantly worse overall survival compared to patients without RA. Further refinement of the cohort and further analyses of this dataset, including modeling, that incorporate prior lines of cancer therapy, receipt of concomitant chemotherapy and treatment with RA disease modifying antirheumatic drugs will be needed to confirm these findings.

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Abstract Number: 0968

Risk of Incident Heart Failure and Heart Failure Subtypes in Patients with Rheumatoid Arthritis

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Background/Purpose: Patients with rheumatoid arthritis (RA) are at increased risk of cardiovascular (CV) disease including heart failure (HF). HF is a heterogeneous condition that is categorized into two main subtypes: HF with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF). Unlike HFrEF which arises primarily from ischemic myocardial

Table 1: Baseline characteristics of RA and non-RA comparators* at index date

	Non-RA (N=1919)	RA (N=1919)
Age (mean, SD)	50.5 (13.7)	50.2 (13.7)
Female (%)	78.7	78.7
Self-reported race (%)		
White	87.2	84.5
Black	5.0	5.7
Asian	1.7	2.2
Other	3.0	3.3
Missing	3.1	4.2
Comorbidities** (%)		
Hypertension	19.0	19.9
Hyperlipidemia	20.6	20.7
Diabetes	6.8	6.9
Chronic kidney disease	2.3	2.7
Atrial fibrillation	2.6	1.9
Coronary artery disease	6.6	8.3
Stroke	4.6	4.3
Ever smoker† (%)	23.0	23.6

RA, rheumatoid arthritis; SD, standard deviation; EHR, electronic health record
*Non-RA comparators were matched to the RA cohort by birth year, sex, and EHR entry year
**Comorbidities were defined by the presence of ≥ 1 diagnosis codes prior to index date
†Smoking status was determined based on natural language processing of unstructured EHR data for positive mentions of concepts related to smoking prior to the index date

injury, the pathophysiology of HFpEF is less well understood but systemic inflammation is thought to play a role. RA may confer risk of HFrEF via ischemic heart disease and and HFpEF via systemic inflammation, but most prior epidemiologic studies have studied HF in RA as a single entity. Therefore, we sought to investigate the risk of HF and HF subtypes among patients with RA compared to non-RA patients.

Methods: Using an electronic health record (EHR)-based cohort at a large academic U.S. health system, we identified RA patients and non-RA comparators matched by age, sex, and year of entry into the EHR. Index date was defined as the RA diagnosis date (RA cohort) or an encounter date closest to the matched RA patient's index date (non-RA cohort). The primary outcome was incident HF as ascertained using a previously validated algorithm with a positive predictive value of 90%. HF subtypes were categorized based on EF extracted using natural language processing from clinical notes and cardiology reports closest to the HF incident date (HFpEF, EF ≥ 50%; HFrEF, EF ≤ 40%). Patients with prevalent HF at the index date were excluded. Covariates included age, sex, race, and CV risk factors. Patients were followed from the index date until incident HF, death, last EHR encounter, 20 years of follow up, or end of study (October 26, 2021). We estimated the incidence rate of HF and HF subtypes and used Cox proportional hazards model to estimate the adjusted hazard ratios (HR) for incident HF and HF subtypes.

Results: We studied 1919 RA patients and 1919 matched non-RA comparators (mean age 50 years, 78.7% female). Baseline characteristics, including the proportion of patients with CV risk factors, were similar between the two groups (**Table 1**). Over 42,858 person-years of follow up, we identified 128 incident HF diagnoses (6.7%) in the RA cohort and 87 in the non-RA cohort (4.5%). HFpEF was the most common HF subtype in both cohorts (64.1% in RA, 60.9% in non-RA). The overall incidence rate of HF was higher in the RA cohort than the non-RA cohort (6.11 per 1000 person-years vs. 3.97 per 1000 person-years). Patients with RA had a 56% higher rate of incident HF overall (95% CI: 1.18 - 2.06) compared to those without RA, even after adjusting for established CV risk factors (**Table 2**). Examining the HF subtypes, we found that RA patients had a 62% higher rate of HFpEF (95% CI: 1.13 - 2.30), but there was no significant difference in HFrEF rate between the RA and non-RA cohorts (95% CI: 0.81 - 2.75).

Conclusion: RA was associated with higher rate of HF overall compared to non-RA comparators, even after adjustment for CV risk factors. The elevated risk was driven by HFpEF, highlighting an opportunity to reduce HF risk in RA by targeting HFpEF. More studies are needed to identify modifiable HFpEF risk factors in RA and methods for earlier detection before clinical HF.

Table 2: Risk of incident HF and HF subtypes in RA and non-RA comparators

	Non-RA (N = 1919)	RA (N = 1919)
Follow up time (person-years)	21,901	20,957
Overall HF		
Cases (n)	87	128
Incidence rate (per 1,000 person-years)	3.97	6.11
Unadjusted hazard ratio	1.00	**1.54 (1.17 - 2.02)**
Adjusted hazard ratio*	1.00	**1.56 (1.18 - 2.06)**
HF with reduced EF**		
Cases (n)	18	25
Incidence rate (per 1,000 person-years)	0.82	1.19
Unadjusted hazard ratio	1.00	1.46 (0.80 - 2.68)
Adjusted hazard ratio*	1.00	1.49 (0.81 - 2.75)
HF with preserved EF†		
Cases (n)	53	82
Incidence rate (per 1000 person-years)	2.42	3.91
Unadjusted hazard ratio	1.00	**1.62 (1.14 - 2.28)**
Adjusted hazard ratio*	1.00	**1.62 (1.13 - 2.30)**

HF, heart failure; RA, rheumatoid arthritis; EF, ejection fraction
*Adjusted for sex, age, race, and CV risk factors: baseline history of coronary artery disease, diabetes, hypertension, hyperlipidemia, atrial fibrillation, chronic kidney disease, stroke, smoking
**Defined as having EF ≤ 40%
†Defined as having EF ≥ 50%. Those with a moderately reduced EF of 41 – 49% were included in the overall HF but excluded from the HF subtypes above

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Abstract Number: 0969

Tumor Necrosis Factor-α Inhibitors Reduces Obstructive Sleep Apnea in Patients with Juvenile Idiopathic Arthritis: A Population-based Cohort Study

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SESSION INFORMATION

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Background/Purpose: Tumor necrosis factor-α (TNF-α) plays a role in the pathogenesis of and serves as a biomarker for obstructive sleep apnea (OSA). Moreover, patients with juvenile idiopathic arthritis (JIA) had a numerically elevated risk of OSA. Given TNF-α inhibitors have been widely used to treat JIA, the aim of the present study was to assess the risk of OSA among patients with JIA on TNF-α inhibitors.

Methods: This was a population-based cohort study of patients with JIA diagnosed following the International League of Associations for Rheumatology (ILAR) classification criteria. Subjects treated between 2008 and 2023 at 92 United States hospitals were screened. Propensity score matching was used to balance the baseline differences in age of JIA onset, sex, comorbidities, and past medical history between the two groups. The primary predictor variable was any use of TNF-α inhibitor therapy. The primary outcome of interest was the occurrence of new-onset OSA during the follow-up period. A Kaplan-Meier analysis and log-rank tests were utilized to compare the incidence and risk of OSA between the two arms. A Cox proportional hazards model was utilized to estimate the association between the use of TNF-α inhibitors and new-onset OSA.

Results: A total of 608,190 patients with JIA underwent propensity score matching. This resulted in 1,299 included subjects with JIA treated with TNF-α inhibitors, 514 patients developed new-onset OSA after the use of TNF-α inhibitors. In comparison, 594 TNF-α inhibitor non-users developed incident OSA during the follow-up period. Survival analysis suggested a significantly lower incidence of OSA in TNF-α inhibitor users over non-users (log-rank test, p-value < 0.001). Cox proportional hazard regression showed subjects receiving TNF-α inhibitors were associated with a significantly lowered risk of new-onset OSA as compared to non-users (HR=0.87, 95% CI: 0.78, 0.98; RR=0.86, 95% CI: 0.76, 0.96)

Conclusion: Findings in the present study suggested that subjects with JIA treated with TNF-α inhibitors presented with a significantly decreased risk of OSA. This finding was consistent with previous studies reporting that the use TNF-α inhibitors resulted in a significantly lowered risk of OSA and better sleep quality in patients with other inflammatory arthritis such as spondyloarthritis and rheumatoid arthritis. Clinical trials are required to validate the findings.

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Abstract Number: 0970

Comparison of Survival on Treatment and Severe Infection Among New Users of Biosimilar vs. Originator Biologics in Inflammatory Arthritis: Population-based Evidence from a Natural Experiment Due to a Policy Change

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Background/Purpose: British Columbia's health policy mandated that all new anti-TNF initiations after June 2017 use biosimilars when available, providing the context for a natural experiment. Our study objective was to compare drug survival and severe infections (as surrogate markers of effectiveness and safety) after the initiation of etanercept and infliximab for inflammatory arthritis in new users of biosimilars versus originators, using historical controls pre- and post-policy change.

Methods: Study Cohort: Using administrative health data, we identified all incident users of a new biologic (i.e., without prior prescriptions over 6 months) with rheumatoid arthritis (RA), psoriasis or psoriatic arthritis (Pso/PsA), or ankylosing spondylitis (AS). The biosimilar cohort includes users starting etanercept or infliximab between 07/01/2017 and 12/31/2019, followed until 12/31/2020 (post period). Historical controls include all incident users of etanercept/infliximab originators between 01/01/2014 and 06/30/2016, followed until 06/30/2017 (pre period). To control for temporal trend, we selected new users of adalimumab (no biosimilar available over the same time periods) as a comparison group.

Outcome: Discontinuation was defined as no prescription renewal for at least 6 months, and severe infection was defined as hospitalization with an infection diagnostic code in any position.

Statistical analyses: People were followed for up to 3 years from anti-TNF initiation until death, moving out-of-province, or the end date of the follow-up, whichever occurred first. Rates were calculated. We applied weighted Cox Proportional Hazard Models to estimate the adjusted hazard ratio (aHR) of discontinuing anti-TNFs and Quasi Poisson Models to estimate the adjusted rate ratio (aRR) of severe infections. We applied propensity overlap weights to control for potential confounders. To control for temporal trend, we employed the difference-in-difference (DID) method, comparing drug survival and severe infections among new users of biosimilar vs. originator etanercept/infliximab with new users of adalimumab post- vs. pre-policy change. The DID computes the difference between the logarithms of the aHRs/aRRs for etanercept/infliximab and for adalimumab, reported as the ratio of the two aHRs/aRRs in Table 1C.

Results: Our sample includes 827 biosimilar etanercept users (RA:576, AS:171, Pso/PsA:80) and 271 infliximab users (RA:150, AS:54,Pso/PsA:67); 1312 etanercept and 230 infliximab originator users; and 2213 adalimumab originator users post- and 1773 pre-policy change. Counts and rates of discontinuation and severe infections are reported in Table 1A. After adjusting for baseline covariates (Table 1B), and after accounting for temporal trends (Table 1C), the likelihood of discontinuation and severe infection was similar for biosimilar vs. originator etanercept and infliximab users.

Conclusion: Real-world population-based data showed that incident users of biosimilar etanercept and infliximab had similar discontinuation and severe infection rates as originators, suggesting comparable effectiveness and safety for inflammatory arthritis.

Disclosure: D. Lacaille: None; **J. Avina-Zubieta**: None; **Y. Zheng**: None; **N. Lu**: None; **H. Xie**: None.

Abstract Number: 0971

Network Meta Analyses of the Effectiveness and Safety Profiles of Janus Kinase Inhibitors and Biologic Agents in Treating Children with Non-systemic Juvenile Idiopathic Arthritis (nsJIA)

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Background/Purpose: Tofacitinib (TOFA, NCT02592434) and Baricitinib (BARI, NCT03773978) are Janus kinase inhibitors (JAKi) that are approved for or being tested for nsJIA treatment. We aim to evaluate the effectiveness and safety profiles of JAKi, vs. biological agent (BA) with or without Methotrexate (MTX) combination in treating children with nsJIA.

Methods: Studies written in English language and published in ClinicalTrial.gov, PubMed, EMBASE, Cochrane are searched from establishment of the databases to May 2023. Randomized studies conducted in the nsJIA population, investigated effectiveness of JAKi or BA, and reported JIA-ACR responses with/without adverse event outcomes are eligible. The primary outcome of clinical efficacy was measured by JIA-ACR70 responses at 16+/-4 weeks and secondary outcomes include serious adverse events (SAE). Bayesian Network meta-analyses (BNMA) evaluate the effectiveness and safety outcomes of JAKis and BAs with/without MTX.BNMA are conducted separately for efficacy and safety outcomes. League table reports results for all pairwise comparisons.

Results: The initial search query yielded 2,475 citations. Fifteen randomized controlled trials (RCT, 6 parallel and 9 withdrawal trials) met the study inclusion criteria. The meta-analyses investigated 6 BA, 3 BA+MTX combination, and two JAKi (i.e. TOFA and BARI). MTX background treatment was allowed, rarely mandated. The trial design and sample characteristics are summarized in Table 1. The aggregate summary statistics reported for the efficacy and safety outcomes are presents in Figure 1. The BNMA analyzed data from a total of 1,796 patients, estimates of odds ratio (OR) and corresponding 90% credible intervals are reported in Table 2 for the efficacy (upper triangle) and safety outcomes (lower triangle).

Conclusion: No significant differences are observed for pairwise comparisons among TOFA, BARI and BAs either alone or in combination with MTX for efficacy and safety outcomes when used for treating children with nsJIA. The BNMA indirect comparisons are limited, given that trials differ greatly in participants age, duration of disease, % of MTX background therapy, whether the trial mandate patients with inadequate responses to composition of DMARD or NSAID to be eligible, as well as the composition of JIA subtypes. The SAE may be defined differently in different studies. Future studies will expand the meta-analyses by including non RCT studies and individual patients' data.

Table 1

Table 1. Trial Design and Sample Characteristics

TRIAL ID^	REGISTRY (REFENCE)	STUDY YEAR	ARMS* (N)	%FEMALE	AGE (YR)	JIA_DUR (YR)	LOM	AJC	MDG# (0-10)	PTWELL# (0-10)	CHAQ	%MTX
1	NCT01166282 (1)	2010-2	ADA (31)	29%	13.4	2.6	5.1	8.4	5.3	5.3	0.8	52%
			PC (15)	40%	11.9	2.7	4.5	6.7	5.3	4.9	0.8	53%
2	EUCTR2015-003384-11 (2)	2015	ETN+MTX (35)	67%	9.8*	2.5*	6*	7*	8*	7.5*	1.5*	100%
			PC (33)	76%	6.62*	3*	6*	7*	6*	7*	1*	100%
3	NTR1574 (3-4)	2009-13	PC1 (32)	75%	8.8*	0.65*	2*	7.5*	4.8*	4.8*	0.88*	100%
			PC2 (32)	59%	10.2*	0.49*	2*	7.5*	5.0*	5.9*	0.94*	100%
			ETN+MTX (30)	67%	8.6*	0.7*	3*	8.5*	5.1*	5.8*	0.88*	100%
4	NCT00443430 (4)	2007-10	ETN+MTX (42)	69%	9.9	0.4	13.6	18.3	7	5.6	1.1	100%
			PC (43)	79%	11.1	0.43	16.3	25.5	7	5.2	1.3	100%
5	NCT00036374 (5)	2001-6	PC (62)	79%	11.1	3.6	17.6	18.5	5	4.1	1.2	100%
			INF (60)	88%	11.3	4.2	18.4	19.5	5.2	4.5	1.2	100%
6	NCT01015547 (6)	2003-7	INF+MTX(19)	68%	10.5	1.5	11	18	4.9	1.8	0.51	100%
			PC1 (20)	70%	8.3	2.3	10	17	5.5	3.1	0.71	100%
			PC2 (20)	55%	10.1	1.8	10	18	6.0	4.1	1.06	100%
7	NCT00095173 (7)	2003-6	ABA (190)	72%	12.4	4.4	16.3	16.2	5.4	4.5	1.3	74%
8	NCT00048542 (8)	2002-5	ADA+MTX(85)	80%	11.4	4.0	12.7	15	5.8	4.2	0.9	100%
			ADA (86)	78%	11.1	3.6	14.3	19.4	6.0	5.3	1.2	0%
9	NCT03780959 (9, 10)	1997-8	ETN (69)	62%	10.5	5.9	10	28	7	5	1.4	0%
10	EUCTR2010-020423-51 (11)	2011-4	ETN (41)	24%	13.3	2.8	5.2	5.4	5	5.8	0.7	0%
11	EUCTR2009-015019-42 (12)	2010-3	GOLI(173)	76%	11.2	>= 0.5	12.2	15	5.6	4.4	1.0	100%
12	NCT03031782 (13)	2018-20	SECU(86)	34%	13.1	>= 0.5	5.5	7.7	4.7	4.9	0.8	65%
13	NCT00988221 (14)	2009-11	TOCI(188)	77%	11.0	4.2	17.6	20.3	6.1	5.2	1.4	79%
14	NCT02592434 (15)	2016-9	TOFA(184)	78%	13*	2.5*	6.0*	10.0*	6*	5.0*	0.9*	65%
15	NCT03773978 (16)	2018-22	BARI(220)	69%	14	2.7	8.8	12	6.5	5.4	1.2	58%

Header Abbreviations. JIA Dur = JIA Duration; LOM = Loss range of motion; AJC = Active joint count; MDG = MD Global; PtWell = Patient wellbeing; CHAQ = Child Health Assessment Questionnaire; %MTX = % of patients used MTX during the trial.

* MTX=Methotrexate; ADA = adalimumab; ETN = Etanercept; GOLI=Golimumab; INF= Infliximab; ABA = Abatacept; TOCI = Tocilizumab; SECU=Secukinumab; TOFA=Tofacitinib; BARI = Baricitinib; PC = placebo control

*Medium is reported instead of mean.

#Studies report MDG or PTWELL on 0-100 scale are converted to 0-10 scale.

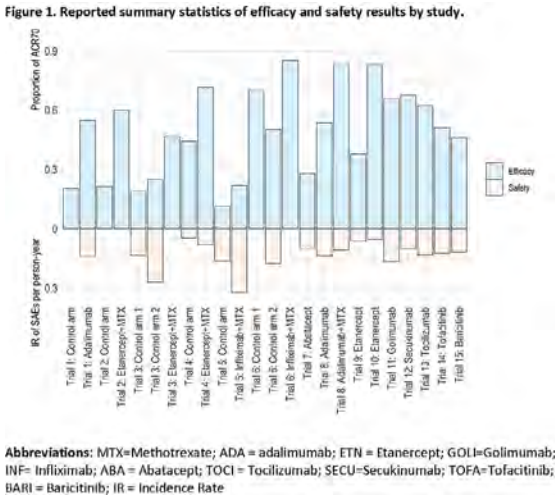
^Trials 1-8 are parallel RCT; 9-15 are withdrawal RCT. For Trials 9-15, only open lead-in phase data are use.

Table 2. League table of estimates for efficacy and safety outcomes from the Bayesian NMAA analyses.

ADA	1.31 (0.23, 7.3)	1.54 (0.18, 12.29)	2.6 (0.85, 7.8)	1.13 (0.3, 4.12)	0.76 (0.18, 3.17)	0.31 (0.04, 2.49)	1.32 (0.16, 10.55)	1.65 (0.2, 12.82)	0.83 (0.1, 6.7)	0.67 (0.08, 5.52)	0.29 (0.09, 0.92)
2.78 (0.3, 31.42)	ETN	1.17 (0.13, 10.84)	1.98 (0.3, 13.16)	0.86 (0.17, 4.15)	0.58 (0.11, 3.17)	0.24 (0.03, 2.22)	1.01 (0.11, 8.89)	1.26 (0.14, 11.42)	0.63 (0.07, 5.58)	0.51 (0.06, 4.61)	0.22 (0.05, 0.97)
0.71 (0.07, 6.89)	0.26 (0.02, 3.21)	GOLI	1.69 (0.18, 16.66)	0.74 (0.1, 5.41)	0.5 (0.06, 4.01)	0.2 (0.02, 2.5)	0.86 (0.07, 10.52)	1.07 (0.09, 12.71)	0.54 (0.04, 6.64)	0.44 (0.04, 5.38)	0.19 (0.03, 1.3)
1.15 (0.14, 9.58)	0.42 (0.03, 5.26)	1.63 (0.12, 22.94)	ADA+MTX	0.44 (0.09, 2.12)	0.29 (0.06, 1.61)	0.12 (0.01, 1.14)	0.51 (0.06, 4.71)	0.63 (0.07, 5.96)	0.32 (0.03, 2.96)	0.26 (0.03, 2.42)	0.11 (0.03, 0.48)
4.08 (0.47, 48.11)	1.47 (0.12, 18.89)	5.75 (0.56, 83.72)	3.53 (0.31, 51.98)	ETN+MTX	0.68 (0.22, 2.11)	0.27 (0.04, 2)	1.17 (0.16, 8.63)	1.46 (0.21, 10.47)	0.73 (0.1, 5.51)	0.59 (0.08, 4.32)	0.26 (0.13, 0.52)
0.95 (0.13, 9.82)	0.34 (0.04, 3.4)	1.34 (0.15, 17.23)	0.82 (0.09, 10.47)	0.23 (0.02, 1.83)	INF+MTX	0.41 (0.05, 3.18)	1.73 (0.22, 13.3)	2.15 (0.28, 16.84)	1.08 (0.13, 8.53)	0.88 (0.11, 7.12)	0.38 (0.15, 0.95)
1.24 (0.11, 14.37)	0.45 (0.03, 4.54)	1.75 (0.13, 27.45)	1.08 (0.07, 15.12)	0.3 (0.02, 2.83)	1.31 (0.12, 11.57)	ABA	4.26 (0.34, 53.23)	5.31 (0.43, 66.89)	2.67 (0.22, 31.79)	2.17 (0.17, 25.72)	0.94 (0.13, 6.29)
0.91 (0.07, 8.98)	0.33 (0.03, 3.76)	1.28 (0.1, 17.18)	0.79 (0.05, 10.57)	0.22 (0.01, 2.32)	0.95 (0.08, 7.8)	0.73 (0.05, 9)	TOCI	1.25 (0.1, 15.1)	0.63 (0.05, 7.5)	0.51 (0.04, 6.34)	0.22 (0.03, 1.48)
1.43 (0.11, 22.19)	0.52 (0.03, 7.62)	2.02 (0.12, 35.56)	1.24 (0.08, 20.77)	0.35 (0.02, 5.24)	1.51 (0.11, 18.61)	1.15 (0.07, 19.49)	1.58 (0.1, 26.98)	SECU	0.5 (0.04, 6.39)	0.41 (0.03, 5.08)	0.18 (0.03, 1.16)
1.01 (0.11, 10.73)	0.36 (0.03, 3.63)	1.42 (0.1, 20.42)	0.87 (0.06, 10.25)	0.25 (0.02, 2.39)	1.06 (0.1, 8.13)	0.81 (0.07, 10.69)	1.11 (0.09, 13.59)	0.7 (0.04, 9.73)	TOFA	0.81 (0.07, 10.61)	0.35 (0.05, 2.43)
1.06 (0.09, 13.31)	0.38 (0.03, 4.84)	1.49 (0.11, 20.41)	0.91 (0.06, 13.14)	0.26 (0.02, 2.76)	1.11 (0.09, 9.48)	0.85 (0.07, 10.69)	1.16 (0.1, 14.83)	0.74 (0.04, 11.89)	1.05 (0.08, 12.59)	BARI	0.43 (0.06, 2.95)
1.68 (0.31, 11.2)	0.61 (0.08, 4.35)	2.37 (0.35, 22.34)	1.46 (0.19, 12.64)	0.41 (0.05, 2.3)	1.77 (0.39, 6.93)	1.36 (0.18, 12.54)	1.86 (0.3, 17)	1.18 (0.12, 12.88)	1.67 (0.25, 13.7)	1.6 (0.23, 14.98)	PC

Abbreviations: MTX=Methotrexate; ADA = adalimumab; ETN = Etanercept; GOLI=Golimumab; INF= Infliximab; ABA = Abatacept; TOCI = Tocilizumab; SECU=Secukinumab; TOFA=Tofacitinib; BARI = Baricitinib; PC = placebo control.

* The upper right triangle (blue shades) reports the odds ratio (OR) and corresponding 90% credible interval (CI) for efficacy (JIA-ACR70) and the lower left triangle (pink shades) reports incidence rate ratio and its 90% CI for safety outcomes (SAE). Bold fonds indicate two-sided 90% CI not including 1. Values <1 suggest the row has better efficacy or safety profile than the column.



Reported summary statistics of efficacy and safety results by study.

References: 1. Burgos-Vargas R, Tse SML, Horneff G, et al. A Randomized, Double-Blind, Placebo-Controlled Multicenter Study of Adalimumab in Pediatric Patients With Enthesitis-Related Arthritis. Arthritis Care Res (Hoboken). 2015;67(11):1503-1512. doi:10.1002/acr.22657 ; 2. Alexeeva E, Horneff G, Dvoryakovskaya T, et al. Early combination therapy with etanercept and methotrexate in JIA patients shortens the time to reach an inactive disease state and remission: results of a double-blind placebo-controlled trial. Pediatr Rheumatol Online J. 2021;19(1):5. doi:10.1186/s12969-020-00488-9 ; 3. Hissink Muller PCE, Brinkman DMC, Schonenberg D, et al. A comparison of three treatment strategies in recent onset non-systemic Juvenile Idiopathic Arthritis: initial 3-months results of the BeSt for Kids-study. Pediatr Rheumatol Online J. 2017;15(1):11. doi:10.1186/s12969-017-0138-4 ; 4. Wallace CA, Giannini EH, Spalding SJ, et al. Trial of early aggressive therapy in polyarticular juvenile idiopathic arthritis. Arthritis Rheum. 2012;64(6):2012-2021. doi:10.1002/art.34343 ; 5. Visvanathan S, Wagner C, Marini J, et al. The effect of infliximab plus methotrexate on the modulation of inflammatory disease markers in juvenile idiopathic arthritis: analyses from a randomized, placebo-controlled trial. Pediatric rheumatology. 2010;8:24-TN: NCT00036374/ClinicalTrials.gov. doi:10.1186/1546-0096-8-24 ; 6. Tynjala P, Vahasalo P, Tarkiainen M, et al. Aggressive combination drug therapy in very early polyarticular juvenile idiopathic arthritis (A-CUTE-JIA): A multicenter randomized clinical trial. Arthritis Rheum. 2009;60((Tynjala P.; Vahasalo P.; Tarkiainen M.; Aalto K.; Kroger L.; Malin M.; Putto-Laurila A.) Helsinki University, Central Hospital, Helsinki, Finland):2051. doi:10.1002/art.27123 ; 7. Ruperto N, Lovell DJ, Quartier P, et al. Abatacept in children with juvenile idiopathic arthritis: a randomised, double-blind, placebo-controlled withdrawal trial. Lancet. 2008;372(9636):383-391. doi:10.1016/S0140-6736(08)60998-8 ; 8. Lovell DJ, Ruperto N, Goodman S, et al. Adalimumab with or without methotrexate in juvenile rheumatoid arthritis. N Engl J Med. 2008;359(8):810-820. doi:10.1056/NEJMoa0706290 ; 9. Lovell DJ, Giannini EH, Reiff A, et al. Etanercept in children with polyarticular juvenile rheumatoid arthritis. Pediatric Rheumatology Collaborative Study Group. N Engl J Med. 2000;342(11):763-769. doi:10.1056/NEJM200003163421103 ; 10. NCT03780959. Safety and Efficacy of Etanercept (Recombinant Human Tumor Necrosis Factor Receptor Fusion Protein [TNFR: fc]) in Children With Juvenile Rheumatoid Arthritis (JRA). https://clinicaltrials.gov/show/NCT03780959. Published online 2018. https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01918680/full ; 11. Horneff G, Foeldvari I, Minden K, et al. Efficacy and safety of etanercept in patients with the enthesitis-related arthritis category of juvenile idiopathic arthritis: results from a phase III randomized, double-blind study. Arthritis Rheumatol. 2015;67(8):2240-2249. doi:10.1002/art.39145 ; 12. Brunner HI, Ruperto N, Tzaribachev N, et al. Subcutaneous golimumab for children with active polyarticular-course juvenile idiopathic arthritis: results of a multicentre, double-blind, randomised-withdrawal trial. Ann Rheum Dis. 2018;77(1):21-29. doi:10.1136/annrheumdis-2016-210456 ; 13. Brunner HI, Foeldvari I, Alexeeva E, et al. Secukinumab in enthesitis-related arthritis and juvenile psoriatic arthritis: a randomised, double-

blind, placebo-controlled, treatment withdrawal, phase 3 trial. Ann Rheum Dis. Published online August 12, 2022: annrheumdis-2022-222849. doi:10.1136/ard-2022-222849 ; 14. Brunner HI, Ruperto N, Zuber Z, et al. Efficacy and safety of tocilizumab in patients with polyarticular-course juvenile idiopathic arthritis: results from a phase 3, randomised, double-blind withdrawal trial. Ann Rheum Dis. 2015;74(6):1110-1117. doi:10.1136/annrheumdis-2014-205351 ; 15. Ruperto N, Brunner H, Synoverska O, et al. Tofacitinib in juvenile idiopathic arthritis: a double-blind, placebo-controlled, withdrawal phase 3 randomised trial. Lancet (london, england). 2021;398(10315):1984-1996. doi:10.1016/S0140-6736(21)01255-1 ; 16. Ramanan AV, Quartier P, Okamoto N, et al. Baricitinib in juvenile idiopathic arthritis: an international multi-centre phase 3, randomized, double-blind, placebo-controlled, withdrawal, efficacy, and safety trial. Lancet, In press.

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Abstract Number: 0972

Increased Incidence of Inflammatory Arthritis After COVID-19 in a Colombian Population

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Epidemiology & Public Health Poster II
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Background/Purpose: An increase in the incidence of autoimmune diseases after COVID-19 has been reported. Since many diseases exhibit population-specific causal effect sizes, we aimed to evaluate the incidence trends of inflammatory arthritis (IA), including rheumatoid arthritis (RA), after COVID-19 in a large admixed Colombian population.

Methods: Data analysis for this retrospective, population-based cohort study was carried out using the COOSALUD EPS registry. COOSALUD EPS is a health insurance company, belonging to the subsidized regime in Colombia. The registry includes demographic and epidemiological data on diagnoses identified during admission and defined by the *International Classification of Diseases* (ICD-10). The following codes were selected for analyses: M059, seropositive RA, defined by the presence of rheumatoid factor (RF) or anti-citrullinated protein antibody (ACPA); M069, unspecified RA, in which RF and ACPA were not confirmed; M060 seronegative RA, in which RF and ACPA were negative; and other RA-related diagnoses: M064, M139, M068, M058, M130 and M053. All the diagnosis were made by qualified rheumatologists. The study period was limited to January 01, 2020, through December 31, 2022. Incidence rates (IRs) and incidence rate ratios (IRRs) were assessed. IRRs were computed by comparing the IR of those who had COVID-19 prior to the IA diagnosis and those who did not have COVID-19 prior to the IA diagnosis. A Cox survival model was built to evaluate the influence of age, gender, and COVID-19 vaccination status on the development of IA.

Table. Incidence rates (IRs) of inflammatory arthritis (IA) during the pandemic period (2020-2022) according to previous diagnosis of COVID-19, and the incidence rate ratios (IRRs).

Diagnosis	IR in patients without previous COVID-19	IR in patients with previous COVID-19	IRR	95% CI
RA, seropositive	1.03	1.65	**1.60**	**1.16 -2.22**
RA, unspecified	0.44	1.29	**2.93**	**2.04 - 4.19**
RA, seronegative	0.06	0.13	2.19	0.71 - 6.81
Other RA-related diagnosis	0.06	0.13	2.08	0.67 - 6.46
Overall IA				
M	0.52	1.16	**2.21**	**1.22 - 3.98**
F	2.61	4.73	**1.81**	**1.40 - 2.33**
Total	1.60	3.21	**2.01**	**1.59 - 2.53**

Bold indicates significance.

Results: The entire population study comprised 3,335,084 individuals, of whom 1,720,579 (51.59%) were women. The IRs of IA during the pandemic period (2020-2022) according to a previous diagnosis of COVID-19 and the respective IRRs are shown in the table. The associations remained significant after controlling for sex. The fitted Cox survival model showed that all the variables considered were significant ($p< 0.05$). The age groups estimates were increased until the age group of 51-60 years (HR: 9,163 95% CI: 7,245 - 11,589) and then decreased in the age group 61 years or older (HR: 5,364, 95% CI: 4,243 - 6,781) compared to those within 18-30 years. Men were less at risk than women to develop IA (HR: 0,2115, 95% CI: 0,182 - 0,246). The greater time since COVID-19 diagnosis was associated with a lower likelihood of developing IA (HR: 0,9986, 95% CI: 0,998 - 0,999). In vaccinated population, the probability of developing IA was reduced from HR: 3.345, 95% CI: 1.617 - 6.918 to HR: 3.232, 95% CI: 1.281 - 8.155 compared to those who did not have COVID-19. The model fitted well (Likelihood ratio test =2.074 $p< 0,05$; concordance = 0.77, $p< 0,05$).

Conclusion: Our findings indicate that the incidence of IA, including RA, increased following COVID-19, with the greatest increase occurring before the first year post-covid. Women were more susceptible than men. COVID-19 vaccination appears to be a protective factor.

Disclosure: J. Marin: COOSALUD EPS, 3; **E. Mazenett**: COOSALUD EPS, 3; **M. Sarmiento**: COOSALUD EPS, 3; **R. Perez**: COOSALUD EPS, 3; **C. Morales**: COOSALUD EPS, 3, 3; **J. Dominguez**: COOSALUD EPS, 3; **J. Salazar**: None; **J. Anaya**: COOSALUD EPS, 3.

Abstract Number: 0973

Real-World Comparative Effectiveness Study of Janus Kinase Inhibitors Compared to Biologic Disease Modifying Antirheumatic Drugs in Korean Patients with Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Although clinical trials have shown similar effectiveness between Janus kinase inhibitors (JAKi) and biologic disease-modifying anti-rheumatic drugs (bDMARDs), the choice between these two options is currently a crucial question in real-world practice. However, there is a lack of sufficient real-world evidence comparing the outcomes and safeties of these treatments in patients with rheumatoid arthritis (RA). This study aimed to assess the efficacy and safety of JAKi compared to bDMARDs in Korean patients with RA who have not previously received either JAKi or bDMARDs.

Methods: In this prospective, multicenter, quasi-experimental study conducted at 17 centers in South Korea, we enrolled patients who had an inadequate response to Methotrexate (MTX) and initiated either Janus kinase inhibitors (JAKi) or biologic disease-modifying anti-rheumatic drugs (bDMARDs). The primary objective of the study was to assess the proportion of patients achieving low disease activity (LDA) at 24 weeks, as measured by the disease activity score (DAS) 28 erythrocyte sedimentation rate (ESR). Secondary endpoints included remission rate at 24 weeks, as well as LDA rates at 12 weeks and 48 weeks. Furthermore, we compared the safety profiles of the two treatment groups during the follow-up period.

Results: A total of 506 patients were enrolled in the study, with 253 patients in each of the JAKi and bDMARDs groups between April 2020 and August 2022. Among the bDMARDs users, 60.1% received TNFi (n = 152), while 39.9% received non-TNFi (n = 101). In the JAKi group, 48.6% received baricitinib (n = 123), 24.9% received tofacitinib (n = 63), and 26.5% received upadacitinib (n = 67). The two groups were comparable in terms of age (53.2 vs. 54.2) and the proportion of females (83.0% vs. 86.2%). Most patients in both groups received combination therapy with MTX (89.3% in both groups) and glucocorticoids (89.3% vs. 83.8%). At baseline, the bDMARDs group had slightly higher DAS28-ESR compared to the JAKi group (6.1 vs. 5.9, p=0.039). The primary endpoint, achieving LDA at 24 weeks, was observed in 48.2% of the JAKi group and 42.7% of the bDMARDs group (p=0.246). Regarding secondary endpoints, the remission rate at 24 weeks was 28.9% in the JAKi group and 27.3% in the bDMARDs group. Among patients receiving glucocorticoids at baseline (n=438), the rates of achieving glucocorticoid-free remission at 24 weeks were similar between the two groups (6.2% in bDMARDs and 8.5% in JAKi). The JAKi group showed a higher rate of achieving LDA at 12 weeks compared to the bDMARDs group, with marginal significance (45.9% vs. 38.3% based on DAS28 ESR, p=0.105). Currently, these patients are undergoing follow-up to gather data on the effectiveness and safety of the treatment at the 48-week mark.

Conclusion: In this real-world study involving Korean patients with RA eligible for targeted therapy, the profiles of JAKi users were similar to those of bDMARDs users. The study found that JAKi demonstrated comparable effectiveness and safety to bDMARDs users.

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Abstract Number: 0974

Validation of Boolean 2.0 Criteria for Assessing Remission and Predicting Quality of Life in Korean Patients with Rheumatoid Arthritis Undergoing Targeted Therapy

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SESSION INFORMATION
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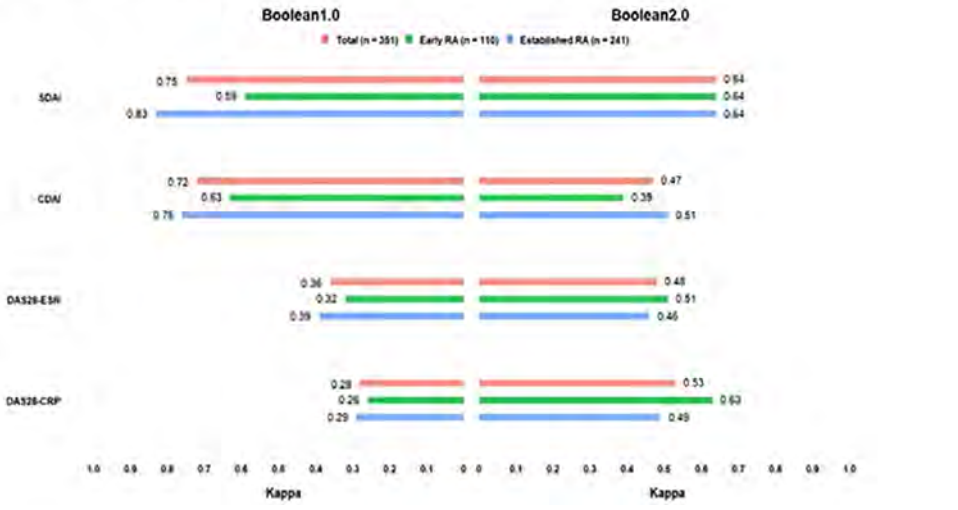
Background/Purpose: The management of rheumatoid arthritis (RA) focuses on achieving remission as a treatment goal. The updated ACR/EULAR remission definition (Boolean criteria 2.0) has raised the threshold for patient global assessment (PtGA) to 2 cm and received endorsement from ACR and EULAR. The revised Boolean 2.0 criteria classify more patients as achieving remission and show increased agreement with index-based criteria in US and European patients. This study aimed to validate the Boolean 2.0 criteria, assess their agreement with index-based remission criteria, and evaluate their predictive value for quality of life (QoL) compared to Boolean 1.0 criteria in Korean patients receiving targeted therapy.

Methods: Data from a multicenter prospective study of Korean patients with RA initiating biologic disease-modifying antirheumatic drugs or Janus kinase inhibitors were analyzed. Remission rates according to Boolean 2.0 and Boolean 1.0 criteria, as well as other index-based remission criteria, were measured at 24 weeks. Agreement between Boolean 2.0 criteria and index-based criteria was analyzed and compared with Boolean 1.0 criteria. Additionally, the likelihood ratio (LR) of Boolean 2.0 criteria in predicting improved QoL (health assessment questionnaire [HAQ] score ≤0.5 or EQ-5D =1) at 48 weeks was estimated and compared to Boolean 1.0 criteria.

Figure. Kappa values representing agreement between Boolean criteria and index based remission.



Results: A total of 351 RA patients were included, with a mean age of 53.2 years, and 86.9% were female. Boolean 2.0 criteria showed better agreement than Boolean 1.0 criteria for remission based on DAS28-ESR (kappa 0.48 vs. 0.36) and DAS28-CRP (kappa 0.53 vs. 0.28). However, Boolean 1.0 criteria exhibited higher concordance with SDAI (kappa 0.75) or CDAI (kappa 0.72) than Boolean 2.0 criteria (kappa with SDAI 0.64 and kappa with CDAI 0.47, respectively). Regarding predictive value for better QoL, remission based on Boolean 1.0 criteria showed higher LR compared to remission based on Boolean 2.0 criteria (6.01 vs. 2.49 for HAQ ≤0.5 and 3.53 vs. 2.37 for EQ-5D =1, respectively).

Conclusion: Among Korean patients with RA initiating targeted therapy, the Boolean 2.0 criteria showed enhanced agreement with remission assessments based on DAS28-ESR or DAS28-CRP, while the agreement with remission based on SDAI or CDAI was not improved compared to the Boolean 1.0 criteria. Furthermore, remission defined by the Boolean 1.0 criteria demonstrated a higher predictive value for improved QoL when compared to the Boolean 2.0 criteria.

Disclosure: S. Cho: None; **Y. Song**: None; **J. Han**: None; **H. Kim**: None; **E. Nam**: None; **Y. Sung**: Bristol-Myers Squibb(BMS), 5, Eisai, 5, JW Pharmaceutical, 5, Pfizer, 5.

Abstract Number: 0975

Association of HLA-DRB1 Alleles with Ischemic Events and Mortality in a Multi-ethnic Community-living Population

Manmeet Kaur[1], Ronit Katz[2], Michael H. Criqui[1], Maripat Corr[1], Wendy S. Post[3], Matthew Budoff[4], Gerald P. Morris[5] and Jan Hughes-Austin[5], [1]University of California San Diego, San Diego, CA, [2]University of Washington, Seattle, WA, [3]Johns Hopkins University School of Medicine, Baltimore, MD, [4]University of California Los Angeles, Los Angeles, CA, [5]University of California San Diego, La Jolla, CA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Epidemiology & Public Health Poster II
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Session Time: 9:00AM–11:00AM

Background/Purpose: Human leukocyte antigen (HLA) DRB1 alleles with specific common amino acids referred to as "the shared epitope (SE)", have been linked to cardiovascular mortality in inflammatory polyarthritis. Thesehaplotypes associate with ST-elevation myocardial infarction in the general population. However, less is known about the HLA-DRB1 alleles with other cardiovascular (CV) events. We aimed to determine associations of the HLA-DRB1 SE alleles (04:04, 04:05, 04:01, 04:08, 01:01, 14:02, 10:01, 03:01, 03:02) with ischemic events and mortality in a multi-ethnic community-living population.

Methods: Within the Multi-Ethnic Study of Atherosclerosis (MESA), a prospective cohort study designed to determine risk factors and progression of subclinical and clinical CVD, a subset of 955 participants who completed the Abdominal Aortic Calcium Ancillary Study and had complete measures of HLA typing and cardiac imaging were evaluated. We defined shared epitope positive [SE(+)] as being positive for any of the HLA-DRB1 SE alleles; and evaluated associations of SE positivity with all-cause mortality, CVD death (defined as secondary to stroke, coronary heart disease, other atherosclerotic death, or other CVD death), non-CVD death, angina, and myocardial infarction (MI) using Cox proportional hazards models. The covariates in our fully adjusted analysis included age, sex, race/ethnicity, diabetes mellitus, systolic blood pressure, current smoking, ever having cancer, eGFR, current use of anti-hypertensive medications, nonsteroidal anti-inflammatory drugs, and IL-6.

All-cause mortality		
Events / P-Y	30 / 520	18 / 435
Event rate (per 1000 P-Y)	3.79	2.71
Age, sex, race/ethnicity	1.00 (ref)	0.69 (0.38, 1.27)
Fully Adjusted	1.00 (ref)	0.74 (0.40, 1.37)
CVD death		
Events / P-Y	8 / 520	3 / 435
Event rate (per 1000 P-Y)	1.01	0.45
Age, sex, race/ethnicity	1.00 (ref)	0.37 (0.08, 1.79)
Fully Adjusted	1.00 (ref)	0.38 (0.08, 1.88)
Non-CVD death		
Events / P-Y	22 /520	15 / 435
Event rate (per 1000 P-Y)	2.78	2.26
Age, sex, race/ethnicity	1.00 (ref)	0.78 (0.40, 1.52)
Fully Adjusted	1.00 (ref)	0.85 (0.43, 1.67)
CVD events		
Angina		
Events / P-Y	22 / 520	28 /435
Event rate (per 1000 P-Y)	2.86	4.39
Age, sex, race/ethnicity	1.00 (ref)	1.45 (0.82, 2.56)
Fully Adjusted	1.00 (ref)	1.40 (0.79, 2.48)
Myocardial infarction		
Events / P-Y	18 / 520	14 / 435
Event rate (per 1000 P-Y)	2.31	2.13
Age, sex, race/ethnicity	1.00 (ref)	0.88 (0.43, 1.81)
Fully Adjusted	1.00 (ref)	0.88 (0.43, 1.81)

Associations of HLA-DRB1 alleles with Mortality and CVD Events in the Multi-Ethnic Study of Atherosclerosis

Results: Among the 955 MESA participants, 46% were positive for the shared epitope—38% carried a single allele, and 8% carried two alleles. Average age was 60±9, 47% were women, 51% were White, 9% were Asian, 16% were Black, and 24% were Hispanic/Latino. Age, sex, blood pressure, cholesterol, and inflammatory markers (CRP, TNF-α, IL 6) were similar between the SE(+) and SE(-) participants, but racial distributions differed where SE(+) had a higher proportion of white (51% vs 38%) and lower proportion of Asian (9% vs 17%) and Black (16% vs 21%) participants compared to SE(-). Both SE (+) and (-) had 24% Hispanic/ Latino. Being positive for the SE was not significantly associated with a higher risk of all-cause mortality, CVD death, non-CVD death, angina, or MI compared to those who were SE negative. The mean follow-up time was 15.3 ± 0.9 years.

Conclusion: HLA-DRB1 SE alleles were not associated with a higher risk of ischemic events or mortality in a multi-ethnic community-living population.

Disclosure: M. Kaur: None; **R. Katz**: None; **M. H. Criqui**: None; **M. Corr**: None; **W. S. Post**: None; **M. Budoff**: None; **G. P. Morris**: CareDx, 5, ThermoFisher/One Lambda, 1, 5, 12, travel support; **J. Hughes-Austin**: None.

Abstract Number: 0976

Sarcopenia and All-Cause Mortality in US Adults with and Without Rheumatoid Arthritis

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SESSION INFORMATION
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Session Title: Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Table 1. Participant characteristics

Characteristic	Non-RA, N = 11351(96%)			RA, N = 558(3.8%)		
	Nonsarcopenic 10215 (93%)[1]	Sarcopenia 1136 (7.1%)[1]	P Value[2]	Nonsarcopenic 464 (88%)[1]	Sarcopenia 94 (12%)[1]	P Value[2]
Age	41 (31, 51)	51 (41, 60)	**<0.001**	51 (42, 59)	54 (49, 65)	0.079
Female	4,953 (49%)	542 (45%)	**0.049**	272 (54%)	60 (65%)	0.2
Race			**<0.001**			**0.001**
Non-Hispanic White	4,978 (72%)	376 (61%)		195 (68%)	32 (67%)	
Non-Hispanic Black	2,333 (11%)	43 (2.3%)		170 (19%)	8 (4.5%)	
Hispanic	2,516 (12%)	673 (29%)		80 (7.7%)	51 (22%)	
Other/multiracial	388 (4.7%)	44 (7.0%)		19 (5.8%)	3 (6.8%)	
Poverty (PIR < 1.85)	3,719 (27%)	601 (39%)	**<0.001**	221 (39%)	62 (55%)	0.076
High school graduate	7,721 (85%)	558 (67%)	**<0.001**	288 (73%)	45 (67%)	0.3
Obesity	3,136 (29%)	697 (67%)	**<0.001**	218 (44%)	59 (72%)	**0.001**
Currently Smoking	2,728 (27%)	224 (22%)	**0.024**	147 (37%)	25 (36%)	>0.9
Physical Activities			**<0.001**			0.063
>300 min/wk	4,486 (48%)	301 (27%)		168 (40%)	21 (23%)	
150 - 300 min/wk	1,629 (17%)	161 (16%)		61 (13%)	14 (20%)	
<150 min/wk	4,100 (35%)	674 (56%)		235 (47%)	59 (57%)	
Hypertension	3,070 (27%)	544 (49%)	**<0.001**	256 (48%)	67 (67%)	**0.015**
Diabetes mellitus	839 (5.8%)	270 (23%)	**<0.001**	88 (12%)	32 (27%)	**0.005**
Cardiovascular Disease	562 (4.6%)	143 (13%)	**<0.001**	84 (16%)	27 (27%)	0.089
Low HDL	3,187 (31%)	457 (40%)	**<0.001**	168 (34%)	34 (38%)	0.4
eGFR < 60	275 (2.2%)	42 (4.5%)	**<0.001**	29 (3.6%)	9 (10.0%)	**0.014**

[1] median (IQR) for Age; n (%) for categorical data; All percentage are weighted, all counts are unweighted

[2] Wilcoxon rank-sum test for complex survey samples; chi-squared test with Rao & Scott's second-order correction

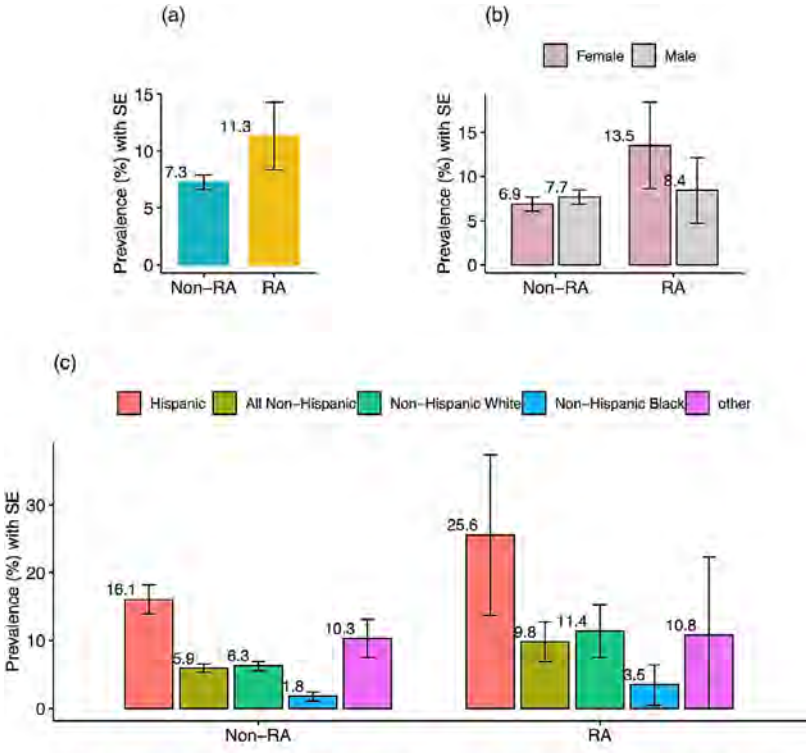

Figure 1. Age-standardized prevalence of sarcopenia among participants with and without RA (a), stratified by sex (b) and race/ethnicity (c): NHANES 1999-2006.

Background/Purpose: Sarcopenia, which refers to the loss of muscle strength and mass, has been linked to adverse health outcomes. Although several systemic reviews have reported a high prevalence of sarcopenia in rheumatoid arthritis (RA) patients, the impact of sarcopenia on all-cause mortality in this population remains unclear. This study aims to determine the prevalence of sarcopenia in RA patients in a nationally representative cohort and evaluate its association with all-cause mortality in US adults with and without RA.

Methods: The study utilized data from the National Health and Nutrition Examination Survey (NHANES) 1999–2006, along with linked mortality data from the National Death Index up to the end of 2019. Sarcopenia was defined using the Foundation for the National Institutes of Health (FNIH) 2014 sarcopenia criteria: appendicular lean mass (ALM) divided by BMI (< 0.789 in men;< 0.512 in women). Rheumatoid arthritis cases were self-reported physician diagnoses. Population estimates, including prevalence and hazard ratio (HR), were generated by incorporating sample weights and cluster information. Four multivariate Cox proportional hazard models were constructed successively to produce adjusted HRs.

Results: The final cohort included 11909 participants aged 20 to 69, among which were 558 cases of rheumatoid arthritis (table 1).Figure 1 indicates that individuals with RA had a significantly higher age-standardized prevalence of sarcopenia compared to those without RA (11.3 % vs. 7.3 %). Notably, Hispanics had a significantly higher prevalence of sarcopenia

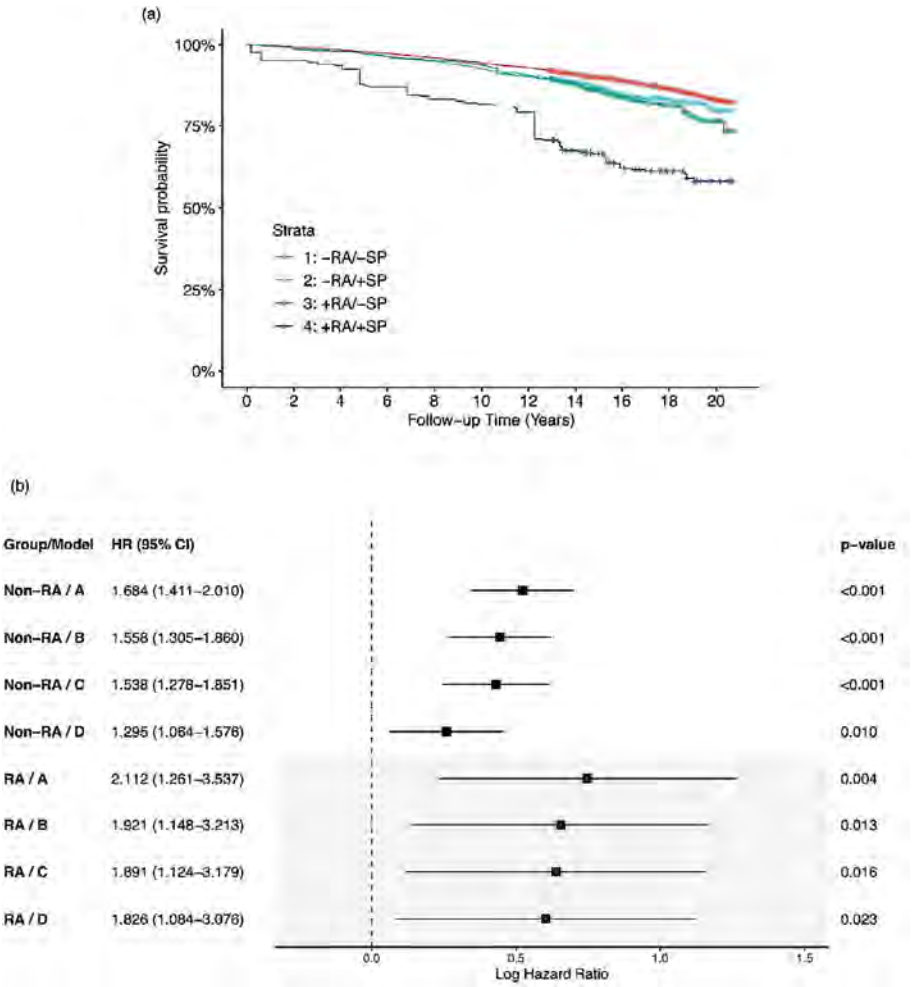

Figure 2. (a) Kaplan-Meier curves of survival probability stratified by rheumatoid arthritis (RA) and sarcopenia (SP) status. (b) Association of sarcopenia with all-cause mortality in non-RA versus RA group, as depicted by forest plot of log hazard ratios across 4 models: Model A adjusted for age and sex; Model B adjusted for age, sex, race/ethnicity, poverty status, and education level; Model C adjusted for all variables in model B, adding health behavior (smoking and physical activity); Model D adjusted for all variables in model C, adding comorbidities including obesity, diabetes mellitus, hypertension, cardiovascular disease, hyperlipidemia, and chronic kidney disease.

than the rest of the population, with rates of 25.6% and 16.1% among individuals with RA and non-RA, respectively. Regarding survival analysis, the median follow-up time for RA and non-RA group was 17 and 16.8 years. After adjusting for age and sex, the unweighted Kaplan-Meier curve revealed that sarcopenic RA patients had the highest overall mortality (Figure 2a). Across all four adjusted Cox models, individuals with sarcopenia had a higher risk of mortality regardless of whether they had RA or not (Figure 2b). Despite all four Cox models providing higher estimates of HRs for sarcopenia in the RA group as compared to the non-RA group, the differences were not statistically significant given the overlapping confidence intervals.

Conclusion: In a nationally representative cohort, the study found a higher prevalence of sarcopenia in individuals with RA, and a significant increase in all-cause mortality associated with sarcopenia with or without RA.

Disclosure: Q. Xu: None; **X. Du**: None.

Abstract Number: 0977

Prevalence of Arthritis in the United States: National Estimates from a Population-based Study

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Arthritis is the number 1 cause of disability among U.S. adults and reported to cost > $300 billion in direct and indirect costs in 2013. Theis et al. found that the prevalence of arthritis in the US grew from 54.4 million in 2013-2015 to 58.5 million in 2016-2018. These estimates were derived from the U.S. CDC National Health Interview Survey (NHIS), which has recently undergone a total redesign. With the updated NHIS, we aimed to query an updated nationally-representative estimate of the prevalence and burden of arthritis in the U.S. adult population.

Methods: We identified patients over the age of 18 years in the 2019 and 2021 National Health Interview Survey (NHIS) who had doctor-diagnosed arthritis (n=15,822; 21.3%; excluded 2020 due to unclear impact of COVID-19 on NHIS completion). Sampling weights were used to create nationally representative estimates. Unadjusted and age-standardized estimates of arthritis prevalence were generated. Sociodemographic and health characteristics were analyzed. We compared with previous years' prevalence estimates.

Results: During 2019 and 2021, an estimated 53.7 million people over the age of 18 had arthritis (21.3%; 18.8% age-standardized; **Table 1**). This represents a 5 million person decrease from 2016-2018 (58.5 million; **Figure 1**), but is similar to the estimates from 2013-2015 (54.4 million; **Figure 1**). Arthritis prevalence was greater than 50% in adults with ≥3 ADL limitations (65.2%; **Table 1**) and adults with 2 IADL limitations (50.2%; **Table 1**). Arthritis was most prevalent in adults aged ≥65 years (47.6%), non-Hispanic whites (24.9%), adults unable to work or disabled (49.5), and adults who reported fair or poor health (48.9%)

Table 1: Annual prevalence of doctor-diagnosed arthritis[1] in adults ≥18, unadjusted and age-standardized[2], National Health Interview Survey (NHIS), United States, 2019, 2021

Characteristic	Unweighted no. of adults with arthritis	No. of adults with arthritis in population (millions)[3]	Distribution among adults with arthritis (%)[3]	Prevalence of doctor-diagnosed arthritis, % (95% CI)	
				Unadjusted	Age-standardized
Overall	15822	53.7	100	21.3 (20.9-21.8)	18.8 (18.3-19.4)
Sociodemographic characteristics					
Age group, yrs					
18-44	1452	6.5	12.1	5.6 (5.3-6.0)	-
45-64	5505	21.2	39.4	25.9 (25.1-26.7)	-
≥65	8865	26.1	48.6	47.6 (46.7-48.5)	-
Sex					
Male	6113	22.0	40.9	18.1 (17.5-18.7)	16.4 (15.7-17.2)
Female	9709	31.8	59.1	24.4 (23.8-25.1)	21.0 (20.2-21.8)
Race/Ethnicity					
Hispanic or Latino, any race	1198	5.3	9.8	12.5 (11.7-13.4)	14.7 (13.4-16.2)
White, NH	12090	39.4	73.4	24.9 (24.3-25.4)	20.3 (19.6-21.0)
Black, NH	1760	6.1	11.3	20.6 (19.4-21.8)	19.8 (18.2-21.5)
Asian or Other Pacific Islander, NH	374	1.6	2.9	10.6 (9.4-12.1)	10.3 (8.5-12.6)
American Indian or Alaska Native, NH	118	0.4	0.7	22.3 (15.1-31.6)	21.5 (14.5-31.7)
Other/Multiple races, NH	282	1.0	1.8	20.2 (17.6-23.0)	22.9 (18.5-27.8)
Sexual identity					
Lesbian or gay	204	0.6	1.2	15.6 (13.3-18.1)	17.9 (14.1-22.4)
Straight	14753	51.0	96.3	21.6 (21.1-22.2)	18.8 (18.2-19.4)
Bisexual	159	0.6	1.1	12.2 (10.2-14.6)	24.2 (18.7-30.1)
Something else/Don't know the answer	199	0.7	1.4	18.9 (15.9-22.2)	19.5 (15.3-24.6)
Education					
Less than high school graduate	1854	7.5	14.1	27.4 (26.0-28.9)	21.2 (19.3-23.3)
High school graduate or equivalent	4490	16.1	30.1	23.0 (22.2-23.9)	20.1 (19.0-21.3)
Some college or associate degree	4890	16.0	30.0	22.2 (21.5-23.0)	20.7 (19.6-21.7)
Bachelor's degree or greater	4501	13.7	25.8	17.0 (16.4-17.7)	15.3 (14.5-16.1)
Employment status					
Employed/Self-employed	5185	19.6	37.8	12.7 (12.2-13.1)	14.8 (14.0-15.6)
Unemployed	157	0.7	1.3	11.2 (9.3-11.3)	16.6 (12.3-21.7)
Unable to work/Disabled	2046	7.4	14.2	49.5 (47.5-51.4)	41.8 (38.5-45.2)
Other[4]	8007	24.4	46.8	35.7 (34.8-36.6)	20.1 (18.9-21.3)
Income-to-poverty ratio					
Poor/Near poor (<125%)	2918	9.4	17.4	25.7 (24.5-26.9)	25.0 (23.4-26.7)
Low income (125% to <200%)	2550	8.5	15.8	23.7 (22.6-24.8)	20.6 (19.1-22.2)
Middle income (200% to <400%)	4822	16.9	31.5	22.2 (21.5-23.0)	19.7 (18.7-20.7)
High income (≥400%)	5532	19.0	35.3	18.3 (17.8-19.0)	15.7 (15.0-16.5)
Health characteristic					
Body Mass Index (kg/m2)					
Under/Healthy weight (<25.0)	4045	13.0	24.9	15.8 (15.2-16.5)	14.8 (14.0-15.7)
Overweight (25.0- <30.0)	5069	17.2	32.9	20.7 (20.0-21.3)	17.1 (16.2-18.0)
Obese (≥30.0)	6284	22.1	42.2	27.7 (26.9-28.6)	24.8 (23.8-25.9)
Joint symptoms					
Yes	12728	43.3	80.6	37.6 (36.8-38.4)	29.8 (28.9-30.9)
No	3094	10.4	19.4	7.6 (7.3-8.0)	8.0 (7.4-8.5)
Activities of daily living (ADL) disability					
0	5794	20.6	38.3	11.0 (10.6-11.4)	11.6 (11.1-12.2)
1-2	5227	17.4	32.4	43.1 (41.9-44.3)	31.8 (30.0-33.7)
≥3	4801	15.8	29.4	65.2 (63.8-66.6)	52.2 (48.7-55.9)
Instrumental activities of daily living (IADL) disability					
0	11825	40.2	74.8	18.1 (17.6-18.6)	16.5 (15.9-17.0)
1	1803	6.0	11.2	40.3 (38.4-42.2)	34.4 (31.8-37.2)
2	2194	7.6	14.1	50.2 (48.2-52.2)	39.3 (36.3-42.5)
Self-rated health					
Excellent/Very good	5352	17.5	32.6	12.0 (11.6-12.4)	12.3 (11.7-12.9)
Good	5403	18.5	34.4	26.6 (25.8-27.5)	21.7 (20.6-22.8)
Fair/poor	5057	17.7	33.0	48.9 (47.5-50.3)	38.1 (35.9-40.3)

[1] Answered yes to "Have you ever been told by a doctor or other health professional that you had some form of arthritis, rheumatoid arthritis, gout, lupus, or fibromyalgia?"

[2] age-standardized using 2000 U.S. projected adult population, combined into three age groups: 18-24, 45-64, ≥65

[3] may not sum to total due to rounding errors

[4] Retired, student, or taking care of house/family

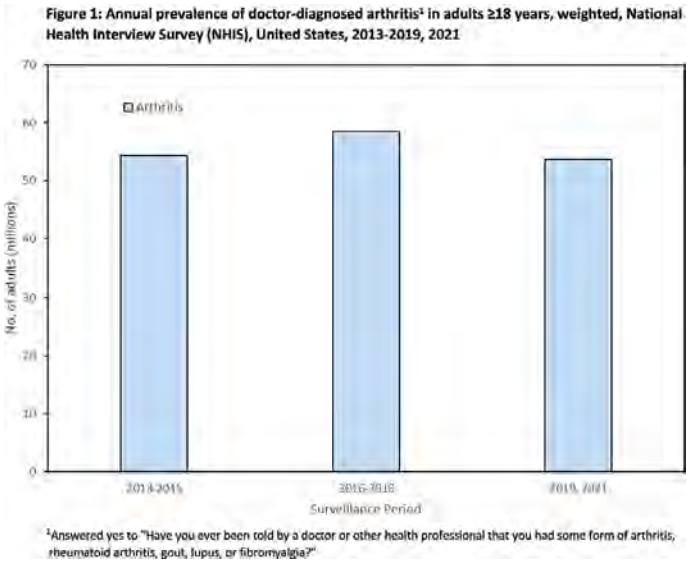

Figure 1: Annual prevalence of doctor-diagnosed arthritis[1] in adults ≥18 years, weighted, National Health Interview Survey (NHIS), United States, 2013-2019, 2021

[1]Answered yes to "Have you ever been told by a doctor or other health professional that you had some form of arthritis, rheumatoid arthritis, gout, lupus, or fibromyalgia?"

Conclusion: Arthritis has significant impact on disability and functional limitation in US adults. Surprisingly, we found stabilization of arthritis prevalence in the U.S. from the 2019 and 2021 national estimates rather than an anticipated increase. Stratified analyses by age, sex, and other demographic characteristics need to be performed to understand as to which subgroup accounts for this recent stabilization/decrease in arthritis prevalence.

Disclosure: S. Chandrupatla: None; **K. Rumalla**: None; **J. Singh**: Other, 2, 6, 11, 11, 12, Adaptimmune Therapeutics, GeoVax Labs, Pieris Pharmaceuticals, Enzolytics Inc., Seres Therapeutics, Tonix, Charlotte's Web, 12, Atai life sciences, kintara therapeutics, Intelligent Biosolutions, Acumen pharmaceutical, TPT Global Tech, Vaxart pharmaceuticals, Atyu biopharma, 12, speaker's bureau of Simply Speaking, other, 12, received institutional research support from Zimmer Biomet Holdings. JAS received food and beverage payments from Intuitive Surgical Inc./Philips Elec, Other, 12, Schipher, Crealta/Horizon, Medisys, Fidia, PK Med, Two labs Inc., Adept Field Solutions, Clinical Care options, Clearview healthcare partners, Putnam.

Abstract Number: 0978

Identifying Important Clinical Features for Predicting Remission in Patients with Rheumatoid Arthritis Treated with Biologics Using Machine Learning Model

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
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Background/Purpose: Biologic disease-modifying antirheumatic drugs (bDMARDs) offer promising results for rheumatoid arthritis (RA) patients in general, but a substantial percentage of patients do not respond to them. It is important to predict the response before the treatment so that unnecessary adversities for the patients and costs for the healthcare system can be avoided. We developed a model to predict remissions in patients treated with bDMARDs and to identify important clinical features associated with remission using several machine learning (ML) models system that works with readily-available demographic and clinical factors for prediction of response to DAS-28.

Methods: We gathered the follow-up data of 1,000 patients treated with bDMARDs (etanercept, adalimumab, golimumab, infliximab, abatacept, and tocilizumab) from KRRD. Patients were recruited from public hospitals in Kuwait between February 2013 to September 2022. Remission (DAS-28 less than 2.6) was predicted at 1-year follow-up using baseline clinical data obtained at the time of enrollment. Machine learning methods system (including: lasso,

Table 1. KRRD RA Patients Demographics

Characteristic	N = 1,968
Gender	
female	1,278 (65%)
male	690 (35%)
BMI	28.4 (25.2, 32.7)
Morning Stiffness (mg)	1 (0, 15)
VAS	0 (0, 3)
ESR	25 (11, 44)
CRP	3.4 (1.0, 7.9)
HAQ	0.88 (0.50, 1.38)
Patient's Global Assessment	0 (0, 4)
Physician's Global Assessment	0 (0, 2)
DAS28	2.55 (1.87, 3.67)
RF	
Negative	405 (22%)
Positive	1,409 (78%)
ANTI CCP	
Negative	508 (33%)
Positive	1,049 (67%)
ANA	
Negative	1,058 (69%)
Positive	471 (31%)
Smoking	150 (10%)
Family History	
Negative	1,178 (82%)
Positive	252 (18%)
MedCond-Thyroid Disease	245 (12%)
MedCond-PUD	33 (1.7%)
MedCond-Osteoporosis	131 (6.7%)
MedCond-OA	160 (8.1%)
MedCond-Hypertension	429 (22%)
MedCond-Hyperlipidemia	213 (11%)
MedCond-DM	393 (20%)
MedCond-B.Asthma	205 (10%)
Age (years)	56 (47, 65)
Disease duration (years)	10 (7, 13)
DAS28.Group	
DAS28 < 3.2	1,328 (68%)
DAS28 >= 3.2	633 (32%)
TNF	
Anti-TNFi	331 (45%)
TNFi	399 (55%)
OnDMARD	1,605 (82%)
onbio	757 (38%)

[1] *n (%); Median (IQR)*

Table 2. Comparison between DAS-28 levels with other rheumatoid factors

Cross Table for Dependent DAS28Group

	N	DAS28 < 3.2 (N=9293)	DAS28 >= 3.2 (N=3858)	Test Statistic
RIT : Yes	13163	0.1 1066/9293	0.1 455/3858	X_1^2=0.28, P=0.60[2]
ADA : Yes	13163	0.1 576/9293	0.1 218/3858	X_1^2=1.44, P=0.23[2]
TOC : Yes	13163	0.2 1902/9293	0.1 411/3858	X_1^2=181.15, P<0.01[2]
ETA : Yes	13163	0.1 472/9293	0.0 131/3858	X_1^2=17.66, P<0.01[2]
ABA : Yes	13163	0.1 537/9293	0.1 337/3858	X_1^2=38.41, P<0.01[2]
INF : Yes	13163	0.0 374/9293	0.0 180/3858	X_1^2=2.78, P=0.10[2]
TOF : Yes	13163	0.0 91/9293	0.0 54/3858	X_1^2=4.42, P=0.04[2]
CER : Yes	13163	0.0 131/9293	0.0 66/3858	X_1^2=1.67, P=0.20[2]
GOL : Yes	13163	0.0 58/9293	0.0 17/3858	X_1^2=1.62, P=0.20[2]

N is the number of non-missing value. [1]Kruskal-Wallis. [2]Pearson. [3]Wilcoxon.

Cross Table for Dependent DAS28Group

	N	DAS28 < 3.2 (N=9293)	DAS28 >= 3.2 (N=3858)	Test Statistic
MTX : Yes	13163	0.6 5955/9293	0.6 2403/3858	X_1^2=3.79, P=0.05[2]
SSZ : Yes	13163	0.1 1181/9293	0.1 519/3858	X_1^2=1.34, P=0.25[2]
LEF : Yes	13163	0.1 1293/9293	0.1 567/3858	X_1^2=1.38, P=0.24[2]
HCQ : Yes	13163	0.3 2573/9293	0.3 1074/3858	X_1^2=0.03, P=0.86[2]
IMUR : Yes	13163	0.0 155/9293	0.0 75/3858	X_1^2=1.21, P=0.27[2]
CYC : Yes	13163	0.0 3/9293	0.0 7/3858	X_1^2=7.98, P<0.01[2]

N is the number of non-missing value. [1]Kruskal-Wallis. [2]Pearson. [3]Wilcoxon.

Cross Table for Dependent DAS28Group

	N	DAS28 < 3.2 (N=9293)	DAS28 >= 3.2 (N=3858)	Test Statistic
Treatment Type	13163			X_2^2=68.91, P<0.01[2]
Combination		0.4 3478/9293	0.3 1254/3858	
Monotherapy		0.2 1718/9293	0.2 598/3858	
No		0.4 4097/9293	0.5 2006/3858	
On Biologics : Yes	13163	0.6 5196/9293	0.5 1852/3858	X_1^2=68.56, P<0.01[2]
On DMARDs : Yes	13163	0.8 7410/9293	0.8 2999/3858	X_1^2=6.63, P=0.01[2]

N is the number of non-missing value. [1]Kruskal-Wallis. [2]Pearson. [3]Wilcoxon.

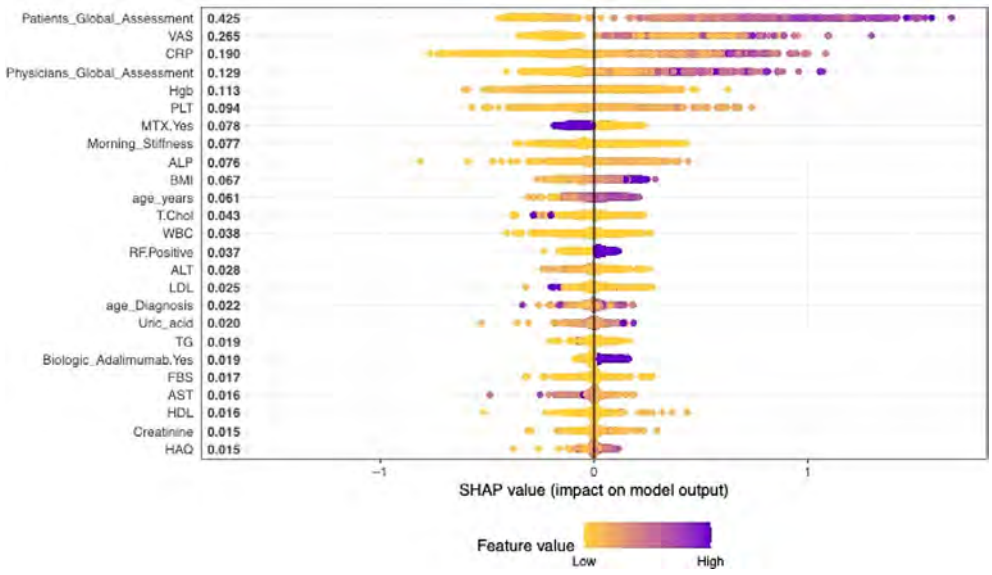

Figure 1. The SHAP results that emphasize the most clinical characteristics of RA patients using rituximab (RIT)

ridge, support vector machine, random forest, XGBoost, and Shapley additive explanation (SHAP)) were used for the predictions.

Results: The ranges for accuracy and area under the receiver operating characteristic of the newly developed machine learning model for predicting remission were 52.8–72.9% and 0.463–0.719, respectively. The Shapley plot in XAI showed that the impacts of the variables on predicting remission differed for each bDMARD. The most important features were age for adalimumab, rheumatoid factor for etanercept, erythrocyte sedimentation rate for infliximab and golimumab, disease duration for abatacept, and C-reactive protein for tocilizumab, with mean SHAP values of – 0.250, – 0.234, – 0.514, – 0.227, – 0.804, and 0.135, respectively.

Conclusion: Our proposed machine learning model system successfully identified clinical features that were predictive of remission in each of the bDMARDs. This approach may be useful for improving treatment outcomes by identifying clinical information related to remissions in patients with rheumatoid arthritis.

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Abstract Number: 0979

Use and Discontinuation of Tumour Necrosis Factor Inhibitors Among Pregnant Women with Chronic Inflammatory Diseases

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SESSION INFORMATION
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Background/Purpose: Early consensus statements recommended discontinuing tumour necrosis factor inhibitors (TNFi) during pregnancy. Despite new guidelines recommending against this, the choice to stop TNFi pre-conception is patient- and provider-dependent. Understanding TNFi discontinuation pre-conception may help inform initiatives to optimize outcomes. We examined calendar trends in TNFi discontinuation pre-conception in women with chronic inflammatory diseases and compared characteristics of those who stopped using TNFi pre-conception (without resuming in pregnancy) compared with those who used TNFi at any time during pregnancy.

Methods: We created a cohort of pregnant women with rheumatoid arthritis, ankylosing spondylitis, psoriasis/psoriatic arthritis, and/or inflammatory bowel disease who delivered between 2011 and 2019 using the MarketScan commercial database. TNFi use was defined as ≥1 filled prescription or infusion procedure claim, categorized as a) TNFi pre-conception only (i.e. ≥1 prescription filled or infusion procedure claim in the 12 weeks preceding the gestational period but not within the gestational period) or b) TNFi use at any time during pregnancy (i.e. any prescription filled or infusion procedure claim during the gestational period, including restarts, new starts, and those continuing from pre-conception).

Table 1 Characteristics of pregnant women with chronic inflammatory diseases who stopped TNFi pre-conception and those who took TNFi at any time during gestation (n=3,372)

	Total (n=3372)	TNFi pre-conception only (n=470)	TNFi any time during pregnancy (n=2902)
Age (years), mean (SD)	32.3 (4.14)	32.5 (4.18)	32.3 (4.13)
Disease Diagnosis, n (%)			
All		470/3372 (14)	2902/3372 (86)
IBD only	1588 (47)	82/1588 (5)	1506/1588 (95)
RA only	807 (24)	187/807 (23)	620/807 (77)
PsA/PsO only	530 (16)	132/530 (25)	398/530 (75)
AS only	117 (3)	27/117 (23)	90/117 (77)
>1 diagnosis	330 (10)	42/330 (13)	288/330 (87)
Corticosteroids, n (%)	1085 (32)	149/470 (32)	936/2902 (32)
Non-biologic DMARDs, n (%)	713 (21)	66/470 (14)	647/2902 (22)
Diabetes, n (%)			
Gestational	376 (11)	54/376 (14)	322/376 (87)
Pre-gestational	137 (4)	23/137 (17)	114/137 (83)
Asthma, n (%)	281 (8)	31/281 (11)	250/281 (89)
Hypertension, n (%)	214 (6)	34/214 (16)	180/214 (84)
Delivery Year, n (%)			
2011-2013			
All	1202 (36)	224/1202 (19)	978/1202 (81)
IBD only	510 (15)	36/510 (7)	474/510 (93)
RA only	345 (29)	96/345 (29)	249/345 (72)
PsA/PsO only	200 (6)	61/200 (30)	139/200 (70)
2014-2016			
All	1138 (34)	148/1138 (13)	990/1138 (87)
IBD only	549 (16)	20/549 (4)	529/549 (96)
RA only	266 (8)	60/266 (23)	206/266 (77)
PsA/PsO only	157 (5)	41/157 (26)	116/157 (74)
2017-2019			
All	1032 (31)	98/1032 (9)	934/1032 (91)
IBD only	529 (16)	26/529 (5)	503/529 (95)
RA only	196 (6)	31/196 (16)	165/196 (84)
PsA/PsO only	173 (5)	30/173 (17)	143/173 (83)

Abbreviations: AS, ankylosing spondylitis; DMARDs, disease-modifying anti-rheumatic drugs; IBD, inflammatory bowel disease; PsA, psoriatic arthritis; PsO, psoriasis; RA, rheumatoid arthritis; SD, standard deviation

Results: We identified 3,372 pregnancies; 14% discontinued TNFi in the 12 weeks before conception and did not restart, and 86% were exposed to TNFi during pregnancy. IBD patients accounted for 47% of all pregnancies. Comparing rheumatologic to non-rheumatologic patients, more RA individuals (difference of 18%, 95% confidence interval, CI, 15-21%) and PsA/PsO (20%, 95% CI 16-24%) discontinued their TNFi than IBD patients. Corticosteroid use was similar in both TNFi exposure groups, and those using TNFi during pregnancy were more likely to use non-biologic disease-modifying agents concomitantly (difference of 8%, 95% CI 5-12%). Across comorbidities (diabetes, asthma, and hypertension), there was no difference in discontinuation. Over time, a lower proportion of patients stopped TNFi pre-conception (2011-2013 19% vs 2014-2016 13% vs 2017-2019 10%; p-value for trend < 0.0001).

Conclusion: In our study, 14% discontinued TNFi in the 12 weeks before conception and did not restart. The proportion of patients stopping TNFi pre-conception decreased over time, possibly reflecting how changes in the observational literature pre-dated (and influenced) guidelines. Further research on TNFi discontinuation in the years after the 2020 ACR guidelines is warranted to establish guideline compliance and monitor perinatal outcomes.

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Abstract Number: 0980

Temporal Trends in Incidence Rates of Seropositive and Seronegative Rheumatoid Arthritis: A Danish Nationwide Population-based Study

Bolette Soussi[1], René Cordtz[2], Kirsten Duch[2], Salome Kristensen[3], Asta Linauskas[4], Christian Bork[5], Erik Schmidt[6] and Lene Dreyer[3], [1]Center of Rheumatic Research Aalborg, Department of Rheumatology, and Clinical Cancer Research Center, Aalborg University Hospital, Aalborg, Denmark, [2]Center of Rheumatic Research Aalborg, Department of Rheumatology, Aalborg University Hospital, Aalborg, Denmark, [3]Center of Rheumatic Research Aalborg, Department of Rheumatology, Aalborg University Hospital, and Department of Clinical Medicine, Aalborg University, Aalborg, Denmark, [4]Department of Rheumatology, North Denmark Region Hospital, and Department of Clinical Medicine, Aalborg University, Hjørring, Denmark, [5]Department of Cardiology, Aalborg University Hospital, Aalborg, Denmark, [6]Department of Medicine and Cardiology, Viborg Regional Hospital, and Department of Clinical Medicine, Aalborg University, Viborg, Aalborg, Denmark

SESSION INFORMATION

Session Date: Monday, November 13, 2023

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Background/Purpose: With growing availability of autoantibody testing and autoantibodies gaining more weight in the 2010 ACR/EULAR classification criteria of rheumatoid arthritis (RA), an increasing incidence rate (IR) of seropositive RA might be expected. We therefore aimed to explore the temporal trends of IRs for patients with seropositive and seronegative RA using various data sources for serostatus definition.

Table 1. Serological information on patients with rheumatoid arthritis

	2000 to 2004 (n = 6216)	2005 to 2009 (n = 7454)	2010 to 2014 (n = 8883)	2015 to 2018 (n = 6559)
Serostatus available from Autoimmune Laboratory at SSI/Register of Laboratory Results for Research	505 (8.1)	2713 (36.4)	4155 (46.8)	5423 (82.7)
Seropositive according to Autoimmune Laboratory at SSI/Register of Laboratory Results for Research*	263 (52.1)	1496 (55.1)	2727 (65.6)	3769 (69.5)
Registered in DANBIO at time of DNPR diagnosis	731 (11.8)	2619 (35.1)	5846 (65.8)	4938 (75.3)
Test result available for anti-CCP and/or IgM-RF in DANBIO	22 (0.4)	922 (12.4)	2401 (27.0)	3430 (52.3)
Seropositive according to DANBIO	15 (68.2)	594 (64.4)	1567 (65.3)	2221 (64.8)
Seropositive according to DNPR ICD-10 code at time of diagnosis	3202 (51.5)	3798 (51.0)	4679 (52.7)	3389 (51.7)
Seropositive according to Autoimmune Laboratory at SSI/Register of Laboratory Results for Research and DNPR**	3282 (52.8)	3964 (53.2)	5245 (59.0)	4301 (65.6)
Seropositive according to Autoimmune Laboratory at SSI/Register of Laboratory Results for Research, DANBIO, and DNPR***	3281 (52.8)	3978 (53.4)	5275 (59.4)	4355 (66.4)

Data are shown as n (%) unless otherwise indicated. * Outcome definition for seropositive rheumatoid arthritis using laboratory-reported autoantibodies from the Autoimmune Laboratory at Statens Serum Institut (SSI) and the Register of Laboratory Results for Research within 15 years before and 14 days after the case definition of RA was fulfilled. ** Outcome definition for seropositive rheumatoid arthritis with weighting of data by laboratory-reported autoantibodies from Autoimmune Laboratory at SSI/Register of Laboratory Results for Research > ICD-10 codes from the Danish National Patient Registry (DNPR). *** Outcome definition for seropositive rheumatoid arthritis with weighting of data by laboratory-reported autoantibodies from Autoimmune Laboratory at SSI/Register of Laboratory Results for Research > physician-reported autoantibodies from DANBIO > ICD-10 codes from DNPR. IgM-RF, immunoglobulin M rheumatoid factor; Anti-CCP, anti-cyclic citrullinated peptide.

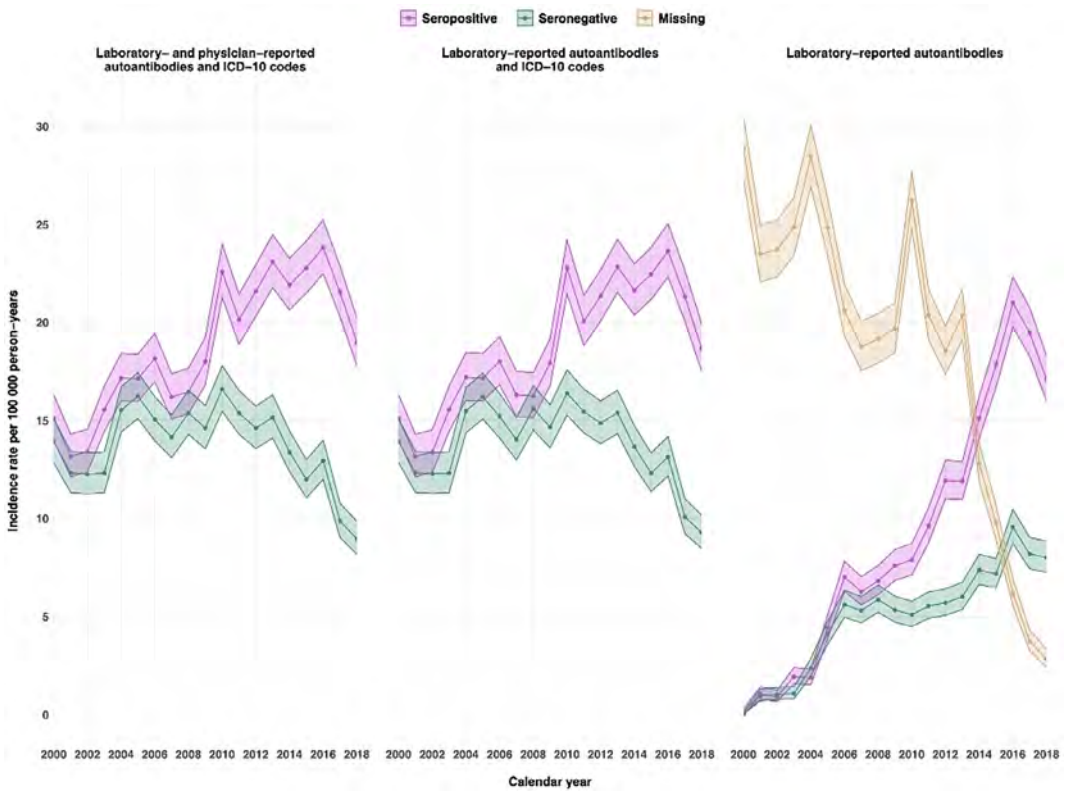

Figure 1. Temporal incidence rates for seropositive and seronegative rheumatoid arthritis using various data sources to distinguish serological subtypes. Laboratory-reported autoantibodies originated from laboratory test results of IgM-RF and/or anti-CCP in the Autoimmune Laboratory Statens Serum Institut and/or the Register of Laboratory Results for Research, physician-reported autoantibodies from physician-reported IgM-RF and/or anti-CCP in DANBIO, and ICD-10 codes from the Danish National Patient Registry. Missing values illustrated the identified patients with rheumatoid arthritis who had no available autoantibodies result in the Autoimmune Laboratory at Statens Serum Institut or the Register of Laboratory Results for Research within 15 years before to 14 days after they fulfilled the case definition of rheumatoid arthritis.

Methods: Danish nationwide population-based cohort study using healthcare and clinical quality registries from 2000 to 2018. RA patients were identified with first-time M05/M06 ICD-10 code (except M06.1) in the Danish National Patient Registry (DNPR) and a redeemed prescription of a csDMARD in the following year in the Danish National Prescription Registry.

Autoantibodies and ICD-10 codes from laboratory and register-based data sources were combined to define the outcome: serological status of each RA case. The definitions used laboratory-reported IgM-RF and anti-CCP registered in the Autoimmune Laboratory at Statens Serum Institut and/or the Register of Laboratory Results for Research. Physician-reported IgM-RF and anti-CCP available in DANBIO were added for those with no laboratory-reported autoantibodies. Imputation of serostatus according to ICD-10 codes in the DNPR, was for those with missing autoantibodies from any of the previous data sources. An outcome definition without DANBIO data was also pre-specified. The robustness of the register-estimated incidences of seropositive and seronegative RA were assessed using solely laboratory-reported autoantibodies. Registration of a positive autoantibody or an M05 diagnosis classified as seropositive RA, whereas negative autoantibody or M06 outlined seronegative RA.

Annual age- and sex-standardised IRs were calculated as the number of incident seropositive and seronegative cases, respectively, divided by number of person-years in the general population in that given year.

Results: In total, 29 112 incident patients with RA were identified from 2000 to 2018 (Table 1). An increasing temporal trend in IR of seropositive RA and decreasing trend of seronegative RA was observed. The IRs were higher for seropositive RA than for seronegative RA from 2009 and onwards with a widening of the IR gap between 2009 and 2016, leading to

approximately twofold higher IR of seropositive RA than of seronegative RA, regardless of the definition of seropositivity (Figure 1). The widening of the IR gap was driven by an initial increase in IRs with a rapid increase to year 2010 followed by a more fluctuating pattern for seropositive RA in combination with a decrease in the IR of seronegative RA. As testing for autoantibodies became more frequent, the rate of RA cases with missing values for autoantibodies decreased significantly over time.

Conclusion: The IR of patients with seropositive RA increased and decreased for seronegative RA during a period where autoantibody testing grew and the presence of autoantibodies received a greater weight in the classification criteria for RA. Temporal IR changes may be caused by a true change in RA serology subtypes, increase in autoantibodies testing or change in registration practice over time, or a combination of these factors.

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Abstract Number: 0981

Time Trends in Overall Infection Risk in Patients with Inflammatory Arthritides Treated with Tumor Necrosis Factor Inhibitors

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Background/Purpose: Infections are a known complication of disease-modifying therapy in rheumatic patients but have also been associated with the diseases being treated. Biosimilars have increased access to TNF inhibitors (TNFi) which may have changed the composition of patients receiving TNFi therapy. We hypothesized that, over time, this could lead to a reduction in the incidence of infections and antibiotic use among patients starting TNFi treatment.

Methods: Information on all biologic-naïve adult patients with RA, SpA, and PsA initiating treatment with a TNFi was extracted from ICEBIO, a nationwide registry. Each patient was randomly matched on age, sex, and calendar time to five general population comparators. Patients were observed for two years before and after TNFi initiation (reference date). All ICD-10 inpatient and outpatient codes for infections and information on filled prescriptions were extracted from nationwide registries maintained by the Icelandic Directorate of Health. Serious infections (SI) were defined as any of the following: hospital admission with an ICD-10 code for infection, intravenous antibiotic administration in an outpatient clinic with a relevant ICD-10 code, or a filled prescription for an intravenous antibiotic. Events occurring within 30 days of one another were considered the same event. To examine time trends we split the data into four-year periods; 2003-2006, 2007-2010, 2011-2014, and 2015-2018. We calculated the incidence rate (IR) per 1000 patient-years (py) for SI and prescriptions for each period. We used Poisson exact test to calculate the 95% confidence interval (CI) and p-value when comparing IR. Incidence rate ratios (IRR) were calculated using a Fisher exact test and a Poisson regression model to adjust for previous infections, age, sex, HAQ score at baseline, diagnosis, time from diagnosis, and steroid use.

Results: We identified 1387 individuals initiating their first treatment episode with a TNFi in 2003-2018; 583 (42%) had RA, 420 (30%) PsA, and 384 (28%) SpA. The mean age ±SD was 48.8 years ± 14.2 (Table 1). There were 6916 matched comparators. We identified 139 SI (58 before vs. 81 after TNFi) in the patients and 329 for the comparators (168 before vs. 161 after the reference date).

When comparing the IR per 1000py of the first and last periods, the antimicrobial use increased among the TNFi-treated patients from 1407 (95% CI 1303 – 1517) to 1674 (1593 – 1758) prescriptions (p< 0.001), while the change was not statistically significant for the number of SI; 35.1 (20.5-50.2) to 21.9 (13.5-33.4), p=0.16 (Figure I).

Multivariate analysis showed that the between-period IRR for SI was 0.46 (0.23 – 0.94, p=0.03) for the TNFi treated patients in the last period compared to the first while it was 1.42 (0.87 – 2.41) for the comparators (Figure II). The IRR for antimicrobial use was stable in the TNFi group at 1.02 (0.93-1.13) while it increased for the comparators 1.15 (1.05-1.16, p< 0.001).

Table I
Patient characteristics between periods

	2003-2006 (N=246)	2007-2010 (N=269)	2011-2014 (N=367)	2015-2018 (N=505)	Overall (N=1387)
Age					
Median [Min, Max]	50.0 [22.0, 83.0]	50.0 [18.0, 85.0]	50.0 [18.0, 83.0]	50.0 [18.0, 87.0]	50.0 [18.0, 87.0]
Sex					
Female	153 (62.2%)	160 (59.5%)	207 (56.4%)	298 (59.0%)	818 (59.0%)
Years from diagnosis					
Median [Min, Max]	8.00 [0, 47.0]	4.00 [0, 42.0]	3.00 [0, 60.0]	3.00 [0, 55.0]	4.00 [0, 60.0]
Diagnosis					
PsA	52 (21.1%)	70 (26.0%)	123 (33.5%)	175 (34.7%)	420 (30.3%)
RA	123 (50.0%)	124 (46.1%)	153 (41.7%)	183 (36.2%)	583 (42.0%)
SpA	71 (28.9%)	75 (27.9%)	91 (24.8%)	147 (29.1%)	384 (27.7%)
HAQ at baseline					
Mean (SD)	0.35 (0.56)	0.61 (0.72)	0.99 (0.74)	1 (0.67)	0.81 (0.73)
DAS28-CRP at baseline					
Mean (SD)	1.87 (2.34)	2.48 (2.25)	3.66 (1.90)	3.38 (1.91)	3.01 (2.16)
DDD of glucocorticoids for 2 years following TNFi					
Mean (SD)	85.5 (155)	91.5 (161)	76.6 (158)	80.1 (147)	82.4 (154)

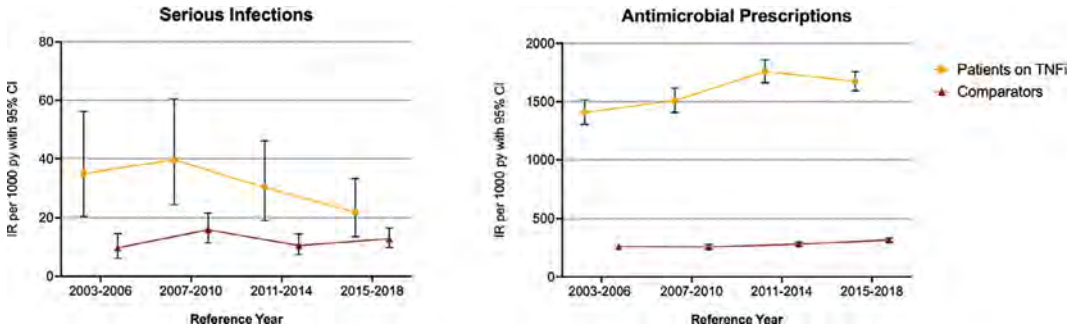

Figure I: Incidence rates (IR) per 1000 patient years (py) by time period for serious infections (left) and antimicrobial prescriptions (right) for rheumatic patients on TNFi (circle) and general population comparators (triangle). Individuals are observed for up to two years following TNFi initiation (reference year)

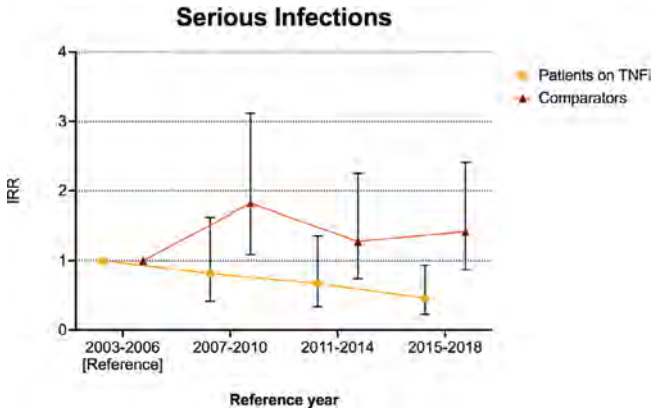

Figure II: Incidence rate ratio (IRR) estimates with 95% CI for serious infections by time period for TNFi patients (circle) and for matched general population comparators (triangle). Individuals are observed up to two years following TNFi initiation (reference year). The model corrects for age, sex, previous infections, HAQ score, time since diagnosis, steroid use, and diagnosis (RA, PsA, or AS).

Conclusion: The risk of serious infections associated with TNFi in patients with inflammatory arthritides has decreased in recent years. This trend of diminishing risk of SI needs to be considered when analyzing data over long periods or when comparing recent research to previously published data.

Disclosure: A. Bjornsson: None; **T. Thrastardottir**: None; **B. Gudbjornsson**: Nordic-Pharma, 6, Novartis, 2, 6; **T. Love**: None.

Abstract Number: 0982

Systemic Autoimmune Rheumatic Diseases (SARD) in the Agricultural Health Study Cohort: Rates of Rheumatoid Arthritis (RA) and Other SARD Among Medicare-linked Participants

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SESSION INFORMATION
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Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Some systemic autoimmune rheumatic diseases (SARD), such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), have been associated with farming, specific pesticides, and other occupational exposures in the Agricultural Health Study (AHS), a prospective cohort of ~89,000 licensed pesticide applicators and spouses in North Carolina and Iowa enrolled in 1993-1997. We previously identified incident RA based on self-report confirmed by DMARD use and case validation, e.g., 220 cases (0.8%) among 26,354 male private pesticide applicators with available follow-up data through 2010. However, incomplete cohort follow-up limits the assessment of disease rates, and many rarer SARD were not included on questionnaires. Thus, we used cohort-linked Medicare claims data to enhance case ascertainment for future analyses of agricultural exposures and risk of SARD.

Methods: The AHS cohort includes licensed pesticide applicators (N=52,394 private and 4,916 commercial, 97% male) and spouses (32,345, 99% female). We assessed SARD prevalence based on Medicare claims data from 1999-2016 in 35,506 participants (21,554 male) who enrolled in Medicare at ages ≥65 years with ≥1 year of Fee for Service coverage (FFS; Parts A and B, but not Part C). We sought to identify cases of 15 SARD using ICD codes, requiring ≥2 disease-specific claims ≥30 days apart. In a subset of 33,398 (20,132 male) with a 24-month clean period (i.e., continuous FFS with no SARD-specific claims), we identified incident cases and calculated age- and sex-standardized incidence rates.

Table 1 - Prevalence of Systemic Autoimmune Rheumatic Diseases in the Agricultural Health Study

	Total N=35,506		Males N=21,514	
Claims based diagnosis of SARD	N	(%)	N	(%)
No SARD[1]	33,609	(94.67)	20,622	(95.85)
Any SARD	1897	(5.26)	892	(4.15)
Rheumatoid arthritis	1032	(2.94)	480	(2.23)
Polymyalgia rheumatica	639	(1.63)	325	(1.51)
Sicca syndrome (Sjögren's)	128	(0.36)	26	(0.12)
Systemic Lupus Erythematosus	111	(0.34)	35	(0.16)
Giant cell arteritis	108	(0.27)	45	(0.21)
Connective tissue disease	71	(0.21)	26	(0.12)
Cutaneous lupus	69	(0.16)	17	(0.08)
Psoriatic arthritis	53	(0.15)	30	(0.14)
Systemic sclerosis	54	(0.13)	11	(0.05)
Polymyositis	33	(0.09)	20	(0.09)
Dermatomyositis	18	(0.04)	<11	—

ARD = Systemic Autoimmune Rheumatic Disease

SARD with 2+ disease-specific claims 30+ days apart; Any SARD = total listed in table plus nclusion body myositis, polyarteritis nodosa, Wegener's/granulomatous polyangiitis, and Still's isease, are not shown due to small numbers of cases (<11) in one or both groups. Numbers do ot add to total due to individuals with more than one diagnosis.

Table 1 - Incidence of Systemic Autoimmune Rheumatic Diseases in the Agricultural Health Study

	Overall		Males	
Claims based diagnosis of SARD	N=33,398 N (%)	Cases per 100,000 PY[2]	N=20,132 N (%)	Cases per 100,000 PY[2]
No SARD[1]	32,093 (96)		19,501 (97)	
Any incident SARD	1305 (3.91)	422	631 (3.13)	344
Rheumatoid arthritis	592 (1.77)	191	287 (1.43)	156
Polymyalgia rheumatica	513 (1.54)	165	273 (1.36)	148
Sicca syndrome (Sjögren's)	92 (0.28)	27.1	18 (0.09)	8.9
Systemic Lupus Erythematosus	65 (0.19)	18.3	27 (0.13)	12.9
Giant cell arteritis	88 (0.26)	27.7	40 (0.20)	20.8
Connective tissue disease	53 (0.16)	15.8	19 (0.09)	10.9
Cutaneous lupus	37 (0.11)	12.5	12 (0.06)	6.7
Psoriatic arthritis	25 (0.07)	7.8	12 (0.06)	5.7
Systemic sclerosis	26 (0.08)	7.6	<11	—

[1]SARD with 2+ disease-specific claims 30+ days apart following 24 months without SARD-specific claims; Any incident SARD = total listed in table plus inclusion body myositis, polyarteritis nodosa, Wegner's granulomatosis, and Stills disease, are not shown due to small numbers of cases (<11) in one or both groups.

[2]Incidence among participants with ≥24 months follow-up time, standardized to the 2010 US population ages ≥65, adjusted for age- and gender.

Results: Overall, we identified 1987 SARD cases (5.33%), including 892 (4.15%) among males (**Table 1**). The top 5 diagnoses were rheumatoid arthritis (1,032; 2.90%), polymyalgia rheumatica (PMR, N=639; 1.80%), sicca syndrome (SS, 128; 0.36%), SLE (111; 0.31%), and giant cell arteritis (GCA; 108; 0.30%). Among males, prevalence was slightly lower for RA (480; 2.23%), PMR (325; 1.51%), and GCA (45; 0.21%), and substantially lower for SS (27; 0.12%) and SLE (35; 0.16%). A total of 1305 (3.91%) met the criteria for incident SARD, including 636 (3.13%) male cases, with 287 (1.43%) incident RA, 273 (1.36%) PMR, and the remaining rarer SARD (0-0.20%; **Table 2**).

Conclusion: In this agricultural cohort, about 1 in 20 older individuals was diagnosed with an SARD based on Medicare claims. Incidence of Medicare-based RA in males was greater than we previously identified by questionnaire. These data will facilitate comparisons of SARD in the AHS with published rates in the Medicare population and will enhance research on the role of pesticides and other exposures in the development of SARD in older AHS participants.

Disclosure: C. Parks: None; **K. Costenbader**: Amgen, 2, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Eli Lilly, 2, Exagen Diagnostics, 5, Gilead, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5; **L. Beane Freeman**: None; **J. Hofmann**: None; **D. Sandler**: None.

Abstract Number: 0983

Association Between Disease-modifying Anti-rheumatic Drugs and Short-term Outcomes of Dengue: A Population-based, Cohort Study

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Dengue is the leading vectorborne disease globally with half of the global population at risk, including Puerto Rico in the United States. Previously, we showed that rheumatoid arthritis and related disease were associated with an increased risk of death after dengue diagnosis. Disease-modifying anti-rheumatic drugs (DMARDs), categorized into conventional-synthetic (cs) DMARDs, biological (b) DMARDs and target-synthetic (ts)DMARDSs, are standard therapy for patients with RA. Rituximab (RTX) therapy has been associated with higher COVID-19 mortality but outcomes associated with dengue have not been reported. The aim of this study was to assess the association between DMARDs and dengue outcomes.

Methods: The Taiwanese National Health Insurance Research Database (NHIRD), covering 99.5% of the Taiwan population was linked to the Notifiable Disease Dataset of Confirmed Cases (NDDCC) to assess associations of short-term dengue outcomes with RTX and other b/tsDMARDs. We identified 51,769 confirmed dengue cases aged ≥ 18 years from January 1, 2014 to December 31, 2015. Those cases were linked to the NHIRD to assess DMARDs use within one year before dengue was diagnosed and study outcomes of mortality and hospitalization within 30 days after dengue diagnosis. We categorized patients with dengue into four mutually exclusive groups based on prior use of DMARDs within one year: (1) RTX use, (2) use of b/tsDMARDs other than RTX ,(3) use of csDMARDs without use of b/tsDMARDs, (4) without use of any DMARDs. We examined the adjusted odds ratios (aORs) with 95% confidence intervals (CIs) for 30-day mortality and hospitalization in dengue patients based on prior use of DMARDs (csDMARDs users as reference) by multivariable logistic regression analysis

Table 1.Incidences of mortality within 30 days after dengue diagnosis based on use of DMARDs within one year before dengue the diagnosis date.

	n	Number of events	Incidence[b]	Crude incidence ratio[b]	Adjusted odds Ratio[c]	95% CI
Mortality						
DMARD group						
csDMARD	304	5	1.6	1.00	Reference	
Rituximab	14	2	14.3	8.69	6.19	1.00–38.10*
b/tsDMARD other than rituximab	153	3	2.0	1.19	1.24	0.28–5.49
No DMARD	51,298	361	0.7	0.43	0.58	0.23–1.45
No DMARD	51,298	14,979	29.2	0.75	0.84	0.66–1.07

[a]csDMARD: conventional synthetic disease-modifying antirheumatic drugs, b/tsDMARD: biological or target-synthetic DMARD.

[b]Incidence: number of events per 100 persons; Ratio of incidence to that of the reference group

[c]Adjusted for age, sex, social economic status, year of diagnosis, and all the other comorbidities

*P-value < 0.05.

Table 1.Incidences of hospitalization within 30 days after dengue diagnosis based on use of DMARDs within one year before dengue the diagnosis date.

	n	Number of events	Incidence[b]	Crude incidence ratio[b]	Adjusted odds Ratio[c]	95% CI
Hospitalization						
DMARD group						
csDMARD	304	119	39.1	1.00	Reference	
Rituximab	14	7	50.0	1.28	1.01	0.34–3.01
b/tsDMARD other than rituximab	153	71	46.4	1.19	1.35	0.90–2.03
No DMARD	51,298	14,979	29.2	0.75	0.84	0.66–1.07

[a]csDMARD: conventional synthetic disease-modifying antirheumatic drugs, b/tsDMARD: biological or target-synthetic DMARD.

[b]Incidence: number of events per 100 persons; Ratio of incidence to that of the reference group

[c]Adjusted for age, sex, social economic status, year of diagnosis, and all the other comorbidities

adjusting for age, sex, socioeconomic status, year of diagnosis and comorbidities: RA and related disease, chronic kidney disease, diabetes, malignancy, coagulation and hemorrhagic disorders, coronary artery disease, hypertension, stroke, congestive heart failure, chronic obstructive pulmonary disease, asthma, major depressive disorder, and liver cirrhosis.

Results: Table 1 shows the numbers and incidences of death within 30 days after dengue diagnosis. Compared with patients treated with csDMARDs only, risk of 30-day mortality was higher in patients with prior rituximab use (aOR, 6.19; 95% CI, 1.00–38.1; $p < 0.05$), but not in patients receiving b/tsDMARDs other than RTX. However, the risk of 30-day hospitalization was not significantly different between patients receiving csDMARDs treatment and patients with prior use of RTX or other b/tsDMARDs (Table 2).

Conclusion: This population-based study showed that use of rituximab was associated with a higher risk of death within 30 days after dengue diagnosis compared with use of csDMARDs.

Disclosure: I. Lin: None; **H. Chen**: None; **T. Tsai**: Takeda Vaccines, Cambridge, Massachusetts, USA, 5; **N. Huang**: None.

Abstract Number: 0984

Factors Associated with 5-year Mortality in Patients with Rheumatoid Arthritis Initiating Their First Biological or Target Synthetic DMARDs: A Nationwide, Population-based Cohort Study of 12,612 Patients

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Epidemiology & Public Health Poster II
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Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease resulting in increased mortality. manifestations. involvement. The National Health Insurance Research Database (NHIRD) in Taiwan provided nationwide, population-based claim data that can be linked to death registry to assess risk factors and cause of death in patients with RA.

The aim of the study was to investigate factors associated with 5-year mortality in patients with RA starting their first biological or target synthetic disease-modifying antirheumatic drugs (b/tsDMARDs).

Methods: Using the 2000–2020 NHIRD, we identified 12,612 RA patients who initiated their first b/tsDMARDs, including tumor necrosis factor inhibitors (TNFi), tocilizumab, abatacept, rituximab and tsDMARD. A multivariable Cox regression model was used to estimate the adjusted hazard ratios (aHRs) with 95% confidence interval (CIs) for the association of the risk of 5-year mortality with the use of 5 categories of b/tsDMARDs (TNFi as a reference) after adjustment of potential confounders including age, sex, urbanization level of residence, income, comorbidities and medications.

Results: We included 8,902 TNFi-treated patients, 974 tocilizumab-treated patients, 994 abatacept-treated patients, 1,462 tsDMARD-treated patients and 280 rituximab-treated patients. Figure 1 showed the 5-year survival curve in patients treated with b/tsDMARDs categorized into 5 groups based on mechanism of actions. Compared with TNFi-treated patients, multivariable Cox-regression analyses showed that 5-year mortality risk was higher in rituximab-treated patients (aHR, 3.47; 95% CI,

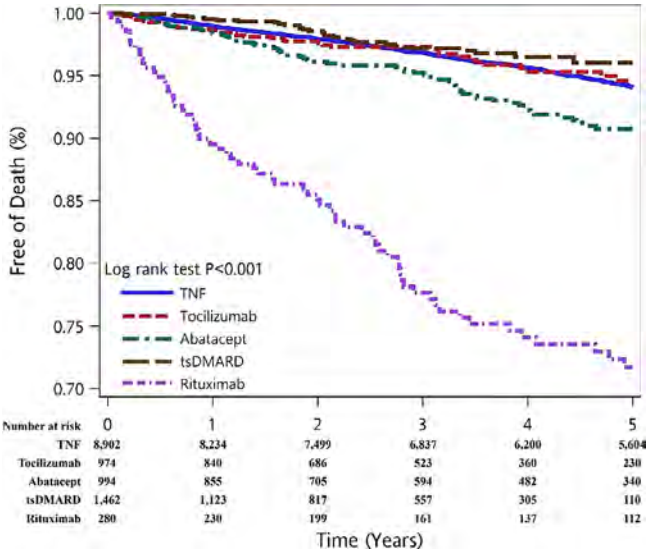

Fig 1. Five-year survival of patients with rheumatoid arthritis initiating their first b/tsDMARDs.

Table 1. Top 4 causes of death in all and each group of patients with rheumatoid arthritis initiating their first b/tsDMARDs.

All b/tsDMARDs		TNFi		Tocilizumab		Abatacept		tsDMARD		Rituximab	
n=623		n=431		n=34		n=63		n=29		n=66	
Neoplasms (G1)	164 (26.3)	G1	90 (20.9)	G6	9 (26.5)	G1	13 (20.6)	G1	9 (31.0)	G1	47 (71.2)
Circulatory system (G6)	110 (17.7)	G6	81 (18.8)	G10	9 (26.5)	G7	12 (19.0)	G6	7 (24.1)	G7	7 (10.6)
The musculoskeletal system and connective tissue (G10)	100 (16.1)	G10	75 (17.4)	G1	5 (14.7)	G6	11 (17.5)	G7	4 (13.8)	G0	4 (6.1)
The respiratory system (G7)	78 (12.5)	G7	53 (12.3)	G3	4 (11.8)	G10	9 (14.3)	G10	4 (13.8)	G10	3 (4.5)
Certain infectious and parasitic diseases (G0)	45 (7.2)										

2.48–4.85) and lower in JAKi-treated patients (aHR, 0.65; 95% CI, 0.44–0.96). Other significant predictors for 5-year mortality included male gender (aHR, 1.90; 95% CI, 1.61–2.24), age (aHR, 1.08; 95% CI, 1.07–1.09), low income (aHR, 1.47; 95% CI, 1.21–1.78), comorbidities within one year before the index date (heart failure: aHR, 1.72; 95% CI, 1.14–2.59; diabetes mellitus: aHR, 1.50; 95% CI, 1.22–1.84; chronic obstructive pulmonary disease: aHR, 1.29; 95% CI, 1.02–1.63; renal disease: aHR, 1.38; 95% CI, 1.02–1.85), a history of sepsis within prior one year (aHR, 2.61; 95% CI, 1.73–3.92), and use of medications within prior one year (methotrexate: aHR, 0.65; 95% CI, 0.51–0.83; prednisolone dose > 5mg/day: aHR, 1.89; 95% CI, 1.33–2.70). Table 1 showed the top 4 causes of death in all and each group of b/tsDMARD-treated patients.

Conclusion: This study showed that among patients with RA initiating b/tsDMARDs, the 5-year mortality risk was higher in rituximab-treated patients and lower in tsDMARD-treated patients compared with TNFi-treated patients.

Disclosure: H. Chen: None.

Abstract Number: 0985

Assessing the Value of Comorbidity Clusters in Predicting Clinical Outcomes in Rheumatoid Arthritis: A Machine Learning Approach Using a Very Large US Registry

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
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Background/Purpose: Comorbid conditions are very common in rheumatoid arthritis (RA) and several prior studies have derived comorbidity clusters using machine learning (ML). Clustering using ML is straightforward, but clusters only have value if they better explain clinical outcomes. We applied various ML algorithms to compare the clusters of comorbidities derived and to assess the value of the clusters for predicting clinical disease activity (CDAI) and function.

Methods: A large US-based RA registry, CorEvitas, was used to identify patients for the analysis. We assessed the presence of 24 comorbidities, and ML was used to derive comorbidity clusters. K-mode, K-mean, regression-based, and hierarchical clustering was used. To assess the value of the clusters, we compared them in clinical outcome models predicting clinical disease activity index (CDAI) and health assessment questionnaire (HAQ). We used data from the first three years of the six-year study period to derive clusters and assess time-averaged values for CDAI and HAQ during the latter three years. Model fit was assessed via adjusted R^2 and Root Mean Square Error for a series of models that included clusters from K-mode and each of the 24 comorbidities separately. K-mode was selected as it was representative of the ML-based clustering algorithms.

Results: 11,883 patients with RA were included who had longitudinal data over 6 years. At baseline, patients were on average 59 (SD 8) years of age, 77% were women, CDAI was 11.1 (SD 3.4, moderate disease activity), HAQ was 0.32 (SD 0.11), and disease duration was 10.9 (SD 4.3) years. During the six years of follow-up, the percentage of patients with various comorbidities increased (**Table 1**). Using five clusters produced by the K-mode ML algorithm, multivariable regression models with time-averaged CDAI as an outcome found that entering K-mode comorbidity clusters produced similarly strong models as models with each of the 24 separate comorbidities entered individually (**Table 2**). The same patterns were observed for HAQ (**Table3**). The other ML-based clustering algorithms produced very similar model results.

Table 1: Comorbidities Among 11,833 Patients with Rheumatoid Arthritis from the CorEvitas Registry Included in the Analyses, at Baseline and During Follow-Up.

	Baseline	Year 2	Year 4	Year 6
	Percentages			
Coronary artery disease	7.1	9.6	11.1	12.7
Heart failure	0.9	1.4	2.0	2.8
Hypertension	36.4	51.8	56.4	60.4
DVT/PE	1.7	2.1	2.4	2.9
Stroke/TIA	2.2	2.9	3.9	4.8
Arrhythmia	0.4	0.5	0.6	0.9
Gastrointestinal bleed	3.6	3.6	3.7	3.7
Liver disease	3.4	4.0	4.0	4.3
Solid tumor	2.0	2.6	3.2	3.9
NMSC	6.3	9.6	12.3	14.4
Lymphoma	0.4	0.5	0.8	1.1
Other cancer	5.0	6.1	7.0	8.1
Melanoma	1.0	1.9	2.8	3.6
Diabetes	9.5	13.6	15.6	17.1
Hyperlipidemia	9.8	10.5	11.1	11.3
Osteoporosis	22.7	23.3	23.3	23.4
Demyelinating	0.4	0.5	0.5	0.5
Mental health	41.8	51.2	55.6	59.1
Fibromyalgia	3.7	6.2	10.4	12.1
Psoriasis	4.3	5.3	5.6	5.7
Asthma/COPD	5.5	5.8	6.3	6.7
RA Lung	2.9	3.1	3.2	3.3
Acute kidney injury	7.0	10.1	13.4	16.7

DVT/PE, deep venous thrombosis/pulmonary embolus; TIA, transient ischemic attack; NMSC, non-melanoma skin cancer; COPD, chronic obstructive pulmonary disease.

Table 2: Multivariable regression comparing models for time averaged CDAI outcome, individual comorbidities versus comorbidity clusters from K-mode algorithm

	No comorbidities	+ Individual comorbids	+ Clustering K-mode
	Beta coefficient (95% confidence interval)		
Race/ethnicity			
Asian	0.23 (-0.62, 1.07)	0.49 (-0.36, 1.33)	0.32 (-0.52, 1.17)
Black	0.10 (-0.36, 0.56)	0.18 (-0.29, 0.64)	0.09 (-0.38, 0.55)
Hispanic	-0.45 (-0.91, 0.002)	-0.38 (-0.83, 0.08)	-0.43 (-0.88, 0.03)
Other	-0.03 (-0.71, 0.65)	0.06 (-0.62, 0.74)	-0.00 (-0.68, 0.68)
White (reference)	0.00	0.00	0.00
Duration of RA, years	0.01 (-0.01, 0.02)	0.00 (-0.01, 0.02)	0.00 (-0.01, 0.02)
Erosions, new	0.38 (0.15, 0.62)	0.43 (0.20, 0.67)	0.37 (0.14, 0.61)
Serologic status, positive	-0.66 (-0.90, -0.41)	-0.59 (-0.83, -0.34)	-0.64 (-0.89, -0.39)
CDAI, baseline	0.67 (0.66, 0.69)	0.66 (0.65, 0.68)	0.67 (0.66, 0.69)
HAQ-DI, baseline	2.13 (1.78, 2.48)	1.56 (1.21, 1.92)	1.95 (1.59, 2.30)
Individual Comorbidities			
Coronary artery disease	---	0.32 (-0.04, 0.69)	---
Heart failure	---	1.10 (0.28, 1.93)	---
Hypertension	---	0.18 (-0.06, 0.41)	---
DVT/PE	---	0.65 (-0.06, 1.37)	---
Stroke/TIA	---	0.57 (-0.02, 1.16)	---
Arrhythmia	---	-0.28 (-1.70, 1.15)	---
GI bleed	---	0.64 (0.42, 0.86)	---
Liver disease	---	0.31 (-0.24, 0.85)	---
Solid tumor	---	-0.30 (-0.93, 0.33)	---
Non-melanoma skin cancer (NMSC)	---	0.07 (-0.28, 0.43)	---
Lymphoma	---	0.87 (-0.43, 2.17)	---
Other cancer	---	-0.10 (-0.53, 0.32)	---
Melanoma	---	0.41 (-0.31, 1.13)	---
Diabetes	---	0.16 (-0.15, 0.48)	---
Hyperlipidemia	---	0.05 (-0.19, 0.28)	---
Osteoporosis	---	-0.03 (-0.30, 0.25)	---
Demyelinating	---	-0.77 (-2.24, 0.71)	---
Mental health	---	0.59 (0.36, 0.81)	---
Fibromyalgia	---	1.34 (0.95, 1.73)	---
Psoriasis	---	-0.02 (-0.48, 0.44)	---
Asthma/COPD	---	-0.08 (-0.53, 0.36)	---
RA Lung	---	-0.12 (-0.74, 0.50)	---
Acute kidney injury	---	0.08 (-0.25, 0.42)	---
Clusters from ML			
1	---	---	0.00
2	---	---	0.07 (-0.35, 0.49)
3	---	---	0.60 (0.20, 1.00)
4	---	---	0.59 (0.14, 1.04)
5	---	---	-0.22 (-0.63, 0.19)
Degrees of freedom	22	46	26
Model fit statistics			
Adjusted R2	0.53	0.54	0.54
Root Mean Square Error	5.78	5.75	5.78

Table 3: Multivariable regression comparing models for HAQ-DI with comorbidity clusters versus individual comorbidities

	No comorbidities	+ Individual comorbidities	+ Clustering K mode
	Beta coefficient (95% confidence interval)		
Race/ethnicity			
Asian	0.02 (-0.01, 0.06)	0.03 (-0.00, 0.06)	0.03 (-0.01, 0.06)
Black	-0.00 (-0.02, 0.02)	-0.00 (-0.02, 0.01)	-0.00 (-0.02, 0.01)
Hispanic	0.00 (-0.01, 0.02)	0.01 (-0.01, 0.02)	0.00 (-0.01, 0.02)
Other	0.04 (0.01, 0.07)	0.04 (0.02, 0.07)	0.04 (0.02, 0.07)
White (reference)	0.00	0.00	0.00
Duration of RA, years	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
Erosions, new	-0.00 (-0.01, 0.01)	-0.00 (-0.01, 0.01)	-0.00 (-0.01, 0.01)
Serologic status, positive	-0.01 (-0.02, -0.00)	-0.01 (-0.02, -0.00)	-0.01 (-0.02, -0.00)
CDAI, baseline	0.00 (0.00, 0.00)	0.00 (-0.00, 0.00)	0.00 (0.00, 0.00)
HAQ-DI, baseline	0.90 (0.89, 0.91)	0.88 (0.87, 0.89)	0.89 (0.88, 0.91)
Individual Comorbidities			
Coronary artery disease	---	0.02 (0.00,0.03)	---
Heart failure	---	0.07 (0.03, 0.10)	---
Hypertension	---	0.01 (0.00, 0.02)	---
DVT/PE	---	0.04 (0.01, 0.07)	---
Stroke/TIA	---	0.05 (0.02, 0.07)	---
Arrhythmia	---	NS	---
GI bleed	---	0.02 (0.01, 0.03)	---
Liver disease	---	NS	---
Solid tumor	---	NS	---
NMSC	---	NS	---
Lymphoma	---	NS	---
Other cancer	---	NS	---
Melanoma	---	NS	---
Diabetes	---	0.02 (0.01, 0.03)	---
Hyperlipidemia	---	NS	---
Osteoporosis	---	NS	---
Demyelinating	---	NS	---
Mental health	---	0.02 (0.01, 0.03)	---
Fibromyalgia	---	0.03 (0.02, 0.05)	---
Psoriasis	---	NS	---
Asthma/COPD	---	NS	---
RA Lung	---	NS	---
Acute kidney injury	---	NS	---
Clusters from ML			
1	---	---	0.00
2	---	---	0.00 (-0.01, 0.02)
3	---	---	0.03 (0.01, 0.04)
4	---	---	0.03 (0.01, 0.05)
5	---	---	-0.01 (-0.02, 0.01)
Degrees of freedom	22	46	26
Model fit statistics			
Adjusted R2	0.70	0.71	0.70
Root Mean Square Error	0.22	0.22	0.22

Conclusion: Clustering comorbidities using ML algorithms is not computationally complex but often results in clusters that are difficult to interpret from a clinical standpoint. While ML clustering is very useful for biologic modeling, using clusters to predict outcomes produces models with similar fit as those with individual comorbidities. Other use cases for comorbidity clusters might help demonstrate underlying biology.

Disclosure: D. Solomon: CorEvitas, 5, Janssen, 5, Moderna, 5, Novartis, 5; **F. Johansson**: None; **H. Guan**: None; **L. Santacroce**: None; **L. Guo**: CorEvitas, LLC, 3; **W. Malley**: None; **H. Litman**: CorEvitas, 3, 12, Shareholder.

Abstract Number: 0986

Medication Use Patterns and Factors Associated with Abnormal Pregnancy Outcomes in Patients with Rheumatoid Arthritis in Korea

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Epidemiology & Public Health Poster II
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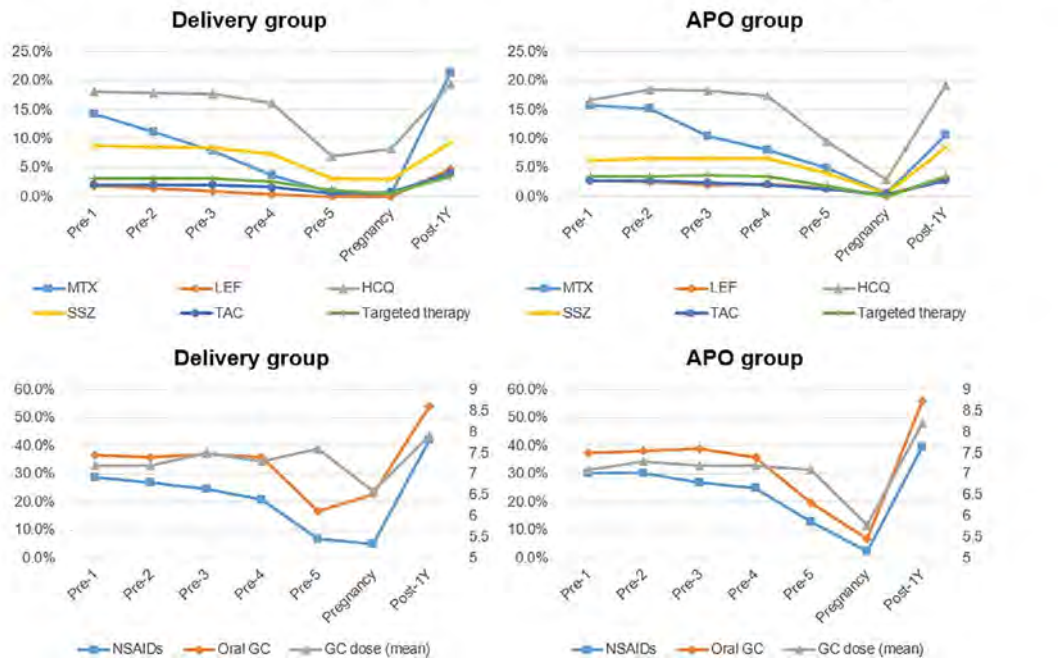
Background/Purpose: As female patients constitute a significant proportion of rheumatoid arthritis (RA) cases, pregnancy management is crucial for women with RA. This study aimed to investigate medication use patterns according to pregnancy outcomes and identify factors associated with abnormal pregnancy outcomes (APO) in female RA patients in Korea.

Methods: Using the Korean national health insurance database, female RA patients aged between 20 and 50 were identified based on the presence of both RA diagnostic codes and prescriptions for any disease-modifying anti-rheumatic drug (DMARD). Pregnancy episodes were selected using diagnostic or procedure codes and divided into two groups: the delivery group and the APO group (including abortion and stillbirth). Characteristics were compared between the two groups, and medication use patterns were analyzed during the preconception period, pregnancy, and one year after delivery. A multivariable logistic regression analysis was conducted to identify factors associated with APO.

Results: A total of 5,728 pregnancy episodes were included, with 4,576 in the delivery group and 1,152 in the APO group. The mean maternal age for all pregnancy episodes was 33.7 years, which was higher in the APO group. Comorbidities such as chronic pulmonary disease and diabetes mellitus were more frequent in the APO group. Hydroxychloroquine was the most commonly used conventional synthetic DMARD during the preconception period and pregnancy in both groups. Except for sulfasalazine and targeted therapies, all DMARDs were more frequently used in the APO group during the preconception period. Methotrexate and leflunomide prescriptions during pregnancy were nearly nonexistent in the delivery group. Within one year after delivery or termination of pregnancy, there was a rapid increase in the use of all DMARDs and oral glucocorticoids. In the multivariable analysis, patients aged 30-39 (adjusted odds ratio [aOR] 1.36, 95% confidence interval [CI] 1.09-1.68) and 40-49 (aOR 5.41, 95% CI 4.21-6.95) had a higher risk of APO compared to those aged 20-29. Methotrexate use (aOR 2.19, 95% CI 1.60-2.99) and leflunomide use (aOR 2.87, 95% CI 1.49-5.54) within three months before conception were associated with APO. Hospital visits for RA during pregnancy were associated with a lower risk of APO (aOR 0.67, 95% CI 0.55-0.82).

Figure. Pattern of medication use according to pregnancy outcome



GC doses are presented as prednisolone-equivalent dose (mg). APO, abnormal pregnancy outcome; MTX, methotrexate; LEF, leflunomide; HCQ, hydroxychloroquine; SSZ, sulfasalazine; TAC, tacrolimus; NSAID, nonsteroidal anti-inflammatory drug; GC, glucocorticoid. (Pre-1: from 12 months to 9 months before conception, Pre-2: from 9 months to 6 months before conception, Pre-3: from 6 months to 3 months before conception, Pre-4: during 3 months before conception, Pre-5: from conception to pregnancy recognization, Pregnancy: during pregnancy, Post-1Y: during 1 year after pregnancy outcome)

Conclusion: Medication use patterns differed between the delivery and APO groups. Methotrexate and leflunomide were associated with a higher risk of APO, emphasizing the importance of appropriate medication adjustment when planning for pregnancy. Regular hospital visits for RA treatment during pregnancy are also crucial in reducing the risk of APO.

Disclosure: Y. Song: None; **S. Cho**: None; **Y. Jung**: None; **J. Keum**: None; **S. Jung**: None; **D. Yoo**: Celltrion, 2, 5, 6; **Y. Sung**: Bristol-Myers Squibb(BMS), 5, Eisai, 5, JW Pharmaceutical, 5, Pfizer, 5.

Abstract Number: 0987

Risk Factors and Predictors of Disease Activity in Rheumatoid Arthritis and Psoriatic Arthritis: Data from the Mexican Adverse Events Registry (BIOBADAMEX)

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Background/Purpose: Genetic, demographic, clinical, and immunological factors have been related with the response to treatment in inflammatory rheumatic diseases, such as rheumatoid arthritis (RA) and psoriatic arthritis (PsA). Among them, obesity and smoking are two potentially modifiable risk factors. Obesity has been associated with persistent activity of the disease and a lower response to TNF inhibitors. Active smoking is associated with disease severity and lower response to conventional treatment. The aim of this study is to evaluate the association of baseline characteristics, particularly obesity, smoking and disease activity in patients with RA and psoriatic PsA using data from the Mexican Adverse Events Registry (BIOBADAMEX).

Methods: In this case-control study from an inception cohort from BIOBADAMEX we included all patients with RA and PsA diagnosis registered from 2016 to April 2023. We compared the clinical characteristics between RA and PsA. Patients were divided in 2 groups: those with remission/low disease activity and those with moderate/high disease activity, patients without disease activity registered were excluded. Sociodemographic, clinical, and treatment characteristics were compared between groups. Chi square and Mann Whitney U tests to analyze differences between the groups. Multivariate model was used to analyze disease activity associated variables.

Table 1: Basal characteristics of RA an PsA patients from BIOBADAMEX

	Patients with rheumatoid arthritis (n = 748)	Patients with psoriatic arthritis (n = 70)	p
Gender, female n(%)	687 (91.8)	38 (54.3)	0.3
Age, median (IQR)	52 (43.8 – 60.2)	52 (42.8 – 57.4)	0.7
Body Mass Index, median (IQR)	26.7 (23.8- 30)	29.4 (25.5 – 32)	0.001
Smoking, n(%)	49 (6.6)	5 (7.1)	0.9
Disease duration, years, median (IQR)	14.2 (8.9 – 21.2)	9.7 (6.2 – 15.7)	0.001
Disease Activity Indexes, median (IQR)			
DAS28[a]	5.2 (4.1 – 6)	4.9 (4.3 – 5.8)	0.8
BASDAI[b]	–	6.8 (5.4 – 8)	NA
ASDAS[b]	–	3.7 (3.2 – 4.5)	NA
Comorbidities, n(%)	347 (46.4)	26 (37.1)	0.1
N of comorbidities, median (IQR)	1 (1 – 2)	1 (1 – 2)	0.2
High blood pressure, n(%)	100 (13.4)	9 (12.9)	0.9
Diabetes mellitus, n(%)	83 (11.1)	6 (8.6)	0.6
High cholesterol, n(%)	59 (7.9)	5 (7.1)	0.8
Use of previous biologic, n(%):	298 (39.8)	27 (38.6)	0.8
Use of steroids, n(%):	296 (39.6)	12 (17.1)	0.001
Dose of steroids (mg), median (IQR)	6 (5 – 7.5)	5.5 (5 – 6)	0.3
Use of DMARD, n(%):	593 (79.3)	54 (77.1)	0.6
N of DMARDs, median (IQR)	1 (1 – 2)	1 (1 – 2)	0.9
Adverse events, n(%):	102 (13.6)	6 (8.6)	0.2
Severe, n(%):	19 (2.5)	1 (1.4)	0.4

[a] Rheumatoid arthritis, peripheric psoriatic arthritis, [b] axial psoriatic arthritis
p: Chi square and Mann Whitney U test.

Table 2: RA patients according to disease activity

	RA patients with remission/low activity (n = 106)	RA patients with moderate/high activity (n = 642)	p
Gender, female n(%)	96 (90.6)	591 (92.1)	0.6
Age, median (IQR)	50.3 (42.3 – 59.8)	52 (43.9 – 60.2)	0.2
Body Mass Index, median (IQR)	26.2 (23.2 – 29.1)	26.9 (24 – 30.2)	0.11
Smoking, n(%)	10 (9.4)	39 (6.1)	0.007
Disease duration, median (IQR)	16.1 (11.3 – 22.8)	13.2 (8.3 – 20.9)	0.002
Comorbidities, n(%)	54 (51)	293 (45.6)	0.93
High blood pressure, n(%)	14 (13.2)	86 (13.4)	0.21
Diabetes mellitus, n(%)	7 (6.6)	71 (11.1)	0.3
High cholesterol, n(%)	16 (15.1)	43 (6.7)	0.68
Use of previous biologic, n(%):	66 (62.3)	232 (36.1)	0.001
Use of steroids, n(%):	35 (33)	261 (40.7)	
Dose of steroids (mg), median (IQR)	5 (5 – 6)	5 (5 – 8.7)	0.52
Use of DMARD, n(%):	81 (76.4)	512 (79.8)	0.001
N of DMARDs, median (IQR)	1 (1 – 1)	1 (1 – 2)	0.14
Adverse events[b], n(%):	17 (16)	85 (13.2)	0.43
Severe[b], n(%):	2 (1.9)	17 (2.6)	0.5
p: Chi square and Mann Whitney U test.			

Table 3: PsA patients according to disease activity

	PsA patients with remission/low activity (n = 7)	PsA patients with moderate/high activity (n = 57)	p
Gender, female n(%)	3 (42.9)	34 (59.6)	0.4*
Age, median (IQR)	53.9 (36.2 – 66.7)	51.7 (42.9 – 56.6)	0.5
Body Mass Index, median (IQR)	29 (23.7 – 33.7)	29.4 (25.9 – 31.7)	0.9
PsA type			
Peripheric	4 (57.1)	24 (42.1)	0.7*
Axial	0	9 (15.8)	N/A
Uveitis	1 (14.3)	2 (3.5)	0.3*
Disease duration, median (IQR)	12.6 (8.6 – 18.7)	8.5 (5.5 – 14.3)	0.2
Smoking, n(%)	2 (28)	3 (5.3)	0.03
Comorbidities, n(%)	3 (42.9)	22 (38.6)	0.6*
High blood pressure, n(%)	1 (14.3)	7 (12.3)	0.6*
Diabetes mellitus, n(%)	1 (14.3)	4 (7)	0.5*
High cholesterol, n(%)	2 (28.6)	3 (5.3)	0.08*
Use of previous biologic, n(%):	5 (71.4)	20 (35.1)	0.07
Use of steroids, n(%):	1 (14.3)	10 (17.5)	0.6*
Dose of steroids (mg), median (IQR)	5	5.5 (5 – 6)	0.2
Use of DMARD, n(%):	7 (100)	43 (75.4)	0.16*
Adverse events[b], n(%):	0	5 (8.8)	N/A
Severe[b], n(%):	0	5 (8.8)	N/A
p: Chi square and Mann Whitney U test. *Fisher test			

Results: A total of 818 patients were included, 748 with RA and 70 with PsA. When comparing both groups, we found that PsA patients had higher BMI (29.4 vs 26.7, p = 0.001), lower disease duration (9.7 vs 14.2, p = 0.001) and lower use of steroids (17.1 vs 39.6, p = 0.001). Variables like gender, age, smoking, disease activity, comorbidities were similar (Table 1). When we compared RA patients with remission/low activity and moderate/high activity (Table 2), we found that moderate/high activity patients had lower smoking habit (6.1 vs 9.4, p = 0.007), lower disease duration (13.2 vs 16.1, p = 0.002), and lower use of previous biologic (36.1 vs 62.3, p = 0.001). Comparison between PsA patients with remission/low activity and moderate/high activity (Table 3) showed lower smoking frequency in moderate/high activity (5.3 vs 28, p = 0.03). For the adjusted multivariable analysis, we included age, sex, BMI, smoking, disease duration and previous use of biologic therapy. In RA patients we found that longer disease duration (p = 0.03) and previous use of biologic (p = 0.001) were associated with lower risk of disease activity. In PsA patients we found that smoking habit (p = 0.007) was associated with lower risk of disease activity.

Conclusion: In Mexican RA and PsA patients enrolled in BIOBADAMEX, we found that most of the patients have BMI >25. However, higher BMI did not show an association with disease activity. Further studies comparing BMI levels and activity, as well as comparing Mexican BMI with other regions will be conducted. On the other hand, we found that smoking was associated with lower disease activity, especially in PsA patients. This finding correlates with the Choi HK study where smokers had slower radiographic progression. This finding needs further investigation.

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Abstract Number: 0988

Elderly Patients' Discontinuation of Biologic DMARDs in Patients with Rheumatic Diseases: Data from the Mexican Adverse Events Registry (BIOBADAMEX)

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SESSION INFORMATION

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Background/Purpose: The approach to elderly patients (≥60 years) with rheumatic diseases offers certain difficulties and uncertainties. Older adults are a particularly vulnerable group who often have multimorbidity and polypharmacy. In addition, geriatric syndromes, such as malnutrition, sarcopenia, and frailty, significantly affect the quality of life, which is already compromised by rheumatic diseases. Furthermore, the use of antirheumatic drugs (synthetic or biological) in this group of patients is a major concern due to their potential adverse events. The aim of this study is to Determine if drug discontinuation of bDMARDs differs in elderly patients compared to younger patients with rheumatic diseases registered in the Mexican Adverse Events Registry (BIOBADAMEX).

Methods: In this case-control study from an inception cohort from BIOBADAMEX we included all patients registered from 2016 to April 2023 with at least two assessments. We divided the patients in 2 groups: younger than 60 years and older than 60 years. Survival on similar or originator bDMARDs was estimated using Kaplan-Meier analysis. Predictors of discontinuation, including use of biosimilar drugs were investigated by Cox regression analysis.

Results: Among 1041 patients in the registry, 630 had at least two assessments. Of patients analyzed, 128 (20.3%) were older than 60 years old and 512 (81.3%) were women. The most common diagnoses were RA in 407 (64.6%), ankylosing spondylitis in 83 (13.2%) patients and psoriatic arthritis in 44 (6.9%). At baseline, patients had a median (IQR) age of 50.5 (40.1-58.1) years old, median disease duration of 6.9 (2.7-13.9) years. The most common bDMARDs received were adalimumab 122 (19.4%), certolizumab 96 (15.2), tocilizumab 95 (15.1), abatacept 82 (13.0) and rituximab 67 (10.6). At the time of analysis, the median bDMARDs treatment duration was 58.8(38.6-70.7) months, 264 (41.9%) had discontinued treatment, 135 for inefficacy, 108 for adverse events and 21 for others. Fig 1 shows discontinuation rate curves in patients younger and older than 60 years old.Cox proportional-hazards demonstrated no significant differences regarding age older than 60 years old (HR 1.0, 95% CI 0.8-1.2, p=0.7), age as continuous variable (HR 0.9, 95% CI 0.9-1.0, p=0.07), use of corticosteroids (HR 1.2, 95% CI 0.9-1.4, p=0.05) or comorbidities (HR 0.9, 95% 0.6-1.5, p=0.78). To have a disease duration shorter than the median (≤6.9 years) (HR 1.2, 1.1-1.4 p=0.03), history of an adverse event (HR 2.4, 1.1-4.8, p=0.02) and high disease activity (HR 1.5,95%CI 1.2-1.7, p< 0.001) were characteristics associated with discontinuation. In the multivariable Cox regression analysis history of adverse event and high disease activity were the only variables that remained associated.

Conclusion: This analysis did not show a role of elderly age on discontinuation of bDMARDs in Mexican patients with rheumatic diseases. Survival analysis showed that in our population high disease activity and history of adverse events are associated with the discontinuation of bDMARDs.

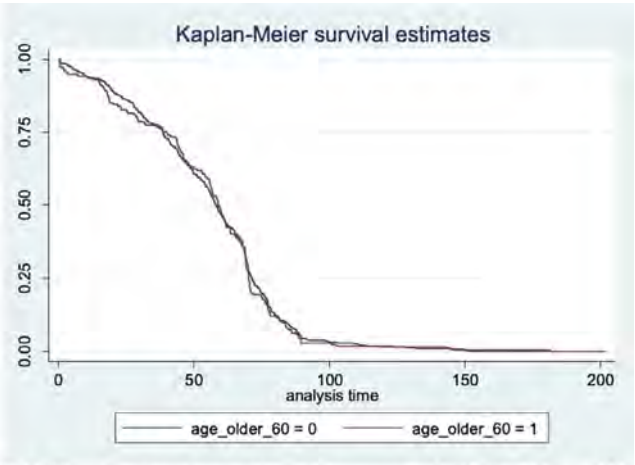

Fig 1. Discontinuation rate curves in patients younger and older than 60 years old

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Abstract Number: 0989

Rheumatoid Arthritis and Risk of Migraine: A Population-based Nationally Representative Cohort

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SESSION INFORMATION

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Background/Purpose: Migraine is the second most prevalent neurologic disorder and is known to be associated with neurogenic inflammation. Previous studies suggest an association between migraine and chronic inflammatory rheumatic diseases. However, the relationship between rheumatoid arthritis (RA) and migraine has yet to be determined. This study aimed to evaluate the association between RA and subsequent migraine risk specifically in the Korean population.

Methods: This was a retrospective cohort study using the Korean National Health Insurance Service database. Participants were enrolled from 2010 to 2017 and followed up until 2019 (median follow up 4.4 years after a 1-year lag period). RA was defined using ICD-10 codes, prescription of any disease modifying anti-rheumatic drug, and enrollment in the Rare and Intractable Disease program. A total of 42,674 patients who had undergone a health checkup within 2 years prior to the initial diagnosis of RA were included in the study, after applying the exclusion criteria (previous migraine, other rheumatic disease, missing variables that were of interest). Among them, there were 29,744 patients with seropositive RA (SPRA) and 12,900 patients with seronegative RA (SNRA). A non-RA control was obtained by age- and sex- matching (1:5), resulting in the inclusion of 213,370 non-RA participants as controls. Primary outcome was the occurrence of incident migraine, defined using the ICD-10 code of migraine (G43) in the claim database. Cox proportional hazards regression analyses and Kaplan Meier curve were used for analysis.

Results: A total of 22,294 migraine cases (17,912 control and 4,382 RA) had developed. RA participants had a 1.2-fold higher risk of migraine compared with controls (adjusted hazard ratio [aHR] 1.2, 95% confidence interval [CI] 1.17-1.26). Increased risk of migraine was found in both patients with SNRA and SPRA compared with controls (aHR 1.20, CI 1.15-1.24 in SPRA; aHR 1.26, CI 1.20-1.33 in SNRA). Compared to the SNRA group, those with SPRA did not demonstrate

a heightened risk (aHR 0.94, CI 0.88-1.01). The association between RA and incident migraine was statistically significant in males (aHR 1.3 in male, 1.2 in female, p for interaction 0.04), current smokers (aHR 1.35 in current smoker, 1.31 in ex-smoker, 1.2 in never smoker, p for interaction 0.02), those with diabetes mellitus (aHR 1.33 in DM, 1.2 in non-DM, p for interaction 0.04,) and those with hyperlipidemia (aHR 1.31 in hyperlipidemia, 1.17 in non-hyperlipidemia, P for interaction 0.002).

Conclusion: RA was associated with increased risk of migraine. There was no difference in the risk of developing migraine based on seropositivity for rheumatoid arthritis.

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Abstract Number: 0990

Association of Treatment and Disease Activity with Antibiotic Use and Hospitalized Infection Among People Living with Rheumatoid Arthritis: Baseline Data from a Longitudinal Study in the ArthritisPower Registry

Kelly Gavigan[1], Esteban Rivera[2], Odette Kolenky[3], Cassie Clinton[4], Emily Holladay[4], David Curtis[5], Laura Stradford[6], Jeffrey Curtis[4], W. Benjamin Nowell[6], Christian Curtis[7] and Michael George[8], [1]Global Healthy Living Foundation, Upper Nyack, NY, [2]Global Healthy Living Foundation, Long Island City, NY, [3]Hospital of the University of Pennsylvania, Philadelphia, PA, [4]University of Alabama at Birmingham, Birmingham, AL, [5]Global Healthy Living Foundation, San Francisco, CA, [6]Global Healthy Living Foundation, Nyack, NY, [7]Illumination Health, Birmingham, AL, [8]University of Pennsylvania, Philadelphia, PA

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Session Time: 9:00AM–11:00AM

Background/Purpose: Infections are a major contributor to morbidity and mortality in patients (pts) with rheumatoid arthritis (RA). Little is known about the risk of non-serious infections, however, which are much more common than serious infections. This study aimed to use baseline data from an ongoing longitudinal study to identify factors associated with both serious infection in the past year and recent non-serious infection.

Methods: Pts with RA from a national rheumatology community practice-based research network, the Excellence Network in RheumatoloGY (ENRGY), were remotely recruited July 2022 to May 2023 to join a prospective 6-month study. Results of baseline surveys are reported, with longitudinal data collection ongoing. Interested pts were asked to join the ArthritisPower research registry to complete monthly assessments about their physical, mental, and social health, physical function, infections, and medication use. At baseline, pts reported recent antibiotic use in the preceding 3 months and hospitalization due to infection in the preceding year, as proxies for non-serious and serious infection, respectively. We hypothesized that older age, glucocorticoid use, DMARD type, comorbidities, and measures of more severe disease would be associated with greater frequency of both serious and non-serious infection.

Results: At time of analysis, 307 pts with RA completed the baseline assessments. The mean (SD) age was 59 (14), 84% female, 86% non-Hispanic white (Table 1). TNF inhibitors were used by 47% of pts and 23% of pts were taking glucocorticoids, most commonly at doses ≤5 mg/day. Thirty-one pts (10%) reported permanently stopping RA medication in the past because of an infection. A total of 85 pts (28%) reported antibiotic use in the preceding 3 months and 17 (6%) reported

Table 1. Participant Demographic and Clinical Characteristics at Baseline ‡ PROMIS measures are T scores with range 1-100, general US population mean 50 with standard deviation of 10 ^ Patient Global Assessment of disease activity score range from 0 to 10 with higher scores indicating more severe disease activity ϕ Patient reported flare in past 30 days

Table 1. Participant Demographic and Clinical Characteristics at Baseline

	N=307
Age, mean (SD)	59.1 (13.8)
Female, n (%)	257 (83.7)
Race/Ethnicity, n (%)	
White, non-Hispanic	265 (86.3)
Hispanic	27 (8.8)
Black, non-Hispanic	10 (3.3)
Other	5 (1.6)
Years since diagnosis, mean (SD)	13.1 (11.8)
Glucocorticoid use, n (%)	
≤5 mg	50 (16.3)
>5 mg	22 (7.2)
Disease Modifying Anti-Rheumatic Drugs (DMARDs), n (%)	
Conventional synthetic DMARD without biologic/JAKi	70 (22.8)
TNF inhibitor	145 (47.2)
Non-TNF inhibitor biologic	61 (19.9)
JAK inhibitor	31 (10.1)
Comorbidities, n (%)	
Asthma/COPD	65 (21.2)
Depression	72 (23.5)
Diabetes	37 (12.1)
Smoking Status, n (%)	
Current Smoker	17 (5.5)
Previous Smoker	104 (33.9)
Never Smoked	186 (60.6)
Patient-Reported Outcomes at Baseline, mean (SD)	
PROMIS Physical Function ‡	43.1 (8.2)
PROMIS Fatigue ‡	56.9 (9.8)
PROMIS Depression ‡	50.5 (10.4)
PROMIS Ability to Participate Social ‡	48.4 (9.6)
Patient Global Assessment^	4.1 (2.4)
RA Flare in the past 30 days ϕ	162 (52.8)
Influenza vaccine in past year, n (%)	209 (68.1)
Received one or more doses of COVID-19 vaccine, n (%)	270 (88.0)
Young children at home, n (%)	47 (15.3)
Ever permanently stopped an RA medication due to infection, n (%)	31 (10.1)

‡ PROMIS measures are T scores with range 1-100, general US population mean 50 with standard deviation of 10

^ Patient Global Assessment of disease activity score range from 0 to 10 with higher scores indicating more severe disease activity

ϕ Patient reported flare in past 30 days

hospitalization for infection in the preceding year (Table 2). Antibiotic use was associated with current glucocorticoids [OR 2.2 (95% CI, 1.2, 3.8)], recent RA disease flare [2.0 (1.2, 3.3)], worse PROMIS physical function < 40 [OR 2.5 (1.5, 4.1)], worse patient global ≥4 [1.9 (1.1, 3.2)], and asthma/COPD [OR 2.1 (1.2, 3.7)]. These factors were similarly associated with hospitalization although differences were not statistically significant (Table 2). Associations between DMARD type and both outcomes were modest and not statistically significant (Table 2).

Conclusion: Patients with RA with glucocorticoid use, recent disease flares, and poorer physical function and disease severity measures were more likely to report recent antibiotic use in the preceding 3 months and hospitalization in the past year. Both disease activity and treatment, particularly glucocorticoids, may affect both risk of serious infections and more common non-serious infections. Infections also influence treatment decisions, however, and pts not infrequently reported stopping medications because of infections. Accounting for disease activity and the potential that certain medications may

Table 2. Results of Univariate Regression Models for Antibiotic Use in Prior 3 Months and Hospitalization for Infection in Prior Year *p <0.05 a Patient reported flare in past 30 days b PROMIS measures are T scores with range 1-100, general US population mean 50 with standard deviation of 10 c Patient Global Assessment of disease activity score range from 0 to 10 with higher scores indicating more severe disease activity

Table 2. Results of Univariate Regression Models for Antibiotic Use in Prior 3 Months and Hospitalization for Infection in Prior Year

	Antibiotic use in past 3 months # Outcomes = 85 (27.7%) OR (95% CI)	Hospitalization for infection in past year # Outcomes = 17 (5.5%) OR (95% CI)
Age >65 years old	1.06 (0.63, 1.78)	0.75 (0.26, 2.17)
Female	1.26 (0.62, 2.54)	0.44 (0.15, 1.31)
Glucocorticoid use		
None	Reference	Reference
Any dosage	2.16 (1.23, 3.77)*	2.42 (0.89, 6.62)
Disease Modifying Anti-Rheumatic Drugs (DMARDs)		
Conventional synthetic DMARDs without biologic/JAKi	Reference	Reference
TNF inhibitor	1.45 (0.74, 2.84)	1.09 (0.32, 3.68)
Non-TNFi biologic	1.79 (0.82, 3.91)	0.28 (0.03, 2.53)
JAK inhibitor	1.50 (0.57, 3.93)	1.77 (0.37, 8.42)
RA flare past month[a]	1.97 (1.18, 3.30)*	3.08 (0.98, 9.65)
PROMIS Physical Function[b] <40	2.46 (1.47, 4.10)*	2.41 (0.89, 6.51)
Pt Global Assessment[c] ≥4.0	1.89 (1.11, 3.22)*	2.39 (0.76, 7.52)
Diabetes	1.12 (0.53, 2.38)	0.97 (0.21, 4.43)
COPD or Asthma	2.07 (1.16, 3.68)*	2.14 (0.76, 6.01)
Young children at home	1.27 (0.65, 2.49)	1.77 (0.55, 5.68)

*p <0.05

[a] Patient reported flare in past 30 days

[b] PROMIS measures are T scores with range 1-100, general US population mean 50 with standard deviation of 10

[c] Patient Global Assessment of disease activity score range from 0 to 10 with higher scores indicating more severe disease activity

be avoided in high risk patients (confounding by indication) are important when assessing infection risk with medications, and will be a focus of the longitudinal analysis from this cohort.

Disclosure: K. Gavigan: Global Healthy Living Foundation, 3; **E. Rivera**: Global Healthy Living Foundation, 3; **O. Kolenky**: None; **C. Clinton**: None; **E. Holladay**: None; **D. Curtis**: Global Healthy Living Foundation, 3; **L. Stradford**: Global Healthy Living Foundation, 3; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Cor-Evitas, 2, 5, Eli Lilly and Company, 2, 5, Janssen, 2, 5, Myriad, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **W. Nowell**: AbbVie/Abbott, 2, 5, Amgen, 5, Janssen, 2, 5, Scipher Medicine, 5; **C. Curtis**: None; **M. George**: AbbVie/Abbott, 2, GlaxoSmithKlein(GSK), 5, Janssen, 5.

Abstract Number: 0991

Trends in Arthroplasty Utilization for Inflammatory Arthritis Including Rheumatoid Arthritis and Spondyloarthritis in China: Analysis of a Large National Database

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Epidemiology & Public Health Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: For end-stage inflammatory arthritis (IA) including rheumatoid arthritis (RA) and spondyloarthritis (SpA), joint arthroplasty is the only treatment option, but is considered to be a failure of medical treatment. Country-level socioeconomic factors play an important role in treatment options and long-term outcomes of IA. Though trends in arthroplasty utilization for RA and SpA have been well-studied in high-income countries, the data are still scarce in low- or middle-income countries. Understanding the trends in arthroplasty utilization in low- or intermediate-income countries would add epidemiological data on this topic and have important implications for health policy in these countries. Using the Chinese national inpatient database (i.e., the Hospital Quality Monitoring System), we aimed to examine trends in arthroplasty utilization among patients with RA, SpA, and a composite group of the IA, compared with these trends among those without IA.

Methods: Patients receiving elective primary total knee arthroplasty and total hip arthroplasty for IA or non-inflammatory conditions between 2013 and 2019 were included. The International Classification of Diseases, Tenth Revision codes were used to identify RA and SpA. Comparisons between groups were performed using the Student's t-test for continuous

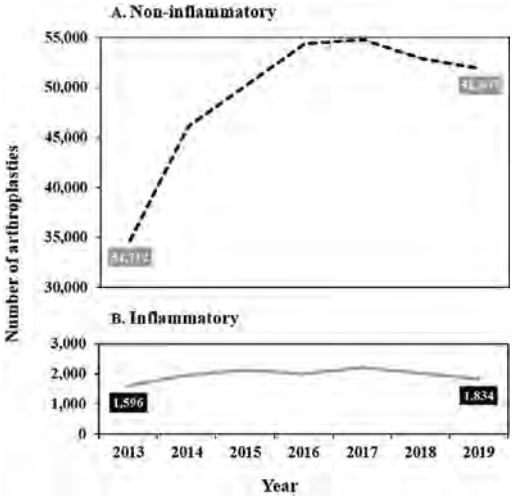

Figure 1. Trends in the number of arthroplasties in the non-inflammatory group (A) and the IA group (B).

variables and chi-square test for categorical variables. A generalized estimating equation model was used to examine trends over time.

Results: Of 358,891 arthroplasties performed between 2013 and 2019, 3.8% (13,747) were performed for IA **(Table 1)**. From 2013 to 2019, the number of arthroplasties for IA slightly increased from 1,596 to 1,834 (average yearly increase rate, 2.0%), and the number of arthroplasties for non-inflammatory conditions significantly increased from 34,712 to 51,907 (average yearly increase rate, 5.9%) ($P < 0.001$) **(Figure 1)**. The proportion of arthroplasty for IA declined from 4.4% to 3.4%. In the IA group, the mean age at arthroplasty increased from 55.8 years to 59.5 years ($P < 0.001$), and a similar result was also found in the non-inflammatory group. The number of arthroplasties for RA increased from 1,366 to 1,701 (average yearly increase rate, 3.2%) ($P < 0.001$). This contrasted with the findings of SpA (average yearly decrease rate, 7.5%) ($P < 0.001$) **(Figure 2)**. Age at arthroplasty increased from 58.5 years to 60.5 years in the RA group ($P < 0.001$) and from 39.5 years to 47.2 years in the SpA group ($P < 0.001$). In addition, a decrease in the proportion of arthroplasty before 50 years among RA and SpA patients was observed.

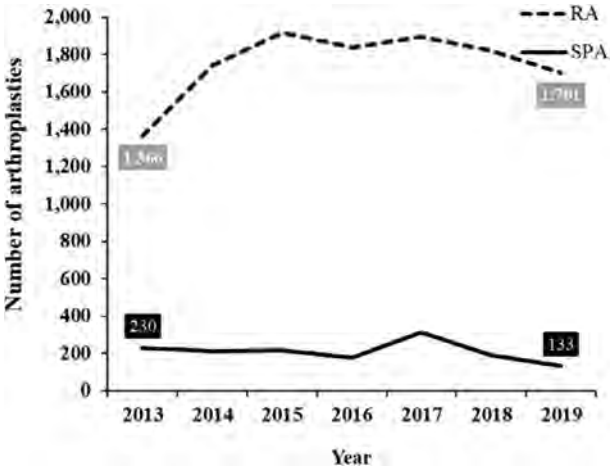

Figure 2. Trends in the number of arthroplasties in the RA group and the SpA group.

Table 1. Characteristics of patients with RA, SpA, IA and non-inflammatory conditions who received TKA or THA

	RA	SpA	IA	Non-inflammatory	*P* value
n (% of total)	12,279 (3.4)	1,468 (0.4)	13,747 (3.8)	345,144 (96.2)	<0.001
Age, mean (SD), years	59.5±11.1	44.7±17.8	57.9±12.8	63.0±11.7	<0.001
Age group, %					
<50	16.3	65.5	21.6	11.4	
50-59	29.5	15.9	28.1	20.4	
60-69	36.9	12.6	34.3	39.3	
70-79	15.5	5.2	14.4	25.2	
≥80	1.8	0.9	1.7	3.7	
P for trend	<0.001	<0.001	<0.001	<0.001	
Male, %	15.3	78.1	23.6	35.7	<0.001
TKA, %	84.3	17.5	77.2	54.9	<0.001
Hospital regions, %					<0.001
Beijing	11.2	9.5	11.0	9.4	
North	9.2	3.5	8.6	8.1	
East	35.3	32.3	35.0	40.4	
North-East	5.1	5.7	5.1	5.7	
South-Central	19.2	31.3	20.5	21.3	
South-West	11.5	5.0	10.8	9.2	
North-West	8.5	12.8	9.0	6.0	
Provincial hospital, %	61.0	62.8	62.6	37.4	<0.001

IA: inflammatory arthritis; TKA: total knee arthroplasty; THA: total hip arthroplasty; RA: rheumatoid arthritis; SpA: spondyloarthritis; IA: inflammatory arthritis; SD: standard deviation.

Conclusion: This nationwide inpatient-based study found that arthroplasty utilization slightly increased in RA, but significantly decreased in SpA in China. The increase in arthroplasty utilization for RA may be driven by the popularity of arthroplasty because a significant decrease in the proportion of arthroplasty for RA was observed. The decrease in arthroplasty utilization for SpA is conceivable given that economic development expanded the access to medical resource. Additionally, an increase in age at arthroplasty for RA and SpA was also found, suggesting long-term outcomes of RA and SpA are improving.

Disclosure: D. Xie: None; **Q. Jiang**: None; **Y. Wang**: None; **H. Long**: None; **H. Chen**: None; **J. Wei**: None; **X. Li**: None; **H. Wang**: None; **C. Zeng**: None; **G. Lei**: None.

Abstract Number: 0992

Association Between Metabolic Syndrome and the Presence of Enthesophytes on Musculoskeletal Ultrasound Compared to Joint X-ray

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Enthesophytes consist of calcium deposition on tendons or ligaments that are proposed to form in response to localized inflammation of the enthesis, either idiopathic or in response to repetitive strain. The exact etiology of these deposits is unknown, but it has been proposed that they form as a result of tendon degeneration or a cell-mediated reactive process, and one working theory postulates that enthesophyte formation could be correlated with metabolic disorders. It is suggested that metabolic syndromes contribute to enthesopathy through tendon degeneration, aging and overuse. While joint X-ray is known to identify enthesophytes, musculoskeletal ultrasound (MSUS) offers dynamic testing due to its non-invasive nature, decreased radiation burden, affordability and versatility. There is limited research that focuses on ultrasound identification of enthesophytes in relation to metabolic syndrome and compared to other imaging modalities.

Methods: This pilot study compared the prevalence of metabolic syndrome, (characterized as hypertension, hyperlipidemia, diabetes mellitus, elevated Body Mass Index (BMI)) and enthesophytes identified on imaging between MSUS examinations and joint X-rays. The patients were identified through retrospective data collection taken from General Rheumatology Clinic and Rheumatology MSUS Clinic. 49 joints evaluated for joint pain by X-ray demonstrated enthesophytes and 5 joints evaluated for joint pain by MSUS demonstrated enthesophytes. We aimed to evaluate how many patients with joint pain found to have enthesophytes also had comorbid metabolic syndrome.

Results: Of the 49 joints demonstrating enthesophytes on X-ray, this population showed a prevalence of comorbid metabolic syndrome per joint as follows: pelvis - 17/18, knee - 9/10, and ankle - 21/21. The joint X-ray population showed evidence of enthesophytes according to age range per joint as follows: pelvis - < 40yo: 0/8, 40-70yo: 15/71, and >70yo: 3/11, knee - < 40yo: 0/8, 40-70yo: 6/71, >70yo: 4/11, and ankle - < 40yo: 0/8, 40-70yo: 16/71, and >70yo: 5/11.

Of the 5 joints demonstrating enthesophytes with MSUS, this population showed a similar prevalence of comorbid metabolic syndrome in isolated studies of the hip/pelvis (n=1), ankle (n=3).

Conclusion: As a pilot study, we found that X-ray is useful in detecting enthesophytes as a pathologic cause of pain in patients with metabolic syndrome. This highlights the need to investigate further the mechanism that drives this force. Joint X-ray showed a correlation of metabolic syndrome and age with the presence of enthesophytes. In our early MSUS evaluations, detection is achievable as well and demonstrates the high prevalence metabolic syndrome and the presence of enthesophytes, which indicates that there may be a safer, faster, more affordable way to evaluate for this underlying comorbid condition.

Disclosure: S. Brown: None; **J. Hardin**: None; **S. Mahmood**: Qiagen, 6.

Abstract Number: 0993

Successful Implementation of a New Patient Video Triage Program

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Health Services Research Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Many factors contribute to long wait times for new patient rheumatology visits including the increasing number of rheumatology referrals and new patient visits. Through a separate retrospective analysis, we found that many new patients (32%) in our rheumatology clinics likely did not need to see rheumatology and could have been evaluated via e-Consult (72%). In addition, with the expansion and acceptance of telemedicine, we postulated a new patient video triage program could facilitate appropriate care while also avoiding unnecessary in-person rheumatology appointments.

Table 1: Comparison of referral reason and referral source between rheumatology follow-up needed vs not needed groups

No Rheum Follow up needed (n=103)				Rheum Follow up needed (n=57)		
Referral source:						
Primary care	60%			60%		
Self-referred	24%			26%		
Specialist referral	16%			14%		
Referral reason:						
Joint pain	39	37.9%		Joint pain	25	43.9%
ANA+	20	19.4%		Rheumatoid arthritis	10	17.5%
Fibromyalgia	8	7.8%		ANA+	7	12.3%
Rash	4	3.9%		Gout	3	5.3%
Rheumatoid arthritis	3	2.9%		Psoriatic arthritis	2	3.5%
elevated ESR or CRP	3	2.9%		Osteoporosis	2	3.5%
Osteoarthritis	3	2.9%		Other	8	14.0%
Fatigue	3	2.9%				
Back pain	2	1.9%				
Numbness/paresthesia	2	1.9%				
myalgia	2	1.9%				
chronic pain	2	1.9%				
Autoimmune disease	2	1.9%				
Other	10	9.7%				

Methods: New patients scheduling a rheumatology appointment from December 2022 through May 2023 were offered a video triage appointment option with a rheumatology provider at our tertiary academic medical center. Patients were advised this appointment would determine whether they would need subsequent evaluation or follow-up with rheumatology. If appropriate after evaluation, they were scheduled for an in-person appointment (average of 2 weeks later). Subsequently, a chart review was completed to validate our primary outcome of interest: need of in-person rheumatology follow-up. We also compared the 2 groups of patients: those that needed in-person rheumatology follow up vs. those that did not need follow-up to evaluate for differences in terms of visit reason and referral source. Lastly, we measured the difference in median wait times for video vs in-person new appointments.

Results: A total of 225 patients were included in the rheumatology new patient video triage program. Of these, 103 (46%) patients were found to not require an in-person rheumatology follow up and were referred back to their primary care provider or another specialty for follow-up. Only 57 (25%) patients required a subsequent in-person rheumatology follow up. A total of 26 (12%) patients did not show to or cancelled their appointments. 14 (6%) patients did not complete follow-up testing after the video appointment. The remaining 25 patients are currently being assessed to determine if ongoing rheumatology care is needed. Referral sources were similar between patients who required rheumatology follow-up and those who did not (Table 1). Reasons for initial visit are shown in Table 1. The top diagnoses that did require rheumatology follow-up were joint pain, rheumatoid arthritis (RA), and +ANA, whereas those that did not require an in-person follow-up were joint pain, +ANA, and fibromyalgia. The current median wait for a new in-person rheumatology appointment in our division is 80 days compared to a 30 day wait time for a new patient video triage appointment.

Conclusion: Through a new patient video triage program for rheumatology patients, we have shown that only 25% of the video patients needed a subsequent in-person rheumatology follow up. The referral sources and most common reason for visit were similar between the 2 groups. Of note, the average wait time for a video triage appointment is less than half of an in-person new patient appointment. Given these findings, we plan to continue this successful new patient video program to help facilitate more timely initial rheumatology evaluation and facilitate more appropriate in-person rheumatology visits.

Disclosure: D. Sharma: None; **A. Dore**: AbbVie/Abbott, 1, 6, Bristol-Myers Squibb(BMS), 1, Exagen, 6, Novartis, 1; **C. Rossi**: None; **J. Heintzinger**: None.

Abstract Number: 0994

Narrative Medicine and Pediatric Rheumatology: Addressing Burnout and Bias

Aviya Lanis, Natalie Rosenwasser and Esi Morgan, Seattle Children's Hospital, Seattle, WA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Health Services Research Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Burnout, a syndrome of emotional exhaustion and depersonalization, adversely impacts healthcare and results in mood disturbances, poor patient and provider satisfaction and high turnover. Studies have shown burnout also plays a critical role in physician bias, with increased bias among those with higher rates of burnout. The SARS-CoV-2 pandemic increased levels of burnout and exposed the high prevalence of racial bias in healthcare. There is a critical need

for methods to address burnout and bias in healthcare. Narrative medicine (NM) incorporates the stories of human experience into the medical realm and has been proven to strengthen relationships and increase empathy. To date, limited data investigating narrative medicine's impact on burnout and bias has been promising. This pilot study aims to investigate the use of NM as a tool to address burnout and explore bias amongst a pediatric rheumatology division.

Methods: Physicians, nurses, medical assistants and staff at a single center enrolled in a series of six monthly 1-hour video-based sessions lead by co-facilitators (AL, and a NM-trained facilitator) after informed consent. Sessions utilized poetry, photography, paintings, and spoken word to inspire writing prompts around the medical experience. A Plan-Do-Study-Act approach was used to guide intervention adjustments based on participant post-session feedback. Demographics were collected, and standard surveys were administered at baseline, and after the third and sixth sessions, specifically: Mini Z Burnout, Copenhagen Burnout Inventory (CBI), Provider Health Questionnaire-9 (PHQ-9) as well as Implicit Association Testing (IAT) and explicit bias Feeling Thermometer (FT).Survey data were assessed for differences with a Wilcoxon signed rank test.

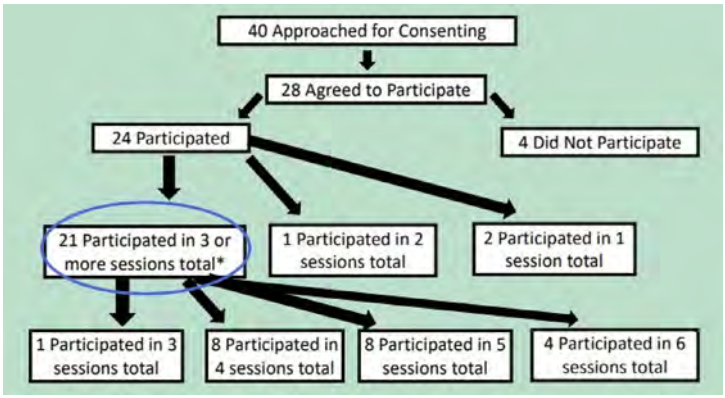

Figure 1: Breakdown of individuals consented compared to those who participated.

Table 1: Pre-, intra- and post-participation questionnaire results including observations, mean, standard deviation (SD), median, range, and Wilcoxon signed-rank test p-values. For Mini Z Burnout, a score of 20 or higher is considered to be a joyful work environment. For the CBI, a score of 50-74 is concerning for moderate burnout, 75-99 with high burnout, and a score of 100 shows severe burnout. For the PHQ-9, a score of 1-4 demonstrates minimal depression, 5-9 demonstrates mild depression, 10-14 demonstrates moderate depression and 20-27 demonstrates severe depression.

	Mini Z Burnout			Copenhagen Burnout Index (CBI)			Patient Health Questionnaire-9 (PHQ-9)		
	Pre	Intra	Post	Pre	Intra	Post	Pre	Intra	Post
Observations	21	20	16	21	19	17	21	18	17
Mean	29.2	29.5	31.4	42.8	38.4	34.5	6.0	4.6	4.2
SD	6.4	6.2	5.2	13.2	16.7	17.2	5.0	3.8	3.9
Median	30	30	32	39.5	34.2	28.9	5.0	3.5	3.0
Range	15-38	18-38	23-39	25-75	17.1-84.2	5.26-81.58	0-17	0-13	0-13
Wilcoxon Signed Rank Test P-value Pre/Intra	0.775			0.258			0.727		
Wilcoxon Signed Rank Test P-value Intra/Post		0.703			0.185			0.858	
Wilcoxon Signed Rank Test P-value Pre/Post	0.375			0.052			0.680		

Results: Twenty-four participants with 21 females, 2 males and one non-binary were divided amongst 6 narrative medicine groups for the 6 total sessions. Data analysis was completed for those who attended 3 or more sessions (n=21) (See Figure 1). Self-identified race included 18 White, 4 Asian, 1 Black, and 1 who preferred not to answer. Participants included 8 attendings, 4 fellows, 2 nurses, 2 medical assistants, and 8 staff members. While no statistical significance was seen when evaluating questionnaires for the Mini Z Burnout, CBI, or PHQ-9 when comparing questionnaires from baseline and after 6 months into participation, there was a trend toward improvement with median CBI improved from 39.5 to 28.9, and median PHQ-9 score improved from 5 to 3. (Table 1). IAT showed a statistically significant shift towards positive association with African Americans following participation (p-value= 0.012), while FT showed a non-statistically significant explicit bias shift away from positive association with European Americans (p=0.096).

Conclusion: Narrative medicine is a feasible intervention that warrants further study as a means to address bias. Additional long-term analysis is needed to understand if these changes are durable.

Disclosure: A. Lanis: None; **N. Rosenwasser**: None; **E. Morgan**: None.

Abstract Number: 0995

Rheumatoid Arthritis Early Diagnostic Clinic: A Web-based Referral Tool Serving Ethnic Minority Patients

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Health Services Research Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis (RA) data indicate a "window of opportunity" during which DMARD therapy is most effective in achieving early and sustained remission, hence expedited access and early diagnosis is essential. Health status disparities exist in ethnic minority (EM) patients with rheumatic disease, inclusive of RA, particularly with early access and referral to specialty care. RA early referral tools have led to decreased wait times and increased numbers with the diagnosis. Therefore expedited referral in EM RA populations would be advantageous for early diagnosis and intervention. We evaluated a web-based referral tool developed to facilitate referrals of EM patients with symptoms of inflammatory arthritis to specialty care.

Methods: We designed an online referral tool, RHEUMATOID ARTHRITIS EARLY DIAGNOSTIC CLINIC [RAEDC], for primary care physicians (PCPs) at clinics serving EM patients. Based on the 4 domains of the ACR/EULAR 2010 RA Classification Criteria, the tool included a joint homunculus for PCP input of swollen and tender joints. PCPs received a RA educational lecture emphasizing the importance of early referral as well as joint exam techniques. Patients who received a score of ≥6 were scheduled for a RAEDC visit within 2 weeks. PCPs received feedback within 48 hours of the visit regarding RA diagnosis and accuracy of joint exam. Demographic data, RA disease status (Anti-CCP, RF), tender and swollen joint counts (TJC, SJC), ESR, CRP, and disease activity measures (RAPID-3, CDAI) were collected at baseline and compared to Ethnic Minority RA Consortium (EMRAC), an established disease cohort. Treatment patterns for the RAEDC cohort RA patients were assessed at baseline and at 3, 6, and 12 months. PCPs completed a 10-point Likert scale assessing utility of the referral tool.

Baseline Data for RAEDC patients vs. EMRAC cohort

	RAEDC referrals (N=35)		RA diagnosis (N=11)		Non-RA diagnosis (N=24)		EMRAC (N=97)		RA vs. EMRAC
	Obs	Statistic	Obs	Statistic	Obs	Statistic	Obs	Statistic	P-value:
Age (years)	35	49.8(12.6)	11	48.4 (13.7)	24	50.4(12.3)	85	58.0 (16.2)	0.064
Female (%)*	35	25 (71.4%)	11	10(91%)	24	15 (62.5%)	97	80 (82.5%)	0.687
Black / African-American (%)*	35	12 (34.3%)	11	3 (27.3%)	24	9 (37.5%)	95	80 (84.2%)	**<0.001**
Hispanic / Latino (%)*	35	19 (54.3%)	11	7(63.6%)	24	12 (50%)	95	11 (11.3%)	**<0.001**
Disease Duration (years)	35	0 (0.0)	11	0 (0.0)	24	0 (0.0)	57	10.0 (10.9)	**0.004**
Education (years)	23	12.2(7.4)	10	11.1(5.7)	13	13.1(8.6)	94	12.6 (3.8)	0.205
Function [0-10]	31	3.2(2.2)	11	3.5(2.3)	20	3.1(2.2)	75	2.2 (2.2)	0.072
Pain [0-10]	31	6.7(2.9)	11	7.6(2.2)	20	6.3(3.2)	79	4.3 (3.3)	**0.002**
Fatigue [0-10]	20	4.7 (3.8)	8	4.6 (4.3)	12	4.8 (3.6)	80	3.2 (3.2)	0.256
Patient Global [0-10]	30	6.2(3.1)	11	6.3(2.9)	19	6.1(3.3)	82	3.3 (3.1)	**0.003**
Physician Global [0-10]	26	4.3(2.7)	9	5.5(2.5)	17	3.6(2.7)	66	3.6 (2.6)	**0.043**
Morning Stiffness (min)	31	127.1(309.8)	11	46.4(42.7)	20	171.5(380.5)	78	41.1 (65.8)	0.796
Tender Joints [0-28]	32	7.4(8.9)	11	11.9(9.6)	21	5.1(7.8)	97	1.5 (3.3)	**<0.0001**
Swollen Joints [0-28]	32	2.7(4.5)	11	6.5(6.0)	21	0.7(1.1)	97	2.6 (3.5)	**0.002**
Rheumatoid Factor Positive (%)*	31	12 (38.7%)	11	10(90.9%)	20	10 (50%)	24	22 (91.7%)	0.999
Anti-CCP Positive (%)*	23	13(56.5%)	9	6 (66.7%)	14	7(50%)	21	18 (85.7%)	0.329
Sedimentation Rate (mm/hr)	30	35.4(32.5)	10	37.1(28.7)	20	34.6(35.0)	57	31.1 (26.2)	0.512
C-Reactive Protein (mg/L)	24	16.5(23.2)	8	12.3(15.8)	16	18.7(26.6)	56	9.9 (17.1)	0.709
RAPID3 [0-30]	30	16.5(6.9)	11	17.3(6.0)	19	16.1(7.5)	73	9.8 (7.6)	**0.003**
CDAI [0-76]	26	20.8(13.2)	9	30.9(13.5)	17	15.4(9.7)	64	12.3 (9.9)	**<0.0001**
Prednisone Use at Enrollment (%)*	11	2 (18.1%)	11	2 (20%)	24	0 (0.0%)	97	13 (13.4%)	0.649
Methotrexate Use at Enrollment (%)*	11	0 (0.0%)	11	0 (0.0%)	24	0 (0.0%)	97	23 (23.7%)	0.116
Other DMARD Use at Enrollment (%)*	11	0 (0.0%)	11	0 (0.0%)	24	0 (0.0%)	97	17 (17.5%)	0.207
Biologic Use at Enrollment (%)*	11	0 (0.0%)	11	0 (0.0%)	24	0 (0.0%)	97	8 (8.2%)	0.999

*N(%) reported and Chi-Square [†Fisher's Exact] reported. Otherwise, Mean (SD) reported and t-test reported.

Baseline Data for RAEDC patients vs. EMRAC cohort

Medication Use for RAEDC Referrals Diagnosed with RA

	Enrollment (N=11)		Baseline (N=11)		First Follow Up (N=9)**		3 months (+/- 1 month) (N=8)**		6 months (+/- 1 month) (N=5)		12 months (+/- 2 months) (N=5)	
	Obs	Statistic	Obs	Statistic	Obs	Statistic	Obs	Statistic	Obs	Statistic	Obs	Statistic
Follow Up (Months)					9	1.2 (0.6)	8	3.0 (0.5)	5	5.9 (0.5)	5	11.1 (0.9)
Prednisone Use (%)*	11	2 (18.2%)	11	4 (36.4%)	9	3 (33.3%)	8	4 (50.0%)	5	1 (20.0%)	5	1 (20.0%)†
Methotrexate Use (%)*	11	0 (0.0%)	11	5 (45.4%)	9	5 (55.5%)	8	6 (75.0%)	5	4 (80.0%)	5	5 (100.0%)
Other DMARD Use (%)*	11	0 (0.0%)	11	3 (27.3%)	9	3 (33.3%)	8	5 (62.5%)	5	3 (60.0%)	5	4 (80.0%)
Biologic Use (%)*	11	0 (0.0%)	11	0 (0.0%)	9	1 (11.1%)	8	1 (12.5%)	5	0 (0.0%)	5	1 (20.0%)

*N(%) reported. Otherwise, Mean (SD) reported. **One patient's first follow-up visit was at the 3-month time point. †Patient had a one-time dose of 40 mg IM Methylprednisolone at this visit.

Medication Use for RAEDC Referrals Diagnosed with RA

Results: Of 51 referrals, 35 were evaluated, and 16 did not keep their appointment. Of the 35 patients seen, 11 met ACR/EULAR RA Classification Criteria (31%). Whereas RAEDC patients were evaluated within 2-4 weeks of referral, the average time to diagnosis for the EMRAC cohort was 4 months. Compared to EMRAC, RAEDC patients were mostly Hispanic, with lower educational levels, higher pain/fatigue/patient global scores, TJC, SJC, ESR, CRP, and disease activity scores RAPID-3 (17.3 [6.0] vs. 9.8 [7.6], p=0.003) and CDAI (30.9 [13.5] vs. 12.3 [9.9], $p < 0.0001$) (Table 1). At initial visit, 72.7% received a DMARD (45.4% MTX, 27.3 % other DMARD), with 100% on a DMARD within a year (Table 2). Only 20% remained on Prednisone at 12 months. Alternate inflammatory diagnoses included Gout, PMR, and SS, despite ~50% of the referral cohort with a positive RA serology. PCPs indicated favorable utility of the online tool (Likert 7.8).

Conclusion: An online referral tool accompanied by initial teaching of PCP end-users served to increase RA awareness and early referral. The early access to specialty care led to initiation of DMARDs in all patients, with limited Prednisone use by one year. Our tool served to advocate for EM patients with low education status and emphasized the importance of joint exam by PCPs in the presence of RA serologies. Evaluations of improved accuracy in joint exam by PCPs and patient opinion in use of the online tool are planned.

Disclosure: M. Quinones: Bristol-Myers Squibb(BMS), 5, CVS Health - CVS Caremark, 2, Pfizer, 5; **S. Dowell**: Aurinia, 6, Bristol-Myers Squibb(BMS), 5, Janssen, 1; **I. Jileaeva**: None; **O. Kadiri**: None; **C. Swearingen**: Biosplice Therapeutics, Inc, 3; **G. Kerr**: AstraZeneca, 2, Aurinia, 6, Horizon, 2, Janssen, 2, Pfizer, 1, Sanofi, 2.

Abstract Number: 0996

Will Patients Engage with Digital Technologies as Part of Routine Healthcare?

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Health Services Research Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

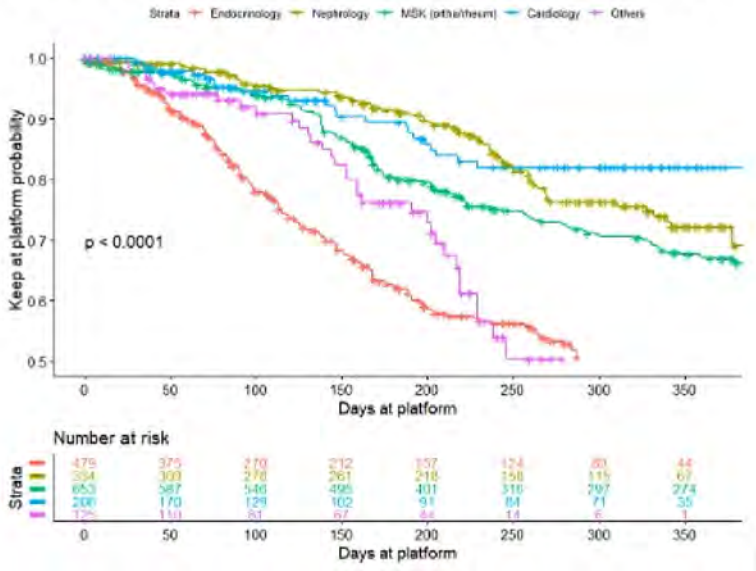
Background/Purpose: Remote Physiologic Monitoring (RPM) and Remote Therapeutic Monitoring (RTM) are new care delivery options by which patients can provide data to their provider via a biosensor device and/or smartphone app in an insurance reimbursable fashion. However, patients' willingness and persistence to engage in RPM/RTM over time is unclear.

Table 1: Characteristics of Patients Enrolled in RPM/RTM

	Endocrinology	Nephrology	MSK (ortho/rheum)	Cardiology	Other
N	479	334	653	206	125
Age, years (Mean (SD))	58.6 (15.3)	75.1 (11.7)	70.4 (10.9)	77.6 (8.8)	67.8 (14.2)
Women, %	296 (62.8%)	171 (54.6%)	429 (66.7%)	136 (66.0%)	78 (62.9%)
Median National Area Deprivation Index (ADI) ADI >=80 (deprived)*, %	50 (10.5%)	0 (0.0%)	24 (3.9%)	29 (14.2%)	14 (11.2%)

RPM = remote physiologic monitoring; RTM = remote therapeutic monitoring; MSK = musculoskeletal
**proportions shown of those with data available*

Figure 2: Persistence with RPM and RTM Over Time, Stratified by Specialty



Methods: Using data from 9/2020 - 5/2023, we examined characteristics of patients who enrolled in a national RPM/RTM program as part of routine care, stratified by medical specialty. Time on the program began at the time patients were first enrolled in the program and contributed data and continued until they voluntarily withdrew from the program, were lost to follow up (i.e. became inactive) or were censored. Kaplan Meier curves described persistence over time, stratified by medical specialty, combining musculoskeletal (orthopedics and rheumatology) and Others (e.g. pulmonology, primary care) into a single group. Cox proportional hazards models evaluated the time to discontinuation by medical specialty, adjusting for age and sex.

Results: A total of 1797 patients were enrolled, with characteristics as described in table 1.Mean age was greater than 70 years for all cohorts except endocrinology. Persistence with RPM/RTM significantly differed by specialty (Figure). Approximately 80% of patients being monitored for musculoskeletal conditions were approximately 80% adherent at 6 months. Referent to patients being monitored for musculoskeletal conditions (e.g. rheumatology), persistence with RPM/RTM was worse for patients being monitored for endocrinology conditions (age-sex-adjusted hazard ratio for non-persistence=2.3, 95% CI 1.8-2.8) and was not different for other specialties.

Conclusion: Most patients with musculoskeletal or other chronic health conditions are persistent with digital health care delivery systems such as remote physiologic and remote therapeutic monitoring. Strategies to optimize patient engagement with such programs are important to maximize the health benefits of these new digital healthcare delivery mechanisms.

Disclosure: J. Curtis: AbbVie, 2, 5, Amgen, 2, 5, BMS, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Genentech, 2, 5, Janssen, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB Pharma, 2, 5; **S. Sodhi**: None; **Y. Su**: None; **S. Laster**: None; **F. Xie**: None; **Y. Liu**: None; **C. Patrick**: None.

Abstract Number: 0997

Impact of Depression on Healthcare Utilization in Members with Underlying Rheumatoid Arthritis, Psoriatic Arthritis and Systemic Lupus Erythematosus

W. Cliff Rutter, Jean Park, Elisea Avalos-Reyes, Chen Liu, Will Cavers, Dorothea Verbrugge and Kjel Johnson, CVS Health, Woonsocket, RI

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Health Services Research Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and systemic lupus erythematosus (SLE) have higher rates of psychiatric comorbidities, particularly depression and anxiety. Comorbid depression has been associated with increased disease activity in patients with rheumatic conditions. What isn't known, is how comorbid depression impacts healthcare utilization in these patients. The objective of this study was to assess the impact of depression on healthcare utilization in patients with RA, PsA and SLE.

Methods: This cohort study included fully insured commercial or Medicare members of a large national health plan between 1/1/2018 and 1/1/2023. Members ≥ 18 years old were included if they had at least 2 visits for RA (ICD-10 code: M05 or M06), PsA (L40.5), or SLE (M32) during the study period. Members were excluded if they did not maintain continuous

Table 1. Demographic characteristics

Variable	No MDD N(%)= 76797 (70.5)	MDD N(%) = 32209 (29.5)	P-Value
Gender, n (%)			<0.001
F	51744 (67.4)	25739 (79.9)	
M	25053 (32.6)	6470 (20.1)	
Age, mean (SD)	57.5 (15.4)	58.2 (15.5)	<0.001
Age, median [Q1,Q3]	59.0 [47.0,69.0]	59.0 [48.0,69.0]	<0.001
Age category, n (%)			<0.001
18-45	17037 (22.2)	6682 (20.7)	
46-55	15475 (20.2)	6337 (19.7)	
56-65	19573 (25.5)	8223 (25.5)	
66-75	15421 (20.1)	6668 (20.7)	
>75	9291 (12.1)	4299 (13.3)	
Person time (months), mean (SD)	23.9 (14.5)	24.8 (14.4)	<0.001
Person time (months), median [Q1,Q3]	21.0 [12.0,33.0]	22.0 [13.0,35.0]	<0.001
Charlson Comorbidity Index, mean (SD)	2.8 (2.6)	3.8 (3.1)	<0.001
Charlson Comorbidity Index, median [Q1,Q3]	2.0 [1.0,4.0]	3.0 [1.0,5.0]	<0.001
Region, n (%)			<0.001
Midwest	12871 (16.8)	6306 (19.6)	
Northeast	23455 (30.5)	7930 (24.6)	
South	31415 (40.9)	14575 (45.3)	
West	9056 (11.8)	3398 (10.5)	
SES Index, n (%)			<0.001
Very Low	10670 (13.9)	4770 (14.8)	
Low	24113 (31.4)	11364 (35.3)	
Medium	22119 (28.8)	9100 (28.3)	
High	14712 (19.2)	5312 (16.5)	
Very High	5183 (6.7)	1663 (5.2)	
Primary condition, n(%)			<0.001
PSA	9629 (12.5)	3531 (11.0)	
RA	56980 (74.2)	23744 (73.7)	
SLE	10188 (13.3)	4934 (15.3)	

Table 2. Healthcare utilization by depression status

Utilization metric	No MDD N(%)= 76797 (70.5)	MDD N(%) = 32209 (29.5)	P-Value
Telemedicine users, n (%)	21591 (28.1)	11399 (35.4)	<0.001
Telemedicine claims in users, mean (SD)	9.9 (15.6)	23.3 (39.7)	<0.001
Telemedicine claims in users, median [Q1,Q3]	5.0 [2.0,11.0]	11.0 [4.0,26.0]	<0.001
Telemedicine (claims per 100 PY), rate (95% CI)	139.9 (139.3-140.5)	399 (397.5-400.6)	
Rate difference (95% CI)	-259.1 (-260.5, -257.8)		<0.0001
Rate ratio (95% CI)	0.351 (0.349-0.353)		<0.0001
ER users, n (%)	26447 (34.4)	17438 (54.1)	<0.001
ER days in users, mean (SD)	2.5 (3.1)	3.7 (4.9)	<0.001
ER days in users, median [Q1,Q3]	2.0 [1.0,3.0]	2.0 [1.0,4.0]	<0.001
ER (days per 100 PY), rate (95% CI)	42.7 (42.4-43)	96.9 (96.1-97.6)	
Rate difference (95% CI)	-54.2 (-54.9, -53.5)		<0.0001
Rate ratio (95% CI)	0.441 (0.436-0.445)		<0.0001
Inpatient users, n (%)	15407 (20.1)	11928 (37.0)	<0.001
Inpatient days in users, mean (SD)	7.9 (13.3)	13.0 (23.9)	<0.001
Inpatient days in users, median [Q1,Q3]	3.0 [1.0,8.0]	5.0 [2.0,14.0]	<0.001
Inpatient (days per 100 PY), rate (95% CI)	79.2 (78.7-79.6)	233 (231.8-234.1)	
Rate difference (95% CI)	-153.8 (-154.8, -152.8)		<0.0001
Rate ratio (95% CI)	0.34 (0.337-0.342)		<0.0001

eligibility for 6 months before or after entrance into the study, had multiple conditions of interest, or had missing socioeconomic status (SES) data. Members were stratified by presence of a visit for depression and anxiety (MDD). Healthcare utilization metrics were examined as use of telemedicine, emergency department (ER), or inpatient services and were identified by place of service codes on medical claims. Telemedicine utilization included both medical and behavioral health visits. ER and inpatient claims were aggregated by day and are presented by days utilizing the service. Utilization rates were calculated based on total person years observed in each cohort and the sum of telemedicine claims. ER days and inpatient days are presented as claims or days per 100 person years observed. Rate differences and rate ratios (RR) were calculated with 95% confidence intervals (CI). Continuous variables were assessed utilizing t-tests; categorical variables were assessed with the Chi^2 test. P-values < 0.05 are significant.

Results: Of the 109,006 members included, 32,209 (29.5%) had a visit for depression (MDD). Table 1 demonstrates significant differences in baseline demographics between disease states, with MDD members being older (mean age (standard deviation (SD)): 58.2 (15.5) vs. 57.5 (15.4) years; p< 0.001) and having more comorbidities at baseline (mean Charlson Comorbidity Index (SD): 3.8 (3.1) vs. 2.8 (2.6); p< 0.001). Table 2 demonstrates the differences in healthcare utilization between cohorts. Members in the MDD group had significantly higher telemedicine (RR [95% CI]: 2.85 [2.83 – 2.86]; p< 0.0001), ER (RR [95%CI]: 2.27 [2.25-2.29]; p< 0.0001), and inpatient (RR [95% CI]: 2.94 [2.92-2.97]; p< 0.0001) utilization.

Conclusion: Members diagnosed with RA, PsA, or SLE with visits for depression and anxiety utilized significantly more healthcare services than those that did not have depression. These findings highlight the importance of managing depression and anxiety when treating patients with RA, PsA and SLE.

Disclosure: W. Rutter: CVS Health, 3, 11; **J. Park**: CVS Health, 3, 11; **E. Avalos-Reyes**: AstraZeneca, 11, CVS Health, 3, 11, GlaxoSmithKlein(GSK), 11, Haleon, 11, Johnson & Johnson, 11, Moderna, 11, Novavax, 11, Pfizer, 11, Viatris, 11; **C. Liu**: CVS Health, 3, 11; **W. Cavers**: Amedisys Inc, 11, Baxter, 11, Conmed Corp, 11, CVS Health, 3, 11; **D. Verbrugge**: CVS Health, 3, 4, 11; **K. Johnson**: CVS Health, 3, 4, 11, HC Technology Patent, 10.

Abstract Number: 0998

Barriers and Facilitators for Osteoporosis and Sarcopenia Care for Persons Living with HIV in Peru: HIV Physician and Coordinator Perspectives

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Health Services Research Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Persons living with HIV (PLWH) have a higher risk of developing age-related non-communicable diseases (NCDs), such as osteoporosis and sarcopenia. In Peru, HIV providers are the primary point of medical care for PLWH. Using a qualitative approach, we examined health system barriers and facilitators for osteoporosis and sarcopenia care for PLWH in Peru from the perspective of HIV physicians and coordinators.

Methods: HIV regional program coordinators and physicians affiliated with Peru's National HIV, STI and Hepatitis Program were recruited from the Program's physician and coordinator registry and by peer referral. All coordinators (N=31) were contacted for a semi-structured in-depth interview over Zoom by a trained Peruvian research assistant. Physicians were purposefully sampled to ensure adequate regional representation. Interviews continued until thematic saturation was reached in both groups. The interviews were recorded and transcribed using Sonix.ai and checked for accuracy. Transcripts were translated to English following a standardized protocol by a team of bilingual translators, and then coded in English by two

Table 1. Interviewee Demographics

	Coordinators N=25	Physicians N=14
Age (mean) +/- SD [range]	46 +/- 9.1 [31-65]	46 +/- 9.5 [32-59]
Sex N (%) Male Female	 7 (28%) 18 (72%)	 9 (64%) 5 (35%)
Region N (%) Coast Highlands Jungle	 13 (52%) 8 (32%) 4 (16%)	 7 (50%) 4 (29%) 3 (21%)
Professional Training N (%)	RN/Midwife 23 (92%) MD 2 (8%)	Infectious Disease 12 (86%) Generalist/Internist 2 (14%)

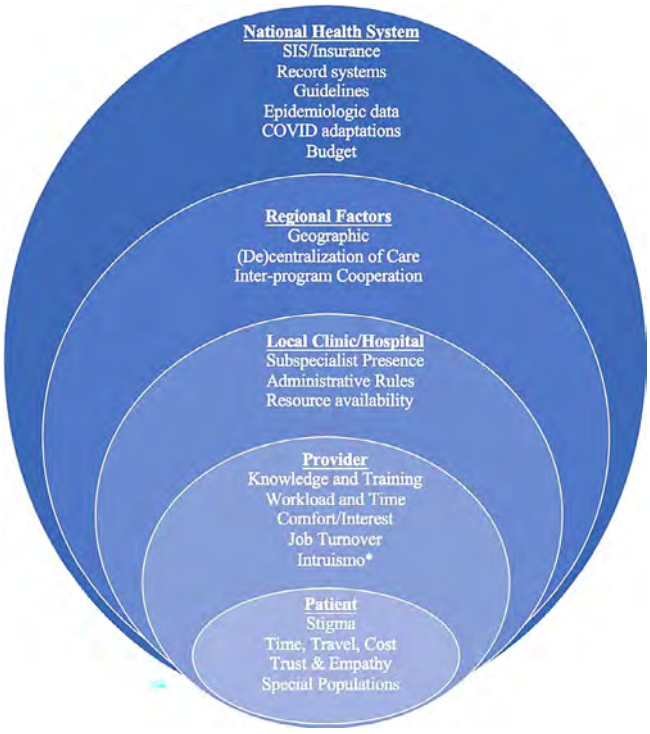

Figure 1. Socioecological Model Applied to Barriers and Facilitators of Osteoporosis and Sarcopenia Care for Persons Living with HIV. Emerging themes and sub-themes from physician and coordinator interviews were visualized using this adapted socioecological model. *Translates to the idea that one should not overstep the boundaries of their specialty.

independent coders, one of which was Peruvian to ensure culturally appropriate codes. All codes were discussed, and discrepancies were resolved by consensus. The emerging themes and sub-themes were visualized using an adapted socioecological framework.

Results: Twenty-five regional coordinators and 14 physicians were interviewed to reach thematic saturation (Table 1). Barriers and facilitators discussed by both groups were organized into major themes following a socioecological model: patient, provider, local clinic/hospital, regional, and national health system (Figure 1). Coordinators highlighted health system components such as budget, resources, the impact of the pandemic, existing NCD programs, lack of epidemiologic data on NCDs, and a motivation to improve care for PLWH. While some physicians were enthusiastic about learning more and providing osteoporosis/sarcopenia care themselves or were already providing some direct management, others felt that the patient was better served by referral to a specialist. Physicians noted barriers of knowledge/training, interest, time, workload, lack of guidelines, available medications and DXA, and an inclination to stay within the scope of their specialty, which is encouraged by their health system at the local and national levels. Physicians reported that they were aware of the growing burden of NCDs in patients aging with HIV. They described a unique position of trust with their patients, who preferred their HIV provider to manage their NCDs to simplify their care and avoid stigma, especially in areas lacking access to NCD-trained specialists.

Conclusion: This study highlights the complex interplay between patient, provider, local, regional, and national factors that influence care delivery to PLWH in Peru. Addressing the barriers of osteoporosis and sarcopenia management in PLWH will require support from HIV physicians and coordinators as well as health system level interventions such as national guidelines, training, and increased access to screening resources.

Disclosure: R. Slotkin: None; **D. Granda Calderón**: None; **J. Malca Hernandez**: None; **D. Cabrera**: None; **C. Benites Villafane**: None; **P. García**: None; **E. Hsieh**: None.

Abstract Number: 0999

Race, Payer, and Hospital Factors Are Associated with Post-primary Total Hip Arthroplasty Healthcare Utilization

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Health Services Research Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Over 450,000 primary total hip arthroplasties (THA) are performed each year. One major indication for primary THA is the presence of osteoarthritis (OA). Patient characteristics, insurance payer status, and regional and hospital level factors can lead to disparities in outcomes and costs of primary THA in patients with OA. We aimed to examine the association of these factors to extended lengths of stay and increased hospital costs after primary THA.

Methods: We utilized the National Inpatient Sample (NIS) to identify patients with OA who underwent primary THA in 2019. Diagnoses and procedures were identified using the International Classification of Disease (ICD-10) codes. We stratified healthcare/resource utilization by the occurrence of an extended length of stay (eLOS) and the presence of an increased

Table-1: Baseline Hospital and Patient Characteristics with Osteoarthritis who undergo Primary Total Hip Replacement in the Nationwide Inpatient Sample (2019, N=424,555)

Variables	
Age (standard error)	66 (0.1)
Sex	
Male	186080 (43.8)
Female	238475 (56.2)
Race & Ethnicity	
White	355940 (86.2)
Black	32630 (7.9)
Hispanic	13020 (3.2)
Asian or Pacific Islander	3695 (0.9)
Native American	1360 (0.3)
Other	6350 (1.5)
Region	
Northeast	83650 (19.7)
Midwest	108920 (25.7)
South	144535 (34.0)
West	87450 (20.6)
Payer	
Medicare	243645 (57.5)
Medicaid	20115 (4.7)
Private	146090 (34.4)
Self-pay or other	14220 (3.4)
Median Income Quartile by Patient ZIP Code	
1st (Highest Income)	83435 (19.9)
2nd	103775 (24.8)
3rd	115455 (27.6)
4th (Lowest Income)	115930 (27.7)
Hospital Bed Size	
Small	142770 (33.6)
Medium	116655 (27.5)
Large	165130 (38.9)
Location & Teaching Status	
Rural	35715 (8.4)
Urban Non-Teaching	93825 (22.1)
Urban Teaching	295015 (69.5)
Hospital Control	
Government (Public)	35450 (8.3)
Private, Not-for-Profit (Voluntary)	325735 (76.7)
Private (Proprietary)	63370 (14.9)
Extended Length of Stay (> 2 days)	82110 (19.3)
Increased Total Charge (> $76,000)	105640 (25.0)
Non-Routine Discharge	53015 (12.5)
Perioperative Complication	9015 (2.1)
Mortality	280 (0.1)

Data are reported as raw numbers with proportions (%) for comparison

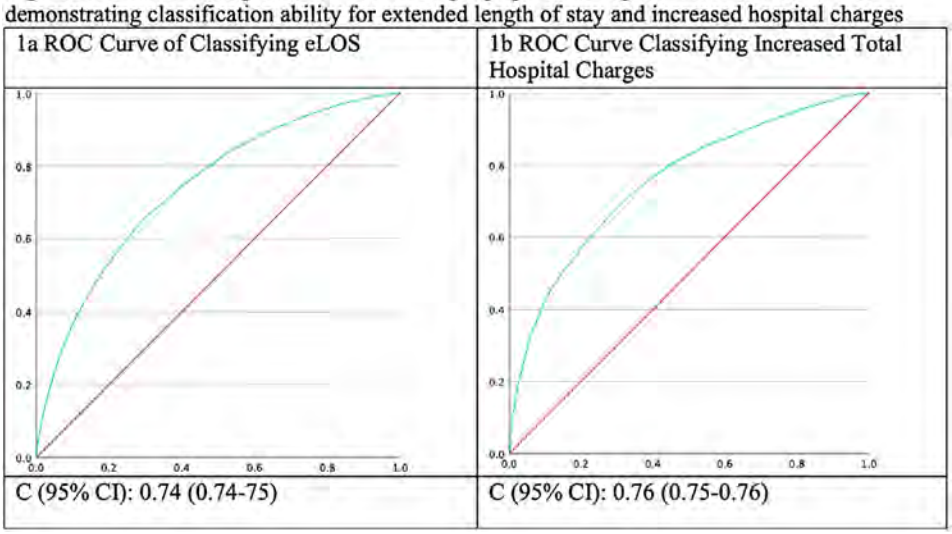
Table-2: Multivariable analysis of regional characteristics for primary outcomes extended length of stay and increased hospital charge (2019, N=424,555)

	Extended LOS (> 2 days)		Increased Hospital Charge (> $78,000)	
Variables	aOR (95% CI)	p-value	aOR (95% CI)	p-value
Age	1.63 (1.58-1.69)	<0.001	0.95 (0.91-0.98)	0.001
Sex		<0.001		<0.001
Male	Ref		Ref	
Female	1.57 (1.50-1.63)		0.91 (0.88-0.95)	
Race & Ethnicity		<0.001		<0.001
White	Ref		Ref	
Black	1.86 (1.70-2.03)		1.15 (1.00-1.30)	
Hispanic	1.39 (1.21-1.59)		1.67 (1.42-1.98)	
Asian or Pacific Islander	1.41 (1.09-1.82)		1.37 (1.02-1.84)	
Native American	1.85 (1.29-2.65)		0.74 (0.52-1.07)	
Other	1.30 (1.07-1.59)		1.74 (1.39-2.19)	
Region		<0.001		<0.001
Northeast	Ref		Ref	
Midwest	0.89 (0.76-1.04)		0.72 (0.48-1.09)	
South	0.69 (0.58-0.82)		1.61 (1.07-2.41)	
West	0.45 (0.38-0.55)		3.17 (2.09-4.81)	
Payer		<0.001		0.003
Medicare	1.39 (1.29-1.49)		1.11 (1.03-1.20)	
Medicaid	2.91 (2.61-3.23)		1.22 (1.06-1.42)	
Private	Ref		Ref	
Self-pay or other	1.65 (1.42-1.91)		0.92 (0.77-1.09)	
Median Income Quartile by Patient ZIP Code		<0.001		0.488
1st (Lowest Income)	1.41 (1.27-1.55)		1.01 (0.84-1.22)	
2nd	1.31 (1.20-1.43)		0.97 (0.82-1.16)	
3rd	1.21 (1.12-1.30)		0.94 (0.81-1.08)	
4th (Highest Income)	Ref		Ref	
Hospital Bed Size		0.770		0.004
Small	1.03 (0.90-1.19)		0.58 (0.42-0.80)	
Medium	1.05 (0.92-1.18)		0.91 (0.71-1.17)	
Large	Ref		Ref	
Location & Teaching Status		<0.001		<0.001
Rural	1.533 (1.34-1.75)		0.38 (0.29-0.51)	
Urban Non-Teaching	0.91 (0.80-1.04)		0.87 (0.67-1.14)	
Urban Teaching	Ref		Ref	
Hospital Control		<0.001		<0.001
Government (Public)	1.60 (1.35-1.91)		0.55 (0.38-0.79)	
Private, Not-for-Profit (Voluntary)	Ref		Ref	
Private (Proprietary)	0.70 (0.57-0.86)		4.19 (2.98-5.91)	
Perioperative Complication	2.27 (2.02-2.56)	<0.001	1.29 (1.13-1.48)	<0.001
Length of Stay	-	-	1.37 (1.26-1.49)	<0.001
Total Hospital Charge	1.17 (1.14-1.20)	<0.001	-	-

Column data reported as no. patients (% proportion) unless otherwise specified

Unit of change for age = 10; Unit of Change for Total Hospital Charge = 10,000

Figure-1: Multivariable prediction models of geographic and regional level characteristics demonstrating classification ability for extended length of stay and increased hospital charges



hospital charge (IHC), i.e., the upper quartile each outcome. Univariate and multivariable analyses compared patient-level, regional, and hospital characteristics associated with an eLOS or IHC. Predictive probabilities from multivariable analyses were used in Area Under the Curve (AUC) analysis.

Results: There were 424,555 patients with OA who underwent primary THA in 2019. Patient race/ethnicity, Medicaid or Medicare payer status, income, age/sex and nearly all regional, and hospital, characteristics were independently associated with eLOS (ROC C-statistic = 0.74). Significant independent predictors for IHC were race & ethnicity ($p < 0.001$), hospital region ($p < 0.001$), hospital location & teaching status ($p < 0.001$), and hospital control ($p < 0.001$). The ROC curve classifying IHC had a C-statistic of 0.76.

Conclusion: Patient race/ethnicity and insurance payer status are important determinants of longer LOS for primary THA hospitalizations in the US. Well-known geographical and hospital-level disparities are negatively associated with the outcomes and costs of primary THA in patients with OA. Policy and other interventions targeting these factors may help reduce utilization for elective THA.

Disclosure: K. Rumalla: None; **S. Chandrupatla**: None; **J. Singh**: Other, 2, 6, 11, 11, 12, Adaptimmune Therapeutics, GeoVax Labs, Pieris Pharmaceuticals, Enzolytics Inc., Seres Therapeutics, Tonix, Charlotte's Web, 12, Atai life sciences, kintara therapeutics, Intelligent Biosolutions, Acumen pharmaceutical, TPT Global Tech, Vaxart pharmaceuticals, Atyu biopharma, 12, speaker's bureau of Simply Speaking, other, 12, received institutional research support from Zimmer Biomet Holdings. JAS received food and beverage payments from Intuitive Surgical Inc./Philips Elec, Other, 12, Schipher, Crealta/Horizon, Medisys, Fidia, PK Med, Two labs Inc., Adept Field Solutions, Clinical Care options, Clearview healthcare partners, Putnam.

Abstract Number: 1000

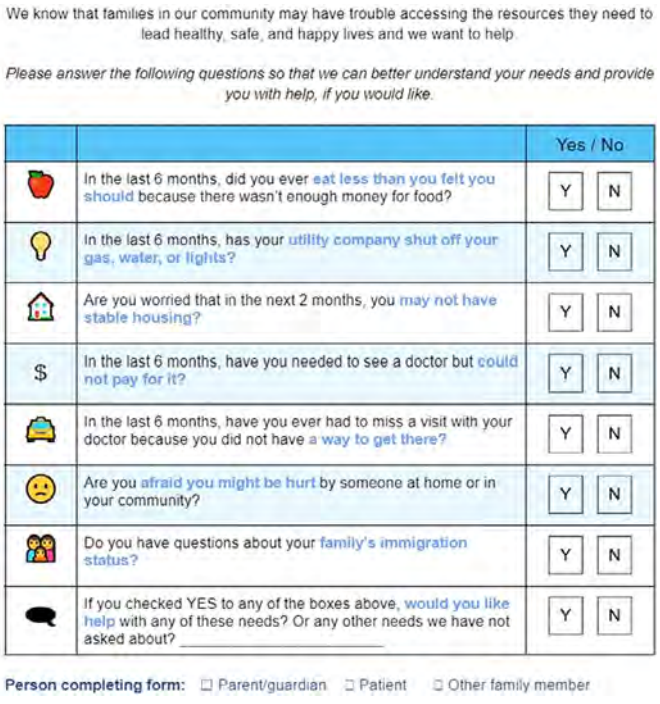
Incorporation of Social Drivers of Health Screening into a Structured Healthcare Transition Program for Adolescents and Young Adults with Chronic Rheumatic Disease

Morayah Ciprien[1], Sarah Barrientos[2], Cori Christenholz[2], Elinore Benett[2] and Rosemary Peterson[1], [1]Dell Medical School at UT Austin, Austin, TX, [2]Dell Children's Medical Center, Division of Rheumatology, Austin, TX

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Health Services Research Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Social drivers of health (SDoH) such as access to housing and food, may significantly influence safe and timely transition to adult healthcare, yet routine screening for psychosocial barriers is uncommon in the pediatric setting. This study aims to successfully implement SDoH screening and proactive social work support into an existing standardized transition program and to assess correlations between positive SDoH screening and transition readiness among pediatric rheumatology patients.

Methods: As part of the clinic's transition program, established patients aged 14 and older with chronic rheumatic disease complete the transition readiness assessment questionnaire (TRAQ) and meet with a child life specialist every 6 months to learn healthcare self-management skills. A physician associate helps the patient schedule their first adult rheumatology visit. Starting August 2022, the SDoH screener, adapted from the Health Leads Screening Toolkit, was given to this same group of eligible patients, or legal guardians if under age 18 (Figure 1). The primary process measure was the percentage of eligible patients who completed the SDoH screener each month and the primary outcome measure was the percentage of positive



We know that families in our community may have trouble accessing the resources they need to lead healthy, safe, and happy lives and we want to help.

Please answer the following questions so that we can better understand your needs and provide you with help, if you would like.

		Yes / No
🍎	In the last 6 months, did you ever eat less than you felt you should because there wasn't enough money for food?	Y N
💡	In the last 6 months, has your utility company shut off your gas, water, or lights?	Y N
🏠	Are you worried that in the next 2 months, you may not have stable housing?	Y N
$	In the last 6 months, have you needed to see a doctor but could not pay for it?	Y N
🚗	In the last 6 months, have you ever had to miss a visit with your doctor because you did not have a way to get there?	Y N
😟	Are you afraid you might be hurt by someone at home or in your community?	Y N
👨‍👩‍👧	Do you have questions about your family's immigration status?	Y N
🗨️	If you checked YES to any of the boxes above, would you like help with any of these needs? Or any other needs we have not asked about? _____	Y N

Person completing form: ☐ Parent/guardian ☐ Patient ☐ Other family member

Figure 1. SDoH screener, adapted from HealthLeads Screening Toolkit

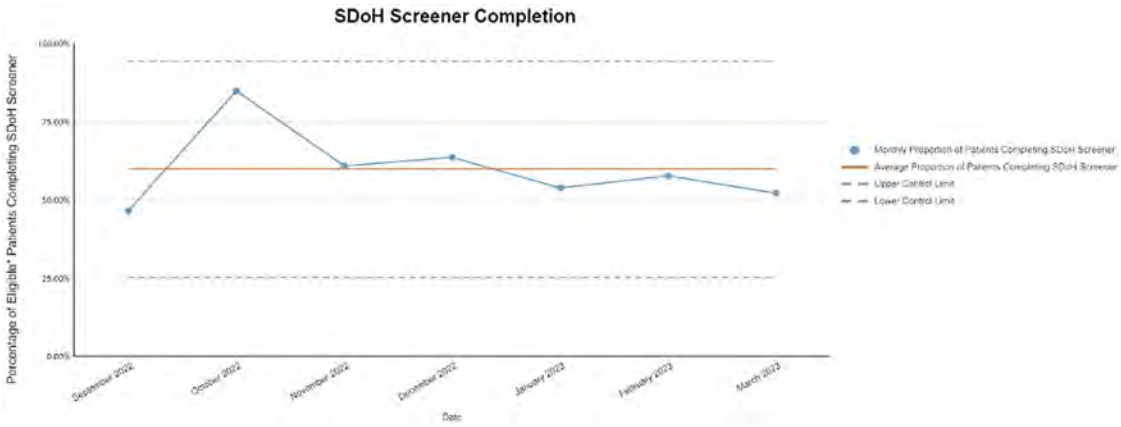


Figure 2. Statistical process control chart of percentage of eligible patients (>= 14 years, established patient, chronic rheumatic disease, present with legal guardian) completing SDoH screener each month.

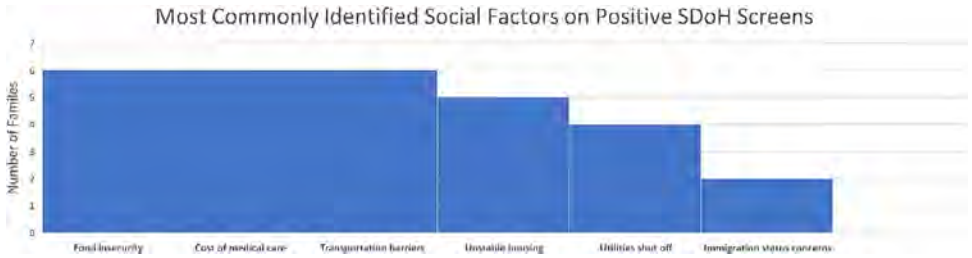


Figure 3. Frequency count of most commonly identified social factors on positive SDoH screeners

SDoH screens. A secure daily message was sent to providers, social work and medical assistants to confirm patient and family suitability to receive screeners. Results of SDoH screening were shared in the same morning text thread at time of rooming and families with positive screens were offered a meeting with the social worker. Two-sample t-test was used to determine the correlation between TRAQ scores and SDoH positivity.

Results: A total of 94 patients/families (median patient age 17 years, IQR 16-18.0) completed the SDoH screener from August 2022 through March 2023 with an average of 59.9% eligible patients per month (Figure 2). Of the completed SDoH screeners, 14.9% (n=14) were positive and 64.2% (n=9) of those families met with social work. Most common social needs included transportation issues (n = 6), food insecurity (n = 6) and financial barriers (n = 6) (Figure 3). Average TRAQ score was 3.43/5 (SD = 0.76) for all patients. There was not a significant difference in mean TRAQ score for patients with positive SDoH screen (mean 3.23 +/- 0.66) and negative SDOH screen (mean 3.52 +/- 0.77; p = 0.2). There was not an association between primary rheumatologic diagnosis and SDoH screen positivity. Since implementation of SDoH screening, only 11 patients have completed their final pediatric rheumatology visit, limiting further analysis of correlation between transition success and SDoH screening.

Conclusion: Implementation of an SDoH screener facilitated proactive social work support for a vulnerable population at risk for an unstable transition to adult care. Transportation, food insecurity, and financial barriers were the most commonly identified needs, informing clinic resource preparation. Next steps include continued long-term follow up of patient cohort, addressing barriers to social work interface with families and collecting patient-facing data regarding SDoH screening acceptability and process to explore possible underreporting bias in our patient population.

Disclosure: M. Ciprien: None; **S. Barrientos**: None; **C. Christenholz**: None; **E. Benett**: None; **R. Peterson**: None.

Abstract Number: 1001

Distance Not Travelled in a Tele-Rheumatology Shared Care Model: Leveraging the Expertise of an Advanced Clinician Practitioner in Arthritis Care (ACPAC)-trained Extended Role Practitioner (ERP) in Rural-remote Ontario

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Health Services Research Poster II
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Session Time: 9:00AM–11:00AM

Background/Purpose: A shortage of Rheumatologists has led to gaps in inflammatory arthritis (IA) care in Canada. Amplified in rural-remote communities, the number of Rheumatologists practicing rurally cannot be meaningfully increased. Alternate care strategies must be adopted. The economic impact of a shared-care Telerheumatology model, utilizing a community-embedded Advanced Clinician Practitioner in Arthritis Care (ACPAC)-ERP and an urban-based Rheumatologist, is described in terms of the estimated travel cost-savings (distance not traveled) for both patients and the healthcare system.

Methods: A Rheumatologist and an ACPAC-ERP located 463 kilometers distally, established a monthly half-day Hub-and-Spoke-Telerheumatology clinic to care for patients with suspected IA, triaged by the ACPAC-ERP. Subsequent collaborative visits occurred with the Rheumatologist (Hub-St. Michael's Hospital, Toronto) attending virtually. Geospatial information for individual patients was obtained using regional postal codes collected through demographic data. Calculations of hypothetical distances between these locations and St. Michael's Hospital were based on the most efficient and cost-effective driving route utilizing Google Maps©. Aggregate data were used to calculate distances not travelled due to the virtual care delivery model. An estimation of further cost-savings of this Telerheumatology shared model of care was based on Ministry of Health (MOH) travel grants that would have been reimbursed to these patients should they have traveled for in-person care.

Results: Data from 124 patients seen between January 2013-January 2022 were collected: 98.0% (n=496/504 visits) were virtual. An estimated 493,470 km of patient-related travel was avoided (basedon 494 Telerheumatology visits). The loci where more than 5 patients resided is represented in Figure 1.A theoretical estimate of the MOH travel grant cost was $276,428, calculated based on the total number of patient visits that would have been incurred should these patients have been followed by the Rheumatologist in-person.

Conclusion: Half of a million kilometers (493,470 km) of travel was avoided for the patients involved in this Telerheumatology study, significantly reducing the carbon footprint and environmental impact by not travelling to access specialist rheumatology care. The estimated $276,428 cost-savings in this study represents a minimal base fiscal value of the ACPAC-trained ERP working within a Telerheumatology model of care. Other indirect costs need to be further captured

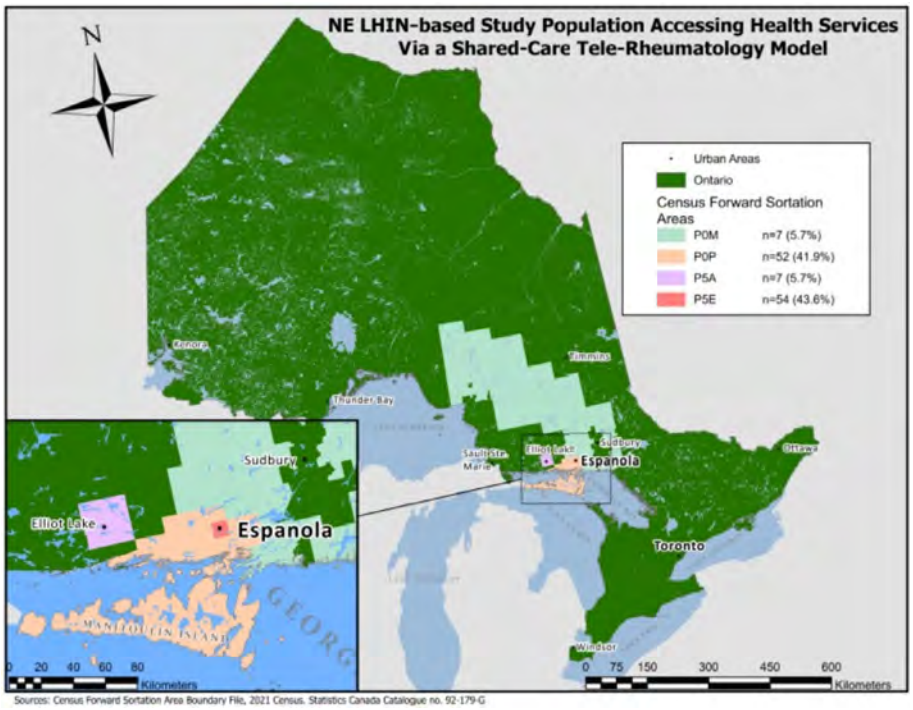

Figure 1.

in a more robust economic analysis. There is a compelling fiscal argument to support scaling-upof this model to deliver comprehensive and cost-effective virtual rheumatologic care in underserved communities provincially and beyond.

Disclosure: A. Steiman: AstraZeneca, 1, GlaxoSmithKlein(GSK), 6, Pfizer, 5; **J. Murdoch**: None; **R. Shupak**: None; **T. Inrig**: Pfizer, 12, I was hired by Unity Health as a Research Coordinator, my salary was supported by a Pfizer unrestricted investigator-initiated grant; **K. Lundon**: None.

Abstract Number: 1002

Optimizing Rural Rheumatology Access: Collaborative Tele-Health Clinic Between University of North Carolina and Piedmont Health 1 Year Extension and Opportunities for Improvement

Prarthana Jain[1], Eli Tiller[2], John Doughton[3], Rumey Ishizawar[4] and Alfredo Rivadeneira[4], [1]University of North Carolina at Chapel Hill, Division of Rheumatology, Allergy and Immunology, Thurston Arthritis Research Center, Pittsboro, NC, [2]University of North Carolina Department of Family Medicine, Piedmont Health Services, Siler City, NC, [3]University of North Carolina Department of Family Medicine, Piedmont Health Services, Prospect Hill, NC, [4]University of North Carolina at Chapel Hill, School of Medicine, Division of Rheumatology, Allergy, and Immunology, Thurston Arthritis Research Center, Chapel Hill, NC

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Health Services Research Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Access to healthcare is challenging for racial and ethnic minorities, especially in medically underserved rural areas.[1] This issue is particularly prevalent in North Carolina where 40% live in rural counties.[2] To address this disparity, a pilot project supported by the Arthritis Foundation was initiated in January 2022, to enhance access to rheumatology specialty care. The project focused on shared telehealth visits between the University of North Carolina (UNC) Rheumatology Clinic and Piedmont Health Services (PHS), a federally qualified health center catering to rural NC patients. This extension of the pilot project evaluates the follow-up data from the past year with expansion to 81 patient encounters and assess limitations of the pilot.

Table 1: Baseline Characteristics (n=81)

Table 1: Baseline Characteristics (n=81)	
Age	
Average Age, n (range)	49. 49 (18-83)
Female, n (%)	68 (84)
Race	
White, n (%)	39 (52.7)
Black, n (%)	2 (2.7)
No response, n (%)	33 (44.6)
Ethnicity	
Hispanic/Latino, n (%)	59 (75.6)
Non-Hispanic / Latino, n (%)	19 (24.4)
Language	
Spanish	51 (67.0)
English	25 (32.9)
Insurance	
No insurance, n (%)	52 (70.3)
Medicaid/Medicare/Tricare, n (%)	11 (14.9)
Private, n (%)	11 (14.9)
Education Level	
< 7 years of school, n (%)	17 (29.3)
Less than a high school diploma, n (%)	7 (12.1)
High school diploma/GED, n (%)	18 (31.0)
College or associate, n (%)	13 (22.4)
Graduate or professional degree, n (%)	3 (5.2)
Type of Visit	
New	33 (67.3)
Return	16 (32.7)
Evaluation	
RA	43 (57.3)
Undifferentiated arthritis	4 (5.6)
SLE	11 (14.7)
PMR	3 (4.0)
Other	14 (18.7)
Medications	
Methotrexate	25 (29.4)
Prednisone	7 (8.2)
TNF alpha inhibitors	17 (20.0)
Tofacitinib	3 (3.5)
Other	15 (17.6)
No response	18 (21.2)
Transportation Time	
<30 minutes, n (%)	3 (3.9)
30-40 minutes, n (%)	28 (36.8)
50-60 minutes, n (%)	31 (40.8)
>60 minutes, n (%)	14 (18.4)
Appointment Wait Time	
<1 month	58 (92.1)
3-6 months	4 (6.3)
>6 months	1 (1.6)
Telehealth Access	
Computer, Tablet, or Smartphone Access at Home, n (%)	62 (82.7)
Internet Access at home, n (%)	54 (81.8)

Methods: Patients eligible for the rheumatology telehealth clinic were established patients with a history of rheumatic disease who had been lost to follow up or new patients requiring rheumatology evaluation who faced transportation and/or financial barriers. Monthly clinic sessions were conducted between the on-site PHS provider and the off-site UNC

Table 2: Patient Satisfaction Response (n=71)

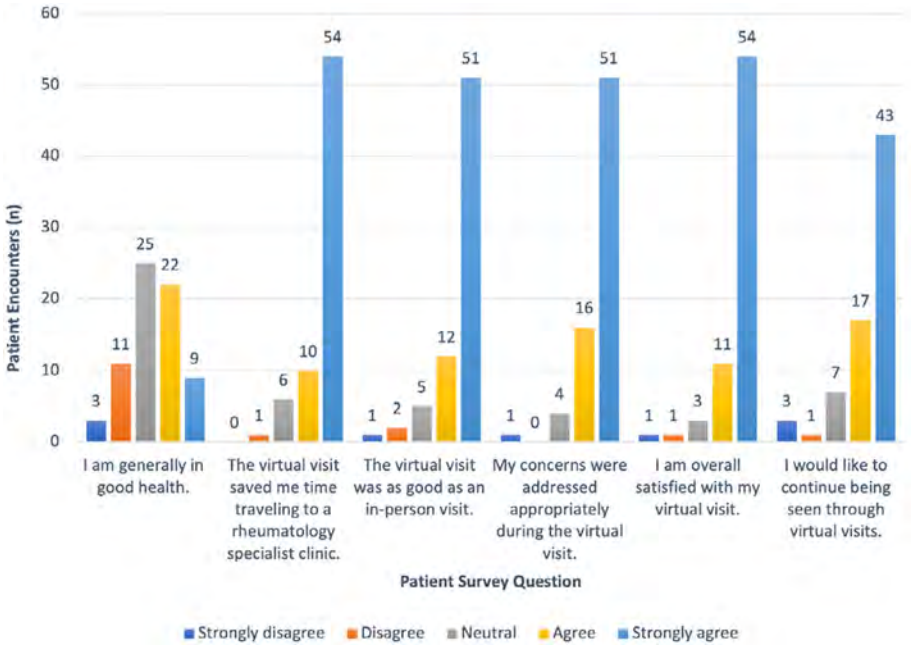

Table 3. PHS Provider Post-Didactic Survey

Table 3. PHS Provider Post-Didactic Survey	
Average Attendees Per Session	
n (%)	3.5 (7.7)
Questions	**Average score**
1. The didactic session enhanced my knowledge of evaluating and managing/co-managing rheumatological illnesses.	4.5
2. I feel comfortable applying the knowledge learned through didactics to patients with similar diseases in my clinic.	4.3
3. Participating in didactics and open forums for patient management questions is an effective way to enhance rheumatology expertise.	4.5
4. I am overall satisfied with the didactic session.	4.5

Scores are calculated from responses on a Likert scale where 1 = Strongly Disagree, 2 = Disagree, 3 = Neutral, 4 = Agree, and 5 = Strongly Agree.

rheumatologist. The PHS provider facilitated the physical examination and relayed objective data while receiving rheumatology guidance over video. The rheumatologist assisted real time with workup and management. Non-identifying patient demographics were also collected. Monthly virtual didactic sessions on core topics in rheumatology were conducted by UNC rheumatologists. PHS provider satisfaction after didactic sessions was evaluated using 5-point Likert surveys.

Results: Between January 2022 and March 2023, a total of 81 encounters (new and return) were completed. Majority of patients identified as female (84%), Hispanic (75.6%), and Spanish-speaking (67.1%). Most patients reported being uninsured (70.3%). The most encountered rheumatic conditions were RA (57.3%), SLE (14.6%), undifferentiated arthritis (5.6%), and other (21.7%). Wait time from referral to visit completion was short, with 92.1% of patients reporting less than a 1-month wait. In contrast, average wait times for new patient visits at UNC was 6 months or greater. Patient satisfaction scores were high and there was a strong interest in continuing to use this telehealth clinic for future visits. Didactic sessions received high satisfaction scores from providers, but attendance was low with an average of 4-5 community providers present per session out of the 45 invited.

Conclusion: This project supported by the Arthritis Foundation employs a unique model connecting an on-site primary care provider with a virtual rheumatologist to address barriers related to transportation, medical costs, internet access and time. Patients reported high satisfaction with this model. This project entailed educational sessions to empower the local community workforce to manage rheumatic conditions. While didactic sessions were rated favorably, provider attendance was low. Future directions include a needs assessment to evaluate barriers faced by community providers to expand rheumatology knowledge and ability to manage basic rheumatic conditions; and therefore, enhance the local community workforce serving the rural medically underserved.

Disclosure: P. Jain: None; **E. Tiller**: None; **J. Doughton**: None; **R. Ishizawar**: None; **A. Rivadeneira**: None.

Abstract Number: 1003

A Multidisciplinary Obstetric-Medicine/Rheumatology Specialty Clinic in the United States: A Five Year Analysis

Griffin Reed[1], Joyce Mathew[1], Kelsey Rigby[2], **Mery Deeb**[3], Elena Cravens[1], Anthony Reginato[4], Gofran Tarabulsi[5] and Joanne Cunha[6], [1]Brown University, Providence, RI, [2]Dartmouth Hitchcock Medical Center, Falmouth, MA, [3]Brown University, Warwick, RI, [4]The Warren Alpert Medical School of Brown University, Providence, RI, [5]Women and Infants Hospital, The Warren Alpert Medical School of Brown University, Providence, RI, [6]The Warren Alpert Medical School of Brown University, Riverside, RI

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Health Services Research Poster II
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Background/Purpose: Rheumatic disorders frequently affect women of childbearing age. These diseases and medications used to treat them can have adverse effects on fertility and fetuses. At The Women and Infant's Hospital in Providence, Rhode Island, the Specialty Care in Pregnancy (SCIP) clinic provides a multidisciplinary patient care team consisting of obstetric-medicine internists collaborating with rheumatologists to care for women with rheumatologic conditions who are pregnant or hoping to become pregnant. At a national level, clinics combining these specialties are scarce with an internet search revealing only three other programs in the United States (The Brigham and Women's Hospital, Tufts Hospital, and

The Hospital for Special Surgery). The purpose of this study was to characterize the population cared for in this unique clinic, identify interventions provided by this clinic, and analyze pregnancy outcomes for the mother and child.

Methods: We performed a 5-year retrospective chart review of patients seen in the multidisciplinary obstetric-medicine/rheumatology clinic at The Women and Infants Hospital in Providence, Rhode Island, from January 1, 2016 through December 31, 2021. Outcomes extracted from the charts included: age, change to diagnosis, changes to medications, medical comorbidities, laboratory results, birth outcomes and complications, and services provided by the clinic.

Table 1. Maternal characteristics of the 87 patients seen in the shared obstetric-medicine/rheumatology shared clinic at Women and Infants Hospital in Providence, Rhode Island.

Characteristic	n=87
Age, median (IQR), years	35 (32-39)
Ethnicity, n (%)	
White	50 (58%)
Black or African American	7 (8%)
Asian	4 (5%)
Multiracial	6 (7%)
Unknown / Not Reported	19 (22%)
Ethnicity, n (%)	
Hispanic / Latino	28 (33%)
Not Hispanic / Latino	51 (59%)
Unknown/ Not Reported	7 (8%)
Non-rheumatologic conditions, n (%)	
Asthma	10 (12%)
Hypertension	6 (7%)
Obesity	5 (6%)
Diabetes	2 (2%)
Tobacco Use	2 (2%)
Alcohol Use	2 (2%)
Rheumatologic diagnosis, n (%)	
Systemic lupus erythematosus	15 (17%)
Rheumatoid arthritis	16 (18%)
ANA abnormality (≥1:160), undifferentiated	11 (13%)
Psoriatic arthritis	5 (6%)
Ankylosing spondylitis	5 (6%)
Antiphospholipid syndrome	4 (5%)
Panuveitis	2 (2%)
Drug induced lupus	2 (2%)
Discoid lupus	1 (2%)
Behcet's disease	1 (1%)
Mixed connective tissue disease	1 (1%)
Other	24 (28%)

Table 2. Frequency of medications initiated, changed, or discontinued at the shared obstetric-medicine/rheumatology shared clinic in 87 women at Women and Infants Hospital in Providence, Rhode Island.

Medications **initiated** at shared visit, n (%)	
Hydroxychloroquine	12 (14%)
Prednisone	8 (9%)
Aspirin	6 (7%)
Sulfasalazine	5 (6%)
Amitriptyline	3 (3%)
Azathioprine	2 (2%)
Medications **changed** or **discontinued** at shared visit, n (%)	
Prednisone	5 (6%)
Hydroxychloroquine	4 (5%)
Adalimumab	2 (2%)

Table 3. Outcomes from 87 pregnant women seen in the shared obstetric-medicine/rheumatology clinic at Women and Infants Hospital in Providence, Rhode Island

Pregnancy outcome, n (%)	
Live Birth	47 (54%)
Miscarriage	9 (10%)
Unknown	31 (36%)
Mode of delivery, n (%)	
Cesarean section	16 (18%)
Normal vaginal delivery	13 (15%)
Assisted vaginal delivery	2 (2%)
Unknown	51 (59%)
Fetal complications, n (%)	
Prematurity (<37 weeks)	9 (10%)
Intrauterine growth restriction	4 (5%)
Respiratory complications	2 (2%)
Infection	1 (3%)
Fetal demise	1 (3%)

Results: *Demographics* The data from 87 patients were extracted (**Table 1**). Additionally, the median gestational age at first visit was 17 weeks (IQR 11-26 weeks). 47% of patients had a primary rheumatologist prior to evaluation in clinic. *Interventions* 38 patients (44%) had a medication initiated at the clinic, 9 (10%) had a medication discontinued, and 7 (8%) had a change in dose of a medication (**Table 2**). 18 patients (21%) were referred to another specialist from the shared clinic, and 3 (3%) received fertility counseling and were referred to a fertility specialist. 8 patients (9%) were diagnosed with a new autoimmune condition. *Outcomes* Pregnancy outcomes are listed in **Table 3**. Additionally, 5 patients (6%) developed preeclampsia.

Conclusion: The Specialty Care in Pregnancy (SCIP) clinic is among the first obstetric-medicine/rheumatology multidisciplinary clinics in the United States (US) and the first to publish analysis of their data. Interventions were made in the majority of patients despite nearly half already having established care with a primary rheumatologist, which highlights the critical importance of this clinic. The most commonly initiated medications were hydroxychloroquine and prednisone, which underscores the safety and efficacy of these medications in preventing and treating flares during pregnancy. Compared with a similar clinic in the United Kingdom, our preeclampsia incidence was 6 times higher (6% vs 1%) and miscarriage incidence was 8 times higher (16% vs 2%) (1). These discrepancies may be attributed to differences in socioeconomic and racial diversity. Multidisciplinary clinics of this type are needed in the US to provide further care and research to this patient population.
References: Hum RM, et al. Pregnancy outcomes of a joint obstetric and rheumatology clinic. Rheum Adv Pract. 2022 PMID: 35474882

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Abstract Number: 1004

Telerheumatology Shared-Care Model: Leveraging the Expertise of an ACPAC-Trained Extended Role Practitioner (ERP) in Rural-Remote Ontario

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SESSION INFORMATION

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Background/Purpose: A shortage of Rheumatologists has led to gaps in inflammatory arthritis (IA) care in Canada. Amplified in rural-remote communities, the number of Rheumatologists practicing rurally cannot be meaningfully increased. Alternate care strategies must be adopted. In this retrospective chart review, we describe the impact of a shared-care

Table 1: Demographics and Clinical Characteristics of Cohort

Demographic and Clinical Description of Cohort	
	n=124
Age at first Rheumatologist visit, years	
Mean (SD)	55.6 (16.2)
Biological Sex: n(%)	
Female	94 (75.8%)
Male	30 (24.2%)
Marital Status: n(%)	
Married	77 (62.1%)
Single	15 (12.1%)
Widowed	10 (8.1%)
Ethnicity:	
Identified as Indigenous peoples of Canada n(%)	26 (21.0%)
Employment Status: n(%)	
Employed/Self-Employed	51 (41.1%)
Retired	42 (33.9%)
Disability	9 (7.3%)
Homemaker	7 (5.7%)
Geography: n(%)	
Postal Codes in Rural Settings Overall	60 (48.4%)
Postal Code P0P -Manitoulin Island and Rural areas North	52 (41.9%)
Postal Code P5E-Espanola	54 (43.6%)
Postal Code P5A-Elliot Lake	7 (5.7%)
Postal Code P0M- Rural municipalities NW of Sudbury	7 (5.7%)
IA (OHIP billing code) at First Visit: n (% of whole sample)	n=80 (64.0%)
RA(714)	36 (29.0%)
CTD (710)	16 (12.9%)
PSA/Reactive Arthritis (721)	10 (8.1%)
Gout (274)	7 (5.7%)
Ankylosing Spondylitis (720)	7 (5.7%)
Vasculitis/PMR (447/725)	4 (3.2%)
Non-IA Diagnosis (OHIP billing code) at First Visit: n (% of whole sample)	n=43 (35.0%)
Tendonitis/Tenosynovitis (739/727)	7 (5.7%)
MSK disorder not yet determined (781)	6 (4.8%)
Frozen Shoulder (729)	8 (6.5%)
Disc Disease (722)	8 (6.5%)
OA (715)	14 (11.3%)
Diagnosis (billing code at last recorded visit): n(%)	
Stayed the same	94 (75.8%)
Changed	22 (17.7%)
Only had one consult	7 (5.7%)
Comorbid Conditions: n(%)	
Hypertension	40 (31.0%)
Diabetes	18 (14.0%)
Kidney Disease	7 (5.4%)
Cancer	11 (8.5%)
Depression	24 (18.6%)
Anxiety	17 (13.2%)
Smoking (cigarettes or marijuana): n(%)	
Unknown	6 (5.0%)
No History of Smoking	39 (32.2%)
Quit	39 (32.2%)
Currently Smoking	40 (33.1%)
Patient Reported Outcome Measures (first visit)	
MDHAQ Mean/3 (SD)	0.7 (0.5)
Range	0-2
Mean Pain VAS Mean/10 (SD)	5.7(2.6)
Range	0-10
Mean Fatigue VAS Mean/10(SD)	5.2 (3.2)
Range	0-10
Mean Patient Global VAS Mean/10(SD)	5.0 (2.6)
Range	0-10
Morning Stiffness in minutes Mean (SD)	49.5 (59.3)
Range	0-240

Telerheumatology model, utilizing a community-embedded Advanced Clinician Practitioner in Arthritis Care (ACPAC)-ERP and an urban-based academic Rheumatologist.

Methods: A Rheumatologist and an ACPAC-ERP established a monthly half-day Hub-and-Spoke-Telerheumatology clinic to care for patients with suspected IA, triaged by the ACPAC-ERP. Comprehensive initial assessments were conducted in-person by the ACPAC-ERP (Spoke);investigations were completed prior to the Telerheumatology visit. Retrospective analysis of demographics, time-to-key-care-indicies, patient-reported outcomes, clinical data, and estimated travel savings was performed.

Table 2: referral, Assessment and Follow-up visits Some patients presented at first clinic visit alrady on DMARDS; of 21 who were eligible for new DMARD thrapy, treatment commenced on average in 52 days.

Referral, Assessment, and Follow Up Visits	
Visits	**n=124**
Range All Visits	1-20
Mean (SD)	4.0 (4.0)
Range Telerheumatology Visits	1-20
Mean Telerheumatology Visits (SD)	4.0 (3.0)
Range In-person Visits	n=10 (0-1)
Mean In-person Visits (SD)	0.1 (0.25)
T1 (Days from PCP Referral to ERP Assessment)	**n=119**
Range	0-513 days
Mean (SD)	68.9 days (81.4)
75th Percentile	84 days
T2 (Days from ERP Assessment to Telerheumatology Visit)	**n=95**
Range	0-658 days
Mean (SD)	79.7 days (103.2)
75th Percentile	92 days
T3 (Days from Telerheumatology Visit to DMARD)*	**n=21**
Range	0-371 days
Mean (SD)	52.0 days (87.8)
75th Percentile	70 days

*Some patients presented at the first clinic visit already on DMARD; of the 21 who were eligible for new DMARD therapy, treatment commenced on average in 52 days.

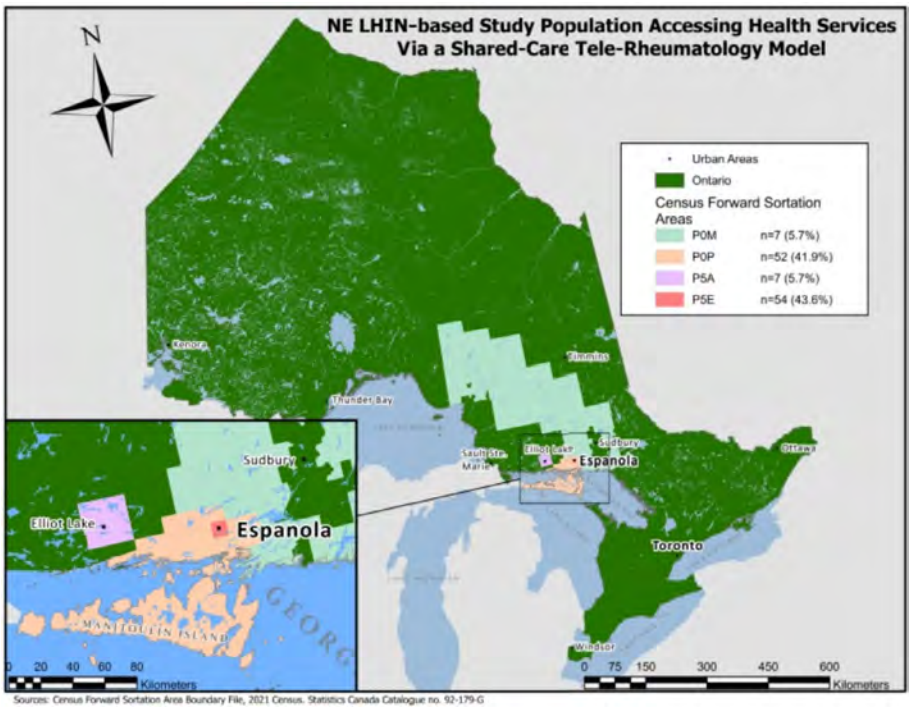

Figure 1: North East LHIN-based Study Population Accessing Health Services via Shared-Care Telerheumatology Model

Results: Data from 124 patients seen between January 2013-January 2022 were collected: 98% (n=496/504 visits) were virtual. Average age at first visit was 55.6 years, 75% were female. IA/Connective Tissue Disease (CTD) disease was confirmed in 80/124 (64.5%) patients. Mean time from primary care referral to ACPAC-ERP assessment was52.5 days and mean time from ACPAC-ERP assessment to the Telerheumatology visit was 64.5 days. An estimated 493,470 kilometers of patient-related travel was avoided.

Conclusion: A feasible, equitable, and effective ACPAC-ERP (Spoke) and Rheumatologist (Hub) Telerheumatology model of care assessing and managing patients with suspected IA in rural/remote Ontario was described. This model can be leveraged to increase capacity to deliver comprehensive virtual rheumatologic care in underserviced communities.

Disclosure: A. Steiman: AstraZeneca, 1, GlaxoSmithKlein(GSK), 6, Pfizer, 5; **T. Inrig**: Pfizer, 12, I was hired by Unity Health as a Research Coordinator, my salary was supported by a Pfizer unrestricted investigator-initiated grant; **K. Lundon**: None; **J. Murdoch**: None; **R. Shupak**: None.

Abstract Number: 1005

Telemedicine for Rheumatology Care: A Randomized, Single-Blind, Parallel Group, Noninferiority Trial

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Background/Purpose: In the wake of the COVID-19 pandemic, telemedicine rapidly became standard of care for people with rheumatic diseases. Observational data on effectiveness and acceptability of telemedicine for rheumatology care is mixed. We aimed to determine whether satisfaction with telemedicine visits was noninferior to in-person visits for delivery of rheumatologic care.

Methods: We conducted a parallel group, randomized, single-blind, noninferiority trial in rheumatology clinics at a tertiary academic medical center. Eligible patients were age ≥ 18 years with one of several rheumatic diseases, and completed ≥ 2 clinic visits in ≤ 18 months (telemedicine or in-person) including ≥ 1 prior visit in-person in ≤ 18 months. The primary outcome was high post-visit satisfaction rate (9 or 10 on a 0 – 10 satisfaction scale). Using an administered survey, we also collected date on preference for the next visit type, self-efficacy for managing medications, and medication adherence. Preference for the next visit type was defined as: same as the group allocation, different than the group allocation or no preference. Success was determined if the satisfaction rate with telemedicine versus in-person visits was non-inferior, using a noninferiority margin of -10%. We performed modified intent-to-treat (mITT), and per protocol (PP) analyses to account for those that crossed over, with age adjustment on the PP population.

Results: Out of 599 randomized participants, 451, 38.9% Black, 84.3% women, mean age 55.6 completed surveys. In the mITT analysis, telemedicine visits were not non-inferior to in-person visits for the proportion of people that were highly satisfied, 77.4% vs. 90.5%, difference -13.1% (95% CI, -19.8% to -6.5%). 35 participants crossed over in the in-person group and 55 in the telemedicine group. In the PP analysis, the satisfaction rate for telemedicine visits was also not non-inferior to in-person visits, age-adjusted difference -16.2% (95% CI, -23.8% to -8.6%). In the mITT analysis, most participants in both arms preferred an in-person visit for their next visit. The proportion of participants who indicated they preferred the same type of visit for their next visit compared to a different visit type and no preference

Table 1. Demographic characteristics of participants who completed phone surveys and were included in the modified intent to treat analysis; p < 0.05 in bold font.

	In-person (N=221)	Telemedicine (N=230)	p
Age, mean (SD)	56.4 (13.9)	54.7 (13.6)	0.2
Age group No. (%)			0.2
<45 years	48 (21.7)	60 (26.1)	
≥45 years to <65 years	106 (48.0)	116 (50.4)	
≥65 years	67 (30.3)	54 (23.5)	
Sex, female, No. (%)	185 (83.7)	195 (84.8)	0.8
Race, No. (%)			0.6
White	133 (60.2)	129 (56.3)	
Black	83 (37.6)	92 (40.1)	
Native American, Asian, Latinx	5 (2.3)	8 (3.5)	
Education, some college or more, No. (%)			0.6
High school graduate or less	48 (23.2)	55 (25.5)	
Some college	73 (35.3)	74 (34.3)	
4-year degree	53 (25.6)	47 (21.8)	
More than 4-year college degree	33 (15.9)	40 (18.5)	
Health literacy, inadequate*, No. (%)	20 (9.3)	23 (10.5)	0.7
Employment status, employed[5], No. (%)	74 (35.4)	94 (43.1)	0.1
Annual income, No. (%)			0.4
Low, < $29,999	26 (21.7)	37 (29.4)	
Medium, $30,000-79,999	41 (34.2)	39 (31.0)	
High, > $80,000	53 (44.2)	50 (40.0)	
Area deprivation index (ADI) ranking, state decile, median (Q 25-Q 75)#	4 [2, 7]	4 [2, 7]	0.7
Area deprivation index (ADI) ranking, national percentile, median (Q 25-Q 75)##	67 [47, 85]	68 [51.3, 86]	0.4

Table 2. Patient experience with in-person or telemedicine visits, modified intent-to-treat (mITT) and per protocol analyses; No (%) represented unless otherwise stated.

	Modified Intent-to-treat			Per Protocol		
	In-person (N=221)	Telemedicine (N=230)	p	In-person (N=186)	Telemedicine (N=175)	p
Primary Outcome						
Satisfaction rate, score ≥ 9	200 (90.5)	178 (77.4)	**0.0001**	170 (91.4)	131 (75.9)	**<0.0001**
Satisfaction, mean (SD)	9.6 (0.8)	9.2 (1.5)	**<0.0001**	9.6 (0.8)	9.1 (1.6)	**<0.0001**
Satisfaction, median (IQR)	10 (9.5, 10)	10 (9, 10)	**<0.0001**	10 (10, 10)	10 (8, 10)	**<0.0001**
Secondary Outcomes						
Preference for next visit, No (%)			0.2			**0.009**
In-person	122 (55.2)	108 (47.0)		105 (56.5)	71 (40.6)	
Telemedicine	36 (16.3)	46 (20.0)		29 (15.6)	42 (24.0)	
No preference	63 (28.5)	76 (33.0)		52 (28.0)	62 (35.4)	
Self-efficacy for managing medications, mean (SD)*	57.2 (8.7)	57.4 (8.0)	0.7	56.5 (8.9)	57.6 (7.9)	0.2
Medication adherence, always take medication as prescribed, No (%)**	162 (74.7)	168 (76.4)	0.7	141 (76.6)	121 (72.9)	0.4
Exploratory						
Missed work for appointment, No (%)	39 (18.0)	33 (14.7)	0.4	37 (20.2)	15 (8.9)	**0.002**
Expenses incurred related to visit, No (%)						
Meals	72 (32.6)	28 (12.2)	**<0.0001**	70 (37.6)	10 (5.7)	**<0.0001**
Lodging	0 (0)	0 (0)	-	0 (0.0)	0 (0.0)	-
Childcare	1 (0.5)	2 (0.9)	1.0	1 (0.5)	0 (0.0)	1.0
Transportation	142 (64.3)	62 (27.0)	**<0.0001**	139 (74.7)	15 (8.6)	**<0.0001**

IQR, Interquartile range; SD, standard deviation. *PROMIS self-efficacy for managing medication/treatment, reported as the T-score that represents a standardized score with mean of 50 and a standard deviation of 10, and higher scores associated with higher self-efficacy; **from the Medication Adherence Questionnaire. Self-efficacy for managing medications missing for 15 participants, medication adherence missing for 14 participants.

was significantly greater for those who had in-person visits (55.2% vs 20.0% in-person vs telemedicine, $p < 0.0001$). There were no differences between groups in self-efficacy for managing medications or medication adherence in either the mITT or PP analyses. Significantly more individuals in the in-person group vs. the telemedicine group reported expenses related to meals and transportation.

Conclusion: Among a large group of diverse, established rheumatology patients, who uniquely were randomized to visit type, high satisfaction rate with rheumatology clinic visits was significantly lower for telemedicine than for in-person visits. A meaningful minority of patients (about 20%) preferred that their next visit be telemedicine. Future studies should focus on factors associated with optimal visit type and how to achieve best outcomes for people with rheumatic diseases, including identifying subgroups that may prefer or benefit most from telemedicine.

*Inadequate health literacy grouped the following answers: ''Somewhat'', ''A little bit'', and ''Not at all''; $Employed is full-time, part-time, or temporary work; #State decile from 1 (least disadvantaged) to 10 (most disadvantaged); ##National percentile from 1 (least disadvantaged) to 100 (most disadvantaged). Race missing for 1 participant; education missing for 28 individuals; health literacy missing for 16 individuals; income missing for 205 participants; ADI missing for 132 participants.

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Use of Implementation Strategies to Promote Adherence of Knee Osteoarthritis Guidelines and Improve Patient Outcomes: A Systematic Review

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Background/Purpose: Despite the development of care models and practice guidelines the translation of knee osteoarthritis guidelines to practice remains suboptimal. Theoretically informed implementation strategies may facilitate the translation of guidelines to practice however their selection and use present challenges for clinicians and health systems aiming to improve patient quality of care for patients with knee osteoarthritis. Therefore, the purpose of this systematic review was to describe the use of implementation strategies to promote knee osteoarthritis guideline recommendations and evaluate their impact on guideline adherent care and patient-reported outcomes.

Methods: An electronic search was performed using MEDLINE (via PubMed), Embase (Elsevier), CINAHL(EBSCO), and Web of Science (Clarivate) databases to identify studies that included the use implementation strategies to improve knee osteoarthritis guideline recommendations and or patient reported outcomes. Implementation strategies were categorized based on the nine implementation domains and 73 implementation strategies as described by the Expert Recommendations for Implementing change (ERIC) taxonomy. Risk of bias was assessed using the Cochrane Effective Practice and Organization of Care(EPOC) criteria.

Results: Twenty-one studies were included in the final review. Eight implementation domains and 36 implementation strategies were represented within the twenty one studies with six strategies represented in ten or more studies. Seventy-one percent of implementation interventions were theoretical informed with an average of ten strategies used per study. "Develop educational materials", "Conduct educational meetings", "Make training dynamic", "Distribute educational material" and "Prepare patients/consumers to be active participants" were the top represented strategies. "Utilize financial strategies" and "Provide interactive assistance" domains were the least represented of the included studies. Eight implementation domains demonstrated a positive effect on clinician adherence to knee osteoarthritis guidelines, quality of life(3 domains), disability(8 domains), and reduction of pain intensity(3 domains). "Train and educate stakeholders" and "Engage consumers" had positive effects on both clinician adherence to guidelines and patient reported outcomes. The majority of studies had a low to moderate risk of bias.

Conclusion: This review highlights the use of strategies to improve the quality of care and outcomes for patients with knee osteoarthritis. The findings suggests that using multifaceted implementation strategies appear to be effective for improving knee osteoarthritis clinical practice guideline adherence and patient-reported outcomes. The findings also suggest only 50% of the 73 strategies recommended by the ERIC taxonomy have been used in improving guideline adherence and outcomes in the context of knee osteoarthritis care management, demonstrating a need for further research. In general, the use of implementation strategies in the context of knee osteoarthritis management, may guide future initiatives to improve quality of care and patient outcomes.

Disclosure: M. Ramirez: None; **R. Fillipo**: None; **C. Drake**: None; **L. Skalla**: None; **K. Allen**: None; **A. Nelson**: None; **M. Horn**: None.

Abstract Number: 1007

Telehealth Conversion: A Strategy for Optimizing Ambulatory Access

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Background/Purpose: With the rapid uptake of telehealth at the beginning of the pandemic, our group operationalized a simple strategy to convert appointments for patients who were not present at the time of their in-person visit to a telehealth visit in order to provide timely access to care amid constrained access.

Methods: Patients with late cancellations or impending no-show visits were asked if they'd like to convert their visit to telehealth. If enrolled in the electronic patient portal a video visit was offered, and if not enrolled, a telephone visit was offered. The project was piloted at 1 clinic site through 8/31/2021 before broader implementation to 2 clinics. Procedure visits were excluded. Demographics including age, gender, race/ethnicity, insurance status, and language, were analyzed using Chi-square and Fischer's exact tests to examine variations in telehealth visit type by group.

Results: Between 9/1/2023 and 3/31/2023, we successfully contacted patients across 624 visits eligible for telehealth conversion (554 unique patients) converting 83% (516/624). Of the 516 telehealth visits completed, 56% were by telephone (n= 282) and 46.2% by video (n = 234). Patients who were older or with Medicare and Medicaid public insurance were more likely to select phone visits (72.1%, 59.3%), while patients with commercial insurance were more likely to choose video visits (56%) ($p < 0.001$). Younger and urban patients were more likely to have video visits, while older and rural patients were more likely to have phone visits (Table 1) . There was no difference in the video vs telehealth visit selection by race, ethnicity, or sex. The intervention resulted in at least 258 additional hours of patient care, avoided reschedules and zero payment clinic time, with a modest revenue loss reduction

Table 1: Sociodemographics of no-show or late cancellation visits converted to telehealth n=516

	Phone	Video	p-value
Overall n, (%)	282 (54)	234 (46)	

	Phone	Video	p-value
Overall n, (%)	282 (54)	234 (46)	

Age			
18 - 39	29 (31)	64 (69)	<0.00001
40 - 59	105 (49)	108 (51)	
60 - 79	125 (69)	57 (31)	
> 80	23 (82)	5 (18)	
Gender			
Female	203 (53)	182 (47)	0.13
Male	79 (60)	52 (40)	
Race/ethnicity			
Native American, American Indian or Alaska Native	7 (39)	11 (61)	0.29
Asian American, Pacific Islander	5 (71)	2 (28)	
Black or African American	23 (51)	22 (49)	
Latino/a/x	8 (40)	12 (60)	
White	282 (55)	233 (45)	
Insurance Status			
Medicare	124 (70)	52 (30)	<0.00001
Medicaid	35 (59)	24 (41)	
Commercial Insurance	121 (44)	154 (56)	
Geography			
Rural	84 (65)	46 (36)	0.01
Urban	196 (51)	186 (49)	
Language			
English	277 (54)	234 (46)	0.067[1]
Limited English Proficiency	5 (100)	0 (0)	

[1] 5 patients with limited English proficiency all choose phone and not video system data shows lower portal enrollment in this population

Sociodemographics of no-show or late cancellation visits converted to Telehealth

Figure 1: Telehealth conversion visit volume across time

for telemedicine of $7298 ($39.19 per appointment). Figure 1 shows overall gains and seasonal variation with higher winter demand. Monthly variability may also reflect clinic staff shortages during this period impacting outreach capacity.

Conclusion: Our simple, targeted strategy of converting appointments to telehealth when an in-person appointment is identified as at-risk resulted in significant access gains and modest revenue loss reduction. Clinic patients who are older, on Medicare or Medicaid, or rural preferred phone visits. Per literature, those with limited English proficiency are less likely to be actively enrolled in patient portals, which may impact their ability to convert to a video visit, a potential area to optimize in the future. Higher rates of telephone visits for rural patients, who may have less access to high-speed internet, highlight the equity considerations in offering telehealth modalities to patients.

: Telehealth conversion visit volume across time

Disclosure: S. Ferguson: None; **A. Nanes**: None; **L. Zemlicka**: None; **C. Bartels**: Pfizer, 5.

Abstract Number: 1008

Identifying Inflammatory Arthritis Ambulatory Care Service Model Enhancements Needed to Reduce Avoidable Emergency Department Use

Emilie Pianarosa[1], Pamela Roach[1], Patrick McLane[2], Meghan Elliott[1], Brian Holroyd[3], Shanon McQuitty[4], Steven Katz[3], Nazret Russon[2], Katie Lin[1], Claire Barber[1] and Cheryl Barnabe[1], [1]University of Calgary, Calgary, AB, Canada, [2]Alberta Health Services, Edmonton, AB, Canada, [3]University of Alberta, Edmonton, AB, Canada, [4]Arthritis Research Canada, Vancouver, BC, Canada

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Health Services Research Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Emergency departments (ED) become a location for non-urgent care when ambulatory care systems are not sufficient. We aim to describe contributing factors to the decision taken by persons with inflammatory arthritis (IA) to present to the ED, their experiences of ED care, and propose enhancements in ambulatory models of care to better support patients and improve system efficiency.

Methods: An invitation to complete an online survey was distributed by the health authority in October 2021 and March 2022 to a sample of individuals with an IA condition who had visited an ED within the previous year. Descriptive statistics were used to summarize quantitative data. Thematic analysis of free text responses was conducted

to contextualize decision making and experiences of ED care, and generate system-level recommendations to reduce avoidable ED use.

Results: 82 persons (48% RA, 12% PsA, 6% SpA, 34% Gout; 63% aged 16-55 years; 48% female; 50% urban residents) completed the survey. Over 1/3 (37%) of visits were for arthritis flare or other musculoskeletal symptoms, with other primary symptoms being chest pain (15%), injury (12%) and infection (11%). Of all visits, 28% of persons reported they proceeded directly to the ED, 32% made a return visit, and 36% were completed after accessing ambulatory care, primarily a primary care provider. For visits specific to arthritis flare or other musculoskeletal symptoms, 19% of patients proceeded directly to the ED as they could not access ambulatory care (after business hours, or call to provider not returned), 36% were a return visit of which 64% were for symptoms being unresolved or worsening and with 27% not being able to follow-up with their rheumatologist. For 39% they had accessed primary or specialty care for assessment and management first but then presented to the ED anyways. The rheumatology service was contacted by the ED provider in 9% of events of patients presenting with arthritis flare. Challenges in healthcare system coordination, system processes and pressures, and communication and relationality between IA patients and healthcare providers led to negative experiences of ED care (Table 1). After an ED visit patients had remaining concerns about not having been assessed comprehensively, and not having the cause of their symptoms being explained to them. They felt they were being discharged too soon, did not have a symptom management plan, and had the responsibility to coordinate multiple further assessments with different ambulatory providers. They perceived symptoms were not being appropriately attributed to their arthritis condition, Recommendations to reduce avoidable ED use include improving access to rheumatology care for both initial visits and urgent concerns, introducing initiatives for improved ambulatory care coordination and service delivery, resourcing EDs at appropriate levels to provide quality care, and to enhance provider education about arthritis condition assessment and management.

Conclusion: We present initial recommendations to develop systems and procedures to reduce the need for ED use by IA patients. Modifying current models of care may improve patient outcomes while simultaneously decreasing utilization and cost to the healthcare system.

Main Theme	*Subtheme*	*Description*	*Quotes*
Continuity & Coordination of Care	Lack of coordination in the healthcare system	It becomes the patient's responsibility to navigate the healthcare system for their arthritis condition.	"It's a hopeless feeling to be told that there is nothing that can be done. Medications are not changed at the hospital because the rheumatologist makes that decision. Pain meds are only assessed by your personal physician. It's endless rounds of medical visits which never really end up addressing the base causation. You learn to try to handle it by yourself." "I've been in the ER plenty of times, and it's always the same thing. You're EXTREMELY lucky if you see a Rheum, instead they [referring to the ED provider] just give you pain meds and send you home and expect you to deal with it on your own time."
	Expectations of being discharged only when safe to do so	The patient needs to mobilize safely, access necessary prescriptions, and have transportation home, however they experience being discharged quickly.	"I was still very unwell however they felt there was nothing more they could do. I was unsteady and was not escorted out or asked how I was getting home. Then had to wait at the pharmacy for 45 until the prescriptions were filled. It was not ideal so I sat in the hospital reception for one hour until I felt like I could drive." "It was after 7:00 PM I believe and didn't feel I was well enough from the drugs they had given me. I told them I lived alone."
	Expectations of having a symptom management plan and follow up arranged	The patient wants to understand how they should self manage symptoms after discharge, and have any necessary follow-up arranged.	"No reassurance was given that I would be okay until I saw rheumatology. The best suggestion was ibuprofen." "They would just send me home with more pain medication and no follow up plan." "[I knew that follow up in the community with specialists would not happen/ would not happen in a timely manner."
System Process & Pressures	Long wait times for both ambulatory and acute care assessment	Patients experience prolonged wait times for assessment in the ED, yet this is accepted as there is a need for reassurance about symptoms while awaiting a rheumatology assessment.	"I spent over 95 percent of the time waiting [in the ED] for who knows what." "I was waiting to see a rheumatologist and was in a great deal of pain and was scared. I wanted reassurance I wasn't becoming more ill while waiting on rheumatology."
	Expectations of a comprehensive assessment to determine the cause for their symptoms	Patients with complex conditions and treatment anticipate having a complete history taken, with appropriate investigations completed and interpreted. However, the focus during an ED visit is on acute symptoms and/or issues only rather than being chronic disease oriented. The patients feel that the cause of their symptom onset is not explored nor explained to them. Symptoms that seem severe to the patient are not explained.	"They were unsure what was happening but sent me home and told me to come back when/if it started again so I returned 3 times for the same issues with chest pain before a doctor figured it out." "I left with NO answers to my abdominal pain, feeling just as ill as I did when I went in." "No results, communication was lacking, no answers or investigation to why I flared up." "There was still no explanation for why I was experiencing severe stomach pains, chest pains and brain fog, and no further inquiry into why I have an assortment of other symptoms that don't fully correlate to my Rheumatoid Arthritis diagnosis."
Communication & Relationality	Expectations of a respectful interaction with healthcare providers	Patients experience interactions that are short in duration, and they feel ignored and rushed out.	"Gone are the days of hospitals actually treating anyone, it's all just temporary bandaids, so you can get out of there fast enough so they can see the next person." "The doctors are always rushing and make you feel like you on an assembly line not an actual person."
	Attitudes and knowledge about arthritis	Patients experience that either every symptom they present with is attributed to arthritis by the healthcare provider even when the patient doesn't think this to be true, or that they are not believed when they indicate their symptoms are arthritis related. They feel there is a negative perception when the ED is used as a resource for chronic disease management.	"Didn't feel like they were listening to me about my symptoms not feeling like my RA and I really felt that something else was wrong." "Doctor said interesting interesting that I suggested a "rheumatoid perspective" and said I must have just over worked it. Did not make any sense which left me extremely confused and upset." "I do struggle if I go to different ER where my doctor doesn't work as sometimes they don't treat me well due to my chronic illness."

Themes and Representative Quotes for Emergency Department Experience

Disclosure: E. Pianarosa: None; **P. Roach**: None; **P. McLane**: None; **M. Elliott**: None; **B. Holroyd**: None; **S. McQuitty**: None; **S. Katz**: None; **N. Russon**: None; **K. Lin**: None; **C. Barber**: None; **C. Barnabe**: None.

Abstract Number: 1009

More Implementation Strategies Are Not Associated with Better Implementation Outcomes: Implementing the Lupus Patient Decision Aid

larry hearld, **Jasvinder Singh** and Mark Beasley, University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Health Services Research Poster II
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Background/Purpose: To assess the association of the number of implementation strategies for a patient lupus decision aid (DA) with perceived implementation outcomes, and the moderating effect of the organizational climate on this relationship.

Methods: We implemented a lupus patient DA across 15 U.S. rheumatology clinics made available during a regular patient clinic visit. In addition to the standardized implementation strategies provided uniformly by the research team to each site (e.g., training on DA use, designation of a clinic champion and refresher training course), each clinic could choose from a 'menu' of implementation strategies directed to both clinic personnel and patients, customized to their clinic. We examined the effect of the number of implementation strategies with clinic-personnel-reported implementation outcomes (acceptability, appropriateness, feasibility), and the extent of impact of the organizational climate (e.g., learning environment, readiness for change) on this relationship.

Results: At the 4-month post-implementation period, the average perceptions of the lupus DA were as follows: acceptability, 3.49; appropriateness, 3.37; and feasibility, 3.40. The mean number of total strategies implemented by the participating clinics was 3.37, with 2.07 clinic-focused strategies and 1.29 patient focused strategies, that remained stable during follow-up. Adjusted for clinic and clinic personnel characteristics, and time since implementation, we found the following associations for implementation strategies: (1) total strategies not significantly associated with lupus DA acceptability, appropriateness, feasibility, success, or permanence; (2) the number of clinic-focused strategies associated positively and significantly with lupus DA acceptability, appropriateness, and feasibility; and (c) the number of patient-focused strategies was negatively significantly associated with lupus DA acceptability and feasibility but not appropriateness. We found significant moderation of the relationship between implementation strategies and implementation outcomes by the learning environment and readiness for change.

Conclusion: We found that the overall number of implementation strategies was not associated with perceptions of DA acceptability, appropriateness, and feasibility; however, these relationships did differ for different implementation targets and under different organizational conditions. Our findings highlight the importance of the context but suggest that a very nuanced consideration of contextual characteristics is needed as aggregated factors such as organizational readiness for change and its learning climate contribute to implementation success in different ways and for different implementation outcomes.

Disclosure: I. hearld: None; **J. Singh**: Other, 2, 6, 11, 11, 12, Adaptimmune Therapeutics, GeoVax Labs, Pieris Pharmaceuticals, Enzolytics Inc., Seres Therapeutics, Tonix, Charlotte's Web, 12, Atai life sciences, kintara therapeutics, Intelligent Biosolutions, Acumen pharmaceutical, TPT Global Tech, Vaxart pharmaceuticals, Atyu biopharma, 12, speaker's bureau of Simply Speaking, other, 12, received institutional research support from Zimmer Biomet Holdings. JAS received food and beverage payments from Intuitive Surgical Inc./Philips Elec, Other, 12, Schipher, Crealta/Horizon, Medisys, Fidia, PK Med, Two labs Inc., Adept Field Solutions, Clinical Care options, Clearview healthcare partners, Putnam; **M. Beasley**: None.

Abstract Number: 1010

Advanced Clinician Practitioners in Arthritis Care: A Workforce Profile

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Background/Purpose: The Advanced Clinician Practitioner in Arthritis Care (ACPAC) Program is a post-licensure, competency-based academic and clinical educational program that prepares physiotherapists, occupational therapists, nurses, and chiropractors for extended practice roles in the diagnosis and management of patients with arthritis, autoimmune and other musculoskeletal (MSK) conditions. Since 2005, the program has graduated extended role providers (ERPs) to manage a growing population of patients with MSK conditions; address a progressive decline in MSK specialists and better utilize health professionals to improve access to care. The objective of this study was to profile the current ACPAC workforce with respect to 1) demographics, including aspects of ethnicity, diversity and inclusion; 2) practice setting and clinical roles; 3) health system integration and 4) remuneration.

Methods: ACPAC graduates from 2006 to 2022 were sent an electronic questionnaire from February to April 2023 using Research Electronic Data CAPture software. The questionnaire was developed based on review of workforce literature and was reviewed by the investigative team for face and content validity, clarity, relevance and format. Univariate statistics were used to summarize data. All analyses were conducted in SAS v9.4.

Results: Seventy-two of 103 graduates completed the questionnaire (response rate 69.9%). *Demographics*: Most respondents were from Ontario, Canada (95.8%) and were physiotherapists (78.8%). Mean age was 49.4 (SD 9.2) years. The majority identified as women (77.8%) and White-North American/European ethnicity (71.8%). No respondents identified as North American Indigenous. *Practice setting and clinical roles:*Most reported current employment in an ERP role (76.4%). There were inconsistencies regarding ERP title. The majority (80%) were working in hospital-based settings (80%). Across all settings, 89.1% worked with adult populations, and provided either orthopaedic (54.5%) or rheumatology (40%) care. Only 12.2% reported working in rural or remote settings. *Health system integration:* Respondents reported working in various orthopaedic and rheumatology models of care including triage, interprofessional collaborative care programs and transition clinics from paediatric to adult care. *Remuneration*: Most funding models were from government sources (90.9%) with almost half (47.2%) reporting an annual salary of at least $100,000 CAD.

Conclusion: Most ACPAC ERPs are physiotherapists working in urban publicly-funded, hospital-based practices providing adult orthopaedic and rheumatology care. Opportunity exists to maximize employment of existing graduates and further expand ERP roles beyond hospital-based settings, and in rural and remote areas. Examples include family medicine clinics, community-based clinics, geriatric care, and emergency departments. A small proportion of respondents identified as non-white, with Indigenous individuals not represented in this workforce. There is value in targeting recruitment strategies to attract program candidates representative of diverse ethnic backgrounds and inclusive of Indigenous populations.

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Abstract Number: 1011

A Rheumatology Model of Care Re-design: Integrating the Advanced Practice Provider

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SESSION INFORMATION
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Background/Purpose: There is a lack of guidance surrounding integration of Advanced Practice Providers (APPs) into specialty practices utilizing interprofessional Models of Care (MoC). Due to current and projected workforce shortages combined with rising patient need in the field of Rheumatology, multiple methods were utilized to engage both APP and physician perspectives to develop a MoC specific to an academic Rheumatology practice. Initial goals included understanding the current and desired MoC, as well as integration of APPs into optimized models.

Figure 1
Blueprint for Model of Care Re-Design

Methods: Utilizing a mixed methods sequential-exploratory design through a quality improvement lens, a blueprint for a MOC re-design was developed and will be presented here. Quality Improvement (QI) strategies planned: 1. Needs assessment 2. Baseline data collection 3. Dissemination 4. Team building 5. Implementation 6. Evaluation with ongoing improvements as needed (Figure 1). Phases one through four were completed as part of this project with divisional consideration for implementation of phases five and six in the future.

Results: In the needs assessment phase, we interviewed key stakeholders (divisional leadership) to develop shared goals for the optimal MoC. These goals included quality of patient care, access, and addressing barriers at the patient, physician, APP, environmental, and organizational levels. In the next phase, data collection, we distributed a survey to 12 physicians and 8 APPs in our practice addressing eleven domains: 1. Models of Care 2. Physician 3. Appropriateness of an APP to see 17 common Rheumatological diagnoses as a new or return visit 4. Logistical Considerations 5. Staff Utilization

Figure 2
Model of Care: Team Blueprint and Strategies for Formation

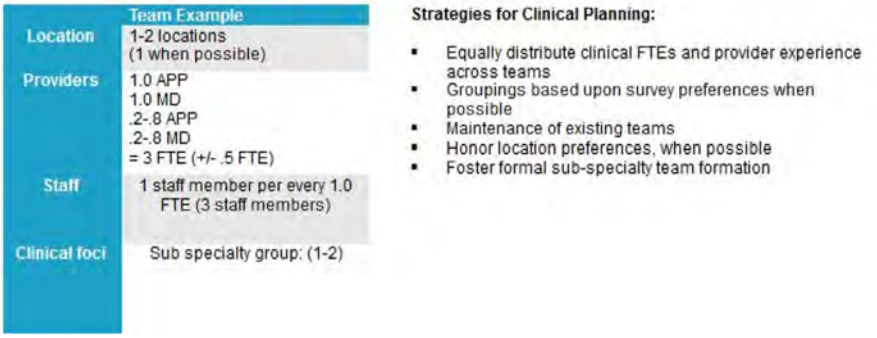

Table 1
Rheumatology Model of Care Results

Clinician Type	MD	APP
	N (%)	N (%)
	12 (100)	8 (100)
MoC Currently Utilized (Can select more than 1)		
Independent	**8 (66.7)**	**6 (75)**
Tandem	3 (25)	0 (0)
Parallel	**8 (66.7)**	**5 (62.5)**
Follow-up	0 (0)	1 (12.5)
Leverage	0 (0)	0 (0)
Specialty Specific	1 (8.3)	1 (12.5)
No Current MoC	2 (16.7)	1 (12.5)
Satisfaction with MoC		
Satisfied	2 (16.7)	0 (0)
Neutral	4 (33.3)	**5 (62.5)**
Dissatisfied	**6 (50)**	3 (37.5)
Preferred MoC (Can select more than 1)		
Independent	3 (25)	3 (37.5)
Tandem	5 (41.7)	0 (0)
Parallel	**9 (75)**	**6 (75)**
Follow-up	3 (25)	2 (25)
Leverage	3 (25)	0 (0)
Specialty Specific	2 (26.7)	1 (12.5)
Should MoC be standardized		
Yes	**9 (75)**	8 (100)
No	**3 (25)**	0 (0)
Interest in structured MoC incorporating the APP		
	MD (n=10)	APP (n=7)
Yes	**6 (60)**	6 (85.7)
No	**4 (40)**	1 (14.3)

MD (Medical Doctors), APP (Advanced Practice Provider), MoC (Model of Care), RVU (Relative Value Unit), Staff (Registered Nurse, Licensed Practical Nurse, Medical Assistant)

6. Provider Satisfaction 7. Telehealth Preferences 8. Patient Impact 9. Burnout Inventory 10. Work Life Balance and 11. Joy in Work. During phase three, key findings were communicated with divisional leadership and then with clinicians and staff followed by an iterative process for team building and design in phase four. Surveys showed low satisfaction with the current MoC. These findings suggest that the APP is being utilized in variable MoC and that many physicians are dissatisfied with current MoC. Additionally, strong preferences for parallel and independent practice, standardization of MoC, and a formal structure that integrates the APP was preferred by both APPs and Physicians (Table 1). The top two clinician foci for the MoC included quality of care and prevention of burnout. Clinicians agreed that the main barriers to implementing a MoC were a lack of a well-defined and documented MoC, clinic space and communication. Based upon these findings, a proposed team-based MoC was developed (Figure 2).

Conclusion: Using a mixed methods QI approach is effective to elicit clinical needs and barriers with significant clinician buy-in. Improved understanding of clinicians' desired MoC and what this MoC should focus on impacts team-based structures, for which the APP is a critical component. As the role of the APP is predominantly geared towards the clinical mission, improving full scope integration of the APP via MoC re-design in specialty practices, including Rheumatology, is pivotal to improve the quality of patient care and access.

Disclosure: L. Carnago: None; **K. Holbrook**: None; **D. Leverenz**: Pfizer, 5, Rheumatology Research Foundation, 5, Sanofi, 2; **N. Rivera**: None; **A. Dimsdale**: None.

Abstract Number: 1012

Leveraging Cues and Rewards to Form Habits to Improve Medication Adherence in Gout: An Adaptive Behavioral Pilot Trial

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Background/Purpose: Adherence to urate-lowering therapy (ULT) reduces the incidence of debilitating gout flares. Providing a cue for a behavior, reinforcing the behavior with a reward, and then repeating this process is known as the cue-reward-repetition principle. Over time, cues become more important and rewards less because the activity becomes automatic (a habit). We conducted a randomized, adaptive pilot trial to test whether leveraging cues and rewards to establish medication taking as a habit improves adherence to ULT.

Methods: We enrolled adults 18 with gout and a uric acid level of >6mg/dL within 6 months, on a stable dose of ULT (allopurinol or febuxostat), who received rheumatology and/or primary care at a multisite medical center. Participants received electronic pill caps and were randomized to 3 arms: 1) the nonadaptive intervention where they received assistance selecting a cue (e.g., "place your medication near your toothbrush") and a reward (charitable donation of $0.50/ULT adherent day) with text message reminders about their cue and the amount donated every 4 days, 2) the adaptive intervention with the

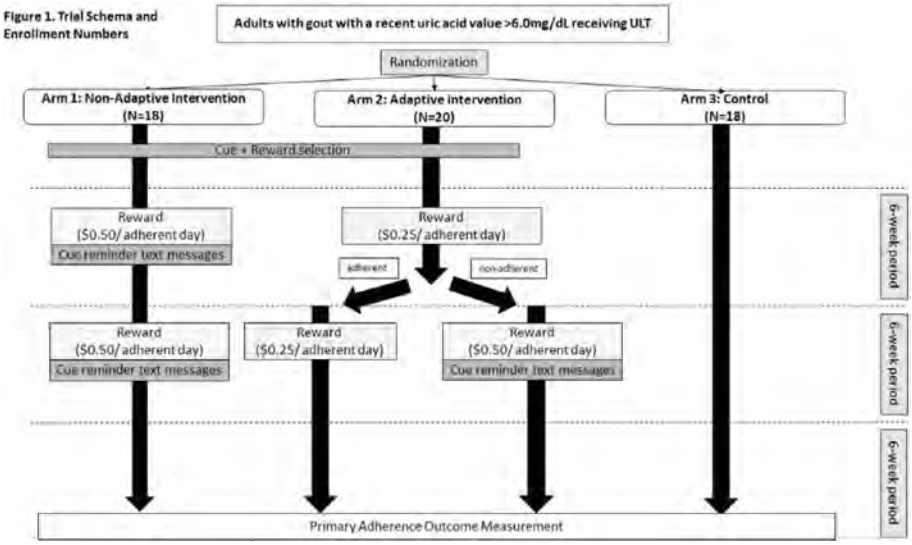

Table 1. Characteristics of Individuals with Gout on Urate Lowering Therapy Enrolled in the Randomized Adaptive Behavioral Pilot Trial

Characteristics	**Non-Adaptive Arm** (N=18)	**Adaptive Arm** (N=20)	**Control Arm** (N=18)
Age – mean (SD)	50.7 (12.4)	60.2 (11.8)	54.8 (12.5)
Female – N (%)	4 (22)	5 (25)	2 (11)
Race/Ethnicity – N (%)			
White	13 (72)	17 (75)	14 (78)
Black/African American	4 (22)	2 (10)	3 (17)
Asian	1 (6)	0	0
Hispanic/Latinx	2 (11)	1 (5)	1 (6)
Educational Level- N (%)			
High School Diploma	2 (11)	3 (15)	3 (17)
Some College	4 (22)	2 (10)	3 (17)
College Degree	6 (33)	7 (35)	5 (28)
Graduate Degree	6 (33)	8 (40)	7 (39)
Employment – N (%)			
Employed	14 (78)	10 (50)	13 (72)
Job seeking	0	0	1 (6)
Not job seeking	2 (11)	7 (35)	0
Retired	2 (11)	7 (35)	3 (17)
Disabled	1 (6)	1 (5)	(6)
Baseline uric acid – mean (SD)	7.9 (2.3)	7.4 (1.1)	7.1 (0.9)
Low adherence by self-report at baseline- N (%)	7 (39)	2 (10)	2 (11)
Baseline automaticity score* – mean (SD)	2.09 (1.75)	2.80 (1.15)	2.63 (1.41)
Baseline medication intention* score – mean (SD)	3.97 (0.30)	3.82 (0.38)	3.91 (0.31)
Baseline medication taking routine score* – mean (SD)	6.13 (0.60)	6.30 (0.64)	6.02 (0.81)

p-values were all >0.05 across arms
*Higher scores indicate greater automaticity, stronger intention to take medications and greater association of medication taking with a routine

Table 2. Randomized Adaptive Behavioral Trial Outcomes				
	Non-Adaptive Arm (N=18)	**Adaptive Arm** (N=18)	**Control Arm** (N=18)	**p-value**
Primary Outcome				
Adherence# at 18 weeks – mean (SD)	0.79 (0.23)	0.83 (0.18)	0.76 (0.26)	0.75
Secondary Outcomes				
Adherence# at 12 weeks – mean (SD)	0.84 (0.22)	0.87 (0.17)	0.81 (0.25)	0.60
Change in uric acid level- mean (SD)	-1.13 (1.66)	-0.55 (1.88)	-1.21 (1.31)	0.71/0.17*
Change in medication taking intention score – mean (SD)	0.02 (0.30)	0.05 (0.28)	-0.12 (0.50)	0.25/0.28*
Change in automaticity – mean (SD)	0.62 (0.96)	0 (0.85)	-0.13 (0.50)	**<0.001**/0.45*
Change in medication taking routine – mean (SD)	0 (0.86)	0.14 (0.65)	-0.22 (0.86)	0.43/0.18
*Non-adaptive vs. control/Adaptive vs. control #Adherence measured using pill caps as the number of times the pill cap was opened divided by the number of doses prescribed per day				

same strategy but the reward started at $0.25/ULT adherent day and was doubled at 6 weeks if adherence was 75% 3) the control arm (pill cap monitoring only) (**Fig. 1**). The intervention ended at 12 weeks and adherence was monitored for the next 6 weeks. The primary outcome was adherence (number of times the pill cap was opened/number of doses prescribed per day) at 18 weeks. Secondary outcomes included adherence at 12 weeks, changes in automaticity, medication-taking routines and intentions, and uric acid level from baseline. We interviewed 14 patients who completed the trial to understand their experiences.

Results: Fifty-six individuals were randomized (non-adaptive arm (N=18), adaptive arm (N=20), and control arm (N=18)) (**Fig. 1**). Participants were 21% female, 81% White, 15% Black, 8% Latinx with similar demographics across arms (**Table 1**). The mean (SD) baseline uric acid was 7.47 (1.55) mg/dL. We did not observe statistically significant improvement in ULT adherence across intervention arms at 18 weeks (primary outcome) or at 12 weeks (secondary outcome) (**Table 2**). Mean (SD) adherence at 18 weeks was 0.79 (0.23) in the nonadaptive arm, 0.83 (0.18) in the adaptive arm, and 0.76 (0.26) in the control arm. Compared to the control arm, automaticity scores were higher post vs. pre intervention for the non-adaptive arm ($p< 0.001$) but not the adaptive arm ($p=0.45$); changes in other secondary outcomes were not significant. Exit interviews revealed limited intervention impact due to preestablished medication-taking habits, independent reasons to take ULT (e.g., prevention of painful gout flares) and ineffective reward (charity donation). Participants in all groups noted awareness of being monitored with the pill caps.

Conclusion: We did not observe significantly improved adherence to ULT among individuals enrolled in this habit formation intervention. High adherence in all arms and small sample size limited power. Larger studies over longer time frames are needed in diverse patient populations with varied baseline adherence to understand whether leveraging automaticity can enhance medication-taking behaviors.

Disclosure: C. Feldman: BMS Foundation, 5, Curio Bioscience, 12, My husband is one of the founders and will receive equity (but has not received anything to date)., OM1, Inc., 2, Pfizer, 5; **K. Crum**: None; **K. Hanken**: None; **C. Fontanet**: None; **E. Sears**: None; **T. Oduol**: None; **S. Vine**: None; **J. Mastrorilli**: None; **G. Bhatkhande**: None; **J. Lauffenburger**: None; **R. Oran**: Blue Cross Blue Shield of Massachusetts, 3; **T. Robertson**: None; **W. Wood**: None; **N. Choudhry**: Decipher Health, 2, 8, RxAnte, 2, 11, Veracity Healthcare Analytics, 2.

Abstract Number: 1013

Implementation of a Rheumatology-Based Social Determinants of Health Screening Program to Uncover and Address Needs in a Multihospital Health Care System

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SESSION INFORMATION

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Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Social determinants of health (SDoH) contribute to inequities in rheumatic disease care and outcomes. Most SDoH screening occurs in primary care where resources may exist to meet related needs. Individuals with rheumatic conditions receive extensive care in the subspecialty setting where SDoH are infrequently documented and infrastructure to address needs is often lacking. We implemented SDoH screening in 9 rheumatology clinics to determine feasibility, associated factors, and the ability to address SDoH needs in a subspecialty setting.

Methods: We implemented an electronic health record-based SDoH questionnaire at e-check in, or on arrival with an iPad, at 3 hospital-based adult rheumatology clinics and 6 satellite clinics. To ensure sufficient resources to meet needs uncovered, we first focused on visits for RA, then expanded to other rheumatic conditions. Patients screened within the year in primary care were not rescreened, however our team responded to incompletely addressed needs. Patients who indicated SDoH needs received resource sheets in their primary language and those requesting assistance received outreach from the rheumatology-based community resource specialist (rCRS). Rheumatologists and primary care physicians were informed of their patients' needs and actions taken to address them. We assessed prevalence of SDoH needs, used multivariable logistic regression to examine factors associated with ≥1 SDoH need (vs. 0), and used multilevel, multivariable logistic regression to examine the association between census tract social vulnerability index (SVI) quartile and presence of needs, adjusting for demographics. We categorized actions taken by the rCRS.

Results: From 6/23/22-4/18/23, 7,146 adults (≥18 years) completed the SDoH questionnaire. 6,309 (88%) were associated with rheumatology visits and 837 (12%) with primary care and re-reviewed in rheumatology. There were 2,015 SDoH needs among 1,143 (16%) patients; 120 others requested resources without specifying needs. SDoH needs varied by demographic factors and insurance status (**Table 1**). 417 (36% of patients with needs) indicated food insecurity, 340 (30%) had difficulty paying utility bills, 297 (26%) had difficulty paying for medications (**Fig. 1**). We observed significantly higher odds of ≥1 SDoH need vs. no needs among Black (vs. White) and Hispanic (vs. non-Hispanic) individuals, Medicaid and Medicare beneficiaries (vs. Commercially insured) and Spanish speakers (vs. English) (**Table 1**). While SDoH needs were present among individuals in all neighborhoods, living in the most vulnerable SVI quartile (vs. the least) was associated with 4.92 times higher odds (95% CI 1.43-16.92) of SDoH needs. The rCRS connected patients to varied resources to address needs (**Table 2**).

Conclusion: Screening and addressing SDoH in rheumatology clinics is feasible and has revealed a significant burden of needs not being met elsewhere. While needs were concentrated among individuals living in more vulnerable neighborhoods and among historically marginalized populations, they were not limited to these groups suggesting the importance of inclusive screening and connections to resources to improve care for all patients.

Table 1. Characteristics of patients screened and odds ratios (OR, 95% CI) for presence of one or more SDoH need vs. no needs from multivariable logistic regression models

Characteristics*	Overall screened (N=7,146)	≥1 SDoH need (N=1,143)	No SDoH needs (N=6,003)	OR# (95% CI)
Age – mean (SD)	58 (16)	54 (15)	58 (16)	**0.98 (0.98-0.99)**
Female – N (%)	5,518 (77)	932 (17)	4,586 (83)	1.11 (0.93-1.32) *Reference=Male*
Race - N (%)				
White	5,836 (82)	736 (13)	5,100 (87)	*Reference*
Black/African American	379 (5)	139 (37)	240 (63)	**3.21 (2.54-4.07)**
Asian	309 (4)	45 (15)	264 (85)	0.98 (0.70-1.39)
More than one race	84 (1)	34 (40)	50 (60)	**3.10 (1.93-4.97)**
Other/Missing**	538 (8)	189 (35)	349 (65)	**1.69 (1.29-2.22)**
Ethnicity – N (%)				
Non-Hispanic	6,125 (86)	886 (14)	5,239 (86)	*Reference*
Hispanic	484 (7)	204 (42)	280 (58)	**1.64 (1.23-2.20)**
Unknown/Other	537 (8)	53 (10)	484 (90)	**0.63 (0.46-0.85)**
Primary Language – N (%)				
English	6,864 (96)	1,011 (15)	5,853 (85)	*Reference*
Spanish	162 (2)	96 (59)	66 (41)	**2.69 (1.78-4.06)**
Other/Declined	120 (2)	36 (30)	84 (70)	**2.21 (1.43-3.41)**
Insurance - N (%)				
Commercial	4,599 (64)	602 (13)	3,997 (87)	*Reference*
Medicaid	455 (6)	228 (50)	227 (50)	**4.04 (3.25-5.04)**
Medicare	2,061 (29)	303 (15)	1,758 (85)	**1.67 (1.39-2.00)**
Other/Missing	31 (0.4)	10 (32)	21 (68)	**2.41 (1.07-5.43)**
Rheumatic Condition* - N(%)				
Osteoarthritis	754 (11)	106 (14)	648 (86)	*Reference*
Rheumatoid arthritis	3,640 (51)	577 (16)	3,063 (84)	1.15 (0.90-1.45)
SLE and Connective Tissue Diseases	1,089 (15)	218 (20)	871 (80)	1.23 (0.94-1.62)
Other inflammatory arthritis	1,056 (15)	142 (13)	914 (87)	1.03 (0.78-1.38)
Vasculitis, Myositis, Behcet's, PMR	183 (3)	21 (11)	162 (89)	0.83 (0.49-1.41)
Crystalline arthritis	111 (2)	11 (10)	100 (90)	0.79 (0.40-1.57)
Other	313 (4)	68 (22)	245 (78)	1.34 (0.93-1.92)
Social Vulnerability Index** – N (%)				
Quartile 1- Least vulnerable	2,138 (35)	240 (11)	1,898 (89)	*Reference*
Quartile 2	1,775 (29)	207 (12)	1,568 (88)	1.45 (0.43-4.82)
Quartile 3	1,363 (22)	279 (20)	1,084 (80)	2.63 (0.83-8.28)
Quartile 4- Most vulnerable	811 (13)	290 (36)	521 (64)	**4.92 (1.43-16.92)**

#Primary multivariable logistic regression model includes age, gender, race, ethnicity, primary language, insurance, and rheumatic condition. Odds ratios (ORs) for the social vulnerability index are from a separate multilevel, multivariable logistic regression model adjusted for age, gender, race, and ethnicity.

*Overall percentages are by column, SDoH percentages are by row within overall characteristic-specific Ns; all categories except rheumatic condition demonstrate statistically significant differences (p<0.01) between ≥1 SDoH need vs. no need using descriptive statistics

**Other includes Native Hawaiian and other Pacific Islander and American Indian/Alaska Native due to small sample size and individuals who indicated Other or declined to answer

*Mutually exclusive categories for analyses (i.e., if a person had a systemic rheumatic condition and osteoarthritis, they were identified as having the systemic rheumatic condition)

**Social vulnerability index quartiles restricted to addresses in MA (N=6,087) and uses MA-based references

Figure 1. Percentage of Rheumatology Patients with Specific SDoH Needs among those Indicating Any Need (N=1,143)

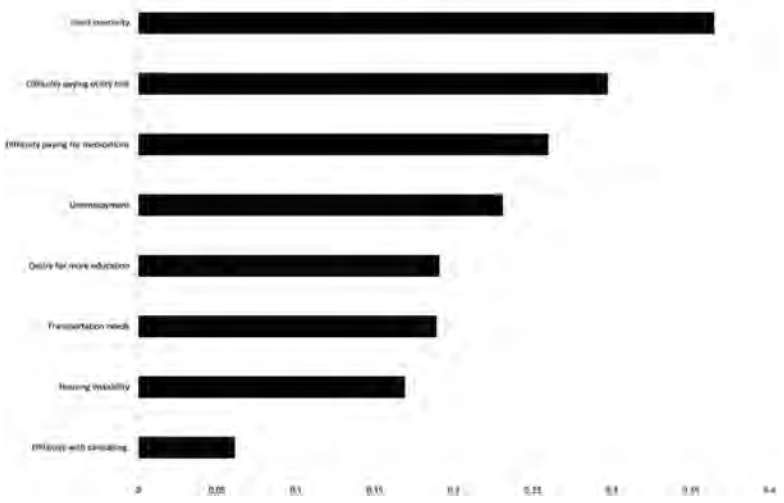

Table 2. Rheumatology-based Community Resource Specialist (rCRS) Activities to Address Social Determinants of Health (SDoH) Needs

SDoH Need	# Reached by rCRS*	Categories of Services Provided by rCRS
Food insecurity	81	• Determined eligibility for state and federal programs • Assisted with SNAP and patient assistance program applications • Assisted with packaged meal delivery application to community-based organization • Connected patients with local food pantries
Difficulty paying utility bills	76	• Facilitated access to utility payment assistance programs (e.g., Low Income Home Energy Assistance Program) • Reviewed finances and monthly bills to plan payments
Difficulty paying for medications	72	• Connected patients with organizations such as GoodRx and NeedyMeds for copayment assistance • Connected patients with multihospital-based specialty pharmacy program staff members • Connected patients with pharmaceutical company patient assistance programs when indicated • Aided in determining whether certain over the counter medications could be more affordable with prescriptions and conveying this to providers
Transportation needs	49	• Assisted with PT-1 applications • Connected patients with local public transportation ADA services • Provided information on other transportation assistance programs including Age Strong Commission Shuttle, The RIDE/RIDE Flex and planning ways to help them get to rheumatology or other subspecialty appointments
Housing instability	34	• Consulted with Harvard Center for Health Law and Policy Innovation housing legal expert for guidance regarding tenants' rights in MA • Aided with CHAMP, RAFT and Section 8 housing applications • Provided contact information for organizations offering volunteer legal services • Obtained housing letters from rheumatologists and primary care providers
Unemployment	38	• Connected patients with local hiring offices in their respective towns and with job listing websites
Desire for more education	39	• Investigated training programs based on patients' needs and loan/payment assistant programs for these programs
Difficulty with child/family-caretaking responsibilities	17	• Referred patients to elder services/Council on Aging • Assisted with SSDI application • Researched local early education resources (e.g., HeadStart, YMCA, private preschools) and provided them to patients

*Patients who indicated having ≥1 SDoH need and asked for assistance addressing needs were referred to the rCRS

Disclosure: C. Feldman: BMS Foundation, 5, Curio Bioscience, 12, My husband is one of the founders and will receive equity (but has not received anything to date)., OM1, Inc., 2, Pfizer, 5; **R. Summit**: None; **K. Retzel**: None; **H. Gim**: None; **L. Santacroce**: None; **S. Patel**: None; **S. Wilkie**: None; **V. Bills**: None; **S. Case**: None; **C. Wasserman**: None; **D. Todd**: None; **N. Sadick**: Abbvie, 5, AQtual, 5, BMS, 5, Janssen, 5; **S. Schoenfeld**: None.

Abstract Number: 1014

Rheumatic Immune-Related Adverse Events Following Immune Checkpoint Inhibitor Therapy and Subsequent Referrals to Rheumatologists at a Private vs Public Medical Center in Los Angeles: Ramifications for Health Disparities

Laura Kobashigawa[1], Nicole Zagelbaum[2], Katherine Ruddy[3], Martha Delgado[1], Baljeet Rai[4], Victoria Gevorgyan[5], Kiana Mortezaei[6], William Stohl[7] and Elizabeth Taylor-Albert MD[8], [1]LAC+USC Internal Medicine Residency, Los Angeles, CA, [2]Beverly Hills Arthritis Associates, Beverly Hills, CA, [3]LAC+USC Internal Medicine Residency, Los Angeles, MD, [4]University of California San Francisco, San Francisco, CA, [5]Los Angeles County Hospital, Los Angeles, CA, [6]Keck Medical Center of USC, Los Angeles, CA, [7]University of Southern California Keck School of Medicine, Division of Rheumatology, Los Angeles, CA, [8]University of Southern California, Santa Monica, CA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Healthcare Disparities in Rheumatology Poster II: Socioeconomic Determinants

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitors (ICIs) represent a breakthrough in cancer therapies. However, ICIs may be associated with significant immune-related adverse events (irAEs), including rheumatic irAEs. The frequency, severity, and treatment of rheumatic irAEs are not well characterized among racial and ethnic minorities. Accordingly, we

Table 1. Characteristics Among Patients at LAG and KMC with irAEs vs. No irAEs

	LAG irAEs (n=30) n (%)	LAG No irAEs (n=106) n (%)	KMC irAEs (n=74) n (%)	KMC No irAEs (n=403) n (%)
Age at Cancer Diagnosis (years ± SD)	56.8 ± 11.2	57.1 ± 11.8	60.7 ± 13.9	62.2 ± 13.1
Age at Initiation of ICI Treatment (years ± SD)	59.2 ± 10.3	59.4 ± 11.4	64.0 ± 13.4	65.5 ± 12.5
Sex				
Male	13 (43.3)	60 (56.6)	38 (51.4)	248 (61.5)
Female	17 (56.7)	46 (43.4)	36 (48.6)	155 (38.5)
Ethnicity				
Hispanic	17 (56.7)	69 (65.1)	12 (16.2)	88 (21.8)
Non-Hispanic	13 (43.4)	37 (35.9)	62 (83.8)	311 (77.2)
Unknown	0 (0)	0 (0)	0 (0)	4 (1.0)
Type of Cancer				
Melanoma	6 (20.0)	13 (12.3)	12 (16.2)	35 (8.7)
NSCLC	7 (23.3)	27 (25.5)	6 (8.1)	44 (10.9)
Renal	4 (13.3)	14 (13.2)	15 (20.3)	74 (18.4)
Urothelial	0 (0)	7 (6.6)	2 (2.7)	32 (7.9)
Pulmonary	0 (0)	7 (6.6)	4 (5.4)	40 (9.9)
Breast	0 (0)	1 (0.9)	1 (1.4)	11 (2.7)
Oral Squamous Cell	0 (0)	3 (2.8)	1 (1.4)	13 (3.2)
Ovarian	0 (0)	0 (0)	4 (5.4)	7 (1.7)
Endometrial	2 (6.7)	5 (4.7)	4 (5.4)	13 (3.2)
Hepatocellular	1 (3.3)	4 (3.8)	2 (2.7)	24 (6.0)
Gastric	1 (3.3)	2 (1.9)	1 (1.4)	14 (3.5)
Other*	9 (30.0)	23 (21.7)	22 (29.7)	96 (23.8)
Pre-Existing Autoimmune Condition	2 (6.7)	2 (1.9)	15 (20.3)	55 (13.7)
Comorbidities				
Hypertension	11 (36.7)	45 (42.5)	37 (50.0)	202 (50.1)
Obesity	7 (23.3)	15 (14.2)	25 (33.8)	96 (23.8)
Hyperlipidemia	10 (33.3)	27 (25.5)	12 (16.2)	93 (23.1)
Asthma	1 (3.3)	0 (0)	3 (4.1)	10 (2.5)
ESRD	0 (0)	2 (1.9)	0 (0)	13 (3.2)
COPD	1 (3.3)	3 (2.8)	1 (1.4)	25 (6.2)
CHF	2 (6.7)	7 (6.6)	2 (2.7)	11 (2.7)
Diabetes	7 (23.3)	32 (30.2)	12 (16.2)	91 (22.6)
CKD	8 (26.7)	11 (10.4)	7 (9.5)	42 (10.4)

*Other: unknown primary (5), adrenal (1), anal (5), basal cell carcinoma (2), cardiac angiosarcoma (1), cervical (11), cholangiocarcinoma (1), chordoma (1), CNS lymphoma (1), colon (8), cutaneous SCC (1), cystic carcinoma maxillary sinus (1), desmoplastic round small cell tumor (1), duodenal (1), esophageal (5), follicular lymphoma (1), Hodgkin lymphoma (6), neuroendocrine (4), perivascular epithelioid cell (1), maxillary sinus SCC (1), Merkel cell (1), mesothelioma (4), thyroid (3), mucoepidermoid (1), nasopharyngeal (4), nerve sheath tumor (1), osteosarcoma (1), Pancoast tumor (1), pancreatic (1), penile (1), rectal (3), cutaneous SCC (3), sarcoma (7), fallopian tube (1), vulvar (2), testicular (1), thyroid (1), thymic (2), prostate (4), multiple cancers (48)

Table 2. Demographics and Outcomes Among Patients with Rheumatic iRAEs

	Patients with Rheumatic irAEs at LAG (n=8) n (%)	Patients with Rheumatic irAEs at KMC (n=15) n (%)	P-value
Ethnicity			0.068
Hispanic	5 (62.5)	2 (13.3)	
Non-Hispanic	3 (37.5)	13 (86.7)	
Referred to a Rheumatologist	1 (12.5)	10 (66.7)	0.013
Treatment of irAE			0.466
None	2 (25.0)	3 (20.0)	
Steroid monotherapy	3 (37.5)	1 (6.7)	
NSAIDs Only	1 (12.5)	2 (13.3)	
Steroid + NSAIDs	0 (0)	1 (6.7)	
DMARD	2 (25.0)	7 (46.6)	
Opioid	0 (0)	1 (6.7)	
Cancer Outcome			0.711
Complete response	1 (12.5)	1 (6.7)	
Partial response	1 (12.5)	1 (6.7)	
Stable	2 (25.0)	4 (26.6)	
Progression	4 (50.0)	6 (40.0)	
Death	0 (0)	3 (20.0)	

investigated the nature of rheumatic irAEs among patients treated with ICIs and subsequent referrals to rheumatologists at 2 medical centers located in the same geographic region of Los Angeles, both staffed by faculty from the same medical school: Los Angeles General Medical Center (LAG), a safety-net public hospital, and Keck Medical Center (KMC), a private hospital.

Methods: The electronic medical records of patients 18+ years of age seen at LAG and KMC from May 2015 through May 2021 were screened for treatment with ICIs (nivolumab, pembrolizumab, and/or atezolizumab) by ICD-10 codes, and 613 individual patients (136 at LAG and 477 at KMC) were identified. Of these patients, 30 (22.1%) and 74 (15.5%) developed irAEs at LAG and KMC, respectively. We compared patient demographics, type of iRAEs, and cancer outcomes between the irAE and no-irAE groups at each institution. Among the 30 + 74 patients with irAEs, we identified 23 patients (n=8, 5.9% at LAG; and n=15, 3.1% at KMC) who developed rheumatic irAEs. We compared referral rates to a rheumatologist and management of rheumatic iRAEs between these 2 groups.

Results: No significant differences in demographics and comorbidities were detected between the irAE and no-irAE groups at either institution (Table 1). Across both medical centers, the most common rheumatic irAEs were arthritis (70.0%) followed by myositis (13.0%). Compared to patients at KMC, patients at LAG with rheumatic iRAEs were more likely to be of Hispanic ethnicity (62.5% vs. 13.3%, p=0.068), less likely to be referred to a rheumatologist (12.5% vs. 62.5%, p=0.013) and more likely to be treated with steroid monotherapy for management of rheumatic iRAEs (37.5% vs. 12.5%, p=0.466). There were no significant differences in cancer outcomes between patients with rheumatic iRAEs at each institution (Table 2).

Conclusion: While ICIs have revolutionized therapy for many different types of cancers, they may lead to the development of significant iRAEs, including rheumatic irAEs. To our knowledge, this is the first study to investigate differences in rheumatic irAEs between a public and a private institution located in the same geographic region and staffed by the same group of physicians. The significantly lower rate of referral to rheumatologists among patients with rheumatic irAEs at a public medical center compared to patients at a neighboring private institution raises concern for health care disparities between patients seeking care at a private vs public institution. Studies with larger cohorts of racially and ethnically diverse patient populations are necessary to enhance our understanding of rheumatic irAEs and to ensure equitable care for all patients.

Disclosure: L. Kobashigawa: None; **N. Zagelbaum**: None; **K. Ruddy**: None; **M. Delgado**: None; **B. Rai**: None; **V. Gevorgyan**: None; **K. Mortezaei**: None; **W. Stohl**: GSK, 5, Pfizer, 5; **E. Taylor-Albert MD**: AliveCor, 3, 4.

Abstract Number: 1015

Health Care Access in an Indigenous North American Population of Rheumatoid Arthritis Patients and Their At-risk First-Degree Relatives

Dana Wiens[1], David Robinson[1], Irene Smolik[1], Cheryl Barnabe[2], Hani El-Gabalawy[1] and **Liam O'Neil**[1], [1]University of Manitoba, Winnipeg, MB, Canada, [2]University of Calgary, Calgary, AB, Canada

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Healthcare Disparities in Rheumatology Poster II: Socioeconomic Determinants
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis (RA) is a chronic autoimmune disease that requires access to subspecialty care. Although Canada has a universal healthcare system, there are complex and interrelated factors that lead to inequitable healthcare access and delivery. These factors are particularly relevant to Canada's geographically dispersed First Nations People (FN), who bear a disproportionate burden of RA and its complications. In the context of a longitudinal study of RA onset in a FN population, we sought to identify factors that influence access to healthcare in a cohort of FN RA patients and their First-Degree Relatives (FDR).

Methods: A longitudinal cohort of FN RA patients (n = 214) and their FDR (n = 617) was recruited between 2005 and 2017 to participate in a prospective study of RA risk in the FDR (total n = 831). Study participants were recruited in both urban and rural locations in Manitoba, Canada. The study enrollment visit included a healthcare access survey which measured access on a Likert scale (Figure 1). Overall access difficulty was determined using a binary variable, where if *any* of the 7 questions scored moderate or higher, the individual was deemed to have 'access difficulty', otherwise they were classified as 'adequate access'. Modified health assessment questionnaire (mHAQ) and disease duration were collected for RA patients. Data were analyzed using chi-square test and logistic regression.

Have any of the following been a problem for you with respect to healthcare? (Please check the best answer for you.)	No problem	A bit of a problem	A moderate problem	A big problem
Wait Domain	❑	❑	❑	❑
Q1: Waiting to be seen at your nursing station?	❑	❑	❑	❑
Q2 Waiting list to be seen by a family doctor?	❑	❑	❑	❑
Q3: Waiting list to be seen by a specialist?	❑	❑	❑	❑
Travel Domain	❑	❑	❑	❑
Q4: Traveling to see a family doctor?	❑	❑	❑	❑
Q5: Traveling to see a specialist?	❑	❑	❑	❑
Medication Domain	❑	❑	❑	❑
Q6: Cost of medications?	❑	❑	❑	❑
Q7: Access to medications?	❑	❑	❑	❑
Q8: Cost of medical devices? (e.g., braces, wheelchairs, etc.)	❑	❑	❑	❑

Figure 1: Access to care questionnaire.

Results: Overall, RA and FDR participants living in rural communities reported more difficulties with healthcare access compared to urban dwellers (overall access difficulty, 53.5% vs 33.5%, p< 0.0001), and rural RA patients reported more access difficulty than unaffected rural FDR (Figure 1A, 66.9% vs 50.5%, p=0.002). In contrast, there were no differences reported between RA patients and FDR living in urban locations (Figure 2B). In the entire RA cohort, no differences in access were reported based on disease duration, age, or sex, although those with higher mHAQ scores tended to report worse access. A logistic regression model of the entire RA and FDR cohort suggested that variables which independently associated with healthcare access difficulty were *female sex* (Figure 2A, OR 1.47, 1.07-2.01), *older age* (OR 1.51, 1.12-2.04) and *living in a rural community* (OR 1.99, 1.45-2.71). The model suggested that females living in rural locations, irrespective of an RA diagnosis, were particularly disadvantaged for healthcare access, but also that males with an RA diagnosis experienced substantially more access difficulty compared to FDR males (Figure 2B).

Conclusion: Perceived difficulties in accessing healthcare were reported more frequently in FN RA patients as well as their unaffected at-risk FDR who were living in rural locations compared to those living in urban locations. We also identified sex, age and location of residence-based differences in perceived healthcare access for FN persons irrespective of disease state. In order to achieve equitable healthcare delivery in the context of a universal healthcare system, interventions to address geographic factors, such as transportation and availability of healthcare providers, need to also incorporate complex factors related to sex, gender and age.

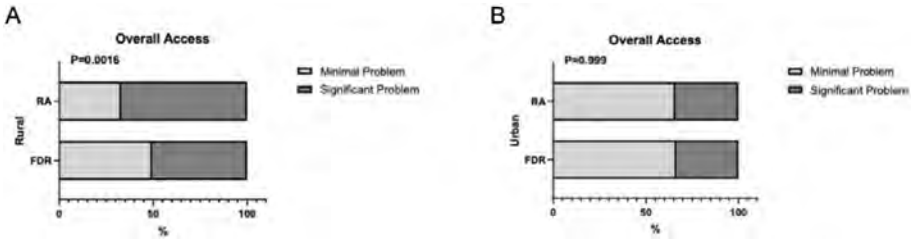

Figure 2: Poor access to care in First Nation RA patients is restricted to rural communities. (A) Overall access difficulty in RA patients compared to first-degree relatives (FDR) in rural communities. (B) Overall access difficulty in RA patients compared to first-degree relatives (FDR) in the urban setting. Differences calculated by chi-square test.

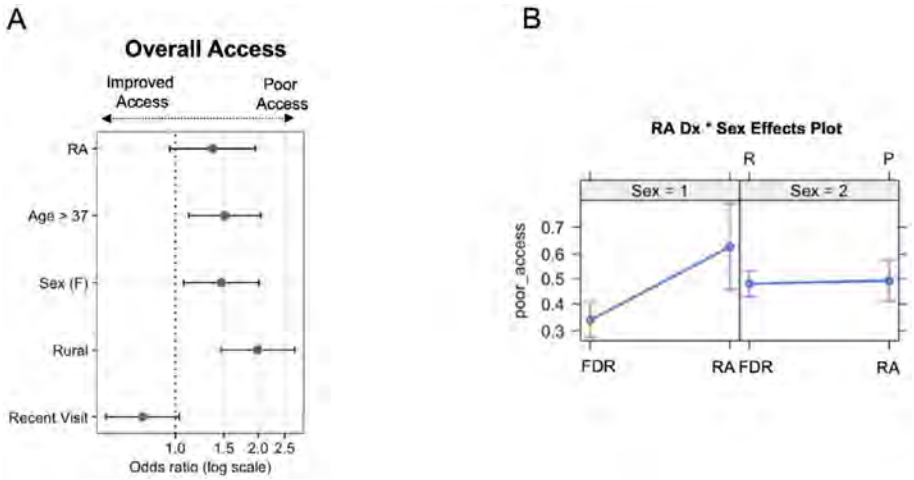

Figure 3: Poor access to care in First Nations RA patients and first-degree relatives is predominantly mediated by older age, female sex and living in a rural community. (A) Results of a logistic regression analysis that included the variables Age, Sex, RA diagnosis, and timing of the visit displaying OR with 95% confidence interval. Statistically significant OR were observed for age, sex and rural. (B) Effects plots for logistic regression interaction term between Sex and RA diagnosis. Differentially poor access was observed for males with RA, while females with RA and FDR displayed similar access.

Disclosure: D. Wiens: None; **D. Robinson**: None; **I. Smolik**: None; **C. Barnabe**: None; **H. El-Gabalawy**: None; **L. O'Neil**: None.

Abstract Number: 1016

Cost-related Medication Burden for Patients with and Without Systemic Autoimmune Rheumatic Diseases

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Healthcare Disparities in Rheumatology Poster II: Socioeconomic Determinants
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Medication nonadherence is a challenging issue in the management of systemic autoimmune rheumatic diseases (SARDs), leading to poor clinical outcomes. Although it is complex and multifaceted, cost is a significant barrier to medication adherence. We investigated cost-related medication burden in patients with SARDs, compared to that in patients without SARDs in a large diverse cohort across the U.S..

Methods: Among the participants with baseline survey and electronic health records in the All of Us (AoU) research program v7, we identified patients with SARDs who had ≥2 International Classification of Diseases (ICD)-9/10 and Systematized Nomenclature of Medicine (SNOMED) codes ≥ 60 days apart within two years.Cost-related medication burden was assessed in 3 ways using self-reported questionnaire data collected at enrollment: 1) unaffordability of prescription medicines, 2) cost-related medication nonadherence—skipping medications, taking less medicines, or delaying filling a prescription, and 3) cost-reducing strategies—asking for a lower cost medication, buying prescription drugs from another country, or using alternative therapies. Self-reported responses to each question were compared between patients with and without SARDs using Chi-squared tests. Logistic regression analyses calculated odds ratios (ORs), adjusting demographic, socioeconomic, and multiple clinical factors.

Results: Among respondents who fully answered these questionnaires, a total of 4,428 SARDs patients and 110,109 participants without SARDs were analyzed (**Table 1**). Patients with SARDs had lower socioeconomic status than those without SARDs. Among those with SARDs, 18.2% did not get prescription medicines due to cost, whereas this was 11.6% of those without SARDs (**Figure 1**). 18.7% of those with SARDs vs. 12.8% without SARDs reported cost-related medication nonadherence, while 29.9% with vs. 25.2% without SARDs reported using medication cost-reducing strategies. After adjusting for multiple demographic and clinical factors, patients with SARDs had 1.6-fold (95% CI 1.4-1.7) odds of reporting unaffordability of prescription medicines, 1.5-fold (95% CI 1.3-1.6) odds of reporting cost-related medication nonadherence, and 1.2-fold (95% CI 1.1-1.3) odds of reporting using cost-reducing strategies, than those without SARDs (**Figure 2**). Full adjustment reduced the odds of all 3 cost-reducing behaviors the most for those with SLE, likely as this is a younger, more diverse population of lower socioeconomic status than other SARDs groups.

Conclusion: Higher proportions of patients with SARDs self-reported unaffordability of prescription medicines, cost-related medication nonadherence, and cost-reducing strategies than did patients without SARDs in the large AoU research program, even after adjusting for multiple demographic and clinical factors. Ongoing research is investigating how cost-related

Table 1. Demographic and survey data of participants with and without systemic autoimmune rheumatic diseases

	Participants with systemic autoimmune rheumatic diseases (n=4,428)	Participants without systemic autoimmune rheumatic diseases (n=110,109)	Standardized mean difference
Age category, years, (%)			0.313
18-49	1,170 (26.4)	45,174 (41.0)	
50-64	1,653 (37.3)	32,985 (30.0)	
65-	1,605 (36.2)	31,950 (29.0)	
Female, (%)	3,508 (81.3)	70,240 (65.1)	0.372
Self-reported race/ethnicity (%)			0.062
Hispanic	495 (11.5)	13,417 (12.5)	
Non-Hispanic Black	477 (11.1)	10,817 (10.1)	
Non-Hispanic Other	233 (5.4)	6,951 (6.5)	
Non-Hispanic White	3,082 (71.9)	75,999 (70.9)	
Index year			0.015
~2018	1,214 (27.4)	30,172 (27.4)	
2019	1,489 (33.6)	37,459 (34.0)	
2020	447 (10.1)	11,159 (10.1)	
2021	773 (17.5)	19,233 (17.5)	
2022	505 (11.4)	12,086 (11.0)	
Annual household income, $			0.124
<35k	1,152 (30.5)	24,255 (25.3)	
35k-<100k	1,425 (37.7)	36,938 (38.5)	
≥100k	1,202 (31.8)	34,659 (36.2)	
Education level			0.145
High school graduate or less	723 (16.7)	16,010 (14.9)	
Some college	1,283 (29.7)	26,275 (24.4)	
College graduate or above	2,316 (53.6)	65,206 (60.7)	
Insurance type[a]			0.231
Private	2,126 (55.2)	59,055 (62.0)	
Public	1,671 (43.4)	32,553 (34.2)	
Uninsured	54 (1.4)	3,658 (3.8)	
Unemployed	2,566 (59.6)	47,208 (44.0)	0.316
Region			0.164
Northeast	1,708 (38.6)	34,125 (31.0)	
Midwest	1,160 (26.2)	31,419 (28.5)	
South	622 (14.1)	16,737 (15.2)	
West	936 (21.1)	27,771 (25.2)	
Area deprivation index, median (IQR)	0.30 (0.07)	0.30 (0.08)	0.058
Ever smoking	1,742 (40.0)	38,206 (35.3)	0.097
Obesity[b]	1,974 (46.0)	42,211 (39.8)	0.124
Charlson comorbidity index[c]	2.85 ± 3.04	1.38 ± 2.36	0.537
Number of medications			0.655
0	431 (9.7)	36,119 (32.8)	
1-4	1,736 (39.2)	43,247 (39.3)	
5-9	983 (22.2)	14,598 (13.3)	
10+	1,278 (28.9)	16,145 (14.7)	
Types of SARDs			
Rheumatoid arthritis	1,469 (33.2)	-	
Systemic lupus erythematosus	518 (11.7)	-	
Psoriatic arthritis	315 (7.1)	-	
Ankylosing spondylitis	321 (7.2)	-	
Other SARDs	917 (20.7)	-	
2 or more SARDs	888 (20.1)	-	

[a]People covered by both private and public insurance considered to have private insurance, and people having only Indian Health Service coverage considered uninsured
[b]Obesity by body mass index (BMI) ≥30 kg/m² from physical measurement data
[c]Charlson comorbidity index calculated using 16 comorbidities, excluding rheumatic disease.

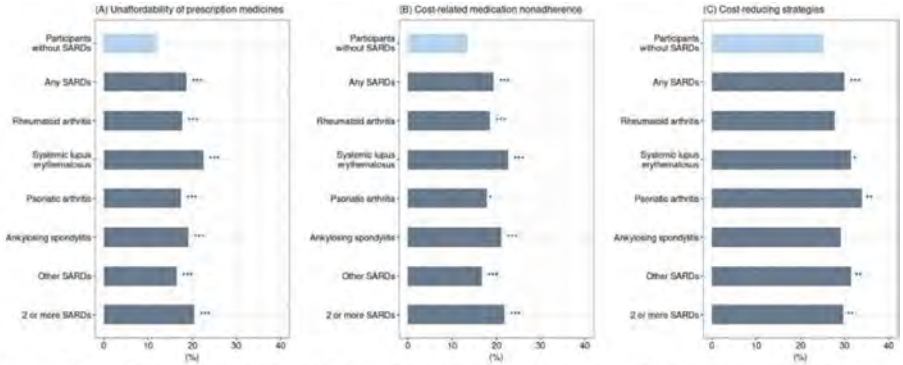

Figure 1. Prevalence (%) of cost-related medication burden reported by patients with and without systemic autoimmune rheumatic diseases (SARDs) in All of Us (v7). (A) Unaffordability of prescription medicines. (B) Cost-related medication nonadherence. (C) Cost-reducing strategies. *p<0.05, **p<0.01, *p<0.001 compared to general population.

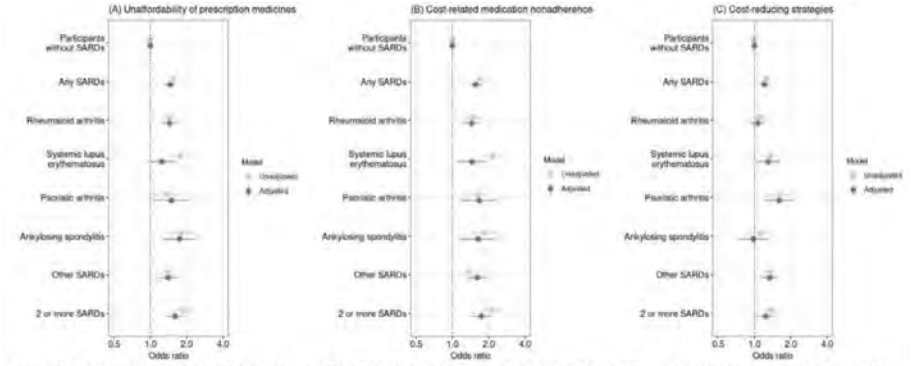

Figure 2. Unadjusted and adjusted odds ratio (95% CI) for cost-related medication burden in patients with systemic autoimmune rheumatic diseases (SARDs) compared to patients without SARDs in All of Us (v7). (A) Unaffordability of prescription medicines. (B) Cost-related medication nonadherence. (C) Cost-reducing strategies. Adjusted model included age, sex, race/ethnicity, index year, annual household income, education level, insurance type, employment status, geographical region, area deprivation index, smoking status, obesity, Charlson comorbidity index, calculated using 16 comorbidities excluding rheumatic diseases, and number of medications.

medication burden influences adherence and clinical outcomes for patients with SARDs. Clinicians and other stakeholders should consider the financial burden of medications faced by patients with SARDs to improve medication adherence and thus clinical outcomes.

Disclosure: J. Yee: None; **C. Feldman**: BMS Foundation, 5, Curio Bioscience, 12, My husband is one of the founders and will receive equity (but has not received anything to date)., OM1, Inc., 2, Pfizer, 5; **E. Oakes**: None; **J. Ellrodt**: None; **M. Choi**: AbbVie/Abbott, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 6, Mallinckrodt, 2, Merck/MSD, 2, MitogenDx, 2, Organon, 6, Pfizer, 2, 6, Roche, 2, Werfen, 2; **E. Karlson**: None; **K. Costenbader**: Amgen, 2, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Eli Lilly, 2, Exagen Diagnostics, 5, Gilead, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5.

Abstract Number: 1017

Cross Country Differences in b/tsDMARD Prescription Behavior: Associations Between Socioeconomics, Real World b/tsDMARD Use and Disease Outcomes

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Healthcare Disparities in Rheumatology Poster II: Socioeconomic Determinants
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The development of biologic and targeted synthetic (b/ts)DMARDs contributed to improved treatment outcomes in rheumatoid arthritis (RA). However, high medication costs may limit their use. Previously we showed less b/tsDMARD use in countries with a lower socioeconomic status (SES), than in countries with higher SES. Here we take a more detailed look at b/tsDMARD use across countries and explore cross-country relationships between Gross Domestic Product (GDP)-per-capita, indicators of b/tsDMARD use and disease outcomes in RA-patients

Methods: This multinational, observational study included countries contributing ≥100 patients using b/tsDMARDs, with available follow-up, to one of two registries: METEOR, an international registry capturing daily practice data of patients with a clinical diagnosis of RA, and JAK-POT, an investigator-initiated collaboration between national registries aiming to evaluate clinical aspects of b/tsDMARDs in RA. On a per-country basis, mean DAS28 was calculated from the last available follow-up visit per patient. B/tsDMARD usage was determined as mean time to start b/tsDMARD therapy since date of diagnosis, number of b/tsDMARDs tried per patient and duration of b/tsDMARD therapy. To calculate the time to start a first b/tsDMARD per country included from JAK-POT, only bionaïve patients were included. Possible associations between GDP per capita, indicators of b/tsDMARD use and DAS28 were tested using univariable linear regression. Regression coefficients (β) are interpreted as the numerical increase in the outcome per one point increase in the predictor.

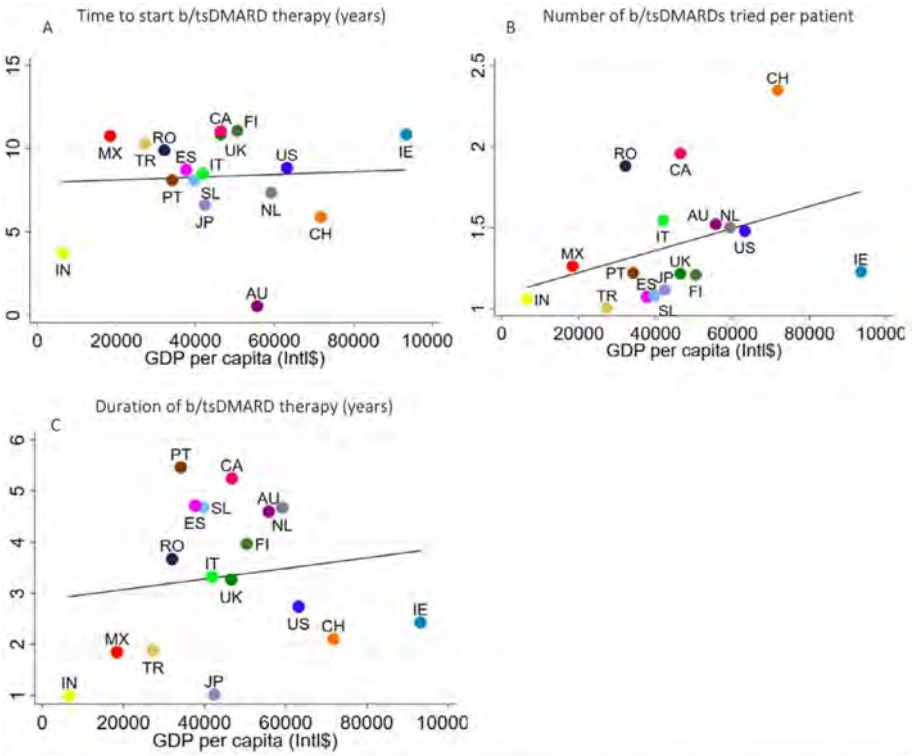

Figure 1. Associations between 'GDP per capita (Intl$)' and the 'Time to start b/tsDMARD therapy (years)' (A), 'Number of b/tsDMARDs tried per patient' (B) and 'Duration of b/tsDMARD therapy (years)' (C)

AU, Austria; CA, Canada; CH, Switzerland; ES, Spain; FI, Finland; GB, United Kingdom; IE, Ireland; IN, India; IT, Italy; JP, Japan; MX, Mexico; NL, Netherlands; PT, Portugal; RO, Romania; SL, Slovenia; TR, Turkey; US, United States

Results: Data from 25,832 patients from 17 different countries showed varying b/tsDMARD prescriptions. GDP-per-capita ranged from 6505 (India) to 93350 Intl$ (Ireland). Time to start b/tsDMARD therapy ranged from 0.5(Austria) to 11.1 (Finland) years. Mean number of b/tsDMARDs tried per patient ranged from 1.0 (Turkey) to 2.4 (Switzerland). Duration of b/tsDMARD therapy ranged from 0.9 (India) to 5.5 (Portugal) years (fig 1). Baseline DAS28 ranged between 3.7 and 6.1, but was not related to any of the indicators of b/tsDMARD use: time to start a b/tsDMARD β 0.08 (95% CI -0.7; 0.9), number of prescribed b/tsDMARDs β 0.06 (95% CI -0.03; 0.2), duration of b/tsDMARD treatment β 0.1 (95% CI -0.3; 0.5).No statistically significant associations were observed between GDP-per-capita and time to start b/tsDMARD therapy (fig 1A, β 0.09 CI 95% -0.7; 0.9), number of b/tsDMARDs tried per patient (fig 1B, β 0.07 CI 95% -0.02; 0.2) or duration of b/tsDMARD therapy (fig 1C, β 0.1 CI 95% -0.3; 0.5). None of the indicators of b/tsDMARD prescription were significantly related to DAS28 at the end of follow up: time to start a b/tsDMARD β 0.02 (95% CI -0.05; 0.1), duration of b/tsDMARD therapy β -0.03 (95% CI -0.2; 0.1) and number of b/tsDMARDsβ -0.03 (95% CI -0.6; 0.6).

Conclusion: This study showed varying b/tsDMARD prescription behavior and disease activity across 17 countries worldwide. Overall, differences in b/tsDMARD prescription behavior was not related to socioeconomic welfare and disease activity at a country level. This seems to indicate that once patients start a b/tsDMARD, socioeconomic welfare has less impact on b/tsDMARD use.

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Abstract Number: 1018

Recognizing Rural Healthcare Disparities in Pain Assessment for Autoimmune Rheumatologic Diseases

Lydia Yang[1], Bharat Kumar[2] and Melissa Swee[1], [1]University of Iowa Carver College of Medicine, Iowa City, IA, [2]University of Iowa Hospitals and Clinics, Iowa City, IA

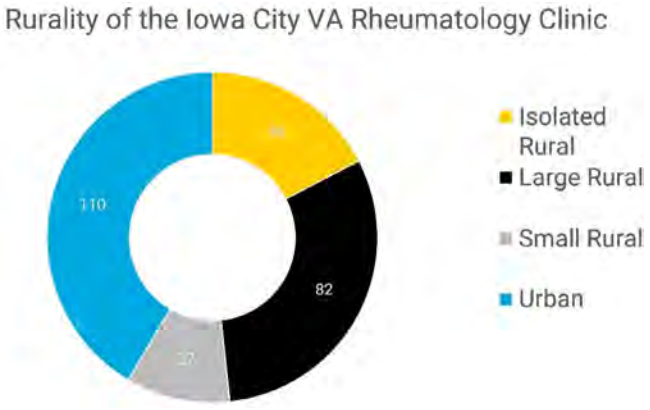
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Healthcare Disparities in Rheumatology Poster II: Socioeconomic Determinants
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Pain is a common complaint seen in many autoimmune rheumatologic conditions, along with decreased function and decreased sense of well-being. Pain is a highly person-specific symptom without well-validated biomarkers, making it difficult to assess and use as a standardized metric in guiding immune modulatory therapy. Multiple lines of evidence suggest that rural-dwelling patients may conceptualize and relay pain differently than non-rural-dwelling patients, which may complicate the delivery of optimal care and further healthcare disparities. Within a clinic that serves predominantly rural-dwelling patients, we aim to determine if rural-dwelling status correlates with self-reported levels of pain,

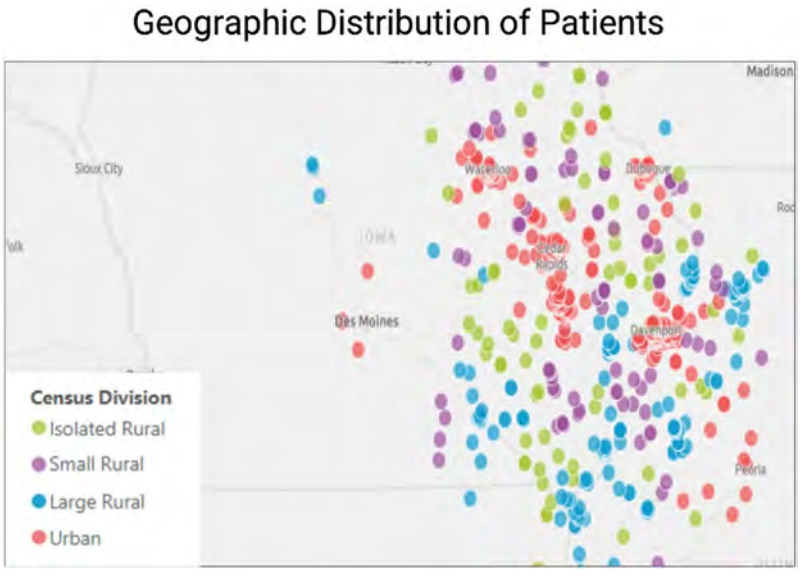
function, and sense of well-being in patients with autoimmune rheumatologic diseases. We additionally aim to determine if there is a statistically significant difference in functional activity, pain levels, and sense of well-being between rural-dwelling patients and non-rural-dwelling patients. These correlations will empower quality improvement initiatives within our clinic.

Methods: We correlate rurality with elements of the RAPID-3 form. Rurality is determined by RUC (Rural-Urban Commuting) Codes based on the patient's home address. Using RUC, patients were classified into four categories: (1) urban, (2) large rural town, (3) small rural town, and (4) isolated small rural town. The RAPID-3 is a validated questionnaire consisting of three parts: (1) functional status, (2) pain level, and (3) global well-being. All items are self-reported by patients.

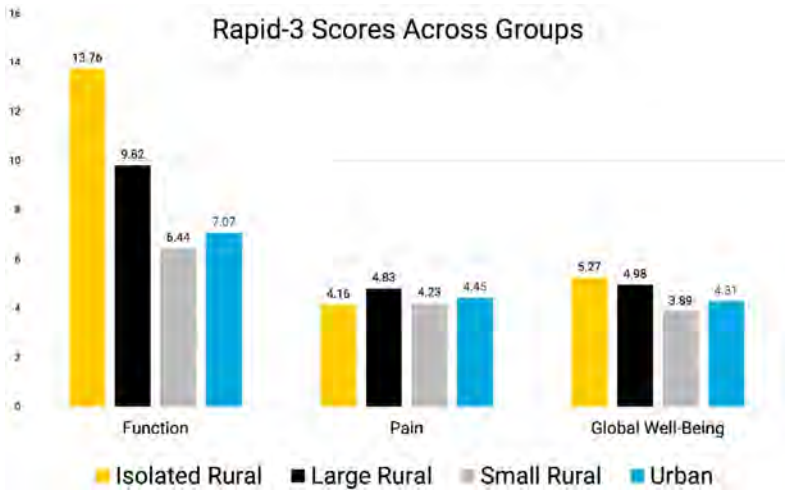
Results: Among the 265 rheumatology patients seen between May 1, 2022, to November 1, 2022, 110 were urban-dwelling and 155 were rural-dwelling (large [82], small [27], or isolated [46]).Percentages of self-reported gender and ethnicity/race (Non-Hispanic White, Hispanic, Black) were comparable as well as average age. Isolated rural-dwelling patients had the highest degree of dysfunction (13.76/20) and sense of poor well-being (5.27/10) compared to small rural-dwelling patients (6.44/20 and 3.89/10, respectively), who had the lowest degree of dysfunction and poor sense of well-being, and



Pie chart displaying the proportion of patients in each rurality classification.



Dot plot displaying the geographic distribution of patients' homes seen at the VA Rheumatology Clinic in Iowa City, IA



Bar graphs depicting differences in self-reported function, pain, and global well-being across groups.

urban-dwelling patients (7.07/20 and 4.31/10, respectively) [p-value< 0.01).In contrast, dwellers of large rural towns report the highest levels of pain (4.84/10) compared to those in isolated rural communities, who had the lowest (4.16/10).However, differences in levels of pain were not statistically significant.

Conclusion: In this clinic, there exist healthcare disparities in measuring pain, dysfunction, and sense of well-being among rural-dwelling patients with autoimmune rheumatologic diseases. Those that live in isolated rural communities tend to report lower amounts of pain despite having higher levels of poor well-being and dysfunction, compared to those living in larger rural and urban settings. These findings suggest that we may be systematically underestimating the burden of pain in patients living in isolated rural communities that obtain care through our clinic. These results empower quality improvement initiatives to better solicit pain and dysfunction among rural-dwelling patients.

Disclosure: L. Yang: None; **B. Kumar**: None; **M. Swee**: None.

Abstract Number: 1019

Association of Historical Redlining and Present-Day Neighborhood Inequities with Missed Outpatient Appointments Among Individuals with Rheumatic Conditions

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Healthcare Disparities in Rheumatology Poster II: Socioeconomic Determinants
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Structural racism pervades U.S. history with continued effects on health inequities. Residential segregation serves as an example, where redlining maps outlined areas with high concentrations of Black and immigrant residents as hazardous for investment, which precluded access to mortgages and home ownership. This exclusionary

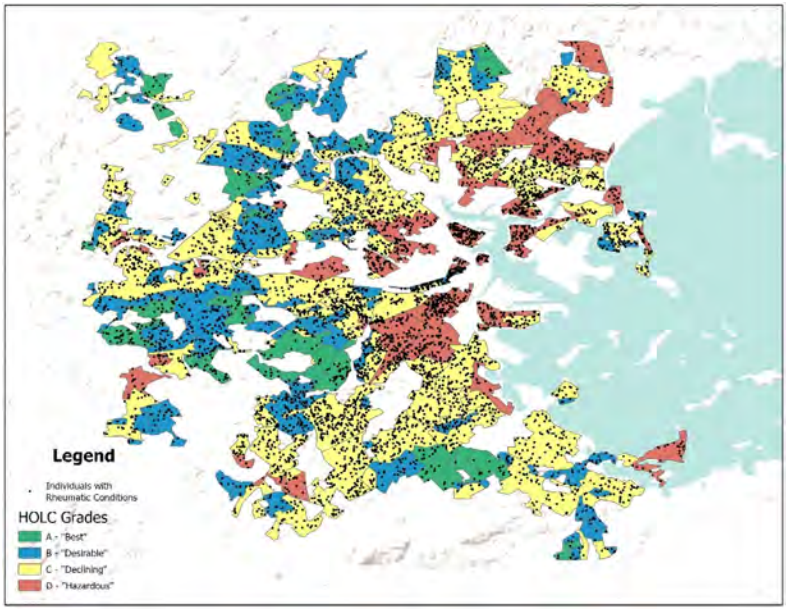

Figure 1. Current distribution of individuals with rheumatic conditions receiving care in a Massachusetts-based multihospital medical system on a 1930s Home Owners' Loan Corporation redlining map

Table 1. Characteristics of individuals with rheumatic conditions (n = 5,598) overall and by HOLC grade

Characteristics	Overall (n = 5,598)	HOLC classification A "Best" (n = 304)	B "Still Desirable" (n = 1,047)	C "Definitely Declining" (n = 2,952)	D "Hazardous" (n = 1,295)
Age, mean ± SD years	63 (16)	65 (16)	64 (16)	62 (16)	63 (16)
Legal sex - N (%)					
Male	1,654 (30)	100 (33)	347 (33)	821 (28)	386 (30)
Female	3,944 (70)	204 (67)	700 (67)	2,131 (72)	909 (70)
Race* - N (%)					
Asian	258 (5)	13 (4)	64 (6)	122 (4)	59 (5)
Black	657 (12)	9 (3)	49 (5)	416 (14)	183 (14)
White	3,855 (69)	270 (89)	868 (83)	1,969 (67)	748 (58)
Other/Unknown/Missing	828 (14)	12 (4)	66 (6)	445 (15)	305 (23)
Ethnicity - N (%)					
Hispanic	224 (4)	1 (0)	9 (1)	123 (4)	91 (7)
Non-Hispanic	4,698 (84)	251 (83)	880 (84)	2,506 (85)	1,061 (82)
Unknown/Missing	676 (12)	52 (17)	158 (15)	323 (11)	143 (11)
Insurance - N (%)					
Medicaid	868 (16)	5 (1.6)	58 (6)	473 (16)	332 (26)
Medicare	1,742 (31)	89 (29)	341 (33)	911 (31)	401 (31)
Commercial	2,703 (48)	198 (65)	602 (57)	1,414 (48)	489 (38)
Other/Unknown/Missing	285 (5)	12 (4)	46 (4)	154 (5)	73 (6)
DCCI, mean ± SD	1.05 (1.93)	1.00 (1.73)	0.89 (1.68)	1.08 (1.98)	1.12 (2.03)
Rheumatic condition‡ - N (%)					
Osteoarthritis	3,009 (54)	166 (55)	511 (49)	1,587 (54)	745 (58)
Crystalline arthritis	1,152 (21)	67 (22)	202 (19)	574 (19)	309 (24)
Inflammatory arthritis	2,800 (50)	140 (46)	510 (49)	1,502 (51)	648 (50)
SLE/Connective tissue disease	1,935 (35)	101 (33)	387 (37)	1,018 (34)	429 (33)
Vasculitis	520 (9)	28 (9)	106 (10)	272 (9)	114 (9)
ICE racialized economic segregation§ - N (%)					
Q1 (most Black and low-income)	1,780 (32)	8 (3)	59 (6)	1,158 (39)	555 (43)
Q2	969 (17)	13 (4)	100 (10)	574 (19)	282 (22)
Q3	938 (17)	20 (6)	169 (16)	532 (18)	217 (17)
Q4	934 (17)	39 (13)	308 (29)	440 (15)	147 (11)
Q5 (most non-Hispanic White and high-income)	977 (17)	224 (74)	411 (39)	248 (9)	94 (7)

HOLC = Home Owners' Land Corporation; DCCI = Deyo-Charlson Comorbidity Index; SLE = systemic lupus erythematosus; ICE = Index of Concentration at the Extremes

* Race was characterized by self-identification in the medical record. "Other" racialized group includes individuals who self-identified as American Indian or Alaska Native, Native Hawaiian or Pacific Islander, two or more races, selected "some other known race," or declined to report race

‡ Rheumatic conditions are not mutually exclusive categories

§ ICE quintiles were constructed using self-reported race and incomes of ≤ $30,000 and ≥ $150,000 for 20th and 80th percentile cut-offs, respectively per 2021 American Community Survey data

Table 2. Multilevel multinomial models estimating the odds of recurrent missed outpatient appointments by HOLC grade and Index of Concentration at the Extremes for racialized economic segregation (n = 5,598)

Variable	Number of Missed Outpatient Appointments *(Ref=0)*	Model 1 Overall Odds Ratio OR (95% CI)	Model 2 Overall Odds Ratio OR (95% CI)
Race (*Ref=White*)			
Black	1-3	**2.44 (1.87, 3.18)**	**2.27 (1.72, 2.99)**
	4+	**4.95 (3.81, 6.43)**	**4.09 (3.13, 5.36)**
Ethnicity (*Ref=Non-Hispanic*)			
Hispanic	1-3	1.48 (0.87, 2.51)	1.42 (0.83, 2.42)
	4+	**2.91 (1.81, 4.67)**	**2.79 (1.74, 4.47)**
Insurance (*Ref=Commercial*)			
Medicaid	1-3	**1.58 (1.23, 2.02)**	**1.50 (1.17, 1.93)**
	4+	**5.44 (4.31, 6.87)**	**5.15 (4.08, 6.51)**
Medicare	1-3	1.16 (0.99, 1.36)	1.15 (0.98, 1.34)
	4+	**2.03 (1.71, 2.40)**	**2.02 (1.70, 2.39)**
Deyo-Charlson Comorbidity Index (DCCI, *Ref=at or below mean*)			
DCCI	1-3	**1.28 (1.07, 1.53)**	**1.28 (1.07, 1.53)**
	4+	**2.18 (1.83, 2.61)**	**2.16 (1.81, 2.59)**
HOLC Grade (*Ref=Grade A, "Best"*)			
Grade = B ("Still Desirable")	1-3	0.93 (0.70, 1.24)	--
	4+	1.19 (0.81, 1.75)	--
Grade = C ("Definitely Declining")	1-3	1.00 (0.77, 1.32)	--
	4+	**1.62 (1.13, 2.33)**	--
Grade = D ("Hazardous")	1-3	0.89 (0.66, 1.19)	--
	4+	**1.79 (1.22, 2.62)**	--
Index of Concentration at the Extremes (ICE), Racialized Economic Segregation *(Ref= Quintile 5- highest concentration non-Hispanic White high-income)*			
Quintile 4	1-3	--	1.02 (0.83, 1.26)
	4+	--	1.16 (0.89, 1.51)
Quintile 3	1-3	--	1.17 (0.94, 1.45)
	4+	--	**1.44 (1.11, 1.88)**
Quintile 2	1-3	--	1.06 (0.85, 1.32)
	4+	--	**1.71 (1.32, 2.21)**
Quintile 1 (highest concentration Black low-income)	1-3	--	**1.24 (1.00, 1.53)**
	4+	--	**2.27 (1.77, 2.90)**

Model 1: Adjusted for age, Asian and other/unknown race, and ethnicity, includes HOLC grades; **Model 2**: Adjusted for age, Asian and other/unknown race, and ethnicity, includes ICE for racialized economic segregation; Multilevel models account for clustering of individuals by census tract; Bolded values indicate statistically significance.

disinvestment in communities of color has led to the racial wealth gap. We studied the effects of historical redlining policies and present-day racialized economic segregation, measured by the Index of Concentration at the Extremes (ICE), on missed outpatient appointments, an indicator of access to sustained care, among individuals with rheumatic conditions.

Methods: Using a multihospital clinical data repository, we identified adults 18 years with New England addresses and 1 ICD-10 code for a rheumatic condition who received rheumatology care within 3 years of 1/2023. We defined the index date as the date of the third code for the same rheumatic condition and the baseline period as one year prior to the index date. Home addresses were geocoded and overlaid with 1930s Home Owners' Loan Corporation (HOLC) redlining vector files. The ICE for extreme high vs. low combined racial and income polarization at the census tract level was constructed using 2021 American Community Survey data. We used multilevel, multinomial logistic regression models to examine the odds of 1-3 and 4 missed outpatient appointments (Ref.=0) over 2 years post index date separately by historical HOLC

grade (A "best" to D "hazardous") and ICE quintile (most deprived (Q1) to most privileged (Q5) area for combined race and income), adjusting for demographics, insurance, and comorbidities.

Results: Among 5,598 individuals with rheumatic conditions, 1,935 had SLE/connective tissue disease, 2,800 inflammatory arthritis, 1,152 crystalline arthritis, and 3,009 osteoarthritis. The mean age was 63 (SD 16) years, 70% were female, 12% Black, and 4% Hispanic **(Table 1)**. 23% lived in the most historically redlined areas **(Figure 1)**, and 33% in areas with the most extreme present-day racialized economic deprivation (ICE Q1). Among 1,780 individuals living in ICE Q1 areas, 96% were in areas that were historically deemed hazardous (HOLC D) or declining (HOLC C). 1,915 (34%) individuals had 0 missed appointments, 1,783 (32%) had 1-3, and 1,900 (34%) had 4. Accounting for individual-level factors, patients living in the most historically redlined areas vs. the least had 1.79 times greater odds (95% CI 1.22-2.62) of 4 missed appointments. Individuals living in areas with the greatest concentration of lowest-income Black households vs. highest-income White households had 2.27 times greater odds (95% CI 1.77-2.90) of 4 missed appointments **(Table 2)**.

Conclusion: Individuals with rheumatic conditions living in historically redlined areas and current areas with highly concentrated racialized economic deprivation had significantly greater odds of repeated missed appointments. Legacies of residential segregation persist and contribute to rheumatic disease disparities. Policy interventions that dismantle structural racism are needed to address inequities in consistent access to care for patients with rheumatic conditions.

Disclosure: S. Yang: None; **L. Santacroce**: None; **C. Feldman**: BMS Foundation, 5, Curio Bioscience, 12, My husband is one of the founders and will receive equity (but has not received anything to date)., OM1, Inc., 2, Pfizer, 5.

Abstract Number: 1020

An Increase in Safety Outcome Trials and the Issue of Informed Consent

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
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Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The randomized controlled trial (RCT remains a most important research tool and a necessary document for drug licensing. Informed consent is an integral component of this tool. Its exact wording is not currently in the public domain as we and others had previously voiced (1, 2). Such transparency is important not only from the point of maintaining the public trust but also for an organized skepticism, an essential element of scientific inquiry (3). Moreover,

	1990-1991 (n=309)	2019-2020 (n=581)	OR; 95% CI
Total number of RCTs	309	581	
A trial	284 (91.9%)	501 (86.2%)	0.6; 0.3-1.0
B trial	9 (2.9%)	39 (6.7%)	2.4; 1.1-5.0
Non-A trial*	25 (8.1%)	80 (13.8%)	2.0; 1.1-2.1
ICU trial	12 (3.8%)	52 (8.9%)	2.4; 1.3-4.6

* B + C trials

we had also indicated that this transparency was even more important in safety outcome trials (SOTs) (4). We have the impression that such SOTs are becoming more frequent and, in some, the outcome measure can be as severe as stroke or death. We aimed to tabulate the temporal frequency of RCTs with the primary outcome of primarily safety versus primarily efficacy, in 4 mainline general medicine journals.

Methods: RCTs published in 1990-1991 vs 2019-2020 in NEJM, JAMA, LANCET and BMJ were surveyed by 2 independent reviewers (AO, SNE). Phase 1-2 RCTs, post-hoc analyses of RCTs and RCTs reporting long term follow-up data were excluded. RCTs with an undisputable study aim and a primary endpoint of efficacy with no appreciable risk of harm to the patients were defined as an 'A trial'. Those trials in which we unanimously considered the presence of serious harm to the enrolled patients were defined as a 'B trial'. The trials that we could not unanimously decide whether to designate as an A or B, were called a 'C trial'. Discrepancies were resolved after discussion with HY and if there was no consensus, the trial was designated as 'non-A'. We compared the frequencies of the types of RCTs published in 1990-1991 vs 2019-2020. Other salient features of these RCTs were also tabulated. Of these, only data related to the intensive care unit (ICU) settings are presented in this abstract.

Results: There were 309 RCTs published in 1990-1991 and 600 RCTs published in 2019-2020. 19 RCTs on COVID-19 infection were excluded for fair comparisons. As seen in the Table there was a significant increase in the number SOTs in the later years. Moreover, the number of ICU trials, a setting in which obtaining informed consents can often be problematic, evento the degree of being *post-hoc*, were significantly increased.

Conclusion: There is a significant increase in the number of SOTs. Moreover, more RCTs are conducted in the ICUs. We re-emphasize that the informed consents of all RCTs, particularly those related to the SOTs should be in the public domain. We strongly consider that such action is necessary a. to continue receiving the necessary public trust for scientific inquiry and b. for adequately addressing the organized skepticism of our peers.

References

1. Yazici Y, Yazici H. Informed consent: time for more transparency. Arthritis Res Ther 2010;12: 121.
2. Kotz D, et al. Details about informed consent procedures of RCTs should be reported transparently. J Clin Epidemiol 2019;109: 133-5.
3. Merton, et al. Science and technology in a democratic order. J Legal and Political Sociology 1942; 1:115–26.
4. Ozdede A, Yazıcı H. Cardiovascular and Cancer Risk with Tofacitinib in Rheumatoid Arthritis. NEJM 2022; 386:1766.

Disclosure: A. Ozdede: None; **S. Esatoglu**: None; **H. Yazici**: None.

Abstract Number: 1021

Racial Disparities Between Black and White Patients in Joint Replacement Surgery: A Systematic Review

Max Krall[1], Samuel Good[1], Collin Brantner[2], Diyu Pearce-Fisher[2], Susan Goodman[2], Michael Parks[2], Peter Sculco[2], Cynthia Kahlenberg[2], Ajay Premkumar[2], Michelle Demetres[3] and John FitzGerald[1], [1]University of California Los Angeles, Los Angeles, CA, [2]Hospital for Special Surgery, New York, NY, [3]Weill Cornell Medicine, New York, NY

SESSION INFORMATION
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Background/Purpose: Despite the documented efficacy of joint replacement surgery (JRS) for the management of refractory hip or knee osteoarthritis (OA), multiple studies have documented lower rates of JRS among Black patients with refractory hip or knee OA. The purpose of this research is to investigate how differences in patient characteristics, cultural characteristics, outcomes after joint replacement surgery (JRS), and structural barriers between Black and White patients may affect the decision to undergo JRS and how those decisions contribute to differences in utilization in JRS.

Methods: Original searches ran on April 8, 2019, April 7, 2020 and updated October 11, 2022 in the following databases: Ovid MEDLINE (ALL - 1946 to Present); Ovid EMBASE (1974 to present); and The Cochrane Library (Wiley). Our population of interest was black patients with hip and/or knee OA, our comparator was white patients with hip and/or knee OA, and our primary outcome was disparities in decisions regarding JRS. We registered the protocol under the PROSPERO international

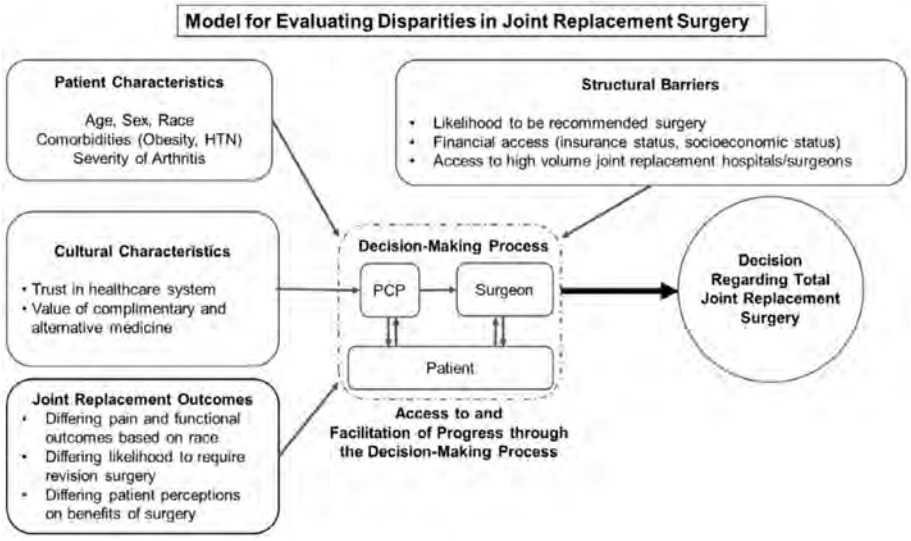

Figure 1: model for evaluating disparities in joint replacement surgery.

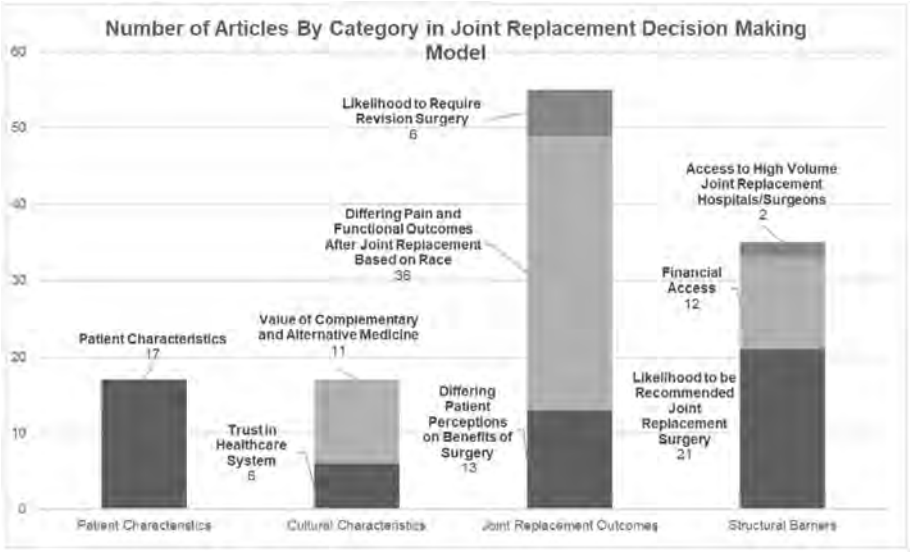

Figure 2: number of articles by category in joint replacement decision making model.

register and followed the Preferred Reporting Items of Systematic reviews and Meta-Analyses (PRISMA) guidelines. We included any articles which fit within our model (Figure 1).

Results: Searches across the chosen databases retrieved 21,390 results, 14,252 after results after de-duplication, 351 pulled for full text, and 96 selected for inclusion in this review. We then categorized these articles using our conceptual model (Figure 1): 17 in patient characteristics, 17 in cultural characteristics, 55 in joint replacement outcomes and 35 in structural barriers. We further subclassified articles within each category, as outlined in Figure 2.

Relative to white patients, Black patients had higher levels of pain catastrophizing, disability, lower levels of physical function, longer length of stay post total knee arthroplasty (TKA) and total hip arthroplasty (THA), increased ED visits post THA and TKA, decreased proportions of JRS performed as outpatients, higher rates of discharge to post-acute care facilities, and higher risk of revision after TKA. In certain analyses, the effect of race was shown to be mediated by socioeconomic disadvantage and comorbidity burden.

Conclusion: Preliminary review of the data finds that Black patients undergo JRS at lower rates than White patients. While some of this difference can be explained by lower preference for JRS vs. other arthritis treatments among Black patients, there are significant structural, financial, provider and patient factors that contribute to this difference. Some of these factors could be targeted for intervention to improve access to JRS for Black patients. The articles included for review primarily investigated differences in joint replacement outcomes and structural barriers, with less research studying baseline patient and cultural characteristics.

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Abstract Number: 1022

Lower Rates of Statin Therapy Initiation in Dermatomyositis/ Polymyositis vs. Rheumatoid Arthritis Patients with Hyperlipidemia: A Multicenter USA-Based Study (2018-2023)

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
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Background/Purpose: Despite the proven cardioprotective benefits of statin therapy in RA, concern for statin-associated muscle symptoms (SAMS) might deter clinicians from prescribing them to DM/PM patients with Hyperlipidemia (HLD), particularly those with disease-derived myopathy. This analysis aims to quantify and compare the initiation rates of statin therapy in patients with RA-HLD and DM/PM-HLD, with a focus on whether a diagnosis of DM/PM leads to the underutilization of these drugs.

Methods: Utilizing the TriNetX Research Network, we analyzed de-identified electronic health records from U.S.-based entities over the last five years. Inclusion criteria required the HLD diagnosis to follow the initial RA or DM/PM diagnosis by one day to five years. All patients included were on immunosuppressive medications, and we excluded patients with a second autoimmune disease diagnosis or on treatment with lipid-lowering medications other than statins. The detection of NormRx code for HMG CoA reductase inhibitors identified statin initiation. The analysis considered the HLD diagnosis (Index Event) point following RA or DM/PM diagnosis and the succeeding one month to five years (Time Window). Propensity score matching was employed for age, race, sex, ethnicity, cardiovascular risk factors, and cardiovascular diseases. TriNetX

	Unadjusted Baseline Characteristics				Adjusted Baseline Characteristics			
	RA-HLD (n= 16,590)	DM/PM-HLD (n= 576)	p value*	Std diff.**	RA-HLD (n=573)	DM/PM-HLD (n=573)	P value*	Std diff.**
Age at Index Mean ± SD	62.1 ± 12.7	58.4 ± 13.7	<0.0001	0.001	59.1 ± 13.9	58.5 ± 13.7	0.427	0.047
			Sex					
Female	12,473 (75.32%)	409 (70.96%)	0.017	< 0.0001	407 (71.03%)	408 (71.20%)	0.324	0.045
Male	4,108 (24.68%)	167 (29.04%)	0.017	0.257	166 (28.97%)	165 (28.80%)	0.948	0.004
			Race					
White	11,966 (72.49%)	369 (63.80%)	< 0.0001	0.990	385 (67.19%)	366 (63.88%)	0.263	0.066
Black	2,044 (12.32%)	101 (17.50%)	0.001	0.607	91 (15.881%)	100 (17.34%)	0.429	0.047
Asian	1376 (7.21%)	32 (5.50%)	< 0.0001	0.055	37 (6.457%)	30 (5.30%)	0.378	0.0521
American Indian	75 (0.38%)	10 (1.70%)	< 0.0001	0.003	3 (0%)	10 (1.70%)	0.001	0.189
Native Hawaiian	19 (0.15%)	0(0%)	0.416	0.001	0(0%)	0(0%)		
Unknown	2,063 (12.45%)	74 (13.86%)	0.763	0.309	60 (10.471%)	73 (12.69%)	0.198	0.076
	Cardiovascular Risk Factors and Cardiovascular disease							
	Unadjusted Risk Ratio				Adjusted Risk Ratio			
Hypertension	9,609 (58.26%)	296 (51.78%)	0.001	0.136	304 (53.05%)	296 (51.66%)	0.636	0.028
Diabetes Mellitus	3,464 (21.00%)	169 (29.39%)	< 0.0001	0.194	161 28.09%)	168(29.32%)	0.648	0.027
Smoking	2,349 (14.24%)	35 (6.09%)	< 0.0001	0.272	28 (4.88%)	35 (6.11%)	0.364	0.054
CAD	2,251 (13.65%)	69 (12%)	0.257	0.049	62 (10.82%)	69 (12.04%)	0.516	0.038
Heart Failure	1,485 (9.00%)	59 (10.26%)	0.302	0.042	48 (8.37%)	57 (9.95%)	0.357	0.055
Myocardial Infarction	604 (3.66%)	21 (3.65%)	0.990	0.001	27 (4.71%)	20 (3.49%)	0.297	0.062
Stroke	613 (3.72%)	19 (3.30%)	0.607	0.022	10 (1.74%)	19 (3.31%)	0.091	0.100
PVD	664 (4.03%)	14 (2.44%)	0.055	0.090	10 (1.74%)	14 (2.44%)	0.469	0.049
CKD	1,624 (9.85%)	35 (6.09%)	0.003	0.139	23 (4.01%)	35 (6.10%)	0.106	0.096
Fatty Liver	758 (4.59%)	43 (7.48%)	0.001	0.121	35 (6.80%)	43 (7.50%)	0.647	0.027
Liver Cirrhosis	207 (1.25%)	10 (1.74%)	0.309	0.039	10 (1.74%)	10 (1.74%)	1.000	< 0.0001

* p is significant if <0.05
** If the standard mean difference was less than 0.1, it means the groups were well matched

Baseline characteristics of RA-HLD and DM/PM-HLD before and propensity score matching

Unadjusted Risk Ratio				Adjusted Risk Ratio			
RA-HLD (n=10,431)	DM/DM-HLD (n=419)	p value*	CI	RA-HLD (n=387)	DM/DM-HLD (n=414)	p value*	CI
2,15 (20.62%)	52 (12.41%)	< 0.0001	4.96%,11.46%	76 (19.69%)	50 (12.08%)	0.003	2.51%,12.61%

* p is significant if <0.05

Statin initiation following HLD diagnosis among RA-HLD and DM/DM-HLD

Statin	RA-HLD	DM/PM-HLD	p value*	CI
Atorvastatin	1,665/12,494 (13.33%)	41/479 (8.56%)	0.002	2.20%,7.34%
Pravastatin	246/15,918 (1.55%)	10/564 (1.77%)	0.668	-1.33%,0.88%
Rosuvastatin	766/15,537 (4.93%)	23/535 (4.30%)	0.507	-1.12%,2.38%
Lovastatin	15/16,439 (0.091%)	0/575 (0%)	0.469	0.05%,0.14%
Simvastatin	135/15,702 (0.86%)	0/557 (0%)	0.028	0.72%,1.00%
Fluvastatin	10/16,586 (0.6%)	10/576 (1.736%)	< 0.0001	-2.74%,-0.61%
Pitavastatin	10/16,564 (0.6%)	0/575 (0%)	0.556	0.02%,0.10%

* p is significant if <0.05

Distribution of statin NormRX codes among RA-HLD and DM/PM-HLD cohorts

software aided in cohort matching and statistical computations. The measure of association was the Risk Ratio of statin initiation post the Index Event. A confidence interval of 95% was used, with a significance level of $p < 0.05$ (2-sided).

Results: The study included 16,590 RA-HLD and 576 DM/PM-HLD patients from 2018-2023, with average ages at HLD diagnosis being 62 (RA-HLD) and 58 (DM/PM-HLD). Both groups were predominately female and of White race (75% RA-HLD and 71% DM/PM-HLD), with a higher proportion of Black and Asian patients in the DM/PM-HLD cohort (Table 1). Statin initiation therapy was significantly higher among the RA-HLD cohort (20.6%) compared to the DM/PM-HLD cohort (12.4%) [CI 4.96%,11.46%, $p < 0.0001$], excluding those already on statin therapy. This trend persisted even with propensity score matching, with initiation rates of 19.6% for the RA-HLD groups and 12%, for the DM/PM-HLD groups [CI 2.51%, 12.61%, p 0.003] (Table 2). Regarding specific statin therapy, Atorvastatin was more commonly detected in the RA-HLD group (13% vs 8.5%), while Fluvastatin was more prevalent in the DM/PM-HLD cohort (1.73% vs 0.6%). Notably, Simvastatin nor Pitavastatin were not detected to DM/PM-HLD patients, whereas rates of Pravastatin, Rosuvastatin, and Lovastatin were similar among both groups (Table 3).

Conclusion: Despite the inherent limitations of an electronic health records-based database this study shows a concerning signal of disparity in statin initiation rates in DM/PM-HLD compared to RA-HLD patients. These results emphasize the urgent need for improved cardiovascular disease risk assessment and the development of guidelines for targeting DM/PM-HLD patients. Future research should explore factors contributing to this under-treatment and evaluate the potential risks and benefits of utilizing statins in this unique patient population.

Disclosure: J. Fares: None; **r. Summer**: None; **G. Loizidis**: None.

Abstract Number: 1023

Characterization of Phenotypic Differences in IgG4-Related Disease Across the Sexes

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Background/Purpose: IgG4-related disease (IgG4-RD) is a multi-organ fibroinflammatory disease with an autoimmune basis that can affect essentially any organ. Differences in phenotypic expression between males and females have been observed in case series features of individual organ involvement. We aimed to characterize sex differences in IgG4-RD using baseline data from the Massachusetts General Hospital (MGH) IgG4-RD cohort.

Methods: Subjects were recruited between 2008 and 2023 and classified by ACR/EULAR Classification Criteria. Age at diagnosis, disease activity, treatment status, organ involvement, pre-treatment laboratory values, and blood plasmablast concentrations were collected at baseline. Active disease was defined as IgG4-RD-associated inflammation in at least one organ, such that the IgG4-RD Responder Index score was > 0. Laboratory values are reported only on patients who had active IgG4-RD and were untreated at baseline. The study was approved by the MassGeneral Brigham IRB.

Results: Of the 564 participants enrolled in the MGH Registry for IgG4-RD, 328 fulfilled ACR/EULAR Classification Criteria and were included. There was a strong male predominance: 226 males (69%) versus 102 (31%) females [**Table 1**]. This M:F ratio of 2.2:1.0 contrasts markedly with both that of the general population (1:1) ($P < 0.001$) and our general clinic population (0.4:1.0) ($P < 0.001$). Male patients were five years older on average at the time of diagnosis (61.6 vs 56.6; $P < 0.01$) and disproportionately more likely to have involvement of the pancreas, kidneys, lymph node, aorta, large blood vessels, coronary arteries, and retroperitoneum. Females had higher involvement in the lacrimal and submandibular glands than males (for all organ involvement comparisons, $P < 0.05$) [**Figure 1**]. We examined laboratory values in 127 (39%) subjects who had active IgG4-RD and were untreated at baseline. Males were more likely to be serologically active at baseline as defined by serum IgG4, IgG1, and IgE concentrations. The mean serum IgG4 concentration in males was 620 mg/dl (±684) versus 412 mg/dl (±543) for females ($P = 0.095$). Forty-seven percent of males had serum IgG4 concentrations 5 times the upper limit of normal (ULN), compared with 29% of the female subjects. Male subjects also had higher mean concentrations of IgE and IgG1 [**Table 1**]. Mean serum lipase values were lower among the male subjects ($P = 0.020$). A greater degree of plasmablast expansion was observed in males [**Figure 2**].

Conclusion: In its predilection for affecting males more often than females, IgG4-RD bears a striking contrast to most other forms of autoimmune disease, which typically have strong female predilections. Male patients with IgG4-RD also appear more likely than females to have multi-organ involvement, to have disease affecting major organs, and to be serologically active as defined by immunoglobulin concentrations in the blood. The lower lipase levels observed in males are consistent with greater degrees of pancreatic damage. Further study is required to understand these sex differences.

Table 1. Demographics and Baseline Laboratory Values, By Sex

	Male	Female	P-Value
Demographics			
Subjects - N (%)	226 (69%)	102 (31%)	<0.001
Age at Diagnosis Avg (SD)	61.6 (13.3)	56.6 (15.1)	<0.01
Race (%)			
White	73%	73%	
Asian	16%	12%	
Black or African American	4%	4%	
American Indian/ Alaskan Native	0%	1%	
Unknown	4%	7%	
Other	4%	3%	
Ethnicity			
Hispanic or Latino	12%	16%	
Not Hispanic or Latino	83%	73%	
Unknown/Not Reported	5%	12%	
Laboratory Values [mean (SD)]			
IgG4 (F: N=24, M: N=70)	620 (684)	412 (543)	0.095
Percentage in normal range (4-86 mg/dL)	14%	25%	
Percentage > ULN but < 2x ULN	16%	25%	
Percentage 2-5x ULN	23%	21%	
Percentage >5x ULN	47%	29%	
IgG1 (F: n=24, M: n=70)	890 (529)	828 (820)	
IgE (F: n=30, M: n=73)	409 (625)	318 (520)	
C3 (F: n=22, M: n=62)	119 (43)	130 (37)	
% C3 hypocomplementemic	15	14	
C4 (F: n=21, M: n=59)	24 (11)	25 (8)	
% C4 hypocomplementemic	12	10	
Eosinophils (0-8%) (F: n=31, M: n=81)	4.6 (3.9)	4.8 (5.0)	
Lipase (F: n=19, M: n=56)	37 (46)	72 (96)	0.020

Abbreviations:
SD = standard deviation
ULN = upper limit of normal
NS = not significant

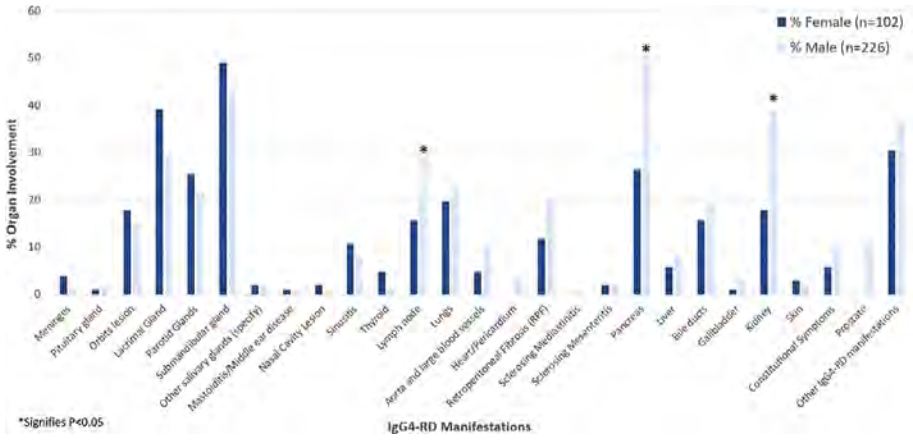

Figure 1. Organ Involvement in female and male patients with IgG4-RD

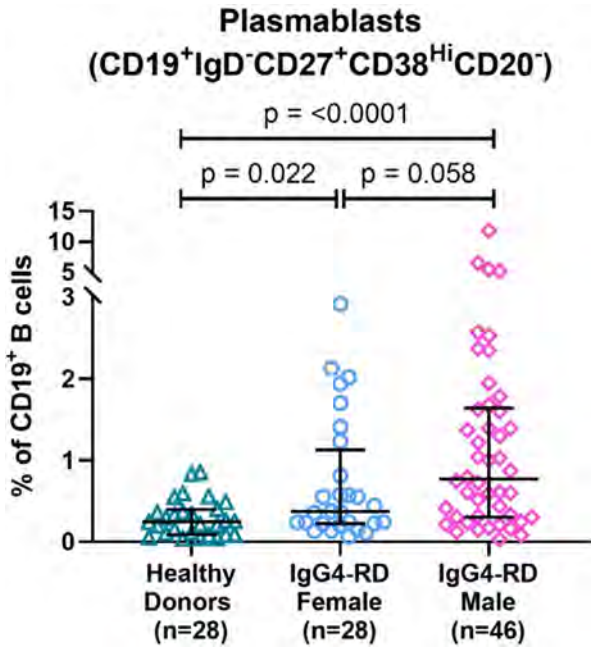

Figure 2. Plasmablast quantitation plot of females and males with active and untreated IgG4-RD

Disclosure: G. McMahon: None; **I. Jha**: None; **A. McMahon**: None; **A. Fernandes**: None; **Z. Wallace**: BioCryst, 2, Bristol-Myers Squibb(BMS), 5, Horizon, 1, 2, 5, MedPace, 2, Novartis, 1, PPD, 2, Sanofi, 1, 5, Shionogi, 1, Visterra, 1, 2, Zenas, 1, 2; **G. Katz**: None; **C. Perugino**: Horizon Therapeutics, 2; **J. Stone**: Abvie, 2, Amgen, 1, 2, Argenx, 2, Aztrazeneca, 2, Bristol Myers Squibb, 2, 5, Celgene, 2, Chemocentryx, 2, Chugai, 2, GSK, 2, Horizon Therapeutics, 1, 2, 5, InflaRx, 2, IQVIA, 1, 2, Kyverna, 2, Mirabio, 2, NIH, 5, Novartis, 2, PPD, 2, Prometheus, 2, Q32, 2, Regeneron, 2, Roche-Genentech, 2, Roivant, 2, Sanofi, 2, 5, Spruce Biosciences, 2, Star Therapeutics, 2, Steritas, 12, Chair, Scientific Advisory Board (no fiduciary responsibilities), ZenasBio, 2.

Abstract Number: 1024

Relationship Between Race and Ethnicity, Time to Diagnosis, and Disease Activity for Children with Juvenile Idiopathic Arthritis in the CARRA Registry

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Healthcare Disparities in Rheumatology Poster II: Socioeconomic Determinants
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Compared to non-Hispanic White children, Black children diagnosed with juvenile idiopathic arthritis (JIA) have more severe disease at diagnosis and worse outcomes, such as long-term disability. We aimed to determine if time to JIA diagnosis was longer in Black and Hispanic/Latinx populations and helped explain higher disease activity scores in minoritized populations.

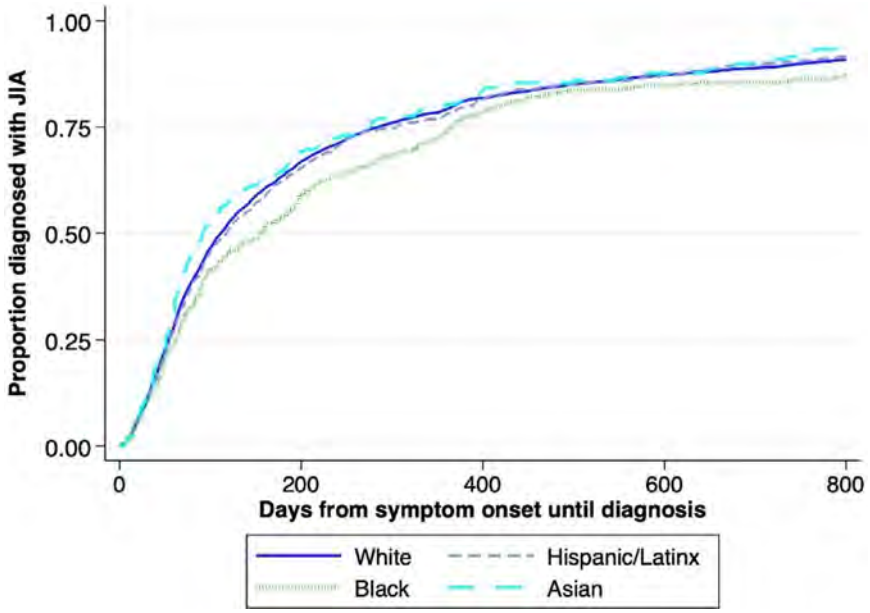

Figure. Time to JIA diagnosis in the CARRA Registry by race and ethnicity. Kaplan-Meier curves were generated to represent days from symptom onset to JIA diagnosis among US participants of the CARRA Registry, stratified by Non-Hispanic White children (blue), Hispanic/Latinx children (light purple dash), Non-Hispanic Black children (green dots), and Non-Hispanic Asian (cyan dash and dots).

Table 1. Select characteristics of the study population. NH, Non-Hispanic; IQR, interquartile range; JIA, Juvenile Idiopathic Arthritis; RF, rheumatoid factor; RUCA, Rural-Urban Commuting Area. 1 P-values from chi-square testing unless indicated; 2 P-values from Wilcoxon rank-sum testing; 3 Highest level of education completed by parent/guardian; 4 Oligoarticular JIA or RF- polyarticular arthritis; 5 Enthesitis-related arthritis (ERA) or psoriatic arthritis (PsA).

Characteristic	NH White (n = 5,308)	Hispanic/ Latinx (n = 763)	P-value[1]	NH Black (n = 315)	P-value[1]	NH Asian (n = 172)	P-value[1]
Female gender, %	70%	67%	0.07	67%	0.28	70%	0.98
Age, median years (IQR)	7.5 (3.3, 12.3)	9.1 (4.2, 13.0)	<0.01 [2]	10.7 (6.0, 14.1)	<0.01 [2]	8.6 (3.3, 12.8)	0.41
Household income, annual gross, %							
<$25,000	6%	18%	<0.01	23%	<0.01	4%	0.40
$25,000 - $50,000	11%	18%	<0.01	19%	<0.01	11%	0.94
$50,000 - $100,000	26%	21%	<0.01	17%	<0.01	14%	<0.01
$100,000 - $150,000	20%	10%	<0.01	5%	<0.01	15%	0.13
>$150,000	17%	6%	<0.01	4%	<0.01	22%	0.06
Prefer not to answer/unknown	22%	27%	<0.01	33%	<0.01	34%	<0.01
Missing	0.5%	0.5%	0.14	0%	0.49	0%	0.61
Education[3], %							
High school equivalent or less	14%	31%	<0.01	25%	<0.01	9%	0.06
College attendance	43%	32%	<0.01	32%	<0.01	29%	<0.01
Graduate school degree	23%	13%	<0.01	11%	<0.01	39%	<0.01
Prefer not to answer	14%	17%	<0.01	20%	<0.01	20%	0.01
Missing	7%	7%	0.65	11%	<0.01	3.5%	0.08
Insurance, %							
Public insurance	21%	47%	<0.01	58%	<0.01	22%	0.78
Private insurance	74%	47%	<0.01	39%	<0.01	76%	0.45
Other/no insurance	6%	6%	0.67	3%	0.12	3%	0.14
Missing	4%	2%	0.88	2.2%	0.67	0.5%	0.21
RUCA, %							
Metropolitan	77%	77%	0.94	76%	0.80	76%	0.71
Micropolitan	8%	8%	0.91	8%	0.68	8%	0.95
Small Town	4%	4%	0.28	7%	0.03	3%	0.35
Rural	3%	3%	0.47	3%	0.92	4%	0.40
JIA type, %							
Systemic JIA	7%	9%	0.07	17%	<0.01	13%	<0.01
Polygo JIA[4]	66%	59%	<0.01	49%	<0.01	60%	0.07
RF-positive JIA	5%	16%	<0.01	19%	<0.01	11%	<0.01
Juvenile spondyloarthritis[5]	20%	15%	<0.01	12%	<0.01	13%	0.03
Undifferentiated JIA	2%	2%	0.64	4%	0.21	4%	0.35

Table 2. Comparison of times to diagnosis between racial and ethnic groups. aHR, adjusted hazard ratio; CI, confidence interval; IQR, interquartile range; uHR, unadjusted hazard ratio. 1 p-values from Wilcoxon rank-sum testing; 2 Cox proportional hazards model adjusted for age, sex, household income, highest educational level attained in household, insurance type, JIA type, calendar year of diagnosis, diagnosis of uveitis, Area Deprivation Index quintile (measure of local socioeconomic disadvantage), local population density, and time from date of JIA diagnosis to date of enrollment in the CARRA Registry. Missing data were imputed using multiple imputation.

Race/Ethnicity	Days to JIA diagnosis, median (IQR)	p-value[1]	uHR (95% CI)	aHR[2] (95% CI)	p-value
Non-Hispanic White (ref)	112 (54, 286)				
Hispanic/Latinx	119 (56, 305)	0.46	1.01 (0.93, 1.09)	0.99 (0.92, 1.08)	0.88
Non-Hispanic Black	158 (63, 365)	0.006	0.87 (0.77, 0.97)	0.87 (0.77, 0.98)	0.02
Non-Hispanic Asian	91.5 (51, 266)	0.21	1.07 (0.92, 1.25)	1.04 (0.89, 1.22)	0.59

Methods: We performed a retrospective cohort study using the CARRA registry, which contains sociodemographic, clinical, and patient/caregiver-reported data on children with pediatric-onset rheumatic diseases across the US and Canada. Eligible participants needed to have JIA, live in the US, and have complete data on self-reported race, ethnicity, and dates of symptom onset and diagnosis. We compared time to diagnosis among children in different racial and ethnic groups using Wilcoxon rank-sum testing, Kaplan-Meier curves, and multivariable Cox regression adjusted for age, sex, insurance type, self-reported household income and parental education, JIA type, calendar year of diagnosis, presence of uveitis, and local area-linked urban-rural status and socioeconomic disadvantage (Area Deprivation Index). To examine whether time to diagnosis mediated the relationship between race/ethnicity and disease activity at enrollment, we used a product of coefficients model, adjusting for the above covariates and time since JIA diagnosis, with bootstrapping to create bias-corrected 95% confidence intervals (CIs). Disease activity was assessed by Clinical Juvenile Arthritis Disease Activity Score 10 (cJADAS10). Missing data was imputed in 10 datasets using multiple imputation by chained equations.

Results: Of 9,037 US Registry participants with JIA, 6,558 (73%) were included. Groups differed in baseline characteristics, including age, income, education, insurance status, and JIA type (Table 1). Compared to non-Hispanic White participants, non-Hispanic Black participants had higher median times to JIA diagnosis (156 days [interquartile range (IQR) 62, 365] vs. 112 days [IQR 54, 286], p=0.006) while times to diagnosis among other racial/ethnic groups were similar (Figure, Table 2). In adjusted models, non-Hispanic Black participants had a significantly longer time to diagnosis than non-Hispanic White participants (aHR 0.87, 95% CI 0.77, 0.98) (Table 2). Time to diagnosis partially mediated the association between Black race and cJADAS10 at enrollment (indirect coefficient = 0.08, bias-corrected 95% CI 0.03, 0.17), but this effect was considerably smaller than the direct relationship between Black race and cJADAS10 (direct coefficient = 1.67, 95% CI 1.50, 1.84).

Conclusion: In a large US cohort, Black children with JIA were more likely to experience delays in diagnosis independent of clinical, geographic, and socioeconomic factors. Higher disease activity scores in Black children at enrollment were modestly explained by longer times from symptom onset to diagnosis, but other factors appeared to contribute more substantially to these disparities. Future research should examine the role of systemic racism and other factors driving racial disparities in JIA diagnosis and disease activity as well as ways to address these factors.

Disclosure: S. McGuire: None; **T. Atanassova**: None; **J. Madej**: None; **M. Jimenez**: None; **D. Horton**: Childhood Arthritis and Rheumatology Research Alliance, 1, 5, 12, Salary support for serving as JIA Committee Vice Chair and Steering Committee Member, Danisco USA Inc., 5; **f. the CARRA TMJ Arthritis Workgroup**: None.

Abstract Number: 1025

Embedding Treat to Target Principles in Rheumatoid Arthritis Patient Education in Routine Care of Ethnic Minority Patients

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Healthcare Disparities in Rheumatology Poster II: Socioeconomic Determinants

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: A successful treat to target (T2T) strategy in ethnic minority (EM) patients with rheumatoid arthritis (RA) could improve patient outcomes and help reduce healthcare disparity but requires patient engagement. In one prospective EM RA database, a low rate of meaningful clinical response was due in part to decreased biologic DMARD (bDMARD) utilization. Other known contributors include distrust of the medical system and medication hesitancy embedded in cultural norms. Education is a critical factor in encouraging self-active participation, medication adherence, and commitment to healthcare goals, but often requires lengthy one-on-one sessions with a provider. The aim of this study was to observe the effect of a Rheumatology Care Coordinator (RCC)-led education program on patient outcomes before and after a targeted education program focused on the T2T paradigm in RA.

Methods: Participants with RA and moderate-to-high disease activity (CDAI >10, RAPID3 >6) were enrolled. Each participant completed 5 T2T-focused education sessions scheduled with routine rheumatology office visits and facilitated by a RCC who completed 6 weeks of training on RA patient education. Translation services were utilized for non-English speaking participants. Demographic and clinical characteristics were recorded, as well as race and ethnicity of providers. Disease activity measures (CDAI and RAPID3), the Arthritis Community Research Evaluation Unit (ACREU) Patient Knowledge Questionnaire (PKQ), Compliance questionnaire and Trust in Physician Scale scores were recorded at Visit 1 and Visit 5. Meaningful clinical reduction in RAPID3 (-3.8) and CDAI (- 6) at Visit 5 was calculated. Descriptive statistics were used for demographic and clinical characteristics. Student's t-test was used to assess RA-related knowledge acquisition, change in compliance, and change in disease activity.

Results: Over a mean study enrollment period of 10 (±3.4) months, there were 29 participants of mean age 57.52 ± 13.81 years, predominantly of African descent and female sex (83%) (Table 1). Most had at least high school education, one with a post graduate degree. The 4 participating providers were non-White. There was a high level of physician trust, which remained stable at the end of the study. There was no significant difference in ACREU scores ($t = -0.07$, p-value = 0.94), and although compliance scores improved, the difference was not significant ($t = -1.94$, p-value = 0.06). A significant decrease in RAPID3 ($t = 2.70$, p-value < 0.05, mean difference -3.98) and CDAI ($t = 4.36$, p-value < 0.05, mean difference -8.60) was seen, with meaningful clinical reduction in disease activity in 48% and 58% of patients, respectively. Almost 50% of participants had a change in DMARD, with 5 patients starting a new biologic therapy.

Conclusion: In a small urban cohort of predominantly African American patients with high school education, a successful T2T regimen was independent of educational level and targeted patient education. Achieving meaningful reduction in disease activity can be achieved in a setting where high physician trust enables shared decisions. The role of patient-provider race and ethnicity in achieving disease remission needs further evaluation.

Table 1. Clinical Characteristics of Participants in the Rheumatoid Arthritis Treat to Target Education Program		
N		29
Age [mean (SD)]		57.52 (13.82)
Female [N(%)]		24 (82.7)
Race [N(%)]		
	African American	22 (75.9)
	Asian	1 (3.4)
	White	6 (20.7)
Ethnicity [N(%)]		
	Hispanic	5 (17.2)
	Non-Hispanic	24 (82.8)
Tobacco [N(%)]		
	Yes	12 (41.4)
	No	17 (58.6)
Education [N(%)]		
	< High School	9 (31.0)
	High School	12 (41.4)
	> High School	8 (27.5)
Seropositive [N(%)]		
	Double	18 (62.1)
	Yes	5 (17.2)
	No	6 (20.7)
Disease Activity [mean (SD)]		
	Baseline Rapid3	15.19 (5.96)
	Baseline CDAI	19:08 (9.89)
Baseline *csDMARD use [N(%)]		26 (89.7)
Baseline *bDMARD use [N(%)]		12 (41.4)
*DMARD change [N(%)]		14 (48.3)
Baseline **ACREU_PKQ [mean (SD)]		14.97 (4.52)
Baseline **Compliance Score [mean (SD)]		15.17 (3.32)
Baseline **Physician Trust Score [mean (SD)]		47.90 (7.12)

*Disease modifying antirheumatic drug (DMARD), conventional synthetic DMARD (csDMARD), Biologic DMARD (bDMARD) **The Arthritis Community Research Evaluation Unit Patient Knowledge Questionnaire (ACREU_PKQ) is scored out of 31. Compliance questionnaire is scored out of 20, and the Trust in Physician Scale is scored out of 55.

Disclosure: S. Dowell: Aurinia, 6, Bristol-Myers Squibb(BMS), 5, Janssen, 1; **M. Quinones**: Bristol-Myers Squibb(BMS), 5, CVS Health - CVS Caremark, 2, Pfizer, 5; **T. Jamshidi**: None; **I. Jileaeva**: None; **O. Kadiri**: None; **G. Kerr**: AstraZeneca, 2, Aurinia, 6, Horizon, 2, Janssen, 2, Pfizer, 1, Sanofi, 2.

Abstract Number: 1026

Patients' Barriers to Total Joint Arthroplasty: Associations with the Orthopedic Consultation

Insa Mannstadt[1], J. Alex Gibbons[2], Troy Amen[1], Mangala Rajan[3], Sarah Young[4], Michael Parks[1], Mark Figgie[1], Anne Bass[5], Linda Russell[1], Bella Mehta[5], iris Navarro-Millán[1] and Susan Goodman[1], [1]Hospital for Special Surgery, New York, NY, [2]Columbia University Vagelos College of Physicians & Surgeons, New York, NY, [3]Weill Cornell Medicine, New York, NY, [4]Binghamton University, Binghamton, NY, [5]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Healthcare Disparities in Rheumatology Poster II: Socioeconomic Determinants

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Table 1: Characteristics of cohort stratified by consultation with an orthopedist

	No orthopedic consultation (N=358)	Orthopedic consultation (N=338)	p-value*
Age (years) (mean, SD)	58.28 (10.54)	60.34 (10.71)	p<0.05
Female (n, %)	310 (86.6%)	303 (90.2%)	
Race/Ethnicity (n, %)			p<0.05
White	284 (79.3%)	272 (80.5%)	
Black	33 (9.2%)	43 (12.7%)	
Hispanic	41 (11.5%)	23 (6.8%)	
Arthritis characteristics			
VAS Pain score (0-100) (mean, SD)	58.28 (10.54)	60.34 (10.71)	p<0.05
HOOS/KOOS score (100-0) mean, SD)	66.16 (21.4)	67.07 (23.2)	
Provider history (n, %)			
Primary care physician	148 (41%)	197 (58%)	p<0.01
Rheumatologist	243 (68%)	161 (48%)	p<0.01
No one	33 (9%)	1 (0%)	p<0.01
Other	33 (9%)	24 (7%)	
Discussed TJA	112 (31%)	249 (74%)	p<0.01
Education (n, %)			
College grad or above	172 (48%)	205 (61%)	p<0.01
Some college	148 (41%)	109 (32%)	
Some HS	37 (10%)	24 (7%)	
Insurance (n, %)			
Medicare	151 (42%)	175 (52%)	p<0.05
Medicaid	73 (20%)	54 (16%)	
Private	183 (51%)	168 (50%)	
Uninsured	18 (5%)	14 (4%)	
Treatment history (n, %)			
Over the counter drugs	291 (81%)	285 (84%)	
Physical therapy	173 (48%)	261 (77%)	p<0.01
Acupuncture	47 (13%)	57 (17%)	
Braces	54 (15%)	119 (35%)	p<0.01
Joint injections	170 (47%)	250 (74%)	p<0.01
Topical salves/creams	226 (63%)	234 (69%)	
Prescription drugs	265 (74%)	266 (79%)	
None	15 (4%)	4 (1%)	p<0.05

**p-value represents the statistical significance of the differences observed in values between groups*

Background/Purpose: While racial/ethnic disparities in total joint arthroplasty (TJA) utilization are well-documented, the impact of orthopedic specialists on patients' perceptions of TJA is poorly understood. We aimed to assess the relationship between orthopedic consultation and patients' perspectives on TJA barriers.

Table 2: Odds ratios with 95% Confidence intervals of orthopedic consultation on rated importance of barriers to TJA ††

	Orthopedic Consultation Odds Ratio (OR)	
Barrier to arthroplasty	**Crude OR (95% C.I.)**	**Adjusted OR (95% C.I.)***
1. Trust in surgeon	0.97 (0.72, 1.31)	1.08 (0.77, 1.51)
2. Recovery	1.03 (0.75, 1.42)	1.17 (0.78, 1.75)
3. Cost and Insurance	0.50 (0.37, 0.69) ***	0.51 (0.36, 0.76)***
4. Outcome of surgery	0.98 (0.71, 1.35)	1.12 (0.78, 1.59)
5. Timing for surgery	0.46 (0.31, 0.68) ***	0.49 (0.31, 0.79)***

† Models adjusted for sex, age, education, HOOS KOOS score, insurance, discussion of TJA with doctor
*††Statistical significance markers . p<0.10; * p<0.05; ** p<0.01; *** p<0.001*

Methods: This multi-institutional prospective cohort study was conducted from 2/2020 to 7/2022. We surveyed patients at 2 large urban academic institutions (Hospital for Special Surgery; New York Presbyterian-Brooklyn Methodist Hospital) and 2 national arthritis cohorts (ArthritisPower; CreakyJoints Español). The electronic questionnaire was developed through thematic analysis of semi-structured interviews conducted with minority patients experiencing advanced osteoarthritis. The questionnaire assessed participants' barriers to TJA were using a 5-level Likert scale. Responses were categorized through a top-2 box analysis: "Highly important" (very or extremely important) and "Not as important" (bottom 3 levels). We evaluated differences in characteristics between those who had and those who had not consulted an orthopedist. Multiple logistic regression models were used to analyze the adjusted odds ratios (aOR) of orthopedic consultation on patients' ratings of barriers to TJA. Models controlled for patient factors, including race, age, HOOS, JR/KOOS, JR, insurance, education, and prior discussion of TJA with any doctor.

Results: 696 participants who completed the survey were included in the analysis (94% of respondents; 24% of total queried). Most were female (88%), average age 59.3 years, 77% White participants, 11% Black, and 9% Hispanic. 49% reported having had an orthopedic consultation. The questionnaire examined five TJA barriers: 1. *Trust in surgeon*, including factors like finding a qualified surgeon; 2. *Cost/insurance*, such as challenges related to co-pays and insurance coverage; 3. *Recovery concerns*, such as insufficient social support; 4. *Surgical outcome*, such as the potential need for additional TJA due to young age; and 5. *Timing of surgery*, whereby other health concerns take precedence over TJA. Participants who had consulted with an orthopedist were older ($p< 0.05$), more likely to be college graduates ($p< 0.01$), Medicare beneficiaries ($p< 0.05$), have consulted with a primary care physician ($p< 0.01$), and have attempted arthritis treatments, such as joint injections ($p< 0.01$), braces ($p< 0.01$), and physical therapy ($p< 0.01$) **(Table 1**). After adjusting for patient factors, orthopedic consultation was a significant predictor of lower barriers relating to *cost/insurance* (aOR (95% CI): 0.52 (0.36, 0.76)) and *timing of surgery* (aOR (95% CI): 0.49 (0.31, 0.79)). (**Table 2**) Patient factors, including race and insurance, did not have significant interaction with orthopedic consultation (all $p >0.05$).

Conclusion: While those with an orthopedic consultation were able to overcome *cost/insurance* and *timing* barriers to consider TJA, significant barriers persisted. Developing strategies to identify and address the TJA barriers among minority groups may help increase utilization within these groups.

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Abstract Number: 1027

Single-Payer Health Insurance May Not Mitigate Income-Based Differences in Total Hip Arthroplasty Utilization: A Transnational Analysis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

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Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Access to care varies across health systems. Countries with universal health insurance are thought to have less wealth-based health disparities, but it is unclear if this applies to total hip arthroplasty (THA) utilization and outcomes. The purpose of this study was to determine whether a single-payer healthcare system would mitigate income-based disparities in THA utilization and outcomes.

Methods: We retrospectively compared all patients undergoing THA from 1/2012 to 9/2018 in Ontario (ON), Canada and Pennsylvania (PA), United States. We obtained PA patient data from Pennsylvania Health Care Cost Containment Council and ON patient data from Ontario's Institute for Clinical Evaluative Sciences. Patient-level data were linked to Census data of median household income of the ZIP code or postal code of patients' residence. We then analyzed whether community income-based differences in THA utilization were reduced in Ontario compared to Pennsylvania due to Canada's single-payer healthcare system. We used logistic regression to examine the relative risks for lowest community income of outcomes such as rates of 1-year revision, 90-day mortality, and 90-day readmission in the two regions.

Results: Among all THAs, 13,280 patients (15.8%) and 16,850 patients (16.0%) lived in communities within the lowest income quintile in Ontario and Pennsylvania, respectively (**Table 1).** Overall THA utilization was lower in Ontario compared to Pennsylvania across income groups **(Figure 1)**. In Ontario, patients in the highest income quintile utilized THA 43.2% more than those in the lowest income quintile (12.6 vs 8.8); this difference in utilization was slightly greater than the difference in Pennsylvania, where patients in the highest income quintile utilized THA 41.7% more than patients in the lowest income quintile (21.4 vs. 15.1) ($p < 0.001$). Patients in the lowest community income quintile in Pennsylvania had a greater rate of 1-year revision, 90-day mortality, and 90-day readmission compared to patients in the lowest income quintile of Ontario. However, after adjusting for age, sex, hospital volume, and rural vs. urban hospital, the odds for patients in the lower-income group compared to the higher-income group of 1-year revision (ON: OR 1.70, 95% CI: [1.34, 2.15]. PA: 1.30 [1.12, 1.52]), 90-day mortality (ON: 1.92 [1.24, 2.98]. PA: 1.66 [1.18, 2.33]), and 90-day readmission (ON: 1.48 [1.34, 1.62]. PA: 1.43 [1.34, 1.54] were greater in Ontario compared to Pennsylvania **(Figure 2)**.

Conclusion: Income-based differences in THA utilization were greater in Ontario than in Pennsylvania. Additionally, patients in low-income communities in Ontario were at greater risk relative to higher community income patients for adverse outcomes. These findings suggest that a single-payer insurance system may not be sufficient to eliminate income-based differences in utilization and complications of THA.

Table 1: Characteristics of patients who underwent total hip arthroplasty in Ontario and Pennsylvania by community income level

	Lowest quintile community Income			Highest quintile community Income		
Variable, n (%)	**Ontario N = 13,280**	**Pennsylvania N = 16,850**	**p**	**Ontario N = 18,110**	**Pennsylvania N = 33,836**	**p**
Age, mean (SD)	68.22 ± 11.43	63.9 (11.7)	<0.001	66.05 ± 10.72	65.7 (11.0)	<0.001
Age group:						
Age <50	708 (5.3%)	1716 (10.2%)	<0.001	1,078 (6.0%)	2231 (6.59%)	0.004
Age 50-64	4,019 (30.3%)	6994 (41.5%)	<0.001	6,852 (37.8%)	13073 (38.6%)	0.074
Age >=65	8,553 (64.4%)	8140 (48.3%)	<0.001	10,180 (56.2%)	18532 (54.8%)	0.002
Sex: Female	8,160 (61.4%)	9290 (55.1%)	<0.001	9,296 (51.3%)	18100 (53.5%)	<0.001
Elixhauser index:						
0	8,048 (60.6%)	2373 (14.1%)	<0.001	12,079 (66.7%)	6309 (18.6%)	<0.001
1-4	5,204 (39.2%)	13306 (79.0%)	<0.001	6,013 (33.2%)	25918 (76.6%)	<0.001
>=5	28 (0.2%)	1171 (6.95%)	<0.001	18 (0.1%)	1609 (4.76%)	<0.001
Volume of cases (by facility and year):						
< 25 procedures	35 (0.3%)	1042 (6.18%)	<0.001	8 (0.0%)	545 (1.61%)	<0.001
25-99 procedures	1,645 (12.4%)	4462 (26.5%)	<0.001	893 (4.9%)	4131 (12.2%)	<0.001
100-199 procedures	3,731 (28.1%)	4876 (28.9%)	0.11	4,121 (22.8%)	9003 (26.6%)	<0.001
200-299 procedures	3,899 (29.4%)	2431 (14.4%)	<0.001	5,482 (30.3%)	9769 (28.9%)	0.001
>= 300 procedures	3,970 (29.9%)	4039 (24.0%)	<0.001	7,606 (42.0%)	10388 (30.7%)	<0.001
Urban / rural (based on patient ZIP codes): urban	11,381 (85.7%)	12369 (73.4%)	<0.001	17,407 (96.1%)	33761 (99.8%)	<0.001

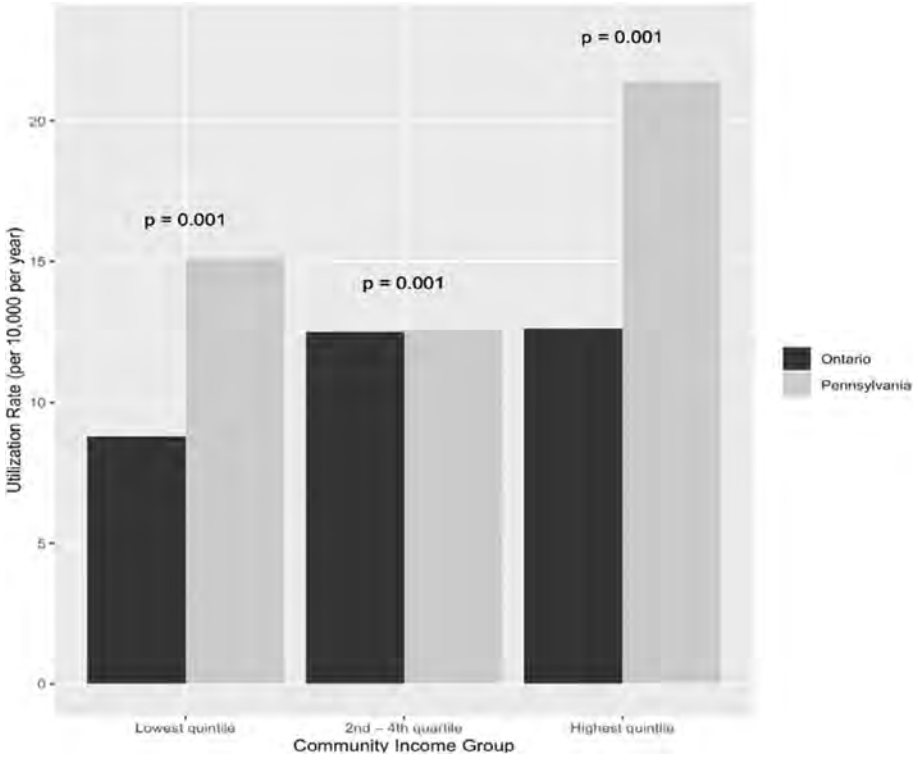

Figure 1: Utilization rate of total hip arthroplasty for patients in Ontario and Pennsylvania by community income level

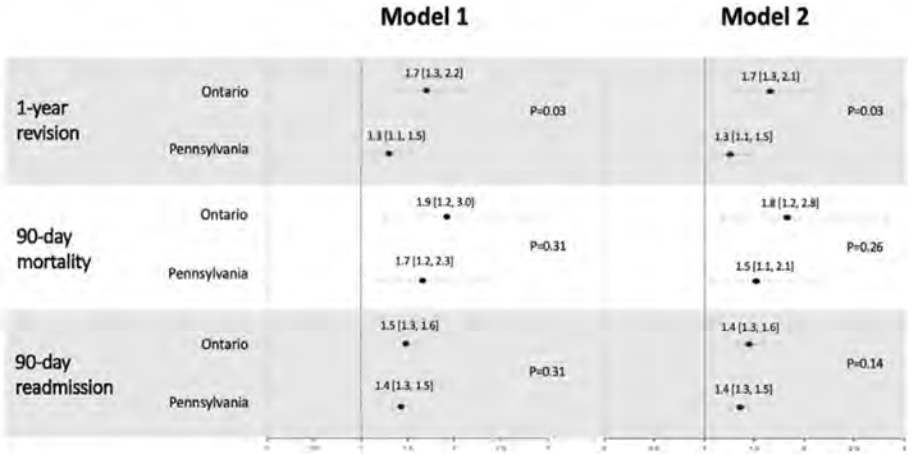

Figure 2: Adjusted odds ratios and 95% confidence intervals for risk of adverse outcomes in lowest community income group compared to highest community income group. Note: Model 1 adjusts for income group, age, sex, hospital volume, rural / urban hospital. Model 2 adjusts for income group, age, sex, hospital volume, rural / urban hospital, and Elixhauser index.

Disclosure: B. Mehta: Janssen, 1, Novartis, 5; **K. Ho**: None; **J. Gibbons**: None; **V. Ling**: None; **S. Goodman**: NIH, 5, Novartis, 5; **M. Parks**: None; **B. Ravi**: None; **F. Wang**: None; **S. Ibrahim**: None; **P. cram**: None.

Abstract Number: 1028

Barriers to Total Joint Arthroplasty for Patients Residing in High-Poverty Communities

J. Alex Gibbons[1], Insa Mannstadt[2], Troy Amen[2], Mangala Rajan[3], Sarah Young[4], Michael Parks[2], Mark Figgie[2], Anne Bass[5], Linda Russell[2], Bella Mehta[5], Iris Navarro-Millán[6] and Susan Goodman[2], [1]Columbia University Vagelos College of Physicians & Surgeons, New York, NY, [2]Hospital for Special Surgery, New York, NY, [3]Weill Cornell Medicine, New York, NY, [4]Binghamton University, Binghamton, NY, [5]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [6]Weill Cornell Medicine, Hospital for Special Surgery, New York, NY

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Healthcare Disparities in Rheumatology Poster II: Socioeconomic Determinants

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients from lower socioeconomic status (SES) backgrounds have low access to total joint arthroplasty (TJA), delays in undergoing TJA, and a higher risk of adverse outcomes compared to those from high-SES backgrounds. The specific barriers to care perceived by patients from lower-SES backgrounds are not well understood, despite the significance of addressing these barriers in reducing disparities in TJA utilization and outcomes. We aimed to assess differences in patient-reported barriers to TJA by patient community poverty level.

Methods: We developed a survey by analyzing interviews with underrepresented minority patients with symptomatic osteoarthritis regarding their concerns about TJA. The 21-question survey assessed five barriers to TJA: 1) trust in surgeon (such as finding a qualified surgeon), 2) recovery (such as lack of social support), 3) cost / insurance (such as concerns about co-

Table 1. Demographic and clinical characteristics by proportion of community residents living below the national poverty line Note: Figures represent N (%) unless stated otherwise. SD = standard deviation. HOOS, JR = Hip Disability and Osteoarthritis Outcome Score. KOOS, JR = Knee Injury and Osteoarthritis Outcome Score. VAS = visual analogue scale.

Variable, N (%)	Participants from low-poverty (<20%) communities	Participants from high-poverty (≥20%) communities
	N = 584	N = 118
Age, mean (SD)	59 (11)	59 (13)
Sex: female	511 (88%)	106 (90%)
Race / Ethnicity		
Black	65 (11%)	9 (8%)
White	461 (80%)	72 (62%)
Hispanic	29 (5%)	27 (23%)
Asian or Other	21 (4%)	8 (7%)
Education		
College grad or above	309 (53%)	62 (53%)
Some college	225 (39%)	42 (36%)
Some high school	47 (8%)	14 (12%)
Insurance		
Medicare	278 (48%)	54 (46%)
Medicaid	104 (18%)	22 (19%)
Private	289 (49%)	56 (47%)
Uninsured	25 (4%)	8 (7%)
HOOS, JR / KOOS, JR, mean (SD)	33 (13)	31 (13)
Pain VAS (0-100), mean (SD)	55 (21)	55 (23)
% of census tract living below poverty line, mean (SD)	6 (5.1)	32 (10)

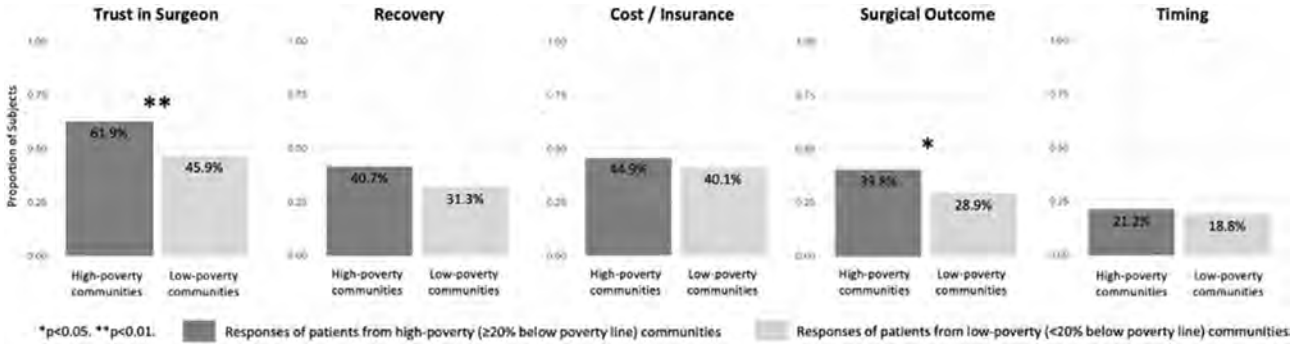

Figure 1. Proportion of participants indicating each barrier to arthroplasty as "highly important" stratified by proportion of community residents living below the national poverty line

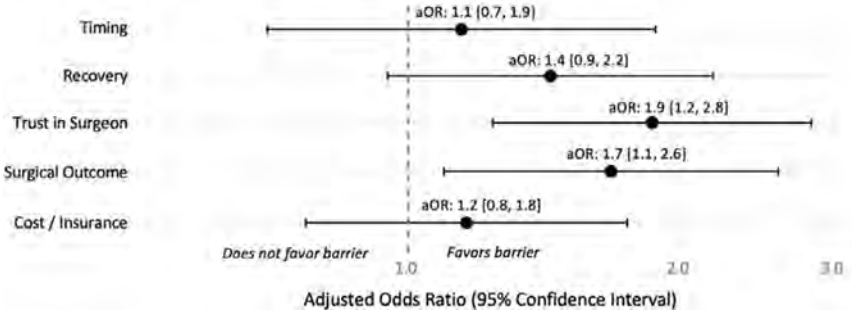

Figure 2. Adjusted odd ratios with 95% confidence intervals of participants from high-poverty communities indicating each barrier as "highly important" Note: Models adjust for age, sex, and HOOS, JR / KOOS, JR.

pay), 4) fear of poor surgical outcome (such as fear of a future revision), and 5) timing (such as not having severe enough joint pain). Participants indicated whether a barrier was important on a 5-point Likert scale, which we then dichotomized so that "Extremely" and "Very" important were defined as "*highly important,*" and other responses were "*not as important*." The survey was distributed to patients at New York City hospitals and nationally via an arthritis support group. Home addresses were geocoded and linked to census tracts; "high-poverty community" was defined as ≥20% of residents in a community living below the poverty level (American Community Survey data). Multiple logistic regression models were used to evaluate adjusted odds ratios (aOR) of community poverty to rating barriers as "*highly important*", adjusted for age, sex, Hip Disability and Osteoarthritis Outcome Score (HOOS, JR) and Knee Injury and Osteoarthritis Outcome Score (KOOS, JR).

Results: Of the 702 participants who provided an address that could be geocoded, 118 (16.8%) were residents of high-poverty communities **(Table 1**). Participants from 46 states and Puerto Rico were represented across 658 unique census tracts. All five barriers were more frequently considered "*highly important*" by residents of high-poverty communities compared to those from low-poverty communities, with differences in surgeon- and outcome-related barriers being the most pronounced (**Figure 1**). After adjusting for age, sex, and HOOS, JR / KOOS, JR, residents of high-poverty communities had a higher risk of perceiving barriers related to limited or lack of trust in a surgeon (aOR: 1.9, 95% CI: [1.2, 2.8]) and fear of poor surgical outcome (aOR: 1.7, 95% CI: [1.1, 2.6]) as "*highly important*" (**Figure 2**).

Conclusion: Residents from high-poverty communities prioritized lack of trust in surgeon and fear of poor surgical outcomes as more significant barriers to TJA compared to residents from low-poverty communities. Our work suggests that facilitating the selection of a trustworthy surgeon and providing education about the process of recovery from TJA among residents from low-income communities could be effective strategies for increasing the uptake of TJA in these communities.

Disclosure: J. Gibbons: None; **I. Mannstadt**: None; **T. Amen**: None; **M. Rajan**: None; **S. Young**: None; **M. Parks**: None; **M. Figgie**: hs2, 8, joint effort aso, 8, lima, 2, 9, wishbone medical, 2, 4, 8, 9, 10; **A. Bass**: None; **L. Russell**: None; **B. Mehta**: Janssen, 1, Novartis, 5; **I. Navarro-Millán**: None; **S. Goodman**: NIH, 5, Novartis, 5.

Abstract Number: 1029

Social Determinants of Health in Children with Rheumatic Disease: A Single Center Cohort

Kristina Ciaglia[1], Elizabeth Sloan[1] and Tracey Wright[2], [1]UT Southwestern and Scottish Rite for Children, Dallas, TX, [2]UT Southwestern, Dallas, TX

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Healthcare Disparities in Rheumatology Poster II: Socioeconomic Determinants
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatic disease disproportionately impacts certain socioeconomic, racial, and ethnic groups frequently resulting in health care inequities. Social determinants of health (SDOH) are conditions in the environment where people exist that encompass a wide range of systems, and influence quality of life, outcomes, and risks. Aligning with health

Table 1: SDOH Survey Responses from Patients Seen in Rheumatology Clinic

Table 1: SDOH Survey Responses from Patients Seen in Rheumatology Clinic

Social Determinant of Health Survey Questions	Responses: Number of patients (%)
In the last 12 months, was there a time when you were not able to pay the mortgage or rent on time?	Yes: 109 (12.7%) No: 569 (66.1%) Refused to answer/blank: 183 (21.2%)
In the last 12 months, how many places have you lived?	1: 606 (70.4%) 2: 58 (6.7%) 3+: 6 (0.7%) Refused to answer/blank: 191 (22.2%)
In the last 12 months, was there a time when you did not have a steady place to sleep or slept in a shelter (including now)?	Yes: 19 (2.2%) No: 674 (78.3%) Refused to answer/blank: 168 (19.5%)
In the past 12 months, has lack of transportation kept you from medical appointments or from getting medications?	Yes: 39 (4.5%) No: 621 (72.2%) Refused to answer/blank: 201 (23.3%)
In the past 12 months, has lack of transportation kept you from meetings, work, or from getting things needed for daily living?	Yes: 35 (4.1%) No: 629 (73%) Refused to answer/blank: 197 (22.9%)
Within the past 12 months, you worried that your food would run out before you got the money to buy more.	Never true: 508 (59%) Sometimes true: 121 (14.1%) Often true: 19 (2.2%) Refused to answer/blank: 213 (24.7%)
Within the past 12 months, the food you bought just didn't last and you didn't have money to get more.	Never true: 542 (63%) Sometimes true: 92 (10.6%) Often true: 11 (1.3%) Refused to answer/blank: 216 (25.1%)

equity literature, children from disadvantaged socioeconomic backgrounds experience worse outcomes and delays in care.1 In adult SLE, the negative impacts of SDOH are well described with unfavorable determinants leading to more severe disease and increased mortality.2 We aimed to identify SDOH in a cohort of children with rheumatic disease followed at a single center to begin to explore risk factors for disparities in our patient population.

Methods: Patient caregivers completed a SDOH survey prior to the start of the clinic visit. Survey results from February to May 2023 were extracted from the EMR. Patient demographics, diagnosis, and survey responses were analyzed using standard descriptive statistics.

Results: We analyzed SDOH surveys (n=861) completed during the initial survey roll out. Most patients surveyed were female (70%), and the average age was 11.7 years. Seventy percent reported White race, and 38% identified their ethnicity as Hispanic/Latino. Eleven percent of respondents had no high school degree, and 7.6% reported they need help with reading materials. Approximately 4% of patients reported needing help with cost of care, utilities, food, housing, or

Table 2: SDOH Demographics and Responses in Patients with Pediatric Rheumatic Disease by Diagnosis

Table 2: SDOH Demographics and Responses in Patients with Pediatric Rheumatic Disease by Diagnosis

	Overall Cohort (n = 861)	SLE Cohort (n = 66)	JDM Cohort (n = 50)	JIA Cohort (n = 371)
Mean Age (SD)	11.7 (4.4)	14.9 (3.1)	11.4 (4.9)	11.7 (4.3)
Race/Ethnicity Number (%)				
Non-Hispanic White	311 (36.1%)	8 (12%)	26 (52%)	173 (46.6%)
Black/African American	65 (7.5%)	11 (16.7%)	5 (10%)	32 (8.6%)
Asian	36 (4.2)	4 (6%)	2 (4%)	13 (3.5%)
American Indian	7 (0.8%)	1 (1.5%)	1 (2%)	4 (1.1%)
Other Race	129 (15%)	6 (9.1%)	2 (4%)	33 (8.9%)
Hispanic/Latino	310 (36%)	38 (57.6%)	24 (48%)	117 (31.5%)
Sex Number (%)				
Male	259 (30%)	7 (10.6%)	16 (32%)	106 (28.9%)
Female	602 (70%)	59 (89.4%)	34 (68%)	265 (71.4%)
Insurance Status Number (%)				
Government/None	369 (42.9)	73 (65.2%)	25 (50%)	148 (39.9%)
Commercial	492 (57.1%)	23 (34.8%)	25 (50%)	223 (60.1%)
SDOH Responses Number (%)				
"I need help with reading materials"				
Yes	66 (7.6%)	10 (15.2%)	6 (12%)	18 (4.9%)
No	632 (73.4%)	35 (53%)	24 (48%)	240 (64.7%)
Refused to answer/blank	163 (18.9%)	21 (31.8%)	20 (40%)	113 (30.4%)
"Do you have a High School degree?"				
Yes	592 (68.8%)	32 (48.5%)	24 (48%)	228 (61.4%)
No	101 (11.7%)	11 (16.7%)	6 (12%)	31 (8.4%)
Refused to answer/blank	168 (19.5%)	23 (34.9%)	20 (40%)	112 (30.2%)

transportation. Twenty-one percent reported being often or sometimes worried about food security (Table 1). Of the patients surveyed, 66had a diagnosis of SLE,50 had JDM, and 371 had JIA(Table 2). In comparison with JIA and JDM families, SLE caregivers disclosed a statistically significant higher rate of needing help with reading materials (p=0.0136) and lack of high school degree (p=0.0355).

Conclusion: Patients seen in our center come from diverse socioeconomic, racial, and ethnic backgrounds. The SDOH survey identified critical barriers to patient care including health literacy, food security, and living costs such as transportation, housing, and utilities. Health literacy may be an essential limiting factor for our families with children who have SLE. Further study is needed to understand the impact of SDOH on outcomes for children with rheumatic disease and how it varies by diagnosis. Future efforts to improve the management and outcomes of children with rheumatic disease should focus on specific SDOH that could influence health inequities.

1. Akinsete AM, Woo JMP, Rubinstein TB. Disparities in Pediatric Rheumatic Diseases. Rheum Dis Clin North Am. Feb 2022;48(1):183-198. doi:10.1016/j.rdc.2021.09.014
2. Williams JN, Drenkard C, Lim SS. The impact of social determinants of health on the presentation, management and outcomes of systemic lupus erythematosus. Rheumatology (Oxford). Mar 29 2023;62(Suppl 1):i10-i14. doi:10.1093/rheumatology/keac613

Disclosure: K. Ciaglia: None; **E. Sloan**: None; **T. Wright**: None.

Abstract Number: 1030

Patterns in the Prescription, the Denials of Coverage, and the Delays in Dispensation of Janus Kinase Inhibitors

Thomas Riley[1], Igor Dombrovsky[2], Michael George[3] and Joshua Baker[3], [1]Hopsital of the University of Pennsylvania, Springfield, PA, [2]Pennsylvania Hospital, Philadelphia, PA, [3]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Healthcare Disparities in Rheumatology Poster II: Socioeconomic Determinants
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Janus kinase inhibitors (JAKi) have therapeutic benefits in autoimmune conditions. Access to these medications is controlled by insurance carriers through requirements for prior authorizations and the use of restricted formularies which are difficult to navigate and may lead to denials of coverage and/or delays in dispensation.This study sought to characterize the real-word coverage denials and delays in dispensation of JAKi in patients with rheumatologic diseases, hypothesizing that there would be differences in denials of prescriptions and delays in dispensation related to drug type, race, and insurance status.

Methods: A retrospective cohort was created from patients at an academic tertiary care rheumatology practice who were prescribed a JAKi between 2014 and 2023. Patients were included in this analysis if they had a documented visit with a rheumatologist documented in the electronic health record (EHR) and for the initial prescription of a JAKi (tofacitinib, baricitinib, upadacitinib) but did not include patients renewing an existing prescription. Patients were selected irrespective of underlying disease. Demographics and current/prior disease-modifying anti-rheumatic drug (DMARD) use were extracted from the EHR. To provide confirmation of insurance approval and determine the time to dispensation, pharmacy and nursing-based communications related to the processing of prior authorization and coordination with specialty pharmacies were also extracted from the EHR.

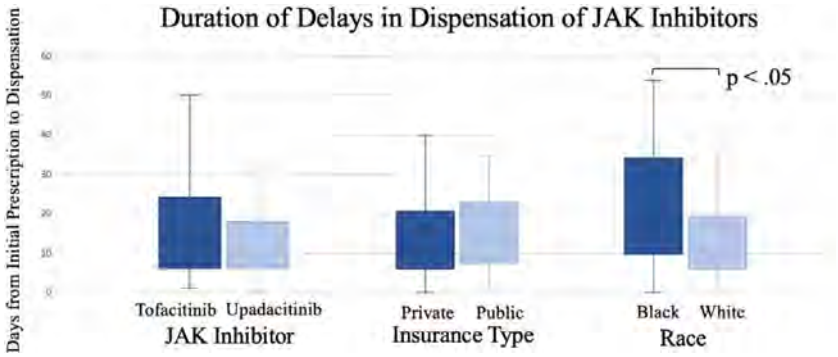

Figure 1. In evaluating the delays from time to prescription to time to dispensation, there were no significant differences comparing tofacitinib to upadacitinib (19.8 vs 15.2, p =0.34) or the insurance type the patient was enrolled in (16.7 vs 21.3, p = 0.32). However, patients who were Black experienced a longer delay in initial dispensation compared to those who were Non-Hispanic White (30.6 vs 15.8, p = 0.013)

Results: We identified a total of 118 new prescriptions for JAKi among 90 patients (81 tofacitinib, 36 upadacitinib, 1 baricitinib).Of these 118 prescriptions, 10 (8%) had coverage denied by insurance, and 5 (4%) were not dispensed for other reasons [2 were limited by co-pay, 1 changed insurance, 1 developed a severe infection, and 1 opted not to start due to personal preferences]. Patients with an approved prescription experienced, on average, an 18-day delay [IQR 6-22] between initial prescription and dispensing of a JAKi. 14 prescriptions (11%) had delays longer than 30 days. Patients who were Black experienced a longer delay in initial dispensing compared to those who were Non-Hispanic White (30.6 vs 15.8, p = 0.013). Comparing private vs public insurance, there were not differences in rates of coverage denial (10% vs 7%, p = 0.61), nor were there differences in delays in dispensation (21.3 vs 16.7, p = 0.32). There were not differences in delays in dispensation for tofactinib compared to upadacitinib (19.8 vs 15.2, p =0.34).

Conclusion: While rates of coverage denial of JAKi were low, there was an average delay in dispensing prescriptions of 18 days. Patients who were Black experienced an almost 2-fold longer delay in dispensing of JAKi compared to those who identified as Non-Hispanic White. Further evaluation is needed to identify the potential factors at play contributing to this observed disparity and the key drivers of delays in medication dispensing.

Disclosure: T. Riley: None; **I. Dombrovsky**: None; **M. George**: AbbVie/Abbott, 2, GlaxoSmithKlein(GSK), 5, Janssen, 5; **J. Baker**: CorEvitas, 2, Cumberland Pharma, 2, Horizon Pharmaceuticals, 5.

Abstract Number: 1031

Geographic Socioeconomic Influences on Disease Activity in Rheumatoid Arthritis in an Academic and Safety-Net Hospital System

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Healthcare Disparities in Rheumatology Poster II: Socioeconomic Determinants
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is associated with increased morbidity and mortality, particularly if RA is poorly controlled. The effects of socioeconomic deprivation have not been well studied in the context of RA. We analyzed the impact of the Area Deprivation Index (ADI) on disease activity and cardiovascular comorbidity in RA.

Table 1. Demographics of each cohort

	Academic State ADI (n=542)	Academic National ADI (n=502)	Safety net State ADI (n=496)	Safety net National ADI (n=354)	Academic vs Safety net (n=1158)
Age, mean ± SD	60.3±13.8	60.6±13.7	58.6±12.8	58±13.3	62±13.9
Sex, % Female	446 (82.3%)	411 (81.9%)	407 (82.1%)	292 (82.5%)	964 (83.3%)
Ethnicity, %					
Hispanic	98 (18.1%)	88 (17.5%)	230 (46.4%)	172 (48.6%)	385 (33.3%)
Non-Hispanic	414 (76.4%)	376 (74.9%)	264 (53.2%)	182 (51.4%)	763 (65.9%)
Unknown	30 (5.5%)	38 (7.6%)	2 (0.4%)	0 (0%)	10 (0.9%)
Race, %					
White	330 (60.9%)	327 (65.1%)	301 (60.7%)	234 (66.1%)	607 (52.4%)
Black	205 (37.8%)	169 (33.7%)	173 (34.9%)	104 (29.4%)	504 (43.5%)
Asian	2 (0.4%)	0 (0%)	22 (4.4%)	0 (0%)	39 (3.4%)
Other	5 (0.9%)	6 (1.2%)	0 (0%)	16 (4.5%)	8 (0.7%)
Charlson Comorbidity Index, mean ± SD (au)	5.1±3.6	5.2±3.7	4.9±3.5	4.7±3.2	6±3.9
Insurance Class					
Medicaid/Charity	16 (3%)	14 (2.8%)	332 (66.9%)	225 (63.6%)	186 (16.1%)
Medicare/Similar	513 (94.7%)	483 (96.2%)	153 (30.9%)	113 (31.9%)	921 (79.5%)
Unknown	13 (2.4%)	5 (1%)	11 (2.2%)	16 (4.5%)	51 (4.4%)
Rheumatoid Factor (RF), % Positive	126 (47.7%)	112 (46.7%)	315 (69.1%)	226 (67.7%)	513 (64.3%)
Cyclic Citrullinated Peptide (CCP), % Positive	141 (55.1%)	116 (50.4%)	354 (77.6%)	259 (77.5%)	574 (72.1%)

SD: standard deviation; ADI: area deprivation index

Cohort Demographics

Table 2. State ADI for academic cohort

	RA with high ADI ≥8 (n=271)	RA with low ADI ≤3 (n=271)	P-Value
Emergency Department Visits, mean ± SD	0.7±2.7	0.3±1.2	0.0502§
Hospital Visits, mean ± SD	0.37±1.2	0.4±1.7	0.6747§
Language, n (%)			
English	258 (95.2%)	262 (96.7%)	0.1326*
Spanish	12 (4.4%)	5 (1.9%)	
Other	1 (0.4%)	4 (1.5%)	
MyChart Status, Active n (%)	203 (74.9%)	234 (86.4%)	**0.0008**
Smoking History, n (%)			
Ever Smoked	124 (45.8%)	92 (34%)	**0.0054***
Never Smoked	144 (53.1%)	178 (65.7%)	
Unknown	3 (1.1%)	1 (0.4%)	
Has Primary Care Provider, n (%)	245 (90.4%)	242 (89.3%)	0.6696
RAPID 3 Score, mean ± SD (au)	13.8±6.9	11.2±7.4	**<.0001§**
CDAI Score (au)	12±11.7	9.4±8	**0.0173§**
MDHAQ Average, mean ± SD (au)	0.93±0.68	0.72±0.67	**0.0003§**
Cardiovascular Disease, n (%)	103 (38%)	87 (32.1%)	0.1498
Medication Ever Used, n (%)			
Prednisone	225 (83%)	214 (79%)	0.2285
NSAID	210 (77.5%)	221 (81.6%)	0.2417
CSDMARD	224 (82.7%)	208 (76.8%)	0.0875
BDMARD	136 (50.2%)	135 (49.8%)	0.9315
TSDMARD	33 (12.2%)	47 (17.3%)	0.09

RA: rheumatoid arthritis; ADI: area deprivation index; RAPID3: routine assessment of patient index data; CDAI: clinical disease activity index; MDHAQ: multidimensional health assessment questionnaire; NSAIDS: nonsteroidal anti-inflammatory drugs; CSDMARDS: conventional synthetic disease modifying anti-rheumatic drugs; BDMARDS: biologic DMARD; TSDMARD: targeted synthetic DMARD
Note: § by t-test; * by Fisher's Exact Test; Otherwise by Chi-Square Test

State ADI for academic cohort

Table 3. State ADI for safety net cohort

	RA with high ADI ≥8 (n=248)	RA with low ADI ≤3 (n=248)	P-Value
Emergency Department Visits, mean ± SD	2.3±3.3	2.7±3.7	0.1612§
Hospital Visits, mean ± SD	0.5±1.2	0.7±1.5	0.1013§
Language, n (%)			
English	153 (61.7%)	159 (64.1%)	0.8049
Spanish	85 (34.3%)	81 (32.7%)	
Other	10 (4%)	8 (3.2%)	
MyChart Status, Active n (%)	148 (59.7%)	156 (62.9%)	0.4608
Smoking History, n (%)			
Ever Smoked	96 (38.7%)	94 (37.9%)	**0.0119**
Never Smoked	113 (45.6%)	135 (54.4%)	
Unknown	39 (15.7%)	19 (7.7%)	
Has Primary Care Provider, n (%)	209 (84.3%)	200 (80.7%)	0.5505
CDAI Score (au)	12.8±10.2	15.3±12.2	0.1020§
HAQ-II Average, mean ± SD (au)	1.23±0.8	1.23±0.76	0.9790§
Cardiovascular Disease, n (%)	90 (36.3%)	79 (31.9%)	0.2974
Medication Ever Used, n (%)			
Prednisone	144 (58.1%)	142 (57.3%)	0.8558
NSAID	182 (73.4%)	177 (71.4%)	0.6156
CSDMARD	197 (79.4%)	182 (73.4%)	0.1126
BDMARD	116 (46.8%)	95 (38.3%)	0.0565
TSDMARD	6 (2.4%)	7 (2.8%)	0.7787

RA: rheumatoid arthritis; ADI: area deprivation index; RAPID3: routine assessment of patient index data; CDAI: clinical disease activity index; MDHAQ: multidimensional health assessment questionnaire; NSAIDS: nonsteroidal anti-inflammatory drugs; CSDMARDS: conventional synthetic disease modifying anti-rheumatic drugs; BDMARDS: biologic DMARD; TSDMARD: targeted synthetic DMARD

Note: § by t-test; * by Fisher's Exact Test; Otherwise by Chi-Square Test

State ADI for safety net cohort

Methods: We conducted a retrospective analysis of RA patients, defined by ICD-10 codes, seen at our academic practice and safety-net hospital system clinics in the past 5 years and are 18-89 years old. We collected age, ethnicity, race, gender, insurance plan, primary language, address, RA medications, MyChart engagement, primary care physician presence, emergency department/inpatient visits, RA disease activity and functional scores (CDAI, MDHAQ/HAQII, RAPID3), Charlson comorbidity index (CCI), and cardiovascular disease (CVD) presence. ADI was used as a proxy for socioeconomic deprivation and was assigned using 9-digit zip codes. Patients were divided by the upper ADI tertile vs lower ADI tertile and matched by gender, race/ethnicity, age, insurance and CCI using propensity score analysis. Two-sample t test and Chi-square test were conducted for final group comparisons.

Results: Patients from our academic practice (n=542) and from our safety-net hospital system (n=496) were assessed using state ADI. The mean state ADI score was 5.3 and 5.6 for academic and safety-net, respectively (range 1-10). In the academic cohort, those with high ADI scores (>8, more deprived) had higher RA disease activity (RAPID3: High 13.834±6.943 vs Low 11.166±7.370, $p< 0.0001$, CDAI: High 11.970±11.738 vs Low 9.400±7.968, $p< 0.05$) and RA functional impairment (MDHAQ: High 0.933±0.676 vs Low 0.722±0.667, $p< 0.001$) and had lower MyChart utilization ($p< .001$) compared to those with low ADI scores (< 3, less deprived). There were also statistically significant differences in smoking status ($p< .01$). In the safety-net cohort, there was a statistically significant difference in smoking status ($p< 0.05$). Otherwise, for the safety-net cohort, there were no significant differences between the high ADI and low ADI group in any of the other measured variables.

Conclusion: We found significant differences in RA disease activity and function in patients from more socioeconomically deprived areas in the academic system. The absence of these differences in safety-net patients raises important questions as to whether certain hospital specific factors influence the role ADI plays in various health outcomes. The results suggest that ADI may not be as effective at predicting RA disease activity at a safety-net hospital. Identifying the discrepancies between the two hospital systems may elucidate areas of improvement for patient care.

Disclosure: J. Kim: None; **S. Zhang**: None; **E. Solow**: None.

Abstract Number: 1032

"Not of Your Ethnicity": A Qualitative Study Exploring Diverse Patient Experiences in Axial Spondyloarthritis (axSpA)

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Healthcare Disparities in Rheumatology Poster II: Socioeconomic Determinants

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthritis (axSpA) can result in significant morbidity. Existing studies suggest functional impairment and inflammation may be worse in Black and Latine patients. However, no studies have focused on the experiences of diverse patients with axSpA. This study fills a critical knowledge gap by utilizing qualitative methods to describe the experiences of patients with axSpA from diverse racial-ethnic groups.

Methods: We identified a sampling frame of 128 adult patients with: ≥1 rheumatology visit in a university healthcare system within 3 years with a linked ICD code (spondylopathies) and patient-identification of race as Black, African American, Asian, Native American, American Indian, Alaska Native, Native Hawaiian, or Pacific Islander, or ethnicity of Hispanic or Latino. Twenty-eight patients were excluded due to not meeting diagnostic criteria or language preference other than English or Spanish. We used qualitative methods with a grounded theory approach (Figure 1). Sampling was purposive. We performed semi-structured individual interviews of 20 patients, conducted in English or Spanish. Analysis of interview transcripts was ongoing and iterative. Participants were recruited until thematic saturation was reached.

Results: Qualitative data analysis indicated six major themes (figure 2): 1) nebulous diagnostic definitions; 2) diversity and intersectionality; 3) road to rheumatology; 4) barriers to diagnosis; 5) limitations in treatment options; 6) coping with chronic illness.

Within nebulous diagnostic definitions, minor themes included: patient difficulty in understanding diagnosis, provider gaps in knowledge of axSpA, inconsistency in diagnostic language, and provider failure to query for or disbelief of inflammatory symptoms.

For diversity and intersectionality, minor themes included: the role of healthcare outside the US, provider-patient discordance, bias along age, gender and race/ethnic/cultural axes, the impact of a gendered and racialized illness script for axSpA and the importance of unique social stressors for patients.

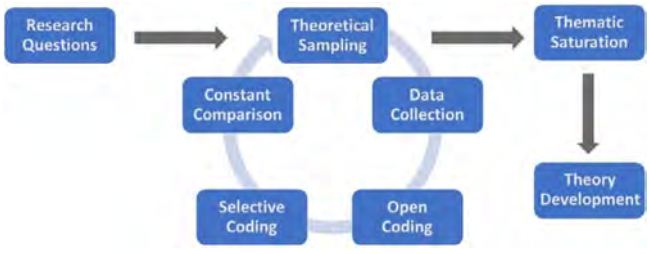

Figure 1: Schematic representation of grounded theory methodology in qualitative research

Regarding the road to rheumatology, minor themes included: reliance on positive HLA-B27 or recurrent uveitis for referral to rheumatology care, the burden of seeing multiple providers, and financial barriers to supportive diagnostic testing.

In barriers to diagnosis, minor themes included: patients' internalized communication failure, provider disbelief of symptoms or misattribution, and overall mistrust in the medical system

Within limitations in treatment, minor themes included: overreliance on physical therapy and NSAID use, difficulty understanding medication options and difficulty understanding systemic nature of disease.

About coping with chronic illness, minor themes included: chronic and incurable disease, fear and anxiety over prognosis, use of complementary therapies, protective strategies, and the importance of safety net services.

Conclusion: Our study identified six major themes of diverse patient experiences. Studying patient experiences is critical for understanding mechanisms of health disparity, targeting interventions and, ultimately, improving quality of care.

Table 1: Descriptive characteristics of study participants

	Participants (n=20)
Age, years (mean)	33.5
Sex assigned at birth	
Male	11 (55%)
Female	9 (45%)
Primary language	
English	17 (85%)
Spanish	3 (15%)
Race-ethnicity (per patient-identified pre-existing medical record categories)	
Asian or Asian American	10 (50%)
Hispanic or Latino	6 (30%)
Black or African American	3 (15%)
American Indian or Native American	1 (5%)
Primary diagnosis	
Ankylosing spondylitis	12 (60%)
Axial spondyloarthritis	6 (30%)
Psoriatic arthritis	1 (5%)
Inflammatory bowel disease-associated arthritis	1 (5%)
Disease manifestations	
Age at symptom onset, years (mean)	22.9
Time from symptom onset to diagnosis, years (mean)	8.2
HLA-B27 Positive	16 (80%)
Radiographic axSpA (positive sacroiliac joint x-ray findings)	9 (45%)
History of uveitis	6 (30%)

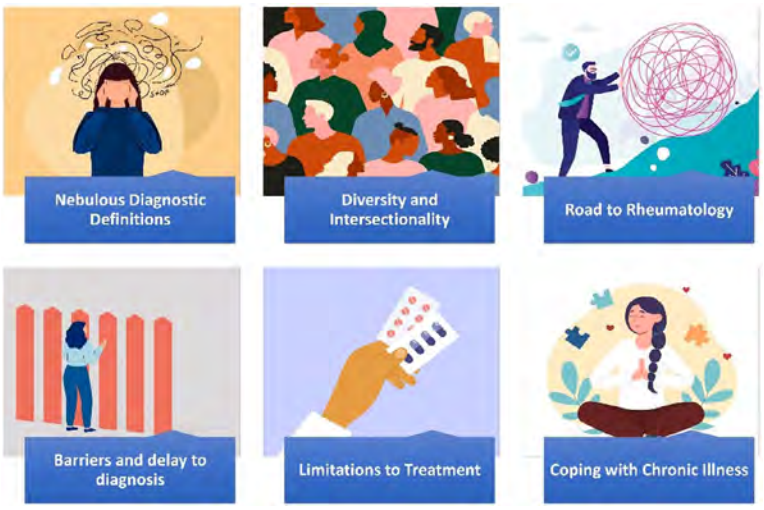

Figure 2: Six major themes identified from qualitative interview analysis

Disclosure: B. Mantilla: None; **K. Wysham**: None; **J. liew**: None; **G. Hughes**: Janssen, 3.

Abstract Number: 1033

The Detection of Subclinical Joint Inflammation by Thermal and Ultrasound Imaging at the Metacarpophalangeal Joints in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: While magnetic resonance imaging and ultrasound (US) imaging have been shown to be useful in the detection of subclinical joint inflammation in rheumatoid arthritis (RA), the literature on the use of thermal imaging (TI) in detecting subclinical disease in RA is presently lacking. The purpose of this RA study is to investigate whether there exists any correlation(s) between thermographic parameters and US-detected joint inflammation at clinically non-tender and non-swollen metacarpophalangeal joints (MCPJs).

Methods: RA patients (fulfilling the 2010 RA classification criteria) with clinically non-tender and non-swollen MCPJs underwent TI and US imaging of their 10 MCPJs on the same study visit. The thermographic parameters (maximum (Tmax), minimum (Tmin) and average (Tavg) temperatures in degree Celsius) were recorded from the dorsal surface of each MCPJ and summed up to obtain the respective Total Tmax, Total Tmin and Total Tavg per patient. Ultrasound power Doppler (PD) and grey-scale (GS) joint inflammation were scored semi-quantitatively (0-3) at the dorsal aspect of each MCPJ and summed up to obtain the respective Total PD and Total GS scores per patient. At each MCPJ, US synovitis is defined as PD ≥1 or GS ≥2 [1]. At the patient level, Pearson's correlation coefficient was used to correlate Total Tmax, Total Tmin and Total Tavg with Total PD score, Total GS score and the number of joint(s) with US synovitis (PD ≥1 or GS ≥2). Among associations which were statistically significant, simple linear regression was applied to characterise relationship between variables.

Results: A total of 340 MCPJs (clinically non-tender and non-swollen) were examined among 34 RA patients. In this cross-sectional study, the patients' baseline characteristics are as follows: age, mean (SD) 58.3 (12.5) years; Chinese (n = 25, 73.5%); female (n = 30, 88.2%); DAS28, mean (SD) 3.13 (0.84); disease duration, mean (SD) 36.9 (58.1) months. Table 1 summarises the results from the correlation analysis. Total Tmax correlated significantly (P < 0.05) with Total PD score (r = 0.38), Total GS score (r = 0.41) and the number of joint(s) with PD ≥1 or GS ≥2 (r = 0.41). Total Tmin correlated

Table 1. Results from the Pearson's correlation coefficient analysis.

Thermographic parameter	Total PD		Total GS		Number of joint(s) (PD ≥1 or GS ≥2)	
	Correlation coefficient	P-value	Correlation coefficient	P-value	Correlation coefficient	P-value
Total Tmax	0.38	0.03*	0.41	0.02*	0.41	0.02*
Total Tmin	0.33	0.06	0.40	0.02*	0.39	0.02*
Total Tavg	0.34	0.051	0.41	0.02*	0.40	0.02*

*Statistically significant at P < 0.05

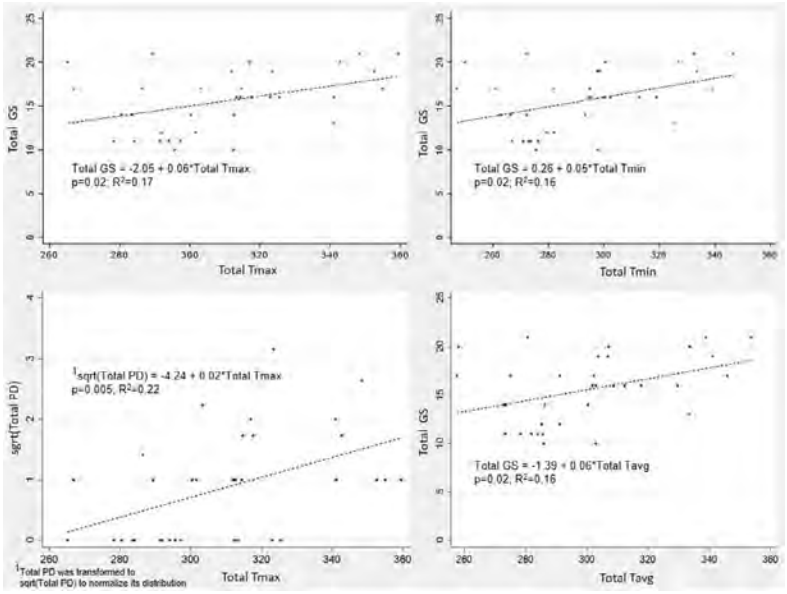

Figure 1. The relationship between thermographic parameters and ultrasound PD and GS variables.

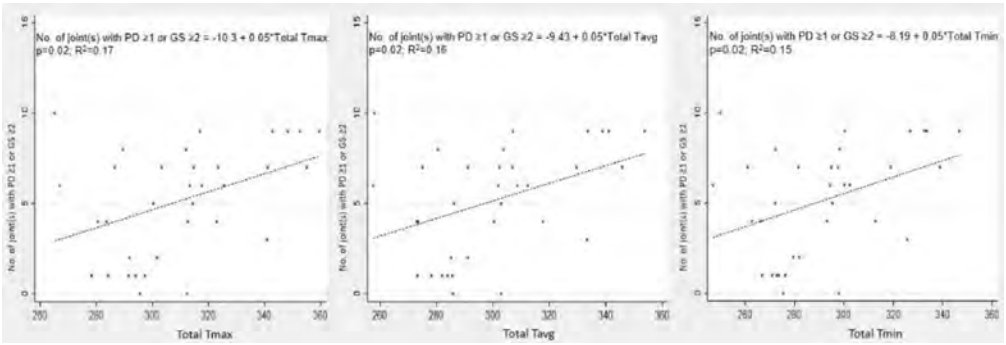

Figure 2. The relationship between thermographic parameters and number of joint(s) with PD ≥1 or GS ≥2.

significantly ($P < 0.05$) with Total GS score ($r = 0.40$) and the number of joint(s) with PD ≥1 or GS ≥2 ($r = 0.39$). Total Tavg correlated significantly ($P < 0.05$) with Total GS score ($r = 0.41$) and the number of joint(s) with PD ≥1 or GS ≥2 ($r = 0.40$). The relationship (only associations which were statistically significant are shown) of thermographic parameters with US variables and number of joint(s) with PD ≥1 or GS ≥2 are shown in Figure 1 and 2, respectively.

Conclusion: To the best of our knowledge, our RA study is the first to show that results from TI correlates significantly with US PD and GS joint inflammation as well as the number of joint(s) with ultrasound synovitis (PD ≥1 or GS ≥2) at the MCPJs. Like US imaging, TI can help detect subclinical joint inflammation at clinically non-tender and non-swollen MCPJs and further investigative work using TI in the detection of subclinical disease in RA appears warranted.

1. Hirata A, et al. Arthritis Care Res (Hoboken). 2017;69:801-806.

Disclosure: Y. Tan: None; **G. Lim**: None.

Abstract Number: 1034

The Relationship Between the Extent of Ground Glass to Fibrosis Ratio and Treatment Response to Immunomodulatory Therapy in Three Separate Autoimmune Interstitial Lung Disease Cohorts

Scott Matson[1], Stephen Humphries[2], joyce Lee[3], Michael Roth[4], Donald Tashkin[4], Grace Kim[4], Jonathan Goldin[4], Mei Leng[4] and **Elizabeth Volkmann**[4], [1]University of Kansas School of Medicine, Kansas City, MO, [2]National Jewish Health, Denver, CO, [3]University of Colorado Anschutz Campus, Denver, CO, [4]University of California Los Angeles, Los Angeles, CA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Imaging of Rheumatic Diseases Poster I

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: For patients with autoimmune interstitial lung disease (ILD), the clinician's interpretation of the extent of ground glass relative to fibrosis on imaging often influences the choice of treatment (immunomodulatory vs. antifibrotic therapy). However, it is unknown if the ground glass to fibrosis ratio affects treatment response for patients with different types of autoimmune ILDs. The purpose of this study is to examine the relationship between quantitative ground glass opacity to fibrosis ratio on baseline imaging and treatment response to immunomodulatory therapy in patients with ILD associated with systemic sclerosis (SSc) and rheumatoid arthritis (RA).

Methods: Participants of three independent cohorts were included in the present study: (1) Scleroderma Lung Study (SLS) I, which compared cyclophosphamide with placebo for SSc-ILD; SLS II, which compared cyclophosphamide with mycophenolate for SSc-ILD; and a retrospective cohort of patients with rheumatoid arthritis RA-ILD treated with immunomodulatory

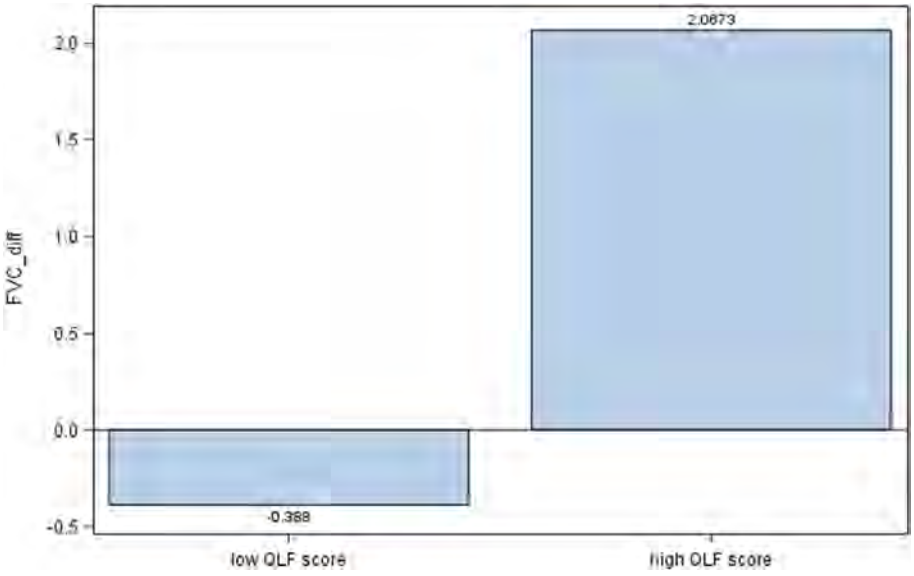

Figure 1. Bar chart that compares the mean forced vital capacity (FVC) percent predicted change at 12 months in SLS I and SLS II participants randomized to cyclophosphamide based on high versus low fibrosis (QLF) score. Patients in the high QLF score group (N=49) experienced a mean improvement in FVC%-predicted of 2.07 (SD 6.8), while patients in the low QLF group (N=53) experienced a slight mean decline in FVC %-predicted of -0.39 (SD 7.2) (P-value for between group difference [P=0.08])

therapy (azathioprine, mycophenolate mofetil or rituximab). Pretreatment high-resolution computed tomography (HRCT) scans underwent quantitative image analysis to determine whole lung ground glass and fibrosis extent. Forced vital capacity (FVC) and diffusion capacity for carbon monoxide (DLCO) percent predicted were measured at baseline and 12-months. Logistic regression analysis was used to examine the relationship between baseline ground glass to fibrosis ratio and the following outcomes: FVC improvement of 3% or greater, FVC decline of 3% or greater, and FVC decline of 5% or more or

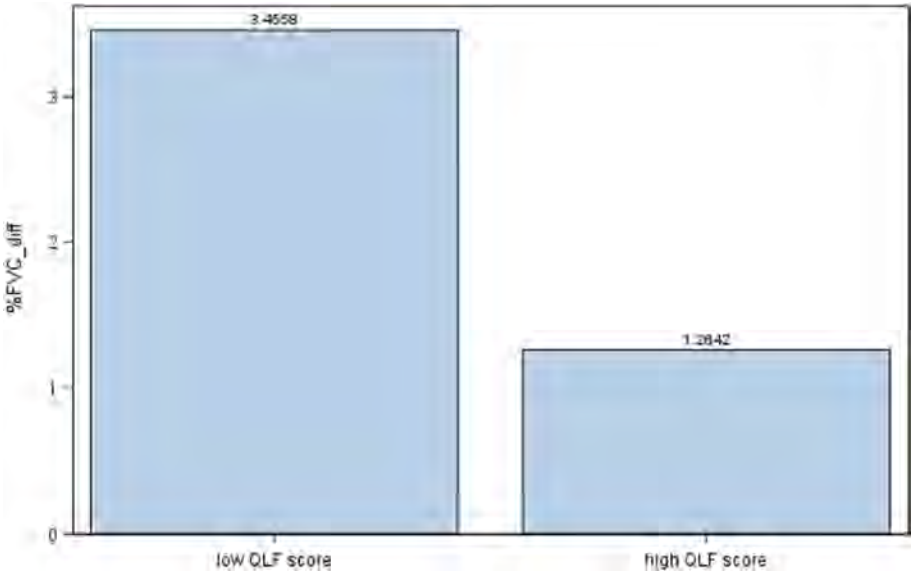

Figure 2. Bar chart that compares the mean forced vital capacity (FVC) percent predicted change at 12 months in SLS II participants randomized to mycophenolate based on high versus low fibrosis (QLF) score. Patients in the high QLF score group (N=26) experienced a mean improvement in FVC%-predicted of 1.26 (SD 7.4), while patients in the low QLF group (N=30) experienced a mean improvement in FVC%-predicted of 3.46 (SD 7.5) (P-value for between group difference [P=0.28]).

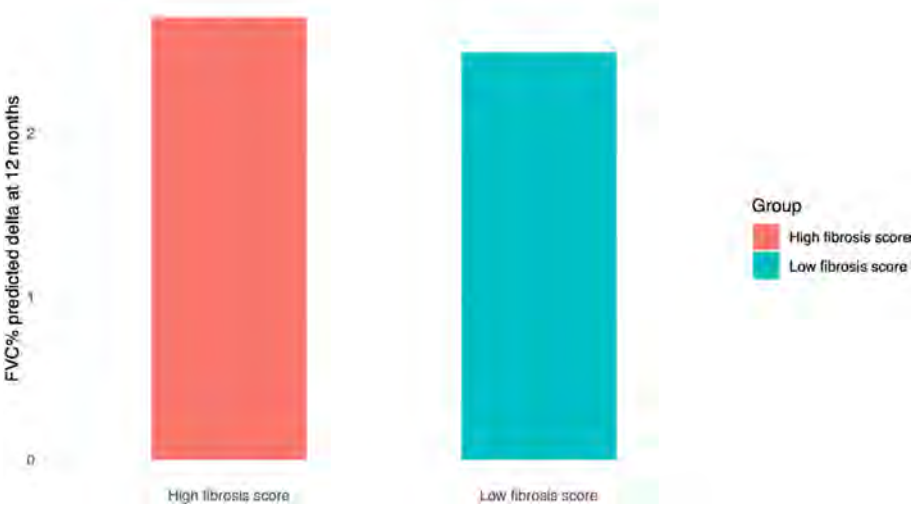

Figure 3. Bar chart that compares the mean forced vital capacity (FVC) percent predicted change at 12 months in RA-ILD participants based on high versus low fibrosis scores. Patients in the high QLF score group experienced a mean improvement in FVC%-predicted of 2.70 (SD 1.7), while patients in the low QLF group experienced a mean improvement in FVC%-predicted of 2.49 (SD 1.3) (P-value for between group difference [P=0.76]).

DLCO decline of 10% or more. Two sample t-tests were performed to compare the mean change from baseline in FVC %-predicted between patients with high versus low fibrosis scores based on the median.

Results: The total cohort included 354 patients with autoimmune ILD. The mean baseline quantitative ground glass to fibrosis ratio at baseline was higher in the SSc cohorts (SLS I: 5.3 [SD 5.5], SLS II: 5.0 [SD 5.2]) than in the RA-ILD cohort (0.62 [SD 1.2]). No significant association was observed between the quantitative ground glass to fibrosis ratio and FVC improvement ≥3% or decline ≥3%, nor the physiologic criteria for progressive pulmonary fibrosis (FVC decline of 5% or more or DLCO decline of 10% or more) at one year in any of the cohorts. Participants with high fibrosis scores demonstrated improved response to treatment with CYC in SLS I and II (Figure 1), while participants with high versus low fibrosis scores experienced a similar improvement in FVC%-predicted in the SLS II-MMF arm (Figure 2) and the RA-ILD cohort (Figure 3).

Conclusion: The extent of ground glass relative to fibrosis does not appear to affect treatment response to immunomodulatory therapy in patients with SSc-ILD and RA-ILD; whereas, higher fibrosis extent was associated with improved response to CYC in SSc-ILD. While the presence of ground glass opacity may signify an underlying inflammatory process, the etiologies of this radiological phenomenon are diverse in these two diseases and additional research is needed to understand how to predict treatment response using radiological parameters in patients with autoimmune ILD.

Disclosure: S. Matson: None; **S. Humphries**: None; **j. Lee**: Blade, 2, Boehringer-Ingelheim, 1, 5, Eleven P15, 2, Pliant, 5, United Therapeutics, 1; **M. Roth**: Genentech, 5; **D. Tashkin**: None; **G. Kim**: MedQIA, 2; **J. Goldin**: MedQIA, 12, Founder; **M. Leng**: None; **E. Volkmann**: Boehringer-Ingelheim, 2, 5, 6, CSL Behring, 2, GlaxoSmithKline, 2, Horizon, 5, Prometheus, 5, Roche, 2.

Abstract Number: 1035

Diagnostic and Educational Utility of an Ultrasound Protocol for Evaluation of Hand Pain in Systemic Sclerosis

Meridith Balbach, Tracy Frech, Nicholson Chadwick, Kevin Byram and Erin Chew, Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Hand impairment is a prevalent issue among systemic sclerosis (SSc) patients and contributes to disability and diminished quality of life. Managing hand pain can be challenging due to the coexistence of various manifestations such as inflammatory arthritis, tendinopathies, joint contractures, sclerodactyly, calcinosis, acro-osteolysis, Raynaud's phenomenon (RP), digital ulcers (DU), and chronic pain. The physical examination and radiographs are the primary methods for evaluating hand pain but are limited in scope. We hypothesized that joint ultrasound (US) is more sensitive than combined joint exam and hand radiograph for identification of acro-osteolysis, articular disease (synovitis, erosions, osteophytes), and periarticular disease (tendinopathies, calcinosis) and can assist in targeted treatment strategies.

Table 1: Patient clinical characteristics and physical exam, radiograph, and ultrasound findings. Yr= years; lcSSc= limited cutaneous systemic sclerosis; dcSSc= diffuse cutaneous systemic sclerosis; NVC= nailfold videocapillaroscopic pattern; DIP= distal interphalangeal; CMC= carpometacarpal; OA= osteoarthritis; MCP= metacarpophalangeal; CPPD= calcium pyrophosphate deposition. *Summarized ultrasound findings are displayed in Table 1 with specific pathologic features detected on ultrasound represented in Figure 1. PIP= proximal interphalangeal; MCP= metacarpophalangeal; TFCC= triangular fibrocartilage complex; DIP= distal interphalangeal

Patient	Age (yr)	SSc Disease Duration (yr)	Clinical Subset (serologies)	NVC Pattern	Fixed Contractures	Synovitis Physical Exam	Radiographic Findings & Diagnosis	Ultrasound Findings*
A	74	23	lcSSc (centromere)	Late	No	No	Non-uniform DIP and CMC joint space narrowing, osteophyte formation; OA	Flexor tendon sheath effusion
B	46	2	dcSSc (RNApol3)	Active	Yes	No	CMC degenerative change, subchondral cystic change; OA	Skin and soft tissue thickening
C	79	20	dcSSc (RNApol3, SSa52)	Late	Yes	No	MCP erosions, chondrocalcinosis	Pseudo double contour sign, fibrocartilage and hyaline calcification, calcinosis
D	37	3	dcSSc (SCL70, dsDNA)	Early	No	Yes	Normal	Inflammatory MCP synovitis, wrist tenosynovitis
E	29	2	dcSSc (SCL70)	Active	No	No	Normal	Normal

Methods: Five randomly selected SSc patients with nonspecific hand pain were referred for musculoskeletal US exam. SSc clinical features were recorded. Joint US was compared to physical exam features of synovitis, tendinopathy, digital ulcers, or calcinosis and radiographic features of erosions, osteophytes, and acro-osteolysis. A pre- and post-ultrasound survey assessed patient and provider perception of diagnostic understanding and treatment needs.

Results: Baseline characteristics, exam findings, radiographs, and ultrasound findings are noted in **Table 1**. No patients had digital ulcers or calcinosis on physical exam or acro-osteolysis on radiograph. Ultrasound exam was able to detect diverse manifestations of hand pathology (**Figure 1)**. Ultrasound review improved the referring provider's confidence in treatment decision improved in all cases (**Table 2**). Patient A was diagnosed with mechanical osteoarthritis, patient B with sclerodactyly, patient C with calcium pyrophosphate arthropathy, Patient D with inflammatory arthritis, and Patient E with chronic pain. The treatment plan was modified in all five patients. US improved patients' understanding of the cause of their joint pain in four patients. After undergoing US, all patients reported feeling that their joint problem had been more thoroughly examined and being more likely to adhere to their provider's treatment recommendations.

Conclusion: The physical exam and radiographs are not sufficient for the evaluation of hand pain in systemic sclerosis. Standardized US assessment in SSc can accurately evaluate hand pain and quantify acro-osteolysis, articular disease, and periarticular disease. Detection of these features can improve provider confidence in management decisions and advance patient understanding of disease, potentially improving treatment adherence and outcomes.

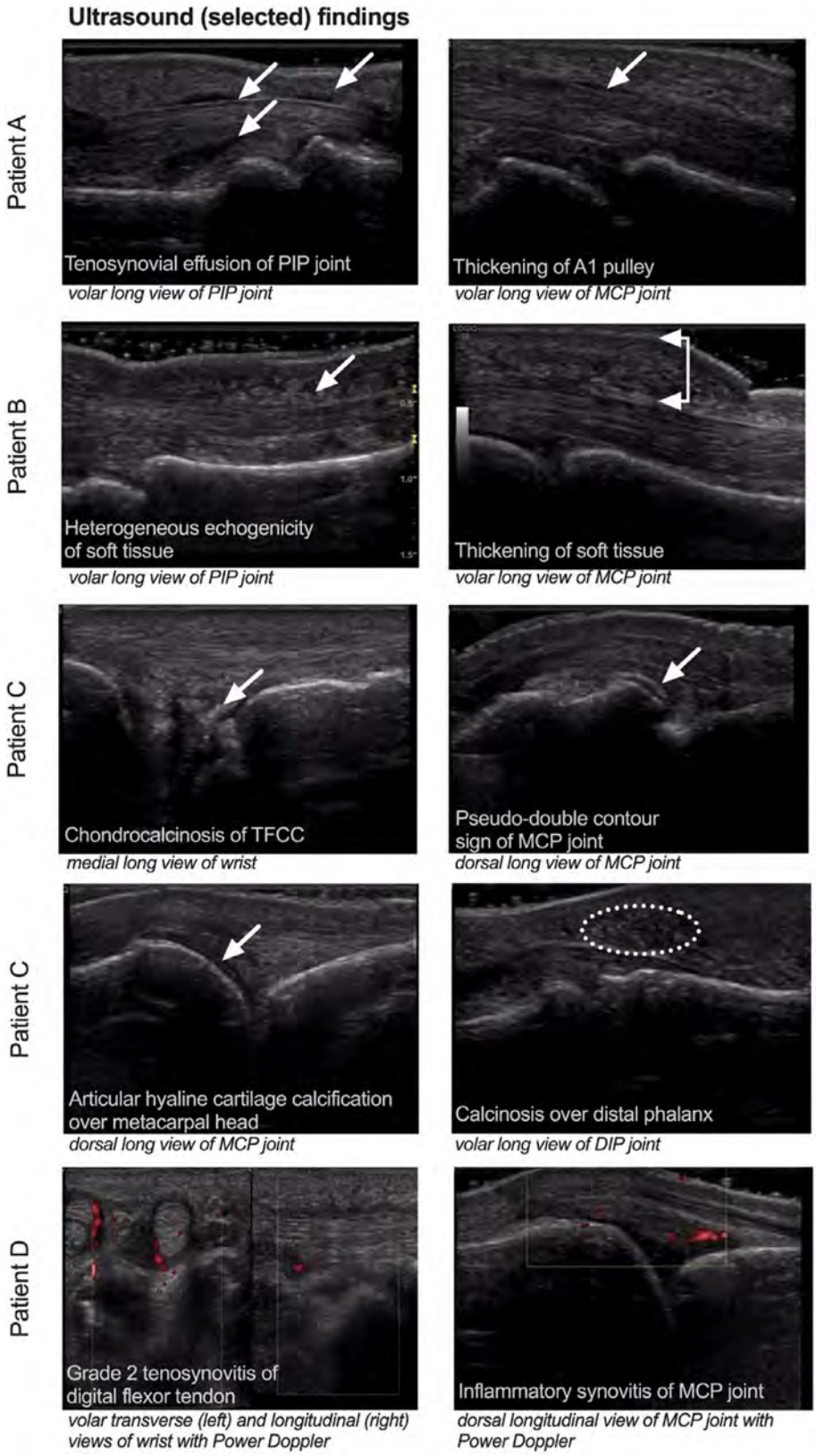

Figure 1: Selected pathologic findings on musculoskeletal ultrasound exam for patients A-D. Relevant features are indicated by white arrows or dotted oval and imaging view is labeled in italics. PIP= proximal interphalangeal; MCP= metacarpophalangeal; TFCC= triangular fibrocartilage complex; DIP= distal interphalangeal

Table 2: Patient and provider perception survey results after ultrasound exam.

Patient	Improved Patient Understanding of Hand Pain	Improved Provider Understanding of Hand Pain	Change in Care Plan Based on US Results
A	Yes	Yes	Yes
B	Yes	Yes	Yes
C	Yes	Yes	Yes
D	Yes	Yes	Yes
E	No	Yes	Yes

Disclosure: M. Balbach: None; **T. Frech**: None; **N. Chadwick**: None; **K. Byram**: None; **E. Chew**: None.

Abstract Number: 1036

The Prevalence of Shoulder and Hip Joints Ultrasound Findings in Polymyalgia Rheumatica: A Multicenter International Study

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Musculoskeletal ultrasound (US) is a validated method for the objective assessment of the pathological changes occurring in PMR. It assists the diagnosis of the disease and increases the performance of 2012 ACR/EULAR classification criteria for PMR(1). The aim of our international multicenter study was to determine the prevalence of US findings characteristic for PMR in a cohort of newly diagnosed PMR patients.

Methods: Our PMR cohort included 390 consecutive clinically diagnosed patients from eight rheumatology centers.At diagnosis, patients underwent a bilateral US examination of shoulder and hip joints. Only patients who had no missing data were included in the analysis. The presence of joint effusion (hip, glenohumeral), bursitis (subdeltoid, trochanteric) and tenosynovitis (long biceps tendon) was recorded.

Results: A complete US examination was performed in 289 PMR patients. Mean (SD) age was 73.1 (9.7) years and 159 patients were female (55.0%). All PMR patients had at least one pathologic US finding. The presence of biceps tendosynovitis (mostly bilateral) was the most frequently recorded abnormality, disclosed in 240 patients (83.0%). The prevalence of individual pathologic US findings is reported in Table 1. The two US items included in the PMR classification criteria "at least 1 shoulder with subdeltoid bursitis and/or biceps tendosynovitis and/or glenohumeral synovitis and at least 1 hip with synovitis and/or trochanteric bursitis" (item 1) and "bilateral shoulder with subdeltoid bursitis, biceps tendosynovitis, or

Pathology	n	% (from 289)	Unilateral / Bilateral (n)
Hip effusion	137	47.4%	44 / 82
Trochanteric bursitis	55	19.0%	18 / 37
Glenohumeral joint effusion	128	44.3%	46 / 82
Subdelotid bursitis	227	78.5%	61 / 166
Biceps tenosynovitis	240	83.0%	56 / 184

n = number of cases

glenohumeral synovitis" (item 2) were fulfilled in 153 cases (52.9 %) and 269 cases (93.1%), respectively. Patients who fulfilled item 1 of US classification criteria had a higher CRP level compared to those who did not ((mean (SD) CRP 59.4 (48.1)vs 42.0 (40.7) mg/l ($p < 0.001$) for patients that not fulfilled this item, since No other associations regarding US criteria, sex, age, ESR and CRP were found.

Conclusion: At least one US abnormality of shoulder or hip joints was found in all our PMR patients, with bilateral tendosynovitis of long biceps tendon being the most common finding 83%. Ultrasound PMR classification criteria were met in 52.9% patients for item 1 and in 93.1% patients for item 2.

References:

1 Dasgupta B et al. 2012 provisional classification criteria for polymyalgia rheumatica: a European League Against Rheumatism/American College of Rheumatology collaborative initiative. Ann Rheum Dis. 2012; 71: 484–92.

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Abstract Number: 1037

Dual Energy Computed Tomography (DECT) Urate Volume Predicts Fulfillment of Gout Remission After Two Years of Intensive Urate-Lowering Therapy

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Imaging of Rheumatic Diseases Poster I

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Preliminary gout remission criteria have been developed using OMERACT core outcome domains for long-term gout studies. This study aimed to identify variables that predict gout remission in patients receiving intensive urate-lowering therapy.

Methods: We analysed data from a 2-year, double-blind randomized controlled trial of 104 people with erosive gout. Participants were randomized to an intensive serum urate target of < 0.20mmol/L or a standard target of < 0.30mmol/L using oral urate-lowering therapies (allopurinol, probenecid, benzbromarone, and febuxostat). All participants had a dual energy CT (DECT) scan of the feet and ankles at baseline. The proportion of participants achieving gout remission according to the preliminary gout remission criteria and simplified gout remission criteria without the patient reported outcomes at Year 1 and Year 2 was calculated **(Table 1).** The simplified gout remission criteria were developed following a qualitative study examining patient perspectives of gout remission. Logistic regression models were used to evaluate independent predictors of gout remission at Year 2; these included baseline variables associated with remission in bivariate analysis and baseline values for each remission domain.

Results: The preliminary gout remission criteria were fulfilled in 11 (11%) of all participants at Year 1 and 21 (23%) of all participants at Year 2. The simplified criteria were fulfilled in 26 (27%) participants at Year 1 and 40 (44%) participants at Year 2. Similar rates of remission were observed in the two randomization groups (P >0.99). In regression models, baseline DECT urate volume was a significant predictor of gout remission at Year 2, using either criteria. Each one cm^3 increase in the baseline DECT urate volume decreased the odds of fulfilling the preliminary gout remission criteria with an odds ratio of 0.65 [95% CI 0.44-0.96], P=0.029. Likewise, each one cm^3 increase in the baseline DECT urate volume decreased the odds of fulfilling the simplified gout remission criteria with an odds ratio of 0.56 [95% CI 0.39-0.77], P< 0.001.

Conclusion: In people with erosive gout on urate-lowering therapy, high baseline MSU crystal volume measured by DECT is associated with lower odds of gout remission after two years of treatment, defined by both the preliminary gout remission criteria and simplified gout remission criteria.

Table 1. Preliminary gout remission criteria (1) and the simplified gout remission criteria used in this analysis

Preliminary gout remission criteria	Simplified gout remission criteria
Absence of gout flares in the last 12 months	Absence of gout flares in the last 12 months
Absence of tophi	Absence of tophi
Serum urate <0.36mmol/L measured at least twice in the last 12 months,	Serum urate <0.36mmol/L measured at least twice in the last 12 months
Pain due to gout <2 at least twice the last 12 months and no value 2 or more, using a 10-cm visual analogue scale or 10-point Likert scale.	
Patient global assessment <2 at least twice the last 12 months and no value 2 or more, using a 10-cm visual analogue scale or 10-point Likert scale.	

1 de Lautour H, et al. Arthritis Care Res (Hoboken). 2016;68:667-72.

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Abstract Number: 1038

Improved Assessment of Structural Damage in the Spine in Patients with Axial Spondyloarthritis by MRI-based Synthetic CT: A Comparison with Low-dose CT and X-ray

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SESSION INFORMATION

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Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Whether a therapy has bone structure-modifying effects in the spine is crucial to determine since this is a prerequisite for a therapy to reduce development of permanent disability in patients with axial spondyloarthritis (axSpA). The current imaging modality for assessing structural progression in axSpA is conventional radiography (X-ray), using the modified Stoke Ankylosing Spondylitis Structural Score (mSASSS). However, this method is only able to show change over a minimum of two years, i.e. has a very low sensitivity to change. Alternative modalities are MRI and CT. MRI, unfortunately, cannot reliably visualize small syndesmophytes. CT is considered the gold standard but delivers substantial ionizing radiation. However, modern CT scanners allow the use of lower radiation doses (low-dose CT, ldCT).

Table 1. Occurrence, sensitivity, and specificity of new bone formation lesions, as detected by various imaging modalities, for each reader

	Number of new bone formation lesions scored (low-dose CT/synthetic CT/x-ray)					*Sensitivity/specificity for synthetic CT (low-dose CT gold standard)*					*Sensitivity/specificity for X-ray (low-dose CT gold standard)*				
Entire spine	All[1] (n=3128)	Anterior (n=782)	Central (n=782)	Posterior (n=782)	Facet joints (n=782)	All[1]	Anterior	Central	Posterior	Facet joints	All[1]	Anterior	Central	Posterior	Facet joints
Reader 1	191/ 209/ 45	141/ 147/ 44	11/ 14/ 0	21/ 32/ 1	18/ 16/ 0	0.76/ 0.93	0.82/ 0.91	0.80/ 0.94	0.48/ 0.92	0.61/ 0.94	0.05/ 0.99	0.06/ 0.97	0/ 1.0	0/ 1.0	0/ 1.0
Reader 2	169/ 262/ 29	114/ 141/ 29	5/ 25/ 0	7/ 17/ 0	43/ 79/ 0	0.46/ 0.96	0.53/ 0.92	0.20/ 0.99	0.14/ 0.98	0.35/ 0.91	0.06/ 0.99	0.04/ 0.97	0/ 1.0	0/ 1.0	0/ 1.0
Reader 3	219/ 170/ 47	188/ 138/ 41	5/ 5/ 1	10/ 13/ 3	16/ 14/ 2	0.57/ 0.99	0.60/ 0.97	0/ 1.0	0.7/ 0.99	0.56/ 0.99	0.07/ 0.99	0.06/ 0.97	0/ 1.0	0.1/ 1.0	0.13/ 1.0
Reader 4	166/ 187/ 28	130/ 143/ 26	8/ 2/ 0	13/ 17/ 2	15/ 25/ 0	0.52/ 0.98	0.65/ 0.94	0/ 1.0	0.07/ 0.99	0.30/ 0.98	0.04/ 0.99	0.04/ 0.98	0/ 1.0	0/ 1.0	0/ 1.0
Cervical & lumbar spine	All[1] (n=1632)	Anterior (n=408)	Central (n=408)	Posterior (n=408)	Facet joints (n=408)	All[1]	Anterior	Central	Posterior	Facet joints	All[1]	Anterior	Central	Posterior	Facet joints
Reader 1	62/ 74/ 43	41/ 44/ 42	4/ 6/ 0	9/ 18/ 1	8/ 6/ 0	0.71/ 0.93	0.73/ 0.92	1.0/ 0.94	0.56/ 0.92	0.63/ 0.94	0.13/ 0.98	0.22/ 0.94	0/ 1.0	0/ 1.0	0/ 1.0
Reader 2	55/ 133/ 27	27/ 61/ 27	2/ 16/ 0	4/ 11/ 0	22/ 45/ 0	0.36/ 0.95	0.48/ 0.92	0.50/ 0.98	0/ 0.98	0.27/ 0.90	0.16/ 0.99	0.15/ 0.96	0/ 1.0	0/ 1.0	0/ 1.0
Reader 3	57/ 74/ 43	41/ 34/ 38	2/ 2/ 0	5/ 9/ 3	9/ 7/ 2	0.49/ 0.99	0.49/ 0.98	0/ 1.0	1.0/ 0.99	0.33/ 0.99	0.25/ 0.99	0.27/ 0.95	0.20/ 1.0	0/ 1.0	0.22/ 1.0
Reader 4	50/ 55/ 24	32/ 31/ 22	2/ 2/ 0	8/ 12/ 2	8/ 10/ 0	0.31/ 0.98	0.53/ 0.98	0/ 1.0	0/ 0.98	0.1/ 0.96	0.08/ 0.99	0.13/ 0.97	0/ 1.0	0/ 1.0	0/ 1.0

[1] Anterior: Anterior vertebral corners, Central: Central vertebral corners, Posterior: posterior vertebral corners, Facet joints

The purpose of this study was, with ldCT as the gold standard reference, to assess and compare the ability of a novel deep-learning MRI-based method ("synthetic CT", sCT), ldCT, and X-ray, in the assessment of structural damage in the spine in patients with axSpA.

Methods: X-ray (lumbar and cervical spine), ldCT, and sCT of the entire spine were performed in patients with axSpA (according to ASAS criteria) in a prospective observational cohort. sCT was made using the BoneMRI application (v1.6, MRIGuidance BV, Utrecht, NL) a quantitative 3D MRI technique based on a multiple gradient-echo sequence and a machine learning processing pipeline that can generate CT-like MR images. All images were scored by four readers for new bone formation (NBF; such as syndesmophytes and ankylosis). NBF was recorded as present vs. absent at the anterior, central, and posterior locations as defined by the Canada Denmark (CANDEN) MRI scoring system for the spine and at the facet joints. Images were anonymized and read blinded to information from other imaging modalities and to clinical information. Readers were trained before the exercise by mutual evaluation of 3 other ldCT and sCT image sets. Sensitivity and specificity of sCT and X-ray were calculated, with ldCT as the gold standard. Inter-reader agreement was assessed using kappa statistics.

Results: 17 patients with axSpA were included (8 women, 9 men; mean age 34.4 ± 9.5 [SD]). The mean overall number of NBF lesions scored was 186 for ldCT, 207 for sCT, and 37 for X-ray. Most findings were located at the anterior vertebral corners with a mean of 143 lesions on ldCT, 142 on sCT, and 35 on X-ray (Table 1). With ldCT as the reference, the overall sensitivity for sCT to detect NBF was 0.58, with a corresponding specificity of 0.97. sCT had the highest sensitivity (0.65) at the

Table 2. Inter-reader agreement (kappa, κ)
(Mean agreement all readers)

	All[1]	Anterior vertebral corners	Central vertebral segment	Posterior vertebral corners	Facet joints
Low-dose CT	0.64	0.68	0.04	0.39	0.50
Synthetic CT	0.39	0.51	0.08	0.13	0.24
X-ray	0.55	0.57	0	0.11	0

[1] Anterior: Anterior vertebral corners, Central: Central vertebral corners, Posterior: posterior vertebral corners, Facet joints

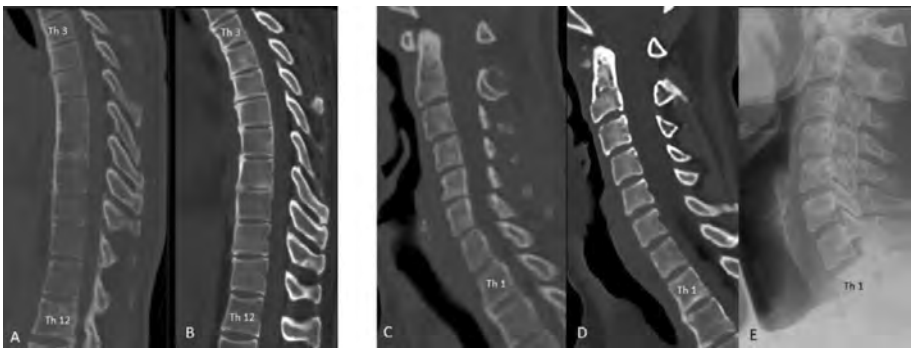

Figure 1: A-B: Low-dose CT (A) and MRI-based synthetic CT (sCT, B) of the thoracic spine. Ankylosis is seen anteriorly at several upper thoracic vertebral levels, with both modalities. C-E: Low-dose CT (C), sCT (D), and X-ray (E) of the cervical spine. Anterior ankylosis is seen at the Th1/Th2 level, both on low-dose CT and sCT, while this level is not visualized adequately by X-ray. Note: Low-dose CT versus sCT slice positioning (A-D) differ slightly at some levels. All images are from the same axSpA patient.

anterior corners (specificity 0.94). For levels that were assessable on X-ray (C2-Th1 and Th12-S1), the sensitivity was 0.47 for sCT and 0.16 for X-ray, with similar high specificities (>0.90) for both methods.

The mean inter-reader agreement for all locations was 0.64 for ldCT, 0.39 for sCT, and 0.55 for X-ray, and best for the anterior corners (Table 2).

Conclusion: MRI-based synthetic CT showed very high specificity and a sensitivity much higher than X-ray, despite limited reader training. With more training, calibration, and optimization of the scoring procedure, sCT could become highly valuable in axSpA clinical trials.

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Abstract Number: 1039

Cross-Sectional Associations of Ultrasound Features with Symptom Outcomes at the Knee: A Community-based Study

Katherine Yates[1], Carolina Alvarez[2], Todd Schwartz[3], Serena Savage-Guin[4], Jordan Renner[4], Catherine Bakewell[5], Minna Kohler[6], Janice Lin[7], Jonathan Samuels[8] and Amanda Nelson[4], [1]University of North Carolina Medical Center, Chapel Hill, NC, [2]University of North Carolina at Chapel Hill, Miami, FL, [3]University of North Carolina-Chapel Hill, Chapel Hill, NC, [4]University of North Carolina at Chapel Hill, Chapel Hill, NC, [5]Intermountain Healthcare, Salt Lake City, UT, [6]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [7]Stanford University, Palo Alto, CA, [8]NYU Langone, Rye Brook, NY

SESSION INFORMATION
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Background/Purpose: Ultrasound (US) allows for visualization of many features of knee osteoarthritis (KOA) including osteophytes, meniscal extrusion, synovitis, and articular cartilage damage. Additionally, US is more sensitive than radiography and less expensive than MRI. The current analysis aimed to determine the association of features of KOA on US with patient reported symptoms and quality of life.

Methods: The Johnston County Health Study (JoCoHS) is an actively enrolling population-based study in Johnston County, North Carolina built on the infrastructure of the longstanding Johnston County Osteoarthritis Project, but with a focus on younger individuals (35-70) and a range of chronic health conditions. All JoCoHS participants provide demographic information, symptomatic and functional assessments (Knee Injury and Osteoarthritis Outcome Score (KOOS)), and imaging (knee US and multiple joint radiographs). Posteroanterior semi-flexed radiographs are read for Kellgren Lawrence Grade (KLG) by an expert musculoskeletal radiologist (JBR). Standardized knee US images are obtained by a trained sonographer (SSG). Each participant's set of images is read by 2 randomly selected expert readers (CJB, MJK, JL, JS) with disagreements adjudicated by a 3rd independent reader. For this preliminary analysis, we took the first US read for each participant (complete

Table 1. Descriptive statistics on person-level characteristics of JoCoHS sample

Knee Injury & Osteoarthritis Outcome Score (KOOS) thinking about your worst knee (N=552)	*n* or mean	*% or ±SD*
Pain subscale, median (IQR)—range=19.4-100 (missing=2)	89.1	(72.2-100)
Pain subscale categories		
100 (none)	175	31.7
75-<100 (mild)	230	41.7
50-<75 (moderate)	100	18.1
25-<50 (severe)	38	6.9
0-<25 (extreme)	7	1.3
Symptoms subscale, median (IQR)—range=14.3-100 (missing=2)	85.7	(67.9-96.4)
Symptoms subscale categories		
100 (none)	117	21.2
75-<100 (mild)	246	44.6
50-<75 (moderate)	147	26.6
25-<50 (severe)	33	6.0
0-<25 (extreme)	7	1.3
ADL function subscale, median (IQR)—range=5.6-100 (missing=1)	88.9	(69.4-100)
ADL function subscale categories		
100 (none)	188	34.1
75-<100 (mild)	207	37.5
50-<75 (moderate)	95	17.2
25-<50 (severe)	47	8.5
0-<25 (extreme)	14	2.5
QOL subscale, median (IQR)—range=0-100 (missing=1)	75.0	(56.3-100)
QOL subscale categories		
100 (none)	159	28.8
75-<100 (mild)	168	30.4
50-<75 (moderate)	125	22.6
25-<50 (severe)	62	11.2
0-<25 (extreme)	37	6.7

SD=standard deviation; IQR=interquartile range

reads are not yet available). The worst US feature score was defined at the person-level and negative binomial models of KOOS outcomes were used to produce adjusted odds ratios and 95% confidence intervals.

Results: The first 552 individuals (33% men, 23% Black, 9% Hispanic, mean age 55 [range 35-70] years, mean BMI 33.1 kg/m^2, 52% with less than a college degree, 33% with previous knee injury) enrolled in the JoCoHS with complete data (1083 knees with at least one US read) were included in this preliminary analysis. About one-third of the knees (330/1083) had radiographic KOA (KLG ≥ 2), while nearly half reported at least some pain, aching, or stiffness. The frequency (n, %) of each of the US features is shown in **Table 1.**

The symptoms and QOL subscales of KOOS were where participants reported the most impactful effects of KOA. Associations between each US feature with KOOS symptoms and Quality of Life subscales are shown in **Table 2.**

Except for the presence of suprapatellar power Doppler (PD), all evaluated US features were associated with worse KOOS scores. Participants with large or very large osteophytes, particularly in the medial joint, were more likely to report worse symptoms and quality of life scores. Lateral cartilage damage of any severity was associated with increased symptoms. Findings followed a similar pattern for other KOOS scales and when adjusted for KLG, although statistical significance was attenuated.

Table 2. Adjusted associations for US features for separate, KOOS outcome models, N=552, K=1083

US Knee feature main effect	KOOS symptoms subscale	KOOS QOL subscale
	IDR (95% CI)	IDR (95% CI)
GS effusion/synovitis (vs no joint capsular distension (JCD))		
1: JCD parallel to bone	1.28 (0.98, 1.67)	1.06 (0.77, 1.47)
2: JCD horizontal	**1.50 (1.12, 2.00)**	1.37 (0.96, 1.96)
3: convex or bulging JCD	1.28 (0.81, 2.03)	1.24 (0.71, 2.16)
GS synovitis (vs no synovitis)		
1: minimal recess distention by abnormal internal anechoic material	1.26 (0.97, 1.65)	1.05 (0.76, 1.46)
2: moderate distention as above, with flat/concave superficial limit	**1.50 (1.12, 2.00)**	1.36 (0.96, 1.94)
3: severe distention as above, with bulging superficial limit	1.24 (0.77, 1.97)	1.23 (0.70, 2.17)
GS effusion	**1.45 (1.18, 1.80)**	**1.38 (1.07, 1.79)**
Suprapatellar PD (vs no intra-articular signal)		
1: trace to 10% of intra-articular area with color signal	0.94 (0.74, 1.19)	0.86 (0.64, 1.15)
2-3: >10% of the intra-articular area filled with color signal	0.89 (0.54, 1.47)	0.92 (0.50, 1.71)
Osteophytes, medial (vs none)		
1: small but distinct	1.16 (0.90, 1.50)	1.14 (0.83, 1.56)
2: larger	**2.02 (1.46, 2.80)**	**1.77 (1.19, 2.63)**
3: very large	**2.11 (1.40, 3.18)**	**2.00 (1.20, 3.33)**
Osteophytes, lateral (vs none)		
1: small but distinct	1.08 (0.84, 1.41)	1.10 (0.79, 1.52)
2: larger	**1.90 (1.41, 2.58)**	**1.72 (1.18, 2.51)**
3: very large	**2.32 (1.38, 3.89)**	1.79 (0.95, 3.41)
Meniscal extrusion, medial	1.23 (0.95, 1.59)	1.07 (0.78, 1.47)
Meniscal extrusion, lateral	1.14 (0.90, 1.45)	1.09 (0.81, 1.45)
Cartilage damage, medial (vs normal cartilage)		
1: minimal thinning	1.03 (0.73, 1.47)	1.10 (0.72, 1.68)
2: mild/local thinning	1.27 (0.88, 1.84)	1.24 (0.79, 1.94)
3: complete loss of cartilage	1.26 (0.79, 2.01)	1.28 (0.72, 2.25)
Cartilage damage, lateral (vs normal cartilage)		
1: minimal thinning	**1.35 (1.01, 1.81)**	1.39 (0.98, 1.99)
2: mild/local thinning	**1.48 (1.06, 2.07)**	**1.50 (1.00, 2.24)**
3: complete loss of cartilage	**1.89 (1.22, 2.94)**	**1.72 (1.00, 2.94)**
Popliteal cyst (vs absent)		
1: small/possible	1.16 (0.92, 1.45)	1.09 (0.82, 1.44)
2: definite	**1.84 (1.21, 2.79)**	1.55 (0.93, 2.60)
Calcium crystal deposition, suprapatellar transverse	1.13 (0.72, 1.77)	1.15 (0.66, 2.00)
Calcium crystal deposition, medial	1.24 (0.82, 1.90)	1.02 (0.61, 1.71)
Calcium crystal deposition, lateral	1.00 (0.73, 1.37)	1.00 (0.69, 1.47)
Calcium crystal deposition, posterior transverse	ne	ne
Double contour sign, suprapatellar transverse	1.17 (0.70, 1.96)	0.99 (0.53, 1.87)

IDR =incidence density ratio; CI=confidence interval; ne=not estimable if <5 cells

IDR >1 indicates how many times worse the KOOS subscale outcome is for US group indicated; significant effects at alpha=0.05 shown in **BOLD**; Person-level, negative binomial models modeling KOOS outcome to produce adjusted odds ratios and 95% confidence intervals, OR (95% CI); All models include covariables for: sex, race/ethnicity, age, BMI, <College degree education, and knee injury.

Conclusion: US features of KOA, except for suprapatellar PD, are associated with worse KOOS scores. Large and very large osteophytes and lateral cartilage thinning are significantly associated with worse patient reported symptoms and decreased quality of life. Future work will provide more accurate population-based estimates for the presence of these features and their effects on patient reported outcomes.

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Abstract Number: 1040

Impact of Ultrasound Limitation to Assess Aortitis in Patients with Giant Cell Arteritis: Comparative Study with FDG-PET/CT

Juan Molina-Collada[1], Isabel Castrejon[2], Irene Monjo[3], Elisa Fernandez-Fernandez[4], Gabriela Torres[5], JULIA MARTINEZ BARRIO[6], Jose María Alvaro-Gracias[7] and Eugenio De Miguel[5], [1]Hospital General Universitario Gregorio Marañón, Madrid, Spain, [2]Hospital Universitario Gregorio Marañón, Madrid, Spain, [3]University Hospital La Paz, Madrid, Spain, [4]La Paz University Hospital, Madrid, Spain, [5]Hospital Universitario La Paz, Madrid, Spain, [6]Rheumatology, Gregorio Marañon University Hospital, Madrid, Spain, [7]Hospital General Universitario Gregorio Marañon, Madrid, Spain

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Background/Purpose: Aortitis is a serious potential complication of patients with giant cell arteritis (GCA) and may lead to dilation, aneurysms or dissection. Since ultrasound (US) has limited access to detect aortitis, comparative studies with other imaging modalities to determine the clinical impact of this limitation and the specific situations warranting their use are needed. Our aim was to determine the impact of US intrinsic limitation to assess aortitis vs FDG-PET/CT in patients with US-proven GCA and to identify factors associated with aortic involvement.

Methods: Retrospective observational study of patients referred to US fast-track clinics at two academic centres over a four-year period. Only patients with GCA confirmed by US were included. Temporal (TA) and extracranial arteries US were performed at baseline. FDG-PET/CT was performed according to clinician's criteria. An FDG artery uptake at the aorta higher than liver uptake was considered positive for aortitis.

Table 1. Clinical, laboratory and histology findings of patients with and without aortic involvement.

	Total n=72	Patients with aortic involvement in FDG-PET/CT n=24 (33.3%)	Patients without aortic involvement in FDG-PET/CT n=48 (66.7%)	p
Demographics				
Age, mean (SD)	77 (9.1)	68.9 (8.1)	81 (6.5)	**<0.001**
Female, n (%)	38 (52.8%)	19 (79.2%)	19 (39.6%)	**0.002**
Clinical variables				
PMR diagnosis before US examination, n (%)	15 (20.8%)	3 (12.5%)	12 (25%)	0.432
Headache, n (%)	49 (68.1%)	14 (58.3%)	35 (72.9%)	0.211
Scalp tenderness, n (%)	16 (22.2%)	3 (12.5%)	13 (27.1%)	0.232
Jaw claudication, n (%)	16 (22.2%)	4 (16.7%)	12 (25%)	0.423
Visual symptoms, n (%)	15 (20.8%)	0 (0%)	15 (31.2%)	**0.001**
Ocular ischaemia, n (%)	6 (8.3%)	0 (0%)	6 (12.5%)	0.07
Constitutional symptoms, n (%)	42 (58.3%)	17 (70.8%)	25 (52.1%)	0.128
Fever, n (%)	19 (26.4%)	9 (37.5%)	10 (20.8%)	0.130
Morning stiffness in shoulders/neck, n (%)	38 (52.8%)	10 (41.7%)	28 (58.3%)	0.182
Abnormal TA clinical examination, n (%)	11 (15.3%)	3 (12.5%)	8 (16.7%)	0.643
Fulfilled 1990 ACR GCA classification criteria, n (%)	38 (52.8%)	9 (37.5%)	29 (60.4%)	0.066
Fulfilled 2022 ACR/EULAR GCA classification criteria, n (%)	68 (94.4%)	22 (91.7%)	46 (95.8%)	0.467
Laboratory findings				
CRP (mg/L), mean (SD)	85.8 (79.6)	101.8 (77.8)	77.8 (80.4)	0.230
ESR (mm/h), mean (SD)	68.6 (33.6)	69.7 (31.8)	68 (34.7)	0.839
Haemoglobin (g/dL), mean (SD)	11.9 (1.6)	11.5 (1.5)	12.1 (1.7)	0.139
Platelets 10^9/L, mean (SD)	345.7 (152.1)	413.4 (169.7)	311.11 (131.1)	**0.014**
Histology				
Temporal artery biopsy positive n=22, n (%)	9 (40.9%)	2 (28.6%)	7 (46.7%)	0.421

Table 2. US patterns of vascular involvement in patients with or without aortitis in FDG-PET/CT.

	Total n=72	Patients with aortic involvement in FDG-PET/CT n=24 (33.3%)	Patients without aortic involvement in FDG-PET/CT n=48 (66.7%)	p
Positive cranial GCA US, n (%)	50 (69.4%)	10 (41.7%)	40 (83.3%)	**<0.001**
Positive LV-GCA US, n (%)	42 (58.3%)	22 (91.7%)	20 (41.7%)	**<0.001**
Negative LV-GCA US, n (%)	30 (41.7%)	2 (8.3%)	28 (58.3%)	**<0.001**
Isolated positive LV-GCA US, n (%)	22 (30.6%)	14 (58.3%)	8 (16.7%)	**<0.001**
Positive cranial + LV-GCA US, n (%)	20 (27.8%)	8 (33.3%)	12 (25%)	0.457

GCA: giant cell arteritis; US: ultrasound; LV: large-vessel.

Results: Seventy-two of 186 patients with US-proven GCA underwent an FDG-PET/CT; 29 (40.3%) had a positive FDG-PET/CT and 24 (33.3%) presented aortitis. Only 6 (20.7%) patients with positive FDG-PET/CT had negative US findings of large vessel (LV)-GCA. Among patients with aortitis in FDG-PET/CT, only 2 (8.3%) had negative US findings of LV-GCA. Patients with aortitis were younger (68.9 *vs* 81;p< 0.001), more frequently females (79.2% *vs* 39.6%;p=0.002) and had higher platelets count (413.4 *vs* 311.1;p=0014) (Table 1). Patients with aortitis presented positive TA US less frequently (41.7% *vs* 83.3%;p< 0.001), but more LV US involvement (91.7% *vs* 41.7%; p< 0.001) versus patients without aortitis (Table 2). None of the patients with aortitis exhibited visual symptoms (0% *vs*31.2%;p=0.001).

Conclusion: FDG-PET/CT can detect aortitis in 1 out of every 3 patients with US-proven GCA. However, a negative US examination for LV-GCA suggests a low risk of aortitis. Younger and female GCA patients with thrombocytosis, absence of visual manifestations and LV-GCA on US may more frequently present aortitis by FDG-PET/CT.

Disclosure: J. Molina-Collada: None; **I. Castrejon**: Bristol Myers Squibb, 1, 6, Galapagos, 2, GlaxoSmithKline, 1, 6, Lilly, 1, 6, Merck Sharp & Dohme, 6, Pfizer, 1, 2, 6; **I. Monjo**: Amgen, 6, Gedeon Richter, 6, Janssen, 6, Novartis, 6, Roche, 6, UCB, 6; **E. Fernandez-Fernandez**: None; **G. Torres**: None; **J. MARTINEZ BARRIO**: None; **J. Alvaro-Gracias**: Abbvie, 2, 6, AstraZeneca, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, GSK, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **E. De Miguel**: None.

Abstract Number: 1041

Efficacy of Apremilast on Peripheral and Axial Inflammation in Patients with Psoriatic Arthritis Based on Whole-Body Magnetic Resonance Imaging

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SESSION INFORMATION

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Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: Poster Session B
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Background/Purpose: Apremilast is an oral phosphodiesterase 4 inhibitor with a unique immunomodulatory mechanism of action and is approved for the treatment of psoriatic arthritis (PsA). Whole-body magnetic resonance imaging (WB-MRI) is a promising tool for inflammatory arthritis management and may provide a more thorough picture of total inflammatory burden than standard MRI or clinical assessment. Here, we evaluate the efficacy of apremilast 30 mg BID (APR) on peripheral and axial inflammation in patients with PsA.

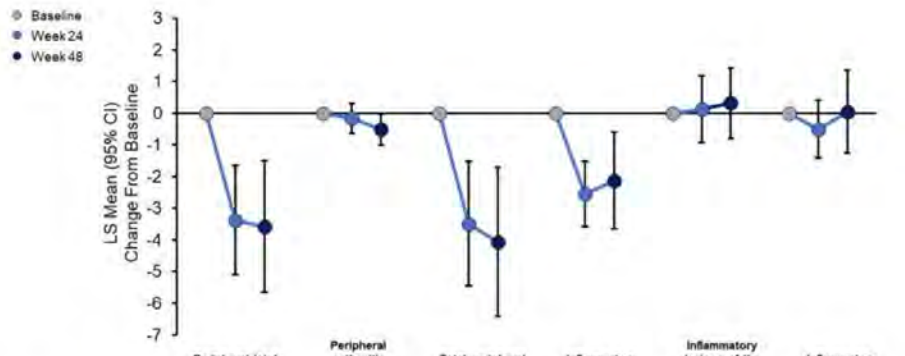
Methods: The MOSAIC study was a phase 4, multicenter, single-arm, open-label trial that evaluated up to 48 weeks of APR treatment (monotherapy or with stable methotrexate) on MRI outcomes in patients with active PsA (≥3 months but ≤5 years since diagnosis, meeting the CASPAR criteria for PsA). Contrast-enhanced WB-MRI was performed at baseline, Week 24, and Week 48, and images were read and adjudicated by two blinded, experienced readers. Using the OMERACT MRI whole-body scoring system for inflammation in peripheral joints and entheses (MRI-WIPE), WB-MRI results were used to calculate the change from baseline in the peripheral enthesitis inflammation index (33 entheses), peripheral joint inflammation index (83 joints), and total peripheral inflammation index (enthesitis + joint inflammation). In patients deemed to have PsA spondylitis by the investigator and a baseline BASDAI Item 2 (pain) ≥4), MRI axial inflammation was assessed by calculating

Table 1. Demographics and Baseline Characteristics

Parameter	APR N=122
Age, mean (SD), y	46.6 (12.9)
Female, n (%)	67 (54.9)
Weight, mean (SD), kg	84.9 (21.2)
Duration of PsA, mean (SD), y	1.9 (1.7)
BASDAI score[a], mean (SD)	6.4 (1.5)
WB-MRI measures	—
Total peripheral inflammation index[b], mean (SD)	28.8 (22.5)
Peripheral enthesitis inflammation index[c], mean (SD)	4.7 (3.7)
Peripheral joints inflammation index[d], mean (SD)	24.1 (20.3)
CANDEN spine inflammation score[e,f], mean (SD)	5.8 (11.6)
SPARCC sacroiliac joint inflammation score[e,g], mean (SD)	2.7 (5.0)
SPARCC spine score[e,h], mean (SD)	5.4 (10.9)

APR, apremilast 30 mg BID; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BME, bone marrow edema; CANDEN, Canada-Denmark scoring system; PsA, psoriatic arthritis; SD, standard deviation; SPARCC, Spondyloarthritis Research Consortium of Canada scoring system; WB-MRI, whole-body magnetic resonance imaging.
[a]BASDAI score calculated for patients deemed to have PsA spondylitis by the investigator and a BASDAI item 2 ≥4 at baseline, n=40.
[b]Sum of the peripheral joint inflammation index (BME + synovitis in 83 joints) and peripheral enthesitis inflammation index (BME and soft tissue inflammation at 33 entheses). Score ranges from 0 to 738.
[c]Includes BME and soft tissue inflammation at 33 entheses. Score ranges from 0 to 201.
[d]Includes BME and synovitis in 83 joints. Score ranges from 0 to 537.
[e]Based on patients deemed to have PsA spondylitis by the investigator and a BASDAI item 2 ≥4 at baseline.
[f]Score ranges from 0 to 614, with higher scores reflecting greater disease activity.
[g]Score ranges from 0 to 72, with higher scores reflecting greater disease activity.
[h]Score ranges from 0 to 414, with higher scores reflecting greater disease activity.

Figure 1. Peripheral and Axial Inflammation Indices as Assessed by WB-MRI (FAS)[a]



	Peripheral joint inflammation index[a]		Peripheral enthesitis inflammation index[b]		Total peripheral inflammation index[c]		Inflammatory lesions of the spine (CANDEN)[d,e]		Inflammatory lesions of the sacroiliac joint (SPARCC)[d,f]		Inflammatory lesions of the spine (SPARCC)[d,g]	
Baseline Mean (SD)	n=117	24.1 (20.3)	n=117	4.7 (3.7)	n=117	28.8 (22.5)	n=39	5.8 (11.6)	n=39	2.7 (5.0)	n=39	5.4 (10.9)
Week 24 LS Mean Change (95% CI)	n=100	-3.4 (-5.1, -1.7)	n=100	-0.2 (-0.7, 0.3)	n=100	-3.5 (-5.5, -1.5)	n=32	-2.6 (-3.6, -1.5)	n=32	0.1 (-0.9, 1.2)	n=32	-0.5 (-1.4, 0.4)
Week 48 LS Mean Change (95% CI)	n=84	-3.6 (-5.7, -1.5)	n=84	-0.5 (-1.0, -0.02)	n=84	-4.1 (-6.4, -1.7)	n=27	-2.1 (-3.7, -0.6)	n=27	0.3 (-0.8, 1.4)	n=27	0.04 (-1.3, 1.4)

Full analysis set, defined as all patients who received at least one dose of study medication. Based on mixed-effect model for repeated measures with change from baseline as the response variable and including scanner type, time as fixed effects, baseline composite score as a covariate.
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BME, bone marrow edema; CANDEN, Canada-Denmark scoring system; LS, least-squares; PsA, psoriatic arthritis; SD, standard deviation; SPARCC, Spondyloarthritis Research Consortium of Canada scoring system; WB-MRI, whole-body magnetic resonance imaging.
[a]Includes BME and synovitis in 63 joints. Score ranges from 0 to 537.
[b]Includes BME and soft tissue inflammation at 33 entheses. Score ranges from 0 to 201.
[c]Sum of the peripheral joint inflammation index (BME + synovitis in 63 joints) and peripheral enthesitis inflammation index (BME and soft tissue inflammation at 33 entheses). Score ranges from 0 to 738.
[d]Based on patients deemed to have PsA spondylitis by the investigator and a BASDAI item 2 ≥4 at baseline.
[e]Score ranges from 0 to 614, with higher scores reflecting greater disease severity.
[f]Score ranges from 0 to 72, with higher scores reflecting greater disease severity.
[g]Score ranges from 0 to 414, with higher scores reflecting greater disease activity.

the change from baseline in the Canada-Denmark (CANDEN) spine score, the Spondyloarthritis Research Consortium of Canada (SPARCC) spine score, and the SPARCC sacroiliac joint (SIJ) inflammation score.

Results: A total of 122 patients were enrolled and treated with APR. Demographics and baseline disease characteristics are shown in **Table 1**. WB-MRI results showed significant reductions in peripheral joint inflammation at 24 and 48 weeks, and a significant reduction in peripheral enthesitis at 48 weeks (**Figure 1**). Taken together, a significant reduction in the total peripheral inflammation index was observed at both 24 and 48 weeks (**Figure 1**). At baseline, 40 patients were deemed by the investigator to have PsA spondylitis and a BASDAI Item 2 ≥4; 39 patients were analyzed for axial inflammation. WB-MRI using the CANDEN scoring system showed a reduction in axial inflammation at 24 and 48 weeks (**Figure 1**). There was no significant change in either SPARCC spine or SPARCC SIJ scores (**Figure 1**).

Conclusion: This is the first PsA study applying WB-MRI of both peripheral and axial joints and entheses. Patients treated with APR experienced significant improvement from baseline in peripheral joint and entheseal inflammation. These outcomes demonstrate the efficacy of APR on inflammatory manifestations of PsA and the value of using WB-MRI as an objective measure in PsA management.

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Squibb, 12, Investigator, Celgene, 2, Eli Lilly, 2, Genentech, 2, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, Merck, 2, MLKCDT, 12, Investigator, Novartis, 2, Pfizer, 2, Regeneron, 2, Sanofi, 2, UCB, 2; **M. Bubb**: Amgen, 5, Bristol-Myers Squibb, 5, Eli Lilly, 5, Gilead, 5, GlaxoSmithKline, 5, Janssen, 5, Novartis, 5, Pfizer, 5, UCB, 5; **O. Kubassova**: Image Analysis Group, 3, 11; **J. Reddy**: Amgen, 3, 11; **S. Colgan**: Amgen, 3, 11; **Y. Klyachkin**: Amgen, 3, 11; **C. Deignan**: Amgen, 3, 11; **Z. Zhou**: Amgen Inc., 3, 11; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2.

Abstract Number: 1042

B-line of Lung Ultrasound Reflects Different Morphological Features on Chest HRCT Between Interstitial Lung Disease Associated with Systemic Sclerosis and Myositis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Session Type: Poster Session B
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Background/Purpose: Lung ultrasound (LUS) is a non-invasive imaging tool to evaluate distribution and severity of interstitial lung disease (ILD). Utility of LUS has been examined mainly in patients with systemic sclerosis (SSc), and B-line scores assessed by LUS were shown to correlate with semiquantitative scores of chest high-resolution computed tomography (HRCT). However, little is known about performance of LUS in ILD associated with idiopathic inflammatory myopathy (IIM) or anti-synthetase syndrome (ASS). The aim of this study was to investigate utility of LUS in patients with IIM/ASS, by focusing on correlations of B-line score with morphological features on HRCT.

Methods: A total of 64 patients, including 30 with SSc-ILD and 34 with IIM/ASS-ILD were selected from a prospective LUS registry of Nippon Medical School Hospital based on fulfillment of one of classification criteria for SSc, IIM, or ASS and availability of chest HRCT and LUS images performed simultaneously. The degree of B-line was semiquantitatively scored using a 4-8 MHz microconvex transducer, and a sum of the B-line at 14 scan sites was used as a total B-line score. ILD images on HRCT were scored according to the method proposed by the Scleroderma Lung Study (SLS) by two investigators in a

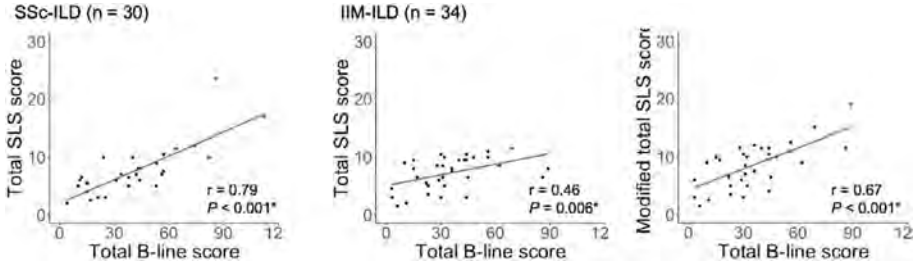

Figure 1. Single regression analysis to evaluate correlation between total B-line score and HRCT semiquantitative score. LUS: lung ultrasound; HRCT: high-resolution computed tomography; SSc systemic sclerosis; IIM: idiopathic inflammatory myopathy; ASS: anti-synthetase syndrome; ILD: interstitial lung disease; SLS: Scleroderma Lung Study. *P < 0.05

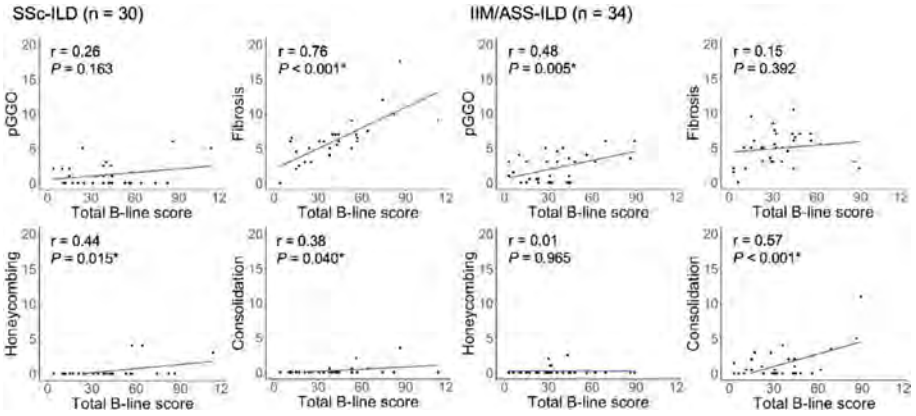

Figure 2. Single regression analysis to evaluate correlation between total B-line score and SLS scores of individual morphologies by underlying disease. SSc: systemic sclerosis; IIM: idiopathic inflammatory myopathy; ASS: anti-synthetase syndrome; ILD: interstitial lung disease; pGGO: pure ground-glass opacity; LUS: lung ultrasound; SLS: Scleroderma Lung Study. * P < 0.05

blinded fashion. The scores assessed included pure ground-glass opacity (pGGO), fibrosis, honeycombing, and consolidation, and the sum of pGGO, fibrosis, and honeycombing scores was regarded as total SLS score. In some analyses, the original SLS score was modified to include the consolidation score. Single regression analysis was used to evaluate correlations of total B-lines with SLS scores of individual morphologies and the total score. Multiple regression analysis was carried out to identify independent morphological features of HRCT contributing to total B-lines.

Results: Total B-line score correlated with total SLS score in patients with SSc-ILD (r = 0.79, P < 0.001), but the correlation was much weaker in patients with IIM/ASS-ILD (r = 0.46, P = 0.006) (Figure 1). When correlations of total B-line score with individual morphological patterns on HRCT were examined, total B-line score was significantly correlated with fibrosis (r = 0.76, P < 0.001) and weekly with honeycombing (r = 0.44, P = 0.015) and consolidation (r = 0.38, P = 0.040) in patients with SSc-ILD. On the other hand, in patients with IIM/ASS-ILD, total B-line score was correlated with pGGO (r = 0.48, P = 0.005) and consolidation (r = 0.57, P < 0.001) (Figure 2). Multiple regression analysis revealed contribution of different morphological patterns on HRCT to total B-line score: fibrosis (β = 0.743, P < 0.001) and honeycombing (β = 0.326, P = 0.007) in SSc-ILD, while consolidation (β = 0.497, P = 0.006) and fibrosis (β = 0.320, P = 0.040) in IIM/ASS-ILD. Finally, inclusion of the consolidation score in the original total SLS score resulted in improvement of correlation with total B-line score in patients with IIM/ASS-ILD (r = 0.67, P < 0.001) (Figure 1).

Conclusion: B-lines detected by LUS reflect different HRCT morphological features in patients with SSc and IIM/ASS. This difference should be considered upon interpreting total B-lines upon evaluation of ILD in clinical practice.

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Abstract Number: 1043

Comparison of Optical and Ultrasound Imaging in Lupus Arthritis

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SESSION INFORMATION
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Background/Purpose: Almost all patients with SLE experience joint problems and arthritis, 12% suffer permanent joint damage. The wide variability in SLE arthritis and the limitations of existing assessment tools make it difficult to identify musculoskeletal involvement in clinical care and clinical trials. Identifying lupus arthritis based on physical exam remains challenging. Clinicians need a robust, easy-to-use imaging technique to diagnose and monitor arthritis in SLE. Ultrasound (US) and magnetic resonance (MRI) allow for more objective assessments but are plagued by operator dependence and high cost. With the support of a DoD award, we are developing a prototype imaging system that uses lasers and light detectors to evaluate finger joints in SLE. Here we describe preliminary data on comparisons between optical imaging and US evaluations of affected and unaffected proximal interphalangeal (PIP) joints.

Methods: Fifteen SLE patients were evaluated, 8 PIP joints (bilateral PIP 2-5)/patient were imaged, with a total of 120 images. A systematic multiplanar grey-scale (GS) and power doppler (PD) examination of PIP joints was performed using the Outcome Measures in Rheumatology (OMERACT) consensus definitions for joint pathologies, and a combined PDGS score was calculated. Immediately after the US, joints were examined using optical imaging. The instrumentation uses a 670nm, 8mW laser with a 1 mm diameter beam modulated at 300 MHz as light source. The laser beam is focused on the dorsal surface of each finger and scans across the PIP joints (as shown in Figure 1, left). The transmitted light is collected by an intensified charge-coupled device camera and the absorption and scattering distributions inside the finger are reconstructed (Fig.1 shows absorption) using a radiative transfer equation model.

Results: The PDGS scored 34 joints 0, 44 – 1, 20 – 2 and 22 – 3. The absorption and scattering data were obtained from the reconstructed images. Figure 2 shows a cross section through an unaffected joint (PDGS=0) on the left and an affected joint (PDGS=3) on the right. The average absorption coefficient of joints with PDGS = 0 or 1 was 0.52±0.19 cm^{-1}, while joints with

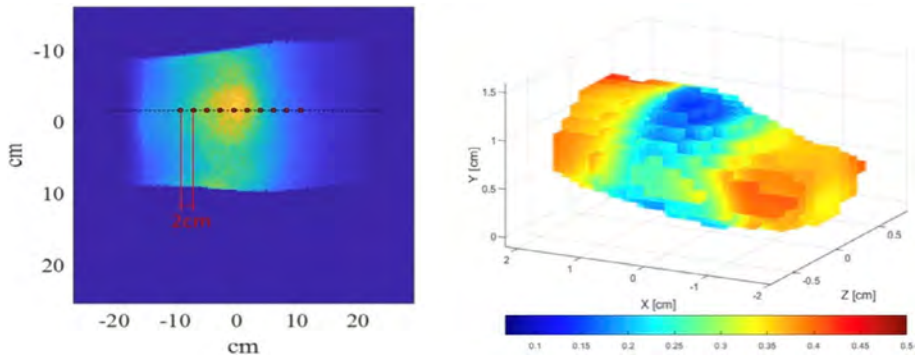

Figure 1. Left, example of the collected raw signal from the system, with the red dots indicating the different positions of the laser during the acquisition protocol. Right, example of a three-dimensional reconstruction of a joint's absorption properties.

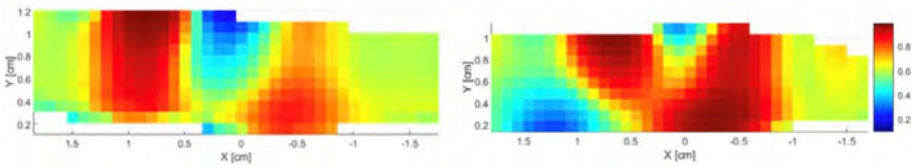

Figure 2. Representative cross-sectional images of "unaffected" (PDGS=0, left) and "affected" (PDGS=3, right) PIP joints absorption properties.

PDGS = 2 or 3 the absorption was 0.60±0.19 cm^{-1}, $p < 0.05$. Similarly, we found that the difference in the scattering coefficients between the two groups was also statistically significant (10.8±1.9 cm^{-1} versus 11.8±2.1 cm^{-1}, $p< 0.01$).

Conclusion: Optical imaging correlated with PDGS findings in 120 evaluated lupus arthritis PIP joints. Further examination of SLE arthritis using the new US OMERACT criteria that includes a tenosynovitis score and MRI will allow for better definitions of PIP arthritis and improve the correlations with optical imaging. The system, which could take the form of an ergonomic glove, will allow the investigators to image lupus arthritis, both in the office and at home, to diagnose and monitor arthritis progress. The goal is to create a portable, wearable, imaging device that permits real-time monitoring of SLE arthritis to improve patient care and outcomes.

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Abstract Number: 1044

Prevalence and Distribution of Sonographic Elementary Lesions in PsA – Results of 2 Cohorts

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Imaging of Rheumatic Diseases Poster I
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Background/Purpose: Psoriatic arthritis (PsA) can manifest with different musculoskeletal (MSK) features. Ultrasound (US) optimizes the assessment of the different MSK features in PsA. However, there is no consensus on which MSK sonographic lesions and what locations should be evaluated by US. The group for research and assessment of psoriasis and psoriatic arthritis (GRAPPA) have set a goal of defining the most prevalent locations for the various US lesions in order to reduce the number of scanned sites.

The aim of the study was to describe the prevalence and distribution of key sonographic MSK lesions in patients with PsA.

Methods: This study analyzed data from two prospectively recruited PsA cohorts. Cohort 1 included 101 patients with active PsA (DAPSA >14) and cohort 2 included 94 patients with active PsA prior to initiation of therapy. All underwent a comprehensive US assessment, including both gray scale (GS) and power Doppler (PD) of 50 joints, 40 tendons and

14 entheses. The following sonographic lesions were assessed by two sonographers blinded to clinical data: I. Inflammatory lesions - synovitis, tenosynovitis, peritenonitis and enthesitis and II. Structural lesions – periarticular erosions and bone proliferations. Presence or Absence of these lesions was determined based on previously suggested definitions by OMERACT (when available) or other publication and their prevalence by joint/tendon site was reported.

Results: In cohort 1, mean ± SD age was 52.7 ± 13 and 55.7% were females. In cohort 2, mean ± SD age was 47.5 ± 13.2 and 48.8% were females (Table 1). The most prevalent locations of the inflammatory lesions in both cohorts were (figure 1): Synovitis (small joints) – MCP2 (cohort 1: 13.5%, cohort 2: 27%), MCP 3 (cohort 1: 11%, cohort 2: 26%), IP1 (cohort 1: 5%, cohort 2: 24.5%) PIP 3 (cohort 1:3%, cohort 2: 16%), MTP 1 (cohort 1: 35.5%, cohort 2: 35%), MTP2 (cohort 1: 24%, cohort 2: 30%), MTP3 (cohort 1: 18.5%, cohort 2: 22%); Synovitis (medium-large joints) – wrist (cohort 1: 31.5%, cohort 2: 29%)

Table 1: Baseline and clinical characteristics

	Cohort 1 (n=101)	Cohort 2 (n=94)
Age, years, mean (± SD)	52.7 (13)	47.5 (13.2)
Sex (%)	55.7	48.8
PsA duration, years, mean (± SD)	12 (12)	3.8 (17)
Tender joint count, mean (± SD)	12 (10)	7 (5)
Swollen joint count, mean (± SD)	2 (3)	5 (3)
Enthesitis (SPARCC), mean (± SD)	3.8 (4)	2 (2)
CRP mg/dl	1 (2)	0.9 (1)
DAPSA	29 (13)	30 (21)
Current cDMARD therapy, n (%)	42 (41.6)	22 (23.4)
Current Biologic therapy, n (%)	31 (30.7)	1 (1.1)

DAPSA – Disease activity in Psoriatic Arthritis; cDMARD – conventional Disease Modifying anti-Rheumatic Drugs

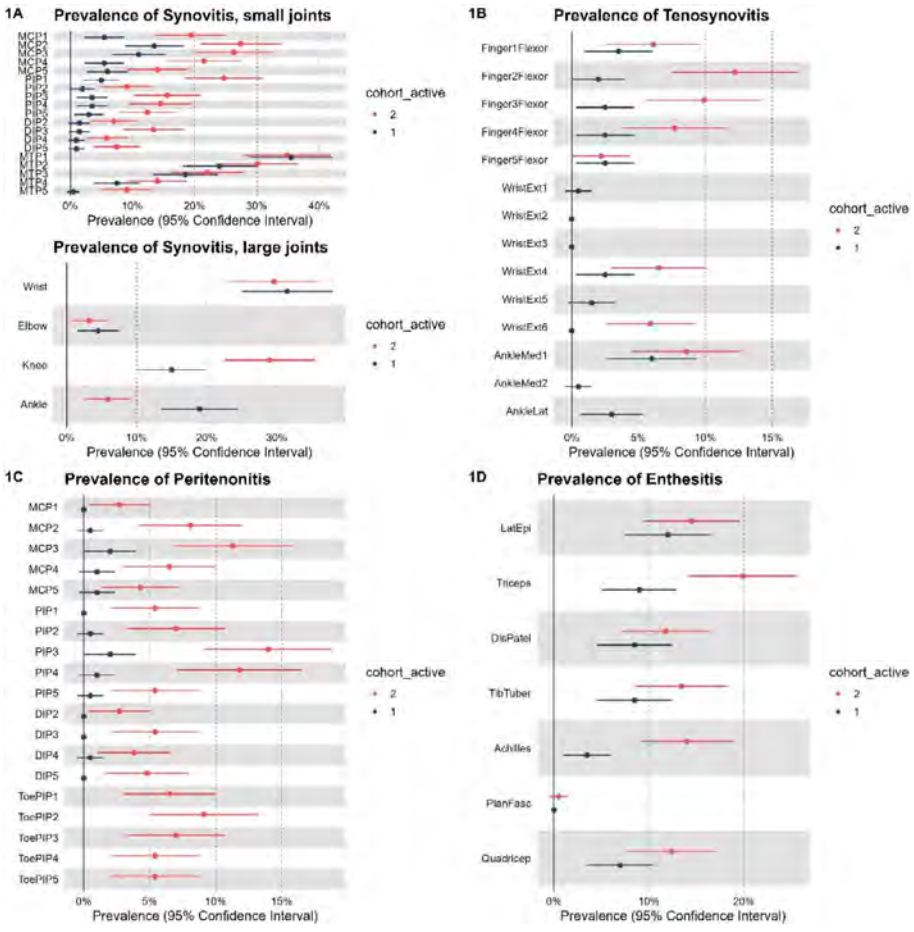

Figure1: Prevalence and distribution of sonographic inflammatory lesions in PsA

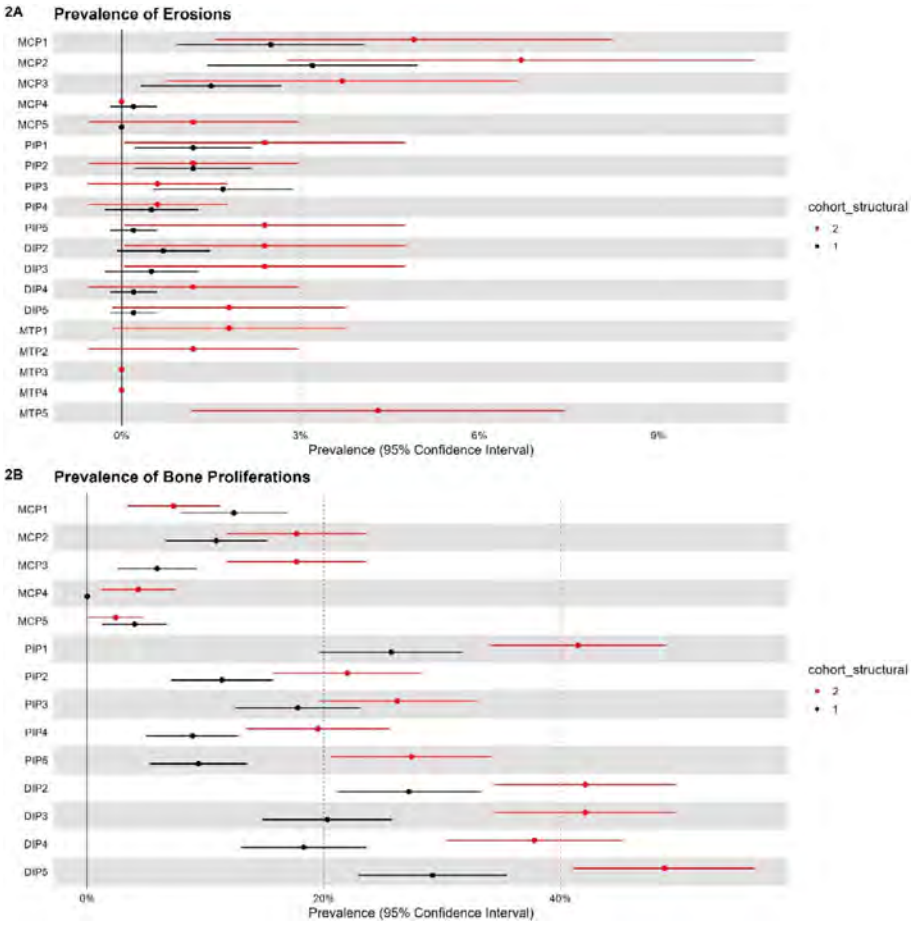

Figure2: Prevalence and distribution of sonographic structural lesions in PsA

and knee (cohort 1: 15%, cohort 2: 29%); Tenosynovitis – 2nd finger flexors (cohort 1: 2%, cohort 2: 8%) 3rd finger flexor (cohort 1: 2%, cohort 2: 6%), extensor digitorum (cohort 1: 2.5%, cohort 2: 6%), tibialis posterior (cohort 1: 6%, cohort 2: 8.5%); extensor peritenonitis –MCP3 (cohort 1: 2%, cohort 2: 12%), PIP 3 (cohort 1: 2%, cohort 2: 14%), PIP4 (cohort 1: 1%, cohort 2: 12%); Enthesitis – lateral epicondyle (cohort 1: 12%, cohort 2: 14%) and triceps (cohort 1: 9%, cohort 2: 20%). The most prevalent locations of the structural lesions (figure 2): Erosions – MCP1 (cohort 1: 4%, cohort 2: 4%), MCP2 (cohort 1: 6.5%, cohort 2: 6%), MCP3 (cohort 1: 3%, cohort 2: 3%), MTP5 (cohort 2: 4%); Bone proliferations – IP1 (cohort 1: 25%, cohort 2: 36%), DIP2 (cohort 1: 27.5%, cohort 2: 37%), DIP3 (cohort 1: 19.5%, cohort 2: 37%) and DIP5 (cohort 1: 28%, cohort 2: 44%).

Conclusion: This descriptive study provides comprehensive information on the most commonly affected sites for key inflammatory and structural domains in PsA. This information can inform efforts to develop reduced sonographic score to diagnose or monitor disease activity in PsA.

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Abstract Number: 1045

Ultrasound Findings in Patients with Difficult to Treat Rheumatoid Arthritis

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SESSION INFORMATION

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Background/Purpose: In recent years, the concept of D2T RA (difficult-to-treat rheumatoid arthritis) has become widespread, and D2T RA patients are defined as a state in which activity cannot be controlled even with the use of various molecular-targeted drugs. In this study, we investigated the ultrasound synovial findings in D2T RA patients. However, ultrasound findings in D2T RA patients are unknown. In this study, we investigated the ultrasound findings of D2T RA patients.

Methods: A total of 750 RA patients who underwent ultrasound examination from January 2017 to August 2020 were continuously included. Ultrasound examination was performed at the of bilateral first to fifth metacarpophalangeal (MCP) joints, first interphalangeal (IP) and second to fifth proximal interphalangeal (PIP) joints, wrist joints (three part of radial, medial and

Table 1. Patients characteristics of D2T RA and non D2T RA patients

	D2TRA (n=40)	non D2TRA (n=477)	p value
Age (years)	61.2±17.3	65.0±14.1	0.113
Female, %	77.5	82.1	0.390
BMI (kg/m²)	22.5±4.9	22.3±3.4	0.750
Disease duration (years)	17.6±9.6	14.9±12.7	0.199
RF+, %	95.0	89.9	0.410
RF titer (mg/dL)	754.3±1284.7	301.2±423.4	0.032
CCP+, %	94.8	85.2	0.144
CCP titer (U/mL)	227.0±183.2	134.0±165.6	0.001
MTX use, %	50.0	70.9	0.011
MTX dose (mg/week)	8.9±2.6	9.2±3.6	0.581
Glucocorticoid use, %	32.5	12.6	0.002
Glucocorticoid dose (mg/day)	7.7±4.4	3.1±1.8	0.003
DAS28 ESR	3.2±1.9	3.0±1.4	0.668
DAS28 CRP	2.8±1.4	2.7±1.2	0.438
SDAI	13.4±12.6	10.1±9.5	0.120
CDAI	12.6±12.0	9.8±9.3	0.166
HAQ	0.90±0.98	0.66±0.74	0.137
ESR (mm/h)	26.2±30.2	17.6±20.6	0.085
CRP (mg/dL)	0.79±2.67	0.28±0.77	0.233
MMP-3 (ng/mL)	295.6±611.9	105.8±157.2	0.057
GSUS	16.2±15.7	9.5±9.5	0.011
PDUS	11.0±13.0	6.4±7.7	0.034

ulnar) and first to fifth metatarsophalangeal (MTP) joints. Both grayscale (GS) and power Doppler (PD) findings were scored to grade 0-3 by a semi-quantitative method, and the sum of GS was defined as the GSUS score and the sum of PD as the PDUS score. Of all 750 RA patients, 517 RA patients (68.9%) who treated bDMARDs/JAKi were included and devided in D2T RA patients and non-D2T RA patients. The patients' characteristics, GSUS and PDUS score were compared between D2T RA patients and non-D2T RA patients.

Results: There were 40 D2T RA patients and 477 non-D2T RA patients. Mean age was 61.2 vs. 65.0 years (p=0.133), mean disease duration of RA was 17.6 vs. 14.9 years (p=0.199), CDAI was 12.6 vs. 9.8 (0.166), and CRP level was 0.79 vs. 0.28 mg/dL (p=0.233), MMP-3 level was 295.6 vs 10.8ng/mL (p=0.057), respectively. In the D2T RA group, concomitant use ratio of MTX was low (50.0 vs 70.9 %, p=0.011), but there was no difference in the average dose of MTX (8.9 vs 9.2 mg/w, p=0.581). The concomitant use ratio of glucocorticoid (32.5 vs 12.6 %, p=0.002) and the average dose of glucocorticoid (7.7 vs 3.1 mg/d, p=0.003) were higher in D2T RA group. Regarding ultrasound findings, GSUS score (16.2 vs 9.5, p=0.011) and PDUS score (11.0 vs 6.4, p=0.034) were significantly higher in the D2T RA group.

Conclusion: The definition of D2T RA is resistant to multiple mode of bDMARDs/JAKi. Although, disease activity and inflammatory markers tended to be worse in the D2T RA group, there was no statistically significant difference in this study. However, ultrasound findings were significantly worse in D2T RA. Suppression of synovitis might be important to prevent D2T RA.

Disclosure: T. Okano: None; **K. Mamoto**: None; **Y. Yamada**: None; **S. Anno**: None; **A. Yagami**: None; **Y. Domae**: None; **S. Washida**: None; **Y. Yoshida**: None; **T. Koike**: None; **H. Nakamura**: None.

Abstract Number: 1046

The Level of RF or Anti-CCP Antibody Affect Ultrasound Synovial Findings in Patients with Rheumatoid Arthritis?

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Background/Purpose: Positive for auto-antibodies such as rheumatoid factor (RF) and anti-citrullinated peptide antibodies (CCP) or having high autoantibody titers is associated with the progression of joint destruction in patients with rheumatoid arthritis (RA) (van Steenbergen HW, et al. Ann Rheum Dis. 2015;74:e3. and Hecht C, et al. Ann Rheum Dis. 2015;74:2151-6.). Therefore, we evaluated the relationship between RF or CCP levels and ultrasound synovial findings.

Methods: A total of 750 RA patients who underwent ultrasound examination from January 2017 to August 2020 were continuously included. Ultrasound examination was performed at the of bilateral first to fifth metacarpophalangeal (MCP) joints, first interphalangeal (IP) and second to fifth proximal interphalangeal (PIP) joints, wrist joints (three part of radial, medial and ulnar) and first to fifth metatarsophalangeal (MTP) joints. Both grayscale (GS) and power Doppler (PD) findings were scored to grade 0-3 by a semi-quantitative method, and the sum of GS was defined as the GS score and the sum of PD as the PD

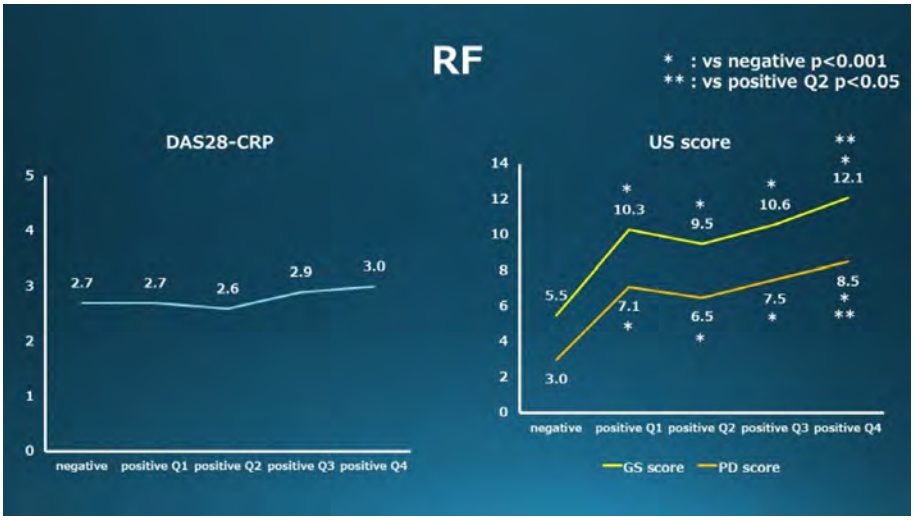

Figure 1. The relattionship between RF titer and disease activity or ultrasound findings.

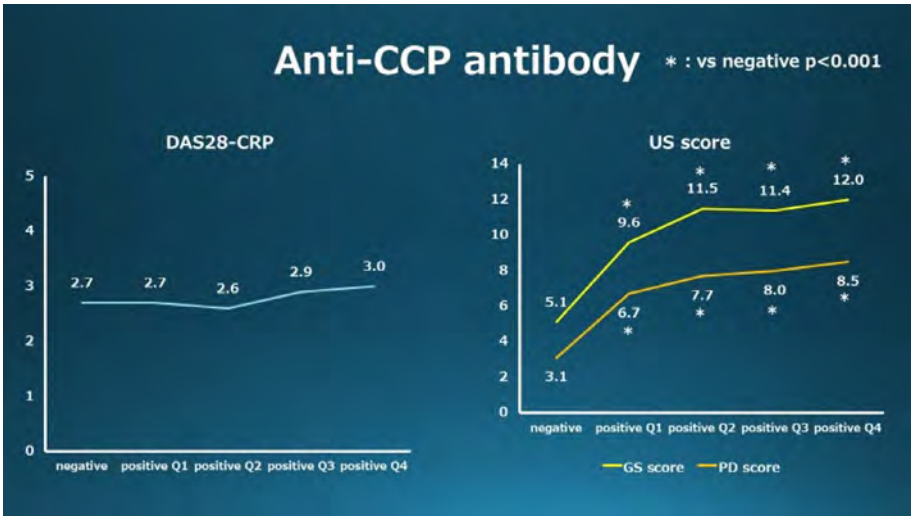

Figure 1. The relattionship between anti-CCP antibody titer and disease activity or ultrasound findings.

score. Patients were classified into a negative group and a positive group according to RF and CCP titers, and the positive group was further classified into quartiles (Q1-Q4) according to those levels, and disease activity and ultrasound synovial findings were compared.

Results: There were 655 cases in the RF positive group and 565 cases in the CCP positive group. RF positive group were divided into quartiles such as Q1: 15 < RF ≤ 72, Q2: 72 < RF ≤ 158, Q3: 72 < RF ≤ 379, Q4: 379 < RF ≤ 8160, and CCP positive group were divided into quartiles such as Q1: 4.5 ≤ CCP ≤ 36.0, Q2: 36.0 < CCP ≤ 95.6, Q3: 95.6 < CCP ≤ 308.0, Q4: 308.0 < CCP. There was no difference in disease duration or disease activity both in the RF and CCP positive group and the negative group, but the ultrasound synovitis scores were significantly worse in both GS and PD score in the positive groups. Among the RF and CCP positive groups, the ultrasound synovitis score tended to be high in the high RF and CCP group, and the highest in the Q4 group.

Conclusion: We evaluated the relationship between RF or CCP levels and ultrasound synovitis. Ultrasound synovial findings were significantly worse in positive group than negative group on both RF and CCP, regardless of disease activity. Moreover, high titer of RF or CCP levels tended to be higher ultrasound synovitis. Patients with high titer of RF or CCP levels should be considered to treat more earlier and intensively.

Disclosure: T. Okano: None; **K. Mamoto**: None; **Y. Yamada**: None; **S. Anno**: None; **Y. Domae**: None; **S. Washida**: None; **A. Yagami**: None; **Y. Yoshida**: None; **T. Koike**: None; **H. Nakamura**: None.

Abstract Number: 1047

Infrared Thermography Imaging Discriminates Between Inflamed and Non-inflamed Joints

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Background/Purpose: Infrared thermography (IRT) is an emerging technology that has the potential to rapidly assist in identifying joint inflammation in patients with joint symptoms. However, its use in clinical practice is currently limited due to the lack of a true gold standard (e.g., musculoskeletal ultrasound [MSUS]) confirming the presence of joint inflammation. We aimed to determine whether there are differences in IRT measurements between joints categorized as inflamed or not based on Power Doppler (PD) ultrasound imaging.

Methods: We conducted a cross sectional study among patients at a tertiary academic medical center. Eligible patients were age ≥ 18 years, had a rheumatologist-diagnosis of rheumatoid arthritis or a non-inflammatory joint condition (e.g. osteoarthritis) or healthy controls, and had at least one swollen joint in the hands or wrists or feet (RA patients only). IRT images were obtained using a FLIR E75 3400 camera. A manual segmentation approach was employed to place rectangular regions of interests (ROIs) over each of the 32 target joint sites. FLIR software was used to determine IRT temperature (^{0}C) parameters including ROI maximum (max), minimum (min), mean (mean), center (center) and within joint variability (STD). MSUS was obtained at the same visit by a rheumatologist with RhMSUS certification. MSKUS erosions (presence/absence), joint inflammation (PD) and synovial hypertrophy (SHT) was scored using a 0-3 severity scale (none =0, mild =1, moderate=2, and severe =3) for each wrist, metacarpophalangeal (MCP), proximal interphalangeal (PIP) and metatarsophalangeal (MTP) joint. We used mixed effects logistic regression to determine whether IRT parameters were able to discriminate between inflamed (i.e. PD score ≥ 1) and not inflamed joints (PD=0), accounting for clustering of joints within patients and adjusting for demographic factors including age, sex, and race.

Results: A total of 50 patients with RA (n=30), OA (n=10), healthy controls mean (SD) age 54.8 (14.20) years, mostly women (90.0%), 22 (44%) Black participated in the study. A total of 1598 joints were included in the analysis including 103 joints with a PD ≥ 1. A total of 248 joints had erosions. IRT measurements by PD score are presented in the Table. The c-statistic for the area under the receiver operator curve was 0.82 (Figure). After multivariable adjustment, the minimum, maximum and the within-joint variability (STD) of the thermography camera temperature readings were significantly associated with joint

Table: Infrared thermography measurements by Power Doppler (PD) score.

Table: Infrared thermography measurements by Power Doppler (PD) score.

Variable	Overall N = 1598	PD = 0 N = 1495	PD = 1 N = 97	PD = 2 N = 6
Study group:				
Patients with rheumatoid arthritis	958 (59.9%)	868 (58.1%)	84 (86.6%)	6 (100.0%)
Healthy controls	320 (20.0%)	319 (21.3%)	1 (1.0%)	0 (0.0%)
Patients with Osteoarthritis	320 (20.0%)	308 (20.6%)	12 (12.4%)	0 (0.0%)
Mean Temperature (°C):				
Mean (SD)	30.96 (3.18)	30.87 (3.21)	32.09 (2.43)	33.96 (0.86)
Median (IQR)	31.80 (29.00, 33.36)	31.76 (28.76, 33.30)	32.67 (30.99, 33.98)	34.03 (33.63, 34.55)
Minimum-Maximum Difference	0.00-36.11	0.00-36.11	23.22-35.58	32.54-34.93
Within joint variability (STD) (°C):				
Mean (SD)	0.20 (0.15)	0.20 (0.14)	0.26 (0.17)	0.47 (0.32)
Median (IQR)	0.17 (0.11, 0.26)	0.16 (0.11, 0.26)	0.23 (0.14, 0.30)	0.38 (0.31, 0.40)
Minimum-Maximum Difference	0.00-1.94	0.00-1.94	0.03-0.92	0.27-1.12
Center Temperature (°C)				
Mean (SD)	30.97 (3.10)	30.89 (3.13)	32.07 (2.45)	34.19 (0.92)
Median (IQR)	31.82 (28.96, 33.37)	31.74 (28.72, 33.31)	32.61 (31.00, 33.93)	34.21 (33.46, 34.84)
Minimum-Maximum Difference	21.07-36.11	21.07-36.11	23.21-35.82	33.08-35.40
Maximum Temperature (°C)				
Mean (SD)	31.36 (3.51)	31.26 (3.55)	32.68 (2.47)	34.78 (0.38)
Median (IQR)	32.32 (29.37, 33.86)	32.22 (29.17, 33.78)	33.18 (31.47, 34.53)	34.67 (34.62, 34.93)
Minimum-Maximum Difference	0.00-36.87	0.00-36.87	23.32-36.05	34.30-35.40
Minimum Temperature (°C)				
Mean (SD)	30.50 (3.39)	30.43 (3.44)	31.55 (2.41)	32.70 (1.54)
Median (IQR)	31.37 (28.49, 32.92)	31.32 (28.40, 32.88)	31.97 (30.50, 33.34)	33.20 (32.93, 33.52)
Minimum-Maximum Difference	0.00-35.86	0.00-35.86	23.12-35.25	29.63-33.73

Figure: Receiver Operator Curve comparing thermography with musculoskeletal ultrasound for classifying joint inflammation (PD = 1 or 2)

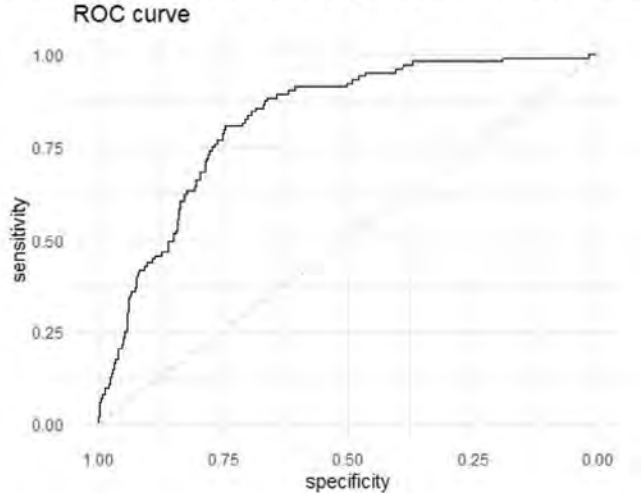

Figure: Receiver Operator Curve comparing thermography with musculoskeletal ultrasound for classifying joint inflammation (PD = 1 or 2)

inflammation compared to the gold standard of PD={1,2} by MSUS. Older age, female sex, and black race also were significantly associated with the outcome.

Conclusion: We found that a commercially-available infrared thermography camera had reasonable accuracy to discriminate between inflamed versus non-inflamed joints among people with RA, OA, and healthy controls. These findings can help inform future use of IRT in clinical practice to discriminate between inflammatory and non-inflammatory joint disease in settings where a rheumatologist physical exam may not be feasible.

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Abstract Number: 1048

The Prediction of Response to Advanced Therapies on a Joint Level in Rheumatoid Arthritis: The Interpretation of Tenderness and Doppler Ultrasound

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SESSION INFORMATION
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Background/Purpose: Ultrasound (US) has emerged as a sensitive method, especially when compared to clinical examination, for evaluating disease activity in Rheumatoid Arthritis (RA). Several studies have shown discrepancies between the physical examination and US in detecting inflammation. In this study, we aimed to understand a) for joints that are tender at baseline, what is the response rate (same joint being non-tender at follow up), according to the presence of Doppler signal positivity at therapy initiation; b) for joints that are not tender at baseline, what is the risk of flare (being tender) at follow up, according to the presence of Doppler signal positivity at the therapy initiation.

Methods: At the ORCHESTRA (**O**ttawa **R**heumatology **C**ompre**HE**n**S**ive **TR**eatment and **A**ssessment) Clinic RA patients starting a new advanced bDMARD/tsDMARD therapy are assessed using a comprehensive screening process which includes a protocoled US scan. Patients are evaluated in the same clinic three months after new therapy initiation. For this analysis, we included all MCP, PIP and wrist joints of every patient. Analysis was performed on a joint level. Tenderness of the joint as baseline and at follow up were grouped according to having Global OMERACT-EULAR Synovitis Score (GLOESS) grade ^{3} 2 Doppler signals at baseline. Odds ratio (confidence intervals) were calculated a) for joints that were tender at baseline to understand the prediction of response; b) for joints that were not tender at baseline to understand the prediction on flare.

Results: There were 40 RA patients (70% female) included in the analysis, with 878 joints being analyzed. The median (IQR) tender and swollen joint counts were 8(11) and 7.5(5), respectively, with a DAS28 score of 3.76 (1.58). The mean (SD) age was 60.1(15.6), with a median (IQR) disease duration of 14.5 (21.3) years. Twenty-one patients (52.5%) were bionaive at baseline and 7(17.5%), 4(10%) and 8(20%) patients had failed 1, 2 or ^{3}3 biologic therapies, respectively.

TENDER at baseline	MCP, PIP and wrists		
	Good response		
	No (still tender at follow up)	Yes (not tender at follow up)	Response rate %
Baseline No Doppler	49	122	71
Doppler (+)	26	22	46

Table 1: Response rates in tender joints at baseline, according the initial Doppler positivity

Not TENDER at baseline	MCP, PIP and wrists		
	Follow up		
	Still no pain	New onset pain	Risk of flare %
Baseline No Doppler	492	59	10.1
Doppler (+)	82	26	24.1

Table 2: Flare rates in non-tender joints at baseline, according the initial Doppler positivity

219/878 joints were tender at baseline, 48 (21.9%) of whom had Doppler signals. Among the Doppler positives, the response rate was 46%. The response rate of the joints with no Doppler signals at baseline was 71%, meaning they were no longer tender at follow up. The odds of achieving response on a joint level was lower if there were Doppler signals at baseline (OR 0.34 (CI:0.18-0.66)) (table 1).

Among the 659 joints that were not tender at baseline, 108 (16.4%) had Doppler signals. Within these, 24.1% became tender at follow up. Among the 551 patients who were Doppler negative, 10.1% became symptomatic. The odds of flaring on a joint level that was previously non-tender was higher if there were Doppler signals at baseline (OR 2.64 (CI:1.58-4.44)) (table 2).

Conclusion: Our study shows that the Doppler signals at the initiation of an advanced therapy has two important meanings on a joint level: Doppler positive tender joints are more resistant to therapies (then Doppler negatives) and Doppler positive non-tender joints have a higher risk of becoming symptomatic. It is still not clear how the US should be incorporated in the treatment algorithms, but the US information suggest a different patient phenotype.

Disclosure: S. Acikgoz: None; **U. Gazel**: None; **R. Sabido-Sauri**: None; **O. Bayindir Tsechelidis**: Janssen, 5; **A. Zahrai**: None; **C. Ivory**: None; **E. Hepworth**: None; **s. aydin**: AbbVie/Abbott, 6, Celgene, 6, Clarius, 11, Novartis, 6, Pfizer, 6, UCB, 6.

Abstract Number: 1049

Enhanced Diagnostic Confidence with High Frequency Temporal Artery Ultrasound in Diagnosis of Cranial Giant Cell Arteritis (GCA)

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: A previous survey of Australian Rheumatologists indicated low confidence (60% of Australian Rheumatologists) in the use of Temporal artery ultrasound provided by their Radiology services in the diagnosis of giant cell arteritis. There is limited published information on multimodal imaging to enhance diagnostic confidence of GCA. The aim of this study was to determine the utility of standardized high-resolution temporal artery scanning protocols for diagnosis of GCA and the role of multimodal imaging in increasing the confidence of GCA diagnosis.

Methods: Consecutive patients from 2020 to 2022 with suspected GCA based on 3/5 1990 ACR classification criteria were enrolled. Patients underwent ultrasound of bilateral common superficial temporal arteries (**CSTA**) and main branches with a 22MHz linear ultrasound probe to determine the arterial intima-media thickness (**IMT**) at the CSTA and the presence of a non-compressible halo on color Doppler.Bilateral axillary artery (**AA**) IMT was measured in some patients. Additional diagnostic tests included dedicated 3Tesla MRI of scalp arteries time of flight sequence with grading of gadolinium enhancement of temporal artery (TA) wall and temporal artery biopsy (TAB) or 18FDG PET scan. Final diagnosis of GCA was determined at case-note review at 6 months by consultant rheumatologist. At least two diagnostic tests were performed on most patients. GCA diagnostic confidence was enhanced by employing multimodality imaging and biopsy. Optimal IMT cut-off measurements for GCA diagnosis were determined by Receiver Operating Characteristic analysis.

Results: 82 patients were included in the study (mean age 72 years, 66% female). Mean age was higher in the 31 (38%) patients with confirmed GCA diagnosis than those without GCA confirmation (79 vs 68 years, p=0.0002).

Of the 82 patients, 78 (95%) underwent ultrasound, 41 MRI (50%), 15 PET (18%) and 35 TAB (43%). 71% had at least two diagnostic procedures and 33% had three. The optimal IMT cut-off measurements were 0.4mm for CSTA (n=74, 86% sensitivity, 91% specificity) and 1mm for AA (n=42, 62% sensitivity,100% specificity). Sensitivity and specificity of TA halo for GCA (n=78) was 80% and 94% respectively and 63% and 95% respectively for Grade 2 Gadolinium enhancement of TA (n=41).

Conclusion: High resolution ultrasound TA Halo, and the more objective TA IMT, both performed well for cranial GCA diagnosis with excellent sensitivity and specificity.

Figure 1. GCA Diagnostic Test Results

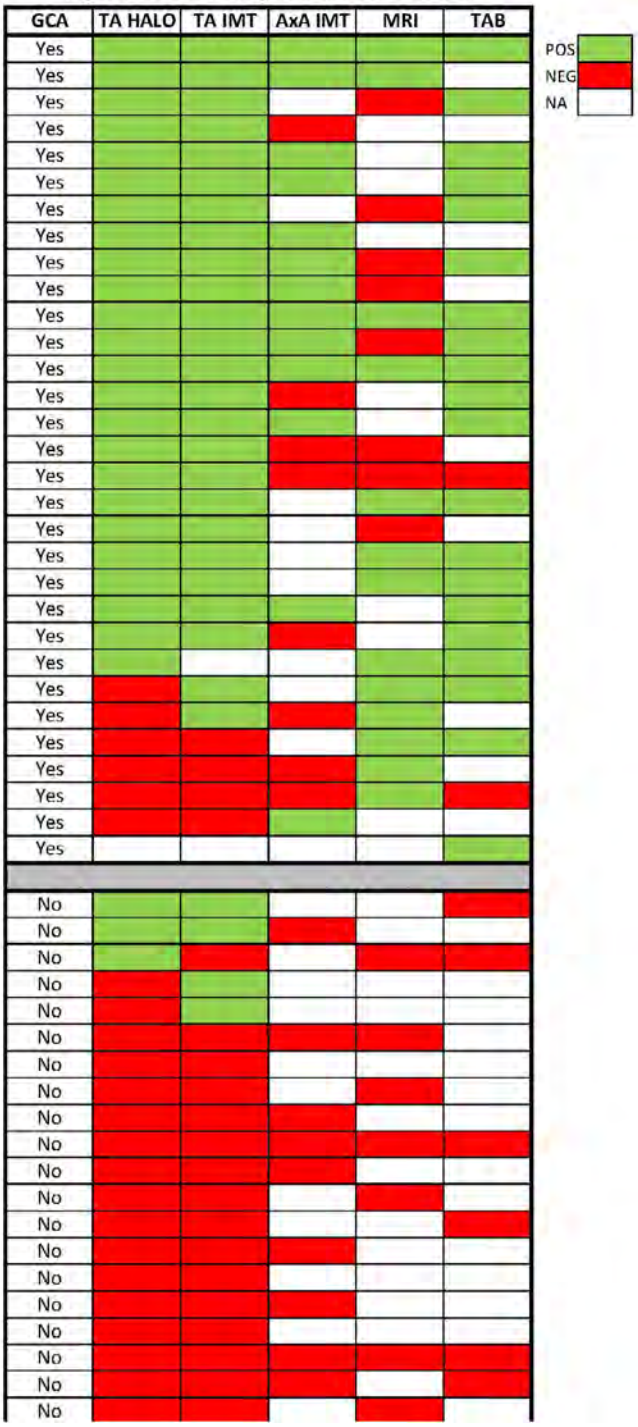
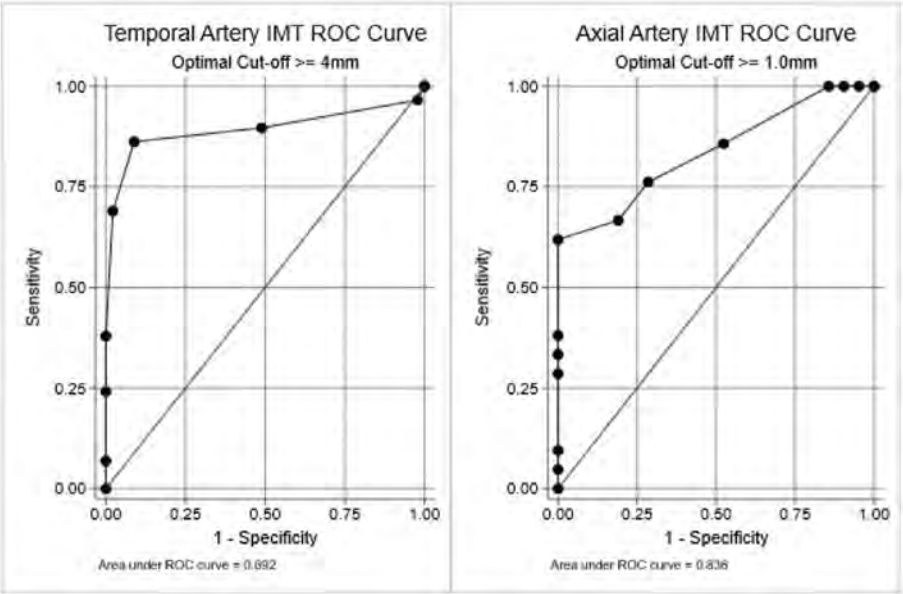


Table 1. GCA Diagnostic Test Performance

	TA_Halo	TA_IMT	AxA_IMT	MRI	TAB
N	78	74	42	41	35
case_testpos	24	25	13	13	20
case_testneg	6	4	8	8	2
control_testpos	3	4	0	0	0
control_testneg	45	41	21	20	13
%correct	88%	89%	81%	80%	94%
Sensitivity	80.0% (61.4, 92.3)	86.2% (68.3, 96.1)	61.9% (38.4, 81.9)	63.2% (38.4, 83.7)	90.9% (70.8, 98.9
Specificity	93.8% (82.8, 98.7)	91.1 (78.8, 97.5)	100% (83.9, 100))	94.7% (74.0, 99.0)	100% (75,3,100)
Positive Predictive Value	88.9% (70.8, 97.6)	86.2 (68.3, 96.1)	100% (75.3, 100)	92.3% (64.0, 99.8)	100% (73.2,100)
Negative Predictive Value	88.2% (76.1, 95.6))	91.1 (78.8, 97.6)	72.4 (52.8, 87.3)	72.0% (50.6, 87.9)	86.7% (59.5, 98.3)



Disclosure: J. Ninan: None; **S. Lyne**: None; **J. McNeil**: None; **J. Tieu**: Vifor, 5; **V. Limaye**: None; **S. Proudman**: None; **S. Lester**: None; **C. Hill**: None.

Abstract Number: 1050

Diagnostic Accuracy of Lung Ultrasound for Detecting Interstitial Lung Disease Among Patients with Systemic Sclerosis: A Comparative Study of Two Scanning Protocols

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Imaging of Rheumatic Diseases Poster I

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: *Lung ultrasound (LUS) has proven useful to detect interstitial lung disease (ILD) among patients with SSc when compared to high-resolution computerized tomography (HRCT) as the gold standard; it also exhibits advantages as a tool in clinical practice owing to its accessibility and innocuity. Nevertheless, a key drawback is currently the lack of a standardized methodology to perform LUS. Our objectives were to evaluate diagnostic accuracy of LUS for ILD by comparing the systematic evaluation of 14 intercostal spaces (ICS) against 12 postero-basal ICS; and to correlate the grade of severity of ILD assessed through LUS with findings on HRCT, both as a global score and evaluating specific concordant lung zones*.

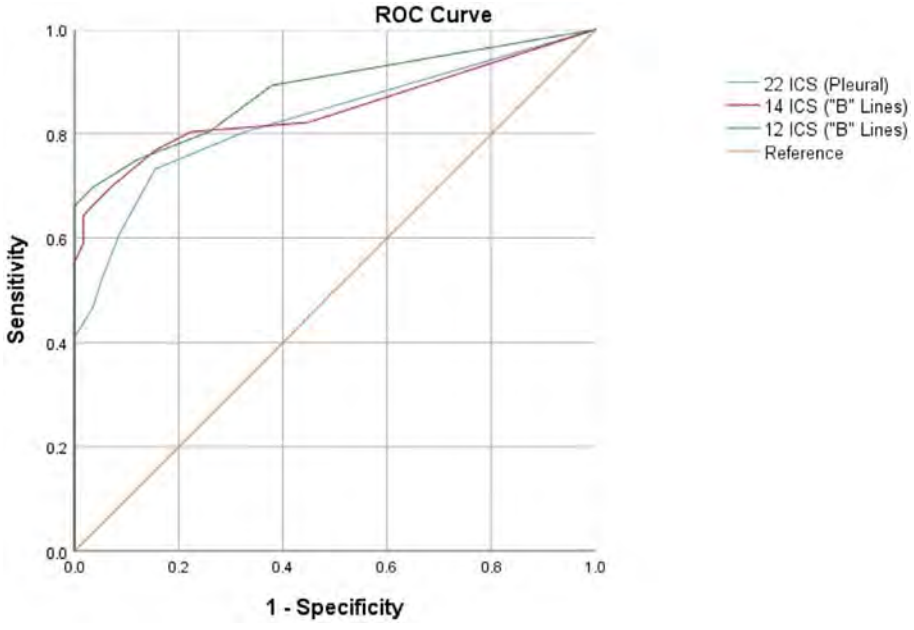
Methods: *Patients with SSc, according to current classification criteria, were recruited from the outpatient rheumatology clinic at a referral hospital. Demographic, clinical, serological, and imaging variables were collected. LUS was performed using two scanning methods: 14 predetermined ICS and 12 postero-basal ICS. "B" lines (BL) and pleural abnormalities (PA) were documented for each ICS. HRCT was performed with a maximum 3 month-interval from the time of recruitment (before or after). Descriptive statistics, multivariate analysis, a Pearson correlation test (to compare findings between LUS and HRCT), and ROC curves (to show diagnostic accuracy) were carried out*.

Table 1. General characteristics

Variable	w/o ILD (*n*= 58)	ILD (*n*= 56)	*p*
Age	53 (43.5-60.5)	59 (50.8-66.2)	**0.007**
Gender (female)	58 (52.3)	53 (47.7)	0.07
Body Mass Index	23.8 (20.7-25.4)	23.1 (20.5-25.9)	0.97
SSc variant (n=105)			
Limited	45 (57)	34 (43)	**0.008**
Diffuse	7 (26.9)	19 (73.1)	
Anti-Scl-70 (n= 92)	31 (43.1)	41 (56.9)	0.069
Anti-centromere (n= 99)	45 (52.9)	40 (47.1)	0.532
Pulmonary Hypertension (n= 70)	5 (26.3)	14 (73.7)	**0.02**
Medsger global score (n= 69)	1.5 (1-2)	2 (1-2.5)	**0.017**
Warrick score	3 (0-6)	13 (9-18)	**<0.001**
BL count in 14 ICS	0 (0-1)	7 (3-12.8)	**<0.001**
BL count in 12 ICS	0 (0-2)	6.5 (2.3-15.5)	**<0.001**
PA (22 EIC)	0 (0-1)	4 (1-9)	**<0.001**
Immunosuppresants, no. (n= 71)	1 (0-2)	1 (0-2)	0.48
Mycophenolate mophetil (n=104)	9 (36)	16 (64)	0.084

Continuous variables: Mean ± DE, Median (25-75), Categorical variables: Frequency (%)

ILD: Interstitial Lung Disease, SSc: Systemic Sclerosis.



Results: *We included 114 patients with a median age of 55 (IQR 48-63) years; 97.4% were women. Prevalence of ILD was 49.1%. Relevant baseline characteristics are shown in Table 1. Acknowledged risk factors for ILD were pulmonary hypertension (*OR 3.4, CI 95% 1.04-11.14, *p*=0.04) and diffuse SSc (OR 2.5, CI 95% 0.84-7.6 *p*= 0.10). A strong correlation was shown between the BL count in 14 ICS and the Warrick score (0.62), and the BL count in 12 ICS and Warrick score (0.61).

The AUC were 0.85 (95% CI, 0.77-0.92), 0.88 (95% CI, 0.82-0.95) and 0.83 (95% CI, 0.75-0.91) for the evaluation of the number of BL in 14 ICS, 12 ICS and the number of ICS with PA (22 EIC), respectively.

Conclusion: Our study confirms the robustness of LUS as a tool for the detection of ILD through the quantification of BL and PA when using any of two different scanning protocols (14 and 12 ICS). A reasonable diagnostic accuracy was also proven for the finding of PA, but more studies are required to elucidate their added value over BL for the diagnosis of ILD by LUS.

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Abstract Number: 1051

Validation of Handheld Ultrasound Devices for Point of Care Use in Rheumatology: Interim Analysis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Ultrasonography (US) has experienced a rapid evolution in rheumatology. Despite many advantages being shown repeatedly, several barriers persist and stand in the way of a wider use of US in rheumatology, equipment cost being an important one. Hand-held US technology promises to take this cost down substantially. However, before it can be specifically used for rheumatology, its performance needs to be validated against gold-standard devices for key interventions. We aim to test the concurrent validity of a handheld US device versus a gold-standard device to detect characteristic features of healthy and rheumatic joints (i.e., anatomical structures and vascular flow).

Methods: Adult patients with peripheral PsA presenting with at least one tender and swollen joint were included. Each patient had consecutive US examinations using a handheld (Clarius Mobile Health Inc, HD3 L20 and L15 scanners) and a gold standard US device (GE LogicE9) for detecting synovitis, nail disease, and erosions. B mode and power Doppler images were saved for each site and lesion. Every image was given a unique identifier number at the end. Image reading was performed at least 2 weeks after the acquisition of US in all patients. A random order slide show was conducted for

scoring, irrespective of the machine used or the anatomical site or patient assessed, to ensure blindness. Scoring was done using previously validated methods. Here we present interim analysis for the first 10 patients to detect synovitis (n=240), nail disease (n=20), and erosions (n=40).

Results: Patients had a mean±SD age of 55.2±8.6, with a median (IQR) disease duration of 7(12) years. 40% were female. On the day of the US, the median (IQR tender joint count was 8.5(18.5) and swollen joint count was 4.5(5.75).At least moderate agreement was observed between the handheld and gold standard devices in all elementary lesions assessed (table). Specifically, both detecting synovitis, the L15 and L20, had a kappa of 0.499 and 0.535 compared to the GE machine, respectively, with absolute agreement rates of 76.7-77.8%. For detecting the intrasynovial Doppler signals, the L15 had a substantial agreement (kappa: 0.667, absolute agreement: 93.9%); and L20 had moderate agreement (kappa: 0.428, absolute agreement: 89.3%). The nail lesions were compared with L20, which showed a moderate agreement to detect the loss of trilaminar appearance (kappa: 0.490, absolute agreement: %75) and substantial agreement to detect nail bed vascularity (kappa: 0.732, absolute agreement: 89.5%). For erosions, there was an almost perfect agreement with the L15 (kappa: 0.876, absolute agreement: 94.1%) and moderate agreement with L20 (kappa: 0.486, absolute agreement: 77.5%). Investigating the individual discrepancies, the L20 seemed to be more sensitive to detecting erosions (fig).

Conclusion: In this interim analysis, the handheld US devices show moderate-substantial agreement to detect synovitis, nail lesions and erosions, and Doppler signals. The final analysis will be conducted after 30 PsA patients are enrolled, and enthesitis will also be analyzed. These interim results encourage testing the use of handheld US devices for wider use.

Table: The frequency, kappa and percent absolute agreement of elementary lesions on all three devices.

		Handheld							
		L20 Scanner				L15 Scanner			
GE LogicE9	Erosion								
		Absent	Present	Kappa	% Absolute agreement	Absent	Present	Kappa	% Absolute agreement
	Absent	23	7	0.486	77.5	10	0	0.876	94.1
	Present	2	8			1	6		
	Nail- loss of tri-laminar appearance								
	Absent	9	2	0.490	75				
	Present	3	6						
	Nail Doppler								
	Absent	4	2	0.732	89.5				
	Present	0	13						
	Synovitis-B Mode								
	Absent	69	27	0.535	76.7	50	12	0.499	77.8
	Present	10	53			12	27		
	Synovial Doppler								
	Absent	134	5	0.428	89.3	86	2	0.667	93.9
	Present	12	8			4	7		

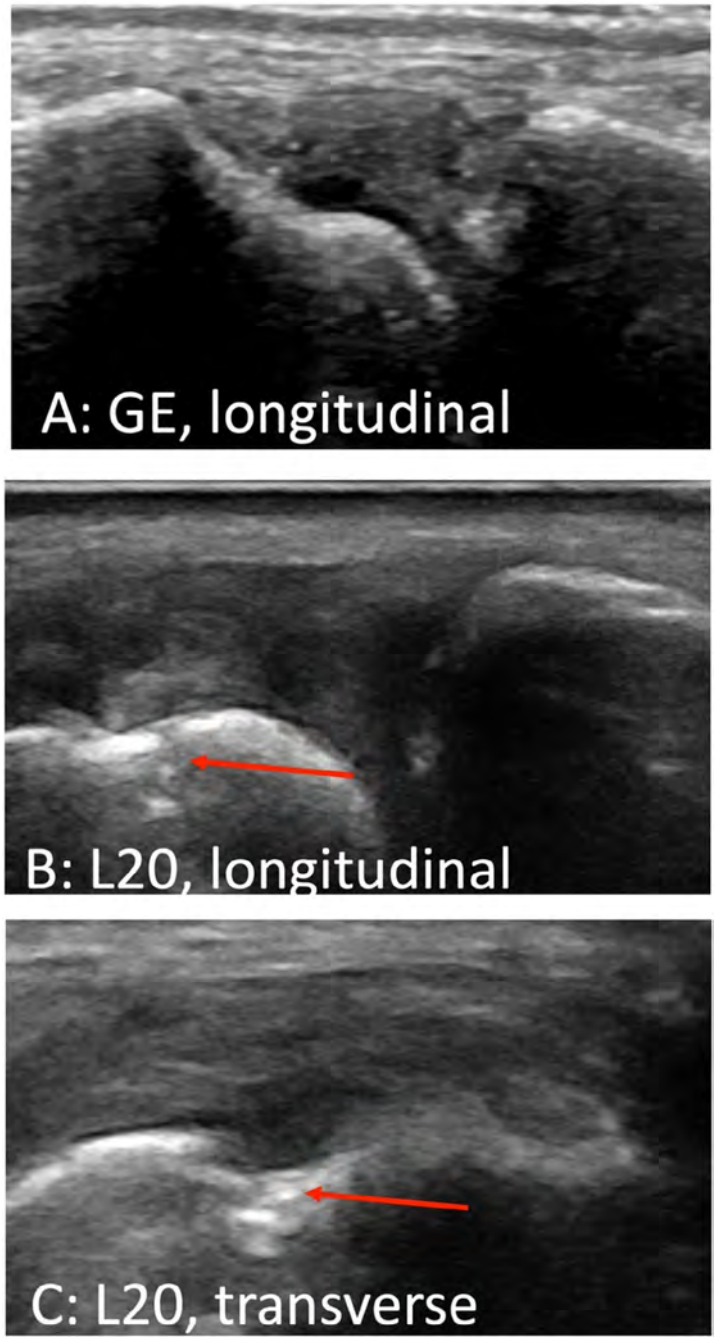

Figure: Lateral view of the same 2nd MCP joint. A) Longitudinal view using GE LogicE9, with no erosions; B) Longitudinal view using the L20 scanner, showing the erosion (arrow); C) transverse view of the erosion with L20 scanner.

Disclosure: s. aydin: AbbVie/Abbott, 6, Celgene, 6, Clarius, 11, Novartis, 6, Pfizer, 6, UCB, 6; **s. acikgoz**: None; **U. Oguz**: None; **a. Vieira**: Novartis, 3; **p. Leclerc**: Novartis, 3; **S. Shah**: Novartis, 3; **L. Eder**: AbbVie, 2, 5, Eli Lilly, 2, 5, Fresenius Kabi, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Sandoz, 5, UCB, 2, 5; **G. S Kaeley**: Abbvie, 5, Gilead, 5, Janssen, 5.

Abstract Number: 1052

Unique Cellular and Autoantibody Signatures in Patients with irAEs Revealed by Longitudinal Immune Tracking

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The use of anti-PD-1 (aPD-1) immunotherapy has seen significant success in clinical practice, corresponding with a continued rise in clinical indications for multiple cancer diagnoses. Immune-related adverse events (irAEs) are a type of secondary autoimmune toxicities arising in the setting of cancer immunotherapy. They can cause significant morbidity and disruption of the treatment of oncologic patients. They also offer a controlled setting for dissecting the cellular and signaling networks of autoimmunity development.

Methods: To better understand irAEs in the setting of aPD-1 immunotherapy, we established a prospective, longitudinal cohort at the University of Pennsylvania enrolling patients before immunotherapy and following them for a year. We stratified the responses in two groups: patients that developed at least one irAE event ($irAE^+$) and patients that never developed an irAE event ($irAE^-$) during that time period.

Results: Using high-dimensional cytometry, we found that $irAE^+$ patients had a larger increase in their activated CD4 T cells after PD-1 inhibition compared to $irAE^-$ patients. In addition, plasmablast generation following immunotherapy was higher for $irAE^+$ patients. Using PhIP-Seq, an autoantigen screening assay, we found that $irAE^+$ patients demonstrated robust enrichment in autoantibodies against various tissue antigens after immunotherapy with unique patterns for each patient. Finally, a large-scale proteomic analysis revealed that $irAE^+$ patients at baseline have increased levels of circulating inflammatory mediators.

Conclusion: These results indicate that there are distinct cellular and serological imprints of $irAE^+$ patients that reflect their heightened autoimmune reactivity and can be used to uncover the underlying pathogenic mechanism of irAEs and design predictive algorithms.

Disclosure: S. Apostolidis: None; **K. Sacksith**: None; **B. Fulmer**: None; **Z. Quandt**: None; **M. Anderson**: MedTronic, 11, Merck, 11; **T. Laufer**: None; **E. Wherry**: Arsenal Biosciences, 12, Founder, Danger Bio, 1, 12, Founder, Janssen, 1, Marengo, 1, Pluto Immunotherapeutics, 1, Related Sciences, 1, Rubius Therapeutics, 1, Surface Oncology, 1, 12, Founder, Synthekine, 1.

Abstract Number: 1053

Outcomes of Immune Check Point Inhibitor Use in US Veterans with Pre-Existing Inflammatory Muscle Disease

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Data on Immune Checkpoint inhibitor (ICI) use in patients with previously diagnosed inflammatory muscle disease (IMD) is limited as these patients were excluded from clinical trials. There is a concern that use of ICIs in patients with pre-existing IMD may have flares of their disease, increased morbidity, and/or higher mortality with ICI treatment. We identified all patients diagnosed with IMD prior to ICI infusion in the Veterans Health Administration (VHA) and analyzed these patients' demographics, diagnoses, laboratory findings, clinical course, and mortality in comparison to other Veterans treated with ICIs.

Methods: This analysis used data from the VHA Corporate Data Warehouse (CDW) for demographics, ICD codes, and pharmacy information, VA cancer registry for cancer diagnosis, and all-cause mortality from the Death Ascertainment File (DAF). Veterans who received one or more ICI infusions between 6/6/2011 and 2/14/2023 were evaluated as potential IMD cases if they had two or more myositis ICD-9 or ICD-10 codes associated with a rheumatology or neurology clinic visit at least 30 days apart and both visits occurred prior to the ICI treatment. Cases meeting these criteria underwent electronic medical record review using the Compensation and Pension Record Interchange (CAPRI) to determine if the case met American College of Rheumatology (ACR) criteria for IMD. Demographic features and mortality of confirmed cases were compared to patients receiving ICI without pre-existing IMD. IMD cases were also reviewed to determine if patients developed a myositis flare.

Results: We identified 29,539 patients who received at least one ICI infusion in the VHA. Of these patients, 13 met IMD screening criteria with 8 patients having confirmed IMD by ACR criteria (dermatomyositis 3, polymyositis 2, anti-synthetase syndrome 2, and RA/myositis overlap 1). All patients were white males with an average age of 71.7 years at the time of first ICI infusion. Primary cancer diagnoses were lung - 2, melanoma - 2, head and neck - 2 kidney/other urinary - 1, and mesothelioma - 1. Four patients were treated with nivolumab and four patients with pembrolizumab (Table 1). Diagnosis of IMD was made on average 3.1 years prior to treatment with ICI. One patient with dermatomyositis had an IMD flared after two doses of ICI and was treated successfully with steroids and IVIG. No IMD flares were identified in the other seven patients. There was no difference in Kaplan Meier Survival Analysis for IMD patients in comparison to patients treated with ICI without IMD (p=0.40 by log rank test) (Figure 1).

Conclusion: Overall mortality in these 8 patients with IMD treated with an ICI was similar to other ICI treated Veterans. Among the 8 IMD patients, only one developed an IMD flare after ICI treatment that responded to glucocorticoids and IVIG therapy. These findings suggest that ICI therapy can be considered in IMD patients with close monitoring. Future research is needed to better understand the risk of IMD flare and outcomes in patients with established IMD treated with ICIs.

Table 1: Comparison of Patients with Established Inflammatory Muscle Disease (IMD) Prior to ICI Treatment to Patients without IMD

Comparison of Patients with Established Inflammatory Muscle Disease (IMD) Prior to ICI Treatment to Patients without IMD

	IMD (N=8)	No IMD (N=29,531)	
	Means (SD)/ N (%)	Means (SD)/ N (%)	p=value
Age At First ICI	71.7±10.9	70.0±8.8	0.71
Gender			
Male Gender	8 (100%)	28,493 (96.5%)	0.59
Race			
White	7 (87.5%)	22,172 (75.1%)	0.40
Black	0 (0%)	5,126 (17.4%)	
Other/Unknown	1 (12.5%)	2,233 (7.5%)	
Smoking History			
Current/Former Smoker	3 (37.5%)	15,866 (53.8%)	0.56
Never Smoker	1 (12.5%)	4,010 (13.6%)	
Unknown	4 (50.0%)	9,635 (32.6%)	
Cancer			
Lung	2 (50.0%)	13,409 (45.4%)	0.23*
Melanoma	2 (25.0%)	2,710 (9.2%)	
Kidney & Other Urinary	1 (12.5%)	4,042 (13.7%)	
Head And Neck	2 (25.0%)	1,516 (5.1%)	
Mesothelioma	1 (12.5%)	107 (0.4%)	
Other/Miscellaneous	0 (0.00%)	7,747 (26.2%)	
First ICI Received			
Nivolumab	4 (50%)	8,851 (30%)	0.19
Pembrolizumab	4 (50%)	12,630 (42.8%)	
Other Agents	0 (0%)	8,049 (27.3%)	

* Comparison of Lung, Melanoma, and other Cancers

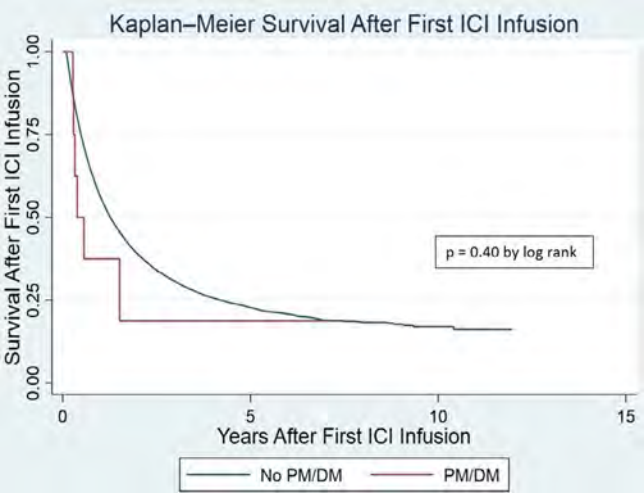

Figure 1: Comparing Survival of Patients on ICI Therapy with Pre-Existing IMD to those without IMD

Disclosure: D. Krutko: None; **S. Rubino**: None; **B. Sauer**: None; **J. Rojas Jr**: None; **G. Kunkel**: None; **J. Walsh**: AbbVie, 5, Amgen, 2, Eli Lilly, 2, Janssen, 2, Merck, 5, Novartis, 2, Pfizer, 2, 5, UCB Pharma, 2; **S. Patel**: None; **G. Cannon**: None; **T. Braaten**: None.

Abstract Number: 1054

Immune Checkpoint Inhibitor Induced Polymyalgia Rheumatica Demonstrates a Similar Scintigraphic Appearance to Classical Polymyalgia Rheumatica on 18F-Fluorodeoxyglucose PET/CT

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Of the rheumatic immune-related adverse events that follow immune checkpoint inhibitor (ICI) cancer immunotherapy, de novo PMR-like episodes without inflammatory arthritis (ICI-PMR) appear to comprise a small subset, distinct from other irAEs. ICI-PMR also appear distinct from classical PMR, given they are temporally related to ICI exposure and occur at far greater incidence than expected for classical PMR alone. ICI-PMR have previously been associated with findings consistent with inflammatory morphological change on [18F] Fluorodeoxyglucose-PET/CT (FDG-PET/CT), a modality used for cancer staging. Classical PMR also has highly accurate diagnostic scintigraphic features on FDG-PET/CT. It is not known to what extent the detailed inflammatory morphological changes in ICI-PMR correlate with those in classical PMR.

Methods: A comparison was made of FDG-PET/CT images from active ICI-PMR and active classical PMR patients. Images in ICI-PMR patients were obtained from a retrospective repository of routine care FDG-PET/CT incidentally obtained for cancer staging. Images were selected where the time of image acquisition correlated with ICI-PMR active disease. Both

Table 1: Scintigraphic comparison (comparison of PMR and irAE cohorts performed by ranking 7 sites in order of average SUVmax - 5 classical PMR sites and 2 intra-articular sites)

Table 1:
Scintigraphic comparison (comparison of PMR and irAE cohorts performed by ranking 7 sites in order of average SUVmax - 5 classical PMR sites and 2 intra-articular sites)

		Rank		
Location	SUVmax (SD)	irAE	PMR	SUVmax (SD)
Ischial tuberosity	1.79 (0.49)	2	1	3.58 (1.38)
Hip capsule	1.65 (0.51)	4	2	3.39 (1.79)
Shoulder capsule	2.04 (0.53)	1	3	3.36 (1.33)
Interspinous bursa	1.60 (0.71)	5	4	2.92 (1.58)
Trochanteric bursa	1.75 (0.55)	3	5	2.50 (0.90)
Glenohumeral joint	1.48 (0.34)	6	6	1.93 (0.98)
Hip joint	1.39 (0.41)	7	7	1.84 (1.17)

diagnosis and disease activity assessment for ICI-PMR patients were determined by a rheumatologist expert in irAEs, without reference to FDG-PET/CT. Patients with clinically apparent inflammatory arthritis were excluded. Images in classical PMR were obtained from a prospective research cohort, after diagnosis and prior to glucocorticoid therapy. All patients met the 2012 ACR/EULAR PMR Classification Criteria. Seventeen sites specific to classical PMR FDG-PET/CT assessment were assessed by a nuclear medicine physician expert in assessment of PET/CT for PMR, blinded to clinical context, and were combined into seven regional sites for comparison.

Results: This analysis captured nine patients with ICI-PMR who had an incidental FDG-PET/CT when their ICI-PMR was active. The median age was 79 (69-85). The ICI indication was melanoma in 5 patients, and non-small cell lung cancer in 4 patients. The ICI agent was nivolumab in 4, pembrolizumab in 4, and durvalumab in 1; only one was receiving combination therapy with ipilimumab. There were 31 patients in the classical PMR cohort. While the overall intensity of uptake was lower in the ICI-PMR cohort, notable morphological similarities existed between both sets of patients (Table 1). Of the seven sites, shoulder capsule and ischial tuberosity ranked in the top three for both groups. For both ICI-PMR and classical PMR, intra-articular uptake at shoulder and hip joints was lower than periarticular sites classical for polymyalgia rheumatica.

Conclusion: ICI-PMR and classical PMR demonstrate similar patterns of scintigraphic uptake on FDG-PET/CT. This close similarity in inflammatory morphological change implies that classical PMR properties might inform ICI-PMR research, and that insights from ICI-PMR might prove useful for classical PMR research, as a model of induced disease.

Disclosure: D. Liew: None; **A. Poon**: None; **C. McMaster**: None; **R. Buchanan**: None; **V. Yang**: None; **A. Scott**: None; **C. Owen**: AbbVie/Abbott, 1, 6, Janssen, 6, Novartis, 6.

Abstract Number: 1055

Cancer Outcomes in Cancer Patients with Immune Checkpoint Inhibitor-induced Inflammatory Arthritis Treated with Glucocorticoids: Data from the CanRIO Retrospective Cohort

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitors (ICI) have revolutionized the treatment of cancer. A drawback of ICI therapy is their off-target effects known as immune-related adverse events (irAEs), including inflammatory arthritis (ICI-IA). Glucocorticoids (GC) are among the first-line treatment for most irAEs, including ICI-IA. However, given the

immunosuppressive properties of GC, there is concern that they may blunt the anti-tumor effects of ICI. There is a paucity of evidence on the safety of GC to treat ICI-IA. The aim of this study was to examine the impact of dose, timing of initiation and duration of GC on cancer outcomes in patients with ICI-IA. We hypothesized that highmaximal dose, early initiation and prolonged duration of GC exposure after onset of ICI-IA would be associated with worse outcomes.

Table 1: Baseline characteristics of subjects exposed to glucocorticoid (GC) within 90 days after onset of ICI-IA (N=76).

Female, n (%)	29 (38.2%)
Age (years), mean (SD)	68.2 (11.3)
Tumor type, n (%)	
Melanoma	30 (39.5%)
Lung	25 (32.9%)
Genito-urinary	12 (15.8%)
Breast	1 (1.3%)
Gastro-intestinal	1 (1.3%)
Gynecological	2 (2.6%)
Other	5 (6.6%)
Type of ICI, n (%)	
Single	51 (67.1%)
Combination	22 (29.0%)
Missing	3 (4.0%)
Treatment, n (%)	
csDMARD	49 (64.5%)
bDMARD	5 (6.6%)
Other	4 (5.3%)
Maximal GC dose (mg), median (IQR)	25 (20-50)
Time to GC initiation after IA onset (days), median (IQR)	26.5 (5-51)
Duration of GC exposure during the 90 days after IA onset (days), median (IQR)	59.5 (30-82)
Duration of follow-up (weeks), median (IQR)	123.2 (67.8-190.7)

csDMARD=conventional synthetic disease-modifying anti-rheumatic drugs; bDMARD= biologic disease-modifying anti-rheumatic drugs; IQR=interquartile range i.e. (25% 75%)

Table 2: Disease progression and death in GC users by maximal GC dose, time to initiation of GC and duration of GC exposure after ICI-IA onset.

		Maximal GC dose		Time to GC initiation after IA onset		Duration of GC exposure during the 90 days after IA onset	
		≤ median (25 mg)	> median (25 mg)	≤ median (26.5 days)	> median (26.5 days)	≤ median (59.5 days)	> median (59.5 days)
Progression	N (%)	13/37 (35.1%)	14/37 (37.8%)	17/38 (44.7%)	10/36 (27.8%)	13/36 (36.1%)	14/38 (36.8%)
	p-value[1]	1.0000		0.1530		1.0000	
Estimate of survival time at which 25% of the patients have progressed (weeks)		22.4	62.0	43.1	123.9	77.7	36.3
Estimate of survival time at which 50% of the patients have progressed (weeks)		NE	297.2	297.2	NE	297.2	NE
P-value for equality of the progression free survival functions (see figures)		0.7791		0.3785		0.8913	
Death	N (%)	8/39 (20.5%)	10/37 (27.0%)	10/38 (26.3%)	8/38 (21.1%)	10/38 (26.3%)	8/38 (21.1%)
	p-value[1]	0.5937		0.7879		0.7879	
Estimate of survival time at which 25% of the patients have died (weeks)		152.5	120.2	120.2	127.2	125.7	224.0
Estimate of survival time at which 50% of the patients have died (weeks)		NE	NE	NE	NE	NE	NE
P-value for equality of the overall survival functions (see figures)		0.8019		0.7844		0.8540	

[1]p-value for comparison of progression/death between groups (≤ vs. > median).
NE=Not estimable because less than 25% or 50% of the patients failed (progressed or died).

Methods: The CanRIO retrospective cohort includes adult subjects with rheumatic irAEs after exposure to ICI, seen at one of 10 rheumatology clinics across Canada between Jan 2013 and Aug 2022, who have had standardized chart data extraction. In this sub-study, participants with *de novo* ICI-IA (without pre-existing IA), who were exposed to GC within 90 days after onset of IA, and in whom there was at least 3 months of follow up after onset of ICI-IA were analyzed. Data on maximal GC dose (max-GC dose), timing of GC initiation (time-GC) and duration of GC exposure (dur-GC) during the 90 days after the onset of ICI-IA were extracted. Median values for each were determined and used to dichotomize the exposure variables into above and below the median. Kaplan Meier analysis were used to evaluate the association between max-GC, time-GC and dur-GC with progression-free survival and overall survival.

Results: Data on 76 participants with *de novo* ICI-IA were available for analysis (Table 1). The median max-GC dose was 25 mg daily (interquartile range (IQR) 20-50 mg), median time-GC was 26.5 days (IQR 5-51 days) and median dur-GC was 59.5 days (IQR 30-82 days). Median follow up of the participants was 123.2 weeks. Max-GC dose, time-GC and dur-GC exposure had no association with progression-free and overall survival (Table 2 and Figure 1).

Conclusion: In this study of participants with *de novo* ICI-IA who were treated with GC, dose of GC, timing of initiation of GC and duration of GC exposure after onset of ICI-IA did not impact tumour outcomes. Although the confidence intervals were wide, our findings provide some reassurance about the safety of short-term GC for the management of ICI-IA. Further

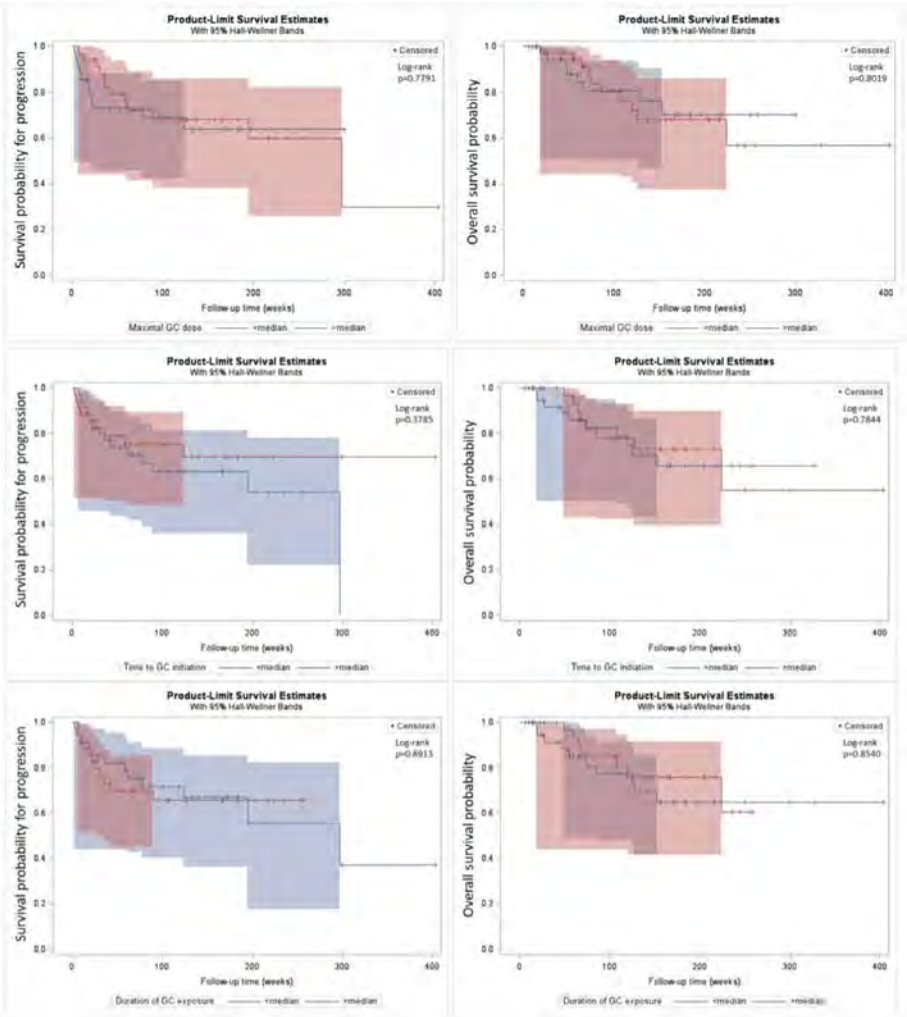

Figure 1: Progression-free and overall survival in weeks after onset of ICI-IA, stratified by the median of maximal dose, time to initiation and duration of GC within 90 days after ICI-IA onset.

studies with larger sample size and longer term follow up are needed to corroborate our results, and additional studies comparing to ICI-IA patients *unexposed* to GC are needed to optimize management.

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Abstract Number: 1056

Immune Checkpoint Inhibitor Rechallenge in Patients Who Previously Experienced Immune-Related Inflammatory Arthritis: A Multicenter Observational Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitors (ICI) improve overall survival in many cancer patients by activating their immune system. However, they can cause off-target immune-related adverse events (irAEs) including inflammatory arthritis (ICI-IA), sometimes prompting ICI discontinuation. Another course of ICI is now often considered in patients with cancer progression and previous irAEs, but there are limited data regarding the safety of ICI rechallenge in this context[1]. We aimed to assess the rate and clinical features associated with ICI-IA flare/recurrence upon ICI rechallenge.

Methods: We conducted a multicenter observational study including cancer patients with ICI-IA (defined by either the presence of at least one synovitis on physical exam and/or on imaging or polymyalgia rheumatica (PMR)-like symptoms) who started a second course of ICI more than 3 months after ICI discontinuation in 4 french university hospitals. Patients with a follow-up of < 3 months after ICI rechallenge were excluded. Charts were manually reviewed to extract data on baseline characteristics, investigations, management and both ICI-IA and tumor outcomes. Patients who experienced a flare or recurrence of ICI-IA upon rechallenge were compared to those who did not.

Table 1. Clinical characteristics and outcomes of patients who flared ICI-IA upon rechallenge and those who did not flare

		ICI-IA flare after rechallenge (N=11)	No ICI-IA flare after rechallenge (N=12)
Sex	Male	7 (63.6)	6 (50)
	Female	4 (36.4)	6 (50)
Age		69.0 (8.7)	64.9 (12.9)
Tumor type	Melanoma	3 (27.2)	7 (58.3)
	Lung	5 (21.7)	2 (16.6)
	Genito-urinary	2 (18.2)	1 (8.3)
	Other	1 (9.1)	2 (16.6)
ICI	CTLA-4	0 (0.0)	1 (8.3)
	PD1/PDL-1	10 (89.9)	9 (75.0)
	Combination	1 (9.1)	2 (16.6)
Type of ICI-IA	Symmetrical polyarthritis	3 (27.3)	4 (33.3)
	Psoriatic arthritis	1 (9.1)	1 (8.3)
	Oligoarthritis	1 (9.1)	1 (8.3)
	Monoarthritis	0 (0.0)	1 (8.3)
	PMR-like	6 (54.5)	5 (41.7)
ICI-IA treatment at the moment of rechallenge	No treatment	5 (45.5)	7 (58.3)
	Prednisone	5 (45.5)	5 (41.7)
	csDMARDs	2 (18.2)	1 (8.3)
	bDMARDs	0 (0.0)	0 (0.0)
	tsDMARDs	0 (0.0)	0 (0.0)
ICI-IA disease activity at the moment of rechallenge	No symptom	9 (81.8)	9 (75.0)
	Minor symptoms	2 (18.2)	3 (25)
	Moderate/severe symptoms	0 (0.0)	0 (0.0)
Progression after ICI rechallenge		7 (63.6)	9 (75.0)
Death		3 (27.3)	1 (8.3)

Abbreviations: ICI-IA, Immune checkpoint inhibitor-induced inflammatory arthritis; ICI, Immune checkpoint inhibitors; PMR, polymyalgia rheumatica; cs DMARDS, conventional synthetic disease modifying anti-rheumatic drugs; bDMARDs, biologic DMARDs; tDMARDs, targeted DMARDs; irAE, immune-related adverse events

Results: 23 patients were included with a median follow-up duration of 7 months from ICI rechallenge. The most frequent ICI-IA presentations were PMR-like (n=11, 48%) and symmetric polyarthritis (n=7, 30.4%), which occurred after a mean time of 6.6 months during the first course of ICI. Almost all patients were treated with prednisone (n=20, 87%), 2 with csDMARDs (8.7%) and 1 with biologics (4.3%). Reason for ICI discontinuation was ICI-IA (n=8; 35%), cancer progression (n=7; 30%), other irAE (n=4; 17%) and cancer stable or in remission (n=3; 13%).

Reason for ICI rechallenge was cancer progression in all patients. At the time of ICI rechallenge, 18 patients reported no symptoms of ICI-IA (78%), 5 had minor symptoms (22%) and none had moderate or severe symptoms. Regarding baseline ICI-IA treatment, 12 patients (52%) were not receiving any ICI-IA treatment at the time of ICI rechallenge, 10 (43%) were still on prednisone and 3 (13%) were on csDMARDs. ICI-IA flare/recurrence occurred in 12 patients (52%) with a mean time of 2.2 months after ICI rechallenge. Only one patient discontinued ICI due to ICI-IA recurrence. When comparing patients who experienced ICI-IA flare/recurrence with those who did not, there was no difference in terms of baseline ICI-IA treatment or disease activity (Table 1). Laboratory and imaging data are currently being analyzed.

Conclusion: In this first observational study of ICI-IA patients rechallenged with ICI, about half of the patients experienced ICI-IA flare/recurrence which occurred earlier than the first episode of ICI-IA but allowing ICI continuation in all but one patient. Patients still on prednisone or csDMARDs to control their ICI-IA at the time of rechallenge did not seem at increased risk of flaring. Larger studies are needed to clarify risk factors of ICI-IA flare with ICI rechallenge.

References:

1. Dolladille C. et al., JAMA Oncology 2020

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Abstract Number: 1057

Melanoma and Combination Immune Checkpoint Inhibitors Are More Clearly Associated with the Development of Chronic Inflammatory Arthritis Than Pre-existing Autoimmune Disease: A Cross-Sectional Study of Administrative Health Data

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

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Background/Purpose: Immune checkpoint inhibitors (ICIs) improve survival in many malignancies[1], by augmenting the immune system's anti-tumor response. However, ICI can result in immune-related adverse events (irAEs), including inflammatory arthritis (IA)[2], affecting 3-7% of ICI users[3]. Since half of ICI-IA fails to resolve and becomes chronic, we aimed to

Table 1. Baseline characteristics and ICI-IA treatment within the first 90 days of ICI-IA patients with acute and chronic ICI-IA

		No ICI-IA tx* within the first 90 days of ICI-IA onset n (%) or mean (SD)	ICI-IA tx* within the first 90 days of ICI-IA onset n (%) or mean (SD)	OR (95% CI)	Acute ICI-IA n (%) or mean (SD)	Chronic ICI-IA n (%) or mean (SD)	OR (95% CI)
		N=238	N=157		N=327	N=68	
Sex	Male	104 (43.7)	88 (56.1)	1.0 (ref)	171 (52.3)	32 (47.1)	1.0 (ref)
	Female	134 (56.3)	69 (43.9)	0.6 (0.41-0.91)	156 (47.8)	36 (53.0)	0.8 (0.48-1.37)
Age		62.76 (11.3)	62.12 (11.1)	1.0 (0.98-1.01)	62.70 (11.2)	61.70 (11.3)	1.0 (0.98-1.01)
Pre-existing autoimmune disease	Non arthritic rheumatic	14 (5.9)	9 (5.7)	1.1 (0.42-2.80)	18 (5.5)	5 (7.4)	1.3 (0.36-3.72)
	Dermatologic	7 (2.9)	9 (5.7)	2.0 (0.73-5.73)	11 (3.4)	5 (7.4)	2.3 (0.70-6.50)
	Ophthalmologic	19 (8.0)	9 (5.7)	0.7 (0.30-1.55)	25 (7.7)	3 (4.4)	0.6 (0.13-1.65)
	Endocrine	9 (3.8)	8 (5.1)	1.4 (0.50-3.65)	13 (4.0)	4 (5.9)	1.5 (0.42-4.43)
	GI	35 (14.7)	21 (13.4)	0.9 (0.49-1.59)	49 (15.0)	7 (10.3)	0.7 (0.26-1.42)
	Other	6 (2.5)	3 (1.9)	0.7 (0.16-2.9)	8 (0.3)	1 (1.5)	0.6 (0.32-3.32)
Tumor type	Melanoma	65 (27.3)	68 (43.3)	2.2 (1.41-3.3)	103 (31.5)	30 (44)	1.7 (1.00-2.92)
	Lung	91 (38.2)	42 (26.8)	0.58 (0.37-0.91)	115 (35.1)	18 (26.5)	0.7 (0.35-1.16)
	Genito-urinary	39 (16.4)	40 (25.5)	1.5 (0.90-2.62)	66 (20.2)	13 (19.1)	1.0 (0.45-1.88)
	GI	16 (6.7)	12 (7.8)	1.3 (0.53-3.05)	22 (6.7)	6 (8.8)	1.9 (0.65-4.78)
	Other	27 (11.3)	42 (26.8)	2.0 (1.06-3.66)	21 (6.4)	1 (1.5)	1.2 (0.52-2.51)
Type of ICI	PD-1/PDL-1	202 (84.9)	113 (72.0)	1.0 (ref)	271 (82.3)	44 (64.7)	1.0 (ref)
	CTLA-4	16 (6.7)	13 (8.3)	1.5 (0.66-3.1)	21 (6.4)	8 (11.8)	2.3 (0.99-4.37)
	Combination	20 (8.4)	31 (19.8)	2.8 (1.52-5.15)	35 (10.7)	16 (23.5)	3.7 (2.04-6.47)
Other irAE prior to ICI-IA	Non arthritic rheumatic	5(2.1)	5 (3.2)	1.5 (0.42-5.60)	10 (3.1)	0 (0.0)	NE
	Dermatologic	3 (1.3)	6 (3.8)	3.1 (0.81-14.9)	6 (1.8)	3 (4.4)	2.5 (0.51-9.61)
	Ophthalmologic	2 (0.9)	5 (3.9)	3.9 (0.83-27.33)	6 (1.8)	1 (1.5)	0.8 (0.04-4.78)
	Endocrine	9 (3.8)	14 (8.9)	2.5 (1.07-6.12)	16 (4.9)	7 (10.3)	2.2 (0.83-5.5)
	GI	21 (8.8)	22 (14.0)	1.7 (0.89-3.20)	34 (10.4)	9 (13.3)	1.3 (0.57-2.78)
	Other	3 (1.3)	11 (7.0)	4.8 (1.40-27.73)	12 (3.7)	2 (2.9)	1.0 (0.15-3.75)

Abbreviations: tx, treatment; ICI-IA, Immune checkpoint inhibitors-induced inflammatory arthritis; OR, odds ratio; CI, confidence interval; GI, gastrointestinal, irAE, immune-related adverse event, NE, not estimable

* tx include glucocorticosteroids (GC), DMARDs and biologics

evaluate whether new ICI-IA occurring in patients with a pre-existing (non-IA) autoimmune disease was associated with a greater likelihood of chronicity compared to ICI-IA occurring in patients without any pre-existing autoimmune disease.

Methods: In the MarketScan Commercial Claims, Medicare Supplemental, and Multi-State Medicaid administrative health databases, we identified all adults (18+) with at least one filled prescription for an ICI (ipilimumab, nivolumab, etc.) from Jan. 1st 2011-Dec. 31st, 2021. We excluded those without continuous health insurance coverage and those with any International Classification of Diseases (ICD) billing/hospitalization code for any IA or for DMARDs and/or biologics in the year prior to ICI initiation. The primary exposure of interest was a diagnosis of any non-IA autoimmune condition (e.g. multiple sclerosis, hypothyroidism, etc.) prior to ICI initiation. We evaluated the data between 0 and 90 days and at 180 days post-ICI-IA. Chronic ICI-IA was defined as current use of systemic glucocorticoids (GC), DMARDs and/or biologics 180 days after ICI-IA diagnosis.

Results: During the study period, 29,598 individuals were newly exposed to ICI and 395 (1.3%) of these had one or more ICD code for IA after ICI initiation. One hundred forty-nine (N=149, 38%) individuals with ICI-IA had a pre-existing autoimmune disease. The most frequent autoimmune diseases were gastrointestinal (N=56, 38%), ophthalmologic (N=28, 19%), other rheumatic diseases (N=23, 15%) and endocrine (N=17, 11%). One hundred fifty-seven (N=157, 40%) of those with ICI-IA received treatment with GC, DMARDs and/or biologics within the first 90 days after ICI-IA onset. Sixty-eight (N=68, 17% of the 395) were still under one of these treatments at 180 days post ICI-IA diagnosis. Table 1 demonstrates that men were more likely than women to receive GC, DMARDs and/or biologics treatment within the first 90 days after ICI-IA. Table 1 shows that melanoma and treatment with combination ICI (as well as a strong trend for anti-CTLA-4) were associated with chronic ICI-IA, but no pre-existing autoimmune disease was clearly associated with this outcome.

Conclusion: In univariate cross-sectional analyses of patients followed from 90 days post ICI-IA to 180 days, pre-existing autoimmune disease was not clearly associated with increased chronicity according to our definition. Melanoma, combination ICI, and possibly anti-CTLA-4 was associated with chronic ICI-IA. Multivariate hazard regression analyses are under way.

References: 1. Sharma P. et al., Cancer Discov 2021 2. Roberts J. et al., Autoimmun Rev 2020 3. Suarez-Almazor ME. et al., Support Care Cancer 2020

Disclosure: A. Ladouceur: None; **M. Hudson**: AstraZeneca, 6, Boehringer-Ingelheim, 1, 5, 6, Bristol-Myers Squibb(BMS), 5, Merck, 6, UCB, 5; **H. Behlouli**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, CorEvitas, 2, 5, Eli Lilly and Company, 2, 5, Janssen, 2, 5, Myriad, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **L. Pilote**: None; **S. Bernatsky**: None.

Abstract Number: 1058

Resolution of Immune Checkpoint Inhibitors-Induced Inflammatory Arthritis While Maintaining Active Treatment with Checkpoint Inhibitors

Alexandra Ladouceur[1], Thomas Barnetche[2], Sorilla Mary-Prey[3], Caroline Dutriaux[4], Emilie Gerard[3], Anne Pham-Ledard[3], Marie Beylot-Barry[3], Maeva Zysman[3], Rémi Veillon[3], Charlotte Domblides[5], Amaury Daste[5], Marine Gross-Goupil[5], Baptiste Sionneau[5], Félix Lefort[5], Mathieu Larroquette[5], Christophe Richez[6], Marie-Elise Truchetet[2], Thierry Schaeverbebke[7] and Marie Kostine[2], [1]Department of Rheumatology of McGill University and CHU-Bordeaux, Montréal, QC, Canada, [2]Bordeaux University Hospital, Bordeaux, France, [3]Department of Dermatology, Bordeaux University Hospital, Bordeaux, France, [4]CHU-Bordeaux, Bordeaux, France, [5]Department of Medical Oncology, Bordeaux University Hospital, Bordeaux, France, [6]Université de Bordeaux, Bordeaux, France, [7]University Hospital of Bordeaux, Bordeaux, France

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitors (ICI) are a revolutionary treatment that boost a patient's own immune system to fight cancer. However, activation of the immune system often induces off-target immune-related adverse events (irAEs). ICI-induced inflammatory arthritis (ICI-IA) affects about 5% of ICI recipients and can lead to ICI discontinuation which might potentially negatively affect tumor outcomes. We aimed 1) to characterize the evolution of ICI-IA while ICI treatment is maintained and 2) to assess how ICI-IA influences ICI management across time.

Methods: All ICI-treated patients referred to rheumatology at Bordeaux University Hospital were identified and patients with ICI-IA defined by either the presence of at least one synovitis on physical exam and/or on imaging or polymyalgia rheumatica (PMR)-like symptoms with a follow-up of ≥ 6 months after ICI-IA onset were included. Charts were manually reviewed to extract data on baseline characteristics, investigations, management and both ICI-IA and tumor outcomes.

Results: Out of 281 referred patients, 80 fulfilled the inclusion criteria, of which 49 (61.3%) were male. The median duration follow-up after ICI-IA onset was 108 weeks [ranging from 26-330 weeks]. The most common tumor was melanoma (n=38, 47.5%), followed by lung cancer (n=16, 20.0%). The mean time from ICI-IA onset to ICI-IA treatment was 8.6 weeks and ICI was continued in 63 patients (78.8%) or temporary held in 11 (13.8%). Prednisone was prescribed in 74 patients (92.5%), csDMARDs in 22 (27.5%) and biologics in 2 (2.5%). ICI-IA resolved allowing ICI-IA treatment discontinuation in 27 patients (33.8%) while still being treated with ICI. Among those, 26 (96.3%) were treated with prednisone (median maximal dose 15 mg and median duration 52.0 weeks), 3 (11.1%) with csDMARDs and 1 (3.7%) with biologics. In patients with persistent ICI-IA while on ICI, 20 (40%) and 34 (68%) had resolved at 6 and 12 months post ICI discontinuation, respectively. During follow-up, the main reason for ICI discontinuation was a cancer stable or in remission in 31 patients (38.8%), cancer progression in 22 (27.5%), other irAE in 7 (8.8%) and ICI-IA in 4 (5.0%). Of note, ICI-IA treatment and ICI management were similar between those with active arthritis and those with resolved arthritis at 6 and 12 months post ICI discontinuation.

Conclusion: In this cohort, ICI was safely continued in most patients experiencing ICI-IA. Over one third of ICI-IA resolved despite maintaining active ICI treatment allowing arthritis treatment discontinuation. Larger studies are needed to determine predicting factors of resolving ICI-IA as this could help minimize exposure to immunosuppressive treatment.

Disclosure: A. Ladouceur: None; **T. Barnetche**: Eli Lilly, 2; **S. Mary-Prey**: Bristol-Myers Squibb(BMS), 2, 12, Congress fees participation, Merck/MSD, 2, 12, Congress fees reimbursement; **C. Dutriaux**: Bristol-Myers Squibb(BMS), 1, 2, 12, Clinical trials, travel and accomodation fees, Merck/MSD, 2, 12, Clinical trials, travel and accomodation fees for boards or congress, Novartis, 2, 12, Clinical trials, travel and accomodation fees; **E. Gerard**: Bristol-Myers Squibb(BMS), 1, 12, Clinical trials, travel to scientific meetings, Merck/MSD, 1, 12, Clinical trials, travel to scientific meetings; **A. Pham-Ledard**: Bristol-Myers Squibb(BMS), 12, conference participation fees, Merck/MSD, 12, Congress participation fees; **M. Beylot-Barry**: None; **M. Zysman**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2; **R. Veillon**: AbbVie/Abbott, 5, Amgen, 6, AstraZeneca, 6, 12, Travel, accomodations, expenses, Bristol-Myers Squibb(BMS), 5, 5, 6, GlaxoSmithKlein(GSK), 5, Janssen, 2, Merck/MSD, 5, Novartis, 5, Roche, 6; **C. Domblides**: Amgen, 4, 12, travel/congress, AstraZeneca, 1, 12, travel/congress, Bristol-Myers Squibb(BMS), 1, 12, Travel/congress, Janssen, 1, Merck/MSD, 4, 12, Travel/congress, Pfizer, 12, Travel/congress, Roche, 12, Travel/congress; **A. Daste**: Bristol-Myers Squibb(BMS), 2, Merck/MSD, 2; **M. Gross-Goupil**: Amgen, 6, Bristol-Myers Squibb(BMS), 1, 6, 12, Clinical research, Merck/MSD, 1, 6, 12, Clinical research, Pfizer, 1, 12, Clinical research, Roche, 12, Clinical research; **B. Sionneau**: None; **F. Lefort**: AstraZeneca, 1, 2, 12, Clinical trials, Bristol-Myers Squibb(BMS), 12, Clinical trials, Merck/MSD, 1, 2, 12, Clinical trials, Pfizer, 12, Travel and accomodation fees, Roche, 12, Clinical trials; **M. Larroquette**: None; **C. Richez**: AbbVie/Abbott, 2, 6, Amgen, 6, AstraZeneca, 2, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, 12, receipt of drugs, GlaxoSmithKlein(GSK), 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **M. Truchetet**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Gilead, 5, 6, Merck/MSD, 6, UCB, 6, 12, support for conferences; **T. Schaeverbebke**: AbbVie/Abbott, 1, 6, 12, Clinical trials, Bristol-Myers Squibb(BMS), 1, 1, 6, 6, Eli Lilly, 1, 5, 6, 12, Clinical trials, Janssen, 6, Merck/MSD, 12, Clinical trials, Novartis, 1, 6, 12, Clinical trials, Pfizer, 1, 5, 12, Clinical trials; **M. Kostine**: None.

Abstract Number: 1059

Identification of Patients with Immune Checkpoint Inhibitor-Associated Inflammatory Arthritis Using Medicare Claims Data

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SESSION INFORMATION
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Session Title: Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitor (ICI) associated inflammatory arthritis (ICI-IA) has been suggested to occur in approximately 3-6% of ICI-treated patients with cancer[1] but most studies of ICI-IA are hampered by small numbers conducted at single centers. In this study, we aimed to identify cases of ICI-IA using administrative claims data to facilitate larger studies.

Methods: We used the Medicare 5% random sample from 2015-2019 to identify patients using ICIs. Cancer patients were identified by having at least 2 diagnosis codes from an oncologist for lung cancer, urothelial cancer or melanoma using ICD-9/10-CM codes. ICI-IA was defined as having two Medicare claims at least 30 days apart with combinations of ICD-9/10-CM diagnosis codes that favored specificity. Results were stratified by whether patients had i.) inflammatory arthritis after the date of ICI initiation and ii.) no diagnosis of a rheumatic disease or musculoskeletal complaint in the one year prior to the date of ICI initiation.

Table 1. Incidence rate of suspected de novo inflammatory arthritis among ICI-treated patients with cancer using various inclusion and exclusion criteria and outcome definitions.

Table 1: Incidence rate of suspected *de novo* inflammatory arthritis among ICI-treated patients with cancer using various inclusion and exclusion criteria and outcome definitions.

Inclusion	Exclusion	Outcome	Cohort size, n	Cases, n	Incidence Rate per 100 person years
2+ cancer diagnoses	Any prior evidence (using all available prior data) of a specific rheumatic disease, or evidence in the prior year of any non-specific joint symptoms	2+ visits for any specific or sensitive ICD9/10 diagnosis code for inflammatory arthritis	3119	193	6.8 (5.9-7.9)
2+ cancer diagnoses	Any prior evidence (using all available prior data) of any specific or non-specific joint symptom diagnosis	2+ visits for any specific or sensitive ICD9/10 diagnosis code for inflammatory arthritis	1515	65	4.5 (3.5-5.7)
No specific cancer diagnosis required (only ICI use)	Any prior evidence (using all available prior data) of a specific rheumatic disease, or evidence in the prior year of any non-specific joint symptoms	2+ visits for any specific or sensitive ICD9/10 diagnosis code for inflammatory arthritis	4422	264	6.9 (6.1-7.8)
No specific cancer diagnosis required (only ICI use)	Any prior evidence (using all available prior data) of any specific or non-specific joint symptom diagnosis	2+ visits for any specific or sensitive ICD9/10 diagnosis code for inflammatory arthritis	2171	96	4.9 (4.0-6.0)
2+ cancer diagnoses	No rheumatology visit in the prior year	Any visit with a rheumatologist (for any condition)	4286	70	1.9 (1.5-2.4)

Table 2: Characteristics of ICI-treated cancer patients with and without ICI-IA identified in the Medicare 5% sample

Table 2: Characteristics of ICI-treated cancer patients with and without ICI-IA identified in the Medicare 5% sample*

Variable	**ICI-IA patients*** N=193 (6%)	**Non-ICI-IA** N=2,926 (94%)	P value
Age - mean (SD) years	73.5 (7.2)	73.4 (8.0)	0.984
Sex (female) (%)	93 (48.2)	1294 (44.2)	0.283
Race			0.281
White	176 (91.2)	2576 (88.0)	
Black	12 (6.2)	203 (6.9)	
Other	5 (2.6)	147 (5.0)	0.495
Hispanic ethnicity	1 (0.5)	36 (1.2)	
Cancer type			**0.015**
Lung cancer	111 (57.5)	1,979 (67.6)	
Melanoma	42 (21.8)	417 (14.3)	
Urological cancer	38 (19.7)	494 (16.9)	
Other	2 (1.0)	36 (1.2)	
First ICI type			0.056
PD1	153 (79.3)	2,226 (76.1)	
PDL1	19 (9.8)	459 (15.7)	
CTLA4	21 (10.9)	241 (8.2)	

* ICD-9/10-CM codes for inclusion: 696.0, L405, 714, M05, M06, 720.0, M45, M46.8, M46.9, 725, M35.3, M31.5, 099.3, M02.9, 716, M13, 719.0, M25.4, 719.4, M25.5, 719.9, M25.9.

Results: We identified individuals with cancer initiating ICI 2016-2019 with a >= 12-month baseline. The incidence of ICI-IA varied modestly depending on the definition used and was generally in the range of 4-7 per 100 patient years (**Table 1**). The incidence rates were similar when all cancer were included. Patients with ICI-IA had mean (SD) age 73.5 (7.2) years, 48% women, 91% white (**Table 2**). More than half of patients (57.5%) had lung cancer, 21.8% had melanoma, and 19.7% urothelial cancer. The median (IQR) time from ICI initiation to first ICI-IA diagnosis was 147 (58, 320) days. The mean (SD) number of provider visits with an ICI-IA diagnoses was 5.3 (6.0), spanning a median (IQR) of 240 (105,461) days. Of the 193 ICI-IA patients identified using our preferred cohort definition, 14.5% used any conventional disease modifying anti-rheumatic drug (DMARD), and fewer than 5% (total) used any TNFi, IL-6Ri, JAKi, or rituximab; none used abatacept. Only 31 (16.1%) received care from a rheumatologist. Median time from ICI initiation to seeing a rheumatologist was 229 (105, 483) days and these patients had a mean (SD) of 11.7 (11.3) visits with the rheumatologist.

Conclusion: We created a simple claims-based algorithm for the preliminary identification of ICI-IA cases using national Medicare claims that results in an incidence similar to that found using registry data.[1] While validation of this algorithm using patient level clinical data linked to administrative claims may be useful to identify suspected cases of irAEs, it is likely that more sophisticated methods (e.g. natural language processing run on unstructured data) or manual medical rec

[1] Kostine M et al Ann Rheum Dis. 2018 Mar;77(3):393-398.

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Abstract Number: 1060

Impact of Troponin Monitoring on Cardiac Outcomes in Patients Receiving Immune Checkpoint Inhibitors

Maja Ivanovic[1], Antonia Chan[2], Miguel Franquiz[1], Sidra Xu[3], Carissa Lee[3], Muhammad Fazal[4], Jonathan You[1], Ronald Witteles[4], Joel Neal[5], Sean Wu[4], Sarah Waliany[1] and Han Zhu[4], [1]Department of Medicine, Stanford University, Stanford, CA, [2]Stanford Medical School, Stanford, CA, [3]Stanford University, Stanford, CA, [4]Department of Cardiology, Stanford University, Stanford, CA, [5]Department of Oncology, Stanford University, Stanford, CA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
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Background/Purpose: Immune checkpoint inhibitors (ICI) are an increasingly used form of anti-cancer therapy, but they have been associated with a range of cardiac immune-related adverse events (iRAEs). Early detection of cardiac iRAEs may lead to prompt intervention and improved patient outcomes. In this study, we investigate the association between regular troponin monitoring and major adverse cardiac events (MACE) detection and overall survival (OS) in patients receiving ICI.

Methods: We performed a retrospective study of 825 patients receiving ICI from January 2018 to March 2022. Of these patients, 428 (52%) were evaluated via a standard troponin monitoring protocol with Troponin I measured at baseline and prior to each ICI dose. The control group included 397 (48%) patients who underwent ICI therapy prior to initiation of this

troponin monitoring protocol. We collected outcomes in all patients for nine months following their first dose of ICI. Primary outcomes included severe MACE (defined as grade ≥ 4 Cardiovascular Adverse Events (CV AEs) according to the National Cancer Institute's Common Terminology Criteria for Adverse Events version 5) and OS. To investigate whether troponin monitoring was associated with discontinuation of ICI therapy, we compared time-to-treatment-failure (TTF) between monitored and unmonitored patients in a subgroup of patients with melanoma. TTF was defined as the interval from ICI initiation to discontinuation for any reason. Additionally, we studied the relationship between troponin elevation and MACE by comparing the rates of MACE (defined as grade ≥3 CV AEs) between all patients with a positive troponin measurement during the monitoring period versus patients with negative or no troponin measurement. A positive troponin was defined as Troponin I >0.055.

Results: We found a lower rate of severe MACE in patients who underwent troponin monitoring (0.5%) compared to patients who underwent no troponin monitoring (1.8%), (HR 0.17, 95% CI 0.02-0.79). There was no difference in OS at nine months between monitored patients (81%) and unmonitored patients (82%), (HR 1.04, 95% CI 0.75-1.44). In patients with melanoma (N=89), we found no difference in TTF at nine months between patients who were monitored (54% discontinued ICI) and unmonitored (53% discontinued ICI) (p = 0.91). There were 71 patients (8.6%) with positive troponin measurement

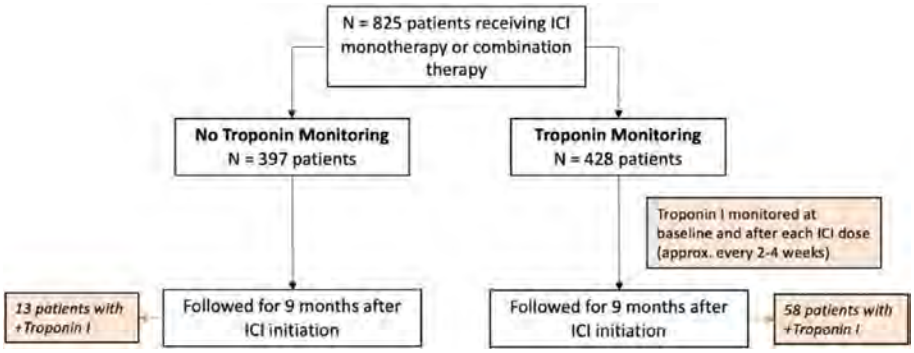

Figure 1. Troponin monitoring algorithm.

Table 1. There was a significantly lower rate of severe MACE in the troponin monitoring group compared to the unmonitored group. There was no difference in all MACE and overall survival between the two groups.

Table 1
MACE and OS within 9 Months of ICI initiation

	No Troponin Monitoring (n = 397)	Troponin Monitoring (n = 428)	Multivariable Hazard Ratio (95% CI)	P value
Death	71 (17.9%)	80 (18.7%)	1.03 (0.75 - 1.43)	0.84
Severe MACE (grade ≥ 4 CV AEs)	7 (1.8%)	2 (0.5%)	0.17 (0.02 – 0.79)	0.04
Arrhythmia	3 (0.7%)	2 (0.5%)	-	-
Myocarditis	3 (0.7%)	0 (0%)	-	-
Congestive Heart Failure	0 (0%)	0 (0%)	-	-
Acute Coronary Syndrome	0 (0%)	0 (0%)	-	-
Stroke	1 (0.2%)	0 (0%)	-	-
Pericardial Effusion	0 (0%)	0 (0%)	-	-
All MACE (grade ≥ 3 CV AEs)	11 (2.8%)	16 (3.7%)	1.34 (0.62 - 3.00)	0.47
Arrhythmia	4 (1%)	2 (0.4%)	-	-
Myocarditis	3 (0.7%)	5 (1.2%)	-	-
Congestive Heart Failure	1 (0.2%)	4 (0.9%)	-	-
Acute Coronary Syndrome	1 (0.2%)	2 (0.4%)	-	-
Stroke	1 (0.2%)	1 (0.2%)	-	-
Pericardial Effusion	1 (0.2%)	2 (0.4%)	-	-

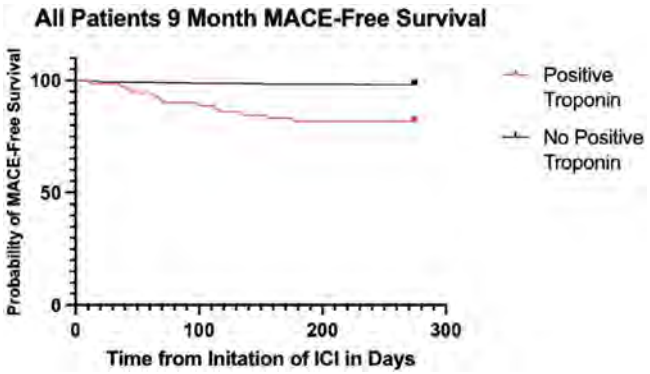

Figure 2. There was a significantly higher rate of in MACE in patients with a positive troponin compared to patients with no troponin or negative troponin within 9 months of first ICI dose ($p < 0.001$).

during the evaluated interval. Patients with positive troponin had a higher risk of MACE compared to those with negative or no troponin measurement (HR 7.20, 95% CI 2.99–17.55). This finding remained consistent when evaluated in the monitored subgroup alone (HR 4.34, 95% CI 1.578 – 12.38).

Conclusion: We found that patients undergoing regular troponin monitoring with ICI therapy had a lower rate of severe MACE compared to those without monitoring. Troponin elevation was significantly associated with MACE. Additionally, there was no difference in OS between those who were monitoring or unmonitored, and there was no difference in TTF between these two groups in patients with melanoma.

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Abstract Number: 1061

Vasculitis as an Immune-Related Adverse Event: Unraveling the Complexities at the Intersection of Immunology and Vascular Pathology

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Immunological Complications of Medical Therapy Poster

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Background/Purpose: Vasculitis as an immune-related adverse event (irAE) from checkpoint inhibitor therapy (ICI) to treat cancer is a rare clinical event, and little is known regarding its nosology, clinical manifestations, or response to treatment and outcomes. In an attempt to address these gaps, we used the Preferred Reporting Items for Systemic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) framework to further define this complication.

Methods: Two independent PUBMED searches in September and November of 2022 revealed 127 publications with 37 excluded from title by relevance, 43 excluded by article type, and 23 excluded due to lack of biopsy results, or biopsy negative for vasculitis. Twenty nine documented cases from 24 publications were included for final analysis. Basic demographics, ICI details, timing of onset of vasculitis symptoms, irAE treatment and outcomes were collected. The vasculitides were classified using 2022 ACR/EULAR Vasculitis Classification Criteria as well as 2012 Revised Chapel-Hill Nomenclature. Naidoo et al 2023 consensus definitions for irAEs were used for early versus delayed irAEs, and efforts were made to classify steroid-responsive versus unresponsive irAEs.

Results: Of the 29 cases reviewed, the average age of patients was 62.1±11.0, composed of 58.6% (17) male and 41.3% (12) female. Prominent cancer types were lung cancer (41.4%; n=12), melanoma (41.4%; n=12), and renal cancer (10.3%; n=3), with vast majority being stage 4 (75.9%, n=22) and Stage 3 (10.3%, n=3). Only 8 cases met the ACR/EULAR criteria, and by Chapel-Hill Nomenclature, approximately a third were small-vessel vasculitis (31.0%; n=9) with n=4 positive for ANCA. Most biopsies were taken from the skin (37.9%, n=11) and kidney (24.1%, n=7). Patients were either treated with single (65.5%, n=19), dual (17.2%; n=5), or sequential (17.2%; n=5) ICI regimen which included anti-PD-1 therapy in all but one case, with mean of 8.7 ± 10.5cycles received. Mean time to onset of symptoms from start ofICI was 7.2 ± 7.8 months, with delayed irAE (>3 months of initial immunotherapy) occurring in 55.2% of cases. Treatment most commonly included glucocorticoids in 96% of cases and immunotherapy was often discontinued (44.8%; n=13). Clinical improvement of irAE was documented in 86.2% (n=25). Data were missing in terms of fate of ICI (34.5%; n=10) and tumor outcomes (41.4%; n=12). Cancer progressed in 20.7% (n=6),stable in 34.5% (n=10) cases, and 6 patients died of all-causes.

Conclusion: Vasculitis as an irAE appears clinically heterogeneous and rare. Among reported cases with adequate documentation, vasculitis is of delayed onset following the initiation of immunotherapy. Outcomes of ICI-vasculitis were generally favorable, responding to glucocorticoids and immunotherapy withdrawal. There is an urgent need for more standardized reporting of rare irAEs such as vasculitis to clarify clinical risks,classification, relationship to immunotherapy and outcomes.

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Abstract Number: 1062

Antiretinal Autoantibodies in Hydroxychloroquine Eye Toxicity

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
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Table 1. Presence of anti-retinal autoantibodies in sera of SLE subjects.

Antibody to retinal antigen	Diagnosis of HCQ retinal toxicity n=28	No retinal toxicity n=241	P value	Frequency in Historic controls (Adamus et al. 2020 PMID: 31770612)
Aldolase	39.3% (11)	33.2% (80)	ns	2%
Enolase	57.1% (16)	41.4% (100)	0.11	13%
Arrestin	**60.7 (17)**	**30.7% (74)**	**0.001**	**2%**
Tubulin	17.9% (5)	16.2% (39)	ns	2%
PKM2	**46.4% (13)**	**28.2% (68)**	**0.047**	**4%**
GAPDH	21.4% (6)	14.9% (36)	ns	11%
HSP	17.9% (5)	13.7% (33)	0.23	1%
CAII	35.7% (10)	27.4% (66)	ns	15%

Background/Purpose: Autoimmune retinopathy (AIR) is a disease process in which circulating autoantibodies (AAbs) against retina-specific antigens cause local inflammation and can lead to blindness. Hydroxychloroquine (HCQ), likewise, can cause retinal toxicity, typically in a dose-dependent manner, for which routine screening is recommended in systemic lupus erythematosus (SLE) patients. AIR has been reported in patients with SLE but the frequency of antiretinal AAbs in SLE patients is not well described. Furthermore, the role of antiretinal AAbs in HCQ related eye toxicity has not been described. The objective of this study is to determine whether patients diagnosed with HCQ retinal toxicity are more likely to have circulating antiretinal AAbs compared to controls.

Methods: This study was conducted at two academic institutions within the United States. Patients in this study were enrolled in a longitudinal cohort study of cardiovascular risk factors. We performed antiretinal AAbs testing on 269 SLE plasma samples collected at baseline. We retrospectively reviewed charts of these patients for the presence of HCQ retinal toxicity, as well as the baseline presence of risk factors for HCQ toxicity. Our primary goal was to determine frequency of specific antiretinal AAbs in SLE patients with HCQ retinal toxicity compared to SLE patients without retinal toxicity.

Results: Patients with a diagnosis of HCQ retinal toxicity had a higher likelihood of testing positive for anti-arrestin AAbs (60.7% of patients vs. 30.7% of patients, p=0.001) and PKM2 antibodies (46.4% of patients vs. 28.2% of patients, p=0.047) compared to patients without a diagnosis of retinal toxicity (see table 1). Patients with a history of HCQ eye toxicity also had a trend towards a higher number of AAbs, with a mean of 2.96 ± 2.40 vs. 2.05 ± 1.74 in the group with no history of toxicity. In multivariate analysis accounting for risk factors associated for HCQ eye toxicity, including renal disease, BMI, average HCQ dose per year of disease duration, and disease severity using the Lupus Severity Index (LSI), we found that the presence of arrestin AAbs was associated with OR 3.2 for developing HCQ eye toxicity.

Conclusion: Antiretinal AAbs, especially arrestin and PKM2, were more common in SLE patients with HCQ retinal toxicity compared to patients without HCQ retinal toxicity. The pathogenesis and clinical significance of these autoantibodies is not clear. However, even when controlling for other risk factors associated with HCQ eye toxicity, anti-arrestin AAbs were associated with increased odds for the development of eye toxicity, suggesting a potential role for antiretinal AAbs as a biomarker of HCQ eye toxicity risk. Further prospective studies are needed to evaluate the risk of developing HCQ retinal toxicity in patients with known circulating antiretinal AAbs.

Disclosure: S. Good: None; **G. Adamus**: None; **M. Gorin**: None; **J. Jacquez**: None; **J. Grossman**: None; **B. Skaggs**: None; **A. Hasan**: None; **M. McMahon**: None.

Abstract Number: 1063

Impact of Aging on Rheumatic Immune-related Adverse Events Secondary to Immune Checkpoint Inhibitors: Experience from the Canadian Research Group of Rheumatology in Immuno-Oncology (CanRIO)

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SESSION INFORMATION

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Background/Purpose: Immune checkpoint inhibitors (ICI) have revolutionized cancer therapy. Their use is complicated by development of immune-related adverse effects (irAEs), including rheumatic irAEs (Rh-irAE). Aging is known to be associated with an increase in chronic inflammation, likely driven by age-related changes in inflammatory networks and proinflammatory pathways, referred to as "inflammaging". Older age has been implicated with the development of more frequent and severe irAEs. In this study, we aim to examine whether older patients with Rh-irAEs develop more severe Rh-irAEs or greater number of irAEs compared to younger patients.

Table 1: Baseline characteristics of patient cohort

Characteristics	Younger Group < 65 years (n = 58)	Older Group ≥ 65 years (n = 81)
Age median (range)	58.5	72
Sex (% female)	30 (52%)	31 (38%)
Cancer Type, n (%)		
• Melanoma	17 (29%)	22 (27%)
• Non-Small Cell Lung Cancer	8 (14%)	20 (25%)
• Renal Cell Carcinoma	9 (16%)	14 (17%)
• Non- Melanoma Skin Cancer	1 (2%)	4 (5%)
• Other	23 (40%)	21 (26%)
Cancer Therapy, n (%)		
• Nivolumab only	10 (17%)	11 (14%)
• Pembrolizumab only	0 (0%)	0 (0%)
• Nivolumab and Ipilimumab	16 (28%)	15 (19%)
• Pembrolizumab in another combination	23 (40%)	42 (52%)
• Durvalumab	0 (0%)	3 (4%)
• Other combination	2 (3%)	2 (2%)
• Other	7 (12%)	8 (10%)
Duration of immune checkpoint inhibitor therapy, months (median, 25th percentile, 75th percentile)	7, 2, 11	7.5, 2.75, 12

ICI = immune checkpoint inhibitor

Methods: Adults who develop new Rh-irAEs after ICI exposure are prospectively followed at 9 academic sites across Canada as part of the CanRIO prospective cohort. We compared the severity and number of irAE between patients ≥65 years and < 65 years, using logistic regression and Poisson regression, respectively. As part of secondary analysis, we compared the immunosuppression and cancer treatment received in both groups.

Table 2: Characteristics of Rh-irAE stratified by age

Characteristics	< 65 years n=58 (42%)	≥ 65 years n=81 (58%)	p-value
Rh-irAE[a]			
• Ir-Arthritis	45 (78%)	72 (89%)	
• Ir-Connective tissue disease	5 (9%)	5 (6%)	
• Ir-Myositis	3 (5%)	3 (4%)	
• Ir-Vasculitis	6 (10%)	3 (4%)	
• Ir-Sarcoid-like reaction	2 (3%)	1 (1%)	
Other irAE[b]	n = 30	n = 35	
• Skin	10 (17%)	14 (17%)	
• Thyroid	10 (17%)	10 (12%)	
• Other	21 (36%)	21 (26%)	
Rh-irAE severity (CTCAE grade), n (%)			0.875
• 1 to 2	43 (74%)	61 (75%)	
○ 1 (asymptomatic/mild)	11 (19%)	29 (36%)	
○ 2 (moderate)	32 (55%)	32 (40%)	
• 3 to 4	15 (26%)	20 (25%)	
○ 3 (severe)	15 (26%)	20 (25%)	
○ 4 (life-threatening)	0 (0%)	0 (0%)	
Number of irAE:			0.283
• 1	30 (52%)	46 (57%)	
• 2	14 (24%)	24 (30%)	
• 3+	14 (24%)	11 (14%)	
Treatment for irAE:			
• Prednisone (>10 mg) monotherapy	12 (21%)	15 (19%)	
• CsDMARD monotherapy	12 (21%)	13 (16%)	
• Prednisone (>10 mg) PO and csDMARDs	9 (16%)	20 (25%)	
• Biologic DMARDs (+/- Prednisone and csDMARDs)	2 (3%)	2 (2%)	
• Other / Untreated	23 (40%)	31 (38%)	
ICI continuation:			
• ICI held	18 (31%)	27 (33%)	
• ICI discontinued	15 (26%)	15 (19%)	
• ICI continued / unaffected	25 (43%)	39 (48%)	
Patients with joint-related Rh-irAEs (n = 107)	n = 41	n = 66	0.400
Rh-irAE severity (CTCAE grade), n (%)			
• 1 to 2	28 (68%)	50 (76%)	
• 3 to 4	13 (32%)	16 (24%)	
Patients with non-joint-related Rh-irAEs (n = 25)	n = 17	n = 15	0.292
Rh-irAE severity (CTCAE grade), n (%)			
• 1 to 2	15 (88%)	11 (73%)	
• 3 to 4	2 (12%)	4 (26%)	

a. Three people in each of the younger and older group have 2 Rh-irAEs each. b. Eleven people from the younger group and 10 people from the older group have ≥2 non-Rh-irAEs each. IrAE = immune-related adverse event; Rh-irAE = rheumatic immune-related adverse event; Ir = immune-related; CTCAE = Common Terminology Criteria for Adverse Events; ICI = immune checkpoint inhibitor

Results: 139 Patients with de novo Rh-irAEs recruited between Jan 2020 and March 2023 were included, 58 in the "younger" (< 65 years) and 81 in the "older" (≥65 years) group (Table 1).There was no significant difference in severity of Rh-irAE (p =0.86) or number of irAEs in each group (p = 0.283) (Table 2). Treatment of irAEs was similar between the two groups, with most patients receiving prednisone monotherapy, conventional synthetic DMARD (csDMARD) monotherapy, or combinations of prednisone/csDMARDs. Biologic DMARDs were infrequently used in both groups. ICI use was similar in both groups. There was a trend towards more severe joint-related Rh-irAEs in the younger group (32% vs 24%, p-value = 0.400), and more severe non-joint related Rh-irAEs (12% vs. 26%, p-value = 0.292) in the older group.

Conclusion: There is growing literature on the role of aging and autoimmunity, but limited data on the relationship between aging and autoimmune reactions, especially after exposure to ICI. In this prospective cohort study, we found similar numbers of overall irAE and severity of Rh-irAE in older and younger patients and similar treatment in both groups. As the role of immunotherapy continues to expand, further investigations in this area can provide insight on whether age-related changes in the immune system influence the development, severity, and clinical course of irAE, which may impact patient counselling and underlying cancer therapy.

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Abstract Number: 1064

Seroconversion Rates in Rituximab-Treated Rheumatic Patients Receiving COVID-19 Vaccination

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SESSION INFORMATION
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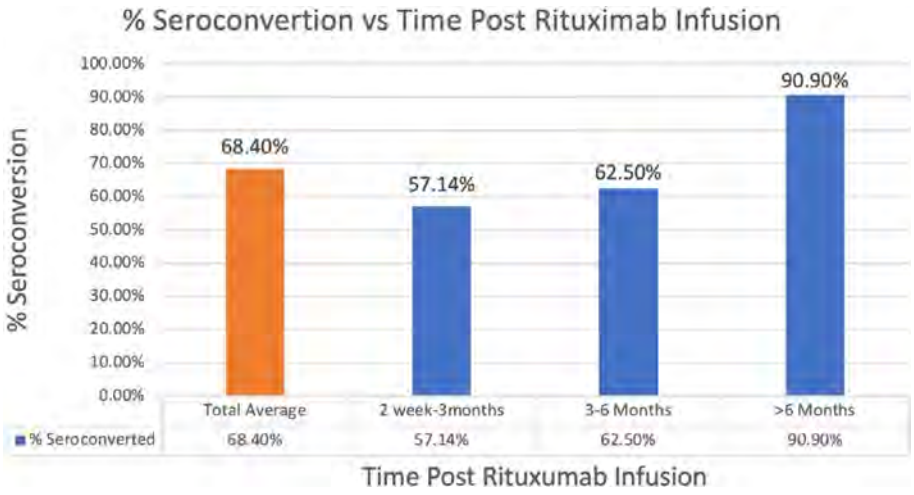
Background/Purpose: COVID-19 has increased the mortality rates among rheumatic patients, mainly those immunocompromised or with underlying comorbidities. During the COVID-19 vaccine development, patients on immunomodulatory drugs such as rituximab (RTX) were excluded from the trials due to their “high risk” categorization.

Aim: Assess the seroconversion rate of RTX-treated rheumatic patients on the COVID-19 vaccine.

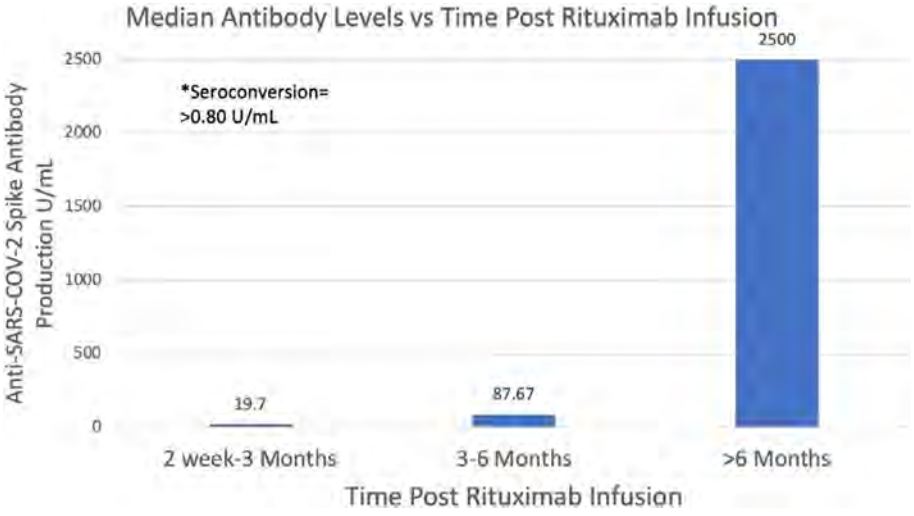
Methods: An observational cohort study on adult patients with various established inflammatory rheumatic diseases at UL Hospitals Group, Limerick receiving ≥2 COVID-19 vaccination and on scheduled RTX infusion (received ≥1 dose). Patients were stratified based on time post-immunization (< 1 month, 1-3 months, 3-6 months, and >6 months post-vaccination).

Samples (taken ≥14 days after the latest vaccination) were analyzed using the Elecsys anti-SARS-CoV-2 immunoassay for in vitro qualitative detection of IgG antibodies to SARS-COV-2, and screened for quantitative detection of anti-SARS-COV-2 nucleocapsid antigen (for previous COVID-19 infection) and anti-SARS-COV-2 spike protein (for immune response to the vaccine). The control group included patients on anti-TNF and tocilizumab (TOC). Seroconversion in response to the SARs-COV-2 is determined at >0.80 U/mL based on the manufacturer's guidelines.

Results: 49 patients were included (38 on RTX, 8 anti-TNFs, 3 TOC). Seroconversion rates were higher in the 1-3-month (75%) and 3-6-month (77%) RTX timelines; however, rates at 1 and 6 months were equal (60%) indicating antibody waning over this time period may not be significant in affecting seroconversion rates (levels remained ≥0.80 U/mL threshold). Whilst average seroconversion for the entire RTX cohort is 68.4%, the highest rates were seen in patients with a 6-month gap (90.9%). The lowest rates were seen in patients receiving immunization in the 2 week-3 months following RTX (57.14%), while the 3-6 months group showed slight improvement (62.5%). The patient population receiving anti-TNFs and TOC showed a 100% seroconversion rate.



Analysis of rates of seroconversion in rituximab patients from the time of infusion to vaccination.



Analysis of median antibody levels in rituximab patients from the time of infusion to vaccination.

Conclusion: Our data shows that a third of RTX patients treated didn't achieve seroconversion following immunization against SARS-COV-2 while the highest rates were seen in patients who had a 6-month gap. This data suggests benefit for delaying RTX infusion greater than the standard 6-month interval in suitable patients, prior to vaccination, to allow patients to reach adequate seroconversion against COVID-19 before reinitiating treatment.

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Association Between COVID-19 and Disease-Modifying Antirheumatic Drugs

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SESSION INFORMATION

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Background/Purpose: Describe patients(pts) hospitalized with COVID-19C(C19) who were on disease modifying antirheumatic drugs (DMARDs) before admission(BA); assess if clinical outcomes differed from pts without BA DMARD exposure

		G1 n(%) n=465	G2 n(%) n=464	P-value	Total n(%) n=929
Sex	Female	205 (44.1)	211 (45.5)	0.671	416 (44.8)
	Male	260 (55.9)	253 (54.5)		513 (55.2)
Race	Caucasian	435 (93.5)	435 (93.8)	0.140	870 (93.6)
	Black or African American	15 (3.2)	22 (4.7)		37 (4.0)
	Asian	4 (0.9)	4 (0.9)		8 (0.9)
	American Indian or Alaska native	2 (0.4)	0 (0)		2 (0.2)
	Native Hawaiian or other Pacific Islander	1 (0.2)	2 (0.4)		3 (0.3)
	Unknown/Other	8 (1.7)	1 (0.2)		9 (1.0)
Ethnicity	Hispanic	26 (5.6)	17 (3.7)	0.118	43 (4.6)
	Non-Hispanic	424 (91.2)	439 (94.6)		863 (92.9)
	unknown	15 (3.2)	8 (1.7)		23 (2.5)
Age	Mean	61.6	61.6	0.928	61.6
	SD	12.4	12.6		12.5
Insurance type	Government-funded	316 (68.0)	310 (66.8)	0.641	626 (67.4)
	Private	145 (31.2)	152 (32.8)		297 (32.0)
	Self-paying	4 (0.9)	2 (0.4)		6 (0.6)

Table 1. Demographics. G1 (prior to admission DMARD use), G2 (no prior to admission DMARD use).

Methods: Retrospective review. Inclusion: admitted with C19, 18-85 years, 01/01/2020-12/31/2021, use of BA DMARDs (G1); without BA DMARD exposure age- & sex-matched to G1 (G2)

		G1 n(%) n=465	G2 n(%) n=464	P-value	Total n(%) n=929
Smoking history	Former smoker	198 (42.6)	201 (43.3)	0.037	51 (5.5)
	Current smoker	22 (4.7)	43 (9.3)		34 (3.7)
	Never smoker	240 (51.6)	217 (46.8)		830 (89.3)
	Unknown	5 (1.2)	3 (0.6)		14 (1.5)
BMI	Mean	35.1	33.8	0.0265	34.4
	SD	9.2	8.9		9.1
Chronic kidney disease	Yes	107 (23.0)	92 (19.8)	0.237	199 (21.4)
	No	358 (77.0)	372 (80.2)		730 (78.6)
Diabetes	Yes	170 (36.6)	176 (37.9)	0.665	346 (37.2)
	No	295 (63.4)	288 (62.1)		583 (62.8)
Hypertension	Yes	220 (47.3)	228 (49.1)	0.578	448 (48.2)
	No	245 (52.7)	236 (50.9)		481 (51.8)
Heart failure	Yes	49 (10.5)	63 (13.6)	0.155	112 (12.1)
	No	416 (89.5)	401 (86.4)		817 (87.9)
Chronic lung disease	Yes	44 (9.5)	72 (15.5)	0.005	116 (12.5)
	No	421 (90.5)	392 (84.5)		813 (87.5)

Table 2. Comorbidities. G1 (prior to admission DMARD use), G2 (no prior to admission DMARD use).

		G1 n(%) n=465	G2 n(%) n=464	P-value	Total n(%) n=929
ICU admission	Yes	313 (67.3)	158 (34.1)	<0.001	471 (50.7)
	No	152 (32.7)	306 (65.9		458 (49.3)
Intubation and mechanical ventilation	Yes	221 (47.5)	93 (20.0)	<0.001	314 (33.8)
	No	244 (52.5)	371 (80.0)		615 (66.2)
Non-invasive ventilation	Yes	326 (70.1)	169 (36.4)	<0.001	495 (53.3)
	No	139 (29.9)	295 (63.6)		434 (46.7)
Bacterial pneumonia	Yes	62 (13.3)	83 (17.9)	0.056	145 (15.6)
	No	403 (86.7)	381 (82.1)		784 (84.4)
Hospital stay length (days)	Mean	17.4	12.2	<0.001	14.8
	SD	16.7	9.6		13.9
Admission-to-ICU hours	Mean	63.4	74.7	0.231	67.2
	SD	89.1	109.9		96.6
Duration of ICU stay (days)	Mean	12.7	10.7	0.041	12.0
	SD	10.3	10.1		10.2
Admission-to-vent hours	Mean	116.1	114.3	0.911	115.6
	SD	125.3	124.1		124.7
Duration of ventilation (days)	Mean	13.9	11.9	0.299	13.3
	SD	17.6	9.8		15.7
In-hospital mortality	Yes	179 (38.5)	96 (20.7)	<0.001	275 (29.6)
	No	286 (61.5)	368 (79.3)		654 (70.4)

Table 3. Admission-associated variables. G1 (prior to admission DMARD use), G2 (no prior to admission DMARD use).

Results: In total, 929 pts were included; 44.8% were female, and 55.2%, male. Most were Caucasian(93.6%); 4.0% were Black, 0.9% Asian. Most were non-Hispanic (91.2%). Mean age was 61.6(standard deviation(s) 12.5). G1 composed 50.1% and G2 49.9%. No differences existed between groups(grps) when age (p 0.928), sex (p 0.671), race (p 0.140) or ethnicity (p 0.118) were compared. Mean BMI was 34.4 (s 9.1); greater in G1(35.1(s 9.2)) than G2(33.8 (s 8.9)) (p 0.025). Smoking history was seen in 49.9%; of these, 86.0% were former smokers and 14.0% were current smokers. Never-smokers composed 49.2% and 0.9% had unknown smoking status. G1 had more never-smokers (51.6%) than G2 (46.8%); G1 had fewer current smokers (4.7%) than G2(9.3%) (p 0.037). Prevalence of chronic kidney disease (21.4%, p 0.237), diabetes (37.2% , p 0.665), hypertension (48.2%, p 0.578), and heart failure (12.1%, p 0.155) were similar between grps. Chronic lung disease(CLD) in 12.5%; more G2 pts had CLD(15.5%) than G1(9.5%) (p 0.005). Mean Charlson Comorbidity Index (CCI) was 3.9(s 3.2) and was similar between grps (p 0.357). Mean hospital stay length(HSL): 14.8 days(s 13.9); HSL was longer in G1(17.4(s 16.7)) than G2(12.2 (s 9.6)) p< 0.001. ICU admission occurred in 50.7%; mean duration of ICU stay: 12.0 days(s 10.2); mean admission-to-ICU(ATI) interval: 67.2 hours(s 96.5). G1 had more ICU admissions (67.3% vs 34.1%, p< 0.001), and longer ICU stays (12.7 days, s 10.3) than G2 (10.7, s 10.0), p 0.0413; the ATI was similar between grps(p 0.231). Intubation and mechanical ventilation (IMV) occurred in 33.8%; more G1 pts had IMV(47.5%) than G2(20.0%), p< 0.001. Mean admission-to-ventilation interval(IAV) was 115.6 hours(s 124.5) and was similar between grps(p 0.911). Mean vent duration was 13.3 days (s 15.7) and was similar between grps(p 0.299). Non-invasive ventilation(NIV) occurred in 53.3%; more G1 pts (70.1%) received NIV than G2(36.4%), p< 0.001. Mean admission-to-NIV duration was 70.7 hours(s 118.9) and was similar between grps(p 0.322). Mean admission respiratory rate(RR) was 23.3 (s 6.6), and similar between grps (p 0.385). Mean RR during admission was 21.8(s 3.3); G1 was greater (22.6, s 3.4) than G2(21.0, s 3.0), p< 0.001. Mean maximum RR was 38.5(s 14.6); G1 was greater (40.5, s 13.2). than G2(36.5, s 15.6), p< 0.001. In-hospital mortality occurred in 29.6%. G1 was greater (38.5%) than G2 (20.7%); p< 0.001

Conclusion: Comorbidity burden was similar between grps. Although more G2 pts had CLD, G1 pts had worse respiratory outcomes including greater RR, longer HSL, greater IMV and NIV, and overall greater mortality. Our study suggests that BA DMARD exposure may predispose to worse respiratory outcomes and survival outcomes in pts hospitalized with C19 and this subset of pts may require closer monitoring when hospitalized.

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Abstract Number: 1066

Biologic Drug and Anti-Drug Antibody Monitoring: All 5 TNF-Inhibitors, Infliximab, Adalimumab, Golimumab, Etanercept, Certolizumab Pegol, in 63,930 Patient Samples

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Session Time: 9:00AM–11:00AM

Background/Purpose: Biologic therapeutic drug monitoring (TDM) of TNF-inhibitor drug and anti-drug antibody provides patient-specific pharmacokinetic and immunogenic assessment. In suboptimal response, drug and anti-drug antibody concentrations discern the underlying mechanism of failure as: 1) *Pharmacokinetic Insufficiency*, not enough drug (low drug) 2)

Mechanistic Mismatch, wrong type of drug (as evidenced by sufficiently high drug) or 3) *immunogenicity* (anti-drug antibodies) As such, biologic TDM informs the very different medication decisions of whether to increase the same biologic or to switch drug, in- or out-of class.

Methods: Drug (in µg/mL) and anti-drug antibody (in ng/mL) were measured by lab developed chemiluminescent immunoassays (Table 1). Of note, all drug assays measure the antibody-unbound fraction of drug when serum anti-drug antibodies are present. All anti-drug antibody assays are drug-tolerant and drug-specific as verified by a confirmatory test. Blood

Table 1. Biologic TNF-Inhibitor Drug and Anti-Drug Antibody Assays: Performance Characteristics and Interpretation

Table 1: Biologic Anti-TNF Drug and Anti-Drug Antibody Assays: Performance and Interpretation

Performance of Biologic Drug Assays					
	IFX	**ADL**	**GOL**	**CTZ**	**ETN**
Assay Sensitivity LLOQ (µg/mL)	0.4	0.6	0.5	1.0	0.2
Inter-Assay Precision %CV	<8.5	<7.1	<7.4	<8.0	<13.8
Inter-Assay Accuracy % Bias	<4.9	<9.5	<6.8	<8.3	<13.7
Interpretive Comment	This drug assays measures the antibody-unbound fraction of drug that is pharmacodynamically active when anti-drug antibodies are present in serum.				
Performance of Anti-Drug Antibody Assays					
	Anti-IFX	**Anti-ADL**	**Anti-GOL**	**Anti-CTZ**	**Anti-ETN**
Assay Sensitivity LLOQ (ng/mL)	22	25	20	40	75
Inter-Assay Precision %CV	<9.7	<11.5	<5.9	<8.4	<9.5
Inter-Assay Accuracy % Bias	<4.1	<7.9	<8.1	<10.7	<14.3
Inverse Relationship with Drug?	Yes	Yes	Likely	Yes	No
Observed Immunogenicity Rate	45.2%	39.4%	4.4%	67.6%	72.3%
Proposed Titer Designation Cut-points	Low: <200 High: >1000	Low: <100 High: >800	Insufficient data to determine	Low: <1000 High: >5000	Low: <1000 High: >1000 *But no inverse relationship
Interpretive Comments	Anti-drug antibody levels should be interpreted in the context of the concomitant trough free drug concentration. Low titer anti-drug antibodies may be transient while high titers are likely to be more consequential.				
	Some immunogenicity is reversible. Elimination of intermediate titer some high titer Abs has been achieved with dose escalation and/or methotrexate or thiopurine.		Mean GOL with low (<50) or high (>50) anti-GOL were 0.51 and 0.36, respectively.	Non-neutralizing anti-pegol Abs cannot be ruled out.	Mean ETN with low (<1000) or high (>1000) anti-ETN were 2.11 and 1.97, respectively.

Figure 1: Distribution of Drug Concentrations in Anti-Drug Antibody-Negative Samples

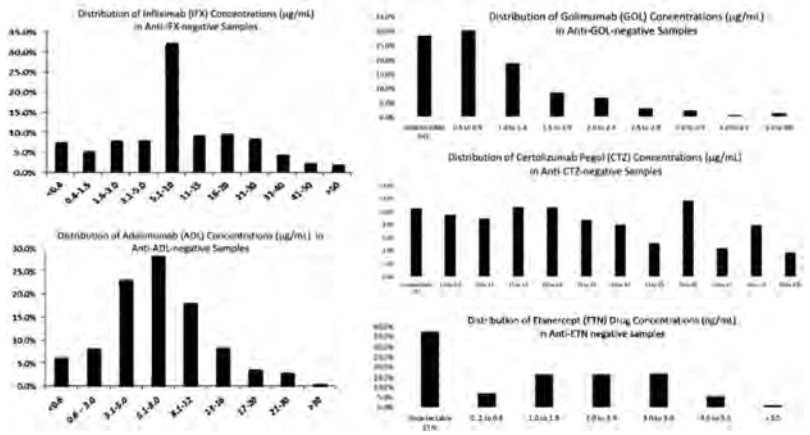

Figure 1. Distribution of Biologic Drug Concentrations in Anti-Drug Antibody-Negative Samples

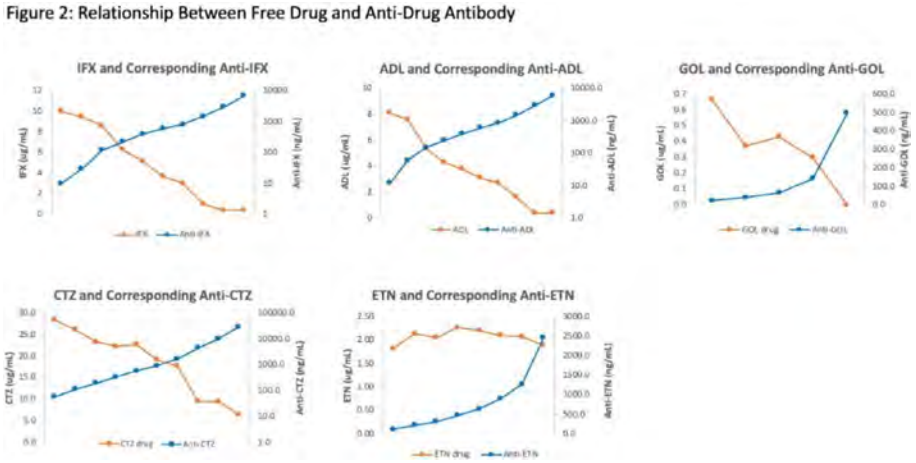

Figure 2. The Relationship between Biologic Drug and Anti-Drug Antibody Concentrations

collection just prior to next infusion/injection is recommended because target ranges have been set by studies using trough concentrations.

Results: Serum samples from 37,165, 22,412, 1032, 2587, and 734 patients were analyzed for IFX, ADL, GOL, CTZ or ETN and corresponding anti-drug antibodies. Distribution of drug levels (Figure 1) demonstrates that even in the absence of immunogenicity, many patients may be subtherapeutic when using reasonable, if not well-established, therapeutic targets of 3 for IFX, 5 for ADL, 3 for GOL, 20 for CTZ, and 3 for ETN. Immunogenicity rates were 45.2%, 39.4%, 4.4%, 67.6% and 72.3% for IFX, ADL, GOL, CTZ and ETN, respectively (Table 1). High immunogenicity of ETN and CTZ may be explained by their uniqueness as fusion and pegylated molecules, respectively. Figure 2 demonstrates the relationship between free drug and anti-drug antibody. Analysis of this inverse relationship yielded cut-points for titer designations of low, intermediate, and high for anti-IFX, anti-ADL, and anti-CTZ (Table 1). Of note, ETN alone lacked this inverse relationship. Anti-ETN, even in high titer, had no effect on concomitant ETN. Anti-CTZ were the highest numerically, but many may be non-neutralizing antibodies against pegol where only >5000 appears to be impactful. As a good rule, anti-drug antibodies should be interpreted in the context of the concomitant free drug trough concentration.

Conclusion: Here, we report TNF-inhibitor and their anti-drug antibody levels in >60,000 patients. Though clinical histories and blood collection timing are not known, Figure 1 showed that many patients may have insufficient drug levels. Observed immunogenicity rates to IFX, ADL, CTZ and ETN were high and all anti-drug antibodies except anti-ETN adversely affect free drug levels. Numeric antibody results should be interpreted with the help of titer designations (low/high) by the laboratory because low titer antibodies have less impact on drug levels and may be transient or reversible whereas high titers with nil or very low drug indicate refractory immunogenicity. In this way, biologic TDM elucidates the mechanism of suboptimal response and should be used to optimize drug efficacy and longevity by informing and expediting adjustments to medication.

Disclosure: K. Chun: None; **J. Yang**: None.

Abstract Number: 1067

A Comparison of Joint Involvement Patterns in Immune Checkpoint Inhibitor-Induced Inflammatory Arthritis and Rheumatoid Arthritis

Carlos Aude[1], Deanna Jannat-Khah[2], Karmela Kim Chan[2], Nilasha Ghosh[1], Clifton Bingham[3], Vivian Bykerk[2] and Anne Bass[1], [1]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [2]Hospital For Special Surgery, New York, NY, [3]Johns Hopkins University, Baltimore, MD

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitors (ICIs) have transformed cancer treatment but may trigger immune-related adverse events (irAEs) such as ICI-induced inflammatory arthritis (ICI-IA). Although ICI-IA and rheumatoid arthritis (RA) exhibit clinical similarities, it remains uncertain if ICI-IA represents an early form of RA or a distinct disease. Our study aimed to elucidate their relationship by comparing joint involvement patterns in patients with ICI-IA and early RA.

Table 1. Demographic and Clinical Characteristics of Early RA and ICI-IA Patients

Characteristic	Early RA n=163[1]	ICI-IA n=89[1]	p-value[2]
Age	43.8 (33.5 - 56.4)	67.9 (60.7 - 77.0)	**<0.001**
Sex			**<0.001**
Male	25 (15%)	46 (52%)	
Female	137 (85%)	43 (48%)	
Race			**0.045**
White	103 (72%)	76 (85%)	
Black	12 (8.4%)	6 (6.7%)	
Asian	17 (12%)	2 (2.2%)	
Other/Declined	11 (7.7%)	5 (5.6%)	
Ethnicity			0.13
Hispanic	22 (14%)	7 (7.9%)	
Not Hispanic	131 (86%)	82 (92%)	
BMI	24.4 (21.3 - 28.7)	26.3 (23.4 - 29.5)	**0.027**
Seropositive (RF+ and/or CCP+)	124 (77%)	20 (25%)	**<0.001**
Steroid Use at Study Inclusion	33 (20%)	34 (38%)	**0.002**
DMARD Use at Study Inclusion	137 (84%)	14 (16%)	**<0.001**
Swollen Joint Count (SJC)	2.0 (1.0 - 4.0)	2.0 (1.0 - 4.0)	0.24
Tender Joint Count (TJC)	2.0 (0.0 - 4.0)	1.0 (0.0 - 3.0)	0.23
Total Joint Involvement Count[3]	4.0 (2.0 - 6.0)	4.0 (2.0 - 6.0)	0.90
Symptom Onset to Study Inclusion (wks)	31.6 (19.4 - 43.9)	17.2 (7.5 - 29.3)	**<0.001**
ICI Initiation to Study Inclusion (wks)	--	46.0 (26.3 - 93.4)	
ICI Regimen			
Anti-PD(L)1 + Anti-CTLA4	--	23 (26%)	
Anti-PD(L)1 Monotherapy	--	63 (71%)	
Other	--	3 (3.4%)	
Cancer Type			
Melanoma	--	24 (27%)	
Non-small cell lung cancer	--	15 (17%)	
Renal cell carcinoma	--	20 (22%)	
Urothelial carcinoma	--	6 (6.7%)	
Other	--	24 (27%)	

[1] Median (IQR); n (%)

[2] Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

[3] Joint involvement = joint is swollen and/or tender

Table 2. Distribution of Swelling and Tenderness for Individual Joints in Early RA and ICI-IA Patients

Joint	Early RA n=163[1]	ICI-IA n=89[1]	Adj. p-value[2,3]
Swelling/Tenderness			
Shoulders	21 (13%)	16 (18.0%)	0.7
Elbows	13 (8%)	11 (12.4%)	0.7
Wrists	55 (34%)	37 (41.6%)	0.7
MCPs	91 (56%)	50 (56.2%)	0.7
PIPs	97 (60%)	40 (44.9%)	**0.03**
Knees	44 (27%)	48 (53.9%)	**0.03**
Swelling			
Shoulders	5 (3.1%)	2 (2.2%)	0.8
Elbows	10 (6.1%)	5 (5.6%)	0.8
Wrists	42 (25.8%)	33 (37.1%)	0.6
MCPs	80 (49.1%)	43 (48.3%)	0.6
PIPs	81 (49.7%)	32 (36.0%)	**0.04**
Knees	37 (22.7%)	44 (49.4%)	**0.008**
Tenderness			
Shoulders	20 (12.3%)	15 (16.9%)	0.5
Elbows	10 (6.1%)	8 (9.0%)	0.5
Wrists	39 (23.9%)	18 (20.2%)	0.9
MCPs	65 (39.9%)	27 (30.3%)	0.5
PIPs	71 (43.6%)	30 (33.7%)	0.5
Knees	31 (19.0%)	19 (21.3%)	0.5

[1] n (%)

[2] Pairwise Fisher's exact test

[3] Benjamini-Hochberg procedure for multiple comparisons

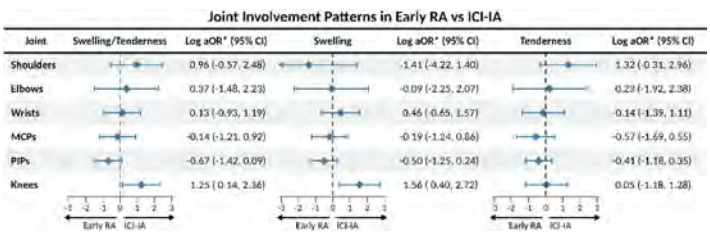

Figure 1. Forest Plot and Log Adjusted Odds Ratios (aOR) with 95% Confidence Intervals for Joint Swelling and Tenderness Comparing Early RA and ICI-IA Patients (*Adjusted for demographics, BMI, seropositivity, steroid use, DMARD use, and time from arthritis onset to study inclusion)

Methods: Clinical data from 89 ICI-IA patients in our institutional rheumatic irAE registry and 163 early RA patients from the Consortium of early ArThritis CoHorts-USA (CATCH-US) cohort were analyzed. Rheumatologists recorded the Swollen and Tender Joint Counts (SJC, TJC) at the patients' baseline visit. A multivariable logistic regression model was first utilized to identify variables associated with specific joint swelling and/or tenderness in the ICI-IA cohort. Separately, we compared the overall joint involvement pattern of ICI-IA and early RA using Fisher's exact test, while SJC, TJC, and joint symmetry were compared using multivariable linear and logistic regressions, correspondingly. Specific joint comparisons were compared with multivariable logistic regression models. All models were adjusted for demographics, BMI, seropositivity, steroid use, DMARD use, and time from symptom onset to study inclusion; ICI-IA-exclusive models were additionally adjusted for cancer type, ICI regimen, and time from ICI initiation to study inclusion.

Results: ICI-IA patients were older, more likely to be male, and less frequently seropositive than early RA patients (Table 1). In the ICI-IA-exclusive analysis, female patients exhibited a higher probability of knee tenderness (aOR=9.02, p=0.03) and a lower probability of PIP swelling (aOR=0.11, p=0.005) relative to male patients. Additionally, younger patients showed an increased likelihood of knee swelling (aOR=0.93, p=0.03) compared to their older counterparts. Notably, no other variables, including the ICI treatment regimen, were associated with specific joint involvement among ICI-IA patients. Comparative analysis between ICI-IA and early RA patients revealed higher odds of symmetrical swelling in early RA (aOR=2.44, p=0.02), despite no substantial differences in either SJC or TJC. There was a significant difference in the overall swollen joint distribution between the two cohorts (p=0.008), particularly with regard to PIP (45% vs. 60%, p=0.02) and knee involvement (54% vs. 27%, p=0.03) (Table 2). After adjusting for confounding variables, ICI-IA patients continued to exhibit higher odds of knee swelling (aOR=4.76, p=0.007), though PIP involvement did not significantly differ (p=0.08) (Figure 1). A subanalysis comparing ICI-IA and seronegative early RA patients yielded similar results.

Conclusion: We demonstrated distinct joint involvement patterns between ICI-IA and early RA patients, with more frequent knee swelling in ICI-IA and more PIP and symmetrical joint involvement in early RA. These results could inform the development of ICI-IA classification criteria, thereby enhancing differential diagnosis and treatment strategies.

Disclosure: C. Aude: None; **D. Jannat-Khah**: AstraZeneca, 12, stock ownership, Cytodyn, 12, stock ownershil[, Walgreens Boots Alliance, 12, stock ownership; **K. Chan**: None; **N. Ghosh**: None; **C. Bingham**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 2, Janssen, 2, Pfizer, 2, Sanofi, 2; **V. Bykerk**: Abbvie, 2, BMS, 2, Pfizer, 2; **A. Bass**: None.

Abstract Number: 1068

Multidisciplinary Prospective Study of Patients Treated with Immune Checkpoint Inhibitors Who Developed Rheumatic Immune-related Adverse Events

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitors (ICIs), by activating the immune system (specifically, T-cells), foster the reaction against tumor cells. However, parallelly, autoimmune phenomena, known as immune- related adverse effects (ir-AEs) (PMID 33902919, 29442540), can be triggered and manifest in any organ or tissue. The most common rheumatic manifestations are inflammatory arthritis, polymyalgia rheumatica, and myositis, but other inflammatory cases have also been described (PMID 32403289). More data on their frequency and characterization are needed.

Our objective was to prospectively evaluate the incidence of rheumatic ir-AEs during ICIs treatment, along with clinical characterization, management required, and outcomes.

Methods: An observational, prospective study was conducted at a tertiary center in Spain, led by the oncology department with the participation of several specialties, to evaluate the occurrence of ir-AEs in patients starting ICIs between January 2019 and April 2022. Participants were routinely followed at oncology clinics to detect ir-AEs through pre-specified clinical and laboratory assessments. For rheumatic symptoms, ir-AEs were studied by records review and evaluated in person at rheumatology clinics for those with a degree of involvement of ≥2, according to the ASCO guidelines (3). The incidence - with a 95% confidence interval (CI) - and characterization of defined rheumatic ir- AEs are presented here.

Results: Of 181 patients, 21 (11.6%, 95%CI 7.7-17.1%) developed rheumatic ir-AEs, 13 men (61.9%) with a median age of 62.3 years (p25-75 51.8-75.0). The median time from the start of ICIs to the development of rheumatic ir-AEs was 85 days (p25-75 51.5-165).The incidence rate was 0.92 cases per 100 patient-months. Blood tests for autoimmunity were positive in 69.2% of available cases (9/13), but all at a low titer (table). According to ASCO guidelines, most patients had a toxicity grade 1-2, but 3 (14.3%) patients presented with severe manifestations (grade 3): 1 (4.8%) case of inflammatory arthritis, 1 (4.8%) of xerostomia, and 1 (4.8%) of Raynaud's phenomenon with ulcers. 9 (42.9%) patients also presented with concurrent ir-AEs of different types. Rheumatic ir-AEs were successfully settled, though infliximab and intravenous vasodilators were required for some cases. While discontinuing ICIs was mostly due to neoplasm progression (47.6%), in 3 cases (14.3%) it was due to grade-3 rheumatic manifestations. 7 (33.3%) patients died during follow-up due to the oncological disease, no case due to rheumatic toxicity.

Type of tumor n (%)	Drug n (%)	Clinical presentation (%)	Antibodies n (%)	Treatment n (%)	Outcome n (%)
Lung 9 (42.9)	Pembrolizumab 8 (38.1)	Inflammatory arthritis 7 (33.3)	ANA 8 (38.1)	No rheumatological treatment 10 (47.6)	Discontinuation of ICI due to progression 10 (47.6)
Melanoma 4 (19.0)	Nivolumab 7 (33.3)	Xerostomia 5 (23.8)	Anti-centromere 1 (4.8)	Glucocorticoids 8 (38.1)	Discontinuation of ICI due to severe ir-AEs 3 (14.3)
Hodgkin's lymphoma 2 (9.5)	Nivolumab + Ipilimumab 3 (14.3)	Polymyalgia-like syndrome 5 (23.8)	Rheumatoid factor 1 (4.8)	Hydroxychloroquine 3 (14.3)	ICI is currently ongoing 4 (19.0)
Kidney 2 (9.5)	Atezolizumab 3 (14.3)	Myositis 4 (19.0)	ACPA 1 (4.8)	Pilocarpine 2 (9.5)	Completed ICI regimen 2 (9.5)
Esophagus 1 (4.8)		Raynaud's phenomenon with ulcers 1 (4.8)	Anti-TIF1γ 1 (4.8)	NSAIDs 2 (9.5)	Lost to follow-up 1 (4.8)
Bladder 1 (4.8)				Infliximab 1 (4.8)	
Mesothelioma 1 (4.8)				Vasodilators 1 (4.8)	

Conclusion: In this prospective and multidisciplinary study, 11.6% of patients treated with ICIs developed rheumatic ir-AEs. We estimated an incidence rate of 0.92 cases per patient-month. The majority experienced mild or moderate involvements, although severe cases were also observed. Therefore, a coordinated approach with oncologists is essential for patients treated with ICIs who are at risk of developing rheumatic ir-AES.

Disclosure: M. López-González: None; **N. Martínez Banaclocha**: None; **M. García Araque**: None; **Y. Montoyo Pujol**: None; **M. Andrés**: None.

Abstract Number: 1069

Exploring the Risk of Demyelination Associated with TNF Alpha Inhibitors: Analysis of the FDA Adverse Event Reporting System (FAERS)

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

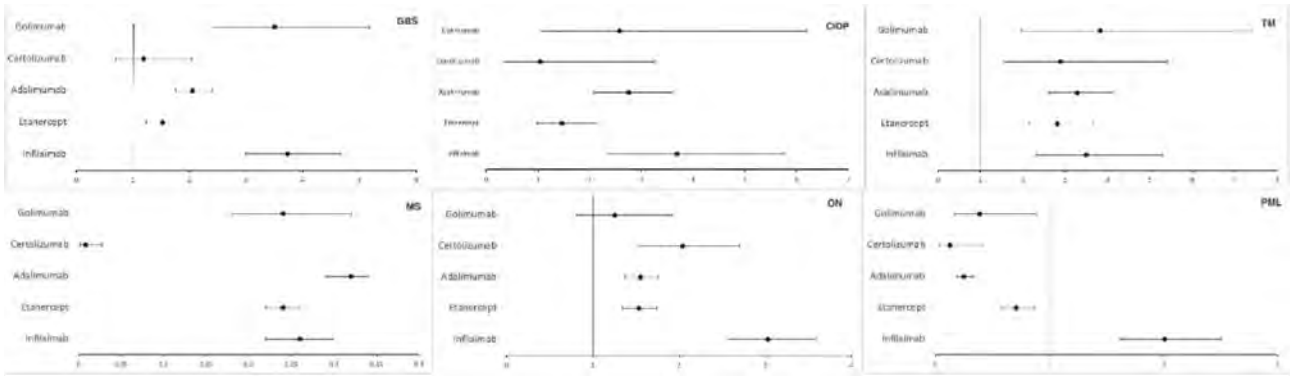
Background/Purpose: Tumor necrosis factor-alpha (TNF-α) inhibitors, a widely used class of biological immunomodulating agents targeting TNF-α, have revolutionized the treatment of various autoimmune and inflammatory conditions. However, emerging evidence suggests a potential association between TNF-α inhibitors and demyelination, a critical factor in the development and progression of neurological disorders. This abstract analyzes data from the FDA Adverse Event Reporting System (FAERS) and helps understand the potential risks underlying this association.

Methods: We performed a retrospective pharmacovigilance study that analyzed the FAERS database from 2009-2023 to investigate the association of demyelinating adverse events (AE), namely Guillain-Barre syndrome (GBS), chronic inflammatory demyelinating polyneuropathy (CIDP), transverse myelitis (TM), multiple sclerosis (MS), optic neuritis (ON), and progressive multifocal leukoencephalopathy (PML) in patients treated with FDA-approved TNF-α inhibitors (infliximab, adalimumab, etanercept, golimumab, and certolizumab). Disproportionality analysis was performed using reporting odds ratio (ROR).

Results: A total of 1,372,262 AEs were reported with TNF-α inhibitors, of which 170,109 were neurological AEs. Most AEs were among patients in the 18-64 age group (38-64%). The death rate was 4-7 % for all demyelinating categories except PML, in which the death rate was 18-22% with infliximab, etanercept, and adalimumab. GBS, CIDP, ON, and PML were

Table depicting the calculated RORs of various demyelinating adverse events associated with TNF-α inhibitors

Adverse Event	Infliximab	Etanercept	Adalimumab	Certolizumab	Golimumab
GBS	3.73(2.98-4.68)	1.52(1.24-1.85)	2.05(1.75-2.40)	1.19(0.69-2.05)	3.5(2.39-5.17)
CIDP	3.69(2.37-5.76)	1.46(0.98-2.15)	2.75(2.09-3.61)	1.04(0.33-3.25)	2.57(1.06-6.19)
TM	3.49(2.31-5.28)	2.81(2.16-3.66)	3.28(2.61-4.12)	2.89(1.55-5.39)	3.82(1.98-7.37)
MS	0.26(0.22-0.30)	0.24(0.22-0.26)	0.32(0.29-0.34)	0.008 (0.002-0.027)	0.24(0.18-0.32)
ON	3.03(2.56-3.58)	1.53(1.34-1.74)	1.55(1.37-1.75)	2.04(1.54-2.70)	1.25(0.81-1.92)
PML	2.01(1.62-2.50)	0.71(0.58-0.87)	0.25(0.19-0.34)	0.13(0.04-0.42)	0.39(0.17-0.88)



Forest plot depicting the association of demyelinating adverse events with TNF-α inhibitors

disproportionately associated with the use of infliximab with a ROR (95% CI) of 3.73 (2.98-4.68), 3.69 (2.37-5.76), 3.03 (2.56-3.58) and 2.01 (1.62-2.50) respectively. Golimumab had the highest reported association with TM, with a ROR of 3.82 (1.98-7.37). We observed a negative association of all TNF-α inhibitors with MS (ROR< 1).

Conclusion: Our study found that using certain biologic agents is associated with an increased risk of specific demyelinating disorders. While a temporal relationship between anti-TNF-α treatment and demyelinating events is suggested, the overall number of published cases is small compared to the total number of treated patients. In most cases, demyelination either progressed slowly or resolved after discontinuing anti-TNF-α therapy, indicating a potential protective effect or short-lasting harmful impact in patients already suffering from latent MS. Genetic predisposition and overlapping syndromes in autoimmune diseases also cast doubt on a direct relationship. We suggest a thorough neurological assessment of candidates considered for TNF-α blockers before initiation and periodically during treatment and avoiding the use in patients with a history or family history of demyelinating diseases. Limitations of the study include reporting bias, confounding of the observed associations, and the observational nature of the study that prevents establishing causal relationships. Further controlled studies, such as randomized clinical trials or prospective cohort studies, are needed to confirm our findings and establish causality.

Disclosure: M. Sondhi: None; **R. Vyas**: None; **A. Thakre**: None; **S. Hayat**: None.

Abstract Number: 1070

Safety of DMARDs in Rheumatologic Immune-related Adverse Events Associated with Immune Checkpoint Inhibitors: Data from a Monocentric Cohort in Hospices Civils De Lyon

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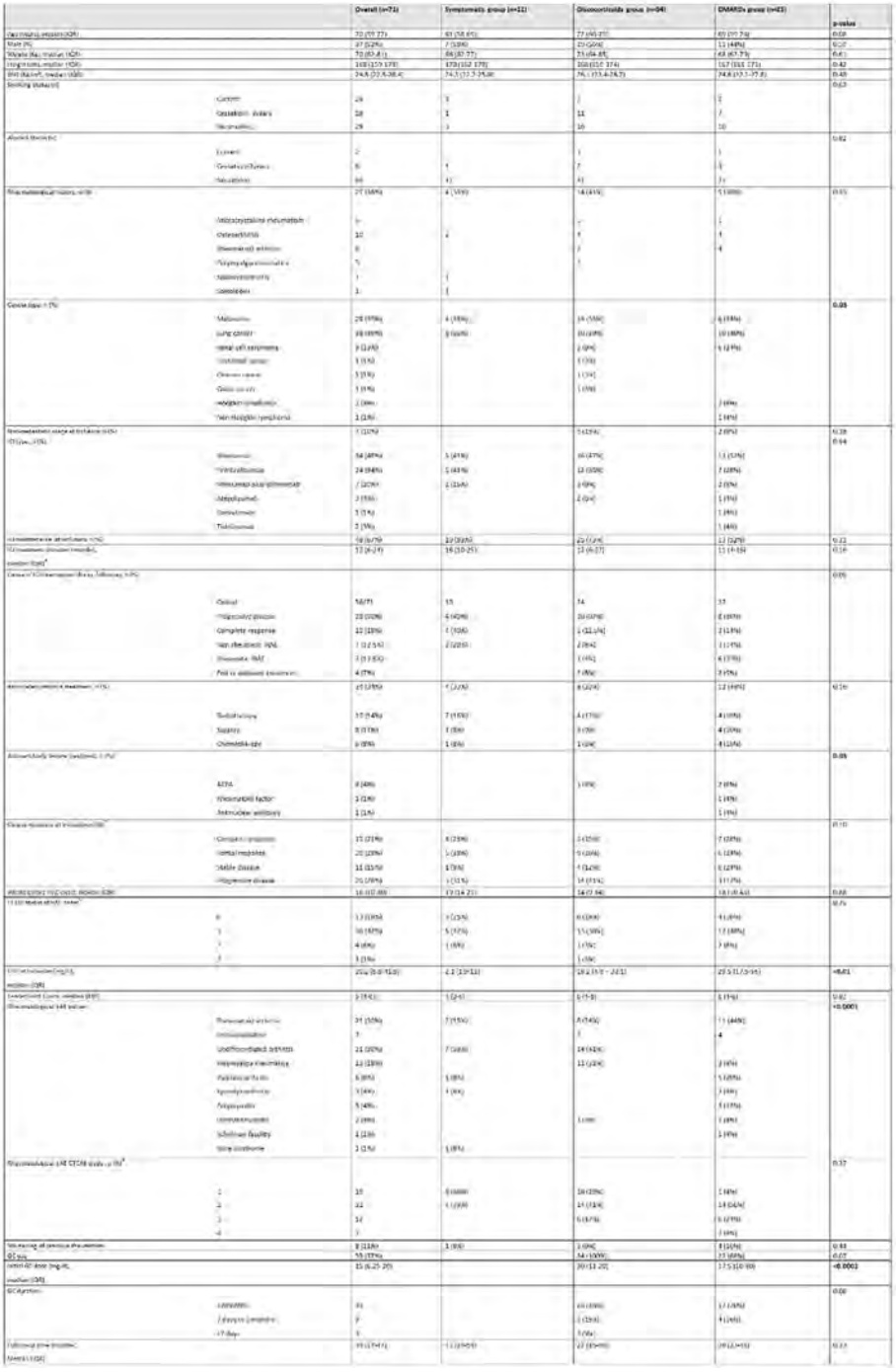
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Since Immune Checkpoint Inhibitors (ICI) revolution, oncologists face immune-related adverse events (irAEs) including rheumatologic irAEs with inflammatory arthritis. Treatment of rheumatologic irAE can be challenging, using glucocorticosteroids (GC), conventional synthetic (cs-) or biological (b-) DMARDs without impeding ICI antitumoral efficiency. The objective of our study was to assess the safety of current rheumatologic irAE treatments.

Table 1 – Patients characteristics. a. 1 missing data. b. 5 missing data. c. 23 missing data. d. 6 missing data. Results are presented with median and interquartile range.



Methods: We conducted a monocentric retrospective observational study at the Centre Hospitalier Lyon Sud, Hospices Civils de Lyon, Lyon, France. Eligible patients were adult patients treated with ICI presenting rheumatologic irAE. Patients with active inflammatory rheumatologic disease and who were not assessed by a rheumatologist were excluded. Data were obtained from medical charts using a standardized data collection. Kruskal-Wallis and Wilcoxon tests were used for comparing continuous variables. Fisher's exact test was used for comparison between categorical variables. Spearman coefficient was used for correlation test. Survival analysis was performed using Kaplan Meier method.

Results: Between July 2016 to October 2022, 71 patients were included **(Table 1)**. Patients were allocated to 3 groups regarding the treatment of their rheumatologic irAE: symptomatic group when treated with analgesics or NSAIDs (n=12), GC group when treated with systemic corticosteroids (n=34) and DMARD group when treated with csDMARD and/or bDMARD (n=25). Eighteen (72%) patients were treated with methotrexate. Ten patients were treated with bDMARD: 5 with infliximab (20%), 4 with tocilizumab (16%), 1 with etanercept (4%). No significant difference was found between different groups **(Figure 1)** regarding overall survival (OS, p=0.43), and progression free survival (PFS, p=0.46). We realized subset survival analysis including GC group, patients treated csDMARD alone (n=15) and patients treated with csDMARD and/or bDMARD (n=10), with no difference for OS and PFS. However, OS was positively correlated with time between irAE and bDMARD onset (R=0.88, p< 0.0001) unlike other groups. Based on this result, we compared patients treated with early

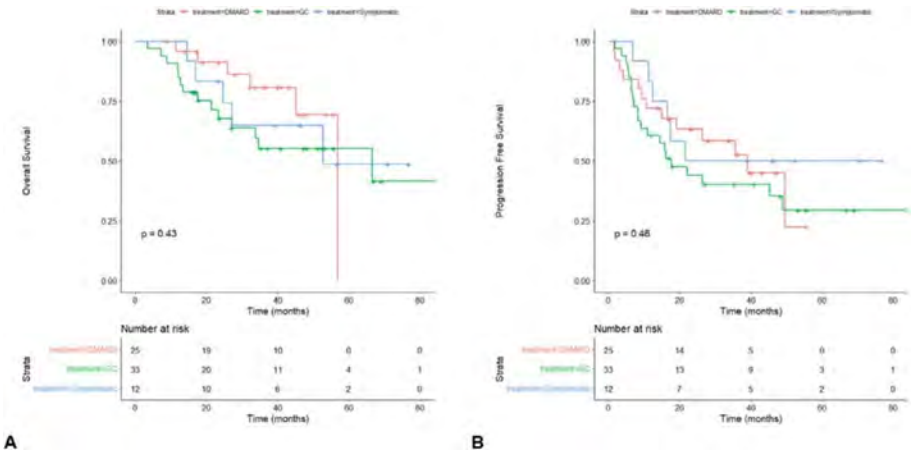


Figure 1 – Kaplan-Meier plots for A. Overall Survival and B. Progression Free Survival for types of rheumatological IRAE treatment. Corresponding risk tables are outlined below the plots.

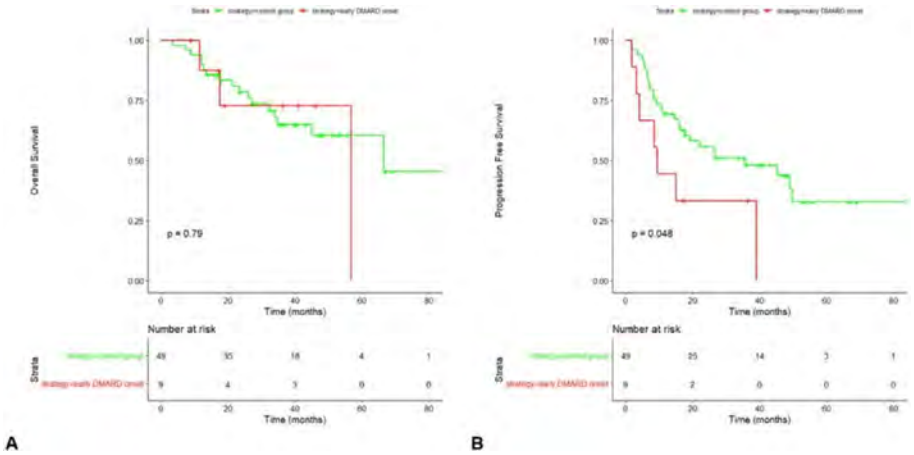


Figure 2 – Kaplan-Meier plots for A. Overall Survival and B. Progression Free Survival between early DMARD onset (<6 weeks) and control group. Corresponding risk tables are outlined below the plots.

DMARD onset (< 6 weeks after irAE onset, n=9) with a control group composed of patients with later DMARD onset after irAE and patients treated with GC (n=50). Patients in early DMARD group were mostly treated with csDMARD: 5 with methotrexate, 2 with immunoglobulins, 1 with hydroxychlororquine. One patient was treated with tocilizumab alone. Survival analysis realized between early DMARD group and control group **(Figure 2)** did not show significant difference for overall survival (p=0.79), but progression free survival was lower in early DMARD group than in control group (p=0.048).

Conclusion: Our data support concerns previously raised about cancer progression in irAE treated with bDMARD and suggest precautions for using DMARD during the first 6 weeks after rheumatologic irAE onset.

Disclosure: J. Seiller: None; **E. Massy**: None; **J. Peron**: None; **C. Confavreux**: None.

Abstract Number: 1071

No Increase in Mortality in US Veterans with Rheumatoid Arthritis Treated with Immune Checkpoint Inhibitors (ICIs)

Madeline O'Sullivan[1], Grant Cannon[1], Brian Sauer[2], Jorge Rojas Jr[3], Gary Kunkel[4], Jessica A Walsh[5], Punyasha Roul[6], Bryant England[6], Ted R Mikuls[7], Joshua Baker[8] and Tawnie Braaten[4], [1]University of Utah and Salt Lake City VA, Salt Lake City, UT, [2]Salt Lake City VA/University of Utah, Salt Lake City, UT, [3]Puget Sound VA and University of Utah, Seattle, WA, [4]University of Utah, Salt Lake City, UT, [5]Salt Lake City Veterans Affairs Health and University of Utah Health, Division of Rheumatology, Salt Lake City, UT, [6]University of Nebraska Medical Center, Omaha, NE, [7]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE, [8]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Background/Purpose: Immune checkpoint inhibitors (ICIs) are used to treat multiple cancers with increasing frequency and have led to improved survival. However, there is limited data on the use of ICIs in patients with pre-existing autoimmune disease, specifically rheumatoid arthritis (RA), as these patients were excluded from most clinical trials. There is concern that RA patients may experience higher mortality with ICI treatment. The objective of this investigation was to compare all-cause and cause-specific mortality following ICI treatment in patients with and without pre-existing RA in the Veterans Health Administration (VHA).

Methods: This analysis employed data from the VHA Corporate Data Warehouse (CDW) for demographic and pharmacy information, VA Central Cancer Registry for cancer diagnosis, Death Ascertainment File (DAF) for all-cause mortality rates, and National Death Index (NDI) for cause of death. We identified Veterans with RA in the VHA with two ICD codes at least 30 days apart, at least one ICD code from a rheumatologist, and treatment with a disease modifying anti-rheumatic drug. Each RA case was matched up to 10:1 based on year of birth, sex, and year of VHA enrollment to Veterans without RA. RA and non-RA patients receiving ICI therapy between 6/6/2011 and 2/14/2023 were identified.All-cause mortality up to 4/30/2023 was obtained from the DAF and cause specific mortality from NDI through 12/31/2019. Demographic, ICI treatment, and cancer type were compared using student t-test or Chi square. Survival from the time of ICI initiation was evaluated using Kaplan-Meier curves and log rank testing.

Results: The cohort of Veterans with RA included 73,677 patients matched to 727,627 controls. There were 301 (0.41%) among the RA patients and 2,114 (0.29%) among the non-RA controls treated with an ICI. There were no differences in demographics, smoking status, first ICI drug, or cancer diagnosis between these groups at the time of initial ICI infusion

(Table 1). The Veterans were majority white, non-Hispanic, male, and current or former smokers. Lung cancer was the most common malignancy type and pembrolizumab was used most frequently as the first ICI in both groups. Both groups had high mortality with one-year survival 51.2% [45.2% - 56.7%] vs. 54.5% [45.3% - 56.7%] and two-year survival 35.0% [29.3% - 40.7%] vs. 37.5% [35.2% - 39.7%] in the RA and non-RA groups, respectively. There was no significant survival difference between the groups (p=0.29)(Figure 1). The NDI cause of death was similar in both groups (p=0.96) with the most common being neoplasm in 91.9% and 91.2% of patients, respectively (Table 2). Deaths due to infection were rare in both groups (1.2%).

Table 1. Demographic and clinical information of RA and non-RA patients at time of first immune checkpoint inhibitor infusion

Table 1 - Demographic and clinical information of RA and non-RA Patients at time of first immune checkpoint inhibitor infusion

	RA (n=301)	non-RA (n = 2114)	
Age at First Infusion	71.4±6.5	71.1±7.1	p = 0.49
Gender			p = 0.12
Male	286 (95%)	1956 (92.5%)	
Race			p = 0.10
White	237 (78.7%)	1546 (73.1%)	
Black	47 (15.6%)	434 (20.5%)	
Other	17 (5.6%)	134 (6.3%)	
Ethnicity			p = 0.23
Not Hispanic	279 (92.6%)	1990 (94.1%)	
Hispanic	15 (4.9%)	66 (3.1%)	
Unknown/Other	7 (2.3%)	58 (2.7%)	
Smoking Status			p = 0.38
Current/Former	160 (53.1%)	1140 (53.9%)	
Never Smoker	45 (14.9%)	258 (12.2%)	
Unknown	96 (31.8%)	716 (33.8%)	
ICI Class			p = 0.58
CTLA-4	11 (3.6%)	99 (4.6%)	
PD-1	218 (72.4%)	1550 (73.3%)	
PD-L1	72 (23.9%)	465 (21.9%)	
ICI - First Infusion			p = 0.48
Atezolizumab	38 (12.6%)	232 (10.9%)	
Avelumab	2 (0.6%)	6 (0.2%)	
Cemiplimab	5 (1.6%)	16 (0.7%)	
Durvalumab	32 (10.6%)	227 (10.7%)	
Ipilimumab	11 (3.6%)	99 (4.6%)	
Nivolumab	83 (27.5%)	620 (29.3%)	
Pembrolizumab	130 (43.1%)	914 (43.2%)	
Cancer Type			p = 0.08
Lung	154 (51.1%)	1043 (49.3%)	
Melanoma	37 (12.2%)	171 (8%)	
Genitourinary	41 (13.6%)	280 (13.2%)	
Gastrointestinal	22 (7.3%)	218 (10.3%)	
Head and Neck	14 (4.6%)	124 (5.8%)	
Other	33 (10.9%)	278 (13.1%)	

Table 2. Specific cause of death from the National Death Index in RA patients treated with ICIs among those with available data from NDI

Table 2 - Specific cause of death from the National Death Index in RA patients treated with ICIs among those with available data from NDI

	RA (n=81)	non-RA (n=545)	
Neoplasms	75 (92.5%)	499 (91.5%)	p=0.96
Circulatory System Diseases	2 (2.4%)	19 (3.4%)	
Respiratory system Diseases	2 (2.4%)	10 (1.8%)	
Infectious Diseases	1 (1.2%)	6 (1.1%)	
Other	1 (1.2%)	11 (2%)	
TOTAL	81 (100%)	545 (100%)	

Figure 1. Kaplan-Meier Survival Analysis After First ICI Infusion

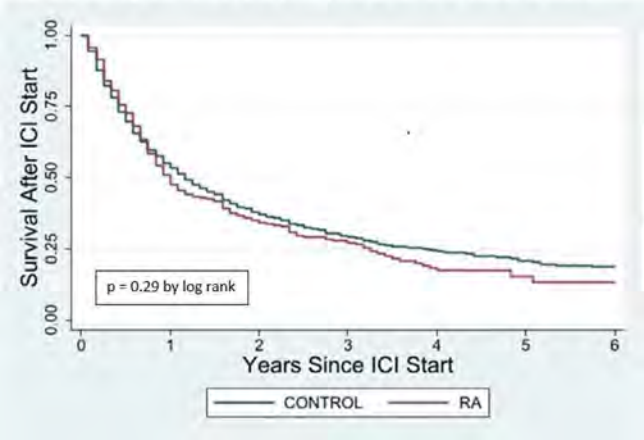

Figure 1. Kaplan-Meier survival analysis after first ICI infusion

Conclusion: Veterans with pre-existing RA who received ICIs for cancer did not experience excess mortality or differences in cause of death compared to Veterans without RA receiving ICI treatment. These preliminary data suggest that a diagnosis of RA alone should not serve as a contraindication to ICI therapy in the context of comorbid cancer.

Disclosure: M. O'Sullivan: None; **G. Cannon**: None; **B. Sauer**: None; **J. Rojas Jr**: None; **G. Kunkel**: None; **J. Walsh**: AbbVie, 5, Amgen, 2, Eli Lilly, 2, Janssen, 2, Merck, 5, Novartis, 2, Pfizer, 2, 5, UCB Pharma, 2; **P. Roul**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **J. Baker**: CorEvitas, 2, Cumberland Pharma, 2, Horizon Pharmaceuticals, 5; **T. Braaten**: None.

Abstract Number: 1072

Increase in Major Osteoporotic Fractures After Therapy with Immune Checkpoint Inhibitors

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SESSION INFORMATION
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Background/Purpose: Immune checkpoint inhibitors (ICI) have revolutionized the treatment of cancer. Despite their efficacy on tumor outcomes they can cause severe and sometimes long-standing immune-related adverse events (irAE). Enhanced immune activation from ICI can conceivably induce expression of the receptor activator of nuclear factor kappa-B ligand (RANK-L) resulting in osteoclast activation, bone loss and fracture. Our objective was to determine the incidence rates of major osteoporotic fractures (MOF) in patients with melanoma treated with ICI, before and after initiation of ICI treatment.

Methods: We analyzed 2011-2022 data from the Optum's de-identified Clinformatics® Data Mart Database (a large commercial healthcare claims dataset from the United States). We identified patients who received one or more ICI currently approved by the Food and Drug Administration (FDA), on at least one occasion. We excluded off-label drug regimens (e.g. non approved combinations). We required that patients have a minimum of 12 months of observable data before receiving the ICI therapy. We used International Classification of Diseases (ICD 9/10) diagnostic codes to identify a diagnosis of melanoma, and we also required a minimum of 90 days follow-up after ICI initiation. We identified MOF which included fractures of the hip, forearm, humerus or vertebrae using ICD 9/10 diagnostic codes. To define a fracture event, we required at least 2 codes for a fracture in the same anatomical site within 90 days. We compared MOF rates in the year before ICI initiation with rates in the year after initiation of ICI, using proportional hazard models with robust sandwich estimate of the covariance matrix to account for correlated outcomes between the pre- and post- ICI treatment periods in the same patient. Patients were censored at last follow-up or death.

Results: We identified 34,864 patients who had received ICI and had continuous enrollment of at least 12 months prior to ICI initiation. Of these, 3,362 had a diagnosis of melanoma and had a minimum of 90 days follow-up after treatment initiation. Of the 3,362 patients with melanoma, 2,143 (64%) were male, mean age was 67 years (SD:14), 2,315 received monotherapy, 176 received combination therapy, and 871 received both therapeutic regimens in sequence. Forty-eight (1.4%) patients had a fracture in the year before ICI initiation, and 57 (1.7%) had a fracture in the year after initiation of treatment. The hazard ratio (HR) for fracture over the year after versus the year before the first ICI dose was 1.69 [95% CI 1.14 – 2.41].

Conclusion: Our findings suggest that patients who receive ICI are at increased risk of MOF during the first year after receiving therapy. Further research is needed to determine whether there are additional risk modifiers, such as concomitant treatment with steroids for irAE or metastatic bone disease, and to develop strategies for risk reduction.

Disclosure: M. Suarez-Almazor: Celgene, 1, Eli Lilly, 2, Pfizer, 2, Syneos Health, 1; **C. Ye**: None; **B. Zhao**: KMK Consulting Inc., 3; **J. Ruiz**: None; **H. Zhao**: None; **N. Abdel-Wahab**: ChemoCentryx, 2, 6; **W. Leslie**: None.

Abstract Number: 1073

Risk of Inflammatory Central Nervous System Diseases Among New Users of Biologic and Targeted Synthetic Disease-Modifying Antirheumatic Drugs

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SESSION INFORMATION
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Background/Purpose: Inflammatory and demyelinating central nervous system (CNS) adverse events have been observed among new users of tumor necrosis factor (TNF) inhibitors. No studies to date have defined the risk of these adverse events after initiation of TNF inhibitors as compared to other biologic and synthetic disease-modifying antirheumatic drugs (b/tsDMARD).

Methods: Data were derived from the US-based TriNetX electronic health records database. Patients were included if they had a disease for which TNF inhibitors are indicated (rheumatoid arthritis, psoriasis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis) and received a b/tsDMARD with regulatory approval for one of those diseases. Inflammatory CNS events were identified using ICD9-CM/ICD10-CM codes and unadjusted incidences were calculated. The adjusted risk among new users of TNF inhibitors was compared to other b/tsDMARDs using weighted Cox proportional hazards models.

Table 1: Characteristics of Included Patients, n = 132,015

Patient Characteristics	**n (%)**
Age at Diagnosis, mean (SD)	51.6 (16.1)
Sex	-
Male	47,387 (35.9%)
Female	84,628 (64.1%)
Race/Ethnicity	-
White	95,709 (72.5%)
Black or African American	12,275 (9.3%)
Hispanic or Latino	8,748 (6.6%)
Asian	2,459 (1.9%)
Other / NA	12,824 (9.7%)
Years with Disease, mean (SD)	3.5 (4.3)
Admissions during Prior Year, mean (SD)	0.4 (1.7)
Comorbidities at Diagnosis	-
Charlson Comorbidity Index	0.8 (1.7)
Chronic Obstructive Pulmonary Disease	18,017 (13.6%)
Diabetes	16,448 (12.5%)
Obesity	15,397 (11.7%)
Renal Disease	8,416 (6.4%)
Liver Disease	8,302 (6.3%)
Congestive Heart Failure	5,271 (4.0%)
Autoimmune Disease	-

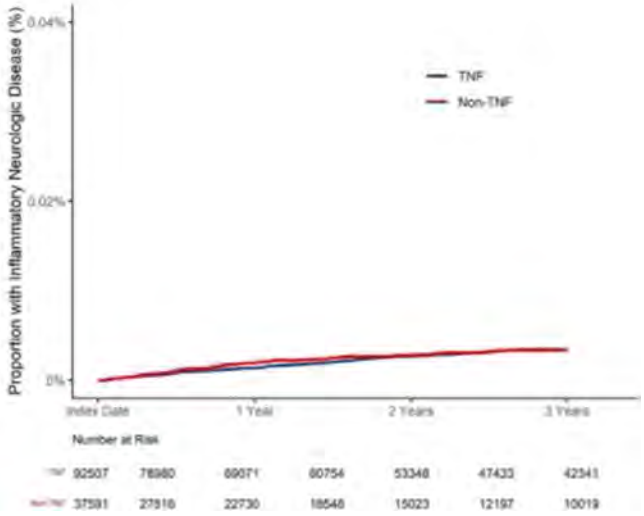
Results: Among 132,015 patients included in the analysis (84,628 female [64.1%]; mean age 51.6 [standard deviation{SD}, 16.1]), the most common first biologic agent was a TNF inhibitor (93,661, [70.9%]) followed by IL 12/23 inhibitor (7,949, [6.0%]) and Janus kinase inhibitors (6,900, [5.2%]). Patients were followed for an average of 1.85 years (SD 1.17) and contributed 244,038 patient-years of exposure time. In the primary analysis, there were 348 patients who had an inflammatory CNS event (mean time to event 388 days [SD 285 days]). The unadjusted incidence of inflammatory CNS events was numerically lower among new users of TNF inhibitors (185,909 total exposure years; 250 events, incidence 1.34 per 1,000

Table 2: Incidence of inflammatory neurologic lesions among patients who received targeted synthetic or biologic DMARDs

Class	Exposure (py)	Events	Incidence (per 1,000 py)
TNF	185,909	250	1.3
IL1223	12,094	15	1.2
CD20	10,913	36	3.3
JAK	9,439	9	1.0
Integrin	8,481	9	1.1
CTLA4	7,564	14	1.9
IL6	4,191	7	1.7
IL17	2,601	2	0.8
IL23	2,205	2	0.9
IL1	625	4	6.4
S1PR	18	0	0

Abbreviations: **TNF** = tumor necrosis factor; **IL** = interleukin; **JAK** = Janus kinase; **CD 20** = Cluster of differentiation 20; **CTLA4** = cytotoxic T lymphocyte associated protein 4; **S1PR** = sphingosine 1-phosphate receptor modulator

Figure 1: Proportion of Patients with Inflammatory Neurologic Events over Time, Stratified by TNF or non-TNF Exposure



patient-years) as compared to the combined non-TNF group (58,130 exposure years, 98 events, incidence 1.69 per 1,000 patient-years).The incidence per 1,000 person-years varied by drug class (Table 2). In a weighted Cox proportional hazards regression with TNF exposure as the referent, there was no association between TNF exposure and inflammatory CNS events as compared to the combined non-TNF b/tsDMARDs (hazard ratio [HR] 1.01, 95% confidence interval [CI] 0.75-1.36). These results persisted in subset analyses of patients with rheumatoid arthritis (HR 1.03, 95% CI 0.67-1.59), psoriasis, psoriatic arthritis, and ankylosing spondylitis (HR 1.02, 95% CI 0.47-2.19), and Crohn's disease or ulcerative colitis (HR 1.02, 95% CI 0.41-2.57).

Conclusion: This large real-world analysis of patients initiating b/tsDMARDs did not identify an increased risk of inflammatory CNS events among new users of TNF inhibitors compared to other b/tsDMARDs. Meta-analyses of randomized trials should be conducted to corroborate these findings, which may be affected by channeling bias.

Disclosure: M. Casey: None; **S. Pannu**: None; **S. Bajwa**: None; **A. Duarte-Garcia**: None; **M. Putman**: AbbVie/Abbott, 12, Trial participation, AstraZeneca, 12, Trial participation, Novartis, 2.

Abstract Number: 1074

Baseline Clinical Features, but Not Shared Epitope or HLA B27, Predict Severe Outcomes for Immune Checkpoint Inhibitor-induced Inflammatory Arthritis

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SESSION INFORMATION
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Background/Purpose: Immune checkpoint inhibitors (ICI) can cause inflammatory arthritis (IA) of varying severity. Many patients with ICI-IA require immunosuppression beyond corticosteroids, but there is no way to identify these patients at initial presentation. We determined baseline risk factors for requiring immunosuppression and having persistent arthritis in ICI-IA.

Methods: participants were adults with rheumatologist diagnosed ICI-IA. The primary outcome was requirement of conventional synthetic (cs) or biologic (b) DMARDs; other outcomes were persistence of IA >6 months after ICI cessation and requirement of corticosteroids. Logistic regression models evaluated associations between clinical/genetic features and primary and secondary outcomes, with adjustment for potential confounders, as appropriate. Finally, we evaluated the relationship between maximum prior dose of steroids and primary and secondary outcomes with simple logistic regression.

Results: 126 patients with ICI-IA were included; 53 patients (42%) required a csDMARD/bDMARD (demographic and clinical features by DMARD group in Table 1).In univariate logistic regressions, higher CDAI, tenosynovitis, longer symptom duration before first rheumatology visit, and longer ICI duration were significantly associated with a higher likelihood of requiring DMARDs; there was a trend toward those treated with prior chemotherapy being less likely to need DMARDs (Table 2). After adjustment, tenosynovitis, longer symptom duration, and higher CDAI remained associated with requiring DMARDs, while those with prior chemotherapy were significantly less likely to require DMARDs (Table 2). Combination anti-CTLA-4/

Table 1: Demographic features, cancer history, shared epitope/HLA B27 status, and selected arthritis clinical variables by DMARD requirement

Variable	Total (n=126)	No DMARD (n=73)	csDMARD and/or bDMARD (n=53)	p-value
Age: Mean (SD)	60.0 (13.0)	60.0 (12.9)	60.1 (13.3)	0.98
Female gender: N (%)	70 (56%)	37 (51%)	33 (62%)	0.20
Race: N (%)				0.10
White	116 (92%)	65 (89%)	51 (96%)	
Black	6 (5%)	6 (8%)	0 (0%)	
Other	4 (3%)	2 (3%)	2 (4%)	
Smoking status				0.81
Never	66 (57.9%)	37 (56.9%)	29 (59.2%)	
Ever	48 (37.7%)	28 (43.1%)	20 (40.8%)	
ICI class				0.14
Anti-PD-1/PD-L1	89 (70.6%)	52 (71.2%)	37 (69.8%)	
Anti-CTLA-4	4 (3.2%)	4 (5.5%)	0 (0%)	
Combination	31 (24.6%)	15 (20.6%)	16 (30.2%)	
Other	2 (1.6%)	2 (2.7%)	0 (0%)	
Cancer type				0.20
Melanoma	41 (32.5%)	18 (24.7%)	23 (43.4%)	
Lung cancer	30 (23.8%)	20 (27.4%)	10 (18.9%)	
GU cancer	7 (5.6%)	6 (8.2%)	1 (1.9%)	
GI cancer	17 (13.5%)	13 (17.8%)	4 (7.6%)	
Breast cancer	6 (4.8%)	2 (2.7%)	4 (7.6%)	
SCC	8 (6.4%)	4 (5.5%)	4 (7.6%)	
Other	17 (13.5%)	10 (13.7%)	7 (13.2%)	
ICI Duration at baseline in months	9.7 (9.4)	7.9 (8.4)	12.1 (10.3)	**0.014**
Prior chemotherapy: N (%)				0.08
No	56 (46.7%)	28 (40%)	28 (56%)	
Yes	64 (53.3%)	42 (60%)	22 (44%)	
Prior radiation: N (%)				0.65
No	86 (68%)	51 (69.9%)	35 (66%)	
Yes	40 (32%)	22 (30.1%)	18 (34%)	
Additional irAEs				0.32
0	76 (60.3%)	48 (65.8%)	28 (52.8%)	
1	31 (24.6%)	18 (24.7%)	13 (24.5%)	
2+	19 (15.1%)	7 (9.6%)	12 (22.6%)	
Presence of Shared Epitope Alleles (N=98)	46 (47.0%)	24 (43.6%)	22 (51.2%)	0.46
Presence of HLA B27 (N=98)	3 (3.1%)	2 (3.6%)	1 (2.3%)	0.71
Symptom duration at baseline in months	12.7 (10.0)	10.3 (7.5)	16.0 (12)	**0.001**
Tender joint count (28)	3.4 (4.0)	2.7 (4.0)	4.3 (3.9)	**0.024**
Swollen joint count (28)	7.0 (5.5)	6.1 (5.1)	8.2 (5.8)	**0.034**
Patient global disease activity VAS	39.7 (27.2)	37.7 (26.4)	42.4 (28.4)	0.35
Physician global disease activity VAS	25.5 (15.7)	22.4 (12.9)	29.5 (18.1)	**0.02**
CDAI	17.0 (10.2)	14.8 (8.8)	19.8 (11.4)	**0.008**
Pain VAS	48.3 (29.4)	48.9 (28.5)	47.4 (30.7)	0.78
Stiffness Severity VAS	52.2 (27.2)	51.1 (27.8)	53.5 (26.7)	0.65
Tenosynovitis Y/N	23 (18.3%)	7 (10%)	16 (30.8%)	**0.008**
Enthesitis Y/N	28 (22.9%)	19 (26.8%)	9 (17.0%)	0.20
Dactylitis	5 (4.0%)	2 (2.8%)	3 (5.8%)	0.40
Stenosing tenosynovitis	13 (10.7%)	5 (7.3%)	8 (15.1%)	0.16
Inflammatory back pain Y/N	3 (2.4%)	3 (4.2%)	0 (0%)	0.13
Rheumatoid factor positive	12/10 4%)	8 (11.8%)	4 (8.5%)	0.58
Anti-CCP positive	7 (6.1%)	5 (7.8%)	2 (4.2%)	0.40
ANA positive	27 (24.8%)	15 (23.4%)	12 (26.7%)	0.70

Table 2: Unadjusted and adjusted Odds Ratios for association with primary and secondary outcomes

Primary Outcome: Requiring csDMARD or biologic DMARD				
	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age	1.00 (0.97, 1.03)	0.977	0.99 (0.96, 1.03)	0.931
Female sex	1.61 (0.78, 3.30)	0.198	1.31 (0.52, 3.40)	0.56
Prior Chemotherapy	0.52 (0.25, 1.09)	0.085	**0.34 (0.14, 0.85)**	**0.022**
Already on steroids at baseline visit	1.99 (0.89, 4.44)	0.094	1.97 (0.73, 5.31)	0.182
Presence of tenosynovitis	**4.00 (1.50, 10.63)**	**0.005**	**3.80 (1.05, 13.76)**	**0.042**
CDAI	**1.05 (1.01, 1.09)**	**0.01**	**1.06 (1.01, 1.11)**	**0.017**
ICI duration	**1.05 (1.01, 1.10)**	**0.02**	1.03 (0.98, 1.09)	0.30
Symptom duration	**1.06 (1.02, 1.11)**	**0.004**	**1.06 (1.01, 1.12)**	**0.027**
Secondary Outcome: Persistent IA >6 months after ICI cessation				
	Unadjusted OR	p-value	Adjusted OR	p-value
Age	0.99 (0.96, 1.03)	0.593	0.98 (0.93, 1.02)	0.277
Female sex	1.27 (0.52, 3.08)	0.600	0.61 (0.18, 2.03)	0.419
Already on steroids at baseline visit	**5.28 (1.16, 23.96)**	**0.031**	**5.51 (1.02, 29.90)**	**0.048**
Combination ICI therapy	**5.28 (1.16, 23.96)**	**0.031**	**5.43 (1.04, 28.43)**	**0.045**
Presence of tenosynovitis	6.43 (0.81, 50.71)	0.078	7.09 (0.77, 65.16)	0.083
ICI duration	1.07 (0.99, 1.14)	0.065	1.08 (0.99, 1.18)	0.068
Symptom duration	**1.13 (1.03, 1.24)**	**0.009**	1.11 (0.99, 1.24)	0.067

PD-1 therapy and steroid use at baseline were associated with a higher risk of persistent IA (Table 2). For 98 patients with HLA typing data, there was no significant association with HLA DRB1 shared epitope alleles or HLA B27 and primary or secondary outcomes. For 62 patients reporting systemic steroid use after starting ICI therapy, but prior to their baseline visit with rheumatology, there were no differences between those treated with low dose (prednisone or equivalent ≤ 10 mg/daily), moderate dose (10 mg< prednisone daily ≤60 mg), or high dose (prednisone daily > 60 mg) corticosteroids in either requiring a csDMARD/biologic or having persistent ICI-IA.

Conclusion: Higher levels of disease activity, tenosynovitis, and longer symptom duration prior to baseline were associated with requiring DMARDs for ICI-IA, while those treated previously with chemotherapy were less likely to require DMARDs. Known genetic risk factors for traditional forms of IA were not predictive. The presence of risk factors for severe disease at baseline may indicate a role for higher initial steroid dose, earlier rheumatology referral, and adoption of immunosuppression beyond steroids to improve outcomes.

Disclosure: L. Cappelli: Bristol-Myers Squibb(BMS), 5, Mallincrkrodt, 2; **o. Kamal**: None; **M. Jones**: None; **C. Bingham**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 2, Janssen, 2, Pfizer, 2, Sanofi, 2; **A. Shah**: Arena Pharmaceuticals, 5, Eicos Sciences, 5, Kadmon Corporation, 5, Medpace LLC, 5.

Abstract Number: 1075

Impact of Immunosuppression on the Safety and Efficacy of Immune Checkpoint Inhibitors in Patients with Rheumatic Autoimmune Disease: Experience from the Canadian Research Group of Rheumatology in Immuno-Oncology (CanRIO)

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitors (ICI) have changed the landscape of treatment for many cancers. However, most cancer clinical trials for ICI excluded patients with pre-existing autoimmune diseases (PAD). Efficacy and safety data on the use of ICI in patients with rheumatic PAD (Rh-PAD) is limited to retrospective case series and reports, and many do not differentiate between Rh-PAD and non-rheumatic PAD. In one study of a large French retrospective cohort, patients on immunosuppression (IS) at baseline had poorer tumor outcomes (1).

Objectives: To explore the impact of baseline IS on the safety and efficacy of ICI in patients with Rh-PAD using data from the CanRIO retrospective and prospective cohorts.

Table 1. Summary of demographic, pre-existing rheumatic autoimmune disease, cancer and outcomes data a 3 patients who were on baseline IS had more than one Rh-PAD; 1 patient who was not on baseline IS had more than one Rh-PAD b Missing data for 3 patients in the baseline IS group and 1 patient in the no baseline IS group c 13 patients on baseline IS experienced a flare of their Rh-PAD and a de-novo irAE; 3 patients not on baseline IS experienced a flare of Rh.PAD and de-novo irAEs d 5 patients on baseline IS experienced both de-novo Rh-irAE and other irAEs; 12 patients not on baseline IS experienced de-novo Rh-irAE and other irAEs e Including skin, endocrinological (other than thyroid), heart and eyes f Missing tumor response information for 7 patients on baseline IS and 5 in no baseline IS

Characteristics [n (%)]	Baseline IS (n=50)	No Baseline IS (n=52)
Demographics		
Age, years (mean, SD)	69.4 (12.1)	70.5 (9.5)
Male	25 (50.0%)	29 (55.8%)
Caucasian	29 (58.0%)	37 (71.2%)
Rheumatic Pre-existing autoimmune disease [a]		
Rheumatoid arthritis	18 (36.0%)	12 (23.1%)
Psoriasis/psoriatic arthritis	13 (26.0%)	12 (23.1%)
Polymyalgia rheumatica	5 (10.0%)	5 (9.6%)
Ankylosing spondylitis	5 (10.0%)	5 (9.6%)
Vasculitis	1 (2.0%)	3 (5.8%)
Uveitis	2 (4.0%)	0 (0.0%)
Others	9 (18.0%)	18 (34.6%)
Cancer type		
Melanoma	17 (34.0%)	15 (28.8%)
NSCLC (lung)	19 (38.0%)	19 (36.5%)
Renal cell carcinoma	4 (8.0%)	9 (17.0%)
Non-melanoma skin	1 (2.0%)	3 (5.8%)
Other	9 (18.0%)	6 (11.5%)
Cancer stage [b]		
1	1 (2.0%)	0 (0.0%)
2	5 (10.0%)	1 (1.9%)
3	13 (26.0%)	22 (42.3%)
4	28 (56.0%)	28 (53.8%)
Cancer therapy [b]		
Nivolumab	10 (20.0%)	10 (19.2%)
Pembrolizumab	25 (50.0%)	16 (30.8%)
Nivolumab and ipilimumab	5 (10.0%)	10 (19.2%)
Pembrolizumab in another combination	2 (4.0%)	8 (15.4%)
Durvalumab	0 (0.0%)	1 (1.9%)
Other	8 (16.0%)	7 (13.5%)
Duration of ICI therapy, months (median, IQR)[b]	3.0, 2.0 – 12.5	3.0, 1.0 – 9.5
Immune-related adverse events		
No irAE	11 (22.0%)	10 (19.2%)
Any irAE [c]	39 (78.0%)	42 (80.8%)
Flares	29 (58.0%)	20 (38.5%)
New irAE [d]	22 (44.0%)	25 (48.1%)
New rheumatic irAE	19 (38.0%)	24 (46.2%)
New other irAE [e]	11 (22.0%)	20 (38.5%)
CTCAE grade (Rh-PAD flares)		
1 – 2 (non-severe)	9 (18.0%)	11 (21.2%)
3 – 5 (severe)	6 (12.0%)	6 (11.5%)
CTCAE grade (de-novo Rh-irAE)		
1 – 2 (non-severe)	4 (8.0%)	5 (9.6%)
3 – 5 (severe)	2 (4.0%)	9 (17.3%)
CTCAE grade (de-novo other irAE)		
1 – 2 (non-severe)	4 (8.0%)	8 (15.4%)
3 – 5 (severe)	1 (2.0%)	4 (7.6%)
Tumor response to ICI therapy [f]		
Favorable response (stabilization, partial or complete)	22 (44.0%)	21 (40.4%)

Methods: We evaluated patients with Rh-PAD treated with at least one dose of ICI, including CTLA-4, PD-1, or PDL-1 inhibitors. 45 patients were recruited prospectively between Jan 2020 and Apr 2023 across 9 Canadian academic sites and followed at regular intervals as per a standardized study protocol. 57 patients were retrospectively recruited using data extracted from patients referred to rheumatology specialists between Jan 2013 and Jun 2022 across 10 Canadian sites. We used logistic regression to compare the occurrence and severity of flares and de-novo immune-related adverse events (irAE), as well as tumor response, between patients on baseline IS and not on baseline IS.

Results: One hundred and two patients with Rh-PADs were followed for a median of 32 months; 50 were on baseline IS prior to ICI start, and 52 were not. The most common Rh-PADs were rheumatoid arthritis and psoriasis/psoriatic arthritis (Table 1).

Cancer type, cancer stage, ICI type, and ICI exposure time were similar in both groups (Table 1). The flare rate of patients on baseline IS was 58%, compared to only 38% in the group without baseline IS (adjusted OR=2.1; 95% CI = 0.9-5.0; p=0.09). There were no statistically significant differences in the risk of a severe flare (CTCAE grade ≥3) (p = 0.3), development of a de-novo Rh-irAE (p = 0.4) or a severe de-novo Rh-irAE (p = 0.4) (Tables 1 & 2). Tumor follow-up data was available for 38 of the 50 patients on baseline IS and 37 of the 52 patients without baseline IS. The rate of tumor progression was 42% (16 of 38) in the IS group and 27% (10 of 37) in the no IS group (HR=1.4; 95% CI = 0.6-3.1; p=0.437) but there was no difference in progression free survival between groups.

Conclusion: Early data from patients with Rh-PAD in the multicenter prospective and retrospective CanRIO cohorts suggest that 1) ICI can be effective for cancer treatment in patients with Rh-PAD, and should be offered as indicated; 2) Baseline IS does not seem to protect from flares of Rh-PAD; 3) Baseline IS does not seem to change the risk of developing de-novo irAE, nor the severity of flares/de-novo irAEs; 4) There was a non-significant trend towards baseline IS increasing the hazard of tumor progression but no difference in progression free survival between groups.

[1] Tison A, et al. Safety and efficacy of immune checkpoint inhibitors in patients with cancer and preexisting autoimmune disease: A nationwide, Multicenter Cohort Study. Arthritis & Rheumatology. 2019;71(12):2100–11.

Table 2. Flare and de-novo irAEs rates and flare and de-novo irAEs severity according to baseline immunosuppression a Adjusted for Rheumatic Pre-existing autoimmune disease (*) Indicates significance at p 0.05. OR calculated using logistic regression

Characteristics [n (%)]	Baseline IS (n=50)	No Baseline IS (n=52)	OR (95% CI) p-value
Occurrence			
Flare (unadjusted)	29 (58.0%)	20 (38.5%)	2.2 (1.0 – 4.9) p=0.050*
Flare (adjusted)[a]			2.1 (0.9 – 5.0) p=0.093
De-novo irAE	22 (44.0%)	25 (48.1%)	0.8 (0.4 – 1.9) p=0.680
De-novo Rh-irAE	19 (38.0%)	24 (46.2%)	0.7 (0.3 – 1.6) p=0.405
De-novo other	11 (22.0%)	20 (38.5%)	0.5 (0.2 – 1.1) p=0.074
Severe (CTCAE grade ≥3)			
Flare	13 (46.4%)	6 (30.0%)	2.0 (0.6 – 7.1) p=0.254
De-novo Rh-irAE	7 (38.9%)	9 (52.9%)	0.6 (0.1 – 2.2) p=0.406
De-novo other	4 (44.4%)	4 (28.6%)	2.0 (0.3 – 12.2) p=0.438

Disclosure: L. Gonzalez Arreola: None; **C. Ye**: None; **M. Hudson**: AstraZeneca, 6, Boehringer-Ingelheim, 1, 5, 6, Bristol-Myers Squibb(BMS), 5, Merck, 6, UCB, 5; **J. Roberts**: None; **J. Pope**: AbbVie, 1, 2; **T. Appleton**: AbbVie/Abbott, 1, 2, 6, AstraZeneca, 1, 1, Celgene, 1, Eli Lilly, 1, Janssen, 1, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, 6, Roche, 1, UCB, 1, 2, 6; **S. Hoa**: Boehringer-Ingelheim, 5; **A. Fifi-Mah**: Bristol-Myers Squibb(BMS), 5, Celltrion, 1, Frenesius-Kabi, 6, Novartis, 1, Otsuka, 1, Pfizer, 5, Sanofi, 1; **N. Maltez**: None; **A. Saltman**: None; **M. Himmel**: None; **I. Colmegna**: None; **A. Ladouceur**: None; **A. Obrzut**: None; **J. Tan**: None; **D. Moon**: None; **T. Nevskaya**: None; **E. Schmidt**: None; **L. Cho**: None; **N. Toban**: None; **S. Jamal**: AbbVie/Abbott, 1, 6, Eli Lilly, 1, GlaxoSmithKlein(GSK), 1, Merck/MSD, 1, 5, Pfizer, 1, 2, 6, UCB, 1, 2, 6.

Abstract Number: 1076

Rituximab-Associated Hypogammaglobulinemia in Patients with Rheumatic Diseases: A Multicenter Retrospective Observational Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Rituximab (RTX) is a murine/human chimeric monoclonal antibody directed against the CD20 receptor expressed on pre-B and mature B cells. Rituximab is used effectively in the treatment of different rheumatic diseases, but it can induce hypogammaglobulinemia as a side effect. The purpose of our study was to analyze the prevalence of hypogammaglobulinemia and its association with infections in patients with rheumatic diseases treated with RTX.

Methods: Multicenter, retrospective, observational study. Patients with rheumatic diseases treated with RTX in 4 centers in Madrid, in which serum immunoglobulin counts were available were included. Demographic and clinical variables of the sample were analyzed, changes in immunoglobulin G concentrations during treatment from baseline were assessed. The

Table 1. Hypogammaglobulinemia and infections in patients with rheumatic diseases treated with Rituximab.

Table 1. Hypogammaglobulinemia and infections in patients with rheumatic diseases treated with Rituximab.

	No infection(N, %)	Mild infection(N, %)	Serious infection(N, %)
Patients **without** hypogammaglobulinemia	55 (58.51)	24 (25.53)	15 (15.96)
Patients **with** hypogammaglobulinemia	7 (58.33)	3 (25)	2 (16.67)
p value		p=0.991	p=0.950

chi-square test was used to examine the relationship between variables, considering a p value < 0.05 as statistically significant. Logistic regression models were used to analyze the association between hypogammaglobulinemia and sample characteristics.

Results: One hundred and seven patients were included: 18 men (16.8%) and 89 women (83.2%), with a mean age of 55.9 (±13.9) years, a mean disease duration of 13.1 (±0.8) years, and a mean age of 51 (±14.4) years at the start of treatment. The most prevalent diagnoses were rheumatoid arthritis (RA) (50.5%), primary Sjogren's syndrome (pSS) (10.3%), and systemic lupus erythematosus (SLE) (10.3%). Fourteen (13%) patients were treated with RTX monotherapy. The rest of the patients received concomitant treatment with other immunomodulators such as corticosteroids (64.5%), methotrexate (29%), hydroxychloroquine (27%), leflunomide (9.3%), sulfasalazine (1.9%), or mycophenolate mofetil (2.8%). Twelve (11.21%) patients developed hypogammaglobulinemia (IgG< 600 mg/dl): 6 (50%) had RA, 1 (8.3%) SLE, 1 (8.3%) ANCA vasculitis, 1 (8.3%) leukocytoclastic vasculitis, 1 (8.3%) IgG4-related disease, 1 (8.3%) dermatomyositis, and 1 (8.3%) pSS. Patients with hypogammaglobulinemia had significantly lower mean serum IgG concentrations at the start of treatment (876.3 vs 1249.4 mg/dl; p=0.05). In the multivariate analysis no variable related to hypogammaglobulinemia was found. Fifty-three (49.5%) patients presented infection, of which 17 (15.9%) were serious infections (those that required admission). The distribution of infection by groups (patients with and without hypogammaglobulinemia) is shown in Table 1. No significant differences were found in the development of infections or serious infections between patients with and without hypogammaglobulinemia. Only corticosteroid doses equivalent to ≥7.5 mg/day of prednisone were found as a risk factor for the development of infections (OR 3.48, 95% CI: 1.20-0.11; p=0.02).

Conclusion: Patients with hypogammaglobulinemia had significantly lower mean IgG concentrations at the start of treatment with RTX than those who did not develop it. No greater frequency or severity of infections was observed between patients with and without hypogammaglobulinemia. Prednisone equivalent daily dose ≥7.5 mg/day was a risk factor for occurrence of infections. Larger sample size studies are needed to confirm these findings.

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Abstract Number: 1077

Anti-drug Antibodies Formation During Tapering and Stopping of Methotrexate in Rheumatoid Arthritis Patients with Longstanding Use of Adalimumab

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SESSION INFORMATION

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Session Title: Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Due to better effectiveness and longer drug survival, a TNF inhibitor (TNFi) should preferably be combined with methotrexate (MTX). MTX has been found to reduce the development of anti-drug antibodies (ADAs), which decreases the risk of treatment failure. ADA formation, however, predominately occurs during treatment initiation. To our knowledge, the effect of tapering or stopping MTX on the formation of ADAs after longstanding treatment with TNFi is not yet known. Therefore, the aim of this study was to assess the effect of tapering and stopping MTX on the formation of ADA in rheumatoid arthritis (RA) patients with longstanding use of adalimumab (ADL).

Methods: For this study we used data from the TApering strategies in Rheumatoid Arthritis (TARA) trial. The TARA trial was a multicenter, single-blinded randomized trial that included established RA patients with a well-controlled disease, defined as a disease activity score (DAS) ≤2.4 and a swollen joint count ≤1, which was achieved with conventional synthetic (cs) DMARDs and a TNFi. Eligible patients were randomized into gradual tapering csDMARD (mainly methotrexate) followed by the TNFi, or vice versa. Tapering of MTX was realized by cutting the dosage into half, a quarter and thereafter it was stopped. The TNF inhibitor was tapered by doubling the dose interval, followed by cutting the dosage into half, and thereafter it was stopped. The total tapering schedule took 6 months, with dose adjustments every 3 months as long as there was still a controlled disease. ADA and ADL serum levels were measured at each 3-monthly visit, if serum samples were available, by a drug tolerant enzyme-linked immunosorbent assay.

Results: Of the 46 included RA patients, 21 patients did not experience a disease flare. Among patients who did not experience a flare, 10 patients tapered ADL first, while 11 patients tapered their csDMARD first. Patients had an average symptom duration of 6,5 years and were predominantly female 71% with an average age of 54 years. At baseline, the DAS (standard deviation) was 1,0 (0,6) and the mean MTX dosage before tapering was 16.5 mg/week. In the group tapering ADL first, detectable ADA prevalence remained unchanged between 10 to 20 % (Figure 1A). On the other hand ADA detection in serum increased from 18% to 68% in the RA patients who were tapering and stopping the MTX first (Figure 1B). Despite the increase in ADA formation, the mean ADL concentration showed a minor decrease from 8.3 (T0) to 7,8 (T9) ug/mL (Figure 1B). In the second year, when also ADL is tapered, patients with detectable ADA seems to have faster clearance of ADL (figure 1B).

Conclusion: Our data shows that there is an increase in detectable ADA after tapering and stopping MTX in patients with longstanding use of ADL, but this seems not to have a major effect on the clearance of ADL in the standard dose.

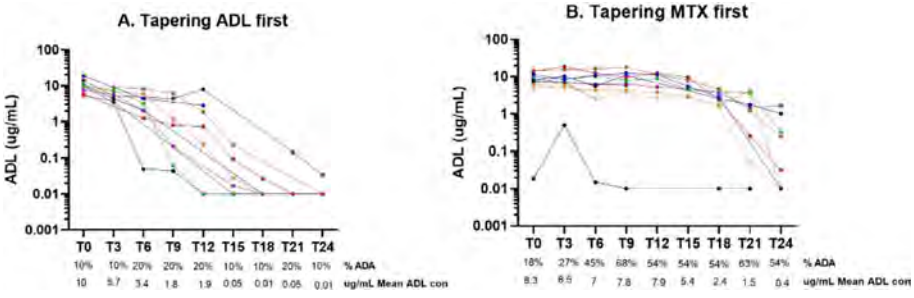

Figure 1: Anti-Drug Antibodies formation during tapering of treatment in RA patients with a well-controlled disease who did not experienced a disease flare"Each dot represents an ADL drug level measurement per individual RA patient. Measurements within each individual patient are connected by a coloured line. Abbreviations: ADL, adalimumab; con., concentration; ADA, anti-drug antibodies

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Abstract Number: 1078

Outcomes of COVID-19 Infection in Hospitalized Autoimmune Patients and Transplant Patients on Immunosuppression

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Coronavirus disease 2019 (COVID-19) can have varying outcomes. Patients with chronic conditions or immunosuppression experience more severe illness. Both organ transplant recipients and patients with certain autoimmune rheumatic diseases (ARD) require immunosuppressive therapy. We investigated the outcome of COVID-19 infections in hospitalized transplant patients and autoimmune immunosuppressed patients.

	Autoimmune Patients (n=49)		Transplant Patients (n=119)	
	n	% [95% CI]	n	
Sex				
Male	13	26.5 [15.8, 40.9]	72	60.5 [51.0, 68.7]
Female	36	73.5 [59.1, 84.1]	47	39.5 [31.3, 49.0]
Race/ethnicity				
White	14	28.6 [17.48,43.0]	47	39.5 [31.0, 48.6]
Black/ African American	19	38.7 [26.0, 53.0]	27	22.6 [16.0, 31.2]
Hispanic or Latino	14	28.6 [17.48, 43.0]	38	31.9 [24.1, 40.9]
Other or not available	2	4.1 [1.0, 15.4]	5	4.2 [1.7, 9.8]
Asian	0		2	1.7 [0.4 6.6]
Current Smoking				
Yes	2	4.1 [1.0, 15.4]	2	1.7 [93.4, 99.6]
No	47	95.9[74.6, 99.0]	117	98.3 [0.4, 6.6]
BMI				
Less than 25	9	18.4[9.7, 32.1]	32	26.9 [19.6, 35.6]
25-29.9	11	22.5[12.7, 36.6]	36	30.3 [22.6, 39.2]
30.0-34.9	11	22.5[12.7, 36.6]	35	29.4 [21.9, 38.3]
35.0-39.9	9	18.4[9.7, 32.1]	12	10.1 [57.8, 17.0]
>40	9	18.4[9.7, 32.1]	4	3.4 [1.3, 8.7]
Comorbidity				
Hypertension	34	69.4 [54.9, 80.9]	104	87.3 [80.0, 92.3]
Diabetes mellitus type II	11	22.5 [12.7, 36.6]	63	53.0 [43.9, 61.8]
Lung disease	16	32.7[20.8, 47.2]	22	18.5 [12.4, 26.6]
Chronic kidney disease	15	30.6 [19.1, 45.1]	95	80.0 [71.6, 86.2]
Heart failure	6	12.2 [5.5, 25.1]	33	27.7 [20.34, 36.5]
Liver disease	4	8.2[3.0, 20.2]	15	12.6 [7.7, 20.0]
Malignancy	6	12.2 [5.5, 25.1]	13	10.9 [6.4, 18.0]
Type of Autoimmune disease (n=47)				
Rheumatoid Arthritis	16	32.7[20.8, 47.2]		
SLE	9	18.4[9.7, 32.1]		
Sarcoidosis	7	14.3 [2.8, 27.5]		
Sjogren Syndrome	2	4.1[1.0, 15.4]		
IPAF	2	4.1[1.0, 15.4]		
Systemic sclerosis	1	2.0[0.3, 13.7]		
Dermatomyositis	1	2.0[0.3, 13.7]		
UCTD	1	2.1[0.3, 13.7]		
Vasculitis	1	2.1[0.3, 13.7]		
Other	9	18.4[9.7, 32.1]		

Table 1. 95% CI = 95% Confidence interval; SLE = systemic lupus erythematosus; IPAF= interstitial lung disease with autoimmune features; UCTD= Undifferentiated connective tissue disease

Baseline Characteristics of Patients with Autoimmune diseases versus Transplant Patients

Methods: This is a retrospective chart review of outcomes for adult patients admitted to our institution with COVID-19 infection from March 2020 to September 2021 on immunosuppressive drugs. Patients were categorized into either a transplant or ARD group. Baseline characteristics, comorbidities, and severe outcomes during admissions were evaluated. Chi2 tests were used to compare outcomes. Odds ratios were adjusted for age, sex, and race.

Results: Of 2,140 cases reviewed, 49 patients with ARD requiring immunosuppression and 119 transplant patients were identified. The ARD group had a higher proportion of females than the transplant group (Table 1). More transplant patients had hypertension, diabetes mellitus, or chronic kidney disease (CKD). In the ARD group, 4.1% were current smokers, but seven patients (43.8%) with any history of smoking died compared with 2 (6.0%) non-smokers, although the adjusted odds ratio did not reach significance. The most common ARD was RA. Among 9 ARD patients who died, 3 had RA and SLE each. The mean age of ARD patients who died was 65.2 years. ARD patients with renal and respiratory failure were more likely to die than those without these adverse events (Table 2). Comorbidities with significantly increased risk of death in ARD patients were hypertension, CKD, and heart failure (Table 2). A history of heart failure or transplant was also associated with respiratory and renal failure. In the transplant group, a history of heart failure was associated with death, and patients with a history of CKD or heart failure were more likely to develop renal failure (Table 3). When comparing death, renal or, respiratory failure and thromboembolic events between transplant and ARD patients, there was an increase in renal failure for transplant patients compared to ARD patients (17.0 versus 4.8%, p= .017). While 14.3% of ARD patients and 16.9% of transplant

Comorbidity	Outcome	With comorbidity (95% CI)	Without comorbidity (95% CI)	aOR (95%CI)	P value (chi2)
Hypertension	**Death**	**26.5 (14.1, 44.0)**	**0**	**	**0.027**
	Respiratory failure	23.5 (12.0, 41.0)	6.7 (0.9, 36.4)		0.160
	Renal failure	11.8 (4.4, 28.0)	6.7 (0.9, 36.4)		0.59
	DVT/ PE	2.9 (0.4, 18.9)	6.7 (0.9, 36.4)		0.54
Diabetes	Death	27.3 (8.8, 59.4)	15.8 (7.1, 3.14)		0.39
	Respiratory failure	18.2 (4.4, 51.7)	8.4 (8.9, 34.4)		0.99
	Renal failure	0	13.2 (5.5, 28.5)		0.20
	DVT/PE	9.1 (1.2, 45.2)	2.6 (0.4, 17.2)		0.34
Lung disease	Death	12.5 (3.0, 39.5)	21.2 (10.3, 38.8)		0.46
	Respiratory failure	12.5 (3.0, 39.5)	21.2 (10.3, 38.8)		0.46
	Renal Failure	6.3 (0.8, 34.7)	12.1 (4.5, 28.7)		0.52
	DVT/PE	0	6.1 (1.5, 21.9)		0.32
CKD	**Death**	**40.0 (18.8, 65.8)**	**8.8 (2.8, 2.5)**	**5.9 [1.01, 34.34]**	**0.009**
	Respiratory failure	26.7 (10.1, 54.1)	14.7 (6.1, 31.3)		0.32
	Renal failure	20 (6.4, 47.8)	5.9 (1.4, 21.3)		0.13
	DVT/PE	0	5.9 (1.4, 21.3)		0.34
Heart failure	**Death**	**66.7 (26.0, 91.9)**	**11.6 (4.8, 25.5)**	**24.4 [1.55, 384.72]**	**0.001**
	Respiratory failure	**50 (16.2, 83.8)**	**14.0 (6.3, 28.2)**	**5.62 [0.75, 42.0]**	**0.033**
	Renal failure	**50 (16.2, 83.8)**	**4.7 (1.1, 17.3)**	**28.1 [1.46, 543.1]**	**0.001**
	DVT/PE	0	4.7 (1.1, 17.3)		0.59
Cirrhosis	Death	0	20.0 (10.6, 34.6)		0.32
	Respiratory failure	0	20.0 (10.6, 34.6)		0.32
	Renal failure	0	11.1 (4.6, 24.5)		0.48
	DVT/PE	0	4.4 (1.1, 16.6)		0.67
Cancer	Death	33.3 (8.1, 74.0)	16.3 (7.8, 30.9)		0.31
	Respiratory failure	16.7 (2.2, 64.4)	18.6 (9.4, 33.4)		0.91
	Renal failure	0	11.6 (4.8, 25.5)		0.38
	DVT/ PE	0	4.7 (1.1, 17.3)		0.59
Transplant	Death	33.3 (10.8, 67.4)	10.0 (3.7, 24.3)		0.071
	Respiratory failure	42.9 (13.9, 77.7)	14.3 (6.4, 28.8)		0.071
	Renal failure	**42.9 (13.9, 77.7)**	**14.3 (6.4, 28.8)**	**23.8 [1.43, 393.73]**	**0.002**
	DVT/ PE	0	4.7 (1.1, 17.7)		0.56
History of DVT/PE	Death	12.5 (1.7, 54.9)	18.0 (9.5, 31.4)		0.92
	Respiratory failure	0	20.4 (10.8, 35.3)		0.26
	Renal failure	20 (25.7, 70.3)	9.1 (3.4, 22.3)		0.45
	DVT/ PE	0	4.5 (1.1, 16.9)		0.63

Table 2. aOR= adjusted odds ratio, adjusted for age, sex, and race. ** Hypertension perfectly predicted death in this model.

Comorbidity	Outcome	% With comorbidity (95% CI)	Without comorbidity (95% CI)	aOR (95%CI)	P value (chi2)
Hypertension	Death	17.3 (11.1, 25.9)	13.3 (3.3, 40.9)		0.70
	Respiratory failure	23.1 (15.9, 32.2)	13.3 (3.3, 40.9)		0.39
	Renal failure	17.3 (11.1, 25.9)	26.7 (10.3, 53.6)		0.38
	DVT/ PE	7.7 (2.6, 3.9)	0		0.27
Diabetes	Death	20.6 (12.3, 32.5)	12.5 (6.0, 24.1)		0.24
	Respiratory failure	25.4 (16.1, 37.7)	17.9 (9.8, 30.3)		0.32
	Renal failure	19.0 (11.1, 30.1)	17.9 (9.8, 30.3)		0.87
	DVT/PE	9.5 (4.3, 19.8)	3.6 (0.0, 13.4)		0.196
Lung disease	Death	18.2 (6.9, 40.0)	16.5 (10.3, 25.3)		0.85
	Respiratory failure	12.5 (3.0, 39.5)	21.2 (10.3, 38.8)		0.46
	Renal Failure	93.8 (65.3, 99.2)	87.9 (71.3, 95.5)		0.52
	DVT/PE	0	6.1 (1.5, 21.9)		0.32
CKD	Death	16.8 (10.5, 25.8)	16.7 (6.3, 37.2)		0.98
	Respiratory failure	22.1 (8.9, 41.6)	20.8 (8.9, 41.6)		0.89
	Renal failure*	**22.1 (14.8, 31.6)**	**4.2 (0.6, 24.7)**	**6.11 [0.77, 48.73]**	**0.043**
	DVT/PE	7.4 [3.5, 14.8]	4.2 [0.6, 24.7]		0.58
Heart failure	**Death**	**30.3 (17.0, 47.9)**	**11.6 (6.3, 20.4)**	**3.04 [1.05, 8.79]**	**0.015**
	Respiratory failure	27.3 (14.7, 44.8)	19.8 (12.6, 29.6)		0.38
	Renal failure	**36.4 (21.8, 53.9)**	**11.6 (6.3, 20.4)**	**6.50 [2.16, 19.56]**	**0.002**
	DVT/PE	3.0 (0.4, 18.9)	8.1 (0.4, 16.2)		0.32
Cirrhosis	Death	6.7 (0.9, 35.7)	18.3 (11.9, 27.0)		0.26
	Respiratory failure	6.7 (0.9, 35.7)	24.0 (16.7, 33.3)		0.128
	Renal failure	13.3 (3.3, 40.9)	19.2 (12.7, 28.0)		0.58
	DVT/PE	0	7.7 (3.9, 14.7)		0.27
Cancer	Death	7.7 (1.0, 4.0)	17.9 (11.7, 26.5)		0.35
	Respiratory failure	7.7 (7.4, 10.5)	23.6 (16.4, 32.7)		0.191
	Renal failure	7.7 (7.4, 10.5)	19.8 (13.2, 28.6)		0.29
	DVT/ PE	0	7.5 (3.8, 14.5)0		0.31
DVT/PE	Death	17.8 (11.6, 26.3)	0		0.15
	Respiratory failure	10.0 (1.4, 47.3)	22.4 (15.5, 31.4)		0.36
	Renal failure	30.0 (9.8, 62.7)	17.8 (11.6, 26.3)		0.34
	DVT/ PE	10.0 1.6, 47.3)	5.6 (2.5, 12.0)		0.58

Table 3. *there was no distinction between patients with CKD and those who were already on dialysis prior to admission. 16.4% of transplant patients who experienced renal failure were renal transplant recipients (versus 20.7% who were non-renal transplant recipients).

Proportion of Transplant Patients Who Experienced an Adverse Outcome During COVID-19 Infection

patients died, and 21.8% of transplant patients required intubation, compared to 14.3% of ARD patients, these trends did not reach statistical significance. In transplant patients who died during their admission, the most common organ transplant was heart (22.7%) followed by kidney and lung (18 and 15%).

Conclusion: Studies have evaluated risk factors for severe COVID-19 outcomes in immunosuppressed patients, but there is limited literature comparing autoimmune disease and transplant patients that also evaluate severe outcomes such as renal failure and thromboembolic events. Besides renal failure, severe outcomes from COVID-19 were not significantly different between ARD and transplant patients. Risk factors for death, however, did differ between these groups. This study gives further insight into similarities and differences of immunosuppression's impact on COVID-19 outcomes in autoimmune and transplant patients.

Disclosure: Y. KC: None; **R. Ostrowski**: None.

Abstract Number: 1079

Identification of Immune Checkpoint Inhibitor-Induced Myositis Patients Using Electronic Health Records Is Most Successful When Employing Multiple Data Elements

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Immune Checkpoint Inhibitor (ICI)-induced myositis (ICI-myositis) is a rare, but potentially fatal complication of ICI therapy.Electronic health record (EHR) databases are essential to accrue sufficient patients for clinical investigations regarding phenotypical presentations, associated risks, prognosis, and management and have not yet been fully employed in this area of research.To meet this critical need, this study assessed the factors most effective in identifying ICI-myositis in the Veterans Health Administration (VHA) with the goal of developing an algorithm to accurately identify these patients.

Table 1: Sensitivity, Positive Predictive Value, and F1 Score for Individual Factors Involved in ICI-Induced Myositis Identification

Table 1: Sensitivity, Positive Predictive Value, and F1 Score for Individual Factors Involved in ICI-Induced Myositis Identification

Factors involved in ICI myositis identification	Patients Meeting Criteria	Cases meeting Criteria	Sensitivity % (95% CI)	Positive Predictive Value % (95% CI)	F1 Score
Screening Sources					
10x ULN* Creatinine Kinase	60	33	55.0% (41.6%, 67.8%)	55.0% (41.6% 67.9%)	55.0%
Myositis text in Discharge Summary	176	46	76.7% (63.9%, 86.6%)	26.1% (19.8%, 33.3%)	39.0%
Myositis text in Clinic Notes	477	40	66.7% (53.3%, 78.3%)	8.4% (6%, 11.2%)	14.9%
Lab Data during 6 months after first ICI infusion					
Creatinine Kinase					
3x ULN Creatinine Kinase	181	48	80.0% (67.6%, 89.2%)	26.5% (20.2%, 33.6%)	39.8%
1x ULN Creatinine Kinase	430	54	90.0% (79.5%, 96.2%)	12.6% (9.6%, 16.1%)	22.0%
Creatinine Kinase ordered	4549	56	93.3% (83.8%, 98.2%)	1.2% (0.9%, 1.6%)	2.4%
Aldolase					
3x ULN Aldolase	5	2	3.3% (0.4%, 11.5%)	40% (5.2%, 85.3%)	6.2%
1x ULN Aldolase	25	4	5.0% (1%, 13.9%)	16% (4.5%, 36.1%)	9.4%
Aldolase ordered	79	5	8.3% (2.7%, 18.3%)	6.3% (2.1%, 14.2%)	7.2%
Anti-Jo					
Anti-Jo - positive	0	0	0% (0%, 6.0%)	N/A	N/A
Anti-Jo ordered	39	5	8.3% (2.7%, 18.3%)	12.8% (4.2%, 27.4%)	10.1%
Troponin - I					
3x ULN Troponin I	415	10	16.7% (8.2%, 28.5%)	2.4% (1.1% 4.3%)	4.2%
1x ULN Troponin I	761	12	20.0% (10.7%, 32.3%)	1.5% (0.8%, 2.7%)	2.9%
Troponin I ordered	3410	15	25.0% (14.7%, 37.8%)	0.4% (0.2% 0.7%)	0.9%
Troponin - T					
3x ULN Troponin T	227	1	1.7% (0%, 8.9%)	0.4% (0%, 2.4%)	0.7%
1x ULN Troponin T	310	1	1.7% (0%, 8.9%)	0.3% (0% 1.7%)	0.5%
Troponin T ordered	481	1	1.7% (0%, 8.9%)	0.2%, (0%, 1.1%)	0.4%

*ULN = Upper Limit of Normal

Table 2: Sensitivity, Positive Predictive Value, and F1 Scores for Combined Factors Involved in ICI-Induced Identification Ranked by F1 Score

Table 2: Sensitivity, Positive Predictive Value, and F1 Scores for Combined Factors involved in ICI-Induced Identification Ranked by F1 Score

Factors involved in ICI identification	Patients Meeting Criteria	Cases meeting Criteria	Sensitivity % (95% CI)	Positive Predictive Value % (95% CI)	F1 Score
Note* OR Dis Sum**	597	46	76.7% (63.9%, 86.6%)	7.7% (5.7%, 10.2%)	14.0%
Note OR Dis Sum OR CK 10xULN***	637	60	100% (94%, 100%)	9.4% (7.3%, 11.9%)	17.2%
Note AND CK tested****	213	38	63.3% (49.9%, 75.4%)	17.8% (12.9%, 23.7%)	27.8%
Note AND Dis Sum AND CK 10xULN	11	11	18.3% (9.5%, 30.4%)	100% (73.5% 100%)	31.0%
(Note OR Dis Sum AND CK tested) OR CK 10xULN	282	56	93.3% (83.8%, 98.2%)	19.9% (15.4%, 25.0%)	32.7%
Dis Sum AND CK 10xULN	12	12	20.0% (10.7%, 32.3%)	100% (73.5%, 100%)	33.3%
Note AND Dis Sum	56	23	38.3% (26.1%, 51.7%)	41.1% (28.1%, 55.0%)	39.7%
Dis Sum AND CK Tested	61	25	41.7% (29.1%, 55.1%)	41.0% (28.6%, 54.3%)	41.3%
Note AND CK 10xULN	19	18	30.0% (18.8%, 43.2%)	94.7% (73.9% 99.8%)	45.6%
(Note AND Dis Sum) AND CK 1xULN*****	23	21	35.0% (23.1%, 48.4%)	91.3% (72.0%, 98.9%)	50.6%
Dis Sum AND CK 1xULN	27	24	40.0% (27.5%, 53.5%)	88.9% (70.8%, 97.6%)	55.2%
Note AND CK 1xULN	64	37	61.7% (48.2%, 73.9%)	57.8% (44.8%, 70.1%)	59.7%
(Note OR Dis Sum) AND CK 1xULN	68	40	66.7% (53.3%, 78.3%)	58.8% (46.2%, 70.6%)	62.5%
(Note AND CK 1xULN) OR CK 10xULN	105	52	86.7% (75.4%, 94.1%)	49.5% (39.6%, 59.4%)	63.0%
(Note OR Dis Sum AND CK 1xULN) OR CK 10xULN	108	54	90.0% (79.5%, 96.2%)	50.0% (40.2%, 59.8%)	64.3%
(Note AND Dis Sum AND CK 1xULN) OR CK 10xULN	72	43	71.6% (58.6%, 82.5%)	59.7% (47.5%, 71.1%)	65.2%
(Dis Sum AND CK 1xULN) OR CK 10xULN	75	45	75.0% (62.1%, 85.3%)	60.0% (48.0%, 71.1%)	66.7%

* Note = Clinic Note with term "myositis" in text
** Dis Sum = Discharge summary with "myositis" in text
*** CK 10xULN = Creatinine Kinase value at least 10 x Upper Limit of Normal
**** CK tested = Creatinine Kinase test with value either within or over the normal range
***** CK 1xULN = Creatinine Kinase value at least 1 x Upper Limit of Normal

Methods: The VA Corporate Data Warehouse (CDW) containing clinical, laboratory, pharmacy, and administrative records from the VHA's EHR, identified Veterans treated with an ICI between 6/2011 and 2/2023.Patients at high risk for ICI-myositis underwent electronic medical record review.High risk was defined by having one or more of the following: creatine kinase (CK) over 10 times the upper limit of normal (ULN) (312 U/L) within 6 months after the first ICI, the term "myositis" in a discharge summary text any time after first ICI, and/or the term "myositis" in a progress note text within six months after ICI treatment. Criteria for diagnosis of ICI-myositis were a provider ICI-myositis diagnosis in clinical notes and laboratory evidence of myositis without alternate etiologies.Levels of CK, aldolase, troponin, and Anti-Jo1 antibodies during 6 months after first ICI infusion were extracted from the CDW.Sensitivity, positive predictive value (PPV), and F1 score for individual variables and combinations of variables were calculated in comparison to the gold standard chart review diagnosis.

Results: In the 29,562 Veterans receiving an ICI, 60 (0.2%) patients were identified with ICI-myositis.In the 60 patients with CK 10xULN, 33 had ICI-myositis with a sensitivity of 55% and PPV of 55% with F1 score of 55% which was the highest F1 score of any single variable.In the 176 patients with a discharge summary with "myositis" and 477 patients with "myositis" in a clinic note the sensitivities were 76.7% and 66.7% and the PPVs were 26.1% and 8.4% with F1 score of 39.0% and 14.9% respectively.There was a wide range of sensitivity, PPV, and F1 score with the individual lab values (Table 1).The combination of factors demonstrated increased sensitivity, PPV, and F1 score with five combinations having an F1 score greater than 60% which was much higher than the F1-scores seen with individual elements (Table 2).

Conclusion: The multiple factors evaluated for the identification of ICI-myositis had varying degrees of performance with factor combinations performing best. Building on this foundational work, future work will detect and include additional clinical and laboratory factors to enhance the effectiveness of an algorithm to identify ICI-myositis patients in large databases. This work suggests that similar methods may be used to identify other immune related adverse events which can be used for further epidemiological studies.

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Abstract Number: 1080

Prevalence and Incidence of Paradoxical Side-effects of TNF-α Inhibitors: A Cross-sectional Study

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Tumor necrosis factor alpha inhibitors (TNFi) are used to treat a variety of inflammatory conditions ranging from rheumatoid arthritis to sarcoidosis. Paradoxical side-effects (PSE) of TNFi include the development of conditions normally treated by the therapeutic agent, such as psoriasis and uveitis. Most prevalent among these adverse effects is paradoxical psoriasis, described as having a prevalence of 4.6%[1] in patients with inflammatory bowel disease (IBD). Our objective was to validate the prevalence and incidence of PSE in TNFi treatment of rheumatic diseases (RD) patients and to identify risk factors.

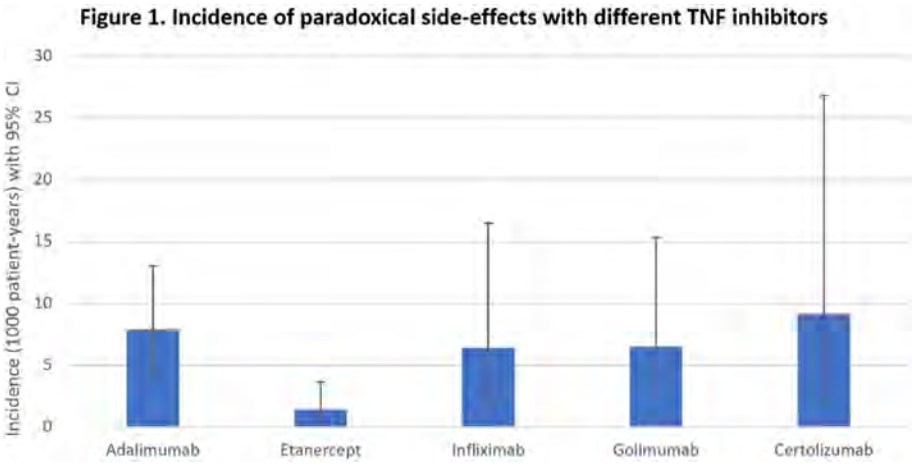
Methods: Using our institution's database on biologic agents in RD, patients that used TNFi were identified. Chart review was performed to identify PSE, which were either documented by the treating clinician or defined as the onset of a condition treatable by the biologic agent (psoriasis, uveitis, hidradenitis suppurativa (HS) or IBD). To identify risk factors, demographic information, diagnosis, and duration of treatment were recorded.

Results: From 2003 to 2023, 1184 patients used at least one TNFi. Median age at diagnosis was 46.1 years old, and females made up 55% of the population. 39% of patients had rheumatoid arthritis while 61% of patients had spondyloarthritides (37% psoriatic arthritis; 63% with other spondylarthropathies). 35 PSE were identified, including 23 cases of psoriasis, 4 cases of Crohn's disease, 3 psoriasis exacerbations , 2 palmoplantar pustulosis, 2 uveitis and 1 HS. The prevalence of PSE across our population was 3.0% (95% CI 2.1 – 4.1). Patients in the SpA group were three times more likely to experience a PSE when compared to RA with a prevalence of 5.1% vs 1.7% (OR (95% CI) = 3.06 (1.36 – 6.92), p< 0.01). A

Table 1. Demographic and clinical patient characteristics (n=1184)

Age at diagnosis (years) - med. (IQR)	46.1 (32.8-56.7)
Female sex - no. (%)	651 (55)
Smoking - no. (%)	
• Current smoker	267 (23)
• Former smoker	218 (18)
• Never smoker	492 (42)
• Unknown	207 (17)
Rheumatoid arthritis - no. (%)	464 (39)
• Rheumatoid factor positive	204 (44)
• Rheumatoid factor negative	177 (38)
• Unknown	83 (18)
Spondylarthritis - no. (%)	451 (38)
• HLA-B27 positive	205 (45)
• HLA-B27 negative	115 (26)
• Unknown	131 (29)
Psoriatic arthritis - no. (%)	269 (23)

Med.: Median, IQR: Interquartile range (25th-75th percentiles)



difference was also observed when comparing prevalence in SpA versus PsA (OR=3.56 (1.22 – 10.41), p=0.02) , while patients younger than 50 years old were more likely to experience PSE (OR=2.34 (1.16 – 2.75), p=0.02).Smoking was a risk factor (OR=2.19 (1.02 – 4.83), p=0.05). Etanercept was less likely to be used in the SpA group compared to the RA group (OR=0.27 (0.20 – 0.36), p< 0.01). Incidence of PSE per 1000 patient-years was 7.9 (95% CI : 4.4 – 13.1) for adalimumab, 2.9 (1.2 – 5.7) for etanercept, 6.4 (1.8 – 16.5) for infliximab, 6.5 (2.1 – 15.3) for golimumab and 9.2 (1.9 – 26.8) for certolizumab. The incidence rate ratio between adalimumab and etanercept was statistically significant (IRR=2.76 (1.10 – 7.52), p=0.02).

Conclusion: Our results identify an overall prevalence of 3.0% for PSE, with a prevalence of 5.1% in SpA, closely matching the prevalence previously reported in IBD. Our results suggest a higher prevalence of PSE in SpA compared to RA. Predisposition to psoriasis in SpA or cutaneous psoriasis appearing after diagnosis of PsA are likely explanations for these results. The use of the decoy receptor, etanercept, compared to monoclonal antibodies was an important protective factor, explained in part by its lesser use in the SpA group. 1. Xie W, Xiao S, Huang H, Zhang Z. Incidence of and Risk Factors for Paradoxical Psoriasis or Psoriasiform Lesions in Inflammatory Bowel Disease Patients Receiving Anti-TNF Therapy: Systematic Review With Meta-Analysis. *Front Immunol*. 2022;13:847160.

Disclosure: A. Minier: None; **G. Boire**: Eli Lilly, 1, Janssen, 6, Organon, 1, Orimed Pharma, 1, 6, Otsuka, 1, Pfizer, 1, 5, Sandoz, 1, Teva, 1, Viatris, 1, 6; **S. ROUX**: Amgen, 6, Kyowa kirin, 12, Journal Club, Novartis, 6; **N. Carrier**: None; **H. Allard-Chamard**: AbbVie/Abbott, 1, 5, 6, Amgen, 1, 6, AstraZeneca, 1, 6, Bristol-Myers Squibb(BMS), 1, 5, 6, Celltrion, 1, 6, Eli Lilly, 1, 5, 6, Fresenius Kabi, 5, 6, GlaxoSmithKlein(GSK), 1, Hoffmann-La Roche, 1, 6, Janssen, 1, 6, Mantra Pharma, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Sanofi, 5, Sobi, 6, Viela Bio, 5, Xencor, 5.

Abstract Number: 1081

Clinical Consequences of Infliximab Immunogenicity and the Impact of Proactive Therapeutic Drug Monitoring: Secondary Analyses of a Randomised Clinical Trial

Marthe Brun[1], Kristin Hammersbøen Bjørlykke[2], Johanna E. Gehin[3], David John Warren[3], Rolf A. Klaasen[3], Joseph Sexton[1], Øystein Sandanger[4], Tore Kvien[1], Cato Mørk[5], Jørgen Jahnsen[2], Nils Bolstad[3], Kristin Kaasen Jørgensen[2], Espen Haavardsholm[1], Guro Goll[1] and Silje Watterdal Syversen[1], [1]Center for Treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway, [2]Department of Gastroenterology, Akershus University Hospital, Oslo, Norway, [3]Dept. of Medical Biochemistry, Oslo University Hospital, Oslo, Norway, [4]Section of Dermatology, Oslo University Hospital, Oslo, Norway, [5]Akershus Dermatology Center, Lørenskog, Norway

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Formation of anti-drug antibodies (ADAb) to biological drugs is a clinical problem. Proactive therapeutic drug monitoring (TDM) allows for timely detection of ADAb and may reduce the negative clinical consequences. The aim of the study was to explore the relation between ADAb and treatment outcomes and adverse events, and to assess the impact of proactive TDM.

Methods: Patients (n=615) with spondyloarthritis (n=181), rheumatoid arthritis (n=120), psoriatic arthritis (n=72), ulcerative colitis (n=114), Crohns disease (n=83) and psoriasis (n=45) on infliximab therapy were included in the Norwegian Drug Monitoring (NOR-DRUM) trials[1,2] and randomised to TDM or standard infliximab therapy. Patients were followed for 30/52 weeks in the NOR-DRUM A (induction therapy) and NOR-DRUM B (maintenance therapy) trials, respectively. Neutralising ADAb were assessed with a drug-sensitive assay at each infusion. The outcomes of this study were: remission 30 weeks after initiation of infliximab, having a disease worsening during 52 weeks of maintenance therapy, having an infusion reaction and infliximab treatment discontinuation. Regression and Kaplan-Meier survival analyses were used to assess the association between ADAb and the outcomes, and the impact of proactive TDM. Remission and disease worsening were defined by disease specific composite scores[1,2].

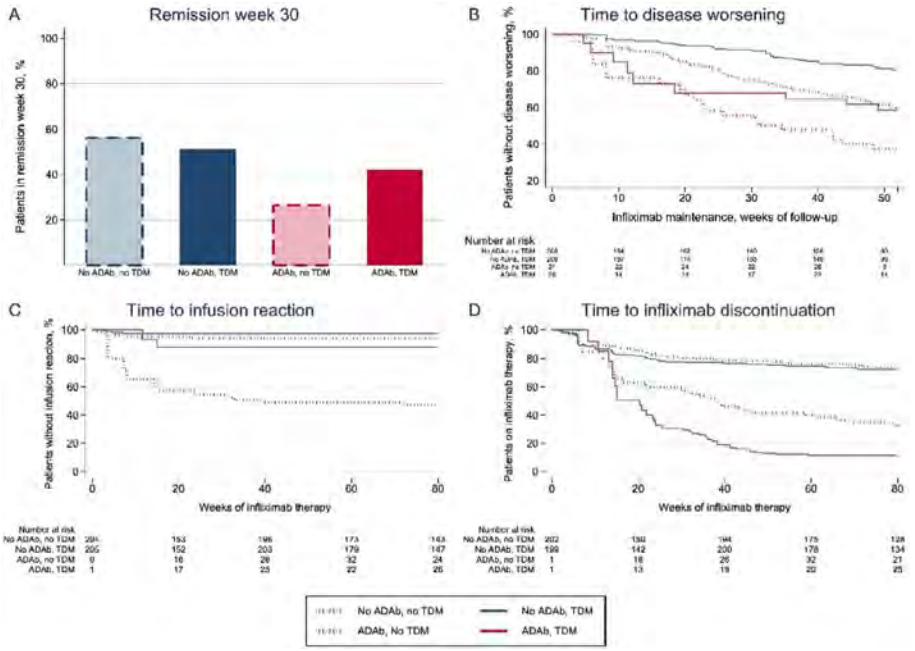
Results: ADAb were detected in 147/615 (24 %) patients. A lower proportion with ADAb achieved remission at week 30 (odds ratio (OR) 0.4, 95 % confidence interval (CI) 0.2-0.7, P< 0.01) (Table, Figure 1A) compared to ADAb negative. The risk of having a disease worsening was increased in ADAb positive (hazard ratio (HR) 2.0, CI 1.3-3.7, P< 0.01) (Table, Figure 1B) or an infusion reaction (HR 17, CI 7-41, P< 0.001) (Table, Figure 1C) was increased in patients with ADAb as compared to ADAb negative. The risk of infliximab treatment discontinuation was increased in ADAb positive patients (HR 6.6, CI 4.8-9.1, P< 0.001) (Table, Figure 1D). Patients developing ADAb in the TDM group had lower risk of having a disease worsening (HR 0.4, CI 0.3-0.6, P< 0.001) or an infusion reaction (HR 0.3, CI 0.1-0.7, P< 0.01) compared to patients with ADAb in the standard therapy group (Table, Figure 1B and C). Patients with ADAb discontinued infliximab treatment more often in the TDM group than in the control group (HR 1.4, CI 1.0-1.8, P=0.04) (Table, Figure 1D).

Conclusion: Formation of ADAb led to poorer clinical outcomes during infliximab treatment and increased the risk of infusion reactions. Early detection of ADAb by proactive TDM reduced the negative consequences of ADAb, both on infliximab effectiveness and safety. Our results highlight the role of proactive TDM in optimising TNFi therapy.

Table. Treatment and safety outcomes related to ADAb formation and TDM

Outcome: Remission week 30	**OR (CI)**	**P**
ADAb	0.4 (0.2-0.7)	<0.001
TDM	1.0 (0.7-1.5)	0.9
Outcome: Disease worsening	**HR (CI)**	**P**
ADAb	2.0 (1.3,3.1)	<0.01
TDM	0.4 (0.3-0.6)	<0.001
Outcome: Infusion reaction	**HR (CI)**	**P**
ADAb	17 (CI 7.0-41)	<0.001
TDM	0.3 (0.1-0.7)	<0.01
Outcome: Treatment discontinuation	**HR (CI)**	**P**
ADAb	6.6 (4.8-9.1)	<0.001
TDM	1.4 (1.0-1.8)	0.04

Results from multivariable logistic- or cox regression models including the covariates: ADAb, TDM, age, sex, diagnosis, comedication. Only results for ADAb and TDM are shown.
ADAb=Anti-drug antibodies; TDM=therapeutic drug monitoring



References

1. Syversen SW et al. JAMA 2021;326(23)
2. Syversen SW et al. JAMA 2021;325(17)

Disclosure: M. Brun: None; **K. Bjørlykke**: Janssen-Cilag, 6; **J. Gehin**: None; **D. Warren**: None; **R. Klaasen**: None; **J. Sexton**: None; **Ø. Sandanger**: None; **T. Kvien**: AbbVie/Abbott, 1, 2, 6, Bristol-Myers Squibb(BMS), 5, Galapagos, 2, 5, Gilead, 2, grunenthal, 6, Janssen, 2, 6, Novartis, 5, Pfizer, 2, 5, sandoz, 2, 6, UCB, 2, 5, 6; **C. Mørk**: None; **J. Jahnsen**: AbbVie/Abbott, 1, 6, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 1, 6, Galapagos, 1, 6, Gilead, 1, 6, Janssen, 1, 6, Pfizer, 1, 6, Roche, 1, 6, Sandoz, 1, 6, Takeda, 1, 6; **N. Bolstad**: None; **K. Jørgensen**: Bristol-Myers Squibb(BMS), 6, Roche, 6; **E. Haavardsholm**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Eli Lilly, 2, Gilead, 2, Pfizer, 6, UCB, 6; **G. Goll**: AbbVie/Abbott, 1, 6, Galapagos, 1, 6, Novartis, 6, Pfizer, 1, Union Chimique Belge, 1, 6; **S. Syversen**: AstraZeneca, 1.

Abstract Number: 1082

Reducing No-shows and Late Cancellations at an Academic Medical Center Subspecialty Clinic

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patient no-shows and late cancellations, defined as less than 24 hours from the visit, reduce operational efficiency, revenue generation, and lead to negative clinical outcomes. There has been an increasing trend in no-show and late cancellation rates at the University of Cincinnati Hoxworth rheumatology clinic. For fiscal year 2021, monthly rates ranged from 6.2-32.7%. Since each unused slot is not reimbursable, this has resulted in a negative financial impact. When extrapolated to all of Internal Medicine, this has led to a $2 million revenue loss. Previously, reminders for visits involved automated calls and mailing letters. Using Vizient clinical database to identify performance gaps, our smart aim was to integrate phone call reminders to decrease median benchmark for no-shows and late cancellation rates from 18.47% to 14.6% from October 31, 2022 to February 1, 2023.

Methods: The 1st Plan-Do-Study-Act (PDSA) involved identifying the optimal lead time to call and was from October 31, 2022 to December 31, 2022. The 2nd aimed to refine phone call and messaging scripts and was from January 1 to February 1, 2023. Patients were called from 1 to 6 days prior to the visit. Alternate numbers or patient portals were used if they could not be reached. Conversations and barriers were documented in the medical record. To assess for common and special cause variations, baseline rates were plotted on a run chart starting from November 22, 2021 to April 14, 2023 (Figure 1).

Results: Monthly attendance ranged from 64.3-96.3% from October 31, 2022 to February 1, 2023 (N=11-30 patients per visit). The lowest rates were during Thanksgiving at 72.7% (N=22) and Christmas at 64.3% (N=14). Data for Thanksgiving and Christmas for 2021 were similarly low with median attendance of 74.55% (N=33-66). When excluding these holidays, the median rate was above the set benchmark of 85%. We concluded that low rates during holidays are special cause variations and can show positive shift if project is of a longer duration. After the project ended on February 1, 2023, rates dropped again below the benchmark to median of 80.6%. During PDSA #1 the optimal time to call was 5 to 6 days prior allowing for identification of barriers, some of which included transportation or work obligations. If barriers could not be resolved, patients on wait lists filled the open slots. During PDSA #2, late cancellations became increasingly higher than no-shows since they were unaware of the policy. There was a positive trend in attendance once scripts were refined to explicitly inform all patients of the policy. Also, phone calls were more effective than mailed letters or patient portal messaging due to the lead time and ability to identify barriers.

Conclusion: Monthly attendance ranged from 64.3-96.3% from October 31, 2022 to February 1, 2023. When excluding no-shows and late cancellations during Thanksgiving and Christmas, the median attendance rate was above the set benchmark of 85%. Low rates during holidays are special cause variations and can show positive shift if the next phase of the

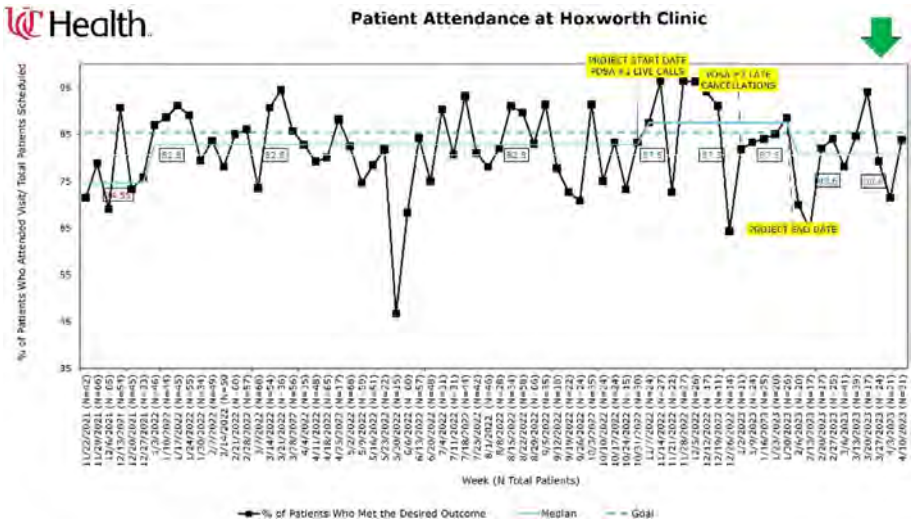


Figure 1. Monthly Attendance Rates Run Chart

project is longer. The optimal time to call is 5 to 6 days prior and are opportunities to identify barriers and to fill open slots. There was a positive trend once scripts included explanation of the policy.

Disclosure: N. Jackson: None; **M. James**: None; **K. Nguyen**: None; **P. Vashisht**: None; **A. Ware**: None.

Abstract Number: 1083

A Patient-Centered Approach to Increase Herpes Zoster Vaccination in Patients on Janus Kinase Inhibitors: A Fellowship Quality Improvement Initiative

Rachel Dayno[1], Sarah Capponi[2], Stephanie Song[3], Sarah Bayefsky[4], Thomas Riley[5], Marta Bean[1], John Oghene[3], Jonathan Kotzin[1], Ellen Romich[6], Paula Breslin-Perry[1], Nora Sandorfi[1], Preethi Thomas[7] and Michael George[1], [1]University of Pennsylvania, Philadelphia, PA, [2]Hospital of the University of Pennsylvania, New Hope, PA, [3]Hospital of the University of Pennsylvania, Philadelphia, PA, [4]University of Pennsylvania/Children's Hospital of Philadelphia, Philadelphia, PA, [5]Hopsital of the University of Pennsylvania, Springfield, PA, [6]Hospital of the University of Pennsylvania, Media, PA, [7]University of Pennsylvania, Conshohocken, PA

SESSION INFORMATION

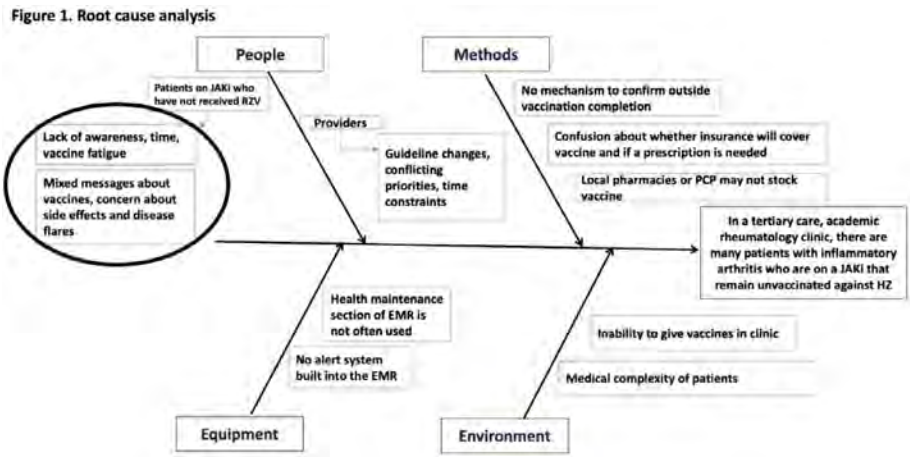
Session Date: Monday, November 13, 2023

Session Title: Measures & Measurement of Healthcare Quality Poster I

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: People with systemic rheumatologic diseases are more susceptible to herpes zoster (HZ) infection and its complications due to their underlying diseases and the medications used to treat them. Janus kinase inhibitors (JAKi) confer a substantial risk for HZ, resulting in morbidity and cost to the healthcare system. The Division of Rheumatology at the study site recognized the rate of recombinant zoster vaccine (RZV) uptake among people receiving JAKi was unacceptably low. The goal of this quality improvement study was to increase the number of RZV prescriptions written for patients on JAKi via a streamlined patient outreach campaign.



A fishbone diagram was created to assist in performing a root cause analysis of the low rate of recombinant zoster vaccine (RZV) uptake in patients on janus kinase inhibitors (JAKi). This figure depicts the several barriers to vaccination, including the barriers targeted in this quality improvement study (circled).

Methods: In September 2022, patients in a tertiary care, academic rheumatology clinic with inflammatory arthritis and a current prescription for a JAKi were identified using a query of the electronic medical record (EMR). A process map and root cause analysis were created to understand why there was a low rate of RZV uptake. Lack of awareness and vaccine fatigue were the main barriers identified (Figure 1). On January 10, 2023, a customized EMR message or letter was sent to the identified patients outlining the importance of RZV, including efficacy and safety, and requesting a reply from those interested in a prescription for RZV (Figure 2). A standardized nursing protocol was used to process responses. The outcome measure was the percentage of patients who received a RZV prescription by April 10, 2023 (goal >10%, starting from 5%).

Results: There were 194 patients identified as being on a JAKi for inflammatory arthritis. Seventy-five (39%) had documentation of RZV, and 119 (61%) did not have documentation of RZV. A message was sent via the EMR to 113 patients and via mailed letter to 6 patients without EMR access. Thirteen of 119 patients (11%) responded with a request for RZV vaccination and received a prescription for RZV between January 10, 2023 and April 10, 2023, which met the outcome measure. A total of 90 patients (46%) had documentation of RZV following the intervention (Figure 3). Fifty-one patients (43%) had a rheumatology follow-up appointment by April 9, 2023. Three patients expressed vaccine hesitancy when discussed with the provider at their appointment. One patient was concerned about side effects of RZV. Twenty-two patients (18%) had a recommendation for RZV documented in follow-up clinic notes.

Conclusion: Utilizing a targeted EMR message is a low-cost intervention that helps address barriers to recombinant zoster vaccination in patients on janus kinase inhibitors without increasing provider burden. This intervention helps empower patients who are motivated to improve their health, allowing vaccination between clinic visits or prompting discussions with providers at subsequent visits. These results will inform a broader multi-modality, patient- and provider-facing program to increase vaccination rates at the study institution, including offering in-clinic vaccinations.

Figure 2. Quality improvement study profile

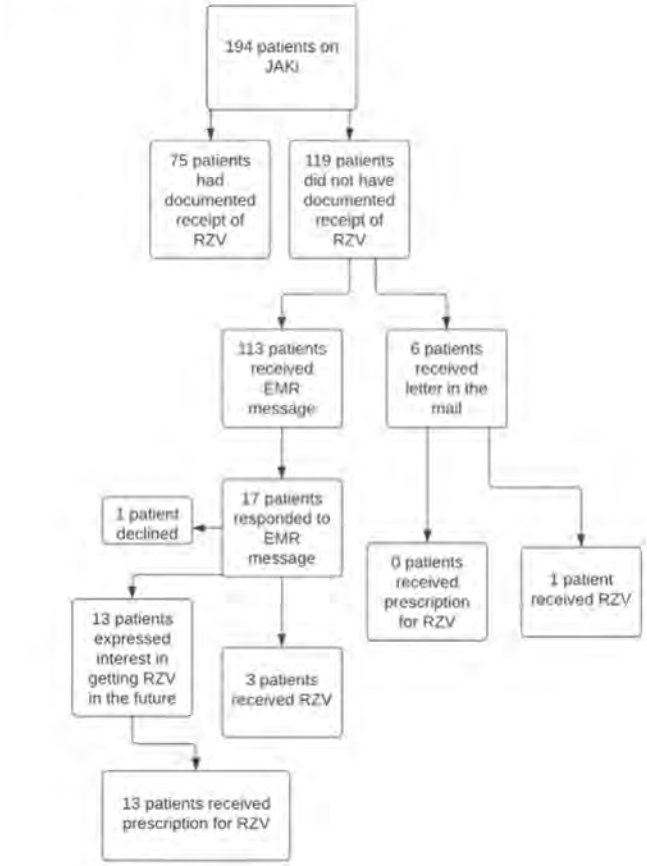
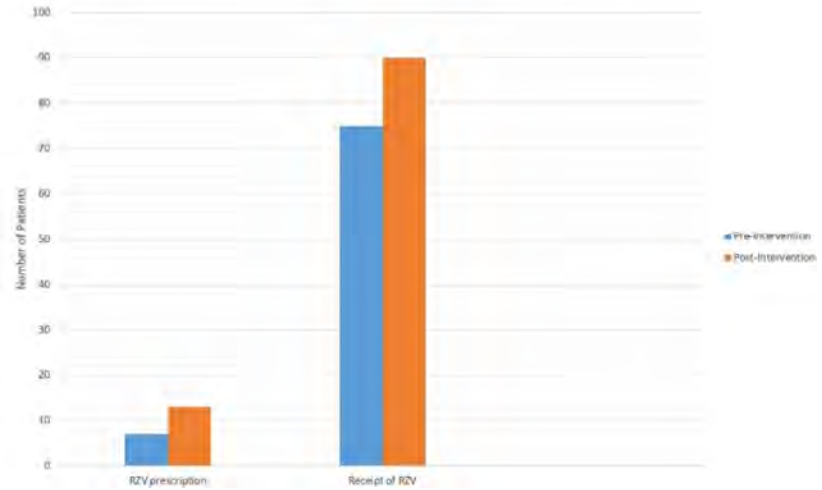


Figure 3. Recombinant Zoster Vaccine (RZV) both pre and post intervention



This figure shows the increase in number of patients who received RZV after the intervention (receipt of RZV). Not every patient who received RZV was given a prescription.

Disclosure: R. Dayno: None; **S. Capponi**: None; **S. Song**: None; **S. Bayefsky**: None; **T. Riley**: None; **M. Bean**: None; **J. Oghene**: None; **J. Kotzin**: None; **E. Romich**: None; **P. Breslin-Perry**: None; **N. Sandorfi**: None; **P. Thomas**: None; **M. George**: AbbVie/Abbott, 2, GlaxoSmithKlein(GSK), 5, Janssen, 5.

Abstract Number: 1084

Identifying and Addressing Disparities in Health Literacy in Patients with Rheumatic Diseases Through Point of Care Distribution of Patient Education Materials

Kelly Corbitt[1], Abhimanyu Amarnani[2], Jammie Law[3], Cristina Sorrento[3], Nicole Leung[4], Catherine Howe[3], Tasneem Ahmed[3], Meghan Anderson[3] and Sara Stream[3], [1]New York University, El Portal, FL, [2]NYU Langone Medical Center, New York, NY, [3]New York University, New York, NY, [4]New York University Langone Hospital, New York, NY

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Improving health literacy in patients with rheumatic diseases is important as many have chronic, complex diagnoses treated with high-risk medications. Poor health literacy may be due to education level, language barriers, socioeconomic status, and/or inadequate access to health education material. Many of these factors are non-modifiable, putting patients at risk for healthcare disparity. We aimed to create a quality improvement initiative to (1) better characterize those with poor health literacy and (2) improve their diagnosis and medication understanding via physician provided education material.

Methods: Patients from three distinct healthcare systems in New York City (Bellevue, NYU, the VA; Table 1) with documented rheumatologic diagnoses were administered health literacy surveys during rheumatology clinic visits from September 2022 to May 2023. A baseline survey assessed the patient's ability to identify their diagnosis and medication

from a list of options, as well as self-reported level of health literacy, desire for more printed education material, primary language, and education level. Printed patient education materials, in English or Spanish, were provided in real-time with counseling on knowledge gaps. Repeat surveys are being administered at follow-up visits to assess the effectiveness of education materials. Those completed during the study period are included for preliminary analysis.

Results: 116 patients completed the baseline survey. There were fewer native English speakers and fewer patients with higher education at Bellevue. Overall, 20% of patients incorrectly selected their diagnosis and medication from the provided list. While incorrect diagnosis selection did not vary by site, incorrect medication selection differed with 5% incorrect at the VA, 14.7% at NYU, and 27.6% at Bellevue (Table 1). Across sites, medication literacy significantly differed by education level and primary language (Table 2). 38.9% of all patients reported being unsure about holding medication during infection. On average, patients from all sites self-rated their health literacy at least a 4, on a 1-5 scale (higher=better). At baseline, 54.5%

Table 1: Comparisons amongst three diverse healthcare systems in New York City. Bellevue is a public service teaching hospital. The VA is a government run hospital serving veterans and their families. New York University (NYU) Hospital is a private, not-for profit, teaching hospital. All values are represented as n (%). N is specified where it differs from the overall sample. All p-values represent chi-square analyses. For perceived level of diagnosis and medication understanding, chi-square testing compared response levels 1-3, 4, vs, 5 to ensure statistical testing validity where all expected values are greater than 1.0 and at least 20% of the expected values are greater than 5.

	Bellevue n=60	Veterans Affairs (VA) Hospital n=22	NYU n=34	p-value (Bellevue v. VA)	p-value (Bellevue v. NYU)	p-value (VA v. NYU)
Wrong Diagnosis	11 (18.3)	4 (18.2)	8 (23.5)	1	0.55	0.63
Wrong Medication	16 (26.7)	1 (5) n=20	5 (14.7)	0.03	0.14	0.27
Native English Speaker	26 (43.3)	21 (95.5)	26 (81.3) n=32	<0.001	<0.001	0.13
Any higher education	19 (35.2) n=54	17 (85) n=20	19 (59.4) n=32	<0.001	0.03	0.05
Self-reported level of diagnosis understanding (mean)	4.0 n=55	4.0 n=20	4.3 n=33	0.76	0.01	0.22
Self-reported level of medication understanding (mean)	4.2 n=55	4.2 n=21	4.4 n=33	0.68	0.1	0.63
Wants more diagnosis education material	39 (69.6) n=56	8 (38.1) n=21	13 (39.4) n=33	0.02	0.004	0.88
Wants more medication education material	43 (76.8) n=56	9 (47.4) n=19	14 (43.8) n=32	0.008	<0.001	0.68

Table 2. Results of correct medication result, organized by language and education level. All statistics Chi-square analyses.

		Correct, n (%)		Incorrect, n (%)	Significance (p)
Total	N	Count (%)	N	Count (%)	
English – Primary Language	74		15		<0.05
Yes		53 (71.6)		9 (60)	
No		21 (28.4)		6 (40)	
Education – Greater than HS	79		26		<0.01
Yes		33 (41.8)		3 (11.5)	
No		46 (58.2)		23 (88.5)	

wanted more diagnosis education and 61.7% wanted more medication education; percentages were significantly higher among patients at Bellevue than other sites (Table 1). Of those who completed the repeat survey (n=27), 74.1% found the diagnosis education materials helpful and 63% found the medication education materials helpful. Those with higher education found these more helpful overall.

Conclusion: There is a discrepancy between perceived and actual health literacy in patients with rheumatic diseases, as there were notable knowledge gaps in the survey results and uncertainty about medication use during infection, despite reports of adequate understanding. This highlights the importance of providing consistent education to all patients. Medication literacy may be a particular area for improvement, as this varied by factors that engender healthcare disparity, including lower education level and primary language. The optimal way to improve patient literacy in varied settings is an important topic for future study.

Disclosure: K. Corbitt: None; **A. Amarnani**: None; **J. Law**: None; **C. Sorrento**: None; **N. Leung**: None; **C. Howe**: None; **T. Ahmed**: None; **M. Anderson**: None; **S. Stream**: None.

Abstract Number: 1085

Utilizing a Maintenance of Certification (MOC) Part 4 Quality Improvement Project to Improve Data Completeness in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry

Hemalatha Srinivasalu[1], anne dennos[2], alan Russell[3], Mary Beth Son[4] and Mara Becker[2], [1]Children's National Hospital, Washington, DC, [2]Duke University, Durham, NC, [3]Duke Clinical Research Institute, Duke, NC, [4]Division of Immunology, Boston Children's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Minimizing missing data in research registries is a universal challenge. Enrolling patients into a research registry with poor data quality is wasteful and potentially unethical, as it incurs risks and cost with minimal to no benefit. Data quality is a central focus for the CARRA Registry, and we aimed to improve data completion rates for the Registry's critical variables using quality improvement (QI) methodology and obtained approval for a large group MOC Part 4 QI project through the American Board of Pediatrics to obtain credit for maintenance of board certification.

Methods: The *CARRA Registry Critical Variable MOC 4 Improvement Project* is designed to improve data completion rates for critical variables in the CARRA Registry that are required to calculate disease activity outcomes in JIA (Physician Global and Patient/Parent Global scores) and SLE (Calculable SLEDAI Score and SLE Physician & Patient/Parent Global scores). The goal is to close the gap in data completion by 50% over a 12-month period (9/1/2022-8/31/2023).Participation in each project earns 25 MOC part 4 points. Outcome Measures are data completion rates at the Registry level; Process Measures are data completion rates at the site level in addition to completion rates of monthly site engagement surveys where site-specific Plan-Do-Study-Act (PDSA) cycles are documented. At the Registry level, two PDSA cycles were completed thus far: 1) development of site-specific critical variable reports with graphs to illustrate change over time and 2) initiation of monthly office hours/Q&A sessions. Participation is voluntary and each site can choose to participate in one or both projects. The final analysis will include run charts for each sub-project to display improvement over time, and data reflecting overall improvement will be analyzed by chi-square analysis. Data reported herein is an interim analysis as of May 2023.

Figure 1: Key Driver Diagram depicting the drivers and the site-specific interventions

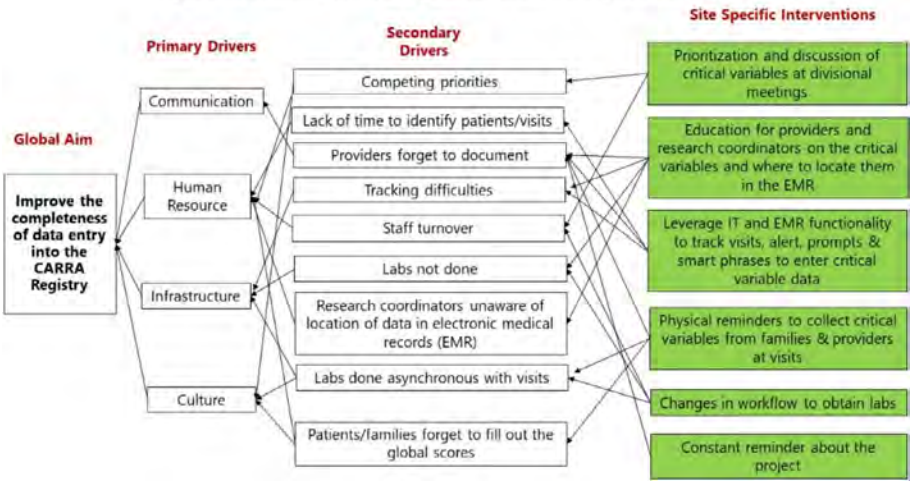


Figure 2A-2E: Run charts showing the trend in the completion rates of the critical variables from September 2022 to May 2023.

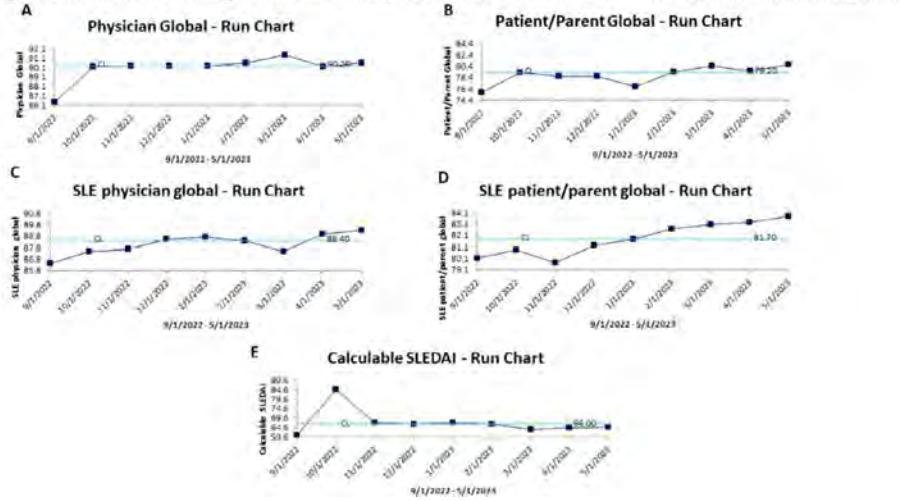


Table 1: Overall critical variable completion rates

Critical Variable	Baseline completion rate (Prior to Sep 2022) %	Interim completion rate (As of May 2023) %
Physician Global	86.4	90.5
Patient/Parent Global	75.7	80.7
SLE Physician Global	86.4	89.3
SLE Patient/Parent Global	80.1	83.7
Calculable SLEDAI	60.5	64.7

Results: Out of 71 active CARRA Registry sites, 42 (59%) are participating. Baseline completion rates were calculated from approximately 38,000 visits across participating sites. There have been 5,067 follow up visits entered into the Registry (13% of total) since MOC project initiation. Key drivers and examples of site-specific PDSA interventions are indicated in **Fig 1**. Interim run charts for each critical variable show a trend towards improvement (**Fig 2A-2E**). Averaged critical variable completion rates at baseline and May 2023 are noted in **Table 1.**

Conclusion: Interim analysis reveals a trend towards improvement in completion rates of all targeted critical variables, but the rate of improvement is slower than originally anticipated. This is likely due to the limited cross-section of new visits occurring during the 8-month project period compared to the aggregated visits accumulated from Registry inception to September 2022. As sites accrue additional follow-up visits, and continue to trial site specific interventions, we hope to observe sustained improvement in critical variable completion rates within the CARRA Registry.

Disclosure: H. Srinivasalu: None; **a. dennos**: None; **a. Russell**: None; **M. Son**: None; **M. Becker**: None.

Abstract Number: 1086

Increase Shingrix Vaccination Rate in Patients on JAK Inhibitors: A Quality Improvement Project at the Rheumatology Practice of an Urban Institution

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The 2022 ACR guidelines for vaccination strongly recommend recombinant VZV vaccination for all patients > 18 years old who are taking immunosuppressive medication. Studies have shown that there is a higher risk of shingles in patients on JAK inhibitors. To assess the Shingrix vaccination rate at the rheumatology outpatient practice of an urban academic institution and improve adherence, we initiated a quality improvement project in patients who are on JAK inhibitors.

Methods: The primary aim of our QI project was to increase the Shingrix vaccination rate by 10%. We also attempted to identify the risk factors for eligible patients not receiving Shingrix despite guideline recommendations. We acquired data quarterly from electronic health records, including patients' MRN, age, sex, race, Shingrix vaccination status, and last visit dates. Vaccination status was further validated with manual chart review. Data obtained from 4/1/2022 to 6/30/2022 were considered the baseline. We implemented interventions via Plan-Do-Study-Act (PDSA) method: 1) provide posters at clinics to improve awareness, 2) remind eligible patients during the encounter 3) notify patients' primary rheumatologists quarterly. Data were obtained from 9/1/2022-11/30/2022 and 12/1/2022-2/28/2023 respectively. We used descriptive statistics and analyzed the data via Stata/SE 17.0, stratified by Shingrix vaccination status. We also studied the trend of the Shingrix vaccination rate.

Results: From 4/1/2022 to 2/28/2023, the Shingrix vaccination rate raised from 22.22% (14/63) to 39.19% (29/74) after two cycles of PDSA, meeting our goal of a 10% increase. (Figure 1) After PDSA #1 in 9/2022, the overall vaccination rate slightly declined to 19.67%. After PDSA #2 in 12/2022, it significantly improved. Among all the patients (N = 198) seen from

4/1/2022 - 2/28/2023, 55.56% (110) of them were ≥ 50 years old while 44.44% (88) were < 50 years old. 14.14% (28) were male, while 85.86% (170) were female. 41.41% (82) of the patients were Caucasian, 10.61% (21) were African American, and 9.09% (18) of the patients identified as AAPI.

Patients ≥ 50 years old had higher vaccination rate than patients < 50 years old. (Figure 1) From 4/1/2022 to 2/28/2023, patients ≥ 50 years old had a significant increase in vaccination rate from 29.73% to 56.41%. Male and female patients had similar vaccination rates, with 41.67% male and 38.71% female vaccinated. Despite the improvement in the 12/2022 – 2/2023 period, patients who identified as African American had a lower vaccination rate than their Caucasian counterparts. 25% (2/8) African American patients were vaccinated compared to 46.97% (15/32) Caucasian patients. (Figure 2)

Conclusion: Our interventions improved the Shingrix vaccination rate. Congress's new bill eliminating the cost of vaccines covered by Medicare Part D may have also played a role. Besides achieving our goal of a 10% increase, we identified the risk factors for lower vaccination rates: patients < 50 years old and African American patients. As the PDSA cycle continues, targeted interventions will be implemented to address disparities and improve adherence to Shingrix vaccination.

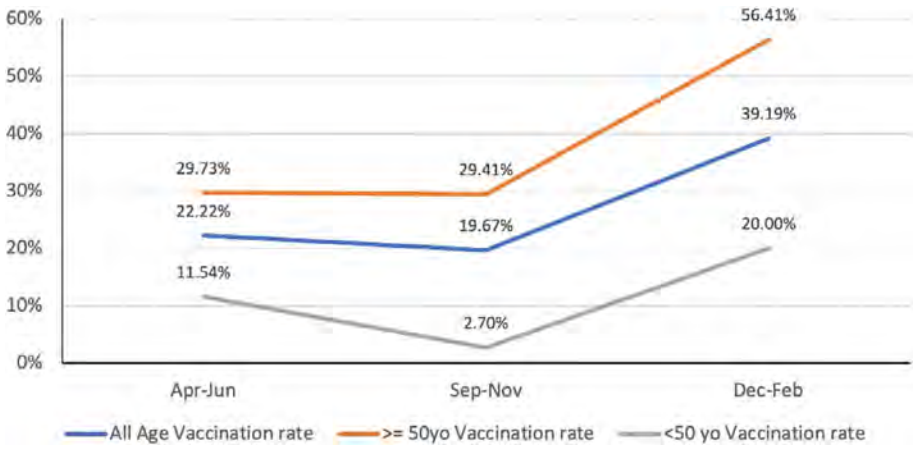

Figure 1. The trend of Shingrix vaccination rate stratified by age

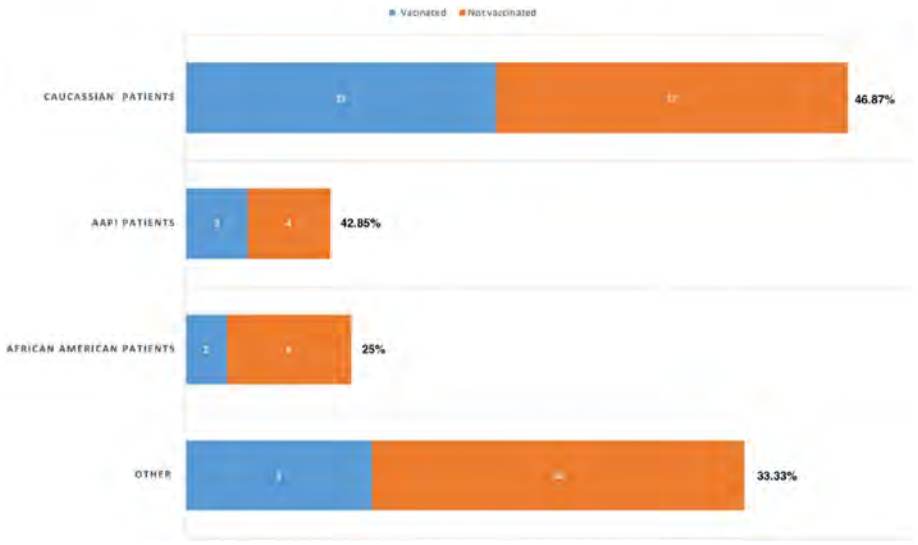

Figure 2. Shingrix vaccination rates by race/ethnicity in PDSA #2 (12/2022 - 2/2023)

Disclosure: J. Feng: None; **K. Koci**: None.

Abstract Number: 1087

Characterizing Herpes Zoster Vaccination Patterns in Rheumatoid Arthritis Patients in a Tertiary Care Clinic: A Quality Improvement Approach

Sara Faghihi-Kashani, Arooj Babar and Janice Lin, Stanford University, Palo Alto, CA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) face an increased risk of herpes zoster (HZ) infection, notably those on immunosuppressive therapy. Herpes zoster infection is associated with comorbidities and a significant economic burden. The American College of Rheumatology recommends the recombinant herpes zoster vaccine for all immunocompromised adults above 18. We aimed to assess the current state of herpes zoster vaccination rates among RA patients at the Stanford Rheumatology Clinic and identify barriers to vaccination.

Methods: We retrospectively collected data from 1,449 consecutive RA patients seen at the Stanford Rheumatology Clinic from October 2017 to October 2022. We reviewed electronic medical records (EMR) to determine patients' characteristics and HZ vaccination status. We categorized medication history based on ever being prescribed; 1) Janus Kinase inhibitor (JAKi), 2) biologic DMARDs (bDMARD), including anti-TNF, anti-IL6, anti-IL1, and anti-CD20, 3) conventional synthetic DMARDs (csDMARD) and 4) Hydroxychloroquine. We surveyed 19 current physicians (attendings and fellows) in the Rheumatology clinic to evaluate their practice patterns on vaccine discussions.

Results: Seventeen providers responded to the physician survey. We found that 61% "sometimes" discuss HZ vaccination with their RA patients, and 46% depend on primary care providers for vaccine discussions. Figure 1 shows the physician-reported HZ vaccination discussion rate based on the medication group. Our RA patient population were mostly female (82%) and 50 years old or older (71%). Among the 1,449 RA patients, only 547 (37.7%) have had HZ vaccination. Among

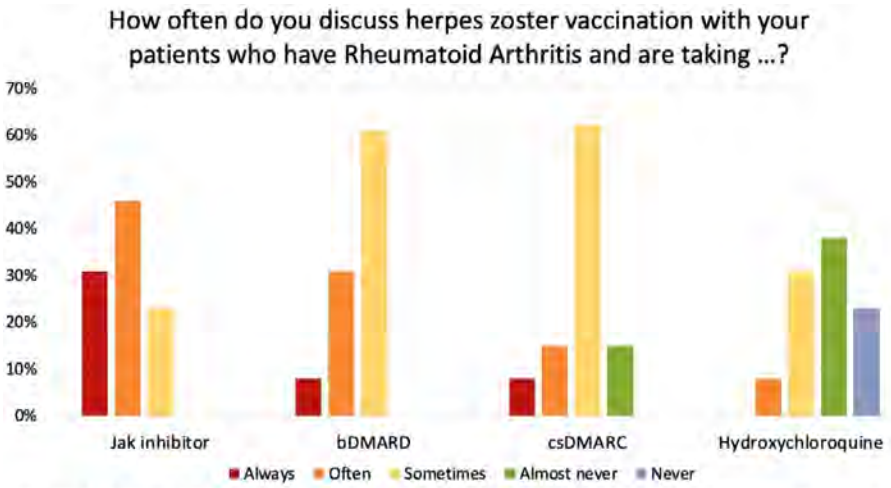

Figure 1. Frequency of herpes zoster vaccination discussion reported by physicians (n=17)

Figure 2. Shingrix vaccination rates by race/ethnicity in PDSA #2 (12/2022 - 2/2023)

those aged below 50 years, only 23 (5.5%) were vaccinated. Among the 178 patients who had ever been prescribed a JAKi, only 79 (44.4%) had the HZ vaccine, and most (90%) were aged 50 years or older (Table 1). The rate of Herpes Zoster vaccination was statistically different based on gender, ethnicity, primary language (English, Spanish, other), insurance type (Medicare, MediCal, Other/Commercial), PCP type (internal, external), and history of Herpes Zoster infection. We did not observe a statistically significant association between vaccination rate and specific immunosuppressive medication.

Conclusion: We identified a suboptimal herpes zoster vaccination rate among RA patients in our clinic, particularly those younger than 50 years on immunosuppressive therapy, including JAKi. We initiated an intervention to improve vaccine awareness by having the medical assistants inquire about the patient's herpes zoster vaccine history during the clinic pre-calls. Patients were also encouraged to have further discussions with their rheumatologists. In addition to promoting patient education and physician awareness, potential future strategies to improve the vaccination rate include fostering collaboration with primary care providers, engaging with pharmacies on campus to make the HZ vaccine readily accessible, and developing automatic reminders in the electronic medical system. Additional efforts, e.g., overcoming insurance barriers, may be needed for at-risk patients younger than 50.

Table 1. Demographic of patients with rheumatoid arthritis based on herpes zoster vaccination status.

Table 1. Demographic of patients with rheumatoid arthritis based on herpes zoster vaccination status.

	Vaccinated (N = 547)	Unvaccinated (N = 902)	P-value	Total (N = 1449)
Age			<0.001	
Younger than 50	23 (4%)	396 (44%)		419 (29%)
50 years or older	524 (96%)	506 (56%)		1030 (71%)
Gender			0.001	
Female	426 (78%)	763 (85%)		1189 (82%)
Male	121 (22%)	139 (15%)		260 (18%)
Race			0.097	
White	291 (54%)	433 (49%)		724 (51%)
Black	12 (2%)	22 (3%)		34 (2%)
Asian	99 (18%)	147 (17%)		246 (17%)
Native Hawaiian	10 (2%)	9 (1%)		19 (2%)
Native American/Alaskan	4 (1%)	5 (1%)		9 (1%)
Other	125 (23%)	262 (29%)		387 (27%)
Ethnicity			0.004	
Hispanic	87 (16%)	194 (23%)		281 (20%)
Non-Hispanic	441 (84%)	650 (77%)		1091 (80%)
Language			0.006	
English	462 (85%)	802 (89%)		1264 (87%)
Spanish	30 (5%)	48 (5%)		78 (5%)
Other	55 (10%)	50 (6%)		105 (8%)
Insurance			0.003	
Medicare	76 (14%)	74 (8%)		150 (10%)
MediCal	9 (2%)	15 (2%)		24 (2%)
Other/Commercial	462 (84%)	813 (90%)		1275 (88%)
PCP type			<0.001	
Internal	272 (50%)	303 (35%)		575 (41%)
External	267 (49%)	566 (65%)		833 (59%)
History of herpes zoster infection			<0.001	
Yes	40 (7%)	29 (3%)		69 (5%)
No	507 (93%)	873 (97%)		1380 (95%)
Medications (ever prescribed)				
JAKi			0.051	
Yes	79 (14%)	99 (11%)		178 (12%)
No	468 (86%)	803 (89%)		1271 (88%)
bDMARD			0.056	
Yes	264 (48%)	482 (53%)		746 (52%)
No	283 (52%)	420 (47%)		703 (48%)
csDMARD			0.054	
Yes	455 (83%)	189 (21%)		1168 (81%)
No	92 (17%)	713 (79%)		281 (19%)
Hydroxychloroquine			0.601	
Yes	297 (54%)	477 (53%)		774 (53%)
No	250 (46%)	425 (47%)		675 (47%)

JAKi: Tofacitinib, Upadacitib, and Baricitinib. bDMARD: Infliximab, Adalimumab, Etanercept, Golimumab, Certolizumab, Tocilizumab, Anakinra, Abatacept, and Rituximab. csDMARD: Methotrexate, Azathioprine, Leflunomide, and Mycophenolate mofetil.

Disclosure: S. Faghihi-Kashani: None; **A. Babar**: None; **J. Lin**: None.

Abstract Number: 1088

Improving JIA Outcomes Assessments in a Large Pediatric Rheumatology Practice: A Fellow Quality Improvement Project

Anna Costello[1], Hallie Carol[1], Dori Abel[2], Sarah Bayefsky[3], Sarah Capponi[1], Adam Mayer[1], Julia Rood[1], Kirsten Spichiger[1], Joshua Madas[1], Lynsey Cecere[1], Megan Roman[1], Beth Rutstein[4] and Jon Burnham[2], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]Children's Hospital of Philadelphia, Philadelphia, PA, [3]University of Pennsylvania/ Children's Hospital of Philadelphia, Philadelphia, PA, [4]Division of Rheumatology at Children's Hospital of Philadelphia, Philadelphia, PA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Measures & Measurement of Healthcare Quality Poster I
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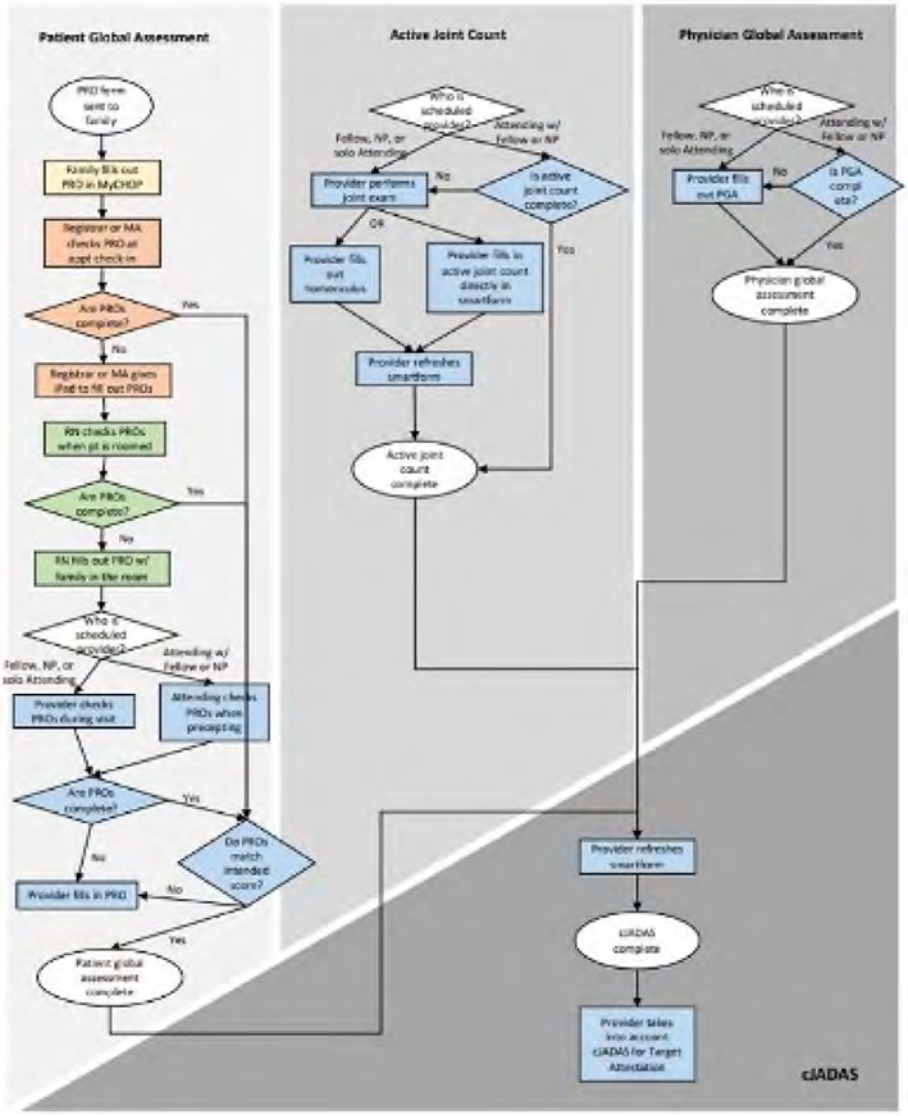
Background/Purpose: Juvenile idiopathic arthritis (JIA) is a chronic autoimmune disease that can result in long-term joint damage if inadequately treated. Collecting validated outcomes data at the point of care can facilitate a "Treat to Target" approach and allow for pre-visit planning and population management. The clinical Juvenile Arthritis Disease Activity Score (cJADAS) is a validated outcome measure that helps rheumatologists assess disease activity. It is a score that is calculated based on three inputs: provider global assessment of disease activity, patient/parent global assessment of wellbeing, and active joint count. We identified a baseline cJADAS completion rate of only 55% in our practice. Our goal was to increase the proportion of JIA visits with cJADAS completion from 55% to 70% by February 2023.

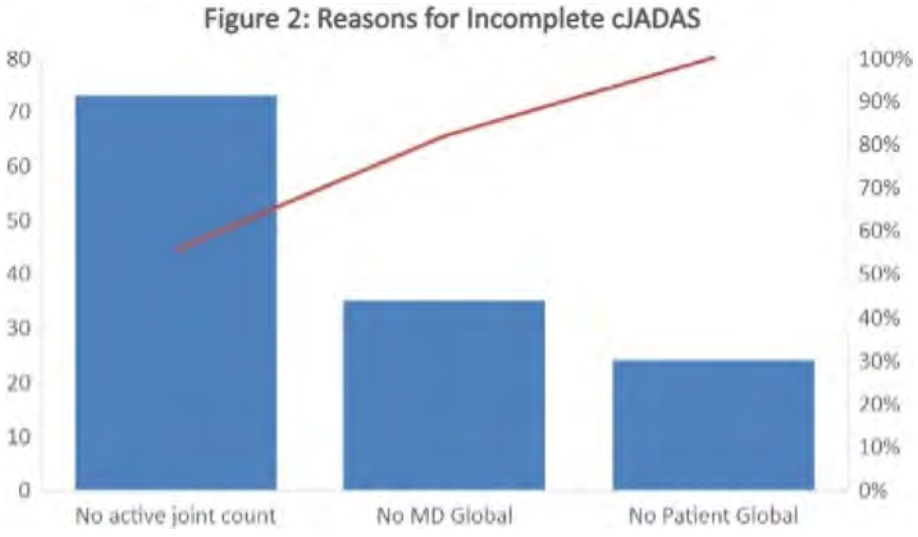
Methods: Through process mapping (Figure 1) and a Pareto analysis (Figure 2),we found that provider cJADAS components were the most common contributor to incomplete scores. Several technical elements within the electronic health record (EHR) were also noted to be limiting cJADAS completion. Through discussions with key divisional stakeholders, we identified methods to engage clinicians in the project, including education, data distribution (monthly reports), inclusion of cJADAS completion as ongoing professional practice evaluation metric, and incorporating the metric in providers' yearly incentive. Our process measure was the proportion of clinic visits with a visit-specific diagnostic code for JIA in which documentation of a cJADAS was completed.

Results: Beginning in September2022, we began educational interventions to promote cJADAS completion. The education included technical components required to complete the scores. Additionally, providers were informed that these outcome measures are critical for ongoing high-quality care and assessment of health disparities. Providers began receiving reports on monthly performance and were allowed to backfill cJADAS scores based on existing documentation. We noted a significant shift in the cJADAS metric beginning in August 2022 from a median of 56% to 79% that has been sustained through February 2023 (Figure 3).

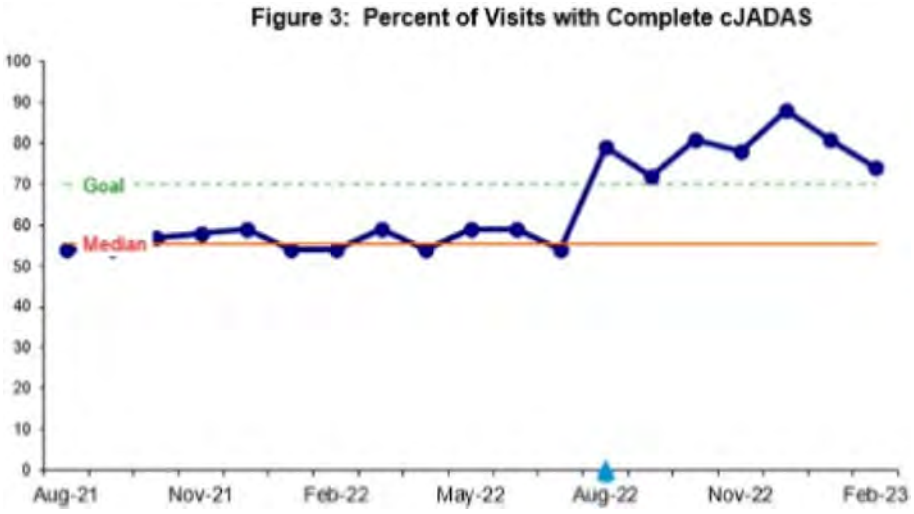
Conclusion: Utilization of multiple change management techniques led to a rapid increase in completion of the cJADASin our patients with JIA. Moving forward, we will continue to monitor the rate of cJADAS completion to assess the sustainability of these changes. We plan to operationalize the scheduling workflow to ensure that patients with elevated cJADAS values remain engaged in rheumatology care and hope that this may help mitigate health disparities.



Process mapping



Pareto analysis demonstrating reasons for incomplete cJDASA score



Run chart demonstrating percent of visits with completed cJADAS scores before and after interventions

Disclosure: A. Costello: None; **H. Carol**: None; **D. Abel**: None; **S. Bayefsky**: None; **S. Capponi**: None; **A. Mayer**: None; **J. Rood**: None; **K. Spichiger**: None; **J. Madas**: None; **L. Cecere**: None; **M. Roman**: None; **B. Rutstein**: None; **J. Burnham**: None.

Abstract Number: 1089

Improving Recombinant Zoster Vaccination Rates Among Immunosuppressed Veterans in an Academic Rheumatology Clinic

Nagendra Pokala[1], Benjamin Gardner[2], Avni Amratia[1], Daniel Emesiani[3], Jiby Mathew[4], Rashmi Arora[5], Una Makris[6] and Swathi Reddy[7], [1]Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, TX, [2]Department of Internal Medicine, Baylor University Medical Center, Dallas, TX, [3]Baylor Scott and White Medical Center McKinney, Dallas, TX, [4]VA North Texas Healthcare System, Dallas, TX, [5]Department of Internal Medicine, UT Southwestern Medical Center; VA North Texas Healthcare System, Dallas, TX, [6]UT Southwestern Medical Center and Dallas VA, Dallas, TX, [7]UT Southwestern Medical Center / Dallas VA Medical Center, Colleyville, TX

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Due in part to immunosuppressant medications, patients with rheumatic diseases not only carry a higher risk of herpes zoster reactivation but also worse outcomes. In July 2021 the FDA extended the indication for the recombinant zoster vaccine (Shingrix) to include immunosuppressed adults aged 18 years or older. Shingrix vaccination rates among eligible patients in our rheumatology clinic at the Veterans Affairs (VA) Medical Center remained low. The goal of this quality improvement project is to increase vaccination rates to at least 30% fully vaccinated over a period of 12 months in immunosuppressed patients seen in our rheumatology clinic.

Methods: Patients above the age of 18 seen in the VA Dallas rheumatology clinic and on disease-modifying antirheumatic drugs (DMARDs), excluding hydroxychloroquine, were eligible for inclusion. Patients were considered due for vaccination if they were unvaccinated or partially vaccinated (one vaccine dose received at least two months prior to clinic visit). Shingrix vaccination rate was defined as the percentage of patients due for vaccination at time of clinic visit who received a Shingrix vaccine

within one week after clinic visit. Baseline data were obtained via chart review of patients seen in our rheumatology clinic during the month of October 2021. We implemented three interventions: a) educating rheumatology fellows and attendings regarding the project and the expanded FDA indication in April 2022, b) attaching a Shingrix vaccination patient information sheet to intake forms from May 2022 to October 2022 and c) providing patients with a detailed map with directions to the separate vaccine clinic. Post-intervention data were collected during the months of June, September, October, and November 2022.

Results: For the baseline month of October 2021, our population sampled (n = 100) was on average 61.7 years old (median 64), 79% were men, 53% white, and 43% had rheumatoid arthritis. At baseline, 12% of eligible patients were fully vaccinated and 77% were unvaccinated at time of clinic visit. The Shingrix vaccination rate of due patients within one week after clinic

Table 1. Patient demographics for pre-intervention and post-intervention groups

	Pre-Intervention (n = 100)	Post-Intervention (n = 405)
Patient Characteristics		
Average age (years)	61.7	61.5
Men n (%)	79 (79.0%)	333 (82.2%)
Race		
White n (%)	53 (53.0%)	228 (56.3%)
Black n (%)	34 (34.0%)	124 (30.6%)
Hispanic n (%)	7 (7.0%)	16 (4.0%)
Rheumatic Disease		
Rheumatoid Arthritis n (%)	43 (43.0%)	176 (43.5%)
Seronegative Spondyloarthritis n (%)	34 (34.0%)	133 (32.8%)
Polymyalgia Rheumatica/Giant Cell Arteritis n (%)	6 (6.0%)	25 (6.2%)

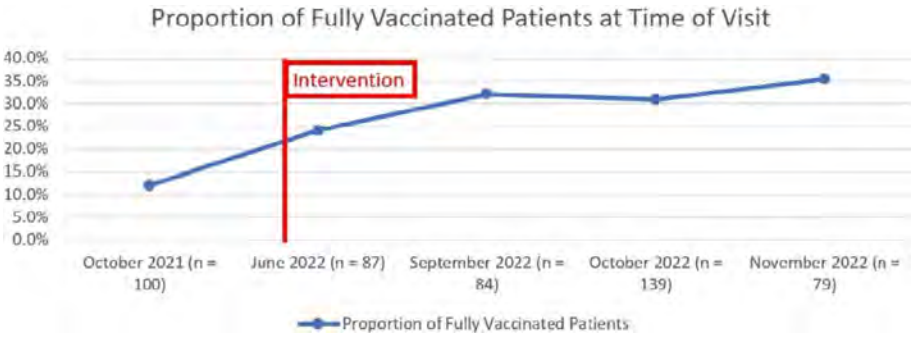


Figure 1. Proportion of fully vaccinated patients at time of visit during pre-intervention (October 2021) and post-intervention (June, September, October, November 2022) months.

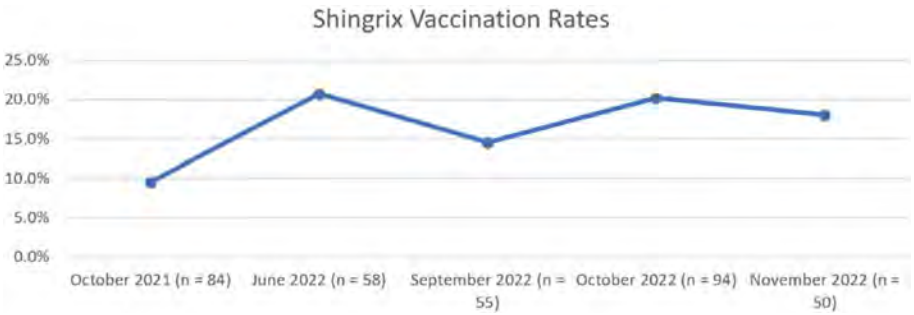


Figure 2. Percentage of patients due for vaccination at time of clinic visit who received a Shingrix vaccine within one week during pre-intervention (October 2021) and post-intervention (June, September, October, November 2022) months.

visit was 9.5% (n = 84). During post-intervention, our population sampled (n = 405) had similar demographics to the baseline (Table 1). For the post-intervention months of June, September, October, and November 2022, the proportion of fully vaccinated patients at time of clinic visit increased from baseline (Figure 1). Vaccination rates also increased during the post-intervention months (Figure 2).

Conclusion: The baseline proportion of fully vaccinated patients and vaccination rates were low among immunosuppressed patients seen in our rheumatology clinic. While our post-intervention evaluation showed an increase in the proportion of fully vaccinated patients as well as vaccination rates, overall post-intervention vaccination rates remained low at < 50%, leaving room for improvement. Our next steps will include streamlining our vaccination processes, and considering alternative communication approaches to educate our patients, especially those with vaccine hesitancy.

Disclosure: N. Pokala: None; **B. Gardner**: None; **A. Amratia**: None; **D. Emesiani**: None; **J. Mathew**: None; **R. Arora**: None; **U. Makris**: None; **S. Reddy**: None.

Abstract Number: 1090

Improved Patient and Team Satisfaction and Pharmacy Outcomes After Implementing a Rheumatology Clinical Pharmacist in a Large Academic Medical Center

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SESSION INFORMATION
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Background/Purpose: We embedded a clinical pharmacist into our university rheumatology clinics beginning in June 2022 to improve patient experience and reduce provider burden based on projected improved medication access and improved organizational financial health. The objective was to demonstrate how implementing a rheumatology clinical pharmacist with a medication access team can impact patient, provider, staff, and pharmacy outcomes.

Methods: In this mixed methods study at two academic clinics in 2022-23, we employed pre-post surveys and electronic health record (EHR) data review. We conducted a pre-implementation pharmacy services satisfaction survey and baseline needs assessment with providers and clinical staff to set priorities and leveraged existing patient surveys pre-post. Based on survey results, we categorized outcome measures of clinical pharmacist and medication access team impact into four groups: patient, provider, clinic staff, and pharmacy. EHR data included prior authorization quantity and turnaround time, manufacturer assistance referrals, time to infusion, and number of new patient enrollments, and prescriptions captured within the organizational specialty pharmacy. At six-months post-implementation, providers and clinic staff were asked to complete a post-implementation survey to assess the impact of the embedded clinical pharmacist.

Results: Patient and EHR data showed improvement after the clinical pharmacist joined the rheumatology clinic team. When asked "How well the staff worked together to care for you?" 83.3% after vs. 77.2% baseline (Q2 2022 n=298 vs. Q2 2023, n = 277) responded "extremely well" (p=0.047). The time from order to infusion decreased 9-13 days for infusions of 4 hours

or less (Table 1). Prior authorizations with a turnaround time greater than 5 days decreased by 27% (from 40 to 29/month); prior authorizations resulting in appeal decreased by 86% (from 7 to 1/month, Table 1). Our medication assistance program assisted many more patients (n=55 over 6 months) in obtaining medications through free drug programs. Prescription capture rate increased by 15% and patients enrolled in our specialty pharmacy increased from 27.8% (204/734) in Q1 2022, to 31.8% (228/718) in Q1 2023 (Figure 1).

Table 1. Medication Access

Table 1. Medication Access

Infusion Therapy- Mean Time from Order to Administration			
Treatment Duration	Pre-Implementation	Post-Implementation	Mean Improvement
2-hour infusions	20 days	7 days	13 d
4-hour infusions	21 days	12 days	9 d
6-hour infusions	32 days	34 days; Urgent spots now avail.	NA
Prior Authorization (PA) Turnaround Time and Appeals			
	Pre-Implementation	Post-Implementation	Improvement
PAs with turnaround > 5 days	40 per month	29 per month	27%
Number of Appeals	7 per month	1 per month	86%

Figure 1. Specialty Pharmacy Outcomes

Table 2. Provider and Clinic Staff Satisfaction Mean Response Pre-Post Pharmacist Implementation

Table 2. Provider and Clinic Staff Satisfaction Mean Response Pre-Post Pharmacist Implementation

Staff	Domain	Pre-Implementation	Post-Implementation	p-value t-test of means
Provider n=9/15		n=9/15	N=8/15	p<0.001
	Availability	5.89	9.8	
	Prior Authorization	5.67	9.6	
	Support for Appeals	5.11	9	
	Support for Infusions	7.61	9	
Clinic Staff/ Nurses n=5/5		n=5/5	n=5/5	p=0.015
	Support for Infusions	5.7	9.5	
	Prior Authorization	6.75	9.5	
	Confidence on Lab Monitoring for Anti-Rheumatic Medications	8.4	9.6	

Provider and staff satisfaction also significantly improved. All provider items on medication communication, prior authorization assistance, and support for appeals and infusions rose (Table 2, p< 0.001). Clinic staff satisfaction also improved in the prior authorization process (mean 9.5 vs 6.75 on scale of 1-10 best) and support for infusions (5.7 vs 9.5; pooled p=0.015,). Nurses also reported being more comfortable on anti-rheumatic medication lab monitoring after education from our clinical pharmacist.

Conclusion: The addition of an embedded rheumatology clinical pharmacist with direct support from a medication access team has improved patient, provider, and clinical staff satisfaction and outcomes. Specialty pharmacy prescription capture improved, and the cost to support the position was covered by improved financial outcomes.

Disclosure: S. Gomez: None; **T. Ludwig**: None; **K. Hartkopf**: None; **S. Ferguson**: None; **L. Zemlicka**: None; **M. Jones**: None; **C. Bartels**: Pfizer, 5.

Abstract Number: 1091

Prevalence of Loss to Follow up of Systemic Lupus Erythematosus Patients and Its Effect on Quality of Care

Raphael Kirou, Cesar Avalos and Ellen Ginzler, SUNY Downstate Health Sciences University, Brooklyn, NY

SESSION INFORMATION
Session Date: Monday, November 13, 2023
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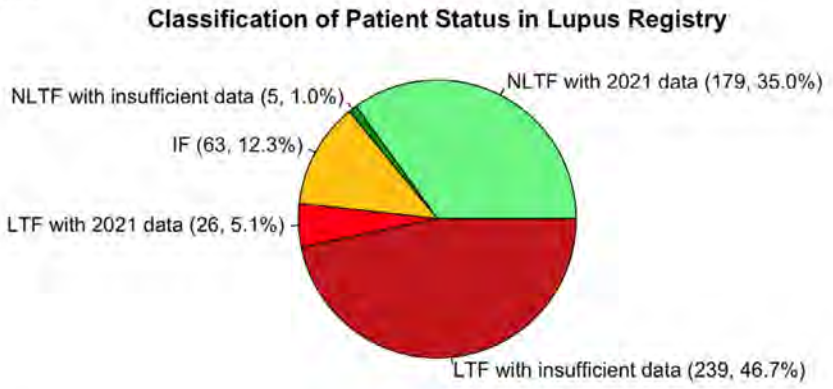
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Quality of care (QoC) in SLE patients has been studied by Schmajuk et al. (*Arthritis Care Res*2022), who developed six quality measures assessing blood pressure, lupus nephritis screening, hydroxychloroquine prescription, and corticosteroid dosing. In this study, prompted by the increased loss to follow up and disruption in care associated with the COVID-19 pandemic, we quantify the effect of loss to follow up from the rheumatology clinic at University Hospital Brooklyn (UHB) on QoC of our SLE patients.

Methods: Using the Lupus Registry at UHB rheumatology clinic, we identified all SLE patients who had any rheumatology visits between 2007 and 2019, excluding patients reported dead in 2021 or earlier. We stratified these patients into three groups based on their follow-up status: lost to follow up (all-LTF; no rheumatology visits in 2020 and 2021), not lost to follow up (all-NLTF; ≥1 rheumatology visits in each year 2019, 2020, and 2021), and inconsistently followed (IF; remaining patients). Within all-LTF, we selected all patients who had ≥2 outpatient visits to UHB at least 30 days apart in 2021 (LTF; n=26). We then matched these patients 1:2 by age and sex to all-NLTF patients with ≥2 outpatient visits to UHB at least 30 days apart in 2021 (NLTF; n=52). Finally, we completed a chart review to identify whether the six SLE quality measures outlined by Schmajuk et al. were met for these patients. To compare LTF and NLTF patients, we used chi-square analyses and a two-sample t-test ($\alpha = 0.05$).

Results: We determined that of 512 eligible patients in the registry, all of whom satisfied either the 1995 ACR or SLICC criteria for SLE, 265 (52%) were all-LTF and 184 (36%) were all-NLTF [Figure 1]. As expected, the average age (49) and the female prevalence (89%) did not differ between LTF and matched NLTF [Table 1]. Notably, 50% of LTF patients had ESRD (47% with renal transplant), compared to 2% of NLTF patients (2% with renal transplant). NLTF patients received blood pressure measurements and hydroxychloroquine prescriptions at significantly greater rates (96% and 96% respectively) than LTF patients (81% and 36% respectively) [Table 2]. Although not statistically significant, they also tended to receive more urine studies (88%) than LTF patients (76%), but also higher frequency of high dose corticosteroids (27%) than LTF patients (12%). Overall, NLTF patients received a greater proportion of eligible quality measures (0.81) than did LTF patients (0.66).

Figure 1



Notes: all-LTF comprises "LTF with 2021 data" and "LTF with insufficient data". All-NLTF comprises "NLTF with 2021 data" and "NLTF with insufficient data". Matched NLTF (n=52) taken from "NLTF with 2021 data" (n=179).

Table 1

	LTF (n = 26)	Matched NLTF (n = 52)
Sex	• Male: 3 (11.5%) • Female: 23 (88.5%)	• Male: 6 (11.5%) • Female: 46 (88.5%)
Race	• Black/African-American: 26 (100.0%)	• Black/African-American: 47 (90.4%) • White: 3 (5.8%) • Undisclosed: 2 (3.8%)
Age (Mean ± SD)	49.39 ± 15.74	49.09 ± 16.03
ESRD	13 (50.0%)	1 (1.9%)
Renal Transplant	12 (46.2%)	1 (1.9%)
Total Number of visits in 2021 (Mean ± SD)	8.73 ± 6.50	11.52 ± 8.09

Table 2

Quality Measures (2021)	LTF (n = 26)	Matched NLTF (n = 52)	p-value
BP Measurement [≥2 BP measurements ≥30 days apart]	21/26 (80.77%)	50/52 (96.15%)	0.025[1]
BP Control [Not having ≥2 blood pressure measurements ≥30 days apart with SBP>140 or DBP>90][3]	11/21 (52.38%)	30/50 (60.00%)	0.553[1]
Lupus Nephritis Screening [≥1 documented urine study (urinalysis, urine protein, or urine protein:creatinine ratio)][4]	19/25 (76.00%)	46/52 (88.46%)	0.158[1]
HCQ Prescription [At least one HCQ prescription][5]	9/25 (36.00%)	45/47 (95.74%)	<0.001[1]
HCQ Safe Dosing [HCQ dose ≤5 mg/kg/day at last visit][6]	8/9 (88.89%)	37/45 (82.2%)	0.624[1]
Corticosteroid Safe Dosing [No more than 90 days of >7.5 mg/day of prednisone]	23/26 (88.46%)	38/52 (73.08%)	0.121[1]
All eligible quality measures met	3/26 (11.54%)	14/52 (26.92%)	0.121[1]
Proportion of eligible quality measures met (Mean ± SD)	0.66 ± 0.23	0.81 ± 0.16	0.005[2]

Notes:
Quality measures adapted from Schmajuk et al. (2022) and measured for the calendar year 2021.
SBP = systolic blood pressure; DBP = diastolic blood pressure; HCQ = hydroxychloroquine.

[1]Chi-squared test
[2]Two sample t-test (unequal variances)
[3]Only patients that met "BP Measurement" measure were eligible for "BP Control" measure
[4]Patients on hemodialysis were excluded from "Lupus Nephritis Screening" measure
[5]Patients with HCQ toxicity were excluded from "HCQ Prescription" measure
[6]Only patients that met "HCQ Prescription" measure were eligible for "HCQ Safe Dosing" measure

Conclusion: Only 36% of SLE patients at UHB were consistently followed from 2019-2021. This by itself is an indicator of poor QoC, and may portend poor outcomes. In addition, LTF patients met fewer quality measures than NLTF patients. Conversely, LTF patients tended to have lower corticosteroid doses than NLTF patients, which may be indicative of fewer symptoms, another explanation for their loss to follow up. However, the possibility of subclinical SLE progression, such as lupus nephritis, means that loss to follow up can still be detrimental to these patients. We conclude that loss to follow up is a significant threat to QoC in SLE patients, and that efforts to address follow-up barriers should be made by rheumatologists in collaboration with other health care providers.

Disclosure: R. Kirou: None; **C. Avalos**: None; **E. Ginzler**: None.

Abstract Number: 1092

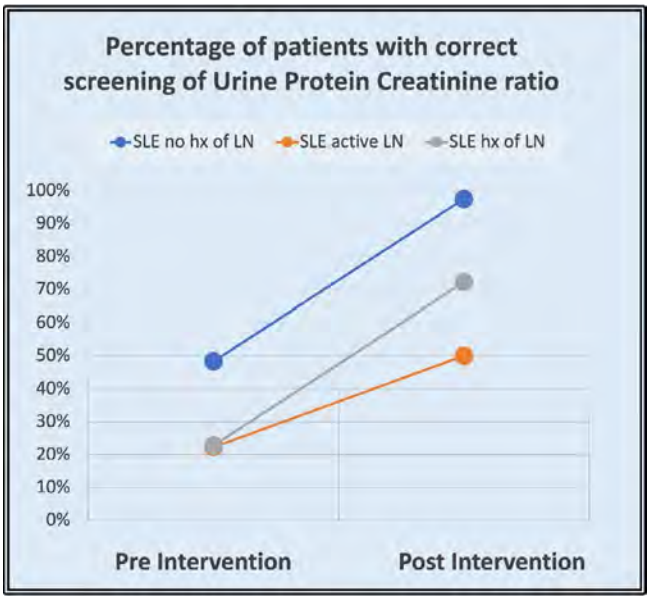
Improving Screening of Lupus Nephritis in Patients with Systemic Lupus Erythematous

Lilian Otalora Rojas[1], Gurjit S Kaeley[2] and Myint Thway[3], [1]University of Florida, Ponte Vedra Beach, FL, [2]University of Florida College of Medicine – Jacksonville, Ponte Vedra Beach, FL, [3]UF Jacksonville, Ponte Vedra, FL

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Nephritis remains one of the most devastating complications of Systemic lupus erythematosus (SLE). Lupus nephritis (LN) significantly reduces overall survival to approximately 88% at 10 years. The ACR guideline suggests that the frequency of follow-up visits is determined by the activity and severity of the disease and its complications. Current recommendations for monitoring lupus nephritis include UA (urine analysis with microscopy) and urine Protein/creatinine ratio (UPCR). This test should be obtained every 6 months for patients with SLE without active LN, every 3 months



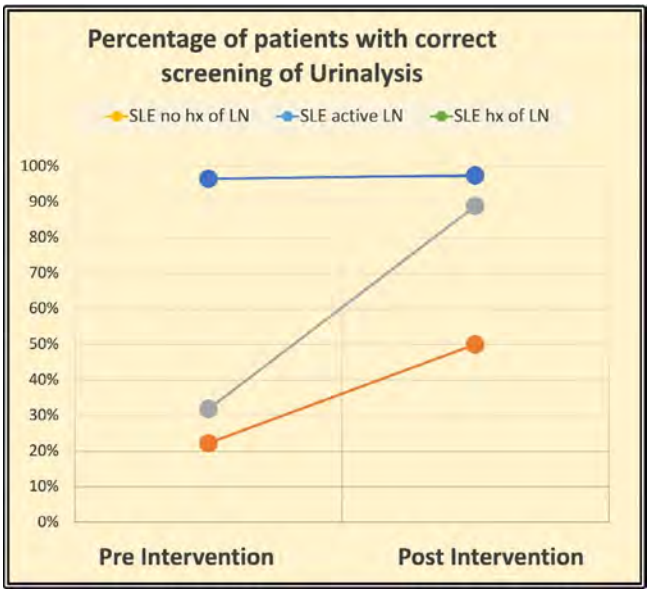
Improvement on screening rate of proteinuria

in patients with non-active LN, and every month in patients with active LN. Our overall goal was to increase the appropriate monitoring of LN in patients with SLE in our rheumatology clinic.

Methods: This quality improvement project retrospectively analyzed the medical records of 60 patients diagnosed with SLE who were seen at the rheumatology clinic at the University of Florida in Jacksonville, FL, from January 2019 to December 2019. Patients were classified as SLE without LN, non-active LN, and with active LN. The frequency of performed UA and UPCR, were recorded in each subject. After identifying baseline values, we worked with clinicians and clinic support staff on intervention. Interventions included educating fellows, faculty, and staff about current guidelines for LN screening and monitoring, creating flyers, and generating a panel order in the electronic health system (EPIC) for SLE, including UA and UPCR tests. A subsequent retrospective chart review of 60 patients was performed after 12 months to analyze the impact of interventions.

Results: Initial data showed the need for improvement in monitoring/screening laboratory parameters (UPCR and UA) for LN in our patients with SLE. Preintervention analysis showed that less than 50% of patients were correctly monitored for UPCR in the three groups, and less than 40% were monitored for UA in patients with active LN and with a history of LN as recommended per ACR guidelines. Just one group of patients: SLE patients with no LN history had a high UA monitoring rate (97%). After the intervention, monitoring/screening for LN in patients with SLE improved: Regarding UPCR, preintervention results were 48% (no history of LN), 23% (history of LN), and 22% (active LN), and it increased to 97%, 72% and 50% respectively. Adequate monitoring of UA preintervention results were 97% (no history of LN), 32% (history of LN), and 22% (active LN, and postintervention 97%, 89%, 50%. A separate chart review of those patients suggested that compliance of patients is the major issue of proper testing intervals.

Conclusion: LN is associated with increased mortality and morbidity in SLE patients. Survival of SLE has improved in the past few decades with advanced treatment, including early diagnosis of LN. ACR developed recommendations for screening LN and follow-up tests. Adherence to proper screening may help renal survival by treating exacerbations on a timely basis. This study employed various interventional methods to increase the screening of Urinalysis and proteinuria. However, patient compliance remains a challenge.



Improvement on screening rate of Urine analysis

Disclosure: L. Otalora Rojas: None; **G. S Kaeley**: Abbvie, 5, Gilead, 5, Janssen, 5; **M. Thway**: None.

Abstract Number: 1093

Development of Adaptive Immunity Against Different SARS-CoV-2 Variants over the Course of Three COVID-19 Vaccinations in Patients with Inflammatory Rheumatic Diseases

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Measures & Measurement of Healthcare Quality Poster I

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Even though individuals with inflammatory rheumatic diseases (IRDs) were excluded from the SARS-CoV-2 vaccine trails, studies have shown that these individuals at risk of a severe course of infection do show an immune response after vaccination. The goal of our study was to show the development of the adaptive immunity over time and its activity towards different variants of concern (VoC).

Methods: For this retrospective study, patients with IRDs and a healthy control group were recruited. To evaluate the immunity induced by SARS-CoV-2 vaccination the antibody titres against the S1-domain of the spike protein of SARS-CoV-2 (BAU/ml) and the IC_{50} neutralization of different VoCs (EU1, Delta, Omicron-BA.5, BQ1.1, BF.7) were quantified at different time points before and after each vaccination. The study period started before the first and ended 26 weeks after the third vaccination.

Results: In total 187 patients with IRDs [mean age (standard deviation (SD)) 54.5 (±14.8) years, 65.8% female] and 84 healthy controls [46.7 (±13.2) years, 78.7% female] were included into the study (Table 1). Even though both patients and controls showed high antibody titres after the first two vaccinations [median (interquartile range (IQR)) 1600 BAU/ml (378.2-3468); 4446 BAU/ml (1943-7200)] the titres of the patients were significantly lower ($P< 0.0001$). After declining over the next 24 weeks, the titres showed another significant rise after the third vaccination in both groups [patients: 4344 BAU/ml (933.2-8023); controls: 5795 BAU/ml (3779-12209)]. However, the levels reached by the patients were still significantly lower compared to the controls ($P=0.04$). The decline of titres after the third vaccination was not as operand as after the second in either group (Fig. 1). Both groups displayed robust neutralization activities after the first two vaccinations for EU1, Delta and BA.5 that increased after the third dose of the mRNA vaccine. However, the controls showed a rise in neutralization capacity until 16 weeks after the second vaccination while it already started declining after the 2-week measurement in patients resulting in a significant difference. Notably, neutralization of Delta and BA.5 were significantly lower compared to the ancestral EU1. Good neutralization capacity of BQ1.1 in both groups were only reached after the third vaccination, while neither group presented reliable neutralization of the highly immunoevasive BF.7 after any vaccination. (Fig. 2) Individuals treated with rituximab were not able to mount a reliable humoral immune response after any vaccination. However, they did show adaptive T-cell responses which were comparable to the controls.

Table 1: Study population

	IRD[1] patients	Healthy control group
n	187	84
Age mean (SD[2])	54,5 (±14,8)	46,7 (±13,2)
Sex % (n)	65,8 (123)	78,7 (66)
IRDs: % (n)		
Arthritis	62,0 (116)	
Soft connective tissue disorders	15,5 (29)	
Vasculitis	16,0 (30)	
Other	7,5 (14)	
Immunosuppressant therapy: % (n)		
MTX	35,3 (66)	
RTX	9,6 (18)	
TNF-inhibitors	21,9 (41)	
IL-6R-inhibitors	8,6 (16)	
JAK-inhibitors	4,8 (9)	
HCQ	10,2 (19)	
Azathioprine	6,4 (12)	
Ixekizumab	2,7 (5)	
MMF	3,2 (6)	
Glucocorticoids	19,3 (36)	
Infections % (n)	21,9 (41)	25,0 (21)

[1]inflammatory rheumatic diseases
[2]standard deviation

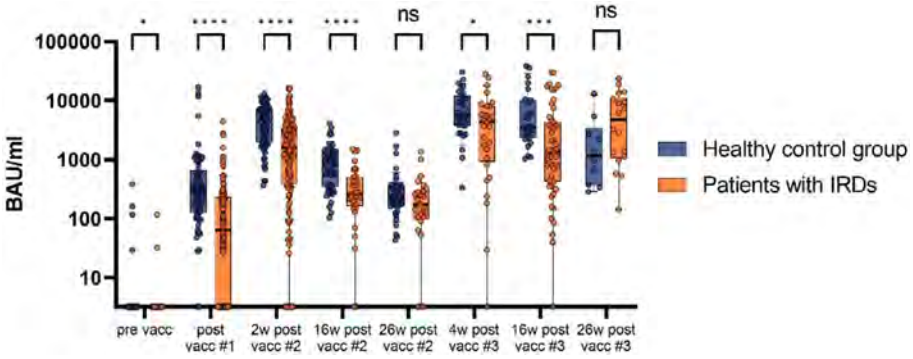

Figure 1: Antibody titres against the S1-domain of the spikeprotein of SARS-CoV-2 over time

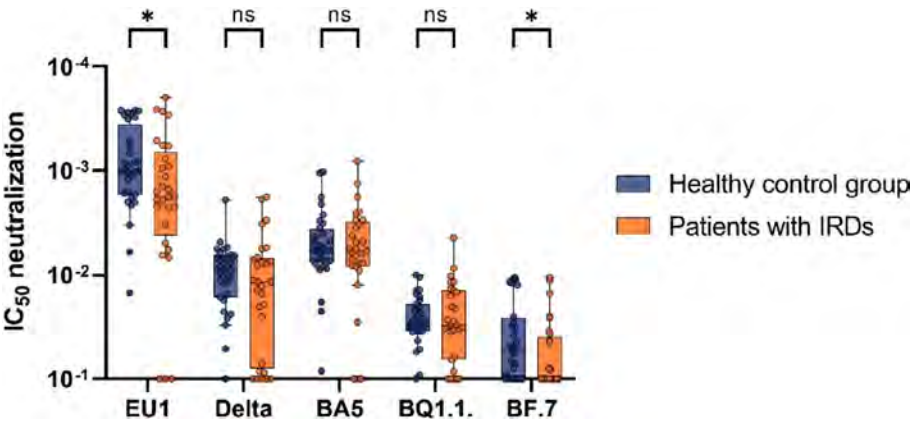

Figure 2: Neutralization capacity for different SARS-CoV-2 variants of concern four weeks after the third vaccination

Conclusion: Although patients with IRDs show lower anti-SARS-CoV-2 spike antibody titres and partly lower IC_{50} neutralization compared to healthy controls, most of them mount a robust immune response against SARS-CoV-2, indicating some level of protection from a severe course of infection. However, the original vaccines did not induce a robust neutralization capacity for the recently emerged BF.7 variant in patients or controls. Thus, variant-adapted vaccines should be considered, in particular, in high-risk patient groups, including individuals with IRDs.

Disclosure: L. Huppke: None; **P. Wratil**: None; **M. Bischof**: None; **S. Wolfrum**: None; **F. Ullrich**: None; **D. Singh**: None; **J. Lichtnekert**: None; **L. Grümme**: None; **C. Gebhardt**: None; **K. Krüger**: AbbVie/Abbott, 2, 6, Biogen, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, CellTrion, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Hexal, 2, Janssen, 6, Medac, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Rheumaakademie, 6, Roche, 6, Sandoz, 6, Sanofi-Aventis, 2, 6, UCB, 6, Update GmbH, 6; **F. Wiesent**: None; **A. Skapenko**: None; **O. Keppler**: None; **H. Schulze-Koops**: AbbVie, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Pfizer, 2, 6.

Abstract Number: 1094

"Lupus Doesn't Have Me, I Have Lupus" a Patient Centered Quality Improvement Project to Increase Medication Adherence for Patients with Lupus Nephritis

Christopher Macko[1], Patty Chen[2], Roger Santos[3], Nirmala Ramalingam[4], Nicole Tran[5] and Sijie Zheng[6], [1]Kaiser Oakland Internal Medicine Residency, Piedmont, CA, [2]Kaiser Oakland Medical Center Department of Rheumatology, Orinda, CA, [3]Kaiser East Bay Department of Pharmacy, Oakland, CA, [4]Kaiser Oakland Medical Center Department of Graduate Medical Education, Oakland, CA, [5]Kaiser Oakland Department of Adult and Family Medicine, Oakland, CA, [6]Kaiser Oakland Medical Center Department of Nephrology, Oakland, CA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session B
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Background/Purpose: Lupus nephritis (LN) is the most common cause of kidney injury in patients with systemic lupus erythematous (SLE) and is associated with higher morbidity and mortality. Low adherence to treatment regimens is common amongst patients with LN and is correlated with high rates of relapse, increased hospitalizations, and poor renal outcomes. Our objective was to assess and identify barriers to medication adherence for our patients with LNon mycophenolate mofetil (MMF).We used this data to design targeted interventions aimed at improving medication adherence for our patients with LN on MMF in our large integrated health system at Kaiser Permanente Oakland Medical Center, California.

Methods: We identified patients with a diagnosis of LN, who were taking MMF between 11/30/21 and 11/30/22. We collected demographic information including age, gender, 30-day copay, ethnicity, requirement of renal replacement therapy, and proportion of days covered (PDC) for MMF. We identified patients with a PDC of less than80% and surveyed them for barriers to medication adherence. Our survey questions sought to elucidate barriers such as medication side effects, cost, refill processes, and lab draws. We also asked open-ended questions to gain insight into how SLE has affected their lives.

Results: Of 37 patients with LNon MMF, almost a third (12/37) had PDC less than 80%. More than half (7/12) of these patients agreed to be interviewed. They identified the following barriers to medication adherence: forgetfulness57% (4/7), incompletelabwork28% (2/7),medication cost 14% (1/7),and intentionally missed doses 14% (1/7). No patients identified

Table 1: Characteristics of patients with LN on MMF

	Patients on MMF (N=37)	Patient on MMF with PDC <80% (N=12)	Patients on MMF with PDC <80% who agreed to be interviewed (N=7)
Median age (yrs)	47	44.5	40
Female sex %	89%	84%	100%
RRT %	3%	0%	0%
Ethnicity %			
Asian	46%	25%	14%
Black	22%	25%	43%
Hispanic	32%	50%	43%
NHW	0%	0%	0%
30-day co-pay range:	$0-$14.63	$0-$14.63	$0-$14.63
Median 30-day co-pay:	$3.33	$3.94	$4.55

Abbreviations: RRT- renal replacement therapy, MMF- Mycophenolate Mofetil, LN- Lupus Nephritis

Figure 1: Proportion of days covered (PDC) for patients with LN on MMF

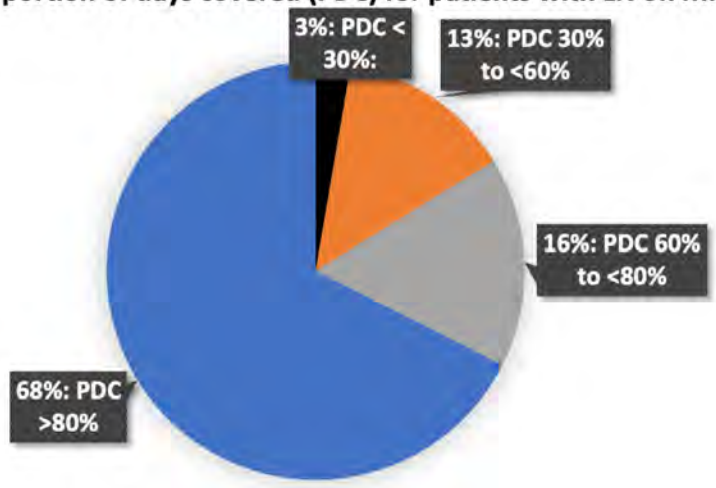
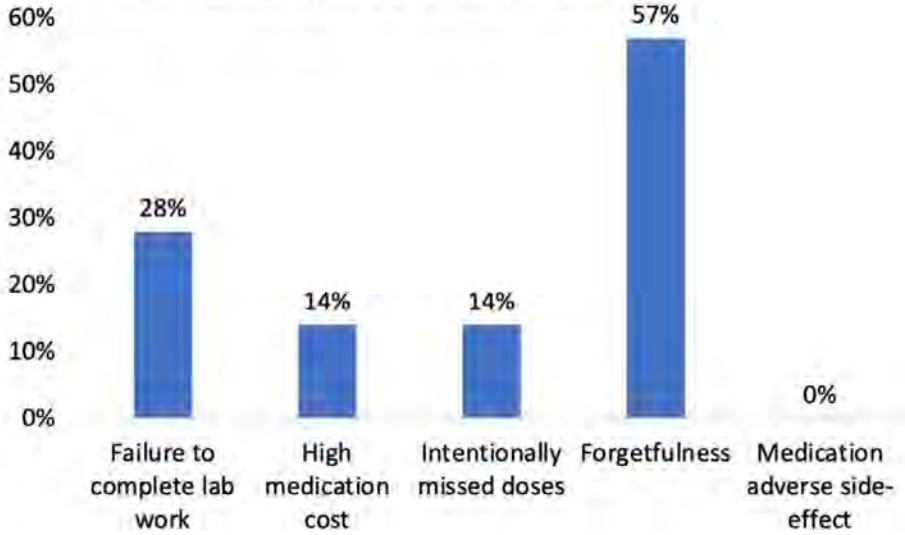


Figure 2: Patient reported barriers to medication adherence



medication side effects as a barrier. More than two thirds (5/7) reported no issues with obtaining new prescriptions from the pharmacy. The median 100-day co-pay for MMF was $13.13 and 2/7 (28%) patients paid $0 for their medications.

Conclusion: At KP Oakland, two thirds of our patients with LNare adherent to their MMF; forgetfulness appears to be a challenge for our non-adherent patients. The next steps to our quality improvement initiatives will focus on the following: 1) patient and provider education about tools (medication and lab reminder apps) to promote medication adherence and 2) creating a multidisciplinary rheumatology and nephrology committee to identify and discuss patients with LN who are at risk of disease progression.

Disclosure: C. Macko: None; **P. Chen**: None; **R. Santos**: None; **N. Ramalingam**: None; **N. Tran**: None; **S. Zheng**: None.

Abstract Number: 1095

Engagement with the RISE Registry Clinician Dashboard Is Associated with Higher Performance on Rheumatology Quality Measures

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The American College of Rheumatology's Rheumatology Informatics System for Effectiveness (RISE) EHR-based registry facilitates quality measure calculation and reporting for rheumatology practices in national pay-for-performance programs. Participating practices can leverage RISE's web-based clinician dashboard to monitor performance on quality measures, benchmark performance against registry means, and explore patient-level data to identify gaps in care. Despite substantial investment in these dashboards, the extent to which they help improve performance on quality measures remains unclear. We investigated the relationship between practice engagement with the RISE web-based dashboard and performance on rheumatology-specific measures in 2021.

Methods: Eligible practices were categorized into 3 engagement groups based on practice personnel's dashboard interactions (number of sessions and actions performed, such as drilldowns and exports) during the study period: no engagement (0 sessions), some engagement (≤ median actions), high engagement (> median actions) (**Table**). Practice performance was assessed on both individual and composite measures, utilizing all available rheumatology-specific measures (range 1 to 8) per practice that had ≥20 eligible patients. The composite measure incorporated all rheumatology-specific measures per practice and was denominator-weighted, i.e., based on the number of patients included in each individual measure denominator. Individual measure performance analysis was restricted to measures with data from ≥5 practices per engagement group. Linear regression models were used to calculate predictive margins and 95% confidence intervals for quality performance for each engagement group. Differences in performance across engagement groups were assessed via pairwise comparisons; linear trends were evaluated using orthogonal polynomial contrasts (**Figure**).

Results: Most of the 204 included practices were single-specialty (59.8%) or solo practices (29.4%), with a median of 2 providers and 4970 patients (**Table**). Among these practices, 11% had no dashboard engagement, 76% had some engagement, and 12% were highly engaged. Performance on individual rheumatology-specific measures ranged from 28%-72%

(median (IQR) 60% (47-66%)). The majority of practices' (75%) composite scores included ≥3 out of 8 possible rheumatology-specific measures with a median (IQR) performance of 65% (40-79%). We observed a pattern of higher measure performance with more dashboard engagement: 3 out of 5 individual rheumatology-specific measures and the composite measure exhibited a significant linear trend at the 5% level (**Figure**).

Table. RISE registry Practice Characteristics by Level of RISE Dashboard Engagement

	Total Practices (N)	Dashboard Engagement (N(%))		
		None	*Some*	*High*
	204	23 (11.2)	156 (76.4)	25 (12.3)
Dashboard Interactions (median (IQR))				
Total Sessions	9.0 (3.0 - 20.0)	0.0 (0.0 - 0.0)	9.0 (5.0 - 17.0)	43.0 (33.0 - 56.0)
Total Actions[1]	3.0 (0.0 - 18.0)	0.0 (0.0 - 0.0)	3.0 (0.0 - 12.5)	86.0 (58.0 - 116.0)
Practice Characteristics				
Practice Type (N(%))				
Single-Specialty	122 (59.8)	12 (52.2)	94 (60.3)	16 (64.0)
Solo Practitioner	60 (29.4)	8 (34.8)	46 (29.5)	6 (24.0)
Multi-Specialty	22 (10.7)	3 (13.0)	16 (10.3)	3 (12.0)
Practice Size (median (IQR))				
Total Patients	4970 (2710 - 9035)	5682 (1318 - 8225)	4673 (2678 - 8923)	7217 (3788 - 12906)
Total Providers	2 (1 - 5)	2 (1 - 4)	2 (1 - 5)	4 (1 - 8)
Patient Casemix (median (IQR))				
Age, median	62.0 (60.0 - 65.0)	63.0 (60.0 - 64.0)	63.0 (61.0 - 66.0)	61.0 (59.0 - 63.0)
Female, %	75.1 (73.1 - 77.3)	74.6 (73.6 - 79.1)	75.1 (72.5 - 77.1)	75.2 (73.3 - 77.2)
Medicare Insurance, %	33.2 (25.9 - 41.9)	27.1 (23.3 - 40.1)	33.5 (25.8 - 42.3)	34.3 (29.4 - 39.5)
National ADI[2], median	45.5 (29.5 - 59.3)	41.0 (30.0 - 65.0)	46.0 (29.0 - 59.5)	45.0 (39.0 - 58.0)

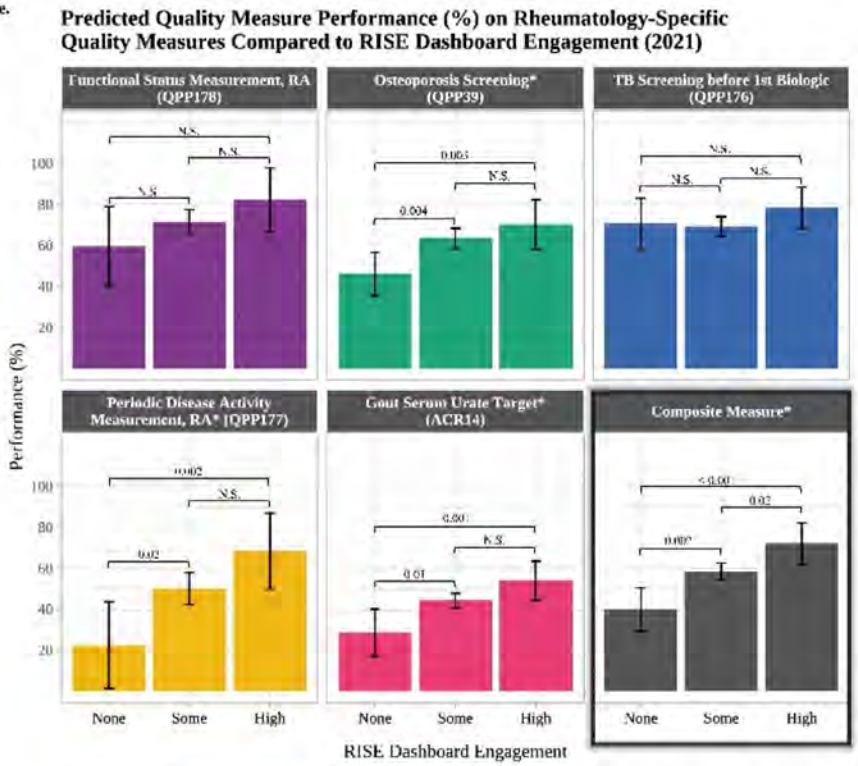
Table. summarizes dashboard interactions (total logins and actions) and practice characteristics of the affiliated RISE web-dashboard users stratified by level of engagement. Median and interquartile range (IQR), and frequency (N) and percent (%) are displayed for continuous and categorical variables, respectively.

[1]Total actions completed on the RISE dashboard during a login session included the following: total views of quality performance on selected measures at the patient-level, total exports of quality performance on selected measures at the patient-level, and total exports of a summary-level report of selected quality measures.

[2]National ADI (Area Deprivation Index) is a proxy for socioeconomic status (SES) and is derived from the University of Wisconsin School of Medicine and Public Health, Neighborhood Atlas. A higher ADI indicates lower SES (more neighborhood-level disadvantage).

Disclaimer: This data was supported by the ACR's RISE Registry. However, the views expressed represent those of the authors, not necessarily those of the ACR.

Figure.



*Significant linear trend at the 5% level between RISE dashboard engagement and quality measure performance. **Rheumatology-specific measures** were defined as measures that aligned with care routinely provided by rheumatologists. The **composite measure** included the following measures, if reported by practices: QPP178 (Functional Status Screening for RA), QPP39 (Osteoporosis Screening for patients 65–), QPP176 (TB Screening before first Biologic), QPP177 (Periodic Disease Activity Measurement for RA), ACR14 (Gout Serum Urate < 6mg/dL), ACR10 (Hepatitis B screening), ACR12 (PsA Periodic Disease Activity Assessment), and ACR15 (Hydroxychloroquine Dosing).

Conclusion: This cross-sectional analysis revealed a dose-response between degree of dashboard engagement and practice-level quality performance: RISE practices with higher levels of dashboard engagement exhibited better quality performance. Further investigation is needed to determine whether more dashboard engagement yields meaningful quality improvement over time, and whether performance is determined by engagement or vice versa.

Disclosure: E. Kersey: None; **J. Li**: None; **J. Kay**: Pfizer, 12, Own Stock; **J. Adler-Milstein**: None; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, Gilead, 5, Pfizer, 2; **G. Schmajuk**: None.

Abstract Number: 1096

A Quality Improvement Project About Medication Adherence to Understand What Questions Rheumatology Patients Have About Their Medications, and How They Answer Them

Lena Eder[1], Kai Sun[2], Sonali Bracken[3], Ann Cameron Barr[4], Jeffrey Shen[4], Dahima Cintron[4], Mithu Maheswaranathan[4], Catherine Sims[2], Poorva Apte[4], Megan Milne[5], Nathaniel Harris[4] and David Leverenz[6], [1]Duke University, Chapel Hill, NC, [2]Duke University, Durham, NC, [3]Duke University Hospital, Apex, NC, [4]Duke University Hospital, Durham, NC, [5]Costal Carolina Health Care, New Bern, NC, [6]Duke University School of Medicine, Durham, NC

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Medication non-adherence remains high among rheumatology patients, yet little is known about adherence barriers faced by patients or interventions that improve adherence. As part of a quality improvement initiative, we aimed to better understand questions rheumatology patients have about their medications, how they seek answers, and factors associated with self-reported medication adherence.

Methods: Patient surveys were administered at a fellows; continuity clinic at periodic intervals between 5/5/2022 – 4/26/2023. The survey consisted of 5 items assessing length of time taking rheumatic medications, self-reported confidence with taking medications correctly, what patients would like to learn about their medications, how patients find answers to questions about their rheumatic medications, and adherence to rheumatic medications over the past month. Survey responses were analyzed to determine differences in patient needs based on their years of experience taking rheumatic medications (0-5 years vs. >5 years) and their self-reported adherence with rheumatic medications (< 80% adherence vs. >=80%). Comparisons were performed with Fisher's exact test.

Results: Of the 88 surveys that were administered, 80 patients answered at least one question (response rate 91%). Of all respondents, 74% reported taking rheumatic medications for five years or less, 82% reported feeling "very confident" in taking their medications, and 80% reported adherence over the past month (Table 1). The top categories of information that patients wanted to learn about were "side effects I could experience" (46%) and "how the medications work" (37%). To answer questions about rheumatic medications, most respondents "ask [their] rheumatology provider directly" (83%) or turn to "Google or other internet search engine" (59%). There were no significant differences in confidence, questions about medications, or methods of answering questions according to experience taking rheumatic medications (Table 2). Patients reporting non-adherence were significantly less likely than those reporting adherence to ask their provider directly about their rheumatic medications (57% vs. 88%, p=0.01) and more likely to turn to internet searches (86% vs. 52%, p=0.03) and social media (29% vs. 5%, p=0.02) for information (Table 3).

Table 1: Overall survey results among 80 respondents.

	n (%)
How long have you been taking medications that treat a rheumatology disease?	
Total number of respondents to this question*	n=78
Less than 1 year, n (%)	32 (41%)
Between 1 to 5 years, n (%)	26 (33%)
Between 5 to 10 years, n (%)	5 (6%)
More than 10 years, n (%)	15 (19%)
How confident are you that you are taking your rheumatology medications correctly?	
Total number of respondents to this question*	n=76
Not at all confident, n (%)	0 (0%)
Slight confident, n (%)	3 (4%)
Moderate confident, n (%)	11 (14%)
Very confident, n (%)	62 (82%)
What would you like to learn about your rheumatology medications?	
Total number of respondents to this question*	n=70
How the medications work, n (%)	26 (37%)
Why am I taking each medication, n (%)	15 (21%)
How to take the medications correctly, n (%)	8 (11%)
Side effects I could experience, n (%)	32 (46%)
How to reduce the cost of my medications, n (%)	12 (17%)
Other, n (%)	22 (31%)
How do you find answers to questions you have about your rheumatology medications?	
Total number of respondents to this question*	n=78
I ask my rheumatology provider directly, n (%)	65 (83%)
I use resources my rheumatology provider gives me, n (%)	14 (18%)
I ask my family or friends for advice, n (%)	5 (6%)
Google or other internet search engine, n (%)	46 (59%)
Social media, n (%)	9 (12%)
Support groups, n (%)	4 (5%)
Other, n (%)	2 (3%)
How much of your rheumatology medications did you take in the past month?	
Total number of respondents to this question*	n=76
Self-reported adherence >=80%, n (%)	61 (80%)
Self-reported adherence <10%, n (%)	11 (14%)

*Not all respondents answered every question. Percentages reflect the proportion of respondents who answered that individual question (blank answers are excluded).

Overall survey results among 80 respondents.

Table 2: Survey responses based on years of taking rheumatology medications (0-5 years vs. >5 years).

	0-5 years (n=58)	>5 years (n=20)	p value
How confident are you that you are taking your rheumatology medications correctly?			
Total number of respondents to this question*	n=58	n=20	
Not at all confident, n (%)	0 (0%)	0 (0%)	0.8
Slight confident, n (%)	2 (4%)	1 (5%)	
Moderate confident, n (%)	8 (14%)	3 (15%)	
Very confident, n (%)	46 (82%)	16 (80%)	
What would you like to learn about your rheumatology medications?			
Total number of respondents to this question*	n=53	n=17	
How the medications work, n (%)	21 (40%)	5 (29%)	0.6
Why am I taking each medication, n (%)	12 (23%)	3 (18%)	0.7
How to take the medications correctly, n (%)	7 (13%)	1 (6%)	0.7
Side effects I could experience, n (%)	23 (43%)	9 (53%)	0.5
How to reduce the cost of my medications, n (%)	8 (15%)	4 (24%)	0.5
Other, n (%)	16 (30%)	6 (35%)	0.8
How do you find answers to questions you have about your rheumatology medications?			
Total number of respondents to this question*	n=57	n=20	
I ask my rheumatology provider directly, n (%)	47 (82%)	17 (85%)	1
I use resources my rheumatology provider gives me, n (%)	13 (23%)	1 (5%)	0.1
I ask my family or friends for advice, n (%)	4 (7%)	1 (5%)	1
Google or other internet search engine, n (%)	37 (65%)	9 (45%)	0.2
Social media, n (%)	8 (14%)	1 (5%)	0.4
Support groups, n (%)	3 (5%)	1 (5%)	1
Other, n (%)	1 (2%)	1 (5%)	0.5
How much of your rheumatology medications did you take in the past month?			
Total number of respondents to this question*	n=54	n=20	
Self-reported adherence >=80%, n (%)	44 (81%)	17 (85%)	1
Self-reported adherence <10%, n (%)	10 (19%)	3 (15%)	

*Not all respondents answered every question. Percentages reflect the proportion of respondents who answered that individual question (blank answers are excluded).

Survey responses based on years of taking rheumatology medications (0-5 years vs. >5 years).

Table 3: Survey responses based on self-reported medication adherence (>80% adherent vs. <80% adherent).

	<80% adherent (n=15)	>=80% adherent (n=61)	p value
How long have you been taking medications that treat a rheumatology disease?			
Total number of respondents to this question*	n=13	n=61	
Less than 1 year, n (%)	3 (23%)	26 (43%)	0.4
Between 1 to 5 years, n (%)	7 (54%)	18 (30%)	
Between 5 to 10 years, n (%)	1 (8%)	4 (7%)	
More than 10 years, n (%)	2 (15%)	13 (21%)	
How confident are you that you are taking your rheumatology medications correctly?*			
Total number of respondents to this question*	n=13	n=61	
Not at all confident, n (%)	0	0	0.7
Slight confident, n (%)	1 (8%)	2 (3%)	
Moderate confident, n (%)	2 (15%)	9 (14%)	
Very confident, n (%)	10 (77%)	52 (83%)	
What would you like to learn about your rheumatology medications?			
Total number of respondents to this question*	n=12	n=55	
How the medications work, n (%)	5 (42%)	21 (38%)	1
Why am I taking each medication, n (%)	3 (25%)	12 (22%)	1
How to take the medications correctly, n (%)	3 (25%)	5 (9%)	0.1
Side effects I could experience, n (%)	7 (58%)	25 (45%)	0.5
How to reduce the cost of my medications, n (%)	3 (25%)	9 (16%)	0.4
Other, n (%)	2 (17%)	20 (36%)	0.3
How do you find answers to questions you have about your rheumatology medications?			
Total number of respondents to this question*	n=14	n=61	
I ask my rheumatology provider directly, n (%)	8 (57%)	54 (88%)	**0.01**
I use resources my rheumatology provider gives me, n (%)	3 (21%)	11 (18%)	0.7
I ask my family or friends for advice, n (%)	0 (0%)	5 (8%)	0.6
Google or another internet search engine, n (%)	12 (86%)	32 (52%)	**0.03**
Social media, n (%)	4 (29%)	3 (5%)	**0.02**
Support groups, n (%)	2 (14%)	2 (3%)	0.2
Other, n (%)	0 (0%)	2 (3%)	1

*Not all respondents answered every question. Percentages reflect the proportion of respondents who answered that individual question (blank answers are excluded).

Survey responses based on self-reported medication adherence (>80% adherent vs. <80% adherent).

Conclusion: The majority of patients taking rheumatic medications are primarily interested in learning about how their medications work and potential side effects, regardless of how long they have been taking rheumatic medications or how adherent they are to their rheumatic medications. Non-adherent patients are more likely to seek out this information through internet searches and social media, rather than asking their rheumatologist directly. These data are crucial for designing quality improvement initiatives to improve patients' knowledge and adherence when taking rheumatic medications.

Disclosure: L. Eder: None; **K. Sun**: AstraZeneca, 6; **S. Bracken**: None; **A. Barr**: None; **J. Shen**: None; **D. Cintron**: None; **M. Maheswaranathan**: AstraZeneca, 2; **C. Sims**: None; **P. Apte**: None; **M. Milne**: None; **N. Harris**: None; **D. Leverenz**: Pfizer, 5, Rheumatology Research Foundation, 5, Sanofi, 2.

Abstract Number: 1097

Improving Vaccine Uptake of the Pneumococcal 20-valent Conjugate Vaccine (PCV20) in Young Rheumatic Disease Patients Using a Brief Intense Partnership Program

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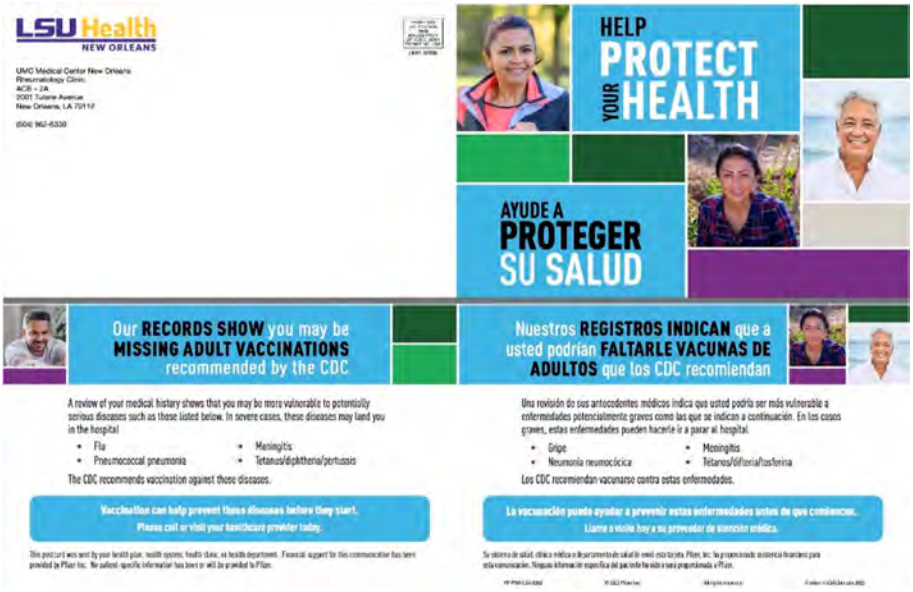
SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with inflammatory rheumatic diseases (IRDs) are at increased risk of infection. The Centers for Disease Control and Prevention (CDC) and the ACR strongly recommend vaccination to decrease risk of invasive Streptococcus pneumoniae infections. Vaccine hesitancy is common, has multiple causes, and made more evident by the recent pandemic. Younger adults ages 19-64, including those with IRDs, have reduced pneumococcal vaccine uptake even though it has been recommended for them since 2012. Recent CDC data from 2020 shows 67% of patients 65 years of age and older have the pneumococcal vaccination, but only 23.9% of patients ages 19-64. The objective of this project was to increase pneumococcal vaccination uptake in our high-risk patients in the 19-64 age range, in accordance with recommendations regarding the newer PCV20 vaccine. We hypothesized that using a targeted intense outreach strategy would increase vaccine uptake compared to the current standard of care.

Methods: The Vaccine Brief Intense Partnership (V-BIP) Program was created and started in January 2023. The program included a partnership between our clinic and industry. The target intervention population was identified by electronic health records. We identified unvaccinated patients seen in the University Medical Center- New Orleans Rheumatology Clinic January 2022- January 2023, ages 19-64. All patients without vaccination documentation were contacted using an automated call system and post cards were sent to their homes alerting them of their need to update their vaccinations. Post cards were mailed February and patient calls started March 2023. Number of calls and patient's responses to call attempts are tracked, along with vaccination uptake in the original cohort from January- June 2023.

Results: Of the 1,464 rheumatology patients seen in that year ages 19-64, 580 or 39.6% were unvaccinated. Of the 580 unvaccinated patients, 138 or 26% have been successfully vaccinated within the first 4 months of the V-BIP quality improvement program. This represents a 10% increase in the receipt of the PCV20 vaccine in our 19-64 cohort. The entire automated vaccine promotion message was listened to by 65% of patients. Of postcards mailed, few were returned undeliverable. Increased awareness was discussed with providers, but no changes to the ongoing Epic Best Practice Advisory were made.



Conclusion: Our data demonstrates a significant increase in pneumococcal vaccination after a 4-month intervention of the V-BIP quality improvement project. The V-BIP program provided multi-point patient contact and information delivery, providing additional interaction with patients to increase awareness and the opportunity to schedule a vaccination appointment. The program will extend to the end of 2023. The project supports that partnerships with other entities, in addition to industry, such as specialty pharmacies, PBMs, and other organizations should be explored as ways to improve quality of care.

Disclosure: K. Pasch: None; **S. Lindsey**: None; **T. Ferguson**: None.

Abstract Number: 1098

Improving Osteoporosis Screening in Patients with Polymyalgia Rheumatica and Giant Cell Arteritis

Kelly Tran[1], Ellen Ann Sockman[1], Rachel Salyer[1], Megan Young[1], Aisha Abbasi[1] and Devanshu Verma[2], [1]West Virginia University Hospital, Morgantown, WV, [2]West Virginia University, Morgantown, WV

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoporosis is a medical condition associated with decreased bone mass and bone architecture, which increases incidence of fragility fractures(4). It is associated with 1.5 million fractures in the United States annually and thus a major public health concern(1). Osteoporosis most often occurs in post-menopausal women; however autoimmune diseases and glucocorticoid treatment are also independent risk factors(2). Glucocorticoids remain the main treatment for giant cell arteritis (GCA) and polymyalgia rheumatica (PMR), and typically at high doses with an extended period of exposure.

Table 1.

Variables	Pre n=87	Post n=34	p-value
Age: mean (range)	72.6 (51-91)	71.4 (50-90)	0.512
Gender: n (%) Female Male	 51 (58.6) 36 (41.4)	 22 (64.7) 12 (35.3)	 0.680
Diagnosis: n (%) GCA PMR GCA/PMR	 12 (13.8) 9 (10.3) 66 (75.9)	 9 (26.5) 2 (5.9) 23 (67.6)	 0.235
Appropriate screening with DEXA scan: n (%)	50 (57.5)	24 (70.6)	0.217
Tobacco Use History: n (%)	33 (37.9)	9 (26.5)	0.291
Alcohol Use History: n (%)	25 (28.7)	2 (5.9)	0.003
Inclusion criteria*	Patients with GCA/PMR or both, those on prednisone treatment of at least 7.5 mg/day for duration of greater than 3 months		
Exclusion criteria *	Patients with GCA/PMR or both, those on prednisone treatment of less than or equal to 7.5 mg/day or duration less than or equal to 3 months		

Prolonged use of glucocorticoids induces a low bone turnover state causing more pronounced impact on the synthesis rather than the resorption, leading to net loss of bone strength(5). Thus, high and prolonged doses of glucocorticoid treatment in GCA/PMR substantially increases the risk of fractures (3,5). Current guidelines for osteoporosis screening for patients on glucocorticoid treatment were published by the American College of Rheumatology (ACR). Nevertheless, rheumatologists and primary care providers often defer responsibility to one another or to other parties, leading to a lack of osteoporosis screening in GCA/PMR patients(5).This project aimed to increase the rate of ordering recommended screening for osteoporosis by at least 10% in patients diagnosed with GCA/PMR within the West Virginia University hospital system who have been treated with high dose glucocorticoids.

Methods: Patients (n=87) diagnosed with GCA/PMR and treated with high dose of glucocorticoids (≥ 7.5 mg of prednisone for greater than 3 months) were identified via chart review from 06/24/2020 to 12/13/2021. All patients with GCA/PMR included in our study met ACR diagnostic criteria. The number of DEXA scans ordered for patients diagnosed with GCA/PMR was measured pre-intervention. The PDSA (plan-do-study-act) model was then used to implement a quality improvement (QI) initiative at the provider level, which included provider education (email and verbal) coupled with an EPIC best practice alert for this specific patient population. The number of DEXA scans ordered was assessed two months after QI implementation in post-intervention patients (n=34).

Results: Only 57.5% of pre-intervention patients (n = 87, 72.6 ± 8.4 years old) had an appropriate screening completed with a DEXA scan. Within two months after QI implementation, the screening rate in post-intervention patients (n=34, 71.4 ± 9.2 years old) increased to 70.6% (p = 0.217).

Conclusion: Screening for osteoporosis is an important preventive measure for GCA/PMR patients, especially those on high doses of glucocorticoids. Our study demonstrates an improvement in DEXA screening rates by 13.1% over a period of two months by implementing reminders and education for providers in both rheumatology clinics and primary care clinics settings. Future implementation could be expanded at the patient level, through education and sending reminders to discuss the appropriateness of osteoporosis screening with their providers.

Disclosure: K. Tran: None; **E. Sockman**: None; **R. Salyer**: None; **M. Young**: None; **A. Abbasi**: None; **D. Verma**: None.

Abstract Number: 1099

Improving Hydroxychloroquine Dosing and Eye Screening Compliance in Patients with Connective Tissue Disorder

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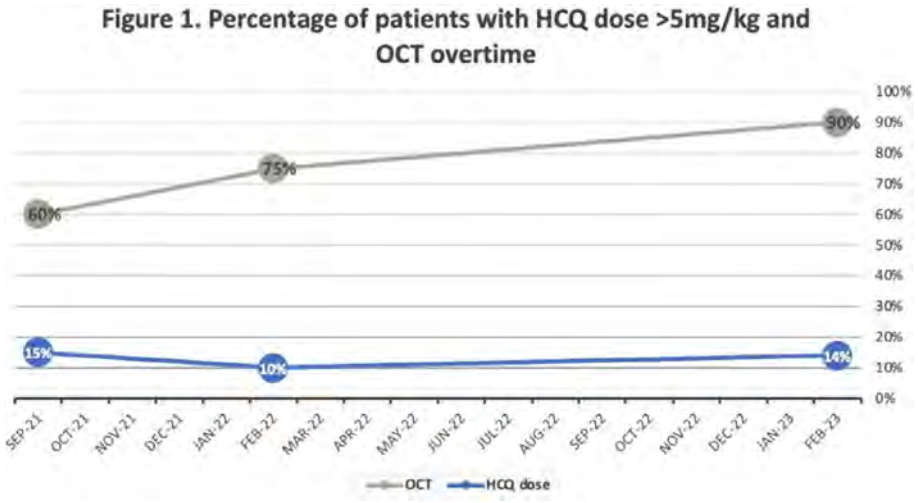
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) is a key treatment for patients with lupus and other rheumatic diseases. To minimize the risk of retinal toxicity, the American College of Ophthalmology (ACO) guidelines published in 2016 recommends using a maximum HCQ daily dose of ≤5mg/kg of actual body weight and to begin annual retinopathy screening after 5 years of HCQ use with automated visual fields plus optical coherence tomography (OCT). The aim of this quality



Percentage of patients with HCQ dose >5mg/kg and OCT overtime

improvement project was to assess if an educational intervention could improve the adherence to ACO dosing recommendations and retinal toxicity monitoring in a large VA Medical Center.

Methods: Patients above 18 years old with a connective tissue disorder diagnosis and who were actively using HCQ were evaluated. HCQ dosing above 5 mg/kg, and eye screening status were reviewed. Two different interventions were implemented twelve months apart: 1) An educational intervention using a personal email with the ACO guidelines was sent to each provider with patients requiring screening testing or HCQ dose adjustment. 2) Second intervention using a "system alert" in the medical record with the correct HCQ dosing and annual OCT was created as a reminder when prescribing or renewing HCQ. Changes in compliance from pre- to post-interventions were assessed.

Results: A total of 258 patients with an active HCQ prescription were included. Forty patients (15%) had a HCQ dose above 5mg/kg. Among this group, HCQ was mainly prescribed by a Rheumatologist (35/40).From the forty patients with HCQ dose above 5mg/kg, 24 (60%) had at least one OCT screening. After the first intervention, the number of patients who required HCQ dose adjustment went down by 5% (15% vs 10%). Most of the patients who required HCQ dose adjustment were receiving a HCQ dose between 5-5.9 mg/kg (60%). More patients had an updated OCT (75% post vs 60% pre). After the second intervention, the number of patients who required HCQ dose adjustment went up by 4%. However, more patients had an updated OCT (90% post vs 75% pre) (Figure).

Conclusion: Educational interventions, including the review of guidelines, or system alerts on different medical records were associated with a notable improvement in retinal toxicity screening but had modest or no effect on adherence to ACO HCQ dosing recommendations.

Disclosure: M. Salgado Guerrero: None; **A. Gaffo**: None.

Abstract Number: 1100

A Comparison of Characteristics of Patients with Crystalline and Septic Arthritis Confirmed by Synovial Fluid Analysis: Towards the Development of a Diagnostic Rule

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Distinguishing crystalline from septic arthritis is a common challenge in patients admitted with acute joint inflammation. Arthrocentesis for synovial fluid analysis is considered the gold standard for both entities, but it is not always available. The aim of this study was to compare the demographic, clinical, and laboratory characteristics of patients admitted with septic and crystalline arthritis confirmed by synovial fluid analysis to identify factors to develop a diagnostic rule.

Methods: Our study population consisted of patients admitted to our institution between 1999-2020 with the diagnosis of gout, pseudogout and septic arthritis identified using ICD9 and 10 codes. We reviewed medical records and included those with diagnoses confirmed by synovial fluid analysis. Demographic data including sex, race, body mass index, comorbidities, distribution of affected joints, physical exam characteristics, medications, and laboratories including estimated glomerular filtration rate, white cell and neutrophil count, inflammatory markers, and serum urate were recorded. We summarized continuous variables with medians and interquartile ranges (IQR) and categorical variables with frequencies and proportions. We used Wilcoxon rank sum and Fisher's exact test to analyze for differences between the septic and crystalline groups. We considered significant a p value of < 0.05, but we further adjusted the assessment of significance for multiple comparisons using the Bonferroni correction. All analysis was completed using R studio.

Results: Of the 256 patients identified, 51 had a diagnosis of septic arthritis and 205 a diagnosis of crystalline arthritis. Two hundred and fifty-four (99%) were men, one hundred forty-four (60%) were African-American, and ninety-six (40%) self-identified as White. The median duration of symptoms was 4 days. Compared to patients with crystalline arthritis, septic arthritis patients were more commonly of White race (Table) (54 vs 36% p=0.02), had longer symptom duration (median of 5 versus 3 days, p=0.002), tended to have fewer joints affected (p=0.001), had higher proportion of involvement of elbows (24 vs 12%) and hips (8 versus 1%), and lower proportion of knee involvement (55 versus 76%). Patient with septic arthritis had more joint erythema (47 versus 29%) but less joint swelling (84 versus 96%) and had higher proportions of history of prior surgery in the affected joint (29% vs. 3%, $p< 0.001$), and involvement of a prosthetic joint (22% vs. 0%, $p= < 0.001$). Absolute leukocyte counts and neutrophil counts were higher in patients with septic arthritis. After adjustment for multiple comparisons only the proportion of prior surgery and involvement of a prosthetic joint met the more stringent significance threshold.

Conclusion: History of prior surgical intervention in the affected joint, and prosthetic joint were strongly associated with septic arthritis. Many other demographic, clinical, and laboratory factors were also different between patients with septic and crystalline arthritis. Future steps will include the development of a prediction model for septic and crystalline arthritis when synovial fluid analysis is not available.

Table 1. Demographic and Clinical Characteristics of Patient with Acute Crystalline Arthritis and Septic Arthritis in the Inpatient Setting Prior to Joint Fluid Analysis

	All	Septic	Crystalline	p value**
	n = 256	n = 51	n = 205	
Demographics				
Male sex, n (%)	254 (99)	51 (100)	203 (99)	1
Age at presentation, median (IQR), years	67 (58-76)	65 (56-73)	67 (57-76)	0.1
Race / Ethnicity, n (%)				
Black or African American	144 (60)	22 (44)	122 (64)	0.02
White	96 (40)	27 (54)	69 (36)	0.02
American Indian or Alaska Native	1 (0.4)	0	1 (0.5)	1
Hispanic	0	0	0	
BMI, median (IQR), kg/m2	28 (24-32)	30 (25-36)	28 (24-32)	0.07
Clinical presentation				
Symptom duration, median (IQR), days	4 (1.5-6.5)	5 (0.5-10)	3 (5.5-28)	0.002
Number of joints affected, n (%)	1 (0.5-1.5)	1 (1-1)	1 (0.5-1.5)	0.01
Joint affected, n (%)				
Hand/Wrist	40 (15)	4 (8)	36 (18)	0.13
Elbow	37 (15)	12 (24)	25 (12)	0.05
Shoulder	8 (3)	2 (4)	6 (3)	0.66
Hip	6 (2)	4 (8)	2 (1)	0.02
Knee	183 (72)	28 (55)	155 (76)	0.01
Foot/Ankle	57 (22)	10 (20)	47 (23)	0.71
Symptoms / signs, n (%)				
Swelling	238 (93)	43 (84)	195 (96)	0.02
Erythema	85 (33)	24 (47)	61 (29)	0.04
Limited ROM	28 (5)	23 (45)	105 (52)	0.44
Fever	39 (15)	10 (20)	29 (14)	0.38
Tophi	7 (3)	0 (0)	7 (3)	0.35
Comorbidities, n (%)				
Gout	131 (51)	20 (39)	111 (54)	0.06
Pseudogout	4 (2)	1 (2)	3 (2)	0.59
Diabetes mellitus	96 (38)	22 (43)	74 (36)	0.42
Hypertension	206 (81)	37 (73)	169 (82)	0.12
Congestive heart failure	60 (23)	9 (18)	51 (25)	0.36
Hyperlipidemia	122 (48)	20 (39)	102 (50)	0.21
Dialysis	12 (5)	7 (14)	5 (2)	0.003
Past surgical history, n (%)				
History of prior surgery in affected joint	21 (8)	15 (29)	6 (3)	p<0.001
Prosthetic joint	11 (4)	11 (22)	0 (0)	p<0.001
Medications, n (%)				
Diuretics	133 (44)	14 (28)	99 (48)	0.007
Glucocorticoids	24 (9)	7 (14)	17 (8)	0.28
Other immunosuppressive therapy*	14 (6)	4 (8)	10 (5)	0.49
Laboratory results				
WBC, median (IQR),mg/dL	9.1 (6.6-11.6)	10 (6-13.9)	8.8 (6.6-11)	0.009
WBC > 10K, n (%)	85 (39)	26 (53)	59 (35)	0.03
Neutrophil count, median (IQR), mg/dL	6 (4.2-7.8)	6.8 (5-8.6)	5.8 (4-7.5)	0.05
C-reactive protein, median (IQR), mg/L	10.5 (3-18.5)	14.8 (2-26.8)	8.5 (2.1-14.9)	0.07
ESR, median (IQR), mm/hr	55 (22-88)	68 (30-105)	51 (23-79)	0.11
GFR by CKD EPI, median (IQR), mL/min/1.73r	70 (43-96)	65 (33-97)	70 (44-96)	0.84
GFR by CKD EPI <30 mL/min/1.73m2, n (%)	33 (13)	9 (18)	24 (12%)	0.35
Serum urate, median (IQR), mg/dL	7.9 (6.2-9.6)	6.3 (4.6-7.9)	8 (6.3-9.7)	0.09

* Other than glucocorticoids such as methotrexate, azathioprine, rituximab, mycophenolate mofetil, cyclosporine, tacrolimus, cyclophosphamide, and any chemotherapy for cancer treatment.

**p value threshold adjusted for multiple comparisons 0.0013

Abreviations: BMI, body mass index; WBC, white cell count; CKD EPI, Chronic Kidney Disease Epidemiology Collaboration equation , ESR = sedimentation rate

Demographic and Clinical Characteristics of Patient with Acute Crystalline Arthritis and Septic Arthritis in the Inpatient Setting Prior to Joint Fluid Analysis

Disclosure: M. Salgado Guerrero: None; **M. Urquiaga**: None; **N. Panchani**: None; **A. Gaffo**: None.

Abstract Number: 1101

Systemic Inflammation Associated with Silent Deposition of Monosodium Urate Crystals in Asymptomatic Hyperuricemia

Maria-Luisa Peral-Garrido[1], Paula Boix-Navarro[2], Silvia Gómez-Sabater[3], Rocío Caño-Alameda[3], Alejandra Bermúdez-García[4], Teresa Lozano[4], Ruth Sanchez-Ortiga[4], Miguel Perdiguero[4], Elena Caro-Martínez[5], Carolina Ruiz-García[6], Eliseo Pascual[4], Rubén Francés[2] and **Mariano Andrés**[4], [1]Vinalopó University Hospital, Novelda, Spain, [2]Miguel Hernandez University, San Juan de Alicante, Spain, [3]Rheumatology Department, Dr. Balmis University General Hospital, Alicante. Institute for Health and Biomedical Research (ISABIAL), Alicante, Spain, [4]Dr Balmis Alicante General University Hospital-ISABIAL, Alicante, Spain, [5]San Vicente Hospital-HACLE, San Vicente del Raspeig, Spain, [6]Campoamor Health Centre, Alicante, Spain

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Whether the presence of subclinical monosodium urate (MSU) crystal deposition leads to a pro-inflammatory state in asymptomatic hyperuricemia (AH) is unknown. We aimed to compare the inflammatory state in peripheral blood between AH patients with and without sonographic deposits.

Methods: Observational, cross-sectional study. Patients with current serum urate ≥7 mg/dl and no history of acute arthritis were consecutively recruited from internal medicine, cardiology, nephrology, endocrinology, rheumatology, and primary care. We excluded those on urate-lowering treatment or colchicine, another inflammatory rheumatic disease, or being under immunosuppressive therapy (including transplants).

Two comparative groups were predefined. ***Group 1***: **AH without deposits**; and ***Group 2***: **AH with deposits**. As sonographic deposits, we considered grade 2-3 double-contour sign and/or tophus according to 2021 OMERACT definitions[1], after a 10-location scanning (knees, tibiotalar joints, 1st and 2nd metatarsophalangeal joints, patellar and Achilles tendons) by a trained sonographer blinded to clinical and laboratory data. We measured serum levels of high-sensitivity C-reactive protein (hsCRP) in mg/dl (by immunoturbidimetry), serum amyloid-A in ng/ml (by nephelometry), and erythrocyte sedimentation rate (ESR) in mm/1h, as acute phase reactants. Later, using commercial ELISA kits, we analyzed: ***i)*** inflammasome

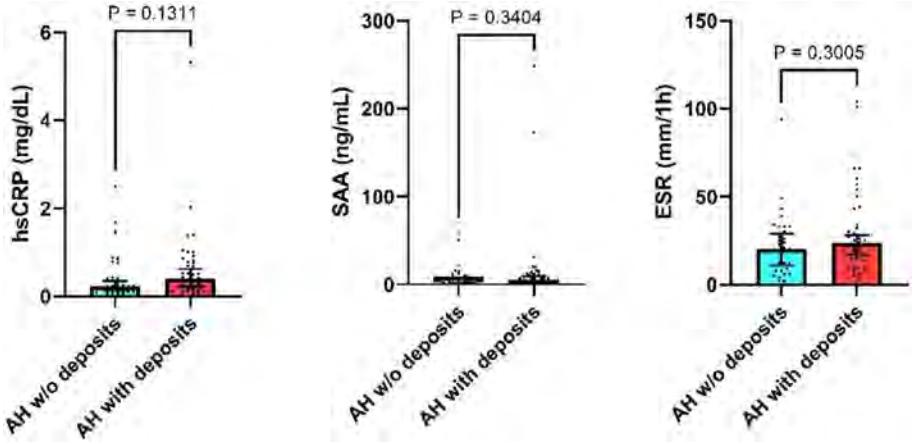


Figure 1. Comparison of acute phase reactants between groups of asymptomatic hyperuricemia. Bars show medians with their 95% confidence intervals. hsCRP: high-sensitivity C reactive protein; SAA: serum A-amyloid protein; ESR: erythrocyte sedimentation rate.

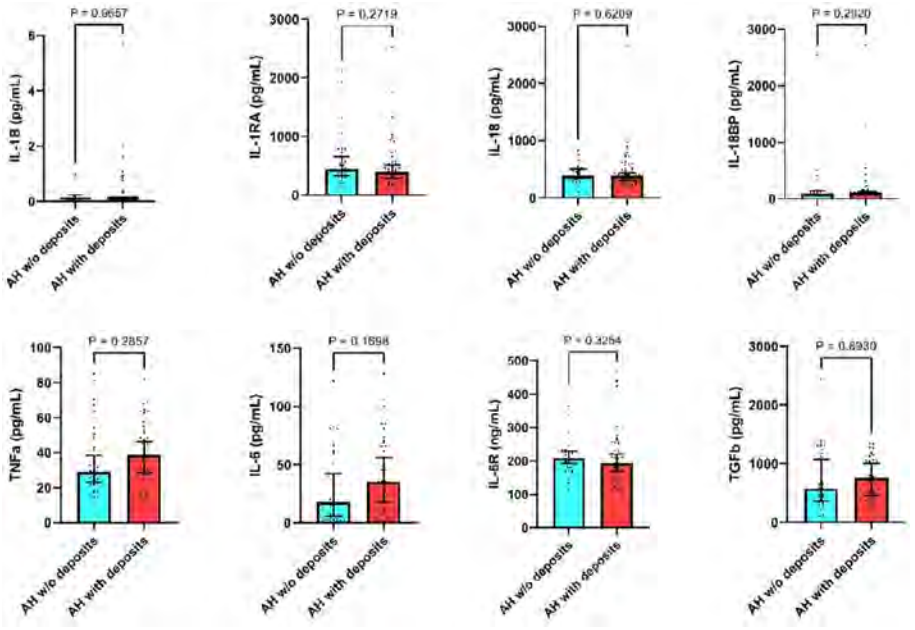


Figure 2. Comparison of cytokines between groups of asymptomatic hyperuricemia. Bars show medians with their 95% confidence intervals. IL-1β: interleukin-1β; IL1-1RA: IL-1 receptor antagonist; IL-18: interleukin-18; IL-18BP: IL-18 binding protein; TNF-α: tumor necrosis factor-α; IL-6: interleukin-6; sIL-6R: soluble IL-6 receptor; TGF-β: transforming growth factor-β.

NLRP3-related cytokines: interleukin **(IL)-1β**, IL-1 receptor antagonist (**IL-1RA**), **IL-18**, IL-18 binding protein (**IL-18BP**); and ***ii)*** general pro-inflammatory and anti-inflammatory cytokines: tumor necrosis factor **(TNF)-α**, **IL-6**, soluble IL-6 receptor (**sIL-6R**), and transforming growth factor **(TGF)-β.**

GraphPad Prism (version 9.5.1) was used to compare AH groups, through Mann-Whitney U's and Chi^2 tests.

Results: 77 subjects with AH were recruited, 71.4% men, with a mean age of 59.8 years (SD 17.3) and body mass index (BMI) of 31.2 kg/m^2 (SD 5.2). 37.7% and 29.9% had cardiovascular (CVD) and renal disease, respectively. Their mean uric acid was 7.6 mg/dl (SD 1.6).

Patients were classified into **group 1** (n=35, 45.5%) or **group 2** (n=42, 54.5%). There were no differences (group 2 vs. group 1) in age (67 vs. 56 years), men (69% vs.74.3%), BMI (31.7 vs. 29.9 kg/m^2), CVD (38.1% vs. 37.1%), estimated glomerular filtration rate (73.42 vs. 75.03 ml/min/1.73m^2), or current serum urate levels (7.35 vs. 7.40 mg/dl). The results of inflammatory markers and cytokines are presented in ***Figures 1 and 2***. There were no differences between groups, but we observed numerical differences for hsCRP, IL-6, and TNF-α.

Conclusion: The inflammatory state was comparable in AH between those with and without sonographic deposits. Some hints were noted for hsCRP, IL-6, and TNF-α that further studies with larger sizes must confirm to establish the relevance of subclinical crystal deposition in AH.

Reference: [1] Christiansen SN. Semin Arthritis Rheum. 2021;51:644.

Disclosure: M. Peral-Garrido: None; **P. Boix-Navarro**: None; **S. Gómez-Sabater**: None; **R. Caño-Alameda**: None; **A. Bermúdez-García**: None; **T. Lozano**: None; **R. Sanchez-Ortiga**: None; **M. Perdiguero**: None; **E. Caro-Martínez**: None; **C. Ruiz-García**: None; **E. Pascual**: None; **R. Francés**: None; **M. Andrés**: None.

Abstract Number: 1102

Finding Lost-to-Care Gout Patients in a Large Community Rheumatology Network: Patient Re-engagement Initiative with Metrics (PRIME)

Amy S. Mudano[1], Jessica Ryan[1], Emily Holladay[2], Kathleen Methric[3], Danielle Grauer[4], Brian LaMoreaux[3], Fenglong Xie[1] and **Jeffrey R Curtis**[5], [1]Illumination Health, Hoover, AL, [2]University of Alabama at Birmingham, Birmingham, AL, [3]Horizon Therapeutics, Deerfield, IL, [4]Illumination Health, Boca Raton, FL, [5]Division of Clinical Immunology and Rheumatology, University of Alabama, Birmingham, AL

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Treatment of patients with gout can be complex and, given the episodic nature of gout attacks, gout patients may not always return for regular appointments, making long-term management and fostering medication adherence more difficult.We sought to identify and describe patients with gout who were lost-to-care in the Excellence Network in RheumatoloGY (ENRGY), a large community rheumatologist practice-based research network,as preparatory to an intervention to re-engage these patients in care.

Methods: We conducted a retrospective analysis of gout patients who had at least one rheumatology visit from 01/01/2020 to 05/31/2022 using electronic health records (EHRs). Eligible patients meeting our definition of presumed lost-to-follow-up must have >1 ICD10 gout diagnosis (M10* or M1A*), previous use of gout medications (e.g.allopurinol and febuxostat), most recent rheumatology visit >365 daysprior,and no future visit scheduled. We analyzed demographics for the eligible cohort and stratified by the most recent serum urate (SU) value (if available) using descriptive statistics. Serum urate value of ≤6 mg/dL indicated that the gout treatment target was achieved. A scatter plot shows the distribution of patients by rheumatology office and last SUvalue.

Results: From a total of 52,504 gout patients who had a specialist gout visit since 1/1/2020, we identified 25,421(48%) gout patients from 201 sites nationwide (Figure 1) who had not been seen in a year or more. After limiting to patients without a future appointment scheduled (98%) and those who had been on therapy (80%), there were 19,883 (38% of the overall cohort) patients that met all inclusion criteria for being lost-to-care. Patients were mostly male (74%), white (66%), with a

Table 1: Baseline Demographics

	Cohort	Last SUA ≤6 mg/dL	Last SUA >6 mg/dL	Labs not available	
N	19883	9022	5473	5388	p-value
Age, Years, Mean (SD)	65.0 (14.2)	66.2 (13.4)	61.7 (14.8)	66.3 (14.2)	<.0001
White, N (%)	15106 (66)	6171 (68)	3408 (62)	3527 (66)	<.0001
Male, N (%)	14765 (74)	6594 (73)	4197 (77)	3974 (74)	<.0001
BMI, N (%)					<.0001
<25	1996 (11)	957 (11)	479 (9)	560 (12)	
25 to <30	5657 (30)	2752 (32)	1417 (27)	1488 (31)	
30 to <35	5560 (30)	2550 (29)	1595 (30)	1415 (29)	
35 to <40	3104 (17)	1388 (16)	941 (18)	775 (16)	
≥40	2537 (14)	1089 (13)	860 (16)	588 (12)	
Tophi, N (%)	1069 (5)	445 (5)	334 (6)	290 (5)	0.01
Medication Use Ever, N (%)					
Allopurinol	17849 (90)	8073 (89.5)	4961 (90.6)	4815 (89.4)	0.04
Colchicine	10861 (55)	5003 (56)	3460 (63)	2398 (45)	<.0001
Febuxostat	3767 (19)	1748 (19)	1153 (21)	866 (16)	<.0001
Pegloticase	419 (2)	204 (2)	175 (3)	40 (1)	<.0001
Probenecid	296 (2)	130 (1)	111 (2)	55 (1)	<.0001
Lesinurad	22 (0.1)	12 (0.1)	5 (0.1)	5 (0.1)	0.76
Serum Urate, mg/dL, Mean (SD)	6.1 (9.7)	4.6 (9.8)	8.6 (15.4)	NA	<.0001
Days since last visit, Median (IQR)	749 (529, 964)	728 (502, 944)	740.0 (537, 964)	781 (560, 999)	<.0001

SD = standard deviation, BMI = body mass index, IQR = interquartile range.

mean (SD) age of 65(14.2) (Table 1). In patients where structured SU lab data was available (73% of the lost-to-care cohort), 38% were poorly controlled at their last visit (SU >6). The median (IQR) days since the most recent rheumatology provider visit was 749 (529, 964) days. Gout with tophi was coded in about 5% of patients and was slightly higher in the SUA >6 group. The scatter plot (Figure 2) shows the difference in distribution patterns among practices of patients who may have met their treatment target (SU<6) compared to those whose last SU was greater than 6.

Figure 1: Attrition Flowchart describing gout patients potentially lost to follow-up

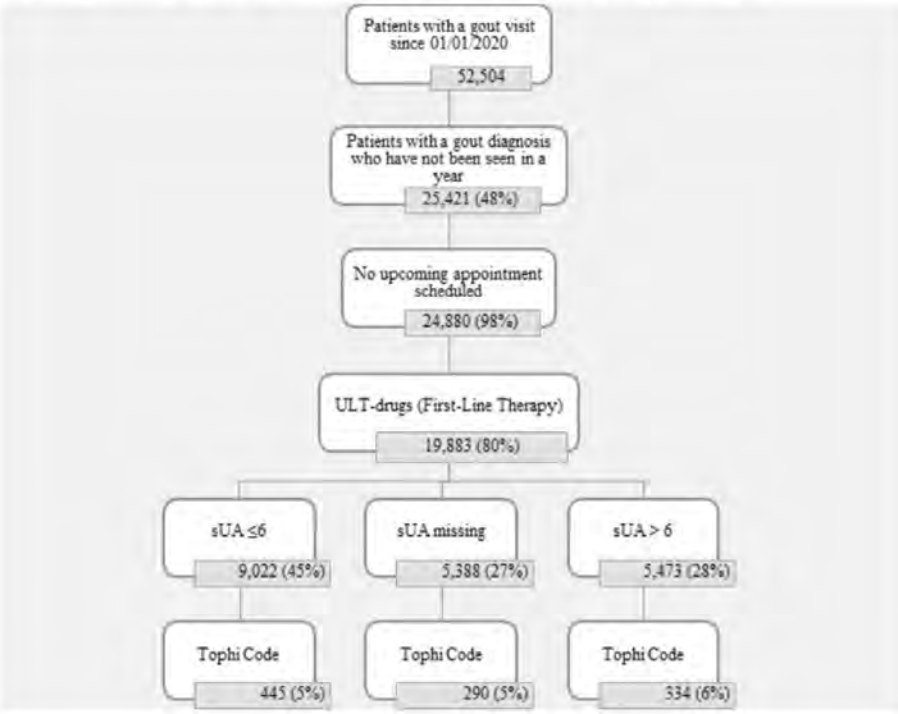
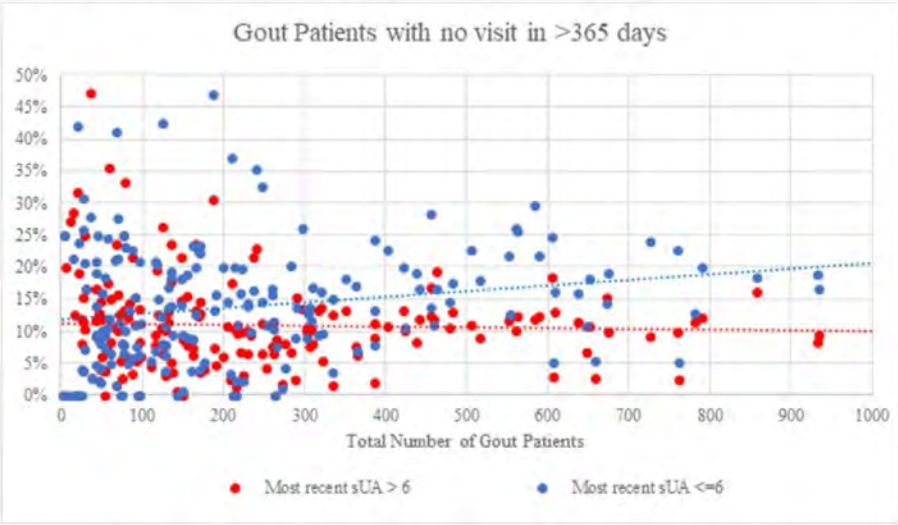


Figure 2: Clustering of gout patients by provider describing proportion who were well controlled (sUA <=6 vs. >6) at the time of their last lab test (n=192 providers). Each rheumatology provider contributed 2 dots to the scatterplot, one for the proportion of patients with the most recent sUA >6mg/dL, and a second for the proportion of their patients <=6mg/dL.



Conclusion: In this large community practice-based rheumatology network, a meaningfully large proportion of gout patients appeared lost to care. Many of these patients were sub-optimally controlled (SU >6 mg/dL) at their last rheumatologist visit, suggesting that they may benefit from further rheumatology involvement. A quality improvement initiative is in development to better understand these patients' gout care needs and offer them an expedited visit with their rheumatology provider to re-engage them in care and potentially improve outcomes.

Disclosure: A. Mudano: None; **J. Ryan**: None; **E. Holladay**: None; **K. Methric**: Horizon Therapeutics, 3, 11; **D. Grauer**: cardinal health, 8; **B. LaMoreaux**: Horizon Therapeutics, 3, 11; **F. Xie**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, BMS, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Genentech, 2, 5, Janssen, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB Pharma, 2, 5.

Abstract Number: 1103

Evaluation of Outcomes Following Discontinuation of Pegloticase Therapy

Emily Holladay[1], Amy S. Mudano[2], Fenglong Xie[2], Jingyi Zhang[1], Ted R Mikuls[3], Brian LaMoreaux[4], Lissa Padnick-Silver[4] and Jeffrey Curtis[1], [1]University of Alabama at Birmingham, Birmingham, AL, [2]Illumination Health, Hoover, AL, [3]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE, [4]Horizon Therapeutics, Deerfield, IL

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Little is known about the long-term effects of pegloticase therapy or what urate-lowering therapy (ULT) patients subsequently receive when they discontinue pegloticase. This analysis examined alternative ULT use, serum urate (SU) changes, systemic inflammatory measures, and renal function following pegloticase discontinuation.

Methods: We conducted a retrospective analysis of gout patients discontinuing pegloticase using the ACR's Rheumatology Informatics System for Effectiveness (RISE) registry from 01/2016 through 06/2022. We defined pegloticase discontinuation as a gap ≥12 weeks after a pegloticase infusion. We examined outcomes beginning two weeks after the last dose of pegloticase (defined as the 'index date'), an interval selected based on its typical every other week dosing schedule. Changes in lab values (treatment effect) following pegloticase discontinuation were examined by comparing measurements obtained within 15 days of the second pegloticase dose and those obtained after pegloticase discontinuation. We analyzed changes in SU, eGFR, CRP, and ESR using descriptive statistics. A Sankey plot was used to describe ULT medication use after the index date, and Kaplan Meier curves assessed the probability of starting post-pegloticase ULT over time.

Results: We identified 375 patients with gout who discontinued pegloticase and had paired labs. We observed lab changes in patients who discontinued pegloticase with median (IQR) differences of SU: 2.4 mg/dL (0.0, 6.3); eGFR: -1.9 mL/min (-8.7, 3.7); CRP: -0.8 mg/L (-12.8, 0.0); and ESR: -4.0 mm/hr (-13.0, 0.0), compared to pre-discontinuation values.

Of those who discontinued pegloticase, 83% started other ULTs (Figure 1), and 8% restarted pegloticase. Of those that started oral ULTs, 63% began allopurinol and 34% began febuxostat. The time to starting (or restarting) ULT is shown in Figure 2. With SU measured at least >=30 days following ULT start, 53% of patients had an SU ≤6 mg/dL with a median SU of 5.8 mg/dL (IQR: 3.6, 8.4).

After starting a new ULT, post-ULT median (IQR) SU values were 5.8 (4.7, 7.0) and,5.8 (4.5, 7.9) mg/dL for users of allopurinol and febuxostat, respectively. In contrast, patients who restarted pegloticase achieved a median SU of 0.9 mg/dL (IQR: 0.2, 9.7) after a median of 156 days (IQR: 131.0, 609.0) since prior discontinuation.

Figure 1: ULT Initiation Over Time After Pegloticase Discontinuation

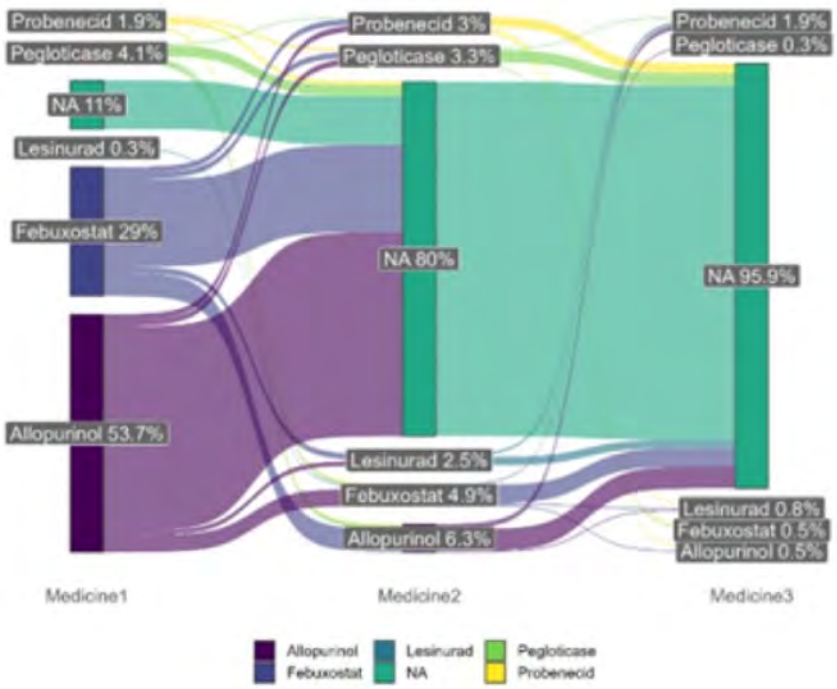
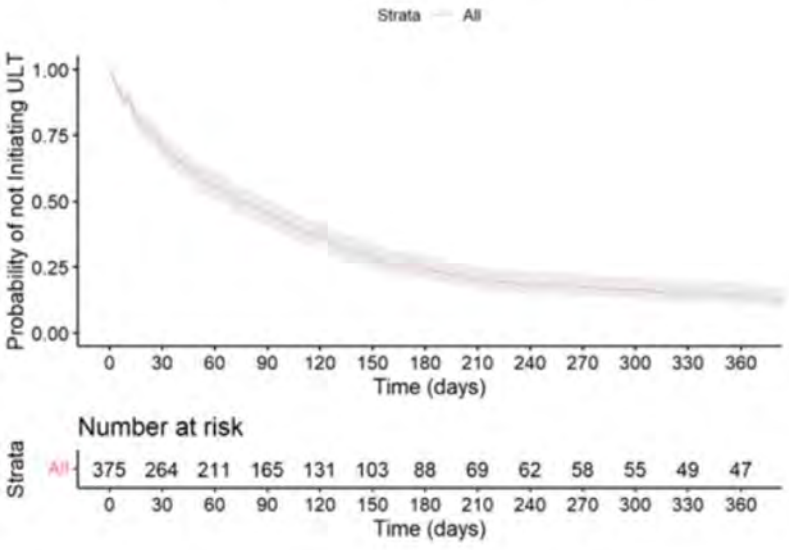


Figure 2: Probability of Not Restarting a ULT* after Pegloticase Discontinuation



*ULT includes pegloticase

Conclusion: Pegloticase treats uncontrolled gout in patients who fail to respond to xanthine oxidase inhibitors, but the development of anti-drug antibodies, and subsequent loss of urate-lowering response may require pegloticase discontinuation. An important minority of patients fail to receive any ULT after cessation of pegloticase. Additionally, many patients who were able to restart restarting pegloticase after a prolonged gap in therapy achieved had its expected resulting SU-lowering effect with therapy even after a gap in therapy, although the context for the interruption needs to be further explored. Future studies should focus on the optimal management of gout patients who discontinue or have meaningful gaps in pegloticase treatment.

Disclosure: E. Holladay: None; **A. Mudano**: None; **F. Xie**: None; **J. Zhang**: None; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **B. LaMoreaux**: Horizon Therapeutics, 3, 11; **L. Padnick-Silver**: Horizon Therapeutics, 3, 12, Stockholder; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, 5, CorEvitas, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 1104

Dotinurad, a Potent and Selective Uricosuric Agent, Exhibited Promising Pharmacokinetics and Pharmacodynamic Profiles to Significantly Reduce Serum Urate Levels Following Once Daily Dosing in Healthy U.S. Subjects in a Phase 1 Clinical Trial

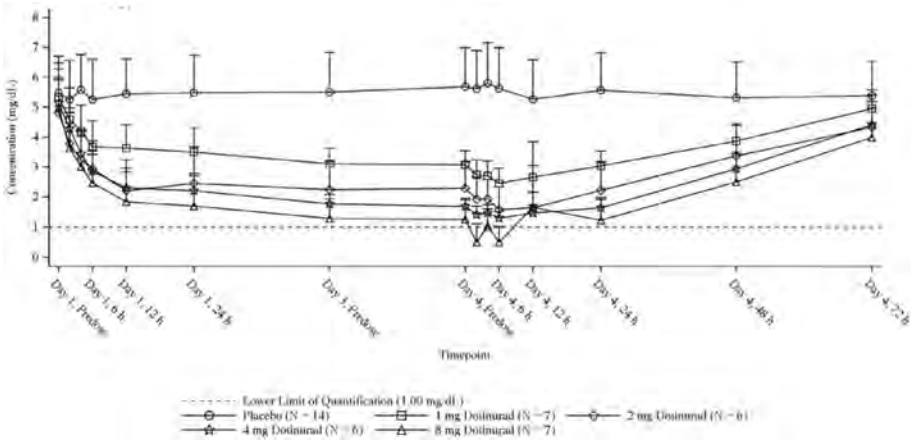
Scott Baumgartner, Raymond Zheng, Mark Harnett and **Jay Kranzler**, Urica Therapeutics Inc., New York, NY

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Dotinurad is a potent and selective URAT1 inhibitor that has been approved as a once-daily drug for the treatment of hyperuricemia with or without gout in Japan since 2020, based on results of 17 clinical trials conducted in Japan with more than 1000 patients exposed with up to 58 weeks in treatment duration. In the Japanese dossier, 4mg dotinurad reduced serum urate to < 6 mg/dL in 100% of patients after long-term treatment. No significant cardiovascular, renal or hepatic adverse events were observed with dotinurad at approved doses in the Japanese studies. This Phase 1 study is the first performed in a 'western' population, initiating the development of dotinurad for eventual use in North America and EU.

Methods: Randomized, double-blind, placebo-controlled, three-period crossover multiple-dose in 15 healthy male and female volunteers (age 18 to 55 years), doses included placebo, 1, 2, 4, and 8 mg once-daily in the morning for 4 days. Serial blood samples were collected to measure pharmacokinetic concentrations of dotinurad as well as serum and urine uric acid levels.Maximum concentration (C_{max}), area under the curve ($AUC_{0-\tau}$), half-life ($t_{1/2}$) were determined.Study drug accumulation from Day 1 to Day 4 was assessed. Safety monitoring was performed throughout.

Results: Dotinurad concentrations exhibited an increase in dotinurad exposure for AUC and C_{max} that was proportional to dose.Plasma-concentration time profiles following multiple oral doses of dotinurad were characterized by a rapid absorption phase, with median T_{max} of 2.5 to 3 hours. When normalized for dose, C_{max} was consistent across the dose range. The rate of elimination appeared to be consistent across the dose groups on Day 4, with geometric mean $T_{1/2}$ values ranging from



Mean serum urate concentrations across all days in the pharmacodynamic population

7.73 to 8.82 hours. The range of accumulation ratios for $AUC_{0-\tau}$ and C_{max} were also found to be similar across all doses administered (1.18 to 1.26 and 1.07 to 1.21, respectively), demonstrating that dotinurad shows little to no accumulation in the plasma following multiple daily dosing.

As dotinurad dose increased, a respective reduction in serum urate concentrations and overall exposure to urate was observed. Steady state of reduced serum urate levels was achieved in day 3. Up to 90% sUA reduction from baseline was observed with dotinurad treatment.

Dotinurad was well tolerated with no observed serious adverse event. No treatment related adverse event was observed with 1-4 mg of dotinurad.

Conclusion: Following 4 consecutive once-daily treatments, dotinurad has exhibited a pharmacokinetic profile, in western healthy subjects, comparable to that from Japanese healthy men. All tested doses of dotinurad (1, 2, 4 & 8 mg QD) significantly reduced serum urate levels. These results support the potential application of dotinurad as a once-daily treatment for hyperuricemia in western population. Another clinical study is currently underway to further establish the safety, efficacy and drug interaction of dotinurad in U.S. gout patients.

Disclosure: S. Baumgartner: Urica Therapeutics Inc., 2; **R. Zheng**: Urica Therapeutics Inc., 3; **M. Harnett**: Urica Therapeutics Inc., 2; **J. Kranzler**: Urica Therapeutics Inc., 3.

Abstract Number: 1105

Effects of Uric Acid Lowering Treatment on Vascular Stiffness in Gout Patients

Jinseok kim, Division of Rheumatology, Department of Internal Medicine, Jeju National University Hospital, Jeju National University School of Medicine, Jeju, South Korea

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Many studies have reported that gout and hyperuricemia are associated with an increase in all-cause mortality and cardiovascular mortality.Increased vascular stiffness is closely related to the occurrence of cardiovascular disease. Many studies have shown a significant correlation between uric acid levels and arterial stiffness. However, there is no study on whether vascular stiffness is improved by uric acid-lowering treatment in gout patients. Few studies have reported that uric acid-lowering treatment reduces vascular stiffness in chronic kidney disease patients. The aim of this study is to evaluate the effect of uric acid lowering treatment on vascular stiffness in gout patients.

Methods: Between June 2017 and June 2019, patients who visited Jeju National University Hospital for treatment of gout were measured for augmentation index (AIx) and follow-up to evaluate changes in vascular stiffness by uric acid lowering treatment.

Results: One hundred twenty patients participated in the study and AI was measured. At the time of the enrollment, the average age of patients was 55.1 ± 12.9 years, the mean duration of gout was 7.0 ± 6.4 years, the mean duration of uric acid lowering treatment was 27.8 ± 34.0 months, the average of uric acid level was 5.8 ± 1.9, the average of initial AIx was 22.5 ± 10.1 and the average of follow-up duration of AIx was 19.1 ± 2.1 months. When compared with the AIx improved and non-improved groups, there was a higher percentage of smokers in the improved group (16.7% vs 45.5%, p=0.007), and there was no significant difference in age, duration, and uric acid value between the two groups. However, in the group with improved AIx, the initial AIx level was significantly higher (20.6 ± 7.6 vs 26.9 ± 7.2, p< 0.001) and more people (63.6% vs 40.5%, p=0.046) had higher AIx than predicted AIx. When multivariate logistic regression analysis was performed, disease duration (b=0.714, 95% CI 0.528-0.965, p=0.029), ULT duration (b=1.059, 95% CI 1.003-1.118), smoking (109.972, 95% CI 3.693-3274.940, p=0.007) are predictor of improvement of vascular stiffness.

Conclusion: Our results show that long-term uric acid lowering treatment in patients with long gout disease duration can improve vascular stiffness.

Disclosure: J. kim: None.

Abstract Number: 1106

Monosodium Urate and Calcium Pyrophosphate Crystal-induced Inflammation Relies on Cell Volume Regulation and LRRC8/VRAC Channel Activation

Twinu Wilson Chirayath[1], mete kayatekin[2], Isabelle Rubera[3], Nghia Pham[4], FREDERIC LIOTE[4], Pascal Richette[5], Vincent COMPAN[6], François Rassendren[7], Christophe Duranton[3] and Hang Korng EA[4], [1]INSERM, Paris, France, [2]CNRS-UMR7370, Nice, France, [3]CNRS-UMR 7370, Nice, France, [4]INSERM-BIOSCAR, Paris, France, [5]Lariboisière Hospital, Paris, France, [6]CNRS-IGF, Montpellier, France, [7]CNRS UMR 5203, Montpellier, France

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Monosodium urate (MSU) and calcium pyrophosphate (CPP) crystals are responsible for interleukin (IL)-1β dependent acute arthritis. The release of mature IL-1β is dependent on the NLRP3 inflammasome, which can be activated by other sterile stimuli such as hypo-osmolarity and ATP. During extracellular hypotonic stress, there is cellular swelling secondary to water influx. The cell sets up a defence mechanism, called regulatory volume decrease (RVD), allowing it to

return to its initial volume. RVD depends on the anion channel VRAC, a hetero-hexamer composed of members of the LRRC8 family. LRRC8A is the obligatory key protein required to form active VRAC channel. Activation of LRRC8/VRAC channel results in an efflux of anions (mainly chloride) and **osmolytes** leading to water efflux and cell volume reduction. We evaluate the role of the LRRC8/VRAC channel in cell volume regulation and IL-1β release induced by MSU and CPP crystals.

Methods: In-vitro, primed THP-1 monocytes were stimulated by synthetic sterile MSU and CPP and cytokine production was quantified by ELISA. Cell volume variations were visualized by live video recording and cell surface was measured using ImageJ software. The role of the LRRC8/VRAC channel was evaluated using a pharmacological inhibitor DCPIB or by silencing the LRRC8A subunit (shLRRC8A RNA) in these cells. In vivo, MSU and CPP crystals were injected into air pouches created subcutaneously (mimicking synovial cavity) in wild-type mice and conditional LRRC8A Knock-out mice in the macrophage lineage (Cxcr3Cre_Lrrc8aflox/flox). Supernatants and pouch lavages were used to measure cytokine production by ELISA.

Results: MSU-and CPP-induced NF-κB activation was reduced in WT THP-1 cells treated with DCPIB and in THP-1 cells where *LRRC8A* expression was silenced. Similarly, IL-1β production induced by MSU and CPP crystals was substantially decreased in WT THP-1 treated with DCPIB (MSU 5200 vs 1080 pg/ml; CPP 11500 vs 4980, $p< 0.0001$) and in shLRRC8A THP-1 cells compared to crystal-treated WT cells. MSU and CPP crystals exposure induced a biphasic cell volume change characterised by a significant increase followed by a RVD-like phenomenon. These cell volume changes were abolished in the presence of DCPIB and not observed in shLRRC8A THP-1 cells. In vivo, inflammation induced by MSU and CPP crystals assessed in lavage fluid and conventional histology was lower in Cxcr3Cre_Lrrc8aflox/flox mice as compared with wild-type mice in terms of IL-1β production and cell infiltrate.

Conclusion: These results suggested that MSU and CPP crystal-induced inflammation involves cell volume variation regulated by VRAC/LRRC8 channel.

Disclosure: T. Wilson Chirayath: None; **m. kayatekin**: None; **I. Rubera**: None; **N. Pham**: None; **F. LIOTE**: None; **P. Richette**: None; **V. COMPAN**: None; **F. Rassendren**: None; **C. Duranton**: None; **H. EA**: None.

Abstract Number: 1107

Predictors of Pegloticase Urate-lowering Response in the Presence and Absence of Methotrexate Co-therapy

James Mossell[1], Mai Duong[2], Katie Obermeyer[2], Lissa Padnick-Silver[2], **Brian LaMoreaux**[2] and Sanjay Chabra[3], [1]Arthritis and Osteoporosis Center of South Georgia, Tifton, GA, [2]Horizon Therapeutics, Deerfield, IL, [3]Texas Arthritis Center, El Paso, TX

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Pegloticase can lower serum urate (SU) in patients with uncontrolled gout who are refractory to/intolerant of oral urate-lowering therapies. However, antidrug antibodies (ADAs) can limit pegloticase treatment response and put patients at risk for infusion reactions (IRs).[1,2] Co-administering methotrexate (MTX) with pegloticase attenuates ADAs, resulting in improved response rates (71% vs. 39% during Month 6) and decreased IR risk (4% vs. 31%).[3] Here we examine potential baseline factors that may influence urate-lowering response to pegloticase.

Methods: These analyses included uncontrolled gout patients who received biweekly pegloticase (8 mg) in the Phase 3 pegloticase registration[1] and MIRROR RCT[2] trials. Patients were included if they had received ≥1 pegloticase infusion. Treatment response was defined as SU < 6 mg/dL for at least 80% of Month 6. A classification and regression tree (CART) analysis was performed in patients who did (MIRROR RCT MTX arm) and did not (Phase 3, MIRROR RCT PBO arm) receive MTX co-therapy with pegloticase. CART analyses split datasets based on data homogeneity, providing insight on outcome prediction factors. The following pre-treatment factors were considered: patient age, sex, weight, BMI, SU, and ADA status (positive/negative).

Results: Baseline characteristics in pegloticase monotherapy (N=134; age: 54.9±14.5 years, 82.1% men, BMI: 33.0±7.5 kg/m^2, weight: 99.2±23.3 kg) and pegloticase+MTX (N=96; age: 56.0±12.5 years, 91.7% men, BMI: 32.8±5.6 kg/m^2, weight: 102.6±19.4 kg) groups were similar. 57 monotherapy (42.5%) and 71 MTX (74.0%) patients were treatment responders. For the pegloticase monotherapy group, CART analysis selected an age cut-off of 46 years (< 46 years: 14.7% response, ≥46 years: 59.0% response) as a first-level predictor and a body weight cut-off of 85 kg as a second level predictor (**Figure, Part A**). For the pegloticase+MTX group, CART analysis returned no decision tree. This finding indicates that no examined factors predicted pegloticase treatment response in the presence of MTX co-therapy. Although age did

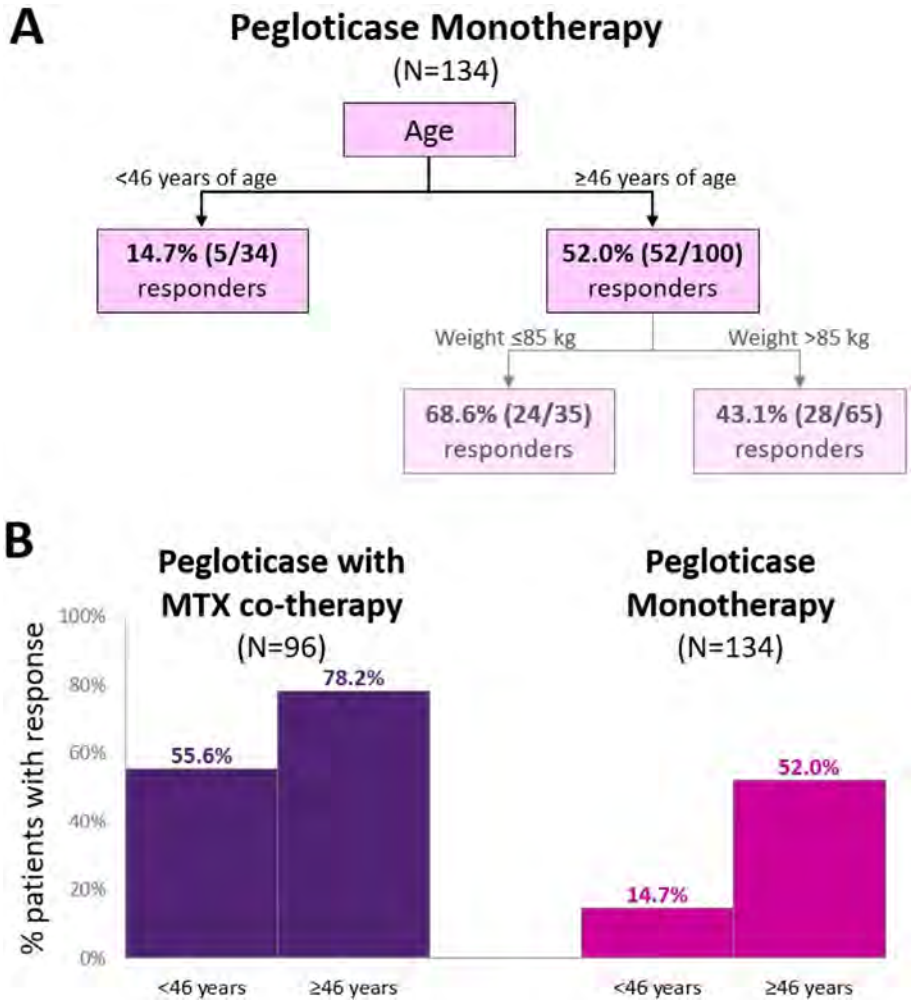


Figure. A. CART decision tree for treatment response in patients receiving pegloticase monotherapy. Pre-treatment factors examined included patient age, sex, weight, BMI, serum urate, and anti-drug antibody status (positive/negative). No decision tree was formed for patients receiving pegloticase+MTX (no examined pre-treatment factor predicted treatment response). B. Proportion of pegloticase treatment responders during Month 6 in pegloticase monotherapy CART age groupings (≥46 years, <46 years). MTX co-therapy led to increased response rate during Month 6 in both age groups.

not predict treatment response in patients receiving MTX co-therapy, those ≥46 years of age had a higher response rate than those < 46 years of age (cutoff identified in the monotherapy group, 78% vs. 56%; **Figure, Part B**).

Conclusion: With pegloticase monotherapy, younger patient age and higher body weight were predictors of treatment failure. These findings are in agreement with pharmacokinetic studies showing an influence of ADAs and body surface area on serum pegloticase concentrations. However, in the presence of MTX-co-therapy, neither patient age nor body weight predicted response to pegloticase. These findings further support the importance of MTX co-administration with pegloticase to maximize the number of patients who may benefit from this often last-line therapy.

Disclosure: J. Mossell: Abbvie, 6, Amgen, 6, ANI, 6, Aurinia, 6, Boehringer-Ingelheim, 6, Glaxo Smith Klein (GSK), 6, Horizon Therapeutics, 6, Mallinckodt, 6, Scipher, 6, UCB, 6; **M. Duong**: Horizon Therapeutics, 3, 12, Stockholder; **K. Obermeyer**: Horizon Therapeutics, 3, 12, Stockholder; **L. Padnick-Silver**: Horizon Therapeutics, 3, 12, Stockholder; **B. LaMoreaux**: Horizon Therapeutics, 3, 12, Stockholder; **S. Chabra**: Horizon Therapeutics, 6.

Abstract Number: 1108

Minimal Clinically Important Difference (MCID) of Quality of Life Assessments in Patients with Uncontrolled Gout

Brian LaMoreaux[1], Chelsea McKibbon[2], Katie Obermeyer[1], Lissa Padnick-Silver[1], Gerald Smith[2], Jiaxuan Wang[2] and Haridarshan Patel[1], [1]Horizon Therapeutics, Deerfield, IL, [2]Cytel Inc., Vancouver, BC, Canada

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is an inflammatory arthritis that results in severe joint inflammation, pain, disability, and lower quality of life (QoL). Determining minimal clinically important differences (MCIDs) for QoL metrics is essential for effectively evaluating gout patient QoL and the impact of therapy. Here, we determine and examine potential predictors of MCID for Health Assessment Questionnaire (HAQ)-Disability Index (DI), -Pain, and -Health using data from adult uncontrolled gout patients treated with pegloticase during the MIRROR Randomized Controlled Trial(RCT)[1].

Methods: MIRROR RCT participants received ≤52 weeks of pegloticase+methotrexate (MTX) orpegloticase+placebo (PBO) co-therapy[1].The change from baseline in HAQ scores were obtained at prespecified time points, including Weeks 24 and 52. HAQ scores range from 0-3 for DI, 0-100 for Pain, and 0-100 for Health, with a higher score indicating worse

Table 1. Determined MCID values for HAQ-DI, -Pain, and -Health and the proportion of patients reaching MCID at Week 24 and 52 using a distribution-based approach (0.5SD) for patients with uncontrolled gout.

	MCID Threshold	Pegloticase+MTX, n (%)	Pegloticase+PBO, n (%)
Week 24	(N=120)	(N=80)	(N=40)
HAQ-DI	-0.232	37 (46.3%)	20 (50.0%)
HAQ-Pain	-15.619	41 (51.3%)	13 (32.5%)
HAQ-Health	-14.863	46 (57.5%)	15 (37.5%)
Week 52	(N=110)	(N=76)	(N=34)
HAQ-DI	-0.278	34 (44.7%)	15 (44.1%)
HAQ-Pain	-15.596	50 (65.8%)	19 (55.9%)
HAQ-Health	-16.569	48 (63.2%)	16 (47.1%)

HAQ score range (higher score indicates worse quality of life): DI: 0-3, Pain: 0-100, Health: 0-100. HAQ, Health Assessment Questionnaire; DI, Disability Index; MTX, Methotrexate; PBO, placebo; MCID, Minimal Clinically Important Difference; SD, Standard deviation.

Table 2. Influence of examined baseline parameters on the likelihood of reaching MCID in uncontrolled gout patients receiving pegloticase therapy (MTX and PBO groups combined).

Baseline parameter	HAQ-DI OR* (p-value)	HAQ-Health OR* (p-value)	HAQ-Pain OR* (p-value)
Week 24 (test vs. reference)	(N=120)	(N=120)	(N=120)
Age (≥50 vs. <50 years)	0.73 (0.561)	0.52 (0.243)	0.63 (0.423)
BMI (≥30 vs. <30 kg/m²)	0.80 (0.630)	0.75 (0.567)	0.65 (0.39)
Tophi (Presence vs. absence)	0.80 (0.156)	1.00 (0.998)	**0.30 (0.032)**
Gout duration† (continuous)	1.02 (0.388)	1.00 (0.908)	1.02 (0.463)
Serum urate (continuous)	1.01 (0.935)	0.84 (0.264)	0.83 (0.252)
PhGA (continuous)	0.91 (0.433)	0.97 (0.824)	0.89 (0.391)
HAQ score‡ (continuous)	**12.28 (<0.001)**	**1.07 (<0.001)**	**1.07 (<0.001)**
Week 52 (test vs. reference)	(N=110)	(N=110)	(N=110)
Age (≥50 vs. <50 years)	0.50 (0.230)	1.018 (0.980)	0.34 (0.145)
BMI (≥30 vs. <30 kg/m²)	1.29 (0.614)	0.88 (0.836)	1.09 (0.889)
Tophi (Presence vs. absence)	0.75(0.593)	1.59 (0.472)	1.88 (0.357)
Gout duration† (continuous)	1.03 (0.243)	0.98 (0.505)	1.02 (0.454)
Serum urate (continuous)	0.84 (0.238)	1.10 (0.617)	1.06 (0.764)
PhGA (continuous)	1.00 (0.993)	0.92 (0.595)	0.94 (0.702)
HAQ score‡ (continuous)	**9.28 (<0.001)**	**1.08 (<0.001)**	**1.09 (<0.001)**

*OR <1 denotes a lower chance of meeting MCID in the test group for categorial parameters and a lower chance of meeting MCID with lower baseline values for continuous parameters by multivariate adjusted analysis. †Time from first gout diagnosis. ‡Baseline HAQ score of the category being examined. BMI, Body mass index; HAQ, Health Assessment Questionnaire; DI, Disability Index; OR, odds ratio; MCID, minimal clinically important difference; PhGA, Physician Global Assessment.

QoL. MCIDs were calculated using two distribution-(0.5 standard deviation[SD], standard error of the mean)and two anchor-based (change difference, receiver operator curve) approaches, with physician global assessment(PhGA), serum urate response, and number of gout flares considered as anchors. Time-to-MCID was evaluated by treatment group using Kaplan-Meier curves. A logistic model and a multicollinearity test including seven covariates were used to assess baseline factors that potentially influenced reaching MCID.

Results: A total of 80 and 76 patients in the MTX group and 40 and 34 patients in the PBO group had Week 24 and 52 HAQ data, respectively. Across analysis methods, MCID values were similar. Herein, results for the0.5SDapproach are presented. MCID thresholds for all HAQ measures were established, with notable differences in the proportion of MTX and PBO patients achieving -Health and -Pain MCID at Week 24 and 52 (Table 1). Time-to-MCID for HAQ-DI and -Pain did not differ between treatment groups but was shorter for -Health in the MTX group through Week 52 (median: 20 vs. 24 weeks).Worse baseline QoL was a significant predictor of reaching MCID during therapy for all HAQ measures(Table 2). Additionally, patients with tophi at baseline were significantly less likely to reach MCID for HAQ-Pain at Week 24, but not Week 52.

Conclusion: For the first time, MCID values for HAQ-DI, -Pain, and -Health scores in an uncontrolled gout population were established. Pegloticase administered as monotherapy or with MTX co-therapy resulted in 33-66%ofpatients achieving MCID in all HAQ measures. Both treatment groups had similar median times-to-MCID ,further supporting the effect of pegloticase on QoL measures. Few assessed parameters were predictive of achieving HAQ MCIDs, but worse baseline QoL was associated with an increased likelihood of reaching all HAQ MCIDs at Week 24 and 52 and the presence of tophi at baseline was associated with a decreased likelihood of reaching HAQ-Pain MCID at Week 24. Further exploration is needed on how tophi influence levels of and changes in patient pain. These analyses are of importance for assessing potential QoL benefits during pegloticase and other urate-lowering therapies in both the clinical trial and practice settings.

[1]Botson, J. K. et al. Arthritis Rheumatol2023;75:293-304.

Disclosure: B. LaMoreaux: Horizon Therapeutics, 3, 12, Stockholder; **C. McKibbon**: None; **K. Obermeyer**: Horizon Therapeutics, 3, 12, Stockholder; **L. Padnick-Silver**: Horizon Therapeutics, 3, 12, Stockholder; **G. Smith**: None; **J. Wang**: None; **H. Patel**: Horizon Therapeutics, 3, 12, Stockholder.

Abstract Number: 1109

Genetic Risk Variants in Hyperuricemia and Gout: Common Disease, Multiple Common and Rare Variant Hypothesis

Blanka Stiburkova[1], Katerina Pavelcova[2], Jana Masinova[1], Marketa Pavlikova[3] and Karel Pavelka[4], [1]Institute of Rheumatology, Prague, Czech Republic, [2]Institute of Rheumatology, Praha 2, Czech Republic, [3]Department of Probability and Mathematical Statistics, Faculty of Mathematics and Physics, Charles University, Prague, Czech Republic, [4]Institut of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Praha, Czech Republic

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Hyperuricemia is a central feature in the pathogenesis of gout. Hyperuricemia results from an imbalance between endogenous production and excretion of urate; however, the main cause of hyperuricemia is reduced renal excretion of urate. Accumulating evidence suggests that the net amount of excreted uric acid is regulated mainly by urate transporters, such as urate transporter 1 (URAT1, a renal urate re-absorber), solute carrier family 2 member 9 (SLC2A9, also known as glucose transporter member 9), and ATP-binding cassette subfamily G member 2 (ABCG2, which is high capacity urate exporter expressed in the kidneys and intestines). Decreased extra-renal urate excretion caused by ABCG2 dysfunction is a common mechanism of hyperuricemia.

Methods: In both the hyperuricemia and gout Czech subcohort, partly previously described (1, 2) we analyzed genetic variants that are strongly associated with the transition from asymptomatic hyperuricemia to gout (3). 13 independent single nucleotide polymorphisms in *ABCG2* (rs2231142, rs131204000, rs7672194), *SLC2A9* (rs16890979, rs16891234), *SLC22A11* (rs2078267), *GCKR* (rs1260326), *MEPE* (rs114580333), *PPM1K-DT* (rs4693211, rs28793136, rs1545207), *LOC105377323* (rs114791459) and *ADH1B* (rs1229984) were genotyped using direct DNA sequencing with generic sequencing primers by ABI 3130 automated sequencer. The frequencies of polymorphisms were evaluated using Lasergene software and results were compared between a group of patients with primary hyperuricemia and patients with gout and data of the European population from the 1000 Genomes Project.

Results: We are currently completing a genetic analysis of patients with primary hyperuricemia and gout, consisting of more than 450 patients (60% gout patients). Most of the examined variants occur with significantly different frequencies in our cohort of patients with primary hyperuricemia and gout compared to the European population. Variants rs13120400, rs16890979, rs2078267, rs1260326,rs114791459, and rs1229984 showed a significantly lower frequency ($p \leq 0.0001$) in our cohort compared to the European. On the contrary, variants rs2231142, rs7672194, rs4693211 ($p \leq 0.0001$), rs28793136 ($p = 0.0021$), and rs114580333 ($p = 0.0286$) showed a significantly higher frequency in our cohort compared to the European. There was no significant difference in the frequency of these SNPs between the subcohort of patients with primary hyperuricemia and those with gout.

Conclusion: The preliminary results of our study are not entirely consistent with the findings of the GWAS study, which looked for loci associated with asymptomatic hyperuricemia to gout transition and described 13 such SNPs (3). We confirmed only a significantly higher incidence of 5 of these variants in a cohort of patients with primary hyperuricemia/gout, and the frequency of none of the 13 variants differed between subcohorts.

References:

1. Pavelcova K, et al. J Clin Med. 2020 Aug 4;9(8):2510.
2. Horváthová V, et al. J Clin Med. 2019 Nov 14;8(11):1965.
3. Sandoval-Plata G, et al. Ann Rheum Dis. 2021 Sep;80(9):1220-1226.

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Disclosure: B. Stiburkova: None; **K. Pavelcova**: None; **J. Masinova**: None; **M. Pavlikova**: None; **K. Pavelka**: Abbvie, 2, 6, Amgen, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Egis, 2, 6, MSD, 2, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 6.

Abstract Number: 1110

Pharmacokinetics and Pharmacodynamics of AR882 Following 12-Week Treatment in Patients with Gout

Roy Fleischmann[1], James Cheng-Chung Wei[2], **Zancong Shen**[3], sarah Morris[4], Elizabeth Polvent[5], Andrea Clouser-Roche[4], Vijay Hingorani[6], Rongzi Yan[7], Shunqi Yan[8], Robert Keenan[9] and Li-Tain Yeh[10], [1]Division of Rheumatology, University of Texas Southwestern Medical Center, Metroplex Clinical Research Center, Dallas, TX, [2]Chung Shan Medical University Hospital, Department of Rheumatology, Taichung, Taiwan, [3]Arthrosi Therapeutics, San Diego, CA, [4]Arthrosi Therapeutics Inc, San Diego, CA, [5]Arthrosi Therapeutics, Inc., Roseville, CA, [6]Vanguard Healthsciences, Inc., San Diego, CA, [7]Arthrosi Therapeutics, Inc, Irvine, CA, [8]Arthrosi Therapeutics, Inc., Laguna Hills, CA, [9]Arthrosi Therapeutics, Chapel Hill, NC, [10]Arthrosi Therapeutics, Inc., Irvine, CA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: In early phase studies AR882 exhibited good dose proportionality, long half-life and dose-dependent serum urate (sUA) lowering effect in a broad range of doses in healthy subjects and gout patients. In a phase 2b study, following once-daily dosing up to 3 months, the pharmacokinetics (PK) and pharmacodynamics (PD), including sUA lowering effect of AR882, were evaluated in all patients; in a subset of these patients more frequent laboratory monitoring was done.

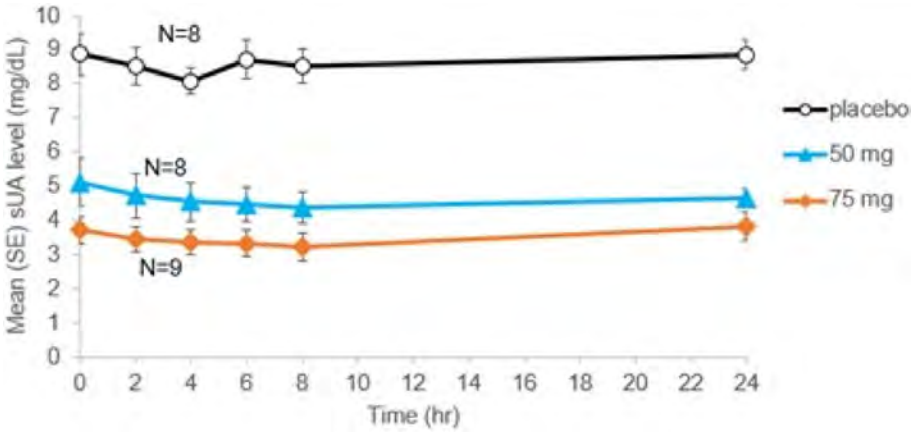

Figure 1. Mean (SE) sUA levels following 8-week dosing of AR882

Table 1. Similar response in sUA lowering between gout patients in phase 2b PKPD subset and phase 2a studies.

Study	Group	N	Mean (SD) value			sUA response, %			
			Baseline (mg/dL)	lowest sUA (mg/dL)	% change	< 6 mg/dL	< 5 mg/dL	< 4 mg/dL	< 3 mg/dL
Phase 2b	50 mg	8	8.7 (1.1)	4.1 (1.0)	-52.5 (9.3)	100	88	38	13
	75 mg	9	8.2 (1.2)	3.2 (1.1)	-62.2 (9.9)	100	89	78	67
	Placebo	8	8.4 (1.1)	8.2 (1.3)	-0.65 (12)	0	0	0	0
Phase 2a	50 mg	28	8.9 (1.1)	4.2 (0.9)	-52.7 (8.8)	96%	93%	39%	0%
	75 mg	8		3.2 (0.9)	-61.5 (7.9)	100%	100%	88%	50%

Methods: In the phase 2b, 12-week study, 140 subjects were enrolled into three treatment groups: placebo (n=47), AR882 50 mg (n=46) and AR882 75 mg (n=47) at approximately 1:1:1 ratio. A single blood sample was collected for PK/PD assessment at each clinical visit (every 2 weeks) through Week 12. In addition, a total of 25 gout patients participated in an optional sub-study with more frequent sampling occurring on baseline, Week 2, and Week 8 visits.Serial blood samples were collected up to 24 hours post-dose for AR882 and sUA measurements.

Results: Following long-term treatment, AR882 showed stable exposure across the entire treatment period. At steady-state, AR882 was readily absorbed with median T_{max} of 1.50 to 3.50 hours post-dose. AR882 demonstrated dose-dependent increase in plasma exposure. Average half-life of AR882 ranged between approximately 14 and 22 hours. Its active metabolite AR896 was formed with median T_{max} between 5- and 8-hours post-dose. Consistent with observations in the early phase studies, AR896 constituted of approximately 9% of C_{max} and 10-12% of AUC exposures with longer half-life (29-36 hours) than the parent drug.

In the sub-study group with more frequent sampling, sUA lowering effect in both AR882 treatment groups showed a smooth, consistent and flat profile across 24 hours with the lowest mean sUA reduced from baseline 8.6 mg/dL to 4.1 mg/dL (-53%) in the 50 mg group and to 3.2 mg/dL (-62%) in the 75 mg group (**Figure 1**). sUA lowering effects and the response rates in these patients were similar to those observed in an earlier, well-controlled, 3-week, cross-over design phase 2a study (**Table 1**). Mild or moderate adverse events including gout flares, diarrhea, headache, and upper respiratory infection were observed. None of the AEs led to discontinuation of investigational product.

Conclusion: In a subset of patients with full PK/PD collection, AR882 showed potent sUA lowering effect with similar exposures to those observed in closely monitored early-phase studies. AR882 50 mg and 75 mg doses were well tolerated during the entire study with an unremarkable safety profile.

Disclosure: R. Fleischmann: AbbVie, 1, 2, 5, Amgen, 1, 2, 5, Bristol Myers Squibb, 1, 2, 5, Eli Lilly, 1, 2, 5, Galapagos, 1, 2, 5, Galvani, 1, 2, 5, Gilead, 1, 2, 5, GlaxoSmithKline, 1, 2, 5, Janssen, 1, 2, 5, Novartis, 1, 2, 5, Pfizer, 1, 2, 5, UCB, 1, 2, 5, Vyne, 1, 2, 5; **J. Wei**: Abbvie, 2, 5, 6, Amgen, 5, AstraZeneca, 6, BMS, 2, 5, 6, Celgene, 2, Chugai, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 5, 6, Gilead, 5, GSK, 2, 5, Janssen, 2, 5, 6, Novartis, 2, 5, Pfizer, 2, 5, 6, Sanofi-Aventis, 2, SUN pharma, 5, TSH Taiwan, 2, UCB pharma, 2, 5; **Z. Shen**: Arthrosi therapeutics, 3; **s. Morris**: Arthrosi Therapeutics, 3; **E. Polvent**: Arthrosi Therapeutics, 3; **A. Clouser-Roche**: Arthrosi Therapeutics Inc, 3; **V. Hingorani**: None; **R. Yan**: Arthrosi Therapeutics, 3; **S. Yan**: Arthrosi Therapeutics, 3; **R. Keenan**: Arthrosi Therapeutics, 3; **L. Yeh**: Arthrosi Therapeutics, 3.

Abstract Number: 1111

Urate-Lowering Therapy Is Associated with a Reduced Risk of Arrhythmias: A Systematic Review and Meta-analysis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
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Background/Purpose: Recent studies have suggested that hyperuricemia is significantly associated with an increased prevalence of atrial and ventricular arrhythmias and urate-lowering therapy (ULT) may provide cardioprotective effects by lowering uric acid level and via drug's direct effects. However, research on the effects of ULT and arrhythmia risk is limited. We aim to conduct a systematic review and meta-analysis exploring the relationship between ULT and incident arrhythmias.

Methods: Potentially eligible studies were identified from PubMed and Embase databases from inception to May 2023. Search terms were derived from terms related to "Arrhythmias" and "Urate-lowering therapy". The eligible study must be cohort study that consists of one cohort of patients with ULT use and another cohort of comparators without ULT use. The study must compare the prevalence of cardiac arrhythmias in each group and report effect size with 95% confidence intervals (95% CIs). The Newcastle-Ottawa quality assessment scale was used to evaluate the quality of the included studies. We performed the meta-analysis by using a random-effects model. The heterogeneity of effect size estimates was assessed using forest plots and the Q and I^2 statistics.

Results: Six studies were included in the analysis with a total of12,435 subjects (7,404 subjects in ULT group and 5,031 in non-ULT group). Our results showed that ULT users had significant reductions in the risk of arrhythmias (pooled RR 0.79, 95% CI: 0.67–0.93, p = 0.004, I^2= 8.4%) compared to non-ULT users (Figure 1). Subgroup analysis showed that ULT users had a reduced risk of atrial fibrillation (pooled RR 0.76, 95% CI: 0.59–0.98, p = 0.034 with I^2 =12.2%) compared to non-ULT users (Figure 2), and that allopurinol users had a reduced risk of arrhythmia (pooled RR 0.66, 95% CI: 0.46–0.95, p = 0.024 with I^2= 39.6%) compared to non-allopurinol users (Figure 3).

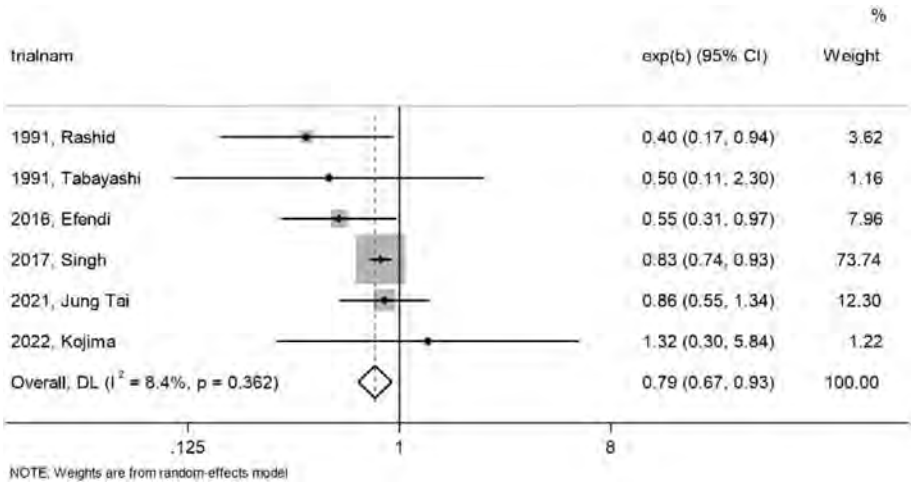


Figure 1. Forest plot of the meta-analysis for urate-lowering therapy and risk of arrhythmias

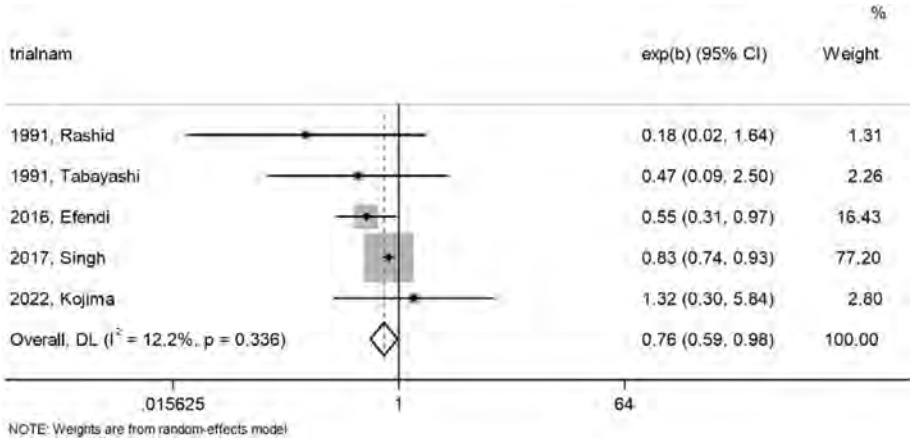


Figure 2. Forest plot of the meta-analysis for urate-lowering therapy and atrial fibrillation

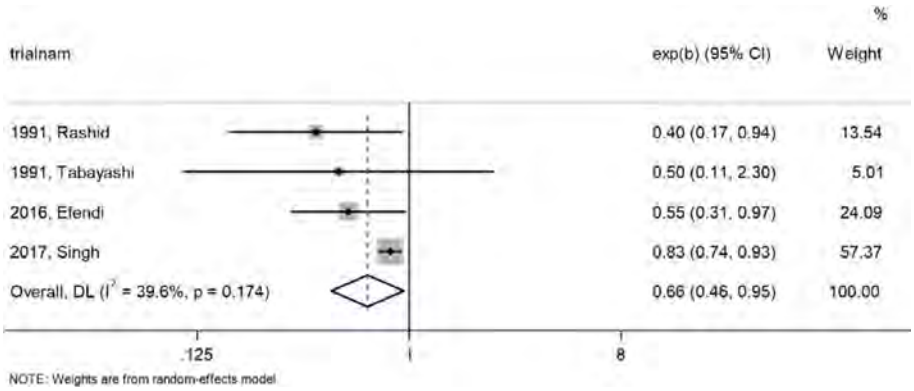


Figure 3. Forest plot of the meta-analysis for allopurinol and arrhythmias

Conclusion: Our results indicate that ULT may play a potential role in protecting arrythmias in addition to lowering uric acid level. Further investigation is needed to elucidate our results and explore the detailed mechanisms.

Disclosure: P. Waitayangkoon: None; **T. Kanthajan**: None; **T. Leesutipornchai**: None.

Abstract Number: 1112

AR882, a Potent Uricosuric Agent, Shows Favorable Uric Acid Excretion Profile Following Multiple Doses

Zancong Shen[1], Elizabeth Polvent[2], sarah Morris[3], Rongzi Yan[4], Shunqi Yan[5], Robert Keenan[6] and **Li-Tain Yeh**[7], [1]Arthrosi Therapeutics, San Diego, CA, [2]Arthrosi Therapeutics, Inc., Roseville, CA, [3]Arthrosi Therapeutics Inc, San Diego, CA, [4]Arthrosi Therapeutics, Inc, Irvine, CA, [5]Arthrosi Therapeutics, Inc., Laguna Hills, CA, [6]Arthrosi Therapeutics, Chapel Hill, NC, [7]Arthrosi Therapeutics, Inc., Irvine, CA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: The uric acid transporter inhibitor (URAT1) is responsible for the reabsorption of filtered uric acid from the renal tubular lumen. Uricosuric agents inhibit URAT1 consequently lowers serum urate (sUA). With previous uricosurics, bolus dumping of drug to the target site caused spontaneous accumulation of uric acid in renal tubules, which posed a potential influx of uric acid at high concentration leading to renal toxicity.[1] AR882 is a potent and selective URAT1 transporter inhibitor in late-phase clinical development. To illustrate the renal safety of AR882 the uric acid excretion profiles across multiple studies were collected to assess the uric acid excretion amount and rate following once-daily dosing.

Methods: In phase 1 healthy subject studies, uric acid excretion profiles were collected following 25, 50 and 75 mg once-daily doses for 10 days in a multiple-ascending dose study (n=24) and following 75 mg once-daily for 14 days (n=16) with every 2-hour collection intervals in a renal impairment study. In a phase 2b study, urine samples were collected at every 2-hour intervals up to 8 hours post-dose from 25 gout patients to evaluate the excretion amount, rate and fractional excretion of uric acid following 8 weeks of once-daily dosing at 50 and 75 mg.

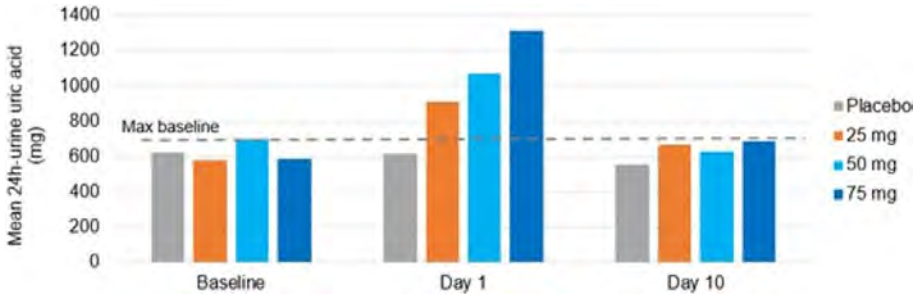


Figure 1. Mean 24-h urine uric acid excretion amount (mg) following AR882 once-daily doses for 10 days in phase 1 subjects

Figure 2. Mean urine uric acid excretion rate (mg/h) following 75-mg AR882 once-daily doses for 14 days in healthy and albuminuria phase 1 subjects

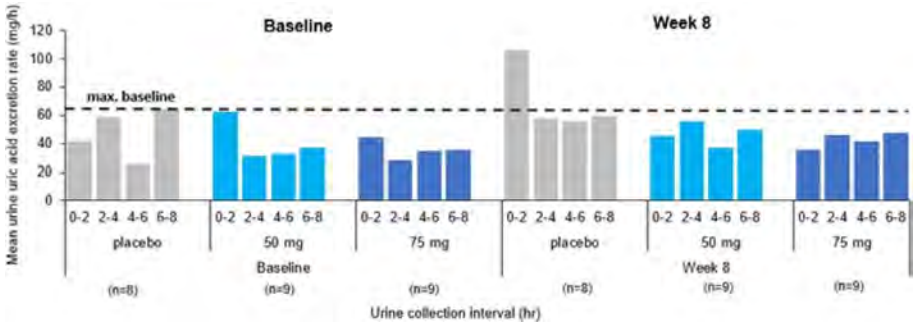


Figure 3. Mean urine uric acid excretion rate (mg/h) following 50 or 75-mg AR882 once-daily doses for 8 weeks in phase 2b gout patients

Results: In phase 1 studies, AR882 showed a relatively flat exposure profile with a slow rise to peak concentrations and slow decline over time. The fraction of dose excreted into tubules was evenly distributed across the day, mirroring the PK profile and supported its sustained sUA reduction and long-lasting URAT1 inhibitory pattern. Following 10 or 14 days of dosing, AR882 showed similar excretion amount to baseline (**Figure 1**) and similar intra-day excretion rate (**Figure 2**). In gout patients, the maximum uric acid excretion rate at baseline was under approximately 60 mg/hr. After 8-week treatment, AR882 at either 50 mg or 75 mg showed consistently low excretion rate across 8 hours post-dose which was similar to baseline or under the maximum baseline value (**Figure 3**) while maintaining significant uric acid lowering effect.

Conclusion: With its unique, slower elimination in PK, AR882 maintains a smooth intra-day uric acid excretion profile that was similar to baseline or to that in placebo patients, resulting in a lasting inhibitory effect without any high concentration of uric acid influx in the kidney tubules. The lack of daily transient increase in uric acid excretion confirms AR882, as a new uricosuric agent, possessing a favorable and safe renal profile over existing and other approved uricosuric agents.

Reference: 1. Sanchez-Niño MD, Zheng-Lin B, Valiño-Rivas L, et al. Lesinurad: what the nephrologist should know. Clin Kidney J. 2017 Oct;10(5):679-687.

Disclosure: Z. Shen: Arthrosi therapeutics, 3; **E. Polvent**: Arthrosi Therapeutics, 3; **s. Morris**: Arthrosi Therapeutics, 3; **R. Yan**: Arthrosi Therapeutics, 3; **S. Yan**: Arthrosi Therapeutics, 3; **R. Keenan**: Arthrosi Therapeutics, 3; **L. Yeh**: Arthrosi Therapeutics, 3.

Abstract Number: 1113

Comparing a Capillary Urate Point-Of-Care Device to Standard Laboratory-based Serum Urate Test for Dose Titration in Gout Patients

Amanuel Kehasse[1], **Sayali Dhamne**[2], Michael LaValley[3], Jean Liew[2] and Tuhina Neogi[4], [1]Boston Medical Center, Boston, MA, [2]Boston University, Boston, MA, [3]Boston University School of Public Health, Arlington, MA, [4]Boston University School of Medicine, Boston, MA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The management of gout remains poor despite the availability of effective medications and recommendation of a treat-to-target treatment strategy using of urate-lowering therapy (ULT). A serum urate level is required to make ULT dose adjustments. However, requiring lab work prior to a clinic visit can be burdensome for patients, while waiting for laboratory test results after the visit makes face-to-face counseling regarding any medication dose changes at the time of the visit impossible. Introducing a point-of-care (POC) device, much like a glucometer, would allow providers to perform serum urate testing during the clinic visit and make therapy adjustments as needed in real-time. Our purpose was to assess the accuracy, reliability, and acceptability of a POC device as compared to standard laboratory-based serum urate tests.

Methods: We measured serum urate levels in patients with gout using both a capillary POC device (Nova Max Uric Acid Monitoring System) that is FDA-approved for home use (but not approved for use in the clinic) and a standard laboratory-based test on the same day. A Bland-Altman analysis was conducted to identify whether the variability of the difference between tests was affected by the level of serum urate and to identify the limits of agreement between the two tests. We plotted the difference of the two values against the average value for each participant. Correlation between the two

measurements of serum urate was evaluated using intraclass correlation coefficients with 95% confidence intervals (CI). In addition, we assessed the patient acceptability and convenience of device use through a self-reported standard Likert scale questionnaire.

Table 1. Participants characteristics

Sample Characteristics (n=30)	Mean (SD), n (%)
Demographics	
Age	61.3 (± 12.3)
Sex	
Male	25 (83.3%)
Female	5 (16.7%)
Race	
Asian	2 (6.7%)
Black/African American	14 (46.7%)
White	7 (23.3 %)
Unknown/Not reported	7 (23.3%)
Ethnicity	
Hispanic or Latino	6 (20.0%)
Not Hispanic or Latino	23 (76.7%)
Unknown/Not reported	1 (3.3%)
Clinical characteristics	
Chronic kidney disease or end stage kidney disease	12 (40.0%)
Type 2 diabetes	7 (23.3%)
Coronary heart disease	2 (6.7%)
Heart failure	7 (23.3%)
Outcomes	
SUA on POC device	5.6 (± 2.3)
SUA from lab	7.2 (± 2.5)
Acceptability Questionnaire Completed	30 (100%)

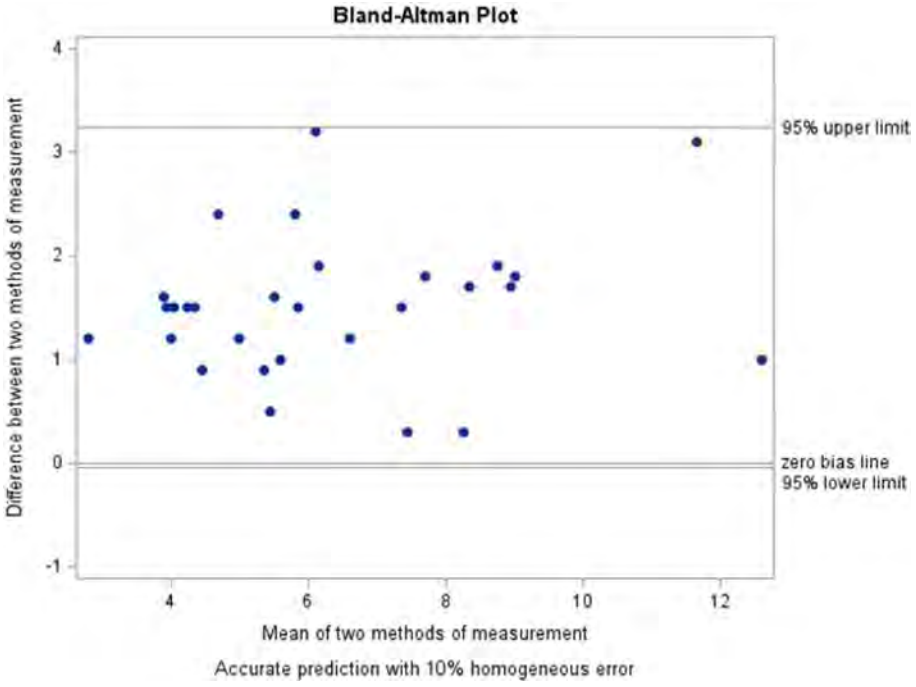


Figure 1. Bland-Altman Plot – Difference in Serum Urate Plotted Against the Average.

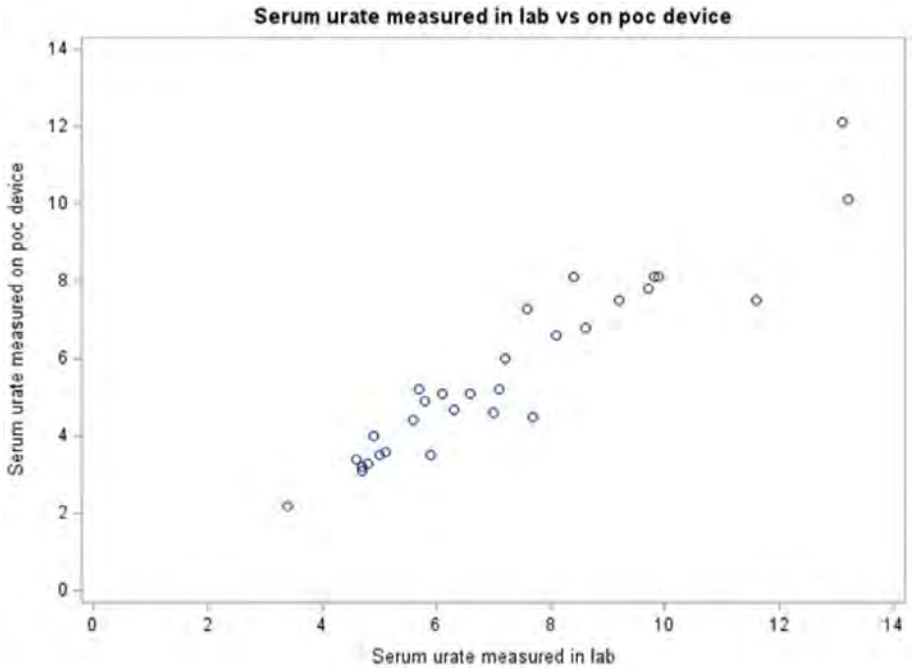


Figure 2. Scatter plot of POC and Laboratory Measures of Serum Urate

Results: We enrolled 30 patients with gout (mean age 61 ± 12.32, 83% male and 17% female; Table 1). The mean ± SD serum urate measured on the POC device was 5.65 ± 2.30 mg/dL and in the laboratory was 7.25 ± 2.52 mg/dL. The Bland-Altman plot (Figure 1) shows limits of agreement close to 0 and 3 indicating consistently lower measurements with the POC device. The intraclass correlation coefficient was 0.75 (95% CI 0.55 - 0.87), indicating moderate agreement (Figure 2). The results from the acceptability questionnaire suggest that the device was acceptable and liked by 97% of the participants. All the participants found it comfortable and 80% preferred the POC device over standard lab tests.

Conclusion: In this small pilot study, the POC device and the standard laboratory tests for serum urate were moderately correlated, though the POC device values were generally >1mg/dL lower than the laboratory values. This discrepancy in serum urate values indicates that this POC device is not suitable at the present time for making treatment decisions in the clinical setting for real-time dose titrations in patients with gout. Nonetheless, patients generally preferred a POC approach; thus, with improved accuracy, POC urate measurements could benefit real-time treat-to-target gout management.

Disclosure: A. Kehasse: None; **S. Dhamne**: None; **M. LaValley**: None; **J. Liew**: None; **T. Neogi**: None.

Abstract Number: 1114

Role of Dual-energy Computed Tomography (DECT) in Detection of Carotid Artery Monosodium Urate Deposition in Patients with Gout

Muhammad Danish Sarfraz, Lee Treanor, Savvas Nicolaou and Adnan Sheikh, University of British Columbia, Vancouver, BC, Canada

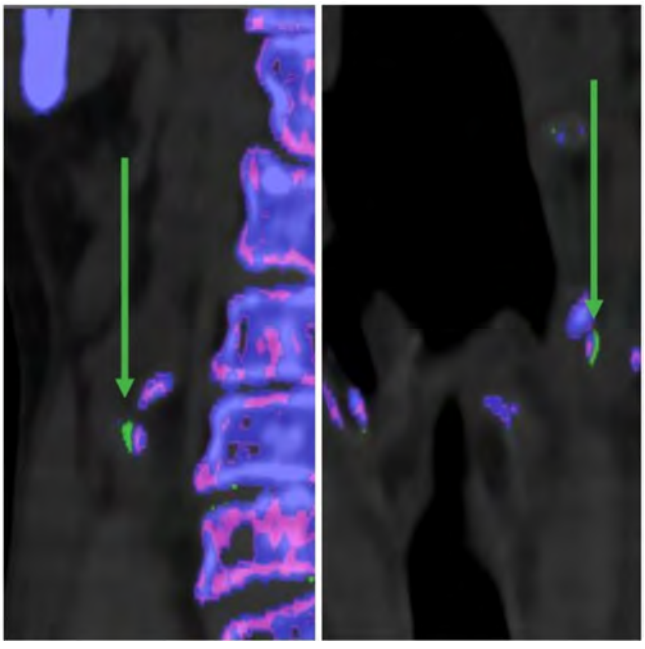
SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: To find out if a Dual energy CT can detect monosodium urate deposition in carotid arteries and whether the presence of monosodium urate crystals has any effect on atherosclerotic disease in terms of plaque volume.

Methods: This is a retrospective study. All patients who underwent any Dual energy neck imaging (like carotid angiogram, neck soft tissues or cervical spine) from January 2015 to December 2022 were included. All patients' charts were reviewed to determine to find gout patients with clinical and laboratory evidence. Charts were also rigorously reviewed to find potential confounding variables like hypertension, dyslipidemia, CKD and smoking as these may have effect on plaque volume. Patients with a smoking history were excluded as it has a well-established role in atherosclerotic disease. Non-smokers with either hypertension, dyslipidemia, CKD or either of two were included as most of the patients have similar comorbidities. Comprehensive data extraction was done to allow multivariable regression analysis for confounding variables. Same number of healthy controls (without a clinical history of gout or other rheumatic diseases) were included during same study period which were then age (within 5 years), sex and confounders-matched to gout patients using MedCalc. Patients with any extensive artefacts, spinal metal implants, carotid stents, carotid endarterectomy prior to scan date or prior radiotherapy to the head and neck were excluded. DECT datasets were post-processed using Syngo.ViaVB30 with gout application class at default factory settings including a DECT iodine ratio of 1.27, minimum HU at 130, resolution of 3mm, and air distance 5. Volumetric analysis of atherosclerotic plaque was performed using Syngo.ViaVB30 with Calcium scoring application in matched gout patients with carotid monosodium deposition, gout patients without carotid monosodium deposition and control/non-gout patients.

Results: Out of total 2157 patients who underwent dual energy neck imaging during study period, 85 were established gout cases with confirmed clinical and laboratory evidence. Of 85 gout cases, 2 were excluded due to presence of streak artefacts from dentures hence, n=83. Out of 83, Monosodium urate deposition was detected in carotid arteries of 10 patients (12%). None of the matched control patient demonstrated monosodium crystal deposition. Volumetric analysis of atherosclerotic plaque demonstrated larger plaque volumes in gout patients with monosodium urate deposition (n=10) than matched gout patients without monosodium urate deposition (n=10) and matched control/non-gout patients (n=10) (p value of 0.03).



Positive MSU carotid plaque on DECT

Conclusion:

1. Dual energy CT is an effective tool to detect monosodium urate deposition in carotid arteries.
2. Carotid arteries are not a common site for monosodium urate deposition but if present, can lead to increased atherosclerosis in the involved vessel.

Disclosure: M. Sarfraz: None; **L. Treanor**: None; **S. Nicolaou**: None; **A. Sheikh**: None.

Abstract Number: 1115

EULAR Recommendations for the Use of Imaging in the Diagnosis and Management of Crystal-induced Arthropathies in Clinical Practice

Peter Mandl[1], Maria-Antonietta D'Agostino[2], Victoria Navarro-Compán[3], Irina Gessl[1], Garifallia Sakellariou[4], Abhishek Abhishek[5], Fabio Becce[6], Nicola Dalbeth[7], Hang-Korng Ea[8], Emilio Filippucci[9], Hilde Berner Hammer[10], Annamaria Iagnocco[11], Annette De Thurah[12], Esperanza Naredo[13], Sebastien Ottaviani[14], Tristan Pascart[15], Fernando Perez-Ruiz[16], Irene Pitsillidou[17], Fabian Proft[18], Juergen Rech[19], Wolfgang Schmidt[20], Luca Sconfienza[21], Lene Terslev[22], Brigitte Wildner[23], Pascal Zufferey[24] and Georgios Filippou[25], [1]Department of Rheumatology, Medical University of Vienna, Vienna, Austria, [2]Universita Cattolica del Sacro Cuore Rome, Courbevoie, France, [3]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain, [4]Department of Internal Medicine and Therapeutics, Università di Pavia, Istituti Clinici Scientifici Maugeri IRCCS, Pavia, Italy, [5]University of Nottingham, Nottingham, United Kingdom, [6]Lausanne University Hospital (CHUV), Lausanne, Switzerland, [7]University of Auckland, Auckland, New Zealand, [8]Hôpital Lariboisière, APHP-Nord, Service de Rhumatologie, Université de Paris Cité, Paris, France, [9]Polytechnic University of Marche, Jesi, Italy, [10]Center for Treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway AND University of Oslo, Faculty of Medicine, Oslo, Norway, [11]University of Turin, Roma, Italy, [12]Aarhus University Hospital, Aarhus, Denmark, [13]Hospital Fundación, Madrid, Spain, [14]Assistance Publique Hopitaux de Paris, Paris, France, [15]Department of Rheumatology, Saint-Philibert Hospital, Lille Catholic University, Lille, France, [16]Rheumatology Division, Osakidetza, OSI-EE Cruces, Cruces University Hospital, Barakaldo, Spain, [17]EULAR Patient Research Partner, Executive Secretary of Cyprus League Against Rheumatism, Nicosia, Cyprus, [18]Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [19]University Clinic Erlangen, Erlangen, Germany, [20]Rheumatology, Immanuel Krankenhaus Berlin, Medical Centre for Rheumatology Berlin-Buch, Berlin, Germany, [21]Dipartimento di Scienze Biomediche per la Salute, Università degli Studi di Milano AND IRCCS Istituto Ortopedico Galeazzi, 20161, Milan, Italy, [22]Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup, Denmark, [23]University Library, Medical University of Vienna, Vienna, Austria, [24]Rheumatology Department, University of Lausanne, CHUV, Lausenne, Switzerland, [25]IRCCS Galeazzi - Sant'Ambrogio Hospital, Milan, Italy

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: The multifaceted clinical presentation in crystal-induced arthropathies (CiA) poses challenges to imaging. Our goal was to formulate evidence-based recommendations on the use of imaging in the diagnosis and management of CiA.

Methods: An international task force of 25 rheumatologists, radiologists, methodologists, health care professionals and patient research partners from 11 countries was formed according to the EULAR standard operating procedures. Fourteen key questions on the role of imaging in the most common forms of CiA were generated (Table 1). The CiA assessed included gout, calcium pyrophosphate dihydrate deposition and basic calcium phosphate deposition. Imaging modalities included conventional radiography, ultrasound, magnetic resonance imaging and computed tomography. Experts applied research

evidence obtained from 4 systematic literature reviews using MEDLINE, EMBASE and CENTRAL after assessing for risk of bias. Task force members provided level of agreement (LoA) anonymously by using a numeric scale.

Table 1. Research questions. BCPD: basic calcium-phosphate deposition; CiA: crystal-induced arthropathy; CPPD: calcium-pyrophosphate deposition; RQ: research question

RQ 1	What is the diagnostic value, above other diagnostic tests of individual imaging modalities in gout?
RQ 2	What is the ability and added value of individual imaging modalities for monitoring inflammation, damage or crystal deposition in gout? In case there is additional value, how frequently and at which timepoints should imaging be applied to monitor inflammation, damage or crystal deposition in gout?
RQ 3	What is the ability and added value above other measures of individual imaging modalities to predict outcome (severity) in gout?
RQ 4	What is the ability and added value above other measures of individual imaging modalities to predict treatment effect in gout?
RQ 5	What is the diagnostic value, including differential diagnosis above other diagnostic tests of individual imaging modalities in CPPD?
RQ 6	What is the ability and added value of individual imaging modalities for monitoring inflammation and damage (including crystal deposition) in CPPD? In case there is additional value, how frequently and at which timepoints should imaging be applied to monitor inflammation and damage in CPPD?
RQ 7	What is the ability and added value above other diagnostic measures of individual imaging modalities to predict outcome (severity) in CPPD?
RQ 8	What is the ability and added value above other measures of individual imaging modalities to predict treatment effect in CPPD?
RQ 9	What is the diagnostic value, including differential diagnosis, above clinical criteria of individual imaging modalities in BCPD (including calcific tendonitis of the supraspinatus tendon, calcific tendonitis of the Achilles tendon, Milwaukee shoulder syndrome and knee, etc.)?
RQ 10	What is the ability and added value of individual imaging modalities for monitoring inflammation and damage (including crystal deposition) in BCPD? In case there is additional value, how frequently and at which timepoints should imaging be applied to monitor inflammation and damage in BCPD?
RQ 11	What is the ability and added value above other diagnostic measures of individual imaging modalities to predict outcome (severity) in BCPD?
RQ 12	What is the ability and added value above other measures of individual imaging modalities to predict treatment effect in BCPD?
RQ 13	What is the ability and added value above conventional measures of individual imaging modalities in guiding diagnostic aspiration and guiding delivery of drugs in CiA?
RQ 14	What is the ability and added value above standard care of individual imaging modalities to facilitate patient education & understanding of disease in CiA?

Table 2. EULAR Recommendations for the use of imaging in crystal-induced arthropathies in clinical practice. *1a for gout, 1a for CPPD, 5 for BCPD; $1a for US, 1a for CR, 1b for CT; #A for gout, A for CPPD, C for BCPD; §A for CR, A for US, B for CT Numbers in column 'LoA' indicate the mean and SD (in parenthesis) of the LoA (range 0–10 with 0='completely disagree' to 10='completely agree'), BCPD: basic calcium phosphate deposition; CPPD: calcium pyrophosphate dihydrate deposition; DECT: dual-energy computed tomography; GoR: grades of recommendation; LoA: level of agreement; LoE: level of evidence; MTP1: first metatarsophalangeal; n.a., not applicable;

Overarching principles	**LoE**	**GoR**	**LoA**
A. Crystal-induced arthropathies are typically characterized by intermittent, acute episodes of inflammation, but may also exhibit a persistent disease course with or without superimposed flares.	n.a.	n.a.	9.83 (0.48)
B. Imaging in crystal-induced arthropathies provides useful information on crystal deposition, inflammation and structural damage.	n.a.	n.a.	9.83 (0.48)
C. The presence of imaging abnormalities, in particular, those related to crystal deposition may not always be related to clinical manifestations.	n.a.	n.a.	9.79 (0.51)
D. Patient information (medical history, physical/ laboratory examination, synovial fluid/tissue analysis, etc.) should be taken into account when imaging is considered in crystal-induced arthropathies.	n.a.	n.a.	9.75 (0.74)
E. Imaging in crystal-induced arthropathies should be performed and interpreted by trained health care professionals.	n.a.	n.a.	9.92 (0.41)
Recommendations			
1. When performing imaging in crystal-induced arthropathies, both symptomatic areas and disease-specific target sites (i.e., MTP1 joint in gout, knee and wrist in CPPD, shoulder in BCPD) should be considered.	1a*	A[§]	9.71 (0.55)
2. In the diagnostic assessment of gout, ultrasound and DECT are both recommended imaging modalities.	1a	A	9.75 (0.61)
3. When characteristic features of monosodium urate crystal deposition on ultrasound (i.e., double contour sign or tophi) or on DECT are identified, synovial fluid analysis is not needed to confirm a diagnosis of gout.	1a	A	8.79 (1.82)
4. In the diagnostic assessment of CPPD, conventional radiography and ultrasound (or computed tomography if axial involvement is suspected) are recommended imaging modalities.	1a[#]	A[$]	9.63 (0.92)
5. In the diagnostic assessment of BCPD, imaging is necessary; conventional radiography or ultrasound are the recommended modalities.	2b	C	9.08 (1.69)
6. In gout, ultrasound and DECT can be used to monitor crystal deposition and in case of ultrasound, also inflammation. Both modalities provide additional information on top of clinical and biochemical assessment. In case ultrasound/DECT are not available conventional radiography can be used to assess structural damage due to gout. The decision on when to repeat imaging depends on the clinical circumstances.	2b	B	9.33 (1.17)
7. In CPPD and BCPD serial imaging is not recommended, unless there is an unexpected change in clinical characteristics.	2a	B	9.42 (1.21)
8. In gout, assessing the amount of monosodium urate crystal deposition by ultrasound or DECT may be used to predict future flares.	2b	B	8.46 (1.67)
9. If synovial fluid analysis is required in the assessment of crystal-induced arthropathies, ultrasound guidance should be used in cases where aspiration based on anatomical landmarks is challenging.	5	D	9.71 (0.55)
10. Showing and explaining imaging findings of crystal-induced arthropathies to people with such conditions may help them understand their condition and improve treatment adherence in gout.	2b	C	9.38 (0.92)

Results: Five overarching principles and 10 recommendations were produced on the role of imaging in making a diagnosis, monitoring inflammation, structural damage and crystal deposition, predicting severity and treatment effect, guiding intervention, and patient education in CiA (Table 2). Level of evidence and grade of recommendation was evaluated. Overall, the LoA for the recommendations was very high (8.5-9.9).

Conclusion: These are the first recommendations that encompass all common forms of CiA and guide the use of established imaging modalities in this disease group.

Disclosure: P. Mandl: AbbVie/Abbott, 5, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 6, Eli Lilly, 6, Janssen, 6, Novartis, 5, 6, Pfizer, 5, Roche, 6, UCB, 5, 6; **M. D'Agostino**: None; **V. Navarro-Compán**: AbbVie, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, Janssen, 6, MoonLake, 2, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6; **I. Gessl**: None; **G. Sakellariou**: None; **A. Abhishek**: Cadilla Pharmaceuticals, 12, lecture fees, Inflazome, 2, Limbic, 2, NGM Biopharmaceuticals, 2, Springer, 9, UpTodate, 9; **F. Becce**: Horizon Therapeutics, 2, Siemens Healthineers, 2; **N. Dalbeth**: Arthrosi, 2, AstraZeneca, 2, Dyve Biosciences, 2, Hikma, 6, Horizon, 2, JW Pharmaceutical Corporation, 2, LG, 2, Novartis, 6, Novotech, 5, PK Med, 2, Protalix, 2, PTC Therapeutics, 2, Selecta, 2, Unlocked Labs, 2; **H. Ea**: None; **E. Filippucci**: None; **H. Hammer**: None; **A. Iagnocco**: None; **A. De Thurah**: None; **E. Naredo**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 6, Eli Lilly, 5, 6, Janssen, 6, Novartis, 6, Pfizer, 6, Roche, 6, UCB, 6; **S. Ottaviani**: None; **T. Pascart**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 6, Pfizer, 6, Roche, 5, Sanofi, 6; **F. Perez-Ruiz**: None; **I. Pitsillidou**: None; **F. Proft**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celgene, 2, 6, Eli Lilly, 5, Hexal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 6, UCB Pharma, 2, 5, 6; **J. Rech**: AbbVie, Biogen, BMS, Chugai, GSK, Janssen, Lilly, MSD; Mylan, Novartis, Roche, Sanofi, Sobi, UCB, 2, 6, Novartis, Sobi, 5; **W. Schmidt**: AbbVie/Abbott, 1, 5, 6, Amgen, 1, 6, Bristol-Myers Squibb(BMS), 6, Chugai, 6, GlaxoSmithKlein(GSK), 1, 5, 6, Janssen, 6, Medac, 6, Novartis, 1, 5, 6, Roche, 6, UCB, 6; **L. Sconfienza**: Abiogen, 6, Bracco Imaging Italia, 6, Esaote, 6, Fidia, 6, Janssen, 6, Merck Serono, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, Samsung, 6; **L. Terslev**: Eli Lilly, 1, Janssen, 1, 6, Novartis, 6, UCB, 1; **B. Wildner**: None; **P. Zufferey**: None; **G. Filippou**: None.

Abstract Number: 1116

The Current State of Sodium-Glucose Cotransporter Type 2 Inhibitor Use Among Patients with Gout at a Tertiary Academic Healthcare System

Chio Yokose[1], Baijun Zhou[1], Natalie McCormick[1], Sruthi Tanikella[1], Minna Kohler[2], Janeth Yinh[1], Yuqing Zhang[3] and Hyon K. Choi[4], [1]Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [3]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, MA, [4]Massachusetts General Hospital and Harvard Medical School, Lexington, MA

SESSION INFORMATION

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Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: A substantial proportion of gout patients have type 2 diabetes (T2DM), heart failure (HF), and chronic kidney disease (CKD), for which SGLT2i treatment is recommended. Proactive use of SGLT2i among gout patients would have multiple benefits, including lowering the risk of HF and CKD progression, major adverse cardiovascular events (MACE), cardiovascular and all-cause mortality, in addition to their potential to lower serum urate and the risk of recurrent gout flares. We sought to examine the current state of SGLT2i use among gout patients with existing FDA-approved indications.

Methods: Using the Mass General Brigham (MGB) electronic health record, we identified two cohorts of gout patients with >1 gout-related encounter from 1/1/2021 to 1/4/2023 in the 1) Mass General Hospital rheumatology clinic (MGH rheum) or 2) anywhere within the MGB system (MGB gout). We used a combination of ICD codes, clinical variables, and laboratory values (**Table 1**) to determine the prevalence of FDA-approved indications for SGLT2i treatment: 1) T2DM and atherosclerotic cardiovascular disease (ASCVD); 2) T2DM and ASCVD risk factors; 3) T2DM and CKD; 4) CKD, defined as eGFR 20-44 mL/min/1.73m^2 or 45-89 mL/min/1.73m^2 with urinary albumin-to-creatinine ratio (UACR) ≥200 mg/g (regardless of T2DM); and 5) HF. We then determined the proportion of those patients with indications who were prescribed an SGLT2i.

Results: The MGH rheum and MGB gout cohorts included 1,212 and 21,301 gout patients, respectively (**Table 2**). The mean age was 64.9 and 68.1 years, respectively, and both groups were predominantly male. Of the patients in the MGH rheum and MGB gout cohorts, 41.8% and 45.6% had ≥1 FDA-approved indication for SGLT2i, respectively. However, only 10.7% and 9.7% of the patients with an SGLT2i indication (or 4.5% and 4.4% of the entire cohort) were actually prescribed one in the MGH rheum and MGB gout cohorts, respectively. The prevalence of SGLT2i indications was largely similar between the two cohorts. In both cohorts, CKD was the least prevalent indication at 16.2% and 16.0%, respectively. T2DM with ASCVD risk factors was the most prevalent indication in the MGB gout cohort at 28.4%, whereas T2DM with

Table 1. Definitions Used to Identify Indications for SGLT2i Treatment

Comorbidity	Definition
T2DM	≥2 ICD codes ever and/or hemoglobin A1c ≥6.5 ever
ASCVD	≥2 ICD codes for ASCVD ever
ASCVD risk factors	Age ≥55 and two or more of the following: obesity, hypertension, smoking, hyperlipidemia, UACR 30-300 mg/g
Obesity	Body mass index ≥30 kg/m^2
Hypertension	≥2 ICD codes for hypertension ever
Smoking	Variable available in clinical data warehouse
Hyperlipidemia	≥2 ICD codes for hyperlipidemia ever
CKD	eGFR 20-44 mL/min/1.73m^2 or eGFR 45-89 mL/min/1.73m^2 and UACR ≥200 mg/g
HF	≥2 ICD codes for HF ever

UACR = urinary albumin-to-creatinine ratio
eGFR = estimated glomerular filtration rate

Table 2. Cohort Characteristics and Indications for SGLT2i Treatment

	MGH rheum	MGB gout
N	1,212	21,301
Age, years	64.9 (14.5)	68.1 (13.7)
Male, n (%)	975 (80.5)	17076 (80.2)
Urate-lowering therapy use	659 (54.4)	7659 (36.0)
SGLT2i use	57 (4.7)	972 (4.6)
At least 1 indication for SGLT2i	507 (41.8)	9706 (45.6)
On SGLT2i‡	10.7%	9.7%
T2DM with ASCVD	244 (20.1)	4537 (21.3)
On SGLT2i‡	16.0%	13.1%
T2DM with ASCVD risk factors	287 (23.7)	6057 (28.4)
On SGLT2i‡	12.9%	11.5%
T2DM with CKD*	208 (17.2)	4134 (19.4)
On SGLT2i‡	16.8%	14.0%
CKD†	196 (16.2)	3404 (16.0)
On SGLT2i‡	16.3%	11.5%
HF	288 (23.8)	4670 (21.9)
On SGLT2i‡	14.6%	13.0%

*CKD defined as eGFR 20-59 and/or UACR ≥30 mg/g
†CKD defined as eGFR 20-44 or 45-89 with UACR ≥200 mg/g
‡Indicates proportion among those with indication listed immediately above

ASCVD risk factors and HF were similarly prevalent in the MGH rheum cohort at 23.7% and 23.8%, respectively. In both cohorts, T2DM with CKD was the indication for which the highest proportions of patients were appropriately prescribed an SGLT2i, although it still represented a minority of patients at 16.8% and 14.0%, respectively.

Conclusion: In this retrospective study from a large tertiary academic healthcare system, >40% of gout patients had ≥1 indication for SGLT2i. However, only about 10% of those with an indication for SGLT2i (or approximately 4.5% of the entire cohort) were prescribed one. Because SGLT2i have a myriad of proven cardiometabolic-kidney benefits, more proactive use of SGLT2i among patients with gout with an existing indication could improve their comorbidity outcomes and prevent premature mortality, while simultaneously yielding potential gout-related benefits. Future studies on the use of SGLT2i among gout patients are required, given the rapidly expanding indications for SGLT2i in cardiometabolic-kidney comorbidity care.

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Serum Urate Change Among Gout Patients Initiating Sodium-Glucose Cotransporter Type 2 Inhibitors (SGLT2i) vs. Sulfonylureas: A Comparative Effectiveness Analysis

Chio Yokose[1], Gregory Challener[2], Baijun Zhou[2], Natalie McCormick[2], Sruthi Tanikella[2], Kila Panchot[2], Minna Kohler[3], Janeth Yinh[2], Yuqing Zhang[4], David Bates[5], James Januzzi[2], Meghan Sise[2], Deborah Wexler[2] and Hyon K. Choi[6], [1]Massachusetts General Hospital, Waltham, MA, [2]Massachusetts General Hospital, Boston, MA, [3]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [4]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, MA, [5]Brigham and Women's Hospital, Boston, MA, [6]Massachusetts General Hospital and Harvard Medical School, Lexington, MA

SESSION INFORMATION

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Background/Purpose: Sodium-glucose cotransporter type 2 inhibitors (SGLT2i) are currently indicated as second-line therapy for type 2 diabetes and are also approved for the treatment of heart failure and chronic kidney disease, all comorbidities prevalent among gout patients. SGLT2i have also been found to reduce serum urate (SU), the causal mediator of gout, by up to 1.8 mg/dL among those with hyperuricemia (Doehner et al., Eur Heart J, 2022). However, no data are available specifically among patients with gout. We sought to determine the SU change among gout patients treated with SGLT2i or sulfonylurea (SFU, another second-line diabetes agent).

Methods: Using the Mass General Brigham electronic health record database, we identified all gout patients initiating SGLT2i or SFU who had SU measured within 3 months before and after the initiation through 2/2/2023. Gout patients were identified using an algorithm with a positive predictive value of 0.9 against the 2015 ACR/EULAR gout criteria and were required to have baseline SU ≥6 mg/dL. A rheumatologist reviewed all identified patient records to confirm their gout diagnosis and the initiation and continuation of SGLT2i or SFU treatment during the study period (up to 6 months). Patients who had SU measured < 7 days after the initial prescription or in the setting of an acute gout flare were excluded, as were patients who initiated or changed the dose of urate-lowering therapy (ULT) just prior to or during the study period. We first

calculated the within-group SU change. Then, we compared the two groups for SU change using multivariable linear regression adjusting for age, sex, baseline SU, and ULT use. We additionally adjusted for each of the other covariates for robustness and conducted subgroup analyses per ULT use and key comorbidities.

Results: There were 23 patients with gout who initiated SGLT2i and 24 patients who initiated SFU. The SGLT2i-initiators were slightly older, while the SFU-initiators included more females and had higher baseline SU (**Table 1**). Among SGLT2i-initiators, the mean SU change was -1.6 mg/dL (95% CI, -2.2 to -0.9), compared with 0.3 mg/dL (95% CI, -0.5 to 1.0) among SFU-initiators (**Figure 1**). During the study period, 43.5% of SGLT2i-initiators reached target SU < 6 mg/dL compared to 4.2% of SFU-initiators. The adjusted SU change associated with SGLT2i initiation was -1.6 mg/dL (95% CI, -2.6 to -0.7)

Table 1. Baseline Characteristics of Initiators of SGLT2i vs. Sulfonylurea

	SGLT2i (n=23)	Sulfonylurea (n=24)
Age, years, mean (SD)	66.7 (9.0)	61.6 (13.9)
Female, n (%)	1 (4.3)	4 (16.7)
Race, n (%)		
White	16 (69.6)	12 (50.0)
Other	7 (30.4)	12 (50.0)
BMI, mean (SD)	34.9 (6.7)	33.6 (5.5)
Serum urate, mg/dL, mean (SD)	7.8 (1.4)	8.3 (1.4)
Hemoglobin A1c, %, mean (SD)	7.5 (1.7)	8.6 (1.7)
eGFR, mL/min/1.73m^2, mean (SD)	47.5 (22.5)	48.8 (16.4)
Hypertension, n (%)	8 (34.8)	11 (45.8)
Type 2 diabetes, n (%)	16 (69.6)	24 (100.0)
Chronic kidney disease stage ≥3, n (%)	16 (69.6)	17 (70.8)
Heart failure, n (%)	13 (56.5)	4 (16.7)
Medications, n (%)		
Diuretics	19 (82.6)	15 (62.5)
Urate-lowering therapy (with no recent change)	17 (73.9)	9 (37.5)
Aspirin	10 (43.5)	8 (33.3)
Losartan	1 (4.3)	3 (12.5)
Colchicine	9 (39.1)	8 (33.3)
NSAIDs	7 (30.4)	10 (41.7)
DPP4i	2 (8.7)	0 (0.0)
GLP1-RA	5 (21.7)	0 (0.0)
Insulin	10 (43.5)	7 (29.2)

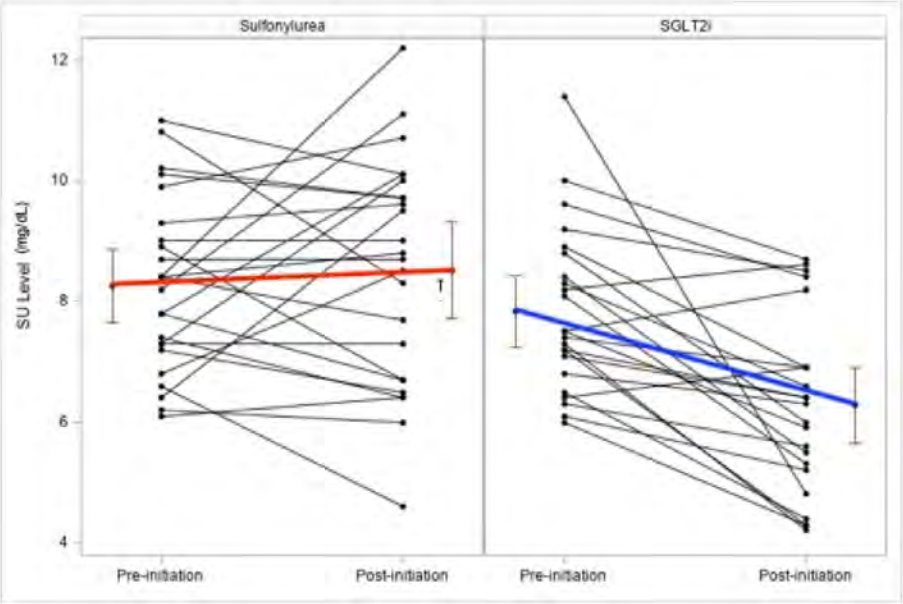
DPP4i = dipeptidyl peptidase 4 inhibitors; GLP1-RA = glucagon-like peptide-1 receptor agonists

Table 2. Adjusted Serum Urate Change Among Initiators of SGLT2i vs. Sulfonylurea

	Age, Sex adjusted	Multivariable 1*	Multivariable 2*
Overall	-1.7 mg/dL (-2.7 to -0.7)	-1.9 mg/dL (-2.8 to -0.9)	-1.6 mg/dL (-2.6 to -0.7)
ULT Use	-1.7 mg/dL (-3.1 to -0.2)	-1.7 mg/dL (-3.1 to -0.3)	—
No ULT Use	-1.6 mg/dL (-3.0 to -0.1)	-1.7 mg/dL (-3.1 to -0.4)	—
Diuretic Use	-1.9 mg/dL (-3.1 to -0.8)	-2.2 mg/dL (-3.3 to -1.1)	-1.8 mg/dL (-2.9 to -0.8)
Type 2 Diabetes	-1.2 mg/dL (-2.2 to -0.2)	-1.3 mg/dL (-2.3 to -0.3)	-1.1 mg/dL (-2.1 to -0.1)
CKD	-1.3 mg/dL (-2.2 to -0.3)	-1.6 mg/dL (-2.6 to -0.6)	-1.4 mg/dL (-2.4 to -0.4)
Prescriptions after March 2013†	-2.1 mg/dL (-3.4 to -0.8)	-2.1 mg/dL (-3.3 to -1.0)	-1.8 mg/dL (-2.9 to -0.7)

Multivariable 1: age, sex, and baseline SU
Multivariable 2: age, sex, baseline SU, and ULT use
†FDA-approval of first SGLT2i in the US

Figure 1. Serum Urate Change Among Initiators of SGLT2i vs. Sulfonylurea



compared with SFU initiation, and remained similar when stratified by ULT use (**Table 2**). These results did not change materially with additional adjustments for other covariates but were slightly attenuated but still significant among those with diabetes.

Conclusion: In this comparative effectiveness analysis of gout patients, SGLT2i use was associated with a notable reduction in SU over several months, whereas SFU use was not. With their proven multiple cardiometabolic-kidney benefits, these results suggest that SGLT2i could be a much-needed multi-purpose medication for the synergistic treatment of gout and its comorbidities, regardless of ULT use, and call for randomized clinical trials to test this hypothesis.

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Abstract Number: 1118

The Nomenclature of Calcium Pyrophosphate Deposition (CPPD) Disease – Results of a Systematic Literature Review for the Gout, Hyperuricemia and Crystal-Associated Disease Network (G-CAN) CPPD Nomenclature Project

Silvia Sirotti[1], Charlotte Jauffret[2], Edoardo Cipolletta[3], Daniele Cirillo[4], Luca Ingrao[4], Alessandro Lucia[4], Antonella Adinolfi[5], Debora Pireddu[4], Emilio Filippucci[6], Tristan Pascart[2], Sara Tedeschi[7], Robert Terkeltaub[8], Nicola Dalbeth[9] and Georgios Filippou[1], [1]IRCCS Galeazzi - Sant'Ambrogio Hospital, Milan, Italy, [2]Saint-Philibert Hospital, Lille Catholic University, Lille, France, [3]Polytechnic University of Marche, Ancona, Italy, [4]Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milan, Italy, [5]Rheumatology Unit, Grande Ospedale Metropolitano Niguarda, Milano, Italy, [6]Polytechnic University of Marche, Jesi, Italy, [7]Brigham and Women's Hospital, Boston, MA, [8]University of California San Diego, San Diego, CA, [9]University of Auckland, Auckland, New Zealand

SESSION INFORMATION

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Background/Purpose: Despite prior attempts at standardising terminology of calcium pyrophosphate deposition (CPPD) disease (including the 2011 EULAR recommendations for CPPD terminology and diagnosis), many different terms are still used interchangeably to describe the disease, its elements, and its states. This confusing nomenclature has important implications for research and for patient care. The Gout, Hyperuricemia and Crystal-Associated Disease Network (G-CAN) has developed a CPPD Nomenclature Project which aims to achieve international consensus about the nomenclature of CPPD. In this first step of the project, the aim was to identify the definitions, the disease elements and the clinical states of CPPD and their corresponding labels in the scientific literature.

Methods: A systematic literature search was performed in the PubMed database starting from 01/01/2000 to 31/01/2022. The search was restricted to studies on humans and in the English language. Eight reviewers independently extracted terms related to disease definition, aetiology, pathogenesis, clinical presentation, imaging features and clinical states of CPPD. An *a priori* list of disease elements and clinical states was generated by the authors and further elements were added during data collection as appropriate. Labels for each identified disease element and clinical state were extracted and analysed to determine their frequency.

Results: A total of 2392 articles were identified using the search criteria, 1028 articles were included. The complete list of evaluated elements is showed in **Figure 1**. There was great inconsistency in the terminology used for the disease, its elements and its states. The 3 most common labels used to identify the disease were "pseudogout", "calcium pyrophosphate deposition disease" and "chondrocalcinosis". The most common acronym used was "CPPD", mostly with the meaning of "calcium pyrophosphate deposition disease" or "calcium pyrophosphate deposition" (**Table 1**). The 2 most commonly used labels describing "an episode of acute CPPD arthritis" were "pseudogout" (31%), and "acute calcium pyrophosphate crystal arthritis" (10%). For "more than one episode of acute CPPD arthritis", "recurrent pseudogout" (17%) or "recurrent

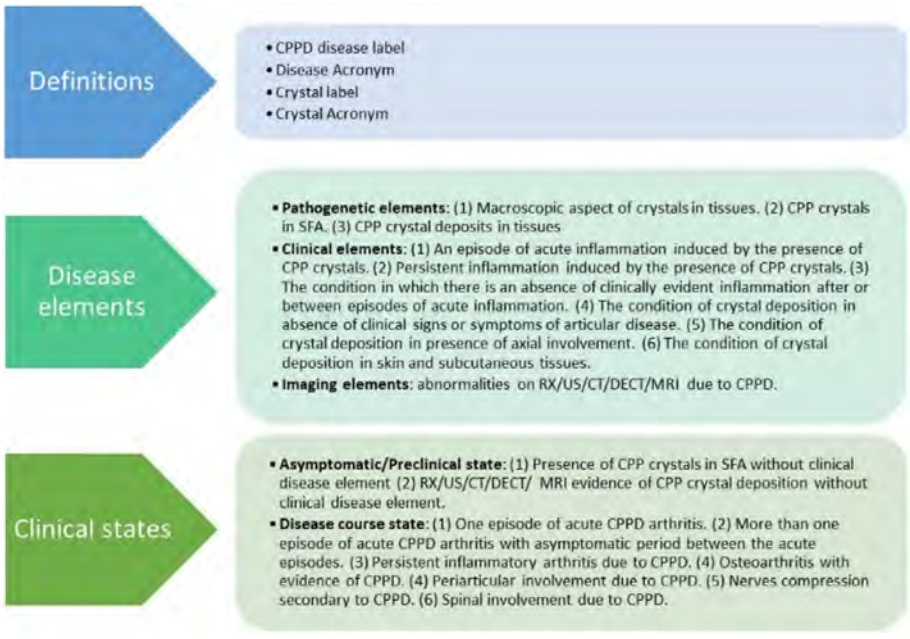

Figure 1: List of definitions, disease elements and clinical states

Table 1: Example of labels extracted for calcium pyrophosphate deposition disease

Element	More frequent labels	Frequency
Disease label	**Pseudogout**	**43.4%**
	Calcium pyrophosphate deposition disease	22.3%
	Chondrocalcinosis	21.5%
	Calcium pyrophosphate dihydrate deposition disease	12.8%
	Calcium pyrophosphate dihydrate crystal deposition disease	12.7%
	Other	57%
Acronym	**CPPD**	**63.9%**
	CC	8.4%
	CPDD	8.1%
	CPPDD	1.9%
	CPPD-CDD	1.6%
	Other	24%
Acronym meaning	**Calcium pyrophosphate deposition disease**	**24.1%**
	Calcium pyrophosphate deposition	16.1%
	Calcium pyrophosphate dihydrate deposition disease	7.1%
	Chondrocalcinosis	5.6%
	Calcium pyrophosphate crystal deposition	5%
	Other	47.3%

arthritis'' (10%) were the most used labels. ''Chronic calcium pyrophosphate crystal arthritis'' (13%) and ''pseudo-rheumatoid arthritis'' (11%) were the most commonly used labels to describe ''persistent inflammatory arthritis due to CPPD''. The most used labels used to identify ''osteoarthritis with evidence of CPPD'' were ''pseudo-osteoarthritis'' (11%) and ''calcium pyrophosphate crystal deposition with osteoarthritis'' (9%).

Conclusion: These results demonstrate the variability and lack of precision in the labels used to describe CPPD disease. The next steps of the project will be to achieve agreement about CPPD disease nomenclature through a Delphi exercise and consensus meeting, and to develop an easily understandable common language definition to increase scientific understanding and awareness of this condition and to facilitate communication with patients.

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Abstract Number: 1119

Preliminary Descriptive Analysis of the RADIAL Cohort Study About the Prevalence and the Clinical Characteristics of Patients with CPPD in Daily Clinical Practice

Silvia Sirotti[1], Joao Madruga-Dias[2], Antonella Adinolfi[3], Garifallia Sakellariou[4], Davide Rozza[5], Greta Carrara[5], Gianpiero Landolfi[5], Carlo Alberto Scire[5], Annamaria Iagnocco[6] and Georgios Filippou[1], [1]IRCCS Galeazzi - Sant'Ambrogio Hospital, Milan, Italy, [2]Centro Hospitalar do Médio Tejo, NOVA Medical School, Lisbon, Portugal, [3]Rheumatology Unit, Grande Ospedale Metropolitano Niguarda, Milano, Italy, [4]Department of Internal Medicine and Therapeutics, Università di Pavia, Istituti Clinici Scientifici Maugeri IRCCS, Pavia, Italy, [5]Società Italiana di Reumatologia, Epidemiology Research Unit, Milan, Italy, [6]University of Turin, Roma, Italy

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Background/Purpose: The RADIAL study is aimed to evaluate the performance of a composite approach, based on clinical, laboratory and ultrasound (US) data in the differential diagnosis among the main inflammatory arthropathies and Osteoarthritis (OA). In this preliminary analysis, based on partial data, we present the prevalence and the clinical characteristics of the patients affected by Calcium Pyrophosphate Deposition (CPPD) as diagnosed by US.

Methods: The RADIAL study is a multicenter, international, mixed design (retrospective, cross-sectional, prospective) diagnostic accuracy study. Consecutive patients reaching the rheumatology outpatients clinic for the first time, with suspicion of an inflammatory arthropathy, aged 18 or older and with recent standard blood exams were enrolled in the study. All patients underwent a US examination of an extended set of target joints for the assessment of specific lesions for Rheumatoid Arthritis, Psoriatic Arthritis, Gout, CPPD, Polymyalgia Rheumatica and OA. Demographic and clinical data were also collected. The presence of typical deposits in at least one joint classified patient as affected by CPPD for this preliminary analysis. After the first visit, all patients entered in routine follow up and treatment strategies were adopted according to guidelines after the diagnosis was made. To increase certainty of the diagnosis, patients will be classified after one year of follow-up (ongoing at the time of submission). In this analysis, we assessed the prevalence of CPPD in the cohort of the RADIAL study, stratified by age and US findings.

Results: 550 patients were enrolled, 58.9% female with a mean age of 60.1 yo (±14.4). 57.8% of the patients were affected by CPPD (318/550) considering the entire cohort, with a mean age of 63 yo (±13.1), significantly higher when compared to no CPPD patients [mean age 56.2 yo (±15.3)]. Stratifying by ageing, the prevalence increases to 66.2% considering the patients older than 60 (188/284) and 73% considering 80 yo or older subjects (30/41). From the US point of view, patients with CPPD had a significantly higher inflammatory involvement of wrists and knees at US (both in grey scale and power Doppler assessment - $p < 0.001$) compared to patients with any other disease and no CPPD, while no differences have been emerged between CPPD and the other arthropathies about the comorbidities and the general clinical profile.

Conclusion: CPPD is commonly encountered in a routine rheumatological setting, reaching a prevalence of more than 65% in patients older than 60. Symptom attribution is challenging as many conditions may be associated and even a higher presence of synovitis in patients with CPPD cannot be unequivocally attributed to it. There is an impellent need to raise awareness on CPPD and its possible implications. We expect RADIAL study to supply additional data on these findings.

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Abstract Number: 1120

Target Serum Urate Levels, Recurrent Gout Flare Rates, and Gout-Primary Hospitalizations: Nationwide Prospective Cohort Study of 3,613 Gout Patients

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Despite rheumatology guidelines' emphasis on treat-to-target-serum-urate (SU) levels (<6 or <5 mg/dL, urate crystal sub-saturation points), this pathophysiology-based recommendation is not accepted in primary care practice (where >90% of gout care occurs) or endorsed by the American College of Physicians.To that end, proportions of

Table 1. Rate and Rate Ratio (RR) for Recurrent Gout Flares According to Serum Urate Level and Follow-Up Time from Baseline. No, number; PY, person years; 95% CI, 95% confidence interval.

Table 1. Rate and Rate Ratio (RR) for Recurrent Gout Flares According to Serum Urate Level and Follow-Up Time from Baseline

	No of Gout Patients	Follow-up, Person years (PY)	No of Flares	Flares per 1000 PY	Crude RR (95% CI)	Age, Sex, and Race Adjusted RR (95% CI)
1 Year						
<6 mg/dL	1057	1057	10	9.5	1.0 (ref)	1.0 (ref)
6 to 7	781	780	42	53.9	5.69 (2.86 to 11.34)	5.03 (2.52 to 10.07)
7 to 8	872	870	109	125.3	13.24 (6.93 to 25.29)	11.64 (6.06 to 22.35)
8 to 9	609	609	77	126.4	13.36 (6.91 to 25.81)	11.81 (6.08 to 22.92)
9 to 10	212	212	41	193.8	20.47 (10.26 to 40.87)	18.95 (9.46 to 37.97)
≥10 mg/dL	82	82	25	306.7	32.40 (15.57 to 67.46)	29.13 (13.94 to 60.87)
Per mg/dL	3613	3608	304	84.3	1.60 (1.49 to 1.71)	1.59 (1.48 to 1.71)
2 Years						
<6 mg/dL	1057	2110	22	10.4	1.0 (ref)	1.0 (ref)
6 to 7	781	1554	77	49.5	4.75 (2.96 to 7.63)	4.28 (2.66 to 6.90)
7 to 8	872	1735	184	106.0	10.17 (6.54 to 15.83)	9.15 (5.86 to 14.29)
8 to 9	609	1217	155	127.3	12.21 (7.81 to 19.09)	11.08 (7.07 to 17.39)
9 to 10	212	421	81	192.3	18.45 (11.51 to 29.55)	17.41 (10.83 to 27.97)
≥10 mg/dL	82	162	44	272.4	26.13 (15.66 to 43.59)	24.12 (14.42 to 40.37)
Per mg/dL	3613	7200	563	78.2	1.60 (1.52 to 1.68)	1.59 (1.51 to 1.68)
5 Years						
<6 mg/dL	1057	5230	58	11.1	1.0 (ref)	1.0 (ref)
6 to 7	781	3845	168	43.7	3.94 (2.92 to 5.31)	3.55 (2.63 to 4.80)
7 to 8	872	4299	407	94.2	8.54 (6.48 to 11.24)	7.66 (5.80 to 10.11)
8 to 9	609	3023	368	121.4	10.98 (8.32 to 14.48)	9.91 (7.49 to 13.10)
9 to 10	212	1041	172	165.2	14.90 (11.06 to 20.06)	13.86 (10.27 to 18.71)
≥10 mg/dL	82	397	76	188.9	17.26 (12.27 to 24.30)	15.80 (11.20 to 22.8)
Per mg/dL	3613	17,836	1249	69.8	1.56 (1.51 to 1.61)	1.55 (1.49 to 1.60)
10 Years						
<6 mg/dL	1057	8833	94	10.6	1.0 (ref)	1.0 (ref)
6 to 7	781	6458	257	39.8	3.74 (2.95 to 4.73)	3.38 (2.66 to 4.29)
7 to 8	872	7260	595	82.0	7.70 (6.20 to 9.57)	6.93 (5.56 to 8.63)
8 to 9	609	5106	516	101.1	9.50 (7.62 to 11.83)	8.57 (6.86 to 10.71)
9 to 10	212	1756	220	125.3	11.77 (9.25 to 14.99)	10.93 (8.57 to 13.95)
≥10 mg/dL	82	663	88	132.8	12.47 (9.33 to 16.68)	11.40 (8.51 to 15.28)
Per mg/dL	3613	30,076	1770	58.9	1.50 (1.46 to 1.54)	1.49 (1.45 to 1.53)

No, number; PY, person years; 95% CI, 95% confidence interval.

gout flares associated with these target levels, including those requiring hospitalization, are unknown. We quantified associations of target SU with recurrent flares, including gout-primary hospitalizations, among gout patients nested in a prospective nationwide cohort.

Methods: This was a prospective cohort study of UK adults recruited over 2006-2010 and followed-up through primary care medical record linkage. As done previously [Cipolletta *et al. JAMA* 2022], flares among prevalent gout patients were ascertained by (1) hospitalization with gout (ICD-10 M10) as primary discharge diagnosis; (2) diagnosis of gout flare in primary care records; or (3) diagnosis of gout in primary care records and prescription issued on the same day for corticosteroids, colchicine, or non-steroidal anti-inflammatory drugs (NSAIDs).We also investigated flares requiring hospitalisation. Poisson regression was used to assess the relation between baseline SU levels and rates of recurrent gout flares over 1, 2, 5, and 10 years of follow-up.

Results: We followed 3,613 prevalent gout patients (86% male, mean age 60 years), among whom we documented 1,770 gout flare events over 10 years.95% (1,676/1,770) and 98% (1,728/1,770) of flares occurred in baseline SU ≥6 and ≥5 mg/dL, respectively. Rate ratio (RR) for flares with SU levels of < 6.0, 6.0-6.9, 7.0-7.9, 8.0-8.9, 9.0-9.9, and ≥10 mg/dL were

Table 2: Rate and Rate Ratio (RR) for Recurrent Gout Flares per mg/dL of Serum Urate, According to Subgroups over 10 Years. CKD, chronic kidney disease; ULT, urate-lowering therapy; SD, standard deviation.

Table 2: Rate and Rate Ratio (RR) for Recurrent Gout Flares per mg/dL of Serum Urate, According to Subgroups over 10 Years.
CKD, chronic kidney disease; ULT, urate-lowering therapy.

		10 Years					
Subgroup		No of Gout Patients	Follow-up, Person years (PY)	No of Flares	Flares per 1000 PY	Age, Sex, and Race Adjusted RR, per mg/dL (95% CI)	P for interaction
Age	<60	1345	11,390	664	58.3	1.46 (1.39 to 1.53)	0.17
	≥60	2268	18,690	1106	59.2	1.52 (1.46 to 1.58)	
Sex	Men	3104	25,803	1675	64.9	1.48 (1.44 to 1.53)	0.17
	Women	509	4,277	95	22.2	1.61 (1.44 to 1.79)	
Race	Non-White	152	1,250	88	70.4	1.40 (1.24 to 1.59)	0.42
	White	3461	28,830	1682	58.3	1.50 (1.45 to 1.54)	
CKD Stage ≥ 3	Present	233	1,849	124	67.0	1.39 (1.28 to 1.52)	0.36
	Absent	3380	28,231	1646	58.3	1.46 (1.41 to 1.52)	
Diuretic Use	Yes	434	3,558	199	55.9	1.48 (1.36 to 1.61)	0.49
	No	3179	26,522	1571	59.2	1.51 (1.46 to 1.55)	
ULT Use	Yes	749	6,227	148	23.8	1.46 (1.32 to 1.62)	0.26
	No	2864	23,853	1622	68.0	1.51 (1.46 to 1.56)	

Table 3: Rate and Rate Ratios (RR) for Recurrent Gout Flares Requiring Hospitalization No, number; PY, person years; SD, standard deviation; 95% CI, 95% confidence interval. Hospitalizations were ascertained through March 5, 2020 (max 12.8 years follow-up)

Table 3: Rate and Rate Ratios (RR) for Recurrent Gout Flares Requiring Hospitalization

	No of Gout Patients	Follow-up, Person years (PY)	No of Flares	Flares per 1000 PY	Crude RR (95% CI)	Age, Sex, and Race Adjusted RR (95% CI)
<6 mg/dL	1057	11,198	2	0.18	1.0 (ref)	1.0 (ref)
6 to 7	781	8214	8	0.97	5.45 (1.16 to 25.68)	4.77 (1.00 to 22.65)
7 to 8	872	9226	17	1.8	10.32 (2.38 to 44.65)	9.02 (2.06 to 39.42)
8 to 9	609	6450	14	2.2	12.15 (2.76 to 53.47)	10.58 (2.38 to 47.04)
9 to 10	212	2229	15	6.7	37.68 (8.62 to 164.76)	34.36 (7.79 to 151.67)
≥10 mg/dL	82	825	8	9.7	54.30 (11.53 to 255.72)	46.43 (9.77 to 220.78)
Per mg/dL	3613	38,142	64	1.7	1.78 (1.55 to 2.05)	1.77 (1.53 to 2.05)

No, number; PY, person years; 95% CI, 95% confidence interval. Hospitalizations were ascertained through March 5, 2020 (max 12.8 years follow-up).

1.0, 5.03, 11.64, 11.81, 18.95, and 29.13, respectively during first year of follow-up (1.59 [1.48-1.71] per mg/dL), and 1.0, 3.38, 6.93, 8.57, 10.93, and 11.40, respectively, over whole 10-year follow-up (1.49 [1.45-1.53] per mg/dL) (**Table 1**).Associations persisted irrespective of sex, race, age group, chronic kidney disease status, and diuretic and urate-lowering therapy use (all P for interaction >0.17) (**Table 2**). 97% (62/64) and 100% (64/64) of flares requiring hospitalization occurred in baseline SU ≥6 and ≥5 mg/dL, respectively (**Table 3**); corresponding RR were 1.0, 4.77, 9.02, 10.58, 34.36, and 46.43, respectively (1.77 [1.53-2.05] per mg/dL).

Conclusion: In this prospective cohort of gout patients treated in primary care, 95% and 98% of flares occurred in baseline SU ≥6 and ≥5 mg/dL, respectively. Associations were more prominent for hospitalized flares, with no cases among those with SU < 5mg/dL; higher serum urate levels are strongly associated with frequency of recurrent flares in a graded manner. These findings support the utility of these target urate levels for gout patient care, consistent with a treat-to-target approach recommended by rheumatology societies in the US and Europe, but not the American College of Physicians.

Disclosure: N. McCormick: None; **C. Yokose**: None; **G. Challener**: None; **A. Joshi**: Regeneron, 3; **S. Tanikella**: None; **H. Choi**: Ani, 2, Horizon, 2, 5, LG, 2, Protalix, 2, Shanton, 2.

Abstract Number: 1121

Cardiovascular Safety of Febuxostat in Patients with Gout or Hyperuricemia: A Systematic Review of Randomized Controlled Trials

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
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Background/Purpose: To this date, a causal relationship between febuxostat and cardiovascular disease remains controversial as comparison between trials can be challenging and may lead to misleading conclusions especially when facing heterogeneous cardiovascular outcomes. We aimed to compare the cardiovascular outcomes in the most pertinent trials of Febuxostat compared to controls.

Methods: We searched electronic databases using a PICOS-style approach search strategy of randomized controlled trials on cardiovascular outcomes of Febuxostat in patients with gout or hyperuricemia. We conducted a quality and risk of bias assessment of the included clinical trials. The definition of MACE as well as all reported cardiovascular outcomes were retrieved from every involved trial.

Results: Of the 1173 records identified from all sources, 20 RCTs were included in the analysis. Mean duration of follow-up was 69.7 ± 81.5 weeks and Febuxostat dose ranged from 10 to 240 mg with 80 mg being the most commonly used dosage. Overall, the quality of evidence deriving from all RCTs showed concerns in most studies (65%). Major cardiovascular event (MACE) was defined in 7 of the 20 RCTs (35%) and cardiovascular outcome reporting was very heterogeneous. Overall, data of cardiovascular safety of Febuxostat were reassuring.

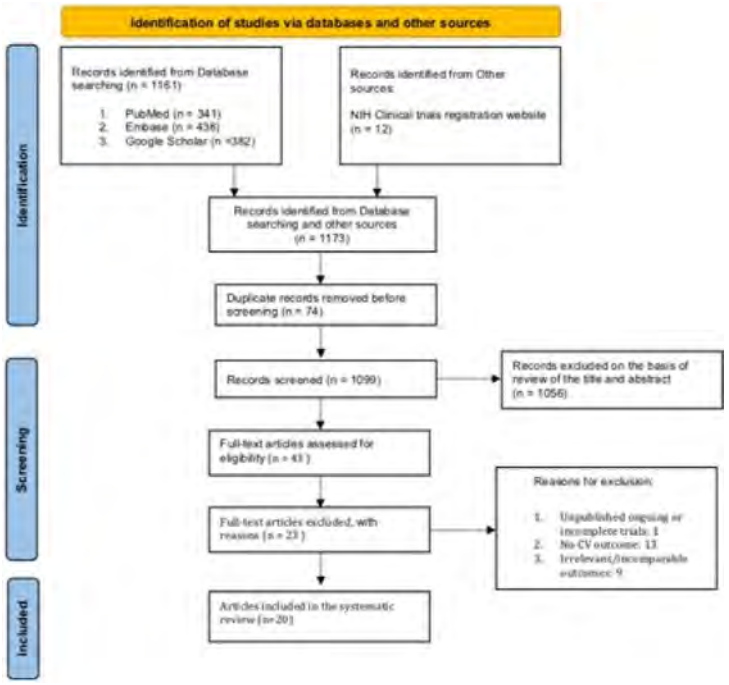

Figure 1: Flowchart of the included studies NIH: National Institutes of Health; CV: Cardiovascular

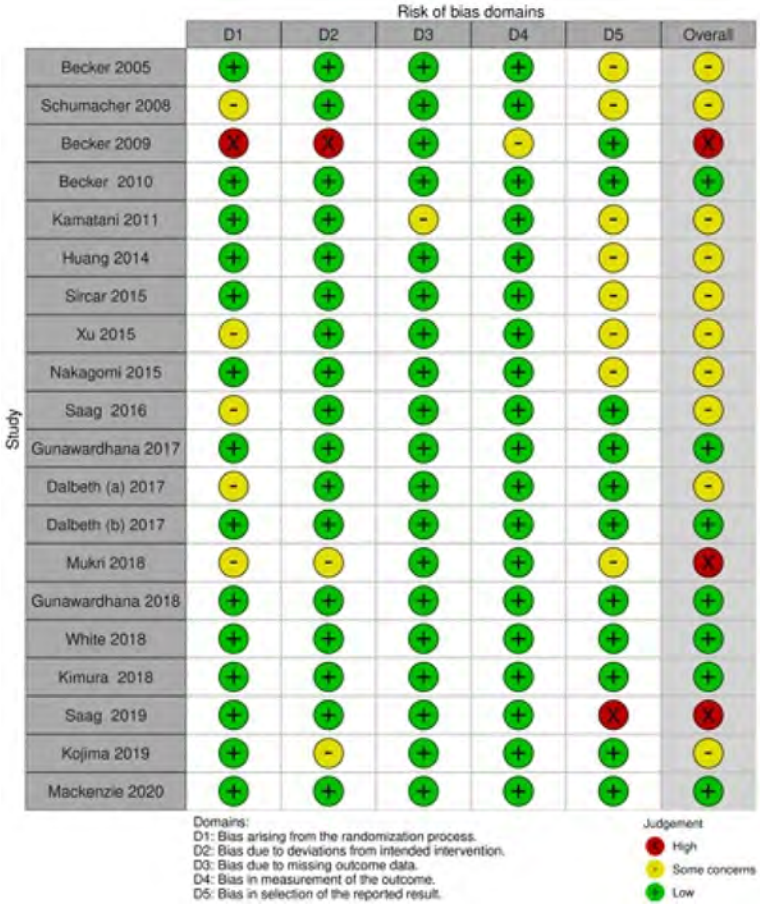

Figure 2: Risk of bias of included randomized trials

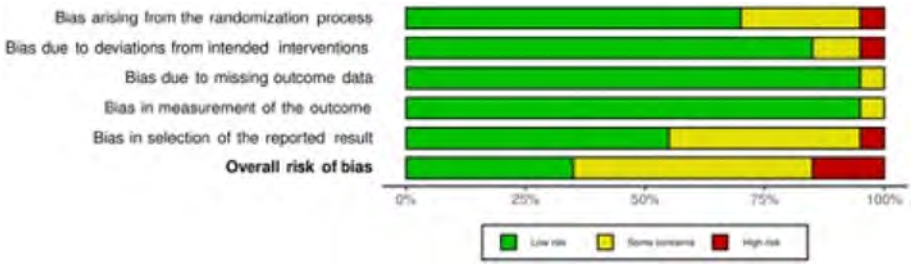

Figure 2: Risk of bias of included randomized trials

Conclusion: Our systematic review showed no alarming increase of cardiovascular mortality and outcomes in Febuxostat treated patients except for the CARES trial in which the credibility of the results is biased by the high rate of drug discontinuation and of most importantly, withdrawal from follow-up. FAST trial results, backed up with real-world data cohort studies, were robust and reassuring with regard to the cardiovascular safety of Febuxostat in most white males with gout including elderly patients. This should lead the regulatory agencies to reconsider the limitations imposed on the use of Febuxostat in patients with non-severe CV burden

Disclosure: R. Ghossan: None; **O. Aitisha Tabesh**: None; **F. Fayad**: None; **P. Richette**: None; **T. Bardin**: None.

Abstract Number: 1122

The Tophus Impact Questionnaire (TIQ-20): Responsiveness to Change During Urate-Lowering Therapy

Cindy Cao[1], Greg Gamble[1], Anne Horne[1], Opetaia Aati[1], Anthony Doyle[1], Jill Drake[2], Lisa Stamp[3] and **Nicola Dalbeth**[1], [1]University of Auckland, Auckland, New Zealand, [2]Te Whatu Ora Waitaha, Christchurch, New Zealand, [3]University of Otago, Christchurch, New Zealand

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
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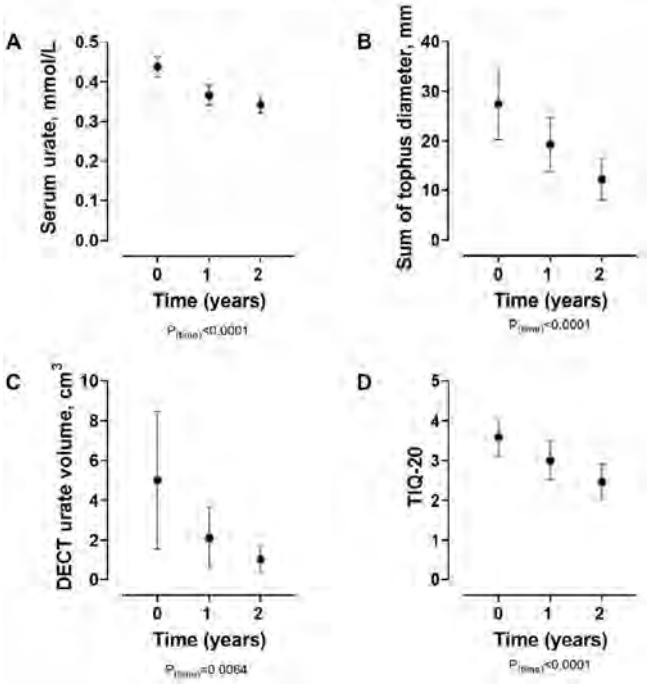
Session Time: 9:00AM–11:00AM

Background/Purpose: In 2015, the 20-item Tophus Impact Questionnaire (TIQ-20) was developed as a tophus-specific patient reported outcome measure (Aati et al., 2015). Initial analysis of the TIQ-20 showed good psychometric properties, with high internal, face and construct validity, reproducibility, and feasibility. To date, responsiveness over time has not been reported. The aim of this study was to determine whether the TIQ-20 changes during urate-lowering therapy.

Methods: We analysed data from a two-year randomized controlled trial of allopurinol dose escalation (Stamp et al, 2017). Briefly, participants with gout on allopurinol with serum urate ≥0.36mmol/L (6mg/dL) were randomised to immediate allopurinol dose escalation to achieve a serum urate of < 0.36mmol/L, or a control group with no change in allopurinol dose. After one year, participants in the control group also had allopurinol dose escalation to achieve a serum urate of < 6mg/dL.

For participants with tophaceous gout, the longest diameter of up to three index tophi was measured using Vernier calipers and the TIQ-20 was recorded at study visits. Participants at the one site were invited into an imaging sub-study with dual energy CT (DECT) of the feet at baseline, Year 1, and Year 2.

Figure. Mean (95% CI) values for A. serum urate, B. sum of index tophus diameter, C. DECT urate volume, D. TIQ-20.



Participants were included in this analysis if they had tophaceous gout and TIQ-20 scores available at baseline, Year 1, and Year 2 (n=58, 39 with DECT data). Data from these visits were analysed using mixed model analysis. Cohen's d was calculated as a standardized effect size for assessing the difference between the baseline and Year 2 tophus mean values. Rasch modelled TIQ-20 scores were used throughout the analysis.

Results: The mean (SD) serum urate reduced over the two-year period from 0.44 (0.10) to 0.34 (0.08) mmol/L, P< 0.001 (Figure). Improvements were observed in all tophus measures including the TIQ-20 over the two-year period, with no difference between the two treatment groups (P >0.34 for treatment allocation). For the entire group, the mean (SD) sum of the index tophi diameter reduced from 27.4 (27.2) to 12.2 (16.4) mm, P< 0.0001, and the DECT urate volume reduced from 5.01 (9.85) to 1.04 (2.03) cm^3, P=0.006 (Figure). The TIQ-20 scores also reduced over two years from 3.59 (1.77) to 2.46 (1.73), P< 0.0001 (Figure), and the mean (95% CI) TIQ-20 change over the two years was -1.13 (-1.54, -0.71). Cohen's d for the sum of the index tophi diameter was 0.68, for DECT urate volume was 0.5, and for the TIQ-20 was 0.71.

Conclusion: For people with tophaceous gout treated with allopurinol using a treat to target serum urate approach, improvements in TIQ-20 occur, as well as improvements in physical and imaging tophus measures. These findings demonstrate that the TIQ-20 is a responsive instrument of tophus burden.

Disclosure: C. Cao: None; **G. Gamble**: None; **A. Horne**: None; **O. Aati**: None; **A. Doyle**: None; **J. Drake**: None; **L. Stamp**: None; **N. Dalbeth**: Arthrosi, 2, AstraZeneca, 2, Dyve Biosciences, 2, Hikma, 6, Horizon, 2, JW Pharmaceutical Corporation, 2, LG, 2, Novartis, 6, Novotech, 5, PK Med, 2, Protalix, 2, PTC Therapeutics, 2, Selecta, 2, Unlocked Labs, 2.

Abstract Number: 1123

Real-world Trends in the Use of Immunomodulation as Co-therapy to Pegloticase: Claims-based Findings Since 2016

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Session Date: Monday, November 13, 2023
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Background/Purpose: Pegloticase can treat uncontrolled gout but anti-drug antibodies limit urate-lowering response and put patients at risk for infusion reactions (IRs).[1, 2] The first case series of pegloticase+methotrexate (MTX) co-administration was presented in Nov 2018, showing a 100% response rate with no IRs.[3, 4] Real-world[5] and clinical trial data[6-8] have continued to support pegloticase+immunomodulation (IMM) co-therapy, with MIRROR RCT confirming pegloticase+MTX superiority (month 6 response rate: 71% vs. 39%; IR rate: 4% vs. 31%).[9] The pegloticase label was updated to include MTX co-therapy in July 2022.[10] Here, we examine real-world IMM co-therapy adoption through Nov 2022 using a large insurance claims database.

Methods: The Merative™ MarketScan® Research Databases (closed claims data, commercially-insured patients) were searched for patients with ≥1 pegloticase infusion code (J2507) between Jan 2016 and Nov 2022. Patients who had data within 180 days before and within 60 days after first J-code were included (not all patients who received pegloticase included). The use of IMM co-therapy (≥1 pharmacy claim [based on NDC code] for MTX, mycophenolate mofetil [MMF], azathioprine, leflunomide and/or cyclosporin ≤60 days before/after first J-code) was examined. Data are presented as mean(±SD) or n(%) as appropriate.

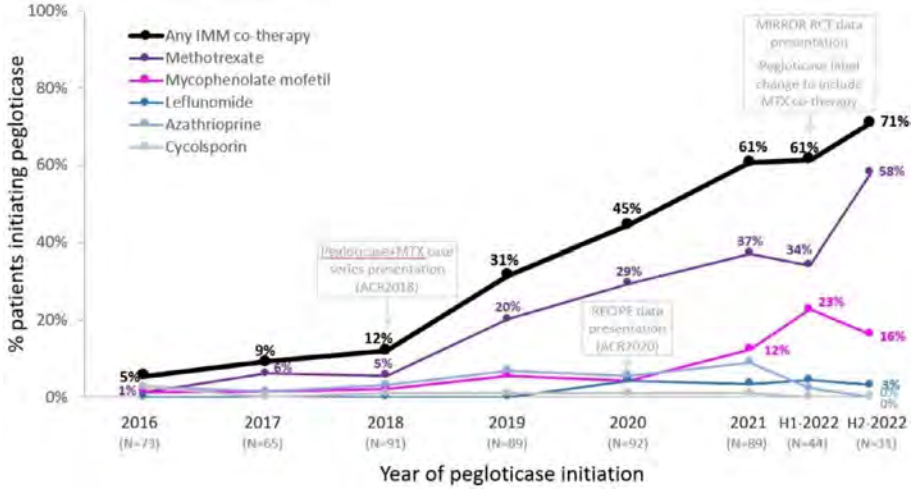

Figure. Proportion of patients with ≥1 pharmacy claim for an IMM agent within 60 days before or after initiating pegloticase therapy (a small proportion of patients received >1 IMM agent). All patients had claims in database within 180 days before and within 60 days after first pegloticase infusion (data do not include all patients who received pegloticase). MIRROR RCT, randomized controlled trial of pegloticase+MTX vs. pegloticase +placebo (N=152) [9]; RECIPE, randomized controlled trial of pegloticase+mycophenolate mofetil vs. pegloticase+placebo (N=32) [12]; IMM, immunomodulation; MTX, methotrexate; ACR, American College of Rheumatology

Results: 574 patients (91% men, 53.0±11.5 years old) met inclusion criteria. Diagnosis codes for hypertension, CKD, and cardiovascular disease were identified in 73%, 38%, and 32% of patients. Few patients (≤12%) received IMM co-therapy through 2018, but rates began to rise in 2019, presumably due to initial pegloticase+MTX case series (MTX use: 5% in 2018, 20% in 2019) and subsequent pegloticase+IMM data presentations; **Figure**). The proportion receiving IMM co-therapy continued to rise through 2022, with notable increases in MMF use following RECIPE presentation in Nov 2020 (ACR) and MTX use following MIRROR RCT presentation in Jun 2022 (EULAR) and pegloticase label update to include MTX in Jul 2022. After 2018, the majority of patients receiving IMM co-therapy had received MTX, followed by MMF and leflunomide (**Figure**).

Conclusion: Compelling real-world[5, 11] and clinical trial[9] efficacy/safety data has led to wide-spread awareness and adoption of IMM co-administration with pegloticase, often a last-hope therapy for patients suffering from uncontrolled gout. In the last part of 2022, over 70% of patients beginning pegloticase were co-administered IMM, with the majority of these patients receiving MTX.

ReferenceS 1. Sundy JS et al. *JAMA* 2011, 306:711-20 2. Lipsky PE et al. *Arthritis Res Ther* 2014;16:R60 3. Botson J, Peterson J. *Arthritis Rheumatol* 2018;70(supp 9) 4. Botson JK, Peterson J. *J Clin Rheumatol* 2022;28:e129-e34 5. Keenan RT et al. *Semin Arthritis Rheum* 2021;51:347-52 6. Botson JK et al. *J Rheumatol* 2021;48:767-74 7. Khanna P et al. *Arthritis Rheum* 2020;72(supp 10) 8. Rainey H et al. *Ann Rheum Dis* 2020;79(suppl 1):438 9. Botson JK et al. *Arthritis Rheumatol* 2023;75:293-304 10. Horizon Therapeutics USA. Pegloticase package insert 2022 11. Peterson J et al. *Semin Arthritis Rheum* 2021;51:1386-8 12. Khanna PP et al. *Arthritis Rheumatol* 2021;73:1523-32

Disclosure: J. Botson: Abbvie, 2, 6, Allena, 5, Amgen, 2, 6, Aurinia, 2, 6, Chemocentryx, 2, 6, Horizon Therapeutics, 2, 5, 6, 9, 10, Lilly, 2, 6, Novartis, 2, 6, Radius Health, 5; **Q. Fu**: Horizon Therapeutics, 3, 12, Stockholder; **K. Zhu**: Horizon Therapeutics, 3, 12, Stockholder; **L. Padnick-Silver**: Horizon Therapeutics, 3, 12, Stockholder; **B. LaMoreaux**: Horizon Therapeutics, 3, 11.

Abstract Number: 1124

A Double-blind, Placebo-parallel Controlled Phase III Clinical Study of the Efficacy and Safety of Hemay005 Tablets in Patients with Moderate to Severe Chronic Plaque Psoriasis in China

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Hemay005 is an orally active selective PDE4 inhibitor under clinical development for treating chronic inflammatory diseases. Hemay005 significantly inhibits the activation of T lymphocytes, which play a vital role in the pathogenesis of psoriatic diseases. It also inhibits Th1-type pro-inflammatory cytokines TNF-α, IFN-γ, IL-2, IL-12, and IL-23. Improvements in the side effect /efficacy ratio vs Apremilast are anticipated to improve the efficacy of Apremilast, which was side effect limited at doses >30mg.

Methods: This phase III, multicenter, double-blind, placebo-controlled study randomized adults (2:1) to Hemay005 or placebo according to the Study Design Fig 1 with the primary efficacy endpoint at 16 weeks.

Results: Efficacy: Based on FAS, the proportion of subjects with sPGA score of cleared (0) or almost cleared (1) with a decrease ≥2 points (i.e., sPGA improved) at Week 16 Efficacy Results are shown in Table 1.

Safety: During the double-blind core treatment, drug-related AEs were reported in 141 (66.8%) in the test group and 37 (39.4%) in placebo, respectively (P< 0.0001). Drug-related AEs with an incidence ≥10% in either the test or placebo group includednausea (test group vs placebo group: 23.2% vs 1.1%), diarrhea (11.4% vs. 1.1%), and vomiting (10.0% vs 0). The incidences of all these events had statistically significant differences between groups (P< 0.05), being significantly higher in the test group than in the placebo group. The severity of drug-related AEs reported during double-blind treatment phase was primarily Grade 1 or 2. Drug-related AEs ≥Grade 3 reported in the test group included hypertriglyceridemia (0.5% each for Grades 3 and 4) and hypokalemia (0.5%, Grade 3); drug-related AEs ≥Grade 3 reported in the placebo group

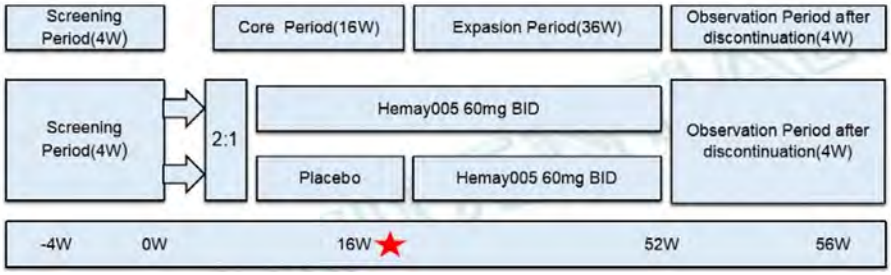

Fig 1 Study Design

At week 16	Hemay005 60mg BID (N=211)	Placebo (N=94)	P	The differernce in the response rate
PASI-75,n(%)	113(53.6)	15(16.0)	<0.0001	37.6% (95%IC:26.42%-47.15%)
sPGA0/1,n(%)	66(31.3)	6(6.4)	<0.0001	24.9% (95%IC:15.29%-32.73%)

Primary Endpoint (Efficacy) at 16 Weeks PASI75

Efficacy response (E-R)	PASI-75Efficacy prediction (%)	95% CI
15mgBID	24.77	21.12~31.91
30mg BID	33.58	25.35~51.27
60mg BID	54.38	33.86~83.52

Efficacy Model predicted response rates (PASI 75)

included soft tissue infection (1.1%, Grade 3). A population pharmacokinetics model was developed from the combined PK Phase II and Phase III data sets. The model was consistent with a one-compartment first-order absorption and linear elimination model, with an estimated elimination half-life of 12.28h.

The results showed that the PASI-75 rate at 16 weeks increased with exposure, and the efficacy signal in the 60 mg BID group was greater than in the placebo or low dose groups Table 2. In the safety analysis, the frequency of defecation and vomiting increased significantly with increasing exposure. However, there was no significant correlation between exposure and the incidences of headache, dizziness, or occult blood positive.

Conclusion: Hemay005 has the potential to be the best-in-class oral PDE4 in the management of psoriasis. The results from this study showed that Hemay005 significantly reduced the severity of moderate to severe plaque psoriasis over 16 weeks. Most AEs were mild. The severity of drug-related AEs reported during the double-blind treatment phase was primarily Grade 1 or 2. The most common drug-related AE was gastrointestinal reactions, and E-R analysis showed that the optimal dose of Hemay005 was 60 mg.

Disclosure: C. Jones: Hemay Pharmaceutical, 3; **J. Zhang**: None; **L. Wang**: None; **X. Dai**: None; **H. Wang**: None; **X. Bi**: None; **X. Duan**: None; **Z. Meng**: None; **Z. Tian**: None; **A. Xu**: None; **B. Yang**: None; **S. Guo**: None; **W. Li**: None; **Q. Diao**: None; **H. Fang**: None; **Y. Liu**: None; **J. Fan**: None; **M. Yan**: None; **S. Lin**: None; **M. Zhu**: Hemay Pharmaceutical, 3; **x. Hu**: Hemay Pharmaceutical, 3; **J. Lin**: Hemay Pharmaceutical, 3; **M. Bi**: None.

Abstract Number: 1125

A Rheumatologic Clinical Profile of the VEXAS Syndrome: Results from a Survey Conducted Among Rheumatologic Units of 126 Hospitals Across Spain

Marta López I Gómez[1], Paula García Escudero[2], Marta López[3], Berta Magallanes López[4], Meritxell Salles Lizarzaburu[5], Beatriz Frade Sosa[6], Elena Riera[7], Ernesto Trallero Araguás[8], MARIA ELVIRA DIEZ ALVAREZ[9], Francisco Javier Toyos Sáenz de Miera[10], Alicia Garcia Dorta[11], José Ángel Hernández Beriain[12], Marta Ibáñez Martínez[13], carolina Merino[14], PALOMA VELA[15], Ana Victoria Orenes Vera[16], Diego Dios Santos[17], Jose Alberto Miranda Filloy[18], Clara García Belando[19], María Rodríguez Laguna[20], Ignacio Vázquez[21], Joaquin Belzunegui[22], Judit Font[23], Carlos de Miguel Sánchez[24], Zuriñe Ortiz de Zárate Caballero[25] and Jaime Calvo Alén[26], [1]Hospital Universitario de Araba, Pamplona, Spain, [2]Hospital Universitario Araba, Bilbao, Spain, [3]Hospital Universitario Arava, Pamplona, Spain, [4]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, [5]C. H. de Manresa - Fundació Althaia, Barcelona, Spain, [6]Hospital Clínic de Barcelona, Barcelona, Spain, [7]H. U. Mútua Terrasa, Barcelona, Spain, [8]Department of Rheumatology, Hospital Universitario Vall d'Hebron, Barcelona, Spain, [9]Rheumatology, Hospital Universitario de León, León, Spain, [10]Hospital Virgen Macarena, Sevilla, Spain, [11]Rheumatology Unit, Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [12]Rheumatology, Hospital Insular de Gran Canaria, Las Palmas de Gran Canaria, Spain, [13]C. A. U. de Salamanca, Salamanca, Spain, [14]Rheumatology Department Hospital Universitario Puerta de Hierro, Majadahonda (Madrid), Spain, [15]Rheumatology, Hospital General Universitario Alicante, Alicante, Spain, [16]H. Arnau de Vilanova, Valencia, Spain, [17]Rheumatology department, Complexo Hospitalario Universitario A Coruña (CHUAC). Instituto de Investigación Biomédica A Coruña (INIBIC), A Coruña, Spain, [18]C. H. U. Lucus Augusti, Lugo, Spain, [19]Hospital Los Arcos del Mar Menor, Murcia, Spain, [20]H. Clínico San Carlos, Madrid, Spain, [21]H. U. Dr. Peset, Valencia, Spain, [22]H. C. Alto Deba, Donostia, Spain, [23]Hospital Universitario Germans Trias i Pujol, Badalona, Spain, [24]Hospital Universitario de Araba, Hematology, VItoria, Spain, [25]Hospital Universitario de Araba, Internal Medicine, Vitoria, Spain, [26]Hospital Universitario Araba, Vitoria, Spain

SESSION INFORMATION

Session Date: Monday, November 13, 2023

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Session Type: Poster Session B

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Background/Purpose: The newly described VEXAS syndrome is a very heterogenous disease with rheumatologic and hematologic manifestations, caused by somatic mutations affecting UBA1 gene, that still requires a precise definition. Our objective was to describe the clinical profile of VEXAS patients (VP) diagnosed and monitored in rheumatologic units in Spain.

Methods: A comprehensive survey covering the whole country, which included 126 Spanish hospitals with rheumatologic units, was performed to identify all the VP observed in those units. VP were defined as compatible clinical picture plus characteristic BMB and/or confirmed UBA1 gene mutations. Demographic, clinical, laboratory and outcome data were collected from medical records. Descriptive analyses were performed employing standard tests.

Results: A total of 28 VP were identified. All of them were men and had a Caucasian origin, with a mean age at diagnosis of 70.96 (±SD 8.92) years. Constitutional symptoms and fever were detected in 26 (92.85%) patients, while arthritis was present in 23 (82.14%) of them, and chondritis (including nasal chondritis, perichondritis and epiglottis' chondritis) was found in

Table 1. Baseline clinical characteristics.

CLINICAL MANIFESTATIONS	Total number and percentage
Constitutional symptoms	23 (82.14%)
Fever	22 (78.57%)
Arthritis	23 (82.14%)
Chondritis	16 (57.14%)
Skin	26 (92.85%)
Pulmonary involvement	10 (35.71%)
Renal involvement	5 (17.85%)
Periorbital edema	10 (35.7%)
Ocular manifestations	12 (42.9%)
Cardiac manifestations	1 (3.6%)
Hepatomegaly	1 (3.6%)
Splenomegaly	6 (21.4%)
Thromboembolic disease attributed to VEXAS syndrome	8 (28.6%)
Hearing loss	6 (21.4%)
Medium vessel vasculitis	4 (14.3%)

Table 2. Laboratory tests.

LABORATORY	Median and standard deviation (SD)
Haemoglobin gr/dL	10.45 (±SD 2.3)
Medium corpuscular volume fL	106.85 (±SD 10.14)
Platelets 10^3/ µL	116 (±SD 78.72)
Leukocytes / µL	5265 (±SD 2265)
CRP mg/dL	6.25 (±SD 6.44)
ESR mm/h	73 (±SD 42)

16 (57.14%) cases. Twenty-six (92.85%) patients presented 1 or more skin manifestations, being the most frequent ones: Sweet syndrome (n=18, 64.28%), leukocytoclastic vasculitis (n=8, 28.57%), erythema nodosum (n=3, 10.71%), Jessner's lymphocytic infiltration of the skin (n=2, 7.14%), and lupus-like skin lesions (n=2, 7.14%). Pulmonary involvement was found in 10 (35.71%) cases; patients presented 1 or more findings, including lung infiltrates (n=5), interstitial lung disease (n=5), pleurisy (n=2), and alveolar hemorrhage (n=1). It is worth remarking the finding of renal involvement (acute renal failure n=3, IgA nephropathy n=1, nephrotic syndrome n=1) attributed to VEXAS syndrome in 5 patients out of 28 (17.85%), complication which has not been previously described in other studies to our knowledge at the time of this publication. Other clinical manifestations are included in Table 1. Anaemia was found in 27 (96.42%) cases, being macrocytic in 22 of them; 19 (67.85%) presented thrombocytopenia as well; furthermore, 18 (64.28%) met criteria for MDS. Other laboratory findings are included in Table 2.

Conclusion: The clinical manifestations identified within our cohort of VEXAS syndrome, focusing on the rheumatologic aspect, exhibit similarities to those previously documented in this condition. However, a noteworthy observation in our study is the presence of renal involvement attributed to VEXAS syndrome in nearly 20% of our patients. This complication has not been reported in previous studies, as far as our knowledge extends at the time of this publication.

Disclosure: M. López I Gómez: None; **P. García Escudero**: None; **M. López**: None; **B. Magallanes López**: None; **M. Salles Lizarzaburu**: None; **B. Frade Sosa**: None; **E. Riera**: None; **E. Trallero Araguás**: None; **M. DIEZ ALVAREZ**: None; **F. Toyos Sáenz de Miera**: None; **A. Garcia Dorta**: None; **J. Hernández Beriain**: None; **M. Ibáñez Martínez**: None; **c. Merino**: None; **P. VELA**: AbbVie/Abbott, 5, AstraZeneca, 5, Eli Lilly, 5, 6, GlaxoSmithKlein(GSK), 6, Novartis, 5, Pfizer, 5; **A. Orenes Vera**: None; **D. Dios Santos**: None; **J. Miranda Filloy**: None; **C. García Belando**: None; **M. Rodríguez Laguna**: None; **I. Vázquez**: None; **J. Belzunegui**: None; **J. Font**: None; **C. de Miguel Sánchez**: None; **Z. Ortiz de Zárate Caballero**: None; **J. Calvo Alén**: None.

Abstract Number: 1126

Identification of Clinical Phenotypes in Behçet's Disease Using a Cluster Analysis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Behcet's disease (BD) is a variable-vessel vasculitis with a high variability of clinical manifestations. The objective of our study was to identify clinical phenotypes using cluster analysis.

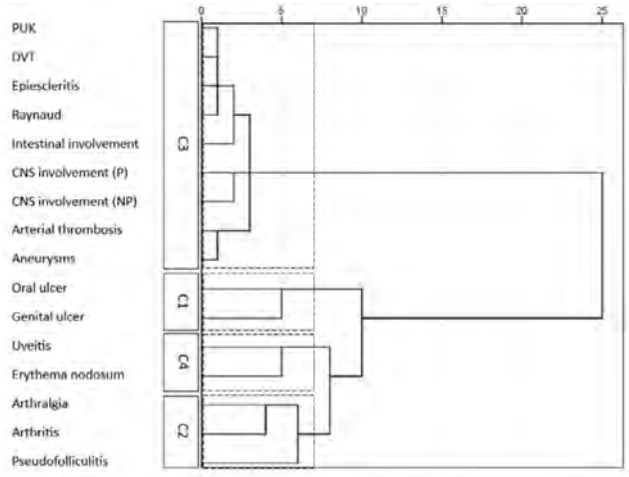
Methods: A model-based clustering relaying on 16 clinical variables was performed in a retrospective cohort of 120 BD patients, diagnosed and follow-up from January 1, 1980 to December 31, 2019 in 3 hospital at Northern Spain (Cantabria). Chi-square test and ANOVA were used to compare categorical and continuous variables among groups. Two-sample t-tests and the partition of Pearson's chi-square statistic were used in pairwise comparisons.

Results: Cluster analysis identified four groups: C1 (n=47; 39.2%), C2 (n=33; 27.5%), C3 (n=33; 27.5%) and C4 (n=7; 5.8%). The clusters were defined as follows: C1 as mucosal involvement, C2 as joint involvement and pseudofolliculitis, C3 as neurological and vascular involvement and C4 as uveitis and erythema nodosum. There were no baseline demographic differences between clusters and no differences in the application of classification criteria were observed (**TABLE**

Table 1: Characteristics of patients with Behçet's syndrome after clustering on clinical manifestations.

	Whole cohort (N=120)	C1 (n=47)	C2 (n=33)	C3 (n=33)	C4 (n=7)	p-value
Demographics						
Age at diagnosis, years±SD	37.6±13.8	37.0±16.0	36.6±11.0	39.2±13.6	38.9±12.3	0.9
Gender, females (%)	58 (48.3)	19 (40.4)	15 (45.5)	20 (60.6)	4 (57.1)	0.3
Classification criteria						
ISG (%)	59 (49.2)	25 (53.2)	18 (54.5)	13 (39.4)	3 (42.9)	0.6
ITR-ICBD (%)	96 (80.0)	39 (83.0)	22 (66.7)	28 (84.8)	7 (100)	0.1
ITR-ICBD score, mean±SD	4.8±1.6	4.8±1.6	4.7±1.6	4.9±1.6	5.6±1.3	0.6
HLA-B51 (%)	43 (35.8)	19 (40.4)	13 (39.4)	10 (30.3)	1 (14.3)	0.5
Clinical manifestation						
Oral ulcer (%)	113 (94.2)	45 (95.7)	32 (97.0)	30 (90.9)	6 (85.7)	0.5
Genital ulcer (%)	71 (59.2)	32 (68.1)	14 (42.4)	22 (66.7)	3 (42.9)	0.08
Ocular involvement (%)	54 (45.0)	18 (38.3)	17 (51.5)	15 (45.5)	4 (57.1)	0.6
Episcleritis (%)	4 (3.3)	2 (4.3)	1 (3.0)	1 (3.0)	0	0.9
PUK (%)	1 (0.8)	0	1 (3.0)	0	0	0.4
Uveitis (%)	47 (39.2)	16 (34.0)	13 (39.4)	14 (42.4)	4 (57.1)	0.7
Anterior	17 (35.4)	4 (25.0)	7 (53.8)	5 (33.3)	1 (25.0)	
Intermediate	3 (6.3)	1 (6.3)	0	2 (13.3)	0	
Posterior	15 (31.3)	4 (25.0)	4 (30.8)	6 (40.0)	1 (25.0)	
Panuveitis	13 (27.1)	7 (43.8)	2 (15.4)	2 (13.3)	2 (50.0)	
Skin lesions (%)	76 (63.3)	27 (57.4)	32 (97.0)	11 (33.3)	6 (85.7)	<0.001
Erythema nodosum	32 (26.7)	6 (12.8)	12 (36.4)	8 (24.2)	6 (85.7)	<0.001
Pseudofolliculitis	57 (47.5)	22 (46.8)	31 (93.9)	3 (9.1)	1 (14.3)	<0.001
Raynaud	3 (2.5)	3 (6.4)	0	0	0	0.2
Joint involvement (%)	79 (65.8)	10 (21.3)	33 (100)	32 (97.2)	4 (57.1)	<0.001
Arthralgia	73 (60.8)	4 (8.5)	33 (100)	32 (97.0)	4 (57.1)	<0.001
Arthritis	46 (38.3)	7 (14.9)	21 (63.6)	14 (42.4)	4 (57.1)	<0.001
Neurological involvement (%)	23 (19.2)	6 (12.8)	2 (6.1)	14 (42.4)	1 (14.3)	0.001
Parenchymal	13 (10.8)	3 (6.4)	2 (6.2)	8 (24.2)	0	0.03
Non.parenchymal	13 (10.8)	3 (6.4)	0	9 (27.3)	1 (14.3)	0.03
Vascular involvement (%)	12 (10.0)	3 (6.4)	0	8 (24.2)	1 (14.3)	0.08
Arterial thrombosis	14 (11.7)	2 (4.3)	2 (6.1)	3 (9.1)	7 (100)	<0.001
DVT	1 (0.8)	0	0	1 (3.0)	0	0.4
Aneurysms	7 (5.8)	0	0	0	7 (100)	<0.001
Intestinal involvement (%)	8 (6.7)	2 (4.3)	2 (6.1)	4 (12.1)	0	0.5

SD: standard deviation; ISG: International Study Group; ITR-ICBD: International Team For The Revision of The International Criteria; DVT: Deep venous thrombosis.



PUK: peripheral ulcerative keratitis; DVT: deep venous thrombosis; CNS: central nervous system; NP: non-parenchymal; P: parenchymal

FIGURE 1: Dendrogram of the hierarchical clustering leading to four clusters.

1). The presence of oral ulcers was predominant in all clusters, ranging from 85.7% (C4) to 95-97% (C1-C2), with no significant differences. However, a higher frequency of genital ulcers was observed in C1 compared to the other clusters. Similarly, a significantly higher frequency of erythema nodosum was observed in C4 (85.7%) and of pseudofolliculitis in C2 (93.9%) ($p< 0.001$). In addition, arterial involvement was more prevalent in C4 (100%, $p< 0.001$) but there were no differences in venous thrombotic involvement. Aneurysms were only observed in the C4 cluster (**FIGURE 2**).

Conclusion: We have defined 4 BD phenotypes in our study. This cluster approach may be useful for better patient management due to early identification of clinical patterns.

Disclosure: A. Serrano-Combarro: None; **J. Martin-Varillas**: None; **R. Fernandez-Ramon**: None; **L. Sanchez-Bilbao**: None; **C. Alvarez Reguera**: None; **E. Aurrecoechea**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6.

Abstract Number: 1127

Factors Associated with Vision-Related Quality of Life in Patients with Non-infectious Uveitis: A Longitudinal Analysis

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Background/Purpose: Non-infectious uveitis (NIU) are characterized by inflammation of the middle layer of the eye wall and have a significant impact on patients' visual-related quality of life (VRQoL). Objective measures of vision, such as visual acuity, do not fully account for the impact of these diseases on the patients' perceived QoL, as it includes other relevant and important aspects not evaluated in routine clinical practice. The assessment of the patient's QoL through standardized and validated questionnaires allows us to evaluate objectively the actual burden of the disease. Several cross-sectional studies have shown that the VRQoL of NIU patients is reduced. However, the evidence regarding how QoL evolves in real life clinical practice and what characteristics influence this evolution is scarce. Therefore, our objective is to describe the evolution of the VRQoL in subjects with NIU and to identify factors associated with increased or decreased VRQoL during follow-up.

Methods: Prospective longitudinal observational study including consecutive NIU patients from a tertiary uveitis clinic from Madrid (Spain). Main outcome was the composite score of the Visual Functioning Questionnaire 25 (VFQ25), measured at baseline and after 1 and 2 years of follow-up. Influence of demographic, clinical, and treatment-related variables (assessed at the same time points) in repeated measures of VRQoL was analyzed using bivariable and multivariable generalized estimating equations (GEE) models nested by patient.

Results: One hundred and forty five patients were included in the analysis, with 422 visits. In the two years of follow up, no significant changes were observed in the evolution of the VFQ25 (Figure). In the multivariate analysis, lower best corrected visual acuity, presence of permanent work disability, being unemployed, cells in anterior chamber ≥2+, previous cataract surgery, previous glaucoma surgery, other intraocular surgeries, and prescription of synthetic immunosuppressive drugs were independently associated with lower VFQ25 (Table).

Table. Multivariate analysis to assess the influence of socio-demographic and clinical related variables in the VRQoL of a cohort of NIU patients.

Variable	Coef (95% IC)	p-value
Women	1.82 (-0.98 to 4.63)	0.21
BCVA (logMAR)	-8.18 (-10.93 to -5.43)	$5.68x10^{-9}$
Baseline visit	Ref.	
1 year visit	-0.18 (-1.68 to 1.32)	0.81
2 year visit	-0.9 (-1.50 to 1.11)	0.77
BCVA X 1 year visit	4.61 (2.30 to 6.93)	$9.5x10^{-5}$
BCVA X 2 year visit	4.46 (3.03 to 5.88)	$9.18x10^{-10}$
Married	1.96 (-0.34 to 4.26)	0.09
Permanent work disability	-27.42 (-36.90 to -17.93)	$1.47x10^{-8}$
Unemployed	-7.04 (-10.82 to -3.27)	$2.6x10^{-4}$
Cells in anterior chamber ≥ 2 +	-3.85 (-7.03 to -0.67)	0.02
Cataract surgery	-4.61 (-8.15 to -1.07)	0.01
Glaucoma surgery	-14.51 (-24.72 to -4.30)	0.01
Other intraocular surgery	-6.77 (-10.53 to -3.01)	$4.2x10^{-4}$
No ISD use	Ref.	
Synthetic ISDs	-5.38 (-8.19 to -2.56)	$1.9x10^{-4}$
Biological ISDs	3.11 (-0.59 to 6.81)	0.01
Synthetic and biological ISDs	-2.22 (-5.79 to 1.34)	0.22

VA: visual acuity; BCVA: best corrected visual acuity; logMAR: logarithm of the minimum angle of resolution; ISDs: immunosuppressive drugs; Coef: correlation coefficient

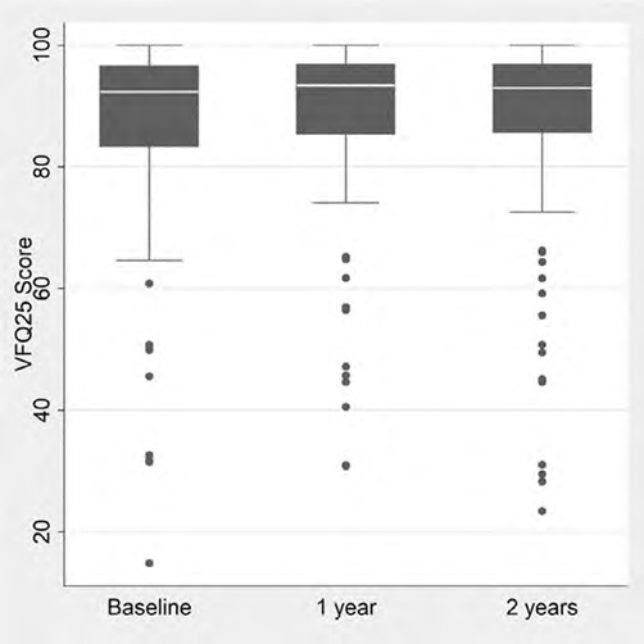

Figure. VFQ25 during follow-up

Conclusion: In the two years follow-up of our study, we did not identify significant changes in the evolution of the VRQoL in NIU patients. Nevertheless, we found some social factors that could contribute to a decreased VQ25 during follow-up. Essentially, work status and financial well-being. Clinical variables were also identified, such as lower visual acuity and factors that might reflect active disease (cells in anterior chamber ≥2+ and prescription of synthetic immunosuppressive drugs). We also detected that previous ocular surgery might contribute to a lower VQ25 score. This preliminary data allows us to evaluate other variables that contribute to the burden of the disease and the extent of the patient's suffering regarding their vision and reflect the importance of identifying them to improve our patients' quality of life.

Disclosure: M. Alvarez Hernandez: None; **I. Pérez Sancristóbal**: None; **A. Madrid García**: None; **L. Borrego Sanz**: None; **C. Hormigos martín**: None; **B. García Tirado**: None; **M. Ariño Gutiérrez**: None; **C. lajas Petisco**: None; **P. Arriola Villalobos**: None; **E. Pato Cour**: None; **L. Rodríguez Rodríguez**: None.

Abstract Number: 1128

Refractory Inflammatory Ocular Pathology and Treatment with Janus Kinase Inhibitors. Multicenter Study and Literature Review

Carmen Lasa-Teja[1], Lara Sanchez-Bilbao[2], Jose Luis Martin-Varillas[3], Vanesa Calvo Río[4], José Luis Álvarez-Vega[5], Emma Beltran-Catalan[6], María del Mar Esteban-Ortega[7], Santiago Muñoz[7], Olga Maiz[8], Ignacio Torre-Salaberri[9], Ana Urruticoechea[10], Elia Valls-Pascual[11], Raúl Veroz[12], Carmen Alvarez Reguera[13], Rosalía Demetrio[13] and Ricardo Blanco[14], [1]Hospital Universitario Marqués de Valdecilla. IDIVAL, Immunopathology Group, Santander, Spain, [2]Hospital Universitario Marques de Valdecilla, Santander, Spain, [3]Hospital de Laredo, Laredo, Spain, [4]Valdecilla Hospital, Santander, Spain, [5]Complejo Hospitalario Universitario de Badajoz, Badajoz, Spain, [6]HOSPITAL DEL MAR, Barcelona, Spain, [7]Hospital Infanta Sofia, Madrid, Spain, [8]Hospital Universitario de Donostia. San Sebastián, Spain., Donosti, Spain, [9]Hospital Universitario de Basurto, Bilbao, Spain, [10]Hospital Can Misses, Ibiza, Spain, [11]Hospital Universitario Doctor Peset. Alicante, Spain., Valencia, Spain, [12]Hospital de Mérida, Mérida. Spain., Mérida, Spain, [13]Hospital Universitario Marqués de Valdecilla, Santander, Spain, [14]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain

SESSION INFORMATION

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Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammatory ocular pathology (IOP) includes internal (uveitis) and external [mainly ocular surface pathology such as epi/scleritis and peripheral ulcerative keratitis (PUK)] involvement. IOP may be severe ocular conditions refractory to conventional immunosuppressants and even biological therapy. Janus Kinase inhibitors (JAKINIB) had shown efficacy in refractory cases of different immune-mediated inflammatory diseases (IMID).

Study, year (Ref)	Cases	Age/Sex	Underlying Disease	JAKINIB	Ocular involvement	Previous immunosuppressive treatment	Ocular Evolution
Meadow et al. 2014 (1)	1	59, F	Rheumatoid Arthritis	TOFA	PUK	MTX, ABA, MP	Partial improvement
Bauernfeind et al. 2018 (2)	1	22, F	Juvenile Idiopathic Arthritis	TOFA	Anterior uveitis, CME	MTX, ADA, RTX, GOLI, IFX, CsA, TCZ, MMF	Complete improvement
Paley et al. 2019 (3)	2	1 40, F 2 45, F	1.Idiopathic 2.Idiopathic	1.TOFA 2.TOFA	1.Scleritis 2.Anterior uveitis, CME	1.MTX, MMF, AZA, CYP 2.MTX, LFN, AZA, MMF, ADA, IFX, CZP, intravitreal fluocinolone acetonide	1.Complete improvement 2.Complete improvement
Liu J et al. 2020 (4)	1	30, M	Behçet syndrome	TOFA	Scleritis	SSZ, MTX, AZA, LFN, THD, COL, GLM	Partial improvement
Majumder et al. 2020 (5)	1	26, F	Vogt-Koyanagi-Harada disease	TOFA	Posterior uveitis	MP	Complete improvement
Miserocchi et al. 2020 (6)	4	1. 9, F 2. 1, F 3. 2, F 4. 10, M	Juvenile Idiopathic Arthritis	1. TOFA 2. BARI 3. BARI 4. BARI	1. Panuveitis 2. Panuveitis 3. Panuveitis 4. Panuveitis	1. IFX, ADA, LFN, ABA, RTX, TCZ 2. MTX, ADA, IFX, RTX, ABA 3. MTX, AZA, IFX, ADA, TCZ 4. ETN, MTX, CsA, IFX, ADA, ABA, TCZ, RTX	1. Complete improvement 2. Complete improvement 3. Complete improvement 4. Complete improvement
Pyare et al. 2020 (7)	1	45, F	Idiopathic	TOFA	Necrotizing scleritis	MMF	Complete improvement
Kaneko et al. 2022 (8)	1	35, M	Rheumatoid Arthritis	BARI	Panuveitis	MTZ, SSZ, ADA, IFX	Complete improvement
Xiao-Bao et al. 2022 (9)	1	18, F	Idiopathic	TOFA	Panuveitis	MTX, MMF, CsA, ADA	Complete improvement
Present study, 2023	11	1. 25, F 2. 85, F 3. 41, F 4. 65, F 5. 59, M 6. 40, F 7. 55, M 8. 45, F 9. 49, F 10. 62, F 11. 67, M	1. Blau Syndrome 2. Rheumatoid Arthritis 3. Relapsing polychondritis 4. Idiopathic 5. Ankylosing Spondylitis 6. Spondyloarthritis and ulcerative colitis 7. Ankylosing Spondylitis 8. Ankylosing Spondylitis 9. Rheumatoid Arthritis 10. Rheumatoid Arthritis 11. Rheumatoid Arthritis	1. TOFA/BARI 2. BARI 3. BARI 4. BARI 5. UPA 6. TOFA 7. UPA 8. UPA 9. UPA 10. UPA 11. BARI	1. Panuveitis 2. PUK 3. PUK 4. Panuveitis 5. Anterior uveitis 6. Anterior uveitis 7. Anterior uveitis 8. Scleritis 9. Scleritis 10. PUK 11. PUK	1.MTX, ETN, ANA, ABA 2.MTX, LFN, CZP, ADA, w MP 3. MTX, CsA, SSZ, MMF, AZA, IFX, TCZ, CZP, ABA, ADA 4. MTX, AZA 5. MTX, ADA 6. MTX, AZA, ADA 7. MTX, IFX, GOLI 8. MTX, ADA, 9. MP, MTX, TCZ, ADA, GOLI, CZP 10. MTX 11. MTX, LFN	1. Complete improvement 2. Complete improvement 3. Complete improvement 4. Complete improvement 5. Complete improvement 6. Complete improvement 7. Complete improvement 8. Complete improvement 9. Complete improvement 10. Complete improvement 11. No improvement

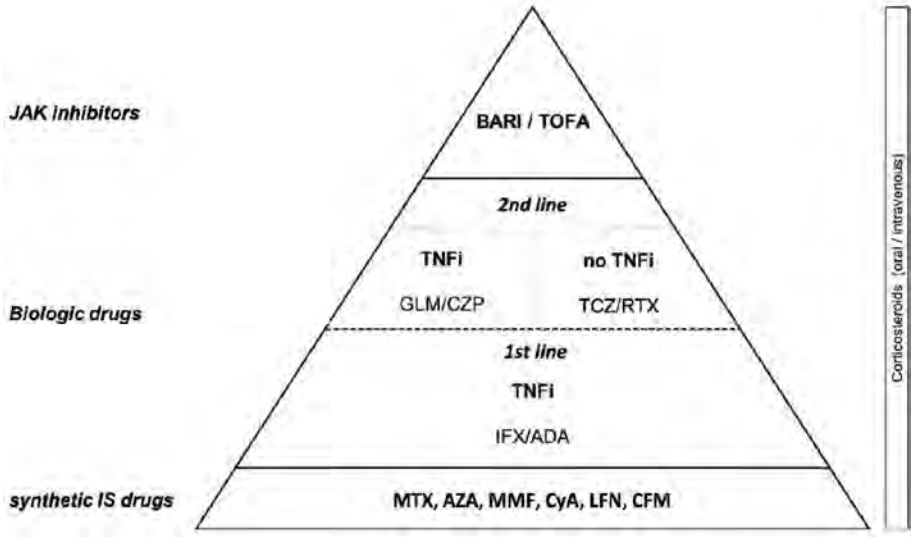

FIGURE. Therapeutical approach of refractory inflammatory ocular pathology.

In patients with refractory IOP treated with JAKINIB our aims were **a)** to assess the patients of Spanish referral centers, **b)** Literature review.

Methods: Multicenter study of 11 patients with refractory IOP treated with JAKINIB. For Literature review a search was conducted in PubMed, Embase and the Cochrane library from their inception to 1st January 2023. Original research articles studying JAKINIB treatment in patients with IOP were included. In addition, a therapeutical approach of refractory IOP is proposed.

Results: We have identified 11 cases in eight University Hospitals and 13 cases in the literature review. These 24 patients (17 women/ 7 men) (35 affected eyes), mean age 38.9±21.9 years, had different refractory IOP (uveitis=14; scleritis=5, PUK=5). Most of IOP were associated with IMID (n=19, 79.2%) while 5 cases (20.8%.), were idiopathic. The main underlying IMID were rheumatoid arthritis (n=6, 25%), juvenile idiopathic arthritis (n=5, 20.8%) and spondyloarthritis (n=4; 16.7%) **(TABLE).** Uveitis (n=14) followed by ocular surface pathology (n=10) were the most frequent subtypes of IOP. Patterns of uveitis were panuveitis (n=8), anterior uveitis (n=5; 2 of them with Cystoid macular), and posterior (n=1). Ocular surface pathology was due to scleritis (n=5) and PUK (n=5). In addition to systemic corticosteroids, before JAKINIB, conventional (n= 23; 95.8%) and biologicalimmunosuppressive drugs (n=18; 75%) were required. The JAKINIB most widely used was tofacitinib (n= 11; 45.8%) followed by baricitinib (n=8; 33.3%). In one patient with Blau Syndrome and uveitis, tofacitinib was switched to baricitinib due to severe lymphopenia.In two other patients, UPA was discontinued due to anemia and skin adverse reaction. Finally, only in one patient baricitinib was withdrawn due to lack of improvement. After starting JAKINIB treatment, 23 patients presented clinical improvement, complete (n=21, 87.5%) or partial (n= 2; 8.3%). Based on these data a therapeutical approach of refractory IOP was proposed **(FIGURE).**

Conclusion: JAKINIB may be an effective and safe therapy in IOP refractory to conventional or even biological immunosuppressive therapy.

Disclosure: C. Lasa-Teja: None; **L. Sanchez-Bilbao**: None; **J. Martin-Varillas**: None; **V. Calvo Río**: None; **J. Álvarez-Vega**: None; **E. Beltran-Catalan**: None; **M. Esteban-Ortega**: None; **S. Muñoz**: None; **O. Maiz**: None; **I. Torre-Salaberri**: None; **A. Urruticoechea**: None; **E. Valls-Pascual**: None; **R. Veroz**: None; **C. Alvarez Reguera**: None; **R. Demetrio**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6.

Abstract Number: 1129

Accuracy and Performance Characteristics of Administrative Codes for the Diagnosis of Autoinflammatory Syndromes: A Discovery and Validation Study

Saeyun Lee[1], Sujin Kim[2], Suzanne Segerstrom[2], Polly Ferguson[1] and **Aleksander Lenert**[3], [1]University of Iowa Carver College of Medicine, Iowa City, IA, [2]University of Kentucky, Lexington, KY, [3]University of Iowa, Iowa City, IA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoinflammatory syndromes (AIS), a group of rare rheumatic diseases driven by the innate immune system, remain understudied due to the lack of prospective cohorts. Electronic medical record (EMR) and administrative health databases represent an opportunity for clinical outcomes and pharmacoepidemiologic research but rely on accurate cohort building. We sought to determine and validate the accuracy and performance characteristics of administrative claims codes for the diagnosis of AIS.

Methods: Potential AIS patients were identified from the EMR at the University of Iowa Hospitals and Clinics and the Stead Family Children's Hospital from 2009 through July 2022 using a screening filter comprised of the 10th edition of the *International Classification of Diseases* (*ICD-10*) codes. We filtered based on the following ICD-10 codes for AIS subtypes: M06.1 (adult onset Sill's disease, AOSD), M08.2 (systemic juvenile idiopathic arthritis, SJIA), M35.2 (Behçet's disease, BD), M04.1 (familial Mediterranean fever, FMF), M04.2 (cryopyrin-associated periodic syndrome, CAPS); and combination of L40.3, L70.9, M65.9, M85.80 and M86.9 for SAPHO syndrome and chronic nonbacterial osteomyelitis (SAPHO-CNO). Medical records were reviewed to determine whether a patient met published criteria for AOSD, SJIA, BD, FMF, CAPS and SAPHO-CNO. Patients age < 18 at last follow-up visit or without supporting documentation to confirm their diagnoses were excluded from the analysis. Patients who did not meet AIS subtype diagnostic criteria, but who were treated for AIS by their specialist were categorized as Other AIS. Otherwise, they were categorized as non-AIS. We determined sensitivity,

Figure 1. Patient identification and screening flowchart.

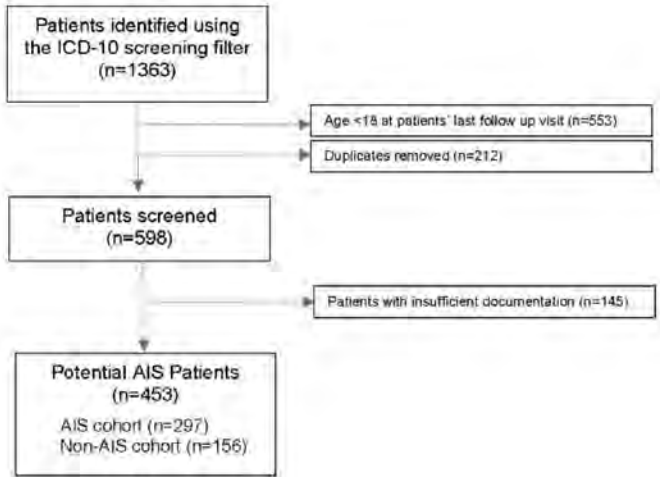

Table 1. Baseline demographics and disease characteristics of the adult AIS and non-AIS cohorts.

	AIS (n=297)	AOSD (n=56)	SJIA (n=22)	[illegible] (n=78)	BD (n=111)	FMF (n=15)	CAPS (n=9)	SAPHO-CNO (n=23)	Other AIS (n=65)	Non-AIS (n=156)
Age, median (IQR), years	39 (28-54)	41 (34-58)	27 (23-30)	36 (27-50)	45 (36-57)	30 (25-55)	37 (39-63)	42 (22-54)	31 (22-40)	47 (34-60)
Gender, female (%)	204 (69)	36 (64)	15 (68)	51 (65)	83 (75)	7 (47)	5 (56)	17 (74)	43 (66)	93 (60)
Non-Hispanic (%)	255 (86)	45 (80)	19 (86)	64 (82)	88 (79)	12 (80)	9 (100)	23 (100)	63 (97)	136 (87)
White (%)	245 (82)	38 (68)	15 (68)	53 (68)	85 (88)	8 (60)	9 (100)	20 (87)	62 (95)	132 (85)

AIS: autoinflammatory syndrome; AOSD: adult onset Still's disease; SJIA: systemic juvenile idiopathic arthritis; BD: Behçet's disease; FMF: familial Mediterranean fever; CAPS: cryopyrin-associated periodic syndrome; SAPHO: Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis; CNO: chronic nonbacterial osteomyelitis. IQR: interquartile range. Continuous variables are presented as median (IQR). Categorial variables are presented as number (percentage).

Table 2. Sensitivity, specificity, predictive values, and accuracy for identifying AIS from administrative codes (n = 453) compared with the reference standard labels (using medical chart review).

AIS Subtype (ICD-10)	True Positives	False Positives	True Negatives	False Negatives	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	AUC (95% CI)[a]
AOSD (M06.1)	49	20	377	7	88 (76-95)	95 (92-97)	71 (61-79)	98 (96-99)	0.91 (0.86-0.96)
SJIA (M08.2)	21	49	382	1	95 (77-100)	99 (95-91)	30 (24-36)	100 (99-100)	0.92 (0.84-1.00)
AOSD/SJIA (M06.1 or M08.2)	76	26	349	2	97 (91-100)	93 (90-95)	74 (67-81)	99 (98-100)	0.95 (0.92-0.99)
BD (M35.2)	111	36	304	0	100 (97-100)	98 (85-92)	75 (68-80)	100	0.94 (0.91-0.97)
FMF (M04.1)	15	81	357	0	100 (78-100)	82 (78-85)	16 (13-19)	100	0.81 (0.61-1.00)
CAPS (M04.2)	8	2	442	1	89 (52-100)	100 (99-100)	80 (50-94)	100 (99-100)	0.94 (0.83-1.00)
SAPHO-CNO (L40.5, L70.4, M45.1, M85.5, M86.6)	17	6	422	6	74 (53-90)	98 (96-99)	68 (51-81)	99 (97-99)	0.86 (0.76-0.96)

AIS: autoinflammatory syndrome; ICD-10: 10th edition of the International Classification of Diseases; CI: confidence interval; PPV: positive predictive value; NPV: negative predictive value; AUC: area under the receiver operating characteristic curve; AOSD: adult onset Still's disease; SJIA: systemic juvenile idiopathic arthritis; BD: Behçet's disease; FMF: familial Mediterranean fever; CAPS: cryopyrin-associated periodic syndrome; SAPHO: Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis; CNO: chronic nonbacterial osteomyelitis. IQR: interquartile range. Continuous variables are presented as median (IQR). [a]For null hypothesis, area under the curve = 0.5.

specificity, positive predictive values (PPV), negative predictive values (NPV), and area under the receiver operating characteristic curve (AUC) of each ICD code or combination of codes for diagnosing each AIS.

Results: The study's screening flowchart is presented in Figure 1. Baseline demographics of the AIS and non-AIS cohorts are presented in Table 1. Out of the 453 patients with potential AIS, 297 patients had a true AIS diagnosis (AIS prevalence 66%), while 156 patients did not have AIS (non-AIS). The AIS cohort was predominantly female (68.7%) and white (82.5%) with median age of 39 (IQR, 28-54) years. Performance characteristics and accuracy of ICD codes are presented in Table 2. Sensitivity was ≥88% for AOSD, SJIA, BD, FMF and CAPS, while slightly lower for SAPHO-CNO (74%). Specificity was ≥89% for AOSD, SJIA, BD, CAPS and SAPHO-CNO, while slightly lower for FMF (82%). PPV ranged from 68% to 80% for AOSD, BD, CAPS and SAPHO-CNO; in contrast, PPVs were very poor for SJIA (30%) and FMF (16%). NPVs was excellent for all 6 AIS subtypes (≥98%). All ICD codes or a combination of ICD codes for the diagnosis of specific AIS subtypes showed excellent AUCs (≥0.86).

Conclusion: This study validated the performance characteristics and accuracy of ICD-10 administrative codes for diagnosing AOSD, BD, and FMF, and examined novel codes for diagnosing SJIA, CAPS, and SAPHO-CNO. Administrative codes have high accuracy for identifying AIS patients and can be used to construct comprehensive AIS cohorts for future clinical outcomes research.

Disclosure: S. Lee: None; **S. Kim**: None; **S. Segerstrom**: None; **P. Ferguson**: None; **A. Lenert**: None.

Abstract Number: 1130

Interobserver Reliability and Sensitivity to Change of a Composite Ocular Inflammatory Activity Index: UVEDAI

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

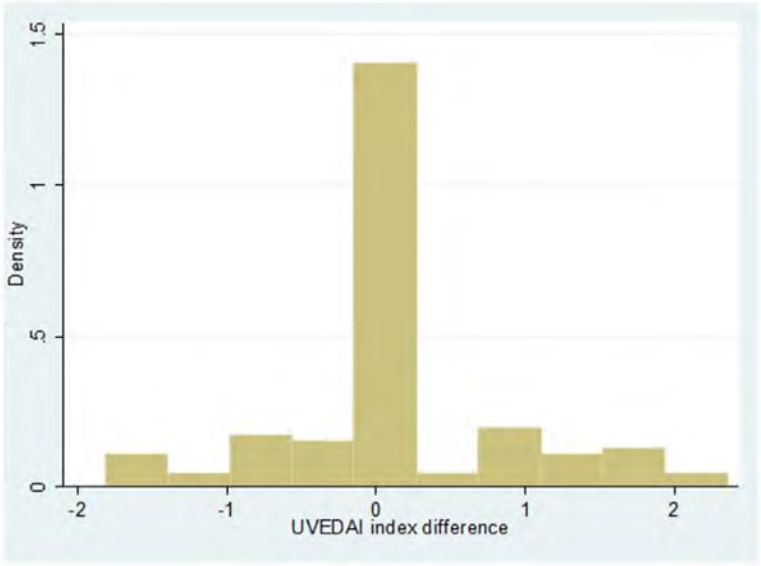
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Standardized and validated outcome measures of disease activity are lacking in the treatment and assessment of uveitis, making it difficult to compare efficacy and response to treatment. In 2014, this working group developed a composite index of ocular inflammatory activity: UVEDAI (1). The index was validated in a subsequent study conducted in 2019. The objective to this study was to determine the interobserver reliability and to demonstrate the sensitivity to change of the UVEDAI index in patients with anterior and non-anterior uveitis who undergo pharmacological treatment.

Methods: The design is an observational, longitudinal, prospective study in 7 Spanish hospitals. Patients over 18 years of age diagnosed with active uveitis were included. A complete baseline visit was performed by two ophthalmologists who determined ocular inflammatory activity with the UVEDAI index. Ophthalmologist 1 made a new visit at 4 weeks to determine



Interobserver Reliability: Differences obtained in the UVEDAI index score by ophthalmologist 1 and 2 at the baseline visit

Anatomical Location	Anterior	Intermediate / Posterior/Panuvetis	Total
UVEDAI INDEX baseline.opht.1*	1.2 ± 1.6	2.8 ± 1.8	1.9 ± 1.8
UVEDAI INDEX visit 4 wks.opht1*	0.2 ± 0.5	1.2 ± 1.5	0.6 ± 1.1
UVEDAI difference	1.04	1.54	1.25
p-value	0.00	0.00	0.00

**mean ± standard deviation*

Sensitive to Change: Mean value and difference in UVEDAI index value measured by ophthalmologist 1 in the active eye at baseline and at 4 weeks

the change in the level of uveal inflammatory activity using the UVEDAI index. The interobserver reliability analysis was performed by calculating the Intraclass Correlation Coefficient (ICC) with the values of the UVEDAI index obtained by ophthalmologist 1 and ophthalmologist 2 in the most inflamed eye at the baseline visit. Sensitivity to change in the UVEDAI index was assessed at 4 weeks from the start of pharmacological treatment by determining the Clinically Relevant Change defined as a change in UVEDAI of 0.8 points between the baseline visit and the 4-week visit.

Results: A total of 111 patients were included (54.1% male). The mean age at the time of the visit was 49.9 years. 36.9% of uveitis were idiopathic uveitis and 58.6% were anterior uveitis. The UVEDAI value was calculated from the score obtained in the 7 variables of the index. The mean value recorded in the most inflamed eye at the baseline visit by ophthalmologist 1 was 1.9 (1.2 anterior uveitis and 2.8 intermediate/posterior uveitis). The ICC for the UVEDAI value was 0.9 and when compared the mean UVEDAI values obtained by the two ophthalmologists for the most inflamed eye at the baseline visit no statistically significant differences were found (p-value >0.05), neither for the total sample nor differentiating by anatomical location. As for sensitivity of UVEDAI change, statistically significant differences (p-value=0.00) were found when comparing the mean values of the index measured by ophthalmologist 1 at the baseline visit and at 4 weeks, both in the overall sample and differentiating by anatomic location of uveitis. In all cases, the index value decreased significantly by more than 1 point at the 4-week visit after pharmacological treatment.

Conclusion: The interobserver reliability of the UVEDAI was high in the total sample and in the different variables. Furthermore, the index was sensitive in determining the change in inflammatory activity after treatment in both anterior and intermediate/posterior uveitis. We believe it is an index of activity that could be used both in routine clinical practice and in clinical studies and trials to compare results objectively

1: Pato-Cour E et al. Development of an activity disease score in patients with uveitis (UVEDAI). Rheumatol Int. 2017

Disclosure: E. Pato: None; **L. Borrego-Sanz**: None; **M. Domínguez**: None; **F. Alonso**: None; **F. Rodríguez-Gonazález**: None; **M. Tejera-Santana**: None; **M. Esteban-Ortega**: None; **I. García-Lozano**: None; **L. Martinez-Costa**: None; **S. Gonzalez-Ocampo**: None; **M. Sainz de la Maza**: None; **A. Moll-Udina**: None; **Z. Plaza**: None; **A. Fonollosa-Calduch**: None; **J. Artaraz**: None; **T. Díaz-Valle**: None; **M. Gurrea-Almela**: None; **D. Diaz-Valle**: None; **R. Méndez-Fernández**: None.

Abstract Number: 1131

Clinical Phenotypes of IgG4-related Disease in a Multi-ethnic Singapore Cohort

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: IgG4-related disease (IgG4-RD) is an immune-mediated condition that is heterogenous and can result in organ failure. To understand the disease profile of our local population better, a multi-disciplinary team was formed to review the IgG4-RD patients seen in our hospital.

Methods: A chart review was undertaken for all IgG4-RD patients seen between 1 January 2015 and 30 September 2021 at a major tertiary hospital in Singapore. All patients included fulfilled the 2020 revised comprehensive diagnostic (RCD) criteria for IgG4-RD for at least possible IgG4-RD and then scored according to the 2019 ACR/EULAR classification.

Results: Of the 58 patients included in this study, 28 scored at least 20 (i.e. completely fulfilled) for the 2019 ACR/EULAR classification criteria. 45/58 (77.6%) were male, 43/58 (74.1%) were Chinese, and median age at onset of symptoms and at diagnosis were 60.4 [inter-quartile range (IQR) 49.4-66.1] and 61.5 (IQR 50.8-67.8) years respectively. 27/58 (46.6%) were smokers, 7/58 (12.1%) had cancers, and 40/58 (69.0%) had underlying metabolic co-morbidities. Patients who completely fulfilled the ACR/EULAR classification criteria scored between 21 and 44 (median 25.5), and those who did not fulfil had a score of 4 to 19 (median 10.5). The distribution of clinical phenotypes were: 22/58 (37.9%) head and neck, 20/58 (34.5%) pancreato-biliary, 12/58 (20.7%) Mikulicz/systemic, and 4/58 (6.9%) retro-peritoneal fibrosis/aortitis. The three commonest sites of involvement were pancreato-hepato-biliary 26/58 (44.8%), ocular 17/58 (29.3%) and lymph nodes 14/58 (24.1%). The median maximum serum IgG4 level and median IgG4/total IgG ratio were 220mg/dL (IQR 98-335) and 0.149 (IQR 0.078-0.236) respectively. Patients with Mikulicz/systemic phenotype had significantly higher median total serum IgG, IgG1, IgG2 and IgG3 ($p< 0.050$). The median maximum serum IgG4 level for those who fulfilled the ACR/EULAR criteria was 280.5mg/dL (IQR 160-816.5) and those who did not fulfil was 187.5mg/dL (87-235) ($p=0.014$). Histological samples were suggestive/conclusive of IgG4-RD in 68% of patients who completely fulfilled the ACR/EULAR classification criteria and 65.4% of patients who did not ($p=0.843$). Prednisolone was the commonest treatment prescribed to patients (49/58, 84.5%). Steroid-sparing immunosuppressants were given to 32/58 (55.2%), for which azathioprine was the commonest (25/58, 43.1%) followed by rituximab (7/58, 12.1%). Surgical excision was done in 23/58 (39.7%). 44/58 (75.9%) patients achieved disease remission after first presentation and 16/58 (27.6%) were in drug-free remission. Mortality was 4/58 (6.9%) with one case attributable to complications of IgG4-RD.

Conclusion: The head and neck IgG4-RD phenotype was the commonest one in our cohort, followed by pancreato-biliary. This condition occurred more commonly in males with no gender pre-dilection in any clinical phenotype. The ACR/EULAR classification criteria appeared too restrictive and the 2020 RCD was better able to capture the full spectral of IgG4-RD patients. The overall prognosis for IgG4-RD is good and histological investigation remains important for the diagnosis of this disease.

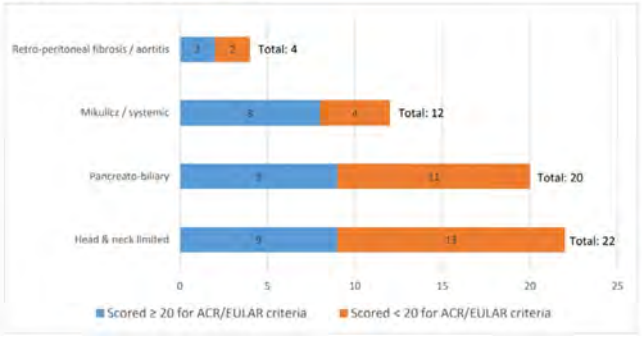
Table 1. Description of patients

Characteristics	All patients (n=58)	Scored ≥ 20 for ACR/EULAR criteria (n=28, 48.3%)	Scored < 20 for ACR/EULAR criteria (n=30, 51.7%)	P-value
Demographics				
Male gender	45 (77.6%)	21 (75.0%)	24 (80.0%)	0.648
Race				0.913
Chinese	43 (74.1%)	22 (78.6%)	21 (70.0%)	
Malay	4 (6.9%)	2 (7.1%)	2 (6.7%)	
Indian	4 (6.9%)	1 (3.6%)	3 (10.0%)	
Others	7 (12.1%)	3 (10.7%)	4 (13.3%)	
Median age at onset of symptoms in years (IQR)	60.4 (49.4 – 66.1)	60.6 (50.3 – 64.4)	60.4 (49.1 – 67.8)	0.938
Median age at diagnosis in years (IQR)	61.5 (50.8 – 67.8)	61.3 (52.4 – 66.4)	62.2 (49.4 – 68.7)	0.950
Social and medical history				
History of smoking	27 (46.6%)	15 (53.6%)	12 (40.0%)	0.300
History of alcohol consumption	16 (27.6%)	8 (28.6%)	8 (26.7%)	0.871
History of cancer	7 (12.1%)	3 (10.7%)	4 (13.3%)	1.00
History of metabolic co-morbidities	40 (69.0%)	18 (64.3%)	22 (73.3%)	0.457
Hypertension	25 (43.1%)	11 (39.3%)	14 (46.7%)	0.571
Hyperlipidaemia	37 (63.8%)	16 (57.1%)	21 (70.0%)	0.309
Type II diabetes	21 (36.2%)	10 (35.7%)	11 (36.7%)	0.940
Investigations				
Biopsy performed	51 (87.9%)	25 (89.3%)	26 (86.7%)	1.000
Histology suggestive or conclusive of IgG4RD	34 (66.7%)	17 (68.0%)	17 (65.4%)	0.843
Max median IgG in mg/dL (IQR)				
Total	1675 (1420 – 2140)	1955 (1495 – 2385)	1500 (1370 – 1960)	0.088
IgG1	921 (734 – 1150)	952 (750 – 1280)	844.5 (678 – 1020)	0.287
IgG2	627.5 (484 – 861)	711.5 (507.5 – 1210)	585.5 (484 – 690)	0.169
IgG3	79 (50 – 110)	87 (53 – 111)	68 (48 – 109)	0.304
IgG4	220 (98 – 335)	280.5 (160 – 816.5)	187.5 (87 – 235)	0.014
Max IgG4/total IgG ratio	0.149 (0.078 – 0.236)	0.215 (0.117 – 0.403)	0.121 (0.059 – 0.178)	0.005
Median ACR/EULAR classification score (IQR)	19 (10 – 25)	25.5 (23 – 28.5)	10.5 (6 – 14)	<0.001
Treatment				
Prednisolone	49 (84.5%)	26 (92.9%)	23 (76.7%)	0.147
Azathioprine	25 (43.1%)	15 (53.6%)	10 (33.3%)	0.120
Methotrexate	3 (5.2%)	3 (10.7%)	0	0.106
Mycophenolate mofetil	3 (5.2%)	2 (7.1%)	1 (3.3%)	0.605
Ciclosporin	1 (1.7%)	1 (3.5%)	0	0.483
Methylprednisolone	7 (12.1%)	1 (3.6%)	6 (20.0%)	0.104
Rituximab	7 (12.1%)	2 (7.1%)	5 (16.7%)	0.425
Surgery	23 (39.7%)	10 (35.7%)	13 (43.3%)	0.553
Outcome				0.154
Controlled following treatment after first presentation	28 (48.3%)	18 (64.3%)	10 (33.3%)	
Drug free remission after first presentation	16 (27.6%)	5 (17.9%)	11 (36.7%)	
Active with or without treatment	4 (6.9%)	1 (3.6%)	3 (10.0%)	
Relapsed	5 (8.6%)	3 (10.7%)	2 (6.7%)	
Death	4 (6.9%)	1 (3.6%)	3 (10.0%)	
Lost to follow-up	1 (1.7%)	0 (0.0%)	1 (3.3%)	

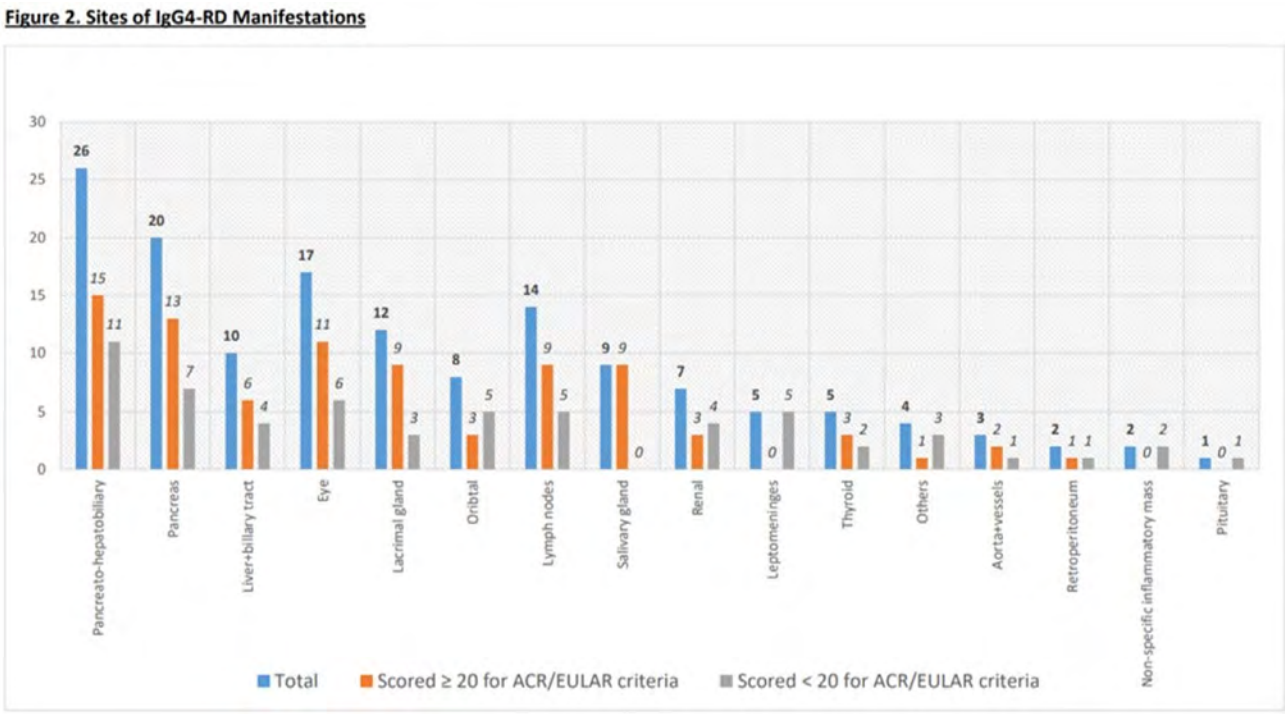
IQR: inter-quartile range

Description of patients

Figure 1. Distribution of IgG4-RD Phenotypes



Distribution of IgG4-related disease phenotypes



Sites of IgG4-related disease manifestations

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Abstract Number: 1132

Preclinical Profiles of FZ007-119, a Highly Potent and Selective Tyk2 Inhibitor, for the Treatment of Immune Mediated Inflammatory Diseases

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Tyrosine Kinase 2 (TYK2) is a signaling protein within the Janus kinase (JAK) family. It plays a crucial role in transmitting signals from pro-inflammatory cytokines like IL-23, IL-12, and Type I IFN, which contribute to Immune Mediated Inflammatory Diseases (IMIDs). Here we report a novel oral TYK2 inhibitor called FZ007-119, unlike traditional kinase inhibitors that target the catalytic domain, which acts through an allosteric mechanism by binding to the pseudokinase Janus homology 2 regulatory domain (JH2) of the TYK2 enzyme. This specific mode of action allows selective inhibition of TYK2 without affecting other kinases. Current preclinical studies indicate that FZ007-119 shows promise as a treatment for IMIDs while avoiding the side effects associated with non-selective JAK inhibitors.

Methods: We employ our AI-driven structure-based drug design tool to discover selective Tyk2 inhibitors. These compounds are characterized for their drug-like properties, potency, selectivity in both enzyme and cell-based assays, DMPK in vitro and in vivo as well as in mouse models of psoriasis and atopic dermatitis.

Results: FZ007-119 exhibits high potency and specificity for binding to TYK2 JH2 (IC50=0.19nM). It does not show activity against JH1 (protein kinase domain) of JAK1, JAK2, JAK3 and TYK2 (IC50 >10μM) based on HTRF kinase assays. Cell-based assays on human PBMCs demonstrate that FZ007-119 is a potent inhibitor of IFNα stimulated TYK2 dependent signaling (IC50 = 12.2 nM) and is selective over GM-CSF induced JAK2 dependent signaling (IC50>30μM) and IL-2 induced JAK1/3 dependent signaling (IC50>30μM). FZ007-119 exhibits excellent selectivity against a panel of 207 kinases (less than 50% inhibition at 1μM) and a safety panel of 90 targets (less than 50% inhibition at 10μM). FZ007-119 demonstrates dose-dependent inhibition of ear thickness in an IL-23-induced psoriasis mice model (0.3 mg/kg, 1.0 mg/kg and 3.0 mg/kg). It also shows strong efficacy in reducing psoriasis clinical score in an imiquimod-induced mice psoriasis model (3 mg/kg, 10 mg/kg and 30 mg/kg). In a DNFB-induced Atopic Dermatitis model, FZ007-119 (1 mg/kg, 3 mg/kg and 10 mg/kg) significantly reduced lesion scores. FZ007-119 has favorable DMPK profiles, with low risk of drug-drug interactions, no significant inhibition of cytochrome P450 isozymes, and limited inhibition of BCRP or p-gp (IC50 >10μM). It is not a substrate for various transporters (OATP1B1, OATP1B3, OAT1, OAT3, OCT2, MATE1, or MATE2-K). In addition, FZ007-119 exhibits remarkable PK properties and has demonstrated good oral bioavailability in rodents and dogs.

Conclusion: Using our AI-driven drug design tools, we rapidly identified a highly potent and selective TYK2 inhibitor, FZ007-119. Preclinical data support the potential of FZ007-119 as a promising candidate for the treatment of IMIDs such as psoriasis and atopic dermatitis, offering an attractive therapeutic approach with improved efficacy and safety compared to non-selective JAK inhibitors.

Disclosure: W. Zhong: None; **J. Lu**: None; **D. Chen**: None; **S. Zhang**: None; **D. Deng**: None.

Abstract Number: 1133

Exploring the Clinical Characteristics and Correlation with Corticosteroid Dependence in Polymyalgia Rheumatica (PMR) Patients: Insights from an Academic Center

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Polymyalgia rheumatica (PMR) treatment is primarily based on long-term corticosteroids, which results in significant toxicities. Studies[1,2] have shown that patients with PMR are exposed to years of corticosteroid treatment. In a single academic center cohort, we found that 76% of patients remained on steroids at the end of two years.[3] In a second cohort of PMR patients, we explored the baseline characteristics and established the success rate in discontinuing steroid treatment at years one and two after initiating the treatment.

Methods: A retrospective observational study was conducted using data collected from a rheumatology clinic at an academic Medical Center. We included patients with a primary diagnosis of PMR or PMR associated with Giant cell arteritis (GCA) and a minimum of 1-year follow-up. Patients with other rheumatological disorders were excluded. Out of 403 PMR charts reviewed from 2011 to 2021, 346 patients met the inclusion criteria.

Results: The mean age of the patient population was 71 years, with 59% being females and 41% males. Approximately 20% of the patients experienced an abrupt onset of symptoms. Among the PMR patients, 17.1% had a concurrent diagnosis of GCA, which usually developed alongside or after the PMR diagnosis. Only 2% of patients presented with Remitting Seronegative Symmetrical Synovitis with Pitting Edema (RS3PE). At the beginning of treatment (T0), the mean prednisone dose was 24 mg daily. At one year (T1), it decreased to 6.4 mg, and at two years (T2), it further reduced to 4.3 mg daily.

Table 1 Baseline characteristics (n=346)

Mean age (years)	70.8 ± 7.9
Male: Female	1:1.4
Overnight onset of symptoms (%)	19.7%
Association with GCA (%)	17.1%
Mean dose of prednisone at T0 (mg)	24 ± 15.6
Mean dose of prednisone at T1 (mg)	6.4 ± 6.5
Mean dose of prednisone at T2 (mg)	4.4 ± 6.6
% Patients off prednisone at T12 (95% CI)	17.7 (13.9-22.3)
% Patients off prednisone at T24 (95% CI)	38.2 (32.3-44.4)
% of patients with elevated CRP and elevated ESR	45.4
% of patients with normal CRP and normal ESR	14.6
% of patients with elevated CRP and normal ESR	18.3
% of patients with normal CRP and elevated ESR	15.8

*T0= Prednisone dose at the start, T1= Prednisone dose at the end of one year, T2= Prednisone dose at the end of two years, CI= Confidence interval, ESR= Erythrocyte sedimentation rate, CRP= C-reactive protein, GCA= Giant cell arteritis

Table 2. Odds Ratios of Successfully Discontinuing Prednisone as determined by Fisher's Exact Test

Characteristic	12 Months			24 Months		
	OR	95% CI	p-value	OR	95% CI	p-value
Gender*	0.71	0.38, 1.32	0.3123	1.41	0.83, 2.41	0.1994
Smoking†	1.15	0.61, 2.11	0.6576	1.14	0.66, 1.98	0.6896
ESR at Baseline	0.89	0.46, 1.75	0.7527	0.91	0.51, 1.64	0.7792
CRP at Baseline	0.84	0.43, 1.66	0.6269	0.85	0.46, 1.58	0.6605
Overnight onset of symptoms	0.89	0.39, 1.89	0.8592	1.73	0.88, 3.39	0.1029
Taking other DMARDs	0.71	0.23, 1.88	0.6587	0.57	0.22, 1.35	0.2413

* Reference group = Female

† Reference group = nonsmoker

At the end of one year, 17.7% of patients had discontinued prednisone, while only 38% had achieved discontinuation by the end of two years. The majority of patients exhibited elevated markers of inflammation (ESR or CRP), with only 14.6% presenting with normal values initially. The only patient characteristic associated with successful discontinuation was the initial steroid dose. Multivariable logistic regression analysis showed that with each unit increase in the initial prednisone dose, the odds of successfully discontinuing prednisone at 12 months decreased by 3% ($p = 0.034$). However, the significance of this association was not sustained at the 24-month mark. No other baseline characteristics were associated with successful prednisone discontinuation.

Conclusion: The clinical course of PMR is characterized by prolonged corticosteroid use, with a discouraging rate of successful prednisone discontinuation. Our study validates previous observations[3] and provides additional insights into the clinical characteristics of PMR patients. Similar to prior research[4,5], our study demonstrates that the initial corticosteroid dosage predicts the likelihood of successful discontinuation. However, the significance of this association diminishes at the 24-month mark, highlighting the need for further investigation. We acknowledge the limitations of our retrospective study, including potential selection bias due to the inclusion of patients with only one year of follow-up. Nonetheless, these findings underscore the urgency for additional research to identify and incorporate alternative disease-modifying anti-rheumatic drugs (DMARDs) into the PMR treatment regimen.

Disclosure: W. Rigby: None; **T. Mackenzie**: None; **E. Campbell**: None; **J. Skydel**: None; **B. Savage**: None; **M. Dimambro**: None; **V. Tiwari**: None.

Abstract Number: 1134

Pilot Study Investigating Adenosine Deaminase-2 as a Disease Activity Biomarker for Cardiac Sarcoidosis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Sarcoidosis is a heterogenous granulomatous inflammatory disease that is especially dangerous when it affects the heart where it may cause fatal arrythmias and heart failure. Prompt initiation of therapy is frequently necessary, but treatment goals or targets are unclear, and there is currently no standardized approach for measuring disease activity. Imaging modalities such as PET or cardiac MRI have been used but are expensive and not always accessible. Laboratory tests such as serum calcium or serum ACE level are nonspecific. Activated macrophages are important in the pathogenesis of sarcoidosis granuloma formation and macrophages secrete adenosine deaminase 2 (ADA2) in plasma. ADA2 has been shown to correlate with disease activity in other macrophage-activated diseases such as macrophage activation syndrome and tuberculosis; however, ADA2 activity levels in systemic and cardiac sarcoidosis are not known. Total ADA levels have been shown to correlate with systemic sarcoidosis disease activity. We hope to investigate whether ADA2 may fill the gap that is needed for better diagnostics to assess disease activity and/or treatment responsiveness in cardiac and/or systemic sarcoidosis.

Methods: Patients with cardiac sarcoidosis and a control group of systemic sarcoidosis were examined.Plasma ADA2 levels for normal controls have been previously established since the ADA2 test at Duke University is CLIA certified. ADA2 activity was assessed by spectrophotometric assay and high-performance liquid chromatography. Disease activity at the time of ADA2 lab draw was retrieved by chart review for patients at our institution.

Results: Thirty-five patients with sarcoidosis have currently been studied – eleven from outside of our institution and twenty-four from within. All patients with systemic sarcoidosis had a higher mean ADA2 level (19 ± 13mU/mL) than all patients with isolated cardiac sarcoidosis (13 ± 4 mU/mL). Duke patients with untreated systemic sarcoidosis (23 ± 14 mU/mL) and those with untreated isolated cardiac sarcoidosis (16 ± 10 mU/mL) had mean ADA levels higher than controls. TNF inhibition lowered ADA2 levels in all Duke patients (mean of 16 mU/mL untreated vs. 10 mU/mL treated). All results did not reach statistical significance due to small sample size.

Conclusion: This pilot study suggests that the Duke CLIA-certified plasma ADA2 measurement could serve as a cost-effective, accessible, plasma-based biomarker for cardiac and systemic sarcoidosis that correlates with disease activity and treatment responsiveness. Our data is limited by sample size but suggest that future study in larger numbers of patients is warranted.

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Abstract Number: 1135

The Prescribing Patterns and Role of TNF-α Inhibitors in Treatment of Cardiac Sarcoidosis Patients

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
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Background/Purpose: Cardiac sarcoidosis is one of the most common causes of mortality from sarcoidosis. In this retrospective study, we describe prescribing patterns and compare outcomes between patients treated with conventional immunosuppressive therapies (IS), and tumor necrosis factor-α inhibitors (anti-TNF) therapy.

Methods: This is a retrospective analysis of cardiac sarcoidosis patients evaluated at Northwell Health Rheumatology. Diagnosis was validated by manual chart review. Clinical characteristics, echocardiogram (ECHO) and PET CT results were collected at baseline and yearly. EF was derived from ECHO and PET CT. Annualized relative percent change of EF from baseline to final year was calculated based on PET EF, or ECHO EF. Correlation between PET CT EF and ECHO EF with R = 0.56 permitted us to use ECHO as substitution when PET CT was not available. Definition of improvement (DOI) was defined as improvement of EF by > 10%, by PET CT or ECHO no new FDG uptake, and decreased standardized uptake value (SUV) when available on PET. Definition of worsening (DOW) was defined as decline in EF by > 10% on PET CT or

ECHO, new or worsening of FDG uptake, and increased SUV on PET. Descriptive statistics, T-tests, ANOVA tests, Fisher's exact and Spearman's correlation tests were used for statistical analysis.

Results: Baseline demographic and clinical characteristics of the 29 patients that met inclusion criteria are outlined in Table 1. Twenty-two patients had at least two PET/ECHO data for analysis, of whom 15 received anti-TNF. Duration of follow up was 1-3 years. Majority of patients had 2 years of follow up (11/22 patients). Four of 22 patients met DOI, and 3 of those patients had received anti-TNF (p = 0.99). 2 patients met DOW, of whom one received anti-TNF.

There was no difference in baseline EF between the two groups (p= 0.88). EF did not change from baseline to year 1 in both anti-TNF group (p = 0.2) and non-TNF group (p = 0.71). Statistically significant improvement of EF was observed at year 2 in the anti-TNF group as compared to baseline (mean EF: 46.8% vs. 51.2%, p=0.03) and the trend of improvement continued to year 3 (mean EF: 44.0% vs. 52.0%, p=0.05). The non-TNF group had improvement in mean EF, but it was not statistically

Table 1. Baseline Characteristics of Cardiac Sarcoidosis Cohort in Northwell Health System

	Total (n=29)	Anti-TNF group (n=18)	Non-TNF group (n=11)
Demographics			
Age, in years (Mean)	57	55	60
Female	11 (35%)	8 (40%)	3 (27%)
Race			
Black	7 (24%)	3 (17%)	4 (36%)
White	16 (55%)	10 (56%)	6 (55%)
Asian	5 (17%)	4 (22%)	1 (9%)
Multicultural	1 (3%)	1 (6%)	0
Cardiovascular risk factors			
BMI	29.0	29.0	29.6
Previous smoker	5 (17%)	3 (17%)	3 (27%)
Hypertension	10 (34%)	5 (28%)	4 (36%)
Type II Diabetes Mellitus	15 (52%)	9 (50%)	6 (55%)
Duration of Cardiac Sarcoidosis			
	5.4 years	5.9 years	4.6 years
EKG Findings on Presentation			
Atrioventricular block	11 (38%)	6 (33%)	5 (45%)
Ventricular Tachyarrhythmia	8 (28%)	5 (28%)	3 (27%)
Atrial arrythmia	5 (17%)	3 (17%)	2 (18%)
Right bundle branch block	4 (14%)	3 (17%)	1 (9%)
Left bundle branch block	1 (3%)	0	1 (9%)
Extra-cardiac Sarcoid Organ Involvement			
Pulmonary	18 (62%)	10 (56%)	7 (64%)
Lymphadenopathy	19 (66%)	12 (67%)	6 (55%)
Liver	4 (14%)	2 (11%)	2 (18%)
Spleen	2 (7%)	2 (11%)	0
Myositis	1 (3%)	1 (6%)	0
Neurosarcoid	1 (3%)	1 (6%)	0
Skin	6 (21%)	4 (22%)	2 (18%)
Joint	1 (3%)	1 (6%)	0
Renal	2 (7%)	1 (6%)	1 (9%)

Eye	2 (7%)	1 (6%)	0
Laboratory Values			
BNP * at diagnosis	723 pg/mL (n=14)	450 pg/mL (n=7)	1236 pg/mL (n=7)
BNP 6 months after diagnosis	1053 pg/mL (n=5)	99 pg/mL (n=2)	2856 pg/mL (n=3)
BNP 12 months after diagnosis	358 pg/mL (n=5)	447 pg/dL (n=3)	211 pg/dL (n=2)
ACE at diagnosis	20 U/L (n=10)	13 U/L (n=5)	33 U/L (n=5)
Calcium at diagnosis	8.4 mg/dL (n=25)	8.1 mg/dL (n=15)	8.7 mg/dL (n=10)
Creatinine at diagnosis	0.89 mg/dL (n=25)	0.77 mg/dL (n=15)	1.06 mg/dL (n=10)
AST at diagnosis	25 U/L (n=24)	25 U/L (n=15)	24 U/L (n=9)
ALT at diagnosis	31 U/L (n=24)	33 U/L (n=15)	30 U/L (n=9)
TNF-alpha Inhibitors			
Adalimumab		13 (72%)	
Infliximab		4(22%)	
Golimumab		1 (6%)	
Etanercept		0	
Immunosuppressive Medications			
Prednisone	27 (93%)	17 (94%)	10 (91%)
Methotrexate	19 (66%)	15 (83%)	3 (27%)
Leflunomide	1 (3%)	1 (6%)	0
Azathioprine	3 (10%)	3 (17%)	0
Mycophenolate	9 (31%)	5 (28%)	3 (27%)
Hydroxychloroquine	5 (17%)	5 (28%)	0
Cardiac Device			
Pacemaker Placement	27 (93%)	16 (89%)	11 (100%)

Legend:
BNP – B-type Natriuretic peptide
ACE – angiotensin converting enzyme
ALT – alanine transaminase
AST – Aspartate transaminase

significant (41.7% vs 55.0%, p = 0.30) likely due to a small sample size. No statistically significant change was seen by calculating annualized relative EF change (Mean = 4.1, SD 11.89) in the anti-TNF group as compared to the non-TNF group (Mean = - 0.7, SD 29.38).

Conclusion: We describe clinical characteristics and prescribing patterns of cardiac sarcoidosis cohort across Northwell Health System. Interestingly, the average baseline B-type Natriuretic Peptide of patients treated with anti-TNF was lower than patients treated with conventional IS, likely due to avoidance of anti-TNF in decompensated heart failure. No significant change was seen in EF after a year, irrespective of the treatment choice. By year 2, improvement of EF was seen in the anti-TNF group and the trend continued to year 3. Further analysis is planned to compare clinical outcomes of cardiac sarcoidosis patients treated with anti-TNF versus conventional IS.

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Abstract Number: 1136

Challenges in Diagnosing VEXAS Syndrome: Delayed Diagnosis, Misdiagnosis, and Associations with Specific Gene Mutations

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SESSION INFORMATION

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Background/Purpose: The newly described VEXAS syndrome is a very heterogenous disease with rheumatologic and hematologic manifestations, caused by somatic mutations affecting UBA1 gene, that still requires a precise definition. This report aims to address diagnostic challenges such as delays in diagnosis, misdiagnosis, and the clinical associations observed between specific genetic mutations and VEXAS patients (VP).

Methods: A comprehensive survey covering the whole country, which included 126 Spanish hospitals with rheumatologic units, was performed to identify all the VP observed in those units. VP were defined as compatible clinical picture plus characteristic BMB and/or confirmed genetic UBA1 gene mutations. Demographic and clinical data, along with the timing of

Table 1. Most frequent diagnostics prior to VEXAS.

Relapsing polychondritis	6
Seronegative arthritis	5
Sweet syndrome	4
Systemic lupus erythematosus	3
Large vessel vasculitis	2
Medium vessel vasculitis	2
Small vessel vasculitis	1
Autoinflamatory disease	1

Table 2. Clinical associations according to mutation type.

	LEUCINE MUTATION	TREONINE MUTATION
Fever	44.4%*	87.5%
Constitutional syndrome	66.7%	87.5%
Chondritis	33.3%	87.5%*
Skin lesions	100%	87.5%
° Sweet syndrome	77.8%	50%
Arthritis	88.9%	87.5%
Hearing loss	0%*	50%*
Edema	33.3%	75%
Lung involvement	22.2%	50%
Orquitis	0%	25%
Epidimitis	0%	25%
Kidney involvement	11.1%	37.5%
Thrombosis	11.1%	62.5%
Myocarditis	0%	12.5%
Splenomegaly	33.3%	12.5%
Hepatomegaly	0%	0%

* Statistically significant differences **p<0.05.**

initial symptoms, initial and final diagnoses, and specific gene mutations identified in each case, were gathered from medical records. Descriptive analyses were conducted employing standard tests.

Results: Twenty-eight VP were identified. Mean age at onset of symptoms was 65.46 (±SD 9.44/range 40-78) years of age, while mean age at final diagnostic was 70.96 (±SD 8.92/range 46-83) years of age.Median diagnostic delay was 65.34 (±SD 41.73) months and median time from first symptom appearance to Rheumatology referral was 26.29 (±SD 41.73) months. Diagnoses prior to VEXAS syndrome are summarised in Table 1. Twenty-six (92.85%) patients underwent bone marrow biopsy; presence of at least 1 cytoplasmic vacuole was described in 23 cases. Genetic tests were performed in 23 (82.14%) patients. Within our cohort, among the three primary causative variants, 10 patients exhibited an M41L mutation, 8 patients had an M41T mutation, and 3 patients presented an M41V mutation. One patient presented a novel variation affecting c.209T >A, causing a leucine to histidine change, this alteration has not been previously described in other studies to our knowledge at the time of this publication. Finally, data regarding specific mutation was missed in a case. The mutation causing a change to leucine was associated with a phenotype more limited to the skin and joints, with absence of other manifestations as chondritis, hearing loss, or pulmonary involvement. In contrast, the threonine mutation was associated with a broader repertoire of clinical manifestations. Most of these associations were numerical rather than statistically significant (with the exceptions of negative association between hearing loss and leucine mutation and the positive one of chondritis with threonine) due to sample size limitations (Table 2). Finally, out of the 3 (10.71%) patients who died, 2 had leucine and 1 threonine mutations.

Conclusion: The VEXAS syndrome presents a significant delay in its detection as it is quite common its misdiagnosis for other multisystemic entities. Leucine mutation seems to be more associated with cutaneous and articular involvement, whereas the threonine mutation is more associated with chondritis and a more multi-organ clinical picture. These associations need further clarification through larger cohorts, which should also investigate the role of the novel mutation (c.209T >A: p.L70H) identified in this particular cohort.

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Abstract Number: 1137

Association Between Nailfold Videocapillaroscopy Findings and sKL-6 Levels in Patients with Idiopathic Inflammatory Myopathies–Related Interstitial Lung Disease

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SESSION INFORMATION

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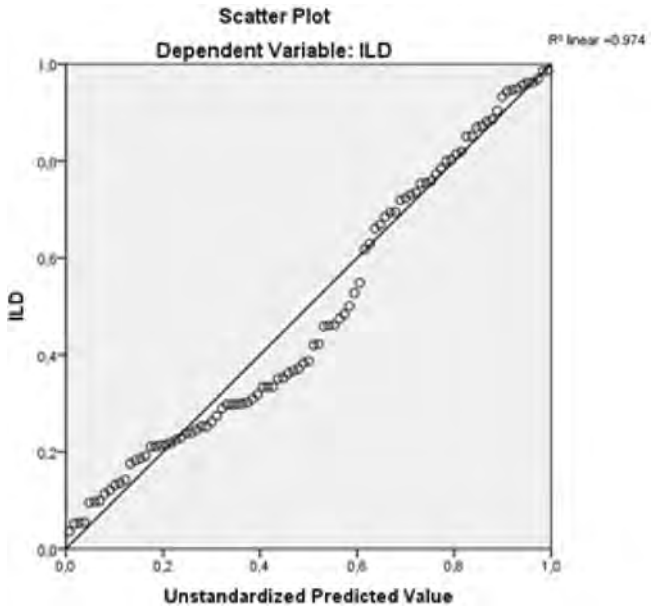
Background/Purpose: Interstitial lung disease (ILD) is a frequent pulmonary manifestation in idiopathic inflammatory myopathies (IIM) (IIM-ILD) and considerably influences morbidity and mortality. Krebs von den Lungen 6 (sKL-6) has been proposed as a potential biomarker reflecting the severity of ILD in connective tissue diseases. Raynaud's phenomenon is very frequent and the presence of microvascular changes in IIM have been described however, the role of nailfold videocapillaroscopy (NVC) in diagnosis and prognosis in IIM is not clearly established. We aim to determine if there is any association between NVC findings, sKL-6 levels and pulmonary involvement in patients with inflammatory myopathies.

Methods: We performed a retrospective study of IIM patients followed in a reference center and compared them according to the presence of ILD. Epidemiological, clinical and immunological data, pulmonary function tests, sKL-6 levels and NVC finding were retrieved. NVC findings including loss of capillary density, enlarged and giant capillaries, ramified capillaries, haemorrhages, thrombosis, avascular areas, disorganization of capillary architecture and subpapillary venous plexus presence were recollected, if present. Statistical analysis was performed by T-test and Fisher's exact test to compare qualitative and/or quantitative variables and multiple logistic regression modelling to identify correlation between pulmonary function tests, NVC findings and sKL-6 levels. Values of $p< 0.05$ were considered statistically significant

Table 1. Significant logistic regressions for predictors for IIM-ILD

Predictor	B value	P value
Male sex	0.186	0.036
Respiratory symptoms	0.40	0.002
%FVC	-0.322	0.01
%DLCO	-0.59	0.001
sKL-6 levels	0.53	0.002
Anti-Jo 1	0.28	0.03
Avascular areas	0.72	0.006
Enlarged capillaries	0.49	0.04



Results: 95 patients were included, 47 patients (49%) with ILD. 34% were male with a median age at inclusion of 55.3 ±24 years and a median disease duration of 6.8±7 years. Avascular areas and capillary loss showed a significant association with the presence of ILD (OR 2.43, 95% CI 1.3-5.7, p 0.004) and (OR 1.7, 95% CI 1.48-3.1, p 0.04). A negative correlation between capillary loss and enlarged capillaries was also found with FVC% (β=-0.46, p 0.001 and β=-0.57, p <0.0001) and DLCO% (β=-0.32, p 0.04 and β=-0.23, p 0.03), respectively**.** When we studied the correlation between sKL-6 levels, positive correlations with the presence of ILD (β=0.77, p 0.0004), the presence of hemorrhages (β =0.21, p 0.04) and avascular areas in NVC (β =0.64, p 0.03) and negative correlations with FVC% (β=-0.47, p 0.001) and DLCO% (β=-0.59, p, 0.005) were found. Multiple logistic regression identified as predictors for developing IIM-ILD are summarized in table 1 and represented in the scatter plot in figure 1. Male sex, respiratory symptoms, %FVC and %DLCO, sKL-6 levels, anti-Jo1 positivity and the presence of avascular areas and enlarged capillaries in NVC were identified as IIM-ILD predictors (R^2=0.974, p =0.006).

Conclusion: Capillary loss and avascular areas showed a significant association with the presence of ILD, worse FVC and DLCO values and sKL-6 levels. We identified 9 predictors for developing ILD in IIM. NVC assessment and sKL-6 levels can have a predictive role for studying pulmonary function and assessing the prognosis of IIM-ILD.

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Nailfold Capillaroscopy Findings in Patients with Idiopathic Inflammatory Myopathies and Its Association to Autoantibodies

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SESSION INFORMATION
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Background/Purpose: Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of acquired muscle diseases, which have distinct clinical, pathological and histological features. Autoantibodies are clinically useful biomarkers to help the diagnosis of IIM. Raynaud's phenomenon is very frequent and the presence of microvascular changes in IIM have been described however, the role of nailfold videocapillaroscopy NVC) for diagnosis and prognosis in IIM is not clearly established. The aim of this study was to study the relationship between clinical and immunological characteristics and nailfold videocapillaroscopy (NVC) abnormalities in patients with idiopathic inflammatory myopathies (IIMs).

Methods: We performed a retrospective study of IIM patients followed in a University Hospital. Patients underwent a NVC at 200x magnification. Epidemiological, clinical data and antibody status, including myositis and scleroderma antibody panel of all patients was retrieved. NVC findings including loss of capillary density, enlarged and giant capillaries, ramified capillaries, haemorrhages, thrombosis, avascular areas, disorganization of capillary architecture and subpapillary venous plexus

Clinical features	
Muscle weakness	79 (83%)
Skin findings	30 (32%)
ILD	47 (49%)
Dysphagia	18 (19%)
Raynaud's phenomenon	37 (39%)
CK elevation	45 (47%)
Cardiac disease	4 (4%)
NFC features	
Loss of capillary density	27 (28%)
Enlarged and giant capillaries	37 (39%)
Haemorrhages	36 (38%)
Thrombosis	19 (20%)
Avascular areas	26 (27%)
Disorganization of capillary architecture	24 (25%)
Subpapillary venous plexus	36 (38%)
Antibody status	
Disease-specific antibodies	
Anti-MDA5	8 (8%)
Anti-TIF1G	11 (12%)
Anti-MI2	11 (12%)
Anti-NXP2	6 (6%)
Anti-synthetase antibodies	
Anti-Jo1	13 (14%)
Anti-PL7	9 (9%)
Anti-PL12	5 (5%)
Disease-associated antibodies	
Anti-Ro52	27 (28%)
Anti-KU	6 (6%)
Antinuclear antibodies	61 (64%)
Others (EJ, SRP, PM-SCL75, PM-SCL100, CN1A)	22 (23%)

Table 1: Epidemiological, clinical, immunological and NFC features and autoantibody status from patients with IIM

presence were recollected, if present. For the comparison of qualitative and/or quantitative variables Fisher's exact Test or T-test was performed when necessary.

Results: 95 patients with NVC performed during the follow-up were included (66% female) with a median age at inclusion of 55.3±24 years. Median IIM duration was 6.8±7 years. 39% had Raynaud's phenomenon at first clinical evaluation and 58% of them showed NVC pathological findings. Table 1 Summarizes the epidemiological, clinical, and autoantibody status of the patients. We found an association between the presence of dysphagia and avascular areas (p=0.02) or abnormal capillary organization (p< 0.01) on NVC. ILD was associated with capillary loss (p=0.04) and avascular areas (p=0.004). Anti-MDA5+ was associated with capillary loss (p=0.03), thrombosis (p=0.02) and ramified capillaries (p=0.04). Anti-Mi2+ and anti-Th/To was associated with abnormal capillary organization (p=0.017 and p=0.001). The presence of haemorrhages was associated with anti-Ku+ (p=0.048) and anti-PL12+ (p=0.046). The presence of enlarged capillaries was associated with anti-RNA-pol III (p=0.04) and anti-NXP2 (p=0.044). A significant association between anti-Ro52 (OR 2.69, CI 95% 1.05-6.8, p 0.03) and anti-Jo1 (OR 7.03 CI 95% 1.46-33.7, p 0.01) with ILD was found. Anti-PML (OR 4.32 CI 95% 1.35-10.42, p 0.038) and anti-Th/To (OR 5.82 CI 95% 1.89-13.24, p 0.04) were associated with dysphagia. Anti-MDA5 (OR 5.85 CI 95% 1.92-14.21, p 0.044) was associated with skin involvement.

Conclusion: The presence of certain autoantibodies is related to the degree of microangiopathy in IIM and associates with capillaroscopic changes. Studying the association between capillaroscopic changes with diagnostic and pathogenic auto-antibodies in IIM can provide useful information regarding the current knowledge about pathogenesis, classification, and prognosis of the disease.

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Abstract Number: 1139

From Skin to Bone Lesions: A Pioneer Study Unraveling the Underdiagnosis of SAPHO Syndrome in the Dominican Republic

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Background/Purpose: SAPHO syndrome is a rare chronic inflammatory condition that affects the skin and osteoarticular structures. Despite being first described over 30 years ago, it remains poorly recognized in clinical practice. This study aims to comprehensively update and analyze the disease in the Dominican Republic to improve diagnosis. It dissects the socio-demographic characteristics, preferred diagnostic imaging modalities, and detailed descriptions of bone and skin lesions in the first diagnosed patients. Furthermore, this study is noteworthy for being the first to explore a correlation between dermatological and imaging findings and their interdependence.

Methods: This retrospective study reviewed electronic medical records from 2015 to 2022 to identify patients with skin conditions related to acne and psoriasis. Patients who met Kanh's and Benhamou's criteria for SAPHO syndrome, identified through imaging studies, were included in the sample population. Data on sociodemographics, comorbidities, laboratory tests, and imaging findings were collected and analyzed. Spearman correlations and chi-square tests were calculated along with their corresponding *P* values using Rstudio, with a significance level of $p< 0.05$ considered statistically significant.

Results: Among the patients reviewed, 21 of 1,340 (1.5%) met the criteria and were diagnosed with SAPHO syndrome, with a majority being females (71%). Laboratory tests, including ESR, C-reactive protein, C3, and C4, were not determining factors for diagnosis. MRI and X-ray (48%) were the preferred diagnostic tools for the disease, with sonography (10%) emerging as an alternative option for younger patients. The study identified hyperostosis (52%), osteitis (29%), and arthritis (19%) as common osteoarticular manifestations, with the dorsal column being the most commonly affected bone (82%). The most common dermatoses were severe acne (57%) and psoriasis vulgaris (29%), which commonly affected the face (62%), thorax (33%), scalp (24%), extremities (19%), back (19%), and palmoplantar region (5%). Most patients displayed one or two affected skin areas.

Conclusion: SAPHO syndrome requires a multidisciplinary approach involving rheumatologists, dermatologists, and radiologists, who rely on clinical and imaging findings for an accurate diagnosis. The disease is commonly seen in females aged 34-38, and the preferred imaging modalities for diagnosis were MRI and X-ray. This study found that severe acne exhibited

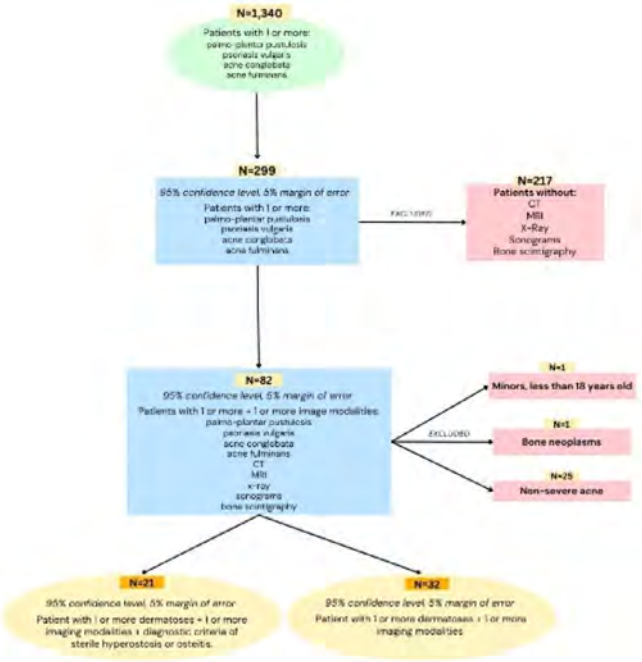

Figure 1. Flowchart illustrating the selection process of patients with SAPHO syndrome, based on inclusion and exclusion criteria.

N=53	PSORIASIS VULGARIS		PUSTULAR PSORIASIS		SEVERE ACNE	
	CHI-SQUARE	*P*-VALUE	CHI-SQUARE	*P*-VALUE	CHI-SQUARE	*P*-VALUE
HYPEROSTOSIS	2.0562	0.1516	0.61299	0.4337	0.35198	0.553
OSTEITIS	0.047409	0.8276	0.19734	0.6569	0.27696	0.5987
HYPEROSTOSIS & OSTEITIS	0.65089	0.4198	0.0004746	0.9826	0.43312	0.5105

Figure 2. Illustration of the statistical analysis performed using chi-square and p-values to evaluate the association between dermatoses and radiological manifestations. The analysis demonstrates the independence of each presentation.

N=21	OUTPUT	P-VALUE
SPEARMAN CORRELATION	0.6363961	0.001925
CHI SQUARE	8.505	0.003542

Figure 3. Illustration of Spearman and chi-square correlation analysis, demonstrating for the first time a positive correlation between dermatoses in the extremities and palmoplantar region and bone lesions in long bones, revealing the interdependence between these variables.

the highest percentage of radiological findings. However, no significant correlation was observed between dermatological and radiological variables within our sample, indicating the independence of each variable from the other. We also investigated a possible correlation between affected bone areas and areas affected by dermatoses, uncovering a positive correlation between dermatoses of the extremities and palmoplantar region with radiological findings on the long bones and the pelvis. The results of this study, representing the first investigation of this topic in the Dominican Republic, hold the potential to enhance diagnostic strategies and provide valuable statistical data for both local and global understanding of SAPHO syndrome.

Disclosure: L. Maletta: None; **D. Jimenez**: None; **R. de Jesus**: None.

Abstract Number: 1140

Inflammation Is More Prominent Than Joint Damage at Initial Visits of Patients with Inflammatory Arthritides, but Organ Damage Is More Prominent and Patient Distress Is as Prominent as Inflammation in Overall Rheumatology Care: Data from a Feasible Physician RheuMetric Checklist

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Background/Purpose: Patients consult rheumatologists for symptoms which may result from inflammatory activity or reversible problems (INF), joint or other organ damage or irreversible problems (DAM), and/or distress with neither INF nor DAM (STR), e.g., fibromyalgia. Many patients may have clinically important DAM and/or STR in addition to INF. However, quantitative assessment in routine rheumatology care is directed primarily (often exclusively) to INF, e.g., DAS28, CDAI, SLEDAI, ASDAS, and DAPSA. DAM and STR are recognized in many patients, but generally recorded only as narrative descriptions, rather than as quantitative data. INF indices are effective in clinical trials. However, measures and indices designed to assess INF may be elevated by comorbid DAM and/or STR, often despite little or no INF, particularly in routine care patients. A RheuMetric checklist includes 4 0-10 visual numeric scales (VNS) for physician global assessment (DOCGL), inflammation (DOCINF), damage (DOCDAM), and patient distress (DOCSTR), and estimates of the percent of DOCGL attributed to INF, DAM, and STR. We analyzed RheuMetric scores in routine care patients with all diagnoses at initial or return visits to recognize levels of DOCGL, INF, DAM, and STR at initial vs follow-up visits.

Methods: A retrospective cross-sectional study was performed of RheuMetric checklist 0-10 VNS estimates for DOCGL and estimates of %INF, %DAM, and %STR (total=100%) completed in routine care by the treating rheumatologist. Mean levels of these estimates were analyzed according to primary diagnosis, classified as INF (RA, SLE, SpA, vasculitis and gout), osteoarthritis (OA), primary fibromyalgia (FM), and "other," at initial or return visits, using descriptive and chi-square statistics.

Results: Highest DOCINF was in inflammatory diseases, DOCDAM in OA, and DOCSTR in primary FM (Table). The % of DOCGL attributed to INF, DAM, and STR was highest in INF diseases, OA, and primary FM, respectively ($p< 0.001$) (Table). At initial visits of patients with inflammatory diseases, mean DOCGL was 4.3, attributed 62% to INF, 24% to DAM and 14% to STR, respectively. At return visits of patients with inflammatory diseases, mean DOCGL was 3.7, attributed 33% to INF, 49% to DAM and 18% to STR (Table). In patients with all diagnoses, 36%, 36%, and 28% of DOCGL were attributed to INF, DAM, and STR, respectively, at first visits, vs 22%, 51%, and 28% at return visits (Table). RheuMetric estimates required 15-20 seconds to complete.

Conclusion: RheuMetric physician estimates for INF, DAM, and STR are feasibly recorded in 15-20 seconds in routine care, with face validity documented by significantly higher DOCINF in inflammatory diseases, DOCDAM in OA, and DOCSTR in FM. DOCINF was higher at first vs return visits, reflecting strong anti-inflammatory therapies at this time, while % DOCDAM was higher at return vs first visits. At return visits of all patients, INF accounted for 22% of DOCGL vs 50% for DAM and 28% for STR, indicating that control of inflammation is not the primary rheumatology activity after the first visit. Physician 0–10 estimates of inflammation, damage, and patient distress, in addition to DOCGL, can give a more complete quantitative patient assessment than only measures of inflammation.

Table: Cross sectional analyses of mean (standard deviation) for 0-10 physician global estimate (DOCGL) and % of DOCGL attributed to inflammation (%INF), damage (%DAM), and patient distress (%STR) (Total=100%) at 244 first visits compared to 319 return visits Δ p<0.001 at both initial and return visits. *p<0.001 vs initial visits, ◊p=0.05 vs initial visits

Table: Cross sectional analyses of mean (standard deviation) for 0-10 physician global estimate (DOCGL) and % of DOCGL attributed to inflammation (%INF), damage (%DAM), and patient distress (%STR) (Total=100%) at 244 first visits compared to 319 return visits

	Initial visits					Return visits				
Primary rheumatic physician ICD-10 diagnosis	N (%)	DOC GL	Mean (SD) % of DOCGL attributed to...			N(%)	DOC GL	Mean (SD) % of DOCGL attributed to...		
		DOC GL	% INF	% DAM	% STR		DOC GL	% INF	% DAM	% STR
Inflammatory diseases (RA, SLE, SpA, Vasc, Gout)	67 (27%)	4.3 (2.5)	62%Δ (33%)	24% (24%)	14% (24%)	127 (40%)	3.7 (2.6)	33%Δ (31%)	49% (35%)	18%* (27%)
Osteoarthritis	45 (18%)	4.4 (2.0)	14% (19%)	72%Δ (28%)	14% (18%)	69 (22%)	5.0 (2.2)	7% (14%)	69%Δ (30%)	24% (28%)
Fibromyalgia	32 (13%)	4.9 (2.6)	14% (22%)	12% (16%)	74%Δ (28%)	36 (11%)	5.0 (2.0)	12% (21%)	20% (21%)	68%Δ (26%)
Other diagnosis	100 (41%)	3.0 (2.1)	37% (33%)	35% (31%)	29% (33%)	87 (27%)	3.5 (2.4)	26% (29%)	52% (35%)	22% (30%)
TOTAL	244 (100%)	3.9 (2.4)	36% (35%)	36% (33%)	28% (34%)	319 (100%)	4.1 (2.5)	22% (28%)	51% (35%)	28%0 (32%)

Δ p<0.001 at both initial and return visits. *p<0.001 vs initial visits, ◊p=0.05 vs initial visits

Disclosure: T. Pincus: None; **T. Li**: None; **J. Schmukler**: None.

Abstract Number: 1141

COVID-19 Vaccination Status and Adverse Events Following SARS-CoV-2 Vaccine in Autoimmune Inflammatory Rheumatic Disease (AIRD) Patients: A Single Center Experience

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SESSION INFORMATION

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Background/Purpose: Autoimmune inflammatory rheumatic diseases (AIRD) were associated with an increased risk for COVID-19 infection, worse clinical outcomes, and COVID-19- related deaths. Vaccines carry the potential benefit of reducing disease transmission and disease severity. Issues on vaccine safety, trigger of an autoimmune reaction or disease flares has been a long issue. Thus this study describes the COVID-19 vaccination status and adverse events following SARS-COV 2 vaccine in a tertiary hospital in Manila, Philippines.

Table 1. Clinicodemographic profile of the patients when grouped according to age, sex, and rheumatologic diagnosis (N=204)

	N (%)
Gender	
Male	30 (15)
Female	174 (85)
Age Group	
19-35	101(50)
36-50	58(28)
51 - 65	31(15)
>65	14(7)
Rheumatologic Diagnosis	
SLE	129(63)
Rheumatoid Arthritis	22(11)
Psoriatic Arthritis	17(8)
Ankylosing Spondylitis	13(6)
Other Systemic Autoimmune Diseases	13 6)
Inflammatory Myopathies	8 (4)
Scleroderma	2(1)

Table 2. Vaccination status, types of COVID-19 vaccines received and side effects following vaccination.(N=204)

	N (%)
Vaccination status	
Fully vaccinated	204(100)
Partially vaccinated	0
Types of vaccines	
Inactivated vaccine Sinovac	87(43)
Viral Vector Astra Zeneca J&J Sputnik V	41(20) 21(10) 1(0.5)
mRNA vaccine Pfizer Moderna	39 (19) 15 (7)
Side effects/Adverse events	
None	**133 (65.2)**
Experienced Adverse Events/Side Effects	**71 (34.8)**
Constitutional Symptoms (fever, headache, body malaise)	36 (38.3)
Musculoskeletal (joint pains, joint swelling, myalgia, muscle weakness)	38(40.4)
Cutaneous/Dermatologic (rashes, ulcers (skin, oral)	12(12.7)
Respiratory (difficulty of breathing, shortness of breath, cough)	3(3.2)
Gastrointestinal (abdominal pain, diarrhea)	4(4.3)
Cardiovascular (occasional chest pain)	1 (1)

Table 3. New onset autoimmune reactions and disease flares and the time-interval of the adverse events following SARS-COV -2 vaccination (N=9)

	N (%)
Days of onset post vaccination 0-30 days 31-60 days 61-90 days 91-120 days >120 days	 9 (100) 0 0 0 0
New onset autoimmune reaction: • Amyopathic dermatomyositis	 1 (11.1)
Disease Flares • SLE (severe hematologic, cutaneous and renal flare) • Rheumatoid arthritis flare • Spondyloarthritis • Inflammatory arthritis • Henoch Schonlein purpura	 3 (33.33) 2 (22.22) 1 (11.1) 1 (11.1) 1 (11.1)

Table 4. COVID-19 infection, disease severity and time interval of COVID-19 infection after receiving SARS-COV-2 vaccine: (N=22)

	N (%)
Days of onset post vaccination 0-30 days 31-60 days 61-90 days 91-120 days >120 days	 3 (13.6) 2 (9.1) 2 (9.1) 6 (27.3) 9 (40.9)
Severity: Asymptomatic Mild Moderate Severe	 19 (86.4) 2 (9.1) 1 (4.5)

1.

Methods: This retrospective cross-sectional study included patients diagnosed with AIRD and seen in the clinics over 12 months (March 2021-March 2022).We collected data from patients' clinic records and analyzed the clinicodemographic profile, vaccination status, adverse events and development of new onset autoimmune reaction and disease flares post vaccination and those who developed COVID-19 infection even after vaccination.

Results: There were 204 respondents included in this study. Majority were female (85%). SLE, rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis were the common AIRD. The median age is 38.4 years. 100% of the respondents were fully vaccinated; 42.6% received inactivated vaccine, 30.8% viral vector vaccine and 26.4% mRNA vaccine. 65.2% reported no adverse events while 34.8% experienced constitutional, musculoskeletal, cutaneous, respiratory, gastrointestinal and cardiovascular symptoms after vaccination. There were 9 (4.4%) of the respondents who developed new onset autoimmune reaction and disease flares 7-28 days post vaccination; 1patient had new onset amyopathic dermatomyositis; 3SLE patients developed severe hematologic, cutaneous and renal flare; 2 rheumatoid arthritis, 1 spondyloarthritis, and 1 inflammatory patients in long remission had disease flares and 1 patient with henoch schonlein purpura developed flare. Twenty two of the respondents developed COVID-19 infection after 30-120 days post vaccination; of whom 86.4% developed mild symptoms, 9.1% moderate infection and 4.5% had severe infection. All of the patients recovered with no complications.

Conclusion: This study showed that patients with AIRD experienced varied organ system adverse events ranging from mild side effects to new onset autoimmune reactions and disease flares. Even after a complete vaccination, some patients still had COVID-19 infection, however preventing them from worse complications, hospitalization and death.

Disclosure: V. Luceño: None; **P. Daleon**: None; **S. Navarra**: Astellas, 6, AstraZeneca, 6, Biogen, 2, Boehringer-Ingelheim, 2, GSK, 6, Novartis, 6, Pfizer, 6.

Abstract Number: 1142

A Retrospective Analysis of Radiographic and Serologic Findings in Patients with Scleroderma and Interstitial Lung Disease

Nikita Jhawar, **Claire Wilson**, Andy Abril, Li Zhuo and Yaohua Ma, Mayo Clinic, Jacksonville, FL

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Connective tissue diseases such as scleroderma are frequently associated with interstitial lung disease (ILD). Detection of autoantibodies is crucial in characterizing disease phenotypes, but there remains a lack of substantial data on the association of some autoantibodies present in scleroderma patients with specific ILD patterns. We sought to investigate possible association, describe the phenotypes of scleroderma seen in our study cohort, and review findings from other studies.

Methods: The cohort included adults with scleroderma and ILD who were treated at Mayo Clinic between January 2011 and December 2021. Baseline demographic, serologic, and imaging data were extracted from the electronic medical record. Continuous variables were summarized with median and range, and categorical variables were summarized with frequency and percentage (%). The Kruskal-Wallis Rank Sum test was used for continuous measures and the Chi-square test

was used for categorical measures. All tests were two-sided and p-values less than 0.95 were considered to be statistically significant. Analysis programming was performed by R-studio with R version 4.1.2.

Results: A total of 454 patients with both scleroderma and ILD were included in the study. The study cohort had a mean age of 62 years, and 103 patients (22.7%) were males. ILD patterns analyzed included NSIP (83.3%), UIP (11%), probable UIP (2.9%), indefinite UIP (2.9%), OP (1.5%) and LIP (2%). The antibody and symptoms were determined for patients with and without each of these ILD patterns. NSIP patients were more likely to have anti-Scl70 antibodies compared to patients

Table 1A: Frequency of percentage of antibodies and symptoms by ILD pattern

Table 1A: Frequency of percentage of antibodies and symptoms by ILD pattern

Antibodies and Symptoms	Summary by NSIP group			Summary by UIP group			Summary by probably UIP group			Summary by indefinite UIP group			Summary by OP group			Summary by LIP group		
	No (N=76)	Yes (N=378)	P.val	UIP.no (N=404)	UIP.yes (N=50)	P.val	No (N=441)	Yes (N=13)	P.val	No (N=441)	Yes (N=13)	P.val	OP.no (N=447)	OP.yes (N=7)	P.val	LIP.no (N=445)	LIP.yes (N=9)	P.val
Anti-Scl70	17 (22.4%)	143 (37.8%)	0.01	150 (37.1%)	10 (20.0%)	0.017	156 (35.4%)	4 (30.8%)	0.732	156 (35.4%)	4 (30.8%)	0.732	158 (35.3%)	2 (28.6%)	0.71	160 (36.0%)	0 (0.0%)	0.025
Anti-centromere	14 (18.4%)	48 (12.7%)	0.185	56 (13.9%)	6 (12.0%)	0.718	59 (13.4%)	3 (23.1%)	0.316	58 (13.2%)	4 (30.8%)	0.068	61 (13.6%)	1 (14.3%)	0.961	60 (13.5%)	2 (22.2%)	0.45
Anti-U1.snRNP	2 (2.6%)	14 (3.7%)	0.644	14 (3.5%)	2 (4.0%)	0.847	16 (3.6%)	0 (0.0%)	0.484	16 (3.6%)	0 (0.0%)	0.484	16 (3.6%)	0 (0.0%)	0.61	14 (3.1%)	2 (22.2%)	0.002
Anti-PM.scl	2 (2.6%)	22 (5.8%)	0.257	23 (5.7%)	1 (2.0%)	0.271	24 (5.4%)	0 (0.0%)	0.387	23 (5.2%)	1 (7.7%)	0.694	22 (4.9%)	2 (28.6%)	0.006	24 (5.4%)	0 (0.0%)	0.474
Anti-RNA.Pol.III	8 (10.5%)	57 (15.1%)	0.301	60 (14.9%)	5 (10.0%)	0.358	63 (14.3%)	2 (15.4%)	0.911	63 (14.3%)	2 (15.4%)	0.911	64 (14.3%)	1 (14.3%)	0.998	65 (14.6%)	0 (0.0%)	0.215
Digital Ulcers	19 (25.0%)	110 (29.1%)	0.47	118 (29.2%)	11 (22.0%)	0.286	124 (28.1%)	5 (38.5%)	0.415	124 (28.1%)	5 (38.5%)	0.415	126 (28.2%)	3 (42.9%)	0.393	127 (28.5%)	2 (22.2%)	0.677
Esophageal Dysmotility	38 (50.0%)	183 (48.4%)	0.801	193 (47.8%)	28 (56.0%)	0.232	216 (49.0%)	5 (38.5%)	0.455	215 (48.8%)	6 (46.2%)	0.853	218 (48.8%)	3 (42.9%)	0.756	215 (48.3%)	6 (66.7%)	0.275
Raynaud's	68 (89.5%)	346 (91.5%)	0.563	367 (90.8%)	47 (94.0%)	0.457	403 (91.4%)	11 (84.6%)	0.396	403 (91.4%)	11 (84.6%)	0.396	409 (91.5%)	5 (71.4%)	0.063	406 (91.2%)	8 (88.9%)	0.806
Pulmonary Hypertension	14 (18.4%)	65 (17.2%)	0.797	69 (17.1%)	10 (20.0%)	0.607	75 (17.0%)	4 (30.8%)	0.197	78 (17.7%)	1 (7.7%)	0.349	77 (17.2%)	2 (28.6%)	0.432	77 (17.3%)	2 (22.2%)	0.7

Notes: Chi-square test for categorical variables; P.val= P value.

Table 1B: Frequency and percentage of ILD pattern by antibody and symptom group

Table 1B: Frequency and percentage of ILD pattern by antibody and symptom group

Antibodies and Symptoms	NSIP	UIP	Probably.UIP	Indefinite.UIP	OP	LIP
Anti-Scl70						
0 (N=294)	235 (79.9%)	40 (13.6%)	9 (3.1%)	9 (3.1%)	5 (1.7%)	9 (3.1%)
1 (N=160)	143 (89.4%)	10 (6.2%)	4 (2.5%)	4 (2.5%)	2 (1.2%)	0 (0.0%)
P value	0.01	0.017	0.732	0.732	0.71	0.025
Anti-centromere						
0 (N=392)	330 (84.2%)	44 (11.2%)	10 (2.6%)	9 (2.3%)	6 (1.5%)	7 (1.8%)
1 (N=62)	48 (77.4%)	6 (9.7%)	3 (4.8%)	4 (6.5%)	1 (1.6%)	2 (3.2%)
P value	0.185	0.718	0.316	0.068	0.961	0.45
Anti-U1.snRNP						
0 (N=438)	364 (83.1%)	48 (11.0%)	13 (3.0%)	13 (3.0%)	7 (1.6%)	7 (1.6%)
1 (N=16)	14 (87.5%)	2 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (12.5%)
P value	0.644	0.847	0.484	0.484	0.61	0.002
Anti-PM.scl						
0 (N=430)	356 (82.8%)	49 (11.4%)	13 (3.0%)	12 (2.8%)	5 (1.2%)	9 (2.1%)
1 (N=24)	22 (91.7%)	1 (4.2%)	0 (0.0%)	1 (4.2%)	2 (8.3%)	0 (0.0%)
P value	0.257	0.271	0.387	0.694	0.006	0.474
Anti-RNA.Pol.III						
0 (N=389)	321 (82.5%)	45 (11.6%)	11 (2.8%)	11 (2.8%)	6 (1.5%)	9 (2.3%)
1 (N=65)	57 (87.7%)	5 (7.7%)	2 (3.1%)	2 (3.1%)	1 (1.5%)	0 (0.0%)
P value	0.301	0.356	0.911	0.911	0.998	0.215
Digital Ulcers						
0 (N=325)	268 (82.5%)	39 (12.0%)	8 (2.5%)	8 (2.5%)	4 (1.2%)	7 (2.2%)
1 (N=129)	110 (85.3%)	11 (8.5%)	5 (3.9%)	5 (3.9%)	3 (2.3%)	2 (1.6%)
P value	0.47	0.286	0.415	0.415	0.393	0.677
Esophageal Dysmotility						
0 (N=233)	195 (83.7%)	22 (9.4%)	8 (3.4%)	7 (3.0%)	4 (1.7%)	3 (1.3%)
1 (N=221)	183 (82.8%)	28 (12.7%)	5 (2.3%)	6 (2.7%)	3 (1.4%)	6 (2.7%)
P value	0.801	0.272	0.455	0.853	0.756	0.275
Raynaud's						
0 (N=40)	32 (80.0%)	3 (7.5%)	2 (5.0%)	2 (5.0%)	2 (5.0%)	1 (2.5%)
1 (N=414)	346 (83.6%)	47 (11.4%)	11 (2.7%)	11 (2.7%)	5 (1.2%)	8 (1.9%)
P value	0.563	0.457	0.396	0.396	0.063	0.806
Pulmonary Hypertension						
0 (N=375)	313 (83.5%)	40 (10.7%)	9 (2.4%)	12 (3.2%)	5 (1.3%)	7 (1.9%)
1 (N=79)	65 (82.3%)	10 (12.7%)	4 (5.1%)	1 (1.3%)	2 (2.5%)	2 (2.5%)
P value	0.797	0.607	0.197	0.349	0.432	0.7

Notes: P values from Chi-square test

Supplementary table 1: Summary of demographic descriptions

	Overall (N=454)
Age	
N-Miss	2
Mean (SD)	61.56 (13.08)
Gender	
Female	351 (77.3%)
Male	103 (22.7%)
NSIP	
0	76 (16.7%)
1	378 (83.3%)
UIP	
0	404 (89.0%)
1	50 (11.0%)
Probable UIP	
0	441 (97.1%)
1	13 (2.9%)
Indefinite UIP	
0	441 (97.1%)
1	13 (2.9%)
OP	
0	447 (98.5%)
1	7 (1.5%)
LIP	
0	445 (98.0%)
1	9 (2.0%)

Supplementary table 1: Summary of demographic descriptions

without NSIP (p=0.01). OP patients were more likely to have anti-PM/Scl antibodies compared to patients without OP (p=0.006), and LIP patients were more likely to have anti-U1 snRNP antibodies compared to patients without LIP (p=0.002). LIP patients were significantly less likely to have antiScl70 antibodies than patients without LIP (p=0.025). Additionally, UIP patients were also less likely to have anti-Scl70 antibodies than patients without UIP (p=0.017). There were no clinically significant findings of anti-centromere antibodies or anti-RNA Pol III antibodies in any of the ILD patterns. No symptoms had a clinically significant association with the ILD pattern groups.

Conclusion: Our study examined associations between serologic data and ILD patterns and demonstrated a statistically significant association of anti-Scl70 antibodies with NSIP and antiPM/Scl antibodies with OP. There also appears to be an association between anti-U1 snRNP antibodies and LIP, which has not been demonstrated in the literature thus far aside from another observational study. LIP and UIP patterns were significantly less likely to have association with anti-Scl70 antibodies. We did not find any statistically significant association between anticentromere antibodies and specific ILD patterns. Finally, our study suggests that antibodies may develop in scleroderma but are not necessarily associated with development of ILD. Autoantibodies offer an invaluable tool in predicting disease outcomes and further studies are needed to elucidate this, especially with regards to scleroderma-associated ILD.

Disclosure: N. Jhawar: None; **C. Wilson**: None; **A. Abril**: None; **L. Zhuo**: None; **Y. Ma**: None.

Abstract Number: 1143

Nationwide Analysis of Adult-Onset Still's Disease with and Without Hemophagocytic Lymphohistiocytosis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Adult-Onset Still's Disease (AOSD) commonly manifests with fever, arthritis, rash, liver dysfunction, lymphadenopathy, and hematologic abnormalities. AOSD is also associated with Hemophagocytic Lymphohistiocytosis (HLH). We aimed to study the characteristics and outcomes of adult AOSD hospitalizations with HLH, as well as independent predictors of inpatient mortality.

Methods: We utilized the 2016 to 2019 National Inpatient Sample (NIS) database to obtain hospitalizations with a principal or secondary diagnosis of AOSD. We subdivided AOSD hospitalizations into those with and without HLH. ICD-10 codes were used to identify diagnoses. Demographics, complications of interest, total hospital charges (THC) and length of stay (LOS) were collected and compared. Variables with a p value ≤ 0.2 in the univariable screen were included in a multivariable logistic regression model for in-hospital death. Results were reported as odds ratios (OR).

Results: We identified 5,495 adult AOSD hospitalizations, of which 340 (6.2%) had HLH, and 5,155 (93.8%) did not have HLH (table 1). Relative to the non-HLH group, HLH group was younger (median age 33 vs 51 years; p< 0.001), had similar percentage of females (69.1% vs 59.4%; p=0.133), had less whites (45.6% vs 58.3%; p=0.045), similar percentage of African Americans (11.8% vs 12.2%; p=0.919), but had more Hispanics (26.5% vs 15.7%; p=0.027), had longer median LOS in days (7 vs 4; p< 0.001) and a higher median THC ($73,156 vs $41,840; p=0.001). The HLH group had higher prevalence of

Hospitalization Characteristics	AOSD without HLH (n=5,155)	AOSD with HLH (n=340)	P-value
Age, median (IQR) in years	51 (35-63)	33 (26-53)	<0.001
Age Groups (%)			
Age 18-40 years	33.2%	63.2%	<0.001
Age 40-60 years	34.4%	20.6%	0.021
Age 60-80 years	29.3%	16.2%	0.022
Age > 80 years	3.1%	0%	---
Female, n (%)	3,060 (59.4%)	235 (69.1%)	0.133
Race/Ethnicity (%)			
White	58.3%	45.6%	0.045
African American	12.2%	11.8%	0.919
Hispanic	15.7%	26.5%	0.027
Asian or PI	6.3%	5.9%	0.890
Native American	0.7%	NR	0.393
Other Race	4.3%	NR	0.599
Length of Stay, median (IQR)	4 (3-8)	7 (4-12)	<0.001
Total Charges, median (IQR)	$41,840 (22,066- 80,610)	$73,156 (40,681- 131,124)	0.001
Income Q1 (%)	26.6%	26.5%	0.985
Income Q2 (%)	21.5%	26.5%	0.368
Income Q3 (%)	24.7%	25.0%	0.962
Income Q4 (%)	26.1%	22.1%	0.456
In-hospital Mortality, n (%)	75 (1.5%)	30 (9.0%)	----
CCI, median (IQR)	2 (1-3)	2 (1-3)	0.215
Predictors of Interest, n (%)			
AKI	845 (16.4%)	140 (41.2%)	<0.001
DIC	35 (0.7%)	25 (7.4%)	<0.001
Encephalopathy	210 (4.1%)	20 (5.9%)	0.474
Hepatic failure	70 (1.4%)	40 (11.8%)	<0.001
Infections	1,995 (38.7%)	215 (63.2%)	<0.001
Myocarditis	0 (0%)	0 (0%)	----
Respiratory failure	595 (11.5%)	105 (30.9%)	<0.001
TMA	15 (0.3%)	NR	0.005

Abbreviations: AKI= acute kidney insufficiency; AOSD=Adult Onset Stills Disease; CCI= Charlson Comorbidity Index; DIC= Disseminated intravascular coagulation; HLH= Hemophagocytic Lymphohistiocytosis; NR=not reported because below permitted reporting threshold (≤10); IQR=interquartile range; n= number; PI=Pacific Islander; IQR=interquartile range; TMA=thrombotic microangiopathy

Weighted Descriptive Characteristics of AOSD Disease Hospitalizations from the 2016-2019 National Inpatient Sample (n=5,495)

acute kidney insufficiency (AKI) (41.2% vs 16.4%; p< 0.001), disseminated intravascular coagulation (DIC) (7.4% vs 0.7%; p< 0.001), hepatic failure (11.8% vs 1.4%; p< 0.001), infections/pneumonia/sepsis (63.2% vs 38.7%; p< 0.001), respiratory failure (30.9% vs 11.5%; p< 0.001), and thrombotic microangiopathy (TMA) (2.9% vs 0.3%; p=0.005). Univariable analyses

Variables	Odds Ratio	P value	95% CI
Age	0.99	0.558	0.964-1.020
HLH	6.66	<0.001	2.477-17.919
CCI	1.32	0.003	1.102-1.591
Female	0.60	0.251	0.253-1.431
Income Q1	1.72	0.235	0.703-4.200
Income Q2	0.18	0.090	0.023- 1.315
Income Q3	1.90	0.155	0.783- 4.633
Income Q4	0.67	0.475	0.223- 2.011
Race/Ethnicity			
White	1.21	0.678	0.497-2.934
African American	0.35	0.315	0.047-2.680
Hispanic	1.61	0.354	0.588-4.412
Asian or PI	0.74	0.772	0.098-5.606
Native American	No deaths	---	---
Other Race	No deaths	---	---
Predictors of Interest			
AKI	6.43	<0.001	2.668-15.492
DIC	19.78	<0.001	4.945- 79.096
Encephalopathy	7.90	<0.001	2.750-22.672
Hepatic Failure	26.52	<0.001	9.144-76.946
Infections	6.52	0.001	2.184-19.47
Respiratory Failure	19.04	<0.001	7.221- 50.206
TMA	13.41	0.030	1.295- 138.954

Abbreviations: AKI=acute kidney insufficiency; AOSD= Adult Onset Stills Disease; CCI= Charlson Comorbidity Index; CI= Confidence Interval; DIC= Disseminated intravascular coagulation, HLH= Hemophagocytic Lymphohistiocytosis; PI=Pacific Islander; Q=quartile; TMA=thrombotic microangiopathy

Univariable Analysis for In-hospital Death of AOSD Patients

Variables	Odds Ratio	P-value	95% CI
AKI	1.51	0.426	0.549-4.148
CCI	1.22	0.185	0.910-1.625
DIC	6.13	0.050	1.002-37.499
Encephalopathy	3.58	0.062	0.940-13.617
Hepatic Failure	7.16	0.014	1.487-34.479
HLH	2.24	0.175	0.699-7.191
Income Q2	0.18	0.064	0.029-1.105
Income Q3	2.08	0.201	0.678-6.361
Infection	3.72	0.012	1.332-10.402
Respiratory Failure	6.89	<0.001	2.353-20.168
TMA	14.05	0.022	1.463-135.008

Abbreviations: AKI=acute kidney insufficiency; AOSD= Adult Onset Stills Disease; CCI= Charlson Comorbidity Index; CI= Confidence Interval; DIC= Disseminated intravascular coagulation; HLH= Hemophagocytic Lymphohistiocytosis; Q=quartile; TMA= thrombotic microangiopathy

Multivariable Analysis for In-hospital Death of AOSD Patients

for predictors of in-hospital mortality in AOSD hospitalizations are shown in table 2. Multivariable analysis showed that DIC (OR 6.13; 95% C.I. 1.002-37.499), hepatic failure (OR 7.16; 95% C.I. 1.487-34.479), infection/pneumonia/sepsis (OR 3.72; 95% CI 1.332-10.402), respiratory failure (OR 6.89; 95% C.I. 2.353-20.168) and TMA (OR 14.05; 95% CI 1.463-135.008) were associated with higher odds of in-hospital death among AOSD hospitalization (table 3).

Conclusion: We found that HLH only occurred in 6.2% of AOSD inpatients. Inpatients with both AOSD and HLH had a higher rate of concurrent AKI, DIC, hepatic failure, infections, respiratory failure, and TMA. They were also younger, had a higher proportion of Hispanics, longer LOS, greater total hospital charges, and a 9% in-hospital mortality in contrast to 1.5% in those without HLH. Despite a large difference in mortality between the groups, HLH itself was not found to be an independent risk factor for in-hospital death. Multivariable analysis in AOSD inpatients showed DIC, hepatic failure, infection/pneumonia/sepsis, respiratory failure, and TMA to be associated with higher odds of death. This information can help clinicians by improving awareness of these life-threatening complications since early recognition and prompt management may improve outcomes.

Disclosure: F. Sami: None; **M. Manansala**: None; **S. Arora**: None; **A. Manadan**: None.

Abstract Number: 1144

Deucravacitinib in Plaque Psoriasis: Maintenance of Response over 3 Years

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Deucravacitinib, a first-in-class, oral, selective, allosteric tyrosine kinase 2 inhibitor, is approved in multiple countries for the treatment of adults with plaque psoriasis. Deucravacitinib was superior to placebo and apremilast in the global, 52-week, phase 3 POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751) trials in psoriasis. Deucravacitinib is being investigated in several immune-mediated diseases and has shown efficacy compared with placebo in phase 2 trials for SLE (NCT03252587) and PsA (NCT03881059). The POETYK long-term extension (LTE) trial (NCT04036435) showed that deucravacitinib maintained long-term efficacy through 2 years with no new safety signals. Here, we report clinical efficacy up to 3 years (148 weeks) in the POETYK LTE trial in a subset of patients who received continuous deucravacitinib from day 1 in the parent trials.

Table. PASI 75, PASI 90, and sPGA 0/1 response rates with continuous deucravacitinib in Week 16 (n=313) and Week 24 (n=336) PASI 75 responders[a]

	PASI 75 responders at week 16, % (95% CI, %)			PASI 75 responders at week 24, % (95% CI, %)		
Parameter	Week 16 (n = 777)	Week 52 (n = 277)	Week 148 (n = 277)	Week 24 (n = 305)	Week 52 (n = 305)	Week 148 (n = 305)
PASI 75	100 (NE–NE)	87.0 (NE–NE)	84.5 (79.8–89.2)	100 (NE–NE)	90.2 (NE–NE)	86.0 (81.6–90.3)
PASI 90	57.8 (NE–NE)	60.6 (NE–NE)	60.0 (53.9–66.1)	63.3 (NE–NE)	61.6 (NE–NE)	60.4 (54.6–66.3)
sPGA 0/1	84.1 (NE–NE)	70.8 (NE–NE)	62.8 (56.7–68.9)	83.0 (NE–NE)	74.1 (NE–NE)	64.5 (58.7–70.3)

[a]Response rate was reported using modified nonresponder imputation. The Clopper-Pearson method was used to calculate 95% CIs.
NE, nonestimable; PASI 75/90, ≥75%/90% reduction in Psoriasis Area and Severity Index; sPGA, static Physician's Global Assessment.

Methods: In POETYK PSO-1 and PSO-2, patients were randomized 1:2:1 to placebo, deucravacitinib 6 mg once daily (QD), or apremilast 30 mg twice daily. At week 52, patients could enter the POETYK LTE trial and receive open-label deucravacitinib 6 mg QD. Deucravacitinib efficacy through week 148 was evaluated in patients from pooled POETYK PSO-1 and PSO-2 populations who received continuous deucravacitinib from day 1, achieved ≥ 75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) at week 16 (primary endpoint) or week 24 (peak response), and enrolled in the POETYK LTE trial. Maintenance of response was assessed through data cutoff (June 15, 2022) and included PASI 75 and PASI 90 (≥ 90% reduction from baseline in PASI). Static Physician's Global Assessment (sPGA) score of 0 (clear) or 1 (almost clear) with a ≥ 2-point improvement from baseline was assessed.

Results: A total of 513 patients completed 52 weeks in the parent trials and received continuous deucravacitinib from day 1, including 313 (61.4%) patients (95% CI, 57.0–65.6) who achieved PASI 75 at week 16 and 336 (66.5%) patients (95% CI, 62.2–70.6) who achieved PASI 75 at week 24. Among these patients, PASI 75 response rates were maintained from week 52 to week 148 (**Table**). PASI 90 response rates were maintained in > 50% of patients from the start of the POETYK LTE trial (**Table**). Response rates for sPGA 0/1 were maintained from week 52 to week 148 (**Table**).

Conclusion: Clinical efficacy was maintained for up to 148 weeks with continuous deucravacitinib in most patients who were week 16 and week 24 PASI 75 responders from the parent trials and enrolled in the POETYK LTE trial. These findings further support the long-term use of once-daily oral deucravacitinib as an effective treatment for patients with psoriasis.

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Abstract Number: 1145

Human Cardiovascular Disease Model Provides Transcriptomic Evidence of Cardiovascular Risk Associated with Febuxostat

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SESSION INFORMATION
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Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is a chronic inflammatory arthritis that is undertreated and managed with the xanthine oxidase inhibitors febuxostat or allopurinol. Despite the United States Food and Drug Administration (FDA) mandating febuxostat carry its most prominent warning for serious side effects that include cardiovascular-related death, febuxostat is widely prescribed. A large, manufacturer-sponsored clinical trial (CARES) led to the febuxostat FDA warning label; however, a recent, large clinical trial (FAST) did not replicate these data in patients without pre-existing cardiovascular risk. Whether febuxostat increases cardiovascular risk remains an important question and to date there are few mechanistic studies designed to resolve this controversy.

Methods: We compared the transcriptomic signature of oral gout medications alongside 107 other clinical stage compounds, 33 of which are FDA labelled for increased cardiovascular risk, in an *in vitro* human primary cell-based cardiovascular disease model to clarify the potential risk of febuxostat.

Results: Febuxostat significantly modulated more signaling pathways associated with cell stress and cardiovascular risk than allopurinol or topiroxostat, gout medications not associated with increased cardiovascular risk. Moreover, these signaling pathways were commonly regulated by other drugs FDA labelled for cardiovascular risk. Lastly, these results were replicated with a febuxostat analog.

Conclusion: Together, these data support the FDA warning for febuxostat and suggest that cardiovascular risk associated with gout medications stems from chemical structure of the medication, itself, rather than the target, xanthine oxidase.

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Abstract Number: 1146

Gene X Environment Paradigm: Exemplified by Selected Cases of Autoinflammatory Diseases

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Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II
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Background/Purpose: The current scientific opinion holds that gene and environment (G X E) interactions contribute to certain human diseases. Systemic autoinflammatory diseases (SAIDs) are usually associated with genetic variations. Unlike classic monogenic disease (Huntington's disease), some genetic mutations associated with SAIDs are of low frequency and low penetrance. In other words, a small proportion of healthy people carry these mutations. Therefore, a gene of interest or candidate gene, genetic background, and environment are hypothesized to collectively cause disease. COVID19 is an environmental factor. Herein, we report a case series of SAID patients to support the above proposition.

Methods: In this retrospective single center study, a cohort of adult patients were enrolled and fulfilled the diagnostic criteria for certain SAIDs as confirmed by molecular analysis. After extensive negative workup for systemic autoimmune and related diseases, genetic testing of periodic fever syndrome 6-gene panel and an extended SAID gene panel were performed at Commercial Diagnostic Molecular Laboratories.

Results: Of the 6 Caucasian patients, there were 4 females and 2 males with a mean age of 46.5(26 to 76). These patients were essentially healthy prior and developed autoinflammatory features following COVID19 infection (4 cases) or vaccinations (2). They experienced recurrent symptoms such as fever, rash, arthralgia and gastrointestinal symptoms among others. All patients were identified to carry *NOD2* mutations, and 3 of them carried concurrent mutations in other SAID genes, such as MEFV, NLRP3, NLRP12, TNFRSF1A, and UBA1(**Table 1** to be presented). Two of the *NOD2* mutations are rare and other mutations are of low frequency/penetrance and are known to increase susceptibility to certain SAIDs, such as Yao syndrome (NOD2), Familial Mediterranean fever (MEFV E148Q, R408Q, P369S), NLRP3-autoinflammatory disease (NLRP3 Q703K), and NLRP12-autoinflammatory disease (NLRP12 F402L). UBA1 mutation is associated with VEXAS syndrome. These SAIDs associated with the low penetrance variants are currently regarded in the new category of Genetically Transitional Disease, where mutation is necessary but not sufficient to cause disease. Genetic background refers to all other related genes that may interact with the gene of interest to potentially influence specific phenotype in concert with environment. Since all our patients carry *NOD2* variants as the denominator, the *NOD2* is considered as the gene of interest, and other SAID gene variants may be entertained as genetic background. Although most *NOD2* variants are low penetrants in this study, their penetrance could be upwardly influenced by genetic background. While these patients carry germline mutations, their disease onsets started following the COVID19 infection or vaccination. These data strongly suggest that candidate genes, genetic background and environment together may contribute to these SAIDs. Our data may also explain some patients with Long COVID Syndrome.

Conclusion: Our study supports the interactive role of genes and environment in the pathogenesis of some autoinflammatory diseases. Further study of large cohort patients is warranted.

Disclosure: Q. Yao: None; **P. Gorevic**: None.

Abstract Number: 1147

Blood-Based Biomarkers of Inflammation and Tissue Remodeling Can Discriminate Between Rheumatoid Arthritis, Psoriasis, and Psoriatic Arthritis and Are Associated with Hand Function

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SESSION INFORMATION

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Background/Purpose: Inflammatory musculoskeletal diseases including rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are characterized by physical function impairment due to progressive inflammatory and structural changes. This becomes apparent even in the early disease stages before arthritis onset, such as in psoriasis (PsO). Chronic inflammation triggers an accelerated remodeling of the extracellular matrix (ECM), resulting in the release of specific degradation products of proinflammatory and collagen molecules that can be measured in blood. In this study, we explored whether levels of ECM biomarkers differ among patients with RA, PsA and PsO, and controls. In addition, we investigated the association between biomarkers and functional impairment by measures of hand function.

Methods: This is a secondary analysis of serum samples obtained from participants of three hand function studies with identical study conditions for sample collection and assessments (FAU ethics approval #125_16B, #357_20B). Serum samples from patients with RA, PsA, and PsO, and controls were obtained in the outpatient clinic of the Rheumatology and Dermatology Department, Universitätsklinikum Erlangen, Germany. Serum ECM catabolic markers (C1M, C2M, C3M, C4M, PRO-C4, C6M, ARG), formation markers (PRO-C1, PRO-C3, PRO-C6), and inflammation markers (VICM) were measured by immunoassay (Nordic Bioscience, Herlev, Denmark). Fine motor skills were assessed by the Moberg-Picking-Up Test (MPUT) and isometric grip strength was measured using a dynamometer. The Michigan Hand Questionnaire (MHQ) was used to evaluate patient-perceived hand function. The best out of two and three attempts was used for the analysis of MPUT and grip strength, respectively. Linear regression models with robust standard errors were used to compare biomarker levels between groups, adjusting for age and gender. Correlations between biomarker data and hand function were assessed by Spearman's rank correlation (ρ) and p-values were adjusted by false discovery rate method.

Results: 85 patients with RA, 115 with PsA, 102 with PsO and 110 controls (mean age, years: 58.4, 53.7, 45.8, 46.6; % male: 35.3, 49.6, 60.8, 45.0, respectively) were included. VICM levels were significantly higher in RA, PsA, and PsO than in controls (Figure 1, $p < 0.0001$). PsA and PsO showed significantly higher C4M levels compared to RA and controls, while C6M was lower in patients with RA and PsA than in controls (Figure 1, $p < 0.001$). C1M presented higher levels in PsO

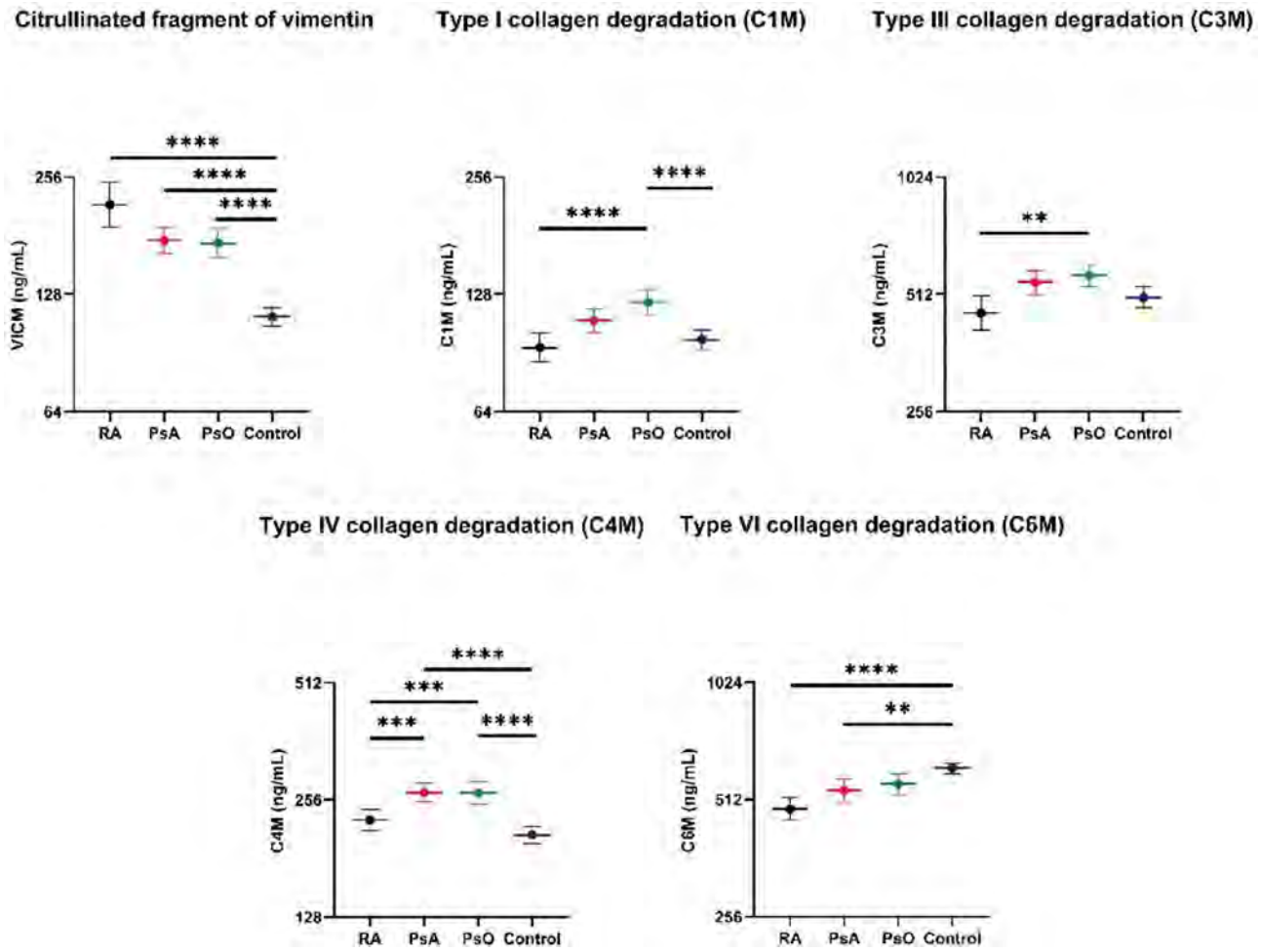

Figure 1. ECM biomarkers in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and psoriasis (PsO), and controls. Data is shown as mean ± 95% confidential intervals.Linear regression models using robust standard errors were performed to compare biomarker levels within the groups with age and gender as covariates. P-values were adjusted by Holm correction and significance threshold was set at 0.004 considering that 12 biomarkers were analyzed. Significance is shown as ** p< 0.004, ***p< 0.001 and ****p<0.0001.

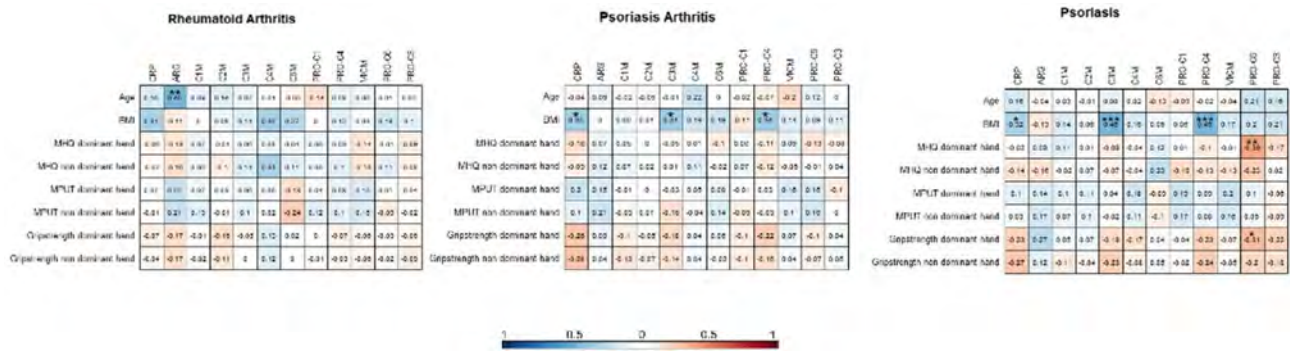

Figure 2. Spearman's correlations between serological metabolites and clinical scores were performed. Spearman's rho (ρ) is shown. The significance of correlations are shown as * p< 0.05, **p< 0.01, and ***p< 0.001. Abbreviations: BMI, body mass index; MHQ, Michigan Hand Questionnaire; MPUT, Moberg Picking-Up Test; CRP, C-reactive protein; ARG, aggrecan ADAMTS degradation; C1M, MMP-2/9/13-degraded type I collagen; C2M, MMP (multiple) -degraded type II collagen; C3M, MMP-9-degraded type III collagen; C4M, MMP (multiple)-degraded type IV collagen; C6M, MMP (multiple)-degraded type IV collagen; PRO-C1, Type I collagen N-terminal propeptide; PRO-C4, Type IV 7S domain collagen; VICM, citrullinated and MMP-degraded vimentin; PRO-C6, Type VI collagen, alpha-3 chain, C5 domain; PRO-C3, type II collagen N-terminal propeptide.

compared to controls, and together with C3M higher levels than RA (Figure 1, $p< 0.004$). The remaining biomarkers did not show any significant differences. Weak correlations were observed between the biomarkers and the hand function scores (all $\rho<\pm0.2$-0.3, Figure 2), while only PRO-C6 showed a significant negative correlation with MHQ ($\rho=-0.39$, $p< 0.01$) and grip strength ($\rho=-0.31$, $p< 0.05$) in patients with PsO.

Conclusion: Patients with RA, PsA, and PsO showed significant alterations in ECM remodeling biomarkers and specially PsA and PsO had higher levels of inflammatory biomarkers compared to RA and controls. Furthermore, predominantly in PsO, ECM formation biomarkers were associated with hand function impairment.

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Abstract Number: 1148

A Comparative Study of Clinical Phenotype in Relation to NOD2 Sub-genotypes in Yao Syndrome

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Background/Purpose: Yao syndrome (YAOS, OMIM 617321) is formerly designated NOD2-associated autoinflammatory disease. A spectrum of NOD2 mutations have been associated with this disease. Most patients carry compound variants and a minority carry monoallelic variant. This study aimed to compare clinical manifestations between patients with certain NOD2 sub-genotypes.

Methods: A single center retrospective study of a cohort of adult patients with YAOS was conducted.All patients underwent genetic testing for periodic fever syndrome gene panel. YAOS was diagnosed based on our published criteria, i.e., the presence of characteristic clinical phenotype and genotype with exclusion of other related diseases. This study was approved by the Institutional Review Board of Stony Brook University.

Results: There were a total of 47 patients who carried NOD2 mutations, and nearly all were Caucasian with female 74%. Mean age at diagnosis was 38±23 years and disease duration 16±25 years. All patients possessed complete or incomplete constellations of autoinflammatory features, such as recurrent fever, rash, polyarthralgia, myalgia, gastrointestinal symptoms and chest pain among others. Approximately 50% of patients had elevated acute phase reactants. Based on our prior publications and experience, most patients with YAOS carry the NOD2 variant, IVS8+158 and another concurrent NOD2 variant, such as R702W or 1007fs. In this study, 47 patients were divided into two groups:patients with carriage of NOD2 IVS8+158

Table 1. Clinical comparison of patients with monoallelic vs compound variants

Table 1. Clinical comparison of patients with monoallelic vs compound variants

Variable	Level	Total (N=47)	Group 1 (N=30, 63.8%)	Group 2 (N=17, 36.2%)	P-value*
Age at diagnosis (year)		38±23	43±19	35±22	0.2314
Disease duration at diagnosis (year)		16±25	22±31	11±8	0.2537
Sex	Female	35 (74%)	23 (77%)	12 (71%)	0.6461
	Male	12 (26%)	7 (23%)	5 (29%)	
Race	Asian	1 (2%)	1 (3%)	0 (0%)	1.0000
	Caucasian	46 (98%)	29 (97%)	17 (100%)	
Fatigue	Yes	42 (89%)	26 (87%)	16 (94%)	0.6491
Night sweats	Yes	13 (28%)	10 (33%)	3 (18%)	0.3147
Headaches	Yes	21 (45%)	13 (43%)	8 (47%)	0.8050
Fever	Yes	35 (74%)	23 (77%)	12 (71%)	0.6461
Skin rash	Yes	45 (96%)	29 (97%)	16 (94%)	1.0000
Arthritis	Yes	47 (100%)	30 (100%)	17 (100%)	-
Lower extremity swelling	Yes	26 (55%)	18 (60%)	8 (47%)	0.3912
Myalgia	Yes	20 (43%)	12 (40%)	8 (47%)	0.6381
Oral ulcer	Yes	18 (38%)	13 (43%)	5 (29%)	0.3455
Gastrointestinal symptoms	Yes	39 (83%)	24 (80%)	15 (88%)	0.6927
Pain	Yes	33 (70%)	20 (67%)	13 (76%)	0.5284
Diarrhea	Yes	29 (62%)	19 (63%)	10 (59%)	0.7599
Sicca	Yes	28 (60%)	18 (60%)	10 (59%)	0.9371
Eyelid swelling	Yes	21 (45%)	13 (43%)	8 (47%)	0.8050
Hearing loss/decrease	Yes	2 (4%)	2 (7%)	0 (0%)	0.5297
Chest pain	Yes	11 (23%)	7 (23%)	4 (24%)	1.0000
Pleuritis	Yes	3 (6%)	3 (10%)	0 (0%)	0.2941
Pericarditis	Yes	4 (9%)	3 (10%)	1 (6%)	1.0000
Asthma	Yes	8 (17%)	4 (13%)	4 (24%)	0.4372
Proteinuria/hematuria	Yes	4 (9%)	4 (13%)	0 (0%)	0.2729
Raised ESR/CRP/ferritin	Yes	24 (51%)	16 (53%)	8 (47%)	0.6793
Drug allergy	Yes	31 (66%)	21 (70%)	10 (59%)	0.4372
Food allergy/intolerance	Yes	14 (30%)	8 (27%)	6 (35%)	0.5343
Allergist evaluation	Yes	19 (40%)	12 (40%)	7 (41%)	0.9371

*: For continuous variables, p-values were based on Wilcoxon's rank sum test; for categorical variables, p-values were based on Monte Carlo simulation from a Chi-squared test.
Note: median+/-IQR were reported for continuous variables; column percentages were reported for categorical variables.

only (N=30, 63.8%, Group1) and those with compound variants, IVS8+158/R702W or 1007fs (N=17, 36.2%, Group 2). We asked whether there would be differences of clinical manifestations between the two groups. Our study has found no statistically significant differences (**Table 1**). This study result was in agreement with our clinical observation that patients had similar clinical phenotype regardless of the sub-genotypes. Because these NOD2 variants are of low penetrance, YAOS has been recently reclassified as the new category of genetically transitional disease, where mutation is necessary but not sufficient to cause disease. The pathogenesis of YAOS may involve the interaction of the candidate gene, genetic background and environment.

Conclusion: Our study suggests that clinical phenotype is similar between YAOS patients with NOD2-subgenotypes. These variants serve as useful diagnostic markers for the disease.

References

Yao Q, et al. Genetically transitional disease: a new concept in genomic medicine. Trends Genet 2023; 39(2):98-108 Yao Q, Shen B. A Systematic Analysis of Treatment and Outcomes of NOD2-Associated Autoinflammatory Disease. Am J Med. 2017;130(3):365 e13-365 e18. Navetta-Modroc B, et al.A novel nucleotide-binding oligomerization domain 2 genetic marker for Yao syndrome. J Am Acad Dermatol. 2023 Feb 28:S0190-9622(23)00282-7.

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Abstract Number: 1149

Tumor Necrosis Factor Inhibitors as First Line Steroid-Sparing Therapy for Neurosarcoidosis: A Case Series

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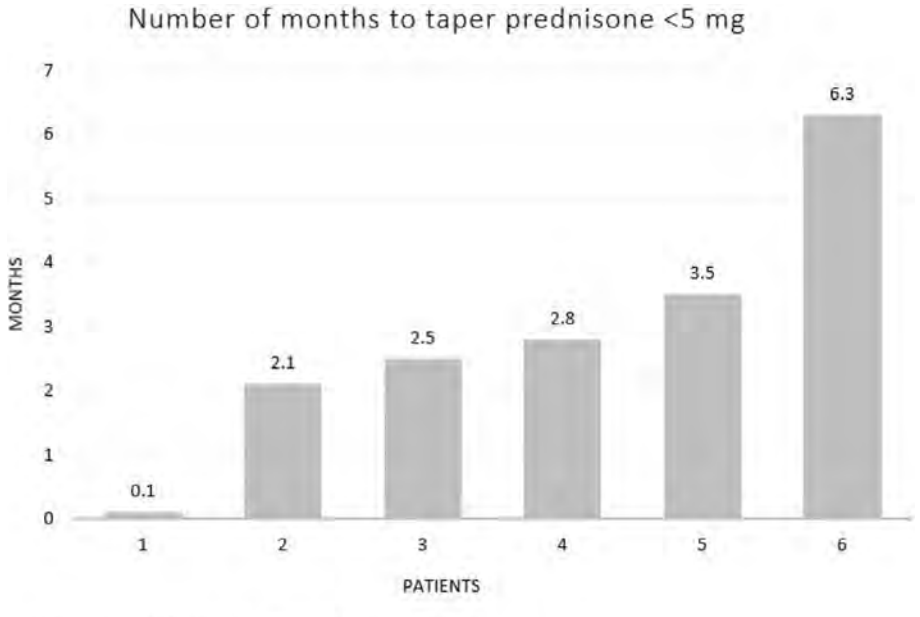
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Sarcoidosis is a systemic inflammatory disease characterized by non-necrotizing granuloma formation affecting the lung, lymphatics, heart, skin, eye, kidney, and, in neurosarcoidosis, the nervous system. Neurosarcoidosis has varied manifestations, including central and peripheral neuropathies, parenchymal disease, meningitis, and myelopathy. Despite the complications of chronic steroid use, there is currently no consensus on preferred steroid-sparing treatments for



neurosarcoidosis.We aim to describe the clinical course of patients treated with tumor necrosis factor (TNF) inhibitors as the first steroid-sparing agent.

Methods: This is a case series of 8 adults with probable or definite neurosarcoidosis based on Neurosarcoid Consortium Consensus Group criteria. Patients were seen between January 1, 2010 and December 31, 2022 in our rheumatology or neurology clinic, had at least one follow up visit, and received TNF inhibitor therapy as first steroid-sparing agent. Data collected through chart review included demographics, disease characteristics, treatment course, and treatment response.

Results: Of our 8 patients, most were male (n=6) and the median age at diagnosis was 55 (IQR 23). Half were definite diagnoses (n=4), confirmed by brain biopsy. The most commonly involved neurologic tissues were parenchymal (n=7), meningeal (n=4), and spinal (n=3). Outside of neurologic involvement, most patients had lung involvement (n=6) and some had musculoskeletal (n=2) involvement. Based on available cerebrospinal fluid studies, most had elevated protein (n=6), elevated white blood cell counts (n=6), and negative angiotensin converting enzyme (n=7), IgG (n=8), and oligoclonal bands (n=8). Most patients were started on infliximab (n=7), initiated a median of 5.7 months (IQR 8.2) after sarcoidosis diagnosis, and were co-treated with methotrexate (n=7). Most patients were able to wean to < 5 mg of prednisone (n=6) in a median of 2.6 months (IQR 1.3). Most patients had one or fewer relapses (n=7) and achieved partial or complete clinical remission (n=7). A minority of patients had adverse reactions, including pulmonary infection (n=3) and skin infections (n=1); 1 patient died 12 years after diagnosis.

Conclusion: Our study provides further evidence that TNF inhibitors can be used effectively as first-line steroid sparing therapy for neurosarcoidosis. Among our neurosarcoidosis patients treated with TNF inhibitors, most were able to wean from steroids within 6 months and had significant resolution of their symptoms.

Disclosure: T. Morrison: None; **T. Lakusta-Wong**: None; **C. Roy-Hewitson**: None; **J. Gosselin**: None; **A. Nevares**: None.

Abstract Number: 1150

A Comparative Study of Cryofibrinogenemia Before and After COVID-19 Era

Carmen Lasa[1], Maria Enriqueta Peiró[2], Juan Irure-Ventura[2], Amparo Sánchez[2], Adrian Martin-Gutierrez[2], carmen secada[2], monica renuncio garcia[2], Marcos Lopez-Hoyos[3] and Ricardo Blanco[4], [1]Hospital Universitario Marqués de Valdecilla, IDIVAL., La Cavada, Spain, [2]Hospital Universitario Marqués de Valdecilla, Santander, Spain, [3]Marques de Valdecilla University Hospital-IDIVAL, Santander, Spain, [4]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain

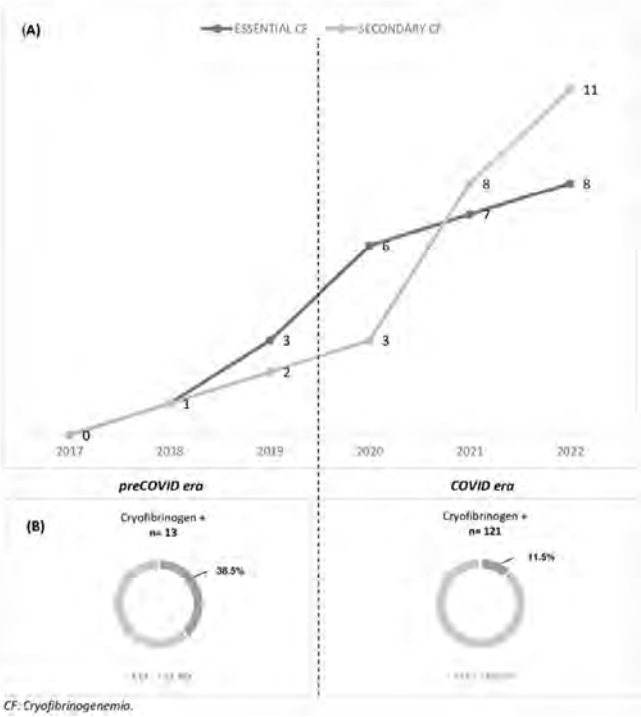
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Cryofibrinogenemia (CF) is an under-recognized syndrome due to the lack of definitive criteria and the rarity of disease. CF may be primary (essential) or secondary to autoimmune, neoplastic or infections conditions. Skin manifestations, mainly ulceration, are the most common and may be a pseudovasculitic syndrome. During COVID-19 era the number of cases with skin lesions get increased. Further studies are needed to characterize this association between CF and SARS-CoV-2.

Table. Number of cases and clinical features of Cryofibrinogenemia (CF) in preCOVID-19 era and COVID-19 era.

	PRECOVID-19 (n= 5)	COVID-19 (n=14)	p
Cryofibrinogen test; positive/performed, (%positive) (N=134)	5/13 (38.5)	14/121 (11.5)	0.008
Age, years, mean±SD	60.6±11.2	43.6±21.0	0.195
Sex			
Male, n (%)	2 (40)	9 (64.3)	0.345
Female, n (%)	3 (60)	5 (35.7)	
Male-to-female ratio	0.7:1	1.8:1	
CF Essential, n (%)	3 (60)	5 (35.7)	0.345
CF Secondary, n (%)	2 (40)	9 (64.3)	0.345
COVID19, n (%)	0	3 (33.3)	0.239
Connectivopathy, n (%)	2 (100)	3 (33.3)	0.418
Vasculitis, n (%)	0	3 (33.3)	0.259
Clinical expression			
Cutaneous manifestations			
Location			
Hands	3 (60)	7 (50)	0.701
Feet	1 (20)	2 (14.3)	0.764
Hands and feet	1 (20)	5 (35.7)	0.516
Clinical pattern			
Purpuric macules, n (%)	4 (80)	6 (42.9)	0.153
Raynaud, n (%)	2 (40)	3 (31.4)	0.418
Distal ulceration, n (%)	1 (20)	6 (42.9)	0.363
Others, n (%)	1 (20)	2 (14.3)	0.764
General symptoms, n (%)	1 (20)	1 (7)	0.383
Gastrointestinal symptoms, n (%)	1 (20)	3 (21.4)	0.659
Rheumatologycal symtoms, n (%)	2 (40)	2 (14.3)	0.486
Treatment			
Antiaggregant treatment, n (%)	4 (80)	4 (28.6)	0.131
Corticosteroid treatment, n (%)	3 (60)	4 (28.6)	0.577
Other treatments, n (%)	3 (60)	4 (28.6)	NA

Figure. (A) Number of cases of essential CF vs secondary CF in preCOVID-19 and COVID-19 era. **(B)** Proportion of positive cryofibrinogen in both eras.



CF: Cryofibrinogenemia.

Methods: Observational single-center study in northern Spain University Hospital of 134 patients with at least one positive cryofibrinogen determination, between January 2017 and March 2020 (preCOVID era) and March 2020 and December 2022 (COVID era). CF diagnosis was confirmed accordingly to reported criteria**.**Clinical conditions, laboratory parameters, including immunological and serological analysis were collected from all patients. Blood was collected in citrated tubes for cryofibrinogen detection. Stadistical analysis was performed using SPSS software. Quantitative variables were expressed as mean±SD. Qualitative variables were compared using the Fisher's exact test or the chi-squared test, according to sample size. Quantitative variables were compared using the student's *t*.

Results: CF was confirmed in 19/134 (14.2%) patients with at least one positive cryofibrinogen test determination (preCOVID-19 era=5; COVID-19 era=14). Patients of COVID-19 era were more frequently male (64.3% vs 40%) and younger (43.6 vs 60.6). Main features are shown in **Table 1**. We observed a change in the distribution cases. In preCOVID-19 era most of cases were essential CF (60%) and in COVID-19 era most of them were secondary ones (64.3%). The 33.3% of secondary CF were mainly due to COVID-19. Cutaneous manifestations were similar in both subgroups, especially as purpuric macules (perniosis-like) in acral distributions and no significant association was noted between both eras. Antiaggregant drugs and corticosteroids were used more frequently in preCOVID-19 era. The comparative incidence after and before COVID-19 is shown in **Figure 1.** From patients with positive cryofibrinogen test, a greater proportion in preCOVID-19 had a CF.

Conclusion: CF is a rare disorder with a low prevalence. This study showed the change in the trend of CF subtypes, probably due to the influence of the COVID-19 infection. In COVID-19 era the number of positive cryofibrinogen test had envolved due to SARS-CoV2 infection, CF cases were not increased. Clinical expression of the disease has not changed in both groups.

Disclosure: C. Lasa: None; **M. Peiró**: None; **J. Irure-Ventura**: None; **A. Sánchez**: None; **A. Martin-Gutierrez**: None; **c. secada**: None; **m. renuncio garcia**: None; **M. Lopez-Hoyos**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6.

Abstract Number: 1151

Revised IWOS Criteria for Ocular Sarcoidosis: A 2019 Review of the 2009 Criteria in a Study of 384 Patients from a Single University Hospital

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

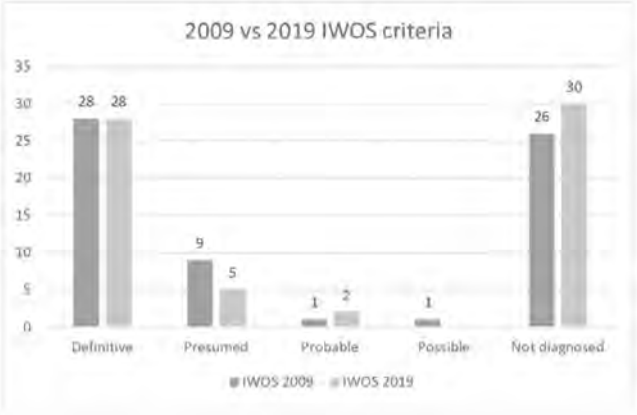
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Sarcoidosis is a systemic inflammatory disorder which involves many organs, including eyes. Uveitis and optic neuropathy are the main manifestations. International Workshop on Ocular Sarcoidosis (IWOS) criteria for diagnosis of ocular sarcoidosis (OS) were first published in 2009 and revised in 2019. (question-based survey and panel discussion). IWOS criteria is a remarkable tool to relate uveitis to sarcoidosis, especially when ocular is the first manifestation in the systemic disease. Due to the consequences of OS, identify and initiate appropriate therapy is essential.

Figure. Results of 2009 and 2019 IWOS criteria on a defined population.



Methods: We studied a large cohort (n=384) of all consecutive patients diagnosed with sarcoidosis from January 1, 1999, to December 31, 2019. Finally, 344 patients were included according to the ATS/ERS/WASOG criteria. First (2009) and revised (2019) IWOS criteria were applied to patients diagnosed with Sarcoidosis and ocular symptoms and the results were compared in both groups for our population. Concordance between 2009 and 2019 IWOS criteria was evaluated by calculating Cohen´s kappa coefficient.

Results: 65 (51% men) of 344 patients had ocular involvement (18.9%), mean age 56.7±16.3 years. As for nationality, 92.3% were Spaniard and 7.7% were South American. A positive biopsy for sarcoidosis was obtained in 75.4% (n=49) and a negative biopsy in 6.2% (n=4). There was no statistically significative difference between diagnostic groups for IWOS 2009/IWOS 2019 in age (p=0.738/p=0.495), sex (p=0.534/p=0.459) nor nationality (p=0.529/p=0.393). When applied 2009 IWOS criteria, 60% (39 patients) met any of the diagnostic categories (43.1% *Definitive*, 13.8% *Presumed*, 1.5% *Probable*, 1.5% *Possible*). When 2019 IWOS criteria was applied, 53.8% (35 patients) met any of the new diagnostic categories (43.1% *Definitive*, 7.7% *Presumed*, 3.1% *Probable*). Sensitivity for IWOS 2009 was 0.6 and for IWOS 2019 was 0.53. There was statistically significative concordance between 2009 and 2019 IWOS criteria (p< 0.0001) with a strong consistency level (kappa = 0.824). When analyzing IWOS categories separately, we found total concordance in the *Definitive* category. *Probable* and *Possible* categories in 2009 criteria have been merged in only probable in 2019 criteria and there is a total concordance when comparing both. *Presumed* category represent the bigger change in the revised criteria. We found statistically significative concordance (p=0.000008) with a moderate consistency level (kappa = 0,524).

Conclusion: The revised 2019 IWOS criteria is less sensitive in our population; however, the main difference is in the category *Presumed*: the requirement of at least 2 intraocular signs of uveitis led to a change of 9 patients (13,8%) in 2009 IWOS down to 5 (7.7%) in 2019. In our population IWOS criteria is still has a low sensitivity.

Disclosure: C. Lasa: None; **J. Gaitán**: None; **L. Sanchez-Bilbao**: None; **D. Martínez-Lopez**: None; **I. Gonzalez-Mazon**: None; **J. Martin-Varillas**: None; **R. Demetrio**: None; **R. Fernandez-Ramon**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6.

Abstract Number: 1152

Relation Between Positive MPO-ANCA Antibodies And: Associated Diseases, Anca-associated Vasculitis Specificty, Severity and Prognosis. Study from a Single University Hospital

Fabricio Benavides[1], Monica Renuncio-García[1], Salma Al Fazazi[2], clara escagedo Cagigas[1], maria rodriguez Vidriales[1], Vanesa Calvo Río[3], Juan Irure-Ventura[1], luis martin penagos[4], Marcos Lopez-Hoyos[5] and Ricardo Blanco[6], [1]Hospital Universitario Marqués de Valdecilla, Santander, Spain, [2]Hospital Universitario Puerta Del Mar, Cádiz, Spain, [3]Valdecilla Hospital, Santander, Spain, [4]Division of Nephrology, Immunopathology Group, Hospital Universitario Marqués de Valdecilla-DIVAL, Santander, Spain, [5]Marques de Valdecilla University Hospital-IDIVAL, Santander, Spain, [6]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain

SESSION INFORMATION

Session Date: Monday, November 13, 2023

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Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: ANCA-associated vasculitis (AAV) is a group of pathologies characterized by necrotizing inflammation that mainly affects small and medium-sized vessels. Serum anti-neutrophil cytoplasmic antibodies (ANCA), mainly anti-myeloperoxidase (anti-MPO) and anti-proteinase 3, levels may correlate to severity and prognosis of the disease. Our objective was to identify the diseases associated with positive anti-MPO antibodies detected in a single university hospital and

Group	Disease	Number (n)	Frequency (%)
Vasculitis (n=77)	Microscopic polyangiitis	34	33.7
	Granulomatosis with polyangiitis	10	8.9
	Eosinophilic granulomatosis with polyangiitis	9	9.9
	Pauci-immune glomerulonephritis	13	12.9
	Unclassified vasculitis	11	10.9
No vasculitis (n=24)	Ulcerative colitis	4	3.9
	Chron's disease	1	0.9
	Rheumatoid arthritis	2	1.9
	Sjogren's syndrome	1	0.9
	Autoimmune hepatitis	1	0.9
	Intestinal ischemia	2	1.9
	Psoriasis	1	0.9
	Lung fibrosis	1	0.9
	Pleural effusion	1	0.9
	Silicosis	1	0.9
	Infection	3	2.9
	Neoplasm	5	4.9
	Pachymeningitis	1	0.9

TABLE 1. Diseases associated with positive anti-MPO antibodies (n=101).

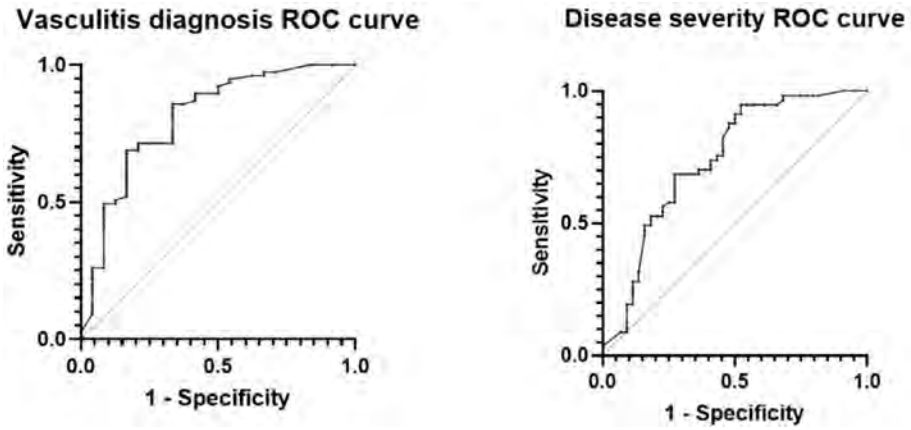

FIGURE 1. Receiver Operating Characteristic (ROC) plots for AAV and positive MPO-antibodies (AUC=0.8084) and disease severity at diagnosis (AUC=0.7160).

attempt to establish whether there is a cut-off point that correlates anti-MPO antibody levels with disease severity and prognosis.

Methods: Table 1 summarizes the frequency of positive anti-MPO antibodies, using laboratory established cut-off value, in different diseases based on a retrospective investigation of 101 positive anti-MPO antibody patients. Then, anti-MPO specificity to vasculitis was evaluated. Furthermore, data of renal disease (hematuria and/or proteinuria) and pulmonary involvement (hemoptysis, asthma and/or respiratory insufficiency) were collected at vasculitis diagnosis, as well as whether the illness progressed to the stage of requiring dialysis, transplantation, or mortality.

Results: For anti-MPO antibodies with a diagnosis of vasculitis (n=77), an area under the curve (AUC) was calculated (AUC=0.8084), and a cut-off point of 41.5 IU/ml was determined (**Figure 1**). When the analysis was restricted to exclusively microscopic polyangiitis diagnoses (n=34), the cut-off point was 36.5 IU/ml with an AUC of 0.6435. There were significant differences in anti-MPO levels between patients with renal or pulmonary dysfunction (n=65) versus those without them (n=36) (p=0.0003), and a cut-off threshold of 60 IU/ml was established. Finally, after evaluating the illness's prognosis, an AUC= 0.5546 was found, being no significant differences between those patients who had a worse disease progression (n=19) and those who did not (n=82) (p=0.4643).

Conclusion: Anti-MPO levels at the moment of vasculitis diagnosis are related with disease severity but not with disease outcome.

Disclosure: F. Benavides: None; **M. Renuncio-García**: None; **S. Al Fazazi**: None; **c. escagedo Cagigas**: None; **m. rodriguez Vidriales**: None; **V. Calvo Río**: None; **J. Irure-Ventura**: None; **l. martin penagos**: None; **M. Lopez-Hoyos**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6.

Abstract Number: 1153

Unmasking SAPHO: A Case Series Revealing the Clinical Spectrum and Treatment Approaches

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SESSION INFORMATION

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Background/Purpose: SAPHO (synovitis, acne, pustulosis, hyperostosis, and osteitis) is a relatively rare and often underdiagnosed inflammatory disorder. Its diagnosis can be challenging due to its wide range of osteoarticular and cutaneous manifestations. Managing SAPHO syndrome often necessitates a multidisciplinary approach, considering its diverse manifestations across multiple systems. Given the rarity of SAPHO syndrome, treatment approaches are primarily informed by observational studies and case reports. In this study, we present a series of five patients diagnosed with SAPHO syndrome and highlight the distribution of lesions and their response to various therapeutic agents.

Methods: In our retrospective single-center study, we examined SAPHO patients under rheumatology care from 2018 to 2023. We screened patients aged 18 or older using specific ICD-10 codes related to sacroiliitis, sternoclavicular joint pain, inflammatory spondylopathy, inflammatory arthritis, acne vulgaris, hidradenitis suppurativa, pustulosis, palmar pustulosis, and palmoplantar pustulosis. Patients with alternate diagnoses or lost to follow-up were excluded. Our analysis identified a cohort of five SAPHO patients and thoroughly characterized their articular and dermatologic manifestations. Additionally, we evaluated the treatment responses in these patients.

Results: We conducted a study on five patients (four female, one male) with SAPHO syndrome, with a mean age of 49 years (range 28-68). The average follow-up period was 56 months (range 21-130). Among the patients, three (60%) exhibited sternoclavicular joint involvement, while one (20%) had sacroiliitis. Peripheral joint involvement was reported in two patients (40%). Acne was present in three patients (60%) in the arms and legs, while one patient (20%) had hidradenitis suppurativa. One patient (20%) had comorbid Crohn's disease. All five patients (100%) were treated with methotrexate, with three patients (60%) also receiving adalimumab and one patient (20%) receiving infliximab. Four out of five patients (80%) showed improvement in bone lesions with methotrexate. Skin lesions improved in two patients (40%) with methotrexate and in two

Age/Sex/ Follow up	Bone Involvement	Skin lesions	Inflammatory Bowel disease	Treatment	Response to treatment	
					Bone lesions	Skin lesions
68/F/58 months	Knees, Feet	Hidradenitis suppurativa in the right axilla and groin	N/A	Methotrexate Adalimumab Infliximab	Improved on Adalimumab	Worsened on MTX and Adalimumab. Improved on Infliximab
54/F/26 months	Sternoclavicular Involvement	Acne in lower legs	N/A	Methotrexate	Improved on Methotrexate	Improved on Methotrexate
28/F/21 months	Lower back pain (Sacroiliitis)	Acne in arms and legs	N/A	Methotrexate Adalimumab	Improved on Methotrexate	Improved on Adalimumab
68/M/130 months	Sternoclavicular Involvement, Knees	Acne in lower legs	N/A	Methotrexate	Improved on Methotrexate	Improved on Methotrexate
29/F/47 months	Sternoclavicular Involvement	Negative	Present	Methotrexate Adalimumab	Improved on Methotrexate	Improved on Adalimumab

A cumulative table highlighting the distribution of lesions and their response to various therapeutic agents.

patients (40%) with adalimumab. In one patient, infliximab was initiated when adalimumab failed to improve the skin lesions, resulting in improvement. Three patients (60%) required treatment with two or more agents.

Conclusion: In our study, the most frequent involvement observed was in the sternoclavicular joints, followed by peripheral joints and the lower back. Acne was more commonly reported than hidradenitis suppurativa. We found that bone lesions showed favorable responses to treatment with methotrexate, while a significant proportion of skin lesions also demonstrated positive results. Adalimumab was effective in treating skin lesions, except in one case where infliximab proved to be more effective. It is important to note that the lack of validated response criteria specific to SAPHO syndrome currently hinders the objective assessment of therapeutic response. Further research is needed to develop better methods for evaluating the response to various treatment modalities in SAPHO patients.

Disclosure: M. Sondhi: None; **W. Maqsood**: None; **S. Umer**: None.

Abstract Number: 1154

Clinical Presentation of IgG4-Related Disease. Single Referral Hospital Experience and Literature Review

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

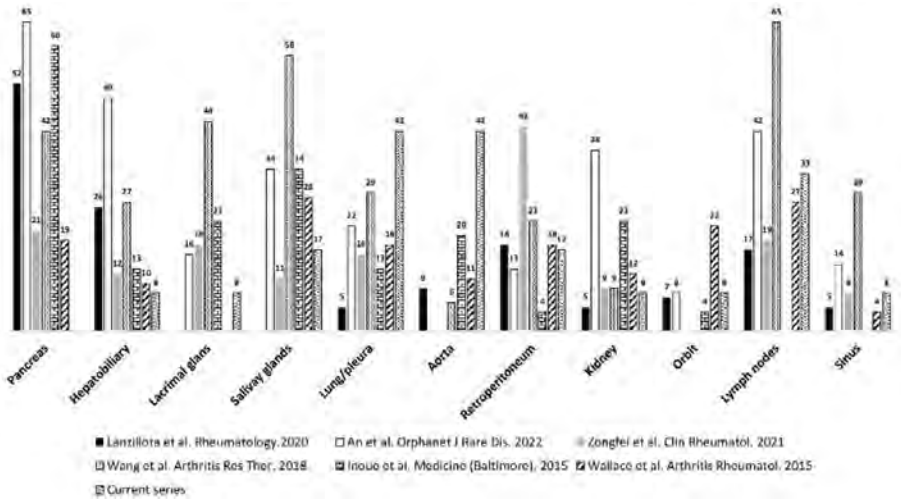
Background/Purpose: IgG4-related disease (IgG4-RD) is an inflammatory and fibrosing entity with very heterogeneous clinical manifestations. It was recognized as a new disease entity only 12 years ago. Its pathogenesis remains unknown, clinical features are heterogeneous and unspecific, and recently released classification criteria are invaluable in early recognition

TABLE. Main features of the patients with IgG4-RD in series of more than 100 patients and in current series

Reference	Cases	Sex Female (F)/ Male (M)	Age, median [IQR] or mean±SD	Diagnosis criteria	Number of organs affected	Level of serum IgG4 (mg/dL), median [IQR]
Lanzillotta et al. Rheumatology 2020	131	F (n=36), M (n=95)	62 [53-70]	-Umehara: possible (46%), probable (2%), definitive (52%)	-1 organ (26%) -More of 1 organ (74%)	224 [115-382]
Arvel et al. Orphanet J Rare Dis 2022	127	F (n=35), M (n=92)	63 [55-69]	-Umehara: possible (82.6%), probable (2.3%), definitive (11.8%)	-1 organ (20%) -2-4 organs (66%) -More of 5 organs (9%)	980 [360-1520]
Zongke et al. Clin Rheumatol 2021	102	F (n=25), M (n=77)	62 [54.1-65.8]	-Okazaki (100%)	Median [IQR]: 2 [1-3]	399 [199-776]
Wang et al. Arthritis Res Ther 2015	215	F (n=67), M (n=148)	54 [46-62]	-Umehara: possible (47.9%), probable (4.7%), definitive (47.4%)	-1-2 organs (36%) -3-4 organs (47%) -5 or more organs (17%)	896 [350-1880]
Inoue et al. Medicine (Baltimore) 2015	235	F (n=169), M(n=46)	67	-Symptoms+laboratory+image/ Compatible histology (100%)	-1 organ (41%) -2 or more organs (59%)	470 [ND]
Wallace et al. Arthritis Rheumatol 2015	125	F (n=49) M (n=76)	50.3±14.9	- Symptoms+laboratory+image/ Compatible histology (100%)	-1 organ (38%) -2 organs (24%) -3 or more organs (38%)	ND
Current series	12	F (n=8), M (n=4)	61 [54.7-76]	-Okazaki: 50% -Umehara: possible (25%), probable (17%), definitive (8%) -ACR/EULAR 2020 (1%) -Symptoms+laboratory+image/ Compatible histology (50%)	-1 organ (33%) -2 organs (25%) -3 or more organs (42%)	48 [21.9-107.5]

Abbreviations: ND: no data

Main features of the patients with IgG4-RD in series of more than 100 patients and in current series



of the disease. Therefore, regrettably IgG4 related disease continues underdiagnosed. The purpose of this study is to evaluate the clinical characteristics of patients diagnosed with IgG4-RD in a single University Hospital as well as to compare it with other large series.

Methods: Study of patients from a referral hospital and literature review of cases diagnosed with IgG4-RD. Diagnosis was made accordingly to these criteria**: a)** Okazaki; **b)** Umehara; **c)** ACR/EULAR 2020; and/or **d)** clinical, laboratory and imaging suggestive findings **(ref. 1-3)**. For the literature review, we searched PubMed and the Cochrane library from its inception until 30 April 2023, selecting those series with the largest number of patients

Results: We include 12 patients (8 females/4 males) (mean±SD age; 62.4±15.5 years) diagnosed with IgG4-RD. The organs affected at diagnosis were: aorta (n=5), pleura/lung (n=5), lymph nodes (n=4), salivary glands (n=2), retroperitoneum (n=2), pericardium (n=2), lacrimal glands (n=1), bile duct (n=1), kidney (n=1), orbit (n=1), subglottis (n=1), mesentery (n=1), maxillary sinuses (n=1). IgG4 values were increased in 2 (17%) patients (median [IQR]; 250.5 [201.0-300.1] mg/dL) (normal value < 135 mg/dL). Blood plasmablasts were increased in 8 (67%) patients (median; 808 [767-1152] cells/mL) (normal values < 653 cells/mL). In the literature review, 6 series of more than 100 patients each were selected. The main data from the different series are listed in **table**. The **figure** shows the most frequently affected organs in the different series. The pancreas was one of the most frequently involved. In contrast, in our series, aortic involvement and lung/pleura were the most frequent.

Conclusion: IgG4-RD is a very heterogeneous disease with involvement of virtually every organ of the anatomy, usually presenting with involvement of more than one organ. Despite the name of the entity, serum IgG4 is not always elevated.

References:

1. Okazaki K et al. Int J Rheumatol. 2012. PMID: 22690221
Umehara H, et al. Mod Rheumatol. 2012. PMID: 21881964
Wallace ZS et al. Arthritis Rheumatol. 2020. PMID: 31793250

Disclosure: F. López: None; **J. Loricera**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6.

Abstract Number: 1155

Identification of Serum Biomarkers Associated with Muscle Damage Detected on MRI in Polymyositis/dermatomyositis

Haruna Matsuo[1], Toshimasa Shimizu[2], Tomohiro Koga[3], Nozomi Oki[4], Mari Kamiya[5], Natsuka Umezawa[5], Shinsuke Yasuda[6], Masataka Uetani[7] and Atsushi Kawakami[8], [1]Nagasaki University, Nagasaki City, Japan, [2]Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, [3]Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University, Nagasaki, Japan, [4]Department of Radiological Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki City, Japan, [5]Department of Rheumatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University (TMDU), Tokyo, Japan, [6]Department of Rheumatology, Graduate School of Medical and Dental Science, Tokyo Medical and Dental University (TMDU), Tokyo, Japan, [7]Department of Radiological Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, [8]Nagasaki University, Nagasaki, Japan

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

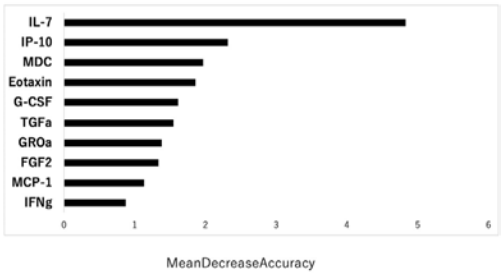
Session Time: 9:00AM–11:00AM

Background/Purpose: Polymyositis/Dermatomyositis (PM/DM) is a chronic inflammatory disease characterized by muscle weakness, and cutaneous manifestations. Although PM/DM exhibits distinct disease phenotypes based on autoantibodies, assessing the severity of muscular symptoms and predicting prognosis solely through autoantibody analysis remains challenging. The aim of this study is to identify potential biomarkers associated with muscle damage in patients with PM/DM.

Methods: This study employed a cross-sectional design to investigate a cohort of patients diagnosed with PM/DM. The initial screening involved a total of 150 PM/DM patients who had visited the Department of Immunology and Rheumatology, and the Department of Respiratory Medicine at Nagasaki University Hospital between August 2008 and June 2021, and had serum samples available for analysis. To assess muscle involvement, bilateral thigh muscles were evaluated using an MRI scoring system described by Andresson et al. Two radiologists independently conducted the scoring process. Serum cytokine levels were measured using a 43-item bead array in both the PM/DM patient group and a control group consisting of 101 healthy subjects from the residents of Saza in Nagasaki prefecture.

Exclusion criteria encompassed cases without disease activity, those complicated by rapidly progressive interstitial pneumonia, or those with underlying malignancies. Ultimately, a total of 43 patients were included in the study, as their femoral MRI images were available for analysis alongside the collected serum samples. Furthermore, an investigation involving immunostaining of muscles obtained from mice with C protein-induced myositis, as previously reported by Sugihara et al., was conducted to identify potential biomarkers.

Figure. 1



Results: Out of the total of 43 cytokines examined, 38 cytokines were deemed appropriate for further analysis. Through RandomForest analysis, it was determined that Interleukin (IL) -7, among the cytokines studied, exhibited the highest significance in distinguishing between the two groups categorized by median MRI score (Figure 1). Moreover, patients with elevated MRI scores exhibited significantly higher levels of serum IL-7 compared to healthy individuals. Correlation analysis revealed a correlation coefficient of 0.3551 (p=0.019) between MRI score and IL-7. Immunohistochemical assessment of muscle tissues in mice with C protein-induced myositis showed the expression of IL-7 and IL-7 receptor on infiltrating mononuclear cells in the muscles.

Conclusion: Our findings indicate that IL-7 can be as a reliable indicator of muscle damage. Assessing IL-7 levels has the potential to serve as a biomarker for predicting muscle damage in patients with PM/DM, particularly when combined with the measurement of other cytokines.

Disclosure: H. Matsuo: None; **T. Shimizu**: None; **T. Koga**: None; **N. Oki**: None; **M. Kamiya**: None; **N. Umezawa**: None; **S. Yasuda**: Abbvie, 5, 6, Asahi-Kasei, 5, 6, Astellas Pharma Inc., 6, AstraZeneca, 6, AYUMI Pharmaceutical Corporation, 5, 6, Bayer Yakuhin, Ltd, 6, Chugai, 1, 5, 6, CSL Behring K.K, 5, 6, Eisai, 2, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Human Life CORD Japan Inc., 5, Immunoforge Inc., 1, Janssen, 6, Japan Blood Products Organization, 5, Kyowa Kirin Co., Ltd., 6, NIPPON KAYAKU Co., Ltd., 5, Novartis, 6, Ono Pharmaceutical, 6, Otsuka Pharmaceutical Co., Ltd, 2, Pfizer, 6, Seed Planning, Inc., 1, Stratoimmune Co., Ltd, 1, SYSMEX CORPORATION, 6, TAISHO PHARMACEUTICAL Co., Ltd., 5, 6, Takeda Pharmaceutical Co., Ltd, 5, Tanabe-Mitsubishi, 5, 6, TEIJIN PHARMA LIMITED, 2, 5, UCB, 5, 6; **M. Uetani**: None; **A. Kawakami**: None.

Abstract Number: 1156

Presentations and Outcomes of Idiopathic Inflammatory Myopathies in Hong Kong

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are a group of heterogeneous autoimmune diseases with cutaneous, musculoskeletal, and systemic involvements. The Hong Kong Myositis Registry (MyoHK) was established to collect longitudinal data on Hong Kong adult IIM patients to enhance our knowledge on the clinical courses and prognosis in IIM.

Methods: This was a retrospective multicentre cohort. Consecutive adult IIM patients followed up in 7 rheumatology centers in Hong Kong were reported voluntarily to the MyoHK registry from January 2018 to May 2023. Additional IIM patients were identified by the Clinical Data retrieval system. Electronic patient records were reviewed. Demographics, clinical data, myositis-specific antibodies (MSAs) and mortality were documented.

Results: 456 patients were included with a mean age at diagnosis of 53.9 ± 13.5 years and 71.1% were female. The median follow-up duration was 72 months (IQR 37-148.8). The most common clinical subtype was dermatomyositis (39.9%), followed by polymyositis (36.4%) and amyopathic dermatomyositis (21.9%). 330 (77.5%) had at least one positive MSA. Anti-melanoma-differentiation-associated gene 5 (Anti-MDA5) and anti-Jo1 were the most prevalent MSAs, both identified in 58 patients (12.7%), followed by anti-transcription-intermediary-factor-1-gamma (Anti-TIF1g) (12.3%) and non-Jo-1

Table 1. Frequencies of different clinical manifestations of Idiopathic Inflammatory Myopathies

Table 1. Frequencies of different clinical manifestations of Idiopathic Inflammatory Myopathies

Clinical manifestations	No of Patients (%)	Clinical manifestations	No of Patients (%)
Weakness	323 (70.8%)	Mechanic Hands	65 (14.0%)
Skin Rash	284 (62.3%)	Raynaud phenomenon	70 (15.4%)
Heliotrope Rash	167 (36.6%)	Arthritis	179 (39.3%)
Gottron's Rash	182 (39.9%)	Vasculitis	58 (12.7%)
Violaceous Rash	52 (11.4%)	Cutaneous ulcers	33 (7.2%)
Periungual Erythema	94 (20.6%)	Interstitial Lung disease	251 (55%)
Refractory Rash	56 (12.3%)	Rapidly progressive ILD	39 (8.6%)
Calcinosis	12 (2.6%)	Pneumomediastinum	9 (2%)
Dysphagia	109 (23.9%)	Fever	102 (22.1%)

Table 2. Clinical manifestations associated with different myositis-specific antibody

MSA	MSA Prevalence	Positive Association	Odds ratio (95% CI)	Negative Association	Odds ratio (95% CI)
MDA5	58 (12.7%)	RP-ILD Hellotrope Rash Cutaneous ulcers	9.461 (2.436 – 36.748) 5.124 (1.43 – 18.331) 15.584 (3.198 – 75.950)	Weakness	0.111 (0.032 – 0.386)
TIF1g	56 (12.3%)	Cancer Rash Refractory Rash	4.156 (1.734 – 9.960) 8.188 (2.576 – 26.032) 3.817 (1.463 – 9.956)	Arthritis ILD	0.239 (0.065 – 0.887) 0.207 (0.079 – 0.545)
SRP	36 (7.9%)	Dysphagia	3.973 (1.778 – 8.875)	Arthritis Rash	0.105 (0.030 – 0.365) 0.096 (0.037 – 0.251)
Jo1	58 (12.7%)	Arthritis Mechanic hands ILD	4.028 (1.874 – 8.658) 2.806 (1.257 – 6.262) 7.921 (2.620 – 23.953)	/	/
Non-Jo1 anti-synthetase	54 (11.8%)	ILD	4.50 (2.245 – 9.020)	/	/
NXP2	10 (2.2%)	/	/	ILD	0.220 (0.058 – 0.842)
SAE	7 (1.5%)	Cancer	4.739 (1.157 – 19.412)	/	/

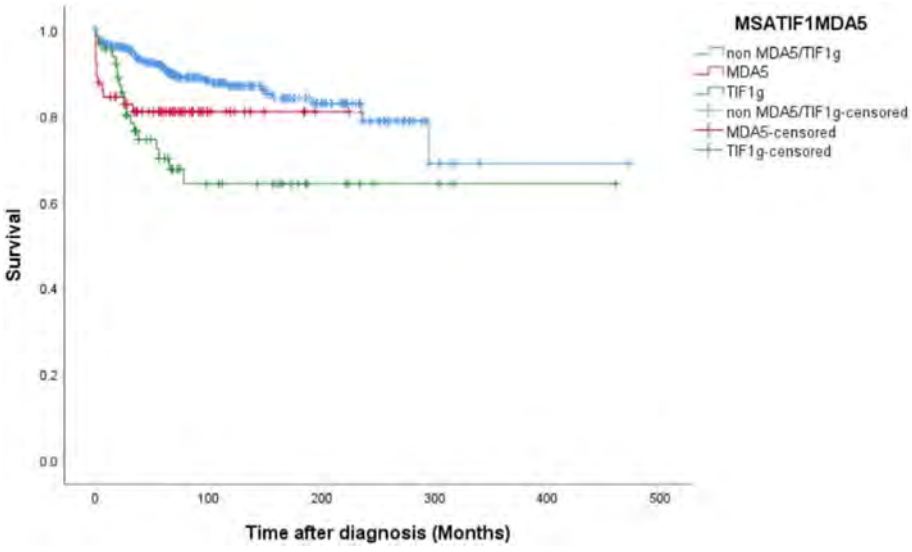

Figure 1. Kaplan-Meier curve of survival of anti-MDA5 antibody positive, anti-TIF1g antibody positive and the rest of IIM patients

anti-tRNA-synthetase antibodies (11.8%). Interstitial lung diseases (ILD) affected 55% of IIM patients, of which 39 patients (8.6%) had rapidly progressive ILD (RP-ILD). Cancer occurred in 84 patients (18.4%), with Nasopharyngeal cancer and lung cancer accounting for 22.6% and 20.2% of all malignancies respectively. Mortality was reported in 74 IIM patients (16.2%) with 22 (4.8%) reported within 6 months of IIM diagnosis. The leading causes of overall mortality were infection (25.6%), malignancies (23.0%) and respiratory failure (18.9%), whereas respiratory failure accounted for 40.9% of deaths occurring within six months of IIM diagnosis. The presence of anti-Jo1 [OR 7.92 (95% CI 2.62-23.95)] and non-Jo1 anti-synthetase MSAs [OR 4.50 (95% 2.24-9.02)] were associated with the development of ILD, whereas anti-MDA5 was associated with RP-ILD [OR 9.46 (95%CI 2.44-36.75)]. Anti-TIF1g [OR 4.16 (95%CI 1.73-9.96)] and anti-SAE [OR 4.74 (95%CI 2.25-9.02)] were associated with malignancy. Tables 1 &2 summarized the clinical manifestations and association with MSAs. Cox regression analysis confirmed older age [HR 1.09 (95% CI 1.06 – 1.11)], RP-ILD [HR 5.79 (95% CI 2.77 – 12.10)], and cancer [HR 3.85 (95% CI 2.19 – 6.77)] to be independent predictors of mortality while anti-MDA5 tended to associate with mortality [HR 1.98(95% CI 0.96 – 4.12)]. Multivariate analysis revealed RP-ILD [HR 7.59 (95% CI 1.77 – 32.53)], MDA5 positivity [HR 5.06 (95% CI 1.05 – 24.24)] and age at diagnosis [HR 1.06 (95% CI 1.00 – 1.13)] were associated with mortality within 6 months of diagnosis. Figure 1 showed the survival between anti-MDA5, anti-TIF1g and rest of IIM patients.

Conclusion: Anti-MDA5 and anti-Jo1 antibodies are the commonest MSA among Hong Kong IIM patients. Older age, presence of cancer and RP-ILD were predictors of mortality. Anti-MDA5 was associated with early mortality.

Disclosure: I. Tang: None; **H. So**: None; **T. li**: None; **V. Tang**: None; **C. Ho**: None; **R. Ho**: None.

Abstract Number: 1157

Experience of Pain in Adults with Idiopathic Inflammatory Myopathies, Myositis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Knowledge of pain in myositis is limited. Recent research suggest that pain is a common symptom in adults with myositis and deemed as one of the most important symptoms to assess in clinical trials and clinical care[1]. The aim of this study was to explore experience of pain in adults with myositis.

Methods: Informants were strategically identified to represent women and men, various age, myositis-diagnosis, diagnosis duration and self-reported pain (≥ 30 mm VAS). 10 adults with polymyositis (n=5), dermatomyositis, (n=3), and antisynthetase syndrome (n=2), 6 women, age range 24-68 years, participated in an individual interview. A semi-structured interview guide was used. Interviews were audiotaped and transcribed verbatim and analyzed by inductive qualitative content analysis. Briefly, transcripts were read by MT,HA separately, identifying meaning bearing units and discussed until consensus, developing condensates, codes and categories. Data were triangulated until consensus (HA,MR,HP).

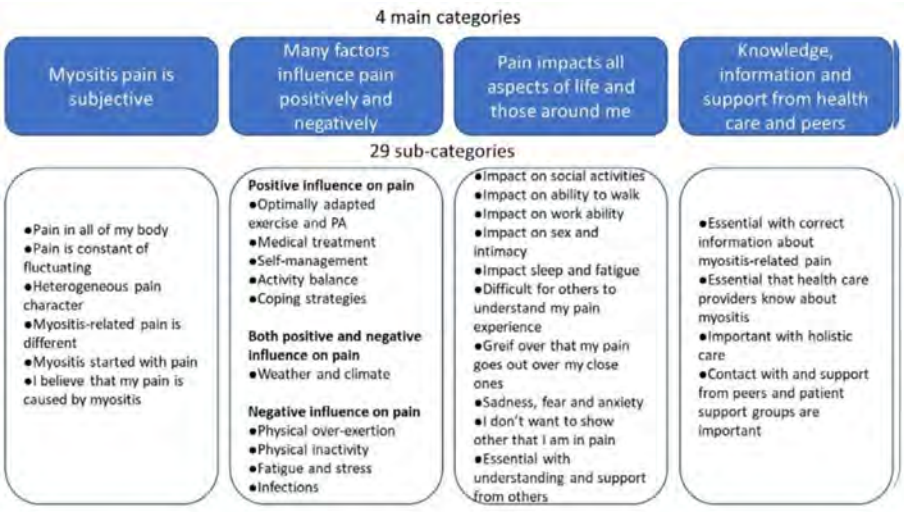

Figure 1. Main categories and sub-categories identified from qualitative content analysis.

Results: Four main categories and 29 sub-categories were identified (Figure 1). Main categories: **1. Myositis pain is subjective***(example codes: Burning pain, tenderness and tensed muscles, Constant pain in my arms, Pain was first symptom of myositis.)***2. Factors influencing myositis positively and negatively***(Exercise reduce pain, Balancing activities and rest reduce pain, Be positive and happy and not focus on the pain, Prednisolone reduce pain, but pain return with tapering of dose,increased pain when I am inactive.)***3. Pain impacts all areas of my life and those around me***(Pain hinders family activities, Difficult to accept that sex no longer is part of my life, Pain reduces sleep quality, Sad that I feel like a burden to others.)***4. Knowledge, information and support from health-care and peers***(Lost a lot of time due to incorrect information, Listen to your doctor, Meet others with myositis for support and tips)*.

Conclusion: Pain is an important symptom in myositis affecting many aspects of life and family/friends. Myositis-related pain is heterogeneous as to character, localization, and duration. Although relieved by medical treatment and adapted exercise, pain can remain as a chronic symptom. Health-care professionals should ask patients about myositis-related pain, and address pain by adequate treatment and information.

Disclosure: H. Alexanderson: None; **M. Tasaroffi**: None; **H. Pettersson**: None; **M. Regardt**: None.

Abstract Number: 1158

Dermatomyositis Flares After COVID-19 Vaccination and/or SARS-CoV-2 Infection

Maximiliano Diaz Menindez[1], Megan Sullivan[2], Benjamin Wang[3], Andy Abril[3], Vikas Majithia[2], Ronald Butendieck[3], Colleen T. Ball[4] and Florentina Berianu[2], [1]Mayo Clinic, Phoenix, AZ, [2]Mayo Clinic Florida, Jacksonville, FL, [3]Mayo Clinic, Jacksonville, FL, [4]Mayo Clinic Jacksonville, Jacksonville, FL

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Dermatomyositis (DM) is an autoimmune disorder part of the group of idiopathic inflammatory myopathies. It is characterized by proximal muscle weakness and skin involvement. Part of the diagnosis includes clinical features, muscle biopsy, electromyography, myositis specific antibodies and laboratory findings. We have seen an association of active DM disease (either new diagnosis or relapse of previously controlled disease) after COVID-19 infection and vaccination. The first cases reported in the literature were by Gokhale et al., who reported 5 cases in India. Other studies have seen a correlation between the vaccine and the positivity of anti-MDA5 antibodies.

Our study aimed to observe the characteristics of a DM cohort after COVID-19 infection and vaccination.

Methods: A retrospective chart review was performed on patients treated between March 1, 2020, and October 31, 2022, for DM. New DM diagnosis or relapse of preexisting DM symptoms following either SARS-CoV-2 infection or COVID-19 vaccination was documented as active DM disease. Qualifying DM symptoms included characteristic rash, muscle weakness, and increased creatine kinase.

For the analysis of our primary aim, we estimated the proportion of patients who had active DM symptoms within 4 weeks after COVID-19 infection or vaccination; a two-sided 95% confidence interval for the single proportion was estimated using the score method. In an exploratory analysis we reported the number and percentage of patients who developed active DM symptoms within 4 weeks following COVID-19 infection or vaccination according to patient characteristics where continuous characteristics were categorized according to the sample median.

Results: 101 patients were treated for DM at our institution in the Division of Rheumatology. 15/101 patients (14.9%) had symptoms related to DM (relapse or new diagnosis) following SARS-COV-2 infection or vaccination. Three (3.0%) patients developed symptoms both with vaccination and infection, 10 (9.9%) patients developed symptoms post SARS-COV-2 infection and 8 (7.9%) developed symptoms post COVID-19 vaccination.

14/15 (93.3%) patients had a positive myositis antibody (see Figure 1). The ten patients who presented with symptoms post infection had a younger mean age of 50 compared to 62 in patients without a flare post infection (p=0.047) (see Table 1).

Of those who developed symptoms post-vaccination (3 patients had symptoms following both infection and vaccination), demographics and vaccine type are presented in Table 2.

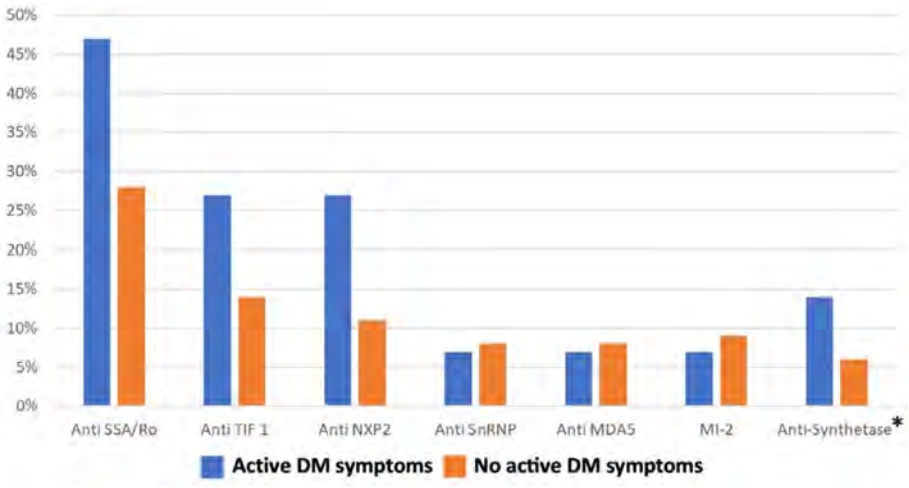

Figure 1. Percentage of positive antibodies in patients with or without active DM symptoms after infection / vaccination * Anti-Synthetase included anti-Jo-1, anti-PL-7, anti-PL-12, anti-OJ, anti-EJ, anti-KS, anti-SRP, anti-Zo, anti-HA, and anti-Ku

The mean onset of symptoms following SARS-COV-2 infection was 2.6 days with a median of 1 (Q1: 0; Q3: 5) and following COVID-19 vaccination was 1.38 days, median of 1 (Q1: 0.5; Q3: 2).

Conclusion: This retrospective study revealed a strong temporal relationship between DM symptoms and Covid-19 infection or vaccination in 14.9% of all DM patients evaluated in our clinic during the pandemic. The higher prevalence of NXP2 in our cohort is unique from prior reports. Additional studies are required to understand the possible pathophysiology behind this association.

Table 1. Demographics & Clinical Characteristics after COVID-19 infection

	Active DM symptoms (n=8)	No active DM symptoms (n=93)	*p*-value
Age			
Median (Q1, Q3)	70 (59, 71)	60 (47, 69)	0.161
Sex			
Female subjects	7 (88%)	71 (77%)	0.679
Male subjects	1 (12%)	21 (23%)	
Race/ethnicity			
White	8 (89%)	75 (82%)	
African American	0 (0%)	6 (7%)	0.682
Asian	0 (0%)	4 (4%)	
Hispanic or Latino	0 (0%)	5 (5%)	
Nondisclosure	1 (11%)	2 (2%)	
Vaccine Number			
Median (Q1, Q3)	2.5 (1.75, 3)	2 (0, 3)	0.647
Type of COVID vaccine			
N-Miss	0	26	
Pfizer	3 (38%)	35 (53%)	
Pfizer and Moderna	0 (0%)	3 (5%)	0.555
Moderna	4 (50%)	23 (35%)	
Moderna and Jansen	0 (0%)	2 (3%)	
Jansen	1 (12%)	3 (5%)	
New Onset disease (n)	4 (50%)	NA	

Table 2. Demographics & Clinical Characteristics after post vaccination

	Active DM symptoms (n=8)	No active DM symptoms (n=93)	*p*-value
Age			
Median (Q1, Q3)	70 (59, 71)	60 (47, 69)	0.161
Sex			
Female subjects	7 (88%)	71 (77%)	0.679
Male subjects	1 (12%)	21 (23%)	
Race/ethnicity			
White	8 (89%)	75 (82%)	
African American	0 (0%)	6 (7%)	0.682
Asian	0 (0%)	4 (4%)	
Hispanic or Latino	0 (0%)	5 (5%)	
Nondisclosure	1 (11%)	2 (2%)	
Vaccine Number			
Median (Q1, Q3)	2.5 (1.75, 3)	2 (0, 3)	0.647
Type of COVID vaccine			
N-Miss	0	26	
Pfizer	3 (38%)	35 (53%)	
Pfizer and Moderna	0 (0%)	3 (5%)	0.555
Moderna	4 (50%)	23 (35%)	
Moderna and Jansen	0 (0%)	2 (3%)	
Jansen	1 (12%)	3 (5%)	
New Onset disease (n)	4 (50%)	NA	

Disclosure: M. Diaz Menindez: None; **M. Sullivan**: None; **B. Wang**: None; **A. Abril**: None; **V. Majithia**: AbbVie/Abbott, 2, Novartis, 2, UCB, 2; **R. Butendieck**: None; **C. Ball**: None; **F. Berianu**: None.

Abstract Number: 1159

Expanded Cytotoxic CD8+ T Cell Clones Characterize the Blood of Inclusion Body Myositis Patients

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Inclusion body myositis (IBM) is an inflammatory myopathy, characterized by CD8+ T cell infiltration of muscle and patients present with progressive muscle weakness and atrophy, leading to disability due to no FDA-approved therapies. Patients with IBM have been noted to frequently exhibit aberrant expansion of circulating CD8+ T cells, even satisfying classification criteria for T cell large granular lymphocytic leukemia (T-LGL) in >50% of cases, in one study. However, high-resolution profiling of the transcriptome and TCR repertoire in IBM are lacking.

We aim to evaluate the TCR repertoire of circulatory CD8+ T cells, allowing us to simultaneously define the transcriptomes of expanded and non-expanded clonotypes in blood of IBM patients.

Methods: 12 IBM patients and 8 age-matched healthy controls were sorted for non-naïve CD8+ T cells by flow cytometry. Single-cell RNA and TCR sequencing was performed to profile the whole gene expression, coupled with paired TCRa and TCRb chains, at single-cell resolution. Additional markers during flow cytometry allowed for further identification of aberrant populations in IBM compared to age-matched healthy controls.

Results: Our results found IBM CD8+ T cell were highly expanded compared to age-matched healthy controls. These CD8+ T cells were identified in both the broad non-naïve T cell population, as well as the specific CD8+ CD57+ T cell subset. Enrichment of T-LGL leukemia genes, in addition to CD8+ effector function, cytotoxicity and inflammatory chemokines and cytokines were found in expanded clonotypes, with a higher gene expression found in hyperexpanded clones compared to minimally expanded clonotypes. Absence of common TCR clonotypes between patients in IBM was found, a pattern also seen in T-LGL leukemia. GSEA analysis also confirmed a downregulation of cell apoptosis processes in hyperexpanded clonotypes, a feature of T-LGL leukemia clones.

Conclusion: Significant clonal expansion of CD8+ T cells in the blood was found in our IBM cohort compared to our age-matched healthy controls. Additionally, these hyperexpanded clonotypes have elevated cytotoxic and T cell activation genes in comparison to their minimally expanded counterparts. These results highlight how the blood compartment of IBM, a progressive muscle disease, is important in IBM and how future studies and therapies should be targeting these aberrant CD8+ T cell clones.

Disclosure: M. Fein: None; **L. Donlin**: Bristol-Myers Squibb(BMS), 2, Stryker, 2; **D. Fernandez**: None; **L. Shakib**: None.

Abstract Number: 1160

Antibody Predictors of Prognosis in a Large Multi-centre Cohort of Idiopathic Inflammatory Myopathy Associated Interstitial Lung Disease

Jennifer Hannah[1], Alexandra Lawrence[2], Jennifer Martinovic[2], Marium Naqvi[2], Saadia Sasha Ali[3], Carmel Stock[4], Cara Owens[4], Anand Devaraj[4], Louise Pollard[2], Sangita Agarwal[2], Belén Atienza-Mateo[5], Amit Patel[6], Alex West[2], Kate Tinsley[2], Hasti Robbie[7], Felix Chua[4], Boris Lams[2], Athol Wells[4], Sam Norton[7], James Galloway[7], Elisabetta Renzoni[4] and Patrick Gordon[8], [1]King's College London, London, United Kingdom, [2]Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom, [3]King's College Hospital, Epsom, United Kingdom, [4]Royal Brompton and Harefield Hospitals NHS Trust, London, United Kingdom, [5]Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain, [6]King's College Hospital, London, United Kingdom, [7]King's College London, London, United Kingdom, [8]NHS, London, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

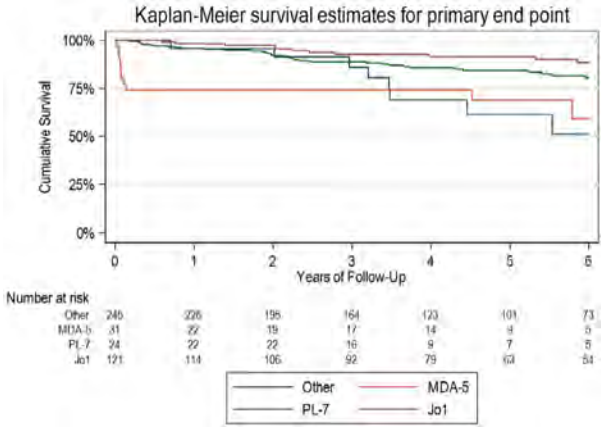
Session Time: 9:00AM–11:00AM

Background/Purpose: IIM-ILD follows a varied clinical course. Serological profile can help predict clinical phenotype, but impact on ILD prognosis is less clear. This multicentre UK cohort study examines whether serological profile can predict mortality and change in lung function over time.

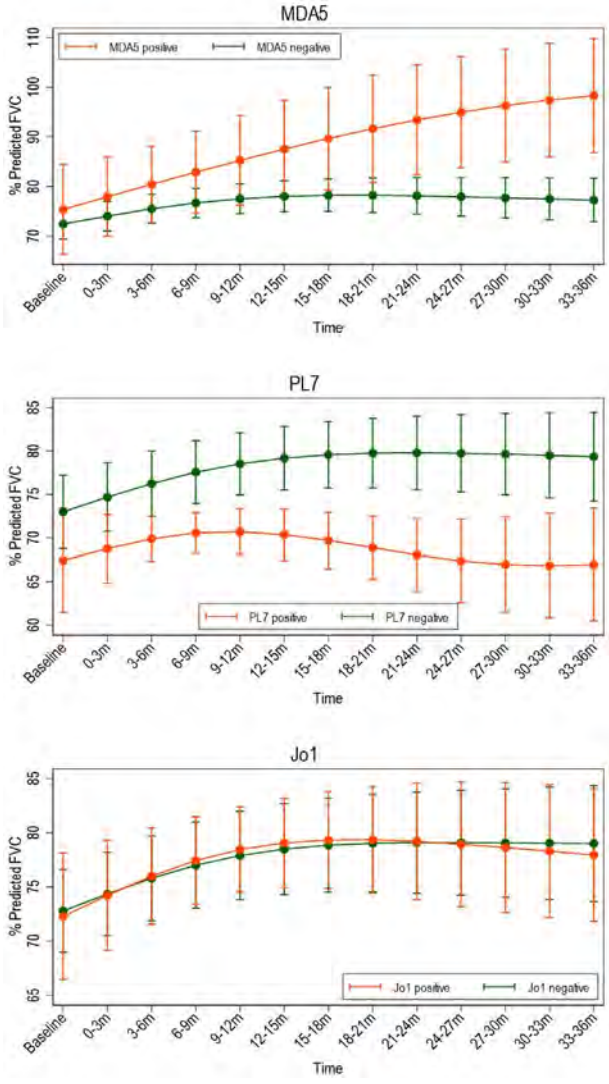
Methods: Patients with IIM-ILD were identified in 3 NHS trusts from local databases. Adults with ILD meeting IIM diagnostic criteria or Interstitial Pneumonia with Autoimmune Features (IPAF) with Myositis Specific Antibodies (MSA) were included. Baseline characteristics from time of presentation were compared across antibody groups and across survivors/deceased at 2 years. Survival analysis looking at time to death (or lung transplant) for duration of available follow-up was modelled by Cox-Proportional Hazards comparing each antibody individually to all others. Models were adjusted for age, gender,

Antibody	Number of patients	Number Reaching End Point	Univariate Model HR	Univariate Model p value	Multivariate Model HR	Multivariate Model p value
Primary End Point						
Jo1	126	21	0.56 (0.35, 0.91)	**0.020**	0.61 (0.42, 0.87)	**0.006**
PL12	44	10	0.90 (0.47, 1.73)	0.748	1.06 (0.90, 1.26)	0.482
PL7	26	11	2.29 (1.22, 4.31)	**0.010**	2.06 (1.42, 2.99)	**0.000**
EJ	16	*	0.63 (0.15, 2.56)	0.517	0.65 (0.30, 1.38)	0.262
OJ	9	*	0.51 (0.07, 3.68)	0.505	0.42 (0.22, 8.01)	0.562
Mi2	19	*	1.31 (0.48, 3.58)	0.603	0.89 (0.27, 2.90)	0.846
SRP	16	*	1.00 (0.32, 3.17)	1.000	0.81 (0.17, 3.76)	0.783
MDA5	32	11	2.90 (1.53, 5.49)	**0.001**	4.61 (2.10, 10.01)	**0.000**
PMScl	40	8	0.89 (0.43, 1.85)	0.764	0.65 (0.40, 1.06)	0.086
RNP	30	12	1.48 (0.80, 2.72)	0.208	1.90 (1.24, 2.93)	**0.003**
Ku	13	*	1.16 (0.37, 3.66)	0.804	1.81 (0.37, 8.85)	0.463
Negative	32	7	0.96 (0.45, 2.08)	0.924	0.90 (0.49, 1.65)	0.733
Ro52	195	40	1.13 (0.75, 1.70)	0.568	1.15 (0.74, 1.79)	0.523
All ARS	215	39	0.58 (0.38, 0.87)	**0.009**	0.64 (0.52, 0.77)	**0.000**

Univariate and multivariate hazard ratios for primary endpoint of death/transplant according to presence or absence of each antibody. Statistically significant results are in bold type. *Counts of <5 suppressed to maintain anonymity



Kaplan-Meier survival curves for death/transplant according to antibody for the three antibodies showing statistically significant differences in survival on both univariate and multivariate analysis



Time trends in % predicted FVC in a) MDA5, b) PL7, and c) Jo1 using multi-level mixed effects models for repeated measures over time, showing slow improvement in MDA-5 FVC, whereas PL-7 deteriorates.

ethnicity, presence of overlap CTD/malignancy, smoking and site. Regression models were also used to observe trends in lung function parameters over time.

Results: Of 430 included patients, 68% were female, 46% were of White ethnicity. 81% met IIM criteria, 19% were IPAF. Mean follow up duration was 4.3 years. Common antibodies were to Ro52, Jo1, PL12, MDA5 (n=195, 126, 44 & 32 respectively). 10% had evidence of pulmonary hypertension within 1 year of diagnosis, 4% had malignancy within 3 years. Baseline characteristics of survivors vs fatal cases at 2 years showed survivors were younger (51.4 vs 61.7 years), more likely to have never smoked (69% vs 44%), less likely to have been hospitalised at diagnosis (15% vs 52%) and had a lower Charleson Comorbidity Index. Survivors had lower CRP, higher CK & higher baseline FEV1/FVC/TLCO. Imbalance in age, BMI, CK and comorbidity status were seen across antibody groups. MDA5 had the highest adjusted hazard ratio (HR) for mortality of 4.59 (95%CI 2.10-10.01). Kaplan-Meier curve shows high early mortality in this group. Anti-synthetase antibodies (ARS) carried a reduced risk of mortality (HR 0.63), however individually Jo1 had low HR (0.61, 95%CI 0.4-0.87) and PL7 had high HR (2.07, 95%CI 1.44-2.99). RNP showed worse prognosis on adjusted analysis (HR 1.88, 95%CI 1.25-2.84) (Table 1). Regression models suggest that compared to other antibodies, %pred FVC in MDA5 improves over the first 3 years, in PL7 it drops, and in Jo1 it is no different (Figure 1). MDA5 % pred FEV1 also showed improvement, but in Ku it was lower than other antibodies from 21 months. There were no significant differences in % pred TLCO between antibodies.

Conclusion: There is strong evidence that antibody status associates with clinical outcomes, both in terms of progression of lung disease and mortality, suggesting pathogenetic differences. MDA5 predicts a high risk of death early on in disease course, whilst Jo1 associates with lower mortality. PL7 and RNP were additional antibodies associating with higher mortality. Difference between Jo1 and PL7 highlights variation within anti-synthetase syndrome. Paradoxically, if an MDA5 positive person survived the early disease phase, there was evidence that lung function can recover, which may reflect different MDA5 subpopulations.

Disclosure: J. Hannah: None; **A. Lawrence**: None; **J. Martinovic**: None; **M. Naqvi**: None; **S. Ali**: None; **C. Stock**: None; **C. Owens**: None; **A. Devaraj**: Boehringer-Ingelheim, 2, Brainomix, 2; **L. Pollard**: None; **S. Agarwal**: None; **B. Atienza-Mateo**: None; **A. Patel**: None; **A. West**: None; **K. Tinsley**: None; **H. Robbie**: None; **F. Chua**: None; **B. Lams**: None; **A. Wells**: Boehringer-Ingelheim, 2, 6, Roche, 2, 6, Veracyte, 2, 6; **S. Norton**: Janssen, 6, Pfizer, 6; **J. Galloway**: AbbVie, 2, 5, 6, AstraZeneca, 5, Biogen, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **E. Renzoni**: None; **P. Gordon**: Celltrion, 12, Support to attend EULAR conference 2023, Galapagos, 1.

Abstract Number: 1161

Proteasome Inhibitor Repurposed for Dermatomyositis: Results of a Drug Repurposing Analysis Based on the Transcriptomic Signature of Patients' Perifascicular Fibers Validated in Pre-clinical Models

Léa Debrut[1], Margherita Giannini[2], Céline Keime[1], Daniela Rovito[1], Béatrice Lannes[3], Anne-Laure Charles[4], Daniel Metzger[1], Bernard Geny[5], Gilles Laverny[1] and Alain Meyer[6], [1]Institut de Génétique et de Biologie Moléculaire et Cellulaire (IGBMC), Illkirch, France, [2]Nouvel Hopital Civil, Strasbourg, Strasbourg, France, [3]Hôpital de Hautepierre - Hôpitaux Universitaires de Strasbourg, Strasbourg, France, [4]UR3072, Centre de Recherche en Biomédecine de Strasbourg (CRBS), Strasbourg, France, [5]Nouvel Hôpital Civil, Strasbourg, France, [6]Hôpitaux Universitaires de Strasbourg, Strasbourg, France

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

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Background/Purpose: Dermatomyositis (DM) is an autoimmune myopathy responsible for muscle weakness associated with decreased quality of life and increased mortality. DM muscular histology is characterized by specific lesions of perifascicular fibers consisting of atrophy, type I interferon (IFN-I) signature, expression of major histocompatibility complex class I (MHC-I) and mitochondrial dysfunctions (1). The origin of these lesions is not understood. Current treatments are empirical, partially effective, expose to a risk of side effects and present a high rate of relapse upon discontinuation. The objective of the study was to identify innovative therapeutic strategies for DM, based on the identification of the molecular pathways that underlie perifascicular fibers lesions and the repositioning of drugs already approved in humans.

Methods: To reveal the molecular pathways underlying DM perifascicular fibers lesions, perifascicular and endofascicular fibers from muscle biopsy of 19 patients with recent and untreated myositis (DM, other myositis) or without myopathy were microdissected by laser, their transcriptome was established by RNA sequencing and analyzed by bioinformatic methods. To identify innovative therapeutic strategies based both on DM pathophysiological mechanisms and on existing drugs, the transcriptomic signature specific to DM perifascicular fibers obtained by microdissection experiments was used for a drug repositioning analysis as described by Karatzas et al. (2). To validate the predications obtained, the effect of drug candidates already used in humans was tested in *in vitro* and *in vivo* preclinical models: in 1) cultured human muscle cells treated with IFN-β and in 2) a mouse model of myositis experimentally induced by immunization against skeletal muscle fast-type C protein.

Results: Transcriptomic analysis of patient's muscle fibers combined with topographic information (perifascicular VS endofascicular localization) revealed that a proteasome deregulation predominant in the perifascicular fibers is a hallmark of DM. The integration of 3 computer databases of drug repositioning allowed the identification of 9 molecules predicted to reverse the pathological signature of the DM perifascicular fibers. The drug with the highest therapeutic potential was a proteasome inhibitor (Ixazomib). A second proteasome inhibitor (MG-132) was also identified. 2 drugs already used for DM (prednisolone and a JAK inhibitor) was identified with a lower therapeutic score. In the cellular model (human myotubes treated with IFN-I), ixazomib reversed the atrophy, IFN-I signature, MHC-I expression and mitochondrial dysfunctions induced by IFN-β treatment. In the mouse model of myositis, ixazomib restored muscle strength and decreased blood creatine kinase level.

Conclusion: Proteasome inhibition could be a new effective therapeutic strategy for DM.

(1) Meyer et al. 2017. IFN-β-Induced Reactive Oxygen Species and Mitochondrial Damage Contribute to Muscle Impairment and Inflammation Maintenance in Dermatomyositis. *Acta Neuropathol*. 134 (4): 655-66. < ! (2) Karatzas et al. 2019. An Application of Computational Drug Repurposing Based on Transcriptomic Signatures. Methods Mol Biol 1903, 149-177.

Disclosure: L. Debrut: None; **M. Giannini**: None; **C. Keime**: None; **D. Rovito**: None; **B. Lannes**: None; **A. Charles**: None; **D. Metzger**: None; **B. Geny**: None; **G. Laverny**: None; **A. Meyer**: None.

Abstract Number: 1162

Serial Imaging Changes in Skeletal Muscle Composition and Their Association with Clinical Outcomes in Idiopathic Inflammatory Myopathies

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Muscle weakness in inflammatory myopathies (IIM) is due to muscle-edema, atrophy and fatty-infiltration among which edema is the predominant cause at baseline. Some IIM pateints do not achieve full muscle power even with immunosupressive treatment which mainly targets edema. Serial changes occuring in skeletal muscles visualized on thigh MRI can help understand the failure of complete recovery. Role of Dual energy X-ray Absorptiometry (DXA) assessed skeletal muscle compositon as outcome measure in IIM was not studied previously.

Objectives: To see the changes in skeletal muscle composition over 6 months in IIM patients using imaging and to assess the agreement of MRI and DXA scores with each other and with clinical outcome measures

Methods: Patients satisfying 2017 ACR-EULAR classification criteria for IIM were prospectively enrolled. All patients underwent thigh MRI(t-MRI) STIR and T1 weighted sequences (axial and coronal) at baseline, 3 and 6 months and DXA scan at baseline and 6 months. Manual muscle testing-8(MMT-8), Functional index-3(FI-3), 2-minute walk distance (2MWD) were

Table 1: Serial change in t-MRI scores, DXA assessed lean mass and clinical outcome measures

	Baseline	3 months	6 months	P-value
Muscle edema	17.03(7.4-32.4) *	0.37(0.00-11.11) *	0.00(0.00-5.37)	**0.000**
Fascial edema	46.66(15.0-57.7) *	7.77(0.00-25.55) *	4.44(0.00-23.88)	**0.004**
Muscle atrophy	0.00(0.00-1.67)	0.00(0.00-2.22)	0.00(0.00-2.22)	0.670
Fatty infiltration	6.66(0.00-15.00) *	8.88(2.22-21.66) *	8.88(2.22-23.33)	**0.001**
Appendicular lean mass/Ht^2	5.5(3.9-6.2) *	-	5.6(4.8-7.3) *	**0.007**
Lean body mass/Ht^2	12.6(10.7-14.4) *	-	13.4(11.1-15.6) *	**0.021**
Manual Muscle Testing-8	56(51.5-70.5) *	78(71.50-80) *	78(76-80)	**0.000**
Functional Index-3	33.88(9.7-57.2) *	56.6(29.4-77.2) *	72.2(50-83.3) *	**0.000**
2-Minute Walking Distance	122(40-141) *	142(126.5-177) *	150(138-161)	**0.002**

*indicates significant change between 2 time points

Table 2: Correlation between t-MRI scores and Coreset measures at baseline and 3 months

	Baseline				3 months			
	Muscle edema	Fascial edema	Muscle atrophy	Fatty infiltration	Muscle edema	Fascial edema	Muscle atrophy	Fatty infiltration
MMT-8	**.631****	-.353	-.264	-.177	**-.673****	-.430	**-.732****	**-.575***
PhyGA	**.632****	.203	.259	-.044	**.488***	.289	**.627****	.463
PGA	**.715****	.341	.307	.105	**.490***	.334	**.585***	.438
HAQ-DI	**.681****	.287	.382	.277	.442	.137	**.613****	**.740****
EMGA	.356	.197	-.107	-.260	-.040	.198	.226	-.099
FI-3	**-.698****	-.434	-.390	-.119	-.382	-.057	**-.488***	-.315
2MWD	**-.485***	-.200	-.276	-.424	**-.591***	-.262	**-.577***	**-.743****

** p<0.01, * p<0.05

MMT-8 - Manual Muscle testing-8; PhyGA - Physician Global assessment; PGA - Patient Global assessment; HAQ-DI - Health assessment Questionnaire Disability index; EMGA- Extra muscular Global assessment; FI-3- Functional Index-3; 2MWD- 2 minute walking distance

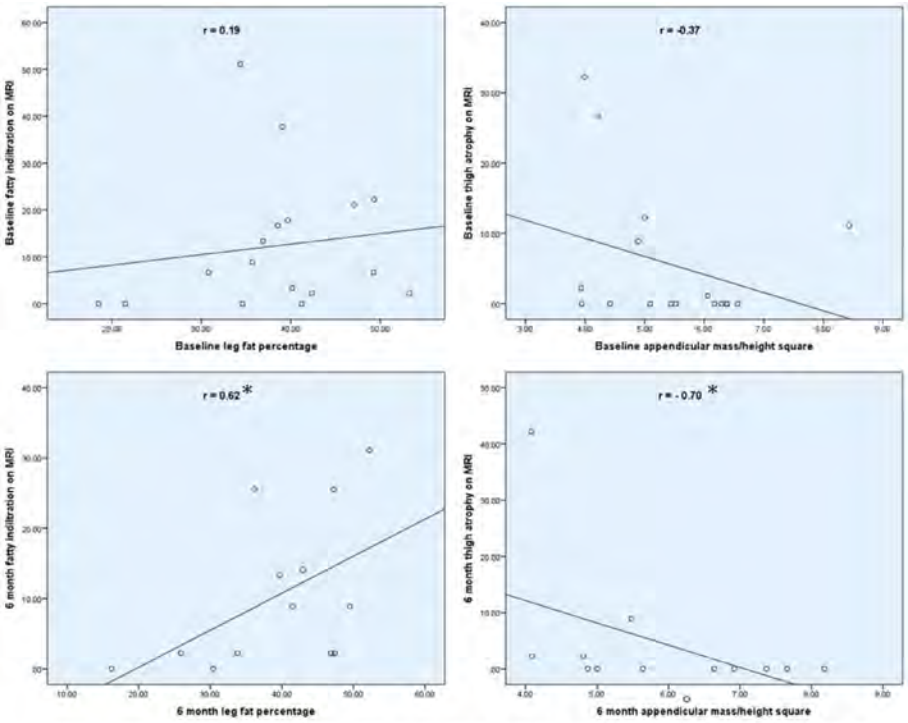


Figure 1: Correlation of MRI assessed fatty infiltration and atrophy with DXA assessed leg fat percentage and appendicular mass/height^2 at baseline and 6 months
* Indicates p<0.05

assessed at baseline, 3 and 6 months. t-MRI was scored using a semi-quantitative score for muscle edema, fascial edema, muscle atrophy and fatty infiltration. Friedman test was used to compare variables at baseline, 3 and 6 months and Spearman correlation was done for agreement of MRI and DXA scores with each other and clinical outcome measures.

Results: 17 patients (12 females) were enrolled and all of them completed 3-months follow-up while only 13 completed 6-months follow-up. Median (IQR) age was 38 (27-46) years, disease duration was 6 (2-24). The study group comprised of 10 dermatomyositis, 5 antisynthetase syndrome and 3 immune mediated necrotizing myopathy patients MRI assessed muscle-edema and fascial-edema decreased significantly and fatty-infiltration increased significantly ($p < 0.01$) from baseline to 3-months. Muscle atrophy showed no change. Improvement in MMT-8 and 2MWD was significant between baseline and 3-months($p< 0.001$) whereas FI-3 continued to improve till 6-months($p< 0.001$) (Table 1). At baseline MMT-8($r=-0.631$; $p< 0.01$), FI-3($r=-0.698$; $p< 0.01$) and 2MWD ($R=-0.485$; $p< 0.05$) negatively correlated with only muscle edema. At 3-months MMT-8 and 2MWD negatively correlated with muscle-edema ($r=-0.673$, $r=-0.591$), atrophy ($r=-0.732$, $r=-0.577$) and fatty-infiltration ($r=-0.575$, $r=-0.743$) ($p< 0.05$) respectively (table 2). MRI fatty-infiltration score and atrophy score did not correlate with DXA assessed leg fat percentage and appendicular mass/ht2 respectively at baseline but had significant correlation ($p< 0.05$) at 6- months (Figure 1).

Conclusion: In IIM, edema decreased but fatty infiltration increased significantly in first 3-months. DXA assessment of fat and lean mass did not agree with MRI atrophy and fatty infiltration at baseline probably due to concomitant muscle edema.

Disclosure: M. Gorijavolu: None; **C. Kavadichanda**: None; **R. Ananthakrishnan**: None; **C. Mariaselvam**: None; **M. Thabah**: None; **V. Negi**: None.

Abstract Number: 1163

Anti-melanoma Differentiation Associated Gene 5 (Anti-MDA5) Antibody Dermatomyositis: Clinical Features and Outcome in a Racially Diverse Patient Cohort

Sai Koyoda[1], Dawn Wahezi[2], Xianhong Xie[3], Anand Kumthekar[4], Clement Tagoe[3] and **Bibi Ayesha**[5], [1]Essen Medical Center, Rahway, NJ, [2]Children's Hospital at Montefiore, New Rochelle, NY, [3]Albert Einstein College of Medicine, Bronx, NY, [4]Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY, [5]Montefiore Medical Center, Bronx, NY

SESSION INFORMATION

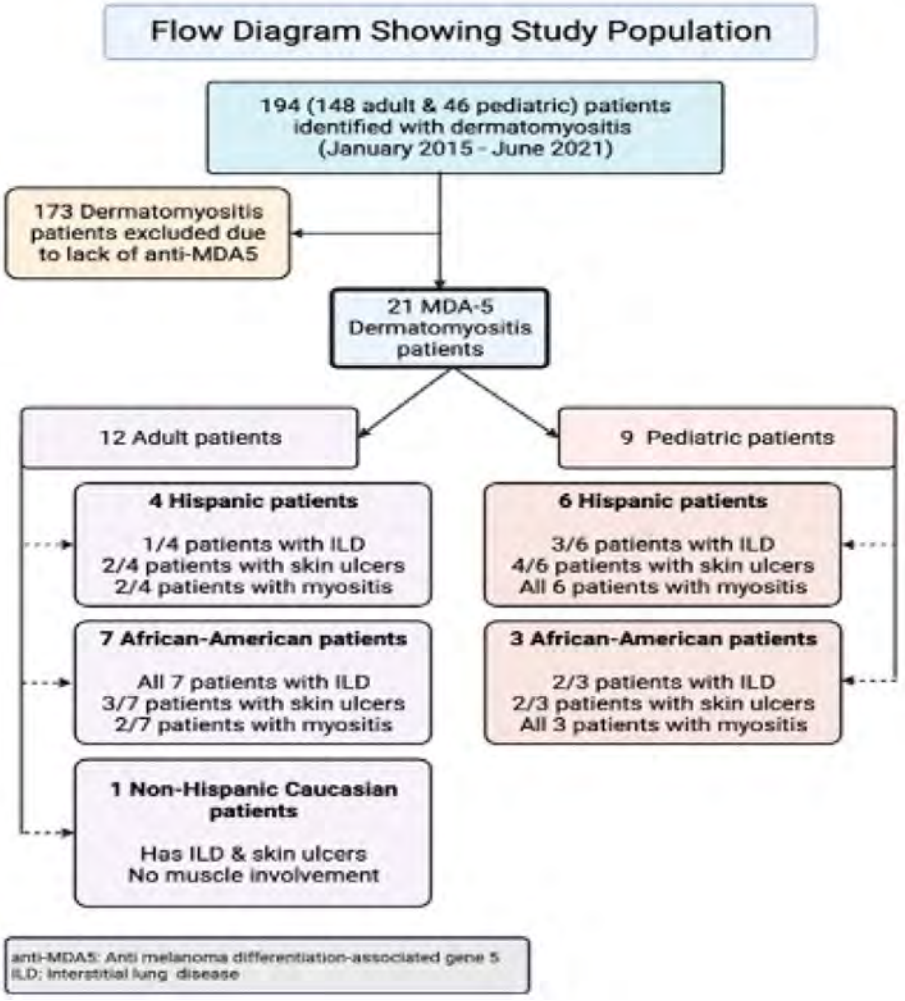
Session Date: Monday, November 13, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-melanoma differentiation-associated gene 5 (anti-MDA5) antibody dermatomyositis typically expresses rapidly progressing interstitial lung disease (RP-ILD) and ulcerative skin lesions, with or without muscle involvement. There is a lack of understanding on early diagnosis and treatment to avoid untoward outcomes. Our objective was



Flow Diagram Showing Study Population

Ulcerative Skin Lesion in MDA-5 Dermatomyositis

to identify distinguishing clinical and laboratory features to assess disease progression amongst a diverse cohort with anti-MDA5 dermatomyositis based on serologic, histopathologic, and radiographic status.

Methods: We studied the disease phenotype in a racially diverse juvenile and adult population with anti-MDA5 dermatomyositis at our institution through a retrospective chart review. We identified 194 dermatomyositis patients, 21 of whom were MDA5 antibody positive. Data were analyzed by Fischer's exact test and ANOVA.

Results: Twelve adult patients represented 8% of all adult dermatomyositis cases (12/148) and 9 represented 19 % of the pediatric dermatomyositis cases (9/46). In adult patients, the mean age of disease onset was 45.2 years (SD 14.4 years). Nine adult ILD cases were noted, of which 2 were RP-ILD. The presence of the Ro52 antibody was associated with rapid disease progression. In the pediatric group, the mean age of onset was 6.6 years (SD 4.9 years). All children had muscle weakness, and 5 had ILD. Myositis was noted to be more prevalent in the pediatric population, compared to adults respectively (9/9 Vs. 4/12 cases; p=0.05). ILD was statistically significant in the African American population (9/10 Vs. 5/11 cases, p=0.03) and of these 3 cases had fatal RP-ILD. The combined mortality rate of 14.2% was more favorable than the 40-60% reported in the literature.

Conclusion: The general disease characteristics of our cohort were similar in both adult and pediatric patients except for myositis, which was more common in the pediatric population. The incidence of ILD was higher in adults, especially in the African American population who had worse outcomes. The rapid escalation of therapy and use of rituximab may have improved our outcomes over historic controls.

Disclosure: S. Koyoda: None; **D. Wahezi**: None; **X. Xie**: None; **A. Kumthekar**: None; **C. Tagoe**: None; **B. Ayesha**: None.

Abstract Number: 1164

Can We Differentiate Patients with Dysferlinopathies and Inflammatory Myopathies by Muscle Ultrasound? A Discriminant Analysis Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

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Background/Purpose: Immune-mediated myopathies (IMM) are a heterogeneous group of diseases characterized by inflammation and muscle weakness; among their differential diagnoses are the dysferlinopathies, which are autosomal recessive neuromuscular disorders caused by mutations in the DYSF gene that present muscle weakness and significant increase of CK, just like IMM. The aim of this research is to determine the sonographic differences between dysferlinopathies and immune-mediated myopathies and whether these allow their classification.

Methods: Observational, cross-sectional, and analytical study in which we evaluated 20 muscles from 11 patients with dysferlinopathies and 11 with IMM. They were matched for age, sex, and time of disease evolution. Clinical and laboratory variables were analyzed. GE LOGIQ^{TM}e equipment with a 4-12 MHz linear transducer was used, and the thickness of each muscle was measured. A semiquantitative scale evaluated elementary lesions: atrophy, edema, power Doppler, and the Heckmatt scale (0-4) was calculated. Descriptive statistics were performed. Finally, discriminant analysis was performed to determine which ultrasound variables best predicted the diagnoses.

Table 1. Characterization of patients with dysferlinopathies and inflammatory myopathies

	Dysferlinopathies n=11	IMM n=11	
General characteristics			*p
Women	9 (81.8%)	9 (81.8%)	
Males	2 (18.18%)	2 (18.18%)	
Ages (years)	39.54±11.24	37.36±10.62	.971
Evolution (years)	16±8.43	16.55±8.25	.852
Manual Muscle Testing Scores (MMT8 (mean))	100 (79-112)	145 (136-147)	.007
Laborstories			
CK (mcg/L)	2785.50 (1052.75-4378.75)	162.00 (72.00-311.00)	.000
LDH (U/L)	289.00 (192.00-411.75)	170.00 (156.00-196.00)	.001
TGO (U/L)	52.75 (42.25-71.55)	25.30 (16.90-29.70)	.011
TGP (U/L)	78.30 (64.90-113.80)	20.10 (15.50-28.00)	.016
Muscle size			
BB (cm)	1.67±0.63	2.76±0.49	*<0.0001*
CD (cm)	2.70±0.84	3.45±0.87	*.040*
GC (cm)	1.88±0.42	3.16±0.42	***<0.001***
Discriminant analysis	Function	Function	**CP
BB	7.434	13.926	≤2.44
CD	-1.117	-4.250	≤2.72
GC	13.489	25.399	≤2.29
Constant	-18.051	-52.935	

- Group 1: -18.051+7.434(B/B)+1.117(CD)+13.489(GC)
- Group 2: -52.953+13.926(B/B)-4.250(CD)+25.399(GC)

Results: A total of 40 muscles were evaluated, finding a greater degree of atrophy and a higher Heckmatt scale in patients with dysferlinopathies compared to MII (Table 1). Discriminant analysis showed that the set of 3 muscles, Right biceps/brachialis (BB), Right quadriceps (CD), and Gastrocnemius/right soleus (GC), had a diagnostic accuracy of 100% (sensitivity 100%, specificity 100%, canonical coefficient 0.733 p=.000). We present a set of 2 formulas that allow classifying with the highest score according to the measurement of the muscles in group 1 (dysferlinopathy) or group 2 (MII). Finally, a COR analysis was performed to determine the cut-off points of each muscle to classify as dysferlinopathies.

Conclusion: The study of 3 muscle groups (BB, CD, GC) presents high diagnostic accuracy in differentiating dysferlinopathies from MII, especially when no genetic study or antibodies are available and diagnostic doubt exists.

Disclosure: C. Soto-Fajardo: None; **S. Solorzano Flores**: None; **A. Angeles-Acuña**: None; **F. Carranza Enriquez**: None; **R. Escobar-Cedillo**: None; **S. Renan-Leon**: None; **K. Arias Callejas**: None; **A. Enriquez-Luna**: None; **G. Ramon-Diaz**: None; **C. Pineda**: None.

Abstract Number: 1165

Long-term Changes in Lung Function in Melanoma Differentiation-associated Protein 5 (MDA5) Antibody Positive Dermatomyositis Patients: Experience of a Single Center Longitudinal Cohort in North America

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) associated with antibodies to melanoma differentiation-associated protein 5 (MDA5 ab) in patients with dermatomyositis (DM) has been associated with a rapid decline in lung function and high mortality early in disease. The current work evaluated long-term changes in lung function in a longitudinal MDA5 ab positive DM cohort in North America.

Methods: We identified DM patients with MDA5 ab in a single center longitudinal cohort of 355 adult patients with idiopathic inflammatory myopathies (IIM). Patient clinical characteristics and longitudinal pulmonary function tests (PFT), echocardiograms, and high-resolution computed tomography (HRCT) chest scan results were collected by chart review.

Results: 30 DM patients (8.5%) of the IIM cohort had confirmed positive MDA5 ab testing. The clinical characteristics of patients with ILD (n=24, 80%) and without ILD (n= 6, 20%) by HRCT are shown in Table 1. Patients without ILD were younger and more likely to present with inflammatory arthritis. Patients with ILD had an aggressive disease phenotype with 75% (22/24) requiring initial hospitalization. Two ILD patients died of rapidly progressive ILD within 3 months of cohort entry. ILD patients were treated predominantly with combination immunotherapy (Table 1) during longitudinal follow-up and remained on combination immunotherapy with 3.1 ± 1.3 (mean ± SD) individual therapies at the last follow-up visit available for this analysis. Non-ILD patients remained on a mean combination of 2.0 ± 1.3 therapies at the last follow-up visit (p =0.06 vs ILD group). 18 ILD patients had short-term (∼2 yr) follow-up PFT data available (1.8 ± 0.6 years from baseline PFT), and

10 ILD patients had both short-term (~2 yr) and long-term follow-up PFT data available (2.0 ± 0.6 and 6.8 ± 3.4 years from baseline PFT, respectively).In analysis of both cohorts, significant improvements in % predicted DLCOHg, FVC, and FEV1 were noted over time (Tables 2-3). In the long-term cohort, continued improvement in pulmonary function beyond the initial follow-up visit at ~2 years with progressive increases in % predicted DLCOHg, FEV1, and FVC at ~ 7 years were noted (Table 3).

Conclusion: A low mortality rate and significant improvements in pulmonary function over long-term follow-up were observed in a North American cohort of MDA5 ab positive patients with ILD treated predominantly with combination immunomodulatory therapy. These results emphasize the importance of early identification and aggressive treatment of MDA5 ab positive DM patients with ILD who may have reversible impairment in lung function.

Table 1. Clinical data for MDA5 ab positive dermatomyositis patients with and without interstitial lung disease (ILD)

	ILD (n=24)	No ILD (n=6)
Demographics		
Age, years	49 ± 3	30 ± 5 *
Sex, female	16(67)	4(67)
Ethnicity, Hispanic	1(17)	5(19)
Race, white	13(54)	3(50)
Clinical Characteristics†		
Required Hospitalization for DM	18(75)	5(83)
Inflammatory Arthritis	15(63)	6(100) *
Proximal Muscle Weakness	21(88)	4(67)
Rash	24(100)	6(100)
Dysphagia	6(25)	2(33)
Voice Hoarseness	9(38)	3(50)
Calcinosis	4(17)	1(17)
Cutaneous Ulcerations	9(38)	1(17)
Fever	5(21)	1(17)
Weight Loss	8(33)	2(33)
Myalgia	8(33)	0(0)
Oral Ulcers	6(25)	0(0)
Heart Failure	0(0)	1(17) *
Pulmonary Hypertension	1(4)	0(0)
Raynaud's Phenomenon	5(21)	2(33)
Medications ††		
Corticosteroids	15(63)	2(33)
Mycophenolate Mofetil	16(67)	4(67)
Intravenous Immunoglobulin	19(79)	4(67)
Rituximab	14(58)	1(17)
Cyclophosphamide (oral)	2(8.3)	0(0)
Tofacitinib	2(8)	1(17)
Tacrolimus	1(4)	0(0)
Hydroxychloroquine	3(13)	0(0)
Leflunomide	1(4)	0(0)
Azathioprine	0(0)	0(0)
Methotrexate	0(0)	0(0)
TNF-inhibitor	0(0)	0(0)
Disease duration at last follow-up (yrs)	6.7 ± 1.8	4.0 ± 0.8

Values are mean±SEM or n (%). * p <0.05 versus ILD group.
†Clinical features noted on disease presentation.
†† Medications at most recent follow-up visit.

Table 2. Longitudinal Pulmonary Function Test Results in Short-Term Follow-up Cohort

	Baseline (n=18)	2-year follow up (n=18)
DLCO Hg (% predicted)	55.4±3.6	72.2±4.0*
FVC (% predicted)	73.3±4.6	89.2±4.1*
FEV1(% predicted)	75.9±4.6	91.4±4.8*
FEV1/FVC	89.3±3.4	84.4±2.1
FVC/DLCO	1.4±0.1	1.3±0.1

Values are mean±SEM. * p <0.05 versus baseline. N= 17 per group for FEV1/FVC analysis.
Disease duration from baseline PFT to 2-year follow-up PFT = 1.8 ± 0.6 years (Mean ± SD).

Table 3. Longitudinal Pulmonary Function Test Results in Long-Term Follow-up Cohort

	Baseline (n=10)	2-year follow-up (n=10)	Long-term follow-up (n=10)
DLCO Hg (% predicted)	57.7±5.8	65.5±4.4	77.7±4.6*
FVC (% predicted)	72.4±6.7	85.3±6.4	96.4±4.9*
FEV1(% predicted)	75.8±6.5	87.7±6.9	96.1±4.9*
FEV1/FVC	94.5±5.0	86.6±3.6	77.9±1.4 *
FVC/DLCO	1.4±0.1	1.3±0.1	1.3±0.1

Values are mean±SEM. * p <0.05 versus baseline. N= 9 per group for FEV1/FVC analysis.
Disease duration from baseline PFT to 2-year follow-up PFT = 2.0 ± 0.6 years (Mean ± SD).
Disease duration from baseline PFT to long-term follow-up PFT= 6.8 ± 3.4 years (Mean ±SD).

Disclosure: J. Cheah: None; **S. Bae**: None; **T. De Leon**: None; **Y. Lee**: None; **C. Charles-Schoeman**: AbbVie, 2, 5, Alexion, 5, BMS, 2, 5, Boehringer Ingleheim, 2, 5, CSL Behring, 5, Galapagos, 2, Pfizer, 2, 5, Priovant, 2, 5, Recludix, 2.

Abstract Number: 1166

Patients with COVID-19 and Polymyositis Inpatient Outcomes and Hospital Cost: Nationwide Inpatient Sample 2020

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SESSION INFORMATION
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Background/Purpose: During the COVID-19 pandemic, there were growing concerns regarding the impact of SARS-CoV-2 on not only patients with rheumatic diseases but also the national hospital system. Research from prior studies on rheumatic and musculoskeletal diseases have identified higher rates of COVID-19 infection and higher mortality rate on a global scale; however, there is scant information on the economic burden on patients and the hospital system. In our study, we aim to analyze the demographic trend and inpatient hospital impact in the United States among patients admitted with concomitant COVID-19 infection and polymyositis.

Methods: We used the National Inpatient Sample (NIS), which is the largest public inpatient database of community hospitals, from 2020 and extracted adult patients (age 18 years and older) with the principal diagnosis of COVID-19 and secondary diagnosis of polymyositis based on the International Classification Disease version 10 (ICD-10) codes. All diagnoses were weighted to be nationally representative. Demographic characteristics, length of stay, hospitalization cost, and co-morbidities were analyzed using STATA, version 17. Pearson chi-squared test was used to compare categorical variables and studentt-test was used to compare continuous variables. Multivariable logistic regression was used to compare mortality with p-value set at < 0.05 for statistical significance.

Results: 32,355,827 hospitalizations were included in the NIS 2020 database and 1,644,600 patients met our inclusion criteria. 365 patients with COVD-19 and polymyositis were admitted in 2020. Patients with COVID-19 as a primary diagnosis and polymyositis as a secondary diagnosis had a 1.98 times higher mortality than those with a diagnosis of COVID-19 alone (OR: 1.98, 95% CI: 1.15-3.42, p=0.01). COVID-19 cohort had average age of 63 years and 52.1% male compared to COVID-19 and polymyositis cohort who had average age of 62 years and 68.5% female. For COVID-19 patients, they were predominantly White, average hospital stay of 8days,and hospital cost $91,446. For COVID-19 and polymyositis cohort, they had a greater percentage of Black patients, predominantly female, average hospital stay of 8 days, and hospital cost $106,700. For co-morbidities, COVID-19 and polymyositis patients had a higher percentage of coronary artery disease and previous myocardial infarction (Table 1).

Conclusion: Both cohorts were predominantly treated at large teaching hospitals, approximate mean age of 60 years old, and over half of each cohort had hospital cost greater than their median household income. Despite these similarities between both groups, patients with pre-existing diagnosis of polymyositis with concomitant COVID-19 infection had almost double the inpatient mortality compared to patients who were hospitalized for COVID-19 alone. Our study highlights the importance of targeting at-risk patient demographics, particularly Black women who were more likely to be hospitalized for concomitant polymyositis and COVID-19 infection. This study not only augments prior research on inflammatory myopathy and COVID-19 infection, but also underlines the increased mortality risk and hospital cost in the American population.

Table 1: Baseline characteristics of COVID-19 patients with and without polymyositis

	COVID-19	COVID-19 and polymyositis	*p*-value
n	1,644,235	365	
Age (mean)	63.2	62.2	
Sex (%)			< 0.0001
Male	856,646 (52.1)	115 (31.5)	
Female	787,589 (47.9)	250 (68.5)	
Race (%)			0.129
White	835,271 (50.8)	147 (40.3)	
Black	312,404 (19.0)	147 (40.3)	
Hispanic	355,154 (21.6)	66 (18.1)	
Asian or Pacific Islander	54,260 (3.3)	0 (0.0)	
Native American	16,442 (1.0)	0 (0.0)	
Other	70,702 (4.3)	5 (1.4)	
Median household income by quartile (%)			0.000
Quartile 1 ($1-42,999)	559,040 (34.1)	125 (34.3)	
Quartile 2 ($50,000-64,999)	445,588 (27.2)	100 (27.4)	
Quartile 3 ($65,000-$85,999	366,664 (22.2)	80 (21.9)	
Quartile 4 ($86,000+)	272,943 (16.6)	60 (16.4)	
APR-DRG Mortality Score (%)			0.000
Score = 0-1 (Minor)	0 (0.0)	0 (0.0)	
Score = 2 (Moderate)	292,674 (17.8)	15 (4.1)	
Score = 3 (Major)	764,569 (46.4)	220 (60.3)	
Score = 4 (Extreme)	586,992 (35.7)	130 (35.6)	
Payer status			0.000
Medicare	831,983 (50.6)	214 (58.4)	
Medicaid	238,414 (14.5)	30 (8.3)	
Private insurance	435,722 (26.5)	81 (22.2)	
Self-Pay	62,481 (3.8)	10 (2.8)	
No Charge	3,288 (0.2)	0 (0.0)	
Other	72,346 (4.4)	30 (8.3)	
Hospital Region (%)			0.003
Northeast	304,184 (18.5)	50 (13.7)	
Midwest	361,731 (22.0)	90 (24.7)	
South	675,781 (41.1)	145 (39.7)	
West	302,539 (18.4)	80 (21.9)	
Hospital location and teaching status (%)			0.000
Rural	161,135 (9.8)	15 (4.1)	
Urban non-teaching	307,472 (18.7)	80 (21.9)	
Urban teaching	1,175,628 (71.5)	270 (74.0)	
Hospital bed size (%)			0.000
Small	401,193 (24.4)	60 (16.5)	
Medium	476,828 (29.0)	91 (25.0)	
Large	766,214 (46.6)	214 (58.6)	
Co-morbidities			
Coronary artery disease	210080 (12.8)	80 (21.9)	< 0.0001
Chronic kidney disease	213585 (13.0)	25 (6.8)	< 0.0001
Chronic obstructive pulmonary disease	54300 (3.3)	20 (5.5)	< 0.0001
Hypertension	578190 (35.2)	100 (27.4)	< 0.0001
Obesity	342185 (20.8)	60 (16.4)	< 0.0001
Previous myocardial infarction	39570 (2.4)	10 (2.7)	< 0.0001
Type 2 diabetes mellitus	248725 (14.5)	25 (6.8)	< 0.0001

Disclosure: E. He: None; **V. Sandhu**: Exagen, 2, 5.

Abstract Number: 1167

Transcriptome Analysis of Peripheral Blood Reveals Superiority of the Triple Combination of Baricitinib, Rituximab, and Tacrolimus Therapy (BRT-Tx.) for anti-MDA5 Antibody-positive Dermatomyositis (MDA5-DM)

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

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Background/Purpose: MDA5-DM is characterized by high mortality due to rapid progressive ILD. We reported that in MDA-5DM, (1) RIG-1-like receptor signaling is enhanced, (2) antiviral responses are also enhanced, and (3) the key for survival is suppression of RIG-I-like and IFN signaling (ACR2022, Oral 0508).Our experience with an autopsy case suggests that uncontrolled activation of macrophages may play a role in the etiology of ILD. Recently, it has been reported that tacrolimus (TAC) and cyclophosphamide (CY) combination therapy (TC-Tx) administered early in the course of the disease improved the prognosis, however, some cases could not be saved.

Therefore, we devised BRT therapy (BRT-Tx).The regimen of the treatment combines baricitinib (BAR), which inhibits GM-CSF and IFN signaling and effectively suppresses uncontrolled macrophages, with rituximab (RTX) and TAC, which rapidly inhibits B cell-T cell interaction and ultimately prevents anti-MDA5 antibody production. In this report, we determine the differences in gene expression between BRT- and TC-Tx for MDA5-DM patients in peripheral blood.

Methods: Transcriptome of peripheral blood from 6 MDA5-DM (TC: 3, BRT: 3) patients with multiple poor prognostic factors were analyzed. Differentially expressed genes (DEGs) were identified between pre- and 2-3 months after treatment. Geneontology (GO), clustering, and gene set variation analysis(GSVA) were performed for the DEGs. As one BRT case was added since our last year's presentation, we reanalyzed the difference between surviving and fatal cases. The IFN signature was scored separately for Types 1, 2, and 3, and the changes between pre- and post-treatment were investigated.

Results: Two of three cases with TC died during treatment, while all three cases on BRT recovered. Cluster analysis of DEGs separated fatal cases from survivors, not by the type of treatment. Comparing surviving and fatal cases, GO analysis revealed that the immune system via immunoglobulins and B cells was significantly suppressed in surviving cases. GO analysis of DEGs in each therapeutic group showed that expression of B cell-related genes were significantly suppressed after BRT-Tx. Meanwhile, TC-Tx significantly suppressed such pathways as cell proliferation, and was less specific for the target cells than BRT-Tx. The changes in IFN signature score after treatment showed an increase in type 2 and 3 IFN scores in all fatal cases and an increase in type 1 IFN score in one fatal case.

Conclusion: BRT-Tx significantly suppressed gene expression associated with B cells, while TC-Tx was characterized by low specificity of therapeutic targets. Comparison of surviving and fatal cases revealed that the combination of RTX was a key to success, as suppression of the immune system via immunoglobulins and B cells is the critical for survival. Analysis of the IFN signature revealed an increase in the IFN score after treatment in fatal cases, indicating that the combination of BAR is beneficial. The superiority of BRT-Tx seems clear from the fact that all patients survived while only one/three patients survived with TC therapy. This regimen is also superior to the existing TC regimen in terms of cytotoxicity and can become the standard of care in the future.

Disclosure: Y. Koyama: AbbVie/Abbott, 5, 6, Asahikasei, 6, Ayumi, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 5, Mitsubishi Tanabe, 6, Novartis, 5; **Y. Sato**: None; **Y. Nakai**: None; **M. Tokunaga(Sakamoto)**: None.

Abstract Number: 1168

Evaluation of Agreement Between Functional and Radiological Changes in Idiopathic Inflammatory Myositis (IIM) Associated Interstitial Lung Disease (ILD)

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SESSION INFORMATION

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Background/Purpose: ILD is a major cause of morbidity and mortality in IIM. The diagnosis and progression of ILD often relies on high resolution computed tomography (HRCT) and pulmonary function tests (PFT). The goal of this study is to assess the agreement between functional and radiological changes longitudinally in patients with IIM-ILD.

Methods: This is a retrospective study on patients in the Northwell Myositis cohort. All patients met 2017 EULAR/ACR classification criteria for IIM. ILD diagnosis was identified by chart review and by presence of NSIP, COP/BOOP, UIP, and unspecified patterns on HRCT. We included 22 patients who had >2 corresponding HRCT and PFT, performed within 6 months of each other. Qualitative ILD patterns are reported using descriptive statistics.

Baseline FVC, FEV1, and DLCO values were collected, and percent changes were calculated for subsequent PFTs from baseline. Improvement or worsening was defined as ≥ 10% increase or decrease in 1 variable with no more than 5% decrease or increase in other variables. HRCT scans were categorized as improved, stable or worsened compared to the previous scan per radiologist assessment.

There were 65 matched HRCT/PFT pairs, ranging from 2 to 5 pairs per patient. Using initial HRCT and PFT as baseline, improvement, stability or worsening were assessed for 43 matched pairs using the above definition. Kappa statistics was calculated to measure the agreement between the changes seen on PFT versus HRCT.

Results: A total of 22 patients with median age of 57.5 years were included in the study. The average follow-up time was 5 years (range: 1-13years). The most common HRCT finding at baseline was bilateral groundglass opacities (77.3%, 17/22), followed by reticular opacities (36.4%, 8/22). The most common initial immunosuppressive agent in addition to steroid was mycophenolate mofetil (54.5%, 12/22), followed by methotrexate (18.2%, 4/22), azathioprine (9%, 2/22), and rituximab (9%, 2/22). Two patients received steroids alone and 1 patient declined treatment.

At baseline, mean FVC was 67% (SD:19. 3), mean FEV1 was 68.6% (SD:21.1), mean DLCO was 48.5% (SD:16.9). On PFT, 13.6% (3/22) patients worsened, 27.3% (6/22) were stable, and 59.1% (13/22) improved. On HRCT, 22.7% (5/22) patients worsened, 54.5% (12/22) were stable, 22.7% (5/22) improved.

Table 1 showed HRCT and PFT status change

		HRCT status		
		Worsened	Stable	Improved
Overall PFT status	Worsened	2	6	0
	Stable	3	10	2
	Improved	0	15	5

Agreement of improvement, stability or worsening for the follow-up pairs of HRCT and PFT is shown in Table 1. Kappa coefficient between these pairs was 0.071 (SE = 0.102, 95% CI -0.129 to 0.272), indicating poor agreement. When analysis was performed by combining improved and stable in one category, the coefficient marginally increased to 0.192 (SE = 0.181, 95% CI -0.129 to 0.272)

Conclusion: When comparing the agreement of HRCT and PFT to assess change in ILD status over time in this study, we found that more patients showed improvement on PFT than HRCT. While PFT was more likely to detect improvement, HRCT was more likely to document stability. The poor agreement between functional and radiological changes demonstrated in this study suggested the deficiency in current methods for monitoring ILD progression. More sensitive modalities are needed to detect change over time in patients with immune-mediated ILD.

Disclosure: S. Narain: None; **C. Hu**: None; **M. Liu**: None; **H. Vashistha**: None; **K. Shargani**: None; **G. Marder**: None.

Abstract Number: 1169

All-cause Mortality and Risk Factors for Death in a Large Multi-center Prospective Registry Cohort of Idiopathic Inflammatory Myositis in China

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SESSION INFORMATION
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Background/Purpose: Our study depicted the mortality and independent risk factors of IIM patients in a large multi-center prospective registry cohort in China.

Methods: Patients registered before 31st, December 2021 in the Chinese Rheumatism Data Center-Myositis Registry (CRDC-MYO) were included. Juvenile patients, patients with malignancy at baseline, or patients complicated with other CTD were excluded. Baseline and follow-up data were collected from CRDC-MYO registry database. Death information was obtained from the Chinese Center for Disease Control and Prevention's disease surveillance points system. Kaplan-Meier Curves and Log-rank test was used to compare the mortality. Univariable and multivariable Cox hazards regression analysis were used to identify potential risk factors for death.

Results: 4534 IIM cases were finally enrolled, including 2902 dermatomyositis (64.0%), 592 polymyositis (13.1%), 927 anti-synthetase syndrome (20.4%), and 113 immune-mediated necrotising myopathy (2.5%). 510 deaths in total were recorded. The cumulative survival at 1, 3, 5 and 10 years were 92.6%, 88.6%, 86.2%, and 80.5% (Figure 1a). Significant differences ($P < 0.05$) in survival between different subgroups (Figure 1b) as well as different myositis-specific antibodies were confirmed by log-rank test (Figure 1c). Malignancy (18.8%), interstitial lung disease (18.8%), cardiovascular diseases (18.8%), and infections (18.6%) were the most common causes of deaths (Figure 2a). We observed a shift in the predominant causes of death from pulmonary interstitial disease and infection within the initial three-year period to tumor and cardiovascular

diseases in the subsequent years as the follow-up time extended (Figure 2b). There is significant variation in the composition of causes of death among myositis patients with different antibodies (Figure 2c). Patients with positive anti-TIF1γ antibody commonly succumb to malignancies, whereas patients with positive anti-MDA5 antibody and anti-Jo-1 antibody frequently experience mortality due to interstitial lung disease. Multivariable Cox regression analysis confirmed male (HR=1.53, 95%CI 1.27-1.83), ferritin≥420ng/ml (2.95 [1.85-4.71]), lymphocytopenia (1.89 [1.51-1.38]), ILD (1.28 [1.02-1.60]), anti-MDA-5 antibody (1.53 [1.21-2.20]), and anti-TIF1γ antibody (1.75 [1.16-2.64]) as independent risk factors, and anti-Jo-1 antibody (0.56 [0.40-0.78]) as protective factor for mortality after adjusting for age (Figure 3).

Conclusion: Patients with positive anti-MDA5 antibody exhibited the most rapid decline in survival rate during the first year, whereas patients with anti-TIF1γ antibody had a worse prognosis over a longer follow-up period. This might be attributed to the fact that causes of mortality among myositis patients vary over time, with anti-TIF1γ-positive patients being more susceptible to malignancies. In addition to interstitial lung disease, myositis-specific antibodies appeared to exert a more deci-

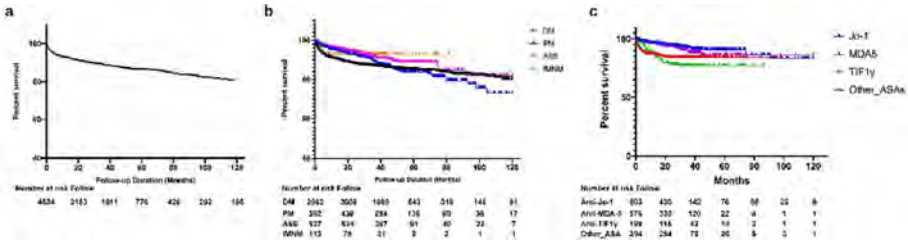

Figure 1 Kaplan-Meier curves for: a. the entire idiopathic inflammatory myositis patients in Chinese Rheumatism Data Center-Myositis Registry (CRDC-MYO); b. patients in different myositis subtypes; c. patients with different myositis-specific antibodies.

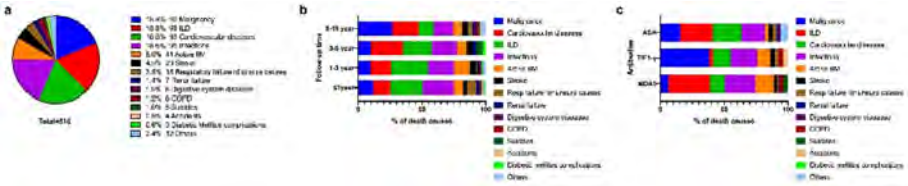

Figure 2 a. Death causes of IIM patients in CRDC-MYO registry. b. Death causes during various follow-up periods. c. Death causes among patients with varying myositis-specific antibody profiles.

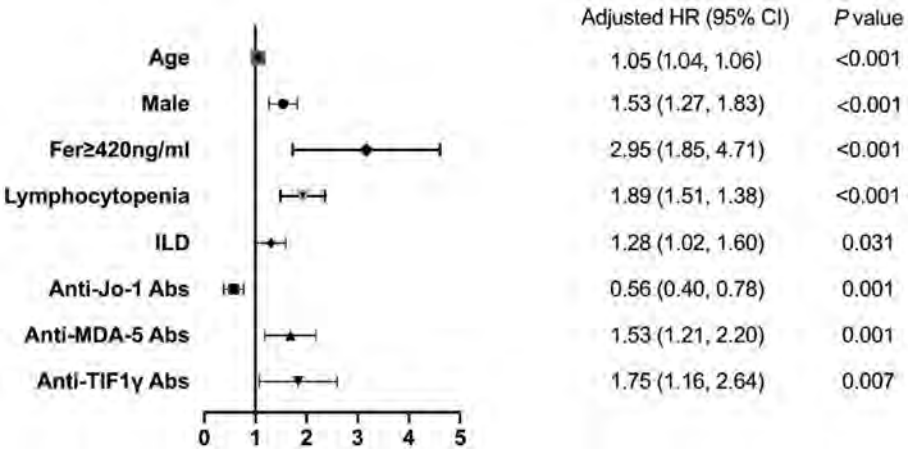

Figure 3 Independent risk factors for death after adjusting for age using multivariable Cox regression analysis.

sive influence on the prognosis of myositis patients compared to other clinical manifestations. This suggests that future classification of myositis patients based on myositis-specific antibodies might be more rational.

Disclosure: L. Peng: None; **P. Yin**: None; **M. Li**: None; **Q. Wang**: None; **Y. wang**: None; **S. Zhou**: None; **c. wu**: None; **J. zhao**: None; **D. xu**: None; **M. Li**: None; **x. Zeng**: None.

Abstract Number: 1170

Damage Accrual in Idiopathic Inflammatory Myopathies: Data from a Monocentric Cohort and Impact on Patients' Quality of Life

Chiara Cardelli[1], Simone Barsotti[2], Elenia Laurino[1], Michele Diomedi[1], Federico Fattorini[1], Alessandra Tripoli[1], Linda Carli[1] and Marta Mosca[1], [1]Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy, [2]Internal Medicine, Ospedale di Livorno, Pisa, Italy

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
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Background/Purpose: Although the prognosis of Idiopathic Inflammatory Myopathies (IIMs) has noticeably improved over time, their chronicity may still expose a considerable number of patients to the development of persistent damage. The purpose of the study was a retrospective analysis of damage accrual in a monocentric cohort of IIM patients, with the aim of also finding possible correlations with epidemiological and clinical data and assessing the impact of damage on patients' quality of life (QoL).

Methods: Consecutive adult patients with a diagnosis of IIM (2017 EULAR/ACR criteria) for at least one year and regularly followed at our Myositis Clinic were recruited. Demographic and clinical features were recorded. At the last follow-up, the Myositis Damage Index (MDI) was applied. IIM activity was evaluated according to the International Myositis Assessment and Clinical Studies Group Disease Activity Core Set Measures. To investigate QoL, patients were asked to fill in generic Patient Reported Outcomes (PROs). Results were reported as mean±SD or median (IQR) for continuous variables and as percentage for categorical variables. Intergroup comparisons were assessed by using chi-square and Mann-Whitney tests, as appropriate. Spearman's coefficient was used to analyse correlations between variables. P values < 0.05 were considered significant.

Results: Eighty IIM patients were enrolled. Demographic and clinical features of the cohort are shown in Table 1. Overall, 78 patients (97.5%) developed at least one item of damage. Using the MDI tool, the damage was represented as follows: global damage VAS 0.75 (0.92); MDI extent of damage score 10.8% (±6.9); MDI severity of damage score 8.2% (10.0). As expected, damage correlated positively with patients' age ($r=0.467$, $p< 0.001$) and disease duration ($r=0.302$, $p=0.007$). A greater damage was associated with cumulative muscle ($p=0.044$) and oesophageal ($p=0.005$) involvement. A positive correlation emerged between damage and the cumulative dose of glucocorticoids ($r=0.404$, $p=0.003$), even when adjusted for patients' age. Correlations were also found between a greater damage accrual and a history of treatment with mycophenolate mofetil ($p=0.039$), cyclophosphamide ($p=0.045$) and immunoglobulins ($p=0.007$). Among disease activity measures, damage correlated with Physician and Patient Global Assessment, Health Assessment Questionnaire (all $r\geq0.322$, $p\leq0.015$) and Manual Muscle Testing-8 ($r< -0.436$, $p< 0.001$) at the last follow-up. As for patients' QoL evaluated by PROs, a higher global damage correlated negatively with several domains of the Short Form-36 and with fatigue assessed by the Functional Assessment of Chronic Illness Therapy (all $r\leq-0.332$, $p\leq0.021$) and positively with the depression subscale score of the Hospital Anxiety and Depression Scale and with activity impairment assessed by the Work Productivity and Activity Impairment Questionnaire (all $r\geq0.367$, $p\leq0.023$).

Table 1. Demographic and clinical characteristics of the cohort of IIM patients.

IIMs cohort (N=80)	
Female	47 (58.8%)
Mean age	66.5 ± 13.4 years
Mean disease duration	8.2 ± 5.6 years
Disease subset	
Polymyositis	40 (50%)
Dermatomyositis	37 (46.3%)
Inclusion body myositis	3 (3.7%)
Anti-synthetase syndrome	21 (26.3%)
Cumulative organ involvement	
Muscular involvement	75 (93.8%)
Cutaneous involvement	37 (46.3%)
Oesophageal involvement	53 (66.3%)
Pulmonary involvement	39 (48.8%)
Cardiac involvement	11 (13.8%)
Microvascular involvement	37 (46.3%)
Articular involvement	16 (20.0%)
Cumulative treatments	
Glucocorticoids (GCs)	80 (100%)
Mean cumulative GCs dose (methylprednisolone equivalent)	10.4±10.3 g (min. 0.4 – max. 57.2)
Mean GCs daily dose (at the last follow-up)	4.4±3.3 mg (min. 1 – max. 20)
Methotrexate	45 (56.3%)
Azathioprine	13 (16.3%)
Cyclosporin A	29 (36.3%)
Mycophenolate mofetil	15 (18.8%)
Cyclophosphamide	30 (37.5%)
Leflunomide	1 (1.3%)
Rituximab	12 (15.0%)
Tofacitinib	1 (1.3%)
Anakinra	1 (1.3%)
Hydroxychloroquine	32 (40.0%)
Immunoglobulins (intravenous or subcutaneous)	37 (46.3%)

Conclusion: IIMs are conditions burdened by a significant damage accrual that can lead to disability and significantly impact patients' QoL, emphasising the need for appropriate strategies to reduce its accumulation, that still represents an unmet need for these patients.

Disclosure: C. Cardelli: None; **S. Barsotti**: None; **E. Laurino**: None; **M. Diomedi**: None; **F. Fattorini**: None; **A. Tripoli**: None; **L. Carli**: None; **M. Mosca**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, GlaxoSmithKlein(GSK), 2, Otsuka, 2, UCB, 2.

Abstract Number: 1171

Cardiac Biomarkers Are a Useful Initial Screening Tool for Myocarditis in Patients with Idiopathic Inflammatory Myopathies

Caoilfhionn M. Connolly[1], Jana Lovell[2], Melody Chung[3], Brittany Adler[2], Jemima Albayda[2], Eleni Tiniakou[2], Christopher Mecoli[1], Stefan Zimmerman[2], Lisa Christopher-Stine[2], Nisha Gilotra[2] and Julie Paik[2], [1]Johns Hopkins University School of Medicine, Baltimore, MD, [2]Johns Hopkins University, Baltimore, MD, [3]Kaiser Permanante, Baltimore, MD

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

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Background/Purpose: Myocarditis in idiopathic inflammatory myopathies (IIM) is poorly understood despite its associated morbidity and mortality. As manifestations of myocarditis can be mild or subclinical in IIM, early detection is crucial to inform clinical decision-making. Currently, there is a paucity of guidance on optimal myocarditis screening among IIM patients, and there is a critical need to enhance early detection of this potentially fatal disease manifestation to improve clinical outcomes. Thus, we sought to prospectively screen newly diagnosed IIM patients in a rigorously phenotyped cohort to (i) determine the prevalence of myocarditis, (ii) identify risk factors associated with myocarditis and (iii) assess the utility of baseline serum cardiac biomarkers as initial screening to inform the need for advanced cardiac evaluation

Methods: Consecutive patients with a clinician verified new diagnosis of IIM based on either ACR/EULAR or Bohan and Peter classification criteria for IIM evaluated at a single center were recruited from 7/1/2022-3/30/2023; new diagnosis was defined as within one year of symptom onset. IIM subgroups ofpolymyositis (PM), dermatomyositis (DM), antisynthetase syndrome (ASyS), immune-mediated necrotizing myopathy (IMNM), and overlap systemic sclerosis (SSc)/myositis were included; those with inclusion body myositis were excluded. Eligible patients underwent cardiac serum biomarkers (troponin I/high-sensitivity troponin and NT-proBNP), electrocardiography, transthoracic echocardiogram (TTE) and cardiac MRI (cMR). Lake Louise Criteria was used for the diagnosis of myocarditis by cMR requiring 2 of 3 positive criteria for

Table 1. Clinical characteristics of 26 newly diagnosed IIM patients stratified by presence/absence of myocarditis

	Myocarditis present n=6	Myocarditis absent n=20	p-value*
Age median (IQR)	51 (35.5-57.5)	51 (40-64)	0.41
Female	5 (83.33)	17 (85)	0.67
Race			0.29
Black	0 (0)	5 (25)	
Hispanic	1 (16.67)	1 (5)	
White	5 (83.33)	14 (70)	
Diagnosis category			0.26
Antisynthetase syndrome	2 (33.33)	2 (10)	
Dermatomyositis	1 (16.67)	4 (20)	
Immune mediated necrotizing myopathy	0 (0)	7 (35)	
Overlap SSc/IIM	3 (50)	7 (35)	
Presentation in hospital	4 (66.67)	1 (5)	0.01
*Immunosuppressive agent included in regimen.^*			0.68
Mycophenolate mofetil	4 (66.67)	9 (45)	
Methotrexate	1 (16.67)	3 (15)	
Intravenous immunoglobulin	2 (33.33)	8 (40)	
Rituximab	0 (0)	2 (10)	
Combination therapy^$	4 (66.67)	7 (35)	0.64
Not on immunosuppressive therapy^	2 (33.33)	4 (20)	0.59
Peak CK (U/L) median (IQR)	2075.00 (336-4206)	1201.5 (178-8435.5)	0.71
Troponin positive	6 (100)	7 (35)	0.02
pBNP positive	6 (100)	6 (31.5)[&]	0.01
Both troponin/pBNP positive	6 (100)	4 (21)[&]	0.01
Reduced ejection fraction on echocardiogram	2 (33.33)	0 (0)	0.05
Cardiac events**	3 (50)	0 (0)	0.01

*Differences in population characteristics between those with myocarditis and those without were compared using Wilcoxon rank-sum test for continuous variables, and Fisher's exact test for binary or categorical variables. ^Therapy at the time of cardiac evaluation $More than 1 simultaneous immunomodulatory agent &1 missing value thus denominator 19 **includes heart failure event, cardiac hospitalization, arrhythmia and death

evidence of hyperemia, edema, and myocardial necrosis/fibrosis. Clinical cardiac events, including heart failure events, arrhythmia events, cardiac hospitalization and death were monitored throughout follow up to 6/7/2023.

Results: Among 26 patients, 85% were female (22/26) and the most common diagnosis was that of overlap SSc/IIM (11/26; 42%) followed by IMNM (6/26; 23.1%). 15/26 (57.7%) had elevation in at least one serum biomarker, most commonly troponin I (13/15; 86.7%). 6/26 (23.1%) patients met Lake Louise Criteria by cMR for myocarditis. When compared to patients without myocarditis, those with myocarditis had numerically higher median CK (U/L) (2075.00 [IQR 336-4206] versus1201.5 [IQR 178-8435.5], p=0.71) and more frequently had elevations in both cardiac biomarkers (100% versus 21%; p=0.01) (Table 1). Among those with myocarditis, anti-Ku was the most common autoantibody (3/6), followed by anti-Scl70, anti-PL12 and anti-Zo (1/6 each). All patients with myocarditis received escalation in immunosuppressive therapy. Three patients (all with myocarditis) experienced clinical cardiac events; two were admitted for heart failure, while the other experienced arrythmia.

Conclusion: The frequency of myocarditis in this cohort was 23%. SSc/IIM overlap was the most prevalent subgroup among patients with myocarditis, suggesting that these patients may be at greater risk. All patients with myocarditis were positive for both cardiac biomarkers, which may represent a useful initial screening tool to inform the need for advanced cardiac imaging.

Disclosure: C. Connolly: None; **J. Lovell**: None; **M. Chung**: None; **B. Adler**: None; **J. Albayda**: Amgen, 5, Janssen, 5; **E. Tiniakou**: None; **C. Mecoli**: None; **S. Zimmerman**: None; **L. Christopher-Stine**: None; **N. Gilotra**: Kiniksa Pharmaceuticals, 2; **J. Paik**: None.

Abstract Number: 1172

Relapse Rate After Glucocorticoid-free Remission in Idiopathic Inflammatory Myopathies with Validation of the International Myositis Assessment & Clinical Studies Group (IMACS) Criteria for Remission and Relapse

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SESSION INFORMATION

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Background/Purpose: Our aim was to explore whether maintenance of remission in patients with idiopathic inflammatory myopathy (IIM) depends on glucocorticoids (GCs) after achieving remission. Therefor we aimed to evaluate long-term outcomes after GC-free remissions in patients with IIM and to determine factors associated with relapses. Secondly since the IMACS criteria for remission and relapse in IIM had not been fully validated [1], we examined their compatibility with statements of physicians.

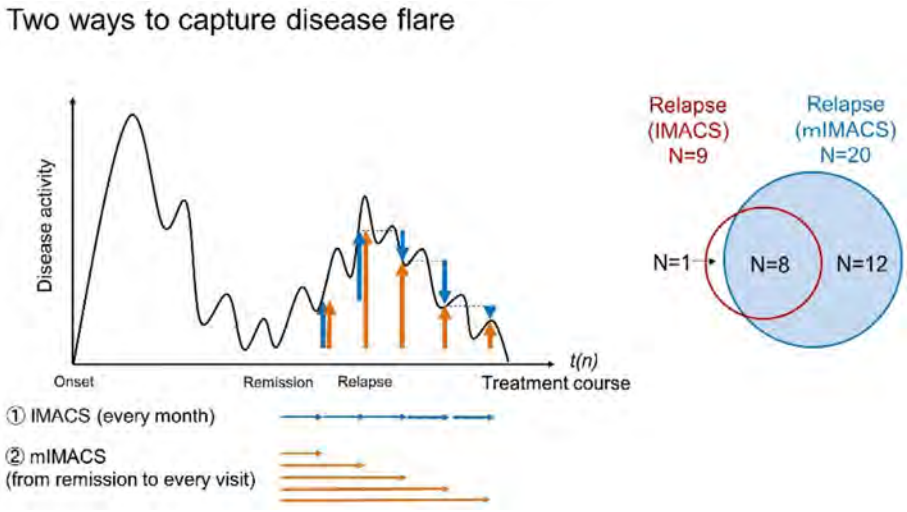
Methods: Data from prospectively followed patients with IIM in the Swedish Rheumatology Quality Register (SRQ) fulfilling the EULAR/ACR classification criteria were extracted and analyzed. For compatibilities of the definition of IMACS-remission, we investigated whether changes in IMACS core sets (CK, MMT8, extramuscular disease activity, patient-/physician-global assessment score (Pt-GA/Ph-GA), and health assessment questionnaire (HAQ)) were within 15% between 6 months before and after the physician's statements of remission/inactive [1].

Relapse was defined as either fulfilling IMACS criteria for relapse (within 20–30% changes in a month) [1] or administration of GC/immunosuppression (IS), which were validated against IMACS relapse criteria. Furthermore, to increase the sensitivity of relapse, a modified IMACS (mIMACS) criteria for relapse was defined as not only changes every month but also changes

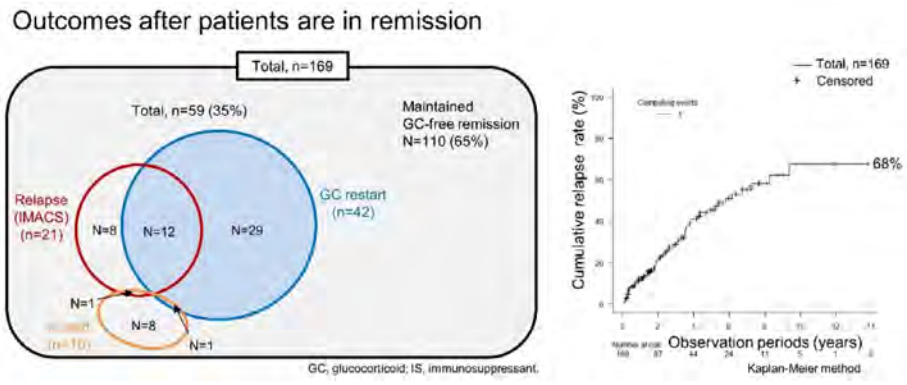
Table 1. IMACS core sets at 6 months before and after remission and their compatibilities to IMACS remission criteria

IMACS core sets at 3 time points								
	6 months before		At remission		6 months later		6M before vs remission	6M later vs remission
	N (%)	mean±SD	N (%)	mean±SD	N (%)	mean±SD	P	P
CK	142 (84%)	25.9±90.7	151 (89%)	2.6±3.6	144 (85%)	3.60±6.82	0.50	0.37
MMT8	143 (85%)	74.7±9.6	140 (83%)	76.7±5.8	139 (82%)	76.8±7.1	0.21	0.42
Extra muscular	7 (4%)	7.7±11.9	3 (2%)	8.3±11.8	0 (0%)	--	1	--
HAQ	147 (85%)	0.72±0.72	147 (85%)	0.51±0.60	149 (87%)	0.49±0.55	0.02	0.99
Pt-GA	146 (86%)	32.4±25.3	148 (88%)	25.6±25.2	145 (86%)	24.6±24.4	0.03	0.93
Ph-GA	143 (85%)	21.3±21.6	137 (81%)	9.2±10.1	145 (86%)	8.3±12.3	<.0001	0.22
Frequencies fulfilled IMACS remission criteria								
	Δ remission - 6 months before			Δ 6 months later - remission				
	N (%)			N (%)			P	
Δ CK	28 (22%)			30 (23%)			0.88	
Δ MMT8	109 (89%)			115 (95%)			0.15	
Δ Extra muscular	2 (100%)			--			1	
Δ Pt-GA	74 (56%)			90 (70%)			0.03	
Δ Ph-GA	76 (64%)			98 (81%)			0.004	
Δ HAQ	55 (42%)			66 (51%)			0.21	
Δ Total	23 (14%)			33 (20%)			0.19	
Periods (days)	241.7±201.8			264.7±184.2			0.03	

Steel-Dwass test for multiple analysis, Mann-Whitiney U test, Fisher's exact test. References: 1) Arthritis Rheum. 2005;52(9):2607-15.



Relapse determined by monthly changes (1, IMACS criteria, blue arrows, red circle), or changes from remission to a time point (2, modified IMACS criteria [mIMACS], orange arrows, blue circle).



Relapse after glucocorticoid-free remission are shown in the left figure (red circle, relapse difined by IMACS; blue circle, glucocorticoid re-start; yellow circle, immunosuppressant admistration). Cumulateve relapse rates during 14 years are shown by Kaplan-Meier method in the right figure. GC, glucocorticoid; IS, immunosuppressant; +, censored patients.

from remission to a visit (Fig. 1). Relapses were examined for up to 14 years, and factors affecting relapses were also explored using logistic regression analyses.

Results: Of 697 patients with IIM, 192 patients were excluded because of lacking outcome data, 169 patients were identified with GC-free remission. Their IMACS core sets were not worsened over 6 months after the physician's statement of remission/inactive. Variables that fulfilled IMACS-remission over 6 months before and after remission were CK (22%, 23%, respectively), MMT8 (89%, 95%), extra-muscular data (100%, no data), Pt-GA (56%, 70%), Ph-GA (64%, 81%), and HAQ (42%, 51%) (Table 1).

After GC-free remission, relapses were observed in 59 of the 169 patients, up to 9.4 years, with a cumulative relapse rate of 68% over 14 years for the Kaplan-Meier curve (Fig. 2). Twenty-one patients (36%) fulfilled IMACS criteria for relapse, including 9 patients with original IMACS criteria and 20 patients with mIMACS criteria (Fig. 1), in which IMACS core set was not significantly different. Relapses other than IMACS-relapse were defined as administration of GC/IS (n=38, Fig. 2). Characteristics in patients with IMACS-relapse were worsened CK, HAQ, Pt-GA, and Ph-GA. In contrast, Ph-GA and CRP worsened in patients with GC/IS defined relapse. Anti-Jo1 autoantibodies were shown as a risk factor for relapses by logistic regression analyses (odds ratio: 6.3, [95%CI: 1.11, 36.0]).

Conclusion: GC free remission using standard of care was achieved in 33% of patients with IIM. Cumulative relapse rate was recorded in 68% of these patients and occurred up to 9.4 years. Especially patients with anti-Jo1 autoantibodies are at risk to relapse. In addition, our real life data suggest that the criteria for remission and relapse in IMACS may need to be modified to fully capture disease flares.

Disclosure: H. Tsuji: ASAHIKASEI, 6, AstraZeneca, 6, Daiichi Sankyo, 6, GlaxoSmithKlein(GSK), 5, Japan college of rheumatology, 5, the Ichiro Kanehara Foundation, 5, the Mochida Memorial Foundation for Medical and Pharmaceutical Research, 5; **F. Espinosa-Ortega**: None; **M. Dastmalchi**: None; **I. Lundberg**: Argenx, 6, Astra-Zeneca, 5, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 1, Corbus Pharmaceutical, 6, EMD Serono Research & Development Institute, 6, Janssen, 6, Kezar, 6, Novartis, 11, Octapharma, 6, Orphazyme, 6, Pfizer, 1, Roche, 11, Xencor, 6; **K. Lodin**: None.

Abstract Number: 1173

Prognostic Biomarkers and Radiological Features of Idiopathic Inflammatory Myopathy Associated Interstitial Lung Disease

Toshimasa Shimizu[1], Haruna Matsuo[2], Tomohiro Koga[3], Noriho Sakamoto[4], Hiroshi Mukae[1] and Atsushi Kawakami[1], [1]Nagasaki University, Nagasaki, Japan, [2]Nagasaki University, Nagasaki City, Japan, [3]Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University, Nagasaki, Japan, [4]Department of Respiratory Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

SESSION INFORMATION

Session Date: Monday, November 13, 2023

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Background/Purpose: Idiopathic inflammatory myopathy (IIM) is a chronic inflammatory disorder involved in skeletal muscles. Interstitial lung disease (ILD) as an organ lesion is a common complication of IIM and may develop into rapidly progressive interstitial lung disease (RPILD), which can be life-threatening. Several myositis-specific antibodies, such as anti-melanoma differentiation-associated gene 5 (MDA5) and anti-aminoacyl-tRNA synthetase (ARS) antibodies, have been associated with developing ILD, which are associated with different prognoses. In addition, patients with IIM-associated ILD are characterized by several radiologic patterns. However, radiological patterns and prognostic biomarkers of IIM-associated ILDs remain obscure, especially in patients with the same antibody positivity. This study aimed to identify the radiological features and specific biomarkers for predicting the short-term prognosis of IIM-associated ILD.

Methods: We enrolled 116 patients with IIM-associated ILD, in either RPILD (n = 55) or non-RPILD (n = 61), who had visited the Department of Immunology and Rheumatology and the Department of Respiratory Medicine at Nagasaki University Hospital between February 2007 and July 2020. We retrospectively obtained the patient's demographics and clinical

Figure 1.

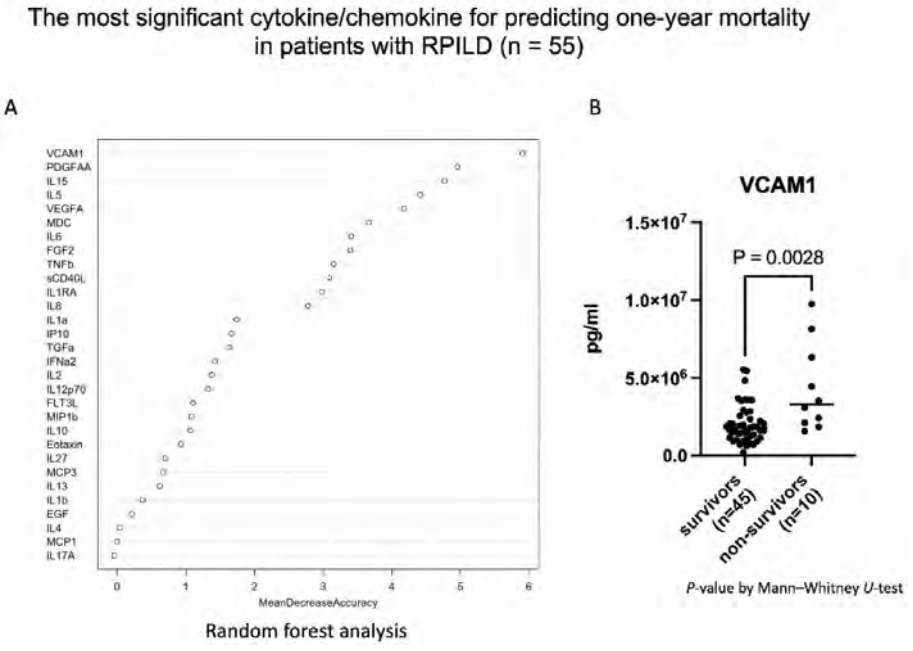

Figure 1. The most significant cytokine/chemokine for predicting one-year mortality in patients with RPILD

Figure 2.

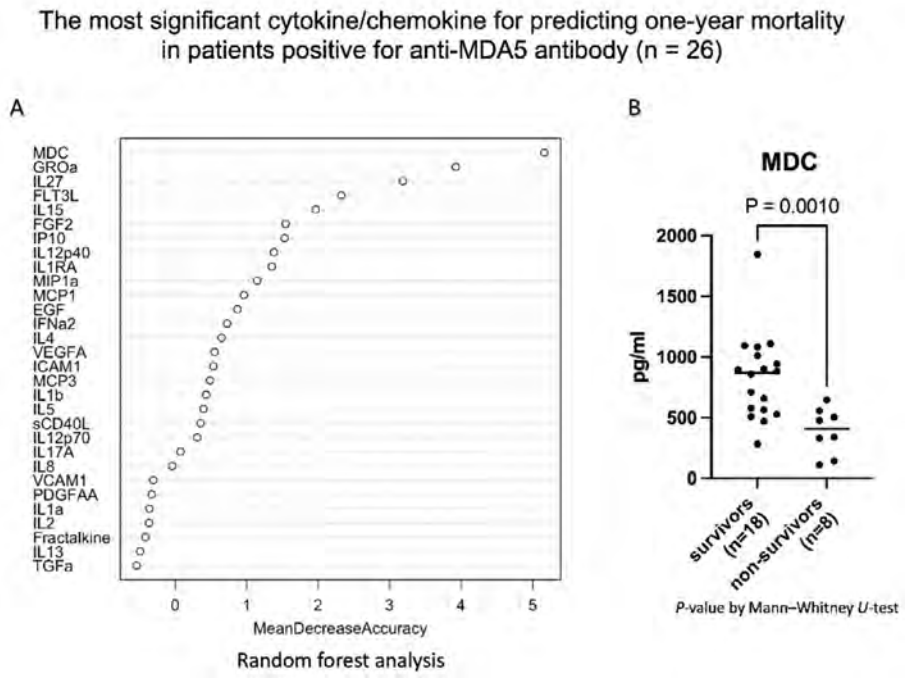

Figure 2. The most significant cytokine/chemokine for predicting one-year mortality in patients positive for anti-MDA5 antibody

characteristics using medical records. The high-resolution CT (HRCT) patterns of ILD, which included diffuse alveolar damage (DAD), nonspecific interstitial pneumonia (NSIP), organizing pneumonia (OP), NSIP with OP, and usual interstitial pneumonia (UIP) pattern, were classified by the experienced pulmonologist. Serum levels of 43 cytokines/chemokines were measured by a multi-suspension cytokine array. These serum variables were ranked by their importance by a multivariate classification algorithm termed random forest analysis.

Results: The one-year mortality rate of patients with RPILD was higher than that with non-RPILD. Within the RPILD group, the HRCT patterns were categorized as follows: NSIP (45.5%), NSIP with OP (25.5%), OP (18.2%), DAD (7.2%), and other (3.6%) patterns. We found the most important cytokine/chemokine for predicting one-year mortality in the RPILD patients was vascular cell adhesion molecule-1 (VCAM-1) using random forest analysis (Fig. 1A). The levels of VCAM-1 were significantly higher in the RPILD groups with survivors than those with non-survivors (Fig. 1B).Among the patients with anti-MDA5 positive ILD, the HRCT patterns were classified as NSIP (46.2%), NSIP with OP (38.5%), OP (11.5%), and DAD (3.8%) patterns. Our random forest analysis revealed macrophage-derived chemokine (MDC), also known as CCL22, was the most significant cytokine/chemokine for predicting one-year mortality in the patients with positive for anti-MDA5 antibody (Fig. 2A). The MDC levels were significantly lower in the patients with survivors than in those with non-survivors (Fig. 2B). In addition, MDC was also the most significant cytokine to predict death within one year in the patients with anti-MDA5 positive RPILD.

Conclusion: This study identified a unique set of serum biomarkers that could predict the short-term prognosis of IIM-associated ILD and characteristic radiological features for each phenotype.

Disclosure: T. Shimizu: None; **H. Matsuo**: None; **T. Koga**: None; **N. Sakamoto**: None; **H. Mukae**: None; **A. Kawakami**: None.

Abstract Number: 1174

Anti-HMGCR Immune-mediated Necrotising Myopathy: Calculation of Incidence and Confirmation of Low Malignancy Risk in Two Independent Cohorts. a Retrospective Case Review

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SESSION INFORMATION

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Background/Purpose: Immune-mediated necrotising myopathy (IMNM) is a rare complication of statin therapy, associated with the development of anti-HMGCR antibodies directed against the enzymatic target of statins (3-hydroxy-3-methylglutaryl-CoA). We sought to calculate the incidence of anti-HMGCR IMNM and determine whether there is a malignancy association in two independent cohorts of anti-HMGCR positive patients presenting to specialist rheumatology services in Greater Manchester (GM), United Kingdom, and South Australia (SA), Australia.

Methods: Patients with detected anti-HMGCR antibodies (January 2018-December 2022) were identified. Demographics, statin exposure, details of any previous or current malignancy, date of self-reported symptom onset and peak creatine kinase (CK) level were recorded. Using population data from 2021 by the Office of National Statistics (GM: 2.9 million people) and the Australian Bureau of Statistics (SA: 1.8 million people), annual incidences were calculated.

Results: The combined incidence of anti-HMGCR IMNM in our cohorts was 0.9-2.4 per million person years over the study period (Table 1). There was more than a doubling of incidence in GM from 2021 to 2022 despite stable testing practices (57-68 tests for anti-HMGCR performed annually). Twenty-four patients (50% female, 71% Caucasian, median age 63.6 years, range: 18.5-89.9 years) from GM and eight (37.5% female, 63% Caucasian, median age 70.3 years, range: 57.9-82.2 years) from SA were identified with a median follow-up of 16.3 months (range: 1.03-58.7 months). The time from first self-reported symptom to anti-HMGCR antibody testing was shorter in SA than GM (median 6.8 *vs* 22.5 months). Three patients (all female, aged 18, 28 and 60 years) were statin-naïve. Most patients (18/29) were exposed to atorvastatin (3/29 to simvastatin, 3/29 to rosuvastatin, 5/29 unknown). The median duration of statin use prior to anti-HMGCR testing was

Table 1: Annual cases of anti-HMGCR myopathy and calculated incidence in Greater Manchester and South Australia

Table 1: Annual cases of anti-HMGCR myopathy and calculated incidence in Greater Manchester and South Australia

Year	Greater Manchester		South Australia		Combined incidence*
	Cases	Incidence*	Cases	Incidence*	
2022	9	3.1	2	1.1	2.4
2021	4	1.4	1	0.6	1.1
2020	4	1.4	2	1.1	1.3
2019	3	1.0	3	1.7	1.3
2018	4	1.4	0	0	0.9

*Incidences reported per million person years. Population for the calculation of incidence derived from 2021 census data (Greater Manchester: 2.9 million people and South Australia: 1.8 million people)

36 months (range: 1-120 months). Five patients had a history of prior malignancy (hepatocellular, parotid, prostate (2), renal); notably all except one (data unavailable) occurred more than five years prior to anti-HMGCR testing. The median peak CK was 5000U/L (range: 964-39076U/L). Where data was available, CK subsequently normalised in 8/27 (29.6%) (time from treatment to stable normal CK: median 12 months, range: 2.3-69.2 months) and 8/25 (32%) had regained normal muscle power. Where data was available, more than half (10/16, 62.5%) remained on prednisolone at time of latest review (median 8 months after anti-HMGCR testing, median dose 5.5mg daily)

Conclusion: We confirm that anti-HMGCR is a rare subtype of inflammatory myopathy and report a recent apparent increase in the incidence of anti-HMGCR IMNM in the GM cohort. We found no temporal association of anti-HMGCR IMNM with malignancy within the timeframes usually defined for cancer-associated myositis. The difference between GM and SA in time from self-reported symptom onset to anti-HMGCR testing likely reflects varying pathways of specialist referral. Further multi-site collaborations will help to clarify the epidemiology of anti-HMGCR IMNM.

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Abstract Number: 1175

Inclusion of All Myositis Specific Autoantibodies or Other Rashes Leads to Better Sensitivity but Lower Specificity of 2017 EULAR/ACR Myositis Classification Criteria for Dermatomyositis

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SESSION INFORMATION
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Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
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Background/Purpose: Idiopathic Inflammatory Myopathies (IIM), collectively known as myositis, are heterogeneous disorders characterized by muscle weakness and muscle inflammation. ACR/EULAR classification criterion for IIM was published in 2016 that showed the sensitivity and specificity for probable diagnosis 87%/82% without biopsies, and 93%/88% with biopsies. The criteria is currently being used in most clinical trials and research studies. However, it has been criticized for its lack of a full panel of autoantibodies as well as the non-inclusion of other Dermatomyositis-specific rashes. The aim of our study was to evaluate if the addition of other myositis-specific antibodies (MSAs) and/or DM rashes other than Gottron papules/sign or heliotrope rash would improve the accuracy of the criteria.

Methods: Data were obtained from a prospectively collected myositis registry at a single tertiary care center but retrospectively extracted in subjects with an initial visit between 1995 to 2020. The classification criteria dataset included all variables of 2017 EULAR/ACR as well as Bohan and Peter myositis classification criteria.Additional variables were verified by chart review if/when required and all variables and scores were cross-checked by 2 physicians. Classification scores were re-calculated by adding:

a. all non-Jo1 MSA/MAA receiving the same score as Jo-1,

b. all other DM rashes except Gottron papule/sign, and heliotrope (i.e., shawl sign, V-neck, holster sign, malar rash not sparing naso-labial fold, mechanics hands, periorbital edema) receiving the same score as Gottron papules.
c. both a & b.

Psychometric properties of the 2017 EULAR/ACR classification criteria and proposed modifications were calculated using the diagnosis made by expert rheumatologist physicians as the gold standard.

Results: 798 patients with IIM including 268 with dermatomyositis, 41 with clinically amyopathic dermatomyositis (CADM). In our analysis, 2017 EULAR/ACR showed 91% accuracy, with high sensitivity (87% and 73%) and specificity (94%, and 93%), with and without muscle biopsy, respectively. Bohan and Peter showed lower sensitivity and specificity of 57% and 74% respectively.

		Sensitivity	Specificity	Positive Predictive Value	Negative Predictive value	Accuracy
Bohan & Peter		57	74	59	72	67
Eular/ACR[1]	With Biopsy	87	94	90	91	91
	Without Biopsy	73	93	88	84	85
2. Eular/ACR with the addition of other MSA/MAA	With Biopsy	88	94	91	91	91.6
	Without Biopsy	77	93	88	86	87
3. Eular/ACR with the addition of other MSA[2]	With Biopsy	88	94	91	91	91.6
	Without Biopsy	77	93	88	86	87
4. Eular/ACR with addition of other DM Rashes	With Biopsy	96	86	84	97	90,7
	Without Biopsy	79	86	79	86	83
5. Eular/ACR with addition of other DM Rashes and all MSA/MAA	With Biopsy	96	86	84	97	90.7
	Without Biopsy	83	85	78	88	84
6. Eular/ACR with addition of other Rashes and other MSA	With Biopsy	96	86	84	97	90.7
	Without Biopsy	82	85	78	88	84

[1] Eular/ACR myositis classification criteria 2017
[2] MSA includes MDA5, TIF1y, NXP2, Mi-2, SAE, PL7, PL12, EJ, OJ, SRP.

Psychometric properties of IIM classification criteria and proposed modifications.

The modification of adding other MSA/MAA along with Anti Jo1 leads to a minor improvement in sensitivity (88% and 77% with and without biopsy respectively) without loss of specificity. Adding other DM rashes with Gottron papules increases sensitivity significantly (96% and 79% with and without biopsy, respectively) but with a decrease in specificity (86%). (Table 1)

The modification of adding other MSA/MAA as well as other DM rashes together improves sensitivity the best but at the cost of specificity.

Conclusion: The addition of other skin rashes and/or MSA to the 2016 EULAR/ACR criteria improves sensitivity but at a cost of specificity. Modification of the EULAR/ACR classification criteria is required to overcome some of the shortcomings of the current criteria.

Disclosure: Y. Hasan: None; **K. Chung**: None; **D. Ascherman**: None; **S. Moghadam-Kia**: None; **C. V. Oddis**: Boehringer-Ingelheim, 5, Cabaletta, 5, EMD Serono, 5, Novartis, 5, Pfizer, 1; **R. Aggarwal**: Actigraph, 2, Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella Bioscience, 2, Corbus, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Mallinckrodt, 5, Merck, 2, Octapharma, 2, Pfizer, 2, 5, Q32, 5, Roivant, 2, Sanofi, 2, Teva, 2.

Abstract Number: 1176

Brepocitinib Prevents Type-I Interferon Induced Damage in Cultured Myocytes and Endothelial Cells Indicating a Potential Role in the Treatment of Dermatomyositis

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SESSION INFORMATION
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Background/Purpose: Dermatomyositis (DM), an idiopathic inflammatory myopathy, is a chronic and often debilitating condition characterized by a hallmark skin rash (e.g., Gottron's sign and heliotrope rash) with perifascicular atrophy and subsequent muscle weakness. The pathogenesis of DM involves dysregulation in signaling of Type I interferon (IFN-I), IFN-ɣ, IL-12, and IL-23. TYK2 and JAK1, are essential for the signaling pathway of these cytokines. Brepocitinib, a selective and potent dual TYK2/JAK1 inhibitor is in development for the treatment of DM and is expected to reduce signaling of these cytokines.A Phase 3 clinical trial of brepocitinib in adults with DM is ongoing (NCT05437263).

Methods: To evaluate the efficacy of brepocitinib in preventing IFN-I induced pathological changes characteristic of DM, human skeletal muscle myoblasts were cultured and differentiated into myotubes then treated with vehicle control or IFN-I to induce cellular damage. Myotubes were also preincubated for 1 hour with brepocitinib (1 μM or 130 nM, the latter represents the average free plasma concentration after brepocitinib 30 mg QD) prior to IFN-I treatment. Immunofluorescence staining followed by image analysis to determine myosin 4 surface area were conducted after 48 hours of IFN-I treatment. Human dermal microvascular endothelial cells (HMEC-1) were cultured and, once vascular networks were established, cells

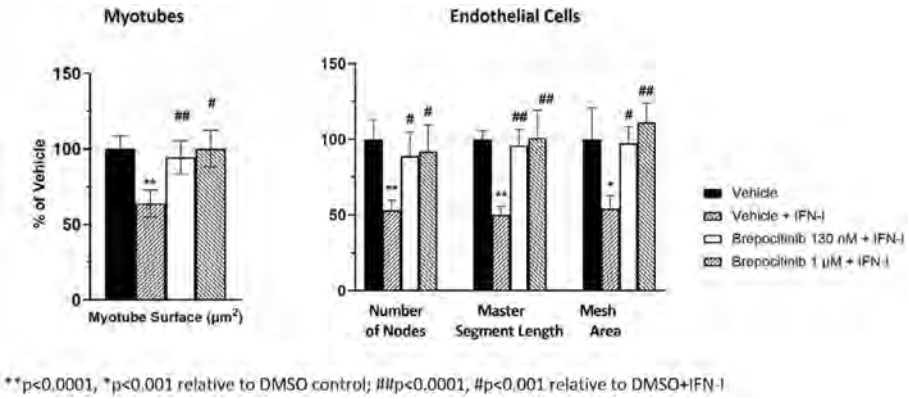

Figure 1. Brepocitinib Effects on IFN-I Induced Myotube and Endothelial Cell Damage

were treated with IFN-I or vehicle control. Cells were also preincubated for 1 hour with brepocitinib as described above. Under light microscopy 9 hours after treatment, the number of nodes, master segment length, and total mesh area were analyzed. One-way ANOVA followed by Tukey's multiple comparison post-hoc analyses were performed.

Results: Myosin surface area was reduced by ~40%, relative to vehicle treated control, in myotubes exposed to IFN-I ($p < 0.0001$). This cytokine induced damage was prevented by brepocitinib preincubation (both 130 nM and 1 μM) with mean myosin surface areas of 96% and 100% of the vehicle control, respectively. The differences between IFN-I treatment alone and brepocitinib were significant ($p < 0.0001$ [1 μM] and $P < 0.001$ [130 nM]). Similarly, HMEC-1 exposure to IFN-I significantly reduced the mean number of nodes, mean master segment length, and mean total mesh area by 47 to 50% relative to vehicle control ($p < 0.0001$ nodes and segments, $p < 0.001$ mesh area). With brepocitinib preincubation, this damage was prevented with the mean number of nodes, master segment lengths, and total mesh area ranging from 89 to 111% of vehicle control. These differences were statistically different from the IFN-I treatment at both brepocitinib concentrations and all endpoints ($p < 0.001$ for all conditions).

Conclusion: One of the most debilitating aspects of DM is muscle weakness resulting from perifascicular atrophy leading to significant impacts on quality of life for these patients. We report here the ability of brepocitinib to prevent IFN-I induced damage in both myocytes and microvasculature in culture at clinically relevant concentrations, providing further pharmacologic rationale for brepocitinib in the treatment of DM.

Disclosure: J. Vencovsky: Argenx, 2, Eli Lilly, 6, Galapagos, 2, Horizon, 2, Merck, 2; **J. Feldman**: Priovant Therapeutics, 3; **L. McConnachie**: Impel Pharmaceuticals, 2, Priovant Therapeutics, 3; **B. Johnson**: Priovant Therapeutics, 3, 3.

Abstract Number: 1177

Anti-HMGCR Autoantibody Levels in the Follow-up of Statin-induced Immune-mediated Necrotizing Myopathy: Multicentric Study of 24 Patients

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SESSION INFORMATION
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Background/Purpose: Statin-induced immune-mediated necrotizing myopathy (IMNM) is associated with anti-3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) autoantibodies. It is characterized by elevated creatine kinase (CK) levels, and severe muscle weakness. Measuring disease activity is problematic, since it is challenging to differentiate it from damage. The utility of the quantitative analysis of anti-HMGCR autoantibodies during the follow-up has not been thoroughly studied.

Our aum was to assess the usefulness of measuring the levels of anti-HMGCR autoantibodies in relation to response to treatment.

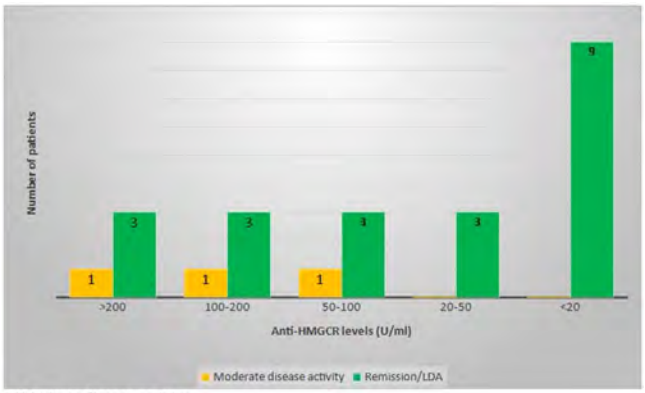
Methods: We included patients all consecutive patients diagnosed with statin-induced IMNM according to the definition of the European Neuromuscular International Workshop 2016 and positivity for anti-HMGCR autoantibodies in two centers from Spain and Sweden from January 2017 to November 2022. All patients were followed for at least 3 months to be included. Clinical data was extracted retrospectively from the patients' clinical records. Remission was defined as no disease activity assessed by expert rheumatologists according to 2016 ACR/EULAR response criteria in myositis. Moderate and high disease activity was defined when physician global activity score was higher than 2 or 3 (on a Likert scale) respectively . Anti-HMGCR autoantibodies level was measured at the time of diagnosis and at a variable period of time after treatment. Results were obtained using the chemiluminescence immunoassay (CLIA) method. Negative anti-HMGCR was considered as levels lower than 20 U/ml.

Results: Our group combined of 24 patients. Main features of the patients are summarized in the **TABLE**. 21 (87.5%) patients reached clinical remission or low disease activity. However, 3 patients (12.5%) remained with moderate activity of the disease. None of the patients had high disease activity. Anti-HMGCR levels at diagnosis were higher than 100 U/ml in 23 patients (95.8%) and above 200 in 11 patients (45.8%). However, anti-HMGCR levels after treatment were significantly lower in patients in remission (p=0.035). Numeric levels in patients at diagnosis of the disease and after treatment are shown in the **FIGURE**. Most of the patients at diagnosis (with high activity of the disease) had high anti-HMGCR levels (22 patients,

Variables	Total (n=24)	Remission / low activity (n=21)	Moderate activity (n=3)	P (remission vs no remission)
Age (years), mean ± SD	68.2 ± 7.2	67.6 ± 7.1	67.3 ± 10.1	0.95
Sex (women), n (%)	10 (42)	9 (42.9)	1 (33.3)	0.89
Analytical values, mean ±SD				
• CK (ukat/L) at diagnosis	114.3 ± 103.9	103.5 ± 100	230.7 ± 84.5	0.51
• Anti-HMGCR levels at diagnosis	214.6 ± 110.8	212.2 ± 89.7	295 ± 127.8	0.24
• Anti-HMGCR levels after treatment	83.8 ± 89	74 ± 80.4	190 ± 100.1	**0.035***
Muscle strength assessment, mean ±SD				
• MMT-8 at diagnosis	64.4 ± 12	65.4 ± 12.7	62.7 ± 13.5	0.73
• MMT-8 after treatment	77.6 ± 4.2	78.6 ± 3.1	74.3 ± 8.1	0.1

CK: Creatine kinase.
Upper limit for CK: < 4.7 ukat/L for men and 3.5 ukat/L for women.
*: p < 0.05

TABLE: General features of 24 patients diagnosed with anti-HMGCR positive IMNM



LDA: Low disease activity

FIGURE: Anti-HMGCR autoantibodies levels according to disease activity after treatment in 24 patients with IMNM.

91.7% had levels above 100 U/ml). After treatment, most patients in remission had low (n=3, 14.3%) or negative (n=9, 42.9%), while patients with moderate activity had higher levels (n=2, 66.7% with levels above 100 U/ml). However, 6 patients in remission (28.6%) still had levels above 100 U/ml.

Conclusion: Anti-HMGCR autoantibodies levels evaluation can be used in parallel with other tools to accurately measure disease activity in patients with statin-induced IMNM. However, more studies are needed to confirm these results.

Disclosure: D. Martinez-Lopez: None; **C. Corrales Selaya**: None; **D. Prieto-Peña**: None; **P. Szczesny**: None; **A. Notarnicola**: None; **M. Lopez-Hoyos**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6; **I. Lundberg**: Argenx, 6, Astra-Zeneca, 5, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 1, Corbus Pharmaceutical, 6, EMD Serono Research & Development Institute, 6, Janssen, 6, Kezar, 6, Novartis, 11, Octapharma, 6, Orphazyme, 6, Pfizer, 1, Roche, 11, Xencor, 6; **M. Dastmalchi**: None.

Abstract Number: 1178

Self-Perceived Knowledge of Myositis Among Social Media Respondents-a Pilot Study on Twitter

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SESSION INFORMATION

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Background/Purpose: Myositis is a rare complex autoimmune disease that is less known and poorly understood, with increased effort required for education of practitioners, students, educators, and patients. Social media platforms offer immense potential for rare disease education, though assessment of baseline knowledge is crucial to develop a comprehensive health education program disseminated through social media. We assessed the current level of knowledge and

understanding of myositis, and explored preferred methods of learning, among social media respondents to develop a social media-based myositis education program.

Methods: A validated, pilot tested baseline self-reporting survey was circulated on Twitter, and all respondents >18 years were invited to participate. The survey collected data on demographics, country of residence, profession, and sources of health-related information used for learning. Respondents reported their perceived level of knowledge of myositis on a 5-point Likert scale from 1 (very low) to 5 (very high). Level of knowledge, pattern of twitter activity, and sources of health information used were compared between the different groups through descriptive statistics.

Results: A total of 504 participants responded to the survey, with 48.2% females, ranging from 18-20 to >70 years, with most in the 30–40-year age group (31.1%), from 66 countries across six continents, mostly from the United States (37.5%), India (15.66%) and the United Kingdom (5.79%) (Fig 1A). Respondents included patients (25.2%), trainees (26.1%) from medical student to residents and fellows, as well as faculty (27.8%) from various specialties (Figure 1B, Table 1). The overall knowledge of myositis increased with a higher level of medical training with mean (SD) score of 2.5 (0.9) in medical students, 2.8 (0.8) in residents, 3.3 (0.6) in fellows, and 3.9 (0.6) among attending rheumatologists, where 1 was 'very low' while 5 was 'very high'. Importantly, the overall knowledge of myositis amongst myositis patients and autoimmune patients were 3.1 (0.9) and 2.1 (1.0) respectively indicating a low to medium level (Fig 2A). Myositis pathogenesis was least understood followed by myositis ILD and myositis complications. Social media was reported as the most common platform to be used amongst all respondents for medical educational content, however traditional in person and online lectures remain important for medical personnel (Fig 2B). Patients clearly favored social media for their knowledge.

Conclusion: The overall knowledge of myositis remains low amongst patients. In the medical community overall myositis knowledge is low to moderate among trainees, though increases medical training progresses. Social media is commonly used by patients, students and doctors to access educational content on myositis, though traditional lectures remain important among the medical community. This provides an excellent means to educate patients and clinicians alike about this rare condition which may in turn may improve patient outcomes.

Table 1. Demographic, level of current knowledge and use of educational platforms of respondents

	Myositis patient (n=106)	Autoimmune disease patient (n=26)	Medical student (n=20)	Resident (n=60)	Fellow (n=52)	Attending Rheum (n=95)	Attending Non Rheum (n=46)	Other (n=99)
Age group (years), n (%)								
<20	0(0%)	0(0.0%)	3(15.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
20-30	7(6.6%)	2(7.7%)	15(75.0%)	36(60.0%)	11(21.2%)	5(5.3%)	2(4.3%)	12(17.1%)
30-40	15(41.2%)	6(23.1%)	1(5.0%)	19(31.7%)	37(71.2%)	41(43.2%)	27(58.7%)	20(28.6%)
40-50	15(14.2%)	8(30.8%)	1(5.0%)	2(3.3%)	1(1.9%)	28(29.5%)	9(19.6%)	15(21.4%)
50-60	30(28.3%)	6(23.1%)	0(0.0%)	0(0.0%)	0(0.0%)	3(3.2%)	3(6.5%)	11(15.7%)
60-70	18(17.0%)	3(11.5%)	0(0.0%)	0(0.0%)	0(0.0%)	4(4.2%)	1(2.2%)	8(11.4%)
>70	15(14.2%)	1(3.8%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	1(22.2%)	1(1.4%)
Undocumented	6(5.7%)	0(0.0%)	0(0.0%)	3(5.0%)	3(5.8%)	14(14.7%)	3(6.5%)	3(4.3%)
Gender, n (%)								
Female	68(64.2%)	22(84.6%)	7(35.0%)	22(36.7%)	22(42.3%)	39(41.1%)	10(21.7%)	37(52.9%)
Male	32(30.2%)	3(11.5%)	13(65.0%)	35(58.3%)	27(51.9%)	41(43.2%)	32(69.6%)	30(42.9%)
Undisclosed	6(5.7%)	1(3.8%)	0(0.0%)	3(5.0%)	3(5.8%)	15(15.8%)	4(8.7%)	3(4.3%)
				Overall Myositis Knowledge, Mean (SD)				
Overall Myositis Knowledge, Mean (SD)	3.1(0.9)	2.1 (1.0)	2.5(0.9)	2.8(0.8)	3.3(0.6)	3.9(0.6)	3.3(0.9)	2.9(1.0)
				Knowledge on various myositis topics, Mean (SD)				
Subtypes	2.9(1.0)	2.0(1.0)	2.5(1.0)	3.0(1.0)	3.6(0.8)	4.2(0.8)	3.4(0.9)	2.8(1.2)
Pathogenesis	2.3(1.0)	1.7(0.9)	2.6(1.1)	2.6(0.9)	3.0(0.8)	3.5(0.9)	3.0(1.0)	2.5(1.1)
Signs and symptoms	3.5(0.9)	2.3(1.0)	3.0(1.0)	3.4(0.9)	3.9(0.7)	4.4(0.6)	3.7(0.9)	3.1(1.1)
Diagnosis & classification	2.9(1.0)	1.9(0.9)	2.4(0.9)	3.0(1.0)	3.6(0.8)	4.3(0.7)	3.3(1.0)	2.8(1.2)
Myositis diagnostic tests	3.0(1.1)	2.1(1.1)	2.4(0.9)	2.7(1.0)	3.3(0.8)	3.8(0.8)	3.2(1.1)	2.7(1.1)
Myositis Autoantibodies	2.6(1.2)	2.1(1.1)	2.7(1.2)	3.1(1.0)	3.6(0.8)	4.1(0.9)	3.3(1.1)	2.7(1.3)
Myositis associated ILD	2.4(1.1)	2.0(1.1)	2.5(1.1)	2.9(1.1)	3.5(0.9)	4.0(0.9)	3.1(1.1)	2.5(1.2)
Myositis Complications	2.8(1.1)	1.9(1.0)	2.7(1.2)	3.0(1.1)	3.4(0.8)	3.9(0.9)	3.0(1.0)	2.6(1.2)
Myositis management	3.0(1.1)	1.8(1.0)	2.5(1.0)	3.0(1.1)	3.5(0.9)	4.1(0.8)	3.3(1.1)	2.8(1.2)
Prognosis and outcomes	3.1(1.0)	1.8(0.9)	2.5(1.1)	2.8(1.0)	3.3(0.9)	4.0(0.9)	3.1(1.0)	2.7(1.2)
				Frequency of use of different educational platforms, Mean (SD)				
Twitter	3.3 (1.4)	4.0 (1.3)	3.8 (1.4)	4.0 (1.3)	4.1 (1.3)	4.0 (1.3)	4.0 (1.3)	3.8 (1.3)
Other social media	3.5 (1.4)	3.5 (1.4)	3.2 (1.5)	3.0 (1.5)	2.6 (1.3)	2.8 (1.4)	3.0 (1.4)	3.5 (1.3)
Traditional online lectures/conferences	2.3 (1.4)	2.9 (1.3)	3.4 (1.2)	3.6 (1.3)	3.7 (1.1)	3.8 (1.1)	3.9 (1.0)	3.1 (1.5)
Traditional in person lectures/conferences	1.5 (0.9)	2.2 (1.4)	3.3 (1.3)	3.7 (1.3)	3.7 (1.1)	3.7 (1.1)	3.6 (1.0)	2.7 (1.5)

Data are presented as mean (SD) for continuous measures, and n (%) for categorical measures.

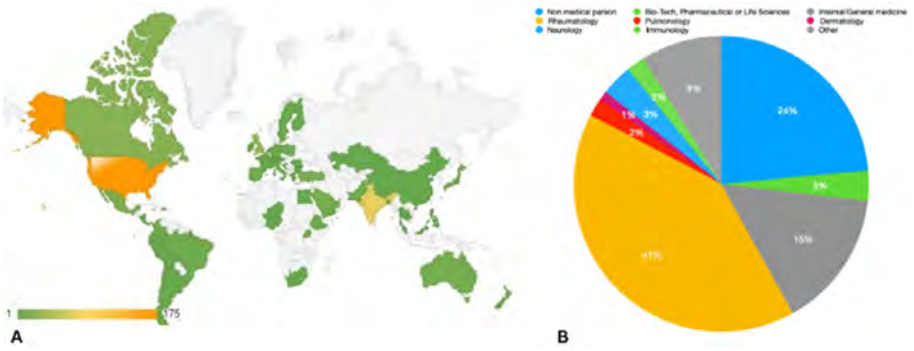


Fig 1. Country-wise (A) and specialty wise (B) distribution of respondents

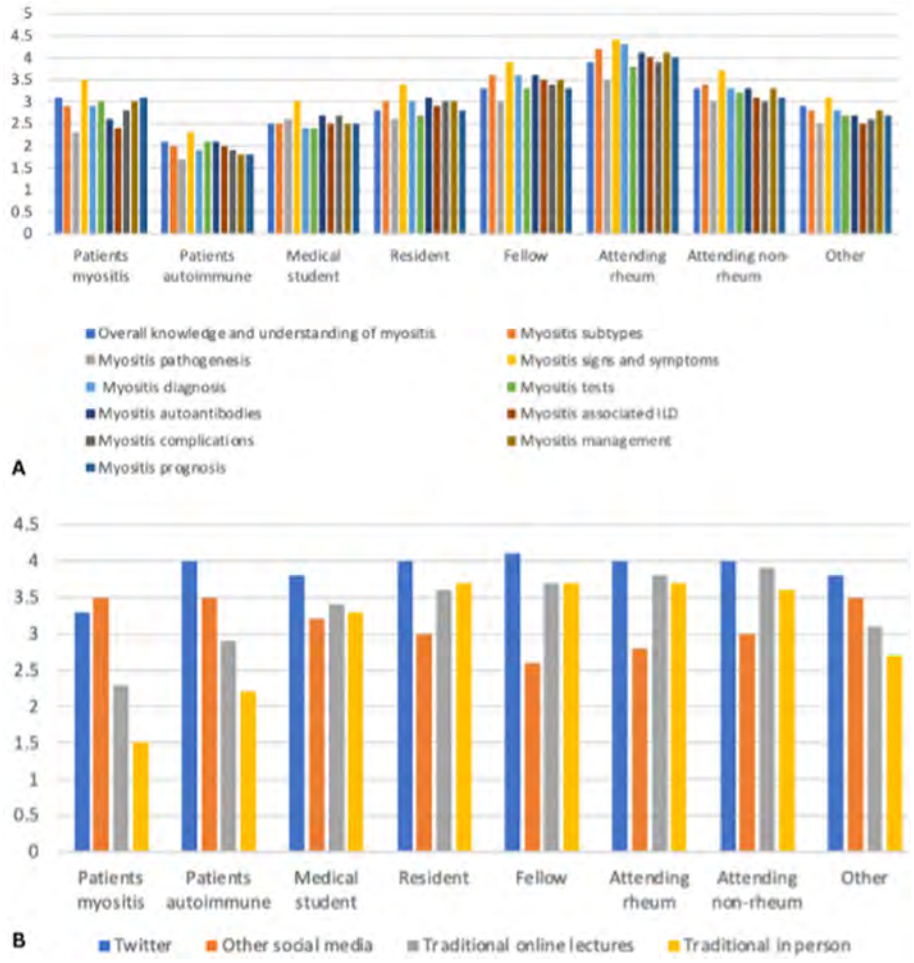


Fig 2. Self-reported level of knowledge on topics in myositis (1 very low, 2 Low, 3 Medium, 4 High, 5 Very High) (A) and use of educational platforms for medical or patient educational content/material by respondent (0 never, 1 rarely, 3 sometimes, 4 often, 5 regularly) (B)

Disclosure: S. Mittal: None; **V. Batra**: None; **P. Sen**: None; **S. Ali**: None; **A. Mago**: None; **M. Russell**: Biogen, 6, Galapagos, 6, Lilly, 6, 12, educational, Menarini, 6, UCB, 12, educational; **E. Gkiaouraki**: None; **R. Aggarwal**: Actigraph, 2, Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella Bioscience, 2, Corbus, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Mallinckrodt, 5, Merck, 2, Octapharma, 2, Pfizer, 2, 5, Q32, 5, Roivant, 2, Sanofi, 2, Teva, 2.

Abstract Number: 1179

Rituximab in the Treatment of Interstitial Lung Disease Associated with the Antisynthetase Syndrome

Javier Narvaez[1], Elena Cañadillas-Sanchez[2], Ivan Castellvi[3], Juan José Alegre[4], Paola Vidal-Montal[5] and Joan Miquel Nolla[5], [1]Hospital Universitario de Bellvitge, Barcelona, Spain, [2]Department of Rheumatology, Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, [3]Rheumatology, Hospital Universitari de la Santa Creu i Sant Pau, Sant Just Desvern, Spain, [4]Department of Rheumatology, Hospital Universitario Dr Peset, Valencia, Spain, [5]Department of Rheumatology, Hospital Universitario de Bellvitge, Barcelona, Spain

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: To assess the real-world, long-term effectiveness of rituximab (RTX) as a rescue therapy in patients with antisynthetase syndrome and interstitial lung disease (ASS-ILD).

Methods: Multicentre observational retrospective longitudinal study of a cohort of patients with ASS-ILD that started treatment with RTX due to recurrent or ongoing progressive ILD despite therapy with glucocorticoids and immunosuppressants.

Results: Twenty-eight patients were analyzed; 15 fulfilled the criteria of progressive pulmonary fibrosis. Ongoing therapy with immunosuppressants remained unchanged. Examining the entire study population, before treatment with RTX the mean decline in %pFVC and %pDLCO from the ILD diagnosis was -6.44% and -14.85%, respectively. After six months of

Table 1. Changes before and after 6 months, 1 and 2 years of treatment with Rituximab vis-à-vis the main outcome efficacy measures evaluated.

Before RTX treatment				
	At time of RA-ILD diagnosis mean ± SD (IQR, 25th-75th)	**At time of RTX onset** mean ± SD (IQR, 25th-75th)	**Delta (mean)**	***P* (95% CI)**
Total sample (N=28)				
%FVC predicted	76,3 ± 21,6 (57,9 – 87,6)	69,8 ± 19,6 (52,5 – 76,7)	-6,44%	0,003 (2,45 to 10,43)
%DLCO predicted	58,3 ± 16,9 (43 – 70)	43,4 ± 14,6 (32 – 52)	-14,85%	<0,001 (10,51 to 19,19)
Mean distance covered in 6MWT (meter)	420 ± 88 (349 – 490)	349 ± 112 (289,5 – 442,5)	-77,08 m	0,021 (13,50 to 141,87)
After 6 months of treatment				
	At time of RTX onset mean ± SD (IQR, 25th-75th)	**6 months post-RTX** mean ± SD (IQR, 25th-75th)	**Delta (mean)**	***P* (95% CI)**
Total sample (N=28)				
%FVC predicted	69,8 ± 19,6 (52,5 – 76,7)	76,1 ± 21,6 (60,7 – 90,9)	+6,29%	0,002 (-10,07 to -2,51)
%DLCO predicted	43,1 ± 14,8 (32 – 52)	49,1 ± 15,8 (35,7 – 55)	+6,15%	0,013 (-10,86 to -1,43)
Mean distance covered in 6MWT (meter)	343 ± 112 (289,5 – 442,5)	433 ± 76 (382,5 – 488)	+90,41 m	0,019 (-197,95 to -22,87)
After 1 year of treatment				
	At time of RTX onset mean ± SD (IQR, 25th-75th)	**12 months post-RTX** mean ± SD (IQR, 25th-75th)	**Delta (mean)**	***P* (95% CI)**
Total sample (N=24)				
%FVC predicted	71,9 ± 20,1 (57 – 80)	83,5 ± 22 (66,7 – 102,5)	+11,63%	<0.001 (-16,91 to -6,36)
%DLCO predicted	45,3 ± 16 (32 – 52,7)	55,6 ± 15,7 (44 – 63)	+10,29%	<0.001 (-14,87 to -5,76)
Mean distance covered in 6MWT (meter)	346 ± 124 (290 – 450)	433,4 ± 73 (361,5 – 471)	+87,16 m	0.061 (-179,21 to 4,88)
After 2 years of treatment				
	At time of RTX onset mean ± SD (IQR, 25th-75th)	**24 months post-RTX** mean ± SD (IQR, 25th-75th)	**Delta (mean)**	***P* (95% CI)**
Total sample (N=22)				
%FVC predicted	74,1 ± 19,5 (60,3 – 82)	84 ± 21,6 (69,9 – 99,2)	+9,93%	0,002 (-15,61 to -4,25)
%DLCO predicted	45,5 ± 14,7 (32 – 54)	53,2 ± 16,8 (41,7 – 63,6)	+7,86%	<0.001 (-11,67 to -3,65)
Mean distance covered in 6MWT (meter)	334 ± 136 (289 – 456)	418 ± 91,5 (367,5 – 528,5)	+103,54 m	0,33 (-197,17 to -9,91)

%pFVC = predicted forced vital capacity, %pDLCO = predicted diffusing capacity for carbon monoxide, corrected for hemoglobin; RTX = rituximab; 6MWT = 6-minute walking test

treatment, RTX reversed the decline in pulmonary function test (PFTs) parameters: Δ%pFVC +6.29% (95% CI: -10.07 to 2.51; p=0.002 compared to baseline) and Δ%pDLCO +6.15% (95% CI: -10.86 to -1.43; p=0.013). Twenty-four patients completed one year of therapy and 22 two years, maintaining the response in PFTs: Δ%pFVC: +9.93% (95% CI: -15.61 to -4.25; p=0.002) and Δ%pDLCO: +7.66% (95% CI: -11.67 to -3.65; p< 0.001) [Table 1]. In addition, there was a significant reduction in the median dose of prednisone, and it could be suspended in 18% of cases. In 33% of patients who required oxygen therapy at the start of treatment, it could be discontinued. The frequency of adverse events reached 28.5% of cases.

Conclusion: Based on our results, RTX appears to be effective as rescue therapy in most patients with recurrent or progressive ASSD-ILD unresponsive to conventional treatment. Use of RTX was well tolerated in the majority of patients

Disclosure: J. Narvaez: None; **E. Cañadillas-Sanchez**: None; **I. Castellvi**: None; **J. Alegre**: None; **P. Vidal-Montal**: None; **J. Nolla**: None.

Abstract Number: 1180

Machine Learning Approach for the Prediction of anti-MDA5 Positive Dermatomyositis Mortality

Xinlei Liu[1], Fumin Qi[2], Wei Wei[1] and Yin Zhao[1], [1]Tianjin Medical University General Hospital, Tianjin, China, [2]Tianjin Medical University, Tianjin, China

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: We describe a single-center clinical cohort of MDA5 positive dermatomyositis(DM) in China and apply a machine learning approach to predict the risk of mortality in patients.

Methods: We conducted a retrospective collection of clinical characteristics from 70 Asian patients diagnosed with MDA5+ DM between June 2017 and March 2023. The collected data encompassed various aspects, including basic information, clinical symptoms and signs, prognosis, treatment methods, imaging information, pulmonary functions, and laboratory examinations. The cohorts were divided into training and validation sets in a 4:1 ratio. Machine learning approaches (Ridge, LASSO, Elastic Net) were employed to identify the optimal variables among the 152 variables, which were used to construct a COX regression model. A Nomogram was subsequently developed to provide guidance for clinical practice.

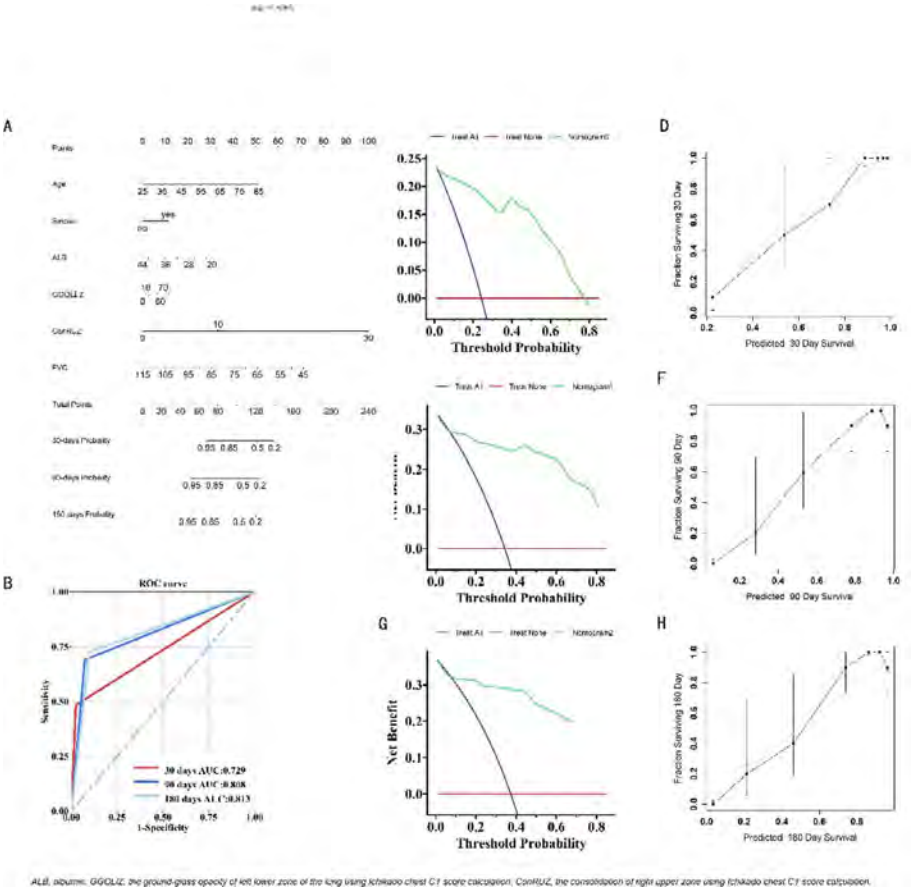
Results: Demographic and disease characteristics of the 70 MDA5 positive DM patients can be found in Table 1. The median follow-up time was 10 months (IQR 2-40, range 0.5-71), and 29 patients (41.4%) died in our study. The deceased patients were older in age, had a shorter duration of disease, exhibited fever, respiratory symptoms, and poorer lung condition, as well as higher levels of inflammatory markers. After comparing three machine learning methods, it was found that the Partial Likelihood Deviance of the Lasso-COX regression model was 5.001, which was not the lowest. However, it was comparable to the other models in terms of deviation and showed good performance with a c-index of 0.7421. This indicates that the model has strong discriminatory power. Therefore, the Lasso-COX model was ultimately chosen to establish the risk prediction model in this study (Fig).

Variables	survive	deceased	p-value
Demographic	41	29	
Sex, female/male	29/12	15/14	0.105
Age of onset, years	51(40,57)	63(50.5,67)	**0.000**
Duration from disease onset to diagnosis, months	3(2,5.5)	2(1,3)	**0.006**
General condition			
Fever, no. (%)	19(46.3)	21(72.4)	**0.030**
Fatigue, no. (%)	26(63.4)	20(69)	0.630
Loss of weight (>5%), no. (%)	22(53.7)	12(41.)	0.311
Skin changes			
Skin lesions, no. (%)	37(90.2)	24(82.8)	0.357
Mechanic's hands, no. (%)	12(29.3)	5(17.2)	0.248
Gottron's sign/papules, no. (%)	28(68.3)	19(65.5)	0.808
Heliotrope rash, no. (%)	16(39)	6(17.2)	0.050
V sign, no. (%)	23(56.1)	11(37.9)	0.134
Shawl sign, no. (%)	17(41.5)	10(34.5)	0.554
Periungual erythema, no. (%)	12(29.3)	5(17.2)	0.248
Raynaud phenomenon, no. (%)	2(4.9)	0	0.508
Skin ulcers, no. (%)	10(24.4)	3(10.3)	0.137
Muscular manifestations			
Proximal weakness, no. (%)	18(43.9)	13(44.8)	0.939
Myalgia, no. (%)	18(43.9)	15(54.7)	0.518
Increased CK levels, no. (%)	19(46.3)	11(37.9)	0.484
CK level, U/L	82(40,261)	89(45.5,276.5)	0.770
Lung manifestations			
Cough, no. (%)	21(48.8)	22(78.6)	**0.017**
Dyspnea, no. (%)	21(51.2)	21(72.4)	0.075
ILD, no. (%)	33(80.5)	29(100)	**0.011**
RP-ILD, no. (%)	11(26.8)	23(79.1)3	**0.000**
FVC %	65.6(73.8,92.1)	72.8(46.8,62.7)	**0.000**
Dlco %	64.2(60.2,83.74)	54.17(48.9,64.5)	**0.044**
PaO2, mmHg	75(60.2,81.8)	70.3(60.2,83.7)	0.190
HRCT scores	115(107,137)	137(114,185)	**0.003**
HRCT type			
NSIP, no. (%)	24(68.6)	9(31)	**0.024**
OP, no. (%)	7(17.11)	7(24.1)	
NSIP+OP, no. (%)	3(7.3)	12(41.3)	
UIP, no. (%)	1(2.4)	1(3.4)	
Other manifestations			
Arthritis/arthralgia, no. (%)	26(63.4)	13(44.8)	0.123
Dysphagia, no. (%)	1(2.4)	4(13.8)	0.152
Dysarthria, no. (%)	6(14.6)	5(17.2)	0.768
Ferritin, ug/L	221.1,1487.9	1636.4(1277.1,3567.5	**0.001**
Lymphocytes count, $\times 10^9$/L	0.83(0,564,1.27)	0.6(0.4,0.85)	**0.007**
CD4 positive T cell count, cells/ul	327(218,327)	250(158,350)	**0.014**
CRP, mg/L	4.8(2.2,7.2)	8.7(4.2,30.4)	**0.008**
ESR, mm/h	34(23,39)	33(24,39)	0.620
KL-6, U/ml	543(272,1000)	592.5(282,4045.5)	0.539

CK, creatine kinase; ILD, interstitial lung disease; RP-ILD, rapidly progressive ILD; FVC= forced vital capacity; Dlco, single-breath diffusing capacity for carbon monoxide; HRCT= high resolution computed tomography; NSIP, nonspecific interstitial pneumonia; OP, organizing pneumonia; UIP, usual interstitial pneumonia; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; KL-6, Krebs von den Lungen-6.

Comparison of clinical and laboratory characteristics between surviving and deceased patients with anti-MDA5-positive

Conclusion: A machine learning approach was applied to construct a mortality prediction model for patients with MDA5 positive DM by variables such as age, smoke, HRCT semiquantitative visual scores, and ALB, with good discrimination and calibration.



Nomogram for predicting 30-, 90-, and 180-day survival (A). ROC curves for 30-day, 90-day 180-day mortality models fitted by Lasso-COX models (B). Calibration curve of nomogram predictions of 30-day (C), 90-day (E) and 180-day (G) survival. Decision curve analysis plots of nomogram predictions of 30-day (D), 90-day (F) and 180-day (H) survival.

Disclosure: X. Liu: None; **F. Qi**: None; **W. Wei**: None; **Y. Zhao**: None.

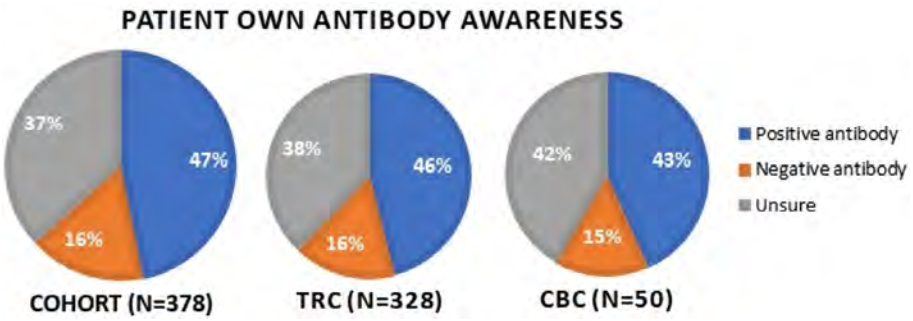
Abstract Number: 1181

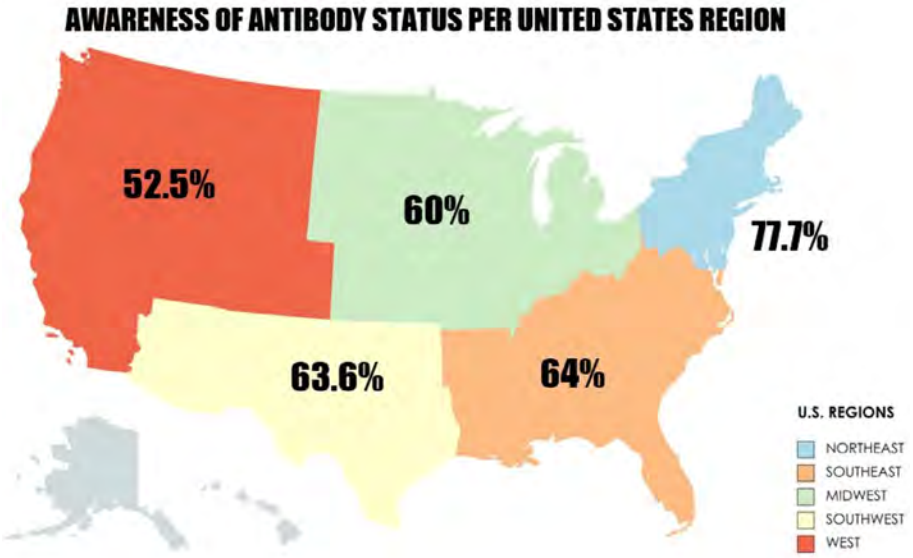
Real-World Myositis Antibody Frequency and Patient Awareness

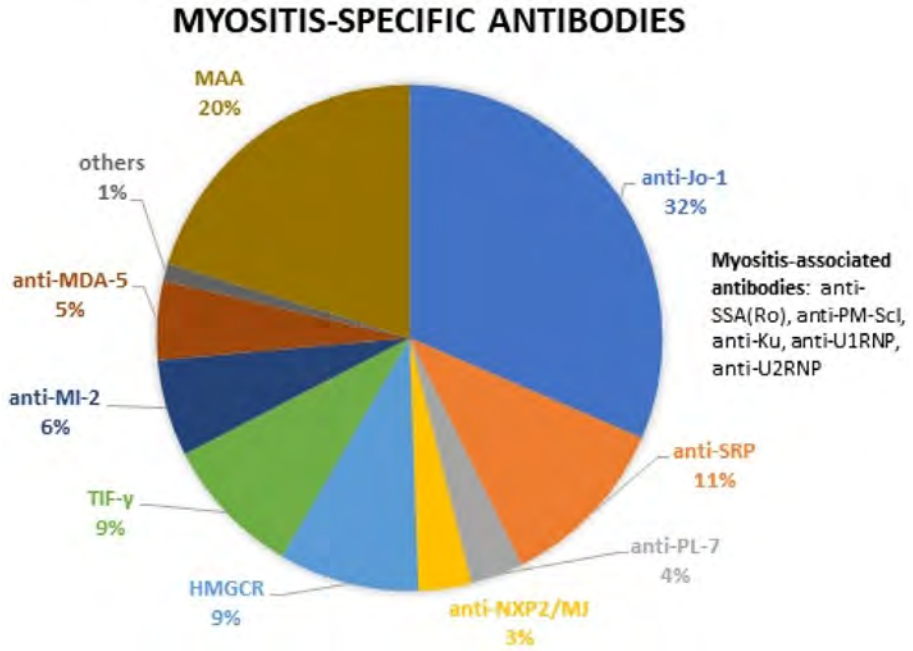
Raisa Lomanto Silva[1], shiri keret[2], Akanksha Sharma[3], Tanya Chandra[4], Siamak Moghadam-Kia[1], Chester V. Oddis[5] and Rohit Aggarwal[5], [1]University of Pittsburgh Medical Center, Pittsburgh, PA, [2]Bnai Zion, Atlit, Israel, [3]UPMC Mercy Hospital, Pittsburgh, PA, [4]Georgetown University Hospital, Washington, DC, [5]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Myositis-specific antibodies (MSA) represent unique phenotypes in idiopathic inflammatory myopathies (IIM). Myositis-associated antibodies (MAA) most commonly occur in IIM overlap syndromes. MSA and MAA should be assessed in all IIM patients, but their real-world frequency, distribution, and patient awareness are not well known. Given the increasing importance of MSA/MAA in IIM diagnosis and management, we examined their real-world vs. expert-center frequency, awareness, and distribution.


PATIENT OWN ANTIBODY AWARENESS
37%
47%
16%
COHORT (N=378)
38%
46%
16%
TRC (N=328)
42%
43%
15%
CBC (N=50)
Positive antibody
Negative antibody
Unsure


AWARENESS OF ANTIBODY STATUS PER UNITED STATES REGION
52.5%
60%
77.7%
63.6%
64%
U.S. REGIONS
NORTHEAST
SOUTHEAST
MIDWEST
SOUTHWEST
WEST


MYOSITIS-SPECIFIC ANTIBODIES
MAA
20%
others
1%
anti-MDA-5
5%
anti-MI-2
6%
TIF-γ
9%
HMGCR
9%
anti-NXP2/MJ
3%
anti-PL-7
4%
anti-SRP
11%
anti-Jo-1
32%
Myositis-associated antibodies: anti-SSA(Ro), anti-PM-Scl, anti-Ku, anti-U1RNP, anti-U2RNP

Methods: Myositis Patient-Centered Tele-Research is a multi-center observational study. Patients were enrolled remotely from anywhere in the U.S. through social media and patient organizations (Tele-Research Cohort, TRC) and traditionally through myositis centers (Center-Based Cohort, CBC). Patients completed a pre-screening questionnaire with MSA/MAA and IIM self-report, the latter being confirmed by a rheumatologist, neurologist, or dermatologist. Patients also self-reported on study disease criteria: proximal muscle weakness, muscle or skin biopsy, electromyography, muscle enzyme, and/or dermatomyositis rashes. A subset of patients had their clinical features, diagnosis, and MSA/MAA results confirmed by physician chart review.

Results: 408 participants completed the pre-screening questionnaire: 317 (77.8%) females, mean age 54.84 (SD +/- 13.8), 378 (92.6%) non-Hispanic, and 328 (80.4%) White, 49 (12%) Black, 13 (3.3%) Asian. Most patients (378, 92.6%) met study IIM criteria. The most common diagnoses were dermatomyositis (195; 51.6%), polymyositis, or necrotizing myopathy (183; 48.4%). A total of 177 (46.8%) reported a positive MSA and/or MAA while 62 (12.4%) were antibody negative and 139 (36.8%) were unsure about their antibody status. The most common MSAs were Jo-1 (31.6%), anti-SRP (11.3%), anti-HMGCR (9%), anti-TIF1-γ (9%), anti-Mi-2 (6.2%), and anti-MDA-5 (5.1%). Regarding MAA, 21 (11.8%) had a positive SSA (Ro), 9 (5.1%) anti-PM-Scl, 3 (1.74%) anti-Ku, and 2 (1.13%) anti-U1RNP. There was no difference in MSA/MAA frequency or distribution by U.S. region or enrollment method (remote vs. from myositis center). Antibody status awareness was significantly higher in the Northeast compared to other regions. Age, gender, ethnicity, and race were not associated with antibody knowledge. There was no difference in antibody awareness between enrollment methods. In a subset of patients (n=94), antibody self-report was highly consistent with physician chart-confirmed MSA/MAA positivity (96.4%) and overall negative or positive status (91.5%).

Conclusion: In a large national real-world IIM cohort, anti-Jo1, -SRP, -HMGCR, -TIF1-γ, -Mi-2, -MDA-5, -SSA, - PM-Scl were the most common MSA/MAA reported by patients. One-third of patients were unaware of their antibody status. There was no difference in antibody frequency, distribution, or awareness by patients enrolled remotely vs. by expert centers. Patients enrolled from the Northeast had significantly more autoantibody awareness. No demographic differences were seen. Patient awareness of their disease and key test results is crucial, as they are important allies in healthcare decision-making.

Disclosure: R. Lomanto Silva: None; **s. keret**: None; **A. Sharma**: None; **T. Chandra**: None; **S. Moghadam-Kia**: None; **C. V. Oddis**: Boehringer-Ingelheim, 5, Cabaletta, 5, EMD Serono, 5, Novartis, 5, Pfizer, 1; **R. Aggarwal**: Actigraph, 2, Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella Bioscience, 2, Corbus, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Mallinckrodt, 5, Merck, 2, Octapharma, 2, Pfizer, 2, 5, Q32, 5, Roivant, 2, Sanofi, 2, Teva, 2.

Abstract Number: 1182

Treatment Trajectories and Patient Outcomes in Idiopathic Inflammatory Myopathies

Kristin Wipfler[1], Michael Feely[2], Gulsen Ozen[3], Urbano Sbarigia[4], Federico Zazzetti[5], Anna Sheahan[6], Iris Lin[7], Evo Alemao[8] and Kaleb Michaud[2], [1]FORWARD, The National Databank for Rheumatic Diseases, Omaha, NE, [2]University of Nebraska Medical Center, Omaha, NE, [3]University of Nebraska Medical Center, Bellevue, NE, [4]Janssen Pharmaceutica, Beerse, Belgium, [5]Janssen Research & Development, LLC, Spring House, PA, [6]Janssen, Raleigh, NC, [7]Janssen, Horsham, PA, [8]Janssen Pharmaceuticals, New Hope, PA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are rare, heterogeneous diseases characterized by chronic skeletal muscle inflammation and weakness. Initial conventional therapy is based on expert opinion and includes glucocorticoids and methotrexate, azathioprine, or mycophenolate. Second line therapy (calcineurin inhibitors or IVIG) and then escalation to third line therapy (rituximab or cyclophosphamide) is considered if initial therapy is insufficient. Adherence to these recommendations and the impact of nonconventional therapies in real-world circumstances is unclear. The aim of this study was to characterize treatment trajectories in IIM and assess changes in patient-reported outcomes (PROs) and symptom frequency among those on conventional vs nonconventional therapies.

Methods: Data were provided by adults with IIM enrolled in the FORWARD Databank. Participants with co-occurring RA, SLE, or SSc were excluded. Participant characteristics and treatment category (none, glucocorticoids alone, first line without glucocorticoid, first line, second line, third line, and other immunomodulator) were assessed at study entry (baseline) and at

Table 1. Characteristics of included participants at study entry by baseline treatment category.

	Conventional Therapy n=57	Nonconventional Therapy n=61	No Therapy n=8	p
Age, years	54.6 (14.3)	57.2 (14.2)	57.0 (8.3)	0.61
Female sex, %	77.8	82.8	37.5	0.02
White race, %	90.6	88.5	75	0.62
IIM subtype				
DM	41.1	44.1	37.5	
PM/IMNM	42.9	32.2	12.5	0.19
Unspecified subtype	16.1	23.7	50	
Time since symptom onset, years	6.5 (6.0)	8.3 (6.3)	4.1 (5.2)	0.2
Study entry prior to 2010, %	55.4	66.1	37.5	0.5
Time from baseline to ultimate treatment, years	3.6 (3.4)	4.4 (4.8)	2.0 (2.4)	0.01
Rural residence, %	30.4	21.1	37.5	0.41
Hx smoking, %	42.9	40.7	75	0.18
Pain VAS, 0-10	3.1 (2.8)	3.2 (2.9)	5.1 (3.5)	0.71
Global severity, 0-10	3.6 (2.8)	3.4 (2.7)	6.3 (2.8)	0.03
HAQ-II, 0-3	1.0 (0.7)	0.9 (0.6)	1.2 (0.7)	0.48
PAS-II, 0-3	3.5 (2.3)	3.3 (2.3)	5.1 (2.6)	0.86

DM=dermatomyositis; PM=polymyositis; IMNM=immune mediated necrotizing myopathy; VAS=visual analog scale; HAQ=Health Assessment Questionnaire; PAS=Patient Activity Scale.

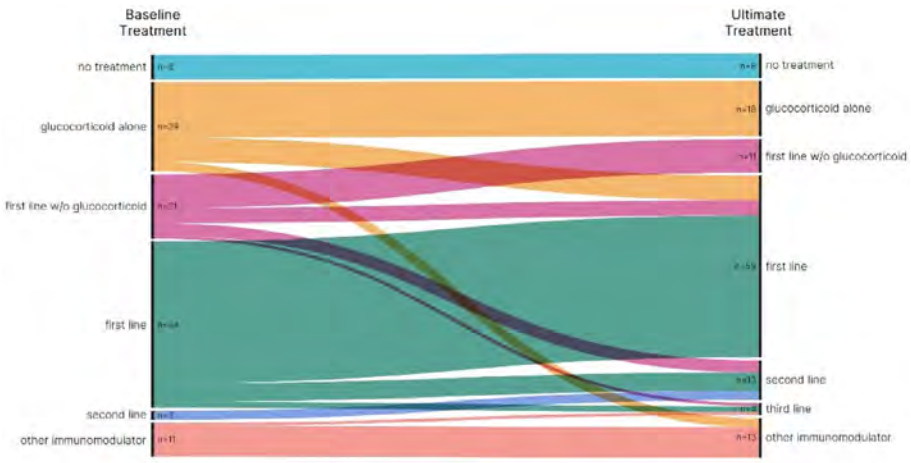


Figure 1. Treatment progression among individuals in FORWARD with IIM. Baseline (at study entry) treatment category is shown on the left, and ultimate treatment category (during observation) is shown on the right. First line = glucocorticoid in combination with methotrexate, azathioprine, or mycophenolate. Second line = calcineurin inhibitors or IVIG. Third line = rituximab or cyclophosphamide. Other immunomodulator = immunomodulator other than those associated with conventional therapy.

Table 2. Changes in patient-reported outcomes and symptoms from baseline to ultimate treatment by treatment trajectory group.

	Stayed on Nonconventional Treatment n=42			Stayed on Conventional Treatment n=57			Switched (Nonconventional to Conventional) n=19		
	Baseline	Ultimate	p	Baseline	Ultimate	p	Baseline	Ultimate	p
PROs, mean (SD)									
Pain VAS, 0-10	3.4 (3.1)	3.3 (3.0)	0.91	3.1 (2.7)	2.9 (3.0)	0.48	3.4 (2.8)	2.7 (1.8)	0.22
Fatigue VAS, 0-10	4.4 (3.6)	4.2 (3.3)	0.64	4.3 (2.9)	3.8 (3.3)	0.05	4.6 (2.9)	4.4 (2.8)	0.81
Patient Global VAS, 0-10	3.5 (2.9)	3.7 (2.9)	0.52	3.6 (2.8)	3.3 (2.7)	0.21	3.8 (2.6)	4.0 (2.1)	0.69
HAQ-II, 0-3	0.9 (0.7)	0.9 (0.7)	0.64	1.0 (0.7)	0.9 (0.8)	0.20	1.1 (0.6)	1.1 (0.6)	0.76
PAS-II, 0-10	3.3 (2.6)	3.4 (2.5)	0.85	3.5 (2.2)	3.1 (2.4)	0.06	3.7 (2.0)	3.6 (1.6)	0.85
RDCI, 0-9	2.2 (1.7)	2.4 (1.6)	0.32	1.9 (1.6)	2.4 (2.1)	0.05	2.0 (1.5)	2.1 (1.8)	0.76
PSD, 0-31	12.8 (9.5)	12.5 (9.2)	0.12	10.2 (7.1)	8.3 (7.4)	0.03	14.0 (5.9)	10.9 (6.5)	0.04
Health satisfaction, 0-4	2.4 (1.4)	2.3 (1.4)	0.64	2.1 (1.3)	2.1 (1.3)	0.70	2.2 (1.1)	2.2 (1.1)	0.82
Symptoms, % (N)									
Muscle pain	57.9 (38)	47.1 (34)	0.13	57.7 (52)	48.8 (43)	0.29	68.4 (19)	46.7 (15)	0.45
Muscle weakness	64.1 (39)	64.7 (34)	1.00	71.2 (52)	47.6 (42)	<0.01	78.9 (19)	80.0 (15)	1.00
Rash	34.2 (38)	21.2 (33)	0.50	21.6 (51)	14.3 (42)	0.73	42.1 (19)	33.3 (15)	1.00
Joint pain	59.5 (37)	57.1 (35)	0.73	69.8 (51)	42.9 (42)	0.07	52.6 (19)	46.7 (15)	1.00
Joint swelling	27.0 (27)	24.2 (33)	1.00	23.5 (51)	23.8 (42)	1.00	31.6 (19)	40.0 (15)	0.63
Depression	31.6 (38)	32.4 (34)	1.00	23.5 (51)	31.0 (42)	0.38	15.8 (19)	13.3 (15)	1.00
Anxiety	23.1 (39)	26.5 (34)	0.63	19.6 (51)	19.0 (42)	1.00	15.8 (19)	13.3 (15)	1.00

PRO=patient-reported outcome; VAS=visual analog scale; HAQ=Health Assessment Questionnaire; PAS=Patient Activity Scale; RDCI=Rheumatic Disease Comorbidity Index; PSD=polysymptomatic distress.

last/most recent observation (ultimate treatment). First, second, and third line treatments were considered "conventional" and glucocorticoid alone, first line without a glucocorticoid, and other immunomodulators were considered "nonconventional." Differences in baseline characteristics between those on conventional, nonconventional, and no therapy were assessed using one-way ANOVA and Fisher's exact tests. Changes in PROs and symptom frequency from baseline to ultimate treatment were evaluated using paired t-tests and McNemar tests.

Results: Among 126 participants who met inclusion criteria, 43% were on first line therapy at baseline, while 23% received glucocorticoids alone. Only 2% were on second line therapy, and none received third line therapy. The remaining participants were on first line therapy without glucocorticoids (17%), nonconventional immunomodulators (9%) or no treatment (6%). Over 504 person-years (from baseline to ultimate treatment), 47% reported first line treatment, 10% reported second line, and 3% reported third line as the most advanced conventional therapy received. The remaining 40% reported nonconventional or no treatment throughout observation. Analyses of PROs and symptom frequencies from baseline to ultimate treatment showed significant improvements in polysymptomatic distress (PSD; 10.2 to 8.3, p=0.03) and muscle weakness (71% to 48%, p< 0.01) among those consistently on conventional therapy. Participants who switched to conventional from nonconventional therapy experienced improved PSD (14.0 to 10.9, p=0.04). No significant changes were observed in the nonconventional treatment group.

Conclusion: Despite recommendations for combination therapy in IIM, a substantial proportion of individuals do not receive concomitant immunomodulators. Our results suggest that individuals who remain on conventional therapies have improved PSD with less muscle weakness over time. The use of nonconventional treatments highlights the need for further investigation of their effectiveness.

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Abstract Number: 1183

CoLchicine for Treatment of OsteoArthritis of the Knee—Updated Data from a Double-blind, Placebo-controlled Trial

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Osteoarthritis – Clinical Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Knee osteoarthritis (OA) has a probable inflammatory role for IL-1b. The presence of calcium and urate crystals may contribute to OA by activating the NLRP3 inflammasome, leading to IL-1b production. Colchicine is a well-tolerated anti-inflammatory drug that inhibits the inflammasome and suppresses IL-1b. Prior studies investigating the efficacy of colchicine on knee OA include some reporting pain relief, others showing improvement in inflammatory markers, but none assessing synovial effusions.

Methods: CLOAK is a randomized, double-blind, placebo-controlled trial of colchicine (0.6 mg daily for 3 months) for knee OA (Fig. 1). We are enrolling individuals ≥ 40 years of age, BMI ≤ 30 kg/m^2, with symptomatic knee OA and Kellgren-Lawrence grade 2 or 3 on radiographs, who are willing to abstain from other anti-inflammatory treatment during the trial. Clinical outcomes include the change in knee pain by visual analog scale (VAS), and in Knee injury and Osteoarthritis Outcome Scores (KOOS) in the colchicine and placebo groups. If present, synovial fluid is aspirated and analyzed. Biologic outcomes to be assessed after study completion include changes in inflammatory markers in plasma, peripheral blood leukocytes, and synovial fluid.

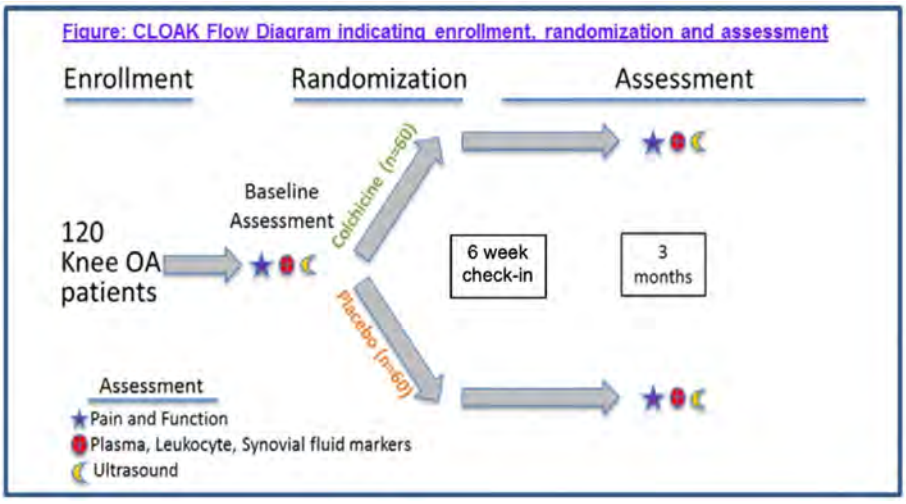

Figure 1. Flow diagram of study plan.

Results: To date, 1,105 potential subjects were contacted, 119 screened, and 97 enrolled. 69 have finished the study with data available: 32% male, 64% White, 24% Black, 4% Asian and 8% other, with mean±SD BMI 27.5±3.9 kg/m^2 and age 68.6±10.1 years. Inclusive of all completing participants (blinded to treatment vs placebo) over the 3 months, mean VAS pain improved (decreased) by -1.04 units in the index knee; 58% demonstrated VAS improvement while 42% had no change or worsened. The mean VAS improvement was concordant with improvements (increases) in all 5 KOOS component subscores (Fig. 2), including mean pain (6.99), symptoms (7.30), activities of daily living (8.01), sports activity (2.45), and quality of life (5.59). Subsets of patients with baseline VAS ≥6 and baseline KOOS ≤60 for pain (i.e., more severe) showed significantly more 3-month mean KOOS pain improvement, even with the blinded inclusion of placebo, than those with less baseline severity (by baseline VAS: 10.8 vs. 1.95, p=0.030; by baseline KOOS 12.2 vs 1.1, p=0.008) (Fig. 3). Sonography was performed on all 69 subjects pre- and post-treatment. Subjects without effusion at baseline were more likely to experience knee pain improvement post treatment than those with effusion (mean KOOS improvement 9.8 vs 1.6, p=0.046).The prevalence of effusions did not differ pre and post treatment (29 vs 26%, ns).

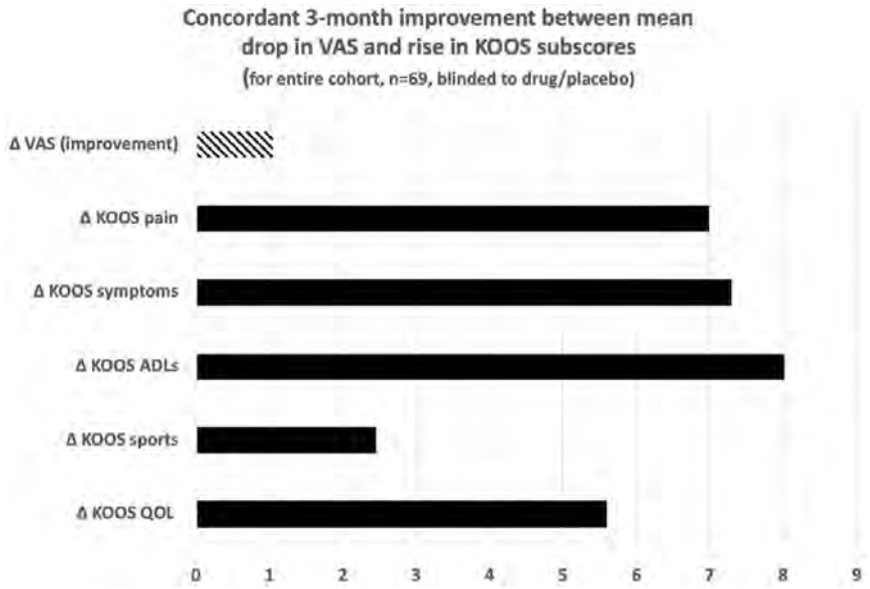

Figure 2. Concordant 3-month improvement with mean drop in VAS and rise in KOOS subscores

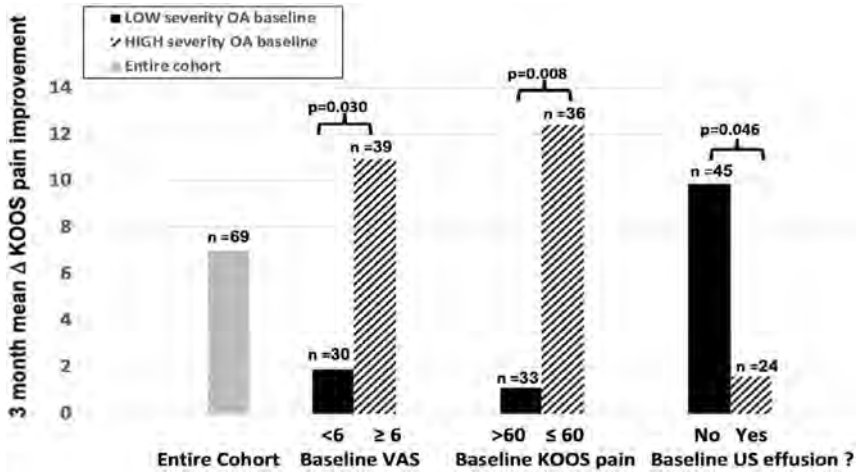

Figure 3. Subject improvement in KOOS score from beginning to end of study, according to high or low baseline severity as measured by VAS and KOOS scores and presence of synovial effusion

Conclusion: The findings of this blinded analysis are consistent with the possibility that colchicine may offer benefit in terms of pain, function, and effusion in subjects with knee OA not taking other anti-inflammatory agents. Patients with higher baseline pain severity were more likely to improve, whereas patients with effusions at baseline were less likely to improve, with regard to post-treatment VAS and KOOS pain scores. Enrollment is ongoing, and the study will be unblinded and fully analyzed upon completion. Supported by an investigator-initiated grant from Hikma Pharmaceuticals.

Disclosure: K. Tse: None; **R. Meidan**: None; **M. Toprover**: ANI Pharmaceuticals, 2, Horizon Therapeutics, 5; **D. Wei**: None; **N. Leung**: None; **M. Coronel**: None; **J. Cai**: None; **A. Jain**: None; **m. Iessa**: None; **R. La Rocca Vieira**: None; **S. Krasnokutsky Samuels**: None; **M. Pillinger**: Federation Bio, 2, Fortress Biotech, 2, Hikma, 5, Horizon Therapeutics, 2, 5, Scilex, 2, Sobi, 2; **J. Samuels**: None.

Abstract Number: 1184

A Wearable-Sensor for Assessment of Gait and Chair Stand Patterns in People with Knee Osteoarthritis: Validation and Responsiveness to Treatment of a Potential Digital Biomarker

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The objectives of this study in people with knee osteoarthritis (OA) were to (a) examine the agreement between measures of gait and chair stand patterns derived from a wearable-sensor and those from gold-standard motion capture, (b) assess the correlation between wearable-sensor derived measures and standard functional measures, and (c) examine the responsiveness of wearable-sensor derived measures to an exercise-based physical therapy intervention.

Table 1. Agreement between sensor and motion-capture derived measures using data from baseline, week 12, and week 18 visits.

Table 1. Agreement between sensor and motion-capture derived measures using data from baseline, week 12, and week 18 visits.

	Sensor-derived (mean [standard deviation])	Motion Capture derived (mean [standard deviation])	% difference	Agreement (ICC[2,1] with 95% confidence intervals
Walking at self-selected pace				
Cadence (steps/min)	120.86 (119.29, 122.42)	123.25 (121.61, 124.88)	1.94	0.835 (0.740, 0.897)
Speed (m/s)	1.33 (1.30, 1.36)	1.54 (1.50, 1.57)	13.66	0.509 (0.298, 0.672)
Stride duration (s)	1.00 (0.98, 1.01)	0.98 (0.97, 0.99)	-1.54	0.850 (0.763, 0.907)
Step duration (s)	0.50 (0.50, 0.51)	0.49 (0.48, 0.50)	-2.20	0.832 (0.735, 0.895)
Initial double support duration (s)	0.14 (0.13, 0.14)	0.14 (0.14, 0.15)	5.20	0.608 (0.423, 0.744)
Terminal double support duration (s)	0.13 (0.13, 0.14)	0.14 (0.14, 0.15)	5.30	0.651 (0.480, 0.774)
Total double support duration (s)	0.27 (0.27, 0.27)	0.29 (0.28, 0.29)	5.36	0.633 (0.456, 0.762)
Single limb support duration (s)	0.37 (0.36, 0.37)	0.35 (0.34, 0.35)	-5.05	0.655 (0.485, 0.777)
Stance duration (s)	0.64 (0.63, 0.65)	0.63 (0.62, 0.64)	-0.81	0.843 (0.751, 0.902)
Swing duration (s)	0.36 (0.36, 0.37)	0.35 (0.34, 0.35)	-3.70	0.724 (0.580, 0.825)
Step length (m)	0.65 (0.64, 0.66)	0.75 (0.73, 0.76)	12.56	0.478 (0.260, 0.649)
Chair stand				
Duration (s)	1.15 (1.07, 1.23)	1.34 (1.29, 1.38)	13.88	0.493 (0.272, 0.665)
Maximum acceleration (m/s^2)	2.17 (2.02, 2.32)	1.95 (1.86, 2.04)	-11.63	0.685 (0.521, 0.800)
Minimum acceleration (m/s^2)	-3.17 (-3.40, -2.94)	-2.27 (-2.41, -2.14)	-39.49	0.566 (0.363, 0.717)

Methods: We conducted a single-arm clinical trial (NCT04243096) of a 12-week exercise intervention in people with symptomatic knee OA (n = 60, age = 66.3±7.4 years; 75% women; BMI = 29.0±4.8 kg/m^2). Participants received 18 sessions of an exercise-based physical therapy intervention over 12 weeks. Spatiotemporal gait parameters and measures of chair stand mechanics (Table 2) were extracted from an inertial sensor worn on the lower back as well as from optical motion capture during walking at self-selected pace and chair stand tasks. Agreement between sensor and motion capture measures was examined using intraclass coefficients (ICC [2,1]). Participants also completed standard functional tests including a walking test (28-meters), 5 times chair stand test, and a 6-minute walk test, while wearing the inertial sensor and correlations between sensor derived measures and functional measures were assessed. The wearable sensor measures with excellent

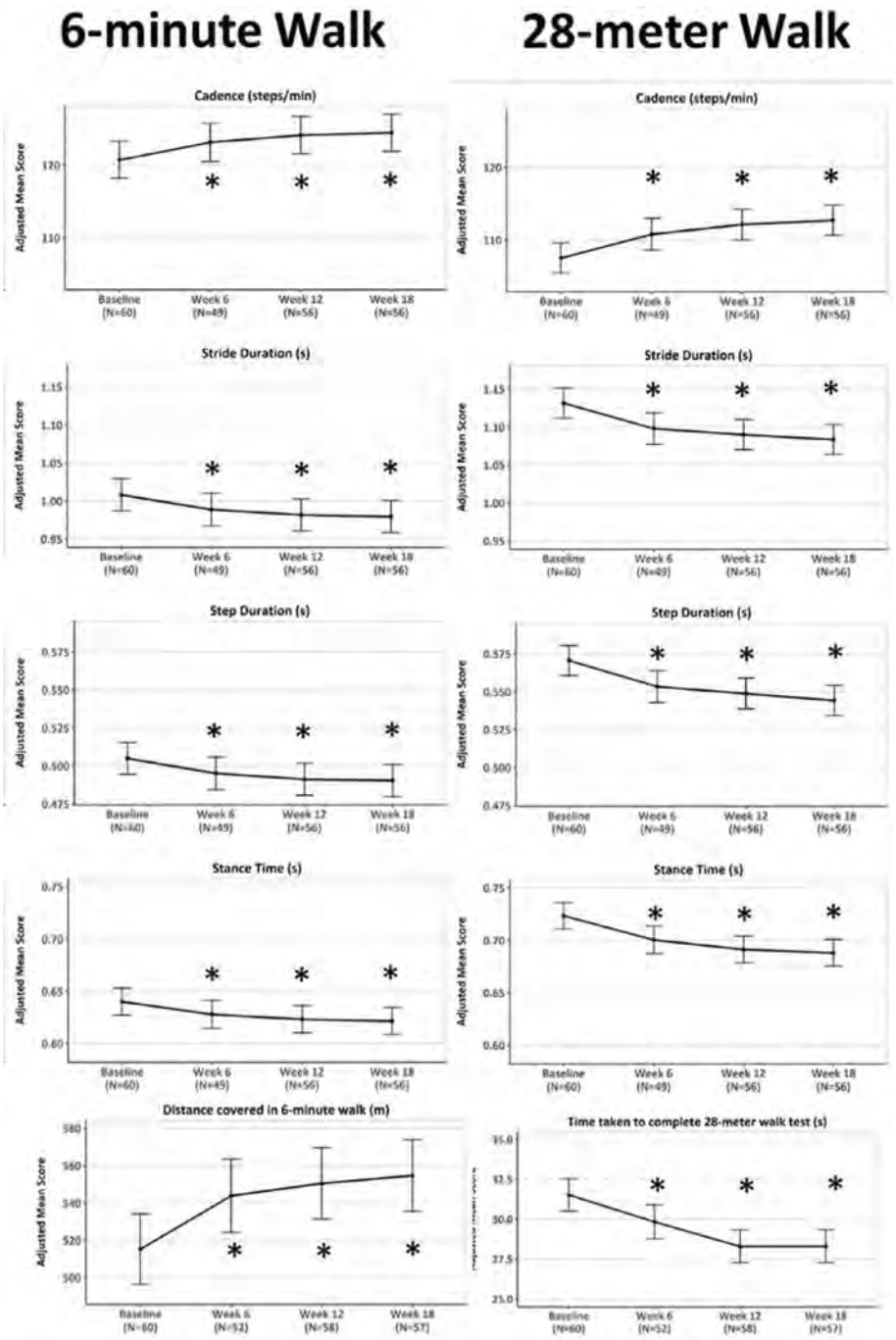

Figure 1. Adjusted means for sensor-derived measures (with excellent agreement) and standard functional measures at baseline, week 6, week 12, and week 18 during the 6-minute walk test (left) and 28-meter walk test (right). * indicates significant change compared to baseline.

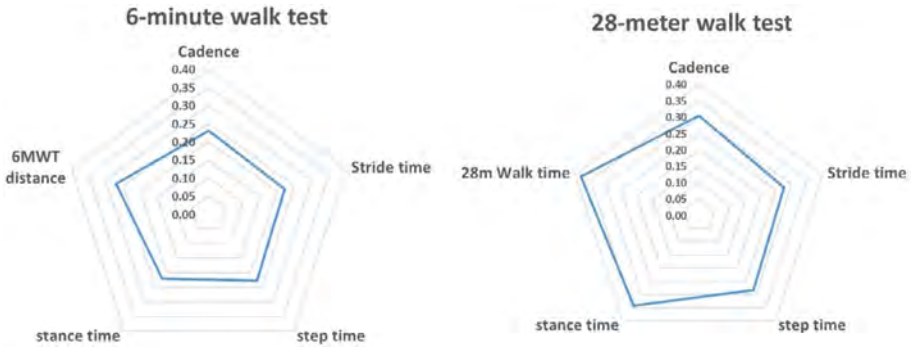

Figure 2. Standardized response means for change from baseline to week 12 in sensor-derived measures (with excellent agreement) and standard functional measures during 6-minute walk test (left) and 28-meter walk test (right)

agreement with motion capture and standard measures during functional tests were evaluated with mixed model repeated measures (MMRM) models with visit as a categorical factor adjusting for age, sex, BMI, and presence of comorbidities.

Results: The agreement between sensor and motion capture derived measures was excellent (ICC ≥ 0.75) for cadence, stride duration, step duration, and stance duration, good (0.6≤ICC≤0.74) for initial double support duration, terminal double support duration, total double support duration, and swing time, and moderate (0.4≤ICC≤0.59) for step length and gait speed (**Table 1**). Sensor derived measures and functional measures were significantly correlated in the expected directions with somewhat stronger correlations during 6-minute walk (range 0.68-0.90) vs. and 5-time chair stand (range 0.67-0.70) vs. 28-meter walk (range 0.46-0.65). With the intervention, all sensor derived measures showed significant improvements in all functional tests with the improvement maintained from 12- to 18-weeks (**Figure 1 and 2**).

Conclusion: Multiple measures of gait and chair stand patterns derived using a single inertial sensor demonstrate good agreement with gold-standard measures derived from motion capture. Spatial measures (step length, speed) performed worse than temporal measures. Sensor derived measures are moderately correlated with standard functional outcomes and may provide additional information not captured by standard measures. Sensor derived measures are responsive to change with an effective treatment and potentially could serve as digital biomarker for monitoring or treatment response.

Disclosure: D. Kumar: Eli Lilly, 5, Pfizer, 5; **L. Adamowicz**: Pfizer, 3; **B. Senderling**: None; **M. Gheller**: None; **M. LaValley**: None; **K. Bacon**: None; **P. Georgiev**: Pfizer, 3, 11; **C. Demanuele**: Pfizer, 3, 11; **P. Wacnik**: Pfizer, 11; **T. Neogi**: None.

Abstract Number: 1185

Soluble Buffered Alendronate After Denosumab Discontinuation in Erosive Hand OA Patients

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: In osteoporotic patients, discontinuation of denosumab is associated with a rapid increase in bone turnover and bone loss. Denosumab was recently proven to have clear structure modifying effects in erosive hand osteoarthritis (OA) patients compared to placebo. So far, the effect of denosumab discontinuation in a non-osteoporotic population is unclear. The objective was to investigate whether buffered soluble alendronate after denosumab discontinuation, can counter potential increase in bone turnover in this non-osteoporotic population.

Methods: Patients with erosive hand OA, who participated in a RCT with denosumab, were randomized to open label treatment with oral effervescent alendronate 70 mg weekly for either 24 or 48 weeks, after discontinuating denosumab treatment. Underlying osteoporosis was excluded at baseline. Serum bone turnover markers (C-terminal telopeptide of type I collagen (CTx-I) and N-terminal propeptide of type I procollagen (PINP) were measured at baseline, week 12, week 24 and week 48. Dual energy X-ray absorptiometry was performed at baseline, week 24 and week 48. The primary end point was the number of patients maintaining serum bone turnover markers within pre-menopausal reference range. Statistical analysis was performed with an intention to treat approach. Secondary end point was change in bone mineral density (BMD). Occurrence of adverse events were recorded.

Results: Fifteen patients were randomized to each treatment group. At week 48, 5 of 15 (33%) patients from alendronate 24 weeks vs 1 of 15 (7%) from alendronate 48 weeks, showed CTx-I values above pre-menopausal ranges. For PINP, 7 of 15 (47%) from alendronate 24 weeks vs. 2 of 15 (13%) from alendronate 48 weeks, showed values exceeding pre-menopausal ranges. The amount of patients above pre-menopausal ranges was not significantly different between both groups (p=0.11 and p=0.17 for CTx-I and PINP respectively). Mean changes of CTx-I levels between baseline and week 48 were significantly lower for alendronate 48 vs 24 weeks (p=0.043). For PINP, mean changes were numerically lower in alendronate 48 weeks but not statistically significant. BMD T-scores did not differ significantly between baseline and week 48, except for T-scores at the lumbar spine in alendronate 24 weeks. No significant differences were seen in mean change BMD between treatment groups. No fractures were reported.

Conclusion: Soluble alendronate 70mg weekly after denosumab discontinuation in this non-osteoporotic population did not maintain bone turnover markers under premenopausal reference range in all patients. Clinical implications of the increase of bone turnover markers in this non osteoporotic remain doubtful, since BMD values did not change over time, except at the lumbar spine in the 24 weeks alendronate group. Longer follow-up is warranted to evaluate clinical consequences on long term.

Disclosure: T. Vanhaverbeke: AbbVie, 6; **D. Elewaut**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 2, galapagos, 5, Janssen, 6; **R. Wittoek**: AbbVie, 2, Amgen, 5, Fresenius Kabi, 6, Galapagos, 6, Merck/MSD, 6, Pfizer, 5.

Abstract Number: 1186

Presence of Erosions Is Not a Risk Factor for the Development of Knee OA in a Hand OA Population: The Framingham OA Study

Tine Vanhaverbeke[1], Gabriela Rabasa[2], Ruth Wittoek[1], Ida Kristin Haugen[3] and David Felson[2], [1]Dept. of Rheumatology, Ghent University Hospital, Ghent University, Ghent, Belgium, [2]Boston University, Boston, MA, [3]Diakonhjemmet Hospital, Oslo, Norway

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is a prevalent musculoskeletal disease and can affect multiple joint sites in one patient. Studies have shown an association between hand and knee OA (1). However, few studies have examined the association between erosive hand OA, a subtype of hand OA considered to be more inflammatory, and knee OA. The goal of this study was to assess the association between erosive hand OA and knee OA and to identify risk factors for the development of knee OA in a hand OA population.

Methods: All subjects were selected from the Offspring and Community cohorts of the Framingham OA study. Bilateral knee and hand radiographs were obtained and scored using the Kellgren-Lawrence grade (KLG). Radiographic tibiofemoral OA was defined as at least one knee having a KLG≥2. Symptomatic knee OA was defined as presence of radiographic OA, in combination with presence of frequent knee pain. Radiographic hand OA (RHOA) was defined as KLG≥2 in at least one hand joint, erosive hand OA as RHOA plus a central erosion and symptomatic hand OA as RHOA plus pain, aching or stiffness in the same joint. Crude prevalence and incidence numbers were calculated. Multivariable logistic regression analysis, adjusted for age, sex and BMI was performed.

Results: In total, 1293 participants were studied. After adjustment for age, sex and BMI, presence of radiographic hand OA was associated with the development of symptomatic knee OA (OR 1.8 [1.4,2.4]). Similar results were found for symptomatic hand OA as the predictor (OR 1.9 [1.3,2.7]). However, compared with nonerosive hand OA, erosive hand OA was not identified as a risk factor for the development of symptomatic knee OA (OR 1.3 [0.7, 2.6]). Other risk factors identified for the development of symptomatic knee OA were: presence of thumb OA (vs. no thumb OA), presence of OA at a distal

Table 1: Risk factors for the development of symptomatic knee osteoarthritis in subjects with symptomatic hand osteoarthritis

Variable	Odds Ratio (OR)	95% Confidence Interval (95% CI)
Presence of Symptomatic Hand OA	1.89	(1.34, 2.67)
Presence of Symptomatic Bilateral Hand OA	1.47	(0.84, 2.57)
Presence of Thumb Base OA	1.98	(1.36, 2.90)
Presence of DIP OA	1.73	(1.20, 2.50)
Presence of PIP OA	1.97	(1.29, 3.03)
Presence of Erosive HOA	1.18	(0.60, 2.34)
Number of Finger Joints Affected-Continuous*	1.17	(1.06, 1.29)
Number of Finger Joints Affected-Dichotomous (1 if 3 or more joints are affected for kl >=2)*	1.84	(1.15, 2.96)
>= 1 Unit Change in KL Grade in At Least One Joint*	2.09	(1.50, 2.91)
>= 1 Unit Change in KL Grade in At Least Two Joints*	2.13	(1.53, 2.97)
>= 1 Unit Change in KL Grade in At Least Three Joints*	2.29	(1.61, 3.26)

* Includes thumb

Table 2: Risk factors for the development of symptomatic knee osteoarthritis in subjects with radiographic hand osteoarthritis

Variable	Odds Ratio (OR)	95% Confidence Interval (95% CI)
Presence of Radiographic Hand OA	1.8	(1.4, 2.4)
Presence of Radiographic Bilateral Hand OA	1.9	(1.4, 2.6)
Presence of Thumb Base OA	1.9	(1.4, 2.6)
Presence of DIP OA	1.6	(1.2, 2.1)
Presence of PIP OA	1.8	(1.2, 2.7)
Presence of Erosive HOA	1.3	(0.7, 2.6)
Number of Finger Joints Affected-Continuous*	1.2	(1.1, 1.3)
Number of Finger Joints Affected-Dichotomous (1 if 3 or more joints are affected for kl >=2)*	1.8	(1.2, 2.7)
>= 1 Unit Change in KL Grade in At Least One Joint*	2.1	(1.6, 2.8)
>= 1 Unit Change in KL Grade in At Least Two Joints*	2.2	(1.7, 2.9)
>= 1 Unit Change in KL Grade in At Least Three Joints*	2.2	(1.6, 3.0)

* Includes thumb

interphalangeal (DIP) joint, presence of OA at a proximal interphalangeal (PIP) joint, the number of finger joints affected and a change of at least 1 unit in KL grade in one or more hand joints (interphalangeal and thumb joints). .

Conclusion: This study confirms presence of hand OA is a risk factor for the development of knee OA. However, in a hand OA population, presence of erosions is not an additional risk factor. Our results may suggest that erosive hand OA is unrelated to OA in the knee.

References

< 1. Hirsch R et al. Association of hand and knee osteoarthritis: evidence for a polyarticular disease subset. Ann Rheum Dis. 1996 Jan;55(1):25-9.

Disclosure: T. Vanhaverbeke: AbbVie, 6; **G. Rabasa**: None; **R. Wittoek**: AbbVie, 2, Amgen, 5, Fresenius Kabi, 6, Galapagos, 6, Merck/MSD, 6, Pfizer, 5; **I. Haugen**: AbbVie/Abbott, 6, GlaxoSmithKlein(GSK), 6, Grünenthal, 6, Novartis, 6, Pfizer, 5; **D. Felson**: None.

Abstract Number: 1187

Post-hoc Analysis of Individual Questions from the Australian/Canadian Osteoarthritis Hand Index from a Randomized, Double-blind, Placebo-controlled Trial of Patients with Hand OA

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Osteoarthritis – Clinical Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Hand osteoarthritis (OA) is a frequently occurring form of OA characterized by symptoms including joint pain, stiffness, and swelling which affect performance of activities of daily living.The Australian/Canadian Osteoarthritis Hand Index (AUSCAN) is a key functional survey for hand OA, consisting of 15 questions organized into three subscales: pain, stiffness, and physical function.While AUSCAN results are typically reported as a total index and/or subscale scores, the individual questions are more granular endpoints which are relevant to patients' daily activities such as getting dressed, turning doorknobs and faucets, and cooking. The purpose of this post-hoc analysis was to evaluate the scores from the individual AUSCAN questions from an 8-week randomized, double-blind, placebo-controlled trial of diclofenac sodium 1% gel (DSG) vs vehicle in the treatment of hand OA (Altman RD, et al. J Rheumatol 2009;36:1991-9).

	Baseline			Week 4				Week 6			
Question	DSG Mean (SD) N=198	V Mean (SD) N=187	Δ	DSG Mean (SD)	V Mean (SD)	Δ	p	DSG Mean (SD)	V Mean (SD)	Δ	p
Pain Subscale: How much pain do you have in your hand-											
-at rest?	51.99 (23.339)	52.28 (22.168)	-0.29	32.32 (26.528)	35.12 (26.522)	-3.81	0.1470	29.30 (27.097)	34.37 (26.894)	-5.07	0.0478
-when gripping objects?	68.08 (19.019)	68.05 (17.718)	0.03	40.52 (28.211)	45.83 (27.297)	-5.31	0.0327	38.44 (28.144)	44.29 (27.716)	-5.85	0.0188
-when lifting objects?	67.61 (20.290)	69.07 (17,895)	-1.46	41.24 (28.882)	48.39 (27.730)	-7.15	0.0136	38.88 (25.669)	45.53 (27.293)	-6.65	0.0231
-when turning objects?	71.30 (18.661)	71.46 (17.779)	-0.16	42.59 (28.385)	50.54 (25.183)	-7.95	0.0026	39.85 (29.276)	47.19 (29.264)	-7.34	0.0054
-when squeezing objects?	72.69 (18.766)	72.90 (18.305)	-0.21	44.15 (29.216)	51.70 (28.843)	-7.55	0.0049	40.96 (26.738)	48.96 (28.945)	-8.00	0.0028
Stiffness Subscale: How severe is your stiffness in your hand-											
-after first wakening in the morning?	66.03 (22.779)	66.62 (23.888)	-0.59	40.96 (28.639)	48.40 (29.153)	-7.44	0.0066	38.36 (28.412)	46.82 (30.491)	-8.46	0.0019
Physical Function Subscale: How much difficulty do you have-											
-when turning taps/faucets on?	56.70 (25.698)	54.73 (24.292)	1.97	34.92 (27.097)	42.41 (28.046)	-7.49	0.0009	31.94 (27.074)	40.08 (28.000)	-8.14	0.0004
-when turning a round doorknob or handle?	61.70 (22.953)	58.48 (23.168)	3.22	36.95 (27.891)	44.37 (28.119)	-7.42	0.0002	34.60 (28.324)	42.37 (28.326)	-7.77	0.0001
-while doing up buttons?	63.33 (24.136)	61.44 (23.939)	1.89	39.17 (28.935)	46.74 (29.075)	-7.57	0.0009	34.55 (28.444)	43.88 (29.985)	-9.33	<0.0001
-while fastening jewelry?	66.02 (22.349)	64.56 (22.703)	1.46	40.53 (29.557)	47.70 (28.541)	-7.17	0.0022	36.53 (29.837)	45.17 (29.510)	-8.64	0.0003
-while opening a new jar?	76.23 (18.929)	76.26 (18.623)	-0.03	49.53 (29.007)	55.11 (29.473)	-5.58	0.0349	46.08 (30.357)	52.96 (29.188)	-6.88	0.0093
-when carrying a full pot with your hand?	74.54 (19.442)	73.91 (18.637)	0.63	47.97 (29.083)	53.40 (29.017)	-5.43	0.0249	45.63 (30.549)	51.88 (29.169)	-6.25	0.0104
-while peeling vegetables/fruits?	65.86 (22.890)	65.07 (20.219)	0.79	41.27 (28.114)	47.27 (29.066)	-6.00	0.0107	38.08 (28.594)	45.26 (29.304)	-7.18	0.0026
-when picking up large heavy objects?	73.27 (20.347)	72.83 (18.325)	0.44	47.72 (29.529)	53.40 (28.672)	-5.68	0.0212	44.45 (30.456)	51.26 (29.011)	-6.81	0.0062
-when wringing out wash clothes?	73.27 (20.127)	73.21 (18.614)	0.06	45.74 (29.295)	52.21 (30.074)	-6.47	0.0141	43.03 (30.318)	49.37 (30.071)	-6.34	0.0160

DSG, diclofenac sodium gel 1%; V, vehicle; Δ, difference (DSG – V); p, p-value; SD, standard deviation
0 = no pain/stiffness/difficulty, 100 = severe pain/stiffness/difficulty

Mean scores for individual AUSCAN questions (0-100 scale)

Methods: Patients diagnosed with hand OA in the dominant hand were randomly assigned DSG (n = 198) or vehicle (n = 187) and applied 2 g to each hand 4 times daily for 8 weeks. Vehicle was identical to DSG except for the absence of diclofenac sodium.AUSCAN questions were scored using a scale of 0 (no pain/stiffness/difficulty)-100 (extreme pain/stiffness/difficulty) at baseline and at weeks 1, 2, 4, 6 and 8.Mean scores for each question were assessed and compared between treatments at each timepoint using Analysis of Covariance (ANCOVA) with baseline as a covariate in the model and with no multiplicity correction.

Results: DSG demonstrated efficacy with reduction of pain subscale question scores at week 6 by 42%-44% (33%-35% for vehicle), stiffness scores by 42% (30% for vehicle) and physical function subscale scores by 39%-45% (27%-33% for vehicle).Statistically significant differences favoring DSG over vehicle were observed at weeks 4 and 6 (the primary endpoints) in all categories and at week 8 in the stiffness and physical function questions. Specifically, the questions with the greatest separation from vehicle at week 6 involved pain when turning and squeezing objects, stiffness upon wakening, difficulty turning doorknobs and faucets, and difficulty getting dressed, all of which are important components of hand functionality in daily living. Questions that did not reach statistical significance demonstrated a trend favoring DSG.

Conclusion: The results from this analysis show that the individual AUSCAN index question scores for DSG reach statistical significance vs vehicle at week 4 and last through week 8.The DSG scores at week 6 demonstrate a 39%-45% improvement from baseline in performing daily activities including turning objects such as doorknobs and faucets, getting dressed, and cooking compared to 27%-35% reductions from baseline for vehicle. These endpoints may be more meaningful to patients than the subscale scores of pain, stiffness and physical function, and may provide healthcare providers better ways to communicate the benefit of using DSG to treat the symptoms of hand OA.

Disclosure: K. Nicholson: Haleon, 3; **E. Sanchez**: Haleon, 3; **W. Wright**: Haleon, 2; **J. Block**: Haleon, 2; **R. Petruschke**: Haleon, 3.

Abstract Number: 1188

Development of a Method to Isolate Functional Mitochondria and Assess Their Functionality and Integration in Joint Tissues: *In Vitro* and *in Vivo* Models

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: There is not cure or an efficient treatment for the osteoarthritis (OA). Mitochondrial damage and dysfunction are described during OA process modulating chondrocyte function and survival contributing to its pathogenesis. As a consequence, mitochondria has proposed as a potential therapeutic target for OA.

Aim: To describe a method to isolate functional mitochondria and assess their functionality and capacity to integrate in joint tissues

Methods: Magnetic beads coupled to anti-TOM22 was used to obtain isolate mitochondria from liver of C57BL/6JOlaHsd after classical tissue digestion. Transmission Electron microscopy (TEM) images and Western blot (WB) were using to stablish the purity and the analysis of Mitotracker Red® staining and ATP were studied in the stablish of mitochondria viability. To evaluated the capacity of mitochondria to integrated in the joint tissues, cartilage and synovial membrane explants were co-incubated in presence of isolated mitochondria labeled with Iron nanoparticles or MitoTarker Red ® during 24, 48 hours (h). Mitochondria labeled with Mitotracker Red® were injected in left knee of 3 C57BL/6JOlaHsd mice and 48 h after the animals were euthanized. The ability of the injected mitochondria to cross the different joint tissues was analyzed, as well as the biological effect and safety of the intra-articular injection.

Results: Normal mitochondrial morphology was obtained when TEM images were analyzed (**Figure 1-A**). WB showed a big signal of *ATP synthase α* in mitochondrial isolated fraction while *BIP* and *Tubulin-α* were detected only in the elution fraction (**Figure 1-B**). These data reflected that isolated mitochondria were purity. The Mitochondria viability was analyzed through the evaluation of MitoTracker Red ® fluorescence and ATP production. Isolated mitochondria labeled with MitoTracker Red ® showed higher fluorescent than the same samples without label (81±6.92 vs 2.51±0.29, p=0.05) (**Figure 1-C**). ATP production in isolated mitochondria was modulated when were incubated in presence of 0.8 µM Rotenone (27.64±3.42 vs 16.76±4.62) (**Figure 1-D**). These results showed that isolated mitochondria were functional.

In vitro analysis showed the presence of isolated mitochondria embedded in the ECM of the superficial and intermedial layer of cartilage and into the ECM of synovial tissue (**Figure 2-A-B**). Morphology of chondrocytes in the different layers of the cartilage and morphology of synoviocytes did not show any change. Intrarticular injection of mitochondria caused low grade of joint inflammatory response as well as any systemic complication, no animal dead. Histologic studies of left joint showed Mitotracker Red® signal in the synovial membrane and in the superficial layer of the cartilage (**Figure 2-C**). Synovitis was not present. Histologic studies of the right knee and organs did not detect any red fluorescence stain.

Conclusion: Isolated mitochondria penetrate ECM of cartilage and synovium. In mice, intraarticular injection of functional isolated mitochondria is safety. These data give us the opportunity to continue studying the mitochondria as a treatment for OA.

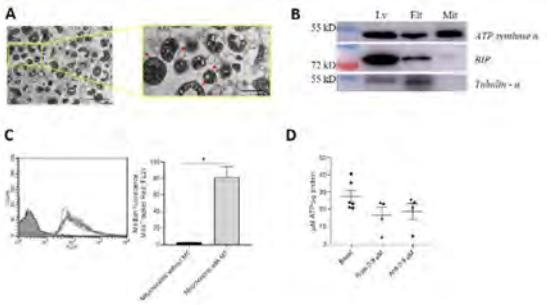

Figure 1. Purity and viability of isolated mitochondria. A Transmission electron microscopy (TEM) image of isolated mitochondria: representative image of purify mitochondria from mouse liver. mitochondria morphology was investigated by transmission electron microscopy. picture was taken at 9,000x (left panel) and the magnification area at 25,000x (right panel), black bars display 2.5 µm (left panel) and 1 µm (right panel) respectively. Black dots at the outer membrane represent anti TOM22 magnetic beads (red arrows). **B. Western blot** of preparations probed with antibodies specific for organelle-cell compartment specific marker proteins: cytosol (Tubulin-α), mitochondria (ATPsintase α) and Endoplasmic Reticulum (GRP78 -BIP). Lv: liver homogenate, Flt: elution fraction, Mit: isolated mitochondria. **C. Mitochondrial membrane potential (ψm)** of isolated mitochondria labeled with MitoTracker Red® was measured by flow cytometry .Graph. represented the the median of fluorescence showed the comparison between mitochondria without and with Mitotracker Red® (MT) (N=4). **D. ATP production** nmol/µg mitochondrial protein was determined by ATP assay in isolated mitochondria (basal) and in isolated mitochondria incubated in presence of 0.8 µM Rotenone (Rote) or 0.8 µM Antimycine A (Anti) during 2 h (N=4) *p≤0.05

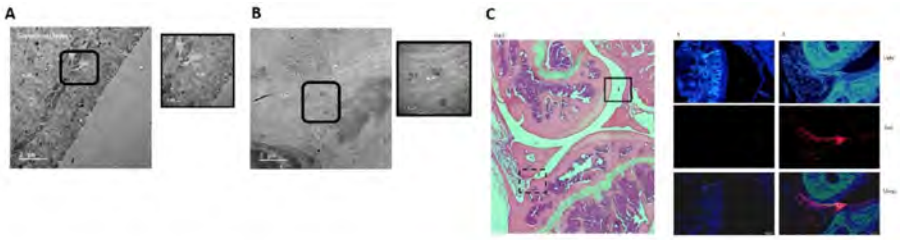

Figure 2. Mitochondria has the capacity in breaking through joint tissue and penetrate in ECM of cartilage and synovium. A. Cartilage with mitochondria injection labeled with iron during 48 h. Images showed the presence of mitochondria in the superficial layer embedded in the extracellular matrix (em), these pictures were taken at 15,000 X and 40,000 X respectively and withe bar display 2 and 1 µm respectively. **B**. Synovial membrane incubated with mitochondria labeled with iron, picture showed the presence of mitochondria embedded in the extracellular matrix (em), picture was taken at 15,000 x (left panel) and the magnification area at 50,000 x (right panel), white bars display 2 (left panel) and 0.5 µm (right panel) respectively. **C**. ***In vivo* model**. Mitochondria obtained from mouse liver were labeled with MitoTracker Red® and injected in the mouse left knee. 48 h later the animal was scarified. The red fluorescence analysis showed the presence of red mitochondria in the superficial layer of the cartilage and in the synovial membrane.

Disclosure: M. Fernandez-Moreno: None; **T. Hermida-Gomez**: None; **S. Paniagua-Barro**: None; **A. Rodriguez-Coello**: None; **C. Vaamonde-garcia**: None; **F. Blanco**: None.

Abstract Number: 1189

Evaluating Neuropathic and Nociplastic Pain in Patients with Hip and Knee Osteoarthritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session B
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Background/Purpose: Chronic pain in patients with hip and knee osteoarthritis (OA) has been classically attributed to nociceptive pain pathways. Emerging evidence has demonstrated influence from additional pain pathways in OA (Table 1). In this study, we screened for pre-operative neuropathic and nociplastic pain in patients who subsequently underwent hip or knee arthroplasty.

Methods: Participants filled out two surveys reflecting pre-surgical pain: 1) the PainDETECT questionnaire (PD-Q) to assess neuropathic pain, and 2) the Fibromyalgia Survey Questionnaire (FSQ). The FSQ is comprised of the Widespread Pain Index (WPI) assessing widespread musculoskeletal pain and the Symptom Severity Scale (SSS) assessing comorbid symptoms (e.g., fatigue). The 2016 fibromyalgia criteria were used as inclusion criteria for fibromyalgia diagnosis.

Results: Overall, 89 participants were included in our analysis (23 hip OA, 66 knee OA). The mean age was 66.0 ± 9.01 (mean ± SD), 50 were female (56.2%), 84 were Caucasian Non-Hispanic (94.4%), the mean BMI was 30.43 ±5.56 (Table 2). Of this cohort, 18.0% had widespread pain (WPI ≥ 7), 7.9% met diagnostic criteria for fibromyalgia, 25.8% had possible neuropathic pain (PD-Q 13-18), and 12.4% had probable neuropathic pain (PD-Q ≥19) (Figure 1). This represented 34 (38.2%) unique individuals. We did not find significant differences in age, BMI, sex or site of OA among those with versus without widespread pain, fibromyalgia or neuropathic pain.

Conclusion: Among patients with hip or knee OA who underwent joint arthroplasty, more than a third had evidence of pre-operative nociplastic and/or neuropathic pain. This has clinical relevance, as nociplastic and neuropathic pain may have decreased responsiveness to peripherally directed therapies such as surgery. Given the evidence that there are multiple

Table 1. Pain Mechanism Definitions

Table 1. Pain Mechanism Definitions	
Nociceptive	Related to tissue damage
Nociplastic	Related to central pain modulation
Neuropathic	Related to nerve damage or dysfunction

Table 2. Demographics

Table 2. Demographics	N = 89
Age, mean (±SD)	66.0 (±9.01)
Sex	
Female	50 (56.2%)
Male	39 (43.8%)
Race/Ethnicity	
African American	2 (2.2%)
Asian	1 (1.1%)
Caucasian	84 (94.4%)
Hispanic	2 (2.2%)
BMI, mean (±SD)	30.43 (±5.56)
Primary OA site	
Hip	23 (25.8%)
Knee	66 (74.2%)

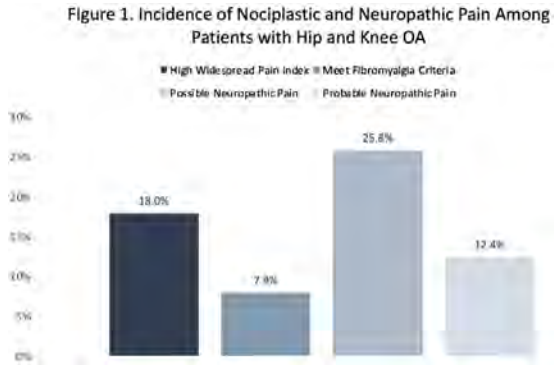

FIgure 1. Incidence of Nociplastic and Neuropathic Pain Among Patients with Hip and Knee OA

mechanisms of pain within individuals, this implies a need for multiple therapeutic targets in many patients. Elucidating these pain pathways in future studies will be key to more effectively treating hip and knee OA pain.

Disclosure: C. Conran: None; **L. Moreland**: Boehringer-Ingelheim, 12, member of independent Data Safety Monitoring Board, Celltrion, 12, member of independent Data Safety Monitoring Board; **A. Clauw**: None; **J. Seifert**: None; **C. Keeter**: None; **C. Hogan**: None; **M. Dayton**: None.

Abstract Number: 1190

Worsening of Pain as Perceived by Patients Is Not Reflected by an Annual Standardized Questionnaire

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The course of pain in hand osteoarthritis (OA) is often investigated with repeated validated pain questionnaires. However, it is unknown whether these questionnaires reliably reflect patients' experience of changes in pain. This experience may be influenced by amongst others recall and a shift in the patients' perception of the pain over time. In order to improve patient outcomes, it is important to ensure that what is measured as a decrease in pain is also experienced as such. Therefore, this study aimed to compare yearly changes on a validated pain questionnaire with the pain course recalled by the patient.

Methods: Four year data of the ongoing HOSTAS (Hand OSTeoArthritis in Secondary care, patients with primary hand OA diagnosed by rheumatologist) cohort were used.

Pain was measured with the Australian/Canadian hand Osteoarthritis index (AUSCAN) pain subscale (range 0-20) annually from baseline. Change in cross-sectional AUSCAN pain scores between years were categorized using the minimal clinical important improvement (MCII, 1.6). Additionally, an anchor question asking participants whether pain had worsened, improved, remained stable or if they had never had pain, compared with the year before, was collected annually. Patients were included in the current analysis if change in AUSCAN pain and the anchor question were available for at least one year.

Changes in annual AUSCAN scores were compared to answers on the anchor questions Cohen's kappa was calculated. Annual results were comparable between years, so the years were pooled.

Results: Over 4 years, 708 annual intervals (307 patients, mean age 61.0 (SD 8.2), 82% women, mean BMI 27.3 (SD 4.8), baseline AUSCAN pain 9.1 (SD 4.2)) with change in AUSCAN and anchor questions were available. Of 307 patients, 95 provided one interval, 74 provided two, 87 provided three and 51 provided four. In 203 intervals 172 patients reported an increase in AUSCAN pain (of which in 151 intervals patients (74%) indicated their pain had worsened), in 293 intervals 199 patients reported a stable level of pain (of which in 96 intervals (33%) indicated their pain had not changed) and in 212 intervals 176 patients reported a decrease in pain (of which 39 (19%) indicated their pain had improved) (table 1). The most frequent answer was worsening pain. In 422 (60%) of intervals, the anchor question was not in concordance with the AUSCAN pain (Cohen's kappa of 0.12).

Table 1. Change in AUSCAN pain compared with change in pain on anchor question

		Change in AUSCAN pain			
		Improvement	Stable	Worsening	Total
Anchor question	Worse – more pain	98 (14)	173 (24)	**151 (21)**	422 (60)
	No change	74 (10)	**96 (14)**	41 (6)	211 (30)
	Better – less pain	**39 (6)**	20 (3)	11 (2)	70 (10)
	Never had this symptom	1 (0)	4 (1)	0 (0)	5 (1)
	Total	212 (30)	293 (41)	203 (29)	708 (100)

Table 1. Change in AUSCAN pain vs anchor questions. The number and % of concordant answers in bold.

Conclusion: Changes in yearly AUSCAN pain measured differ greatly from the course of pain over the last year perceived by the patient. The patients described deterioration more often than is reflected in the differences between AUSCAN pain measurements. Further investigations to understand pain development, how patients perceive pain development and how best to evaluate it, are warranted.

Disclosure: C. van der Meulen: None; **L. van de Stadt**: None; **F. Rosendaal**: None; **M. Kloppenburg**: None.

Abstract Number: 1191

A Phase 1b, Randomized, Double-Blind, Placebo-Controlled, Multiple-Dosing, Ascending-Dose Study Evaluating the Safety, Tolerability and Pharmacokinetics of XG004 Applied Topically in Participants with Osteoarthritis of the Knee

Guang-Liang Jiang[1] and Feng Xu[2], [1]Xgene Pharmaceutical Inc., Lexington, MA, [2]Xgene Pharmaceutical Inc., Altos Hills, CA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Globally osteoarthritis affects about 302 million patients, knee osteoarthritis accounts for 263 million and ranks the highest in disability and pain compared to OA of other joints. Efficacious and safe therapeutics for chronic management of OA symptoms are still needed. Topical therapies remain the first line of recommendation for pharmacological management of OA. The current study was to assess a topical gel formulation of XG004, a new chemical entity inhibiting both the COX enzymes and the calcium a2d-subunit, in knee OA patients.

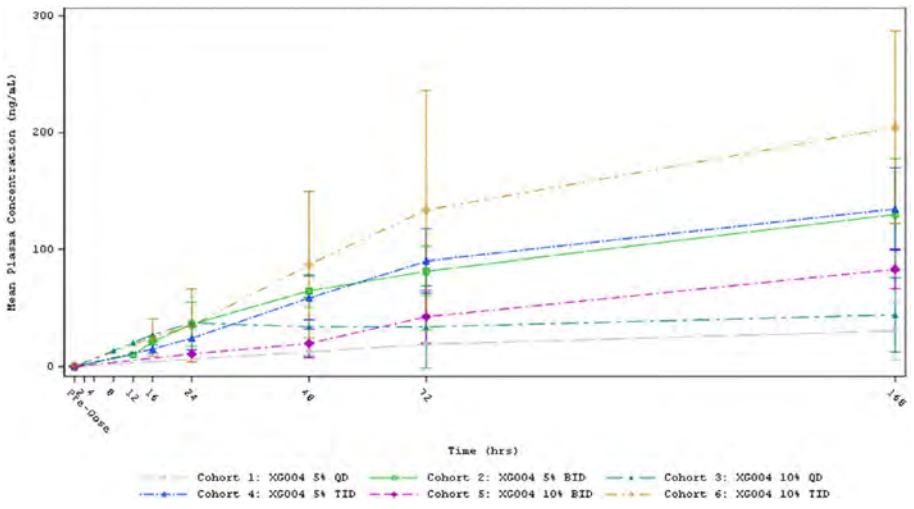


Figure 1. Plasma Concentrations (mean +/- SD) of Naproxen (linear)

Methods: The Phase 1b study (NCT054540200) was a randomized, double-blind, placebo-controlled, single-center, parallel-group trial, evaluating the safety, PK and efficacy of topical application of XG004 gel in Australian patients with OA of the knee. Patients with moderate to severe OA pain and Kellgren-Lawrence (KL) grade of II-IV were randomized in a 3:1 ratio to receive 4 mL of 5% or 10% topical gel of XG004 or placebo qd, bid, or tid over one week period. Trough plasma and synovial fluid (SF, withdrawn on day 8) PK was assessed with up to 24 hours interval from the last dosing. The exploratory efficacy was measured by changes from baseline in daily walking pain, sleep interference, the WOMAC scores, and the Patient Global Impression of Change (PGIC).

Results: 32 randomized patients had a mean baseline walking pain of 5.7 (0-10 NRS scale), 25% patients had KL grade IV, 56.2% patients had painDETECT score ≥ 13 (indicating neuropathic pain components), those and other baseline characteristics were well balanced between active and placebo arms. All reported good tolerability and safety without SAEs or discontinuation to the study drug. While pregabalin (an active metabolite) was only measurable in plasms of 10% TID dosing cohort, XG004 and another active metabolite naproxen were readily assessable in both plasma and SF. Plasma concentration increased over time in a dose-frequency- and drug-content-dependent way (Fig. 1). The magnitude of symptom improvement was greater in BID or TID dosing cohorts than in the QD cohorts. Over placebo, the BID or TID drug applications resulted in symptom relief in WOMAC pain, physical function, stiffness, total score, and daily walking pain with standard

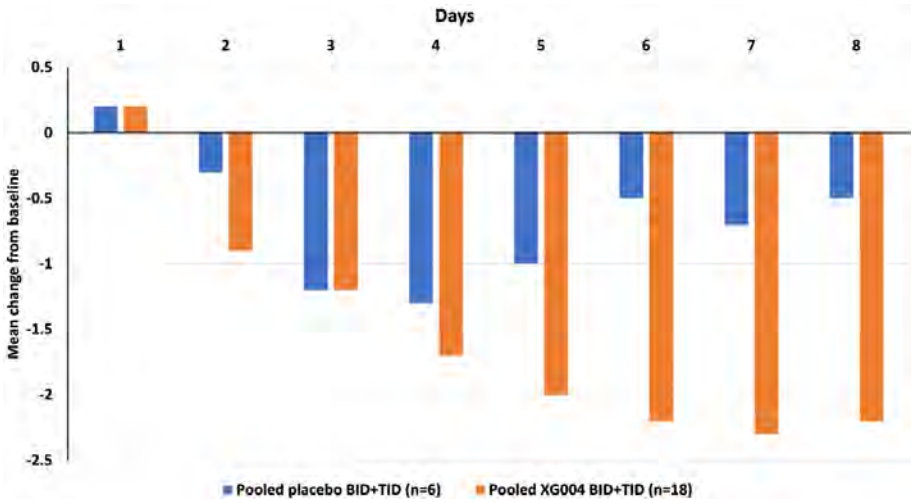


Figure 2. Sleep Interference Score Changes from Baseline in Pooled BID+TID Cohorts (0-10 NRS scale)

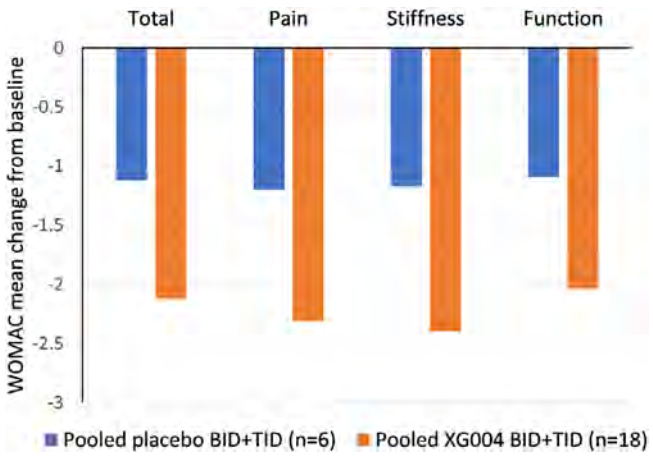


Figure 3. WOMAC Total and Subscore Changes from Baseline in Pooled BID+TID Cohorts (0-10 NRS scale)

effect sizes of 0.639, 0.444, 0.528, 0.508, and 0.343 by the end of 7 days treatment, respectively (Fig. 3). Meantime, these treatment regimens improved pain-induced sleep interference with an effect size of 0.752 (Fig. 2). 72.2% patients with XG004 BID or TID treatment reported at least "minimally improvement" and 27.8% reported "no change", while 50% reported at least "minimally improved" and 50% reported "no change" or "minimally worse" in the placebo-treated patients.

Conclusion: XG004 topical gel in knee OA patients showed good tolerability and safety. XG004 and its active metabolites were detectable in sparse plasma and/or SF samples. 5% or 10% BID or TID dosing showed substantial improvement in knee pain, stiffness, physical function, as well as sleep quality. With novel dual targeting on both nociceptive and neuropathic pain signals, XG004 topical could be a promising more efficacious and safer addition to chronic OA pain management.

Disclosure: G. Jiang: Xgene Pharmaceutical, 3; **F. Xu**: Xgene Pharmaceutical, 3.

Abstract Number: 1192

Autoimmune Thyroid Disease Associates with Symptomatic Hand Osteoarthritis in Older Persons in the Third National Health and Nutrition Examination Survey

Clement Tagoe[1] and Wanyi Wang[2], [1]Albert Einstein College of Medicine, Bronx, NY, [2]Elite Research, LLC, Irving, TX

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) of the hand is associated with the presence of bony deformities in the proximal interphalangeal joints, distal interphalangeal joints, and first carpometacarpal joints, frequently with joint pain and stiffness (1). The factors conferring risk and determining the joint distributions in hand OA are not well understood. Due to similarities in the epidemiology of hand OA and autoimmune thyroid disease (AITD) we investigated for the first time, a possible association between the two conditions in participants representative of the US population. The purpose of the study was to examine whether the AITD autoantibodies, anti-thyroid peroxidase antibody (TPOAb) and anti-thyroglobulin antibody (TgAb), associate with hand OA and symptomatic hand OA in the Third National Health and Nutrition Examination Survey (NHANES III).

Methods: NHANES III interviewed a sample of 33,994 participants, 3128 of whom were aged 60 years and over in Phase 2 (1991 – 1994) of the study where data for osteoarthritis were collected. A total of 2429 persons ≥60 years of age had no missing data for TPOAb and TgAb. Clinical hand OA (46.6% of participants) was defined using the American College of Rheumatology Classification Criteria modified for the NHANES III data set following the experience of Dillon et al. (2). Symptomatic hand OA (8.6% of participants) was defined as hand OA with the presence of chronic hand pain recorded as the presence of a "yes" response to the question, "Have you ever had pain in your hands on most days for at least 6 weeks? This also includes aching and stiffness". Data on hand OA or symptomatic hand OA were examined with respect to their associations with TPOAb and TgAb. Log binomial and modified Poisson regression models were fit to examine the associations between the anti-thyroid autoantibodies, and hand OA or symptomatic hand OA.

Results: Higher levels of TPOAb were associated with a higher prevalence of symptomatic hand OA in the unadjusted (*PR*=1.182, *p*=0.024) and adjusted models, after controlling for age, gender, and diabetes (*PR*=1.174, *p*=0.039). The significance of the association was no longer observed when positive TPOAb was classified into four levels and was compared

with negative TPOAb. TgAb analyzed as a continuous variable showed a trend to being positively associated with symptomatic hand OA (p< 0.10) in both the unadjusted and adjusted models. When positive TgAb was stratified as a categorical variable with four levels and compared with negative TgAb the highest quartile was associated with a higher prevalence of symptomatic hand OA than negative TgAb in the unadjusted (*PR*=2.242, *p*=0.008) and adjusted models (*PR*=2.045,*p*=0.038). There was no significant association between TPOAb or TgAb and hand OA.

Conclusion: Higher levels of TPOAb may be associated with the presence of symptomatic hand OA in persons ≥60 years. Persons ≥60 years with the highest quartile levels of TgAb may be more likely to present with symptomatic hand OA. Neither TPOAb nor TgAb was significantly related to the presence of hand OA.

Table 1. Associations between TPOAb/TgAb and Hand OA/Symptomatic Hand OA

	Hand OA			Symptomatic hand OA		
Models	β	*PR*	*p*	β	*PR*	*p*
Model 1						
TPOAb	0.004	1.004	0.934	0.167	1.182	**0.024**
Model 2						
TPOAb	-0.001	0.999	0.999	0.160	1.174	**0.039**
Age	0.444	1.558	**<0.001**	0.518	1.678	0.068
Female[a]	0.226	1.253	**<0.001**	0.304	1.356	0.242
Diabetes (Yes)[b]	-0.062	0.940	0.468	0.107	1.113	0.654
Model 3						
Positive TPOAb (Q1)[c]	0.095	1.100	0.371	0.056	1.057	0.895
Positive TPOAb (Q2)[c]	0.106	1.112	0.375	0.270	1.310	0.356
Positive TPOAb (Q3)[c]	0.005	1.005	0.975	0.297	1.345	0.416
Positive TPOAb (Q4)[c]	0.060	1.062	0.681	0.423	1.527	0.338
Model 4						
Positive TPOAb (Q1)[c]	0.033	1.033	0.999	-0.056	0.946	0.894
Positive TPOAb (Q2)[c]	0.083	1.086	0.393	0.175	1.192	0.494
Positive TPOAb (Q3)[c]	-0.065	0.937	0.666	0.210	1.233	0.599
Positive TPOAb (Q4)[c]	0.061	1.063	0.614	0.384	1.469	0.386
Age	0.448	1.565	**<0.001**	0.512	1.669	**0.041**
Female[a]	0.222	1.249	**<0.001**	0.301	1.351	0.178
Diabetes[b]	-0.067	0.935	0.434	0.098	1.103	0.724
Model 1						
TgAb	-0.014	0.986	0.771	0.086	1.089	0.071
Model 2						
TgAb	-0.020	0.980	0.733	0.085	1.089	0.094
Age	0.444	1.559	**<0.001**	0.499	1.648	0.088
Female[a]	0.225	1.253	**<0.001**	0.330	1.390	**0.038**
Diabetes (Yes)[b]	-0.063	0.939	0.462	0.102	1.108	0.669
Model 3						
Positive TgAb (Q1)[c]	-0.070	0.933	0.674	-0.595	0.552	0.393
Positive TgAb (Q2)[c]	-0.043	0.958	0.800	-0.054	0.947	0.893
Positive TgAb (Q3)[c]	0.192	1.212	0.272	-0.454	0.635	0.464
Positive TgAb (Q4)[c]	0.123	1.131	0.293	0.807	2.242	**0.008**
Model 4						
Positive TgAb (Q1)[c]	-0.079	0.924	0.627	-0.618	0.539	0.389
Positive TgAb (Q2)[c]	-0.080	0.923	0.608	-0.113	0.893	0.772
Positive TgAb (Q3)[c]	0.104	1.110	0.523	-0.560	0.571	0.359
Positive TgAb (Q4)[c]	0.031	1.032	0.816	0.715	2.045	**0.038**
Age	0.500	1.648	**<0.001**	0.463	1.589	0.066
Female[a]	0.225	1.252	**<0.001**	0.333	1.395	0.159
Diabetes[b]	-0.067	0.935	0.472	0.126	1.134	0.651

Note. Q: Quartile; [a] compared with male; [b] compared with non-diabetes; [c] compared with negative cases; β: beta level; PR: prevalence ratio; OA: osteoarthritis.

Figure 1. Prevalence of symptomatic hand OA by A). TPOAb levels and B). TgAb levels separated by negative level and positive quartiles.

Figure 1a

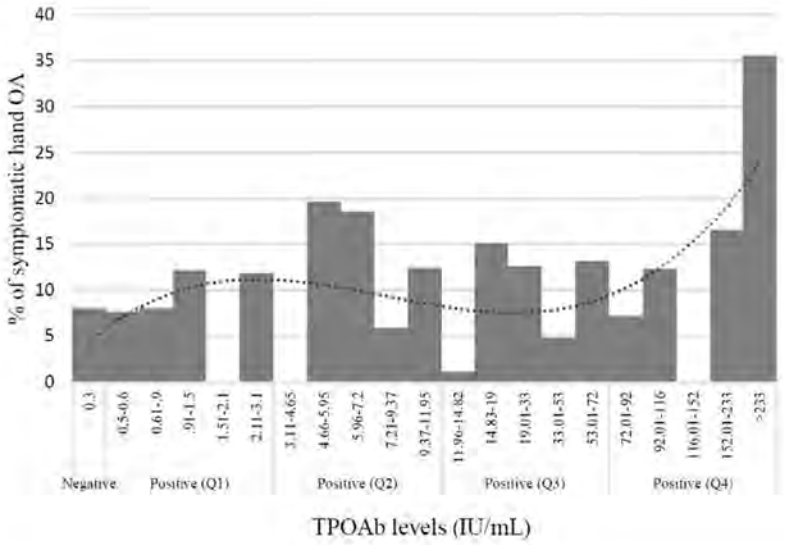
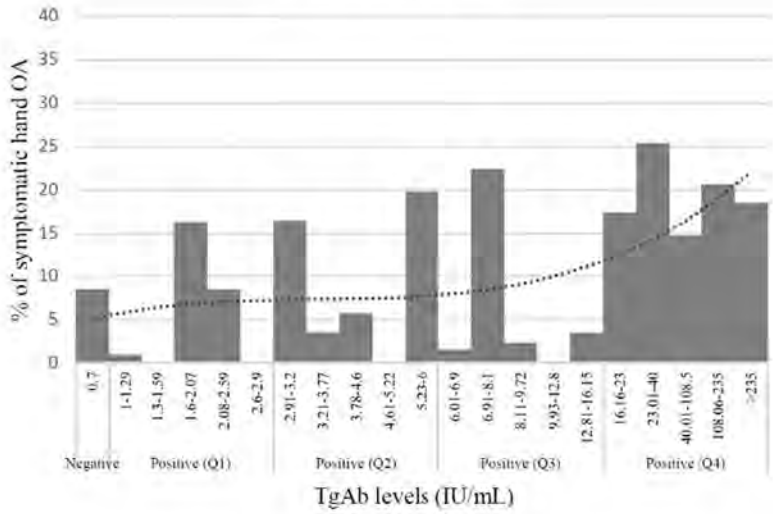


Figure 1b



References:

1. Altman R, Alarcon G, Appelrouth D, Bloch D, Borenstein D, Brandt K, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand. Arthritis Rheum. 1990;33(11):1601-10.
2. Dillon CF, Hirsch R, Rasch EK, Gu Q. Symptomatic hand osteoarthritis in the United States: prevalence and functional impairment estimates from the third U.S. National Health and Nutrition Examination Survey, 1991-1994. Am J Phys Med Rehabil. 2007;86(1):12-21.

Disclosure: C. Tagoe: None; **W. Wang**: None.

Abstract Number: 1193

The Association of Peak Forces and Loading Rates During Walking with MRI-Based Structural Worsening of the Knee: The Multicenter Osteoarthritis Study

Lauren Sara[1], David Felson[1], Michael LaValley[2], Gabriela Rabasa[1], Beth Lewis[3], John Lynch[4], Neil Segal[5], Ali Guermazi[1], Frank Roemer[6], Joshua Stefanik[7] and Cara Lewis[1], [1]Boston University, Boston, MA, [2]Boston University School of Public Health, Arlington, MA, [3]University of Alabama at Birimingham, Birmingham, AL, [4]University of California San Francisco, San Francisco, CA, [5]University of Kansas, Kansas City, KS, [6]Friedrich-Alexander University Erlangen-Nürnberg, Erlangen, Germany, [7]Northeastern University, Boston, MA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Osteoarthritis – Clinical Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Mechanical loading is an important, modifiable risk factor for knee osteoarthritis (OA). Walking loads have been previously proposed as a risk factor for developing OA; however, there is a scarcity of literature exploring the longitudinal relation of baseline walking kinetics on structural worsening in the knee joint. Thus, our purpose was to analyze peak vertical ground reaction force (GRF) and average slope of the force (i.e., average loading rate (ALR)) during walking in persons with and without knee OA, and to explore the relation of these exposure variables to changes in MRI-based structural outcomes two years later. We hypothesized that increased peak GRF and ALR would be associated with greater odds of MRI-based structural worsening.

Methods: Data from the Multicenter Osteoarthritis Study (MOST), an NIH-funded cohort study, were used. Participants were included if they had walking GRF data at baseline (i.e., year 12 of MOST) and had obtained knee MRIs at baseline and follow-up (i.e., years 12 & 14 of MOST). Participants were excluded if they underwent total knee arthroplasty of either knee, whether prior to or during the study period.

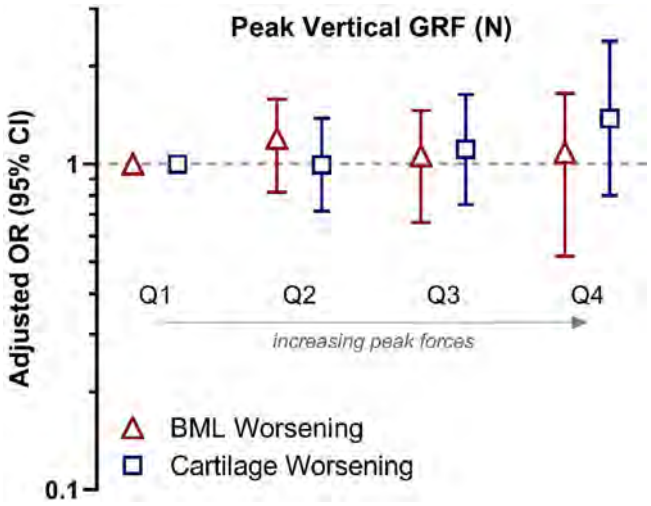


Figure 1. Adjusted odds ratios for BML and cartilage worsening across quartiles of peak vertical ground reaction force (GRF) during walking. Quartile 1 (Q1) is the reference quartile and has the lowest peak GRF, while Q4 has the highest peak GRF.

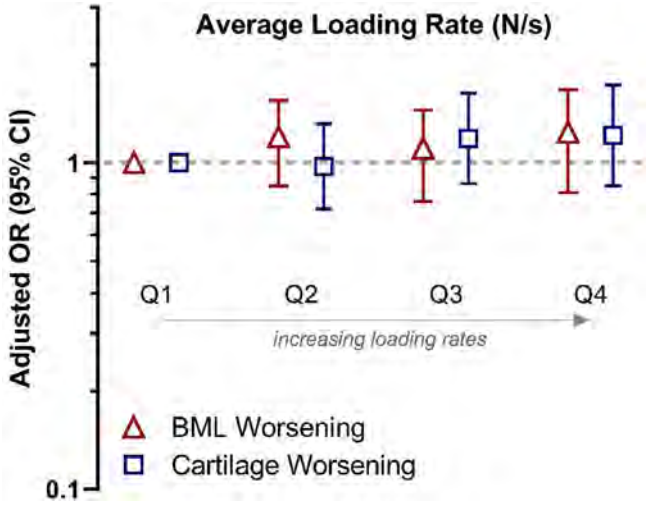


Figure 2. Adjusted odds ratios for BML and cartilage worsening across quartiles of average vertical ground reaction force loading rates during walking. Quartile 1 (Q1) is the reference quartile and has the lowest average loading rate, while Q4 has the highest average loading rate.

Peak vertical ground reaction force (GRF) and average loading rate were evaluated during the first ~10% of the gait cycle following initial contact, averaged across four trials per knee, grouped into sex-specific quartiles (Q1-Q4), and analyzed in relation to structural outcomes. MRIs were read paired by experienced musculoskeletal radiologists using the MOAKS scales. Structural worsening was operationalized in two ways: (1) increase in size of bone marrow lesions (BMLs); and (2) cartilage worsening, defined as an increase in cartilage score anywhere in the knee including incident damage. BML and cartilage worsening were separately dichotomized as Y/N (i.e., any increase in BML size or any cartilage loss) at 2-year follow-up. Analyses were conducted using logistic regression adjusting for specific covariates (gait speed, age, sex, body weight, race, and mechanical alignment). For both exposure variables, peak GRF and ALR, Quartile 1 is the reference group and represents the lowest magnitudes of force and loading rate.

Results: 1577 participants (age: 61(9) years, BMI: 28(5) kg/m^2; 56% female, 86% white) met criteria for inclusion; 8 observations were removed from analyses due to missing exposure and/or outcome data. At follow-up, 46% had BML worsening, and 45% had cartilage worsening. There were no between-quartile differences (p=0.29-0.69) or linear trends for BML worsening in either of the exposure variables (Chi Square=0.04-0.54, p=0.46-0.83). The odds of cartilage worsening were 11% higher in Q3 and 38% higher in Q4 of peak GRF (see figures) (test for linear trend: Chi Square=1.23, p=0.27). For ALR, the odds of cartilage worsening were 19% higher for Q3 and 21% higher for Q4 (test for linear trend: Chi Square=1.85, p=0.17).

Conclusion: Peak vertical GRF and GRF loading rate were not associated with worsening BMLs in the knee joint in persons with mild or no knee OA. Though not significant, the odds of cartilage worsening suggest a modestly elevated risk of cartilage worsening at higher peak GRF and higher loading rates when walking.

Disclosure: L. Sara: None; **D. Felson**: None; **M. LaValley**: None; **G. Rabasa**: None; **B. Lewis**: None; **J. Lynch**: None; **N. Segal**: Pacira Biosciences, 1, 2, 5, 6, Trice Medical, 6; **A. Guermazi**: BICL, LLC, 11, ICM, Coval, TrialSpark, TissueGene, Medipost, 2, Novartis, 2, Pfizer, 2; **F. Roemer**: Boston Imaging Core Lab (BICL) LLC., 8, Grünenthal GmbH, 2; **J. Stefanik**: None; **C. Lewis**: None.

Abstract Number: 1194

Extent of Subregional Involvement of Subchondral Bone Marrow Lesions in Incident Knee OA Is Associated with Weight-Bearing Knee Pain

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Subchondral bone marrow lesions (BMLs) have been associated with incident and progressive pain and reported to fluctuate along with concurrent fluctuations in symptoms. While associated with other structural, cellular, and biochemical features of OA that cause pain, BMLs may contribute directly to OA pain via cytokines, NGF, and altered biomechanics in knee OA, though evidence surrounding the role of BMLs and weight-bearing pain, specifically, is limited. Our objective was to estimate the effect of BML involvement on weight-bearing knee pain following radiographic KOA development, across the whole knee and by bone plate.

Methods: The OAI is a longitudinal observational study of participants with or at risk of symptomatic KOA. We identified incident cases of radiographic KOA, defined as KLG 2 or 3 on centrally graded x-rays. Participants underwent bilateral posteroanterior fixed-flexion weight-bearing knee radiography and non-contrast 3T MRI over 10 years of follow-up. MSK radiologists graded BMLs, effusion-synovitis (ES), Hoffa-synovitis (HS), cartilage and meniscal damage using the MRI Osteoarthritis Knee Score (MOAKS). BML involvement was assessed in 15 subregions (Figure 1). The WOMAC questionnaire includes pain assessment during 3 weight-bearing activities: walking on a flat surface, going up/down stairs, and standing, rated as none (0), mild (1), moderate (2), severe (3), or extreme (4). The weight-bearing knee pain score was defined as the

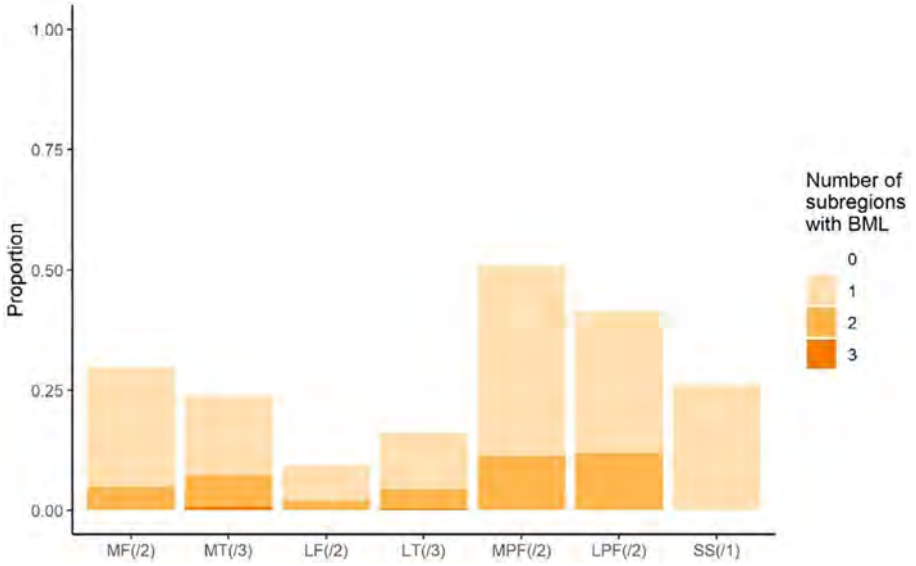

Figure 1. Prevalence of BML involvement in each bone plate, including 15 subregions: medial femur (MF) [FemCentMed, FemPostMed]; medial tibia (MT) [TibAntMed, TibCentMed, TibPostMed]; lateral femur (LF) [FemCentLat, FemPostLat]; lateral tibia (LT) [TibAntLat, TibCentLat, TibPostLat]; medial patellofemoral (MPF) [FemAntMed, PatellaMed]; lateral patellofemoral (LPF) [FemAntLat, PatellaLat]; subspinous (SS) [TibSubSpCent]

sum of reported pain scores during these activities (0-12). We fit a proportional odds logistic regression to model weight-bearing knee pain using penalized maximum likelihood estimation; predictors included the number of subregions with BML involvement, other structural damage scores, KLG, age, and BMI at the same clinic visit, as well as sex and race. We similarly fit a model with the number of subregions with BML involvement at the bone-plate level. Models were compared with and without the number of subregions with BML involvement using a likelihood ratio test (LRT). The predicted probability of weight-bearing pain score 4 or greater is reported with nonparametric bootstrap 95% confidence intervals with cluster sampling at the participant-level.

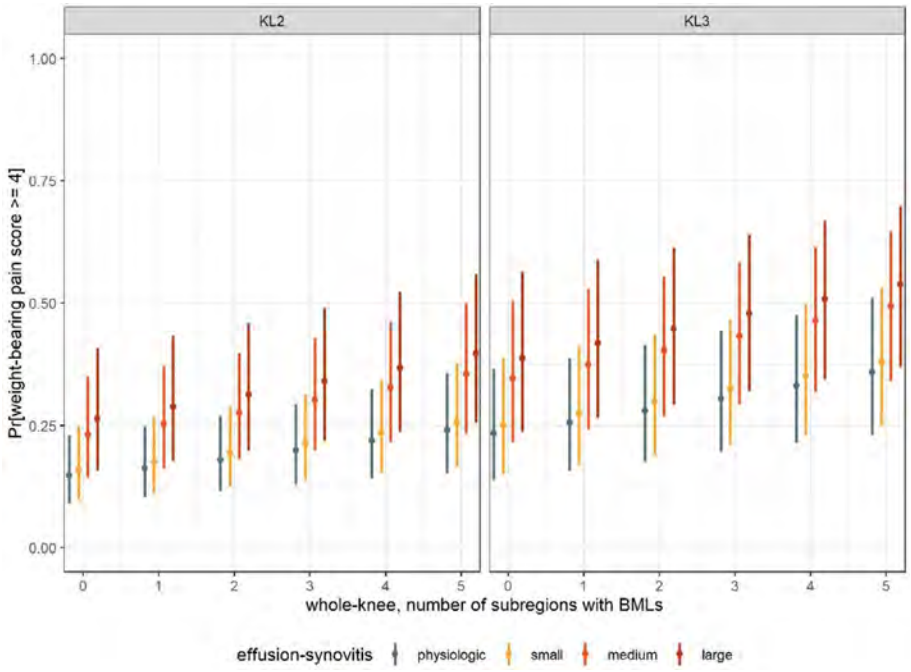

Figure 2. Weight-Bearing Knee Pain and Subregional BML Involvement By Amount of Effusion-Synovitis and Kellgren-Lawrence Grade

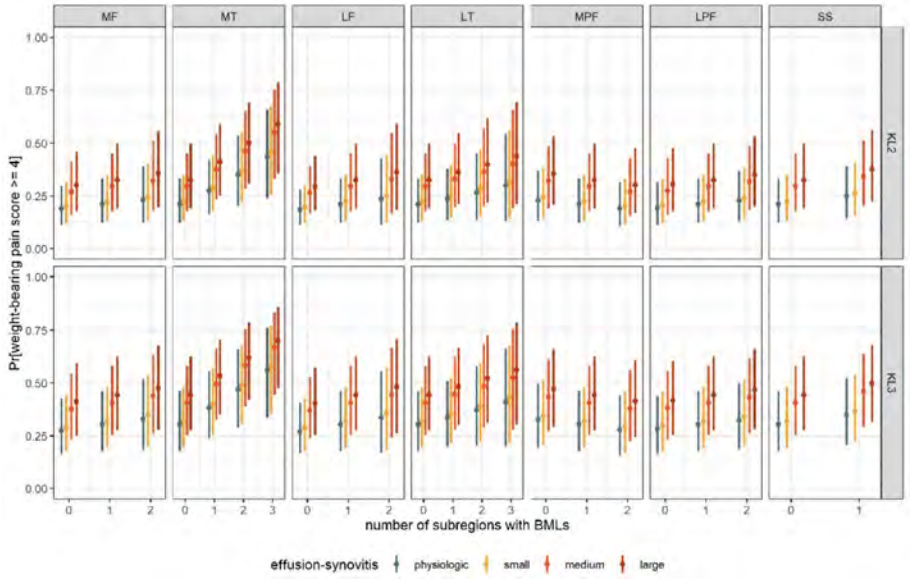

Figure 3. Weight-Bearing Knee Pain and Subregional BML Involvement within Bone Plates By Amount of Effusion-Synovitis and Kellgren-Lawrence Grade

Results: We identified 690 knees contributed by 623 participants with radiographic KOA (i.e., KL2 or KL3 at the time of MRI). The mean participant age was 65 years (SD 9), mean BMI was 29.3 (SD 4.8), 66% reported female sex, and 83% self-identified as white.The prevalence of BML involvement in our sample is shown for each bone plate (Figure 1). Predicted probability of weight-bearing pain is reported based on BML involvement, ES, and KLG, from fully adjusted models (Figures 2-3). The number of subregions in the whole knee with BML involvement was associated with weight-bearing pain (LRT p=0.006). The model that included affected subregions in each bone plate implicated BML involvement in the MT (LRT p=0.002).

Conclusion: Our findings suggest that the probability of weight-bearing knee pain increases with increasing subregional involvement of BMLs, largely driven by MT BMLs.

Disclosure: K. Kwoh: Express Scripts, 2, Kolon Tissue Gene, 12, IDMC, Moebius, 2, Novartis, 1, Trial Spark, 2, Xalud, 1; **F. Roemer**: Boston Imaging Core Lab (BICL) LLC., 8, Grünenthal GmbH, 2; **E. Ashbeck**: None; **A. Guermazi**: BICL, LLC, 11, ICM, Coval, TrialSpark, TissueGene, Medipost, 2, Novartis, 2, Pfizer, 2.

Abstract Number: 1195

Relationship of Depth-Specific Subchondral Bone Mineral Density to MRI Cartilage Worsening: The Multicenter Osteoarthritis Study

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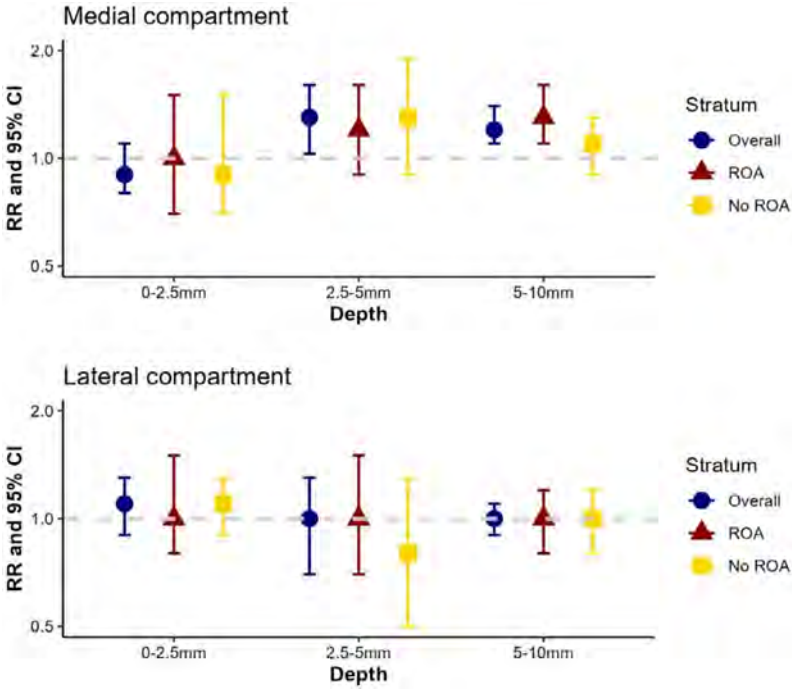
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: While OA has been considered a disease of cartilage, early subchondral bone changes may precede cartilage abnormalities. Although higher systemic BMD has a known association with radiographic OA severity, the relation of local subchondral BMD measures at the knee with structural changes on MRI is not well studied. CT topographic mapping of subchondral density is a 3D imaging tool that precisely measures subchondral cortical and trabecular BMD in relation to depth from the subchondral surface, allowing for the study of local knee BMD and its impact on important OA structural outcomes. This study aims to evaluate compartment- and depth-specific subchondral knee BMD in relation to cartilage worsening on knee MRI, with the hypothesis that higher local subchondral knee BMD will be associated with higher risk of cartilage loss in the same compartment.

Methods: Participants from the Multicenter Osteoarthritis (MOST) study, a NIH-funded longitudinal prospective cohort of older adults with or at risk of knee OA, who had knee CTs and MRIs at the 12th year study visit were included in this longitudinal analysis. A 3D imaging tool measuring BMD in relation to depth from the subchondral surface was used to assess proximal tibial subchondral BMD at depths of 0-2.5 mm, 2.5-5.0 mm, and 5-10 mm. Regional analyses of each medial and lateral plateau, at each depth were performed to calculate average BMD. Cartilage worsening on MRI was defined as any increase in the MRI OA Knee Score (MOAKS) subregion score between the 12th year visit and 2-year follow-up, considering the medial and lateral compartment separately. We evaluated the relation of subchondral BMD to compartment-specific cartilage worsening using binomial regression with generalized estimating equations to account for 2 knees within individuals,



Multivariable analyses for the association of subchondral BMD and compartment-specific cartilage worsening, overall and stratified by the presence of radiographic OA

for each compartment and depth in separate models, and adjusted for age, sex, and body mass index (BMI). We additionally stratified by radiographic OA (ROA) status in separate models.

Results: We included 1659 participants (mean age 61 years, 56% female, mean BMI 29 kg/m^2). At baseline, 90% of knees had any cartilage damage on knee MRI and 10% had any cartilage worsening at 2-year follow-up. In the medial compartment, at depths of 2.5-10mm below the subchondral surface, the risk of MRI cartilage worsening was 1.2-1.3 times higher for each standard deviation increase in the average subchondral BMD, after confounder adjustment. This association was not seen in the most superficial medial compartment depth (0-2.5mm), nor in the lateral compartment. Analyses stratified by ROA status did not differ substantially from the main results.

Conclusion: Higher subchondral tibial BMD measures were associated with higher risk of cartilage loss in the medial compartment at deeper depths of 2.5-10mm beneath the subchondral surface. These results support differential depth- and compartment-specific contributions from subchondral BMD involved in the pathogenesis of cartilage damage in knee OA.

Disclosure: J. Liew: None; **J. Johnston**: None; **G. Rabasa**: None; **B. Lewis**: None; **J. Lynch**: None; **J. Torner**: None; **T. Neogi**: None.

Abstract Number: 1196

Association of Long-Term Use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) with Worsening Symptoms and Structural Changes of Knee Osteoarthritis: An Individual Patient Data Meta-Analysis of Cohort Studies

Zubeyir Salis[1] and Amanda Sainsbury[2], [1]The University of New South Wales, Kensington, Australia, [2]The University of Western Australia, Crawley, Australia

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are commonly prescribed for short-term management of symptoms of knee osteoarthritis (KOA), but they are often used long-term, and the long-term effects are unclear. Therefore, we aimed to investigate the association of long-term use of NSAIDs with KOA symptoms and structural changes.

Methods: We performed individual patient data meta-analysis of three independent cohort studies: Osteoarthritis Initiative (OAI); Multicenter Osteoarthritis (MOST); and Cohort Hip and Cohort Knee (CHECK). The participants had or were at risk of developing KOA. A participant was classified as long-term user of NSAIDs if they were using them at baseline and during all follow-up visits. The follow-up visits occurred annually over 4 years in OAI, over 5 years in CHECK, and every 2.5 years over 5 years in MOST. A participant was classified as a non-user of NSAIDs if they did not use it at baseline and at any follow-up visits. There were 435 participants (with 870 knees) identified as long-term users of NSAIDs, and 3,762 participants (with 7,524 knees) identified as non-users. Outcomes included worsening pain, disability, and stiffness, assessed by the Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores, structural changes assessed by Kellgren/Lawrence (K/L) grades, and incidence of total knee replacement. Generalized estimating equations were used to assess the association of long-term use of NSAIDs with the change in outcomes between baseline and the 4-to-5-year follow-up, accounting for the clustering of left and right knees within each participant. The analyses were adjusted for sex; race; baseline values of age; body mass index (BMI); smoking status; comorbidity score; walking for leisure or activity; the pain, disability, and stiffness scores on WOMAC; the severity of osteoarthritis as assessed by K/L grades; and study cohort (OAI, MOST, and CHECK).

Results: Compared to non-users, long-term users of NSAIDs had significantly increased odds of worsening pain, disability, and stiffness that was of a clinically meaningful degree. The odds ratios (OR) were 2.04 (95% confidence intervals [CI]: 1.66 to 2.49) for pain, 2.21 (95% CI: 1.74 to 2.80) for disability, and 1.58 (95% CI: 1.29 to 1.93) for stiffness. For structural changes, compared to non-users, long-term users of NSAIDs had significantly increased odds of worsening in both severity of structural changes of KOA (OR: 1.43; 95% CI: 1.15 to 1.77) and incidence of total knee replacement (OR: 3.13; 95% CI: 2.08 to 4.70).

Conclusion: Long-term use of NSAIDs may have detrimental effects on KOA, including worsening symptoms and structural changes. Although NSAIDs are useful for short-term management of KOA symptoms, our findings highlight potential adverse effects of long-term use. Therefore, healthcare providers should weigh the benefits and risks of long-term NSAID use in patients with KOA and consider alternative strategies to improve patient outcomes in the long term.

Disclosure: Z. Salis: Zuman International Pty Ltd, 8, 9; **A. Sainsbury**: Zuman International Pty Ltd, 6, 8, 9.

Abstract Number: 1197

Efficacy and Safety of a Single Intra-Articular Injection of MM-II, a Novel Suspension of Large, Empty, Multilamellar Liposomes, in People with Painful Knee OA: Results of a 26-Week, Phase 2b, Placebo-Controlled, Double-Blind, Randomized Trial

Schnitzer Thomas[1], Helene Rovsing[2], Edith Lau[3], Sidsel Boll[4], Ballari Brahmachari[5], Richard Chou[6], Tarini Joshi[5], Roni Wechsler[7], Siu-Long Yao[5], Sveta Weiner[5], Asger Bihlet[8] and Philip Conaghan[9], [1]Northwestern University Feinberg School of Medicine, Chicago, IL, [2]Sanos Clinic, Gandrup, Denmark, [3]Hong Kong Center for Clinical Research, Hong Kong, China, [4]Sanos Clinic, Vejle, Denmark, [5]Sun Pharmaceutical Industries, Inc., Princeton, NJ, [6]Jacobs School of Medicine and Biomedical Sciences, University of Buffalo, Buffalo, NY, [7]Moebius Medical, Tel Aviv, Israel, [8]NBCD, Soeborg, Denmark, [9]University of Leeds, Leeds, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Osteoarthritis – Clinical Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Safe and effective therapies are needed for OA pain. MM-II, a novel suspension of large, empty, multilamellar liposomes composed of dimyristoylphosphatidylcholine and dipalmitoylphosphatidylcholine, effectively reduced cartilage degeneration in OA animal models administered weekly IA injections. A single IA injection of MM-II lowered knee pain in OA patients for up to 3 months in a first-in-human study. This phase 2b study evaluated dosing, safety, and efficacy of MM-II through 26 weeks in patients with symptomatic knee OA.

Methods: Consenting patients were enrolled in a 6-arm, randomized, double-blind, placebo (PBO)-controlled, 26-week trial evaluating one IA injection of 1, 3, and 6 mL of MM-II (150 mM lipids) and corresponding volumes of PBO. Key inclusion criteria were age ≥40 years, radiographic Kellgren-Lawrence grades 2 or 3 in the index knee, ACR criteria for OA, WOMAC A pain level ≥2/4 within 24 hours of baseline (BL), index knee visual analog scale pain score of 50 to 90 mm for ≥5/7 days prior to BL, and intolerance or inadequate response to NSAIDs or acetaminophen. Patients with moderate to large effusions in the index knee

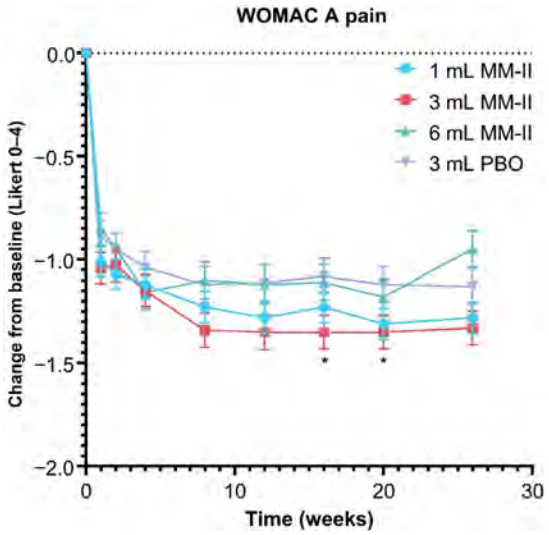


Figure 1. Change in baseline WOMAC A pain score over time. Data points represent least square means; error bars represent standard error. *P <0.05, multiplicity-unadjusted pairwise comparison of MM-II 3 mL to PBO 3 mL. PBO, placebo.

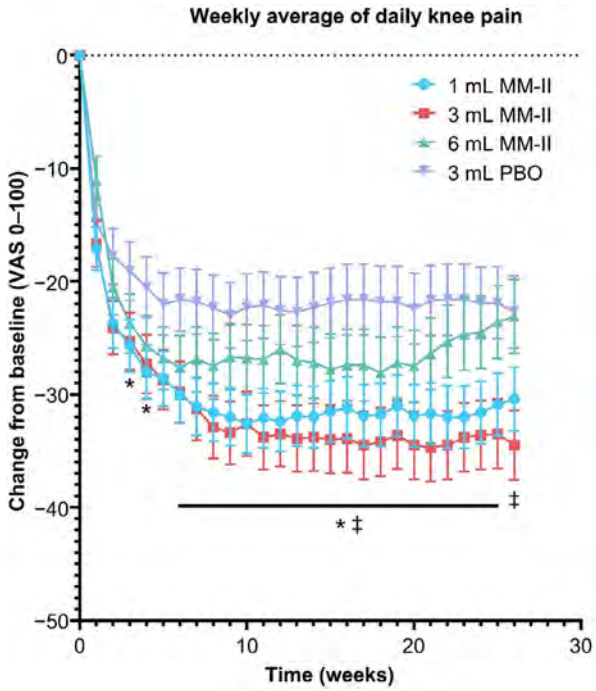


Figure 2. Change from baseline weekly average of daily pain over time. Data points represent least square means; error bars represent standard error. *P <0.05, 1 mL MM-II vs 3 mL PBO (not adjusted for multiplicity); ‡P <0.05, 3 mL MM-II vs 3 mL PBO (not adjusted for multiplicity). PBO, placebo; VAS, visual analog scale.

or with moderate to severe pain in another joint were excluded. The primary endpoint was change in WOMAC A pain score at week 12; secondary endpoints included change from BL in WOMAC A pain, weekly average daily knee pain score, and use of rescue medication. Randomization was stratified by BMI and BL index knee pain. The primary endpoint was analyzed for all patients who received MM-II or PBO (full analysis set) using mixed models for repeated measures. Treatment differences were estimated with least square means (LSM), and multiplicity-adjusted *P*-values were calculated for MM-II vs PBO 3 mL WOMAC A scores using step-down Dunnett's hierarchical testing. Nominal *P*-values were not adjusted for multiplicity.

Results: Of 397 enrolled patients, 258 (65.0%) were female and 266 (67.0%) were White. Mean age and BMI were 62.7 years (standard deviation [SD], 8.1) and 30.8 kg/m^2 (SD, 6.1), respectively. Treatment groups did not significantly differ at BL. Overall, 7.1% of patients discontinued the study. At week 12, LSM change from BL WOMAC A pain was –0.24 for the MM-II 3 mL group (95% confidence interval [CI], –0.476 to –0.004; $P = 0.085$), –0.16 for the 1 mL group (95% CI, –0.390 to 0.061; $P = 0.850$), and –0.02 for the MM-II 6 mL group (95% CI, –0.269 to 0.222; $P = 0.850$). In the 3 mL group, results were sustained until week 26 with nominal significance at 2 time points (**Figure 1**). When comparing MM-II 3 mL to the pooled PBO groups, LSM difference in change from BL of WOMAC A pain at week 12 was –0.28 (95% CI, –0.484 to –0.068; $P = 0.018$). LSM differences in weekly average daily pain scores for the MM-II 3 mL group were nominally significant from week 6 through 26 (nominal $P < 0.05$ for all; **Figure 2**). Changes in rescue medication use reflected changes in symptoms. Treatment-emergent serious adverse events (AEs) were reported in 2.67% of MM-II and 2.99% of PBO patients; incidence of injection site AEs were 1.91% and 2.99%, respectively.

Conclusion: MM-II treatment was well tolerated and may provide durable, clinically relevant pain relief. These data support phase 3 studies.

Disclosure: S. Thomas: AstraZenica, 2, Eli Lilly, 2, GlaxoSmithKline, 2, Horizon, 2, IBSA Group, 2, Merck, 2, Moebius Medical, 2, Orion, 2, Paradigm Biopharmaceuticals, 5, Pfizer, 1, 2, Regeneron, 2, Xalud Therapeutics, 2; **H. Rovsing**: None; **E. Lau**: None; **S. Boll**: None; **B. Brahmachari**: Sun Pharmaceutical Industries, Inc, 3, 11; **R. Chou**: Sun

Pharmaceutical Industries, Inc, 2; **T. Joshi**: Sun Pharmaceutical Industries, Inc, 3, 11; **R. Wechsler**: Moebius Medical, 3, 11; **S. Yao**: Sun Pharmaceutical Industries, Inc, 3, 11; **S. Weiner**: Sun Pharmaceutical Industries, Inc, 3, 11; **A. Bihlet**: NBCD, 8, Nordic Biosciences, 3, 11; **P. Conaghan**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, Genascense, 2, GlaxoSmithKlein(GSK), 2, Grunenthal, 2, Janssen, 2, Levicept, 2, Merck/MSD, 2, Moebius Medical, 2, Novartis, 2, 6, Stryker, 2, Takeda, 2, TrialSpark, 2.

Abstract Number: 1198

Bicycling Is Not Associated with New Knee Pain or Disease Progression over 48 Months in Those with Knee Osteoarthritis: Data from the Osteoarthritis Initiative

Colin McLaughlin[1], **Grace Lo**[1], Jeffrey Driban[2], Timothy McAlindon[3], Andrea Kriska[4], Bonnie Rockette-Wagner[4], Marc Hochberg[5], Michael Nevitt[6], Kent Kwoh[7] and Charles Eaton[8], [1]Baylor College of Medicine, Houston, TX, [2]Tufts Medical Center, Westborough, MA, [3]Tufts Medical Center, Arlington, MA, [4]University of Pittsburgh, Pittsburgh, PA, [5]University of Maryland School of Medicine, Baltimore, MD, [6]University of California San Francisco, Orinda, CA, [7]University of Arizona, Tucson, AZ, [8]Brown University, Pawtucket, RI

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Osteoarthritis – Clinical Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

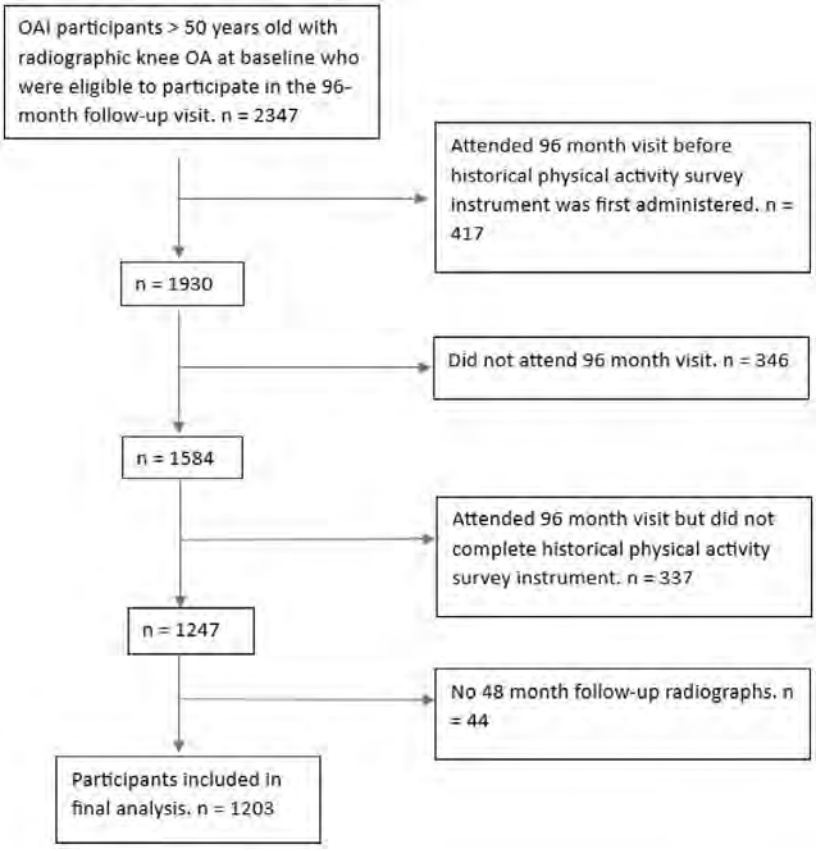


Figure 1: flow diagram indicating the selection process.

Background/Purpose: Bicycling is viewed as a non-weight bearing exercise and is often recommended as a preferred exercise for those with knee osteoarthritis (OA).However, there is no long-term epidemiologic evidence to support this recommendation.Therefore, we evaluated the relationship of bicycling with symptomatic and structural progression in those with pre-existing radiographic knee OA in the Osteoarthritis Initiative (OAI), a longitudinal observational study designed to identify biomarkers for the development and progression of symptomatic and structural knee OA.

Methods: This is a nested cohort study within the OAI, which included participants over the age of 50 years at OAI baseline who had radiographic OA in at least one knee (excluding those knees that already had undergone joint arthroplasty) at the time of OAI enrollment. Bicyclists were defined using a self-administered questionnaire completed at the 96-month visit, identifying people who had participated in the activity at least 10 times for at least 20 minutes each time. The flow diagram illustrates those who were included in the analysis. At baseline and 48-months, symptoms were assessed using the frequent knee pain question, and radiographs were scored using the Kellgren-Lawrence (KL) grade (2-4) and medial joint space narrowing (JSN) score (0-3) to determine the following outcomes of interest, including KL grade worsening (increase of KL by at least 1 grade), medial JSN worsening (any increase in medial JSN score, including within grade worsening), new knee pain

Table 1: Baseline and 48-month Characteristics of non-bicyclers and bicyclers

Baseline Characteristics	Non-bicyclers	Bicyclers	p-value
Person Based Characteristics	(n = 961)	(n = 242)	
Age in years mean (SD)	63.5 (7.9)	61.7 (7.7)	0.002
Sex (% Male)	42.4%	56.6%	<0.0001
BMI (kg/m²)	29.5 (4.6)	29.1 (4.7)	0.3
BMI<25	169/961 (17.6%)	50/242 (20.6%)	0.5
BMI>=25 / <30	376/961 (39.1%)	89/242 (36.8%)	
BMI>=30	416/961 (43.2%)	103/242 (42.6%)	
Knee Based Characteristics at baseline			
KL grade	(n=1451)	(n=357)	
2	933/1451 (64.3%)	220/357 (61.6%)	0.6
3	420/1451 (29.0%)	109/357 (30.5%)	
4	98/1451 (6.8%)	28/357 (7.9%)	
Medial JSN			
0	518/1451 (35.7%)	120/357 (33.6%)	0.6
1	523/1451 (36.0%)	125/357 (35.0%)	
2	345/1451 (23.8%)	92/357 (25.8%)	
3	65/1451 (4.5%)	20/357 (5.6%)	
Frequent knee symptoms (%)	546/1451 (37.6%)	130/357 (36.1%)	0.7
48-month characteristics			
Frequent knee symptoms (%)	588/1451 (40.5%)	141/357 (38%)	0.7
TKR	55/1451 (3.8%)	22/357 (6.1%)	0.05

Table 2: Odds Ratios of Worsening or Improving Outcomes in Non-bicyclists vs. bicyclists			
	Prevalence of Outcome, no./total (%)	Unadjusted Odds Ratios (95% CI)	Adjusted Odds Ratios* (95% CI)
Worsening Outcomes			
Outcome: New knee pain			
Non-Bicyclists	260/905 (28.7%)	Referent	Referent
Bicyclists	66/227 (29.1%)	1.2 (0.7 – 1.5)	1.2 (0.7 – 1.5)
Outcome: KL grade worsening			
Non-Bicyclists	275/1451 (19.0%)	Referent	Referent
Bicyclists	64/357 (19.8%)	1.2 (0.7 – 1.2)	1.2 (0.7 – 1.3)
Outcome: Medial JSN worsening			
Non-Bicyclists	329/1451 (22.7%)	Referent	Referent
Bicyclists	89/357 (24.9%)	1.2 (0.8 – 1.5)	1.2 (0.8 – 1.5)
Improving Outcome			
Outcome: Improving knee pain			
Non-Bicyclists	546/1451 (37.6%)	Referent	Referent
Bicyclists	130/357 (36.4%)	1.1 (0.7 – 1.7)	1.3 (0.7 – 1.7)
*adjusted for age, sex between OAI baseline and 48-month follow up visit			

(transitioning from no knee pain to knee pain), and improved knee pain (transitioning from knee pain to no knee pain). We evaluated the association of bicycling with the outcomes of interest using a knee-based analysis with logistic regression with generalized estimating equations to account for correlation between knees within a given person.We present crude results and those adjusted for age and sex.

Results: 1203 participants contributed 1808 knees to the study with 20% self-identifying as bicyclists. Table 1 shows the demographics of the two groups; both KL grade and JSN grade were well balanced between the groups. Notable differences were male predominance and increased number of TKR in the bicycling group compared with controls. Table 2 shows that there were no significant associations between bicycling and any of the four outcomes

Conclusion: Among individuals 50 years old and older with known radiographic knee OA, self-reported bicycling was not associated with worsening knee pain or radiographically defined structural progression. These findings support that bicycling is not harmful to knees in those with radiographic OA.

Disclosure: C. McLaughlin: None; **G. Lo**: None; **J. Driban**: None; **T. McAlindon**: None; **A. Kriska**: None; **B. Rockette-Wagner**: None; **M. Hochberg**: TrialSpark, 2; **M. Nevitt**: None; **K. Kwoh**: Express Scripts, 2, Kolon Tissue Gene, 12, IDMC, Moebius, 2, Novartis, 1, Trial Spark, 2, Xalud, 1; **C. Eaton**: None.

Abstract Number: 1199

Association of Dipeptidyl Peptidase-4 Inhibitor Use for Type 2 Diabetes and Incidence of OA in Taiwan

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Cellular senescence is involved in osteoarthritis (OA) development. Dipeptidyl Peptidase-4 (DPP4) is associated with senescence in OA chondrocytes. It is uncertain whether DPP4 inhibitor use is associated with reduced risk of OA in patients with type 2 diabetes mellitus. We aimed to establish whether DPP4 inhibitor use was associated with a reduced risk of OA among these patients.

Table 1. Characteristic Baseline of Cohorts

Table 1. Characteristic Baseline of Cohorts

		DPP-4 Non-User N = 166,987		DPP-4 user N =166,987		
		N	%	N	%	P Value
Gender						1.000
	Male	93624	56.07	93624	56.07	
	Female	73363	43.93	73363	43.93	
AGE Group (Years)						0.9987
	<40	35954	21.53	35996	21.56	
	41–50	71671	42.92	71713	42.95	
	51–60	38487	23.05	38429	23.01	
	61–70	15803	9.46	15776	9.45	
	>70	5072	3.04	5073	3.04	
	Mean ± SD	58.60 ± 9.53		58.60 ± 9.53		0.7852
	Median (IQR)	57	13	57	13	0.7431
DPP-4 Use						
Nonusers (<28 cDDDs)		166987	100	0	0	
Users		0	0	166987	100	
Follow-Up Time (year)						
	Median (IQR)	3.25	2.77	3.61	3.00	<.0001
Comorbidity						
	Cirrhosis	1565	0.94	1627	0.97	0.2702
	COPD	6432	3.85	5464	3.27	<.0001
	IHD	26455	15.84	23024	13.79	<.0001
	Hypertension	88607	53.06	96814	57.98	<.0001
	Chronic kidney disease	5600	3.35	7115	4.26	<.0001
	Dyslipidemia	70338	42.12	93226	55.83	<.0001
Medication						
	NSAIDs	138795	83.12	139161	83.34	0.0901
	Corticosteroid	87871	52.62	117865	70.58	<.0001
	Metformin	87551	52.43	108465	64.95	<.0001
	GLP-1RA	313	0.19	2788	1.67	<.0001
	SGLT2	642	0.38	3210	1.92	<.0001

Methods: We selected patients with type 2 diabetes mellitus that was diagnosed between 2008 and 2018 from the Taiwan National Health Insurance Research Database.We used Individual Matching (1:1), age ±1, same gender, same index year, same Diabetes Compilations Severity Index to balancepotential confounders between DPP4 inhibitor users and nonusers. We assessed the risks of incident OA using Cox proportional hazards regression between DPP4 inhibitor users and nonusers.

Results: We included 166,987 participants who were not treated with DPP4 inhibitor and 166,987who were treated with DPP4 inhibitor (mean age 58.60yr, standard deviation 9.53yr; 56.07% were men). In the DPP4 inhibitor use cohort, 5953 patients developed OA during a median follow-up of 3.61years (Table 1). Compared with participants who did not use DPP4 inhibitor, those who used DPP4 inhibitor had lower risks of incident OA (adjusted hazard ratio [HR] 0.43, 95% confidence interval [CI]0.42∼0.45(Table 2).Furthermore, the use of concurrent medications, such as Glucagon-like peptide-1receptor agonist (GLP-1RA; 0.22 [0.15∼0.31]) and Corticosteroid (0.66 [0.64∼0.68]), was associated with a lower OA risk (Table 3).We observed no relationship between a dose-dependent effect of DPP4 inhibitor use and OA(Table 3).

Table 2. Association of Comorbidities and Concurrent Medications with Osteoarthritis Risk

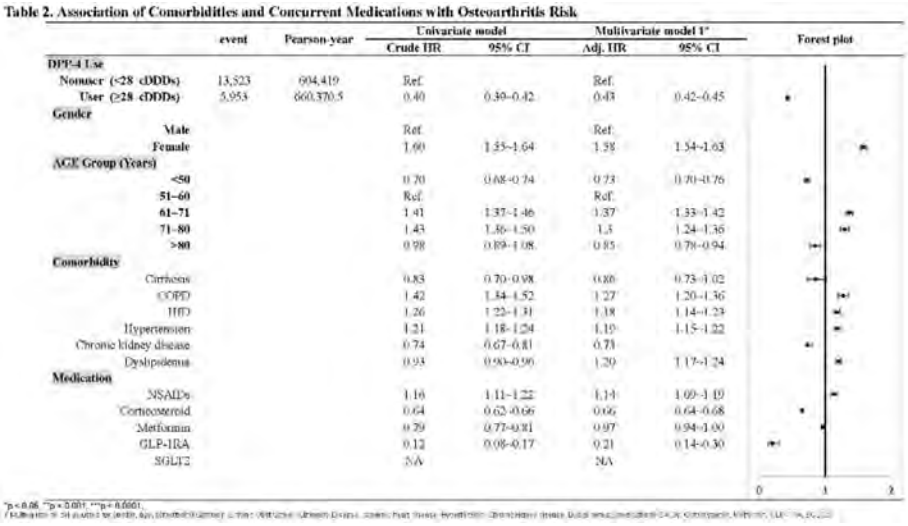

Table 2. Association of Comorbidities and Concurrent Medications with Osteoarthritis Risk

	event	Pearson-year	Univariate model		Multivariate model 1*		Forest plot
			Crude HR	95% CI	Adj. HR	95% CI	
DPP-4 Use							
Nonuser (<28 cDDDs)	13,523	604,419	Ref.		Ref.		
User (≥28 cDDDs)	5,953	660,370.5	0.40	0.39–0.42	0.43	0.42–0.45	
Gender							
Male			Ref.		Ref.		
Female			1.60	1.55–1.64	1.58	1.54–1.63	
AGE Group (Years)							
<50			0.70	0.68–0.74	0.73	0.70–0.76	
51–60			Ref.		Ref.		
61–71			1.41	1.37–1.46	1.37	1.33–1.42	
71–80			1.43	1.36–1.50	1.3	1.24–1.36	
>80			0.98	0.89–1.08	0.85	0.78–0.94	
Comorbidity							
Cirrhosis			0.83	0.70–0.98	0.86	0.73–1.02	
COPD			1.42	1.34–1.52	1.27	1.20–1.36	
IHD			1.26	1.22–1.31	1.18	1.14–1.23	
Hypertension			1.21	1.18–1.24	1.19	1.15–1.22	
Chronic kidney disease			0.74	0.67–0.81	0.73		
Dyslipidemia			0.93	0.86–0.99	1.20	1.17–1.24	
Medication							
NSAIDs			1.16	1.11–1.22	1.14	1.09–1.19	
Corticosteroid			0.64	0.62–0.66	0.66	0.64–0.68	
Metformin			0.79	0.77–0.81	0.97	0.94–1.00	
GLP-1RA			0.12	0.08–0.17	0.21	0.14–0.30	
SGLT2			NA		NA		

Table 3. Association of Comorbidities and Concurrent Medications with OA Risk

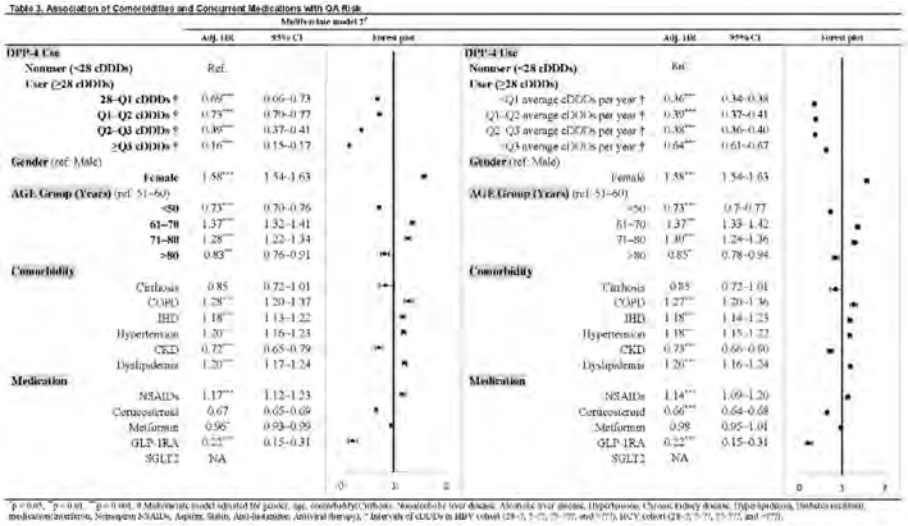

Table 3. Association of Comorbidities and Concurrent Medications with OA Risk

Multivariate model 2*

	Adj. HR	95% CI	Forest plot		Adj. HR	95% CI	Forest plot
DPP-4 Use				**DPP-4 Use**			
Nonuser (<28 cDDDs)	Ref.			**Nonuser (<28 cDDDs)**	Ref.		
User (≥28 cDDDs)				**User (≥28 cDDDs)**			
28–Q1 cDDDs †	0.69***	0.66–0.73		<Q1 average cDDDs per year †	0.36***	0.34–0.38	
Q1–Q2 cDDDs †	0.73***	0.70–0.77		Q1–Q2 average cDDDs per year †	0.39***	0.37–0.41	
Q2–Q3 cDDDs †	0.39***	0.37–0.41		Q2–Q3 average cDDDs per year †	0.38***	0.36–0.40	
≥Q3 cDDDs †	0.16***	0.15–0.17		≥Q3 average cDDDs per year †	0.64***	0.61–0.67	
Gender (ref: Male)				**Gender** (ref: Male)			
Female	1.58***	1.54–1.63		Female	1.58***	1.54–1.63	
AGE Group (Years) (ref: 51–60)				**AGE Group (Years)** (ref: 51–60)			
<50	0.73***	0.70–0.76		<50	0.73***	0.7–0.77	
61–70	1.37***	1.32–1.41		61–70	1.37***	1.33–1.42	
71–80	1.28***	1.22–1.34		71–80	1.30***	1.24–1.36	
>80	0.83***	0.76–0.91		>80	0.85***	0.78–0.94	
Comorbidity				**Comorbidity**			
Cirrhosis	0.85	0.72–1.01		Cirrhosis	0.85	0.72–1.01	
COPD	1.28***	1.20–1.37		COPD	1.27***	1.20–1.36	
IHD	1.18***	1.13–1.22		IHD	1.18***	1.14–1.23	
Hypertension	1.20***	1.16–1.23		Hypertension	1.18***	1.15–1.22	
CKD	0.72***	0.65–0.79		CKD	0.73***	0.66–0.80	
Dyslipidemia	1.20***	1.17–1.24		Dyslipidemia	1.20***	1.16–1.24	
Medication				**Medication**			
NSAIDs	1.17***	1.12–1.23		NSAIDs	1.14***	1.09–1.20	
Corticosteroid	0.67	0.65–0.69		Corticosteroid	0.66***	0.64–0.68	
Metformin	0.96*	0.93–0.99		Metformin	0.98	0.95–1.01	
GLP-1RA	0.22***	0.15–0.31		GLP-1RA	0.22***	0.15–0.31	
SGLT2	NA			SGLT2	NA		

Conclusion: DPP4 inhibitor use in patients with type 2 diabetes mellitus was associated with a significantly reduced risk of OA. Randomized controlled clinical trials in patients with osteoarthritis are warranted to determine whether DPP4 inhibitor is effective in decreasing the incidence of OA.

Disclosure: H. Lee: None; **C. Chang**: None; **T. Lin**: None; **T. Ku**: None; **J. Chen**: None; **Y. Chen**: None; **S. Chen**: None; **C. Chang**: None.

Abstract Number: 1200

Self-Reported Effectiveness of Cannabis for Arthritis-Related Pain

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SESSION INFORMATION
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Session Title: Patient Outcomes, Preferences, & Attitudes Poster II
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Background/Purpose: Pain management remains a significant challenge for individuals with rheumatic diseases (RDs), often causing patients to seek complementary or alternative treatments to traditional medications. Cannabis has been investigated as a potential option due to its immunomodulatory and analgesic effects, and arthritic pain is a commonly reported reason for cannabis use.[1] However, little is known about its safety or effectiveness in this population, and existing products are incredibly diverse and often unregulated. The objective of this study was to assess differences in self-reported effectiveness of cannabis or cannabis-derived products (hereafter simply "cannabis") for the treatment of arthritis-related pain by the presence or absence of tetrahydrocannabinol (THC).

Methods: The study population included adults in the FORWARD Databank who reported use of cannabis for treating arthritis-related pain. Participants were categorized into two groups: those who used products containing cannabidiol (CBD) but not THC, and those who used products containing THC with or without CBD. Univariate analyses were performed to examine differences between these groups, as well as between those who found cannabis effective or ineffective. Characteristics that varied significantly (chi-square or t-test $p < 0.05$) were included in a multivariable logistic regression model to assess the relationship between the presence of THC and effectiveness of cannabis in treating arthritic pain.

Results: Among 1,718 participants using cannabis for arthritis-related pain, 811 used THC-containing products while 907 used CBD-only products. In univariate analysis, THC users were significantly more likely to find cannabis effective compared to CBD-only users (62% v 39%, $p < 0.001$; Figure 1). THC users were younger, more likely to be male, more likely to live in a state where cannabis is legal, more likely to smoke, vape, or ingest cannabis, less likely to use topical cannabis, and more likely to use cannabis for other reasons in addition to pain relief (Table 1). After adjusting for confounders, logistic regression showed that participants using cannabis products with THC had significantly higher odds of finding cannabis effective for pain reduction (OR 2.2 [1.5, 3.1]; $p < 0.001$; Figure 2). Participants who used topical cannabis or who also used cannabis to treat insomnia or anxiety had significantly higher odds of finding cannabis effective, while participants with higher global VAS scores were less likely to find cannabis effective.

Conclusion: This study provides valuable insights into the use of cannabis for pain management in individuals with RDs. Our findings suggest that cannabis products containing THC and/or that are applied topically are more likely to be perceived by patients as effective. These results highlight the importance of considering the specific formulation of cannabis products as

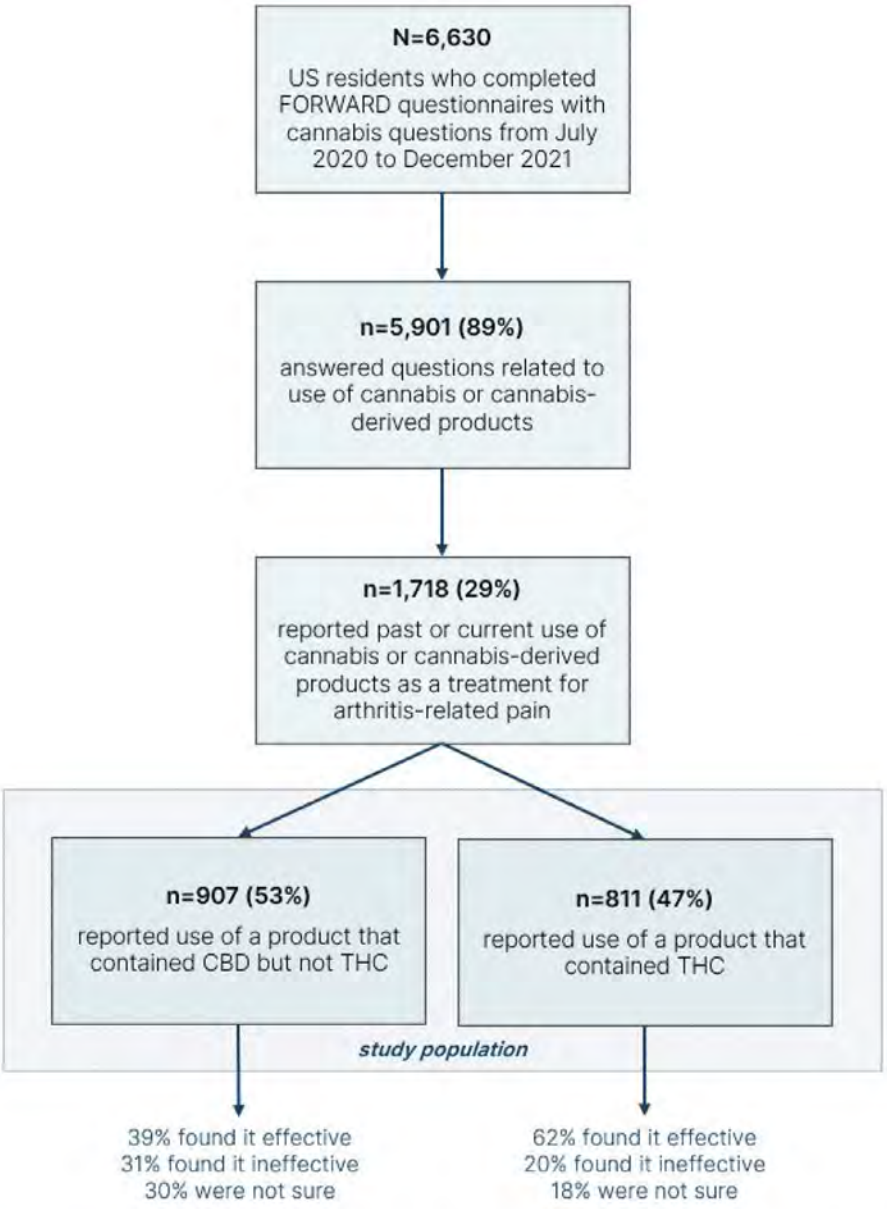

Figure 1. Inclusion criteria and study population selection. The final study population included FORWARD participants living in the US who completed questionnaires from July 2020 to December 2021 and reported using cannabis or cannabis-derived products for the treatment of arthritis-related pain. Participants who reported use of products containing THC were significantly more likely to find the product effective compared to participants who reported the use of CBD-containing products that did not contain THC (chi-square $p<0.001$).

well as their route of administration when evaluating their therapeutic potential. Prospective studies, particularly randomized controlled clinical trials, are needed to better understand efficacy and potential risks of cannabis use in this population.

1. Wipfler, K. *et al*. *Arthritis Care & Research***74**, 2091–2099 (2022)

Table 1. Characteristics of FORWARD participants who have reported using cannabis or cannabis-derived products to treat arthritis-related pain. Summary statistics are presented by whether the product did or did not contain THC, and by whether the participant reported finding the product effective or not. Significance testing was performed with Student's t-tests or chi-square tests, as appropriate.

	CBD Only n=907	Contains THC n=811	p	Not Effective n=440	Effective n=860	p
Demographics						
Age, years	67.5 (11.4)	62.9 (10.5)	<0.001	66.9 (10.4)	63.9 (11.2)	<0.001
Female, %	89.9	84.6	<0.01	87.3	87.2	0.96
Caucasian, %	91.9	90.5	0.32	93.6	88.9	<0.01
Education, years	14.8 (2.4)	14.8 (2.3)	0.54	14.7 (2.6)	14.7 (2.3)	0.77
History of smoking, %	41.0	59.3	<0.001	48.9	51.4	0.39
BMI, kg/m2	29.4 (7.1)	29.5 (7.3)	0.77	29.5 (7.2)	29.7 (7.5)	0.64
RDCI, 0-9	2.2 (1.6)	2.3 (1.7)	0.09	2.2 (1.6)	2.3 (1.7)	0.50
Primary Diagnosis, %						
Rheumatoid arthritis	62.8	61.4		61.4	62.1	
Osteoarthritis	17.8	15.7		18.4	15.9	
Fibromyalgia	6.3	6.8		7.5	7.1	
Lupus	4.7	5.3	0.23	5.2	4.9	0.74
Psoriatic arthritis	2.2	4.0		2.7	3.1	
Ankylosing spondylitis	0.7	1.4		0.7	1.2	
Other	5.5	5.6		4.1	5.7	
State Cannabis Legality, %						
Not legal	37.7	27.5		32.3	31.4	
Medical only	36.7	39.3	<0.001	38.4	38.0	0.89
Recreational	25.6	33.2		29.3	30.6	
Route of Administration, %						
Smoked	0.4	48.5	<0.001	17.3	30.0	<0.001
Vaped	0.6	17.6	<0.001	4.5	12.5	<0.001
Ingested	47.0	66.9	<0.001	59.8	58.6	0.68
Topical	64.2	51.5	<0.001	51.8	59.8	<0.01
Additional Reasons For Use, %						
Insomnia	9.5	28.4	<0.001	9.3	25.7	<0.001
Anxiety	6.7	22.7	<0.001	5.9	21.0	<0.001
Depression	4.3	13.4	<0.001	4.5	12.1	<0.001
Recreational	0.1	20.5	<0.001	8.4	10.1	0.32
Medications, %						
csDMARD	48.2	44.6	0.13	48.3	45.0	0.28
TNFi bDMARD	18.5	17.7	0.67	16.7	18.1	0.54
nTNFi bDMARD	15.1	14.2	0.63	14.2	13.6	0.78
JAKi	7.0	8.5	0.25	8.8	6.8	0.20
Glucocorticoid	20.1	18.3	0.37	20.4	17.8	0.27
Nonopioid analgesic	47.9	43.9	0.11	45.5	45.5	0.99
Opioid	25.5	28.6	0.17	29.9	25.5	0.09
PROs						
Fatigue VAS, 0-10	4.7 (3.0)	5.0 (3.0)	0.04	4.9 (3.0)	5.0 (3.1)	0.89
Pain VAS, 0-10	4.5 (2.7)	4.7 (2.8)	0.37	4.8 (2.8)	4.6 (2.8)	0.39
Global severity VAS, 0-10	4.1 (2.4)	4.3 (2.6)	0.23	4.5 (2.5)	4.1 (2.6)	0.02
HAQ-II, 0-3	1.0 (0.7)	1.0 (0.7)	0.13	1.0 (0.6)	1.0 (0.7)	0.90
PAS-II, 0-10	4.0 (2.1)	4.0 (2.2)	0.96	4.2 (2.1)	4.0 (2.2)	0.15

Cannabis legality categories were determined as of January 2020. Cannabis use may have been decriminalized and/or available in certain formulations in states in the "not legal" category. CBD=cannabidiol; THC=tetrahydrocannabinol; BMI=Body Mass Index; RDCI=Rheumatic Disease Comorbidity Index; DMARD=disease-modifying antirheumatic drug; csDMARD=conventional synthetic DMARD; TNFi=tumor necrosis factor inhibitor; bDMARD=biologic DMARD; nTNFi=non-TNFi; JAKi=Janus kinase inhibitor; PRO=patient-reported outcome; VAS=visual analog scale; HAQ-II=Health Assessment Questionnaire II; PAS-II=Patient Activity Scale II.

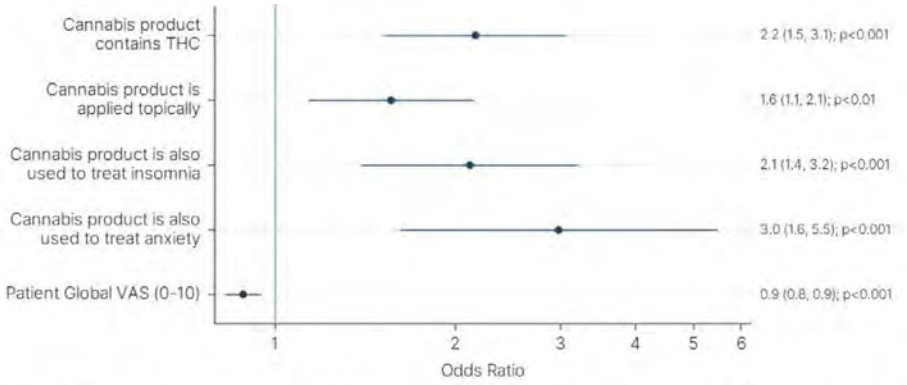

Figure 2. Factors associated with self-reported effectiveness of cannabis products in treating arthritis-related pain from multivariable analysis. The phrase "cannabis product" is used to describe cannabis or cannabis derived products that may or may not include tetrahydrocannabinol (THC). The multivariable logistic regression model included all covariates from Table 1 with p<0.05 (age, sex, race, history of smoking, state cannabis legality, routes of administration, additional reasons for use, fatigue, and global severity). Statistically significant (p<0.05) covariates are presented with their associated odds ratio (95% confidence interval) and p-value.

Disclosure: K. Wipfler: None; **J. Zeiger**: None; **K. Michaud**: None.

Abstract Number: 1201

Frailty and Its Impact on Patient Reported Outcomes in Polymyalgia Rheumatica

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Session Date: Monday, November 13, 2023
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Background/Purpose: Frailty is an increasingly important construct in the field of rheumatology, aiding the identification of individuals with increased vulnerability to accelerated clinical decline and overall worse disease outcomes.

The aim of this research was to explore the prevalence of frailty, and its potential associated impact on patient reported outcomes (PRO's) in a cohort of patients with Polymyalgia Rheumatica (PMR).

Methods: Patients with a diagnosis of PMR (fulfilling the 2012 EULAR/ACR Classification Criteria), who were in clinical remission and on active treatment with glucocorticoids were recruited from two centres. Patients were ≥3 months and ≤12 months from diagnosis.

Frailty was defined by the 5 criteria of the widely validated Fried Phenotypic Frailty Index.

Patient reported outcomes included anxiety, using the Generalised Anxiety Disorder Assessment (GAD-7), mood, using the Patient Health Questionnaire (PHQ-9), fatigue using the Functional Assessment of Chronic Illness Therapy - Fatigue Scale (FACIT-F), pain, using the Visual Analogue Scale (VAS) and overall health related quality of life, using the Health Assessment

Table 1: Baseline characteristics by frailty classification according to Fried Phenotypic Frailty Index.

Table1. Baseline characteristics by frailty classification according to Fried Phenotypic Frailty Index				
Characteristic	**Robust (n=33)**	**Pre-frail (n=14)**	**Frail (n=4)**	**p-value**
Sex, female, n(%)	18(54.5%)	7 (50%)	4 (100%)	
Age, median (IQR)	72 (69-76)	67 (59- 71.8)	66.5 (63-73.2)	0.049
Body Mass Index, median (IQR)	25.4 (23.8-28.4)	30.8(26.4-32.2)	34.1 (25.8-36.1)	0.040
Rheumatic disease comorbidity index (RDCI), median (IQR)	2.0 (1-3)	1.5 (0.2-2.8)	3.5 (2.5-4.2)	0.262
GAD-7 score, median (IQR)	0 (0-2)	0 (0-4.8)	11.5 (9-14.2)	0.003
PHQ-9 score, median (IQR)	1 (0-3)	3.5 (2.2-7.8)	1.45 (12.2-17.5)	0.001
HAQ-DI score, median (IQR)	0 (0-0)	0.6 (0-0.8)	1.4 (1.1-1.8)	<0.001
VAS pain score, median (IQR)	0 (0-0)	4 (2-4)	2 (2-2.5)	<0.001
FACIT-F score, median (IQR)	48 (45-50)	40.5(36.8-43.8)	18.5 (16-24.8)	0.001

Questionnaire-Disability Index (HAQ-DI). The associations between categorical variables were compared using chi-squared or Fishers exact test where appropriate. The association between continuous variables and categorical variables were assessed using the Kruskal-Wallis test. Correlations were calculated using Pearson's r. All analyses were conducted using R (R Core Team, 2022). A p-value of < 0.05 was considered as statistically significant.

Results: 51 consecutive patients were recruited, of which 56.9% (n=29) were female. Using the Fried Phenotypic index, 64.7% (n=33) were classified as robust, 27.5% (n=14) as pre-frail, and 7.8% (n=4) as frail. All patients classified as frail were female, and had a statistically significant higher BMI (p=0.040) than those in the robust and pre-frail categories. Compared to robust individuals, those who were frail had statistically significant higher median GAD-7 (p=0.003), PHQ-9 (p=0.001), VAS (p=< 0.001) and HAQ-DI (p< 0.001) scores. FACIT-F scores were also worse in those who were frail versus robust (p=0.001).

Conclusion: Over one third of patients with PMR in this cohort were classified as pre-frail or frail. Increased frailty status was significantly correlated with worse PRO's, including mood, pain, fatigue and overall quality of life. As frailty is a potentially reversible state, accurately identifying frailty, and implementing appropriate interventions is of utmost importance to ensure improved clinical outcomes in those with PMR.

Disclosure: P. Harkins: Janssen, 5; **S. Cowley**: None; **D. Kane**: None; **R. Conway**: AbbVie/Abbott, 5, 6, Celltrion, 5, Fresenius Kabi, 6, Galapagos, 6, Janssen, 5, 6, Nordic Pharma, 5, Novartis, 5, UCB, 6, Viatris, 6.

Abstract Number: 1202

Goal Concordant Patient-clinician Dyads Have Higher Odds of Communication Around Rheumatoid Arthritis Goals

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SESSION INFORMATION

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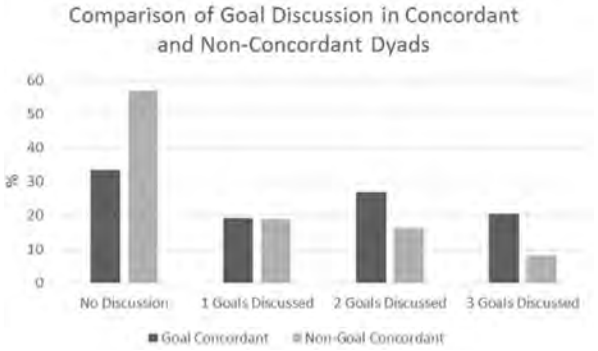
Background/Purpose: Goal concordance between patients with chronic disease and their clinicians is linked to improved outcomes, however, less is known about goal concordance and goal communication in rheumatoid arthritis (RA). Our objective was to explore the relationship between goal concordance and actual conversation of patient goals during the clinic visit.

Methods: Patients with RA seen at one of two rheumatology clinics were enrolled in a cross-sectional survey study. Prior to the visit, enrolled patients and their clinicians independently ranked their top 3 goals for RA treatment. After the visit, patients completed a survey question that asked if any of their goals were discussed during the visit. Concordance was defined as the patient's #1 goal being among any of the top 3 listed by the clinician. Additional survey items included a measure of health literacy, demographics, and self-reported adherence. Goal concordance and number of goals discussed were analyzed using both descriptive statistics and statistical analysis using a Chi^2 test, in which we compared rates of communication between concordant and non-concordant patient-clinician dyads.

Results: 178 patient-clinician dyads included 15 clinicians. Of the 178 patients, 58% were female, 16% Spanish speaking, and 29% with limited health literacy. The majority of dyads (79%) were goal concordant. Among goal-concordant dyads, 33% did not discuss any goals during the visit, while 19% discussed 1 goal, 27% discussed 2 goals, and 21% discussed 3 goals. In contrast, 57% of non-goal concordant dyads did not discuss any goals during the visit, compared with 19% who discussed one goal, 16% discussed 2 goals, and 8% discussed 3 goals. Goal concordant dyads were more likely to discuss at least one goal during the visit (OR 2.63, p-value 0.009).

Conclusion: Goal concordant dyads were more likely to discuss RA patient goals during the clinic visit compared with discordant dyads. Tools to elicit RA patient goals prior to a clinic visit that can be incorporated into real-time discussions with clinicians have potential to improve patient engagement in care and RA outcomes.



Disclosure: J. Barton: None; **D. ZuZero**: None; **D. Molina Ochoa**: None; **R. Matsumoto**: None; **E. Yelin**: None.

Abstract Number: 1203

Vaccination Against SARS-CoV-2 in Inflammatory Arthritis and Factors Determining Its Decision

Olivier FAKIH[1], Charlotte Bourgoin[2], Violette Benier[1], Thomas Lohse[1], Cerise Guillochon[1], Elodie Bouvier[2], Jean-Charles Balblanc[1], Thierry Conrozier[1] and Anne Lohse[1], [1]Service de rhumatologie, Hôpital Nord Franche-Comté, Trévenans, France, [2]Unité de recherche clinique, Hôpital Nord Franche-Comté, Trévenans, France

SESSION INFORMATION

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Background/Purpose: DMARDs, which are essential for controlling the progression of inflammatory arthritis (IA), are mostly immunomodulators that significantly increase the risk of severe infections. Therefore, several vaccinations are recommended for patients receiving these treatments. In the recent pandemic context of Covid-19, vaccination of these patients against SARS-Cov2 seems to be a major issue in their management and is recommended by scientific societies. Better identification of patients reluctant to receive this vaccination would make it possible to adapt the information to encourage their adherence.

Methods: An observational cross-sectional monocentric study in current practice was conducted to include 150 adult patients treated with DMARDs for IA at the rheumatology outpatient clinic of the Hôpital Nord Franche-Comté between June and December 2021. The main objective of this study was to determine the factors associated with refusal of vaccination against SARS-CoV-2. During routine visits, a questionnaire was administered to the patients after obtaining their consent. This questionnaire contained demographic and pathology-related data (type of IA, activity level, disease duration), treatment-related data (type of DMARD, use of corticosteroids, number of targeted therapies, number of DMARD lines), other vaccinations, and recommended follow-ups during IA (gynecological, oral, etc.), as well as diets (vegetarian, vegan, etc.). Patients who did not wish to be vaccinated answered questions regarding the reasons for their refusal. The primary endpoint was willingness to be vaccinated against SARS-CoV-2. The factors associated with willingness or refusal were also studied. Statistical analyses were performed using R++ software (ClinicalTrials.gov Identifier: NCT04970550).

Results: 100 women and 49 men, mean age of 57.9 years, with a mean BMI of 27.0 were included. The percentage of vaccinated patients was 72.5%. There was no difference between vaccinated and non-vaccinated patients in terms of sex, type of current DMARD, number of lines of DMARDs, level of education, other vaccinations (hepatitis, pneumococcus), recommended follow-up (gynecological, dermatological, oral), diet, or use of alternative medicines. The non-vaccinated patients were significantly younger (p=0.03), more worried about adverse effects (among others, cancer, and vaccine-related Covid contamination), and that it triggered a flare-up of IA (all p=0.0004). They had less confidence in the pharmaceutical industry and in new technologies (p=0.0004). They were less likely to be vaccinated against influenza (p=0.003). Their partners were less frequently vaccinated against Covid-19 (p=0.002).

Conclusion: Slightly less than 75% of patients were vaccinated against Covid-19. The factors associated with refusal of vaccination were younger age, unvaccinated spouse, fear of adverse events, and refusal of the influenza vaccination. The type of DMARD or IA (RA, AS, PsA, or other SpA) did not influence the decision to vaccinate. However, non-vaccinated patients were not less compliant with other vaccinations (except for influenza) and follow-up recommendations inherent to their treatment.

Disclosure: O. FAKIH: None; **C. Bourgoin**: None; **V. Benier**: None; **T. Lohse**: None; **C. Guillochon**: None; **E. Bouvier**: None; **J. Balblanc**: None; **T. Conrozier**: None; **A. Lohse**: None.

Abstract Number: 1204

Understanding Community Perspectives on Disease Management: A Social Media Analysis of Gout Care Strategies

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Background/Purpose: To comprehensively understand the impact of disease management strategies, it is essential to understand the patient perspective. Gout is a chronic inflammatory arthritis characterized by painful joint flare-ups secondary to uric acid accumulation. Virtually all subspecialty groups recommend a proactive "treat-to-target" strategy to reduce serum urate levels, but many individuals living with gout adhere to a "treat-to-no symptoms" strategy. Here, we aimed to characterize gout community perspectives on various management approaches to gout care.

Methods: We evaluated 2 online social media communities using a proprietary analytics engine that evaluates social media conversations using natural language processing. Sources included a private Facebook group, The Gout Support Group of America (15,000+ members), which had 50,000 posts/comments from 2021 to 2023; and a public subreddit, r/gout (9,000+ members), with 125,000 posts/comments from 2011 to 2023. The engine used a topic modeling approach to identify the most frequent conversation themes across groups. Topics related to disease management were then tagged. All management topics were subject to sentiment analysis in which posts/comments were scored from −1 (most negative) to 1 (most positive) using a pretrained sentiment tagger. A final exploratory analysis identified the number of questions in each topic.

Results: Topic modeling yielded more than 30 topics that had at least 300 total posts/comments. Fourteen topics related to disease management (others related to disease burden, etc.). Polarity analysis showed the most positive management topics, in rank order, to be *uric acid monitoring*, *weight loss*, *cbd/thc*, *allopurinol*, and *prednisone*. Statistically significant differences were found between topic polarities as determined by 1-way ANOVA [$F(4,10543) = 16.74$, $P = .0001$]. A Tukey post hoc test revealed that *uric acid monitoring* conversation polarity was significantly higher [0.15 (0.24), $P = .008$] than *cbd/thc* conversations, as well as *allopurinol* and *prednisone* conversations but not *weight loss* conversations. Exploratory analysis showed that about 40% of all posts/comments in *diseasemanagement* topics included questions, compared with 20% in *disease burden* topics.

Conclusion: Using a proprietary analytics engine, we identified the most prevalent topics of conversation across 2 online gout communities. In comparing the top 5 most positive management topics, *uric acid monitoring* achieved the highest mean sentiment. Though the functional impact of sentiment differences is not easily appraised, these contrasts could suggest that gout community members tend to prefer uric acid monitoring over reactive management approaches such as prednisone. *Disease management* topics were composed of about 40% questions (vs 20% for *disease burden* topics),

suggesting that increased awareness of various management strategies could benefit community members. Further work is needed to continue investigation of the patient perspective on gout management, which could be an important factor for patients having greater autonomy and participation in controlling their disease.

Disclosure: M. Flurie: TREND Community, 3, 12, Shareholder; **M. Converse**: TREND Community, 3, 12, Shareholder; **C. Parker**: Gout Support Group of America, 6, 12, Co-founder; **B. LaMoreaux**: Horizon Therapeutics, 3, 12, Stockholder; **D. Hernandez**: Global Healthy Living Foundation, 3; **N. Edwards**: Horizon Therapeutics, 2, United Rheumatology, 12, Medical Policy Committee Member; **G. Ho**: Gout Support Group of America, 1, 5, 8, 12, Grant funded from Horizon Therapeutics, plc, TREND Community, 3, 12, Shareholder; **K. Davidson**: Horizon Therapeutics, 3, 12, Stockholder; **E. Wassman**: TREND Community, 3, 12, Shareholder; **C. DeFelice**: TREND Community, 3, 12, Shareholder; **M. Picone**: TREND Community, 3, 12, Shareholder.

Abstract Number: 1205

Universal Social Determinants of Health Screening in a Pediatric Rheumatology Specialty Clinic: A Feasibility Study

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Background/Purpose: Social determinants of health (SDoH) significantly impact health outcomes. Practice guidelines from a national pediatric organization and federal agencies recommend routine assessment of SDoH. Screening is increasingly prevalent in the pediatric primary care setting. However, little evidence exists to suggest that pediatric specialty clinics can successfully screen for and address SDoH needs routinely. This study aimed to 1) test the feasibility of universal SDoH

1.	Do you/your child have frequent emotional or behavior concerns?	Yes	No
2.	Do you worry about your/your child's adjustment to illness?	Yes	No
3.	Do you worry about school attendance or school performance related to medical issues?	Yes	No
4.	Do you worry about where you live being unaffordable or unstable?	Yes	No
5.	Do you worry about your living conditions affecting you/your child's health (i.e. mold, bugs)?	Yes	No
6.	Do you worry about your heat or electricity being shut off where you live?	Yes	No
7.	Do you worry that your/your child's food supply will run out?	Yes	No
8.	Do you/your child have trouble with transportation for medical appointments?	Yes	No
9.	Do you worry about work attendance or work performance related to medical issues?	Yes	No
10.	Do you worry about paying for your/your child's health care? Do you need assistance obtaining health insurance coverage? ***Please circle cost, coverage, or both***	Yes	No

Please return this form to your doctor.

Figure 1: Needs Assessment Questionnaire – English Version

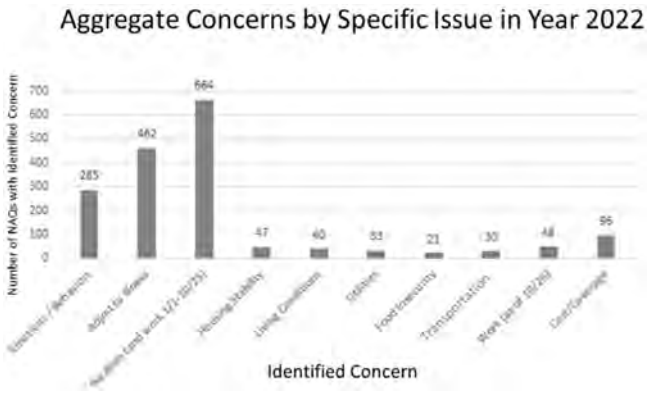

Figure 2: Identified Concerns from the Needs Assessment Questionnaire in Year 2022

screening and 2) understand the burden of SDoH-related needs in a large academic pediatric rheumatology subspecialty clinic.

Methods: As part of a quality improvement project to understand the burden of and address unmet social needs at a large pediatric academic medical center, the study team developed a SDoH needs assessment questionnaire (NAQ) via the nominal group technique. The study team included a full-time social worker and pediatric rheumatologists, including a SDoH/health equity physician researcher. The NAQ and the process outlining the distribution and return of the NAQ to the social worker were piloted. Iterative changes to the NAQ and to the process map were made to optimize the return rate. The brightly colored paper-based NAQ, translated into English and Spanish, was distributed by front desk staff to every patient/family at each in-person visit conducted in the main campus of a pediatric rheumatology outpatient clinic. Completed surveys were returned by the rheumatology providers to a single designated receptacle and then collected by the social worker within 1-2 business days. The responses from all NAQs were analyzed to understand the burden of unmet SDoH-related needs. The social worker addressed any non-urgent unmet needs identified on returned NAQs by way of the electronic health record patient portal or phone call. Acute needs identified in the clinic prompted a direct page or message to the social worker for urgent follow-up.

Results: The NAQ consists of 10 questions assessing the presence or absence of family/patient concernsabout SDoH-related needs: emotional/behavioral, adjustment to illness, school attendance or performance, housing insecurity, living conditions, utilities (heat and electric) insecurity, food insecurity, transportation access, work attendance or performance, and health care insurance/health care costs (Figure 1). Nearly 2/3 of rheumatology outpatient clinic visits between January 1-December 31, 2022, resulted in a completed NAQ (2355/3738). At least 1 unmet SDoH-related need was identified on 903 (38%) of the completed NAQs. School attendance/performance was the most frequently identified concern (Figure 2). The social worker responded to all 903 (100%) NAQs that identified unmet needs.

Conclusion: There is a significant burden of SDoH-related needs among patients presenting to a large academic outpatient pediatric rheumatology specialty clinic. Universal screening of social and behavioral determinants of health with subsequent follow-up to address unmet needs is feasible with a dedicated, full-time social worker on staff.Given the high burden of SDoH-related needs, further studies are needed to assess the effectiveness and impact of social work interventions over time.

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Abstract Number: 1206

Self-Perceptions of Aging and Physical Activity in Older Adults with Arthritis: Does General Health Matter?

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SESSION INFORMATION
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Session Title: Patient Outcomes, Preferences, & Attitudes Poster II
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Background/Purpose: Negative self-perceptions of aging are generally associated with decreased physical function in older adults. Whether self-perceptions of aging (i.e., "awareness of age-related change" including gains and losses) impact physical activity (PA) in older adults with arthritis, for whom activity is particularly important, is not well understood [1]. We examined associations between self-reported PA and awareness of age-related change, self-reported general health, and individual characteristics (e.g., sociodemographic features and comorbidity) among older adults with self-reported arthritis. We also explored whether self-reported general health mediated the relationship between awareness of age-related change losses and self-reported PA.

Methods: This cross-sectional study analyzed baseline data from a randomized controlled trial of a digitally delivered intervention designed to enhance PA versus an educational control. Adults ≥60 years of age enrolled at 2 sites. Participants with arthritis of any type were included. Sociodemographic characteristics and comorbid conditions were self-reported. PA levels

Table 1

Table 1. Participant characteristics

Domain	N = 99	
	N (%)	Mean (standard deviation)
Age (years)		70.5 (7.0)
Gender		
Female	81 (81.8)	
Race		
Black or African American	17 (17.2)	
White	77 (76.7)	
Other	5 (5.1)	
Ethnicity		
Hispanic or Latino	13 (13.1)	
Current employment	33 (33.7)	
Educational attainment		
Vocational training	1 (1.0)	
Secondary degree	6 (6.1)	
Some college	25 (25.3)	
College degree	21 (21.2)	
Graduate or doctoral degree	46 (46.5)	
Multimorbidity	72 (72.7)	
Self-reported general health[a]		2.6 (0.7)
Pain level and interference[b]		2.3 (0.9)
Social support[c]		25.4 (6.7)
Awareness of age-related change[d]		
Gains		4.3 (0.7)
Losses		2.3 (0.7)
Self-reported physical activity[e] (MET-minutes/week)		2368.7 (5822.7)

[a]Question 1 of 36-Item Short Form Survey Instrument: Ranges from 1 ("excellent") to 5 ("poor").
[b]Composite of questions 21 and 22 of 36-Item Short Form Survey Instrument: Question 21 (bodily pain) ranges from 1 ("none") to 6 ("very severe"); question 22 (pain interference) ranges from 1 ("not at all") to 5 ("extremely").
[c]12-Item Interpersonal Support Evaluation List: Ranges from 0-48; higher score indicates more social support.
[d]Awareness of age-related change: Ranges from 0-5; higher score indicates more perceived positive or negative changes.
[e]Global Physical Activity Questionnaire

quantified as MET-minutes/week, awareness of age-related change gains and losses, general health, pain level and interference, and social support were assessed using validated questionnaires. Pearson correlations were used to evaluate relationships between PA and sociodemographic characteristics, multimorbidity, awareness of age-related changes, general health, pain level and interference, and social support. Awareness of age-related change losses (independent variable), general health (mediator), and PA (dependent variable) were included in a mediation model.

Results: Significant correlations were observed between PA and general health ($r = -0.29$; $p < 0.01$), social support ($r = 0.27$; $p < 0.01$), and awareness of age-related change losses ($r = -0.27$; $p < 0.01$). General health significantly mediated the negative effect of greater awareness of age-related change losses on PA, i.e., for each 1-unit increase in awareness of age-related change losses, physical activity is expected to decrease by 582.61 MET-minutes/week when mediated by general

Table 2

Table 2. Pearson correlations between self-reported physical activity[a] and sociodemographic variables, multimorbidity, self-reported general health[b], pain level and interference[b], social support[c], and awareness of age-related change[d] (N=99)

Domain	r	p
Age	-0.15	0.14
Gender	0.09	0.36
Race		
Black or African American	0.27	<0.01
Other	-0.03	0.74
Ethnicity		
Hispanic or Latino	-0.001	0.99
Multimorbidity	0.02	0.82
General health	-0.29	<0.01
Pain level and interference	-0.18	0.07
Social support	0.27	<0.01
Awareness of age-related change		
Gains	0.11	0.28
Losses	-0.27	<0.01

[a]Global Physical Activity Questionnaire
[b]36-Item Short Form Survey
[c]12-Item Interpersonal Support Evaluation List
[d]Awareness of age-related change

Table 3

Table 3. Mediation model relating awareness of age-related change losses[a] and self-reported general health[b] to self-reported physical activity[c] (N=99)

Model domain	Standardized ß coefficient	Unstandardized ß coefficient [95% confidence interval]
Direct effects on general health		
Awareness of age-related change losses	0.29	0.25 [0.05, 0.45]
Race and ethnicity		
Black or African American	0.17	0.3 [-0.05, 0.65]
Other	0.09	0.24 [-0.34, 0.83]
Hispanic or Latino	0.09	0.17 [-0.23, 0.56]
Social support[d]	-0.14	-0.01 [-0.04, 0.01]
Direct effects on physical activity		
Awareness of age-related change losses	-0.06	-471.06 [-2320.80, 1378.69]
General health	-0.25	-2315.12 [-4184.8, -445.44]
Race and ethnicity		
Black or African American	0.27	4318.67 [1132.69, 7504.66]
Other	-0.01	-285.35 [-5527.6, 4956.89]
Hispanic or Latino	0.01	159.46 [-3356.69, 3675.6]
Social support	0.15	129.8 [-67.71, 327.3]
Indirect effect of age-related change losses on physical activity mediated by general health	-0.07	-582.61 [-1502.88, -24.82]

[a]Awareness of age-related change
[b]36-Item Short Form Survey General Health Scale
[c]Global Physical Activity Questionnaire
[d]12-Item Interpersonal Support Evaluation List

health (indirect effect of general health on PA unstandardized ß = -582.61; 95% confidence interval [-1502.88, -24.82]).

Conclusion: Negative self-perceptions of aging were associated with less PA in older adults with arthritis, but the impact of these negative self-perceptions was attenuated by general health. Interventions to improve PA in arthritis patients may need to target self-perceptions of aging, as well as general health.

Reference: 1. Kaspar et al. Gerontologist 2019;59:e130-40.

Disclosure: S. Lieber: None; **J. Moxley**: None; **L. Mandl**: Annals of Internal Medicine, 12, Associate Editor, Regeneron Pharmaceuticals, 5, Up-to-Date, 9; **M. Reid**: None; **S. Czaja**: None.

Abstract Number: 1207

Cardiovascular Mortality of Acute Myocardial Infraction and Acute Heart Failure Hospitalization in Rheumatic Diseases Patients Evaluation from the 2016-2020 National Inpatient Sample (NIS) Database

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SESSION INFORMATION

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Session Title: Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatic diseases such as rheumatoid arthritis (RA) and Systemic lupus erythematosus (SLE) were known for increased prevalence and risk of death from cardiovascular disease (CVD) due to systemic inflammation in conjunction with other environmental risk factors and genetic predispositions. [1] The COVID-19 pandemic is of the leading causes for the increased age-adjusted mortality rate in 2020 due to various unforeseeable conditions including unequitable healthcare resource distribution, decrease access to medical treatment other than for COVID-19 infection. [2]

Table 1: International Statistical Classification of Disease 10 (ICD-10)

Table 1: International Statistical Classification of Disease 10 (ICD-10)

Diagnosis	ICD-10 Codes
Acute MI (STEMI/NSTEMI/ Coronary Thrombosis) Acute Heart Failure	I21.01, I21.02, I21.09 I21.1, 11, 19, I21.2, .21, .29; I21.3, I21.4 I50.21, I50.23, I50.31, I50.33, I50.41, I50.43
Rheumatoid Arthritis	M05.80 , M05.89 , M05.9 ,M06.09, M06.00
Systemic lupus erythematosus	M32.0 –M32.9
Psoriasis/Psoriatic Arthritis	L40.9, L40.50, L40.53, L40.59
Gout	M10.9
Myositis	M33.10, M33.11
Vasculitis	I77.6, M31.5, M31.6, I79.1
Sarcoidosis	D86.9
Scleroderma	M 34.0, M34.1, M34.2, M34.81-M34.89, M35.0
COVID-19	Z11.52, Z11/59, Z20.822, Z 86.16, M86.19, M35.81, M35.89, J12.82, U07.10, B97.29

To investigate if the presence of the COVID-19 had an impact on the mortality outcome of acute myocardial infraction (AMI) and acute heart failure (AHF) in rheumatic diseases (RDs) including patients with RA, SLE, scleroderma, psoriasis/psoriatic arthritis, gout, myositis and vasculitis, and sarcoidosis in the United States using the NIS inpatient database from 2016-2020.

Methods: Using NIS database from 2016-2020, which stratifies 20% of the total national hospital admissions, we identified patients with a primary admission diagnosis (s) of AMI or AHF (with concurrent COVID-19 infection for 2020 data) using ICD-10 codes. (Table.1) For each admission, we calculated the baseline characteristics including mortality risk with independent variable for present or absence of RDs' ICD10 codes as the secondary diagnosis. The association of RDs with inpatient mortality was calculated using multivariable logistic regression.

Results: For 2016-2019, there were 484,775 AMI admissions without underlying RDs comparing to 23,538 AMI with RDs. During this pre-COVID-19 pandemic time, the inpatient mortality was significantly higher in the non-RDs (4.6% vs. 3.8%, $p< 0.001$). For AHF hospitalizations, 204,848 admissions were non-RDs compared to 15,799 RDs. There was no

Table.2A: Demographic, Outcomes, and Adjusted Odd Ratio of Hospitalization Mortality of AMI/AHF in patient without and with RD's in 2016-2019

Table.2A: Demographic, Outcomes, and Adjusted Odd Ratio of Hospitalization Mortality of AMI/AHF in patient without and with RD's in 2016-2019

Characteristics/ Outcomes	AMI Without RDs =484,775	AMI With RDs =23,538	*p*-value	AHF Without RDs = 204,848	AHF With RDs =15,799	p-value	Characteristics/ Outcomes	Odd Ratio (OR)	95% C/I	p-value
Mortality (%)	**4.6%**	**3.8%**	**<0.001**	2.8%	2.7%	**0.3**	**Mortality**	0.76	0.72-0.81	<0.001
Age (Year)(Mean)	67	70	**<0.001**	73	73	**0.8**	Length of Stay	1.01	1.01-1.01	<0.001
Race (%)			**<0.001**			<0.001	Hyperlipidemia	1.19	1.17-1.22	<0.001
Asian	2.7%	4.6%		2.0%	3.2%		Diabetes Mellitus	0.96	0.93-0.99	0.003
Black	11%	15%		17%	25%		Tobacco Use	0.93	0.86-1.01	0.11
Hispanic	8.9%	6.0%		7.4%	5.1%		Alcohol use	0.64	0.57-0.71	<0.001
Native American	0.6%	0.4%		0.6%	0.4%		Other substance	0.35	1.32-1.40	0.071
White	74%	72%		71%	65%		Obesity	1.36	1.32-1.40	<0.001
Male (%)	62%	68%	**<0.001**	52%	59%	**<0.001**				
Length of Stay (Day)	**3**	**2**	**<0.001**	**4**	**4**	**<0.001**				

Table.2B: Demographic, Outcomes, and Adjusted Odd Ratio of Hospitalization Mortality of AMI/AHF/COVID-19 Infection in patient without and with RD's in 2020

Table.2B: Demographic, Outcomes, and Adjusted Odd Ratio of Hospitalization Mortality of AMI/AHF/COVID-19 Infection in patient without and with RD's in 2020

Characteristics/ Outcomes	AMI +COVID Without RDs = 25,149	AMI+ COVID With RDs = 1,1164	*p*-value	AHF +COVID Without RDs = 4,401	AHF +COVID With RDs =204	p-value	Characteristics/ Outcomes	Odd Ratio (OR)	95% C/I	p-value
Mortality (%)	**5.6 %**	**4.2%**	**0.042**	3.2%	1.0%	**0.3**	**Mortality**	0.67	0.58-0.78	<0.001
Age (Year)(Mean)	67	70	<0.001	66	66	0.7	COVID-19	0.93	0.87-0.99	0.027
Race (%)			**<0.001**				Length of Stay	1.01	1.01-1.01	<0.001
Asian	3.1%	4.9%		1.8%	5.0%		Hyperlipidemia	1.23	1.16-1.30	<0.001
Black	12%	16%		15%	20%		Diabetes Mellitus	0.79	0.72-0.85	<0.001
Hispanic	11%	6.2%		7.9%	5.5%		Tobacco Use	0.89	0.71-1.09	0.3
Native American	0.5%	0.4%		0.6%	0%		Alcohol use	0.83	0.60-1.10	0.2
White	70 %	70%		72%	65%		Other substance	0.37	0.02-1.66	0.3
Male (%)	63%	72%	<0.001	55%	55%	**0.9**	Obesity	1.34	1.25-1.44	<0.001
Length of Stay (Day)	**3**	**3**	<0.001	**4**	**4**	**0.6**				

significance in term of mortality between these two groups. (2.8% vs. 2.7%, p=0.3) The odd of dying from AMI and AHF in patients with RDs was less compared to patients in the non-RDs group after adjusting for age, race, gender, regions and other confounders. (OR=0.76, p< 0.001) (Table.2A) For the pandemic year, there were 26,313 total AMI/COVID-19 infection hospitalizations, whereas 1,164 of these admissions were from patients with RDs. The mortality was still more significant in the non-RDs group. (5.6% vs. 4.2%, p=0.042) For the AHF/COVID-19 infection hospitalization, total of 4,405 with 204 of them were from the non RDs group. Due to smaller sample size, the mortality was not significant higher in the non-RDs group. (3.2% vs. 1.0%, p=0.073) In terms of the combined mortality OR of AMI/AHF/COVID-19 infection for 2020, the non-RDs group was still having lower odd compared to RDs group (Table.2B).

Conclusion: Based on our analysis, the presence of co-morbid RDs was not associated with increase mortality in patients hospitalized with AMI even with coexisting COVID-19 infection. For the AHF cohort, there was no significance in mortality in both groups. A detailed cardiovascular review of systemic during each rheumatology clinic visit may have helped to implement early intervention on CVD complications in RDs by early referral to cardiology.

Disclosure: Z. Li: None; **S. Huang**: None; **s. Gokcebel**: None; **A. Reginato**: None.

Abstract Number: 1208

Investigating the Experiences of Patients Living with Antiphospholipid Antibodies: A Qualitative Study

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Session Type: Poster Session B
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Background/Purpose: Substantial morbidity and mortality affect those with aPLs and APS, yet the patient experience remains poorly understood. This research investigated patient experiences of aPL/APS 1) diagnosis; 2) effects on daily life; and 3) healthcare and treatment.

Methods: Patients aged ≥18 years with ≥1 positive aPL on ≥2 occasions or those meeting the Revised Sapporo criteria for APS were purposefully recruited from a Canadian multidisciplinary APS clinic to participate in semi-structured in-depth interviews. Interviews were conducted virtually and transcribed verbatim for subsequent thematic analysis using NVivo software.

Results: Twelve patients with aPLs/APS were interviewed; 91.7% were female, mean (SD) age was 47.1 (16.1) years, 66.7% had aPLs/APS with SLE (per 1997 ACR or 2012 SLICC criteria), and 33.3% had aPLs/APS without SLE (Table 1). Patients experienced a range of challenges (e.g., obstetric and thrombotic complications) and emotional impacts (e.g., relief, anxiety) around the time of aPL/APS diagnosis (*It's been a traumatic experience (Participant #050)*) (Figure 1). In addition to the physical and psychosocial impacts of living with aPLs/APS, patients reported modified leisure activities, altered employment trajectories, and both positive and negative impacts on relationships (*My relationship with my family has become stronger, my relationship with the family that I'm potentially marrying into has become weaker (#040)*). The past and future impacts on family planning were critical to how patients experienced living with aPLs/APS; specifically, they shared experiences of miscarriage and other pregnancy complications, fear of future impacts on pregnancy, and

medication-related challenges, such as with low-molecular-weight heparin injections (*I would have these bruises, it made it awkward when I would go for ultrasounds (#029)*). Challenging aspects of aPL/APS healthcare and treatment were also discussed (Figure 1), particularly related to the lifestyle impacts, side effects, and emotional burden associated with medication use (*I hate it, I hate it. It's awful (#059)*). Although a lack of aPL/APS resources was described, participants expressed trust in

Table 1: Patient characteristics

Characteristic	Total sample
All aPLs/APS, n (%)	12 (100%)
APS with SLE, n (%)	5 (41.7%)
aPLs with SLE, n (%)	3 (25.0%)
APS only, without SLE, n (%)	4 (33.3%)
aPLs only, without SLE, n (%)	0 (0.0%)
Age (years) at time of interview, mean (SD)	47.1 (15.1)
aPLs/APS disease duration (years) at time of interview, mean (SD)	8.9 (7.4)
Female, %	91.7%
SLE + aPLs/APS: medications taken in the past year[a], % (n = 8)	
Antimalarials, n (%)	8 (66.7%)
Anticoagulants, n (%)	5 (41.7%)
Antiplatelets, n (%)	5 (41.7%)
Immunosuppressants/steroids[b], n (%)	4 (33.3%)
aPLs/APS only, without SLE: medications taken in the past year[a], % (n = 4)	
Antimalarials, n (%)	1 (8.3%)
Anticoagulants, n (%)	2 (25.0%)
Antiplatelets, n (%)	2 (25.0%)
Immunosuppressants/steroids[b], n (%)	0 (0.0%)

[a]*Categories are not mutually exclusive.*
[b]*Immunosuppressants/steroids include: belimumab, mycophenolate mofetil or mycophenolic acid, and steroids.*

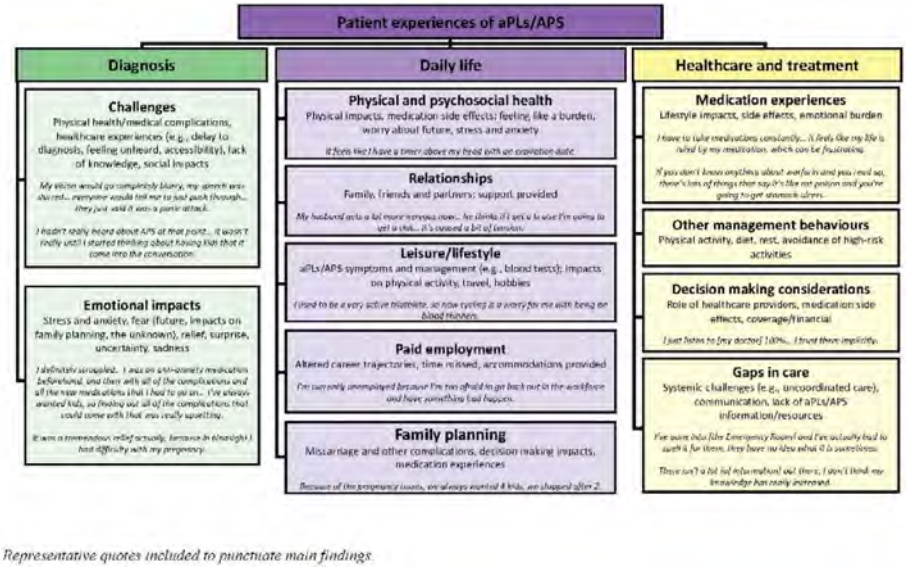

Figure 1: Overview of themes emerging through qualitative analysis

healthcare providers when making management decisions or when seeking information. Suggestions for resources included the need for additional medication-related information (long-term risks, dietary requirements; *Being able to speak with somebody who knows how warfarin works in relation to Vitamin K… that was my biggest battle (#059)*), examples to help contextualize management behaviours (*Can I sit on the couch and watch a movie? Do I have to be constantly moving around? I think more situational examples would have been helpful (#041)*), and additional information for those with aPLs/APS without SLE (*There might be a whole different resource instead of just always focusing on the lupus patients (#050)*).

Conclusion: Patients highlighted how the diverse manifestations of aPLs/APS, accentuated by management-related challenges, impose considerable physical and psychosocial burdens. Results will inform the development of patient resources and decision aids aligned with patient priorities.

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Abstract Number: 1209

The Role of Kinesiophobia on Ankylosing Spondylitis Disease Activity, Exercise Habits, and Quality of Life

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Session Title: Patient Outcomes, Preferences, & Attitudes Poster II
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Background/Purpose: Patients with Ankylosing Spondylitis (AS) consistently report exercise frequencies that are lower than healthy controls and ACSM/EULAR recommended frequencies; even though exercise has consistently been demonstrated to improve function and disease activity in patients with AS. This study explored the presence of kinesiophobia in populations with AS, specifically exploring if kinesiophobia has any correlation with disease activity, functionality, quality of life, and exercise habits of individuals with AS.

Methods: This study recruited 182 participants with AS via digital AS support groups and social media organizations. Recruited participants responded to a survey via Qualtrics that included the following validated patient reported outcome measures (PROMs): Tampa Scale of Kinesiophobia 11 (TSK-11), Baths Ankylosing Spondylitis Functional Index (BASFI), Baths Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Quality of Life Questionnaire (AS QoL), and a modified National Health Interview Survey (NHIS) to assess exercise habits.

Results: The results of this study suggest a high level of kinesiophobia in this population with a mean TSK-11 score of 29.45 ± 6.18, with 20% reporting "severe" (>35/44) scores for kinesiophobia. Participants with high kinesiophobia also demonstrated more active disease (r=.419, p >0.001), more functional limitations (r=.532, p >0.001), and more Quality-of-Life limitations (r=.611, p >0.001).Participants with high kinesiophobia also demonstrated less activity frequency for vigorous, moderate, and strengthening activities (r=-.279, r=-.256, r=.400; p >0.001).Patients that did report engaging in moderate activity 3 or more times a week also reported significantly better results in all 4 outcome measures versus patients who did

not.A similar significant improvement in outcome measures was found for patients who reported engaging in strengthening activity 2 or more times per week versus patients who did not.

Conclusion: This study shows a significant correlation of TSK-11 scores with other clinical measures in AS patients and self-reported exercise habits. Thus, kinesiophobia may play a role in the clinical presentation of AS and so tests such as the TSK-11 may be a valuable screening tool for AS treatment.

Conservative treatment with physical therapy and regular activity is an important aspect of management of autoinflammatory disorders such as AS. Studies in populations with general low back pain (LBP) have showed success in treating chronic LBP by treating the biopsychosocial aspects associated with kinesiophobia when patients demonstrate kinesiophobia and fear-avoidant behaviors. Understanding the presence and characteristics of kinesiophobia in populations with AS can help shape and drive effective intervention models for clinicians and so the TSK-11 can be a valuable tool in screening and evaluating patients in the AS population.

Disclosure: J. Thompson: None.

Abstract Number: 1210

Assessing Patient-Reported Drug Efficacy and Adherence Among IL-23 Inhibitors for Psoriasis and Psoriatic Arthritis

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Background/Purpose: Data suggest that patient satisfaction with drug therapy in psoriasis (Pso) and psoriatic arthritis (PsA) is associated with treatment compliance and, ultimately, disease response. Biologics, including IL-23 inhibitors such as risankizumab and guselkumab, have shown efficacy for both plaque psoriasis and psoriatic arthritis. However, meta-analyses reporting patient adherence to prescribed biologic therapy range from 61% to 70%, with limited data elucidating patients' reasons for non-adherence. The objective of this study was to characterize patient-reported factors associated with adherence and efficacy among IL-23 inhibitors for psoriasis and psoriatic arthritis.

Methods: Data were collected from 37 consecutive adult patients with Pso and PsA treated with an IL-23 inhibitor (either risankizumab or guselkumab) from a single clinic at our institution from 2019 onwards. Patient-reported therapy satisfaction was assessed using an adapted Treatment Satisfaction Questionnaire for Medication (TSQM-9). The TSQM-9 is a validated instrument used to assess patient satisfaction with medication across three domains: effectiveness, convenience, and global satisfaction. TSQM-9 domain scores are calculated as recommended by the instrument authors and range from 0 to 100, with higher scores indicating increased satisfaction in that domain. Medication non-adherence was defined as at least one missed injection over the study period. Exploratory factor loading was conducted to identify specific attributes of therapy associated with adherence. Statistical analysis was performed using logistic regression.

Results: Our cohort consisted of 37 patients with a mean age of 49.7 ± 15.9 (standard deviation) years, of whom 54.1% were male. The mean treatment duration from drug initiation to the study period was 14.1 months ± 10.0, with 22 patients prescribed risankizumab and 15 patients prescribed guselkumab. In our cohort, 32% of patients reported at least one missed dose, and 5% of patients reported multiple missed doses. The overall TSQM-9 scores by domain were as follows: effectiveness 93.4 ± 7.9, convenience 93.4 ± 9.1, and global satisfaction 89.6 ± 15.9. Mean scores for TSQM-9 statistically differed ($p < 0.05$) between fully compliant patients and non-compliant patients for convenience (96.5 ± 5.4 vs. 87.6 ± 11.8). There were no intra-drug differences in satisfaction or adherence within our cohort despite variations in dosing regimens. Factor loading revealed medication planning, medication administration, and side effects as the top three variables responsible for satisfaction variance between groups.

Conclusion: This study suggests that differences in biologic therapy adherence among patients with psoriasis and psoriatic arthritis may be influenced by patient therapy convenience and satisfaction as defined by medication planning, administration, and side effects. Larger studies should further attempt to characterize and address specific barriers identified.

Disclosure: F. Ahmed: None; **S. Rahman**: None; **S. Trent**: None; **L. Pham**: None; **N. Memon**: None; **H. Chung**: None; **A. Haque**: None.

Abstract Number: 1211

Description of Self-Efficacy for Managing Symptoms and Emotions in a Large Rheumatology Clinic Population

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II
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Background/Purpose: Self-efficacy (SE) is the inner belief in one's ability to succeed in specific situations and tasks. SE for managing the symptoms and emotions associated with chronic disease has considerable impact on health-related quality of life (HRQoL) and health outcomes. The goal of this study was to describe SE for people living with various rheumatologic diseases with comparison across insurance type and clinic setting and correlation with HRQoL.

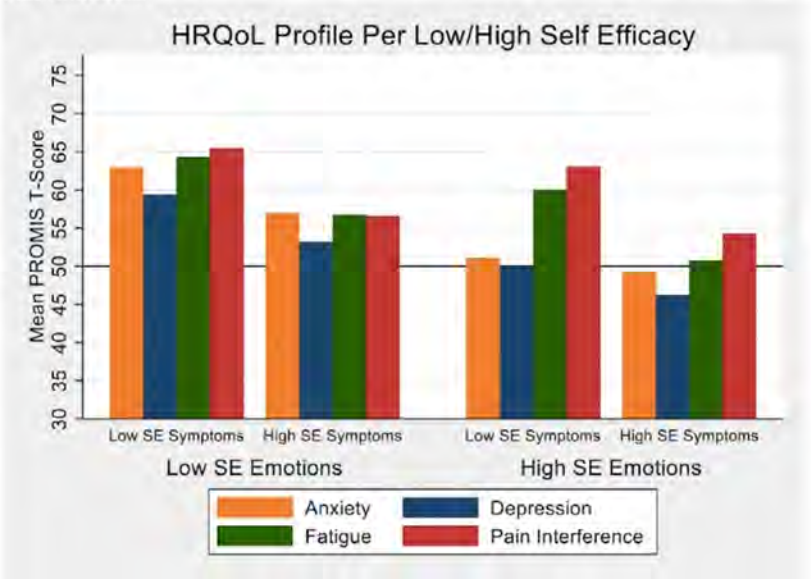
Methods: This study was a retrospective, cross-sectional analysis of patients in the rheumatology division at a large academic medical center who had office visits and completed self-efficacy PROMIS questionnaires from July 1, 2022 to January 1, 2023. Outpatient clinic locations were urban and suburban. Questionnaires included the Patient Reported Outcome Measurement Information System (PROMIS)-29 V2.1 collection of short, fixed forms (physical function, anxiety, depression, fatigue, sleep disturbance, ability to participate in social roles and activities, pain interference) and PROMIS Self-Efficacy for Managing Symptoms (SE Symptoms) and Emotions (SE Emotions) Computer Adaptive Tests. PROMIS T-scores are based on United States (US) population normative values with a mean (SD) T-score of 50 (10). Rheumatologic diagnosis was confirmed by the treating rheumatologist at the time of the encounter. Mean PROMIS T-scores were compared across gender, race, ethnicity, clinic location, rheumatologic diagnosis and insurance type using t-tests vs ANOVA or Kruskal-Wallis, where applicable.

Table 1. Population attributes and HRQoL domains of included patients per disease (n=647).

Characteristic	OA* (n= 70)	RA (n=194)	PsA (n=46)	SLE (n=100)	DM (n=77)	SSc (n=25)	Sjo (n=135)	p
Mean Age (SD)	63.9 (12.5)	54.0 (15.6)	51.0 (15.4)	41.7 (14.2)	57.4 (11.3)	54.5 (17.1)	55.3 (15.1)	<0.001
Sex F, n (%)	52 (74.3)	146 (75.6)	21 (45.7)	100 (100)	64 (83.1)	18 (72)	128 (94.8)	<0.001
Race, n (%)*								
White	53 (75.7)	135 (68.5)	34 (73.9)	23 (23.0)	41 (53.2)	16 (64.0)	100 (73.0)	
Black	10 (14.3)	27 (13.7)	2 (4.3)	57 (57.0)	9 (11.7)	7 (28.0)	21 (15.3)	<0.001
Other	2 (2.9)	13 (6.6)	4 (8.7)	9 (9.0)	15 (19.5)	0 (0)	8 (5.8)	
Not identified	5 (7.1)	22 (11.2)	6 (13.0)	11 (11.0)	12 (15.6)	2 (8.0)	8 (5.8)	
Disease Duration, mean months (SD)	*	26.5 (8, 48)	13 (4, 36)	26 (4, 82)	20 (6, 56)	15 (12, 63)	33 (5, 136)	0.300
Comorbidities n (%)								
Diabetes Mellitus	9 (13)	22 (11.3)	8 (17.4)	9 (9.0)	12 (15.6)	3 (12.0)	10 (7.4)	0.300
HLD	34 (49.3)	78 (40.2)	12 (26.1)	24 (24.0)	18 (23.4)	7 (28.0)	32 (23.7)	0.009
CVD/CHF/Stroke	0 (0)	33 (16.8)	5 (10.9)	12 (12.0)	7 (9.1)	5 (20.0)	13 (9.5)	0.008
COPD	4 (5.8)	23 (11.9)	0 (0)	0 (0)	0 (0)	4 (16.0)	6 (4.4)	<0.001
Anxiety	19 (27.5)	60 (30.9)	6 (13.0)	28 (28.0)	3 (3.9)	6 (24.0)	27 (20.0)	<0.001
Depression	5 (7.2)	24 (12.4)	2 (4.3)	14 (14.0)	1 (1.3)	2 (8.0)	7 (5.2)	0.005
Fibromyalgia$	39 (56.5)	112 (57.7)	18 (39.1)	60 (60.0)	27 (35.1)	14 (56.0)	61 (45.2)	0.002
Patient Reported Outcomes mean (SD)								
PROMIS-29#								
Fatigue	55.6 (9.3)	56.1 (10.9)	57.1(10.5)	60.6 (9.8)	54.3 (11.2)	53.8 (9.2)	58.1 (10.7)	<0.001
Sleep Disturbance	53.6 (7.6)	54.6 (8.8)	53.5 (7.5)	58.0 (8.3)	53.1 (9.9)	53.9 (6.8)	55.5 (8.5)	0.002
Anxiety	53.5 (10.1)	54.6 (11.0)	50.5 (7.0)	58.1 (10.4)	53.1 (8.1)	50.9 (6.4)	55.9 (10.5)	<0.001
Depression	51.3 (8.9)	51.9 (9.2)	50.0 (7.9)	53.5 (9.4)	50.8 (7.9)	47.1 (6.5)	52.2 (9.9)	0.045
Pain interference	60.2 (8.4)	60.2 (8.8)	60.6 (9.1)	60.7 (7.5)	57.3 (10.7)	55.6 (9.2)	57.6 (10.3)	0.004
Physical Function	41.1 (8.7)	41.5 (9.0)	40.8 (6.3)	40.9 (7.3)	43.1 (9.7)	41.6 (6.6)	44.4 (10.1)	0.019
Social Participation	46.5 (8.6)	46.2 (9.1)	44.4 (6.2)	45.9 (7.0)	47.7 (10.1)	49.7 (8.9)	47.0 (9.2)	0.110
PROMIS Self-Efficacy for Symptoms	44.7 (8.5)	44.1 (8.6)	42.5 (7.3)	43.1(7.5)	45.6 (8.4)	47.6 (5.8)	43.4 (8.0)	0.065
PROMIS Self-Efficacy for Emotions	47.3 (8.0)	46.6 (8.2)	48.1 (6.8)	45.4 (8.3)	48.4 (7.1)	51.8 (5.8)	46.1 (8.4)	0.005

OA=Osteoarthritis, RA=Rheumatoid Arthritis, PsA=Psoriatic Arthritis, SLE=Systemic Lupus Erythematosus, DM=Dermatomyositis, Ssc=Systemic Sclerosis, Sjo=Sjogrens Disease, HLD=Hyperlipidemia, CVD=Cardiovascular disease, CHF=Congestive Heart Failure, COPD=Chronic Obstructive Pulmonary Disease *Missing data. Other is defined as Native America, Alaskan, Asian, and "other" per patient report. Not identified is defined as missing or listed as "patient declined" per chart review. $Extracted via chart review and not necessarily confirmed by rheumatologist. #Higher PROMIS measures reflect more of a concept and lower PROMIS measures reflect less of a concept (ex., higher PROMIS physical function T-scores denote better physical function).

Figure 1: HRQoL Domains per Low and High Self-Efficacy (SE) for Managing Symptoms and Emotions.



Higher PROMIS measures reflect more of a concept, and lower PROMIS measures reflect less of a concept.

Table 2. Mean PROMIS T-Scores for patients with rheumatologic disease across insurance type (n=571).

	Insurance Type			
PROMIS Measure#	Private N=342	Medicare N=168	Medicaid N=61	P value*
Fatigue	56.0 (9.6)	55.6 (11.9)	67.8 (7.4)	<0.001
Sleep Disturbance	54.1 (7.8)	54.6 (10.1)	62.1 (6.8)	<0.001
Anxiety	53.4 (9.3)	54.4 (10.8)	64.0 (9.0)	<0.001
Depression	50.4 (8.2)	51.7 (9.3)	60.0 (9.4)	<0.001
Pain Interference	57.6 (9.0)	59.7 (9.4)	66.6 (7.0)	<0.001
Physical Function	43.7(8.3)	40.9 (10.0)	37.7 (6.5)	<0.001
Social Participation	47.8 (8.0)	45.7 (10.1)	41.7 (7.1)	<0.001
Self-Efficacy Symptoms	44.4 (7.0)	45.7 (9.0)	37.1 (7.8)	<0.001
Self-Efficacy Emotions	47.6 (7.2)	47.8 (9.0)	40.7 (7.0)	<0.001

Results shown are mean (SD) of PROMIS T-scores. Excludes patients with self-pay. *Significance determined by ANOVA. #Higher PROMIS measures reflect more of a concept, and lower PROMIS measures reflect less of a concept (ex., higher PROMIS physical function T-scores denote better physical function).

Results: There were 1,619 patients who completed office visits during the study timeframe and 647 patients (40%) completed PROMIS measures. Mean age, sex, race, disease duration, and comorbidities varied significantly between diagnoses and patients with osteoarthritis were significantly older (Table 1). The median (IQR) T-score for SE Emotions was 46 (43, 52) and the median (IQR) T-score for SE Symptoms was 43 (39, 48) for those with rheumatologic disease, below US population normative values. All PROMIS domains statistically differed between disease groups except for SE Symptoms (p=0.065) (Table 1). Compared to those with high SE for managing symptoms and high SE for managing emotions (T-scores >43 and 46, respectively) those with low SE had significantly worse HRQoL in all PROMIS domains by 5-10 mean T-score units (p< 0.001) (Figure 1). Specifically, patients with low SE Emotions had more mood disturbance and patients with low SE Symptoms had worse pain and fatigue. Patients who had low SE Emotions/low SE Symptoms had the worst HRQoL profiles overall. HRQoL including SE domains were significantly worse for individuals with Medicaid (Table 2) but not by clinic location.

Conclusion: Self-efficacy (SE) for managing symptoms and emotions was lower than expected for people living with rheumatologic disease and especially lower for those with Medicaid insurance. This suggests that SE may be impacted by socioeconomic status but needs to be explored further. SE can be measured as part of routine rheumatology clinical care, and physician awareness and interventions to strengthen SE have the potential to improve patient outcomes.

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Abstract Number: 1212

Racial Disparities in Comorbidities and Perception of Physical Health in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II

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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic multisystemic immune-mediated disease with often nonspecific symptoms, associated with recurrent flares that can be life threatening. Prevalence of SLE in women and minorities especially African Americans (AA) are higher with a higher disease severity index [(1)]. Studies have shown that higher morbidity scores correlate with lower perceived physical health score [(2)]. Our study aims to assess racial disparities in perception of health using morbidity index scores and perceived physical health in SLE patients.

Methods: We included 258,188 patients from *All of Us* dataset 6 from May 6, 2018 to January 1, 2022 who had available electronic health records data. SLE patients were identified with ICD 9/10 codes. We calculated average Charlson Comorbidity Index (CCI) for SLE patients and prevalence of the following common comorbidities by race: chronic pulmonary disease (CPD), peripheral vascular disease (PVD), renal disease (RD), diabetes (DM), and congestive heart failure (CHF). From the survey data, we calculated average PROMIS-PH scores to assess the degree of self-reported physical health, with responses ranging from 2 to 10. Analysis was performed in the web-based platform Jupyter Notebook using the programming language R.

Results: Of 4,959 patients with SLE, Whites (N=1,430) had the highest average CCI of 5.44, followed by 5.34 in AA (N=857) and 4.55 in Asians (N=85). AA showed the lowest average PROMIS-PH score of 5.82, representing worse perception of physical health, compared to Whites (6.32) and Asians (6.45). Asians had the lowest prevalence of CPD (30.6%) compared to AA (45.3%) and Whites (46.8%). PVD prevalence was similar in Asians (24.6%) and in AA (25.6%) but higher in Whites (29.8%). Of note, RD in Whites was the lowest with 23.9%, higher in AA (34.2%) and Asians (40%). For DM, AA had the highest prevalence at 37.1%, followed by 20.7% in Whites and 20% in Asians. Prevalence of CHF was notably high in AA (25.9%), 15.1% in Whites and less than 15% in Asians.

Conclusion: Despite similarity in average CCI between AA and White SLE patients, self-perception of physical health was significantly lower in AA. Our study shows that morbidity indices do not always correlate with perception of health. Differences in the types of comorbidities, such as CHF and DM in African Americans could be responsible for the disparities in perceived health.

References 1.Izmirly PM, Parton H, Wang L, McCune WJ, Lim SS, Drenkard C, Ferucci ED, Dall'Era M, Gordon C, Helmick CG, Somers EC. Prevalence of Systemic Lupus Erythematosus in the United States: Estimates From a Meta-Analysis of the Centers for Disease Control and Prevention National Lupus Registries. Arthritis Rheumatol. 2021 Jun;73 (6):991-996. doi: 10.1002/art.41632. Epub 2021 Apr 23. PMID: 33474834; PMCID: PMC8169527.

2.Pak SS, Miller MJ, Cheuy VA. Use of the PROMIS-10 global health in patients with chronic low back pain in outpatient physical therapy: a retrospective cohort study. J Patient Rep Outcomes. 2021 Sep 6;5(1):81. doi: 10.1186/s41687-021-00360-8. PMID: 34487270; PMCID: PMC8421489.

Disclosure: O. AKPOIGBE: None; **Y. EUN**: None; **C. ANIM-KORANTENG**: None; **A. SAMMUT**: None.

Abstract Number: 1213

Using Patient-Reported Disease Activity in a Population-Based Cohort to Predict Systemic Lupus Erythematous Hospitalization and Emergency Room Visits

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

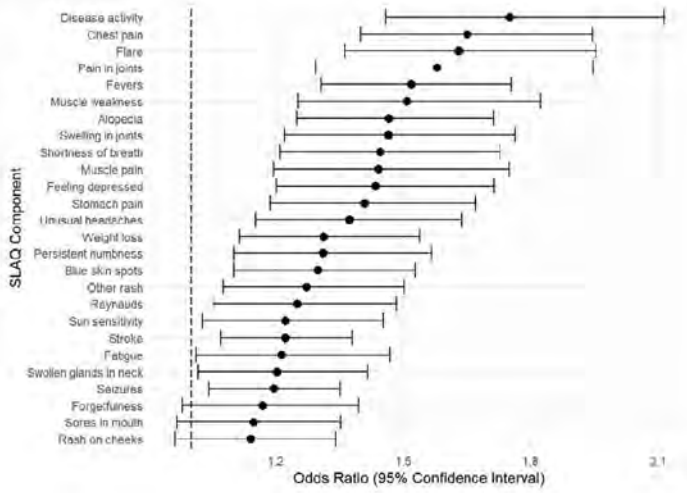
Background/Purpose: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease that has a large range of clinical manifestations, some of which can be severe. Reducing SLE flares leading to emergency room (ER) visits and hospitalizations is often difficult for clinicians given the heterogeneity of symptoms that can identify at-risk patients. The SLE Activity Questionnaire (SLAQ), a validated patient-reported instrument designed to screen disease activities in the clinical settings, may be a novel way to predict SLE-related healthcare utilization; but such association and application has not been studied and there have been few data to support its use in the clinical setting. The purpose of this analysis was to assess the patient-reported disease activity symptoms using SLAQ components in a population-based lupus cohort and develop a predictive model to identify patients at a higher risk for SLE-related hospitalization and ER visits.

Table 1 SLAQ components by SLE-related hospitalization or ER visit

	Overall N = 1,456	No SLE-related hospitalization/ER N = 1,350	≥ 1 SLE-related hospitalization/ER N = 106
SLAQ score* (Mean, SD)	17 (9)	17 (9)	22 (9)
SLAQ Components (N, %)			
Rash			
No Problem	502 (34%)	476 (35%)	26 (19%)
Mild	386 (26%)	358 (27%)	28 (21%)
Moderate/Severe	569 (37%)	478 (35%)	77 (57%)
Weight loss			
No Problem	907 (61%)	847 (63%)	60 (44%)
Mild	240 (16%)	207 (15%)	33 (24%)
Moderate/Severe	318 (21%)	276 (20%)	42 (31%)
Fatigue			
No Problem	161 (11%)	149 (11%)	12 (9%)
Mild	306 (21%)	282 (21%)	24 (18%)
Moderate/Severe	993 (67%)	895 (66%)	98 (72%)
Fevers			
No Problem	1011 (69%)	945 (70%)	66 (48%)
Mild	259 (17%)	226 (17%)	33 (24%)
Moderate/Severe	202 (14%)	166 (12%)	36 (26%)
Sores in mouth/nose			
No Problem	886 (60%)	820 (61%)	66 (50%)
Mild	312 (21%)	273 (20%)	39 (29%)
Moderate/Severe	274 (18%)	247 (18%)	27 (20%)
Rash on cheeks			
No Problem	978 (68%)	889 (67%)	79 (58%)
Mild	217 (15%)	190 (14%)	27 (20%)
Moderate/Severe	270 (18%)	243 (18%)	27 (20%)
Dark blue spots on skin			
No Problem	856 (58%)	794 (59%)	62 (48%)
Mild	242 (16%)	217 (16%)	25 (18%)
Moderate/Severe	370 (25%)	323 (24%)	47 (35%)
Sensitivity to the sun			
No Problem	659 (45%)	588 (44%)	47 (35%)
Mild	291 (20%)	265 (20%)	26 (19%)
Moderate/Severe	544 (37%)	463 (36%)	81 (46%)
Alopecia			
No Problem	906 (61%)	846 (63%)	60 (44%)
Mild	225 (15%)	200 (15%)	23 (17%)
Moderate/Severe	341 (23%)	289 (21%)	52 (38%)
Swollen glands in neck			
No Problem	887 (60%)	820 (61%)	67 (49%)
Mild	271 (18%)	236 (17%)	35 (26%)
Moderate/Severe	312 (21%)	280 (21%)	32 (24%)
Shortness of breath			
No Problem	482 (32%)	456 (34%)	26 (19%)
Mild	371 (25%)	336 (25%)	35 (26%)
Moderate/Severe	616 (41%)	542 (40%)	74 (54%)
Chest pain with deep breath			
No Problem	752 (51%)	712 (53%)	40 (29%)
Mild	309 (21%)	278 (21%)	31 (23%)
Moderate/Severe	413 (28%)	349 (26%)	64 (47%)
Raynaud's			
No Problem	696 (47%)	646 (48%)	48 (35%)
Mild	243 (16%)	215 (16%)	28 (21%)
Moderate/Severe	533 (36%)	475 (35%)	58 (43%)
Stomach pain			
No Problem	642 (43%)	608 (45%)	34 (25%)
Mild	329 (22%)	288 (21%)	41 (30%)
Moderate/Severe	486 (33%)	437 (32%)	49 (43%)
Persistent numbness or tingling			
No Problem	552 (37%)	519 (38%)	33 (24%)
Mild	309 (21%)	279 (21%)	30 (22%)
Moderate/Severe	616 (41%)	546 (40%)	70 (51%)
Seizures			
No Problem	1389 (93%)	1272 (94%)	117 (86%)
Mild	54 (4%)	42 (3%)	12 (9%)
Moderate/Severe	30 (2%)	25 (2%)	5 (4%)
Stroke			
No Problem	1387 (93%)	1267 (94%)	120 (88%)
Mild	46 (3%)	41 (3%)	5 (4%)
Moderate/Severe	38 (3%)	29 (2%)	9 (7%)
Forgetfulness			
No Problem	417 (28%)	387 (29%)	30 (22%)
Mild	444 (30%)	407 (30%)	37 (27%)
Moderate/Severe	606 (41%)	549 (40%)	66 (48%)
Feeling depressed			
No Problem	476 (32%)	453 (34%)	23 (17%)
Mild	383 (26%)	348 (26%)	35 (26%)
Moderate/Severe	619 (42%)	542 (40%)	77 (57%)
Unusual headaches			
No Problem	523 (35%)	494 (37%)	29 (21%)
Mild	381 (26%)	342 (25%)	39 (29%)
Moderate/Severe	596 (41%)	509 (38%)	86 (64%)
Muscle pain			
No Problem	334 (22%)	314 (23%)	20 (15%)
Mild	314 (21%)	294 (22%)	20 (15%)
Moderate/Severe	825 (56%)	732 (54%)	93 (69%)
Muscle weakness			
No Problem	400 (27%)	378 (28%)	22 (16%)
Mild	301 (20%)	279 (21%)	22 (16%)
Moderate/Severe	770 (52%)	679 (50%)	91 (67%)
Pain or stiffness in joints			
No Problem	179 (12%)	170 (13%)	9 (7%)
Mild	314 (21%)	292 (22%)	22 (16%)
Moderate/Severe	987 (68%)	883 (65%)	104 (76%)
Swelling in joints			
No Problem	415 (28%)	389 (29%)	26 (19%)
Mild	322 (22%)	294 (22%)	28 (21%)
Moderate/Severe	735 (49%)	649 (48%)	86 (63%)
Self-report disease activity† (Mean, SD)	4.0 (3.4)	3.8 (3.3)	5.7 (3.4)

*SLAQ score is a composite variable calculated using the individual SLAQ components. Disease activity scores can range from 0-47, with 47 indicating the highest disease activity.
†Self-reported disease activity is collected on a scale from 0 (no/low activity) to 10 (severe/high activity).

Figure 1. Unadjusted association between SLAQ components and SLE-related hospitalizations/ER visits



Estimated odds ratio (and 95% CI) for each SLAQ component from unadjusted logistic regression model predicting SLE-hospitalization or ER visits. All components were standardized to the same numeric scale of 0-3 of increasing severity.

Methods: This study used data from two surveys (2011-2013) of the Georgians Organized Against Lupus (GOAL) cohort, a Centers for Disease Control and Prevention supported population-based cohort of validated SLE patients in Atlanta who complete annual surveys, including sociodemographic and the SLAQ. This database was linked with the Georgia Hospital Discharge Database to obtain ER visits and hospitalizations within 6 months of each survey. An SLE-related hospitalization or ER visit is defined based on diagnosis of SLE-related condition in the primary position within 6 months of GOAL survey completion. The unadjusted association between SLAQ components and SLE-hospitalizations or ER visits was assessed using logistic regression to identify the strongest SLAQ predictors. A classification and regression tree (CART) model generated a decision tree for predicting SLE-hospitalization or ER risk based on the SLAQ components.

Results: Of the 1,486 GOAL participants, 136 (9.2%) had an SLE-related hospitalization or ER visit within 6-months of survey completion. The mean age at survey completion was 47 (SD: 13) years, 94% of patients were female, 78% of patients were Black, and had SLE for 14 (9) years. Patients with ≥1 SLE-related hospitalizations or ER visits had higher SLAQ scores than those without hospitalization (22 vs. 17; Table 1). The risk of SLE-related hospitalization or ER visit was higher among patients with higher disease activity scores, chest pain with deep breath, and those with more SLE flares (Figure 1). CART modeling suggests patients who had chest pain with deep breath and fevers as the high-risk group with 18.8% likelihood of an SLE-related hospitalization or ER visit in the next 6 months. The high-risk group have a 2-fold increased risk than the average patients (Pr=9.2%), and a 4-to-6-fold risk than those identified as low-risk (Pr=3.2-4.5%).

Conclusion: Patients who reported chest pain with deep breath and fevers were at the highest risk of having anSLE-related hospitalization or ER visit within 6 months. The inclusion of the SLAQ in routine care may provide physicians and patients with valuable information that could help mitigate healthcare utilization and improve outcomes.

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Abstract Number: 1214

Using Patient Self-Reported Measures to Predict All-Cause Hospitalization in a Population-Based Lupus Cohort

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

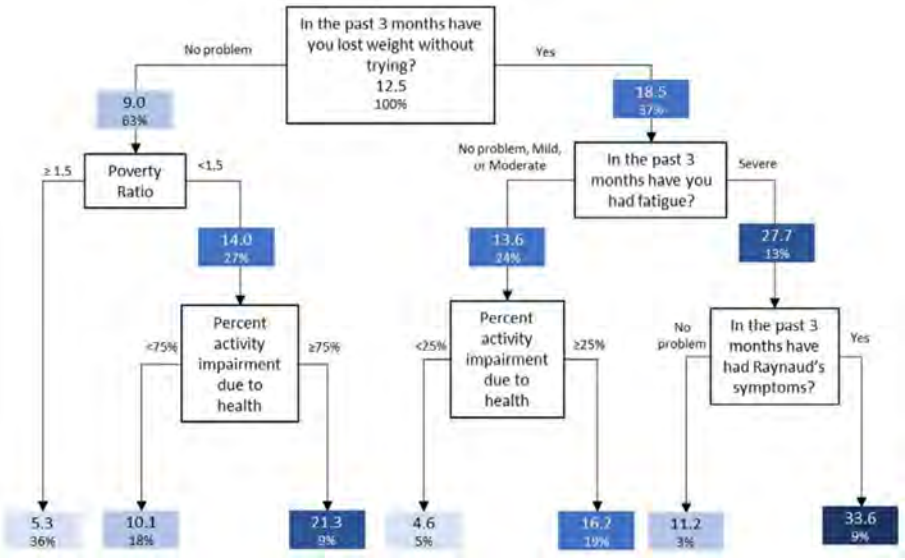
Background/Purpose: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease that affects the skin, joints, kidneys, lungs, central nervous system, and hematopoietic system. As a result of disease activity, patients with SLE have a 2- to 3-fold increased risk of hospitalization compared with the general population. Previous research has aimed to identify potential biomarkers or clinical factors that could be used to predict SLE flares that correlate with hospitalizations, but to date there has been little consistency. The purpose of this study was to develop a patient-centric predictive model that can be easily integrated into the clinical setting to identify patients that are at a higher risk for hospitalization.

Methods: Georgians Organized Against Lupus (GOAL) is a Centers for Disease Control and Prevention supported population-based cohort of validated SLE patients in Atlanta who complete annual surveys. From two surveys (2011-13), demographic, social-economic, clinical information and self-reported outcomes including Short-Form Survey (SF-12) and the SLE Activity Questionnaire (SLAQ) were obtained. This database was linked with the Georgia Hospital Discharge Database to obtain all-cause hospitalizations within 6 months of each survey. Those who died during a hospitalization were censored at the time of death.

Following descriptive analyses, a multivariable model examined the predictors of interest and all-cause hospitalization. Automated variable selection methods, the lowest Akaike Information Criterion (AIC) and selection through penalized regression (LASSO), were used. Variables of low importance across methods were excluded from further analysis. A classification and

Table 1. Characteristics of GOAL Participants, by 6-month Hospitalization Status

	Overall N = 1,486	No Hospitalization N = 1,300	≥ 1 Hospitalization N = 186
Age at Survey, years (Mean, SD)	47 (13)	48 (13)	44 (14)
Race Category (N, %)			
Black or African American	1,160 (78%)	1,005 (77%)	155 (83%)
White	303 (20%)	277 (21%)	27 (15%)
Other	22 (1.5%)	18 (1.4%)	4 (2.2%)
Disease Duration, years (Mean, SD)	14 (9)	14 (9)	13 (9)
Marital Status (N, %)			
Single	513 (35%)	429 (33%)	84 (45%)
Married	525 (35%)	476 (37%)	49 (26%)
Divorced/Separated/Widowed	443 (30%)	390 (30%)	53 (28%)
Other/Unknown	5 (0.3%)	5 (0.4%)	0 (0%)
Education (years) (Mean, SD)	14 (3)	14 (3)	14 (2)
Unknown (N)	6	5	1
Work Status (n, %)			
Working Full or Part Time	357 (24%)	308 (24%)	49 (26%)
Unemployed/Disabled	607 (41%)	509 (39%)	98 (53%)
Other/Unknown	522 (35%)	483 (37%)	39 (21%)
Poverty Ratio (Mean, SD)	2.1 (1.8)	2.1 (1.8)	1.6 (1.6)
Unknown (N)	61	50	11
Percent Activity Impairment (Mean, SD)	53 (32)	52 (32)	64 (29)
Unknown (N)	61	53	8
Insurance Type (N, %)			
Private Insurance	581 (39%)	518 (40%)	63 (34%)
Medicare	412 (28%)	357 (27%)	55 (30%)
Medicaid	204 (14%)	165 (13%)	39 (21%)
Other	40 (2.7%)	36 (2.8%)	4 (2.2%)
None/Unknown	249 (17%)	224 (17%)	25 (13%)



regression tree (CART) model generated a decision tree for predicting hospitalization risk based on a combination of components from SLAQ, SF-12, and sociodemographic characteristics.

Results: Of the 1,486 GOAL responses, 186 (12.5%) had an all-cause hospitalization within 6-months after survey completion. The mean age at survey completion was 47 (SD: 13), 94% of patients were female, 78% of patients were Black, and had SLE for 14 (9) years (Table 1). CART modeling identified patients with weight loss, fatigue, and Raynaud's symptoms as having the highest probability of having a hospitalization within 6 months (Pr=33.6%) (Figure1). Among those without weight loss, an increased probability of hospitalization was seen among those that had a poverty ratio < 1.5 and had more than 75% activity impairment due to health (Pr=21.3%).

Conclusion: In a population-based SLE cohort with a large proportion of Black patients, those who had weight loss, fatigue, and Raynaud's symptoms in the previous 3 months were at high risk of being hospitalized within the next 6 months. Collection of these symptoms that may not often be deemed clinically significant can be utilized in the clinical setting to identify SLE patients at higher risk of hospitalization and guide providers and patients accordingly.

Disclosure: S. Lim: None; **S. Wu**: AstraZeneca, 3; **R. Ross**: None; **G. Bao**: None; **M. Richards**: None; **L. Palmer**: None; **G. Bryant**: AstraZeneca, 3.

Abstract Number: 1215

Efficacy of Pharmacological Interventions: A Systematic Review Informing the 2023 EULAR Recommendations for the Management of Fatigue in People with Inflammatory Rheumatic and Musculoskeletal Diseases

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
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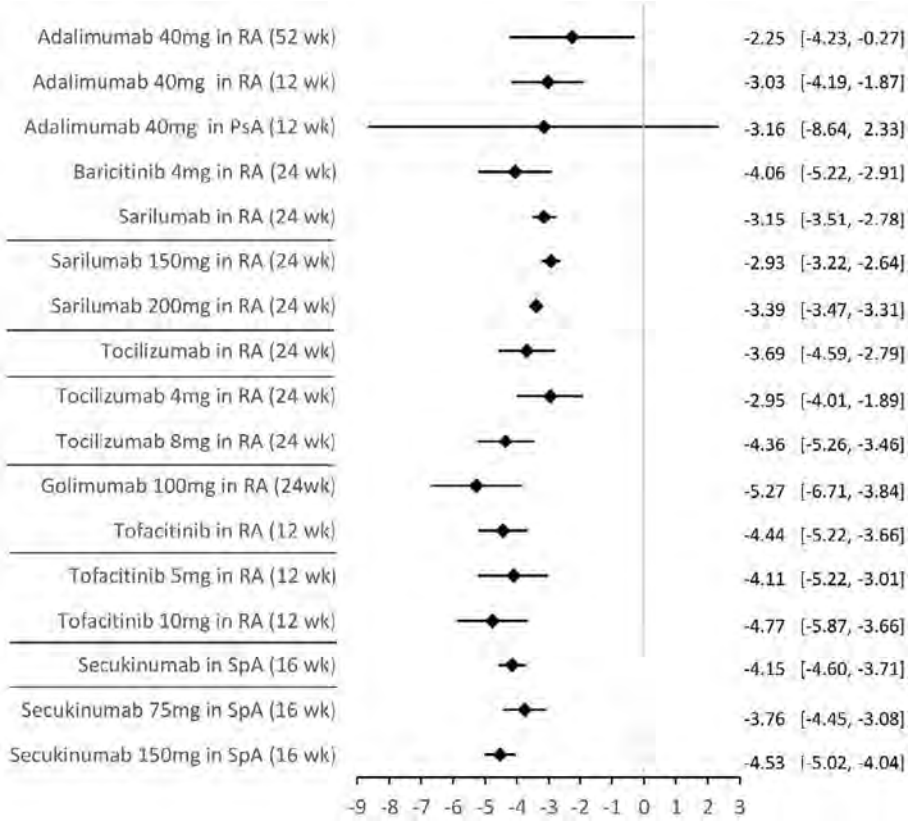
Background/Purpose: To identify the best evidence on the efficacy of pharmacological interventions in reducing fatigue in people with I-RMDs and to summarise their safety in the identified studies to inform EULAR recommendations for the management of fatigue in people with inflammatory rheumatic and musculoskeletal disease (I-RMD).

Methods: Systematic review of adults with I-RMD conducted according to the Cochrane Handbook. Search strategy ran in Medline, Embase, Cochrane Library, CINAHL Complete, PEDro, OTseeker and PsycINFO. Assessment of risk of bias, data extraction, and synthesis performed by two reviewers independently. Data pooled in statistical meta-analyses.

Results: From a total of 4,150 records, 454 were selected for full-text review, 105 fulfilled the inclusion criteria, and 19 RCTs were included in meta-analyses. Adalimumab was superior to placebo in reducing fatigue at 52 and 12 weeks (wk) in rheumatoid arthritis (RA) (mean difference [MD]=-2.25, p=0.03; MD=-3.03, p< 0.001; respectively) and psoriatic arthritis (MD=-3.16, p=0.26). Golimumab (24wk: MD=-5.27, p< 0.001), baricitinib (24wk: MD=-4.06, p< 0.001), sarilumab (24wk: MD=-3.15, p< 0.001), tocilizumab (24wk: MD=-3.69, p< 0.001) and tofacitinib (12wk: MD=-4.44, p< 0.001) were also superior to placebo in reducing fatigue in RA. A dose/effect relationship was observed for sarilumab, tocilizumab and tofacitinib. In spondyloarthritis, secukinumab was superior to placebo in reducing fatigue at 16wk (MD=-4.15, p< 0.001), with a dose/



effect relationship also observed (**Figure**). The narrative results of the RCTs not included in the meta-analysis indicated that several other pharmacological interventions were efficacious in reducing fatigue, with reassuring safety results.

Conclusion: Pharmacological interventions are efficacious and safe for the management of fatigue in people with I-RMD.

Disclosure: B. Farisogullari: None; **E. Santos**: None; **E. Dures**: None; **R. Geenen**: None; **P. Machado**: AbbVie/Abbott, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Orphazyme, 2, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 6.

Abstract Number: 1216

"I Call It Zombie Hands and Feet, That's Actually How I Found out I Had This Disease": Disease Symptoms and Treatment Side Effects in a Diverse Sample of Patients with Early Limited Cutaneous and Diffuse Cutaneous Systemic Sclerosis

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SESSION INFORMATION
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Background/Purpose: Systemic sclerosis (SSc) is a multisystem autoimmune rheumatic disease with heterogeneous manifestations, including common symptoms such as pain, fatigue, dyspnea, and Raynaud's phenomenon. It can also include rare but life-threatening complications such as renal failure and pulmonary hypertension. While the ACR Composite Response Index in Systemic Sclerosis (ACR CRISS), an existing clinical outcome assessment (COA), has shown favorable

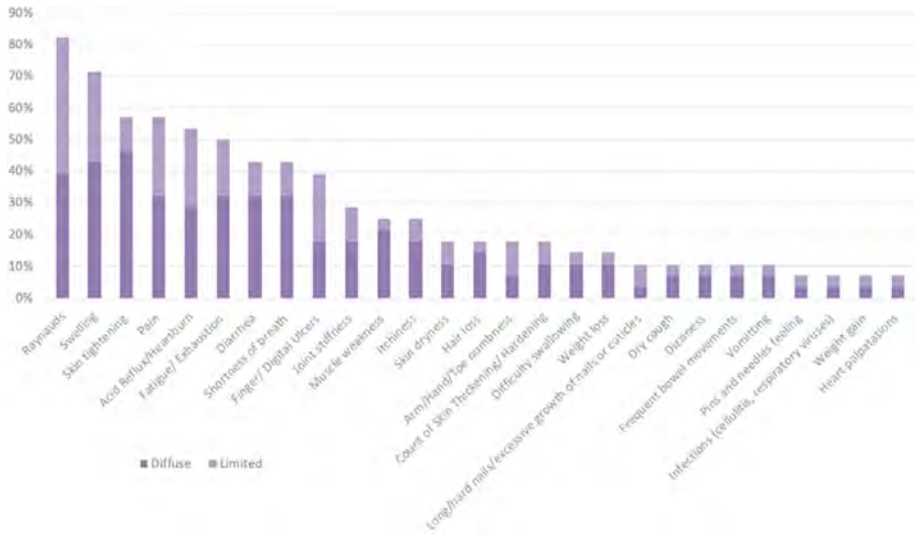

Figure 1. Disease Symptoms and Treatment Side Effects Reported by Participants with Both Subtypes of Systemic Sclerosis (N=27)

Table 1. Frequently Reported Disease Symptoms, Treatment Side Effects, and Bother Ratings by Participants with Both Subtypes of Systemic Sclerosis

Disease symptom/Treatment side effect	Number (%) who mentioned DS/TSE during interview	Mean Bother rating and range (0-10)	
Raynaud's disease	23 (82.1%)	6.1	1-10
Swelling[1]	20 (71.4%)	6.1	1-10
Pain[2]	16 (57.1%)	6.8	0-10
Skin tightening	16 (57.1%)	5.4	1-10
Acid reflux/heartburn/GERD	15 (53.6%)	5.6	0-10
Fatigue/exhaustion	14 (50.0%)	7.8	2-10

[1]Swelling includes hands, fingers, face, ankles, feet, joints.
[2]Pain includes abdominal, joint, jaw, hips, feet, ankles, hand, skin, whole body aches, nerve, muscle aches/soreness/cramps, generalized.

performance in SSc clinical trials, research is needed to develop a COA to more fully assess the way a patient feels, functions, and/or survives, per the FDA guidance. The purpose of this research is to comprehensively identify the disease symptoms (DS) and treatment side effects (TSE) that are most bothersome for patients with SSc toward the development a new and robust COA.

Methods: Concept elicitation interviews were conducted from February 2023 to May 2023 with 28 participants with SSc (15 participants with diffuse cutaneous SSc and 13 participants with limited cutaneous SSc). The 90-minute interviews focused on DS and TSE, how bothersome they were (0 = not at all bothersome to 10 = extremely bothersome), and their impacts on participants' lives. Interview data were summarized and results were analyzed thematically.

Results: The sample had a mean age of 54 years (range: 34-69) and was primarily women (82.1%), consistent with the broader gender distribution of SSc. The sample was diverse, including White (75.0%), Black (17.8%), Hispanic (7.1%), and American Indian (3.6%) participants. Overall, the sample reported 76 unique concepts (DS/TSE). After combining similar concepts for analytic purposes (e.g., sleep disturbances combined insomnia, hypersomnia) participants reported 66 DS/TSE. Participants with diffuse SSc reported an average of 13 DS/TSEs, while participants with limited SSc reported an average of 7 DS/TSEs. As presented in Figure 1, the most described DS/TSE across all participants was Raynaud's disease (82.1%), followed by swelling (71.4%), pain (57.1%), skin tightening (57.1%), acid reflux/heartburn/GERD (53.6%), and fatigue/exhaustion (50%). Of those DS/TSEs, fatigue was described as the most bothersome (M=7.8), followed by pain (M=6.8), swelling (M=6.1), Raynaud's (M=6.1), acid reflux/heartburn/GERD (M=5.6), and skin tightening (M=5.4). See Table 1 for more detail. Fatigue was the top bothersome DS/TSE for both diffuse and limited groups (M=7.8 and M=7.6 respectively). Both groups reported DS/TSE unique to their respective groups. Participants in the diffuse group uniquely reported contractures (46.7%), headaches (33.3%), skin discoloration (26.7%), and bloating/cramping (26.7%). Participants in the limited group uniquely reported eczema/red dots/blood vessels on skin (30.8%), and facial rash (15.4%).

Conclusion: These findings were consistent with symptoms described in the "Voice of the Patient" report for systemic sclerosis (2021) developed for the FDA's Patient-Focused Drug Development Initiative. This research will aid the creation of a new SSc COA measure using existing FACIT, PROMIS, and Neuro-QoL measurement systems, and new SSc-specific items, which will be capable of assessing multiple patient-centered domains.

Disclosure: C. Perschon: Boehringer-Ingelheim, 5, Merck/MSD, 5; **E. Jaeger**: Boehringer-Ingelheim, 5; **G. Greene**: None; **A. Lescoat**: None; **Y. Chen**: None; **S. Murphy**: None; **S. Shaunfield**: None; **D. Cella**: None; **D. Khanna**: AbbVie, 12, DSMB, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb, 2, 5, CSL Behring, 2, Genentech, 2, Horizon Therapeutics, 2, 5, Janssen, 2, 6, Pfizer, 5, Prometheus, 2.

Abstract Number: 1217

Sex Differences in Perceptions of Psoriatic Arthritis Disease Impact, Management, and Physician Interactions: Results from a Global Patient Survey

Lihi Eder[1], Pascal Richette[2], Laura Coates[3], Valderilio Feijó Azevedo[4], Joseph C. Cappelleri[5], Megan Hoang[6], Jade Moser[7] and Meriem Kessouri[8], [1]Women's College Research Institute, Division of Rheumatology, University of Toronto, Toronto, ON, Canada, [2]Lariboisière Hospital, Paris, France, [3]University of Oxford, Oxford, United Kingdom, [4]Department of Internal Medicine, Hospital de Clínicas at the Federal University of Paraná, Curitiba, Paraná, Brazil, [5]Pfizer Inc., Groton, CT, [6]Pfizer Inc., New York, NY, [7]The Harris Poll, Rochester, NY, [8]Pfizer Inc., Paris, France

SESSION INFORMATION

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Session Title: Patient Outcomes, Preferences, & Attitudes Poster II

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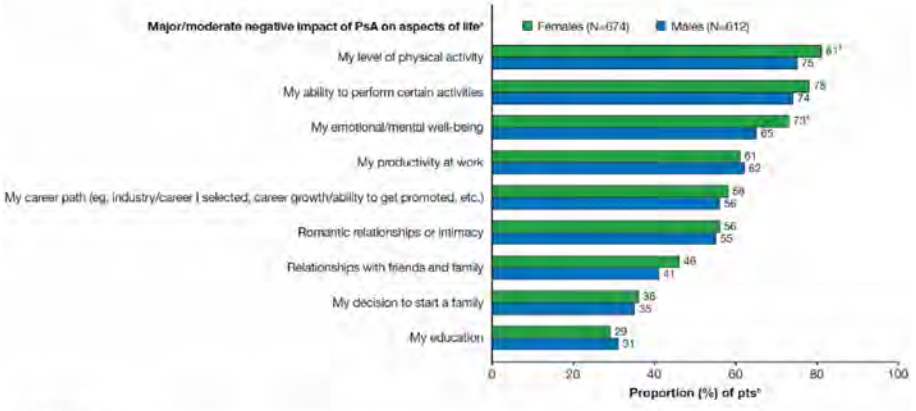
Background/Purpose: Women with PsA have more severe disease activity and lower health-related quality of life vs men.[1] This post hoc analysis assessed sex differences in disease impact perceptions and physician interactions with patients (pts) with PsA using global survey data.

Methods: An online survey by The Harris Poll (Nov 2, 2017–Mar 12, 2018) included 1,286 pts from 8 countries, aged ≥ 18 years, who had PsA for > 1 year, visited a rheumatologist/dermatologist in the past 12 months, and had used ≥ 1 DMARD for PsA.[2] Results were stratified post hoc by sex; analyzed descriptively and by binomial (chi-squared) tests. Percentages/binomial tests of the final global data were adjusted for size of each country's adult population. Statistically significant differences ($p < 0.05$) were described as more/higher.

Results: 52% of pts were female; 24% from Europe (France/Spain/UK). Mean age of females/males (41.3/41.0 years) and time since diagnosis (9.2/8.8 years) were similar. More females had anxiety (32% vs 24%), osteoarthritis (17% vs 9%), had taken a steroid (57% vs 43%), and were taking any DMARD (biologic and oral DMARDs; 20% vs 15%). More females vs males reported a major/moderate negative PsA impact on physical activity (81% vs 75%) and emotional/mental well-being

Fig. Major/moderate negative impacts of PsA for female vs male pts



*p < 0.05 for females vs males
†How much of a negative impact, if any, has PsA had on each of the following aspects of your life?
‡% based on weighted n (adjusted for size of each country's adult population)
N, number of pts that answered question; pts, patients

Table. Communication satisfaction[a] with rheumatologist, and discussion topics[b] between pts and their rheumatologist

n, yes, (%)[c]	Female (N=620)	Male (N=552)
Satisfaction[a]		
Very satisfied	371 (60)*	281 (51)
Somewhat satisfied	174 (28)*	214 (39)
Somewhat dissatisfied	40 (6)	33 (6)
Very dissatisfied	36 (6)	24 (4)
Discussion topics[b]		
Treatment goals	515 (83)*	428 (78)
Overall health	507 (82)	444 (80)
Physical exam of musculoskeletal symptoms	509 (82)	432 (78)
Impact on ability to conduct daily activities	510 (82)*	403 (73)
Response to and/or satisfaction with treatment regimen	500 (81)*	396 (72)
Impact on physical activity	491 (79)	413 (75)
Physical exam of skin/nail symptoms	469 (76)	406 (74)
Back pain (pain/stiffness)	467 (75)	411 (74)
Disease management plan	448 (72)	411 (74)
Unusual fatigue	430 (69)	370 (67)

*$p < 0.05$ for females vs males

[a]How satisfied are you with the communication you currently have with your rheumatologist regarding PsA? (Among pts who visited a rheumatologist in the past 12 months

[b]In the last 12 months, have you discussed/conducted the following with your rheumatologist regarding PsA?

[c]% and binomial tests based on weighted data (adjusted for size of each country's adult population)

N, number of pts that answered question; n, number of pts with satisfaction level or who participated in each discussion topic; pts, patients

(73% vs 65%); major/moderate impact on other life aspects, such as work productivity, was similar between sexes (Fig). More females vs males reported the following because of PsA: emotional distress (65% vs 50%), stopped social activities (49% vs 41%), and went on permanent work disability (14% vs 9%); more males vs females reported lower work productivity (47% vs 38%) because of PsA. Switching treatment due to joint symptoms (41% vs 28%) and side effects (35% vs 22%) were higher in females vs males; switching due to potential serious side effect concerns (29% vs 16%) and symptoms being under control (18% vs 9%) were higher in males vs females. More females vs males were very satisfied with their rheumatologist's communication (60% vs 51%), and discussed treatment goals (83% vs 78%), impact on ability to conduct daily activities (82% vs 73%), and response to and/or satisfaction with treatment regimen (81% vs 72%; Table). Pt ability to describe their PsA diagnosis/recall symptoms may limit the study.

Conclusion: More women vs men reported a major/moderate PsA impact on physical and emotional/mental well-being. More women were very satisfied with communication and discussed treatment goals with their rheumatologist. It is important to consider how sex impacts a pt's experience with PsA.

1. Orbai et al. Arthritis Care Res 2020; 72: 1772–9

2. Coates et al. Health Qual Life Outcomes 2020; 18: 173

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Abstract Number: 1218

Discovering the Potential Application of Digital Biomarkers for Inflammatory Arthritis Patients, a Design Thinking Approach; Preliminary Results of the Patients' Perspective

patty de Groot[1], ilja Tchetverikov[2], Yvonne P. M. Goekoop-Ruiterman[3], Wendy Olsder[4], Rien Bakker[5], Marc r. Kok[6], Jasper Foolen[7] and Jolanda J. Luime[1], [1]Erasmus Medical Center, Rotterdam, Netherlands, [2]Albert Sweitzer Hospital, Dordrecht, Netherlands, [3]Haga Ziekenhuis, The Hague, Netherlands, [4]Erasmus School of Health Policy and Management, Rotterdam, Netherlands, [5]Consortium Beroepsonderwijs, Information Communication Technology, Amersfoort, Netherlands, [6]Maasstad Hospital, Rotterdam, Netherlands, [7]Eindhoven University of Technology deparment of Biomedical Engineering, Eindhoven, Netherlands

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II
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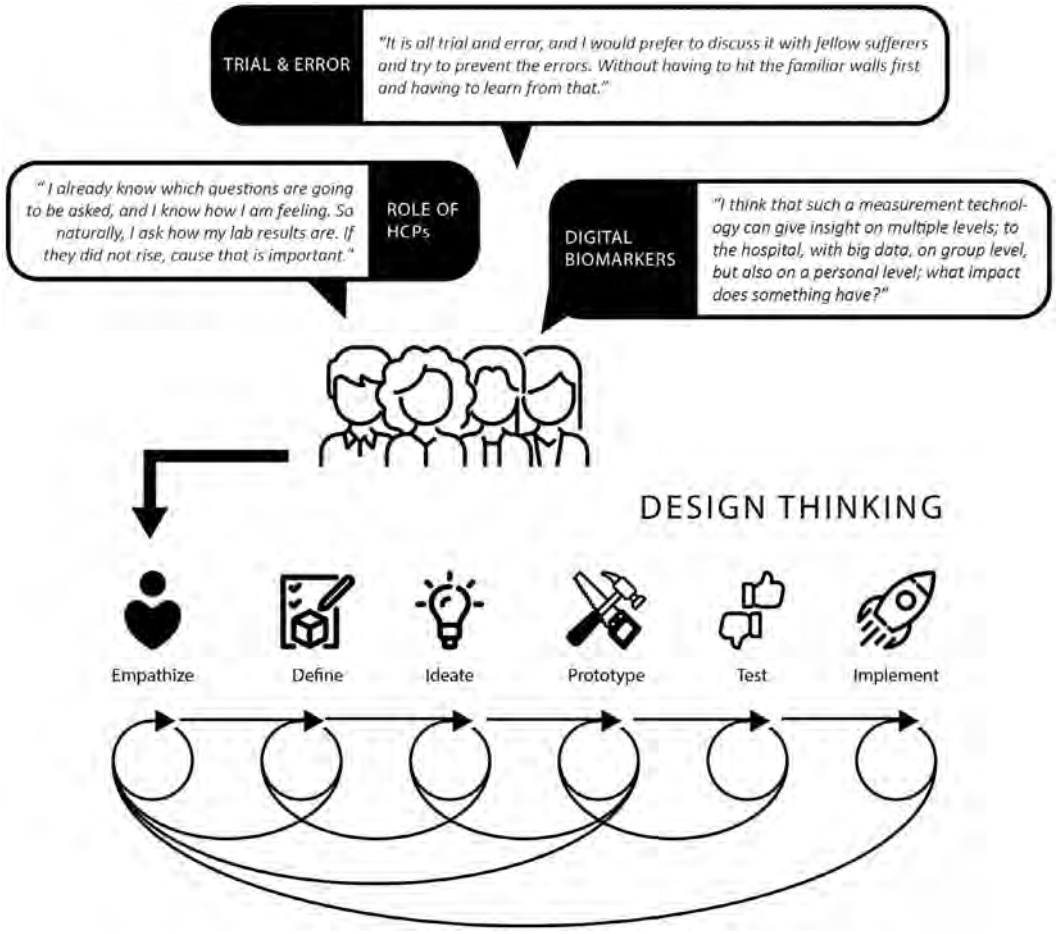
Session Time: 9:00AM–11:00AM

Background/Purpose: The Inflammatory Arthritis (IA) patient population is growing, whilst facing a shortage of health care professionals (HCPs). It is impossible to meet the future care demand. *Digital Biomarkers (DBs)* are objective, quantifiable, physiological and behavioural data that are collected and measured with digital devices. They can support continuous measurements outside the physical confines of clinical environments and help close the gap in healthcare demands.

This study aims to obtain the patients' insights on disease activity, disease management and care needs; and to empathise with their attitude towards DBs in order to obtain future directions for DB development.

Methods: Design Thinking is followed for the development of DBs in rheumatology. It is a human-centered problem-solving approach that leverages empathy and collective idea generation to tackle complex challenges. Sixty minute online semi-structured focus group discussions, based on the Common Sense Model of Self-Regulation were conducted (Leventhal et al. 2016). All interviews were audio-recorded, transcribed to verbatim, coded and discussed with our patient partners.

Results: Six focus groups were organised, with a total of 30 IA patients (22 PsA; 8 RA, age 51± 11 years, 48% male, time since diagnosis 7 (3:12,5) years). The main findings were: *Trial and error;* life after diagnosis is marked by trial and error. Learning how and when to listen to their bodies, uncovering potential inflammation-triggers and developing appropriate disease management. Needs are discussions on lifestyle adjustments, career choices and life adaptations with their HCPs and fellow patients. T*he HCPs role;* patients visited their HCP for affirmation, reflection and future directions. They often doubted whether their symptoms were rheumatic. Secondly, they wanted assurance adverse drug reactions are absent, blood tests



Quotes from patient focus groups and the design thinking process

brought peace of mind. Furthermore, consultations were indicated as obligatory self-reflection. Conversing with their HCP was seen as a reality check and a conversation about (new) options. *DBs;* attitudes towards DBs varied. Some patients thought it could provide them with deeper insights and reminders before crossing a line. Some patients thought it relevant only for their HCP. They did not want a constant disease reminder. Others did not see any additional value. They knew themselves well enough, no device should tell them whether their feelings are justified.

Conclusion: The following problem statement from the patients' perspective can be formulated; "we suffer from a disease that turned our lives upside down, we have to cope with it daily. Our learning is by trial and error. We must know which activities to avoid and how to predict flares. It is difficult to discriminate ordinary pain, from pain preceding a flare. Affirmation from our HCPs and our blood results bring peace of mind. Perhaps, by applying technology, we can speed up our learning process and triggers of flare could be identified. However, one should be mindful of the purpose, the amount of notifications and the data representation." In general there is no strong resistance to DBs. However, for future uptake the recorded data should be of clear benefit for the patient.

Disclosure: p. de Groot: None; **i. Tchetverikov**: None; **Y. Goekoop-Ruiterman**: None; **W. Olsder**: None; **R. Bakker**: None; **M. Kok**: None; **J. Foolen**: None; **J. Luime**: None.

Abstract Number: 1219

Patient Experience of Brain Fog to Inform the Development of a De Novo Patient Reported Outcome (PRO) in Patients with Sjögren's Disease

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Background/Purpose: Brain fog is commonly reported by SJD patients, though limited evidence exists to understand patient experiences. Various terms may be used to describe brain fog, including mental or cognitive fatigue and cognitive dysfunction. While cognitive difficulties are typically assessed via battery testing, there is no brain fog PRO to assess related patient symptoms and impacts experienced by patients. The purpose of this study was to explore concepts related to brain fog among SJD patients, and attempt to discern whether brain fog is related to fatigue or may be a separate manifestation as experienced by SJD patients.

Methods: A cross-sectional qualitative study among adults with clinician-confirmed SJD consisted of 30-minute semi-structured concept elicitation (CE) interviews and a pile-sort exercise. A thematic approach, a codebook, and MAXQDA software were used to organize, code, and analyze anonymized CE interview transcripts. In the sorting exercise, patients ranked all items from the Neuro-QoL-Cognitive Function and PROMIS-Cognitive Fatigue item banks as most, somewhat, or not relevant to their brain fog experience. Cultural consensus analysis (CCA) was used to determine whether there were items that participants agreed were most relevant (consensus) that may be considered for a de novo PRO instrument.

Figure 1. Patient-Reported Symptoms of Brain Fog in SJD by Cognitive Domain

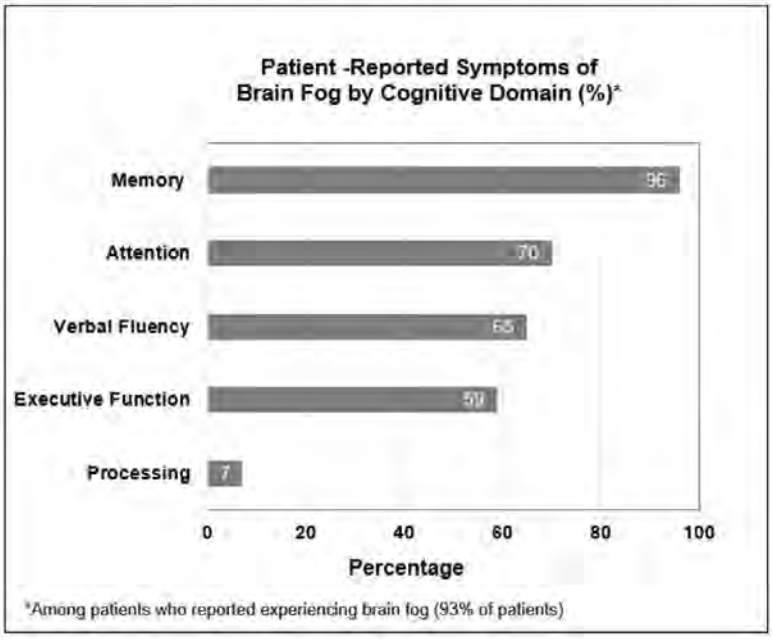

Table 1. Selected Patient Descriptions of Brain Fog Symptoms by Cognitive Domain

Memory	*"[…] and brain fog, brain fog is another one. […]* ***Forgetting—forgetting what I [laughs] was going to say constantly****. So, I'm not sure, I forgot where I was going with all this. We were talking about dry mouth?" (Patient 001)*
Attention	*"I basically check out or* ***I can't focus*** *on what I'm doing. That's what I consider brain fog, anyway, is* ***lack of focus****. Just feeling maybe not physically tired but just* ***tired of concentrating****. It's just a lot of work." (Patient 015)*
Verbal Fluency	*"So, there are sometimes, yes, the speech doesn't want to come out properly or* ***I'll stumble over words or it's like I'm not speaking clearly****." (P001)*
Executive Function	*"If there are multiple things going on, I do. If I* ***can focus on one thing*** *then I'm fine, but I* ***can't multitask anymore****." (Patient 040)*

Results: Of N=29 SJD patients interviewed (mean age, 63 yrs; 97% female; 79% Caucasian; mean length of time since diagnosis, 13.6 yrs), 75% spontaneously used the term "brain fog" to describe their cognitive difficulties. Symptoms included deficits in memory (96%), concentration (70%), verbalizing (65%), and executive function (59%) (Figure 1, Table 1). Patients reported experiencing brain fog all the time (12%), daily (24%), weekly (36%), monthly (20%) or annually (8%). Results indicated patients generally do not associate brain fog directly with fatigue; of 11 (44%) patients describing brain fog and fatigue as somewhat related, 9 (82%) stated brain fog and fatigue can occur separately while 5 felt fatigue was triggering or causing their brain fog (45%). CCA results from the pile sort exercise indicated that consensus, defined as an Eigenvalue ratio of >3.1, existed among a participant subset (n=10; ER 4.05). Comparing results based on this subset and all patients demonstrated a nearly identical overlap in highly ranked items between the two groups. Neuro-QoL items consistently ranked higher than PROMIS items; 17 of the top 20 highest ranked items were based on the Neuro-QoL, indicating items of cognitive dysfunction were more relevant than those of cognitive fatigue for SJD patients.

Conclusion: Brain fog commonly affects SJD patients with symptoms impacting memory, concentration, verbalization and executive function. Participant endorsement of items from the Neuro-QoL suggests brain fog may be attributable to independent cognitive dysfunction rather than cognitive fatigue. The results support exploring the use of highly ranked Neuro-QoL items to develop a draft de-novo Brain Fog PRO for further research in SJD patients.

Disclosure: D. Kruzikas: AbbVie/Abbott, 3, 11; **A. Eldred**: AbbVie/Abbott, 3, 11; **S. Kafka**: AbbVie/Abbott, 3, 11; **J. Church**: Sjögren's Foundation, 3; **K. Hammitt**: Sjögren's Foundation, 3; **P. Koochaki**: ICON Clinical Research LLC, 3, the healthcare business of Merck KGaA, Darmstadt, Germany, 2; **C. O'Donnell**: ICON plc, 3.

Abstract Number: 1220

Sjögren's Patients' Experiences and Content Validity of the Dry Eye Disease Symptom Questionnaire (DED-SQ)

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Dry eye is one of the most important and prevalent symptoms experienced by patients with Sjögren's Disease (SJD). The DED-SQ is a 12-item patient reported outcome (PRO) measure developed to assess dry eye disease. The purpose of this study was to identify the most important dry eye concepts to SJD patients and assess content validity of the DED-SQ for use in SJD populations.

Methods: Recruitment was conducted in partnership with the Sjögren's Foundation, with patients self-selecting for participation. US patients with physician-confirmed diagnosis of SJD and symptoms of dry eye were recruited. Combined concept elicitation (CE) and cognitive interviews (CI) were conducted by phone or online platform with 29 adult SJD patients. During CE, patients reported the most important dry eye symptoms and the impact of dry eye on their daily lives and ability to function. During CI, patients completed the DED-SQ followed by discussion of the relevancy of items, clarity of wording, ease of completion, selection of response options, comprehensiveness, and appropriateness of the recall period. Interviews

Table 1. Selected Patient Descriptions of Dry Eye

*"It feels like, at its best it feels as if **your eyes are really tired** and it also means that you're **struggling sometimes to focus on things**." (Patient 006)*
*"Well, in the beginning it felt like there was **sand in your eye**, and now it feels, it's a **burn** that is beyond, and yet I, it's very difficult to get relief anymore." (Patient 009)*
*"It's **painful** if I don't medicate—it can be so painful that I **can't read**, can't keep my eyes open." (Patient 040)*
*"They're going to get irritated; I end up having **blurry vision**, and then they'll get **swollen**, they'll get **red and irritated**." (Patient 001)*
*"My eyes would become so dry that I **could not remove the contacts**, they would **stick to my eyeballs**, even using the rewetting solution." (Patient 038)*
*"It feels like your lids are sticking closed. It looks like you're **looking through a fog**. You could read an eye chart and blink and get a totally different response five seconds later, because the **dry eyes just distorts your vision** to that degree. It also **feels like gritty and itchy**, yeah." (Patient 016)*

were audio recorded, transcribed, and anonymized. Thematic analysis of the CE data was conducted using MAXQDA, software designed to organize and facilitate qualitative data analysis, and a codebook, developed from the interview guide and supplemented with additional codes derived from patient comments. An item tracking matrix was used to facilitate a systematic evaluation of the individual items, instructions, recall period and response options to make recommendations for revision.

Results: The study participants were predominantly female (96%), White (79%), and held a bachelor's degree or higher (90%). On average, participants were 62.8 years of age. Patients reported multiple symptoms of dry eye (Table 1), including general dryness (100%), pain, soreness, or an ache in their eyes (41%), as well as a gritty and/or sandy feeling in their eyes (45%). Patients also reported that dry eye caused their vision to be blurry, distorted, foggy, or fuzzy making it difficult to read text (38%). The reported dry eye symptom descriptions mapped well onto concepts/items in DED-SQ and patients found most items in the DED-SQ relevant to their experiences. Some patients suggested concepts that may be less relevant to SJD ("red eyes" (56%), "itchy eyes" (31%), or "crustiness" (52%) or that may be difficult to distinguish from causes other than SJD ("stinging/sharp feeling", "burning" (28%)). Apart from items on stinging and burning, patients interpreted the items as intended (≥93%) and found the items easy to answer (≥81%). Patients felt the past 24-hour recall period was appropriate (82%).No additional dry eye symptoms beyond those included in the DED-SQ were identified.

Conclusion: These results reveal dry eye consists of a constellation of symptoms. A PRO covering the multifaceted concept of dry eye may be needed to appropriately assess SJD patients' experiences. These findings suggest a revised DED-SQ may be fit-for-purpose for assessing dry eye in SJD. Further research can help assess the content validity of a revised DED-SQ in SJD patients.

Disclosure: D. Kruzikas: AbbVie/Abbott, 3, 11; **A. Eldred**: AbbVie/Abbott, 3, 11; **S. Kafka**: AbbVie/Abbott, 3, 11; **J. Church**: Sjögren's Foundation, 3; **K. Hammitt**: Sjögren's Foundation, 3; **P. Koochaki**: ICON Clinical Research LLC, 3, the healthcare business of Merck KGaA, Darmstadt, Germany, 2; **C. O'Donnell**: ICON plc, 3.

Abstract Number: 1221

Familial Clustering of Dysbiotic Oral and Fecal Microbiomes in Juvenile Dermatomyositis (JDM)

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: JDM is a rare immune-mediated disease of childhood that is thought to result from genetic predisposition and environmental drivers, with documented links to microbial exposures. In this multi-center, prospective, observational cohort study, we evaluated whether JDM is associated with discrete oral and gut microbiome signatures using siblings to control for family-associated microbial communities.

Methods: We generated 16S rRNA sequence data from fecal, saliva, supragingival, and subgingival plaque samples from JDM probands (*n*=28, age range 3-18 years, mean age 10 years, 46% female). To control for genetic and environmental determinants of microbiome community structure, we also profiled microbiomes of their unaffected family members (*n*=27 siblings, *n*=26 mothers, and *n*=17 fathers). We performed paired within-family comparisons as well as unpaired analyses of different cohorts.

Results: Family unit was the predominant factor explaining variance in both weighted and unweighted UniFrac distances between samples for each sample type ($p< 0.001$ in fecal, saliva, supragingival swab, and posterior subgingival dental plaque samples; $p< 0.01$ in anterior subgingival dental plaque samples, permutational multivariate analysis of variance. Unweighted UniFrac distances between siblings was significantly smaller than the distances between JDM probands in our cohort ($p< 0.002$, two-tailed Student's *t*-test).

In fecal samples, 4% of bacterial amplicon sequence variants (ASVs) were differentially abundant in microbiomes between JDM probands and their siblings (**Figure 1A, Table 1**). In the case where ASVs that were initially classified as unannotated bacteria during the analyses, taxonomy was assigned based on BLAST results.Approximately 8% of ASVs identified in the ***anterior*** subgingival dental plaque were significantly different between JDM probands and their healthy siblings (**Figure 1B).** In ***posterior*** subgingival dental plaque samples, approximately 7% of identified ASVs were significantly differentially

Table 1. Differential 16s rRNA Microbial amplicon sequence variants (ASVs) in children with JDM compared to healthy siblings (Percent ± SEM).

Table 1. Differential 16s rRNA Microbial amplicon sequence variants (ASVs) in children with JDM compared to healthy siblings (Percent ± SEM).

Microbial Species	JDM	Siblings
Fecal		
Unannotated *Ruminococcaceae* or *Oscillospiraceae* [*]	0.08 ± 0.03%	0.05 ± 0.03%
Faecalibacterium in the *Oscillospiraceae* family [*]	1.13 ± 0.15%	0.95 ± 0.12%
Unannotated *Roseburia*	0.15 ± 0.05%	0.02 ± 0.02%
Unannotated *Ruthenibacterium lactatiformians*	0.03 ± 0.007%	0.007 ± 0.005%
Unannotated *Agathobacter* [*]	0.02 ± 0.02%	0.07 ± 0.04%
Unannotated *Anaerostipes*	0.55 ± 0.13%	0.83 ± 0.25%
Unannotated *Fusicatenibacter*	0.9 ± 0.2%	1.7 ± 0.3%
Streptococcus [*]	0.1 ± 0.05%	0.4 ± 0.2%
Streptococcus [*]	0.007 ± 0.008%	0.02 ± 0.01%
Streptococcus [*]	0.007 ± 0.004%	0.02 ± 0.02%
Subdoligranulum	0.0004 ± 0.0004%	0.01 ± 0.01%
Anterior Subgingival Plaque		
Unannotated *Parvimonas* species [*]	0.03 ± 0.03% [#]	0.006 ± 0.006%
Corynebacterium matruchotii	1.9 ± 0.3%	2.4 ± 0.1%
Corynebacterium matruchotii	1.4 ± 0.2%	1.8 ± 0.08%
Porphyromonas pasteri [*]	0.95 ± 0.1%	0.1 ± 0.1%
Porphyromonas pasteri [*]	0.6 ± 0.1%	0.7 ± 0.1%
Granulicatella	0.3 ± 0.03%	0.4 ± 0.04%
Prevotella loeschelii	0.3 ± 0.1%	0.4 ± 0.2%
Unclassified with sequence identity to *Prevotella* [#]	0.1 ± 0.07%	0.3 ± 0.1%
Posterior subgingival dental plaque		
Actinomyces [*]	1.0 ± 0.2%	0.8 ± 0.1%
Actinomyces [*]	0.6 ± 0.1%	0.5 ± 0.07%
Gemella	0.7 ± 0.1%	0.6 ± 0.1%
Streptococcus pneumoniae	3.6 ± 0.5%	3.3 ± 0.4%
Unclassified with sequence identity to *Lautropia* [#]	0.08 ± 0.08%	0.03 ± 0.03%
Actinomyces dentalis	0.01 ± 0.01%	0.05 ± 0.01%
Leptotrichia [#]	0.03 ± 0.03%	0.09 ± 0.09%
Unclassified with identity to *Prevotella*	0.05 ± 0.03%	0.2 ± 0.09%
Saliva		
Veillonella [#]	0.07 ± 0.06%	0.05 ± 0.02%
Prevotella shahii [#]	0.02 ± 0.008%	0.009 ± 0.009%
Prevotella melaninogenica [#]	0.005 ± 0.003%	0.01 ± 0.01%
Supragingival		
Neisseria oralis	0.2 ± 0.07%	0.09 ± 0.06%
Unclassified with sequence identity to *Corynebacterium*	0.03 ± 0.01%	0.02 ± 0.01%
Prevotella	0.04 ± 0.02%	0.02 ± 0.01%

[*] Multiple ASVs were identified for these species
[#] Significantly different between JDM and siblings

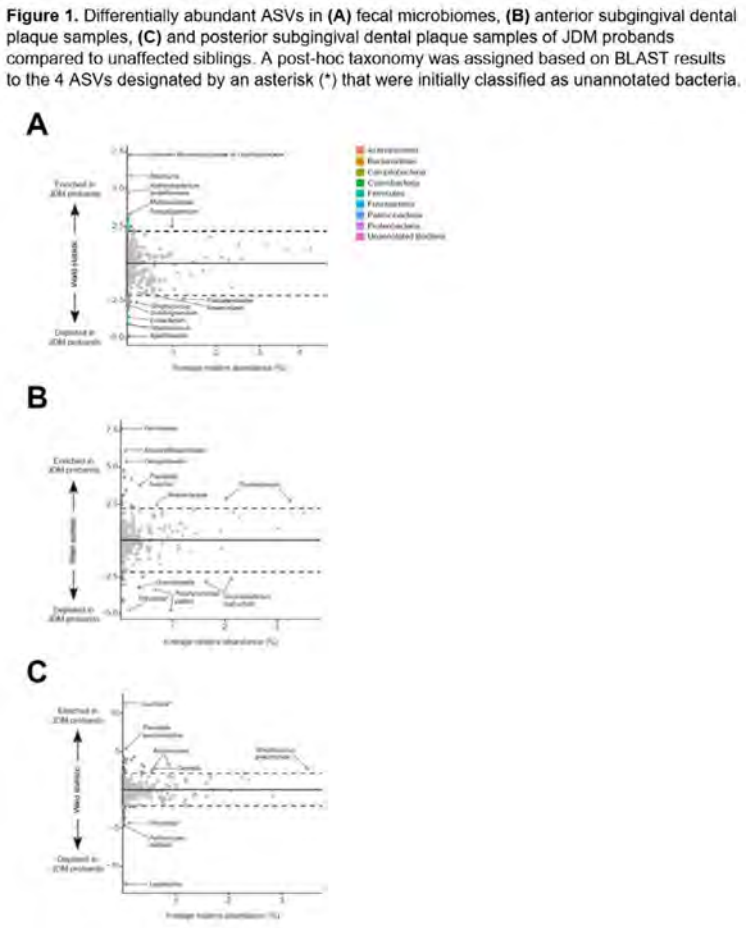

Figure 1. Differentially abundant ASVs in (A) fecal microbiomes, (B) anterior subgingival dental plaque samples, (C) and posterior subgingival dental plaque samples of JDM probands compared to unaffected siblings. A post-hoc taxonomy was assigned based on BLAST results to the 4 ASVs designated by an asterisk (*) that were initially classified as unannotated bacteria.

abundant between JDM probands and their siblings (**Figure 1C)**. We also observed differentially abundant ASVs in the saliva and supragingival swab samples from JDM probands, all of which were found in very low abundances, including salivary enrichment of *Veillonella* and *Prevotella shahii* and depletion of *Prevotellamelaninogenica*.

Conclusion: The oral and gut microbiomes of JDM probands were more similar to their own unaffected siblings than they were to the microbiomes of other JDM probands, suggesting family unit has a significant effect on microbiome community structure. Nonetheless, in a sibling-paired analysis, several potentially immunomodulatory bacterial taxa were differentially abundant in the microbiomes of JDM probands, including *Faecalibacterium* in the gut and *Streptococcus* in the oral cavity. The loss or gain of specific fecal and oral bacteria may potentially play a role in disease pathogenesis and/or be secondary to immune dysfunction in susceptible individuals.

Disclosure: A. Chow: None; **S. Koester**: None; **E. Pepper-Tunick**: None; **P. Lee**: None; **M. Eckert**: None; **L. Brenchley**: None; **P. Gardner**: None; **N. Li**: None; **a. Schiffenbauer**: None; **R. Volochayev**: None; **N. Bayat**: None; **J. McLean**: None; **L. Rider**: AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Hope Pharmaceuticals, 5; **S. Shenoi**: None; **A. Stevens**: Janssen, 2, 5; **N. Dey**: None.

Abstract Number: 1222

The Association Between Gingival Inflammation and Clinical Signs of Active Juvenile Dermatomyositis (JDM)

Albert Chow[1], Hyun Song[2], Laurie Brenchley[3], Nastaran Bayat[4], Mary Eckert[5], Sean Koester[6], adam Schiffenbauer[7], Rita Volochayev[7], Pamela Gardner[3], Peggy Lee[8], Jeffrey McLean[9], Susan Shenoi[10], Lisa Rider[11], Anne Stevens[12] and Neelendu Dey[13], [1]Loma Linda University, Loma Linda, CA, [2]Department of Dentistry, Seattle Children's Hospital, Seattle, WA, [3]Office of the Clinical Director, NIDCR, National Institutes of Health, Bethesda, MD, [4]Social Scientific Systems, DLH Holdings Corp, Silver Spring, MD, [5]Center for Clinical and Translational Research, Seattle Children's Research Institute, Seattle, WA, [6]Translational Science and Therapeutics Division, Fred Hutchinson Cancer Center, Seattle, WA, [7]Environmental Autoimmunity Group, Clinical Research Branch, National Institute of Environmental Health Sciences, National Institutes of Health, Bethesda, MD, [8]Department of Oral Medicine, School of Dentistry, University of Washington, Seattle, WA, [9]Department of Periodontics, University of Washington, Seattle, WA, [10]Seattle Childrens Hospital, Mercer Island, WA, [11]NIEHS, NIH, Bethesda, MD, [12]Janssen, Hansville, WA, [13]Department of Medicine, Division of Gastroenterology, University of Washington, Seattle, WA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease

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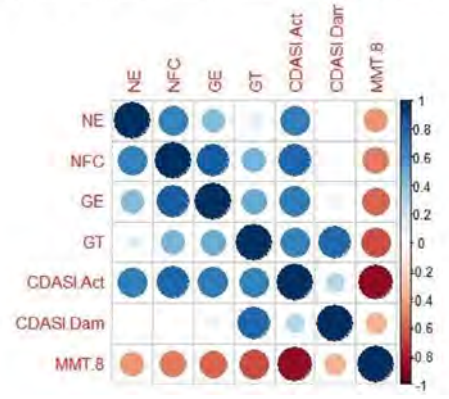
Session Time: 9:00AM–11:00AM

Background/Purpose: JDM is a rare vasculopathy of unknown etiology characterized by typical rashes and proximal weakness. JDM has been associated with gingivitis, which can be triggered by microbial dysbiosis and has been implicated in the etiology of systemic autoimmune disease. This study aimed to characterize the relationship between oral inflammation and vasculopathy with JDM disease activity.

Methods: A prospective pilot observational study was conducted at two centers. Patients met probable or definite Bohan and Peter criteria for JDM, and were excluded for co-existing autoimmune diagnoses, antibiotics within 3 months of enrollment, or gingival erythema secondary to tooth eruption or orthodontic appliances. Gingival erythema, telangiectasias, gingival index, and plaque index were scored by dentists and dental hygienists. Myositis disease activity measures such as manual muscle testing of 8 core groups (MMT8), Cutaneous DM Disease Area and Severity Index (CDASI), and nailfold

Figure 1: Associations of nailfold and gingival capillary scores in patients with JDM.

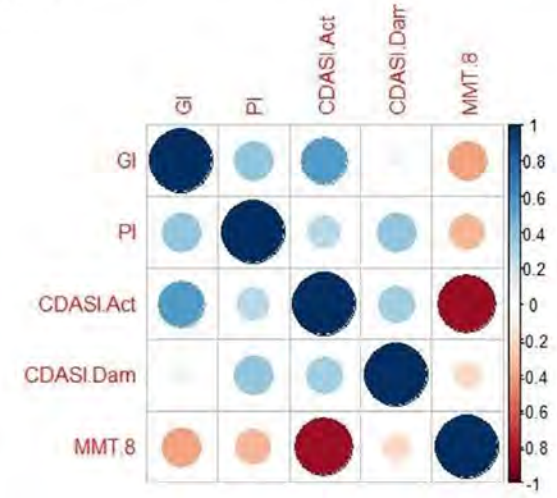
Central readings of nailfold and gingival capillary scores were conducted in patients with JDM via photographs (N=14). NFC, nailfold capillary abnormalities; NE, nailfold erythema; GE, gingival erythema; GT, gingival telangiectasis; CDASI.Act, CDASI total activity score; CDASI.Dam, CDASI total damage score; MMT.8, manual muscle testing of 8 core groups. Diagonal dark blue circles indicate 1:1 Spearman correlation. Color intensity, effect size; circle radii, statistical significance; Blue, positive effect; Red, negative effect. Note the red (negative) correlation between MMT8 and other clinical findings.



Associations of nailfold and gingival capillary scores in patients with JDM.

Figure 2: Associations of Gingival Index and Plaque Index in patients with JDM.

Associations of Gingival Index, Plaque Index with JDM disease outcomes in 17 patients with JDM evaluated during clinical examinations and N=17. GI, gingival index; PI, plaque Index; CDASI.Act, CDASI total activity score; CDASI.Dam, CDASI total damage score; MMT.8, manual muscle testing of 8 core groups.



Associations of Gingival Index and Plaque Index in patients with JDM.

capillaroscopy (NFC) were assessed by pediatric rheumatologists. To conduct parallel evaluations of vasculopathy in nailfolds and gingiva, we developed a central dichotomous scoring system averaging the presence or absence of erythema and telangiectasias from photographs over 6 anterior teeth and 10 fingers. With uncertain distribution and variance patterns in JDM, we elected to use Spearman's correlation despite small sample size.

Results: Seventeen subjects ages 3.8-15.5 (mean 8.9) years, with 9 females were included. The mean MMT8 was 140; eleven met PRINTO criteria for clinically inactive disease. The mean CDASI activity score was 6.5 and mean CDASI damage score 1.8.In evaluation of photographs, reliability was good: with Cohen's Kappa k=0.860 and 0.940 for NFC telangiectasia and erythema and k=0.840 and 0.814 for gingival telangiectasias and erythema. Excellent correlation was found between gingival erythema and presence of NFC abnormalities (r=0.85, p=0.003) and between the presence of gingival telangiectasias and CDASI Damage (r=0.74, p=0.009), with moderate correlation between gingival erythema and MMT8 (r=-0.36, p=0.012) (Figure 1).There was a moderate correlation between Gingival Index and CDASI Activity (r=-0.56, P=0.02) (Figure 2).

Conclusion: We systematically quantified gingival and NFC vasculopathy in JDM and found correlations between signs of oral vasculopathy and both skin and muscle disease, suggesting related pathogenic processes. Future mechanistic studies are needed to elucidate mechanisms, including whether gingival vasculopathy remains an underrecognized primary vasculopathic manifestation of JDM.

Disclosure: A. Chow: None; **H. Song**: None; **L. Brenchley**: None; **N. Bayat**: None; **M. Eckert**: None; **S. Koester**: None; **a. Schiffenbauer**: None; **R. Volochayev**: None; **P. Gardner**: None; **P. Lee**: None; **J. McLean**: None; **S. Shenoi**: None; **L. Rider**: AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Hope Pharmaceuticals, 5; **A. Stevens**: Janssen, 2, 5; **N. Dey**: None.

Abstract Number: 1223

Extracorporeal Life Support for Childhood-Onset Systemic Lupus Erythematosus: An ELSO Registry Analysis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a heterogeneous multisystemic autoimmune disorder that can cause life-threatening complications. There is a paucity of data on the utility of extracorporeal membrane oxygenation (ECMO) in children with SLE. The Extracorporeal Life Support Organization (ELSO) 2023 International summary reported an overall pediatric survival to discharge for 61% pulmonary support, 55% cardiac support, and 41% extracorporeal cardio-pulmonary resuscitation (eCPR). A recent systematic analysis on the use of ECMO in children with immune-mediated

Table 1: Demographics by Survival at Discharge

	Non-survivors (N =23)			Survivors (N =25)			
	N	Median	(IQR)	N	Median	(IQR)	p-value
Age year	23	15.5	(13.1,16.9)	25	14.1	(12.1,16.7)	0.245
BMI	17	20.1	(19.5,32.4)	21	21.5	(20.2,27.5)	0.652
	N	(%)		N	(%)		p-value
Sex							1.000
Female	20	(87.0)		21	(84.0)		
Male	3	(13.0)		4	(16.0)		
Race							0.563
Asian	3	(13.0)		1	(4.0)		
Black	8	(34.8)		8	(32.0)		
Hispanic	3	(13.0)		7	(28.0)		
Middle Eastern	1	(4.3)		0	0.0		
Multiple	3	(13.0)		1	(4.0)		
Native American	0	0.0		1	(4.0)		
Other	2	(8.7)		1	(4.0)		
Unknown	0	0.0		1	(4.0)		
White	3	(13.0)		5	(20.0)		
Comorbidities*							
Pulmonary	5	(21.7)		7	(28.0)		0.743
Renal	6	(26.1)		12	(48.0)		0.145
Cardiac	2	(8.7)		4	(16.0)		0.668
SLE Primary Diagnosis*	8	(34.8)		5	(20.0)		0.335

disorders showed a 50% survival to discharge, including 53% pulmonary support, 55% cardiac support, and 34% eCPR. We aim to describe the use and outcomes of ECMO in childhood-onset SLE.

Methods: After approval by the ELSO Registry Committee, a retrospective cohort study from the registry database included patients < 18 years of age who had International Classification of Diseases Ninth Revision (ICD9) and Tenth Revision (ICD10) codes consistent with SLE from 2012-2022. The decision to use ECMO was made independently at each center. The primary outcome was survival to hospital discharge. Descriptive analysis on demographic information, pre-ECMO variables, ECMO mode and support indications, complications, and survival was performed using Stata v 15.1 (StataCorp, College Station, TX, USA). ECMO patient and mechanical complications were predefined by ELSO. Data on severity of illness or immunosuppression therapy was not included as it is not available in the registry.

Table 2: ECMO Characteristics by Survival at Discharge

	Non-survivors (N =23)			Survivors (N =25)			
	N	Median	(IQR)	N	Median	(IQR)	p-value
PEEP	18	12	(8.0,15.0)	16	12	(10.0,15.0)	1.000
MAP	13	20	(15.0,28.0)	12	22	(16.5,25.0)	0.641
Hours	23	139	(39.0,303.0)	25	158	(94.0,197.0)	0.803
		N	(%)		N	(%)	p-value
Mode							0.731
VA		13	(56.50)		16	(64.00)	
VV		8	(34.80)		8	(32.00)	
Conversion		2	(8.70)		1	(4.00)	
Support Type							0.163
Cardiac		4	(17.40)		11	(44.00)	
ECPR		5	(21.70)		4	(16.00)	
Pulmonary		14	(60.90)		10	(40.00)	
Complications*							
Cardiovascular							0.338
No		20	(87.00)		24	(96.00)	
Yes		3	(13.00)		1	(4.00)	
Hemorrhage							0.736
No		17	(73.90)		20	(80.00)	
Yes		6	(26.10)		5	(20.00)	
Infectious							0.224
No		21	(91.30)		25	(100.00)	
Yes		2	(8.70)		0	0.00	
Limb							1.000
No		21	(91.30)		23	(92.00)	
Yes		2	(8.70)		2	(8.00)	
Metabolic							0.091
No		18	(78.30)		24	(96.00)	
Yes		5	(21.70)		1	(4.00)	
Neurologic							0.338
No		20	(87.00)		24	(96.00)	
Yes		3	(13.00)		1	(4.00)	
Pulmonary							0.091
No		18	(78.30)		24	(96.00)	
Yes		5	(21.70)		1	(4.00)	
Renal							1.000
No		9	(39.10)		9	(36.00)	
Yes		14	(60.90)		16	(64.00)	
Mechanical							1.000
No		17	(73.90)		18	(72.00)	
Yes		6	(26.10)		7	(28.00)	

Results: During the study period, 48 children with SLE received ECMO. Table 1 show the demographics and patients comorbidities. Table 2 show ECMO characteristics for patients by survival status at discharge. Overall, 52% survived to discharge, 50% received ECMO for respiratory support (40% survival), 31% received cardiac support (44% survival), and 18% received eCPR (16% survival). The most common complications were renal dysfunction (61% non-survivors vs 64% survivors), followed by hemorrhagic (26% non-survivors vs 20%), and mechanical (26% non-survivors vs 28% survivors) complications. No ECMO parameters or patient characteristics differentiated survivors from non-survivors.

Conclusion: ECMO can be used as a life supporting therapy in children with SLE, with similar outcomes to the experience in children with immune-mediated disorders. The decision to use ECMO in this population remains challenging due to the nature of the systemic disease and potential complications related to immunosuppression. Additional analyses comparing survival rates in children and adults with lupus are underway.

*Comorbid and SLE primary diagnoses were entered via ICD9/10 coding. Pulmonary involvement was defined using codes for pulmonary hemorrhage, hemoptysis, acute respiratory distress syndrome, pulmonary hypertension. Renal involvement was defined using codes for acute kidney injury, chronic kidney disease, end-stage renal disease, glomerulonephritis. Cardiac disease was defined using codes for pericarditis, pericardial effusion, endocarditis, myocarditis.

*ECMO patient and mechanical complications were predefined by ELSO. Mechanical defined as those requiring interventions such as change of equipment or circuit components. MAP: mean airway pressure, PEEP: positive end-expiratory pressure, ECPR: extracorporeal cardiopulmonary resuscitation, VA: veno-arterial, VV: venous-venous.

Disclosure: C. Levin: None; **A. Ontaneda**: None; **D. Guffey**: None; **P. Rycus**: None; **M. Anders**: None; **E. Muscal**: Sobi, 1, 11; **M. Pereira**: None.

Abstract Number: 1224

Mental Health Screening Follow-Up in the Childhood-Onset Systemic Lupus Clinic

Audrea Chen[1], Tala El Tal[2], Asha Jeyanathan[1], Holly Convery[1], Stephanie Wong[1], Linda Hiraki[1], Deborah Levy[1] and Andrea Knight[1], [1]The Hospital for Sick Children, Toronto, ON, Canada, [2]Children's Hospital of Eastern Ontario (CHEO), Ottawa, ON, Canada

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Common barriers to conducting mental health (MH) screening in pediatric clinics include provider uncertainty with follow-up after screening, and concern with increasing burden of referrals to MH services. However, regular MH screens help identify patients who need MH care and engage them in follow-up. In the childhood-onset systemic lupus erythematosus (cSLE) clinic at The Hospital for Sick Children, a new MH screening and referral system was recently implemented. This project aims to describe MH screening results and assess patient satisfaction with their MH care in the cSLE clinic.

Methods: Patients followed in the cSLE clinic aged ≥12 received a MH screen with validated assessment tools for depression (PHQ-9) and anxiety (GAD-7). Referral to MH services (psychology, social work, psychiatry and adolescent medicine) was based on symptom severity (Fig.1) and discussion with the patient. All patients who completed the MH screen received

a handout with free online MH resources. An anonymous survey to assess patient satisfaction with their MH care was sent to patients ≥8 weeks after their initial screen. Repeat screens were performed for patients after 6 months. 66 surveys were distributed to 100 eligible patients. Data were collected from January 2022 to May 2023.

Results: 153 MH screens were completed, 37 patients were screened twice and 2 patients were screened 3 times. Most patients (60%) had minimal or no symptoms of depression and anxiety (Fig. 2). About a third of patients had mild symptoms, 14% of patients had moderate to severe symptoms and 8 patients (5%) reported suicidal ideation (primarily passive) (Fig.2). 12 patients (11%) were referred to adolescent medicine, 4 (4%) to social work and 1 (1%) to psychiatry. 28 satisfaction surveys were completed for a response rate of 42%. While 21% of patients felt that the MH screen brought up unwanted feelings, 100% found the MH screen to be a positive experience. 71% of patients were interested in follow-up or resources after their screen. 8 (28%) patients who completed the survey were referred to MH providers and were all satisfied with the services received. 5 patients had their appointment >4 weeks after referral, 2 patients had an appointment < 4 weeks after their referral and 1 patient had their appointment the same day as cSLE clinic. 2 patients seen >4 weeks after the referral felt that

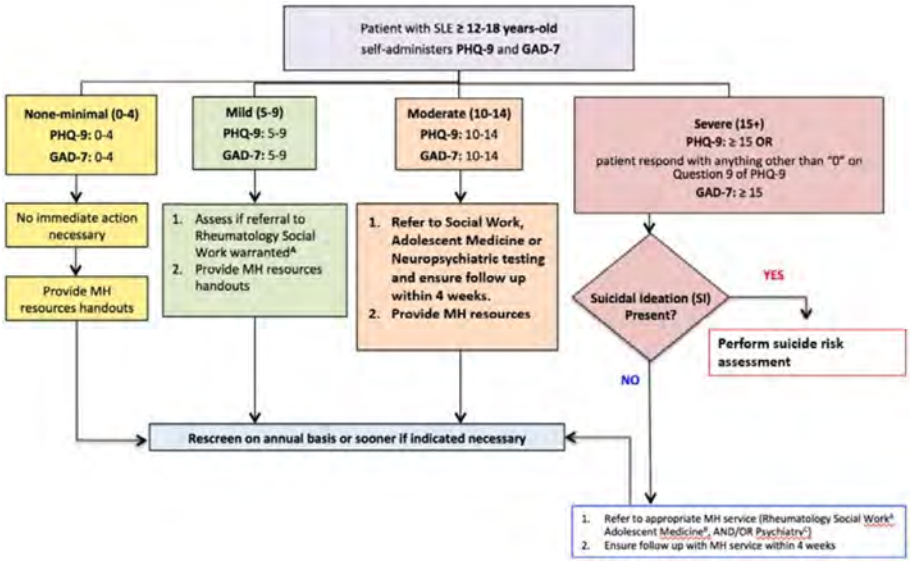

Figure 1. Pediatric rheumatology MH screen referral algorithm based on PHQ-9 and GAD-7 screening scores.

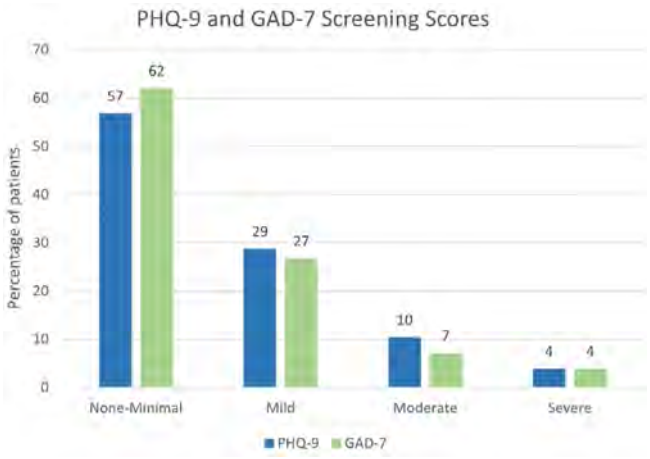

Figure 2. PHQ-9 and GAD-7 scores for depression and anxiety symptoms among the screened cSLE patients. Categories: None-minimal represents a score of 0-4, Mild 5-9, Moderate 10-14, Severe >15.

time to their MH appointment was too long. Suggested improvements to the MH process included making the physical space more welcoming and private, and asking about MH at every clinic visit.

Conclusion: While most patients had mild or no symptoms of depression and anxiety, MH screens detected 14% of patients with moderate to severe symptoms, and 16% were referred to MH services. MH screening was a positive experience and receiving MH resources was important to patients. Patients' MH concerns were adequately addressed with MH services, although time to follow-up could be improved. Overall, the new MH screening process has identified important concerns for patients with cSLE and initiated appropriate referral to MH services with high rates of patient satisfaction. We hope to further improve this process based on patient feedback by changing the physical space and increasing the frequency of screens.

Disclosure: A. Chen: None; **T. El Tal**: None; **A. Jeyanathan**: None; **H. Convery**: None; **S. Wong**: None; **L. Hiraki**: None; **D. Levy**: None; **A. Knight**: Pfizer, 6.

Abstract Number: 1225

Nailfold Video Capillaroscopy and Its Association with Autoantibodies and Rheumatic Diseases in Pediatric Patients

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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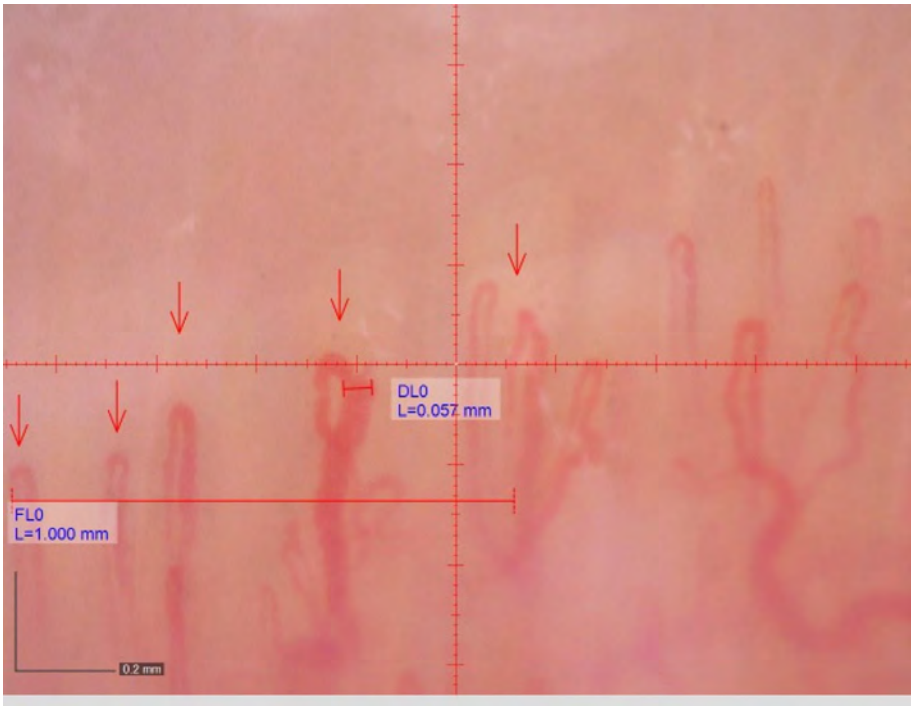
Background/Purpose: Nailfold video capillaroscopy (NVC) is useful in diagnosing secondary Raynaud's phenomenon (RP) and predicting systemic sclerosis (SSc) and other CTD in adults. Recent studies indicate its potential application in children with positive antinuclear autoantibodies (ANA), irrespective of the presence of RP. We aimed to evaluate microvascular abnormalities in children using NVC in a cohort of pediatric Chilean patients.

Methods: This cross-sectional study included children between 5 to 18 years with diagnosis of CTD, RP and/or positive ANA. Using a 200 magnification DinoLite microscope, NVC findings were according to the standardized international consensus definitions from the EULAR Study Group on Microcirculation in Rheumatic Diseases into normal, non-specific and SSc patterns. ANA were detected through routine clinical care by indirect immunofluorescence techniques on HEp-2 substrate and/or immunoblotting ANA Profile 23 Ag. Extractable nuclear antibodies (ENA) were detected by Enzyme-Linked Immunosorbent Assay.

Results: 28 children were consecutively included. Median age was 12 years (interquartile range (ICR) 8-14), and 79% were female (n=22). 57% of the patients had CTD/RP (n=16) and 43% (n=12) had a positive ANA without features of CTD/RP. Non-specific abnormalities were the most frequent pattern (n=25, 89%). The SSc pattern was found in 2 patients, and 1 patient had a normal NVC pattern. The patient with normal pattern was a healthy child without CTD and with high titers of DFS70 antibody on ANA immunoblotting. The 2 patients with SScPattern had a clinical diagnosis of MCTD with RP and high titers of RNP/Sm antibody, and exhibit an active SSc pattern on NVC. Patients with positive ANA without CTD/RP had a median of 6.5 capillaries/mm (ICR 6-7) and a median apical diameter of 21,5 μm (ICR 17-24) . Most of them had a non-specific NVC pattern (n=11, 92%), and dilated capillaries were present in 50% (n=6), without microhemorrhages or giant capillaries. Patients with CTD/RP had a median apical diameter of 22.5 μm (ICR 17.5-24). Most of them had dilated capillaries (75%, n=12), and 88% (n=14)



had a non-specific pattern. Patients with a positive ANA without CTD/RP had significantly lower median apical diameters than those with CTD/RP (p=0.0091). In univariate analysis, CTD/RP (p=0.0091), and the presence of RP (p=0.0048) were associated with higher median apical diameters. High titers of RNP/Sm antibodies on ENA panel (p=0.0376), positive Sm (p=0.0376), and positive La autoantibodies (p=0.0376) were associated with higher apical diameters. In the ENA panel, high titles of RNP/Sm (p=0.0211), positive Sm (p=0.0211) and positive La (p=0.0211) were associated with fewer capillaries.

Conclusion: This study adds further knowledge of NVC technique and methodology in children and adolescents. Our results highlight the potential utility of regular use of NVC in pediatric patients with positive ANA, RP and CTD.

Disclosure: Y. Espinosa: None; **S. Concha**: None; **C. Schulze**: None; **A. Valenzuela**: None.

Abstract Number: 1226

Examining the Relationship Between Socioenvironmental Factors and Cognitive Functioning in Youth with Childhood-Onset Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease

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Session Time: 9:00AM–11:00AM

Background/Purpose: Problems with cognitive functioning are common in childhood-onset systemic lupus erythematosus (cSLE); these may be attributed to many factors including underlying brain inflammation. Socioenvironmental factors are known to impact disease outcomes, with poorer outcomes associated with those from disadvantaged groups. However, little is known about how socioenvironmental disadvantage may be related to cognition in cSLE. We examined the associations between socioenvironmental disadvantage, disease factors, and cognitive functioning in a pediatric cSLE cohort.

Methods: We examined a cross-sectional sample of youth with cSLE aged 10-17 years from a major tertiary hospital SLE outpatient clinic between January 2020 and April 2023. All patients met ACR or SLICC classification criteria for SLE. Area-level indicators of socioenvironmental disadvantage were obtained using the Ontario Marginalization Index, which measures levels of poverty (material deprivation) and proportion of immigrants or minoritized ethnic groups within a region (ethnic concentration). Cognition was evaluated using standardized measures of sustained attention (Conners Continuous Performance Test – Third Edition), working memory (Digit Span subtest from the age-appropriate Wechsler intelligence Scale), and inhibitory control (Color-Word Interference test from the Delis Kaplan Executive Function System).The associations between cognitive function scores, disease activity (SLEDAI-2K), disease damage (SDI) and each socioenvironmental factor were examined using separate multivariable linear regression models. P-values < .05 were considered statistically significant.

Results: A total of 49 youth with cSLE (86% female) with a mean age of 15.3 years (SD=1.7) were included in the study; mean disease duration was 22.6 months (SD=25.9), 33% had active disease (SLEDAI-2K >4) and 8% had disease damage (SDI >0). 28.6% of patients lived in the highest quintile of material deprivation, and 61.2% lived in the highest quintile of ethnic concentration (Table 1, Figure 1).

In multivariable analysis, higher material deprivation was associated with poorer working memory (β = -0.415, 95% CI -0.69, -0.14, p=0.004) (Table 2).Ethnic concentration was not associated with the cognitive outcomes. The covariate for presence of disease damage showed independent statistically significant associations with worse attention and poorer inhibitory control in both of the models for material deprivation and ethnic concentration (Table 2).

Conclusion: In keeping with known health disparities in cSLE, our data shows that higher levels of material deprivation were associated with poorer working memory performance, even when adjusting for current disease activity, damage and duration of disease. In our small cohort, disease damage was associated with worse attention and inhibitory control; replication

Table 1. Demographic and Clinical Characteristics of the Total Sample (n=49)

Demographic Characteristic	**Descriptive Statistics**
Age in years, mean (SD)	15.29 (1.71)
Female sex, n (%)	42 (86)
Race, n (%)	
Black	4 (8)
South Asian	8 (16)
Southeast Asian	16 (33)
Hispanic	2 (4)
White	13 (27)
Mixed race/Other	6 (12)
Ontario-Marginalization Index – n (%) in most marginalized quintile[a]	
Material Deprivation[b]	14 (28.6)
Ethnic Concentration[c]	30 (61.2)
Clinical Characteristics	
Disease Duration in months, mean (SD)	22.62 (25.88)
Active Disease (SLEDAI-2K >4), n (%)	17 (35)
Presence of Disease Damage (SDI >0), n (%)	4 (8)

[a]Patients were assigned a quintile based on the distribution of z-scores for each dimension in the province of Ontario
[b]Material deprivation: indicator of poverty and the inability to meet basic needs
[c]Ethnic concentration: proportion of residents who are recent immigrants and/or belong to a visible minority group

Table 2. Multivariable Regression Analyses for Association between Socioenvironmental Factors and Cognition

	Sustained Attention (CPT-3)[1]	Working Memory (WISC-V/WAIS-IV Digit Span)[2]	Inhibitory Control (DKEFS Color-Word Interference)[3]
Model 1	**Adjusted β, 95% CI, *p*-value**		
Predictor: Material Deprivation	0.233, (-0.03,0.50), *p*=0.082	**-0.415, (-0.69,-0.14), *p*=0.004**	-0.088, (-0.36,0.19), *p*=0.520
Disease Duration	-0.085, (-0.35, 0.19), *p*=0.530	-0.142, (-0.42,0.14), *p*=0.309	-0.218, (-0.49,0.06), *p*=0.116
Active Disease	0.154 (-0.12,0.43), *p*=0.262	0.025, (-0.26,0.30), *p*=0.860	-0.040, (-0.32,0.24), *p*=0.771
Disease Damage	**0.358, (0.09,0.62), *p*=0.009**	-0.029, (-0.31,0.25), *p*=0.834	**-0.386, (-0.66,-0.11), *p*=0.007**
Model 2:	**Adjusted β, 95% CI, *p*-value**		
Predictor: Ethnic Concentration	0.114, (-0.18,0.41), *p*=0.440	0.057, (-0.25,0.37), *p*= 0.712	0.170, (-0.11,0.45), *p*= 0.220
Disease Duration	-0.074, (-0.36,0.21), *p*=0.600	-0.121, (-0.43,0.19), *p*= 0.433	-0.189, (-0.46,0.09), *p*=0.172
Active Disease	0.153, (-0.13,0.44), *p*=0.283	-0.007, (-0.32,0.30), *p*= 0.963	0.066, (-0.34,0.21), *p*=0.627
Disease Damage	**0.421, (0.15,0.70), *p*=0.003**	-0.094, (-0.40, 0.21), *p*= 0.538	**-0.371, (-0.64,-0.10), *p*= 0.008**

[1]CPT-3 detectability T score with mean = 50, SD=10; Higher scores are indicative of worse attention.
[2]WISC/WAIS Digit Span subtest scaled score with mean=10, SD=3; Higher scores are indicative of better working memory.
[3]DKEFS Color-Word Interference trial 3 scaled score with mean =10, SD=3; Higher scores are indicative of better inhibitory control.
Statistically significant results with *p*<0.05 are in bold font.

of this finding is needed with larger samples. Continued examination of the range of disparate outcomes in cSLE over time is essential for better understanding how we can best provide care for all youth with cSLE, and mitigate both disease-related and socioenvironmental risk factors.

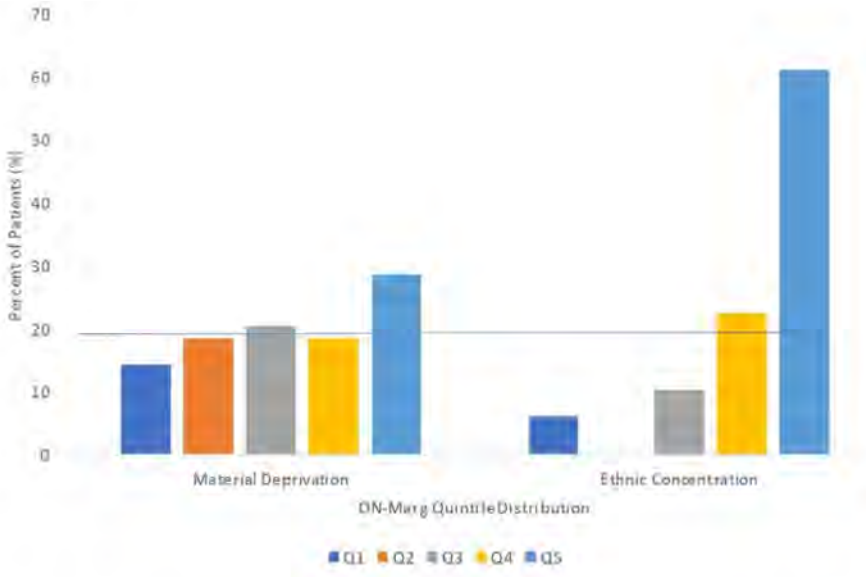

Figure 1. Quintile distribution of the Ontario Marginalization Index dimension z-scores[1] for the cSLE cohort (n=49). Ontario Marginalization Index z-scores represent the number of standard deviations from the expected mean of 0 on a given dimension, with higher scores indicating that the patient resides in an area of greater than average material deprivation or ethnic concentration. The blue line indicates the expected proportion of patients that should belong in each quintile (Q1-Q5) based on provincial census data.

Disclosure: A. Danguecan: None; **I. Mohamed**: None; **S. Mossad**: None; **T. El Tal**: None; **A. Davis**: None; **A. Jeyanathan**: None; **S. Sandhu**: None; **L. Ng**: None; **P. Moaf**: None; **D. Levy**: None; **L. Hiraki**: None; **A. Knight**: Pfizer, 6.

Abstract Number: 1227

Serious Infections Following Rituximab Administration in Children with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rituximab has been associated with high rates of infection among adults with systemic lupus erythematosus. However, studies of infection risk following rituximab among children with pediatric lupus (pSLE) are lacking. We conducted a retrospective study to assess incidence of hospitalized serious infections following rituximab among children with pSLE, and to assess changes in rituximab use over time.

Table 1: Characteristics of Children with pSLE who Received Rituximab and were Hospitalized with Serious Infection

Variable	Total Rituximab Cohort (2,708 hospitalizations with rituximab administered among 1,567 children)	Serious Infection Following Rituximab (339 hospitalizations with infection among 219 children in first year after rituximab)
Age at Admission (years)	16 [13 - 17] median [IQR]	16 [14 - 18]
Female	2243 (83%)	281 (83%)
Race/Ethnicity		
Asian	166 (6%)	11 (3%)
Hispanic	779 (29%)	127 (37%)
Multiracial	34 (1%)	3 (1%)
Non-Hispanic Black	1089 (40%)	123 (36%)
Non-Hispanic White	435 (16%)	55 (16%)
Other	168 (6%)	18 (5%)
Unknown	37 (1%)	2 (1%)
Insurance Status		
Private	850 (33%)	97 (29%)
Public (non-military)	1633 (60%)	220 (65%)
Military	71 (3%)	9 (3%)
Self-pay/Uninsured	51 (2%)	1 (0%)
Other/Unknown	63 (2%)	12 (4%)
Household Income		
<25k	237 (9%)	19 (6%)
25 to 50k	1611 (61%)	213 (64%)
50 to 75k	672 (25%)	85 (26%)
75 to 100k	92 (3%)	14 (4%)
100k or more	25 (1%)	1 (0%)
Lupus Nephritis	1634 (60%)	225 (66%)
End Stage Renal Disease	131 (5%)	38 (11%)
ICU admission during hospitalization	446 (16%)	88 (26%)

Methods: Children and adolescents ages 2-21 years with an ICD-9 or ICD-10 code for SLE (710.0, M32*) and who received at least one dose of rituximab during admission to a Pediatric Health Information System (PHIS)-participating hospital from 2009-2020 were included. The PHIS includes in-hospital administrative data from >50 freestanding U.S. children's hospitals. Serious infections were defined by ICD-9 and ICD-10 codes for infections during an inpatient, observation or admission encounter. Antimicrobial medication use was also required for bacterial or fungal infections. The study period for infections was 12 months following the index hospitalization when rituximab was administered. Summary statistics were used to describe children with pSLE who received rituximab, and the subset who developed a serious infection. Incidence rates for infections requiring hospitalization over the 12 months following first rituximab administration were calculated using exposure time truncated at time of death, first hospitalized infection, or 12 months after index hospitalization for rituximab administration. Rituximab use by year of hospital discharge was assessed from 2009-2021.

Table 2: Hospitalization Outcome by Type of Infection

Variable	**All Hospitalized Infections (n=339)**	**ICU Stay (n=88)**	**Death during Hospitalization (n=7)**
	N (% of total hospitalization)	*N (% of hospitalization with ICU)*	*N (% of total deaths)*
Type of Infection			
>1 serious infection code	61 (18%)	31 (35%)	5 (71%)
Bacterial			
Bacterial pneumonia	78 (23%)	26 (30%)	2 (29%)
Sepsis	69 (20%)	45 (51%)	5 (71%)
Cellulitis	66 (19%)	14 (16%)	2 (29%)
Urinary Tract Infection	43 (13%)	4 (5%)	0 (0%)
Septic arthritis	3 (1%)	0 (0%)	0 (0%)
Endocarditis	3 (1%)	3 (3%)	0 (0%)
Bacterial meningitis	1 (0%)	1 (1%)	0 (0%)
Bacterial encephalitis	1 (0%)	0 (0%)	0 (0%)
Osteomyelitis	0 (0%)	0 (0%)	0 (0%)
Fungal			
Aspergillosis	20 (6%)	7 (8%)	0 (0%)
Candidiasis	17 (5%)	7 (8%)	2 (29%)
Non-tuberculosis or unspecified mycobacterial	6 (2%)	0 (0%)	0 (0%)
Other mycoses	4 (1%)	4 (5%)	1 (14%)
Pneumocystis jirovecii pneumonia	2 (1%)	2 (2%)	1 (14%)
Cryptococcus	2 (1%)	1 (1%)	0 (0%)
Histoplasmosis	1 (0%)	0 (0%)	0 (0%)
Coccidiomycosis	1 (0%)	0 (0%)	0 (0%)
Tuberculosis	0 (0%)	0 (0%)	0 (0%)
Viral			
Herpes simplex	45 (13%)	9 (10%)	1 (14%)
Influenza	15 (4%)	3 (3%)	0 (0%)
COVID	12 (4%)	2 (2%)	0 (0%)
Herpes zoster	11 (3%)	1 (1%)	0 (0%)
Cytomegalovirus	11 (3%)	1 (1%)	1 (14%)
Other viral pneumonia	11 (3%)	6 (7%)	1 (14%)
Varicella	7 (2%)	1 (1%)	0 (0%)
Adenovirus	1 (0%)	1 (1%)	0 (0%)
Epstein-Barr virus	0 (0%)	0 (0%)	0 (0%)
Progressive multifocal leukoencephalopathy (PML)	0 (0%)	0 (0%)	0 (0%)
Other viral encephalitis	0 (0%)	0 (0%)	0 (0%)

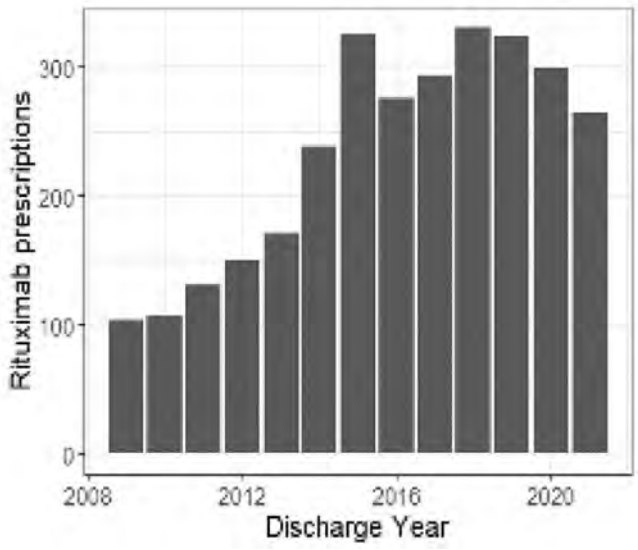

Figure 1: Hospitalizations with Rituximab Administered by Discharge Year

Results: We identified 1,567 children with pSLE who received rituximab. Demographic and clinical characteristics of the study cohort are presented in Table 1. 624 (40%) children with pSLE received cyclophosphamide in the 3 months prior to, and up to 1 year after index hospitalization. Hospitalizations with rituximab administered decreased from 2019 to 2020 and 2021 (Figure 1). Among 1,567 rituximab-treated children with pSLE, 219 (representing 339 hospitalizations) were admitted with a serious infection within 1 year after the first rituximab administration (exclusive of index hospitalization) for an incidence rate of 140 cases per 1,000 patient-years. Median [IQR] time to hospitalization with serious infection following rituximab was 1.83 [0.61, 5.84] months. 7 children with pSLE (0.44%) died during a hospitalization with an infection in the year following rituximab administration. The most common serious infections were bacterial pneumonia, sepsis and cellulitis (Table 2). There were 12 children with pSLE hospitalized with COVID-19 (4% of hospitalizations) and no in-hospital deaths with COVID-19.

Conclusion: We observed high rates of serious infection in the year following first rituximab administration in a large multi-center cohort of youth with pSLE. Rituximab use declined during the COVID-19 pandemic, though no fatalities during hospitalizations with COVID-19 were observed. Concomitant use of other highly immunosuppressive medications was common in our cohort. Further research is needed to identify risk factors for serious infection following rituximab among children with pSLE.

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Abstract Number: 1228

Validation of the PEDiatric Behçet's Disease Classification Criteria (PEDBD): An International Consensus-based Approach

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SESSION INFORMATION

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Background/Purpose: Behçet's disease (BD) is an autoinflammatory disease characterized by a variable vessel vasculitis. In the past, several criteria have been created for adult BD classification. In 2015, the first set of BD paediatric classification criteria, the PEDBD, was proposed by an international Expert consensus. The aim of the study was to perform an external validation of the PEDBD classification criteria in a cohort of internationally validated pediatric BD, through an international Expert-based consensus process.

Methods: 210 patients (70BD, 40 PFAPA (Periodic Fever-Apthous stomatitis-Pharingytis-Adenopathies), 35 FMF, 26 HyperIgD syndrome, 22 TNF-receptor associated periodic fever syndrome, 17 undefined recurrent fevers) were randomly selected from the Eurofever Registry (patients excluded if disease onset > 16 years and if included in the first PEDBD study). A set of 11 Experts blinded to the original diagnosis, were chosen to evaluate the patients: in the 1st round, clinical and serological data were evaluated; in the 2nd round genetic data were added; in the 3rd round the other Experts' votes and comments were shown. Using the expert consensus as gold standard (agreement >80%), the PEDBD, the ISG and the ICBD criteria were applied to BD patients and to confounding diseases with a consensus, in order to define their sensitivity, specificity and accuracy.

Results: At the end of the 3rd round, a consensus on the initial diagnosis was reached in 66.2% of patients. The BD patients with an agreement (24) were classified as confirmed-BD, and those with an agreement of 60-70% (10) as probable-BD.In confirmed-BD patients, oral ulcers were present in all the patients, genital ulcers in 77%, skin manifestations in 50%, a positive pathergy reaction in 39%, ocular manifestations in 54%, with a reesulting impaired vision in 17%, venous thrombosis in 8%, neurological manifestations in 21%, gastrointestinal manifestations in 38%, articular manifestations in 33% and fever in 50% of patients. The patients with ocular and vascular involvement were all males. HLA-B51 was positive in 69% of patients. When comparing these patients with the confounding diseases, an older age at disease onset, the presence of oral and genital ulcers, skin papulo-pustular lesions, a positive pathergy test and posterior uveitis were BD distinctive elements.

The ISG, ICBD and PEDBD criteria were applied to confirmed-BD and to the confounding disease controls, resulting in the following test characteristics (Table).

Criteria	Sensitivity	Specificity	Accuracy
ISG	0.50	1.0	0.91
ICBD	0.79	0.97	0.94
PEDBD	0.58	0.99	0.92

Conclusion: the PEDBD were very specific in classifying BD patients, while the ICBD had a better sensitivity, especially for patients with only bipolar aphtosis. One limitation is that specific monogenetic BS mimics were not included as disease controls, thus the true accuracy of all these criteria may be lower in practice. The complexity of childhood BD suggests larger prospective international cohorts to foster the performance of the criteria, and to understand if BD clusters and ethnic variables should be added to the criteria.

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Abstract Number: 1229

Longitudinal Assessment of Self-reported Executive Function in Youth with Childhood-Onset Lupus

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SESSION INFORMATION

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Background/Purpose: Cognitive dysfunction (including executive dysfunction) affects up to 60% of youth with childhood-onset systemic lupus erythematosus (cSLE), with potential adverse effects on health-related quality of life, and medication adherence. Patients with cSLE are often diagnosed during a critical period of neurodevelopment, and changes in executive

Table 1. Demographics and disease characteristics

	cSLE Participants (n=22)	Controls (n=10)
Age, mean (SD) years	15.7 (1.5)	14.8 (1.8)
Female, n (%)	19 (86)	8 (80)
Race / ethnicity, n (%)		
Black/African-American	3 (13.6)	1 (10)
Asian	10 (45.5)	1 (10)
White	5 (22.7)	6 (60)
Other	4 (18.1)	2 (20)
Disease Characteristics of cSLE participants (n=22)		
Disease duration in years, median (IQR)	2 (1.2-4.3)	
SLEDAI-2K, median (IQR)	2 (2-4)	
Active disease (SLEDAI-2K>4), n (%)	4 (18)	
SLICC Damage Index (score>0), n (%)	1 (45)	
Glucocorticoid use at visit (mg/d), median (IQR)	0 (0-2.25)	
Cumulative glucocorticoid use (g), median (IQR)	3 (0.85-8.66)	

Table 2: BRIEF-2 Executive Function Scores Over Time for cSLE Participants and Controls

BRIEF-2 Executive Function (EF)	Mild elevated T-Score*, n (%)	Potentially/ Clinically elevated T-Score*, n (%)	Baseline T-score, mean (SD)	1 year T-score, mean (SD)	Within-group comparisons Test Statistic, p-value
cSLE Participants (n=22)					
GEC	4 (18)	9 (41)	58.5 (13)	55.9 (10.3)	0.72, p=0.47
BRI	2 (9)	6 (27)	55 (12.6)	53.4 (9.3)	0.46, p=0.64
CRI	5 (22)	8 (36)	60 (14.1)	56.1 (10.2)	0.98, p=0.33
ERI	4 (18)	5 (22)	55.7 (10.4)	56.7 (10.2)	- 0.29, p=0.77
Controls (n=10)					
GEC	1 (10)	3 (30)	57.8 (8.9)	56.1 (11.8)	0.16, p=0.88
BRI	3 (30)	3 (30)	54.7 (11.6)	53.4 (10)	0.19, p=0.85
CRI	0 (0)	3 (30)	55.3 (10.3)	55.7 (12.5)	0, p=1
ERI	1 (10)	4 (40)	57.1 (12.4)	55.3 (14.8)	0.25, p=0.80

*Patients with elevated scores include those occurring at either the baseline or 1-year timepoints according to the following categories for Behavior Rating Inventory of Executive Function 2 (BRIEF-2) T-scores: 60-64 = mildly elevated, 65-69= potentially clinically elevated; ≥ 70 = clinically elevated. A higher T-score indicates a greater degree of difficulty in executive functioning.

function (EF) over time have not been well-studied in cSLE compared to typically developing children. We aimed to characterize the course of EF over time in cSLE patients matched to healthy controls.

Methods: We examined a prospective longitudinal sample of patients with cSLE (ages 12-17, met ACR or SLICC classification criteria for SLE), along with age and sex-matched healthy controls over two time points (baseline and 1 year later) collected from January 2020 to May 2023. Participants completed the self-report Behavior Rating Inventory of Executive Function 2 (BRIEF-2) that generated overall EF difficulties index score (global executive composite (GEC)), and three subindices – behavioral regulation index (BRI), cognitive regulation index (CRI), and emotion regulation index (ERI)). T-scores are transformations of raw scores based on age and sex norms. A higher T-score indicates a greater degree of difficulty in executive functioning. Disease measures including SLE Disease Activity Index 2000 (SLEDAI-2K), SLICC/ACR damage index (SDI), glucocorticoid use at visit and cumulative use, and disease duration were collected. The primary outcome was EF measured by GEC, BRI, CRI, and ERI T-scores, with a focus on GEC. T-tests were performed to examine within-group and between-group comparisons of mean scores at baseline and 1-year, and of change in mean scores (1 year minus baseline) respectively, for cSLE participants and controls.

Results: Twenty-two patients with cSLE and 10 controls were included. For cSLE, the mean age was 15.7 ± SD 1.5 years, 86% were female, median SLEDAI-2K score was 2 (IQR 2-4) and median disease duration was 2 years (IQR 1.2-4.3) (Table1). In cSLE patients compared to controls, mildly elevated GEC T-scores were present in 18% (n=4) vs. 1 (10%); potentially and/or clinically elevated GEC T-scores were present in 41% (n=9) vs 30 %(n=3) (Table2) at baseline or 1-year timepoints. While the mean CRI T-score showed a small improvement from baseline and 1 year later (60 vs 56.1), there were no statistically significant differences for within-group comparisons of any of the BRIEF-T scores over time for both cSLE and controls (Table 2). There were also no significant differences between the cSLE and control groups for mean change in the BRIEF-T scores over time (GEC, t-value=0.78, p=0.43; BRI t-value= -0.28, p=0.77, CRI t-value= -1.2, p=0.20, ERI t-value 0.99, p=0.32).

Conclusion: Self-reported EF was stable over a one-year period in this small cohort of patients with cSLE and controls. Although no significant differences in mean scores for EF were found between cSLE and controls, 59% (versus 40% of HC) had at least mild difficulties in EF. More longitudinal research is needed with longer follow up to identify cognitive function trajectories and at-risk groups for executive dysfunction in cSLE.

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Abstract Number: 1230

Differences in Nailfold Capillary Morphology Distinguish Juvenile Dermatomyositis Patients That Are Myositis-Specific Autoantibody Positive

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Background/Purpose: Juvenile dermatomyositis (JDM) is characterized by multiorgan vasculopathy, and degree of vasculopathy can indicate more severe disease. Nailfold capillaroscopy is a non-invasive method to directly evaluate abnormalities in the microvasculature. While the majority of children with JDM present with nailfold capillary (NFC) abnormalities, we do not fully understand whether NFC patterns and characteristics might differentiate JDM from other pediatric autoimmune diseases or lend insight into distinct JDM subgroups. In this study, we utilized high-resolution nailfold video capillaroscopy paired with a machine learning approach to (1) generate patient subgroups based on NFC features and (2) characterize clinical features defining each patient subgroup.

Methods: We utilized nailfold video capillaroscopy at 200x to obtain images from JDM (n=23), childhood systemic lupus erythematosus (SLE) (n=9), mixed connective tissue disease (MCTD) (n=5) and healthy control (n=17) patients at the University of Michigan Pediatric Rheumatology Clinic (1/1/23 – 5/31/23). We quantified NFC features from images using a convolutional neural network via an automated method, including density of normal and giant capillaries, microhemorrhages, and

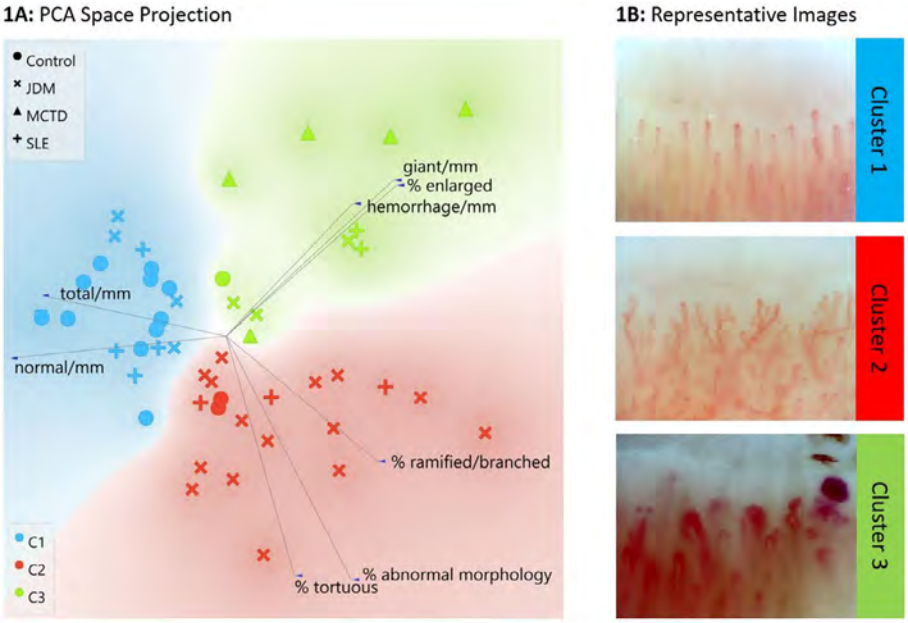

Figure 1: (1A) Principal Component Analysis (PCA) plot from Louvain cluster analysis visualized by linear projection. Symbols represent each patient, localized by alignment toward or away from each feature along its axis. (1B) Representative images demonstrating predominant NFC pattern and features from patients in each cluster.

percentage of enlarged, tortuous or ramified capillaries. We then performed unsupervised cluster analysis to identify patients with similar NFC features. Following this, clinical variables were grouped by cluster with differences between means assessed for significance by ANOVA ($p \leq 0.05$).

Results: We identified 3 patient clusters distinguished by a predominant NFC pattern of either higher relative capillary density (cluster 1 (C1)), abnormal morphology (C2) or enlarged capillaries (C3) (**Figure 1**). Upon review of JDM clinical features by cluster, we found JDM patients were primarily assigned to C2 (65%), with the remainder in C1 (22%) and C3 (13%). MCTD patients were entirely assigned to C3 (100%). Patients with SLE were distributed more evenly, with 44%, 33%, and 22% in C1, 2, and 3, respectively. The majority of control patients were assigned to C1 (82%) (**Figure 2A**). Interestingly, we found that all JDM patients with presence of a positive MSA (TIF-1γ, MDA5, NXP2, Mi-2, Ku) were assigned to C2, while those with negative MSAs were spread between C1, 2 and 3 (**Figure 2B**). We assessed CK values by cluster, revealing a trend toward higher CK in C3 (mean 550.8 u/L) than C2 (mean 201.2 u/L) or C1 (mean 83.6) (**Figure 3A**, p=0.073). Aldolase and LDH levels were similar between clusters (p=0.65 and p=0.77, respectively). Skin disease activity as assessed by Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) scores trended toward higher values in C3 (mean 5.7) as compared to C2 (mean 1.5) and C1 (mean 2.5) (**Figure 3B**, p=0.124).

Conclusion: We demonstrate 3 distinct groupings of NFC patterns that align with clinical diagnosis and MSA positivity. A predominant pattern of tortuosity and ramification is most pronounced in JDM as compared to MCTD, SLE and control patients. Further investigation into NFC morphology and patterns within a larger JDM cohort may hold the potential to assist in diagnosis, disease subtyping, monitoring and prognostication.

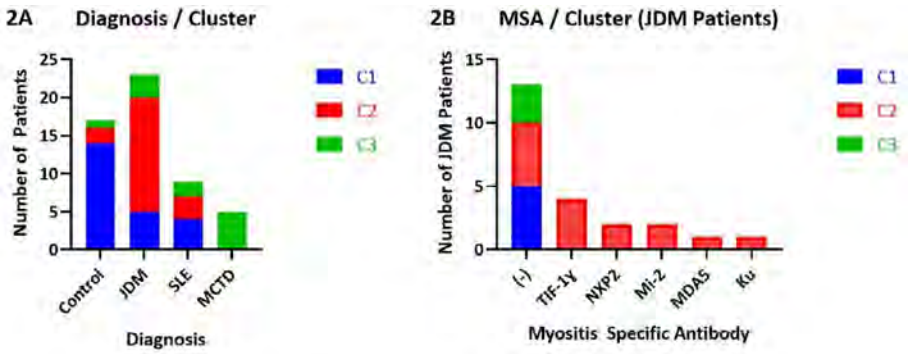

Figure 2: Stacked columns representing patients in each assigned cluster, separated by diagnosis (2A, left) and by myositis specific antibody (2B, right).

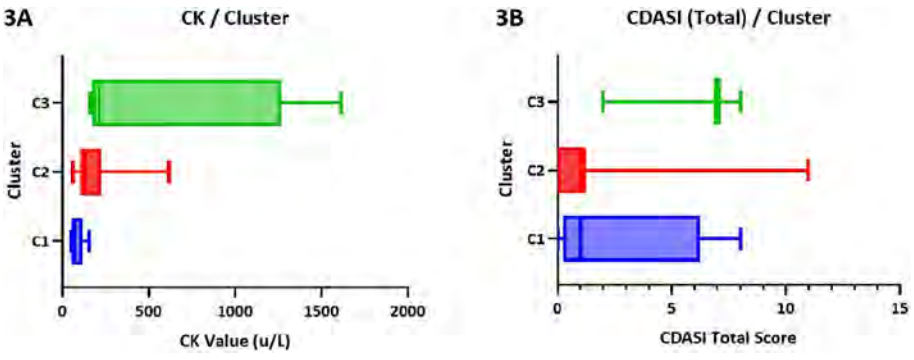

Figure 3: Box-and-whisker plots of CK values by cluster (3A, left) and total CDASI score (3B, right)

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Abstract Number: 1231

Successful Implementation of a Mental Health Screening Program for Youth with Juvenile Dermatomyositis

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Background/Purpose: High levels of emotional distress have been reported in children with juvenile myositis (JM). Inadequate recognition of mental health concerns by healthcare providers (HCPs) can contribute to poor disease outcomes. A recent multicenter study confirmed the feasibility and acceptability of mental health screening (MHS) in patients with JM. The global aim of this quality improvement project was to implement MHS with referrals to an integrated social worker as standard of care for patients ≥5 years of age seen in the SickKids JM clinic. The specific aims were to 1) increase the rate of MHS from 0 to ≥50% in a 90-day period, and 2) ensure that all patients with moderate or severe screening results received referrals for social work assessment.

Table 1. MHS Implementation in Juvenile Myositis Clinic: Results Across PDSA Cycles Over a 3-Month Period

Table 1. MHS Implementation in Juvenile Myositis Clinic: Results Across PDSA Cycles Over a 3-Month Period

PDSA Cycle	Patients Completing MHS	Number with Completed AVS Documentation	Number with Completed EHR Documentation	Number Receiving Handout	Number of Positive Screens Referred to Social Work	Barriers to Implementation and Post-Cycle Changes
#1 (Mar 7 - Apr 4)	12 (100%)	4 (25%)	12 (100%)	12 (100%)	2/3 (66.7%)	Limited HCP time → Speed buttons in EHR Rotating trainees HCPs not knowing the process → Educational infographic for rotating trainees Need for interpreter → Obtain screener in other languages HCPs not sure which format of handouts to distribute → Patients receive both digital (in AVS) and physical copies of the handout
#2 (Apr 18)	7 (100%)	4 (57.1%)	5 (71.4%)	7 (100%)	2 of 2 (100%)	HCPs needing a reminder to complete documentation → Pre-clinic dot phrase → HCPs with incomplete documentation receive reminder emails
#3 (May 16 - May 30)	13 (100%)	12 (92.3%)	13 (100%)	13 (100%)	2 of 2 (100%)	In progress

Methods: A multidisciplinary stakeholder team (rheumatologists, physical therapists, nurse, social worker, research coordinators, and patient/caregiver advisors) iteratively developed screening and referral workflows, and educational resources for HCPs and families. Patients attending the JM clinic were to be screened for anxiety and depression [12-18 years old: Generalized Anxiety Disorder-7 (GAD-7) and Patient Health Questionnaire (PHQ-9); caregivers of patients 5 to < 12 years old: Pediatric Symptom Checklist (PSC-17)]. All patients were to receive a mental health resource handout and patients with positive screens were to be reviewed by physicians who decided whether to refer to the social worker. HCPs were to document MHS in patients' After Visit Summary (AVS) and electronic health record (EHR). Feedback was sought from HCPs and patients/caregivers who agreed to participate in surveys, which informed successive plan, do, study, and act (PDSA) cycles.

Results: Prior to implementation we did not perform MHS as standard care in JM clinic. We conducted three PDSA cycles from March 7 to May 30, 2023. All 32 patients (100%) seen in the clinic received MHS and the resource handout (Table 1). Documentation of MHS in the AVS and EHR rose from 25% to 92.3% and 71.4% to 100%, respectively. There were seven positive screens (22%), of which, six(86%) were referred to the integrated social worker and one was not as they were being seen at our clinic for a secondary opinion. All patient/caregiver survey participants (n=16) indicated that they were satisfied with the MHS process.

Conclusion: The JM clinic has successfully implemented MHS for all its patients within 90days and achieved timely referral to integrated social work. Additional PDSA cycles are needed to support its sustainability as well as build a robust culture of documentation. Future work will include development of tailored mental health resources to address the needs of patients with JM, caregivers, and siblings.

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Abstract Number: 1232

Improvement Across Organ System, Physician and Patient Reported Outcome Measures over a 36-time Period in the Juvenile Systemic Scleroderma Inception Cohort

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Background/Purpose: Juvenile systemic sclerosis (jSSc) is an orphan disease with a prevalence of 3 in 1, 000, 000 children. The Juvenile Systemic Scleroderma Inception cohort (jSScC) is the largest cohort of jSSc patients in the world. The jSScC collects longitudinal data prospectively in jSSc, allowing the evaluation of the development of organ involvement and patients and physician reported outcomes in jSSc over time.

Table 1. Clinical characteristics and patient and physician related outcome over time

	0 month N=74	36-month follow-up N=74	P Value
Female/Male	3.6:1 (58/16)		
Cutaneous subtype			
Diffuse subtype	74% (55/74)		
Limited subtype	26% (19/74)		
Median Disease duration (years), IQR	2.3 (0.8 – 4.2)		
Median age at onset of Raynaud´s (years), IQR	9.3 (5.7 – 12.5)		
Median age at onset of non-Raynaud´s (years), IQR	10.3 (6.7 – 13.3)		
Disease modifying drugs	90% (64/71)	90% (66/73)	
MRSS, median (IQR)	10 (3 – 20)	7 (2 – 20)	0.041
Presence of Swollen joints	16% (12/74)	4% (3/74)	0.014
Muscle Weakness	16% (10/62)	3% (2/69)	0.009
Elevated CK	25% (13/52)	9% (4/44)	0.042
Patient Reported Outcome (median, IQR)			
Patient global disease activity	40 (20 – 50) n=52	20 (10 – 30) n=61	0.014
Patient global disease damage	40 (20 – 60) n=52	20 (10 – 30) n=61	0.005
Patient Raynaud activity	20 (10 – 50) n=65	10 (0 – 20) n=64	0.034
Physician Reported Outcome (median, IQR)			
Physician global disease activity	30 (20 – 45) n=58	15 (5 – 25) n=69	0.001
Organ involvement with nonsignificant change			
History of ulceration	49% (36/74)	64% (47/73)	0.054
Pulmonary Hypertension (Ultrasound)	4% (3/71)	7% (4/57)	0.490
Only Cardiac involvement	3% (2/74)	3% (2/74)	-
Hypertension assessed by RR	0% (0/74)	0% (0/74)	-
Renal Crisis	0% (0/74)	0% (0/74)	-
Gastrointestinal Involvement			
Overall	38% (28/74)	39% (29/74)	0.866
BMI ≤ - 2 z score	17% (12/71)	20% (13/65)	0.641

Methods: The jSScC enrolls jSSc patients who developed the first non-Raynaud´s symptom before the age of 16 years and are under the age of 18 years at the time of inclusion. We reviewed jSScC patient clinical data and patient and physician reported outcomes of those with 36 months follow up from the time of inclusion until 1st of April 2023.

Results: We could extract data of 74 patients, 74% with diffuse cutaneous subtype. The female/male ratio was 3.6:1. 89% of the patients were Caucasian. Median age of onset of Raynaud symptom was 9.3 years and the median age of onset of non-Raynaud symptom was 10.3 years. Median disease duration was 2.3 years at the time of inclusion in the cohort (T0). Ninety percent of the patients were treated with disease modifying anti-rheumatic drugs at T0 and 90% after 36months (T36). Four clinical parameters improved significantly over time: the median modified Rodnan skin score decreased from 10 to 7 (p=0.041), the number of patients with swollen joints decreased from 16% to 4% (p=0.014), the number of patients with elevated CK value decreased from 25% to 9% (p=0.042) and the number of patients with muscle weakness decreased from 16% to 3% (p=0.009). All other organ involvement did not show any statistically significant change from T0 to T36.

Three of the four patient reported outcomes improved significantly from T0 to T36: patient reported disease activity (VAS 0 – 100) from 40 to 20 (p=0.014), patient reported disease damage (VAS 0 – 100) from 40 to 20 (p=0.005), patient reported Raynaud activity (VAS 0 – 100) from 20 to 10 (p=0.034). One of the three physician reported outcomes improved significantly: the physician global disease activity (VAS 0 – 100) from 30 to 15 (p=0.001).

Conclusion: Skin and musculoskeletal clinical features improved significantly over 36 months. It is reassuring that major internal organ manifestations, such as cardiac, pulmonary and gastrointestinal were stable. No renal crisis occurred over the 36-month time period. The patient and physician-reported outcomes had the most positive impact over the 36 months period in this large international cohort.

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Disclosure: I. Foeldvari: Novartis, 2; **J. Klotsche**: None; **O. Kasapcopur**: Novartis, 6, Pfizer, 6; **A. Adrovic**: None; **K. Torok**: None; **B. Feldman**: AB2Bio, 2, Janssen, 2, Novo Nordisk, 2, Pfizer, 2; **M. TErreri**: None; **A. Sakamoto**: None; **J. Anton**: Abbvie, 6, Amgen, 6, GSK, 2, Lilly, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Roche, 6, Sobi, 2, 5, 6; **S. Appenzeller**: None; **E. Marrani**: None; **M. Katsikas**: Novartis, 6, Pfizer, 6; **M. Santos**: None; **F. SZTAJNBOK**: None; **L. Berntson**: None; **J. Brunner**: None; **S. Johnson**: None; **M. Kostik**: None; **K. Minden**: Amgen, 6, Medac, 6, Novartis, 6, Pfizer, 6; **F. Nuruzzaman**: None; **N. Helmus**: None.

Abstract Number: 1233

The Pattern of Medication Use Significantly Changed over 36 Months Observation Period. Result from the Juvenile Scleroderma Inception Cohort

Ivan Foeldvari[1], Jens Klotsche[2], Ozgur Kasapcopur[3], Amra Adrovic[4], Brian Feldman[5], Kathryn Torok[6], Maria Teresa TErreri[7], Ana Sakamoto[8], Jordi Anton[9], Simone Appenzeller[10], Edoardo Marrani[11], Maria Jose Santos[12], FLAVIO SZTAJNBOK[13], Lillemor Berntson[14], Juergen Brunner[15], Mikhail Kostik[16], Farzana Nuruzzaman[17] and Nicola Helmus[18], [1]Hamburger Zentrum für Kinder- und Jugendrheumatologie, Hamburg, Germany, [2]German Rheumatism Research Center, Berlin, Germany, [3]Department of Pediatric Rheumatology, Cerrahpasa Medical School, Istanbul University-Cerrahpasa, Istanbul, Turkey, [4]Istanbul University - Cerrahpasa, Istanbul, Turkey, [5]The Hospital for Sick Children, Toronto, ON, Canada, [6]University of Pittsburgh, University of Pittsburgh Medical Center, Pittsburgh, PA, [7]UNIFESP, São Paulo, Brazil, [8]Federal University of São Paulo (UNIFESP), São Paulo, Brazil, [9]Hospital Sant Joan de Déu, Pediatric Rheumatology Department, Universitat de Barcelona, Barcelona, Spain, [10]UNICAMP, Campinas, Brazil, [11]University of Florence, Firenze, Italy, [12]Hospital Garcia de Orta, Almada, Lisboa, Portugal, [13]UFRJ/UERJ, São Paulo, Brazil, [14]Dept. of Women's and Children's Health, Uppsala University, Uppsala, Sweden, [15]Medical University Innsbruck; Department of

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile systemic sclerosis (jSSc) is an orphan disease with a prevalence of 3 in 1,000,000 children. Currently no medications are licensed for the treatment of jSSc. Due to its rarity, only recently the first management and treatment guidelines have been published, the jSSc SHARE (Single Hub and Access point for paediatric Rheumatology in Europe) recommendations, reflecting consensus opinion upon pediatric rheumatologists(1). We reviewed the applied medication in the treatment of the patients in the juvenile systemic scleroderma inception cohort (jSScC) up to April 2023.

Methods: We reviewed the change of the applied medication in the treatment of jSSc patients over 36 months in the jSScC. The frequency of medications was calculated across the cohort at timepoint 0 (enrollment), and 36 months. jSScC is a prospective cohort of jSSc patients, who developed the first non-Raynaud́ s symptom before the age of 16 years and are under the age of 18 years at the time of inclusion.

Results: We extracted data from 71 patients from the jSScC who were followed for 36 months, 75% had diffuse subtype. At the time of inclusion in the cohort the median disease duration was 2.4 years, median age of the first non-Raynaud symptom was 10.3 years. We captured the recorded medications at 0 months and 36 months. 64/71(90%) received any kind of Disease modifying drug (DMARD).

MEDICATIONS	Time point 0 N =71	T36 months N=71	P value
Any Medication	90% (64/71)	90% (64/71)	
Vascular medications			
Endothelin receptor antagonist	17% (11/64)	22% (14/64)	0.504
PDE-5-Blocker	3% (2/64)	9% (6/64)	0.144
Immunomodulators			
Glucocorticoids	56% (36/64)	31% (20/64)	0.004
All csDMARDs:			
Methotrexate	53% (34/64)	25% (16/64)	0.001
Mycophenolate Mofetil	22% (14/64)	67% (43/64)	<0.001
Hydroxychloroquine	13% (8/64)	20% (13/64)	0.233
Cyclophosphamide	14% (9/64)	0% (0/64)	0.002
Azathioprine	3% (2/64)	3% (2/64)	
All bDMARDs:			
Tocilizumab	0% (0/64)	17% (11/64)	0.001
Rituximab	0% (0/64)	0% (0/64)	
Adalimumab	2% (1/64)	0% (0/64)	0.315
Autologous Stem cell transplantation	0% (0)	1% (1)	

csDMARDs: Conventional synthetic disease-modifying antirheumatic drugs
bDMARDs: Biological disease-modifying antirheumatic drugs

The glucocorticoid use decreased from month 0 to 36 months from 56% to 31% (p=0.004).The methotrexate use decreased from 53% to 25% (p=0.001), in opposite the mycophenolate use increased from 22% to 67% (p< 0.001). The cyclophosphamide use decreased from 14% to 0% (p=0.002). Tocilizumab use increased from 0% to 17% (p=0.001). All other medication use showed no significant changes. Endothelin receptor antagonist was used in 17% patients at time point 0 and 22% at 36 months. PDE-5 blocker use increased from 3% to 9%.

Conclusion: At baseline half of the patients were on glucocorticoids. This is more frequent than typical adult SSc practice but coincides with jSSc SHARE treatment recommendations (#1) (1). After 36 months observation in the cohort over 90% of patients received a DMARD therapy. Methotrexate and mycophenolate mofetil were the most commonly prescribed DMARDs, which also reflects the SHARE treatment recommendations (#2 and #3).At 36 months the use of glucocorticoids, methotrexate and cyclophosphamide decreased, and the use of mycophenolate and tocilizumab increased. In general, biological DMARDs are typically considered in severe or refractory disease (SHARE recommendation #7), reflecting the lower percentage compared to csDMARDs. Endothelial receptor antagonists, such as bosentan, were used over time in approximately 20% of the patients, reflecting SHARE recommendation #6 for pulmonary hypertension and/or digital tip ulcers. This is the first evaluation looking at clinical medication practice pattern in jSSc over 36 months, and its comparison to recently published consensus guidelines.

This project was supported by an unrestricted grant from "Joachim Herz Stiftung"

1 Foeldvari I, Culpo R, Sperotto F, Anton J, Avcin T, Baildam E, et al. Consensus-based recommendations for the management of juvenile systemic sclerosis. Rheumatology (Oxford). 2021;60(4):1651-8.

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Abstract Number: 1234

Cognitive Performance Score of the Pediatric Automated Neuropsychological Assessment Metrics Software in a Brazilian Cohort and Its Association with Disease Activity

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The PedAnam (Pediatric Automated Neuropsychological Assessment Metrics) is an automatic software to evaluate cognitive performance that has recently been validated into Portugues (Brazil). The purpose of this study was to (1) Explore and test Cognitive Performance Score (CPS) in childhood-onset systemic lupus erythematosus (cSLE). (2) Compare different CPS scores between cSLE and to determine if there is an association with disease activity.

Methods: Consecutive cSLE and healthy controls responded to the PedAnam. We performed the calculation of four scores: (1) PedANAM-CPSUWA using unweighted averages of the accuracy score; (2) PedANAM-CPSPCA principal component analysis; (3) PedANAM-CPSlogit used logistic regression; (4)PedANAM-CPSmultiscore logistic models based on performance parameters with selected subtests. After these calculations, we observed the correlation between the CPS indices and compared the performance of patients and healthy controls. Cognitive impairment was determined by z-scores and considered present if ≤2 SD from healthy controls. Disease activity was evaluated through SLE disease activity score and cutoff of 3 was considered active disease.

Results: We included a total of 50 consecutive cSLE (45 [90%] women; median age = 14 years; age range = 9–18 years) and 50 healthy controls (44 [88 %] women; median age = 15; age range = 9-18 years). We observed a correlation between the PedANAM-CPSUWA and the PedANAM-CPSPCA (r = 0.99), PedANAM-CPSPCA and PedANAM-CPSmultiscore (r = -0.60) logit and PedANAM-CPSUWA (r = -0.56). We observed statistically significant differences between patients and healthy controls in the PedANAM-CPSUWA and PedANAM-CPSPCA scores (P = 0.001). Cognitive impairment was observed in12 (24%) cSLE patients and 1 (2%) healthy controls (p < 0.001) by the PedANAM-CPSUWA index and using the PedANAM-CPSPCA index. An association between disease activity and PedANAM-CPSUWA index (p=0.01) and PedANAM-CPSPCA index (p=0.002) was observed**.**

Conclusion: After the translation and validation process, this is the first study using the CPS in Brazilian version of PedANAM and we identified two of the metrics that were able to differentiate between cSLE and healthy controls. Worse performance with disease activity was observed. Funding FAPESP (CEPID BRAINN 13/07559-3)

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Abstract Number: 1235

Apparent Diffusion Coefficient (ADC) from Diffusion Weighted Imaging (DWI) as an Objective Tool to Differentiate Normal Maturational Subchondral Signal from Inflammation at the Sacroiliac Joint in Youth

Michael L. Francavilla[1], Dmitry Khrichenko[2], Timothy G. Brandon[2], Nancy A. Chauvin[3], Rui Xiao[4] and **Pamela F. Weiss**[5], [1]University of South Alabama College of Medicine, Mobile, AL, [2]Children's Hospital of Philadelphia, Philadelphia, PA, [3]The Cleveland Clinic, Hummelstown, PA, [4]University of Pennsylvania, Philadelphia, PA, [5]Children's Hospital of Philadelphia, Philadelphia, PA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: There is a critical need for tools to distinguish between maturational changes mimicking subchondral edema from pathologic inflammation within the SI joints on MRI. We aimed to establish standards for interpretation of diffusion weighted imaging (DWI) in healthy children.

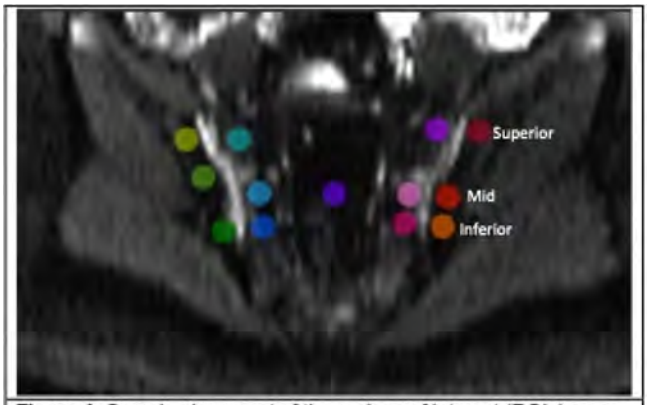

Figure 1. Sample placement of the regions of interest (ROIs) on a control patient in the mid SI joint. Analogous ROI placement performed on 1 anterior and 1 posterior slice of the SI joint.

Table 1. Apparent diffusion coefficient (ADC) values by region of interest (ROI) on anterior, mid, and posterior slices in superior, mid, and inferior locations of the ilium and sacrum. Each subject contributed data from right and left sacroiliac joints.

			Anterior Median (IQR)	Mid Median (IQR)	Posterior Median (IQR)
Type I	Iliac	***Superior Mid***		335.3 (210.6-533.4)	
		Inferior		630 (491.1-879.5)	
	Sacrum	***Superior Mid Inferior***	845.4 (751.9-985.6)	710.9 (655.9-803.9)	728.6 (560.2-804.0)
Type II	Iliac	Superior		366.6 (291.9-459.4)	
		Mid		340.5 (230.5-380.0)	
		Inferior		577.8 (454.0-670.3)	
	Sacrum	***Superior Mid Inferior***	837.0 (764.2-1073.0)	749.5 (621.2-773.5)	684.7 (499.3-769.4)
Type III	Iliac	***Superior Mid***		320.7 (225.5-403.0)	
		Inferior		518.3 (336.8-665.7)	
	Sacrum	***Superior***	489.1 (315.5-727.8)		556.0 (280.4-794.9)
		Mid	672.5 (375.4-784.6)		795.7 (425.7-1008.8)
		Inferior	489.1 (315.5-727.8)		556.0 (280.4-794.9)
Type IV	Iliac	***Superior Mid***	291.3 (65.7-412.1)		435.9 (210.6-495.3)
		Inferior	517.1 (344.8-593.1)		418.5 (375.0-569.0)
	Sacrum	***Superior Mid Inferior***		497.3 (381.0-514.8)	

Legend. Regions of interest (ROIs) that were not significantly different across slices (anterior/mid/posterior) or across joint sites (superior/mid/inferior) were combined to create a representative value of those regions. The combinations are shown in the table through merged columns across anterior, mid, and posterior slices and by bold and italicized region names across superior, mid, and inferior locations for each bone and maturational type.

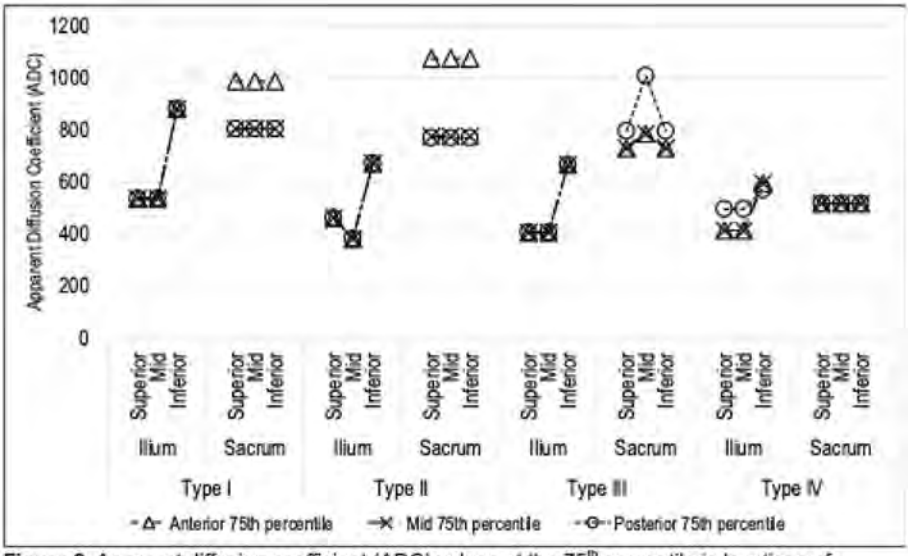

Figure 2. Apparent diffusion coefficient (ADC) values at the 75th percentile in locations of interest among patients with normal MRI scans of the sacroiliac joints.

Methods: This was a retrospective cross-sectional study of MRI scans of healthy controls identified from a prior study that evaluated the appearance of MRI in healthy children (Chauvin et. al, 2019) and through query of the digital archiving system at a single center across a range of bone maturation. DWI and short-tau inversion recovery (STIR) images were analyzed independently by 2 pediatric radiologists using custom software (Parametric MRI, Philadelphia, PA; https://www.parametricmri.com/). DWI series performed in the axial plane were reformatted by the software into a semi-coronal plane. To establish normative ranges of apparent diffusion coefficient (ADC) in controls, circular regions of interest (ROIs) of 0.15-0.22 cm^2 were placed at the superior, mid, and inferior portions of the anterior, mid, and posterior ilium and sacrum along the cartilaginous SI joint (Figure 1), avoiding sclerosis. ADC was calculated using a linear log model and all available b values. The type (I-IV) of sacral apophyseal/periarticular maturational signal was recorded. Mixed effects regression models with subject-specific random effect to account for clustering were used to determine if the ROIs (average ADC from the 2 raters) for the superior, mid, and inferior locations for the anterior, mid, posterior portions of the sacrum and ilium differed significantly for each maturational type.

Results: DWI and STIR sequences from 63 healthy children were assessed. Table 1 lists the ADC for each part of the SI joint for maturational types I-IV. Figure 2 shows the 75th percentile of normative values. ADC at the superior, mid, and inferior portions of the anterior, mid, and posterior of the sacrum were not significantly different for type I, II, and IV maturation; for type III, ADC from the posterior sacrum was significantly higher than the anterior and mid slices. The median ADC values in the sacrum were significantly different between maturational types ($p < 0.001$) and decreased from type I to type IV. ADC values were significantly different in the ilium between the inferior, mid, and superior parts of the SI joint ($p < 0.001$) with higher ADC values observed in the inferior locations compared to the superior or mid portion of the joint in anterior, mid, and posterior slices for all 4 maturational types.

Conclusion: We established ADC normative values for the superior, mid, and inferior portions of the anterior, mid, and posterior sacrum and ilium along the cartilaginous SI joint by maturational type. Observed trends with more variable ADC in the ilium and higher ADC at the inferior aspect of the ilium are in accordance with prior observations on STIR in the maturing SI joint; however, the ADC from DWI goes beyond prior STIR observations by quantifying the difference(s). Next steps are to establish empirical cut-offs to distinguish normal maturational changes from pathologic inflammation to improve the specificity and confidence in the diagnostic interpretation of the MRI.

Disclosure: M. Francavilla: None; **D. Khrichenko**: None; **T. Brandon**: None; **N. Chauvin**: None; **R. Xiao**: None; **P. Weiss**: Eli Lilly, 2, Novartis, 2, Pfizer, 2.

Abstract Number: 1236

Melanoma Differentiation-Associated Protein-5 in Juvenile Dermatomyositis: A Single Center Cohort

Dawn Gist[1], Sarah Molina[2], Maria Pereira[3], Andrea Ramirez[3], Cagri Yildirim-Toruner[4] and Marietta De Guzman[3], [1]Baylor College of Medicine Pediatrics Residency, Houston, TX, [2]Baylor College of Medicine - Pediatrics Residency Program, Houston, TX, [3]Baylor College of Medicine, Houston, TX, [4]Baylor College of Medicine, Texas Children's Hospital, Houston, TX

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease

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Background/Purpose: Juvenile dermatomyositis (JDM) is an idiopathic inflammatory myopathy that causes muscle weakness, rash, vascular changes, or other organ involvement. The phenotypes may vary, and studies suggest a correlation between myositis-specific antibodies (MSA), clinical presentation, and course. This is thought to be due to specific cytokine profiles activated by these antibodies. Melanoma Differentiation-Associated Protein-5 (MDA5) is an MSA associated with clinically amyopathic dermatomyositis and lung disease with high risk for rapidly progressive interstitial lung disease. This study aims to highlight the clinical manifestations of MDA5+ JDM and disease course in a racially and ethnically diverse population. We also aim to assess racial disparities in time-to-diagnosis from cutaneous symptom onset.

Methods: After Institutional Review Board approval was obtained, we conducted a retrospective chart review of patients diagnosed with MDA5-positive JDM at Texas Children's Hospital.Clinical characteristics at the time of diagnosis, 6-month, 12-month, and most recent visits were recorded.

Results: Nineteen patients were included, with a mean age of 9.9 years (range 3-18), 68% female, 21% Black, 79% White, and 68% Hispanic. Figure 1 shows the clinical findings at presentation. All had cutaneous and vascular features, 78% had muscle disease, 74% had interstitial lung disease, and 47% had gastrointestinal (GI) symptoms. Most common skin findings were Gottron's papules (95%), palmar papules (47%), and heliotrope rash (47%). Median time in months from onset of cutaneous symptoms to diagnosis was 5.5 among Black patients, 5 among Hispanic, and 3 among White Non-Hispanic. Three

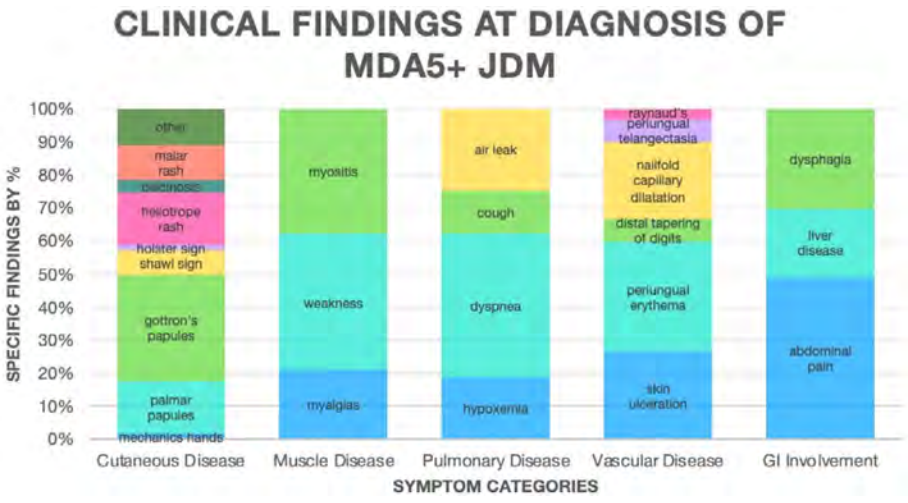

Figure 1: Clinical Findings at Diagnosis of MDA5+ JDM

patients had a lung biopsy, with the most common findings of organizing pneumonia and diffuse alveolar damage. Figure 2 summarizes induction treatment given. 8% of patients had clinical remission at 6-month follow-up, 30% at 12 months, and 50% at last visit (mean of 31.1 months, range: 6-70).Two patients diagnosed at age 3 years had progressive, diffuse alveolar damage resulting in death shortly after diagnosis. At last follow up, 20% still required corticosteroids, 30% required intravenous immunoglobulin (IVIG), and 20% required rituximab. While arthritis, cutaneous symptoms, and GI symptoms improved over time, vascular, muscular, and lung disease were persistent at last visit (Figure 3).

Conclusion: MDA5+ JDM patients in this cohort presented with prominent cutaneous and vascular disease. Lung disease was present early and persisted late in disease course. Half of patients had not reached remission at the last visit, and several continued to require steroids, IVIG, and B-cell depletion. Further studies comparing these patients to non-MDA5 controls may help characterize the role of MDA5 in these findings. While this study does not show a significant difference in time to

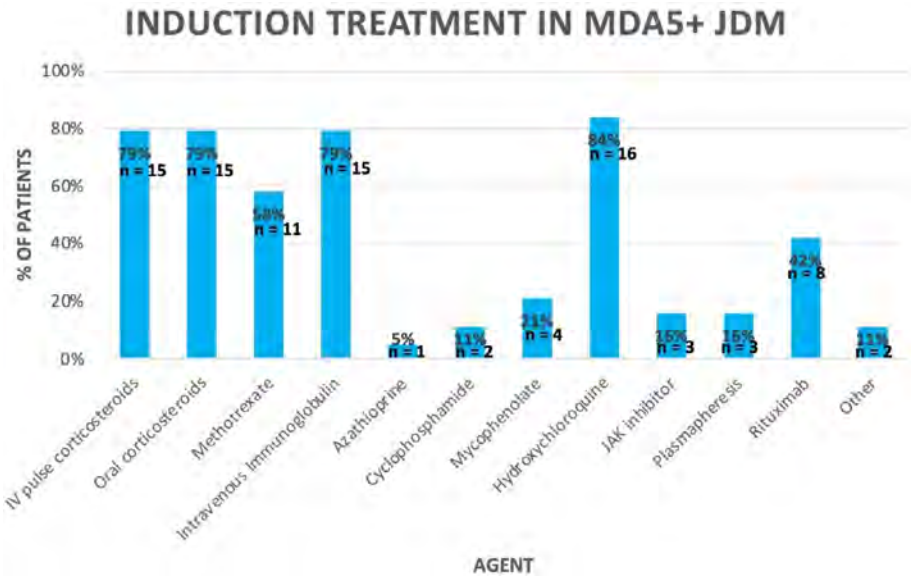

Figure 2: Induction Treatment in MDA5+ JDM

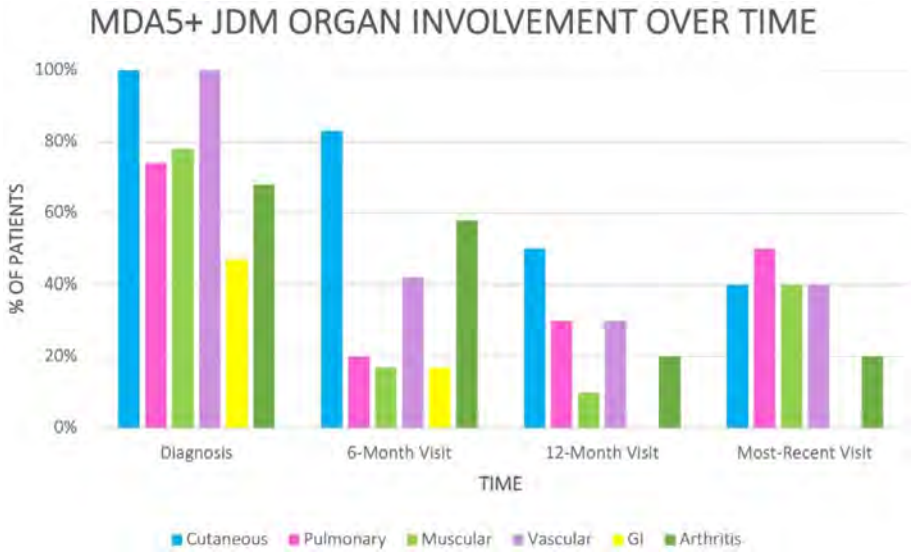

Figure 3: MDA5+ JDM Organ Involvement Over Time

diagnosis from onset of cutaneous symptoms between racial and ethnic groups, the sample sizes were small. More data on time to diagnosis, especially in Black and Hispanic patients, is needed to assess for delays in diagnosis, as there continues to be a need for education and recognition of cutaneous features in dark skin tones.

Disclosure: D. Gist: None; **S. Molina**: None; **M. Pereira**: None; **A. Ramirez**: None; **C. Yildirim-Toruner**: None; **M. De Guzman**: None.

Abstract Number: 1237

The Associations Between Depressive Symptoms and Executive Function and Academic Outcomes in Children with SLE

Hannah Bradfield[1], Paola Sparagana[2], Elizabeth Sloan[1], Chanhee Jo[3], Tracey Wright[1] and Sheryl Frierson[2], [1]UT Southwestern, Dallas, TX, [2]Scottish Rite for Children, Dallas, TX, [3]Texas Scottish Rite Hospital, Dallas, TX

SESSION INFORMATION
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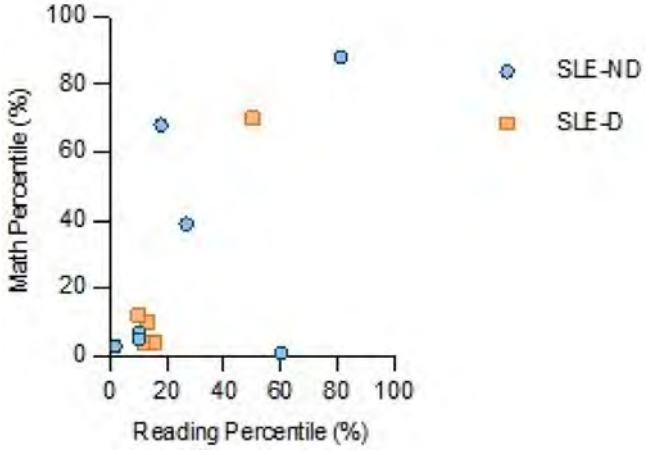
Background/Purpose: Children with juvenile-onset SLE (jSLE) have high rates of depression.[1-2] Adolescents with depression, but without a chronic illness, have lower academic engagement, efficacy, and school functioning.[3] While academic outcomes have been studied in children with jSLE, no studies have explored the associations between depression and academic outcomes in this population. [4] This pilot study aimed to evaluate the relationship between depressive symptoms and executive function and academic outcomes in jSLE.The study also explored the relationship of depressive symptoms to other disease/patient-specific variables, including age at onset, disease duration, and disease activity.

Methods: jSLEpatients, 9-18 years of age, completed the Wide Range Achievement Test 5th Edition (WRAT5) and the Center for Epidemiological Studies – Depression Scale (CESD). Their parent completed the Behavior Rating Inventory of Executive Function 2nd Edition (BRIEF2) and a questionnaire gathering demographics and academic performance. The SLEDAI

Figure 2



and SLICC/ACR Damage Index, were obtained. Two-sample T-test was used to identify associations between depressive symptoms and academic outcomes, including WRAT5 and BRIEF scores, and disease/patient-specific variables.

Results: Of the 12 patients enrolled, 42% screened positive for significant depressive symptoms.Forty percent of patients who screened positive for depressive symptoms reported receiving mental health treatment. The WRAT5 mean math computation and reading composite percentile ranks were higher for participants without significant depressive symptoms (SLE-ND) compared to those with significant depressive symptoms (SLE-D), but this difference was not significant (see figure 1). The mean BRIEF Initiate scale percentile was higher for participants with significant depressive symptoms compared

Figure 2A

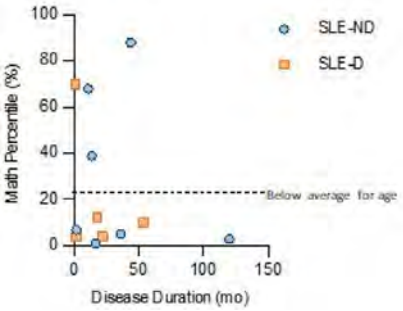


Figure 2B

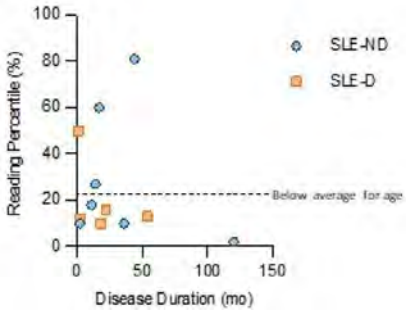


Table 1A

Variable		N	Percent
Sex	Female	11	91.67
	Male	1	8.33
Racial Background	Hispanic or Latino	11	91.67
	White	12	100.00
Primary insurance	Medicare/Medicaid	10	83.33
	Uninsured	2	16.67
Current annual household income	< $35,000	7	58.33
	$35,000 - $69,999	5	41.67
Highest household education level	<9 years	1	8.33
	Some High School	1	8.33
	High School Graduate or GED	6	50.00
	Education Beyond High School	4	33.33
Oral steroid dose at time of enrollment	None	2	16.67
	<10 mg	5	41.67
	10-20 mg	5	41.67

Table 1B

Variable	N	Mean	Med	Min	Max
Age	12	14.58	15.00	9.00	18.00
Age at onset of jSLE (years)	12	12.08	12.00	8.00	17.00
Disease Duration (months)	12	28.42	17.50	1.00	120.00
Number of Hospitalizations in the last year	12	1.08	0.00	0.00	8.00
Childhood Health Assessment Questionnaire (CHAQ)	12	0.18	0.07	0.00	1.13
MD global assessment scale for disease activity (MDG)	11	0.55	0.00	0.00	3.00
Disease activity score (SLEDAI)	12	5.25	2.50	0.00	18.00
Damage Index (SLICC/ACR DI)	12	0.33	0.00	0.00	2.00
Patient VAS - Pain	10	0.90	0.00	0.00	3.00
Patient VAS - Illness	10	2.60	3.00	0.00	5.00
Patient VAS - Fatigue	10	4.80	5.00	0.00	8.00
General QOL Score	10	7.10	7.50	4.00	10.00
HRQOL Score	10	6.30	6.50	1.00	10.00
Number of school absences in the last 6 months	12	6.17	5.00	1.00	15.00

to those without, but this difference was also not significant. Patients with significant depressive symptoms tended to be older at disease onset and have shorter disease duration (see figures 2A-B).

Conclusion: Depressive symptoms, often untreated, were common in this cohort with jSLE. While there may be clinically meaningful differences in academic outcomes in jSLE patients with significant depressive symptoms, the small sample size precluded us from detecting significant differences. However, this pilot study demonstrated the feasibility of administering tools to assess depressive symptoms, executive function, and academic outcomes in jSLE. Larger studies are needed to better understand these trends.

1. Knight AM, et al. Depression risk in young adults With juvenile- and adult-onset LUPUS: Twelve years of followup. *AC&R*. 2018;70 (3):475-480.
2. Knight A, et al. Identifying differences in risk factors for depression and anxiety in pediatric chronic disease. *J of Ped*. 2015;167 (6):1397-1403.
3. Jaycox LH, et al. Impact of Teen depression ON ACADEMIC, social, and physical functioning. *Ped*. 2009;124(4):596-605.
4. Zelko F, et al. Academic outcomes in childhood-onset systemic lupus erythematosus. *AC&R*. 2012;64(8):1167-1174.

Disclosure: H. Bradfield: None; **P. Sparagana**: None; **E. Sloan**: None; **C. Jo**: None; **T. Wright**: None; **S. Frierson**: None.

Abstract Number: 1238

Prevalence of Celiac Disease Among Children and Adolescents with Systemic Lupus Erythematosus (SLE)

Oscar Mwizerwa[1], Andrea Knight[2], Daniela Dominguez[2], Deborah Levy[2], Holly Convery[2], Kendal Thompson[2], Nicholas Gold[2], Catherine M Walsh[2] and Linda Hiraki[2], [1]University of Toronto, The Hospital for Sick Children, Toronto, ON, Canada, [2]The Hospital for Sick Children, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) and celiac disease (CD) are autoimmune diseases characterized by the presence of specific autoantibodies. We aimed to investigate the prevalence of CD in a multiethnic cohort of children and adolescents with SLE.

Methods: We completed a retrospective cohort study of patients under 18 years of age who were diagnosed and followed for SLE at The Hospital for Sick Children between January 2010 and June 2022. We restricted to patients screened for CD with immunoglobulin A antibodies against tissue transglutaminase (tTG-IgA) within one year of SLE diagnosis. We recorded tTG-IgA titers and reviewed medical records for additional investigations, including pathology reports of duodenal biopsies. CD was confirmed by duodenal histology based on the modified Marsh-Oberhuber classification (Marsh ≥3). Demographic and SLE disease features were extracted from the dedicated Lupus database. We calculated the prevalence of clinical features, positive tTG-IgA results, and biopsy-confirmed CD, and compared SLE features between CD and non-CD groups with Fisher's exact tests.

Results: CD screening was completed in 74% (300/404) of children diagnosed with SLE. Thirteen (4%) had positive tTG-IgA serology (ranging from 38 to >100 U/ml [positive >8U/ml] for Enzyme-linked immunoassay testing and 34 to >4965 CU [positive >30 CU] using the Chemiluminescent Immunoassay). Ten of 13 (77%) patients with positive anti-tTG autoantibodies

Table 1. Clinical Presentation

Table 1. Clinical Presentation

Symptoms	
Constitutional symptoms, n (%)	20 (95.5)
Fever	8 (38.1)
Weight loss	16 (76.2)
Fatigue	20 (95.2)
Musculoskeletal symptoms, n (%)	16 (76.2)
Arthralgia	8 (38.1)
Myalgia	7 (33.3)
Arthritis	4 (19)
Other[1]	3 (14.3)
Neurologic symptoms, n (%)	11 (52.4)
Headache	9 (42.9)
Numbness/paresthesias	1 (4.8)
Claudication, n (%)	1 (4.8)
Exam findings	
Hypertension, n (%)	8 (38.1)
Malignant hypertension[2]	2 (9.5)
BP differential[3], n (%)	8 (38.1)
Decreased pulse, n (%)	8 (38.1)
Absent pulse, n (%)	2 (9.5)
Bruit, n (%)	7 (33.3)
Carotid artery tenderness, n (%)	0 (0)
Laboratory results	
Anemia[4], n (%)	12 (57.1)
Hemoglobin in g/dL, mean (SD)	10.5 (1.6)
Leukocytosis[5], n (%)	9 (42.8)
WBC count x10^3/uL, mean (SD)	9.01 (1.5)
Elevated CRP[6], n (%)	17 (81)
CRP in mg/dL, mean (SD)	5.2 (4.2)
Elevated ESR[7], n (%)	20 (95.2)
ESR in mm/hr, mean (SD)	82.5 (35)

Legend. [1]Other: morning stiffness, muscle spasm
[2]Malignant hypertension: stage 2 hypertension with severe examination or laboratory evidence of ≥ 1 organ damaged (per APP 2017 criteria)
[3]BP differential: difference in systolic BP of ≥ 10 mmHg between any two limbs
[4]Anemia: Hgb < 10.6 for females > or = 6 years to < 12 years; Hgb < 10.8 for females > or = 12 years to < 18 years; Hgb < 10.6 for females > or = 18 years; Hgb < 10.6 for males > or = 6 years to < 12 years.
[5]Leukocytosis: WBC > or = 11.40 for females > or = 6 years to < 12 years; WBC > or = 9.43 for females > or = 12 years to < 18 years; WBC > or = 9.68 for females > or = 18 years; WBC > or = 11.40 for males > or = 6 years to < 12 years.
[6]CRP: upper limit of normal = 1.0 mg/dL
[7]ESR: upper limit of normal = 20 mm/hr

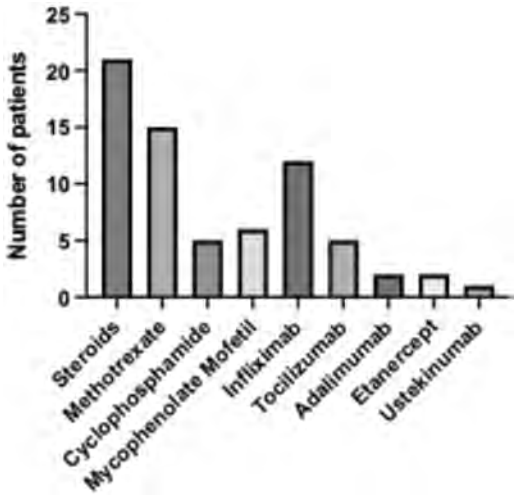


Figure 1. Medications used throughout Takayasu Arteritis course

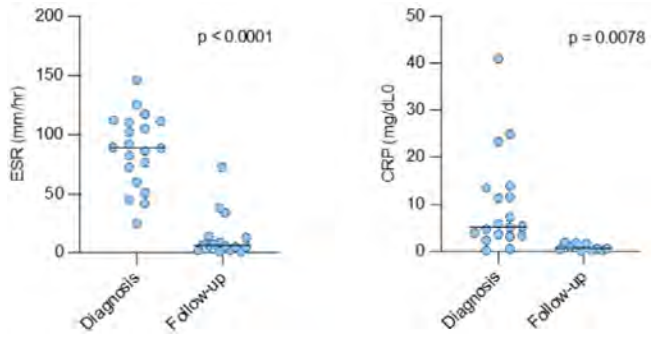


Figure 2. Differences in ESR and CRP from diagnosis to last follow-up visit compared by Wilcoxon signed-rank test.

had an endoscopy and duodenal biopsy. Of those biopsied, eight had histopathologic evidence of CD which represents 62% of patients with positive serology, and 2.6% of the screened SLE population. Among patients with CD, only 50% had GI symptoms and 62% (8/13) had positive anti-endomysial antibodies. All patients with biopsy-proven CD were diagnosed within one year of SLE diagnosis. There were no significant differences in SLE features observed between those with and without CD.

Conclusion: Biopsy-proven CD was diagnosed in 2.6% of children and adolescents with SLE, which is higher than the reported prevalence in the general population of 1.4% by seroprevalence and 0.7% by biopsy. Only half of the patients with biopsy-proven CD had GI symptoms, highlighting the utility of screening in the childhood SLE population.

Disclosure: O. Mwizerwa: None; **A. Knight**: Pfizer, 6; **D. Dominguez**: None; **D. Levy**: None; **H. Convery**: None; **K. Thompson**: None; **N. Gold**: None; **C. Walsh**: None; **L. Hiraki**: None.

Abstract Number: 1239

Clinical Manifestations and Management of Takayasu Arteritis: A Multicenter Pediatric Cohort

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Takayasu arteritis (TA) is a rare granulomatous vasculitis that affects large vessels, including the aorta, its major branches, and the pulmonary artery. Data on the presentation and clinical course of pediatric TA are limited, and children present with different clinical features than their adult counterparts.

Methods: With institutional review board approval, a retrospective cohort study of children who were diagnosed with TA at two large pediatric centers between 2005-2022 and 2016-2023 was performed. Data were abstracted from the electronic medical record. Patient demographics, presenting symptoms and signs, imaging findings, and management data were evaluated using standard descriptive statistics.

Results: Twenty-one patients were included. The majority were female (90.45%), with a mean age at diagnosis of 13.5 years (range 9-17). Most were Hispanic or Latino (71.4%). Diagnosis occurred a median of 4 months following symptoms onset (IQR 1-15), and the mean follow-up period was 38 months (range 5-112). The most prevalent symptoms at initial presentation were constitutional (95.5%), with fatigue being almost universally present (Table 1). A history of claudication was only elicited from one patient at presentation. Over half (54.5%) presented with hypertension, BP differential, and/or decreased pulses. All but one patient had an elevated ESR (mean 82.5 mm/hr, range 25-146), and all but four had an elevated CRP (mean 5.2, range 0.2-13.6) (Table 1). All patients had imaging evidence of aortic involvement, including the abdominal (76.2%), ascending thoracic (71.4%), and descending thoracic (66.7%) segments. Seven patients (33.3%) had renal artery stenosis. All patients were initiated on systemic corticosteroids at diagnosis. The most common initial steroid-sparing immunomodulatory regimen included a combination of methotrexate and infliximab (42.9%). Eighty-one percent were treated with a biologic DMARD (bDMARD) at some point (Figure 1). Many patients switched steroid-sparing agents throughout their disease course. Reasons for addition or change of therapy included poor disease control or flare, inability to wean steroids, new disease manifestations, adverse effects, and patient preference. Five patients (23.8%) required surgical management. At the most recent follow-up visit, 10 patients remained on steroids. Five patients were still symptomatic. One patient achieved drug-free clinical remission. There was a statistically significant decrease in ESR ($p< 0.0001$) and CRP ($p=0.0078$) from the initial to final visit (Figure 2).

Conclusion: Like prior pediatric studies, patients in our cohort presented predominantly with constitutional symptoms, musculoskeletal involvement, hypertension, and elevated inflammatory markers. bDMARDs were introduced earlier than in previously reported cohorts. Our cohort was demographically different from other pediatric case series as we report majority Hispanic/Latino patients. While many patients were asymptomatic at the last follow-up, approximately half still required steroids for disease control.

Disclosure: A. Altaffer: None; **K. Ciaglia**: None; **E. Sloan**: None; **M. De Guzman**: None.

Abstract Number: 1240

Obvious Only in Retrospect: A Cohort of STING Associated Vasculopathy in Infancy (SAVI) Without Typical Rash

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

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Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: STING-associated vasculopathy with onset in infancy (SAVI) is characterized by systemic inflammation, skin vasculopathy and interstitial lung disease. However, since the initial description knowledge and clinical spectrum of this disease has substantially broadened. Here we present the clinical and laboratory characteristics of 2 families with SAVI presenting with autoimmunity and lung disease without significant cutaneous vasculopathy

Methods: We performed a retrospective chart review of patients with a genetic diagnosis of SAVI followed at the Rheumatology division of Cincinnati Children's Hospital Medical Center (CCHMC). We collected demographic, clinical, laboratory and radiological information.

Results: We identified 9 patients from 2 families. *Family A* consisted of 7 individuals (the father (patient G), 3 sons and 3 daughters) carrying the heterozygous variant in STING1 c.463G >A, previously reported as cohort with undiagnosed interstitial lung disease, arthritis, and atopic dermatitis. The diagnosis was confirmed reviewing their medical records and performing genetic testing for SAVI. *Family B* consisted of 2 individuals (father (patient I) and daughter (patient H)), carrying the c.842G >A variant (see table 1). The median age at onset of symptoms in these 9 patients was 18 months (range 1-adulthood). The first symptom was eczema in 5 (55.5%), lung disease in 3 (33.3%), failure to thrive in 2 (22.2%), and arthritis in 1 (11.1%). Eight patients showed skin involvement (7 eczema and alopecia and 1 blistering rash), 7/9 lung involvement, 5/9 arthritis, 7/9 arthralgia and 1/9 increased liver enzymes. Seven patients underwent to lung CT that showed an interstitial lung disease of different severity characterized by minimal ground glass or nodular lesion up to diffuse cystic lesions to

Table 1: Main demographic, clinical and laboratory characteristics of patients with SAVI.

Variable in study	FAMILY A							FAMILY B	
	Pt A	*Pt B*	*Pt C*	*Pt D*	*Pt E*	*Pt F*	*Pt G*	*Pt H*	Pt I
Sex	M	F	F	M	F	M	M	F	M
Ethnicity	Black-african	Black-african	Black-african	Black-african	Black-african	Black-african	Black-african	Caucasian	Caucasian
Mutation	c.463G>A p.(Val155Met)	c.463G>A p.(Val155Met)	c.463G>A p.(Val155Met)	c.463G>A p.(Val155Met)	c.463G>A p.(Val155Met)	c.463G>A p.(Val155Met)	c.463G>A p.(Val155Met)	c.842G>A p.(Arg281Gln)	c.842G>A p.(Arg281Gln)
Age at onset (months)	3	infancy	12	16	60	3	Unknown	1	Adulthood
Current age (year)	15.5	10	18	18	14	Death at 9	35	12	Adult
First manifestation	eczema	eczema	Failure to thrive, eczema, lung involvement	Eczema and alopecia	Eczema and alopecia	Lung involvement	Alopecia and eczema	Failure to thrive	Arthritis
Failure to thrive	-	-	+	+	-	+	-	+	NA
Fever	-	-	-	-	-	+	+	-	NA
Recurrent infections	-	-	-	-	-	+	+	-	NA
Skin involvement	Eczema, alopecia totalis	Eczema, alopecia totalis	Eczema, alopecia	Eczema, alopecia	Eczema, alopecia	Eczema, alopecia	Eczema, alopecia	Blistering rash	None
Lung involvement	+	+	+	+	+	-	-	+	-
	Lung nodules	Intraparenchymal cysts, and small nodules and tree in buds aspect	Diffuses intraparenchymal cysts and small nodules. Some honeycomb aspect	Diffuse ground glass opacities with peripheral nodules. Diffuse cysts	Diffuse cystic lesion, with subsegmental bronchiectasis and blebs	Complete changes in the architecture of the lung with bronchiectasis, nodules, diffuse fibrosis		Centrilobular ground glass opacities with multifocal parenchymal bands	
Arthritis	-	-	+	+	-	+	-	-	-
ANA positivity	-	+	+	+	+	+	-	-	-
RF positivity	-	+	+	+	+	+	-	-	-
B cells	Increased	Normal	NV	Increased	Increased	Increased	Increased	Increased	NA
CD3+CD4+ cells	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	NA
CD3+CD8+ cells	Normal	Decreased	Decreased	Decreased	Decreased	Decreased	Normal	Decreased	NA
CD4+/CD8+cells ratio	Normal	Increased	Normal	Increased	Increased	Normal	Increased	Increased	NA

List of abbreviations: pt patient, M male, F female, ANA antinuclear antibody, RF rheumatoid factor.

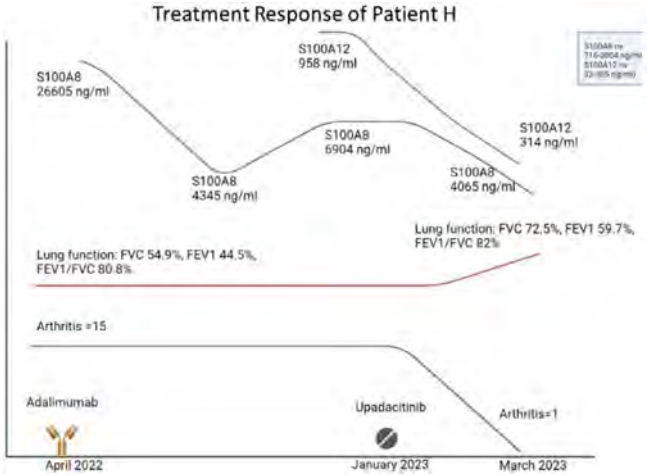

Figure1: visual presentation of response to treatment of patient H (adalimumab and Upadacitinib) in terms of articular response, lung response and some inflammatory biomarkers.

complete disruption of parenchyma. Lung biopsy performed in 5 patients showed chronic inflammatory bronchiolitis. Laboratory tests were available in 8 patients: all had increased ESR, 75% ANA and rheumatoid factor positivity, and 62.5% hypergammaglobulinemia. Lymphocyte subset showed expanded B cells in 75% (median 38.5% Range 31-53%), with decreased CD8+T in 71% (median 14%, R 10-38%) and 57% with increased CD4+/CD8. Plasma cytokines performed in 7 patients, showed increased value of IL1b (1/7), IL2 (2/7), IL4 (2/7), IL5 (4/7), IL8 (3/7) IL6 (5/7), TNFa (4/7). One patient of *Family A* died at age 9 years because of lung disease. The daughter of *family B (patient H),* after failing anti-TNF, received a JAK-inhibitor upadacitinib, with resolution of arthritis and improvement of lung function (spirometry) after 1.5 months of treatment.

Conclusion: The phenotype of SAVI may be extremely variable even within the same family. It is essential to reconsider prior cases with familial ILD and autoimmunity in order to identify the correct diagnosis and tailored treatment.

Disclosure: I. Maccora: None; **P. Vega-Fernandez**: None; **K. Risma**: None; **G. Schulert**: IpiNovyx, 5, SOBI, 2.

Abstract Number: 1241

Adverse Childhood Experiences in a Paediatric Systemic Lupus Erythematosus Cohort

Stephanie Fevrier[1], Olivia Hendrikx[1], Ashley Danguecan[1], Asha Jeyanathan[1], Lawrence Ng[1], Ibrahim Mohamed[2], Paris Moaf[1], Sondos Ayyash[1], Chelsea DeCoste[3], Deborah Levy[1], Linda Hiraki[1] and Andrea Knight[1], [1]The Hospital for Sick Children, Toronto, ON, Canada, [2]The Hospital for Sick Children, Brampton, ON, Canada, [3]IWK Health Centre, Halifax, NS, Canada

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic, multiorgan autoimmune disease in which 20% of cases are diagnosed in childhood. Adverse childhood experiences (ACEs) are traumatic events or experiences occurring in childhood. While adult SLE patients with a history of ACEs report higher levels of depression, ACEs' more immediate impact on adolescents with childhood-onset SLE (cSLE) is unknown. Research posits that ACEs and cSLE can be detrimental to the rapidly developing adolescent brain as they are both associated with an increased risk of cognitive impairment and mood disorders. This study aims to: 1) determine the prevalence of ACEs and 2) examine the relationship between ACEs and cognitive performance and mood disorder symptoms in cSLE.

Methods: We conducted a retrospective cohort study of participants ages 10-18 years who met the ACR or SLICC classification criteria for SLE. We identified 18 types of ACEs according to the CDC-Kaiser and Philadelphia ACEs frameworks through electronic medical records and responses from the PTSD section of the Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS). Outcomes of interest were: i) executive function (EF, measured by the Delis-Kaplan Executive Function System (D-KEFS)), ii) depression (Beck Depression Inventory-II (BDI-II), Children's Depression Inventory-II (CDI-II) and Center for Epidemiological Studies Depression Scale for Children (CES-DC)), and iii) anxiety (Screen for Childhood Anxiety and Related Emotional Disorders (SCARED)), each available for subsets of the cohort. We tabulated the prevalence, types, and timing of ACEs. Multivariable regression analyses examined the relationship between binary ACEs exposure and EF (D-KEFS scaled scores) and the presence of clinically elevated depression and anxiety symptoms; all models were adjusted for sex and age at cSLE diagnosis.

Results: The study involved 224 patients; 85% were female, and 83% identified as non-white, with a median age at diagnosis of 13.2 (IQR 4.4) years and a median disease duration of 2.7 (IQR 5.9) years. Forty-one percent (n=92) of the cohort had at least one documented ACE, of which 60% (n=37) had ≥2 ACEs; 55% of these ACEs occurred before cSLE diagnosis. Of all ACEs types, parental separation/divorce, bullying, and parental mental illness were the most frequent (Figure 1).

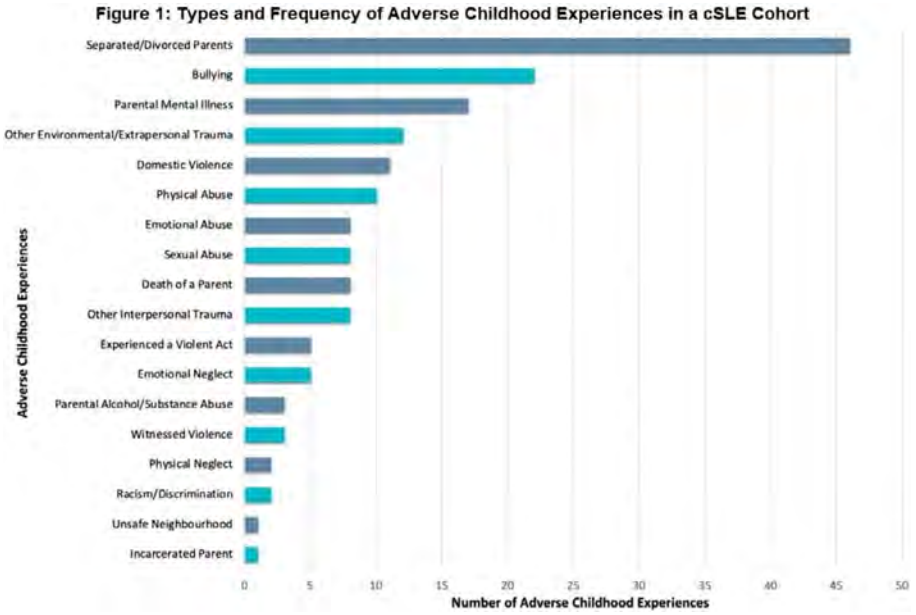

Figure 1. Bar chart showing the 18 ACEs types (adopted from the CDC-Kaiser and Philadelphia ACEs frameworks) and the frequency of each ACE among participants with documented ACEs. A total of n=172 ACEs events were identified among n=224 patients with cSLE.

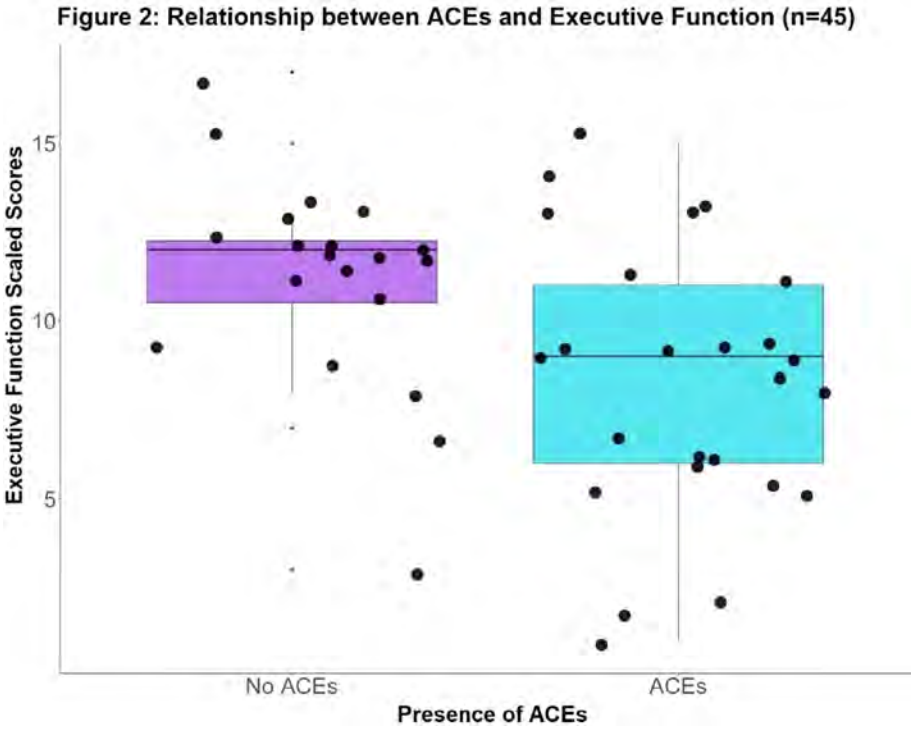

Figure 2. Box plot showing findings from a multivariable linear regression model examining the associations between ACEs exposure and EF scores, adjusting for sex and age at cSLE. Scaled scores from the D-KEFS Colour-Word Interference Test (CWIT) were measured as a continuous variable (scores of ≤7 indicate below-average performance). EF data were available for a subset of 45 participants.

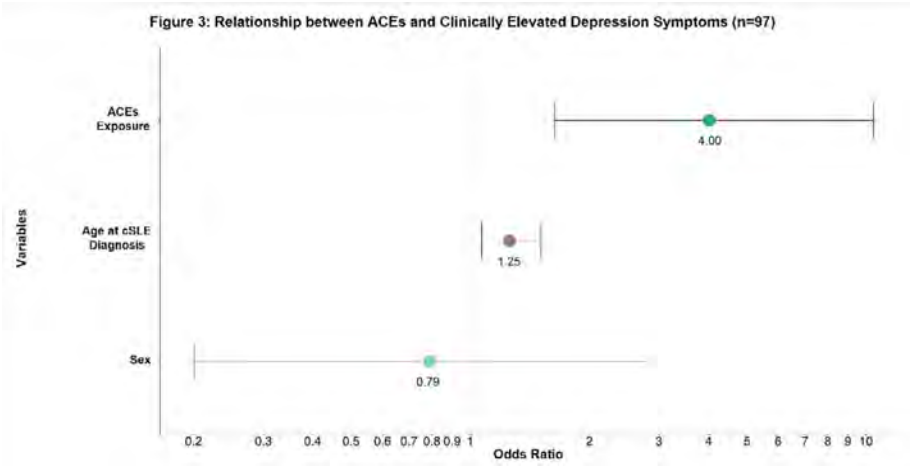

Figure 3. Odds plot showing findings from a multivariable logistic regression model examining the associations between ACEs exposure and the presence of clinically elevated depression symptoms, adjusting for sex and age at cSLE. Depression scores based on the BDI-II, CDI-II and CES-DC score classifications were measured as a binary variable and categorized as clinically elevated depression symptoms or not clinically elevated depression symptoms. Depression data were available for a subset of 97 participants.

Multivariable linear regression analysis (sample n=45) showed a significant association between ACEs exposure and worse EF performance on D-KEFS (β = -2.93, 95% CI [-5.04, -0.82], p = 0.008) (Figure 2). ACEs exposure was significantly associated with clinically elevated depression symptoms (OR = 4.00, 95% CI [1.63, 10.43], p = 0.003, sample n=97) (Figure 3). No association was found between ACEs exposure and clinically elevated anxiety symptoms (OR = 1.07, 95% CI [0.47, 2.46], p = 0.868, sample n=99).

Conclusion: ACEs negatively impact EF performance and mental health in children and adolescents with SLE. Further investigation is required into the neuropsychiatric consequences of ACEs and potential biological pathways that enable these deleterious outcomes in youth with cSLE and other chronic illnesses.

Disclosure: S. Fevrier: None; **O. Hendrikx**: None; **A. Danguecan**: None; **A. Jeyanathan**: None; **L. Ng**: None; **I. Mohamed**: None; **P. Moaf**: None; **S. Ayyash**: None; **C. DeCoste**: None; **D. Levy**: None; **L. Hiraki**: None; **A. Knight**: Pfizer, 6.

Abstract Number: 1242

Agreement Between Parent- and Self-Report of Executive Function in Adolescents with Childhood-Onset Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Executive functions (EFs) are a set of cognitive skills that enable successful problem solving and goal-directed behavior. EFs are predictive of academic success, mental and physical health, self-care, medical adherence, and transition from the pediatric to adult medical system, thereby impacting capacity for disease self-management and quality of life. One method of measuring EF is standardized questionnaires, completed by parents or youth. Agreement between raters is not yet well known in childhood-onset systemic lupus erythematosus (cSLE) and would provide clinically valuable information about parental concern and youth's self-awareness. Questionnaires could inform which patients may require follow-up for cognitive concerns, but it is not yet established whether these should be collected from parents, youth, or both. The aim of this study was to examine the agreement between parent and self-report ratings of EF.

Methods: Participants were youth aged 12-17 who met the ACR or SLICC criteria for SLE, and their parents. The Behavior Rating Inventory of Executive Function, Second Edition (BRIEF-2) parent- and self-report versions were collected. The BRIEF-2 is a standardized questionnaire assessing EFs in daily life with parent- and self-report versions (Figure 1). Intraclass correlation coefficients (ICCs) were calculated for the General Executive Composite (GEC), Behavior Regulation Index (BRI), Emotion Regulation Index (ERI), Cognitive Regulation Index (CRI), and six subscales. Mean T-scores between patients and parents were compared with paired-sample t-tests.

Table 1. Demographic and Clinical Characteristics

Variable	Mean (SD)
Current age (years)	15.4(1.7)
Sex (females; n[%])	32(88.9%)
Race/ethnicity n[%])	
American Indian or Alaskan Native	1(2.8%)
Asian	19 (50%)
Black or African-American	4 (11.1%)
White	9 (25%)
Other/Mixed	4 (11.1%
Disease duration (months)	26.6(28.5)
Disease Activity (SLEDAI-2K)	3.6(3.7)
Disease Damage (SDI)	0.2(0.6)

Table 2. Intraclass Correlation Coefficients and Mean Differences between Parent-Report and Self-Report

BRIEF-2 Index/Scale	ICC	Parent-Report M(SD)	Self-Report M(SD)	Mean Difference
General Executive Composite	.567***	50.2(11.3)	57.2(11.9)	-6.94**
Indices				
Behaviour Regulation Index	.580***	49.2(10.7)	54.5(11.3)	-5.23**
Emotion Regulation Index	.362*	52.7(11.9)	56.4(10.6)	-3.69
Cognitive Regulation Index	.566***	50.2(11.7)	58.1(13.3)	-7.89**
Scales				
Inhibit	.478***	48.8(9.8)	55.2(11.3)	-6.47***
Self-Monitor	.550***	50.1(11.9)	52.8(10.2)	-2.17
Shift	.098	52.9(12.3)	55(10)	-2.13
Emotional Control	.580***	52.1(10.9)	57.1(12.1)	-4.12**
Working Memory	.681***	53.1(12.6)	59.9(14.2)	-6.81***
Plan/Organize	.574***	49.3(11.4)	55.1(11.5)	-5.69**

Note: ICC= intraclass correlation coefficient, ICCs are classified as ≤ 0.40 poor to fair agreement, 0.41-0.60 moderate agreement, 0.61-0.80 good agreement, 0.81-1.00 excellent agreement

* p ≤ .05; **p ≤.01; ***p ≤ .001

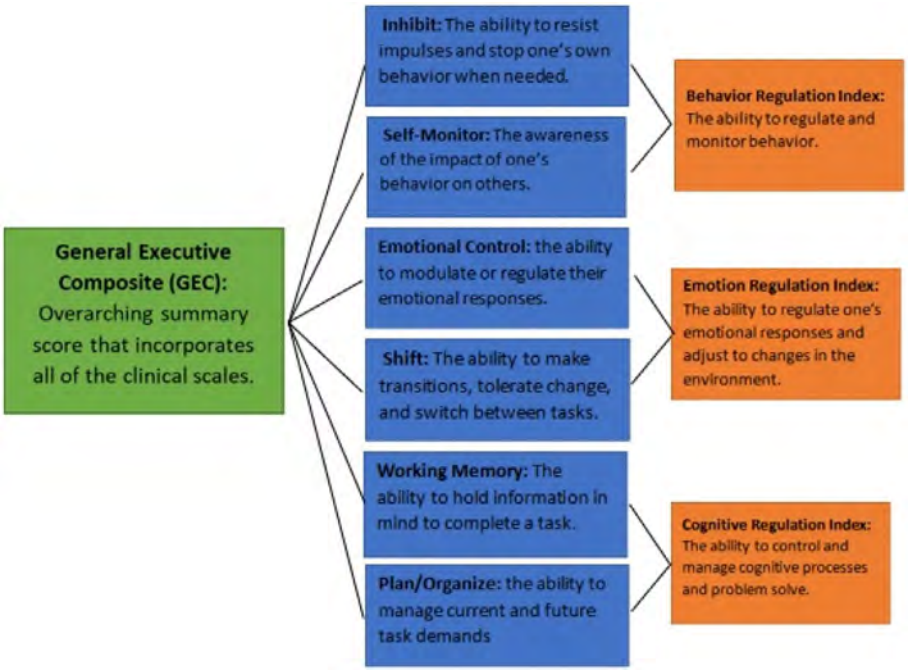

Figure 1. Structure and Definitions of the BRIEF-2 Scales and Indices

Results: Among 36 youth-parent dyads (Mean= 15.4 [SD1.7] years), ICCs between parent- and self-report (Table 2) showed moderate agreement for the overall GEC, BRI and CRI, however, the ERI showed poor agreement. For subscales, agreement was good for working memory, and moderate for inhibit, self-monitor, emotional control, and planning/organization, while ratings for the shift scale were discrepant. Mean T-score comparisons (Table 2) showed that youth rated themselves as having significantly more difficulties relative to parent-report on the GEC, BRI and CRI, as well as the inhibit, emotional control, working memory, and planning/organization subscales.

Conclusion: While ICCs indicated moderate to good consistency between most EF ratings on parent- and self-report, agreement for the ERI was poor and the shift scale was discrepant. Further analyses demonstrated that youth rated themselves as having more EF difficulties relative to parent's report across several EF domains. Our findings suggest that direct youth self-report is needed for comprehensive assessment using the BRIEF-2 and highlights the importance of considering the youth's own perspective of their cognitive functioning rather than relying on parent report alone. Future directions include comparing parent- and self-report BRIEFs with performance-based measures of EF.

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Abstract Number: 1243

Tubulointerstitial Inflammation Is Associated with End-Stage Renal Disease in Pediatric Lupus Nephritis: A Single Center Retrospective Cohort Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease
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Background/Purpose: Lupus nephritis (LN) is associated with significant morbidity and mortality. The 2018 International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification criteria and the NIH chronicity activity indices are used for LN classification. Some adult studies report tubulointerstitial (TI) inflammation is an independent predictor of renal outcomes in LN. However, its impact in pediatric LN remains unexplored.

Methods: We conducted a retrospective, observational cohort study utilizing a subgroup analysis of patients with biopsy-confirmed LN. Inclusion criteria encompassed all patients with biopsy-confirmed lupus nephritis, where the renal biopsies were performed at the University of Chicago between January 1, 2006, and September 6, 2022. Patients were required to be ≤ 21 years of age at the time of their initial kidney biopsy. Exclusion criteria consisted of a follow-up duration of

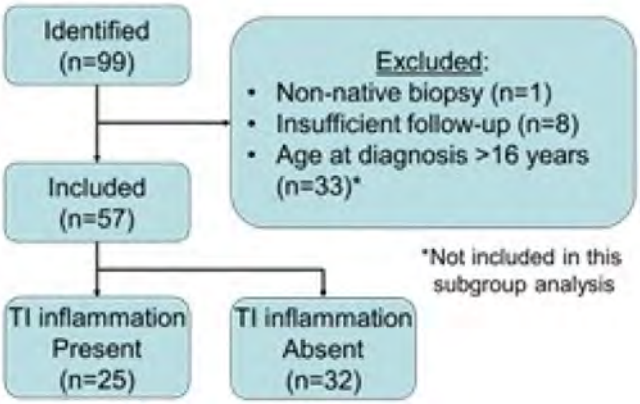

Figure 1. Study Flow Diagram

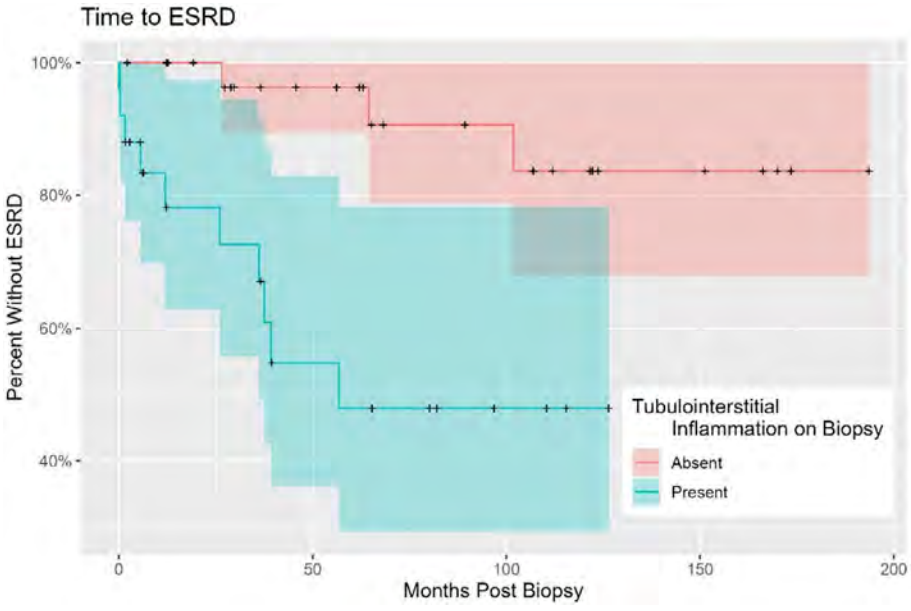

Figure 2. Time to ESRD

≤ 3 months and an age ≥ 16 years at the time of initial lupus diagnosis. Non-native renal biopsies were also excluded. The primary outcome measures were end-stage renal disease (ESRD) and/or the need for dialysis.

Results: Out of 99 identified biopsies, 42 were excluded, leaving 57 patients for analysis (see figure 1). The mean follow-up duration was 74 months (SD 26, max 210). TI inflammation was present for 25 (44%) and absent for 32 (56%). Of those with TI inflammation, 10 (40%) developed ESRD while only 3 (9.4%) without inflammation developed ESRD. Survival analysis showed a significant association with ESRD, with a positive likelihood ratio of 6.6 (95% CI 1.8, 24.3). Patients with TI inflammation experienced a shorter time to ESRD (mean 21.51 months, SD 20.32) compared to those without TI inflammation (mean 64.33 months, SD 37.65; see figure 2). ESRD was correlated with the NIH activity index (LR 1.9, 95% CI 1.1 - 1.3) and the NIH chronicity index (LR 3.1, 95% CI 1.8 - 5.4). Hemoglobin, C3 level, and proteinuria at 3 months and obesity at

Table 1: Demographics, baseline/biopsy characteristics, and select significant variables

Table 1: Demographics, baseline/biopsy characteristics, and select significant variables					
		Overall	ESRD		
			No	Yes	p
	n	57	44	13	
Demographic data					
Age at biopsy (mean (SD))		14.25 (3.20)	13.93 (3.14)	15.32 (3.28)	0.169
Age at lupus diagnosis (mean (SD))		12.86 (2.56)	12.63 (2.70)	13.67 (1.90)	0.201
Female (%)		45 (78.9)	36 (81.8)	9 (69.2)	0.555
Hispanic (%)		15 (26.3)	13 (29.5)	2 (15.4)	0.122
Race (%)					0.348
	African-American	39 (68.4)	28 (63.6)	11 (84.6)	
	Multiracial	11 (19.3)	10 (22.7)	1 (7.7)	
	Caucasian	7 (12.3)	6 (13.6)	1 (7.7)	
Baseline Characteristics					
CKD class (%)					<0.001
	G1	26 (60.5)	24 (70.6)	2 (22.2)	
	G2	8 (18.6)	8 (23.5)	0 (0.0)	
	G3a	5 (11.6)	1 (2.9)	4 (44.4)	
	G3b	2 (4.7)	1 (2.9)	1 (11.1)	
	G5	2 (4.7)	0 (0.0)	2 (22.2)	
SLEDAI (mean (SD))		16.51 (9.47)	14.90 (9.05)	22.00 (9.13)	0.021
Biopsy					
TI inflammation (%)		25 (43.9)	15 (34.1)	10 (76.9)	0.016
NIH activity index (mean (SD))		4.70 (5.14)	3.41 (4.24)	9.08 (5.65)	<0.001
NIH chronicity index(mean (SD))		0.86 (1.96)	0.39 (0.87)	2.46 (3.41)	<0.001
Treatments					
Cyclophosphamide infusions (mean (SD))		4.36 (2.22)	4.91 (1.81)	3.10 (2.64)	0.029
No ACEi in proteinuric pt at 36 months (%)		5 (13.2)	1 (3.3)	4 (50.0)	0.004
Non-adherence at 36 months (%)		10 (26.3)	5 (16.7)	5 (62.5)	0.03
Weight status at 12 months					0.009
	Healthy	13 (33.3)	12 (37.5)	1 (14.3)	
	Overweight	14 (35.9)	8 (25.0)	6 (85.7)	
	Obese	12 (30.8)	12 (37.5)	0 (0.0)	
Lab values at 3 months (mean (SD))					
	Hemoglobin	11.70 (1.79)	12.06 (1.70)	10.33 (1.50)	0.009
	Urine Pro:Cr ratio	1639 (2732)	1062 (1862)	3877 (4300)	0.008
	C3 level	93.3 (27)	97.5 (27.7)	75.8 (15.1)	0.039

12 months was associated with ESRD. ESRD was not correlated with ISN/RPS classification, race, sex, Hispanic ethnicity, or induction treatment (see table 1). It should be noted that 35 patients (62%) had missing data for non-outcome variables at certain timepoints. This study had a considerable amount of missing data for non-outcome variables, leading to wide confidence intervals due to the high proportion of right-censored data and limited number of events.

Conclusion: Our findings indicate a significant association between tubulointerstitial (TI) inflammation and the primary endpoint of ESRD or dialysis in our pediatric lupus nephritis cohort. Further evaluation of TI inflammation may provide valuable insights into the pathogenesis, prognosis, and treatment of pediatric lupus nephritis patients. However, these conclusions are constrained by the retrospective nature of the study and the significant amount of missing data.

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Abstract Number: 1244

Characterizing Lupus in African American Children in Southern United States

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease
Session Type: Poster Session B
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Background/Purpose: African-American (AA) ethnicity is a known predisposing factor for childhood onset systemic lupus erythematosus (cSLE) and a predictor of poor outcomes. In addition to ethnicity, income and geographical location are known drivers of health care disparities in cSLE. Despite this knowledge, there is lack of literature describing demographic and clinical features of cSLE in a predominant AA cohort. This study aims to characterize demographic and clinical features of cSLE patients in the Southeast United States (US) compared to current literature describing predominantly Caucasian cohorts.

Methods: Cross sectional study of cSLE patients from 2 centers in Southeast United States – University of Mississippi Medical center (UMMC) and University of Alabama at Birmingham (UAB). Prevalent and incident patients with cSLE at UMMC were consented for the study. Demographic, social and clinical data was retrospectively collected by chart review. Similar

	Study cohort N=45 N (%)	1000 faces of lupus cohort N=213 N (%)	Chi-square test results
Female sex	37 (82)	176 (83)	0.26, p= 0.6
African American ethnicity	37 (82)	22 (11)	87.29, **p < 0.00001**
Renal involvement present	14 (31)	72 (36)	0.12, p=0.72
Neurologic involvement present	9 (20)	26 (13)	1.92, p=0.16
SDI > 0	23 (51)	32 (16)	25.79, **p < 0.00001**
SDI > 2	20 (44)	14 (7)	42.82, **p < 0.00001**
Social vulnerability grade >2	38 (84)	NA	NA

	Study cohort (N=36) Mean (+/- SD)	1000 faces of lupus cohort (N= 199) Mean (+/- SD)	Unpaired t test results
Age at diagnosis (years)	13.5 (2.8)	12.6 (3)	**p=0.04**
ACR criteria	5.1 (1.27)	NA	NA
SLEDAI baseline	13.06 (9.3)	3.1 (2.1)	**p<0.0001**
SLEDAI at 6 months	7.4 (6.81)	NA	NA
SLEDAI at 1 year	4.7 (3.94)	NA	NA
Social vulnerability index score	0.74	NA	NA

data was obtained for the cSLE UAB cohort via the CARRA registry database. Data from both cohorts was combined and analyzed using SPSS statistical software. Descriptive statistics were used for demographic and clinical features. Unpaired t test and chi square test were used to compare outcomes in this cohort with those reported in the literature.

Results: Results are described for a total cohort of 45 patients, comprising 26 from UMMC and 19 from UAB. 37/45 (82.2%) were female, 37/45 (82.2%) were of AA ethnicity, and 30/45 (66.7%) had Medicaid insurance. Mean age at diagnosis (+/- SD) of SLE for the cohort was 13.5 years (+/- 2.8). Mean ACR score at diagnosis was 5.1 (+/- 1.27), SLICC score was 8.4 (+/- 2.5). Average baseline SLEDAI score was 13.06 (+/- 9.3), while SLEDAI score at 6 months and 1 year respectively were 7.4 and 4.7. Average distance traveled to see a rheumatologist was 74.83 miles compared to a national average of 42.8 miles. 37/45 patients (82%) belonged to medium-high or high Social Vulnerability Index (SVI) group based on zip code.

Average baseline SLEDAI compared to a multiethnic Canadian cohort with 10% black population, was significantly higher: 13.06 versus 3.1 ($p < 0.0001$, $t=10.99$). 23/45 had SDI > 0 (51.11%) versus 16% reported in the literature ($p < 0.00001$, chi-square 25.79). 20/45 (44.4%) had SDI >/= 2 compared to 7% reported in the literature ($p < 0.00001$, chi-square 42.82).

Patients from UMMC were offered depression and anxiety screening by a counselor in a multi-disciplinary clinic. 15/26 (57.7%) patients were screened with Revised Children's Anxiety and Depression Scale (RCADS). 5/15 (33.3%) and 6/15 (40%) had elevated scores for depression and anxiety respectively.

Conclusion: Compared to multiethnic cohorts of cSLE from Canada, this predominantly AA patient population from two centers in the Southern United States has significantly higher disease activity and greater damage accrual. Social risk factors for this population include a higher SVI, longer distance from an academic pediatric rheumatology center and having Medicaid insurance. The effect of these factors on disparity of disease outcomes needs to be further explored with larger cohorts.

Disclosure: A. Dhanrajani: None; **T. Long**: None; **S. Hagwood**: None; **C. Karlson**: None; **C. Foreman**: None.

Abstract Number: 1245

Evaluating a Diagnostic Algorithm for Childhood Sjögren's Disease

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease
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Background/Purpose: There are no widely accepted diagnostic or classification criteria for childhood Sjögren's disease (cSjD). To address the urgent need for consensus, the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Sjogren's Workgroup created a clinical diagnostic algorithm for cSjD. This study evaluates the sensitivity of the diagnostic algorithm to diagnose cSjD using an international cohort of patients.

Methods: The diagnostic algorithm was developed per expert opinion and has four distinct clinical pathway entry points: Parotitis (P), Systemic/Neurologic Manifestations (SN), Sicca symptoms (SIC) and Incidental Salivary or Lacrimal Gland Inflammation on Imaging (INC). The algorithm classifies patients as cSjD, probable cSjD, and negative for cSjD. The validation cohort was an international cohort of 300 cSjD cases, which includes extensive demographic and clinical information. De-identified clinical data from the cSjD cohort was put through the diagnostic algorithm. A response of Sjögren's disease (SjD) and probable SjD was classified as "positive" for SjD and all other responses were classified as "negative". Two analyses for the sensitivity of the algorithm for diagnosis were performed, one putting all patients through all pathways, and the other with patients only being put through the pathway they would meet criteria for entry into.

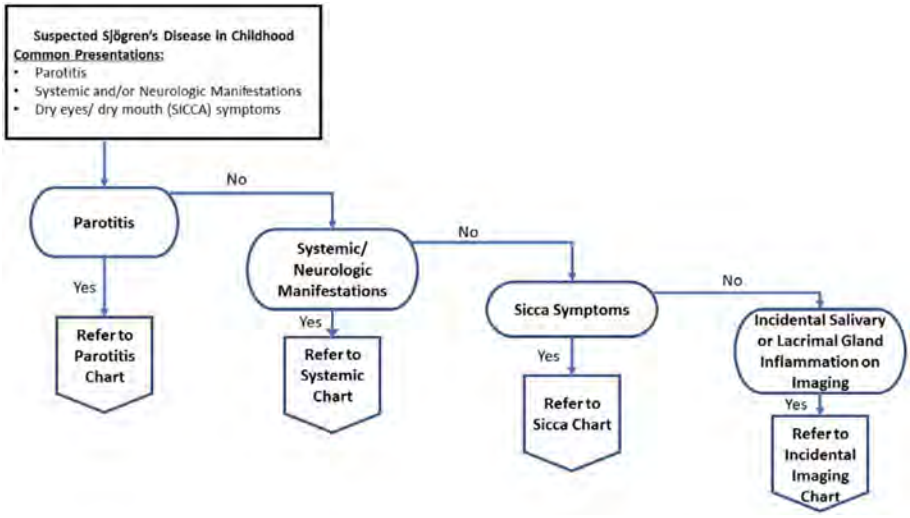
Results: The cSjD cohort (n=300) is 83% female with a mean age of diagnosis of 12 (9,15) years. Among the 300 cSjD cases, 100 (33%) were positive based on the algorithm across all pathways. 100 patients had adequate data allowing them to complete at least one of the 4 pathways, 75% of whom were positive across all pathways. Within each pathway, sensitivity of the algorithm ranged from 23-43% (all cases, Table 1) and 50-82% (limited to cases with complete data, Table 2). The proportion of patients without information for each variable is as follows: parotid biopsy (98%), ocular or oral screen (91%), minor salivary gland biopsy (65%), salivary gland ultrasound (65%) and positive SSA or SSB (2%).

Table 1: Sensitivity of the algorithm to diagnose Sjögren's Disease using the complete cohort where missing data is classified as NO

	Run all Patients through the pathways.		*Run all patients who fit specifically through that pathway*	
Pathway	**Total number of people with complete Info**	**Number with Positive Sjogren (Sensitivity out of complete Info (%))**	**Total number of people with complete Info**	**Number with Positive Sjogren (Sensitivity out of complete Info (%))**
Aggregated Diagnosis	300	100 (33.33)	-	-
Parotitis	300	71 (23.67)	140	41 (29.29)
Systemic Neurologic	300	89 (29.67)	244	70 (28.69)
SICCA	300	89 (29.67)	198	62 (31.96)
Incidental	300	69 (23)	96	41 (42.71)

Table 2: Sensitivity of algorithm to diagnose Sjögren's Disease where cases were excluded if unable to complete pathway due to missing data

	Run all Patients through the pathways.		*Run all patients who fit specifically through that pathway*	
Pathway	**Total number of people with complete Info**	**Number with Positive Sjogren (Sensitivity out of complete Info (%))**	**Total number of people with complete Info**	**Number with Positive Sjogren (Sensitivity out of complete Info (%))**
Aggregated Diagnosis	100	75 (75)	-	-
Parotitis	83	61 (73.49)	54	38 (70.37)
Systemic Neurologic	18	10 (10)	25	13 (52)
SICCA	26	19 (73.08)	22	18 (81.82)
Incidental	68	46 (67.65)	40	26 (65)



Conclusion: The sensitivity of the algorithm was limited by the lack of completion of diagnostic studies commonly performed in adults with SjD. The P and SIC arms of the algorithm were the most sensitive arms of the algorithm. The SN arm was the least sensitive arm, possibly due to the inhomogeneous and rare presentations in cSjD. Invasive and difficult testing were the least likely to be completed. This algorithm has adequate sensitivity in the setting of complete data, suggesting it is an appropriate diagnostic algorithm for cSjD until a more sensitive, pediatric specific classification criterion can be developed.

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Abstract Number: 1246

Assessment and Outcomes of 63 Cases of Juvenile Dermatomyositis-Associated Calcinosis

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SESSION INFORMATION

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Background/Purpose: Calcinosis is a poorly understood and morbid complication of juvenile dermatomyositis (JDM). As there is no consensus treatment approach for calcinosis, and limited knowledge of outcomes, we seek to inform future treatment guidance for this significant complication of JDM. We performed a multi-institutional retrospective review of treated cases of JDM calcinosis to assess outcomes as they relate to JDM severity, myositis autoantibody, initial treatment, and calcinosis-directed treatment.

Methods: Collaborators of Childhood Arthritis and Rheumatology Research Alliance (CARRA) submitted retrospectively reviewed cases with data collected at timepoints of JDM and calcinosis diagnoses, respectively, as well as the determined outcome of each specific calcinosis treatment.All cases were sourced from electronic health record searches of clinical terms or billing codes. Only cases diagnosed and treated from 2003 to 2019 were included to capture the contemporary era of JDM treatment. Cases were required to have probable/definitive JDM by Bohan and Peter criteria and calcinosis. Outcome was assessed in univariable and multivariable analyses as time to improvement by clinician judgement utilizing all available follow-up. Proportion with improvement along with 95% confidence intervals was estimated using Kaplan-Meier analysis. Multivariable Cox models were used to assess the association between patient characteristics and time to improvement beginning at calcinosis diagnosis.

Table 1 – Patient, disease, and treatment characteristics*

	Overall (N=63)
Age at calcinosis diagnosis, years	9.4 [5.7, 13.3]
Age at JDM diagnosis, years	7.8 [4.1, 11.1]
Duration of calcinosis symptoms prior to calcinosis diagnosis, years	0.2 [0.1, 0.3]
Duration of JDM symptoms prior to JDM diagnosis, years	0.5 [0.2, 1.0]
Male sex, n (%)	18 (29.6)
Race, n (%)	
White	25 (39.7)
Hispanic, Latino or Spanish origin	17 (27.0)
Black, African American, African or Afro Caribbean	12 (19.0)
Middle Eastern or North African	6 (9.5)
Asian	1 (1.6)
Unknown	2 (3.2)
Disease course, n (%)	
Monocyclic	2 (3.2)
Polycyclic	10 (15.9)
Chronic	44 (69.8)
Not applicable	7 (11.1)
Any myositis antibody (n=60), n (%)	25 (50.0)
Jo-1 (n=47)	3 (6.4)
MDA5 (caDM140) (n=33)	5 (15.2)
Mi-2 (n=42)	3 (7.1)
NXP2 (MJ) (n=32)	12 (37.5)
TIF1-gamma (P155/140) (n=35)	5 (14.3)
U1 RNP (n=36)	1 (2.8)
Characteristics at JDM diagnosis, n (%)	
Calcinosis present	20 (31.7)
Aggressive treatment of JDM†	38 (60.3)
Characteristics at calcinosis diagnosis, n (%)	
Active JDM (n=62)	47 (75.8)
Moderate to severe JDM	33 (52.4)
Active muscle involvement	31 (49.2)
Active skin involvement	51 (81.0)
Background medication(s)‡	41 (65.1)
Treatment at calcinosis diagnosis, n (%)	
None	11 (17.6)
Immunomodulatory agent(s)§	28 (44.4)
Immunomodulatory agent(s) plus Ca-modifying treatment(s)	19 (30.2)
Calcium modifying treatment(s)¶	5 (7.9)
Immunosuppressant(s)	30 (47.6)
Bisphosphonates	13 (20.6)
IVIG	20 (31.7)
Biologics	4 (6.3)
Surgical excision resulting from referral	7 (11.1)

* Continuous variables are summarized as median [interquartile range]. Categorical variables are summarized as frequency (percentage). Observations with complete information are presented when fewer than 63.
† Within the first 3 months of JDM diagnosis, receiving IV methylprednisolone ≥2 mg/kg/day continued for more than 1 week, and/or cyclophosphamide, and/or IVIG and/or rituximab
‡ Includes glucocorticoids, immunomodulatory drugs, IVIG, and biologics
§ Includes glucocorticoids, immunosuppressants (Methotrexate, Leflunomide, Azathioprine, Mycophenolate mofetil, Mycophenolic acid, Sirolimus, Tacrolimus, Thalidomide, Lenalidomide, Cyclosporine, Hydroxychloroquine, Sulfasalazine, Cyclophosphamide, Colchicine), non-biologic DMARDs (tofacitinib, baricitinib, ruxolitinib), IVIG, Biologic DMARDs (Rituximab, Etanercept, Infliximab, Adalimumab, Certolizumab, Golimumab, Anakinra, Canakinumab, Rilonacept, Abatacept, Tocilizumab).
¶ Includes agents that effect calcium or phosphorus (Bisphosphonates, Vitamin D, Vitamin C, Calcium-channel blocker, Sodium thiosulfate, Aluminum hydroxide, Warfarin, Minocycline, Probenecid).

Table 2 - Summary of Adjusted Univariable Analyses of Significant Improvement and Disease/Patient Characteristics*

Disease/Patient Characteristics	*HR (95% CI, adjusted)*	*P*
Female Sex	1.42 (0.68, 2.99)	*0.521*
Calcinosis at JDM diagnosis	1.21 (0.51, 2.91)	0.665
Active JDM at calcinosis diagnosis	1.42 (0.60, 3.38)	0.425
Moderate to severe JDM severity at calcinosis diagnosis	1.07 (0.52, 2.20)	0.850
Aggressive treatment of JDM at JDM diagnosis	1.45 (0.74, 2.84)	0.276
Any myositis antibody	1.36 (0.65, 2.83)	0.411
NXP2 (MJ) or MDA5 antibody	0.67 (0.26, 1.72)	0.401

*Results are from Cox proportional hazards models adjusted for age, sex, and time between initial JDM diagnosis and calcinosis diagnosis. Significant improvement was defined as moderate/significant improvement or complete/total resolution in the survey. Association between characteristics and improvement was assessed using time-dependent indicators for the given characteristics. Hazard ratios represent the multiplicative increase in hazard for improvement associated with the given treatments.

Table 3. Summary of Adjusted Univariable Analyses of Time-dependent Treatment Regimens*

Treatment Regimen	*HR (95% CI, adjusted)*	*P*
None	Ref.	
Immunomodulatory Agent(s)	2.57 (0.74, 8.96)	0.139
Calcium modifying treatment(s)	1.79 (0.38, 8.32)	0.458
Immunomodulatory Agent(s) + Ca-modifying treatment(s)	3.08 (0.90, 10.55)	0.074
Types of Immunomodulatory Agent		
Immunosuppressant(s)	1.40 (0.78, 2.49)	0.259
IVIG	1.95 (1.10, 3.45)	0.022
Biologics	1.40 (0.66, 3.00)	0.382
Bisphosphonates	1.23 (0.67, 2.24)	0.506
Surgical Excision	0.82 (0.24, 2.79)	0.751

*Results are from Cox proportional hazards models adjusted for age, sex, and time between initial JDM diagnosis and calcinosis diagnosis. Association between treatment and improvement was assessed using time-dependent indicators for the given treatments. Hazard ratios represent the multiplicative increase in hazard for improvement associated with the given treatments.

Results: Data for 63 patients were collected from 11 institutions. Median age was 7.8 years at JDM diagnosis and 9.4 years at calcinosis diagnosis. Calcinosis was present at JDM diagnosis in 32%. JDM was considered active in 76% of cases at the time of calcinosis diagnosis. Fifty percent of patients had a positive myositis autoantibody, with anti-nuclear matrix protein 2 (NXP2) antibody being the most common (38%) (Table 1). The presence of NXP2 or anti-melanoma differentiation-associated gene 5 (MDA5) antibodies did not reach statistical significance to influence outcomes but trended to lower likelihood of improvement (Table 2). Patients received multiple treatment regimens including immunomodulating agents with or without other calcium modifying treatments. Seventy nine percent of patients ultimately showed improvement. IVIG was associated with greater probability of calcinosis improvement (p=0.02) compared to treatment without IVIG (Table 3). The improvement was largely determined based on history and physical exam (93%), whereas imaging was used in a small number of cases (14%).

Conclusion: NXP2 antibody was the most common myositis antibody in our JDM calcinosis population. Those with NXP2/MDA5 antibody were less likely to respond to treatment, although not statistically significant. Our cohort received multiple treatment regimens including both immunomodulating therapies and calcium modifying agents. Reassuringly, most patients showed improvement over time, especially with IVIG; however standardized measures of defining improvement are warranted. Improved knowledge of treatment choices and outcomes can support future prospective studies.

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Abstract Number: 1247

Pharmacokinetic, Pharmacodynamic, and Safety Profile of Subcutaneous Belimumab in Pediatric Patients with Systemic Lupus Erythematosus: Analysis of Data from a Multicenter, Open-Label Trial

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SESSION INFORMATION

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Background/Purpose: Belimumab (BEL) is an approved treatment for SLE, in addition to standard therapy. Intravenous (IV) BEL is approved in patients (pts) ≥5 years of age, and subcutaneous (SC) BEL is approved in adults.[1] This study aimed to evaluate the pharmacokinetics (PK), pharmacodynamics (PD), and safety of SC BEL in pediatric pts with SLE.

Methods: This was a multicenter, open-label trial (GSK Study 200908; NCT04179032) of pediatric pts (5–17 years of age) with active SLE who received SC BEL, plus standard therapy, over 52 weeks (wks). A 3-weight band dosing regimen was planned to correct for higher exposure expected with low body weight (≥15–< 30 kg: 200 mg/2 wks; ≥30–< 50 kg: 200 mg/10 days; ≥50 kg: 200 mg/wk). Pts received SC BEL for the first 12 wks (Part A) and could then choose to enter a 40-wk extension (Wk 12–52; Part B). Primary outcome was PK; a population PK (popPK) model (2-compartmental with 1st order absorption, distribution, and elimination) was developed using data from the pediatric IV BEL PLUTO trial (NCT01649765)[2] and the current trial, and was informed by a previous model developed for IV BEL in pediatrics.[3] Exposures were compared with those in the adult BLISS-SC trial (NCT01484496).[4] Secondary outcomes: safety (adverse events [AEs], serious AEs [SAEs], and AEs of special interest [AESI]); PD (percentage change from baseline [BL] in biomarker levels).

Results: Of the 25 pediatric pts enrolled, 84.0% were female; mean (standard deviation, SD) age at screening was 14.0 (2.1) years. Approximately half of pts were ≥50 kg (52.0%) and 48.0% were ≥30–< 50 kg; no pts were enrolled in the < 30 kg cohort. All pts completed Part A and continued into Part B; 92.0% of pts completed Part B. Mean BEL concentrations were generally higher in pts ^{3}50 kg compared with ^{3}30 to < 50 kg (**Table 1, Figure A**). However, across a pediatric population, the

popPK analysis showed that exposures for the 3-weight band SC regimen were expected to be consistent with adult SC exposures from BLISS-SC (**Figure B**). Most pts had ≥1 AE (88.0%; **Table 2**). Nine (36.0%) pts had mild or moderate COVID-19. One (4.0%) pt had a single SAE (mild COVID-19) and was hospitalized, and 3 (12.0%) had an AESI (all post-injection systemic reaction). No infections of special interest, malignancies, depression/suicide/self-injury, or deaths were reported. From BL to Wk 52, there were median percent decreases in Ig levels (IgA: –13.1%; IgG: –12.3%; IgM: –30.8%) and anti-dsDNA antibody levels (–58.9% among those positive at BL). In pts with low complement (C) at BL, there were median percent increases in C3 (+23.5%) and C4 (+67.5%) levels at Wk 52.

Conclusion: SC BEL exposure in pediatric pts with SLE was consistent with the adult SC (200 mg/wk) population. The PD and safety profiles of SC BEL 200 mg in children 5–17 years of age with SLE were consistent with the known profiles of BEL in SLE. No new safety concerns were identified in this population.

Table 1. PopPK model-derived exposures and observed BEL concentrations at Wk 12. AUC.ss, area under the curve at steady state calculated over the dosing period; Cavg.ss, average concentration at steady state; Cavg (Wk 0–12), average concentration over the first 12 wks of treatment; Cmax.ss, maximum concentration at steady state; Cmin.ss, minimum concentration at steady state; CV, coefficient of variation.

Geometric mean (CV%), range	All pts (N=25)	Pts ≥50 kg (n=13)	Pts ≥30–<50 kg (n=12)
Cmin.ss (µg/mL)	112 (41.7%), 38.7–203	138 (26.2%), 89.0–203	90.1 (43.9%), 38.7–159
Cavg.ss (µg/mL)	124 (37.3%), 47.9–214	146 (25.2%), 95.6–214	103 (39.8%), 47.9–173
Cmax.ss (µg/mL)	131 (34.9%), 54.1–220	151 (24.7%), 99.4–220	111 (37.6%), 54.1–182
AUC.ss (µg day/mL)	1027 (32.1%), 479–1733	1024 (25.2%), 669–1498	1031 (39.8%), 479–1733
Cavg (Wk 0–12) (µg/mL)	82.7 (32.0%), 39.1–140	95.4 (25.4%), 60.1–140	70.8 (31.5%), 39.1–113
Observed Wk 12 concentration (µg/mL)	106.4 (49.3%) (27.3, 224.4)	134.2 (34.7%) (65.3, 224.4)	82.8 (49.3%) (27.3, 155.3)

Table 2. Summary of treatment-emergent AEs. *Last injection date – first injection date + X, where X is 7, 10 or 14 for pts ≥50 kg, pts ≥30–50 kg and pts ≥15–<30 kg, respectively. Only complete dates are used. First and last injection dates are used, regardless of any missed doses; †per Custom MedDRA query (version 25.1); ‡includes opportunistic infections, herpes zoster, tuberculosis, and sepsis; §per Standard MedDRA query (version 25.1). MedDRA, Medical Dictionary for Regulatory Activities; PISR, post-injection systemic reaction.

n (%)	BEL 200 mg SC (N=25)
Duration (days) of study drug exposure*, mean (SD)	357.8 (43.0)
≥1 AE	22 (88.0)
≥1 related AE	14 (56.0)
≥1 SAE	1 (4.0)
≥1 severe AE	0
≥1 AE resulting in drug discontinuation	1 (4.0)
AESI	
All malignancies†	0
PISR†	3 (12.0)
All infections of special interest†,‡	0
Depression (including mood disorders and anxiety)†	0
Suicide/self-injury§	0
Death	0

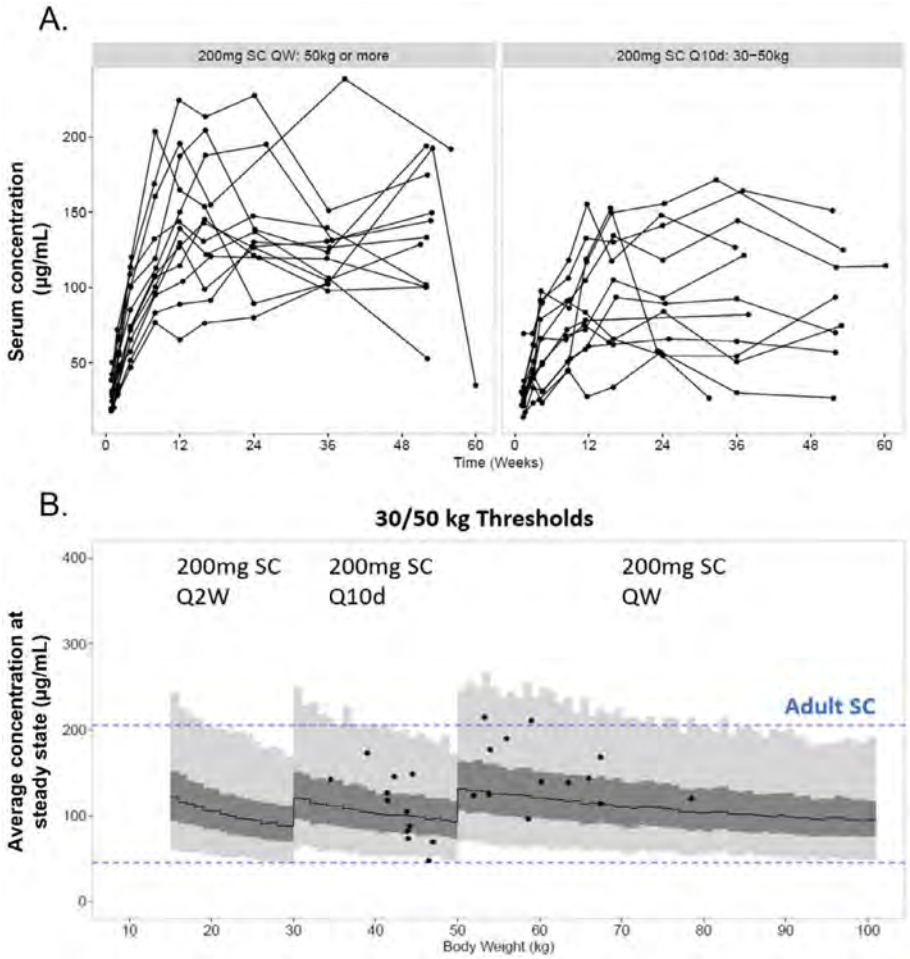

Figure. (A) Observed serum concentrations, (B) predicted Cavg versus body weight. (B) Individual predicted Cavg of patients (points, N=25); model predicted median (solid line), interquartile range (dark gray) and 95% prediction interval (light gray, and dotted line). Cavg, average concentration; QW, every week; Q2W, every 2 wks; Q10d, every 10 days.

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References

1 Levy RA et al. *Lupus* 2021;30:1705–21
2 Brunner HI et al. *Ann Rheum Dis* 2020;79:1340–8
3 Dimelow R et al. *Clin Pharmacol Drug Dev* 2021;10:622–33
4 Stohl W et al. *Arthritis Rheumatol* 2017;69:1016–27

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Abstract Number: 1248

Thrombotic Manifestations in Pediatric Behçet Disease Patients: A Multicentre Comparative Study from EUROFEVER Registry

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

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Background/Purpose: Arterial and venous thrombosis occurs in 6.6 to 38.4% of pediatric Behçet disease (BD) and cerebral sinus is one of the most involved districts. The aim of our study was to report clinical features and outcomes of a pediatric BD multicentre cohort with thrombosis, to identify possible predictive factors of thrombosis

Methods: A retrospective data collection of pediatric BD patients with thrombosis (T+) included in the EUROFEVER registry was conducted. Clinical data of BD patients without thrombosis (T-), belonging to the same contributing rheumatology units have been retrieved from EUROFEVER registry. T+ and T- groups were matched in a 2:1 ratio.

Results: 37 T+ patients were compared to 74 T- patients across 13 European pediatric rheumatology centers. BD onset occurred at a median age of 153 months (IQR±57) and 156 months (IQR±51) in the T+ and T- group, respectively. At onset, ICBD criteria fulfillment was significantly higher in the T- group compared to the T+ ($p=0.015$), whereas no differences were detected in ISG and PEDBD criteria frequencies. No gender differences were observed, Caucasian ethnicity significantly recurred in T- group while Middle Eastern in T+ group ($p=0.002$). HLA-B51 haplotype positivity was significantly reported in T- patients ($p=0.04$). At onset, pustulosis was most frequently observed in the T- group ($p< 0.001$) as well as gastrointestinal symptoms ($p< 0.001$) and ocular involvement ($p=0.022$). Conversely, neurological symptoms were more often described in T+ patients ($p=0.034$). As for T+ group, thrombosis was reported at BD presentation in 8/37 patients (29.6%). For the remaining patients, who developed thrombosis later in the disease course, the comparison of symptoms revealed that oral aphtosis ($p=0.003$), genital aphtosis ($p=0.014$) and posterior uveitis ($p=0.050$) were more frequently observed at BD onset than at thrombosis presentation, while pustulosis ($p=0.02$) and fever

(p=0.019) significantly coexisted with thrombosis. Thrombosis type was mainly venous (26/37,70.3%), predominantly involving the cerebral sinuses (21/37, 56.8%). 16/29 (55.2%) T+ patients were on treatment before thrombosis onset with at least one systemic, non-steroid treatment. After thrombosis occurence, 35/37 (94.6%) T+ patients underwent or added an immunomodulatory treatment. 26/32 (81.3%) and 26/33 (21.2%) started anticoagulant and antiplatelet therapy, respectively. At a median follow up of 4 months (IQR±10), 9/28 (32.1%) T+ patients resolved thrombosis, 8/28 (28.6%) had a partial regression and 11/28 (39.3%) a persistence. A recurrence was reported in 6/31(19.4%) as venous thrombosis.

Conclusion: Middle Eastern ethnicity significantly recurred in T+ group, pustolosis and fever were more frequently concomitant to thrombosis. Neurological symptoms at onset could be related to thrombosis development in the BD course. Sinus veins were confirmed as the most frequent thrombosis site. Larger studies are required to better define predictive risk factors of thrombosis in pediatric BD.

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Cross-Sectional Associations of Emotional Distress and Cardiovascular Health in Juvenile Lupus and Dermatomyositis

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SESSION INFORMATION

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Background/Purpose: Juvenile lupus (JSLE) and dermatomyositis (JDM) patients are at high risk for cardiovascular disease (CVD). The American Heart Association cardiovascular health (CVH) construct is the sum of protective factors against CVD. JSLE/JDM patients are at risk of premature loss of CVH that may increase lifetime risk for CVD. Emotional distress is often elevated in JSLE/JDM patients and may be a modifiable factor that adversely impacts CVH in this population. We hypothesize that emotional distress is associated with worse CVH in JSLE/JDM.

Methods: JSLE/JDM patients (5-22yo) were enrolled at Duke and UNC Children's Hospitals. PROMIS® Pediatric (self-report) and/or Parent-Proxy measures of emotional distress were administered, including Psychological Stress Experiences, Depressive Symptoms, and Anxiety (PROMIS-Str/-Depr/-Anx). CVH indicators included CVH Behaviors (diet quality screener; PROMIS Physical Activity) and CVH Factors (body mass index, blood pressure, non-HDL cholesterol, HbA1c). CVH Summary (CVH-S, all 6 indicators), Behaviors (CVH-B) and Factors (CVH-F) scores were derived (range 0-100, higher scores indicate better CVH). Spearman's correlations between PROMIS emotional distress measures and CVH scores were calculated for the overall cohort and for subgroups (race/ethnicity, age, diagnosis, gender, steroid use). Rank sum tests

Table 1: Participant Characteristics

Table 1: Participant Characteristics

	n (with data)	n (%) or median (IQR)
Diagnosis		
JSLE	83	48 (58%)
JDM	83	35 (42%)
Age (years)	83	16 (12-18)
Female Gender	83	66 (80%)
Race/Ethnicity	83	
White		29 (35%)
Black, African-American, African, Afro-Carribean		38 (46%)
Hispanic, Latino/Latina/Latinx, or Spanish origin		10 (12%)
Asian		8 (10%)
Native Hawaiian or Other Pacific Islander		1 (1.2%)
Other		2 (2.4%)
Medical & Psychiatric History:		
History of Any Cardiovascular Comorbidities	83	47 (56.6%)
Current Antihypertensive Medication Use	83	22 (26.5%)
Current Lipid-Lowering Therapy Use	83	2 (2.4%)
History of Any Psychiatric Comorbidity	83	45 (54.2%)
Current Psychiatric Medication Use	83	18 (21.7%)
On/off corticosteroids	83	36 (43.4%)
Disease Activity:		
Physician's Global Assessment of Disease Activity (JSLE and JDM)	83	0.5 (0-2)
Physician's Global Assessment of Disease Activity (JSLE only)	48	0.5 (0-1.5)
Physician's Global Assessment of Disease Activity (JDM only)	35	1 (0-2.2)
PROMIS Self-Report		
Psychological Stress Experiences	73	58.3 (50.6-64.3)
Moderate to Severe Stress		42 (57.5%)
Depressive Symptoms	75	51.9 (40.7-61.7)
Moderate to Severe Depressive Symptoms		36 (48%)
Anxiety	75	51.6 (38.8-59.8)
Moderate to Severe Anxiety Symptoms		37 (49.3%)
PROMIS Parent-Proxy Report		
Psychological Stress Experiences	56	58.7 (53.4-66.4)
Moderate to Severe Stress		31 (55.4%)
Depressive Symptoms	55	45.4 (36.2-58.1)
Moderate to Severe Depressive Symptoms		21 (38.2%)
Anxiety	55	49.2 (43.3-56.8)
Moderate to Severe Anxiety Symptoms		25 (45.5%)
CVH Scores:		
CVH Summary Score (CVH-S)	82	69.6 (60.2-78.1)
CVH Behaviors Subscore (CVH-B)	83	45 (30-55)
CVH Factors Subscore (CVH-F)	82	82.5 (71.2-93.8)

compared median CVH scores between patients with minimal vs moderate/severe emotional distress in the overall cohort. Rank sum tests also compared median CVH scores by subgroup among patients with moderate/severe emotional distress. Minimal vs moderate/severe emotional distress groups were based on published PROMIS T-score cutoffs. Variation of the association of PROMIS-Str/-Depr/-Anx with CVH by subgroups was assessed via interactions in regression models.

Results: Data were analyzed for 83 patients (Table 1). In the overall cohort, PROMIS-Anx modestly correlated with CVH-F (rho -0.26, p = 0.019) (Table 2) and patients with moderate/severe PROMIS-Anx scores had worse median CVH-F than those with minimal PROMIS-Anx (90 vs 77.5, p = 0.011). CVH-B scores were most strongly related to PROMIS-Str scores

Table 2: Spearman's Correlations Between CVH Scores and PROMIS T-scores, Stratified by Participant Subgroups

Table 2: Spearman's Correlations Between CVH Scores and PROMIS T-scores, Stratified by Participant Subgroups*

			CVH Summary (CVH-S)		CVH Behavior (CVH-B)		CVH Factors (CVH-F)	
	Participant Subgroups	Group	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value
PROMIS Pediatric Psychological Stress Experiences (PROMIS-Str)	All Participants	n/a	NS	NS	-0.19	0.081	NS	NS
	Race/Ethnicity	Non-Hispanic White	-0.38	0.057	NS	NS	NS	NS
		Any US Minority Racial/Ethnic Background	NS	NS	NS	NS	NS	NS
	Gender	Female	-0.25	0.041	NS	NS	NS	NS
		Male	NS	NS	NS	NS	NS	NS
	On Corticosteroids	Yes	NS	NS	-0.45	0.007	NS	NS
		No	NS	NS	NS	NS	NS	NS
PROMIS Pediatric Depressive Symptoms (PROMIS-Depr)	Race/Ethnicity	Non-Hispanic White	NS	NS	-0.4	0.043	NS	NS
		Any US Minority Racial/Ethnic Background	NS	NS	NS	NS	NS	NS
	Gender	Female	-0.24	0.051	NS	NS	NS	NS
		Male	NS	NS	NS	NS	NS	NS
PROMIS Pediatric Anxiety (PROMIS-Anx)	All Participants	n/a	-0.21	0.064	NS	NS	-0.26	0.019
	Race/Ethnicity	Non-Hispanic White	NS	NS	NS	NS	NS	NS
		Any US Minority Racial/Ethnic Background	NS	NS	NS	NS	-0.25	0.062
	Age	< 16 yo	NS	NS	NS	NS	-0.34	0.034
		> or = 16 yo	NS	NS	NS	NS	NS	NS
	Diagnosis	JSLE	NS	NS	NS	NS	-0.24	0.1
		JDM	NS	NS	NS	NS	-0.3	0.082
	Gender	Female	-0.25	0.044	NS	NS	-0.31	0.011
		Male	NS	NS	NS	NS	NS	NS
	On Corticosteroids	Yes	-0.34	0.044	NS	NS	-0.39	0.019
		No	NS	NS	NS	NS	NS	NS

*Spearman's rho calculated between PROMIS-Str/-Depr/-Anx and CVH-S/-B/-F scores for all participants and by subgroups including race/ethnicity (Non-Hispanic white vs Any US Minority Racial/Ethnic Background), Age (< 16 yo vs > or = 16 yo), Diagnosis (JSLE vs JDM), Gender (Female vs Male), Corticosteroid Use (Yes vs No), with results displayed if p < or = 0.1

p <0.05 | p >0.5 but < or = 0.1 | NS = Not Significant

Table 3: Comparison of Median CVH Scores For Participants with Moderate/Severe Emotional Distress, Stratified By Subgroups

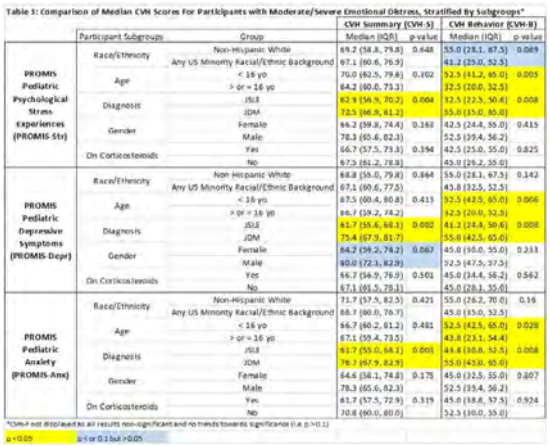

Table 3: Comparison of Median CVH Scores For Participants with Moderate/Severe Emotional Distress, Stratified By Subgroups*			CVH Summary (CVH-S)		CVH Behavior (CVH-B)	
	Participant Subgroups	Group	Median (IQR)	p-value	Median (IQR)	p-value
PROMIS Pediatric Psychological Stress Experiences (PROMIS-Str)	Race/Ethnicity	Non-Hispanic White	69.2 (58.8, 79.8)	0.648	55.0 (28.1, 67.5)	0.089
		Any US Minority Racial/Ethnic Background	67.1 (60.6, 76.9)		41.2 (25.0, 52.5)	
	Age	< 16 yo	70.0 (62.5, 79.8)	0.102	52.5 (31.2, 65.0)	0.005
		> or = 16 yo	64.2 (60.0, 73.1)		32.5 (20.0, 32.5)	
	Diagnosis	JSLE	62.9 (56.9, 70.2)	0.004	32.5 (22.5, 50.4)	0.008
		JDM	72.5 (66.9, 81.2)		55.0 (35.0, 65.0)	
	Gender	Female	66.2 (59.8, 74.4)	0.163	42.5 (24.4, 55.0)	0.415
		Male	70.3 (65.6, 82.3)		52.5 (39.4, 56.2)	
	On Corticosteroids	Yes	66.7 (57.5, 73.3)	0.394	42.5 (25.0, 55.0)	0.825
		No	67.5 (61.2, 78.8)		43.0 (26.2, 55.0)	
PROMIS Pediatric Depressive Symptoms (PROMIS-Depr)	Race/Ethnicity	Non-Hispanic White	64.8 (55.0, 79.8)	0.864	55.0 (28.1, 67.5)	0.142
		Any US Minority Racial/Ethnic Background	67.1 (60.6, 77.0)		43.8 (32.5, 52.5)	
	Age	< 16 yo	67.5 (60.4, 80.8)	0.413	52.5 (42.5, 65.0)	0.006
		> or = 16 yo	66.7 (59.2, 74.2)		32.5 (20.0, 52.5)	
	Diagnosis	JSLE	61.7 (55.6, 68.1)	0.002	41.2 (24.8, 50.6)	0.008
		JDM	75.4 (67.9, 81.7)		55.0 (42.5, 65.0)	
	Gender	Female	66.2 (59.2, 74.2)	0.067	45.0 (30.0, 55.0)	0.233
		Male	80.0 (72.1, 82.9)		32.5 (47.5, 37.5)	
	On Corticosteroids	Yes	66.7 (56.9, 76.9)	0.501	45.0 (34.4, 56.2)	0.562
		No	67.1 (61.5, 78.1)		45.0 (28.1, 55.0)	
PROMIS Pediatric Anxiety (PROMIS-Anx)	Race/Ethnicity	Non-Hispanic White	71.7 (57.5, 82.5)	0.421	55.0 (26.2, 70.0)	0.16
		Any US Minority Racial/Ethnic Background	68.7 (60.0, 76.7)		45.0 (35.0, 52.5)	
	Age	< 16 yo	66.7 (60.2, 81.2)	0.481	52.5 (42.5, 65.0)	0.028
		> or = 16 yo	67.1 (59.4, 73.5)		43.8 (23.1, 54.4)	
	Diagnosis	JSLE	61.7 (55.0, 68.1)	0.001	41.8 (30.6, 53.5)	0.008
		JDM	78.7 (67.9, 82.9)		55.0 (43.0, 65.0)	
	Gender	Female	64.6 (58.1, 74.8)	0.175	45.0 (32.5, 55.0)	0.807
		Male	78.3 (65.6, 82.3)		52.5 (39.4, 56.2)	
	On Corticosteroids	Yes	61.7 (57.5, 72.9)	0.319	45.0 (38.8, 57.5)	0.924
		No	70.8 (60.0, 80.0)		52.5 (30.0, 55.0)	

*CVH-F not displayed as all results non-significant and no trends towards significance (i.e. p >0.1)

p <0.05 | p ≤ or 0.1 but >0.05

in patients on steroids relative to those who were not, and with PROMIS-Depr scores in non-Hispanic White relative to minority race/ethnicity patients (Table 2). Among patients with moderate/severe emotional distress, CVH-S/-B scores were lower in JSLE vs JDM patients and CVH-B scores were lower in older (≥16yo) vs younger (< 16yo) JSLE/JDM patients (Table 3). Interactions indicated JSLE diagnosis and non-Hispanic White race/ethnicity were associated with stronger inverse relationships between PROMIS-Depr scores and CVH-S ($p = 0.043$) and CVH-B ($p = 0.017$) respectively.

Conclusion: Moderate/severe emotional distress is associated with worse CVH, driven by lower CVH-B, in JSLE as well as ≥16yo JSLE/JDM patients. We also noted differences by race/ethnicity in the association of emotional distress with CVH-B. Future analyses will identify social determinants of health and clinical features that influence associations of emotional distress with CVH in JSLE/JDM patients.

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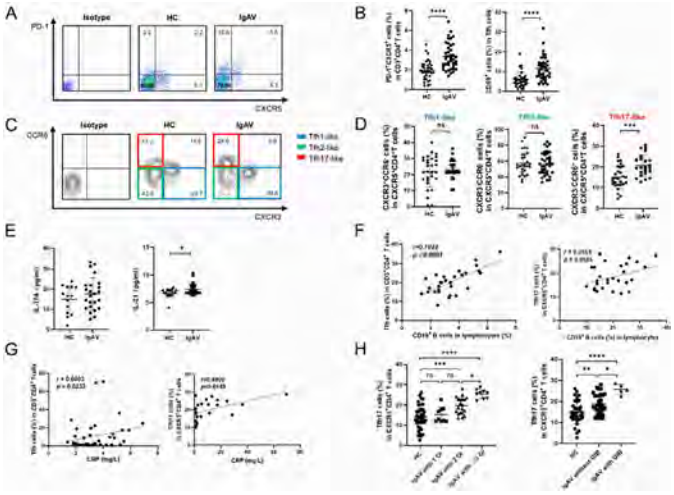
Abstract Number: 1250

Local Inflammatory Response Mediated by the Homing of Tfh17 Cells Is Involved in Tissue Injury of Immunoglobulin a Vasculitis

Xiaoxue Ma, Qinglian Jiang and Xuyang Chi, The First Hospital of China Medical University, Shenyang, China

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM



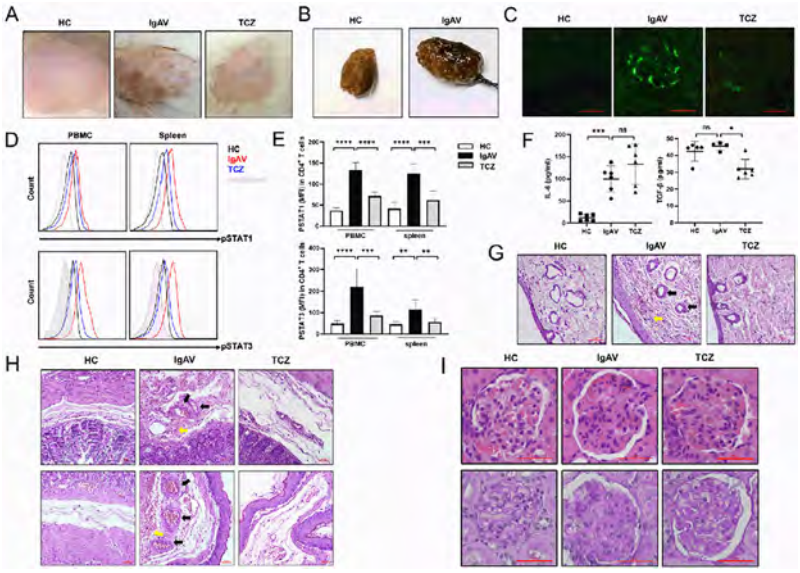
Circulating CD4+CXCR5+CCR6+ Tfh17 cells are increased and associated with IgAV disease severity. PBMCs and serum were isolated from the peripheral blood of IgAV patients and HCs without incubation. (A) Representative flow cytometry plots showing the percentage of circulating PD-1+CXCR5+ Tfh cells in CD3+CD4+ T cells. (B) Scatter plots showing the frequencies of circulating PD-1+CXCR5+ Tfh and CD69+ activated cTfh cells in CD3+CD4+ T cells. (C, D) Representative flow cytometry plots and scatter plots showing the percentages of cTfh1, cTfh2, and cTfh17 subsets in circulating CD3+CD4+CXCR5+ Tfh cells. (E) Serum levels of IL-17A and IL-21 evaluated by ELISA (25 of 40 IgAV patients were randomly selected and tested). Correlations of (F) frequencies of CD19+ B cells in lymphocytes (32 of 40 IgAV patients were randomly selected and tested) and (G) serum CRP levels with the percentages of cTfh cells and cTfh17 cells from IgAV patients. (H) Frequencies of circulating CXCR3–CCR6+ Tfh17 cells in circulating CD3+CD4+CXCR5+ Tfh cells from HC and IgAV patients grouped by the organ involvement (OI) number or the presence of gastrointestinal bleeding (GIB). ns: not significant; *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001.

Background/Purpose: Immunoglobulin A vasculitis (IgAV), also named Henoch–Schönlein purpura, is a systemic vasculitis characterized by the deposition of IgA1-dominant immune complexes in small vessels that often involves the skin, joints, gastrointestinal tract, and kidney. Research indicated increased frequencies of circulating activated B cells and plasmablasts in IgAV, which may serve as the source of

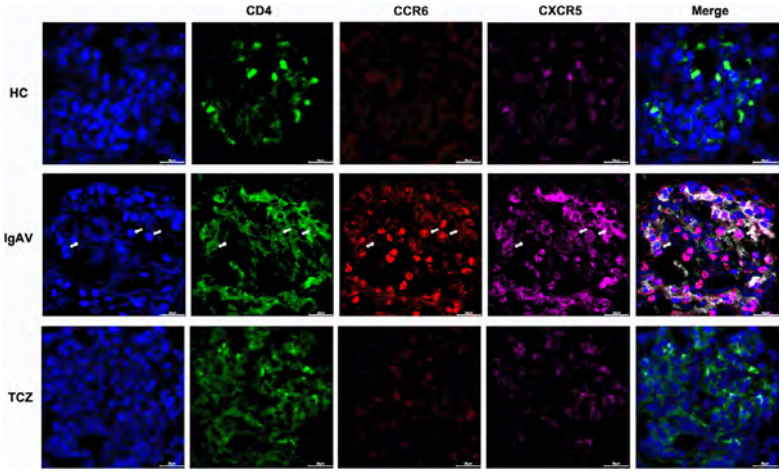
the rising IgA levels. T follicular helper (Tfh) 17 cells are considered to support B cells to switch to high-affinity IgA production. Previous study has confirmed that Tfh17 cells increase in the peripheral blood of IgAV patients. To evaluate the pathological role and the contribution in local tissue damage of Tfh17 cells in IgAV, we investigated the mechanism responsible for the differentiation of Tfh17 and the production of IgA in IgAV patients and IgAV rats respectively, and explored how to ameliorate IgAV by modulating Tfh17 generation.

Methods: Renal biopsy samples and peripheral blood mononuclear cells from IgAV patients were analyzed respectively by immunofluorescence staining and flow cytometry. In vitro culture was performed to assess the modulation of cytokine-induced phenotypes. IgAV rat model was established by intragastric administration of mixed solution, intraperitoneal injection of ovalbumin and Freund's adjuvant. IgAV rats were used to explore the therapeutic effects of regulating Tfh17 cells. Serum cytokine and IgA levels were measured by ELISA while histopathological changes were evaluated by H&E and PAS staining. Flow cytometry and immunofluorescence staining were used to detect T cell and GC B cell phenotypes and homing characteristics in circulation and tissues of IgAV rats.

Results: Frequency of CD4+CXCR5+CCR6+Tfh17 cells were increased in the circulation and organization of IgAV patients and associated with disease severity. The increased expressions of CD103, CCR6, CCR9 lead to the homing and residence characteristics of Tfh17 cells, resulting in local inflammatory response. Suppression of Tfh17 cells reduced the production of IgA and greatly ameliorated clinical symptoms and decreased IgA deposition and mesangial proliferation in the kidney in IgAV rats.



Suppressing Tfh17 using tocilizumab ameliorates symptoms in the IgAV rat. SD rats were respectively assigned to HC, IgAV, and TCZ groups. Representative photographs showing (A) hemorrhagic rash and (B) bloody stool from the three groups. Representative immunofluorescence images (C) showing renal IgA deposition from the three groups. (D, E) PBMCs and spleen cells were isolated from the three groups. Representative flow cytometry line graphs (D) and bar graphs (E) showing the expression of pSTAT1 and pSTAT3 in CD4+ T cells. (F) Serum levels of IL-6 and TGF-β in the three groups (the serum TGF-β level was tested in 5 rats from the HC group, 4 rats from the IgAV group, and 6 rats from the TCZ group). Representative photomicrographs showing H&E-stained sections of (G) skin and (H) intestinal (upper) and gastric (lower) tissues from the three groups. Black arrows indicate thickened vessel walls, hemangiectasis, and hyperemia; yellow arrows indicate extravasated erythrocytes. (I) Representative photomicrographs showing H&E-stained (upper) and PAS-stained (lower) sections of the kidney from the three groups. Scale bar = 50 μm. MFI: mean fluorescence intensity; ns: not significant; *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001.



Expression of Tfh17 cells in the renal tissue of IgAV rat. Multichannel confocal immunofluorescence staining of human renal tissue for CD4, CCR6 and CXCR5 with composite multiplexed images (scale bar: 20 lm). Arrowheads indicate representative CD4+CCR6+ CXCR5+ Tfh17 cells.

Conclusion: Our findings suggest that suppression of Tfh17 differentiation can alleviate IgA-mediated vasculitis and inflammatory tissue damage, which may permit the development of tailored medicines for treating IgAV.

Disclosure: X. Ma: None; **Q. Jiang**: None; **X. Chi**: None.

Abstract Number: 1251

Neurologic Manifestations of Pediatric Sjogren's Disease Patients: Case Series from an Academic Children's Hospital

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The prevalence of Sjogren's disease (SD) is becoming increasingly recognized in pediatric rheumatology. Despite fewer sicca symptoms, it has been shown that pediatric SD (pSD) patients experience neurologic manifestations at a rate higher than their adult counterparts. This case series aims to identify the neurologic manifestations and associated characteristics of pediatric patients with SD at a single academic institution.

Methods: Billing codes, age parameters, and encounter dates were used to identify patients diagnosed with SD prior to 18 years of age and seen between November 1, 2011 and August 15, 2022. 79 charts were initially identified (Figure 1). Charts were reviewed to confirm that patients had a diagnosis of pSD or connective tissue disease (CTD) with SD features. Set search terms were then applied to find patients who met inclusion criteria for neurologic manifestations. Patient demographics, serologies, neurologic manifestations, evaluation, and management were manually extracted. IRB approval was obtained for retrospective chart review.

Results: Twenty-eight pediatric patients were evaluated in the specified time frame and diagnosed with pSD/CTD. Thirteen of these patients (46%) had neurologic manifestations. Of these, 62% (8/13) had sicca symptoms and 77% (10/13) had arthralgia at diagnosis. 85% of patients with neurologic manifestations were female. 46% of patients were identified as white,

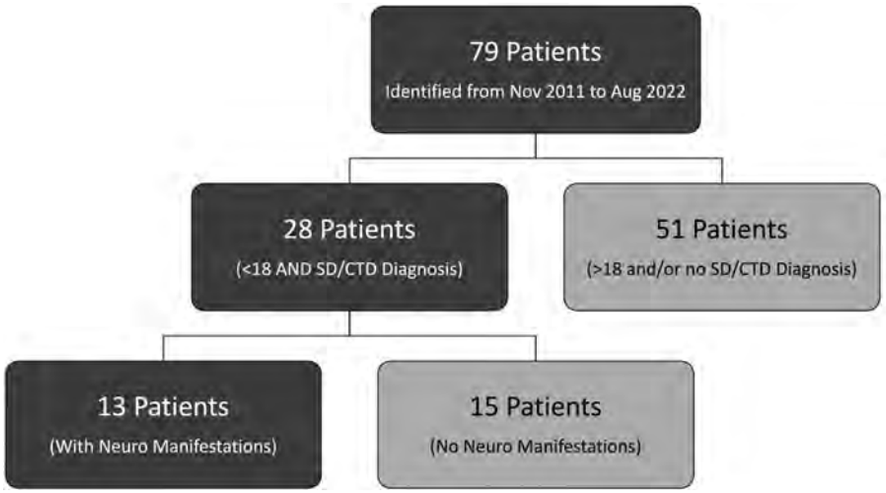

Figure 1

31% as black, and 23% as Hispanic/Latina/o/x. Additional demographic information and testing results can be found in Table 1. The most common neurologic manifestations in pSD patients were headaches and sensory changes, which occurred in eight patients (62%) and seven patients respectively (54%). Six of the eight patients with headaches were

Table 1

Table 1. Patient Demographics and SD Diagnostic Testing

Patient	Age at Other Diagnoses (Years)	Age at SD Diagnosis (Years)	Sex	Race/Ethnicity	Sicca Sx	Arthralgia	ANA	Anti-Ro/SSA	Anti-La/SSB	Anti-Smith	Anti-RNP	Anti-dsDNA	RF	C3	C4	CRP	ESR	IgG	Total Protein	SD Diagnostic Testing	ACR/EULAR Criteria
1	15 (UCTD)	22	F	White	+	+	+	+	+	-	-	-	+	103 mg/dL	**10 mg/dL**	4 mg/L	16 mm/hr	**2220 mg/dL**	8.2 g/dL	None	-
2	-	10	M	Black	+	+	+	+	+	-	-	-	+	153 mg/dL	18 mg/dL	**40 mg/L**	**66 mm/hr**	**1573 mg/dL**	7.1 g/dL	Schirmer - Negative	-
3	-	16	M	White	After Dx	After Dx	+	+	-	-	-	-	-	150 mg/dL	23 mg/dL	<3 mg/L	4 mm/hr	1136 mg/dL	7.9 g/dL	Schirmer - Negative	-
4	10 (JIA) 19 (SLE)	14	F	Black	After Dx	+	+	+	+	-	-	-	NP	**77 mg/dL**	**14 mg/dL**	<3 mg/L	**48 mm/hr**	NP	**9.2 g/dL**	None	-
5	16 (UCTD)	20	F	White	+	+	+	+	+	-	-	-	NP	95 mg/dL	19 mg/dL	-	8 mm/hr	NP	7.1 g/dL	None	-
6	15 (CTD)	13	F	White	+	+	-	-	+	-	-	-	-	140 mg/dL	28 mg/dL	NP	2 mm/hr	NP	7.5 g/dL	None	-
7	18 (UCTD)	14	F	Black	After Dx	After Dx	+	+	+	-	+	-	+	111 mg/dL	22 mg/dL	NP	**28 mm/hr**	**2849 mg/dL**	NP	US - Positive	-
8	-	11	F	White	+	+	+	+	+	-	-	-	+	-	-	**10 mg/L**	**33 mm/hr**	**2380 mg/dL**	8.3 g/dL	US - Positive	-
9	-	15	F	White	+	+	+	+	-	-	-	-	+	119 mg/dL	22 mg/dL	**12 mg/L**	**42 mm/hr**	**2228 mg/dL**	**9.3 g/dL**	Schimer - Negative	-
10	-	17	F	Hispanic/Latinx	After Dx	+	+	+	NP	NP	NP	NP	-	133 mg/dL	**14.9 mg/dL**	2.6 mg/L	**28 mm/hr**	835 mg/dL	7.2 g/dL	None	-
11	-	14	F	Hispanic/Latinx	+	+	+	+	-	-	+	-	-	**15 mg/dL**	**<1.7 mg/dL**	3 mg/L	11 mm/hr	**2570 mg/dL**	**8.9 g/dL**	None	-
12	-	16	F	Black	-	-	+	+	-	-	-	-	-	189 mg/dL	53.3 mg/dL	**17.8 mg/L**	**58 mm/hr**	1490 mg/dL	**8.5 g/dL**	None	-
13	-	14	F	Hispanic/Latinx	+	+	+	+	-	-	-	-	-	92 mg/dL	**17 mg/dL**	<3 mg/L	2 mm/hr	1151 mg/dL	6.9 g/dL	• Schirmer – Positive but Did Not Meet Criteria • US - Positive	-

Legend:
NP = Not performed + = Performed and positive - = Performed and negative **Bold** = Elevated based on individual lab range

Table 2

Table 2. Neurologic Manifestations and Treatment

Patient	Time from Diagnosis to Neuro Symptoms	Neuro Symptoms	Work-up	Neuro Consult	Timing of Consult	Diagnoses	SD Meds	SD Med Changes for Neuro Symptoms	Other Med Changes for Neuro Symptoms
1	4 years	• Confusion • Stuttering	• MRI/MRA/MRV Brain	N	-	• No neuro diagnosis	• GC • HCQ	• None	-
2	At diagnosis	• Dysmetria • Speech difficulty • Unsteady gait • Tongue fasciculations	• MRI/MRA Brain • LP	Y	R → N	• Aseptic meningitis	• MTX • HCQ	• GC added	
3	Prior: 2 years	• Headaches	• MRI Brain	Y	R → N	• Migraine	• HCQ	• None	• Topiramate (Prior to Diagnosis) • Amitriptyline (Migraine)
4	At diagnosis	• Ataxia • Antalgic gait • Sensory deficit • Decreased proprioception • Adie tonic pupil • Bladder incontinence	• MRI Brain • MRI Complete Spine • LP • EMG • Sural nerve biopsy	Y	R → N	• Sensory Neuropathy • Sensory Ataxia • Mononeuritis multiplex	• GC • HCQ • MTX	• RTX added • IVIg added	
5	Prior: 1 year	• Headaches with intermittent aura • Lightheadedness • Memory impairment	• MRI/MRA Brain	Y	R → N	• Migraine • Tension Headache	• HCQ	• None	• Butalbital/Acetaminophen/Caffeine (Migraine)
6	Prior: 10+ years	• Headaches	• MRI Brain + Orbits	Y	R → N	• Migraine • NSAID overuse headache	• GC • HCQ • MTX	• None	• Flexeril (Headache) • Butalbital (Headache) • CoQ10 (Migraine)
7	Prior: 3 years	• Headaches	• MRI/MRA Brain	Y	R → N	• Migraine	• HCQ	• None	• CoQ10 (Migraine) • Magnesium (Migraine) • Amitriptyline (Migraine)
8	2 months	• Tingling and burning in arms and legs		Y	R → N	• Small fiber neuropathy	• HCQ • MTX • AZA • Belimumab	• GC added	
9	1 month	• Headaches • Tingling in hands and feet	• MRI/MRA/MRV Brain • Serum NMO/AQP4 testing	Y	R → N	• Generalized headaches • Small fiber neuropathy	• GC • HCQ	• GC increased • HCQ increased	-
10	Prior: 5 years	• Tremors • Pins and needles sensation • Weakness in arms/legs • Headache	• MRI Brain + C-Spine • EMG	Y	R → N	• Paresthesia, • Migraine	• GC • HCQ • AZA	• None	
11	2 weeks	• Tingling and burning in hands and feet • Decrease to pinprick and temperature sensation • Memory impairment • Headaches	• MRI/MRA/MRV Brain • Neuropsych testing	Y	R → N	• Chronic headache • Small fiber neuropathy • Mild neurocognitive disorder	• GC • HCQ • AZA • RTX	• GC added/increased • RTX restarted	• Gabapentin (Neuropathic Pain) • B12/Magnesium Supplement (Headache)
12	Prior: 2 years	• Loss of motor function on half of face • Loss of taste on half of tongue • Sensation changes on half of face	• CT Brain • MRI Brain	Y	N → R	• Recurrent Bell's palsy	• HCQ	• None	• GC (Prior to Diagnosis) • Acyclovir (Prior to Diagnosis)
13	Prior: 1 year	• Headaches • Shooting pains • Decreased sensation	• MRI Brain + C-Spine	Y	N → R	• Migraine • Neuropathic pain • Small fiber neuropathy	• GC • HCQ • MTX	• None	• Sertraline (Chronic Pain) • B12/Mag Supplement (Migraine) • Cymbalta (Chronic Pain/Neuropathic Pain) • Gabapentin (Neuropathic Pain)

Legend:
GC = Glucocorticoids HCQ = Hydroxychloroquine MTX = Methotrexate AZA = Azathioprine RTX = Rituximab
N → R = Neurology referral to Rheumatology R → N = Rheumatology referral to Neurology

diagnosed with migraines, and four of the seven patients affected by sensory changes were diagnosed with small fiber neuropathy. Other diagnoses included mononeuritis multiplex (1/13), aseptic meningitis (1/13), recurrent Bell's palsy (1/13), and mild neurocognitive disorder (1/13). All neurologic manifestations, timing with regard to pSD diagnosis, work-up, and treatments are in Table 2. For ~70% of patients (9/13), neurologic manifestations began prior to or at the time of their pSD diagnosis. For patients with symptoms occurring prior to pSD diagnosis, all symptoms occurred one or more years prior. Five patients (38%) had treatment regimen changes due to their neurologic manifestations. Adjustments included the addition or increase of glucocorticoids (4/13), the addition of rituximab (2/13), the addition of IVIg (1/13), and an increase in hydroxychloroquine dose (1/13).

Conclusion: Neurologic manifestations occurred in nearly half of pSD patients. Migraines and small fiber neuropathy, which are more frequently seen in SD patients, were the most common pSD neurologic manifestations. For pediatric patients with neurologic symptoms of unknown etiology and pediatric patients with other rheumatologic diagnoses, pSD should remain in the differential as a possible diagnosis to explain their neurologic symptoms.

Disclosure: M. Faison: None; **C. Lavallee**: None; **J. McDonald**: None; **C. Edens**: None.

Abstract Number: 1252

Physician Global Assessment of Disease Activity in Childhood-Onset Systemic Lupus Erythematosus – Does the Approach Matter?

Ekemini Ogbu[1], Hermine Brunner[2], Jennifer Huggins[3], Angela Merritt[3], Megan Quilan-Waters[3], Catherine Robben[3], Chen Chen[3], Daniel J Lovell[4] and Bin Huang[3], [1]Cincinnati Children's Hospital Medical Center, University of Cincinnati School of Medicine, Johns Hopkins University, Cincinnati, OH, [2]Cincinnati Children's Hospital Medical Center, Division of Rheumatology, Cincinnati, OH, [3]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [4]UC Department of Pediatrics, Cincinnati Children's Hospital, University of Cincinnati, Cincinnati, OH

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Physician Global Assessment of Disease Activity (PhGA) are commonly used outcome measures in pediatric rheumatology. For childhood-onset systemic lupus erythematosus (cSLE), the traditional visual analog scale (range: 0 – 10; 0=inactive; 10=very active; $PhGA_{0\text{-}10}$) but also the SELENA-SLEDAI (range: 0-3; 0= none, 1=mild, 2=moderate, 3=severe; $PhGA_{0\text{-}3}$) are used to measure treatment response, flare, and Lupus Low Disease Activity Status (LLDAS) with $PhGA_{0\text{-}3} \leq 1$. Thus, the purpose of this study was to compare the measurement properties of the $PhGA_{0\text{-}10}$ and the $PhGA_{0\text{-}3}$ in cSLE and with scores of the SLEDAI-2k, and the SELENA-SLEDAI.

Methods: Secondary data analysis from a convenience sample of 100 cSLE followed every 3 months for up to 7 visits (1). Ratings of $PhGA_{0\text{-}10}$, $PhGA_{0\text{-}3}$, parent assessment of patient well-being (ParGA; range: 0= very poorly, 10=very well), SLEDAI-2k and SELENA-SLEDAI were compared. After linear transformation of $PhGA_{0\text{-}10}$ to a 0-3 range ($tPhGA_{0\text{-}10}$) frequency of $PhGA_{0\text{-}3} \leq 1$ were compared.

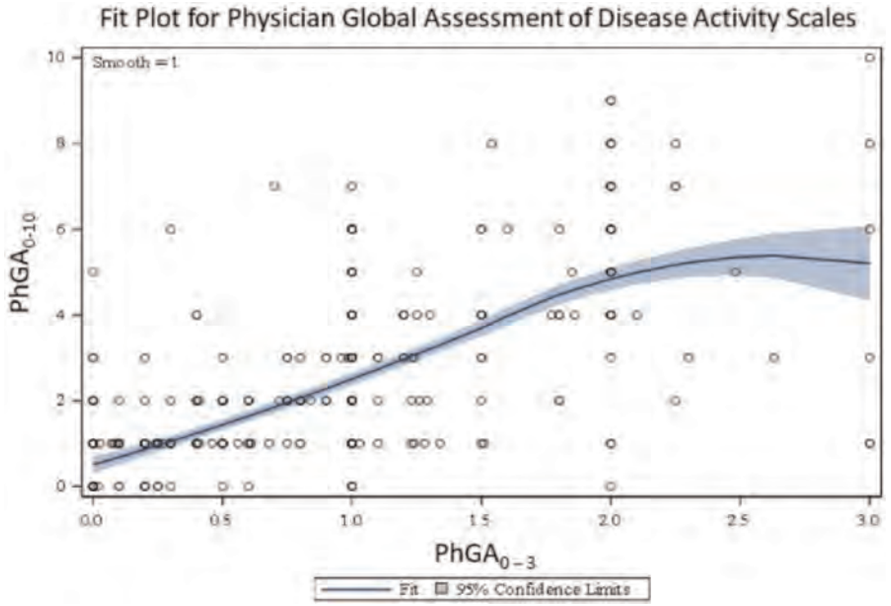

Figure 1: Relationship of Physician Global Assessment of Disease Activity traditional visual analog scale (PhGA0-10) with the SELENA-SLEDAI scale (PhGA0-3)

Results: In 601 visits, mean (SD)/median (range) of $PhGA_{0-10}$, $PhGA_{0-3}$, SLEDAI-2K and SELENA-SLEDAI were 2.13 (1.87)/2 (0-10), 0.79 (0.64)/1(0-3), 4.63 (4.14)/ 4 (0-28) and 4.51 (4.1) / 4 (0-32) respectively. $PhGA_{0-10}$ were moderately correlated with $PhGA_{0-3}$ (r=0.73; p< 0.0001; Figure 1) with more variability for $PhGA_{0-3} \geq 2$. ParGA was weakly correlated with $PhGA_{0-10}$, $PhGA_{0-3}$, SLEDAI-2k and SELENA-SLEDAI scores (r = -0.34, -0.30, -0.19 and -0.20). SELENA-SLEDAI and SLEDAI-2k scores were highly (r=0.98) correlated with each other. However, SLEDAI-2K/SELENA-SLEDAI scores were weakly correlated with $PhGA_{0-3}$ (r=0.28/0.28; p < .001) and moderately correlated with $PhGA_{0-10}$ (r= 0.56/0.54; p < .0001). There were 490/497 of 601 visits with $PhGA_{0-3} \leq 1$ / $tPhGA_{0-10} \leq 1$ [Kappa (SE) =0.59 (0.04), McNemar p=0.4].

Conclusion: Using the traditional $PhGA_{0-10}$ in cSLE yields almost identical LLDAS rates compared to the $PhGA_{0-3}$. Given its closer association with the scores of disease activity indices in cSLE, use of the $PhGA_{0-10}$ may be preferable in pediatric populations.

References: (1) Mina R, Klein-Gitelman MS, Nelson S, Eberhard BA, Higgins G, Singer NG, Onel K, Tucker L, O'Neil KM, Punaro M, Levy DM, Haines K, Martini A, Ruperto N, Lovell D, Brunner HI. Validation of the systemic lupus erythematosus responder index for use in juvenile-onset systemic lupus erythematosus. Ann Rheum Dis. 2014 Feb;73 (2):401-6. PMID: 23345596.

Disclosure: E. Ogbu: None; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb (BMS), 2, 5, Celgene, 2, Eli Lilly, 2, 5, EMD Serono, 2, F-Hoffman La Roche, 2, 5, GlaxoSmithKlein (GSK), 2, 5, 6, Horizon, 2, 2, Janssen, 5, Merck, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6; **J. Huggins**: None; **A. Merritt**: None; **M. Quilan-Waters**: None; **C. Robben**: None; **C. Chen**: None; **D. Lovell**: Abbott, 2, 6, AbbVie, 2, Amgen, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Canadian Arthritis Society, 1, Celgene, 2, Forest Research, 1, GlaxoSmithKlein(GSK), 2, Hoffmann-La Roche, 2, Janssen, 2, NIH-NIAMS, 1, Novartis, 2, 6, Pfizer, 2, United Bioscience Corporation, 2, Wyeth, 2; **B. Huang**: None.

Abstract Number: 1253

The Novel Florida Scoring System: A Machine Learning-Based Stratification of Clinical and Laboratory Features in Children with Suspected Sjögren's Disease

Akaluck Thatayatikom[1], Wenjie Zeng[2], Tyler Lovelace[3], Nicole Winn[4], Ankit Shah[5], Thomas Schrepfer[6], Indraneel Bhattacharyya[7], Renato Gonik[8], Panayiotis Benos[2] and Seunghee Cha[9], [1]AdventHealth for Children, Orlando, FL, Orlando, FL, [2]University of Florida College of Public Health and Health Professions and College of Medicine, Gainesville, FL, [3]Department of Computational & Systems Biology, University of Pittsburgh School of Medicine, Pittsburgh, PA, [4]Division of Oral Medicine, Department of Oral and Maxillofacial Diagnostic Sciences, University of Florida College of Dentistry, Gainesville, FL, [5]Department of Ophthalmology, University of Florida College of Medicine, Gainesville, FL, [6]Division of Pediatric Otolaryngology, University of Florida College of Medicine, Gainesville, FL, [7]Department of Oral & Maxillofacial Diagnostic Sciences, University of Florida College of Dentistry, Gainesville, FL, [8]Division of Pediatric Neurology, University of Florida College of Medicine, Gainesville, FL, [9]Department of Oral & Maxillofacial Diagnostic Sciences, University of Florida College of Dentistry and Center for Orphaned Autoimmune Disorders (COAD), Gainesville, FL

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Childhood Sjögren 's disease (cSjD) is a poorly defined systemic autoimmune disorder. Due to the absence of diagnostic criteria, heterogeneous presentations, and the dissimilarity between adult- and childhood-onset diseases, diagnosing and managing symptomatic children suspected of having cSjD is challenging. Currently, no clinical guidelines for these children are available. The study aims to propose a novel Florida Scoring System (FSS) for the stratification of heterogenous clinical and laboratory features of children with suspected cSjD condition.

Methods: A total of 191 clinical and laboratory variables from 217 patients enrolled between January 2018 and March 2022 were subject to our machine learning analysis. These patients with suspected cSjD were referred from Pediatric Rheumatology Clinics at the University of Florida (UF) in Gainesville and AdventHealth for Children in Orlando to the UF Center for Orphaned Autoimmune Disorders to rule out/rule in cSjD with further work-ups. In the absence of any established cSjD diagnostic criteria, the final cSjD diagnosis was made based on the 2016 ACR/EULAR criteria for adult SjD.Latent class analysis (LCA) was performed on 33 clinical/laboratory variables from 191 variables to stratify heterogeneous patient features. Artificial neural networks (ANN) and other machine learning models were constructed for internal validation and ranking of variable importance. Along with LCA and internal validations, causal graphical learning identified key variables, which became the foundation for the final FSS.

Results: Three distinct classes were defined by the LCA model. Machine learning models, including random forest, gradient-boosted decision tree, partial least square discriminatory analysis, LASSO-penalized ordinal regression, and ANN, accurately predicted three classes and ranked similar variable importance consistently. The causal graph model identified eight essential variables for inferring LCA-derived patient classes. FSS was developed using weighted points with a maximum of 24. As shown in Table 1,the final FSS score is the summation of subjective and objective features without requiring a lip biopsy, Schirmer test, SICCA ocular staining, and/or sialometry. If the FSS score >11, children with suspected cSjD are classified as Class I. Those with score >6 and ≤11 are classified as class II, and those with score < 6 are classified as class III. Out of the patients who fulfilled the 2016 criteria, the percentages in Classes I, II, and III were 70%, 18%, and 14%, respectively ($p < 0.001$). The characteristics of each class are listed in Table 2.

Table 1. Proposed Florida Scoring System (FSS) for children with clinical suspicion of cSjD using weighted points between the minimum of 0 and maximum of 24

Table 1. Proposed Florida Scoring System (FSS) for children with clinical suspicion of cSjD using weighted points between the minimum of 0 and maximum of 24.

Item	Weighted Points[†]
***Subjective score*[‡]**. *Each ESSPRI score will be multiplied by the weighted points and added together. The final sum will be divided by 10.*	
ESSPRI-Dryness	4
ESSPRI-Fatigue	3
Objective score. *Each present item will be weighted by the point below and added together.*	
Cytopenia[§]	5
Hypergammaglobulinemia[**]	4.5
Anti-SSA	3
ESSDAI Articular Domain[††]	2.5
SGUS	2
Final Classification	**Summation of subjective and objective scores**
Class I	FSS score >11
Class II	6 < FSS score ≤ 11
Class III	FSS score ≤ 6

[†] Points for weighting were generated by the coefficients from the ordinal regression model.

[‡] In the case of children who cannot report ESSPRI scores, parents can report subjective dry mouth and fatigue as "yes" or "no". If "yes", dry mouth will be weighed as "4" and fatigue as "3".

[§] Cytopenia: defined as the reduction of one or more mature blood cell types (e.g., neutropenia, lymphopenia, thrombocytopenia, and any type of anemia) in the peripheral blood.

[**] Hypergammaglobulinemia: above the reference range by age.

[††] Articular domain in ESSDAI (arthritis or arthralgia with morning stiffness) objectively evaluated by a specialist.

Conclusion: We propose the novel FSS, a physician-friendly scoring system, to stratify clinical/laboratory features of children with cSjD. Further evaluation of FSS with new cohorts will ensure the clinical usefulness of FSS for early recognition, diagnostic workup, and monitoring.

Table 2. Clinical characteristics of three classes

Table 2. Clinical characteristics of three classes

	Class I (n = 27)	Class II (n = 98)	Class III (n = 92)
FSS score			
	FSS score >11	6 < FSS score ≤ 11	FSS score ≤ 6
Patients fulfilling the 2016 criteria (%)			
	70% (n = 19/27)	18% (n = 18/98)	14% (n = 13/92)
Overall characteristics			
	Prominent glandular and systemic symptoms with high prevalence of positive labs & SGUS	Prominent sicca/systemic symptoms and low prevalence in positive labs	Low prevalence of sicca, systemic symptoms, and labs
Clinical and laboratory characteristics*			
Laboratory features	High prevalence of: anti-SSA (81.5%) anti-SSB (40.7%) low C3 (30.8%) low C4 (38.5%) high IgG (55.6%) cytopenia (40.7%)	Low prevalence of: anti-SSA (8.6%) anti-SSB (5.2%) low C3 (1.1%) low C4 (8.7%) high IgG (1.0%) cytopenia (1.0%)	Low prevalence of: anti-SSA (6.7%) anti-SSB (7.8%) low C3 (1.3%) low C4 (7.9%) high IgG (3.3%) cytopenia (1.1%)
Positive SGUS	Highest (90.9%)	Lowest (5.41%)	21.0%
Sicca prevalence	55.6%	Highest (77.6%)	Lowest (13.2%)
Focus score	Highest:4.90 (SD 4.6)	Lowest: 0.96 (1.5)	1.25 (1.6)
ESSPRI	• Dryness (3.48) • Fatigue (3.30) • Pain (2.62)	Highest: • Dryness (5.63) • Fatigue (7.14) • Pain (4.82)	Lowest: • Dryness (1.62) • Fatigue (2.94) • Pain (1.35)
ESSDAI	Highest in: • Renal (51.9%) • Cutaneous (11.1%)	Highest in: • Articular (98%) • Muscular (63.0%) • Neurological (98%) such as dysautonomia (35.7%) • Gastrointestinal (82.7%)	Lowest in: • Articular (63%) • Muscular (26%)
Miscellaneous	• Articular (74.1%) • Highest prevalence of AIHA (18.5%)	• Highest prevalence of HSD/EDS (76.6%)	

Disclosure: A. Thatayatikom: None; **W. Zeng**: None; **T. Lovelace**: None; **N. Winn**: None; **A. Shah**: None; **T. Schrepfer**: None; **I. Bhattacharyya**: None; **R. Gonik**: None; **P. Benos**: None; **S. Cha**: None.

Abstract Number: 1254

Outcome of Pediatric Lupus in South Asia: Data from Indian SLE Inception Cohort for Research (INSPIRE)

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile onset SLE (jSLE) has more severe disease and has poorer outcome as compared to adults SLE. Ethnicity affects clinical course and disease outcome in SLE. There is a lack of data on outcomes from inception cohort of jSLE from South Asia.

Methods: Patients with SLE with ≥4 ACR classification criteria for SLE, who were enrolled in the Indian SLE inception cohort for research (INSPIRE) and had onset of symptoms before the age of 18 years were included. Data on their clinical features, autoantibodies, activity as well as short term outcome including death was extracted from the database at baseline and at every 6 months follow up for 24 months. Lupus low disease activity (LLDAS) was calculated. Baseline predictors of attainment of LLDAS and flare at 1 year were also studied. All variables with p=0.1 were put in multivariate analysis using binary logistic regression.

Results: Among 2503 patients enrolled in INSPIRE cohort 491(19.6%) had jSLE. Their mean age at onset of disease was 14.58+2.69 years and median duration of symptoms was 10 months. Major clinical features were : fever (84.5%). malar rash/ACLE (64.3%), oral ulcers (69%), pleural effusion (21%), Seizures (13%), Leucopenia (33%), and Class III/IV LN (17%) (Table 1), BILAG (A/B) in neuropsychiatric domain was present in 55, renal domain in 195, and gastrointestinal domain in 29 patients. Among autoantibodies, antibodies to dsDNA (71.9%), nucleosome (39%), histones (35%), RO_52 (30%), RO_60 (35%), La (11%), ribosomal P protein (38%), nRNP (51%), Sm (42%), Scl-70 (3%). The mean SLEDAI score was 13.05+ 8.19 and PGA score was 1.22+0.89. There were 47 deaths during 2-year follow-up period. The actuarial survival at 2 years was 83.6%. There was no difference in survival between patients with LN or those without it. (Figure 1). LLDAS was achieved at 1 year by 57.4% and at 2 years by 65.2% in patients who had completed that point of follow up (Table 2). Among those who achieved LLDAS at 12 months, in 78 where 24 month follow up was available, 59 (75%) had sustained remission. None of the clinical features or antibodies at baseline were major predictors of achieving LLDAS at 1 year. Presence of SCLE (p=0.049) and anti-Ro 52 antibody (p=0.049) reduced the odds of achieving LLDAS while presence of psychosis (p=0.033) and acute confusional state (p=0.022) increased the odds of achieving LLDAS at 12 months. The baseline factors associated with flare at 12 months were discoid rash (p=0.002), leucopenia (p=0.007), low C3 (p=0.027), low C4 (p=0.005) and anti-nucleosome antibodies (p=0.014). On multivariate analysis only anti-nucleosome antibodies (OR 0.503 (CI 0.270-0.935), serum C3 levels (OR 0.987 (0.976-0.998) and discoid rash (OR 2,617 (1.336-5.126) were significantly associated with flare.

Table 1: Baseline clinical features of the cohort

Feature	Value
Females: Males	433:58
Mean age (Years)	14.58+2.69
Median duration of symptoms (months)	11
Clinical features: number (%)	
Fever > 38.3 C	415 (84.5)
Oral ulcers	340 (69%)
Subacute cutaneous lupus	38(8%)
Acute cutaneous lupus	316(64.3%)
Discoid rash	90(18%)
Proteinuria>0.5g/24hr	193(39%)
Class II or V lupus nephritis	83(17%)
Class III or IV lupus nephritis	41(8 %)
Delirium	16(3%)
Psychosis	11(2%)
Seizure	65(13%)
Pleural effusion	105(21%)
Pericardial effusion	54(11%)
Leukopenia	602 (32%)
Thrombocytopenia	116 (24%)
Autoimmune hemolysis	93 (19%)
Low C3	375 (76.3%)
Low C4	296 (60.2%)

Conclusion: jSLE in India is associated with significant early mortality. Almost one-third patients do not achieve low disease activity even at 2 years of treatment. Thus, there is a need for better therapeutic options for lupus

Table 1: Baseline clinical features of the cohort

	6 months (N=381)	12 months (N=282)	18 months (N=189)	24 months (N=141)
Number of patients with				
SLEDAI =0	149	117	77	62
SLEDAI 1-4	152	98	69	45
SLEDAI 5-8	47	41	21	20
SLEDAI>8	33	26	22	14
Death	22	9	6	10
Prednisolone ≤7.5 mg	200 (53.84)	195 (69.1%)	137 (73.5%)	110(78.1%)
LLDAS	144 (37.7%)	162 (57.4%)	113 (59.8%)	92 (65.2%)
Disease flare	66	67	34	26

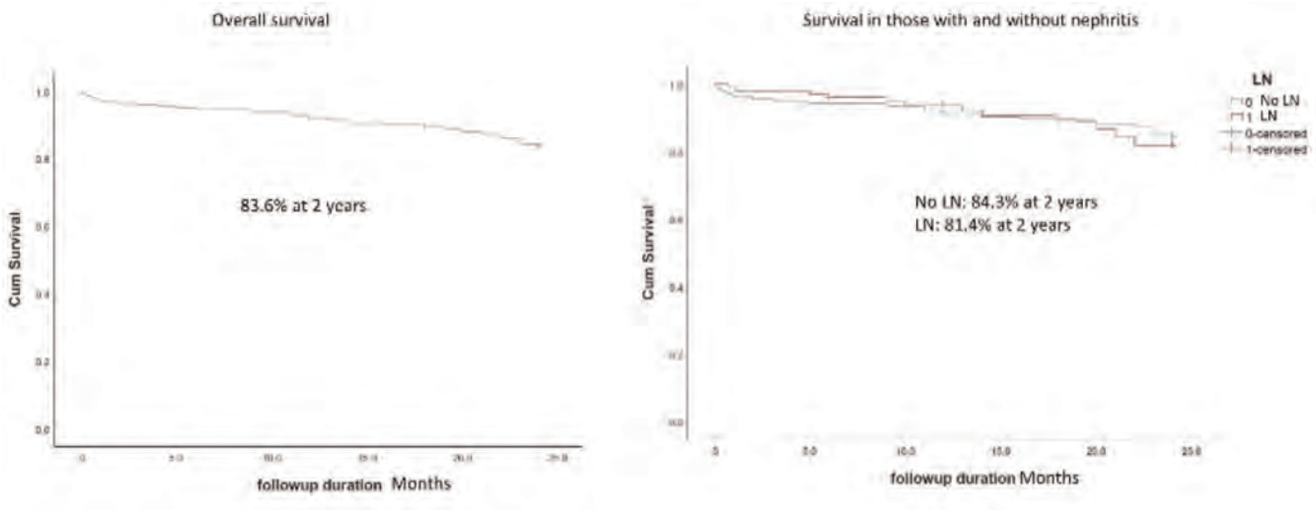

Figure 1: survival curve in total patients and in patients with and without nephritis

Disclosure: A. Aggarwal: None; **R. Gupta**: None; **L. Rajasekhar**: None; **A. Mathew**: None; **P. Ghosh**: None; **C. Kavadichanda**: None; **V. Shobha**: None; **B. Das**: None; **M. Rathi**: None; **A. Jain**: None; **A. Lawrence**: None.

Abstract Number: 1255

Clinical Characteristics and Disease Outcomes of anti-NXP2 Positive Juvenile Dermatomyositis: A Single Center Cohort

Sarah Molina[1], Dawn Gist[2], Marietta De Guzman[3], Eyal Muscal[4], Jamie Lai[2] and Maria Pereira[3], [1]Baylor College of Medicine - Pediatrics Residency Program, Houston, TX, [2]Baylor College of Medicine / Texas Children's Hospital, Houston, TX, [3]Baylor College of Medicine, Houston, TX, [4]Division of Rheumatology, Department of Pediatrics, Baylor College of Medicine, Houston, TX

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Pediatric Rheumatology – Clinical Poster II: Connective Tissue Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile dermatomyositis (JDM) is a rare idiopathic inflammatory myopathy with clinically heterogeneous presentations that can be categorized by myositis-specific antibodies (MSAs). NXP2 is among the more common of MSAs, seen in approximately 20-25% of cases. It is associated with an increased risk of severe muscle weakness, dysphagia, and vasculopathy which may cause gastrointestinal ulceration and bleeding. Children with NXP2 are described to be more resistant to conventional therapies and at risk for prolonged active disease. This retrospective chart review aims to provide additional data on 18 patients at one institution regarding clinical presentation, management, and outcomes.

Methods: With approval from our IRB, we reviewed the presentation, management, and outcomes of patients with positive NXP2-antibody JDM before 18 years old between January 2012 - May 2023. Data abstracted include clinical features, diagnostic studies, therapy at initial and follow up at 6-month, 12-month, and last clinic visit. Muscle strength was measured by muscle manual testing (MMT) and Childhood Myositis Assessment Scale (CMAS). Remission defined as CMAS >48 and/or documented full strength, absence of active skin and vascular disease, and normalized muscle enzymes.

Results: A total of 18 patients were included: 66% female, 50% Hispanic, with a median age of 8 years [4-12] at presentation; median time to diagnosis was 1.5 months [1-3]. All had progressive proximal lower extremity and neck muscle weakness. Proximal upper extremity weakness was seen in 83%, with bulbar weakness in 44% (*see Figure 1*). Initial median CMAS was 12 [10-18]. All had abnormal MRIs, with 83% showing diffuse myositis. 56% of patients had a muscle biopsy, which all but 1 were diagnostic of JDM. 83% of patients presented with cutaneous manifestations, two with calcinosis. 61% had periungual vascular changes. Gastrointestinal features were seen in 61%. Median duration of follow up was 36.5 months [24 –77]. CMAS at 12 months and the last visit were 43 and 48 [43-52], respectively. 56% reported dysphagia over time. Two patients required invasive feeding methods. Two developed skin ulcerations, 1 had bowel ulceration with perforations requiring partial colectomy with end-ileostomy creation, and 2 developed SMA syndrome from excessive weight loss. No lung or cardiac disease reported. Only 2 patients had a monophasic course. Progressive calcinosis was seen in 41% (*see Figure 2*). All received steroids and methotrexate, 94% IVIG, 89% hydroxychloroquine, 50% rituximab, and 22% required other biologic therapies (*see Figure 3*). Remission achieved in 44% after a median of 44 months of therapy [25.5 - 52.5]. No malignancy or deaths reported.

Demographics	Age (years)	8 (2 - 16)		
	Sex	Female, Male	56%, 44%	
	Race	Caucasian	72%	
		Black	17%	
		Asian	6%	
		American Indian	6%	
	Ethnicity	Hispanic	50%	
Clinical Characteristics	Cutaneous findings		83%	
		Gottron's Papules	61%	
		Heliotrope	56%	
		Shawl Sign	11%	
		Calcinosis	11%	
	Muscle disease		100%	
		Proximal Upper Extremities	83%	
		Proximal Lower Extremities	100%	
		Dysphagia	28%	
	Gastrointestinal symptoms		61%	
	Vascular changes		67%	
Diagnostic Studies at Presentation	Muscle Enzyme Abnormalities	CK median	1304 (144 - 2487)	*(normal 55 - 215)*
		Aldolase median	19 (13 - 25)	*(normal 3.4 - 8.6)*
		AST median	116.5 (75- 184)	*(normal 12 - 32)*
	MRI Dermatomyositis	Diffuse myositis	15/18	
		Abnormal subcutaneous fat signal	11/18	
		Fascial edema / abnormality	7/18	
	Miscellaneous tests	ANA positive	17/17	
		Other antibodies positive*	2/17	
		IgG elevated	3/11	

*positive includes TIF1, anti-Jo1, Scl70, RNP

Figure 1: Clinical Presentation in NXP2+ JDM

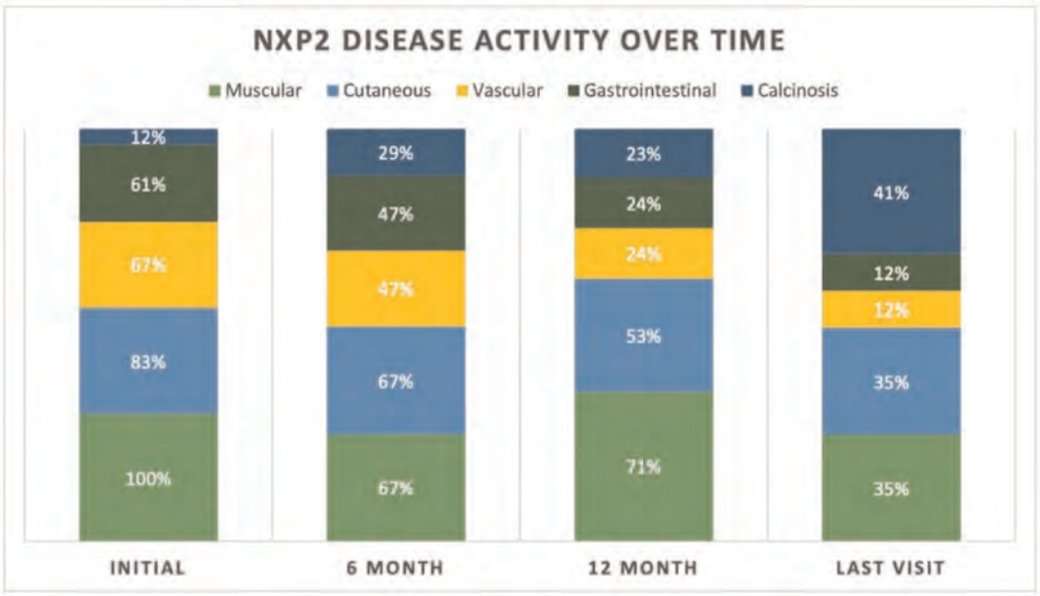

Figure 2: NXP2 Disease Activity Over Time

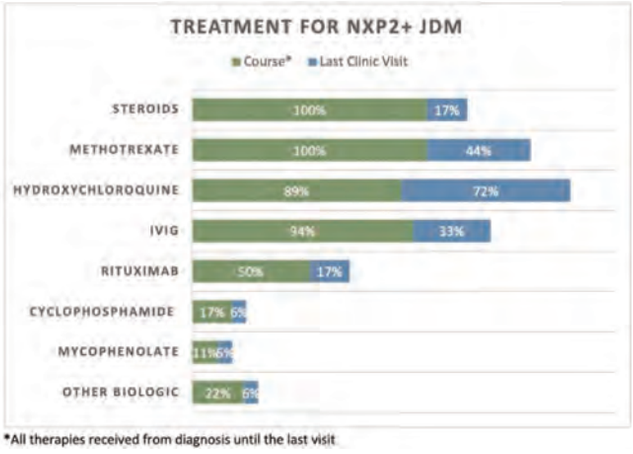

Figure 3: Treatment for NXP2+ JDM

Conclusion: Children with NXP2+ JDM in our cohort developed a chronic disease course where gastrointestinal features were common with complications that could be severe. Progressive calcinosis was seen despite aggressive therapies. Remission was achieved in 44% after prolonged therapy. Our patients provided information as to the challenges for supportive and multimodal immunotherapy. Additional large multi-center cohort studies are needed to determine the optimum treatment course with validated remission criteria.

Disclosure: S. Molina: None; **D. Gist**: None; **M. De Guzman**: None; **E. Muscal**: Sobi, 1, 11; **J. Lai**: None; **M. Pereira**: None.

Abstract Number: 1256

Self-esteem and Body Image of Young People with Rheumatic Diseases: A Systematic Review

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Psychology/Social Science – Interprofessional Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Little is known about the self-esteem and body image impact in young people with rheumatic and musculoskeletal diseases (RMD). Studies in chronic illness suggest that chronic health conditions can develop changes in appearance, or social activities disruption, consequentially body image and self-esteem can be altered mainly in young people. The purpose of this study was to synthesize existing research related to self-esteem and body image in young people with RMD.

Methods: Databases (MEDLINE, Embase, PsycINFO, and CINAHL) were searched until April 2023. Results were limited to English-language studies. Studies were screened and evaluated for inclusion by two investigators. The systematic review included: a) All original articles reporting self-esteem or body image of young people with RMDs ; b) Qualitative studies (data obtained through individual interview and/or focus groups), quantitative studies (information obtained through questionnaires) or c) mixed designs (articles including qualitative and quantitative methods) Case studies, letters to the editor and commentaries were excluded. Additionally, a manual search was undertaken wherein reference lists of selected articles were screened for inclusion.

Results: Twelve articles were eligible for inclusion in the present review. Eligible studies were identified for juvenile idiopathic arthritis (6), lupus (3), scleroderma (2), and vasculitis (1). As main results we highlight the following: Glucocorticoids use was found to consistently associate with poor body image, in all conditions (due to visible side-effects of medication). Greater body image concerns were associated with facial lesions, and the resulting perceived stigma (this appearance concern was also related to depression). Females showed lower self-esteem than males. Anxiety and apprehension about their physical and sexual attractiveness was associated with lower self-esteem. Feeling of restrictions in their experimentation with drinking and sexual relations also impacted their self-esteem. A lower self-esteem was associated with poor QoL, and regarding DMARDs treatments, use of IL-6 treatment improved self-esteem.

Conclusion: The use of disease-specific measures and the heterogeneous group of studies complicated the synthesis of the findings. However, some factors appeared most associated with poorer self-esteem and body image across disease groups. Young people with RMD, who already face additional medical and psychosocial burden, might benefit from monitoring tools and interventions designed to improve their body image and bolster self-esteem in the ongoing context of self-care and adherence. Moreover, understanding these issues can help in treatment planning, and clinical decision-making for this population.

Disclosure: L. Leon: Pfizer, 6; **D. clemente Garulo**: Eli Lilly, 5, GlaxoSmithKlein(GSK), 6, Pfizer, 6, Sanofi, 5; **C. Heredia**: None; **I. Abasolo**: None.

Abstract Number: 1257

The Psychological Experience of Work for People with Inflammatory Arthritis (IA)

Joan Westreich[1], Adena Batterman[1], Anna Balakrishnan[1], Roberta Horton[1], Minerva Nong[1], Vivian Bykerk[2] and Theodore Fields[1], [1]Hospital for Special Surgery, New York, NY, [2]Department of Rheumatology, Hospital for Special Surgery, New York, NY

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Psychology/Social Science – Interprofessional Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: A large body of research reports that people with inflammatory arthritis (IA) are at increased risk for work disability, which profoundly affects all aspects of life. While researchers describe the challenges that people with IA face in maintaining employment, these studies largely focus on addressing concrete barriers and strategies and inadequately explore psychosocial factors that may influence the ability to continue working. A EULAR taskforce recently released points

Table 1. Demographic Characteristics

Table 1. Demographic Characteristics (n=20)

Characteristic	N (%)	Characteristic	N (%)
Age		**Education**	
Median (IQR)	49 (37-59)	Some College	2 (10%)
20-29	2 (10%)	Graduated College	6 (30%)
30-39	3 (15%)	Post-graduate	12 (60%)
40-49	5 (25%)	**Employment Status***	
50-59	5 (25%)	Employed outside the home	2 (10%)
60-69	5 (25%)	Work full-time	9 (45%)
Gender		Work part-time	4 (20%)
Female	15 (75%)	Self-employed	5 (25%)
Male	4 (20%)	Not currently working	2 (10%)
Gender non-conforming	1 (5%)	Retired	1 (5%)
Race*		**Main source of financial support***	
American Indian/Alaska Native	2 (10%)	Own salary	14 (70%)
Asian	2 (10%)	Partner's salary	6 (30%)
Black or African American	6 (30%)	Social security	2 (10%)
White	13 (65%)	Retirement	1 (5%)
Other	1 (5%)	Other	3 (15%)
Ethnicity		**Years since diagnosis****	
Hispanic/Latino(a)/LatinX	3 (15%)	Median (IQR)	8.5 (5.0-18.0)
Not Hispanic/Latino(a)/LatinX	17 (85%)	0-5	6 (30%)
Relationship Status		6-10	5 (25%)
Married	7 (35%)	11-15	2 (10%)
Single	9 (45%)	15-20	3 (15%)
Divorced	4 (20%)	21+	2 (10%)
Insurance			
Commercial/Private	16 (80%)		
Medicare	2 (10%)		
Medicaid	2 (10%)		

*Race, Employment Status, and Main source of financial support: Categories are not mutually exclusive, so totals may add up to >100%

**Missing two responses for years since diagnosis

Table 2. Preliminary Themes and Illustrative Quotes

Table 2: Preliminary Themes and Illustrative Quotes

Theme	Illustrative Quote
Challenges to identity and pride *(The important role work plays in sense of identity, pride in achievements, struggle coping with IA and its impact at work.)*	"I always wanted to be a cop. I worked hard for about four years to try to get into an agency. It's very competitive. So, it was a long road to get there. I worked very hard to get there, worked very hard in the academy to finish and get certified. I loved what I did. ... In the position I currently hold, I am still able to go above and beyond because there are things that I can physically and emotionally do. If I am reassigned to other positions, such as doing surveillance or sitting in a car all day long for like seven or eight hours, obviously I will not be able to do that." (Female, works full-time)
Guilt, shame and ableism *(Guilt, shame and internalized ableism about one's diminished capacity and its impact at work)*	"There are still times, though, when it was tougher to do things, especially when my hands were bad, and I would have to help move things. You would feel guilty if you didn't help move things because, here I am, a guy in my 30s, and you know: 'Can you help me move this?' 'Kind of.' You don't want to look like you are being unhelpful, and so there's that psychological component to it as well." (Male, works full-time)
Managing perceptions *(Attempts to process and cope with real or imagined perceptions of family and/or colleagues)*	"I would want people to understand that when someone has RA and they go to work, they're really working two jobs or even three. One of them is performing as well as everyone else ... and then there is another job of having to manage one's energy and having to manage the perception of others." (Female, works part-time and self-employed)
Grappling with disclosure *(Weighing decisions re: whether or not to disclose condition at work, and the potential consequences)*	"I'm going to be honest. I have lied because with early childhood education they do not want you calling out if you don't feel well, or they don't want to hire someone who is older or not physically capable, because someone else has to pick up the slack. ... I had to be honest about the skin aspect, obviously, because it's there. So, I'll be like: 'Oh, I have psoriasis and blah blah,' but I will conveniently leave out how all-encompassing it can be. It's not just this, you know." (Female, self-employed)
Pushing through *(Internal/external pressure to be productive at work, presenteeism, absenteeism)*	"I think that I would never have been able to decrease my full-time hours. I think that I would never have been able to go part-time. I would have kept pushing because I would have had to. You know, there's no one to back me up. It's just me, right? And I would have never let up. And I would have eventually, I really believe, would have been on disability at some point because I would have pushed so hard that I wouldn't have been able to walk." (Female, not currently working)
Financial security *(The imperative to maintain employment to sustain living costs, medical insurance and healthcare)*	"I'm really glad I can work, and I earn enough money, and have insurance, but I'm also kind of upset that it's such a necessity...for me, I mean, I know it's a necessity for everybody, but it just feels like I have even less of a choice than I imagine other people might have." (Female, works full-time) "So, if I ever need motivation, to get motivated to get up and go to work in the morning, that might be the thing... I enjoy working, I feel like I may be more driven because, you know, the fact that I literally cannot afford to be unemployed and uninsured. (Female, works full-time)
Mental health impact *(Stress, anxiety, anger, depression, reflected in all study themes)*	"I would cry every Sunday before I would go in on Monday. I couldn't do it, like it was impacting how I was at home. I couldn't do it." (Female, self-employed)
Personal/professional support *(Plays an important role in an individual's ability to manage their IA at work. Support is complex, variable, vital to maintaining work, and often inadequate)*	"I feel a bit more supported by my family. It's as simple as someone having dinner for me now. Like, I don't have to worry about fixing dinner for myself, or you know, laundry or household chores." (Female, works full-time)
New perspectives, transformations, meaning-making *(Evolving priorities and values, shift in perspective, privileging self-care, and turning to spiritual practices and other forms of meaning-making)*	"Actually, one of my sons said I'm 'more human.' I'm choking up a little bit because when they were growing up I was not there, I was working. I'd come home at 3 o'clock [in the morning] and when I woke up they were already gone, they were at school. Sometimes I would pick them up, but it was rare... My younger son said I used to be very angry. I feel wholeheartedly that now they see the real me because before it was the 'worker me.' Before, I was a human working, now it is a human being." (Male, works part-time and self-employed)

to consider to support people with rheumatic and musculoskeletal diseases, highlighting that "work outcomes comprise … physical and mental health … but also personal and environmental factors. These contextual factors can be barriers as well as facilitators, and are of special interest if they are modifiable." (Boonen, 2023). This study, therefore, explores the psychological experience of people with IA in their efforts to maintain sustainable work while coping with their illness. Our aim is to report key psychosocial areas of exploration to be considered in a comprehensive evaluation of IA patients.

Methods: In a mixed methods qualitative study, a clinical social work researcher conducted semi-structured interviews with MD-diagnosed IA patients (18+ years, currently employed or within the past 5 years). Interviews were conducted via Zoom, averaged 1 hour in duration, and were recorded and transcribed verbatim. Participants were recruited from an NYC academic hospital by MDs, SWs, and by a community partner.

Using thematic analysis and NVivo software, 4 reviewers conducted preliminary analysis of data of 20 interviews to identify emerging themes. We also collected demographic information (*Table 1*).

Results: While 40 IA patients participated, we include here preliminary results from 20 interviews. Nine interrelated themes emerged *(Table 2)*: **Challenges to identity and pride** (achievements, coping with illness' impact on work); **Guilt or shame** (diminished capacity, internalized ableism); **Managing perceptions** (attempts to process and cope with perceptions of others); **Grappling with disclosure** (and potential consequences); **Pushing through** (internal/external pressure to function, presenteeism); **Financial security** (living costs, healthcare); **Mental health impact** (stress, anxiety, anger, depression reflected in all study themes); **Personal/professional support** (complex, variable, vital to sustaining work, often inadequate); and **New perspectives, transformations and meaning-making** (evolving priorities and values).

Conclusion: Preliminary findings demonstrate a significant psychological impact related to IA patients' efforts to maintain employment while coping with the challenges of their illness. This nuanced perspective is an important area of inquiry for a more holistic patient assessment and can inform multidisciplinary interventions to support IA patients at work. Continued analysis will further describe the diverse needs of people with IA across job type, gender, orientation, race, ethnicity and other factors.

Disclosure: J. Westreich: None; **A. Batterman**: None; **A. Balakrishnan**: None; **R. Horton**: None; **M. Nong**: None; **V. Bykerk**: AbbVie, 2, Bristol Myers Squibb, 1, 2, 5, Pfizer, 1, 2; **T. Fields**: Horizon Therapeutics, 2.

Abstract Number: 1258

"What Is My Risk Really?": A Qualitative Exploration and Ideal-Type Analysis of Preventive Interventions Among Individuals at Risk of Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Psychology/Social Science – Interprofessional Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: A preclinical phase of rheumatoid arthritis (RA), in which 'at-risk' individuals develop autoantibodies and/or symptoms and progress to clinical arthritis and classifiable RA, is well established (1). Emerging evidence suggests intervention in the pre-arthritis phase could reduce the risk of RA developing, delay onset and progression of RA, or reduce the severity of the condition should it develop (2). Preventive interventions include drug therapies and lifestyle changes. It is important that potential treatments are acceptable to at-risk individuals, particularly as RA prevention trials to date have demonstrated recruitment challenges (2). This study aimed to explore factors that would influence at-risk individuals' engagement with potential preventive interventions, including RA medication, antibiotics, probiotics, oral health treatment and maintenance, dietary changes, and smoking cessation.

Methods: This was a qualitative study employing a phenomenological approach. Anti-cyclic citrullinated peptide (anti-CCP) positive at-risk individuals with musculoskeletal symptoms but no synovitis were recruited from the Leeds CCP cohort. Individual semi-structured interviews were conducted via video or telephone between March-June 2022. Interviews were audio-recorded and transcribed verbatim and data were analyzed using reflexive thematic analysis. A secondary ideal-type analysis was subsequently conducted to understand different approaches to health-related behaviors.

Results: Nineteen CCP+ at-risk individuals (ten women; age range 35-70) participated. Three overarching themes were identified (Figure 1). Participants described distress related to ongoing symptoms and a burden of uncertainty regarding disease progression. Many participants had concerns about side effects of preventive RA medication and preventive antibiotics. In contrast, most participants expressed willingness to take a probiotic, and to make oral health and dietary changes with the aim of preventing RA. Participants' perceived engagement with preventive measures was influenced by symptom severity, personal risk level, comorbidities, experiences of taking other medications or supplements, knowledge of risk factors, and perceived effort. Three 'types' of participants were identified from the data: pro-active preventers (health-conscious, seek information and act on knowledge about being at-risk); change considerers (deal with health issues as they happen, rely on direct medical advice to make changes); fearful avoiders (worry about the future, limited engagement).

Conclusion: Our study suggests that having more severe symptoms, a higher personal risk level, increased knowledge about risk factors, and positive experiences of taking other medications would increase engagement with preventive interventions among CCP+ at-risk individuals, but that an individual's overall orientation to health behaviors also impacts on their

Figure 1. Themes

attitude towards preventing RA. These findings could inform recruitment and retention in pre-RA research and promote uptake of preventive interventions in clinical practice.

References

1. MankiaK. Arthritis Rheumatol 2016.
2. Falahee M. Front Immunol. 2022.

Disclosure: L. Chapman: None; **H. Siddle**: None; **S. Serban**: None; **K. Mankia**: Abbvie, 6, Eli Lilly, 5, Galapagos, 6, Gilead, 5, Serac Lifesciences, 6; **C. Rooney**: None; **Z. Mustufvi**: None; **S. Pini**: None; **K. Vinall-Collier**: None.

Abstract Number: 1259

Voices Unheard: Unmasking the Hidden Challenges of Youth with Rheumatic Diseases

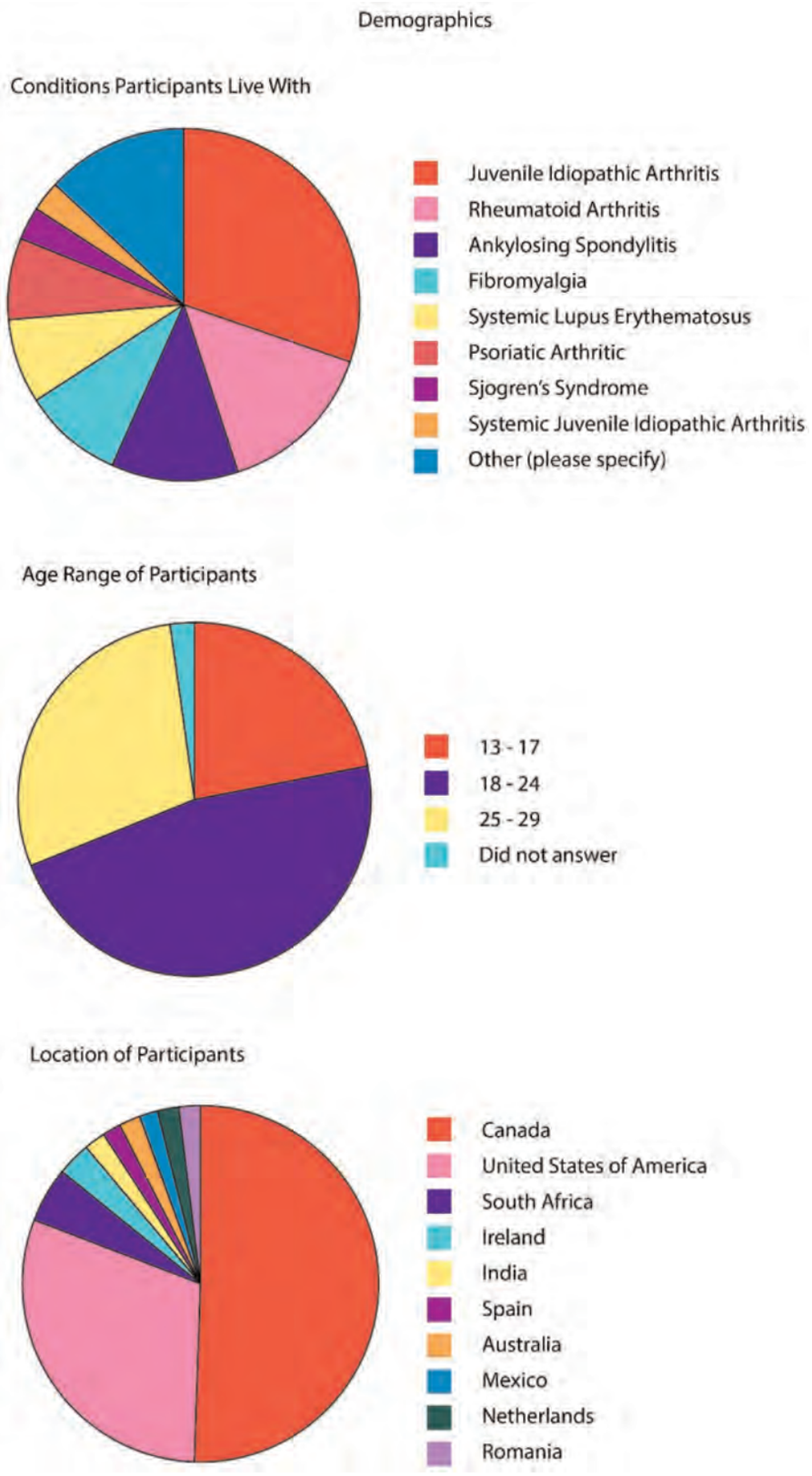
Natasha Trehan[1], Laurie Proulx[2] and Isabel Dukes[3], [1]University of Ottawa, Take a Pain Check Foundation, Toronto, ON, Canada, [2]Canadian Arthritis Patient Alliance, Ottawa, ON, Canada, [3]CAPA & TAPC, Freelance, Ottawa, ON, Canada

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Psychology/Social Science – Interprofessional Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

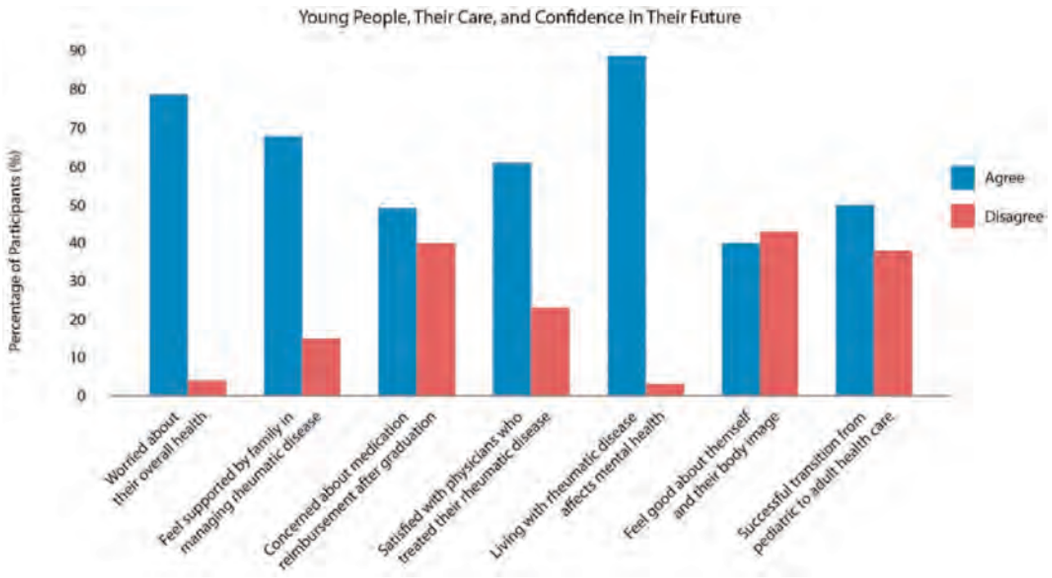
Background/Purpose: Rheumatic disease doesn't merely present physical challenges—it also significantly impacts various psychological and social aspects of one's life, often disrupting academic progress, straining friendships, and fostering a sense of social isolation for youth and young adults. Take a Pain Check Foundation (TAPC) and the Canadian Arthritis Patient Alliance (CAPA) are grassroots, patient-driven, and managed organizations. This effort illuminates the collaboration of these organizations, shining a light on their dedication to uplifting young lives and increasing awareness about the hurdles they face. The objective of this effort was to gain a comprehensive understanding of the needs of youth and young adults with rheumatic diseases to identify strategies in support of mental health and psychosocial well-being.

Methods: A survey was developed and young people with lived experience of rheumatic disease were consulted. The survey covered several domains including navigating the healthcare system, mental health and social support, self-confidence and self-image, and the transition from pediatric to adult care. The survey was opened in September 2022 and closed in January 2023. During this time, 67 participants completed the survey. Descriptive statistics were used to analyze the data per domain and sub-group analysis based on age, disease type, and geographic area (Figure 1).

Results: Over one in two participants (52%) lived with Juvenile Idiopathic Arthritis and others lived with Rheumatoid Arthritis (25%), Ankylosing Spondylitis (20%), Fibromyalgia (16%) and Systemic Lupus Erythematosus (13%) and Psoriatic Arthritis (13%). Findings revealed that a significant proportion (79%) of respondents expressed worry about their health, and 89% said their rheumatic disease affects their mental health. Self-perception and body image were reported as dissatisfactory for over 40% of youths. While a considerable number of participants (69%) felt supported by their families in managing their condition, 20% did not feel supported by romantic partners and friends. The majority of respondents (61%) expressed satisfaction with physicians who treated their rheumatic disease. Nearly half of the respondents (48%) felt ready for the transition from pediatric to adult care transition, while an equal proportion reported a successful transition experience (50%). Significant concerns were raised regarding medication reimbursement after graduating from school, as nearly half of the participants (49%) expressed unpreparedness (Figure 2).



Three pie graphs indicating demographic information gathered in the study. Demographic information includes age, location, and conditions participants live with.



A double bar graph showing how many participants agree or disagree with a variety of questions related to their care, mental health, and confidence in their future.

Conclusion: The survey provides valuable insights into the experiences and perceptions of young individuals living with rheumatic diseases and shows the need for targeted interventions and enhanced social support. Survey findings also suggest the need for innovative and tailored interventions about healthcare navigation and drug reimbursement faced by this population. Addressing this multifaceted challenge, TAPC and CAPA are creating the necessary tools and resources to aid young people with rheumatic conditions.

Disclosure: N. Trehan: AbbVie/Abbott, 5, Pfizer, 5; **L. Proulx**: AbbVie/Abbott, 5, ESDC, 5, IMC, 5; **I. Dukes**: None.

Abstract Number: 1260

Optimal Approaches for Reducing Depressive Symptoms in Rheumatoid Arthritis Patients Based on Psychological Interventions: A Systematic Review and Network Meta-analysis

Zhang Lijuan and Wu Beiwen, Shanghai Jiao Tong University School of Medicine, Shanghai, China

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Psychology/Social Science – Interprofessional Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: In recent years, numerous psychological interventions for rheumatoid arthritis (RA) patients have been developed. However, it remains unclear which psychological interventions are effective and preferred for their depressive symptoms. The purpose of this study was to identify the optimal psychological interventions approach for reducing depressive symptoms in RA patients.

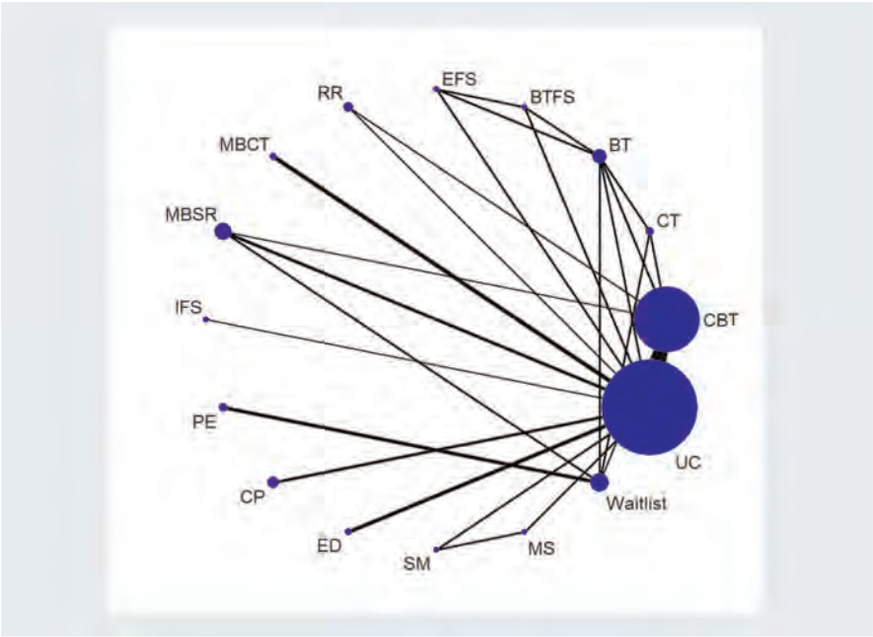


Figure 1 Network plots of depression at post-intervention. CBT: Cognitive behavioral Therapy; CT: the cognitive therapy; BT: the behavior therapy; BTFS: the behavior therapy with family support group; EFS: the education family support group; RR: Relaxation response training; MBCT: Mindfulness-Based Cognitive Therapy; MBSR: Mindfulness-Based Stress Reduction; IFS: Internal Family Systems; PE: Patients education; CP: Combined psychological intervention; ED: Emotional disclosure; SM: Stress Management; MS: Mutual Support; UC: Usual care.

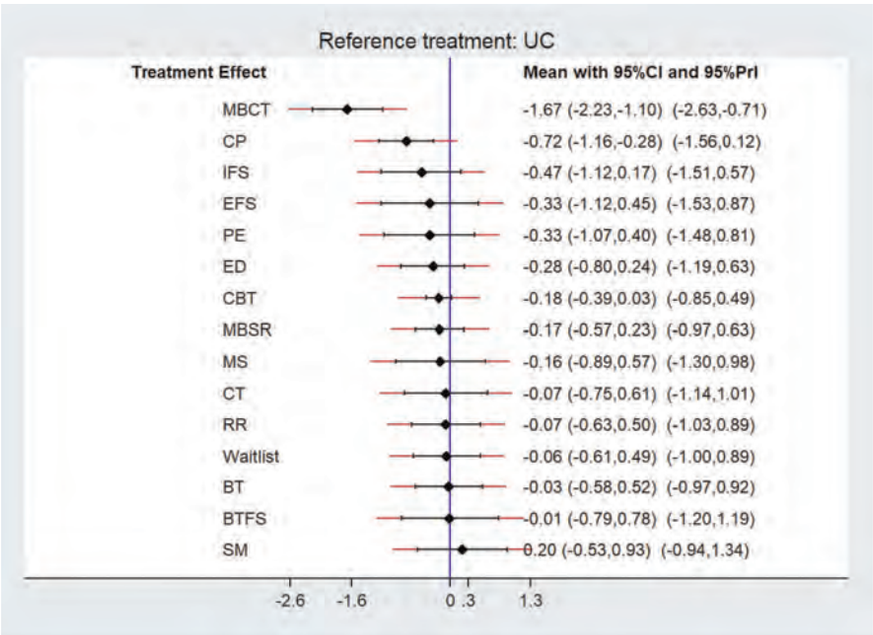


Figure 2 Efficacy of different psychological intervention approaches compared to UC group. CBT: Cognitive behavioral Therapy; CT: the cognitive therapy; BT: the behavior therapy; BTFS: the behavior therapy with family support group; EFS: the education family support group; RR: Relaxation response training; MBCT: Mindfulness-Based Cognitive Therapy; MBSR: Mindfulness-Based Stress Reduction; IFS: Internal Family Systems; PE: Patients education; CP: Combined psychological intervention; ED: Emotional disclosure; SM: Stress Management; MS: Mutual Support; UC: Usual care.

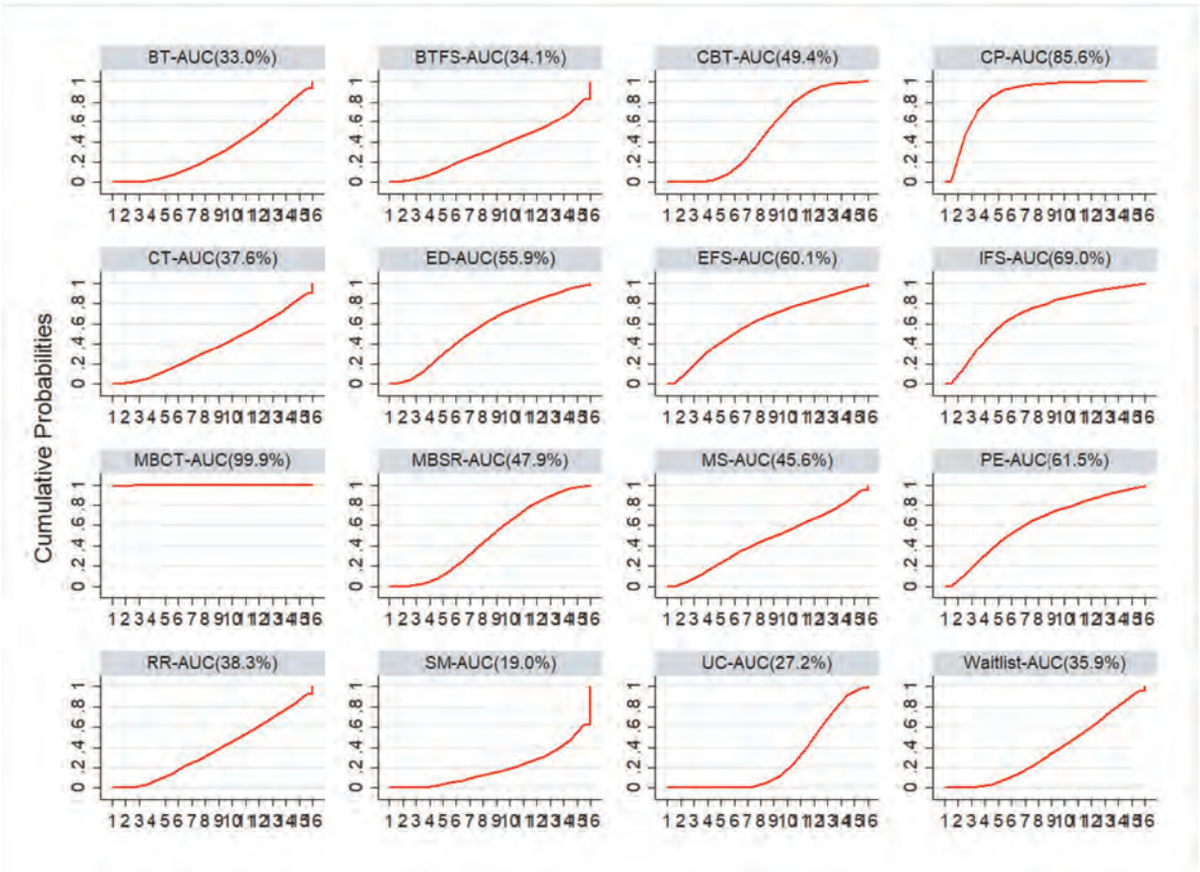


Figure 3 The SUCRA plot and values based on cumulative probabilities of interventions. AUC: Area under curve; CBT: Cognitive behavioral Therapy; CT: the cognitive therapy; BT: the behavior therapy; BTFS: the behavior therapy with family support group; EFS: the education family support group; RR: Relaxation response training; MBCT: Mindfulness-Based Cognitive Therapy; MBSR: Mindfulness-Based Stress Reduction; IFS: Internal Family Systems; PE: Patients education; CP: Combined psychological intervention; ED: Emotional disclosure; SM: Stress Management; MS: Mutual Support; UC: Usual care.

Methods: The PubMed, Embase, PsycINFO, the Cochrane Library, China National Knowledge Infrastructure (CNKI), Wanfang databases, and grey literature were searched between inception and 31 December 2022. Pairs of reviewers screened studies, abstracted aggregate level data, and appraised risk of bias with the Cochrane risk of bias tool. The network meta-analysis was conducted using STATA software version 14.0.

Results: A total of 23 randomized controlled trials, involving 1885 participants and 16 psychological interventions were included in our analyses. In this network meta-analysis, two interventions were associated with a greater reduction in symptoms of depression compared with treatment as usual care group: mindfulness-based cognitive therapy (MBCT) (standardized mean difference –1.67, 95% credible interval -2.23 to -1.10) and combined psychological intervention (CP) (–0.72, –1.16 to –0.28). Although most psychological interventions showed non-significant effects, the surface under the cumulative ranking curve (SUCRA) values revealed that the best psychological intervention for depression was MBCT (99.9%), followed by CP (85.6%), and Internal Family Systems (IFS) psychotherapeutic intervention (69.0%).

Conclusion: MBCT was the most recommended psychological intervention to accompany the depression among RA patients according to our network meta-analysis results.

Disclosure: Z. Lijuan: None; **W. Beiwen**: None.

Abstract Number: 1261

Network Analysis of Depression and Anxiety Symptoms in Chinese Rheumatoid Arthritis Patients

Zhang Lijuan and Wu Beiwen, Shanghai Jiao Tong University School of Medicine, Shanghai, China

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Psychology/Social Science – Interprofessional Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) patients are susceptible to comorbid anxiety and depression. From the network model perspective, comorbidity is due to direct interactions between depression and anxiety symptoms. The objective of this study was to assess the network structure of depression and anxiety symptoms in Chinese RA patients and identify the central and bridge symptoms as well as how depression and anxiety symptoms are related to quality of life (QoL) in the network.

Methods: A total of 402 Chinese RA patients were included in this study. Depression and anxiety symptoms were measured by the Hospital Anxiety and Depression Scale (HADS).R software was used to estimate the network. Specifically, we computed the predictability, expected influence (EI) and bridge expected influence (BEI) for each symptom and showed a flow network of "QoL".

Results: Our network revealed that the strongest edge was D2 "See the bad side of things"-D3 "Not feeling cheerful" across the whole network. For centrality indices, D3 "Not feeling cheerful" and D6 "Feeling down" had the highest EI values in the network, while A4 "Trouble relaxing" and D6 "Feeling down" had the highest BEI values of their respective community. As to "QoL", the strongest direct edge related to it was A1 "Nervousness".

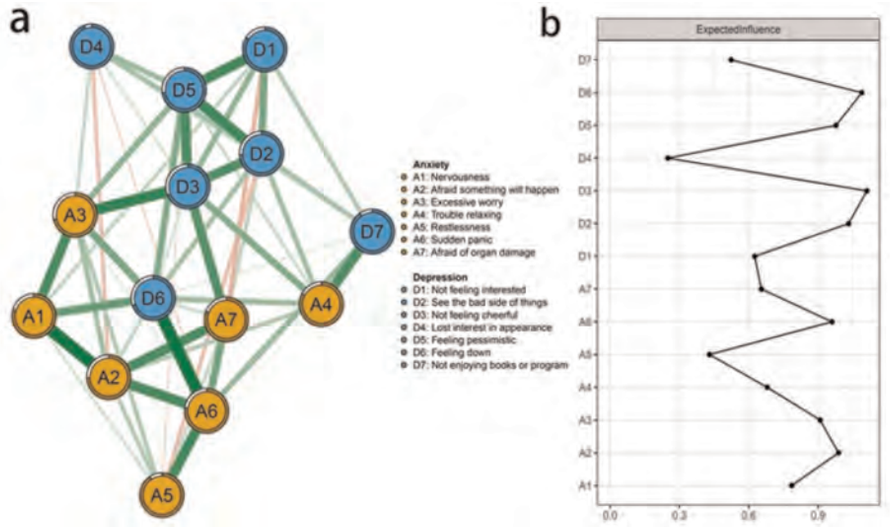


FIGURE 1 The anxiety-depression network structure and the expected influence indices in Chinese RA patients. (a) The anxiety-depression network structure of the Chinese RA patients. The nodes in the network represent symptoms of anxiety and depression, and the edges represent correlations of symptoms. Green edges and red edges represent positive and negative correlations, respectively, and thicker edges represent higher correlations. (b) The expected influence indices in the anxiety-depression network of Chinese RA patients.

Conclusion: Network analyses highlighted specific associations between symptoms of depression and anxiety in Chinese RA patients. D3 "Not feeling cheerful" and D6 "Feeling down" were the core symptoms in the network; A4 "Trouble relaxing" and D6 "Feeling down" were the most critical bridge symptoms. A1 "Nervousness" was also identified as key priority due to its significant association with QoL. Our study emphasizes the necessity of implications for clinical prevention and intervention based on these symptoms in Chinese RA patients.

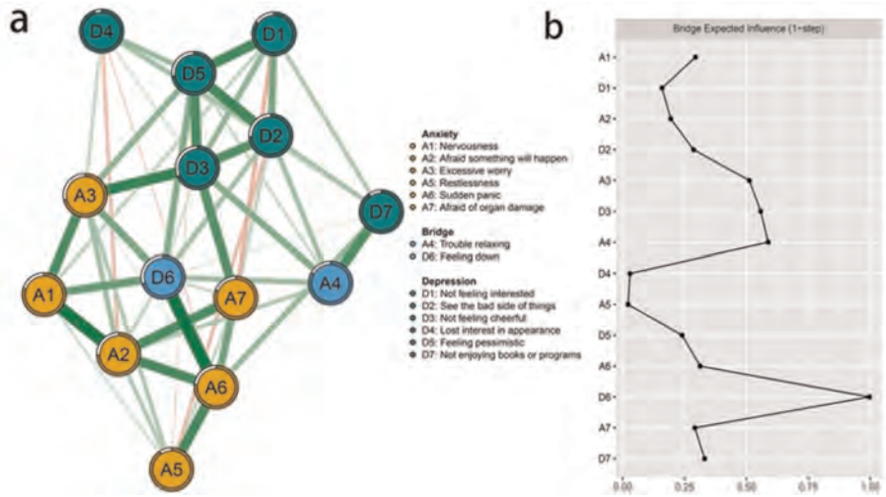


FIGURE 2 The anxiety-depression network structure highlighting the bridge symptoms and the bridge expected influence indices in Chinese RA patients. (a) The anxiety-depression network structure highlighting the bridge symptoms. The nodes in the network represent symptoms of anxiety and depression, and bridge symptoms are highlighted in blue. The edges represent correlations of symptoms, green edges and red edges represent positive and negative correlations, respectively, and thicker edges represent higher correlations. (b) The bridge expected influence indices in the anxiety-depression network of Chinese RA patients.

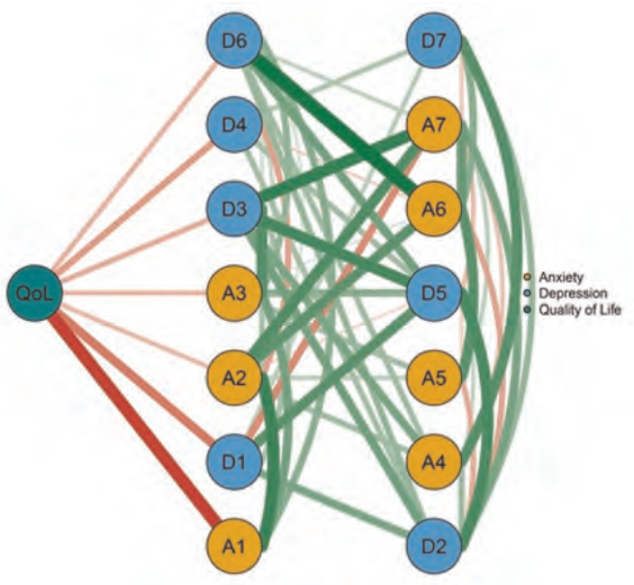


FIGURE 3 The flow network of quality of life in Chinese RA patients. The nodes in the network represent symptoms of anxiety and depression, and the edges represent correlations of symptoms. Green edges and red edges represent positive and negative correlations, respectively, and thicker edges represent higher correlations. A1-Nervousness, A2-Afraid something will happen, A3-Excessive worry, A4-Trouble relaxing, A5-Restlessness, A6-Sudden panic, A7-Afraid of organ damage, D1-Not feeling interested, D2-See the bad side of things, D3-Not feeling cheerful, D4-Lost interest in appearance, D5-Feeling pessimistic, D6-Feeling down, D7-Not enjoying books or programs, QoL-quality of life.

Disclosure: Z. Lijuan: None; **W. Beiwen**: None.

Abstract Number: 1262

"Somebody Who's Been There and Can Understand the Challenges That You're Going Through": Participant Perspectives of a Resilience-Based Energy Management Online Intervention for Systemic Sclerosis with Peer Health Coaches

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Psychology/Social Science – Interprofessional Poster
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Background/Purpose: People with systemic sclerosis (SSc) often experience fatigue, which impacts daily life functioning and quality of life. We developed a 12-week, resilience-based energy management intervention to promote well-being (RENEW) that focuses on healthy behaviors and resilience skills. Participants worked with a trained peer health coach, who also has SSc, setting healthy goals and tracking progress. We conducted interviews to explore participant experience and the impact of RENEW on SSc symptom management.

Methods: From a clinical trial *(ClinicalTrials.gov: NCT04908943)* testing the effectiveness of the RENEW program versus a waitlist control, we purposively selected RENEW program participants who scored high or low on the Patient Global Impression of Change (PGIC) scale. We then conducted virtual interviews (N = 21). Transcripts were analyzed using the rigorous and accelerated data reduction (RADaR) technique combined with thematic content analysis. During the coding process, codes were refined collaboratively by coders, including a patient partner. Any discrepancies were resolved through discussions. Codes with similar content were merged and organized into subthemes and themes to better understand the data.

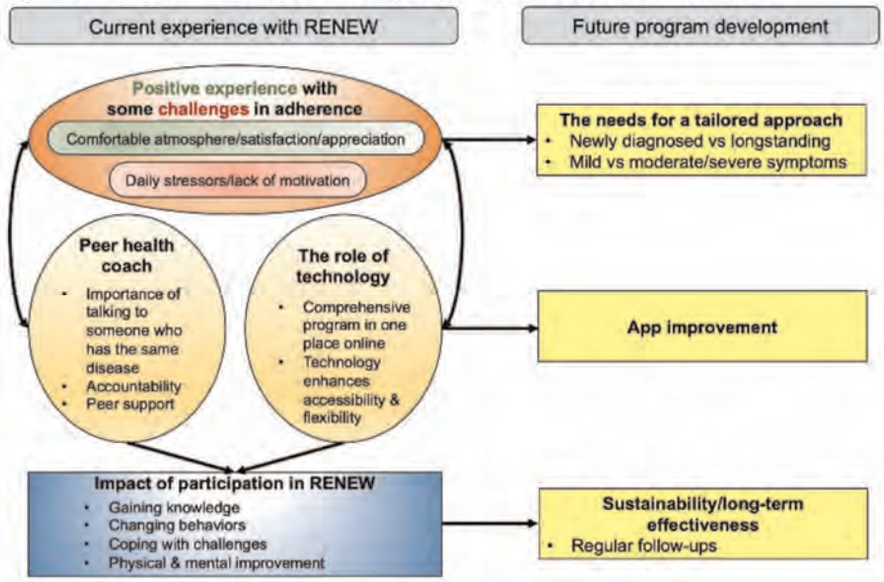
Results: Twenty-one participants (mean age = 57 ± 14 years; 18 females; 13 diffuse SSc subtype; 11 early disease duration ≤ 5 years) with 12 reported high PGIC (Table 1). Five themes were identified (Figure 1). 1) *Peer health coaches*: Participants valued support provided by peer health coaches. The coaches understood their needs and provided guidance throughout the program, helping them set achievable goals and develop strategies to overcome challenges. 2) *Impact of participation*: RENEW had a positive impact on managing fatigue. Participants reported gaining knowledge and skills in developing healthy behaviors that improved their overall physical and mental health. 3) *Program experiences*: Participants expressed overall satisfaction with comprehensiveness and relevance to SSc. However, they faced difficulties in managing everyday life stressors and obligations, which sometimes affected their motivation and/or ability to participate in RENEW. 4) *Need for a tailored approach*: Although results were generally positive, participants suggested tailoring the approach to optimize effectiveness of RENEW. They recommended tailored information for newly diagnosed patients versus those with a longer disease duration to better address specific needs. 5) *Role of technology*: Participants appreciated the convenience of Zoom and easy accessibility of the program through an online platform or app. However, some participants mentioned that the app was not user-friendly and suggested improvement.

Table 1. Participants PGIC, demographics and SSc characteristics, and change in fatigue score from baseline to 12 weeks (n = 21)

PGIC score		ID	Age	Sex	Race	SSc subtype	SSc duration	Fatigue Change[a]
Low	1	1	59	F	African American	Diffuse	11+ years	17.4
	2	2	69	F	White	Diffuse	11+ years	1.8
	3	3	72	M	White	Diffuse	11+ years	1.7
	3	4	58	F	White	Limited	11+ years	0
	3	5	44	F	White	Limited	≤ 5 years	-1.8
	3	6	63	F	White	Limited	6-10 years	-2.2
	3	7	78	F	White	Overlap	11+ years	-2.6
	3	8	56	F	White	Diffuse	11+ years	-2.8
	3	9	87	F	White	Diffuse	≤ 5 years	-3.6
High	6	10	40	F	African American	Diffuse	11+ years	5.3
	6	11	54	F	African American	Overlap	≤ 5 years	-1.6
	7	12	61	F	White	Diffuse	≤ 5 years	-8.2
	6	13	51	M	White	Diffuse	≤ 5 years	-8.9
	6	14	59	F	African American	Diffuse	≤ 5 years	-9.8
	6	15	31	F	Asian & other	Diffuse	≤ 5 years	-10.3
	6	16	35	F	African American	Diffuse	11+ years	-11.0
	6	17	63	M	White	Diffuse	≤ 5 years	-12.0
	7	18	58	F	African American	Diffuse	≤ 5 years	-12.2
	6	19	65	F	Asian & other	Limited	≤ 5 years	-12.5
	7	20	40	F	White	Limited	≤ 5 years	-14.4
	7	21	47	F	White	Limited	11+ years	-16.1

a. To assess change in fatigue, we calculated the difference between the fatigue score at baseline and the score at the 12-week. Negative values indicated a favorable change, suggesting an improvement or decreased in fatigue.
PGIC, Patient Global Impression of Change: 1= No change (or condition has gotten worse); 2 = Almost the same, hardly any change at all; 3 = A little better, but no noticeable change; 4 = Somewhat better, but the change has not made any real difference; 5 = Moderately better, and a slight but noticeable change; 6 = Better and a definite improvement that has made a real and worthwhile difference; 7 = A great deal better and a considerable improvement that has made all the difference.

Figure 1. A conceptual model representing the participants' experiences in RENEW



Conclusion: Our findings highlighted the importance of the peer health coach component to our self-management intervention. Participation in the program led to improved fatigue management and well-being for individuals with SSc. However, we identified a need to tailor RENEW based on different SSc duration groups. While the virtual program was convenient, suggestions for improving the app were noted. These findings contribute to the development and refinement of future interventions for people with SSc.

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Abstract Number: 1263

Depression and Anxiety Risk Assessment in Patients with Rheumatic Diseases

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Background/Purpose: Depression is one of the most common psychiatric comorbidities in patients with rheumatic diseases. A study has shown that almost a third of patients with Rheumatoid Arthritis (RA) present symptoms of major depressive disorder, making it more prevalent than general population. (1) Early and continuous screening could help reduce the prevalence of mental health disorders. (2) The objective of this study was to evaluate and identify patients at risk of developing anxiety and/or depressive disorders.

Methods: We conducted a cross-sectional study at the outpatient rheumatology clinic of Hospital Universitario Dr. José Eleuterio González. Patients aged 18 and older with at least one rheumatic disease were included. Sociodemographic and disease activity data were collected from records. We administered the Hospital Anxiety and Depression Scale (HADS): a score of 0 is classified as no risk, 1-7 points low risk, 8-10 intermediate risk, and >11 high risk. For fatigue, we utilized The Functional Assessment of Chronic Illness Therapy scale (FACIT). Those identified as high risk were referred for psychiatric evaluation.

Results: We enrolled a total of 893 patients. Based on their scores, 42.70% (382) showed no risk of anxiety, while 57.22% (511) had a low, intermediate, or high risk (Table 1). Among the patients without anxiety symptoms, 89.3% (341) were female, with a mean disease duration of 7.2 +/- 7.9 years and a mean age of 49.9 +/- 15.1 years. Rheumatoid Arthritis (RA) was the most common diagnosis, accounting for 48.7% (186). On the other hand, only 152 patients (16.57%) were classified as high risk for anxiety, with 97.4% of them being female. The mean age in this group was 53.7 +/- 14.8 years, and mean disease duration was 6.9 +/- 7 years. Among those at high risk, RA was the most prevalent diagnosis, affecting

Table 1. HADS A Demographics and clinical characteristics.

	No risk	Low risk	Intermediate risk	High risk	
Total	***382***	***239***	***120***	***152***	
Sex, n (%)					0.002
Female	341 (89.3)	229 (95.8)	111 (92.5)	148 (97.4)	
Male	41 (10.7)	10 (4.2)	9 (7.5)	4 (2.6)	
Age	49.9 ± 15.1	52.0 ± 14.6	51.8 ± 13.6	53.7 ± 14.8	0.045
Marital status					0.436
Married	186 (48.7)	121 (50.6)	63 (52.5)	72 (47.4)	
Cohabitation	37 (9.7)	22 (9.2)	13 (10.8)	15 (9.9)	
Widowed	33 (8.6)	17 (7.1)	5 (4.2)	22 (14.5)	
Single	91 (23.8)	60 (25.1)	26 (21.7)	26 (17.1)	
Divorced	24 (6.3)	9 (7.5)	9 (7.5)	12 (7.9)	
Separated	11 (2.9)	8 (3.3)	4 (3.3)	5 (3.3)	
Rheumatic disease, n (%)					0.079
Rheumatoid Arthritis (RA)	216 (56.5)	145 (60.7)	70 (58.3)	80 (52.6)	
Osteoarthritis (OA)	28 (7.3)	19 (7.9)	10 (8.3)	16 (10.5)	
Systemic Lupus Erythematosus (SLE)	69 (18.1)	24 (10)	15 (12.5)	18 (11.8)	
MII	14 (3.7)	7 (2.9)	3 (2.5)	2 (1.3)	
Arthralgia	13 (3.4)	14 (5.9)	6 (5)	10 (6.6)	
Sjögren Syndrome	10 (2.6)	6 (2.5)	4 (3.3)	8 (5.3)	
SSc	8 (2.1)	6 (2.5)	3 (2.5)	1 (0.7)	
SpA / PsA	6 (1.6)	2 (0.8)	2 (1.7)	5 (3.3)	
Others	18 (4.71)	7 (6.69)	7(5.83)	12 (7.89)	
Years since diagnosis, n (SD)	7.2 ± 7.9	6.6 ± 7.5	6.1 ± 6.9	6.9 ± 7.0	0.527
Comorbidities					0.112
No	228 (59.7)	132 (55.2)	59 (49.2)	86 (56.6)	
Yes					
Fatigue (FACIT)					<0.001
No	376 (98.4)	233 (97.5)	111 (92.5)	130 (85.5)	
Yes	6 (1.6)	6 (2.5)	9 (7.5)	22 (14.5)	
Depression (HADS)					<0.001
No risk	375 (98.2)	160 (66.9)	47 (39.2)	11 (7.2)	
Low risk	7 (1.8)	79 (33.1)	68 (56.7)	93 (61.2)	
Intermediate	-	-	3 (2.5)	25 (16.4)	
High risk	-	-	2 (1.7)	23 (15.1)	
Menopause* (827)	***340***	***229***	***110***	***148***	0.132
Yes	224 (65.9)	165 (72.1)	82 (74.5)	110 (74.3)	
No	116 (34.1)	64 (27.9)	28 (25.5)	38 (25.7)	

52.25% (80) of the patients (Table 1). Regarding risk of depression, 66.40% (593) of all patients presented no risk of depression, while 33.57% (300) had a low, intermediate, or high risk. Among those without depression symptoms, 91.6% were female, with a mean age of 50.1 +/- 15 years. RA was the most frequent diagnosis, accounting for 58.2% of the patients. In the group with a high risk of depression, we found 2.79% (25) of patients, with a mean age of 56.4 +/- 18 years and a mean disease duration of 7.7 +/- 7.8 years (Table 2). Fatigue and depression risk were more prevalent in individuals with higher anxiety scores ($p < 0.001$)

Conclusion: Our findings revealed that in our patient population, risk for anxiety and depression increases with age, and is more prevalent in women. Additionally, we observed that fatigue was associated with both anxiety and depression risk scores. Furthermore, there was a positive association between high-risk scores for anxiety and high-risk scores for depression. Based on these results, we strongly recommend the regular screening of patients who are at high risk of developing mental health problems

Table 2. HADS D: Demographics and clinical characteristics

	No risk	Low risk	Intermediate risk	High risk	sig
Total	593	247	28	25	
Sex, n (%)					0.15
Female	543 (91.6)	234 (94.7)	28 (100)	24 (96)	
Male	50 (8.4)	13 (5.3)	0	1 (4)	
Age, mean (SD)	50.1 ± 15	53.8 ± 13.5	52.3 ± 17.5	56.4 ± 14.8	0.005
Marital Status					0.516
Married	297 (50.1)	117 (47.4)	13 (46.4)	15 (60)	
Cohabitation	61 (10.3)	23 (9.3)	3 (1.7)	-	
Widowed	46 (7.8)	22 (8.9)	4 (14.3)	5 (20)	
Single	139 (23.4)	55 (22.3)	5 (17.9)	4 (16)	
Divorced	34 (5.7)	20 (8.1)	2 (7.1)	-	
Separated	16 (2.7)	10 (4)	1 (3.6)	1 (4)	
Rheumatic disease (RD), n(%)					0.015
Rheumatoid Arthritis (RA)	345 (58.2)	142 (57.5)	13 (46.4)	11 (44)	
Osteoarthritis (OA)	50 (8.4)	17 (6.9)	5 (17.9)	1 (4)	
Systemic Lupus Erythematosus (SLE)	95 (16)	21 (8.5)	4 (14.3)	6 (24)	
MII	18 (3)	6 (2.4)	1 (3.6)	1 (4)	
Arthralgia	21 (3.5)	19 (7.7)	1 (3.6)	2 (8)	
Sjögren Syndrome	16 (2.7)	8 (3.2)	2 (7.1)	2 (8)	
SSc	12 (2)	5 (2)	-	1 (4)	
SpA / PsA	6 (1)	8 (3.2)	-	1 (4)	
Others	30(5.05)	21 (8.50)	2(7.14)	-	
Years since diagnosis, n (SD)	7 ± 7.7	6.2 ± 5.8	8.4 ± 8.5	7.7 ± 7.8	0.541
Comorbidities					0.002
No	344 (58)	133 (53.8)	15 (53.6)	13 (52)	
Yes	249(41.98)	114(46.15)	13(46.42)	15 (60)	
Menopause* (827)	***541***	***234***	***28***	***24***	0.078
Yes	365 (67.5)	179 (76.5)	21 (75)	16 (66.7)	
No	176 (32.5)	55 (23.5)	7 (25)	8 (33.3)	
Fatigue (FACIT)					<0.001
Yes	15 (2.5)	17 (6.9)	3 (10.7)	8 (32)	
No	578 (97.5)	230 (93.1)	25 (89.3)	17 (68)	
Anxiety (HADS)					<0.001
No risk	375 (63.2)	7 (2.8)	-	-	
Low risk	160 (27)	79 (32)	-	-	
Intermediate Risk	47 (7.9)	68 (27.5)	3 (10.7)	2 (8)	
High risk	11 (1.9)	93 (37.7)	25 (89.3)	23 (92)	

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Abstract Number: 1264

Nomination of Biomarkers for Self-testing Disease Activity in Rheumatoid Arthritis Using Patient Similarity Networks: A Pilot Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II

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Session Time: 9:00AM–11:00AM

Background/Purpose: Although telemedicine in rheumatoid arthritis (RA) could improve disease control with lower healthcare costs, knowledge of suitable parameters for self-testing disease activity still remains limited. The alteration in lipoproteins among RA patients seems to be associated with disease activity and severity. Objective: To explore the relationship between disease activity and a set of serum inflammatory and lipid biomarkers and patient and physician evaluations in RA.

Methods: Activity markers (CRP, ESR, swollen (SJC) & tender (TJC) joint counts), serum lipids and patient health status evaluation using the visual analogous scale (VAS) completed by the patient and clinician were analysed at two-time points in a real-world cohort of patients with RA (n=22, males/females, 4/18) using patient similarity networks (PSNs). Disease activity was assessed by DAS28 at each visit, and most patients were treated with biologics (inhibitors of TNFa/JAK/IL6/others: 12/3/2/5).

Results: When comparing patient and physician evaluations, patient evaluations differed significantly from physician evaluations in ∼1/3 of patients (differences in SJC >5, TJC >3, and/or VAS >30), mainly with overestimated values of SJC and VAS health status by patients. Therefore, we constructed a PSN based only on laboratory parameters and revealed three clusters (subgroups) of patients who differed in CRP, low-density lipoprotein cholesterol (LDL-C), and apolipoprotein-AI (apoA-I) levels, all three of which have been associated with RA disease activity in previous studies. One subgroup (CI) characterised by a low CRP and high LDL-C and apoA-I included predominantly non-active patients (6/9, confidence C=67%, support S=41%). The majority of these patients changed to active after the 3-month follow-up. Two subgroups: CII) with low CRP and LDL-C (5/6, C=83%, S=27%), and CIII) with high CRP and LDL-C and low apoA-I (6/7, C=86%, S=32%) included predominantly active patients. Our data support a key role for serum apoA-I levels in activity assessment, as these levels are strongly related to disease activity at follow-up. The expansion of the study cohort is ongoing.

Conclusion: Our study shows the utility of serum biomarkers for assessing disease activity, independent of the patient and clinician evaluations. Whether the nominated biomarkers are suitable for the automated approach, clinical use and/or interpretation of cardiovascular risk or even sorting active patients in telemedicine approach, deserves future validation on a larger patient cohort.

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Abstract Number: 1265

Changes in the Endocannabinoid Tone in Rheumatoid Arthritis and Osteoarthritis – Discovery of a Novel Target for the Treatment of Pain and Inflammation?

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Background/Purpose: Inflammation is a complicated physiological process that results in a variety of disorders. Several inflammatory mediators are produced during this process, which is responsible for long-term inflammatory conditions like osteoarthritis (OA) and rheumatoid arthritis (RA). Endocannabinoids (ECs) and the endocannabinoid system play a pivotal role in the physiological response to pain and inflammation. A clinical study was performed to investigate changes in endocannabinoid tone and related lipid meditators in OA and RA compared to age-matched healthy participants.

Methods: A clinical study with 80 subjects (53 Female and 27 male) was performed including 25 RA and 18 OA patients and 37 healthy participants. Venous blood was drawn, plasma was generated, and one aliquot of plasma was acidified using 0.5% formic acid to preserve/stabilize endocannabinoids and related lipid mediators. An in-house developed and validated HPLC-MS/MS-based assay for the analysis of 20 ECs and congeners was performed as. Moreover, we applied a lipid mediator multiplex assay for the analysis of 131 oxylipins many of which are related to the ECs pathway. Data were analyzed using ANOVA in combination with the LSD post-hoc test (SPSS 28.0).

Results: Average age of study participants was 55.8±10.6 years with 57.2±8.3, 62.2±6.6 and 52.0±12.0 for the RA, OA and control group, respectively. The female/male ratio was 53/27 with 16/9, 15/3 and 22/15 for the RA, OA and control group, respectively. The endocannabinoid analysis revealed significantly decreased levels of 2-arachidonoylglycerol (2-AG, see Figure 1). In contrast, EC levels of the ethanolamide (EA) group (anandamide (AEA), docosahexaenoyl-EA, palmitoleoyl-EA and other EAs) were increased in the RA group and to a lesser extent in the OA group (Figure 1 lower part).This analysis of oxylipins revealed decreased levels of the inflammation resolving lipid 9-oxo-octadecadienoic acid (9-oxoODE) in RA compared to all other study groups. In contrast, proinflammatory lipids 11-hydroxy docosahexaenoic acid (11-HDHA) and 12-hydroxy-eicosatetraenoic acid (12-HETE) were significantly increased in both the RA and OA group as compared to healthy controls.

Conclusion: ECs have very short half-lives. The study design included addition of stabilizer solution to plasma that enabled us to accurately determine the EC levels, specifically 2-AG. Using this approach, we found decreased levels of the major antinociceptive and anti-inflammatory endocannabinoid 2-AG in RA and OA subjects. 2-AG is a key regulator of nociception

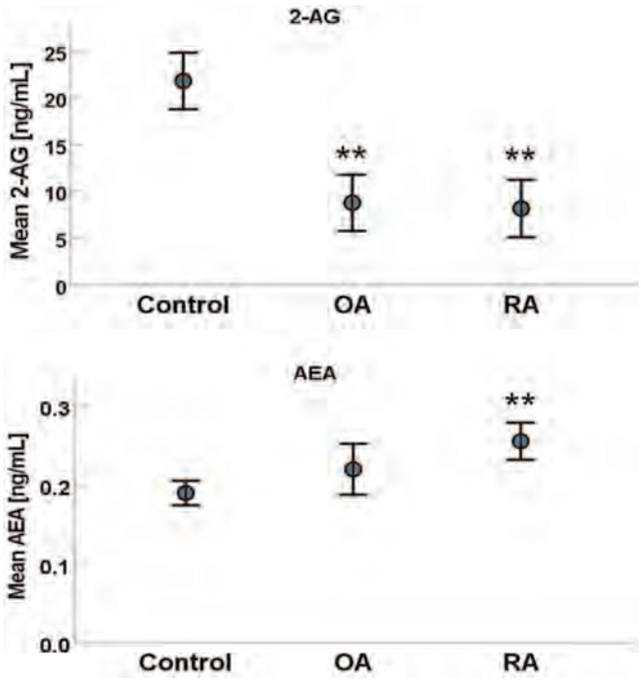

Figure 1: Mean 2-AG (upper) and AEA (lower) plasma levels in osteoarthritis (n=17), rheumatoid arthritis (n=25) and in age matched healthy controls (n=37). Data are shown as mean ± SEM.**p<0.01 post-hoc LSD.

and inflammation, and decreased levels could be a major mechanistic contributor to pain and inflammation in RA and OA. In addition, we observed increased levels of ethanolamide endocannabinoids (EA-ECs). This may be an indicator for decreased FAAH (fatty acid amide hydrolase) activity, the major EA-ECs regulating enzyme. Although anandamide (the major EA-EC) functions as a CB1 receptor agonist in the CNS, it shows vanilloid TRPV1 receptor agonism peripherally. Overall, our results suggest the involvement of ECs in inflammation and pain in patients with RA and OA and may present a potential treatment target.

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Abstract Number: 1266

The Anti-inflammatory Effect of High-density Lipoprotein Is Blunted by Delivery of Altered MicroRNA Cargo to Macrophages in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: High-density lipoprotein (HDL) has well-characterized anti-atherogenic cholesterol efflux and anti-oxidant functions. Another function of HDL uncharacterized in RA is its ability to transport microRNAs (miRNAs) between cells and thus alter cellular function. The study's purpose was to determine if HDL-miRNA cargo is altered and affects inflammation in RA.

Methods: HDL-miRNAs were characterized in 30 RA and 30 control subjects by next generation sequencing and quantitative PCR. The most abundant differentially expressed miRNA was evaluated further. The function of miR-1246 was assessed by miRNA mimics, antagomiRs, siRNA knockdown and luciferase assays. Monocyte-derived macrophages were treated with miR-1246-loaded HDL, and unmodified HDL from RA and control subjects to measure delivery of miR-1246 and its effect on IL-6.

Results: The most abundant miRNA on HDL was miR-1246; it was significantly enriched 2-fold on HDL from RA versus control subjects. HDL-mediated miR-1246 delivery to macrophages significantly increased *IL6* expression 43-fold. miR-1246 delivery significantly decreased *DUSP3* 1.5-fold and *DUSP3* siRNA knockdown increased macrophage *IL6* expression. Luciferase assay indicated *DUSP3* is a direct target of miR-1246. Unmodified HDL from RA delivered 1.6-fold more miR-1246 versus control subject HDL. Unmodified HDL from both RA and control subjects attenuated activated macrophage *IL6* expression, but this effect was significantly blunted in RA so that *IL6* expression was 3.4-fold higher after RA versus control HDL treatment.

Conclusion: HDL-miR-1246 was increased in RA versus control subjects and delivery of miR-1246 to macrophages increased *IL-6* expression by targeting *DUSP3*. The altered HDL-miRNA cargo in RA blunted HDL's anti-inflammatory effect.

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Abstract Number: 1267

Lower Herpes Zoster Rate of Tocilizumab and Tofacitinib in Patients Undergoing Treatment for Rheumatoid Arthritis

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Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Biological disease-modifying antirheumatic drugs (bDMARDs) have become the primary treatment option for rheumatoid arthritis (RA) from 2010 in Taiwan. Tocilizumab is an interleukin-6 receptor inhibitor (IL-6Ri) and Tofacitinib is Janus kinase inhibitor (JAKi), in treating RA patients. They have much similar mechanism and efficacy. To address this concern, we conducted a comparison of the safety outcomes of Tocilizumab and Tofacitinib in RA patients in real-world clinical settings.

Table 1. Baseline characteristics of patients in the Tocilizumab and Tofacitinib.

	Tofacitinib	Tocilizumab	SMD	Tofacitinib	Tocilizumab	SMD
	n=611	n=463		n=579.983	n=425.075	
Age, year			-0.0573			-0.0031
Mean (STD)	53.32 (13.19)	52.57 (12.94)		53.21 (12.57)	53.17 (12.32)	
Median (IQR)	53 (20)	53 (18)		54 (19)	53 (19)	
Range	19-80	18-79		19-80	18-79	
Sex			0.0643			0.002
Female	486 (79.54%)	356 (76.89%)		457.05 (78.8%)	334.63 (78.72%)	
Male	125 (20.46%)	107 (23.11%)		122.94 (21.2%)	90.45 (21.28%)	
Comorbidity						
Diabetes	100 (16.37%)	66 (14.25%)	-0.0587	87.25 (15.04%)	62.11 (14.61%)	-0.0121
Chronic kidney disease	31 (5.07%)	25 (5.4%)	0.0146	27.37 (4.72%)	20.34 (4.78%)	0.0031
Hypertension	216 (35.35%)	164 (35.42%)	0.0014	204.81 (35.31%)	150.17 (35.33%)	0.0003
Pre-cancer	14 (2.29%)	15 (3.24%)	0.0579	15.48 (2.67%)	11.91 (2.8%)	0.0081
Concomitant medication						
Hydroxychloroquine	426 (69.72%)	335 (72.35%)	0.0581	413.49 (71.29%)	306.35 (72.07%)	0.0172
Sulfasalazine	95 (15.55%)	71 (15.33%)	-0.0059	84.41 (14.55%)	61.76 (14.53%)	-0.0007
Methotrexate	517 (84.62%)	381 (82.29%)	-0.0626	493.06 (85.01%)	359.26 (84.52%)	-0.0138
Leflunomide	108 (17.68%)	96 (20.73%)	0.0777	106.32 (18.33%)	79.89 (18.79%)	0.0119
Cyclosporine	30 (4.91%)	37 (7.99%)	0.1257	29.80 (5.14%)	23.93 (5.63%)	0.0217
Azathioprine	8 (1.31%)	5 (1.08%)	-0.0211	6.90 (1.19%)	4.92 (1.16%)	-0.003
Penicillamine	0 (0%)	1 (0.22%)	0.0658	0.00 (0%)	1.07 (0.25%)	0.0712

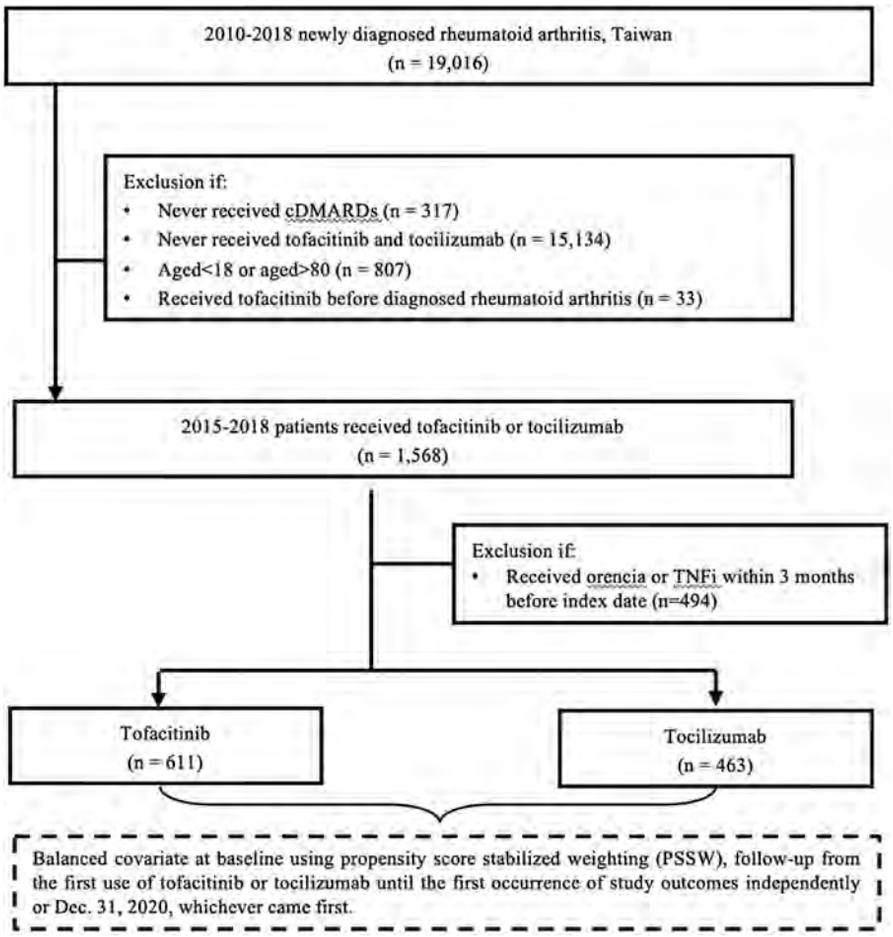

Figure 1. Flowchart for identifying patients with rheumatoid arthritis in the Taiwan National Health Insurance Research Database during the period 2010–2018.

Methods: Patients diagnosed with RA between 2010 and 2018 were identified from the Taiwan National Health Insurance Research Database and followed till 2020. Propensity score stabilized weighting (PSSW) was used to balance the baseline characteristics of the Tocilizumab and Tofacitinib groups. The incidences of safety outcomes, namely cardiovascular (CV) events, total hip replacement (THR), total knee replacement (TKR), tuberculosis (TB), herpes zoster infection, cancer and all-cause mortality, were compared between the study groups.

Results: A total of 1,074 patients with RA who were administered Tocilizumab (n = 463) and Tofacitinib (n = 611) were included in this study. The mean follow-up duration was 1.96 years in Tocilizumab group and 1.98 in the Tofacitinib group. A lower incidence rate of herpes zoster infection was observed in the Tocilizumab group than in the tofacitinib group. All-cause mortality, CV events, THR and TB infection had higher incidence rate but all without statistical significance.

Conclusion: Although, the mechanism of Tocilizumab and Tofacitinib are much similar. Lower herpes zoster incident rate was observed in Tocilizumab group compared with Tofacitinib. Other safety issues and mortality rates revealed comparable incidences in both groups with RA patients treated in real-world settings.

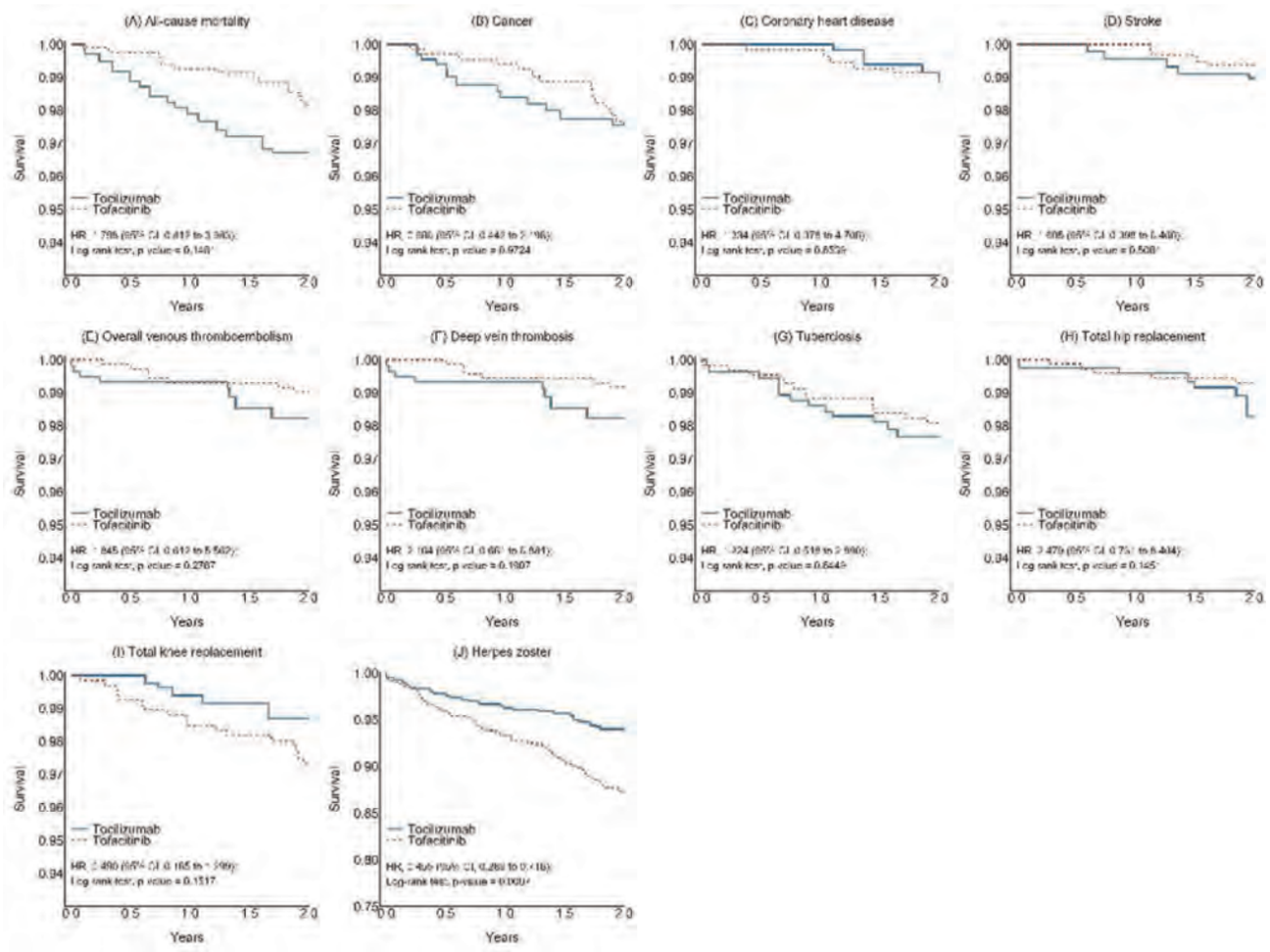

Figure 2. Survival curve of safety outcomes in the Tocilizumab and Tofacitinib groups.

Disclosure: Y. Fang: None; **L. See**: None; **S. Chang**: None.

Abstract Number: 1268

Clinical Characteristics of Patients with Rheumatoid Arthritis (RA) Who Rate Their Global Assessment of Disease Activity Substantially Lower Than Their Physicians (Negative Discordance) Based on a Large RA Database in Japan: A Rare but Important Subgroup

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Discordance between patient global assessment (PGA) and physician global assessment (PhGA) regarding the disease activity of rheumatoid arthritis (RA) can be divided into three groups: positive discordance, concordance, and negative discordance. Several studies have demonstrated that the major determinants of positive discordance (PGA > PhGA) are pain and functional impairment. The clinical manifestations of negative discordance (PGA < PhGA) have not yet been fully elucidated. This study identifies determinants of this discordance using a nationwide RA database in Japan (*NinJa*).

Methods: The data of 13,945 patients with RA registered in *NinJa* in 2014 with available joint counts were analyzed. Data from patients with RA registered in both *NinJa* in 2014 and 2018 (n=4,923) were analyzed to study the radiographic progression of RA. The clinical variables used for the analysis included age, sex, disease duration, radiographic stage, functional class, pain visual analog scale (VAS) score, tender joint count (TJC), swollen joint count (SJC), disease activity score in 28 joints, C-reactive protein (DAS28-CRP), modified Health Assessment Questionnaire (mHAQ), and rheumatoid factor and anti-citrullinated peptide antibody (ACPA) levels. The affected joint distribution was investigated using joint indices (JI) x, y, and z, which were calculated as indices for the upper and lower joints and large joint involvement, respectively (Int J Rheum Dis 21(6):1237-45, 2018).

Results: Using a PGA-PhGA cutoff of 3 on a 10-cm scale, the numbers of patients with RA classified into positive discordance (PGA-PhGA > 3), concordance (-3 < PGA-PhGA < 3), and negative discordance (PGA-PhGA < -3) were 2,049 (14.7%), 11,785 (84.5%), and 111 (0.8%), respectively. There were no significant differences in age or disease duration between the three groups; however, the proportion of male patients was significantly higher in the negative-discordance group (19.9%, 16.5%, and 28.8%, respectively; $p< 0.01$). The TJC ($p< 0.01$), SJC ($p< 0.01$), and DAS28-CRP ($p< 0.01$) scores were higher in the negative discordance group than in the concordance group, while the PGA ($p< 0.05$) scores were lower in the negative discordance group than in the concordance group. JI x was significantly higher in the negative discordance group than in the other groups ($p< 0.01$). The proportion of patients with radiographic progression was significantly higher in the negative discordance group (33.3%) than in the concordance and positive concordance groups (13.7% and 11.5%, respectively; $p< 0.01$).

Conclusion: Negative discordance is prevalent in males and associated with higher disease activity, especially in the upper extremities, though the patients rated their disease activities substantially lower than their attending physicians. As negative discordance is associated with the progression of joint destruction, this rare but important discordance status can be regarded as a potential factor of poor prognosis.

Disclosure: T. Sawada: AbbVie/Abbott, 5, 6, Asahikasei, 5, 6, AstraZeneca, 6, Chugai, 5, 6, Eisai, 6, Eli-Lily, 6, Jansen, 6, Mitsubishi-Tanabe, 6, Ono Pharmaceutical, 6, Pfizer, 6, Taisho, 6, UCB, 6, Viatris, 6; **S. Nishiyama**: AbbVie/Abbott, 6, Asahi Kasei Pharma Corporation, 1, AstraZeneca, 6, AYUMI Pharmaceutical Corporation, 12, Financial support for the OKAYAMA medical conference., Chugai Pharma Manufacturing Co., Ltd., 6, Eisai Co., Ltd., 6, GlaxoSmithKlein(-GSK), 1, 6, Kissei PharmaceuticalCo., Ltd., 6, Santen Pharmaceutical Co., Ltd., 6, Taisho Pharmaceutical Co., Ltd., 6; **S. Yamashita**: None; **T. Matsui**: Abbie, 6, Asahikasei Pharma Corp., 5, 6, Astellas, 6, Chugai Pharmaceutical Co, Ltd., 5, 6, Eisai Co., Ltd., 6, Eli Lilly Japan, 6, Ono Pharmaceutical Co., Ltd., 6, Pfizer Japan Inc., 6; **S. Tohma**: AbbVie/Abbott, 5, AsahiKASEI Co., Ltd., 6, Chudai Pharmaceutical Co., Ltd., 5, Mitsubishi Tanabe Pharma Corporation, 5, Pfizer Japan Inc., 6.

Abstract Number: 1269

The Impact of Sex, Serostatus, and Smoking on Risk for Rheumatoid Arthritis-associated Interstitial Lung Disease Subtypes

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: RA-associated interstitial lung disease (RA-ILD) is a heterogenous condition encompassing multiple subtypes with varying histopathology, prognosis, and potential treatment options. The most common RA-ILD subtypes are usual interstitial pneumonia (UIP) and nonspecific interstitial pneumonia (NSIP). RA-UIP is characterized by fibrosis and

Table 1. Characteristics at index date* for RA-ILD cases and RA-noILD controls.

	All RA-ILD cases (n=201)	RA-UIP cases (n=69)	RA-NSIP cases (n=34)	Other† RA-ILD subtypes or indeterminate subtype (n=98)	RA-noILD controls (n=547)
Mean age at RA diagnosis, years (SD)	51.0 (14.4)	54.3 (15.6)	50.6 (14.8)	48.7 (13.0)	49.1 (14.8)
Female sex, n (%)	133 (66.2%)	37 (53.6%)	25 (73.5%)	71 (72.4%)	427 (78.1%)
Race, n (%)					
White	176 (87.6%)	59 (85.5%)	29 (85.3%)	88 (89.8%)	473 (86.5%)
Black	14 (7.0%)	7 (10.1%)	2 (5.9%)	5 (5.1%)	36 (6.6%)
Asian	3 (1.5%)	1 (1.4%)	1 (2.9%)	1 (1.0%)	7 (1.3%)
Other	8 (4.0%)	2 (2.9%)	2 (5.9%)	4 (4.1%)	31 (5.7%)
Smoking status, n (%)					
Never	67 (33.3%)	24 (34.8%)	12 (35.3%)	31 (31.6%)	257 (47.0%)
Past	119 (59.2%)	40 (58.0%)	20 (58.8%)	59 (60.2%)	247 (45.2%)
Current	15 (7.5%)	5 (7.2%)	2 (5.9%)	8 (8.2%)	43 (7.9%)
Median pack-years (IQR)	8 (0, 25)	10 (0, 25)	2.7 (0, 17.5)	10 (0, 30)	0.4 (0, 16.5)
Median RA duration at index date*, years (IQR)	8.6 (0.3, 20)	5.0 (0, 14.1)	4.1 (0, 17.5)	12.9 (2.0, 20.8)	8.9 (2.5, 17.7)
Seropositive, n (%)	155 (77.1%)	53 (76.8%)	27 (79.4%)	75 (76.5%)	328 (60.0%)
RF positive, n (%)	133/198 (67.2%)	45 (65.2%)	23/33 (69.7%)	65/96 (67.7%)	246/543 (45.3%)
Median RF level, -fold above ULN (IQR)	2.0 (1.0, 20.2)	4.5 (1.0, 25.8)	8.3 (1.3, 23.4)	3.1 (1.0, 12.2)	1.1 (1.0, 6.2)
Anti-CCP positive, n (%)	131/191 (68.6%)	48/66 (72.7%)	22/33 (66.7%)	61/92 (66.3%)	270/519 (52.0%)
Median anti-CCP level, -fold above ULN (IQR)	7.4 (0.5, 15.3)	9.3 (0.8, 16.4)	5.8 (0.4, 12.3)	8.2 (0.5, 15.1)	1.5 (0.3, 11.4)

Anti-CCP = anti-cyclic citrullinated peptide, ILD = interstitial lung disease, IQR = interquartile range, NSIP = nonspecific interstitial pneumonia, RF = rheumatoid factor, SD = standard deviation, UIP = usual interstitial pneumonia, ULN = upper limit of normal

*Index date was date of RA-ILD for cases and date of HRCT for RA-noILD controls
† includes 61 unknown/indeterminate subtypes, 19 organizing pneumonia, 8 respiratory bronchiolitis interstitial lung disease, 9 other interstitial lung disease subtypes, and 1 lipoid interstitial pneumonia

Table 2. Multivariable* odds ratios for RA-ILD and major subtypes.

	Multivariable OR for all RA-ILD (95%CI)	Multivariable OR for RA-UIP (95%CI)	Multivariable OR for RA-NSIP (95%CI)
Age at RA diagnosis (per year)	1.00 (0.99, 1.02)	1.01 (0.99, 1.04)	0.99 (0.98, 1.02)
Male (vs. female)	**1.63 (1.12, 2.37)**	**2.69 (1.56, 4.67)**	1.21 (0.53, 2.74)
Seropositive (vs. seronegative)	**2.23 (1.52, 3.28)**	**2.44 (1.32, 4.50)**	**2.87 (1.21, 6.84)**
RF+ (vs. RF-)	**2.40 (1.68, 3.44)**	**2.49 (1.43, 4.35)**	**3.21 (1.46, 7.07)**
Anti-CCP+ (vs. anti-CCP-)	**2.03 (1.41, 2.92)**	**2.87 (1.37, 5.24)**	2.01 (0.94, 4.33)
RA duration (per year)	0.99 (0.97, 1.004)	0.98 (0.95, 1.004)	0.98 (0.94, 1.02)
Smoking status			
Never	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
Ever	**1.71 (1.19, 2.45)**	1.45 (0.82, 2.57)	1.55 (0.72, 3.33
Pack-years (per unit)	1.00 (0.99, 1.01)	0.99 (0.98, 1.01)	0.99 (0.97, 1.01)

*Adjusted for age at RA diagnosis, sex, serostatus, RA duration at index date (RA-ILD diagnosis for cases or HRCT for RA-noILD controls), smoking status, pack-years, and cohort.

Anti-CCP = anti-cyclic citrullinated peptide, CI = confidence interval, ILD = interstitial lung disease, NSIP = nonspecific interstitial pneumonia, OR = odds ratio, RA = rheumatoid arthritis, RF = rheumatoid factor, UIP = usual interstitial pneumonia

Table 3: Association of male sex, seropositivity for RA-related autoantibodies, and smoking with risk of RA-ILD and major subtypes

	Multivariable OR for all RA-ILD (95%CI)	Multivariable OR for RA-UIP (95%CI)	Multivariable OR for RA-NSIP (95%CI)
0 risk factors (female sex, never smoker, seronegative)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
1 risk factor	**1.93 (1.003 to 3.71)**	3.08 (0.89 to 10.7)	0.90 (0.26 to 3.08)
2 risk factors	**3.41 (1.78 to 6.51)**	**4.19 (1.21 to 14.5)**	2.24 (0.70 to 7.11)
3 risk factors (male sex, ever smoker, seropositive)	**6.09 (2.95 to 12.6)**	**12.8 (3.5 to 46.8)**	2.96 (0.77 to 11.5)
p for trend	<0.0001	<0.0001	0.022

ILD = interstitial lung disease, NSIP = nonspecific interstitial pneumonia, OR = odds ratio, RA = rheumatoid arthritis, UIP = usual interstitial pneumonia

portends the worst prognosis but may be treated with antifibrotic therapy. RA-NSIP is more likely to have inflammatory features on lung imaging. Despite these differences, most prior research studied RA-ILD as a single entity rather than examining individual subtypes. Therefore, we investigated differences in demographic, serologic, and lifestyle risk factors for RA-ILD and major RA-ILD subtypes.

Methods: We systematically identified RA-ILD cases and RA-noILD controls from two established RA cohorts. RA-ILD and subtypes (including UIP, NSIP, and other/indeterminate) were determined by clinical imaging reports and research review of clinically-indicated chest high-resolution computed tomography (HRCT) by at least two thoracic radiologists using a sequential reader method. RA-ILD cases met criteria for definite/probable RA-ILD (Bongartz, *A&R*, 2010). RA-noILD controls had no evidence of ILD on clinical review of medical records AND research HRCT review. Demographics, RA-related autoantibody testing, and smoking were extracted from study questionnaires or electronic health records. We investigated associations between RA-ILD and subtypes with demographic, serologic, and lifestyle factors using multivariable logistic regression, pooling both cohorts due to limited sample size.

Results: From 3328 RA patients, we identified 201 RA-ILD cases (mean age 51 years, 66.2% female) and 547 RA-noILD controls (mean age 49 years, 78.1% female). Of the RA-ILD cases, 69 (34.3%) had RA-UIP, 34 (16.9%) had RA-NSIP, and 98 (48.8%) had other subtypes or were indeterminate (**Table 1**). RA-ILD was associated with male sex (OR 1.63, 95%CI 1.12 to 2.37), seropositivity for RF and/or anti-CCP (OR 2.23, 95%CI 1.52 to 3.28) and ever smoking (OR 1.71, 95%CI 1.19 to 2.45, **Table 2**). Having all three risk factors (male, seropositive, smoking) was strongly associated with RA-ILD (OR 6.09, 95%CI 2.95 to 12.58, **Table 3**) and particularly with RA-UIP (OR 12.8, 95%CI 3.50 to 46.8) compared to RA-NSIP (OR 2.96 95%CI 0.77 to 11.56). RA-UIP was associated with male sex (OR 2.69, 95%CI 1.56 to 4.67) and positive

anti-CCP (OR 2.23, 95%CI 1.52 to 3.28, **Table 2**). RA-NSIP was associated with positive RF (OR 3.21 95%CI 1.46 to 7.07) but not male sex (OR 1.21, 95%CI 0.53 to 2.74).

Conclusion: In this study comparing systematically phenotyped RA-ILD cases with RA-noILD controls confirmed by HRCT, we found distinct risk factor profiles for RA-UIP and RA-NSIP. Male sex and elevated anti-CCP were strongly associated with RA-UIP, the most severe RA-ILD subtype. The combination of male sex, seropositivity, and smoking conferred nearly 13-fold increased risk of RA-UIP. These findings suggest that RA-ILD sex differences are specific to RA-UIP and may help clarify RA-ILD heterogeneity to optimize screening and treatment approaches.

Disclosure: G. McDermott: None; **K. Hayashi**: None; **P. Juge**: None; **R. Gill**: None; **S. Byrne**: None; **S. Gagne**: None; **K. Vanni**: None; **E. Kowalski**: None; **G. Qian**: None; **K. Bade**: None; **A. Saavedra**: None; **Y. Kawano**: None; **M. Diiorio**: None; **T. Wolfgang**: None; **E. Kim**: Bayer, 5, Novartis, 12, Spouse is employee; **P. Dellaripa**: None; **M. Weinblatt**: Abbvie, 2, 5, Aclaris, 2, Amgen, 2, Aqtual, 5, Bristol Myers Squibb, 2, 5, Canfite, 11, Corevitas, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, 2, Glaxo Smith Kline, 2, Horizon, 2, Inmedix, 11, Janssen, 5, Johnson and Johnson, 2, Pfizer, 2, Prometheus Laboratories, 2, Rani, 2, Revolo, 2, Sanofi, 2, Sci Rhom, 2, Scipher, 2, 11, Set Point, 2, UCB, 2; **N. Shadick**: Abbvie, 5, AQtual, 5, Bristol-Myers Squibb(BMS), 5, Janssen, 5; **T. Doyle**: None; **J. Sparks**: AbbVie, 2, Amgen, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, 5, Gilead, 2, Inova Diagnostics, 2, Janssen, 2, Optum, 2, Pfizer, 2, ReCor, 2.

Abstract Number: 1270

Identification of Subclinical Atherosclerosis by Six Cardiovascular Risk Calculators in Rheumatoid Arthritis Patients

Natalia Guajardo-Jauregui[1], José Ramón Azpiri-López[2], Dionicio A. Galarza-Delgado[2], Iris Colunga[2], Jesus Alberto Cardenas-De la Garza[3] and Rosa Arvizu-Rivera[4], [1]Hospital Universitario Dr. José Eleuterio González, Monterrey, Mexico, [2]Hospital Universitario UANL, Monterrey, Mexico, [3]Hospital Universitario "Dr. José Eleuterio González", San Nicolas, Mexico, [4]Hospital Universitario \"Dr. José Eleuterio Gonzalez\", Escobedo, Mexico

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Current EULAR recommendations for cardiovascular risk (CVR) assessment in rheumatoid arthritis (RA) patients indicate that the CVR evaluation should be performed according to national guidelines; however, there was no algorithm designed for the Mexican population until 2019, when the World Health Organization (WHO) published the CVR charts for 21 world regions, including Mexico. The aim of this study was to determine the capacity of the WHO and other five algorithms for the detection of carotid plaque in RA patients.

Methods: This was a cross-sectional study. We included 164 patients with RA diagnosis according to the 2010 ACR/EULAR classification criteria, aged 40-75 years. CVR was calculated with six algorithms: WHO, FRS-lipids, FRS-BMI, SCORE, ACC/AHA and QRISK3. The result was multiplied by 1.5, according to current guidelines. Carotid ultrasound was performed to all patients to identify the presence of carotid plaque, which was defined as a cIMT ≥ 1.2 mm or a focal thickness ≥ 0.5 mm. A ROC-curve analysis was performed, and the cutoff points to detect carotid plaque of each algorithm were determined using Youden's Index. Area under the curve (AUC), sensitivity, specificity, and likelihood ratios were calculated. A p-value < 0.05 was considered statistically significant.

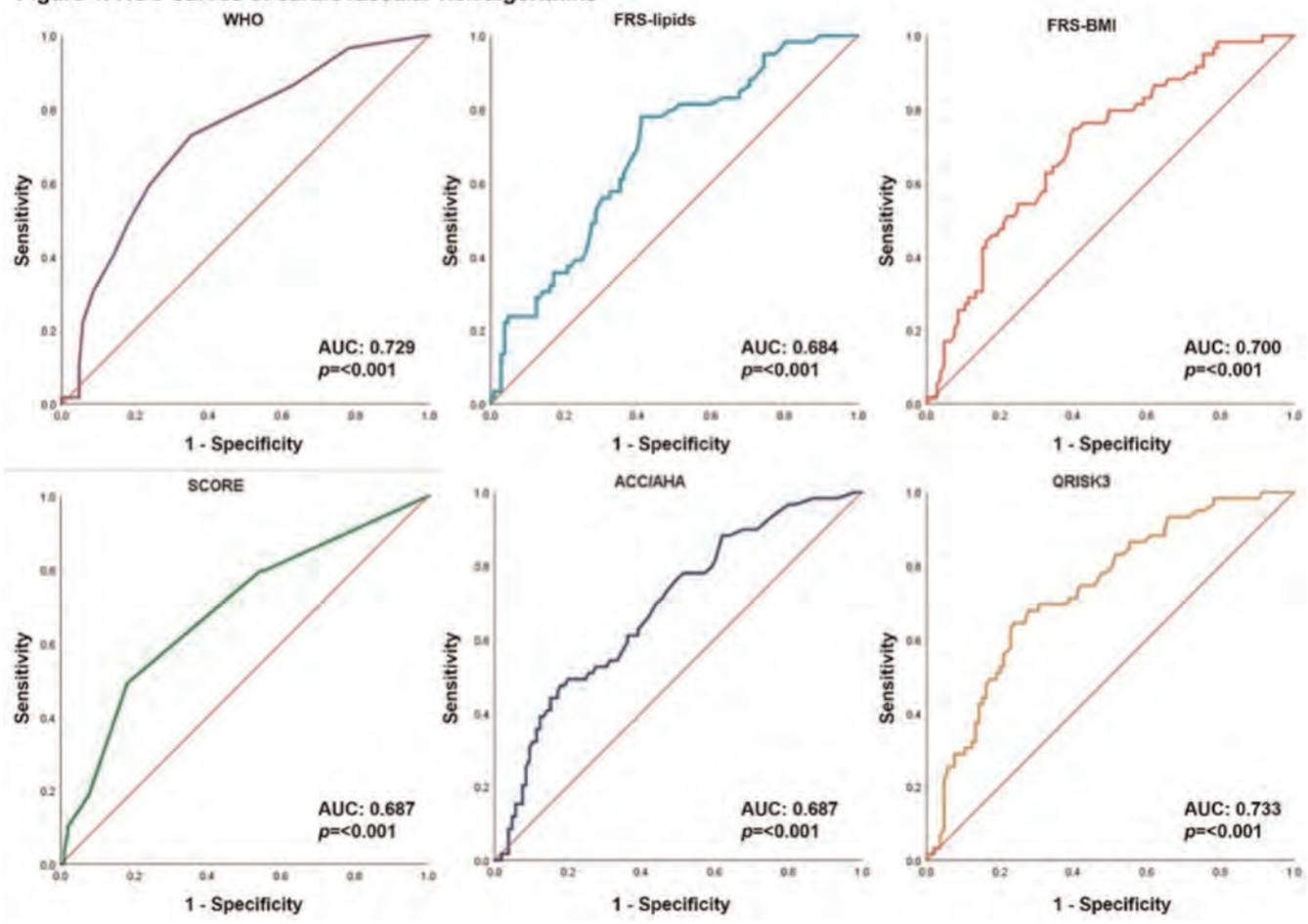
Table 1. Capacity of cardiovascular risk algorithms to detect presence of carotid plaque in rheumatoid arthritis patients.

Algorithms (cut-off points)	High risk cut-off point	AUC	CI 95%		p	Sensibility	Specificity	Likelihood ratio	
			Inferior limit	Superior limit				+	-
WHO (5.25)	≥ 10%	0.729	0.649	0.809	<0.001	72.9%	64.8%	2.07	0.42
FRS-lipids (8.62)	≥ 20%	0.684	0.601	0.767	<0.001	67.8%	61.0%	1.74	0.53
FRS-BMI (11.55)	≥ 20%	0.700	0.618	0.781	<0.001	72.9%	61.0%	1.87	0.44
SCORE (1.5)	≥ 5%	0.687	0.601	0.773	<0.001	79.7%	45.7%	1.47	0.44
ACC/AHA (3.82)	≥ 20%	0.687	0.604	0.770	<0.001	62.7%	61.0%	1.61	0.61
QRISK3 (6.05)	≥ 20%	0.733	0.654	0.811	<0.001	71.2%	61.0%	1.82	0.47

AUC, area under the curve; WHO, World Health Organization; FRS, Framingham Risk Score; BMI, body mass index.

AUC, area under the curve; WHO, World Health Organization; FRS, Framingham Risk Score; BMI, body mass index.

Figure 1. ROC-curves of cardiovascular risk algorithms



Results: The prevalence of carotid plaque was 35.9%. Mean age was 55.8 ±8.9 years, 156 (95.1%) patients were women, 27 (16.5%) patients had diagnosis of type 2 diabetes mellitus, 53 (32.3%) patients had hypertension, 58 (35.4%) had dyslipidemia, 56 (34.1%) had obesity and 15 (9.1%) were active smokers. The ROC-curve analysis of the algorithms is shown in table 1 and figure 1. All the algorithms tested in this study demonstrated significant discrimination for the presence of carotid plaque, with p-values < 0.001.

Conclusion: Among the various algorithms evaluated, the WHO calculator stood out as one of the most effective tools for detecting carotid plaque, demonstrating superior positive and negative likelihood ratios; however, similar to the other algorithms, a lower cut-off point than the one established by the official guidelines was needed to identify high-risk patients with the presence of CP who were initially classified as low-moderate risk by the CVR algorithm, even though the results were multiplied by 1.5 as established by EULAR recommendations, with the exception of QRISK-3, considering the fact that the disease itself is considered a CVR factor. The utilization of carotid ultrasound remains essential in order to accurately identify high-risk patients and provide them with timely treatment.

Disclosure: N. Guajardo-Jauregui: None; **J. Azpiri-López**: None; **D. Galarza-Delgado**: None; **I. Colunga**: None; **J. Cardenas-De la Garza**: None; **R. Arvizu-Rivera**: None.

Abstract Number: 1271

Upregulation of IFNγ-Response Genes in Monocytes and T Cells Identified by Single-Cell Transcriptomics in Patients with Anti-CCP Antibody-Positive Rheumatoid Arthritis (RA)

Bong-Ki Hong[1], Sungyong You[2], Naeun Lee[1], Jung Gon Kim[3], Kijun Lee[4], Ji Hyeon Ju[5], Wan-Uk Kim[1] and **Ho-Youn Kim**[6], [1]The Catholic University of Korea, Seoul, South Korea, [2]Cedars-Sinai Medical Center, Los Angeles, CA, [3]Inje University Ilsan Paik Hospital, Goyang, South Korea, [4]YiPSCELL, Secho, South Korea, [5]Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea, [6]HoYoun Kim's Clinic for Arthritis Rheumatism, Seoul, South Korea

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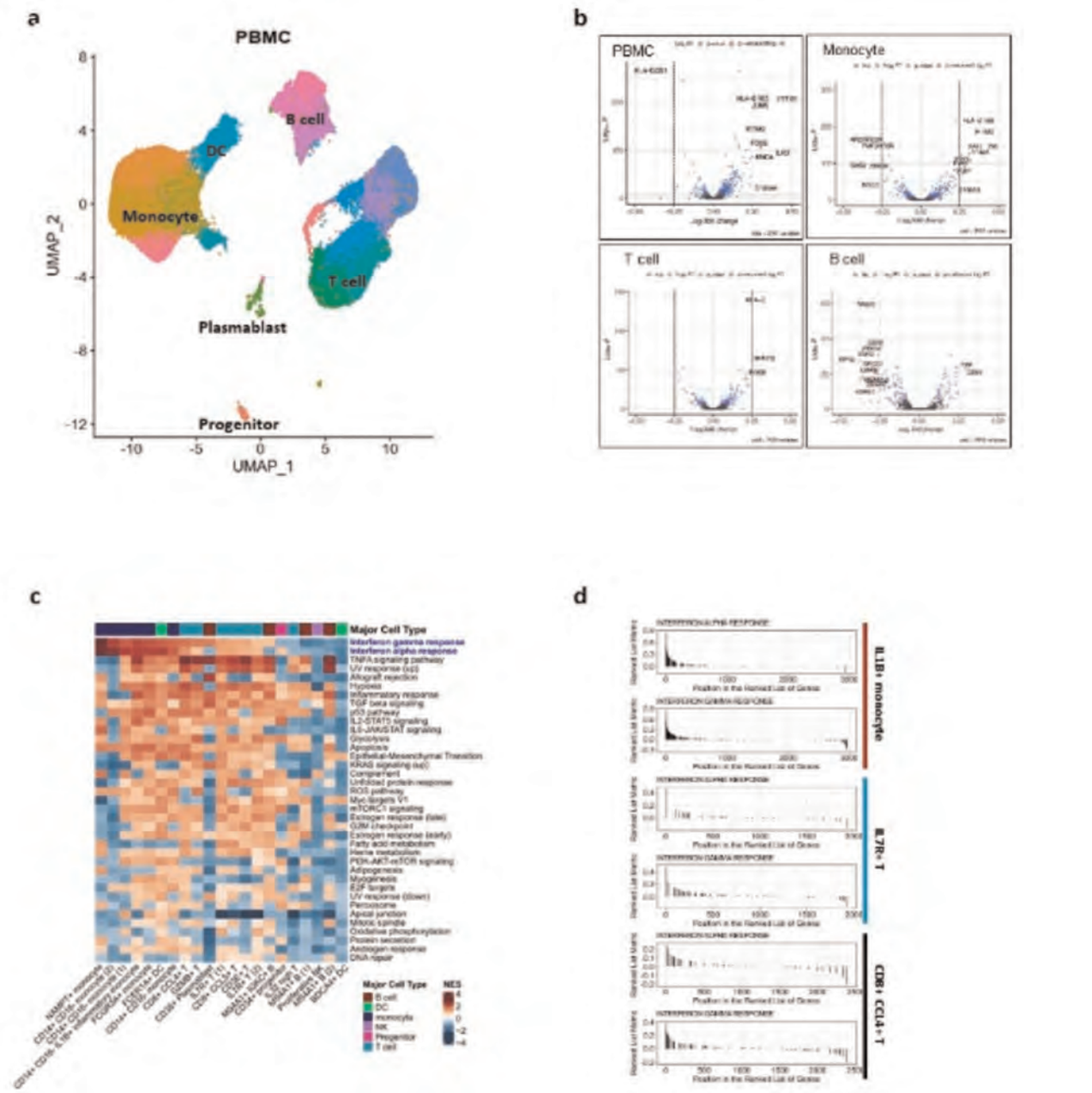
Background/Purpose: Recent research has revealed a significant upregulation of IFNγ-related genes in RA patients, though the underlying mechanisms and implications are still unclear. To further investigate these gene expression alterations, we implemented single-cell RNA sequencing and performed an analysis on the peripheral blood mononuclear cells (PBMCs) of RA patients.

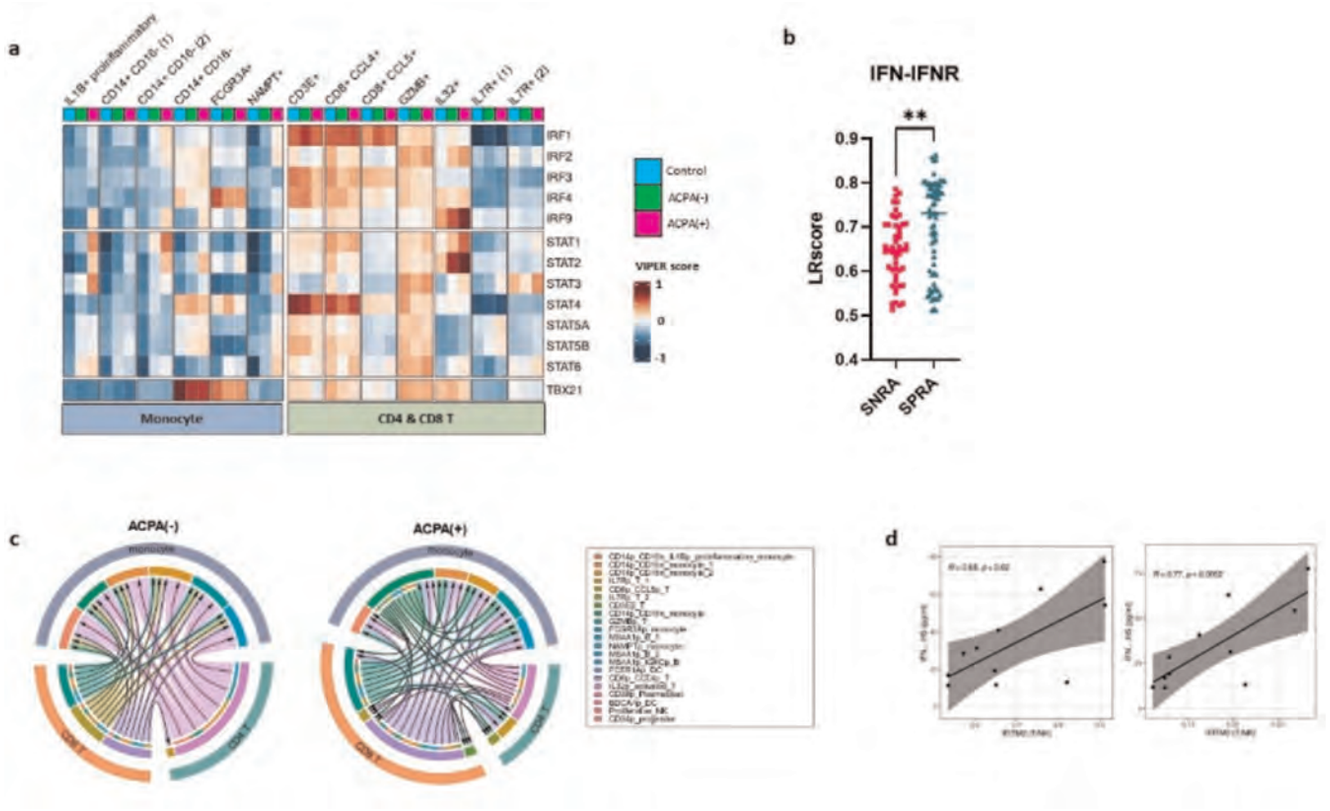
Methods: We executed a single-cell RNA sequencing study on peripheral blood samples from patients with anti-citrullinated protein antibody positive (ACPA+) and negative (ACPA-) RA. Cell subsets were identified, and their distribution and functional characteristics were compared based on ACPA presence.

Results: Our analysis identified 37,318 single cells grouped into 17 different cell types. We observed an expanded proportion of IL1B+ monocytes, IL7R+ T cells, and CD8+ CCL4+ T cells in ACPA+ RA patients. Enrichment analysis scores of interferon-gamma (IFNγ) response genes increased in nearly all monocytes and T cell subsets in ACPA+ RA. These patients exhibited heightened interactions between IFNγ and IFNγ receptors upstream of IFNγ response genes. Cell-cell interaction

was significantly amplified between monocytes and T cells in ACPA+ RA. Additionally, we discovered upregulated IFNγ-driven transcription factors (TFs) such as STATs and IRFs in ACPA+ RA. Major target genes of STATs and IRFs were identified, with IFITM3 and IFITM2 standing out as strongly associated target genes. A significant positive correlation was also found between IFITM2, IFITM3, and elevated serum levels of IFNγ, a signature cytokine of Th1 cells. This finding supports their potential clinical implications in ACPA+ RA.



Landscape of peripheral blood mononuclear cells of patients with RA and differentially expressed gene sets of each cell subset based on Gene Ontology terms (a) t-SNE map based on single-cell RNA-seq data obtained from PBMC of 16 rheumatoid arthritis (RA) patients, with or without anti-CCP antibody, showing 17 different cell types after clustering with 37,318 cells. (b) Volcano plot for PBMC, T, B, and monocyte, comparing ACPA+ vs. ACPA- groups, showing differentially expressed genes obtained by comparison. (c) The heatmap displays the results of gene set enrichment analysis for genes whose expression levels change in ACPA-compared to ACPA+ for 17 cell types. Column annotation of heatmap showing the major cell types (T, B, DC, monocyte, NK, progenitor) indicated for each cell type. (d) The GSEA graph shows the results of IFN-alpha and IFN-gamma response gene sets for three types of subcellular groups that increase in ACPA+ patient groups.



Ligand-receptor score and cell-cell interaction patterns with regard to interplays of IFN and IFN receptor (a) Heatmap representing the activity score of STAT and IRF families predicted to regulate the expression of IFITM2 and IFITM3. (b) The bar graph represents the LR score for IFN-IFNR in the ligand-receptor analysis results. (c) Chord diagram showing the difference in the interaction of IFN-IFNR between monocyte-T cells in ACPA- and ACPA+ groups. The legend on the left side of the diagram represents the subcellular types of monocyte and T cells seen in the second layer of the diagram. (d) Graph showing the correlation between the degree of mRNA expression of IFITM2/3 for each patient and Interferon concentration measured in serum.

Conclusion: Our findings offer novel insights emphasizing the critical role of IFNγ in regulating Th1 skewing in the pathogenesis of ACPA+ RA, as compared to ACPA- RA. The increased interactions between monocytes and T cells and high serum levels of IFNγ, particularly in ACPA+ RA, provide a more comprehensive understanding of the pathogenesis of ACPA+ RA.

Disclosure: B. Hong: None; **S. You**: None; **N. Lee**: None; **J. Kim**: None; **K. Lee**: None; **J. Ju**: None; **W. Kim**: None; **H. Kim**: None.

Abstract Number: 1272

Immunomodulators and Risk for Breakthrough COVID-19 After a Third SARS-CoV-2 mRNA Vaccine Among Patients with Rheumatoid Arthritis: A Cohort Study

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SESSION INFORMATION

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Background/Purpose: In August 2021, the CDC recommended a third SARS-CoV-2 mRNA vaccine dose to complete the initial vaccine series for immunosuppressed patients who had previously received 2 mRNA doses. Despite this, some rheumatoid arthritis (RA) patients may remain at increased risk for breakthrough COVID-19 infection, due to use of immunomodulators which lead to blunted immune responses to vaccination and infection. Identifying patients at highest risk for

Table 1. Baseline demographic and clinical characteristics at date of 3rd mRNA vaccine receipt among patients with rheumatoid arthritis.

Characteristic	All RA patients that received at least 3 mRNA vaccine doses (n=5781)	COVID-19 after index date (n=1173)	No COVID-19 after index date (n=4608)
Age (mean, SD, years)	64.2 (14.2)	62.3 (14.9)	64.6 (14.0)
Female	4555 (78.8%)	933 (79.5%)	3622 (78.6%)
Race			
White	4869 (84.2%)	1016 (86.6%)	3853 (83.6%)
Black or African American	268 (4.6%)	43 (3.7%)	225 (4.9%)
Asian	169 (2.9%)	28 (2.4%)	141 (3.1%)
Other or multiple	294 (5.1%)	50 (4.3%)	244 (5.3%)
Unknown	181 (3.1%)	36 (3.1%)	145 (3.2%)
Hispanic or Latinx ethnicity	334 (5.8%)	53 (4.5%)	281 (6.1%)
Charlson Comorbidity Index (CCI) (median [IQR])	1 (1, 3)	2 (1, 4)	1 (1, 3)
Comorbidities			
Hypertension	2586 (44.7%)	593 (50.6%)	1993 (43.3%)
Diabetes	828 (14.3%)	176 (15.0%)	652 (14.2%)
Malignancy excluding non-melanoma skin cancer	759 (13.1%)	190 (16.2%)	569 (12.4%)
Asthma	786 (13.6%)	231 (19.7%)	555 (12.0%)
Coronary artery disease	662 (11.5%)	161 (13.7%)	501 (10.9%)
Interstitial lung disease	303 (5.2%)	74 (6.3%)	229 (5.0%)
Median RA duration, years (IQR)	5 (2, 10)	5 (2, 10)	5 (2, 10)
Immunomodulatory medications			
Conventional synthetic DMARDs			
Methotrexate	2669 (46.2%)	543 (46.3%)	2126 (46.1%)
Antimalarials	1686 (29.2%)	342 (29.2%)	1344 (29.2%)
Hydroxychloroquine monotherapy	803 (13.9%)	158 (13.5%)	645 (14.0%)
Leflunomide	429 (7.4%)	74 (6.3%)	355 (7.7%)
Sulfasalazine	308 (5.3%)	62 (5.3%)	246 (5.3%)
Mycophenolate mofetil/mycophenolic acid	78 (1.4%)	20 (1.7%)	58 (1.3%)
Azathioprine	58 (1.0%)	15 (1.3%)	43 (0.9%)
Cyclophosphamide	9 (0.2%)	1 (0.1%)	8 (0.2%)
Biologic DMARDs			
TNF inhibitor	1727 (29.9%)	364 (31.0%)	1363 (29.6%)
CTLA-4 immunoglobulin	282 (4.9%)	51 (4.4%)	231 (5.0%)
IL-6 receptor inhibitor	238 (4.1%)	51 (4.4%)	187 (4.1%)
CD20 inhibitor	172 (3.0%)	55 (4.7%)	117 (2.5%)
JAK inhibitor	490 (8.5%)	99 (8.4%)	391 (8.5%)
Oral glucocorticoid	792 (13.7%)	205 (17.5%)	587 (12.7%)
Previous COVID-19	340 (5.9%)	30 (2.6%)	310 (6.7%)
Calendar date of 3rd vaccine			
Feb 1, 2021 – Dec 16, 2021	4348 (75.2%)	945 (80.6%)	3403 (73.8%)
Dec 17, 2021 – Jan 31, 2022	1115 (19.3%)	193 (16.5%)	922 (20.0%)
Feb 1, 2022 – Jul 6, 2022	318 (5.5%)	35 (3.0%)	283 (6.1%)
Median zip-code area household income ($USD, IQR)	88,395 (68,865, 110,025)	92,327 (73,525, 113,417)	87,516 (67,589, 107,444)
Median number of healthcare encounters in previous year (IQR)	14 (1, 31)	23 (6, 41)	12 (1, 29)

breakthrough infection despite 3 vaccines can prioritize resources for prevention. Therefore, we investigated the risk of breakthrough COVID-19 among RA patients with at least 3 vaccine doses using disease-modifying antirheumatic drugs (DMARDs), especially TNF inhibitors (TNFi) and CD20 inhibitors (CD20i), during the Omicron wave.

Methods: We performed a retrospective cohort study investigating DMARDs and risk for breakthrough COVID-19 among RA patients who had received 3 mRNA vaccines at a large health care system. A previously validated algorithm was used to identify RA patients using a combination of diagnosis codes and DMARD/glucocorticoid prescription (PPV 90%). COVID-19 was identified systematically from positive PCR tests or patient reports to the hospital/clinic of home rapid antigen tests. Patients were followed from the date of 3rd vaccine (index date) until breakthrough COVID-19, non-COVID death, or end of follow-up (January 18, 2023). A previously defined hierarchical algorithm was used to categorize DMARD exposures. Covariates included demographics, lifestyle, comorbidities, and prior COVID-19. We used Cox proportional hazards models to estimate the risk of COVID-19 among different DMARD users. We then used propensity scores and overlap-weighting to further account for confounding when comparing the risk among users of CD20i vs. TNFi.

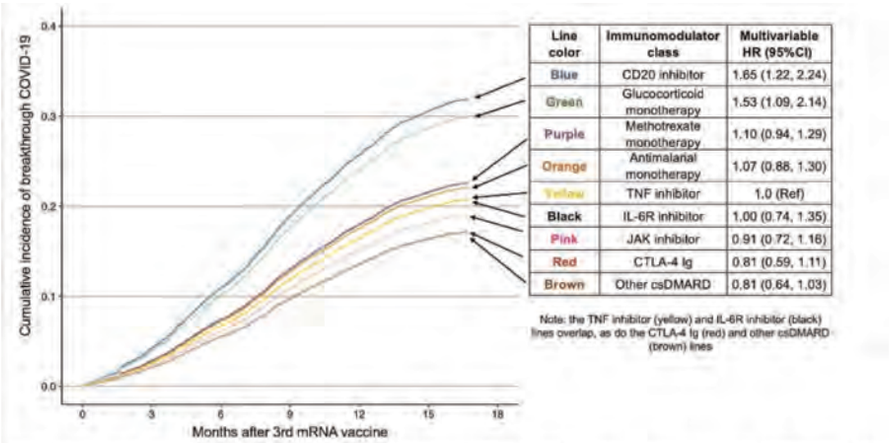

Figure 1. Cumulative incidence and hazard ratio for breakthrough COVID-19 by immunomodulator use at 3rd COVID mRNA vaccine dose.

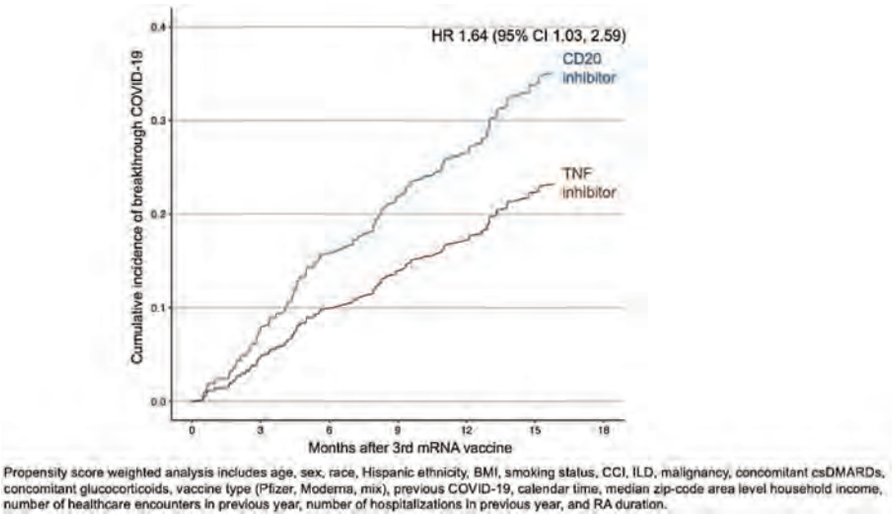

Figure 2. Propensity-score weighted cumulative incidence of COVID-19 after 3rd mRNA vaccine, comparing CD20 inhibitor users vs. TNF inhibitor users.

Results: We identified 5781 patients with RA who used DMARDs/glucocorticoids and received 3 mRNA vaccine doses (78.8% female, mean age 64.2 years). During mean follow up of 12.8 months, 1173 (20.2%) had a SARS-CoV-2 infection (incidence rate 15.7 per 1000 person-months) (**Table 1**). Users of CD20i were more likely than TNFi users to have COVID-19 after the index date (adjusted HR 1.74, 95%CI 1.30-2.33), as were users of steroid monotherapy (adjusted HR 1.47, 95%CI 1.09-1.98) (**Figure 1**). After using propensity scores for overlap weighting to account for baseline differences, CD20i users remained at higher risk for COVID-19 than TNFi users (HR 1.62, 95%CI 1.02-2.56; **Figure 2**). In a sensitivity analysis excluding patients with cancer or interstitial lung disease, the findings were similar.

Conclusion: In this RA-specific study evaluating the impact of DMARD use on the risk of COVID-19 during the Omicron phase of the pandemic, we identified CD20i and steroid monotherapy use as risk factors for breakthrough COVID-19. This contemporary study highlights the excess risk associated with glucocorticoid monotherapy or CD20 inhibitor use for RA treatment and identifies important subgroups for counseling and additional risk mitigation strategies.

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Abstract Number: 1273

Long-term Follow-up of Treated-to-target RA and UA: Results of the BeSt and IMPROVED Studies

Sascha Heckert[1], Johanna Maria Maassen[1], Isabell Nevins[2], F. Fodili[3], Margreet Steup-Beekman[4], Thomas Huizinga[1], Sytske Anne Bergstra[1] and CF Allaart[1], [1]Leiden University Medical Center, Leiden, Netherlands, [2]Leiden University Medical Center, Amsterdam, Netherlands, [3]Stichting ReumaZorg ZWN, Roosendaal, Netherlands, [4]Leiden University Medical Center, Den Haag, Netherlands

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Background/Purpose: In 2 trials with an original follow-up of 5-10 years, patients with early arthritis were treated to target, resulting in low disease activity or remission in the majority of patients and limited radiographic progression. We invited former participants for a long-term follow-up ('RECALL') visit.

Methods: In BeSt (inclusion 2000-2002) 508 patients with early RA were randomized to: 1. Sequential DMARD monotherapy; 2. Step-up combination therapy; 3. Initial csDMARD combination therapy with prednisone or 4. Initial combination of MTX + infliximab, and treated-to-target DAS≤2.4 for 10 years. In IMPROVED (inclusion 2007-2010) 610 patients with early RA or UA received induction therapy with MTX + prednisone, with DAS< 1.6 as a treatment target. After 4 months 67% were in DAS remission (early remission). From 2019 to 2022 patients from both trials were invited for follow-up (after 20/12 years respectively). Outcomes were functional ability (HAQ), disease activity (3-component DAS) and radiographic damage (Sharp/Van der Heijde score, SHS, based on hands/feet X-rays of BeSt/IMPROVED at baseline & RECALL study visit, assessed by one reader (intrareader coefficient 0.98)). All outcomes had < 6% missing. In BeSt, SHS was compared

	Arm 1, sequential monotherapy (n=33)	Arm 2, step-up combination therapy (n=31)	Arm 3, initial combination with prednisone (n=39)	Arm 4, initial combination with infliximab (n=50)	p-value
Age, mean (SD)	48 (10)	45 (10)	45 (11)	47 (12)	0.54
Symptom duration in weeks, median (IQR)	31.7 (16.6-89.0)	25.1 (9.3-40.3)	23.3 (11.9-50.7)	25.1 (14.6-56.1)	0.13
Sex, %	76	84	67	64	0.22
BMI, mean (SD)	25.6 (5.7)	25.2 (3.6)	25.6 (3.9)	25.9 (3.8)	0.90
Ever smoker, %	28	45	26	18	0.067
Disease activity score (DAS), mean (SD)	4.4 (0.8)	4.6 (1.0)	4.4 (1.0)	4.0 (0.6)	0.024
ESR, mean (SD)	46.4 (32.6)	35.3 (24.7)	35.5 (21.2)	31.7 (21.7)	0.070
CRP, mean (SD)	41.8 (42.4)	25.1 (30.6)	37.9 (46.5)	24.6 (30.3)	0.12
Health Assessment Questionnaire, mean (SD)	1.3 (0.6)	1.6 (0.6)	1.3 (0.6)	1.3 (0.6)	0.076
ACPA positive, %	73	45	62	73	0.048
RF positive, %	76	55	69	62	0.31
SHS, mean (SD)	2.7 (5.6)	1.5 (2.0)	1.3 (3.6)	1.7 (3.8)	0.53

BeSt baseline characteristics of RECALL participants

between treatment arms with a generalized linear model, adjusted for unequally distributed patient characteristics across treatment arms (baseline DAS, ACPA; table 1). In IMPROVED, SHS was compared between patients that had been in early remission vs. not in early remission, adjusted for possible confounders (baseline DAS, ACPA, BMI).

Results: 45% (153/339) of alive BeSt patients participated (table 1). Their mean age at BeSt baseline was 46±11 years (non-participants/deceased: baseline age 58±13 years). At 20-year follow-up, median HAQ was 0.75, IQR 0.25-1.25; 0.54±0.7 lower than at baseline. Mean DAS was 1.5±0.6, with 137/151 (91%) of patients with DAS≤2.4 and 102/151 (68%) in DAS remission. Overall median SHS at RECALL visit was 13 (IQR 6-36) with a median progression of SHS 11 (IQR 5-30) since

	Early remission (n=177)	No early remission (n=104)
Age, mean (SD)	49 (12)	49 (12)
Symptom duration in weeks, median (IQR)	18.0 (9.0-34.0)	21.0 (10.0-37.0)
Sex, %	63	82
BMI, mean (SD)	25.5 (4.1)	26.9 (5.0)
Ever smoker, %	26	25
Disease activity score (DAS), mean (SD)	3.0 (0.8)	3.6 (0.9)
ESR, mean (SD)	25.3 (20.5)	29.1 (23.2)
CRP, mean (SD)	18.8 (23.5)	23.0 (32.4)
Health Assessment Questionnaire, mean (SD)	1.1 (0.6)	1.4 (0.7)
ACPA positive, %	66	48
RF positive, %	64	54
SHS, mean (SD)	1.9 (3.0)	2.1 (3.3)

IMPROVED baseline characteristics of RECALL participants

baseline. Compared to the other arms, SHS was lower in arm 4 (median SHS (IQR) 17 (8-58) in arm 1, 14 (3-28) in arm 2, 22 (7-42) in arm 3 and 9 (3-27) in arm 4). After adjusting for baseline differences this difference was statistically significant for arms 1 (p=0.02) and 3 (p=0.01), but not for arm 2 (p=0.16). 54% (282/523) of alive IMPROVED patients participated (table 2). Their mean age at IMPROVED baseline was 49±12 years (non-participants/deceased: 55±15 years). At 12-year follow-up, median HAQ was 0.50, IQR 0-1.0; 0.56±0.7 lower than at baseline. Mean DAS was 1.4±0.7, with 255/279 (91%) of patients with DAS≤2.4 and 189/279 (68%) in DAS remission. Overall median SHS was 8 (IQR 3-16) with a median SHS progression since baseline of 6 (IQR 3-13). Median SHS (IQR) was 10 (IQR 4-17) in the early remission group vs 6 (IQR 2-15) in patients that had not been in early remission. There was no statistically significant difference after adjusting for possible confounders (p=0.28).

Conclusion: 91% of patients who attended long term follow-up of BeSt/IMPROVED after respectively 20 and 12 years were in remission or low disease activity, with a median HAQ of 0.75/0.50 and clinically significant SHS progression of median 11/6 points.

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Rheumatoid Arthritis Patients, Achieving Low Disease Activity State or Remission, Still Demonstrate Significant Hand Disability, as Assessed by Functional Dexterity Test: A Disconnection Between CDAI and Functional Hand Assessment

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SESSION INFORMATION
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Background/Purpose: Direct functionality of the hand is not commonly assessed in daily practice or clinical trials in patients with rheumatoid arthritis (RA). Functional dexterity test (FDT), developed to assess a patient's ability to use the hand for daily tasks and widely used in rehabilitation medicine, has also been suggested as a legitimate tool for RA patients [Aaron et al, J Hand Ther. 2003]. *Aim:* To examine the value of FDT in a cohort of RA patients and to study the correlation between the results of FDT and RA activity.

Methods: Patients with established RA were followed in the outpatient clinic of Bnai Zion Medical Center performed the FDT during their regular follow-up visits. All patients were given 100 seconds (sec) to complete the test; the performance was measured in seconds separately for the dominant and non-dominant hands. FDT results were compared among 28 patients with active RA and clinical disease activity index(CDAI) greater than 10, 20 RA patients with controlled disease activity (CDAI of less than or equal to 10), and 20 volunteers with no rheumatic disease from the hospital personnel who agreed to perform the FDT.

Table 1. Corresponding FDT results for the dominant and non-dominant hand

	FDT dominant hand mean (range) in *sec* and comparison with control group, p value		FDT non-dominant hand mean (range) in *sec* and comparison with control group, p value	
RA, CDAI>10	43 (24-100)	0.0001	50 (22-100)	0.0001
RA, CDAI≤ 10	35 (27-70)	0.001	38 (24-68)	0.013
Control group	25 (20-40)		29 (22-45)	
Normal FDT	Up to 25		Up to 27	

Results: A group of patients with active RA was younger than other groups, with a median age of 56 years (range 30-88 years) vs. 65 years (range 41-78 years) in the controlled RA group vs. 62 years (range 40-82 years) in the control group, $p < 0.03$. The mean disease duration was 11 years (range 3-26 years) in the active disease group and 11 years (range 1-47 years) in the controlled RA group, p=0.97. The gender composition of the groups was similar, with female patients comprising 70% to 82% (p=0.67). All 28 RA patients with CDAI >10 and 16 of 20 patients with CDAI< or equal to 10 were treated with biologics (p=0.02). Mean FDT for the dominant hand was 43 sec (range 24-100 sec) in the active RA group, 35 sec (range 27-70 sec) in the controlled RA group, and 25 sec (range 20-40 sec) in persons without arthritis. Corresponding FDT results for the non-dominant hand were 50 sec (range 22-100 sec), 38 sec (range 24-68 sec), and 29 sec (22-45 sec), respectively (Table 1). The difference in the FDT results between the two RA groups was non-significant for the dominant hand (p=0.28) but reached statistical significance for the non-dominant hand (p=0.02). Individuals without arthritis performed FDT either by dominant or non-dominant hand significantly better than any RA group (p values from 0.013 to 0.0001). FDT results significantly correlated with CDAI in the group of active RA only, with R=0.47/p=0.01 for the dominant hand and R=0.49/p=0.007 for the non-dominant hand vs. R=0.29/p=0.2, and R=0.4/p=0.08, respectively, in the controlled RA group. Minimally or non-functioning dominant hand, as predefined by FDT, was observed in 17 of 28 patients with active RA (61%), 11 of 20 patients (55%) with controlled disease, and 3 of 20 (15%) volunteers with no rheumatic disease.

Conclusion: FDT revealed a significant decrease in hand function in most RA patients. In patients with high or moderate RA activity, FDT correlated well with CDAI scores, while this correlation was lost in the group of patients with low disease activity or remission, where 55% of patients still demonstrated a significant loss in the dominant hand function.

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Abstract Number: 1275

Prevalence of Frailty Among Individuals Living with Rheumatoid Arthritis: A Population-based Cohort Study

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Studies have demonstrated a link between frailty and chronic inflammation, raising the question of whether chronic inflammatory diseases like rheumatoid arthritis (RA) may be associated with increased rates of frailty. Our objective was to evaluate the prevalence of frailty among individuals living with RA compared to the general population without RA.

Methods: We conducted a population-based cohort study using administrative health data for a Canadian province from 1990 - 2018. A previously validated case definition based on physician billing data was used to assemble an incident cohort of all cases with RA onset from 1996 - 2008. To capture the health state of individuals living with RA, the baseline date was defined as 5 years after the index date for RA diagnosis. A random sample of 50% of incident RA cases was included in this analysis, none of which were used for the derivation of our frailty measure. Each RA individual was matched 2:1 by sex, birth year, and index year with randomly selected individuals from the general population with no physician visits for any type of inflammatory arthritis. For controls, the index date was defined as the date of a randomly selected health care encounter occurring in the same calendar year as the index year of the RA case to which they were matched, and the baseline date was defined as 5 years after this index date. Frailty was measured using a frailty index (FI), which we previously developed using a combination of data-driven and consensus-based methods. The FI includes 40 health deficits, the presence of which was evaluated using administrative health data for the 3 years prior to the baseline date. Each deficit was scored from 0 (absent) to 1 (present) and individual deficit scores were summed and divided by the total number of deficits to produce a baseline FI score for each individual. Frailty was defined as a baseline FI score > 0.21. We compared the prevalence of frailty among RA patients and non-RA controls using conditional logistic regression. The number of health deficits present was compared between RA patients and non-RA controls using negative binomial regression. Multivariable models were stratified by age, sex, and calendar year, and were adjusted for rurality, socioeconomic status, and baseline scores for the Romano version of the Charlson comorbidity index (CCI).

Table 1. Baseline characteristics of individuals living with rheumatoid arthritis (RA cases) versus age- and sex-matched individuals without inflammatory arthritis (non-RA controls).

Table 1. Baseline characteristics of individuals living with rheumatoid arthritis (RA cases) versus age- and sex-matched individuals without inflammatory arthritis (non-RA controls).

	RA cases n=13367	Non-RA controls n=26734
Age at baseline (years), mean (SD)	60.2 (14.4)	60.2 (14.4)
Female, n (%)	9213 (68.9%)	18420 (68.9%)
Rurality		
Urban, n (%)	11064 (82.8%)	23275 (87.1%)
Rural, n (%)	2303 (17.2%)	3458 (12.9%)
Neighbourhood income quintile		
Lowest 20%, n (%)	2878 (21.5%)	4882 (18.3%)
20-40%, n (%)	2667 (20.0%)	5104 (19.1%)
40-60%, n (%)	2922 (21.9%)	5755 (21.5%)
60-80%, n (%)	2541 (19.0%)	5411 (20.2%)
Highest 20%, n (%)	2359 (17.6%)	5582 (20.9%)
Baseline Romano CCI [a]		
Mean (SD) score	0.83 (1.60)	0.65 (1.43)
Median (IQR) score	0 (0-1)	0 (0-1)
Score ≥ 1, n (%)	4933 (36.9%)	8003 (29.9%)
Baseline frailty index (FI) [a]		
Mean (SD) score	0.078 (0.070)	0.053 (0.058)
Median (IQR) score	0.0625 (0.025-0.1125)	0.0375 (0.0125-0.075)
Frail (FI > 0.21), n (%)	744 (5.6%)	703 (2.6%)

[a] Calculated using administrative health data for the 3-year assessment period prior to the baseline date.
SD = standard deviation; IQR = interquartile range; CCI = Charlson comorbidity index.

Table 2. Conditional logistic regression models for frailty status among individuals with rheumatoid arthritis (RA cases; n=13367) versus matched individuals without inflammatory arthritis (non-RA controls; n=26734).

Table 2. Conditional logistic regression models for frailty status among individuals with rheumatoid arthritis (RA cases; n=13367) versus matched individuals without inflammatory arthritis (non-RA controls; n=26734).

	Odds ratio (95% CI)
Model 1: Unadjusted	
RA cases (versus non-RA controls)	2.29 (2.05 – 2.56)
Model 2: Adjusted for rurality, neighbourhood income quintile	
RA cases (versus non-RA controls)	2.27 (2.04 – 2.54)
Model 3: Adjusted for rurality, neighbourhood income quintile, baseline CCI score	
RA cases (versus non-RA controls)	2.30 (2.03 – 2.60)

Frailty defined as a baseline frailty index (FI) score > 0.21, calculated using administrative health data for the 3 years prior to the baseline date.
All models stratified by the matching variables (birth year, sex, and year of index date).
CCI = Charlson comorbidity index; CI = confidence interval.

Table 3. Negative binomial regression models for the number of health deficits present at baseline among individuals with rheumatoid arthritis (RA cases; n=13367) versus matched individuals without inflammatory arthritis (non-RA controls; n=26734).

Table 3. Negative binomial regression models for the number of health deficits[a] present at baseline among individuals with rheumatoid arthritis (RA cases; n=13367) versus matched individuals without inflammatory arthritis (non-RA controls; n=26734).

	Rate Ratio (95% CI)
Model 1: Unadjusted	
RA cases (versus non-RA controls)	1.52 (1.49 – 1.55)
Model 2: Adjusted for rurality, neighbourhood income quintile	
RA cases (versus non-RA controls)	1.51 (1.48 – 1.54)
Model 3: Adjusted for rurality, neighbourhood income quintile, baseline CCI score	
RA cases (versus non-RA controls)	1.47 (1.44 – 1.50)

[a] Based on 40 health deficits included in the frailty index (FI), evaluated using administrative health data for the 3 years prior to the baseline date.
All models stratified by the matching variables (birth year, sex, and year of index date).
CCI = Charlson comorbidity index; CI = confidence interval.

Results: Baseline characteristics for RA patients (n=13367) and non-RA controls (n=26734) are shown in **Table 1**. Baseline FI scores were significantly higher among RA patients compared to non-RA controls and a greater proportion of RA patients were considered frail at baseline **(Table 1)**. The odds of frailty were significantly higher among RA patients compared to non-RA controls, and this relationship was unchanged following adjustment for potential confounders **(Table 2)**. Similar results were obtained for the number of health deficits present at baseline **(Table 3)**.

Conclusion: Frailty is significantly more common among individuals living with RA when compared to age- and sex-matched individuals without inflammatory arthritis. Future work will aim to better understand the reasons for these differences and identify strategies to prevent and treat frailty in RA.

Disclosure: A. Legge: None; **D. Lacaille**: None.

Abstract Number: 1276

Multimorbidity Burden Predicts Lower Likelihood of Remission in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
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Background/Purpose: Seropositivity has historically been associated with poor disease outcomes in patients with rheumatoid arthritis (RA). Seronegative RA is on the rise and is associated with higher rates of multimorbidity (i.e., 2 or more chronic conditions). However, little is known about the association between multimorbidity and RA disease activity. We aimed to assess the association between multimorbidity and RA disease flares and remission.

Methods: This retrospective, population-based study included residents of a geographically well-defined area with incident RA in 1999-2014 who fulfilled 1987 ACR criteria for RA. Flare/remission were defined using OMERACT definitions and were manually abstracted from medical records. Flare was defined as a worsening of disease requiring initiation, change, or escalation of therapy or documentation of 'flare up' or 'active' disease. Remission was defined as an absence of disease activity (e.g., 'remission', 'quiescent', 'no activity') and/or based on ≤1 tender/swollen joints and normal inflammatory markers. Multimorbidity at RA incidence was defined using 55 chronic conditions published previously and was categorized as MM2+ (2 or more comorbidities) or MM5+ (5 or more comorbidities). Binomial mixed models with random effects accounting for multiple visits per patient adjusted for age, sex, RA duration, seropositivity, incidence year, and smoking status were used to assess the association between flare/remission and multimorbidity.

Results: The study included 625 patients with RA (mean age 55.5 years, 70% female, 88% white, 68% seropositive, 47% current/former smokers, 40% obese). Among 7841 visits over a mean follow-up of 8.7 (SD 4.3) years, 2793 were in flare (36%) and 1929 (25%) were in remission. Multimorbidity was modestly associated with flare, but these associations did not reach statistical significance (MM2+: OR 1.22;95% CI: 0.97-1.53, p=0.08; MM5+: OR 1.16; 95%CI 0.94-1.44, p=0.16). Multimorbidity was significantly associated with decreased odds of remission for both MM2+ (OR 0.63; 95%CI 0.46-0.87, p=0.0048) and MM5+ (OR 0.64 [95%CI 0.48-0.87, p=0.0046). Seropositivity was not significantly associated with flare (OR 1.13; 95%CI 0.93-1.40; p=0.21) or remission (OR 1.00; 95%CI 0.75-1.34, p=0.99). Male sex, longer RA duration, and increased age were associated with significantly greater odds of remission and smoking at baseline was associated with significantly decreased odds of remission. RA duration, increased age, and increased year of RA index were associated with significantly lower odds of flare and current smoking with significantly increased odds of flare.

Conclusion: Patients with RA and multimorbidity were less likely to achieve remission. Multimorbidity was a stronger predictor of poor prognosis than seropositivity. These results underscore the importance of considering multimorbidity and not just seropositivity when assessing prognosis for patients with RA. Further research is needed to elucidate the underlying mechanisms of these associations (e.g., whether certain morbidities are associated with poor prognosis, or the impact of patient complexity on adherence or other issues are playing a role).

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Abstract Number: 1277

Relationship Between Quality of Life and the Region of the Affected Joints in Japanese Patients with Rheumatoid Arthritis: A Cross-sectional Study

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SESSION INFORMATION
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Background/Purpose: This clinical study aimed to investigate the relationship between affected joints and the quality of life (QOL) in patients with rheumatoid arthritis (RA) in Japan.

Methods: We analyzed data from 15,553 RA patients registered in the NinJa database in 2020 to investigate the relationship between affected joints and the quality of life (QOL). QOL was assessed using the EuroQol 5-Dimensions (EQ-5D) questionnaire. Patients for whom EQ-5D data were acquired were included in this study. The affected joints, based on a 68-joint count, were categorized into four regions: upper/large, upper/small, lower/large, and lower/small. The presence or absence of swelling or tenderness in the joints within each region was evaluated as a binary variable. We performed multivariable regression analysis with EQ-5D scores as the dependent variable. The independent variables included demographic factors (age, sex), disease duration, pain visual analogue scale (pain VAS), C-reactive protein (CRP) levels, positivity of rheumatoid factor (RF) and anti-citrullinated peptide antibody (ACPA), scores from the hospital anxiety and depression scale (HADS-A and HADS-D), modified health assessment questionnaire (mHAQ), Steinbrocker's stage, and the presence/absence of swelling or tenderness in the affected joints within each region.

Results: The study included 11,709 RA patients, with a mean age of 67.0 years (SD = 12.9), and 79.2% were women. The mean disease duration was 14.0 years (SD = 11.2). (Table 1) After adjusting for covariates, the activity of upper/large joints region (β = -0.02, 95% CI: -0.02 to -0.01, $p < 0.01$), lower/large (β = -0.03, 95% CI: -0.04 to -0.02, $p < 0.01$), 65 to 74 years old (β = -0.03, 95% CI: -0.05 to -0.00, $p = 0.02$), 75 years old or older (β = -0.05, 95% CI: -0.07 to -0.03, $p < 0.01$), women sex (β = -0.01, 95% CI: -0.02 to -0.00, $p < 0.01$), pain VAS (β = -0.02, 95% CI: -0.02 to -0.02), CRP (β = -0.01, 95% CI: -0.01 to -0.00, $p < 0.01$), HADS-A (β = -0.01, 95% CI: -0.01 to -0.01, $p < 0.01$), HADS-D (β = -0.01, 95% CI: -0.01 to -0.00, $p < 0.01$), and mHAQ (β = -0.15, 95% CI: -0.16 to -0.14, $p < 0.01$) were found to be significantly associated with lower EQ-5D scores, indicating worse QOL. (Table 2)

Conclusion: In this study, we found significant associations between various factors and QOL of RA patients in Japan. Specifically, among the demographic factors, being aged 65 or older and female, along with higher scores on pain VAS, elevated CRP levels, increased scores on HADS-A and HADS-D, and higher mHAQ scores were all associated with decreased EQ-5D scores, indicating lower QOL. Furthermore, we observed that the presence of swelling or tenderness in the affected joints within both the upper and lower extremities, particularly in the large joints, was significantly associated with lower EQ-5D scores. By considering these factors and the specific joint distribution, healthcare professionals can tailor interventions and treatment strategies to improve the QOL of RA patients, focusing on mitigating pain, reducing inflammation, and addressing functional limitations associated with affected joints.

Table 1. Characteristics of Participating RA Patients

N		11709
age (years old) (SD)		66.99 (12.85)
age (%)	16-39 (years old)	365 (3.1)
	40-64 (years old)	3626 (32.7)
	65-74 (years old)	4013 (34.3)
	<74 (years old)	3505 (29.9)
sex, women (%)		9272 (79.2)
disease duration (years)		13.96 (11.22)
pain VAS (0-10 cm) (SD)		2.26 (2.23)
PGA (0-10 cm) (SD)		2.31 (2.20)
CRP (mg/dL) (SD)		0.47 (1.06)
ESR (mm/hr) (SD)		24.73 (21.07)
RF positive (%)		6509 (72.0)
ACPA positive (%)		3622 (72.5)
HADS-A (SD)		3.80 (3.48)
HADS-D (SD)		5.51 (3.69)
EQ-5D (SD)		0.76 (0.19)
mHAQ (SD)		0.35 (0.57)
DAS28 (SD)		2.78 (1.15)
stage (%)	I	3380 (32.4)
	II	2928 (28.0)
	III	1773 (17.0)
	IV	2366 (22.6)
class (%)	1	4317 (41.2)
	2	4350 (41.5)
	3	1607 (15.3)
	4	208 (2.0)
swollen joint count 68 (SD)		0.95 (2.23)
tender joint count 68 (SD)		1.60 (3.84)
upper/large (%)		3659 (31.2)
upper/small (%)		3098 (26.5)
lower/large (%)		2339 (20.0)
lower/small (%)		721 (6.2)

ACPA: anti-cyclic citrullinated peptide antibody; CRP: C-reactive protein; DAS28: disease activity score 28; ESR: rythrocyte sedimentation rate; EQ-5D: EuroQol 5 dimension; HADS-A; hospital anxiety and depression Scale-anxiety; HADS-D; hospital anxiety and depression Scale-depression; mHAQ; modified health assessment questionnaire; PGA: patients global assessment; RA: rheumatoid arthritis; RF: rheumatoid factor; SD: standard deviation; VAS: visual analogue scale

Table 2. Estimates of Partial Regression Coefficients in Multiple Regression Analysis with EQ-5D as the Dependent Variable

Factor		Estimate (95% CI)	p value
age	16-39 (years old)	Reference	
	40-64 (years old)	-0.01 (-0.04, 0.01)	0.218
	65-74 (years old)	-0.03 (-0.05, -0.00)	0.02
	<74 (years old)	-0.05 (-0.07, -0.03)	<0.001
sex, women		-0.01 (-0.02, -0.00)	0.003
disease duration		0.00 (-0.00, 0.00)	0.576
pain VAS		-0.02 (-0.02, -0.02)	<0.001
CRP		-0.01 (-0.01, -0.00)	<0.001
RF positive		0.00 (-0.01, 0.01)	0.76
ACPA positive		0.01 (-0.00, 0.02)	0.143
HADS-A		-0.01 (-0.01, -0.01)	<0.001
HADS-D		-0.01 (-0.01, -0.00)	<0.001
mHAQ		-0.15 (-0.16, -0.14)	<0.001
stage	I	Reference	
	II	0.00 (-0.01, -0.00)	0.287
	III	0.00 (-0.01, 0.02)	0.743
	IV	0.00 (-0.01, 0.02)	0.567
affected joints region	upper/large	-0.02 (-0.02, -0.01)	<0.001
	upper/small	0.00 (-0.01, 0.01)	0.98
	lower/large	-0.03 (-0.04, -0.02)	<0.001
	lower/small	-0.01 (-0.02, 0.01)	0.27

ACPA: anti-cyclic citrullinated peptide antibody; CI: confidence interval; CRP: C-reactive protein; EQ-5D: EuroQol 5 dimension; HADS-A; hospital anxiety and depression Scale-anxiety; HADS-D; hospital anxiety and depression Scale-depression; mHAQ; modified health assessment questionnaire; RF: rheumatoid factor; VAS: visual analogue scale

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Abstract Number: 1278

Nature and Severity of Activity Limitations According to the Health Assessment Questionnaire Disability Index in Patients with Rheumatoid Arthritis and Functional Disability

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SESSION INFORMATION

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Background/Purpose: Not withstanding modern treatment, some Rheumatoid Arthritis (RA) patients have severe disability due to persistently high disease activity, joint destruction/deformities and/or comorbidities. Insight into the severity and nature of their functional limitations is important to treat this subgroup adequately. The aim of this research was to describe the severity and nature of functional limitations in RA patients with severe functional limitations, according to the Health Assessment Questionnaire Disability Index (HAQ-DI).

Methods: Baseline data from RA patients with severe functional limitations participating in a randomized controlled trial on the (cost-)effectiveness of longstanding physical therapy compared to usual care were used (Netherlands Trial Register NL8238). Participants completed the HAQ-DI, a questionnaire reflecting problems in activities of daily living and consisting of 20 items divided over eight domains (Dressing and grooming, Arising, Eating, Walking, Personal hygiene, Reaching, Gripping and Usual activities). Each item is scored on a 4-point scale (0-3, no difficulty-unable to perform), with the total HAQ-DI score ranging from 0-3 (no disability-severe disability). Demographic characteristics were administered and the EuroQol 5-Dimensions 5-Levels (EQ-5D-5L, index score (-0.446-1.000), and Visual Analogue Scale (EQ-VAS, 0-100)) were used to estimate health-related quality of life.

Results: 215 participants were included (n=194; 90% women, age 58.8 (SD 12.9) years, median disease duration 19 (IQR 9-27) years). The median EQ-5D-5L index and EQ-VAS were 0.6 (0.3-0.7) and 59 (41 -70). The median total HAQ-DI score was 1.5 (1.1-1.9) and the majority (83%, n=179) had a total HAQ-DI score ≥1, indicating moderate to severe functional limitations. Figure 1 shows the mean HAQ-DI scores per domain and the percentage of patients reporting no/some/much difficulty or inability to perform daily activities within each domain. More than half of the participants had a domain score ≥1 in all 8 domains (52%, n=111), 24% (n=52) in 7 domains, 13% (n=28) in 6 domains and 11% (n=24) in 5 or less domains. The domains Personal hygiene and Reaching had the highest percentage of participants with a maximum score of 3 (42% and 28%).

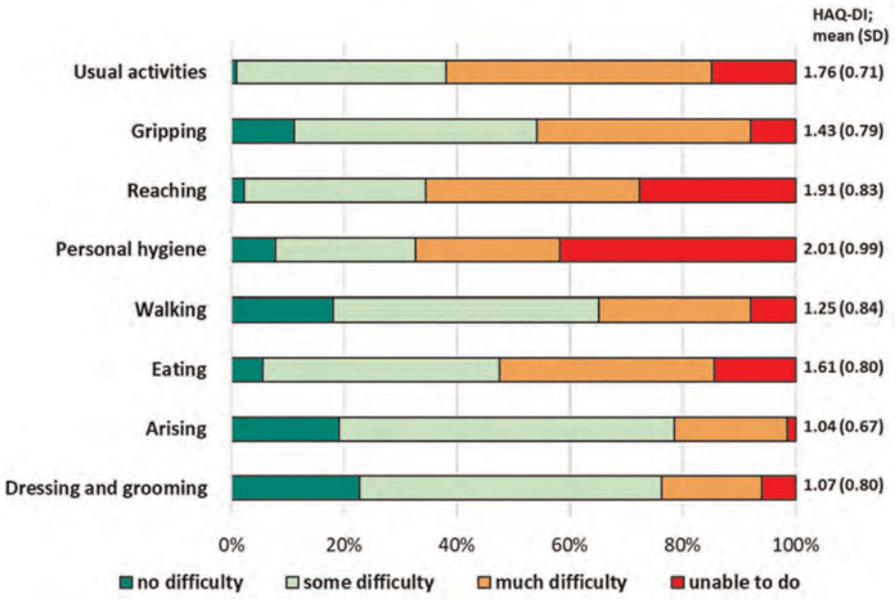

Figure 1. Mean HAQ-DI scores for each HAQ-DI domain and the percentage of patients that reported to have either no/some/much difficulty or unable to perform everyday activities represented for each domain.

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Conclusion: In this subgroup of RA patients with severe functional limitations, the majority had limitations in almost all domains of the HAQ-DI. Mostly, limitations were seen in Personal hygiene and Reaching. In clinical practice, a comprehensive assessment of all areas of daily activities might thus be warranted, as well as shared decision-making between patients and clinicians to prioritize functional limitations and set personalized treatment goals.

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Abstract Number: 1279

What Is the Nature of Functional Problems in People with Rheumatoid Arthritis and Severe Disability; An Analysis Using the International Classification of Functioning, Disability and Health as a Reference

Max Teuwen[1], Salima van Weely[1], Thea Vliet Vlieland[2], Thom Douw[3], Manja van Wissen[1], Alfons den Broeder[4], Dirkjan van Schaardenburg[5], Cornelia van den Ende[4] and Maaike gademan[1], [1]Leiden University Medical Center, Leiden, Netherlands, [2]Leids University Medical Center, Leiden, Netherlands, [3]Leiden University of Applied Sciences, Leiden, Netherlands, [4]Sint Maartenskliniek, Nijmegen, Netherlands, [5]Reade, Amsterdam, Netherlands

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Background/Purpose: There is a lack of knowledge about the limitations in activities and participation experienced by a subgroup of people with rheumatoid arthritis (RA) and severe functional disability, such as those with difficult-to-treat RA. More insight is essential to optimize their treatment, in particular non-pharmacological care, of which exercise therapy is an essential element. The International Classification of Functioning, Disability and Health (ICF) offers a common framework to classify functional limitations. Therefore, the aim of the study was to describe limitations in activities and participation of people with RA with severe functional disability using the ICF as a reference.

Methods: Baseline data from n=206 people with RA and severe disability, participating in an exercise trial were used. In that trial, the Patient Specific Complaint (PSC) was used as an instrument to identify and quantify limitations in activities and participation. For each participant, the three most limited activities as derived from the PSC were linked to the ICF. Two researchers independently identified meaningful concepts within each PSC activity and linked them to the most specific ICF category within the "Activities and Participation" component, following standardized linking rules. The frequencies of ICF categories were calculated and compared with activities and participation elements of the Comprehensive and Brief ICF Core Sets for RA.

Results: Of 206 RA patients (90.8% female, 58.7 (12.9) years of age, 1.5 (0.5) HAQ-DI score), 618 PSC activities were linked to 909 (72 unique) ICF categories. Taking into account all three activities, the five most prevalent ICF categories concerned the ICF domain Mobility (d4) and included d4501 walking long distances (n=121/909; 13.3%); d4502 walking on different

Table 1. Frequencies and nature of most prevalent limitations within the ICF component activities and participation of people with RA and severe disability (n=909 ICF categories)

Total of 3 PSC activities	N (%)	PSC activity 1	N (%)	PSC activity 2	N (%)	PSC activity 3	N (%)
d4501 walking long distances	121 (13.3)	d4501 walking long distances	75 (23.7)	d4501 walking long distances	28 (9.5)	d4103 changing basic body position from sitting	28 (9.4)
d4502 walking on different surfaces	79 (8.7)	d4502 walking on different surfaces	47 (14.9)	d451 stair climbing	25 (8.5)	d451 stair climbing	27 (9.0)
d451 stair climbing	62 (6.8)	d4500 walking short distances	33 (10.4)	d4103 changing basic body position from sitting	20 (6.8)	d4402 manipulating	20 (6.7)
d4103 changing basic body position from sitting	60 (6.6)	d4401 grasping	14 (4.4)	d4750 driving human-powered transportation	19 (6.4)	d4401 grasping	19 (6.4)
d4401 grasping	51 (5.6)	d4103 changing basic body position from sitting	12 (3.8)	d4401 grasping	18 (6.1)	d4501 walking long distances	18 (6.0)

PSC: Patient specific complaints

Funding

This project is financially supported by the Netherlands Organization for Health Research and Development (ZonMw; 852004018), Ministry of Health, Welfare and Sport (Ministerie van Volksgezondheid, Welzijn en Sport), the Royal Dutch Society for Physical Therapy (KNGF) and the Dutch Arthritis Society (ReumaNederland).

surfaces (n=79/909; 8.7%); d451 stair climbing (n=62/909; 6.8%); d4103 changing basic body position from sitting (n=60/909; 6.6%); and d4401 grasping (n=51/909, 5.6%) (Table 1). Considering the top-5 of the three individual PSC activities, three additional ICF categories (driving human-powered transportation, manipulating, walking short distances) were found to be relatively frequent. All of the most frequent ICF categories were included in the ICF RA Core Sets, except for stair climbing.

Conclusion: Most limitations of patients with RA with severe disability were seen in the ICF domain Mobility. Except for stair climbing, most of the identified ICF categories were covered by the related sections of the ICF RA Core sets. Clinicians should thus be aware that some relatively common problems in selected groups of RA patients may not be included in the Core Sets.

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Abstract Number: 1280

Systemic Inflammation Is Associated with Incident Valvular Heart Disease in Patients with Rheumatoid Arthritis: A Multicenter, Prospective Cohort Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: The risk of aortic stenosis is increased in people with RA and valvular heart disease (VHD) is among the most over-represented causes of cardiovascular death in RA. Thus, VHD is an under-appreciated extra-articular manifestation in RA, whose risk factors in RA are largely unknown. Because aortic and mitral valve disease comprise the majority of the VHD burden in the U.S., we examined the associations of RA-related clinical variables with the risk of incident aortic and mitral valve disease in a large cohort of U.S. Veterans with RA.

Methods: We studied participants in the Veterans Affairs RA (VARA) registry, a multicenter, prospective cohort of U.S. Veterans with RA. Using diagnostic and procedural codes in linked VA, Medicare, and National Death Index data, a composite VHD outcome was defined as the development of aortic stenosis or insufficiency, non-rheumatic mitral stenosis, mitral insufficiency, aortic or mitral valve procedural intervention, or death related to aortic or mitral valve disease. Participants who experienced the VHD outcome prior to enrollment were excluded. Included participants were followed from registry enrollment to the first of the composite outcome, death, or end of study period (12/2020). RA disease activity was assessed using DAS28-CRP (DAS28-ESR if missing) and CDAI. From banked serum at enrollment, rheumatoid factor, anti-CCP, and hsCRP concentrations were measured using nephelometry or ELISA. We examined the association of these RA-related clinical variables with VHD risk in multivariable Cox regression models, adjusting for demographics, BMI, smoking status, hypertension, diabetes, coronary artery disease, and medication (methotrexate, hydroxychloroquine, TNFi, prednisone, statin) use at baseline.

Results: Among 2,848 eligible participants (mean age 71.6 years, 88% male, mean DAS28 3.8), we observed 128 composite VHD events over a mean follow up of 6.7 years (IR 6.67 [5.61-7.93] per 1000 person years). The incidence of aortic (IR 3.72 [2.95-4.68]) and mitral disease (IR 3.25 [2.54-4.16]) were similar. After multivariable adjustment, hsCRP concentration was significantly associated with incident VHD (**Table 1;** aHR 1.21 [1.02-1.43] per log unit increase; aHR 1.88 [1.10-3.23] for highest hsCRP quartile). Non-significant trends toward elevated VHD risk were observed in those who were RF (aHR 1.26 [0.78-2.03]) or anti-CCP positive (aHR 1.27 [0.80-2.03]), whereas higher autoantibody concentrations were not associated with VHD (**Table 2**). Referent to participants in DAS28 remission, those with higher DAS28 categories demonstrated trends toward higher VHD risk. DAS28 and CDAI scores, as well as high CDAI disease activity, similarly demonstrated non-significant trends with VHD risk.

Table 1. Association of systemic inflammation and composite disease activity measures with incidence valvular heart disease in U.S. Veterans with rheumatoid arthritis

Table 1. Association of systemic inflammation and composite disease activity measures with incident valvular heart disease risk in U.S. Veterans with rheumatoid arthritis	
Variable	**aHR (95% CI)***
DAS28 (per 1-unit)	1.06 (0.94-1.19)
DAS28 category	
Remission	*Ref*
Low	**1.84 (1.03-3.27)**
Moderate	1.29 (0.77-2.15)
High	1.38 (0.77-2.48)
CDAI (per 1-unit)	1.01 (1.00-1.02)
CDAI category	
Remission	*Ref*
Low	0.88 (0.46-1.67)
Moderate	0.97 (0.51-1.84)
High	1.26 (0.66-2.37)
hsCRP (per log unit)**	**1.21 (1.02-1.43)**
hsCRP quartiles	
1 (lowest)	*Ref*
2	1.69 (0.99-2.89)
3	1.32 (0.75-2.32)
4 (highest)	**1.88 (1.10-3.23)**
Variables assessed in separate models. *Adjusted hazard ratios (aHR) estimated in multivariable Cox regression models adjusting for age, sex, race, body mass index, smoking status, hypertension, diabetes, coronary artery disease, RF positivity, and medications (methotrexate, hydroxychloroquine, TNFi, prednisone, statins) at enrollment. **hsCRP concentration log-transformed prior to analysis **Bold indicates p<0.05** Abbreviations: CCP, cyclic citrullinated peptide; hsCRP, high sensitivity C-reactive protein; DAS28, Disease Activity Score with 28-Joint Count; Ref, referent	

Table 2. Association of RA-related autoantibody positivity and concentration with the risk of valvular heart disease in rheumatoid arthritis.

Table 2. Association of RA-related autoantibody positivity and concentration with the risk of valvular heart disease in rheumatoid arthritis.	
Variable	**aHR (95% CI)***
Rheumatoid factor	
Positive (vs. negative)	1.26 (0.78-2.03)
Strong positive (>3x ULN; vs. negative)	0.90 (0.62-1.30)
Concentration** (per log unit)	1.05 (0.96-1.14)
Anti-CCP	
Positive (vs. negative)	1.27 (0.80-2.03)
Strong positive (>3x ULN; vs. negative)	1.15 (0.75-1.77)
Concentration** (per log unit)	0.93 (0.83-1.05)
*Adjusted hazard ratios (aHR) estimated in multivariable Cox regression models adjusting for age, sex, race, body mass index, smoking status, hypertension, diabetes, coronary artery disease, DAS28, and medications (methotrexate, hydroxychloroquine, TNFi, prednisone, statins) at enrollment. **Distribution of autoantibody concentrations skewed, thus were log-transformed prior to analysis Abbreviations: CCP, cyclic citrullinated peptide; CI, confidence interval; IU, international unit; mL, milliliter; ULN, upper limit of normal.	

Conclusion: In this prospective RA cohort, baseline systemic inflammation as assessed by hsCRP was associated with a higher risk of incident VHD. Composite clinical RA disease activity measures were not significantly associated with incident VHD, though estimates were imprecise and only baseline disease activity measures were evaluated. Continued study is warranted to identify mediators that drive VHD risk in RA.

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Abstract Number: 1281

Risk of Cancer in Patients with Rheumatoid Arthritis Under Tocilizumab: Data from the French National Registry REGATE

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

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Background/Purpose: Our study aimed to estimate the incidence and risk factors of cancer among rheumatoid arthritis (RA) patients treated with tocilizumab (TCZ) and followed for five years in the French registry (REGATE), which assessed the effectiveness and safety of TCZ.

Methods: We specifically focused on solid cancers, hematological malignancies, and skin cancers including non melanoma skin cancers (NMSC). To collect these data, we developed a pre-defined data collection form and distributed it to participating centers that reported malignancies in REGATE. To identify potential risk factors associated with cancer, we performed a univariate analysis and a multivariate analysis using logistic regression analysis.

Results: Our study included 1496 patients with RA who were treated with TCZ for a mean duration of 32.0 (±22.0) months and followed for an average of 47 (±15.2) months, resulting in a total exposure of 3990.9 patient-years (PY). Of these patients, 63 (4.2%) were diagnosed with a total of 75 cancers during the follow-up period (35 solid neoplasms, 11 hematological malignancies, 3 melanomas, and 26 NMSC). The overall incidence of cancer excluding NMSC was 8.3 /1000 PY, which was calculated after excluding patients who developed cancer more than 90 days after the last TCZ administration Our multivariate analysis revealed that high age (OR=1.06 [1.03-1.09], p=0.001) and smoking exposure (OR=2.80 [1.38-5.68], p=0.004) were independent risk factors for the group of cancers excluding NMSC.

Conclusion: Our study identified an incidence of cancer comparable to that observed in RA patients treated with other bDMARD and no other risk factor than those known in the general population

Table 1 : Baseline characteristics of RA patients

Group n= patients	Cancer excluding NMSC (n=47)	p	NMSC (n=22)	p	Cancer free Patients (n=1433)	
Age, years	63.4 (10.5)	**0.01**	68.5 (9.1)	**0.01**	56.2 (13.6)	*Ref*
MD, n (%)	0 (0)		0 (0)		0 (0)	
Female	29 (61.7)	**0.01**	17 (77.3)	0.43	1154 (80.5)	*Ref*
MD, n (%)	0 (0)		0 (0)		0 (0)	
Weight in kilogram	73.0 (16.4)	**0.16**	70.7 (16.9)	0.75	69.6 (15.9)	*Ref*
MD, n (%)	2 (4.3)		0 (0)		73 (5.1)	
Current smoker	17 (36.2)	**0.02**	2 (9.1)	**0.16**	303 (20.3)	*Ref*
MD, n (%)	1 (2.1)		2 (9.1)		33 (2.3)	
History of cancer	5 (10.6)	**0.09**	2 (9.1)	0.31	72 (5.0)	*Ref*
MD, n (%)	0 (0)		0 (0)		0 (0)	
Charlson's Index	3.6 (1.4)	**0.001**	3.7 (1.2)	**0.01**	2.9 (1.4)	*Ref*
MD, n (%)	3 (6.4)		1 (4.5)		244 (17.0)	
RA duration (months)	144.2 (129.9)	0.65	156.5 (98,8)	0.88	152.5 (120.3)	*Ref*
MD, n (%)	0 (0)		1 (4.5)		74 (5.2)	
ACPA+ and/or RF+	39 (83.0)	0.65	16 (72.7)	0.21	1146 (80.0)	*Ref*
MD, n (%)	2 (4.3)		2 (9.1)		134 (9.4)	
csDMARDs	2.0 (1.2)	**0.16**	2.3 (1.2)	0.81	2.3 (1.3)	*Ref*
MD, n (%)	1 (2.1)		0 (0)		0 (0)	
MTX, n (%)	40 (85,1)	**0.02**	22 (100)	0.38	1351 (94,3)	*Ref*
MD, n (%)	1 (2.1)		0 (0)		20 (1.4)	
Previous bDMARDs	1.7 (1.1)	0.6	1.9 (1.3)	0.63	1.8 (1.3)	*Ref*
MD, n (%)	0 (0)		0 (0)		0 (0)	
Duration of follow-up in REGATE (months)	46.3 (16.6)	0.77	55.9 (8.2)	**0.01**	46.9 (15.2)	*Ref*
MD, n (%)	0 (0)		0 (0)		6 (0.4)	
Total dose (mg)	563.8 (143.9)	0.57	540.1 (146.0)	0.64	553 (127)	*Ref*
MD, n (%)	0 (0)		0 (0)		333 (23.2)	
Exposure (months)	23,0 (19.5)	**0.005**	36.5 (21.9)	0.38	32.2 (22.0)	*Ref*
MD, n (%)	0 (0)		0 (0)		0 (0)	

Table 2: Incidences of cancer in REGATE registry

	Events	Incidence (/1000 PY)
Cancers diagnosed during all follow-up		
Cancer excluding NMSC	49	12.28
Solid cancer	35	8.76
Hematologic malignancy	11	2.76
Melanoma	3	0.75
NMSC	26	6.51
Cancers diagnosed within 90 days after last TCZ		
Cancer excluding NMSC	30	7.52
Solid cancer	21	5.26
Hematologic malignancy	8	2.00
Melanoma	1	0.25
NMSC	20	5.01
Cancers excluding NMSC diagnosed according to the time since the last TCZ		
within 60 days	26	6.51
within 180 days	32	8.01
within 360 days	33	8.27

Table 3. Risk factors of cancers associated with TCZ: multivariate analysis.

	Cancers excluding NMSC N = 1148 (42 events/1106 controls)		NMSC N=1111 (18 events/1093 controls)	
	OR	p	OR	p
Age	1.06 [1.03-1.09]	0.001	1.22 [1.12-1.34]	0.001
Female	0.509 [0.261-0.995]	0.048	-	-
Smoking exposure	2.80 [1.38-5.68]	0.004	-	-
Charlson's index	-	-	0.45 [0.23-0.89]	0.021
Prior MTX exposure before inclusion	0.31 [0.12-0.82]	0.019	-	-
Prior RTX exposure before inclusion	-	-	3.53 [1.26-9.92]	0.017
Exposure to TCZ	0.981 [0.966-0.996]	0.013	-	-
Follow-up duration in registry	-	-	1.07 [1.01-1.132]	0.023

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Abstract Number: 1282

Proteomic Signature in Peripheral Blood and Sputum in Rheumatoid Arthritis Patients with and Without Lung Involvement

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II

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Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) related lung manifestations have a significantly impact the morbidity and mortality. Male gender and RF/ACPA positivity are known risk factors but so far, no specific biomarkers, which could predict the future development of lung involvement in RA have been identified. We aimed to explore if proteome signature in peripheral blood and sputum differs in RA patients with and without lung involvement and if possible, biomarkers for RA-related lung disease could be identified.

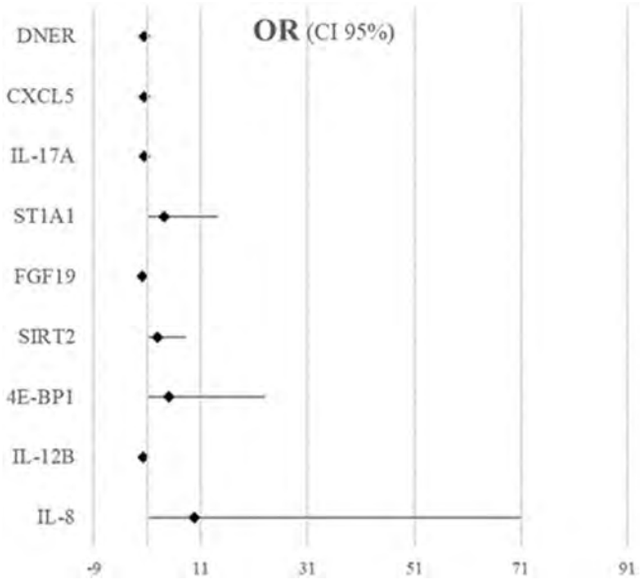
Methods: Peripheral blood and sputum samples were obtained from RA patients with (n=33, 73% female, mean age 68 years, 94% ACPA positive) and without (n=7,100% female, mean age 69 years, 86% ACPA positive) pulmonary manifestations in a single-centre explorative and cross-sectional study. A simultaneous proteome analysis targeting 92-plex inflammatory proteins in peripheral blood and in sputum was performed using proximity extension immunoassay (PEA) (Proteomics, Uppsala, Sweden) (ref). The associations between the levels of possible biomarkers and lung involvement were studied using logistic regression analysis.

Results: Significant differences between the groups were found for the levels of eight proteins in blood and for four proteins in sputum. Separate logistic regression models revealed significantly increased levels of 4 proteins in plasma: IL8, 4EBP1, SIRT2, and ST1A1 with an OR of having RA related lung involvement of 2,9-9,9. Additional 5 proteins (IL12B and FGF19 in plasma, and IL17A, CXCL5 and DNER in sputum) were associated with significantly lower risk of lung involvement (OR 0,1-0,3) (Figure).

Conclusion: The results from this study confirm the feasibility of proximity extension immunoassay (Proteomics) for proteome analysis in peripheral blood and sputum in RA patients with or without lung involvement. The difference in proteomics signature in blood and sputum indicate the analysis may be applied in the search for effective predictors of RA related lung diseases. Despite limitations we identified a number of promising biomarkers of lung involvement in RA in blood and sputum.
Ref. Assarsson E, Lundberg M, Holmquist G, et al. Homogenous 96-plex PEA immunoassay exhibiting high sensitivity, specificity, and excellent scalability. PLoS One. 2014 Apr 22;9(4):e95192.

	RA - no lung involvement (n=7)	**RA - lung involvement (n=33)**	**p-value**
Age, mean ± SD (range), years	68,9 ± 7,3 (22)	67,6 ± 7,9 (29)	0,735
Female gender, n (%)	7 (100)	24 (72,7)	0,117
RF-pos, n (%)	6 (85,7)	28 (84,8)	0,954
ACPA-pos, n (%)	6 (85,7)	31 (93,9)	0,453
Duration of RA, mean ± SD (range), yrs	11,2 ± 10,4 (28,9)	18,4 ± 11,9 (46,1)	0,182
DAS28 score, mean ± SD (range)	2,7 ± 0,9 (2,8)	3,6 ± 1,4 (5,1)	0,143
HAQ score, mean ± SD (range)	0,5 ± 0,6 (1,4)	0,9 ± 0,7 (2,5)	0,1
1 or more noduli, n (%)	1 (14,3)	9 (27,3)	0,471
Skel. CT findings, n (%)	4 (66,7)	19 (61,3)	0,804
Ongoing DMARD, n (%)	6 (85,7)	22 (66,7)	0,318
Ongoing bDMARD, n (%)	4 (57,1)	26 (78,8)	0,23
Ongoing prednisolone, n (%)	0 (0)	16 (48,5)	**0,017**
Prednisolone dose (mg/day), mean ± SD (range)	.	6,3 ± 4,7 (18,3)	.
Previous DMARDs, n (%)	7 (100)	31 (93,9)	0,504
Previous bDMARDs, n (%)	3 (42,9)	25 (75,8)	0,084
Symptom, n (%)	0 (0)	26 (78,8)	**<0,001**
Lung-related comorbidity, n (%)	1 (14,3)	7 (21,2)	0,677

Baseline disease and treatment characteristics



Biomarkers predicting lung involvement in rheumatoid arthritis

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Abstract Number: 1283

Atherogenic Index of Plasma Identifies Patients with Rheumatoid Arthritis and Increased Carotid Intima-Media Thickness

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The atherogenic index of plasma (AIP) is a novel marker to identify cardiovascular disease. Recently, AIP was reported to be related to long-term cardiovascular disease risk in women with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). We aimed to evaluate if RA-patients with high AIP present a higher prevalence of carotid plaque than patients with RA and low AIP.

Methods: A cross-sectional and comparative study including RA-patients aged 40 to 75 who fulfilled the ACR/EULAR 2010 classification criteria for RA. Patients with previous cardiovascular disease were excluded. Carotid ultrasound was performed on all study participants. The presence of carotid plaque (CP) was defined as diffuse carotid intima-media thickness (cIMT) ≥1.2 mm or focal thickness ≥0.5 mm. Subclinical atherosclerosis was defined as the presence of CP or an increased cIMT (≥0.8mm). Cardiovascular disease risk was evaluated using 6 algorithms: ACC/AHA 2013, FRS-Lipids, FRS-BMI,

RRS, QRISK3, and SCORE2. AIP was defined by log (TG/HDL-C) mg/dL, and levels ≥0.21 were considered as high AIP. Patients were divided into two groups according to AIP levels. The distribution between groups was assessed with the Kolmogorov-Smirnov test. Comparisons with Chi-square or Fisher's exact test and Student's t-test or Mann Whitney's U-test, accordingly. A value of $p \leq 0.05$ was considered statistically significant.

Results: A total of 144 patients with RA were included, most of which were women (n=133, 94%). There was no difference between sex, traditional cardiovascular risk factors, disease activity, or disease duration between patients with high AIP and those RA-patients with low AIP (Table 1). The prevalence of CP (37.5% vs 25.0%, p=0.106) and overall subclinical atherosclerosis (58.3% vs 62.5%, p=0.609) was similar between groups (Table 1). However, the prevalence of increased cIMT was higher in RA-patients with high AIP (29.2% vs 54.2%, p=0.002). Cardiovascular risk was increased in patients with high AIP using FRS-Lipids Score (7.6 vs 9.6, p=0.037) and RRS (1.5 vs 1.5, p=0.009) (Table 2).

Conclusion: The prevalence of increased cIMT was higher in RA-patients and had a high atherogenic index of plasma (AIP). AIP could be a helpful marker for the early identification of patients with increased cIMT.

Table 1. Demographic characteristics.

Characteristics	RA patients with low AIP (n=72)	RA patients with high AIP (n=72)	*p*-value
Age, years, ± SD	56.7 ± 9.7	55.8 ± 9.7	NS
Women, n (%)	71 (98.6)	65 (90.3)	NS
Diabetes, n (%)	12 (16.7)	12 (16.7)	NS
Hypertension, n (%)	24 (33.3)	23 (31.9)	NS
Dyslipidemia, n (%)	24 (33.3)	21 (29.2)	NS
Active smoking, n (%)	6 (8.3)	9 (12.5)	NS
Time of evolution, years, median (IQR)	8.4 (3.0-15.0)	10.0 (4.1-17.8)	NS
DAS28-CRP, ± SD	3.3 ± 1.3	3.2 ± 1.4	NS
Carotid plaque, n (%)	27 (37.5)	18 (25.0)	NS
Unilateral CP, n (%)	14 (19.7)	10 (13.9)	NS
Bilateral CP, n (%)	13 (18.3)	8 (11.1)	NS
Hyperplasia cIMT, n (%)	21 (29.2)	39 (54.2)	**0.002**
Unilateral high cIMT, n (%)	11 (15.5)	25 (34.7)	**0.008**
Bilateral high cIMT, n (%)	10 (14.5)	14 (19.4)	NS
Subclinical atherosclerosis, n (%)	42 (58.3)	45 (62.5)	NS

RA, rheumatoid arthritis; SD, standard deviation; IQR, interquartile range; NS, no significative; AIP, atherogenic index of plasma; DAS28-CRP, 28-joint Disease Activity Score based on C-reactive protein; CP, carotid plaque; cIMT, intima-media thickness.

Table 2. Cardiovascular risk algorithms.

Characteristics	RA patients with low AIP (n=72)	RA patients with high AIP (n=72)	*p*-value
ACC/AHA 2013, median (IQR)	2.2 (1.0-5.8)	3.7 (1.8-9.9)	NS
High risk, n (%)	4 (5.8)	9 (12.5)	NS
FRS-Lipids, median (IQR)	7.6 (3.7-11.4)	9.6 (4.9-16.0)	**0.037**
High risk, n (%)	2 (3.1)	10 (15.2)	**0.030**
FRS-BMI, median (IQR)	10.9 (6.9-21.1)	11.4 (5.4-20.8)	NS
High risk, n (%)	15 (23.1)	19 (27.5)	NS
SCORE2, median (IQR)	4.5 (3.0-7.5)	4.5 (3.0-10.5)	NS
High risk, n (%)	8 (13.1)	14 (21.5)	NS
QRISK3, median (IQR)	5.8 (3.6-9.7)	5.6 (2.7-10.5)	NS
High risk, n (%)	2 (2.9)	6 (8.3)	NS
RRS, median (IQR)	1.5 (1.5-1.5)	1.5 (1.5-4.5)	**0.009**
High risk, n (%)	0 (0.0)	2 (2.8)	NS

RA, rheumatoid arthritis; SD, standard deviation; IQR, interquartile range; NS, no significative; AIP, atherogenic index of plasma; FRS, Framingham Risk Score; BMI, body mass index; RRS, Reynolds Risk Score.

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Abstract Number: 1284

Baseline Data's Role in Predicting All-cause Mortality in Chinese Rheumatoid Arthritis Patients: Findings from the China Registry of Rheumatoid Arthritis (CREDIT) Study

Kangping Huang[1], Mucong Li[1], Chen Yu[1], Nan Jiang[1], Jiuliang zhao[1], Qian Wang[1], Peng Yin[2], Xinping Tian[1], Mengtao Li[1] and Xiaofeng Zeng[1], [1]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China, [2]Chinese Center for Disease Control and Prevention, Beijing, China

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

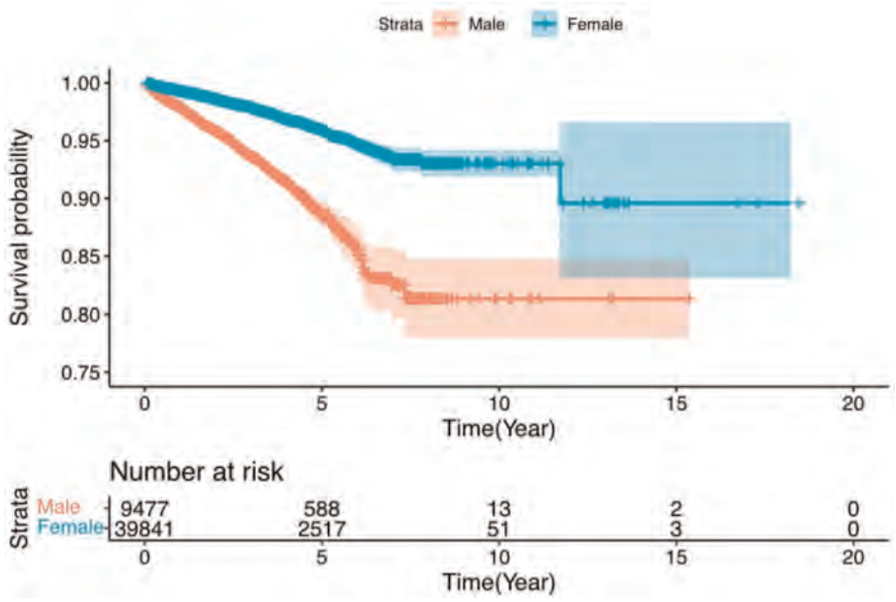

Figure 1. Kaplan-Meier analysis of sex factor. Shades of the curves shows 95% confidential intervals.

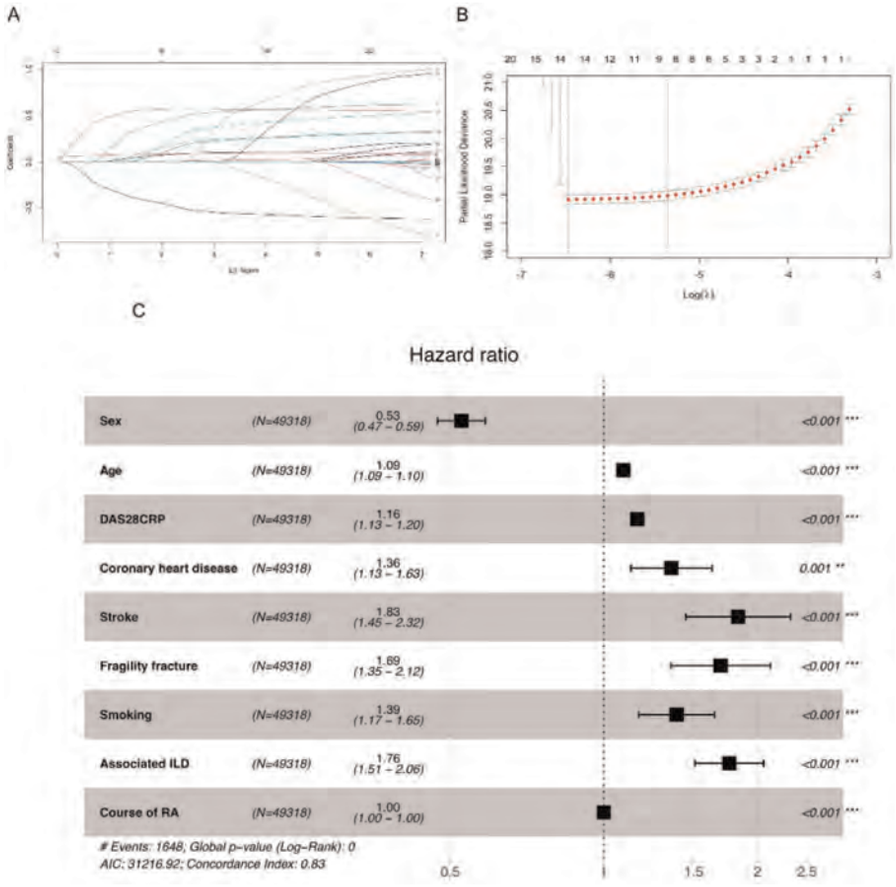

Figure 2. Variable selection using the least absolute shrinkage and selection operator (LASSO) model and results from Cox model. (A) LASSO model coefficient profiles of the 33 candidate variables. (B) Cross-validation in the LASSO model. The error bars represent the partial likelihood deviance standard error (SE). (C) Forest plot of hazard ratio according to Cox model.

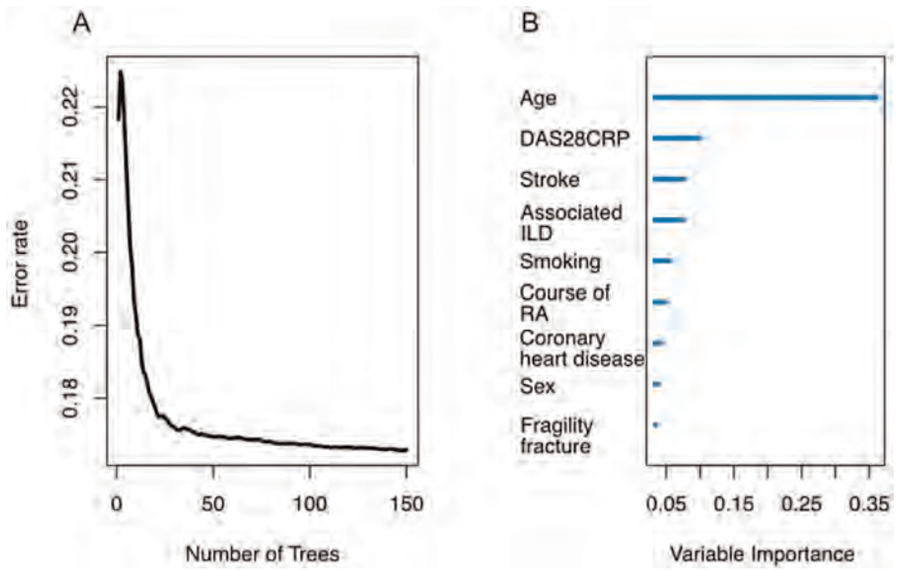

Figure 3. Random survival forest (RSF) model. (A) Out-of-bag (OOB) error rate to number of trees. (B) Bar plot of variable importance (VIMP).

Background/Purpose: Rheumatoid arthritis (RA) poses significant challenges for patients in China due to prolonged disease duration prior to a definitive diagnosis, resulting in comorbidities and increased mortality rates in RA management. Although the ACR/EULAR guideline has identified certain laboratory results as poor prognostic factors (PPFs), their availability is limited in community-based centers, particularly in rural areas. Moreover, comprehensive patient follow-up remains a challenge. Consequently, the utilization of readily accessible baseline data assumes paramount importance in the nationwide management of RA. This study seeks to predict mortality rates by leveraging baseline data obtained from a nationwide cohort of RA patients.

Methods: The clinical data utilized in this study were obtained from the database of the Chinese Registry of Rheumatoid Arthritis (CREDIT), while the survival outcome data were from the Chinese Center for Disease Control and Prevention. The datasets were linked based on the diagnosis ID, and the baseline data were extracted based on the first recorded follow-up date. Data cleaning was performed to ensure data quality. To identify the most crucial features, the least absolute shrinkage and selection operator (LASSO) technique was employed. Subsequently, two modeling approaches, the Cox proportional hazards model (Cox model) and random survival forest (RSF), were simultaneously applied to develop predictive models using the selected features. The performance of these models was evaluated by Harrell's concordance index (C-index) and compared.

Results: The registry was initiated on October 9, 2003, and is currently ongoing. Survival outcomes were collected until December 31, 2021, with no loss to follow-up observed. A total of 49,318 patients (Mean age: 51.96 (IQR: 44.00-61.00); Female sex: 39.841, 80.78%) diagnosed with RA from 125 medical centers across China were included in this study. 1,648 deaths were recorded, while 47,670 patients remained under observation (Figure 1). The LASSO technique identified 9 variables within 1 standard error, which were utilized in model construction. Notably, the variables demonstrating significant importance were sex, smoking status, stroke, and the presence of associated interstitial lung disease (ILD), as evidenced by the beta coefficients in the Cox model and the Variable Importance (VIMP) in the RSF model (Figure 2 and 3). The Cox model exhibited a C-index of 0.831 (95% confidence interval [CI]: 0.808-0.852), while the RSF model achieved a C-index of 0.879 (95% CI: 0.829-0.916).

Conclusion: This study shows that the risk of mortality in RA patients can be predicted based on demographic factors and comorbidities from baseline data. Specifically, male sex, smoking, stroke, and the presence of associated ILD were identified as factors associated with a higher risk of mortality. Both the Cox model and RSF proved to be effective methods for

mortality prediction while the RSF model exhibited higher accuracy but lower explainability. Future research could focus on exploring the prediction of comorbidities within the same cohort, further enriching our understanding of their impact on mortality risk in RA patients.

Disclosure: K. Huang: None; **M. Li**: None; **C. Yu**: None; **N. Jiang**: None; **J. zhao**: None; **Q. Wang**: None; **P. Yin**: None; **X. Tian**: None; **M. Li**: None; **X. Zeng**: None.

Abstract Number: 1285

PROMIS Symptom Clusters Predict Disease Activity in the First 6 Months in Newly Diagnosed RA Patients Starting MTX Therapy: Data from the Canadian Early Arthritis Cohort

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

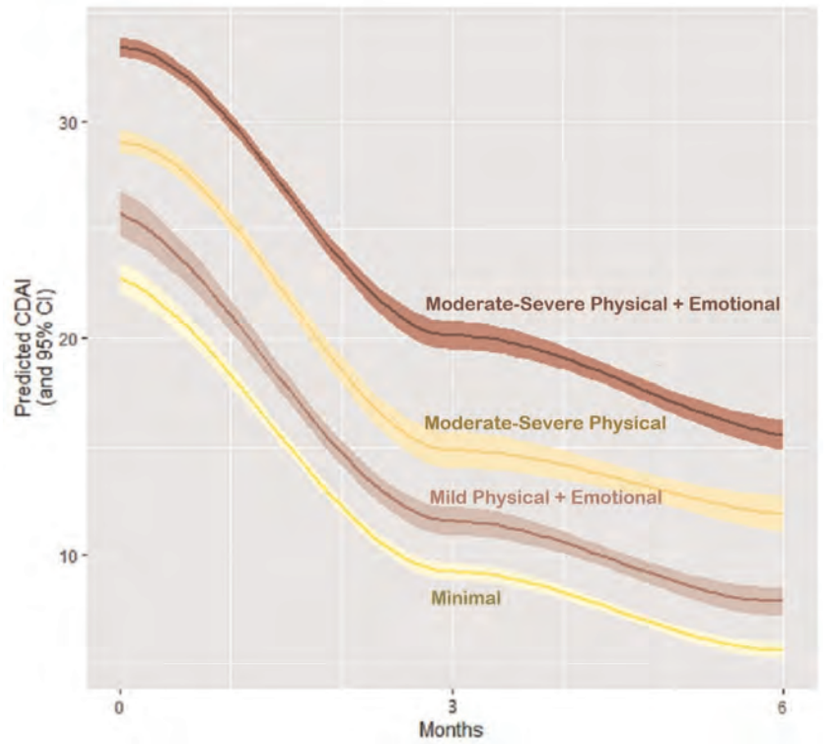
Background/Purpose: We have previously shown that PROMIS-29 physical (pain, fatigue) and emotional (depression, anxiety) symptom clusters can be used to identify 4 distinct early RA patient sub-groups, and that patient sub-groups with higher emotional symptoms experienced greater physical and emotional symptom burden despite all receiving conventional RA treatment with MTX over 6-months follow up. Here, we examine whether these 4 identified patient subgroups also follow distinct trajectories of disease activity over the first 6 months of MTX therapy.

Methods: Data were from adults with newly diagnosed early RA (symptoms < 1 year) enrolled in the Canadian Early Arthritis Cohort (CATCH) study who were initiating treatment with MTX for the first time and had complete clinical and PRO measures at baseline, 3- and 6-month follow up. PROMIS-29 anxiety, depression, fatigue, and pain scores were used to classify patients into 4 patient sub-groups using latent transition analysis: Group 1: **Minimal Sx**; Group 2: **Mild Physical + emotional Sx**; Group 3: **Moderate-Severe Physical Sx**; and Group 4: **Moderate-Severe Physical + emotional Sx**. Linear mixed effects

CDAI Disease Activity Over the First 6-Months of Methotrexate Treatment Across Early RA Patient Sub-Groups

	CDAI Mean Difference (95% CI)^
Class (reference – Group 1: Minimal Symptoms)	
Group 2:Mild Physical + Emotional	2.90 (0.19, 5.61)
Group 3:Moderate-Severe Physical	5.89 (3.44, 8.33)
Group 4: Moderate-Severe Physical and Emotional	10.74 (8.00, 13.48)

^ Adjusted for: age, sex, race, education, smoking status, obesity, comorbidities, serology status and symptom duration.



Predicted change in CDAI over the first 6 months of MTX therapy in adults with new-onset RA (n=310).

regression was used to estimate trajectories of CDAI disease activity over the first 6 months of MTX treatment across groups adjusting for age, sex, race, education, smoking status, obesity, comorbidities, serology status and symptom duration.

Results: The sample included 310 early RA patients initiating MTX treatment for the first time. Participants had a mean age of 56, CDAI of 29.3, and symptom duration of 5 months; 67% were women and 78%were White. At baseline, average disease activity was high across all 4 patient groups though mean CDAI scores were highest for patients in Group 3 (**Moderate-Severe Physical Sx**) (mean (sd) CDAI: 29.2 (12.7)) and Group 4 (**Moderate-Severe Physical + emotional Sx**) (mean (sd) CDAI: 32 (14.0). Disease activity improved for all groups over 6-months of treatment with MTX though not to the same degree across groups. Compared with patients in Group 1 (**Minimal Sx)**, mean CDAI was nearly 3 points higher for participants in Group 2 (**Mild Physical + emotional Sx)** was nearly6-points higher for Group 3 (**Moderate-Severe Physical Sx)** and nearly 11 points higher for Group 4 (**Moderate-Severe Physical + emotional sx)** (FIGURE).

Conclusion: We found that despite being treated with the same conventional RA MTX treatment, early RA patients displayed varying levels of physical (pain, fatigue) and emotional symptoms [anxiety, depression] and that these symptom clusters could be used to identify distinct patient sub-groups with substantial differences in disease activity over 6-months of follow up. Results suggest that both the presence and intensity of physical symptoms plus the levels of anxiety and depression may indicate more complex subtypes of RA with a less favorable prognosis. Evaluating both physical and emotional symptoms at the time of diagnosis may help providers better tailor RA treatment by potentially combining medications and supportive interventions that reduce overall symptom burden and improve treatment outcomes and QOL.

Disclosure: S. Bartlett: Janssen, 6, Merck/MSD, 2, 6, Novartis, 2, Organon, 1, 6, PROMIS Health Organization, 4, Sandoz, 2, 6; **C. Bingham**: None; **O. Schieir**: None; **M. Valois**: None; **G. Boire**: Eli Lilly, 1, Janssen, 6, Organon, 1, Orimed Pharma, 1, 6, Otsuka, 1, Pfizer, 1, 5, Sandoz, 1, Teva, 1, Viatris, 1, 6; **L. Bessette**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol

Myers Squibb, 2, 5, 6, Eli Lilly, 2, 5, 6, Fresenius Kabi, 2, 6, Gilead, 2, 5, 6, JAMP Pharma, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Organon, 2, 6, Pfizer, 2, 5, 6, Sandoz, 2, 6, Sanofi, 2, 5, 6, Teva, 2, 6, UCB, 2, 5, 6, UCBA, 5; **J. Pope**: AbbVie, 1, 2; **D. Tin**: None; **C. Thorne**: Abbvie, 1, Biogen, 2, Nordic Pharma, 1, Pfizer, 1, 5, Roche, 1, Sandoz, 1, 2; **G. Hazlewood**: None; **C. Hitchon**: Astra Zeneca, 1, Pfizer, 5; **E. Keystone**: AbbVie/Abbott, 2, 6, Amgen, 2, 6, celltrion, 2, 6, Eli Lilly, 2, 6, Fresenius Kabi, 2, 6, Pfizer, 2, 6, Samsung Bioepsis, 2, sandoz, 2, 6; **V. Bykerk**: Abbvie, 2, BMS, 2, Pfizer, 2.

Abstract Number: 1286

Impact of Body Mass Index (BMI) on Upper versus Lower Extremity Joints Assessed Using Clinical and Musculoskeletal Ultrasound Measures in Rheumatoid Arthritis Patients

Nicolette Morris[1], Elena Saab[2], Lucia Chen[1], Jenny Brook[1], Gurjit S Kaeley[3], David Elashoff[1] and Veena Ranganath[1], [1]David Geffen School of Medicine, UCLA, Los Angeles, CA, [2]Wake Forest University School of Medicine, Los Angeles, CA, [3]University of Florida College of Medicine – Jacksonville, Ponte Vedra Beach, FL

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Tender and swollen joints counts may be differentially affected in rheumatoid arthritis (RA) patients with obesity. A prior study demonstrated an association between increased BMI and swelling of the lower extremity joints (Ranganath et al. 2019). To our knowledge, there are no publications describing the impact BMI has on musculoskeletal ultrasound (MSUS) measures of the upper and lower extremity (UE and LE) joints. This study aimed to examine the association of BMI with clinical and MSUS joint assessments of the UE/LE joints in a large cohort of RA patients.

Methods: We examined a cross-sectional cohort of 268 patients meeting American College of Rheumatology 2010 RA classification criteria who completed screening visits for clinical trials. Patients were grouped by BMI: < 25, 25 to 30, and ≥ 30. Demographic data and DAS28/ESR were collected including 28 and 44 tender and swollen joint counts (TJC28, SJC28, TJC44, SJC44). Following the LAJAX protocol (Ben-Artzi et al. 2021), grayscale and power Doppler ultrasound (GSUS and PDUS) images were obtained from 34 joints: bilateral radioulnar joint midline of the wrists, proximal interphalangeal joints, interphalangeal joints, metacarpophalangeal joints, knees, and metatarsophalangeal joints (excluding MTP1).

Table 1. Number of upper and lower extremity joints analyzed per composite joint characteristic across BMI. BMI = body mass index, N = number, GSUS = grayscale ultrasound, PDUS = power Doppler ultrasound, TJC28 = 28 tender joint count, SJC28 = 28 swollen joint count, TJC44 = 44 tender joint count, SJC44 = 44 swollen joint count.

	Normal Weight BMI <25 N = 66		Overweight BMI 25-30 N = 62		Obese BMI >30 N = 140	
Composite Joint Characteristic Analyzed	Upper Extremity Joint N	Lower Extremity Joint N	Upper Extremity Joint N	Lower Extremity Joint N	Upper Extremity Joint N	Lower Extremity Joint N
GSUS	1584	660	1488	620	3360	1400
PDUS	1584	660	1488	620	3360	1400
TJC28	1716	132	1612	124	3640	280
SJC28	1716	132	1612	124	3640	280
TJC44	1980	924	1860	868	4200	1960
SJC44	1980	924	1860	868	4200	1960

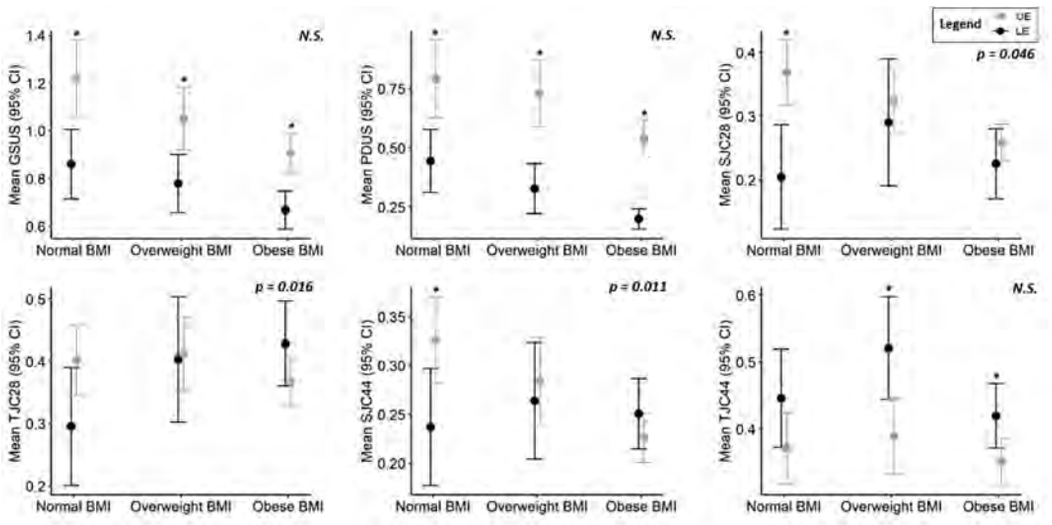


Figure 1. Upper versus lower extremity joints across BMI categories for musculoskeletal ultrasound measures and joint counts. N.S. = ANOVA not significant ($p > 0.05$), * = significant difference ($p < 0.05$), LE = lower extremity, UE = upper extremity, CI = confidence interval, BMI = body mass index, N = number, GSUS = grayscale ultrasound, PDUS = power Doppler ultrasound, TJC28 = 28 tender joint count, SJC28 = 28 swollen joint count, TJC44 = 44 tender joint count, SJC44 = 44 swollen joint count.

Each image was scored on a scale of 0-3. For joints with multiple views, the highest PDUS and GSUS score was used. Joints were categorized as either UE or LE. GSUS and PDUS scores were calculated by taking the average of all individual joint scores per UE or LE group. SJC and TJC scores were calculated using the proportion of swollen or tender joints out of all joints per UE or LE group. Differences between UE and LE joints for both ultrasound (GSUS and PDUS) and clinical joint measures (TJCs and SJCs) were calculated across BMI groups using t-tests. For each joint assessment, interaction effects were tested between UE/LE joint categories and BMI via analysis of variance (ANOVA).

Results: Within the cohort, mean age was 54.8 years, 90.2% were female, 45% Caucasian, 78.7% seropositive and mean disease duration was 11.9 years. Patients overall had moderate disease activity with an average DAS28/ESR of 4.8. A total of 11,792 joints were examined by MSUS and/or joint counts. A breakdown of the UE and LE joint distribution per measure among BMI groups is shown in Table 1. Analyses comparing UE versus LE joints demonstrated a higher MSUS burden (GSUS and PDUS) in the UEs regardless of BMI (Figure 1) ($p< 0.05$), although there was not a significant UE/LE by BMI interaction ($p>0.05$). For SJC28 and SJC44 the UE/LE difference was significantly different across BMI categories ($p< 0.05$ for interaction). Normal weight patients had significantly higher joint swelling in the UEs (both $p< 0.03$), but this was not seen for overweight or obese patients (all $p>0.05$). Significant differences in individual joints of TJC28 for UE/LE were observed across BMI groups ($p=0.02$).

Conclusion: We observed a significant differential effect of BMI in the UE versus LE comparisons for clinical joint assessments (TJC 44, SJC 28, and SJC44), which are thought to be more subjective measures. However, for more objective measurements of joints by MSUS (PDUS and GSUS), this differential effect of UE/LE across BMI was not seen.

Disclosure: N. Morris: None; **E. Saab**: None; **L. Chen**: None; **J. Brook**: None; **G. S Kaeley**: Abbvie, 5, Gilead, 5, Janssen, 5; **D. Elashoff**: None; **V. Ranganath**: Bristol-Myers Squibb(BMS), 5, mallinckrodt, 5.

Abstract Number: 1287

Impact of Body Mass Index (BMI) on Rheumatoid Arthritis Disease Activity and Musculoskeletal Ultrasound Measures

Nicolette Morris[1], Elena Saab[2], Lucia Chen[1], Jenny Brook[1], Gurjit S Kaeley[3], David Elashoff[1] and Veena Ranganath[1], [1]David Geffen School of Medicine, UCLA, Los Angeles, CA, [2]Wake Forest University School of Medicine, Los Angeles, CA, [3]University of Florida College of Medicine – Jacksonville, Ponte Vedra Beach, FL

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) patients with obesity are less likely to respond to therapy and achieve remission. Obesity is a known driver of inflammatory processes and is also associated with conditions such as osteoarthritis, fibromyalgia, and other comorbid conditions. The objective of this study was to comprehensively examine various disease

Table 1. Demographic characteristics and disease activity among BMI categories. BMI = body mass index, SD = standard deviation, RF = rheumatoid factor, ACPA = anti-cyclic citrullinated peptide, GSUS = grayscale ultrasound, PDUS = power Doppler ultrasound, TJC28 = 28 tender joint count, SJC28 = 28 swollen joint count, TJC44 = 44 tender joint count, SJC44 = 44 swollen joint count, DAS28/ESR = 28 joint disease activity score with erythrocyte sedimentation rate, DAS44/ESR = 44 joint disease activity score with erythrocyte sedimentation rate, HAQ-DI = Health Assessment Questionnaire Disability Index, and RAPID3 = Routine Assessment of Patient Index Data 3.

	Normal Weight BMI <25 N = 66	Overweight BMI 25-30 N = 62	Obese BMI >30 N = 140	*p*-value
Background characteristics				
Age (years), mean (SD)	54.3 (16.8)	55.3 (11.9)	54.8 (13.2)	0.93
Disease duration (years), mean (SD)	12.7 (13.2)	11.7 (9.9)	11.6 (10.8)	0.81
Female, %	90.6%	87.1%	91.4%	0.64
Seropositivity (RF or ACPA), %	71.4%	84.2%	79.7%	0.21
Current or past smoking, %	39.1%	38.7%	42.9%	0.81
Race and ethnicity, %				0.02
Hispanic/Latino	18.8%	27.9%	19.4%	
Asian	18.8%	9.8%	7.2%	
Black	4.7%	19.7%	16.5%	
White/Caucasian	43.8%	36.1%	49.6%	
Other	14.1%	6.6%	7.2%	
Disease Activity Measures				
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	***p*-value**
GSUS-34	37.8 (20.1)	32.9 (15.9)	28.3 (14.3)	<0.001
PDUS-34	23.3 (20.7)	20.7 (16.1)	14.9 (12.8)	0.001
DAS28/ESR	4.8 (1.2)	4.8 (1.2)	4.8 (1.0)	0.96
DAS44/ESR	6.1 (1.5)	6.2 (1.6)	6.1 (1.3)	0.82
TJC28	11.1 (6.4)	11.6 (6.5)	10.5 (6.4)	0.51
SJC28	10.1 (5.6)	9.1 (5.4)	7.3 (5.0)	<0.001
TJC44	17.4 (9.9)	19.0 (10.4)	16.4 (9.7)	0.24
SJC44	13.1 (7.6)	12.2 (7.5)	10.3 (6.9)	0.02
ESR	29.0 (22.9)	29.9 (26.0)	29.7 (28.4)	0.87
HAQ-DI	1.1 (0.7)	1.2 (0.7)	1.2 (0.7)	0.65
RAPID3	8.4 (5.7)	9.9 (9.4)	5.8 (6.6)	0.005

activity measures (composite clinical measures, patient surveys, and musculoskeletal ultrasound (MSUS)) across BMI in a large RA cohort. Prior studies evaluating this question have been small with conflicting findings.

Methods: Clinical and MSUS data were obtained from 268 RA patients meeting American College of Rheumatology 2010 RA classification criteria who completed screening visits for RA clinical trials at an academic center. Patients were grouped by BMI categories: < 25, 25 to 30, and ≥ 30. Laboratory measurement of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), anti-cyclic citrullinated peptide (ACPA) and rheumatoid factor (RF) levels were performed. 28- and 44-joint count Disease Activity Scores using ESR (DAS28/ESR and DAS44/ESR), Health Assessment Questionnaire Disability Index (HAQ-DI) and Routine Assessment of Patient Index Data 3 (RAPID3) scores were calculated. Grayscale and power Doppler ultrasound (GSUS and PDUS) scores were calculated using the LAJAX 34 joint protocol (Ben-Artzi et al. 2021). Images were scored semi-quantitatively on a scale of 0–3. Total PDUS and GSUS scores were calculated via summation of all 34 joint scores (range 0–102). Demographic and clinical characteristics were categorized across BMI groups using the Kruskal-Wallis test (KW) for continuous variables and chi-square tests for categorical variables. Multiple linear regressions were used to assess factors influencing PDUS and GSUS.

Results: Demographics were similar across BMI categories except for race/ethnicity (p=0.02). GSUS and PDUS scores significantly differed across BMI groups, with obese patients showing the lowest MSUS activity (p< 0.001 and p=0.001, respectively). DAS28/ESR, DAS44/ESR, TJC28, TJC44 were not different across BMI. However, SJC28 and SJC44 were significantly different across BMI groups and numerically lower in BMI >30. RAPID3 demonstrated a significant difference across BMI where obese patients were numerically lower, while HAQ-DI did not differ. In the regression models, BMI was significantly negatively associated with PDUS and GSUS after accounting for demographic characteristics, DAS28/ESR, disease duration, and seropositivity. In these models race, sex, smoking, seropositivity and DAS28/ESR were also significantly associated with MSUS findings.

Conclusion: In this large cohort of RA patients, DAS28/ESR and DAS44/ESR were similar across BMI categories. However, active synovitis as measured by PDUS and GSUS scores were independently negatively associated with BMI, after accounting for DAS and other demographic factors. These results suggest there is less MSUS joint inflammation in obese patients, which is consistent with prior findings of reduced radiographic damage observed in obese RA patients. Further study is warranted to confirm these findings.

Disclosure: N. Morris: None; **E. Saab**: None; **L. Chen**: None; **J. Brook**: None; **G. S Kaeley**: Abbvie, 5, Gilead, 5, Janssen, 5; **D. Elashoff**: None; **V. Ranganath**: Bristol-Myers Squibb(BMS), 5, mallinckrodt, 5.

Abstract Number: 1288

Frailty Is Associated with Higher Risk of Readmission in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: With the advent of new therapies and increasing life expectancy, there is a rising number of older adults living with rheumatoid arthritis (RA). Patients with RA are at a higher risk for developing frailty[1], and frailty in RA has been linked with increased risk of hospitalization[2]. However, little is known regarding the association between frailty status and a patient's hospitalization outcomes. Our study investigated whether frailty increases risk for readmission and inpatient mortality in RA patients.

Methods: Using the 2018 Nationwide Readmissions Database, we identified adult patients (age ≥18 years) admitted with a primary or secondary diagnosis of RA (using ICD 10 codes) between January to June 2018. Utilizing validated claim-based Hospital Frailty Score[3], patients' frailty risk score was calculated at the time of index admission and individuals were categorized into frail (score ≥ 5) and non-frail (score < 5) groups. Our primary outcome of interest was risk of readmission following discharge after index hospitalization. Secondary outcomes of interest included inpatient mortality, prolonged length of

Characteristics at the time of index hospitalization	Non-frail patients (N = 69056)	Frail patients (N = 64131)	P-value
Age (years) (mean ± st. dev)	64.52±14.256	71.13±13.023	< 0.01
Age categories (%)			< 0.01
<40	6.92%	2.37%	
40-64	38.82%	25.61%	
>64	54.26%	72.02%	
Female (%)	72.69%	74.63%	< 0.01
Urban (%)	91.83%	90.99%	< 0.01
Primary expected payer (%)			< 0.01
Medicare	62.98%	79.20%	
Medicaid	9.98%	6.87%	
Private insurance	23.13%	11.48%	
Self-pay	1.48%	0.86%	
Other	2.44%	1.59%	
Median household income (%)			0.0168
0-25th percentile ($1- $45,999)	27.12%	27.52%	
26th - 50th percentile ($46,000 - $58,999)	28.16%	28.06%	
51st - 75th percentile ($59,000 - $78,999)	24.92%	24.25%	
76th - 100th percentile ($79,000+)	19.80%	20.170997	
Hospital characteristics (%)			< 0.01
Metropolitan non-teaching	23.51%	23.15%	
Metropolitan teaching	68.32%	67.84%	
Non-metropolitan hospital	8.17%	9.01%	
Hospital size/capacity (%)			0.0102
Small	18.80%	18.30%	
Medium	28.25%	28.88%	
Large	52.95%	52.82%	
Length of stay			
Median	3	4	< 0.01
IQR	2-4	3-8	
Elixhauser Index	7.91	12.87	< 0.01
Hypertension	53.16%	53.41%	0.3670
Heart Failure	15.31%	27.06%	< 0.01
Diabetes mellitus	25.64%	32.78%	< 0.01
COPD	30.99%	36.63%	< 0.01

Baseline patient demographics, hospital characteristics, and comorbidities at time of index hospitalization by frailty status

Outcomes	Non-frail patients	Frail patients	P-value
Readmission	30.61%	56.60%	<0.01
Inpatient mortality at index hospitalization	0.39%	3.36%	<0.01
LOS > 7 days at index hospitalization	7.82%	26.24%	<0.01
Average days to readmission	91.9	82.5	<0.01
Cost of hospitalization			
Mean	$13,014.80	$17,028.21	<0.01
Median	$9,534	$10,511	
IQR	$5,396 - 16,053	$6,251 - 19,024	

Longitudinal hospital based related outcomes in patients with RA

Variables	Hazard Ratio* (95% Confidence Interval)	P-value
Frailty	1.09 (1.08 – 1.11)	<0.005
Age	0.99 (0.99 – 1.00)	<0.005
Female	0.97 (0.96 – 0.98)	<0.005
Median Household Income	1.00 (0.99 – 1.00)	0.85
Hospital Characteristics	0.98 (0.97 – 1.00)	0.01
Primary Expected Payer	0.99 (0.98 – 0.99)	<0.005
Hospital Size/Capacity	1.01 (1.00 – 1.02)	0.02
Elixhauser Index	1.01 (1.01 – 1.01)	<0.005
Diabetes	0.99 (0.98 – 1.00)	0.18
Heart Failure	1.04 (1.02 – 1.05)	<0.005
Chronic Lung Disease	0.97 (0.95 – 0.98)	<0.005
Obesity	0.99 (0.98 – 1.01)	0.28

**Model adjusted for age, sex, household income, hospital characteristics (teaching status, capacity, location), and Elixhauser comorbidities index.*

Cox Proportional Hazard Analysis Evaluating Risk of Readmission by Frailty Risk Score

admission (≥ 7 days), mean days to readmission, and costs of hospitalization. We used descriptive statistics to compare patient demographics, admission characteristics, and hospital characteristics at index hospitalization in frail vs non-frail groups. Multivariable Cox proportional hazard analysis was performed to evaluate the independent effect of frailty on readmission after controlling for age, sex, household income, hospital characteristics (teaching status, capacity, location), and Elixhauser comorbidities index.

Results: 133,187 patients with RA met our inclusion criteria. Of these, 64,131 (48.15%) patients were categorized as frail, and 69,056 (51.85%) patients were non-frail. Frail patients were older, female, predominantly with Medicare coverage, and had higher Elixhauser comorbidity index (**Table 1**). Frail patients had a higher rate of readmission (56.60%) compared to the non-frail group (30.61%). After readmission, frail patients also had significantly higher inpatient mortality compared to non-frail patients (3.36% vs 0.39%, $p < 0.005$) and a longer length of stay (7.82% vs 26.24%, $p < 0.005$) (**Table 2**). On multivariate analysis, frailty was independently associated with a 9% increased risk of readmissions (adjusted hazard ratio, 1.09; 95% confidence interval, 1.08 – 1.11) (**Table 3**).

Conclusion: Frailty is associated with a higher risk of readmissions in patients with RA. In addition, frail patients with RA have higher likelihood for poorer outcomes after hospitalization (such as increased inpatient mortality) relative to non-frail patients. These findings are crucial in identifying hospitalized patients with RA who are at a higher risk of worse outcomes. Future studies should explore modifiable factors to mitigate these risks.

References:

1. van Onna M, et al. PMID: 35314796.
2. Hanlon P, et al. PMID: 35292529.
3. Gilbert T, et al. PMID: 29706364

Disclosure: W. Tahir: None; **Y. Rosli**: None; **C. Leung**: None; **K. Wysham**: None; **J. Lee**: None; **R. Goulabchand**: None; **U. Makris**: None; **S. Singh**: None; **N. Singh**: None.

Abstract Number: 1289

Increases in Serum Levels of Tartrate-Resistant Acid Phosphatase 5b Reflected Radiographic Progression of Joint Damage in Treated Rheumatoid Arthritis

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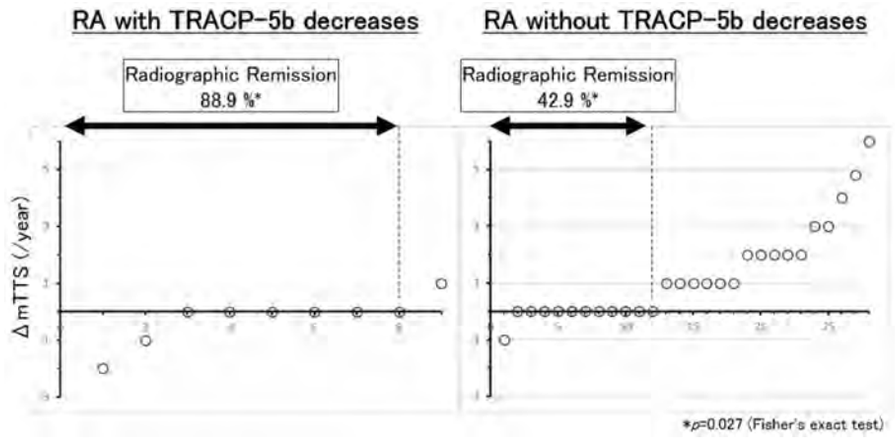
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis (RA) is one of inflammatory arthritis, and this autoimmune-mediated polyarthritis results in structural joint destruction. Articular bone erosion leading to joint destruction in RA is caused by bone resorption of osteoclasts activated by synovial inflammation. Joint damage is usually evaluated by imaging studies, but there are few reports in which joint damage was assessed by bone resorption markers that reflect osteoclast activity. Tartrate-resistant acid phosphatase (TRACP) 5b is a bone resorption marker localized only in osteoclasts and is released during bone resorption, so it directly reflects the number and active state of osteoclasts. Recently, serum levels of TRACP-5b have been reported to correlate with the severity of radiographic damage and the number of articular bone erosion of computed tomography in RA patients. However, the relationship between TRACP-5b and joint damage progression is still unclear. Therefore, we investigated whether TRACP-5b is useful for evaluating the progression of articular damage in RA.

Methods: 37 RA patients were registered, who filled RA criteria 2010, were premenopausal women and men younger than 55 years at enrollment (M0), didn't have metabolic bone diseases or malignancies, were in the treatment with DMARDs, and were followed up until month 12 (M12). Serum TRACP-5b level measurement and radiographic joint damage assessment were performed at M0 and M12. A significant decrease in TRACP-5b titers was defined as a decrease of 12.4% (the minimum significant change; MSC) or more in one year. Radiographic remission of join damage was defined as yearly modified total Sharp score (mTSS) progression below 0.5. Their medical records were reviewed retrospectively.

Results: Subjects at M0 were 31 female, were median age 45.7 years with 5.4 years of disease duration, and were treated with MTX, glucocorticoid, biological/targeted synthetic DMARD and bisphosphonate/denosumab (n=30, 9, 12 and 6, respectively). RA disease activity of median SDAI was 3.29 at M0 and 4.09 at M12 (p=0.670), and median mTSS changed from 15 to 14 (p=0.027). Serum TRACP-5b titers (median) were 253 mU/dl at M0 and 294 at M12 (p=0.672). TRACP-5b levels at M0 and M12 didn't correlated with mTSS at M0 and M12. Increases in TRACP-5b titers between M0 and M12 were positively correlated with changes in erosion score of mTSS (ρ=0.5166; p=0.0011). 20 of 37 subjects (54.1%) achieved



remission in radiographic evaluation. In univariate analysis, increases in TRACP-5b titers were negatively associated with radiographic remission (OR=0.980; 95% confidence interval: 0.961-0.993, for each 1 mU/dl increase in TRACP-5b titers; p=0.001). Only 9 of 37 patients showed significant decreases in TRACP-5b titers. 8 of these 9 patients (88.9%) had radiographic remission, but only 42.9% of 28 cases without TRACP-5b decreases showed structural remission (p=0.027).

Conclusion: Changes in serum TRACP-5b levels were related to aggravation of joint damage in RA during treatment. TRACP-5b is useful for assessing progression of RA joint destruction. In the absence of significant TRACP-5b reduction, joint damage progresses in about 60% of RA patients.

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Abstract Number: 1290

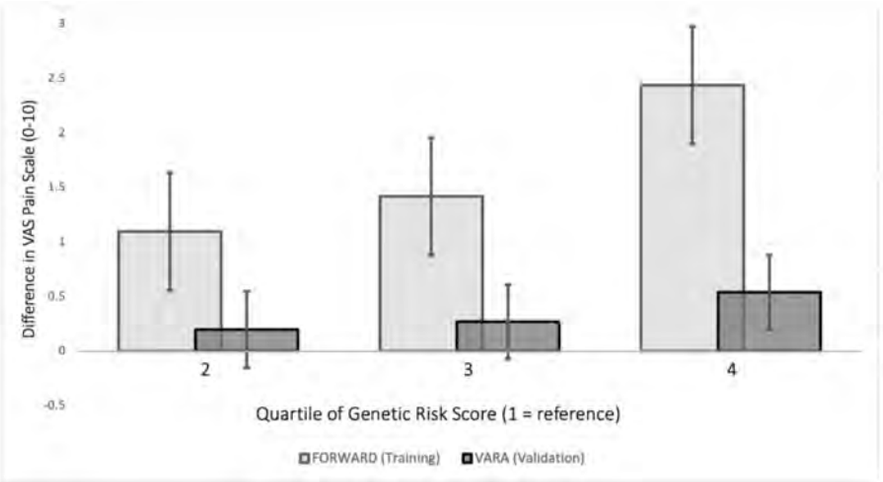
Development of a Genetic Risk Score for Pain in Rheumatoid Arthritis

Katie McMenamin[1], Kristin Wipfler[2], Austin Wheeler[3], Grant Cannon[4], K Wysham[5], Brian Sauer[6], Bryant England[3], Kaleb Michaud[3], Ted R Mikuls[7] and Joshua Baker[8], [1]Boston University, Boston, MA, [2]FORWARD, The National Databank for Rheumatic Diseases, Omaha, NE, [3]University of Nebraska Medical Center, Omaha, NE, [4]University of Utah and Salt Lake City VA, Salt Lake City, UT, [5]VA Puget Sound/University of Washington, Seattle, WA, [6]Salt Lake City VA/University of Utah, Salt Lake City, UT, [7]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE, [8]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Pain in rheumatoid arthritis (RA) is multifactorial and involves processes beyond inflammation such as peripheral and central pain processing. Several genes have been associated with pain processing through studies of fibromyalgia (FM), but it is largely unknown how genetics may affect pain in other rheumatic diseases. The aim of this study was to determine if single nucleotide polymorphisms (SNPs) associated with FM also have an impact on pain and disease activity in patients with RA.

Methods: Participants with RA with whole genome SNP data were included from two independent cohorts: 1) *FORWARD* (National Data Bank for Rheumatic Diseases) and 2) Veterans Affairs RA registry (VARA). Linear regression was used to determine the relationship between 30 individual SNPs previously associated with FM (Jannsen et al. *An Acad Bras Ciênc*. 2021) and baseline pain scores in *FORWARD* adjusting for age, sex and race. A genetic risk score (GRS) was generated using all 30 SNPs, weighted by the coefficients for each SNP from this regression. Linear regression was then used to assess the relationship between the GRS and cross-sectional (baseline) pain (visual analogue scale, range 0-10) in *FORWARD* (training dataset) and VARA (validation dataset). Similarly, the association of GRS with pain during longitudinal follow-up was determined using regression with generalized estimating equations adjusting for age, sex and race. In addition, the associations between GRS and disease activity, at enrollment and during longitudinal follow-up in each study were determined.



Difference in baseline mean VAS pain score by quartile of genetic risk score for FORWARD (training) and VARA (validation) cohorts

	Training		Validation	
	***FORWARD* (PAS-II)**		**VARA (RAPID3)**	
Baseline				
Genetic Risk Quartile	**β (95% CI)**	**P**	**β (95% CI)**	**P**
1	ref	--	ref	--
2	0.79 (0.35, 1.23)	<0.01	0.46 (-0.33, 1.26)	0.25
3	0.97 (0.54, 1.40)	<0.01	0.40 (-0.39, 1.19)	0.32
4	1.28 (1.26, 2.13)	<0.01	1.06 (0.33, 1.26)	<0.01
Longitudinal				
Genetic Risk Quartile	**β (95% CI)**	**P**	**β (95% CI)**	**P**
1	ref	--	ref	--
2	0.43 (0.07, 0.8)	0.02	0.21 (-0.36, 0.77)	0.48
3	0.78 (0.41, 1.16)	<0.01	0.17 (-0.39, 0.74)	0.54
4	1.17 (0.8, 1.55)	<0.01	0.72 (0.16, 1.28)	0.01

Genetic risk score quartile and disease activity score at baseline and throughout all observations for FORWARD (training) and VARA (validation) datasets

Results: This study included 765 patients from *FORWARD* (mean age 56.8 years, 89.4% female) and 2176 from VARA (mean age 71.7 years, 11.0% female). Several SNPs were associated with pain scores in each cohort, but no single SNP was associated in both cohorts. For example, VARA participants with the homozygous major allele of the *BDNF* rs6265 polymorphism (brain-derived neurotrophic factor) had less pain [B: -2.16 (95% CI: -4.06, -0.25, p=0.02)] compared to those with the homozygous minor allele, but a similar association was not observed in *FORWARD*.*FORWARD* participants with a higher GRS had significantly more pain, with those in the highest quartile having higher baseline pain scores [+2.44 (95% CI: (1.91, 2.97) p< 0.01 (range 0-10)] (Figure). VARA participants in the greatest quartile of GRS also had modestly higher baseline pain scores [+0.54 (95% CI: 0.20, 0.89), p< 0.01]. Participants in the highest GRS quartile from both cohorts also had significantly greater pain scores throughout follow-up. The GRS was associated with higher baseline and longitudinal patient-reported disease activity as measured by the PAS-II (*FORWARD*) and RAPID3 (VARA) (Table).

Conclusion: A genetic risk score based on previously identified pain-related SNPs modestly predicted greater pain in an external independent cohort. These observations suggest that more comprehensive genetic scores may eventually provide meaningful clinical value in understanding pain in RA patients. More accurate prediction may be possible through more advanced methods such as machine learning and with an increasing understanding of the genes involved in pain processing.

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Abstract Number: 1291

Risk Factors for Major Adverse Cardiovascular Events and Malignancies in Patients with Rheumatoid Arthritis in a Real-World Setting in Japan

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients (pts) with RA are at an increased risk of major adverse cardiovascular events (MACE) and malignancies vs the general population.[1,2] However, risk factors for MACE and malignancy in pts with RA may differ by geographic location; to date, limited real-world data (RWD) assess this. Thus, this study aimed to identify risk factors for MACE and malignancy (including non-melanoma skin cancer) in pts with RA using RWD in Japan.

Methods: This was a cohort study of pts with RA using a RW database (electronic medical records, claims, and discharge abstract data) of medical institutions in Japan (maintained by the Health, Clinic, and Education Information Evaluation Institute; supported by the RWD Co. Ltd). Eligible pts from January 2013–December 2021 had ≥ 1 RA diagnosis, were aged ≥ 18 years, were prescribed ≥ 1 RA drug, had no psoriasis diagnosis, and had a record after the index date. For the MACE cohort, pts had no myocardial infarction or stroke diagnosis ≤ 31 days before index. For the malignancy cohort, pts had no

malignancy diagnosis < 1 year before index. Outcomes were the incidence of initial MACE and malignancy during follow-up (up to July 1, 2022). Known/exploratory risk factors/variables, including demographics, comorbidities, medications, administration of imaging techniques (eg X-rays), and laboratory tests, were selected using Cox regression models.A sequential variable selection technique with univariate analysis, variance inflation factors, and correlation coefficients was used to select exploratory risk factors. Sensitivity analyses were conducted with and without using laboratory tests as risk factors to identify consistent findings. Adjusted hazard ratios with 95% confidence intervals were calculated.

Results: Across MACE (16,012 pts) and malignancy (14,545 pts) cohorts, most pts were female (64.69–66.90%) and aged ≥ 65 years (69.78–68.88%); the most common comorbidities (all ≥ 29.60%) were hypertension, hyperlipidemia, and malignancies (MACE cohort only; Table). In total, there were 214 MACE over 43,964.7 pt-years (PY; incidence rate [IR] 0.49/100 PY) and 315 malignancies over 40,251.6 PY (IR 0.78/100 PY). Significant variables associated with increased MACE risk were male sex, older age, hypertension, renal disease, cerebrovascular disease, and X-ray administration (Fig 1). Significant variables for increased malignancy risk were male sex, older age, NSAID use, emphysema, serious infection, history of malignancies, and X-ray administration; steroid use and fracture diagnosis were significant for reduced malignancy risk (Fig 2).

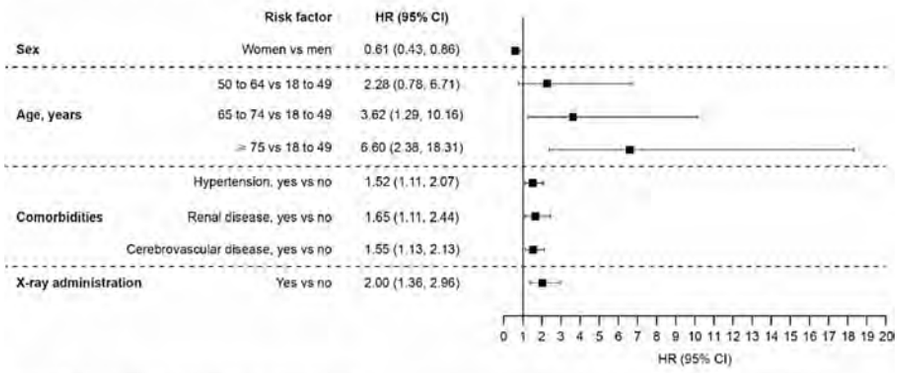
Table 1. Demographics and pt characteristics

	MACE cohort (N=16,012)		Malignancy cohort (N=14,545)	
	n	%	n	%
Female	10,358	64.69	9,730	66.90
Age, years				
18 to 49	1,649	10.30	1,582	10.88
50 to 64	3,190	19.92	2,945	20.25
65 to 74	4,593	28.68	4,009	27.56
≥ 75	6,580	41.09	6,009	41.31
BMI, kg/m²				
< 18.5	771	4.82	655	4.50
≤ 18.5 to < 25	2,771	17.31	2,352	16.17
≥ 25	959	5.99	814	5.60
NA	11,511	71.89	10,724	73.73
Smoking status				
Non-smoker	3,181	19.87	2,843	19.55
Smoker	1,242	7.76	927	6.38
NA	11,589	72.38	10,775	74.08
Comorbidities				
Diabetes	2,589	16.95	2,378	16.35
Cerebrovascular disease	2,492	15.56	2,632	18.10
Cardiovascular disease	4,331	27.05	4,271	29.36
Fracture diagnosis	2,436	15.21	2,250	15.47
Hypertension	6,383	39.86	5,741	39.47
Hyperlipidemia	4,740	29.60	4,305	29.60
Malignancy	4,762	29.74	N/A	N/A
Renal disease	1,388	8.67	1,181	8.12
Unspecified chronic bronchitis	1,212	7.57	1,013	6.96
Emphysema	491	3.07	340	2.34
Other COPD	540	3.37	408	2.81
Serious infection	4,015	25.07	3,496	24.04
Medications				
NSAIDs	9,125	56.99	8,230	56.58
Steroids, daily dose, mg				
0	6,018	37.58	5,644	38.80
> 0 to < 5	8,112	50.66	7,316	50.30
≥ 5 to < 10	1,126	7.03	947	6.51
≥ 10	756	4.72	638	4.39
bDMARDs	900	5.62	867	5.96
csDMARDs	8,505	53.12	7,941	54.60
Methotrexate, weekly dose, mg				
0	11,733	73.28	10,472	72.00
> 0 to ≤ 8	3,730	23.30	3,554	24.43
> 8	549	3.43	519	3.57
JAK inhibitor	49	0.31	48	0.33
Calcineurin inhibitor	1,086	6.78	1,002	6.89
History of malignancy	4,731	29.55	3,362	23.11
X-ray administration	11,100	69.32	9,855	67.76

bDMARD, biologic DMARD; COPD, chronic obstructive pulmonary disease; csDMARD, conventional synthetic DMARD; JAK, Janus kinase; MACE, major adverse cardiovascular events; N, total number of eligible pts; n, number of pts with characteristic; NA, not applicable; pt, patient

Conclusion: In pts with RA in RW settings in Japan, male sex, older age, and X-ray administration were associated with increased risk for MACE and malignancies. Hypertension and cerebrovascular disease increased MACE risk; emphysema increased malignancy risk. Missing data may have reduced potential associations, eg BMI/smoking. 1. Aviña-Zubieta et al. Ann Rheum Dis 2012; 71: 1524–9 2. Simon et al. Arthritis Res Ther 2015; 17: 212 Study sponsored by Pfizer. Medical writing support provided by L Rodgers, CMC Connect; funded by Pfizer.

Fig 1. Statistically significant risk factors for MACE in sensitivity analyses

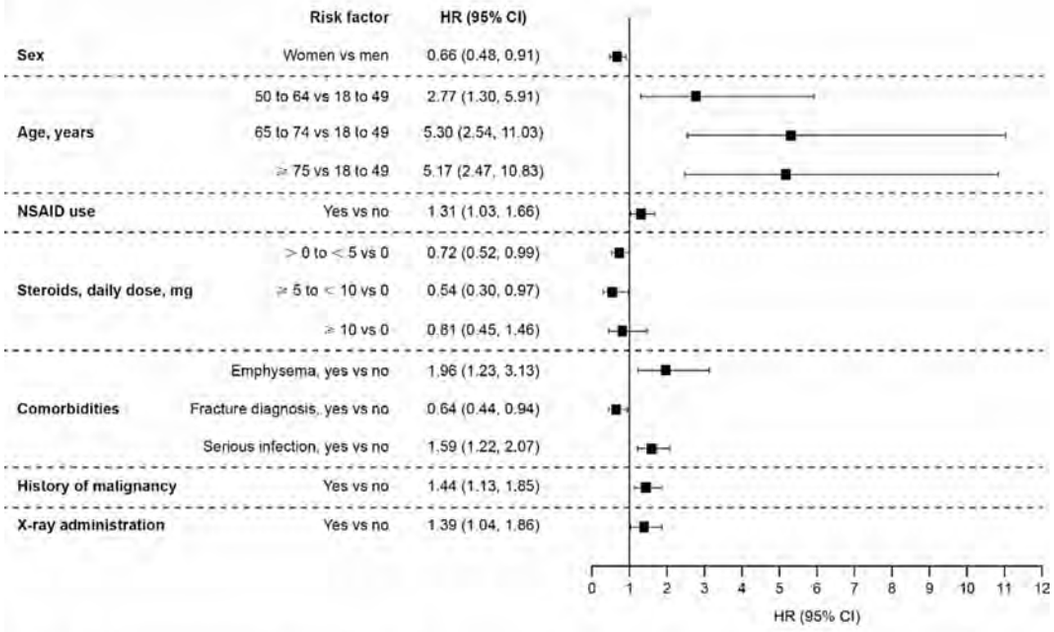


Analyses without laboratory tests included as risk factors are shown

The covariate assessment window for sex and age was the index date. For comorbidities and X-ray imaging, the covariate assessment window was the period from 1 year prior to the index date to the index date

CI, confidence interval; HR, hazard ratio; MACE, major adverse cardiovascular events

Fig 2. Statistically significant risk factors for malignancies in sensitivity analyses



Analyses without laboratory tests included as risk factors are shown

The covariate assessment window for sex and age was the index date. For NSAIDs and steroids, the covariate assessment window was the period from 3 months prior to the index date to the index date. For comorbidities and X-ray administration, the covariate assessment window was the period from 1 year prior to the index date to the index date. For history of malignancy, the covariate assessment window was the period from the initial date in the database to 1 year prior to the index date

CI, confidence interval; HR, hazard ratio

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Abstract Number: 1292

Active Rheumatoid Arthritis Patients Exhibit an Altered Serum Lipidomic Profile Directly Linked to Disease Activity, Which Is Reversed by Biologic and Targeted Synthetic DMARD

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Lipid metabolism impacts immune cell plasticity, activation, differentiation, and function, making the analysis of the lipidomic profile crucial in understanding chronic inflammatory diseases like Rheumatoid Arthritis (RA). High throughput metabolomic techniques offer a comprehensive view of lipid metabolism and can contribute to characterizing the pathogenesis of RA.

This study aimed to analyze the lipidomic profile in the serum of RA patients, examine its association with disease activity, and investigate how biological and targeted synthetic therapies modulate this profile.

Methods: A total of 250 consecutive RA patients participated, providing serum samples and clinical data (disease activity, acute phase reactants, autoimmune profile). Nightingale LTD's nuclear magnetic resonance (NMR) spectroscopy, covering over 200 lipid markers, was used to analyze the lipidomic profile. Additionally, a subgroup of active RA patients underwent prospective monitoring after receiving biologics (anti-TNF: n=50, anti-IL6R: n=15) or JAK inhibitors (JAKi: n=20). Serum samples collected before and after therapy evaluated changes in the lipid and clinical profiles. In vitro studies using an oil red staining assay examined lipid accumulation in HepG2 liver cells treated with serum from RA patients with varying disease activity.

Results: RA patients were divided into high (68), moderate (117), and low (65) disease activity groups. Approximately 100 lipid markers showed significant alterations across these groups. Interestingly, patients with high disease activity exhibited reduced levels of numerous lipid markers, including apolipoproteins, cholesterol, fatty acids (SFA, MUFA, PUFA, Omega 3 and 6, LA, DHA), triglycerides, cholines, phospholipids, lipoproteins (HDL, LDL, VLDL), and total lipid content in lipoproteins. Strong correlations were found between these lipid markers and inflammatory (CRP, ESR) and autoimmune parameters (ACPAs, RF). After six months of therapy, lipid markers significantly increased alongside clinical and analytical improvements in RA patients. Each drug demonstrated both common and distinct molecules that reversed the altered lipid metabolism. In vitro studies showed lipid accumulation in HepG2 liver cells treated with serum from RA patients with high disease activity compared to those with low disease activity, suggesting inflammation-induced altered hepatocyte metabolism as a potential contributor to reduced circulating lipid profiles.

Conclusion: Active RA patients exhibit a significantly reduced lipidomic profile directly linked to disease activity, inflammatory markers, and autoimmune parameters. Biological therapies and JAK inhibitors restore the altered lipid metabolism concurrently with clinical improvement. In vitro studies support the hypothesis that inflammation-induced lipid accumulation in the liver may partially explain the reduction in circulating lipid profiles in active patients. Ongoing studies aim to uncover the underlying mechanisms of these effects. Supported by ISCIII (PI21/0591, CD21/00187, RD21/0002/0033), RYC2021-033828-I, J. Andalucía (P20_01367) co-financed by FEDER; Fundacion Andaluza de Reumatología.

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Abstract Number: 1293

Single Camera Hand Motion Capturing as a Digital Biomarker for Disease Activity in Rheumatoid Arthritis Using Computer Vision: The Proof-of-Concept MeFisto Study

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Computer vision technology offerspromising possibilities for remotely assessing disease activity in rheumatoid arthritis (RA) patients, enabling telemedicine and improving access to care. The objective of this proof-of-concept study was to investigate the association between hand motion tracking features obtained through computer vision and disease activity in RA patients.

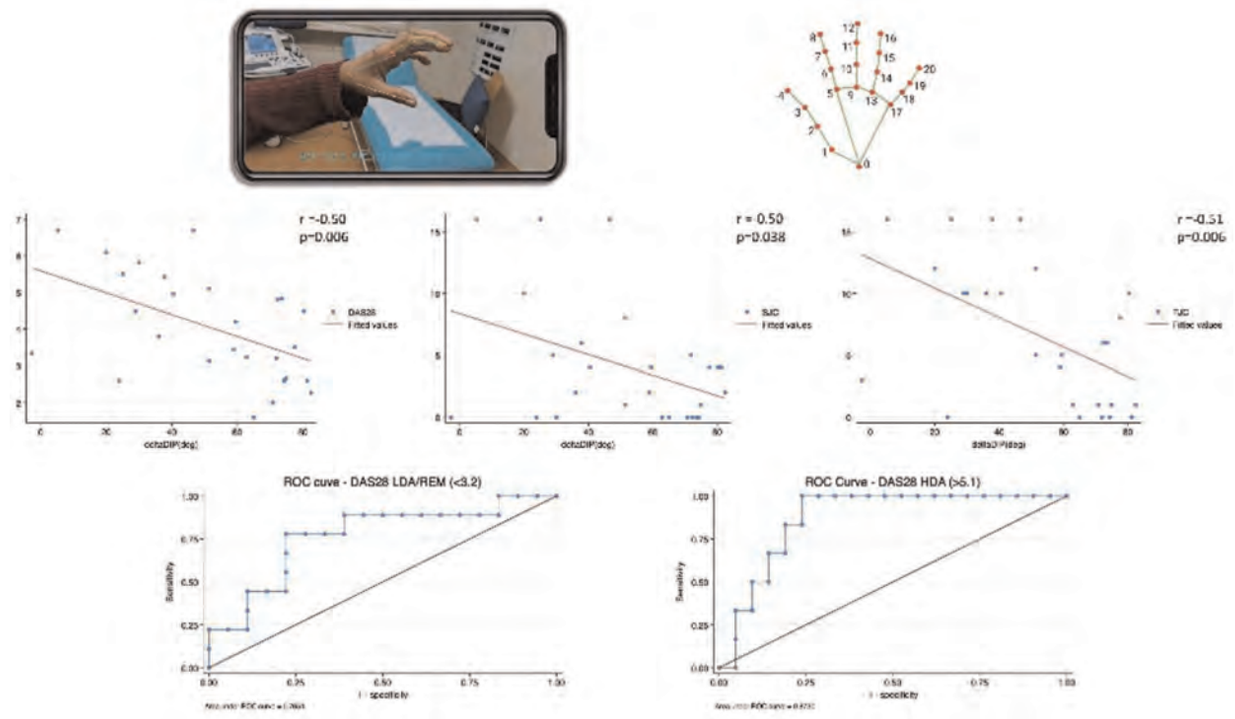

Figure 1. Single Camera algorithm for the detection of range of motion and speed. Correlation with disease activity as well as swollen and tender joint counts.

Methods: This proof-of-concept study included a total of 28 patients with classified rheumatoid arthritis (RA) from three European rheumatology centers. Disease activity was assessed using the Disease Activity Score 28 (DAS28), the Swollen Hand Joint Count (SJC), and the Tender Hand Joint Count (TJC). An ad-hoc hand motion analysis app based on the MediaPipe API was developed in a Python 3.9 environment and deployed on Windows 11, enabling computer vision inference of hand motion data. Upon smartphone single camera recording, the algorithm tracked the mean degree change of joint angle on flexion and the mean time to maximal flexion for each joint (sample video available: https://tinyurl.com/4hux35ze). The prediction performance was further analyzed using the area under the receiver operating characteristic (AUROC) curve.

Results: Among the 28 patients, 9 (32.14%) were classified as having low disease activity (LDA) or being in remission, 6 (21.42%) had high disease activity (HDA), and the remaining 13 (46.42%) fell within the moderate disease activity range. The flexion of the distal interphalangeal (DIP) joint demonstrated a strong correlation with disease activity measures, including DAS28, SJC, and TJC ($p = 0.006$, $r = -0.50$; $p = 0.03$, $r = -0.50$; $p = 0.006$, $r = -0.51$, respectively). Additionally, DIP flexion was found to be a significant predictor of LDA/remission (OR 1.05, 95% CI 1.01-1.10) and HDA (OR 0.93, 95% CI 0.89-0.99). AUROCs have been depicted in Figure 1.

Conclusion: This proof-of-concept study highlights the potential of computer vision technology for remotely assessing disease activity in RA patients. Integrating hand motion tracking into telemedicine platforms could enable rheumatologists to remotely assess disease activity, thereby improving access to care for RA patients. This approach has the potential to enhance telemedicine services, particularly in situations where in-person visits are challenging or limited.

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Abstract Number: 1294

Patient Reported Outcome Measures for Rheumatoid Arthritis Disease Activity: Using Rasch Measurement Theory and Cognitive Interviewing to Achieve More Meaningful Measurement

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Background/Purpose: Disease Activity (DA) monitoring is a standard of care in Rheumatoid Arthritis (RA). A systematic review of Patient Reported Outcome Measures (PROMs) for RA DA demonstrated a lack of sufficient evidence for content validity. The aim of this study was to use Rasch measurement theory (RMT) to develop a valid item pool for measurement of RA DA, and then explore patients' views on the relevance, comprehensiveness and comprehensibility of these items.

Methods: Questionnaires were sent to people aged 18 or over with RA in 2020/21, which included items from identified PROMs from a systematic review - RADAI5, RADAI, RADAI-SF, PDAS2, GAS, PAS, PAS-II, RAPID3, RAPID4, PRO-CLARA, PROM-score, RADAR, RADAI-F5, FLARE-RA and RA-FQ - and others suggested by patient feedback. Items were grouped into core domains established by OMERACT and included in exploratory factor analyses (EFA). By domain, psychometric properties were assessed by RMT analyses, which provided results on targeting, model fit, internal consistency, local dependency, unidimensionality and item threshold ordering. Sampling used a maximal variation approach across various demographics from the questionnaire-returning participants. Individual cognitive interviews took place in 2022/23. The think aloud technique was used as participants answered items, who were then asked about relevance, comprehensiveness and comprehensibility.

Results: A test dataset of n=398 and a validation dataset of n=293 were available. EFA of the test dataset showed that 30 items across the tenderness and swelling, patient global, pain, fatigue, physical functioning and stiffness domains loaded together. RMT analyses in the test dataset indicated that the patient global domain comprised two domains: general health and disease activity. In assessing the now seven domains, 12 items were discarded. Subtest analyses in the validation dataset indicated that patient global general health and fatigue could not be used to measure RA DA but the remaining five domains, containing 12 items, could. 20 participants were interviewed using a questionnaire containing the 12 identified RA DA items, six additional RA DA items, and six general health and fatigue items, which were presented to elicit views on their potential for inclusion. No consistent concerns were identified with the 12 RA DA items with regards relevance, comprehensiveness and comprehensibility. Some participants would prefer longer timeframes (> one week) for symptom reporting to fully capture their DA, a 'don't know' option, and asking about symptoms at different times of day due to diurnal patterns in symptoms. One participant noted that 'disease activity' was a confusing term.

Conclusion: Patient global items relating to general health and disease activity were two separate domains. RA DA can be measured using tenderness and swelling, patient global disease activity, pain, physical functioning and stiffness items, but not with fatigue and patient global general health items. These results provide initial evidence of content validity of the item pool in terms of relevance, comprehensiveness and comprehensibility. The next step is to develop a computer adaptive test based on anchored locations calculated using these data.

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Abstract Number: 1295

Having More Tender Than Swollen Joints Is Associated with Worse Functional Outcomes in Patients with Early RA in a Prospective Real-World Cohort

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Background/Purpose: Early RA patients may present with more tender than swollen joints, which can persist during DMARD therapy. Elevated TSJD (tender-swollen joint difference) is often challenging for rheumatologists, as there may be multiple causes, and in some, it may contribute to overestimating disease activity scores and ineffective treatment decisions.Little is known about the phenotype and impact of TSJD on patient function. Our objective was to evaluate the distribution and impact of TSJD on functional outcomes in the first year following RA diagnosis, and to determine whether associations vary by joint size. A better understanding of pain patterns relating to TSJD may help identify patients who could benefit from adjunctive treatments targeted at different pain pathways.

Table: Every 1-point increase of TJSD associated with Worsening Functional Outcome*

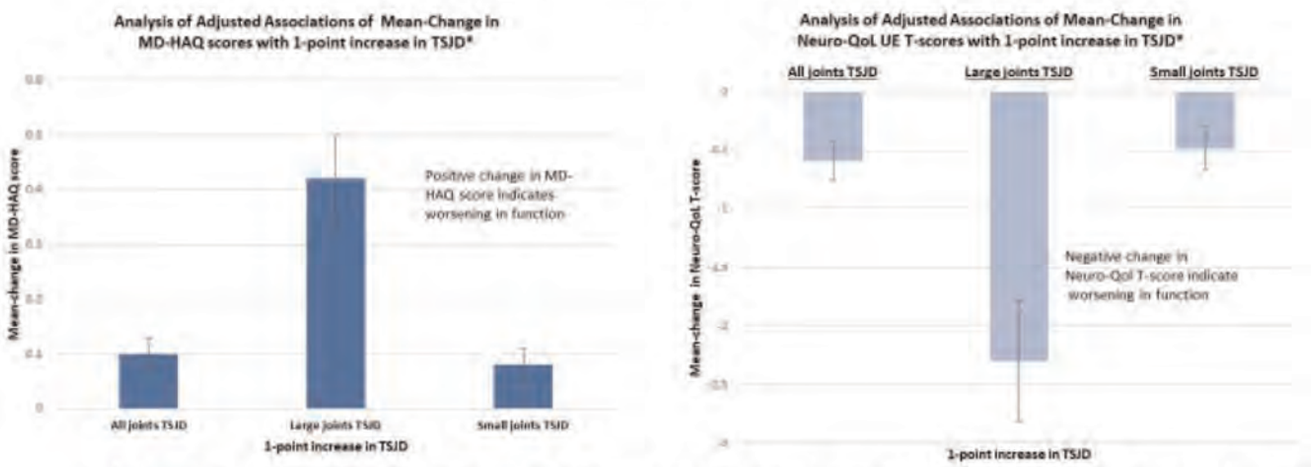
Outcome (Mean Change) for Functional Measures	All 28 joints		Large joints		Small joints	
	MC	95% CI	MC	95% CI	MC	95% CI
Function						
MDHAQ – physical function (0-10)						
TSJD (0-28)$^{\Phi}$	0.10	(0.08, 0.13)	0.42	(0.33, 0.50)	0.08	(0.05, 0.11)
NeuroQoL Upper Extremity T-score (0-100)						
TSJD (0-28)$^{\Phi}$	-0.59	(-0.76, -0.43)	-2.30	(-2.81, -1.79)	-0.49	(-0.67, -0.30)

MC - mean change for a 1-point increase in TSJD

*Multivariate mixed effects models adjusted for time, age at baseline, sex, education, current smoker at baseline, RDCI at baseline, osteoarthritis/back pain at baseline as well as time variant treatment at previous visit of oral steroids, methotrexate and advanced therapy.

$^{\Phi}$unit increase of linear TSJD of 1

Figure: Functional Outcomes in Patients with RA Worsen with Having More Tender than Swollen Joints



*Multi-variate mixed effects models adjusted for time, age at baseline, sex, education, current smoker at baseline, RDCI at baseline, osteoarthritis/back pain at baseline and time-variant treatment

Methods: Data were from patients with active, early RA enrolled in the Canadian Early Arthritis Cohort (CATCH), who completed assessments of general function (MDHAQ, range 0-10), upper extremity (UE) function of small and large joints (Neuro-QoL UE index, T-scores 0-100) over 1-year. 28 tender and swollen joint counts including 6 large joints (shoulders, elbows, knees) and 22 small joints (wrists, MCPs, PIPs) were performed. TSJDs were calculated by subtracting SJC from TJC at each visit. Adjusted associations between TSJD and functional outcomes (MD-HAQ and Neuro-QoL UE function T-score) were estimated in separate multivariable mixed effects models adjusted for age, sex, education, smoking, comorbidities, osteoarthritis/back pain and RA treatment. Separate analyses were performed for large versus small joint TSJD to examine potential differential impacts by joint size.

Results: Patients (n=549) were 70% female, mean (SD) age 56 (15) years, disease duration 5.3 (2.9) months. At baseline, 287 (52%) had TSJD >0, persisting in 32% at 12-months. 43% involved small joints and 34% had large joints, persisting at 12 months in 25% and 15% respectively. Higher TSJD was significantly associated with worse function [adjusted mean-changes (95%CI): MD-HAQ increase of 0.10 (0.08, 0.13) and decrease in Neuro-QoL UE function T-scores by -0.59 (-0.76, -0.43)] for every 1-point increase in TSJD (Table, Figure). Higher large joint TSJDs in particular were associated with the worst functional outcomes.

Conclusion: Having more tender than swollen joints is common in early RA. Higher TSJD score is associated with progressive worsening of functional outcomes, particularly when large joints are affected. Early identification and targeted intervention of predominantly tender joints may be needed to prevent long-term dysfunction.

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Abstract Number: 1296

Decline in Incidence of Extraarticular Manifestations of Rheumatoid Arthritis: A Population-Based Cohort Study

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Background/Purpose: Extraarticular manifestations of rheumatoid arthritis (ExRA) are associated with increased disease burden and mortality. They are also common, affecting about half of patients with RA. Two primary risk factors for developing ExRA include high disease activity and seropositivity.Given advancements in RA management in the last two decades,

Table 1. Baseline demographics, clinical characteristics, and comorbidities

Variable	Period of RA Incidence		
	1985-1999 (N=296)	2000-2014 (N=611)	Total (N=907)
Age (mean ± SD), years	57.6 ± 16.03	55.3 ± 15.27	56.1 ± 15.55
Female, n (%)	198 (67%)	430 (70%)	628 (69%)
Follow up, years (SD)	9.1 (3.61)	7.4 (4.06)	7.9 (4.00)
RF positive, n (%)	208 (70%)	349 (58%)	557 (62%)
Percent tested for RF	100%	98%	99%
Cigarette smoking, n (%)			
Never	127 (43%)	326 (53%)	453 (50%)
Former	113 (38%)	187 (31%)	300 (33%)
Current	56 (19%)	98 (16%)	154 (17%)
Obesity (body mass index ≥30 kg/m^2), n (%)	76 (26%)	247 (40%)	323 (36%)
Periarticular erosions, n (%)			
In the 1st year after RA diagnosis	70 (24%)	175 (29%)	245 (27%)
Percent with radiographs	93%	95%	94%
Highest ESR in the 1st year after RA incidence, mm/h (SD)	32.9 (25.2)	30.1 (24.7)	31.0 (24.9)
Medication exposure in the first year after RA incidence, n (%)			
Methotrexate	73 (25%)	319 (52%)	392 (43%)
Other DMARDs	173 (58%)	286 (47%)	459 (51%)
bDMARD	4 (1%)	68 (11%)	72 (8%)
Glucocorticoids	161 (54%)	328 (54%)	489 (54%)

Abbreviations: RA = rheumatoid arthritis; SD = standard deviation; RF = rheumatoid factor; ESR = erythrocyte sedimentation rate; DMARDs = disease modifying antirheumatic drugs; bDMARDs = biologic disease modifying antirheumatic drugs

epidemiologic data indicating an increasing incidence of seronegative RA, and lack of recent population-based epidemiologic studies evaluating ExRA over time, it is unclear if either the frequency of ExRA or mortality associated with ExRA has changed in recent years. This study aims to assess changes in the cumulative incidence of ExRA and associated mortality risk.

Methods: Trends in ExRA occurrence were evaluated using a population-based inception cohort. All adult patients with incident RA from 1985 through 2014 meeting the 1987 American College of Rheumatology criteria were included. Patients were divided into two cohorts based on the incidence date of RA, 1985-1999 and 2000-2014. Patients were followed until the earlier of death, migration from the region, or 12/31/2000 (for patients with incident RA from 1985-1994), 12/31/2008 (for patients with incident RA from 1995-2007), or 10/15/2022 (for patients with incident RA from 2008-2014). The occurrence of ExRA was determined by manual chart review. The 10-year cumulative incidence was estimated for each ExRA in both cohorts. Cox proportional hazard models were used to determine associations between specific demographic and RA disease characteristics and ExRA and between ExRA and mortality.

Results: A total of 907 patients were included in this study. There were 296 in the 1985-1999 cohort and 611 in the 2000-2014 cohort (table 1). The earlier cohort had a median follow up of 9.5 years (interquartile range [IQR] 6.7-12.0) and the later cohort had a median follow up of 7.4 years (IQR 4-10.3 years). The 10-year cumulative incidence of any ExRA

Table 2. Cumulative incidence of extraarticular rheumatoid arthritis at 10-year follow up

	Period of RA Incidence				
	1985-1999 (n = 296)		2000-2014 (n = 611)		
Extraarticular Manifestations*	Number of Events	10-year Cumulative Incidence %, (95% CI)	Number of Events	10-year Cumulative Incidence %, (95% CI)	HR for time period (95% CI)**
Any ExRA	138	45.1 (39.4, 51.6)	201	31.6 (27.3, 36.5)	**0.65 (0.51, 0.82)**
Severe ExRA	23	7.1 (4.7, 10.9)	33	6 (3.8, 9.3)	0.72 (0.40, 1.29)
Pericarditis	5	2 (0.8, 4.7)	10	2.2 (1.0, 4.6)	1.09 (0.36, 3.29)
Pleuritis	7	2.1 (1.0, 4.8)	7	0.7 (0.03, 1.9)	0.51 (0.15, 1.68)
Felty's syndrome	2	0.7 (0.2, 2.7)	0	0	--
Vasculitis¥	5	1.8 (0.7, 4.2)	2	0.4 (0.1, 1.8)	--
Neuropathy	5	1.4 (0.5, 3.6)	8	0.8 (0.3, 2.4)	0.65 (0.19, 2.28)
Scleritis	0	0	3	1.4 (0.5, 4.5)	--
Episcleritis	2	0.3 (0.05, 2.4)	6	0.6 (0.1, 2.4)	--
Other ExRA	119	41.4 (35.9, 47.9)	151	28.8 (24.8, 33.5)	**0.67 (0.53, 0.86)**
Keratoconjunctivitis sicca	49	15.8 (11.9, 20.9)	86	14.8 (11.5, 19.1)	0.90 (0.62, 1.31)
Xerostomia	1	0.3 (0.05, 2.4)	19	3.6 (2.1, 6.3)	--
Sjogren's syndrome	32	10.1 (7.1, 14.3)	47	8.2 (5.7, 11.7)	0.70 (0.44, 1.13)
Pulmonary fibrosis	15	5.2 (3.1, 8.7)	20	2.8 (1.7, 4.8)	0.62 (0.30, 1.31)
Bronchiolitis obliterans	2	0.7 (0.2, 3.0)	1	0.2 (0.02, 1.2)	--
Organizing pneumonia	2	0.3 (0.05, 2.4)	2	0.3 (0.09, 1.4)	--
Cervical myelopathy	4	1.4 (0.5, 3.8)	1	0.2 (0.03, 1.6)	--
Subcutaneous nodules	90	30.9 (25.8, 37.1)	94	15.8 (12.9, 19.4)	**0.52 (0.39, 0.70)**
Other nodules	0	0	9	1.2 (0.5, 3.0)	--

Abbreviations: ExRA = extraarticular manifestation of rheumatoid arthritis, HR = hazard ratio; RA = rheumatoid arthritis, CI = confidence interval. HR reaching statistical significance in bold.
*There were no cases of retinal vasculitis, glomerulonephritis, or amyloidosis in either cohort; **Adjusted for age and sex. Must have at least 5 events in each group; ¥Included major cutaneous and internal organ vasculitis

Figure 1. Risk of developing any extraarticular manifestation of rheumatoid arthritis based on year of rheumatoid arthritis incidence.

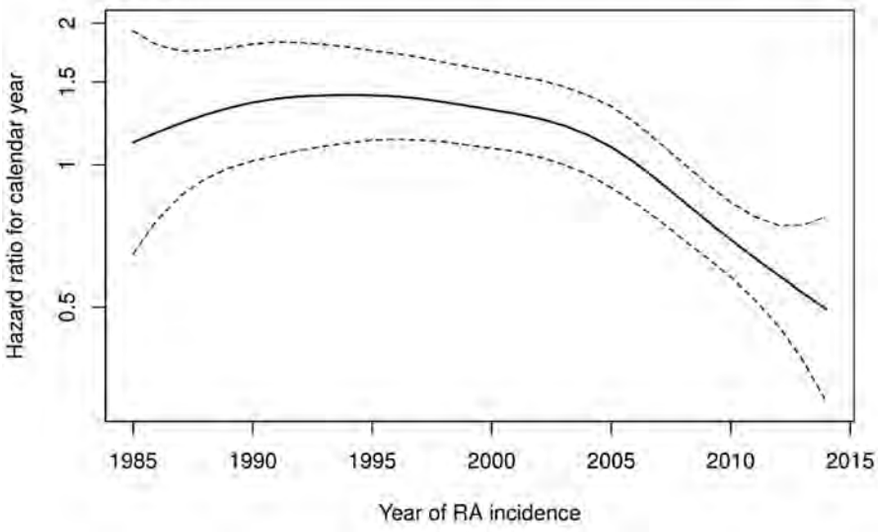

Figure demonstrating the changing hazard ratios (solid black line) and associated 95% confidence intervals (dotted lines) for the development of any extraarticular manifestation of rheumatoid arthritis as a linear trend based on year of rheumatoid arthritis incidence.

decreased significantly between the earlier and later cohorts (45.1% vs 31.6%, p< 0.001; table 2 and figure 1). This was largely driven by significant declines in subcutaneous rheumatoid nodules (30.9% vs 15.8%, p< 0.001) and non-severe ExRA (41.4% vs 28.8%, p=0.001). Several risk factors for the development of any ExRA were identified, including RF positivity (hazard ratio [HR] 2.02, 95% confidence interval [CI] 1.43-2.86), current smoking (HR 1.61, 95% CI 1.10-2.34), and erosions (HR 1.46, 95% CI 1.05-2.04). Mortality was increased in patients with either non-severe (HR 1.83, 95% CI 1.18-2.85) or severe ExRA (HR 3.05, 95% CI 1.44-6.49).

Conclusion: The incidence of ExRA has decreased over time. Despite improvements in RA therapeutics and management strategies, mortality remains increased in patients with ExRA.

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Abstract Number: 1297

COVID-19 Vaccination-related Delayed Adverse Events Among Patients with Rheumatoid Arthritis: Results from the COVAD Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

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Background/Purpose: COVID-19 vaccines have been proven to be safe in the healthy population. Data on longer-term AEs in people with autoimmune diseases (AIDs), including rheumatoid arthritis (RA) are lacking. COVID-19 vaccination-related AEs in patients with RA, rheumatic (rAIDs), and non-rheumatic AIDs (nrAIDs) and healthy controls (HC) greater than seven days post-vaccination were assessed in the COVID-19 Vaccination in Autoimmune Diseases (COVAD)-2 study.

Methods: The COVAD-2 study group comprised 157 collaborators across 106 countries. The study was conducted between February and June 2022. An online survey captured self-reported data related to COVID-19 vaccination-related AEs in RA, AIDs, and HCs. rAIDs included connective tissue diseases, inflammatory myopathies and inflammatory arthritis. nrAIDs comprised inflammatory bowel disease, multiple sclerosis etc. We compared COVID-19 vaccination-related delayed AEs among RA, other rAIDs, nrAIDs and HCs, adjusting for age, gender and ethnicity, using multivariable binary regression. Statistically significant results are reported.

Results: Among 7203 participants, 1423 (19.7%) RA, 2620 (36.4%) rAIDs, 426 (5.9%) nrAIDs and 2734 (38%) HCs were included from a total of 17612 respondents, with 75% female and 42.2% Caucasian (Table 1). People with RA were older [median age 51 (40-62); rAIDs, 48 (37-59); nrAIDs 43 (34-53); HC 38 (30-49)]. When compared to HCs, people with RA reported higher overall major AEs in the multivariable analyses [OR 1.3 (1.0-1.7)], especially throat

Table 1: Socio-demographic and vaccination data of survey respondents. RA: rheumatoid arthritis; rAID: rheumatic autoimmune disease; nrAID: non-rheumatic autoimmune disease; HC: health controls.

Variable	Total, n (7203)	(%) (100)	RA, n (1423)	% (19.7)	rAIDs, n (2620)	% (36.4)	nrAIDs, n (426)	% (5.9)	HC, n (2734)	% (38)
Age (Me, IQR), years	44 (34-56)	-	51 (40-62)	-	48 (37-59)	-	43 (34-53)	-	38 (30-49)	-
Gender F:M	5310:1799 3:1	-	1192:210 5.7:1	-	2155:438 5:1	-	351:70 5:1	-	1611:1081 1.5:1	-
Etnicity n (%)										
African American or of African origin (Black)	336	4.7	49	3.4	186	7.1	4	0.9	97	3.5
Asian	1632	22.7	322	22.6	542	20.7	57	13.4	710	26.0
Caucasian (White)	3039	42.2	784	55.1	1274	48.6	227	53.3	754	27.6
Do not wish to disclose	262	3.6	49	3.4	84	3.2	14	3.3	115	4.2
Hispanic	1200	16.7	104	7.3	293	11.2	83	19.5	720	26.3
Native American/Indigenous/Pacific Islander	53	0.7	8	0.6	21	0.8	4	0.9	20	0.7
Other	628	8.7	98	6.9	206	7.9	34	8.0	290	10.6

closure [OR 2.9 (1.1-7.3)], and increased number of several minor AEs (Table 2). People with RA had fewer reported episodes of fever [OR 0.7 (0.5-1.0)]. When compared to rAIDS, people with RA had fewer episodes of rash [OR 0.6 (0.4-1.0)], and when compared to nrAIDs, had increased reported injection site pain [OR 1.7 (1.0-2.6)], myalgia [OR 1.9 (1.1-3.4)], body ache [OR 2.2 (1.3-3.7)], joint pain [OR 2.7 (1.5-4.8)], fever [OR 1.8 (1.0-3.3)] and swelling of extremities [OR 4.9 (1.1-21.4)]. ChadOx1 nCOV-19 (Oxford/ AstraZeneca) led to significantly increased minor AEs in the RA group [OR 1.9 (1.4-2.6)], compared to other vaccines, while the Moderna vaccination was associated with increased hospitalisation in people with RA [OR 2.4 (1.3-4.3)]. People with active RA had increased major AEs [OR 1.8 (1.1 – 3.0)] and hospitalisation [OR 4.1 (1.3 – 13.3)], compared to inactive RA. RA patients without autoimmune comorbidities had significantly fewer major and minor AEs compared to those with other rAIDs (Table 3). People with RA and mental health diagnoses had increased reported chills [OR 1.8 (1.1 – 3.0)] and chest pain [OR 2.5 (1.1 – 6.0)]. Decreased incidence of hospitalisation was seen in patients taking methotrexate [OR 0.5 (0.3-0.9)] or TNF inhibitors [OR 0.1 (0.02-0.9)] compared to hydroxychloroquine, sulfasalazine and leflunomide.

Conclusion: COVID-19 vaccination is safe with minimal to no risks of delayed AEs in patients with RA compared to HCs, and fewer compared to other rAIDs. Active RA and presence of co-existent rAIDs were both associated with increased risk of delayed AEs.

Table 2: Effects of COVID-19 vaccination in patients with rheumatoid arthritis (RA) vs healthy controls (HCs). Factors included as covariates in multivariable binary logistic regression analysis included age, sex, ethnicity.

	RA		HCs		Univariable		Multivariable	
	N 1423	% 100	N 2734	% 100	OR (95% CI)	P value	OR (95% CI)	P value
Minor ADEs	211	14.8	456	16.7		0.122		0.499
Injection site (arm) pain and soreness	124	8.7	305	11.2	**0.8 (0.6-0.9)**	**0.014**		0.065
Myalgia	91	6.4	164	6.0		0.615		
Body ache	111	7.8	176	6.4		0.101		0.354
Joint pain	113	7.9	120	4.4	**1.9 (1.4-2.4)**	**<0.001**	**1.8 (1.3-2.5)**	**<0.001**
Fever	79	5.6	205	7.5	**0.7 (0.6-0.9)**	**0.018**	**0.7 (0.5-1.0)**	**0.048**
Chills	63	4.4	127	4.6		0.748		
Cough	24	1.7	34	1.2		0.249		
Difficulty in breathing or Shortness of breath	26	1.8	33	1.2		0.109		0.184
Nausea/vomiting	34	2.4	36	1.3	**1.8 (1.1-2.9)**	**0.011**		0.170
Headache	91	6.4	142	5.2		0.111		0.321
Rash	25	1.8	21	0.8	**2.3 (1.3-4.1)**	**0.004**	**2.3 (1.1-4.5)**	**0.022**
Fatigue	111	7.8	136	5.0	**1.6 (1.2-2.1)**	**<0.001**	**1.5 (1.1-2.0)**	**0.018**
Diarrhoea	25	1.8	33	1.2		0.152		0.574
Abdominal pain	20	1.4	16	0.6	**2.4 (1.3-4.7)**	**0.007**	**2.6 (1.2-5.7)**	**0.018**
High pulse rate or palpitations	26	1.8	45	1.6		0.670		
Rise in blood pressure	16	1.1	19	0.7		0.151		0.370
Fainting	2	0.1	9	0.3		0.261		
Dizziness	45	3.2	51	1.9	**1.7 (1.1-2.6)**	**0.008**	**1.7 (1.0-2.7)**	**0.040**
Chest pain	23	1.6	29	1.1		0.127		0.223
Swelling in the extremities	24	1.7	17	0.6	**2.7 (1.5-5.1)**	**0.001**	**3.7 (1.8-7.7)**	**<0.001**
Weakness and tingling in the feet and legs	32	2.2	49	1.8		0.313		
Pricking or pins and needles in the hands and feet	25	1.8	28	1.0	**1.7 (1.0-3.0)**	**0.046**		0.232
Visual disturbances (loss of vision, blurring of vision, etc.)	18	1.3	21	0.8		0.115	**2.4 (1.1-5.0)**	**0.022**
Bleeding/bruising on the body	13	0.9	9	0.3	**2.8 (1.2-6.5)**	**0.014**	**3.2 (1.2-8.5)**	**0.024**
Petechial rash	6	0.4	5	0.2		0.155		0.254
Major ADEs	159	11.2	224	8.2	**1.4 (1.1-1.7)**	**0.002**	**1.3 (1.0-1.7)**	**0.046**
Anaphylaxis	9	0.6	19	0.7		0.815		
Marked difficulty in breathing	22	1.5	42	1.5		0.982		
Throat closure	12	0.8	13	0.5		0.146	**2.9 (1.1-7.3)**	**0.029**
Severe rashes	17	1.2	29	1.1		0.696		
Hospitalisation	52	3.7	57	2.1	**1.8 (1.2-2.6)**	**0.003**		0.592

Table 3: Effects of COVID-19 vaccination in patients with rheumatoid arthritis (RA) and no autoimmune comorbidities vs RA with rheumatic autoimmune disease (rAIDs). Factors included as covariates in multivariable binary logistic regression analysis included age, sex, ethnicity.

	RA without AIDs		RA + rAID		Univariable		Multivariable	
	N (965)	100 %	N (334)	100 %	OR (95% CI)	P value	OR (95% CI)	P value
Minor ADEs	126	13.1	69	20.7	**0.6 (0.4-0.8)**	**0.001**	**0.6 (0.4-0.8)**	**0.001**
Injection site (arm) pain and soreness	71	7.4	41	12.3	**0.6 (0.4-0.9)**	**0.006**	**0.6 (0.4-0.8)**	**0.005**
Myalgia	53	5.5	28	8.4	-	0.060		0.079
Body ache	65	6.7	39	11.7	**0.5 (0.4-0.8)**	**0.004**	**0.5 (0.4-0.8)**	**0.006**
Joint pain	66	6.8	37	11.1	**0.6 (0.4-0.9)**	**0.013**	**0.6 (0.4-0.9)**	**0.017**
Fever	46	4.8	27	8.1	**0.6 (0.4-0.9)**	**0.023**	**0.6 (0.4-1.0)**	**0.043**
Chills	34	3.5	23	6.9	**0.5 (0.3-0.9)**	**0.010**	**0.5 (0.3-0.8)**	**0.010**
Cough	10	1.0	12	3.6	**0.3 (0.1-0.7)**	**0.002**	**0.3 (0.1-0.7)**	**0.004**
Difficulty in breathing or Shortness of breath	12	1.2	10	3.0	**0.4 (0.2-1.0)**	**0.033**		0.089
Nausea/vomiting	18	1.9	13	3.9	**0.5 90.2-1.0)**	**0.036**	**0.5 (0.2-1.0)**	**0.039**
Headache	47	4.9	37	11.1	**0.4 (0.3-0.6)**	**<0.001**	**0.4 (0.3-0.7)**	**<0.001**
Rash	13	1.3	11	3.3	**0.4 (0.2-0.9)**	**0.023**	**0.4 (0.2-0.9)**	**0.021**
Fatigue	54	5.6	47	14.1	**0.4 (0.2-0.5)**	**<0.001**	**0.4 (0.2-0.6)**	**<0.001**
Diarrhoea	13	1.3	11	3.3	**0.4 (0.2-0.9)**	**0.023**	**0.4 (0.2-0.9)**	**0.029**
Abdominal pain	8	0.8	9	2.7	**0.3 (0.1-0.8)**	**0.010**	**0.3 (0.1-0.8)**	**0.017**
High pulse rate or palpitations	12	1.2	11	3.3	**0.4 (0.2-0.8)**	**0.014**	**0.4 (0.2-1.0)**	**0.041**
Rise in blood pressure	9	0.9	6	1.8	-	0.203		
Fainting	1	0.1	1	0.3	-	0.432		
Dizziness	25	2.6	17	5.1	**0.5 (0.3-0.9)**	**0.026**		0.053
Chest pain	8	0.8	11	3.3	**0.2 (0.1-0.6)**	**0.001**	**0.3 (0.1-0.7)**	**0.005**
Swelling in the extremities	13	1.3	9	2.7	-	0.100		0.133
Weakness and tingling in the feet and legs	18	1.9	13	3.9	**0.5 (0.2-1.0)**	**0.036**		0.099
Pricking or pins and needles in the hands and feet	16	1.7	8	2.4	-	0.389		
Visual disturbances (loss of vision, blurring of vision, etc.)	7	0.7	10	3.0	**0.2 (0.1-0.6)**	**0.002**	**0.3 (0.1-0.7)**	**0.008**
Bleeding/bruising on the body	7	0.7	5	1.5	-	0.204		
Petechial rash	2	0.2	4	1.2	**0.2 (0.03-0.9)**	**0.021**	**0.2 (0.03-0.9)**	**0.034**
Major ADEs	96	9.9	48	14.4	**0,7 (0.5-1.0)**	**0.026**	**0.7 (0.5-1.0)**	**0.032**
Anaphylaxis	2	0.2	6	1.8	**0.1 (0.02-0.6)**	**0.001**	**0.1 (0.02-0.6)**	**0.009**
Marked difficulty in breathing	8	0.8	9	2.7	**0.3 (0.1-0.8)**	**0.010**	**0.3 (0.1-0.8)**	**0.015**
Throat closure	3	0.3	7	2.1	**0.1 (0.03-0.6)**	**0.001**	**0.1 (0.03-0.6)**	**0.005**
Severe rashes	8	0.8	9	2.7	**0.3 (0.1-0.8)**	**0.010**	**0.3 (0.1-0.8)**	**0.012**
Hospitalisation	32	3.3	16	4.8	-	0.219		

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Abstract Number: 1298

Risk Factors Associated with Venous Thromboembolism in Rheumatoid Arthritis in Clinical Practice

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SESSION INFORMATION

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Background/Purpose: Increased risk of venous thromboembolism (VTE) has been reported in rheumatoid arthritis (RA) compared to the general population. However, factors associated with the risk of VTE have been barely studied in RA. Our objective was to identify classical or disease-related risk factors of VTE in RA patients in clinical practice.

Methods: Retrospective observational study performed on all RA patients fulfilling the 2010 ACR/EULAR clarification criteria attending the one-day hospitalization program of the Rheumatology department, Cochin hospital, in 2021. We used the electronic medical report to identify the occurrence of VTE in 2021 and collect RA disease characteristics and risk factors for VTE. Multivariate analysis by logistic regression was performed to determine the factors independently associated with VTE.

Results: We included 405 RA patients (330 females, 81%), with a mean age of 59±14 years and a mean disease duration of 16±13 years. Positive rheumatoid factor and positive anti-CCP antibodies were detected in 331 (82%) and 347 (86%) patients respectively. 252 patients (62%) had bone erosions. The mean DAS28 was 3.5±1.4 ; 218 patients (48%) received corticosteroids (mean dose 2.6±3.3 mg/L), 247 (61%) methotrexate, and 151 (54%) targeted biologic or synthetic DMARDs (b/tsDMARDs), including 72 on TNF inhibitors, 70 on rituximab and 39 on JAK inhibitors (13 baricitinib, 7 tofacitinib 17 upadacitinib and 2 filgotinib). We identified 15 (4%) venous thromboembolic events that occurred in 2021, including 11 PVT and 8 PE (incidence of 3.7 for 100 patient/year). The mean duration between the occurrence and VTE and the visit was 3.6 ±4.8 months. Among these 15 VTE patients, 11 were women (73%, vs. 82% in patient without VTE), with a mean age of 65±12 years (vs. 59±14, p=0.11). Age >65 years was more frequent in patient with VTE (60% vs. 33%, p=0.030); 4 (27%) patients with VTE had a history of previous VTE (vs. 3%, p< 0.001), 9 (60%) were hospitalized up to 6 months before the event (vs. 6%, p< 0.001), 5 (33%) experienced surgery up to 3 months bfore the event (vs. 2%, p< 0.001) and 4 (33%) had a history of fracture (vs. 3%, p< 0.001). No difference was oberved regarding body mass index, the frequency of

Table 1: results of the logistic regression analysis including VTE as the dependent variable

Variable	Odd ratio (95% CI)	p-value
Age >65 years	1.37 (0.38-4.84)	0.63
Male sex	1.15 (0.26-5.04)	0.85
Extra-articular manifestation	2.64 (0.72-9.64)	0.14
CRP levels	4.41 (0.51-31.28)	0.39
Corticosteroids	1.31 (0.33-5.42)	0.36
JAK inhibitors	7.69, (1.21-81.15)	0.027
History of previous VTE	33.06 (3.57-96.56)	0.002
Hospitalization up to 3 months	11.62 (2.89-46.71)	0.005
Surgery up to 6 months	8.02 (1.16-55.22)	0.034
History of fracture	0.56 (0.07-4.34)	0.58

smoking, neoplasia, recent travel (up to 3 months) and estrogen/antidepressant therapies. No patient had thrombophilia. Regarding RA characteristics, patients with VTE were more likely to present extra-articular manifestations (67% vs. 35%, p=0.011) and higher CRP levels (18±35 mg/L vs. 6.3±13 mg/L, p=0.007). They also received more frequently corticosteroids (73% vs. 47%, p=0.048) and JAKi (27% vs. 9%, p=0.021). Disease duration, autoantibody status, frequency of erosions, DA28 and treatment with methotrexate or bDMARDs did not differ between these 2 groups. Logitic regression analysis identified history of previous VTE, hospitalization, surgery and treatment with JAKi as independently associated with the occurrence of VTE (**Table 1**).

Conclusion: History of VTE was identified as the strongest risk factor of the occurrence of VTE. Our results suggest a specific warning on recent hospitalization and surgery as precipitating events to VTE.As recommended by the PRAC JAKi should be used with caution in patients with risk factors for VTE.

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Rheumatoid Arthritis Patients Who Never Use a Biological During Their Disease Course Represent a Subgroup of Patients Likely to Achieve Sustained DMARD-free Remission

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Background/Purpose: According to the 2022 EULAR recommendations for the management of rheumatoid arthritis (RA) complete cessation of DMARDs is not advisable due to a high risk of disease flares. On the other hand, DMARD-free remission (DFR) is proven to be achievable and sustainable in 10-20% of RA patients. This paradoxical notion can possibly be explained by the fact that the EULAR recommendations refer to evidence from RCTs investigating ACPA-positive RA-patients with high disease activity at inclusion. Generally, this subgroup is treated more often with biologicals, while in daily practice only part of RA patients use a biological (ascertainment bias). We therefore hypothesized that RA patients who are treated with biologicals are less capable of achieving sustained DFR (sDFR) than patients who are not treated with biologicals. We studied this in two different cohorts.

Methods: Patients who fulfilled the 1987 and/or 2010 criteria for RA from the Leiden Early Arthritis Clinic (EAC) and from the treatment in the Rotterdam Arthritis Cohort (tREACH) trial were selected. The EAC is a population-based inception cohort that includes early arthritis patients who are treated according to general guidelines. The tREACH was a treat-to-target strategy trial in which RA patients were treated according to protocol that included treatment intensification as well as tapering. RA patients that had been treated with a biological at any point in time during 5 (EAC) and 3 (tREACH) years of follow-up

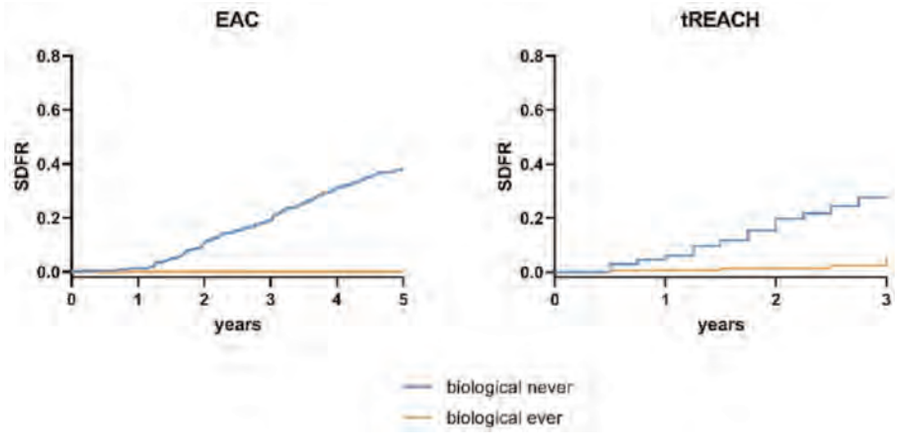

Figure 1. Kaplan Meier curves for achievement of sustained DFR in the EAC and tREACH. Orange lines indicate patients with a history of biological use. Blue lines indicate patients without a history of biological use. Follow-up time was 5 years in the EAC and 3 years in the tREACH. DFR, DMARD-free remission.

were compared to RA patients who had never used a biological in this period for the outcome of achieving sDFR. sDFR was defined as the sustained (≥12 months) absence of clinical arthritis after discontinuation of DMARD in both the EAC and tREACH. Differences in sDFR were visualised with Kaplan-Meier curves and tested with log rank tests.

Results: In the EAC 627 RA patients were followed for 5 years. None of the RA patients who ever used a biological achieved sDFR (0%), while 30% (162/538) of the patients who never used a biological achieved sDFR (p-value < 0.001; Figure 1). In the tREACH trial 425 patients were followed for 3 years; 3.2% (5/154) of patients who ever used a biological achieved sDFR, while 22% (60/271) of patients who never used a biological achieved sDFR (p-value < 0.001; Figure 1).

Conclusion: RA patients who use/used a biological have a negligible chance of achieving sDFR; in contrast to the large proportion of RA patients without biological use. Since the current RA management guidelines may suffer from ascertainment bias, future guidelines may be amended such that DMARD cessation is not discouraged in RA-patients without biologicals.

Disclosure: J. Heutz: None; **P. de Jong**: None; **A. van der Helm-van Mil**: None; **E. van Mulligen**: None.

Abstract Number: 1300

Bone Marrow Edema in MRI Is More Associated with Rapid Radiographic Progression Than Clinically Relevant Radiographic Progression

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rapid radiographic progression (RRP) is selected as one of the risk factors for difficult- to- treat RA, which needs to be resolved as soon as possible. On the other hand, EULAR recommendations for imaging were published, in which MRI bone oedema was an independent and strong predictor for joint destruction.

To clarify, association of BE with RRP using the clinical data in RA patients treated with conventional synthetic (cs) DMARDs. This study was undertaken for patients as post-hoc analysis of the paper (Trial Registration Number: UMIN000012200): Etiology of autoimmune diseases: Commensal bacterial pathogens overwhelming antibody defence function evoke serological marker levels and aggravate disease activity in rheumatoid arthritis. (K. Terato et al. Published: February 6, 2018, https://doi.org/10.1371/journal.pone.0190588).

Methods: All patients were mainly treated with methotrexate (MTX) or MTX +other csDMARDs combination therapy. The majority of patients did not respond to medication. None of the patients received biologics during the study. Hand and feet X-rays were taken for all patients and MRI was taken for affected hand. The modified total Sharp score (mTSS) was evaluated by KK and TO over a period of one year. MRI hand BE (rarely other large joints) were also checked by same reader by OMERACT MRI method as BE score.

Results: 1) At first, baseline data of 108 non-RRP patients and 47 Clinically relevant radiographic progression (CRRP:5 >ΔmTSS /year≥3)+RRP patients (ΔmTSS /year ≥5) were statistically compared. Short duration, high BE rate and MRI BE score (hand), high DAS28-ESR , high CRP levels, high mTSS, high yearly progression of mTSS were significantly increased in RRP+CRRP group compared with non RRP group. Secondly, background data of 13 CRRP and 34 RRP patients were compared. Only percentages of BE, MRI BE score (hand) were significantly increased in RRP group compared with CRRP group (table 1)

2)Secondly, patient data were divided into 5 groups according to rate of 1) ΔmTSS/year-- ≥10, 2)< 10 and ≥5 (both 1)2) are in RRP group), 3) < 5 and ≥3 (in CRRP group), 4) < 3 and >0.5, and 5)) ≤ 0.5(both 4)5) are in non RRP group). Mean of DAS28-ESR in the group of ΔmTSS /year ≥10 was significantly lower in the group of ΔmTSS /year < 10 and ≥5 and < 3 and >0.5, respectively(P< 0.05). No significant changes were observed in SJC (x10), CRP value (x10), RF, MMP3 (ng/ml) (figure 1A). We also compared mean BRI BE score (hand)(x10), ΔmTSS /year (x10), mTSS, age, disease duration among

Figure 1

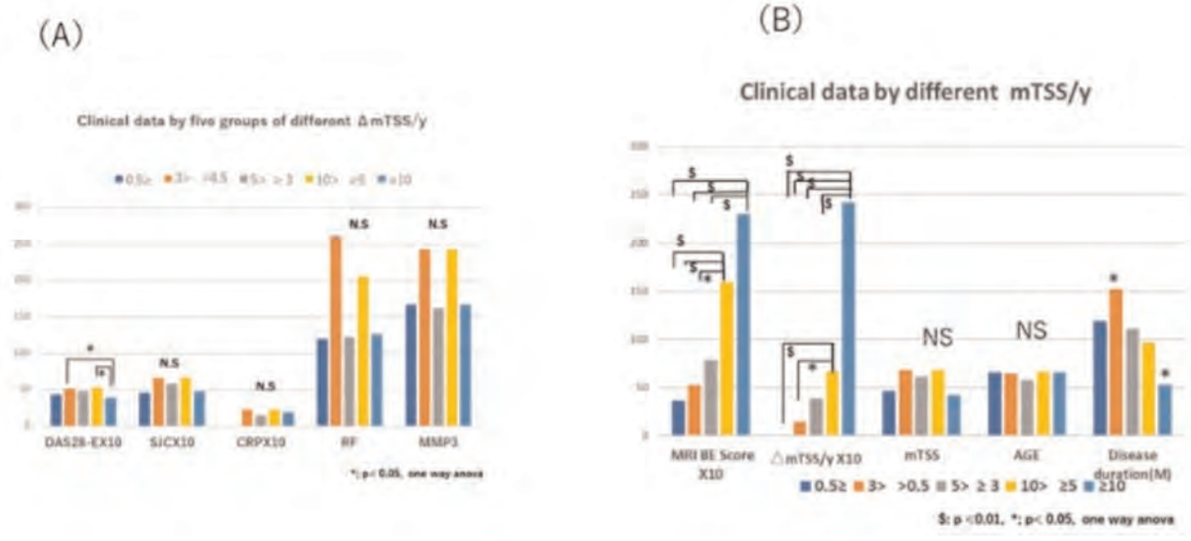

Figure 1.

5 groups. As a results, MRI BE score (hand) and and ΔmTSS /year in the group of ΔmTSS /year-≥10 or < 10 and ≥5 (both 4) 5) are in RRP group) was significantly higher than another group (figure 1B).

3) Finally, we investigated correlation between MRI BE score and ΔmTSS /year(x10). We found slight correlation between them. r = 0.57 P = 0.001(Pearson Correlation Coefficient) (Figure 2).

Figure 2

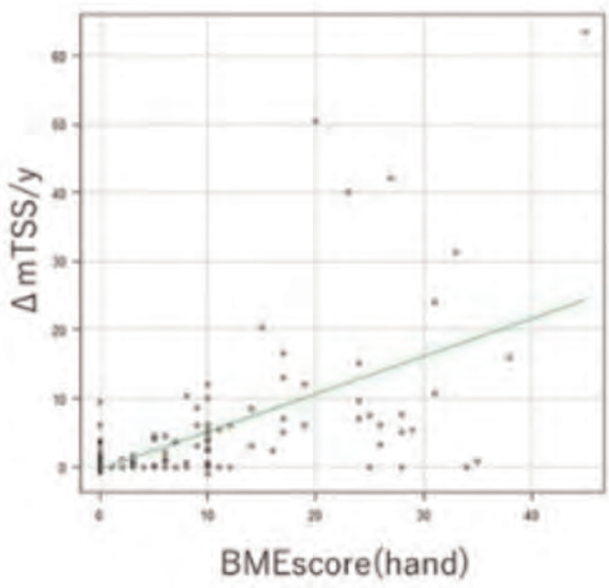

Figure 2.

Table 1.

item	RRP group(N=34)	CRRP group(N=13)	P value	
sex(F,M)	31, 3	12, 1	N.S	fisher
age (years)	65.9(±13.6)	57.6(±9.22)	N.S	t
duration(month)	41.5(13.8-135)	96.0(60.0-156)	N.S	mann-whitney U
MTX dose (mg/w)	8(0-11.5)	8(6-10.0)	N.S	mann-whitney U
complication(-,+)	13, 21	3, 10	N.S	fisher
MRI BE(-,+)	3, 31	5, 8	<0.05	fisher
MRI BE score(hand)	19(10.5-26.5)	7(5.0-10.0)	P<0.01	mann-whitney U
DAS28-ESR	4.63(±1.50)	4.80(±1.40)	N.S	t
DAS28-ESR (not high, high)	17, 14	7, 6	N.S	fisher
SJC	5.79(±3.27)	5.77(±3.19)	N.S	t
SJC(≥7, 7>)	13, 21	5, 8	N.S	fisher
TJC	5.21(±5.12)	6.00(±5.92)	N.S	t
pVAS	46.8(±25.4)	41.4(±22.4)	N.S	t
RF (IU/ml)	168.5(±178.0)	122.1(±145.7)	N.S	t
RF (-,+)	6, 28	3, 10	N.S	fisher
CRP (mg/dl)	0.92(0.16-2.59)	1.00(0.49-1.64)	N.S	mann-whitney U
CRP(negative, positive)	11, 23	3, 10	N.S	fisher
ESR (mm/hr)	37.7(±26.6)	37.0(±27.9)	N.S	t
mTSS	39(19.5-63.8)	46(31.0-95.0)	N.S	mann-whitney U
ΔmTSS/Y	9.55(6.0-15.8)	3.70(3.5-4.00)	P<0.01	fisher
MMP-3 (ng/ml)	207.6(±223.1)	162.1(±94.4)	N.S	t

Conclusion: BE may be a possible prognostic factor for RRP and more associated with RRP than CRRP.

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Abstract Number: 1301

The Relationship Between Socioeconomic Factors and Persistent Active Rheumatoid Arthritis: Results from (NEIAA) a Large UK Cohort of Early Inflammatory Arthritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Psychosocial factors may interplay with biological factors to drive a refractory disease state in patients with inflammatory arthritis1. We aim to explore which socioeconomic, and disease related factors associated with persistent active rheumatoid arthritis (PactiveRA) in the first year, despite use of conventional synthetic DMARDs.

Methods: NEIAA is an observational cohort of adult patients with early RA patients in England and Wales. Data from May 2018 until Oct 2022 were acquired. All patients fulfilled the ACR/EULAR 2010 criteria for RA. Patients were defined as having PactiveRA based on three consecutive Disease Activity Scores (DAS28) of >3.2 at baseline, three and 12 months of follow up. Controlled RA (contRA) was defined as patients started with high DAS28 >3.2 at baseline then entered remission (DAS28 ≤ 3.2 at the three and 12 month time-points). PactiveRA status was used as the primary outcome variable.

Table. The association between PactiveRA with socioeconomic, clinical and treatment variables

Independent predictors at baseline	Univariable analysis OR (95% CI)	Multivariable analysis OR (95% CI)
Age (years)	0.99 (0.98,0.99)	0.99 (0.98,0.99)
Female gender	1.37 (1.15,1.63)	1.38 (1.16,1.64)
IMD (less social deprivation)	0.91 (0.88,0.94)	0.92 (0.89,0.95)
Ever smoked (referent never-smoked)	1.21 (1.02,1.43)	1.22 (1.02,1.47)
Depression	2.30 (1.67,3.17)	2.15 (1.54,3.01)
Lung disease	1.46 (1.14,1.86)	1.44 (1.12,1.85)
Stomach ulcer	1.71 (1.17,2.50)	1.72 (1.17,2.52)
CCP and RA seropositivity	0.80 (0.67,0.94)	0.69 (0.58,0.83)
Corticosteroids	1.52 (1.18,1.96)	1.50 (1.16,1.94)

Persistent active (pactiveRA) defined as DAS28 >3.2 at baseline, 3 and 12 moths of follow-up. CCP: cyclic citrullinated peptide; IMD: index of multiple deprivation; RF: rheumatoid factor. (p<0.05 for all predictors).

Univariable, followed by multivariable analyses stepwise forward logistic regression to explore associations with PactiveRA. Age and gender were included in the models as a priori, with socioeconomic variables handled as the main independent variables (social deprivation, smoking-status and comorbidities) of interest, followed by disease related factors.

Results: A total of 15,626 patients had a diagnosis of RA in NEIAA. Of which, 682 patients with pactiveRA and 1,026 patients with contRA were analysed. Compared to contRA, patients with PactiveRA were younger (aged 58, interquartile range (IQR): 49, 67) vs (62, IQR: 52,72), included more females 471 (69%) vs 607 (59%), were current or ex-smokers, and more likely to have depression, lung and gastrointestinal disease.

Also, patients with PactiveRA had worse scores in Patient Reported Outcomes at baseline and Patient Health Questionnaire Anxiety and Depression Screener. Logistic regression results are summarised in the table. Age, gender, living in a socially deprived area and being an ex or current smoker, were associated with PactiveRA in models controlling for markers of disease severity (seropositivity). Baseline corticosteroid use was also associated with PactiveRA ($p< 0.05$ for all) and having a concomitant diagnosis of depression, odds ratio (OR) 2.30 (95%CI: 1.67,3.17), lung disease OR 1.46 (95%CI: 1.14,1.86) and gastric ulcer OR 1.71 (95%CI: 1.17,2.50) were significantly related to PactiveRA**.**

Conclusion: Sociodemographic factors and living in socially deprived areas were all associated with PactiveRA, independent of clinical and disease characteristics. Identifying 'adverse' socioeconomic factors that could drive persistent active disease early in the disease process, can help better guide interventions that would be suitable for individual patients and their respective needs.

Disclosure: M. Adas: None; **S. Norton**: Janssen, 6, Pfizer, 6; **A. Cope**: Bristol-Myers Squibb(BMS), 2, 5, 6; **M. Buch**: AbbVie, 2, 6, 12, All paid to host institution, Boehringer Ingelheim, 2, 6, 12, Paid to host institution, Galapagos, 2, 6, 12, Paid to host institution, Gilead, 2, 5, 6, 12, Paid to host institution, Lilly, 2, 6, 12, All paid to host institution, National Insitute for Health and Care Research (NIHR), 3, 12, Maya H Buch is a National Institute for Health and Care Research (NIHR) Senior Investigator. The views expressed are those of the authors and not nece, Pfizer, 2, 12, Paid to host institution; **J. Galloway**: AbbVie, 2, 5, 6, AstraZeneca, 5, Biogen, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **E. Nikiphorou**: AbbVie/Abbott, 6, Celltrion, 6, Eli Lilly, 6, fresenius, 6, Galapagos, 6, Gilead, 1, 6, Pfizer, 6, Sanofi, 6.

Abstract Number: 1302

Biomarkers of Cardiovascular Risk in Patients with Rheumatoid Arthritis: Results from the TARGET Trial Biomarker Study

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular (CV) disease remains an important source of morbidity and the most common cause of mortality in patients with rheumatoid arthritis (RA). It has been well recognized that traditional risk models for CV events do not perform well in RA patients. Prior attempts to improve risk prediction have not explored a wide range of

Table 1: Linear Regression Results Assessing Relationship Between Each Candidate Biomarker at Baseline and Change in Target to Background Ratio in the TARGET Trial Cohort, with Increasing Adjustment

	All biomarkers only	Baseline PCE only	Biomarkers + PCE
Cytokine/Inflammation	**Beta estimate (95% CI)**		
IL-6	0.03 (-0.10, 0.16)	...	0.03 (-0.10, 0.17)
sTNF-R1	-0.10 (-0.22, 0.02)	...	-0.12 (-0.24, 0.01)
SAA	**-0.18 (-0.35, -0.02)**	...	**-0.18 (-0.35, -0.01)**
CRP	**0.19 (0.01, 0.38)**	...	**0.19 (0.00, 0.38)**
CD-40 ligand	-0.07 (-0.19, 0.05)	...	-0.06 (-0.19, 0.08)
Adipokines			
Adiponectin	**-0.11 (-0.20, -0.01)**	...	**-0.12 (-0.22, -0.01)**
Leptin	-0.04 (-0.14, 0.07)	...	-0.03 (-0.15, 0.08)
Resistin	0.07 (-0.03, 0.17)	...	0.08 (-0.03, 0.19)
Atherothrombosis			
Antithrombin III	0.04 (-0.07, 0.15)	...	0.05 (-0.07, 0.17)
PAI 1	-0.05 (-0.17, 0.06)	...	-0.05 (-0.18, 0.07)
Lipids Parameters			
Apolipoprotein A1	0.06 (-0.05, 0.17)	...	0.06 (-0.06, 0.17)
Apolipoprotein A2	0.02 (-0.13, 0.17)	...	0.02 (-0.14, 0.17)
Apolipoprotein B	0.02 (-0.10, 0.13)	...	0.01 (-0.12, 0.13)
Lp (a)	0.04 (-0.06, 0.13)	...	0.04 (-0.06, 0.13)
LDL	-0.03 (-0.14, 0.07)	...	-0.04 (-0.15, 0.07)
Other Analytes			
Cardiac troponins	-0.12 (-0.33, 0.09)	...	-0.12 (-0.35, 0.10)
nt-pro-BNP	0.03 (-0.08, 0.13)	...	0.03 (-0.09, 0.15)
VCAM-1	0.04 (-0.08, 0.16)	...	0.04 (-0.08, 0.17)
VEGF-A	-0.01 (-0.12, 0.09)	...	-0.01 (-0.12, 0.10)
MMP-1	-0.04 (-0.14, 0.06)	...	-0.04 (-0.15, 0.06)
MMP-3	0.08 (-0.04, 0.20)	...	0.08 (-0.05, 0.20)
YKL-40	**0.15 (0.05, 0.25)**	...	**0.15 (0.04, 0.25)**
Cystatin-C	-0.02 (-0.12, 0.08)	...	-0.03 (-0.14, 0.08)
Osteopontin (OPN)	-0.03 (-0.13, 0.07)	...	-0.02 (-0.13, 0.09)
Osteoprotegrin (OPG)	**-0.10 (-0.19, 0.00)**	...	-0.10 (-0.19, 0.10)
Pooled cohort equation	...	0.00 (-0.02, 0.01)	0.00 (-0.02, 0.02)
Model Fit Statistics			
R^2	0.53	0.21	0.52
Adjusted R^2	0.35	0.20	0.33
Root Mean Square Error	0.348	0.450	0.351

NOTES: All models include the baseline target to background ratios values from the most diseased segment (MDS TBR). PCE, Pooled Cohort Equation, includes age, sex, race, diabetes status, cigarette use, systolic blood pressure, treatment for hypertension, and high-density lipoprotein value. R^2 indicates better model fit when larger and Root Mean Square Error is better when smaller.

candidate biomarkers shown in prior literature to be associated with both RA and CV disease. These analyses tested a wide range of candidate biomarkers against CV risk assessed by arterial inflammation using a FDG PET/CT scan at baseline and 24 weeks.

Methods: These analyses leveraged data from TARGET trial (NCT02374021). Subjects had RA and were inadequate responders to methotrexate (MTX); they were then randomized to add a TNF inhibitor or triple therapy (MTX + sulfasalazine + hydroxychloroquine). Both treatment strategies demonstrated significant suppression of arterial inflammation, measured as the change in target to background ratio in the most diseased segment (MDS TBR) on the FDG PET/CT. However, we observed no significant differences in change in arterial inflammation between the arms. In this analysis, both arms were combined into a single cohort and candidate biomarkers (see **Table 1**) were tested at baseline and 24 weeks. First, progressively adjusted models tested baseline candidate biomarker values (per standard deviation) as predictors of change in MDS TBR between baseline and 24 weeks. Second, change (also 0 to 24 weeks) in candidate biomarker values (per standard deviation) were tested against change in MDS TBR. Models with only biomarkers, only traditional CV risk factors (Pooled Cohort Equation), and both were tested.

Table 2: Linear Regression Results Assessing Relationship Between Change in Each Candidate Biomarker from Baseline and Change in Target to Background Ratio in the TARGET Trial Cohort, with Increasing Adjustment

	Change in biomarkers only	Baseline PCE only	Change in biomarkers + PCE
Cytokine/Inflammation	**Beta estimate (95% CI)**		
IL-6	-0.19 (-0.58, 0.21)	…	-0.20 (-0.61, 0.21)
sTNF-R1	0.13 (-0.07, 0.33)	…	0.13 (-0.08, 0.34)
SAA	0.26 (-0.19, 0.70)	…	0.25 (-0.22, 0.72)
CRP	0.09 (-0.31, 0.48)	…	0.09 (-0.32, 0.51)
CD-40 ligand	0.06 (-0.16, 0.27)	…	0.06 (-0.16, 0.29)
Adipokines			
Adiponectin	-0.07 (-0.22, 0.08)	…	-0.07 (-0.23, 0.09)
Leptin	-0.00 (-0.14, 0.14)	…	-0.00 (-0.15, 0.15)
Resistin	0.1 (-0.15, 0.17)	…	0.1 (-0.16, 0.18)
Atherothrombosis			
Antithrombin III	0.02 (-0.11, 0.14)	…	0.02 (-0.11, 0.15)
PAI 1	0.01 (-0.21, 0.23)	…	0.01 (-0.24, 0.24)
Lipids Parameters			
Apolipoprotein A1	**-0.14 (-0.28, -0.01)**	…	**-0.14 (-0.28, 0.00)**
Apolipoprotein A2	0.00 (-0.16, 0.16)	…	0.01 (-0.16, 0.18)
Apolipoprotein B	-0.01 (-0.14, 0.12)	…	-0.01 (-0.15, 0.14)
Lp (a)	0.02 (-0.12, 0.16)	…	0.02 (-0.13, 0.17)
LDL	0.12 (-0.02, 0.26)	…	0.12 (-0.03, 0.27)
Other Analytes			
nt-pro-BNP	-0.01 (-0.16, 0.14)	…	-0.01 (-0.16, 0.15)
VCAM-1	-0.04 (-0.20, 0.13)	…	-0.03 (-0.21, 0.14)
VEGF-A	0.02 (-0.15, 0.20)	…	0.03 (-0.16, 0.22)
MMP-1	**-0.16 (-0.30, -0.02)**	…	**-0.16 (-0.30, -0.02)**
MMP-3	0.00 (-0.20, 0.21)	…	0.01 (-0.21, 0.23)
YKL-40	0.01 (-0.19, 0.22)	…	0.02 (-0.20, 0.25)
Cystatin-C	-0.02 (-0.17, 0.13)	…	-0.01 (-0.17, 0.15)
Osteopontin (OPN)	0.01 (-0.16, 0.18)	…	0.01 (-0.18, 0.19)
Osteoprotegrin (OPG)	0.03 (-0.11, 0.17)	…	0.02 (-0.13, 0.18)
Pooled cohort equation	…	0.00 (-0.2, 0.01)	0.00 (-0.02, 0.02)
Model Fit Statistics			
R^2	0.64	0.21	0.63
Adjusted R^2	0.23	0.20	0.19
Root mean squared error	0.306	0.450	0.309

NOTES: All models include the baseline target to background ratios values from the most diseased segment (MDS TBR) and the baseline biomarker values. PCE, Pooled Cohort Equation, includes age, sex, race, diabetes status, cigarette use, systolic blood pressure, treatment for hypertension, and high-density lipoprotein value. R^2 indicates better model fit when larger and Root Mean Square Error is better when smaller.

Results: 115 patients had both biomarker data and FDG PET/CT data at baseline and 24 weeks. The patients in TARGET were similar to typical RA patients: 58-year median age; 71% women; 16 months median duration RA; and baseline DAS28 4.8. From the candidate biomarkers tested, we found significant adjusted associations between baseline values of SAA (b = -0.18, 95% CI -0.35, -0.01), CRP (b = 0.19, 95% CI 0.00, 0.38), and YKL-40 (b = 0.14, 95% CI 0.04, 0.25) (see **Table 1**) and change in arterial inflammation. We found significant adjusted associations between change from baseline to 24 weeks and change in MDS TBR for the following biomarkers (see **Table 2**): serum apolipoprotein A1 (b = -0.14, 95% CI -0.28, -0.01) and MMP-1 (b = 0.16, 95% CI -0.30, -0.02)**.** Model fit (R^2 and Root Mean Square Error, RMSE) was substantially improved when biomarkers were added to traditional CV risk factors.

Conclusion: A broad candidate biomarker scan among patients with RA demonstrated statistically and potentially clinically significant associations with change in arterial inflammation on FDG PET/CT. These biomarkers will be further tested in a large clinical RA cohort with confirmed CV events.

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Abstract Number: 1303

Patient's and Physician's Evaluation of Global Assessment of Disease Activity over Follow up and Across Disease Activity Levels in Recent-Onset Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Composite measures (e.g. SDAI) to assess Rheumatoid Arthritis (RA) disease activity incorporate patient (PGA) and evaluator (EGA) global assessments. EGA and PGA are often discordant, reflecting divergent perspectives on evaluation of disease impact and potentially towards therapeutic goals. We evaluated the stability of PGA minus EGA (PGA-EGA) concordance or discordance from baseline to up to 5 years, and across all levels of disease activity in 822 patients (≥ 90% confirmed RA) from the prospective longitudinal Early Undifferentiated PolyArthritis (EUPA) cohort.

Table. Characteristics of patients according to Baseline PGA-EGA discordance (n=822)

Baseline characteristics	< -1 (n=205)	[-1 to 1] (n=224)	]1 to 3] (n=213)	> 3 (n=180)	p-value
Age (years)	64.7 (54.9-74)	62.8 (53-70.2)	58.6 (47.8-68.3)	59.8 (49.8-70.8)	**0.0027**
Women	108 (52.7)	134 (59.8)	134 (62.9)	118 (65.6)	0.0539
Body mass index (kg/m2)	25.8 (23.4-29.1)	26.6 (23.3-30.3)	27 (23.3-31)	26.6 (23.6-29.9)	0.3876
Scolarity (years)	12 (9-14)	12 (9-14)	12 (9-14)	11 (9-15)	0.8392
Tobacco					
Current smoker	36 (18.1)	31 (14.4)	44 (21)	26 (15)	0.3357
Ex-smoker	91 (45.7)	104 (48.1)	81 (38.6)	84 (48.6)	
Non-smoker	72 (36.2)	81 (37.5)	85 (40.5)	63 (36.4)	
Symptom duration, months	4 (2.4-6.1)	3.7 (2-6.1)	3.4 (1.9-6.8)	3.1 (1.8-5.4)	0.1322
M-HAQ ≥ 1	62 (31.3)	92 (41.3)	105 (50.2)	82 (46.3)	**0.0009**
66-Swollen joint count	14 (9-22)	12 (7-19)	10 (6-16)	8 (5-13)	**<.0001**
68-Tender joint count	15 (7.5-24)	12 (6-22)	12 (6-18)	8 (5-15)	**<.0001**
PGA	2.8 (1.4-4.8)	4.3 (2.9-6.8)	6.4 (5-8.3)	8 (6.8-9.5)	**<.0001**
EGA	6.2 (4.5-7.7)	4.4 (2.7-6.8)	4.3 (2.9-6.3)	3.1 (2.3-4.2)	**<.0001**
Anti-CCP2 positive	76 (37.1)	81 (36.5)	72 (34)	51 (28.7)	0.2954
Rheumatoid factor positive	80 (39.2)	90 (40.4)	76 (35.7)	62 (34.4)	0.5623
ESR, mm/h	28 (16-45.5)	26 (15-45.5)	26 (16-44.5)	30 (15-46)	0.9330
CRP, mg/L	11.3 (4.6-29)	10.9 (4-29.5)	12.4 (4.5-28.8)	9 (3.3-27.2)	0.3623
DAS28-CRP	5.1 (4-6.1)	5 (3.9-6.1)	5 (4.2-6.1)	5 (4.3-5.9)	0.7755
SDAI	33.3 (23-49.3)	29.5 (17.1-45.5)	29.1 (19.6-43.5)	26.2 (19.6-38.6)	**0.0017**
CDAI	32.3 (21.8-45.3)	28 (15.8-43.4)	27.7 (17.8-39.1)	25.2 (17.5-35)	**0.0015**
Sharp score Erosions ≥ 5	36 (18.7)	30 (14.2)	32 (16)	18 (10.8)	0.2015
Sharp score Narrowing ≥ 5	47 (24.4)	47 (22.2)	40 (20)	31 (18.6)	0.5502
Sharp score Total ≥ 5	80 (41.5)	77 (36.3)	62 (31)	54 (32.3)	0.1357
Pain (0-100 mm)	32.5 (17-52)	48 (29-72)	61 (46-79)	74 (60-89)	**<.0001**
Fatigue (0-100 mm)	38 (10-59)	46 (27-72)	61 (43-80)	68 (48-86)	**<.0001**
Sleep disturbance (0-10 cm)	4.5 (2-7)	5 (2-8)	6 (3-8)	7 (5-9)	**<.0001**
CES-D score	15 (8-23)	15 (10-24)	18 (11-24)	18 (13-30)	**0.0033**

Variables were presented with median (IQR: Interquartile range) or with frequencies n (%). CES-D: Center for Evaluation Studies - Depression

Methods: Demographics, clinical and serological variables, radiographic damage (Sharp van der Heijde scores), treatments, comorbidities, and Patient-Reported Outcomes (pain, function, depression, sleep quality) were collected at baseline (median symptom duration 3.7 months) and at 12, 18, 30, 42 and 60 months from symptom onset. PGA and EGA were reported using a 0-10 cm visual analog scale (VAS). PGA-EGA discordance was divided in four subgroups: **negative** discordance group (< -1 cm), **concordance** group (≥-1cm and ≤+1 cm), positive **discordance group I** (>1 cm and ≤3 cm) and **group II** (>3 cm).

Results: At baseline, concordance was present in 27.3%, negative discordance in 24.9% while 47.8% expressed positive discordance (25.9 % group I and 21.9% group II). Over 60 months, concordance increased to 45.7%, negative discordance decreased to 7.7%, while positive discordant groups remained stable (still 46.4 % at 5 years). In positive discordant groups at baseline, patients were younger (median 58.6 years group I and 59.8 years group II, $p < 0.003$), had higher functional impact (M-HAQ ≥1, 46.3 % to 50.2 % $p < 0.001$), fewer tender and swollen joints ($p < 0.0001$), but rated higher for pain, fatigue, sleep disturbances ($p < 0.0001$) and depression (CES-D, median score 18 for both groups, $p < 0.005$). Only 20% (117/583) remained in the same subgroups between 18 and 60 months. The majority of those who remained stable were patients with concordance (79/117) and with positive discordance group II (25/117). Concordance was most frequent in remission, negative discordance in high disease activity, while group I positive discordance appeared independent of disease activity. Group II positive discordance was highest (35-38%) with low or moderate disease activity.

Conclusion: In this study of patients with early arthritis, almost half evaluated their global disease activity worse than the evaluator (positive discordance) and this proportion remained stable over the first 60 months of disease. Patients in positive discordant group were younger and reported higher functional impact, pain, fatigue, poor sleep and more symptoms of

Figure 1. Evolution of discordance and concordance over time

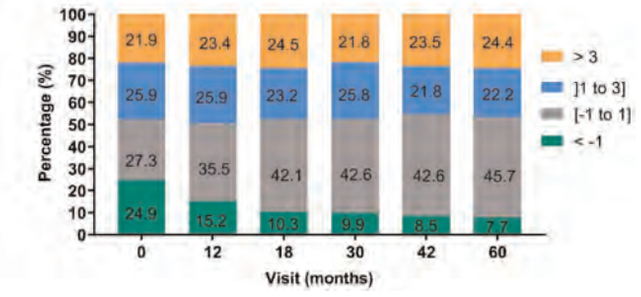
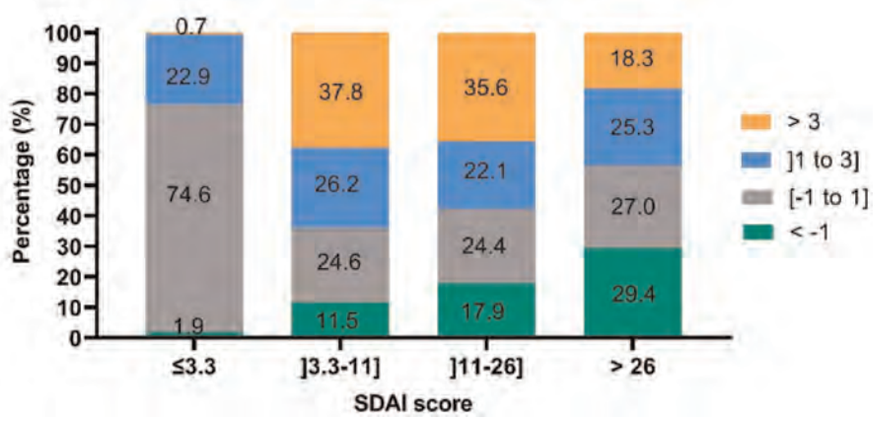


Figure 2. Distribution of concordance/discordance according to SDAI



depression but had lower tender and swollen joint counts. Concordance was best when the patients were in SDAI remission. Negative discordance increased with disease activity. Over time, the relative proportions of each group remained similar, but only a small number of individual patients remained in the same group, most frequently in the concordance group but also among those who invariably rated their disease markedly more active than their physicians (group II), a subgroup important to identify early on to improve their management.

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Abstract Number: 1304

Window of Opportunity to Achieve Better Functional Outcomes in Patients with RA: Effectiveness of an Early Treatment Strategy

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: RA is a chronic disease that can lead to irreversible damage and functional decline with delayed or inadequate treatment.[1] Abatacept + MTX is effective for many patients (pts) with RA[2,3] and may better preserve functional status when introduced early in the disease course[4]. The HAQ-disability index (DI) is a pt-reported outcome delineating physical function impacted by RA.[3,5] This study assessed the relationship between baseline (BL) disease duration after initiating abatacept + MTX and improved physical function using HAQ-DI scores in RA over 8 yrs.

Methods: This pooled analysis included data from 15 randomized controlled trials (RCTs) in pts with RA (ACR/EULAR 2010 criteria[6]) treated with abatacept + MTX. Included pts had data available on BL disease duration, HAQ-DI scores (0–3 scale), and demographic characteristics. Trends in mean HAQ-DI and mean change in HAQ-DI from BL over time were modelled using mixed-effect linear regression models, fitted to BL disease duration and the log of treatment duration as fixed effects and subject identities as random effects. Analyses were repeated in subgroups categorized by age, sex, race, and BMI.

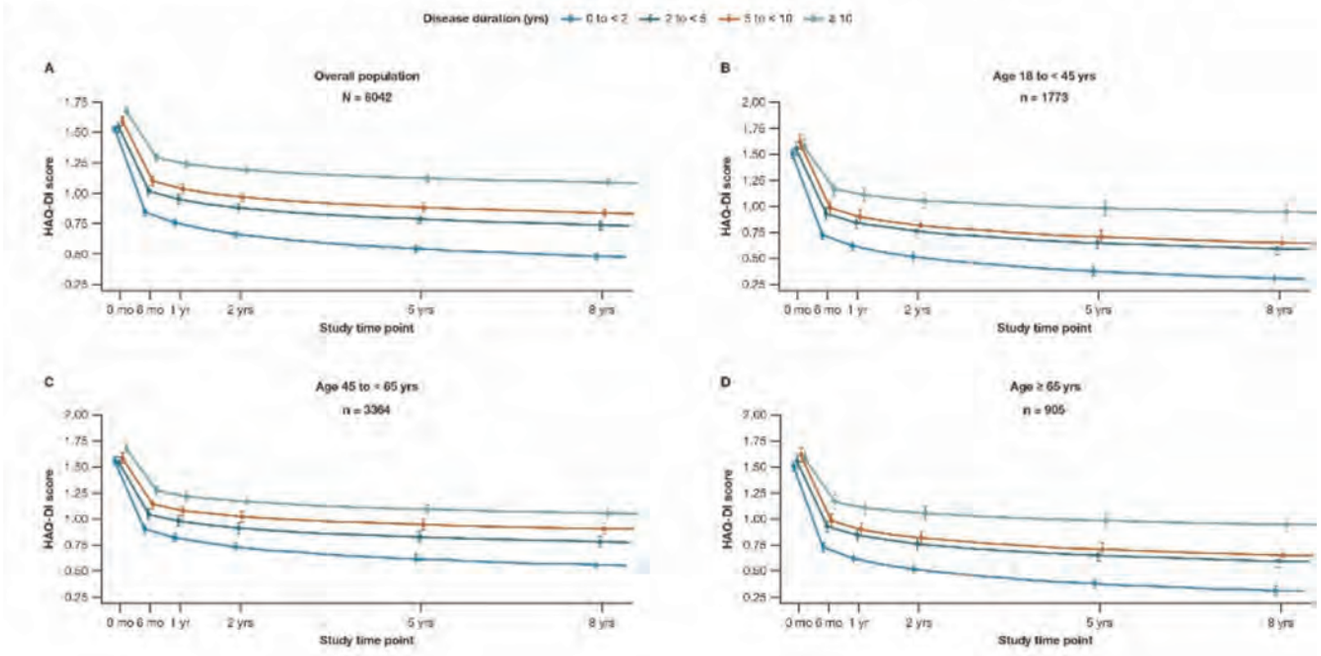
Results: Of the 6042 pts included, most had a disease duration < 2 yrs (34.5%), a normal BMI of 18.5 to < 25 kg/m^2 (29.6%), were of female sex (80.3%) and White (82.1%) (mean age: 51.2 yrs; **Table 1**). In the overall population, HAQ-DI decreases were associated with shorter disease duration (**Fig 1A**): the magnitude of changes in HAQ-DI scores decreased as disease duration increased at all time points (**Fig 2A**). A similar trend was observed for subgroups categorized by age (**Figs 1B–D, 2B–D**), sex, race, and BMI (data not shown). BL HAQ-DI scores for all disease duration categories were higher among females (95% CI: 1.6–1.7 vs 1.3–1.5 in males), and the trend in HAQ-DI reductions was more gradual in male versus female pts (data not shown). In the overall population and subgroups categorized by age, the greatest reduction in HAQ-DI

Table 1. BL demographic and disease characteristics of the pooled study population[a]

Characteristics	Overall population (N = 6042)
Disease duration, yrs, n (%)	
< 2	2083 (34.5)
2 to < 5	1109 (18.4)
5 to < 10	1143 (18.9)
≥ 10	1707 (28.3)
Age, yrs, mean (95% CI)	51.2 (50.9–51.5)
Sex, n (%)	
Male	1191 (19.7)
Female	4851 (80.3)
Race, n (%)	
White	4960 (82.1)
Black/African American	282 (4.7)
Asian/Native Hawaiian/Other Pacific Islanders	394 (6.5)
Others	401 (6.6)
BMI, kg/m², n (%)	
< 18.5 (underweight)	129 (2.1)
18.5 to < 25 (normal)	1788 (29.6)
25 to < 30 (overweight)	1740 (28.8)
≥ 30 (obese)	1613 (26.7)

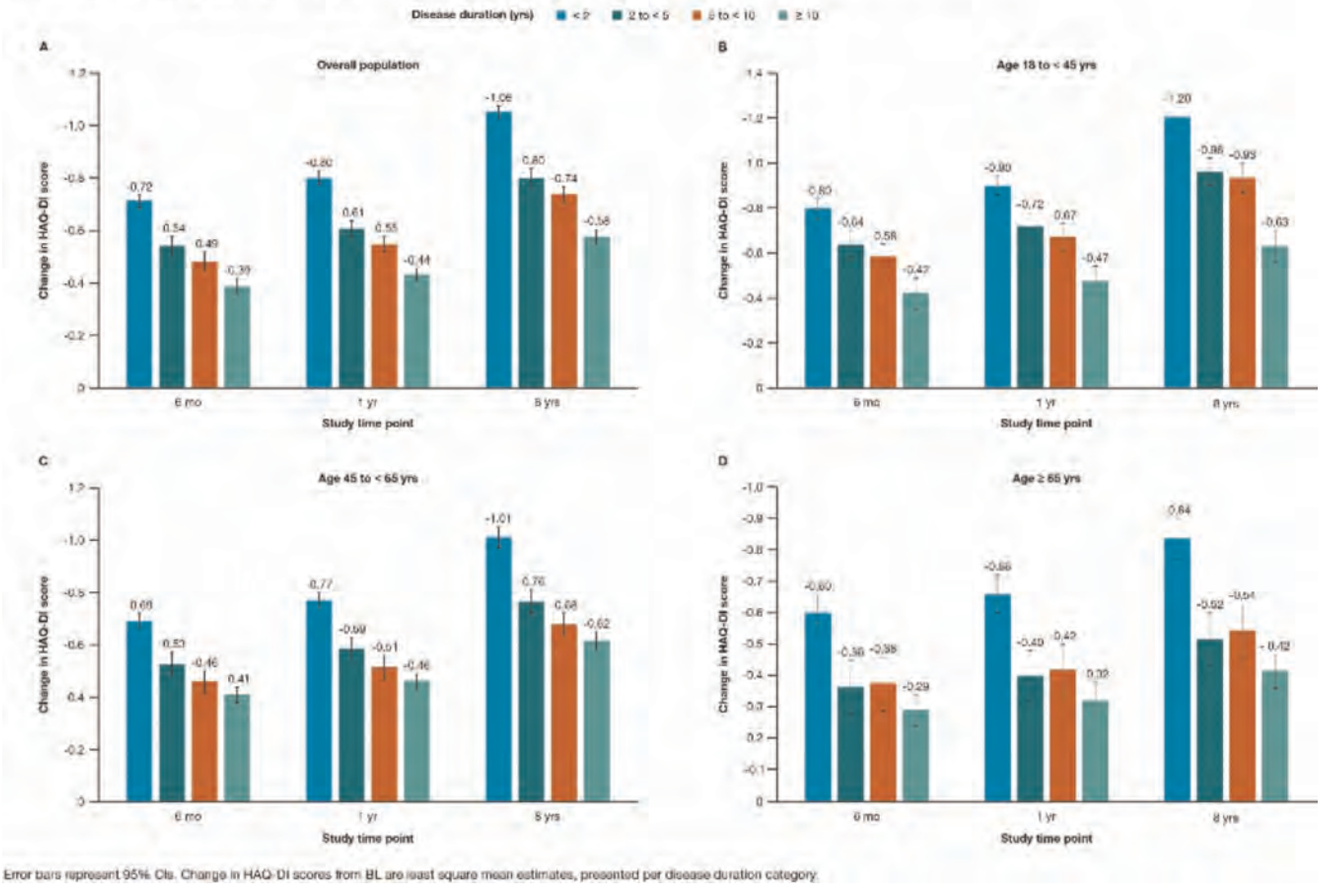
[a]Pooled data from 15 randomized controlled trials: IM101-023, IM101-029, IM101-031, IM101-043, IM101-064, IM101-100, IM101-101, IM101-102, IM101-167, IM101-173, IM101-174, IM101-226, IM101-235, IM101-550, and IM101-567.

Fig 1. Estimated mean HAQ-DI scores from BL to yr 8 by BL disease duration for (A) the overall population and population grouped by age: (B) 18 to < 45 yrs, (C) 45 to < 65 yrs, and (D) ≥ 65 yrs



Error bars represent 95% CIs. Study time points are approximated using 30-day mos and 365-day yrs. For identical time points, x-axis offset was applied to improve visibility and avoid overlap of the curves. HAQ-DI scores are least square mean estimates.

Fig 2. Change in HAQ-DI scores from BL to yr 8 for (A) the overall population and population grouped by age: (B) 18 to < 45 yrs, (C) 45 to < 65 yrs, and (D) ≥ 65 yrs



Error bars represent 95% CIs. Change in HAQ-DI scores from BL are least square mean estimates, presented per disease duration category.

scores occurred between BL and 6 mo, followed by gradual reductions until 8 yrs (**Figs 1, 2**). Differences between disease duration categories were notable from 6 mo and increased with follow-up time (**Figs 1, 2**). The largest reductions in HAQ-DI scores were reported by pts with RA disease duration < 2 yrs and the smallest reductions, by those with RA disease duration ≥ 10 yrs (**Fig 2A**).

Conclusion: Pts with RA receiving earlier abatacept treatment (within 2 yrs of diagnosis) reported greater improvements in and better maintenance of physical function over time. In all groups analyzed, pts with the shortest disease duration at BL who received abatacept + MTX had the best outcomes. Among currently available RA treatments, abatacept + MTX notably improves physical function in pts with early RA. Our findings support the need for prospective RCTs to evaluate abatacept + MTX as an early-line treatment for RA.

References

1. Quinn MA, et al. *Rheumatology(Oxford)* 2001;40:1211–20.
2. Westhovens R, et al. *Clin Exp Rheumatol* 2014;32:553–62.
3. Cagnotto G, et al. *Arthritis Res Ther* 2020;22:15.
4. Aletaha D, et al. *Ann Rheum Dis* 2008;67:238–43.
5. Pope JE, et al. *J Rheumatol* 2009;36:254–9.
6. Aletaha D, et al. *Arthritis Rheum* 2010;62:2569–81.

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Abstract Number: 1305

Variations in Macrophage Cholesterol Loading over Time Are Linked to Dynamic Changes in Coronary Atherosclerotic Plaque in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

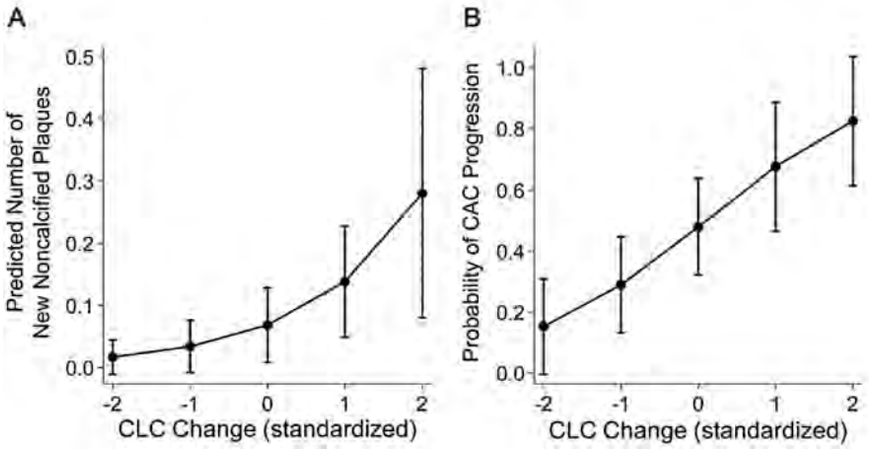
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: The ability of serum to deliver cholesterol to cells is known as cholesterol loading capacity (CLC) and associates with foam cell formation. In rheumatoid arthritis (RA), CLC was linked to long-term cardiovascular risk as well as coronary atherosclerosis burden and vulnerable plaque composition, particularly in biologic nonusers[1]. The relationship between changes in CLC over time and plaque progression is unknown.

Figure 1 Noncalcified plaque increase **(A)** and probability of CAC progression (B) per standard deviation increase in CLC change from baseline to follow-up



Methods: Atherosclerosis (noncalcified, partially or fully calcified plaques and coronary artery calcium [CAC] score) was evaluated with coronary computed tomography angiography in 140 patients without cardiovascular disease and reassessed in 100 after 6.9±0.4 years. Presence of 5 or more plaques in a patient and lesions rendering greater than 50% luminal stenosis were considered extensive and obstructive disease respectively. CLC was measured as intracellular cholesterol content in serum treated human THP-1 monocyte-derived macrophages with a fluorimetric assay during baseline and follow-up atherosclerosis assessments. Multivariable negative binomial and robust linear regression tested the associations between changes in CLC from baseline to follow-up and coronary plaque and CAC progression and new extensive or obstructive disease respectively.

Results: CLC decreased in 68% and increased in 32% of patients at follow-up. All subjects (34/34) at the highest tertile of baseline CLC showed decrease at follow-up whereas 25/33 (75.8%) of patients at the lowest CLC tertile showed increase ($p< 0.0001$). CLC change (per standard deviation) associated with noncalcified plaque increase after adjusting for atherosclerotic cardiovascular disease (ASCVD) score, baseline plaque burden, obesity and duration of prednisone exposure throughout follow-up (incident rate ratio [IRR] 2.03, 95% confidence interval [95%CI] 1.27-3.24, p=0.003); risk of CAC increase after adjustments for ASCVD, baseline CAC, time-averaged c-reactive protein (TA-CRP), weighted daily-average atorvastatin equivalent dose and obesity (odds ratio [OR] 2.26, 95%CI 1.25-3.24, p=0.007) and risk of new extensive or obstructive disease at follow-up after adjusting for ASCVD, baseline plaque and TA-CRP (OR 3.17, 95%CI 1.01-9.94, p=0.048). Incrementally higher CLC at follow-up compared to baseline associated with progressively more new noncalcified plaques, greater risk of CAC increase and new extensive or obstructive disease. In contrast, greater decreases in follow-up CLC associated with significantly fewer new noncalcified plaques (Figure 1A), gradually lower risk of CAC increase (Figure 1B) and new extensive or obstructive disease.

Conclusion: Increasing CLC and therefore rising cholesterol content in arterial wall macrophages over time associates with coronary atherosclerosis progression in a dose-dependent manner, and particularly higher burden of lipid rich noncalcified plaques and extensive or obstructive disease conveying the greatest cardiovascular risk.

[1]Karpouzas GA et al. RMD Open 2022;8:e002411

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Abstract Number: 1306

Statin Use Attenuates the Impact of Systemic Inflammation on Ischemic Cardiovascular Risk in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Baseline and cumulative inflammation have both been associated with increased cardiovascular event (CVE) risk in patients with rheumatoid arthritis (RA). Statin therapy reduced systemic inflammation, attenuated coronary atherosclerosis progression and promoted plaque calcification and stabilization[1] both in general as well as RA patients. We here explored whether baseline statin use influenced the impact of baseline C-reactive protein (CRP) on long-term cardiovascular risk in patients with RA.

Methods: We evaluated 4,357 patients without known cardiovascular disease upon registration to *A*n Int*e*rnationa*l C*ardiovascular *C*onsortium for people with *RA* (ATACC-RA) and who were followed prospectively. The primary outcome was ischemic CVE defined as the composite endpoint of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, coronary revascularization, stable angina pectoris, transient ischemic attack, and peripheral arterial disease with or without revascularization. Missing data were imputed using multiple imputation with 10 repetitions. Multivariable Cox models stratified by center evaluated the effect of natural logarithm of CRP, statin use and their interaction on CVE risk after adjusting for age, gender, hypertension, diabetes, family history, smoking, age at RA diagnosis, and total cholesterol to high-density lipoprotein (TC/HDL)ratio. A sensitivity analysis was performed using inverse probability of treatment weights to balance differences between statin treated and untreated patients.

Results: At baseline 462 patients were treated with statins whereas 3,895 were not. Statin therapy inversely associated with low density lipoprotein cholesterol (p< 0.001), TC/HDL ratio (p< 0.001) and CRP(ln) (p=0.048). Over 26,356 patient years (PY) of follow-up, 361 total ischemic CVE were recorded, 321 over 24,235 PY in statin nonusers and 40 over 2,121 PY in statin users. Incidence of any ischemic CVE was 13.3 (95% CI 11.9-14.8)/1000PY among statin nonusers and 18.9 (95% CI 13.8-25.7)/1000PY in statin users (incidence rate difference 5.62 [95% CI -0.41 to 11.64]). In the entire cohort, baseline CRP(ln) was not associated with ischemic CVE risk, [adjusted hazards ratio- aHR 1.07 (95% CI 0.98-1.17), p=0.138]. However, higher CRP(ln) associated with greater risk of the composite outcome exclusively in statin nonusers [aHR 1.10 (95% CI

Figure 1 Cardiovascular event risk in main (unweighted) and sensitivity analyses (inverse probability-IP weighted) with increasing CRP

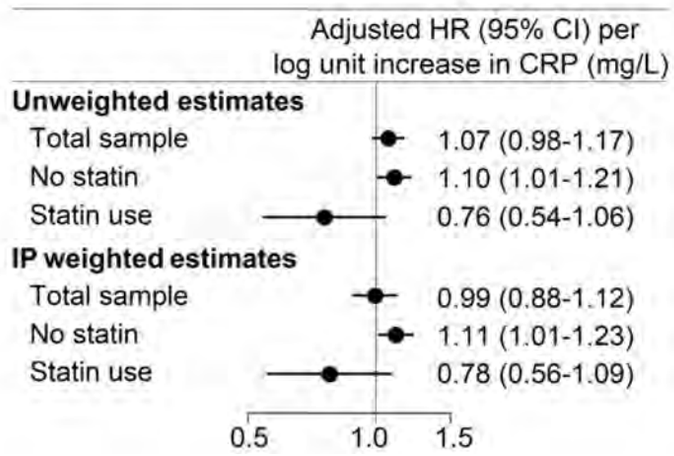
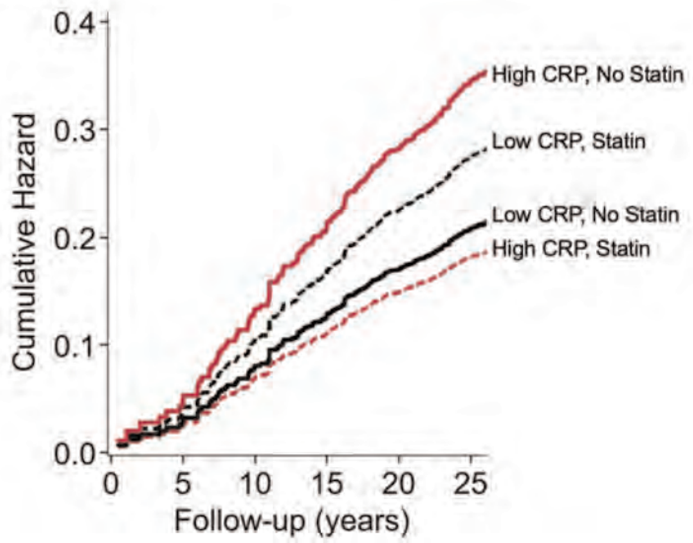


Figure 2 Cumulative probability of ischemic cardiovascular event in statin users and nonusers at high (+1-SD) and low (-1-SD) baseline CRP



1.01-1.21), p=0.036] but not in statin users (p-interaction=0.032, Figures 1 and 2). While CRP(ln) was not different between statin groups after inverse probability weighting adjustment (p=0.333), the sensitivity analysis yielded similar results: higher CRP(ln) associated with greater ischemic CVE risk in statin nonusers [aHR 1.11 (95% CI 1.01-1.22), p=0.030] but not among statin users (p-interaction=0.046).

Conclusion: Higher inflammation at baseline associated with greater risk of any ischemic CVE among statin nonusers but not in users. This points to the potential of statin-specific effects directly on atherosclerotic plaque—such as lower progression and stabilization[1]—above and beyond effects on cholesterol metabolism and systemic inflammation.

Reference: Karpouzas GA et al. Rheumatology (Oxford) 2022;61(5):1857-1866

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Abstract Number: 1307

Impact of Comorbidities on the First bDMARD Effectiveness and Retention Rate After 2 Years of Follow-up in Patients with Rheumatoid Arthritis. Data from the Spanish Registry BIOBADASER

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster II

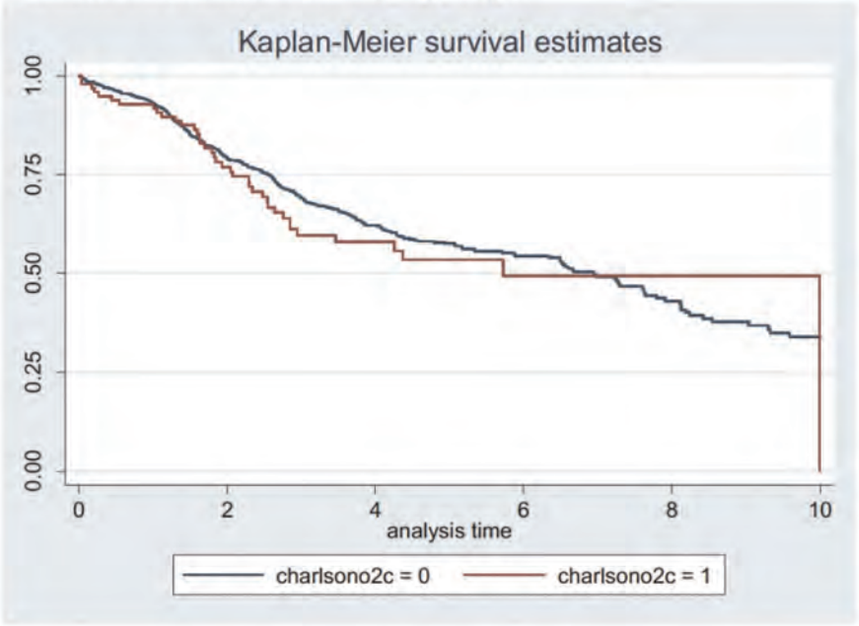
Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with Rheumatoid Arthritis (RA) have a higher prevalence of comorbidities, compared to the general population. The presence of such comorbidities has been directly associated with an increased disease activity. However, little is known about the impact of comorbidities in the therapeutic response and in the retention rate. *Objectives:* a) To evaluate the effect of comorbidities on the first biologic disease-modifying antirheumatic drug (bDMARD) effectiveness in patients with RA after 2 years of follow-up, and b) to determine the influence of such comorbidities on the first bDMARD retention rate.

Methods: The study population consisted of patients with a diagnosis of RA and exposed to a first bDMARDs, included in BIOBADASER. BIOBADASER is a prospective, large national drug safety registry of patients with rheumatic diseases exposed to b- or tsDMARDs. Patients were classified in two groups at baseline according to the Charlson Comorbidity index (CCI) score: < 3 and ≥3. Patients achieving remission (DAS28< 2.6) at 1 and 2-years timepoints after the anti-TNF initiation were compared between the two groups using chi-square test. The absolute DAS28 score over time was compared between both groups of patients using a linear regression model adjusted for sex and age, and considering the follow-up visit as covariate. Finally, the first bDMARD retention rate was compared between patients < 3 and ≥3 using Log-Rank test and Kaplan-Meier curve.

Figure 1. Kaplan Meier curve comparing the first bDMARD retention rate between the two groups.



Results: A total of 1253 patients initiating bDMARD were included (76.6% female and mean age 56 years at the beginning of therapy). Overall, 107 (9%) patients had a CCI ≥3, being diabetes the most frequent comorbidity (5.0%). No differences were found in DAS28< 2.6 between patients with CCI< 3 and CCI≥3 after 1 year of follow-up (48.2% vs. 44.2%, p-value=0.457), nor after 2 years (50.8% vs. 40.7%, p-value=0.135). The linear regression model showed significant higher scores in DAS28 over the two years in patients with a CCI ≥3 after adjusting for age and sex (beta coefficient 0.27, 95%CI: 0.02-0.51; p-value=0.034). Finally, no differences in the bDMARD retention rate were found between both groups (median 2.6 years [IQR: 1.5-4.1] in CCI< 3 vs. 2.1 years [IQR: 0.6-3.7] in CCI≥3; log rank test p-value 0.467) (Figure).

Conclusion: These data suggest that a higher CCI in patients with RA is associated with greater DAS28 scores during the first two years after bDMARD initiation, although no differences in remission status were found. In addition, a slightly shorter retention rate was found in patients with CCI≥3, although the difference was non-significant. These results suggest a lower probability of disease activity control in patients with comorbidities after the initiation of bDMARD.

Disclosure: C. López Medina: AbbVie, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 6, MSD, 6, Novartis, 2, 5, 6, UCB Pharma, 2, 5, 6; **J. Calvo**: None; **L. Otero-Valera**: None; **A. Escudero Contreras**: None; **R. Ortega Castro**: None; **L. Ladehesa Pineda**: None; **C. Campos**: None; **P. Bernabeu-Gonzálvez**: None; **C. Bohorquez**: None; **A. Garcia Dorta**: None; **D. Ruiz-Montesinos**: None; **M. Pombo Suarez**: Janssen, 6, MSD Spain, 6; **I. Ros**: Janssen, 6, novartis, 6, Pfizer, 6; **F. Alonso**: None; **I. Castrejon**: Bristol Myers Squibb, 1, 6, Galapagos, 2, GlaxoSmithKline, 1, 6, Lilly, 1, 6, Merck Sharp & Dohme, 6, Pfizer, 1, 2, 6.

Abstract Number: 1308

Certolizumab Pegol Shows Longer Retention Rate in Comparison with Other TNF Inhibitors in Patients with Rheumatoid Arthritis and High Rheumatoid Factor Titers at Baseline. a Multicentre and Retrospective Study

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SESSION INFORMATION

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Session Title: RA – Treatments Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Factor (RF) is an antibody against the Fc fragment of IgG that contributes to the Rheumatoid Arthritis (RA) development. RF can bind the Fc fragment of infliximab, suggesting the hypothesis that it can also bind other monoclonal antibodies (mAB (Adalimumab, Golimumab and Infliximab)) and fusion proteins (FP (Etanercept)), leading to a lower drug levels and potential early withdrawal. Conversely, the absence of Fc fragment in Certolizumab Pegol (PEG) may lead to a higher retention rate in comparison with other drugs in RA patients (pts) with high RF titers. Objectives: a) to compare the retention rate to PEG vs. mAB and vs. FP in AR pts with high RF titers; b) to conduct the similar analysis but stratifying in naïve and non-naïve pts.

Methods: Longitudinal, retrospective and multicentre study including pts with RA and treated with any TNFi (mAB, FP or PEG) between 2010-2022. RF levels before TNFi initiation and the dates of both initiation and treatment withdrawal were collected. Log-rank test and Kaplan-Meier curves were conducted to evaluate the retention rate to the three molecular structures according to the level of RF considering the quartiles of the baseline titres as cut-offs: < 15, >60 and >200 UI/ml (negative, high, and very high levels, respectively). A sensitivity analysis was performed using a Propensity Score (PS) matching the PEG, mAB and FP populations according to the age, sex and previous TNFi use.

Results: A total of 755 pts with RA treated with TNFi (132 PEG, 441 mAB and 182 FP) and with available titres of RF were included (mean age 53 (12) years, 80.2% female and 70.7% naïve). In the total population, a similar retention rate to PEG, mAB and FP was found (6.1y (95%CI 3.7-NA), 4.2y (95%CI 3.3-8.7) and 4.6y (95%CI 2.9-7.8), respectively, p=0.380). According to the RF levels, the retention rate to the three molecular structures were similar in seronegative pts(F.1A), and in those with high (F.1B) and very high levels (F.1C). When selecting non-naïve pts, those with negative RF titres showed similar retention rates across molecular structures (F.2A). However, in non-naïve ptswith high levels of RF, those treated with PEG showed a significant longer retention rate in comparison with mAB and FP (median 11.0y (95%CI 6.3-NA), 1.4y (95%CI 1.1-NA) and 3.1y (95%CI 0.8-8.8) respectively, p=0.017)(F.2B). Similar results were obtained in non-naïve ptswith

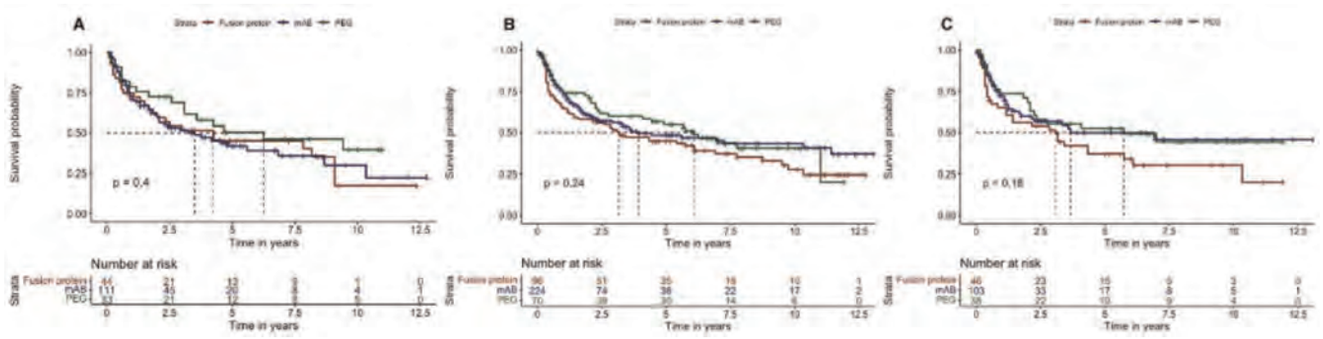

Figure 1. Retention rate to the three molecular structures according to the baseline RF titers: (A) <15 IU/ml, (B) >60 IU/ml and (C) >200 UI/ml.

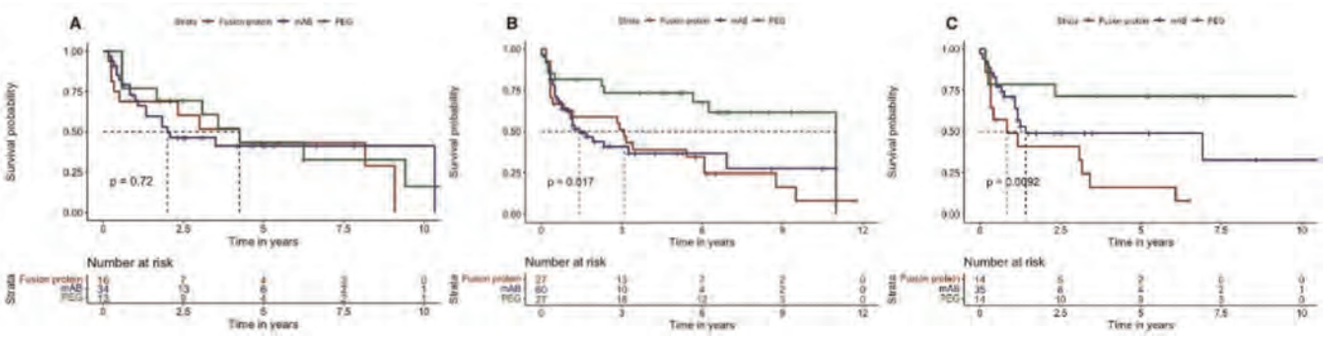

Figure 2. Retention rate to the three molecular structures according to the baseline RF titers in non-naïve patients: (A) <15 IU/ml, (B) >60 IU/ml and (C) >200 UI/ml.

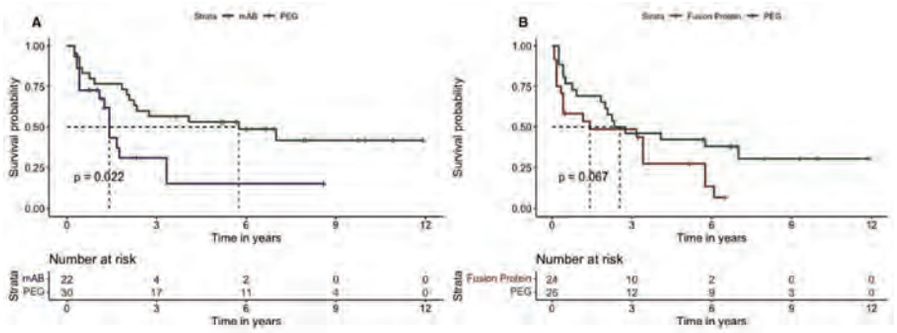

Figure 3. Sensitivity analysis in patients with very high baseline levels of RF (>200 UI/ml) using the PS: (A) PEG vs. mAB and (B) PEG vs. fusion protein.

very high titres of RF (F.2C). In ptswith very high levels of RF, the sensitivity analysis using the PS showed a significant longer retention rate to PEG vs. mAB (median 5.8y (95%CI 2.3-NA) vs. 1.4y (95%CI 1.3-NA), respectively, p=0.022) irrespectively of the previous use of TNFi (F.3A). Likewise, PEG vs. FP showed a longer retention rate, although these differences were non-significant (median 2.5y (95%CI 1.8-NA) vs. 1.4y (95%CI 0.4-5.8), p=0.067)(F.3B).

Conclusion: High or very high RF titers before TNFi initiation were associated with a longer retention rate in non-naïve pts treated with PEG in comparison with mAB and FP. When matching the population using PS, very high levels of RF were associated with longer retention rate to PEG vs. mAB irrespectively of the previous use of TNFi. These results confirm the possible effect of the RF in binding the Fc fragment of the drug.

Disclosure: C. López Medina: AbbVie, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 6, MSD, 6, Novartis, 2, 5, 6, UCB Pharma, 2, 5, 6; **J. Calvo**: None; **M. Abalos-Aguilera**: None; **F. Cepas**: None; **C. Plasencia-Rodríguez**: Abbvie, 5, 6, Eli Lilly, 6, Novartis, 5, Pfizer, 5, 6, Roche, 6; **A. Martinez Feito**: None; **A. Balsa**: AbbVie/Abbott, 1, 2, 5, 6, Bristol-Myers Squibb(BMS), 1, 5, Eli Lilly, 1, 5, 6, Merck/MSD, 1, 5, Novartis, 5, Pfizer, 1, 5, 6, UCB, 1, 5, 6; **R. Faré-García**: None; **A. Juan Mas**: None; **V. Ruiz-Esquide**: None; **L. Sainz-Comas**: None; **C. Díaz-Torné**: None; **J. Godoy**: None; **I. Anon Onate**: None; **N. Mena Vazquez**: None; **S. MANRIQUE**: None; **M. Moreno Garcia**: None; **R. Ortega Castro**: None; **A. Escudero-Contreras**: None.

Abstract Number: 1309

Refractory RA Patients for Targeted Therapies in Real Life

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
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Background/Purpose: Despite the increasing number of available targeted therapies (TT) in rheumatoid arthritis (RA), a proportion of RA patients fail to respond to their first TT, and response decreases with increasing TTs exposures. The definition of refractory RA (refRA) patients is complex; however, recent EULAR guidance defines "difficult-to-treat RA" (D2T RA) as a failure of two or more TTs with differing mechanisms of action (TTDMA) with signs suggestive of active disease, and the management of signs and/or symptoms is perceived as difficult by the rheumatologist and/or the patient.

We aimed to determine the clinical and therapeutic profile of refRA, to describe the patterns of drug sequencing in terms of loss of response, non-response or adverse effects that are associated with RefRA.

Methods: Observational retrospective study with a single-center cohort of RA patients (ACR/EULAR 2010 criteria) exposed to TT since 2000 was performed. We defined refRA as failure of at least 2 TTDMA with moderate/high activity at the TT onset. Demographic and clinical variables were extracted from the electronic medical record, and we analyzed the different lines of treatment with TTs, its duration treatment and reasons for treatment discontinuation.

Results: 537 RA patients undergoing TTs were included, 81 from them were considered as refRA. Clinical and demographic characteristics are listed in table 1.

In a multivariate logistic regression analysis RefRA patients showed younger age at diagnosis, higher proportion of female sex and Sjögren Syndrome, and higher Das28-ESR values than non-refRA (P< 0.001). No differences in CRP and ESR levels, rheumatoid factor or anti-CCP positivity, cardiovascular events, depression, fibromyalgia or pulmonary affection were observed. A Kapplan-Meier survival analysis showed a shorter length of TT in RefRA than non-RefRA (P< 0.0001).

Anti-TNF was the treatment of choice for the 1sr and 2nd TTs, however is less likely to be administered in non-RefRA rather than RefRA (P< 0.001) (table 2), and RefRA showed more incidence of switches (P< 0.001). The absence of conventional DMARD treatment is more likely in Non-RefRA (P=0.046).

Table1

Variable	Non-D2T RA N=456	D2T RA N=81	
	Mean (SD) / n(%)	Mean (SD) / n(%)	P-value
Age at diagnosis (years)	47.6 (12.87)	41.78 (11.37)	<0.001
Age at the beginning of the 1st TT (years)	55.84 (11.99)	48.68 (10.57)	<0.001
Time of disease evolution until the 1st TT (months)	100.54 (102.12)	84.43 (96.52)	0.188
Duration of TT (months)	72.84 (69.23)	42.17 (47.41)	<0.001
Sex (female)	348 (76.32%)	72 (88.89%)	0.01216
C-Reactive Protein	17.85 (23.61)	25.6 (31.23)	0.0346
Erythrocyte sedimentation rate	35.1 (22.88)	47 (31.97)	<0.001
Das28-ESR	5.01 (1.23)	5.55 (1.13)	0.0014
Primary non-response treatment	21 (9.05%)	11 (13.58%)	0.0016
Secondary non-response treatment	91 (39.22%)	40 (49.38%)	<0.001
Discontinuation by adverse event	75 (32.33%)	28 (34.57%)	<0.001
Sjögren syndrome	75 (32.33%)	28 (34.57%)	0.1154
Raynaud's phenomenon	11 (2.41%)	1 (1.23%)	0.7677
Pulmonary affection	81 (17.76%)	18 (22.22%)	0.3681
Cardiovascular event	81 (17.76%)	17 (20.99%)	0.5193
Fibromyalgia	20 (4.39%)	6 (7.41%)	0.4195
Depression	35 (7.68%)	7 (8.64%)	0.9999
Diabetes	58 (12.89%)	7 (12.5%)	0.9886
Dyslipidemia	185 (41.11%)	21 (37.5%)	0.8636
Arterial hypertension	177 (39.33%)	19 (33.93%)	0.6803

Loss of response in 1sr and 2nd TTs were the main reason for discontinuing treatment in refRA, being the adverse event and other causes no related to TT the more frequent as cause of discontinuing TT in non-refRA (P=0.006). When we analyze the reason for discontinuing treatment and excluding the "other causes", if the cause of discontinuing treatment in refRA is a primary non-response, near of the 30% of patients discontinue in second-line by the same reason; and if the cause for discontinuation in first-line is an adverse effect, the 33% of patients discontinue in second-line by the same reason.

Table2

	Non-RefRA				RefRA							
	1st line N=456	2nd line N=164	3rd line N=42	4th line N=8	1st line N=81	2nd line N=81	3rd line N=81	4th line N=65	5th line N=38	6th line N=19	7th line N=9	8th line N=5
	Mean (SD) / n(%)	Mean (SD) / n(%)	Mean (SD) / n(%)	Mean (SD) / n(%)	Mean (SD) / n(%)	Mean (SD) / n(%)	Mean (SD) / n(%)	Mean (SD) / n(%)	Mean (SD) / n(%)	Mean (SD) / n(%)	Mean (SD) / n(%)	Mean (SD) / n(%)
Targeted therapies												
ANTI-TNF	289 (63.4%)	78 (47.6%)	15 (35.7%)	3 (37.5%)	64 (79%)	46 (56.8%)	21 (25.9%)	8 (12.3%)	4 (10.5%)	4 (21.1%)	2 (22.2%)	3 (60%)
ANTI-JAK	80 (17.5%)	31 (18.9%)	7 (16.7%)	1 (12.5%)	1 (1.2%)	6 (7.4%)	18 (22.2%)	15 (23.1%)	16 (42.1%)	11 (57.9%)	7 (77.8%)	2 (40%)
ANTI IL6	51 (11.2%)	22 (13.4%)	13 (30.9%)	3 (37.5%)	10 (12.4%)	11 (13.6%)	19 (23.5%)	21 (32.3%)	5 (13.2%)	3 (15.8%)	0 (0%)	0 (0%)
Others	36 (7.9%)	33 (20.1%)	7 (16.7%)	1 (12.5%)	6 (7.4%)	18 (22.3%)	23 (28.4%)	21 (32.3%)	13 (34.2%)	1 (5.3%)	0 (0%)	0 (0%)
Cycling	0 (0%)	72 (43.9%)	20 (47.6%)	4 (50%)	0 (0%)	36 (44.4%)	16 (19.8%)	8 (12.3%)	2 (5.3%)	4 (21.1%)	5 (55.6%)	1 (20%)
Switching	0 (0%)	92 (56.1%)	22 (52.4%)	4 (50%)	0 (0%)	45 (55.6%)	65 (80.3%)	57 (87.7%)	36 (94.7%)	15 (78.9%)	4 (44.4%)	4 (80%)
Conventional DMARD												
Methotrexate	222 (48.7%)	87 (53.05%)	25 (59.52%)	3 (37.5%)	41 (50.62%)	40 (49.38%)	36 (44.44%)	29 (44.62%)	17 (44.74%)	8 (42.11%)	3 (33.33%)	4 (80%)
Leflunomide	66 (14.5%)	24 (14.63%)	7 (16.67%)	0 (0%)	18 (22.22%)	19 (23.46%)	17 (20.99%)	10 (15.38%)	3 (7.89%)	0 (0%)	1 (11.11%)	0 (0%)
Others	15 (3.3%)	4 (2.44%)	2 (4.8%)	3 (37.5%)	5 (6.2%)	4 (4.9%)	5 (6.2%)	8 (12.3%)	7 (18.1%)	4 (21.1%)	0 (0%)	0 (0%)
Discontinued TT by:												
Non-response	21 (9.1%)	10 (12.7%)	3 (21.4%)	0 (0%)	11 (13.6%)	21 (25.9%)	12 (18.2%)	10 (23.8%)	6 (27.3%)	2 (18.2%)	2 (40%)	0 (0%)
Loss of response	91 (39.2%)	23 (29.1%)	6 (42.9%)	0 (0%)	40 (49.4%)	39 (48.2%)	36 (54.6%)	16 (38.1%)	10 (45.5%)	5 (45.5%)	3 (60%)	1 (50%)
Adverse events	75 (32.3%)	29 (36.7%)	5 (35.7%)	1 (50%)	28 (34.6%)	18 (22.2%)	18 (27.2%)	14 (33.3%)	5 (22.7%)	4 (36.3%)	0 (0%)	1 (50%)
Other causes*	45 (19.4%)	17 (21.5%)	0 (0%)	1 (50%)	2 (2.4%)	3 (3.7%)	0 (0%)	2 (4.8%)	1 (4.5%)	0 (0%)	0 (0%)	0 (0%)

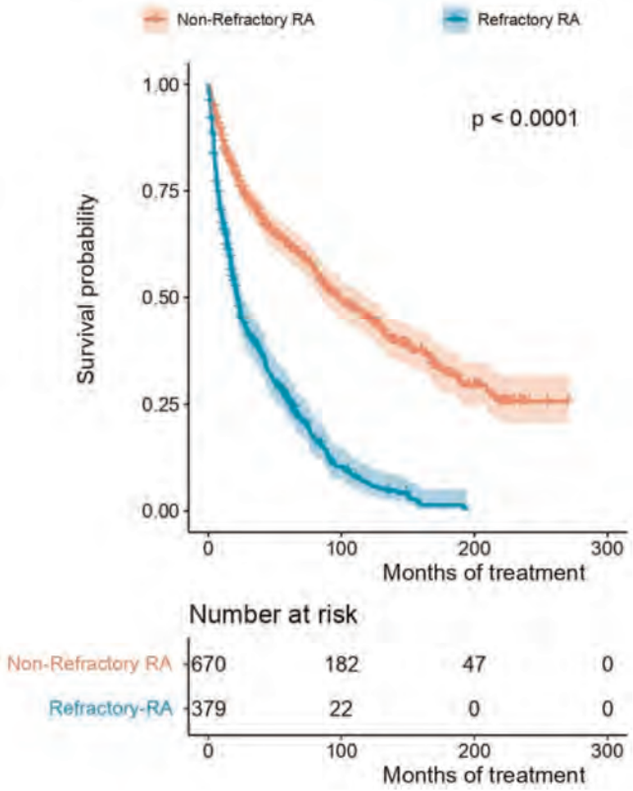

Figure1

Conclusion: RefRA patients in this study showed lower age at diagnosis, higher proportion of female sex and Sjögren Syndrome. With an exposition of 4 TTs as an average in refRA, the duration of TT is shorter and anti-TNF was the most frequent TT both in first and second line of treatment with more incidence of switching. Loss of response is the most common cause of discontinuation in refRA, with lower rate of adverse events and other causes of discontinuation than non-RefRA.

Disclosure: E. Grau Garcia: None; **L. Mas Sanchez**: None; **P. Muñoz Martínez**: None; **C. Riesco Barcena**: None; **A. Torrat Noves**: None; **D. Ramos Castro**: None; **A. Huaylla Quispe**: None; **I. Alcantara Alvarez**: None; **B. Villanueva Mañez**: None; **E. Tovar Sugrañes**: None; **E. Vicens Bernabeu**: None; **H. Charia**: None; **M. De la Rubia Navarro**: None; **L. Gonzalez Puig**: None; **J. Ivorra Cortes**: None; **S. Leal Rodriguez**: None; **I. Martinez Cordellat**: None; **R. Negueroles Albuixech**: None; **J. Oller Rodriguez**: None; **I. Canovas Olmos**: None; **C. Najera Herranz**: None; **J. Roman Ivorra**: None.

Abstract Number: 1310

Comparison of Two Methotrexate Initiation Strategies in Rheumatoid Arthritis in Current Practice

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: To compare the efficacy and tolerance at 3 and 6 months of two methotrexate (MTX) initiation strategies in rheumatoid arthritis (RA).

Methods: Retrospective,monocentric,cross-sectionalstudy including patients with RA who initiated MTX as first-line therapy during the last 2 years according to one of the following 2 strategies: a "conventional" strategy (CS) defined by an initiation of oral MTX at a dose of 10-15 mg/week or an "aggressive" strategy (AS), defined by an initiation of subcutaneous (SC) MTX at a dose of 15 mg/week SC or >15 mg/week either orally or SC. Each strategy allowed the possibility to increase the doses and/or switch to the SC route at 3 months. Efficacy was assessed at 3 and 6 months using the DAS28-CRP. The tolerance of each strategy was also assessed at month 3 and 6.

Results: We included 101 patients (85 women) with a mean age of 55±12 years and disease duration of 5±6 months. The frequency of rheumatoid factors, anti-CCP antibodies and erosions was 83%, 81% and 38% respectively. 61 patients initiated MTX according to the CS, with an increase of dose and/or a switch to the SC route at 3 months for 31 patients, and 40 patients started treatment according to the AS, with an increase of dose and/or switch to the SC route at 3 months for 14 patients. There was no difference between these 2 groups in terms of age, gender, disease duration, antibody status, frequency of bone erosions, body mass index, comorbidities and disease activity at baseline. Efficacy at 3 months was significantly higher with the AS (reduction of the DAS28-CRP from 4.34±0.91 to 2.39±0.75, mean difference of 1.95±1.21, $p< 0.001$) compared to the CS (reduction of the DAS28-CRP from 4.09±0.62 to 2.88±0.73, mean difference of 1.21 ±0.90, $p=0.12$) (**Figure 1**). The improvement of tender/swollen joint counts, patient global assessment and CRP levels

was also significantly more important at 3 months with the AS (**Table 1**). At 6 months, although the DAS28-CRP was similar in the 2 groups (**Figure 1**), less patients from the AS subgroup required an escalation to a targeted biologic/synthetic therapy compared to the CS (12/40, 30% vs. 29/61, 48%, p=0.073). The frequency of digestive side effects at 3 months was significantly lower in the AS (3/40, 7,5% vs. 16/61, 26%, p=0.021). The frequency of hepatic cytolysis at 3 month was higher in the AS (4/40, 10% vs. 1/61,1,6%, p=0.057). The frequency of asthenia at 3 months was similar in both groups (7/4, 18% vs. 6/61, 10%, p=0.25). Only one infection was observed in the CS and no hematological side effect was recorded. At 6 months, the cumulative incidence of side effects was 23% with the AS compared to 46% with the CS (p=0.015). Only one treatment discontinuation was noted in the AS subgroup vs. 9 in the CS subgroup (p=0.042).

Conclusion: This study suggests that it is possible to use a more aggressive initiation strategy of MTX in RA in routine clinical practice. This strategy allows to obtain an earlier clinical response and it is associated with a better tolerance than the conventional strategy. These results need to be confirmed in prospective studies.

Table 1: Evaluation of efficacy parameter at 3 months according to the methotrexate initiation strategy

	"Conventional" strategy (n=61)	"Aggressive" strategy (n=40)	p-value
Variation of tender joint count	-2.6±3.4	-4.4±4.9	0.032
Variation of swollen joint count	-2.0±5	-4.7±4.0	0.005
Variation of PGA-VAS	-24±25	-40±35	0.009
Variation of CRP (mg/L)	-1.8±13	-15±20	<0.001

PGA-VAS: patient Global Assessment - Visual Analogic Scale

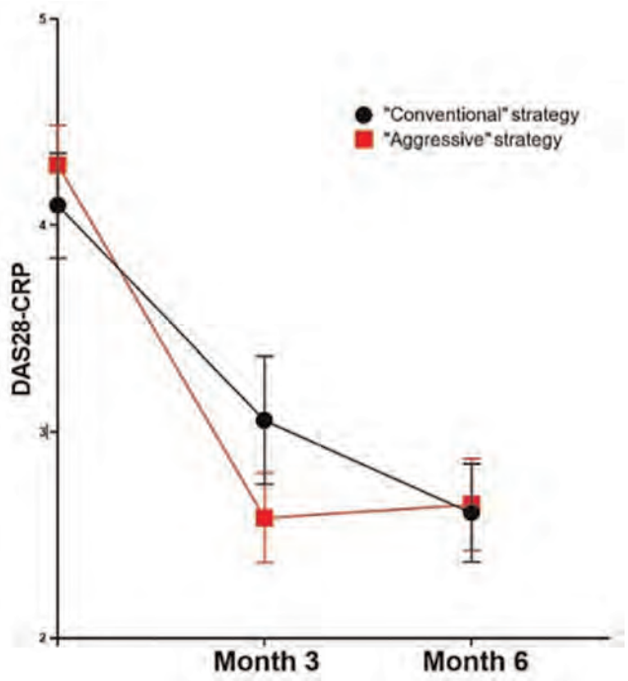

Figure 1: Evolution at 3 and 6 months of DAS28-CRP index according to the methotrexate initiation strategy

Disclosure: P. Vidal-Montal: None; **A. Combier**: None; **A. STEELANDT**: None; **M. THOMAS**: None; **J. Narvaez**: None; **J. Nolla**: None; **Y. ALLANORE**: AbbVie/Abbott, 2, Alpine Immunoscience, 5, AstraZeneca, 2, Bayer, 2, Boehringer-Ingelheim, 2, Janssen, 2, Medsenic, 2, 5, Mylan, 2, OSE Immunotherapeutics, 5, Prometeus, 2, Roche, 2, Sanofi, 2; **J. AVOUAC**: AbbVie, 1, 2, 4, 6, BMS, 4, 5, 6, Fresenius Kabi, 4, 5, Galapagos, 1, 2, 4, 6, Lilly, 6, Novartis, 5, 6, Pfizer, 5, 6, Sanofi, 4, 6.

Abstract Number: 1311

T Cell Subset Signatures Predicted Clinical Response to Etanercept-biosimilar Yisaipu in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Our study aimed to use machine-learning approaches to characterize the immune cell profiles of patients who were inadequate responders to Etanercept-Biosimilar Yisaipu (Yisaipu-IRs) and develop an Yisaipu-IR risk model based on immune cell signatures in rheumatoid arthritis (RA).

Methods: The study included RA patients from the Department of Rheumatology and Immunology, Peking University People's Hospital between July 1, 2022 and May 3, 2023. All the patients fulfilled the 2010 American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) classification criteria for RA. All the patients received Yisaipu 25mg twice a week for 6 months. Patients who didn't achieve ACR20 improvement at 3rd month after enrollment were defined as Yisaipu-IRs and others were defined as Yisaipu adequate responders (Yisaipu-ARs). Immunophenotyping profiles (24 immune cell subsets) of peripheral blood mononuclear cell from Yisaipu-IRs and Yisaipu-ARs were determined by flow cytometry. Spearman correlation analysis was used to test the association between immune phenotypes. Sparse partial least squares-discriminant analysis (sPLS-DA) was used to assess classification and parameter selection. Univariate and multivariate logistic regression analyses were performed to identify immune cell signatures associated with Yisaipu-IRs to build a risk model. Study design and analysis plan flow diagram was shown in **figure1**.

Results: Peripheral blood was collected from 30 Yisaipu-ARs and 8 Yisaipu-IRs. The demographic data and clinical features of the patients were described in **table 1**. The mean age was 51.8±12.4 years for Yisaipu-ARs and 52.5±12.8 years for Yisaipu-IRs. In-depth immune cell phenotyping showed that Yisaipu-IRs had a disrupted immune cell profile, compared with Yisaipu-ARs, including alteration in total CD8$^+$ T-cell, regulatory T-cell (Treg), effector T-cell (Teff) and total B-cell (**figure 2**). Correlation analysis displayed significant disruption in the relationship among total CD8$^+$ T-cell, Treg and B-cell with each other in Yisaipu-IRs compared to Yisaipu-ARs (**figure 3**). The top-ranked immunological features discriminated by sPLS-DA included total CD8$^+$ T-cell, Treg and CLA$^+$ Treg and Teff (**figure 4)**. Logistic regression analysis was applied to confirm that total CD8$^+$ T-cell, CLA$^+$ Treg and foxp3$^+$Treg were significantly associated with ETN-IRs, substantiating the global immunological difference between Yisaipu-IRs and Yisaipu-ARs (**figure 5**). A multi-parametric prediction model for Yisaipu-IRs was established based on weighted immunological signatures including total CD8$^+$ T-cell, CLA$^+$ Treg and foxp3$^+$ Treg. Receiver operating characteristic curve (ROC) analysis of the model showed an area under the curve (AUC) of 0.874 (accuracy 87.4%) (**figure 6**), indicating good performance in discriminating Yisaipu-IRs from Yisaipu-ARs.

Table 1. Characteristics of the patients in the adequate and inadequate responders to Yisaipu at enrollment.

Characteristics	Adequate responders (AR, n=30)	Inadequate responders (IR, n=8)	P
Basic information			
Age, years	51.8±12.4	52.5±12.8	0.848
Sex, % female	76(23/30)	80 (5/8)	0.566
Disease duration, months	111.8±102.9	209.5±143.3	0.066
Clinical features			
DAS28-CRP	3.4±1.7	5.4±1.2	0.002
Tender joint count(t28)	8.9±7.6	13.8±9.9	0.062
Swollen joint count(s28)	4.3±4.2	5.9±2.4	0.213
No. of joint deformity(d28)	3.1±5.0	4.6±6.1	0.577
Tender joint count(t68)	10.3±7.3	20.3±19.8	0.026
Swollen joint count(s68)	4.4±4.2	8.5±7.5	0.045
No. of joint deformity(d68)	3.1±5.0	5.6±2.5	0.325
Wrist involvement	80(24/30)	100 (8/8)	0.134
Global health score (10-cm VAS)	6.1 ±2.5	8.3±2.2	0.021
Laboratory data			
WBC, ×10 9 /L	7.3±2.9	8.1 ±1.7	0.461
Percentage of neutrophils, %	64.5±9.1	71.6±4.5	0.035
Percentage of lymphocytes, %	27.1±8.3	19.5±3.4	0.011
Percentage of monocytes, %	6.2±2.1	6.6±1.8	0.428
Neutrophil count, x10 9 /L	4.9±2.8	5.2±1.2	0.772
Lymphocyte count, x10 9 /L	1.9±0.7	1.4±0.4	0.046
Monocyte count, x10 9 /L	0.4±0.2	0.5±0.2	0.461
Hb, g/L	129.2±14.8	111.9±14.9	0.01
PLT, ×10 9 /L	288.5±80.5	384.6±113.6	0.016
ALT, U/L	20.6±18.6	21.6±32.3	0.956
AST, U/L	22.4±15.6	21.3±16.3	0.814
BUN, mmol/L	5.2±1.4	4.5±1.0	0.304
Cr, umol/L	60±14.6	58.6±8.6	0.743
ESR, mm/hour	22.7±17.7	69.4±25.8	0.000
CRP, mg/liter	5.5±8.5	50.2 ±31.0	0.000
ACPA positive, %	100(30/30)	75(6/8)	0.009
RF positive, %	100(30/30)	75(6/8)	0.009
RF and ACPA double positive, %	100(30/30)	51.2(5/8)	0.001
Medication			
No. of conventional synthetic DMARDs received, %			
0	6.6(2/30)	12.5(1/8)	
1	23.3(7/30)	37.5(3/8)	
2	20(6/30)	25(2/8)	
≥3	50(15/30)	25(2/8)	0.634
No. of biological DMARDs received, %			
0	66.7(20/30)	75(6/8)	
1	30(9/30)	25(2/8)	
≥2	3(1/30)	0	0.825
Receiving steroids at the time of entry, %	10(3/30)	25(2/8)	0.265

Abbreviations: DAS28-CRP, disease activity Score indexed by C-reactive protein; WBC, white blood cell; Hb, hemoglobin; PLT, platelet; ALT, alanine aminotransferase; AST, aspartate amino transferase. Cr, creatinine; BUN, blood urea nitrogen; ESR, erythrocyte sedimentation rate; CRP. C-reactive protein; ACPA, anti-cyclic citrullinated peptide antibody; RF, rheumatoid factor; DMARDs, disease -modifying anti-rheumatic drugs.

Conclusion: T cell signatures might promisingly predict the clinical response to Yisaipu in RA patients and facilitate better stratification of patients for optimal treatment choices in the future.

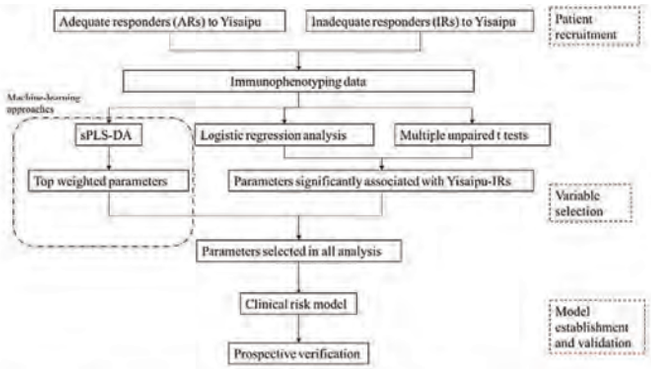

Figure 1. Study design and analysis plan flow diagram. sPLS-DA, sparse partial least squares-discriminant analysis. Yisaipu-IR, inadequate responder to Yisaipu.

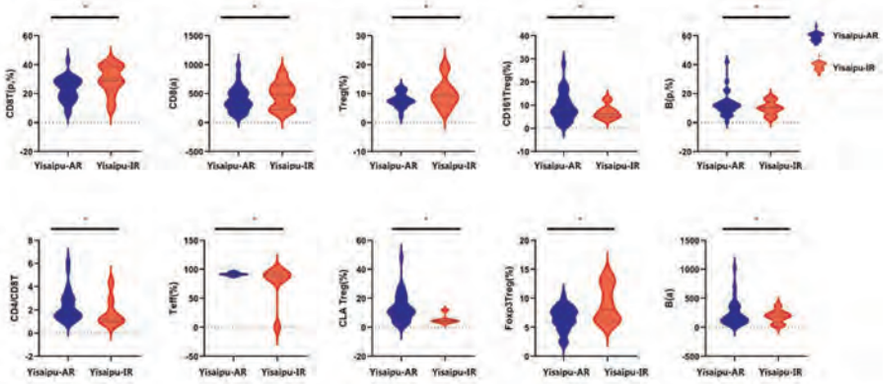

Figure 2. Comparison analyses of the peripheral cell subset profiles between Yisaipu-ARs and Yisaipu-IRs by unpaired t test. Violin plots displayed that total CD8+ T-cell, regulatory T-cell (Treg), effector T-cell (Teff) and total B-cell were significantly different between Yisaipu-ARs and Yisaipu-IRs. Asterisks indicated significant correlations, p<0.05. Yisaipu-IR, inadequate responder to Yisaipu; Yisaipu-AR, adequate responder to Yisaipu; p, percentage; a, absolute count.

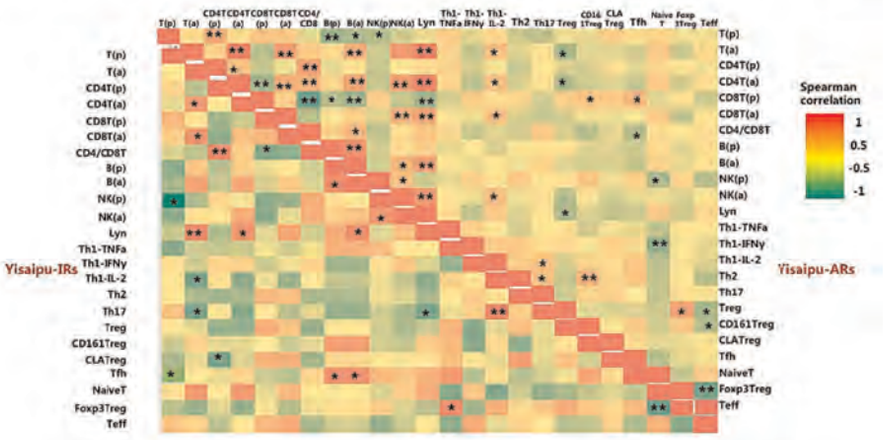

Figure 3. Correlation comparison analysis were performed on immune phenotyping data. The bottom left of the heat map showed the correlation between immune cell types in Yisaipu-IRs and the upper right of the heat map showed the correlation between immune cell types in Yisaipu-ARs. Spearman correlation coefficients for each pair of cell types were represented by colure. Asterisks indicated significant correlations, p<0.05. Yisaipu-IR, inadequate responder to Yisaipu; Yisaipu-AR, adequate responder to Yisaipu; p, percentage; a, absolute count.

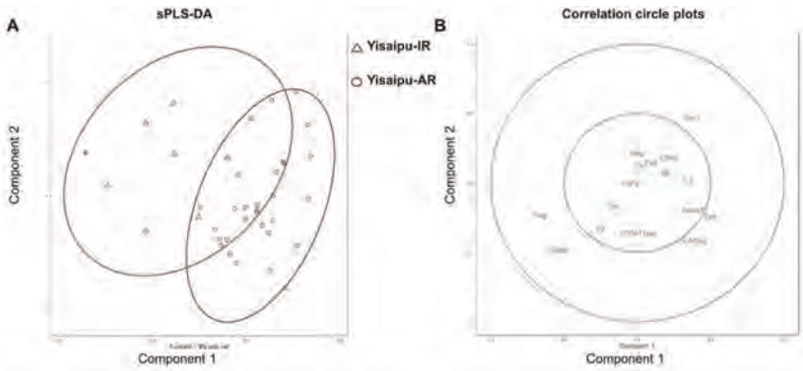

Figure 4. Top hits validated with sparse partial least squares-discriminant analysis (sPLS-DA) based on immunological parameters.**(A)** Individual distribution points and confidence ellipses (ovals) were plotted for the Yisaipu-ARs (red circle) and Yisaipu-IRs(purple triangle). **(B)** Using this analysis, the weighting of each cell type in component 1 and 2 was displayed (inner circle is the 0·5 cutoff). Yisaipu-IR, inadequate responder to Yisaipu; Yisaipu-AR, adequate responder to Yisaipu; p, percentage; a, absolute count.

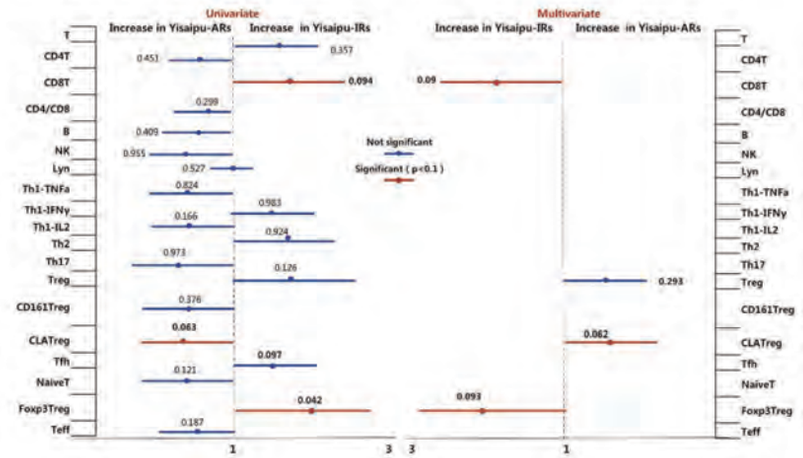

Figure 5. Odds ratios (error bars indicate 95% CIs) of 19 immunological parameters were computed with univaraite and multivariate logistic regression analysis. Yisaipu-IR, inadequate responder to Yisaipu; Yisaipu-AR, adequate responders to Yisaipu.

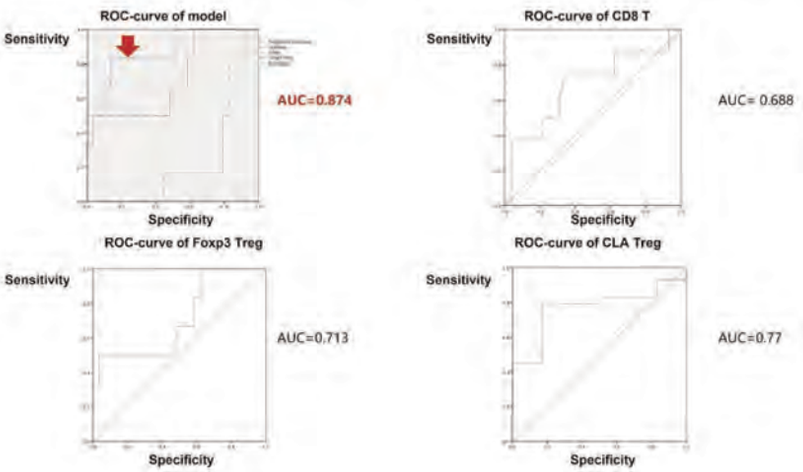

Figure 6. Receiver operating characteristic curve (ROC) with area under the curve (AUC) from univariate models showed the sensitivity and specificity of the top three markers (including total $CD8^+$ T-cell, CLA^+ Treg and $foxp3^+$Treg) identified by Yisaipu-IR risk model. Yisaipu-IR, inadequate responder to etanercept.

Disclosure: H. Zhu: None; **S. Tang**: None; **G. Cheng**: None; **Y. Li**: None; **Y. Li**: None; **F. Sun**: None; **X. Sun**: None; **J. Cheng**: None; **R. Li**: None; **Z. Li**: Abbott, 2, 9, Abbvie, 2, 9, BMS, 2, 9, Celgene, 2, 9, Eli Lilly, 2, 9, GSK, 2, 9, Janssen, 2, 9, MSD, 2, 9, Novartis, 2, 9, Pfizer, 2, 9, Roche, 2, 9, UCB Pharma, 2, 9.

Abstract Number: 1312

Uncovering Risk Factors for Adverse Events and Infections in Rheumatoid Arthritis and Rheumatoid Arthritis with Interstitial Lung Disease Under Biologics or Targeted Synthetic DMARDs: Insights from the KOBIO Registry

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: This study aimed to identify risk factors associated with adverse events (AEs) and infections in patients with rheumatoid arthritis (RA) and comorbid interstitial lung disease (ILD) receiving biologics or targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs), using data from the Korean College of Rheumatology Biologics (KOBIO) registry.

Methods: We analyzed data from a cohort of 2,266 adult RA patients who received b/tsDMARDs between December 2012 and December 2021, including 169 patients having comorbid ILD. We identified risk factors for AEs and infections in the whole RA group and RA-ILD group and investigated the impact of infections on mortality in patients with RA and comorbid ILD.

Figure 1. Kaplan-Meier curve for mortality according to ILD in total RA patients (N=2,266) (A) and for mortality according to having infection in RA-ILD patients (n=169) (B)

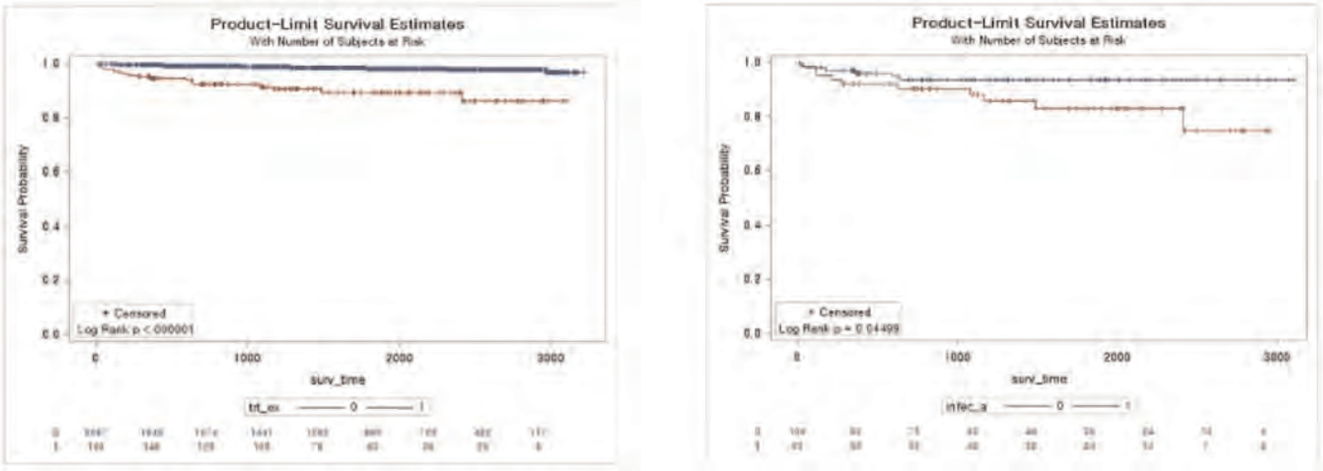

Table 1. Risk factors of infection in total RA and RA with ILD

	Total RA (N=2,266)				RA-ILD (n=169)			
	Univariable model*		Multivariable model*		Univariable model*		Multivariable model*	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
ILD	**1.97 (1.42, 2.74)**	**<0.001**	**1.76 (1.20, 2.59)**	**0.004**				
Elderly (vs. <65years)	1.18 (0.94, 1.48)	0.153	1.00 (0.77, 1.29)	0.968	1.20 (0.64, 2.24)	0.566		
Male (vs. female)	1.07 (0.84, 1.38)	0.580			1.15 (0.60, 2.19)	0.676		
BMI	1.00 (0.97, 1.03)	0.898			0.97 (0.88, 1.07)	0.562		
Current smoking (vs. non-smoking)	1.28 (1.00, 1.64)	0.047	1.03 (0.78, 1.36)	0.825	1.90 (0.99, 3.65)	0.054	2.21 (1.12, 4.40)	**0.023**
Disease duration	1.00 (0.99, 1.02)	0.832			1.00 (0.96, 1.04)	0.937		
Biologics								
Abatacept (vs. TNFi)	**0.71 (0.53, 0.96)**	**0.026**	**0.59 (0.42, 0.83)**	**0.003**	0.59 (0.28, 1.30)	0.193	0.54 (0.24, 1.23)	0.141
Tocilizumab (vs. TNFi)	**0.79 (0.62, 1.00)**	**0.046**	**0.74 (0.57, 0.96)**	**0.023**	0.63 (0.28, 1.42)	0.265	0.45 (0.19, 1.09)	0.077
JAK inhibitors (vs. TNFi)	**0.52 (0.36, 0.75)**	**<0.001**	**0.47 (0.31, 0.72)**	**0.001**	0.72 (0.23, 2.22)	0.593	0.65 (0.19, 2.19)	0.486
Rituximab (vs. TNFi)	0.49 (0.14, 1.71)	0.265	0.52 (0.15, 1.83)	0.308				
Patient global assessment	1.01 (0.96, 1.06)	0.726			1.07 (0.92, 1.26)	0.362		
Physician global assessment	1.02 (0.97, 1.07)	0.523			0.99 (0.85, 1.19)	0.905		
DAS28-ESR	1.05 (0.96, 1.14)	0.286			1.20 (0.91, 1.60)	0.200		
DAS28-CRP	1.04 (0.95, 1.13)	0.414			1.16 (0.87, 1.54)	0.315		
SDAI	1.00 (0.99, 1.01)	0.720			1.02 (0.99, 1.04)	0.255		
CDAI	1.00 (0.99, 1.01)	0.835			1.02 (0.99, 1.05)	0.274		
RAPID3	1.01 (0.99, 1.02)	0.441			1.04 (0.98, 1.11)	0.163	1.05 (0.99, 1.12)	0.139
Diabetes mellitus	1.31 (0.99, 1.72)	0.060	1.02 (0.74, 1.41)	0.913	1.48 (0.73, 2.99)	0.279		
Hypertension	1.42 (1.16, 1.74)	0.001	1.21 (0.95, 1.54)	0.133	1.07 (0.57, 2.02)	0.833		
Cardiovascular diseases	**1.46 (1.18, 1.82)**	**0.001**	**1.29 (1.00, 1.66)**	**0.049**	0.81 (0.43, 1.54)	0.521		
Cancer	1.29 (0.43, 4.84)	0.582			<0.01(<0.01, >999.9)	0.991		
RF positivity	0.98 (0.75, 1.27)	0.855			0.53 (0.18, 1.60)	0.260		
Anti-CCP Ab positivity	1.16 (0.85, 1.58)	0.356			1.00 (0.31, 3.21)	0.994		
Prior use of methotrexate	0.70 (0.47, 1.04)	0.077	0.82 (0.52, 1.29)	0.390	0.79 (0.36, 1.74)	0.553		
Prior use of sulfasalazine	1.20 (0.99, 1.45)	0.071	1.11 (0.89, 1.37)	0.355	1.27 (0.67, 2.39)	0.461		
Prior use of leflunomide	1.10 (0.91, 1.34)	0.323			1.03 (0.55, 1.93)	0.935		
Prior use of csDMARDs	1.02 (0.57, 1.84)	0.938			0.37 (0.10, 1.38)	0.139	0.32 (0.08, 1.30)	0.112
Prior use of biologic agents	1.09 (0.87, 1.36)	0.456			1.44 (0.71, 2.95)	0.315		
Concomitant methotrexate	**0.72 (0.59, 0.88)**	**0.001**	**0.79 (0.63, 1.00)**	**0.045**	1.30 (0.69, 2.42)	0.417		
Concomitant sulfasalazine	0.93 (0.41, 2.23)	0.910			1.01 (0.23, 4.38)	0.989		
Concomitant leflunomide	1.15 (0.70, 1.90)	0.576			0.46 (0.09, 2.33)	0.348		
Concomitant corticosteroid	1.04 (0.79, 1.36)	0.809			0.61 (0.25, 1.54)	0.298		
Dose of corticosteroid	1.03 (1.00, 1.06)	0.023	1.02 (1.00, 1.05)	0.106	0.99 (0.91, 1.07)	0.767		

Table 2. Risk factors of any adverse events in total RA and RA with ILD

	Total RA (N=2,266)				RA-ILD (n=169)			
	Univariable model*		Multivariable model*		Univariable model*		Multivariable model*	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
ILD	1.68 (1.24, 2.47)	0.009	2.07 (1.46, 2.92)	<0.001				
Elderly (vs. <65years)	1.26 (1.00, 1.57)	0.047	1.04 (0.82, 1.33)	0.728	1.92 (0.88, 4.18)	0.102	2.65 (1.14, 6.17)	0.024
Male (vs. female)	0.87 (0.69, 1.10)	0.258			0.89 (0.41, 1.94)	0.771		
Current smoking (vs. non-smoking)	0.89 (0.70, 1.13)	0.326			1.85 (0.78, 4.41)	0.164	3.33 (0.86, 5.65)	0.091
Disease duration	1.02 (1.01, 1.03)	0.006	1.00 (0.99, 1.01)	0.953	1.00 (0.95, 1.051	0.863		
Abatacept (vs. TNFi)	0.94 (0.71, 1.24)	0.662	0.60 (0.44, 0.83)	0.002	0.99 (0.39, 2.48)	0.975		
Tocilizumab (vs. TNFi)	1.19 (0.94, 1.50)	0.143	0.73 (0.57, 0.94)	0.013	1.34 (0.49, 3.69)	0.570		
JAK inhibitors (vs. TNFi)	0.56 (0.42, 0.75)	<0.001	0.50 (0.34, 0.73)	<0.001	1.19 (0.29, 1.91)	0.809		
Rituximab (vs. TNFi)	1.48 (0.49, 4.50)	0.488	0.19 (0.11, 1.74)	0.272				
Patient global assessment	0.99 (0.95, 1.04)	0.676			0.92 (0.81, 1.17)	0.261		
Physician global assessment	0.95 (0.90, 1.00)	0.034	1.02 (0.96, 1.08)	0.513	0.86 (0.68, 1.08)	0.199		
DAS28-ESR	1.02 (0.94, 1.11)	0.603			0.93 (0.70, 1.37)	0.906		
DAS28-CRP	1.00 (0.92, 1.08)	0.958			1.01 (0.72, 1.42)	0.953		
RAPID3	1.01 (1.00, 1.03)	0.136	1.00 (0.98, 1.02)	0.911	1.03 (0.97, 1.11)	0.338		
Diabetes mellitus	1.19 (0.90, 1.59)	0.220			0.55 (0.21, 1.23)	0.184	0.5 (0.21, 1.25)	0.140
Hypertension	1.42 (1.15, 1.74)	0.001	1.32 (1.06, 1.63)	0.012	0.52 (0.25, 1.12)	0.094	0.44 (0.19, 1.01)	0.052
Cardiovascular diseases	1.37 (1.10, 1.71)	0.005	1.27 (1.00, 1.60)	0.048	0.79 (0.37, 1.70)	0.551		
Cancer	0.65 (0.21, 2.00)	0.454			>999.9(<0.01, >999.9)	0.990		
RF positivity	1.12 (0.88, 1.43)	0.360			0.62 (0.13, 2.93)	0.550		
Anti-CCP Ab positivity	0.99 (0.74, 1.31)	0.917			0.65 (0.14, 3.11)	0.592		
Prior use of methotrexate	1.01 (0.68, 1.51)	0.945			0.37 (0.11, 1.36)	0.121	0.3 (0.09, 1.13)	0.077
Prior use of sulfasalazine	0.92 (0.76, 1.10)	0.342			1.34 (0.61, 2.93)	0.464		
Prior use of leflunomide	1.11 (0.93, 1.33)	0.251			1.05 (0.51, 2.29)	0.859		
Prior use of csDMARDs	0.98 (0.56, 1.70)	0.941			0.42 (0.05, 3.47)	0.424		
Prior use of biologic agents	1.19 (0.96, 1.48)	0.109	1.17 (0.92, 1.49)	0.198	0.86 (0.37, 2.04)	0.737		
Concomitant methotrexate	0.76 (0.63, 0.92)	0.005	0.72 (0.59, 0.89)	0.002	1.33 (0.62, 2.84)	0.467		
Concomitant sulfasalazine	0.81 (0.38, 1.75)	0.599			0.74 (0.14, 3.86)	0.725		
Concomitant leflunomide	1.02 (0.64, 1.71)	0.849			0.46 (0.11, 2.03)	0.319		
Concomitant corticosteroid	1.12 (0.87, 1.45)	0.371			1.25 (0.43, 3.79)	0.653		
Dose of corticosteroid	1.02 (0.99, 1.05)	0.227			1.02 (0.92, 1.14)	0.670		

Results: Among all RA patients, 45.7% withdrew b/tsDMARDs, while in the RA-ILD group, a higher proportion of 57.4% withdrew their regimen. The main reason for withdrawing b/tsDMARDs in the RA-ILD group was adverse events (AEs), with infections being the largest proportion among the reported AEs. In the RA without ILD group, the frequency of AEs was significantly lower compared to the RA-ILD group (ILD: 45.4%, non-ILD: 27.8%, $p < 0.001$), among the AEs, infusion-related reactions were more common than infections. In multivariate analysis of risk factors for AEs and infections in the RA-ILD group, older age was identified as a risk factor for AEs (OR, 2.65, $p = 0.024$), and only current smoking was identified as a risk factor for infections (OR, 2.214, $p = 0.023$). In the whole RA, ILD (OR = 1.97, $p < 0.001$), current smoking (OR = 1.28, $p = 0.047$), abatacept (OR = 0.71, $p = 0.026$), tocilizumab (OR = 0.79, $p = 0.046$), JAK inhibitors (OR = 0.52, $p < 0.001$), hypertension (OR = 1.42, $p = 0.001$), cardiovascular diseases (OR = 1.46, $p = 0.001$), concomitant methotrexate (OR = 0.72, $p = 0.001$), and dose of corticosteroid (OR = 1.03, $p = 0.023$) were associated with infections.

Conclusion: The patients with RA-ILD had a higher rate of withdrawal of b/tsDMARDs due to AEs and infections compared to patients with RA without ILD. In RA-ILD group, older age was identified as a risk factor for AEs, while current smoking was identified as a risk factor for infections.

Disclosure: J. Kim: None; **J. Jung**: None; **C. Suh**: None; **H. Kim**: None.

Abstract Number: 1313

Remotely Supervised Weight Loss and Exercise Training Improves Disease Activity and Patient Reported Outcomes in Older Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Older persons with rheumatoid arthritis (RA) are at increased risk for sarcopenic obesity, physical disability, adverse drug events, and cardiovascular disease; thus, there is a need for novel, non-pharmacologic interventions to improve clinical care in this patient population. Weight loss and exercise training have well-established benefits of improving clinical outcomes in non-RA populations; however, the effects of combined lifestyle interventions for older patients with RA are understudied. In this randomized controlled trial of older patients with RA and overweight/obesity, our goal was to identify the effects of a remotely supervised weight loss and exercise training (SWET) intervention on disease activity and patient reported outcomes.

Methods: Older (age 60-80 years), previously sedentary participants with RA and overweight/obesity (BMI 28-40 kg/m^2), who all satisfied 2010 ACR/EULAR RA classification criteria, were randomized to 16 weeks of SWET or a counseling health as treatment (CHAT) control group. The SWET intervention group completed aerobic training (150 minutes/week moderate-to-vigorous exercise), resistance training (2 days/week), and a hypocaloric diet (7% weight loss target). The CHAT control group completed 2 baseline visits of diet and exercise counseling followed by usual care. Baseline and post-intervention assessments included body composition assessment (BOD POD®), minimal waist circumference measurement, muscle strength assessment (isometric knee extension), RA disease activity (DAS-28-CRP) assessment, and Patient-Reported Outcomes Measurement Information

Table 1. Changes in outcomes pre- and post-intervention

Variable (units)	CHAT control intervention group			Remotely supervised SWET intervention group			
	Pre (0 weeks) n=10	Post (16 weeks) n=10	Within group pre-post p-value	Pre (0 weeks) n=10	Post (16 weeks) n=10	Within group pre-post p-value	Between group absolute change p-value
Weight (kg)	86.3 (11.3)	84.1 (11.3)	0.03	83.0 (7.1)	78.2 (8.1)	0.002	0.03
Fat mass (kg)	42.0 (7.3)	39.8 (7.6)	0.01	37.0 (4.9)	32.3 (4.2)	0.002	0.04
Lean mass (kg)	44.5 (7.8)	44.9 (7.5)	0.43	46.6 (6.8)	46.6 (6.9)	1.0	0.68
Waist circumference (cm)	100.1 (8.5)	98.71 (8.6)	0.20	97.6 (6.4)	91.2 (6.4)	0.003	0.002
Isometric knee extension average torque (Nm)	102.6 (48.1)	111.8 (48.0)	0.23	117.8 (37.8)	127.2 (31.5)	0.16	0.83
DAS-28-CRP	3.1 (1.0)	2.9 (0.8)	0.26	2.9 (1.2)	2.1 (0.9)	0.01	0.03
Tender joints (#)	2.7 (4.8)	1.7 (2.1)	0.75	2.4 (2.9)	0.7 (0.9)	0.03	0.04
Swollen joints (#)	4.3 (3.4)	2.3 (1.7)	0.03	3.2 (3.7)	0.9 (1.2)	0.06	0.05
Patient global assessment VAS (mm)	31.1 (20.3)	22.2 (22.8)	0.16	26.4 (26.5)	13.3 (22.9)	0.03	0.47
CRP (mg/L)	8.2 (13.0)	9.3 (11.5)	0.91	4.7 (9.5)	3.6 (4.4)	0.04	0.24
PROMIS-physical health (T-score)	47.3 (7.3)	45.1 (5.8)	0.31	47.7 (5.7)	52.3 (6.6)	0.08	0.01
PROMIS-physical function (T-score)	41.7 (5.0)	41.7 (6.4)	0.90	42.3 (6.3)	48.1 (6.5)	0.01	0.01
PROMIS-mental health (T-score)	51.6 (6.6)	51.9 (6.6)	0.52	54.1 (8.8)	57.6 (8.4)	0.01	0.02
PROMIS-cognitive function (T-score)	53.6 (7.7)	51.1 (8.7)	0.25	49.3 (9.6)	52.3 (8.0)	0.12	0.16
PROMIS-pain intensity (T-score)	46.5 (6.1)	45.7 (4.0)	0.50	46.3 (5.8)	41.7 (7.9)	0.04	0.11
PROMIS-fatigue (T-score)	49.0 (9.1)	52.0 (6.0)	0.16	49.0 (6.3)	44.0 (9.9)	0.06	0.02

Values are shown as mean (SD). CHAT counseling health as treatment, SWET supervised weight loss and exercise training, DAS-28-CRP disease activity score in 28 joints with C-reactive protein, VAS visual analog scale, CRP C-reactive protein, PROMIS Patient-Reported Outcomes Measurement Information System

System (PROMIS) questionnaires. Within group pre- versus post-intervention changes were assessed using Wilcoxon signed rank tests. Between group comparisons of outcome absolute change (post – pre) were assessed using regression modeling controlling for the baseline outcome. Relationships were assessed using Spearman's correlations. Statistical significance for the primary outcome (between group changes in DAS-28-CRP) was established at $p< 0.05$.

Results: Compared to the CHAT control group (n=10, 9 female, mean age 65.6±5.4), older RA participants who completed the remotely supervised SWET intervention (n=10, 7 female, mean age 67.7±5.4) significantly improved DAS-28-CRP (p=0.03) (Table 1). SWET group participants also comparatively improved patient reported outcomes, including physical health, physical function, mental health, and fatigue ($p< 0.05$ for all) (Table 1). Decreases in DAS-28-CRP among all participants (n=20) were associated with decreases in waist circumference (rho=0.48, p=0.03) and increases in leg muscle strength (rho=-0.57, p=0.01).

Conclusion: In older participants with RA and overweight/obesity, when compared to a lifestyle counseling control intervention, a remotely supervised weight loss and exercise training intervention significantly improved RA disease activity and multiple patient-reported assessments of overall health. Results of this randomized control trial support the use of multifaceted lifestyle interventions in the usual clinical care of older patients with RA.

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Abstract Number: 1314

Safety Results from a Phase 1 Double-blind Randomized Clinical Trial of Allogeneic Mesenchymal Stem Cells in Early RA

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SESSION INFORMATION
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Background/Purpose: The purpose of this study was to evaluate the safety of bone-marrow derived allogeneic mesenchymal stem cells (MSCs) as therapeutic agents in early rheumatoid arthritis (RA). Used to reduced graft-versus-host disease following bone marrow transplantation, MSCs are being clinically tested in multiple sclerosis, Crohn's disease, cystic fibrosis and other diseases for their immune regulatory properties. We designed and conducted a Phase 1 randomized double blind clinical trial (RDBCT) using MSCs in early RA. MSCs have immunomodulatory properties ex vivo and *in vivo*. We hypothesized that a "window of opportunity" would exist in early RA during which immune tolerance could be restored to a "pre-RA-like" state

Methods: We conducted a Phase 1 RDBCT in early RA patients using a single infusion of marrow derived allogeneic MSCs. Donors were pre-screened and MSCs isolated and expanded and tested in functional suppressor assays *ex vivo*. The selected MSC donor had a second bone marrow aspiration and MSCs were expanded in the Case Comprehensive Cancer Center GMP faculty and cryopreserved. MSCs underwent purity and adventitious testing in advance and endotoxin prior to release. Studies were perfumed under IND # 016906 and according to the Declaration of Helsinki. Patients enrolled had symptoms of RA for less than two years and had elevated rheumatoid factor or antibody directed against citrullinated peptides or both. Known DMSO sensitivity, active infection and history of disease modifying drugs (DMARDs) other than methotrexate, hydroxychloroquine and low dose prednisone were exclusionary.

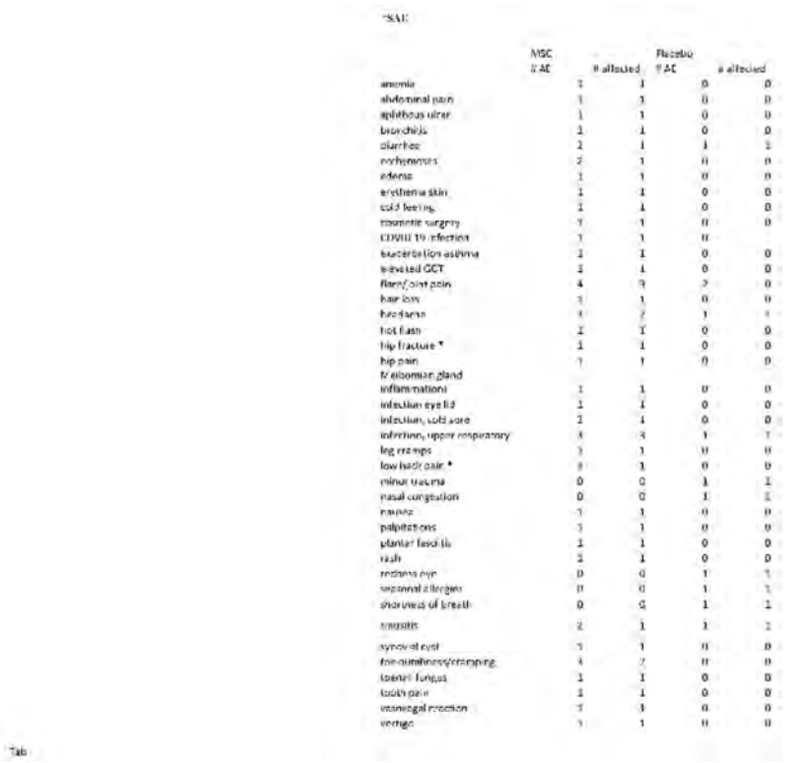
Results: Screening lasted 42 days prior to infusion. Of the ten patients treated, five were administered MSCs at 2 million (M)/kg and three patients at 4M/kg and two received sham infusion. Patients were pre-medicated with acetaminophen and diphenhydramine. There were no dose limiting toxicity and no infusion reactions. Two SAEs were not considered to be study

Table 1 Demographics

Table 1 Demographics

	Age	Male	Female	White	Black	Hispanic	Not Hispanic
MSC	50.75	2	6	5	1	0	6
Placebo	53.5	0	2	1	1	0	2

Table 2 Adverse Events



*SAE	MSC # AE	# affected	Placebo # AE	# affected
anemia	1	1	0	0
abdominal pain	1	1	0	0
aphthous ulcer	1	1	0	0
bronchitis	1	1	0	0
diarrhea	1	1	1	1
erythemas	2	1	0	0
edema	1	1	0	0
erythema skin	1	1	0	0
cold feeling	1	1	0	0
cosmetic surgery	1	1	0	0
COVID 19 infection	1	1	0	
exacerbation asthma	1	1	0	0
elevated GGT	1	1	0	0
flare/joint pain	4	3	2	0
hair loss	1	1	0	0
headache	1	1	1	1
hot flash	1	1	0	0
hip fracture *	1	1	0	0
hip pain	1	1	0	0
IV abdominal gland inflammation	1	1	0	0
infection eye lid	1	1	0	0
infection, cold sore	1	1	0	0
infection, upper respiratory	3	3	1	1
leg cramps	1	1	0	0
low back pain *	3	1	0	0
minor trauma	0	0	1	1
nasal congestion	0	0	1	1
nausea	1	1	0	0
palpitations	1	1	0	0
plantar fasciitis	1	1	0	0
rash	1	1	0	0
redness eye	0	0	1	1
seasonal allergies	0	0	1	1
shortness of breath	0	0	1	1
sinusitis	2	1	1	1
synovial cyst	1	1	0	0
toe numbness/cramping	3	2	0	0
toenail fungus	1	1	0	0
tooth pain	1	1	0	0
vasovagal reaction	1	1	0	0
vertigo	1	1	0	0

Tab

related: 1) acute exacerbation of chronic low back pain; 2) hip fracture in a patient on low dose steroids. Enrollment was halted after ten patients due to stalling during the pandemic. Demographics are included in Table 1. Spirometry post-infusion was discontinued with permission mid-way through the trial as no respiratory AEs occurred in conjunction with or immediately after infusion. No study related AEs related to the therapeutic agent were reported (Table 2). Secondary outcomes including Patient Reported Outcomes and DAS28CRP are under analysis.

Conclusion: Use of "off the shelf" bone marrow derived adult "mesenchymal stem cells" appear safe using dosages up to 4M/Kg. There were no dose limiting toxicities observed and patients tolerated infusion well without pre-conditioning, as is required for use of other cellular therapies. Given the safety of using MSC's, we suggest that allogeneic MSCs should be tested early in RA in a phase 2 study for their ability to induce immune quiescence and induction of host regulatory cells as well as efficacy responses.

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Abstract Number: 1315

Elevated Serum Adiponectin Levels During Olokizumab Treatment in Patients with Rheumatoid Arthritis Correlate with High-density Lipoprotein Lipid Profile Independently of Body Mass Index: Results from the Double-blind, Randomized Controlled Phase III Studies

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SESSION INFORMATION
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Background/Purpose: Active rheumatoid arthritis (RA) is associated with a higher prevalence of insulin resistance (IR). Dysregulation of adipokines driven by low-level systemic inflammation plays a central role in the development of IR. Adiponectin (Adp) is an adipokine exerting anti-inflammatory and insulin-sensitizing activity. However suppression of Adp secretion by IL-6 was shown in previous studies, data on associations of Adp with serum lipid profiles and disease activity in patients with RA treated with biologic DMARDs are controversial. Here we present the changes in serum Adp levels in patients with active RA during treatment with IL-6 inhibitor olokizumab (OKZ).

Methods: Data were extracted from 3 double-blind RCTs (NCT02760368; NCT02760407; NCT02760433). Patients were randomized to receive subcutaneous (SC) injections of OKZ 64 mg every 2 weeks (q2w), OKZ 64 mg once every 4 weeks (q4w), or placebo for 24 weeks, all on background of MTX.

Demographics were assessed at baseline. Body weight and height were assessed at baseline, week 4, 8, 12, 18, and 24. Clinical and laboratory data were collected at baseline, week 4, 12, and 24. Associations with changes in Adp were evaluated by partial correlations adjusted for gender, age, BMI, and lipid-modifying therapy for lipid profiles or for gender, age; BMI; Adp; changes in BMI and cholesterol for disease activity.

Results: Serum Adp measurements were available for 1944 pts (730/765/499 pts in OKZ q2w, OKZ q4w, and placebo groups). Baseline characteristics were equally distributed across treatment groups. In total 18% of patients received lipid modifying agents, with the percentage slightly higher in OKZ groups compared to placebo. Pre-dose Adp levels were positively associated with longer disease duration, and inversely associated with BMI at baseline, however no association was observed with disease activity (Figure 1A).

Significantly elevated levels of triglycerides, total cholesterol, HDL- and LDL-cholesterol were observed at all post-dose timepoints (figure 1B, 1C). After 24 weeks of treatment, Adp increased significantly by 1590.46 (182.90) ug/L, 1743.61 (180.14) ug/L, and 687.58 (238.33) in OKZ q2w, OKZ q4w, and placebo groups. Significant difference with placebo was observed in OKZ q4w group only (difference (SE) 1056.03 (299.37) μg/L, $p = 0.02$).

Adp changes were positively correlated with changes in total and HDL-cholesterol ($r=0.134$ and $r=0.281$, $p< 0.001$), a very weak however significant correlation was seen with changes in LDL-cholesterol ($r=0.067$, $p=0.018$) and probability to reach low disease activity (DAS28-CRP < 3.2) at week 24 ($r=0.061$, $p=0.001$), but not with post-baseline changes in

Table. Demographic and other baseline characteristics of CREDO population included in the Adp analysis (ITT population)

Parameter	OKZ 64 mg q2w N=730	OKZ 64 mg q4w N=765	Placebo N=449
Median age [IQR], years	46.0 [54.0; 61.0]	46.0 [54.0; 62.0]	46.0 [55.0; 62.0]
Females, n(%)	576 (78.9)	612 (80.0)	359 (80.0)
Median BMI [IQR]	24.0 [27.5; 31.3]	24.0 [27.3; 31.6]	24.3 [27.4; 30.9]
BMI ≥ 30, n(%)	233 (31.9)	254 (33.2)	136 (30.3)
Mean RA duration ± SD, years	8.5±8.1	8.5±7.7	7.8±7.4
RA duration ≥ 10 years, n(%)	229 (31.4)	255 (33.3)	133 (29.6)
Very active disease: DAS28-CRP >5.1, n(%)	591 (81.0)	623 (81.4)	356 (79.3)
Mean CRP ± SD, mg/L	20.3±21.7	19.9±20.9	20.0±22.1
Mean ESR± SD, mm/h	47.4±25.5	48.1±26.5	49.6±27.5
Mean total cholesterol (SE), mmol/L	4.92 (0.04)	4.92 (0.04)	4.97 (0.05)
Mean HDL-C (SE), mmol/L	1.48 (0.02)	1.47 (0.02)	1.49 (0.02)
Mean LDL-C (SE), mmol/L	2.79 (0.03)	2.80 (0.03)	2.83 (0.04)
Mean triglycerides (SE), mmol/L	1.41 (0.02)	1.43 (0.03)	1.44 (0.03)
Lipid-lowering agents, n(%)	140 (19.2)**	152 (19.9)**	58 (12.9)

*** p <0.01 in comparison with placebo*
OKZ = olokizumab, q2w = every 2 weeks, q4w = every 4 weeks, RA = rheumatoid arthritis; BMI = body mass index; IQR = interquartile range; HDL-C = high density lipoprotein cholesterol; LDL-C = low density lipoprotein cholesterol

triglycerides or BMI. Adp levels were inversely correlated with DAS28-ESR and ESR at week 24 (r=-0.061, p=0.048, r=-0.082, p=0.004).

Conclusion: Significant elevation of serum Adp was observed after 24 weeks of OKZ treatment in patients with RA. Adp changes positively correlated with elevations of total and HDL-cholesterol, independently of post-treatment changes in BMI. Increased Adp may have protective insulin-sensitizing effects and may contribute to decreasing the risk of CV complications in RA patients.

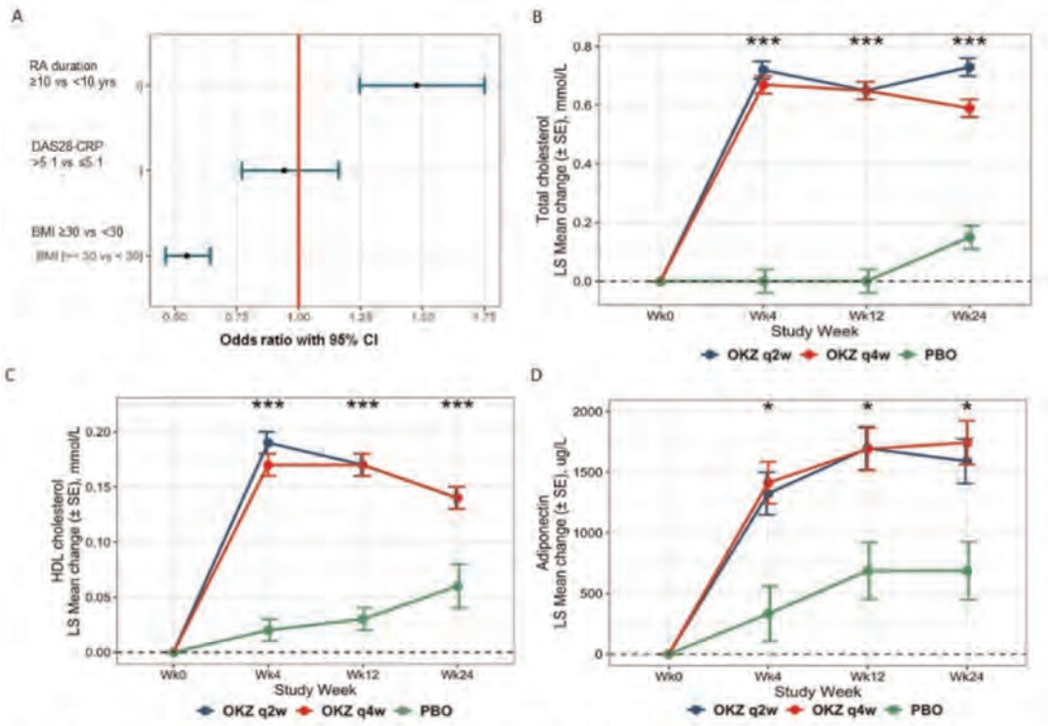

Figure 1 Baseline associations(A) and changes from baseline in lipids(B,C) and Adp (D) in adult patients with moderately to severely active RA receiving OKZ therapy on top of MTX

Comparisons to placebo: * p <0.05; *** p <0.001. Linear mixed model was used to compare change in Adp from baseline between OKZ groups and placebo with adjustments for baseline Adp, baseline BMI, post-baseline dynamic in BMI and total cholesterol. OKZ = olokizumab, q2w = every 2 weeks, q4w = every 4 weeks, PBO = placebo; RA = rheumatoid arthritis; BMI = body mass index; IQR = interquartile range; MTX = methotrexate; LS Mean = least square mean; SE = standard error

Disclosure: E. Zonova: AbbVie/Abbott, 5, 6, Amgen, 5, 6, AstraZeneca, 6, Bayer, 6, Berlin-chemie, 6, Biocad, 5, 6, Boehringer-Ingelheim, 6, Dr. Reddys, 6, Egis, 6, Eli Lilly, 5, 6, Fresenius, 5, 6, Gedeon Richter, 6, Generium, 5, Heel, 5, 6, Janssen, 5, 6, Lancet, 6, Nanolek, 6, Novartis, 5, 6, Pfizer, 6, Pierre Fabre, 6, R-Pharm, 6, Sandoz, 6, Swixx, 6; **A. Abbate**: Applied Clinical Intel, 2, 6, AstraZeneca, 2, 6, Cromos Pharma, 2, 6, Implicit Biosciences, 2, 6, Janssen, 2, 6, Kiniksa, 2, 5, 6, Merck/MSD, 2, 6, Novartis, 5, Novo Nordisk Inc., 2, 6, Olatec, 2, 6, R-Pharm, 5, Serpin Pharma, 2, 6, Swedish Orphan Biovitrum, 2, 5, 6; **E. Feist**: AbbVie, 12, has received honoraria and research grants, BMS, 12, has received honoraria and research grants, Galapagos, 12, has received honoraria and research grants, Lilly, 12, has received honoraria and research grants, MSD, 12, has received honoraria and research grants, Novartis, 12, has received honoraria and research grants, Pfizer, 12, has received honoraria and research grants, Roche, 12, has received honoraria and research grants, Sobi, 12, has received honoraria and research grants; **S. Yakushin**: AbbVie/Abbott, 5, Bayer, 6, Boehringer-Ingelheim, 6, Egis Pharmaceuticals, 6, Eli Lilly, 5, Krka, 6, Merck/MSD, 5, Novartis, 6, R-Pharm, 5, Sanofi, 6, Servier, 6, STADA, 6; **M. Lemak**: R-Pharm, 3; **A. Egorova**: R-Pharm, 3; **D. Bukhanova**: R-Pharm, 3; **S. Grishin**: R-Pharm, 3; **S. Kuzkina**: R-Pharm, 3; **M. Samsonov**: R_Pharm, 3; **E. NASONOV**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 6, Novartis, 6, Pfizer, 6, R-Pharm, 6.

Abstract Number: 1316

Influence of Rheumatoid Factor on Serum Drug Levels of TNF Inhibitors with Different Structures in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Treatments Poster II

Session Type: Poster Session B

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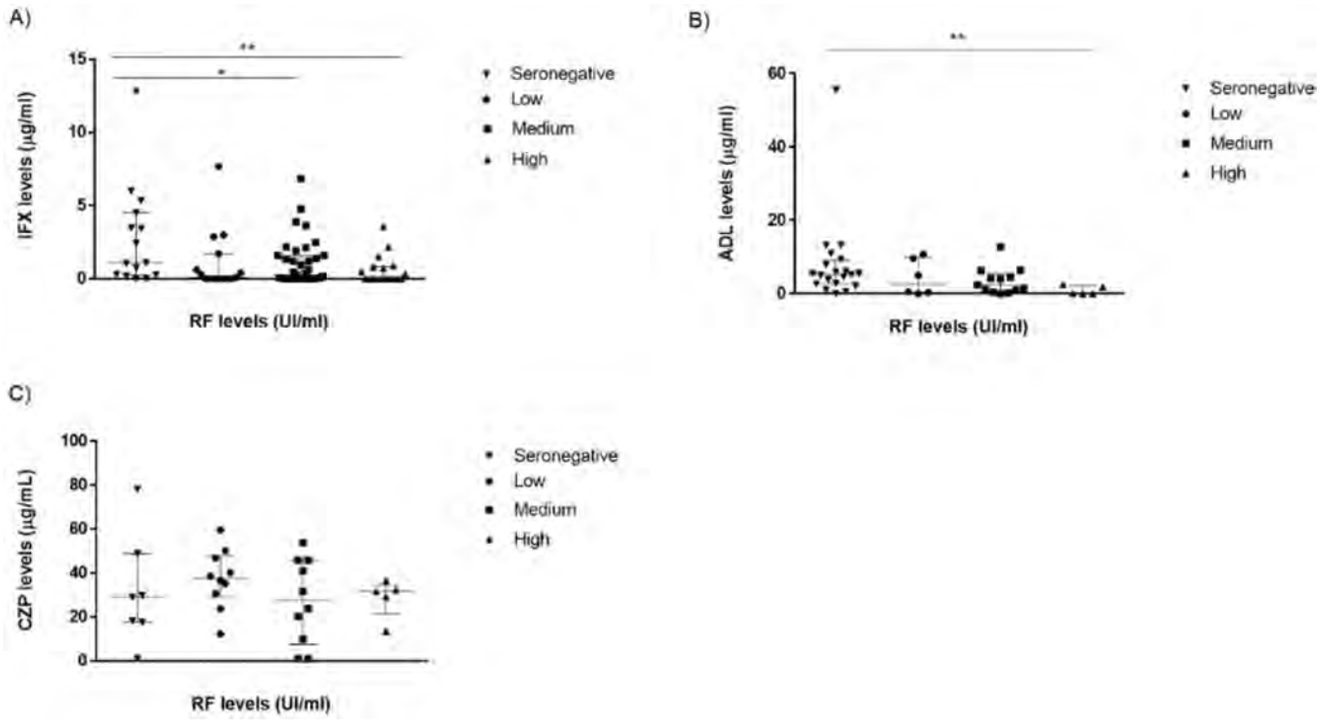
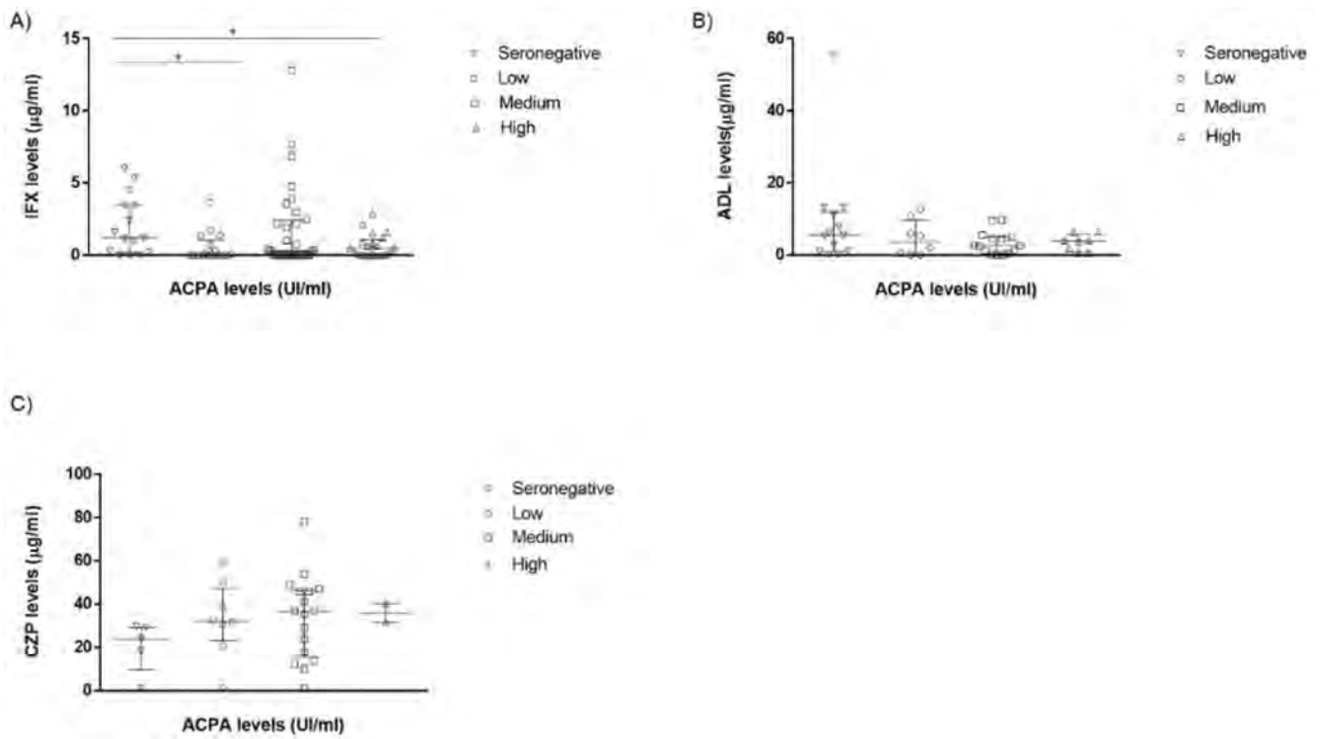
Background/Purpose: Elevated rheumatoid factor (RF) in patients with rheumatoid arthritis (RA) is associated with higher disease activity. A significantly lower efficacy of TNF inhibitors (TNFi) monoclonal antibodies (mAbs), Infliximab (IFX) and Adalimumab (ADL) as well as the fusion protein etanercept, in seropositive RA patients with high RF levels has been described[1,2]. Certolizumab pegol (CZP), a Fc-free pegylated mAb anti-TNF has shown comparable efficacy irrespective of baseline RF status [3]. RF binds the Fc fragment of IgG1 which is the subtype used to engineer the majority of TNFi mAbs. Augmented clearance of mAbs in the presence of high titers of FR, due to the formation of large immune complexes, may likely explain reported negative impact of RF titers in mAbs efficacy. We aim to evaluate in clinical practice whether RF and ACPA levels in RA patients influence serum drug levels of 3 TNFi with differentiated molecular structures.

Characteristics	Total (n=170)	Infliximab (n=90)	Adalimumab (n=48)	Certolizumab pegol (n=32)
Age, years*	55.5 (45.3-66)	57 (46-65)	50 (42-64)	61 (47-70)
Body mass index, Kg/m2*	24.5 (21.7-29)	24.2(21.8-27.7)	24.7 (21.5-30.3)	24.6 (22.2-30.3)
Male, n (%)	28 (17%)	14 (15%)	9 (19%)	5 (17%)
Disease duration, years*	8.7 (4.5-14.3)	8.4 (4.4-14.3)	8.8 (3.9-16)	9.7 (5-12)
Smoking status, n (%)				
Currently or ex-smoker	66 (39%)	29 (32%)	22 (48%)	16 (57%)
Non-smoker	96 (57%)	61 (68%)	24 (52%)	12 (43%)
Rheumatoid factor, n (%)	128 (76%)	75 (83%)	28 (58%)	25 (81%)
ACPA, n (%)	134 (80%)	73 (81%)	35 (73%)	27 (84%)
DAS28 at baseline**	5.1 (1.3)	5.4 (1.3)	4.5 (1.3)	4.9 (1.3)
CRP levels*	7.8 (3-21.8)	10.3 (3.2-25.2)	5.1 (1.4-10.1)	7.8 (2.3-18.2)
Previous bDMARDs, n (%)	26 (15%)	10 (11%)	10 (21%)	6 (20%)
Monotherapy, n (%)	16 (10%)	8 (9%)	8 (17%)	0
csDMARDS, n (%)	152 (90%)	82 (91%)	82 (91%)	32 (100%)
Methotrexate, n (%)	112 (67%)	64 (78%)	33 (83%)	17 (53%)
Other csDMARDs, n (%)	24 (24%)	18 (22%)	7 (18%)	15 (50%)
Prednisone, n (%)	85 (51%)	49 (54%)	21 (44%)	16(50%)

Demographics characteristics of patients with RA treated with infliximab (IFX), adalimumab (ADL) and certolizumab (CTZ) at baseline.



Median drug levels (ng/ml) at 6 months by baseline RF quartiles.



Median drug levels (ng/ml) at 6 months by baseline ACPA quartiles.

[1] Bobbio-Pallavicini F. Ann Rheum Dis 2007;66(3):302–7 [2] Potter C. Ann Rheum Dis 2009;68(1):69–74 [3] Tanaka Y. APLAR 2020. Oral Communication

Methods: We evaluated retrospectively a cohort of consecutive RA patients treated with either IFX, ADL or CZP. Clinical, laboratory and demographic data were collected for all patients at baseline (T0) and after 6 months (T6) of treatment. RF and ACPA titers, serum drug levels were measured at T0 and T6 using nephelometry and ELISA respectively. Patients were stratified into quartiles based on baseline RF [seronegative (< 20 UI/ml, low (20-57.0), medium (57.0-380), and high (> 380)] and ACPA [negative (< 25.0 IU/ml), low (25.0–167 IU/ml), medium (167–1582 IU/ml) and high (>1582 IU/ml)]. Association between baseline RF and ACPA titers and drug levels were assessed using non-parametric test (Mann-Whitney).

Results: A total of 170 patients from a tertiary hospital were evaluated: 90 (66%) received IFX, 48 (35%) ADL and 32 (22%) CZP. Demographic characteristics are shown in **Table 1**. RF and ACPA were positive in 76% and 80 % of patients, respectively. A higher proportion of patients in the IFX group (77%) had both RF+ and ACPA+ status followed by CZP (75%) and ADL (54%) groups. Serum IFX and ADL levels at T6 were significantly lower in patients with higher basal RF titers (Fig 1). In contrast, no differences between drug levels at T6 across baseline RF titers were observed in the CZP group **(Fig. 1).**For ACPA status, only IFX levels at T6 were statistically higher in basal ACPA negative patients **(Fig.2).**Most patients with high ACPA levels had also medium or high RF levels: 11/22 (50%) patients and 1/22 (32%), respectively. Anti-Drug Antibodies (ADA) were detected in 26 patients with IFX, 2 with ADL and 2 with CZP.In the case of IFX, the major percentage of patients with ADA positive had medium or high RF levels patients (39% and 38%, respectively) compared to patients with seronegative andlow RF levels (4% and 19% respectively).

Conclusion: Baseline RF titers do not impact serum drug levels of CZP (a Fc-free anti-TNF) whereas they are significantly linked to low serum drug levels of complete monoclonal antibodies (IFX and ADL) in clinical settings in RA patients. These differences might aid physicians to select suitable treatment for the management of RA.

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Abstract Number: 1317

Discontinuation of Biological Disease Modifying Drugs Due to Adverse Drug Reactions in an Inception Rheumatoid Arthritis Cohort

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: There is a well-known risk of developing adverse drug reactions (ADR) in rheumatic patients due, mainly, to the use of Disease Modifying Drugs (DMARD). In the last two decades, the use of biological DMARDs (bDMARDs) has increased extensively but our knowledge of the ADR to these drugs outside clinical trials setting and in the long term has not at the same rate; especially those that require drug discontinuation. **Purpose.** To describe the incidence and characteristics of ADR to bDMARD, as well as the factors associated to their discontinuation in an inception cohort of patients with RA.

Methods: We conducted an observational longitudinal retrospective study. Patients: all recent onset RA diagnosed between January 1st 2007 and December 31st 2015 followed in outpatient clinic at Hospital Clinico San Carlos until January 1st 2022, which used any bDMARD ≥ 3 months, were included. Primary outcome: development of an ADR that required drug discontinuation (moderate: discontinuation drug, severe: hospitalization or death of the patient due to the ADR). Covariables: sociodemographic, clinical and treatment. Statistical analysis: incidence rates of discontinuation (IR) per 100 patient-years were estimated using survival techniques with their respective 95% confidence interval [CI]. A multivariate Cox regression analysis was used to evaluate the risk factors of discontinuation due to ADR. Results were expressed as HR with their 95% CI.

Table 1. Characteristics at baseline

Age at onset (years), mean (± SD)	52.38 (13.80)
Women %	81.72
Married %	59.24
Active workers %	65.59
Active or ex smoker %	41.80
FR %	63.98
Anti-CCP %	55.80
ESR at diagnosis mm/h (± SD)	41.56 (28.42)
Rosser at diagnosis (± SD)	0.96 (0.06)
Comorbid conditions %	
Hypercholesterolemia	26.34
Hypertension	23.66
Hypothyroidism	17.74
Diabetes Mellitus	9.68
Depression	8.60
Osteoporosis	6.99
Chronic obstructive pulmonary disease	6.99
Cancer	4.84
Fractures	4.30
Gastric ulcer	4.30
Cardiovascular disease	2.15
Liver Disease	1.08
Heart failure	0.54

Results: 186 patients were included (927.86 patient-years), 81.72% were women with a mean age at diagnosis of 52.38 ±13.80. Characteristics at baseline are shown in table 1. They received 347 courses of bDMARD treatment of which 81 were discontinued due to ADR (11.50%; IR 8.73 [7.02-10.85]). 75.30% of the ADR were moderate (IR 6.57 [5.12-8.45]) and 24.69% severe (IR 2.16 [1.39-3.34]). Infection was the most frequent cause of ADR (n=28, 35.44%), followed by allergic reactions (n=16, 20.25%); 2 patients died due to an ADR. Incidence rates are shown in table 2. After performing bivariate and multivariate analysis (table 3) we found that the risk of ADR was higher in patients with heart failure (HR 3.85 [1.48-10.04]) or osteoporosis (HR 2.57 [1.10-5.99]) at diagnosis and in posterior courses of treatment (HR 3.28 [1.92-5.59]); there was a tendency of higher risk to develop ADR with the use of JAK inhibitors (HR 2.15 [0.96-4.85]) compared to anti-TNF, but it did not reach statistical significance. Rituximab had lower risk (HR 0.41 [0.17-0.98]) for the development of ADR compared to anti-TNF.

Conclusion: Discontinuations of bDMARDs in clinical practice due to ADR are common (13.06%) with an estimated IR of 8.73%, most of them moderate. Infection was the main cause of ADR with only 2 deaths registered due to an ADR during follow-up. Higher incidences of ADR to bDMARD were found in the female sex, older patients, concomitant use of corticoids as well as with some bDMARDs (JAKi and Abatacept). We should pay special attention regarding the development of ADR

Table 2. IR of discontinuation due to ADR.

	Patients/year	N	IR	95%CI
Total	927.86	81	8.73	7.02-10.85
Moderate		61	6.57	5.12-8.45
Severe		20	2.16	1.39-3.34
By gender				
Female	759.25	70	9.22	7.29-11.65
Male	168.61	11	6.52	3.61-11.78
By age				
< 46 years	416.93	33	7.92	5.63-11.13
47-69 years	424.17	38	8.96	6.52-12.31
> 70 years	86.76	10	11.53	6.20-21.42
By concomitant use of methotrexate				
No	437.94	41	9.36	6.89-12.72
Yes	489.92	40	8.17	5.99-11.13
By concomitant use of corticoids				
No	194.29	13	6.69	3.89-11.52
Yes	733.57	68	9.27	7.31-11.76
By bDMARDs				
Anti-TNF	618.03	53	8.58	6.55-11.23
Rituximab	158.19	6	3.79	1.70-8.44
Abatacept	42.77	7	16.37	7.80-34.33
Anti-IL6	57.48	6	10.44	4.69-23.23
JAK inhibitors	51.39	9	17.51	9.11-33.66

Table. 3 Bivariate and multivariate analysis

	Bivariate			Multivariate		
	HR	CI 95%	p	HR	CI 95%	p
Age at diagnosis	1.01	0.99-1.03	0.393	1.01	0.98-1.03	0.523
Male gender	0.69	0.31-1.55	0.369	0.78	0.34-1.76	0.548
Rheumatoid factor positive	0.43	0.24-0.76	0.003			
Anti-CCP	0.52	0.29-0.96	0.036			
Heart failure	3.35	2.35-4.77	0.000	3.85	1.48-10.04	0.006
Depression	2.21	0.82-5.93	0.116	2.30	0.91-5.81	0.077
Osteoporosis	2.14	0.81-5.66	0.128	2.57	1.10-5.99	0.029
Posterior courses of treatment	3.52	2.13-5.82	0.000	3.28	1.92-5.59	0.000
Treatment						
Anti-TNF	1	-	-	1	-	-
Rituximab	0.42	1.18-0.99	0.049	0.41	017-0.98	0.044
Abatacept	2.08	0.83-5.24	0.121	1,14	0.44-2.99	0.784
Anti-IL6	1.35	0.57-3.20	0.502	0,93	0.40-2,13	0.861
JAK inhibitors	2.22	0.96-5.12	0.062	2.15	0.96-4.85	0.064
Corticoids use	1.32	0.60-2.91	0.493			
Methotrexate use	0.88	0.49-1.56	0.660			

to patients with certain comorbidities and those using posterior courses of treatment, meanwhile Rituximab seems a safer option of treatment compared to anti-TNF.

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Abstract Number: 1318

Abatacept Modulates Both Global and Citrulline Specific T Cell Signatures: Results from Inhibition of Co-Simulation in Rheumatoid Arthritis Phase IV Trial

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SESSION INFORMATION
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Session Title: RA – Treatments Poster II
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Session Time: 9:00AM–11:00AM

Background/Purpose: Clinical outcomes in Rheumatoid arthritis (RA) have improved with the introduction of biological and targeted synthetic disease modifying anti-rheumatic drugs (b & tsDMARDs). Abatacept (CTLA4-Ig), modulates T cell co-stimulation by interacting with CD80/86 expressed on antigen-presenting cells (APC) and has the potential to interfere both with proinflammatory amplification pathways and autoimmunity. In the Phase IV Inhibition of co-stimulation in RA (ICosRA) trial, we aimed to determine the impact of Abatacept on the peripheral frequencies and phenotypes of citrulline specific T cells in seropositive and shared epitope HLA-DR*04 positive RA patients.

Methods: HLA-DRB1*04:01 or *04:04 $ACPA^+$ RA patients were recruited into a 24-week open label study (n= 25). Peripheral blood mononuclear cells were harvested at baseline, 12 weeks, and 24 weeks after abatacept treatment. A panel of 18 markers expressed on various T-cell subsets and 12 known citrullinated epitope specific HLA class II tetramers was employed to investigate citrulline specific and broad T-cell responses, using spectral flow-cytometry. One-way Anova or Friedman test, with post-hoc tests were used for testing statistical significance.

Results: Evaluation of the global $CD4^+$ T cell compartment revealed that abatacept treatment significantly decreased $CD4^+CD69^+$ recently activated T cells ($p = 0.03$), $CD4^+HLA\text{-}DR^+$ T cells ($p = 0.005$) and $CXCR3^-CCR6^+CD4^+$ Th17 cells ($p = 0.05$). Abatacept treatment also significantly decreased $CD4^+CD25^+CD127^-$ regulatory T cells ($p= 0.03$). This was accompanied by a significant decrease in expression of HLA-DR ($p = 0.0004$), CD137 ($p = 0.003$), CD95 ($p = 0.0004$) and

CD38 (p = 0.03), but not PD1. Characterization of the citrulline specific T cell compartment, demonstrated that citrullinated Tenascin C specific T cells dominated the autoreactive TCR fine-specificities (p< 0.05). Moreover, the frequencies of citrulline specific T cells decreased significantly over time (p= 0.003). Patients responding to therapy showed significantly higher baseline number of citrulline specific T cells than non-responders (p= 0.05). TCR sequencing of *in-vitro* expanded cit-Tenascin C specific T cells from 4 patients at baseline and subsequent follow up, revealed persistence of autoreactive TCR clones.

Conclusion: Abatacept decreases both global and citrulline specific T cell populations. Notably, prior to treatment there were higher numbers of autoreactive T cells in those patients that respond; suggesting that not only do these individuals potentially have a stronger autoimmune disease component but are also more receptive to therapeutic intervention targeting inhibition of co-stimulation. Finally, the persistence of citrulline specific T cell clones underscores the notion that abatacept does not fully abrogate the T cell compartment's propensity to drive autoimmunity.

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Abstract Number: 1319

Real World Data on Antifibrotics in Rheumatoid Arthritis-Interstitial Lung Disease. National Multicenter Study of 73 Patients

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Treatments Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a critical complication of rheumatoid arthritis (RA). Abatacept and rituximab are the preferred disease-modifying antirheumatic drugs (DMARDs) for RA-ILD. However, progression of ILD despite its use is not uncommon. A subgroup analysis of the INBUILD trial has shown a slower decline in forced vital capacity (FVC) in patients with progressive fibrosing autoimmune disease-related ILD with nintedanib (NINTE) [*Arthritis Rheumatol* 2022;74(6):1039-47]. However, data on antifibrotics use for RA-ILD in clinical practice (CP) are scarce. Our aim was: **a)** To assess the efficacy of antifibrotic drugs, NINTE and pirfenidone (PIRFE), in Spanish RA-ILD patients with a progressive phenotype in CP; **b)** To compare the profile of CP RA-ILD patients with those included in the INBUILD trial.

Methods: National multicenter study of RA-ILD patients to whom NINTE or PIRFE were added due to progressive fibrosing ILD. Demographic and clinical variables were collected from all patients. These features were compared with those of RA-ILD patients included in the INBUILD trial (n=89, 42 NINTE and 47 placebo). Forced vital capacity (FVC) evolution was the primary endpoint. Results are expressed as percentage, mean±SD or median [IQR].

Table 1. Baseline characteristics of RA-ILD patients treated with NINTE in clinical practice and RA-ILD patients included in the INBUILD trial.

	Clinical practice (n=66)	INBUILD trial (n=89, 42 NINTE vs 47 PCB)
Age, years mean±SD	68.7±8.8	66.9±9.6
Women, n (%)	29 (43.9)	35 (39.3)
Smoker ever, n (%)	47 (71)	57 (64)
Time since ILD diagnosis, years, mean±SD	4.8±4.1	3.6±3.2
RF, n (%)	60 (91)	-
ACPA, n (%)	55 (83)	-
FVC (% of the predicted), mean±SD	71.4±22.6	71.5±16.2
DLCO (% of the predicted), mean±SD	49.1±13.9	47.7±15.6
Dyspnea Score (mMRC), median [IQR]	2 [2-3]	-
UIP-like fibrotic pattern on HRCT, n (%)	42 (63.6)	77 (86.5)
Concomitant immunosuppressive therapy, n (%)	66 (100)	79 (88.8)
Glucocorticoids	44 (66.7)	65 (73.0)
Conventional DMARD	20 (30.3)	48 (53.9)
Biologic DMARD	43 (65.1)	19 (21.3)
JAKi	4 (6.1)	-

ACPA, anti-citrullinated protein antibodies; DLCO, diffusing capacity of the lung for carbon monoxide; DMARD, disease-modifying antirheumatic drug; FVC, forced vital capacity; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; IQR, interquartile range; JAKi, JAK inhibitor; mMRC: modified Medical Research Council scale; NINTE, nintedanib; PCB, placebo; RA, rheumatoid arthritis; RF, rheumatoid factor; SD, standard deviation; UIP, usual interstitial pneumonia.

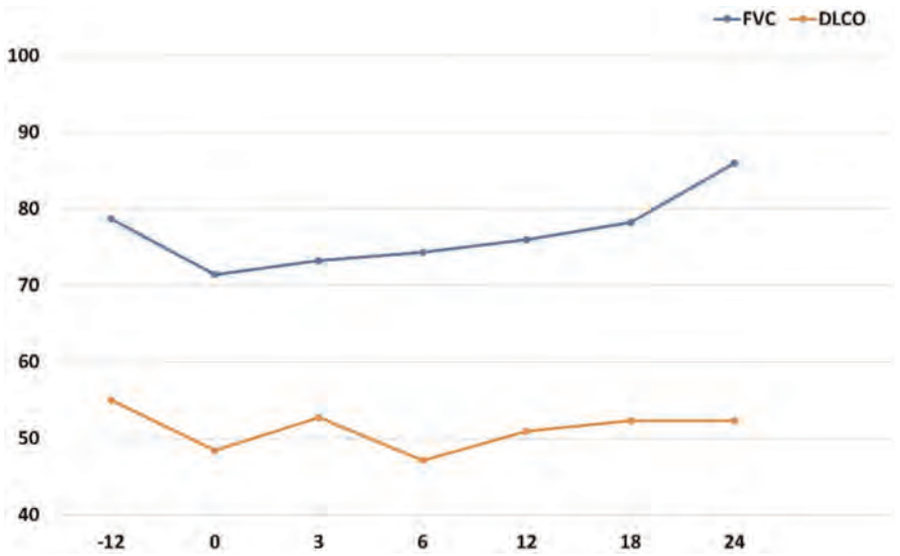

Figure 1. Evolution of FVC and DLCO in 66 patients with RA-ILD treated with nintedanib in clinical practice since the previous year of initiation.

Results: A total of 73 patients (24 women/49 men) from CP were collected, mean age of 69±9 years. The median [IQR] ILD duration up to antifibrotic initiation was of 56.5 [21.5-83] months. NINTE was the most widely used antifibrotic (n=66), combined with immunosuppressive treatment in all cases: corticosteroids in 44, cDMARD in 20 (mycophenolate mofetil=8, leflunomide=6, methotrexate=3, hydroxychloroquine=2, azathioprine=1), bDMARD in 43 (abatacept=31, rituximab=10, anti-IL6R=2) and/or JAKi in 4 (baricitinib=2, tofacitinib=1, filgotinib=1). Mean FVC one year before NINTE start was 80±21 (% pred.), whilst mean baseline FVC was 71±23 (% pred.). **Table 1** shows the comparison of baseline characteristics of RA-ILD patients treated with NINTE in CP and in the INBUILD trial. The evolution of FVC and diffusing capacity of the lungs for carbon monoxide (DLCO) in our patients with NINTE from the previous year of antifibrotic initiation is shown in **Figure 1**. After a median follow-up of 15.5 [3.5-23.5] months, no significant decline in mean FVC or DLCO values was observed. In addition, 86% of the patients presented stabilization or improvement of dyspnea. NINTE was withdrawn in 14 patients due to: gastrointestinal adverse events (11), death (1), hemorrhage risk (1), and stabilization (1). PIRFE was administered to 7 patients (4 men), combined with abatacept in 3 patients, leflunomide in 1, and methotrexate in 1. Mean baseline FVC and DLCO were 69±22 and 49±14 (% pred.), respectively. As with NINTE, a stability in the evolution of lung function was observed. PIRFE was withdrawn in 4 patients due to: gastrointestinal adverse events (2), inefficacy (1), and stabilization (1).

Conclusion: Antifibrotics, especially NINTE, seem to slow ILD progression in patients with RA-ILD. In CP, our patients are treated belatedly in the evolution of the disease, but results are satisfactory. Combination of antifibrotics and DMARDs is feasible and safe.

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Abstract Number: 1320

Evaluation of Circulating Levels of Helper T and Innate Lymphoid Cells Subsets in a Cohort of bDMARDs-naïve Patients with Rheumatoid Arthritis Treated with Abatacept

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Treatments Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Helper T cells (Th) are key players in rheumatoid arthritis (RA). Th17 and Th17.1 have a prominent function in the early phase of inflammation, while Th1 characterize a well-established disease (Kotake S, 2017). Th22, characterized by synthesis of IL-22 (and IL-13 and TNF-α) but not IL-17A or IFN-γ, are still. In RA animal model, IL-22 hampered Th1 plasticity, favoring Th17 maintenance and survival (Justa S, 2014). Th9 are involved in RA synovitis, IL-9 being an enhancer of Th17 cells differentiation in the synovium (Chowdhury, 2018). Innate lymphoid cells (ILC) were recently described as critical in the perpetuation of immune responses during the autoimmune processes, being resident in the tissues and activating without the presence of antigen-specific cell receptors. The three major groups in the ILC family (1, 2, 3) mirror the canonical T helper subsets Th1, Th2, and Th17 (Wu X, 2020). Considering the crucial role played by the CD28 co-stimulation in the process of Th priming and its effect on inflammatory environment, we hypothesized that its

Table 1.
Cell subsets, defined as:
Th9:CD3+CD4+CCR6+CCR4- (%CD3+CD4+); Th22:CD3+CD4+CCR6+CCR4+CXCR3-CCR10+ (%CD3+CD4+CCR6+CCR4+); Th17:CD3+CD4+CCR4+CXCR3-CCR6+CCR10- (%CD3+CD4+CCR4+CXCR3-); Th17.1:CD3+CD4+CCR4-CXCR3+CCR6+CCR10- (%CD3+CD4+CCR4-CXCR3+); Th1:CD3+CD4+CCR4-CXCR3+CCR6-CCR10- (%CD3+CD4+CCR4-CXCR3+); Th2:CD3+CD4+CCR4+CXCR3-CCR6-CCR10- (%CD3+CD4+CCR4+CXCR3-); ILC1: LIN-CD45+CD127+CRTH2-CD161+/-CD117-NKP46- (%LIN-CD45+CD127+CRTH2-CD161+/-); ILC2: LIN-CD45+CD127+CRTH2+CD161+ (%LIN-CD45+CD127+); ILC3: LIN-CD45+CD127+CRTH2-CD161+/-CD117+NKP46+ (%LIN-CD45+CD127+CRTH2-CD161+/-).
LIN=lineage markers.

A Correlation between CRP-DAS28 and cell subsets percentage at baseline in the total cohort. In bold statistically significant comparisons.

Cell Subsets	CRP-DAS28	
	r	p
Th9	0.57	**0.020**
Th22	-0.07	>0.999
Th17	0.52	**0.040**
Th17.1	0.51	**0.041**
Th1	-0.57	**0.022**
Th2	-0.66	**0.005**
ILC1	0.01	0.96
ILC2	0.03	0.90
ILC3	-0.05	0.82

B Comparison between cell subsets percentage at T0 (n=16) and T12 (n=13) in the total cohort. In bold statistically significant comparisons.

Cell Subsets	T0	T12	T0 vs T12, p
Th9	8.77 (6.32-14.2)	9.35 (7.89-11.1)	0.301
Th22	20.1 (17.93-23.53)	16 (14.5-19.4)	**0.016**
Th17	37.65 (30.23-43.43)	35.3 (32.5-42.4)	0.946
Th17.1	22.9 (16.8-36.95)	27.2 (17.9-35.4)	0.466
Th1	58.6 (47.88-75.58)	62.2 (39-70.5)	0.305
Th2	36.35 (28.48-46.03)	38.1 (34.1-49.1)	0.376
ILC1	60.6 (50.05-69.58)	57.4 (50.5-79.5)	1.000
ILC2	11.55 (7.39-18.35)	1.98 (0.82-25.75)	1.000
ILC3	0	0	n.d.

blocker abatacept (ABA) might modulate the circulating levels of Th and ILC cells and their involvement in B-cell maturation and antigen-driven differentiation.

Methods: Sixteen bDMARDs-naïve RA patients [female/male=10/6; median (IQR) age=64 (54.3-67.6) years; disease duration=51 (30-108) months; 13/16 (81.3%) seropositive; C Reactive Protein (CRP)=6 (2.4-11.5) mg/L (normal value < 5 mg/L), CRP-28-joint Disease Activity Score (CRP-DAS28)=4 (3.3-4.4)] were enrolled before starting ABA. Peripheral blood mononuclear cells, obtained from the patients before the start of ABA therapy (T0) and after 12 months (T12), were extracellular stained and evaluated by flow cytometry (FACSCantoII, Beckton Dickinson). EULAR criteria were used to evaluate the treatment response [good and moderate responders (R), n=11 and non-responders (NR), n=5].

Results: Baseline CRP-DAS28 was differently correlated with various T helper cell subsets, but not with ILC (Table 1A). In the whole cohort, Th and ILC subpopulation levels did not significantly change between T0 and T12, except for Th22 levels (expressed as % of CD3+CD4+CCR6+CCR4+) which decreased [20.1 (17.93-23.53) vs 16 (14.1-19.4); p:0.016] (Table 1B), mainly in the R group [19 (17.75-20.5) vs 15.85 (13-17.45); p:0.004]. The same level of circulating subsets was found when comparing NR vs R patients at T0 and T12.

Conclusion: All the circulating Th cells expressing CCR6, which is the main chemokine receptor of Th17 and Th17-related cells, were positively correlated with the disease activity at baseline, except for Th22, a distinct Th lineage that can display plasticity towards Th1 and Th2 lineages under special circumstances, showing regulatory properties and participating to the early RA pathogenesis. The decrease of Th22 after CD28 blockade may suggest the potential role of ABA in targeting one of the earliest phases of the disease pathophysiology.

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Abstract Number: 1321

Effect of Subcutaneous Local Anaesthesia Prior to Intra-Articular Injection: An Open Label, Paired-group, Randomized Controlled Trial

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Intraarticular injections are commonly used both for diagnostic and therapeutic injections of glucocorticoids in patients with inflammatory arthritis. The procedural pain felt by patients may be an important factor for patients to consider future injections. Subcutaneous local anaesthesia given a few minutes prior may reduce the pain felt by the patient, however, has the disadvantage of pricking the patient twice. Once problem of studies comparing pain is that individual perception of pain varies, thus, we planned this study which included patients with two same (paired) joints swollen who were undergoing therapeutic joint injections.

Methods: This was an open-label (patients blinded) randomized controlled trial that included patients with rheumatoid arthritis or spondyloarthritis who had both (paired) medium-large joints swollen - either both knees or ankles or writs or elbows, and planned for therapeutic joint injections. The study design was that patients underwent intra-articular into left joint followed by right joint after a gap of 10-minutes. Whether the left or the right joint got local anesthesia was decided by using randomization (online software, serial permuted blocks). (Figure 1) Local anesthesia consisted of 5 ml lignocaine infiltrated in the skin and subcutaneous tissue using a 23-G needle. Intraarticular injections were given using a 10 ml syringe with a 21 G needle. Primary outcome was immediate procedural pain felt by the patient and secondary endpoints were 1-hour

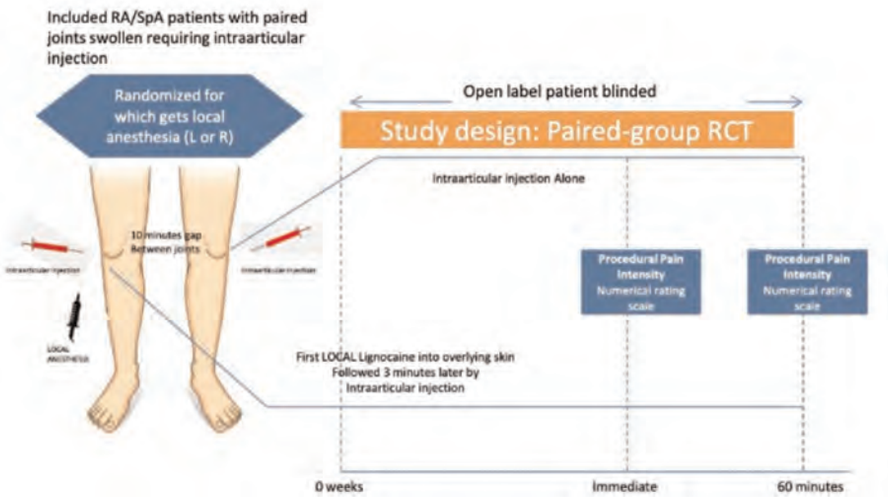

Figure 1: Study design

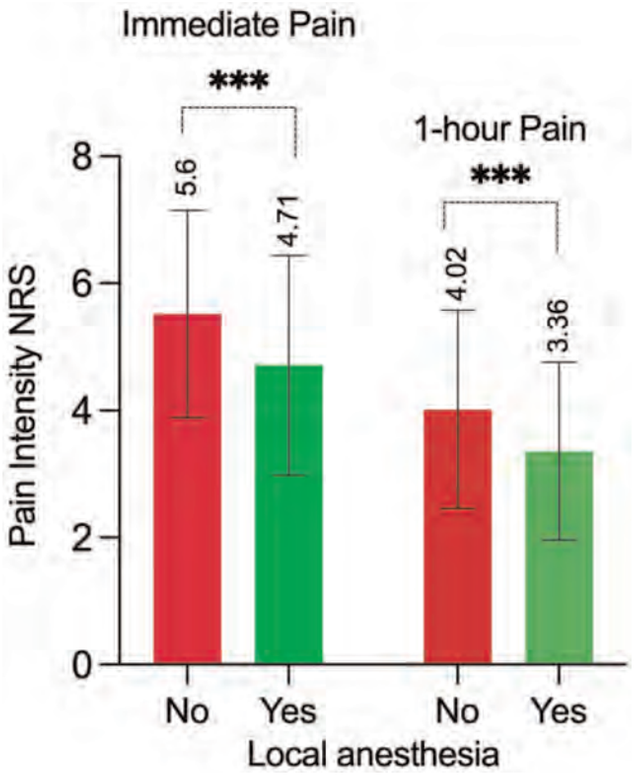

Figure 2: Immediate and 1-hour pain in the joint given prior local anesthesias versus the one not given local

pain assessment, patient preference for future injections (after telling them which joint received LA) and complications. Pain was assessed using numerical rating scale. Paired t-test and Wilcoxon Signed Rank test was used to compare the intensity of pain. Trial registration number CTRI/2021/07/034777

Results: This study included 42 patients undergoing paired joint injections (84 joints). A majority of patients had rheumatoid arthritis (37, 88%), mean age (±SD) was 44.6 ± 14 years and 71% were females. The joints injected were knees (21 patients), wrists (14 patients), ankles (5 patients) and elbows (2 patients). There was a significantly lower immediate pain in the joint given local anaesthesia compared to that not given (difference -0.8, 95 CI -0.6 to -1.0) as well as significantly lower pain at 1-hour (difference -0.7, 95 CI -0.4 to -0.9). (Figure 2) A majority of patients (78.6%) preferred the procedure with local anaesthesia for future injections in their joints. There was no difference in complications of hypopigmentation or purpura nor in residual pain prick-site at 1-month. No significant differences were noted in pain by gender or age, nor by joint injected.

Conclusion: In this study with a unique paired design to obviate individual differences in pain, local anaesthesia of the overlying skin led to a definite but modest reduction (approximately 15%) in pain felt by the patient during intraarticular injection.

Disclosure: A. Shaji: None; **V. Dhir**: None; **C. Prasad**: None; **S. Naidu**: None; **A. Sharma**: None; **S. Sharma**: None; **B. Ghai**: None; **S. Jain**: None.

Abstract Number: 1322

Efzofitimod, a First-in Class NRP2-targeting Immunomodulator, Ameliorates Rheumatoid Arthritis and Associated Lung Fibrosis in Preclinical Models

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Efzofitimod, a novel immunomodulator, has shown clinical proof-of-concept in a Phase 1b/2a clinical trial in patients with pulmonary sarcoidosis and is currently enrolling a global Phase 3 clinical trial. By selectively binding to its target neuropilin-2 (NRP2), a membrane protein that is strongly upregulated on myeloid cells during inflammation, efzofitimod reduces inflammation and fibrosis in a range of animal models of interstitial lung disease (ILD). NRP2 appears to also play a role in other inflammatory diseases such as arthritis [1]. In this work, we confirm that connection utilizing a genetic NRP2 knock-out (KO) mouse model. Based on efzofitimod's anti-inflammatory effects and NRP2's role in the pathology of arthritis, we tested its therapeutic potential in experimental models of rheumatoid arthritis.

Methods: The collagen-induced arthritis (CIA) model was performed in NRP2 WT and KO animals utilizing the Hooke Kit™ for CIA induction. Efzofitimod was dosed at 1 mg/kg weekly intravenously upon emergence of clinical signs. Study animals were scored every other day until termination. Terminal serum samples were analyzed for pro-inflammatory cytokines. To test the effect of efzofitimod in rheumatoid arthritis-associated ILD (RA-ILD), we utilized the SKG mouse model of RA-ILD. The disease was induced via IP injection of 5 mg of zymosan. Efzofitimod was dosed at 3 mg/kg weekly intravenously starting one day prior to disease induction. At termination, lung single cell suspensions were immunophenotyped and lung sections were analyzed for fibrosis.

Results: NRP2 KO animals exhibited heightened sensitivity to disease induction in the CIA model, resulting in excessive mortality. Analysis of serum samples from these animals demonstrated elevated levels of pro-inflammatory cytokines, indicating a deficiency in the negative regulation of the immune response. Based on the impaired immune regulation observed in NRP2 KO animals, we hypothesized that efzofitimod may produce therapeutic benefit in the CIA model via modulation of NRP2. Encouragingly, we observed improved clinical scores in 37.5% of the study animals treated with efzofitimod, compared to only 12.5% in the control group. Additionally, efzofitimod displayed activity in the SKG model of RA-ILD. Treatment with efzofitimod led to a reduction in the number of immune cell populations in the lungs and exhibited a noteworthy reduction in RA-induced lung fibrosis.

Conclusion: The data presented here indicate a critical role for NRP2 in modulating immune responses in autoimmune diseases, such as rheumatoid arthritis and RA-ILD. By targeting NRP2 with efzofitimod, we observed improved disease outcomes, reduced inflammation, and mitigated lung fibrosis, suggesting the potential of efzofitimod as a therapeutic intervention for rheumatoid arthritis and potentially other immune mediated diseases.

1. Fassold, A. *et al*. Soluble neuropilin-2, a nerve repellent receptor, is increased in rheumatoid arthritis synovium and aggravates sympathetic fiber repulsion and arthritis. *Arthritis Rheum*. 60, 2892–2901 (2009).

Disclosure: C. Burkart: aTyr Pharma, 3; **C. Polizzi**: aTyr Pharma, 3; **L. Eide**: aTyr Pharma, 3; **M. Pastenes**: aTyr Pharma, 3; **D. Siefker**: aTyr Pharma, 3; **L. Nangle**: aTyr Pharma, 3.

Abstract Number: 1323

Distinct Treatment Responses in Patients with Rheumatoid Arthritis Receiving Filgotinib 200 Mg over 12 Months: A *Post Hoc* Analysis of FINCH 1

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: FINCH 1 (NCT02889796) was a Phase 3 randomized controlled trial evaluating filgotinib (FIL) in patients with rheumatoid arthritis and an inadequate response to methotrexate (MTX).[1] Patients received background MTX and were randomized 3:3:2:3 to FIL 200 mg (FIL200), FIL 100 mg, adalimumab or placebo. This analysis aimed to identify patterns of response trajectory over 12 months in patients from FINCH 1 receiving FIL200.

Methods: Group-based trajectory modeling is a statistical method which groups individuals based on similar patterns of change in an outcome over time.[2] A group-based trajectory modeling approach was applied to identify five distinct phenotypic groups in terms of observed clinical disease activity index (CDAI) outcomes (and components) over a 12-month period (**Figure**). Responders were recorded as either low disease activity (LDA) or remission, defined as CDAI between ≥ 2.9 and ≤ 10, or ≤ 2.8, respectively, at 6 months.

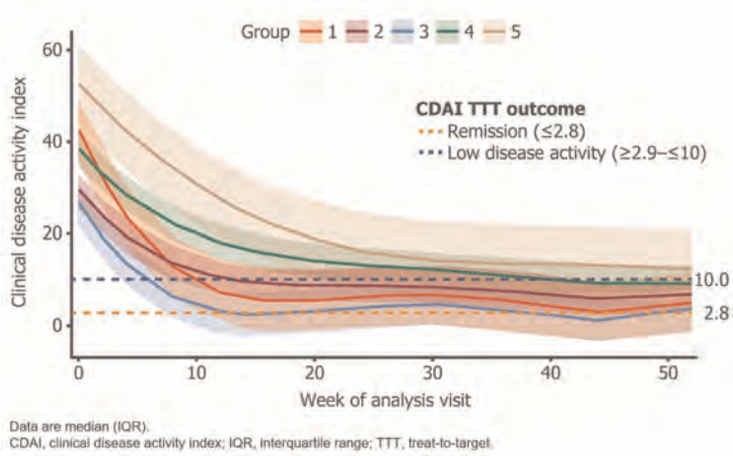

Figure. CDAI trajectory in patients from FINCH 1 receiving FIL200

Table. Efficacy outcomes from baseline to Month 12 in phenotypic patient groups receiving FIL200: CDAI components

	Group 1 N=94	Group 2 N=103	Group 3 N=131	Group 4 N=67	Group 5 N=80
PtGADA					
Baseline	72 (60, 84)	67 (52, 78)	60 (46, 72)	77 (66, 85)	76 (67, 89)
12-month abs change	58 (44, 70)	31 (20, 50)	50 (33, 65)	40 (21, 56)	46 (20, 59)
12-month value	9 (3, 21)	25 (12, 43)	6 (3, 13)	33 (23, 50)	36 (21, 46)
PhGADA					
Baseline	71 (61, 80)	62 (52, 71)	60 (49, 68)	73 (63, 82)	77 (64, 88)
12-month abs change	66 (51, 71)	48 (36, 58)	51 (42, 62)	53 (43, 63)	51 (36, 62)
12-month value	5 (1, 10)	10 (4, 17)	4 (1, 9)	22 (8, 31)	23 (9, 36)
SJC28					
Baseline	14 (11, 18)	8 (6, 9)	8 (6, 11)	10 (8, 12)	16 (12, 20)
12-month abs change	14 (10, 18)	7 (5, 8)	8 (6, 10)	9 (7, 12)	13 (10, 17)
12-month value	0 (0, 0)	0 (0, 1)	0 (0, 0)	0 (0, 2)	2 (0, 3)
TJC28					
Baseline	20 (16, 24)	10 (8, 14)	11 (7, 13)	15 (13, 18)	22 (18, 26)
12-month abs change	18 (15, 22)	9 (7, 12)	11 (7, 13)	13 (10, 16)	16 (12, 22)
12-month value	0 (0, 2)	1 (0, 2)	0 (0, 0)	3 (1, 5)	5 (2, 9)
CDAI responders (LDA and remission), n (%)					
6-months	79 (92)	66 (78)	122 (99)	11 (21)	14 (23)
12-months	75 (91)	75 (90)	119 (99)	27 (52)	20 (34)

Data are median (IQR) unless otherwise stated.
abs, absolute; CDAI, Clinical Disease Activity Index; IQR, interquartile range; LDA, low disease activity; PhGADA, Physician's Global Assessment of Disease Activity; PtGADA, Patient's Global Assessment of Disease Activity; SJC28, swollen joint count in 28 joints; TJC28, tender joint count in 28 joints.

Results: Mean age, the proportion of females and disease duration were similar across all groups. Improvements in efficacy outcome measures were seen for all groups. Baseline (median interquartile range [IQR]) CDAI was highest (worst) in Group 5 (52 [48, 60]), followed by Group 1 (48 [44, 55]). Groups 1 and 3 showed a rapid reduction in CDAI in the first 6 months and sustained response over 12 months. Groups 2, 4 and 5 demonstrated slower response trajectories, with continued improvements in the proportion of CDAI responders between 6 and 12 months; of note, Group 5 constituted 16.8% (80/475) of the total analysis population. **Table** shows that despite substantial and comparable improvements in CDAI components across all 5 groups over 12 months, Group 5 demonstrated some residual disease activity.

Conclusion: A group-based multivariate trajectory model identified five distinct CDAI disease activity trajectories in patients from FINCH 1 receiving FIL200. Patients in all groups demonstrated either fast and sustained response or slower and continued improvements, with no or low numbers of swollen or tender joints at Month 12. The current analysis suggests that patients who do not achieve CDAI LDA within 6-months may still benefit from treatment continuation and informs a range of expectations for times to clinical response. Future work will assess biomarker profiles that may be used to predict the observed clinical response patterns.

References:

1. Combe B, et al. Ann Rheum Dis 2021;80:848–58
2. Nagin DS, et al. Stat Methods Med Res 2018;27:2015–23

Disclosure: P. Taylor: AbbVie, 2, Biogen, 2, Eli Lilly, 2, Fresenius, 2, Galapagos, 2, 5, Gilead Sciences, 2, GSK, 2, Janssen, 2, Nordic Pharma, 2, Pfizer Inc, 2, Sanofi, 2, UCB, 2; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer-Ingelheim, 6, Chugai, 5, 6, Eisai, 5, 6, Eli Lilly, 6, Gilead, 6, GSK, 6, Mitsubishi-Tanabe, 5, Pfizer, 6, Taiho, 6, Taisho, 5, 6; **E. Aiello**: Amgen, 2, Cytel, 3, Galapagos, 2, Genmab, 2, Janssen, 2, Pfizer, 2, UCB, 2; **T. Debray**: Biogen, 2, Galapagos, 2, Gilead, 2; **C. Watson**: Galapagos, 3, 11; **K. Harris**: Galapagos, 3, 11; **G. Burmester**: AbbVie, 2, 6, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Chugai, 6, Galapagos, 2, 6, Lilly, 2, 6, Pfizer, 2, 6, Sanofi, 2, 6.

Abstract Number: 1324

Previous History of Serious Infection Is Associated with the Use of IL-6 Inhibitors in Rheumatoid Arthritis in Wales, UK

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Biologic therapy has revolutionised the treatment of rheumatoid arthritis (RA). Randomised control trials have shown that IL-6 inhibitors are superior to adalimumab, a TNF inhibitor, when used as monotherapy in RA. However more information is required to assess the real-life burden and to predict infection risk in RA patients using biologics and IL-6 receptor antibodies. Here, we describe the characteristics and comorbidities of RA patients treatment with either IL-6 inhibitors, (tocilizumab or sarilumab) versus non-IL-6 (anti-TNF, B-or T-cell therapies) biologic disease modifying anti-rheumatic drugs (bDMARDs).

Methods: A retrospective cohort study of patients with the diagnosis of RA in the Secure Anonymised Information Linkage (SAIL) databank, which includes primary care, secondary care and specialist rheumatology clinic records of over 90% of the population in Wales, UK. Patients treated with IL-6 inhibitors or biologics are compared in a descriptive study and include both biologic/il6-inhibitor naïve and non-naïve patients. Funding and acknowledgement: This study was funded a grant from Sanofi (20190412).

Results: Of 4,922 patients identified with RA in their primary care records, 95.7% (4,691/4,922) received csDMARD treatment. Over a third of patients (36.2%) were treated with bDMARDs (1,784/4,922).Of these biologic-naïve patients, 116 (6.5%) were treated with IL-6 inhibitors. Treatment with IL-6 bDMARDs was associated with previous history of infection (difference: 8.8%, 95% CI 1.1 to 17.8) and kidney disease (14.3% 95% CI 8.0 to 22.5). The rate of treatment failure was significantly higher in the non-IL-6 bDMARDs-treated patients (23.1%) compared to the IL-6 inhibitor treated individuals (18.1%) (difference: 9.4%, 95% CI: 1.1 to 15.7). Orthopaedic surgery pre-treatment and steroid use was associated with non-IL-6 bDMARDs treatment failure (HR: 1.64, 95% CI: 1.00 to 2.68; HR: 1.62, 95% CI: 1.26 to 2.08, respectively). Post-treatment infection rate was higher with non-IL-6 bDMARDs (difference: 10.5%, 95% CI: 3.7 to 19.0) than IL-6 bDMARDs. Orthopaedic surgery was also more common in non-IL-6 bDMARDs (difference: 9.9%, 95% CI: 4.1 to 13.3). No factor was found to be associated with treatment failure in the IL-6 inhibitor treated patients which may be due to fewer number of patients. 385 patients (23%) and 21 patients (18%) switched to alternative bDMARD from the non-IL-6 and IL-6 groups respectively. Of the 385 switchers from the non-IL6 bDMARD group, 298 patients (77.4%) received a second non-IL-6 bDMARDs and 87 patients received IL-6 bDMARDs (22.5%). Treatment failure in biologic-experienced patients was significantly higher in the IL-6 bDMARD treated group (difference: 28.3%, 95% CI: 17.6 to 39.3). The patient characteristics were not significantly different between the two groups.

Conclusion: Comorbidities, previous history of infection and previous history of kidney disease, were associated with choosing IL-6 bDMARDs in biologic naïve RA patients in Wales. IL-6 treated biologic-naïve patients were more likely to continue treatment than non-IL-6 biologic treated patients. The reverse is the case in biologic-experience patients.

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Abstract Number: 1325

Integrated Safety Analysis of Filgotinib in Patients with Moderate to Severe Active Rheumatoid Arthritis with a Maximum Exposure of 8.3 Years

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Filgotinib (FIL) is an oral Janus kinase 1 preferential inhibitor, approved for the treatment of moderate to severe active rheumatoid arthritis (RA). In previous analyses, comparable incidence of selected adverse events (AEs) occurred in FIL 200 mg (FIL200) and 100 mg (FIL100) dose groups, except for herpes zoster.[1] This analysis aimed to provide an update on FIL selected AEs up to a median (max) exposure of 3.8 (8.3) years.

Methods: Integrated FIL RA data from 7 clinical trials are reported: Phase 2 (NCT01888874, NCT01894516), Phase 3 (NCT02889796, NCT02873936, NCT02886728), and the long-term extension studies DARWIN 3 Phase 2 (NCT02065700) and FINCH 4 Phase 3 (NCT03025308). Exposure-adjusted incidence rates (EAIRs)/100 patient-years of exposure (PYE), censored at time of first event, were determined for major adverse cardiovascular event (MACE), venous thromboembolism (VTE), arterial systemic thromboembolism, nonmelanoma skin cancer (NMSC), malignancies excluding NMSC, herpes zoster, serious infections and deaths. Data were as of May 2, 2022 (DARWIN 3) and May 6, 2022 (FINCH 4). MACE and VTE only include positively adjudicated events with a data cutoff of April 3, 2022.

Table. Frequencies and EAIRs of selected AEs in parent and ongoing long-term extension RA clinical trials

	FIL100 (PYE= 4532.4) (n=1647)	FIL200 (PYE= 8008.6) (n=2267)
	n (%), EAIR per 100 PYE (95% CI)	
MACE*	22 (1.3), 0.49 (0.3, 0.7)	27 (1.2), 0.34 (0.2, 0.5)
VTE*	9 (0.5), 0.20 (0.1, 0.4)	15 (0.7), 0.19 (0.1, 0.3)
ASTE	1 (<0.1), 0.02 (0.0, 0.1)	1 (<0.1), 0.01 (0.0, 0.1)
NMSC	9 (0.5), 0.20 (0.1, 0.4)	27 (1.2), 0.34 (0.2, 0.5)
Malignancies (excluding NMSC)	30 (1.8), 0.66 (0.4, 0.9)	57 (2.5), 0.71 (0.5, 0.9)
Herpes zoster	49 (3.0), 1.10 (0.8, 1.5)	114 (5.0), 1.48 (1.2, 1.8)
Serious infections	97 (5.9), 2.18 (1.8, 2.2)	149 (6.6), 1.88 (1.6, 2.2)
All-cause mortality	26 (1.6), 0.57 (0.4, 0.8)	57 (2.5), 0.71 (0.5, 0.9)

*Positively adjudicated MACE/VTE.
AE, adverse event; ASTE, arterial systemic thromboembolism; CI, confidence interval; EAIR, exposure-adjusted incidence rate; FIL100/200, filgotinib 100/200 mg; MACE, major adverse cardiovascular event; NMSC, nonmelanoma skin cancer; PYE, patient-years of exposure; RA, rheumatoid arthritis; VTE, venous thromboembolism.

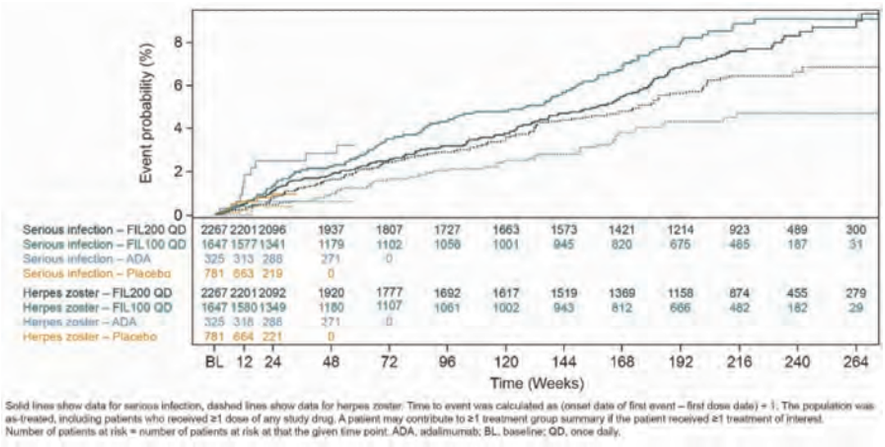

Figure. Event probability of serious infection and herpes zoster

Results: The as-treated population included 3691 patients with 12,541 PYE. Median (max) exposure was 3.8 (8.3) in the pooled FIL group; 3.8 (8.3) years for FIL200 and 3.3 (7.8) years for FIL100. Baseline demographics and disease characteristics were balanced between groups.[2] Small numerical differences were observed between FIL doses for EAIRs of selected AEs. Numerically higher incidences of NMSC, herpes zoster and all-cause mortality were reported with FIL200 vs FIL100; incidences of MACE and serious infections were numerically lower with FIL200 vs FIL100, with overlapping confidence intervals (**Table**). Over 240 weeks, the risks of MACE and VTE were comparable for FIL100 vs FIL200; low event numbers make interpretation difficult. The risk of herpes zoster was higher with FIL200 vs FIL100, and generally similar for serious infection or all-cause mortality (**Figure**).

Conclusion: Over a maximum of 8.3 years, FIL200 and FIL100 continued to show small numerical differences in EAIRs of selected AEs between dose groups in the overall RA population. Slightly higher incidence rates for NMSC, herpes zoster and all-cause mortality were reported in the FIL200 than FIL100 group, with a higher incidence of MACE and serious infections with the lower dose; confidence intervals overlapped between the dose groups.

References:

1. Winthrop KL, et al. Arthritis Rheumatol 2022;74(S9): abstract 0273
2. Winthrop KL, et al. Ann Rheum Dis 2022;81:184–92

Disclosure: K. Withrop: AbbVie, 2, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GSK, 2, Novartis, 2, Pfizer, 2, 5, Regeneron, 2, Roche, 2, Sanofi, 2, UCB, 2; **D. Aletaha**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Janssen, 2, 6, Lilly, 2, 5, 6, Merck, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6, Sandoz, 2, 6, Sanofi, 5, Sobi, 5; **R. Caporali**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celltrion, 2, 6, Fresenius Kabi, 2, Galapagos, 2, 6, Janssen, 2, 6, Lilly, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, Sandoz, 2, 6, UCB, 2, 6; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer-Ingelheim, 6, Chugai, 5, 6, Eisai, 5, 6, Eli Lilly, 6, Gilead, 6, GSK, 6, Mitsubishi-Tanabe, 5, Pfizer, 6, Taiho, 6, Taisho, 5, 6; **T. Takeuchi**: AbbVie, 2, 5, 6, AYUMI, 5, Bristol-Myers Squibb, 6, Chugai, 2, 5, 6, Daiichi Sankyo, 5, Eisai, 5, 6, Eli Lilly Japan, 2, 6, Gilead, 2, 6, Janssen, 6, Mitsubishi-Tanabe, 2, 5, 6, ONO, 5, Pfizer Japan, 6, Taiho, 2; **P. Van Hoek**: Galapagos, 7; **P. Stiers**: Galapagos, 3, 11; **V. Rajendran**: Galapagos, 3, 11; **K. Van Beneden**: Galapagos, 3, 11; **J. Gottenberg**: AbbVie, 2, BMS, 2, 5, Galapagos, 2, Gilead, 2, Lilly, 2, MSD, 2, Novartis, 2, Pfizer, 2, 5; **G. Burmester**: AbbVie, 2, 6, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Chugai, 6, Galapagos, 2, 6, Lilly, 2, 6, Pfizer, 2, 6, Sanofi, 2, 6.

Abstract Number: 1326

Safety and Efficacy of Upadacitinib in Patients with Rheumatoid Arthritis Refractory to Biologic DMARDs: Results Through Week 204 from the SELECT-CHOICE Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Treatments Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

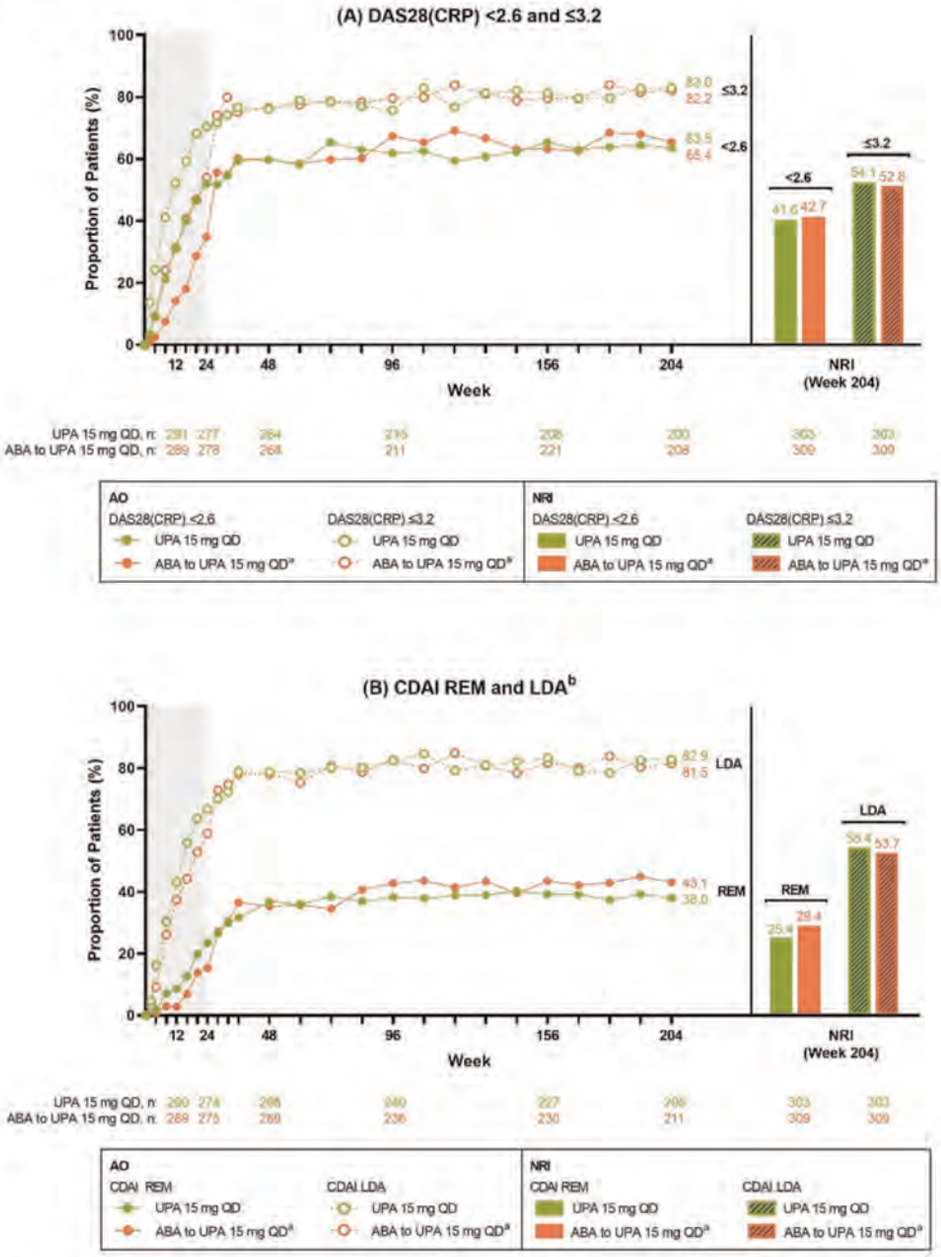
Background/Purpose: To evaluate the long-term safety and efficacy of upadacitinib (UPA), an oral JAK inhibitor, through week 204 in patients with RA from the long-term extension (LTE) of the SELECT-CHOICE study.

Methods: In SELECT-CHOICE (period 1: 24-week, phase 3, double-blind), RA patients refractory to biologic DMARDs were randomized to either upadacitinib 15 mg (UPA15) once daily or intravenous abatacept (ABA).[1] In period 2, open-label LTE patients initially randomized to ABA were switched to UPA15 at week 24, while patients initially randomized to UPA15 continued to receive UPA15 for up to 4 years. Efficacy endpoints, including patient-reported outcomes (PROs) through week 204, were analyzed using as observed (AO) and NRI for binary endpoints or descriptive statistics based on AO and mixed-effect model repeated measures (MMRM) for continuous endpoints. Treatment-emergent adverse events (TEAEs) are summarized through week 204.

Results: In total, 304 patients were randomized to UPA15; 278 (91.4%) patients completed week 24 and 277 (91.1%) continued to the LTE. Of the 309 patients randomized to ABA, 277 (89.6%) patients completed week 24 and entered the LTE. Of the patients who entered the LTE on UPA15 (n=547), 151 (27.6%) patients discontinued UPA15 treatment, with the most common reasons being adverse event (9.1%), withdrawal of consent (5.9%), and other reason(s) (7.3%). Of patients on continuous UPA15, a high proportion achieved DAS28(CRP) < 2.6 or ≤3.2, which was maintained or further improved through week 204 (< 2.6: 63.5%; ≤3.2: 83.0%) (AO) (**Figure 1A**). Greater than one-third of patients achieved CDAI remission (38.0%) and over 80% achieved LDA (82.9%) at week 204 (AO) (**Figure 1B**); similarly, 36.5% of patients achieved SDAI remission and 82.2% achieved LDA (AO) (**Table 1**). At week 204, 90%/75%/58% of patients achieved ACR20/50/70 responses (AO). Boolean remission was achieved at week 204 by 26.7% (95% CI: 20.7, 32.7) of patients (AO); more conservative estimates using NRI showed similar results (19.1% [14.7, 23.6]). Mean change from baseline in HAQ-DI was -0.84 and the patient's assessment of pain was -44.7 at week 204 (AO). Across all efficacy endpoints, similar results were observed in patients who switched from ABA to UPA15, compared to those who continued UPA15. Patients with an inadequate response to ≥1 prior anti-TNF (UPA15: n=263; ABA to UPA15: n=273) showed similar responses to the overall population (data not shown). No new safety risks were identified with long-term exposure to UPA15 in patients with RA through week 204 (**Table 2**). A total of 24 deaths occurred; 18 deaths were treatment-emergent, of which 9 were related to COVID-19.

Conclusion: Efficacy responses with UPA15 were maintained over time, including DAS28(CRP) < 2.6 and ≤3.2, CDAI and SDAI remission and LDA, ACR20/50/70 responses, and PRO outcomes.[1] The safety profile of UPA through week 204 is consistent with previous findings[1] and the broader RA clinical program. These data further support the long-term safety and efficacy of UPA for the treatment of patients with RA.

Figure 1. Proportion of Patients Achieving **(A)** DAS28(CRP) <2.6 or ≤3.2 and **(B)** CDAI REM or LDA Through Week 204 (AO, NRI)



ABA, abatacept; AO, as observed; LDA, low disease activity; QD, once daily; REM, remission; UPA, upadacitinib.
[a]Patients randomized to ABA were switched to UPA 15 mg QD at week 24; shading indicates treatment with ABA.
[b]CDAI REM defined as ≤2.8; CDAI LDA defined as ≤10.

Table 1. Efficacy Endpoints at Week 204 With UPA15 or ABA Switched to UPA15 (AO, NRI or MMRM)

Endpoint	UPA 15 mg QD		ABA to UPA 15 mg QD[a]	
Proportion of patients, % (95% CI)	AO	NRI	AO	NRI
SDAI LDA (≤11), n	197 82.2 (76.9, 87.6)	303 53.1 (47.5, 58.8)	208 82.2 (77.0, 87.4)	309 53.4 (47.8, 59.0)
SDAI remission (≤3.3), n	197 36.5 (29.8, 43.3)	303 23.4 (18.7, 28.2)	208 38.9 (32.3, 45.6)	309 26.2 (21.3, 31.1)
ACR20, n	208 89.9 (85.8, 94.0)	303 59.4 (53.9, 64.9)	210 89.5 (85.4, 93.7)	309 58.3 (52.8, 63.8)
ACR50, n	208 75.0 (69.1, 80.9)	303 49.8 (44.2, 55.5)	209 75.1 (69.3, 81.0)	309 49.5 (43.9, 55.1)
ACR70, n	207 57.5 (50.8, 64.2)	303 38.6 (33.1, 44.1)	208 58.2 (51.5, 64.9)	309 38.5 (33.1, 43.9)
Change from baseline, mean (95% CI)	Descriptive (AO)	MMRM (AO)	Descriptive (AO)	MMRM (AO)
HAQ-DI, n	207 -0.84 (-0.94, -0.74)	303 -0.76 (-0.84, -0.67)	210 -0.91 (-1.02, -0.81)	306 -0.78 (-0.86, -0.70)
Patient's assessment of pain, n	208 -44.7 (-48.7, -40.6)	303 -42.5 (-45.4, -39.5)	210 -50.3 (-54.3, -46.2)	306 -45.6 (-48.5, -42.6)

ABA, abatacept; AO, as observed; CI, confidence interval; LDA, low disease activity; MMRM, mixed effect model repeated measurement; QD, once daily; UPA, upadacitinib.
[a]Patients randomized to ABA were switched to UPA 15 mg QD at week 24.

Table 2. TEAEs in Patients Treated With UPA15 Through Week 204[a]

E/100 PY (95% CI)	UPA 15 mg QD[b] n=579; PY=1833.3
Overall TEAEs	
Any AE	226.1 (219.3, 233.1)
Any serious AE	12.8 (11.2, 14.5)
Any AE leading to discontinuation of study drug	4.2 (3.3, 5.2)
All deaths[c]	1.3 (0.8, 1.9)
≤30 days after last dose of study drug	1.0 (0.6, 1.6)
>30 days after last dose of study drug	0.3 (0.1, 0.7)
TEAEs and AEs of Special Interest	
Any infection	72.7 (68.9, 76.7)
Serious infection	3.5 (2.7, 4.5)
Opportunistic infection[d]	0.2 (0.0, 0.5)
Herpes zoster	4.0 (3.2, 5.1)
COVID-19	8.8 (7.5, 10.3)
COVID-19 related AE	9.7 (8.3, 11.2)
GI perforation (adjudicated)	<0.1 (0.0, 0.3)
CPK elevation	4.3 (3.4, 5.4)
Malignancies (excluding NMSC)	0.8 (0.5, 1.3)
NMSC	0.4 (0.2, 0.8)
MACE (adjudicated)[e]	0.3 (0.1, 0.6)
VTE (adjudicated)[f]	0.4 (0.2, 0.8)

ABA, abatacept; AE, adverse event; CI, confidence interval; CPK, creatine phosphokinase; E, event; GI, gastrointestinal; LTE, long-term extension; NMSC, nonmelanoma skin cancer; PY, patient-year; QD, once daily; TEAE, treatment-emergent adverse event; UPA, upadacitinib.
[a]TEAEs are defined as any AE with onset on or after the first dose of study drug and ≤30 days after the last dose of study drug.
[b]Includes patients who started on UPA 15 mg and patients who switched from ABA to UPA 15 mg at week 24; one patient was randomized to UPA 15 mg but was never treated and one patient randomized to ABA entered the LTE but was never treated with UPA 15 mg.
[c]Includes non-treatment emergent deaths; a total of 24 deaths occurred (18 were treatment-emergent, of which 9 were COVID-19 related; 6 were non-treatment emergent, of which 1 was COVID-19 related).
[d]Excludes tuberculous and herpes zoster infections; no cases of tuberculosis were reported.
[e]MACE defined as non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death.
[f]VTE includes deep vein thrombosis (DVT) and pulmonary embolism (PE).

Reference:

1. Rubbert-Roth A, et al. *N Engl J Med*. 2020;383:1511-21.

Disclosure: A. Rubbert-Roth: AbbVie/Abbott, 2, 6, Amgen, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, 6; **K. Kato**: AbbVie/Abbott, 3, 11; **B. Haraoui**: AbbVie/Abbott, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **M. Rischmueller**: AbbVie/Abbott, 2, 5, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 5, GlaxoSmithKlein(GSK), 5, Janssen, 5, Novartis, 2, 5, 6, Recordati Rare Diseases, 2, 6, Servier, 5, UCB, 5; **Y. Liu**: AbbVie/Abbott, 3, 11; **N. Khan**: AbbVie, 3, 11; **H. Camp**: AbbVie, 3, 11; **R. Xavier**: AbbVie, 2, 6, AstraZeneca, 2, 6, Janssen, 2, 6, Organon, 2, 6, UCB Pharma, 2, 6.

Abstract Number: 1327

Effects of Long-Term Low Dose Glucocorticoid Treatment for Rheumatoid Arthritis on Body Weight and Blood Pressure: A Pooled Analysis of Individual Patient Data from Five Randomised Trials

Andriko Palmowski[1], Sabrina Mai Nielsen[2], Zhivana Boyadzhieva[3], Linda Hartman[4], Judith Oldenkott[5], Björn Svensson[6], Ingiäld Hafström[7], Siegfried Wassenberg[8], Ernest Choy[9], John Kirwan[10], Robin Christensen[11], Maarten Boers[12] and Frank Buttgereit[13], [1]Charité - Universitätsmedizin Berlin, Berlin, Germany, [2]The Parker Institute, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark, [3]Charité Universitatsmedizine - Berlin, Berlin, Germany, [4]Amsterdam University Medical Centers, Amsterdam, Netherlands, [5]Charite - University Medicine Berlin, Berlin, Germany, [6]Lund University, Lund, Sweden, [7]Karolinska Institutet, Stockholm, Sweden, [8]Rheumazentrum Ratingen, Ratingen, Germany, [9]Section of Rheumatology, Cardiff University, Cardiff, United Kingdom, [10]University of Bristol, Bristol, United Kingdom, [11]Musculoskeletal Statistics Unit, The Parker Institute, Copenhagen, Denmark, [12]Amsterdam UMC, Vrije Universiteit, Amersfoort, Netherlands, [13]Charité Universitätsmedizin, Dept. Rheumatology, Berlin, Germany

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Treatments Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: High-dose glucocorticoids (GCs) can cause weight gain and hypertension. It is unclear whether GCs at ≤7.5mg/day prednisone equivalent ("low dose"), administered for rheumatoid arthritis (RA), do as well. Prior studies could not definitively answer this research question: Observational studies are confounded by indication, and individual randomized trials are usually underpowered for small safety signals. The objective was to assess the effects of long-term treatment with low dose GCs in RA on body weight and blood pressure by pooling individual patient data from randomized trials.

Methods: Data from five randomised controlled trials with two-year interventions were pooled.[1-5] Intervention groups received GCs at a dose of ≤7.5mg/day prednisone equivalent. Co-primary outcomes were the difference in change from baseline in a) body weight (kg) and b) mean arterial blood pressure (MAP; mmHg). A secondary outcome was difference in the change of number of administered antihypertensive drugs. Several sensitivity and subgroup analyses were conducted. All analyses were based on analyses of covariance, trial ID was included as a random effects factor to account for clustering of patients within trials. Multiple imputation was used to account for missing data under the Intention-To-Treat approach. No imputations were performed for trials with no data collected or available for the given outcome. A detailed prespecified protocol (dx.doi.org/10.17504/protocols.io.x54v9y4d1g3e/v1) with a gatekeeping procedure for statistical testing was followed. All trials originated in Europe (twelve countries), and all allowed concomitant treatment with disease-modifying antirheumatic drugs.

Results: 1,112 participants were included (mean ± SD age 61 ± 15 years; 68% female). A mean DAS28 of 4.87 ± 1.16 indicates moderate disease activity at baseline. Disability was moderate to severe with a median (interquartile range) health assessment questionnaire score of 1.38 (0.80; 2.25). 64% and 67% of patients with available data were ACPA and

Table. Changes in weight and mean arterial blood pressure in GC and control groups over two years.

Table. Bone mineral density and trabecular bone score in PPI users and non-users.

	PPI use	No PPI use	Contrast	P-value
Crude (unadjusted)				
Left femoral neck T-score	-1.24 (-1.36 to -1.13)	-1.01 (-1.12 to -0.89)	-0.24 (-0.11 to -0.37)	<0.001
Lumbar spine T-score	-0.87 (-1.06 to -0.69)	-0.64 (-0.79 to -0.48)	-0.23 (-0.05 to 0.42)	0.01
Trabecular bone score	1.28 (1.24 to 1.31)	1.30 (1.26 to 1.33)	-0.02 (-0.06 to 0.02)	0.35
Adjusted				
Left femoral neck T-score	-1.24 (-1.36 to -1.13)	-1.08 (-1.27 to -0.88)	-0.17 (-0.35 to 0.01)	0.07
Lumbar spine T-score	-0.87 (-1.06 to -0.69)	-0.62 (-0.83 to -0.41)	-0.25 (-0.47 to -0.04)	0.02
Trabecular bone score	1.28 (1.24 to 1.31)	1.27 (1.24 to 1.31)	0.00 (-0.04 to 0.04)	0.97

Numbers are estimated marginal means and 95% confidence intervals.

rheumatoid factor positive, respectively, and the median (interquartile range) disease duration was 1 year (0.42; 7). Most patients (44%) were never smokers. Baseline values for weight and MAP were 73kg ± 14 and 98mmHg ± 12; median number of antihypertensive drugs was 0 (interquartile range 0; 1). After two years, patients on GCs gained mean 1.1kg (95%CI 0.5 to 1.8; $p < 0.001$; **Table**) more weight than patients in the control groups. Both groups increased MAP by 2-3mmHg, without difference between the groups (–0.4; 95% CI –3.0 to 2.2 mm Hg; $p = 0.19$; **Table**). The change in number of antihypertensive drugs was low and similar in both groups. Results were consistent across sensitivity and subgroup analyses focusing on overweight or hypertensive patients, and when comparing GCs at 5mg/d with 7.5mg/d (data not shown).

Conclusion: We present robust evidence that low dose GCs, taken over two years for the treatment of RA, lead to about one additional kg of weight gain but do not cause changes in blood pressure.

References: 1 Boers et al. Ann Rheum Dis 2022 2 Kirwan et al. NEJM 1995 3 Choy et al. Ann Rheum Dis 2005 4 Wassenberg et al. Arthritis Rheumatol 2005 5 Svensson Arthritis Rheumatol 2005

Disclosure: A. Palmowski: None; **S. Nielsen**: None; **Z. Boyadzhieva**: None; **L. Hartman**: None; **J. Oldenkott**: None; **B. Svensson**: None; **I. Hafström**: None; **S. Wassenberg**: AbbVie/Abbott, 6, Eli Lilly, 2, 6, Galapagos, 2, Medac, 6, Merck/MSD, 6, Pfizer, 5, 6, UCB, 2; **E. Choy**: AbbVie, 2, 6, Amgen, 2, 6, Bio-Cancer, 5, Biogen, 2, 5, Chugai Pharma, 2, 6, Eli Lilly, 2, 6, Fresenius Kabi, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Janssen, 2, Novartis, 5, Pfizer, 5, 6, R-Pharm, 2, Sanofi, 2, 5, 6, Sanofi-Genzyme, 2, UCB, 2; **J. Kirwan**: None; **R. Christensen**: None; **M. Boers**: Celltrion, 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **F. Buttgereit**: AbbVie/Abbott, 6, Horizon Therapeutics, 5, Pfizer, 5, 6, Roche, 6.

Abstract Number: 1328

Switching Biologics or Janus Kinase Inhibitors Is Effective in Difficult-to-treat Rheumatoid Arthritis, Regardless of Inflammation

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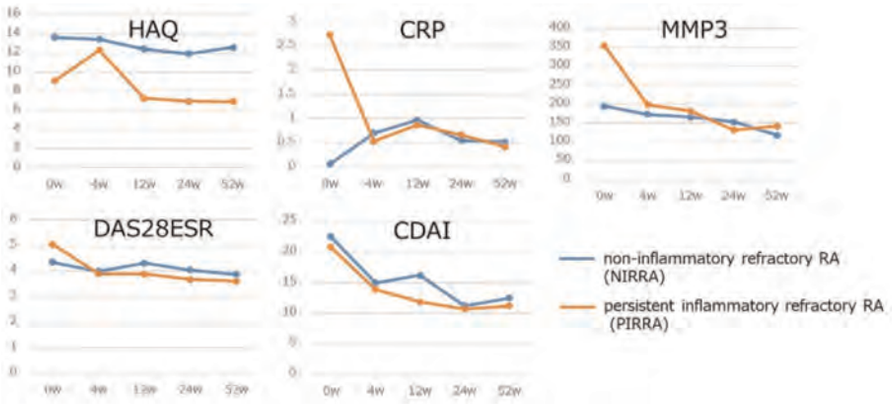
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Although biologics (BIO) or Janus kinase inhibitors (JAKi) have improved treatment for rheumatoid arthritis (RA), there are patients with difficult disease activity control even after using several BIO/JAKi, that is difficult-to-treat rheumatoid arthritis (D2TRA). D2TRA can be divided to two groups by mechanism: persistent inflammatory refractory RA (PIRRA) and non-inflammatory refractory RA with only persistent pain (NIRRA). We investigated these two different types of D2TRA.

Methods: Total of 147 patients switched to another BIO/JAKi because of inadequate response to previous BIO/JAKi and considered as D2TRA in our institution as of 2021. Patients with negative CRP and tender joint count > swollen joint count was defined as NIRRA, otherwise was defined as PIRRA. We investigated clinical characteristics and efficacy of following BIO/JAKi in both types of D2TRA for 52 weeks.

Results: Compared to NIRRA (n=33), PIRRA (n=114) showed significantly low hemoglobin (12.9 vs 12.0, p=0.02) and high DAS28ESR (4.43 vs 5.25, p=0.003) at the time of switching (baseline). There was no significant difference in MMP3 and CDAI. Retention rate at 52w also showed no difference (51.5% vs 45.6%, p=0.48). MMP3 and CDAI significantly improved during 52w in NIRRA, whereas CRP, MMP3, DAS28ESR, CDAI, and HAQ significantly improved in PIRRA. Switched BIO/JAKi consisted of IL6 inhibitors (n=7) and JAKi (n=15) in NIRRA, IL6 inhibitors (n=24) and JAKi (n=70) in PIRRA. Efficacy of switched BIO/JAKi showed no difference regardless of mechanism in both NIRRA and PIRRA.

Conclusion: MMP3 and CDAI improved after switching both in NIRRA and PIRRA. This tendency was similar whichever following BIO/JAKi was IL6 inhibitors and JAKi. Switching BIO/JAKi was effective in both types of D2TRA.



The clinical characteristics and efficacy of BIO/JAKi after switching in two types of D2TRA

Disclosure: K. Onishi: None; **Y. Yamada**: None; **T. Okano**: None; **K. Mamoto**: None; **S. Anno**: None; **T. Koike**: None; **H. Nakamura**: None.

Abstract Number: 1329

R851, a Potent Second Generation IRAK1 and IRAK4 Inhibitor Suppresses IL-6 in Vitro and in Vivo for the Treatment of Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The Toll-Like Receptor family (except TLR3) signal through IRAK4 and IRAK1 to produce an array of cytokines (including IL-6, IL-23 and TNFα in response to pathogen and damage associated molecular patterns (PAMPs and DAMPs).The IRAK proteins are also involved in the signaling cascade of the IL-1 receptor family; therefore, they play a critical role in innate immune response controlling chronic inflammation. As a result, inhibition of IRAK4 has been investigated as a means of attenuating a range of autoimmune diseases including rheumatoid arthritis, with zimlovisertib demonstrating encouraging results in a Phase 2 rheumatoid arthritis study. We identified R835, which has shown proof of mechanism in an LPS challenge study in healthy human volunteers. In this study we report an improved molecule R851 which has been modeled to require five-fold lower dosing for similar efficacy making it suitable for chronic indications such as rheumatoid arthritis.

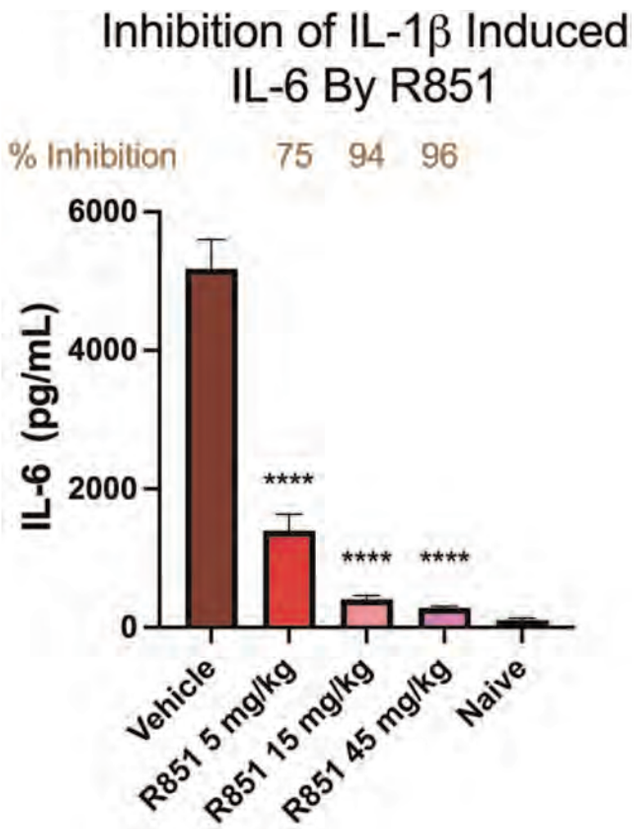

Fig A. The effect of R851 on inhibition of IL-6 production after stimulation with IL-1 in Balb/c mice.

Methods: Prioritizing inhibition of TLR signaling in a cell-based assay in conjunction with IRAK4 biochemical inhibition, we identified a series of potent and selective dual IRAK1 and IRAK4 inhibitors. The results suggested that dual IRAK1/4 inhibition results in a more effective inhibition of TLR signaling than IRAK4 alone. Having identified R835, we undertook a retrospective analysis of our IRAK1/4 inhibitor portfolio to identify R851.

Results: Our first molecule R835, currently being developed for low-risk myelodysplastic syndrome, demonstrated robust efficacy in a number of animal models including a collagen induced arthritis model.R835 not only inhibited disease when dosed prophylactically but also reversed symptoms when dosing was initiated after onset of disease. In the clinic, R835 showed dose-dependent, linear PK and proof of mechanism in humans. While R835 is a promising IRAK1/4 inhibitor with clinical potential, we hoped to identify an alternative molecule with favorable pharmacokinetic characteristics and increased potency for chronic autoimmune indications such as rheumatoid arthritis. A retrospective analysis of the data from the IRAK1/4 inhibitors generated over the program led to R851, a molecule from the R835 scaffold that showed improved potency in both cellular and biochemical assays. Further, R851 demonstrated 7-10 fold improvement in potency in our whole blood assays, driven by reduced plasma protein binding. Building on our understanding of the scaffold we expect R851 to require 5-fold less exposure for a similar effect to R835.The compound has been taken through PK studies across species demonstrating a dose-dependent, linear and predictable PK profile in multiple day dosing. In vivo, R851 shows a robust inhibition of IL-6 after IL-1β stimulation (**Fig. A**) which is expected to translate into efficacy in chronic models.

Conclusion: Using the knowledge gained in the development of R835, we have identified R851 as a second generation dual IRAK1 and IRAK4 inhibitor. The increased potency in whole blood assays is believed to be driven by a reduction in protein binding. We predict that R851 will require a significantly lower exposures for efficacy in humans which should position this molecule for a chronic condition like rheumatoid arthritis.

Disclosure: Y. Chen: Rigel Pharmaceuticals, Inc, 3; **S. Yi**: Rigel Pharmaceuticals, Inc, 3; **V. Markovtsov**: Rigel Pharmaceuticals, Inc, 3; **B. Samant**: Rigel Pharmaceuticals, Inc, 2; **A. Chow**: Rigel Pharmaceuticals, Inc, 3; **E. Masuda**: Rigel Pharmaceuticals, Inc, 3; **S. Shaw**: Rigel Pharmaceuticals, Inc, 3.

Abstract Number: 1330

Certolizumab-pegol, Abatacept, Tocilizumab or Active Conventional Therapy in Early Rheumatoid Arthritis: 48 Week Patient-reported Outcomes of the NORD-STAR Trial

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Treatments Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: The optimal first-line treatment of patients with early rheumatoid arthritis (eRA) is not established.

Methods: In this investigator-initiated, randomized, open-label study (NCT01491815), patients with treatment-naïve eRA with DAS28 >3.2 and RF+/ACPA+/CRP >10mg/L, were randomized 1:1:1:1 to methotrexate (MTX) combined with: 1) oral prednisolone (tapered quickly; discontinued at w36); or: sulphasalazine, hydroxychloroquine and mandatory intra-articular (IA) glucocorticoid injections in swollen joints (ACT); 2) certolizumab-pegol (CZP); 3) abatacept (ABA) or 4) tocilizumab (TCZ). IA glucocorticoid was allowed in all arms except during w20-24 and w44-48. The primary outcome Clinical Disease Activity Index (CDAI) remission and key secondary outcomes at 24 weeks have previously been published (Hetland ML et al, BMJ 2020;371:m4328). Differences between ACT and each of the 3 biological therapies for PRO (pain, patient´s global assessment, HAQ-DI, fatigue (VAS and FACIT) at 48 weeks were tested and descriptive data presented with 95% CI. Longitudinal data points were analyzed using a linear mixed model analysis. The continuous and dichotomous PRO data were adjusted for country, sex and anti-citrullinated protein antibody status. For continuous data, additional adjustment included baseline values of PRO endpoint and treatment arm and time as well as their interaction as categorical covariates.

Table 1. Baseline characteristics for clinical data and 48-week values for selected PROs.

Demographics/baseline characteristics		ACT (n=200)	CZP+MTX (n=203)	ABA+MTX (n=204)	TCZ+MTX (n=188)[§]
Age (y)		55 (15)	55 (15)	55 (14)	52 (15)
Women, %		139 (70%)	139 (69%)	140 (69%)	129 (69%)
Time since diagnosis, days		13 (21)	12 (17)	16 (34)	16 (33)
Anti-CCP/RF positive, %		82% / 76%	82% / 73%	83% / 78%	82% / 72%
CDAI		28.7 (12.1)	27.9 (12.4)	28.6 (11.3)	26.6 (11.7)
Baseline and 48 week values for selected PROs[#] (ITT-population)					
Pain (VAS, mm)	0 weeks	56.4 (53.9, 58.9)	56.4 (54.0, 58.9)	56.5 (54.0, 58.9)	56.1 (53.5, 58.7)
	48 weeks	19.1 (16.4, 21.8)	**13.7 (11.1, 16.4)**	**13.5 (10.9, 16.0)**	**13.5 (10.6, 16.3)**
Patient´s Global assessment of disease activity (VAS, mm)	0 weeks	57.5 (54.9, 60.1)	57.5 (54.9, 60.1)	57.5 (55.0, 60.1)	57.1 (54.4, 59.8)
	48 weeks	19.9 (17.1, 22.7)	16.0 (13.2, 18.7)	15.6 (12.9, 18.2)	16.2 (13.3, 19.1)
HAQ-DI	0 weeks	1.04 (0.99, 1.09)	1.04 (0.99, 1.09)	1.04 (0.99, 1.09)	1.03 (0.98, 1.08)
	48 weeks	0.30 (0.25, 0.35)	0.27 (0.22, 0.32)	0.27 (0.22, 0.32)	0.23 (0.17, 0.28)
Fatigue (VAS, mm)	0 weeks	51.6 (48.6, 54.6)	51.6 (48.6, 54.6)	51.5 (48.6, 54.5)	51.0 (47.9, 54.2)
	48 weeks	25.8 (22.5, 29.0)	20.4 (17.2, 23.5)	20.7 (17.6, 23.8)	19.8 (16.4, 23.2)
Fatigue, FACIT score	0 weeks	18.3 (17.5, 19.1)	18.3 (17.6, 19.1)	18.3 (17.6, 19.1)	18.3 (17.5, 19.1)
	48 weeks	12.2 (11.3, 13.0)	11.5 (10.6, 12.3)	11.2 (10.4, 12.1)	11.3 (10.4, 12.2)

[#]Values are mean (95% CI), if not otherwise indicated, adjusted for country, sex, anti-citrullinated protein antibody status and baseline values of respective PRO endpoint. Bold values show non-overlapping 95% CI vs ACT. ITT: Intention-to-treat population.

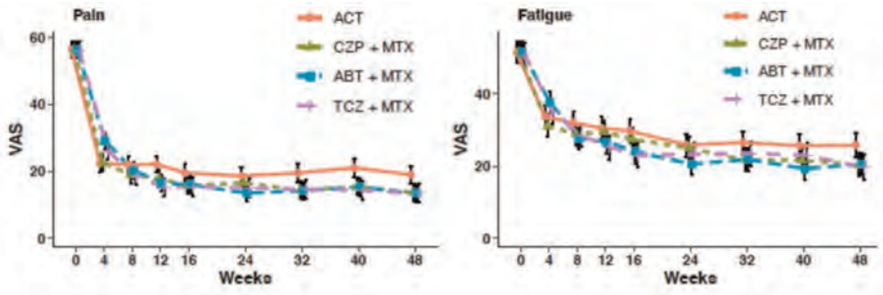

Figure 1. Longitudinal values of pain and fatigue stratified by treatment arms. The values are mean (95% CI)

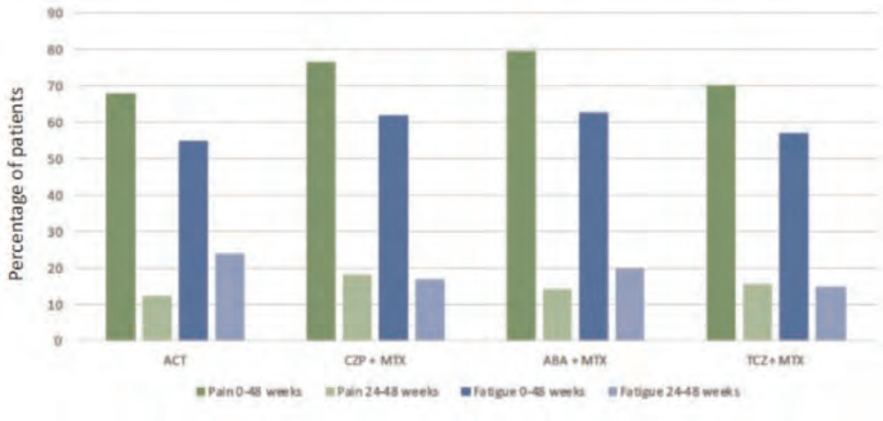

Figure 2. Patients reporting improvement ≥ Minimal Clinical Important Difference for pain and fatigue

MCID for pain and fatigue were defined as: ≥ 10-point decrease for VAS pain (Strand V et al; J Rheumatol 2011;38;1720-7) and ≥10-point decrease for VAS Fatigue (Wells et al, J Rheumatol 2007:34(2);280-9), respectively.

Results: 812 patients were randomized. Baseline characteristics and adjusted baseline and 48-week PRO data are shown in table 1. In the longitudinal analysis there was a trend for greater improvement of pain and fatigue in biological groups compared to ACT (figure 1). Adjusted for baseline values, pain levels and physician global assessment were numerically lower in all biological groups compared to ACT at week 48. The percentage of patients reporting improvements above MCID for pain and fatigue (from baseline until 48 weeks) were numerically higher in biological arms compared to ACT (% and 95% CI), as follows: MCID for pain: ACT 68% (61, 74); CZP+MTX 77% (71, 82); ABA+MTX 80% (74, 85); TCZ+MTX 70% (64, 77); and for fatigue: ACT 55% (48, 62); CZP+MTX 62% (55, 69); ABA+MTX 63% (56, 69); TCZ+MTX 57% (59, 64) (figure 2).

Conclusion: All four different modes of action lead to marked improvements of PROs after 48 weeks. Compared with csDMARD+glucocorticoid treatment pain levels were lower in all biological arms at week 48. Likewise, the percentages of patients with clinically important improvements for pain and fatigue were numerically higher in the treatment arms with biological vs. conventional treatment.

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2, 5, 6, Amgen, 5, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Hospira, 2, 6, Janssen, 2, 6, MEDAC, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Novo Nordisk, 2, 6, Orion, 2, 6, Pfizer, 2, 6, Regeneron, 2, 6, Roche, 2, 6, Sandoz, 2, 6, Sanofi, 2, 6, UCB, 2, 6; **A. Rudin**: AstraZeneca, 12, financial support; **M. Schrumpf Heiberg**: Roche, 6; **M. Nurmohamed**: None; **B. Gudbjornsson**: Nordic-Pharma, 6, Novartis, 2, 6; **K. Lend**: None; **K. Hørslev-Petersen**: None; **T. Sokka-Isler**: None; **G. Grondal**: None; **S. Krabbe**: None; **J. Lindqvist**: None; **A. Hultgård Ekwall**: AbbVie/Abbott, 1, 2, Boehringer-Ingelheim, 6, Pfizer, 1; **D. Glinatsi**: Eli Lilly, 1, 6; **M. Kapetanovic**: None; **C. Gentline**: None; **A. Aga**: AbbVie, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **H. Relas**: None; **T. Lorenzen**: None; **G. Cagnotto**: Bristol-Myers Squibb(BMS), 5, UCB, 5; **J. Back**: None; **O. Hendricks**: AbbVie/Abbott, 6, Eli Lilly, 6, Novartis, 6, Pfizer, 6; **B. Dijkshoorn**: Galapagos, 2, Novartis, 2; **K. Öberg**: None; **M. Ljoså**: AbbVie/Abbott, 1, 12, Advisory board fee; **E. Brodin**: None; **H. Lindegaard**: None; **A. Söderbergh**: None; **M. Rizk**: None; **A. Kastbom**: None; **P. Larsson**: None; **L. Uhrenholt**: None; **S. Just**: None; **D. Stevens**: UCB, 1; **T. Laurberg**: None; **G. Bakland**: UCB, 2; **I. Olsen**: None; **J. Sexton**: None; **T. Uhlig**: Galapagos, 2, 6, Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6.

Abstract Number: 1331

Long-term Effectiveness of a Lifestyle Program for Rheumatoid Arthritis: One-year Follow-up of the "Plants for Joints" Randomized Clinical Trial

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The 16-week Plants for Joints (PFJ) multidisciplinary lifestyle program, based on a whole-food plant-based diet, physical activity, and stress management, significantly reduced 28-joint Disease Activity Score (DAS28) compared to usual care in people with rheumatoid arthritis (RA).[1,2] The objective was to determine the long-term effectiveness of the PFJ lifestyle program on disease activity in people with RA.

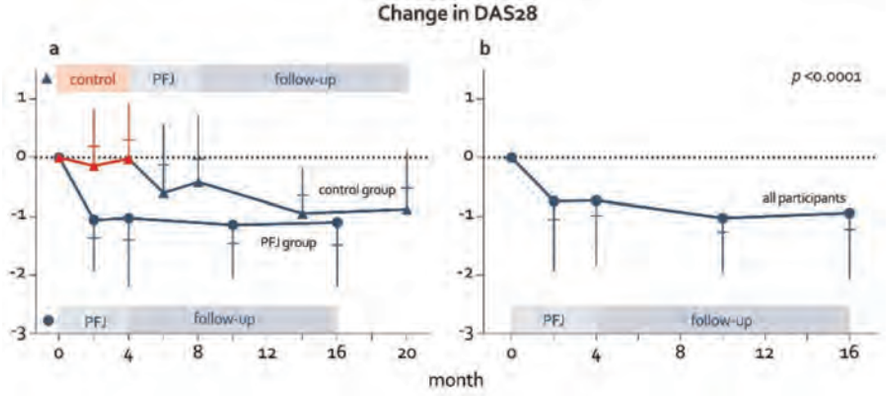

Figure 1. Mean change in DAS28 (a) during the randomized controlled trial phase and one-year follow-up period per trial arm and (b) for the whole cohort before and after completing the lifestyle intervention and one year follow-up.

Table 1. Plants for Joints cohort at start and end of the 16-week intervention period as well as during the one year extension study (6 and 12 months after completing the intervention). Continuous variables reported as mean (SD) when normally distributed or as median [IQR] when skewed. Within-group difference shown between start of the lifestyle intervention and end of the 12-month follow-up determined using the linear-mixed model when model assumptions were met. For variables in which model assumptions were not met (†) a linear-mixed model was performed after log transformation and within group differences were reported as median difference of complete paired values determined using a Wilcoxon test (p-values from the linear mixed model are shown, all were similar to the Wilcoxon test). ESR = Erythrocyte sedimentation rate.

	Intervention			Extension study		Within group	
	Start	Halfway	End	6 months	12 months	difference (95% CI)	*p-value*
n=	77	77	77	69	65		
Rheumatologic measures							
DAS28	3.85	3	3.09	2.79	2.84	−0.9 (−1.2 to −0.7)	<0.0001
Swollen joint count	1	0	0	0	0	−0.9 (−1.7 to −0.1)	0.02
Tender joint count	3	1	1	1	1	−1.6 (−2.5 to −0.7)	<0.001
General health (VAS)	52	29	26	23	22	−24 (−30 to −19)	<0.0001
ESR (mm/hour)	15	12	14	12	12	-2.5 (-5.0 to -0.5)†	0.02
Inflammation							
C-reactive protein (mg/l)	2.4	2.7	2.1	1.7	1.6	-1.0 (−1.8 to −0.45)†	0.005
Anthropometric measurements							
Weight (kg)	74.5	72.2	71.5	73.1	74.6	−0.3 (−1.2 to 0.4)	0.5
Body mass index (kgm−1)	26.3	25.4	25.2	25.9	26.1	−0.1 (−0.4 to 0.2)	0.5
Waist circumference (cm)	91	88	87.6	89	89.8	−1.4 (−2.6 to −0.1)	0.03
Metabolic markers							
HbA1c (mmol/mol)	36.9	36.4	36	36.8	36.5	−0.3 (−0.9 to 0.2)	0.2
Fasting blood glucose (mmol/l)	5.1	4.9	4.9	5.1	4.9	−0.0 (−0.2 to 0.1)	0.7
LDL-cholesterol (mmol/l)	3.1	2.6	2.7	2.8	2.9	−0.1 (−0.2 to 0.0)	0.04
HDL-cholesterol (mmol/l)	1.6	1.5	1.6	1.6	1.7	0.0 (0.0 to 0.1)	0.2
Triglycerides (mmol/l)	1.1	1.1	1	1	1	-0.0 (−0.1 to 0.1)†	0.6
Systolic blood pressure (mmhg)	134	130	128	133	134	0.7 (−2.5 to 3.8)	0.7
Diastolic blood pressure (mmhg)	86	85	84	85	86	−0.4 (−3.1 to 2.2)	0.8

Methods: In the PFJ assessor-blind randomized clinical trial, people with RA (DAS28 ≥ 2.6 and ≤ 5.1) were randomized to receive the PFJ program in addition to usual care, or the control group which received usual care. After this 16-week period the control group also received the program. After completion of the program all participants were followed-up for one year with biannual visits and six adherence-promoting webinars. Participants with a DAS28 < 2.6 were instructed to taper antirheumatic medication following a pre-specified protocol. Medication changes were assessed at one year as an "increase," "stable," or "decrease" compared to baseline by an independent committee. Secondary outcomes included anthropometric and metabolic markers. An intention-to-treat analysis with a linear mixed model was used to analyze within-group differences.

Results: 65 (84%) of the 77 participants, who completed the initial 16-week clinical trial, completed the one-year follow-up. 92% of participants were female with a mean (SD) age of 55 (12) and body mass index of 26 (4) kg/m^2. In the year after the PFJ program the DAS28 continued to improve slightly whereby a within-group difference of –0.9 points was observed after one year compared to baseline ($p < 0.0001$) (Figure 1). All components of the DAS28 improved significantly compared to baseline (Table 1). Of the 56 participants who completed the follow-up and used disease modifying anti-rheumatic medication, 27 (48%) decreased or stopped, 16 had stable, and 13 had increased medication. 45 participants (58%) improved DAS28 scores (20 with DAS28 < 2.6) with stable or less medication compared to baseline. After the 1-year follow-up period waist circumference, LDL cholesterol, and CRP remained significantly lower than baseline values, although there was no longer a significant difference in weight or HbA1c.

Conclusion: The PFJ lifestyle program significantly decreased disease activity in people with RA and its effects were sustained till one year after program completion with on average slightly less antirheumatic medication. Metabolic benefits found after the lifestyle intervention were only partially sustained, possibly indicating attenuated adherence to the program in the follow-up.

References 1. Walrabenstein, Trials 2021 2. Walrabenstein, Rheumatology 2023

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Abstract Number: 1332

Patient-Reported Outcomes, Disease Activity and Safety in 798 Patients with RA Treated with Filgotinib: Up to 1-Year Interim Results from a Prospective Observational Study (FILOSOPHY)

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Treatments Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: The efficacy of filgotinib (FIL) for treating RA has been demonstrated in clinical trials. Real-world data are valuable to assess patient-reported outcomes such as pain, fatigue and work productivity, which are negatively impacted by RA.

Methods: FILOSOPHY (NCT04871919) is an ongoing Phase 4, prospective, observational, European study that will enroll ~1500 patients aged ≥18 years with moderate to severe active RA, prescribed FIL for the first time and in accordance with the product label in general practice. At Week 1, 2 and 3 and Month 1, 3, 6, 9 and 12, we assessed the proportion of patients with clinically meaningful change from baseline in pain (reduction of ≥ 10 on a visual analog scale [VAS]) and Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score (increase of ≥ 4) in advanced therapy (AT)-naïve and -experienced patients. AT-naïve patients had received no prior biologic (b) or targeted synthetic (ts) disease modifying anti-rheumatic drugs (DMARDs) for RA; AT-experienced patients had received ≥ 1 prior bDMARD or tsDMARD for RA. Work productivity was also assessed at these timepoints using the Work Productivity and Activity Impairment Questionnaire. DAS28-CRP was assessed at baseline and Month 1, 3, 6 and 12. Adverse events (AEs) were recorded.

Results: As of Jan 31, 2023, 798 patients had been treated; baseline characteristics are presented in the **Table**. 53.6% of patients received FIL monotherapy and 37.3% FIL + MTX. 38.2% were AT naïve; 61.8% were AT experienced.

Pain and fatigue improved as early as Week 1. At Week 1, 40.0% of AT-naïve and 48.5% of AT-experienced patients had a clinically meaningful change in VAS pain score (**Figure 1A**); 44.0% of AT-naïve and 42.9% of AT-experienced patients had a clinically meaningful change from baseline in FACIT-Fatigue (**Figure 1B**). Clinically meaningful changes in pain and FACIT-Fatigue were maintained until Month 12. Improvements in pain and fatigue were accompanied by changes in work productivity and time spent on daily activities, which increased from as early as Week 1, with further improvements observed until Month 12. Mean (SD) absenteeism decreased between baseline (23.5 [34.1]) and Month 1 (17.0 [30.3]) (**Figure 2**).

Median DAS28-CRP decreased after 1 month, and decreases were maintained through Month 12. Least squares mean change (SE) from baseline in DAS28-CRP was –1.4 (0.1) to Month 1 and –1.9 (0.1) to Month 12. 43 patients (5.4%) discontinued treatment due to AEs. AEs were mainly infections, including COVID-19 (11.0%), herpes zoster (1.0%), active

Table. Baseline characteristics, laboratory measures and prior and current treatment

Parameter	N=798
Female sex, n/N (%)	585/797 (73.3)
Age, mean (SD), years	57.0 (11.8); n=797
BMI, mean (SD), kg/m^2	27.7 (5.9); n=713
RA duration, mean (SD), years	10.7 (9.6); n=786
DAS28-CRP, mean (SD)	4.5 (1.3), n=608
CDAI, mean (SD)	25.2 (12.7), n=614
TJC28, mean (SD)	8.3 (6.8); n=758
SJC28, mean (SD)	5.1 (4.8); n=756
VAS pain, mean (SD)	52.8 (27.8); n=355
RF and/or ACPA positive, n/N (%)*	483/567 (85.2)
Smoking status, n (%)†	
Nonsmoker	329 (41.2)
Former smoker	137 (17.2)
Current smoker	129 (16.2)
Family history of myocardial infarction, n (%)	57 (7.1)
Medical history of, n (%):	
Cardiovascular disease	49 (6.1)
Diabetes	56 (7.0)
Dyslipidemia	91 (11.4)
Hypertension	252 (31.6)
Ischemic CNS vascular disorders	23 (2.9)
Peripheral vascular disease	26 (3.3)
Prior use of DMARDs for RA, n (%)	
At least 1 DMARD for RA	735 (92.1)
At least 1 csDMARD	707 (88.6)
At least 1 bDMARD	469 (58.8)
At least 1 tsDMARD	140 (17.5)
Study treatment, n (%)	
FIL monotherapy	428 (53.6)
With glucocorticoids	170 (21.3)
FIL + MTX	298 (37.3)
With glucocorticoids	142 (17.8)
FIL + other csDMARDs for RA	66 (8.3)
With glucocorticoids	25 (3.1)
FIL dose, n (%)	
200 mg	735 (92.1)
100 mg	63 (7.9)
Current work status, n (%)‡	
Employed full-time	257 (32.2)
Employed part-time	127 (15.9)
Unemployed	98 (12.3)
Retired	251 (31.5)
Full-time student	2 (0.3)
None of the above	46 (5.8)

*Data for RF or ACPA status are missing for 364 participants (45.6%); †Data are missing for 203 participants (25.4%); ‡Data are missing for 17 patients (2.1%).
ACPA, anticitrullinated protein antibody; (b/cs/ts)DMARD, (biologic/conventional synthetic/targeted synthetic) disease-modifying antirheumatic drug; CDAI, Clinical Disease Activity Index; CNS, central nervous system; DAS28-CRP, Disease Activity Score in 28 joints using C-reactive protein; FIL, filgotinib; RA, rheumatoid arthritis; RF, rheumatoid factor; SD, standard deviation; SJC28, swollen joint count based on 28 joints; TJC28, tender joint count based on 28 joints; VAS, visual analog scale.

tuberculosis (0.1%) and opportunistic infections (0.1%). The reported cardiovascular events included stroke (0.5%), transient ischemic attack (0.5%) and unstable angina (0.3%). Neoplasms (excluding NMSC) were reported in 0.8% and fractures in 0.9% of patients. There were 2 deaths.

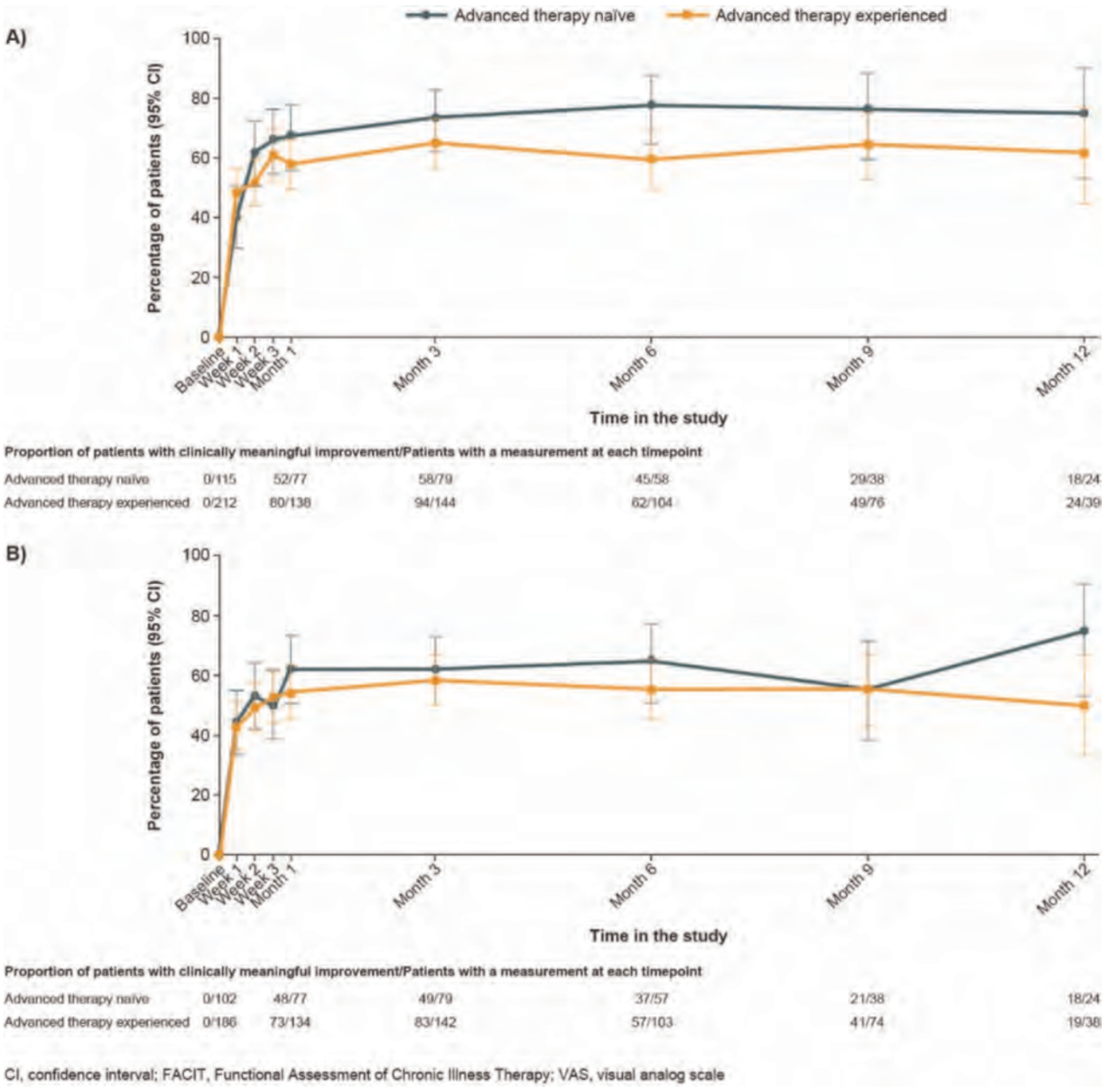
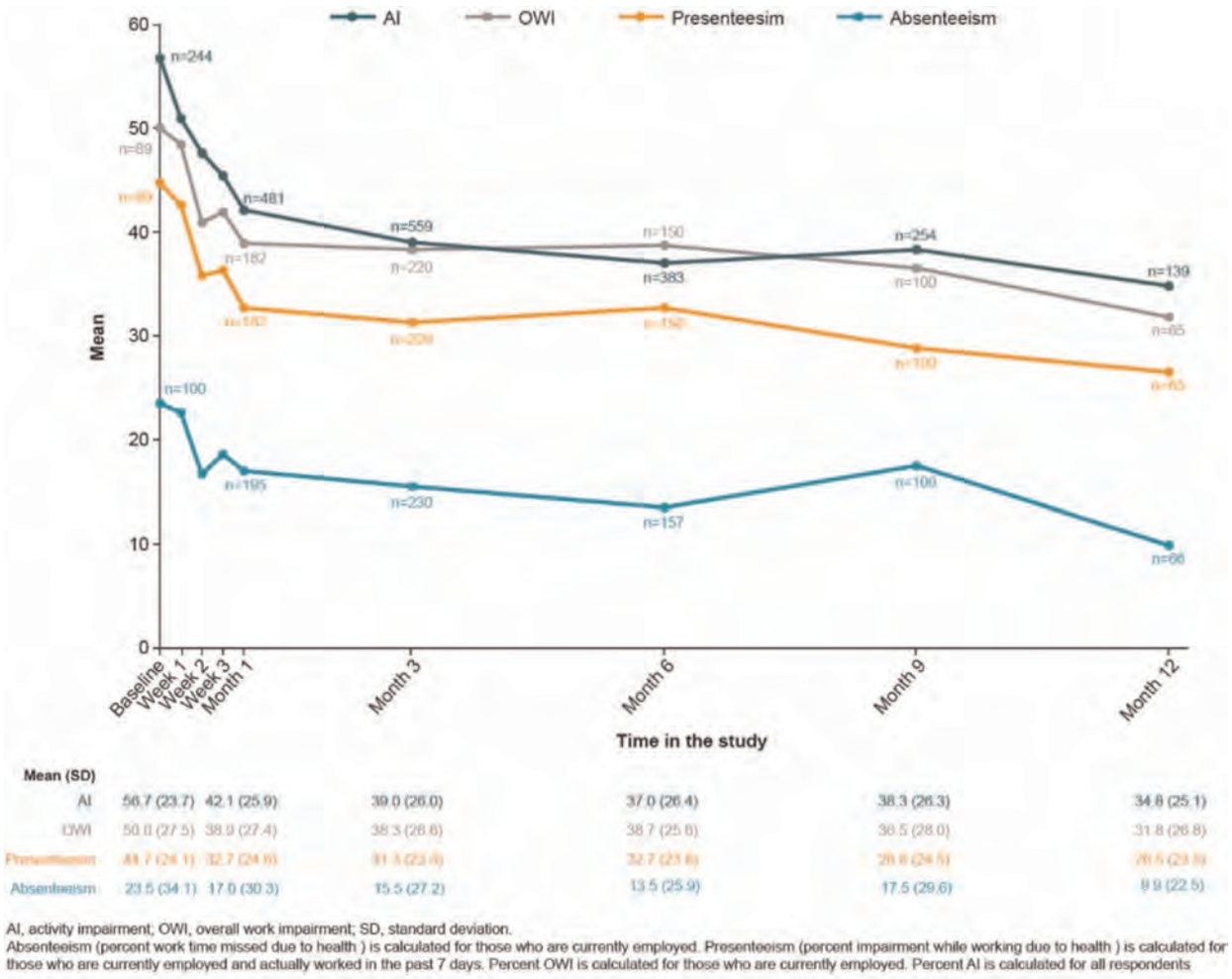


Figure 1. Proportion of patients with a clinically meaningful improvement from baseline in (A) VAS pain score and (B) FACIT-Fatigue score

Conclusion: Interim data from patients treated with FIL show pain, fatigue and work productivity improved as early as Week 1 and DAS28-CRP as early as Month 1, the first timepoint at which DAS28-CRP was assessed; improvements were maintained up to Month 12. No new safety findings were observed up to 12 months. Long-term follow-up is needed to further evaluate effectiveness and safety.



Mean (SD)						
AI	56.7 (23.7)	42.1 (25.9)	39.0 (26.0)	37.0 (26.4)	38.3 (26.3)	34.8 (25.1)
OWI	50.0 (27.5)	38.9 (27.4)	38.3 (28.6)	38.7 (25.6)	36.5 (28.0)	31.8 (26.8)
Presenteesim	48.7 (24.1)	32.7 (24.6)	31.3 (23.4)	32.7 (23.6)	28.8 (24.5)	26.5 (23.8)
Absenteeism	23.5 (34.1)	17.0 (30.3)	15.5 (27.2)	13.5 (25.9)	17.5 (29.6)	9.9 (22.5)

AI, activity impairment; OWI, overall work impairment; SD, standard deviation.
Absenteeism (percent work time missed due to health) is calculated for those who are currently employed. Presenteeism (percent impairment while working due to health) is calculated for those who are currently employed and actually worked in the past 7 days. Percent OWI is calculated for those who are currently employed. Percent AI is calculated for all respondents

Figure 2. Work productivity

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Abstract Number: 1333

Rheumatoid Arthritis-associated Lymphoproliferative Disorders: A Multi-center Analysis of Clinical Outcomes and Evaluation of Anti-rheumatic Drugs After LPD Onset

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

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Session Type: Poster Session B

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Background/Purpose: The largest multi-center collaborative study on lymphoproliferative disorders (LPD) in rheumatoid arthritis (RA) (RA-LPD) in Japan was conducted to characterize its clinical outcomes and identify suitable treatments.

Methods: Patients with RA who developed LPD between January 1999 and March 2021 were retrospectively analyzed in a multicenter collaborative study across 48 hospitals in Japan. Significant differences were evaluated using Fisher's exact test, the Mann-Whitney U-test, the Log-rank test, and a multivariate analysis with the Cox proportional hazard model. Significance was set at $p < 0.05$.

Results: Clinical outcomes of RA-LPD A total of 752 RA-LPD patients were enrolled. Their clinicopathological characteristics were presented at the ACR Convergence 2022. As shown in Figure 1, among 438 patients, 81.4% spontaneously regressed after the withdrawal of immunosuppressive agents, while 32.0% showed regrowth after a median of 12 months (range: 1-92). Among the 439 patients treated with first-line therapy, 365 (77.8%) achieved a complete or partial response to first-line therapy. The 5-year overall survival (OS) rate was 86.3%. The multivariate analysis identified an advanced clinical stage, Hodgkin lymphoma as independent regrowth after spontaneous regression, an older age (>70 years), the T cell phenotype, and a sIL-2R level >1300 U/mL as independent unfavorable prognostic factors. Necessity for re-biopsy in patients with regrowth or relapse Eight patients with RA-LPD developed different histological subtypes after the regression or

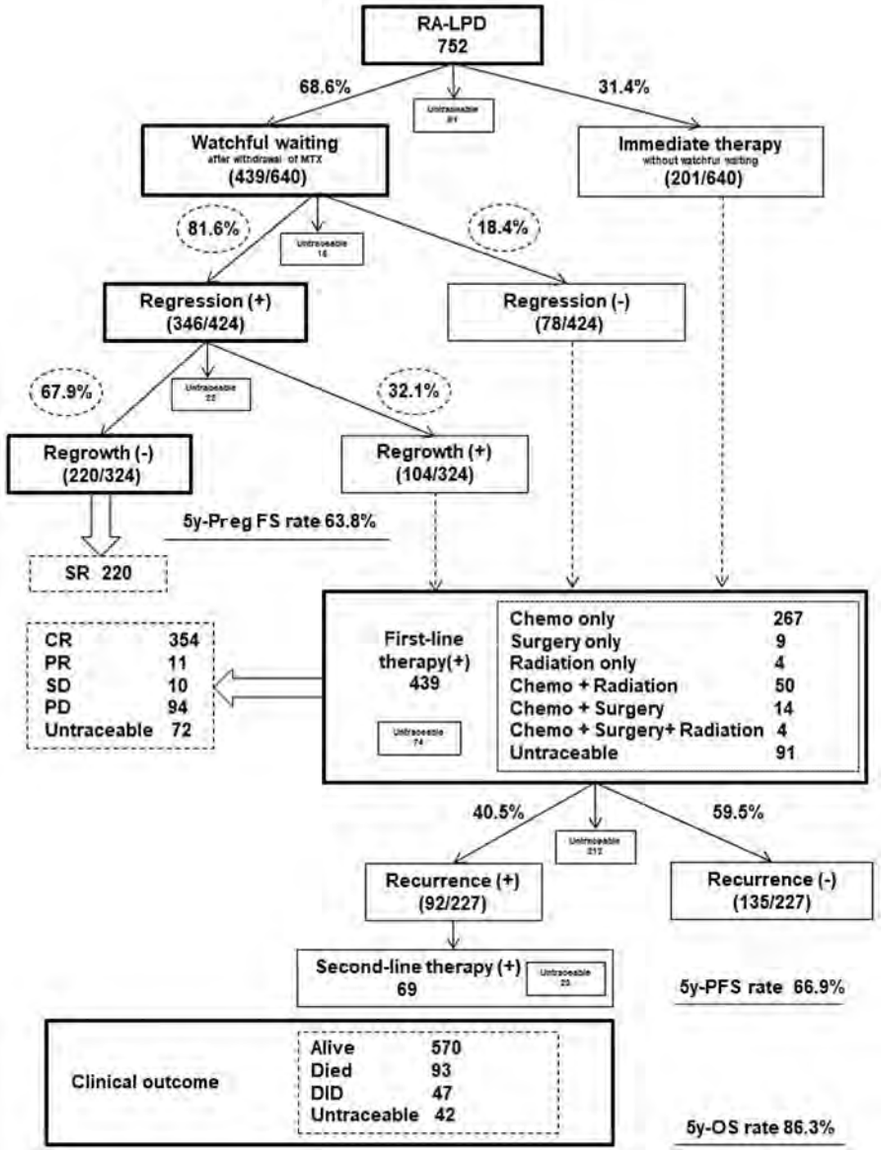

Figure 1. The clinical course of RA-LPD. Among 752 patients with RA-LPD, 68.5% spontaneously regressed after the withdrawal of immunosuppressive agents. Among them, 81.4% showed tumor regression, while 32.0% showed regrowth with a median of 12 months (range: 1-92).

Figure 2. The clinical course after LPD onset

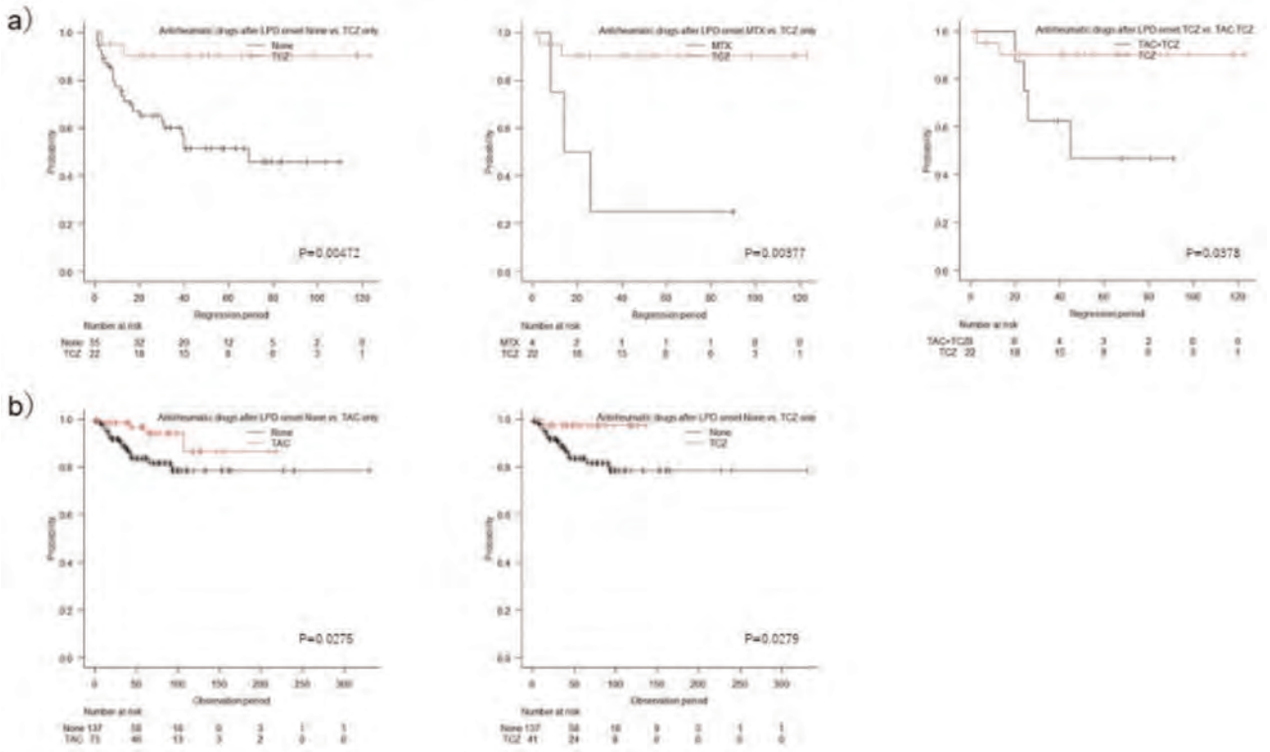

Figure 2. Kaplan-Meier curves of RA-LPD according to antirheumatic drugs administrated after the onset of LPD. a). PSRFS curve of RA-LPD. The rate of spontaneous regression was significantly higher in the TCZ only group than in the none, MTX only, and TCZ plus TAC groups. b) OS curve of RA-LPD. The prognosis of patients after the onset of LPD was better in the TAC only and TCZ only groups than in the none group.

Table 1. Summary of eight patients who developed different histological subtypes after the regression or remission of RA-LPD.

No.	Sex	Age at first LPD onset (y)	Therapy for RA after first LPD onset	Periods from primary LPD to secondary LPD (m)	First LPD		Secondary LPD	First LPD		Secondary LPD	First LPD		Secondary LPD	First LPD		Secondary LPD	Follow-up periods (m)	Outcome
					Histology			primary site			EBER-1			Therapy for LPD				
1	F	76	MTX (30M, 1002mg)	39	EBVMCU	→	HL	Skin	→	Axillary LN	+	→	+	Watching	→	A-AVD	76	A
3	F	77	None	9	AITL	→	HL	Cervical LN	→	LN	+	→	+	Watching	→	ABVD	55	DT
1	F	66	None	77	AITL	→	DLBCL	Cervical LN	→	Systemic LN	-	→	+	CHOP	→	Surgery DEVIC	92	DT
4	M	68	TAC	5	HL-like lesion	→	DLBCL	Cervical LN	→	Cervical LN	+	→	+	Watching	→	R-CHOP R-Devic	35	DT
1	F	57	MTX (4M, 129mg)	17	FL	→	DLBCL	Abdominal LN	→	Abdominal LN	-	→	-	R only	→	R-GDP RT 30Gy	109	DT
4	M	63	None	10	P-LPD	→	Mantle	Axillary LN	→	Cervical LN	+	→	-	watching	→	R-CHOP R-hyper-CVAD/MA	17	DT
1	F	60	TAC	20	HL	→	TRBCL	Inguinal LN	→	Inguinal LN	+	→	+	watching	→	R-CHOP	71	A
4	F	69	None	31	DLBCL	→	MALToma	Stomach	→	Stomach	-	→	-	watching	→	Eradication of HP	157	A

RA-LPD: Rheumatoid arthritis-associated lymphoproliferative disorders; y: Year; m: Month; EBER-1: Epstein-Barr virus-encoded small RNA-1; F: Female; M: Male; MTX: Methotrexate; SASP: Salazosulfapyridine; TAC: Tacrolimus; EBVMCU: Epstein-Barr virus-positive mucocutaneous ulcer; AITL: Angioimmunoblastic T-cell lymphoma; HL-like lesion: Hodgkin lymphoma-like lesion; FL: Follicular lymphoma; P-LPD: Polymorphic lymphoproliferative disorders; HL: Hodgkin's lymphoma; DLBCL: Diffuse large B-cell lymphoma; TRBCL: T-cell rich B-cell lymphoma; MALToma: Mucosa-associated lymphoid tissue lymphoma; LN: Lymph node; CHOP: (C: Cyclophosphamide; H: Doxorubicin Hydrochloride; O: Oncovin; P: Prednisolone); R: Rituximab; A-AVD: ADCetris (brentuximab vedotin)-Adriamycin (doxorubicin) Vinblastine Dacarbazine; ABVD: Adriamycin Bleomycin Vinblastine Dacarbazine; R-GDP:Rituximab + GEM + Dexamethasone + CDDP; RT: radiotherapy; Hyper-CVAD: (C: Cyclophosphamide; V: Vincristine sulfate; A: Adriamy hydroxydaunorubicin Hydrochloride; D: Dexamethasone); MA: MTX+Ara-c; HP: Helicobacter Pylori.

remission of RA-LPD. Among them, 6 patients (5.7%) showed regrowth after temporary tumor regression following the withdrawal of methotrexate (MTX), and 2 (2.2%) relapsed during temporary remission after chemotherapy. The tumor-related death rate was significantly higher in these patients (62.5%) than in those who developed LPD with the same histology (24.6%) (p=0.030) (Table 1). Therefore, re-biopsy is required for patients with regrowth or relapse. Recommended antirheumatic drug regimens after LPD onset The effects of antirheumatic drugs administered after the onset of LPD on the clinical outcomes of RA-LPD were examined in 393 patients with the relevant information available. The trastuzumab (TCZ) only group maintained a significantly higher rate of spontaneous regression than the none, MTX only, and TCZ plus tacrolimus (TAC) groups (Figure 2a). The prognosis of patients after the onset of LPD was better in the TAC only and TCZ only groups than in the none group, which included patients who had never been treated with MTX, TAC, TCZ, tumor necrosis factor inhibitors, abatacept, or a Janus-activating kinase inhibitor (Figure 2b).

Conclusion: The present study showed the clinical outcomes of RA-LPD and identified independent factors associated with post-spontaneous regression (SR)-free survival (PSRFS) and overall survival. Based on the results obtained, TCZ only regimens are recommended after the onset of LPD and re-biopsy is required for patients with regrowth or relapse.

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Abstract Number: 1334

Comparison of Malignancies and Serious Infections Between Etanercept Biosimilar and Bio-Originator Initiators: Population-Based Analyses

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
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Background/Purpose: Treatment safety, particularly malignancy and infections, is an important issue for biologics; hence, surveillance and analyses comparing biosimilar versus bio-originator use in the real world are needed. We aimed to compare malignancy and serious infections among initiators of etanercept originator (ETA-O) versus biosimilar (ETA-B), all users and rheumatoid arthritis (RA) specific.

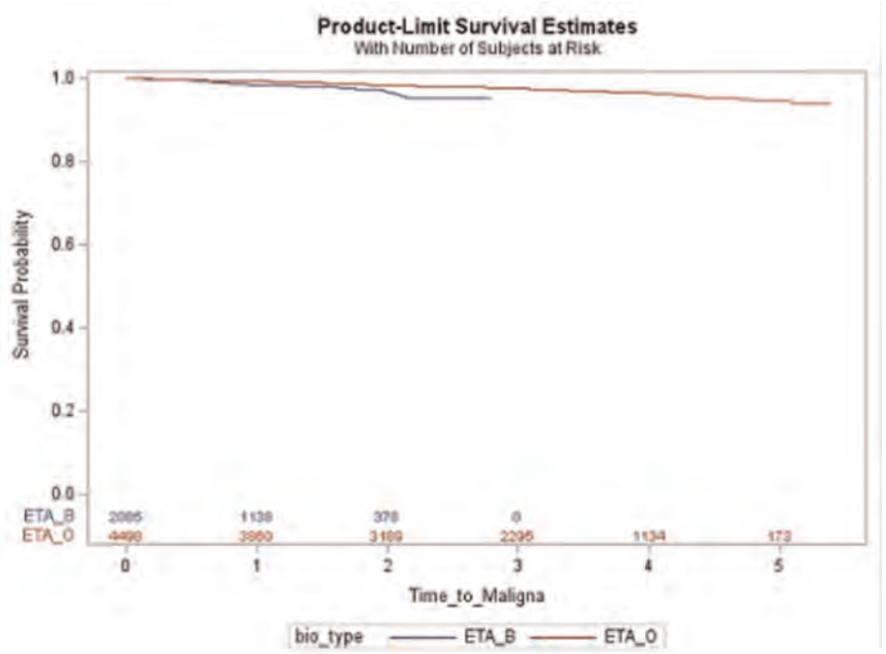

Figure 1. Time to first malignancy event for etanercept biosimilar and originator (all users)

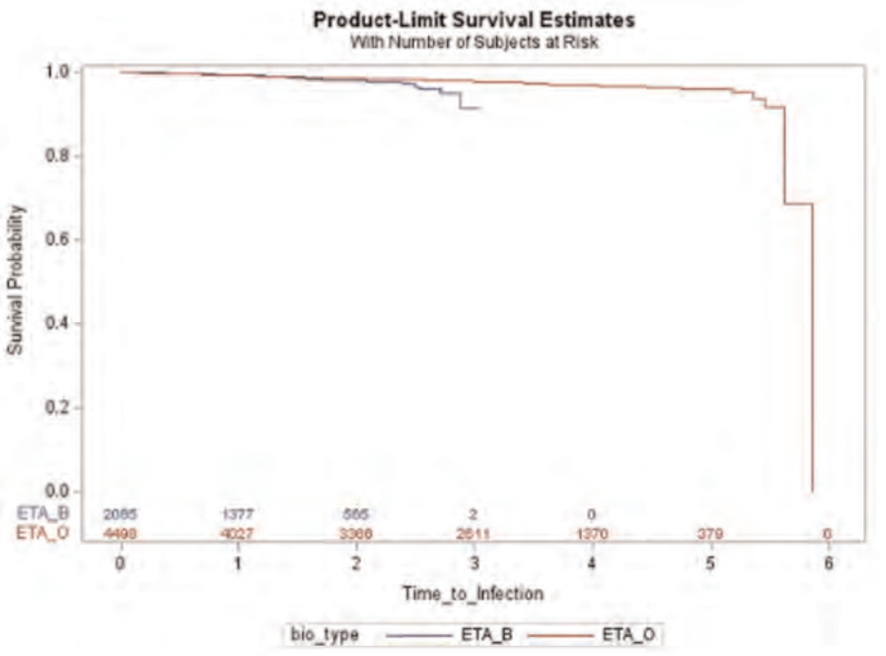

Figure 2. Time to first serious infection for etanercept biosimilar and originator (all users)

Table 1. Unadjusted and adjusted hazard ratio (HR) for serious infection and malignancy, comparing etanercept biosimilar and originator in patients with RA.

Variables	HR (95% CI)	
	Unadjusted	Adjusted*
1. First malignant event (ETA-B vs ETA-O)		
Biosimilar	0.83 (0.31, 2.18)	0.51 (0.14, 1.78)
Female (biological sex)	0.49 (0.22, 1.11)	0.48 (0.21, 1.09)
Age at ETA initiation ≥ 65 years	**1.04 (1.00, 1.08)**	**1.04 (1.01, 1.08)**
Corticosteroids prior to initiation	1.17 (0.50, 2.77)	1.13 (0.47, 2.70)
Biologic prior to initiation	1.04 (0.31, 3.50)	1.09 (0.31, 3.90)
Ontario province	1.49 (0.64, 3.46)	1.38 (0.58, 3.27)
Calendar year ≥2018	1.26 (0.49, 3.27)	1.79 (0.53, 6.06)
2. First serious infection (ETA-B vs ETA-O)		
Biosimilar	1.13 (0.54, 2.34)	1.69 (0.64, 4.49)
Female (biological sex)	0.91 (0.45, 1.82)	0.89 (0.44, 1.78)
Age at ETA initiation ≥ 65 years	1.00 (0.98, 1.02)	1.00 (0.97, 1.02)
Corticosteroids prior to initiation	**2.23 (1.02, 4.88)**	**2.17 (1.00, 4.79)**
Biologic prior to initiation	1.38 (0.57, 3.33)	1.39 (0.55, 3.49)
Ontario province	1.92 (0.96, 3.85)	**2.09 (1.03, 4.24)**
Calendar year ≥2018	0.74 (0.34, 1.60)	0.43 (0.16, 1.22)

Methods: CAN-AIM is a team funded to do high-priority research projects for Health Canada and other stakeholders. We used data from the National Prescription Drug Utilization Information System (NPDUIS), which contains pan-Canadian (except Quebec) claims-level data on prescriptions dispensations paid from public drug programs, linked to the hospital Discharge Abstract Database (DAD) and the National Ambulatory Care Reporting System (NACRS). We studied adults (≥18 years), initiating ETA between January 2015 and December 2019, further restricted to RA (ICD-10 M05, M06, M45, M70, M71, M72, M73andL40). Those with ICD diagnostic codes indicating malignancy, HIV or organ transplant one year before ETA/INF initiation (baseline) were excluded. For infection, follow-up began at treatment initiation and ended at end of data or 90 days after discontinuation or end of study; and for malignancy, 365 days after treatment initiation up to 365 days after discontinuation. Serious infections were defined as the first hospitalization with ICD-10 indicating infectious disease, observed from treatment initiation up to end of data or 90 days after treatment discontinuation. Malignancy was defined by the first record of neoplasm except non-melanoma skin cancer, from 365 days after treatment start up to 365 days after discontinuation. We compared originator and biosimilar using Cox regression models. We presented the adjusted hazard ratio (aHR) - potential confounders or effect modifiers included sex at birth, age at ETA initiation, prior corticosteroids or other biologics, region (Ontario vs other), and calendar year. Kaplan-Meier curves were plotted to compare time to first event between both treatment groups.

Results: The cohort (6,583 users, 695 RA, 31.7% on ETA-B) was mostly female (65%), with a median age (interquartile range, IQR) of 62 (50-69) at treatment initiation. Overall, malignancy incidence was 10.3 (95%CI 8.8-12.1), and infection rate was 8.9 (95%CI 7.5-10.4) per 1,000 person-year. Time to first event between ETA-B and ETA-O is presented in Figures 1-2. The aHR for ETA-B versus ETA-O (reference) was 1.14 (95%CI 0.68-1.91) for malignancy and 1.33 (95%CI 0.77-2.30) for infection. Non-significant results were also found when restricted to RA (Table 1).

Conclusion: In this real-world dataset, we were unable to identify clear differences in serious infections and malignancy comparing biosimilar and originator of etanercept, all users and RA-specific. Limitations include inability to control for residual confounders (e.g., disease severity), potential outcome misclassification and selection bias and short follow-up or treatment exposure to detect malignancy.

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Abstract Number: 1335

Effectiveness of Longstanding Exercise Therapy versus Usual Care in People with Rheumatoid Arthritis and Severe Functional Limitations: A Randomized Controlled Trial (L-EXTRA)

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SESSION INFORMATION
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Session Title: RA – Treatments Poster II
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Background/Purpose: Supervised exercise therapy is an effective and safe treatment option for people with rheumatoid arthritis (RA). However, most studies involve interventions of relatively short duration (≤12 weeks) or in patients with stable disease and a favorable health status. Patients with persistent disease activity, irreversible joint damage, multiple joint replacements and/or severe comorbidities are underrepresented in research, although in particular patients in this subgroup might be in need of exercise therapy, most likely longstanding. However, studies on longstanding exercise interventions in this subgroup are lacking. Therefore, this study aimed to evaluate the effectiveness of longstanding personalized, supervised exercise therapy compared with usual care in people with RA and severe functional limitations.

Table 1: Registration, Acknowledgements and Funding of the L-EXTRA study

Registration number Netherlands Trial Register NL8235, included in the International Clinical Trial Registry Platform (ICTRP) (https://trialsearch.who.int/Trial2.aspx?TrialID=NL8235).

Acknowledgements: This research would not have been possible without the cooperation of many people. We would like to acknowledge the work of:

- All physical and exercise therapist who participated in the training and treatment of patients and/or have made their practice available for the assessments.
- All rheumatologists, nurse specialists, physician assistants and other clinicians that informed patients about the study and/or were involved in active recruitment strategies and/or provided information on participants' characteristics.
- All medical students who voluntarily supported the research team with the enormous amount of administrative tasks
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Methods: Adults with RA and severe limitations in basic activities of daily living were randomized 1:1 to longstanding (>52 weeks) personalized, supervised exercise therapy or usual care. The intervention consisted of exercise therapy tailored to individual goals, combined with self-management support to increase physical activity and fitness levels, and was delivered by specifically trained, primary care physical/exercise therapists. The primary endpoint was the change in the Patient-Specific Complaint (PSC (0-10)) at 52 weeks. Secondary endpoints included the Health Assessment Questionnaire-Disability Index (HAQ-DI), Rheumatoid Arthritis Quality of Life questionnaire Patient (RAQoL), 6-minute walk test (6MWT), Patient Reported Outcome Measurement Information System-Physical Function-10 (PROMIS-PF-10) and the Short Form-36 (SF-36). Results are reported from the 52-week rater-blind treatment period using analysis of covariance, expressed as mean difference between change scores with the 95% confidence interval.

Results: 215 people (90% female, age 58.8 (SD; 12.9) years) with RA and severe functional limitations were randomized. At 52 weeks n=104 (intervention) and n=98 (usual care) participants were included in the intention-to-treat analyses. The improvement in the primary outcome (PCS) was statistically significantly greater in the intervention group vs usual care difference in change score between groups (mean [95% CI] -1.7 [-2.4 – 1.0]) at week 52. Except for the PROMIS-PF-10 and SF-36, all secondary outcomes showed statistically significantly greater improvements in the intervention group vs usual care group at week 52 (HAQ-DI 0.17 [0.05 – 0.29], RAQoL 1.97 [0.62 – 3.32], 6MWT 56 meter [38 – 75]) indicating consistent improvements across domains, with between-group effect sizes ranging from 0.4 to 0.9. No intervention-related (serious) adverse events were reported.

Conclusion: Longstanding, personalized, supervised exercise therapy was more effective than usual care after 52 weeks of treatment in people with RA and severe functional limitations. Improvements were consistently observed across domains.

Disclosure: M. Teuwen: None; **S. van Weely**: None; **T. Vliet Vlieland**: None; **M. van Wissen**: None; **W. Peter**: None; **A. den Broeder**: None; **D. van Schaardenburg**: None; **W. van den Hout**: None; **C. van den Ende**: None; **M. gademan**: None.

Abstract Number: 1336

Adalimumab and Etanercept Serum Levels in Rheumatoid Arthritis Patients with and Without a Disease Flare During Tapering

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Due to the improved management strategies and availability of biologic disease-modifying antirheumatic drugs (bDMARDs), ~60% of the rheumatoid arthritis (RA) patients will achieve sustained remission. To ensure optimal rheumatic care, effective use of bDMARDs is required, which includes tapering for RA patients with stable low disease activity. However, previous tapering trials for TNF inhibitors (TNFi) in RA reported that 51-77% of patients experience a disease flare during tapering and stopping. For personalized tapering approach therapeutic drug monitoring (TDM) might be of added value. TDM is based on pharmacokinetics that uses measurements of circulating drug level to adjust the dose

individually. Unfortunately, current knowledge on pharmacokinetics of TNFi during tapering is incomplete, e.g. what is the minimal drug level that should be aimed for to prevent disease flares. We aimed to assess the serum level of etanercept (ETN) and adalimumab (ADL) in well-controlled RA patients with and without a disease flare during tapering.

Methods: All RA patients who participated in the TApering strategies in Rheumatoid Arthritis (TARA) trial and followed the tapering protocol and had serum samples from ≥3 visits (n=111) were selected. The TARA trial was a multicenter, single-blinded randomized trial that included established RA patients with a well-controlled disease, defined as a disease activity score (DAS) ≤2.4 and a swollen joint count ≤1. Eligible patients were randomized into gradual tapering csDMARD (mainly methotrexate) followed by the TNFi (ETN or ADL), or vice versa. Tapering of the TNFi was done every three months by doubling the dosing interval, then cutting the dosage into half, and finally stopping. TNFi serum levels were measured at each 3-monthly visit, if serum samples were available, by a drug tolerant enzyme-linked immunosorbent assay.

Results: Of the 111 included RA patients 54 tapered their TNFi first, while 57 patients tapered the csDMARD first. The 54 patients who tapered TNFi first had an average symptom duration of 7,2 years and were predominantly female (58%) with an average age of 58 years. At baseline, the DAS (standard deviation) was 1,0 (0,5).Respectively 40% and 60% of the RA patients used ADL and ETN as TNFi. The baseline mean serum concentration for ADL was 7.2 ug/ml (range 0.023-13.4 ug/ml) and 2.7 ug/ml (range 0.5-4.38 ug/ml) for ETN. ADL and ETN serum levels decreased during tapering, but ADL remained longer in the blood circulation after stopping compared to ETN, 6 versus < 3 months respectively (figure 1A and C). Approximately 43% of the patients who tapered the TNFi first flared. At the time of a flare, mean serum level for ADL was 0.6 ug/ml and 0.5 ug/ml for ETN (figure 1B and D).

Conclusion: For both ADL and ETN, the critical serum level below which flares occur seems to be 1 ug/ml. TDM might prevent disease flares during tapering by allowing personalized TNFi dosing targeting levels above this critical threshold. In line with the longer half-live ADL remains longer in the blood circulation after stopping compared to ETN. One should, therefore, be aware that it can take up to 6 months after cessation before the TNFi drops to undetectable levels in blood.

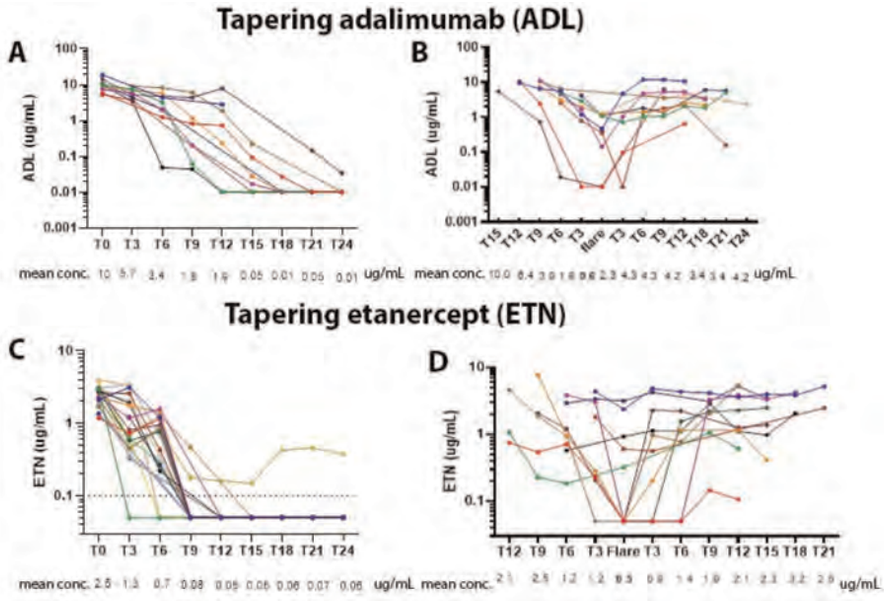

Figure 1: Drug levels of Rheumatoid Arthritis patients with and without a disease flare during tapering of a TNF inhibitor. Each dot represents a drug level measurement per individual RA patient on ADL without (1A) or with a disease flare (1B) or ETN without (1C) or with (1D) a disease flare during tapering. Measurements within each individual patient are connected by a coloured line. Abbreviations: ADL, adalimumab; conc., concentration; ETN, etanercept

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Abstract Number: 1337

Effect of Tofacitinib Therapy on Angiotensin Converting Enzyme Activity in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The Renin-Angiotensin-Aldosterone system (RAAS) has been implicated in the regulation of the cardiovascular system and linked to rheumatoid arthritis (RA). Little information has become available on the effects of Janus kinase (JAK) inhibition on RAAS. here we studied the effects of 12-month tofacitinib treatment on angiotensin converting enzyme (ACE), ACE2 production and ACE/ACE2 ratios in RA along with numerous other biomarkers.

Methods: Thirty RA patients were treated with tofacitinib in this prospective study. Serum ACE concentrations were assessed by ELISA. ACE2 activity was determined by a specific quenched fluorescent substrate. ACE/ACE2 ratios were calculated. We also determined common carotid intima-media thickness (ccIMT), brachial artery flow-mediated vasodilation (FMD) and carotid-femoral pulse-wave velocity (cfPWV) by ultrasound. C-reactive protein (CRP), rheumatoid factor (RF) and anti-citrullinated protein autoantibodies (ACPA) were also determined. All measurements were performed at baseline, as well as after 6 and 12 months of tofacitinib treatment.

Results: After the dropout of 4 patients, 26 completed the study. Tofacitinib treatment increased ACE levels after 6 and 12 months, while ACE2 activity only transiently increased at 6 months. The ACE/ACE2 ratio increased after one year of therapy ($p < 0.05$). Logistic regression analyses identified correlations between ACE, ACE2 or ACE/ACE2 ratios and RF at various time points. Baseline disease duration also correlated with erythrocyte sedimentation rate (ESR) ($p < 0.05$). One-year changes of ACE or ACE2 were determined by tofacitinib treatment plus ACPA or RF, respectively ($p < 0.05$).

Conclusion: JAK inhibition increases serum ACE and ACE/ACE2 ratio in RA. Baseline inflammation (ESR), disease duration and ACPA, as well as RF levels at various time points can be coupled to the regulation of ACE/ACE2 ratio. The effect of tofacitinib on RAAS provides a plausible explanation for the cardiovascular effects of JAK inhibition in RA.

Disclosure: D. Kacsándi: None; **M. Fagyas**: None; **Á. Horváth**: None; **E. Végh**: None; **A. Pusztai**: None; **M. Czókolyová**: None; **B. Soós**: None; **A. Szabó**: None; **A. Hamar**: None; **Z. Peth**ő: None; **N. Bodnár**: None; **G. Kerekes**: None; **K. Hodosi**: None; **S. Szamosi**: None; **G. Szücs**: None; **Z. Papp**: None; **Z. Szekanecz**: Pfizer, 1, 2, 5, 6.

Abstract Number: 1338

The Advantage of Tight Control and Treat-to-Target in New-onset Rheumatoid Arthritis Patients in Daily Rheumatology Practice: Results from a Contemporary University Clinic Inception Cohort

Katarina Friberger Pajalic[1], **Jon Thorkel Einarsson**[1], Caroline Bengtsson[2], Ellen Landgren[3], Elisabeth Mogard[4], Carmen Roseman[5], Johan Karlsson Wallman[4], Elisabet Lindqvist[4], Tor Olofsson[4] and Meliha Kapetanovic[4], [1]Lund University, Institution for clinical sciences, section for rheumatology Lund and Lund University Hospital, Lund, Sweden, [2]Lund University Hospital, section for rheumatology, Lund, Sweden, [3]Lund University, Institution for clinical sciences, section for rheumatology Lund and Skåne University Hospital, Lund, Sweden, [4]Lund University and Skåne University Hospital, Lund, Sweden, [5]Lund University, Institution for clinical sciences, section for rheumatology Lund and Lund University Hospital, Lund, Sweden

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: RA – Treatments Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Since 2018, all patients with new-onset rheumatoid arthritis (RA) at the Department of Rheumatology, Skåne University Hospital, Lund, Sweden, are invited to participate in a ”tight control” and ”treat-to-target” (TC+T2T) follow-up strategy. This strategy includes follow-up visits to a rheumatologist (at diagnosis and 3, 6, 12, 18, 24 months) plus physical/telephone consultations with a rheumatology nurse between physician visits – both with disease activity assessments and, if needed, adjustment of anti-rheumatic treatment, aiming for remission. The aim of the current study was to explore the possible advantages of implementing this TC+T2T strategy over routine care in reaching remission (DAS28 < 2.6, DAS28CRP < 2.4 or CDAI≤2.8) in clinical practice of new-onset RA patients.

Methods: RA patients with symptom duration < 24 months at diagnosis were eligible. Data on disease and treatment characteristics, as well as outcome measures during follow-up, were retrieved from the Swedish Rheumatology Quality register (SRQ). In total, 336 patients entered one of the follow-up strategies between January 1, 2018, and October 31, 2022. Of these, 193 were followed according to the TC+T2T strategy and 143 according to routine care. Percentage females/mean age/mean symptom duration at inclusion were 75%/56 years/4.5 months (TC+T2T) and 71%/62 years/7.6 months (routine

	TC+T2T group (n=193)	Controls (n=143)
Swollen 28 joint count	6.1 (4)	5.8 (5)
Tender 28 join count	8.4 (6)	7.3 (6)
ESR	46.8 (29)	41.3 (28)
CRP	21.7 (30)	20.6 (32)
DAS28	5.4 (1)	4.9 (1)
DAS28CRP	4.7 (1)	4.4 (1)
CDAI	23.5 (11)	21.6 (12)
HAQ	1.0 (0.6)	1.1 (0.7)
Fatigue (VAS)	32.3 (28)	38.1 (30)
Pain (VAS)	28.8 (25)	34.1 (27)
Smoking (ever) (%)	42%	30%
Methotrexate started at diagnosis (%)	75%	66%
Prednisolone started at diagnosis (%)	68%	42%

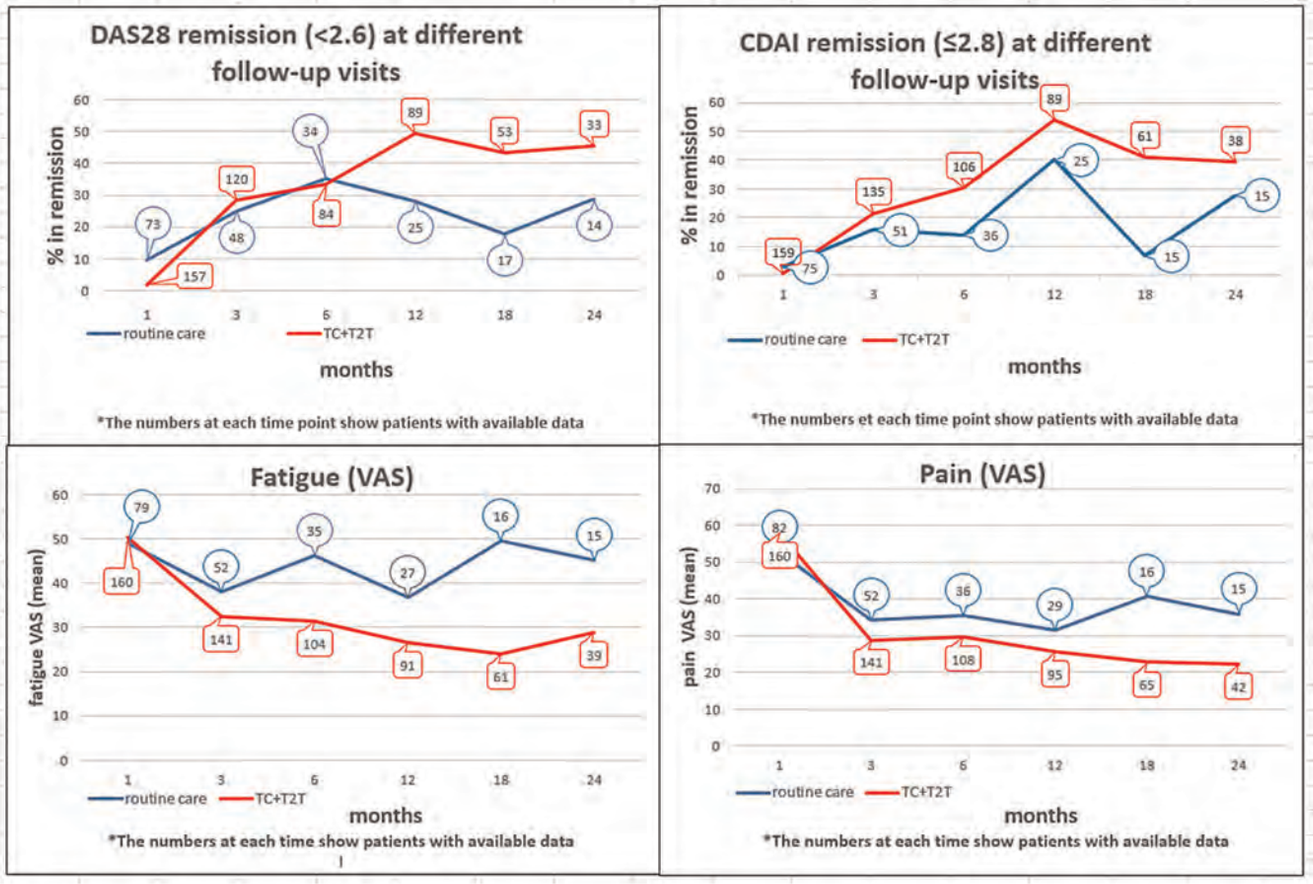
Mean and standard deviation (SD) if not otherwise stated.

Disease and treatment characteristics at diagnosis

care). Achievement of remission was compared between the two strategies using logistic regression, adjusted for sex, age, symptom duration, and DAS28/DAS28CRP/CDAI at diagnosis. In addition, changes in patient-reported outcomes (fatigue and pain) were assessed for the respective strategies.

Results: Disease and treatment characteristics at diagnosis are summarized in Table1.

Percentages of patients reaching DAS28, DAS28CRP and CDAI remission criteria increased in both groups over time, but this was more pronounced in the TC+T2T group (Figure). A similar pattern was seen in the dynamics of fatigue and pain (Figure). Follow-up according to the TC+T2T was associated with a numerical higher odds ratio of achieving remission at all follow-up times regardless the remission criteria used and a significantly higher odds ratio of CDAI remission at 6 months (after adjustment for sex, age, symptom duration and CDAI at diagnosis) (Table 2).



	B	p-value	Odds ratio	95% CI
T2T+TC (vs. routine care)*	**1.5**	**0.032**	**4.32**	**1.1-16.4**
CDAI at inclusion	-0.04	0.083	0.97	0.9-1.01
Female (vs. male)	-0.09	0.854	0.91	0.3-2.6
Age (years)	0.01	0.398	1.01	1.0–1.04
Disease duration (months)	0.00	0.998	1.00	0.9-1.1

*T2T+TC= treat to target and tight control

Achievement of remission between "treat -to-target" strategy and routine rheumatology care (logistic regression analysis)

Conclusion: Compared to routine rheumatology care, the implementation of a ”tight control” and ”treat-to-target” strategy resulted in numerically larger proportions of patients reaching remission at majority of follow-up visits over two years. Similarly, both strategies showed an early and sustained numerical improvement in patient-reported outcomes. Our results suggest that this type of strategy should be integrated into daily clinical practice of new-onset RA.

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Abstract Number: 1339

Neutrophil Activation and Formation of Neutrophil Extracellular Traps Are Associated with Response to Abatacept in Patients with Moderate to Severe Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Neutrophil activation and formation of neutrophil extracellular traps (NETs) have been implicated in the pathogenesis of rheumatoid arthritis (RA). Calprotectin, a neutrophil activation marker, correlates with RA disease activity and is a novel biomarker that can be used to distinguish RA patients in remission and active disease and to predict disease progression. Abatacept is a CTLA-4-Ig fusion protein, which is widely used as a treatment for RA. However, the response rates to abatacept are variable in heterogeneous RA patients. We conducted this study to determine the effect of abatacept on neutrophil-related markers and to explore whether these markers could predict the therapeutic efficacy of abatacept in RA patients.

Methods: A total of 23 RA patients, who had an inadequate response to methotrexate and other conventional DMARDs, were enrolled in this study. All participants fulfilled the 1987 ACR criteria or 2010 ACR/EULAR criteria, with clinical disease activity index (CDAI) ≥16. Plasma samples were collected at baseline, week 6, week 14, and week 24. Levels of calprotectin, myeloperoxidase (MPO)-DNA, and neutrophil elastase (NE)-DNA complexes were determined by ELISA. Responders (n=10) were defined as subjects who achieved ACR50 Response at week 24. Changes in these markers were compared before and after treatment using the Wilcoxon matched-pairs signed rank test. Baseline levels of these markers were compared between the responder and non-responder groups by the Mann-Whitney test.

Results: Plasma levels of calprotectin and MPO-DNA complexes were significantly decreased at week 6 (p=0.0011 and p=0.0025, respectively), week 14 (p=0.0003 and p=0.0002, respectively), and week 24 (p=0.0121 and p=0.0037, respectively) with the treatment of abatacept when compared to baseline. Abatacept reduced the levels of NE-DNA only at week 14 (p=0.0085). Compared to the non-responders, the responders had a numerically higher percentage of anti-CCP antibodies (90% vs 62%, p=0.1790) and RF (90% vs 54%, p=0.0886). Baseline levels of calprotectin (3190 ng/mL vs 2167 ng/mL, p=0.0493) and NE-DNA complexes (6708 pM vs 0 pM, p=0.0305) were significantly higher in responders when compared to non-responders (Figure 1).

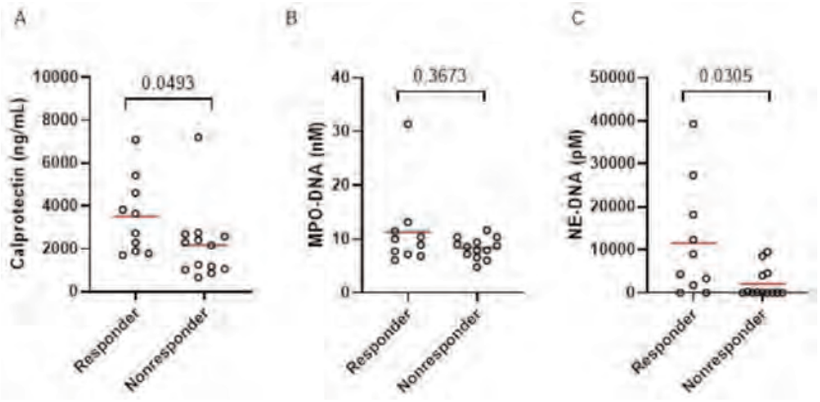

Figure 1. Comparison in baseline plasma levels of neutrophil-related markers between responders and non-responders. Comparison of plasma levels of calprotectin (A), MPO-DNA (B), and NE-DNA in circulation at baseline in patients treated with abatacept. Differences between groups were determined by the Mann-Whitney test.

Conclusion: Abatacept significantly decreased neutrophil activation in RA patients. Calprotectin and NE-DNA complexes may serve as useful markers in predicting the therapeutic efficacy of abatacept in moderate to severe RA patients.

Disclosure: T. Wang: None; **N. Giltiay**: None; **C. Lood**: Amytryx, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Citryll, 2, Eli Lilly, 5, Gilead, 5, Pfizer, 5, Redd Pharma, 2, 5, 11; **B. Han**: None.

Abstract Number: 1340

Recent Trends in Treatment Patterns for Rheumatoid Arthritis in Response to Emerging Data

Stephanie Song[1], Michael George[2], Ted R Mikuls[3], Bryant England[4], Brian Sauer[5], Grant Cannon[6] and Joshua Baker[2], [1]Hospital of the University of Pennsylvania, Philadelphia, PA, [2]University of Pennsylvania, Philadelphia, PA, [3]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE, [4]University of Nebraska Medical Center, Omaha, NE, [5]Salt Lake City VA/University of Utah, Salt Lake City, UT, [6]University of Utah and Salt Lake City VA, Salt Lake City, UT

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Janus kinase inhibitors (JAKi) have demonstrated substantial efficacy in decreasing symptoms and in reducing progressive joint damage in patients with rheumatoid arthritis (RA). In light of the ORAL Surveillance trial, which was published in January 2021, all JAKi (tofacitinib, baricitinib, upadacitinib) now carry black box warnings concerning risks of serious cardiac events, thromboembolism, cancer, and death associated with these agents. The purpose of this study was to determine whether prescribing practices for Janus kinase inhibitors (JAKi), TNF inhibitors (TNFi), and non-TNFi biologic agents changed after the results of the ORAL Surveillance trial were released in January 2021.

Methods: This is a retrospective study in adult patients with RA receiving advanced therapies within the Veterans Affairs (VA) Health System from January 2012 through September 2022. Eligible patients were required to have at least one diagnosis code for RA and to have received a biologic DMARD or JAKi. Treatment courses were defined

from pharmacy dispensing data and the proportion of new courses of each advanced therapy was quantified over time. We assessed changes in the use of each therapy before and after the release of safety data (January 2021).

Results: A total of 88,253 individual drug courses (in 34,656 unique patients) were included. The overall number of new drug courses decreased for most of the 11 advanced therapies in 2020, corresponding to the start of the COVID-19 pandemic, before resuming similar levels in 2021. From January 2021 through December 2020, there were consistent increases in the number and proportion of new courses of JAKi, which was followed by a significant net decrease in the proportion of JAKi use through September 2022 (**Figure 1A**). There were proportionally fewer initiations of tofacitinib after the release of safety data, with a significant difference in the slope of change with time (**Figure 1B**). In contrast, while use of TNFi declined leading up to 2021, TNFi use significantly increased after January 2021 (**Figures 1A and 2A**). The number and proportion of prescribed non-TNFi biologics were more variable over these years, with fluctuations in prescribing patterns observed as a class (**Figure 2B**).

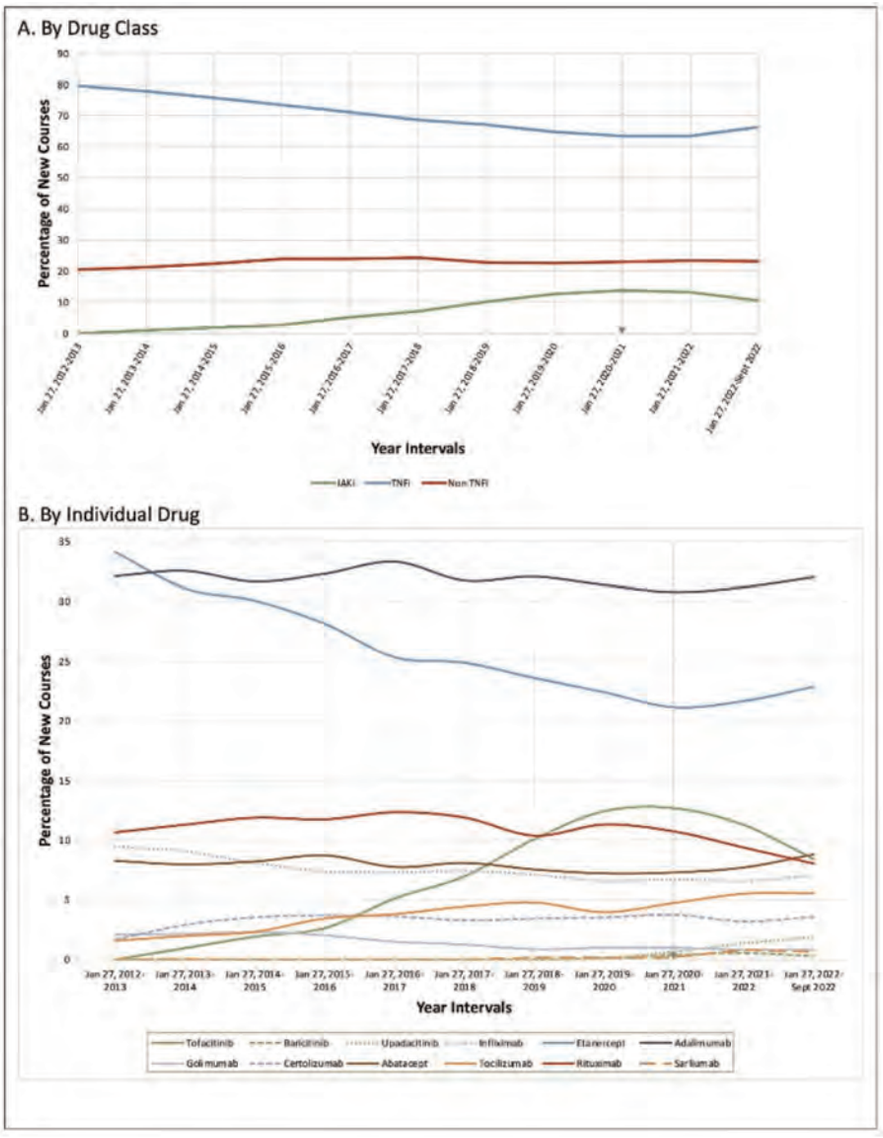

Figure 1. Percentage of Incident Drug Courses from January 2012 through September 2022

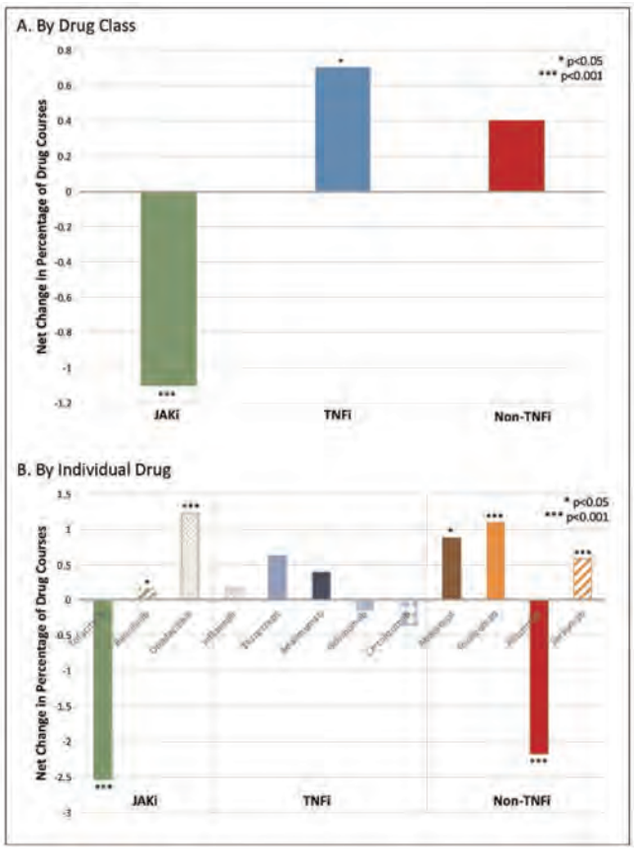

Figure 2. Net Change in Incident Courses of Biologic Agents 664 Days Before vs. After January 2021

Conclusion: The results of this study suggest that the release of safety data in January 2021 regarding adverse effects of JAKi influenced providers' prescribing practices for patients with RA. Changes in prescribing in response to new evidence emphasize the impact that safety trials have on prescribing practices. Ongoing study in this area, with attention to specific patient characteristics and risk profiles, will help characterize these changes in practice.

Disclosure: S. Song: None; **M. George**: AbbVie/Abbott, 2, GlaxoSmithKlein(GSK), 5, Janssen, 5; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **B. England**: Boehringer-Ingelheim, 2, 5; **B. Sauer**: None; **G. Cannon**: None; **J. Baker**: Bristol-Myers Squibb(BMS), 2, Burns-White, LLC, 2, CorEvitas, LLC, 2, Pfizer, 2.

Abstract Number: 1341

Impact of Ultrasound on Physician Assessments of Patients with RA with Elevated Clinical Disease Activity Scores

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Treat-to-target is recommended in RA, but physicians often do not escalate therapy despite elevated disease activity measures due to uncertainty regarding the true degree of joint inflammation. This study evaluated the utility of ultrasound (U/S) in assessing disease activity in patients with RA with moderate disease activity measures but few swollen joints. We aimed to determine the frequency of active synovitis on U/S and compare physician treatment recommendations before and after U/S.

Table 1. Patient Characteristics by Maximum Power Doppler Synovitis Score

Table 1. Patient Characteristics by Maximum Power Doppler Synovitis Score

	Maximum PD Synovitis Score	
	≤1	≥2
Characteristic	n = 11	n = 7
Demographics		
Age, mean (std)	59.5 (11.6)	67.1 (4.3)
Female	10 (90.9%)	5 (71.4%)
Race		
White	7 (63.6%)	3 (42.9%)
Black/African American	2 (18.2%)	4 (57.1%)
Asian	2 (18.2%)	0 (0%)
Ethnicity		
Hispanic or Latino	2 (18.2%)	0 (0%)
RA Characteristics		
RA duration years, mean (std)	12 (11.1)	16.7 (14.1)
BMI, mean (std)	29.5 (7.9)	34.2 (8.4)
Erosions on radiographs	2 (18.2%)	5 (71.4%)
Seropositive (anti-RF or anti-CCP)	4 (36.4%)	7 (100%)
SJC, median [IQR]	2 [1,2]	2 [2,2]
TJC, median [IQR]	6 [2,14]	7 [6,8]
Patient global, median [IQR]	5 [4,6]	4 [2,5]
Physician global, median [IQR]	4 [2,4]	4 [2,5]
CDAI, median [IQR]	14 [12,25]	16 [14,19]
Medication history		
Glucocorticoids	2 (18.2%)	4 (57.1%)
Methotrexate	5 (45.5%)	4 (57.1%)
Biologics	6 (54.6%)	5 (71.4%)
Opioids	1 (9.1%)	3 (42.9%)
Comorbidities		
Smoking		
Current	1 (9.1%)	1 (14.3%)
Former	3 (27.3%)	3 (42.9%)
Fibromyalgia syndrome	2 (18.2%)	0 (0%)
Depression	2 (18.2%)	0 (0%)
Anxiety	1 (9.1%)	0 (0%)
Patient-reported measures		
PROMIS fatigue T-score (std)	58.6 (8.3)	59.5 (10)
PROMIS depression T-score (std)	51.6 (9.0)	52.7 (8.6)
PROMIS Pain interference T-Score (std)	63.6 (6.9)	65.3 (6.7)

std: standard deviation; IQR: inter-quartile range

Methods: This single-center, prospective study enrolled adults who met 2010 ACR classification criteria for RA, had a clinical disease activity index (CDAI) >10 (moderate or high disease activity) but a swollen joint count (SJC) ≤2, and were receiving a DMARD. Patients completed surveys and underwent standardized U/S performed in the musculoskeletal (MSK) ultrasound department by a certified MSK U/S technologist using a high-resolution GE Logiq E10 system. Exams were interpreted by a single MSK U/S radiologist using the validated OMERACT scoring system, grading synovial hypertrophy by grayscale (GS) and hyperemia by power doppler (PD) in each of the bilateral MCPs, PIPs, and wrists as absent (0), minimal (1), moderate (2), or severe (3). Treating rheumatologists were surveyed pre-U/S and again after U/S to capture their impression of disease activity, confidence in their assessment (100-point scale), and treatment recommendations.

Results: We recruited 18 patients with RA: 15 (83%) females, mean age 62 years, and mean RA duration 14 years. U/S revealed moderate or severe synovial hypertrophy (GS grade 2 or 3) of at least one joint in 17/18 (94%) patients. In contrast, moderate or severe hyperemia of at least one joint (PD grade 2 or 3) was found in 7/18 (39%). Patients with active PD signal tended to be older, have longer disease duration, more frequent glucocorticoid use, higher body mass index, and more frequent seropositivity and erosions on radiographs; patient and physician global scores and PROMIS measures were similar (**Table 1**). Although CDAI scores indicated at least moderate disease activity pre-U/S, physician impression was that disease activity was low in 8/18 (44%) of patients pre-U/S. Physician-rated disease activity assessment changed after U/S in 6/18 (33%) patients: 3 to a higher level of disease activity and 3 to a lower level (**Figure 1**). Similarly, treatment decisions changed after U/S in 6/18 (33%) patients: 3 from no change to escalation of therapy and 3 from escalation to no change (**Figure 1**). Mean physician confidence in disease activity assessment increased from 54 pre-U/S to 72 post-U/S ($p< 0.01$).

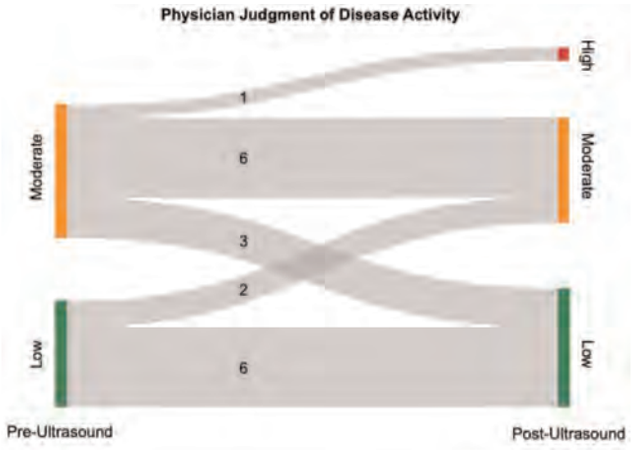

Figure 1. Pre- and Post-Ultrasound Physician Disease Activity Assessments

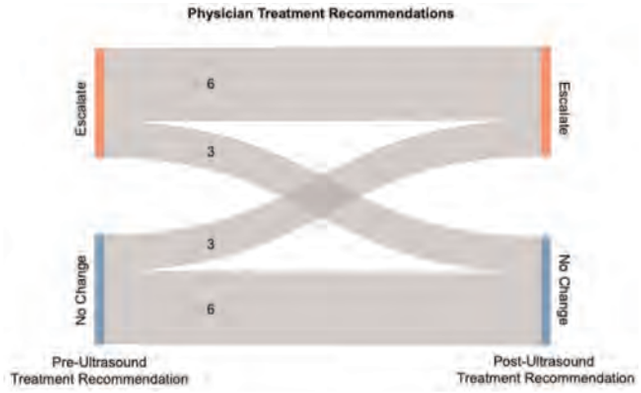

Figure 2. Pre- and Post-Ultrasound Physician Treatment Recommendations

Conclusion: In patients with longstanding RA, U/S demonstrating a moderate to high degree of synovial hypertrophy in at least one joint was nearly universal, but the presence of active PD signal was less common. Musculoskeletal U/S increased physician confidence in the assessment of disease activity and frequently led to a change in assessment and treatment recommendation. Future research should evaluate whether use of U/S to refine assessments of disease activity in patients with RA with high disease activity scores but few swollen joints can improve patient outcomes.

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Abstract Number: 1342

The Delivery of the Super-repressor IκBα by Exosomes Has the Potential to Alleviate Inflammation Associated with Rheumatoid Arthritis

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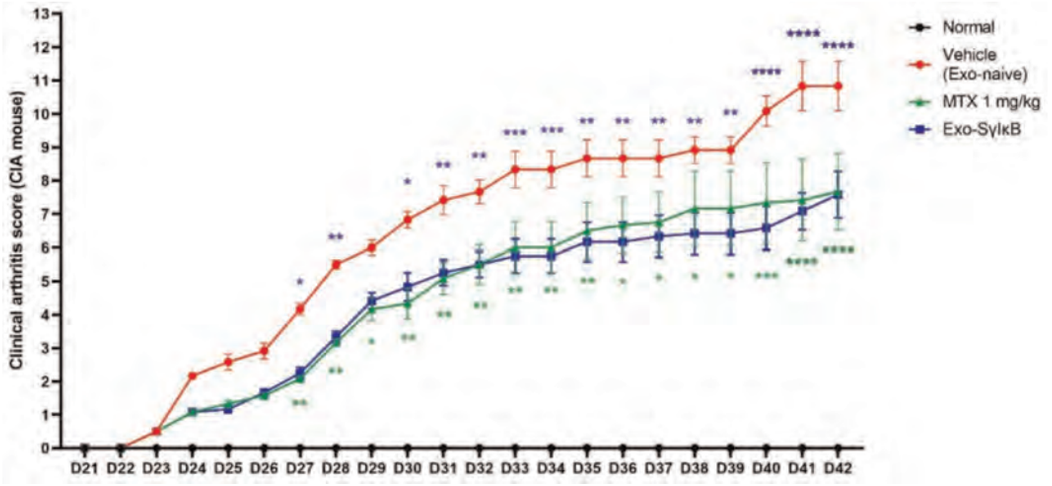
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a persistent inflammatory disease primarily affecting the diarthrodial joints. Nuclear factor-κB (NF-κB) is a family of inducible transcription factors responsible for regulating numerous genes involved in various aspects of immune and inflammatory diseases, including RA. This study aims to evaluate the potential anti-inflammatory properties of suppressor IκB (srIκB), an inhibitor of NF-κB when delivered by exosomes in the context of RA.



Exo-SrIκB treatment resulted in a reduction of clinical symptoms in mice with collagen-induced arthritis (CIA). The severity of arthritis in each group was assessed and scored based on clinical manifestations following treatment with either MTX, Exo-Naïve, or Exo-SrIκB.

Methods: Peripheral blood mononuclear cells (PBMCs) were collected from both healthy controls (HCs) and rheumatoid arthritis (RA) patients, and additional synovial fluid mononuclear cells (SFMCs) were collected from RA patients. Collected PBMCs and SFMCs were pretreated with Exo-srIκB or vehicle (Exo-Naïve) and then evaluated for cell viability. The subset of cells producing inflammatory cytokines, including IFN-γ, IL-17, and GM-CSF, was examined by flow cytometry and quantified by enzyme-linked immunosorbent assay (ELISA). To evaluate the therapeutic potential of Exo-srIκB in vivo, collagen-induced arthritis (CIA) mouse model was used. Mice were treated with Exo-srIκB or vehicle, and arthritis scores were calculated for monitoring disease progression. Histological observations of ankle joints were performed using hematoxylin and eosin (H&E) staining, and radiation damage scores were measured using micro-computed tomography micro-CT) imaging.

Results: Administration of Exo-SrIκB for 7, 24, and 48 hours had no significant effect on cell viability. However, treatment with Exo-SrIκB showed a significant reduction in the frequency of IL-17A- and GM-CSF-producing cells in PBMCs from rheumatoid arthritis patients. Exo-SrIκB treatment also reduced the frequency of GM-CSF-producing cells in SFMCs from RA patients. In the mouse experiment, Exo-SrIκB administration delayed the onset of arthritis and significantly reduced the severity of arthritis compared to the control group **(Figure 1)**. In addition, radiographic arthritis scores were significantly lower in Exo-SrIκB treated mice than in Exo-Naïve treated mice.

Conclusion: Exo-srIκB, which contains IκB as an inhibitor, demonstrates the ability to inhibit inflammatory cytokines in vitro and exhibits inhibitory effects in animal models. These findings suggest that regulation of NF-κB signaling by Exo-srIκB may be a promising therapeutic target for the treatment of RA.

Disclosure: K. Park: None; **J. Kang**: None; **H. Lee**: None; **Y. Lee**: None; **M. Kim**: None; **S. Ahn**: None; **J. Yoo**: None; **C. Choi**: None; **T. Kim**: None.

Abstract Number: 1343

Cardiovascular (CV) and Malignancy Events in the Filgotinib Rheumatoid Arthritis (RA) Clinical Development Program up to 8.3 Years

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

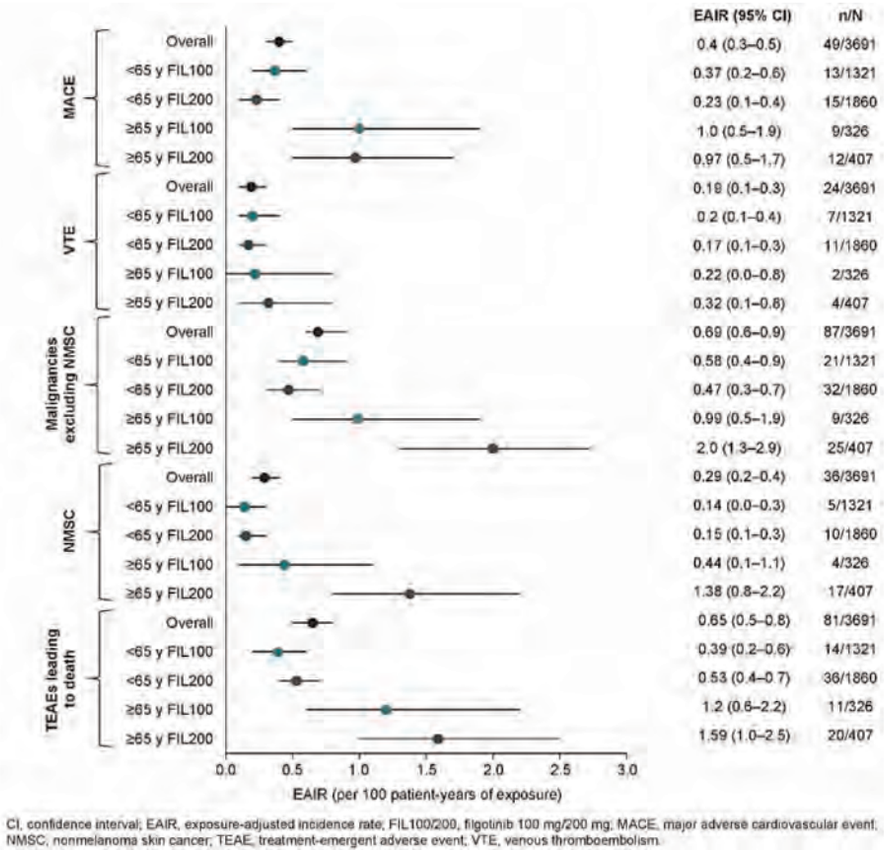
Background/Purpose: Filgotinib (FIL) is a Janus kinase (JAK) 1 preferential inhibitor for the treatment of RA. Data from the ORAL Surveillance post-marketing study (NCT02092467) suggest that in patients with active RA aged ≥50 years with ≥ 1 CV risk factor, the risks of cancer and major adverse cardiovascular events (MACE) are higher

Table. Baseline characteristics

	FIL200		FIL100	
	<65 y (n=1860)	≥65 y (n=407)	<65 y (n=1321)	≥65 y (n=326)
Age, y, mean (SD)	48.8 (10.7)	70.0 (4.4)	49.0 (10.5)	70.2 (4.5)
Female, n (%)	1506 (81.0)	322 (79.1)	1075 (81.4)	244 (74.8)
BMI, kg/m^2, mean (SD)	27.5 (6.3)	28.1 (5.9)	27.7 (6.4)	27.2 (5.1)
Creatinine clearance, mL/min, mean (SD)	122 (37.4)	84 (23.4)	122 (38.1)	83 (22.5)
CRP, mg/L, mean (SD)	19.0 (24.3)	18.4 (25.2)	18.9 (25.9)	17.2 (24.7)
Current smoker, n (%)*	207 (14.4)	37 (10.9)	165 (15.3)	28 (9.7)
CV family history, n (%)†	43 (3.0)	10 (2.9)	47 (4.3)	12 (4.2)
Any CV medical history, n (%)	672 (36.1)	308 (75.7)	540 (40.9)	234 (71.8)
Current alcohol use, n (%)*	296 (20.6)	78 (22.9)	213 (19.7)	54 (18.7)

*FIL200 <65 y: n=1436, ≥65 y: n=340; FIL100 <65 y: n=1081, ≥65 y: n=289.
†FIL200 <65 y: n=1434, ≥65 y: n=339; FIL100 <65 y: n=1081, ≥65 y: n=289.
BMI, body mass index; CRP, C-reactive protein; CV, cardiovascular; FIL100/200, filgotinib 100 mg/200 mg; SD, standard deviation.

with the pan-JAK inhibitor tofacitinib vs tumor necrosis factor inhibitors, with higher rates in those aged ≥ 65 vs < 65 years.[1]



CI, confidence interval; EAIR, exposure-adjusted incidence rate; FIL100/200, filgotinib 100 mg/200 mg; MACE, major adverse cardiovascular event; NMSC, nonmelanoma skin cancer; TEAE, treatment-emergent adverse event; VTE, venous thromboembolism.

Figure. EAIRs for treatment-emergent MACE, VTE, malignancies excluding NMSC, and NMSC overall, and by filgotinib dose and patient age (safety analysis set, as treated)

The objective of this analysis was to assess the incidence of malignancies excluding nonmelanoma skin cancer (NMSC), NMSC, MACE and venous thromboembolism (VTE) in patients treated with FIL 200 mg (FIL200) and FIL 100 mg (FIL100) in RA clinical trials.

Methods: Data were pooled from patients treated with FIL200 or FIL100 from DARWIN 1–3 (NCT01888874, NCT01894516, NCT02065700) and FINCH 1–4 (NCT02889796, NCT02873936, NCT02886728, NCT03025308). Data cuts used for the ongoing DARWIN 3 and FINCH 4 studies were May 2, 2022, and May 6, 2022, respectively. Exposure-adjusted incidence rates (EAIRs) per 100 patient-years of exposure (PYE) were calculated for MACE, VTEs, malignancies excluding NMSC, NMSC and treatment-emergent adverse events (TEAEs) leading to death, according to FIL dose (200 vs 100 mg) and age (< 65 vs ≥ 65 years); no statistical testing was performed, so all differences are numerical. MACE and VTE were adjudicated by an independent committee; the cutoff for adjudication was April 3, 2022.

Results: Overall, 3691 patients were treated with FIL for a total of 12,541 PYEs. Median (max) PYE was 3.8 (8.3) years for FIL200 and 3.3 (7.8) years for FIL100. Baseline characteristics are shown in the **Table**. A greater proportion of those aged ≥ 65 years vs < 65 years had a CV medical history in both the FIL200 (75.7% vs 36.1) and FIL100 (71.8% vs 40.9%) groups. Overall EAIRs (95% confidence interval [CI]) were 0.40 (0.3, 0.5) for MACE, 0.19 (0.1, 0.3) for VTEs, 0.69 (0.6, 0.9) for malignancy excluding NMSC, 0.29 (0.2, 0.4) for NMSC and 0.65 (0.5, 0.8) for TEAEs leading to death. EAIRs of MACE and VTE were higher in patients aged ≥ 65 vs < 65 years but were generally similar for FIL200 and FIL100 within each age group (**Figure**). EAIRs of malignancies, NMSC and TEAEs leading to death were also higher in the ≥ 65- vs < 65-year group. Within the ≥ 65-year group, EAIRs (95% CI) of these events were numerically higher in the FIL200 vs FIL100 group: 2.0 (1.3, 2.9) vs 0.99 (0.5, 1.9) for malignancies, 1.38 (0.8, 2.2) vs 0.44 (0.1, 1.1) for NMSC, and 1.59 (1.0, 2.5) vs 1.20 (0.6, 2.2) for TEAEs leading to death, respectively.

Conclusion: Rates of MACE and VTE in FIL-treated patients were low and similar for FIL200 and FIL100. There was a higher proportion of patients aged ≥ 65 years vs < 65 years with a CV medical history. In patients aged ≥ 65 years, EAIRs of malignancies, NMSC and TEAEs leading to death were higher with FIL200 vs FIL100, although CIs overlapped.

Reference:

1. Ytterberg SR, et al. N Engl J Med 2022;386:316–26

Disclosure: X. Mariette: AstraZeneca, 2, 6, BMS, 2, 6, Galapagos, 2, 6, GSK, 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **S. Borchmann**: Galapagos, 2, Liqomics, 11, Takeda, 6; **S. Aspeslagh**: AstraZeneca, 6, BMS, 6, BSMO, 2, 12, I lead BITOX and my university hospital is paid for the hours I invest in BITOX (a multidisciplinary board for immune related adverse events), Galapagos, 5, Ipsen, 6, MSD, 5, 6, Roche, 6, Sanofi, 5, 6; **J. Calvo- Alén**: AbbVie, 2, AstraZeneca, 2, Biogen, 6, BMS, 5, Galapagos, 6, GSK, 2, 6, Lilly, 2, 6, Novartis, 2, 6, Roche, 5, Sanofi, 2; **R. Moriggl**: Galapagos, 2; **Z. Szekanecz**: AbbVie, 2, 6, Galapagos, 2, 6, Gedeon Richter, 2, 6, Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 5, 6, Roche, 2, 6, Sobi, 2, 6, UCB, 2; **F. De Leonardis**: Galapagos, 3; **N. Verbruggen**: Galapagos, 3, 11; **P. Van Hoek**: Galapagos, 7; **M. Schmalzing**: AbbVie, 2, 6, Boehringer Ingelheim, 2, 5, 6, Chugai/Roche, 2, EUSA-Pharma, 2, 6, Galapagos, 2, 5, 6, Hexal/Sandoz, 2, Janssen-Cilag, 2, 6, Lilly, 2, onkowissen.de, 2, UCB, 2, 5; **A. Stallmach**: AbbVie, 2, 6, Amgen, 2, BMS, 2, 6, Celltrion, 6, CLS Behring, 6, Consal, 2, De Prom, 6, Falk Foundation, 6, Ferring, 6, Galapagos, 2, Gilead, 2, Janssen, 2, 6, Kompetenznetz Darmerkrankungen, 6, Lilly, 2, MedUpdate, 6, MSD, 2, 6, Pfizer, 2, Pharmacosmos GmbH, 2, Recordati, 6, Repha GmbH, 2, Roche, 2, Sobi Rare Strength, 6, Takeda, 2, 6, Tillotts Pharma, 2; **C. Charles-Schoeman**: AbbVie, 2, 5, Alexion, 5, BMS, 2, 5, Boehringer Ingleheim, 2, 5, CSL Behring, 5, Galapagos, 2, Pfizer, 2, 5, Priovant, 2, 5, Recludix, 2; **V. Rajendran**: Galapagos, 3, 11; **C. Rudolph**: Galapagos, 3, 11; **C. Watson**: Galapagos, 3, 11; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer-Ingelheim, 6, Chugai, 5, 6, Eisai, 5, 6, Eli Lilly, 6, Gilead, 6, GSK, 6, Mitsubishi-Tanabe, 5, Pfizer, 6, Taiho, 6, Taisho, 5, 6; **E. Choy**: AbbVie, 2, 6, Amgen,

2, 6, Bio-Cancer, 5, Biogen, 2, 5, Chugai Pharma, 2, 6, Eli Lilly, 2, 6, Fresenius Kabi, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Janssen, 2, Novartis, 5, Pfizer, 5, 6, R-Pharm, 2, Sanofi, 2, 5, 6, Sanofi-Genzyme, 2, UCB, 2.

Abstract Number: 1344

Efficacy and Safety of JAK Inhibitors in Difficult to Treat Rheumatoid Arthritis in Clinical Practice

Omar AL TABAA[1], Sophie HECQUET[2], Marion THOMAS[3], Sandrine CARVES[1], Alice Combier[1], Corinne MICELI[4], Olivier Fogel[3], Anna Molto[3], Yannick ALLANORE[5] and Jerome AVOUAC[6], [1]APHP / Cochin Hospital, Paris, France, [2]APHP / Cochin Hospital / Paris University, Paris, France, [3]HOPITAL COCHIN AP-HP, Service de Rhumatologie, Paris, France, [4]Université de Paris Cité, HOPITAL COCHIN AP-HP, Service de Rhumatologie, Paris, France, [5]Université Paris Cité, Paris, France, [6]Rheumatology A Department, Hôpital Cochin, AP-HP Centre - Université Paris Cité, Paris, France

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: RA – Treatments Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Use of JAK inhibitors (JAKi) may be challenged in difficult to treat rheumatoid arthritis (D2TRA) by the multiplicity of previous treatment lines and the presence of comorbidities that may trigger the occurrence of potentially severe side effects. Our objective was to assess the efficacy and safety profile of JAKi in patients with D2TRA in clinical practice

Methods: Retrospective routine care study carried out between 2018 and 2022 our department. We selected from our electronic medical report database RA patients initiating a JAKi between 2018 and 2022. D2TRA was defined by failure to at least two targeted biological therapies of different mechanisms of action and at least one of the following: active disease, defined by a DAS28 >3.2, signs and/or symptoms suggestive of active disease or inability to taper glucocorticoid treatment below 7.5mg/day (1). D2TRA patients were compared to JAKi-treated patients not fulfilling this D2TRA definition (non-D2TRA). Efficacy was assessed at the first visit (FV) (3 to 6 months following the JAKi initiation) and at the last available visit (LV) up to December 2022 on the basis of the DAS28 and DAS28-CRP composite index and its components. The number of side effects and causes of treatment discontinuations were collected during the exposition period

Results: We included 83 RA patients initiating a JAKi, with a mean age of 58±14 years and a mean disease duration of 16 ±13 years. Among them, we identified 45 D2TRA and 38 non-D2TRA patients (**Table 1**). Patients with D2TRA had longer disease duration and active disease and previous targeted therapies. DAS28 was reduced between baseline and FV in both groups, with a significantly higher extent in non-D2TRA patients, and then remain stable in both groups between FV and the LV, which occurred 15±10 months after the baseline (**Table 2**). These results were similar for other parameters assessing disease activity (**Table 2**). Higher proportion of patients reached remission or low disease activity (LDA, DAS28< 3.2) in the non-D2TRA subgroup (FV: 82% vs. 53%, p=0.012; LV: 71% vs. 33%, p=0.006) compared to D2TRA. A total of 35 patients discontinued the JAKi during a mean observation period of 20±10 months. Mean time to discontinuation was 10±8 months. Frequency of discontinuation was not different for D2TRA and non-D2TRA patients (21/45, 47% vs 14/38, 37%, p=0.36). Discontinuations related to inefficacy and side effects occurred in 20/83 patients (24%) and 11/83 patients (13%), respectively, and were evenly distributed between patients with D2TRA and non-D2TRA. Frequency of infections (n=31), herpes zoster (n=3) myocardial infractions (n=3) and venous thromboembolism (n=3) was similar between groups. These events were more likely to occur in the subgroup of patients aged ≥65 years and/or with at least one CV risk factor (30/39, 77%)

Table 1: Patients' characteristics at inclusion

	Non-D2TRA (n=38)	D2TRA (n=45)	p-value
Baseline demographics			
Age (years), mean ± SD	57±15	59±14	0.53
Women, n (%)	28 (74)	40 (89)	0.077
Baseline disease characteristics			
Disease duration (days), mean ± SD	14±14	21±11	0.012
Positive rheumatoid factor, n (%)	29 (76)	39 (87)	0.19
Positive anti-CCP2 antibodies, n (%)	33 (87)	41 (91)	0.56
Erosions on hand/foot x-rays, n (%)	28 (74)	38 (84)	0.26
Extra-articular manifestations	13 (34)	12 (27)	0.49
Pulmonary involvement / interstitial lung disease, n (%)	3 (8) / 2 (5)	2 (4) / 2 (4)	0.44 / 0.89
Baseline disease activity:			
Tender joints, mean±SD	2.9±3.1	7.9±6.1	<0.001
Swollen joints, mean±SD	3.4±3.9	5.2±4.4	0.054
Pain VAS	57±28	62±25	0.39
Fatigue VAS	65±28	62±29	0.63
PGA	57±26	65±22	0.13
DAS28, mean±SD	3.91±1.34	4.96±1.35	0.001
DAS28-CRP, mean±SD	3.54±1.07	4.46±1.16	<0.001
ESR (mmH1), mean ±SD	32±24	27±24	0.34
CRP (mg/L), mean ±SD	10.1±16.7	8.5±9.9	0.59
Baseline comorbidities			
Active Smokers / former smokers, n (%)	4 (10) / 11 (29)	6 (13) / 9 (20)	0.67 / 0.34
High blood pressure, n (%)	6 (16)	14 (31)	0.11
Diabetes mellitus, n (%)	5 (13)	4 (9)	0.56
Hypercholesterolemia, n (%)	5 (13)	7 (15)	0.79
BMI, kg/m2, mean ±SD	25±5	25±5	0.99
BMI >30 kg/m2, n (%)	6 (16)	11 (24)	0.37
Atherosclerotic cardiovascular disease, n (%)	2 (5)	1 (2)	0.45
History of ischemic stroke, n (%)	3 (8)	0 (0)	0.054
History of venous thromboembolism, n (%)	3 (8)	3 (7)	0.86
History of severe infection, n (%)	3 (8)	1 (2)	0.20
History of herpes zoster, n (%)	5 (13)	4 (9)	0.56
Previous neoplasia, n (%) (Solid/hemopathy)	5 (13) / (2/3)	7 (16) (6/1)	0.70
≥65 years and/or at least one CV risk factor, n (%)	21 (55)	33 (73)	0.089
Treatments received at baseline			
JAKI received			
Baricitinib	12 (32)	17 (38)	0.57
Tofacitinib	3 (8)	5 (11)	0.64
Upadacitinib	20 (52)	23 (51)	0.98
Filgotinib	3 (8)	0 (0)	0.055
Current corticosteroid use, n (%)	29 (76)	30 (67)	0.37
Corticosteroid dose, mg/day, mean±SD	4.7±3.6	4.8±3.0	0.99
Corticosteroid dose ≥7.5 mg/day	7 (18)	10 (22)	0.65
Current conventional DMARD use, n (%)	32 (84)	35 (78)	0.49
Current MTX use, n (%)	22 (58)	30 (67)	0.40
Targeted therapeutic line of the JAKi			
First line	15 (39)	0 (0)	<0.001
Second line	20 (53)	0 (0)	<0.001
Third line	0 (0)	19 (42)	<0.001
>3 line	3 (8)	26 (58)	<0.001
Previous targeted therapies			
TNF inhibitors, n (%)	16 (4)	44 (98)	<0.001
Rituximab, n (%)	5 (13)	17 (38)	0.011
IL6 receptor inhibitors, n (%)	3 (8)	21 (47)	<0.001
abatacept, n (%)	3 (8)	23 (51)	<0.001

VAS: Visual Analogic Scale, PGA: patient Global Assessment, ESR: Erythrocyte Sedimentation Rate, CRP: C-reactive Protein; DAS: Disease Activity Score, SD: Standard Deviation; BMI: Body Ma Index, CV: cardiovascular, DMARD: Disease-Modifying Anti-Rheumatic Drug, MTX: Methotrexate, TNF: Tumor Necrosis Factor

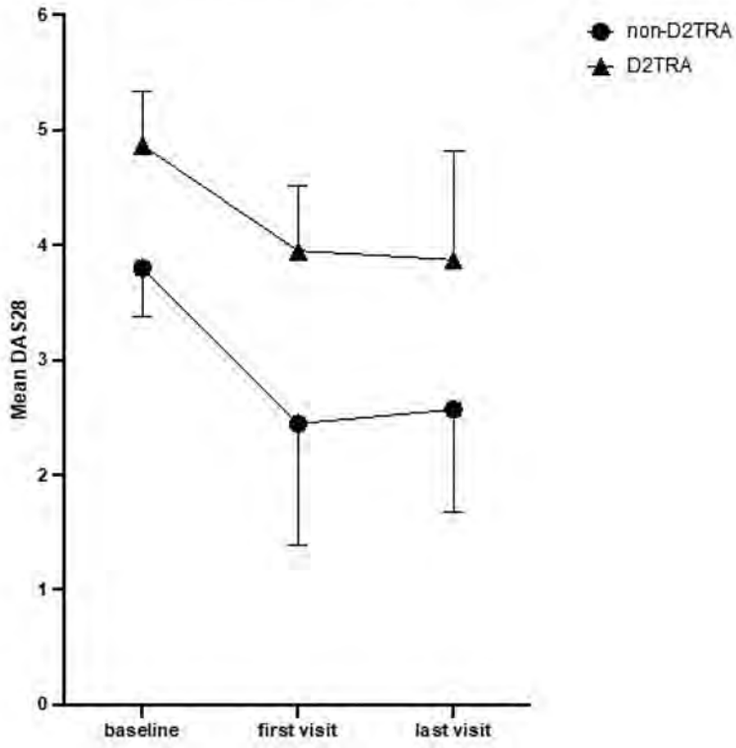
Conclusion: JAKi reduced disease activity parameters of patients with D2TRA. However, disease activity level of these patients remained high, with a proportion of LDA or remission significantly lower compared to non-D2TRA, highlighting the need of improved therapeutic strategies in D2TRA. Tolerance profile of JAKi was not different between patients with D2TRA and non-D2TRA and largely depended on the presence of risk factors

Table 2: Efficacy of JAK inhibitors in D2TRA

	Difference First visit-baseline		p-value	Difference last visit-first visit		p-value
	Non-D2TRA	D2TRA		Non-D2TRA	D2TRA	
Tender joints, mean±SD	-1.5±2.9	-3.6±5.8	0.046	-0.26±2.3	-0.51±3.0	0.67
Swollen joints, mean±SD	-1.8±3.9	-1.3±3.4	0.53	-0.44±2.9	-0.06±2.4	0.51
VAS pain (/100), mean±SD	-33±28	-26±27	0.25	+12±25	+2.05±26	0.079
VAS fatigue (/100), mean±SD	-35±28	-16±26	0.001	+5±25	+9±33	0.54
PGA (/100), mean±SD	-40±18	-24±40	0.025	+9±21	+5±23	0.41
ESR (mm H1), mean±SD	-12±21	+3.4±21	0.001	+2.4±13	-0.1±11	0.34
CRP (mg/L), mean±SD	-3.6±6.0	-2.1±8.5	0.36	-0.9±6	+1.3±8	0.17
DAS28, mean±SD	-1.60±1.21	-0.95±1.54	0.038	+0.15±0.99	-0.10±1.12	0.29
DAS28-CRP, mean±SD	-1.17±0.86	-1.09±1.55	0.78	+0.16±0.67	-0.10±1.05	0.19

VAS: Visual Analogic Scale, PGA: patient Global Assessment, ESR: Erythrocyte Sedimentation Rate, CRP: C-reactive Protein; DAS: Disease Activity Score, SD: Standard Deviation

Figure 1: Course of the DAS28 in patients with D2TRA and non-D2TRA



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Abstract Number: 1345

Maternal and Infant Outcomes Following Abatacept Exposure During Pregnancy

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Background/Purpose: Abatacept is approved for the treatment of moderate to severe rheumatoid arthritis (RA) and psoriatic arthritis. However, there are limited data on the safety of abatacept when used in pregnancy. The purpose of this study was to estimate the incidence/birth prevalence of selected maternal and infant outcomes in pregnancies exposed to abatacept.

Methods: Pregnant women exposed to any dose of abatacept from the first day of the last menstrual period to the end of the first trimester (with or without continued use in pregnancy) and who resided in the U.S. or Canada were enrolled in the Organization of Teratology Information Specialists (OTIS) Abatacept Pregnancy Exposure Registry between 2007 and 2019. Data on maternal characteristics, pregnancy and infant outcomes including major and minor birth defects were collected throughout pregnancy and the first-year post-partum through maternal interviews, medical records abstraction, and dysmorphology examinations.

Results: The study sample was comprised of 30 abatacept-exposed pregnancies (Table 1). Of these, 16 were treated for RA and were enrolled in a prospective cohort, and 14 who did not meet the cohort criteria were enrolled in a "registry group".Reasons that pregnancies did not meet the cohort criteria included retrospective enrollment, co-exposure to an exclusionary medication, or abatacept used for an indication other than RA. In the prospective cohort, 13/16 pregnancies (81.3%) resulted in at least one live birth, 2/16 pregnancies (12.5%) ended in spontaneous abortion, 2/13 pregnancies (15.4%) were delivered preterm (< 37 weeks' gestation) and 1/16 (6.3%) was lost-to-follow-up. One pregnancy of 13 ending in a livebirth (8.3%) involved a child with a major birth defect, congenital chordee (Table 2). In the registry group 14/14 pregnancies (100.0%) resulted in at least one livebirth and 6/14 (42.9%) were delivered preterm. Three of 14 pregnancies (21.4%) ended with a liveborn infant with a major birth defect (pyloric stenosis, cleft lip and palate, and patent foramen ovale).An additional two pregnancies in the registry group (14.3%) ended with an infant with major birth defects in association with a genetic or chromosomal alteration (Table 2). A dysmorphology examination for minor birth defects was completed for 6 infants in the prospective cohort and 7 in the registry group. No patterns of either major or minor birth defects were identified. The number of liveborn infants who were small for gestational age (SGA) ($\leq 10^{th}$ centile for sex and gestational age at birth) or smaller ($\leq 10^{th}$ centile) at about one year of age on weight, length or head circumference was unremarkable.

Conclusion: Although there was no internal comparison group and the sample size was small, no specific risks were identified in the prospective cohort for any of the outcomes examined. In the registry group, selected adverse outcomes were more frequent, likely due to the biases that led to exclusion of these pregnancies from the prospective cohort. However, no patterns of major or minor birth defects were identified in either group. Future studies with a larger sample size are needed.

*One pregnancy involved twins ending in one live birth and one spontaneous abortion; counted only in the outcome of livebirth

Table 1. Outcomes in Pregnancies Exposed to Abatacept (n=30)

	Abatacept-Exposed (N = 16)	Abatacept-Registry (N = 14)
Major Birth Defects in Pregnancies Ending with Live-born Infants	1/13* (7.7)	5/14 (35.7)
Major Birth Defects in All Pregnancies Excluding Lost-to-Follow-up	1/15 (6.7)	5/14 (35.7)
Pattern of Minor Birth Defects in Infants Who Received the Physical Examination	0/6 (0.0)	0/7 (0.0)
Dysmorphology Examination	6/13 (46.2)	7/13 (53.8)
Spontaneous Abortion	2/16 (12.5)	0/14 (0.0)
Stillbirth	0/16 (0.0)	0/14 (0.0)
Termination	0/16 (0.0)	0/14 (0.0)
Preterm Delivery	2/13 (15.4)	6/14 (42.9)
Small for Gestational Age ≤10th centile on Weight	1/13 (7.7)	2/14 (14.3)
Small for Gestational Age ≤10th centile on Length	0/13 (0.0)	0/13 (0.0)
Small for Gestational Age ≤10th centile on Head Circumference	2/11 (18.2)	0/12 (0.0)
Postnatal Growth ≤10th centile on Weight at 1 year of age	0/16 (0.0)	2/14 (14.3)
Postnatal Growth ≤10th centile on Length at 1 year of age	0/16 (0.0)	2/14 (14.3)
Postnatal Growth ≤10th centile on Head Circumference at 1 year of age	0/16 (0.0)	2/14 (14.3)
Lost-to-Follow-Up	1/16 (6.3)	0/14 (0.0)

Table 2. Major Birth Defects in Infants Exposed to Abatacept in Utero

Major Birth Defects in Prospective Cohort
1. Congenital chordee
Major Birth Defects in Registry Group
1. Congenital hypertrophic pyloric stenosis
2. Cleft lip with cleft palate
3. Patent foramen ovale
Major Birth Defects Associated with Chromosomal or Genetic Alterations in the Registry Group
1. Balanced chromosome translocation (46XX, balanced translocation between 14/15) with microcephaly, persistent with right aortic arch, and pulmonary atresia with ventricular septal defect
2. 14Q 11.2 microdeletion with anomalous optic nerves (bilateral) with vascular abnormality and developmental delay

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Abstract Number: 1346

Semen Analysis of Patients with Psoriatic Arthritis, Axial Spondyloarthritis and Healthy Controls

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Background/Purpose: Psoriatic arthritis (PsA) and axial spondyloarthritis (AxSpA) are commonly diagnosed in young males in their reproductive years. However, only a few studies have investigated male fertility in patients with spondyloarthritis (SpA). Our objective was to evaluate the sperm quality in male patients with PsA and AxSpA compared to healthy controls (HC) and to investigate the effects of disease activity and anti-rheumatic drugs on sperm quality.

Methods: Consecutive PsA and AxSpA patients (age range 18-50 years), who fulfilled the classification criteria for PsA (CASPAR) and AxSpA (ASAS) were recruited prospectively. HC were recruited from candidate sperm donors at the male fertility clinic. Each patient was evaluated by a comprehensive clinical assessment that included measurement of disease activity scores (MDA/DAPSA/CPDAI/PASDAS for PsA and ASDAS for AxSpA). Treatments ranged from no treatment to conventional and biologic DMARDs. Sperm collection and analysis were performed on the day of clinical assessment. Sperm analysis was performed according to the World Health Organization 2010 guidelines. In addition, sperm DNA-fragmentation test was performed.

Continuous variables were compared using a t-test or Anova for normally distributed data, otherwise, a non-parametric test was applied. Fisher's exact test was used to compare categorical variables.

Results: 70 patients (40 PsA and 30 AxSpA) and 50 HC were included. Demographics and clinical characteristics are presented in Table 1. Most semen parameters, including concentration, and vitality of PsA and AxSpA patients were similar to those of HC ($p > 0.05$).The proportion of normal morphology in patients was significantly lower compared to HC (3.01 (± 1.39) vs 4.64 (±2.00), $p < 0.0001$). The motility in patients vs. controls was lower (56.89 (± 11.50) vs. 59.54 (± 14.31), $p=0.04$). Nevertheless, values for both groups were within the normal range (>40%) and the total motile count was normal and similar between the groups (Table 2).

Table 1 - Demographic and clinical characteristics of patients with PsA, AxSpA and healthy controls

	PsA n=40	AxSpA n=30	Healthy controls n=50
Demographics			
Age, years, mean (± s.d)	37.75 (±7.27)#	35.02 (± 6.08)#	31.68 (± 1.04)#
BMI, mean (± s.d)	25.65 (±4.38)	24.77 (± 3.80)	-
Smoking, n (%)	5 (13)	9 (30)	-
University education, n (%)	26 (65)	20 (67)	-
Employed, n (%)	39 (98)	27 (90)	-
Married/in relationship, n (%)	24 (60)	13 (43)	-
No. of children, mean (± s.d)	0.95 (± 1.24)	0.7 (± 1.12)	-
No. of spontaneous abortions, mean (± s.d)	0.08 (± 0.27)	0.17 (± 0.38)	-
Clinical			
Psoriasis duration, years, mean (± s.d)	12.20 (± 8.79)	-	-
Disease duration (PsA/AxSpA), years, mean (± s.d)	5.86 (± 5.60)	7.16 (± 6.44)	-
Tender joint count, mean (± s.d)	4.03 (± 6.87)	0.37 (± 0.56)	-
Swollen joint count, mean (± s.d)	1.28 (± 2.40)	0.07 (± 0.25)	-
CRP (mg/L), mean (± s.d)	4.44 (± 5.28)	4.90 (± 8.23)	-
Disease activity scores			
MDA, n (%)	25 (63)	-	-
DAPSA, mean (± s.d)	12.71 (± 13.33)	-	-
CPDAI, mean (± s.d)	4.58 (± 3.07)	-	-
PASDAS, mean (± s.d)	2.89 (± 2.03)	-	-
ASDAS, mean (± s.d)	-	2.20 (± 1.21)	-
Treatment			
No treatment, n (%)	14 (35)	14 (47)	-
CsDMARDs*, n (%)	3 (8)	-	-
CsDMARDs+TNFi**, n (%)	4 (10)	-	-
TNFi**, n (%)	10 (25)	14 (47)	-
Anti-IL17**, n (%)	6 (15)	2 (7)	-
Anti-IL12/23 or anti-IL23**, n (%)	3 (8)	-	-

P-Value<0.05 (vs. healthy controls)
*CsDMARDs= conventional synthetic DMARDs: Methotrexate, Leflunomide
**Biologic therapy= TNFi (Infliximab+Etanercept+Adalimumab+Golimumab), Anti-IL17 (Secukinumab+Ixekizumab), Anti-IL23 (Guselkumab), Anti-IL12/23 (Ustekinumab)

Table 2 - Semen analysis of patients with PsA and AxSpA compared with healthy controls

	Normal values - WHO 2010	PsA+AxSpA n=70	Healthy controls n=50	P-value
PH, mean (± s.d)	>7.2	8.12 (± 0.31)	8.17 (± 0.33)	0.57
Volume (ml), mean (± s.d)	>1.5	2.89 (± 1.32)	2.78 (± 1.46)	0.47
Concentration (million/ml), mean (± s.d)	>15	53.68 (± 29.76)	52.10 (± 33.39)	0.79
Motility, mean (± s.d)	>40%	56.89 (± 11.50)	59.54 (± 14.31)	**0.04**
Total motile count (million), mean (± s.d)	>20	90.35 (± 79.40)	103.41 (± 88.67)	0.42
Vitality, mean (± s.d)	>58%	81.01 (± 8.02)	82.35 (± 7.48)	0.40
Normal morphology, mean (± s.d)	>4%	3.01 (± 1.39)	4.64 (± 2.00)	**<0.0001**
Total DNA fragments, mean (± s.d)	<30%	11.76 (± 4.73)	-	-

	Normal values - WHO 2010	No treatment n=28	CsDMARDs* n=3	CsDMARDs*+ biologic therapy** n=4	Biologic therapy** n=35	P-value
PH, mean (± s.d)	>7.2	8.12 (±0.37)	8.20 (±0.17)	8.33 (±0.29)	8.09 (±0.27)	0.50
Volume (ml), mean (± s.d)	>1.5	2.94 (±1.36)	2.83 (±1.04)	2.88 (±1.90)	2.85 (±1.29)	0.99
Concentration (million/ml), mean (± s.d)	>15	61.68 (±32.87)	41.67 (±22.85)	58.25 (±21.62)	47.79 (±27.64)	0.27
Motility, mean (± s.d)	>40%	62.57 (±7.99)	62.33 (±7.02)	58.75 (±4.99)	51.66 (±12.44)	**0.003**
Total motile count (million), mean (± s.d)	>20	117.18 (±100.45)	68.38 (±48.75)	93.80 (±67.74)	70.37 (±56.47)	0.12
Vitality, mean (± s.d)	>58%	83.43 (±5.62)	83.00 (±3.00)	82.75 (±2.87)	78.71 (±9.65)	0.22
Normal morphology, mean (± s.d)	>4%	2.89 (±1.31)	3.00 (±1.00)	2.75 (±1.71)	3.14 (±1.48)	0.89
Total DNA fragments, mean (± s.d)	<30%	11.75 (±4.80)	8.67 (±0.58)	14.75 (±6.70)	11.69 (±4.60)	0.37

*CsDMARDs= conventional synthetic DMARDs: Methotrexate, Leflunomide
**Biologic therapy= TNFi (Infliximab+Etanercept+Adalimumab+Golimumab), Anti-IL17 (Secukinumab+Ixekizumab), Anti-IL23 (Guselkumab), Anti-IL12/23 (Ustekinumab)

In addition, no differences were observed in semen analysis in the different disease activity states (remission/low and moderate/high disease activity) for PsA and for AxSpA ($p > 0.05$). Finally, a comparison of the different treatment options (no treatment, conventional and biologic DMARDs) showed overall no differences, while motility was slightly lower in patients treated with biologic therapy (62.57 (±7.99), 62.33 (±7.02), 58.75 (±4.99) and 51.66 (±12.44) for no treatment, conventional synthetic DMARDs, conventional synthetic DMARDs+biologic therapy, and biologic monotherapy respectively, $p=0.003$). However, values for all groups were within the normal range (>40%) and the total motile count was normal and similar between the groups (Table 3).

Conclusion: In this relatively large study evaluating semen analysis in spondyloarthropathies, the semen quality of PsA and AxSpA patients was comparable to HC in most parameters. In addition, neither disease activity nor antirheumatic drugs substantially affected sperm quality. Our results do not support cryopreservation of semen before treatment initiation nor a drug free interval prior to conception. Further longitudinal large studies are needed.

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Abstract Number: 1347

Continuing Biologic DMARDs During Pregnancy in Women with Rheumatic Disease Was Not Associated with Increased Unfavorable Pregnancy Outcomes, Serious Infections, and Adverse Effects of Vaccination

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SESSION INFORMATION

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Background/Purpose: It is important to control disease activity during pregnancy in women with rheumatic diseases because its exacerbation is associated with increased adverse pregnancy outcomes. Some of biologic disease-modifying anti-rheumatic drugs (bDMRARDs), especially in TNF inhibitors, are safe to continue during pregnancy, and become key drugs for controlling disease activity during pregnancy. However, there is little evidence whether continuing these drugs really does not affect unfavorable pregnancy outcomes, serious infections for mothers and infants, and adverse events of vaccination. Therefore, we investigated the effects of bDMARDs continuation on them.

Methods: We used the data of patients with rheumatic diseases who had been treated before pregnancy and gave birth in our institution. We extracted cases who were treated with bDMARDs at the time of conception, and divided them into two groups that discontinued bDMARDs at the time of pregnancy confirmed (discontinued group), and continued bDMARDs after pregnancy confirmed (continued group). We retrospectively examined pregnancy outcomes, serious infections requiring hospitalization for mothers and infants, live vaccination for infants in these two groups

Results: Of 238 cases with rheumatic diseases who gave birth in our institution, 32 cases were treated with bDMARDs at the time of conception. Of these, 27 cases were rheumatoid arthritis, 3 cases were Behcet disease, 1 case was juvenile idiopathic arthritis, and 1 case was Takayasu aortitis, which were divided into 17 cases of the continued group, and 15 cases of discontinued group. Table 1 showed patients' characteristics and treatment during pregnancy. In the continued group, certolizumab pegol was administered in 10 cases, etanercept was 3 cases, adalimumab was 3 cases, and tocilizumab was one case. All cases continued into second or third trimester with mean discontinued weeks of 28.5±5.1 weeks. In discontinued group, the mean dose of glucocorticoid was significantly higher compared to continued group (7.7±3.7 vs. 3.6 ±1.6, P=0.03). Table 2 showed pregnancy outcomes. The gestational weeks at delivery and birth weight in continued group were similar with discontinued group, and there was no significant difference of adverse pregnancy outcomes between these two groups. No serious infections requiring hospitalization were observed in either mother and infant in both groups.

Table 1. patients' characteristics and treatment during pregnancy. Values are presented as the mean ± standard deviation or number (%). #Wilcoxon rank sum test; ##Fisher's exact test. *P < 0.05.

	Continued group (n=17)	Discontinued group (n=15)	P value
Mean age at delivery, years old#	33.5 ± 3.8	33.3 ± 4.3	0.66
Mean disease duration, years#	7.2 ± 4.5	5.1 ± 3.3	0.19
Primiparity, n(%)##	8 (47.1)	8 (53.3)	1.00
Treatment during pregnancy			
Glucocorticoid, n(%)##	9 (52.9)	6 (40.0)	0.50
Mean dose of glucocorticoid, mg/day#	3.6 ± 1.6	7.7 ± 3.7	0.03*
Increasing dose of glucocorticoid, n(%)##	3 (17.7)	5 (33.3)	0.42
bDMARDs			
Certolizumab pegol, n(%)	10 (58.8)		
Etanercept, n(%)	3 (17.7)		
Adalimumab, n (%)	3 (17.7)		
Tocilizumab, n(%)	1 (5.9)		

Table 2. Pregnancy outcomes, serious infection, and adverse events of vaccination. Values are presented as the mean ± standard deviation or number (%). #Wilcoxon rank sum test; ##Fisher's exact test. *P < 0.05.

	Continued group (n=17)	Discontinued group (n=15)	P value
Caesarean section, n(%)##	8 (47.1)	3 (20.0)	0.15
Gestational age at delivery, week#	38.5 ± 1.3	38.6 ± 1.5	0.73
Birth weight, gram#	2891.2 ± 372.9	2887.5 ± 469.7	0.92
Adverse pregnancy outcomes, n(%)##	3 (17.7)	2 (13.3)	1.00
preterm birth, n(%)##	1 (5.9)	1 (6.7)	1.00
Low birth weight, n(%)##	2 (11.8)	2 (13.3)	1.00
Small for gestational age, n(%)##	0 (0)	1 (6.7)	0.47
Hypertensive disorder, n(%)##	0 (0)	1 (6.7)	0.47
Congenital malformation, n(%)##	1 (5.9)	0 (0)	1.00
Serious infections for mothers and infants, n(%)	0 (0)	0 (0)	
Adverse evets of vaccination for infants, n(%)	0 (0)	0 (0)	

In addition, the infants received rotavirus vaccine from 2 months after birth, and BCG vaccine after 6 months according to the Japanese vaccine schedule, however, none of the infants had any adverse events due to vaccination.

Conclusion: In patients with rheumatic diseases, continuing bDMARDs had no association with the increase of unfavorable pregnancy outcomes, serious infections, and adverse events of vaccination. It was suggested that the continuation of bDMARDs may be an effective treatment option for rheumatic diseases during pregnancy. Larger number of examinations are needed as to how long to continue bDMARDs during pregnancy.

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Abstract Number: 1348

Reproductive Outcomes for Women with Vasculitis

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Background/Purpose: There are limited data on the reproductive health of women with vasculitis. This study utilized a large, prospective, international vasculitis pregnancy registry to survey women during and after pregnancy to improve characterization of reproductive outcomes.

Methods: The Vasculitis Pregnancy Registry (VPREG) is imbedded within the online Vasculitis Patient-Powered Research Network (VPPRN). Any pregnant woman with a diagnosis of vasculitis can self-enroll. After enrollment, women are invited to complete online surveys at study entry, once each trimester, and post-partum. Survey questions are organized into three categories: pregnancy outcomes and complications, vasculitis medications, and disease activity. VPREG surveys are currently available in five languages.

Results: Since 2015, 147 women with 149 pregnancies have enrolled in VPREG from 16 countries. Seventy-one pregnancies were excluded as nine women have ongoing pregnancies and 62 women were lost to follow-up. Seventy-eight pregnancies have known pregnancy outcomes (live or non-live birth) and were included in this analysis. Of these 78 pregnancies, ANCA-associated vasculitis was the most frequently reported diagnosis (n=35, 45%) followed by Takayasu's arteritis (n=15, 19%), Behcet's (n=7, 9%), and other forms (n=21, 27%). During pregnancy, women experienced low pain related to vasculitis (scale 0-10, mean 3.1 ± 3.0) and preserved feelings of wellness (scale 0-10, mean 3.4 ± 3.1). Nineteen women reported experiencing a flare of vasculitis during pregnancy. Of the 15 women requiring hospitalization during pregnancy outside of delivery, four cited vasculitis activity as the indication for inpatient care. Most women (54/73, 74%) were prescribed medications for vasculitis during pregnancy with glucocorticoids (n=36) and azathioprine (n=18) being the most frequently prescribed. Four women were prescribed rituximab. Nineteen (26%) women took no medications to treat vasculitis during pregnancy. Seventy-six (97%) pregnancies resulted in live births. Of these live births, 63% delivered vaginally and 21% experienced a preterm delivery. The median gestational age at delivery was 38 weeks.

Conclusion: These results demonstrate that most women with vasculitis can have successful pregnancies. During pregnancy, a minority of women reported vasculitis flares or the need for hospitalization due to vasculitis. Medications to treat vasculitis are prescribed in most patients for disease control during pregnancy. These data can be used by rheumatologists to inform and facilitate discussions about reproductive health with women with vasculitis.

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Abstract Number: 1349

Paternal Effects of Anti-TNFs in Inflammatory Arthritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Reproductive Issues in Rheumatic Disorders Poster II
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Background/Purpose: Inflammatory arthritis is a group of rheumatic diseases characterized by the inflammation of joints with systemic manifestations: psoriatic arthritis (PsA), rheumatoid arthritis (RA), and spondyloarthritis (SpA) are included in this group. The use of anti-TNFs in arthritis has become very frequent, especially after the 2000s with established efficacy.

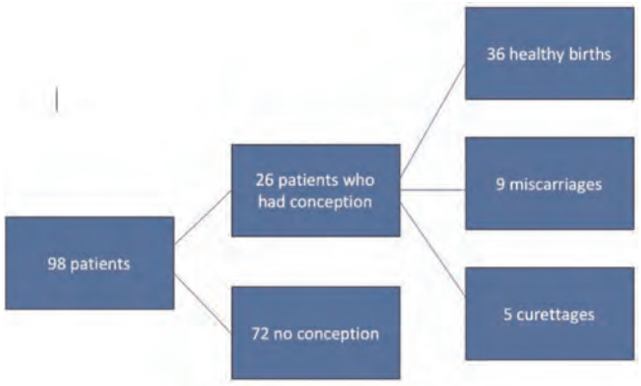

Figure 1.Flow chart of the patients according to conception

However, their effects on fertility in men remain mostly unknown. In this study, we aimed to determine the effect of anti-TNFs on the fertility of men.

Methods: We performed a questionnaire on married male patients who were diagnosed between 1987-2020. The following questions were asked: Did your wife get pregnant while you were using an anti-TNF agent? How many times did she get pregnant? Which drug were you using when your wife got pregnant? Was there any problem during the pregnancy? Were you using any contraception? Have you ever been evaluated for infertility? What drug were you using during the time your wife could not get pregnant? Did you have any children when you were not taking anti-TNF treatments? After this questionnaire, we reevaluated the patient group who had pregnancy under anti-TNF treatment. We recorded any data regarding pregnancy complications and pregnancy-associated situations.

Results: 98 patients were involved in our study. The mean age of the patients was 54. 82 (80.39%) patients had AS, 12 (11.76%) patients had PsA, and 8 patients had RA. 72 patients did not experience pregnancy and 67 of them were using contraception (Figure 1). The number of patients taking anti-TNF treatments (infliximab, etanercept, golimumab, and adalimumab) who could not get pregnant despite trying to conceive was 5.Among those 5 patients, 4 were screened for infertility, revealing unknown etiology for 3, and the remaining 1 was of female origin. 2 of these 5 patients had already conceived and given birth before anti-TNF treatment. The patient who was not screened for infertility had been trying to conceive for the previous 2 months. The total number of conceptions was 50. There were 9 miscarriages under anti-TNF treatment and 5 curettages under anti-TNF treatment (four of them were voluntary and one of them was a medical requirement). There were 36 healthy births (Figure 1). The patients who had miscarriages were using the following medications: certolizumab pegol (2 patients), golimumab (1 patient), etanercept (1 patient), adalimumab (1 patient), etanercept (3 patients), and infliximab (1 patient). The patient who had a curettage due to a medical requirement was using golimumab.

Conclusion: Among the male patients taking anti-TNF treatment, infertility due to paternal origin does not seem to be a major issue according to our limited data. Anti-TNF treatment thus seems to be safe with regards to fertility in male patients.

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Abstract Number: 1350

Identification of ACR Guidelines for SLE Pregnancy Care in the Electronic Health Record

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Reproductive Issues in Rheumatic Disorders Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is an autoimmune disease with an increased risk for poor outcomes in pregnancy. In 2020, ACR specified several recommendations to assist clinicians in preparing patients with SLE and other rheumatic diseases for pregnancy management, with the intention of risk reduction for both the mother and developing fetus (1). Two recommendations that are of particular importance in managing SLE pregnancies are to initiate low dose aspirin (LDA) and continuation of hydroxychloroquine (HCQ) therapy. We investigated whether the rate of adherence to these guidelines increased after their release at a single healthcare site.

Methods: We identified all patients at Northwestern Medicine (NM) with 4 or more encounters billed for SLE, with at least one SLE encounter billed by a rheumatologist. Using diagnosis and procedure codes, we ascertained the approximate start and end dates of pregnancies that occurred following the first SLE diagnosis among these patients from 2012 to 2022. Next, we identified the presence of LDA if a medication order for low dose or baby aspirin occurred from 6 months prior to the beginning of pregnancy up to the end of the first trimester. The presence of HCQ therapy was determined by medication orders for HCQ occurring either 6 months before or during the pregnancy. The presence of antiphospholipid (APL) antibodies was determined if anti-cardiolipin, anti-beta-2-glycoprotein, or lupus anticoagulant were positive on two separate occasions 12 or more weeks apart. Finally, the number of pregnancies during which patients received specific ACR guidelines over the study period were summarized over time, before and after the start of 2020, and further delineated by patient APL status at the time of pregnancy.

Results: We identified 529 pregnancies among people with SLE that occurred over the study period from 3,312 total female patients meeting our SLE identification algorithm. Overall, there was a general upward trend in the rates of patients receiving HCQ, LDA, or both over the study period (Figure 1). The rates of pregnancies during which both LDA and HCQ were administered were 34% and 39% ($p = 0.30$) before 2020 and following the start of 2020, respectively (Table 2). A larger, although non-significant, increase was also observed among patients with two different positive APLs, where the rate increased from 37% to 50% ($p = 0.55$).

Conclusion: Our results suggest that there was only a modest, non-significant increase in implementing ACR guidelines for SLE in pregnancy in our health system following their release. Limitations include the single-center nature of the study, use of only structured and semi-structured data in detecting medication orders, and short follow-up period after implementation of the guidelines. It is anticipated that the recommended care will continue to increase as the guidelines are disseminated more widely. To obtain a sample with adequate size to study changes in prescribing patterns for pregnancy among patients with SLE in a broader context, future work will focus on implementation of our SLE and pregnancy identification strategies in a larger data network derived from multiple healthcare sites and development of more sophisticated tools to detect physician recommended LDA.

Disclosure: N. Forrest: None; **J. Waytz**: None; **A. Barnado**: None; **M. Clowse**: Exagen, 5, GlaxoSmithKlein(GSK), 2, 5, Immunovant, 5, UCB, 2, 5; **T. Walunas**: Gilead Sciences, 5; **R. Ramsey-Goldman**: Ampel Solutions, 2, Calabetta, 2, Exagen, 2, Immunocor, 6.

Abstract Number: 1351

HPV Vaccination in Adolescent and Young Adult Patients Seen in an Academic Rheumatology Center

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Reproductive Issues in Rheumatic Disorders Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Adolescent and young adults (AYAs) with rheumatic disease (RD) may face disproportionate risk of HPV and associated cancers due to immune dysregulation, immunosuppression and gaps in preventive health care delivery. As vaccination is a safe and effective means of prevention, we aimed to evaluate whether having an RD is associated with decreased HPV vaccine uptake in AYAs seen by a rheumatologist.

Table 1. Demographic, Clinical, and Immunization Information About Patients Aged 16-22 Seen in an Academic Rheumatology Clinic with and without Rheumatic Disease (RD)

Variable	RD (N=321)	No RD (N=213)	p-value
Demographics			
Age (at most recent visit) – years, mean (SD)	19.6 (2.1)	18.4 (1.9)	*<0.001*
Female	233 (72.6)	166 (77.9)	0.16
Race			0.24
• Asian	22 (6.9)	7 (3.3)	
• Black	29 (9.0)	14 (6.6)	
• White	195 (60.7)	131 (61.5)	
• Other	52 (16.2)	1 (0.5)	
• *Missing*	*23 (7.2)*	*32 (15.0)*	
Ethnicity			*<0.001*
• Hispanic/Latino	75 (23.4)	23 (10.8)	
• Not Hispanic/Latino	235 (73.2)	167 (78.4)	
• *Missing*	*11 (3.4)*	*23 (10.8)*	
Insurance type			*0.003*
• Medicaid and/or Medicare	70 (21.8)	24 (11.3)	
• Private	246 (76.6)	180 (84.5)	
• *Missing*	*5 (1.6)*	*9 (4.2)*	
Employment status			*0.002*
• Employed	33 (10.3)	10 (4.7)	
• Student	193 (60.1)	99 (46.5)	
• Not employed/Disabled	90 (28.0)	81 (38)	
• *Missing*	*5 (1.6)*	*23 (10.8)*	
Smoking status			0.41
• Current	11 (3.4)	7 (3.3)	
• Former	6 (1.9)	1 (0.5)	
• Never	301 (93.8)	192 (90.1)	
• *Missing*	*3 (0.9)*	*13 (6.1)*	
Clinical Information			
HPV vaccinated	160 (49.8)	75 (35.2)	*<0.001*
Influenza vaccination (ever)	252 (78.5)	131 (61.5)	*<0.001*
COVID-19 vaccination			*<0.001*
• 0 doses	70 (21.8)	92 (43.2)	
• 1-2 doses	104 (32.4)	60 (28.2)	
• ≥3 doses	147 (45.8)	61 (28.6)	

Values are reported as N (%) unless otherwise indicated. A p-value <0.05 was considered statistically significant; missing values were excluded from analysis.

Methods: This retrospective study included individuals aged 16-22 seen in our academic rheumatology center ≥2 times (2020-2022) with New York State (NYS) residence. We used chart review to ascertain demographics, vaccine information (automatically pulled from the NYS Immunization Information System), reason for evaluation by a rheumatologist, and medication information. We descriptively compared demographic and clinical variables between patients with and without an RD diagnosis. We performed a multivariable logistic regression to assess whether having an RD diagnosis was associated with having received 2-3 HPV vaccine doses after adjusting for relevant demographic characteristics and receipt of other elective vaccines.

Results: There were 534 patients aged 16-22 seen by a rheumatologist at our center ≥2 times during the study period with NYS residence (mean age ± 2.1 years, 74.7% female, and 61% White). Compared to those without RD (n=213), patients with RD (n=321) were older (mean age 19.6 vs. 18.4 years, p< 0.001), more frequently Hispanic/Latino (23.4% vs. 10.8%, p< 0.001), more had Medicaid and/or Medicare (21.8% vs. 11.3%, p=0.003), more were employed (10.3% vs. 4.7%) and students (60.1% vs. 46.5; p=0.002) [**Table 1**].

Table 2. Clinical Characteristics of Patients Aged 16-22 with a Rheumatic Disease (RD) Seen in an Academic Rheumatology Center

RD Diagnosis	N (%)
• Inflammatory arthritis[1]	185 (57.6)
• Connective tissue disease[2]	94 (29.3)
• Other[3]	42 (13.1)
Age at RD Diagnosis	
• <11	60 (18.7)
• 11-16	137 (42.7)
• 17-22	124 (38.6)
Immunosuppression (at most recent visit)?	202 (62.9)

Values are reported as N (%) unless otherwise indicated.
1. RA, PsA, SpA, JIA
2. SLE, APS, Sjögren's, Myositis, UCTD, MCTD
3. Chronic recurrent multifocal osteomyelitis, vasculitis, scleroderma, autoinflammatory disease, other inflammatory disease

Table 3. Logistic Regression Model Evaluating the Association Between Rheumatic Disease (RD) Status and HPV Vaccination in Patients Aged 16-22 Seen in an Academic Rheumatology Center

Variable	Odds Ratio	95% Confidence Interval	p-value
RD Status			
• No RD	*Referent*		
• RD	0.74	0.45 – 1.22	0.23
Age (at most recent visit)	1.10	0.98 – 1.22	0.10
Sex			
• Male	*Referent*		
• Female	1.09	0.65 – 1.81	0.75
Race			
• White	*Referent*		
• Asian	2.35	0.86 – 6.47	0.10
• Black	3.09	1.27 – 7.55	*0.01*
• Other	1.76	0.86 – 3.54	0.12
Ethnicity			
• Hispanic/Latino	*Referent*		
• Not Hispanic/Latino	0.94	0.50 – 1.78	0.84
Insurance			
• Private	*Referent*		
• Medicaid and/or Medicare	1.22	0.64 – 2.31	0.55
Influenza vaccination (ever)			
• No	*Referent*		
• Yes	12.68	6.35 – 25.33	*<0.001*
COVID-19 vaccination			
• 0 doses	*Referent*		
• 1-2 doses	3.71	2.00 – 6.87	*<0.001*
• ≥3 doses	4.56	2.52 – 8.26	*<0.001*

A p-value <0.05 was considered statistically significant.

Overall, 235 (44%) patients were HPV vaccinated (49.8% with RD vs. 35.2% without RD, p< 0.001). Compared to non-RD patients, those with RD were more likely to have ever received the influenza vaccine (78.5% vs. 61.5%, p< 0.001) and ≥3 doses of the COVID-19 vaccine (45.8% vs. 28.6%, p< 0.001) [**Table 1**]. Of 321 patients with RD, 86.9% were diagnosed with inflammatory arthritis or CTD; 61.4% were diagnosed with RD before age 17 [**Table 2**].

In adjusted models, RD status was not associated with HPV vaccination (OR 0.74, 95% CI 0.45-1.22, p=0.23). Black vs. White race was associated with HPV vaccination (OR 3.09, 95% CI 1.27-7.55, p=0.01). Influenza vaccination (ever) (OR 12.68, 95% CI 6.35-25.33, p< 0.001) and COVID-19 vaccination (OR 3.71 for 1-2 vs. 0 doses, 95% CI 2.00-6.87, p< 0.001; OR 4.56 for ≥3 vs. 0 doses, 95% CI 2.52-8.26, p< 0.001) were associated with HPV vaccination [**Table 3**].

Conclusion: Among AYAs seen in an academic rheumatology center, less than half were HPV vaccinated, and having an RD was not associated with HPV vaccination in adjusted models. Receipt of HPV and other elective vaccines was more common for patients diagnosed with an RD compared to those who were not. Influenza vaccination (ever) was associated with 13-fold increased likelihood of HPV vaccination, and COVID-19 vaccination (≥3 doses) with 5-fold increased likelihood of HPV vaccination, after adjusting for relevant factors. Interventions are needed to improve HPV vaccine uptake in AYAs, including those with RD at increased risk of vaccine-preventable illnesses; targeting elective vaccine uptake in general may be a fruitful approach.

Disclosure: C. Siegel: UCB, 12, fellowship training is supported by UCB Women's Health Fellowship Program; **L. Robinson**: cynosure, 4; **D. Jannat-Khah**: AstraZeneca, 12, stock ownership, Cytodyn, 12, stock ownershil[, Walgreens Boots Alliance, 12, stock ownership; **A. Mikhaylov**: None; **N. Pan**: None; **L. Sammaritano**: None.

Abstract Number: 1352

Similar Delivery Outcomes in Pregnant Patients with and Without Takayasu Arteritis - A Nationwide Inpatient Database Study

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Reproductive Issues in Rheumatic Disorders Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Takayasu's arteritis (TA) is a large vessel vasculitis which affects women of reproductive age. There is limited information about the effect of TA on pregnancy. We ran an analysis in pregnant women with an already established diagnosis of TA in an effort to determine the effect of TA on delivery outcomes.

Methods: We queried the National Inpatient Sample database in the period between 2016 - 2019. Patients who were admitted for delivery were identified and stratified based on the presence of diagnosis of TA. The adjusted odds ratios (aOR) of in-hospital outcomes and resource utilization were calculated using chi-square statistics in software STATA v.17.

Results: Of 1.44e+07 hospitalizations for pregnancy between 2016-2019; 120 pregnant patients had TA. The mean age of TA patients was older (31 vs. 29, p-value 0.04). Patients with TA had significantly higher rates of gestational hypertension (15.83% vs 6.4%, p-value 0.03), thyroid disorders (12.5% vs 4.14%, p-value 0.04), genitourinary infections (8.3% vs

Baseline characteristics of patients admitted for delivery with and without Takayasu arteritis

	Without Takayasu arteritis	With Takayasu arteritis	P-value
Total	1.44E+07 - 120	120	
Mean Age (years)	29	31	0.04
LOS (days)	2.6	3.7	0.016
Total Charge (Dollars)	20835	27065	0.077
Gestational HTN (n) (%)	917,314 (6.4%)	19 (15.83%)	0.03
DM (n) (%)	1,301,544 (9%)	10 (8.3%)	0.9
Gestational DM (n) (%)	1,139,094 (7.9%)	10 (8.3%)	0.93
Thyroid Disorders (n) (%)	596,870 (4.14%)	15 (12.5%)	0.04
Cervical Incompetence (n) (%)	64,905 (0.5%)	0 (0%)	0.75
Antiphospholipid syndrome (n) (%)	15,670 (0.1%)	0 (0%)	0.87
SLE (n) (%)	19,990 (0.1%)	0 (0%)	0.86
Genitourinary infection (n) (%)	339,975 (2.4%)	10 (8.3%)	0.05

Outcomes of complications of patients admitted for delivery with and without Takayasu arteritis

	Without Takayasu	With Takayasu		Unadjusted		Adjusted*	
	(Total= 1.44E+07)	(Total = 120)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Pre-eclampsia	865,580	15	0.19	2.2 (0.6 - 7.5)	0.19	2 (0.59 - 7)	0.26
Eclampsia	11,005	0	0.9	1	-	1	-
Amniotic Disorders	921,645	10	0.69	1.3 (0.33 - 5.3)	0.69	1.2 (0.32 - 5.0)	0.73
Placental Disorders	1,606,504	20	0.4	1.6 (0.54 - 4.7)	0.4	1.6 (0.54 - 4.55)	0.413
Antepartum hemorrhage	19,385	0	0.86	1	-	1	-
Intrapartum hemorrhage	45,280	0	0.8	1	-	1	-
Postpartum hemorrhage	549,220	0	0.34	1	-	1	-
Cord Disorders	3,197,868	25	0.87	0.92 (0.34 - 2.5)	0.87	0.9 (0.34 - 2.5)	0.85
Prolonged Labor	1,633,819	10	0.64	0.71 (0.16 - 3.03)	0.64	0.7 (0.16 - 2.9)	0.62
Preterm Labor	660,720	0	0.3	1	-	1	-
Postdate Pregnancy	1,871,509	15	0.94	0.96 (0.28 - 3.2)	0.94	1.03 (0.3 - 3.6)	0.95
Fetal Stress	3,318,893	15	0.22	0.48 (0.14 - 1.6)	0.23	0.46 (0.14 - 1.54)	0.21

*Adjusted for age, gestational hypertension, thyroid disorders, gestational diabetes, cervical incompetence, antiphospholipid syndrome, and SLE.

2.4%, p-value 0.05) and longer length of stay (3.7 vs 2.6 days, p-value 0.016) compared to controls. The risk of pre-eclampsia trended higher, however was statistically insignificant (aOR 2, 95% CI 0.59-7.0, p-value 0.26). There was no difference in the rate of amniotic or placental disorders, ante/intra/postpartum hemorrhage, cord disorders, prolonged/preterm/postdate pregnancy or fetal stress.

Conclusion: While TA patients had a significantly higher rate of comorbidities: gestational hypertension, thyroid disorders, and increased incidence of genitourinary infections, TA does not seem to cause adverse outcomes during the delivery period. Interestingly, TA patients were older than non-TA patients.

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Abstract Number: 1353

Sexual Dysfunction in Women with Systemic Lupus Erythematosus: A Cross-Sectional Multicentre Study

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SESSION INFORMATION

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Session Type: Poster Session B

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Background/Purpose: Due to its multisystemic involvement, systemic lupus erythematosus (SLE) can have a significant impact on patients' quality of life (QoL). Sexual (dis)function is a key component of QoL but is often underappreciated. Little is known about sexual disfunction in SLE patients, a condition that primarily affects women during their fertile age.

We aimed at determining the prevalence of sexual dysfunction among women with SLE and predictors thereof.

Methods: We performed a cross-sectional multicenter study in which women (18-70 years-old) with a clinical diagnosis of SLE (according to their treating rheumatologist) were included. An anonymous online questionnaire was perfomed where data on demographics (e.g., age), symptoms of depression and anxiety [Hospital Anxiety and Depression Scale (HADS)), health-related QoL (Short Form Health

	Total (n=194)	No sexual dysfunction (n=66; 34%)	Sexual dysfunction (n=128, 66%)	p-value
Age, mean in years (SD)	44.3 (11)	41.3 (10)	45.8 (11.92)	**0,006**
On menopause, n (%)	44 (23%)	9 (5%)	35 (18%)	**0,05**
Disease duration, mean in years (SD)	13.5 (9)	13.5 (9)	13.6 (9)	0,09
Moderate to severe disease activity according to SELENA-SLEDAI, n (%)	42 (22%)	13 (7%)	29 (15%)	0,75
On cDMARDs, n (%)	182 (94%)	65 (34%)	117 (60%)	0,1
On bDMARDs, n (%)	16 (8%)	6 (3%)	10 (5%)	0,98
On glucocorticoids, n (%)	113 (58%)	37 (19%)	76 (39%)	0,77
Charlson comorbidity index, mean (SD)	1.63 (1)	1.44 (1)	1.73 (1)	**0,05**
SF36 Physical, mean (SD)	70.7 (29)	76.5 (29)	67.7 (29)	**< 0,01**
SF36 Mental, mean (SD)	60.8 (22)	69.8 (17)	56.2 (23)	**< 0,01**
HADS Anxiety, mean (SD)	9.4 (2)	8.8 (2)	9.7 (2)	**0,007**
HADS Depression, mean (SD)	9 (2)	8.5 (2)	9.2 (2)	**0,009**

Descriptive analysis of the population. SD, standard deviation; SELENA-SLEDAI, Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA) – systemic lupus erythematosus disease activity index (SLEDAI); cDMARDs, classic disease-modifying anti-rheumatic drugs; bDMARDs, biologic disease-modifying anti-rheumatic drugs

	Univariable analysis OR (95% CI) (N=192-194)	p-value	Multivariable analysis OR (95% CI) (N=193)
Age	1.04 (1.01; 1.07)	**0.01**	**1.04 (1.01; 1.07)**
Menopause (yes vs no)	2.38 (1.11; 5.61)	0.03	†
SELENA-SLEDAI (remission/LDA vs moderate to severe activity)	1.09 (0.94; 1.28)	**0.24**	**1.18 (1.01; 1.40)**
CCI	1.39 (1.00; 2.02)	0.06	†
bDMARDs (yes vs no)	0.85 (0.30; 2.59)	0.76	*
cDMARDs (yes vs no)	0.16 (0.01; 0.87)	0.09	†
Glucocorticoids (yes vs no)	1.15 (0.63; 2.09)	0.66	*
HADS Depression	1.20 (1.03; 1.42)	**0.02**	**1.20 (1.01; 1.43)**
HADS Anxiety	1.19 (1.04; 1.38)	0.02	†
SF36 Mental	0.97 (0.95; 0.98)	**< 0.01**	**0.97 (0.95; 0.98)**
SF36 Physical	0.99 (0.98;1.00)	0.03	†

Multivariable analysis. * Not selected in the univariable model (p>0.25); † Not selected in the multivariable model (p>0.05); Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA) – systemic lupus erythematosus disease activity index (SLEDAI); CCI, Charlson Comorbidity Index; bDMARDs, biologic disease-modifying anti-rheumatic drugs; cDMARDs, classic disease-modifying anti-rheumatic drugs

Survey Index 36 Item (SF36)]) and sexual function [Female Sexual Function Index (FSFI) - a 19-item patient-report outcome that assesses female sexual function]) were collected. Data on clinical features [disease activity according to the Safety of Estrogens in Lupus National Assessment-SLE Disease Activity Index (SELENA-SLEDAI), organ involvement and evaluation of comorbidity (Charlson Comorbidity Index)] and on treatment status were collected from medical records. The main outcome was sexual dysfunction, defined as FSFI< 26.5 (validated cut-off). A multivariable logistic regression was perfomed to test the association of clinical and demographic characteristics with sexual dysfunction (present vs absent).

Results: In total, 194 female patients with SLE were included (mean age 44 years-old [standard deviation (SD) 11]). The mean SELENA-SLEDAI score was 1.7 (SD: 2.2), corresponding to low disease activity, and 94% of patients were on classical disease-modifying antirheumatic drugs. The mean value of HADS was 9 (0-21), for both depression and anxiety scores. Regarding SF36, the mental component had a mean value of 61 (0-100) and the physical one of 70 (0-100). Sexual disfunction was present in 128 (66%) patients.

In the multivariable analysis (Table 1), older age (OR: 1.04; 95%CI: 1.01; 1.07), higher SELENA-SLEDAI (OR: 1.18; 95%CI: 1.01; 1.40), higher HADS depression score (OR: 1.20; 95%CI: 1.01; 1.43), as well as a lower (that is, worse) SF36 mental component score (OR: 0.97; 95%CI: 0.95; 0.98) were independently associated with sexual dysfunction.

Conclusion: Sexual disfunction is common in women with SLE and is influenced by both physical and mental health components. Clinicians should consider both for the optimal management of their patients in order to improve their sexual QoL.

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Abstract Number: 1354

The Impact of Pregnancy Intention on Depression and Quality of Life in Women with Lupus

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Reproductive Issues in Rheumatic Disorders Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Mental health conditions are the leading cause of maternal mortality across most of the United States. Among individuals with SLE, pregnancy intention has been noted as a risk factor for adverse pregnancy outcomes and infant complications. However, the impact of pregnancy intention on maternal mental health and quality of life in this population is poorly understood.

Methods: We conducted a prospective cohort study using data from a university-based pregnancy registry that enrolls pregnant women with rheumatic disease. Patient reported outcomes including the London Measure of Unplanned Pregnancy (LMUP) and Edinburgh Postnatal Depression Scale (EPDS) were collected at first rheumatology visit of pregnancy. The EPDS is validated in pregnancy. Data for patient measures and physician assessed SLE activity were obtained at each subsequent visit. Pregnancy intention was stratified into two categories: (1) Planned versus unplanned based on LMUP≥10 and (2) Medically optimized versus not optimized. Medically optimized for pregnancy was defined as < 1g of proteinuria, no rheumatic teratogens at conception, and continuing pregnancy compatible SLE medications after conception. We conducted primary and secondary analyses using Fisher's exact test to estimate the association of pregnancy intention with maternal depression, maternal mental health/quality of life, and maternal SLE activity. Multivariable logistic regression models were used to estimate the association of pregnancy intention with each outcome of interest.

Results:

Depression: Individuals with unplanned pregnancy were 2-3 times as likely to have maternal depression as those with planned pregnancy. On the other hand, individuals who were not medically optimized for pregnancy did not have a significant increase in depression (Table 1).

Table 1. Association between pregnancy intention and maternal depression

Table 1. Association between pregnancy intention and maternal depression

	Pregnancy Group		P-value (unadj.)	OR (95% CI)	Adjusted OR (95% CI)
	Pregnancy Planning				
	Unplanned n=40	Planned n=68			
Depression at entry (EPDS ≥10) (n=108)	15 (38%)	12 (18%)	0.04	2.78 (1.15, 6.67)	2.63 (0.99, 7.14)
	Medical optimization				
	Non-optimized n=37	Optimized n=78			
Depression at entry (EPDS ≥10) (n=111)	11 (31%)	17 (23%)	0.5	1.49 (0.61, 3.70)	1.19 (0.46, 3.13)

*Adjusted for marital status, household income, Medicaid/Medicare insurance.

Table 2. Association between pregnancy intention and patient-reported lupus activity*

Table 2. Association between pregnancy intention and patient-reported lupus activity*
*Higher score is higher SLE activity

	Pregnancy Group		p-value (unadj)	β (95% CI)	Adjusted β (95% CI)
	Pregnancy Planning				
	Unplanned n=40	Planned n=68			
Patient-reported activity (0-10) (n=93)	4.3 (2.6)	2.7 (2.9)	0.007	1.62 (0.45, 2.79)	0.96 (-0.31, 2.23)
Joint tenderness and swelling (0-10) (n=102)	3.0 (3.0)	1.7 (2.5)	0.03	1.32 (0.23, 2.40)	0.77 (-0.41, 1.96)
Moderate-Severe Patient-Reported Flare (n=105)	13 (35%)	10 (15%)	0.03	OR 3.13 (1.20, 8.33)	OR 2.86 (0.98, 8.33)
	Medical Optimization			β (95% CI)	Adjusted β (95% CI)
	Non-optimized n=37	Optimized n=78			
Patient-reported activity (0-10) (n=97)	3.6 (3.1)	3.1 (2.8)	0.5	0.46 (-0.77, 1.69)	-0.37 (-1.63, 0.90)
Joint tenderness and swelling (0-10) (n=108)	2.4 (2.9)	2.0 (2.6)	0.5	0.38 (-0.71, 1.46)	0.18 (-1.33, 0.98)
Moderate-Severe Patient-Reported Flare (n=111)	9 (25%)	15 (20%)	0.6	OR: 1.33 (0.52, 3.45)	OR: 1.14 (0.41, 3.23)

Table 3. Association between pregnancy intention and provider-reported disease activity*

Table 3. Association between pregnancy timing and provider-reported SLE disease activity*
*Higher score is higher SLE activity (all provider scored)

	Pregnancy Group		p-value (unadj)	β (95% CI)	Adjusted β (95% CI)
	Pregnancy Planning				
	Unplanned: n=40	**Planned: n=68**			
SLEPDAI[1]	4.0 (4.5)	2.4 (3.0)	0.05	1.60 (0.20, 3.00)	0.82 (-0.70, 2.34)
PGA[2]	0.7 (0.7)	0.4 (0.5)	0.004	0.37 (0.15, 0.59)	0.23 (-0.002, 0.47)
Renal PGA[3]	0.3 (0.6)	0.05 (0.2)	0.005	0.29 (0.14, 0.45)	0.27 (0.09, 0.44)
				OR (95% CI)	**Adjusted OR (95% CI)**
SLEPDAI ≥6	9 (23%)	8 (12%)	0.2	0.46 (0.16, 1.31)	0.73 (0.24, 2.27)
PGA ≥1.0	12 (30%)	7 (10%)	0.02	0.27 (0.10, 0.75)	0.42 (0.14, 1.27)
Renal PGA >1.0	6 (15%)	1 (1%)	0.01		
	Medical Optimization				
	Non-optimized: n=37	**Optimized: n=78**	**p-value (unadj)**	**β (95% CI)**	**Adjusted β (95% CI)**
SLEPDAI	5.4 (4.7)	1.7 (2.2)	<0.0001	3.67 (2.42, 4.89)	3.33 (1.94, 4.73)
PGA	0.8 (0.7)	0.3 (0.4)	0.0002	0.52 (0.31, 0.72)	0.44 (0.21, 0.67)
Renal PGA	0.4 (0.6)	0.01 (0.07)	0.0003	0.43 (0.29, 0.57)	0.44 (0.27, 0.61)
				OR (95% CI)	**Adjusted OR (95% CI)**
SLEPDAI ≥6	12 (32%)	5 (6%)	0.0005	0.14 (0.05, 0.45)	0.19 (0.06, 0.64)
PGA ≥1.0	14 (38%)	5 (6%)	<0.0001	0.11 (0.04, 0.35)	0.16 (0.05, 0.51)
Renal PGA ≥1.0	7 (19%)	0 (0%)	0.0002		

[1]SLEPDAI: SLE Pregnancy Disease Activity Index: 0=none, ≥6 moderate to severe SLE.
[2]PGA: Physician's Global Assessment: 0=none, ≥1.0 moderate, 3=severe
[3]Renal PGA: Physician's Global Assessment for renal disease, recorded within the LFA-REAL: 0=none, ≥1.0 moderate, 3=severe

Patient-reported SLE activity: Higher patient-reported lupus activity was seen in unplanned pregnancy than in planned pregnancy, with three-times as many reporting a moderate or severe flare. However, patient-reported lupus activity was not associated with whether or not pregnancy was medically optimized (Table 2).

Physician-reported SLE activity: When adjusted for marital status, household income, and Medicaid/Medicare insurance, unplanned pregnancies did not have higher SLE activity, despite higher patient-reported symptoms (Table 3).On the other hand, pregnancies that were not medically optimized had significantly higher rates of active SLE, SLEPDAI, and active nephritis, even though the women did not report higher SLE activity.

Conclusion: Early in pregnancy, maternal depression and patient-reported SLE symptoms were associated with unplanned pregnancy, but not whether SLE activity or medications were optimized in pregnancy. On the other hand, physician-reported SLE activity, which is an important predictor of pregnancy outcomes, was not increased in unplanned pregnancies, but was higher in pregnancies not medically optimized. These results suggest that addressing unplanned pregnancy may improve maternal mental health, and increasing medical optimization prior to conception may have more impact on pregnancy outcomes.

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Abstract Number: 1355

Delivering Care for Pregnant Women with Rheumatic and Musculoskeletal Diseases in Ireland: Current Challenges and Practices

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SESSION INFORMATION
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Background/Purpose: Rheumatic disease frequently affects women of childbearing age. Women with pre-existing rheumatic disease who are planning a pregnancy or develop these conditions during pregnancy often require specialist input from maternal-foetal medicine and Rheumatology. The aim of this study is to establish current practices regarding the management and monitoring of women with RMD (Rheumatic and Musculoskeletal disease) in Ireland and to identify current challenges.

Methods: In March 2023, a 17-question anonymised online survey was distributed using a well-recognised electronic survey tool. Rheumatology consultants, Registrars, Clinical Nurse Specialists (CNS), advanced nurse practitioners (ANP) and Allied health professionals currently working in a rheumatology unit in Ireland were invited to participate. The survey collected

demographics and data focusing on current delivery of care in place for pregnant women with RMD in Irish rheumatology units. SPSS was used for statistical analysis.

Results: The response rate was 69 %: 82% (n=54) female, 29% (n=19) Consultant Rheumatologists, 18% (n=12) Registrars, 27% (n=18) CNS, 20% (n=13) ANPs. Significant variability exists across clinical sites for pregnancy care delivery in RMD, with combined rheumatology/obstetric clinics occurring in only 18% of units (Figure 1). Preconception counselling is conducted in the General Rheumatology Clinic setting in 61% (n=40) of hospitals. In 41 % (n=27) of centres, women with RMD are reviewed once per trimester and 27 % (n=18) of centres reported no change to pre-pregnancy care. Less than 5 % (n=3) of clinical centres arranged monthly reviews during pregnancy. In 56% (n=37) of hospitals, there is no named Obstetrician for managing complex RMD patients during pregnancy.

The majority 49% (n=32) of respondents wished to review patients between 6 weeks and 3 months post-delivery and 46% (n=30) of centres reported offering clinical reviews in this period at present (Figure2). In 12 % (n=8) centres, clinicians offered no change to pre-pregnancy care. Professional healthcare role had no association with time to review post-delivery ($p > 0.05$). Challenges identified in delivering desired care included suboptimal communication between Rheumatologists and Obstetricians (23 %, n=15), complex care needs of patients (17 %, n=11), suboptimal infrastructure (17 %, n=11) (Figure 3). Common barriers to implementing a dedicated clinic included lack of clinical space (62 %, n=41), insufficient staffing (46 %, n=30) and maternity hospital not co-located with main hospital (50%, n=33).

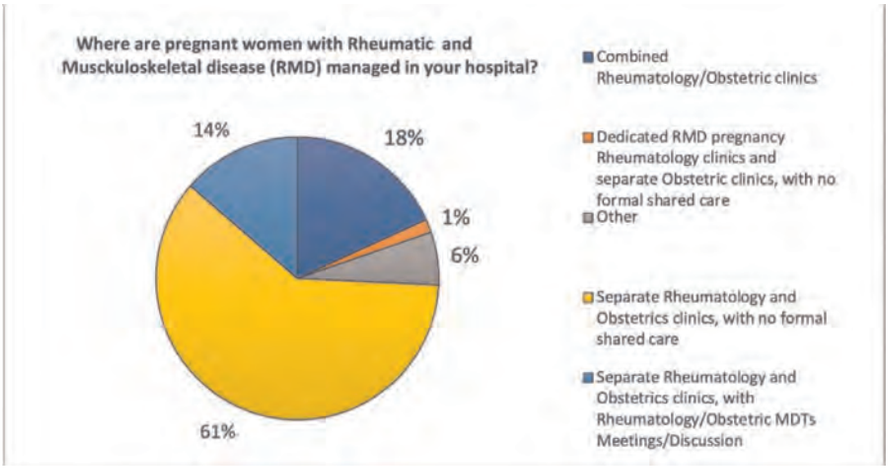

Figure 1.

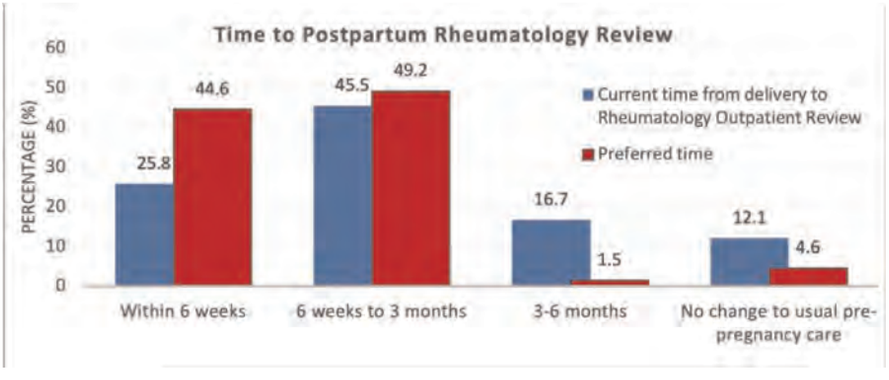

Figure. 2

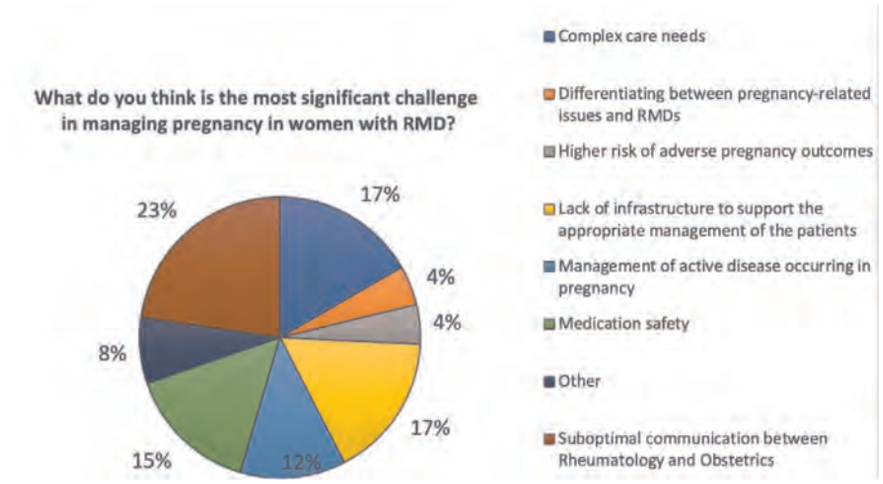

Figure 3.

Conclusion: Significant variation in the delivery of care for pregnant women with RMD is identified in this survey. The delivery of care to patients with RMD may be limited by deficiencies in our current healthcare setting. The development of a national framework for management and monitoring of women with RMD during their pregnancy would unify care, promoting optimisation of maternal health, control of disease and neonatal outcomes.

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Abstract Number: 1356

Reproductive History and HPV Vaccination Awareness Among Women with Systemic Lupus Erythematosus and Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Women with systemic rheumatic diseases (SRDs), particularly those with SLE, may be more vulnerable to HPV infection and HPV-related cervical cancer. However, HPV testing and vaccination rates are low in patients with SLE (Dhar et al. *J. Clin Rheumatol. 2019*). We aimed to assess and compare HPV vaccination status and awareness in female rheumatology patients with systemic lupus erythematosus (SLE) vs. rheumatoid arthritis (RA).

Methods: Women aged 18-65 years seen by a Hospital for Special Surgery rheumatologist ≥2 times between 2020-2022 were recruited to the Rheumatology Women's Reproductive Health and Wellness Cohort; cohort enrollment is ongoing. This interim analysis included cohort members self-reporting rheumatologist-diagnosed SLE or RA (excluding those reporting

both) who responded to questions on rheumatology history, reproductive history, and HPV vaccination awareness. We compared reproductive history and HPV vaccination status and awareness in women with SLE vs. RA.

Results: Of the 812 cohort participants, 711 (87.6%) completed the relevant questionnaires. This analysis included 295 participants: 111 with SLE and 184 with RA. Demographics were similar between the two groups, except those with SLE were younger (45.6 vs. 49.0 years, p=0.02). Women with SLE and RA were similarly likely to be sexually active, report a prior Pap smear, and report similar time since their most recent Pap smear (Table 1). While the two groups had numerically but not statistically different rates of abnormal Pap smears (42.9% vs. 32.8%, p=0.09), women with SLE were more likely to have persistent abnormal smears on follow up (13.3% vs. 1.7%, p=0.04). Gynecologic diagnoses were similar between groups, except two women with SLE and none with RA reported cervical cancer diagnoses (Table 1). Although more women with SLE discussed cervical cancer screening with their rheumatologist (33.3% vs. 11.4%, p< 0.01), women with SLE and RA were similarly due/overdue for cervical cancer screening. HPV vaccination uptake was similar between the groups, with 37% of previously/currently eligible women having completed the vaccine series. Of the 50% of previously/currently eligible women never beginning vaccination, 90% reported it not being offered. Both groups responded similarly to HPV vaccination awareness questions (Table 2).

Conclusion: Compared to women with RA, women with SLE at our tertiary musculoskeletal center reported a higher frequency of persistent abnormal Pap smears and were more likely to have discussed cervical cancer screening with their rheumatologists. Among women previously/currently eligible for HPV vaccination, 37% completed the vaccine series with no

Table 1. Demographic characteristics and reproductive history among women with systemic lupus erythematosus and rheumatoid arthritis

Characteristics	SLE (N = 111)	RA (N = 184)	p-value
Demographics			
Current age (years)	**45.56 (11.45)**	**48.97 (12.39)**	**0.02**
Race (N = 288)			0.11
- White	70 (64.2)	131 (73.2)	
- Non-white (includes multiracial)	39 (35.8)	48 (26.8)	
Ethnicity (N = 293)			0.11
- Hispanic or Latina/x	20 (18.2)	21 (11.5)	
- Not Hispanic or Latina/x	90 (81.8)	162 (88.5)	
Reproductive and Gynecologic History			
Sexually active (N = 276)			
- Currently sexually active	69 (67.6)	105 (60.3)	0.23
- Formerly sexually active	30 (29.4)	64 (36.8)	0.21
- Never sexually active	3 (2.9)	5 (2.9)	1
Sexual partners* (N = 266)			
- Men	96 (97.0)	161 (96.4)	0.62
- Women	7 (7.1)	9 (5.4)	0.62
Ever Pap smear	111 (100.0)	182 (98.9)	0.53
Last Pap smear (N = 287)			0.40
- <1 year ago	54 (50.0)	97 (54.2)	
- 1-3 years ago	47 (43.5)	65 (36.3)	
- >3 years ago	7 (6.5)	17 (9.5)	
Ever abnormal Pap smear (N = 282)	45 (42.9)	58 (32.8)	0.09
Abnormal Pap smear result* (N = 103)			
- Returned to normal	22 (48.9)	24 (41.4)	0.45
- Required colposcopy	27 (60.0)	31 (53.4)	0.51
- Required surgery	14 (31.1)	10 (17.2)	0.10
- **Remained abnormal**	**6 (13.3)**	**1 (1.7)**	**0.04**
Gynecologic diagnosis* (N = 290)			
- PCOS	9 (8.2)	12 (6.7)	0.63
- Endometriosis	10 (9.1)	18 (10.0)	0.80
- Uterine fibroids	25 (22.7)	26 (14.4)	0.07
- Gynecologic cancer	2 (1.8)	5 (2.8)	0.71
Cervical cancer diagnosis	2 (1.8)	0 (0.0)	0.14
Cervical cancer screening*,**			
- Ever had cervical cancer screening	79 (71.2)	135 (73.4)	0.68
- Due or overdue for cervical cancer screening†	22 (19.8)	35 (19.0)	0.86
- **Discussed cervical cancer screening with rheumatologist**	**37 (33.3)**	**21 (11.4)**	**<0.01**

**Subcategories are not mutually exclusive.*
***Cervical cancer screening includes Pap smear, colposcopy, and HPV testing.*
†Of the 57 subjects due or overdue for cervical cancer screening, 29 (50.9%) were due in the past year, 21 (36.8%) 1-3 years ago, 5 (8.8%) 3+ years ago, and 2 (3.5%) were unsure. These subjects reported being overdue for screening for the following reasons: forgot/lost track of timing, do not believe the test is necessary/important to me, concerns about the procedure itself, fear of getting an abnormal result, difficulty scheduling test, concerns regarding COVID-19 pandemic risk, and other.

Table 2. HPV vaccination information and HPV awareness among women with systemic lupus erythematosus and rheumatoid arthritis

Characteristics	SLE (N = 111)	RA (N = 184)	p-value
***HPV Vaccination Awareness†**, N (%) correct*			
HPV vaccination is recommended to begin at 11-12 years of age, but can be started at age 9 (*TRUE*)	97 (87.4)	171 (92.9)	0.11
Very few sexually active adults have been exposed to HPV (*FALSE*)	103 (92.8)	173 (94.0)	0.68
HPV vaccination treats existing HPV (*FALSE*)	96 (86.5)	159 (86.4)	0.99
HPV vaccination is recommended for all women under 26 (*TRUE*)	98 (88.3)	165 (89.7)	0.71
HPV vaccination is never recommended for women older than 26 (*FALSE*)	87 (78.4)	136 (73.9)	0.39
HPV vaccination is never recommended for men (*FALSE*)	93 (83.8)	162 (88.0)	0.30
***HPV Vaccination Information**, N (%) Includes respondents aged 49 or below‡†*	SLE (N = 69)	RA (N = 89)	p-value
HPV vaccination status - HPV vaccine series complete - Did not start HPV vaccine series - Unsure or partial vaccination*	 27 (39.1) 34 (49.3) 8 (11.6)	 32 (36.0) 45 (50.6) 12 (13.5)	0.89
Age at last HPV dose (N = 54) - <13 years - 14-26 years - >26 years	 3 (12.5) 18 (75.0) 3 (12.5)	 8 (26.7) 20 (66.7) 2 (6.7)	 0.35 0.60 0.65
Reason for not starting HPV series (N = 72) - I was not offered the vaccine - Other**	 26 (86.7) 8 (26.7)	 39 (92.9) 5 (11.9)	 0.44 0.11

†Correct responses denoted in parentheses.
‡†Analysis conducted among respondents 49 years or younger given extended eligibility approved in 2019 for ages ≤45 years if clinically appropriate.
*These subjects reported the following reasons for not completing HPV series: I thought the first vaccine dose triggered a flare of my rheumatic disease (4 subjects), I forgot (3 subjects), other reason (2 subjects).
**Subjects reported the following *other* reasons for not beginning HPV vaccination (not mutually exclusive): did not know it was important for me (3 subjects), was concerned about vaccine side effects (3 subjects), other reason (8 subjects).

difference in vaccination rate or awareness between women with SLE and RA. Among the 50% of previously/currently eligible women who did not begin HPV vaccination, 90% reported never having been offered the vaccine although vaccination may have been warranted for those >26 years in certain instances (e.g. immunosuppressive medication use) based on expanded eligibility criteria. Our results suggest the importance of increasing both HPV vaccination and cervical cancer screening discussion in women with SLE and RA.

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Abstract Number: 1357

Systemic Lupus Erythematosus and Assisted Reproductive Technology: A Case Series and Systematic Literature Review

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is one of the most common autoimmune diseases in women of childbearing age and female sex hormones are known to play a role in the pathophysiology of SLE. Multiple studies have suggested impaired ovarian reserve in patients with even mild SLE. Women with SLE may also be advised to defer pregnancy until disease remission; however, the likelihood of conception decreases with advancing age and the use of potentially gonadotoxic immunomodulatory agents. For these reasons, assisted reproductive technology (ART) is an important consideration for women with SLE who desire pregnancy. Patients with SLE utilizing ART are theoretically at increased risk of hormone-associated disease flare or thrombosis. In this study, we aim to evaluate outcomes in women with SLE who have utilized ART in our center. We also performed a systematic literature review regarding safety and efficacy of ART in women with SLE.

Methods: A retrospective chart review was performed at a large tertiary care center. Patients with a diagnosis of SLE whose records included mention of in-vitro fertilization (IVF) or ART between 2010-2023 were reviewed. All included patients had a diagnosis of SLE based on the modified 1997 ACR criteria. In addition, a literature search was performed using electronic databases including PubMed, Web of Science, and Cochrane Library. Studies that reported data for patients with SLE who utilized ART were included. Case reports were excluded. Data collected for both the case series and literature review included type of ART utilized and number of cycles performed, demographic data, obstetric history, autoantibody positivity, etiology of infertility, delivery mode, maternal outcomes including SLE disease activity, and fetal outcomes.

Results: Nine patients were included in the case series and 6 studies in the literature review. Amongst patients included in the case series, ART was performed in 7 patients with SLE and SLE developed after the use of ART in 2 patients. - **Table 1** summarizes the main clinical features of patients. A total of 25 ART stimulation attempts resulted in 10 intrauterine (IU) pregnancies (40%). Of these, 8 resulted in live births. Two patients had SLE flare while receiving hormonal therapy. Our literature review revealed 256 relevant articles. The full text of 25 articles was reviewed resulting in 6 eligible studies. Between these studies and our case series, 283 SLE patients were reviewed. A total of 610 ART cycles were analyzed. These ART cycles resulted in 148 IU pregnancies and clinical pregnancy rate was 24.3%. Live birth occurred in 133 cases (89.9%). **Table 2** summarizes clinical features and major outcomes in the literature.

Conclusion: The rate of SLE flare in patients utilizing ART appears to be like that of SLE patients not receiving hormonal therapy. The success rate of ART in women with SLE is similar to that of the general population. This case series and review of the current literature supports the use of ART in patients with SLE who desire pregnancy.

Table 1. Clinical features of SLE patients.

Race, Age	SLE duration	SLE Abs	ART reason	Total ART cycles	IU pregnancy	Pregnancy complications	Flare	Thr/ OHSS
AA, 36	3 yrs	SSA	FO, MF	2	1	PE, Gest HTN	-	-/-
W, NH, 34	7 yrs	–	?	4	1	No	-	-/-
W, NH, 33	After ART	dsDNA	FO	3	2	Gest Diabetes	-	-/-
NA, 26	NA	dsDNA	POF, EM	3	0	NA	LN	-/-
AS, 34	After ART	dsDNA	?	2	1	PE, Preterm, Club foot	-	-/-
AS, 40	1 yr	SSA	EM	2	2	Fetal loss	-	-/-
W, NH, 34	1 yr	dsDNA	?	1	0	NA	-	-/-
AA, 30	10 yrs	dsDNA, SSA	FO, POF	3	0	NA	Rash	-/-
W, NH, 25	6 yrs	-	?	5	3	Fetal loss, twins	-	-/-

AA: African-American, W: white, AS: Asian, NA: Native American, NH: non-Hispanic, FO: fallopian obstruction, EM: endometriosis, MF: male factor, PE: preeclampsia, HTN: hypertension, POF: premature ovarian failure, LN: lupus nephritis, Thr: thrombosis, OHSS: ovarian hyperstimulation syndrome

Table 2. Summary of SLE patients who utilized ART in the literature.

n (SLE patients)	283
ART cycles	610
Intrauterine pregnancy	148
Infertility reason	
Fallopian obstruction	41
Premature ovarian failure	22
Endometriosis	13
Uterine malformation	2
Male factor	20
Mixed	15
Unexplained	68
Maternal outcome	
Preterm delivery	6
Preeclampsia	5
Gestational DM/HTN	4
Twins	9
OHSS	9
SLE Outcomes	
Flare	30
Nephritis	2
Thrombocytopenia	4
Hemolytic anemia	4
Fetal outcomes	
Live birth	133
IUGR	2
Neonatal lupus	3

Disclosure: E. Coe: None; **E. Petrinec**: None; **O. Pamuk**: None.

Abstract Number: 1358

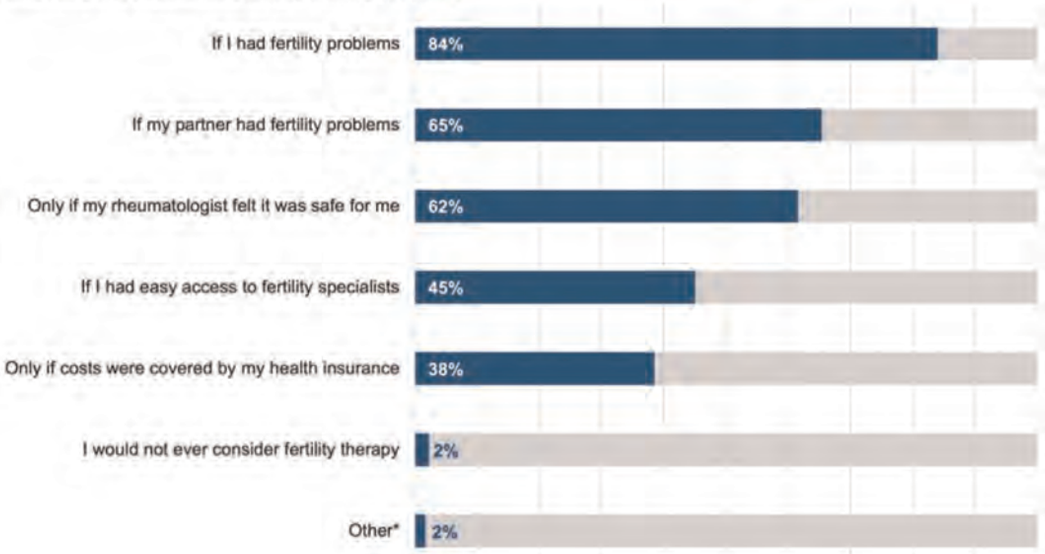
Experiences and Attitudes Related to Assisted Reproductive Technologies Among Women with Systemic Rheumatic Disease

Sanjana Adurty[1], Lucy Masto[2], Amaya Smole[2], Caroline Siegel[2], Sarah Lieber[3], Jonah Levine[2], Bessie Stamm[2], Lisa Mandl[3], Michael Lockshin[3], Medha Barbhaiya[3] and Lisa Sammaritano[3], [1]Weill Cornell Medical College, New York, NY, [2]Hospital for Special Surgery, New York, NY, [3]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Reproductive Issues in Rheumatic Disorders Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic rheumatic disease (SRD) may be associated with decreased fertility. Advances in the safety and efficacy of oocyte cryopreservation (OOC) and other assisted reproductive technologies (ART) make these therapies increasingly appealing. However, few studies have assessed ART utilization among women with SRD. Here, we evaluate how sociodemographic factors and medical history influence OOC experiences and attitudes towards ART among women with SRD.

Figure 1. Relative importance of factors when considering whether to pursue fertility therapies among individuals who have not experienced fertility-related problems†



† The 228 (86%) participants who responded that they had never used other fertility therapies were asked why not, to which 121 (53%) had not previously tried to get pregnant and 61 (27%) had not had fertility problems. These 182 participants were subsequently asked to select the circumstances under which they consider receiving fertility therapies if they had fertility problems. They could select all responses that applied to them.
* The 3 participants who selected 'Other' were able to describe their thoughts in more detail through a free text box. Their responses are as follows:
- "I am egg freezing soon"
- "I would be concerned about egg /embryo freeze for religious and ethical reasons, so would only consider therapies that didn't result in extra eggs/embryos being harvested"
- "If the moment came that I'm prepared for a pregnancy and find difficulties conceiving"

Methods: We enrolled women ages 18-65 seen ≥2 times by a Hospital for Special Surgery rheumatologist from 2020-2022 in the Rheumatology Women's Reproductive Health and Wellness Cohort; cohort enrollment is ongoing. We included women aged 18-45 years with a self-reported SRD in this interim analysis. Using descriptive statistics, we assessed how sociodemographic factors, reproductive history, SRD, and rheumatology medications influence attitudes towards OOC. We also detailed the experiences of women who have undergone OOC, and we explored the relative importance of factors affecting decisions to use ART among women without previous fertility issues.

Results: Out of 815 cohort participants, 641 (79%) provided information on fertility; 265 were reproductive-aged with SRD. Of these, 21 (7.9%) had done OOC, and an additional 102 (38.5%) had contemplated OOC (Table 1). Openness to OOC was associated with no previous pregnancy ($p< 0.01$), greater infertility concern ($p< 0.01$), age< 30 ($p=0.01$), lack of a spouse/partner ($p< 0.01$), bachelor's degree or higher ($p=0.01$), and use of antimalarials ($p=0.04$) or DMARDs/immunosuppressives ($p=0.03$). Previous use of other ART and age ≥40 were associated with either completing OOC or never having considered OOC (both $p< 0.01$). Of participants who had undergone OOC, most (81%) did so before 35 years of age (Table 2). Three women had complications related to OOC, all reporting SRD flares. For those who did not have fertility issues, 112 (64%) reported that, if necessary, they would consider ART only if their rheumatologist felt it was safe (Figure 1). This was the third most important factor influencing consideration of ART, preceded only by the participant or partner experiencing fertility problems.

Conclusion: Almost half of women with SRD in our cohort have either undergone or considered OOC for fertility preservation. Attitudes towards OOC were associated with pregnancy history, fertility concern, experience with other ART, age, marital status, education, and rheumatologic medications. Among women who have completed OOC, most initiated their cycles before age 35. Receiving their rheumatologists' approval regarding the safety of ART is an important factor for many women who have not pursued ART. This analysis provides one of the first reports of OOC use in SRD. Our results highlight the significant role of SRD-related factors on attitudes towards and experiences with ART in women with SRD.

Table 1. Characteristics of reproductive-aged women with SRD who have completed OC compared to those who had not completed OC

Variable[1]	Completed OOC (N=21)	Considered OOC (N=102)	Never Considered OOC (N=140)	p-value[2]
Fertility Attitudes & Experiences				
No previous pregnancy	8 (38)	77 (75)	52 (37)	***<0.001***
Pregnancy plans affected by SRD	9 (43)	52 (51)	51 (36)	*0.06*
Concerned about fertility	12 (57)	68 (67)	48 (34)	***< 0.001***
Previous use of other ART[3]	7 (33)	8 (8)	21 (15)	***0.007***
Sociodemographics & Lifestyle				
Current age (years)				
• 18-29	4 (19)	36 (35)	27 (19)	***0.01***
• 30-39	10 (48)	51 (50)	63 (45)	*0.74*
• 40-45	7 (33)	15 (15)	50 (36)	***0.001***
Married or partnered	10 (48)	47 (46)	104 (74)	***<0.001***
Bachelor's degree or higher	20 (95)	99 (97)	120 (86)	***0.01***
Private medical insurance	21 (100)	96 (94)	129 (92)	*0.38*
Religious affiliation	15 (71)	65 (64)	90 (64)	*0.67*
Medical History				
SRD diagnosis category				
• Inflammatory arthritis[4]	13 (62)	48 (47)	82 (59)	*0.16*
• Lupus and lupus-like conditions[5]	6 (29)	42 (41)	46 (33)	*0.32*
• Vasculitis, myositis, and SSc[6]	1 (5)	8 (8)	8 (6)	
• Other autoinflammatory conditions[7]	0 ()	3 (3)	2 (1)	
• Multiple diagnosis categories	1 (5)	1 (1)	2 (1)	
Disease flare in the last year	16 (76)	77 (75)	102 (73)	*0.75*
Medications in the last year[8]				
• Antimalarials	14 (67)	52 (51)	56 (40)	***0.04***
• Antiplatelets/Anticoagulants	1 (5)	13 (13)	11 (8)	*0.33*
• Biologics[9]	11 (52)	44 (43)	74 (53)	*0.26*
• DMARDs/Immunosuppressives[10]	5 (24)	45 (44)	41 (29)	***0.03***
• Steroids	7 (33)	29 (28)	40 (29)	*0.90*
• JAK inhibitors	1 (5)	6 (6)	5 (4)	
• Other[11]	3 (14)	18 (18)	13 (9)	*0.16*
Teratogenic medication in the last year[12]	5 (24)	35 (34)	32 (23)	*0.11*
Gynecologic comorbidity present[13]	10 (48)	33 (32)	35 (25)	*0.09*

1. All results are reported as N (%) unless noted otherwise
2. P-values were derived from chi-squared testing, which was performed if at least 80% of expected values were ≥5.
3. Other ART: oral/injectable medications for ovarian stimulation, intrauterine insemination, and in vitro fertilization
4. Inflammatory arthritis: Adult Onset Still's Disease, JIA, PsA, RA, spondyloarthritis (i.e. AS, IBD-related arthritis, ReA), inflammatory arthritis - not otherwise specified
5. Lupus and lupus-like conditions: APS, SLE, MCTD, SS, UCTD
6. Vasculitis, myositis, and SSc: Behcet's, myositis (i.e. DM, PM, IBM, or other inflammatory muscle disease), SSc, CREST, vasculitis (including ANCA-associated vasculitis, GCA, Takayasu's vasculitis, PAN)
7. Other autoinflammatory conditions: autoinflammatory syndrome (i.e. CAPS, TRAPS, FMF), IgG-4-related disease, PMR, sarcoidosis
8. Patients could select all medications they had received. As such, these totals are not mutually exclusive
9. Biologics: Abatacept, Adalimumab, Anakinra, Anifrolumab, Belimumab, Canakinumab, Certolizumab, Denosumab, Etanercept, Golimumab, Guselkumab, Infliximab, Ixekizumab, Mepolizumab, Rilonacept, Risankizumab, Rituximab, Sarilumab, Secukinumab, Tocilizumab, Ustekinumab
10. DMARDs/Immunosuppressives: AZA, CYC, Cyclosporine, LEF, MTX, MMF, Tacrolimus, Thalidomide, SSZ, Voclosporin
11. Other: Allopurinol, Apremilast, Avacopan, Colchicine, IVIG, Nintedanib, other rheumatology not otherwise specified (including chemotherapy)
12. Teratogenic medications: CYC, LEF, MTX, MMF, nintedanib, thalidomide, warfarin
13. Gynecologic comorbidities: polycystic ovarian syndrome, endometriosis, uterine fibroids, gynecologic cancer

Table 2. OOC characteristics based on age at initial oocyte retrieval

Variable[1]	<30 years (N=6)	30-34 years (N=11)	35-37 years (N=2)	≥38 years (N=2)
Current age (years), mean ± SD	31.7 ± 5.4	36.8 ± 4.1	41.9 ± 0.3	43.1 ± 0.8
Number of cycles completed				
• One	4 (67)	7 (64)	0 (0)	2 (100)
• Two	0 (0)	2 (18)	1 (50)	0 (0)
• Three or more	2 (33)	2 (18)	1 (50)	0 (0)
Total number of eggs frozen				
• 1 to 5	0 (0)	3 (27)	2 (100)	2 (100)
• 6 to 10	2 (33)	3 (27)	0 (0)	0 (0)
• 11 to 15	1 (17)	3 (27)	0 (0)	0 (0)
• 16 or more	3 (50)	2 (18)	0 (0)	0 (0)
SRD-related complications from OC[2]	1 (17)	2 (18)	0 (0)	0 (0)
• SRD flare	1 (17)[3]	2 (18)[4]		
Use of other ART	2 (33)	4 (36)	1 (50)	0 (0)
• Oral ovarian stimulation	2 (33)	4 (36)	1 (50)	
• Injectable ovarian stimulation	2 (33)	4 (36)	0 (0)	
• Intrauterine insemination	1 (17)	3 (27)	0 (0)	
• IVF	1 (17)	4 (36)	1 (50)	

1. All results are reported as N (%) unless noted otherwise
2. Participants with a complication were asked to specify whether it was a blood clot, SRD flare, or 'Other'
3. This participant had SRD diagnoses within the 'Vasculitis, myositis, and SSc' category
4. These participants both had SRD diagnoses within the 'Inflammatory arthritis' category

Disclosure: S. Adurty: None; **L. Masto**: None; **A. Smole**: None; **C. Siegel**: UCB, 12, fellowship training is supported by UCB Women's Health Fellowship Program; **S. Lieber**: None; **J. Levine**: None; **B. Stamm**: None; **L. Mandl**: Annals of Internal Medicine, 12, Associate Editor, Regeneron Pharmaceuticals, 5, Up-to-Date, 9; **M. Lockshin**: None; **M. Barbhaiya**: None; **L. Sammaritano**: None.

Abstract Number: 1359

Association of Menstrual Cycles and Disease Flare Activity in Women with Systemic Lupus Erythematosus and Rheumatoid Arthritis

Lucy Masto[1], Amaya Smole[1], Caroline Siegel[1], Sarah Lieber[2], Sanjana Adurty[3], Jonah Levine[1], Bessie Stamm[1], Lisa Mandl[2], Michael Lockshin[2], Lisa Sammaritano[2] and Medha Barbhaiya[2], [1]Hospital for Special Surgery, New York, NY, [2]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [3]Weill Cornell Medical College, New York, NY

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Reproductive Issues in Rheumatic Disorders Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Whether the timing of menstruation impacts disease activity or severity among women with SLE or RA is poorly understood. We evaluated systemic rheumatic disease (SRD) flares related to the timing of menses, along with demographic, medical, and lifestyle characteristics among pre-menopausal women with self-reported diagnoses of SLE or RA.

Methods: We enrolled women ages 18-65 evaluated by a Hospital for Special Surgery rheumatologist ≥2 times from 2020-2022 in the Rheumatology Women's Reproductive Health and Wellness Cohort. This analysis includes participants who self-reported SLE or RA diagnoses and provided information on SRD flares and menstrual cycles. We conducted descriptive analyses to compare self-reported demographics, lifestyle factors, medication use, and SRD flare activity overall and related to timing of menstrual cycles, between women with self-reported RA and SLE. We excluded women self-reporting overlapping SLE and RA diagnoses, though participants may have additional SRD diagnoses.

Results: Out of 812 cohort participants,307 (37.8%) pre-menopausal women responded to our questions on menstruation. The current analysis includes 122 of the respondents (40%) who self-reported an SRD diagnosis of SLE (N=49) or RA (N=73). 85 (71.4%) participants were White, 16 (13.2%) were Hispanic or Latina/Latinx, and mean age was 37.6 years. Of those who reported medication use, women with RA were more likely to use biologics, DMARDS/immunosuppressives, or Janus kinase inhibitors within the last year (83.8% RA vs. 67.3% SLE, $p< 0.01$), while those with SLE more commonly used antimalarials (79.6% SLE vs. 43.8% RA $p< 0.01$). Fewer women with SLE used prescription birth control (20.8% vs. 39.7%, $p=0.03$). RA patients were also more likely to report a recent SRD flare within the last 3 months (64.4% vs. 42.9% $p=0.02$); however, SRD flares were most common in this time frame for both groups with comparable flare severity (mild, moderate, severe) between groups (Table). Of those answering our question on timing of SRD flare in their menstrual cycle, 39.1% reported any association of menstrual cycle timing with an SRD flare. Variation in the duration and schedule of menstrual cycles and the impact of participants menstrual cycles on SRD flares was consistent between SLE and RA groups. While the majority of participants in each group reported not experiencing SRD flares related to their menses, those who did typically experienced flares within one week before/during their menses (Table).

Conclusion: Our findings suggest that over a third of women with SLE or RA experience disease flares related to timing of menstruation, with most occurring before/during their menses. Our results highlight an important trend reported by many patients that may inform physician counseling and encourage closer monitoring during vulnerable phases of the menstrual cycle, allowing for timely intervention and better disease control. As cohort recruitment is ongoing, planned multivariable analyses adjusting for demographic, lifestyle, and medical conditions will investigate factors influencing this potential association.

Table. Demographic, Lifestyle, Medical, and Menstrual Cycle Characteristics in Women with SLE versus RA			
	SLE (N=49)	RA (N=73)	p-value
Demographics			
• Age (years), mean (SD)	37.17 (± 7.9)	38.0 (± 8.0)	0.58
Race (N=119)			
• White Only	30 (62.5)	55 (77.4)	0.08
• Non-white (includes multiracial)	18 (37.5)	16 (22.5)	
Ethnicity (N=121)			
• Hispanic or Latina/X	10 (20.4)	6 (8.3)	0.05
Age of first menstrual period			0.89
• <10 years old	6 (12.2)	8 (11.0)	
• 11-15 years old	41 (83.7)	63 (86.3)	
• >16 years old	2 (4.1)	2 (2.7)	
Age at SRD diagnosis			
• <18	5 (10.2)	8 (8.2)	1
• 18 – 35	40 (81.6)	46 (63.0)	0.03
• >36	4 (8.1)	19 (16.4)	0.02
Lifestyle Factors			
• Currently use alcohol	29 (59.2)	54 (74.0)	0.09
• Currently smoke	0	1 (1.4)	N/A
Medical and Medication History			
Medication use in the past year[1] (N=121)			
• Antimalarials	39 (79.6)	32 (44.4)	<0.01
• Biologics, DMARDS / Immunosuppressives, JAK Inhibitors[2]	33 (67.3)	60 (83.8)	0.04
• Steroids	19 (38.8)	17 (23.6)	0.07
• Other[3]	2 (4.1)	3 (4.2)	1
• None	2 (4.1)	0	N/A
• Ever pregnant (N=102)	19 (51.4)	31 (47.7)	0.72
• Currently use prescription birth control[4] (N=121)	10 (20.8)	29 (39.7)	0.03
Most recent flare of SRD			
Current/within the last 3 months	21 (42.9)	47 (64.4)	0.02
>3 months to 12 months	6 (12.2)	15 (20.5)	0.23
>1 year ago	16 (32.7)	7 (9.6)	<0.01
Do not have disease flares / do not recall latest flare	6 (12.2)	4 (5.5)	0.20
Most recent flare severity (N=111)			0.36
• Mild	14 (33.3)	28 (40.5)	
• Moderate	19 (45.2)	33 (47.8)	
• Severe	9 (21.4)	8 (11.5)	
Any Gynecology Diagnosis[1] (N=121)			
• PCOS	7 (14.5)	9 (12.3)	0.72
• Uterine Fibroids	10 (20.8)	9 (12.3)	0.21
• Endometriosis	4 (8.3)	5 (6.8)	0.74
Menstrual Cycle Characteristics and Impact on SRD Flares			
Timing of SRD flare in menstrual cycles (N=117)			
• Within a week before or during menses	17 (36.2)	26 (37.1)	0.91
• Within a week after menses	0	1 (1.4)	N/A
• During ovulation	0	1 (1.4)	N/A
• Do not experience SRD flare related to menses	30 (63.8)	42 (60%)	0.68
Duration and schedule of cycle (N=121)			0.40
• Both are regular	21 (42.9)	31 (43.0)	
• Regular schedule, varied duration	6 (12.2)	7 (9.7)	
• Regular duration, varied schedule	4 (8.2)	10 (13.9)	
• Both irregular	13 (26.5)	11 (15.2)	
• Natural cycle is impacted by hormonal contraceptive	5 (10.2)	13 (18.0)	

1. Not mutually exclusive
2. Biologics, DMARDS/immunosuppressives, Janus kinase inhibitors: Abatacept, Adalimumab, Anakinra, Anifrolumab, Belimumab, Canakinumab, Certolizumab, Denosumab, Etanercept, Golimumab, Guselkumab, Infliximab, Ixekizumab, Mepolizumab, Rilonacept, Risakizumab, Rituximab, Sarilumab, Secukinumab, Tocilizumab, Ustekinumab, Azathioprine, Cyclophosphamide, Cyclosporine, Leflunomide, Methotrexate, Mycophenolate, Tacrolimus, Thalidomide, Sulfasalazine, Voclosporin, Baricitinib, Tofacitinib, Upadicitinib
3. Other medication: Colchicine, IVIG, other rheumatology medication not otherwise specific (including chemotherapy)
4. Nexplanon, IUD, birth control pill, estrogen patch, vaginal ring, DMPA or Depo-Provera

Disclosure: L. Masto: None; **A. Smole**: None; **C. Siegel**: UCB, 12, fellowship training is supported by UCB Women's Health Fellowship Program; **S. Lieber**: None; **S. Adurty**: None; **J. Levine**: None; **B. Stamm**: None; **L. Mandl**: Annals of Internal Medicine, 12, Associate Editor, Regeneron Pharmaceuticals, 5, Up-to-Date, 9; **M. Lockshin**: None; **L. Sammaritano**: None; **M. Barbhaiya**: None.

Abstract Number: 1360

Factors Associated with Medication-related Concerns in Women with Inflammatory Rheumatic Diseases – an Analysis of a Nationwide Pregnancy Cohort

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Reproductive Issues in Rheumatic Disorders Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Pregnancies in women with chronic diseases are often accompanied by concerns about potential complications [1]. This analysis explored medication-related concerns among women with inflammatory rheumatic disease (IRD) and identified influencing factors.

[1] PMID: 26039501

Methods: The German registry Rhekiss is a nationwide, multicentre, web-based cohort study to investigate pregnancies in women with various IRD. Women can participate if they are either planning a pregnancy (cohort 1) or are already pregnant (up to 20 weeks of gestation; cohort 2). Rheumatologist- and patient-reported data are captured at regular, pre-defined follow-up visits.

We analysed data of women who had responded to a question about concerns regarding pregnancy and child's health in relation to medication. Categorical answers and patient characteristics were analysed descriptively. The impact of factors associated with patients' anxieties was estimated by multivariable ordinal logistic regression using the proportional odds model and combining the two cohorts. Missing values were replaced by single imputation.

Table: Characteristics of patients stratified by level of concern.

	Cohort 1 (n=455)				Cohort 2 (n=784)			
Level of concern	Not at all	Not really	A little	A lot	Not at all	Not really	A little	A lot
Number of patients	29 (6.4)	79 (17.4)	193 (42.4)	154 (33.8)	124 (15.8)	159 (20.3)	302 (38.5)	199 (25.4)
Age in years (mean ± SD)	32.3 (4.0)	32.0 (3.8)	32.0 (4.4)	31.9 (4.4)	32.7 (4.2)	32.9 (3.9)	32.7 (4.3)	32.4 (4.3)
Disease duration in years (mean ± SD)	10.6 (9.3)	7.1 (7.0)	8.9 (8.0)	7.1 (7.4)	7.5 (7.0)	7.8 (6.2)	8.2 (7.3)	8.3 (6.9)
Moderate-severe disease	10 (50.0)	33 (49.3)	96 (61.5)	76 (65.5)	33 (31.4)	61 (47.3)	145 (58.7)	110 (65.5)
RAID score* (mean ± SD)	1.3 (1.3)	1.7 (1.6)	2.2 (1.9)	3.0 (2.2)	1.7 (1.7)	1.7 (1.7)	2.2 (1.8)	3.3 (2.3)
Current flare	3 (15.8)	4 (6.7)	15 (10.5)	42 (43.3)	4 (4.3)	4 (3.3)	19 (8.6)	29 (18.7)
Treatment changes**	9 (31.0)	31 (39.2)	112 (58.0)	96 (62.3)	29 (27.4)	47 (36.2)	125 (48.3)	85 (51.2)
Nulligravidae	15 (62.5)	52 (73.2)	111 (66.9)	88 (67.7)	55 (51.9)	65 (53.3)	141 (56.2)	95 (55.9)
Number of comorbidities (mean ± SD)	0.8 (0.9)	0.6 (0.8)	0.7 (1.0)	0.9 (1.0)	0.7 (0.8)	0.8 (0.9)	0.8 (1.0)	0.8 (1.0)

Values are given as number (percentage) unless otherwise indicated.
**RAID score: Patient-reported seven-item composite index originally developed for rheumatoid arthritis and now used for all IRD ranging from 0-10.*
***Treatment change either due to the intention to become pregnant or the ongoing pregnancy.*

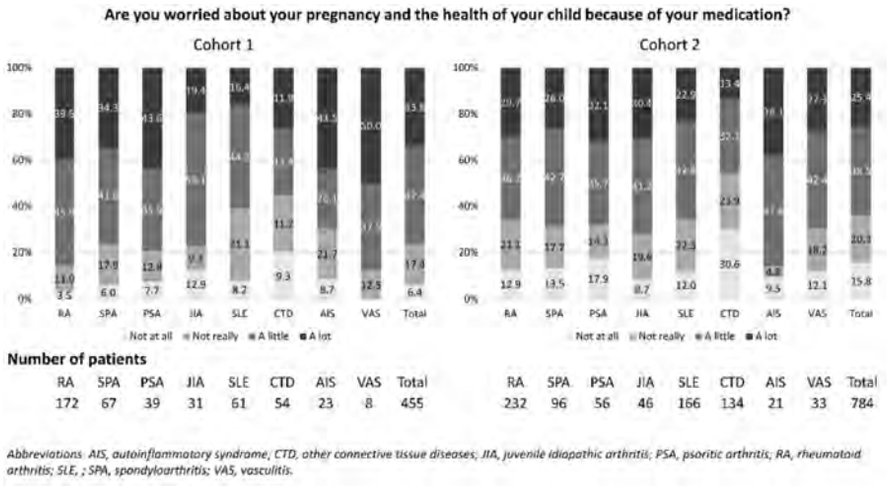

Figure: Level of concerns stratified by cohort and by IRD diagnosis.

Results: Between 09/2015 and 10/2022, a total of 2,240 patients were enrolled (cohort 1: 708, cohort 2: 1,532). Out of those, n=455 and n=784, respectively, were eligible for the analysis.On average, women were 32-33 years old and disease duration was 7-11 years (table).A total of 34% in cohort 1 and 25% in cohort 2 stated that they are concerned "a lot" (figure). Responses varied across different IRD diagnoses.

Treatment changes had the greatest impact on higher levels of worries, (odds ratio 1.72 [95% confidence interval 1.38; 2.14]). Furthermore, a significant association was found for moderate-severe IRD (1.34 [1.17; 1.53]) and a higher disease impact, measured by patient-reported RAID score (per 1-point-increase: 1.31 [1.24; 1.38]). Patients who were already pregnant at enrolment were less worried than patients planning a pregnancy (0.63 [0.51; 0.79]). No significant relationship was found for maternal age, number of prior pregnancies and comorbidities.

Conclusion: At least one in four women with IRD is "very concerned" about pregnancy and infant health due to medications. Treatment changes, moderate-severe disease and higher RAID score were associated with higher levels of concern. Therefore, worries should be an essential part of individual counselling for patients who either wish to become pregnant or are already pregnant.

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Disclosure: Y. Meissner: Eli Lilly, 6, Pfizer, 6; **B. Eickhoff**: None; **C. Glaser**: Galapagos, 6, Novartis, 6, Pfizer, 6, UCB, 5, 6; **J. Henes**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, GlaxoSmithKlein(GSK), 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **J. Richter**: None; **S. Spaethling-Mestekemper**: Abbvie, 6, Astra Zeneca, 6, Bristol-Myers Squibb(BMS), 6, Galapagos, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, Lilly, 6, Novartis, 6, Sanofi, 6, UCB, 6; **C. Specker**: AbbVie, 2, 6, Boehringer-Ingelheim, 2, 6, Bund Deutscher Internisten, 6, Chugai, 2, 6, Eli Lilly, 2, 6, GlaxoSmithKlein(GSK), 2, 6, Janssen-Cilag, 6, Med Update, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Otsuka, 6, Pfizer, 6, Rheumatologische Fortbildungsakademie, 6, Rheumazentrum Rhein-Ruhr, 6, Roche, 6, Sanofi, 6, Sobi, 2, StreamedUp, 6, UCB, 2, Vifor, 6; **R. Fischer-Betz**: None; **A. Strangfeld**: AbbVie/Abbott, 6, Amgen, 6, Bristol-Myers Squibb(BMS), 6, Celltrion, 6, Eli Lilly, 6, Janssen, 6, Pfizer, 6, Roche, 6, Sanofi, 6, UCB, 6.

Abstract Number: 1361

Effect of Zen/Doria Remission and Glucocorticoid Dosage on the Pregnancy Outcome of SLE: Retrospective Study in Two Japanese Tertiary Referral Centers

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Reproductive Issues in Rheumatic Disorders Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Achieving remission is one of the treatment targets in the lupus care and it is also important in preventing the prevalence of adverse pregnancy outcomes (APO).

Table 1: achievement of Zen/Doria remission and its relationship with adverse pregnancy outcome

	Zen/Doria remission			Logistic regression model		
Factor	(-)	(+)	p value	HR	95%CI	P value
n	37	59				
overall APO	26 (70.3)	23 (39.0)	<0.01	0.27	0.11-0.65	<0.01
maternal APO	15 (40.5)	11 (18.6)	0.03	0.34	0.13-0.85	0.02
neonatal APO	23 (62.2)	22 (37.3)	0.02	0.36	0.16-0.85	0.02
PROMISSE APO	10 (27.0)	12 (20.3)	0.47	0.69	0.26-1.81	0.45
flare during pregnancy	8 (21.6)	2 (3.4)	0.01	0.13	0.03-0.638	0.01
flare after delivery	2 (6.7)	1 (1.9)	0.29	0.26	0.23-3.04	0.29
gestational DM	6 (16.2)	4 (6.8)	0.18	0.38	0.10-1.43	0.15
preeclampsia	3 (8.1)	3 (5.1)	0.67	0.61	0.12-3.18	0.56
Gestational hypertension	7 (18.9)	6 (10.2)	0.24	0.49	0.15-1.58	0.23
HELLP syndrome	1 (2.7)	1 (1.7)	1.0	0.62	0.04-10.2	0.74
Oligohydramnios	6 (16.2)	2 (3.4)	0.05	0.19	0.04-0.97	0.05
maternal death	0 (0.0)	2 (3.4)	0.52	NA	NA	NA
live birth	29 (78.4)	54 (91.5)	0.12	2.98	0.89-9.94	0.76
Total duration of gestation	262.0 [242.0, 271.0]	268.0 [262.0, 276.0]	0.02	NA	NA	NA
preterm birth	6 (18.2)	8 (14.8)	0.77	0.78	0.25-2.5	0.67
spontaneous abortion	1 (2.8)	2 (3.4)	1.0	1.25	0.11-14.3	0.86
missed abortion	3 (8.1)	1 (1.8)	0.30	0.20	0.02-2.02	0.17
Iatrogenic abortion	5 (13.5)	2 (3.4)	0.10	0.23	0.04-1.22	0.08
Still birth	0 (0.0)	0 (0.0)	NA	NA	NA	NA
height at birth (cm)	46.0 [43.8, 48.0]	48.0 [46.5, 49.5]	<0.01	NA	NA	NA
weight at birth (g)	2472.0 [2202.0, 2896.0]	2716.0 [2476.5, 3013.8]	0.03	NA	NA	NA
Low birth weight	15 (51.7)	15 (27.8)	0.05	0.36	0.14-0.92	0.03
SGA (%)	6 (20.7)	8 (14.8)	0.55	0.67	0.21-2.15	0.50
Apgar score (1m)	8.00 [8.00, 8.00]	8.00 [8.00, 8.00]	0.53	NA	NA	NA
Apgar Score (5m)	9.00 [9.00, 9.00]	9.00 [9.00, 9.00]	0.55	NA	NA	NA
Apgar.score.1m>7 (%)	27 (93.1)	53 (98.1)	0.28	3.93	0.34-45.3	0.27
Apgar.score.5m>7 (%)	29 (100.0)	54 (100.0)	1.0	1.0	0-inf	1.0

Although there are reports on relationship with LLDAS/DORIS remission and APOs, little is known on the relationship with Zen/Doria remission and APO, so we conducted this study. In addition, we aimed to investigate optimal cutoff glucocorticoid dosage to predict APO prevalence.

Methods: Pregnant with SLE who was followed up at two Japanese tertiary referral centers were included in our study. We divided the patients into two groups according to the achievement of Zen/Doria remission at conception and analyzed the APO prevalence. Furthermore, we investigated the optimal glucocorticoid dosage to minimize APO.

Results: Of the 124 pregnancies, 59 achieved Zen/Doria remission at conception. Baseline characteristics except for glucocorticoid dosage and hydroxychloroquine usage at conception did not differ according to the achievement of Zen/Doria remission. (remission vs not on remission; prednisolone (PSL): 4.0 [0.0, 5.0] mg/day vs 10.0 [8.0, 11.0] mg/day, p< 0.01, hydroxychloroquine: 54.2% vs 37.8%, p=0.14)

	Glucocorticoid dosage at first trimester			Logistic regression model		
Factor	PSL<7.5mg	PSL≥7.5mg	p value	HR	95%CI	P value
n	87	37				
overall APO	**38 (43.7)**	**24 (64.9)**	**0.05**	**2.36**	**1.07-5.28**	**0.03**
maternal APO	23 (26.4)	13 (35.1)	0.39	1.51	0.66-3.44	0.33
neonatal APO	**33 (37.9)**	**23 (62.2)**	**0.02**	**2.69**	**1.22-5.94**	**0.01**
PROMISSE APO	18 (20.7)	11 (29.7)	0.35	1.62	0.68-3.89	0.28
flare during pregnancy	**7 (8.0)**	**9 (24.3)**	**0.02**	**3.67**	**1.25-10.8**	**0.02**
flare after delivery	3 (3.7)	2 (6.7)	0.61	1.88	0.30-11.8	0.5
gestational DM	9 (10.3)	5 (13.5)	0.76	1.35	0.42-4.35	0.61
Preeclampsia	5 (5.7)	3 (8.1)	0.7	1.45	0.33-6.4	0.63
Gestational hypertension	14 (16.1)	6 (16.2)	1	1.01	0.36-2.87	0.99
HELLP syndrome	1 (1.1)	1 (2.7)	0.51	NA	NA	NA
Oligohydramnios	**3 (3.5)**	**6 (16.2)**	**0.02**	**5.35**	**1.26-22.7**	**0.02**
maternal death	0 (0.0)	0 (0.0)	NA	NA	NA	NA
live birth	**82 (94.3)**	**29 (78.4)**	**0.02**	**0.22**	**0.07-0.73**	**0.01**
Total duration of gestation	269.0 [262.0, 276.0]	261.0 [242.0, 269.0]	<0.01	NA	NA	NA
preterm birth	15 (18.3)	6 (18.2)	1.0	0.99	0.35-2.83	1.0
spontaneous abortion	2 (2.3)	1 (2.8)	1.0	NA	NA	NA
missed abortion	**1 (1.2)**	**3 (8.1)**	**0.08**	**7.41**	**0.745-73.8**	**0.09**
Iatrogenic abortion	**2 (2.3)**	**5 (13.5)**	**0.02**	**6.64**	**1.23-36.0**	**0.03**
Still birth	0 (0.0)	0 (0.0)	NA	NA	NA	NA
height at birth (cm)	**47.5 [46.0, 49.2]**	**46.0 [44.2, 47.8]**	**0.01**	NA	NA	NA
weight at birth (g)	**2752.5 [2473.8, 3056.8]**	**2472.0 [2176.0, 2816.0]**	**0.01**	NA	NA	NA
Low birth weight	**24 (29.3)**	**15 (51.7)**	**0.04**	**2.59**	**1.08-6.18**	**0.03**
SGA (%)	11 (13.4)	8 (27.6)	0.09	2.46	0.88-6.91	0.09
Apgar.score.1m>7 (%)	79 (96.3)	27 (93.1)	0.6	0.51	0.08-3.23	0.48
Apgar.score.5m>7 (%)	81 (98.8)	28 (96.6)	0.46	0.35	0.02-5.71	0.46

table 2: glucocorticoid dosage and its relationship with adverse pregnanyc outcome

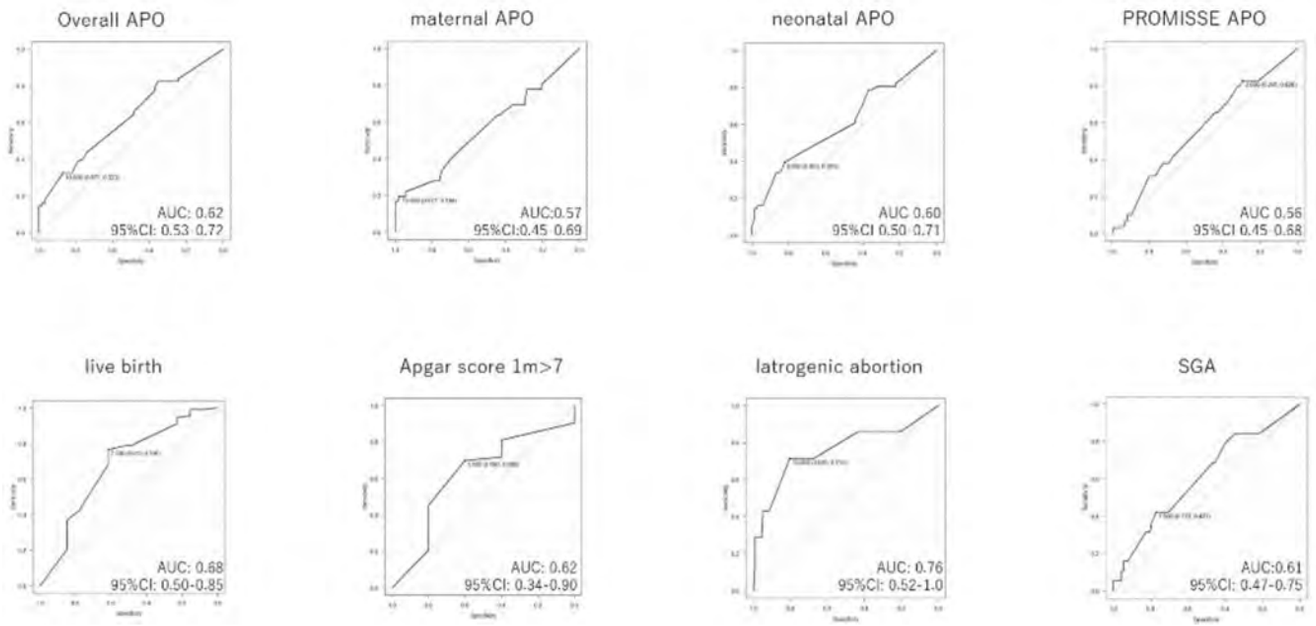

Figure 1 Receiver operating characteristic (ROC) curve for glucocorticoid dosage at first trimester to predict each adverse pregnancy outcomes

Pregnant on Zen/Doria remission showed significant decrease in the APO ratio compared with those without. (overall APO: OR 0.27, 95%CI 0.11-0.65, p< 0.01, maternal APO: OR 0.34, 95%CI 0.13-0.85, p=0.02, neonatal APO: OR 0.36, 95%CI 0.16-0.85, p=0.02, PROMISSE APO: OR 0.69, 95%CI 0.26-1.8, p=0.45)

On the other hand, glucocorticoid dose of prednisolone equivalent≥7.5mg/day at conception was associated with the increase in APO prevalence. (overall APO: OR 2.36, 95%CI 1.07-5.28, p=0.03, maternal APO: OR1.51, 95%CI 0.66-3.44, p=0.33, neonatal APO: OR 2.69, 95%CI 1.22-5.94, p=0.01, PROMISSE APO: OR 1.62, 95%CI0.68-3.89, p=0.28)

ROC curve also showed that prednisolone dosage >7.5mg/day was related to the decrease in live birth rate (AUC 0.68, 95% CI 0.50-0.85, sensitivity 0.77, specificity 0.62)

Conclusion: Achieving Zen/Doria remission can be a clinical target to reduce APOs in patients who wants to be conceived. In addition, if clinically feasible, reducing glucocorticoid dosage to less than 7.5mg/day before conception can be another treatment target.

Disclosure: T. Nakai: None; **N. Honda**: None; **S. Fukui**: None; **A. Kitada**: None; **N. Yokogawa**: None; **M. Okada**: AbbVie/Abbott, 6, Eli Lilly, 6, Pfizer, 6.

Abstract Number: 1362

Improving Reproductive Health Counseling for Pediatric Adolescent Females Prescribed Teratogenic DMARDs

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Reproductive Issues in Rheumatic Disorders Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Several rheumatologic medications routinely prescribed to adolescent females are teratogenic. However, there is no standard method to educate our patients and their families about this risk. This is a significant problem because U.S. teenage females with chronic illnesses engage in sex without contraception, and there are now strict abortion bans in some states prohibiting abortions for fetal anomalies. We performed a quality improvement (QI) project to increase the proportion of reproductive-age females receiving documented reproductive health counseling (RHC) at outpatient clinics in our single-center tertiary care practice. We specifically sought to educate patients about the teratogenicity of their medications and the need for contraception.

Methods: We included female patients aged 13 or older who were being seen as an outpatient and were taking methotrexate, mycophenolate, cyclophosphamide, or leflunomide. Two plan-do-study-act (PDSA) cycles were completed to test the following interventions: (cycle 1) physician and nurse educational seminar and creation of a smart phrase, which is a short template in our electronic health record system that users can pull into their notes on demand, (cycle 2) personal appeal to clinicians via email and development of an electronic health record note template, which automatically populates a note unlike a smart phrase. Chart review was performed at three time periods (baseline and after each round with n=80 each time period) to assess for documentation of "full RHC" (discussed risk of pregnancy AND the need for contraception), "partial

RHC" (discussed risk of pregnancy OR the need for contraception), or "no RHC." Chi-squared test was used for statistical analysis.

Results: In the anonymous pre-intervention questionnaire administered to patients (n=30), 46.7% said a rheumatologist had already discussed the need for contraception and 53.3% of patients knew that their medications may cause birth defects. However, chart review at baseline found that 60 of 80 (75.0%) patients received no documented RHC. After the first PDSA cycle, 26 of 80 (32.5%) patients received documented RHC, which was not a statistically significant improvement from baseline, p=0.5765. After the second PDSA cycle, 39 of 80 (48.8%) patients received documented RHC, which was a statistically significant improvement from the first PDSA cycle, p=0.0002. We found that patients prescribed methotrexate were more likely to receive RHC than those prescribed mycophenolate or leflunomide.

Conclusion: Overall, we learned that the most effective intervention for our group was creating a note template in Epic and sending a division-wide email. This project shows that it can be simple to improve reproductive health counseling because both interventions required no specialized skills or significant investment of resources. The next step in our PDSA cycle is to include RHC on printed after visit summaries (AVS) that are given to patients at the end of each visit.

Table 1: Patient demographic information

		Baseline 1/1/20 - 12/31/20	Post-intervention #1 8/1/21 - 12/31/21	Post-intervention #2 8/1/22 - 2/1/23
Age				
	Mean (SD)	15.8 (2.1)	16.1 (2.0)	16.5 (2.3)
Teratogenic drug				
Methotrexate	N (%)	33 (41.3)	34 (42.5)	37 (46.3)
Leflunomide	N (%)	20 (25.0)	19 (23.8)	19 (23.8)
Cyclophosphamide	N (%)	2 (2.5)	1 (1.3)	0 (0.0)
Mycophenolate	N (%)	25 (31.3)	26 (32.5)	24 (30.0)
Race				
American Indian or Alaska Native	N (%)	0 (0.0)	0 (0.0)	0 (0.0)
Asian	N (%)	1 (1.3)	2 (2.5)	2 (2.5)
Black or African American	N (%)	15 (18.8)	16 (20.0)	7 (8.8)
Hispanic or Latino	N (%)	3 (3.8)	0 (0.0)	0 (0.0)
Native Hawaiian or Pacific Islander	N (%)	0 (0.0)	0 (0.0)	0 (0.0)
White	N (%)	58 (72.5)	54 (67.5)	56 (70.0)
Not enough info	N (%)	3 (3.8)	8 (10.0)	15 (18.8)
Birth control that had already prescribed to the patient at time of pediatric rheumatology visit				
None	N (%)	64 (80.0)	56 (70.0)	53 (66.3)
Depo shot	N (%)	2 (2.5)	2 (2.5)	3 (3.8)
Oral contraceptive pill	N (%)	12 (15)	14 (17.5)	18 (22.5)
Nexplanon	N (%)	0 (0.0)	1 (1.3)	2 (2.5)
IUD	N (%)	2 (2.5)	4 (5.0)	2 (2.5)
Ring	N (%)	0 (0.0)	2 (2.5)	2 (2.5)
Patch	N (%)	0 (0.0)	1 (1.3)	0 (0.0)

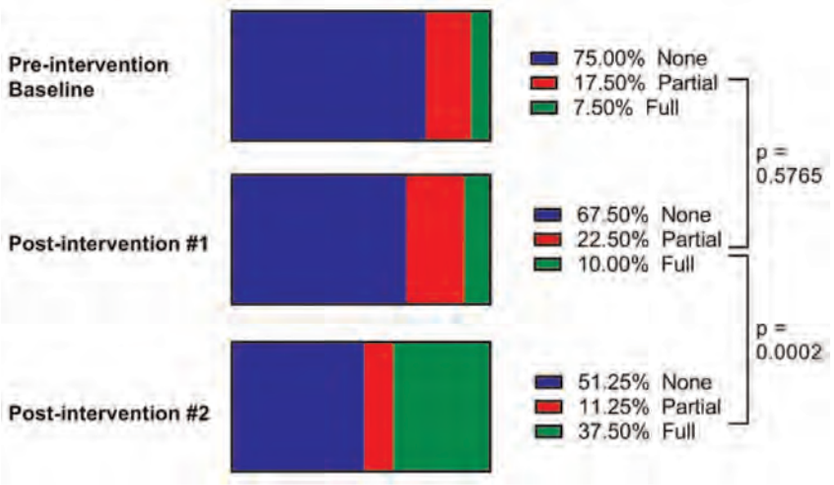

Figure 1: Stacked column chart depicting proportion of patients who received none, partial, or full RHC at three measured timepoints in QI project

Disclosure: R. Ferguson: None; **I. Marmor**: None; **M. Kitcharoensakkul**: None.

Abstract Number: 1363

Plasma Neutrophil Extracellular Trap Remnant Levels Are Lower in Premenopausal Healthy Women Using Oral Contraceptive Pills

SESSION INFORMATION

Session Date: **Monday, November 13, 2023**
Session Title: Reproductive Issues in Rheumatic Disorders Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Women develop RA 3 times more often than men, and several risk factors for RA are female specific. Prior studies demonstrate an association between oral contraceptive pill (OCP) use and a reduced risk of developing RA. However, the etiology of this protective effect remains unexplained. Anti-citrullinated protein antibodies (ACPA) develop prior to arthritis in RA, and their presence is associated with an increased risk of developing RA in the future. Exaggerated

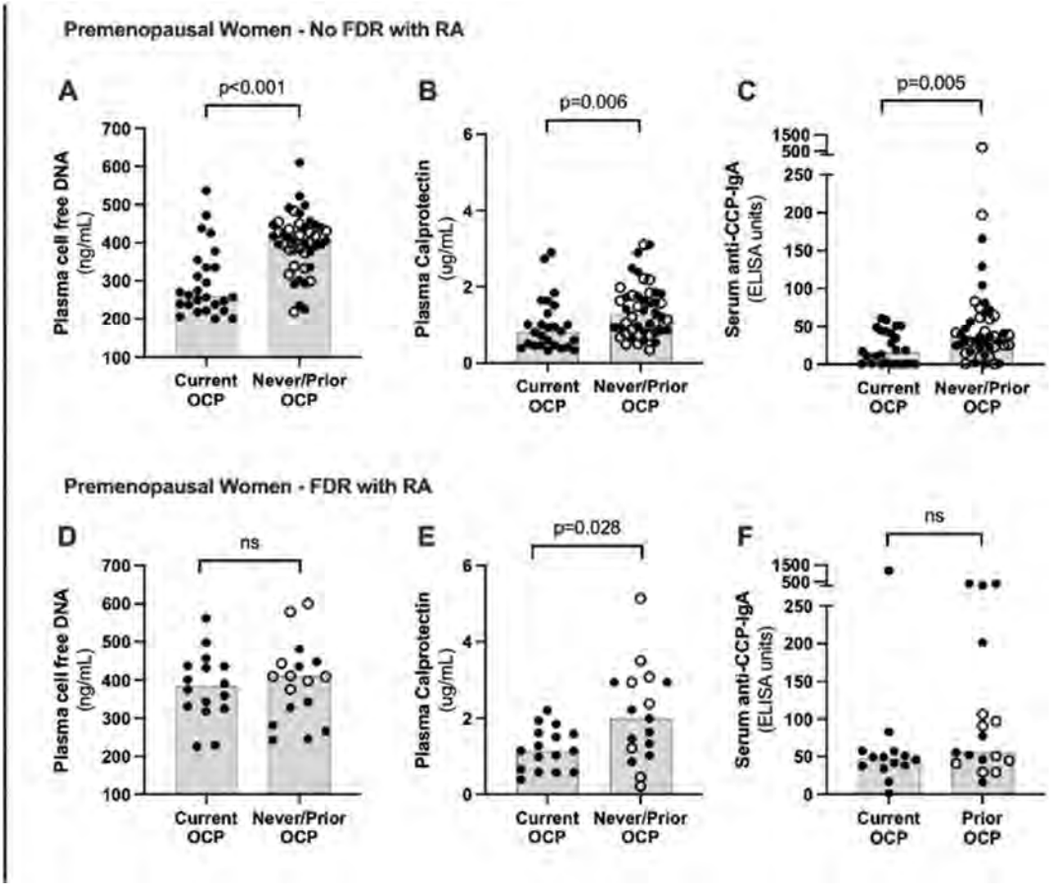

Figure 1. The figure depicts the levels of plasma cell free DNA (Panels A and D), calprotectin (Panels B and E) and serum anti-CCP-IgA (Panels C and F) in premenopausal healthy women (Panels A-C) and premenopausal women with a first degree relative (FDR) with RA (Panels D-F). Closed circles = current or prior OCP users; Open circles = never OCP users. P=values compare levels between groups using Wilcoxon rank sum test. OCP use could include combined OCPs (estrogen and progesterone) or progestin-only OCPs. There was no difference in cfDNA, calprotectin or anti-CCP-IgA levels between prior and never users in non-FDR or FDR groups (p>0.05 for all).

neutrophil extracellular trap (NET) formation has been implicated in RA pathogenesis, in part via externalization of citrullinated proteins targeted by ACPA. Moreover, neutrophils from pre-menopausal women are more prone to undergo NET formation (Blazkova 2017). Therefore, we investigated the relationship between OCPs, NETs and ACPA in pre-menopausal women without RA.

Methods: From the Denver site of the Studies of the Etiologies of RA cohort, we included all premenopausal women without RA and without pre-RA (i.e. serum anti-CCP-IgG positive) who had stored blood and were: 1) 'current OCP' users without prior use of other hormonal contraception, or 2) 'never/prior OCP' users without current/prior use of other hormonal contraception. Thirty-three had a first degree relative (FDR) with RA and 72 had no FDR with RA. Plasma was tested for NET remnants using immunofluorescence for cell free DNA (cfDNA, Quanti-iT PicoGreen dsDNA) and ELISA for calprotectin (Werfen). Serum was tested by ELISA for anti-CCP-IgA (research modification of CCP3.1, Werfen) as a measure of mucosal-based ACPA.

Results: Overall, FDRs were older, more likely smokers and had higher anti-CCP-IgA levels (Table 1). In women without an FDR with RA, cfDNA, calprotectin and anti-CCP-IgA levels were significantly lower in current OCP users compared to never/prior OCP users (Figure 1A-C). In adjusted analyses, cfDNA levels remained significantly inversely associated with current OCP use, while lower calprotectin maintained a trend toward an inverse association with current OCP use (Table 2). In FDRs, current OCP users had lower calprotectin levels but not lower cfDNA or lower anti-CCP-IgA levels (Figure 1D-F). The relationships between cfDNA, calprotectin, and OCP use in non-FDRs and FDRs was maintained in adjusted analyses (Table 2). In current OCP users, there was no correlation between cfDNA, calprotectin or anti-CCP-IgA level and duration of OCP use ($p > 0.05$), although overall median OCP duration was 7 years.

Conclusion: We found lower levels of plasma NET remnants and anti-CCP-IgA levels in current OCP users who were healthy premenopausal women without an FDR with RA. Calprotectin was similarly lower in FDRs currently using OCPs, although cfDNA and anti-CCP-IgA levels in FDRs did not differ by OCP status. Differences between FDRs and non-FDRs did not appear related to age or smoking, based on adjusted analyses, and may instead be related to underlying genetic

Table 1. Clinical characteristics, plasma NET remnants and serum anti-CCP-IgA levels by group

	Non-FDRs (N=72)	FDRs (N=33)	p-value
Age	30 (24 – 38)	36 (27 - 46)	0.03
Ever smoker	3 (4%)	10 (31%)	<0.01
Ever pregnant	28 (39%)	17 (52%)	0.23
Current OCP use	26 (36%)	16 (49%)	0.23
OCP duration	6 (3 - 10)	11 (4 - 24)	0.08
≥1 Shared epitope allele*	22 (43%)	12 (44%)	0.91
cfDNA	383 (271 - 430)	398 (327 - 440)	0.25
Calprotectin	1.0 (0.7 - 1.6)	1.5 (0.9 - 2.2)	0.07
Anti-CCP-IgA	30 (11 - 51)	51 (38 - 91)	<0.01

Results are reported in median (IQR) or N (%)
*Shared epitope testing available in 51/72 non-FDRs and 27/33 FDRs

Table 2. Results of multivariable linear regression for plasma NET remnant levels and current OCP use

	Non-FDRs (N=72)			FDRs (N=33)		
	Adjusted*			Adjusted*		
	Beta	95% CI	p-value	Beta	95% CI	p-value
cfDNA	-0.5	-142, -50	<0.01	-0.1	-95, 41	0.43
Calprotectin	-0.2	-0.7, 0.1	0.09	-0.5	-1.7, -0.3	<0.01

*Linear regression model adjusted for age, history of pregnancy and ever smoking

or environmental predisposition to increased NET formation. These findings support further studies to better understand whether modulation of NETs could explain the previously established relationship between OCP use and reduced RA risk.

Abstract Number: 1364

Both Low and High 25(OH)-Vitamin D Levels Increase Adverse Pregnancy Outcomes in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: We evaluated the role of maternal 25(OH)-vitamin D in adverse pregnancy outcomes in systemic lupus erythematosus (SLE).

Methods: We used a longitudinal cohort that included visits of pregnant patients with assessment of 25(OH)-vitamin D at each visit. Pregnancies were excluded if there was no vitamin D level during pregnancy, if the outcomes of pregnancies were missing (such as data on due date, birth date, gestational age, and complications of pregnancies), or if the pregnancy was terminated. 270 pregnancies were available for the statistical analysis.

Results: We found a U-shape association between the maternal serum 25(OH)-vitamin D level and the combined adverse pregnancy outcomes (P=0.0022), miscarriage (P=0.0048), and preterm delivery (P=0.0003). We also found the same U-shape curve with the low birth weight; but it did not reach statistical significance due to the smaller number of cases. The lowest prevalence of adverse pregnancy outcomes was with 25(OH)-vitamin D in the range of 40-59 ng/dL (Figure 1). The multivariate analysis confirmed the same U-shape association controlling for age, race, and antiphospholipid antibodies (Table 1, Figure 2). The results were similar when we examined the subset in which pre-pregnancy or first trimester BMI were available.

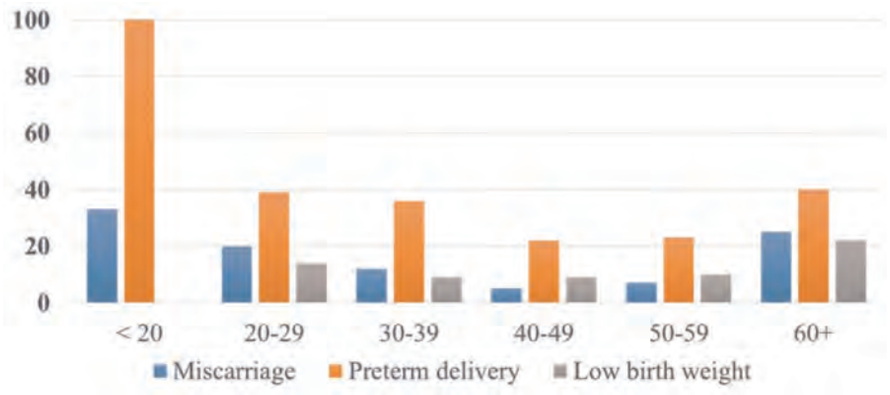


Figure 1. Adverse pregnancy outcomes occurrence (%) by mean 25(OH)-vitamin D (ng/dL) during pregnancy.

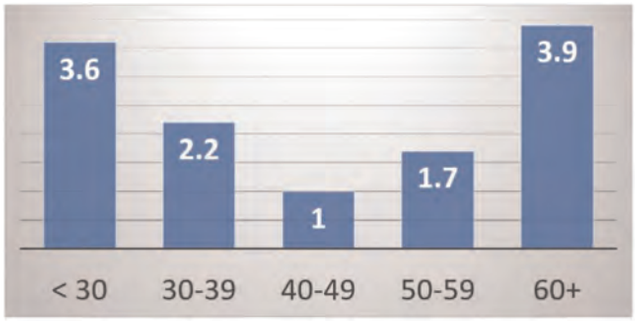


Figure 2. Odds ratios of combined adverse pregnancy outcomes with different mean 25(OH)-vitamin D levels controlling for age, race, and antiphospholipid antibodies.

Table 1. Odds ratios of adverse pregnancy outcomes with different mean maternal 25(OH)-vitamin D levels controlling for age, race, and antiphospholipid antibodies.

Mean 25(OH)-vitamin D during pregnancy (ng/dL)	Odds Ratio (95% Confidence Interval)	P-value
<30	3.6 (1.6-8.0)	0.0014
30-39	2.2 (1.1-4.4)	0.029
40-49	1.00 (reference group)	--
50-59	1.7 (0.7-3.8)	0.21
60+	3.9 (1.3-12.2)	0.018

Conclusion: Our study design cannot prove a cause-and-effect relationship. Most of our patients were prescribed vitamin D supplementation (but obviously many did not take it). We recommend monitoring 25(OH)-vitamin D levels during SLE pregnancies. The ideal 25(OH)-vitamin D range was 40-59 ng/dL.

Disclosure: N. Madanchi: None; **A. Fava**: Annexon Biosciences, 2, Sanofi, 1; **D. Goldman**: None; **L. Magder**: None; **R. Jacobson**: None; **M. Petri**: Alexion, 1, Amgen, 1, AnaptysBio, 1, Annexon Bio, 1, Argenx, 1, Arhros-Focus Med/Ed, 6, AstraZeneca, 1, 5, Aurinia, 1, 5, 6, Axdev, 1, Biogen, 1, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CVS Health, 1, Eli Lilly, 1, 5, Emergent Biosolutions, 1, Exagen, 5, Exo Therapeutics, 2, Gilead Biosciences, 2, GlaxoSmithKlein(GSK), 1, 5, 6, Horizon Therapeutics, 2, Idorsia Pharmaceuticals, 2, IQVIA, 1, Janssen, 1, 5, Kira Pharmaceuticals, 2, MedShr, 6, Merck/EMD Serono, 1, Momenta Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Proviant, 2, Sanofi, 2, Sinomab Biosciences, 2, Thermofisher, 5, UCB, 2.

Abstract Number: 1365

Extraglandular Involvement and Autoantibody Status as Risk Factors for Cardiovascular Disease in Primary Sjogren's Syndrome (pSS): A 20 Year-follow up Study

Cristiana Sieiro Santos[1], Rúben Rego Salgueiro[2], Clara Moriano Morales[3], Carolina Álvarez Castro[3] and Elvira Díez Álvarez[3], [1]Complejo Asistencial Universitario de León, León, Spain, [2]ULS Guarda, Guarda, Portugal, [3]CAULE, León, Spain

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Primary Sjögren's syndrome (pSS) is an autoimmune disorder characterized by chronic multisystem inflammation with shared pathophysiology with SLE and RA. Cardiovascular events have emerged as major causes of morbidity and mortality in patients with autoimmune diseases however, the clinical significance of cardiovascular disease in patients with pSS remains unclear. We aim to study the association between cardiovascular disease and primary Sjögren's syndrome (pSS) and analyze the risk of cardiovascular disease accordingly to glandular/extraglandular involvement and anti-Ro/SSA and/or Anti-La/SSB autoantibody status.

Methods: pSS patients fulfilling the 2016 ACR/EULAR classification criteria for pSS were consecutively evaluated and followed in our department between 2000 and 2022. We evaluated the prevalence and clinical significance of cardiovascular risk factors with primary Sjögren's syndrome (SS), focusing on the possible association with clinical and immunological features, the therapies administered, and the impact on cardiovascular disease. A two-tailed value of $p< 0.05$ was taken to indicate statistical significance. Potential risk factors associated with cardiovascular involvement were determined by multivariate regression analyses.

Results: A total of 102 pSS patients were included. 90% were female, with a mean age of 65±24 years and a disease duration of 9.9 ±7 years. Patients with extraglandular involvement had a higher prevalence of cardiovascular risk factors, including arterial hypertension (OR 2.28 95% CI (1.01-5.09), p 0.04), dyslipidemia (OR 4.4 95% CI (1.67-11.6), p 0.003), higher LDL mean values (116±48 vs 99±44, p 0.038), uric acid (6.58±1.7 vs 4.3±1.03, p 0.04) and higher risk for myocardial ischemia (OR 4.09 95% CI (1.46-11.4), p 0.01) after adjustment for age, sex, disease duration, and the significant variables in the univariate analysis. Patients positive for both Ro/SSA and La/SSB autoantibodies had a substantially higher risk of arrythmia (OR 3.4 95% CI (1.01-10.6), p 0.04), arterial and venous thromboembolism (OR 5.5 95% (1.18-25.7), p 0.03) and stroke (OR 3 95% (1.02-8.8), p 0.04). In the multivariate logistic regression analysis, extraglandular organ involvement (p=0.008), beta2microglobulin levels (p=0.001), hypocomplementemia of C3 (p=0.01), the use of glucorticoids (p=0.02), hypergammaglobulinemia (p=0.02), ESR levels (p=0.007), treatment with HCQ (p=0.03) and an ESSDAI (Sjögren's syndrome disease activity index) >13 (p=0.02) were found to be factors associated with increased or decreased odds ratio forcardiovascular events in pSS patients. Anti-Ro/SSA and anti-La/SSB were significant predictors in univariate but not in multivariate analysis.

Conclusion: pSS patients are more vulnerable to cardiovascular diseases (CVDs). In addition to traditional CVD risk factors, we identified risk factors independently associated with cardiovascular involvement in pSS patients, which suggests the need for early detection and prevention measures to improve the prognosis in those patients.

	OR 95% IC	P value
Extraglandular involvement	16.5 (4.51-28.5)	0.008
Beta2microglobulin (mg/dL)	7.83 (3.16-12.5)	0.001
C3 (mg/dl)	0.92 (0.24-0.98)	0.01
Corticoids	7.2 (2.34-15.7)	0.02
Hypergammaglobulinemia	10.2 (4.5-21.2)	0.02
ESSDAI >13	1.8 (1.13-4.52)	0.02
ESR (mm/h)	1.4 (1.10-3.45)	0.007
HCQ	0.82 (0.26-0.92)	0.03

Table 4. Significant logistic regressions for predictors for CV risk

Disclosure: C. Sieiro Santos: None; **R. Rego Salgueiro**: None; **C. Moriano Morales**: None; **C. Álvarez Castro**: None; **E. Díez Álvarez**: None.

Abstract Number: 1366

A Unique Cluster of Inflammatory Monocytes and Functionally Intact Regulatory T Cells in Rare Childhood Sjögren's Disease

Myung-Chul Kim[1], Umasankar De[2], Nicholas Borcherding[3], Joon Paek[4], Nicole Winn[5], Indraneel Bhattacharyya[6], Qing Yu[7], Ryan Kolb[8], Theodore Drashansky[9], Akaluck Thatayatikom[10], Weizhou Zhang[8] and Seunghee Cha[11], [1]Jeju National University, Jeju-si, South Korea, [2]University of Florida, Gainesville, FL, [3]Washington University School of Medicine in St. Louis, Washington, DC, [4]Department of Oral & Maxillofacial Diagnostic Sciences, Gainesville, FL, [5]Division of Oral Medicine, Department of Oral and Maxillofacial Diagnostic Sciences, University of Florida College of Dentistry, Gainesville, FL, [6]Department of Oral & Maxillofacial Diagnostic Sciences, University of Florida College of Dentistry, Gainesville, FL, [7]The Forsyth Institute, Cambridge, MA, [8]Department of Pathology & Immunology, University of Florida, Gainesville, FL, [9]Cellularity, Inc, Florham Park, NJ, [10]AdventHealth for Children, Orlando, FL, Orlando, FL, [11]Department of Oral & Maxillofacial Diagnostic Sciences, University of Florida College of Dentistry and Center for Orphaned Autoimmune Disorders (COAD), Gainesville, FL

SESSION INFORMATION

Session Date: Monday, November 13, 2023

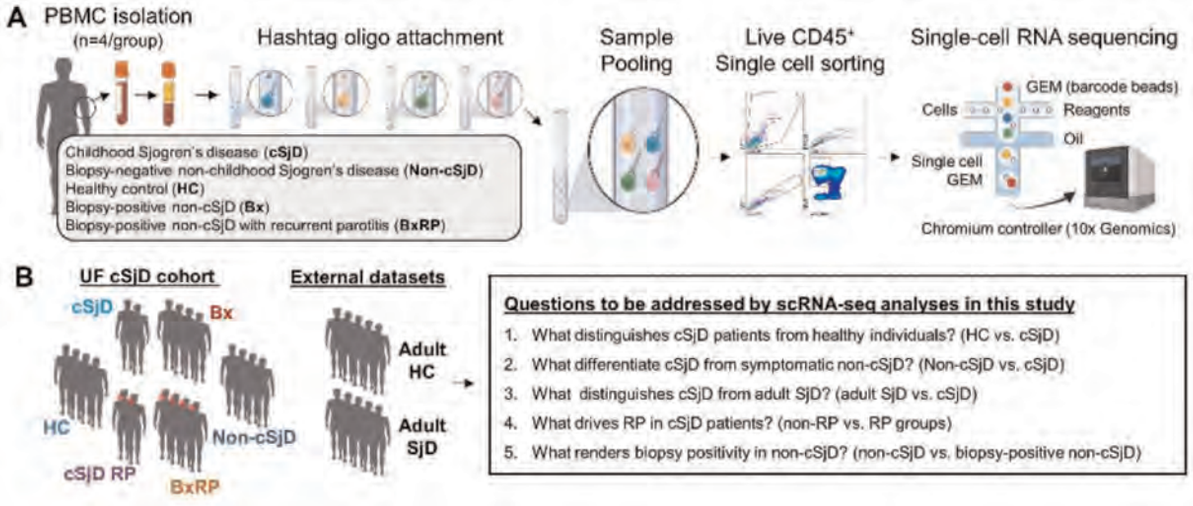
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: This study was performed to characterize key immune cell subsets and their interactions in patients with childhood Sjögren's disease (cSjD) for the first time in the field. Unlike Sjögren's disease (SjD), diagnostic criteria, treatment protocols, and natural history are unavailable in cSjD. In the current study, we aimed to address the following questions: 1) What distinguishes cSjD patients from healthy individuals?, 2) What distinguishes cSjD from symptomatic non-cSjD?, 3) Is cSjD a distinct disease entity from adult SjD?, 4) What involves biopsy positivity in non-cSjD?, and 5) Most importantly, what are the transcriptome and interactome profiles contributing to recurrent parotitis (RP), a chief complaint that prompts the most clinical visits from young children with cSjD?

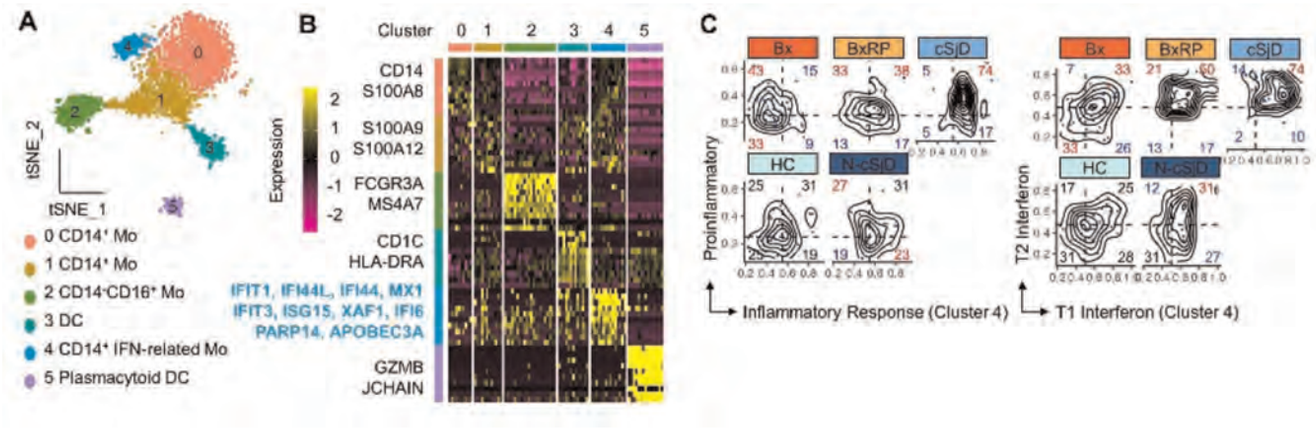
Methods: Five groups of four PBMC samples from the University of Florida (UF) pediatric cohort were profiled by single-cell RNA-seq (scRNA-seq). The groups include: cSjD, non-cSjD, biopsy-positive non-cSjD (Bx), biopsy-positive non-cSjD with RP (BxRP), and healthy controls (HC) (Figure 1). cSjD patients were diagnosed based on the 2016 ACR/EULAR criteria for



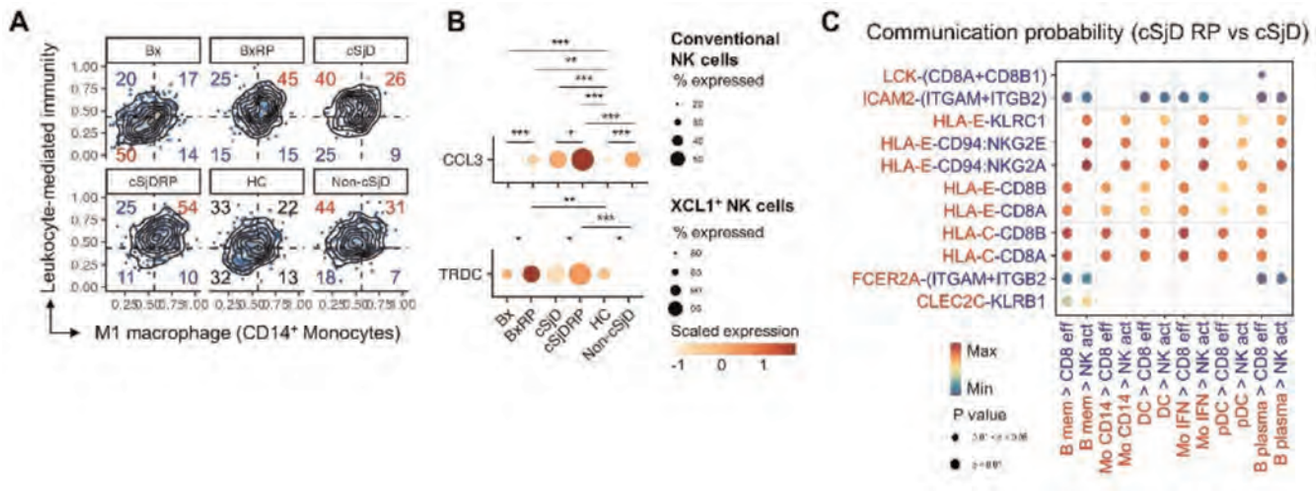
Overall study scheme. (A) Single cell RNA sequencing applied to peripheral blood mononuclear cells from 5 groups of interest is present. (B) Study design, groups, and analyses that will be covered by this study.

primary SjD. The CellChat R package identified cell-to-cell interaction strength and frequency. Flow cytometry for immune subsets and regulatory T cell (Treg) functional assays for Treg suppression were also performed.

Results: Prominent effector memory $CD4^+$ T cells (Tem) noted in cSjD were characterized by genes involving inflammation and cytolysis. A unique cluster of proinflammatory $CD14^+$ monocytes enriched with type I and type II IFN-related genes was highly specific to cSjD compared with the published scRNA-seq dataset from adult SjD (Figure 2). Surprisingly, *in vitro* Treg function in cSjD was intact and distinct from reduced Treg functionality in SjD. The X-C-motif-chemokine-ligand-1 $(XCL1)^+$ NK subset was expanded significantly, exhibiting functional enhancement in NK-mediated cytotoxicity and transmigration. Subjects with RP



Identification and characterization of proinflammatory myeloid subpopulations by scRNA-seq. (A) Six myeloid subsets are presented on the tSNE plot. (B) Among the top 20 DEGs defining each subset, representative genes are presented on the heatmap with Cluster 4 characteristically distinguished from others by the distinct upregulation of IFN-related genes. (C) Hex density enrichment plot reveals enrichment pattern of proinflammatory and inflammatory responses and type I and II IFN signatures in Cluster 4 of each group. Red and blue numbers on each quadrant illustrate upward and downward trends, respectively, compared to HC.



Molecular and interactome characterization of immune subsets involved in recurrent parotitis. (A) Hex density enrichment plot revealing enrichment pattern of "M1 macrophage" and "leukocyte-mediated immunity" in the classic monocyte subsets across the groups. RP exhibits a more inflammatory phenotype than those without, as evidenced by the RP-preferential shift toward the inflammatory signatures. The numbers in red and blue on each quadrant illustrate upward and downward trends, respectively, compared to HC. (B) Dot plot presenting RP-related upregulation of CCL3 and TRDC genes in NK subsets. Statistical significance was obtained by comparing two groups of interest with a non-parametric Wilcoxon rank-sum t-test. * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$. (C) Identification of significant ligand and receptor pairs between immune subsets of interest, including effector CD8+ T and XCL1+ NK subsets. These subsets have shown increased communication probability with B and myeloid subsets via MHC class I-related genes in cSjD RP, compared to the groups without RP.

had more M1-like CD14$^+$ monocytes, Tem, and XCL1$^+$ NK cells. Importantly, effector CD8$^+$ T and XCL1$^+$ NK cells were analyzed to be activated by dendritic cells or memory B cells, based on our interactome analyses (Figure 3). Significant upregulation of CCL3 was noted in NK cells from patients in the RP group, compared to those not in the RP group.

Conclusion: Our study, based on scRNA-seq analysis of PBMC from our UF cohort, revealed that: 1) Enhanced immune cell interactions and inflammatory monocyte clusters enriched with IFN-related genes are the key features in cSjD. 2) M2-polarized monocytes distinguish non-cSjD from cSjD. 3) Tregs in cSjD are functionally competent, whereas the regulatory function of Tregs in adult SjD are suppressed. 4) Biopsy-positive non-cSjD contains proinflammatory M1-polarized monocytes. 5) Patients with RP present inflammatory immune subsets and enhanced interactions similar to cSjD. A subset of more activated NK cell subset might also contribute to RP through preferential recruitment of effector types of T cells, including MAIT-like CD8$^+$ T cells, by CCL3-producing NK cells.

Disclosure: M. Kim: None; **U. De**: None; **N. Borcherding**: Omniscope, 2; **J. Paek**: None; **N. Winn**: None; **I. Bhattacharyya**: None; **Q. Yu**: None; **R. Kolb**: None; **T. Drashansky**: Celularity, Inc., 3, 10, 11; **A. Thatayatikom**: None; **W. Zhang**: None; **S. Cha**: None.

Abstract Number: 1367

Novel Autoantibodies Might Circumvent the Need for Labial Biopsy in a Subset of Seronegative Sjögren's Disease Patients

Maxwell Parker[1], Zihao Zheng[2], Michael Lasarev[3], Roxana Alexandridis[3], Michael Newton[3], Miriam Shelef[3] and **Sara McCoy**[4], [1]University of Wisconsin-Madison, Madison, WI, [2]Google, Sunnyvale, CA, [3]University of Wisconsin, Madison, WI, [4]University of Wisconsin School of Medicine and Public Health, Middleton, WI

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren's disease (SjD) is typically diagnosed by the presence of an anti-SSA antibody or focal lymphocytic sialadenitis in salivary gland tissue. Among SjD patients who are anti-SSA antibody negative (SSA-), a salivary gland biopsy is required for diagnosis. Our objective was to identify novel autoantibodies to non-invasively diagnose SSA- SjD.

Methods: IgG binding to a high density whole human peptidome array was quantified using sera from SSA- SjD (n=8) cases and age- and sex-matched healthy controls (n=8). The highest bound peptides from the array were confirmed by ELISA. Fifteen peptides were selected for external validation by ELISA using an independent cohort of subjects that were age-, sex-, and race-matched from the SICCA biorepository: SSA- SjD subjects (met 2016 ACR/EULAR criteria for SjD; n=76), sicca controls (sicca with negative ANA, rheumatoid factor, SSA, and focus score < 1; n=75), and autoimmune controls (positive ANA [≥1:320], rheumatoid factor, or SSA, but failed to meet 2016 ACR/EULAR criteria for SjD; n=41). Among all subjects, 85/192 (44.3%) had a positive focus score (FS ≥1). Peptide abundance was compared between groups using area under the ROC curve (*c*-index; AUC). Binary decision trees using R trees package were used to generate models predictive of SjD vs. controls. Adaptive Lasso was used for variable selection for binary logistic regression models.

Results: IgG against a peptide from DTD2 (D-aminoacyl-tRNA deacylase 2) and RESF1 (retroelement silencing factor 1) was bound more in SSA- SjD than in sicca controls (p=.004; p=0.045; Fig 1a) and more in SSA- SjD than in combined controls (sicca and autoimmune) (p=0.003, p=0.03; Fig 1b). The top performing classification tree model discriminating SjD vs. sicca

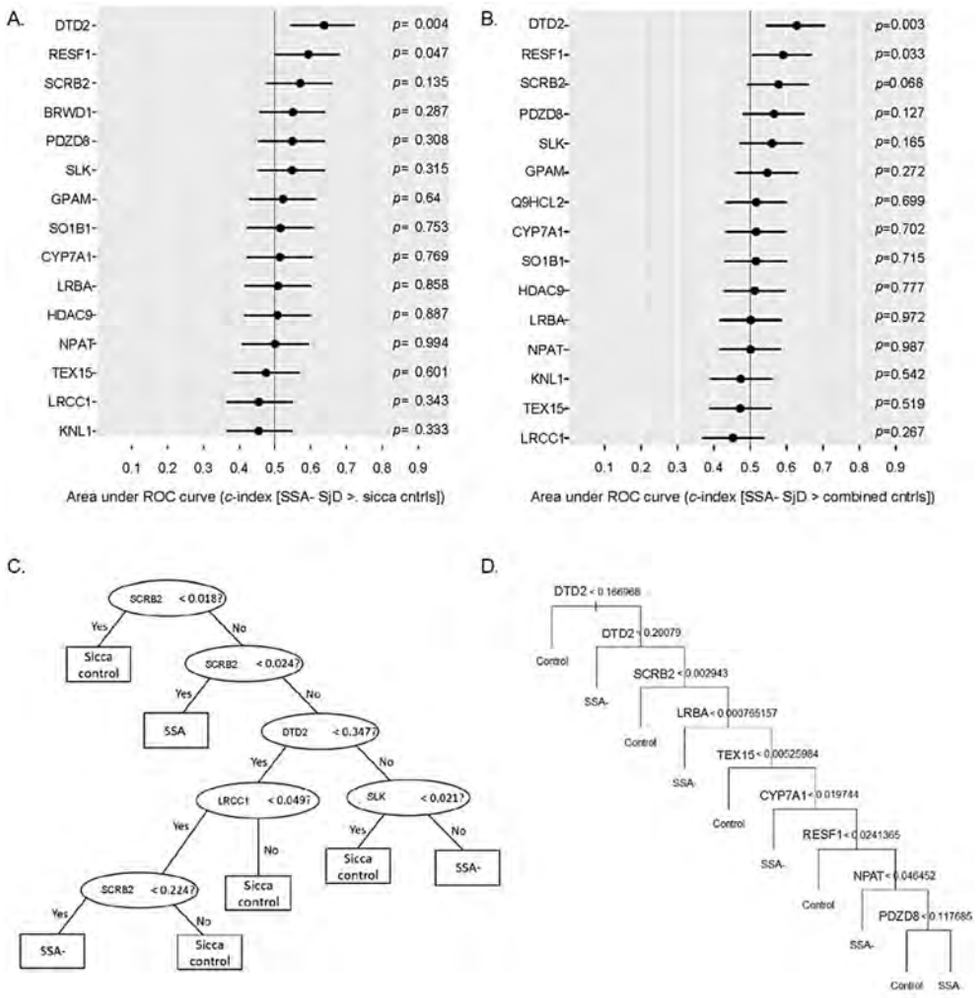


Figure 1. SSA- SjD subjects bind peptides from DTD2 and RESF1 more than controls. A) Area under the ROC curve (AUC) of the adjusted optical density of peptide groups between SSA- SjD (n=76) and sicca controls (n=75); B) AUC of the adjusted optical density of peptide groups between SSA- SjD (n=76) and a combined control comprising sicca and autoimmune controls (n=116); C) Best performing tree discriminating SSA- SjD vs. sicca controls; D) Best performing tree discriminating SSA- SjD vs. combined controls.

control included peptides from proteins SCRB2, DTD2, LRCC1, and SLK (65% accurate on validation set; Fig 1c). The top performing tree (55% accuracy upon validation) to discriminate between SjD and sicca controls involved peptides from proteins DTD2, SCRB2, CYP7A1, LRCC1, and KNL1. The top performing (62% accuracy upon validation) to discriminate between SjD and combined controls included peptides from proteins DTD2, RESF1, SCRB2, LRBA, TEX15, CYP7A1, NPAT, and PDZD8 (Fig 1d). Next, we defined if we could predict a positive FS. IgG against peptides from proteins RESF1, DTD2, and SCRB2 were bound more in patients with FS positive vs. negative (p=.010; p=0.012; p=0.027; Figure 2a). We incorporated peptide binding into a regression model with clinical variables including platelet count, SSB, ANA≥1:320, rheumatoid factor, and unstimulated whole salivary flow. Our dependent variable was FS (positive vs. negative). The final model showed good discrimination between FS positive vs. negative (Fig 2b-c). The AUC for this model is 71.6% (95% CI 63.9-78.2%) and allows flexibility to optimize for specificity, sensitivity, and positive and negative predictive value (Fig 2d-g).

Conclusion: We present novel autoantibodies inSSA- SjD compared to autoimmune- and sicca-controls that can be used to predict an abnormal FS on labial salivary gland biopsy with good predictive value.

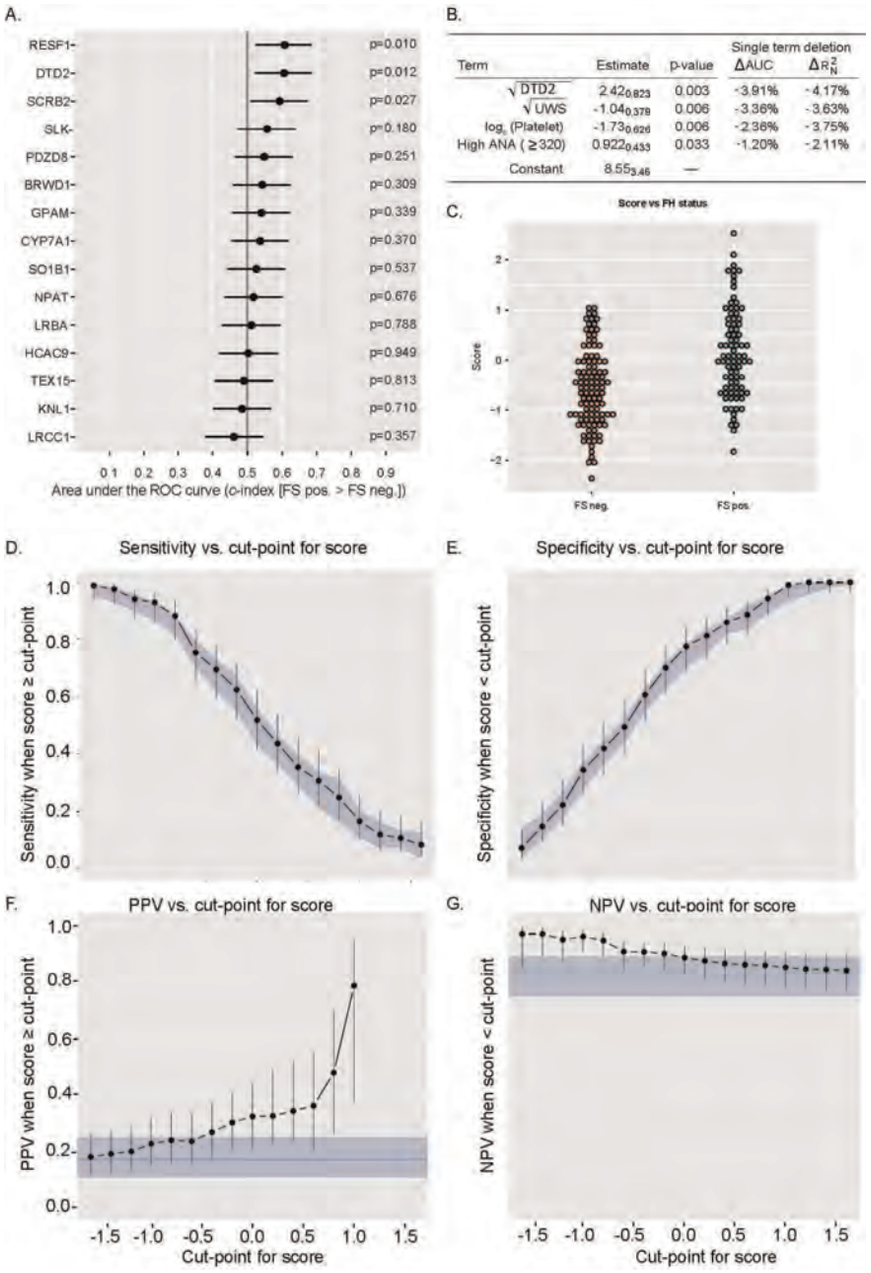


Figure 2. Models that incorporate binding to a peptide from DTD2 yield clinically relevant sensitivity, specificity, and positive and negative predictive value among SSA- patients. A) AUC comparing distributions of adjusted optical density of peptide groups comparing between focus score positive vs. negative (n=85 focus score positive and n=107 focus score negative). The forest plot shows the degree of IgG binding to the peptide of interest differed between focus score positive and focus score negative comparisons; B) Adaptive Lasso reduced variables from 33 to 5 (anti-SSB antibodies, RF, high ANA titer, IgG level, and platelet count) for separate binary logistic regression models. The model incorporated four predictors (binding a peptide form DTD2, unstimulated salivary flow, platelet count, and high ANA) with an AUC of 71.6% (95% CI 63.9-78.2%). The table shows estimated model coefficients and their standard errors in subscript; C) dot plot showing the separation between positive and negative focus score groups; D-E) Specificity and sensitivity graphed separately for cut-points of the score ranging from -1.6 to 1.6. Optimism-corrected values as dotted lines and differ from original values by at most 2.6 or 1.8% for sensitivity and specificity, respectively; F-G) Positive and negative predictive value graphed separately.

Disclosure: M. Parker: JangoBio, 3; **Z. Zheng**: None; **M. Lasarev**: None; **R. Alexandridis**: None; **M. Newton**: None; **M. Shelef**: None; **S. McCoy**: Bristol-Myers Squibb(BMS), 2, Horizon, 2, Kiniksa, 2, Novartis, 2, Otsuka/Visterra, 2, Target RWE, 2.

Abstract Number: 1368

Development of the Sjögren's-related Quality of Life (SRQoL) to Assess Health-related Quality of Life (HRQoL) in Sjögren's

Benjamin A Fisher[1], Linda Stone[2], **Jessica Marvel**[3], Pushpendra Goswami[4], Monia Steenackers[4], Gayle Kenney[4], Chiara Perella[5], Wolfgang Hueber[4], Chloe Howse[6], Elizabeth Gargon[6], Aishwarya Chohan[6], Megan Mayhew[6] and Nicola Williamson[6], [1]University of Birmingham, Birmingham, United Kingdom, [2]The British Sjogren's Syndrome Association, Birmingham, United Kingdom, [3]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [4]Novartis Pharma AG, Basel, Switzerland, [5]Novartis Pharma AG, Riehen, Switzerland, [6]Adelphi Values Patient-Centered Outcomes, Bollington, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I

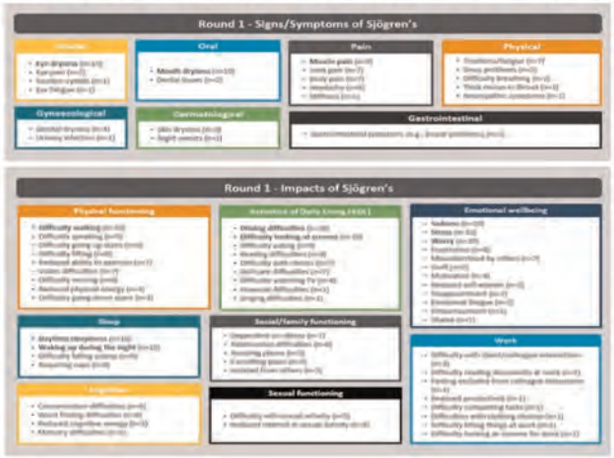
Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren's is a heterogenous chronic auto-immune disease, characterized by excessive dryness of the eyes and mouth, as well as systemic complications which can significantly impact patients' health-related quality of life (HRQoL). Existing patient-reported outcome (PRO) measures focus on the frequency/severity of symptoms but do not capture the impacts that Sjögren's has on patients' HRQoL. To address this gap, the Sjögren's-Related Quality of Life (SRQoL), was developed in line with Food and Drug Administration's Clinical Outcome Assessment (COA) guidance documents.[1-4] Qualitative interviews were conducted to evaluate the content validity and appropriateness of the SRQoL.

Methods: Patient advisory boards, social media listening, previous patient interviews, and findings from a prior literature review were reviewed to gain insights into the patient experience and HRQoL impact of Sjögren's to develop the SRQoL. Global impression of severity (PGI-S) and change (PGI-C) items were developed to inform further validation of the SRQoL. SRQoL and PGI-S/C development involved a patient advocate and physician as research partners. Combined qualitative concept elicitation (CE) and cognitive debriefing (CD) interviews are being conducted with adult (≥18 years) patients with primary Sjögren's from the US and UK, over two rounds. Round-one has been completed (n=10; 70% female; mean age = 52 years).

Figure 1: Conceptual model of signs/symptoms and impacts elicited from CE interviews during development of Sjögren's Related Quality of Life (SRQoL) in patients with Sjögren's



Results: From the review, an initial 36-item draft PRO measure was developed to assess HRQoL across seven hypothesized domains including physical functioning, activities of daily living, cognition, sleep, emotional wellbeing, social/family functioning, and work. Round-one CE results were consistent with Sjögren's related symptoms and HRQoL impacts elicited from the review (difficulty walking, driving difficulties, low mood/sadness, and daytime sleepiness). Concepts from the participant interviews (round one) were organized into a preliminary conceptual model in Figure 1. SRQoL and PGI-S/C items were well understood and relevant to most participants during round-one CD. Participants endorsed the 7-day recall period and frequency and severity response scales.

Conclusion: Initial findings support the content validity and suitability of the draft SRQoL, with round-two interviews currently underway. Following further testing and psychometric evaluation, the SRQoL is intended to provide greater understanding of patient burden and treatment benefit of Sjögren's in randomized clinical trials and may be used in clinical practice to monitor patients' HRQoL and improve patient-physician communication.

References:

1. FDA PFDD: Collecting Comprehensive and Representative Input, 2018
2. FDA PFDD: Methods to Identify What Is Important to Patients, 2022
3. FDA PFDD: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments, 2022
4. FDA PFDD: Incorporating Clinical Outcome Assessments Into Endpoints for Regulatory Decision-Making, 2023

Disclosure: B. A Fisher: Bristol-Myers Squibb(BMS), 2, Celgene, 5, Galapagos, 2, 5, Janssen, 2, 5, Novartis, 2, Roche, 2, Sanofi, 2, Servier, 2, 5, UCB, 2; **L. Stone**: Novartis, 12, Patient advocate, Servier Saclay, 12, Member Patient Board; **J. Marvel**: Novartis, 3; **P. Goswami**: Novartis, 3; **M. Steenackers**: Novartis, 3; **G. Kenney**: Novartis Pharma AG, 3; **C. Perella**: Novartis, 3; **W. Hueber**: Novartis, 3, 11; **C. Howse**: Novartis, 2, 7; **E. Gargon**: Novartis, 2, 7; **A. Chohan**: Novartis, 2, 7; **M. Mayhew**: Novartis, 2, 7; **N. Williamson**: Novartis, 2, 7.

Abstract Number: 1369

Treatment Patterns and Drivers of Biologic Prescriptions in Patients with Primary Sjögren's Disease: Results from a Multinational, Real-World Survey

Sara McCoy[1], Alan Baer[2], **Ann Xi**[3], Giorgio Castellano[4], Victoria Barton[4], Anthony Amatucci[5], Ilias Alevizos[6] and Haridarshan Patel[7], [1]University of Wisconsin School of Medicine and Public Health, Middleton, WI, [2]Johns Hopkins University School of Medicine, Baltimore, MD, [3]Horizon Therapeutics, Indianapolis, IN, [4]Adelphi Real World, Bollington, United Kingdom, [5]Horizon Therapeutics, Cambridge, MA, [6]Horizon Therapeutics, Rockville, MD, [7]Horizon Therapeutics, Deerfield, IL

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Currently, no systemic therapies have been approved for Sjögren's disease (SjD) due to limited evidence regarding efficacy. However, biologics are often used in patients with active systemic involvement. Real-world data on treatment patterns and off-label use of biologics in SjD are lacking. We aimed to describe treatment patterns and identify potential drivers of biologic prescription in patients with primary SjD in real-world clinical settings.

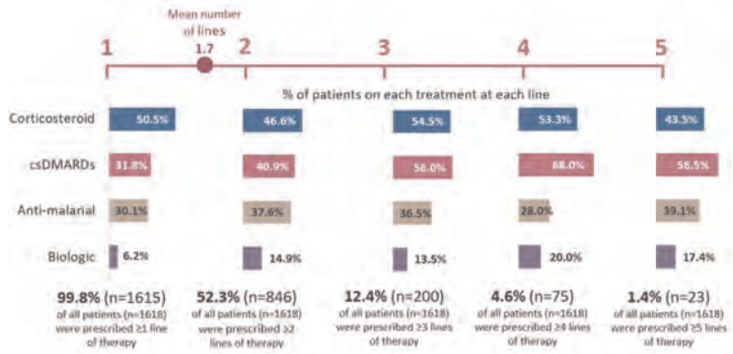


Figure 1. Lines of therapy in patients with primary Sjögren's disease. Progression in line of therapy defined as change in treatment regimen (including addition or removal of any other class of therapy from a regimen). Overall, 1618 patients had complete treatment pattern data. At each line of therapy, the % of patients prescribed each treatment class does not sum to 100% due to concomitant treatment class prescription. csDMARDs (conventional synthetic disease-modifying anti-rheumatic drugs) include azathioprine, methotrexate, cyclosporine, cyclophosphamide, mycophenolate mofetil and other csDMARD. Anti-malarial includes hydroxychloroquine and other anti-malarials.

Table 1. Variables identified from LASSO regression as factors associated with biologic prescription in patients with primary Sjögren's disease. Note that base size differs from main sample due to data completeness for all variables.

Characteristics associated with biologic prescription (N=1187)	Directionality of association with biologic prescription
United States of America (reference), N=320 (27%)	
Germany, N=213 (18%)	Negatively associated
Spain, N=209 (18%)	Positively associated
Patient aged 18-49 and 65+ (reference), N=674 (57%)	
Patients aged 50-64, N=513 (43%)	Positively associated
Physician-reported severity prior to treatment: mild (reference), N=168 (14%)	
Severe, N=230 (19%)	Positively associated
Physician-reported lines of therapy: 1 line (reference), N=585 (49%)	
2 lines, N=476 (40%)	Positively associated
3+ lines, N=126 (11%)	Positively associated
Physician-reported number of organs involved: 1 organ (reference), N=497 (42%)	
4+ organs involved, N=186 (16%)	Positively associated
Physician-reported organ involvement at diagnosis: not experiencing symptom (reference)	
Ulcers, N=18 (2%)	Positively associated
Lachrymal swelling, N=103 (9%)	Positively associated
Thrombocytopenia, N=40 (3%)	Positively associated
Lymphadenopathy, N=115 (10%)	Positively associated
Physician-reported concomitant conditions before diagnosis: not experiencing the concomitant condition (reference)	
Myocardial infarction, N=13 (1%)	Positively associated

Methods: Data were drawn from the Adelphi SjD Disease Specific Programme™, a cross-sectional survey of rheumatologists and their consulting patients with SjD in France, Germany, Italy, Spain, and the United States of America from 2018. Rheumatologists completed patient record forms for their next six SjD patients, reporting on demographics, clinical characteristics, physician-perceived disease severity (mild, moderate, severe), treatment history and reasons for treatment selection. A least absolute shrinkage and selection operator (LASSO) regression model was applied to identify drivers associated with biologic prescription. All other data were analyzed descriptively.

Results: 316 rheumatologists reported data for 1879 patients with SjD; 89% of patients were female, the mean (SD) age was 53 (12.18) years, 89% of patients were white and 67% of patients had moderate SjD as perceived by rheumatologists prior to SjD treatment. Of 1618 patients with complete data on treatment patterns, 99.8% (N=1615) of patients received ≥1 line of therapy (LoT), 52% (N=846) of patients received ≥2 LoTs and 12% (N=200) of patients received ≥3 LoTs. Corticosteroids were prescribed in 44-55% of patients with SjD, while biologics were least prescribed (6-20%) and were typically initiated at LoT 2 or later (**Figure 1**). LASSO regression (N=1187) revealed a higher likelihood of biologic prescription at 2 or later LoT. Patients with physician-perceived severe disease were also more likely to be prescribed a biologic than those with mild disease, as were patients with ≥4 organs involved at diagnosis (**Table 1**).

Rheumatologists' top five reasons for biologic prescription (N=223) included efficacy in treating organ manifestations (55%), reducing pain (51%), intent to slow disease progression (51%), and maintaining quality of life (50%). A further 49% also reported wanting to reduce steroid burden, even though around 50% of patients with biologic prescriptions had concomitant steroid use.

Conclusion: From this international survey, we found that patients with more LoTs, physician-perceived severe primary SjD, and greater organ involvement were more likely to be prescribed biologics. Across all LOTs, biologic use was low reflecting the lack of approved or effective drugs in SjD. Overall corticosteroid use was common, suggesting that available biologics may not be efficacious enough to reduce steroid use in SjD. There remains an unmet need among patients with primary SjD and further research is warranted to fully understand the impact of biologics on corticosteroid use among patients with SjD.

Disclosure: S. McCoy: Bristol-Myers Squibb(BMS), 2, Horizon, 2, Kiniksa, 2, Novartis, 2, Otsuka/Visterra, 2, Target RWE, 2; **A. Baer**: Bristol-Myers Squibb(BMS), 2; **A. Xi**: Horizon Therapeutics, 3, 11; **G. Castellano**: None; **V. Barton**: None; **A. Amatucci**: Horizon Therapeutics, 3, 11; **I. Alevizos**: Horizon Therapeutics, 3, 11; **H. Patel**: Horizon Therapeutics, 3, 12, Stockholder.

Abstract Number: 1370

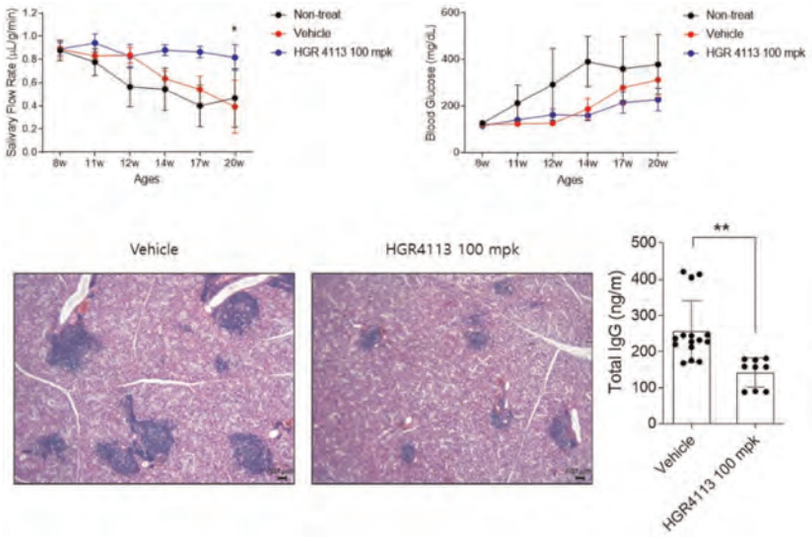
Synthetic Glabridin Derivatives Improves Sjogren's Syndrome by Inducing Salivary Secretion and Salivary Gland Regeneration

Eui-Jong Kwon[1], Jin-Sil Park[2], Ha Yeon Jeong[3], Hye Yeon Kang[4], JeongWon Choi[3], Mi-La Cho[3] and Sung-Hwan Park[5], [1]Division of Rheumatology, Department of Internal Medicine, The Catholic University of Korea Seoul St. Mary's Hospital, Seocho-gu, South Korea, [2]The Rheumatism Research Center, Catholic Research Institute of Medical Science, College of Medicine, The Catholic University of Korea, Seocho-gu, South Korea, [3]Rheumatism Research Center, Catholic Research Institute of Medical Science, College of Medicine, The Catholic University of Korea, Seoul, South Korea, [4]Rheumatism Research Center, Catholic Research Institute of Medical Science, College of Medicine, The Catholic University of Korea, Seocho-gu, South Korea, [5]Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea

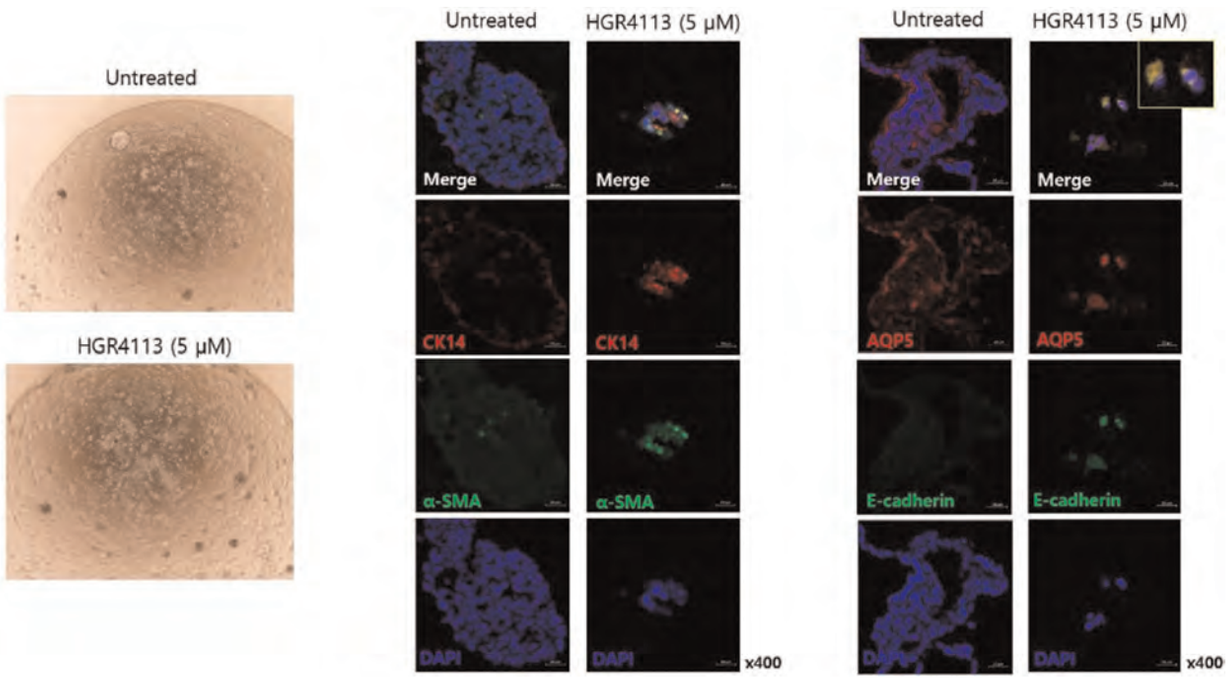
SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjogren's syndrome (SS) is a systemic autoimmune disease characterized by infiltration of lymphocytes into the exocrine gland resulting in progressive lacrimal and salivary estruction and dysfunctional glandular secretion. Metabolic abnormalities of immune cells infiltrated into the salivary gland of patients with SS induce abnormal cell death



HGR4113 attenuates the severity of SS in NOD/ShiLtJ mice

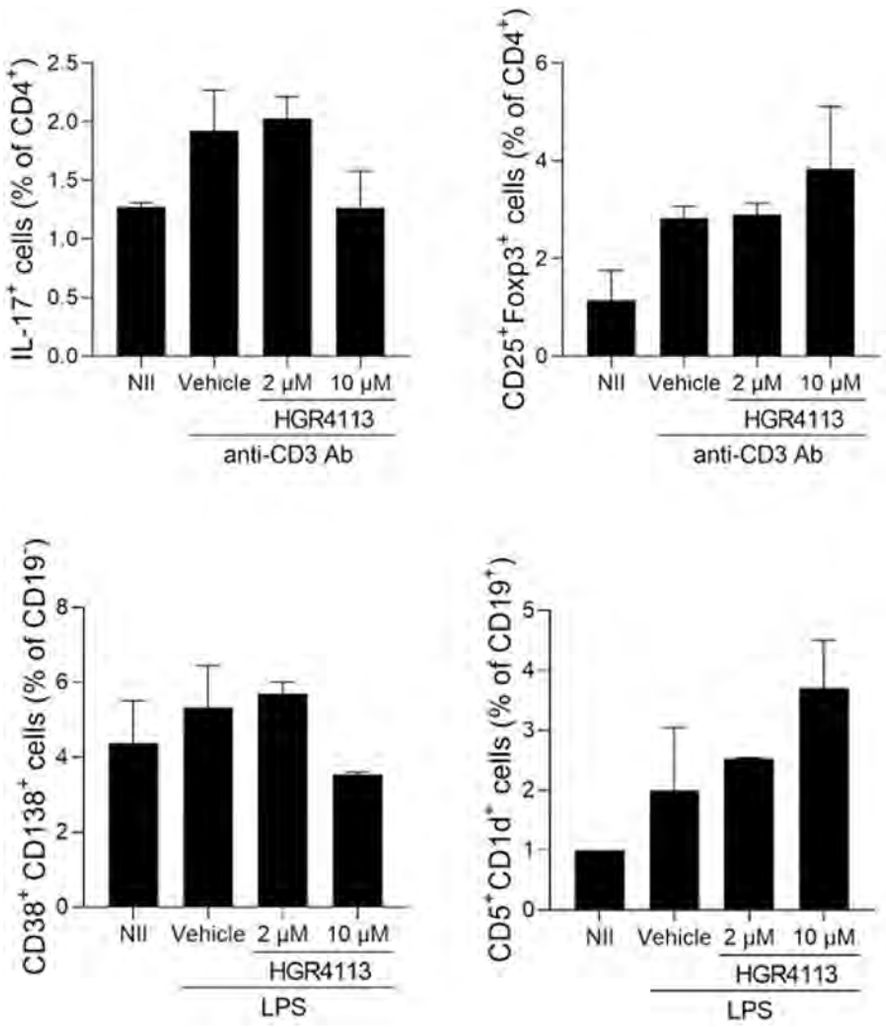


Treatment with HGR4113 promotes the generation of salivary gland organoids in vitro

and hyperactivity, which is involved in the exacerbation of SS. In this study, we investigated the effects of HGR4113, a structural analogue of glabridin under clinical trial for obesity, that promotes mitochondrial function, on the development of Sjogren's syndrome in non-obese diabetic NOD/ShiLtJ (NOD) mice.

Methods: NOD mice were orally administered 100 mg/kg of HGR4113 daily, and body weight, salivary flow rate, and blood glucose levels were measured every 3 weeks. Infiltration of inflammatory cells and levels of inflammation-related factors in salivary gland were histologically analyzed, and the development of salivary gland tissue organoids was investigated. The populations of various T– and B–cell subtypes in the spleen were assessed by flow cytometry. In vitro formation of salivary gland organoids was investigated by treatment with HGR4113.

Results: Oral administration of HGR4113 improved salivary flow rate and the infiltration of lymphocytes and the level of inflammatory cytokines in salivary gland of NOD mice. HGR4113 lowered the frequencies of splenic IL-17-producing T and B cells, germinal center B cells and plasma cells ex vivo in NOD mice. In addition, organoid formation from salivary gland stem cells of NOD mice administered with HGR4113 increased, and the levels of E-cadherin-14, Aquaporin-5, α-SMA, and Cytokeratin-14 increased. Treatment with HGR4113 also promoted the formation of salivary gland organoids in vitro.



Treatment with HGR4113 regulates the frequency of inflammatory cells in humans

Conclusion: These results show that HGR4113 can improve salivary gland hypofunction by inhibiting lymphocyte infiltration and inflammation in the salivary gland and restoring the damaged salivary gland in SS-Like NOD mice.

Disclosure: E. Kwon: None; **J. Park**: None; **H. Jeong**: None; **H. Kang**: None; **J. Choi**: None; **M. Cho**: None; **S. Park**: None.

Abstract Number: 1371

Are Ultrasound Salivary Parenchymal Abnormalities More Severe in Primary Sjögren Patients with a Higher Disease Duration ? A Cross-sectional International Study

Alice TISON[1], sandrine jousse joulin[2], Maëlys Consigny[3], Philipp Moog[4], Benedikt Hofauer[5], Eric Hachulla[6], Christophe Lamotte[7], JACQUES MOREL[8], Gael Mouterde[9], Vera Milic[10], Hendrika Bootsma[11], Alja Stel[12], Benjamin A Fisher[13], Mark Maybury[14], Alan Baer[15], Dana Direnzo[16], Hae-Rim Kim[17], Hong Ki Min[18], Shin-Seok Lee[19], Sung-Eun Choi[19], Guillermo CARVAJAL ALEGRIA[20], Sylvie Boisramé[21], Dewi Guellec[22], Divi Cornec[23], Malin Jonsson[24], Daniel Hammenfors[25], Alain SARAUX[26] and **Valerie Devauchelle**[27], [1]CHU de la Cavale Blanche, Brest, France, [2]Rheumatology, CHU Brest, Brest, France, [3]Biostatistics, CHU Brest, Brest, France, [4]Rheumatology, CHU Munich, Munich, Germany, [5]Otolaryngology, CHU Munich, Munich, Germany, [6]University of Lille, Lille, France, [7]Internal Medicine and Clinical Immunology, CHU Lille, Lille, France, [8]Protocole thérapeutique immuno-rhumatologie, Montpellier, France, [9]CHU Lapeyronie, Montpellier, France, [10]Rheumatology, University of Belgrade, Medical School, Belgrade, Serbia, [11]Department of Rheumatology, University Medical Centre Groningen, Groningen, Netherlands, [12]Rheumatology and clinical immunology, University Medical Center Groningen, Groningen, Netherlands, [13]University of Birmingham, Birmingham, United Kingdom, [14]Rheumatology, Institute of Inflammation and Ageing, University of Birmingham, Birmingham, United Kingdom, [15]Johns Hopkins University School of Medicine, Baltimore, MD, [16]University of Pennsylvania, Bala Cynwyd, PA, [17]Rheumatology, Konkuk University Medical Center, Seoul, South Korea, [18]Konkuk University School of Medicine, Seoul, South Korea, [19]Chonnam National University Medical School & Hospital, Gwangju, South Korea, [20]CHRU de Tours, Tours, France, [21]Ondontology, CHU Brest, France, Brest, France, [22]CHU de Brest, Brest, France, [23]University of Brest, Brest, France, [24]Clinical dentistry, University of Bergen, Bergen, Norway, Bergen, Norway, [25]Rheumatology, Haukeland University Hospital, Bergen, Norway, [26]CHU Brest, Brest, France, [27]UBO, Brest, France

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Salivary gland ultrasonography (SGUS) is commonly used in primary Sjögren Disease (pSD) as a diagnostic tool. It could also be used to monitor disease activity, but severity of SGUS parenchymal abnormalities in relation to disease duration is not well characterized. The objective was to assess transversally the severity of ultrasound salivary parenchymal abnormalities in relation to pSD duration.

Methods: In this prospective cross-sectional international multicentric study, patients with pSD according to 2002 or 2016 ACR/EULAR classification criteria were included. Parenchymal abnormalities assessed by ultrasound within both parotid and sub-mandibular glands were reported on a standardized form and classified according to the semi-quantitative score of the OMERACT. Reliability between experts was measured after online training. Patients were separated into 4 groups according to disease duration from the first buccal dryness symptoms (group A : < 5 years, group B : between 5 and 9 years, group C : between 10 and 20 years, group D : > 20 years of evolution).The association between disease duration groups and SGUS parenchymal abnormalities was quantified in terms of odds ratio and its 95% confidence interval.

Results: 247 patients were consecutively included between May 2019 and February 2022 in 11 international centers. They were 47, 69, 78 and 53 in groups A, B, C and D, respectively. Women represented 94.7% of patients, with a median age of 58 [range 19-89] years old. Oraldryness was reported by 99.6% of patients with an abnormal salivary flow in 75% of patients. The focus score was ≥1/4mm2 in 89% of patients. 85% of patients had positive anti-SSA. The median ESSDAI score was 3 [0-48]. Considering for each patient the most severe gland, there was a global significant association between disease duration and OMERACT score (OR for 5 years duration : 1.23 [IC95% 1.04 ; 1.47], p=0.02). Considering each US parameter, there was not any statistical difference between the 4 groups, notably in relation to the proportion of an/hypoechoic areas in the gland. The only statistical difference between groups was found regarding the proportion of hyperechoic bands (p = 0.002). Proportion of hyperechoic bands was not associated with age (p=0,90) but was associated with visual analogic scale for dryness (p=0,002).

Conclusion: This large international cross-sectional study in patients with pSD found a positive association between the OMERACT score and disease duration, with a significant difference only observed in the proportion of hyperechoic bands, when considering separately each US parameter. This may suggest a progressive fibro-adipous evolution of the gland across disease duration related to pSD itself and not related to older age, while surface of hypoechoic areas could be more linked to inflammation, and could be more usefull in clinical trials to assess SGUS modifications after treatment.

Disclosure: A. TISON: Bristol-Myers Squibb(BMS), 6, galapagos, 2; **s. jousse joulin**: None; **M. Consigny**: None; **P. Moog**: None; **B. Hofauer**: None; **E. Hachulla**: Bayer, 2, CSL Behring, 5, GlaxoSmithKlein(GSK), 2, 5, 6, johnson&-Johnson, 2, 5, 6, Novartis, 2, 5, Otsuka, 6, Roche-Chugai, 2, 5, 6, sanofi-genzyme, 2, 5, Sobi, 5; **C. Lamotte**: None; **J. MOREL**: None; **G. Mouterde**: Bristol-Myers Squibb(BMS), 6; **V. Milic**: None; **H. Bootsma**: None; **A. Stel**: None; **B. A Fisher**: Bristol-Myers Squibb(BMS), 2, Celgene, 5, Galapagos, 2, 5, Janssen, 2, 5, Novartis, 2, Roche, 2, Sanofi, 2, Servier, 2, 5, UCB, 2; **M. Maybury**: GE Healthcare, 2; **A. Baer**: Bristol-Myers Squibb(BMS), 2; **D. Direnzo**: None; **H. Kim**: None; **H. Min**: None; **S. Lee**: None; **S. Choi**: None; **G. CARVAJAL ALEGRIA**: None; **S. Boisramé**: None; **D. Guellec**: None; **D. Cornec**: None; **M. Jonsson**: None; **D. Hammenfors**: None; **A. SARAUX**: None; **V. Devauchelle**: None.

Abstract Number: 1372

Obinutuzumab Efficacy and Tolerance in Patients with Auto-Immune Diseases Immunized Against Rituximab

Mathilde Pezot[1], Gaetane Nocturne[2], Rakiba Belkhir[1], Julien Henry[1], Stephan Pavy[1], Raphaele Seror[3], Xavier Mariette[4] and Samuel Bitoun[5], [1]Rheumatology Department, Université Paris-Saclay, INSERM U1184, Hôpital Bicêtre, APHP, FHU CARE, Le Kremlin-Bicêtre, France, [2]APHP, Le Kremlin-Bicêtre, France, [3]University Hospital Paris Saclay, Le Kremlin-Bicêtre, France, [4]Université Paris-Saclay, Le Kremlin-Bicêtre, France, [5]CHU Bicêtre APHP, Le Kremlin-Bicêtre, France

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Among patients with auto-immune diseases (AID) treated with Rituximab (RTX), anti-drug antibodies (ADAb) leading to inefficacy and infusion reactions (Wincup and al., Ann Rheum Dis, 2019) is a frequent complication. We previously showed that it was more common in systemic AID than in RA (Combier and al, Rheumatology, 2020) In these conditions, targeting B cells with another anti-CD20 molecule is the only option. Obinutuzumab (OBZ) is an anti-CD20 humanized antibody frequently used in hematological malignancies. However, only few studies reported its efficacy and

safety on a limited number of patients with autoimmune diseases, and never in the context of immunization against RTX. (Kvacskay and al., Ann Rheum Dis, 2022 ; Furie and al. Ann Rheum Dis, 2022). The presence of ADAb allows to hypothesize that targeting CD20 can still be efficacious with another molecule to which ADAb against RTX are not cross-reactive.

Methods: This study aims to describe efficacy and tolerance of consecutive patients with confirmed ADAb against rituximab and treated with OBZ between 2019 and 2023 in our tertiary department. Clinical and biological variables were collected before OBZ and 3 months after the first infusion. Response to OBZ was determined by the physician.

Results: Thirteen out of 15 were females (87%), with a median age of 53 years; 13/15 (87%) had Sjogren's syndrome (SS). Among Sjögren patients 3/13 also had systemic lupus erythematosus (SLE), and 2/13 also had anti-synthetases syndrome. The remaining 2 patients did not have Sjogren's and had eosinophilic granulomatosis with polyangiitis and mixed connective tissue disease.Thirteen out of 15 (87%) patients had been tested positively for anti-RTX antibodies. The most frequent symptoms leading to OBZ infusions were polyarthritis for 6/15 (40%) of them, cryoglobulinaemia for 3/15 (20%). The median duration from onset of the disease to first OBZ infusion was 9 years. The median number of cycles of RTX before OBZ was 2. Two patients had also received ofatumumab, another anti-CD20 therapeutic antibody. (Table 1). OBZ was well-tolerated in all patients without any infusion reaction even in patients with previous infusions reactions to RTX. Seven out of 15 (46%) patient presented with non-serious infections (Grade 1-2) mainly respiratory. Eight out of 15 patients (53%) had a clinical response to OBZ at 3 months. Comparing OBZ responders and non-responders at 3 months showed that responders trended to have longer disease duration (11 years vs 6, p=0.08). Number of treatment lines, co-treatments with corticosteroids or methotrexate were not different between groups.

Conclusion: In conclusion, obinutuzumab can be a good therapeutic option for AID patients who are immunized against RTX without symptomatic cross immunogenicity, with good tolerance and with clinical response in half of the patients. Further studies are required to determine which type of patients could respond to this treatment.

Disclosure: M. Pezot: None; **G. Nocturne**: None; **R. Belkhir**: None; **J. Henry**: None; **S. Pavy**: None; **R. Seror**: None; **X. Mariette**: AstraZeneca, 2, 6, BMS, 2, 6, Galapagos, 2, 6, GSK, 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **S. Bitoun**: None.

Abstract Number: 1373

Deltex1 May Involve the Function of T Regulatory Cells and Regulate the Disease Activity of Sjögren's Syndrome

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Deltex1 is a transcription target of nuclear factor of activated T cells in mice and promotes T cell anergy. We have previously reported that silencing of Deltex1 expression enhanced IFN-γ secretion by human T cells after stimulation with anti-CD3 and anti-CD28 antibodies. In this study, we aimed to investigate the role of Deltex1 in patients with Sjögren's syndrome (SjS).

Methods: Peripheral T cells were collected from SjS patients and healthy controls for analysis of Deltex1 gene expression by RT-QPCR. The expression of T regulatory cells (Tregs)-associated molecules, including PD-1, CTLA-4, LAG-3, TIGIT, TIM-3, and cytokines were measured by flow cytometry.

Results: We found that Deltex1 expression in T cells was significantly lower in the primary Sjogren's syndrome patients than inhealthy controls ($p < 0.001$). Interestingly, Deltex1 expression in T cells was negatively correlated with the v*isual analogue scale* (*VAS*) for dryness, VAS for fatigue, European League Against Rheumatism (EULAR) SjS outcome measures, the patient reported index (ESSPRI), and the disease activity index (ESSDAI) ($p < 0.001$, $p = 0.003$, $p = 0.017$, and $p = 0.003$, respectively), but not with VAS for pain ($p = 0.495$). Importantly, we found that Treg-associated molecules expression, including PD-1, CTLA-4, and TIM-3, andanti-inflammatory cytokine interleukin-10 on $CD4^+FoxP3^+$ Tregs was significantly higher in low Deltex1 expression group than high Deltex1 expression group (all $p < 0.05$).

Conclusion: These results suggested that Deltex1 may involve the function of Tregs and regulate the disease activity of SjS.

Disclosure: M. Chen: None.

Abstract Number: 1374

Interstitial Lung Disease Is Frequent in Primary Sjögren's Syndrome and Is Associated with Reduced Survival

Marco Sprecher[1], Florine Weber[2], Kastriot Kastrati[3], Helmut Prosch[4], Natasha Moe[5], Emily Langballe[6], Cosimo Bruni[7], Oyvind Molberg[8], Phuong Phuong Diep[9], Christian Clarenbach[10], Paul Studenic[11], Helena Andersson[8], Oyvind Midtvedt[12], Torhild Garen[8], Karoline Lerang[13], Thomas Frauenfelder[14], Helga Radner[15], Oliver Distler[7] and Anna Maria Hoffmann-Vold[16], [1]Dept of Rheumatology, University Hospital Zurich, University of Zurich, Zürich, Switzerland, [2]Dept of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [3]Dept of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna (Austria), Vienna, Austria, [4]Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna, Vienna, Austria, [5]Dept of Radiology, University Hospital Oslo, Oslo, Norway, [6]Universitetet i Oslo, Oslo, Norway, [7]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [8]Dept of Rheumatology, University Hospital Oslo, Oslo, Norway, [9]Dept of Respiratory diseases, University Hospital Oslo, Oslo, Norway, [10]Dept of Pulmonology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [11]Medical University of Vienna and Karolinska Institutet (sweden), Vienna, Austria, [12]Oslo University Hospital, Oslo, Norway, [13]Department of Rheumatology, Oslo University Hospital, Oslo, Norway, [14]Dept of Radiology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [15]Division of Rheumatology, Medical University of Vienna, Vienna, Austria, [16]Oslo University Hospital, Department of Rheumatology, Oslo, Norway

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) has been reported to be present in 10-15% of patients with primary Sjögren's syndrome (pSS). Knowledge on risk factors predicting the development of ILD in pSS and its impact on long-term outcome is limited and no standardized disease management exists, including screening and monitoring. The aim of this project was to evaluate the presence of ILD in pSS, assess risk factors for the development of ILD and its impact on mortality.

Methods: This is an international multicenter study including patients with pSS with and without ILD from expert centers. All patients fulfilled the 2016 ACR-EULAR classification criteria for pSS. ILD was diagnosed on high resolution computed tomography (HRCT) assessed by expert radiologists in each center. Comprehensive clinical characteristics, lung function tests including forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DLCO) were available. Vital status was assessed at last available observation. We applied multivariable Cox regression to assess risk factors predicting ILD and mortality, presented as hazard ratio (HR) with 95% confidential interval (CI). Survival was assessed using Kaplan-Meier estimates.

Table: Disease characteristics of all patients and patients with ILD

	All pSS (n=843)	pSS-ILD (n=74)
Male sex, n (%)	73 (8.7)	15 (19.7)
Age, yrs (SD)	50.5 (14.7)	52.7 (14.9)
Time from pSS to ILD diagnosis, yrs (SD)	n.a.	6.9 (8.9)
ILD diagnosed after pSS, n (%)	n.a.	48 (65.8)
Anti-Ro-SSA, n (%)	456 (72.6)	58 (90.6)
Anti-Ro-SSA and La-SSB, n (%)	227 (34.6)	34 (50)
CRP, mg/l (SD)	5.2 (13.6)	6.4 (11.2)
ESR, (SD)	23.8 (20.2)	30 (19.4)
Extraglandular manifestation		
Polyneuropathy, n (%)	64 (8.9)	13 (18.6)
Dermal affection, (%)	48 (6.7)	11 (15.5)
Nephritis, n (%)	18 (2.5)	3 (4.1)
Lymphadenopathy, n (%)	62 (8.6)	16 (21.9)
Lymphoma, n (%)	24 (3.3)	7 (9.7)
Death, n (%)	140 (16.6)	13 (17.1)

Results: The study cohort included a total of 843 patients with pSS; 9% were male, age at time of pSS diagnosis was 51.5 (SD 15.1) years, 72.6% were positive for anti-Ro-SSA and 34.6% for both anti-Ro-SSA and anti-La-SSB (Table).

In total, 498 (59%) patients were assessed by HRCT. Of these, 76 (15%) were diagnosed with ILD (Table). Of all pSS-ILD patients, 21 (33%) were diagnosed with ILD at time point of or prior to the diagnosis of pSS, while 48 (67%) were diagnosed in a mean follow-up of 11 (SD 8.2) years after diagnosis of pSS.

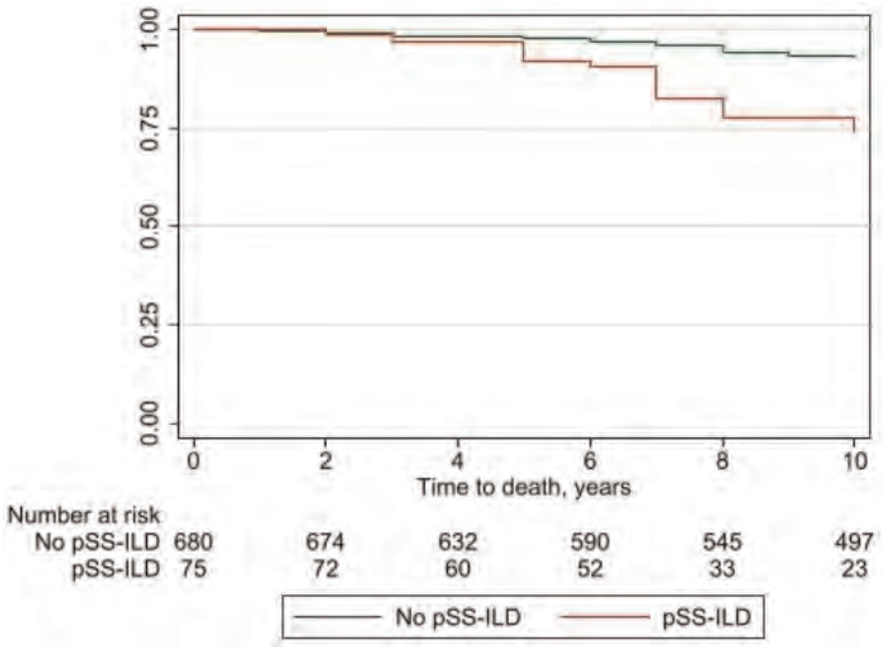

Figure 1: Time to death in pSS patients with (red line) and without ILD (green)

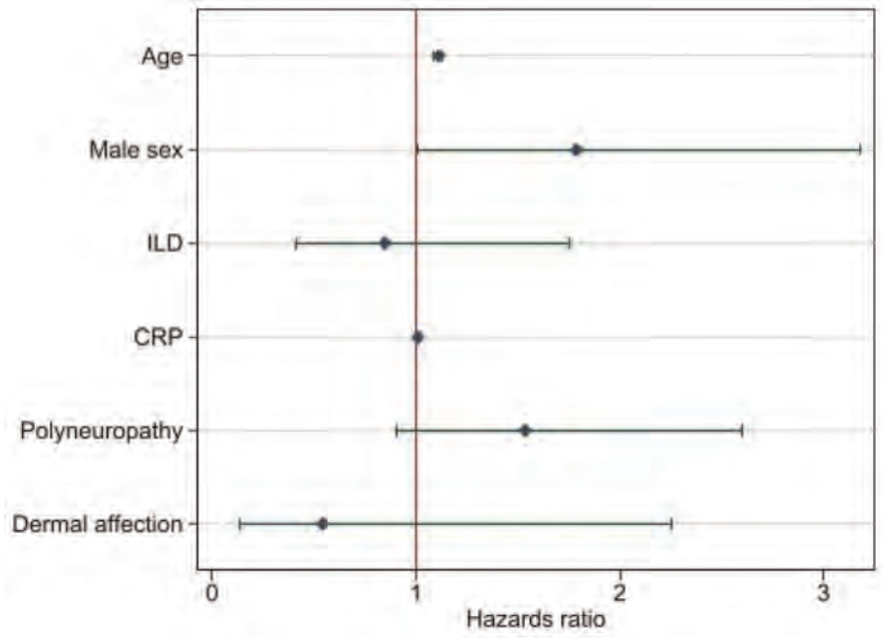

Figure 2: Risk factors predicting mortality in pSS in multivariable Cox regression

In these 48 patients, we assessed risk factors for the development of pSS-ILD and found that male sex, increased inflammatory markers, reduced complement factor C3, presence of interstitial nephritis and absence of arthritis were predicting development of ILD in univariable Cox regression. In multivariable Cox regression, only older age predicted ILD development.

Over mean 15.9 (SD 8.9) years follow up, 140 (16%) pSS patients died. ILD was associated with impaired survival with a reduced 10-year survival from 93% to 74% in patients without and with ILD (p=0.001) (Figure 1). In multivariable Cox regression, male sex, older age and increased inflammatory markers were associated with mortality (Figure 2).

Conclusion: Based on the relatively high prevalence of ILD in pSS and its significant impact on long-term survival, we suggest that screening strategies should be developed and that at least patients at risk of ILD development should be screened on a regular basis. As pSS-ILD patients have a reduced long-term outcome, regular monitoring is of outmost importance.

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Abstract Number: 1375

The Relative Burden of Fatigue Is Associated with High TSH/fT4 Ratio in Korean Patients with Primary Sjogren's Syndrome

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate the prevalence of anti-thyroid autoantibodies, abnormal thyroid function, and their clinical impacts in Korean patients with primary Sjögren's syndrome (pSS).

Methods: One hundred ninety-six pSS patients (190 females; median age 58.6 [IQR, 46.5-67.3]), satisfying the 2016 ACR/EULAR criteria, were consecutively enrolled. Those with a history of overt thyroid disease (n=22) or thyroid cancer (n=4) were excluded. Clinical variables including EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) and Patient Reported Index (ESSPRI) were collected. For the relative contribution of fatigue to ESSPRI, the fraction of fatigue ($F_{fatigue}$)

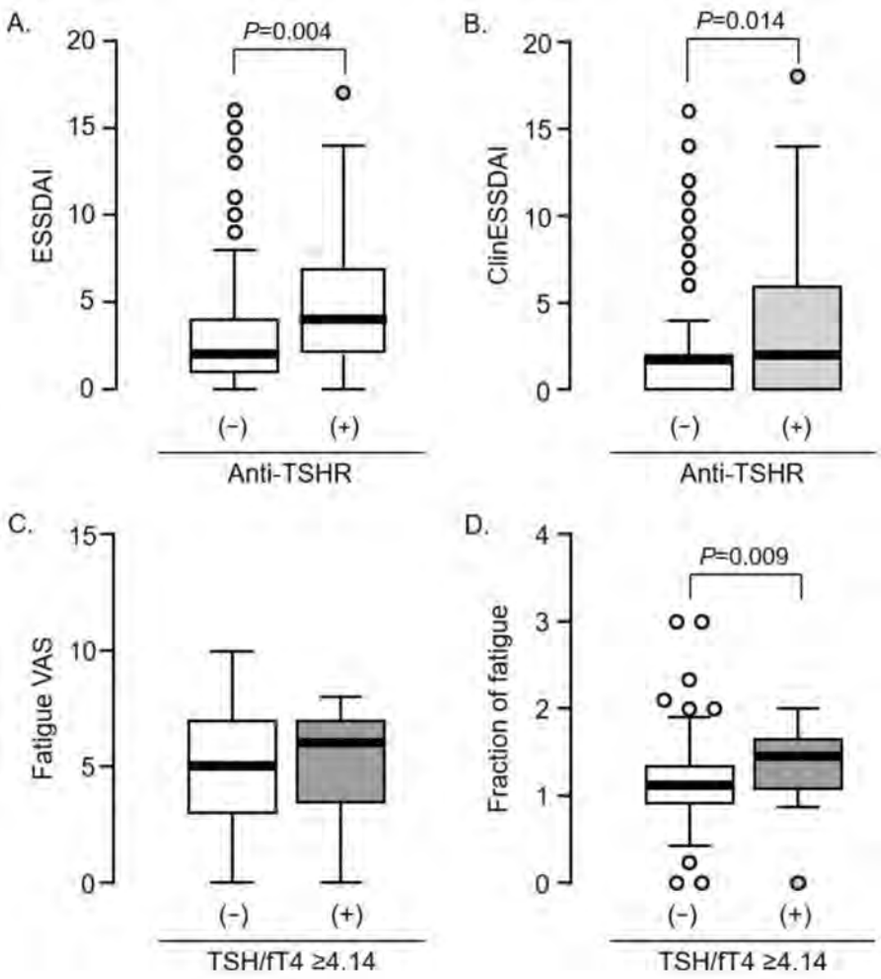

Figure 1. ESSDAI (A) and clinical ESSDAI (ClinESSDAI, B) levels were significantly different according to anti-TSH receptor (TSHR) positivity. Fatigue VAS levels were compatible (C) but fractions of fatigue in ESSPRI were significantly higher in patient with TSH/fT4 ≥4.14 (D) than those with TSH/fT4 <4.14. P values were calculated by the Mann-Whitney test.

Table 1. Logistic regression analysis results for the highest quartile of the fraction of fatigue in ESSPRI. Variables with p <0.1 in univariate analyses were incorporated into the multivariate analysis.

	Univariate		Multivariate			
			Model 1		Model 2	
Variables	OR [95% CI]	*P*	OR [95% CI]	*P*	OR [95% CI]	*P*
Age	0.968 [0.945-0.992]	0.010	0.969 [0.944-0.995]	0.018	0.966 [0.941-0.992]	0.011
ALC	0.999 [0.999-1.000]	0.028	0.999 [0.999-1.000]	0.059	0.999 [0.999-1.000]	0.072
TSH/fT4	1.234 [0.999-1.523]	0.051	1.231 [0.937-1.617]	0.135		
TSH/fT4 ≥ 4.14	5.601 [2.036-15.408]	0.001	-	-	8.001 [2.048-31.263]	0.003
Subclinical hypothyroidism	4.145 [0.895-19.207]	0.069	2.406 [0.336-17.225]	0.382	0.836 [0.105-6.680]	0.866

ALC = absolute lymphocyte counts; OR = odds ratio; CI = confidence intervals.

was calculated using ESSPRI fatigue score/ESSPRI score. Laboratory data including the complete blood count, ESR, and levels of thyroid-stimulating hormone (TSH; uIU/mL), free T4 (ng/dL), IgG, β2-microglobulin, cryoglobulin, and complement C3 and C4 were assessed. TSH/fT4 ratio was calculated. Anti-thyroglobulin (TG), anti-thyroperoxidase (TPO), TSH-binding inhibiting immunoglobulin (TBII), and anti-TSH receptor antibody (TSHR) were measured. Subclinical hypothyroidism (ST) was defined as TSH > 4.0 and the presence of hypothyroidism-related autoantibodies. The Mann-Whitney test, Chi-squared or Fischer's exact test, and logistic regression analysis were performed.

Results: Of 196 patients, 71 (36.2%) had one of the anti-thyroid autoantibodies and 53 (27%) had one of the hypothyroidism-related autoantibodies. The prevalence of anti-TG, anti-TPO, TBII, and anti-TSHR was 31 (15.8%), 28 (14.3%), 8 (4.1%), and 28 (14.3%), respectively. Twenty-four (12.2%) had TSH > 4.0 and 3 (1.5%) had TSH < 0.3. No patients had TSH > 10.0. ST was observed in 7 (3.6%) and was significantly associated with anti-TPO ($p < 0.001$) and TBII ($p < 0.05$). Patients with anti-TSHR had significantly higher levels of ESSDAI or clinical ESSDAI (both $p < 0.05$) and those with TSH/fT4 ≥ 4.14 had significantly higher $F_{fatigue}$ levels ($p < 0.01$; Fig. 1). In multivariate logistic regression analyses, subclinical hypothyroidism (OR=5.61 [95% CI 1.07-29.50]) or TFI ≥ 4.14 (OR=9.01 [2.35-34.56]) was associated with the top quantile of $F_{fatigue}$. Additionally, TSH/fT4 ≥ 4.14 was an independent predictor for the highest quantile of $F_{fatigue}$ (OR=8.00 [2.05-31.26]; Table 1).

Conclusion: Despite a high positive rate of thyroid-related autoantibodies, subclinical hypothyroidism was uncommonly observed in Korean pSS patients. The high TSH/fT4 ratio was significantly associated with "fatigue-dominance" in ESSPRI, and it may be related to the neuroendocrine aspects of fatigue in pSS.

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Abstract Number: 1376

SJOGRENSER Registry: Prospective Evaluation of a Cohort of Patients with Primary Sjögren's Syndrome After 8 Years of Follow-up

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Describe the evolution of patients with Sjögren's syndrome (SS) in relation to the appearance of new systemic manifestations and disease activity, as well as factors associated with an unfavorable outcome.

Methods: SJÖGRENSER PROS (SS-PROS) is an observational, longitudinal, and multicenter study of patients with SS who met 2002 classification criteria under active follow-up in rheumatology clinics of 31 Spanish hospitals that participated in the cross-sectional phase of the study (SJÖGRENSER TRANS; SS-TRANS). For the prospective phase, an 8 years follow-up visit was performed (2021-2022) comparing the results with baseline visit (SS-TRANS 2013-2014, 437 patients). Medical history was reviewed and a medical interview was performed. Epidemiological, clinical and serological variables as well as causes of death were recorded. Continuous and categorical variables were analyzed using means, medians, and frequencies, with their respective deviations and interquartile ranges (Q1-Q3). Student's T test was used to establish statistical associations, considering $p< 0.05$ significant.

Results: Up to January 2023, 180 patients have been included, 96% women, mean age 68 years (SD 11.2) and mean evolution time from diagnosis to inclusion of 18 years (SD 7.27). Newly developed systemic involvement was: joint in 47% of patients (arthritis in 17%), hematological (cytopenia) in 44%, lung involvement in 14%, renal in 13%, digestive in 17%. %, hepatic 6%, central and peripheral nervous system (NS) 4% and 3% respectively, and cardiac 2.7%; parotid inflammation was described in 13%. In the last 8 years, 3 new lymphomas have appeared (3/180, 1.6%).

Mean of the ESSDAI in SS-PROS was lower than in SS-TRANS: 2.78 (SD 4.3; 1-4) vs. 3.66 (SD 5.15; 2-4), respectively. By domains, the greatest variations were observed in the articular, hematological and biological domains; while in the rest of the domains, stability was evidenced in ≥94% of the cases (Figure 1). By organs, the most affected organ during follow-up was the lung, with 8 patients who increased the mean value of this domain.

ESSPRI mean improved: 5.24 (SD 2.35; 3.67-7) vs. 4.47 (SD 2.14; 2.67-6), respectively; being greater in the VAS of pain, 5.16 (SD 3.02; 3- 8) vs. 3.98 (SD 2.95; 1- 7), respectively (Figure 2).

Twenty-seven patients out of 180 have died since their inclusion in SS-TRANS (15%), 89% women, with a mean age of 75 years (SD 11.5; 65-84.5).

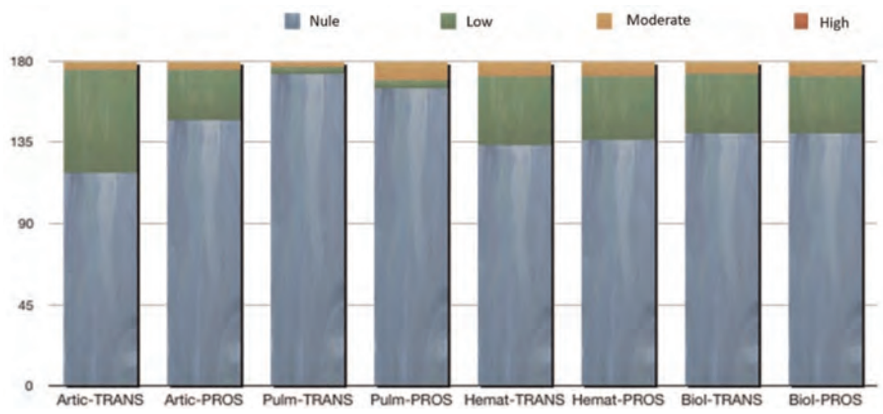

Figure 1: ESSDAI analysis by domains comparing SjögrenSER TRANS vs. SjögrenSER PROS

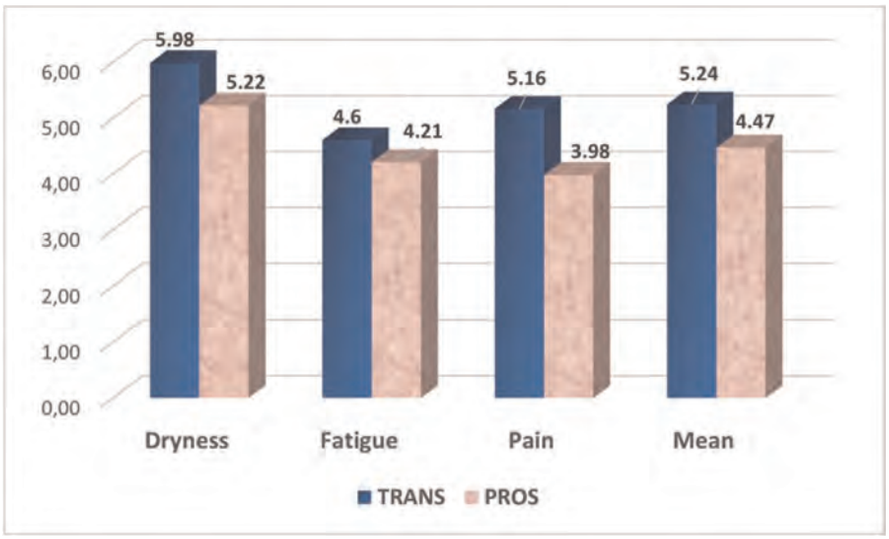

Figure 2: Mean ESSPRI in SjögrenSER TRANS compare with SjögrenSER PROS

Comparing baseline data visit (SS-TRANS) from the group of deceased (during SS-PROS) and of non-deceased (remaining under follow-up in SS-PROS), we observed that age (70 years; SD 11; 59-77), disease evolution time (11.5 years; SD 8; 4-17) and ESSDAI (5.22; SD 6.35; 0-8), were higher in the deceased vs. non-deceased (age 59 years, SD 12, p< 0.001; evolution time 9 years, SD7, p=0.078; ESSDAI 3.38, SD 4.88, 0-4, p0.087). There were no differences in ESSPRI.

Conclusion: Patients with SS develop new systemic manifestations over the years, despite maintaining or improving ESSDAI, suggesting the need of a close follow-up. The ESSPRI varies little over time, which represents a great challenge for the scientific community. Mortality in this cohort is 15%. Greater age, time of evolution and baseline ESSDAI were associated with a worse outcome.

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Abstract Number: 1377

Characterization of Pulmonary Manifestations of Sjögren Syndrome: A Multicenter Retrospective Study

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University Hospital, Strasbourg, France, [10]CHU Lille, Département de Médecine Interne et Immunologie Clinique, Centre de Référence des Maladies Auto-immunes Systémiques Rares du Nord et Nord-Ouest de France (CeRAINO), Lille, France, [11]APHP Hôpital Cochin, Paris, France, [12]Assistance Publique-Hôpitaux de Paris, Bichat-Claude Bernard University Hospital, INSERM UMR1152, University de Paris Cité, Department of Rheumatology, Paris, France, [13]CHU Bichat, Radiology, Paris, France, [14]CHU Kremlin-Bicêtre, Functional Explorations, Le Kremlin-Bicêtre, France, [15]University Hospital Paris Saclay, Le Kremlin-Bicêtre, France, [16]Université Paris-Saclay, Le Kremlin-Bicêtre, France, [17]APHP, Le Kremlin-Bicêtre, France

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren disease (Sjo) is a systemic immune-related disease with pulmonary manifestations occurring in up to 16% of patients [1], including interstitial lung disease (SS-ILD) and airway disease (SS-AD). Our objective was to assess the associated factors with SS-ILD and SS-AD and to describe these manifestations.

Methods: We performed a retrospective multicentric study, involving 9 French centers. We included Sjo patients fulfilling the ACR/EULAR 2016 criteria with a pulmonary disease evidenced by at least one clinician and one computed tomography (CT) report. We collected clinical and biological data at the visit giving access to the most exhaustive collection, pulmonary function test (PFT) and CT scans, that were all reviewed by a radiologist specialist in thoracic diseases. SS-ILD were considered progressive when associating a CT scan worsening and at least a 10% decrease of the forced vital capacity (FVC) between 2 consecutive measurements during follow-up. SS-ILD and SS-AD were compared to Sjo controls with no history of pulmonary involvement, matched on age and disease duration with a 2/1 ratio.

Results: We included 35 SS-ILD, 31 SS-AD and 132 Sjo controls. SS-ILD and SS-AD had significantly higher disease activity (ESSDAI) than control, even when excluding the pulmonary criteria of the score (**Table 1**). Thus, SS-ILD was also associated with anti-RNP antibodies and B cell biological markers at visit time. SS-ILD were mostly nonspecific interstitial pneumonia (NSIP, 26%), with fibrosis features and restrictive lung disease occurring in 46% of cases at baseline. 41% of SS-ILD were considered progressive, independently of Sjo characteristics and CT pattern. On the other hand, SS-AD were mostly diffuse,

Table 1: Characteristics of SS-ILD and SS-AD compared to Sjo controls

	SS-ILD, n=35	Sjo controls, n=70	p	SS-AD, n=31	Sjo controls, n=62	p
Age (years)	52	52	ns	56	56	ns
Women	29 (83)	65 (93)	ns	30 (97)	58 (93)	ns
Mean follow-up (years)	7	7	ns	9	7	ns
Disease duration (years)	4.6	4.3	ns	5.6	6.1	ns
Death during follow-up	5 (14)	4 (6)	ns	2 (7)	3 (5)	ns
History of clinical involvement						
-Articular	15 (44)	26 (37)	ns	18 (58)	34 (55)	ns
-Muscular	6 (18)	4 (6)	ns	3 (10)	3 (5)	ns
-Splenomegaly	4 (12)	1 (1)	**0.04**	2 (6)	2 (3)	ns
Biology						
-Anti-SSA	27 (79)	44 (63)	ns	21 (70)	38/59 (64)	ns
-Anti-RNP	11/32 (34)	1/62 (2)	**<0.001**	0	1/53 (2)	ns
-RF	15/32 (47)	21/67 (31)	ns	7/23 (30)	15/55 (27)	ns
-C3 low	5/30 (17)	2/67 (3)	**0.03**	2/24 (8)	3/56 (5)	ns
-Kappa/lambda ratio	3	1	**<0.001**	1.5	1	ns
-IgG	24	16	**<0.001**	17	14	0.06
-Gammaglobulinemia	24	20	ns	19	18	ns
-Beta-2-microglobulin	4	2	**<0.001**	3	2	**0.002**
ESSDAI	18	4	**<0.001**	10	4	**<0.001**
ESSDAI (pulmonary excluded)	11	4	**<0.001**	7	4	**0.02**
Incident lymphoma	2 (6)	2 (3)	ns	1 (3)	0	ns

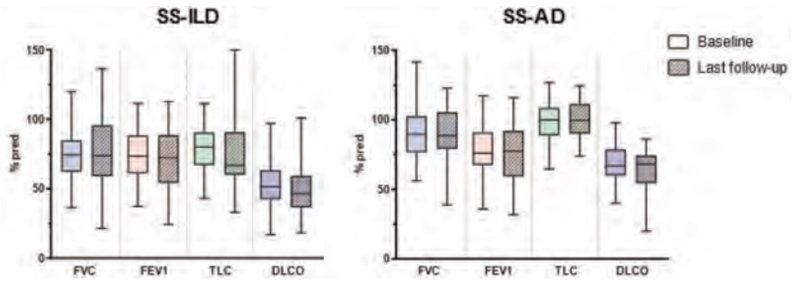

Figure 1: PFT evolution in SS-ILD and SS-AD

associating bronchiolitis and bronchiectasis in 60% of cases, with CT scan worsening observed in 41% of cases. Finally, both were poorly progressive in terms of PFT with respectively five and nine years of follow-up for SS-ILD and SS-AD (**Figure 1**).

Conclusion: SS-ILD are usually fibrosing and progressive manifestations of Sjo, associated with the disease activity and B cell biological markers. SS-AD readily associate proximal and distal airways and associate with the disease activity. Both slowly progress functionally. **Bibliography** 1. Ramos-Casals et al., Rheumatology. 54(12):2230-8.

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Abstract Number: 1378

The UCSD Shortness of Breath Questionnaire Is a Useful Tool for the Assessment of Dyspnea in Primary Sjögren's Syndrome Patients with Interstitial Lung Disease: A Monocentric Cross-Sectional Study

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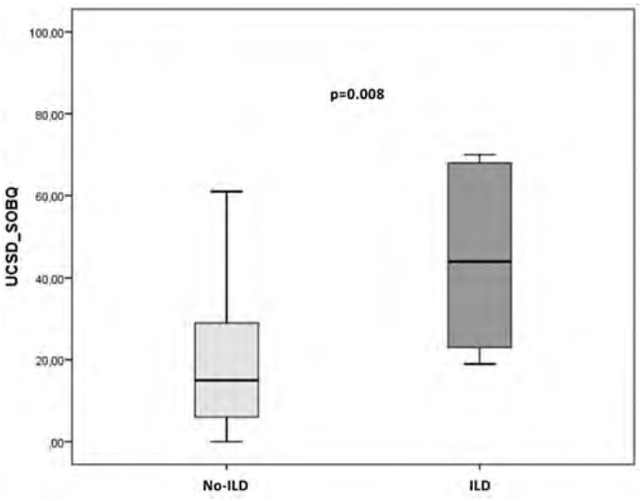
SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

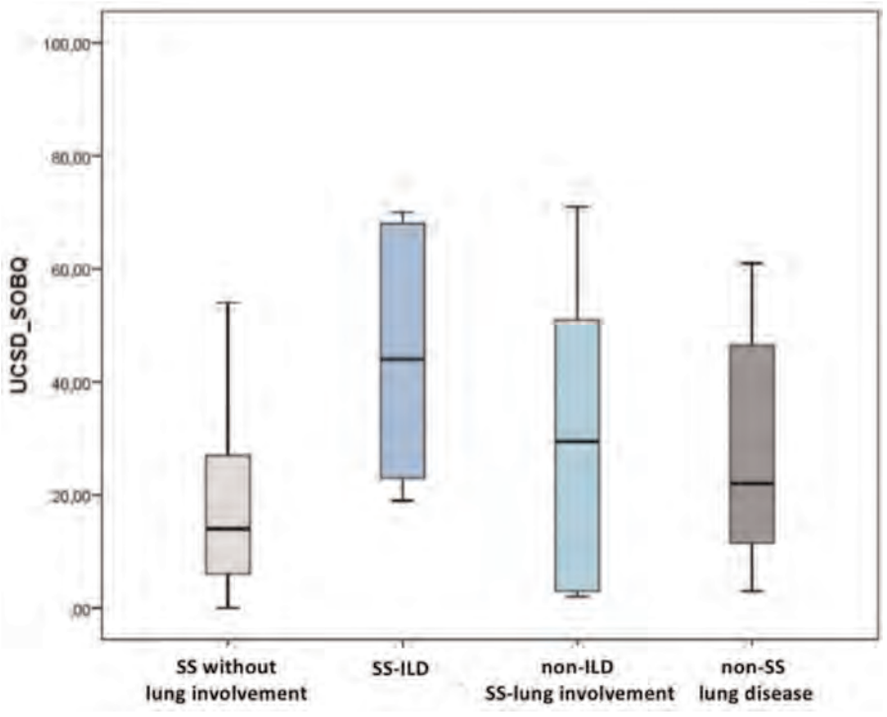
Background/Purpose: In clinical trials investigating new drugs for the management of Interstitial Lung Disease (ILD) patient reported outcomes (PRO) are increasingly employed as outcome measures in addition to objective pulmonary function tests (PFT). The UCSD Shortness of Breath Questionnaire (UCSDSOBQ) is a domain-specific PRO for the evaluation of dyspnea.

It has been recently validated in a large cohort of patients with fibrotic ILD of various etiologies. However, assessing dyspnea in Sjögren's Syndrome (SS) patients is especially challenging since it can be caused by both ILD and airway disease, ranging from xero-trachea to small airway involvement.

Aims: 1) to assess the impact of dyspnea in SS patients by using the UCSDSOBQ; 2) to investigate the correlation of the UCSDSOBQ score with underlying lung involvement and other PRO commonly employed for the multidimensional assessment of SS.



Comparison of UCSDSOBQ total score between SS-ILD patients and non-ILD SS patients



Comparison of UCSDSOBQ total score between SS patients subgroups

Methods: This was an observational cross-sectional study involving consecutive Primary SS patients (2016 ACR/EULAR classification criteria) evaluated in our outpatient clinic from November 2022 to May 2023. Clinical, biological, and imaging data were registered, as well as detailed information regarding smoking and pulmonary history.

Patients were asked to compile the UCSDSOBQ, a 24-item questionnaire assessing the impact of dyspnea on common daily activities with a score from 0 ("not at all") to 5 ("unable to do because of breathlessness") for each question.

PRO including ESSPRI, FACIT and HADS (hospital anxiety and depression scale) were also collected.

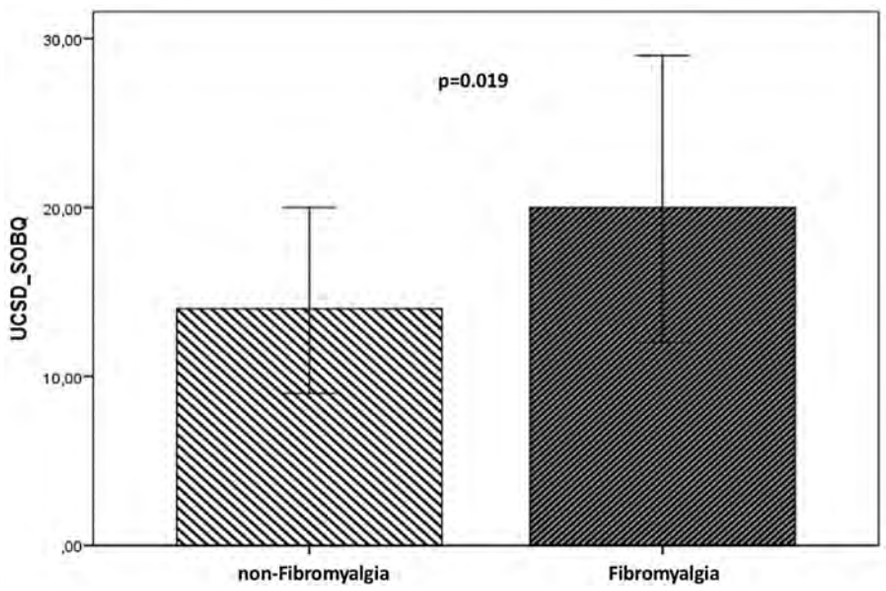
Based on clinical history, PFT and high-resolution computed tomography, we classified patients in the following subgroups: a) absence of lung involvement; b) SS-ILD; c) non-ILD SS-related lung involvement; d) non-SS-related lung disease.

Results: 137 SS patients were enrolled, with a median age of 64 (IQ 57-72) yrs, disease duration of 7 (IQ 5-14) yrs, F:M=133:4, anti-SSA positivity in 97/137 (70.8%). 39/137 (31.7%) patients were current or past smokers. Out of 137 patients 110 (80.3%) were classified as SS without lung involvement, 6 (4.4%) as SS-ILD, 10 (7.3%) as non-ILD SS-related lung involvement and 11 (8%) as non-SS related lung disease, including bronchial asthma and COPD.

The UCSDSOBQ total score was significantly higher in SS-ILD compared to non-ILD SS patients with a median score of 44 (IQR 22-68,5) vs 15 (5,75-29,75) respectively (p=.008).

We observed a trend towards a higher median UCSDSOBQ total score in SS-ILD patients compared to those with non-ILD SS-related lung involvement. However, this difference was not statistically significant. The UCSDSOBQ total score showed a moderate correlation with ESSPRI (r=.449; p< .001), FACIT (r=.564; p< .001) and HADS (r=.417; p< .001). Finally, SS patients with comorbid fibromyalgia exhibited a higher median UCSDSOBQ total score (p= .019) compared to the remaining SS patients.

Conclusion: Dyspnea assessment in SS-ILD patient is challenging due to potential airway involvement and comorbid conditions such as chronic fatigue, anxiety and depression that may alter its perception. Despite these difficulties the UCSDSOBQ seems a promising tool both for screening of lung involvement and as an outcome measure in future clinical trials.



Comparison of UCSDSOBQ total score between SS patients with comorbid fibromyalgia and the remaining SS patients

Disclosure: G. La Rocca: None; **F. Ferro**: None; **E. Elefante**: None; **S. Fonzetti**: None; **G. Fulvio**: None; **I. Navarro Garcia**: None; **C. Romei**: None; **M. Mosca**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, GlaxoSmithKlein(GSK), 2, Otsuka, 2, UCB, 2; **C. Baldini**: GlaxoSmithKlein(GSK), 6, Horizon, 6, Sanofi, 6.

Abstract Number: 1379

Population Pharmacokinetic/Pharmacodynamic Modeling of Dazodalibep, a CD40L Antagonist, in Healthy Volunteers and Patients with Rheumatoid Arthritis and Sjogren's Syndrome

Kenneth Der[1], Ryan Crass[2], Brendan Smith[3], Wonkyung Byon[4], Yan Xin[5] and Jiayin Huang[6], [1]Horizon Therapeutics, Danville, CA, [2]Apellis Pharmaceuticals, Michigan, [3]A2-Ai, Michigan, [4]Amador Bioscience, Michigan, [5]Horizon Therapeutics, South San Francisco, CA, [6]Horizon Therapeutics, Chicago, IL

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren's (SjS) is a chronic, systemic autoimmune disease caused by aberrant activation and infiltration of lymphocytes. Dazodalibep (DAZ), a novel non-antibody biologic antagonist of CD40 ligand (CD40L), inhibits the costimulatory signals between immune cells. The concentration of DAZ and immune biomarker data from existing clinical trials were analyzed using a population pharmacokinetic (PK)/pharmacodynamic (PD) model to inform dose selection for future studies.

Methods: PK and PD data from 4 clinical trials in healthy volunteers (HV) and subjects with rheumatoid arthritis (RA) and SjS were pooled and analyzed to characterize the PK of DAZ, including the effects of demographic covariates, and evaluate the PK/PD relationship on immune biomarkers (Ki67+ B cells, rheumatoid factor [RF], and CXCL13).

Results: Population PK modeling demonstrated that the PK of DAZ was adequately described by a two-compartment model with first-order elimination pathway from the central compartment. Following intravenous administration (IV), estimated clearance (CL; 0.347 L/day), distributional clearance (Q; 0.242 L/day), central volume of distribution (Vc; 3.4 L), and peripheral volume of distribution (Vp; 1.39 L) were consistent with typical biologics. Age, sex, race, ADA (anti-drug antibody) and renal function had no clinically relevant impact on DAZ CL. Body weight and patient population (HV or RA vs SjS) were identified as statistically significant covariates of DAZ PK. DAZ CL and VC increased less than linearly with increasing body weight. Healthy volunteers and RA patients had increase clearance relative to SjS patients. DAZ reduced circulating immune biomarkers which was well described with an indirect response model with DAZ effect applied as an inhibitory maximal effect (Imax) on the zero order production (Kin) for RF and CXCL13 and a direct effect model with DAZ effect applied as a proportional inhibitory maximal effect reduction from baseline for Ki67+ B cells. The proposed phase 3 doses are supported by the PK/PD modeling results and are expected to achieve sustained average drug concentration above the IC50 of Ki67+ B cells and RF within the dose interval.

Conclusion: The PK and PK/PD of DAZ were successfully described by population modeling. The modeling results supported the selection of dose to be further evaluated in upcoming phase 3 studies.

Disclosure: K. Der: Horizon Therapeutics, 3; **R. Crass**: Amador Bioscience, 3, Apellis Pharmaceuticals, 3; **B. Smith**: A2-Ai, 3, Amador Bioscience, 3; **W. Byon**: Amador Bioscience, 3, Pfizer, 3; **Y. Xin**: Horizon Therapeutics, 3; **J. Huang**: Astellas Pharma, 3, Horizon Therapeutics, 3.

Abstract Number: 1380

Synergistic Dose Effects of Extra X Chromosome in Development of Sjogren's Syndrome in Klinefelter and Triple X Syndromes

Anna-Kay Palmer[1] and Irene Tan[2], [1]Albert Einstein Medical Center, Philadelphia, PA, [2]Einstein Medical Center Philadelphia, Bala Cynwyd, PA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Immune-related genes located on the X chromosome are known to be important in the regulation of sex hormones and immune tolerance. It has been postulated that a dose relationship exists between the X chromosome and certain female predominant autoimmune diseases most notable for an increase of SLE in patients with triple X syndrome compared to females with XX karyotype. We investigate the proportion of individuals with Klinefelter syndrome (KS) karyotype 47, XXY and triple X syndrome karyotype 47, XXX who developed Sjogren's syndrome (SjS) compared with the general population.

Methods: This is a retrospective, multicenter, observational study using the TrinetX global research database. Using ICD-10 codes, we identified patients with the karyotype 47, XXY (KS) and 47, XXX (Triple X syndrome) from 6/1/2000 to 6/1/2023 who developed Sjogren's syndrome at any time. This was compared with the prevalence of SjS in the general population within the same time frame.

Table 1. Proportion of Sjogren's syndrome patients in general population, Klinefelter syndrome karyotype 47, XXY and in triple X syndrome karyotype 47, XXX.

Disorders	Affected patients	Total patients	Affected/Total patients	%	# Affected in 100,000	proportion
Sjogren in general population	221,860	121,080,766	0.0018	0.183	183	-
Sjogren in female	188,581	121,080,766	0.00156	0.156	156	5.7
Sjogren in male	33,279	121,080,766	0.00027	0.027	27	1 (reference)
Klinefelter in gen pop	1,634	121,080,766	0.0000135	0.00135	1.35	-
Sjogren in KS	10	1,634	0.0061	0.612	612	22.6
Triple X syndrome in gen pop	2,800	121,080,766	0.000023	0.0023	2.3	-
Sjogren in triple X	13	2,800	0.0046	0.464	464	3

Results: A total of 120,908,054 patients were queried on 6/1/2023 on the Global Collaborative Network. A total of 221,821 patients with Sjogren's syndrome (188,581 or 85% females; 33,279 or 15% males) were found in general population.A total of 1,637 patients have KS identified by 47, XXY karyotype and 2,467 patients have triple X syndrome identified by karyotype 47,XXX. A total of 10 patients with KS were found to have SjS and 13 patients with triple X syndrome have SjS. Prevalence of SjS in general population is 0.18% (0.16% in females; 0.027% in males). There is a 22.6-fold increase in SjS in KS when compared with male patients in the general populations; and a 3-fold increase in SjS in patients with Triple X syndrome compared to females in the general population.

Conclusion: In this real-world, real-time study, extra X chromosome in Klinefelter syndrome and triple X syndrome have a non-proportional, synergistic dose effect on the risk of developing Sjogren's syndrome when compared with males and females in the general population, respectively.

Disclosure: A. Palmer: None; **I. Tan**: None.

Abstract Number: 1381

Fatigue and Associated Factors in Patients with Primary Sjogren's Syndrome Compared to Secondary Sjogren's Syndrome

Hyeji Jeon, Hyun-Sook Kim and Kyung-Ann Lee, Soonchunhyang University Seoul Hospital, Seoul, South Korea

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Fatigue is one of the dominant symptoms of patients with Primary Sjogren's syndrome (pSS). However, whether fatigue is specific to pSS compared to secondary SS (sSS) has not been investigated to date. The severity and risk factors that can affect fatigue may differ in groups between pSS and sSS. In this study, we aimed to evaluate the differences in subjective manifestations including fatigue, dryness, and pain between patients with pSS and sSS, and to determine the risk factors associated with fatigue.

Methods: This single-center, prospective study enrolled patients with pSS and sSS who met the 2016 American College of Rheumatology/European League Against Rheumatism (ACR/ EULAR) classification criteria and were aged ≥19 years. Patients were evaluated using questionnaire with Functional Assessment of Chronic Illness Therapy- Fatigue (FACIT-Fatigue) scale (Version 4), having thirteen items associated with fatigue evaluation with numeric scale of 0 to 4. Additionally, EULAR Sjogren Syndrome Patients Reported Index (ESSPRI), which have numerical scale from 0 to 10 for measurement of musculoskeletal pain, fatigue and dryness, were assessed. The following data were collected from all patients: disease duration, smoking history, autoantibodies, laboratory data, Schirmer's test, whole unstimulated salivary flow rate, focus score, salivary gland ultrasound, organ involvement, medication, and other comorbidities including fibromyalgia and hypothyroidism. A linear regression analysis was performed to determine the factors associated with fatigue.

Results: A total of 72 patients with pSS and 78 sSS patients were included in this study. Patients with pSS had significantly higher scores of FACIT-fatigue scales (7.95 vs 5.88, $p< 0.01$) and ESSPRI (5.56 vs 4.49, $p< 0.01$) compared to those with sSS. Among the thirteen questions of FACIT-fatigue scales, nine questions were proved to be significantly higher in patients with pSS while four (questionnaire number 5-8 related to physical activity) were not. Each score of ESSPRI was also higher in

pSS than sSS: fatigue (6.08 vs 5.10), pain (4.35 vs 3.32), dryness (6.24 vs 5.05) (all $p< 0.05$). In univariate regression analysis, only presence of arthritis (β=2.36, $p< 0.05$) was associated with the FACIT-Fatigue scale. Age, other clinical findings, laboratory findings, severity of glandular involvement, organ involvement, and medication were not associated with fatigue.

Conclusion: Our study confirmed patients with pSS manifest higher subjective discomfort with fatigue, pain, and dryness than those with sSS. Arthritis was an only risk factor associated fatigue in pSS patients, suggesting management of arthritis could improve fatigue.

Disclosure: H. Jeon: None; **H. Kim**: None; **K. Lee**: None.

Abstract Number: 1382

Efficacy of Tofacitinib Immunotherapy Suppresses Tfh and Tph Cells in Patients with Primary Sjögren's Syndrome

Qinghong Liu[1] and Jing He[2], [1]Peking University People's Hospital, Beijing, China, [2]Peking University People's Hospital, Beijing, China

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Primary Sjögren's syndrome (pSS) is an autoimmune disease characterized by systemic involvement and lacks effective treatment options. The Janus kinase (JAK) pathway plays a pivotal role in cytokine signaling pathways that contribute to the pathogenesis of SS. This study aims to investigate the underlying mechanisms and therapeutic efficacy of the JAK inhibitor, tofacitinib, in primary Sjögren's syndrome.

Methods: We enrolled 10 patients with active pSS and administered oral tofacitinib, assessing disease activity scores, laboratory parameters, and immune cell subsets. Additionally, NOD mice were treated with either tofacitinib or vehicle, and we evaluate saliva flow rates, immune cell subsets, and submandibular gland (SMG) pathology.

Results: Following tofacitinib treatment, a significant decrease in ESSDAI scores was observed at the 6th compared to baseline (9(6, 11.25) vs 4(1, 6), (p=0.002)).Additionally, at 6 months, 80% of patients achieved MCII of ESSPRI, which was defined as an improvement of ESSPRI at least one point or 15%.Notably, arthritis exhibited significant improvement at the 6th month compared to baseline (p=0.020). No serious adverse events were observed. In tofacitinib-treated mice, the results demonstrated a significant increase in saliva production compared to the control group from weeks 8 to 14 (4.20(3.29, 4.41)mg/min vs 5.74(4.44,6.15)mg/min, p=0.033), and SMGs exhibited fewer lymphocytic infiltrations and foci under a photomicroscope. Finally, immunological analysis revealed that both NOD mice and pSS patients exhibited a decrease in effector follicular helper T (Tfh) cells and peripheral helper T cells (Tph cells), which correlated positively with the level of pSTAT-3 in CD4+ T cells and disease activity scores.

Conclusion: Our findings demonstrate that the dosage of 5 mg tofacitinib twice a day proven to be effective and safe for the management of pSS. Tofacitinib inhibits the progression of pSS in both murine models and patients, potentially through the regulation of T cell differentiation.

Disclosure: Q. Liu: None; **J. He**: None.

Abstract Number: 1383

Long-term Association Between Physical Activity and Global Functioning in Patients with axSpA: Results of a 2 Year Prospective Study

Kwi Young Kang[1] and Hyoun-Ah Kim[2], [1]Catholic University of Korea, Seoul, South Korea, [2]Ajou University School of Medicine, Suwon, South Korea

SESSION INFORMATION

Session Date: Monday, November 13, 2023

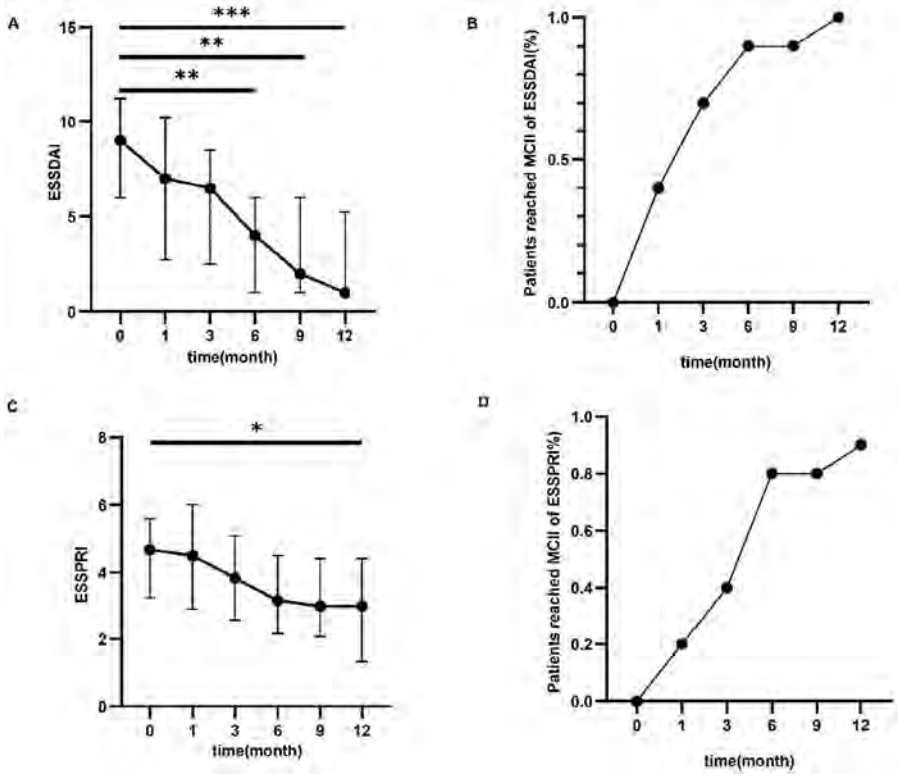
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS

Session Type: Poster Session B

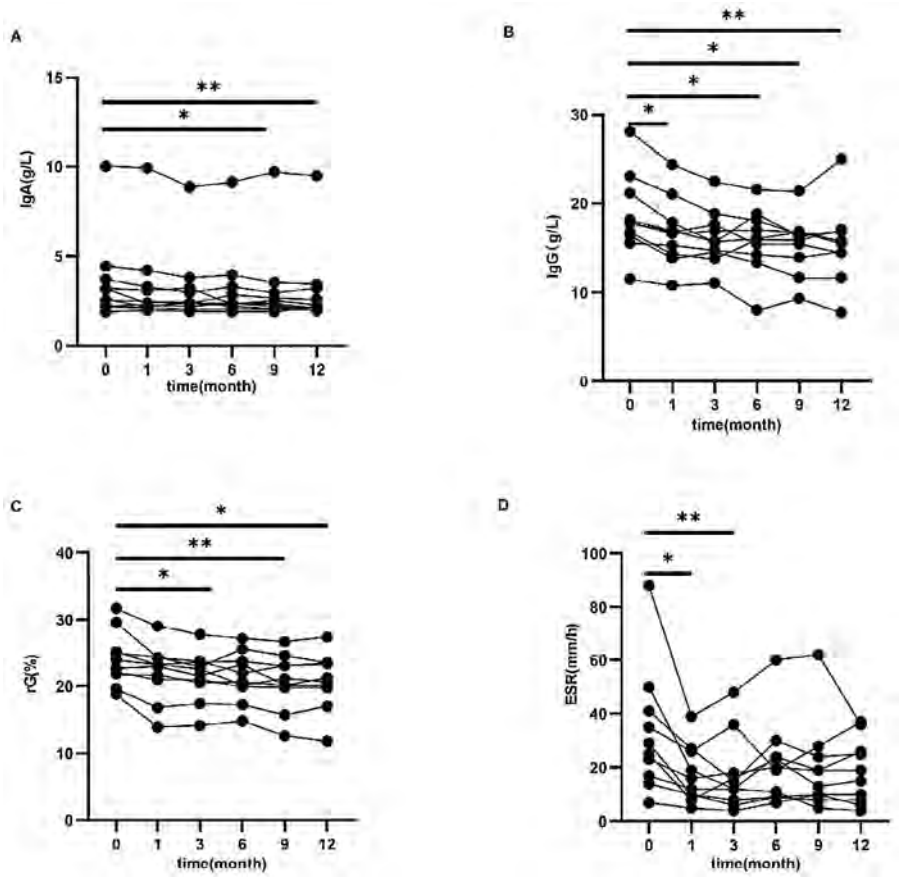
Session Time: 9:00AM–11:00AM

Background/Purpose: To assess the longitudinal association between physical activity and global functioning in patients with axial spondyloarthritis (axSpA) and to identify the subtype of physical activity that is longitudinally related to global functioning.

Methods: Data from 160 patients enrolled in the Incheon Saint Mary's axSpA prospective observational cohort were evaluated. Physical activity was measured using the Global Physical Activity Questionnaire. Global functioning was assessed using the ASAS health index (HI). The amount and subtype of physical activity, disease activity, and ASAS HI were assessed at baseline, and at the 1 year and 2 year follow-ups. Levels of physical activity were categorized as low, moderate, or high. The longitudinal association between physical activity and ASAS HI scores was analyzed using a generalized estimating equation.



Clinical response to tofacitinib treatment. Changes of ESSDAI (A) , ESSPRI (C) score of pSS patients after the treatment of tofacitinib. After 6 months of treatment, 90% patients achieved MCII of ESSDAI (B) and 80% patients achieved MCII of ESSPRI (D). ESSPRI, EULAR primary SS Patient Reported IndESSDAex; ESSDAI, EULAR primary SS Disease Activity Index. (*P<0.05; **p<0.01; ***p<0.001.)



Longitudinal follow-up of laboratory values during the trial. (A) A decrease in the IgA level was observed at the 9th and 12th month compared with that at baseline (p=0.028 and p=0.004, respectively); (B) A decrease in the IgG level was observed at the 1st, 6th, 9th and 12th month compared with that at baseline (p=0.011, p=0.015, p=0.023 and p=0.008, respectively). (C) A decrease in γG level was observed at the 3rd, 9th and 12th month compared with that at baseline (p=0.018,p=0.008 and p=0.013, respectively). (D) A decrease in the ESR level was observed at the 1st, 3rd month compared with that at baseline (p=0.004, p=0.004); (*P<0.05; **p<0.01; ***p<0.001.)

Results: Univariate analysis identified physical activity exceeding moderate levels, disease activity status, and syndesmophyte number as being longitudinally associated with ASAS HI over 2 years. Multivariate analysis identified physical activity exceeding moderate levels as being longitudinal association with ASAS HI (β (95% confidence interval) = -0.244 (-0.423 – -0.065)). Physical activity above moderate levels was associated independently with good global functioning (ASAS HI ≤5). Subgroup analysis revealed a positive association between physical activity and global functioning, which was consistent for both radiographic axSpA and nonradiographic axSpA. Only recreational activity, but not work- and transport-related activity, showed an independent longitudinal relationship with the ASAS HI score.

Conclusion: Physical activity exceeding moderate levels was associated independently with global functioning in axSpA; thus, patients should maintain physical activity above moderate levels to preserve global function.

Disclosure: K. Kang: None; **H. Kim**: None.

Abstract Number: 1384

Functional Status by Sex and Socioeconomic Status in Axial Spondyloarthritis

Rachael Stovall[1], Jing Li[1], zara izadi[1], Lianne Gensler[2], Gabriela Schmajuk[3] and Jinoos Yazdany[4], [1]University of California San Francisco, San Francisco, CA, [2]University of California San Francisco, Department of Medicine, Division of Rheumatology, San Francisco, CA, [3]UCSF / SFVA, San Francisco, CA, [4]University of California, General Department of Medicine, Division of Rheumatology, San Francisco, CA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Women with axial spondyloarthritis (axSpA) tend to have worse patient reported outcomes compared to men. Non-U.S. studies have evaluated functional status (FS) by sex in axSpA, but data are inconsistent. Studies in other rheumatic diseases suggest that lower socioeconomic status (SES) is correlated with worse FS. Yet little is known about the effect of SES in axSpA. We evaluated FS by sex and SES in the U.S. using the Rheumatology Informatics System for Effectiveness (RISE) registry.

Methods: Data were derived from RISE, a large, national electronic health record-based registry from 2016-2022. Patients ages 18+ with ≥2 visits for axSpA or ankylosing spondylitis (AS) with a rheumatologist, ≥ 30 days apart and ≥1 FS measure (Multi-Dimensional Health Assessment Questionnaire or MDHAQ) were included. RAPID3 (of which MDHAQ is a

Table 1. Baseline characteristics and the primary outcome for the cross-sectional analysis: GEE models clustered by rheumatology practice for functional status as measured by the MDHAQ among individuals with axial spondyloarthritis in the RISE Registry.

	N = 5,658 (%)	Coefficients (95% CI)*
Age Mean (SD)	53.8 (15.2)	0.04 (0.001-0.08) per 10 years
Female sex	3155 (55.8)	0.36 (0.23-0.49)
Race and ethnicity		
White	4041 (71.4)	1.0 (ref)
African American	252 (4.5)	0.13 (-0.15-0.41)
Asian	222 (3.9)	-0.21 (-0.41-0.0003)
Hispanic	128 (2.3)	0.35 (0.06-0.64)
Other/mixed	34 (0.6)	-0.16 (-0.89-0.57)
Unknown	981 (17.3)	0.04 (-0.12-0.20)
ADI quintile		
1 (highest SES)	1128 (19.9)	1.0 (ref)
2	1132 (20.0)	0.23 (-0.004-0.46)
3	1138 (20.1)	0.25 (0.05-0.45)
4	1116 (19.7)	0.43 (0.17-0.70)
5 (lowest SES)	1144 (20.2)	0.58 (0.33-0.84)
Smoking status		
Ever smoker	1747 (30.9)	1.0 (ref)
Never smoker	3709 (65.6)	-0.17 (-0.30- -0.04)
Unknown	202 (3.6)	0.009 (-0.27-0.29)
ts/bDMARD use during the study period	4139 (73.2)	0.07 (-0.04-0.18)

Values are expressed as N (%) unless otherwise indicated. MDHAQ: Multi-Dimensional Health Assessment Questionnaire; RISE: Rheumatology Informatics System for Effectiveness; ADI: area deprivation index; ts/bDMARDs: targeted synthetic or biologic disease-modifying anti-rheumatic drugs.
* Adjusted for age, sex, race, ethnicity, smoking status, and targeted synthetic or biologic DMARD use.

component) has been validated in AS. Patients with HIV or cancer were excluded. Area deprivation index (ADI), a zip code-based measure for neighborhood poverty, was used as a proxy for SES. We performed cross-sectional and longitudinal analyses using GEE models in which patients were clustered within rheumatology practices, and adjusting for age, sex, race, ethnicity, ADI quintile, smoking status (ever/never), and targeted synthetic or biologic DMARD (ts/bDMARD) use (yes/no during the study period). In the cross-sectional analysis, the outcome was the most recent MDHAQ score (0-10 scale) during 2019-2022. We tested for a linear trend across ADI quintiles for MDHAQ, with and without interaction for sex. In the longitudinal analysis, the outcome was functional decline (yes/no) defined as a >1.2 point difference in MDHAQ at 2 time points (most recent MDHAQ minus the next most recent MDHAQ ≥12 months prior), adjusted for baseline MDHAQ. We reported predictive margins in both analyses.

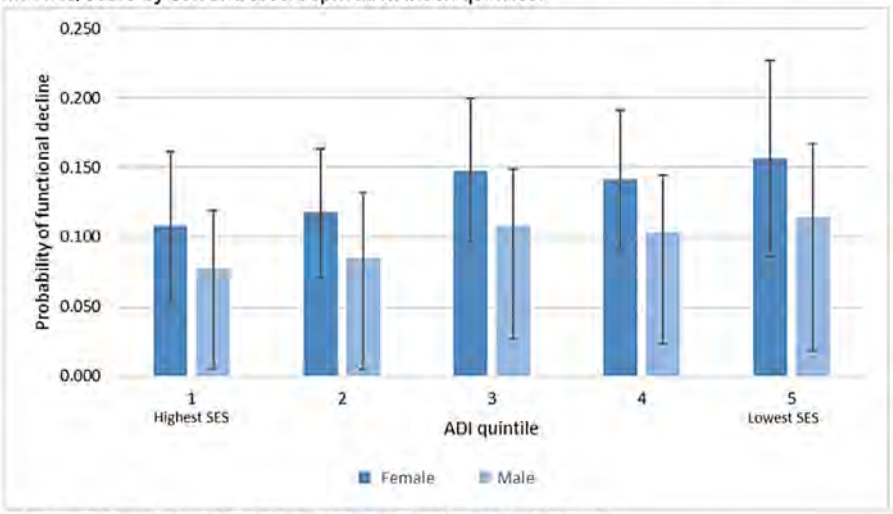
Results: We identified 5,658 adults with axSpA for the cross-sectional analysis and 2,357 were included in the longitudinal cohort. The mean (SD) age was 53.8 years (15.2), 55.8% were female, and 71.4% were non-Hispanic White (**Table 1**). The mean (SD) MDHAQ score for women and men were 2.1 (2.2) and 1.6 (2.0), respectively. There was no evidence of an

Table 2. Predictive margins on ADI quintiles by most recent MDHAQ (cross-sectional) and change in MDHAQ (longitudinal) during the study period.

	Cross-sectional analysis, N = 5,658		Longitudinal analysis, N = 2,357	
	Un-adjusted	Adjusted GEE model*	Un-adjusted	Adjusted GEE model**
ADI quintile	Mean MDHAQ score (95% CI)	Predicted Mean (95% CI)	Proportion of patients with declines in MDHAQ score (95% CI)	Predicted Proportion (95% CI)
1st ADI quintile (highest SES)	1.5 (1.4-1.6)	1.7 (1.4-2.1)	10.2 (7.7-13.2)	10.2 (6.0-14.3)
2nd ADI quintile	1.8 (1.7-2.0)	2.0 (1.6-2.4)	11.7 (9.0-14.8)	11.6 (6.4-16.8)
3rd ADI quintile	1.7 (1.5-1.8)	2.0 (1.6-2.4)	12.8 (9.8-16.3)	13.9 (8.8-19.1)
4th ADI quintile	2.1 (2.0-2.2)	2.2 (1.8-2.6)	14.8 (11.7-18.3)	14.0 (8.4-19.6)
5th ADI quintile (lowest SES)	2.2 (2.0-2.3)	2.3 (1.9-2.7)	15.3 (12.1-19.0)	15.5 (8.8-22.2)

ADI: area deprivation index; MDHAQ: Multi-Dimensional Health Assessment Questionnaire; SES: socioeconomic status.
* Adjusted for age, sex, race, ethnicity, smoking status, and targeted synthetic or biologic DMARD use.
**Longitudinal model additionally adjusted for baseline MDHAQ score.

Figure. Primary outcome for the longitudinal analysis: predicted proportion of decline in MDHAQ score by sex and area deprivation index quintiles.



MDHAQ: Multi-Dimensional Health Assessment Questionnaire; ADI: area deprivation index.

Disclaimer: Data collection was supported by the ACR's RISE Registry. The views expressed represent those of the authors, not necessarily those of ACR.

interaction between sex and SES on FS; instead, women had consistently lower FS than men across all ADI quintiles (**Figure**). In the cross-sectional analysis, the predicted mean MDHAQ score was 2.3 (95% CI 1.9-2.7) for the 5th ADI quintile (lowest SES) compared to 1.7 (95% CI 1.4-2.1) for the 1st ADI quintile (highest SES; **Table 2**). In the longitudinal analysis, the predicted proportion of patients with FS decline were 15.5 (95% CI 8.8-22.2) in the 5th ADI quintile compared to 10.2 (95% CI 6.0-14.3) in the 1st ADI quintile. In the longitudinal analysis, women had 1.65 (95% CI 1.3-2.14) times higher odds of functional decline compared to men.

Conclusion: In this large U.S. sample of adults with axSpA, women had worse FS than men, at baseline and over time, and FS was worse in both sexes with lower SES. Women and individuals with low SES should be prioritized for interventions to reduce FS decline and disability in AS. Future work should assess the mechanisms of SES and sex-based FS differences.

Disclosure: R. Stovall: None; **J. Li**: None; **z. izadi**: Bristol-Myers Squibb(BMS), 3; **L. Gensler**: AbbVie, 2, Acelyrin, 2, Eli Lilly, 2, Fresenius Kabi, 2, Janssen, 2, Novartis, 2, 5, Pfizer, 2, UCB Pharma, 2, 5; **G. Schmajuk**: None; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, Gilead, 5, Pfizer, 2.

Abstract Number: 1385

Where Are We with Implementing Axial Spondyloarthritis Treatment Recommendations and Disease Activity Monitoring in Clinical Practice - Results of an Online Survey Amongst Rheumatology Care Providers

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Several sets of treatment recommendations for axial spondyloarthritis and ankylosing spondylitis (axSpA/AS) have been published. Clinical practice guidelines are not followed consistently by health care providers. Five groups of factors are thought to contribute to poor adherence: guideline, practice setting, patient, health professional and societal factors. To better understand potential barriers to the implementation of treatment guidelines in axSpA/AS, we performed an online survey amongst rheumatology care providers.

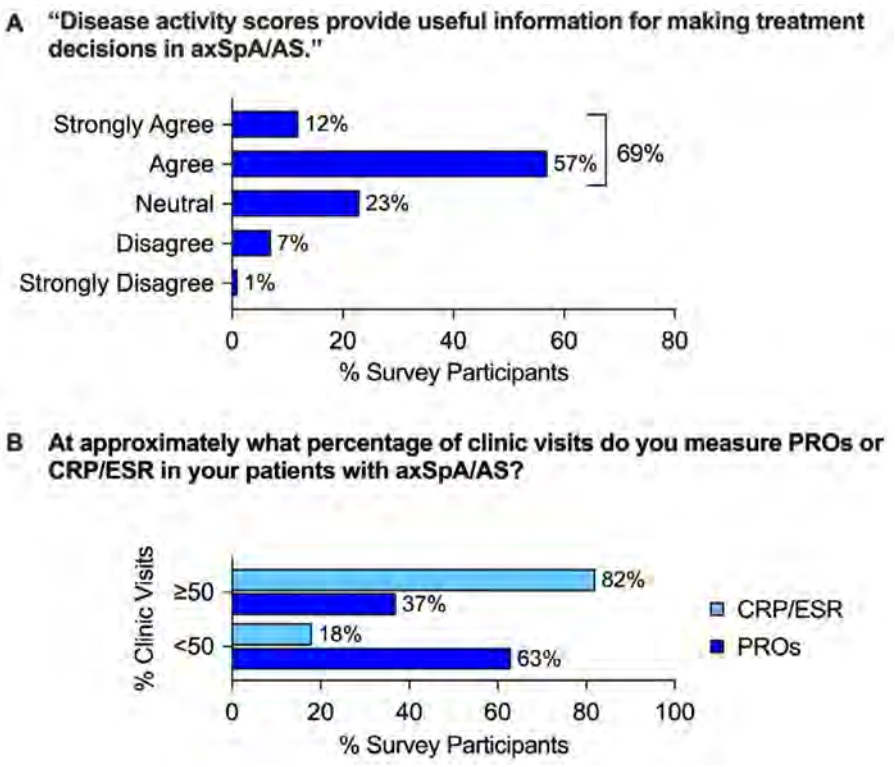
Methods: Based on the results of a focus group, a survey was developed with 20 questions and an estimated completion time of 5-7 minutes. The survey was distributed via email to 441 rheumatology care providers in the New England States (CT, MA, ME, NH, RI, VT) in January 2023. Anonymized data were collected in REDCap.

Results: 104/441 (24%) health professionals participated including 80/104 (77%) board-certified rheumatologist and 20/104 (19%) fellows. 73/104 (70%) participants work in academic medical centers while 27/104 (26%) work in either hospital-based, group or solo practices.

Table 1. Characteristics of respondents (N=104).

Demographics	**n (%)**
Male	50 (48)
Training Level	
Board-certified Rheumatologist	80 (77)
Rheumatology Fellow	20 (19)
Physician Assistant or Nurse Practitioner	3 (3)
Other	1 (1)
Practice Setting	
Academic Medical Center	73 (70)
Hospital-based practice	14 (13)
Group practice	11 (11)
Retired	3 (3)
Solo practice	2 (2)
Other	1 (1)
Number of axSpA/AS patients seen per week	
< 5	65 (63)
5 to 10	33 (32)
> 10	6 (6)
Years Since Rheumatology Board Certification N=80	
1-10 years	34 (43)
11-30 years	23 (29)
31 or more years	23 (29)

Characteristics of survey respondents (N=104).

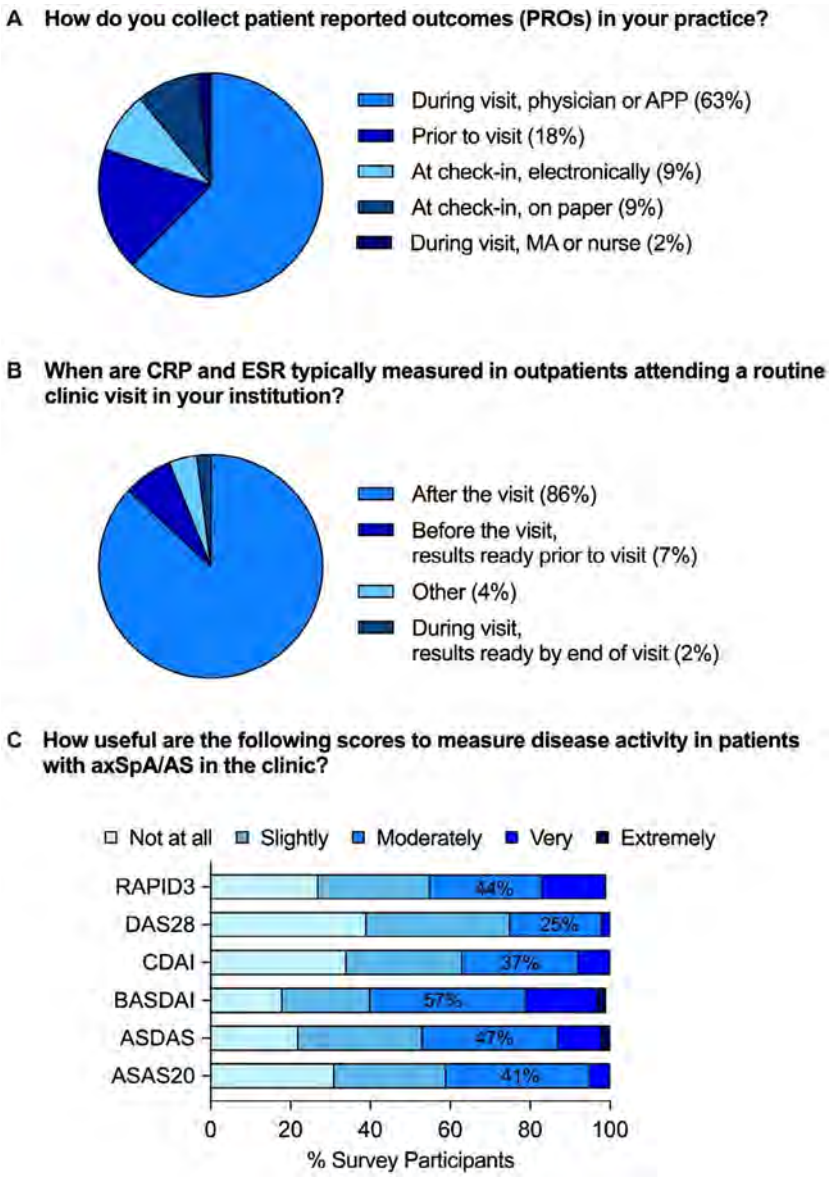


Discrepancy between agreement with the utility of using axSpA/AS disease activity scores and clinical practice.

Survey participants identified UptoDate (85%), treatment guidelines (74%) and colleagues (54%) as relevant sources of knowledge for managing axSpA/AS patients. 64% and 53% of participants considered themselves to be at least moderately familiar with the ACR/SAA/SPARTAN and the ASAS/EULAR recommendations, respectively.

The ACR/SAA/SPARTAN guidelines recommend regular-interval use and monitoring of a validated AS disease activity measure and monitoring of CRP/ESR. While 69% of survey participants agreed or strongly agreed that "disease activity scores provide useful information for making treatment decisions in axSpA/AS", only 38% measure patient-reported outcomes (PROs) frequently (in 50% of clinic visits or more) while 82% measure CRP/ESR frequently. PROs are typically recorded during clinic encounters (63%) while CRP/ESR are obtained after the clinic encounter (86%).

When asked about the utility of specific scores to measure disease activity in patients with axSpA/AS, BASDAI and ASDAS were considered to be at least moderately useful by 57% and 47% of participants, respectively, while 41% thought the same about the ASAS20. BASDAI and ASDAS were considered to very or extremely useful by 20% and 13%, respectively.



Potential barriers to measuring axSpA/AS disease activity in clinical practice.

Conclusion: Treatment guidelines are an important source of knowledge for rheumatologists when managing patients with axSpA/AS. Although there is general agreement that disease activity monitoring is important, implementation of the respective guideline recommendations is lacking. Potential reasons may include lack of familiarity and an underdeveloped infrastructure to efficiently collect PROs prior to clinic visits. Guideline uptake and implementation should be considered in future updates of axSpA/AS treatment recommendations.

Disclosure: J. Ermann: AbbVie, 2, 5, Boehringer Ingelheim, 5, Janssen, 2, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, UCB Pharma, 2; **S. Sinnappan**: None; **A. Forte**: None.

Abstract Number: 1386

Opioid Prescription Rates in Patients with Ankylosing Spondylitis in the UK Between 2001-2020: An Electronic Health Records (EHR) Analysis

Huseyin Berk Degirmenci[1], Christine E. Peloquin[2], Sara Lodi[2], Pedro Machado[3], S. Reza Jafarzadeh[4], Tuhina Neogi[5], Lianne Gensler[6], Maureen Dubreuil[7] and Jean Liew[2], [1]St. Elizabeth's Medical Center, Boston, MA, [2]Boston University, Boston, MA, [3]Centre for Rheumatology & Department of Neuromuscular Diseases, University College London, London, UK. Department of Rheumatology, Northwick Park Hospital, London North West University Healthcare NHS trust, London, UK., London, United Kingdom, [4]Boston University Chobanian & Avedisian School of Medicine, Boston, MA, [5]Boston University School of Medicine, Boston, MA, [6]University of California San Francisco, Department of Medicine, Division of Rheumatology, San Francisco, CA, [7]Department of Rheumatology, Boston University School of Medicine, Milton, MA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS

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Session Time: 9:00AM–11:00AM

Background/Purpose: Although current axial spondyloarthritis (axSpA) management guidelines do not address opioid use for chronic pain, available data show that opioid use is common among this population despite widespread uptake of effective biologic therapies, including TNF inhibitors and IL-17 inhibitors. We examined temporal trends in opioid prescription for individuals with ankylosing spondylitis (AS) in the United Kingdom (UK) before and after effective immunomodulatory agents have become available in the mid-2000s.

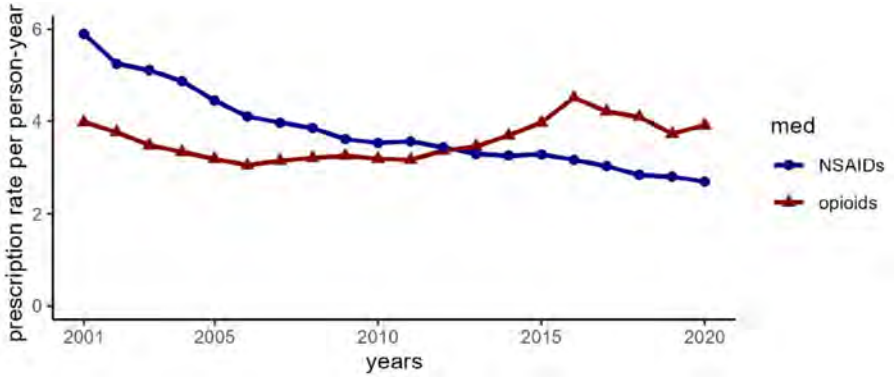

FIGURE Annual prescription rates of opioids and NSAIDs among people with ankylosing spondylitis in the IQVIA Medical Research Database 2001-2020

Methods: We used the IQVIA Medical Research Database (IMRD), incorporating data from THIN, a Cegedim database, an electronic health record database collected by general practitioners throughout the UK. We included adults aged 18-89 from 2000-2020 with AS, defined by ≥2 diagnostic Read codes (coded thesaurus of clinical terms used in the National Health Service since 1985) ≥7 days apart, and ≥1 year data prior to AS diagnosis. Baseline was defined as the date of the second AS diagnosis code. We excluded individuals with ≥2 rheumatoid arthritis Read codes prior to baseline. Individuals were followed until censoring at the date of codes for hospice or palliative care services, death, or end of the study (12/2020). Clinical characteristics included age, gender, baseline treatments for AS (defined within 1 year prior to the index date), and the presence of specific comorbidities (defined using Read codes any time prior to the index date). We calculated annual prescription rates from 2001-2020 for opioids and NSAIDs (comparator drug), as the number of prescriptions in a calendar year divided by person-time contributed by enrolled subjects meeting inclusion criteria for the year. Biologic prescription rates were not adequately captured in this general practitioner-entered database and thus not reported.

Results: We identified 2094 individuals with incident AS (mean age 47 years, 74.6% male, median follow-up time of 6.2 years with interquartile range 2.8-10.6 years). Of these, 395 (18.9%) had history of hypertension, 128 (6.1%) had history of cardiovascular disease, 72 (3.4%) had chronic kidney disease, and 70 (3.3%) had history of cancer. Baseline conventional synthetic DMARD use was present in 10.9% and glucocorticoid use in 10.4%. Opioid prescription rates were relatively unchanged over time with a range of 3.04-4.51 prescriptions per person-year (PY) from 2001-2020 whereas NSAID rates declined over time from 5.90 prescriptions per PY in 2001 to 2.69 per PY in 2020 (**Figure**).

Conclusion: In this UK-based AS cohort, opioid prescription rates remained relatively stable between 2001-2020 whereas NSAID use decreased over time consonant with the uptake of effective biologic therapies. Further, the rates of opioid prescriptions were similar in range to that of NSAID prescriptions. These findings may indicate inadequate pain control in AS despite the introduction and uptake of effective biologic agents.

Disclosure: H. Degirmenci: None; **C. Peloquin**: None; **S. Lodi**: None; **P. Machado**: AbbVie/Abbott, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Orphazyme, 2, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 6; **S. Jafarzadeh**: None; **T. Neogi**: None; **L. Gensler**: AbbVie, 2, Acelyrin, 2, Eli Lilly, 2, Fresenius Kabi, 2, Janssen, 2, Novartis, 2, 5, Pfizer, 2, UCB Pharma, 2, 5; **M. Dubreuil**: Amgen, 2, Pfizer, 5, UCB Pharma, 2; **J. Liew**: None.

Abstract Number: 1387

Power Doppler Musculoskeletal Abnormalities in Patients with Psoriasis at High Risk of Progression to Psoriatic Arthritis

Rebecca Haberman[1], Sarah Moussavi[1], Yan Zhang[1], Sydney Catron[1], Jonathan Samuels[2], Rebecca Blank[3], Michael Toprover[4], Jiyuan Hu[1], Cinty Gong[5], Vincent Piguet[6], Francisco Tausk[7], Jensen Yeung[8], Andrea Neimann[1], Wayne Gulliver[9], Joseph Merola[10], Alexis R Ogdie[11], Proton Rahman[12], Soumya Chakravarty[13], Ralf Thiele[14], Lihi Eder[15], Christopher T Ritchlin[16] and Jose Scher[17], [1]NYU Grossman School of Medicine, New York, NY, [2]NYU Langone, Rye Brook, NY, [3]New York University, New York, NY, [4]New York University Langone Health, New York, NY, [5]Immunology, Janssen Scientific Affairs, LLC, Horsham, PA, USA, Raritan, NJ, [6]Women's College Hospital, Toronto, ON, Canada, [7]University of Rochester Medical Center, Rochester, NY, [8]University of Toronto and Women's College Hospital, Toronto, ON, Canada, [9]Memorial University of Newfoundland, St. John's, NL, Canada, [10]Harvard Medical School, Brigham and Women's Hospital, Newton, MA, [11]University of Pennsylvania, Philadelphia, PA, [12]Craig Dobbin Research Institute, Memorial University, St. John's, NL, Canada, [13]Immunology, Janssen Scientific Affairs, LLC / Division of Rheumatology, Drexel University College of Medicine, Villanova, PA, [14]University of Rochester, Pittsford, NY, [15]Women's College Research Institute, Division of Rheumatology, University of Toronto, Toronto, ON, Canada, [16]University of Rochester Medical School, Allergy, Immunology & Rheumatology Division, Canandaigua, NY, [17]New York University School of Medicine, New York, NY

SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is an immune-mediated disease associated with skin psoriasis that, if untreated, can lead to joint destruction. Up to 30% of patients with psoriasis progress to PsA and, in most cases, psoriasis precedes synovio-entheseal inflammation, providing a unique opportunity for early and potentially preventive intervention in a susceptible and readily identifiable population. The ongoing Preventing Arthritis in a Multicenter Psoriasis At Risk cohort (PAMPA) study (NCT05004727) aims to evaluate the efficacy of the fully human IL-23p19-subunit inhibitor guselkumab in preventing PsA and reducing musculoskeletal ultrasound (US) abnormalities in a population of patients with psoriasis at increased risk of PsA progression (Figure 1). Interim findings from screening US evaluations to date are reported.

Methods: Patients were screened across 5 sites in the US and Canada. PAMPA inclusion required ≥ 3% body surface area (BSA) affected by psoriasis, no current systemic immunosuppressant therapy at time of screening or prior exposure to biologic/JAK inhibitor, and evidence of musculoskeletal abnormalities on US. The US scanned a set of 36 joints and 34 periarticular structures (including tendons and entheses), each scored by 2 independent central readers using the Rochester Modified (RM)-PsASon scoring system (range 0-614). Participants required a mean score of ≥ 3.36 to enroll (the maximized Youden's index based on previous analysis of scores in healthy controls and patients with psoriasis).

Results: Among the 49 participants screened to date, 42 met US criteria. The screened population was mostly male (57.1%), white (83.7%), with an average age of 49.2 (SD 14.3) and a body mass index (BMI) of 30.6 (SD 8.6). Participants had mostly plaque psoriasis (95.1%) at the time of enrollment with a mean BSA of 10.4% (SD 11.9). The mean total US score was 13.55 (SD 10.5, range 1-50), composed of inflammatory and structural subscores (Figure 2A-B). The intraclass correlation coefficient (ICC) assessing reader agreement was 0.89 (95% CI 0.80-0.94) and ICCs on joints, tendons, and entheses were all greater than 0.75 indicating excellent reliability (Figure 2C-F). US scores correlated with increasing age ($r = 0.55$, $p = < 0.001$), but did not correlate with BMI, BSA, FACIT-Fatigue score, patient reported pain intensity, or sex (Figure 3).

Conclusion: In a biologic-naïve cohort of patients with psoriasis at increased risk for PsA progression, 85.7% of those with US evaluation exceeded a score of 3.36, a previously identified threshold to distinguish those with psoriasis from healthy controls. The interrater reliability of the US scoring was excellent. US scores were moderately correlated with increasing age, but not with other demographic or disease activity measures, and the biological meaning of this finding is unclear. While

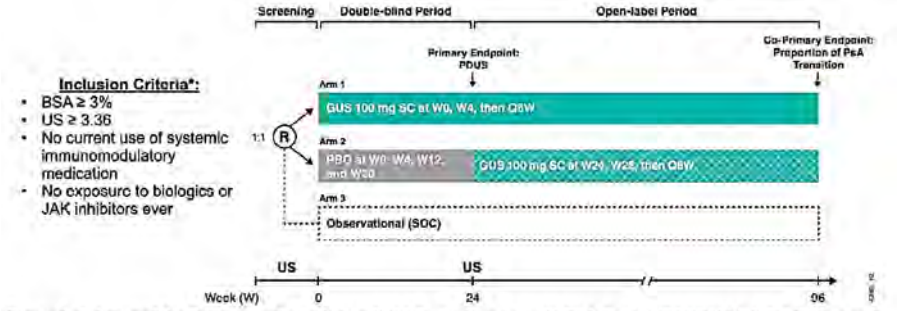

Figure 1. Schema of the Preventing Arthritis in a Multi-Center Psoriasis At-Risk Cohort (PAMPA) trial. PAMPA is a multicenter, randomized, double-blind, placebo-controlled, wait-list, interventional, preventive trial of guselkumab in high-risk psoriasis patients compared to non-biologic standard of care. Participants are eligible if they have a percent body surface area covered by psoriasis (BSA) of at least 3% and a targeted musculoskeletal ultrasound (US) score of at least 3.36. For participants opting for intervention (Arms 1+2), they are randomized (1:1) into drug or placebo for 24 weeks. At 24 weeks, they undergo repeat US and all participants receive active drug for the remainder of the study. For participants who do not want to be on systemic therapy but meet all inclusion criteria, they are enrolled into the observational arm (Arm 3) and are followed every 6 months, also undergoing repeat US at month 6. The primary endpoints are: (1) change in US score at 6 months (Arm 1 vs. Arm 2+3) and (2) proportion of participants transitioning to PsA at 96 weeks (Arm 1+2 vs. Arm 3). *Figure presented previously at CCR-West 2022, San Diego, Ca.*

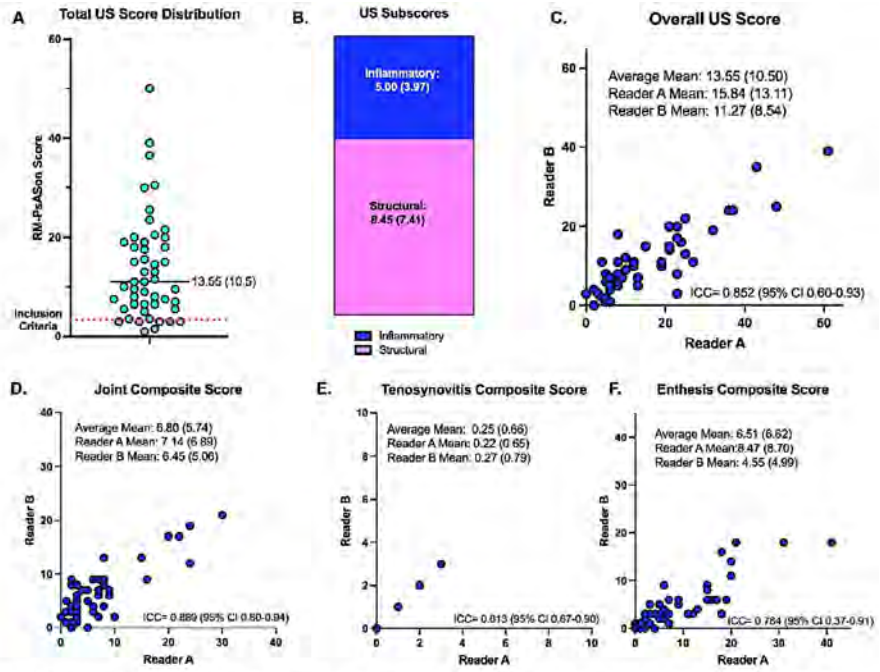

Figure 2. Musculoskeletal Ultrasound (US) Scores. (A) Distribution of the total US scores (an average of the 2 readers, n=49). Pink dashed line indicates the study inclusion threshold of 3.36. Solid black line represents the mean. (B) Total score broken down into inflammatory and structural subscores. Inflammatory subscore includes: joint synovial hypertrophy, joint intra-articular power Doppler, tenosynovitis (gray scale), tenosynovitis (power Doppler), enthesis power doppler, enthesis bursitis, enthesis structure/hypoechogenicity, enthesis thickness, and peritendonitis (gray scale and power Doppler). Structural includes: joint erosions, joint osteophytes, enthesis erosions, and enthesis calcifications. (C) Intraclass correlation coefficient (ICC) between Reader A and Reader B for total US score. Total RM-PsASon score ranges from 0-614. (D-F) ICC between readers for joint composite score, tenosynovitis composite score, and enthesis composite score. Peritendonitis composite score not shown as all scores were 0.

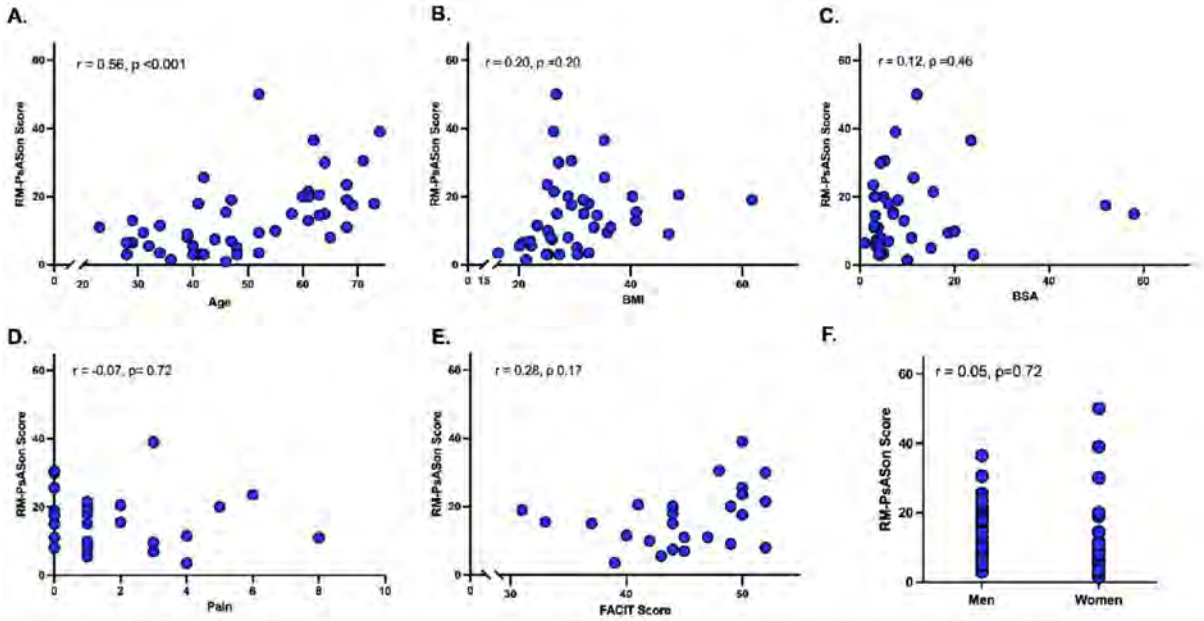

Figure 3. Correlation between total ultrasound score and age (A), body mass index (BMI, B), percent body surface area affected by psoriasis (BSA, C), pain numeric rating scale (D), FACIT Score (measuring fatigue, E) and sex (F). Pain score of 0 indicating no pain and 10 worst pain imaginable. Higher FACIT score indicated higher levels of fatigue. All continuous correlations calculated using Pearson's coefficient. Sex correlation calculated using point biserial correlation.

the ongoing PAMPA study is actively recruiting for a planned enrollment of 350 participants, these preliminary findings suggest that appropriate patients are being enrolled. These data also underscore the need to better characterize clinical and imaging phenotypes of high-risk patients with psoriasis for subclinical soft tissue/structural changes that may foreshadow transition to PsA.

Disclosure: R. Haberman: Janssen, 1, 5, UCB, 1; **S. Moussavi**: None; **Y. Zhang**: None; **S. Catron**: None; **J. Samuels**: None; **R. Blank**: None; **M. Toprover**: ANI Pharmaceuticals, 2, Horizon Therapeutics, 5; **J. Hu**: None; **C. Gong**: Janssen Scientific Affairs, LLC, 3, Johnson & Johnson, 11; **V. Piguet**: AbbVie, 5, Bausch Health, 12, Educational grant paid to the University of Toronto in support of the Dermatology Residency Training Program, Celgene, 12, Educational grant paid to the University of Toronto in support of the Dermatology Residency Training Program, Eli Lilly, 12, Educational grant paid to the University of Toronto in support of the Dermatology Fellowship Program, Incyte, 12, Educational grant paid to the University of Toronto in support of the Dermatology Residency Training Program, Janssen, 12, Educational grant paid to the University of Toronto in support of the Dermatology Residency Training Program, L'Oréal, 12, Equipment donation and educational grant paid to the University of Toronto in support of the Dermatology Residency Training Program, LEO Pharma, 1, 12, Educational grant paid to the University of Toronto in support of the Dermatology Residency Training Program, Novartis, 1, 5, 12, Research grant, educational grant paid to the University of Toronto in support of the Dermatology Residency Training Program, Organon, 12, Educational grant paid to the University of Toronto in support of the Dermatology Residency Training Program, Pfizer, 12, Educational grant paid to the University of Toronto in support of the Dermatology Residency Training Program, Sandoz, 12, Educational grant paid to the University of Toronto in support of the Dermatology Residency Training Program, Sanofi, 1, 5, 12, Research grant, educational grant paid to the University of Toronto in support of the Dermatology Residency Training Program, Union Therapeutics, 1; **F. Tausk**: None; **J. Yeung**: AbbVie/Abbott, 2, Amgen, 2, Anacor, 2, Astellas, 2, Bausche, 2, Baxalta, 2, Boehringer-Ingelheim, 2, Celgene, 2, Centocor, 2, Coherus, 2, Dermira, 2, Eli Lilly, 2, Forward, 2, Galderma, 2, Janssen, 2, Leo, 2, Medimmune, 2, Merck/MSD, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Roche, 2, Sanofi Genzyme, 2, Sun Pharma, 2, Takeda, 2, UCB, 2, Xenon, 2; **A. Neimann**: Sun Pharma, 1, UCB, 1; **W. Gulliver**: AbbVie/Abbott, 2, 5, 12, Clinical Trial Study Fees, Actelion, 2, Amgen, 2, 5, Asna Bioscience, 12, Clinical Trial Study Fees, Astellas, 12, Clinical Trial Study Fees, Bausch Health, 2, Boehringer-Ingelheim, 2, 12, Clinical Trial Study Fees, Celgene, 2, 12, Clinical Trial Study Fees, Cipher, 2, Devonian, 12, Clinical Trial Study Fees, Eli Lilly, 2, 5, 12, Clinical Trial Study Fees, Galapagos, 12, Clinical Trial Study Fees, Galderma, 2, 12, Clinical Trial Study Fees, Janssen, 2, 12, Clinical Trial Study Fees, LEO Pharma, 2, 12, Clinical Trial Study Fees, Merck/MSD, 2, Novartis, 2, 5, 12, Clinical Trial Study Fees, PeerVoice, 2, Pfizer, 2, 5, 12, Clinical Trial Study Fees, Regeneron, 12, Clinical Trial Study Fees, Sanofi-Genzyme, 2, Tribute, 2, UCB, 2, 12, Clinical Trial Study Fees, Valeant, 2; **J. Merola**: Abbvie, 2, 12, Investigator, Amgen, 2, 12, Investigator, Biogen, 2, 12, Investigator, Bristol-Myers Squibb, 2, 12, Investigator, Dermavant, 2, 12, Investigator, Eli Lilly, 2, 6, 12, Investigator, Janssen, 2, 12, Investigator, Leo Pharma, 2, 12, Investigator, Novartis, 2, 12, Investigator, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, 12, Investigator, Sun Pharma, 2, 12, Investigator, UCB Pharma, 2, 12, Investigator; **A. Ogdie**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, UCB, 2; **P. Rahman**: AbbVie, 2, Amgen, 2, Bristol Myers Squibb, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, UCB, 2; **S. Chakravarty**: Janssen Scientific Affairs, 3, Johnson & Johnson, 11; **R. Thiele**: Bioclinica, 2, Novartis, 2; **L. Eder**: AbbVie, 2, 5, Eli Lilly, 2, 5, Fresenius Kabi, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Sandoz, 5, UCB, 2, 5; **C. Ritchlin**: AbbVie, 2, 5, 6, Amgen, 2, BMS, 2, Eli Lilly, 2, Gilead, 2, Janssen, 2, Novartis, 2, Pfizer, 2, 5, 6, UCB, 2, 6; **J. Scher**: AbbVie, 2, Janssen, 2, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 2, UCB, 2.

Abstract Number: 1388

Pain Mechanisms in Psoriatic Arthritis: Differentiating Inflammation Related Pain in Enthesitis Using Ultrasound, in Comparison to Functional MRI

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Background/Purpose: Approximately 50% of PsA patients have persistent pain despite a well-controlled inflammatory state, which has been attributed to non-nociceptive pain and central sensitization. Enthesitis is a key domain in PsA. Unfortunately, physical examination of the entheses is challenging and lacks sensitivity and specificity. Ultrasound (US) is used to differentiate inflammatory enthesitis from widespread or non-specific pain syndromes, however whether "inflammatory enthesitis on US" corresponds to a different underlying pathogenic mechanism is yet to be tested. In this proof-of-concept study, we aimed to compare functional MRI (fMRI) features in response to entheseal pain stimuli in PsA, within patients with or without entheseal inflammation on US.

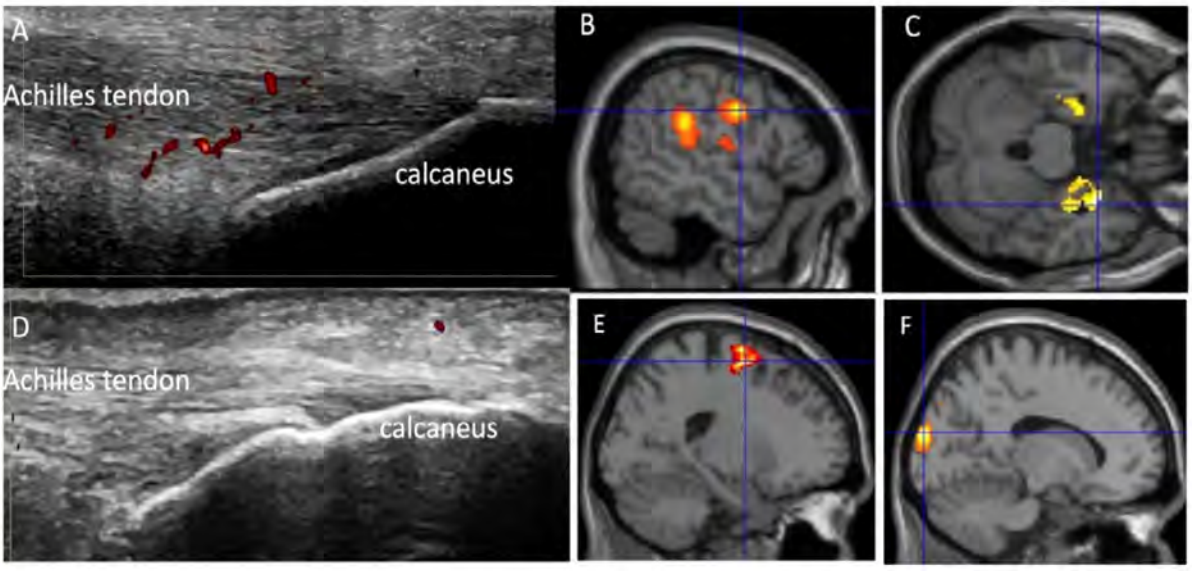

Figure: fMRI and Ultrasound Images in PsA patients with Achilles enthesitis
A-C: Patient with pain on the Achilles enthesis and Doppler positive on US (A). Functional MRI activity with induction of pain on the Achilles entheses: B) in left precentral and supramarginal brain regions C): Functional MRI activity in Amygdala, hippocampus and para hippocampus brain regions.
D-F: Patient with pain on the Achilles enthesis and Doppler negative on US (D). Functional MRI activity with induction of pain on the Achilles entheses : E) and F)

Methods: This study was conducted at the Arthritis Center at The Ottawa Hospital and the Brain Imaging Centre of the Royal Ottawa Mental Health Centre. We recruited two PsA groups; *Group-1:* With Achilles enthesitis on exam and positive US (hypoechogenicity and Doppler signals), *Group-2:* With or without Achilles tenderness on exam, but negative US. Patients had a fMRI with rest and after induction of pain by applying pressure on the Achilles with a blood pressure cuff. Whole brain, between group investigations included a two-sample t-test analysis (second level analyses) conducted at a set threshold of p= 0.05 corrected, with a cluster-wise correction at $p_{FWE} = 0.05$.

Results: Among 12 patients included to the study, five patients were in Group-1 and seven in Group-2. Nine patients were female and mean age was 50.6 (25.2). The mean (SD) TJC and SJC were lower in group-1 (TCJ: 1.80 (2.68), SJC: 1 (2.23)) then group-2 (TJC: 6.86 (8.15); 3 (4.9)). The SPARCC enthesitis score was also numerically lower in group-1 than group-2 (1.40 vs 2.14) Patients who were US (+) had more neural activity when processing pain than US (-) patients. With induction of pain, US (+) patients had significantly more activity in the orbitofrontal gyrus, anterior cingulate, left precentral gyrus, supramarginal gyrus, superior temporal gyrus, and left paracentral lobule than the US (-) group. These regions are related to movement, body representation, and pain. The US (+) patients did not show less activity than US (-) patients in any brain regions.

Conclusion: According to our preliminary results, patients who have pain and inflammatory enthesitis on US, process pain differently than the US negative patients, despite the induction of pain or discomfort on all groups. This pilot study confirms that the US can differentiate different pain mechanisms.

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Abstract Number: 1389

Low Spinal Radiographic Progression After a Mean of 15 Years of Follow-up in a Cohort of Patients with Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthritis (axSpA) is characterized by progressive structural damage on the sacroiliac joints and/or the spine. Conventional radiology allows to assess radiology through available scales such as the mSASSS (modified Stoke Ankylosing Spondylitis Spinal Score) in the spine. However, scarce is the data on long-term radiographic

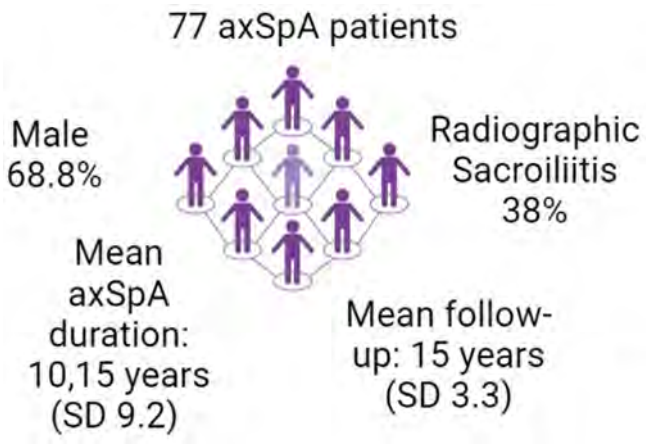

Figure 1. Baseline Characteristics.

Figure 2. Two readers radiographic lecture

progression and factors associated with such progression. The aim of this study was to evaluate the radiographic progression in the spine in patients with axSpA after a mean of 15 years of follow-up as well as the factors associated with such progression.

Methods: Patients with axSpA pertaining to the Reina Sofia University Hospital and included in the multicentre Spanish registry REGISPONSER between 2006-2007 were re-evaluated in 2021-2022. Spine (cervical and lumbar) radiographs were obtained with the aim to be compared with those obtained in 2007. Two trained blinded readers scored the mSASSS in radiographs from both visits (baseline and current). First, intraclass correlation coefficients (ICC) were obtained to evaluate the agreement between both readers in mSASSS. Mean mSASSS of both readers in both timepoints were calculated and the absolute progression (ΔmSASSS) was evaluated. In addition, it was evaluated the mean and median progression per year dividing the ΔmSASSS by the years of follow-up in each patient. Then, the median progression per year was used to divide patients in "low progressors" and "high progressors". Baseline characteristics between these two groups were compared using univariate analysis.

Results: A total of 77 axSpA patients with both baseline and current radiographs were included. A total of 53 (68.8%) were male and the mean disease duration was 10.15 (SD 9.2) years. All of them were naïve to bDMARD at baseline and 38% had radiographic sacroiliitis. The mean years of follow-up (i.e, mean time separating the radiographs) was 15 years (SD 3.3) (Figure 1). ICC between the two readers was moderate for mSASSS at baseline (0.73, 95%CI 0.26-0.88) and at the 15 years visit (0.65, 95%CI 0.11-0.84) (Figure 2). After a mean of 15y of follow-up, the mean progression was 0.54 (SD 0.55) points in mSASSS per year and the median progression was 0.38 points per year. A total of 37 (48%) patients were considered "low progressors" (i.e., median progression < 0.38 points per year) and 40 (52%) were considered as "high progressors"

Table 1. Baseline population characteristics observed by two readers

Baseline Variables		15 year progression according to mSASSS/year		
		Low progressors 37 (48%) (<0,38 points mSASSS/year)	High progressors 40 (52%) (≥0,38 points mSASSS/year)	P-value
Sex	Male	25 (67.6)	28 (70.0)	1.000
	Female	12 (32,4)	12 (30.0)	
Age at diagnosis (mean, SD)		31.1 (9.5)	34.7 (8.1)	0.08
Smoking		1 (2.7)	3 (7.5)	1.000
HLAB27 +		32 (86.5)	34 (85.0)	0.670
Inflamatory low back pain		18 (48.6)	33 (82.5)	**0.003**
Entesitis now or preview		10 (27.0)	8 (20.0)	0.600
Dactilitis now or preview		0 (0.0)	4 (10.0)	0.120
BASDAI median (SD)		4.38 (2.3)	4.3 (2.3)	0.890
BASFI median (SD)		3.8 (2.6)	3.6 (2.4)	0.630
High PCR (mg/L)		18 (48.6)	21 (52.5)	0.450
High VSG (mm/h)		8 (21.6)	14 (35.0)	0.330
NSAID now or preview		34 (91.9)	36 (90.0)	1.000

(i.e., median progression ≥0.38 points per year). The only significant variable associated with "high progression" was low back pain before the diagnosis (82.5% vs. 48.6%, p-value 0.003). Neither sex, smoking, disease duration, HLAB27 or c-reactive protein were associated with the "high progression" group (Table 1).

Conclusion: In this stablished axSpA population, the mean and median progression were 0.54 and 0.38 points in mSASSS per year respectively, which is lower than what has been reported in similar cohorts (i.e., change in 2 points per two years in mSASSS). Only low back pain was found as predictor of spinal radiographic progression.

Disclosure: r. granados: None; **S. Dans-Caballero**: None; **L. Ladehesa Pineda**: None; **M. Puche Larrubia**: None; **D. Ruiz Vilchez**: None; **M. Abalos-Aguilera**: None; **A. Escudero-Contreras**: None; **E. Collantes Estévez**: None; **C. López Medina**: AbbVie, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 6, MSD, 6, Novartis, 2, 5, 6, UCB Pharma, 2, 5, 6.

Abstract Number: 1390

Prediction of Low Disease Activity in Patients with Ankylosing Spondylitis Treated with Secukinumab in Real World – Data from a German Observational Study

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SESSION INFORMATION

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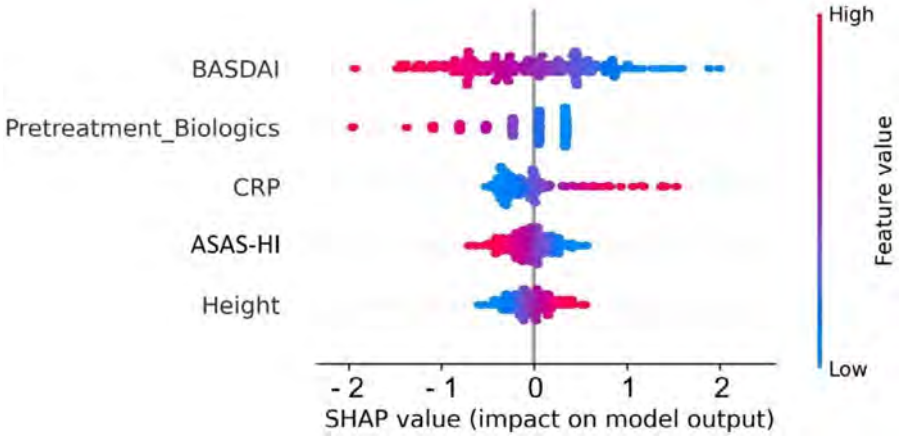
Background/Purpose: Secukinumab (SEC) proved to be an effective treatment for patients suffering from ankylosing spondylitis (AS) in randomized clinical trials [1]. There is only limited knowledge on prediction of low disease activity (LDA) and treatment strategy in AS patients under SEC treatment in routine clinical care.

Using real-world data from the German non-interventional study AQUILA [2], the main objectives were (1) to predict LDA in individual AS patients treated with SEC through machine learning methods and (2) to identify the most important predictors and their influence on the prediction using explainable artificial intelligence (XAI).

Methods: Data of 580 AS patients from the AQUILA study were used. Thirty-two demographic, clinical and treatment parameters at baseline (BL) served as input data to develop prediction models. LDA was defined as Bath ankylosing spondylitis disease activity index (BASDAI) ≤ 2.0 at week (w) 16 (+/- 6 w). Samples were divided into training (70%) and validation (30%) cohorts. Ten different prediction models were applied and compared. Model performance was measured using area under the receiver operating characteristic curve (AUROC) which represents the probability that a randomly selected patient with LDA will have higher prediction to achieve LDA than a patient with moderate/high disease activity. Additionally, sensitivity and specificity of the prediction model were computed and express the proportion of correctly identified patients who reach or don't reach LDA at w16, respectively. Shapley XAI estimated importance and impact of each predictor based on how it affected the change in individual prediction [3].

Results: The most influencing predictor was BASDAI at BL, followed by the number of pretreatments with biologics, C-reactive protein (CRP), assessment of spondyloarthritis international society health index (ASAS-HI) and patient height (**-Figure 1 A**). AUROC of the best performing prediction model was 0.84. Sensitivity and specificity were 0.87 and 0.67, respectively. Applied XAI approach showed that the lower the BL values of BASDAI, ASAS-HI and number of pretreatments with biologics were, the higher the probability of reaching LDA at w16 was. The opposite was the case for BL values of CRP and body height (**Figure 1 A**). The approach also provided visual explanations of patient-individual predictions: Variables with values shown in green color increased probability of reaching LDA at w16, whereas red ones showed the opposite effect (**Figure 1 B)**.



A: Main predictors at baseline and their direction of influence based on Shapley values [3]

B: Explanation of patient-individual prediction of 88% using baseline data

Conclusion: A promising prediction model accuracy of LDA in AS patients treated with SEC could be reached and validated. Identified main predictors at BL, such as BASDAI and number of pretreatments with biologics, and their direction of influence on the prediction of LDA mostly match the existing clinical knowledge [4]. The analysis showed that XAI can provide useful clinical insights into patient-individual predictions, potentially guiding AS treatment decisions in future.

Disclosure: A. Vodencarevic: Novartis, 3; **J. Brandt-Juergens**: AbbVie/Abbott, 2, 6, Affibody, 2, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Gilead, 2, Janssen, 2, 6, Medac, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **D. Peterlik**: Novartis, 3; **B. Gmeiner**: Novartis, 3; **U. Kiltz**: AbbVie, 2, 5, 6, Amgen, 5, Biocad, 2, 6, Biogen, 5, Bristol-Myers Squibb(BMS), 2, 5, Chugai, 2, 6, Eli Lilly, 2, 6, Fresenius, 5, Gilead, 2, 5, GlaxoSmithKline (GSK), 5, Grünenthal, 2, 6, Hexal, 5, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, onkowiessen.de, 2, 5, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Viatris, 2, 5.

Abstract Number: 1391

Rates of Remission in Patients with Axial Spondyloarthritis Treated in Tertiary Care

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SESSION INFORMATION
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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS
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Session Time: 9:00AM–11:00AM

Background/Purpose: Achieving remission is the treatment target for patients (pts.) with axial spondyloarthritis (axSpA). Remission rates over longer periods in a real-life setting have not been studied so far. To evaluate the remission rates in a cohort of axSpA pts. treated in a tertiary care center using retrospective and prospective data.

Methods: Adult pts. with a diagnosis of axSpA were eligible for inclusion when ≥ 2 consecutive ASDAS assessments were documented in the hospital information system in the past. At the next clinical visit, patients and disease characteristics as well as standard assessments using validated outcome parameters for disease activity (ASDAS, BASDAI) and physical function (BASFI) were then prospectively documented. Values of BASDAI, ASDAS and BASFI were taken retrospectively from the hospital information system. ASDAS was calculated either by ASDAS-CRP or alternative-ASDAS the latter one, when patient global assessment was unavailable.1Remission was defined as an ASDAS < 1.3 and sustained remission was defined by ASDAS < 1.3 for at least 6 consecutive months. Multivariable logistic regression was used to estimate ORs, 95% CIs and p-values of achieving remission.

Table 1: Patients demographics and disease characteristics at clinical visit *values are mean (SD) **all of these pts. suffered from severe psoriasis vulgaris, which could not be successfully treated by other bDMARDs

Characteristics*	axSpA patients (n=200)
Age, in years	46.3 (13.3)
Gender female, n (%)	71 (35.5)
Smoker, n (%)	63 (31.5)
Education, university level, n (%)	24 (12.0)
Employment, n (%)	143 (71.5)
Time since symptom onset, years	19.8 (12.9)
Early axSpA status, n (%)	85 (42.5)
HLA-B27 n (%), missings=8	154 (80.2)
At least one syndesmophyte , n (%)	69 (39.0)
NSAR on-demand, n (%)	105 (52.5)
Patients on bDMARD or tsDMARD, n (%)	156 (78)
TNFi, n (%)	130 (65.0)
IL17, n (%)	18 (9.0)
IL12/23**, n (%)	3 (1.5)
JAKi, n (%)	5 (2.5)
No. of previous b- or tsDMARD	0.8 (1.4)
Pain (NRS 0-10)	3.9 (2.6)
Patient Global (NRS 0-10)	3.7 (2.5)
Physician Global (NRS 0-10)	1.4 (1.5)
ASDAS	2.0 (1.0)
ASDAS, n (%)	
Remission	52 (26.0)
Low Disease Activity	59 (29.5)
High Disease Activity	71 (35.5)
Very High Disease Activity	18 (9.0)
BASFI	3.3 (2.5)
physiotherapy, n (%)	96 (48.0)

Results: A total of 200 pts. were consecutively examined at their clinical visit between March and September 2022. Retrospective chart data were available over a period of 82.6 (58.6) months. Mean ASDAS at the clinical visit was 2.0 (1.0) and 52 pts. (26.0%) were in ASDAS remission. 74 (37.0%) pts. showed limitations in physical functioning (BASFI >4) (table 1). 117 pts. (58.5%) achieved ASDAS remission at least once. On average, remission was reached 37.7 (44.5) months after the index visit. 44 pts. achieved remission within the first year (37.6%), 20 in the second (17.1%), 13 in the third (11.1%)

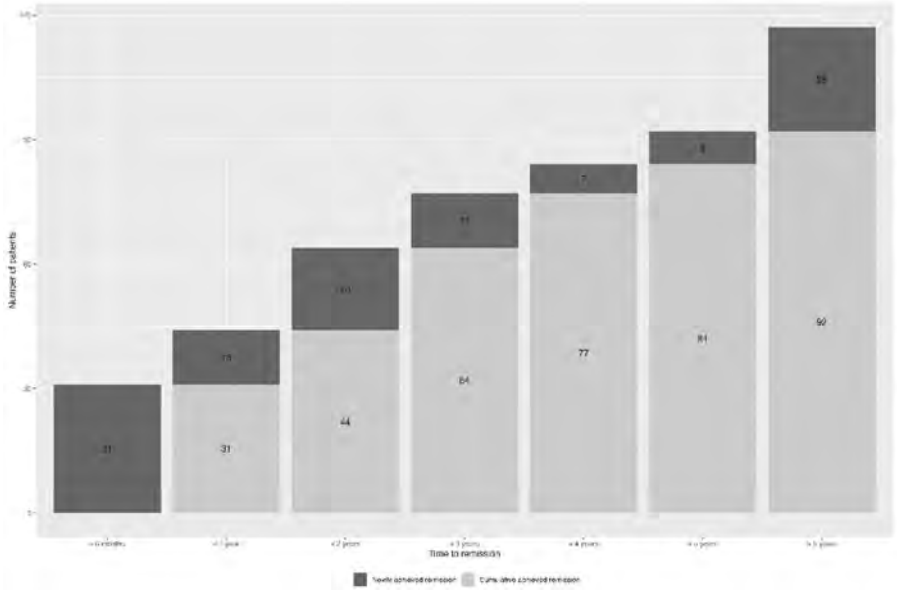

Figure 1: Time to remission

Table 2: Baseline predictors of achieving remission at least once over study period

		Univariable			Multivariable		
Characteristic	N	OR[1]	95% CI[1]	p-value	OR[1]	95% CI[1]	p-value
Sex,	200						
female		0.87	0.48, 1.57	0.65	1.08	0.46, 2.57	0.9
Age, at clinical visit	200	1.00	0.97, 1.02	0.66	1.02	0.99, 1.05	0.2
Symptom duration, clinical visit	200	1.00	0.98, 1.03	0.88			
early axSpA, duration between first symptoms and diagnosis <2 years	200	1.02	0.58, 1.81	0.94	0.89	0.38, 2.05	0.8
HLA-B27	192						
positive		1.79	0.88, 3.68	0.11	2.08	0.79, 5.70	0.14
Smoker, clinical visit	200						
never		—	—		—	—	
former		0.74	0.37, 1.48	0.39	0.49	0.17, 1.41	0.2
current		0.49	0.24, 0.99	**0.048**	0.80	0.30, 2.17	0.7
ASDAS, index visit	135	0.69	0.46, 1.01	0.064			
CRP, index visit	153	1.21	1.04, 1.45	**0.028**	1.35	1.10, 1.73	**0.009**
BASDAI, index visit	165	0.65	0.52, 0.80	**<0.001**	0.72	0.53, 0.97	**0.036**
BASFI, index visit	150	0.80	0.69, 0.93	**0.004**	0.82	0.65, 1.02	0.074
Charlson Comorbidity Index >0, clinical visit	200	0.62	0.33, 1.15	0.13	0.58	0.21, 1.57	0.3

and 40 patients (34.2%) after 3 years (figure 1). 9 (7.7%) pts. achieved their first ASDAS remission at the clinical visit. During the observation period pts. achieved remission for 9.9 (16.8) months or 21.6% (29.9%) of the time, while 51 pts. (43.6%) achieved sustained remission for at least 6 consecutive months, 31 pts. (26.5%) achieved sustained remission for at least 12 consecutive months. 83 pts. (41.5%) never achieved ASDAS remission. In a multivariable model, high CRP (OR=1.35, 95% CI 1.10 to 1.73) and low BASDAI (OR=0.72, 95% CI 0.53 to 0.97) at index visit were associated with higher odds of achieving remission at least once (both $p< 0.05$). Pts. with low BASFI at index visit also tended to have higher odds of achieving remission, however this was not significant (OR=0.82, 95% CI 0.65 to 1.02, p=0.074). Age nor gender was significantly associated with achieving remission (OR=1.02, 95% CI 0.99 to 1.05, p=0.2), (OR=1.08, 95% CI0.46 to 2.57, p=0.9, respectively).

Conclusion: Achievement of remission is an attainable goal for patients with axSpA. High CRP and low BASDAI at index visit were shown to be predictors of ASDAS remission. The majority of patients achieved remission within the first two years after the initial visit. However, also after the fifth year of follow up a quarter of patients achieved ASDAS remission for the first time.

Disclosure: F. Neinert: None; **I. Redeker**: None; **S. Tsiami**: None; **D. Kiefer**: None; **B. Guminski**: None; **X. Baraliakos**: AbbVie, 2, 6, BMS, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, 6, UCB, 2, 6; **J. Braun**: None; **U. Kiltz**: AbbVie, 2, 5, 6, Amgen, 5, Biocad, 2, 6, Biogen, 5, Bristol-Myers Squibb(BMS), 2, 5, Chugai, 2, 6, Eli Lilly, 2, 6, Fresenius, 5, Gilead, 2, 5, GlaxoSmithKline (GSK), 5, Grünenthal, 2, 6, Hexal, 5, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, onkowiessen.de, 2, 5, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Viatris, 2, 5.

Abstract Number: 1392

Improving the Diagnostic Accuracy in Axial Spondyloarthritis: Interim Results of a Nationwide Telemedicine Project

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Background/Purpose: Axial spondyloarthritis (axSpA) is often diagnosed late, while there is also a problem of over- and misdiagnosis in patients with chronic back pain. Imaging, especially magnetic resonance imaging (MRI), is important for diagnosis and differential diagnosis, but interpreting imaging findings in sacroiliac joints requires specific expertise.

The Improve-axSpA project was aimed to assess the effectiveness of telemedicine support in enhancing the diagnostic accuracy of patients suspected of having axSpA.

Methods: We established a central telemedicine platform that allowed the collection of clinical and imaging information from patients who presented to rheumatologists and orthopaedists with suspicion of axSpA. Participating centres were encouraged to recruit appropriate patients consecutively. Collected information included the suspected diagnosis and imaging findings, demographic and laboratory data, information on potential mechanical stress factors, characteristics of back pain

Table 1. Agreement and discrepancies between the local and central assessment of 277 patients with suspicion of axSpA.

		Central diagnosis (N=277)		
		axSpA (n=68)	No axSpA (n=179)	Unclear (n=30)
Local diagnosis (N=277)	axSpA (n=90)	45 50 %	32 35.6 %	13 14.4 %
	No axSpA (n=82)	7 8.5 %	70 85.4 %	5 6.1 %
	Unclear (n=105)	16 15.2 %	77 73.3 %	12 11.4 %

and SpA features as assessed by the local physician. The central expert evaluation included detailed assessment of the submitted data including imaging and the final conclusion on the presence or absence of axSpA.

Results: A total of 25 study centres submitted 277 cases for the central evaluation until March 2023. The distribution of the diagnoses according to the local and central assessment is presented in table 1. A total of 90/277 patients (33%) were locally diagnosed with axSpA. Only in 45 (50%) of those cases axSpA could be confirmed after central evaluation, while in 32 patients (36%) an alternative reason of back pain (in the majority of cases – degenerative / mechanical disorders, non-specific back pain) were found to be more likely. In contrast, among 82 patients with no axSpA according to local assessment, in 70 (85%) of those patients axSpA could be excluded based on central evaluation. In 105 cases with inconclusive local diagnosis, axSpA was more frequently excluded than confirmed (73% vs. 15%). In a total of 30 patients, the diagnosis could not be finally determined after central assessment, this being related in most cases to insufficient imaging. Several important differences could be found between patients with centrally confirmed vs. excluded axSpA: patients without SpA were older, more often females (and more often with a history of pregnancies and 2 and more deliveries), had lower CRP, higher BMI and were less frequently HLA-B27-positive. At the same time, other SpA-characteristics including inflammatory back pain, as well as imaging characteristics as reported by the local rheumatologist were not discriminative between the groups. However, the presence or absence of SpA-compatible active inflammatory and structural changes on MRI of sacroiliac joints according to the central assessment were highly discriminative between the groups with confirmed and excluded SpA.

Conclusion: The Improve-axSpA interim analysis suggests a high risk of overdiagnosis of SpA in daily clinical practice. Telemedicine tools with central evaluation of clinical and imaging information may be helpful in the diagnostic process for patients with suspected axSpA.

Disclosure: D. Poddubnyy: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, MoonLake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 2, UCB Pharma, 2, 6; **M. Kämmerer**: None; **M. Kremers**: None; **B. Schoppen**: None; **C. Arens**: None; **A. Wiedon**: Novartis Pharma GmbH, 3; **I. Redeker**: None; **X. Baraliakos**: AbbVie, 2, 6, BMS, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, 6, UCB, 2, 6.

Abstract Number: 1393

Fully Automated Detection of Active Sacroiliitis in Patients with Axial Spondyloarthritis: A Machine Learning-Based Analysis Magnetic Resonance Image

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Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Magnetic Resonance Imaging (MRI) is a crucial modality for early diagnosis of active inflammation in the sacroiliac joint in patients with axial spondyloarthritis (axSpA). This study focused on developing a fully automated classification model that leverages machine learning to detect sacroiliac joints and determine the presence of bone marrow edema in MRI.

Methods: We collected 815 MRI slices of sacroiliac joints (SIJs) from 60 axSpA patients and 19 healthy subjects. Active sacroiliiitis was identified by bone marrow edema observed in gadolinium-enhanced fat-suppressed T1-weighted oblique coronal images. First, a region of interest (ROI) was manually set, and the ResNet18 model was applied to detect bone marrow edema automatically. The prediction models were evaluated using 5-fold cross-validation sets. In the second phase, we introduced a text-guided cross-position attention module (CPAMTG) that integrates cross-attention into the position attention module (PAM) to localize the ROI automatically. The effectiveness of attention in extracting feature maps was assessed by comparison with backbone networks (U-Net) and PAM.

Results: The semi-automated model demonstrated commendable performance in detecting bone marrow edema, with 77.48% accuracy, 92.15% recall, 73.43% precision, 74.24% specificity, and an F1 score of 81.74% at the image level. At the patient level, active sacroiliiitis was diagnosed with 96.06% accuracy, 100% recall, 94.84% precision, 86.43% specificity, and an F1 score of 97.32%. Remarkably, the fully automated ROI patch exhibited higher accuracy (84.73% vs. 77.48%, $p < 0.001$) and specificity (85.03% vs. 74.24%, $p = 0.004$) and maintained or improved performance in comparison to the semi-automated model, with 92.17% recall, 82.81% precision, and an F1 score of 87.24%.

Conclusion: We presented a fully automated classification model for detecting active sacroiliiitis in MRI, which showed excellent performance. These findings suggest that MRI analysis with machine learning can offer valuable assistance to clinicians, enabling rapid and objective diagnosis of active inflammation in patients with axSpA.

Disclosure: G. Lee: None; **S. Choi**: None; **J. Cho**: None; **S. Kim**: None; **G. Lee**: None; **S. Choi**: None.

Abstract Number: 1394

Comorbidities, Not Long-Term Use of Nonsteroidal Anti-Inflammatory Drugs, May Be Associated with Chronic Kidney Disease in Patients with Ankylosing Spondylitis: A Nationwide Population-Based Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly prescribed as first-line treatment for symptom relief and inflammation reduction in patients with ankylosing spondylitis (AS). However, long-term NSAID use has been linked to an increased risk of developing chronic kidney disease (CKD). This study aimed to identify the risk factors, including cumulative NSAID dosage, associated with CKD in AS patients using data from the National Health Insurance.

Table 1. Hazard ratio of chronic kidney disease by baseline characteristics

Table 1. Hazard ratio of chronic kidney disease by baseline characteristics

	crude HR	95% CI		p-value	Adjusted HR	95% CI		p-value
Age group, year								
<30	Ref.			<.001	Ref.			0.010
30–39	2.16	(0.96	-4.85)	0.062	1.79	(0.79	-4.02)	0.162
40–49	2.69	(1.22	-5.94)	0.015	1.53	(0.68	-3.47)	0.305
50–59	5.55	(2.66	-11.57)	<.001	2.10	(0.96	-4.63)	0.065
60<	13.66	(6.83	-27.33)	<.001	3.27	(1.49	-7.17)	0.003
Sex								
Male	Ref.							
Female	1.10	(0.78	-1.55)	0.597				
Charlson comorbidity index								
0	Ref.			<.001	Ref.			
1 to 2	3.25	(2.18	-4.86)	<.001	1.65	1.049	2.612	0.0303
3 to 4	9.34	(6.14	-14.23)	<.001	2.27	1.27	4.08	0.0058
Comorbidities (1 year prior to index date)								
Dyslipidemia	4.48	(3.25	-6.19)	<.001	1.375	0.922	2.051	0.1182
Hypertension	1.87	(1.08	-3.23)	0.026	2.408	1.595	3.634	<.001
Diabetes mellitus	1.87	(1.08	-3.23)	0.027	1.538	1.016	2.329	0.042
COPD	3.83	(2.39	-6.13)	<.001	0.763	0.431	1.349	0.3518
Ischemic heart disease	3.83	(2.39	-6.13)	<.001	0.945	0.572	1.559	0.8234
Psoriasis	1.38	(0.34	-5.56)	0.652				
Stroke	2.95	(1.45	-6.02)	0.003	0.705	0.431	1.349	0.352
Asthma	0.74	(0.10	-5.25)	0.760				
Immune modulating agents (0-90 days from diagnosis)								
Corticosteroid	1.20	(0.87	-1.66)	0.2619				
Sulfasalazine	0.42	(0.30	-0.60)	<.001	0.682	0.47	0.99	0.0439
Methotrexate	0.86	(0.47	-1.59)	0.631				
TNF inhibitor (ADA, ETN, IFX, GOL)	1.03	(0.57	-1.85)	0.926				
IL-17 inhibitor (Secukinumab, ixekizumab)								
NSAID Index Score (0-90 days from diagnosis)								
NSAID Index Score 0	1.00			< 001	1.00			0.005
NSAID Index Score 0< <33.3	1.11	(0.61	-2.03)	0.725	1.22	(0.67	-2.22)	0.528
NSAID Index Score 33.3≤ <66.6	0.51	(0.28	-0.93)	0.028	0.80	(0.44	-1.48)	0.483
NSAID Index Score ≥66.6	1.29	(0.63	-2.67)	0.484	2.02	(0.97	-4.03)	0.060

Methods: The incidence of CKD was determined in AS patients diagnosed between May 1, 2016, and December 31, 2019, using Korean national health insurance data. The cumulative NSAID dosage was assessed using the ASAS NSAID Intake Score. The ASAS NSAID Intake Score was categorized into four groups based on the score at 3 months, 6 months, and 1-year intervals: = 0, >0 and ≤33.3, >33.3 and ≤66.6, and >66.6. The hazard ratio was used to evaluate the risk of CKD based on baseline characteristics. A nested case-control analysis was performed to investigate the correlation between the ASAS NSAID Intake Score during 3 months, 6 months, and 1 year before CKD diagnosis and the development of CKD.

Results: Out of the initial 12,000 AS patients, 120 were identified with CKD. The incidence rate of CKD was 4.64 per 10,000 patient-years. Factors significantly associated with CKD included age ≥60 (Ref. age< 30, HR 3.27, 95% CI 1.49 – 7.17), Charlson comorbidity index 1–2 (HR 1.65, 95% CI 1.049 – 2.612) and 3–4 (HR 2.27, 95% CI 1.27 – 4.08), hypertension (HR 2.408, 95% CI 1.595 – 3.634), diabetes mellitus (HR 1.538, 95% CI 1.016 – 2.329), and sulfasalazine (HR 0.682.76, 95% CI 0.47 – 0.99) (Table 1). However, the odds ratios adjusted for comorbidity and medication did not show a correlation between the 3-month, 6-month, and 1-year ASAS NSAID Intake Scores and CKD. A 1-year ASAS NSAID Intake Score > 66.6 was associated with a reduced risk of CKD (OR 0.46, 95% CI 0.22–0.94) (Table 2).

Table 2. Odd ratio between cases and matched controls in 3-months, 6-months, and one-year interval

Table 2. Odd ratio between cases and matched controls in 3-months, 6-months, and one-year interval

	OR	95% CI		p-value	adjusted OR	95% CI		p-value
NSAID Index Score (0-90 days from CKD diagnosis)								
NSAID Index Score 0	Ref.			0.0104	Ref.*			0.0673
NSAID Index Score 0< <33.3	1.623	1.081	2.437	0.0194	0.92*	0.578	1.466	0.7272
NSAID Index Score 33.3<= <66.6	0.915	0.512	1.636	0.7656	0.482*	0.246	0.945	0.0337
NSAID Index Score >=66.6+	3.514	1.174	10.522	0.0247	2.078*	0.563	7.663	0.2721
NSAID Index Score (0-180 days from CKD diagnosis)								
NSAID Index Score 0	Ref			0.1049	Ref.*			0.7108
NSAID Index Score 0< <33.3	1.327	0.794	2.219	0.2808	0.696*	0.379	1.277	0.2414
NSAID Index Score 33.3<= <66.6	1.476	0.829	2.628	0.1855	0.839*	0.439	1.604	0.5952
NSAID Index Score >=66.6+	1.934	1.143	3.272	0.014	0.805*	0.435	1.49	0.4907
NSAID Index Score (0-365 days from CKD diagnosis)								
NSAID Index Score 0	Ref.			0.0681	Ref.**			0.1853
NSAID Index Score 0< <33.3	1.166	0.631	2.154	0.6236	0.517**	0.25	1.069	0.0751
NSAID Index Score 33.3<= <66.6	1.334	0.639	2.785	0.4436	0.435**	0.178	1.064	0.068
NSAID Index Score >=66.6+	1.905	1.066	3.403	0.0295	0.448**	0.21	0.957	0.0381

* adjusted for CCI, dyslipidemia, hypertension, diabetes mellitus, ischemic heart disease, use of corticosteriods, TNF inhibitor use

** adjusted for CCI, dyslipidemia, hypertension, diabetes mellitus, ischemic heart disease, use of corticosteriods, sulfasalazine, TNF inhibitor use

Conclusion: The risk of CKD in AS patients was associated with comorbidities. However, long-term NSAID use may not be associated with an increased risk of CKD.

Disclosure: B. Koo: None; **S. Hwang**: None; **Y. Kim**: None; **S. Ahn**: None; **W. Seo**: None.

Abstract Number: 1395

Aerobic Capacity and Its Relation to Disease Characteristics and Lifestyle Habits in Patients with Axial Spondyloarthritis

Elisabet Lindqvist[1], Johan Karlsson Wallman[1], Jonas Sagard[2], Tor Olofsson[1] and Elisabeth Mogard[1], [1]Lund University and Skåne University Hospital, Lund, Sweden, [2]Skåne University Hospital, Lund, Sweden

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Physical activity is part of the treatment of axial spondyloarthritis (axSpA), but despite this almost half of the patients do not meet the required level of physical activity to promote health. (1)Low aerobic capacity (cardiorespiratory fitness) is an important risk factor for cardiovascular disease, morbidity, and mortality. (2) The aim of this study was to

evaluate aerobic capacity in patients with axSpA, and to examine differences between patients with low versus high aerobic capacity.

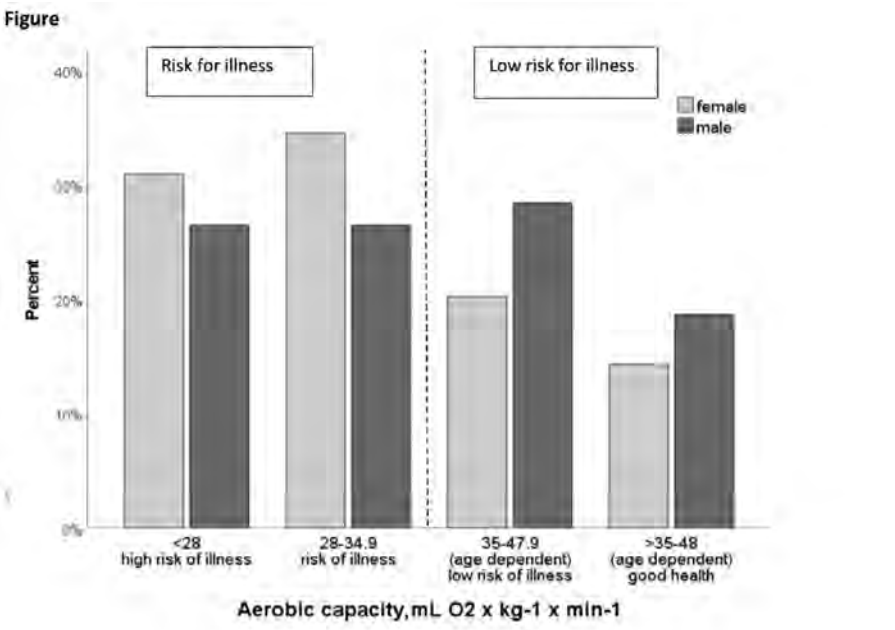
Methods: Patients with clinical axSpA from a defined area of southern Sweden were cross-sectionally examined and classified as non-radiographic axSpA (nr-axSpA; ASAS criteria; n=74) or radiographic axSpA (r-axSpA; modified NY or ASAS criteria; n=112). Aerobic capacity was measured by a submaximal bicycle ergometer test (Åstrand). A value of >28 mL O_2 x kg^{-1} x min^{-1} (mL O_2) is associated with a reduced risk of all-cause mortality, and ≥35 mL O_2 is estimated to be an acceptable level for health in the short term. For health in the long term, a value of 35.1 - 48 mL O_2depending on age, is desirable. (4) Other assessments included spinal mobility, chest expansion, vital capacity (VC), pain sensitivity (by computerized cuff pressure algometry (3)), radiographic assessments (sacroiliac joints [SI-joints]/modified Stoke Ankylosing Spondylitis Spinal

Table. Characteristics of all axial spondyloarthritis (axSpA) patients and stratified on level of aerobic capacity indicating low and high risk for illness, respectively

	All axSpA patients N=186	AxSpA patients with low risk of illness. Aerobic capacity ≥35 mL O_2 x kg^{-1} x min^{-1} n=77	AxSpA patients with high risk of illness. Aerobic capacity <35 mL O_2 x kg^{-1} x min^{-1} n=109
Aerobic capacity,[a] mL O_2 x kg^{-1} x min^{-1}	33.9 (10.4)	43.7 (7.6)	27.0 (5.1)**
Male sex, n (%)	102 (55%)	48 (62%)	54 (50%)
Age, years	47 (11)	41 (10)	51 (10)**
Symptom duration, years	22 (11)	18 (10)	24 (11)**
r-axSpA/AS [b]	112 (60%)	46 (60%)	66 (61%)
HLA-B27 positivity	157 (85%)	68 (88%)	89 (82%)
Vital capacity (VC), L	4.1 (1.0)	4.5 (1.0)	3.8 (0.9)**
Chest expansion, cm	5.4 (1.8)	6.3 (1.6)	4.7 (1,6)**
Modified Schober, cm	4.5 (3.0)	4.4 (0.9)	4.5 (3.9)
Summarized radiographic sacroiliitis score (0-8)[c]	4.4 (2.7)	4.4 (2.8)	4.4 (2.7)
mSASSS, median (IQ-range)	1.0 (0, 7.0	2.0 (0, 5.0)	1.0 (0, 8.5)
ASDAS-CRP	1.7 (1.6)	1.4 (0.76)	1.8 (0.87)*
BASDAI	2.7 (2.0)	2.4 (1.7)	3.0 (2.2)
BASFI	1.6 (1.8)	1.1 (1.3)	2.0 (1.9)*
BASMI	2.6 (1.4)	2.2 (1.0)	2.9 (1.5)**
EQ-5D utility [d]	0.74 (0.22)	0.76 (0.20)	0.72 (0.24)
NRS global health, cm	3.1 (2.5)	2.8 (2.2)	3.3 (2.7)
NRS fatigue, cm	3.4 (2.8)	2.9 (2.5)	3.7 (2.9)
NRS pain, cm	3.0 (2.5)	2.6 (2.2)	3.2 (2.6)
Chronic pain [e]	138 (74%)	58 (75%)	80 (73%)
Pain threshold, kPa [f]	32.4 (14.4)	33.4 (15.0)	31.6 (14.1)
Pain tolerance, kPa [g]	67.9 (27.4)	77.8 (30.4)	60.9 (22.6)**
Charlson comorbidity index [h]	1.3 (0.6)	1.24 (0.6)	1.37 (0.6)
BMI	26 (4)	24 (3)	27 (4)**
Healthy dietary habits, n (%) [i]	150 (86%)	68 (92%)	82 (81%)*
Non-smoking, n (%) [j]	153 (87%)	65 (88%)	88 (87%)
Non-hazardous alcohol consumption, n (%) [k]	149 (85%)	61 (82%)	88 (87%)
Healthy physical activity level, n (%) [l]	135 (77%)	68 (92%)	67 (66%)**
Ongoing csDMARD, n (%)	36 (19%)	13 (17%)	23 (21%)
Ongoing bDMARD, n (%)	82 (44%)	34 (44%)	48 (44%)

Presented as mean (SD) unless otherwise indicated. * $p < 0.05$. ** $p < 0.001$. Missing data ranged from 0-10%. r-axSpA: radiographic axial spondyloarthritis, AS: ankylosing spondylitis, mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score, ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score using C-reactive protein, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, BASMI: Bath Ankylosing Spondylitis Metrology Index, EQ-5D: EuroQol-5 Dimensions, NRS: numeric rating scale, BMI: Body mass index, bDMARD: biologic disease-modifying anti-rheumatic drugs, csDMARD: conventional synthetic disease-modifying anti-rheumatic drugs. [a] Aerobic capacity assessed by Åstrand's submaximal bicycle ergometer test. [b] r-axSpA and AS are merged. 74 patients (40%) have nr-axSpA (non-radiographic axSpA). [c] Sum of left and right radiographic sacroiliitis score, according to the modified New York criteria (value 0-4 at each side). [d] Utilities according to the standard British time trade-off based preference set. [e] Chronic regional or chronic widespread pain for > 3 months registered on a pain mannequin. [f g] Pain threshold and pain tolerance assessed by computerized cuff pressure algometry. [f] The pressure of the cuff in kilopascal when the patients started to feel pain, [g] The pressure of the cuff in kilopascal when the pressure was stopped due to reaching worst tolerable pain. [h] Charlson comorbidity index without age points. [i] Healthy dietary habits equals ≤4/12 points on a dietary questionnaire from the National board of Health and Welfare, Sweden, [j] Non-smoking = never smoked or stopped smoking >6 months ago, smoker = present smoker or stopped <6 months ago. [k] non-hazardous alcohol consumption equals not drinking more than 9 glass per week and/or more than 4 glasses at the same occasion for women and 14 glasses per week and/or more than 5 glass at the same time for men. [l] Healthy physical activity level equals performing ≥150 minutes of moderate physical activity/week or ≥ 75 min/week of vigorous physical activity or a combination of the two.

Figure



Aerobic capacity in mL O_2 x kg^{-1} x min^{-1} for women and men split into 4 groups according to impact on health. We have compared patients with risk for morbidities to patients with low risk for morbidities stratified on aerobic capacity </≥35 mL O_2 x kg^{-1} x min^{-1}, (dotted line)

Score [mSASSS]), lifestyle habits, health-related quality of life, and standard axSpA outcome measures. Comparisons between patents with aerobic capacity ≥/< 35 mL O_2 were performed by Student's t-test/Chi-square test, Mann-Whitney U-test, as appropriate.

Results: Mean aerobic capacity was 33.9 mL O_2, with no differences between nr-axSpA and r-axSpA or men and women (Figure). Only 17% displayed the desirable level of aerobic capacity for health in the long term, and 28% had an aerobic capacity of < 28 mL O_2, indicating a high risk of illness. Patient characteristics, stratified on aerobic capacity ≥/< 35 mL O_2 are presented in the Table. Patients with aerobic capacity ≥35 mL O_2 were younger, had lower disease activity, better physical function, and spinal mobility. Aerobic capacity ≥35 mL O_2 was further associated with better VC and chest expansion, and more healthy body mass index (BMI) and dietary habits, while mSASSS showed borderline significance (p=0.067). No associations were found between aerobic capacity (≥/<35 mL O_2) and grade of radiographic changes in the SI-joints, global health, pain, fatigue, or health-related quality of life. Patients with aerobic capacity ≥35 mL O_2 had higher pain tolerance, while chronic pain was equally common in both groups.

Conclusion: The majority of patients with established axSpA displayed an aerobic capacity indicating a high risk of morbidity. Better chest mobility and vital capacity, as well as healthy BMI and dietary habits were associated with higher aerobic capacity. These findings emphasize the importance of supporting patients with axSpA to a healthy lifestyle and improved aerobic capacity by physical exercise. **References** *1 Mogard*. BMC Rheumatol. *2022;6:29 2 Harber. Prog Cardiovasc Dis. 2017;60:11–20 3 Mogard. J Rheumatol. 2021;48:1672–9 4 Ross. Circulation. 2016;134:e653–e699*

Disclosure: E. Lindqvist: None; **J. Karlsson Wallman**: AbbVie, 5, 6, Amgen, 5, 6, Eli Lilly, 5, Novartis, 5, Pfizer, 5; **J. Sagard**: None; **T. Olofsson**: Merck/MSD, 2, UCB, 2; **E. Mogard**: AbbVie/Abbott, 6, Novartis, 6.

Abstract Number: 1396

Comprehensive Evaluation of the Digital Annular Pulleys: From Ultrasonographical to Anatomical and Histological Evaluation with Special Focus on the Entheses

Luis Coronel[1], Peter Mandl[2], María Isabel Miguel[3], Joan Blasi[4], Maria Lopez-Lasanta[1], Sara Marsal[1], Maria-Antonietta D'Agostino[5] and Ingrid Moller[6], [1]Hospital Universitari Vall d'Hebron, Rheumatology, Barcelona, Spain, [2]Department of Rheumatology, Medical University of Vienna, Vienna, Austria, [3]Universitat de Barcelona - Campus Bellvitge, Unitat d'anatomía i embriología humana, L'Hospitalet de Llobregat, Barcelona, Spain, [4]Universitat de Barcelona - Campus Bellvitge, Histologia, L'Hospitalet de Llobregat, Barcelona, Spain, [5]Universita Cattolica del Sacro Cuore Rome, Courbevoie, France, [6]Instituto Poal de Reumatología, Barcelona, Spain

SESSION INFORMATION

Session Date: Monday, November 13, 2023

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Background/Purpose: The digital annular pulleys (DAP) are anatomical structures of soft connective tissue organized as transverse fibers of variable width, thickness, and configuration that overlay the synovial sheath of the flexor tendons. These structures prevent the flexor tendons from bowing and maintain them in constant relationship with the joint axis of motion. The thickening of DAP has been described as one of the elementary lesions involved in dactylitis in psoriatic arthritis (PsA) patients highlighting the importance of functional pulleys in the pathophysiological manifestations of PsA, as a form of functional enthesis. The present study assesses the ultrasonographic, anatomical and histological characteristics of the DAP anatomical entheses.

Methods: DAP from 20 formalin-embalmed cadaveric hands were assessed with grey-scale ultrasound (US).The US evaluations, performed by 2 expert sonographers, included identification, width, and characterization of insertion sites of the annular pulleys with a newly proposed dynamic maneuver that grants a better exposure of DAP entheses (Figure 1). Then, dissection was performed from the midcarpal area to the distal end of each finger, second to fifth (Figure 2). Measurements of the thickness of the DAP were obtained with a digital caliper. Intra and inter-reader reliability was evaluated using Cohen´s Kappa for all the evaluations. For the histological study, the samples were decalcified using EDTA, sectioned by microtome, and fixed in buffered formalin for two days and, stained with hematoxylin-eosin. The slides were observed and measured with a Leica DMD 108 microscope. Quantitative demographic variables were summarized in means and standard deviations (SD) and qualitative variables in frequencies and percentages (n [%]). Quantitative and qualitative demographic variables

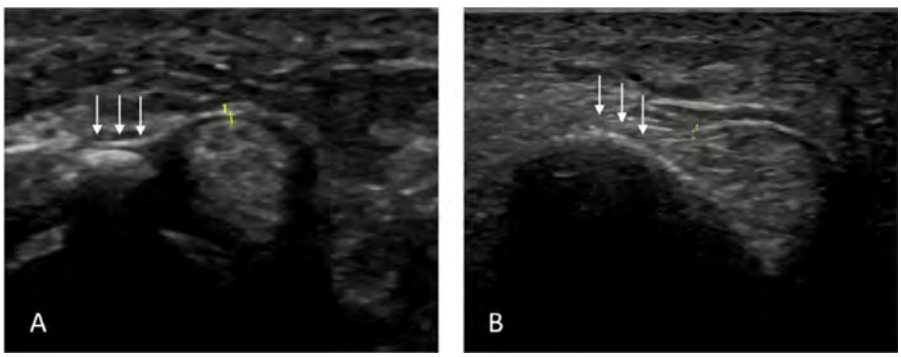

Figure 1. Ultrasound longitudinal scans of the annular pulleys entheses. A) A1 enthesis at the sesamoid bone. B) A2 enthesis in the proximal phalanx. White arrows: Annular pulley entheses. Yellow stars: Dorsal and volar limits of the pulley.

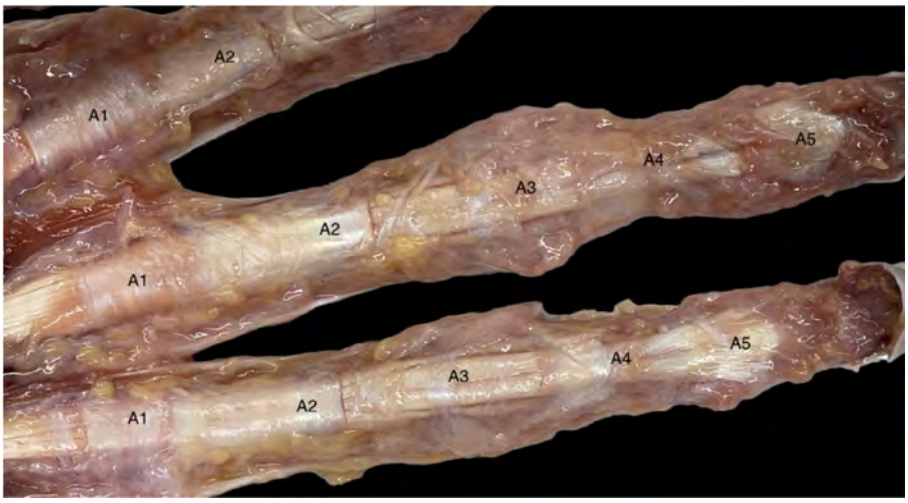

Figure 2. Anatomical dissection of the fingers exposing DAP from A1 to A5.

were compared across groups using Student's t-test and chi-square and Fisher test, respectively.All tests were two-sided and p-values < 0.05 were considered statistically significant. Statistical analyses were performed using R studio (program version RStudio 2022.12.0+353).

Results: The mean age of donors and HC was 81±9 years; range 58–96 years and 11 were females (55%). The mean values of DAP thickness detected by US were analyzed for each finger. Detailed results are presented in Table 1. The intra-reader (mean 0.85, Standard Deviation 0.11) and inter-reader reliability (mean: 0.82, 95% confidence interval: 0.81-0.82) was high. A high correlation between ultrasonographic and anatomical measurements was found (r=0.96). The histological

Table 1. Mean values of pulleys thickness for all annular pulleys (A1-A5) in fingers II-V.

	II	III	IV	V
A1, mean (SD), mm	0.353 (0.066)	0.395 (0.083)	0.378 (0.073)	0.295 (0.09)
A2, mean (SD), mm	0.413 (0.072)	0.455 (0.084)	0.408 (0.086)	0.328 (0.075)
A3, mean (SD), mm	0.135 (0.043)	0.135 (0.056)	0.145 (0.051)	0.128 (0.044)
A4, mean (SD), mm	0.373 (0.072)	0.383 (0.075)	0.358 (0.075)	0.313 (0.086)
A5, mean (SD), mm	0.106 (0.024)	0.113 (0.034)	0.113 (0.033)	0.103 (0.013)

description of the DAP shows a well-vascularized outer surface and a fibrocartilaginous component in the inner surface. The insertion points at the sesamoid or the phalangeal bones demonstrate a diverse nature of the enthesis with fibrocartilaginous and fibrous areas.

Conclusion: These preliminary results show that DAP have a mixed fibrous and fibrocartilaginous enthesis and US is a valuable tool for identifying DAPs' width and anatomical structures, with good correlation with the histological study.

Disclosure: L. Coronel: None; **P. Mandl**: AbbVie/Abbott, 5, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 6, Eli Lilly, 6, Janssen, 6, Novartis, 5, 6, Pfizer, 5, Roche, 6, UCB, 5, 6; **M. Miguel**: None; **J. Blasi**: None; **M. Lopez-Lasanta**: None; **S. Marsal**: None; **M. D'Agostino**: None; **I. Moller**: None.

Abstract Number: 1397

Sustainability of Clinical Response at Week 52 to Upadacitinib Among Patients with Axial SpA: Data from the SELECT-AXIS 1 and SELECT-AXIS 2 Trials

Victoria Navarro-Compán[1], Lianne Gensler[2], Martin Rudwaleit[3], Fabiana Ganz[4], Shirley Chen[4], Jayne Stigler[4], Anna Schmagel[4] and Xenofon Baraliakos[5], [1]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain, [2]University of California San Francisco, Department of Medicine, Division of Rheumatology, San Francisco, CA, [3]University of Bielefeld, Klinikum Bielefeld, Bielefeld, Germany, [4]AbbVie, Inc., North Chicago, IL, [5]Rheumazentrum Ruhrgebiet Herne, Ruhr University Bochum, Bochum, Germany

SESSION INFORMATION

Session Date: Monday, November 13, 2023

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Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Upadacitinib 15 mg (UPA), an oral Janus kinase inhibitor, has shown efficacy and tolerability through 14 weeks in patients (pts) with active radiographic axial SpA (also known as AS), including biological DMARD (bDMARD)-naive pts and pts with intolerance or inadequate response [IR] to bDMARDs, and in pts with non-radiographic axial SpA (nr-axSpA).[1-3] Sustained clinical response is a crucial treatment target. We evaluated the 52-week sustainability of clinical responses in pts with active AS and nr-axSpA from the SELECT-AXIS 1 (NCT03178487) and SELECT-AXIS 2 (NCT04169373) trials who achieved week 14 treatment responses.

Methods: This post hoc analysis included adult pts enrolled in SELECT-AXIS 1 (bDMARD-naive AS) or SELECT-AXIS 2 (comprises 2 studies conducted under a master protocol: 1 in pts with bDMARD-IR AS and 1 in pts with nr-axSpA). Efficacy measures included Assessment of SpA international Society 40 (ASAS40) response, ASAS partial remission (ASAS-PR), AS Disease Activity Score (ASDAS) status (inactive disease [ID] and low disease activity [LDA]) and improvement (clinically important or major improvement), achievement of ≤2.0 score on numerical rating scale (NRS) and minimal clinically important difference (MCID) in total and nocturnal back pain,[4] and achievement of ≤1.5 score and MCID in BASFI.[5,6] Durability of response was assessed at week 52 in pts who achieved a response in each efficacy endpoint at week 14 with UPA. No imputation of missing data was performed. The 95% CIs for durability of response were based on Wald limits without continuity correction.

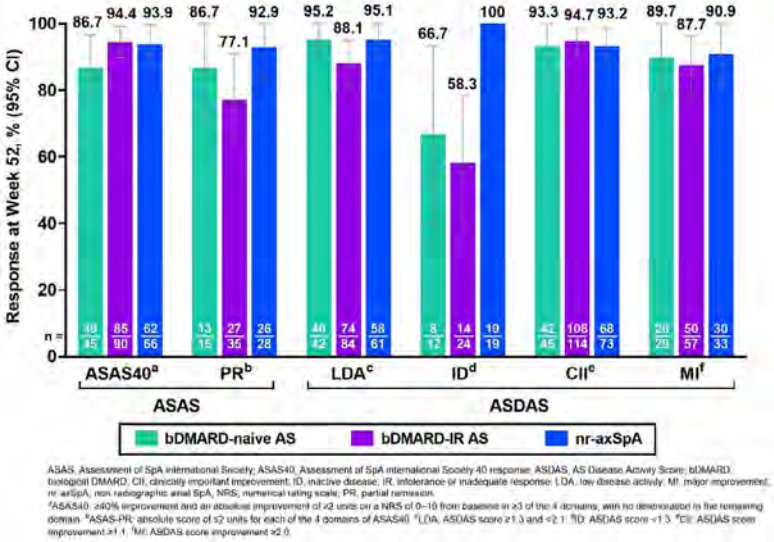
Results: This analysis included 460 pts (bDMARD-naive AS, n=93; bDMARD-IR AS, n=211; nr-axSpA, n=156). In pts who achieved ASAS40 response at week 14 (**Table**), most sustained this response at week 52 (bDMARD-naive AS, 86.7%; bDMARD-IR AS, 94.4%; nr-axSpA, 93.9%; **Fig 1**). Similar results occurred in other disease activity measures with pts

Table. Observed Response Rates in Efficacy Measures at Week 14 With UPA QD

Outcomes, n/N (%)[a]	bDMARD-naive AS	bDMARD-IR AS	nr-axSpA
ASAS			
ASAS40	47/87 (54.0)	94/206 (45.6)	70/143 (49.0)
PR	17/88 (19.3)	37/206 (18.0)	29/143 (20.3)
ASDAS			
LDA	46/86 (53.5)	93/202 (46.0)	66/136 (48.5)
ID	15/86 (17.4)	27/202 (13.4)	22/136 (16.2)
CII	49/85 (57.6)	130/202 (64.4)	81/136 (59.6)
MI	30/85 (35.3)	64/202 (31.7)	37/136 (27.2)
Total back pain			
≤2.0 NRS score	30/88 (34.1)	53/206 (25.7)	39/143 (27.3)
MCID	73/87 (83.9)	169/206 (82.0)	121/143 (84.6)
Nocturnal back pain			
≤2.0 NRS score	40/88 (45.5)	69/206 (33.5)	59/142 (41.5)
MCID	75/87 (86.2)	175/206 (85.0)	113/140 (80.7)
BASFI			
≤1.5 BASFI score	25/88 (28.4)	42/206 (20.4)	40/143 (28.0)
MCID	62/87 (71.3)	157/206 (76.2)	111/143 (77.6)

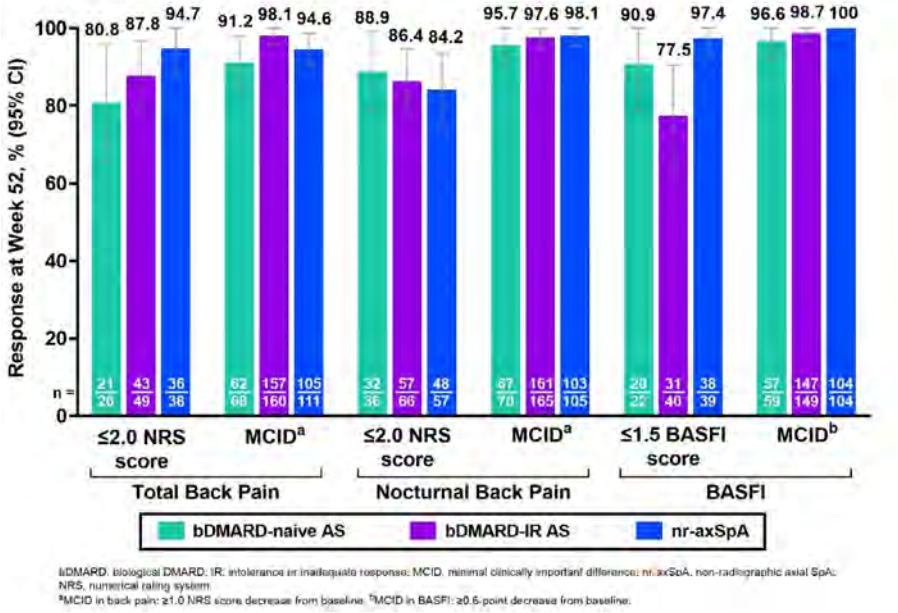
ASAS, Assessment of SpA international Society; ASAS40, Assessment of SpA international Society 40 response; ASDAS, AS Disease Activity Score; bDMARD, biological DMARD; CII, clinically important improvement; ID, inactive disease; IR, intolerance or inadequate response; LDA, low disease activity; MCID, minimal clinically important difference; MI, major improvement; nr-axSpA, non-radiographic axial SpA; NRS, numerical rating scale; PR, partial remission; UPA QD, upadacitinib 15 mg once daily.
[a]Actual observed data are reported here, and no imputation was performed for missing data.
ASAS40: ≥40% improvement and an absolute improvement of ≥2 units on a NRS of 0–10 from baseline in ≥3 of the 4 domains, with no deterioration in the remaining domain.
ASAS-PR: absolute score of ≤2 units for each of the 4 domains of ASAS40.
LDA: ASDAS score ≥1.3 and <2.1.
ID: ASDAS score <1.3.
CII: ASDAS score improvement ≥1.1.
MI: ASDAS score improvement ≥2.0.
MCID in back pain: ≥1.0 NRS score decrease from baseline.
MCID in BASFI: ≥0.6-point decrease from baseline.

Figure 1. Sustainability of Clinical Response at Week 52 in Patients Who Achieved Disease Activity Response at Week 14



ASAS, Assessment of SpA international Society; ASAS40, Assessment of SpA international Society 40 response; ASDAS, AS Disease Activity Score; bDMARD, biological DMARD; CII, clinically important improvement; ID, inactive disease; IR, intolerance or inadequate response; LDA, low disease activity; MI, major improvement; nr-axSpA, non-radiographic axial SpA; NRS, numerical rating scale; PR, partial remission.
[a]ASAS40: ≥40% improvement and an absolute improvement of ≥2 units on a NRS of 0–10 from baseline in ≥3 of the 4 domains, with no deterioration in the remaining domain. [b]ASAS-PR: absolute score of ≤2 units for each of the 4 domains of ASAS40. [c]LDA: ASDAS score ≥1.3 and <2.1. [d]ID: ASDAS score <1.3. [e]CII: ASDAS score improvement ≥1.1. [f]MI: ASDAS score improvement ≥2.0.

Figure 2. Sustainability of Clinical Response at Week 52 in Patients Who Achieved Significant Improvement in Back Pain or Physical Function at Week 14



bDMARD, biological DMARD; IR, intolerance or inadequate response; MCID, minimal clinically important difference; nr-axSpA, non-radiographic axial SpA; NRS, numerical rating system.
[a]MCID in back pain: ≥1.0 NRS score decrease from baseline. [b]MCID in BASFI: ≥0.6-point decrease from baseline.

sustaining effects at week 52: ASAS PR (77.1%–92.9% across pt groups), ASDAS-LDA (88.1%–95.2%), ASDAS-ID (58.3%–100%), ASDAS-CII (93.2%–94.7%), and ASDAS-MI (87.7%–90.9%). At week 52, sustained treatment effects were also observed on back pain (≤2.0 NRS score: total [80.8%–94.7%], nocturnal [84.2%–88.9%]; MCID: total [91.2%–98.1%]; nocturnal [95.7%–98.1%]) and on BASFI (score ≤1.5: 77.5%–97.4%; MCID: 96.6%–100%; **Fig 2**). In the bDMARD-IR AS group, sustainability of more stringent outcomes (ASAS PR, ASDAS-LDA, ASDAS-ID, and BASFI score ≤1.5) were numerically lower vs other pt groups (**Fig 1–2**).

Conclusion: UPA-treated pts with a clinical response at week 14 experienced a sustained response in improvements in disease activity, back pain, and physical function at week 52, supporting the long-term efficacy of UPA across the entire axSpA spectrum.

1. van der Heijde D, et al. *Ann Rheum Dis*. 2022;81:1515–23.
2. van der Heijde D, et al. *Lancet*. 2019;394:2108–17.
3. Deodhar A, et al. *Lancet*. 2022;400:369–79.
4. Salaffi F, et al. *Eur J Pain*. 2004;8:283–91.
5. Wariaghli G, et al. *BMC Musculoskelet Disord*. 2012;13:40.
6. Kviatkovsky MJ, et al. *J Rheumatol*. 2016;43:1680–6.

Disclosure: V. Navarro-Compán: AbbVie, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, Janssen, 6, MoonLake, 2, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6; **L. Gensler**: AbbVie, 2, Acelyrin, 2, Eli Lilly, 2, Fresenius Kabi, 2, Janssen, 2, Novartis, 2, 5, Pfizer, 2, UCB Pharma, 2, 5; **M. Rudwaleit**: AbbVie, 2, 6, Boehringer Ingelheim, 6, Chugai, 6, Eli Lilly, 2, 6, Janssen, 6, Novartis, 2, 6, Pfizer, 6, UCB Pharma, 2, 6; **F. Ganz**: AbbVie, 3, 11; **S. Chen**: AbbVie, 12, Provided statistical analysis support funded by AbbVie, Bristol Myers Squibb, 12, Spouse is an employee, Tigermed-BDM Inc., 3; **J. Stigler**: AbbVie, 3, 11; **A. Schmagel**: AbbVie, 3, 11; **X. Baraliakos**: AbbVie, 2, 5, 6, Bristol Myers Squibb, 2, 6, Celgene, 6, Chugai, 2, 6, Merck, 6, MSD, 2, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6.

Abstract Number: 1398

A Deep Learning Algorithm for MRI Spinal Inflammation in Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Deep learning has achieved wide applications in different areas of medical imaging analysis. Limited studies have explored the use of deep learning for imaging interpretation in axial spondyloarthritis (SpA). This study aims to develop a deep learning algorithm for the detection of active spinal inflammation in short tau inversion recovery (STIR) sequence magnetic resonance imaging (MRI) in patients with axial SpA.

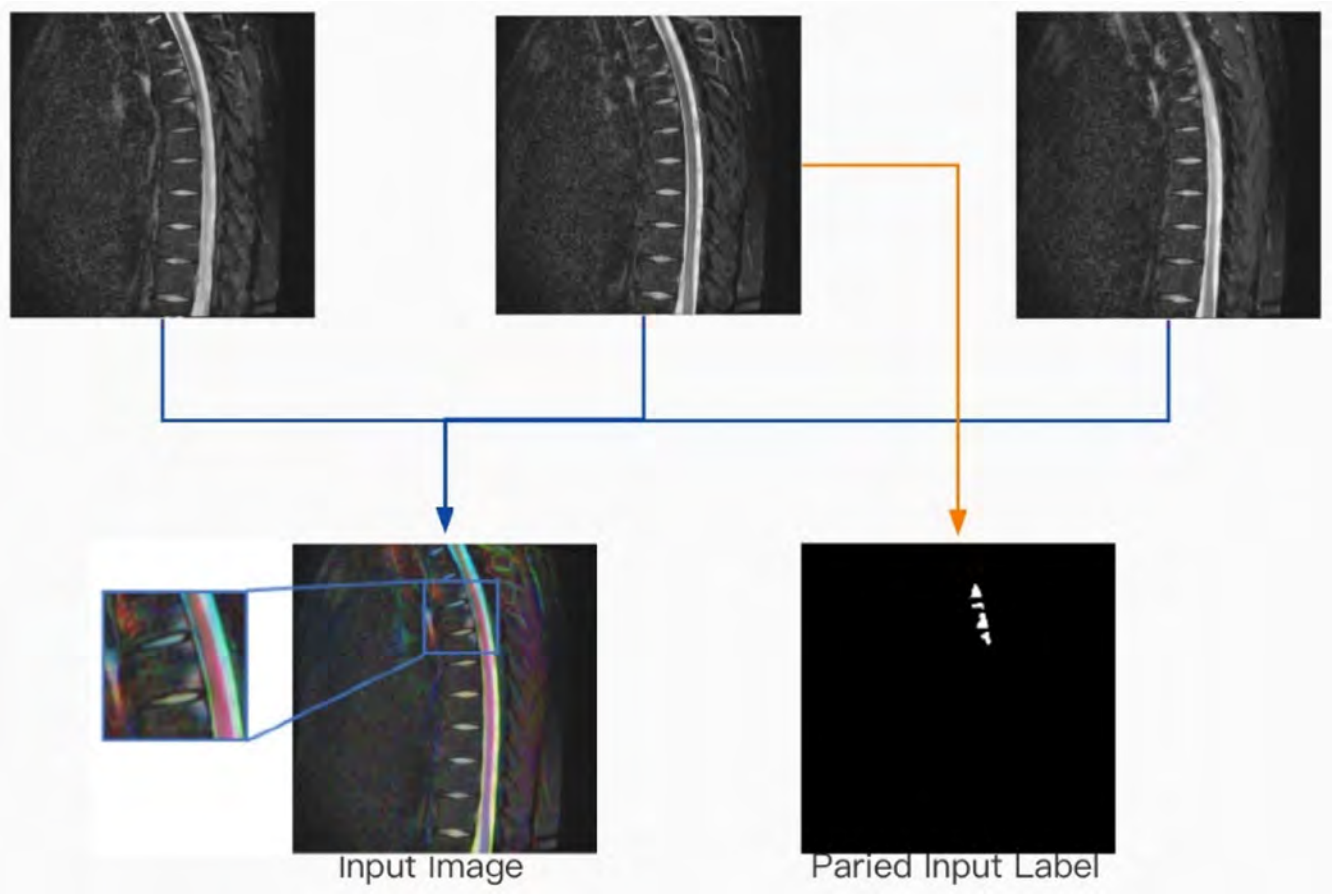

Figure 1: The process of the generation of a 'fake-color' input image and the paired input label. The Blue arrow points to the 'fake-color' image. The orange arrow points to the original image. The blue box shows the zoom-in view.

Methods: A total 330 patients with axial spondyloarthritis (SpA) were recruited. STIR MRI of the whole spine and clinical data were obtained. Spinal inflammation was defined by the presence of an active inflammatory lesion on the STIR sequence. Regions of interests (ROIs) were drawn outlining the active inflammatory lesion. 'Fake-color' images were constructed to mimic adjacent MRI slices (figure 1). Images from 270 patients and 60 patients were separated into the training/validation and testing sets, respectively (table 1). Deep learning algorithms were developed using attention-Unet. The performance of the neural network was compared to the image interpretation by a general radiologist blinded to the ground truth.

Table 1: Baseline characteristics of the training and validation cohort.

Table 1: Baseline characteristics of the training and validation cohort

	Training cohort (N=270)	Validation cohort (N=60)	p-value
Age	44.6±17.8	45.6±14.0	0.323
Male sex	**174/270 (64.4%)**	**27/60 (45.0%)**	**0.005**
Chinese	264/270 (97.8%)	60/60 (100%)	0.244
Age of onset	31.6±12.9	33.3±14.4	0.202
Back pain duration	14.0±14.6	12.4±11.3	0.210
Smoker	88/267 (33.0%)	13/59 (22.0%)	0.101
Drinker	30/261 (11.5%)	6/56 (10.7%)	0.924
HLA-B27	195/252 (77.4%)	34/62 (65.4%)	0.068
CRP	0.89±1.90	1.42±3.62	0.140
ESR	31.6±23.8	34.9±27.0	0.198
BASDAI	4.7±2.2	4.7±2.2	0.398
BASFI	3.0±2.4	3.0±2.4	0.278
Sulphasalazine	62/263 (23.6%)	13/59 (22.0%)	0.800
Other csDMARDs	32/265 (12.1%)	9/60 (15.0%)	0.538

CRP= C-reactive protein; ESR = erythrocyte sedimentation rate; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index (BASDA); BASFI = Bath Ankylosing Spondylitis Functional Index (BASFI); csDMARDs = conventional synthetic disease-modifying anti-rheumatic drugs.

Table 2: Sensitivity and specificity of deep neural network and radiologist in image level and individual spinal vertebral part.

Table 2. Sensitivity and specificity of deep neural network and radiologist in image level and of individual spinal vertebral part

	Radiologist	
	Sensitivity	Specificity
Level of image	0.82	0.87
Level of individual spinal vertebral part	0.87	0.70
	Deep neural network	
	Sensitivity	Specificity
Level of image	0.80+/-0.03	0.88+/-0.02
Level of individual spinal vertebral part	0.85+/-0.04	0.73+/-0.03
	Deep neural network in individual spinal segment	
	Sensitivity	Specificity
Cervical vertebra	0.75+/-0.02	0.81+/-0.02
Thoracic vertebra	0.91+/-0.04	0.62+/-0.04
Lumbar vertebra	0.82+/-0.03	0.74+/-0.02

Results: Active inflammatory lesions were identified in 2891 MR images and were absent in 14590 MR images. The sensitivity and specificity of the derived deep neural network were 0.80±0.03 and 0.88±0.02, respectively. The Dice coefficient of the truth-positive lesions was 0.55±0.02. The area under the curve of the receiver operating characteristic (AUC-ROC) curve of the algorithm was 0.87±0.02. The performance of the developed deep neural network was comparable to the interpretation of a general radiologist with similar sensitivity and specificity (table 2).

Conclusion: A deep neural network was developed to detect spinal inflammation in axial SpA with performance comparable to a general radiologist.

Disclosure: S. Chan: None; **Y. Lin**: None; **H. Chung**: Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Pfizer, 6; **K. Lee**: None; **P. Cao**: None.

Abstract Number: 1399

Trends in Proportionate Cardiovascular Mortality in Patients with Ankylosing Spondylitis in the Era of Biologic Therapies: Analysis of US Death Certificate Data

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing Spondylitis (AS) is associated with an increased risk of cardiovascular disease, partly due to systemic inflammation, and an increased risk of vascular mortality. Since the late 1990s, biologic and targeted therapies have improved outcomes in immune-mediated inflammatory diseases. We sought to investigate cardiovascular mortality trends in AS in the USA in the era of biologic therapies.

Methods: This retrospective cohort study used the Multiple Cause of Death files maintained by the National Center for Health Statistics. The data set contains death certificates for US residents, in which the underlying cause of death is ascertained by the treating physician in the section on the cause of death on the certificate. Each certificate identifies demographic information, a single underlying cause of death, and up to 20 additional contributory causes of death. We investigated temporal trends of proportionate cardiovascular mortality, defined as the number of cardiovascular deaths (the underlying cause of death: International Classification of Diseases, version 10 [ICD10]: I00-I99), divided by the number of all-cause mortality, in patients with AS (defined in multiple causes of death: ICD10 code M45) between 1999 and 2020. Spearman's correlation test was used for trend analysis, and the Chi-square test was used for comparisons.

Results: 4,405 deaths in subjects with AS occurred during the study period, with an age-adjusted mortality rate of 7 per 10 million people. Overall, 984 (22%) died of cardiovascular causes. The mean age of cardiovascular mortality was 73 years. The proportionate cardiovascular mortality decreased from 34% in 1999 to 21% in 2020 (trend P< 0.001), Figure 1. Proportionate cardiovascular mortality was similar in men and women (23% vs. 20%, P=0.08) and in Black and White individuals

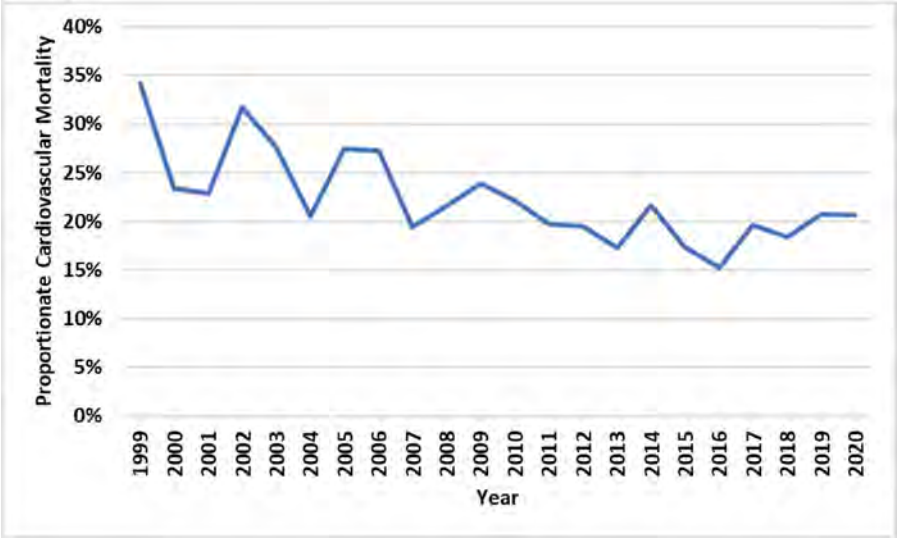

Figure 1. Proportionate Cardiovascular Mortality in Ankylosing Spondylitis from 1999 to 2020

(25% vs. 22%, P=0.47). The most common cardiovascular causes were ischemic heart disease (51%), hypertension and its sequelae (12%), heart failure (7%), stroke (5%), arrhythmia (4%), aortic valve disease (3%), and others (16%).

Conclusion: This national study of death certificate data showed a significant reduction in proportionate cardiovascular mortality in AS in the USA in the era of biologic and targeted therapies. Mechanistic prospective cohort studies are needed to understand the impact of biological therapies on cardiovascular risk in AS.

Disclosure: A. Daoud: None; **S. Al-Kindi**: None; **M. Magrey**: AbbVie, 2, Bristol Myers Squibb, 2, Eli Lilly, 2, Novartis, 2, Pfizer Inc, 2, UCB, 5.

Abstract Number: 1400

Achieving ASDAS Inactive Disease Status in Axial Spondyloarthritis: A Systematic Review and Meta-analysis

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SESSION INFORMATION

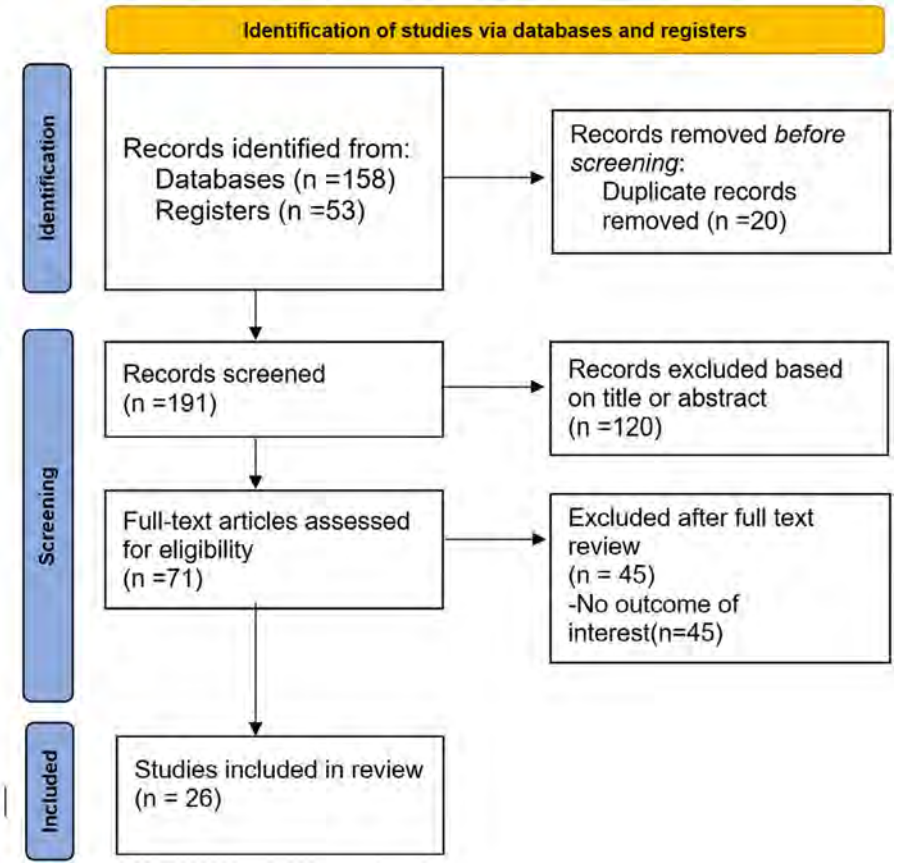
Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: ASDAS-CRP is a composite score that measures disease activity in axial spondyloarthritis (axSpA) and is based on patient-reported outcomes and objective measures of inflammation. An ASDAS-CRP score of < 1.3 indicates inactive disease in axSpA clinical trials and is considered equivalent to clinical remission. We hypothesized that achieving ASDAS-CRP< 1.3 is not feasible in clinical practice. We aimed to evaluate the proportion of patients achieving inactive disease compared to low disease activity (ASDAS< 2.1) with axSpA.



PRISMA Flow chart

Methods: Our PICO question was what proportion of patients with axSpA could reach inactive disease status compared to low disease activity in the treatment group in clinical trials with Biologics and targeted disease-modifying agents. A comprehensive literature search was conducted using electronic databases, including PubMed, Embase, and Cochrane Library, and screening the EU clinical trial registry to identify relevant studies published until May 2023. Clinical trials reporting inactive disease and low disease activity were included. The studies included patients with both radiographic and non-radiographic axSpA treated with different biologic therapies (TNF-i, IL-17-i, JAK-i). The risk of bias was assessed using the Cochrane risk of bias tool. Two independent reviewers screened the articles, and the senior author did conflict resolution. Data were extracted and analyzed using forest plot to compare odds ratios (95% CI). Study heterogeneity was assessed using I^2. All analyses were performed using R Statistical Software meta package (v4.2.1; R Core Team 2022).

Results: Twenty-six clinic trials (randomized and open-label extensions) were identified (PRISMA flow chart attached) with 5024 patients included in the meta-analysis. The proportion of patients reaching inactive disease status in the treatment group at 12-24 weeks was 18% (95% CI:0.16-0.19), and at 52-104 was 24% (95% CI: 0.23-0.26). (Figures 1A and 1B). The odds of achieving inactive disease was 0.28 compared to low disease activity in the treatment group (95% CI 0.22-0.34) (Figure 2A)

Conclusion: The proportion of patients with axSpA achieving inactive disease status was low, suggesting that achieving inactive disease status may be an overarching goal. Hence the definition of clinical remission may need to be revisited with a more feasible outcome.

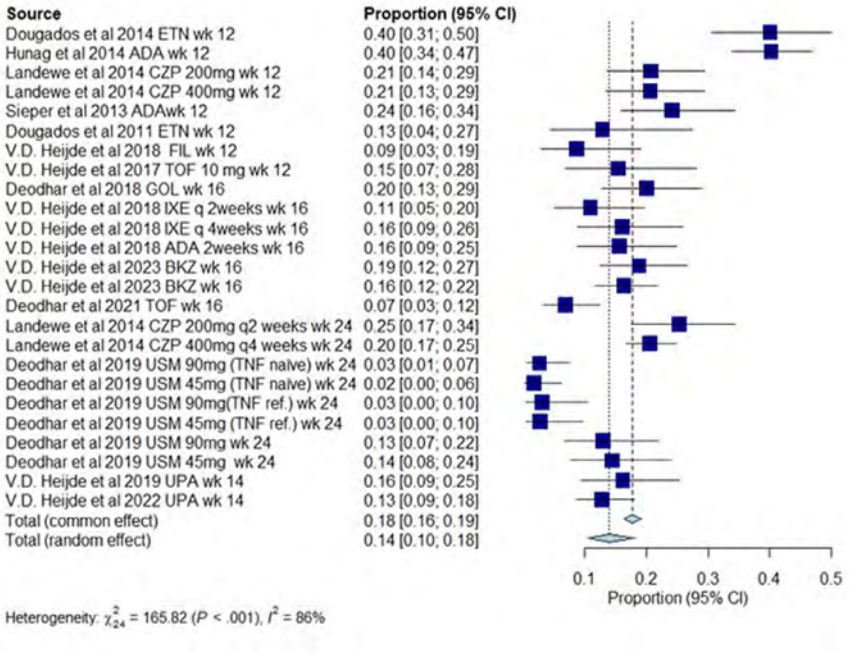


Figure 1A.

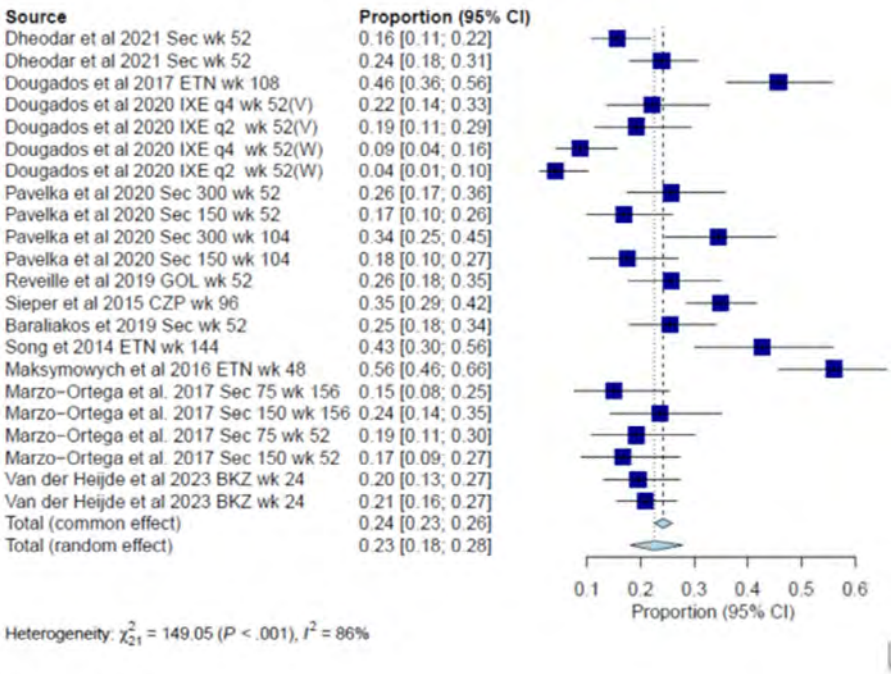


Figure 1B.

Figure 1A. Overall rate of inactive disease in the intervention group in studies ranging from 12-24 Figure 1B. Overall rate of inactive disease in the intervention group in studies ranging from 52-104 weeks

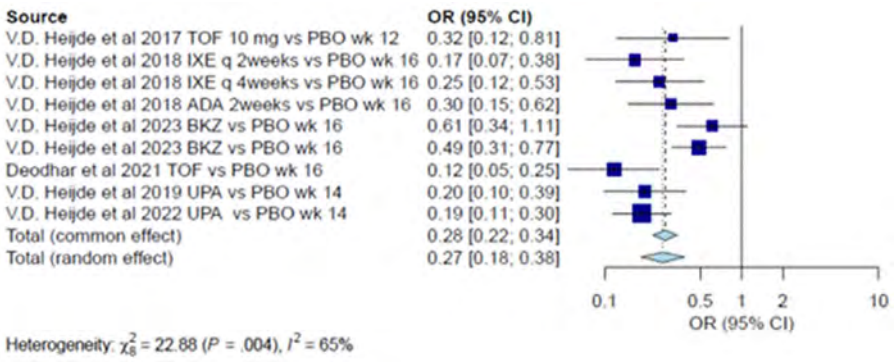


Figure 2A Odds of achieving inactive disease compared to low disease activity in intervention group. All studies including both ASDAS<1.3 and ASDAS<2.1 as outcomes.

Disclosure: S. Abi Doumeth: None; **O. Pamuk**: None; **M. Magrey**: AbbVie, 2, Bristol Myers Squibb, 2, Eli Lilly, 2, Novartis, 2, Pfizer Inc, 2, UCB, 5.

Abstract Number: 1401

The Association of 3VAS/4VAS and DAPSA with Radiographic Progression in Early PsA

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: A feasible, widely accepted, comprehensive disease activity measure is needed for daily use in psoriatic arthritis (PsA). Current measures are either complex (Psoriatic Arthritis Disease Activity Score (PASDAS) and strict (Minimal Disease Activity ((MDA)) for use in daily practice or only joint-oriented (DAPSA). To address this, the 3-item VAS (3VAS) and 4-item VAS (4VAS) were developed. This study investigates the association between 3VAS/4VAS and radiographic progression in early PsA patients. Our aim is to evaluate 3VAS/4VAS having association in terms of radiographic progression over 3 years in early PsA.

Methods: Data were from the DEPAR study which consists of newly diagnosed PsA patients. Radiographic changes were graded with the modified Total Sharp Score (mTSS) for PsA chronologically by two independent assessors. The radiographic progression was defined as a change in mTSS >0.7 (SDC) at any time in 3 years of follow-up. The 3VAS consists of a physician's global VAS, the patient global VAS, and the patient skin VAS. The 4VAS has comprised of a physician global VAS, patient pain VAS, patient joint VAS, and patient skin VAS. Reaching low disease activity (LDA) at 6 months was

Table 1: Baseline Characteristics of Groups

	Non-Progressive Group (n:405)	Progressive Group (n:71)	p-value
BASELINE CHARACTERISTICS			
Age (mean (S.D))	49 (13)	59 (12)	**0.000**
Gender (Female)(%)	51%	52%	0.907
Symptom duration (median(IQR))	9 (4-28)	10 (4-32)	0.190
Body mass index (mean (S.D))	28 (5)	28 (5)	0.247
DISEASE ACTIVITY SCORES			
Baseline 3VAS (mean (S.D))	3.58 (1.85)	3.48 (1.70)	0.449
Baseline 4VAS (mean (S.D))	4.01 (1.84)	3.72 (1.52)	0.151
Baseline DAPSA (mean (S.D))	19.08 (11.5)	19.87 (10.1)	0.488
RADIOGRAPHIC ASSESSMENT			
Baseline mTSS (median(IQR))	0 (0-0)	16 (1-36)	**0.000**
Baseline JSN (median(IQR))	0 (0-0)	7 (1-19)	**0.000**
Baseline Erosion score (median(IQR))	0 (0-0)	5 (0-25)	**0.000**

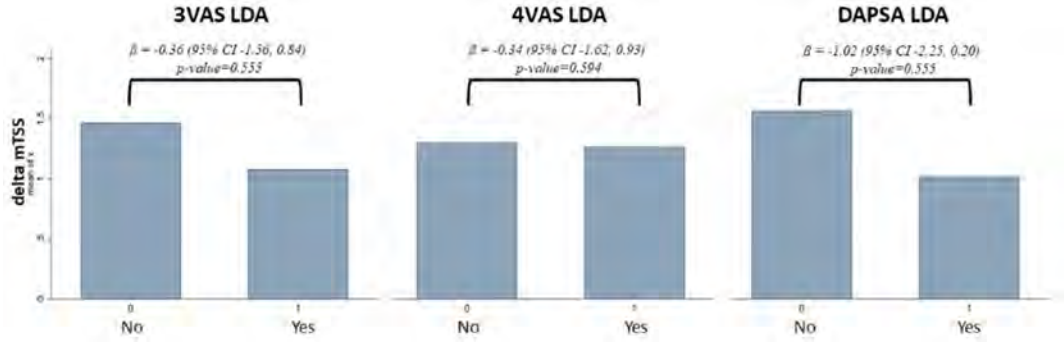

Figure 1. Predicted change in mTSS values over 3 years according to the achievement of LDA at 6 months with GLM results.

determined as 3VAS(< 2.4), 4VAS(< 2.8), and DAPSA (≤14). Comparisons between groups were made by Student's t-test, chi-squared test, or ANOVA. The generalized linear model (GLM) and the Generalized Linear Mix Model (GLMM with a sub-type of negative binomial regression analysis) were adjusted for baseline determinants(age, gender, time (visit time), mTSS, CRP, and biological use at any time point).

Results: In comparing the two groups, a total of 476 patients were included, with 71 patients in the progressive group and 405 patients in the non-progressive group (Table 1). During the first 2-year period, the non-progressive and progressive groups showed similar patterns in terms of disease activity scores. However, in the 2nd year, there was a notable change: the progressive group surpassed the non-progressive group in terms of 3VAS, 4VAS, and DAPSA levels (at 3rd year non-prog. vs prog. (mean(S.D.)); 3VAS: 1.75(1.62) vs 2.17(1.64), 4VAS: 2.03(1.76) vs 2.40(2.00), DAPSA: 7.58(5.88) vs 10.4 (9.30)) (Figure 2).

Even though patients who achieved LDA according to 3VAS, 4VAS, and DAPSA at 6 months had fewer radiographic changes in 3 years, there were no found significant differences (Figure 1).

For longitudinal analysis, 1.758 mTS scores were included from 4 different time points. The generalized linear mixed-effects model showed that there was no significant association between 3VAS/4VAS or DAPSA levels and radiographic changes over time (Figure 2).

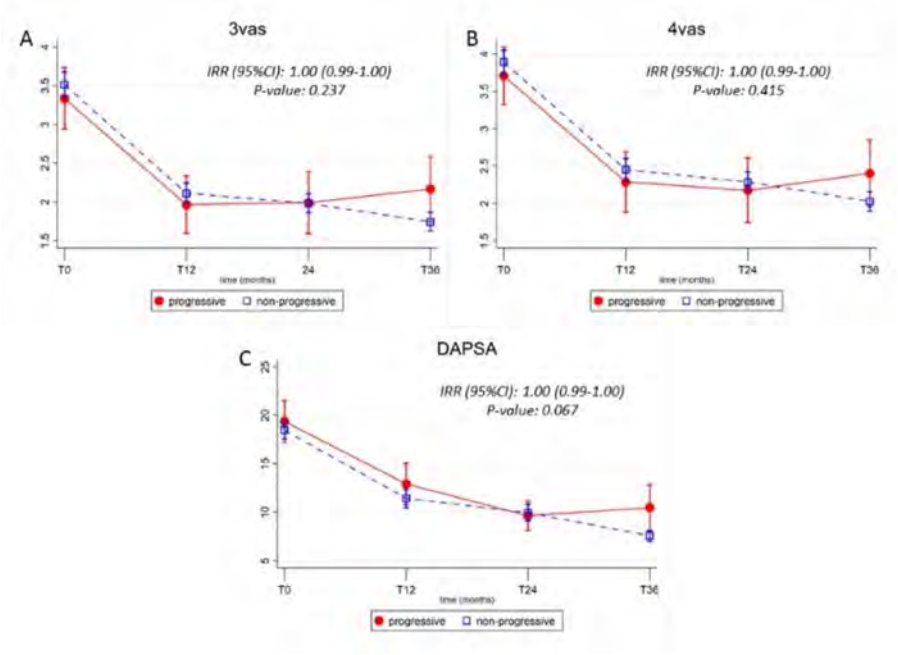

Figure 2. Observed means of A.3VAS, B.4VAS, and C.DAPSA over 3 years according to radiographic progression with GLMM results.

Conclusion: No significant association was observed between the 3VAS and 4VAS measures and radiographic damage in our longitudinal real-world cohort of early PsA patients. This lack of association is likely attributed to the relatively low radiographic progression observed in this cohort rather than being solely influenced by the measures themselves. Furthermore, the articular-oriented measure DAPSA also exhibited no significant association with radiographic damage in early PsA patients.

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Abstract Number: 1402

Exceeding Activity Targets but Missing the Mark with Sleep: Mapping 24-Hour Movement Guidelines in Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: The Canadian 24-Hour Movement Guidelines were recently published in 2022 and integrate evidence-based targets for physical activity, sleep and sedentary behaviours, with recommendations regarding duration, intensity and quality of each activity to achieve health outcomes in adults aged 18-64 years. The purpose of this study was to determine if patients diagnosed with axial spondyloarthritis (axSpA) are meeting these guidelines. The specific objectives were to: 1) profile moderate-vigorous physical activity (MVPA); 2) profile sedentary behaviours and sleep patterns and 3) evaluate discrepancy between objective and subjective measures of activity and sleep.

Methods: Participants with axSpA (meeting ASAS criteria) attending an urban academic rheumatology clinic were provided a wrist-mounted accelerometer, worn for 24 hours over a consecutive 7-day period. The average data validated for a 75% wear-time was used for analysis and included time spent in MVPA per week; time spent in sedentary activity per 24 hours, and sleep/wake duration per 24 hours. Participants completed the International Physical Activity Questionnaire to measure subjective physical activity engagement and a 7-day sleep log to subjectively evaluate sleep quality. Univariate statistics were used to create profiles aligned with the guideline's core recommendations.

Results: Out of 41 people with axSpA who participated in the study, 37 (90%) had validated accelerometer data.Most participants were male (56.7%); mean age of 46.0 years (SD 12.6); mean disease duration 23.9 years (SD 11.4); mean Bath Ankylosing Spondylitis Disease Activity Index was 3.2 (SD.1); mean Bath Ankylosing Spondylitis Functional Index was 2.6 (SD 2.2). 35.1% had a history of peripheral joint involvement; 56.7% were receiving biologic treatment; 51.3% were receiving non-steroidal anti-inflammatories.All of the cohort met the MVPA targets of a minimum of 150 minutes of MVPA per week (mean 978.5 minutes, SD 387.9) and sedentary behaviour limits of no more than 8 hours daily (mean 5.0 hours, SD 0.9).Only 37.8% of participants met the sleep target of 7 to 9 hours of sleep (mean 6.4 hours, SD 2.0), with multiple disruptions per sleep period (mean 17.7, SD 7.1), indicating poor sleep quality. Participants tended to underestimate their subjective engagement in physical activity and overestimate sleep quality.

Conclusion: The results of this study suggest people with axSpA are highly engaged in physical activity and demonstrate minimal sedentary behaviour, both which exceed recommended activity guidelines. These results are considerably higher when compared to the literature. There is discrepancy between subjective and objective measures of activity and sleep.-Sleep quantity and quality are of significant concern, with few people with axSpA meeting recommended targets.Further study that examines sleep-wake patterns, understanding of sleep physiology in this patient population and potential management strategies are recommended to address sleep deficiency in people with axSpA.

Disclosure: L. Passalent: AbbVie/Abbott, 6, Novartis, 6, UCB, 2, 5; **T. Ko**: None; **Y. Deng**: None; **S. Mathur**: None; **M. Abovsky**: None; **I. Jurisica**: None; **N. Haroon**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, UCB Pharma, 2; **R. Inman**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Sandoz, 2.

Abstract Number: 1403

MRI-defined Sacroiliitis in First Degree Relatives of Ankylosing Spondylitis Patients

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS

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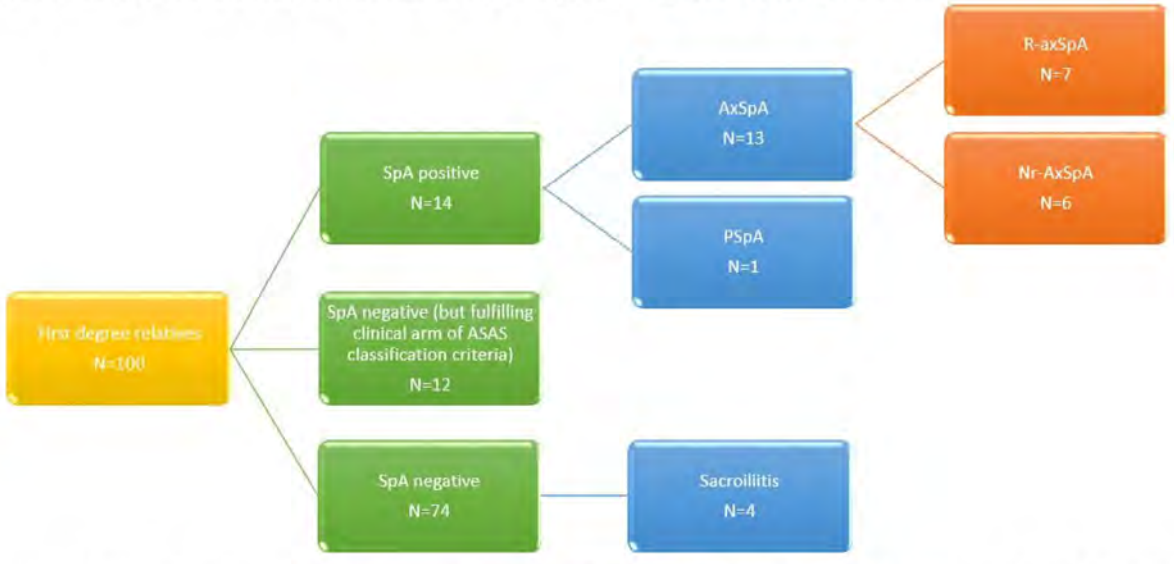
Session Time: 9:00AM–11:00AM

Background/Purpose: Sacroiliitis is a main radiographic finding in axial spondyloarthritis (axSpA) - the inflammatory rheumatic disease with a strong genetic background. The aim of this study was to evaluate the presence of sacroiliitis in first-degree relatives of patients with ankylosing spondylitis (AS) and to determine fulfilment of Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axial and/or peripheral spondyloarthritis (SpA), and the clinical diagnosis of SpA.

Methods: One hundred subjects without a previous rheumatological diagnosis with a first-degree relative treated for AS were included in the study. Clinical data were collected and rheumatological examinations were performed by trained rheumatologists. Magnetic resonance imaging (MRI) of the sacroiliac joints (SIJ) was read by a trained rheumatologist who was blinded to all patient data. Subjects were further divided into both SpA (according to ASAS classification criteria and clinician opinion) and non-SpA subgroups.

Image 1: Distribution of the first degree relatives according to the diagnosis of spondyloarthritis



Abbreviations: N, Number; SpA, Spondyloarthritis; ASAS, The Assessment of SpondyloArthritis international Society; AxSpA, Axial SpA; PSpA, Peripheral SpA, R-axSpA, Radiographic AxSpA; Nr-axSpA, Non-radiographic axSpA

Distribution of the first degree relatives according to the diagnosis of spondyloarthritis

Table 1: Patient characteristics and subsets differences

Characteristic	All N=100	SpA n=14	Non-SpA n=74	P SpA vs non-SpA
Age (years), *mean (SD)*	34.4 (11.3)	36.5 (10.5)	33.7 (11.4)	0.2956
Gender: Males, *number (%)*	54	7 (50)	40 (54)	>0.9999
BMI (kg/m2), *mean (SD)*	28.8 (38.9)	24.8 (4.9)	30.2 (45.1)	0.7069
BASDAI, mean (SD)	2.0 (1.8)	3.1 (1.8)	1.76 (1.78)	0.0054*
CRP (mg/L), *mean (SD)*	3.4 (6.0)	8.8 (10.5)	2.3 (4.1)	0.0048*
BP, *number (%)*	74	14 (100)	48 (65)	0.0082*
IBP, *number (%)*	25	8 (57)	7 (9)	0.0002*
Smokers, *number (%)*	44	7 (50)	20 (27)	0.1185
Spinal distances: Schober *(cm), mean (SD)*	4.8 (1.2)	4.5 (0.9)	4.9 (1.2)	0.276
chin-chest *(cm), mean (SD)*	0.5 (1.4)	0.6 (2.9)	0.4 (1.0)	0.0714
fléche *(cm), mean (SD)*	0.2 (1.0)	0.6 (1.6)	0.1 (1.0)	0.0873
chest expansion *(cm), mean (SD)*	5.4 (1.7)	6.0 (2.0)	5.3 (1.7)	0.2773
HLA-B27 positivity, *number (%)*	56	12 (86)	32 (43)	0.0069*

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, Body mass index; BP, back pain; CRP, C-reactive protein; HLA, human leukocyte antigen; IBP, inflammatory back pain, * P value < 0.05

Patient characteristics and subsets differences

Results: We detected active sacroiliitis defined by MRI in 13 subjects who were further diagnosed with axSpA, 7 (54%) of whom already had advanced radiographic changes on conventional radiographs of the sacroiliac joints. In addition, active sacroiliitis was also present in 4 individuals who did not have back pain. The data are shown in Figure 1. A total of 26 subjects met ASAS classification criteria for SpA, of which the diagnosis of SpA was confirmed in 14 subjects (13 subjects met ASAS classification criteria for axial and 1 subject for peripheral SpA). In addition, 12 individuals met the clinical arm of the ASAS classification criteria for axSpA, but were not diagnosed with axSpA in the clinicians' opinion. Analysis of clinical characteristics showed a significant difference in CRP and BASDAI between the SpA vs. non-SpA subgroups (8.8 (±10.5) vs. 2.3 (±4.1) mg/l, p=0.0048, and 3.1 (±1.8) vs. 1.76 (±1.78), respectively). Individuals diagnosed with SpA were more likely to be HLA-B27 positive and had inflammatory back pain compared to the non-SpA subgroup (87% vs. 43%, p=0.0069 and 57% vs. 9%, p=0.0002, respectively). Individuals who were not diagnosed with SpA but met the clinical arm of the ASAS classification criteria for axSpA were excluded from the analysis. Other clinical characteristics and differences between subgroups are shown in Table 1.

Conclusion: In this cross-sectional study, 17% of first degree relatives of patients with AS had MRI- defined sacroiliitis, however not all of them were diagnosed with SpA due to the absence of back pain. A quarter of the subjects with first-degree AS relative met the classification criteria for SpA, and 14% were diagnosed with SpA based on physician opinion.

Disclosure: K. Bubova: None; **L. Hasikova**: None; **K. Mintalova**: None; **M. Gregova**: None; **S. Forejtova**: None; **L. Senolt**: None; **K. Pavelka**: Abbvie, 2, 6, Amgen, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Egis, 2, 6, MSD, 2, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 6.

Abstract Number: 1404

Factor H-related protein-5 Exacerbates Pathological Bone Formation of Ankylosing Spondylitis

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SESSION INFORMATION
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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The complement factor H-related protein-5 (FHR-5), a member of the human factor H protein family, enhances complement activation. The influence of complement activation on bone and joint was recognized in bone fracture healing, arthritis, and osteomyelitis. Recently, FHR-5 has been linked to eye, kidney, infection, cancer and autoimmune diseases. FHR-5 was also significantly up-regulated in proteomic analysis of serum and synovial fluid for ankylosing spondylitis (AS). Hence, we aimed to evaluate whether FHR-5 exacerbates bone inflammation and ectopic formation of AS.

Methods: The study included 65 patients with AS and 25 healthy controls (HC). Collected sera were divided into three groups according to HC, two AS groups (low CRP and high CRP) based on the CRP 0.8. Human TNF, IL6, IL-17, IL-23, and FHR-5 in three groups were measured with ELISA and human FHR-5 levels were compared to TNF, IL-6, IL-17, and IL-23 levels. In addition, soluble FHR-5 proteins were administered with Curdlan-injected SKG mice 2 time for a week and monitored for 5 weeks *In vivo* model. Foot and ankle were evaluated by micro-CT, Hematoxylin and Eosin for histological observation, and Safranin O for cartilages. Moreover, these finding were further assessed in the AS-osteoprogenitor In vitro model.

Results: In consistent with human data, proinflammatory cytokines (TNF, IL-6, IL-17A, and IL-23) and FHR-5 were elevated in AS group compared to HC group. FHR-5 levels were not significantly correlated with proinflammatory cytokines, whereas FHR-5 levels in AS were only positively correlated with the high CRP group. Notably, treatment with soluble FHR-5 has no effect on clinical arthritis scores and thickness at hindpaw in Curdlan-injected SKG, but significantly increased the ectopic bone formation at the calcaneus and tibia bones of ankle as revealed by micro-CT image and quantification. Basal FHR-5 expression was upregulated in AS-osteoprogenitors compared to control cells. Also, treatment with FHR-5 remarkedly induced bone mineralization status of AS-osteoprogenitors during osteogenic differentiation accompanied by MMP13 expression.

Conclusion: We provide the first evidence demonstrating that FHR-5 can exacerbate pathological bone formation of AS. Therapeutic modulation of FHR-5 could be promising for future treatment of AS.

Disclosure: C. Son: None; **J. Lee**: None; **S. Jo**: None; **T. Kim**: None.

Abstract Number: 1405

Diagnostic Delay of Axial Spondyloarthritis in African American Patients

John Byun[1], Hans Vitzthum von Eckstaedt[1], Kichul Ko[2] and Reem Jan[1], [1]University of Chicago, Chicago, IL, [2]The University of Chicago, Chicago, IL

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS
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Background/Purpose: The identification of axial spondyloarthritis (axSpA) remains challenging. The initial presentation is not always immediately apparent as an inflammatory disease, potentially leading to years of delay in diagnosis. Our hypothesis is that the delay is worse in African American (AA) patients who have a lower disease prevalence of axSpA and lower

frequency of HLA-B27 positivity compared to other racial groups. This retrospective study assessed whether AA patients experience a longer delay in diagnosis from symptom onset to diagnosis of axSpA compared to other ethnic cohorts, and whether they exhibit any significant differences in disease characteristics.

Methods: All adult rheumatology patients evaluated between 2012-2022 with a diagnosis code for ankylosing spondylitis, sacroiliitis, undifferentiated spondyloarthritis, or inflammatory back pain were enrolled. Variables collected include age at diagnosis (years, yrs), time to diagnosis (months, m), ethnicity, sex, HLA-B27 status, CRP at diagnosis (mg/L), history of IBD, psoriasis, uveitis, and family history of axSpA. All enrolled subjects had to have radiographic and/or MRI evidence of sacroiliitis. Fisher's exact test and Mann-Whitney test were performed to compare categorical variables and non-parametric continuous variables respectively, and a multivariate logistic regression analysis was performed to identify independently associated variables with studied outcomes.

Results: 29 AA and 100 sex-matched non-AA subjects were enrolled. The median time to diagnosis from symptom onset was similar at 36 m for both groups. The AA group was older at diagnosis (median 38 yrs [interquartile range {IQR} 26 – 48 yrs] vs 29 years [IQR 23 – 37 yrs], p = 0.03) with higher CRP (15 mg/L [IQR 6 – 32 mg/L] vs 4 mg/L [IQR 2 – 10.5 mg/L], p = 0.001), and lower HLA-B27 positivity rate (36.8% vs 70.5%, p = 0.008). Due to the difference in age at diagnosis, subjects diagnosed at 45 years of age or older were compared to those diagnosed at a younger age. Those diagnosed at an older age had higher proportions of AA subjects (42.3% vs 17.5%, p = 0.015) and HLA-B27 positivity (70.4% vs 31.2%, p = 0.004). A multivariate logistic regression analysis showed that older age at diagnosis (≥45 yrs) was associated with negative HLA-B27 (Odds Ratio [OR] 5.94, 95% Confidence Interval [CI] 0.52 – 7.61) but not with ethnicity. It was also linked to time to diagnosis but the effect was minimal (OR 1.01, CI 1.004 – 1.017).

Conclusion: The time to diagnosis was similar between AA and non-AA groups. However, AA subjects were statistically older at diagnosis; whether this implies a delay in diagnosis or a different disease phenotype is not clear. In addition, AA subjects had a statistically higher degree of CRP elevation and lower HLA-B27 positivity rates. Through a multivariate analysis, older age at diagnosis was associated with negative HLA-B27, and this effect negated the relationship between race and age of diagnosis. Further research is needed to understand the interplay between CRP levels, HLA-B27 positivity and race in terms of disease characteristics vs delay in diagnosis.

Disclosure: J. Byun: None; **H. Vitzthum von Eckstaedt**: None; **K. Ko**: Aurinia Pharmaceuticals, 1; **R. Jan**: Janssen, 6.

Abstract Number: 1406

Temporal Trends in Cardiovascular Events in Axial Spondyloarthritis Patients with Medicare Insurance versus Commercial Insurance: An Analysis Using Claims Data

Rouhin Sen[1], Justin Leach[1], Maria I. (\"Maio\") Danila[2], Fenglong Xie[1], Jasvinder Singh[1], Liron Caplan[3], Iris Navarro-Millán[4] and Jeffrey Curtis[1], [1]University of Alabama at Birmingham, Birmingham, AL, [2]University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL, [3]Rocky Mountain Regional VAMC, Aurora, CO, [4]Weill Cornell Medicine, Hospital for Special Surgery, New York, NY

SESSION INFORMATION

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Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: AS is an inflammatory disorder of the axial skeleton and can cause complications including disabling joint damage. Nearly 20% of people with AS are on Medicare disability insurance[1]. Major adverse cardiovascular events (MACE) are the leading cause of death in AS[2]. Despite the high prevalence of disability in AS, these patients are understudied[1] and may be different than similarly aged commercially insured patients. We sought to compare MACE incidence temporal trends in AS patients who are beneficiaries of Medicare disability insurance against those with commercial insurance in order to understand the excess risk for CVD events in disabled patients.

Methods: We conducted a retrospective longitudinal analysis from 2007-2019 using the Medicare Fee-for-Service and MarketScan claims databases. Subjects were identified by having ≥ 2 AS International Classification of Diseases (ICD)-9/10 diagnosis codes in outpatient visits with age between 18 and 64 years. MACE was defined as an incident hospitalized myocardial infarction or ischemic stroke and identified by validated ICD 9/10 diagnosis codes. Patients with prior MACE were excluded[3]. We reported demographics, cumulative raw incidence/1000 person and determined incidence rate ratios for disabled Medicare enrollees versus commercially insured AS patients. We displayed incidence trends and calculated yearly annual percentage change (APC) based off end-of-year cutpoints; significance was determined using the Monte Carlo Permutations method. SAS v9.4 and Joinpoint Trend Analysis v5.0 software were used for analyses; $p < 0.05$ determined statistical significance.

Results: The total number of AS patients eligible for analysis was 1,097,297 from Medicare and 2,258,212 from MarketScan. Incident MACE was identified in 10,494 subjects in Medicare and 8,860 individuals in MarketScan. The mean age in years at which MACE occurred was 54.8 and 53.3 in patients with Medicare and MarketScan, respectively. Most patients

Table 1. Demographic information of AS patients < 65 years of age with incident MACE enrolled in Medicare and MarketScan (commercial/private insurance).

		Disabled Medicare	Commercially insured
Age in years (mean, SD)	at incident MACE	54.78 (6.96)	53.18 (8.23)
Female, n (%)		6,158 (58.68)	5,069 (58.40)
Race, n (%)			
	American Indian	88 (0.84%)	0
	Asian	77 (0.73%)	0
	Black	1,676 (15.97%)	496 (5.71%)
	White	7,939 (75.65%)	1,471 (16.95%)
	No information	0 (0%)	6,629 (76.37%)
	Unknown	663 (6.32%)	26 (0.30%)
	Other	51 (0.49%)	58 (0.67%)

AS: axial spondyloarthritis; SD: standard deviation; MACE: major adverse cardiovascular events

Table 2. Incidence rate of MACE in AS patients in younger, disabled Medicare enrollees versus commercially insured enrollees

	Medicare with disability			Marketscan			
Year	MACE	Cohort size, n	Incidence/ 1000 pts	MACE	Cohort size, n	Incidence/ 1000 pts	Incidence Rate Ratio
2007	173	16,248	10.65	192	46,059	4.13	2.58
2008	216	21,303	10.14	269	84,078	3.20	3.17
2009	227	24,959	9.09	393	121,547	3.23	2.81
2010	321	31,469	10.20	429	133,959	3.20	3.19
2011	377	39,206	9.62	622	164,243	3.79	2.54
2012	394	50,191	7.85	706	198,094	3.56	2.20
2013	681	83,476	8.16	643	182,431	3.52	2.31
2014	798	104,109	7.67	735	207,062	3.55	2.16
2015	1,165	125,484	9.28	761	198,974	3.82	2.43
2016	1,646	143,532	11.47	1,059	223,774	4.73	2.42
2017	1,708	152,922	11.17	1,035	225,773	4.58	2.44
2018	1,460	154,679	9.44	923	221,919	4.16	2.27
2019	1,328	149,719	8.87	913	224,862	4.06	2.18
Total	10,494	1,097,297	9.56	8,680	2,258,212	3.84	2.49

AS: axial spondyloarthritis; MACE: major adverse cardiovascular events; pts: patients

with MACE were female and White (Table 1). In the disabled Medicare cohort, the incidence of MACE ranged from 7.7-11.5/1000 patients. This cohort showed a significant decrease in incidence from 2007-2014 (-4.1 APC), then a significant increase from 2014-2017 (14.0 APC), then no significant difference from 2017-2019 (Figure 2b). In the MarketScan cohort, the incidence of MACE was between 3.2-4.7/1000 patients and there was a non-significant upward trend (3.4 APC) in the MACE incidence rate (Figure 1c). The incidence rate ratio compared disabled Medicare enrollees with AS to commercially insured AS patients ranged from 2.2-3 (Table 2).

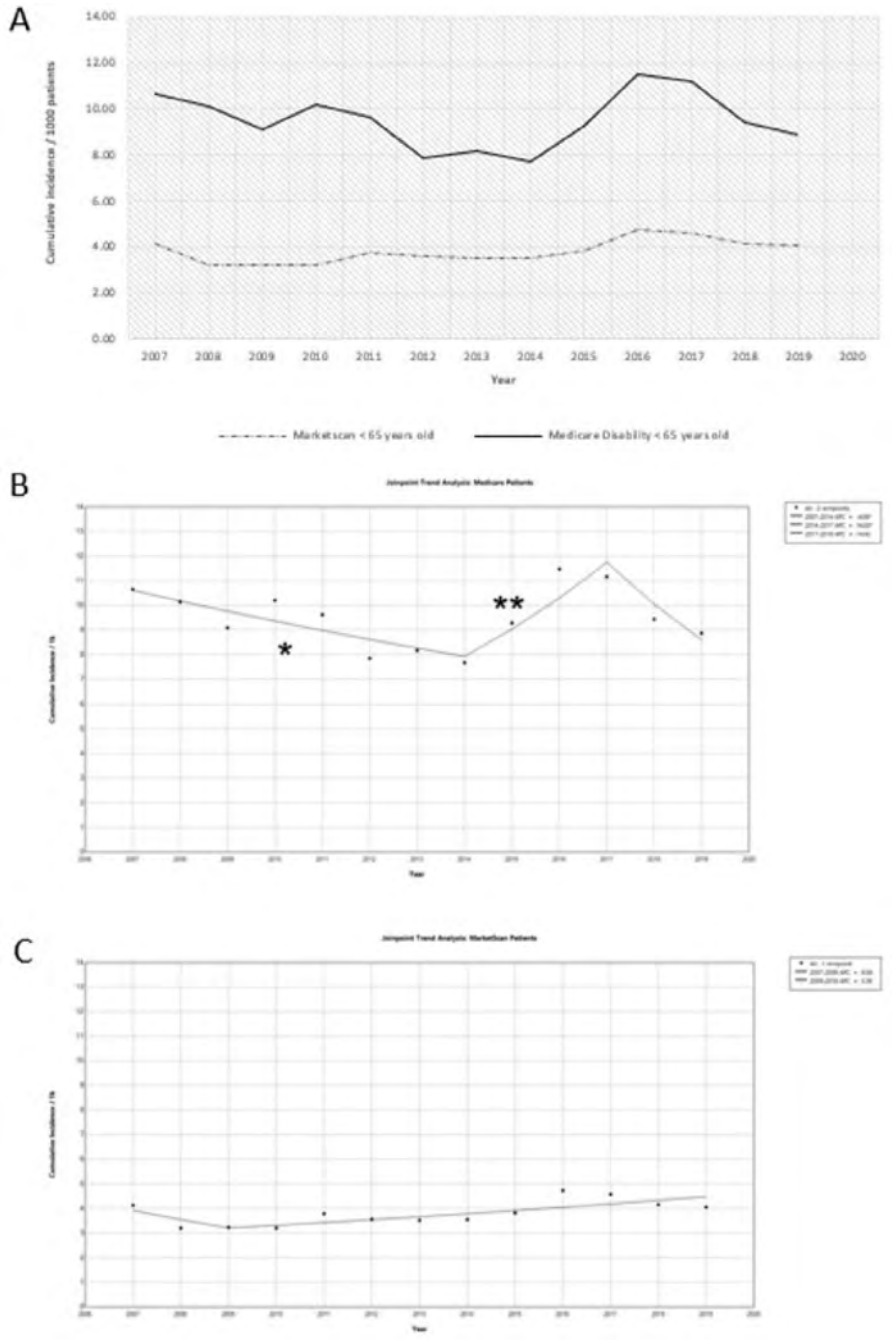

Figure 1. Incidence rate trend of Myocardial infarction and ischemic stroke in AS patients. Panel A: Raw incidence/1000 patients enrolled in Medicare (dark, solid line) versus MarketScan insurance (dashed line). Panel B: JoinPoint analysis of the raw incidence trend for Medicare patients. The single asterisk (*) displayed under the trend line shows a significant decrease in incidence (-4.09 APC) from 2007-2014 while the double asterisk (**) depicts a statistically significant increase in incidence (14.00 APC) from 2017-2019. Panel C JoinPoint analysis of the raw incidence trend for commercially or privately insured MarketScan patients. There was no statistically significant difference in the incidence trend.

Conclusion: Disabled AS patients younger than age 65 years with Medicare experienced a 2-3-fold higher incidence of MACE compared to younger commercially insured patients; unexpectedly, the group of AS patients experiencing MACE events was made up of a high percentage of women. Incidence trend for MACE differed for both groups and did show signs of increase, though not significant. Our future research is to understand why there is a difference between the groups, including differences in the prevalence comorbidities, socioeconomic status, treatment patterns, and healthcare access.

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Abstract Number: 1407

Defining Thresholds of Presenteeism Measures for Unacceptable Work Participation in axSpA

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Presenteeism is associated with lower work satisfaction and future sick leave in axial spondyloarthritis (axSpA). It is generally assessed as a continuous variable; however, despite a lower precision, categorical variables are more meaningful in routine practice.

Table. Optimal thresholds for presenteeism measures and patients correctly classified for unacceptable work status and adverse work outcome at 12 months.

	Optimal threshold (SE/SP)	Correctly classified for unacceptable work status n (%)	Correctly classified for AWO at 12 months n (%)
WPAI presenteeism (0-100)	≥40 (70/86)	283 (83)	215 (76)
QQ method (0-10)	<7 (81/62)	218 (65)	160 (57)
WALS (0-3)	≥0.75 (86/75)	255 (76)	193 (68)
WLQ 25	≥29 (77/80)	266 (79)	201 (71)
BASDAI (0-10)	≥4.7 (81/71)	245 (73)	290 (67)
BASFI (0-10)	≥3.5 (81/67)	232 (69)	185 (66)

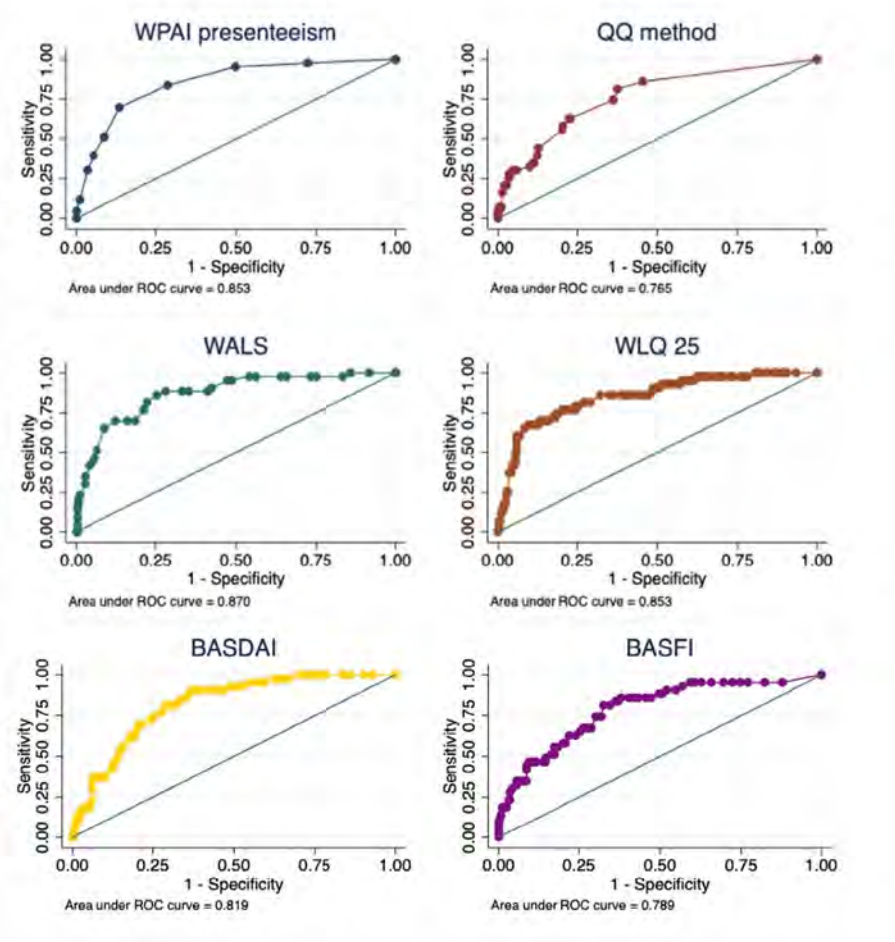
SE, Sensibility; SP, Specificity; AWO, adverse work outcomes.

Our objectives were: 1) To identify thresholds of presenteeism instruments that reflect unacceptable work status in patients with axSpA and whether those thresholds could predict future adverse work outcomes, 2) to compare the performance of these thresholds with thresholds from traditional outcomes for axSpA and 3) to understand whether thresholds are stable across contextual factors.

Methods: We used data from the 1-year multinational prospective study on Patient-Reported Outcomes in Employment Study in Ankylosing Spondylitis (AS-PROSE). Thresholds to determine when patients consider themselves in 'unacceptable work status' were calculated at baseline for 4 presenteeism instruments (Work Productivity and Activity Impairment questionnaire -WPAI-, Quality and Quantity method -QQ-, Workplace Activity Limitations Scale -WALS- and Work Limitations Questionnaire -WLQ 25-); and for BASDAI and BASFI.

We performed receiver operating characteristic (ROC) analysis using as external criteria the Patient Acceptable Work State (PAWS) question 1, addressing ability to perform your current job satisfactorily. We used different approaches (75th percentile, Youden index, Liu method, nearest to 0.1) to determine the optimal cut-off, while balancing over-under diagnosis. Temporal validation was assessed by applying the thresholds in different timepoints. Influence of context (age, gender, nature of work, symptom duration) was explored in subgroup analyses.

Figure. ROC curves for excessive presenteeism and health state from different measurement instruments according to unacceptable work stat



Finally, accuracy of thresholds to predict "future adverse work outcome" throughout 12 months (defined as sick leave or long-term disability) was assessed.

Results: A total of 366 patients were included: 72% males, mean age 43 (SD 10), with a mean symptom duration of 18.2 (11) years. 15% of the patients considered themselves in an unacceptable work status, and 6% had at least one adverse work outcome during the 12 months.

The optimal thresholds of the presenteeism instruments that reflect an unacceptable work status are expressed in the table. BASDAI and BASFI performed similarly to the presenteeism instruments (Figure). Across numerous contextual factors the thresholds were stable, expect for some underdiagnoses among women and persons with a physical loading job by WPAI-, QQ- , BASDAI- and BASFI-thresholds.

The threshold accuracy to predict adverse work outcome over 12 months was similar across all the presenteeism instruments (68-76% of correctly classified patients), except for the QQ (< 60%). BASDAI and BASFI also performed slightly worse (66-67%).

Conclusion: Thresholds for presenteeism and health status representing unacceptable work status have been established, showing stability across contextual factors. Threshold for QQ were insufficiently accurate and for BASDAI and BASFI were slightly worse although acceptable. The capacity of these thresholds to predict future adverse work outcome was somehow lower for all instruments.

Disclosure: D. Capelusnik: None; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, Galapagos, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, UCB Pharma, 2, 5; **E. Nikiphorou**: AbbVie/Abbott, 6, Celltrion, 6, Eli Lilly, 6, fresenius, 6, Galapagos, 6, Gilead, 1, 6, Pfizer, 6, Sanofi, 6; **W. Maksymowych**: AbbVie, 2, 5, 6, BMS, 2, 6, Boehringer-Ingelheim, 2, CARE Arthritis Ltd, 4, CARE Arthritis Ltd., 4, Celgene, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **M. Magrey**: AbbVie, 2, Bristol Myers Squibb, 2, Eli Lilly, 2, Novartis, 2, Pfizer Inc, 2, UCB, 5; **H. Marzo-Ortega**: AbbVie, 2, 6, Biogen, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 5, 6, MoonLake, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Takeda, 2, 6, UCB Pharma, 2, 5, 6; **A. Boonen**: AbbVie, 2, 5, 6, Galapagos, 2, 6, Novartis, 2, 6, Pfizer, 5, 6, UCB Pharma, 2, 6.

Abstract Number: 1408

Impact of Disease Activity on Functional Impairment in Patients with Spondyloarthritis Is Different According to the Degree of Radiographic Progression: Result from SNUH-AS Cohort

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Imaging & AS

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

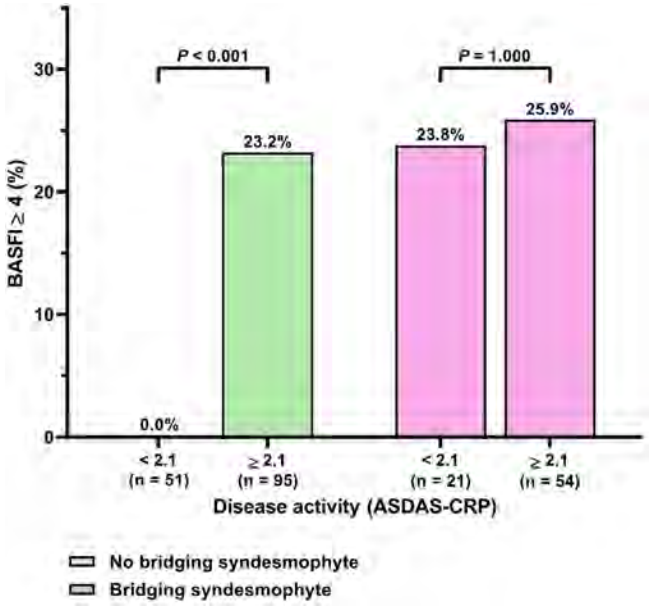
Background/Purpose: Although previous studies suggested that physical functioning is largely driven by disease activity in patients with spondyloarthritis (SpA), its relationship to radiographic progression has not been thoroughly investigated. The aim of this study was to investigate whether the effect of disease activity on physical function varies according to the radiographic progression in SpA patients.

Methods: This cross-sectional study used baseline data from the patients in a single-center, prospective cohort of SpA. Disease activity was assessed through Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Ankylosing Spondylitis Disease Activity Score (ASDAS). Physical function was measured using Bath Ankylosing Spondylitis Functional Index (BASFI) and functional impairment of the patients was defined as BASFI ≥4. Radiographic progression of SpA was assessed using modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). Clinical factors related to functional impairment of the patient were investigated using logistic regression analysis.

Results: A total of 221 patients were analyzed. Mean (SD) age at baseline was 43.4 (14.1) yeas and 176 (79.6%) were male. Mean (SD) disease duration of the included patients was 7.5 (9.5) years. Remission or low disease activity (LDA, ASDAS-CRP < 2.1) was achieved in 149 (67.4%) patients. Mean (SD) mSASSS was 19.5 (20.6) and 96 (43.4%) patients had at least one syndesmophyte on baseline spinal radiographs.

At the baseline, functional impairment was present in 41 (18.6%) patients. Univariable analysis showed that older age at diagnosis, shorter disease duration based on two years, and higher ASDAS-CRP were associated with functional impairment. Although the effect of ASDAS-CRP on the outcome was consistent in the multivariable analysis (adjusted OR 2.46 [95% CI 1.70-3.58]), it was significantly different according to the severity of radiographic progression (*P* value for interaction = 0.001). In the absence of bridging syndesmophyte, increase in ASDAS-CRP was associated with more frequent functional impairment (adjusted OR 5.12 [2.61-10.05]). By contrast, in the subgroup of patients with bridging syndesmophyte, ASDAS-CRP did not increase the likelihood for functional impairment (adjusted OR 1.14 [0.70-1.86]). In fact, in the subgroup without bridging syndesmophyte, no patient with LDA showed a functional impairment. However, in advanced patients with bridging syndesmophyte, the rate of functional impairment was 23.8% despite achieving LDA. (Figure 1)

Conclusion: In the presence of advanced radiographic progression, low disease activity was not significantly associated with less functional impairment in patients with SpA, which suggests that early diagnosis and optimal treatment are critical for better physical function.



Disclosure: J. Jung: None; **J. Kim**: None; **J. Park**: None; **E. Lee**: None; **E. Lee**: Pfizer, 2; **J. Park**: None.

Abstract Number: 1409

Analysis of Soluble Biomarkers in Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

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Background/Purpose: Distinguishing patients with axial spondyloarthritis (axSpA) from patients with other causes of chronic back pain remains a challenge. The lack of reliable biomarkers contributes to the diagnostic delay in axSpA. Recently, macrophage migration inhibitory factor (MIF) has been proposed as a candidate diagnostic and prognostic biomarker. MIF is a proinflammatory cytokine that was shown to be upregulated in several autoimmune/inflammatory diseases including axSpA. The putative role of CD8+ T cells in axSpA pathogenesis suggests further that serum markers of cytotoxicity might have value as biomarkers in axSpA. The goal of this study was to compare serum levels of MIF and other candidate serum proteins in patients with axSpA and controls.

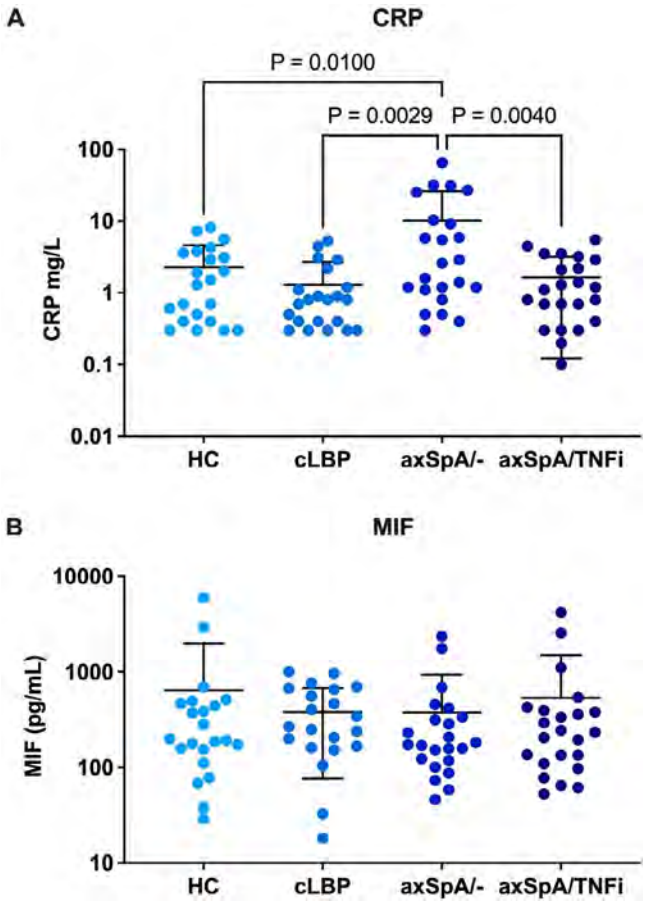
Methods: Study subjects were recruited from our hospital's Orthopedic and Arthritis Center. Four cohorts were compared: healthy controls (HC), patients with chronic low back pain without axSpA (cLBP), axSpA patients not on a biologic (axSpA/-), and axSpA patients treated with a TNF inhibitor (axSpA/TNFi). Study subjects were matched for age, sex and genotyped for HLA-B27 (Table 1). All axSpA patients fulfilled modified New York criteria for ankylosing spondylitis or the 2009 ASAS criteria for axSpA. Serum was evaluated using the LEGENDplex Human CD8/NK panel (BioLegend) for thirteen markers including IL-17A, IL-6, TNF, granzyme B, and perforin. CRP and MIF were evaluated by DuoSet ELISA (R&D Systems).

Results: The severity of back pain in the cLBP controls and axSpA/- patients was comparable (BASDAI Q2 mean 5.0±1.9 vs. 5.0± 3.0). axSpA/- patients had higher back pain, BASDAI and ASDAS scores than axSpA/TNFi patients consistent with higher disease activity in the biologic naïve group. Serum CRP values were significantly higher in axSpA/- patients compared

	Healthy Controls (HC)	Chronic Low Back Pain (cLBP)	axSpA, no biologic (axSpA/-)	axSpA, on TNFi (axSpA/TNFi)
Sample Size (n)	22	22	23	23
Age (years), mean ± SD	37.4 ± 10.5	41.1 ± 15.1	40.1 ± 12.5	40.9 ± 12.6
Male:Female Ratio	13:9	11:11	15:8	14:9
HLA-B27+, n (%)	4 (18.2%)	6 (27.3%)	20 (87.0%)	19 (82.6%)
CRP (mg/L), mean ± SD	2.3 ± 2.4	1.3 ± 1.4	10.2 ± 16.0	1.6 ± 1.5
Severity of Back Pain (BASDAI Q2), mean ± SD	n/a	5.0 ± 1.9*	5.0 ± 3.0*	3.7 ± 2.8
BASDAI, mean ± SD	n/a	n/a	4.2 ± 2.4#	2.9 ± 2.0#
ASDAS, mean ± SD	n/a	n/a	2.7 ± 1.3&	1.9 ± 0.8&

* $P = 0.9058$, # $P = 0.0556$, & $P = 0.0149$

Study subject characteristics.



Serum levels of (A) CRP (mg/L) and (B) MIF (pg/mL) in healthy controls (HC), chronic low back pain (cLBP) controls, axSpA patients not on a biologic (axSpA/-) and axSpA patients on a TNF inhibitor (axSpA/TNFi). Error bars represent mean ± SD, P values by ANOVA with post hoc Tukey's.

with HC, cLBP controls, and axSpA/TNFi patients (P= 0.01, P=0.0029, P=0.004 respectively) (Figure 1A). Serum MIF levels were not statistically different across all four groups (P= 0.8069) (Figure 1B). Additionally, there were no statistically significant differences between the groups for any of the markers included in the LEGENDplex Human CD8/NK panel.

Conclusion: The strength of this study is the comparison of well-characterized groups of axSpA patients with/without biologic therapy and controls including patients with cLBP. In contrast to a previous study, we did not find differences in serum MIF levels between axSpA patients and controls. Of the evaluated serum biomarkers, only CRP values correlated with active axSpA. Our results underscore the need for more research into diagnostic biomarkers in axSpA.

Disclosure: C. Bauchiero: None; **S. Sinnappan**: None; **J. Ermann**: AbbVie, 2, 5, Boehringer Ingelheim, 5, Janssen, 2, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, UCB Pharma, 2.

Abstract Number: 1410

The Use of the ASAS Referral Criteria Together with Increased Education and Training of Its Use Improves Delay to Diagnosis of Axial Spondyloarthritis

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Background/Purpose: Early diagnosis of axial spondyloarthritis (AxSpA) remains a challenge in the management of this condition worldwide. Over the last decade, there remains a significant delay in the diagnosis of the condition. The delay is 8-10 years from symptom onset in Europe. This is contributed by the lack of awareness of the condition, unstructured referral pathways and limited access to diagnostic tests such as MRI. The delayed diagnosis leads to increased complications from AxSpA, delays in treatment and poorer long-term outcomes. Multiple referral strategies are available with the aim of improving the time to diagnosis of AxSpA.

Methods: We reviewed the time from symptom onset to diagnosis of the axial spondyloarthritis over a 12-year period from 2010 to 2023. During this time, we evaluated the effectiveness of the referral strategies we had put in place for use by general practitioners (GPs) to reduce the time to diagnosis. A baseline audit was carried out between January to August 2013 to help understand existing delivery levels against the key National Institute of Clinical Excellence (NICE) recommendations. From 2017, the ASAS referral criteria for suspected AxSpA was implemented in primary care1. This was available as an electronic referral from GPs to the AxSpA clinic. Educational and training events were held to improve the use of the ASAS referral criteria. Follow-up audits were carried out between February to July 2017, January to May 2019 and January to March 2023 to assess the impact of the implementation of the referral strategy with the local AxSpA best practice pathway. Data on length of time of symptoms before seeing the GP, time to referral and diagnosis were captured.

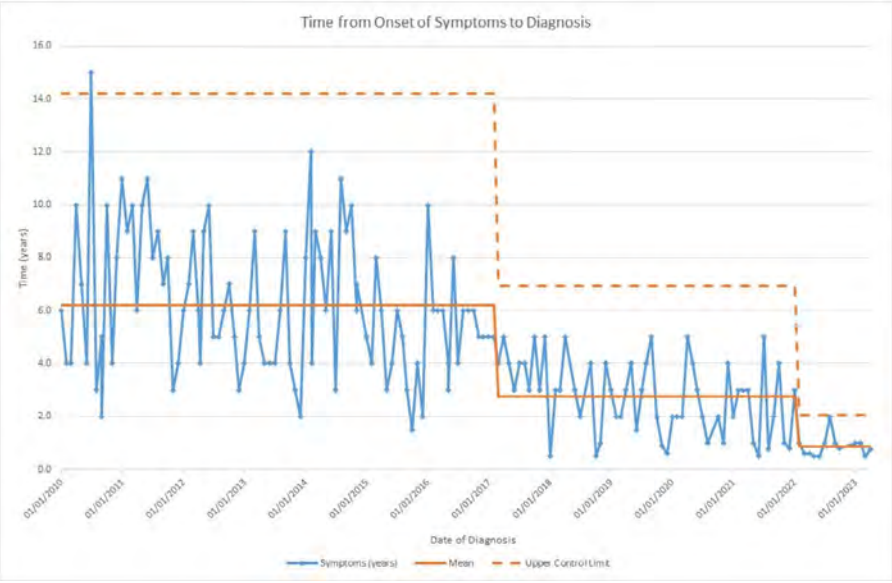

Figure 1. Time to diagnosis from symptom onset over study period

Results: We studied 160 axSpA patients, 87 (54.5%) were male and 73 (45.5%) female. The mean (range) age was 37 (18-52) years. All patients met the ASAS classification criteria for axSpA. Radiographic axSpA (Ankylosing spondylitis) fulfilled the modified New York criteria. There were more patients with radiographic axSpA in the earlier years of diagnosis (100% in 2010) and more of non-radiographic axSpA in the later years (85% in 2022). HLA-B*27 positivity was found in 118 (73.8%) of patients. The majority of referrals were from general practitioners 96 (60.2%), physiotherapists 32 (20.3%), orthopaedics 18 (15.5%) and other specialties 6 (4%). There was no significant difference in the mean (years) delay to diagnosis from the source of the clinic referral. The mean and median delay for time to diagnosis in years were in 2011 (8, 8.5), 2014 (7.8, 8), 2017 (4.2, 4), 2020 (2.5, 2), 2022 (1.1, 0.9) (Figure 1). The majority of the patients were diagnosed between 31-40 years (41%), 22% between 18-30 years, 31% between 41-50 years and 4% after the age of 50 years. We have managed to reduce mean time to diagnosis from a mean of 8 years (2011) to 1.1 years (2022).

Conclusion: The use of the ASAS referral criteria for suspected AxSpA together with increased educational and awareness campaign of its use in primary care and musculoskeletal triage has led to the earlier recognition and referral for suspected AxSpA.

References

Poddubnyy D, van Tubergen A, Landewé R, et al. Ann Rheum Dis 2015;74:1483–1487

Disclosure: A. Chan: None; **K. Rigler**: None; **A. McDougall**: None.

Abstract Number: 1411

Prevalence of Early Axial Spondyloarthritis in the Be-GIANT Cohort Based on the ASAS Consensus Definition of Early Axial Spondyloarthritis

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Background/Purpose: Recently, the Assessment of SpondyloArthritis international Society (ASAS) community, led by the ASAS-SPEAR (SPondyloarthritis EARly definition) working group, endorsed a uniform definition for early axial spondyloarthritis (axSpA). Therefore, in a research setting "early axSpA" should be defined as ≤2 years duration of axial symptoms. The objective was to explore the prevalence of early axSpA as defined by the ASAS community in the prospective Be-GIANT cohort. Additionally, differences in the baseline characteristics of early and late axSpA were analyzed.

Methods: An explorative analysis of all axSpA patients from the prospective Be-GIANT cohort consisting of newly diagnosed adult SpA patients fulfilling the ASAS criteria for axial or peripheral SpA, was performed. Patients were divided in 'early' and 'late' axSpA based on the proposed ASAS definition. Differences in baseline characteristics between these

Table 1. Comparison of baseline characteristics between early axSpA (≤2 years symptom duration) and late axSpA (>2 years symptom duration).

	≤2 years symptom duration (n=162)	>2 years symptom duration (n=204)	p-value
Age, mean (±SD)	29.7 (±7.7)	34.5 (±9.5)	p<0.001
Male, % (n)	51.9 (84)	50.7 (103)	NS
HLAB27 status, % (n)	76.4 (123)	73.0 (146)	NS
Smoking, % (n)	23.4 (37)	20.8 (42)	NS
BASDAI, mean (SD)	4.2 (± 2.0)	4.3 (±1.9)	NS
ASDAS, mean (SD)	2.6 (±1.0)	2.5 (±0.9)	NS
BASFI, median [Q1;Q3]	2.2 [0.9;4.0]	2.7 [1.2;4.6]	NS (p=0.059)
Patient global, mean (SD)	4.9 (±2.8)	4.5 (±2.8)	NS
Physician global, mean (SD)	4.2 (±2.5)	3.7 (±2.4)	p=0.041
Sacroiliitis CR* (ModNY), % (n)	17.3 (27)	32.3 (62)	p=0.001
Sacroiliitis MRI* (ASAS), % (n)	91.1 (143)	84.4 (162)	NS (p=0.06)

Statistically significant test result ($p \leq 0.05$). SD: standard deviation. CR: conventional radiographs; MRI: magnetic resonance imaging.

groups were explored by using the (non) parametric independent- samples T test for continuous variables, and the Chi-square test for categorical variables.

Results: Collected patient data from the Be-GIANT cohort between November 2010 to November 2022 were considered, of which 366 patients with a clinical diagnosis of axial spondyloarthritis and data on symptom duration of axial disease were selected. Overall, 51.2% of patients were male, with mean age of 32.4 ± 9.1 years (mean ± SD). Median axial symptom duration was 30.0 months [10.0; 85.0] (median [Q1;Q3]). HLA-B27 status was positive in 74.5%, with elevated CRP in 41.7% of patients. At baseline, patients exhibited high active disease as indicated by ASDAS 2.5 ± 0.9 (mean ± SD). Strikingly, the definition of early axSpA was met by 44.3% of patients. Regarding imaging, 87,4% fulfilled the ASAS definition of a positive MRI of the sacroiliac joints, whereas 25.6% fulfilled the modified New York criteria for sacroiliitis. When comparing baseline characteristics (Table 1), no significant differences were seen between 'early' and 'late' axSpA regarding BASDAI, ASDAS, patient global or baseline CRP. Likewise, a similar proportion of family history, good response to NSAIDs or previous infection was seen. As expected, patients in the early axSpA group were significantly younger ($p< 0.001$), with significantly less radiographic sacroiliitis ($p=0.001$). Also, physician global was higher in early axSpA as compared to late axSpA ($p=0.041$). No differences were seen in distribution of sex, HLAB-27 status, nor inflammatory back pain features. A trend was seen in favour of insidious onset of back pain ($p=0.051$), lower BASFI ($p= 0.059$) and higher MRI positivity ($p=0.06$) in the early axSpA group.

Conclusion: In the prospective Be-GIANT cohort, almost half of patients met the definition of 'early axSpA'. These patients did not differ in baseline characteristics, except for younger age and lower frequency of radiographic sacroiliitis. Although the disease activity scores at baseline were similar, physicians consider the early disease to be more severe.

Disclosure: G. Varkas: AbbVie/Abbott, 1, 2, 5, 6, Eli Lilly, 6, Novartis, 6, UCB, 1, 2, 6; **A. De Craemer**: None; **Z. Lukasik**: None; **T. Renson**: None; **L. Deroo**: None; **P. Carron**: AbbVie/Abbott, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Merck/MSD, 2, 5, 6, Novartis, 2, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **D. Elewaut**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 2, galapagos, 5, Janssen, 6; **F. Van den Bosch**: AbbVie, 2, 6, Amgen, 2, BMS, 6, Celgene, 6, Eli Lilly, 2, Galapagos, 2, Janssen, 2, 6, Merck, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB Pharma, 2, 6.

Abstract Number: 1412

Improvements in Patient-Reported Outcomes Through 6 Months of Guselkumab Treatment in Patients with Active Psoriatic Arthritis: Real-World Data from the CorEvitas Psoriatic Arthritis/Spondyloarthritis (PsA/SpA) Registry

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Background/Purpose: Guselkumab (GUS) has demonstrated significant efficacy across disease domains in controlled clinical trials of patients (pts) with active PsA.[1,2] Recent CorEvitas PsA/SpA Registry analyses confirmed real-world GUS effectiveness, showing that pts with persistent on-label GUS use at 6 months had significant mean improvements from baseline (BL) in peripheral joint and skin symptoms and pt-reported pain.[3] Here we report secondary findings from the CorEvitas PsA/SpA Registry further assessing changes in pt-reported outcomes (PROs) among pts with persistent GUS use from BL through the 6-month visit (On-Label GUS Persisters).

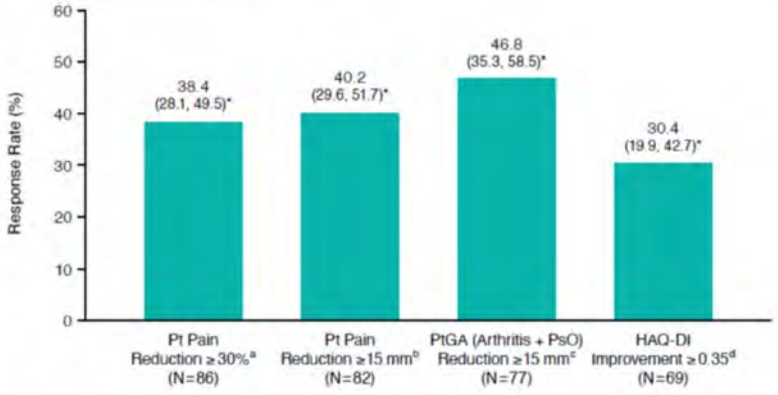
Methods: This analysis includes registry pts who initiated on-label GUS after FDA approval for active PsA (7/13/2020; 100 mg SC at Weeks 0 & 4 then Q8W) and were On-Label Persisters. Demographics, PsA disease activity, PROs, and medication history at GUS initiation (BL visit) were summarized descriptively. Among On-Label GUS Persisters not meeting response criteria at BL, response rates at 6 months were determined for established outcomes related to improvements or achievement of low levels of disease activity in pt-reported pain (0-100 mm visual analog scale [VAS]), pt global assessment of arthritis + psoriasis (PtGA; 0-100 mm VAS), and HAQ-DI (0-3). Unadjusted, nominal p-values were calculated using a single-proportion, one-sided test to determine if response at the 6-month visit differed from 0% at BL. Mean (95% CI) change from BL to 6 months was determined for fatigue (0-100 mm VAS); nominal p-value calculated using a paired t-test at α=0.05.

Results: Among 114 on-label GUS initiators with a 6-month follow-up visit, 90 (79%) had persistent on-label GUS use. On average, pts had longstanding, treatment-resistant, active PsA (**Table 1**). BL pt-reported pain, HAQ-DI, and fatigue scores were 57.0, 0.9, and 56.5, respectively. Substantial proportions of On-Label GUS Persisters experienced clinically meaningful improvements in pain (38% with ≥30% reduction and 40% with ≥15-mm reduction), overall joint and skin disease (47% with ≥15-mm reduction in PtGA), and physical function (30% with HAQ-DI improvement ≥0.35; all nominal p< 0.001; **Figure 1**). Further, up to one quarter of pts achieved the more stringent thresholds of response, generally representing a major response or minimal disease activity, including 22% with ≥50% reduction in pain, 18% with pain score ≤15 mm, 26% with PtGA score ≤20 mm, and 10% with HAQ-DI ≤0.5 (all nominal p< 0.001; **Figure 2**). Mean change (95% CI) in fatigue from BL at 6 months was -8.8 (-14.9, -2.7; nominal p=0.005).

Table 1. BL characteristics of pts with persistent on-label GUS use at 6 months (N=90)	
	Mean (SD)[a]
Demographics at BL visit	
Age, y	55.2 (12.5)
Female sex, n/N (%)	62/89 (69.7%)
White, n/N (%)	82/90 (91.1%)
BMI, kg/m^2	N=88, 33.2 (7.4)
Disease characteristics	
Time since PsA symptom onset, y	N=87, 13.6 (11.2)
Time since PsA diagnosis, y	N=89, 8.9 (7.9)
BSA of PsO, %[b]	N=66, 9.8 (13.5)
cDAPSA score[c]	N=85, 22.0 (15.1)
Pt-reported pain, 0-100 mm VAS	N=89, 57.0 (24.6)
PtGA (arthritis + PsO), 0-100 mm VAS	N=84, 50.3 (24.4)
HAQ-DI, 0-3	N=89, 0.9 (0.6)
Fatigue, 0-100 mm VAS[d]	N=89, 56.5 (25.5)
Medication use and reason for GUS initiation	
Concomitant PsA therapy at BL, n (%)	
GUS monotherapy	63 (70.0%)
GUS + bDMARD or tsDMARD	6 (6.7%)
GUS + csDMARD	20 (22.2%)
GUS + b/tsDMARD + csDMARD	1 (1.1%)
Reason for GUS initiation at BL, n (%)	
Active disease	75 (83.3%)
Alternative mechanism of action	7 (7.8%)
Safety/intolerability	4 (4.4%)
Efficacy	3 (3.3%)
Other (not specified)	1 (1.1%)
Number of prior csDMARDs, n, (%)	
0	34 (37.8%)
1	35 (38.9%)
≥2	21 (23.3%)
Number of prior b/tsDMARDs, n (%)	
0	7 (7.8%)
1	17 (18.9%)
≥2	66 (73.3%)

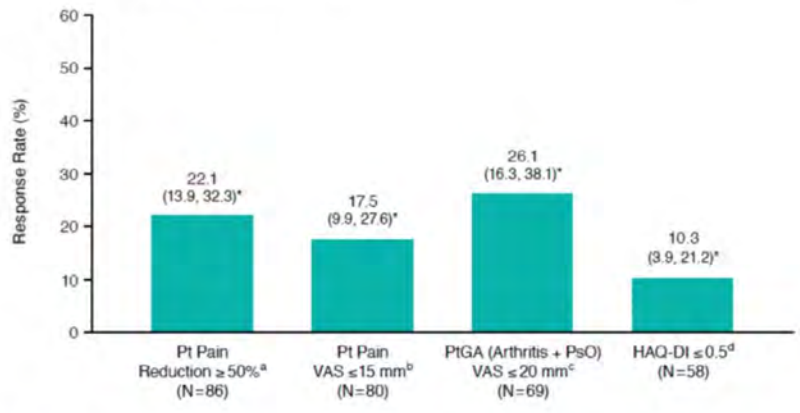
bDMARD, biologic disease-modifying antirheumatic drug; BMI, body mass index; BSA, body surface area; cDAPSA, clinical Disease Activity Index for PsA; csDMARD, conventional systemic DMARD; tsDMARD, targeted synthetic DMARD.
[a]Unless specified otherwise.
[b]In pts with BSA >0 at BL.
[c]cDAPSA score ≤4 indicates remission; score >27 indicates high disease activity.
[d]Based on Question 1 of the BASDAI.

Figure 1. Response rates (95% CI) at the 6-month visit for clinically meaningful improvements in PROs among On-Label GUS Persisters.



* Nominal p<0.001; derived from a one-sided, single-proportion test conducted to determine if the 6-month response rate differed from the BL rate of 0%.
[a] In pts with pt-reported pain (Pt Pain) VAS >0 at BL.
[b] In pts with Pt Pain VAS ≥15 mm at BL.
[c] In pts with a history of PsO with PtGA of arthritis + PsO ≥15 mm at BL.
[d] In pts with HAQ-DI ≥0.35 at BL.

Figure 2. Response rates (95% CI) at the 6-month visit for more stringent thresholds of response among On-Label GUS Persisters.



* Nominal p<0.001; derived from a one-sided, single-proportion test conducted to determine if the 6-month response rate differed from the BL rate of 0%.
[a] In pts with Pt Pain VAS >0 at BL.
[b] In pts with Pt Pain VAS >15 mm at BL.
[c] In pts with a history of PsO with PtGA of arthritis + PsO >20 mm at BL.
[d] In pts with HAQ-DI >0.5 at BL.

Conclusion: In this real-world population of pts with treatment-resistant active PsA and persistent on-label GUS use, consistent with prior results for physician-reported endpoints of joint and skin disease, pts reported meaningful improvements in pain, physical function, and fatigue. These represent difficult-to-treat domains that are important contributors to pts' health-related quality of life.

References:

[1]Deodhar. *Lancet* 2020;395:1115-25
[2]Mease. *Lancet* 2020;395:1126-36
[3]Mease. 6-M Persistence and Multi-Domain Effectiveness of GUS in Adults with PsA: RW Data from the CorEvitas Registry [abstr]. *Maui Derm*; June 21-24, 2023; Colorado Springs, CO

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2; **A. Ogdie**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, UCB, 2; **J. Tesser**: AbbVie, 2, 5, 6, Alpine, 5, Amgen, 2, 5, 6, Anthrosi Therapeutics, 5, AstraZeneca, 2, 6, Aurinia, 2, 6, Bendcare, 5, Biogen, 5, Boehringer Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, 6, Celgene, 5, Corevitas, 5, CSL Behring, 5, DRL, 5, Eli Lilly, 2, 5, 6, Emerald, 5, Exagen, 5, Genentech, 5, 6, Gilead, 5, GlaxoSmithKlein (GSK), 2, 6, Global Health Living Foundation, 5, Horizon, 5, Janssen, 2, 5, 6, Kolon TissueGene, 5, Mitsubishi, 5, Nēsos, 5, Novartis, 2, Organogenesis, 5, Pfizer, 2, 5, 6, Sanofi-Genzyme, 2, 6, Sanumen/Biosplice, 2, 5, Selecta, 5, Setpoint, 5, Sun Pharma, 5, Takeda, 5, UCB, 2; **N. shiff**: AbbVie, 11, Gilead, 11, Iovance, 11, Janssen Scientific Affairs, LLC, 3, Johnson & Johnson, 11, Novo-Nordisc, 11, Pfizer, 11; **I. Lin**: Janssen, 3, Johnson & Johnson, 11; **S. Chakravarty**: Janssen Scientific Affairs, 3, Johnson & Johnson, 11; **M. Kelleman**: CorEvitas, LLC, 3; **R. Dodge**: CorEvitas, LLC, 3; **R. McLean**: CorEvitas, LLC, 3, 11; **A. Broadwell**: AbbVie/Abbott, 2, 6, Amgen, 2, 6, Aurinia, 2, Celgene, 2, Eli Lilly, 2, 6, Horizon, 6, Janssen, 2, 6, Mallinckrodt, 6, Novartis, 2, 6, Pfizer, 2, 6, Radius, 6, Sandoz, 2, Sanofi/Regeneron, 6, UCB, 6; **A. Kavanaugh**: Amgen, 2, BMS, 2, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2; **J. Merola**: AbbVie, 12, Consultant and/or investigator, Amgen, 2, Biogen, 12, Consultant and/or investigator, Bristol Myers Squibb, 2, Dermavant, 12, Consultant and/or investigator, Eli Lilly, 12, Consultant and/or investigator, Janssen, 12, Consultant and/or investigator, LEO Pharma, 12, Consultant and/or investigator,

Novartis, 12, Consultant and/or investigator, Pfizer, 12, Consultant and/or investigator, Regeneron, 12, Consultant and/or investigator, Sanofi, 12, Consultant and/or investigator, Sun Pharmaceuticals, 12, Consultant and/or investigator, UCB Pharma, 12, Consultant and/or investigator.

Abstract Number: 1413

Effect of Apremilast Treatment on the Domains of MDA-Joints in Patients with Early Oligoarticular Psoriatic Arthritis: 16-Week Results from FOREMOST

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The modified minimal disease activity (MDA-Joints) is a novel composite endpoint to assess disease activity and treatment effect in PsA based on a criteria set of mandated tender and swollen joints, and 3/5 items of skin involvement, patient assessments, functionality, and enthesitis.[1] FOREMOST evaluated apremilast 30 mg BID (APR) treatment by MDA-Joints in patients (pts) with early oligoarticular (oligo) PsA.

Methods: FOREMOST (NCT03747939) is a phase 4, multicenter, randomized, double-blind, placebo (PBO)-controlled, parallel-group study. Eligible pts had early disease (PsA duration ≤5 years) and oligo PsA (>1 but ≤4 tender and >1 but ≤4 swollen joint count [TJC and SJC]) despite prior treatment with either nonsteroidal anti-inflammatory drugs and/or ≤2 conventional systemic disease-modifying antirheumatic drugs. Pts were randomized 2:1 to APR or PBO (stratified by concomitant medication use) for 24 weeks, with an early escape at Week 16. The primary endpoint was the proportion of pts at Week 16 who achieved MDA-Joints, a composite of TJC ≤1 and SJC ≤1 plus achieving 3 of the following: psoriasis body surface area (BSA) ≤3%, pt assessment of pain visual analog scale (0–100-mm) ≤15, Pt Global Assessment of Disease Activity (PtGA; 0–100-mm) ≤20, health assessment questionnaire disability index (HAQ-DI) ≤0.5, and enthesitis count ≤1 based on the Leeds Enthesitis Index (LEI). This analysis assesses achievement of each domain in the overall population and only among those with baseline (BL) disease activity. All *P*-values are nominal.

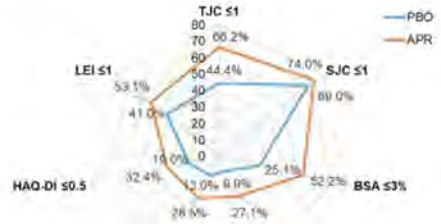
Results: BL values for the overall population and all MDA-Joints domains were comparable between APR and PBO groups (**Table 1**). Improvements were observed across all domains for the entire cohort. In the overall population, more pts achieved TJC ≤1 (66.2% vs 44.4%), SJC ≤1 (74.0% vs 69.0%), BSA ≤3% (70.8% vs 60.5%), pt assessment of pain ≤15 (29.4% vs 13.1%), PtGA ≤20 (30.4% vs 19.1%), HAQ-DI ≤0.5 (47.5% vs 34.2%), and LEI ≤1 (76.0% vs 71.3%) at Week 16 with APR vs PBO. Of pts with BSA >3% at BL, significantly more achieved BSA ≤3% with APR vs PBO at Week 16 (52.2% vs 25.1%; *P*=0.0043) (**Figure 1**). Of pts with a pt assessment of pain score >15 at BL, pt assessment of pain ≤15 was reached by significantly more patients with APR vs PBO at Week 16 (27.1% vs 9.9%; *P*=0.0012) (**Figure 1**). Of pts with PtGA >20 at BL, significantly more achieved PtGA ≤20 at Week 16 with APR vs PBO (28.5% vs 13.0%; *P*=0.0044) (**Figure 1**). Of pts with HAQ-DI >0.5 at BL, 32.4% and 19.0% achieved HAQ-DI ≤0.5 at Week 16 with APR and PBO, respectively (*P*=0.0302) (**Figure 1**). Of pts with LEI >1 at BL, numerically greater proportions achieved LEI ≤1 at Week 16 with APR vs PBO, although this was not significant (53.1% vs 41.0%; *P*=0.3815) (**Figure 1**).

Table 1. Baseline demographics and clinical characteristics

	PBO (n=105)	APR (n=203)
TJC (0–68)		
n	105	203
Mean (SD)	3.2 (0.8)	3.2 (0.8)
SJC (0–66)		
n	105	203
Mean (SD)	2.6 (0.7)	2.7 (0.7)
% BSA		
n	105	198
Mean (SD)	6.3 (10.9)	6.9 (12.3)
Patients with baseline value >3%, n (%)	42 (40.0)	78 (38.4)
Mean (SD)	13.9 (14.2)	15.7 (15.9)
Patient's Assessment of Pain VAS (0–100 mm)		
n	105	198
Mean (SD)	51.1 (22.7)	52.3 (22.0)
Patients with baseline value >15 mm, n (%)	97 (92.4)	184 (90.6)
Mean (SD)	54.7 (19.6)	55.6 (19.0)
PtGA VAS (0–100 mm)		
n	105	198
Mean (SD)	50.5 (20.7)	51.6 (22.0)
Patients with baseline value >20 mm, n (%)	93 (88.6)	179 (88.2)
Mean (SD)	55.0 (17.5)	55.9 (18.4)
HAQ-DI		
n	105	197
Mean (SD)	1.1 (0.6)	1.0 (0.6)
Patients with baseline value >0.5, n (%)	77 (73.3)	145 (71.4)
Mean (SD)	1.4 (0.5)	1.2 (0.4)
LEI		
Patients with baseline value >0, n	38	70
Mean (SD)	2.6 (1.6)	2.4 (1.5)
Patients with baseline value >1, n (%)	27 (25.7)	41 (20.2)
Mean (SD)	3.3 (1.4)	3.4 (1.2)

APR, apremilast; BSA, body surface area; HAQ-DI, health assessment questionnaire disability index; LEI, Leeds enthesitis index; PBO, placebo; PtGA, Patient's Global Assessment of Disease Activity; SD, standard deviation; VAS, visual analog scale.

Figure 1. Achievement of Individual MDA-Joints Domains at Week 16 in Patients With Baseline Disease Activity



	TJC ≤1	SJC ≤1	BSA ≤3%	Patient's Assessment of Pain ≤15	PtGA ≤20	HAQ-DI ≤0.5	LEI ≤1
n, PBO	105	105	42	97	93	77	27
n, APR	203	203	78	184	179	145	41
Adjusted difference, %	22.1	5.1	28.0	17.3	15.9	14.0	11.3

In patients with baseline activity for each respective parameter. Patients who discontinued the study prior to the given week due to an adverse event or lack of efficacy were imputed as non-responders. The remaining missing values at the given week were imputed by multiple imputation.
APR, apremilast; BSA, body surface area; HAQ-DI, health assessment questionnaire disability index; LEI, Leeds enthesitis index; PBO, placebo; PtGA, Patient's Global Assessment of Disease Activity; SJC, swollen joint count; TJC, tender joint count.

Conclusion: Improvements were seen in all MDA-Joints domains with APR vs PBO at Week 16 in pts with early oligo PsA who did not meet any of the thresholds at BL. Improvements were significantly greater for TJC, BSA, pt assessment of pain, PtGA, and HAQ-DI domains and numerically greater for the SJC and LEI domains with APR treatment compared with PBO, possibly related to the small sample size.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2; **A. Ogdie**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, UCB, 2; **K. Callis Duffin**: AbbVie, 2, 4, 5, 6, Amgen, 2, 4, 5, 6, Boehringer Ingelheim, 2, 4, 5, Celgene Corporation, 2, 4, 5, 6, Eli Lilly, 2, 4, 5, 6, Janssen, 2, 4, 5, 6, Novartis, 2, 4, 4, 5, 5, 6, 12, non-promotional speaker, Pfizer, 2, 4, 5, 6, Regeneron, 2, 4, 5, 6, UCB, 2, 4, 5, 6; **J. Reddy**: Amgen, 3, 11; **R. Wang**: Amgen Inc., 3, 8; **S. Jardon**: Amgen Inc., 3, 11; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, Bristol Myers Squibb, 2, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead Sciences, 2, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake, 2, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 1414

Effects of Apremilast on Changes in Cardiometabolic Parameters by Diabetes and Obesity Status in Patients with Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The prevalence of cardiometabolic diseases including obesity and diabetes is higher in patients with psoriatic arthritis (PsA) than those without PsA. Apremilast (APR) is associated with weight loss and a reduction in glycated hemoglobin (HbA1c). The objective of this analysis was to evaluate the effects of APR on cardiometabolic parameters over 52 weeks in patients with active PsA.

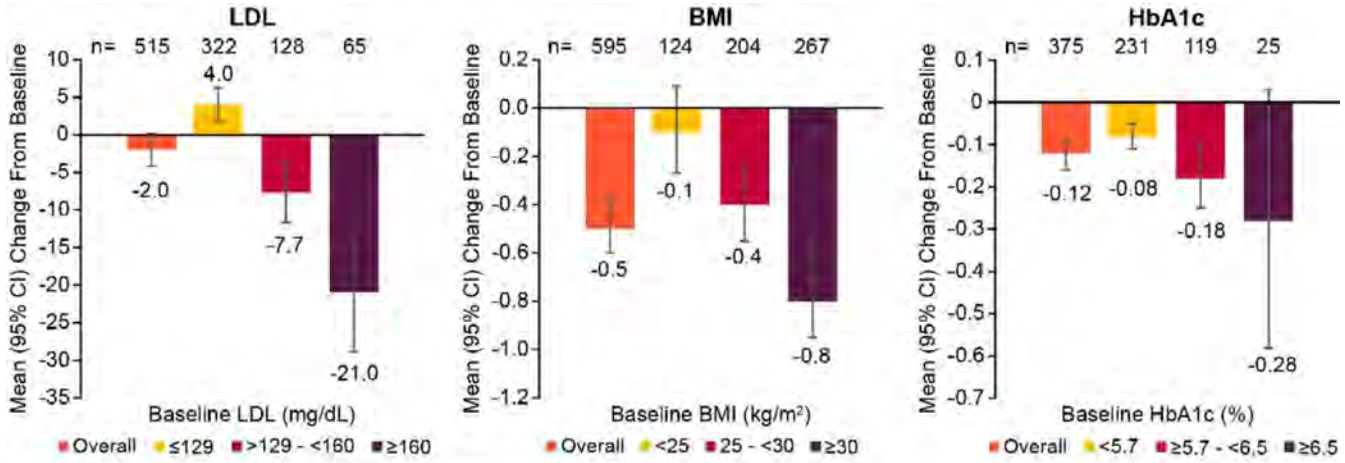
Methods: Data from 5 randomized, placebo-controlled, phase 3 studies (PALACE 1–4 and ACTIVE) in patients with active PsA receiving APR 30 mg twice daily were pooled. Included in this analysis were patients who were treated with APR for 52 weeks. Changes from baseline to Week 52 in low- and high-density lipoprotein (LDL, HDL), body mass index (BMI), and HbA1c were assessed and stratified by baseline level of these parameters and Week 52 disease activity (Clinical Disease Activity Index for Psoriatic Arthritis [cDAPSA] remission/low disease activity [REM/LDA] vs moderate/high disease activity [ModDA/HDA]).

Results: Data from 781 patients with PsA who received APR were pooled (mean age: 50 years, 55% female). Mean LDL was 119.6 mg/dL in the overall population at baseline and decreased by 2.0 mg/dL on average at Week 52 (**Figure**). The greatest decreases in LDL were seen in patients with the highest LDL levels at baseline (**Figure**). Similar favorable changes in HDL were

observed. A total of 34/65 (52.3%) moved from the high LDL category (≥160 mg/dL) at baseline to borderline (>129 – < 160 mg/dL) or normal (≤129 mg/dL) at Week 52 and 49/128 (38.3%) changed from borderline high to normal LDL levels (**Table**).

Mean BMI was 30.3 kg/m^2 in the overall population at baseline and decreased by 0.5 kg/m^2 at Week 52 (**Figure**). A trend was again seen where patients with higher BMI at baseline saw greater decreases in BMI at Week 52 (**Figure**). Additionally, 24/267 (9.0%) patients changed from the obese category (≥30 kg/m^2) to the overweight category (25 – < 30 kg/m^2), and 25/204 (12.3%) patients changed from the overweight category to the normal category (< 25 kg/m^2) (**Table**).

Mean HbA1c was 5.6% in the overall population at baseline and decreased by 0.1% at Week 52 (**Figure**). Greater changes in HbA1c were seen in patients who were pre-diabetic (HbA1c 5.7% – < 6.5%) and diabetic (HbA1c ≥6.5%) at baseline vs those who had normal HbA1c (HbA1c < 5.7%) (**Figure**). Furthermore, 60/119 (50.4%) patients who had pre-diabetes changed to normal HbA1c levels, and 10/25 (40.0%) moved from diabetes to pre-diabetes (**Table**).



Includes patients who were treated with APR for 52 weeks and had both baseline and Week 52 values.
APR, apremilast; BMI, body mass index; HbA1c, glycated hemoglobin; LDL, low-density lipoprotein.

Changes in Cardiometabolic Parameters from Baseline to Week 52 by Baseline Subgroup

	Week 52 LDL (mg/dL), n/N (%)		
Baseline LDL (mg/dL)	Normal (≤129)	Borderline (>129 – <160)	High (≥160)
Normal (≤129)	274/322 (85.1)	41/322 (12.7)	7/322 (2.2)
Borderline (>129 – <160)	49/128 (38.3)	63/128 (49.2)	16/128 (12.5)
High (≥160)	13/65 (20.0)	21/65 (32.3)	31/65 (47.7)
	Week 52 BMI (kg/m^2), n/N (%)		
Baseline BMI (kg/m^2)	Normal (<25)	Overweight (25 – <30)	Obese (≥30)
Normal (<25)	111/124 (89.5)	13/124 (10.5)	0/124 (0.0)
Overweight (25 – <30)	25/204 (12.3)	163/204 (79.9)	16/204 (7.8)
Obese (≥30)	0/267 (0.0)	24/267 (9.0)	243/267 (91.0)
	Week 52 HbA1c (%), n/N (%)		
Baseline HbA1c (%)	Normal (<5.7)	Pre-diabetes (5.7 – <6.5)	Diabetes (≥6.5)
Normal (<5.7)	224/231 (97.0)	6/231 (2.6)	1/231 (0.4)
Pre-diabetes (5.7 – <6.5)	60/119 (50.4)	53/119 (44.5)	6/119 (5.0)
Diabetes (≥6.5)	1/25 (4.0)	10/25 (40.0)	14/25 (56.0)

Includes patients who were treated with APR for 52 weeks.
APR, apremilast; BMI, body mass index; HbA1c, glycated hemoglobin; LDL, low-density lipoprotein.

LDL, BMI, and HbA1c Shift from Baseline to Week 52

Results were consistent across Week 52 cDAPSA psoriatic disease activity subgroups; greater changes in cardiometabolic parameters were seen in patients with higher baseline LDL, BMI, HbA1c, or lower baseline HDL regardless of whether REM/LDA was achieved at Week 52.

Conclusion: APR treatment was associated with improvement in cardiometabolic parameters observed across psoriatic disease activity groups. The most favorable changes were seen in patients with high LDL, low HDL, obesity, or diabetes at baseline. These findings suggest that those with a high burden of comorbid cardiometabolic diseases and active PsA treatment may gain benefit beyond joint disease with APR. However, these findings require larger, prospective studies.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, Gilead Sciences, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5; **I. McInnes**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Bristol Myers Squibb, 2, 5, Cabaletta, 2, 11, Causeway Therapeutics, 2, 11, Celgene, 2, 5, Compugen, 2, 11, Dextera, 11, Eli Lilly, 2, EveloBio, 1, 2, 4, 11, Gilead, 2, Janssen, 2, 5, Moonlake, 2, NHS GGC, 4, Novartis, 2, 5, Pfizer, 2, Sanofi, 2, UCB, 2, 5, Versus Arthritis, 12, Trustee Status; **S. Cheng**: Amgen, 3, 11; **S. Colgan**: Amgen, 3, 11; **Y. Klyachkin**: Amgen, 3, 11; **L. Teng**: Amgen, 3, 11; **N. Mehta**: AbbVie, 12, Investigator, Amgen, 2, Celgene, 12, Investigator, Eli Lilly, 2, Janssen, 12, Investigator, LEO Pharma, 2, Novartis, 12, Investigator.

Abstract Number: 1415

Bimekizumab Treatment Impact on Work Productivity in Biologic DMARD-Naïve and TNFi-IR Patients with Active Psoriatic Arthritis: Results up to 1 Year from Two Phase 3 Studies

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: PsA impacts the physical health and functional ability of patients (pts),which can contribute to reduced work productivity.[1] Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A, and has demonstrated efficacy and tolerability in pts with PsA to 16 weeks (wks), vs placebo (PBO), sustained to 52 wks.[2–5]Here, we report the impact of BKZ treatment on work productivity up to 1 year using data from two phase 3 studies.

Methods: BE OPTIMAL (NCT03895203; biologic DMARD [bDMARD]-naïve pts) and BE COMPLETE (NCT03896581; inadequate response or intolerance to TNF-α inhibitors [TNFi-IR] pts) were PBO-controlled phase 3 studies assessing BKZ in pts with active PsA.[2,3] Pts in BE OPTIMAL were randomized 3:2:1 to subcutaneous (sc) BKZ 160 mg every 4 wks (Q4W), PBO,

Table. Baseline employment status and WPAI-SHP dimension scores for bDMARD-naïve patients (BE OPTIMAL) and TNFi-IR patients (BE COMPLETE) (OC)

	BE OPTIMAL (bDMARD-naïve)		BE COMPLETE (TNFi-IR)	
	PBO/BKZ 160 mg Q4W n=281	BKZ 160 mg Q4W n=431	PBO/BKZ 160 mg Q4W n=133	BKZ 160 mg Q4W n=267
Employment Status, n (%)				
Employed at study start	197 (70.1) (n=281)	280 (65.1) (n=430)	78 (58.6) (n=133)	171 (64.0) (n=267)
WPAI-SHP dimension score,[a] mean % (SD)				
Overall work impairment	34.2 (26.3) (n=181)	37.0 (27.2) (n=262)	40.3 (28.1) (n=73)	40.7 (27.9) (n=158)
Activity impairment[b]	43.2 (24.5) (n=281)	43.2 (24.4) (n=430)	47.1 (26.0) (n=133)	46.5 (25.6) (n=267)
Absenteeism[c]	8.5 (22.1) (n=189)	7.7 (21.4) (n=270)	7.1 (19.7) (n=75)	9.7 (20.4) (n=162)
Presenteeism[d]	32.3 (24.7) (n=181)	34.8 (25.7) (n=262)	38.6 (26.6) (n=73)	38.0 (26.3) (n=158)

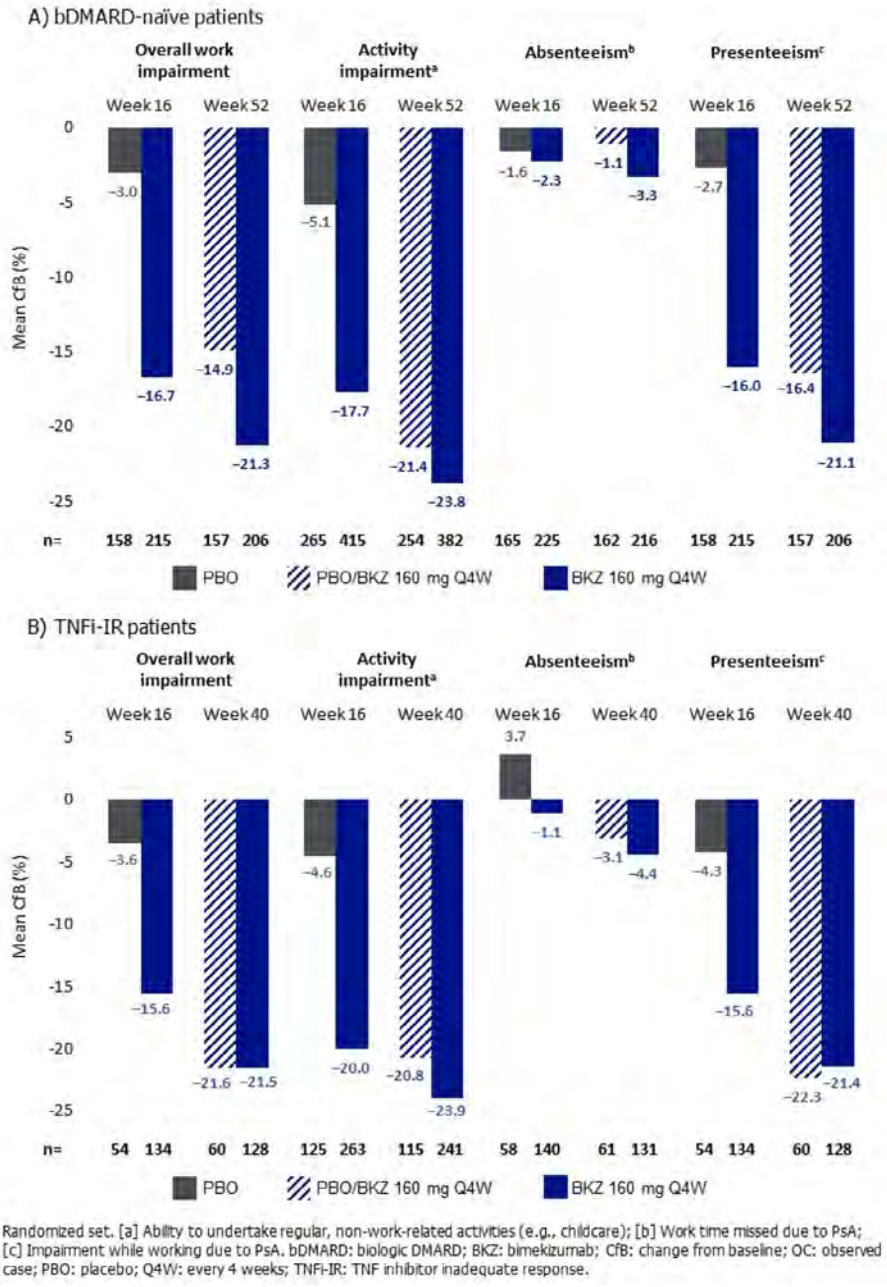
Randomized set. [a] Dimensions were assessed only in patients employed at baseline, with the exception of the activity impairment dimension which was assessed for the entire cohort; [b] Ability to undertake regular, non-work-related activities (e.g., childcare); [c] Work time missed due to PsA; [d] Impairment while working due to PsA. bDMARD: biologic DMARD; BKZ: bimekizumab; OC: observed case; PBO: placebo; Q4W: every 4 weeks; SD: standard deviation; TNFi-IR: inadequate response or intolerance to TNF-α inhibitors; WPAI-SHP: Work Productivity and Activity Impairment Questionnaire – Specific Health Problem v2.0.

or reference (sc adalimumab 40 mg Q2W; not reported here); the study was active treatment-blind to Wk 52, after which pts could enter the ongoing open-label extension BE VITAL (NCT04009499). Pts in BE COMPLETE were randomized 2:1 to sc BKZ 160 mg Q4W or PBO; pts who completed Wk 16 were eligible for BE VITAL. BE COMPLETE plus BE VITAL is referred to as 'BE COMPLETE' hereafter. In both BE OPTIMAL and BE COMPLETE, PBO-randomized pts switched to BKZ 160 mg Q4W at Wk 16 (PBO/BKZ). Pt work productivity is derived from the Work Productivity and Activity Impairment Questionnaire – Specific Health Problem v2.0 (WPAI-SHP), adapted for PsA;[6] collected to Wk 52 in BE OPTIMAL and Wk 40 in BE COMPLETE. Percentage change from baseline in WPAI-SHP scores are reported for four dimensions: overall work impairment, activity impairment, work time missed (absenteeism), and impairment while working (presenteeism).

Results: Baseline WPAI-SHP scores suggest work productivity was impaired in pts: mean overall work impairment was 34.2%–40.7% across studies, with similar rates of activity impairment and presenteeism between treatment arms (**Table**). At Wk 16, BKZ-treated pts in both studies showed numerically greater mean percentage reduction from baseline in overall work impairment compared with PBO-treated pts; bDMARD-naïve: 16.7% BKZ, 3.0% PBO and TNFi-IR: 15.6% BKZ, 3.6% PBO. Work productivity continued to improve up to 1 year; PBO/BKZ pts demonstrated similar reductions in overall work impairment to BKZ-randomized pts at Wk 52 for the bDMARD-naïve population (21.3% BKZ, 14.9% PBO/BKZ) and at Wk 40 for the TNFi-IR population (21.5% BKZ, 21.6% PBO/BKZ). Trends were generally comparable for all dimensions in both studies (**Figure**).

Conclusion: BKZ demonstrated improvements vs PBO in all WPAI-SHP dimensions to Wk 16 which were clinically meaningful,[6] with greatest improvements observed in activity impairment and presenteeism. Work productivity continued to improve with BKZ to 1 year; pts who switched to BKZ at Wk 16 experienced similar levels of improvement to BKZ-randomized pts. Improvements in work productivity were similar in bDMARD-naïve and TNFi-IR pts, demonstrating consistent response.

1. Husni ME. Semin Arthritis Rheum 2017;47:351–60; **2.** McInnes IB. Lancet 2023;401:25–37; **3.** Merola JF. Lancet 2023;401:38–48; **4.**Ritchlin CT. Arthritis Rheumatol 2022;74(S9); **5.** Coates L. Ann Rheum Dis 2023;82(S1); **6.** Tillett W. Rheumatol Ther 2019;6:379–91.



Randomized set. [a] Ability to undertake regular, non-work-related activities (e.g., childcare); [b] Work time missed due to PsA; [c] Impairment while working due to PsA. bDMARD: biologic DMARD; BKZ: bimekizumab; CfB: change from baseline; OC: observed case; PBO: placebo; Q4W: every 4 weeks; TNFi-IR: TNF inhibitor inadequate response.

Figure. Mean change from baseline in work productivity for (A) bDMARD-naïve patients at Week 16 and Week 52 (BE OPTIMAL), and (B) TNFi-IR patients at Week 16 and Week 40 (BE COMPLETE) (OC)

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, Gilead Sciences, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5; **L. Gossec**: AbbVie, 2, 12, Personal fees, Amgen, 2, Biogen, 5, BMS, 12, Personal fees, Celltrion, 12, Personal fees, Eli Lilly, 5, 12, Personal fees, Galapagos, 12, Personal fees, Janssen, 12, Personal fees, MSD, 12, Personal fees, Novartis, 5, 12, Personal fees, Pfizer, 12, Personal fees, Sandoz, 5, 12, Personal fees, UCB Pharma, 5, 12, Personal fees; **P. Nash**: AbbVie, 5, 6, Bristol Myers Squibb, 5, 6, Celgene, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, GSK, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer Inc, 5, 6; **B. Ink**: AbbVie, 11, GSK, 11, UCB Pharma, 3, 11; **J. Coarse**: UCB Pharma, 3, 11; **N. Lyris**: UCB Pharma, 3; **D. Willems**: UCB Pharma,

3; **W. Tillett**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, GSK, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Ovo Pharma, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma, 2, 5, 6.

Abstract Number: 1416

Improvement of Work Absenteeism Following Start of Methotrexate Monotherapy in Newly-Diagnosed Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: In many countries, methotrexate (MTX) monotherapy is the first-line disease-modifying anti-rheumatic drug (DMARD) therapy for psoriatic arthritis (PsA), despite that its efficacy in PsA (in contrast to rheumatoid arthritis [RA]) has not been clearly shown in placebo-controlled trials. In light of this paucity of evidence, data on the effect of MTX on work absenteeism in PsA –relevant to both individual and society – is of interest. Thus, we aimed to investigate absenteeism development in relation to MTX start in newly-diagnosed PsA, and to contrast this to the situation in RA and among general population (GP) comparator-subjects.

Table 1.

Table 1. Characteristics at start of methotrexate monotherapy

	Psoriatic arthritis n=2525	Rheumatoid arthritis n=2525	General population comparator-subjects n=12028
Age; Mean (SD)	47 (11)	47 (11)	48 (10)
Male sex	1217 (48%)	1217 (48%)	5810 (48%)
Days from first diagnosis to MTX start; Mean (SD)	64 (173)	24 (73)	NA
Education			
<10 years	369 (15%)	430 (17%)	1533 (13%)
10-12 years	1386 (55%)	1292 (51%)	5738 (48%)
>12 years	765 (30%)	791 (31%)	4615 (38%)
Patient pain; Mean (SD)	54 (22)	54 (25)	NA
Patient global; Mean (SD)	51 (24)	51 (25)	NA
Tender joints (of 28); Mean (SD)	5.1 (5.0)	6.9 (5.5)	NA
Swollen joints (of 28); Mean (SD)	3.5 (3.7)	6.3 (5.0)	NA
CRP; Mean/Median	12/5.3	17/8.0	NA
Any unemployment during the calendar year before MTX start	219 (8.7%)	207 (8.2%)	965 (8.1%)
Diabetes[2]	98 (3.9%)	135 (5.4%)	325 (2.7%)
Chronic lung disease[1]	7 (0.3%)	21 (0.8%)	58 (0.5%)
Myocardial infarction[1]	16 (0.6%)	26 (1.0%)	91 (0.8%)
Malignancy[1]	51 (2.0%)	54 (2.1%)	356 (3.0%)
Congestive heart disease[1]	5 (0.2%)	3 (0.1%)	18 (0.2%)
Depression/anxiety[3]	407 (16%)	296 (12%)	1350 (11%)

N (%) if not otherwise stated. [1] Based on a registered diagnosis within 5 years prior to MTX start. [2] Based on a diagnosis within 5 years or a prescription within 1 year prior to MTX start. [3] Based on a prescription within 1 year prior to MTX start. Missing data (PsA/RA/GP): Education (0.2/0.5/1%); Patient pain (70/46%); Patient global (70/45%); Tender joints (68/41%); Swollen joints (68/41%); CRP (67/40%). GP, general population; MTX, methotrexate; NA, not applicable; PsA, psoriatic arthritis; RA, rheumatoid arthritis.

Methods: Patients aged 18-62 years (y) with newly-diagnosed PsA in Sweden (≤2y since first main PsA ICD-code from rheumatology/internal medicine), starting MTX monotherapy as their first DMARD 2011-2019, were identified from nationwide registers (with a diagnostic validity of >85% for both PsA and RA). Each PsA case was matched to a corresponding patient with newly-diagnosed RA, starting MTX monotherapy, and to 5 GP comparator-subjects (matching for age, sex, county, and [for RA] MTX start-year). The number of absenteeism days (sick leave or disability pension, due to any reason) per quarter of a year (90 days) was retrieved from the Social Insurance Agency and evaluated from 1y before until 2y after MTX start. In order to assess absenteeism development specifically in relation to MTX monotherapy, in case of switch to/addition of other DMARDs or if stopping MTX, last observation carried forward (LOCF) of the number of absenteeism days in the month when this change occurred, was applied in our main analysis. An alternative analysis without LOCF was, however, also performed, thus reporting the absenteeism development as observed, regardless of further DMARD changes. Within-group changes in absenteeism were analyzed by Wilcoxon´s matched-pair rank-sign test, and comparisons between PsA and RA by bootstrapped ANCOVA, crude and adjusted for relevant confounders (see **Table 2**).

Results: At MTX start, patient-reported outcomes in PsA and RA were similar, while CRP and swollen joints were numerically higher, and time from diagnosis shorter, in RA (**Table 1**). Already 1y prior to MTX start, the PsA cases (but not RA) displayed higher absenteeism levels compared to the GP (**Figure, panel A**). In PsA and RA, absenteeism thereafter increased, peaking in the first quarter after MTX start, but then decreased significantly over the 2y follow-up in the main (**Figure, panel A**) as well as the alternative analysis (**Figure, panel B**), although numerically more in RA. While significant improvements were seen with MTX monotherapy (**Figure, panel A**), the superior outcomes in the as observed analysis (**Figure, panel B**)

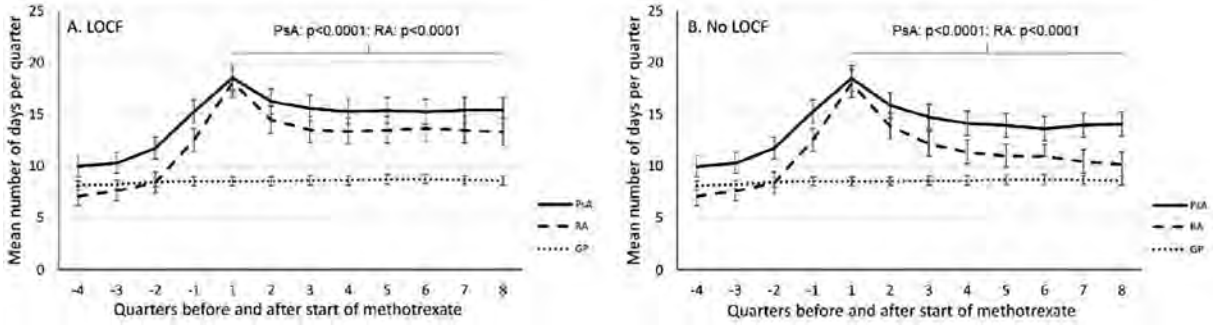

Figure. Mean number of absenteeism days (due to sick leave or disability pension) per quarter of a year (90 days) before and after start of methotrexate. **A.** Main analysis, applying LOCF in case of switch to/addition of other DMARDs or if stopping MTX. **B.** Alternative analysis without LOCF (i.e. as observed, regardless of subsequent DMARD changes). Both analyses censored at death, migration or if receiving the other diagnosis (e.g. a patient with PsA receiving a RA diagnosis). Within-group changes in absenteeism from the 1st to the 8th quarter of a year after MTX start assessed by Wilcoxon's matched-pair rank-sign test. DMARD, disease-modifying anti-rheumatic drug; GP, general population comparator-subjects; LOCF, last observation carried forward; MTX, methotrexate; PsA, psoriatic arthritis; RA, rheumatoid arthritis.

Figure.

Table 2.

Table 2. Mean differences in absenteeism days (due to sick leave or disability pension) between PsA and RA

Main analysis with LOCF. 2525 PsA/RA cases			
Quarter	**Crude**	**Model 1**	**Model 2**
Q-4	**2.9 (1.5 to 4.3)**	1.6 (-0.1 to 3.4)	NA
Q+1	0.4 (-1.5 to 2.3)	-0.8 (-3.3 to 1.6)	-1.3 (-3.6 to 0.8)
Q+8	**2.2 (0.2 to 4.1)**	0.2 (-2.2 to 2.6)	-0.7 (-2.8 to 1.3)
Alternative analysis without LOCF. 2525 PsA/RA cases			
Q-4	**2.9 (1.5 to 4.3)**	1.6 (-0.1 to 3.4)	NA
Q+1	0.5 (-1.5 to 2.3)	-0.7 (-3.2 to 1.7)	-1.2 (-3.5 to 0.9)
Q+8	**3.9 (2.2 to 5.6)**	1.3 (-0.8 to 3.5)	0.4 (-1.4 to 2.3)

Model 1 adjusted for sex, age, county, MTX start-year, level of education, comorbidities (reported in Table 1), any unemployment in the calendar year prior to MTX start and number of days from first PsA/RA-diagnosis to MTX start. Model 2 additionally adjusted for number of absenteeism days in the first quarter of the year preceding the MTX start (i.e. quarter -4) LOCF, last observation carried forward; MTX, methotrexate; NA, not applicable; PsA, psoriatic arthritis, Q, quarter; RA, rheumatoid arthritis.

suggest an added benefit of subsequent DMARD changes. In the adjusted comparisons, absenteeism levels did not differ significantly between PsA and RA at any timepoint (regardless of analysis; **Table 2**).

Conclusion: Our results suggest a significant improvement of work absenteeism, following MTX start in PsA. Considering that work ability is a both prioritized and objectively assessed outcome, this offers additional support for MTX use in PsA, for which trial-based evidence is limited.

Disclosure: U. Lindström: None; **D. Di Giuseppe**: None; **S. Exarchou**: Amgen, 2, Janssen, 2, Novartis, 2, UCB Pharma, 2; **G. Alenius**: None; **T. Olofsson**: Merck Sharp & Dohme, 2, UCB Pharma, 2; **E. Klingberg**: Amgen, 6, Janssen, 6, Pfizer, 6, UCB Pharma, 6; **L. Jacobsson**: Novartis, Eli-Lily and Janssen, 6, Pfizer, Novartis, Eli-Lily and Janssen., 1; **J. Askling**: Abbvie, 5, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 5, Galapagos, 5, Merck/MSD, 5, Pfizer, 5, Samsung bioepis, 5, Sanofi, 5; **J. Karlsson Wallman**: AbbVie, 5, 6, Amgen, 5, 6, Eli Lilly, 5, Novartis, 5, Pfizer, 5.

Abstract Number: 1417

Do Long-term Patient-reported Outcomes Improve Similarly in Psoriatic Arthritis and Axial Spondyloarthritis Patients Treated with Secukinumab? Results from the EuroSpA Collaboration

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patient reported outcomes (PROs) are important in the treatment evaluation of patients with spondyloarthritis, including axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA). For secukinumab, limited real world data on PROs is available – and no comparison between axSpA and PsA patients has been performed. In European patients with axSpA and PsA who initiated secukinumab, we aimed to determine: 1) the proportion of patients achieving 6-, 12- and 24-month pain, fatigue, patient global assessment (PGA) and health assessment questionnaire (HAQ) remission, and 2) the 24-month secukinumab retention rate.

Methods: The study was conducted within the European Spondyloarthritis Research Collaboration Network (EuroSpA)(1). From 16 European registries, patients with axSpA or PsA who initiated secukinumab between 2015 and 2021 were included. Based on the ASAS working group definition of partial remission in axSpA(2), we applied the following definitions of PRO remission: pain≤20, PGA≤20, fatigue≤20 (all on visual analogue scales 0-100 mm) and HAQ≤0.5 for both axSpA and PsA patients, to make comparisons feasible.PRO remission rates were calculated as crude and adjusted for secukinumab adherence (LUNDEX). Comparisons of remission rates were performed with univariable and multivariable (baseline covariates: age, gender, registry, and number of previous b/tsDMARDs)logistic regression analyses. Kaplan-Meier with log-rank test and Cox regression analyses were performed to assess and compare the 24-month secukinumab retention rate between axSpA and PsA patients.

Results: We included 3062 axSpA patients and 3217 PsA patients initiating secukinumab in routine care. At secukinumab treatment start (baseline), axSpA patients had a mean (SD) age of 46.8 (12.0) years, with 52.7% being male. PsA patients had a mean age (SD) of 51.9 (11.9) years and were predominantly female (56.9%). No clinically relevant differences in

Table 1. Baseline characteristics of axSpA and PsA patients

Baseline characteristics*	AxSpA patients (n=3062)		PsA patients (n=3217)	
	Value	N available	Value	N available
Age (years)	46.8 (12.0)	3062	51.9 (11.9)	3216
Gender (male)	1612 (52.7)	3062	1386 (43.1)	3217
HLA-B27 positive	1290 (73.0)	1766	-	-
BMI (kg/m²)	27.6 (5.4)	1580	28.3 (5.9)	1415
Years since diagnosis (years)	9.0 (9.2)	2564	8.6 (7.9)	2465
Previous b/ts DMARDs				
- No previous b/ts DMARDs	802 (26.2)	3062	815 (25.3)	3217
- 1 previous b/ts DMARD	735 (24.0)	3062	784 (24.4)	3217
- ≥ 2 previous b/ts DMARDs	1525 (49.8)	3062	1618 (50.3)	3217
Secukinumab dose				
- 150mg	1033 (50.1)	2060	399 (20.4)	1952
- 300mg	69 (3.4)	2060	339 (17.4)	1952
- Unknown	958 (46.5)	2060	1214 (62.2)	1952
PRO				
- Pain (0-100mm)	65.6 (22.6)	1787	61.6 (24.6)	1861
- Fatigue (0-100mm)	66.6 (23.7)	1535	65.8 (24.9)	1223
- PGA, (0-100mm)	66.0 (22.8)	1891	63.7 (24.3)	2035
- HAQ (0-3)	1.1 (0.6)	1339	1.1 (0.7)	1736
Disease activity measures				
- PhGA, (0-100mm)	44.1 (24.6)	1283	42.1 (25.6)	1525
- 28 tender joint count	2.0 (4.1)	1234	5.9 (6.1)	2095
- 28 swollen joint count	0.7 (2.0)	1313	3.0 (4.0)	2081
- CRP (mg/L)	17.4 (31.0)	2005	12.0 (21.2)	2036
- ESR (mm/hr)	25.9 (23.0)	1496	22.6 (21.2)	1696

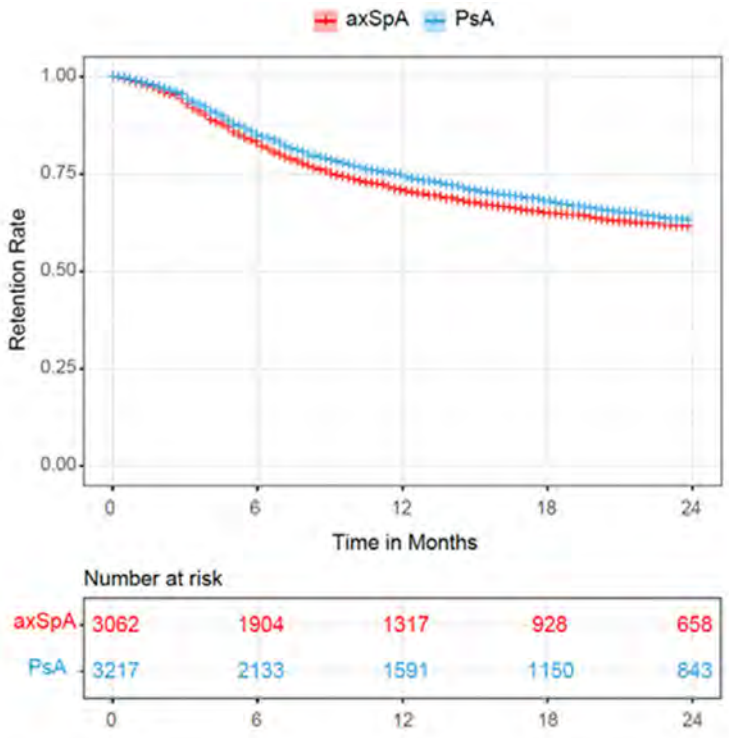
* Values are presented as mean (SD) and n (%) for continuous and categorical variables, respectively. HLA-B27, Human Leukocyte Antigen subtypes B*2701-2759; BMI, Body Mass Index; bDMARD, biologic Disease-Modifying Anti-Rheumatic drugs; tsDMARD, targeted synthetic Disease-Modifying Anti-Rheumatic drugs; PGA, Patient's global assessment of disease activity; HAQ, Health Assessment Questionnaire disability index; PhGA, Physician Global assessment; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PRO, patient reported outcome; N, number.

disease duration, physician global assessment (PhGA), number of previous b/tsDMARDs or PROs values were found at baseline (Table 1). The reductions in pain, fatigue, and PGA values from baseline to 24-month follow-up were greater in axSpA patients compared to PsA patients. While crude PRO remission rates (pain, fatigue, PGA and HAQ) were higher for

Table 2. PROs and PRO remission rates 6, 12 and 24 months after secukinumab initiation in European axSpA and PsA patients.

		PRO values							PRO remission rates								
		AxSpA patients (n=3062)		PsA patients (n=3217)		Estimated difference (95% CI) PsA *vs.* axSpA			AxSpA patients			PsA patients			OR (95% CI) PsA *vs.* axSpA		
	Months	Mean (sd)	N available	Mean (sd)	N available	Unadjusted	Adjusted (age + gender)	Adjusted (all*)	Crude	LUNDEX-adjusted	N available	Crude	LUNDEX-adjusted	N available	Unadjusted	Adjusted (age + gender)	Adjusted (all*)
Pain	0	65.6 (22.6)	1787	61.6 (24.6)	1861	-	-	-	-	-	-	-	-	-	-	-	-
	6	43.7 (26.3)	1473	46.1 (27.4)	1548	2.4 (0.5; 4.3)	1.5 (-0.4; 3.5)	-1.8 (-3.8; 0.2)	26.5	17.9	1473	22.5	15.9	1548	0.8 (0.7; 1.0)	0.9 (0.7; 1.0)	1.1 (0.9; 1.3)
	12	39.7 (26.3)	846	42.9 (26.8)	940	3.2 (0.7; 5.6)	1.9 (-0.6; 4.4)	-1.2 (-3.8; 1.4)	33.1	16.8	846	27.4	15.4	940	**0.8 (0.6; 0.9)**	0.8 (0.7; 1.0)	1.0 (0.8; 1.3)
	24	38.1 (27.0)	397	44.1 (26.2)	455	**6.0 (2.4; 9.5)**	4.5 (0.9; 8.2)	0.0 (-3.6; 3.6)	36.0	12.7	397	25.1	9.6	455	**0.6 (0.4; 0.8)**	**0.6 (0.5; 0.9)**	1.0 (0.7; 1.5)
Fatigue	0	66.6 (23.7)	1535	65.8 (24.9)	1223	-	-	-	-	-	-	-	-	-	-	-	-
	6	47.7 (29.4)	1355	53.6 (28.8)	1115	**6.0 [3.6; 8.3)**	**5.2 [2.8; 7.5)**	-3.0 (-5.3; -0.6)	25.8	17.4	1355	18.3	12.9	1115	**0.6 (0.5; 0.8)**	**0.7 (0.6; 0.9)**	1.3 (1.0; 1.7)
	12	41.9 (28.9)	764	52.1 (30.2)	611	**10.2 (7.0; 13.3)**	**9.3 (6.1; 12.4)**	0.1 (-3.2; 3.4)	32.2	16.3	764	21.9	12.3	611	**0.6 (0.5; 0.8)**	**0.6 (0.5; 0.8)**	1.3 (1.0; 1.8)
	24	42.3 (28.2)	343	51.7 (30)	296	**9.4 (4.8; 13.9)**	**7.6 (3.1; 12.1)**	-1.9 (-6.3; 2.6)	29.7	10.5	343	22.0	8.4	296	0.7 (0.5; 1)	0.7 (0.5; 1.1)	**1.8 (1.1; 3.0)**
PGA	0	66.0 (22.8)	1891	63.7 (24.3)	2035	-	-	-	-	-	-	-	-	-	-	-	-
	6	45.2 (27.2)	1582	47.0 (27.6)	1608	1.8 (-0.1; 3.7)	0.7 (-1.3; 2.6)	-3.0 (-4.9; -1.0)	27.2	18.3	1582	22.4	15.8	1608	**0.8 (0.7; 0.9)**	0.9 (0.7; 1.0)	1.1 (0.9; 1.3)
	12	40.1 (26.6)	926	43.5 (27.5)	1066	**3.4 (1.0; 5.8)**	2.2 (-0.2; 4.7)	-1.8 (-4.2; 0.7)	34.4	17.5	926	28.1	15.8	1066	**0.7 (0.6; 0.9)**	0.8 (0.7; 1.0)	1.1 (0.9; 1.4)
	24	37.9 (27.9)	424	44.6 (27.1)	505	**6.7 (3.1; 10.2)**	**5.1 (1.5; 8.7)**	0.6 (-3.0; 4.1)	41.0	14.5	424	25.9	9.9	505	**0.5 (0.4; 0.7)**	**0.6 (0.4; 0.7)**	0.8 (0.5; 1.1)
HAQ	0	1.1 (0.6)	1339	1.1 (0.7)	1736	-	-	-	-	-	-	-	-	-	-	-	-
	6	0.9 (0.6)	1027	0.9 (0.7)	1447	**0.1 (0.0; 0.1)**	0.0 (-0.0; 0.1)	0.0 (-0.1; 0.1)	35.4	23.9	1027	32.5	23.0	1447	0.9 (0.7; 1.0)	1.1 (0.9; 1.3)	1.1 (0.9; 1.3)
	12	0.8 (0.6)	565	0.9 (0.7)	865	**0.1 (0.3; 0.2)**	0.0 (-0.0; 0.1)	0.0 (-0.1; 0.1)	38.8	19.7	565	32.1	18.0	865	**0.7 (0.6; 0.9)**	0.9 (0.7; 1.2)	1.0 (0.7; 1.3)
	24	0.8 (0.6)	256	0.9 (0.7)	426	**0.1 (0.0; 0.2)**	0.04 (-0.1; 0.1)	0.01 (-0.1; 0.1)	41.8	14.7	256	30.3	11.6	426	**0.6 (0.4; 0.8)**	0.7 (0.5; 1.0)	0.8 (0.6; 1.2)

*Adjustment with age, gender, registries, and number of previous b/tsDMARDS (0/1/≥2). PRO, patient reported outcomes; CI, Confidence Interval; PGA, patient global assessment; HAQ, Health assessment questionnaire; pain, fatigue, PGA, were scored on a 0–100 mm visual analogue scale (VAS); HAQ was scored on a scale ranging from 0–3; PRO remission criteria were defined as following: pain remission ≤ 20mm, PGA ≤ 20mm, fatigue ≤ 20mm, HAQ ≤ 0.5; Significant values are indicated by bold type.



	Retention rates		24-month Hazard ratios [95%CI] PsA *vs.* axSpA		
	axSpA	PsA	Unadjusted	Adjusted Age+gender	Adjusted: All*
24 months	61.2%	62.8%	0.93 [0.85-1.02]	0.92 [0.84-1.01]	0.92 [0.84-1.02]

*Values adjusted for age, gender, registries, and number of previous b/tsDMARDS. (0/1/≥2). CI, Confidence Interval.

Figure 1. Secukinumab retention rates in axSpA and PsA patients, with unadjusted and adjusted hazard ratios

axSpA than for PsA patients at all timepoints, LUNDEX-adjusted remission rates were similar (Table 2). After correction for multiple confounders no difference was found between the groups, except for a higher remission rate for fatigue in PsA at 24 months (OR= 1.8 [95% CI 1.1-3.0]) (Table 2). The 24-month retention rates were similar in axSpA and PsA (61.2% *vs*. 62.8%, HR= 0.92 [95% CI 0.84-1.02], p=0.14 in fully adjusted analyses) (Figure 1).

Conclusion: Our study supports the real-world effectiveness of secukinumab in both axSpA and PsA, as measured by PROs, and suggests that PROs (including pain, PGA and HAQ) and 24-month retention rate after secukinumab initiation are similar in axSpA and PsA patients. Further analyses, aiming to evaluate long-term effectiveness of axSpA and PsA are needed.

References

1. Anon. https://eurospa.eu/.
2. Anderson JJ et al. *Arthritis and Rheumatism* 2001;44:1876–1886.

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Abstract Number: 1418

Efficacy of the Oral, Selective, Allosteric Tyrosine Kinase 2 Inhibitor, Deucravacitinib, on Psoriasis in Patients with Active PsA: Results from a Phase 2 Trial

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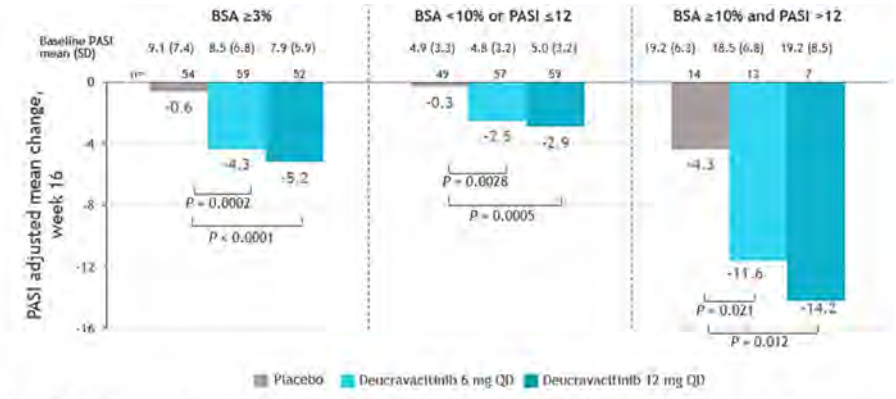
SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Tyrosine kinase 2 (TYK2) mediates signaling of key cytokines involved in plaque psoriasis (PsO) and PsA pathophysiology. Deucravacitinib is a first-in-class, oral, selective, allosteric TYK2 inhibitor approved in multiple countries for the treatment of adults with moderate to severe PsO, based on superiority of deucravacitinib over apremilast and placebo (PBO) in various outcome measures in 4 phase 3 trials, including in China and Japan (NCT03611751, NCT03624127, NCT04167462, NCT03924427) in patients with moderate to severe PsO.[1,2] DEUC also improved multiple measures of disease activity, including in arthritis and PsO, vs PBO in a phase 2 trial (NCT03881059) in patients with active PsA.[3] This analysis further evaluated the efficacy ofdeucravacitinib on PsO in patients with concomitant PsA in the phase 2 trial.

Methods: The phase 2 double-blind trial in PsA randomized patients (N=203) 1:1:1 to PBO, deucravacitinib 6 mg once daily (QD), or deucravacitinib 12 mg QD. After wk 16 (part A), patients could optionally enroll in a double-blind period until wk 52 (part B), where deucravacitinib-treated patients with minimal disease activity at wk 16 continued deucravacitinib treatment to wk 52. PsO disease activity measures, including mean body surface area (BSA), mean Psoriasis Area and Severity Index (PASI) score, and achievement of different treat-to-target PASI and BSA thresholds, were assessed at week 16 in part A.

Results: At baseline (BL), PsO characteristics were generally similar across treatment groups, with most evaluable patients (≥ 74%) having a PASI< 12 or BSA< 10 (**Table**). At wk 16, mean PASI scores significantly decreased from BL and the improvements were significantly greater with deucravacitinib in PBO in patients treated with deucravacitinib vs PBO, even in those with very low BL PASI scores (**Figure**). Deucravacitinib treatment significantly decreased PASI scores from BL in patients with 6 mg QD and 12 mg QD vs PBO, respectively inpatients on background conventional synthetic (cs) DMARD (–4.0 and –4.9 vs –2.3; $P < 0.05$ for both) as well as those without csDMARD use (–3.7 and –4.0 vs +2.5; $P < 0.001$, for both) vs PBO. At wk 16, a greater proportion of patients treated with deucravacitinib at either dose vs PBO achieved PASI ≤ 1 in patients with mild to moderate or moderate to severe PsO. Decreases in mean PASI score at wk 16 were maintained



Modified baseline observation carried forward method was used to handle missing data. Adjusted means and nominal *P* values were derived from an analysis of covariance model with factors for body weight and TNFi use and the baseline value as a covariate.

BSA, body surface area; PASI, Psoriasis Area and Severity Index; PsO, plaque psoriasis; QD, once daily; SD, standard deviation; TNFi, tumor necrosis factor inhibitor.

Figure. PASI mean change from baseline at week 16 by psoriasis severity at baseline

Table. Baseline psoriasis characteristics

Table. Baseline psoriasis characteristics

		Placebo (n = 66)	Deucravacitinib 6 mg QD (n = 70)	Deucravacitinib 12 mg QD (n = 67)
BSA severity	BSA < 3%, n (%)	9 (14)	11 (16)	14 (21)
	BSA ≥ 3% to < 10%, n (%)	32 (49)	37 (53)	29 (43)
	BSA ≥ 10%, n (%)	22 (33)	22 (31)	23 (34)
PASI severity	PASI ≤ 5, n (%)	30 (46)	33 (47)	29 (43)
	PASI > 5 to ≤ 12, n (%)	18 (27)	23 (33)	30 (45)
	PASI > 12, n (%)	15 (23)	14 (20)	7 (10)
	NR, n (%)	3 (5)	0	1 (2)
BSA ≥ 3% (*mild to severe*)	n (%)	54 (82)	59 (84)	52 (78)
BSA < 10%, PASI ≤ 12 (*mild to moderate*)	n (%)	49 (74)	57 (81)	59 (88)
BSA ≥ 10%, PASI > 12 (*moderate to severe*)	n (%)	14 (21)	13 (19)	7 (10)

BSA, body surface area; NR, not reported; PASI, Psoriasis Area and Severity Index; QD, once daily.

through wk 52 in patients who achieved MDA and continued treatment with deucravacitinib 6 mg or 12 mg QD in part B of the study.

Conclusion: Treatment with deucravacitinib significantly improved PsO in patients with PsA, regardless of BL PsO severity and background csDMARD use. Of note, improvement in the moderate to severe PsO patient subgroup was comparable with that observed in the phase 3 POETYK PSO-1 trial in patients with moderate to severe PsO.[1]

References:

1. Armstrong A, et al. *J Am Acad Dermatol* 2023;88:29–39.
2. Strober B, et al. *J Am Acad Dermatol* 2023;88:40–51.
3. Mease PJ, et al. *Ann Rheum Dis* 2022;81:815–822.

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Regeneron, 12, Personal fees, Sanofi Genzyme, 12, Personal fees, Science 37, 12, Personal fees, Sun, 1, 6, Sun Pharma, 12, Personal fees, UCB, 5, Valeant, 12, Personal fees; **J. Merola**: Abbvie, 2, 12, Investigator, Amgen, 2, 12, Investigator, Biogen, 2, 12, Investigator, Bristol-Myers Squibb, 2, 12, Investigator, Dermavant, 2, 12, Investigator, Eli Lilly, 2, 6, 12, Investigator, Janssen, 2, 12, Investigator, Leo Pharma, 2, 12, Investigator, Novartis, 2, 12, Investigator, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, 12, Investigator, Sun Pharma, 2, 12, Investigator, UCB Pharma, 2, 12, Investigator; **A. Napoli**: Bristol-Myers Squibb(BMS), 3, 11; **M. Nowak**: Bristol-Myers Squibb(BMS), 3, 11; **S. Banerjee**: Bristol-Myers Squibb(BMS), 3, 11; **T. Lehman**: Bristol-Myers Squibb(BMS), 3; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2.

Abstract Number: 1419

Impact of Psoriatic Arthritis Manifestations on Perception of Pain Improvement: Pooled Analysis of Two Phase 3, Randomized, Double-Blind, Placebo-Controlled Studies with Guselkumab

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Pain in PsA has multifaceted origins (e.g., peripheral joint inflammation, axial involvement [axPsA], skin lesions, dactylitis, enthesitis, underlying conditions) and can be difficult to treat. Guselkumab (GUS), a fully human IL-23p19 subunit inhibitor, is effective in treating multiple PsA domains and elicited durable improvement in patient-reported pain (PtP) in the DISCOVER-1&2 trials[1,2]. Here, we assessed association between improvement in key PsA manifestations and PtP using 1-year DISCOVER-1&2 data.

Methods: DISCOVER-1&2 enrolled adults with active PsA despite standard therapies[3,4]. Patients were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or placebo with crossover to GUS 100 mg Q4W at W24. Treatment groups were pooled (N=1120). Longitudinal associations of improvement in swollen joint count (SJC,0-66), tender joint count (TJC, 0-68), Leeds enthesitis index (LEI), dactylitis severity score, Psoriasis Area and Severity Index (PASI), axPsA (N=312), and improvement in overall PtP (0-100 mm) and spinal pain (BASDAI question 2 in patients with axPsA) were assessed. Longitudinal associations of improvement in these PsA manifestations with ≥30%/50%/70% improvements in PtP (PtP-30/50/70) were assessed.

Table. Adjusted[1] Associations Between Improvements in Key PsA Manifestations and Pain Improvement Through W52

Pt Population	Predictor (Δ)	Δ PtP (β)[2]	Odds Ratio (OR)[3]			Δ Spinal Pain (β)[2,4]
			PtP-30	PtP-50	PtP-70	
All (N=1120)	PASI	0.41‡	1.05‡	1.04‡	1.04	0.03
	SJC	0.28‡	1.03*	1.03	1.06	0.03
	TJC	0.55‡	1.05‡	1.08‡	1.12‡	0.06‡
BL Enthesitis (N=728)	LEI	1.62‡	1.19‡	1.25‡	1.32‡	0.18*
	PASI	0.47‡	1.06‡	1.06‡	1.06*	0.02
	SJC	0.28‡	1.03*	1.03	1.03	0.03
	TJC	0.39‡	1.04‡	1.05‡	1.08‡	0.05‡
BL Dactylitis (N=473)	DSS	-0.04	0.97*	1.01	1.07	0.01
	PASI	0.31‡	1.04*	1.05*	1.05	0.02
	SJC	0.19	1.03	1.03	1.02	0.05*
	TJC	0.60‡	1.05‡	1.06‡	1.11‡	0.05‡

*p<0.05; †p<0.01; ‡p≤0.0001.

[1]Adjusted for BL values, age, gender, BMI, SF-36 Mental Component Summary score, presence of TJC – SJC ≥7 (central pain sensitization proxy), FACIT-Fatigue score, and treatment group;

[2]β correspond to the incremental increase in pain improvement;

[3]ORs correspond to the incremental increase in the odds of achieving pain endpoints, for every increase in improvement in key PsA manifestations or in the presence (vs absence) of axPsA. Higher β = greater impact on pain improvement;

[4]N=312.

AxPsA, axial involvement of psoriatic arthritis; BL, baseline; BMI, body mass index; DSS, dactylitis severity score; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; LEI, Leeds enthesitis index; OR, odds ratio; PASI, psoriasis area and severity index; PsA, psoriatic arthritis; PtP, patient-reported pain; SJC, swollen joint count; TJC, tender joint count; W, week.

Results: Mean (SD) baseline PtP of 61.2 (19.8) indicated substantial burden. Upon adjusting for potential confounders, greater improvement in PASI, SJC, and TJC (mutually adjusted) were each associated with significantly greater improvement in PtP and higher odds of achieving PtP-30 through W52 **(Table)**. PASI reduction was also associated with greater odds of PtP-50, as was TJC improvement for PtP-50/70. In patients with baseline enthesitis, improvements in LEI, PASI, and TJC were each associated with greater PtP improvement and attaining PtP-30/50/70; SJC reduction was only associated with PtP-30. In patients with baseline dactylitis, PASI and TJC reductions were significantly associated with PtP improvement. Overall, axPsA presence did not impact the extent of PtP improvement (data not shown). In patients with axPsA, significant associations were observed between spinal pain improvement and TJC and LEI improvement.

Conclusion: Improvements in key PsA manifestations were significantly associated with pain reduction, although to varying extents. TJC reduction had the greatest impact on PtP improvement, likely due to overlap of the construct measured. Psoriasis improvement had a greater impact on pain relief than SJC improvement, highlighting the sensory burden of skin lesions, while enthesitis improvement showed a significant association with both overall and spinal pain relief. These findings underscore the importance of utilizing treatments effective across manifestations to address recalcitrant PsA symptoms.

References:

1. Ritchlin CT. *RMD Open* 2022;8:e002195
2. Nash P. *ACR Convergence* 2021 (PO1333)
3. Deodhar A. *Lancet* 2020;395:1115
4. Mease PJ. *Lancet* 2020;395:1126

Disclosure: P. Nash: AbbVie, 5, 6, Bristol Myers Squibb, 5, 6, Celgene, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, GSK, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer Inc, 5, 6; **I. McInnes**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Bristol Myers Squibb, 2, 5, Cabaletta, 2, 11, Causeway Therapeutics, 2, 11, Celgene, 2, 5, Compugen, 2, 11, Dextera, 11, Eli Lilly, 2, EveloBio, 1, 2, 4, 11, Gilead, 2, Janssen, 2, 5, Moonlake, 2, NHS GGC, 4, Novartis, 2, 5, Pfizer, 2, Sanofi, 2, UCB, 2, 5, Versus Arthritis, 12, Trustee Status; **C. T. Ritchlin**: AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, Gilead, 2, Janssen, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5; **L. Tam**: AbbVie, 5, Amgen, 2, 5, Boehringer-Ingelheim, 2, 5, Eli Lilly, 2, GSK, 5, Janssen, 2, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 2; **E. Soriano**: AbbVie, 2, 5, 6, Amgen, 6, Bristol-Myers Squibb, 6, Eli Lilly, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Roche, 2, 5, 6, UCB, 5, 6; **M. Starr**: AbbVie, 1, 6, Eli Lilly, 1, 6, Janssen, 1, 6, Novartis, 1, 6, Pfizer, 1, 6, UCB, 1, 6; **E. Rampakakis**: Janssen, 2, JSS Medical Research, Inc, 3; **F. Lavie**: Janssen, 3, Johnson & Johnson, 11; **M. Shawi**: Immunology Global Medical Affairs, Janssen Pharmaceutical Companies of Johnson & Johnson, 3, Johnson & Johnson, 11; **X. Baraliakos**: AbbVie, 2, 6, BMS, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, 6, UCB, 2, 6; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2.

Abstract Number: 1420

Changes in Serum Cytokines and Collagen Proteins Correlate with Durability of Guselkumab Efficacy and Continued Disease Improvement Through 2 Years in Patients with Active Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: In the phase 3 DISCOVER-2 study of biologic-naïve patients (pts) with active psoriatic arthritis (PsA), guselkumab (GUS), a fully human, selective interleukin (IL)-23p19 subunit inhibitor significantly reduced the signs and symptoms of disease and radiographic progression vs placebo (PBO), with durable response across multiple disease domains through 2 years. GUS also significantly decreased serum levels of collagen turnover markers, which are elevated in PsA pts vs healthy controls. Furthermore, changes in these and other serum cytokine levels through Week 24 (W24) of GUS treatment are associated with clinical response through 2 years. Here, we further assessed effects of GUS on serum cytokine and collagen turnover biomarkers from W24 through W100 (2 years) and explored associations between biomarker levels and longer-term clinical response (W100).

Methods: In DISCOVER-2, biologic-naïve adults with active PsA (swollen joint count ≥5, tender joint count ≥5, CRP ≥0.6 mg/dL) were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4 and then Q8W; or PBO with crossover to GUS Q4W at W24. Blood samples from consenting GUS-treated pts (Q4W and Q8W pooled) were assessed

for serum cytokine levels (N=100), including Th17-related effector molecules (IL-17A, IL-17F, IL-22), β-defensin 2 (BD-2), acute phase proteins (CRP, serum amyloid A [SAA], IL-6), and serum collagen turnover biomarkers (N=174; C1M, C3M, C4M, C6M). Using Spearman linear regression and general linear models, pooled changes from baseline (BL) in biomarkers during GUS treatment, correlations between changes in biomarker levels and reductions from BL at three time points (W24, W52, W100) in disease activity (measured by changes in Disease Activity in Psoriatic Arthritis [DAPSA] score, Psoriatic Arthritis Disease Activity Score [PASDAS], Psoriasis Area and Severity Index [PASI] score) were assessed. Associations between biomarker changes and achievement of American College of Rheumatology (ACR)50 response at W100 were also assessed.

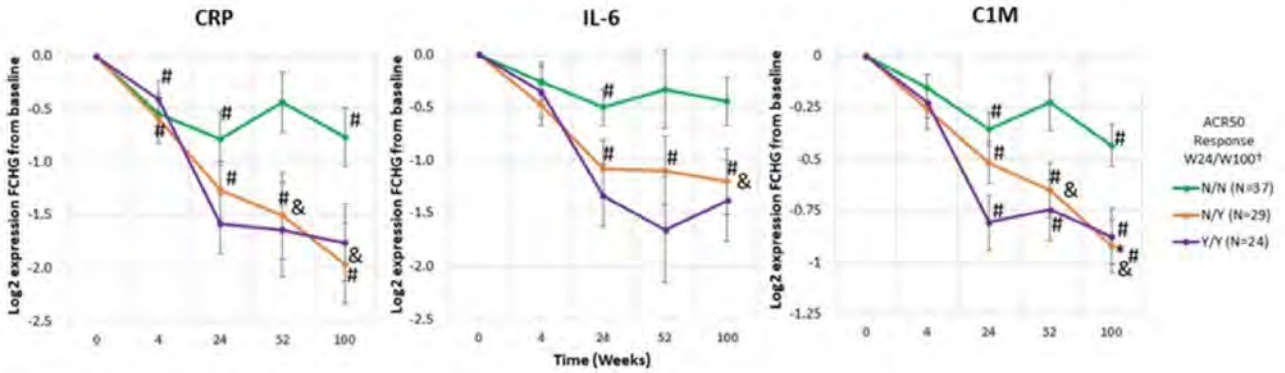
Results: Continued treatment with GUS led to significant and sustained reductions in serum cytokines from W24 through W100. Reductions in CRP and IL-6 were associated with changes in DAPSA score, with a similar trend observed for PASDAS. Reductions in BD-2, IL-17A, IL-17F and IL-22 from BL correlated with improvements in the PASI score, and

Table. Correlation of Change in Serum Biomarker Levels With Change in PsA Disease Activity From BL Through 24, 52 or 100 Weeks of GUS Treatment

	DAPSA	PASDAS	PASI
BD-2	0.08	0.16	**0.58**[a]
CRP	**0.30**[a]	0.24	0.08
IL-17A	0.08	0.21	**0.46**[a]
IL-17F	0.00	0.11	**0.41**[a]
IL-22	0.17	0.22	**0.34**[a]
IL-6	**0.26**[a]	0.17	-0.03
SAA	0.20	0.20	0.14
TNF-α	0.16	0.19	0.14
C1M	**0.27**[a]	**0.27**[a]	0.07
C3M	0.24	**0.27**[a]	0.06
C4M	0.23	**0.27**[a]	0.06
C6M	**0.30**[a]	**0.31**[a]	0.04

[a]Significant correlation between biomarker expression and disease activity; $r>0.25$ and $P<0.05$.

Figure. Reduction in serum cytokine levels and collagen biomarkers in patients who achieved ACR50 response at W24 and through W100.



Statistics based on general linear model. No apparent differential expression was observed across groups at baseline.
*Indicates statistical significance compared to W24 by $P<0.05$ and |fold difference| ≥1.25.
#Indicates statistical significance compared with baseline by $P<0.05$ and |fold difference| ≥1.4.
&Indicates statistical significance of W24 nonresponder→W100 responder compared with W24 nonresponder→W100 nonresponder by $P<0.05$ and |fold difference| ≥1.4.
†Y/N group was not included in this analysis due to a limited number of subjects.

reductions in collagen turnover biomarkers correlated with changes in the PASDAS (Table). Continued disease improvement with long-term GUS treatment, assessed clinically using ACR50 response, was supported by the further reductions in CRP, SAA, IL-6 and collagen turnover biomarkers in ACR50 responders at W100 who were ACR50 nonresponders at W24 (Figure). Among ACR50 responders at W24, mean reductions in CRP, SAA and IL-6 were sustained through W100.

Conclusion: These results provide molecular evidence that sustained reductions in serum acute phase proteins and collagen turnover biomarkers may contribute to the continuous, durable improvements in joint symptoms and that reductions in Th17-related effector molecules contribute to improvements in skin symptoms seen in PsA pts receiving GUS.

Disclosure: S. Siebert: AbbVie, 6, Amgen, 5, 6, AstraZeneca, 6, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 5, 6, GlaxoSmithKlein(GSK), 5, 6, Janssen, 5, 6, UCB, 5, 6; **G. Schett**: None; **S. Raychaudhuri**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, SUN Pharma, 2, 5, 6, UCB, 2, 5, 6; **M. Guma**: Genentech, 5, Gilead, 5, Novartis, 5, Pfizer, 5; **W. Chen**: Janssen, 3, Johnson & Johnson, 11; **S. Gao**: Janssen, 3, Johnson & Johnson, 11; **S. Chakravarty**: Janssen Scientific Affairs, 3, Johnson & Johnson, 11; **M. Shawi**: Immunology Global Medical Affairs, Janssen Pharmaceutical Companies of Johnson & Johnson, 3, Johnson & Johnson, 11; **P. Rahman**: AbbVie, 2, Amgen, 2, Bristol Myers Squibb, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, UCB, 2.

Abstract Number: 1421

Domains Impacting Minimal Disease Activity Non-Achievement in Patients with Psoriatic Arthritis and Inadequate Response to TNF Inhibitors Receiving Guselkumab (COSMOS)

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

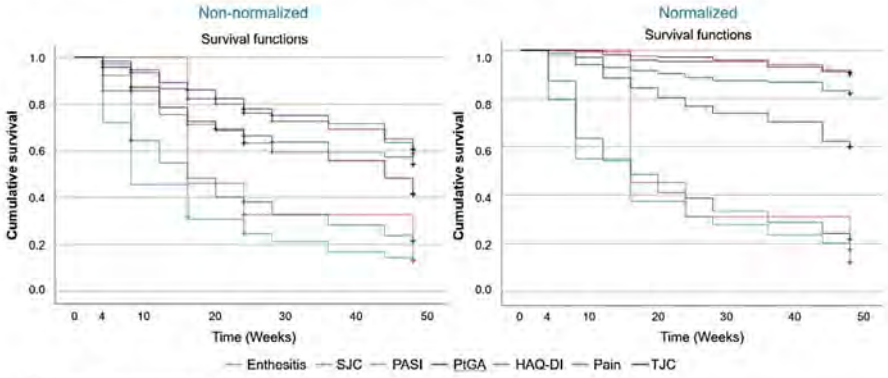
Background/Purpose: Sustained minimal disease activity (MDA) is achieved by a minority of patients (pts) receiving biologics for psoriatic arthritis (PsA). Pt-reported MDA domains are less frequently achieved than physician-reported domains. Here, we assessed MDA achievement in pts with PsA and inadequate response to 1–2 TNF inhibitors (TNFi-IR) to identify PsA disease domains and factors contributing to the lack of MDA achievement at Week (W)48 for TNFi-IR PsA pts treated with guselkumab (GUS) using data from the Phase 3b COSMOS trial.

Methods: In COSMOS, adults with active PsA (swollen/tender joint counts [SJC/TJC] each ≥3) and TNFi-IR were randomized 2:1 to subcutaneous GUS 100 mg or placebo (PBO) at W0, W4, then every 8 weeks. PBO pts crossed over to GUS at W16 (early escape) or W24 (planned). MDA was defined as fulfilment of ≥5/7 domains: tender entheses (Leeds enthesitis

index [LEI]; 0–6) ≤1; Health Assessment Questionnaire-Disability Index (HAQ-DI; 0–3) ≤0.5; pt pain (0–100) ≤15; Psoriasis Area and Severity Index (PASI; 0–72) ≤1; Pt Global Assessment (PtGA; 0–100) ≤20; SJC (0–66) ≤1; and TJC (0–68) ≤1. Primary fibromyalgia (pFM) was defined at baseline (BL) using TJC minus SJC ≥7 as a proxy. A longitudinal trajectory of achieving each MDA domain through W48 was derived (non-responder imputation). Time to achieving each domain was assessed with Kaplan–Meier analyses; to account for differences in scales and domain strictness, scores were also normalized to the SJC (0–66) scale. Response predictors (for pts not meeting each MDA domain criteria at BL) were identified using multivariate regression for time to achievement (Cox proportional hazards) and W48 achievement (logistic) of MDA.

Results: GUS pts (n=189) showed improvement from BL in all MDA domains, with overall W24/48 response rates (%) of: LEI (74.5/79.8), HAQ-DI (26.1/37.0), pt pain (14.7/30.6), PASI (66.8/81.5), PtGA (24.5/39.9), SJC (46.2/63.0), and TJC (14.7/28.3), respectively. Times to achievement of minimal scores for LEI, SJC, and PASI were faster than for PtGA, HAQ-DI, pt pain, and TJC for native-scale scores; when normalized, PtGA, HAQ-DI, and pt pain showed a slower response (Figure 1). Higher BL HAQ-DI and worse fatigue (lower functional assessment of chronic illness therapy [FACIT]-fatigue score) were significantly associated with longer time to HAQ-DI ≤0.5; these factors plus older age predicted W48 non-achievement of HAQ-DI ≤0.5 (Table 1). Worse BL pt pain and fatigue were significant predictors of longer time to pt pain ≤15; these factors plus pFM predicted W48 non-achievement of pt pain ≤15. Worse BL fatigue was also significantly associated with longer time to PtGA ≤20 and W48 non-achievement of PtGA ≤20. Higher TJC, methotrexate (MTX) use, and no

Figure 1. Time to achieve MDA for each domain with GUS treatment



PASI score was assessed at BL and from W16

BL, baseline; GUS, guselkumab; HAQ-DI, Health Assessment Questionnaire-Disability Index; MDA, minimal disease activity; PASI, Psoriasis Area and Severity Index; PtGA, Patient Global Assessment; SJC, swollen joint count; TJC, tender joint count; W, week

Table 1. Predictors of time to achievement and achievement of pt-reported MDA domains at W48 in GUS pts

	BL variable	HAQ-DI ≤0.5	Pt pain ≤15	PtGA ≤20	TJC ≤1
Time to achievement HR (95% CI)	FACIT-fatigue	1.0 (1.0–1.1)*	1.0 (1.0–1.1)*	1.0 (1.0–1.1)†	
	HAQ-DI	0.3 (0.2–0.6)‡			
	Pt pain		1.0 (1.0–1.0)†		
	MTX use				0.6 (0.4–0.9)*
	pFM presence				1.8 (1.0–3.2)*
	TJC				0.9 (0.9–1.0)‡
Achievement at W48 OR (95% CI)	Age	1.0 (0.9–1.0)*			1.0 (1.0–1.0)*
	FACIT-fatigue	1.1 (1.0–1.1)‡	1.1 (1.0–1.1)‡	1.1 (1.0–1.1)‡	
	HAQ-DI	0.2 (0.1–0.5)†			
	Pt pain		1.0 (1.0–1.0)‡		
	MTX use				0.4 (0.2–0.8)†
	pFM presence		0.5 (0.3–1.0)*		
	TJC				0.9 (0.9–1.0)‡

BL, baseline; CI, confidence interval; FACIT, Functional Assessment of Chronic Illness Therapy; pFM, primary fibromyalgia; GUS, guselkumab, HAQ-DI: Health Assessment Questionnaire-Disability Index; HR, hazard ratio; MDA, minimal disease activity; MTX, methotrexate; OR, odds ratio; pt, patient; PtGA, Patient Global Assessment; TJC, tender joint count; W, week
*$P<0.05$; †$P<0.01$; ‡$P<0.001$

pFM at BL were significantly associated with longer time to TJC ≤1; higher BL TJC, MTX use, and older age predicted W48 non-achievement of TJC ≤1.

Conclusion: GUS provided sustainable improvement in all MDA domains through W48. Physician-reported domains (LEI, PASI and SJC) were achieved faster than pt-driven domains (PtGA, HAQ-DI, pt pain, and TJC). BL domain scores, worse fatigue and MTX use (for TJC only) were inversely correlated with MDA in the refractory domains.

Disclosure: L. Coates: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, Bristol Myers Squibb, 2, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead Sciences, 2, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake, 2, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **C. Selmi**: AbbVie, 2, 5, 6, Alfa-Wassermann, 2, 6, Amgen, 2, 5, 6, Biogen, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 5, SOBI, 2, 6; **G. Schett**: None; **P. Richette**: None; **F. Ramirez Garcia**: AbbVie/Abbott, 2, 6, Amgen, 6, Eli Lilly, 6, Janssen, 6, 12, Paid Instructor, Novartis, 2, 6, 12, Paid Instructor, Pfizer, 5, 6, UCB, 2, 6; **W. Noël**: Janssen, 3; **E. Rampakakis**: Janssen, 2, JSS Medical Research, 3; **M. Zimmermann**: Janssen, 3; **M. Sharaf**: Janssen, 3, Johnson & Johnson, 11; **D. McGonagle**: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, 6, 12, Paid Instructor, Janssen, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 1422

Long-Term Safety of Risankizumab in Patients with Psoriatic Disease: Integrated Analysis of Psoriasis and Psoriatic Arthritis Clinical Trial Data

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Risankizumab, an interleukin-23 inhibitor, was efficacious and well tolerated in plaque psoriasis (PsO) and psoriatic arthritis (PsA) clinical trials.The objective of this integrated data analysis of multiple PsO and PsA clinical trials was to report long-term safety of risankizumab in patients with psoriatic disease.

Methods: Integrated risankizumab safety data sets (data cutoff March 25, 2023) were compiled from 20 phase 1–4 clinical trials in PsO and 4 phase 2–3 trials in PsA. Treatment-emergent adverse events (AEs) and AEs of safety interest were reported for patients receiving ≥1 dose of risankizumab. Exposure adjusted event rates are presented as events per 100 patient years (E/100 PY).

Results: Among 3658 patients with PsO (13,329.3 PY exposure), median (range) of treatment duration was 4.1 years (81 days–8.8 years); among 1542 patients with PsA (3803.0 PY exposure), median (range) treatment duration was 2.8 years (84 days–4.0 years). Rates of treatment-emergent AEs (145.5 events [E]/100PY), serious AEs (7.4 E/100PY), and AEs leading to discontinuation (1.9 E/100PY) in patients with PsO were similar to those in patients with PsA (142.6 E/100PY, 8.6 E/100PY, and 1.8 E/100PY, respectively; **Table**). Similar rates of infections (46.2 and 41.3 E/100 PY) and serious infections (1.2 and 2.0 E/100PY) were reported among PsO and PsA groups, respectively. Nasopharyngitis (12.1

Table. Treatment-Emergent AEs in Patients with Psoriasis and Psoriatic Arthritis

	PsO (n=3658, 13,329.3 PY) E (E/100PY) [95% CI]	PsA (n=1542, 3803.0 PY) E (E/100PY) [95% CI]
AEs	19,390 (145.5) [143.4–147.5]	5423 (142.6) [138.8–146.
Serious AEs	986 (7.4) [6.9–7.9]	327 (8.6) [7.7–9.6]
AEs leading to discontinuation	250 (1.9) [1.7–2.1]	68 (1.8) [1.4–2.3]
Infections	6157 (46.2)	1570 (41.3)
Nasopharyngitis	1619 (12.1)	217 (5.7)
URTI	853 (6.4)	156 (4.1)
COVID-19	426 (3.2)	306 (8.0)
Herpes zoster	70 (0.5) [0.4–0.7]	12 (0.3) [0.2–0.6]
Serious infections	165 (1.2) [1.1–1.4]	75 (2.0) [1.6–2.5]
Sepsis	15 (0.1)	3 (<0.1)
COVID-19[a]	13 (<0.1)	8 (0.2)
Pneumonia	13 (<0.1)	7 (0.2)
COVID-19 pneumonia	7 (<0.1)	12 (0.3)
Opportunistic infection[b]	11 (<0.1) [0.0–0.2]	3 (<0.1) [0.0–0.2]
Active tuberculosis	1 (<0.1) [0.0–0.04]	0
Fungal infections	319 (2.4) [2.1–2.7]	61 (1.6) [1.2–2.1]
Tinea infections	186 (1.4)	11 (0.3)
Candida	69 (0.5) [0.4–0.7]	17 (0.4) [0.3–0.7]
Malignant tumors	161 (1.2) [1.0–1.4]	39 (1.0) [0.7–1.4]
NMSC	76 (0.6) [0.5–0.7]	19 (0.5) [0.3–0.8]
Malignant tumors excluding NMSC	85 (0.6) [0.5–0.8]	20 (0.5) [0.3–0.8]
Gastrointestinal cancers[c]	23 (0.2) [0.1–0.3]	2 (<0.1) [0.0–0.2]
Breast cancer	13 (<0.1) [0.1–0.2]	3 (<0.1) [0.0–0.2]
Prostate cancer	12 (<0.1) [0.1–0.2]	5 (0.1) [0.0–0.3]
Melanoma	8 (<0.1) [0.0–0.1]	2 (<0.1) [0.0–0.2]
Serious hypersensitivity[d]	10 (<0.1) [0.0–0.1]	3 (<0.1) [0.0–0.2]
Injection site reaction	373 (2.8) [2.5–3.1]	35 (0.9) [0.6–1.3]

AE, adverse event; E, event; NMSC, non-melanoma skin cancer; PsA, psoriatic arthritis; PsO, psoriasis; PY patient-years; TEAEs, treatment-emergent adverse events; URTI, upper respiratory tract infection.
[a]Clinical trial data for patients with psoriasis mostly pre-dated the onset of the COVID-19 pandemic.
[b]Excluding tuberculosis and herpes zoster.
[c]Events for PsO: pancreatic carcinoma (n=5), adenocarcinoma of colon (n=3), colorectal adenocarcinoma (n=2), colorectal cancer (n=2), gastric cancer (n=2), rectal cancer (n=2), anal cancer (n=1), colon cancer metastatic (n=1), colon cancer stage 0 (n=1), intestinal adenocarcinoma (n=1), esophageal carcinoma (n=1), pancreatic carcinoma stage IV (n=1), and rectal adenocarcinoma (n=1); events for PsA: adenocarcinoma of colon (n=1) and colorectal cancer (n=1).
[d]Events for PsO: eczema (n=2), Steven-Johnson syndrome (n=2), urticaria (n=2), angioedema (n=1), drug hypersensitivity (n=1), erythema multiforme (n=1), and hypersensitivity (n=1); events for PsA: anaphylactic reaction (n=1), hypersensitivity (n=1), and immune thrombocytopenia (n=1).

E/100PY), upper respiratory infection (6.4 E/100PY) and COVID-19 (3.2 E/100PY) were the most common infections in PsO and COVID-19 (8.0 E/100PY), nasopharyngitis (5.7 E/100PY) and upper respiratory infection (4.1 E/100PY) were the most common infections in PsA. The most common serious infections were sepsis, COVID-19, and pneumonia in PsO (0.1, < 0.1, and < 0.1 E/100PY, respectively) and COVID-19 pneumonia, COVID-19, and pneumonia in PsA (0.3, 0.2 and 0.2 E/100PY, respectively). Rates of opportunistic infections excluding tuberculosis (both < 0.1 E/100PY) and herpes zoster (0.5 and 0.3 E/100 PY, respectively) were comparable in PsO and PsA. Rates of non-melanoma skin cancer (NMSC) were 0.6 and 0.5 E/100PY and malignant tumors excluding NMSC were 0.6 and 0.5 E/100PY in PsO and PsA, respectively.

Conclusion: Rates of AEs, AEs of safety interest, and AEs leading to discontinuation remained low in this largest and longest safety reporting for risankizumab in patients with psoriatic disease to date. Rates of AEs of safety interest were within reported benchmarks for both PsO and PsA. Rates of COVID-19 infection were as expected. Overall, these results support the safety profile of risankizumab for the long-term treatment of patients with psoriatic disease.

Disclosure: K. Gordon: AbbVie/Abbott, 2, 5, Almirall, 2, 5, Amgen, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 2, 5, Dermira, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Leo Pharma, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Sanofi-Aventis, 2, 5, Sun, 2, 5, UCB, 2, 5; **A. Blauvelt**: AbbVie/Abbott, 5, 6, Abcentra, 6, Acelyrin, 12, Clinical study investigator, Aclaris, 6, Affibody, 6, Aligos, 6, Allakos, 12, Clinical study

investigator, Almirall, 6, Alumis, 6, Amgen, 5, 6, Anaptysbio, 6, Apogee, 6, Arcutis, 5, 6, Arena, 6, Aslan, 6, Athenex, 5, 6, 12, Clinical study investigator, Bluefin, 6, Boehringer-Ingelheim, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Cara Therapeutics, 6, Concert, 12, Clinical study investigator, CTI Biopharma, 6, Dermavant, 5, 6, EcoR1, 6, Eli Lilly, 5, 6, Escient, 6, Evelo, 6, Evommune, 6, Forte, 6, Galderma, 5, 6, HighlightII Pharma, 6, Incyte, 5, 6, InnoventBio, 6, Janssen, 5, 6, Landos, 6, Leo, 5, 6, Merck/MSD, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Rani, 6, Rapt, 6, Regeneron, 5, 6, Sanofi Genzyme, 6, Spherix Global Insights, 6, Sun Pharma, 5, 6, TLL Pharmaceutical, 6, TrialSpark, 6, UCB, 5, 5, 6, 6, Union, 6, Ventyx, 6, Vibliome, 6, Xencor, 6; **H. Bachelez**: AbbVie/Abbott, 1, 2, 5, 6, Almirall, 1, 2, 5, 6, Amgen, 1, 2, 5, 6, Bayer, 1, 2, 5, 6, Biocad, 1, 2, 5, 6, Boehringer-Ingelheim, 1, 2, 5, 6, Celgene, 1, 2, 5, 6, Dermavant, 1, 2, 5, 6, Eli Lilly, 1, 2, 5, 6, Janssen, 1, 2, 5, 6, Leo Pharma, 1, 2, 5, 6, Menarini, 1, 2, 5, 6, Merck/MSD, 1, 2, 5, 6, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, 6, Pierre Fabre, 1, 2, 5, 6, Sandoz, 1, 2, 5, 6, Sun Pharmaceuticals, 1, 2, 5, 6, UCB, 1, 2, 5, 6; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, Bristol Myers Squibb, 2, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead Sciences, 2, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake, 2, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **B. Kaplan**: AbbVie/Abbott, 3, 11; **W. Koetse**: AbbVie/Abbott, 3, 11; **L. Drogaris**: AbbVie/Abbott, 3, 11; **R. Sinvhal**: AbbVie/Abbott, 3, 11; **K. Papp**: AbbVie, 1, 2, 5, 6, Akros, 1, 2, 5, 6, Amgen, 1, 2, 5, 6, Anacor, 1, 2, 5, 6, Arcutis, 1, 2, 5, 6, Astellas, 1, 2, 5, 6, Bausch Health/Valeant, 1, 2, 5, 6, Baxalta, 1, 2, 5, 6, Boehringer-Ingelheim, 1, 2, 5, 6, Bristol-Myers Squibb, 1, 2, 5, 6, Can-Fite Biopharma, 1, 2, 5, 6, Celgene, 1, 2, 5, 6, Coherus, 1, 2, 5, 6, Dermira, 1, 2, 5, 6, Dow Pharma, 1, 2, 5, 6, Eli Lilly, 1, 2, 5, 6, Evelo, 1, 2, 5, 6, Forward Pharma, 5, Galapagos, 1, 2, 5, 6, Galderma, 1, 2, 5, 6, Genentech, 1, 2, 5, 6, Gilead, 1, 2, 5, 6, GlaxoSmithKlein, 1, 2, 5, 6, Janssen, 1, 2, 5, 6, Kyowa-Hakko Kirin, 1, 2, 5, 6, LEO Pharma, 1, 2, 5, 6, MedImmune, 1, 2, 5, 6, Meiji Seika Pharma, 1, 2, 5, 6, Merck-Serono, 1, 2, 5, 6, Mitsubishi Pharma, 1, 2, 5, 6, Moberg Pharma, 1, 2, 5, 6, MSD, 1, 2, 5, 6, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, 6, PRCL Research, 1, 2, 5, 6, Regeneron, 1, 2, 5, 6, Roche, 1, 2, 5, 6, Sanofi-Aventis/Genzyme, 1, 2, 5, 6, Sun Pharma, 1, 2, 5, 6, Takeda, 1, 2, 5, 6, UCB, 1, 2, 5, 6.

Abstract Number: 1423

Impact of Upadacitinib on Enthesitis and Dactylitis by Location in Patients with Psoriatic Arthritis and an Inadequate Response to Biologic DMARDs from the SELECT-PsA 2 Trial

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Enthesitis and dactylitis are associated with reduced quality of life and greater impairment in daily activities. In the SELECT-PsA 2 phase 3 trial, the JAK inhibitor upadacitinib (UPA) demonstrated greater resolution of enthesitis and dactylitis compared to placebo (PBO) in patients with PsA. However, while the sites of enthesitis and dactylitis involvement are highly variable, relatively limited data are available regarding location-specific resolution of these disease manifestations in PsA. In this post hoc analysis, we evaluated site-specific responses of enthesitis and dactylitis to treatment with UPA over 56 weeks in patients with PsA from SELECT-PsA 2.

Methods: In SELECT-PsA 2, patients with an inadequate response or intolerance to ≥1 biologic DMARD (bDMARD-IR) were randomized to receive once daily UPA 15 mg or PBO.[1] Patients initially randomized to PBO were switched to UPA at week 24. Baseline characteristics were evaluated for patients with enthesitis (defined as Leeds Enthesitis Index [LEI] or

SPARCC Enthesitis Index >0) or dactylitis (defined as Leeds Dactylitis Index [LDI] >0). Among patients with baseline involvement, the presence of enthesitis (shoulders, elbows, hips, knees, and heels) and dactylitis (hands, feet, both hands and feet, and either hands or feet) was assessed at baseline, week 24, and week 56 in patients randomized to UPA 15 mg and in those who switched from PBO to UPA 15 mg at week 24.

Results: Of the 423 patients receiving UPA 15 mg (n=211) or PBO (n=212) in SELECT-PsA 2, 344 (81%) had baseline enthesitis or dactylitis. More patients had baseline enthesitis involvement (n=257) than dactylitis (n=87), although subgroups were non-exclusive, and patients could present with both. The mean LEI and LDI scores at baseline were ~3.1 and ~113.2 for patient subgroups with enthesitis and dactylitis, respectively, indicating a relatively high disease burden (**Table 1**). Across all examined locations, treatment with UPA resulted in greater decreases in the proportions of patients with enthesitis or dactylitis compared to PBO at week 24 (**Figure 1**). Notably, all sites of enthesitis or dactylitis involvement demonstrated improvement with UPA, ranging from a 30-percentage point reduction from baseline for heel enthesitis to a 7-percentage point reduction for hip enthesitis, as well as a 51-percentage point reduction in dactylitis of the hands or feet. The proportions of UPA-treated patients with enthesitis or dactylitis continued to decrease from week 24 to week 56. Additionally,

Table 1. Baseline Demographics and Disease Characteristics of Patients With Enthesitis and Dactylitis in SELECT-PsA 2

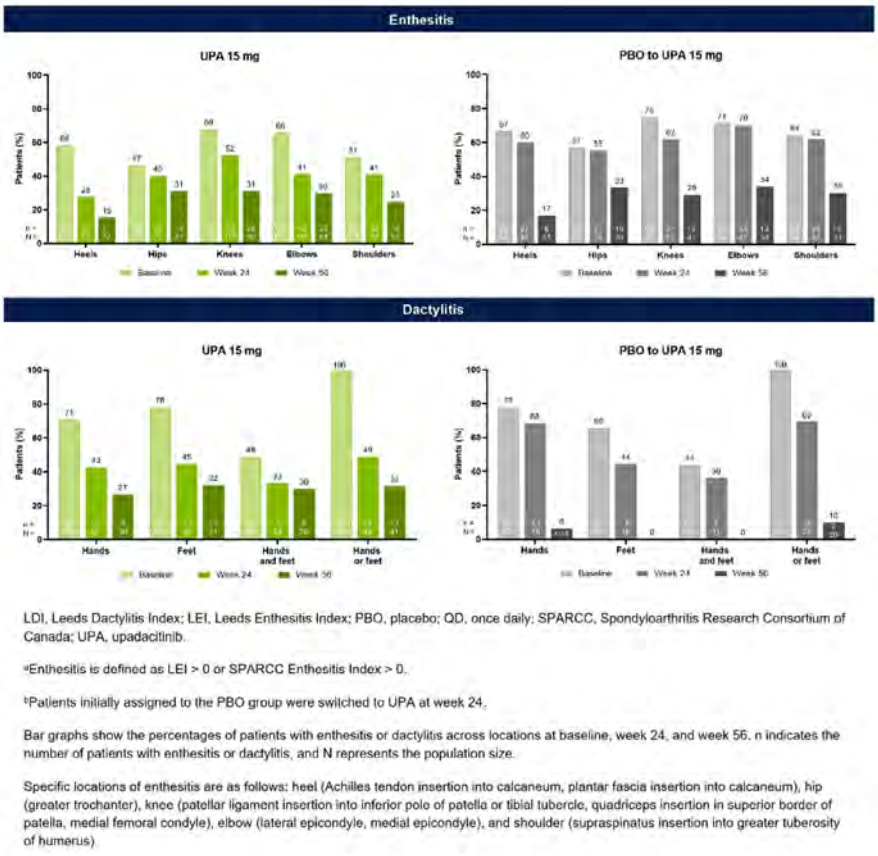
	Enthesitis[b]		Dactylitis	
Characteristic[a]	PBO to UPA 15 mg QD[c] (n = 84)	UPA 15 mg QD (n = 173)	PBO to UPA 15 mg QD[c] (n = 32)	UPA 15 mg QD (n = 55)
Age, years	51.1 ± 11.6	53.4 ± 11.7	51.5 ± 11.6	53.6 ± 12.9
Sex, n (%)				
Female	47 (56.0)	94 (54.3)	18 (56.3)	27 (49.1)
Male	37 (44.0)	79 (45.7)	14 (43.8)	28 (50.9)
Race, n (%)				
Asian	6 (7.1)	14 (8.1)	4 (12.5)	6 (10.9)
Black or African American	3 (3.6)	4 (2.3)	3 (9.4)	0
Multiple	1 (1.2)	0	0	0
Native Hawaiian or other Pacific Islander	0	0	0	1 (1.8)
White	74 (88.1)	155 (89.6)	25 (78.1)	48 (87.3)
Duration since PsA Diagnosis, years	10.4 ± 9.7	10.0 ± 8.7	10.8 ± 10.9	13.0 ± 8.5
Any non-bDMARD at BL, n (%)	42 (50.0)	84 (48.6)	15 (46.9)	29 (52.7)
Number of Prior bDMARD received, n (%)				
1	51 (60.7)	99 (57.2)	20 (62.5)	26 (47.3)
2	15 (17.9)	38 (22)	5 (15.6)	12 (21.8)
≥ 3	18 (21.4)	36 (20.8)	7 (21.9)	17 (30.9)
Prior anti-TNF failure, n (%)	54 (84.4)	116 (90.6)	19 (82.6)	41 (89.1)
SJC66	12.8 ± 9.6	11.3 ± 8.5	14.8 ± 10.2	14.9 ± 10.7
TJC68	29.2 ± 17.8	26.0 ± 17.6	31.1 ± 17.3	29.4 ± 18.3
Patient's Assessment of Pain (NRS 0–10)	6.8 ± 2.0	6.5 ± 2.2	7.2 ± 1.9	6.7 ± 1.8
HAQ-DI	1.3 ± 0.7	1.1 ± 0.6	1.4 ± 0.6	1.1 ± 0.6
LEI > 0, n (%)	71 (84.5)	133 (76.9)	26 (81.3)	39 (70.9)
LEI score (for BL > 0)	3.4 ± 1.7	3.0 ± 1.6	3.7 ± 1.9	3.3 ± 1.9
LDI > 0, n (%)	30 (35.7)	46 (26.6)	32 (100)	55 (100)
LDI (for BL > 0)	145.4 ± 217.2	92.3 (99.4)	137.7 ± 212.3	96.3 ± 97.9
SPARCC Enthesitis Index > 0, n (%)	84 (100)	172 (99.4)	30 (93.8)	46 (83.6)
SPARCC Enthesitis Index score (for BL > 0)	7.3 ± 4.4	6.1 ± 4.3	7.7 (4.9)	7.3 (4.4)
hsCRP	11.0 ± 19.4	11.5 ±19.7	13.8 ± 23.9	16.4 ± 26.7

bDMARD, biologic DMARD; BL, baseline; HAQ-DI, Health Assessment Questionnaire-Disability Index; hsCRP, high-sensitivity C-reactive protein; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; NRS, numeric rating scale; PBO, placebo; QD, once daily; SPARCC, Spondyloarthritis Research Consortium of Canada; UPA, upadacitinib.

[a]Baseline characteristics are reported as mean ± SD unless otherwise noted.

[b]Enthesitis is defined as LEI > 0 or SPARCC Enthesitis Index > 0.

[c]Patients initially assigned to the PBO group were switched to UPA at week 24.



LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; PBO, placebo; QD, once daily; SPARCC, Spondyloarthritis Research Consortium of Canada; UPA, upadacitinib.

[a]Enthesitis is defined as LEI > 0 or SPARCC Enthesitis Index > 0.

[b]Patients initially assigned to the PBO group were switched to UPA at week 24.

Bar graphs show the percentages of patients with enthesitis or dactylitis across locations at baseline, week 24, and week 56. n indicates the number of patients with enthesitis or dactylitis, and N represents the population size.

Specific locations of enthesitis are as follows: heel (Achilles tendon insertion into calcaneum, plantar fascia insertion into calcaneum), hip (greater trochanter), knee (patellar ligament insertion into inferior pole of patella or tibial tubercle, quadriceps insertion in superior border of patella, medial femoral condyle), elbow (lateral epicondyle, medial epicondyle), and shoulder (supraspinatus insertion into greater tuberosity of humerus)

Figure 1. Proportions of PsA Patients With Enthesitis or Dactylitis By Site Over Time in SELECT-PsA 2 (As Observed)

patients who switched from PBO to UPA 15 mg at week 24 were able to achieve similar responses as the continuous UPA group by week 56.

Conclusion: UPA treatment was effective in controlling enthesitis and dactylitis at all evaluated locations in bDMARD-IR PsA patients at week 24, including locations where the disease burden may significantly impact quality of life, with continued improvements evident at week 56. However, results should be interpreted with caution given the small sample size for some subgroups, particularly dactylitis.

References

1. Mease, PJ et al. *N Engl J Med* 2017; 377: 1537-50.

Disclosure: L. Coates: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, Bristol Myers Squibb, 2, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead Sciences, 2, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake, 2, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **C. Bakewell**: AbbVie, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Sanofi Genzyme/Regeneron, 2, 6, UCB, 2, 6; **M. Khraishi**: AbbVie, 2, Amgen, 2, Gilead, 2, Novartis, 2, Pfizer, 2, UCB, 2; **S. Chen**: AbbVie, 12, Provided statistical analysis support funded by AbbVie, Bristol Myers Squibb, 12, Spouse is an employee, Tigermed-BDM Inc., 3; **T. Gao**: AbbVie, 3, 11; **A. Setty**: AbbVie, 3, 11; **H. Jones**: AbbVie, 3, 11; **S. Ciecinski**: AbbVie, 3, 11; **E. Mysler**: AbbVie, 2, 5, Amgen, 2, 5, Astra Zeneca, 2, 5, BMS, 2, 5, GSK, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 2, 5, Sanofi, 2, 5.

Abstract Number: 1424

Early Fatigue Improvement with Guselkumab Associates with Longer Term Disease Control in Patients with Active Psoriatic Arthritis Reporting Substantial Fatigue: Post Hoc Analyses of a Sub-Population of a Phase 3, Randomized, Controlled Trial of Guselkumab in Biologic-Naïve Patients

Dafna Gladman[1], Xenofon Baraliakos[2], Michael Starr[3], Roberto Ranza[4], Emmanouil Rampakakis[5], Natalie shiff[6], Francois Nantel[7], Chenglong Han[8], Andrew James Knowles Ostor[9] and Philip J. Mease[10], [1]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Department of Medicine, University of Toronto, Toronto, ON, Canada, [2]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [3]Division of Rheumatology, McGill University Health Center, Montreal, QC, Canada, [4]Rheumatology Unit, Hospital das Clínicas da Universidade Federal de Uberlândia, Uberlândia, Brazil, [5]McGill University, Department of Pediatrics / JSS Medical Research, Scientific Affairs, Montreal, QC, Canada, [6]Immunology, Janssen Scientific Affairs, LLC / Adjunct, Community Health and Epidemiology, University of Saskatchewan, Horsham, PA, [7]Nantel Medsci Consult, Consultant, Montreal, QC, Canada, [8]Immunology, Janssen Global Services, LLC, Malvern, PA, [9]Cabrini Hospital, Monash University & Emeritus Research / Australian National University, Canberra, Australia, [10]Swedish Medical Center/Providence St. Joseph Health and University of Washington School of Medicine, Seattle, WA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

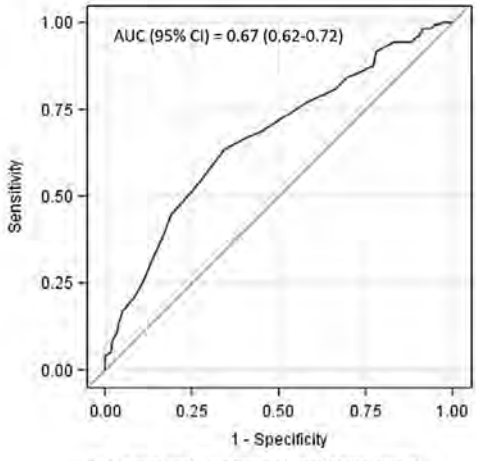
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Fatigue is commonly reported by PsA patients (pts) and contributes to disease burden. The fully human IL-23p19-subunit inhibitor guselkumab (GUS) induces clinically meaningful and sustained fatigue improvements through 1y, with GUS exhibiting a substantial direct effect on fatigue, independent of its impact on other clinical outcomes[1,2]. We previously showed that early fatigue response predicted clinically meaningful improvement (CMI) in fatigue at 2y[3]. In a sub-population of PsA pts with substantial fatigue at baseline (BL), relationships between early fatigue improvement and disease control at 1y were assessed.

Figure 1. ROC Analysis for Discriminatory Power of FACIT-F Score at W8 Using PASDAS at 1 Year as External Criterion (Representative Example) – 448 Pts Randomized to GUS Q4W & GUS Q8W with BL FACIT-F score ≤43

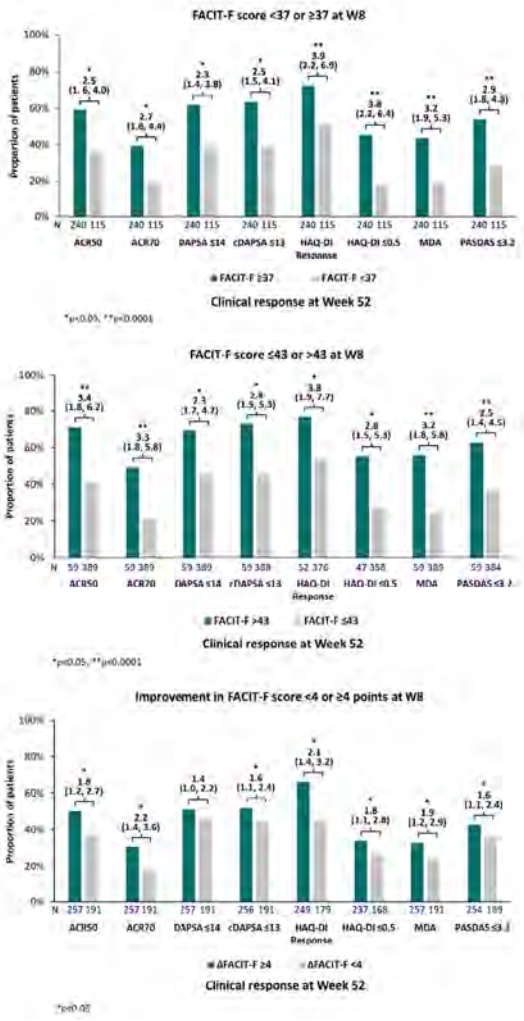


AUC = area under the curve; CI: confidence interval.

Methods: DISCOVER-2 enrolled bionaïve adults with active PsA (≥5 swollen & ≥5 tender joints, CRP ≥0.6 mg/dl). Pts were randomized (1:1:1) to GUS 100mg every 4 weeks (Q4W); GUS 100mg at W0, W4, Q8W; or placebo (PBO). Pts with BL fatigue below normative levels (Functional Assessment of Chronic Illness Therapy – Fatigue [FACIT-F] score ≤43)[3] were included in the analysis. Receiver operating characteristic (ROC) analyses pooling GUS Q4W and Q8W utilized Youden's index to determine optimal FACIT-F cutoffs at W8 (1st post-BL timepoint assessed) for predicting 1y achievement of ACR50/70, Disease Activity (DA) Index for PsA (DAPSA) ≤14 (in pts with BL DAPSA >14), clinical (c) DAPSA ≤13 (in pts with BL cDAPSA >13), PsA DA Score (PASDAS) ≤3.2 (in pts with BL PASDAS >3.2), HAQ-Disability Index (HAQ-DI) response (improvement ≥0.35 in pts with BL HAQ-DI ≥0.35), HAQ-DI ≤0.5 (in pts with BL HAQ-DI >0.5), and MDA. The association of identified and established FACIT-F cutoffs (≥4-point improvement & score >43) with 1y response was assessed via BL-adjusted logistic regression.

Results: In this sub-population of 448/493 GUS-randomized bionaïve PsA pts with BL FACIT-F score ≤43, the mean (SD) BL FACIT-F level of 28.4 (8.7) indicated severe fatigue. ROC analysis **(Figure 1)** identified optimal FACIT-F cutoffs at W8 for predicting 1y disease control with GUS ranging from ≥36 (ACR50, DAPSA≤14, cDAPSA≤13, HAQ-DI≤0.5, PASDAS≤3.2) to ≥41 (HAQ-DI response); intermediary cutoffs were identified for remaining endpoints. The FACIT-F ≥37 cutoff was selected for further analyses as the lowest score (highest fatigue) with a significantly higher probability of achievement with GUS vs PBO (32% vs 24%; p=0.0445).

Figure 2. Early (W8) Achievement of Fatigue (FACIT-F) Targets and 1-Year Clinical Outcomes – 448 Pts Randomized to GUS Q4W & GUS Q8W with BL FACIT-F score ≤43



In pts with BL FACIT-F < 37, W8 FACIT-F ≥37 achievement with GUS associated with significantly higher odds of clinical response at 1y (nominal p< 0.05; odds ratio range: 2.3-3.9) **(Figure 2)**. W8 achievement of normative FACIT-F levels or FACIT-F CMI also associated with significantly greater clinical response rates at 1y.

Conclusion: In this sub-population of bionaïve pts with active PsA enriched for high fatigue levels, early achievement of FACIT-F endpoints with GUS associated with higher rates of clinical response and improved/normalized physical function at 1y. Results of this post hoc analysis further underscore the importance of early improvement in patient-reported outcomes such as fatigue on the trajectory of long-term pt outcome.

References:

1. Ritchlin CT. *RMD Open*. 2022;8;e002195
2. Rahman P. *Arthritis Res Ther*. 2021;23:190
3. Gladman D. *Arthritis Rheumatol*. 2022;74 (suppl 9)

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Abstract Number: 1425

Efficacy and Safety of Tofacitinib in an Open-Label, Long-Term Extension Study in Patients with Psoriatic Arthritis Who Received Adalimumab or Tofacitinib in a Phase 3 Randomized Controlled Study: A Post Hoc Analysis

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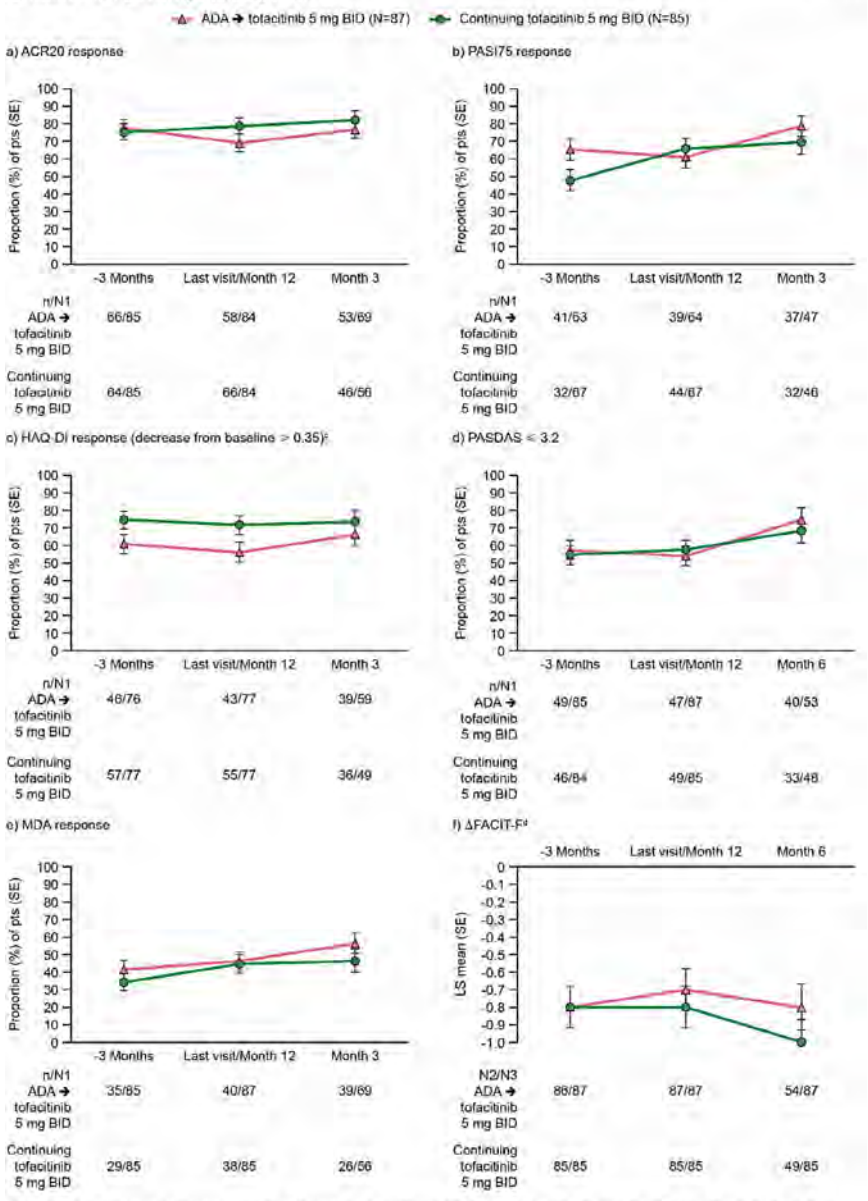
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients (pts) with PsA and an inadequate response (IR) to conventional synthetic DMARDs are routinely treated with TNF inhibitors (TNFi).[1,2] Intolerance/IR to TNFi may require switching treatments.[1,2] Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. Data on whether treatment can be safely and effectively switched from TNFi



-3 months: 3 months prior to the last visit in the P3 study. Last visit/Month 12: the last visit or Month 12 in the P3 study. Month 3: Month 3 in the LTE study. Month 6: Month 6 in the LTE study

Baseline refers to the baseline visit of the P3 study

The LTE SAS includes pts from the P3 study who had at least one dose of treatment in the LTE study with the 14-day gap rule. The 14-day gap rule was defined as the number of days between a pt's last visit in the P3 study and their first dose of tofacitinib 5 mg BID in the LTE study. Pts who met the 14-day gap rule were excluded

[a]LTE study: NCT01976364 (OPAL Balance)

[b]P3 study: NCT01877668 (OPAL Broaden)

[c]In pts with baseline HAQ-DI ≥ 0.35 (N=77)

[d]Results are based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction, geographic location, and baseline value – an unstructured covariance matrix was used

Δ, change from baseline; ACR20, ACR ≥ 20% response criteria; ADA, adalimumab; BID, twice daily; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, HAQ-Disability Index; LS, least squares; LTE, long-term extension; MDA, minimal disease activity; N, number of pts in the LTE SAS; N1, number of pts with non-missing response at visit; N2, number of pts with observations at visit; N3, number of pts included in the mixed model for repeated measures; n, number of pts with response; P, Phase; PASDAS, PsA Disease Activity Score; PASI75, Psoriasis Area and Severity Index 75; pt, patient; Q2W, once every 2 weeks; SAS, safety analysis set; SE, standard error

Table 1. Safety outcomes in pts with PsA who either continued or switched to tofacitinib 5 mg BID in the LTE study after receiving tofacitinib 5 mg BID or ADA 40 mg Q2W in the P3 study

	P3 study[a]				LTE study[b]			
Interval	**To M3**		**To M12**		**To M3**		**To M12**	
	ADA → tofacitinib 5 mg BID (N=91)	**Continuing tofacitinib 5 mg BID (N=89)**	**ADA → tofacitinib 5 mg BID (N=91)**	**Continuing tofacitinib 5 mg BID (N=89)**	**ADA → tofacitinib 5 mg BID (N=91)**	**Continuing tofacitinib 5 mg BID (N=89)**	**ADA → tofacitinib 5 mg BID (N=91)**	**Continuing tofacitinib 5 mg BID (N=89)**
TEAEs								
n (%)	40 (44.0)	31 (34.8)	63 (69.2)	57 (64.0)	26 (28.6)	22 (24.7)	46 (50.6)	41 (46.1)
IR	260.2	193.4	158.7	125.7	161.5	139.9	120.6	115.6
(95% CI)	(185.9, 354.4)	(131.4, 274.5)	(121.9, 203.0)	(95.2, 162.8)	(105.5, 236.6)	(87.7, 211.8)	(88.3, 160.9)	(83.0, 156.9)
Serious AEs								
n (%)	0 (0.0)	0 (0.0)	7 (7.7)	2 (2.3)	3 (3.3)	1 (1.1)	7 (7.7)	3 (3.4)
IR	0.0	0.0	8.8	2.5	15.6	5.3	12.2	5.6
(95% CI)	(0.0, 17.7)	(0.0, 18.0)	(3.6, 18.2)	(0.3, 8.9)	(3.2, 45.6)	(0.1, 29.7)	(4.9, 25.2)	(1.2, 16.4)
Serious infections								
n (%)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (2.2)	2 (2.3)
IR	0.0	0.0	1.2	0.0	0.0	5.3	3.4	3.7
(95% CI)	(0.0, 17.7)	(0.0, 18.0)	(0.0, 6.8)	(0.0, 4.5)	(0.0, 18.9)	(0.1, 29.7)	(0.4, 12.2)	(0.5, 13.4)

Total follow-up time calculated up to the day of the first event, subject to a risk period of 28 days beyond the last dose or to the data cut-off date. Gaps in dosing between treatment switches or between the P3 and LTE studies are included up to 28 days or to the data cut-off date

[a]P3 study: NCT01877668 (OPAL Broaden)

[b]LTE study: NCT01976364 (OPAL Balance)

ADA, adalimumab; AE, adverse event; BID, twice daily; CI, confidence interval; IR, incidence rate (pts with events/100 pt-years); LTE, long-term extension; M, Month; N, number of evaluable pts; n, number of pts with events; P, Phase; pt, patient; Q2W, once every 2 weeks; TEAE, treatment-emergent adverse event

Table 2. TEAEs by Preferred Term[a] (occurring in ≥ 5% of pts in any group) in pts with PsA who either continued or switched to tofacitinib 5 mg BID in the LTE study after receiving tofacitinib 5 mg BID or ADA 40 mg Q2W in the P3 study

	P3 study[b]				LTE study[c]			
Interval	**To M3**		**To M12**		**To M3**		**To M12**	
	ADA → tofacitinib 5 mg BID (N=91)	**Continuing tofacitinib 5 mg BID (N=89)**	**ADA → tofacitinib 5 mg BID (N=91)**	**Continuing tofacitinib 5 mg BID (N=89)**	**ADA → tofacitinib 5 mg BID (N=91)**	**Continuing tofacitinib 5 mg BID (N=89)**	**ADA → tofacitinib 5 mg BID (N=91)**	**Continuing tofacitinib 5 mg BID (N=89)**
Alanine aminotransferase increased								
n (%)	4 (4.4)	1 (1.1)	7 (7.7)	3 (3.4)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)
IR	19.7	4.9	9.1	3.7	5.2	0.0	1.7	0.0
(95% CI)	(5.4, 50.3)	(0.1, 27.4)	(3.6, 18.7)	(0.8, 10.9)	(0.1, 28.8)	(0.0, 19.7)	(0.0, 9.4)	(0.0, 6.8)
Aspartate aminotransferase increased								
n (%)	3 (3.3)	0 (0.0)	7 (7.7)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)
IR	14.7	0.0	9.0	0.0	5.2	0.0	1.7	0.0
(95% CI)	(3.0, 43.1)	(0.0, 18.0)	(3.6, 18.6)	(0.0, 4.5)	(0.1, 28.8)	(0.0, 19.7)	(0.0, 9.4)	(0.0, 6.8)
Blood creatine phosphokinase increased								
n (%)	2 (2.2)	1 (1.1)	3 (3.3)	5 (5.6)	1 (1.1)	1 (1.1)	1 (1.1)	3 (3.4)
IR	9.8	4.9	3.8	6.3	5.2	5.4	1.7	5.7
(95% CI)	(1.2, 35.2)	(0.1, 27.3)	(0.8, 11.0)	(2.0, 14.7)	(0.1, 28.8)	(0.1, 30.1)	(0.0, 9.4)	(1.2, 16.8)
Headache								
n (%)	5 (5.5)	3 (3.4)	7 (7.7)	4 (4.5)	0 (0.0)	1 (1.1)	0 (0.0)	2 (2.3)
IR	24.9	15.0	9.1	5.1	0.0	5.4	0.0	3.8
(95% CI)	(8.1, 58.0)	(3.1, 43.9)	(3.7, 18.7)	(1.4, 13.0)	(0.0, 18.9)	(0.1, 30.0)	(0.0, 6.2)	(0.5, 13.6)
Hypertension								
n (%)	1 (1.1)	0 (0.0)	4 (4.4)	1 (1.1)	2 (2.2)	0 (0.0)	6 (6.6)	2 (2.3)
IR	4.9	0.0	5.0	1.2	10.5	0.0	10.7	3.8
(95% CI)	(0.1, 27.0)	(0.0, 18.0)	(1.4, 12.9)	(0.0, 6.9)	(1.3, 37.8)	(0.0, 19.7)	(3.9, 23.3)	(0.5, 13.6)
Injection site erythema								
n (%)	5 (5.5)	0 (0.0)	5 (5.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
IR	24.8	0.0	6.4	0.0	0.0	0.0	0.0	0.0
(95% CI)	(8.0, 57.8)	(0.0, 18.0)	(2.1, 15.0)	(0.0, 4.5)	(0.0, 18.9)	(0.0, 19.7)	(0.0, 6.2)	(0.0, 6.8)
Nasopharyngitis								
n (%)	5 (5.5)	3 (3.4)	9 (9.9)	6 (6.7)	2 (2.2)	0 (0.0)	8 (8.8)	2 (2.3)
IR	24.6	14.9	11.8	7.6	10.4	0.0	14.1	3.8
(95% CI)	(8.0, 57.4)	(3.1, 43.6)	(5.4, 22.4)	(2.8, 16.6)	(1.3, 37.5)	(0.0, 19.7)	(6.1, 27.8)	(0.5, 13.6)
Pharyngitis								
n (%)	1 (1.1)	0 (0.0)	7 (7.7)	4 (4.5)	1 (1.1)	0 (0.0)	2 (2.2)	0 (0.0)
IR	4.8	0.0	8.8	5.0	5.2	0.0	3.4	0.0
(95% CI)	(0.1, 26.8)	(0.0, 18.0)	(3.6, 18.2)	(1.4, 12.7)	(0.1, 28.9)	(0.0, 19.7)	(0.4, 12.4)	(0.0, 6.8)
Psoriasis								
n (%)	0 (0.0)	0 (0.0)	3 (3.3)	3 (3.4)	1 (1.1)	0 (0.0)	7 (7.7)	1 (1.1)
IR	0.0	0.0	3.7	3.7	5.1	0.0	12.2	1.9
(95% CI)	(0.0, 17.7)	(0.0, 18.0)	(0.8, 10.9)	(0.8, 10.9)	(0.1, 28.6)	(0.0, 19.7)	(4.9, 25.1)	(0.1, 10.4)
Upper respiratory tract infection								
n (%)	2 (2.2)	2 (2.3)	7 (7.7)	10 (11.2)	2 (2.2)	1 (1.1)	4 (4.4)	5 (5.6)
IR	9.8	9.9	8.9	13.0	10.4	5.4	6.9	9.7
(95% CI)	(1.2, 35.2)	(1.2, 35.8)	(3.6, 18.3)	(6.2, 23.9)	(1.3, 37.4)	(0.1, 29.9)	(1.9, 17.5)	(3.2, 22.7)

Total follow-up time calculated up to the day of the first event, subject to a risk period of 28 days beyond the last dose or to the data cut-off date. Gaps in dosing between treatment switches or between the P3 and LTE studies are included up to 28 days or to the data cut-off date

[a]MedDRA (v22.0) coding dictionary applied

[b]P3 study: NCT01877668 (OPAL Broaden)

[c]LTE study: NCT01976364 (OPAL Balance)

ADA, adalimumab; BID, twice daily; CI, confidence interval; IR, incidence rate (pts with events/100 pt-years); LTE, long-term extension; M, Month; MedDRA, Medical Dictionary for Regulatory Activities; N, number of evaluable pts; n, number of pts with events; P, Phase; pt, patient; Q2W, once every 2 weeks; TEAE, treatment-emergent adverse event

to tofacitinib are limited. This post hoc analysis assessed tofacitinib efficacy and safety in pts with PsA in a long-term extension (LTE) study who had received either adalimumab (ADA) or tofacitinib in a Phase (P)3 study.

Methods: Data were analyzed frompts with active PsA who received tofacitinib 5 mg twice daily (BID) or ADA 40 mg once every 2 weeks in aP3 randomized, double-blind, placebo-controlled 12-month study (NCT01877668; OPAL Broaden) and then continued or switched to tofacitinib 5 mg BID and maintained this dose in an open-label LTE study (NCT01976364; OPAL Balance). Efficacy outcomes were assessed 3 months before the last visit and at the last visit/Month (M)12 in the P3 study, and at M3 (or M6 for select outcomes) in the LTE study and included: proportions of pts achieving ACR20, Psoriasis Area and Severity Index 75 (PASI75), HAQ-Disability Index (DI) response (decrease from baseline ≥ 0.35 for pts with baseline HAQ-DI ≥ 0.35), Psoriatic Arthritis Disease Activity Score (PASDAS) ≤ 3.2, minimal disease activity (MDA); and least squares mean change from baseline (Δ) in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F). Safety outcomes were assessed at 3-month intervals to M12 in both studies and included proportions and incidence rates (pts with events/100 pt-years) for: treatment-emergent adverse events (TEAEs), serious AEs, and serious infections. Data reported as observed.

Results: In this post hoc analysis, 180 pts from the P3 study received tofacitinib 5 mg BID in the LTE study (ADAàtofacitinib 5 mg BID: n=91, 50.6%; continuing tofacitinib 5 mg BID: n=89, 49.4%). Baseline characteristics were generally similar across groups. Approximately half of pts were female (50.6%), with a mean (standard deviation [SD]) age of 47.5 (11.3) years and mean (SD) PsA disease duration of 5.9 (6.2) years. Efficacy was similar between groups 3 months before the last visit and at the last visit in the P3 study and was maintained to M3 (or M6 for PASDAS ≤ 3.2 and ΔFACIT-F) in the LTE study (Fig a–f). TEAEs, serious AEs, and serious infections were similar in the P3 and LTE studies, and between groups within each study (Table 1). The most common TEAEs across both studies were nasopharyngitis and upper respiratory tract infection (Table 2).

Conclusion: Tofacitinib efficacy and safety were similar in pts with PsA who continued or switched to tofacitinib 5 mg BID in the LTE study after receiving tofacitinib 5 mg BID or ADA in the P3 study, respectively. These data suggest that treatment can be directly switched from ADA to tofacitinib 5 mg BID. Limitations include the post hoc nature, small sample size and short time frame analyzed.

1. Gossec et al. Ann Rheum Dis 2016; 75: 499–510
2. Coates et al. Arthritis Rheumatol 2016; 68: 1060–71

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Abstract Number: 1426

Distinct Treatment Response Trajectories in Patients with Psoriatic Arthritis Receiving Tofacitinib

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

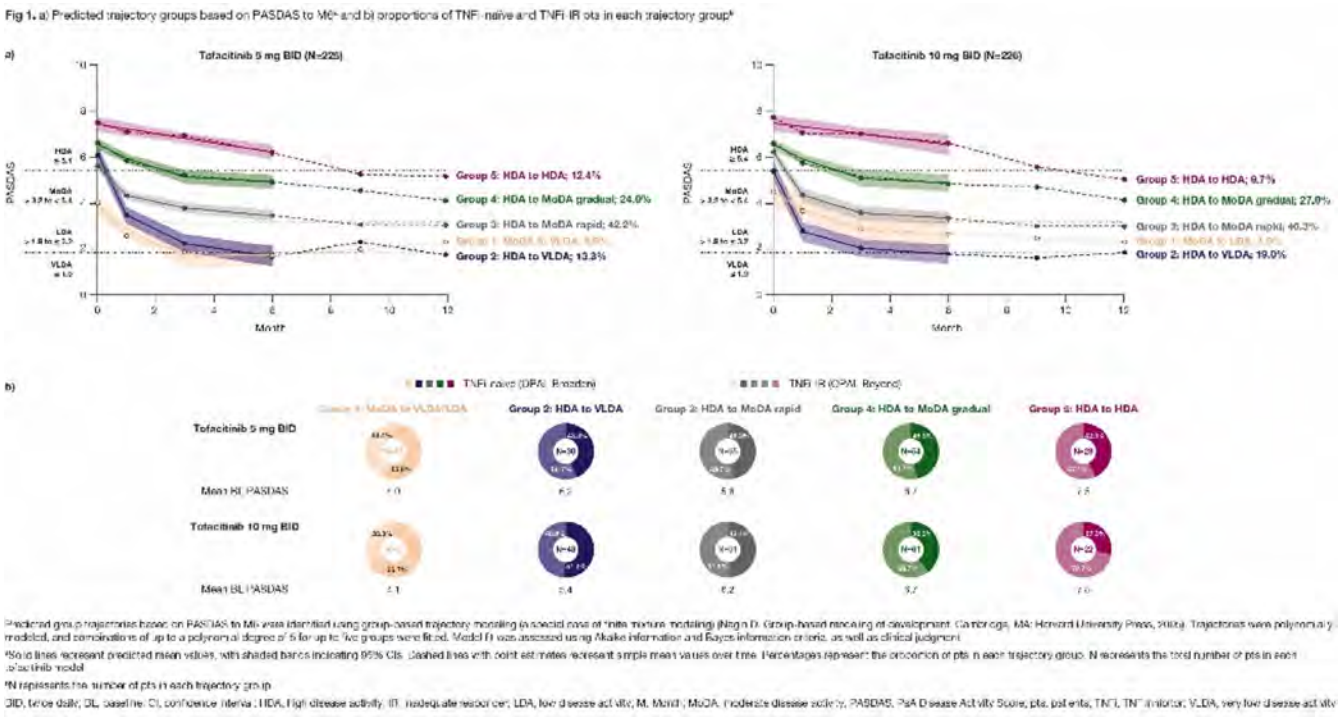
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: PsA is a heterogeneous disease, and identifying clinical phenotypes may assist clinical decision making. Patients (pts) treated with advanced therapies demonstrate varying treatment responses. Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. In this post hoc analysis, we aimed to capture these variations by identifying pt groups with distinct disease activity trajectories; comparisons of associated baseline (BL) variables across groups were used to describe clinical phenotypes in pts with PsA treated with tofacitinib.

Methods: Data were pooled from two Phase 3 randomized controlled trials (RCTs) in pts with PsA who were conventional synthetic DMARD-inadequate responders (IR)/TNF inhibitor (TNFi)-naïve (OPAL Broaden; 12 months (M); NCT01877668) or TNFi-IR (OPAL Beyond; 6M; NCT01882439); pts randomized to tofacitinib 5/10 mg twice daily (BID) were included and analyzed separately. PsA Disease Activity Score (PASDAS) to M6 was used in group-based trajectory modeling (a special case of finite mixture modeling) to identify distinct trajectory groups for each tofacitinib dose. Groups were compared by



Predicted group trajectories based on PASDAS to M6 were identified using group-based trajectory modeling (a special case of finite mixture modeling) (Nagin D. Group-based modeling of development. Cambridge, MA: Harvard University Press, 2005). Trajectories were polynomially modeled, and combinations of up to a polynomial degree of 5 for up to five groups were fitted. Model fit was assessed using Akaike information and Bayes information criteria, as well as clinical judgment.

[a]Solid lines represent predicted mean values, with shaded bands indicating 95% CIs. Dashed lines with point estimates represent simple mean values over time. Percentages represent the proportion of pts in each trajectory group. N represents the total number of pts in each tofacitinib model.

[b]N represents the number of pts in each trajectory group.

BID, twice daily; BL, baseline; CI, confidence interval; HDA, high disease activity; IR, inadequate responder; LDA, low disease activity; M, Month; MoDA, moderate disease activity; PASDAS, PsA Disease Activity Score; pts, patients; TNFi, TNF inhibitor; VLDA, very low disease activity

BL characteristics using t-tests (2-sided) or chi-squared tests, applying a Bonferroni correction for pairwise comparisons for each variable. Safety to M6 across groups was assessed descriptively.

Results: From 225/226 pts with PsA who received tofacitinib 5/10 mg BID, respectively, five disease trajectory groups were identified by PASDAS from BL to M6 for each dose separately; resulting models for either dose were of similar shape with the same polynomial degree and clinical interpretation. Groups progressed from moderate disease activity (MoDA) to very low disease activity (VLDA)/LDA (Group 1), high disease activity (HDA) to VLDA (Group 2), HDA to MoDA rapidly/gradually (Groups 3/4), or remained in HDA (Group 5; Fig 1a). In the tofacitinib 10 mg BID model, proportions of TNFi-naïve and TNFi-IR pts were numerically higher in Groups 1 and 4/5, respectively, vs other groups (Fig 1b). Groups 4/5 vs 1/2/3 had

Table. Demographics and BL disease characteristics across trajectory groups based on PASDAS to M6

	Tofacitinib doses	Group 1: MoDA to VLDA/LDA	Group 2: HDA to VLDA	Group 3: HDA to MoDA rapid	Group 4: HDA to MoDA gradual	Group 5: HDA to HDA
	5 mg BID	N=18	N=30	N=95	N=54	N=28
	10 mg BID	N=9	N=43	N=91	N=61	N=22
Age, years	5 mg BID	47.3	50.1	50.1	49.1	47.7
	10 mg BID	48.8	44.6[5]	49.3	50.2	54.1[5]
BMI, kg/m²	5 mg BID	28.2	28.8	28.6[5]	31.4	33.1[5]
	10 mg BID	28.7	28.8[5]	29.9	30.5	33.9[5]
Female, %	5 mg BID	33.3	43.3	52.6	55.6	53.6
	10 mg BID	66.7	46.5	57.1	59.0	63.6
White (race), %	5 mg BID	88.9[5]	90.0[5]	94.7[5]	96.3	100.0[1,2,3]
	10 mg BID	100.0	90.7	92.3	95.1	95.5
Never smoked, %	5 mg BID	66.7	56.7	54.7	64.8	50.0
	10 mg BID	100.0	62.8	52.7	67.2	50.0
History of alcohol, %	5 mg BID	27.8	30.0	35.8	33.3	32.1
	10 mg BID	55.6	32.6	37.4	34.4	22.7
bDMARD-exposed, %	5 mg BID	44.4	56.7	55.8	55.6	57.1
	10 mg BID	33.3	51.2	53.8	62.3	72.7
Number of bDMARDs	5 mg BID	0.8	0.9	0.9	1.1	1.3
	10 mg BID	0.4	0.7[5]	0.9	1.1	1.6[5]
PsA duration, years	5 mg BID	4.8	10.6	8.9	7.9	8.0
	10 mg BID	4.0	6.0	7.9	8.2	6.6
PROs						
Pt Global Assessment	5 mg BID	35.5[2,4,5]	58.2[1]	50.2[1,5]	64.8[1,3]	66.5[1,3]
	10 mg BID	16.7[2,3,4,5]	48.2[1,4,5]	56.7[1]	60.4[1,3]	69.6[1,3]
HAQ-DI	5 mg BID	0.5[2,3,4,5]	1.2[1]	1.1[1,4,5]	1.4[1,3]	1.6[1,3]
	10 mg BID	0.5[2,3,4,5]	1.0[1,4,5]	1.2[1,4,5]	1.4[1,2,3]	1.8[1,2,3]
Pain	5 mg BID	30.4[2,3,4,5]	53.6[1]	53.1[1,4]	63.6[1,3]	65.7[1]
	10 mg BID	24.7[2,3,4,5]	50.8[1,5]	56.7[1,4]	60.2[1]	71.3[1,3,5]
FACIT-F	5 mg BID	39.1[2,3,4,5]	26.9[1]	29.8[1,4,5]	20.0[1,3]	22.5[1,3]
	10 mg BID	39.3[2,3,4,5]	33.1[1,4,5]	27.4[1,2,3]	24.3[1,2,3]	17.3[1,2,3,4]
PsA clinical domains						
Peripheral arthritis: SJC66	5 mg BID	5.4[1,5]	12.9[1]	9.8[1,5]	15.8[1,3]	21.5[1,2,3]
	10 mg BID	8.0[5]	9.1[5]	11.6[5]	12.6[5]	23.2[1,2,3,4]
Peripheral arthritis: TJC68	5 mg BID	8.2[2,3,4,5]	19.2[1,4,5]	16.6[1,4,5]	28.0[1,2,3]	31.6[1,2,3]
	10 mg BID	12.2[4,5]	12.0[1,4,5]	21.4[1,5]	27.2[1,2,3,5]	45.0[1,2,3,4]
Axial disease: BASDAI	5 mg BID	3.4[2,3,4,5]	6.0[1]	5.5[1,4,5]	6.8[1,3]	6.7[1,3]
	10 mg BID	2.3[2,3,4,5]	5.1[1,4,5]	5.9[1,5]	6.4[1,3]	7.5[1,2,3]
Enthesitis and dactylitis: LEI	5 mg BID	0.4[4,5]	1.4[1,5]	1.5[1,5]	2.6[1,2,3]	3.0[1,2,3]
	10 mg BID	1.0[4,5]	0.8[1,4,5]	1.9[2,4,5]	3.2[1,2,3]	4.1[1,2,3]
Enthesitis and dactylitis: SPARCC	5 mg BID	1.1[4,5]	3.3[1,4,5]	3.2[1,5]	5.8[1,2,3]	7.0[1,2,3]
	10 mg BID	1.9[4,5]	1.8[1,4,5]	4.1[2,4,5]	6.7[1,2,3,5]	10.2[1,2,3,4]
Enthesitis and dactylitis: Dactylitis total score	5 mg BID	1.1[5]	3.1[5]	2.7[5]	5.9[5]	13.3[1,2,3,4]
	10 mg BID	0.7[5]	3.2[5]	3.6[5]	5.4[5]	13.7[1,2,3,4]
Psoriasis: PASI	5 mg BID	5.5	7.9	9.8	9.8	10.2
	10 mg BID	11.1	10.0	10.4	10.4	11.7
Nail disease: NAPSI	5 mg BID	4.3	3.6	3.8	3.6	4.0
	10 mg BID	4.6	4.0	4.2	3.6	4.2

Mean values are presented unless indicated otherwise

A 2-sided Bonferroni correction for multiple comparisons was applied; $p \leq 0.05$ indicated statistical significance

Superscripted numbers represent $p \leq 0.05$ vs the group number

BASDAI, Bath AS Disease Activity Index; bDMARD, biologic DMARD; BID, twice daily; BL, baseline; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, HAQ-Disability Index; HDA, high disease activity; LDA, low disease activity; LEI, Leeds Enthesitis Index; M, Month; MoDA, moderate disease activity; N, number of pts in each trajectory group; NAPSI, Nail Psoriasis Severity Index; PASDAS, PsA Disease Activity Score; PASI, Psoriasis Area and Severity Index; PRO, patient-reported outcome; pts, patients; SJC66, swollen joint count (out of 66 joints); SPARCC, Spondyloarthritis Research Consortium of Canada; TJC68, tender joint count (out of 68 joints); TNFi, TNF inhibitor; VLDA, very low disease activity

Fig 2. Rates of AEs by SOC (occurring in ≥ 5% of pts in any group) to M6 across trajectory groups based on PASDAS to M6

	Tofacitinib 5 mg BID					Tofacitinib 10 mg BID				
	Group 1: MoDA to VLDA/LDA N=18	Group 2: HDA to VLDA N=30	Group 3: HDA to MoDA rapid N=95	Group 4: HDA to MoDA gradual N=54	Group 5: HDA to HDA N=28	Group 1: MoDA to VLDA/LDA N=9	Group 2: HDA to VLDA N=42	Group 3: HDA to MoDA rapid N=91	Group 4: HDA to MoDA gradual N=61	Group 5: HDA to HDA N=22
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
All SOC combined	12 (66.7)	15 (50.0)	67 (70.5)	42 (77.8)	17 (60.7)	6 (66.7)	30 (69.8)	65 (71.4)	44 (72.1)	18 (81.8)
Blood and lymphatic system disorders	1 (5.6)	2 (6.7)	0 (0.0)	2 (3.7)	0 (0.0)	0 (0.0)	3 (7.0)	4 (4.4)	1 (1.6)	1 (4.5)
Cardiac disorders	1 (5.6)	0 (0.0)	2 (2.1)	1 (1.9)	2 (7.1)	1 (11.1)	0 (0.0)	2 (2.2)	1 (1.6)	0 (0.0)
Eye disorders	1 (5.6)	0 (0.0)	3 (3.2)	1 (1.9)	2 (7.1)	0 (0.0)	2 (4.7)	4 (4.4)	2 (3.3)	1 (4.5)
Gastrointestinal disorders	2 (11.1)	1 (3.3)	24 (25.3)	9 (16.7)	7 (25.0)	2 (22.2)	8 (18.6)	14 (15.4)	13 (21.3)	5 (22.7)
General disorders and administration site conditions	0 (0.0)	0 (0.0)	7 (7.4)	6 (11.1)	4 (14.3)	0 (0.0)	4 (9.3)	11 (12.1)	2 (3.3)	2 (9.1)
Infections and infestations	8 (44.4)	16 (53.3)	34 (35.8)	25 (46.3)	8 (28.6)	4 (44.4)	17 (39.5)	40 (44.0)	27 (44.3)	12 (54.5)
Injury, poisoning, and procedural complications	5 (27.8)	5 (16.7)	9 (9.5)	6 (11.1)	6 (21.4)	1 (11.1)	4 (9.3)	9 (9.9)	6 (9.8)	2 (9.1)
Investigations	4 (22.2)	2 (6.7)	9 (9.5)	5 (9.3)	2 (7.1)	2 (22.2)	3 (7.0)	14 (15.4)	6 (9.8)	1 (4.5)
Metabolism and nutrition disorders	0 (0.0)	1 (3.3)	4 (4.2)	3 (5.6)	1 (3.6)	0 (0.0)	4 (9.3)	5 (5.5)	2 (3.3)	0 (0.0)
Musculoskeletal and connective tissue disorders	3 (16.7)	4 (13.3)	13 (13.7)	5 (9.3)	5 (17.9)	2 (22.2)	6 (14.0)	6 (6.6)	8 (13.1)	4 (18.2)
Neoplasms benign, malignant, and unspecified (incl. cysts and polyps)	0 (0.0)	1 (3.3)	2 (2.1)	3 (5.7)	0 (0.0)	1 (11.1)	1 (2.3)	1 (1.1)	0 (0.0)	0 (0.0)
Nervous system disorders	0 (0.0)	0 (0.0)	13 (13.7)	9 (16.7)	5 (17.9)	1 (11.1)	7 (16.3)	15 (14.3)	8 (13.1)	2 (9.1)
Psychiatric disorders	0 (0.0)	0 (0.0)	2 (2.1)	3 (5.6)	2 (7.1)	1 (11.1)	1 (2.3)	1 (1.1)	1 (1.6)	0 (0.0)
Renal and urinary disorders	1 (5.6)	0 (0.0)	2 (2.1)	5 (9.3)	0 (0.0)	0 (0.0)	0 (0.0)	4 (4.4)	1 (1.6)	0 (0.0)
Reproductive system and breast disorders	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.9)	0 (0.0)	1 (11.1)	2 (4.7)	3 (3.3)	2 (3.3)	0 (0.0)
Respiratory, thoracic, and mediastinal disorders	2 (11.1)	2 (6.7)	7 (7.4)	3 (5.6)	1 (3.6)	0 (0.0)	2 (4.7)	6 (6.6)	1 (1.6)	0 (0.0)
Skin and subcutaneous tissue disorders	5 (27.8)	2 (6.7)	12 (12.6)	4 (7.4)	3 (10.7)	1 (11.1)	2 (4.7)	9 (9.9)	7 (11.5)	2 (9.1)
Vascular disorders	2 (11.1)	0 (0.0)	0 (0.0)	1 (1.9)	1 (3.6)	1 (11.1)	0 (0.0)	3 (3.3)	5 (8.2)	1 (4.5)

Heat map color key (rates expressed as percentages)										
0.0	> 0.0–5.0	> 5.0–10.0	> 10.0–15.0	> 15.0–20.0	> 20.0–25.0	> 25.0–30.0	> 30.0–35.0	> 35.0–40.0	> 40.0–45.0	> 45.0–50.0
> 50.0–55.0	> 55.0–60.0	> 60.0–65.0	> 65.0–70.0	> 70.0–75.0	> 75.0–80.0	> 80.0–85.0	> 85.0–90.0	> 90.0–95.0	> 95.0–100.0	

AE, adverse event; BID, twice daily; HDA, high disease activity; LDA, low disease activity; M, Month; MoDA, moderate disease activity; N, number of pts in each trajectory group; n, number of pts with events; PASDAS, PsA Disease Activity Score; pts, patients; SOC, System Organ Class; VLDA, very low disease activity

generally significantly higher BL PsA clinical domain scores, but no significant differences in psoriasis/nail disease scores were seen across groups (Table). In Groups 4 vs 2, which had HDA at BL but distinct responses to M6, significant BL characteristic differences included higher enthesitis scores and tender joint counts (TJC; Table). Across groups, adverse event (AE) rates were generally comparable; most common AEs were infections/infestations (Fig 2).

Conclusion: In pts with PsA treated with tofacitinib, PASDAS response analysis by group-based trajectory modeling identified distinct clinical phenotypes at BL. As expected, higher BL disease burden was associated with poorer responses and differences in BL enthesitis and TJC may impact response to tofacitinib; phenotypes affecting treatment responses were consistent across doses. Trajectory groups showed comparable safety. Limitations included small pt numbers and restricted extrapolation of used RCT data to routine care. Identification of clinical phenotypes may be used to develop personalized treatment algorithms.

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Abstract Number: 1427

Efficacy of Upadacitinib in Patients with Psoriatic Arthritis Stratified by Involvement of Weight-bearing Joint Regions: A Post Hoc Subgroup Analysis of the Phase 3, Randomized, SELECT-PsA 1 and SELECT-PsA 2 Trials

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

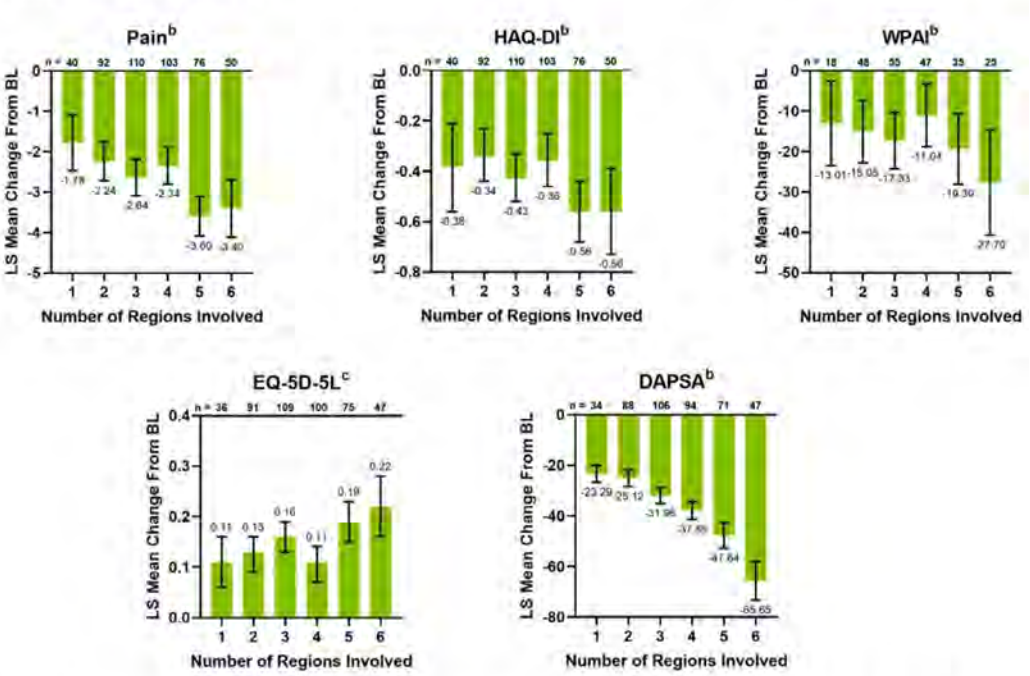
Session Time: 9:00AM–11:00AM

Background/Purpose: Involvement of weight-bearing joints in patients with PsA can be associated with reduced activities of daily living and quality of life. Upadacitinib (UPA) is an oral JAK inhibitor approved for the treatment of active PsA in adults. In the SELECT-PsA 1 and SELECT-PsA 2 trials, treatment with once daily UPA 15 mg (UPA15) or 30 mg (UPA30) resulted in greater improvements in the number of swollen and tender joints as well as other patient- and physician-reported outcomes when compared with placebo.[1–3] The objective of this post hoc analysis was to evaluate the long-term efficacy of UPA in patients with PsA and involvement in 1 or more regions of weight-bearing joints.

Methods: The SELECT-PsA 1 and SELECT-PsA 2 phase 3, randomized, controlled trials enrolled patients ≥ 18 years old with active PsA and intolerance or inadequate response to ≥ 1 nonbiologic disease modifying anti-rheumatic drug (DMARD; SELECT-PsA 1) or biologic DMARD (SELECT-PsA 2). This post hoc analysis of the 2 phase 3 trials stratified patients with involvement in 1 to 6 regions of weight-bearing joints (hips, knees, ankles, midfoot, metatarsophalangeal [MTP], or proximal interphalangeal [PIP]) who were randomized at baseline to receive either UPA15, placebo (PBO), or adalimumab (ADA; only in SELECT-PsA 1); at week 24, PBO-treated patients switched to UPA15 (PBO/UPA15). This analysis did not include patients who received UPA30 or PBO/UPA30. A mixed-effects model with repeated measures was used to analyze the change from baseline to week 104 in 4 patient-reported outcome measures (pain, Health Assessment Questionnaire-Disability Index [HAQ-DI], Work Productivity and Activity Impairment [WPAI] questionnaire, and EuroQol 5 Dimension 5 Level [EQ-5D-5L]) and 1 composite outcome measure (Disease Activity in Psoriatic Arthritis [DAPSA]). UPA safety results in patients with PsA have been previously reported.[1–3]

Results: A total of 1069 patients from the SELECT-PsA 1 trial and 317 patients from the SELECT-PsA 2 trial were included in the pooled analysis. Of all patients with any involvement in regions of weight-bearing joints, > 91% of patients had involvement in ≥ 2 regions. The most common weight-bearing joints with involvement were the PIP (SELECT-PsA 1, 79.8%; SELECT-PsA 2, 84.5%), MTP (71.1%; 73.8%), and knee (62.3%; 64.9%) joints. Improvements from baseline to week 104 were observed with UPA15 treatment in patient-reported outcomes of pain, HAQ-DI, WPAI, EQ-5D-5L, and the DAPSA score across all subgroups of patients with involvement in 1 to 6 regions of weight-bearing joints (**Figure**). In general, the magnitude of improvement in outcome scores with UPA15 was greater in patients with involvement in a higher number of regions. Similar improvements from baseline to week 104 in outcome scores were observed in patients who received PBO/UPA15 or ADA to week 104.

Figure. Mean Change at Week 104 in Outcome Scores Among Subgroups of Patients With Psoriatic Arthritis and Involvement in 1 to 6 Regions of Weight-bearing Joints[a] Treated With UPA 15 mg



[a]Weight-bearing joints include hips, knees, ankles, midfoot, metatarsophalangeal (MTP), or proximal interphalangeal (PIP).
[b]Decrease in score indicates improvement.
[c]Increase in score indicates improvement.
BL, baseline; DAPSA, Disease Activity in Psoriatic Arthritis; EQ-5D-5L, EuroQol 5 Dimension 5 Level; HAQ-DI, Health Assessment Questionnaire-Disability Index; LS, least squares; UPA, upadacitinib; WPAI, Work Productivity and Activity Impairment questionnaire.

Conclusion: UPA15 treatment was associated with long-term improvements in pain, disability, work productivity, disease activity, and quality of life in patients with PsA and involvement in 1 or more regions of weight-bearing joints.

References:

1. McInnes IB, et al. *N Engl J Med*. 2021;384;1227-39.
2. McInnes IB, et al. *RMD Open*. 2021;7:e001838.
3. Mease PJ, et al. *Ann Rheum Dis*. 2022;80:312-20.

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Abstract Number: 1428

Guselkumab Provides Clinically Meaningful Improvents in Patient-Reported Outcomes in Patients with Active Psoriatic Arthritis Who Are Inadequate Responders to Tumour Necrosis Factor Inhibitors: Results Through One Year of a Phase 3b, Randomized, Controlled Study (COSMOS)

Laure Gossec[1], Xenofon Baraliakos[2], James Galloway[3], Lars Erik[4], Vilija Oke[5], Petros Sfikakis[6], Emmanouil Rampakakis[7], Mohamed Sharaf[8], Frederic Lavie[9] and Iain McInnes[10], [1]Sorbonne Université and Pitié Salpêtrière Hospital, Paris, France, [2]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [3]King's College London, London, United Kingdom, [4]Bispebjerg-Frederiksberg Hospital, Vedbæk, Denmark, [5]Karolinska Institutet, Stockholm, Sweden, [6]National Kapodistrian University of Athens Medical School, Athens, Greece, [7]JSS Medical Research, Saint-Laurent, QC, Canada, [8]Immunology, Janssen MEA, Dubai, United Arab Emirates, [9]The Janssen Pharmaceutical Companies of Johnson & Johnson, Paris, France, [10]University of Glasgow, Glasgow, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

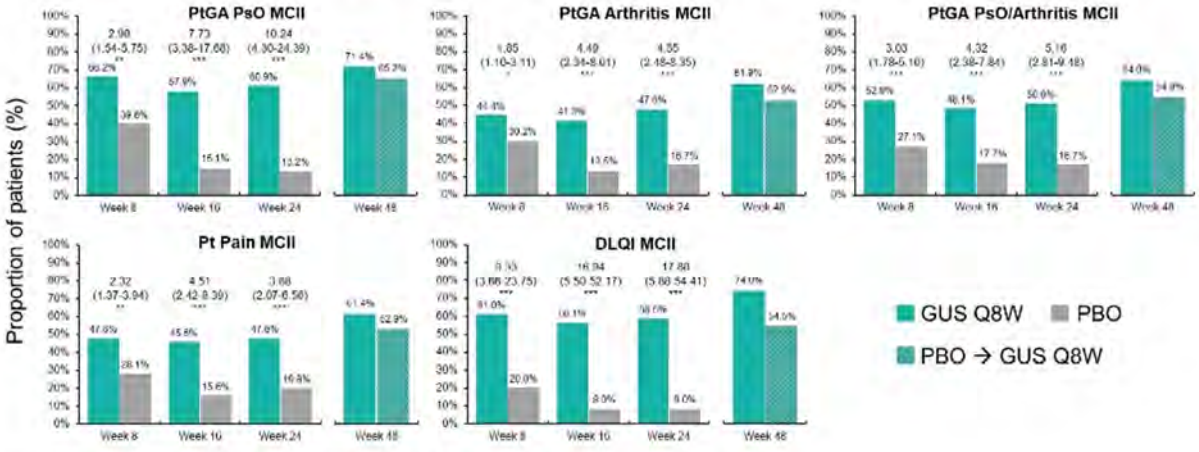
Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: In the Phase 3b COSMOS trial, guselkumab (GUS), a fully human IL-23p19 inhibitor (i), was associated with significantly greater improvements vs placebo (PBO) in joint and skin disease at week (W) 24 in patients (pts) with active PsA with inadequate response (IR) to TNFi[1]. Here, we report GUS effect on achievement of clinically important improvements (CII) in patient-reported outcomes (PROs) through W48 of COSMOS.

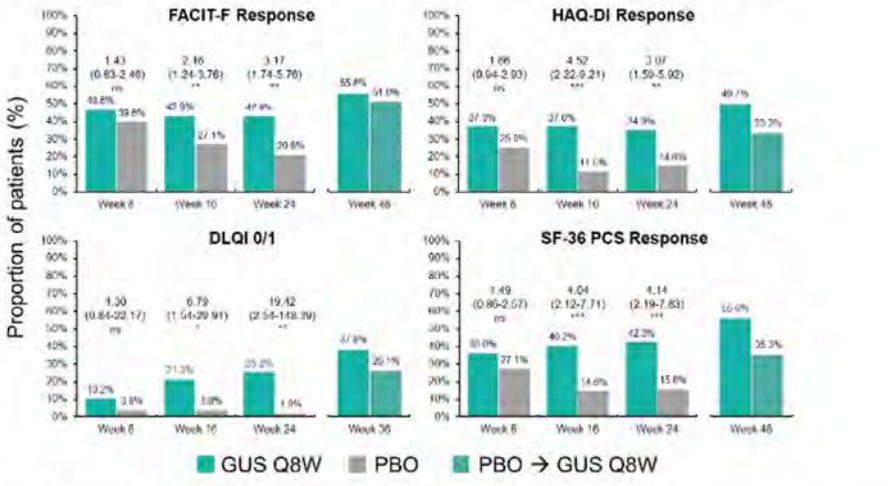
Methods: COSMOS pts had active PsA (≥3 swollen and ≥3 tender joints; SJC/TJC) after discontinuing 1-2 TNFi due to lack of efficacy or intolerance. Pts were randomised (2:1) to GUS 100 mg or PBO at W0, W4, then Q8W through W44. PBO pts crossed over to GUS at W16 (early escape if < 5% improvement in SJC/TJC) or W24. Early response to GUS was assessed

Figure 1. Effect† of GUS Q8W vs. PBO on PRO MCII Achievement (NRI) Through W48‡



ns = p≥0.05; * = p<0.05; ** = p≤0.01; *** = p≤0.0001 vs. PBO.
†Upon adjustment for BL levels, number of prior TNFi, and and concomitant use of conventional synthetic DMARDs.
‡Results for the PBO → GUS group at week 48 are reported for pts without early exit that crossed over to GUS at week 24.
Note: PtGA PsO MCII in pts with BSA ≥3% and IGA ≥2 at BL; DLQI MCII in pts with DLQI score ≥5, BSA ≥3% and IGA ≥2 at BL.
NRI: non-responder imputation.

Figure 2. Effect† of GUS Q8W vs. PBO on PRO Response Achievement (NRI) Through W48‡



ns = p≥0.05; * = p<0.05; ** = p≤0.01; *** = p≤0.0001 vs. PBO.
†Upon adjustment for BL levels, number of prior TNFi, and and concomitant use of conventional synthetic DMARDs.
‡Results for the PBO → GUS group at week 48 are reported for pts without early exit that crossed over to GUS at week 24.
Note: DLQI 0/1 in pts with DLQI score >1, BSA ≥3% and IGA ≥2 at BL.
NRI: non-responder imputation.

with achievement of minimal CII (MCII; 15-point improvements on 0-100 VAS) in Pt Pain, pt global assessment of psoriasis (PtGA PsO), PtGA Arthritis, and PtGA PsO/Arthritis, and Dermatology Life Quality Index (DLQI) MCII (≥5-point-improvement in pts with DLQI ≥5, PsO BSA ≥3% & IGA ≥2 at BL). More rigorous response criteria were used for longer-term pt outcomes: Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F; ≥4-point improvement), Health Assessment Questionnaire Disability Index (HAQ-DI; ≥0.35-point improvement), DLQI 0/1 (in pts with DLQI >1, PsO BSA ≥3%, and IGA ≥2 at BL), and 36-item Short-Form Health Survey physical component summary score (SF-36 PCS; ≥5-point improvement). GUS vs PBO were compared with logistic regression adjusting for BL levels, number of prior TNFi, and concomitant use of conventional synthetic DMARDs. Non-responder imputation (NRI) was used for missing data and pts meeting treatment failure criteria.

Results: The post hoc analysis included 285 randomized pts (GUS Q8W: n=189; PBO: n=96). Mean (SD) BL DLQI (13.1 [7.0]), PtGA PsO (60.9 [23.9]), PtGA Arthritis (64.2 [17.5]), PtGA PsO/Arthritis (66.6 [17.9], Pt Pain (63.2 [18.6]), FACIT-F (29.2 [11.0]), and SF-36 PCS (33.3 [7.3]) scores indicated active disease and impaired health-related quality of life (QoL). GUS treatment was associated with higher rates of PRO endpoint achievement compared with PBO at W8, W16, and W24, as evidenced by significantly greater odds of achieving MCII in PtGA PsO (odds ratio range across timepoints [ORs]: 3.0-10.2), PtGA Arthritis (ORs: 1.8-4.5), PtGA PsO/Arthritis (ORs: 3.0-5.2), Pt Pain (ORs: 2.3-4.5), and DLQI (ORs: 10.4-15.5) as of W8 (**Figure 1**), as well as responses in FACIT-F (ORs: 1.7-3.0), HAQ-DI (ORs: 2.2-2.8), DLQI 0/1 (ORs: 10.6-24.7), and SF-36 PCS (ORs: 1.3-2.9) through W24 (**Figure 2**). Further increases in response rates (NRI) were seen through W48 of GUS, with consistent patterns following crossover from PBO to GUS.

Conclusion: In PsA pts with TNFi-IR, GUS was associated with rapid effect for achievement of MCIIs and sustained achievement of more rigorous response criteria across PROs, including patient-reported skin and joint symptoms, pain, fatigue, functional status, and skin-specific and physical function-related QoL, with increasing response rates from W24 to W48.

References

1. Coates LC. Ann Rheum Dis. 2022;81:359

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Abstract Number: 1429

Longitudinal Evaluation of the Novel Psoriatic Arthritis 5-Thermometer Scale (PsA-5Ts) Domains During Treatment with Guselkumab: Pooled Analysis of Three Phase 3, Randomized, Double-blind, Placebo-Controlled Studies

Carlo Selmi[1], Fausto Salaffi[2], Sibel Aydin[3], Enrique Soriano[4], Emmanouil Rampakakis[5], Mohamed Sharaf[6], Miriam Zimmermann[7], Frederic Lavie[8], Peter Nash[9] and Philip J. Mease[10], [1]Rheumatology and Clinical Immunology, Humanitas Research Hospital / Internal Medicine, Humanitas University, Rozzano, Italy, [2]Polytechnic University of Marche, Department of Clinical and Molecular Sciences, Carlo Urbani Hospital, Ancona, Italy, [3]Department of Medicine, Ottawa Hospital Riverside Campus, Ottawa, ON, Canada, [4]Rheumatology Section, Internal Medicine Services, Hospital Italiano de Buenos Aires, and University Institute Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, [5]McGill University, Department of Pediatrics / JSS Medical Research, Scientific Affairs, Montreal, QC, Canada, [6]Immunology, Janssen MEA, Dubai, United Arab Emirates, [7]Immunology, Janssen Medical Affairs, LLC, Zug, Switzerland, [8]The Janssen Pharmaceutical Companies of Johnson & Johnson, Paris, France, [9]School of Medicine, Griffith University, Brisbane, Australia, [10]Swedish Medical Center/Providence St. Joseph Health and University of Washington School of Medicine, Seattle, WA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: PsA-5Ts is a simple multidimensional composite measure, assessing pain, fatigue, physical function, skin problems, and depression, recently developed to measure overall health in PsA patients (pts) and correlate with established composite measures[1]. We assessed the longitudinal construct validity of the PsA-5Ts domains (PsA-5T-Ds) using data from three Phase 3 trials of the fully human IL-23p19-subunit inhibitor guselkumab (GUS), and evaluated the GUS effect on PsA-5T-Ds through week (W)24.

Methods: Pts in DISCOVER 1&2 (D1/D2; n=1120 ~90% bionaive) and COSMOS (n=285; inadequate response to 1 or 2 TNFi) had active PsA and were randomized to GUS 100 mg every 4 W (Q4W; D1/D2 only); GUS 100 mg at W0, W4, Q8W; or placebo (PBO). A PsA-5T-Ds score (range 0-100) was calculated[1] based on the Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F) scale, Health Assessment Questionnaire Disability Index (HAQ-DI), and question 28 ('*Have you felt downhearted and depressed*') of the 36-Item Short Form Survey (SF-36) to assess fatigue, physical function, and

Figure 1. Correlation of Changes from BL in PsA-5T-Ds Score and PASDAS Through W24 of DISCOVER-1, DISCOVER-2, and COSMOS (N=1405 Pts)

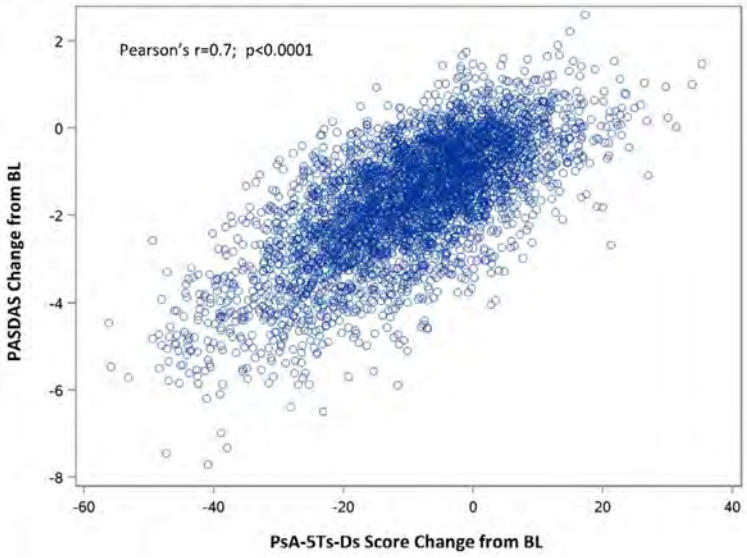
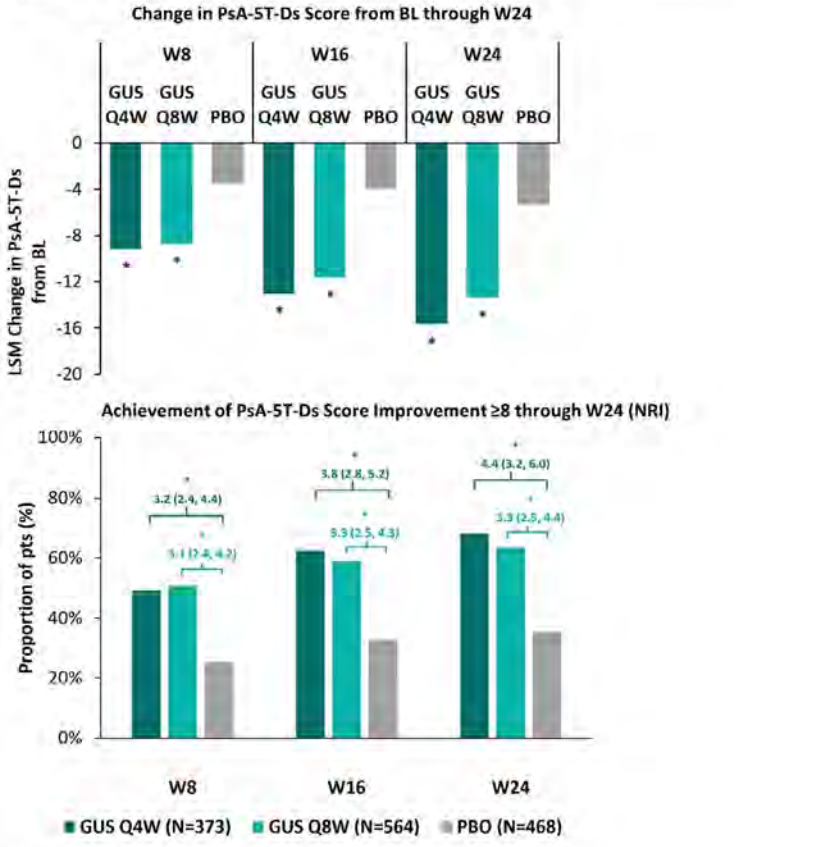


Figure 2. Effect† of GUS vs. PBO on PsA-5T-Ds Score Through W24 of DISCOVER-1, DISCOVER-2, and COSMOS



*p<0.0001 vs. PBO. LSM=least squares mean.

†Upon adjustment for BL PsA-5T-Ds score, age, sex, BL body mass index, prior TNFi use, and concomitant use of conventional synthetic DMARDs at BL.

NRI: non-responder imputation.

depression, respectively, after 0-10 transformation; pt pain and skin disease activity were assessed with native 0-10 visual analogue scales. Correlation of change in PsA-5T-Ds score with changes in PsA disease activity (DA) Score (PASDAS), DA Index for PsA (DAPSA), clinical (c) DAPSA, and SF-36 physical component summary score (PCS) was assessed with Pearson's coefficient. Known-groups validity was assessed with mixed models for repeated measures (MMRM) using change in PsA-5T-Ds score as dependent variable; clinically meaningful improvements (CMI) in PASDAS ($\Delta \leq -0.8$), DAPSA ($\Delta \leq -7.25$), cDAPSA ($\Delta \leq -5.7$), and SF-36 PCS ($\Delta \geq 5$) as independent variables; and age, sex, treatment, and BL PsA-5T-Ds score as covariates. GUS' effect on PsA-5T-Ds score change and CMI achievement was assessed with multivariate MMRM and logistic regression, respectively.

Results: Changes in PsA-5T-Ds score through W24 correlated strongly with variations in PASDAS ($r=0.7$; $p< 0.0001$) **(Figure 1)** and moderately with variations in DAPSA, cDAPSA, and SF-36 PCS ($r=0.5$; all $p< 0.0001$). CMI achievement in PASDAS, DAPSA, cDAPSA, and SF-36 PCS through W24 associated with significantly greater improvements in PsA-5T-Ds score vs non-achievement; corresponding time-weighted least square means (95% CI) differences of -7.9 (-8.5 to -7.3), -7.3 (-7.9 to -6.6), -7.2 (-7.9 to -6.6), and -5.9 (-6.5 to -5.4), respectively, suggested a cutoff of ≥8 points for CMI in PsA-5T-Ds score. Upon adjusting for potential confounders, treatment with GUS Q4W or Q8W associated with significantly greater PsA-5T-Ds improvements through W24 and higher odds of achieving PsA-5T-Ds CMI vs PBO, starting at the first timepoint assessed **(Figure 2)**.

Conclusion: In our first assessment of the PsA-5T-Ds longitudinal construct validity, we observed a strong correlation with PASDAS, which encompasses most core PsA domains, and good ability to discriminate between pts with and without CMI. GUS treatment was associated with greater improvements and higher rates of CMI achievement than PBO, supporting the established GUS efficacy across key PsA domains.

References

1. Salaffi F. *Ann Rheum Dis* 2022;81:218

Disclosure: C. Selmi: AbbVie, 2, 5, 6, Alfa-Wassermann, 2, 6, Amgen, 2, 5, 6, Biogen, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 5, SOBI, 2, 6; **F. Salaffi**: AbbVie/Abbott, 2, 5, 6, Alfa-Wassermann, 2, 6, Biogen, 2, 6, Eli-Lilly, 2, 6, Galapagos, 2, 6, Novartis, 2, 6; **S. Aydin**: AbbVie, 5, 6, Celgene, 5, 6, Eli Lilly, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6; **E. Soriano**: AbbVie, 2, 5, 6, Amgen, 6, Bristol-Myers Squibb, 6, Eli Lilly, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Roche, 2, 5, 6, UCB, 5, 6; **E. Rampakakis**: Janssen, 2, JSS Medical Research, Inc, 3; **M. Sharaf**: Janssen, 3, Johnson & Johnson, 11; **M. Zimmermann**: Janssen, 3, Johnson & Johnson, 11; **F. Lavie**: Janssen, 3, Johnson & Johnson, 11; **P. Nash**: AbbVie, 5, 6, Bristol Myers Squibb, 5, 6, Celgene, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, GSK, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer Inc, 5, 6; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2.

Abstract Number: 1430

A Proof-of-concept Study Evaluating the Use of Functional Brain Magnetic Resonance Imaging in Assessing Treatment Response in Psoriatic Arthritis Patients

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammatory cytokines can alter the way the central nervous system processes pain as shown in patients with rheumatoid arthritis. However, the relationship between TNFα inhibition and pain processing in individuals with psoriatic arthritis (PsA) has not been investigated.

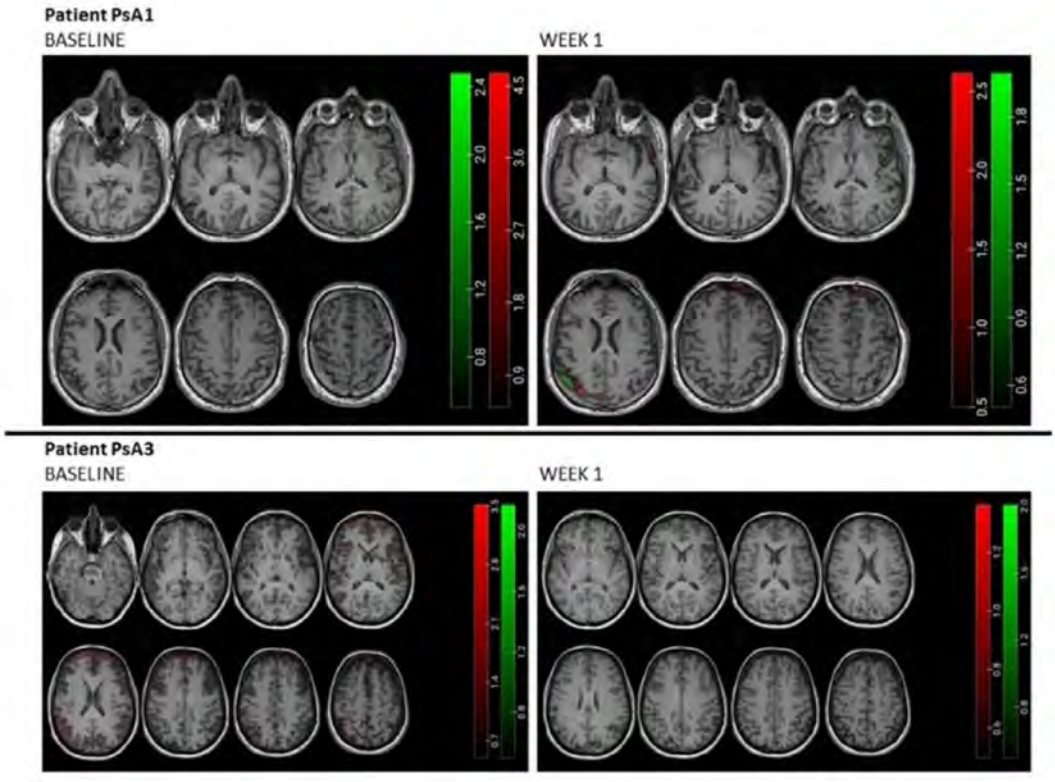

Figure 1. Brain fMRI response to pressure of the non-affected joint (green) and the affected joint (red) overlaid on top of the structural image. Upper panel corresponds to a patient with clinical improvement (PsA1) and lower panel to a patient that did not respond (PsA3) at baseline (left column) and week 1 (right column). Differences are observed in the sensorimotor cortex activation between patients: there is an increase in the activation after week 1 in PsA1 while PsA3 showed activation at baseline but not in week 1.

Table 1. All subject's demographic characteristics ans PsA patients' clinical response

Variables	HS1	HS2	HS3	HS4	PsA1	PsA2	PsA3	PsA4	PsA5	PsA6
Age (year)	48	30	26	59	61	52	47	66	23	63
Gender (F/M)	F	F	F	F	M	F	F	M	F	F
BMI	20	17	20	22	34	24	29	30	19	19
TJC baseline					6	15	13	22	7	8
SJC baseline					5	12	3	11	6	5
CRP baseline (mg/dL)					0.27	0.35	0.80	0.60	0.33	0.45
CRP Week1 (mg/dL)					0.04	0.05	0.44	0.16	0.14	0.20
TNFi naive					Yes	Yes	Yes	No	No	No
DAPSA improvement (%)					57	46.4	22.6	12.8	70.4	16.6
VASp change (Δmm)					-14	-21	-5	0	-51	-7

HS: healthy subject; PsA: psoriatic arthritis patient; F: female; M: male; BMI: body mass index; TJC: tender joint count; SJC: swollen joint count; CRP: C-reactive protein; TNFi: TNF inhibitor; DAPSA: Disease Activity in Psoriatic Arthritis; VASp: visual analogue scale pain

The purpose of this study is to assess the feasibility of functional magnetic resonance imaging (fMRI) paradigm to estimate the respone to pain and the effect of treatment in PsA patients.

Methods: 6 patients with active PsA eligible to start a TNF inhibitor (TNFi) were included: 3 were naïve to biological disease modifying anti-rheumatic drugs and 3 were experienced. Four healthy subjects (HS) were also included. The physician selected a swollen and tender joint (affected joint) and a control joint in the contralateral hand (non-affected joint). Subjects were scanned in a 3.0T scanner at baseline (BL) and week 1 (W1) after starting treatment. First, the brain pain response was investigated pressing the non-affected joint followed by the affected joint. Each acquisition included 2 fMRI runs. The fMRI effect of pressure was represented for each subject individually, for each time point ($p< 0.0001$ uncorrected level, minimum extension 10 voxels). We provided a descriptive analysis of the differences in PsA patients brain response between BL and W1 and the clinical response evaluated by the percentage of improvement of Disease Activity in Psoriatic Arthritis (DAPSA) score and visual analogue scale pain (VASp) change.

Results: All subject's demographic characteristics and PsA patients' clinical response are shown in Table 1. Brain response to pressure in HS produced activation in the sensory motor cortex, with more or less involvement of additional areas in the prefrontal, parietal and temporal cortex. In PsA patients with a higher treatment response (PsA 1, 2, 5), the brain response to pressure did not show any activation at BL whilst sensory motor cortex activation was seen at W1, with amygdala and insula activation in patients PsA 2 and 5 and prefrontal and frontal activity in patients PsA 1 and 2. In those with less response (PsA 3, 4, 6), the sensory motor cortex was activated at BL with little changes when evaluated at W1 (Fig. 1). No evident differences in brain response activation were observed between naïve and TNFi experienced patients.

Conclusion: The proposed fMRI paradigm seems to be a promising candidate to predict response to treatment with TNFi in PsA patients. Studies with more patients are needed to confirm our preliminary results.

Disclosure: E. Espartal López: Pfizer, 5; **X. Michelena Vegas**: Pfizer, 5; **S. Marsal Barril**: Pfizer, 5; **A. Rovira**: Pfizer, 5; **D. Pareto**: Pfizer, 5; **A. Erra Duran**: Pfizer, 5.

Abstract Number: 1431

Izokibep, a Unique IL-17A Inhibitor, Improves Patient-Reported Outcomes in Patients with Active Psoriatic Arthritis up to Week 46 – Phase 2 RCT Results

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Izokibep is a novel small protein IL-17A inhibitor, unique for its high IL-17A binding affinity, a small size at 18.6 kD and albumin binding site enabling access in inflamed tissues and two-week half-life. IL-17A is key in psoriatic arthritis (PsA) pathogenesis and its inhibition is known to improve quality of life. Here, we report results of izokibep treatment to week 46 on patient-reported outcomes (PROs), following a 16-week placebo-controlled period[1]. PRO endpoints include PsAID-9, HAQ-DI, TSQM-9, and patient reported pain, itch, and global disease activity.

Methods: Izokibep doses of 80 mg Q2W or 40 mg Q2W were evaluated to 46 weeks or study termination. The original placebo arm continued to 16 weeks, then switched to 80 mg Q2W in a multicenter trial (NCT04713072). This study was terminated once 16-week results were available to continue to explore the effective dose range in a next P2b/3 trial. The results include as observed analysis evaluating change from baseline to weeks 16, 32 and 46. Patients met CASPAR criteria and had ≥3 swollen (SJC) and ≥3 tender joints (TJC) on a 66/68 joint count and inadequate response to previous NSAIDs, csDMARDs, or TNF inhibitor therapy.

Results: 135 patients were randomized 1:1:1 to izokibep 40 mg, 80 mg or placebo to week 16 when placebo transitioned to 80 mg Q2W. Patients had a mean age of 49 (SD 12) years, a mean BMI of 29 (5) kg/m^2, a mean PsA disease duration of 7 (8) years, a mean SJC of 10 (7) and TJC of 17 (10). At week 32, 96 of 102 eligible patients had evaluable data and at week 46, 59 of 62 eligible patients had evaluable data with similar distribution across groups. Clinically important improvements were evident for pain, patient global disease activity, itch, PsAID-9, treatment satisfaction on the TSQM-9 for those starting on 80 mg at baseline as well as those switching to 80 mg at week 16. The 80 mg dose showed improvements from week 16 to 46, whereas the 40 mg dose was largely stable (Figure 1). Consistent improvements across all PsAID-9 subdomains were evident for the 80 mg doses at week 32 and week 46 (Figure 2). Pain responders, defined as achieving patient reported pain < 30/100, improved from weeks 16 to 32 and 46 for those starting with 80 mg and those switching to 80 mg at week 16 while the 40 mg dose remained largely stable (Figure 3). From week 16 to week 46, the most frequently reported adverse events were injection site reactions, injection site erythema and nasopharyngitis which were distributed similarly across groups. One patient dropped out for ISR over this interval. There were no dose-related infection risks.

Conclusion: Izokibep led to continuing improvements across all PROs from baseline to weeks 16, 32 and 46 with greater improvements in the 80 mg dose groups. The GRAPPA validated PsAID-9 showed clinically important improvements in patient reported quality of life across all subdomains over weeks 16, 32 and 46. More than 70% of patients achieved marked pain control. Izokibep was generally well tolerated with no new safety issues to week 46.

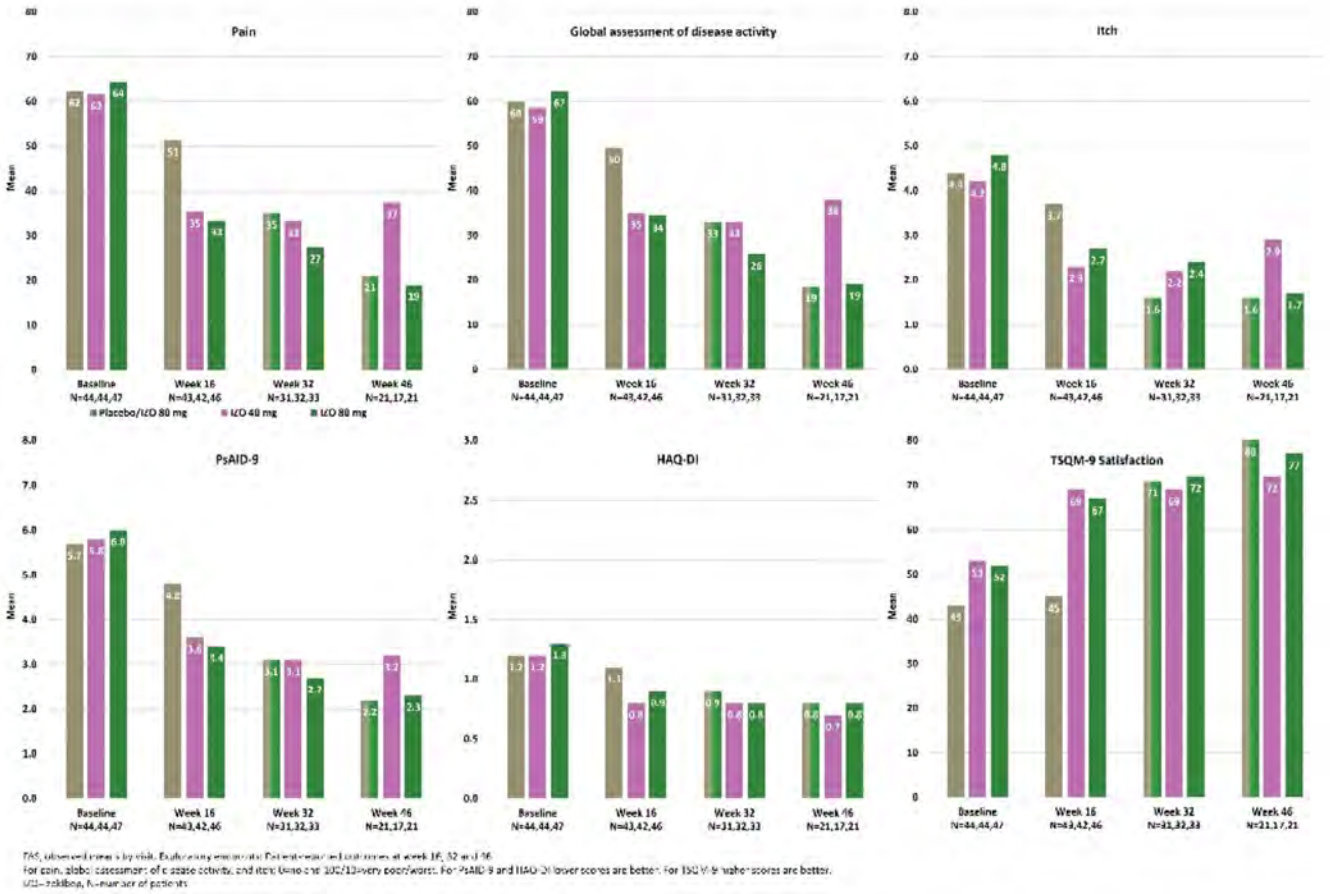

Figure 1. Continued Improvements in Multiple Patient-Reported Outcomes from Baseline to Weeks 16, 32 and 46

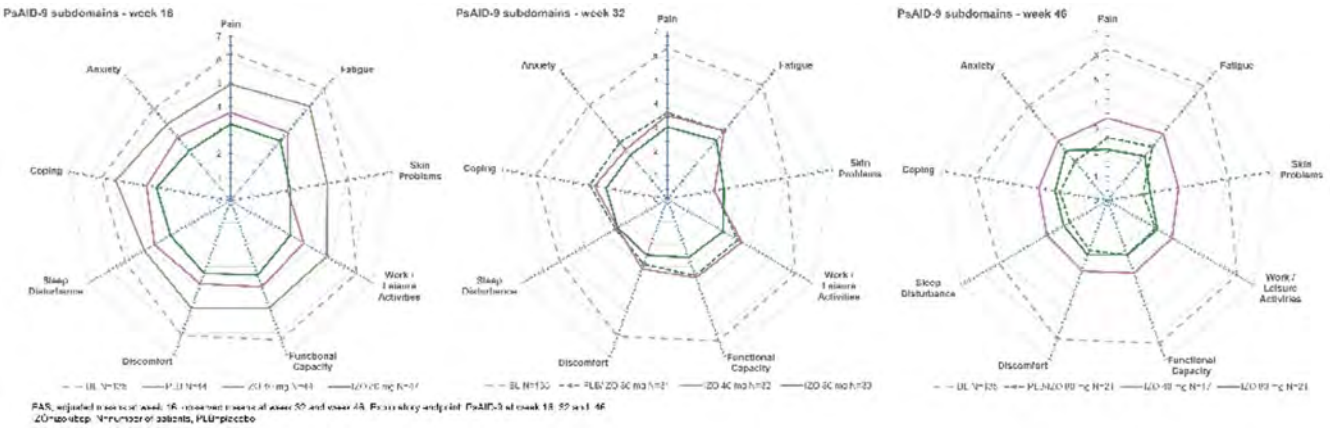

Figure 2. Continued Improvement in the GRAPPA Validated PsAID Quality of Life Index over Weeks 16, 32, 46

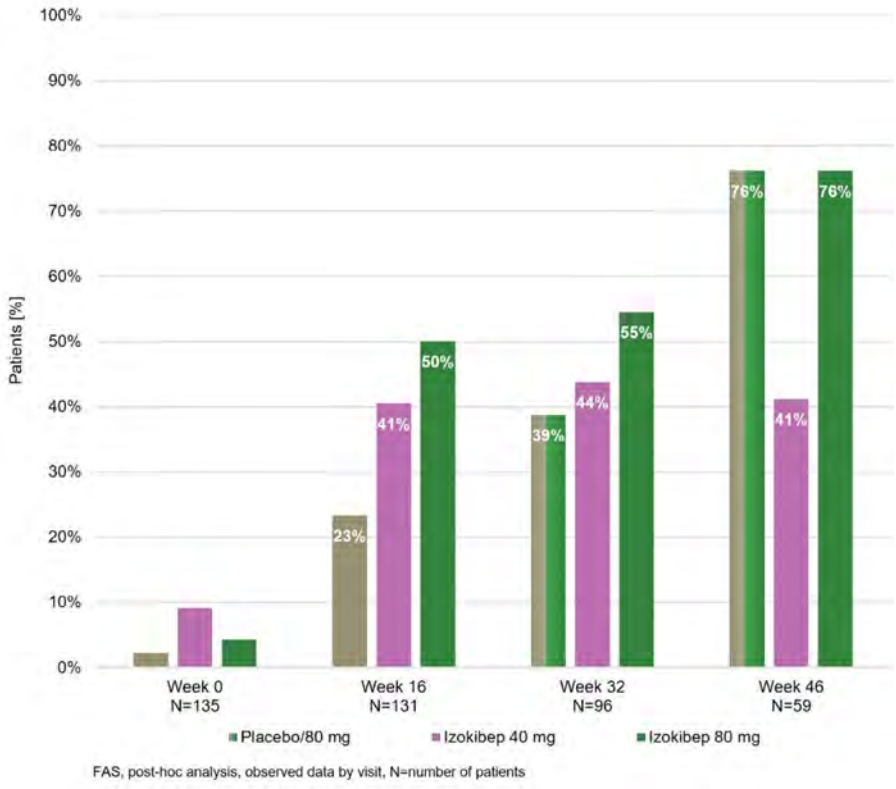

Figure 3. Patient Reported Pain Responders with Pain <30/100 at Weeks 16, 32 and 46

References

[1]Taylor, P C et al. ACR 2022. Abstract 0199. Arthritis Rheumatol. 2022; 74 (suppl 9).

Disclosure: P. Taylor: AbbVie, 2, Biogen, 2, Eli Lilly, 2, Fresenius, 2, Galapagos, 2, 5, Gilead Sciences, 2, GSK, 2, Janssen, 2, Nordic Pharma, 2, Pfizer Inc, 2, Sanofi, 2, UCB, 2; **K. de Vlam**: AbbVie, 2, Amgen, 2, Celgene, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, 5, 6, Novartis, 2, 6, UCB, 2, 6; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2; **P. Peloso**: ACELYRIN, 3, 8, 11; **D. Wetzel**: ACELYRIN, 2, Affibody, 2; **A. Lertratanakul**: AbbVie, 11, ACELYRIN, 3, 11; **N. Brun**: Affibody, 3, 8, 11; **B. Wiens**: ACELYRIN, 3, 8, 11, Horizon Therapeutics, 8; **J. Brandt-Juergens**: AbbVie/Abbott, 2, 6, Affibody, 2, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Gilead, 2, Janssen, 2, 6, Medac, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **E. Drescher**: None; **E. Dokoupilova**: AbbVie/Abbott, 5, Eli Lilly, 5, Galapagos NV, 5, Gilead, 5, GlaxoSmithKlein(GSK), 5, Hexal, 5, Janssen, 5, Novartis, 5, Pfizer, 5, Samsung Bioepis, 5, Sanofi, 5, UCB, 5; **A. Rowińska-Osuch**: None; **N. Abdel-Kader Martin**: None; **F. Behrens**: AbbVie, 2, 6, Affibody, 2, Amgen, 6, Boehringer-Ingelheim, 2, Celgene, 5, Chugai, 5, Eli Lilly, 6, Genzyme, 6, Gilead Sciences, 2, GSK, 2, 6, Janssen, 2, 5, MoonLake, 2, 6, MSD, 2, 6, Novartis, 6, Pfizer, 2, 5, 6, Roche, 5, Sandoz, 2, 6, Sanofi, 2, 6.

Abstract Number: 1432

Experiences and Perspectives of Patients with Psoriatic Arthritis Participating in a Randomized Controlled Trial of Dietary Interventions

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Dietary Interventions in psoriatic arthritis (DIPSA) is a randomized controlled trial (RCT) assessing the efficacy of dietary modifications in patients with psoriatic arthritis (PsA). Ideally, the design of an adjunct therapy trial and the intervention itself should engage patients in a positive experience. We aimed to describe patients' experience participating in a dietary RCT in a rheumatology setting.

Methods: DIPSA (NCT04180904) compares the efficacy of the Mediterranean diet and DASH-low caloric diet as adjunct therapy to the standard of care in PsA. Patients with moderately active PsA (DAPSA > 10) who were overweight or obese (BMI 25-40) were enrolled into the trial for 24 weeks. The trial design is shown in **Figure 1**. At the end of the trial, participants underwent a semi-structured interview regarding their participation including challenges faced, positive aspects of the trial, and recommendations for a future intervention and/or trial. Interviews lasted 20-30 min and were carried out by trained research coordinators. The interviews of first 50 participants who completed the trial (out of intended 90) were analyzed using modified grounded theory by two research coordinators with input from the two PIs.

Results: The mean age of the participants was 54.8 years (SD 12.3 years) and 66% were females. Key themes identified included the benefit of increased wellness from healthy diet, structured intervention, support from dietitian and other staff, self-awareness, barriers to dietary changes, and other lifestyle changes (Figure 2). The themes, subthemes and a few representative quotes are included in **Table 1**. Patients found advice regarding healthy eating habits, setting personal goals, incorporating or avoiding particular food items in the diet to be beneficial for their overall health and well-being. However, most wished for a well-organized and structured diet in the form of recipes, menus, or a booklet. Support from the staff, phone calls from a dietitian and daily text messages motivated participants to adhere to the diet. Participants became more cognizant of the effect of diet on their pain and arthritis which led to higher confidence in controlling pain through dietary modification. Our study identified some important barriers to dietary change in PsA. Psychological barriers included reluctance to change the diet because of taste and habit, and difficulty adhering during times of stress and fatigue. Social issues arose when eating out, traveling or dining with others. Other barriers to healthy eating were related to time constraints and affordability. Finally, participants expressed a desire to continue beneficial dietary changes as well as to commit to other healthy lifestyle choices, e.g., increased physical activity, mindfulness and meditation.

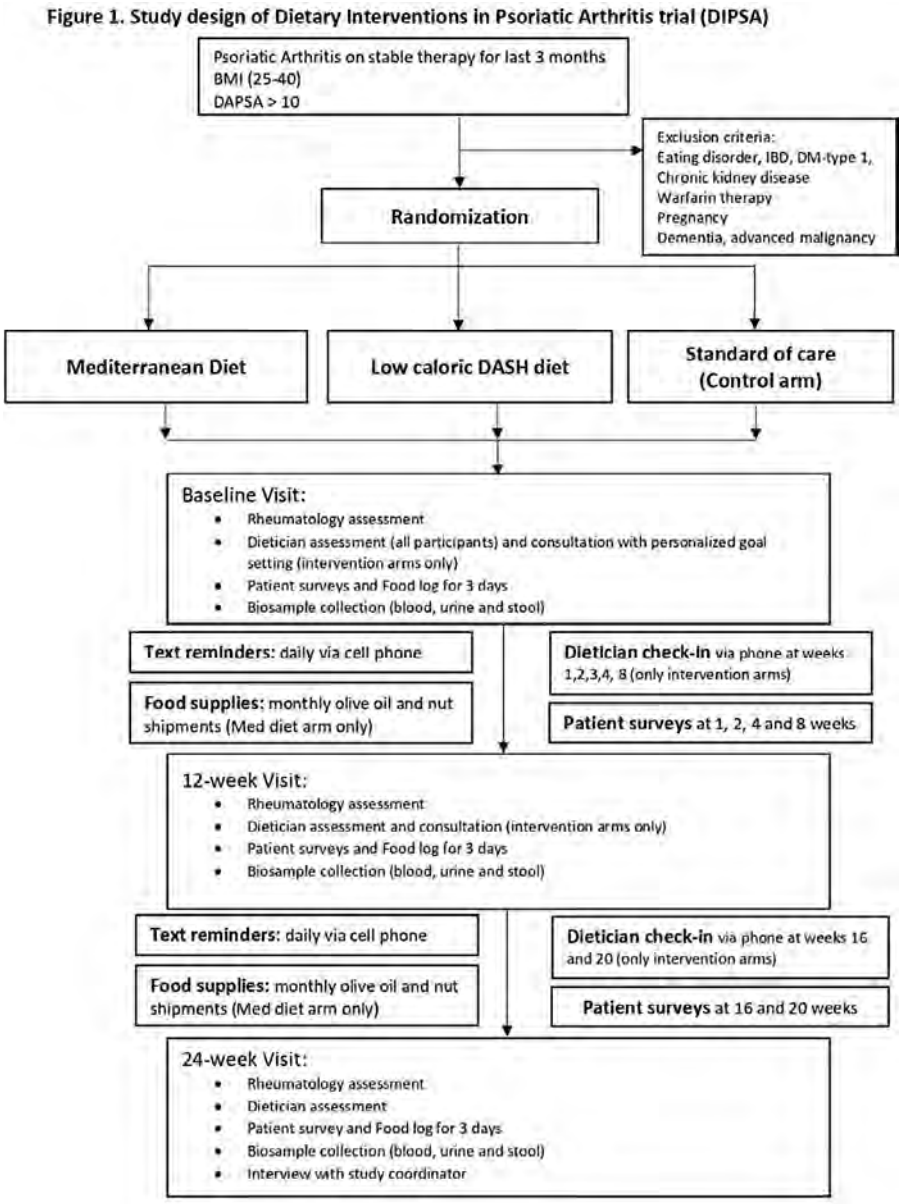

Figure 1: DIPSA study design and procedures

Conclusion: Patients with PsA found the DIPSA interventions to be feasible and valuable. Support from a multidisciplinary team, especially dietitian advice, was deemed crucial. Psychosocial barriers, cost and time constraints prevent patients from implementing healthy dietary changes. Finally, focusing on dietary change had carryover, helping patients to make healthy choices in other aspects of life.

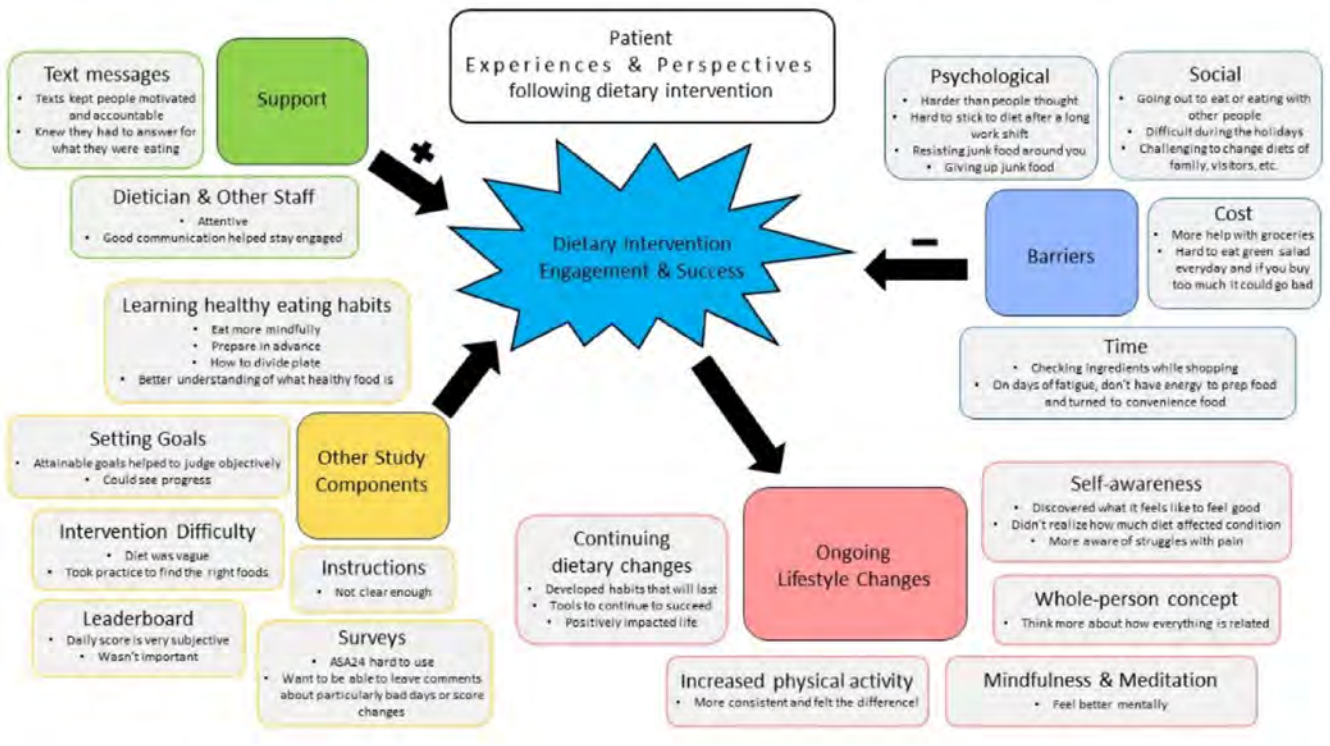

Figure 2: Summary of themes and subthemes that were identified in the interviews of study participants

Disclosure: L. Eder: AbbVie, 2, 5, Eli Lilly, 2, 5, Fresenius Kabi, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Sandoz, 5, UCB, 2, 5; **S. Tarannum**: None; **K. Bush**: None; **S. Cohen**: None; **C. Compher**: None; **H. Emanoilidis**: None; **S. Gillespie**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, Gilead Sciences, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5; **V. Chandran**: AbbVie, 1, 5, 6, Amgen, 1, 5, 6, AstraZeneca, 3, Bristol-Myers Squibb (BMS), 1, 6, Eli Lilly, 1, 5, 6, Janssen, 1, 6, Novartis, 1, 1, 6, UCB, 1, 2; **J. Scher**: AbbVie, 2, Janssen, 2, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **A. Ogdie**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, UCB, 2.

Abstract Number: 1433

Bimekizumab Impact on Core Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) Domains for Patients with Psoriatic Arthritis: 52-Week Results from Four Phase 3 Studies

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: The Group for Research and Assessment of Psoriasis and PsA (GRAPPA) domain-based treatment recommendations for PsA focus on six key domains: peripheral arthritis, axial disease, enthesitis, dactylitis, skin psoriasis, and nail psoriasis, and PsA-related conditions: uveitis and IBD.[1] Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A, has demonstrated superior clinical efficacy vs placebo (PBO) to Week (Wk) 16 in phase 3 clinical trials of patients (pts) with PsA.[2,3] In pts with psoriasis, superior skin domain efficacy has been demonstrated versus secukinumab (IL-17A inhibitor), ustekinumab (IL-12/23 inhibitor), and adalimumab (TNF-α inhibitor [TNFi]).[4–6] The objective of this analysis is to show BKZ efficacy across GRAPPA core domains to Wk 52 from two phase 3 trials in PsA, with axial domain outcomes from two phase 3 trials in axial spondyloarthritis (axSpA).

Methods: Included pts were randomized to receive subcutaneous BKZ 160 mg or PBO every 4 wks (Q4W) in BE OPTIMAL (NCT03895203; biologic DMARD-naïve pts with PsA), BE COMPLETE (NCT03896581; pts with PsA who were TNFi-inadequate responders [TNFi-IR]), BE MOBILE 1 (NCT03928704; non-radiographic axSpA) and BE MOBILE 2 (NCT03928743; radiographic axSpA, i.e. ankylosing spondylitis). BE OPTIMAL included a reference arm (adalimumab 40 mg Q2W) to Wk 52; data not shown.[2,3,7] From Wk 16, all PBO-randomized pts received BKZ 160 mg Q4W to Wk 52 (PBO/BKZ). Wk 16 completers from BE COMPLETE were eligible to enter BE VITAL (NCT04009499; open-label extension). Outcomes are reported by GRAPPA domain (**Table 1**). Missing data are imputed using non-responder and multiple imputation (NRI; MI) for binary and continuous outcomes, or reported using observed case (OC).

Results: Wk 52 completion was high (BE OPTIMAL: 770/852 [90.4%], BE COMPLETE: 347/400 [86.8%], BE MOBILE 1: 220/254 [86.6%], BE MOBILE 2: 298/332 [89.8%]). Baseline demographics and disease characteristics were previously reported.[2,3,7] Across all GRAPPA domains, improvements from Wk 16 were sustained at Wk 52 in BKZ-treated pts across

Table 1. Reported outcomes by core and PsA-related domain

Disease	GRAPPA domain outcome	
PsA	**Peripheral Arthritis**	
	SJC	• CfB
	TJC	• SJC/TJC≤1
	Enthesitis	
	LEI	• CfB • Rates of pts achieving resolution (LEI=0)
	Dactylitis	
	LDI	• CfB • Rates of pts achieving resolution (LDI=0)
	Skin psoriasis	
	PASI	• CfB • Rates of pts achieving resolution (PASI100)
	Nail psoriasis	
	mNAPSI	• CfB • Rates of pts achieving resolution (mNAPSI=0)
	Uveitis[a]	• n (%)
	IBD[a]	• n (%)
PsA and axSpA	**Axial disease**	
	BASDAI	• CfB
axSpA	ASAS40	• Responder rate
	MRI SPARCC SIJ	• CfB
	Nocturnal spinal pain	• CfB

[a] Uveitis and IBD are defined as PsA-related conditions.[1] ASAS40: Assessment in Spondyloarthritis international Society 40% improvement; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CfB: change from baseline; GRAPPA: Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; LDI: Leeds Dactylitis Index; LEI: Leeds Enthesitis Index; mNAPSI: modified nail psoriasis severity index; PASI: Psoriasis Area and Severity Index; PASI100: 100% improvement in PASI; SJC: swollen joint count; SIJ: sacroiliac joint; SPARCC: Spondyloarthritis Research Consortium of Canada; TJC: tender joint count.

Table 2. Efficacy outcomes at Week 16 and 52 from BE OPTIMAL, BE COMPLETE and BE VITAL, BE MOBILE 1, and BE MOBILE 2 by GRAPPA domain [NRI, MI, OC]

	BE OPTIMAL (bDMARD-naive)				BE COMPLETE/BE VITAL (TNFi-IR)			
	PBO → BKZ 160 mg Q4W n=281		BKZ 160 mg Q4W n=431		PBO → BKZ 160 mg Q4W n=133		BKZ 160 mg Q4W n=267	
	Wk16	Wk52[a]	Wk16	Wk52	Wk16	Wk52[a]	Wk16	Wk52
Peripheral arthritis								
SJC score (of 66 joints), BL, mean (SE)	9.5 (0.4)		9.0 (0.3)		10.3 (0.7)		9.7 (0.5)	
CfB, mean (SE) [MI]	−3.0 (0.5)	−7.8 (0.4)	−6.6 (0.3)	−7.6 (0.3)	−2.0 (0.5)	−8.3 (0.6)	−7.0 (0.4)	−7.9 (0.4)
SJC ≤1, n (%) [NRI]	70 (24.9)	189 (67.3)	260 (60.3)	301 (69.8)	25 (18.8)	87 (65.4)	161 (60.3)	166 (62.2)
TJC score (of 68 joints), BL, mean (SE)	17.1 (0.8)		16.8 (0.6)		19.3 (1.2)		18.4 (0.8)	
CfB, mean (SE) [MI]	−3.1 (0.7)	−11.9 (0.7)	−10.0 (0.5)	−12.5 (0.5)	−2.4 (0.9)	−14.1 (1.2)	−10.9 (0.8)	−12.9 (0.8)
TJC ≤1, n (%) [NRI]	24 (8.5)	116 (41.3)	136 (31.6)	198 (45.9)	7 (5.3)	41 (30.8)	66 (24.7)	105 (39.3)
Enthesitis								
LEI score,[b] BL, mean (SE)	2.9 (0.2)		2.5 (0.1)		2.9 (0.3)		2.6 (0.1)	
CfB,[b] mean (SE) [MI]	−1.2 (0.2)	−2.0 (0.2)	−1.3 (0.1)	−1.7 (0.1)	−0.8 (0.3)	−2.1 (0.3)	−1.5 (0.2)	−1.8 (0.2)
Complete resolution of enthesitis, LEI=0,[b] n/N (%) [NRI]	29/70 (41.4)	44/70 (62.9)	72/143 (50.3)	87/143 (60.8)	8/36 (22.2)	21/36 (58.3)	52/106 (49.1)	60/106 (56.6)
Dactylitis								
LDI score,[c] BL, mean (SD)	47.3 (41.1)		46.7 (54.3)		66.4 (127.6)		72.7 (114.4)	
CfB,[c,d] mean (SD) [OC]	−22.9 (34.6)	−48.8 (42.8)	−36.7 (56.1)	−43.7 (55.3)	−25.6 (28.7)	−39.6 (28.1)	−39.8 (82.7)	−64.5 (89.0)
Complete resolution of dactylitis, LDI=0,[c] n/N (%) [NRI]	18/33 (54.5)	29/33 (87.9)	44/56 (78.6)	45/56 (80.4)	6/14 (42.9)	12/14 (85.7)	24/34 (70.6)	29/34 (85.3)
Skin psoriasis								
PASI score,[e] BL, mean (SE)	7.9 (0.5)		8.2 (0.5)		8.5 (0.7)		10.1 (0.7)	
CfB,[e] mean (SE) [MI]	0.0 (0.4)	−7.5 (0.5)	−7.4 (0.5)	−7.7 (0.5)	0.3 (0.5)	−8.2 (0.7)	−9.2 (0.7)	−9.4 (0.7)
PASI100,[e] n/N (%) [NRI]	3/140 (2.1)	91/140 (65.0)	103/217 (47.5)	132/217 (60.8)	4/88 (4.5)	53/88 (60.2)	103/176 (58.5)	116/176 (65.9)
Nail psoriasis								
mNAPSI score,[f] BL, mean (SE)	4.0 (0.2)		4.1 (0.2)		4.5 (0.3)		4.3 (0.2)	
CfB,[f] mean (SE) [MI]	−0.9 (0.2)	−3.5 (0.2)	−2.4 (0.2)	−3.5 (0.2)	−0.4 (0.2)	−3.6 (0.3)	−2.7 (0.2)	−3.6 (0.2)
Complete resolution of nail psoriasis mNAPSI=0,,[f] n/N (%) [NRI]	29/156 (18.6)	111/156 (71.2)	82/244 (33.6)	160/244 (65.6)	12/83 (14.5)	51/83 (61.4)	73/159 (45.9)	107/159 (67.3)
Axial disease								
BASDAI score,[c] BL, mean (SE)	6.2 (0.1)		6.1 (0.1)		6.5 (0.1)		6.2 (0.1)	
CfB,[c] mean (SE) [MI]	−1.1 (0.1)	−3.0 (0.2)	−2.6 (0.1)	−3.2 (0.1)	−0.7 (0.2)	−2.8 (0.3)	−2.6 (0.2)	−2.9 (0.2)

	Pooled BE MOBILE 1 + 2 (nr-axSpA and r-axSpA)			
	PBO → BKZ 160 mg Q4W n=237		BKZ 160 mg Q4W n=349	
	Wk16	Wk52[a]	Wk16	Wk52
ASAS40 responder rate, n (%) [NRI]	52 (21.9)	140 (59.1)	160 (45.8)	207 (59.3)
BASDAI score, BL, mean (SE)	6.6 (0.1)		6.6 (0.1)	
CfB, mean (SE) [MI]	−1.7 (0.1)	−3.7 (0.1)	−3.0 (0.1)	−3.7 (0.1)
Nocturnal spinal pain score, BL, mean (SE)	6.8 (0.1)		6.7 (0.1)	
CfB, mean (SE) [MI]	−1.8 (0.2)	−4.3 (0.2)	−3.5 (0.1)	−4.3 (0.1)

	BE MOBILE 1 (nr-axSpA)		BE MOBILE 2 (r-axSpA)	
	PBO → BKZ 160 mg	BKZ 160 mg Q4W	PBO → BKZ 160 mg	BKZ 160 mg Q4W

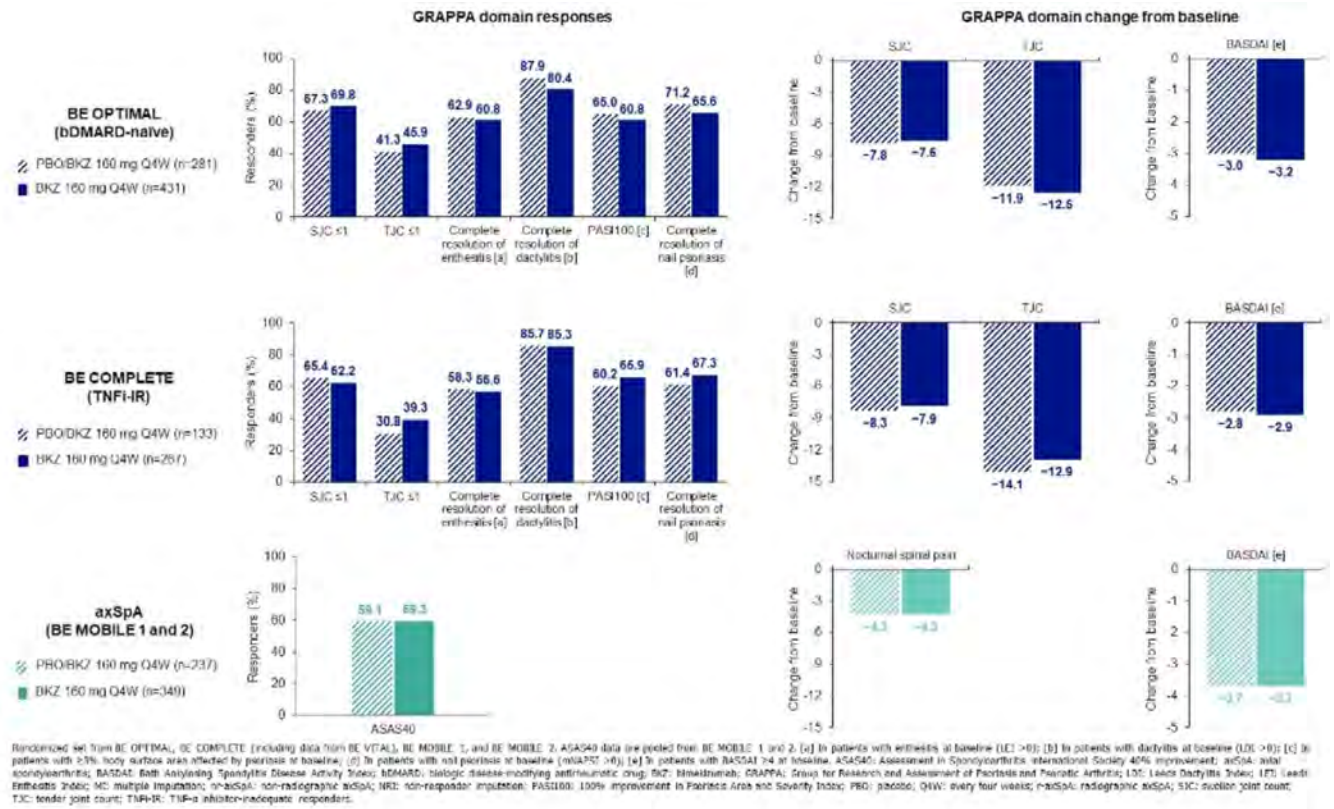

Figure. GRAPPA individual domain response and change from baseline at Week 52 from BE OPTIMAL (bDMARD-naïve), BE COMPLETE (TNFi-IR), BE MOBILE 1 (nr-axSpA) and BE MOBILE 2 (r-axSpA) [NRI, MI]

all studies (**Table 2**). Individual domain responses were generally consistent between bDMARD-naïve and TNFi-IR pts (**Figure**). Results from BE MOBILE 1 and 2 demonstrated BKZ efficacy in pts with axSpA (**Table 2**, **Figure**) and were suggestive of efficacy for axial disease in PsA.[1] Responses were generally consistent between BKZ and PBO/BKZ pts at Wk 52 (**Figure**). To Wk 52, there were no instances of uveitis (BE OPTIMAL; BE COMPLETE). 2 (0.2%) pts in BE OPTIMAL had definite adjudicated IBD; no pts had adjudicated IBD in BE COMPLETE.

Conclusion: Treatment with BKZ resulted in robust and sustained improvements across GRAPPA domains with low rates of IBD and no uveitis to Wk 52 for both bDMARD-naïve and TNFi-IR pts with PsA; results from pts with axSpA support efficacy in the axial domain.

References:1. Coates LC. Nat Rev Rheumatol 2022;18:465–79; **2.** McInnes IB. Lancet 2023;401:25–37; **3.** Merola JF. Lancet 2023;401:38–48; **4.** Reich K. N Engl J Med 2021;385:142–52; **5.** Reich K. Lancet 2021;397:487–98. **6.** Warren RB. N Engl J Med 2021;385:130–41; **7.**Van der Heijde D. Ann Rheum Dis 2023;82:515–26.

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Inc, 2, 5, 6, UCB, 2, 5; **B. Ink**: AbbVie, 11, GSK, 11, UCB Pharma, 3, 11; **C. Fleurinck**: UCB Pharma, 3; **R. Bajracharya**: UCB Pharma, 3, 11; **J. Coarse**: UCB Pharma, 3, 11; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, Bristol Myers Squibb, 2, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead Sciences, 2, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake, 2, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 1434

Long-Term Efficacy and Safety of Risankizumab for Active Psoriatic Arthritis: 148-Week Results from the KEEPsAKE 2 Trial

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: PsA is a chronic systemic inflammatory disease that affects 30% of patients diagnosed with psoriasis, with a clinical burden that includes dactylitis, enthesitis, cutaneous manifestations, chronic pain, progressive joint damage, and disability. Risankizumab (RZB), an antibody that targets the p19 subunit of interleukin-23 with high affinity and specificity, is approved for the treatment of adult patients with active PsA. RZB has been previously reported to show efficacy across several disease domains up to week 100.[1] Here, we report the efficacy and safety results through week 148.

Table 1. Efficacy Results for KEEPsAKE 2 at Week 52, Week 100 and Week 148

	KEEPsAKE 2					
	Week 52		Week 100		Week 148	
	RZB 150 mg (N=224)	PBO to RZB 150 mg (N=219)	RZB 150 mg (N=224)	PBO to RZB 150 mg (N=219)	RZB 150 mg (N=224)	PBO to RZB 150 mg (N=219)
ACR20, % (n)[a]	59.9 (134)	55.7 (122)	57.1 (128)	52.5 (115)	54.0 (121)	46.6 (102)
ACR50, % (n)[a]	33.3 (75)	32.0 (70)	34.8 (78)	33.8 (74)	33.9 (76)	28.8 (63)
ACR70, % (n)[a]	17.4 (39)	21.0 (46)	21.4 (48)	17.4 (38)	19.6 (44)	16.4 (36)
Change in HAQ-DI, mean (95% CI)[b,i]	-0.26 (-0.33, -0.19)	-0.34 (-0.42, -0.27)	-0.26 (-0.33, -0.18)	-0.31 (-0.39, -0.23)	-0.24 (-0.32, -0.16)	-0.27 (-0.36, -0.19)
PASI 90, % (n/N)[a,c]	65.0 (80/123)	59.7 (71/119)	67.5 (83/123)	61.3 (73/119)	65.9 (81/123)	58.8 (70/119)
MDA, n (%)[a]	77.2 (61)	33.8 (74)	33.0 (74)	33.3 (73)	33.0 (74)	28.3 (62)
Change in SF-36 PCS score, mean (95% CI)[b,i]	6.27 (5.22, 7.33)	7.34 (6.26, 8.42)	6.44 (5.28, 7.60)	6.46 (5.25, 7.66)	6.09 (4.83, 7.36)	5.60 (4.27, 6.92)
Change in FACIT-Fatigue score, mean (95% CI)[b,i]	5.7 (4.6, 6.9)	7.0 (5.8, 8.2)	5.4 (4.1, 6.7)	6.4 (5.0, 7.7)	6.0 (4.6, 7.5)	5.1 (3.6, 6.6)
Resolution of enthesitis, % (n/N)[a,d]	43.5 (64/147)	52.5 (83/158)	51.7 (76/147)	52.5 (83/158)	53.1 (78/147)	47.5 (75/158)
Resolution of dactylitis, % (n/N)[a,e]	67.5 (27/40)	70.9 (40/57)	77.5 (31/40)	68.4 (39/57)	82.5 (33/40)	61.4 (35/57)

All changes are least square mean changes from baseline.

[a]Results for binary endpoints are based on as-observed (AO) data with missing data imputed as non-responder imputation incorporating multiple imputation (NRI-MI) if there are missing data due to COVID-19.

[b]Results for continuous endpoints are reported by mixed-effect model repeated measurement (MMRM).

[c]Reported for patients with ≥ 3% of body surface area (BSA) affected by psoriasis at baseline (RZB, N=123; PBO/RZB, N=119).

[d]Defined as Leeds Enthesitis Index (LEI)=0 and reported among patients with LEI >0 at baseline (RZB, N=147; PBO/RZB, N=158).

[e]Defined as Leeds Dactylitis Index (LDI)=0 and reported among patients with LDI>0 at baseline (RZB, N=40; PBO/RZB, N=57).

[i]Number of unique patients contributing to MMRM model estimates: patients with at least one available change from baseline value and no missing data for the factors and covariates in the model. The MMRM N is not visit-specific and is displayed for model estimates for all visits. For change in HAQ-DI (RZB, N=224; PBO/RZB, N=215); for change in FACIT-Fatigue score and change in SF-36 PCS score (RZB, N=223; PBO/RZB, N=213).

ACR20/50/70, ≥20/50/70% improvement in American College of Rheumatology score; BSA, body surface area; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue Questionnaire; HAQ-DI, Health Assessment Questionnaire-Disability Index; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; LS, least square; MDA, minimal disease activity; PASI 90, ≥90% reduction in Psoriasis Area and Severity Index; PBO, placebo; RZB, risankizumab; SF-36 PCS, 36-Item Short Form Health Survey Physical Component Summary.

Methods: KEEPsAKE 2 is an ongoing phase 3 global, multicenter clinical trial evaluating the efficacy and safety of RZB versus placebo (PBO) in patients with active PsA,defined as ≥5 tender joints and ≥5 swollen joints, meeting the Classification Criteria for Psoriatic Arthritis (CASPAR), with symptom onset of ≥6 months before screening, and active plaque psoriasis or nail changes consistent with psoriasis at screening. Eligible patients were 18 years or older and had previous inadequate response or intolerance to 1 or 2 biological therapies (Bio-IR) and/or ≥1 conventional synthetic DMARD (csDMARD-IR). Patients were randomized in a 1:1 ratio to receive double-blinded treatment with subcutaneous RZB 150 mg or matched placebo for 24 weeks, administered at weeks 0, 4 and 16. Starting at week 24, all patients in the ongoing trial receive open-label RZB 150 mg every 12 weeks through week 316. Efficacy and safety analyses were conducted in all randomized patients who received one or more doses of the study drug. Statistical reporting and imputation methods for efficacy assessments are defined in the figures. Safety assessments were based on monitoring of treatment emergent adverse events (TEAEs) and are summarized using exposure-adjusted event rates (EAERs, events/100 patient-years [PYs]).

Results: Patients in KEEPsAKE 2 (RZB N=224; PBO/RZB N=219) maintained similar efficacy results at week 148 to those reported at week 52 and week 100 (**Table 1**). 33.9% of RZB and 28.8% of PBO/RZB patients achieved ACR50 response at week 148 (**Figure 1**). 65.9% of RZB and 58.8% of PBO/RZB patients achieved PASI 90 response at week 148. A consistent change from baseline in HAQ-DI (RZB -0.24, PBO/RZB -0.27), SF-36 PCS (RZB 6.09, PBO/RZB 5.60) and FACIT-

Table 2. Safety Summary for KEEPsAKE 2 through Week 148

	RZB Week 24[a] N=224 PYs=104.3	PBO Week 24[a] N=219 PYs=101.3	RZB and PBO/RZB Week 148 N=419 PYs=1059.0
Any TEAE	286 (274.2)	292 (288.3)	1874 (177.0)
Serious TEAE	14 (13.4)	15 (14.8)	99 (9.3)
TEAE leading to discontinuation of study drug	2 (1.9)	6 (5.9)	12 (1.1)
COVID-19 related TEAE	1 (1.0)	0	124 (11.7)
Any MACE	1 (1.0)	0	4 (0.4)
Cardiovascular death due to acute myocardial infarction	0	0	1 (<0.1)
Non-fatal myocardial infarction	0	0	2 (0.2)
Non-fatal stroke	1 (1.0)	0	1 (<0.1)
Any serious infection	3 (2.9)	5 (4.9)	18 (1.7)
Any serious hypersensitivity	0	0	1 (<0.1)[b]
Opportunistic infections excluding TB and herpes zoster	0	0	2 (0.2)
Active TB	0	0	0
Herpes zoster	0	1 (1.0)	5 (0.5)
Malignant tumors	1 (1.0)	3 (3.0)	17 (1.6)
Including NMSC	1 (1.0)	3 (3.0)	15 (1.4)
Excluding NMSC	0	0	2 (0.2)
Any adjudicated anaphylactic reaction	0	0	0
All Deaths	0	0	1 (0.1)[c]

Treatment-emergent adverse events (TEAE) were defined as any AE with an onset date that was on or after the first dose of risankizumab and up to 140 days after the last dose of risankizumab if the patient discontinued the study drug prematurely.

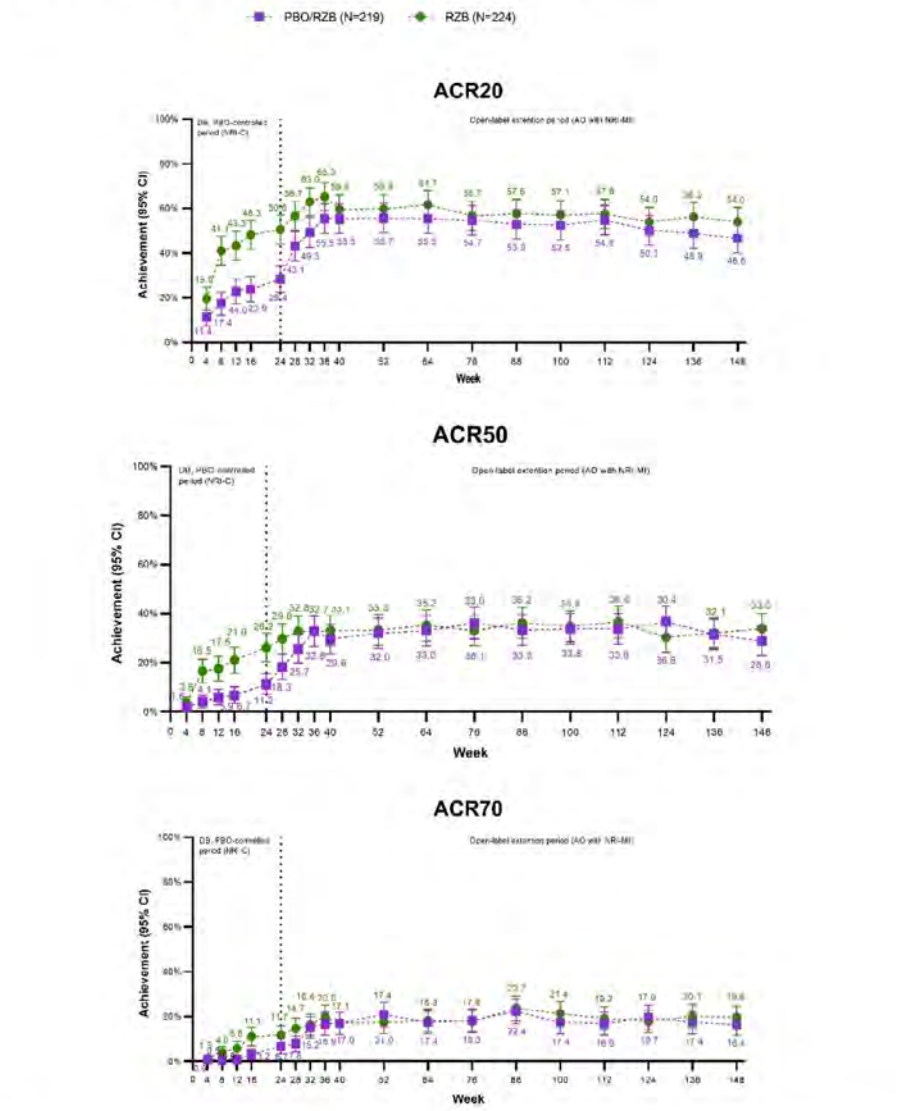
[a]24 week data from KEEPsAKE 2 was previously published in Östör A, et. al. Ann Rheum Dis. 2022;81:351-358.

[b]Event of idiopathic thrombocytopenic purpura assessed as NRP per investigator. Patient remained on study drug.

[c]One death was caused by coronary artery plaque rupture in a patient who had multiple risk factors, including obesity, a long history of smoking, hypertension, hypercholesterolemia, and a family history of cardiovascular disease.

MACE, major adverse cardiovascular events; NMSC, non-melanoma skin cancer; PYs, patient-years; RZB, risankizumab; TB, tuberculosis; TEAE, treatment-emergent adverse events.

Figure 1. ACR20, 50, and 70 Achievement Over 148 Weeks



DB, double-blind; NRI-C, non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19; AO with NRI-MI, as-observed (AO) data with missing data imputed as non-responder imputation incorporating multiple imputation (NRI-MI) if there are missing data due to COVID-19; PBO, placebo; RZB, risankizumab.

Fatigue (RZB 6.0, PBO/RZB 5.1) was observed at 148 weeks. 33.0% of RZB patients and 28.3% of PBO/RZB patients achieved MDA at week 148, consistent with results reported at week 52 and week 100. For those patients with enthesitis at baseline, resolution was observed in 53.1% of RZB and 47.5% of PBO/RZB patients at week 148. For patients with dactylitis at baseline, resolution was observed in 82.5% of RZB and 61.4% of RZB/PBO patients at week 148. The overall rates of TEAEs, serious TEAEs and AEs leading to discontinuation of study drug remained stable and was consistent with the rates reported for the placebo-controlled period (**Table 2**).

Conclusion: Long-term treatment with RZB 150mg shows durable efficacy in patients with PsA through 148 weeks, with no new safety findings.

References:

1. Kristensen, et al. 2022 EADV Congress.

Disclosure: A. Östör: AbbVie, 12, has served as a consultant and/or on advisory boards and/or undertaken clinical trials, GSK, 12, has served as a consultant and/or on advisory boards and/or undertaken clinical trials, Janssen, 12, has served as a consultant and/or on advisory boards and/or undertaken clinical trials, Lilly, 12, has served as a consultant and/or on advisory boards and/or undertaken clinical trials, Novartis, 12, has served as a consultant and/or on advisory boards and/or undertaken clinical trials, Pfizer, 12, has served as a consultant and/or on advisory boards and/or undertaken clinical trials; **F. Van den Bosch**: AbbVie, 2, 6, Amgen, 2, BMS, 6, Celgene, 6, Eli Lilly, 2, Galapagos, 2, Janssen, 2, 6, Merck, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB Pharma, 2, 6; **K. Papp**: AbbVie, 1, 2, 5, 6, Akros, 1, 2, 5, 6, Amgen, 1, 2, 5, 6, Anacor, 1, 2, 5, 6, Arcutis, 1, 2, 5, 6, Astellas, 1, 2, 5, 6, Bausch Health/Valeant, 1, 2, 5, 6, Baxalta, 1, 2, 5, 6, Boehringer-Ingelheim, 1, 2, 5, 6, Bristol-Myers Squibb, 1, 2, 5, 6, Can-Fite Biopharma, 1, 2, 5, 6, Celgene, 1, 2, 5, 6, Coherus, 1, 2, 5, 6, Dermira, 1, 2, 5, 6, Dow Pharma, 1, 2, 5, 6, Eli Lilly, 1, 2, 5, 6, Evelo, 1, 2, 5, 6, Forward Pharma, 5, Galapagos, 1, 2, 5, 6, Galderma, 1, 2, 5, 6, Genentech, 1, 2, 5, 6, Gilead, 1, 2, 5, 6, GlaxoSmithKlein, 1, 2, 5, 6, Janssen, 1, 2, 5, 6, Kyowa-Hakko Kirin, 1, 2, 5, 6, LEO Pharma, 1, 2, 5, 6, MedImmune, 1, 2, 5, 6, Meiji Seika Pharma, 1, 2, 5, 6, Merck-Serono, 1, 2, 5, 6, Mitsubishi Pharma, 1, 2, 5, 6, Moberg Pharma, 1, 2, 5, 6, MSD, 1, 2, 5, 6, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, 6, PRCL Research, 1, 2, 5, 6, Regeneron, 1, 2, 5, 6, Roche, 1, 2, 5, 6, Sanofi-Aventis/Genzyme, 1, 2, 5, 6, Sun Pharma, 1, 2, 5, 6, Takeda, 1, 2, 5, 6, UCB, 1, 2, 5, 6; **C. Asnal**: AbbVie/Abbott, 1, 5, 6, Amgen, 1, 5, 6, Eli Lilly, 1, 5, 6, Genentech, 1, 5, 6, Janssen, 1, 5, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 1, 5, 6, R-Pharm, 1, 5, 6; **R. Blanco**: AbbVie/Abbott, 5, 6, Amgen, 6, AstraZeneca, 2, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, Merck/MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6; **J. Aelion**: AbbVie, 5, 6, Acceleron, 5, Acelyrin, 5, Aclaris Therapeutics, 5, Alpine Immune Sciences, 5, Amgen, 2, 5, AstraZeneca, 5, Biogen, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 5, Galapagos, 5, GlaxoSmithKline, 5, Horizon, 5, Janssen, 2, 5, Novartis, 2, 5, Roche, 5, Selecta, 5, UCB, 5, Ventyx, 5; **V. Stakias**: AbbVie, 3, 11; **T. Iyile**: AbbVie/Abbott, 3, 11; **K. Carter**: AbbVie/Abbott, 3, 11; **A. Soliman**: AbbVie/Abbott, 3, 10, 11; **L. Drogaris**: AbbVie/Abbott, 3, 11; **M. Chen**: AbbVie/Abbott, 3, 11; **B. Padilla**: AbbVie/Abbott, 3, 11; **A. Kivitz**: AbbVie, 6, Amgen, 6, 11, Chemocentryx, 1, Eli Lilly, 6, Fresenius Kabi, 2, Genzyme, 2, Gilead, 2, 11, GlaxoSmithKlein (GSK), 2, 6, 11, Grunenthal, 2, Horizon, 1, 2, Janssen, 1, 2, Novartis, 4, 11, Pfizer, 2, 6, 11, Selecta, 2, Synact, 2, Takeda, 2, UCB, 1, 6.

Abstract Number: 1435

Long-Term Efficacy and Safety of Risankizumab for CsDMARD-IR Patients with Active Psoriatic Arthritis: 148-Week Results from the KEEPsAKE 1 Trial

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Risankizumab (RZB), a humanized immunoglobulin G1 monoclonal antibody that inhibits interleukin-23 by targeting its p19 subunit with high affinity and specificity, is approved for the treatment of adult patients (pts) with active PsA. Pts in the KEEPsAKE 1 trial who received RZB 150 mg achieved the primary efficacy endpoint at week

24. The long-term efficacy, safety and tolerability of RZB has been previously reported through 100 weeks of treatment. Here, we report the efficacy and safety results through week 148.

Methods: KEEPsAKE 1 is an ongoing, global, phase 3, multicenter clinical trial to evaluate the efficacy and safety of RZB versus placebo (PBO) in patients with active PsA. Eligible patients were≥18 years old and demonstrated an inadequate response, intolerance or contraindication to ≥1 conventional syntheticDMARD (csDMARD-IR). Following a 24-week double-blind, PBO-controlled, parallel-group treatment period (period 1), the trial is ongoing with an open-label extension treatment period from week 24 through week 316 (period 2). In period 1, pts were randomized 1:1 to receive subcutaneous RZB 150 mg or PBO at weeks 0, 4 and 16. At week 24, pts who were randomized to RZB received blinded PBO and pts who were randomized to PBO received the first dose of blinded RZB. Starting at week 28, all pts continue to receive open-label RZB 150 mg every 12 weeks until week 316. Beginning at week 36, pts who were classified as non-responders (defined as < 20% improvement in tender or swollen joint count on two consecutive visits vs baseline) were discontinued from the study drug. Efficacy and safety analyses were conducted in all randomized pts who received one or more doses of the study drug. Safety assessments were based on monitoring of treatment-emergent adverse events (TEAEs).

Results: Overall efficacy results were maintained at week 148 of the KEEPsAKE 1 trial, as compared to week 52 and 100 (**-Table 1**). At week 148, 41.1% of RZB and 41.5% of PBO/RZB pts achieved ACR50 and 38.1% of RZB and 35.5% of PBO/RZB pts achieved MDA (**Figure 1**). 69.3% of RZB and 67.1% of PBO/RZB pts achieved PASI90 at week 148. mNAPSI and PGA-F scores improved from baseline by 15.01 and 1.5 points, respectively, for RZB pts and by 13.99 and 1.4 points for PBO/RZB pts. For pts with enthesitis at baseline, resolution was seen in 62.6% of RZB and 62.4% of PBO/RZB pts. For pts with dactylitis at baseline, resolution was seen in 77.5% of RZB and 74.8% of PBO/RZB pts. At week 148, the mean PSA-mTSS score increased by 0.55 from baseline for RZB and by 0.94 for PBO/RZB pts. 88.5% of RZB and 84.4% of

Table 1. Efficacy Results for KEEPsAKE 1 at Week 52, Week 100 and Week 148

	KEEPsAKE 1					
	Week 52		Week 100		Week 148	
	RZB 150 mg (N=483)	PBO to RZB 150 mg (N=481)	RZB 150 mg (N=483)	PBO to RZB 150 mg (N=481)	RZB 150 mg (N=483)	PBO to RZB 150 mg (N=481)
ACR20, % (n)[a]	70.6	63.7	64.4	60.9	58.3	60.7
ACR50, % (n)[a]	43.6	38.3	42.2	44.1	41.1	41.5
ACR70, % (n)[a]	25.9	20.5	27.1	26.9	27.4	26.1
Change in HAQ-DI[c] mean (95% CI)[b]	-0.41 [N=479] (-0.46, -0.36)	-0.32 [N=476] (-0.37, -0.27)	-0.41 [N=479] (-0.45, -0.36)	-0.36 [N=476] (-0.41, -0.31)	-0.41 [N=479] (-0.46, -0.36)	-0.35 [N=476] (-0.40, -0.29)
PASI 90, % (n/N)[a,c]	68 (186/273)	61.1 (166/272)	72.3 (197/273)	68.6 (187/272)	69.3 (189/273)	67.1 (183/272)
Change in mNAPSI[d], mean (95% CI)[b,d]	-12.61 [N=291] (-13.48, -11.74)	-11.34 [N=311] (-12.18, -10.50)	-14.09 [N=264] (-14.94, -13.25)	-13.52 [N=291] (-14.33, -12.70)	-15.01 [N=253] (-15.81, -14.21)	-13.99 [N=280] (-14.75, -13.22)
Change in PGA-F[e], mean (95% CI)[b,e]	-1.2 [N=292] (-1.3, -1.1)	-1.1 [N=311] (-1.2, -1.0)	-1.4 [N=264] (-1.5, -1.3)	-1.3 [N=291] (-1.4, -1.2)	-1.5 [N=253] (-1.6, -1.4)	-1.4 [N=280] (-1.5, -1.3)
MDA, n (%)[a]	38.3 (185)	28.0 (134)	38.5 (186)	35.1 (169)	38.1 (184)	35.5 (171)
Change in SF-36 PCS score[f], mean (95% CI)[b]	8.42 [N=476] (7.73, 9.12)	7.34 [N=473] (6.64, 8.05)	8.43 [N=476] (7.70, 9.16)	7.47 [N=473] (6.74, 8.21)	8.61 [N=476] (7.83, 9.39)	7.78 [N=473] (7.00, 8.57)
Change in FACIT-Fatigue score[g], mean (95% CI)[b]	8.0 [N=476] (7.2, 8.8)	6.5 [N=473] (5.7, 7.3)	7.7 [N=476] (6.9, 8.6)	6.8 [N=473] (5.9, 7.6)	7.4 [N=476] (6.5, 8.2)	6.4 [N=473] (5.5, 7.2)
Resolution of enthesitis, % (n/N)[a,d]	60.6 (180/297)	60.0 (174/290)	61.6 (183/297)	63.4 (184/290)	62.6 (186/297)	62.4 (181/290)
Resolution of dactylitis, % (n/N)[a,e]	79.2 (117/148)	73.5 (108/147)	76.6 (113/148)	77.3 (114/147)	77.5 (115/148)	74.8 (110/147)
Change from baseline PsA-mTSS,[b,h] mean (95%	0.20 [N=365] (0.05, 0.36)	0.35 [N=367] (0.19, 0.51)	0.41 [N=365] (0.09, 0.74)	0.67 [N=367] (0.34, 1.00)	0.55 [N=365] (0.12, 0.97)	0.94 [N=367] (0.52, 1.37)
PsA-mTSS ≤ 0,[i] % [n/N] (95% CI)	91.7 [333/363] (88.9, 94.6)	89.0 [323/363] (85.8, 92.2)	90.0 [325/361] (86.9, 93.1)	86.3 [315/365] (82.8, 89.8)	88.5 [322/364] (85.2, 91.7)	84.4 [308/365] (80.7, 88.1)
PsA-mTSS ≤ 0.5,[i] % [n/N] (95% CI)	94.2 [342/363] (91.8, 96.6)	91.7 [333/363] (88.9, 94.6)	92.2 [333/361] (89.5, 95.0)	89.0 [325/365] (85.8, 92.2)	91.2 [332/364] (88.3, 94.1)	86.6 [316/365] (83.1, 90.1)

All changes are least square mean changes from baseline.

[a]Results for binary endpoints are based on as-observed (AO) data with missing data imputed as non-responder imputation incorporating multiple imputation (NRI-MI) if there are missing data due to COVID-19 or geo-political conflict in Ukraine and Russia.

[b]Results for continuous endpoints are reported by mixed-effect model repeated measurement (MMRM). Number of unique patients contributing to MMRM model estimates: patients with at least one available change from baseline value and no missing data for the factors and covariates in the model. The MMRM N is not visit-specific and is displayed for model estimates for all visits.

[c]Reported for patients with ≥ 3% of body surface area (BSA) affected by psoriasis at baseline (RZB, n=273; PBO/RZB, n=272).

[d]Reported for patients with nail psoriasis at baseline.

[e]Defined as Leeds Enthesitis Index (LEI)=0 and reported among patients with LEI >0 at baseline (RZB, n=297; PBO/RZB, n=290).

[f]Defined as Leeds Dactylitis Index (LDI)=0 and reported among patients with LDI>0 at baseline (RZB, n=148; PBO/RZB, n=147).

[g]Results for PsA-mTSS were recorded from reading session 4 and reported as observed.

[h]For HAQ-DI, lower scores indicate lower difficulty.

[i]For NAPSI, lower scores indicate lower severity of nail psoriasis.

[j]For PGA-F, lower scores reflect lower severity of finger-nail psoriasis.

[k]For SF-36, higher scores reflect better health-related quality of life.

[l]For FACIT-Fatigue, higher scores reflect lower levels of fatigue.

ACR20/50/70, ≥20/50/70% improvement in American College of Rheumatology score; BSA, body surface area; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue Questionnaire; HAQ-DI, Health Assessment Questionnaire-Disability Index; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; LS, least square; MDA, minimal disease activity; PASI 90, ≥90% reduction in Psoriasis Area and Severity Index; PBO, placebo; PGA-F, Physician Global Assessment of Fingernail Psoriasis; PsA-mTSS, psoriatic arthritis modified Total Sharp Score; RZB, risankizumab; SF-36 PCS, 36-Item Short Form Health Survey Physical Component Summary.

PBO/RZB pts showed no radiographic progression (PSA-mTSS ≤0 from baseline). At week 148, HAQ-DI (RZB -0.41, PBO/RZB -0.35), SF-36 PCS (RZB 8.61, PBO/RZB 7.78) and FACIT-Fatigue (RZB 7.4, PBO/RZB 6.4) scores showed consistent increase from baseline. The overall rates of TEAEs, serious TEAEs and AEs leading to discontinuation of study drug have remained stable and comparable to those reported in period 1 (**Table 2**).

Conclusion: The 148-week results of the ongoing KEEPsAKE 1 trial demonstrate the durable efficacy of RZB 150 mg in treating the clinical manifestations and improving health-related quality of life in csDMARD-IR pts with PsA. RZB was well-tolerated, with no new safety signals.

Table 2. Safety Summary for KEEPsAKE 1 through Week 148

Parameter, (Events/100PYs)	RZB Week 24[a] N=483 PYs=224.1	PBO Week 24[a] N=481 PYs=223.5	RZB and PBO/RZB Week 148 N=946 PYs = 2412.2
Any TEAE	398 (177.6)	387 (173.2)	3005 (124.6)
Serious TEAE	15 (6.7)	22 (9.8)	185 (7.7)
TEAE leading to discontinuation of study drug	6 (2.7)	4 (1.8)	45 (1.9)
COVID-19 related TEAE	1 (0.4)	2 (0.9)	215 (8.9)
Any MACE	0	0	5 (0.2)
Cardiovascular death - sudden cardiac death	0	0	2 (<0.1)
Non-fatal myocardial infarction	0	0	2 (<0.1)
Non-fatal stroke	0	0	1 (<0.1)
Any serious infection	6 (2.7)	8 (3.6)	47 (1.9)
Any serious hypersensitivity	0	0	1 (<0.1)
Opportunistic infections excluding TB and herpes zoste	0	0	1 (<0.1)
Active TB	0	0	0
Herpes zoster	2 (0.9)	1 (0.4)	6 (0.2)
Malignant tumors	0	2 (0.9)	18 (0.7)
Including NMSC	0	0	3 (0.1)
Excluding NMSC	0	2 (0.9)	15 (0.6)
Any adjudicated anaphylactic reaction	0	0	0
All Deaths	1 (0.4)	0	9 (0.4)[b]

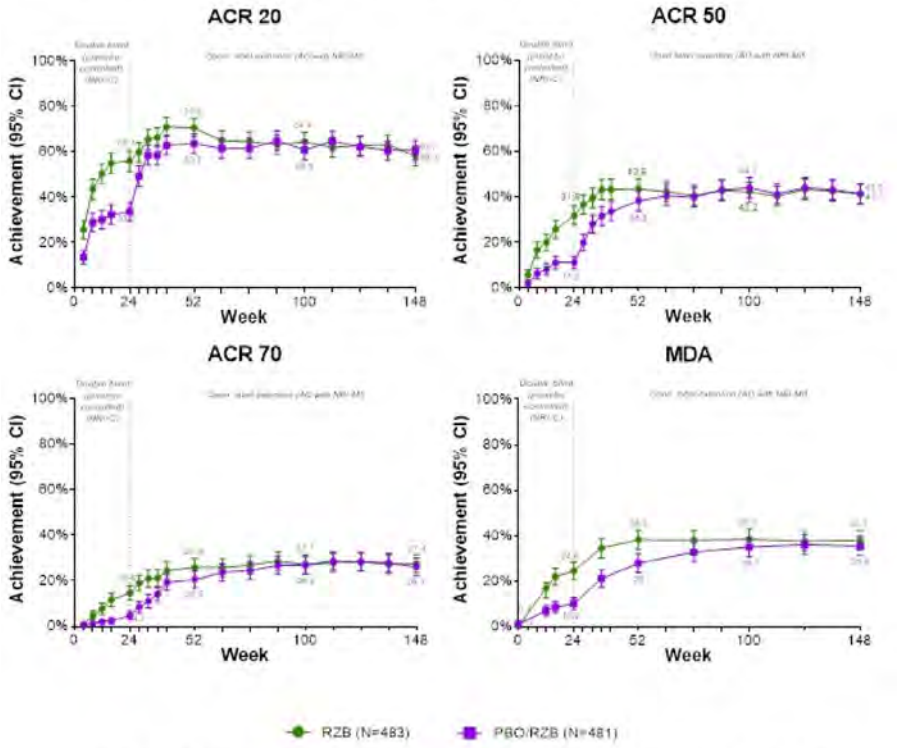
Treatment-emergent adverse events (TEAE) were defined as any AE with an onset date that was on or after the first dose of risankizumab and up to 140 days after the last dose of risankizumab if the patient discontinued the study drug prematurely.

[a]24 week data from KEEPsAKE 1 was previously published in Kristensen, et. al. Ann Rheum Dis. 2022;81(2):225-231.

[b]There were 8 patients reported with fatal TEAEs. 2 deaths were related to COVID 19; 1 was due to complications related to acute leukemia; 1 patient with anemia from diverticulosis died due to multiorgan failure from septicemia as a complication from anastomosis surgery (left hemicolectomy surgery); 1 patient, who was 81 years old with dementia, was hospitalized for pneumonia, developed urosepsis and died from related complications; 1 patient was hospitalized for anxiety and depression, developed septicemia, nausea, vomiting, fever and loss of appetite a week after discharge, and died from unknown causes a week later; 2 patients died of unknown causes (one had a 40 year history of smoking and died after COPD exacerbation). Additionally, 1 patient died on day 363 (166 days after last dose; non treatment emergent) from cardiorespiratory arrest.

MACE, major adverse cardiovascular events; NMSC, non-melanoma skin cancer; PBO, placebo; PYs, patient-years; RZB, risankizumab; TB, tuberculosis; TEAE, treatment-emergent adverse events.

Figure 1. Achievement of ACR 20, 50, 70 and MDA Over 148 Weeks in KEEPsAKE 1



DB, double-blind; NRI-C, non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19; AO with NRI-MI, as-observed (AO) data with missing data imputed as non-responder imputation incorporating multiple imputation (NRI-MI) if there are missing data due to COVID-19; PBO, placebo; RZB, risankizumab

Disclosure: L. Erik: AbbVie, 2, 5, 6, Amgen, 2, 6, Biogen, 2, 6, Bristol-Myers Squibb, 2, 6, Eli Lilly, 2, 5, 6, Gilead, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 5, 6; **M. Keiserman**: AbbVie/Abbott, 1, 2, 5, 6, Amgen, 1, 2, 5, 6, Bristol-Myers Squibb(BMS), 1, 2, 5, 6, Celgene, 1, 2, 5, 6, GlaxoSmithKlein(GSK), 1, 2, 5, 6, Janssen, 1, 2, 5, 6, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, 6, Roche, 1, 2, 5, 6, UCB, 1, 2, 5, 6; **K. Papp**: AbbVie, 1, 2, 5, 6, Akros, 1, 2, 5, 6, Amgen, 1, 2, 5, 6, Anacor, 1, 2, 5, 6, Arcutis, 1, 2, 5, 6, Astellas, 1, 2, 5, 6, Bausch Health/Valeant, 1, 2, 5, 6, Baxalta, 1, 2, 5, 6, Boehringer-Ingelheim, 1, 2, 5, 6, Bristol-Myers Squibb, 1, 2, 5, 6, Can-Fite Biopharma, 1, 2, 5, 6, Celgene, 1, 2, 5, 6, Coherus, 1, 2, 5, 6, Dermira, 1, 2, 5, 6, Dow Pharma, 1, 2, 5, 6, Eli Lilly, 1, 2, 5, 6, Evelo, 1, 2, 5, 6, Forward Pharma, 5, Galapagos, 1, 2, 5, 6, Galderma, 1, 2, 5, 6, Genentech, 1, 2, 5, 6, Gilead, 1, 2, 5, 6, GlaxoSmithKlein, 1, 2, 5, 6, Janssen, 1, 2, 5, 6, Kyowa-Hakko Kirin, 1, 2, 5, 6, LEO Pharma, 1, 2, 5, 6, MedImmune, 1, 2, 5, 6, Meiji Seika Pharma, 1, 2, 5, 6, Merck-Serono, 1, 2, 5, 6, Mitsubishi Pharma, 1, 2, 5, 6, Moberg Pharma, 1, 2, 5, 6, MSD, 1, 2, 5, 6, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, 6, PRCL Research, 1, 2, 5, 6, Regeneron, 1, 2, 5, 6, Roche, 1, 2, 5, 6, Sanofi-Aventis/Genzyme, 1, 2, 5, 6, Sun Pharma, 1, 2, 5, 6, Takeda, 1, 2, 5, 6, UCB, 1, 2, 5, 6; **L. McCasland**: Eli Lilly, 1; **D. White**: AbbVie, 2, 6, Novartis, 1, 2; **V. Stakias**: AbbVie, 3, 11; **T. Iyile**: AbbVie/Abbott, 3, 11; **K. Carter**: AbbVie/Abbott, 3, 11; **A. Soliman**: AbbVie/Abbott, 3, 10, 11; **L. Drogaris**: AbbVie/Abbott, 3, 11; **M. Chen**: AbbVie/Abbott, 3, 11; **B. Padilla**: AbbVie/Abbott, 3, 11; **F. Behrens**: AbbVie/Abbott, 2, 5, 6, Affibody, 2, Amgen, 2, 5, 6, Bionorica, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Chugai Pharma GmbH, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Genzyme, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Iron4u, 2, 5, 6, Leo, 2, 5, 6, Merck/MSD, 2, 5, 6, Moon-Lake, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sandoz, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 1436

Secukinumab Demonstrates a Consistent Safety Profile in Patients with Psoriasis, Psoriatic Arthritis and Axial Spondyloarthritis: Updated Pooled Safety Analysis from Clinical Trials

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Pooled safety data have been reported for secukinumab administration in patients with psoriasis (PsO), psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA).[1,2] The aim of this study is to describe the safety profile of secukinumab after extensive patient exposure in clinical trials. We report safety analysis from a larger pool of patients and more studies than previously published.[3]

Methods: The pooled safety analysis included 48 Phase II/III/IV clinical trials with patients who had received subcutaneous (s.c.) secukinumab 150 mg and / or 300 mg for at least 16 weeks in PsO (31 trials), PsA (9 trials), and axSpA (8 trials), with a cut-off date of June 2022. AxSpA includes data from patients with either radiographic axSpA or non-radiographic axSpA. Adverse events (AEs) were reported as exposure-adjusted incidence rates (EAIRs) per 100 patient-years. Analysis included all patients who received ≥1 dose of secukinumab.

Results: A total of 17,008 patients with PsO (10,150), PsA (4,401) and axSpA (2,457) were included in this analysis. The most frequent AEs reported across all indications were nasopharyngitis (EAIR [95% CI]; PsO, 19.44 [18.66, 20.24]; PsA, 11.36 [10.54, 12.23]; axSpA, 12.88 [11.73, 14.11]) and upper respiratory tract infection (EAIR [95% CI]; PsO, 6.14 [5.75, 6.56]; PsA, 8.1 [7.42, 8.82]; axSpA, 8.28 [7.41,9.22]). EAIRs per 100 patient-years for inflammatory bowel disease (IBD), malignancies and major adverse cardiovascular events (MACE) remained low across all indications. The EAIRs per 100 patient-years for adverse events (AEs) of special interest are reported in **Table 1**.

Conclusion: This pooled safety data analysis of 48 Phase II/III/IV clinical trials demonstrates that secukinumab is well tolerated in patients with PsO, PsA and axSpA, and shows no new signals with longer-term follow-up beyond those already identified in shorter studies.[1,2]

References

1. Deodhar et al. Arthritis Research & Therapy (2019) 21:111.
2. Deodhar et al. EULAR (2020). Eposter no. FRI0272.
3. Gottlieb et al. Acta Derm Venereol (2022) 102: adv00698.

Table 1. Summary of the pooled safety data analysis from Phase II/III/IV clinical trials of secukinumab

Variable	PsO	PsA	axSpA
	Any secukinumab N= 10,150	Any secukinumab N= 4,401	Any secukinumab N= 2,457
EAIR per 100 patient-years (95% CI)			
Any AE	145.22 (141.84, 148.65)	107.78 (103.83, 111.85)	105.07 (100.01, 110.31)
Any serious AE	5.84 (5.46, 6.25)	6.78 (6.18, 7.43)	4.78 (4.14, 5.48)
Most common AEs, EAIR (95% CI)			
Nasopharyngitis	19.44 (18.66, 20.24)	11.36 (10.54, 12.23)	12.88 (11.73, 14.11)
Upper respiratory tract infection	6.14 (5.75, 6.56)	8.1 (7.42, 8.82)	8.28 (7.41, 9.22)
Headache	6.55 (6.13, 6.98)	3.76 (3.32, 4.24)	4.50 (3.88, 5.20)
Arthralgia	5.24 (4.87, 5.62)	4.18 (3.71, 4.68)	3.64 (3.09, 4.27)
Diarrhoea	4.27 (3.95, 4.62)	4.21 (3.74, 4.72)	4.90 (4.25, 5.63)
AEs of special interest, EAIR (95% CI)			
Serious infections[1]	1.4 (1.22, 1.6)	1.65 (1.37, 1.98)	1.07 (0.78, 1.42)
Opportunistic infections	0.2 (0.13, 0.28)	0.16 (0.08, 0.28)	0.11 (0.04, 0.26)
Tuberculosis related events	0.03 (0.01, 0.07)	0.04 (0.01, 0.12)	0.07 (0.01, 0.2)
Candida infections[2]	0.31 (0.23, 0.41)	0.17 (0.09,0.3)	0.04 (0.01, 0.16)
IBD[3] IBD Crohn's disease Ulcerative colitis	0.01 (0.00, 0.05) 0.06 (0.03, 0.12) 0.12 (0.07, 0.19)	0.04 (0.01, 0.12) 0.08 (0.03, 0.18) 0.09 (0.04, 0.19)	0.02 (0.00, 0.13) 0.27 (0.14, 0.47) 0.27 (0.14, 0.47)
MACE[4]	0.3 (0.22, 0.4)	0.28 (0.17, 0.43)	0.29 (0.16, 0.5)
Uveitis[3]	0.02 (0.00, 0.07)	0.09 (0.04, 0.19)	1.35 (1.03, 1.74)
Malignancy[5]	0.72 (0.6,0.87)	1.04 (0.82, 1.3)	0.45 (0.27, 0.7)

[1]Rates for system organ class; [2]Rates for high level term; [3]Rates for preferred term; [4]Rates for Novartis MedDRA Query term; [5]Rates for standardized MedDRA query term – 'malignancies and unspecified tumour.' AE, adverse event; AxSpA, axial spondyloarthritis; CI, confidence interval; EAIR, exposure-adjusted incidence rate per 100 patient-years; IBD, inflammatory bowel disease; MACE, major adverse cardiovascular events; N, number of patients in the analysis; PsA, psoriatic arthritis; PsO, psoriasis.

Disclosure: A. Deodhar: AbbVie, 2, 5, Amgen, 2, Aurinia, 2, Bristol Myers Squibb, 2, 5, Celgene, 5, Eli Lilly, 2, 5, Janssen, 2, 6, MoonLake, 2, 5, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5; **I. McInnes**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Bristol Myers Squibb, 2, 5, Cabaletta, 2, 11, Causeway Therapeutics, 2, 11, Celgene, 2, 5, Compugen, 2, 11, Dextera, 11, Eli Lilly, 2, EveloBio, 1, 2, 4, 11, Gilead, 2, Janssen, 2, 5, Moonlake, 2, NHS GGC, 4, Novartis, 2, 5, Pfizer, 2, Sanofi, 2, UCB, 2, 5, Versus Arthritis, 12, Trustee Status; **X. Baraliakos**: AbbVie, 2, 6, BMS, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, 6, UCB, 2, 6; **A. Gottlieb**: Amgen, 1, 2, AnaptysBio, 1, 2, 5, Avotres Therapeutics, 1, 2, Boehringer Ingelheim, 1, 2, Bristol Myers Squibb, 1, 2, 5, Dice Therapeutics, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, MoonLake Immunotherapeutics, 5, Novartis, 1, 2, 5, Sanofi, 1, 2, UCB Pharma, 1, 2, 5, XBiotech, 1, 2; **U. Kiltz**: AbbVie, 2, 5, 6, Amgen, 5, Biocad, 2, 6, Biogen, 5, Bristol-Myers Squibb(BMS), 2, 5, Chugai, 2, 6, Eli Lilly, 2, 6, Fresenius, 5, Gilead, 2, 5, GlaxoSmithKline (GSK), 5, Grünenthal, 2, 6, Hexal, 5, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, onkowiessen.de, 2, 5, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Viatris, 2, 5; **S. Schreiber**: Abvie, 2, Arena, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, Celltrion, 2, Falk, 2, Fresenius, 2, Gilead, 2, IMAB, 2, Janssen, 2, Merck/MSD, 2, Mylan, 2, Pfizer, 2, Protagonist, 2, provention Bio, 2, Takeda, 2, Theravance, 2; **B. Gopal Sahoo**: Novartis, 3; **W. Bao**: Novartis, 3, 11; **H. Richards**: Novartis, 3, 11; **L. Pricop**: Novartis, 3, 11; **C. Gaillez**: Bristol-Myers Squibb(BMS), 11, Novartis, 3, 11; **V. Dong**: Novartis, 3; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2.

Abstract Number: 1437

Bimekizumab Maintained Efficacy Responses Through 52 Weeks in Biologic Disease-Modifying Antirheumatic Drug-Naïve Patients with Psoriatic Arthritis Who Were Responders at Week 16: Results from a Phase 3, Active-Reference Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

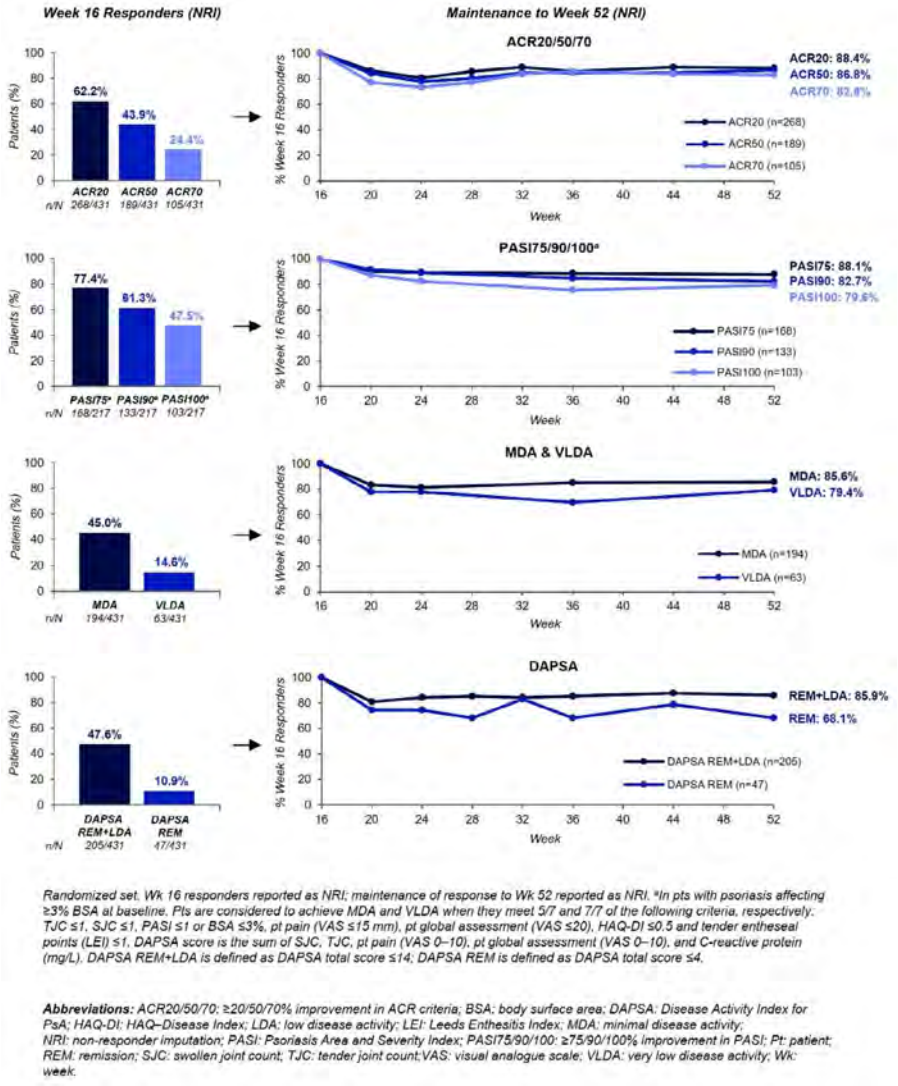
Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Given the chronic nature of PsA, sustaining high levels of disease control with treatment is important. Assessing maintenance of response in patients (pts) that achieve treatment targets is of interest as pts can experience loss of response with long-term therapy.[1] Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A, has demonstrated rapid, clinically meaningful joint and skin efficacy responses at Week (Wk) 16 versus placebo (PBO) in pts with PsA.[2,3] Responses were sustained to Wk 52.[4] We report maintenance of response in joint and skin efficacy outcomes to Wk 52 in BKZ-treated pts with PsA who responded at Wk 16.

Methods: BE OPTIMAL (NCT03895203), which included a 16-wk double-blind, PBO-controlled period and a 36-wk active treatment-blind period, assessed BKZ in patients with active PsA who were biologic DMARD (bDMARD)-naïve. Pts were randomized 3:2:1 to subcutaneous BKZ 160 mg every 4 wks (Q4W), PBO, or reference (adalimumab 40 mg Q2W). At Wk 16, PBO pts switched to BKZ 160 mg Q4W. Maintenance of response is reported as the percentage of BKZ-treated pts who achieved response at Wk 16 and maintained response at Wk 52. Data are reported for pts randomized to BKZ 160 mg Q4W at baseline (BL). Endpoints include ACR20/50/70, Psoriasis Area and Severity Index (PASI)75/90/100, minimal and very low disease activity (MDA, VLDA), and Disease Activity Index for PsA (DAPSA) remission or low disease activity (REM+LDA; ≤14) and remission (REM; ≤4) responses. Wk 16 responders are reported using non-responder imputation (NRI); maintenance of response to Wk 52 is reported using NRI and observed case (OC). Treatment-emergent adverse events (TEAEs) to Wk 52 are reported for pts who received ≥1 dose of BKZ, including pts randomized to PBO at BL.

Results: At BL, 431 pts were randomized to BKZ 160 mg Q4W; 217/431 (50.3%) had psoriasis affecting ≥3% of body surface area (BSA). 414/431 (96.1%) completed Wk 16; 388 (90.0%) completed Wk 52. Most pts who achieved response at Wk 16 maintained response at Wk 52, across a range of outcomes (**Figure**). At Wk 16, ACR20/50/70 was achieved by 268 (62.2%)/189 (43.9%)/105 (24.4%) pts; responses were maintained at Wk 52 by 88.4%/86.8%/82.9% (NRI); 92.9%/91.1%/87.9% (OC). Of 217 pts with psoriasis affecting ≥3% of BSA at BL, 133 (61.3%)/103 (47.5%) achieved PASI90/100 at Wk 16. Most pts maintained response at Wk 52: 82.7%, 79.6% (NRI); 94.0%, 89.1% (OC). The same pattern was observed for the composite measures of efficacy. 194 (45.0%) pts achieved MDA at Wk 16; 85.6% (NRI) and 90.7% (OC) maintained response at Wk 52. A high proportion of Wk 16 responders maintained their response at Wk 52 for VLDA,



Randomized set. Wk 16 responders reported as NRI; maintenance of response to Wk 52 reported as NRI. ªIn pts with psoriasis affecting ≥3% BSA at baseline. Pts are considered to achieve MDA and VLDA when they meet 5/7 and 7/7 of the following criteria, respectively: TJC ≤1, SJC ≤1, PASI ≤1 or BSA ≤3%, pt pain (VAS ≤15 mm), pt global assessment (VAS ≤20), HAQ-DI ≤0.5 and tender entheseal points (LEI) ≤1, DAPSA score is the sum of SJC, TJC, pt pain (VAS 0–10), pt global assessment (VAS 0–10), and C-reactive protein (mg/L). DAPSA REM+LDA is defined as DAPSA total score ≤14; DAPSA REM is defined as DAPSA total score ≤4.

***Abbreviations:** ACR20/50/70: ≥20/50/70% improvement in ACR criteria; BSA: body surface area; DAPSA: Disease Activity Index for PsA; HAQ-DI: HAQ–Disease Index; LDA: low disease activity; LEI: Leeds Enthesitis Index; MDA: minimal disease activity; NRI: non-responder imputation; PASI: Psoriasis Area and Severity Index; PASI75/90/100: ≥75/90/100% improvement in PASI; Pt: patient; REM: remission; SJC: swollen joint count; TJC: tender joint count;VAS: visual analogue scale; VLDA: very low disease activity; Wk: week.*

Figure. Maintenance efficacy responses to Week 52 in Week 16 responders (NRI)

DAPSA REM+LDA, and DAPSA REM (**Figure**). To Wk 52, 555/702 (79.1%) BKZ-treated pts reported ≥1 TEAE; 46 (6.6%) reported serious TEAEs.

Conclusion: With BKZ treatment, Wk 16 responders maintained robust efficacy responses to Wk 52 across joint, skin, and composite efficacy outcomes. The safety profile of BKZ was consistent with previous reports.[2,3]

References:1. Boehncke WH. Am J Clin Dermatol 2013;14:377–88; **2.** McInnes IB. Lancet 2022; 401(10370):25-37; **3.** Merola JF. Lancet 2022; 401(10370):38-48; **4.** Ritchlin C. Arthritis Rheumatol 2022;74(suppl 9).

Disclosure: W. Tillett: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, GSK, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Ovo Pharma, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma, 2, 5, 6; **J. Merola**: Abbvie, 2, 12, Investigator, Amgen, 2, 12, Investigator, Biogen, 2, 12, Investigator, Bristol-Myers Squibb, 2, 12, Investigator, Dermavant, 2, 12, Investigator, Eli Lilly, 2, 6, 12, Investigator, Janssen, 2, 12, Investigator, Leo Pharma, 2, 12, Investigator, Novartis, 2, 12, Investigator, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, 12, Investigator, Sun Pharma, 2, 12, Investigator, UCB Pharma, 2, 12, Investigator; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS,

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Abstract Number: 1438

Efficacy of Guselkumab in Early-Onset and Late-Onset Psoriatic Arthritis: Post Hoc Pooled Analyses of Two Phase 3 Randomized Controlled Trials in Patients with Active PsA

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Late-onset PsA may be associated with elevated acute phase reactants, higher joint count, and erosive disease at diagnosis[1,2]. Given potential phenotype differences and increasing prevalence with aging populations, it is important to establish the efficacy of current treatments in late-onset PsA. Previous analyses of DISCOVER-1&2 (D1&2) have shown the fully human IL-23p19-subunit inhibitor guselkumab (GUS) to be associated with robust and sustained improvement in PsA signs/symptoms over 52 weeks (W) in subgroups of patients (pts) across a variety of baseline (BL) characteristics[3]. These post hoc analyses contrasted early- vs. late-onset PsA pts and evaluated GUS efficacy through W52 in both cohorts.

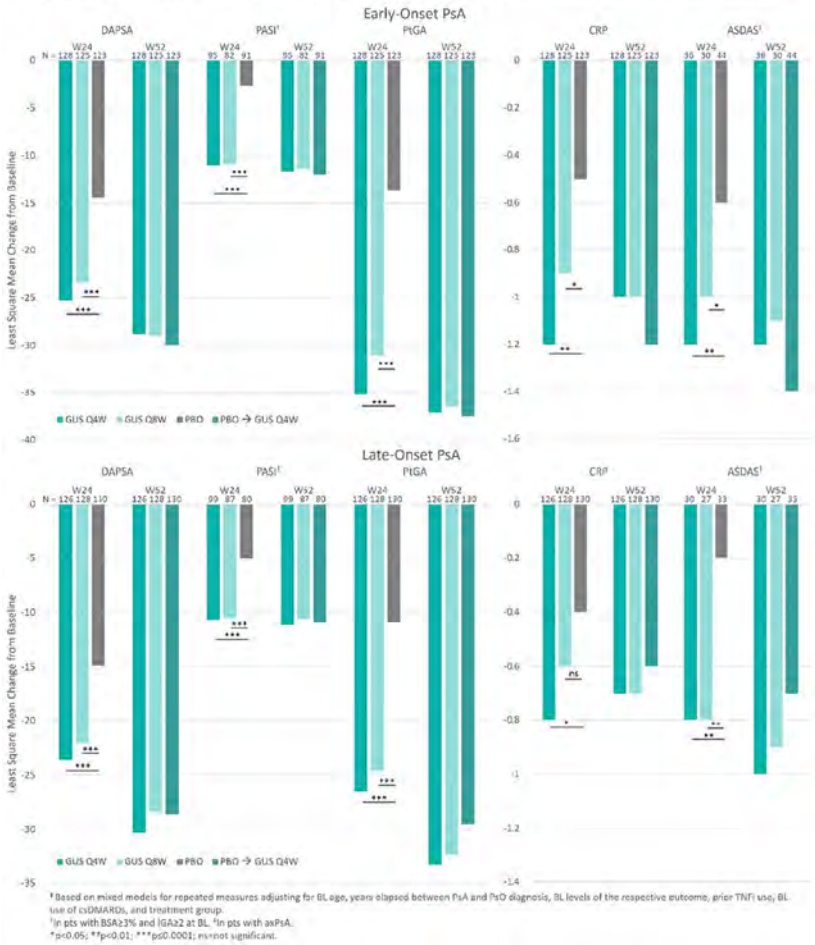
Methods: Adults in D1&2 (90% bionaive) with active PsA despite standard therapies were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, Q8W; or placebo (PBO) with crossover to GUS 100 mg Q4W at W24. The tertile (T) distribution of age at PsA diagnosis in the pooled D1&D2 population informed the definition of early- (T1 < 36y) and late- (T3 ≥47y) onset. W24/52 efficacy assessments included least-square mean changes in Disease Activity Index for PsA (DAPSA), swollen/tender joint counts (SJC/TJC), Psoriasis Area Severity Index (PASI; in pts with BSA≥3% and IGA≥2 at BL), CRP, pt-reported pain (Pt-Pain), pt global assessment of arthritis and psoriasis (PtGA), Short Form 36-item

Table. Baseline Characteristics of Patients with Early-Onset vs. Late-Onset PsA

	Early-Onset PsA (N=376)	Late-Onset PsA (N=384)	Nominal P-value
Age at study BL (years)	35.5 (8.9)	58.1 (6.1)	**<0.001**
Male sex, n (%)	198 (52.7)	181 (47.1)	0.128
Body mass index (kg/m²)	27.4 (6.4)	30.3 (5.3)	**<0.001**
PsA disease duration (years), median (IQR)	5.1 (2.0-11.0)	3.0 (1.2-6.4)	**<0.001**
Years between PsO and PsA diagnosis, median (IQR)	4.0 (0.2-10.3)	8.2 (1.2-22.9)	**<0.001**
DAPSA	46.1 (20.2)	45.4 (20.5)	0.629
SJC (0-66)	11.2 (7.5)	11.1 (6.8)	0.991
TJC (0-68)	20.0 (12.6)	20.5 (13.7)	0.630
% BSA affected by PsO	17.0 (20.4)	14.9 (18.1)	0.145
PASI score (0-72)	9.9 (11.1)	8.6 (9.1)	0.092
CRP (mg/dL)	2.2 (2.6)	1.5 (2.0)	**<0.001**
Pain (VAS, 0-100 mm)	62.4 (19.7)	59.9 (20.8)	0.089
PtGA (VAS, 0-10)	67.7 (19.5)	64.5 (20.9)	**0.032**
Presence of enthesitis, n (%)	247 (65.7)	244 (63.5)	0.600
LEI score (1-6)	2.8 (1.6)	2.9 (1.7)	0.336
Presence of Dactylitis, n (%)	175 (46.5)	135 (35.2)	**0.002**
Dactylitis severity score (1-60)	8.8 (10.8)	8.4 (8.7)	0.772
Axial involvement (axPsA), n (%)	110 (29.3)	90 (23.4)	0.069
BASDAI (0-10) in pts with axPsA	6.7 (1.7)	6.2 (1.7)	**0.031**
ASDAS in pts with axPsA	3.1 (0.7)	2.7 (0.7)	**<0.001**
SF36-PCS (US norm=50; lower=more impairment)	33.3 (8.1)	33.8 (7.5)	0.409

Data are presented as mean (SD) unless stated otherwise.
BSA: body surface area; IQR: interquartile range; LEI: Leeds enthesitis index; PsO: psoriasis.

Figure 1. Least Square Mean Changes[‡] in Key Outcomes Through W52 in Patients with Early-Onset and Late-Onset PsA



[‡] Based on mixed models for repeated measures adjusting for BL age, years elapsed between PsA and PsO diagnosis, BL levels of the respective outcome, prior TNFi use, BL use of csDMARDs, and treatment group.
[†] In pts with BSA≥3% and IGA≥2 at BL. [§] In pts with axPsA.
* p<0.05; ** p<0.01; *** p<0.001; ns=not significant.

Figure 2. Achievement (Using NRI) of ACR Responses and MDA Through W52 in Patients with Early-Onset and Late-Onset PsA

†Odds ratios with corresponding 95% confidence intervals and p-values based on logistic regression adjusting for BL age, years elapsed between PsA and PsO diagnosis, BL levels of the respective outcome, prior TNFi use, BL use of csDMARDs, and treatment group.
*p<0.05; **p<0.01; ***p≤0.0001.

physical component summary score (SF-36 PCS), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI; in pts with axial involvement [axPsA]), and Ankylosing Spondylitis Disease Activity Score (ASDAS; in pts with axPsA), as well as ACR and Minimal Disease Activity (MDA) response rates (employing non-responder imputation [NRI] for missing data).

Results: Relative to pts with late-onset (n=384), those with early-onset (n=376) PsA were significantly younger at BL but had longer PsA duration and a shorter interval between psoriasis and PsA diagnoses **(Table 1)**. The two cohorts had generally comparable joint and skin disease severity at BL, although those with early-onset PsA were more likely to have axPsA and dactylitis, and exhibited higher CRP levels, PtGA, BASDAI and ASDAS.

Irrespective of PsA onset age, GUS Q4W or Q8W was associated with significantly (nominal p< 0.001) greater improvements in DAPSA, PASI, PtGA, CRP, ASDAS **(Figure 1)**, SJC, TJC, Pt-Pain, BASDAI, and SF-36 PCS (data not shown), and higher ACR20/50/70 and MDA response rates vs. PBO at W24 **(Figure 2)**. Further improvements/increased response rates were generally seen through W52 of GUS across early- and late-onset subgroups **(Figure 1, 2)**.

Conclusion: Results of post hoc analyses, conducted in a large cohort of mainly bio-naïve pts with active PsA from D1&2, suggest early-onset PsA may be associated with more aggressive presentation several years post-diagnosis. Irrespective of age of PsA onset and differences in baseline profile, however, GUS was associated with significant and clinically meaningful improvements across key PsA domains, with further enhancements generally seen through W52.

References:

1. Fragoulis GE. *J Rheumatol* 2022;49:1085
2. Polachek A. *Semin Arthritis Rheum* 2019;48:834
3. Ritchlin CT. *RMD Open* 2022;8:e002195

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Abstract Number: 1439

Better Drug Retention on anti-IL17A Compared to Anti-TNF Therapy Despite Its Inferior Effect on Composite Joint Indexes and Quality of Life in Patients with PsA–analysis from the Czech Biologics Registry ATTRA

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II: SpA
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: To compare drug survival, effectiveness and safety of anti-IL17A with anti-TNF drugs as first line biologic therapy in patients (pts) with PsA using real life data from the Czech biologics registry ATTRA. ATTRA is a prospective observational cohort study that captures more than 90% of PSA patients treated with b/tsDMARDs in the Czech Republic (CZ). Anti-IL17A bDMARDs have been reimbursed in CZ since Jan 2016 with the same label and restrictions as anti-TNFs.

Methods: PsA pts who initiated their first bDMARD in Jan 2016–Mar 2022 with at least one year of follow-up were included. By the type of first bDMARD exposure patients were dichotomized to anti-IL17A and anti-TNF cohorts. Effectiveness was assessed every 3-6 months by DAS28-ESR and DAPSA, physician global assessment of psoriasis (PGApso) on numerical rating scale (1-5), and by EQ-5D utility. Incidence of reported AEs and SAEs per 1000 patient-years (p-yrs) was calculated. Propensity score (PS) matching was used to account for differences in baseline characteristics. Drug survival was visualized using Kaplan-Meier curves, and Cox proportional hazards models were used to calculate adjusted Hazard Ratios (HRs) with 95% confidence intervals (CIs) for risk of discontinuing therapy.

Table 1. Baseline characteristics after PS matching

Characteristics	anti-IL17A (n=177)		anti-TNF (n=577)	p-value
Female	85 (48.0%)		289 (50.1%)	0.631
Age at diagnosis, yrs	41.0 (33.0–52.0)		43.0 (34.0–51.0)	0.377
Age at start of 1st line, yrs	49.0 (42.0–57.0)		51.0 (42.0–58.0)	0.697
BMI	28.7 (25.3–33.1)		28.3 (25.3–32.5)	0.741
Tender joint count (66 joints)	12.0 (8.0–20.0)		12.0 (7.0–19.0)	0.439
Swollen joint count (68 joints)	7.0 (3.0–12.0)		8.0 (4.0–12.0)	0.329
ESR (mm/h)	24.0 (11.0–38.0)		26.0 (12.0–40.0)	0.206
CRP (mg/dl)	9.5 (3.9–19.0)		12.0 (5.1–22.0)	0.052
Patient global assessment of disease activity (VAS: 0–100)	70.0 (60.0–80.0)		75.0 (58.0–85.0)	0.671
Physician global assessment of disease activity (0–100)	70.0 (52.0–80.0)		67.0 (50.0–80.0)	0.285
Physician global assessment of psoriasis (scale 0–5: no psoriasis – very severe)	0–1	39 (22.0%)	146 (25.3%)	0.458
	2–3	116 (65.5%)	348 (60.3%)	
	4–5	22 (12.4%)	83 (14.4%)	
Patient assessment of pain (VAS: 0–100)	70.0 (50.0–80.0)		70.0 (55.0–80.0)	0.482
HAQ	1.3 (1.0–1.8)		1.3 (0.9–1.8)	0.668
Nail involvement	No	68 (39.8%)	232 (40.8%)	0.920
	Mild	43 (25.1%)	146 (25.7%)	
	Medium	50 (29.2%)	164 (28.9%)	
	Severe	10 (5.8%)	26 (4.6%)	
Enthesitis	23 (13.0%)		67 (11.6%)	0.620
DAS28-ESR	5.3 (4.6–5.9)		5.4 (4.5–6.1)	0.380
DAPSA	35.0 (26.8–47.6)		36.0 (27.3–45.4)	0.900
Data are median (IQR) or n (percentage).				

Results: 994 PsA pts started first-line anti-IL-17A (n=192) or anti-TNF (n= 802) therapy within period Jan 2016–Mar 2022, and 178 and 719 resp. had non-missing values for the outcomes of interest. Important baseline characteristics were similar between anti-IL17A and anti-TNF cohorts save for swollen joint counts (SJC), and after PS matching (using logistic model with 1 covariate: 68 SJC, matching ratio 1:4, caliper 0.1) 177 pts on anti-IL17A and 577 on anti-TNF were PS-matched and further analyzed. Baseline characteristics of PS-matched cohorts are in table 1. Drug retention on anti-IL7A was significantly better than on anti-TNF drugs with HR (95% CI) 0.57 (0.41; 0.78), see fig. 1. More pts on anti-IL7A discontinued therapy because of primary failure (31% vs 16%), but less of them because of adverse events (9% vs 17%) or other unspecified reasons (13% vs 21%). In pts remaining on first line therapy, mean levels of DAS28-ESR and DAPSA were significantly lower and of utility EQ-5D significantly higher at each time point since month(M)3 until M18 after start of anti-TNF compared with anti-IL-17A therapy (Fig. 2). Skin involvement assessed by PGApso was significantly better in anti-IL17A treated pts at M3 and M12. Incidence of AEs and SAEs was lower in anti-17A than in anti-TNF treated group (93 vs 168/1000 p-yrs, $p< 0.001$; and 7 vs 18 /1000 p-yrs, $p=0.079$, resp.).

Conclusion: We have observed better drug retention on anti-IL17A compared to anti-TNF therapy despite its inferior effect on composite joint indexes and quality of life in pts with PsA. This discrepancy may be explained either by superior safety, tolerability, and effectiveness of anti-IL17A on skin involvement, limited possibility to switch between anti-L17A drugs, or lower confidence of physicians to switch from anti-IL17A to anti-TNF than vice versa.

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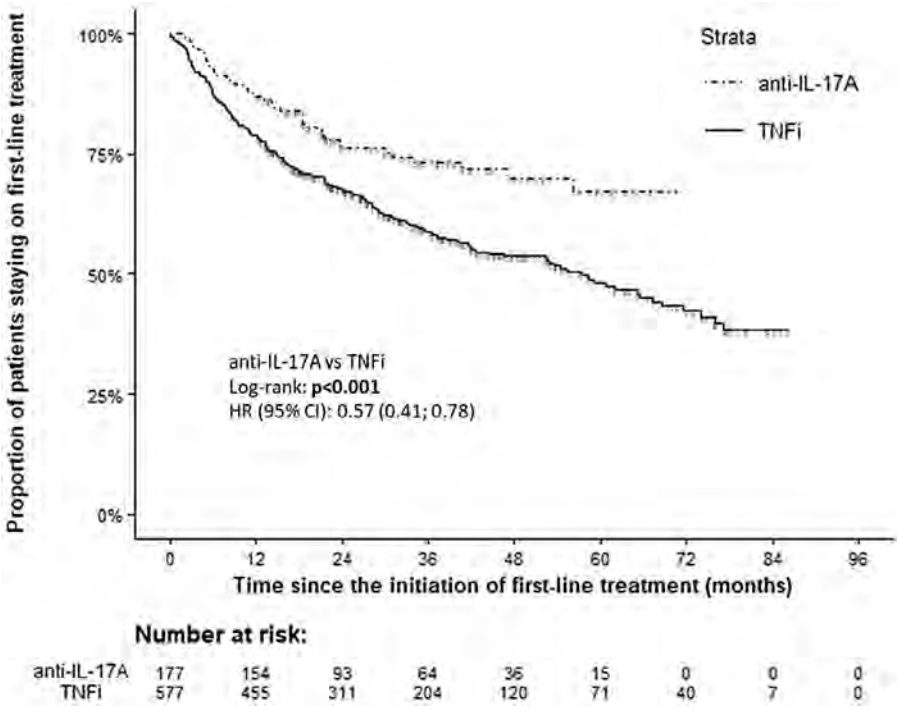

Figure 1. Kaplan-Meier curves of drug survival on first-line treatment – anti-IL-17A vs TNFi

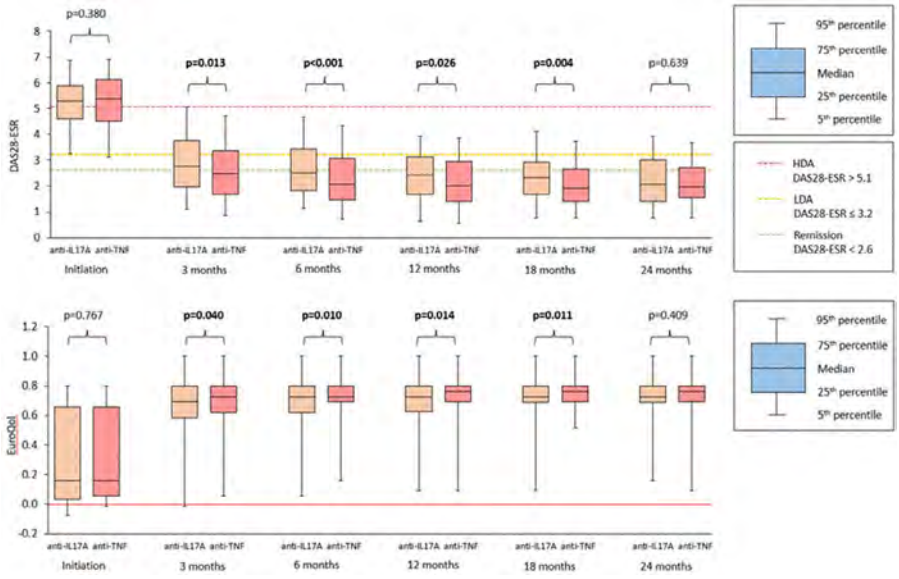

Figure 2. Effectiveness of anti-IL17A and anti-TNF drugs over time in patients remaining on the initial first-line bDMARDs on joint involvement assessed by DAS28-ESR or EuroQol utility.

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Abstract Number: 1440

Removal of Methotrexate in Patients with Active Psoriatic Arthritis with Newly Induced Ustekinumab Treatment Leads to a Delayed Response in DAPSA and DAS28 Within the First 16 Weeks

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Methotrexate (MTX) is often used as first-line DMARD therapy in active psoriatic arthritis (PsA). The value of MTX in combination with different bDMARDs is still unclear. We designed an investigator-initiated, randomized, placebo-controlled trial (IIT) in active PsA to examine if outcomes of treatment with ustekinumab (UST) in combination with MTX (either newly initiated or ongoing) were different from UST only (+Placebo; PBO). It was allowed to include patients with stable MTX treatment. Here, we analyze the data stratified to MTX pretreatment, focusing on early treatment response within the first 16 weeks.

Methods: A total of 186 patients with active PsA (defined as TJC≥4, SJC≥4 [68/66 joint count], and DAS28≥3.2) were screened for eligibility. 173 patients were randomized to UST+MTX (new or ongoing) or UST+PBO. Patients were stratified regarding their previous MTX therapy (blinded continuation of MTX or replacement of MTX with PBO [MTX-pre-treated] or blinded newly initiated MTX or PBO [MTX-naïve]). Demographic data and disease activity status on peripheral arthritis (response rates for LDA and remission for DAS28-CRP, DAPSA) were compared between treatment groups regarding MTX pretreatment. Early response behavior was investigated by identification of DAS28-CRP and DAPSA low disease activity (LDA) and remission rates at weeks 4, 16, and 24.

Figure 1: LDA and Remission rates for DAS28-CRP and DAPSA response at weeks 4, 16, and 24 in the cohort of PsA patients with MTX pretreatment and either discontinuation at the start of UST treatment or continuation of both MTX and UST

Results: BL data were well-balanced between treatment groups (UST+MTX, n=87; UST+PBO, n=79), including gender (42.5% vs. 40.5% female) and mean values for age (49.2 vs. 47.2 years), BMI (29.4 vs. 28.9 kg/m^2), SJC (8 vs. 8), TJC (12 v.s 12), DAS28-CRP (4.6 v.s 4.4), DAPSA (36.7 v.s 34.9), PASI (2.8 .vs 2.4), enthesitis (LEI >0: 50.57% .vs 50.63%), and other domains. BL differences were seen in dactylitis (24.1% .vs 19.0%), BSA (2.9%. vs. 1.0%), and DLQI (8.6. vs 6.9). The patient cohort stratified according to MTX pretreatment was taken out (n=80) for analysis. The proportion of patients who reached LDA and remission rates in DAS28-CRP was slightly lower in the group who discontinued MTX treatment at the study start compared to those who continued MTX (DAS28-CRP 21.62% vs. 25.59%, respectively). This was more prominent in analyzing the achievement of LDA/remission rates in DAPSA at week 4 (10.81% for those discontinuing MTX vs. 25.59 % for those who continued MTX (Figure 1)). At weeks 16 and 24, both treatment groups reached the same levels for LDA/remission rates in DAS28-CRP and DAPSA.

Conclusion: We have previously shown that MTX+UST vs. UST+PBO is non-inferior for efficacy assessments in active PsA. Here we present the data from the analysis focusing on early response behavior to answer whether the overlapping treatment with MTX is of clinical value after the decision to initiate a biological therapy with ustekinumab is made. With a focus on DAS28-CRP and DAPSA response rates (LDA+remission), we can show that an overlapping treatment by the continuation of MTX within the first 12-16 weeks is of clinical value to increase response rates in the early treatment phase of UST treatment. MTX can be stopped at week 12 when UST efficacy increases, independent of MTX use.

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Abstract Number: 1441

Bimekizumab Maintenance of Response and Safety in Patients with Moderate to Severe Plaque Psoriasis: Results from the Open-label Extension Period (Weeks 48–144) of the BE RADIANT Phase 3b Trial

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SESSION INFORMATION

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Background/Purpose: Clinical improvements through Week (Wk)96, with no unexpected safety findings, have previously been reported with bimekizumab (BKZ) in the BE RADIANT phase 3b trial in patients with moderate to severe plaque psoriasis.[1,2] Here, we evaluate the efficacy of BKZ, as measured by complete or near complete skin clearance using the Psoriasis Area and Severity Index (PASI), over 144 weeks, and assess long-term safety of BKZ treatment.

Methods: Patients with moderate to severe plaque psoriasis received BKZ (320mg every 4 wks [Q4W] through Wk16, then Q4W or Q8W) or secukinumab (SEC; 300mg weekly to Wk4, then Q4W) through Wk48, then BKZ (Q4W or Q8W; all received Q8W from Wk64/next scheduled visit). Wks48–144 (open-label extension [OLE]) overlapped with the COVID-19 pandemic. Wk48–144 efficacy data are reported for patients treated with BKZ or SEC to Wk48 who entered the OLE, receiving BKZ Q4W or Q8W. Patients discontinuing due to lack of efficacy/treatment-related adverse events (AEs) were considered non-responders; multiple imputation was used for other missing data (modified non-responder imputation [mNRI]). Wk48–144 safety data (incidence/100 patient-years [PY]) are grouped for patients receiving ≥1 BKZ dose in this period.

Results: 336/373 BKZ-randomized and 318/370 SEC-randomized patients entered the OLE. Among these, 74.9% BKZ vs 52.8% SEC (Wk48) and 68.8% BKZ/BKZ vs 69.1% SEC/BKZ (Wk144) achieved PASI100 (100% improvement from baseline in PASI); 94.3% vs 83.9% (Wk48) and 89.8% vs 87.0% (Wk144) achieved PASI≤2. Wk48–144 serious AE rate with BKZ was low (5.4/100PY).Four deaths (two from coronavirus infection [unvaccinated patients]) occurred; none treatment-related. The most common AEs were: nasopharyngitis (8.4/100PY); oral candidiasis (7.1/100PY); coronavirus infection (5.1/100PY). Most (98.3%) oral candidiasis events were mild/moderate; three led to discontinuation.

Conclusion: Clinical improvements with BKZ were maintained through Wk144; outcomes improved for SEC-treated patients after switching to BKZ (Wk48–144). AEs were consistent with BKZ's safety profile.[1–3]

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385(2):142–52, NCT03536884; **3.**Gordon KB et al. JAMA Dermatol 2022;158(7):735–44.

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12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, Celgene, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, Eli Lilly, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, Gebro, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, Janssen, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, JS BIOCAD, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, LEO Pharma, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, Merck-Serono, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, MSD, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, Mylan, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, Novartis, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, Pfizer, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, Regeneron, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, Roche, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, Samsung-Bioepis, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, Sandoz, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, Sanofi-Genzyme, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:, UCB Pharma, 12, Received consultancy/speaker's honoraria from and/or participated in trials sponsored by:; **A. Blauvelt**: AbbVie/Abbott, 5, 6, Abcentra, 6, Acelyrin, 12, Clinical study investigator, Aclaris, 6, Affibody, 6, Aligos, 6, Allakos, 12, Clinical study investigator, Almirall, 6, Alumis, 6, Amgen, 5, 6, Anaptysbio, 6, Apogee, 6, Arcutis, 5, 6, Arena, 6, Aslan, 6, Athenex, 5, 6, 12, Clinical study investigator, Bluefin, 6, Boehringer-Ingelheim, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Cara Therapeutics, 6, Concert, 12, Clinical study investigator, CTI Biopharma, 6, Dermavant, 5, 6, EcoR1, 6, Eli Lilly, 5, 6, Escient, 6, Evelo, 6, Evommune, 6, Forte, 6, Galderma, 5, 6, HighlightII Pharma, 6, Incyte, 5, 6, InnoventBio, 6, Janssen, 5, 6, Landos, 6, Leo, 5, 6, Merck/MSD, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Rani, 6, Rapt, 6, Regeneron, 5, 6, Sanofi Genzyme, 6, Spherix Global Insights, 6, Sun Pharma, 5, 6, TLL Pharmaceutical, 6, TrialSpark, 6, UCB, 5, 5, 6, 6, Union, 6, Ventyx, 6, Vibliome, 6, Xencor, 6; **D. 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Wang**: UCB Pharma, 3, 11; **V. Vanvoorden**: UCB Pharma, 3, 11; **D. Deherder**: UCB Pharma, 3, 11; **f. Staelens**: UCB Pharma, 3, 11; **S. Wiegratz**: UCB Pharma, 3, 11; **J. Merola**: AbbVie, 12, Consultant and/or investigator, Amgen, 2, Biogen, 12, Consultant and/or investigator, Bristol Myers Squibb, 2, Dermavant, 12, Consultant and/or investigator, Eli Lilly, 12, Consultant and/or investigator, Janssen, 12, Consultant and/or investigator, LEO Pharma,

12, Consultant and/or investigator, Novartis, 12, Consultant and/or investigator, Pfizer, 12, Consultant and/or investigator, Regeneron, 12, Consultant and/or investigator, Sanofi, 12, Consultant and/or investigator, Sun Pharmaceuticals, 12, Consultant and/or investigator, UCB Pharma, 12, Consultant and/or investigator; **C. Paul**: AbbVie, 2, 5, Almirall, 2, 5, Amgen, 2, 5, Boehringer-Ingelheim, 2, 5, Celgene, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Leo Pharma, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Pierre Fabre, 2, 5, Sanofi Regeneron, 2, 5, UCB, 2, 5.

Abstract Number: 1442

Incident Vascular Events in Danish Nationwide Cohort of Patients with Newly Diagnosed Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Awareness of comorbidity in patients with SLE is increasing. Most studies to date have described comorbidity burden in prevalent SLE. We estimated the incidence of vascular events, - by age and sex, - in a large inception cohort of patients with SLE compared with matched general population controls.

Methods: We assembled a cohort of adult patients registered with a first-time diagnosis of SLE (ICD codes) from January 1996 to July 2018 in the Danish National Patient Register (DNPR). SLE patients were age, - and sex-matched to population controls randomly selected from the Danish Civil Registration System. We used ICD codes from the DNPR to determine the presence of cardiovascular disease (Myocardial Infarction (MI)), cerebrovascular disease (CVD), and peripheral vascular disease (PVD) during outpatient and inpatient care. Individuals with prevalent MI, CVD, and PVD at baseline (SLE diagnosis) were excluded from the analyses of incident events. We estimated incidence rates (IRs), incidence rate ratios (IRRs), and incidence rate differences (IRDs) per 1,000 person-years of MI, CVD, and PVD by sex and age (< 50 years vs ≥ 50 years at baseline) during up to 10 years of follow-up. Analyses were done separately for each disease category, e.g., individuals with incident MI were retained for analyses of CVD and PVD. IRRs and IRDs were adjusted for age and sex using Poisson regression and presented with 95% CIs.

Results: We identified 3,178 patients with incident SLE and 60,090 age- and sex-matched general population comparators. 84% of SLE patients and non-SLE controls were female; the mean age at baseline was 47 years. At baseline, the prevalence of MI (2.9% vs 1.40%), CVD (7.0% vs 2.7%), and PVD (5.5% vs 1.4%) was higher in SLE patients compared with the general population controls.

During follow-up, patients with SLE had substantially increased IRs of the above vascular events, with IRRs ranging from 1.7 to 7.6 across sex and age groups (Table 1). Although the absolute rates (IRs) were higher in SLE patients vs controls in the older age group, the IRRs were consistently higher for those aged < 50 at baseline, both females and males. In this age group, female SLE patients had a 5-fold increased risk of CVD and PVD and a 3-fold increased risk of MI. Male SLE patients had an 8-fold increased risk of PVD and a 6-fold increased risk of CVD and MI.

Table 1. Measures of occurrence and association (per 1,000 person-years, with 95% CI) of incident vascular events in patients with incident SLE (n=3,178) compared with matched population controls (n=60,090) during up to 10 years of follow-up after SLE diagnosis, stratified by sex and age group

	IR, SLE	IR, non-SLE	IRR	IRD
Myocardial infarction				
N of eligible persons	N=3086		N=59238	
Females <50	1.0 (0.6-1.7)	0.3 (0.2-0.4)	3.4 (1.8-6.2)	0.7 (0.1-1.3)
≥50 years	4.5 (3.1-6.4)	2.6 (2.3-2.9)	1.7 (1.2-2.5)	1.9 (0.3-3.6)
Males <50	5.8 (2.6-11.3)	1.0 (0.7-1.4)	5.8 (2.5-13.3)	4.8 (0.5-9.1)
≥50 years	13.5 (8.7-20.3)	5.7 (5.0-6.6)	2.4 (1.5-3.7)	7.8 (2.0-13.7)
Cerebrovascular disease				
N of eligible persons	N=2949		N=58459	
Females <50	6.1 (4.7-7.7)	1.2 (1.1-1.3)	5.1 (3.9-6.7)	4.9 (3.4-6.3)
≥50 years	15.5 (12.5-18.9)	7.6 (7.1-8.1)	2.0 (1.6-2.5)	7.9 (4.6-11.1)
Males <50	9.6 (5.1-16.6)	1.7 (1.2-2.2)	5.6 (3.0-11.1)	7.9 (2.2-13.6)
≥50 years	18.2 (12.2-26.2)	12.6 (11.4-13.8)	1.4 (1.0-2.1)	5.6 (1.5-12.7)
Peripheral vascular disease				
N of eligible persons	N=2989		N=59233	
Females <50	2.8 (2.0-4.0)	0.5 (0.5-0.6)	5.2 (3.5-7.6)	2.3 (1.3-3.3)
≥50 years	8.7 (6.6-11.3)	3.4 (3.1-3.8)	2.5 (1.9-3.4)	5.3 (2.9-7.6)
Males <50	5.8 (2.6-11.4)	0.8 (0.5-1.2)	7.6 (3.2-17.9)	5.1 (0.7-9.4)
≥50 years	18.0 (12.2-25.8)	6.6 (5.8-7.4)	2.7 (1.8-4.1)	11.4 (4.6-18.3)

CI: confidence interval; SLE: systemic lupus erythematosus; IR: incidence rate; IRR: incidence rate ratio; IRD: incidence rate difference.

The IRDs ranged from 0.7 (MI in females aged < 50) and 11.4 (PVD in males aged ≥ 50) (Table 1). Interestingly, IRDs were higher in males vs females in both age groups for MI and PVD, and in the younger age group for CVD.

Conclusion: In this nationwide study utilizing prospectively collected registry data, incident patients with SLE were more likely to develop vascular disease than general population controls during up to 10 years of follow-up after SLE diagnosis. This was seen for women and men aged less or more than 50 years at the time of diagnosis but with the highest IRRs of MI, CVD, and PVD in the younger group of SLE patients. Male subjects had a higher incidence of vascular disease, reflected in male SLE patients having the highest IRDs for MI and PVD. Our findings highlight the need for a thorough assessment of vascular comorbidities in SLE patients, at the time of SLE diagnosis and during follow-up, irrespective of sex and age.

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Abstract Number: 1443

Vasculitis Associations Among Patients with Systemic Lupus Erythematous

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Session Type: Poster Session B
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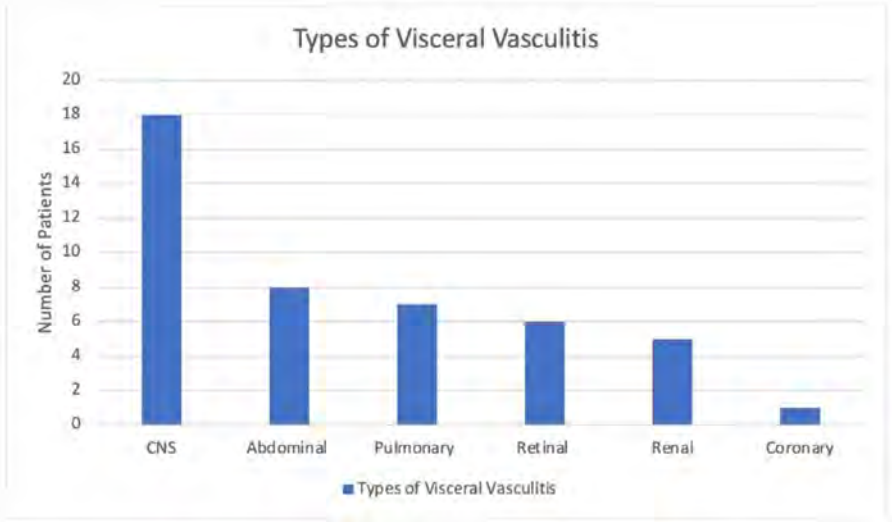
Background/Purpose: Vasculitis is rare manifestation of systemic lupus erythematous (SLE) that often leads to increased morbidity and mortality. Vasculitis prevalence in SLE patients have ranged from 11-36% and can be mild to life-threatening. While there have been limited studies focusing on cutaneous small vessel vasculitis, there are not many studies focusing on risk factors of patients that develop vasculitis within a large longitudinal SLE cohort. The purpose of our study is to identify SLE clinical characteristics associated with vasculitis, testing the hypothesis that certain organ involvement with SLE will be associated with a higher risk of vasculitis.

Characteristics	All patients with SLE N=804	SLE patients with vasculitis n=76	SLE patients without vasculitis n=728	P-value
Male sex (%)	9.5%	10.5%	9.3%	0.737
Black race (%)	74.0%	82.9%	73.1%	0.063
Hispanic Ethnicity (%)	3.1%	4.0%	3.0%	0.723
No High School Diploma (%)	11.2%	14.5%	10.9%	0.228
Uninsured (%)	4.2%	2.6%	4.4%	0.453
History of smoking (%)	24.6%	22.4%	24.9%	0.941
Presence of overlapping autoimmune disorders (%)	**25.9%**	**30.3%**	**25.4%**	**0.028**
Presence of arthritis (%)	**66.2%**	**54.0%**	**67.5%**	**0.043**
Presence of Serositis (%)	28.0%	35.5%	27.2%	0.072
Presence of renal disorder (%)	**47.0%**	**64.5%**	**45.2%**	**<0.01**
Presence of Neurologic disorder (%)	**12.1%**	**23.7%**	**10.9%**	**<0.01**
Presence of heme disorder	51.1%	57.9%	50.4%	0.084
Presence of low complement (%)	**44.7%**	**51.3%**	**44.0%**	**0.026**

Comparison of demographics and disease characteristics between patients with SLE and vasculitis to those without vasculitis.



Prevalence of visceral vasculitis organ involvement among patients with SLE.

Methods: We collected data from consented patients within our institutional longitudinal SLE Database. Data included sex, race, ethnicity, age at lupus onset, SLE classification criteria, medical history, and complications in patients' disease course, including history of vasculitis. If history of vasculitis was present, notes from the database visits and electronic medical record encounters were reviewed to determine what type of vasculitis was present and which organ systems were involved. Once form of vasculitis and organ involvement was confirmed, Stata v15 was utilized to perform descriptive statistics, Chi-squared, Fisher's exact, and t-tests, as appropriate.

Results: Of the 804 patients with SLE included our study, 728 (90.5%) were female, 595 (74%) were Black, and 76 (9.5%) had a history of vasculitis (**Table 1**). 44.7% had visceral vasculitis, 43.4% had cutaneous vasculitis, 7.9% had both cutaneous and visceral vasculitis. Out of the 40 patients that had visceral vasculitis, the breakdown of specific organ involvement was noted (**Figure 1**). Overall, most of patients with vasculitis had CNS, abdominal, or pulmonary involvement. The mean age of SLE onset in patients with vasculitis was 27.3 ± 13.0, compared to 31.5 ± 14.0 in patients without vasculitis. We analyzed the correlation between vasculitis and many factors, including race, ethnicity, symptoms such as arthritis and serositis, smoking history, and others (**Table 1**). We found that presence of other autoimmune disorders, history of renal disorder, and history of neurologic disorder, and low complement was associated with the development of vasculitis. Although mortality rates were higher among patients with vasculitis (21.1% vs 14.0%, p=0.099), the difference was not statistically significant.

Conclusion: Among patients with SLE from a unique population-based cohort, vasculitis was a less common (9.5%) manifestation, yet with important implications for SLE severity and organ involvement. Given the low prevalence of vasculitis, we were limited in ability to identify rare associations, however the strong negative association with arthritis adds to what was previously described in the literature. Based on our findings, presence of low complement, renal, and/or neurologic disorder among patients with SLE could be important clues to the identification of early vasculitis, prompting recognition and treatment which is crucial to improve outcomes.

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Abstract Number: 1444

Identifying Determinants of Favourable and Poor Physical Function in Systemic Lupus Erythematosus: Results from an International Collaborative Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
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Background/Purpose: Systemic lupus erythematosus (SLE) can result in impaired daily physical function through various mechanisms including active disease, chronic damage, and mental health symptoms that are common in the disease. However, the key drivers of reduced physical function are poorly understood, and no large-scale global studies investigating this have been conducted to date. Our objective is to investigate key factors that contribute to impaired physical function in SLE globally.

Methods: SLE patients were identified from the COVAD 2 database, a global register of more than 20,000 respondents. Healthy controls (HC) were included to compare differences in physical function using the Patient Reported Outcome Measurement Information System (PROMIS) questionnaire. Demographics, medication, comorbidities, disease activity, Global Physical Health (GPH) and Global Mental Health (GMH) were collected. Multivariable regression analysis was used to identify contributing factors to favourable or poor physical function (measured by PROMIS Physical Function shortform PF-10a score).

Results: 979 SLE patients and 3358 HCs were included in analysis. Patients with SLE had significantly lower PF-10a score as compared to HCs (median 42, IQR 36-47 vs median 49, IQR 45-50, p< 0.0001), as shown in Figure 1. Determinants of physical function status in patients with SLE are summarised in Table 1. Briefly, factors associated with poor physical function included increasing age (-0.042, 95% CI -0.069 to -0.015, p=0.002) and methotrexate use (-0.928, 95% CI -1.844 to -0.012, p=0.047). Diabetes (-1.862, 95% CI -3.481 to -0.243, p=0.024) and interstitial lung disease (ILD) (-2.441, 95% CI

-4.366 to -0.517, p=0.013), but not asthma or COPD, also contributed to lower PF-10a score. From a mental health perspective, anxiety (-0.970, 95% CI -1.853 to -0.087, p=0.031) but not depression contributed to a lower physical function score. Higher Pain Visual Analogue Scales (VAS) (-2.889, 95% CI -3.107 to -2.671, p< 0.001) and Fatigue VAS (-1.459, 95% CI -1.974 to -0.945, p< 0.001) also contributed to lower PF-10 scores. Hydroxychloroquine use (0.844, 95% CI 0.190 to 1.498, p=0.012) and higher GPH score (2.287, 95% CI 2.079 to 2.494, p< 0.001) were associated with favourable physical function.

Conclusion: Patients with SLE show significantly reduced physical function compared with HCs. Key contributors to poor physical function include intercurrent diabetes and ILD. Screening for, and aggressive early treatment of these conditions may confer improved long-term function. As expected, higher levels of pain and fatigue were associated with poor physical function. Methotrexate use was also identified as a contributing factor to reduced function, which could represent its use in articular manifestations that limit physical function. Importantly, use of hydroxychloroquine was associated with favourable physical function, which might be due to its protective effect in preventing damage, adding to the well-recognised benefits of this drug in SLE.

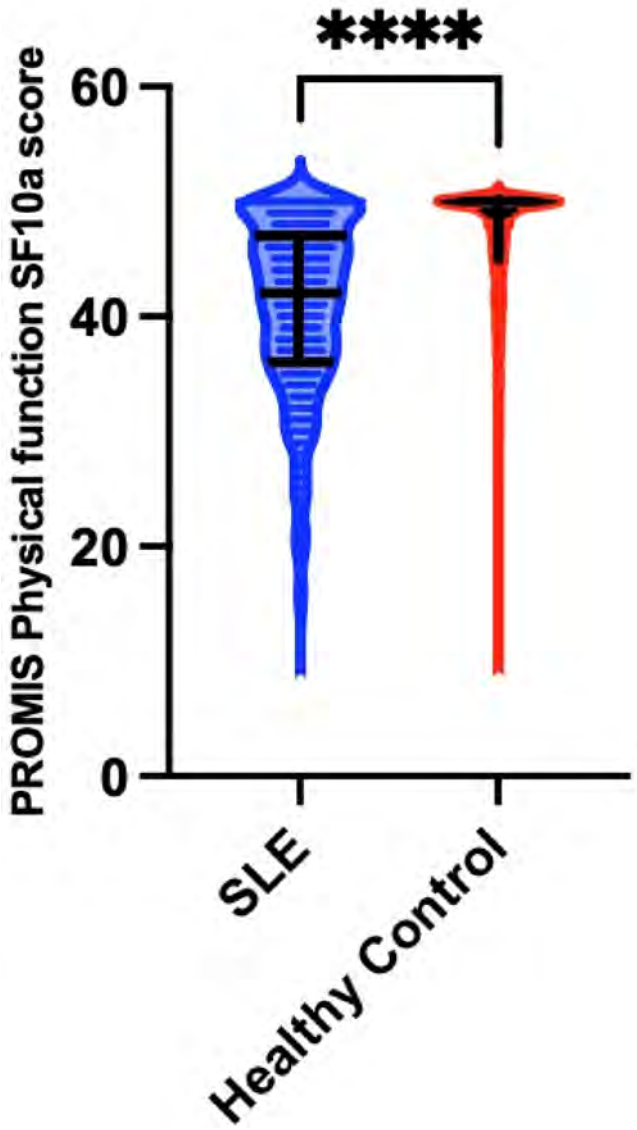

Figure 1: This figure demonstrates that patients with SLE had significantly lower PROMIS Physical Function SF10a scores as compared to healthy controls (median 42, IQR 36-47 vs median 49, IQR 45-50, P<0.0001)

Table 1: This table summarises the determinants of physical function status in patients with SLE

Table 1	Unstandardised B	Beta	95% Confidence Interval for B		Significance
			Lower Bound	Upper Bound	
Age	**-0.042**	**-0.074**	**-0.069**	**-0.015**	**0.002****
Disease Duration (years)	-0.004	-0.005	-0.037	0.029	0.814
Methotrexate	**-0.928**	**-0.040**	**-1.844**	**-0.012**	**0.047***
Mycophenolate mofetil	0.507	0.027	-0.265	1.278	0.198
Azathioprine	0.409	0.022	-0.346	1.164	0.288
Hydroxychloroquine	**0.844**	**0.050**	**0.190**	**1.498**	**0.012***
Steroid Dose	-4.34	-0.044	-.845	-0.023	0.038
Lupus flare within last 6 months	-0.819	-0.039	-1.644	0.007	0.052
Chronic Kidney Disease	-0.430	-0.017	-1.434	0.575	0.401
Interstitial Lung Disease	**-2.441**	**-0.049**	**-4.366**	**-0.517**	**0.013***
Ischaemic Heart Disease	-0.925	-0.020	-2.798	0.947	0.332
Diabetes	**-1.862**	**-0.045**	**-3.481**	**-0.243**	**0.024***
Stroke	-0.663	-0.011	-3.049	1.723	0.586
Anxiety	**-0.970**	**-0.047**	**-1.853**	**-0.087**	**0.031***
Depression	0.594	0.029	-0.290	1.477	0.188
Pain VAS	**-2.889**	**-0.945**	**-3.107**	**-2.671**	**<0.001*****
Fatigue VAS	**-1.459**	**-0.171**	**-1.974**	**-0.945**	**<0.001*****
PROMIS Global Physical Health	**2.287**	**0.634**	**2.079**	**2.494**	**<0.001*****

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Abstract Number: 1445

SLESIS-R: An Improved Score for Prediction of Serious Infection in Patients with Systemic Lupus Erythematosus Based on the RELESSER Prospective Cohort

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) have an increased risk of serious infections that varies with the severity of the disease, use of immunosuppressives, including glucocorticoids (GC), and damage, among others. Estimating the infection risk in these patients is important to balance the immunosuppression but there is no evidence-based and suitable tool available to make a prediction of severe infection in these patients.

The SLESIS score had been previously developed for the prediction of severe infections in SLE and was initially validated in an external cohort[1]. This score had 7 predictors, including the Katz index (SKI), a severity score for SLE with a limited degree of validation and difficult to implement in daily practice. Moreover, its performance was only moderate, with an AUC of 0.63 (95% CI: 0.56 - 0.70).

The objective of our study was to improve the SLESIS score in terms of prediction accuracy and feasibility.

Methods: We used the prospective phase of RELESSER (RELESSER-P), the SLE register of the Spanish Society of Rheumatology, a register that includes patients with SLE or incomplete SLE (91%≥4 ACR 1997 criteria) from 45 centers. The outcome variable was any serious infection identified over the first year of follow up, with serious infection being defined as one leading to hospitalization or death.

The sample was randomly divided into development and validation cohorts. A multivariable logistic model was populated with those variables already forming the SLESIS score, including clinical characteristics, demographic features, hospitalization by SLE comorbidities and treatments [2] plus all other potential predictors identified by literature review and available in the first visit of RELESSER-P.

The most parsimonious model with the least information criteria (AIC and BIC) were chosen as the final model. The performance of the final model was analyzed with C-statistics and AUC. Internal validation was tested using bootstrap techniques.

Table 1. Univariate analysis. Variables associated with serious infection.

Potential predictors	OR (95%CI)	p-value
Aged	**1.04 (1.01 - 1.07)**	**0.006**
Female	1.22 (0.28 - 5.23)	0.789
Latin American	0.90 (0.12 - 6.77)	0.918
Active smoking	1.45 (0.56 - 3.78)	0.446
Charlson's Index	**1.34 (1.15 - 1.56)**	**<0.0001**
Diabetes	0.33 (0.53 - 6.44)	0.333
Malignancy	1.28 (0.21 - 7.67)	0.788
Chronic kidney disease	**3.82 (1.54 - 9.44)**	**0.004**
Disease activity (SELENA-SLEDAI)	1.03 (0.94 - 1.13)	0.559
Damage (SDI)	**1.29 (1.13 - 1.48)**	**<0.0001**
Severity Katz Index (SKI)	**1.33 (1.12 - 1.58)**	**0.001**
SLE-related hospitalization	**15.50 (5.26 - 45.69)**	**<0.0001**
Previous serious infection	**14.78 (6.41 - 34.1)**	**<0.0001**
Creatinine	1.02 (0.88 - 1.19)	0.756
Lymphopenia any time	1.45 (0.57 - 3.68)	0.439
Hypocomplementemia	1.00 (0.43 - 2.30)	1.000
Maximal GC dose over the period (prednisone)	-	-
≤ 5 mg	1	NA
> 5 mg and <10	2.31 (0.68 - 7.81)	0.177
≥ 10 mg and <30	2.00 (0.52 - 7.68)	0.311
≥ 30 mg	**7.47 (1.87 - 29.82)**	**0.004**
Antimalarials	0.64 (0.29 - 1.42)	0.270
Cyclophosphamide	**12.38 (2.57 - 59.70)**	**0.002**
Mycophenolate	**3.04 (1.12 - 8.25)**	**0.029**
Rituximab	1.32 (0.17 - 9.95	0.790
Methotrexate or azathioprine	0.79 (0.23 - 2.65)	0.698

SLE: Systemic lupus erythematosus; SDI: SLICC/ACR DAMAGE INDEX; GC: glucocorticoids

Table 2. Adjusted final multivariate predictive model.

Predictor	OR (95%CI)	p-value
Age	1.03 (1.00-1.06)	0.040
Previous SLE-related hospitalization	3.81 (1.33-10.97)	0.013
Previous serious infection	3.72 (1.58-8.77)	0.003
Having received a GC dose ≥30 mg	4.45 (1.34-14.76)	0.015

SLE: Systemic lupus erythematosus; GC: glucocorticoids

Results: A total of 1459 patients who had completed visit 2 (one year of follow up),or had information on infections or death in the period, were included in the development cohort (mean age of 49 ± 13, 90% females). Twenty-five (1.7%) had experienced at least one serious infection.

The results of univariate analysis are shown in Table 1.According our final, adjusted multivariate model, serious infection in SLE could be predicted from 4 variables (Table 2) and the SKI could be excluded from the model. The model correctly classified 97% of the infections with C-statistic = 0.82 (0.67 - 0.92) and a Hosmer-Lemeshow p=0.997. The AUC was 0.88 (0.80 – 0.96).

Conclusion: The revised SLESIS score (SLESIS-R) is a fairly accurate and feasible instrument to predict infections in SLE patients in the daily clinical practice that could help making informed decisions on the use of immunosuppressive or biological therapy in SLE patients.

[1]Tejera-Segura B, Rúa-Figueroa I, Pego-Reigosa JM, et al. Can we validate a clinical score to predict the risk of severe infection in patients with systemic lupus erythematosus? A longitudinal retrospective study in a British CohortBMJ Open 2019;14;9(6):e028697.

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Abstract Number: 1446

Glucocorticoids Use Is a Major Driver of Self-perceived Depression in Systemic Lupus Erythematosus: Insights from a Large, Prospective and Multicenter Study Using RELESSERPROS Register's Database

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: The prevalence of depression and associated factors in systemic lupus erythematosus (SLE) are not well known and there are no longitudinal studies addressing this relevant subject in SLE.We aimed to evaluate the prevalence of self-perceived depression in patients with SLE and associated factors in a large, multicenter cohort (RELESSER-PROS).

Methods: Prospective longitudinal study. Patients with SLE (1997 ACR criteria) answering positively to the depression question of the Lupus Impact Tracker (LIT) questionary (LITQ7), over 4 years of follow-up (5 annual visits, V1 to V5). Self-perceived depression was addressed as "depression any time" or "depression most of time", according to the kind of answer to the LITQ7 (answers 1,2,3 or 4 and answers 3 or 4 respectively). Only patients with no missing values in the covariates, were included in the multivariable analysis. The following covariates were considered: SLEDAI, age, duration of the disease, SLICC/AR DI (SDI), fibromyalgia, Charlson index, smoking, BMI, menopause, sedentary lifestyle, marital status,

Table 1: best multivariable GEE model

	OR	Lower limit	Upper limit
(Intercept)	0,121	0,028	0,529
SLEDAI	1,066	0,991	1,147
SLICC/ACR DI	1,138	0,962	1,346
Age	1,022	0,994	1,051
Fibromyalgia	2,898	1,576	5,328
BMI	1,485	0,685	3,219
Unemployment	1,86	0,972	3,56
Low incomes	1,726	0,89	3,347
Glucocorticoids use	1,853	1,173	2,928
Single marital status	1,292	0,766	2,179
QICC: 1006.75			
SLICC/ACR DI: SLICC/ACR damage index; BMI: body mass index			

unemployment and glucocorticoid (GC) use. Friedman test was used to test if the change in repeated measures. Generalized estimating equation (GEE) models with binomial response, were built exploring the associations of individual longitudinal determinants with longitudinal assessment of depression. The best model was selected using quasi-likelihood under the independence model information criterion

Results: A total of 1463 were included. Mean age: 55 (DS±13) years, 90% were female. Mean duration of the disease: 14 (±8.59) years. Fibromyalgia was present in 5.7% (76/1343). Corticosteroids use ranged from 49.4% to 57%, depending on the visit. Median SLEDAI ranged from 0 to 2 and SDI ranged from 1 to 2.

Prevalence of "depression any time" was 89.9% (1104/1228) and 34.6% (200/578) were in depression "most of time". Up to 26.5% (153/578) answered to LITQ7 "depression most of time" in the five visits; 89.7% of the patients which perceived themselves as depressed at least in 2 out of 5 visits. Only 6.9% of the patients with previous diagnosis of depression answered "0" to the Q7 of LIT ("none of the time").

Patients with "depression any time" develop more damage at V5 than patients without depression (answer to LITQ7=0) ($p = 0.00931$, T-test). In the GEE binomial analysis considering all the predefined covariates, that included only patients with no missing values for any of them (namely, 155 patients), fibromyalgia (OR 2.79; 95%CI: 1.28-6.05), unemployment (OR 1.95; 95%CI 1.02 -3.73), and GC use (OR 1.88; 95%CI 1.18-2.99) were significant associated with "depression any time".

The best model (according QIC) displayed a statistically significant association only with fibromyalgia (OR 2.90; 95%CI: 1.58-5.33) and GC (OR 1.85; 95%CI 1.17-2.93). (Table 1). Without entering glucocorticoids, SLEDAI turns significant in the model, suggesting collinearity.

Conclusion: The prevalence of self-perceived depression is high in SLE. Longitudinal data analysis suggests a causal relationship between glucocorticoids use, fibromyalgia and self-perceived depression.

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Abstract Number: 1447

Increased Left Ventricular Mass Index in Systemic Lupus Erythematosus Patients with Lupus Nephritis Compared to Those Without Nephritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) and lupus nephritis (LN) are at increased risk of cardiovascular (CV) morbidity and mortality, compared to those without LN due to the additional burden of kidney involvement, inflammation, and potential renal impairment contributing to cardiovascular complications. This elevated risk may be associated to the higher values of left ventricular (LV) mass observed in SLE patients, particularly when compared to age and sex-matched controls. Echocardiographic evaluation is not included in current guidelines for managing CV risk in

Figure 1. Comparison of demographic characteristics between SLE patients with and without LN.

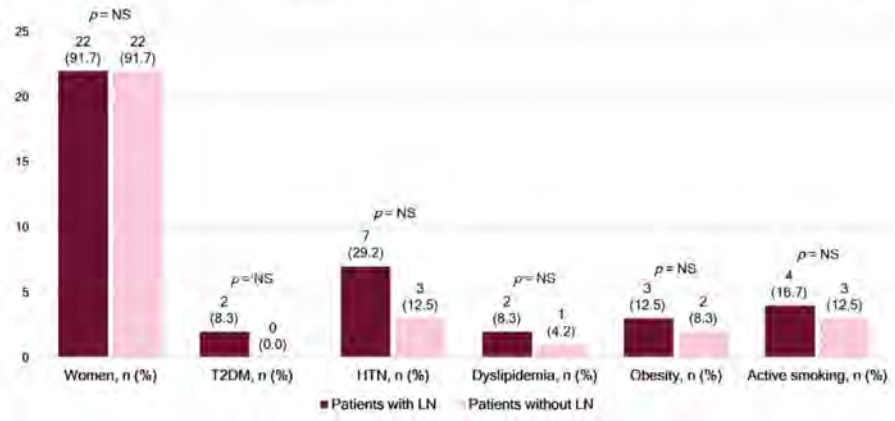

Table 1. Comparison of echocardiographic findings of SLE patients with and without LN.

Variables	Patients with LN (n=24)	Patients without LN (n=24)	*p*-value
LV mass index, g/m^2, mean ± SD	66.9 ± 21.8	54.8 ± 16.1	**0.035**
RWT, mean ± SD	0.37 ± 0.08	0.34 ± 0.10	0.265
LV geometry abnormality, n (%)	7 (29.2)	4 (16.7)	0.303
LAESVI, ml/m^2, mean ± SD	29.72 ± 10.80	26.04 ± 8.76	0.208
LVEF, %, mean ± SD	58.16 ± 7.42	58.04 ± 7.04	0.953
LVESV, ml, median (IQR)	39.0 (26.0-54.5)	32.5 (23.7-39.7)	0.185
LVEDV, ml, mean ± SD	92.10 ± 25.09	81.57 ± 27.80	0.211

SLE, systemic lupus erythematosus; LN, lupus nephritis; LV, left ventricular; RWT, relative wall thickness; LAESVI, left atrial end-systolic volume index; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; LVEDV, left ventricular end-diastolic volume.

SLE, systemic lupus erythematosus; LN, lupus nephritis; LV, left ventricular; RWT, relative wall thickness; LAESVI, left atrial end-systolic volume index; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; LVEDV, left ventricular end-diastolic volume.

patients with rheumatic diseases. This study aimed to compare LV mass and other echocardiographic parameters between SLE-patients with and without LN.

Methods: We performed a nested case-control study among the SLE-cohort from our center. This cohort includes patients older than 18 years who fulfill the 2019 EULAR/ACR Classification Criteria for SLE. Patients with LN were matched with patients without LN by age and gender. A transthoracic echocardiogram was performed by two certified echocardiographers blinded to clinical information. Comparisons were done with Chi-square or Fisher's exact test for qualitative variables, and Student's T-test or Mann-Whitney's U-test for quantitative variables. A p-value < 0.05 was considered significant.

Results: A total of 48 SLE patients, 24 with LN and 24 without LN, were included. Both groups were similar regarding age (36.9 vs 36.5, $p = 0.873$) and prevalence of traditional CV risk factors including type 2 diabetes mellitus, hypertension, dyslipidemia, obesity, and smoking (Figure 1). LV mass index was significantly higher in SLE patients with LN (66.9 g/m^2 vs 54.8 g/m^2, $p = 0.035$) in comparison to those without it. There was no difference regarding other echocardiographic parameters (Table 1).

Conclusion: LV mass measurements were higher in patients with SLE and LN in comparison to patients without LN, regardless of traditional CV risk factors. The consequences of increased LV mass can include an elevated risk of CV events such as heart failure, cardiac arrhythmias, and CV mortality. Further studies are necessary to establish the potential role of echocardiography in the CV assessment of patients with SLE, especially those with LN.

Disclosure: N. Guajardo-Jauregui: None; **D. Galarza-Delgado**: None; **I. Colunga**: None; **J. Azpiri-López**: None; **R. Arvizu-Rivera**: None; **J. Cardenas-De la Garza**: None.

Abstract Number: 1448

Association of Disease Activity and Anti-Double Stranded DNA Antibodies Titers with Echocardiographic Parameters in Systemic Lupus Erythematosus Patients

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic inflammatory disease that involves the deposition of immunocomplexes on vital organs, including the heart. Cardiovascular disease is the leading cause of long-term mortality in SLE patients, and their increased risk of cardiovascular events is attributed to disease characteristics, such as the systemic inflammatory state associated with the disease. In this study we aimed to evaluate the association of disease characteristics, such as the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and anti-double stranded DNA antibodies (anti-dsDNA) titers, with echocardiographic parameters in patients with SLE.

Methods: This was a cross-sectional study. We recruited 75 SLE patients aged ≥ 18 years who fulfill the 2019 EULAR/ACR Classification Criteria for SLE. Patients with a previous cardiovascular event, another connective tissue disease or pregnancy were excluded. A transthoracic echocardiogram was performed by two certified echocardiographers blinded to clinical information. A blood sample was drawn to measure anti-dsDNA antibody titers and disease activity was evaluated with SLEDAI. Correlations were assessed with Spearman's correlation coefficient (rs). A p-value < 0.05 was considered statistically significant.

Results: Median age of SLE patients was 37 (25-44) years with a median SLEDAI of 8.0 (4.0-12.0). The rest of demographic and clinical characteristics are shown in Table 1. We found a positive correlation between SLEDAI and left ventricular mass index (rs=0.243, p=0.036), between SLEDAI and the ratio between early mitral inflow velocity and mitral annular early

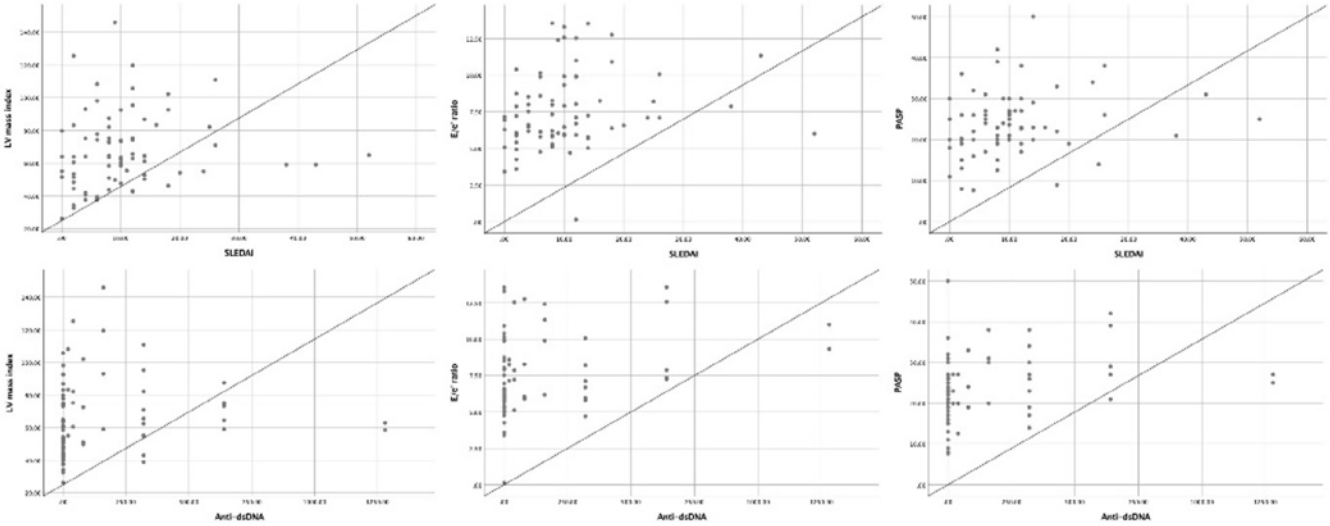
Table 1. Demographic and clinical characteristics.

Variable	SLE patients (n=75)
Women, n (%)	67 (89.3)
Age, median (IQR)	37 (25-44)
T2DM, n (%)	3 (4.0)
Hypertension, n (%)	17 (22.7)
Dyslipidemia, n (%)	8 (10.7)
Obesity, n (%)	12 (16.0)
Active smoking, n (%)	10 (13.3)
Disease duration months, median (IQR)	72 (18-132)
SLEDAI, median (IQR)	8 (4-12)
Anti-dsDNA antibody titers, median (IQR)	0 (0-160)
LV mass index, median (IQR)	63.5 (50.9-79.6)
E/e', median (IQR)	7.1 (5.9-8.7)
LAVI, median (IQR)	25.9 (20.8-31.1)
LVEF, median (IQR)	59.2 (7.9)
TAPSE, median (IQR)	22.0 (20.0-23.0)
PASP, median (IQR)	23.0 (20.0-27.0)

SLE systemic lupus erythematosus; *T2DM* type 2 diabetes mellitus; *SLEDAI* Systemic Lupus Erythematosus Disease Activity Index; *dsDNA* double stranded DNA; *LV* left ventricular; *E/e'* the ratio between early mitral inflow velocity and mitral annular early diastolic velocity; *LAVI* left atrial volume index; *LVEF* LV ejection fraction; *TAPSE* tricuspid annular plane systolic excursion; *PASP* pulmonary arterial systolic pressure.

SLE systemic lupus erythematosus; T2DM type 2 diabetes mellitus; SLEDAI Systemic Lupus Erythematosus Disease Activity Index; dsDNA double stranded DNA; LV left ventricular; E/e' the ratio between early mitral inflow velocity and mitral annular early diastolic velocity; LAVI left atrial volume index; LVEF LV ejection fraction; TAPSE tricuspid annular plane systolic excursion; PASP pulmonary arterial systolic pressure.

Figure 1. Scatter plots of correlations between SLEDAI, anti-dsDNA and echocardiographic parameters.



diastolic velocity (E/e') (rs=0.277, p=0.016) and between SLEDAI and pulmonary arterial systolic pressure (PASP) (rs=0.271, p=0.019). We also found a positive correlation between anti-dsDNA and left ventricular mass index (rs=0.264, p=0.022), between anti-dsDNA and E/e' (rs=0.295, p=0.010), and between anti-dsDNA and PASP (rs=0.292, p=0.011) (Figure 1).

Conclusion: Our study demonstrated significant associations between higher SLEDAI and anti-dsDNA with increased left ventricular mass index, E/e' and PASP, which could lead to the progression of ventricular hypertrophy, diastolic dysfunction, and pulmonary hypertension respectively, suggesting a potential role of disease activity and anti-dsDNA in the development of adverse cardiac remodeling and function in SLE patients. A transthoracic echocardiogram may be helpful to detect early cardiovascular abnormalities, especially in patients with high disease activity and anti-dsDNA titers, and therefore, should be considered as part of the cardiovascular evaluation of SLE patients.

Disclosure: N. Guajardo-Jauregui: None; **I. Colunga**: None; **J. Azpiri-López**: None; **D. Galarza-Delgado**: None; **J. Cardenas-De la Garza**: None; **R. Arvizu-Rivera**: None.

Abstract Number: 1449

Evaluation of Progression from Preclinical to Systemic Autoimmune Rheumatic Disease

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SESSION INFORMATION

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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate the development of a systemic autoimmune rheumatic disease (SARD) in undifferentiated and asymptomatic individuals with antinuclear antibodies (ANA). We evaluated fulfillment of classification criteria and comparatively evaluated manifestations between those who did and did not develop a SARD.

Methods: We conducted a retrospective cohort study of undifferentiated (UCTD) and asymptomatic patients with ANA who were assessed at baseline and annually for developing signs, symptoms, and serology of a SARD. The primary outcome was a physician-based diagnosis of SARD over two years. We assessed fulfillment of classification criteria and used risk ratios (RR) to evaluate differences in manifestations in those who did and did not progress to a SARD.

Results: We evaluated 207 asymptomatic ANA^+ or UCTD subjects, of whom 20 (9.7%) progressed to a SARD while 187 (90.3%) did not progress. Progressors developed systemic lupus erythematosus (SLE) (n=11 (55%)), Sjogren's disease (n=5 (25%)), systemic sclerosis (n=3 (15%)) and rheumatoid arthritis (n=1 (5%)). Fever occurred less frequently in those who progressed to a SARD (RR 0.90, 95%CI 0.86, 0.94). Among SLE patients, 100% fulfilled the EULAR/ACR SLE criteria (sensitivity 91.7%, specificity 100%), whereas 73% fulfilled the 1997 ACR SLE criteria (sensitivity 81.8%, specificity 98.9%). Progressors to SLE had arthritis (91%), hypocomplementemia (45%), alopecia (36%), oral ulcers (27%), acute cutaneous lupus (18%), subacute cutaneous lupus (18%), and pericarditis (18%); while none developed delirium, psychosis, seizures, or lupus nephritis.

Conclusion: Most undifferentiated/asymptomatic individuals with ANA do not progress to a SARD over two years. The EULAR/ACR SLE criteria have improved the ability to identify those who develop SLE. SLE progressors appear to have mild disease in the short term.

Disclosure: J. Wither: None; **D. Bonilla**: None; **Z. Ahmad**: None; **A. Bookman**: GlaxoSmithKline(GSK), 12, Regional Principal Investigator, Novartis, 12, Regional Principal Investigator, VIELA BIO, 12, Regional Principal Investigator; **L. Hiraki**: None; **E. Silverman**: None; **M. Movahedi**: None; **S. Johnson**: None; **H. Alahmari**: None.

Abstract Number: 1450

Clinical Manifestations and Outcomes in Systemic Lupus Erythematosus Patients Who Received Antiviral Therapy During the COVID-19 Omicron Variant Wave: Results from a Single Center Cohort of Puerto Rico

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The impact of COVID-19 in patients with systemic lupus erythematosus (SLE) has been a subject of great concern. Antiviral therapy has emerged as a key approach in the treatment of COVID-19 in the general population, but their efficacy in SLE patients in terms of reducing the risk of hospitalizations, lupus flares, and death remains unclear. Thus, we sought to compare the clinical manifestations and outcomes in SLE patients with COVID-19 that received antiviral therapy to those who did not.

Methods: A cohort of adults (≥21 years) with SLE (per the revised 1997 American College of Rheumatology classification criteria) from a single center in Puerto Rico who had COVID-19 during the Omicron period (December 2021 to December 2022) were studied. SARS CoV-2 infection was confirmed by polymerase chain reaction or antigen tests. Antiviral therapy (nirmatrelvir/ritonavir or molnupiravir) was prescribed to those who presented with mild-to-moderate infection. Demographic parameters, cumulative SLE manifestations, disease activity, damage accrual, lupus treatments, comorbidities, COVID-19 symptoms, emergency room (ER) visits, hospitalizations, SLE flares, and mortality were compared between patients that received antiviral therapy and those who did not using bivariate and multivariate analyses adjusted for age.

Results: Out of 347 SLE patients, 147 (42.4%) had COVID-19 during the Omicron wave. Among these patients, 35 (23.8%) received antiviral therapy as they presented with mild-to-moderate symptoms. The rest of the cohort had mild symptoms. Older age, pleuritis, diabetes mellitus, some COVID-19 symptoms (dyspnea, vomiting, and diarrhea), and ER visits were significantly more common in patients that received antiviral therapy compared to those who did not (Table 1). All these

Table 1. Demographic characteristics, clinical features, and outcomes of SLE patients with COVID-19 who received antiviral therapy versus those who did not.

Table 1. Demographic characteristics, clinical features, and outcomes of SLE patients with COVID-19 who received antiviral therapy versus those who did not.

Characteristics	All patients (n=147)	Antiviral therapy (n=35)	No antiviral therapy (n=112)	p-value
Age, mean (SD)	46.9 (13.0)	52.5 (12.7)	45.2 (12.7)	0.002
Sex, % female	95.9	97.1	95.5	0.675
SLE duration of disease, mean (SD)	15.3 (9.0)	16.1 (6.8)	15.1 (9.6)	0.285
Cumulative SLE manifestations*, %				
Malar rash	53.1	57.1	51.8	0.579
Discoid rash	10.2	2.9	12.5	0.100
Oral ulcers	19.7	17.1	20.5	0.660
Photosensitivity	55.8	68.6	51.8	0.081
Arthritis	68.7	80.0	65.2	0.099
Pericarditis	10.2	14.3	8.9	0.361
Pleuritis	6.8	14.3	4.5	0.044
Proteinuria	36.7	28.6	39.3	0.251
Seizures	4.1	0.0	5.4	0.162
Psychosis	1.4	0.0	1.8	0.426
Other CNS	0.7	0.0	0.9	0.575
Haemolytic anemia	8.2	11.4	7.1	0.419
Leukopenia	37.4	48.6	33.9	0.118
Lymphopenia	61.2	65.7	59.8	0.532
Thrombocytopenia	15.0	20.0	13.4	0.339
SLEDAI, mean score (SD)	1.49 (2.2)	1.69 (2.4)	1.03 (1.9)	0.128
SDI score, mean (SD)	1.38 (1.2)	1.49 (1.3)	1.19 (1.4)	0.130
Current SLE treatment, %				
Corticosteroids	55.1	60.0	53.6	0.505
Hydroxychloroquine	83.7	85.7	83.0	0.708
Mycophenolate mofetil	36.1	34.3	36.6	0.803
Azathioprine	8.8	8.6	8.9	0.948
Methotrexate	3.4	2.9	3.6	0.839
Tacrolimus	3.4	2.9	3.6	0.839
Cyclophosphamide	0.0	0.0	0.0	---
Belimumab	0.7	0.0	0.9	0.575
Rituximab	0.0	0.0	0.0	---
Comorbidities, %				
Smoking	0.7	0.0	0.9	0.575
Overweight/Obesity	64.6	68.6	63.4	0.576
Dyslipidemia	32.0	37.1	30.4	0.452
Arterial hypertension	49.7	51.4	49.1	0.811
Diabetes mellitus	10.9	22.9	7.1	0.009
Chronic kidney disease	4.1	5.7	3.6	0.576
Hypothyroidism	23.8	28.6	22.3	0.449
COVID-19 vaccination, %	95.9	97.1	95.5	0.675
COVID-19 symptoms, n (%)				
Fatigue	50.3	62.9	46.4	0.090
Fever	53.7	60.0	51.8	0.395
Anosmia	11.6	17.1	9.8	0.237
Runny nose	62.6	60.0	63.4	0.717
Sore throat	46.9	57.1	43.8	0.166
Dyspnea	22.4	48.6	14.3	<0.001
Cough	61.2	65.7	59.8	0.532
Arthralgias	34.7	45.7	31.3	0.117
Myalgias	51.0	57.1	49.1	0.406
Headache	47.6	57.1	44.6	0.196
Nausea	13.6	20.0	11.6	0.206
Vomiting	6.8	17.1	3.6	0.005
Diarrhea	18.4	31.4	14.3	0.022
Duration of COVID-19 symptoms, median (25th – 75th percentile)	5.0 (3.0-7.0)	6.0 (4.0-7.0)	5.0 (3.0-7.0)	0.536
Emergency room visit, %	12.9	28.6	8.0	0.002
Hospitalization, %	3.4	8.6	1.8	0.053
SLE flare after COVID-19, %	3.4	8.6	1.8	0.053
Mortality, %	0.7	2.9	0.0	0.073

*As defined in the revised 1997 American College of Rheumatology classification criteria. SLE: Systemic lupus erythematosus; SD: Standard deviation; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; SDI: Systemic Lupus Erythematosus International Collaborating Clinics/ American College of Rheumatology Damage Index

Table 2. Factors associated with antiviral therapy

Table 2. Factors associated with antiviral therapy*

Features	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Pleuritis	3.57 (0.97-13.14)	4.03 (1.03-15.87)
Diabetes mellitus	3.86 (1.33-11.20)	3.27 (1.09-9.84)
Dyspnea	5.67 (2.43-13.24)	5.60 (2.32-13.51)
Vomiting	5.59 (1.48-21.12)	8.90 (2.08-38.04)
Diarrhea	2.75 (1.13-6.69)	2.54 (1.02-6.37)
Emergency room visit	4.58 (1.68-12.46)	5.31 (1.83-15.38)

*No antiviral use is the reference group. Model adjusted for age. OR: Odds ratio; CI: Confidence interval

variables retained significance in the multivariate analysis (Table 2). No significant differences were observed for sex, disease duration, disease activity, disease damage, SLE treatments, hospitalizations, SLE flares, and mortality.

Conclusion: In this cohort of Puerto Ricans with SLE who had COVID-19 during the Omicron period, patients who required antiviral therapy were older and more likely to have pleuritis, diabetes mellitus, and more COVID-19 symptoms than those who did not receive antiviral treatment. Despite having these clinical manifestations and risk factors for severe outcomes, those who were treated with antiviral drugs had a favorable outcome in terms of hospitalizations, SLE flares, and mortality.

Disclosure: L. Serrano-Arroyo: None; **R. Ríos-Rivera**: None; **A. González-Meléndez**: None; **L. Vilá**: None.

Abstract Number: 1451

Evaluation of Changes in SLE Patients' Phenotype at Disease Onset, and Assessment of Disease Activity, Damage and Therapy at Diagnosis and During Follow up in the Last Forty Years: Preliminary Data of a Single Center Experience

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease associated with a high degree of variability at onset, which may make SLE diagnosis challenging, with an estimated time between onset of symptoms and diagnosis of 24 months[1]. Moreover, in SLE early diagnosis and therapeutic advances have led to better improve outcomes, and achievement of persistent low disease activity and/or remission have been associated with reduced long-term organ damage. The aim of this study was to evaluate the changes in the onset pattern of SLE in demographic and clinical terms, and for changes in assessment and therapy at diagnosis and during the f-up.

Methods: Medical records of 125 patients diagnosed between 1970 to 2019 and regularly followed up were reviewed. Patients were divided into 4 groups based on the year of diagnosis: 1970-'89, 1990-'99, 2000-'09, 2010-'19. Disease activity, cumulative organ damage and remission were recorded according to validated indices (SLEDAI-2K, SLEDAS, SLICC Damage Index, LLDAS and DORIS) at the time of diagnosis (T0) and at 1 (T1), 5 (T2) and 10 (T3) years after. GCs (both in absolute terms and daily dosage), hydroxychloroquine (HCQ) and DMARDS use were also evaluated at the same time

Figure 1

	TOTAL (n=125)	Diagnosis 1970-89 (n=16, 12,8%)	Diagnosis 1990-99 (n=19, 15,2%)	Diagnosis 2000-09 (n=32, 25,6%)	Diagnosis 2010-19 (n=58, 46,4%)	p value
Females, N (%)	119 (95,2)	15 (93,75)	18 (94,74)	32 (100)	54 (93,1)	0,5214
Males, N (%)	6 (4,8)	1 (6,25)	1 (5,26)	0 (0)	4 (6,9)	0,5214
Mean age of onset (Std. Dev.)	30,62 (12,91)	22,86 (6,33)	26,42 (10,29)	28 (11,17)	35,59 (14,11)	**0,0011**[1]
Mean age of diagnosis (Std. Dev)	31,95 (12,95)	25,19 (6,15)	28,47 (10,27)	29,09 (11,30)	36,53 (14,47)	**0,0050**[1]
Mean diagnostic delay, months (Std. Dev)	15,83 (32,54)	28,25 (52,26)	24,21 (48,13)	12 (22,06)	11,6 (18,89)	0,9164
Clinical manifestations at onset						
	TOTAL (n=124)[3]	**Diagnosis 1970-89 (n=16, 12,8%)**	**Diagnosis 1990-99 (n=18[3], 15,2%)**	**Diagnosis 2000-09 (n=32, 25,6%)**	**Diagnosis 2010-19 (n=58, 46,4%)**	**p value**
Mucocutaneous, N (%)	88 (70,97)	14 (87,50)	15 (83,33)	21 (65,62)	38 (65,52)	0,1920
Musculoskeletal, N (%)	97 (78,23)	14 (87,50)	15 (83,33)	22 (68,75)	46 (79,31)	0,2540
Constitutional symptoms, N (%)	73 (58,87)	11 (68,75)	10 (55,55)	18 (56,25)	34 (58,62)	0,8449
Renal, N (%)	26 (20,97)	5 (31,25)	5 (26,32)	9 (28,12)	7 (12,07)	0,1521
Cardio-pulmonary, N (%)	8 (6,45)	0 (0)	1 (5,26)	2 (6,25)	5 (8,62)	0,6635
Neurological, N (%)	6 (4,84)	0 (0)	0 (0)	4 (12,50)	2 (3,45)	0,1091

Categorical variables were reported as proportion and/or percentage, continuous variables were expressed as mean (±standard deviation) values. Qualitative variables were compared with Chi-Squared or Fisher's exact test, quantitative variables with one-way Anova or Mann-Whitney test.

[1] a significant difference was found among the groups. Comparing individual group, each other there is a significant difference between "2010-2020" compared to all the other groups: 2010-2020 vs '70- '89 (p= 0.0006), 2010-2020 vs '90- '99 (p=0.0107), 2010-2020 vs 2000-2009 (p=0.0172).

[2]2010-2020 vs '70- '89 (p=0.0025), 2010-2020 vs '90- '99 (p=0.0277), 2010-2020 vs 2000-2009 (p=0.0137).

[3]missing onset data for 1 patient

Figure 2.

	Diagnosis 1970-89 (n=16, 12,8%)	Diagnosis 1990-99 (n=19, 15,2%)	Diagnosis 2000-09 (n=32, 25,6%)	Diagnosis 2010-19 (n=58, 46,4%)	p value
Assessment at diagnosis (T0)					
SLEDAI-2K	9,5 (±6,5)	7,7 (±3,9)	7,6 (±3,9)	9 (±5,3)	0,6877
SLEDAS	10 (±6,9)	9,6 (±7,8)	12,5 (±12)	11,4 (±8,7)	0,8098
SLICC	0 (±0)	0 (±0,2)	0 (±0,2)	0 (±0,2)	0,7575
GCs	12/16 (75%)	16/19 (84,21%)	28/32 (87,5%)	53/57 (92,98%)	0,2471
GCs mg/day	52 (±14,8)	40,1 (±35,8)	25,7 (±18,3)	45,9 (±141,9)	0,8460
HCQ n	5/16 (31,25%)	9/19 (47,37%)	22/32 (68,75%)	42/57 (73,68%)	**0,0069**
DMARDS	7/16 (43,75 %)	8/19 (42,11%)	13/32 (40,63%)	20/57 (35,09%)	0,8899
Assessment 1 year after diagnosis (T1)					
SLEDAI-2K	4 (±2,8)	3 (±1,7)	3,7 (±2,8)	3,9 (±3)	0,8833
SLEDAS	4,9 (±6,3)	1,4 (±0,6)	2,7 (±3,2)	4,1 (±5,7)	0,6523
SLICC	0 (±0,3)	0 (±0,2)	0 (±0,3)	0,1 (±0,3)	0,9219
LLDAS	1/8 (12,5%)	5/12 (41,67%)	5/25 (20%)	18/48 (37,50%)	0,2342
DORIS	1/8 (12,5%)	4/12 (33,33%)	5/25 (20%)	15/48 (31,25%)	0,5390
GCs	12/15 (80%)	15/17 (88,24%)	27/29 (93,10%)	53/57 (92,98%)	0,4397
GCs mg/day	16,7 (±13,3)	13,3 (±7,4)	15,3 (±11,7)	11,7 (±10,7)	0,6361
HCQ n	5/15 (33,33%)	7/17 (41,18%)	21/29 (72,41%)	48/56 (85,71%)	**< 0.0001**
DMARDS	7/14 (50%)	7/17 (41,18%)	16/28 (57,14%)	34/58 (58,62%)	0,6135
Assessment 5 years after diagnosis (T2)					
SLEDAI-2K	4,1 (±3,7)	4,5 (±3,3)	2,7 (±2,9)	2,1 (±2,2)	**0,0120**
SLEDAS	2,8 (±2,1)	2,9 (±3,5)	1,7 (±2,3)	2,9 (±6,1)	0,2324
SLICC	0 (±0,3)	0,2 (±0,3)	0 (±0,3)	0,3 (±0,5)	0,1950
LLDAS	1/11 (9,09%)	6/15 (40%)	16/25 (64%)	49/54 (90,74%)	**< 0.0001**
DORIS	1/11 (9,09%)	3/15 (20%)	14/25 (56%)	44/54 (81,48%)	**< 0.0001**
GCs	11/14 (78,57 %)	16/18 (88,89%)	26/30 (86,67%)	40/56 (71,43%)	0,2580
GCs mg/day	17,3 (±14,3)	9,3 (±6)	5,2 (±2,6)	4,9 (±6,2)	**< 0.0001**
HCQ n	4/14 (28,57%)	10/17 (58,82%)	22/30 (73,33%)	49/56 (87,5%)	**< 0.0001**
DMARDS	6/15 (40%)	8/17 (47,06%)	18/30 (60%)	39/56 (69,64%)	0,1185
Assessment 10 years after diagnosis (T3)					
SLEDAI-2K	3,9 (±2,6)	3,2 (±2,8)	2,6 (±2,6)	2,3 (±2,8)	0,0782
SLEDAS	3,8 (±4,3)	1,6 (±1,213)	2,1 (±2,6)	2,3 (±3,9)	0,3322
SLICC	0,4 (±0,5)	0,4 (±0,8)	0,1 (±0,3)	0,4 (±0,5)	0,1553
LLDAS	3/13 (23,08%)	11/15 (73,33%)	22/30 (73,33%)	23/31 (74,19%)	**0,0053**
DORIS	1/13 (7,69%)	9/15 (60%)	21/30 (70%)	22/31 (70,97%)	**0,0005**
GCs	14/16 (87,5%)	13/18 (72,22%)	23/31 (74,19%)	17/32 (53,13%)	0,0780
GCs mg/day	10,1 (±4,7)	4,9 (±2,4)	6,5 (±8,4)	0,4 (±0,5)	**0,0092**
HCQ n	7/16 (43,75%)	10/19 (52,63%)	25/31 (80,65%)	28/32 (87,5%)	**0,0022**
DMARDS	9/16 (56,25%)	6/19 (31,58%)	18/31 (58,06%)	25/32 (78,13%)	**0,0127**

Categorical variables were reported as proportion and/or percentage, continuous variables were expressed as mean (±standard deviation) values. Qualitative variables were compared with Chi-Squared or Fisher's exact test, quantitative variables with one-way Anova or Mann-Whitney test.

points. Qualitative variables were compared with Chi-Squared or Fisher's exact test, quantitative variables with one-way Anova or Mann-Whitney test

Results: Our cohort consisted of 119 females and 6 males; the mean age of onset was 30,62 years and the mean age of diagnosis was 31,95. Mean age of onset, and consequently mean age of diagnosis, has significantly increased in different groups (p=0,0011) (Figure 1). We observed a decreasing trend in the mean diagnostic delay from 28,25 months to 11,6 although without statistical significance (p=0,5015). Concerning the clinical presentation at onset, the most frequent symptoms observed were musculoskeletal (78,23%) and mucocutaneous (70,97%).

Evaluating patients at the time of diagnosis through the different decades (Figure 2), no significant changes were found in disease activity or damage, nor in the treatment except in the early use of HCQ: from less than 50% before 1999, to more than 70% of patients (p=0.0069). As for disease activity, a significant variation in the different decades appears at T2, with a reduction in SLEDAI (p=0.0120) and a higher number of patients reaching LLDAS and DORIS (both p< 0.0001); similar results were confirmed at T3 for both indexes. As for the use of GCs, no difference was observed in number of patients treated, although a significant reduction in GCs daily dose was observed at T2 and T3 (p< 0.0001 and p=0.0092 respectively). Finally, in patients with a more recent diagnosis, an increased use of HCQ (p< 0.0001 for T2 and p=0.0022 for T3) and DMARDS (p=0.0127 at T3) was observed during f-up

Conclusion: Our preliminary data demonstrated a progressive increase in the mean age at the onset of SLE over the years. However, this increase does not deviate from the mean age range defined in the literature [2].Moreover, our data reflect the therapeutic improvements of the past decades characterized by use of lower doses of GCs, increased use of HCQ and DMARDS and faster achievement of LLDAS and DORIS.

[1] Kapsala et al, CER 2023
[2] Sassi Rh et al, Clin Rheumatol 2017

Disclosure: M. Fredi: None; **S. Della Pina**: None; **C. Barison**: None; **C. Orlandi**: None; **M. Tedeschi**: None; **M. Chiara**: None; **C. Nalli**: None; **F. Franceschini**: None.

Abstract Number: 1452

Inflammatory Markers and Left Ventricular Dysfunction in Systemic Lupus Erythematosus (SLE)

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Women with SLE have an elevated risk of cardiovascular disease. Many women with SLE frequently report chest pain in the absence of obstructive coronary artery disease (CAD) due to coronary microvascular dysfunction (CMD), a form of ischemia with no obstructive CAD (Manchanda et al, 2022). Echocardiographic studies have shown that SLE patients have reduced left ventricular (LV) function, which may also correlate with higher SLE disease activity scores

Table 1: Baseline Characteristics of Female SLE Participants. There was no group difference in clinical and laboratory values in the SLE participants with and without CMD. Complement 3 (C3); Complement 4 (C4); Erythrocyte Sedimentation Rate (ESR); C-Reactive Protein (CRP); Antinuclear antibody (ANA); Ribonucleoprotein (RNP); Smith (Sm); Anti-topoisomerase I antibody (Scl-70).

Mean ±SD [range]	SLE patients (n=13)	CMD (n=5)	No CMD (n=8)	P values
Age	46 ± 6 years	43 [37-51] years	48 [43-57] years	NS
SLICC	1.9 ± 2.5	2.8 ± 3 [0-6]	1.4 ± 2 [0-6]	NS
SLEDAI	0.5 ± 1	0.8 ± 0.8 [0-2]	0.4 ± 1 [0-3]	NS
Clinical Labs				
Fasting Blood Sugar (mg/dl)	77.6 ± 8.6	80.2 ± 6.5 [72-90]	75.5 ± 10.1 [65-91]	NS
Fasting Insulin (mIU/ml)	9.2 ± 11.3	14.8 ± 15.4 [2-42]	4.5 ± 2.5 [1.4-7.6]	NS
Serum Creatinine (mg/dL)	0.70 ± 0.08	0.67 ± 0.12 [0.55-0.84]	0.72 ± 0.03 [0.66-0.76]	NS
Serum Protein (g/dL)	7.29 ± 0.96	7.58 ± 1.47 [6.4-10.1]	7.09 ± 0.40 [6.8-7.9]	NS
C3 (mg/dL)	114 ± 30	124 ± 34 [81-153]	108 ± 26 [77-156]	NS
C4 (mg/dL)	26 ± 12	20 ± 11 [10-32]	29 ± 12 [22-51]	NS
ESR (mm/hr)	20.5 ± 20.5	32 ± 24 [16-73]	14 ± 16 [1-47]	NS
CRP (mg/dL)	3.2 ± 4.8	2.6 ± 2.2 [0.4-5.4]	3.6 ± 6.0 [0.2-17.9]	NS
Anti-ANA	434 ± 273	424 ± 299 [50-640]	440 ± 277 [80-640]	NS
Anti-DNA	<10	<10	<10	—
RNP Antibody	42.3 ± 58	68 ± 70.4 [2-156]	26.3 ± 46.8 [2-133]	NS
Anti-Sm	13.9 ± 18.7	17.2 ± 20.6 [2-52]	11.9 ± 18.6 [1-51]	NS
SSA (Ro)	22.8 ± 38.6	42.8 ± 55 [2-104]	10.4 ± 19.2 [1-56]	NS
SSB (La)	12.2 ± 28.4	22.8 ± 45.5 [2-104]	5.5 ± 8.3 [1-25]	NS
Anti-Scl	6 ± 7	4.2 ± 3.3 [2-10]	1 ± 25 [1-25]	NS

Table 2: Comparison of Cardiac MRI Analysis between SLE Participants and Reference Controls (RC). Left Ventricular (LV) End Diastolic Volume (LVEDV); LV End Systolic Volume (LVESV); LV Systolic Volume (LVSV); Ejection Fraction (EF); LV Mass (LVM); LV End Systolic Diameter (LVESD); Body Surface Area (BSA); LVEDV/BSA (LVEDV index); LVESV/BSA (LVESV index); LVSV/BSA (LVSV index); LVM/BSA (LVM index); CO/BSA (cardiac index), Extracellular Volume Fraction (ECV).

Variable	SLE (n=13)	RC (n=22)	*p*-value
LVEDV (ml)	127 ± 34	114 ± 18	NS
LVESV (ml)	53 ± 20	42 ± 10	0.0339
LVSV (ml)	75 ± 18	73 ± 10	NS
EF (%)	59 ± 7	64 ± 5	0.0242
LVM/LVESD (g/dL)	0.66 ± 0.08	0.62 ± 0.07	NS
LVEDV/BSA (LVEDVi, mL/m2)	72.02 ± 15.4	67.40 ± 9.3	NS
LVESV/BSA (LVESVi, mL/m2)	29.9 ± 10.2	24.5 ± 5.6	0.0481
LVSV/BSA (LVSVi, mL/m2)	42.56 ± 8.2	42.92 ± 5.4	NS
LVM/BSA (LVMi, g/m2)	47.31 ± 9.3	41.34 ± 4.3	0.0141
CO/BSA (CI, L/min/m2)	3 ± 1	2.6 ± 0.3	NS
LVM (g)	83 ± 20	70 ± 9	0.0119
Radial Strain	29.70 ± 6.2	34.37 ± 5.8	0.0306
Circumferential Strain	-17.94 ± 2.5	-19.73 ± 2	0.0251
Longitudinal Strain	-18.40 ± 2.2	-20.10 ± 1.9	0.0202
T1	1263 ± 35	1259 ± 56 (n=11)	NS
ECV	29 ± 3	29.3 ± 2.3 (n=11)	NS

(Gegenava et al, 2020). As such, we used cardiac magnetic resonance imaging (cMRI) to investigate the relationship between SLE, related inflammatory biomarkers, and cardiac function in female SLE patients.

Methods: We performed stress cMRI in women with SLE and chest pain with no obstructive CAD (n=13, all met ACR 1997 criteria, **Table 1**) and reference controls (n=22) using our published protocol (Aldiwani et al, 2022). We evaluated LV function, tissue characterization (T1 mapping, ECV), and delayed enhancement, using CV142 software (Circle Cardiovascular Imaging Inc, Calgary, AB, Canada). Myocardial perfusion reserve index (MPRI) was calculated using our published protocol (Thomson et al, 2015). SLEDAI and SLICC Damage Index (DI) were calculated per validated criteria (Bombardier et al, 1992, Gladman et al, 1997). Serum samples were analyzed for inflammatory markers and autoantibodies (**Table 1**). Independent two-tailed t test was performed on clinical values with CMD and no CMD SLE subjects, and on cMRI values with all SLE subjects and controls. Correlation analysis was done on clinical values, and cMRI values on all SLE subjects.

Results: Overall, 40% of SLE subjects had MPRI values < 1.84, consistent with CMD. Compared to controls, SLE subjects had significantly lower LVEF, and higher LVESVi and LVMi (**Table 2**). Corresponding to this, radial, longitudinal, and circumferential strain were significantly lower in the SLE subjects. In correlation analysis of serum inflammatory biomarkers to cMRI values in the SLE subjects, SLICC DI was related to worse cardiac function (lower radial, circumferential and longitudinal strain) and higher T1 time (**Table 3**). Additionally, fasting insulin and ESR were negatively correlated with LVMi. Fasting insulin also negatively correlated with ECV. CRP had a positive association with LVESV index and CI and a negative association with longitudinal strain.

Table 3: Correlation analysis of cardiac function versus clinical values from SLE participants in the study. The Spearman r coefficient (r) and p value (p) is shown. Ejection Fraction (EF); Cardiac Output (CO); Left Ventricular (LV) Systolic Volume (LVSV); LV mass (LVM); Body Surface Area (BSA); Extracellular Volume (ECV); Systemic Lupus International Collaborating Clinics (SLICC) Damage Index; C-reactive Protein (CRP); Erythrocyte Sedimentation Rate (ESR).

		SLICC	CRP	Fasting Insulin	ESR
EF (%)	*r*	-0.54			
	p	*0.06*			
CO (L/min)	*r*		0.57		
	p		*0.04*		
LVSV/BSA (mL/m^2)	*r*		0.53		
	p		*0.07*		
CO/BSA (L/min/m^2)	*r*		0.57		
	p		*0.05*		
LVMASS/BSA (g/m^2)	*r*			-0.66	-0.60
	p			*0.03*	*0.03*
Radial Strain	*r*	-0.74			
	p	*0.00*			
Circumferential Strain	*r*	0.67			
	p	*0.01*			
Long strain	*r*	0.50	-0.53		
	p	*0.08*	*0.07*		
native T1	*r*	0.62			
	p	*0.03*			
ECV	*r*			-0.66	
	p			*0.03*	

Conclusion: Among women with SLE with chest pain and no obstructive CAD, 40% have CMD. While evaluations of known inflammatory markers (such as ESR and CRP) predictably correlated with decreased cardiac function (Lertratanakul et al, 2014), our study found that decreased fasting insulin levels is a novel marker associated with diminished LV function. In addition, although studies have used SLEDAI as a marker of disease activity when assessing cardiac dysfunction, we are the first to demonstrate that SLICC DI, an assessment of SLE damage, is also correlated with cardiac dysfunction in SLE. This indicates that SLE patients with higher SLICC DI and increased SLE-related damage could potentially have silent involvement in their cardiac tissue, and as such, SLICC DI is another tool that can be used to evaluate the association between SLE and LV dysfunction.

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Abstract Number: 1453

Musculoskeletal Involvement in Systemic Lupus Erythematosus: Insights from a Survey of Lupus Experts

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
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Session Time: 9:00AM–11:00AM

Background/Purpose: Musculoskeletal manifestations of systemic lupus erythematosus (SLE) are common, consisting ofarthralgia and arthritis (95%), myalgia/myositis (17%), tenosynovitis, and bursitis (12%). Joint involvement is a common reason for inclusion in SLE clinical trials. Involvement of ≥2 joints with pain and signs of inflammation satisfies 4 points required to meet trial entry criteria [SLE Disease Activity Index 2000 (SLEDAI-2K) ≥6 points and "Clinical" SLEDAI-2K ≥4 points). Likewise, the SRI-4 response which includes ≥4-point reduction in SLEDAI-2K score can be achieved through joint improvement alone and may allow patients with lower 'initial' joint counts to meet the response threshold of involvement of < 2 joints at the trial end with greater ease compared to those with higher entry joint counts. Additionally, not all joint symptoms in SLE patients are directly attributable to lupus, as comorbid osteonecrosis, osteoarthritis, and fibromyalgia can contribute to joint pain, and may not respond to SLE-directed therapy, thus influencing end-outcome attainment. To gain further perspectives into SLE joint involvement, a survey was conducted among lupus experts within the Lupus Clinical Investigators Network (LuCIN) network, a North American consortium of investigators from 54 academic sites who are actively involved in clinical trials.

Methods: The survey was created in Google Forms with questions focused on the most frequent reasons for therapy change in lupus, the frequency of specific joint involvements that prompted therapy change and enrollment into clinical trials, and the number of active joints necessitating a change in patient care (**Table 1**). The survey was disseminated via email to LuCIN investigators.

Results: Out of 54 LuCIN members, 26 responded to the survey. Joint involvement was identified as the most frequent reason for therapy change in non-renal SLE by 30.8% of respondents, and the 2nd and 3rd top reasons by 46.2% and 15.4% of respondents (**Figure 1**). The combination of joint and mucocutaneous manifestations was cited as the top reason for

Table 1. The survey questionnaire disseminated to the Lupus Clinical Investigators Network (LuCIN) Principal Investigators (PIs)

1. What are the top 3 reasons that have prompted you to change therapy in patients with SLE with non-renal disease?
a. Mucocutaneous manifestations (e.g., inflammatory-type rash, alopecia, oral or nasal mucosal ulcers) b. Musculoskeletal manifestations (tender and swollen joints) c. Combination of mucocutaneous and musculoskeletal manifestations d. Constitutional symptoms (fever, malaise, fatigue, loss of appetite, loss of weight) e. Others (please specify)
2. On a scale of 1 to 10, how frequently have the pain, tenderness and swelling of the following joints prompted you to consider changing the patient's care or enrolling them in a clinical trial?
a. Hand PIPs b. Hand MCPs c. Wrists d. Elbows e. Shoulders f. Feet joints (PIPs, MCPs) g. Ankles h. Knees i. Others
3. In your practice, how many of these active joints would require a change in patient's care when encountering such a situation?
a. Hand PIPs (0-10) b. Hand MCPs (0-10)
4. (Optional) If you have any additional comments regarding the topic of musculoskeletal manifestations in lupus, please share them here.

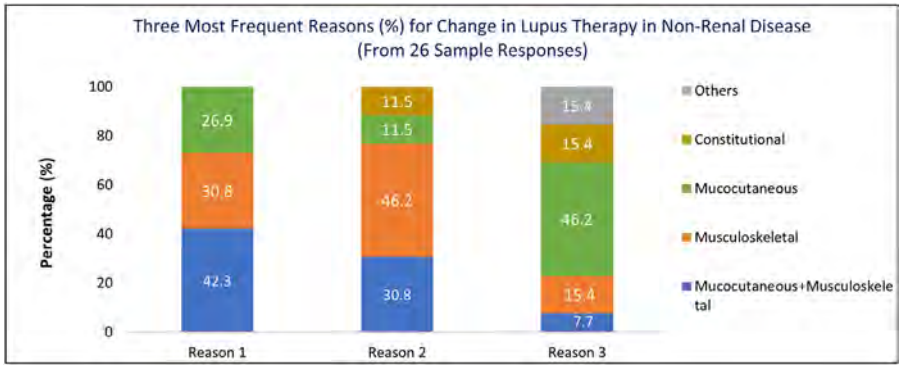

Figure 1. Top Reasons for Therapy Change in Non-Renal Lupus Patients in Clinical Care

therapy change by 42.3% (11/26). MCPs, hand PIPs, wrists, and knees were the joints most frequently associated with therapy change or enrollment in clinical trials (**Figure 2**). The respondents indicated that approximately 3- 4 active MCPs or hand PIPs would prompt a change in therapy.

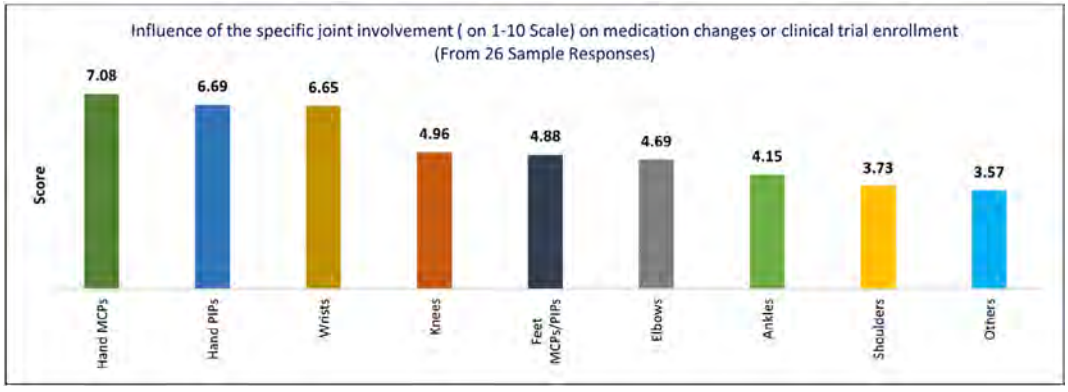

Figure 2. Influence of Specific Joint Involvement (on a 1-10 Scale) on Medication Changes or Clinical Trial Enrollment in Lupus

Conclusion: Joints and the combination of joint and mucocutaneous manifestations were identified as the most common reasons for therapy change in non-renal SLE. MCPs, hand PIPs, wrists, and knees were identified as joints most frequently associated with the decision to change therapy or enroll in a clinical trial. Future Directions: Understanding the pattern and extent of joint involvement over time using data from completed prospective clinical trials may contribute to a more comprehensive understanding of SLE joint manifestations and their influence on trial outcomes. Refined clinical assessment of joints using advanced imaging techniques may improve the characterization of joints and the assessment of interventions in both clinical practice and clinical trials.

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Abstract Number: 1454

Neuropsychiatric Systemic Lupus Erythematosus in Children: A Scoping Review

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SESSION INFORMATION

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Background/Purpose: Neuropsychiatric systemic lupus erythematosus (NPSLE) remains a challenging entity to diagnose and treat. The clinical heterogeneity of NPSLE coupled with the difficulty with attribution of neuropsychiatric symptoms to SLE contribute to the challenges in diagnosis. Furthermore, recommendations for diagnosis and treatment may be limited in their applicability to childhood-onset SLE (cSLE), as there are limited diagnostic tools and treatments and current evidence is largely extrapolated from adult studies. The objective of this scoping review is to review the current literature on NPSLE in cSLE (cNPSLE), grade the level of evidence and identify knowledge gaps in the scope of clinical manifestations, diagnosis, predictors, treatment, and outcomes of cNPSLE.

Methods: An exhaustive search was performed in MEDLINE, Embase, Cochrane, and PsycINFO. Articles were screened in Covidence. We included articles of systematic reviews, cohort, case-control and cross-sectional studies published between 2000 and 2022, studies involving children aged 18 years or younger diagnosed with NPSLE, and only original manuscripts available in English. Five reviewers performed abstract and full-text screening. Eight reviewers performed data extraction. Full text extraction was performed by two reviewers and any conflicts were resolved by a third reviewer. Thirty-four articles met our study eligibility criteria (Figure 1). The certainty of the evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology.

Results: Article characteristics are shown in Figure 2. The prevalence of cNPSLE ranged from 17% to 95%. The mean age in years was 13.7 +/- 4.6. The most common clinical manifestations were cognitive dysfunction (8-100%), headaches (13-85%), and seizures (19-84%). However, some studies did not classify mood disorders or headaches as NPSLE manifestations. Predictive factors of cNPSLE are shown in Table 1. Cerebral and cerebellar volume loss and white matter hyperintensities were the most common findings on MRI, though many patients with active cNPSLE had a normal MRI. PedANAM was the only validated screening tool to assess neurocognitive dysfunction in cNPSLE. Only one study focused primarily on treatment for cNPSLE; this was retrospective and focused on psychosis. Complete recovery of NSPLE ranged from 40-86%, and mortality from 5-45%. Causes of death included status epilepticus, cerebrovascular accident, infection, and brainstem encephalitis.

Conclusion: This scoping review addresses significant knowledge gaps about cNPSLE. Most studies were retrospective, single center studies, with low quality of evidence. The wide range in the prevalence and frequency of cNPSLE manifestations is likely due to the lack of consensus in methods for definition and evaluation of cNPSLE. The evidence of treatment

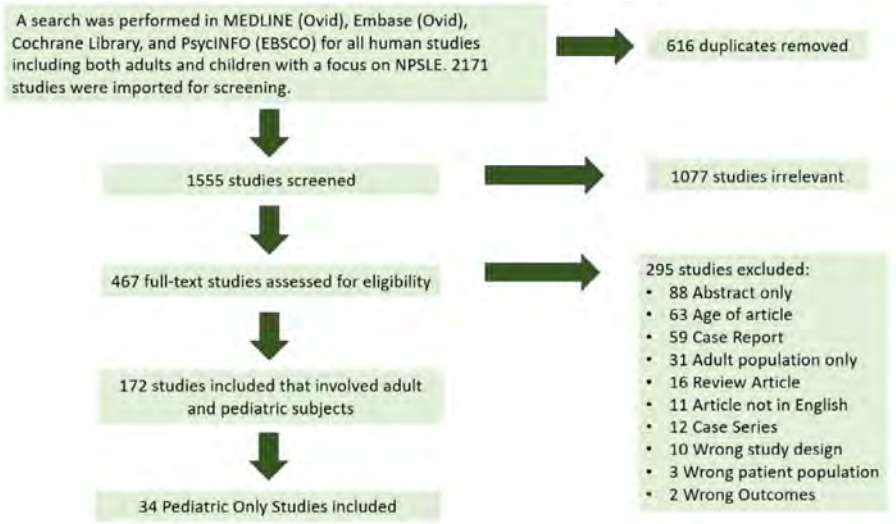

Figure 1: PRISMA Flow Diagram for Scoping Review

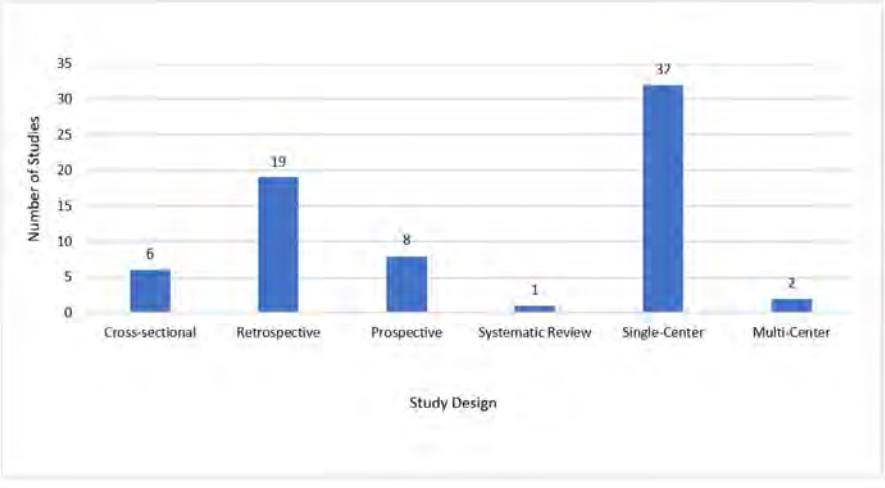

Figure 2: Characteristics of Studies focused on Neuropsychiatric Lupus in Children

Table 1: Articles focused on Predictive Factors for childhood-onset NPSLE

Author and Year	Predictive/Risk Factors	Results	Quality of Evidence
Avcin 2008	anti-B2GP1, LAC	The prevalence of anti-B2GP1 AB was higher in NPSLE compared to those without (p=0.02). There was a significant association between positive LAC and chorea (p=0.02).	Low
Brunner 2014	Serum AP-AB, S100A8/9, ANR2-AB, AGP1-AB, NGAL	aP-AB was more commonly present in SLE with neurocognitive dysfunction than without (p=0.05). There were negative associations between aP-AB, S100A8/9, aNR2-AB, aGP1-AB, and LAC and accuracy rates on Ped-ANAM subtests (p<0.05).	Low
Descloux 2009	Age	The frequency of NPSLE increased when age at disease onset decreased (p=0.037).	Low
Gomes 2016	Age	No differences of NPSLE in three age groups with rates of NPSLE 36%, 25%, and 24% (p=0.236).	Low
Khajezadeh 2018	DsDNA, Platelet count	Higher frequency of dsDNA elevation (p=0.03) and thrombocytopenia (p=0.02) in NPSLE. No difference between NPSLE and SLE as far as sex, age, mortality, or ANA titer (p>0.05).	Low
Knight 2015	Race	Non-White race and longer disease duration were independent risk factors for depression (OR = 3.7, 95% CI 1.5-9.3, P= .005; OR = 1.1, 95% CI 1.01-1.19, P= .02) and suicidal ideation (OR = 7.4, 95% CI 2.3-25.0, P= .001; OR = 1.1, 95% CI1.03-1.27, P= .006). Depression symptoms were associated with increased SLEDAI (OR = 1.1, 95% CI 1.1-1.2, P< .001).	Low
Lisa 2004	RANTES-28G allele	The RANTES −28G allele was more frequent in patients with SLE (23.9% vs 11%; p = 0.006, OR 2.37, 95% CI 1.25–4.28). Patients with −28 C/G RANTES gene had a higher rate of central nervous system SLE (p value not provided).	Low
Mondal 2010	Biologic Sex	The incidence of NPSLE in boys was more than that of girls (66.7% vs. 15.15%; p=0.005).	Very Low
Morsad 2010	HLA-Class II DRB1	Increased HLA-DRB1*15 allele in SLE compared to controls (p=0.004). No association between most frequent HLA-DRB1 alleles and clinical manifestations (including NPSLE) (p=0.41).	Very Low
Mostafa 2009	Antineuronal AB, EEG abnormalities, P300	Antineuronal AB was higher in SLE patients (60%) than controls (3.3%), (p<0.001). Antineuronal AB and abnormalities in EEG and P300 were higher in patients with NPSLE (p < 0.001).	Low
Mostafa 2010	Serum Anti-ganglioside M1 IgG AB, anti-ribosomal P	Patients with and without NPSLE had similar values of anti-ganglioside M1 IgG AB (P= 0.1). Clinical NPSLE had higher anti-ribosomal P AB than patients without clinical NPSLE (p<0.001).	Low
Nowling 2021	Serum Anti-NMDAR AB, Anti-Ribosomal P	Anti-NMDAR AB was higher in SLE patients compared to JIA (p=0.026) but were not associated with any measures of cognitive function in SLE compared with JIA (p>0.05).	Very Low
Singh 2009	Biologic Sex APLA	Male:Female ratio was higher in patients with NPSLE (1:1.125) compared to patients without (1:12), (P<0.0001). No difference in occurrence of APLA in patients with NP events compared to those without (p not provided).	Low
Ulloa 2022	GWAS PRS for Schizophrenia	An increase in GWAS PRS for schizophrenia was not associated with increased odds of having any NPSLE feature vs no features (OR 1.04, 95% CI 0.87–1.26, P = 0.62).	Moderate
Vyas, 2002	Presence of LN+NPSLE	Children with LN and NPSLE had a 5x higher progression rate to ESRD compared to children with LN alone (OR=5.7, P=0.007). There was a higher risk of death in patients with LN + NPSLE than LN alone (p<0.016).	Very Low
Yu, 2007	Lymphopenia, C3 level, DsDNA	Lymphopenia was independently associated with increased risk for NPSLE (OR 7.41, 95% CI 1.99–27.0, P < 0.003). C3 decrease and anti-dsDNA elevation was protective from NPSLE (OR 0.14, 95% CI 0.02-0.87, p=0.035 and OR 0.29, 95% CI 0.1-0.85, p=0.021)	Very Low
Zhu, 2018	SNP-eNOS GT	The genotype GT was higher in NPSLE than in the control group (p=0.028) and the genotype GT rs1808593 was related to pSLE with CNS damage (OR=6.24, 95% CI 1.17-33.15).	Low
Zuniga Zambrano 2014	LAC, APLS	APLS was a risk factor for NPSLE (p=0.03). There were differences regarding the presence of LAC and NPSLE (OR 3.66, 95% CI 1.33-10.03, p=0.01).	Low

AB – antibody; ANA – anti-nuclear antibody; APLA – antiphospholipid antibody; APLS – antiphospholipid syndrome; anti-B2GP1 – anti-beta-2-glycoprotein antibody; CI – confidence interval; CNS – central nervous system; dsDNA – double-stranded DNA; EEG – electroencephalogram; ESRD – end-stage renal disease; GWAS – genome-wide association study; JIA – juvenile idiopathic arthritis; LAC – lupus anticoagulant; LN – lupus nephritis; NMDAR – anti-N-methyl-d-aspartate receptor; NPSLE – neuropsychiatric systemic lupus erythematosus; NP – neuropsychiatric; OR – odd's ratio; SLE – systemic lupus erythematosus; SNP-eNOS – single nucleotide polymorphism of endothelial nitric oxide synthase

for cNPSLE is also sparse. We highlight the need for further prospective, multicenter studies, and consensus regarding approaches to cNPSLE investigation and management. The results of this work also provide the literature background (first phase) in a project to develop a multi-disciplinary, patient-centered prioritized research agenda for cNPSLE.

Disclosure: A. Theisen: None; **E. Ogbu**: None; **E. Beil**: None; **O. Harry**: None; **S. Appenzeller**: None; **R. Kammeyer**: None; **H. Van der Heijen**: None; **A. Knight**: Pfizer, 6; **H. Craven**: None; **M. Rodriguez**: None.

Abstract Number: 1455

Risk Factors of Cytomegalovirus Reactivation and Disease in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

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Background/Purpose: Cytomegalovirus (CMV) infection is classified as an opportunistic infection that occurs in autoimmune diseases. Systemic lupus erythematosus (SLE) is one of the most frequently reported autoimmune diseases that cause CMV reactivation, but no studies have examined the risk factors in patients with SLE. This study aimed to identify the risk factors of CMV reactivation and disease in patients with SLE undergoing remission induction therapy.

Methods: This study reviewed patients with SLE who received remission induction therapy at our institution from May 2010 to October 2022 and enrolled patients whose CMV pp65 antigen levels were measured within 3 months of admission. Patients with CMV reactivation were divided into two groups, namely, CMV disease (presence of symptoms or end-organ disease) and asymptomatic CMV reactivation. We examined the risk factors associated with CMV reactivation and disease.

Results: CMV reactivation was observed in 64 out of 130 patients. Univariate analysis revealed the association between CMV reactivation and old age (46.5 vs. 39.5; P = 0.02), lower serum albumin levels at admission (2.9 vs. 3.3; P< 0.001), higher Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) (17 vs. 10; P = 0.001) at admission, and increased steroid pulse therapy (64.1% vs. 45.5%; P = 0.04) and immunosuppressive drug use (70.3% vs. 50.0%; P = 0.02) (Table 1). Log-rank tests on the above factors revealed significant differences for all except for steroid pulse therapy. Moreover, the Cox proportional hazards regression analysis on the four factors revealed the association of old age (hazard ratio [HR]: 2.03, 95% confidence interval [CI]: 1.09–3.78, P = 0.026), lower albumin (HR: 2.35, 95% CI: 1.09–5.07, P = 0.029),

Table 1. Risk factors of CMV reactivation

	CMV reactivation		
	(+) n=64	(-) n=66	P-value
Age (years)	46.5 (35.8-62.3)	39.5 (31.0-55.8)	0.02
Female, n, (%)	51.0 (77.2%)	49.0 (76.6%)	1.00
BMI (kg/m^2)	20.7 (18.7-23.2)	20.4 (18.9-22.8)	0.69
New-onset SLE, n, (%)	33.0 (51.6%)	27.0 (40.9%)	0.29
SLEDAI	17.0 (9.75-21.0)	10.0 (7.25-15.8)	0.001
Serum albumin (g/dL)	2.90 (2.38-3.30)	3.30 (2.93-3.80)	<0.001
Anti-dsDNA antibodies (IU/mL)	15.3 (3.90-70.8)	20.0 (1.80-84.6)	0.52
Prednisolone dose at admission (mg/kg/day)	0.00 (0.00-0.21)	0.07 (0.00-0.27)	0.38
Use of pulsed methylprednisolone, n (%)	41.0 (64.1%)	30.0 (45.5%)	0.04
Use of immunosuppressant, n, (%)	45.0 (70.3%)	33.0 (50.0%)	0.02
Platelet ($\times 10^4$/μL)	16.4 (9.50-20.6)	15.8 (10.6-20.7)	0.90
Lymphocyte (/μL)	565 (285-919)	590 (317-881)	0.41
Hb (g/dL)	10.6 (8.80-12.0)	11.1 (9.53-12.5)	0.17
CRP (mg/dL)	0.75 (0.18-1.67)	0.44 (0.08-1.89)	0.28
IgG (mg/dL)	1846 (1341-2468)	1617 (1211-2111)	0.13
C3 (mg/dL)	54.0 (35.3-76.8)	58.0 (49.0-78.0)	0.40
C4 (mg/dL)	9.90 (4.50-18.4)	10.1 (6.20-17.8)	0.74

higher SLEDAI (HR: 1.73, 95% CI: 1.00–2.98, P = 0.048), and immunosuppressive drug use (HR: 1.94, 95% CI: 1.12–3.35, P = 0.018) with CMV reactivation. Receiver operating characteristic (ROC) curve analysis using the above four factors revealed that the sensitivity and specificity were 82.8% and 60.6%, respectively (area under the curve = 0.748, 95% CI: 0.664–0.831) for CMV reactivation when all four factors were present. The log-rank test revealed that CMV reactivation developed more frequently when two or more risk factors were present (Figure 1). Among the 64 cases with CMV reactivation, an increased number of CMV pp65 antigen-positive cells was found in the 25 cases with CMV disease than the 39 cases without the disease (6 vs. 2; P = 0.02) (Table 2). ROC curve analysis revealed that the cutoff value for organ damage development was 12 cells out of 2 slides (sensitivity: 36.0% and specificity: 94.9%).

Conclusion: Old age, low albumin levels, high disease activity, and the use of immunosuppressive drugs are possible risk factors of CMV reactivation in patients with SLE. CMV pp65 antigen-positive cells of 12 per 2 slides were determined for the diagnosis of CMV disease.

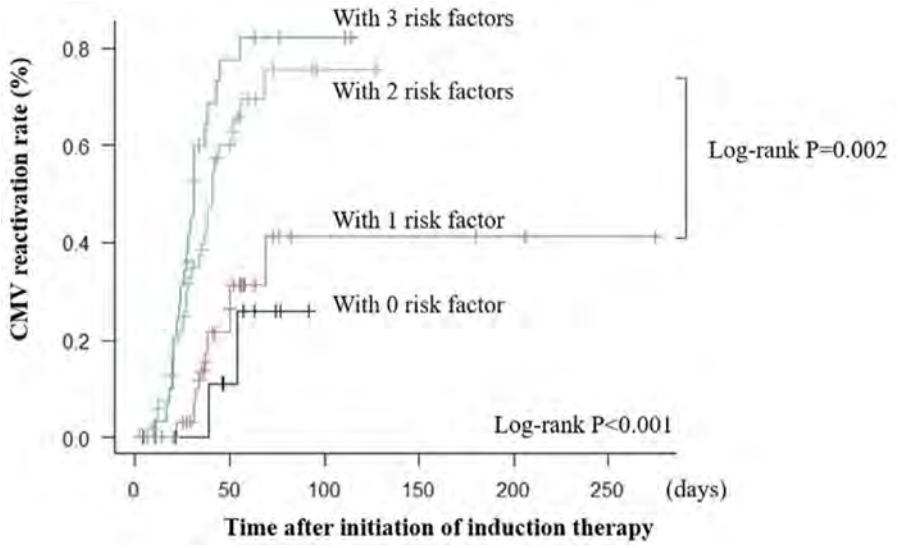

Figure 1. Cumulative probability of CMV reactivation depending on the number of risk factors

Table 2. Comparison of patients with and without CMV disease

	CMV reactivation with disease n=25	CMV reactivation without disease n=39	P-value
Age (years)	48.0 (40.0-62.0)	45.0 (34.0-62.0)	0.60
Female, n, (%)	20.0 (80.0%)	29.0 (74.4%)	0.77
BMI (kg/m^2)	20.8 (20.0-23.0)	20.5 (18.3-23.4)	0.58
New-onset SLE, n, (%)	12.0 (48.0%)	21.0 (53.8%)	0.80
SLEDAI	17.0 (11.0-20.0)	17.0 (9.50-21.0)	0.89
Anti-dsDNA antibodies (IU/mL)	28.8 (3.80-137)	13.4 (4.15-67.9)	0.73
Days from induction remission therapy to reactivation (days)	29.0 (19.0-37.0)	31.0 (22.5-41.0)	0.32
CMV pp65 antigenemia (/3 × 10^5 PMNs)	6.00 (1.00-16.0)	2.00 (1.00-6.00)	0.02
Prednisolone dose at reactivation (mg/kg/day)	0.93 (0.78-1.02)	0.86 (0.70-0.98)	0.38
Use of pulsed methylprednisolone, n (%)	15.0 (62.5%)	26.0 (66.7%)	0.79
Total prednisolone dose (mg)	2145 (1448-3525)	2788 (1493-3525)	0.66
Use of immunosuppressant, n, (%)	18.0 (72.0%)	27.0 (69.2%)	1.00
Serum albumin (g/dL)	2.90 (2.40-3.30)	3.00 (2.40-3.35)	0.76
Platelet (× 10^4/μL)	16.2 (8.60-25.6)	16.8 (9.90-19.2)	>0.99
Lymphocyte (/μL)	608 (222-1069)	533 (315-782)	0.53
Hb (g/dL)	11.1 (8.70-11.8)	10.2 (8.80-12.0)	0.76
CRP (mg/dL)	0.91 (0.36-1.45)	0.48 (0.14-2.54)	0.69
IgG (mg/dL)	1549 (1311-2389)	2089 (1501-2673)	0.31
C3 (mg/dL)	58.0 (46.0-77.0)	48.0 (30.0-76.0)	0.28
C4 (mg/dL)	12.0 (4.00-20.6)	8.60 (4.75-17.0)	0.69

Disclosure: M. Wakatsuki: None; **H. Yamashita**: None; **Y. Akiyama**: None; **S. Oyama**: None; **S. Aozaki**: None; **R. Kuwata**: None; **M. Yamaji**: None; **T. Harada**: None; **K. Motomura**: None; **Y. Nakamichi**: None; **H. Kaneko**: None.

Abstract Number: 1456

Systematic Review of Effects of Systemic Lupus Erythematosus on Brain Structure and Structural Connectivity and Its Relationship with Cognitive Dysfunction Through an Advanced Neuroimaging Lens

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SESSION INFORMATION

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Background/Purpose: Cognitive dysfunction (CD) is highly prevalent in systemic lupus erythematosus (SLE), and advanced structural magnetic resonance imaging (MRI) has revealed brain abnormalities in patients with SLE. We conducted a systematic review of advanced neuroimaging studies to investigate the relationship between structural neuroimaging metrics and CD in SLE.

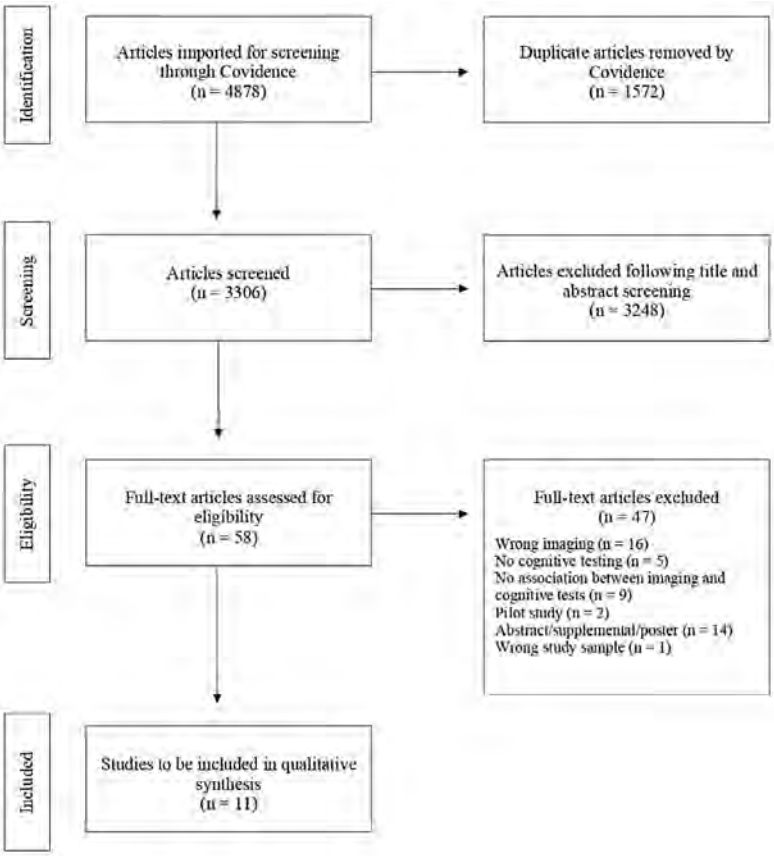

Figure 1: PRISMA flow diagram of the assessed studies.

Methods: A literature search was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The search was performed in PUBMED, MEDLINE, EMBASE, Web of Science, and COCHRANE, between January 2000 and April 2022. Both free-text and expanded medical subject headings were used. The search strategy was developed by the research team with the aid of an experienced librarian and included the following terms: systemic lupus erythematosus (SLE), neuropsychiatric lupus (NPSLE), CNS lupus, magnetic resonance imaging (MRI, sMRI), DRI/dMRI, diffusion tensor imaging (DTI), diffusion-weighted imaging (DWI), brain volume, voxel-based morphometry (VBM), cortical thickness, surface area, tractography, fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD). We included observational, case series, cohort, cross-sectional, longitudinal, retrospective, and prospective studies, and selected for neuroimaging studies using MRI and DTI investigating structural brain correlates of cognitive function in SLE.

Results: We identified 11 articles meeting search criteria (Figure 1); including two longitudinal studies and only one study in childhood-onset SLE (cSLE). Sample sizes ranged from 22 to 119 (SLE samples, n=11 to 75), and 8 studies included non-SLE controls. Neuroimaging techniques and neurocognitive assessments differed across studies. Structural MRI analysis (n=4 studies) showed cognitive impairment in patients with SLE was associated with overall gray and white matter atrophy, as well as regional atrophy (Table 1). DTI and DWI analyses (n=7 studies) showed associations between cognitive impairment and white matter microstructural changes consistent with tissue disorganization/damage of several regions, in SLE patients with and without NPSLE (Table 1).One longitudinal study found progressive regional atrophy over an average 19-month interval, and the other found stable white matter microstructure over an average 15-month interval.

Table 1: Associations between cognitive impairment and regional brain structural metrics in SLE.

Impaired Cognitive Domains	Structural MRI - Regional Atrophy	Diffusion Tensor/Diffusion-weighted Imaging - White Matter Microstructure Findings*
General Cognition	Bilateral hippocampi, left amygdala (2) Overall gray and white matter (3)	- ↑ mean diffusivity (1), and ↓ density, strength, global efficiency, and clustering coefficient (5) of overall white matter - ↓ fractional anisotropy (FA) in right external capsule (8) - NPSLE (neuropsychiatric SLE): ↓ FA in thalamic radiation, corpus callosum, longitudinal fasciculus, forceps major, corona radiata (8)
Executive Function		- NPSLE: ↓ FA in thalamic radiation and longitudinal fasciculus (8) - NPSLE: ↑ FA in the superior white matter pathways (10)
Memory	Left supramarginal superior temporal gyri; right superior frontal, caudal, and rostral middle frontal and precentral gyri (episodic memory) (11)	- NPSLE: ↓ FA in longitudinal fasciculus (verbal memory) and fronto-occipital fasciculus/forceps minor/longitudinal fasciculus (visual memory) (8) - ↓ FA in bilateral parahippocampal area (spatial memory) (9)
Attention		- ↑ free water in callosal regions, fronto-parietal pathway, fronto-temporal pathway, fronto-occipital pathway, cingulum (7) - NPSLE: ↓ FA in corpus callosum, longitudinal fasciculus, major forceps (8)
Visuo-constructual ability		- childhood-onset SLE (cSLE): ↑ blood flow in posterior precuneus (6)
Psychomotor Speed	Left cerebellum (4)	- cSLE: ↑ parenchymal diffusion of water and higher blood flow in posterior precuneus (6)
Processing Speed		- NPSLE: ↓ FA in thalamic radiation, corpus callosum, longitudinal fasciculus, forceps major, corona radiata (8)

*Metrics for white matter microstructure: higher mean diffusivity, lower fractional anisotropy, and increased free water indicate loss of directionality of diffusion due to tissue disorganization/damage.

Included Articles:

1. Wiseman et al. Lupus. 2017;26(6):588-597.
2. Zimmerman et al. *Clin Neuroradiol*. 2017;27(1):23-29.
3. Appenzeller et al. *Neuroimage*. 2007;34(2):694-701.
4. Mårtensson et al. *Brain Sci*. 2021;11(4):510.
5. Wiseman et al. *Lupus*. 2018;27(8):1329-1337.
6. DiFrancesco et al. *Arthritis Res Ther*. 2020;22(1):135.
7. Qian et al. *Rheumatology (Oxford)*. 2022;61(3):1166-1174.
8. Jung et al. *PLoS One*. 2012;7(1):e28373.
9. MacKay et al. *JCI Insight*. 2019;4(1):e124002.
10. Cesar et al. *AJNR Am J Neuroradiol*. 2015;36(10):1874-1883.
11. Bizzo et al. *J Neuroimaging*. 2017;27(1):122-127.

Conclusion: Studies identified in this systematic review showed abnormalities in brain structure in SLE associated with CD. Limitations included small cross-sectional samples, difficulty in comparing findings across studies due to lack of uniformity in neuroimaging techniques and neurocognitive assessments, and the paucity of pediatric data. Larger, longitudinal studies utilizing standardized measures in both adults and children are needed to better understand the impact of SLE on the brain structure and function across the age spectrum.

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Abstract Number: 1457

Obesity Is an Independent Poor Prognostic Factor in Lupus Nephritis

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SESSION INFORMATION
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Session Type: Poster Session B
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Background/Purpose: Up to 50% of patients suffering from systemic lupus erythematosus (SLE) develop lupus nephritis (LN) within the first 10 years of diagnosis and 5 to 20% of them progress to end-stage kidney disease (ESKD) (1,2). Several poor prognostic factors have been identified, such as the presence of tubulointerstitial and/or vascular lesions, a high chronicity index (3), African American descent (4), hypertension (5), absence of renal remission (3),(5) and renal flare(s) (6). Obesity, *per se*, is a risk factor for chronic kidney disease (CKD).Thus, obesity-related glomerulopathy in patients with a body mass index (BMI) ≥30kg/m^2(7)progresses to CKD in up to 50% of the cases (8). In addition, obesity is a risk factor for progression of primary glomerular diseases, such as IgA nephropathy (IgAN) (9). Whether obesity contributes to CKD risk in LN has never been investigated, to the best of our knowledge. We took advantage of the Louvain LN Inception cohort to test this hypothesis.

Table 1. Time-dependent proportional hazards (Cox) regression analysis

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*p*-Value	OR	95% CI	*p*-Value
Male	0.96	0.29-3.16	0.950	-	-	-
Caucasian	-	-	-	-	-	-
African	2.96	1.24-7.06	**0.015**	9.46	3.14-28.44	**<0.001**
Maghrebian	1.43	0.43-4.80	0.563	-	-	-
Asian	0.40	0.05-2.94	0.365	-	-	-
Smoke	1.63	0.79-3.34	0.183	-	-	-
Diabetes	1.60	0.38-6.74	0.525	-	-	-
Hypertension	2.25	1.12-4.50	**0.023**	1.67	0.74-3.76	0.216
Obesity	2.72	1.12-6.65	**0.028**	4.23	1.32-13.59	**0.015**
UPCR at baseline	1.08	0.99-1.18	0.068	1.07	0.95-1.19	0.256
ISN/RPS Class						
III-IV±V	-	-	-	-	-	-
V	0.98	0.23-4.14	0.981	-	-	-
Absence of remission	0.11	0.05-0.25	**<0.001**	0.03	0.01-0.09	**<0.001**
Relapse	1.62	0.80-3.29	0.184	-	-	-

Methods: We retrospectively studied 132 patients with biopsy-proven class III, IV or V incident LN followed for a median period of 140 months (min. 25). Remission was defined as a urine protein to creatinine (uP:C) ratio < 0.5 g/g and a serum creatinine value < 120% of baseline. Renal relapse was defined as the reappearance of a uP:C >1 g/g, leading to a repeat kidney biopsy and treatment change. Poor long-term renal outcome was defined as the presence of CKD. Unpaired

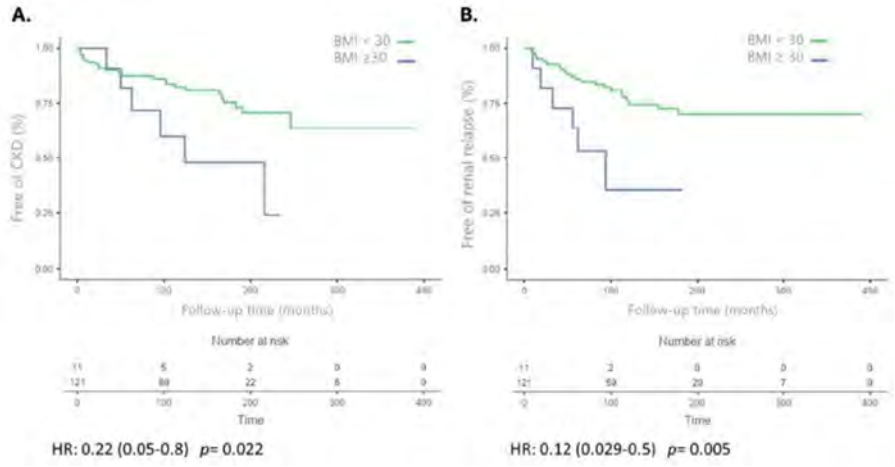

Figure 1. Kaplan-Meier analysis of the probability of survival without CKD (A) and relapse (B) in obese patients compared with non-obese patients. Survival curves were compared with the log-rank test. Hazard ratio (HR) (95% Confidence interval (CI)). Numbers shown on the abscissa are the numbers of patients at risk in each group at each time point.

References

1. Anders HJ, Saxena R, Zhao M-H, Parodis I, Salmon JE, et al. Lupus nephritis. *Nat Rev Dis Primers*. 2020;6:7
2. Fanouriakis A, Kostopoulou M, Cheema K, Anders HJ, Aringer M, et al. 2019 Update of the Joint European League against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of lupus nephritis. *Ann Rheum Dis*. 2020;79:S713–23.
3. Rodríguez-Almaraz E, Gutiérrez-Solís E, Rabadán E, Rodríguez P, Carmona L, et al. Something new about prognostic factors for lupus nephritis? A systematic review. *Lupus*. 2021;30:2256–67.
4. Enfrein A, Pirson V, Le Guern V, Karras A, Tamirou F, et al. Worse long-term renal outcome of lupus nephritis patients of African descent living in Europe. *RMD Open*. 2022;8:e002386.
5. Galindo-Izquierdo M, Rodriguez-Almaraz E, Pego-Reigosa JM, López-Longo FJ, Calvo-Alén J, et al. Characterization of patients with lupus nephritis included in a large cohort from the Spanish society of rheumatology registry of patients with systemic lupus erythematosus (RELESSER). *Medicine*. 2016;95:e2891.
6. El Hachmi M, Jadoul M, Lefèbvre C, Depresseux G, Houssiau FA. Relapses of lupus nephritis: Incidence, risk factors, serology and impact on outcome. *Lupus*. 2003;12:692–6.
7. Weisinger JR, Kempson RL, Eldridge FL, Swenson RS. The Nephrotic Syndrome: A Complication of Massive Obesity. *Ann Intern Med*. 1974;81:440-7.
8. Praga M, Hernández E, Morales E, Peréz A, et al. Clinical features and long-term outcome of obesity-associated focal segmental glomerulosclerosis. *Nephrol Dial Transplant*. 2001;16:1790-8.
9. Zhang J, Wang Y, Liu Z, Huang B, Wang X,et al. Overlapping obesity-related glomerulopathy and immunoglobulin A nephropathy: clinical and pathologic characteristics and prognosis. *Clin Exp Nephrol*. 2021;25:865–74.

t-tests, Wilcoxon's signed rank tests, chi-square tests, Fisher's exact tests, log-rank test and Cox regression were used as appropriate.

Results: The majority of patients were women (89%) and Caucasian (70.5%). Thirty-two patients (24%) developed CKD. Their baseline characteristics did not differ from those without CKD. Nine patients (6.8%) developed ESKD. Eleven patients (8.3%) suffered from obesity, defined by a body mass index (BMI) ≥30kg/m^2. Of note, "dry" weight was considered for patients presenting with oedema related to nephrotic syndrome. None of the obese patients was pregnant at disease onset. Renal remission was achieved in 90% of the cases, but 54% relapsed. Only one obese patient died from lupus-related macrophage activation syndrome. Obesity significantly increased long-term CKD risk [OR= 4.23 (IC95% 1.32-13.59), p = 0.015]. As shown in Table 1, obesity was an independent risk factor of CKD, as were African descent and absence of remission. Time-to-CKD and time-to-renal relapse were shorter in obese patients compared to non-obese patients (Fig 1). By Cox regression, factors independently associated with CKD were African descent, hypertension, absence of remission and obesity, as shown in **Table 1**.

Conclusion: A BMI ≥30 kg/m^2 is an independent poor prognostic factor for CKD in LN and is associated with shorter time to renal relapse. More attention should therefore be paid to weight control in LN patients.

Disclosure: F. Cuervo Gutiérrez: None; **A. Enfrein**: None; **F. Houssiau**: None; **F. Tamirou**: None.

Abstract Number: 1458

Activated Naïve DNA-Reactive B Cells in Lupus Nephritis Patients Are Increased and Associated with Disease Activity

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
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Background/Purpose: Lupus nephritis (LN) is one of the most severe manifestations of systemic lupus erythematosus (SLE), which is characterized by abnormal B-cell activation and their subsequent differentiation into autoreactive plasma blasts/cells. The heterogeneity of autoreactive B cell subsets and their contribution to the pathogenesis of LN are not well elucidated.

Methods: Thirty-five SLE patients, including twenty-eight with positive anti-dsDNA antibodies (80%), and fifteen healthy controls were recruited in this study. Data are represented as median and interquartile range (IQR). To identify DNA-reactive B cells, a surrogate peptide (DWEYSVWLSN) that serves as dsDNA mimotope was used, as previously shown (*Jacobi, Annett M et al. 2009* and *Wangriatisak, Kittikorn et al. 2021*). The phenotype of peripheral B cell subsets (SLE, n = 37 from 35 patients and HCs, n = 15) and DNA-reactive B cells (SLE, n = 10 and HCs, n = 6) was analyzed by spectral flow cytometry. Correlations between different B-cell subsets and Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score, clinical manifestations, and laboratory parameters were assessed.

Results: In SLE patients, the median SLEDAI-2K score was 9 (4-17), median age and disease duration were 34 (28-46) and 9 (1.5-13.0), respectively. Twenty-one patients presented with lupus nephritis (LN), with proliferative (class III, n = 3 and class IV, n = 4), membranous (class V, n = 7) and mixed histological patterns (class III & V, n = 5 and class IV & V, n = 2). Phenotypic analyses showed an expansion of circulating activated naïve (aNAV: $CD11c^{+}CD21^{-}CD27^{-}IgD^{+}$, $p < 0.01$), double negative 2 B cells (DN2: $CD11c^{+}CD21^{-}CD27^{-}IgD^{-}$, $p < 0.05$) and plasmablasts (PB: $CD27^{hi}CD38^{hi}$, $p < 0.05$) in LN patients, especially in class V, compared to non-LN and age-matched HCs. Intriguingly, an upregulation of CD71, as well as a downregulation of CD95, was observed on both DN2 and PB from patients with LN. Further analysis showed that expansion of DNA-reactive B cells was observed in LN patients (median (IQR): 0.13% (0.095-0.160)) compared with non-LN patients (median (IQR): 0.056% (0.042-0.070), $p < 0.05$). Surprisingly, the majority of these autoreactive cells were mostly represented by an activated naïve phenotype ($CD11c^{+}CXCD5^{-}CD21^{-}$), which was more frequent in patients with LN. The percentage of aNAV B cells were positively associated with DN2 ($r = 0.567$, $p = 0.0003$) and PB ($r = 0.498$, $p = 0.002$), especially in patients with LN. These expanded aNAV, DN2 and PB showed a significant positive correlation with the SLEDAI-2K index, and were inversely correlated with C3 and C4 levels in LN patients. Furthermore, DN2 and aNAV B cells were expanded in anti-dsDNA positive patients, while a lower frequency of such cells was found in anti-Smith positive patients.

Conclusion: Our data show that aNAV B cells display autoreactivity to dsDNA. The cooperation between these cells and DN2 and PB might be involved in the generation of anti-dsDNA antibody in LN which proceed of these B cell responses might via the extrafollicular pathway.

Disclosure: K. Wangriatisak: None; **F. Faustini**: None; **C. de Vries**: None; **R. Kumar Sharma**: None; **C. Grönwall**: None; **P. Pisitkun**: None; **P. Chootong**: None; **V. Malmström**: Eli Lilly, 1, Janssen, 5, ONO, 1, Pfizer, 5; **I. Gunnarsson**: None.

Abstract Number: 1459

Unveiling the Impact of Neuropsychiatric Involvement in Systemic Lupus Erythematosus on Damage Accrual

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SESSION INFORMATION

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Background/Purpose: The link between neuropsychiatric involvement in systemic lupus erythematosus (NPSLE) and heightened morbidity, mortality, and organ damage, as well as detrimental impacts on health-related quality of life has been well-documented. However, the direct association between NPSLE and specific SLICC/ACR damage index (SDI) items, especially non-neuropsychiatric items, remains unclear. Herein, we sought to investigate the impact of NPSLE on organ damage accrual in a large lupus cohort.

Methods: We conducted an analysis of baseline data derived from five phase III trials (BLISS-52, BLISS-76, BLISS-SC, BLISS-NEA, EMBRACE), encompassing a total of 3645 SLE participants. NPSLE involvement was defined as NP BILAG A/B/C/D or scores on any of the NP SLEDAI-2K domains (n=372); the non-NPSLE group comprised patients with NP BILAG E and no neuropsychiatric involvement based on the NP SLEDAI-2K domains (n=3273). We employed univariable logistic regression analysis in case of < 30 events, or multivariable analysis to adjust for age, disease duration, sex, and ethnic origin in all other cases.

Results: The median; mean (IQR; SD) SDI score and SLE disease duration were 0.0; 0.6 (0.0–1.0; 1.1) and 4.5; 6.4 (1.6–9.3; 6.3) years, respectively. Compared with the non-NPSLE group, SLE patients with neuropsychiatric involvement had greater SDI scores (adjusted (a)OR: 2.7; 95% CI: 2.1–3.4; p< 0.001). This held true also after suppression of the NPSLE SDI items from the total SDI score (aOR: 1.5; 1.2–1.9; p< 0.001). As expected, neuropsychiatric involvement was associated with damage in the neuropsychiatric domain (aOR: 8.7; 6.6–11.4; p< 0.001). More importantly, neuropsychiatric involvement was associated with damage in the cardiovascular (aOR: 2.4; 1.6–3.7; p< 0.001), musculoskeletal (aOR: 1.8; 1.3–2.4; p< 0.001), and skin (aOR: 1.5; 1.0–2.1; p=0.050) domains. Dissecting the non-neuropsychiatric SDI domains into specific items, neuropsychiatric involvement was associated with established damage in terms of coronary artery disease (aOR: 2.8; 1.3–6.2; p=0.007), myocardial infraction (aOR: 2.9; 1.4–6.0; p=0.004), valvular disease (OR: 4.9; 1.7–14.8; p=0.004), muscle atrophy (aOR: 3.2; 2.1–4.9; p< 0.001), bowel infarction (aOR: 1.8; 1.1–3.0; p=0.018), and scarring alopecia (aOR: 1.7; 1.1–2.6; p=0.013). Lastly, SLE patients with neuropsychiatric involvement were more likely to have developed premature gonadal failure (aOR: 2.0; 1.1–3.7; p=0.032) compared with SLE patients with no history of neuropsychiatric events.

Conclusion: The intricate association between neuropsychiatric involvement in SLE and damage accrual extends beyond the realm of the nervous system, impacting the musculoskeletal, skin, and cardiovascular organ systems. Prospective research, especially survey in non-selected real-world SLE cohorts, would be required to determine the causal relationship between NPSLE and the various components of the SDI. Clarifying this association would contribute to a more comprehensive understanding of the disease and facilitate more targeted management strategies for individuals affected by NPSLE.

Disclosure: D. Nikolopoulos: None; **N. Cetrez**: None; **J. Lindblom**: None; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia Pharmaceuticals, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Elli Lilly and Company, 5, 6, F. Hoffmann-La Roche AG, 5, 6, Gilead Sciences, 5, 6, GSK, 5, 6, Janssen Pharmaceuticals, 5, 6, Novartis, 5, 6, Otsuka Pharmaceutical, 5, 6.

Abstract Number: 1460

Impact of Neuropsychiatric Involvement on Health-related Quality of Life in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
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Background/Purpose: Substantial proportions of systemic lupus erythematosus (SLE) patients report severe fatigue and adverse Health-related Quality of Life (HRQoL). Particularly neuropsychiatric manifestations have been associated with reduced HRQoL. Our objective was to investigate patient-reported outcomes in patients with neuropsychiatric SLE (NPSLE) in comparison to SLE patients without neuropsychiatric involvement.

Methods: We analysed baseline data from four phase III trials (BLISS-52, BLISS-76, BLISS-SC, EMBRACE; N=2968). The NPSLE group comprised individuals with NP BILAG scores A/B/C/D (N=350). The active NPSLE group was defined as individuals with NP BILAG scores A/B or active neuropsychiatric involvement based on NP SLEDAI-2K domains (n=71). The non-NPSLE group consisted of patients with NP BILAG score E (N=2621). HRQoL was assessed utilising the generic instruments Medical Outcomes Study Questionnaire Short Form 36 (SF-36) health survey, the three-level version of EQ-5D (EQ-5D-3L), and the Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue (FACIT-F) scale. Full health state (FHS) was defined as an experience of "no problems" in all five EQ-5D dimensions. Impaired HRQoL by EQ-5D was defined as level 2 or 3 responses in the different dimension.

Results: We observed clinically momentous reduced HRQoL in SLE patients with neuropsychiatric manifestations. NPSLE patients had significantly lower scores of SF-36 physical component summary (PCS) and mental component summary (MCS) compared to the non-NPSLE population [mean (s.d.): 35.7 (9.1) vs. 39.6 (9.6); $p< 0.001$ and 37.3 (12.1) vs. 41.4 (11.0); $p< 0.001$, respectively]. NPSLE patients also exhibited impaired HRQoL in all five EQ-5D dimensions compared to non-NPSLE patients ($p< 0.05$ for all). A substantially lower proportion among NPSLE patients experienced FHS in comparison to the non-NPSLE group (3.3% vs. 14.5%; $p< 0.001$). Neuropsychiatric involvement in SLE was associated with more severe fatigue as measured by FACIT-F [23.8 (12.2) vs. 31.5 (11.6); $p< 0.001$]. Similar associations were detected between active NPSLE patients and the non-NPSLE group with regards to SF-36 PCS/MSC domains, FHS, and FACIT-F scores. However, our findings revealed no discernible distinctions between NPSLE and active NPSLE patients, indicating that impaired HRQoL in patients with NPSLE persists regardless of the disease activity state in the neuropsychiatric domain.

Conclusion: Neuropsychiatric involvement in patients with SLE has a detrimental effect on HRQoL experience and is associated with more severe fatigue. Impaired HRQoL scores remain steady in NPSLE patients regardless of the degree of neuropsychiatric activity. Early intervention strategies are warranted in this specific group of SLE patients to enhance long-term patient-reported outcomes.

Disclosure: D. Nikolopoulos: None; **N. Cetrez**: None; **J. Lindblom**: None; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia Pharmaceuticals, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Elli Lilly and Company, 5, 6, F. Hoffmann-La Roche AG, 5, 6, Gilead Sciences, 5, 6, GSK, 5, 6, Janssen Pharmaceuticals, 5, 6, Novartis, 5, 6, Otsuka Pharmaceutical, 5, 6.

Abstract Number: 1461

Association of Serum Analytes with SLE Cognitive Impairment Phenotypes Formed by Machine Learning: MMP-9, S100A8/A9, IL-6, IL-10, and NGAL

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Background/Purpose: Cognitive impairment (CI) is highly prevalent in patients with SLE [prevalence of 38% (range: 20%-80%)]. The exact mechanisms underlying CI is complex and multifactorial. Understanding the relationship between SLE CI phenotypes and analytes may be crucial for improving patient care and developing targeted interventions. We have previously defined two SLE CI subtypes (A and B) where subtype A performed worst on objective cognitive function compared with subtype B. Subtype A also, had greater levels of disease burden/damage, worse performance on subjective cognitive function, worse HRQoL and psychiatric measures compared with subtype B. We aimed to explore the associations between SLE CI phenotypes and serum analytes levels.

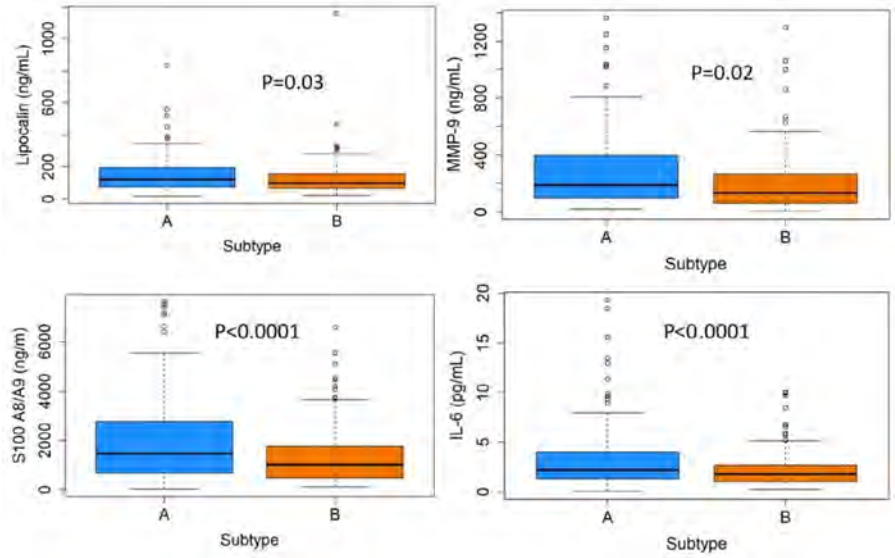

Figure 1 Subtype A (blue) performed worst on objective cognitive function compared with subtype B. Subtype A also, had greater levels of disease burden/damage, worse performance on subjective cognitive function, worse HRQoL and psychiatric measures compared with subtype B (orange).

Methods: SLE patients aged 18-65 years attending a single lupus centre (January 2016 – October 2019) completed the ACR Neuropsychological Battery (ACR-NB) cognitive assessment. Age and gender matched normative data were used to obtain z-scores on all 19 tests of ACR-NB. The ACR-NB tests were reduced using principal component analysis (PCA). Similarity network fusion (SNF) was used to identify patient subtypes on the ACR-NB data, demographic and clinical variables, disease burden/activity, health related quality of life (HRQoL: SF-36, LupusQoL), the PDQ-20 (perceived cognitive deficits), Beck Depression Inventory-II, Beck Anxiety Inventory, and the fatigue severity scale (FSS) in addition to the serum levels of nine analytes (IL-6, IL-10, IFN-ɣ, MMP-9, NGAL/lipocalin, S100A8/A9, S100B, TNF-α, and TWEAK [determined by ELISA]). Differences between the SNF identified subtypes were evaluated using Kruskal-Wallis tests and chi-square tests.

Results: Of the 296 patients, 87% were female, mean age 41.5 ± 18.4 and mean disease duration 13.8 ± 10.1 years at study visit.The level of S100A8/A9, MMP-9, NGAL/lipocalin, and IL-6 were statistically significantly higher in the more severe SLE CI subtype A compared to B (Figure 1). No difference in the levels of IL-10, IFN-ɣ, S100B, TNF-α, and TWEAK were identified between SLE CI subtypes A and B.

Conclusion: This study demonstrated a higher level of serum analytes in association with the SLE CI subtypes identified with machine learning analysis. S100A8/A9, MMP-9, NGAL, and IL-6 levels were higher in the more severe subtype A where patients experience worse objective and and subjective cognitive function with a higher disease burden and damage compared with subtype B. The results of this study will further in deciphering the mechanisms of cognitive impairment in patients with SLE and the identification of targeted therapy.

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Abstract Number: 1462

Cardiovascular Damage in Systemic Lupus Erythematosus Occurs at Early Stages of the Disease. Chronological Analysis of Damage Accrual in a Large Cohort from the Spanish Society of Rheumatology Lupus Registry (RELESSER)

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SESSION INFORMATION

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Background/Purpose: Systemic Lupus Erythematosus (SLE) survival has improved during recent decades, so other outcomes like damage accrual become more relevant. Damage represents that clinical feature that is irreversible and occurs after SLE diagnosis, being present fot at least 6 months. Our approach is to assess damage accrual, with emphasis on the cardiovascular domain over the different stages of the disease in a large SLE cohort.

Table 1. Comparison of patient characteristics with and without damage in the RELESSER-TRANS Cohort

PATIENT CHARACTERISTICS	WITH SOME DAMAGE (n = 2116)	WITHOUT DAMAGE (n = 2103)	p-value
Age at diagnosis, mean (± S.D.), years	37.9 (16.7)	33.9 (12.9)	0.96
Sex, %			
Male	12.4%	8.3%	≈0
Female	87.6%	91.7%	
Race/Ethnicity, n (%)			
Caucasian	94.2%	89.8%	
Afro-Caribbean	0.2%	0.4%	
Latin American	4.8%	5.8%	≈0
Asian	0.3%	1.1%	
Others	0.4%	2.9%	
Disease duration, mean (± S.D.), months	159.7 (109.9)	105.9 (93.1)	0.49
SDI Score, mean (± S.D.)	2.3 (1.8)	0 (0)	≈0
Number of SDI domains affected, mean (± S.D.)	1.8 (1.1)	0 (0)	≈0
Death, n (%)	203 (9.6%)	25 (1.2%)	≈0

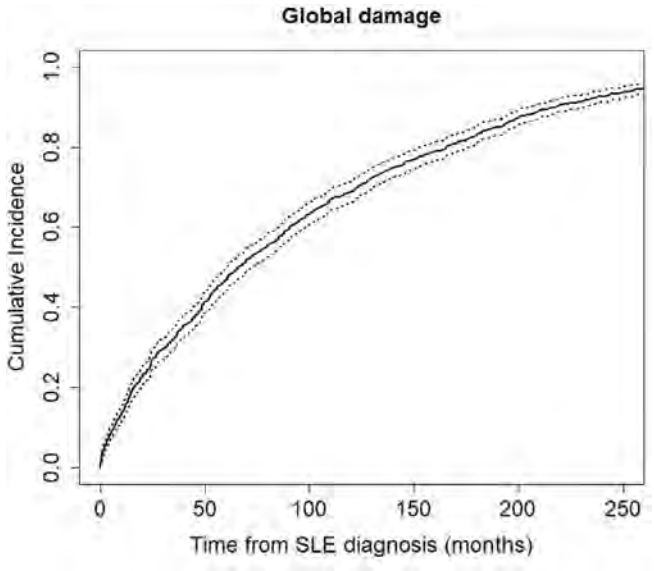

Figure 1.Gobal damage over time

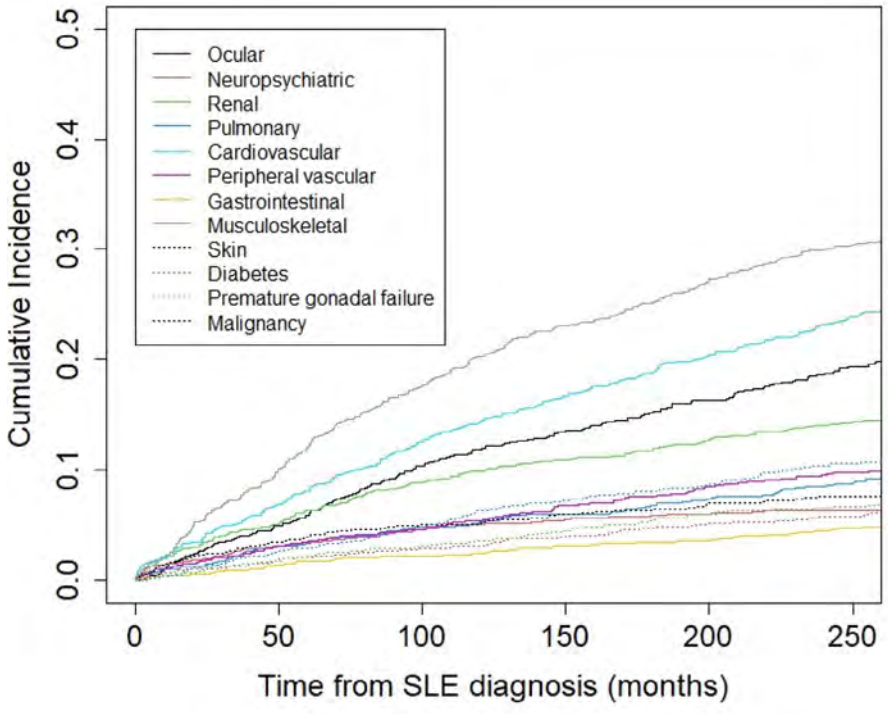

Figure 2. Damage over time by SDI domain

Methods: Multicentre, cross-sectional study of a cohort of 4,219 SLE patients enrolled in the Spanish Society of Rheumatology Lupus Registry (RELESSER) with an average age at diagnosis (±SD) of 35.9 (±15.1) years, 89,6% of women, 92% caucasian and the average duration (±SD) of SLE 133.2 months. Organ damage was ascertained using the SDI (SLICC/ACR Damage Index). For the chronological analysis we considered, globally and for every SDI domain, only those 1,299 patients whose dates of damage events had been recorded.

Results: After 133 months of follow-up, 2,116 (50.1%) of 4,219 patients manifested some damage. Table 1 shows the comparison between patients with and without damage in the RELESSER Cohort . The damage accrual rate was higher during early stages of the disease, with 22.0% and 38.1% of those patients accumulating damage during the first and third year after SLE diagnosis, respectively. Figure 1 graphically represents the cumulative incidence of global damage over the course of the disease.

Analyzing the different domains, musculoskeletal and neuropsychiatric systems were the ones accumulating more damage at those time points. The musculoskeletal system was the one contributing more to damage during late stages.Including "cerebrovascular accident" and "claudication for 6 months" as cardiovascular items, the cardiovascular system became the second one that contributed the most to damage accrual in the early stages of SLE, with 7.0% and 11,1% of the patients who presented damage doing so in this system at year 1 and 3 after diagnosis, respectively. Figure 2 shows the cumulative incidence of damage (per SDI domain) over the course of the disease from the time of SLE diagnosis.

Conclusion: The higher rate of damage accrual occurs during the first year after SLE diagnosis. The cardiovascular system is the second leading cause of damage accrual within the first years. Strategies to prevent cardiovascular damage should be implemented early on starting from the initial SLE diagnosis.

Disclosure: S. garcia Perez: None; **J. Pego-Reigosa**: None; **I. Altabás González**: None; **N. Jiménez**: None; **V. Del campo Perez**: None; **J. MARTINEZ BARRIO**: None; **M. Galindo-Izquierdo**: None; **J. Calvo- Alén**: AbbVie, 2, AstraZeneca, 2, Biogen, 6, BMS, 5, Galapagos, 6, GSK, 2, 6, Lilly, 2, 6, Novartis, 2, 6, Roche, 5, Sanofi, 2; **E. Uriarte Isacelaya**: None; **E. Tomero Muriel**: None; **M. Freire González**: None; **V. Martinez-Taboada**: None; **P. Vela**: None; **A. Fernandez-Nebro**: None; **A. Olivé-Marqués**: None; **J. Narvaez**: None; **R. Menor-Almagro**: None; **G. Santos Soler**: None; **J. Hernández Beriain**: None; **J. Manero ruiz**: None; **E. Aurrecoechea Aguinaga**: None; **O. Ibarguengoitia-Barrena**: None; **C. Montilla-Morales**: None; **G. Bonilla**: None; **V. Torrente-Segarra**: None; **A. Cacheda**: None; **M. García-Villanueva**: AstraZeneca, 6, GSK, 6, Otsuka, 1; **C. Moriano Morales**: None; **C. Fito Manteca**: None; **C. Bohórquez**: None; **N. Lozano Rivas**: None; **I. Rúa-Figueroa**: AstraZeneca, 5, GSK, 1, 6.

Abstract Number: 1463

Predictors of Cognitive Impairment in Individuals with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The purpose of this study was to investigate factors associated with objective cognitive impairment in patients diagnosed with Systemic Lupus Erythematous (SLE). Subjective complaints of changes in cognition are common, being reported by up to 50% of patients with SLE.Previous studies have showed objective declines in immediate memory and total memory.

Methods: This study was conducted using baseline data from ClearMEMory (Clearing Lupus Fog with Memantine), an ongoing clinical trial. Seventy-nine participants who reported neuropsychiatric symptoms on pre-screen and came for in-person screening were included. The dependent variable was the Repeatable Battery for the Assessment of

Variable	N	Value
Sex Female	79	 96% (76)
Ethnicity Not Hispanic or Latino	79	 94% (74)
Age (Median, IQR)	79	51(b)
Race White	79	 70% (55)
ESR	76	19
Anti-dsDNA	63	12.0
PSD Total WPI SSS	77	13.0 5.0 8.0
HADS-Anxiety	78	8
HADS-Anxiety Normal (0-7) Borderline abnormal (8-10) Abnormal (11-21)	78	 44% (34) 29% (23) 27% (21)
HADS-Depression	78	5
HADS-Depression Normal (0-7) Borderline abnormal (8-10) Abnormal (11-21)	78	 72% (56) 15% (12) 13% (10)
RBANS Total Scale	79	86
RBANS Immediate Memory Scale	79	97

IQR = Interquartile range, a b c represent the lower quartile a, the median b, and the upper quartile c for continuous variables. ESR = Erythrocyte sedimentation rate, PSD = Polysymptomatic Distress, WPI = Widespread pain index, SSS = Somatic symptom score, HADS = Hospital Anxiety and Depression Scales, RBANS = Repeatable Battery for the Assessment of Neuropsychological Status. For the RBANS, a score of 100 is the age-adjusted mean.

Factor	Effects	Lower 95% Limit	Upper 95% Limit	p-value
HADS-D (6,12)	-3.9541	-7.8828	-0.0253	0.0486
PSD Total (12,16)	-2.3539	-4.1684	-0.5394	0.0117
Race Non-White:White	-7.7678	-13.0171	-2.5185	0.0043

Overall model P = 0.0004. HADS-D = Hospital Anxiety and Depression Scales – Depression, PSD = Polysymptomatic Distress

Neuropsychological Status (RBANS), a brief, age-normalized, individually administered battery to measure cognitive decline or improvement. Potential predictive variables were sex, race, ethnicity, ESR, anti-dsDNA antibodies, the polysymptomatic distress scale (PSD) and the hospital anxiety and depression scales (HADS-A, HADS-D). Regression models were run to determine covariates that effect the RBANS total and the RBANS immediate memory. The models examined HADS-D scores between 6-12 to determine if there was a statistically significant difference when the scores went from normal to depressed. The models used PSD values 12-16 which are values that cross the threshold for diagnosis of fibromyalgia.

Results: Participant's median age was 51 years, and they were predominantly female (96%), non-Hispanic (94%) and White (70%) (**Table 1**). We used linear regression to model the RBANS total score. A model including HADS-D, PSD, and race was the most significant (p = 0.0004) (**Table 2**). As the HADS-D score increased from 6 to 12, the RBANS total decreased by 3.95 points and as the PSD total increased from 12 to 16, the RBANS total decreased by 2.35 points on average. Non-Whites, when compared to Whites had a decrease in the RBANS total by 7.77 points. The most significant model for RBANS immediate memory included the same factors (p = 0.0004, **Table 3**).

Factor	Effects	Lower 95% Limit	Upper 95% Limit	p-value
HADS-D (6,12)	-4.2360	-9.2266	0.7546	0.0950
PSD total (12,16)	-2.9600	-5.2649	-0.6551	0.0126
Race Non-White:White	-11.3691	-18.0371	-4.7010	0.0011

Overall model P = 0.0004. HADS-D = Hospital Anxiety and Depression Scales – Depression, PSD = Polysymptomatic Distress

Conclusion: Results support race, depression, and polysymptomatic distress as significant contributors to the risk of cognitive impairment in patients with SLE. Disease activity did not appreciably affect cognition in this participant sample. As participant scores crossed thresholds for depression or fibromyalgia diagnosis, measurable declines in cognition, particularly immediate memory, were observed. Further studies with different measures of cognition and larger sample size are necessary to understand the impact of race in these models.

Disclosure: A. Lee: None; **S. Phillips**: None; **L. Crofford**: None.

Abstract Number: 1464

Lupus Flares More Common in Patients on Dialysis Compared to After Renal Transplant: A Systematic Review and Meta-analysis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: End-stage renal disease (ESRD) may develop in up to 20% of patients with lupus nephritis (LN). The SLE disease activity generally declines after the development of ESRD and renal transplantation (RT). However, several studies reported SLE flares could occur after ESRD or RT. In this study, we performed a systematic literature review and meta-analysis to assess the frequency of SLE flares, in patients with ESRD or after RT.

Methods: We used PubMed, Web of Science, and Cochrane Library to search the literature from 1973 to 2023. PRISMA 2020 guidelines and checklist were used to conduct the meta-analysis. Studies investigating frequency of lupus flare in patients after renal replacement therapy (RRT) were included in the analysis. If the information was available, SLE flares were recorded separately for different RRT modalities such as hemodialysis (HD), peritoneal dialysis (PD), and RT. ACR 1997 revised classification criteria was utilized to ascertain SLE diagnosis. We excluded studies that did not mention lupus flares after the development of ESRD or RT. Two authors (O.N.P., A.D.) independently reviewed all articles and evaluated the data for consistency between the abstracts and tables to avoid bias. A forest plot was used to compare odds ratios (95% CI) of SLE flares after ESRD or RT. Study heterogeneity was assessed using I^2. All analyses were performed using the R Statistical Software meta package (v4.2.1; R Core Team 2022).

Results: Our literature review revealed 583 relevant articles, 487 were deemed unsuitable by title or abstract. We reviewed the full text of remaining 96 articles and 69 fulfilled study entry criteria. Twenty-eight studies (862 SLE patients) evaluated clinical SLE disease flares after RRT (HD and PD). Overall 30% of patients with ESRD had at least one flare after RRT (Figure 1). Seven studies (307 SLE patients) compared SLE disease flares after PD or HD initiation. The frequency of SLE flares was similar in both PD (25.6%) and HD (25.3%) (OR: 1.05, 95% CI: 0.57-1.94, p=0.88). Clinical SLE disease flares were evaluated in 5 studies after RT (91 patients). 14.3% of patients had at least one clinical SLE flare (95%CI: 8.5-23.1%). Four studies (204 SLE patients) compared lupus flares in SLE patients with PD/HD or RT. Flare risk was significantly higher in PD/HD

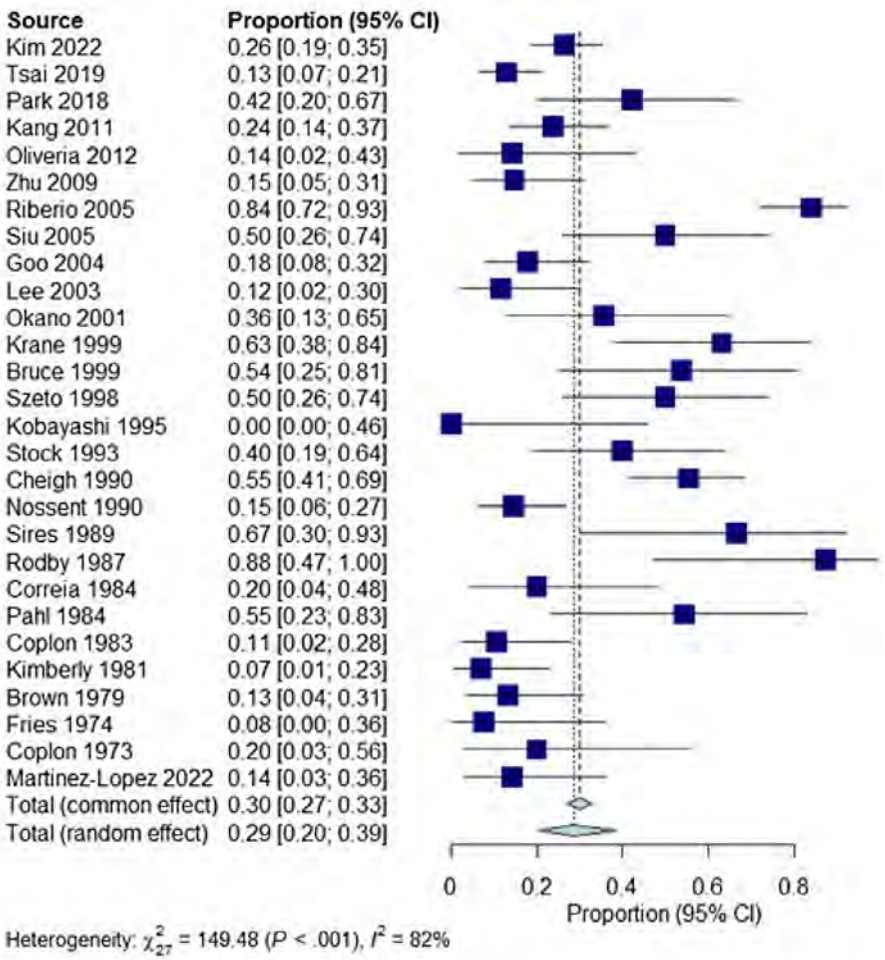
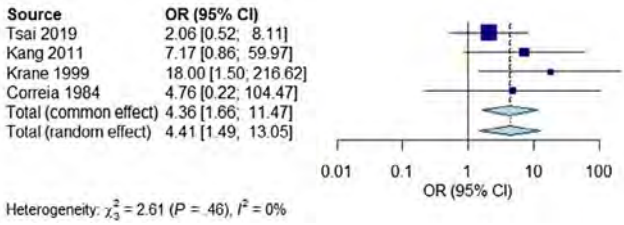


Figure 1. The frequency of SLE flares after renal replacement therapy.



The comparison of lupus disease flares in kidney transplantation and peritoneal dialysis (PD)/hemodialysis (HD) groups

group when compared to RT (OR: 4.36, 95%CI: 1.66-11.47, p=0.0028) (Figure 2). Twenty-nine studies (7890 SLE patients with RT) analyzed the recurrence of the LN after RT. LN had been diagnosed in 3.4% of patients (95%CI: 3-3.8%) (Figure 3).

Conclusion: Our meta-analysis showed lupus flares can still occur in up to 30%of patients with ESRD on RRT. The risk of flare is increased in patients on dialysis as compared to after RT. The flare risk is similar in patients on either HD or PD. A small percentage of SLE patients get recurrence of LN even after transplant.

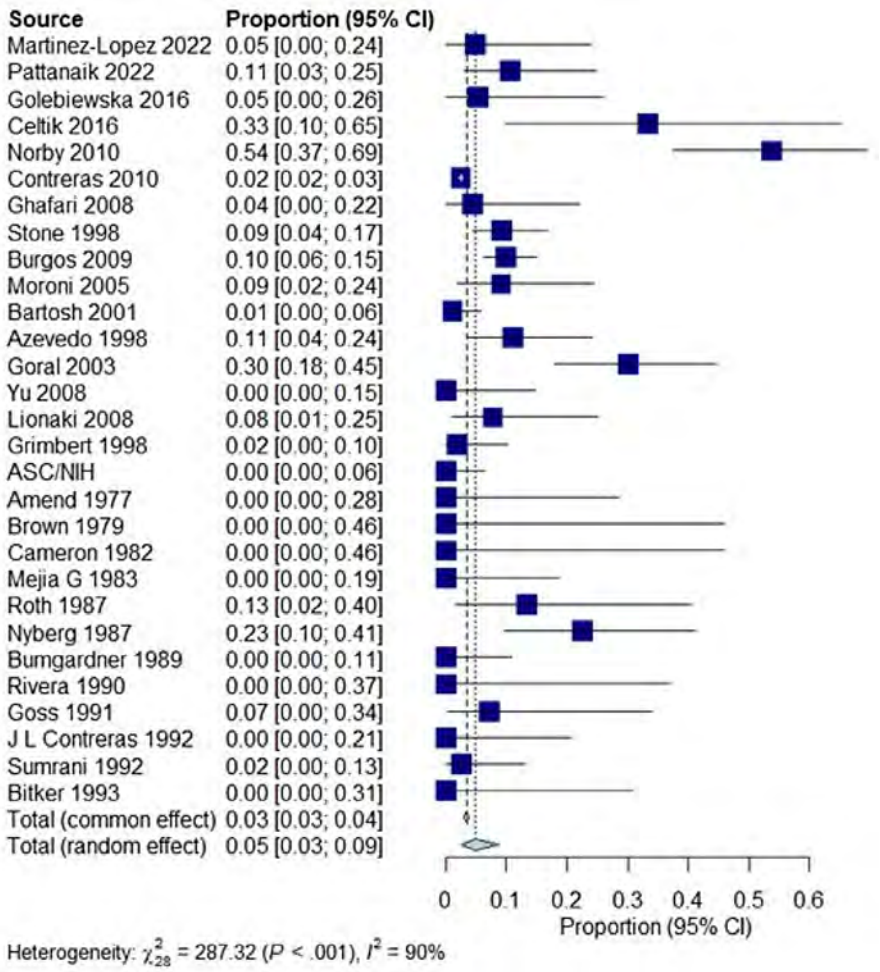


Figure 3. The frequency of lupus nephritis flares after the Renal Transplant.

Disclosure: O. Pamuk: None; **A. Daoud**: None; **L. Dweik**: None; **N. Desai**: None; **s. Hasni**: AstraZeneca, 5.

Abstract Number: 1465

Blood-dominant Disease in Older-onset Lupus: A Systematic Review and Meta-analysis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies have shown that the clinical manifestations of systemic lupus erythematosus (SLE) differ based on age of onset. Late onset SLE has been shown to be milder, with lower frequency of lupus nephritis, cutaneous and neuropsychiatric presentations however with more prevalent pulmonary manifestations. There have been multiple

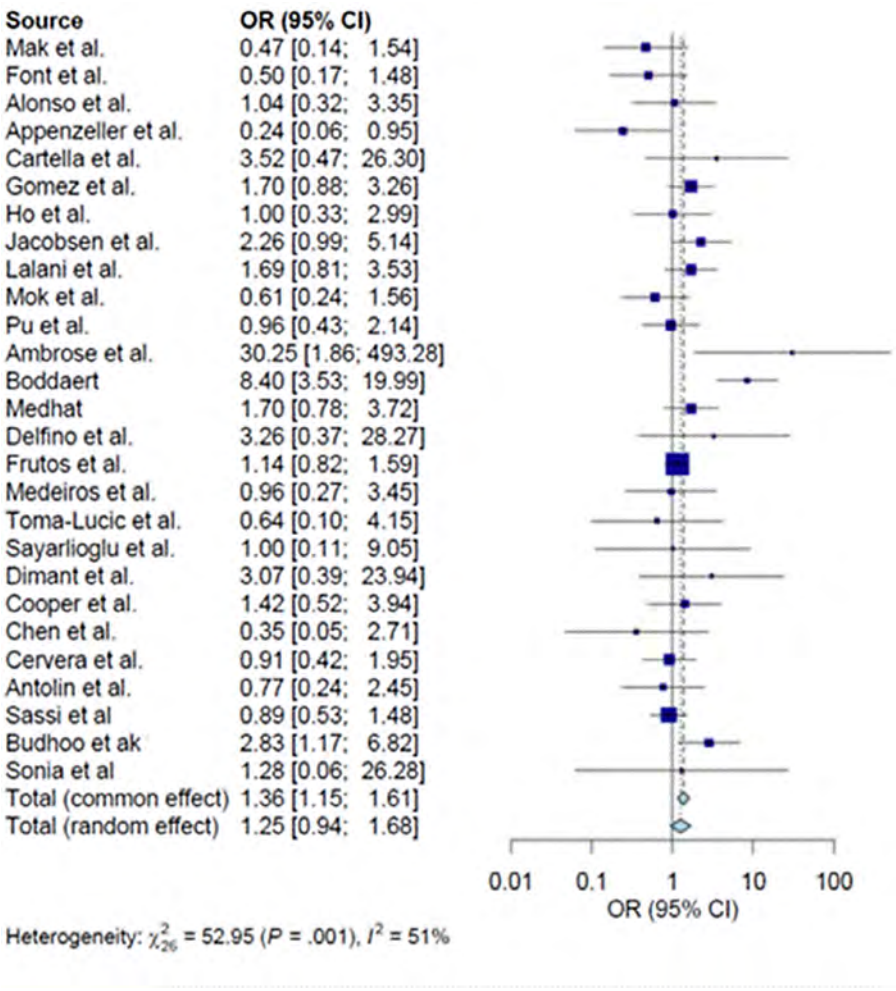

Figure 1. Odd ratios for AIHA in early and late onset SLE patients

retrospective or prospective studies comparing hematological manifestations in early-onset SLE patients (age< 50) with older onset SLE patients (age >50) with varying results. We performed a systematic review and meta-analysis to evaluate the differences in hematologic manifestations (autoimmune hemolytic anemia(AIHA),thrombocytopenia(TP), lymphopenia, leukopenia, lymphadenopathy and thrombosis) in late-onset SLE patients (ltSLE) compared to adult-onset SLE patients (aSLE).

Methods: Literature search was performed using PubMed, Web of Science and Cochrane Library. PRISMA 2020 guidelines and checklist were used. Studies were included if they investigated the frequency of hematological manifestations in ltSLE patients and excluded if they did not include aSLE as control group. The diagnosis of SLE was performed with ACR 1997 revised classification criteria for SLE**.** We included cohort, case-control, and population-based studies. Two authors independently reviewed all articles and evaluated the data for consistency between the abstracts, tables, and text to avoid a bias. Forest plot was used to compare odds ratios (95% CI) of hematological manifestations by age groups. Study heterogeneity was assessed using I^2.All analyses were performed using R Statistical Software meta package (v4.2.1; R Core Team 2022).

Results: 44 eligible studies comprising 20,508 SLE patients (17421 aSLE and 3087 ltSLE) were included in analysis. Among these studies, 27 reported the occurrence of AIHA which was found to be more frequent in the aSLE group compared to ltSLE (OR: 1.36, 95% CI: 1.15-1.61, p=0.0003) (Figure 1). Further analysis of 40 studies revealed a higher frequency of TP in the aSLE group (OR: 1.16, 95% CI: 1.05-1.28, p=0.0045) (Figure 2). 19 studies provided data on lymphopenia which was found to be more frequent in aSLE (OR: 1.16, 95%CI: 1.04-1.30, p=0.0082) (Figure 3). 31 studies included data for

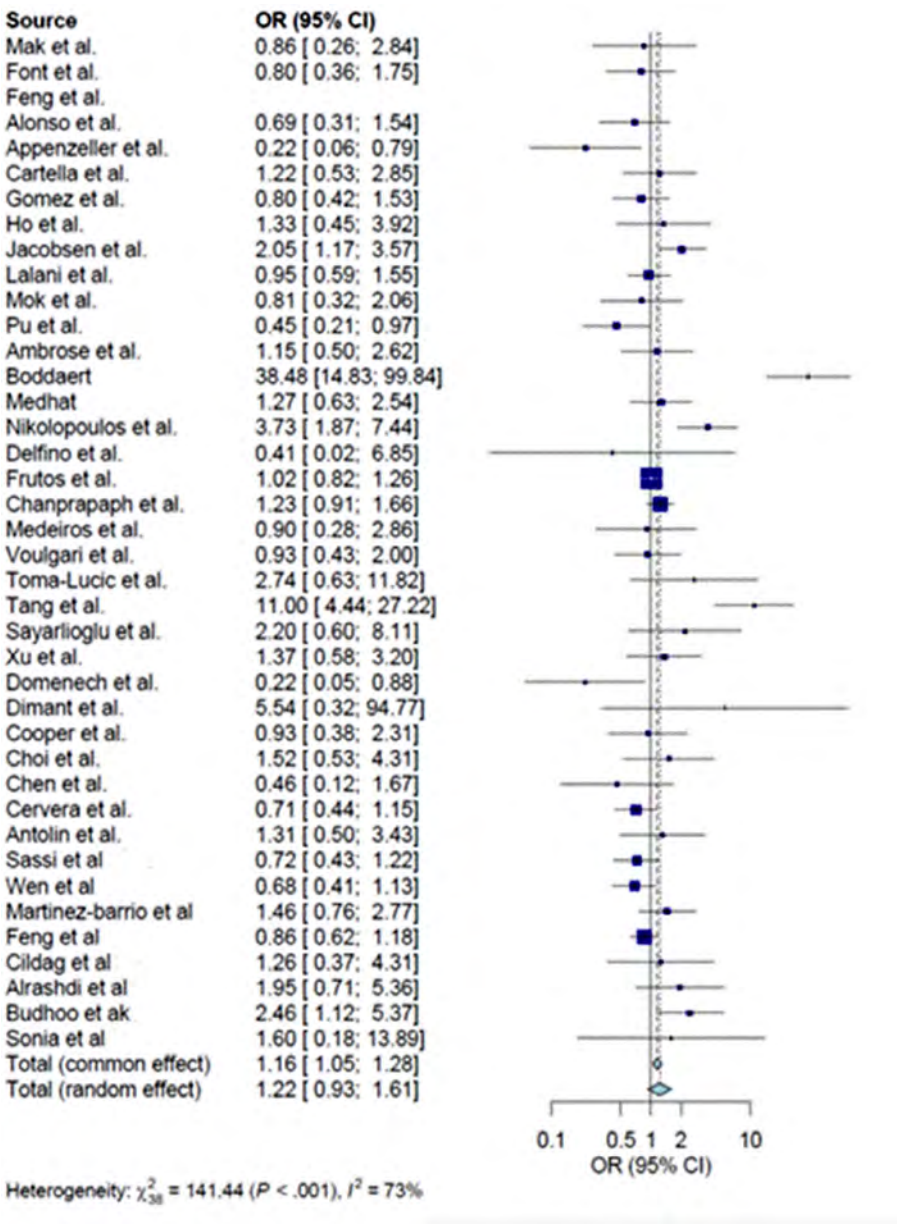

Figure 2. ORs for TP in early and late onset lupus groups.

leukopenia and the frequency was higher in the aSLE (OR: 1.28, 95% CI: 1.17-1.41). Additionally, lymphadenopathy was more commonly seen in aSLE group (OR: 2.18, 95%CI: 1.47-3.24, p=0.0001). However, no significant difference was observed in the frequency of thrombosis between the two groups.

Conclusion: Attributing hematological findings to SLE may be challenging in older onset patients due to comorbidities and polypharmacy. In this study, the overall frequencies of AIHA, TP, lymphopenia, leukopenia and lymphadenopathy were more common in aSLE patients compared to ltSLE.

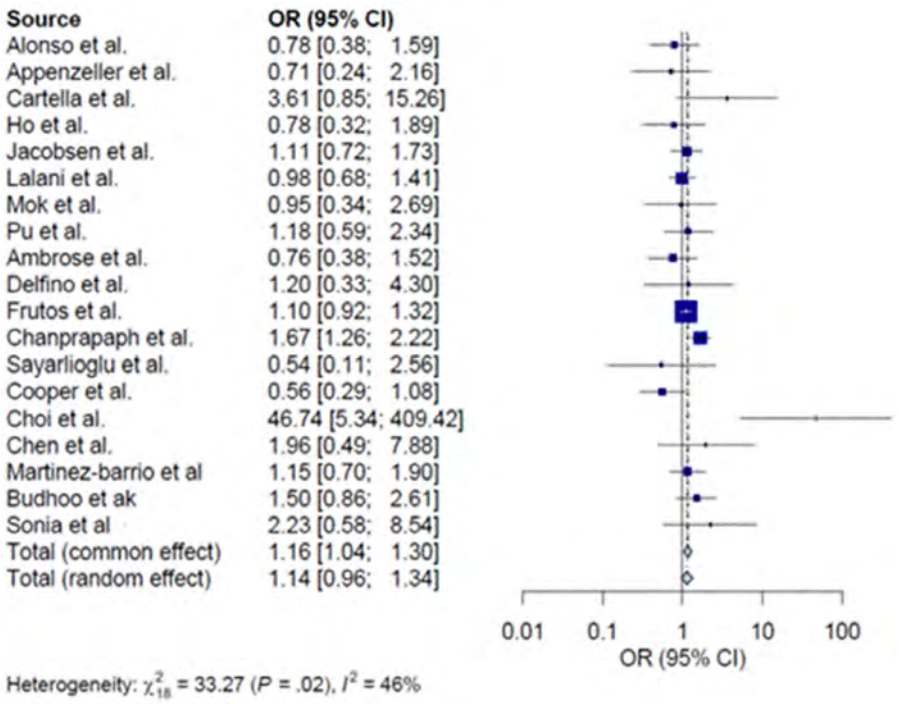

Figure 3. ORs for lymphopenia in aSLE and ltSLE patients.

Disclosure: S. Abi Doumeth: None; **M. Magrey**: AbbVie, 2, Bristol Myers Squibb, 2, Eli Lilly, 2, Novartis, 2, Pfizer Inc, 2, UCB, 5; **O. Pamuk**: None.

Abstract Number: 1466

Impact of Co-morbid Depression on Systemic Lupus Erythematosus Hospitalizations: Insights from National Readmission Database 2020

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SESSION INFORMATION

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Session Type: Poster Session B

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Background/Purpose: SLE patients are prone to hospitalizations and readmissions compared to general population. Depression is highly prevalent among patients with SLE and is an important inpatient comorbidity. Studies have established that depression is an independent risk factor for CVD and premature CVDs are a major cause of mortality in SLE. The additive effect of depression on CVD in SLE remains unknown. Hence, we aimed to investigate the impact of co-morbid depression on SLE hospitalizations in terms of mortality or CVD outcomes and readmissions.

Methods: We performed a retrospective analysis using the 2020 National readmission database (NRD) and identified patients over 18 years of age hospitalized with a principal diagnosis of SLE (ICD 10 code: M32). NRD is a nationally representative database that has discharge data from 31 states and weighted, estimates over 32 million discharges in a year. Depression was identified using ICD 10 codes (F32, F33, F34.1) and SLE patients were divided into two subgroups based on presence or absence of co-morbid depression. Baseline characteristics including demographics, hospital level variables and co-morbidities (table 1) were identified for the two groups. Nearest propensity matching (PSM) was performed using a 1:1 ratio for all baseline characteristics. The primary outcome of interest was mortality. Secondary outcomes include ischemic stroke, acute myocardial infarction, acute heart failure, vasopressor use, acute kidney injury, 30- and 90-day readmissions. T-test and chi-square tests were performed to compare outcomes and p value < 0.05 was considered statistically significant. STATA 18 was used to perform the analysis.

Results: Among 167,825 SLE hospitalizations, 32,619 (19.4%) had co-morbid depression. Baseline characteristics are shown in Table 1. After matching, SLE patients with depression have low all-cause mortality rates (2.05% vs 2.98%, p < 0.001). No significant impact seen on 30- and 90- day readmission rates (8.26% vs 8.09%, p 0.581, and 7.03% vs 6.73%, p 0.267 respectively), and incidence of ischemic stroke (2.00 vs 2.26%, p < 0.100). However, depression reduced acute MI (5.14% vs 6.34%, p< 0.001), acute HF (7.16 vs 7.88%, p 0.012), vasopressor use (0.68% vs 0.93%, p 0.009), and AKI (19.71% vs 21.27%, p < 0.001) (Table 2).

Impact of depression on cardiovascular outcomes in patient with SLE
Table 1

	SLE	
Baseline Characteristics	**Without depression (n=135,206)**	**With depression (n=32,619)**
Age, mean in years	52.6	54.1
Female n (%)	117,792.3 (87.12%)	29,860.1 (91.54%)
Charlson comorbidity index n (%)		
1	35,152.5 (26%)	6,966.3 (21.36%)
2	24,811.3 (18.35%)	6,774.3 (20.77%)
3 and above	75,242.4 (55.65%)	18,878.3 (57.88%)
Insurance provider n (%)		
Medicare	66,997.1 (50.89%)	18,333 (57.43%)
Medicaid	27,500.6 (20.89%)	6,136.7 (19.23%)
Private	33,792.5 (25.67%)	6,767.2 (21.2%)
Uninsured	3,366.1 (2.56%)	683.2 (2.14%)
Hospital bed size n (%)		
Small	21,794.6 (16.12%)	5,522.6 (16.93%)
Medium	32,503.6 (24.04%)	8,257.9 (25.32%)
Large	80,907.9 (59.84%)	18,838.4 (57.75%)
Teaching hospital n (%)		
Metropolitan, non-teaching	21,471.9 (15.88%)	4,869.6 (14.93%)
Metropolitan, teaching	105,187 (77.8%)	25,541.0 (78.3%)
Non-metropolitan	8,547.3 (6.32%)	2,208.2 (6.77%)
Comorbidities		
Atherosclerosis n (%)	2,135.4 (1.58%)	567.8 (1.74%)
Atrial fibrillation - all n (%)	15,093.7 (11.16%)	3,511.0 (10.76%)
Hypertension n (%)	84,412.1 (62.43%)	21,637.0 (66.33%)
Type 2 diabetes mellitus n (%)	28,310.9 (20.94%)	7,811.9 (23.95%)
Chronic lung disorders n (%)	35,330.9 (26.13%)	11,440.4 (35.07%)
CKD n (%)	39,180.1 (28.98%)	8,334.6 (25.55%)
Coagulation disorders n (%)	13,251.6 (9.8%)	3,352.6 (10.28%)
Drug abuse n (%)	9,265.7 (6.85%)	3,229.8 (9.9%)
Fluid electrolyte imbalances n (%)	56,378.8 (41.7%)	14,146.1 (43.37%)
Chronic heart failure n (%)	12,336.2 (9.12%)	3,463.7 (10.62%)
Obesity n (%)	28,320.6 (20.95%)	8,762.3 (26.86%)
Anemia n (%)	48,996.6 (36.24%)	11,892.1 (36.46%)

Impact of depression on cardiovascular outcomes in patient with SLE
Table 2

	SLE		
Outcomes, n (%)	Without depression (n=17,109)	With depression (n=17,109)	p-value
Mortality	510 (2.98%)	350 (2.05)	<0.001
Ischemic stroke	387 (2.26%)	343 (2.00%)	<0.100
90-day readmissions	1,385 (8.09%)	1,413 (8.26%)	0.581
30-day readmissions	1,151 (6.73%)	1,203 (7.03%)	0.267
Acute MI	1,085 (6.34%)	879 (5.14%)	<0.001
Acute HF	1,349 (7.88%)	1,226 (7.16%)	0.012
Vasopressor use	159 (0.93%)	116 (0.68%)	0.009
Acute kidney injury	3,640 (21.27%)	3,372 (19.71%)	<0.001

Conclusion: Depression was highly prevalent among hospitalized SLE patients and traditional CVD risk factors such as DM, HTN, and obesity were noted to be higher in the SLE + depression group. However, co-morbid depression did not impact readmissions, or adverse cardiovascular events. Interestingly, a significant reduction in all- cause mortality was seen. Further studies are warranted to analyze the reasons for hospitalizations and readmission in this subgroup which may help providers predict morbidity and mortality and provide tailored medical care.

Disclosure: S. Gandhi: None; **A. Challa**: None; **S. Kanniyaram**: None; **A. Kamat**: None; **T. Polana**: None; **K. Michaud**: None.

Abstract Number: 1467

Antiphospholipid Antibodies and the Risk of Diffuse Alveolar Hemorrhage in Patients with Systemic Lupus Erythematosus: A Systematic Review and Meta-Analysis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Diffuse alveolar hemorrhage (DAH) is one of the most devastating complications of SLE. The exact pathogenesis leading to DAH in SLE is not well understood. Nonetheless, about a third of the patients with SLE have positive aPL, which are associated with non-thrombotic manifestations, including DAH. We aimed to assess the risk of DAH in patients with SLE based on their aPL profile by performing a systematic review (SR) and meta-analysis (MA).

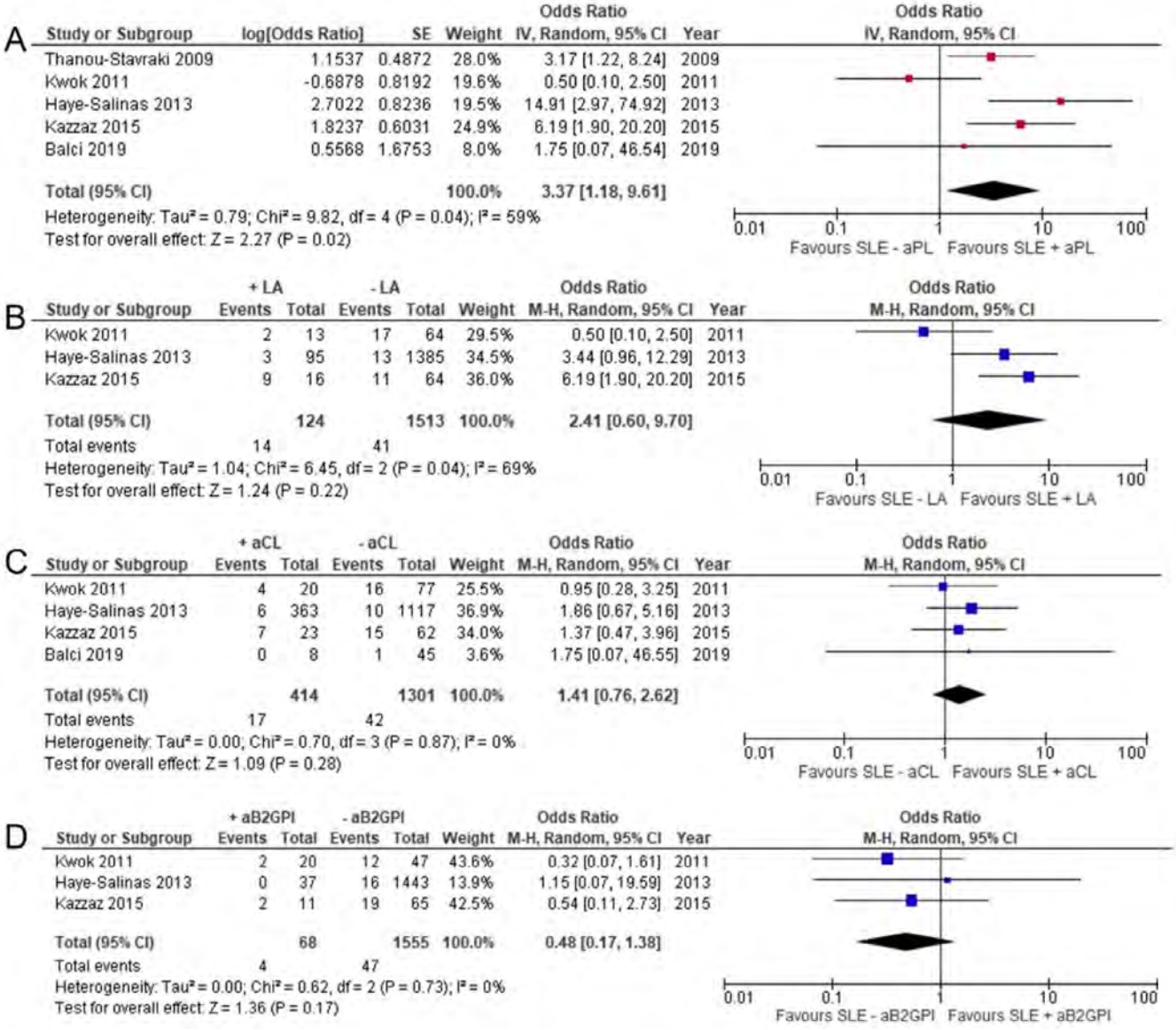
Methods: MEDLINE, EMBASE, CENTRAL, and Scopus were systematically searched from inception to February 2023. Studies were eligible if they included SLE patients (population) with a description of the association of the aPL status (exposure) and DAH (outcome). SLE and DAH were defined as stated by the authors of primary studies. Studies were excluded if they reported findings only for patients with SLE with specific organ involvement. Two reviewers independently screened the studies and extracted data from the reports. The main analysis explored the association between any aPL (overall) and DAH; when multiple aPL subtypes were available in the same study, we prioritized their inclusion in the main analysis in the

Table 1. Characteristics of the included studies.

Author, year	Study design	Type of report	Country	Population	SLE definition	SLE patients, n (%)		Female, n (%)	Exposure to aPL
						DAH	No DAH		
Thanou-Stavraki 2009	Case-control	Abstract	USA	SLE	NR	13	52	50 (76.9)	Overall aPL•
Kwok 2011	Case-control	Full text	South Korea	Hospitalized SLE	1982 ACR criteria	21	83	99 (95.2)	LA•, aCL, aβ2GPI
Haye-Salinas 2013	Cohort	Abstract	Latin America*	SLE	Physician diagnosis	16	1464	1330 (89.9)	LA•, aCL, aβ2GPI
Kazzaz 2015	Case-control	Full text	USA	SLE	1997 ACR criteria	22	66	NR	LA•, aCL, aβ2GPI
Balci 2019	Cohort	Full text	Turkey	Juvenile SLE	1997 ACR criteria	1	52	48 (90.6)	aCL•

aβ2GP1, anti-β2 glycoprotein I antibodies; aCL, anticardiolipin antibodies; aPL, antiphospholipid antibodies; DAH, diffuse alveolar hemorrhage; LA, lupus anticoagulant; NR, not reported; SLE, systemic lupus erythematosus
*Argentina, Brazil, Chile, Colombia, Cuba, Guatemala, Mexico, Peru, and Venezuela
•Included in main analysis

Figure 1. Forest plots for the risk of diffuse alveolar hemorrhage in patients with systemic lupus erythematosus (SLE) according to A) overall antiphospholipid antibodies (aPL), B) lupus anticoagulant (LA), C) anticardiolipin antibodies (aCL), and D) anti-β2 glycoprotein I antibodies (aβ2GPI) positivity.



following order: 1) LA, 2) aCL, and 3) anti-β2 glycoprotein I (aβ2GPI). Subgroup analyses were performed by each aPL subtype. Sensitivity analyses assessed the effect of excluding studies where the population included only a subset of patients with SLE. Estimates were pooled using random-effects models, and the risk of bias was assessed using the Newcastle-Ottawa Scale. We followed the PRISMA guidelines for all stages of the SR and MA.

Results: A total of 399 studies were screened. Only five met inclusion criteria (three case-control and two cohort studies), adding up to 1790 patients with SLE and 73 events of DAH (**Table 1**). Patients with SLE and positive aPL (any) were three times more likely to have DAH than aPL-negative patients with SLE (OR 3.37, 95% CI 1.18-9.61; I^2=59%; 1745 patients; 5 studies). Subgroup analyses based on aPL subtype showed that patients with SLE and positive LA (OR=2.41, 95% CI 0.60-9.70; I^2=69%; 1637 patients, 3 studies), aCL (OR=1.41, 95% CI 0.76-2.62; I^2=0%; 1715 patients; 4 studies), and aβ2GPI (OR=0.48, 95% CI 0.17-1.38; I^2=0%; 1623 patients; 3 studies) had no significant difference in the risk of DAH compared to negative patients (**Figure 1**). Risk of bias assessment showed concerns in the definition and selection of the non-exposed participants and comparability between groups. Sensitivity analysis excluding studies with hospitalized SLE controls showed that patients with SLE and positive LA were four times more likely to present with DAH than negative patients (OR=4.72, 95% CI 1.98-11.22; I^2=0%; 1560 patients; 2 studies).

Conclusion: In patients with SLE, aPL positivity might increase the risk of DAH compared with negative-aPL subjects. The certainty of our findings is limited by the paucity of available evidence exploring the aPL-DAH relationship, decreasing the precision of the risk assessment by aPL subtype.

Disclosure: M. Gonzalez-Trevino: None; **J. Yang**: None; **L. Prokop**: None; **G. Figueroa-Parra**: None; **A. Duarte-Garcia**: None.

Abstract Number: 1468

Prediction of Cardiovascular Disease in Patients with Systemic Lupus Erythematosus Using a Machine Learning Algorithm for Time-to-Event Outcomes: Random Survival Forest

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) have higher risks of developing cardiovascular disease (CVD). Traditional risk factors do not adequately capture the risk of CVD in patients with SLE, and although SLE-specific prediction risk tools have been developed, none has achieved an adequate combination of high sensitivity and specificity. Recently, machine learning techniques, such as random survival forests (RSF), were shown to be effective approaches for the prediction of cardiovascular outcomes in the general population. The purpose of this study was to evaluate the use of RSF in the prediction of CVD events in SLE patients.

Table 1: Descriptive Statistics Data presented as mean ± standard deviation for continuous variables, and N (percentage) for categorical variables. P values were derived from two-sample t-tests for continuous variables, and Chi-squared tests for binary variables. BMI: Body mass index. LDL: Low-density lipoprotein. HDL: High-density lipoprotein. SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000. APLA: Anti-phospholipid antibodies. SLICC: Systemic Lupus International Collaborating Clinics.

Variable	No CVD at 25 years (N=1580)	CVD at 25 years (N=211)	Total (N=1791)	P*
Age	33.6 ± 12.9	41.9 ± 14.1	34.5 ± 13.3	<0.001
SLE duration (years)	4.3 ± 6.1	4.5 ± 6.2	4.3 ± 6.1	0.679
Caucasian	1020 (64.6%)	162 (76.8%)	1182 (66%)	<0.001
Female	1397 (88.4%)	175 (82.9%)	1572 (87.8%)	0.022
Hypertension	483 (30.6%)	92 (43.6%)	575 (32.1%)	<0.001
BMI	25.0 ± 4.5	26.9 ± 5.0	25.2 ± 4.6	<0.001
Diabetes	46 (2.9%)	7 (3.3%)	53 (3%)	0.744
Renal Impairment	137 (8.7%)	49 (23.2%)	186 (10.4%)	<0.001
Smoker	251 (15.9%)	55 (26.1%)	306 (17.1%)	<0.001
Creatinine	81.9 ± 82.7	102.6 ± 108.9	84.3 ± 86.5	0.008
Total Cholesterol	5.0 ± 1.6	5.6 ± 1.8	5.1 ± 1.6	<0.001
Triglycerides	1.7 ± 1.2	2.0 ± 1.2	1.7 ± 1.2	0.001
LDL	2.7 ± 1.1	3.0 ± 1.2	2.7 ± 1.1	<0.001
HDL	1.5 ± 0.5	1.5 ± 0.5	1.5 ± 0.5	0.539
Elevated ds-DNA	730 (46.2%)	80 (37.9%)	810 (45.2%)	0.023
Elevated Anti-Ro	706 (44.7%)	88 (41.7%)	794 (44.3%)	0.414
Elevated Anti-La	278 (17.6%)	49 (23.2%)	327 (18.3%)	0.047
Elevated Anti-SM	389 (24.6%)	44 (20.9%)	433 (24.2%)	0.23
Elevated Anti-RNP	488 (30.9%)	53 (25.1%)	541 (30.2%)	0.087
Elevated CRP	427 (27%)	72 (34.1%)	499 (27.9%)	0.031
Elevated ESR	790 (50%)	132 (62.6%)	922 (51.5%)	<0.001
Elevated homocysteine	158 (10%)	35 (16.6%)	193 (10.8%)	0.004
Low complements	753 (47.7%)	105 (49.8%)	858 (47.9%)	0.565
Positive APLA	426 (27%)	75 (35.5%)	501 (28%)	0.009
SLEDAI-2K score	7.2 ± 6.8	8.9 ± 7.8	7.4 ± 6.9	0.003
SLICC Damage Index	0.2 ± 0.7	0.3 ± 0.8	0.2 ± 0.7	0.393
Corticosteroid therapy	33.6 ± 12.9	41.9 ± 14.1	34.5 ± 13.3	<0.001

Methods: A retrospective analysis was conducted on patients at a single Lupus centre between 1970 and 2018. For each patient, baseline demographic, clinical and laboratory variables were collected using a standard protocol. Multiple imputation by chained equations was used to impute missing variables. Patients were followed for up to 25 years, and CVD event was defined as the development of angina, myocardial infarction, congestive heart failure, stroke, transient ischemic attack, pacemaker insertion or peripheral vascular disease related to atherosclerosis. Patients who had CVD event at baseline, had no follow-up visits after initial visit, or had CVD death and no visits within 10 years prior to death were excluded. To evaluate the risks of developing CVD events, univariate and multivariate survival analyses were conducted using Cox proportional hazard models. In addition, RSF was constructed, and its performance was compared against the multivariate Cox model by calculating the integrated Brier score with bootstrap cross-validation.

Results: Out of the 1791 patients included in the final analyses, 211 (11.8%) developed CVD events over a mean follow-up period of 9.6 years. Patients who developed CVD tended to be older, had higher body mass index (BMI), LDL, homocysteine levels and disease activity, and were more likely to be male, Caucasian, smokers, on corticosteroid treatment, and have hypertension, renal impairment, elevated inflammatory markers, and positive antiphospholipid antibodies (**Table 1**). In ***multivariate Cox regression***, age (HR=1.05, P< 0.001), BMI (HR 1.05, P< 0.000), LDL (HR 1.14, P=0.019), abnormal C-reactive protein (HR=1.36, P=0.040), abnormal erythrocyte sedimentation rate (HR 1.3, P= 0.072), elevated creatinine (HR=1.00, P< 0.001), SLEDAI-2K score (HR=1.04, P < 0.001), and corticosteroid treatment (HR=1.52, P=0.007) were

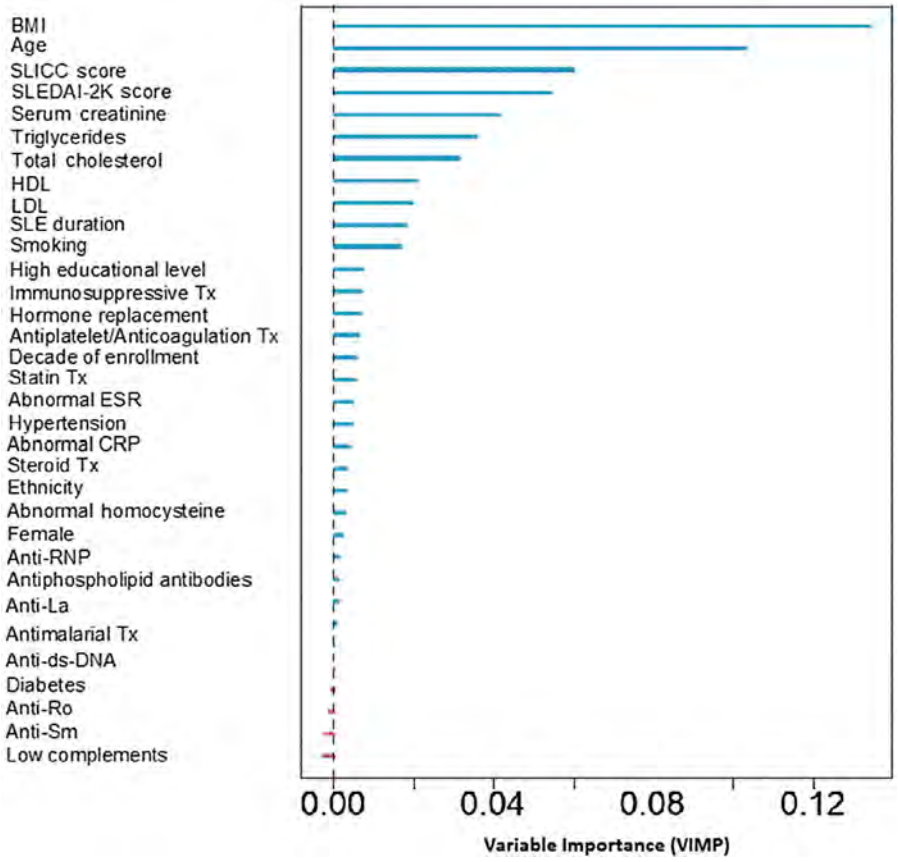

Figure 1: Graph of Variable Importance (VIMP) The greater the VIMP, the more impact a variable has on the prediction accuracy of a model. A value of 0 means that the variable has no impact on the model. A negative VIMP means that the variable decreases prediction accuracy. Tx: Treatment.

associated with increased CVD risk. In the ***RSF model***, the variables with the highest predictive values were: BMI, age, SDI, SLEDAI-2K score and serum creatinine (**Figure 1**). The integrated Brier score was 0.094 for the random survival forest model, compared to 0.100 for the Cox model, suggesting that the RSF yielded lower prediction errors (**Figure 2**).

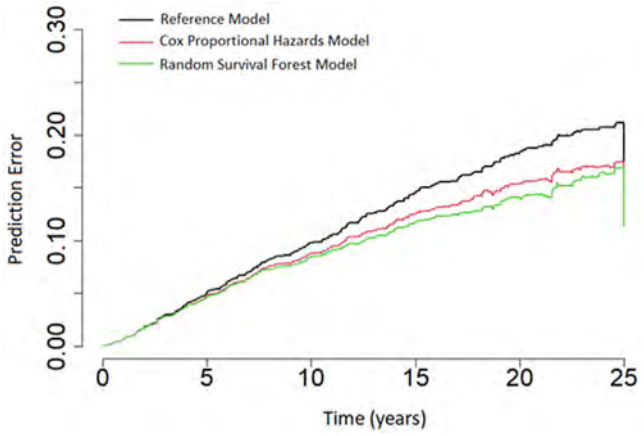

Figure 2: Prediction Error Over Time for Different Models The reference model refers to the marginal Kaplan-Meier prediction model, where no variables were used for stratification. The integrated Brier score (IBS) is calculated based on the integration of the average squared differences between predicted and observed survival, and a lower score is suggestive of overall lower prediction error. The IBS was 0.094 for the random survival forest model, compared to 0.100 for the Cox model.

Conclusion: RSF is a machine learning tool that could help improve the accuracy of CVD event prediction in SLE patients, and could lend insight into important predictors for CVD risk. The random survival forest yielded lower prediction errors compared to the multivariate Cox model.

Disclosure: H. Liu: None; **J. Su**: None; **D. Bonilla**: None; **S. Duaibes**: None; **J. Diaz Martinez**: None; **Z. Touma**: AstraZeneca, 2, GSK, 2.

Abstract Number: 1469

Prevalence of Cardiovascular Disease in a Populations Based Registry of Patients with Systemic Lupus Erythematosus

Daniel Joyce[1], Jeffrey. Berger[2], Allison Guttmann[3], Ghadeer Hasan[4], Jill Buyon[5], H Michael Belmont[1], Jane Salmon[6], Anca Askanase[7], Joan Bathon[8], Laura Geraldino-Pardilla[9], Yousaf Ali[10], Ellen Ginzler[11], Chaim Putterman[12], Caroline Gordon[13], Charles Helmick[14], Kamil Barbour[15], Heather Gold[16], Hilary Parton[17] and Peter Izmirly[2], [1]NYU School of Medicine, New York, NY, [2]New York University School of Medicine, New York, NY, [3]Atlantic Health System, Summit, NJ, [4]Optum, Jersey City, NJ, [5]NYU Grossman School of Medicine, New York, NY, [6]Hospital for Special Surgery, New York, NY, [7]Columbia University Medical Center, New York, NY, [8]Columbia University, New York, NY, [9]Division of Rheumatology, Columbia University Irving Medical Center, New York, NY, [10]Icahn School of Medicine at Mount Sinai, New York, NY, [11]SUNY Downstate Health Sciences University, Brooklyn, NY, [12]Albert Einstein College of Medicine, Bronx, NY, [13]Institute of Inflammation and Ageing, University of Birmingham, Birmingham, United Kingdom, [14]NA, Atlanta, GA, [15]Centers for Disease Control and Prevention, Atlanta, GA, [16]New York University, New York, NY, [17]New York City Department of Health and Mental Hygiene, Queens, NY

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with SLE are at increased risk for cardiovascular disease (CVD). Population estimates of CVD in SLE remains limited for non-White racial/ethnic populations in the United States. The Manhattan Lupus Surveillance Program (MLSP), a population-based retrospective registry of SLE patients, was used to investigate the prevalence of CVD among SLE patients in 2007.

Methods: MLSP patients were identified from rheumatologists, hospitals and population databases using ICD-9 codes. We included prevalent SLE patients aged ≥20 residing in Manhattan in 2007 who met one of the SLE classification criteria: 1997 ACR, SLICC or EULAR/ACR. CVD was captured if documentation existed confirming a myocardial infarction (MI) or cerebrovascular accident (CVA). Crude risk ratios were calculated for sex, age group, and race/ethnicity, and adjusted risk ratios (ARR) controlled for sex, age group, race/ethnicity and number of years since diagnosis. We used data from the National Health and Nutrition Examination Survey (NHANES 2009–2010) and the NYC Health and Nutrition Examination Survey (NYC HANES 2013–2014) to determine the prevalence of MI or CVA nationally and in NYC, respectively. Estimates for those identified as non-Hispanic Asian and non-Hispanic other race/ethnicity were not included, as they were either not available (NHANES) or estimates were unreliable (NYC HANES). We calculated the expected prevalence of MI or CVA by multiplying NHANES and NYC HANES prevalence estimates by strata-specific counts of MLSP SLE patients. We calculated crude prevalence ratios using both national and NYC estimates and age standardized prevalence ratios (ASPR) with three age groups using national estimates. We were unable to calculate age standardized prevalence ratios using the NYC estimates, as prevalence estimates broken down by demographic group and age group were unreliable.

TABLE 1. Demographics of SLE patients with evidence of cardiovascular outcomes - Manhattan Lupus Surveillance Project, 2007

	Any CVD outcome	SLE patients	Percent	Crude risk ratio	Adjusted risk ratio* (95% CI)
Total	179	1,285	13.9		
Male	23	108	21.3	(ref)	(ref)
Female	156	1,177	13.3	0.6	0.6 (0.4-0.8)
Age group					
20-39	41	504	8.1	(ref)	(ref)
40-59	75	540	13.9	1.7	1.4 (1.0-2.0)
60+	63	241	26.1	3.2	2.5 (1.7-3.8)
Race/Ethnicity					
Non-Hispanic White	48	388	12.4	(ref)	(ref)
Non-Hispanic Black	58	331	17.5	1.0	1.8 (1.3-2.6)
Hispanic	62	374	16.6	1.3	1.6 (1.1-2.3)
Non-Hispanic Asian	6	138	4.3	0.4	0.5 (0.2-1.2)
Non- Hispanic Other	5	54	9.3	0.7	2.2 (0.7-6.5)

CVD = cardiovascular disease. Outcomes include myocardial infarction and cerebrovascular disease Patients include residents of Manhattan in 2007 with a new or existing diagnosis of SLE by ACR, EULAR, or SLICC criteria who are aged 20 or older. *Adjusted risk ratios were calculated from a Poisson model which incorporated sex, age group, race/ethnicity, and years since SLE diagnosis. 41 patients were excluded due to missing race/ethnicity information.

Results: Overall 1285 patients met SLE classification criteria (92% female, 30% non-Hispanic White, 26% non-Hispanic Black, 29% Hispanic, 11% non-Hispanic Asian.) CVD occurred in 179 (13.9%), occurred less frequently among women (ARR 0.6, 95% CI 0.4-0.8), and risk increased with age, Table 1. Compared with non-Hispanic White patients, risk of CVD was elevated among non-Hispanic Black (ARR: 1.8, 95%CI 1.3-2.6) and Hispanic SLE patients (ARR: 1.6 ,95%CI

TABLE 2. Crude and age standardized prevalence ratios for SLE patients, overall and by sex and race/ethnicity - Manhattan Lupus Surveillance Project, 2007

	Number of SLE patients	Observed patients	NYC HANES		NHANES			
			Unadjusted		Unadjusted		Adjusted	
			Expected patients	Ratio	Expected patients	Ratio	Expected patients	Ratio (95% CI)
Total	1,285	179	44.7	4.0	62.8	2.8	58.0	3.1 (3.0-3.1)
Sex								
Male	108	23	4.2	5.4	6.9	3.4	6.1	3.8 (3.6-3.9)
Female	1,177	156	36.2	4.3	43.0	3.6	40.2	3.9 (3.8-3.9)
Race/Ethnicity								
Non-Hispanic White	388	48	13.2	3.6	18.7	2.6	21.6	2.2 (2.2-2.3)
Non-Hispanic Black	331	58	17.0	3.4	21.6	2.7	17.9	3.2 (3.2-3.3)
Hispanic	374	62	11.4	5.5	16.0	3.9	14.5	4.3 (4.2-4.4)
Non-Hispanic Asian	138	6						
Non-Hispanic Other	54	5						

Outcomes include myocardial infarction and cerebrovascular disease. Patients include residents of Manhattan in 2007 with a new or existing diagnosis of SLE by ACR, EULAR, or SLICC criteria who are aged 20 or older.

1.1-2.3), Table 1. CVD prevalence was approximately 3 times higher among MLSP patients than national estimates (ASPR: 3.1,9 5%CI 3.0-3.1) and ASPRs did not differ by sex, Table 2. Compared with the national population, the ASPR among SLE patients was most elevated among Hispanics (4.3, 95% CI 4.2-4.4) followed by non-Hispanic Blacks (3.2, 95% CI 3.2-3.3) and non-Hispanic Whites (2.2, 95% CI 2.2-2.3), Table 2. Unadjusted prevalence ratios of CVD were also elevated in comparison with NYC residents (4.0), particularly among men (5.4) and Hispanics (5.5).

Conclusion: These findings provide population-based estimates of CVD amongst a multi-racial/ethnic SLE registry These data can help providers ensure SLE patients are appropriately screened for CVD disease.

Disclosure: D. Joyce: None; **J. Berger**: None; **A. Guttmann**: None; **G. Hasan**: None; **J. Buyon**: Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, Related Sciences, 1; **H. Belmont**: Alexion, 6, Aurinia, 6; **J. Salmon**: None; **A. Askanase**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb, 2, Celgene, 2, Eli Lilly, 2, Genentech, 2, GSK, 2, Idorsia, 2, Janssen, 2, Mallinckrodt, 2, Pfizer, 2, UCB Pharma, 2; **J. Bathon**: None; **L. Geraldino-Pardilla**: None; **Y. Ali**: None; **E. Ginzler**: None; **C. Putterman**: Equillium, 2, KidneyCure, 1, Progentec, 2; **C. Gordon**: AbbVie, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, Sanofi, 2, UCB Pharma, 2; **C. Helmick**: None; **K. Barbour**: None; **H. Gold**: None; **H. Parton**: None; **P. Izmirly**: None.

Abstract Number: 1470

SARS-CoV-2 Antibody Formation After COVID-19 Vaccination in SLE Patients Treated with Belimumab: Single-Center Prospective Observational Study

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) should be more proactive with the administration of the COVID-19 vaccine, as their systemic conditions are prone to developing severe outcomes. However, there are concerns that immunosuppressive agents used in SLE patients could reduce the immune response. Previous data demonstrates that total B-cell depletion impairs the humoral response in patients treated with Rituximab, but there is very limited information about Belimumab. Thus, we aimed to assess the immunogenicity and safety of COVID-19 vaccine in SLE patients treated with Belimumab.

Methods: Between December 14, 2021, and June 17, 2022, patients diagnosed with SLE who were receiving B-cell targeted therapy with Belimumab were recruited. We examined the patients' inoculation history, and antibody titer was measured in patients who had completed the third dose of COVID-19 vaccine. SARS-CoV-2 antibody titers were determined through semiquantitative anti-SARS-CoV-2 S enzyme immunoassay.

Results: As a result of surveying 21 SLE patients receiving Belimumab, only 10 patients completed up to the 3 doses of COVID-19 vaccine. The mean duration between the last (3rd) vaccination date and the date of sample acquisition was 22.5 weeks, and there was no patient with side effect other than mild myalgia. The antibody titer was positive in all

Table 1. Baseline characteristics of 10 SLE patients with Belimumab

Characteristics	Total patients (n=10)
Belimumab & Antibody	
Belimumab duration, month, median (IQR)	7 (2.5)
mRNA 3rd vaccination, n (%)	10 (100)
Vaccine date to serum date (week), median (IQR)	22.5 (2.5)
Side effect (moderate to severe), n (%)	0
COVID infection, n (%)	2 (20)
Antibody positivity (>0.8U/mL), n (%)	10 (100)
High antibody titer (>250U/mL), n (%)	8 (80)
Clinical features	
Age, years, median (IQR)	35.5 (13.28)
Female, n (%)	9 (90)
Duration of SLE, years, median (IQR)	4 (0–8)
SLEDAI, median (IQR)	11 (4.5)
Combined Medication	
Hydroxychloroquine, n (%)	8 (80)
Corticosteroid / Prednisone, n (%)	4 (40)
MMF, n (%)	5 (50)
Azathioprine, n (%)	1 (10)
Tacrolimus, n (%)	3 (30)
History of Rituximab, n (%)	2 (20)
SLE-related manifestations	
Lupus nephritis, n (%)	6 (60)
Cytopenia, n (%)	5 (50)
Pleuritis, n (%)	2 (20)
Anti-phospholipid syndrome, n (%)	2 (20)
Laboratory data	
WBC, mg/dL, median (IQR)	4720 (2645.24)
Hb, mg/dL, median (IQR)	11.67 (2.19)
Platelet, IU/mL, median (IQR)	154.1 (89.01)
C3, mg/dL, median (IQR)	55.02 (22.89)
C4, mg/dL, median (IQR)	10.98 (8.86)
Anti-dsDNA Ab, IU/mL, median (IQR)	242.32 (166.39)
ESR, median (IQR)	26.2 (22.8)
CRP, median (IQR)	0.28 (0.11)

Values are median (interquartile range) or n (%)
SLE, systemic lupus erythematosus, SLEDAI, systemic lupus erythematosus disease activity index; WBC, white blood cell; Hb, hemoglobin; C3/C4, complement 3/4; anti-dsDNA, anti-double strand DNA; ESR, erythrocyte sedimentation rate; CRP, c-reactive protein; IQR, interquartile range

10 patients, and among them, 8 patients showed a high antibody titer of 250 U/mL or more, and the remaining two patients showed a relatively low antibody titer of 117 U/mL and 112 U/mL, respectively. One patient had been treated with Rituximab within one year and the other was using hydroxychloroquine.

Conclusion: Our findings suggest that Belimumab does not compromise the antibody production from the vaccination. SLE patients with Belimumab need not be reluctant to get the COVID-19 vaccines because of worrying about the humoral response impairment.

Disclosure: E. Kang: None; **Y. Kim**: None.

Abstract Number: 1471

A Comparative Study of Lupus Nephritis Class II and IgA Nephropathy: Renal Disease Other Than Lupus Nephritis in Systemic Lupus Erythematosus Patients

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis (LN) is one of major organ involvement of SLE and renal biopsy is commonly performed in SLE patients suspected of having LN to assess the severity of renal damage and guide treatment decisions. However, there have been cases where renal biopsies performed in SLE patients resulted in the diagnosis of other renal diseases, such as IgA nephropathy. The prevalence and similarities between IgA nephropathy and LN in SLE patients have not been extensively studied. This study aims to investigate the characteristics of SLE patients diagnosed with renal disease other than LN, with a focus on IgA nephropathy and its similarities and differences with class II LN.

Methods: A retrospective analysis was conducted on SLE patients who underwent renal biopsies between April 1997 and October 2022 at a single tertiary care academic center. Patients diagnosed with renal diseases other than LN were identified, with a particular focus on IgA nephropathy. Baseline characteristics, laboratory findings, and renal biopsy pathologic findings were collected and statistical analyses were performed.

Results: Among 483 SLE patients who underwent renal biopsies, 25 (5%) were diagnosed with renal diseases other than LN. The most common non-LN pathology was IgA nephropathy, accounting for 28% of cases. A comparison between patients with IgA nephropathy and class II LN showed no significant differences in age, sex, SLEDAI, eGFR or UPCR. In

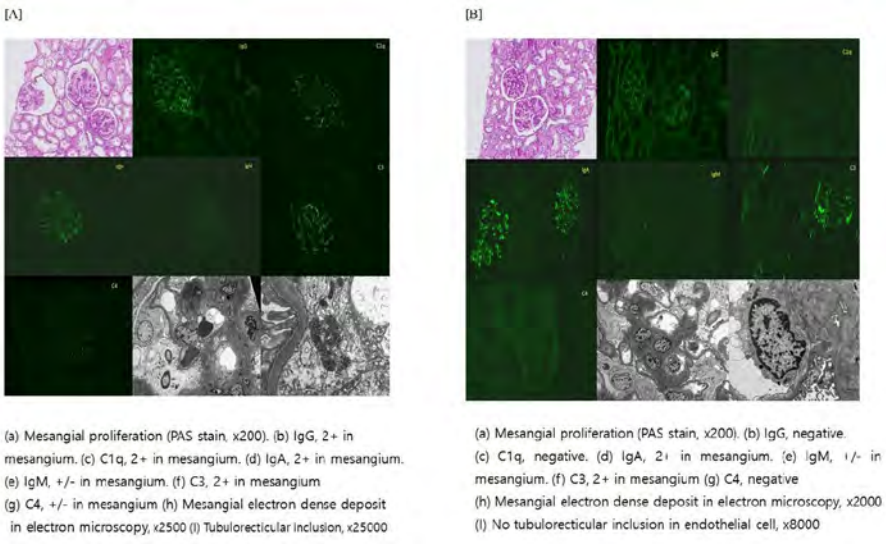

Figure 1. Comparison of Renal outcome of patients with IgA nephropathy and class II Lupus nephritis in SLE patients

Table 1. Kidney biopsy proflie of non-LN in patients with SLE

Total	25
IgA nephropathy	7 (28%)
DM nephropathy	2 (8%)
ANCA-associated GN	2 (8%)
Acute interstitial nephritis	2 (8%)
MPGN	4 (16%)
FSGS	3 (12%)
MGN	2 (8%)
TMA	2 (8%)
MCD	1 (4%)

Abbreviation: LN, lupus nephritis; DM, diabetes mellitus; ANCA-associated GN, anti-neutrophil cytoplasmic antibody-associated glomerulonephritis, MPGN, membranoproliferative glomerulonephritis; FSGS, focal segmental glomerulosclerosis; MGN, membranous nephropathy; TMA, thrombotic microangiopathy; MCD, minimal change disease.

pathologic finding, IgA nephropathy exhibited predominant IgA staining with higher intensity, while class II LN demonstrated "Full house" pattern. Long-term renal outcomes did not significantly differ between the two groups.

Conclusion: SLE patients can have renal diseases other than LN and IgA nephropathy was the most observed non-LN pathology in SLE patients. Comparison between IgA nephropathy and class II LN revealed similarities in clinical and pathological characteristics, although there were differences in immunofluorescence findings. The long-term renal outcomes

Table 2. Comparison of Kidney biopsies between IgA nephropathy and class II lupus nephritis in patients with SLE

	IgA nephropathy (n=7)	Class II LN (n=17)	p-value
Light microscopy[a]			
Hypercellularity, n (%)	3 (42.9)	12 (70.6)	0.084
Neutrophil/karyorrhexis, n (%)	1 (14.3)	2 (11.8)	0.723
Hyaline deposits, n (%)	1 (14.3)	3 (17.6)	0.651
Fibrinoid necrosis, n (%)	0 (0.0)	4 (23.6)	0.098
Cellular crescents, n (%)	2 (28.6)	3 (17.6)	0.522
Interstitial inflammation, n (%)	5 (71.4)	9 (52.8)	0.109
Global glomerulosclerosis, n (%)	4 (57.1)	14 (82.4)	0.191
Fibrous crescents, n (%)	1 (14.3)	3 (17.6)	0.240
Tubular atrophy, n (%)	2 (28.6)	4 (23.6)	0.608
Interstitial fibrosis, n (%)	3 (42.9)	6 (33.2)	0.476
Immunofluorescence			
IgA predominancy[b], n (%)	5 (71.4)	3 (17.6)	**0.021**
IgG predominancy[b], n (%)	0 (0.0)	10 (58.8)	**0.019**
Total count of positive staining, mean	4.1	5.6	**0.009**
IgA intensity, mean	2	1.18	**0.040**
IgG intensity, mean	0.29	1.29	**0.002**
Tubuloreticular inclusion, n (%)	0 (0.0)	6 (35.3)	0.130
Subendothelial deposit, n (%)	3 (42.9)	6 (35.3)	1.000

[a] LM (light microscopic) finding is basically analyzed by NIH activity/chronicity index used in lupus nephritis

[b] Predominant/co-predominant of IgA/IgG among staining

between the two groups have no significant differences. These results contribute to a better understanding of the diagnostic accuracy of renal diseases other than LN in SLE patients.

Disclosure: E. Kang: None; **S. Hong**: None.

Abstract Number: 1472

Prevalence of Hepatic Injury in Patients with Systemic Lupus Erythematosus: A 28-Year Single Center Experience

Asif Hitawala[1], Zerai Manna[2], Yenealem Temesgen-Oyelakin[3], Elaine Poncio[3], Christopher Koh[4], **sarfaraz Hasni**[2] and Theo Heller[4], [1]NIDDK/NIH, Bethesda, MD, [2]Lupus Clinical Trials Unit, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health (NIH), Bethesda, MD, [3]National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD, [4]NIDDK/Liver disease branch, Bethesda, MD

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) are known to have hepatic injury (HI), however large-scale longitudinal studies are lacking.We report our experience of HI in SLE patients.

Methods: A retrospective longitudinal single center study was conducted from 1994-2022 to identify patients enrolled in natural history protocol for SLE. Inclusion: 1) Age ≥ 18 years; 2) Diagnosis of SLE based on 1997 American College of Rheumatology revised criteria. Exclusion: Patients with either < 3 visits or < 6 months of follow-up. Demographic, laboratory, medication and liver histology data (when available) were obtained from the electronic medical records. Patients were divided into two categories- with and without HI. HI was divided into 5 categories- persistent hepatocellular injury, transient hepatocellular injury, persistent cholestatic injury, transient cholestatic injury and mixed. Patients were allowed to be in more than one category. Chi-square test and Kruskal-Wallis tests were used for comparing categorical and numerical variables, respectively. P-value < 0.05 was considered statistically significant and R software was used for all statistical analyses.

Results: Out of 1106 patients, 636 patients were included in the final cohort, with median duration of follow-up of 9.7 yrs (IQR 4.15-16.96). Mean age was 53.85 yrs (±15.31) and majority were females (555, 87.26%). A large proportion of patients (303, 47.64%) developed HI- persistent hepatocellular injury, transient hepatocellular injury, persistent cholestatic injury, transient cholestatic injury and mixed injury were present in 91, 174, 55, 78 and 67 patients, respectively. Patients with HI were older, more likely to be male, Asian, Caucasian or Hispanic and less likely to be African American (Table 1). Patients with HI also had longer follow-up. In majority of patients (230, 75.91%), the cause of HI could not be identified. Of the remaining 73 patients, non-alcoholic fatty liver disease was the most common, followed by drug-induced liver injury, SLE flare and non-alcoholic steatohepatitis (Table 2). On univariable analysis, apart from liver enzymes, age, gender, race, date of SLE diagnosis, duration of follow-up, iron, ferritin, ESR, and ANA were significantly associated with HI (Table 3). However, on multivariable analysis, only alkaline phosphatase, alanine transaminase and duration of follow-up remained associated with higher odds of HI, while older age was associated with lower odds, suggesting patients tend to develop HI at a younger age. All-cause mortality was higher in patients with HI.

Conclusion: A large number of SLE patients develop HI during the course of the disease, with transient hepatocellular injury the most common type of HI. While males and Asians, Caucasians and Hispanics seem to be at a higher risk, African-Americans seem to be at lower risk of HI, although in a majority of patients the cause remains unclear. Fatty liver disease

Table 1: Baseline Characteristics

Table 1: Baseline Characteristics

VARIABLE	HEPATIC INJURY	NO HEPATIC INJURY	p-value
N	303	333	
Age (in yrs)	56.61 ± 15.88	51.35 ± 14.34	<0.0001
Gender			0.02
Male	49	32	
Female	254	301	
Body Mass Index (kg/m^2)	26.6 (23.48, 32.35)	27.55 (23.23, 32.1)	0.5
Race			<0.0001
Asian	29	22	
African/American	67	120	
Multiracial	5	9	
Native Hawaiian	0	1	
Caucasian	151	130	
Unknown	51	51	
Ethnicity			
Hispanic or Latino	95	73	0.01
Not Hispanic or Latino	200	255	
Unknown Ethnic Group	8	5	
All-Cause Mortality	58	24	<0.001
Follow-up Duration (in years)	13.7 (8.28-20.77)	6.35 (2.69, 12.28)	<0.001
Date of SLE Diagnosis			0.22
Before 1997	57	34	
1997-2019	134	107	
After 2019	1	3	
Not available	111	189	
Albumin (g/dL)	3.81 (3.51, 4.07)	3.94 (3.61, 4.18)	0.0015
Alkaline Phosphatase (U/L)	70.25 (60.43, 85.88)	58.5 (48.75, 69.09)	<0.001
Alanine Transaminase (U/L)	25.47 (19.03, 33.75)	15.75 (12.75, 19.59)	<0.001
Aspartate Transaminase (U/L)	23.5 (19.38, 29.5)	18.61 (16.25, 21.25)	<0.001
Total Bilirubin (mg/dL)	0.4 (0.32, 0.51)	0.4 (0.3, 0.51)	0.51
Direct Bilirubin (mg/dL)	0.12 (0.1, 0.19)	0.18 (0.1, 0.2)	<0.001
Prothrombin Time (sec)	13.06 (12.23, 13.74)	13.2 (12.7, 13.9)	0.036
Gamma-glutamyl transferase (U/L)	0 (0, 44.54)	0 (0, 0)	<0.001
Erythrocyte Sedimentation rate (mm/hr)	28.86 (18.65, 42.09)	22 (12.56, 37.88)	0.0003
Iron (mcg/dL)	48.5 (29.25, 68.02)	42.4 (0, 70)	0.062
Ferritin (mcg/L)	46 (11.06, 144.5)	29.62 (0, 80)	0.0004
C-Reactive Protein (mg/L)	1.78 (0, 4.42)	1.195 (0.55, 3.69)	0.02
White Blood Cells (K/μL)	5.81 (4.88, 6.87)	5.56 (4.41, 6.72)	0.026
Hemoglobin (g/dL)	12.23 (11.28, 13.01)	12.23 (11.34, 13.01)	0.157
Platelet Count (K/μL)	241.7 (196.62, 275.04)	236.1 (198.62, 281.5)	0.6
Anti-Nuclear Antibody U)	7.4 (1.01, 11.95)	4.5 (0.9, 11.3)	0.24
Anti-Ribonucleoprotein Antibody (U)	0 (0, 0.2)	0 (0, 0.8)	0.021
Treatment			
Corticosteroid	86	42	<0.001
Hydroxychloroquine	99	75	<0.001
Azathioprine	55	26	<0.001
Methotrexate	27	18	0.12

Table 2; Etiologies of Hepatic Injury

Table 2: Etiologies of Hepatic Injury

Diagnosis	Number of Patients
Non-alcoholic fatty liver disease	29
Non-alcoholic steatohepatitis (liver-biopsy proven)*	9
Drug-Induced Liver injury	14
Lupus flare	13
Alcoholic Hepatitis*	1
Primary biliary cholangitis	1
Nodular Regenerative Hyperplasia	1
Autoimmune hepatitis	1
Chronic Hepatitis C	1
Chronic Hepatitis B	1
Liver metastasis secondary to colon cancer	1
HELLP syndrome	1
Portal vein thrombosis	1

*One patient had both alcoholic hepatitis and Non-alcoholic steatohepatitis on liver biopsy

Table 3: Univariable and multivariable analysis

VARIABLE	UNIVARIABLE ANALYSIS			MULTIVARIABLE ANALYSIS		
	Odds Ratio	95% CI	p-Value	Odds Ratio	95% CI	p-Value
Age	1.02	1.01, 1.03	<0.001	0.97	0.945, 0.998	0.03
Gender	1.81	1.13, 2.92	0.01			
Race	0.42	0.23, 0.79	<0.001			
Body Mass Index	1.00	0.97, 1.02	0.74			
Year of SLE Diagnosis	0.97	0.96, 0.99	0.01	1.04	0.99, 1.09	0.1
Albumin	0.76	0.55, 1.05	0.09			
Alkaline Phosphatase	1.05	1.03, 1.06	<0.001	1.05	1.03, 1.07	<0.0001
Alanine Transaminase	1.20	1.16, 1.24	<0.001	1.22	1.15, 1.3	<0.0001
Aspartate Transaminase	1.17	1.13, 1.21	<0.001			
Total Bilirubin	0.88	0.41, 1.9	0.74			
Direct Bilirubin	0.08	0.01, 0.87	0.03	0.003	0, 8.16	0.155
Prothrombin Time	0.98	0.92, 1.05	0.63			
Gamma glutamyltransferase	1.04	1.03, 1.05	<0.001	1.01	0.996, 1.02	0.097
Erythrocyte Sedimentation Rate (ESR)	1.01	1, 1.02	0.01			
Iron	1.01	1, 1.01	0.02			
Ferritin	1.00	1, 1	<0.001			
C-Reactive Protein (CRP)	1.03	0.99, 1.06	0.10			
White blood cells	1.08	0.99, 1.17	0.07			
Hemoglobin	1.02	0.91, 1.15	0.72			
Platelet Count	1.00	1, 1	0.87			
Anti-nuclear antibody	1.04	1.01, 1.08	0.01			
Anti-Ribonucleoprotein antibody	0.93	0.87, 1	0.05			
Duration of follow-up	1.00	1, 1	<0.001	1.0002	1.00017, 1.0004	<0.0001
All-cause mortality	3.05	1.84, 5.05	<0.001			

Univariable and Multivariable Analysis of Hepatic Injury

was the most common cause of liver disease, although patients were also found to have autoimmune hepatitis, primary biliary cholangitis and nodular regenerative hyperplasia. Higher mortality in patients with liver disease might suggest a more severe SLE disease course and consequently worse outcomes.

Disclosure: A. Hitawala: None; **Z. Manna**: None; **Y. Temesgen-Oyelakin**: None; **E. Poncio**: None; **C. Koh**: None; **s. Hasni**: AstraZeneca, 5; **T. Heller**: None.

Abstract Number: 1473

Mortality from Diseases of the Nervous System in Patients with Lupus in the past Two Decades

Ansaam Daoud[1], Loai Dweik[2], Marina Nighat Magrey[3] and Omer Pamuk[4], [1]University Hospitals, Case Western Reserve University, Akron, OH, [2]Cleveland Clinic Akron General, Akron, OH, [3]Case Western Reserve University, University Hospitals, Cleveland, OH, [4]University Hospitals Cleveland Medical Center, Cleveland, OH

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is a chronic autoimmune disease and affects many organ systems. Juvenile onset disease, male sex, renal involvement, and central nervous system involvement are poor prognostic factors in SLE. ACR defined some neuropsychiatric symptoms in SLE. However, their attribution to SLE is challenging due to confounding factors, especially in

older populations. Atherosclerotic complications, including cardiovascular and cerebrovascular diseases, are important causes of mortality in patients with SLE. Until now, no study has evaluated nervous system mortality causes in SLE patients. This study investigated nervous system-related mortality in SLE in the past two decades in the USA.

Methods: This retrospective cohort study used the Multiple Cause of Death files maintained by the National Center for Health Statistics to investigate the direction of proportionate nervous system-related mortality in SLE, defined as the number of deaths from diseases of the nervous system (the underlying cause of death: International Classification of Diseases, version 10 [ICD10]: G00-G98), divided by the number of all-cause mortality in patients with SLE (defined in multiple causes of death: ICD10 code M32) from 1999-2020. The data set utilizes death certificate data for US residents. To analyze changes in mortality trends, we separated the study period into two decades, the first decade (1999-2009) and the last decade (2010-2020). Spearman's correlation test was used for trend analysis, and the Chi-square test was used for comparisons.

Results: 47,337 deaths in SLE occurred during the study period. 814 (1.72%) died of nervous system causes. The mean age for nervous system-related mortality was 69.3 years. Proportionate nervous system-related mortality in SLE was higher in women than men (1.79% vs. 1.34%, p=0.0087), significantly lower in African-American SLE patients than in other races (1.27% vs. 1.93%, p< 0.00001), and lower in Hispanic SLE patients than non-Hispanic patients (1.24% vs. 1.79%, p=0.0034). Proportionate mortality from nervous system disease increased from 1.33% in the first decade (1999-2009) to 2.11% in the second decade (p< 0.00001) (Figure 1). The most common nervous system cause of death in SLE was Alzheimer's Disease (27%). Table 1 shows other nervous system causes for mortality (Table 1).

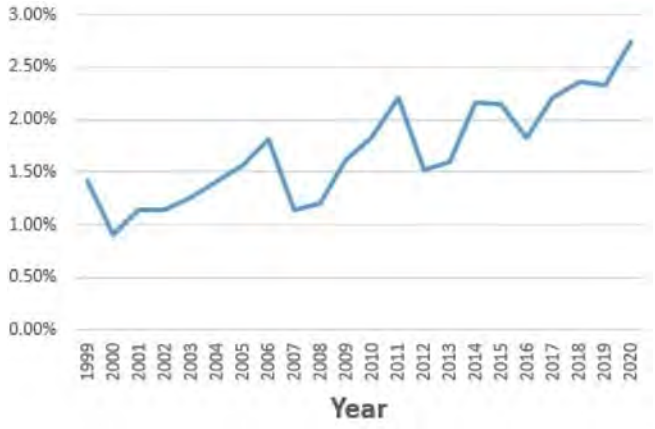

Figure 1. Proportionate Nervous System Disease Mortality in SLE Patients Over the Past Two Decades

Table 1. Mortality in SLE Patients from Diseases of the Nervous System

Mortality cause	N (%)
Alzheimer disease	220 (27)
Others (not listed)	168 (21)
Meningitis/Encephalitis	83 (10)
Epilepsy/status epilepticus	70 (9)
Parkinson disease	60 (7)
Multiple sclerosis	54 (7)
Anoxic brain damage	48 (6)
Senile degeneration of the brain	23 (3)
Acute transverse myelitis	20 (2)
Unspecified Encephalopathy	18 (2)
Guillan-Barre syndrome	14 (2)
Myasthenia gravis	14 (2)
Motor neuron disease	13 (2)
Sequelae of inflammatory diseases of CNS	10 (1)

Conclusion: This national data showed a significant increase in proportionate mortality from nervous system diseases in SLE. SLE patients in ethnic or racial minority groups seem protected from nervous system-related mortality. Prospective cohort studies are required to understand these trends.

Disclosure: A. Daoud: None; **L. Dweik**: None; **M. Magrey**: AbbVie, 2, Bristol Myers Squibb, 2, Eli Lilly, 2, Novartis, 2, Pfizer Inc, 2, UCB, 5; **O. Pamuk**: None.

Abstract Number: 1474

Associations and Outcomes of Critical Peripheral Ischemia in Systemic Lupus Erythematosus (SLE): Data from Indian SLE Inception Cohort for Research (INSPIRE)

Vineeta Shobha[1], Liza Rajasekhar[2], Sandra Manuel[3], Nayana V[3], Ranjan Gupta[4], Bidyut Das[5], Parasar Ghosh[6], Chengappa Kavadichanda[7], Ashish J Mathew[8], Manish Rathi[9], Avinash Jain[10], Sumithra Selvam[3] and Amita Aggarwal[11], [1]St. John's National Academy of Health Science, Bangalore, India, [2]Nizam's Institute of Medical Sciences, Madhapur, India, [3]St. John's Research Institute, Bangalore, India, [4]All India Institute of Medical Sciences, New Delhi, India, [5]SCB medical college, Cuttack, India, [6]Govt of West Bengal, Kolkata, India, [7]Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India, [8]Christian Medical College, Vellore, India, [9]Postgraduate Institute of Medical education and Research, Chandigarh, India, [10]SMS Medical College, Lucknow, India, [11]Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow, India

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Among the cutaneous manifestations of SLE, critical peripheral ischemia (CPI) including digital infarcts and gangrene are considered rare, gangrene occurring only in about 0.2% as initial presentation and in 1.2% in the longest longitudinal cohort with a follow up of 44 years[1]. Whether vasculitis or thrombosis or both contribute to these remains debated. We report the incidence, associations and outcome of digital infarcts and gangrene in the Indian Systemic Lupus Erythematosus(SLE) Cohort.

Methods: From the ongoing prospective INdian SLE inception cohort For Research (INSPIRE), baseline data on CPI was accessed with key terms: 'Digital Infarct' and 'Digital gangrene' in May 2023. Association with other clinical domains and autoantibodies including antiphospholipid antibodies were analysed between cases and controls (all others without digital infarcts or gangrene). Adjusted odds ratios were reported using multivariable logistic regression analysis to identify the factors associated with gangrene and or digital infarcts

Results: Of 2503 patients in the INSPIRE cohort, 79 (3.2%) patients had CPI at initial presentation. Their mean age was 28.7 ±9.5 years including 9 (11.3%) children and 76(96.2%) women. There were 92 events (gangrene 47, digital infarcts 45 and with both gangrene and infarcts in 13). The duration of CPI symptoms was 7.0 ±11.9 days. None of the CPI patients were smokers.

The presence of coexistent thrombosis AOR[10.2(3.91,24.5)]($p< 0.001$), Raynaud's phenomenon AOR[6.41(1.83,17.4)] ($p< 0.006$) and longer disease duration prior to diagnosis AOR[1.01(1.00,1.02)] ($p< 0.007$) were significantly associated with the presence of CPI in SLE patients. The presence of anti Scl-70 antibody AOR[5.34(1.78,13) ($p< 0.008$) and the

Table1: Associations and Outcome of Digital ischemia in SLE Inception cohort

Variables	CPI (N=79)	Controls (N=2424)	P value	Adjusted Odds ratio
Demographics				
Age in years (Mean±SD)	28.72±9.56	27.67±10.23	0.365	
Median duration of illness (months)	12.0(6-32.25)	10.0(4-22)	**0.007**	[1.01(1.00,1.02)]
Clinical parameters				
Fever	53 (67%)	1,654 (68%)	0.8	
Non-Scarring alopecia	67 (85%)	1,881 (78%)	0.13	
Oral Ulcers	43 (54%)	1,444 (60%)	0.4	
Acute Cutaneous Lupus	39 (49%)	1,206 (50%)	>0.9	
Subacute cutaneous or Discoid Lupus	11 (14%)	299 (12%)	0.7	
Arthritis	59 (75%)	1,652 (68%)	0.2	
Proteinuria	24 (30%)	1,002 (41%)	**0.051**	[0.62(0.37,0.99)]
Class 3 or 4 Lupus Nephritis	5 (6.3%)	390 (16%)	**0.019**	[0.35(0.12,0.79)]
Class 2 or 5 Lupus Nephritis	5 (6.3%)	229 (9.4%)	0.3	
Neuropsychiatric Lupus	7(8.9%)	243 (10%)	0.7	
Pleural effusion	13 (16%)	511 (21%)	0.3	
Pericarditis	0	33 (1.4%)	0.6	
Leukopenia	21 (27%)	758 (31%)	0.4	
Thrombocytopenia	19 (24%)	603 (25%)	0.9	
Raynaud's phenomenon	4 (5.1%)	20 (0.8%)	**0.006**	[6.41(1.83,17.4)]
Pulmonary hypertension	4 (5.1%)	65 (2.7%)	0.3	
Coexistent thrombosis	13 (16%)	68 (2.8%)	**<0.001**	[10.2(3.91,24.5)]
Antiphospholipid antibodies				
ACL (IgM or IgG)	12 (15%)	192 (7.9%)	**0.020**	[2.08(1.06,3.78)]
anti B2GPI (IgM or IgG)	15 (19%)	247 (10%)	**0.012**	[2.06(1.12,3.58)]
Lupus anticoagulant	15 (34%)	275 (21%)	**0.032**	[1.98(1.02,3.70)]
Triple positivity	4 (5.1%)	34 (1.4%)	**0.030**	[3.75(1.10,9.70)]
Antinuclear antibodies				
dsDNA	17 (22%)	585 (24%)	0.3	
Nucleosome	13 (16%)	608 (25%)	0.11	
Histone	14 (18%)	473 (20%)	0.9	
Ro-52 (SSA)	27 (34%)	678 (28%)	0.4	
Ro-60 (SSA)	26 (33%)	775 (32%)	0.6	
SSB (LA)	8 (10%)	184 (7.6%)	**0.030**	[1.28(0.56,2.55)]
Ribosomal P	16 (20%)	576 (24%)	0.8	
RNP/Sm	38 (48%)	956 (39%)	0.090	
Sm	21 (27%)	730 (30%)	0.6	
Scl-70	5 (6.3%)	30 (1.2%)	**0.008**	[5.34(1.78,13)]
PM-Scl	2 (2.5%)	10 (0.4%)	0.061	
Jo-1	0	3 (0.1%)	0.9	
CENP-B	0	14 (0.6%)	0.9	
PCNA	2 (2.5%)	25 (1.0%)	0.3	
AMA-M2	2 (2.5%)	76 (3.1%)	0.5	
SLEDAI	13.05±9.25	13.05±8.14	0.997	
Outcome				
Minor Tissue Loss	8 (10%)	0	**<0.001**	
Early Mortality (<6 months)	4 (5.1%)	150 (6.2%)	0.9	

Abbreviations: ACL- Anticardiolipin Antibody , B2GP1- Beta 2 glycoprotein 1, SLEDAI- SLE disease activity index

antiphospholipid antibodies including lupus anticoagulant {AOR for triple positivity [3.75(1.10,9.70)](p< 0.05)} were significantly associated with higher odds of CPI positivity.(Table 1) None of Scl-70 positive patients had features of scleroderma. The disease activity as measured by SLEDAI and the proportion of early mortality were similar in those with and without CPI.

Conclusion: Critical peripheral ischemia occurred in a higher proportion (3.2%) of SLE patients in the INSPIRE cohort as compared to earlier reports. Both prothrombotic state and vasculopathy contribute to its occurrence.

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Abstract Number: 1475

Retrospective Study of Obesity on Clinical and Immunological Features in Systemic Lupus Erythematosus Using AI Software Deep 6 and EPIC Slicer Dicer

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by autoantibodies and systemic inflammation, affecting multiple organs especially kidney. Environmental factors, genetic predisposition, and hormone contribute to lupus pathogenesis. One of the environmental factors, obesity is now considered as a state of chronic low-grade inflammation, but the role of obesity in SLE remains controversial. Studies have shown that adipose tissue contributes to systemic inflammatory status in obese individuals by secreting adipokines, complement components, and other pro-inflammatory mediators. Our recent published studies showed that a high-fat diet exacerbated lupus development and autoimmunity in MRL/lpr lupus-prone mice. Here we compared the clinical features, lab parameters, and autoimmunity in obese and non-obese lupus patients.

Methods: For data abstraction, the AI software Deep6 was used for query building in patients diagnosed with SLE (ICD-10 code: M32.9). Using Slicer Dicer (via EPIC) and Microsoft Excel, data organization resulted in 1126 SLE patients in 2022, with 133 being obese (BMI >30) and 913 being non-obese control (BMI< 25). In a representative sample of patients with SLE in 2022, BMI levels, SLE disease activity (SLEDAI), lupus nephritis involvement, creatinine level, levels of autoantibodies including antinuclear antibody (ANA) and anti-dsDNA antibody, levels of C-reactive protein (CRP) and complement (C3 and C4), levels of triglyceride and cholesterol in patients' serum were extracted from EPIC to REDCap and exported as Excel file. Unpaired Student's *t-test* and multi-variable ANOVA were used for statistical significance analysis among the groups. Two-tailed $p< 0.05$ was considered significant.

Results: Ninety-nine lupus patients were included in this study; 49% were obese (BMI ≥ 30 kg/m^2) with a significantly higher ratio of total cholesterol/HDL and higher triglyceride level, in comparing to the 21% were non-obese (BMI< ![if !msEquation] > < ![endif] >25kg/m^2) patients. A significantly higher frequency of lymphocytes was observed in the blood of obese lupus patients compared to non-obese lupus patients (p< 0.01). There is no difference in SLEDAI, CRP, and ANA levels between obese and non-obese lupus patients. However, anti-dsDNA titer (p< 0.05) and C3 level (p< 0.005) were significantly increased in the obese lupus patients comparing to non-obese patients. Additionally, significant higher level of creatinine (p< 0.005) and significantly increased incidence of lupus nephritis (p< 0.05) and were found in obese patients compared to non-obese lupus patients.

Conclusion: Our results showed that obese lupus patients had a dysfunctional clinical and immunological phenotype with worse outcomes, indicating that obesity may directly influence SLE pathogenesis and autoimmunity. Further study in cellular and molecular levels in obese lupus patients may help us understand the complex mechanism underlying the relationship between SLE and obesity, providing better preventive and treatment strategies for obese lupus patients.

Disclosure: S. Shah: None; **c. keshavamurthy**: None; **S. Ahrens**: None; **D. Reeves**: None; **W. Davis**: None; **R. Quinet**: None; **J. Zakam**: None; **S. Hayat**: None; **T. Leeth**: None; **S. Umer**: None; **S. Hasan**: None; **M. Latsis**: None; **X. Zhang**: None; **G. Lobo**: None.

Abstract Number: 1476

Discriminating Disease Flare from Infection in Febrile Patients with Systemic Lupus Erythematosus Admitted to a Safety-Net Hospital System: A Retrospective, Multicenter Study

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Fever in systemic lupus erythematosus (SLE) patients presents a diagnostic challenge as the differential diagnosis includes disease flare and infection. Identifying laboratory parameters to distinguish between the two is important for clinical care improvement. This study evaluates clinical laboratory parameters in febrile SLE patients admitted to three safety-net hospitals in Los Angeles for their ability to discriminate flare from infection.

Methods: Patients aged over 18 years admitted between August 1, 2016, and July 31, 2019, with a diagnosis of SLE and fever (≥38C) were reviewed for infection versus flare based on viral panels, microbial cultures, antibiotic use, discharge diagnosis, and SLEDAI-2K scores. Laboratory parameters collected within 48 hours of admission (CBC with differential, liver function panel, ESR, CRP, C3, C4, lactate, procalcitonin, and ferritin) were analyzed.

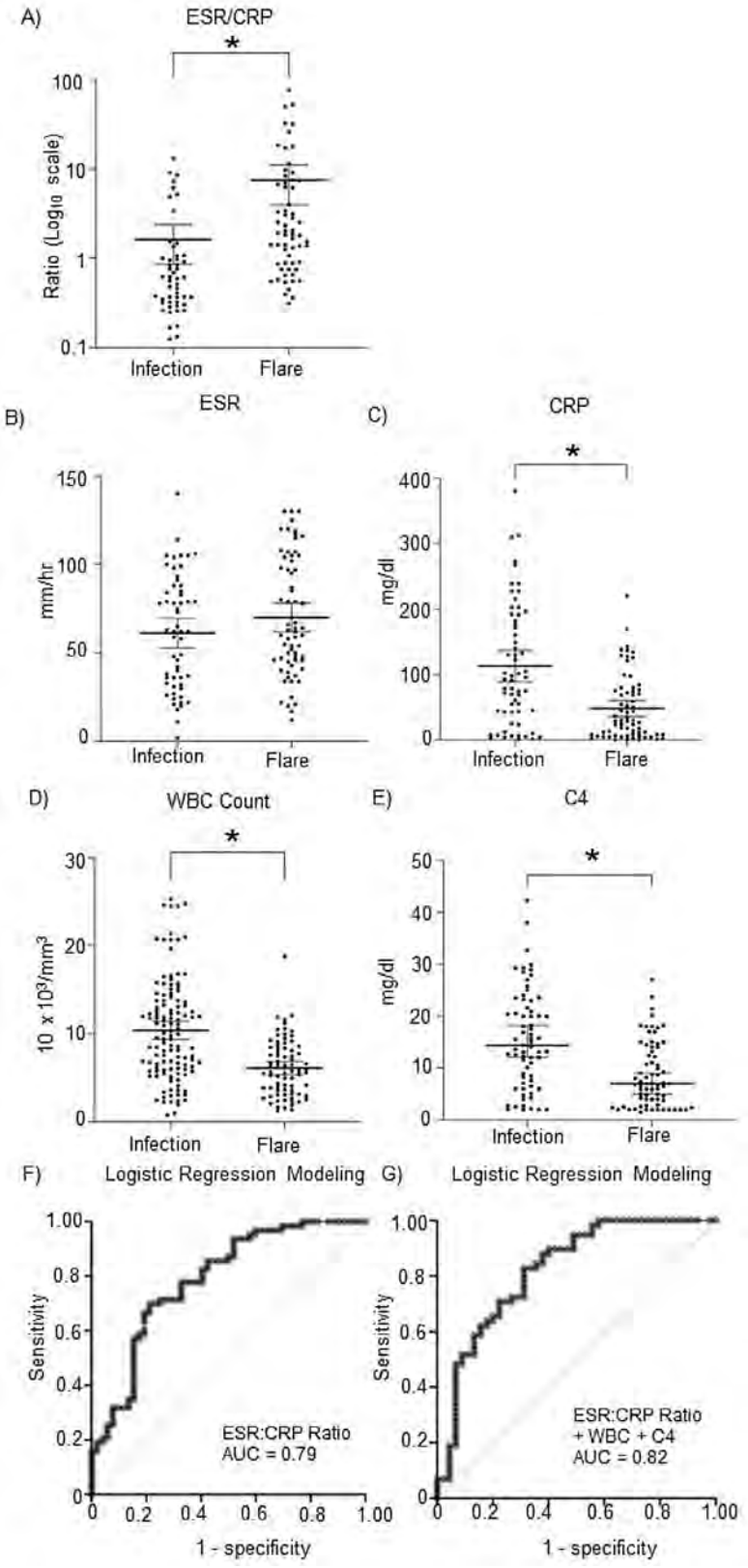

Figure 1. Scatterplots and ROC for variables included in ESR:CRP ratio + WBC count + C4 model. Scatter plots for ESR (A), CRP (B), and variables used in the model (C-E). *p<0.01, independent t-tests, Data are presented as individual points and mean ± 95% confidence interval. The ROC curves for the ESR:CRP ratio alone as well as the ESR:CRP ratio + WBC count + C4 used for logistics regression (F) as well as ESR:CRP ratio + WBC count + C4 vs. CRP + WBC count + C4.

Table 1. Demographics (sex, race/ethnicity, age, hospital site of admission), immunomodulatory medications and prednisone equivalents at time of admission, and proportion of patients discharged with increased steroid use and/or antimicrobials. All numbers represent the first case if the same patient had multiple presentations. All statistics Chi-square, except age which was a independent, t-test shown as mean +/- SD. UCLA = University of California, Los Angeles; LAC = Los Angeles County; USC = University of Southern California; DMARD = disease-modifying antirheumatic drugs; GC = glucocorticoids; mg = milligrams

Table 1. Demographics

		Flare, n (%)		Infection, n (%)	Significance (p)
Total	N	Count (%)	N	Count (%)	
Sex	72		108		0.53
Male		11 (15.3)		13 (12.0)	
Female		61 (84.7)		95 (88.0)	
Race/Ethnicity	72		108		0.62
Black		8 (11.1)		15 (13.9)	
Hispanic		56 (77.8)		73 (67.6)	
White/European		0 (0.0)		2 (1.9)	
Asian/Pacific Islander		3 (4.2)		6 (5.6)	
Caribbean		1 (1.4)		1 (0.9)	
Did not state or Other		4 (5.6)		11 (10.2)	
Age (years, mean ± SD)	72	36.7 ± 13.0	108	44.2 ± 14.8	**<0.01**
Site	72		108		0.88
Harbor-UCLA		21 (29.2)		30 (27.8)	
LAC + USC		34 (47.2)		55 (50.9)	
Olive View-UCLA		17 (23.6)		23 (21.3)	
Admission Immunomodulation	72		108		
None		18 (25)		14 (13.0)	**<0.05**
Anti-malarial use		42 (58.3)		75 (69.4)	0.13
Anti-malarial only		8 (11.1)		11 (10.2)	0.84
1 conventional DMARD		10 (13.9)		12 (11.1)	0.58
1 conventional DMARD + GC		8 (11.1)		21 (19.4)	0.14
2 conventional DMARDs		8 (11.1)		14 (13.0)	0.71
2 conventional DMARDs + GC		16 (22.2)		22 (20.4)	0.77
3 conventional DMARDs		1 (1.4)		0 (0)	0.22
3 conventional DMARDs + GC		1 (1.4)		1 (0.9)	0.77
1 conventional DMARD + biologic + GC		1 (1.4)		4 (3.7)	0.35
Biologic only		1 (1.4)		0 (0)	0.22
GC only		3 (4.2)		8 (7.4)	0.38
Rituximab (within 6 months)		3 (4.2)		8 (7.4)	0.38
Cyclophosphamide (within 6 months)		2 (2.8)		1 (0.9)	0.95
Belimumab (within 6 months)		2 (2.8)		4 (3.7)	0.73
Daily Prednisone Equivalents on Admission (mg)	72		108		0.17
None		40 (55.6)		41 (38.0)	
≤5mg		16 (22.2)		34 (31.5)	
6-10mg		8 (11.1)		21 (19.4)	
11-20mg		5 (6.9)		6 (5.6)	
>20		3 (4.2)		6 (5.6)	
Mortality during admission	72		108		0.53
Y		2 (2.8)		5 (4.6)	
N		70 (97.2)		103 (95.4)	
Discharged with Increased steroid regimen	70		103		**<0.001**
Y		59 (84.3)		17 (16.5)	
N		11 (15.7)		86 (83.5)	

Results: The study population included 200 admissions (123 infection and 77 lupus flare cases), representing 180 unique patients (Table 1). Thirteen percent of patients identified as Black and 72% as Hispanic. Febrile SLE patients with disease flare were younger than those with infection (mean age 37 versus 43, $p < 0.01$). Patients with an SLE flare were more likely using immunomodulatory medications on admission (25% versus 13%, $p < 0.05$) and were more likely to be discharged with an increased steroid regimen (84.3% versus 16.5%, $p < 0.001$) (Table 1). WBC count, hemoglobin, platelet count, neutrophil count, monocyte count, CRP, C3, C4, lactate, neutrophil/lymphocyte ratio, monocyte/lymphocyte ratio, and ESR:CRP ratio were significantly different in febrile SLE patients ultimately diagnosed with an infection from those diagnosed with an SLE flare (Table 2). Multivariable mixed effects logistic regression indicated that optimized differentiation of infection from SLE flare using a single metric is best when considering the ESR:CRP ratio, yielding a receiving operator characteristic (ROC) area under the curve (AUC) of 0.79. Combining the ESR:CRP ratio, C4 level, and WBC count improved the AUC to 0.82 (Figure 1). We defined ideal predictive cut-off point values for ESR:CRP ratio, WBC count, and C4 within the model. The thresholds for predicting flare over infection for each variable are ESR:CRP ratio ≥ 3.4 (Odds Ratio [OR] 1.39, Sensitivity [SE]=0.85, Specificity [SP]=0.35), WBC count ≤ 9.4 10^3/mm3 (OR 2.33, SE=0.52, SP=0.84), and for C4 ≤ 10.9 mg/dl (OR 1.67, SE=0.69, SP=0.69).

Table 2. Laboratory parameters as stratified by diagnosis of infection or flare. All values used are results from the first 48hours of admission. Hypothesis testing was conducted using independent t-tests. Data are presented as mean ± standard deviation. WBC = white blood cells; RDW = red cell distribution width; ESR = erythrocyte sedimentation rate; CRP = c-reactive protein; globulin gap = total protein – albumin

Table 2. Laboratory Parameters stratified by diagnosis.

Laboratory Parameter	n	Flare	n	Infection	Significance (p-value)[1]
Temperature (Celsius)	77	38.5 ± 0.4	123	38.7 ± 0.6	0.056
WBC Count (x10^9/L)	**77**	**6.1 ± 4.0**	**123**	**10.4 ± 2.8**	**<0.001**
Hemoglobin (g/dL)	**77**	**10.0 ± 2.0**	**123**	**10.7 ± 2.0**	**0.048**
Red Cell Distribution Width (%)	77	16.5 ± 4.0	123	16.2 ± 2.8	0.557
Platelet Count (x10^9/L)	**77**	**196.8 ± 99.1**	**123**	**229.6 ± 113.2**	**0.038**
Absolute Neutrophil Count (x10^9/L)	**76**	**4.9 ± 3.1**	**121**	**8.5 ± 5.5**	**<0.001**
Absolute Lymphocyte Count (x10^9/L)	76	0.7 ± 0.4	121	0.9 ± 0.7	0.233
Absolute Monocyte Count (x10^9/L)	**76**	**0.4 ± 0.3**	**121**	**0.6 ± 0.4**	**<0.001**
Erythrocyte Sedimentation Ratio (mm/Hr)	66	70.1 ± 33.2	57	61.2 ± 32.0	0.137
C-Reactive Protein (mg/L)	**67**	**48.3 ± 49.9**	**62**	**112.7 ± 93.0**	**<0.001**
Albumin (g/dL)	73	3.1 ± 0.8	108	3.2 ± 0.7	0.359
Total Protein (g/dL)	73	6.4 ± 1.1	108	6.4 ± 1.1	0.883
Complement C3 (mg/dL)	**71**	**59.0 ± 32.5**	**70**	**82.2 ± 40.4**	**<0.001**
Complement C4 (mg/dL)	**71**	**8.7 ± 6.2**	**70**	**15.5 ± 9.5**	**<0.001**
Lactate (mmol/L)	**74**	**1.3 ±0.5**	**112**	**1.6 ± 1.0**	**0.013**
Procalcitonin (ng/mL)	36	0.7 ± 1.1	44	4.0 ± 11.0	0.079
Ferritin (mg/L)	33	1620 ± 3774	33	571.3 ± 684	0.121
RDW/Platelet Ratio	77	0.1 ± 0.2	123	0.1 ± 0.1	0.149
Neutrophil/Lymphocyte Ratio	**76**	**8.4 ± 7.5**	**120**	**15.9 ± 17.3**	**<0.001**
Platelet/Lymphocyte Ratio	76	347.7 ± 288.3	120	413.1 ± 377.2	0.198
Monocyte/Lymphocyte Ratio	**76**	**0.58 ± 0.5**	**120**	**0.96 ± 0.88**	**<0.001**
Neutrophil/WBC ratio	76	0.76 ± 0.16	121	0.79 ± 0.21	0.436
Monocyte/WBC ratio	76	0.06 ± 0.04	121	0.06 ± 0.05	0.888
ESR:CRP Ratio	**63**	**7.5 ± 14.1**	**52**	**1.6 ± 2.7**	**0.004**
Globulin Gap	73	3.3 ± 1.2	107	3.2 ± 0.9	0.503
Albumin:Globulin Ratio	73	1.1 ± 0.8	107	1.1 ± 0.4	0.898

Conclusion: The ESR:CRP ratio, readily available in clinical settings, has utility in discriminating infection from flare in febrile SLE patients and warrants prospective validation.

Disclosure: A. Amarnani: None; **F. Liu**: None; **M. Wilson**: None; **N. Lim**: None; **W. Stohl**: GSK, 5, Pfizer, 5; **L. Wise**: AstraZeneca, 6, Aurinia Pharma, 2, 6, GlaxoSmithKlein(GSK), 6.

Abstract Number: 1477

Clinical and Economic Burden of Herpes Zoster in Patients with Systemic Lupus Erythematosus: A Retrospective Cohort Study

Nikita Stempniewicz[1], Andrea Steffens[2], Kimvi Kim[1], Christopher Bell[3], Mary DuCharme[2], Helen Trenz[2] and David Singer[1], [1]GlaxoSmithKline, Philadelphia, PA, [2]Optum, Eden Prairie, MN, [3]GlaxoSmithKline, US Value Evidence and Outcomes, Durham, NC

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Herpes zoster (HZ) is characterized by a painful dermatomal rash and is associated with increased healthcare costs and reduced quality of life. Systemic lupus erythematosus (SLE) is associated with an increased risk of HZ. Data on the clinical and economic impact of HZ among people with SLE in the United States (US) is limited. This study aimed to estimate healthcare resource utilization (HRU) and costs in patients with SLE and HZ in comparison to patients with SLE only.

Methods: This retrospective cohort study used US administrative claims data (Optum Research Database) between October 2015 and March 2022 to identify adults (aged ≥18 years) with SLE, based on ≥1 inpatient or ≥2 outpatient claims ≥30 days apart with an International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) diagnosis code for SLE (M32.xx, excluding M32.0). Patients with SLE were either assigned to an SLE+HZ or SLE-only cohort based on ≥1 HZ diagnosis code (ICD-10-CM: B02.xx, excluding B02.2x). Index date was the first observed HZ diagnosis between October 2016 and March 2022 for the SLE+HZ cohort and was assigned for the SLE-only cohort based on the distribution of index dates in the SLE+HZ cohort. All patients were required to have 12 months of continuous enrollment (CE) pre-index (baseline) and ≥1 month of CE post-index (follow-up). Patients with a baseline HZ diagnosis or a HZ vaccine in the up to 5 years pre-index (depending on data availability for patients) were excluded. Clinical and demographic characteristics were measured during baseline. Patients with SLE+HZ were propensity score matched 1:4 to patients with SLE-only with at least as much post-index follow-up time. Propensity scores were calculated using logistic regression with cohort as the outcome and baseline characteristics as predictors. Outcomes included all-cause HRU and costs in the 1-month period post-index and for matched sets with sufficient follow-up time, also in the 3-month period post-index. Outcomes were described overall, and stratified by ambulatory, emergency room, inpatient, and pharmacy HRU and costs.

Results: After matching, 2,126 and 8,504 patients were included in the SLE+HZ and SLE-only cohorts, respectively. No significant differences were observed in demographic and clinical characteristics between the matched cohorts, with similar mean (standard deviation [SD]) age (59 [14]), percent female (91-92%), and baseline HRU and costs (table 1). In the 1-month post-index, mean (SD) HRU was higher in the SLE+HZ vs. SLE-only cohort for ambulatory (SLE+HZ: 4.5 [4.3]; SLE-only: 3.1 [4.1]) emergency (SLE+HZ: 0.41 [0.99]; SLE-only: 0.17 [0.71]), inpatient (SLE+HZ: 0.09 [0.32]; SLE-only: 0.04 [0.20]), and pharmacy HRU (SLE+HZ: 6.23 [4.75]; SLE-only: 4.44 [4.45]). Mean (SD) costs 1-month post-index were

Table1: Baseline characteristics

	SLE+HZ (N=2,126)	SLE-only (N=8,504)	Standardized Difference (%)*
Age (years)			
mean (SD)	58.89 (14.20)	59.19 (4.05)	2.1
Gender, n (%)			
Female	1,943 (91.39)	7,788 (91.58)	0.67
Male	183 (8.61)	716 (8.42)	0.67
Race/ethnicity, n (%)			
Non-Hispanic White	1,318 (61.99)	5,090 (59.85)	4.39
Non-Hispanic Black	382 (17.97)	1,751 (20.59)	6.65
Non-Hispanic Asian	55 (2.59)	218 (2.56)	0.15
Hispanic	266 (12.51)	1,052 (12.37)	0.43
Unknown	105 (4.94)	393 (4.62)	1.49
Insurance type, n (%)			
Commercial	969 (45.58)	3,825 (44.98)	1.2
Medicare	1,157 (54.42)	4,679 (55.02)	1.2
Region, n (%)			
Northeast	235 (11.05)	917 (10.78)	0.87
Midwest	442 (20.79)	1,748 (20.56)	0.58
South	1,152 (54.19)	4,672 (54.94)	1.51
West	297 (13.97)	1,167 (13.72)	0.71
SLE severity level, n (%)			
Mild	420 (19.76)	1,626 (19.12)	1.60
Moderate	1138 (53.53)	4,614 (54.26)	1.46
Severe	568 (26.72)	2,264 (26.62)	0.21
Quan-Charlson comorbidity score[1]			
mean (SD)	2.48 (2.02)	2.48 (1.98)	0.01
All-cause healthcare resource utilization counts, mean (SD)			
Ambulatory visits	36.21 (38.37)	37.42 (36.56)	2.1
Emergency room visits	2.12 (5.79)	2.03 (4.76)	1.56
Inpatient stays	0.42 (0.91)	0.41(0.92)	0.32
Pharmacy fills	52.36 (43.02)	53.04 (44.95)	1.56
All-cause healthcare costs[#] ($, USD), mean (SD)			
Total	36,800.08 (65,047.93)	35,827.14 (65,770.54)	1.49
Medical	27,843.58 (57,178.08)	26,712.48 (55,990.61)	2.00
Ambulatory	13,807.10 (26,660.85)	13,717.72 (30,430.90)	0.31
Emergency room	1,325.59 (4,590.90)	1,233.85 (3,632.09)	2.22
Inpatient	10,160.41 (36,067.59)	9,471.43 (36,587.11)	1.90
Pharmacy	8,956.50 (27,945.20)	9,114.66 (29,522.48)	0.55

*Standardized differences are the difference in means divided by a pooled standard deviation. Standardized differences <10% were considered balanced (Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. Stat Med. 2009).

#Costs computed as the combined health plan and patient paid amounts, and presented in 2021 USD

[1] Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, Januel JM, Sundararajan V. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. Am J Epidemiology. 2011

also higher in the SLE+HZ cohort ($4,383 [$13,737]) vs. SLE-only cohort ($3,033 [$11,337]). Among matched sets with ≥ 3 months of follow-up (93% of overall cohorts), higher HRU and costs in the SLE+HZ vs. SLE-only cohort were also observed in the 3-months post-index (Table 2).

Conclusion: Patients with SLE and HZ had higher HRU and costs than those without HZ, and HZ prevention may be important to consider in this population.

Table 2: Follow-up healthcare resource and costs

Follow-up 1 Month	SLE+HZ (N=2,126)	SLE-only (N=8,504)	p-value*
All-cause healthcare resource utilization counts, mean (SD)			
Ambulatory visits	4.46 (4.33)	3.12 (4.12)	<0.001
Emergency room visits	0.41 (0.99)	0.17 (0.71)	<0.001
Inpatient stays	0.09 (0.32)	0.04 (0.20)	<0.001
Pharmacy fills	6.23 (4.75)	4.44 (4.45)	<0.001
All-cause healthcare costs ($, USD)#, mean (SD)			
Total	4,382.87 (13,737.05)	3,033.48 (11,337.81)	<0.001
Medical	3,606.04 (13,516.22)	2,209.07 (10,583.69)	<0.001
Ambulatory	11,96.74 (3,277.52)	1,120.52 (3,996.05)	0.358
Emergency room	231.18 (844.01)	99.68 (556.19)	<0.001
Inpatient	1,950.62 (12,530.28)	815.81 (9,444.08)	<0.001
Pharmacy	776.83 (2,199.78)	824.41 (3,742.37)	0.448

Follow-up 3 Months	SLE+HZ (N=1,968)	SLE-only (N=7,872)	p-value*
All-cause healthcare resource utilization counts, mean (SD)			
Ambulatory visits	11.44 (11.99)	9.37 (10.79)	<0.001
Emergency room visits	0.75 (1.93)	0.48 (1.60)	<0.001
Inpatient stays	0.15 (0.48)	0.10 (0.37)	<0.001
Pharmacy fills	15.25 (11.96)	13.26 (11.90)	<0.001
All-cause healthcare costs ($, USD)#, mean (SD)			
Total	10,436.73 (31,500.50)	8,679.14 (21,950.28)	0.035
Medical	8,067.55 (30,451.20)	6,346.97 (18,908.88)	0.016
Ambulatory	3,444.22 (7,547.3)	3,491.65 (10,391.28)	0.815
Emergency room	417.47 (1,366.99)	301.7 (1,295.83)	<0.001
Inpatient	3,594.97 (28,046.21)	2,007.34 (13,646.17)	0.015
Pharmacy	2,369.18 (7,576.35)	2,532.17 (9,517.75)	0.421

*P-values compare differences in the SLE+HZ and SLE-only cohorts and were calculated using z-tests with robust standard errors in an ordinary least squares regression.
#Costs computed as the combined health plan and patient paid amounts, and presented in 2021 USD

Disclosure: N. Stempniewicz: GSK, 3, 11; **A. Steffens**: GSK, 2; **K. Kim**: GSK, 3; **C. Bell**: GSK, 3; **M. DuCharme**: GSK, 2; **H. Trenz**: GSK, 2; **D. Singer**: GSK, 3, 11.

Abstract Number: 1478

Presentation and Outcomes of Posterior Reversible Encephalopathy Syndrome in Systemic Lupus Erythematosus: A Multicenter Cohort and a Systematic Literature Review

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: To describe the clinical characteristics, therapies, and outcomes of patients with SLE and Posterior reversible encephalopathy syndrome (PRES).

Methods: We performed a multicenter cohort study in the United States from August 1999 - March 2021. We included patients with SLE who met the 2019 EULAR/ACR criteria and had incident PRES events. A case of incident PRES was defined as 1) the first acute neurological episode attributable to PRES, and 2) confirmation of vasogenic edema with MRI/CT and other causes excluded. A systematic literature review (SLR) was performed according to the PRISMA guidelines. We did a comprehensive search in multiple databases from their inception to October 20, 2021, in any language. Two reviewers independently screened and reviewed the articles and extracted information. We included case reports/case series

Table 1. Demographics and comorbidities of patients with systemic lupus erythematosus (SLE) and posterior reversible encephalopathy syndrome (PRES).

Demographics and comorbidities	n/N (%)
Age at PRES onset, mean (SD)	27.6 (12.28)
Female	276 (91%)
Male	27 (9%)
Comorbidities (history of)	
Hypertension	71/168 (42%)
Dyslipidemia	14/93 (15%)
Diabetes	9/93 (10%)
Ischemic heart disease	3/94 (3%)
Characteristics of SLE	
Duration of SLE, months, median (IQR)	36 (2 – 69)
Disease activity, SLEDAI score at onset (n=77), mean (SD)	17.8 (10.66)
SLE manifestations (history or at onset)	
Lupus nephritis (Biopsy proven)	225/254 (83%)
Available biopsy description (n=132)	
Class IV	85/132 (64%)
Class III	22/132 (17%)
Class IV+V	12/132 (9%)
Class III+V	6/132(5%)
Other (Class I/II or V)	7/132 (5%)
Hematological activity *	112/190 (59%)
Mucocutaneous	86/179 (48%)
Musculoskeletal	83/178 (47%)
Serositis	43/177 (24%)
Secondary antiphospholipid syndrome	25/186 (13%)
Thrombotic microangiopathy	30/206 (17%)
Diffuse alveolar hemorrhage	12/187 (6%)
Immunologic profile (history of)	
Anti-dsDNA antibodies	147/183 (80%)
Anti-Sm antibodies	29/71 (41%)
Antiphospholipid antibodies	57/151 (38%)
Exposure to immunosuppressants (≤ 3 months to PRES onset)	
Any immunosuppressant	219/250 (88%)
Glucocorticoids	199/219 (91%)
Cyclophosphamide	78/219 (36%)
Mycophenolate Mofetil	47/219 (21%)
Antimalarials	38/219 (17%)
Calcineurin inhibitors	20/219 (9%)

Abbreviatures: SD, standard deviation; IQR, Interquartile range; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index.
*Hemolysis, leukopenia, or thrombocytopenia.

reporting cases that met the inclusion criteria used for the cohort. We abstracted demographics, clinical and imaging features, treatment, and disease activity (SLEDAI). We summarized the days to recovery and length of stay (LOS). Neurological symptoms were classified as transient (≤3 days), persistent (≥14 days), or sequelae if permanent. The first available imaging was used to assess the distribution of vasogenic edema and other findings: restricted diffusion, hemorrhages, contrast enhancement, and angiography (MRI/CT). At least two consecutive imaging studies were required to determine the reversibility of edema. Patients were observed until death or last follow-up. The main outcomes after discharge were PRES relapses and all-cause mortality at 90 days. Cases in the cohort were combined with data from the SLR. Descriptive statistics were used to summarize pooled results.

Results: A total of 303 cases were included, 50 (17%) from the cohort, and 253 (83%) from the SLR. The mean age at PRES onset was 27.6 years (SD 12.3), and 91% were women. Comorbidities included hypertension in 42%, dyslipidemia in 15%, and diabetes in 10%. The median (IQR) time between SLE and PRES was 36 months (2-92), and the median follow-up was one month (0.3-12). At onset, SLEDAI was 17.8 (SD 10.7), lupus nephritis was present in 83%, and the autoantibody profile consisted of Anti-dsDNA (80%), Anti-Sm (41%), and aPL (38%) (Table 1). Clinically, 90% had associated high blood pressure (BP) (>140/90 mm Hg), and neurological manifestations were seizures in 78%, headache in 55%, visual disturbance in 45%, altered mental status in 38%, and focal deficits in 9% (Table 2). 97% of the patients survived and recovered after a median of 4 days (2-8), and LOS of 11 days (6-21). Among survivors, symptoms were transient in 45%, persistent in

Table 2. Clinical features of incident posterior reversible encephalopathy syndrome (PRES) in patients with systemic lupus erythematosus (SLE).

Clinical features of PRES at the onset	n/N (%)
PRES as part of initial SLE manifestations.	21/289 (7%)
Neurological symptoms	
Seizures	229/294 (78%)
Headache	163/294 (55%)
Visual disturbance	133/294 (55%)
Altered mental status	112/294 (38%)
Focal deficits	25/294 (9%)
Status epilepticus	15/294 (5%)
Other clinical manifestations at onset	
High blood pressure, >140/90 mm Hg	258/287 (90%)
Systolic blood pressure, mm Hg, mean (SD)	177.8 (30.53)
Diastolic blood pressure, mm Hg, mean (SD)	106.9 (19.32)

Abbreviatures: SD, standard deviation.

Table 3. Imaging features of incident posterior reversible encephalopathy syndrome (PRES) in patients with systemic lupus erythematosus (SLE).

Radiographic features of PRES at the onset	n/N (%)
Distribution of vasogenic brain edema	
Parieto-occipital	275/294 (94%)
Frontal lesions	94/294 (32%)
Temporal lobe	73/294 (25%)
Cerebellum	52/294 (18%)
Basal Ganglia	32/294 (11%)
Brainstem	27/294 (9%)
Asymmetric edema	60 /279 (22%)
Other imaging findings	
Diffuse or focal vasoconstriction on angiography (CT/MRI)	22/64 (34%)
Hemorrhages	27/264 (10%)
Restricted diffusion in DWI, or ADC	21/225 (9%)
Contrast enhancement	11/190 (6%)
Second radiographic assessment	
Improvement or reversible edema	178/183 (97%)
The time between imaging studies (n=159), days, median (IQR)	15 (7 – 49)

Abbreviatures: CT: computed tomography; MRI, magnetic resonance imaging, IQR, Interquartile range; DWI, Diffusion-weighted imaging; ADC, apparent diffusion coefficient.

19%, and 8% had sequelae. In the first imaging study, most had posterior and symmetric vasogenic edema. Among the 183 (60%) with follow-up imaging, brain edema improved in 97% after 15 days (7-49) (Table 3). Treatment strategies for PRES included BP control in 86%, antiepileptics in 64%, and new immunosuppressant therapy in 37%. After discharge, 12% relapsed after a median of 283 days (21-749). The 90-day mortality was 4%.

Conclusion: PRES in SLE develops predominantly in patients who have lupus nephritis. While most cases are reversible, sequelae are possible, and relapses are not uncommon.

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Abstract Number: 1479

Risk Factors for Human Papillomavirus Cervical Infection and Clearance in Patients with Systemic Lupus Erythematosus: The PAPILUP Study

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: An impaired clearance of cervical human papillomavirus (HPV) related to inadequate immune responses may result in persistent infection and increase the risk to develop cervical dysplasia in patients with systemic lupus erythematosus (SLE). We aim to identify risk factors for HPV infection and clearance in patients with SLE.

Methods: All SLE patients have been included in the *ongoing*PAPILUP study (National center for rare immune-mediated inflammatory diseases, Internal Medicine Department, Bichat Hospital, Paris, France) that aimed to improve HPV-related cervical cancer screening (CCS) in SLE patients. All SLE patients aged 30 to 65 who had HPV-related CCS between September 2021 and July 2022 were screened. The frequency of High-Risk (HR)-HPV was assessed in SLE patients in comparison to healthy and HIV-positive controls screened during the same period. The risk factors for persistent infection and clearance of HR-HPV in SLE patients were analyzed.

Results: Overall, 65 of the 107 SLE patients involved in the PAPILUP study were analyzed. The median age at CCS was 45 [39-51]. CCS was up to date in only 36 (55.4%) patients and only one patient (1.5%) had received HPV vaccine. The median SLE disease duration was 12 years [6-21] with a median SLEDAI score of 2 [0-4] at study time. Thirty-one (47.7%) patients had an history of lupus nephritis. Thirty-four (52.3%), 62 (95.4%) and 21 (32.3%) were currently receiving glucocorticoids, hydroxychloroquine and immunosuppressive drugs, respectively. HR-HPV were detected in 19 (29.2%) SLE patients. The frequency of HR-HPV did not differ between SLE patients and healthy controls (119 subjects, median age 43 [37-50], 21.8% of HR-HPV infection, p= 0.291). However the frequencies of multiple HR-HPV (at least 2 coexisting types)and abnormal cervical cytology (ACC, i.e cervical cytology samples enriched with atypical squamous cells, low-grade or high-grade squamous intraepithelial lesions) tended to be higher in SLE patients as compared to healthy controls (15.4% of multiple HR-HPV in SLE vs 6.7 % in healthy p=0.059; 16.9% of ACC in SLE vs 9.2% in healthy, p=0.125). Of note, the

frequency of multiple HR-HPV (15.4% vs 11.5%, p=0.407) and ACC (16.9% vs 11.5%, p=0.255) in SLE patients were in the same range as those in HIV-positive patients (n=192, median age 46 [41-53]). Using multivariable logistic regression model, the only significant risk factor for HR-HPV identified in SLE patients was the duration of the lupus disease (OR 16.1 [1.7-156], p=0.017) . A second HPV screening was performed 12.9 [10.2-14.1] months after the first one in 14 (73.7%) of the 19 HPV +SLE patients. A persistent HR-HPV infection was observed in 11 cases (78.6%). Of note, HR-HPV cleared in 2 of 4 (50%) patients who had never received steroids and immunosuppressive (IS) drugs but in only 1 of 10 (10%, p=0.099) who received long term steroids (median exposure length 9 [5.5-17.7] years) and IS drugs (median exposure length 6 [3.6-10] years).

Conclusion: Multiple HR-HPV and abnormal cervical cytology are frequent in SLE patients comparable to that of HIV-positive patients. The duration of SLE disease increases the risk for HR-HPV regardless of age. Long lasting immunosuppression induced by treatment might impede HPV clearance.

Disclosure: T. Goulenok: None; **V. Ferre**: AstraZeneca, 6, Gilead, 12, Congress accomodation, Moderna, 6; **C. Mendes**: None; **L. Dayan**: None; **M. Bucau**: None; **F. Farhi**: None; **T. Papo**: None; **K. Sacre**: None.

Abstract Number: 1480

Demographic and Clinical Characteristics of Patients with LN: A Multicenter Study from the Gulf Region

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Data from limited studies of LN in the Gulf region suggest that LN manifests more severely in this region than in Caucasian populations, yet there are no treatment recommendations specific to the Gulf region.[1] This study aims to characterize patients with LN in the Gulf region to better understand disease burden and inform treatment recommendations to improve patient outcomes.

Methods: In this prospective, multicenter study (GSK Study 216989), adults with an established diagnosis of LN (biopsy proven or clinician diagnosis) were enrolled from sites in Kuwait, Oman, Qatar, and the UAE. At enrollment, the site physician extracted patient demographics and clinical characteristics retrospectively from medical charts for the previous < 12 months, and patients completed the 36-Item Short Form Health Survey (SF-36). Prospective medical chart follow-up continued for up to 12 months after enrollment. This analysis reports only data collected retrospectively at enrollment.

Results: This analysis comprised 193 patients with LN, the majority of whom were female (83.9%), of Arab ethnicity (85.0%), and with a mean (standard deviation [SD]) age of 37.2 (10.4) years (**Table**). Patients had a mean (SD) age of 27.4 (10.6) years at the time of SLE diagnosis, 30.5 (10.8) at LN diagnosis, and 35.3 (9.9) at ESKD diagnosis (n=11). Comorbidities were reported for 69.4% (n=134) of patients, most commonly endocrine and metabolic disorders (32.1%; n=62). One-third of patients had no kidney biopsy in the year preceding enrollment (35.6%; n=68), and LN class was not available for 26.9% (n=52) of patients, suggesting a potential lack of routine biopsy for some patients. Among available data, the proportions of LN Class III, IV, and V were similar (22.0–25.5%; n=31–36). Renal remission was achieved any time after LN diagnosis in 57.7% (n=101) of patients with available data. The mean (SD) number of prior treatment failures/relapses was 1.4 (3.6)

Table. Summary of demographics and characteristics among patients with LN in the Gulf region. *Those reported for >10% of patients are shown; †for 11 of the 12 patients with ESKD; ‡percentage among those with available data (n=191); §percentage among those with classification (n=141) ||percentage among those with available data (n=175); ¶data missing for 42 patients (n=151). ISN/RPS, International Society of Nephrology and the Renal Pathology Society.

Variable		N=193
Age (years), mean (SD)		37.2 (10.4)
Female, n (%)		162 (83.9)
Ethnicity, n (%)	Arab	164 (85.0)
	Other	27 (14.0)
	Persian	2 (1.0)
Comorbidities present, n (%)		134 (69.4)
Comorbidities, n (%)*	Endocrine/metabolic disorders	62 (32.1)
	Past surgeries	41 (21.1)
	Arterial hypertension	38 (19.7)
	Other autoimmune disorder	27 (14.0)
	Other heart/cardiovascular disorders	25 (13.0)
	Musculoskeletal/extremities disorders	23 (11.9)
	Antiphospholipid syndrome	22 (11.4)
Age at diagnosis (years), mean (SD)	SLE	27.4 (10.6)
	LN	30.5 (10.8)
	ESKD†	35.3 (9.9)
Time from manifestation to SLE diagnosis (years), mean (SD)		2.9 (5.3)
Kidney biopsy in past year, n (%)‡		123 (64.4)
LN pathological type (ISN/RPS 2003 classification), n (%)	Not available	52 (26.9)
	Class I§	6 (4.3)
	Class II§	6 (4.3)
	Class III§	31 (22.0)
	Class III/V§	13 (9.2)
	Class IV§	36 (25.5)
	Class IV/V§	13 (9.2)
	Class V§	35 (24.8)
	Class VI§	1 (0.7)
Renal remission any time after LN diagnosis, n (%)‖		101 (57.7)
Number of prior treatment failures/relapses, mean (SD)¶		1.4 (3.6)

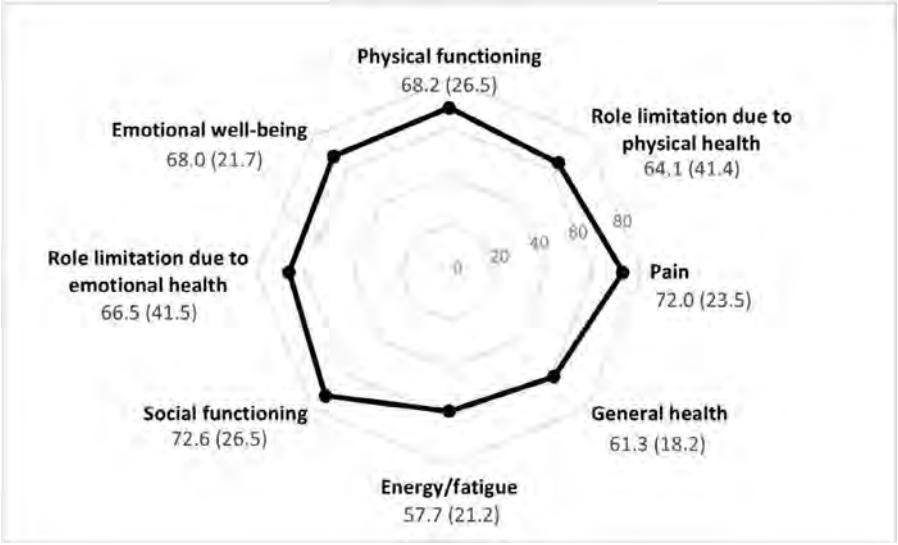

Figure. Mean (SD) SF-36 subscale scores (N=193).

in those with available data. Mean (SD) overall SF-36 score was 66.3 (19.1); scores across domains were generally similar, with energy/fatigue having the lowest score (57.7 [21.2]), and social functioning the highest (72.6 [26.5]; **Figure**).

Conclusion: These retrospective data suggest that approximately one-quarter of patients with LN in the Gulf region did not have sufficient histological classification to guide therapy, and these inconsistencies in histological data make it difficult to compare Gulf patient characteristics to published data from international cohorts. However, age at SLE diagnosis was young, and patients appeared to be similarly impacted across all SF-36 quality of life subscales, whereas a large international inception cohort reported relatively greater impacts in role of physical functioning than other domains.[2] Prospective data generated from this cohort may aid understanding of differences in care and may have the potential to inform LN treatment guideline development in the Gulf region.

Funding: GSK

References

1. Al-Shujairi A et al. *Lupus* 2023;32:155–65
2. Hanly JG et al. *Rheumatology (Oxford)* 2016;55(2):252–62

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Abstract Number: 1481

Racial Disparities in Lupus Nephritis: A Nationwide Analysis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis (LN) is a significant predictor of morbidity and mortality in Systemic Lupus Erythematosus (SLE). Racial disparities are known to exist in SLE in terms of the prevalence of LN, healthcare access, and outcomes. We aimed to study racial disparities in LN and predictors of in-hospital death.

Methods: Data was obtained from the National Inpatient Sample (NIS) between 2016-2019 using ICD-10 codes. All adult hospitalizations with a primary or secondary diagnosis of LN were included and divided into African American (AA) and Hispanic race vs others. Demographics, socio-economic variables, several complications, health care burden, and mortality were compared between the two groups. Univariate and multivariate logistic regression analyses were conducted for predictors of in-hospital death in LN. Variables with a P value ≤0.2 in the univariate analysis were included in the multivariate model and a P value of ≤0.05 was considered to be significant in the final model.

Results: We identified 104, 865 adult LN hospitalizations, of which 66.3% were African Americans or Hispanics (table 1). This group had more females (85.5% vs 79.9%, p< 0.001), were younger (38.4 vs 45.6 years, p< 0.001),were more likely to be from the low-income group (45.8% vs 23.6%, p< 0.001) and more often had Medicaid (30.6% vs 19.4% p< 0.001) in comparison to other races. In-patient mortality was low overall with lower odds of death in the AA-Hispanic group (1.7% vs 2.6%, OR 0.67, p< 0.001) (table 2).AA/ Hispanic LN patients had higher odds of renal failure (82.5% vs 79.1%, OR 1.25, p< 0.001) and end-stage renal disease (ESRD) (44.6% vs 33.9%,OR 1.6, p< 0.001) but were less likely to receive a renal transplant (4.3% vs 5.2%, OR 0.8, p=0.005). They were more likely to leave against medical advice (3.0% vs 1.7%, OR 1.8, p< 0.001,)and less likely to be transferred to a skilled nursing facility (8.7% vs 13.3%,OR 0.6, p< 0.001). Multivariable analysis for predictors of in-hospital death in LN showed following significant variables: Age (OR 1.0, p< 0.001), CCI (OR 1.2, p< 0.001), Medicaid (OR 0.7, p=0.014), small bed size (OR 0.6, p=0.003), sepsis (OR8.54, p< 0.001), PE/DVT (OR 2.8, p< 0.001), and kidney failure (OR4.1, p< 0.001) (table 3).

Conclusion: In the national inpatient sample, almost two-thirds of LN patients were AA or Hispanic. This group had a higher proportion of females, was younger, belonged more often to the lower income quartile, and was more likely to have Medicaid insurance. They had higher odds of renal failure and ESRD in comparison to other races and were less likely to receive renal transplants. The in-hospital mortality was lower in the AA/Hispanic-LN group, but race was not found to be an independent predictor of death in LN. Sepsis, kidney failure, PE/DVT, Charlson comorbidity index, and age were associated with higher odds of in-hospital death in LN.

Hospitalization Characteristics	Adult AA/Hispanic LN N = 69510 (66.29%)	Adult non-AA/Hispanic LN N = 35355 (33.71%)	P-Value Odds ratio (OR)
Female	59,400 (85.5%)	28,245 (79.9%)	<0.001
Age (Mean/SD) (years)	38.4/14.0	45.6/17.2	<0.001
Age Groups 18 – 40	41,325 (59.5%)	14,880 (42.1%)	<0.001
40 – 60	21,730 (31.3%)	12,010 (34.0%)	<0.001
60 – 80	6,120 (8.8%)	7,650 (21.6%)	<0.001
80 or more	335 (0.5%)	815 (2.3%)	
CCI (Mean)	3.5	3.6	0.338
Hospital Bed size Small Bed Size	9050 (13.0%)	5400 (15.3%)	<0.001
Medium Bed Size	16410 (23.6%)	8515 (24.1%)	0.588
Large Bed Size	44050 (63.4%)	21440 (60.6%)	0.009
Income Quartile Q1	31825 (45.8%)	8345 (23.6%)	<0.001
Q2	16105 (23.2%)	9085 (25.7%)	<0.001
Q3	13045 (18.8%)	9210 (26.1%)	<0.001
Q4	7490 (10.8%)	8235 (23.3%)	<0.001
Insurance Medicare	28695 (41.3%)	15190 (43.0%)	0.042
Medicaid	21260 (30.6%)	6860 (19.4%)	<0.001
Private insurance	14955 (21.5%)	11440 (32.4%)	<0.001
Self-pay	3040 (4.4%)	830(2.4%)	<0.001
No charge	305 (0.4%)	85 (0.2%)	0.028
Other insurance	1125 (1.6%)	885 (2.5%)	<0.001
Missing insurance	130 (0.2%)	65 (0.2%)	0.968

Abbreviations: AA=African American; SD=Standard deviation-; LN= Lupus Nephritis; CCI= Charlson Comorbidity

Weighted Descriptive Characteristics of African-American (AA) and Hispanic Lupus Nephritis Hospitalizations compared to non-AA and Hispanic LN Hospitalizations

Outcomes	Adult AA/Hispanic LN	Adult non AA/Hispanic LN	P-Value
Total died	1200 (1.7%)	905 (2.6%)	<0.001
Kidney failure	57370 (82.5%)	27950 (79.1%)	<0.001
Sepsis	9010 (13.0%)	4690 (13.3%)	0.545
PRES	630 (0.9%)	275 (0.8%)	0.351
PE/DVT	1240 (1.8%)	545 (1.5%)	0.198
ESRD	30985 (44.6%)	11995 (33.9%)	<0.001
Renal transplant	2975 (4.3%)	1825 (5.2%)	0.005
Transfer out	6015 (8.7%)	4705 (13.3%)	<0.001
Left against medical advice	2055 (3.0%)	605 (1.7%)	<0.001
Lenght of Stay (Mean/SD)	6.70 (8.7)	6.77 (8.7)	0.591
Total hospital charges (SD)	81,365 (134,023)	84,257 (140, 145)	0.183

Abbreviations: AA=African American; SD=Standard deviation ;OR= Odds Ratio; LN= Lupus Nephritis; PRES= Posterior Reversible Encephalopathy Syndrome; PE/DVT= Pulmonary embolism/Deep venous thrombosis; ESRD= End-stage renal disease

Outcomes of adult African-American (AA) and Hispanic LN Hospitalizations compared to non-African-American (AA) and non Hispanic LN Hospitalizations

Variables	Univariate analysis			Multivariate analysis		
	Odds Ratio	P value	95% CI	Odds Ratio	P Value	95% CI
Age	1.0	<0.001	1.03-1.04	1.0	<0.001	1.02-1.03
Female	0.8	0.110	0.64-1.05	1.1	0.443	0.86-1.43
CCI	1.3	<0.001	1.28-1.39	1.2	<0.001	1.13-1.27
White	1.7	<0.001	1.37-2.09	1.4	0.090	0.95-1.93
African American	0.8	0.076	0.69-1.02	1.0	0.947	0.72-1.42
Hispanic	0.7	0.009	0.54-0.92	0.9	0.678	0.63-1.36
Asian or PI	1.1	0.556	0.74-1.74	-	-	-
Native Americans	0.6	0.507	0.16-2.52	-	-	-
Medicare	1.6	<0.001	1.36-1.99	0.8	0.170	0.66-1.08
Medicaid	0.5	<0.001	0.41-0.69	0.7	0.014	0.50-0.92
Private inusrance	1.0	0.736	0.77-1.20	-	-	-
Self Pay	1.0	0.904	0.62-1.70	-	-	-
Income Q1	0.9	0.457	0.76-1.13	-	-	-
Income Q2	0.9	0.242	0.69- 1.10	-	-	-
Income Q3	1.3	0.042	1.01- 1.56	1.2	0.208	0.92-1.47
Income Q4	1.0	0.983	0.76- 1.30	-	-	-
Small Bed size	0.6	0.002	0.40-0.82	0.6	0.003	0.38-0.82
Medium Bed size	1.1	0.648		-	-	-
Large Bed size	1.2	0.065	0.99-1.49	1.1	0.304	0.89-1.43
Urban Teaching hospital	0.9	0.269	0.67-1.12	-	-	-
Urban Non teaching hospital	1.2	0.322	0.87-1.52	-	-	-
Hypertension	0.6	<0.001	0.45-0.75	1.1	0.733	0.81-1.35
Kidney Failure	7.3	<0.001	4.22-12.78	4.1	<0.001	2.33-7.38
Sepsis	8.8	<0.001	7.23-10.81	8.5	<0.001	6.95-10.50
PRES	0.5	0.392	0.13-2.20	-	-	-
ESRD	1.3	0.024	1.03-1.51	0.9	0.557	0.76-1.16
Renal Transplant	0.8	0.439	0.50-1.35	-	-	-
PE/DVT	2.5	<0.001	1.52-4.13	2.8	<0.001	1.60-4.76

Abbreviations: CI=Confidence Interval; CCI= Charlson Comorbidity; PI=Pacific Islander PRES= Posterior Reversible Encephalopathy Syndrome; PE/DVT= Pulmonary embolism/Deep venous thrombosis; ESRD= End-stage renal disease

Univariate and multivariate analysis for inpatient mortality of LN hospitalizations

Disclosure: F. Sami: None; **S. Sami**: None; **A. Manadan**: None; **S. Arora**: None.

Abstract Number: 1482

Change in the SLE Mortality Rate and Prevalence of Lupus Nephritis Overtime: Single Center Retrospective Study in Japan

Takehiro Nakai[1], Sho Fukui[2], Takahiro Asano[1], Futoshi Iwata[1], Hiroki Ozawa[3], Satoshi Kawaai[1], Yukihiko Ikeda[4], Haruyuki Yanaoka[1], Hiromichi Tamaki[1], Mitsumasa Kishimoto[5], Kenichi YAMAGUCHI[6] and Masato Okada[1], [1]St. Luke's International Hospital, Tokyo, Japan, [2]Brigham and Women's Hospital, Boston, MA, [3]Immuno-Rheumatology Center, St. Luke's International Hospital, Tokyo, Japan, [4]St Luke's international hospital in Japan, Tokyo, Japan, [5]Kyorin University School of Medicine, Yokohoma, Japan, [6]St.Luke's International Hospital, Tokyo, Japan

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Over the past several decades, the treatment of lupus has seen significant advancements, with the approval of belimumab in 2017, and anifrolumab in 2021. Yet, the impact of changes in the standard of care on systemic lupus erythematosus (SLE) mortality and the prevalence of lupus nephritis remains understudied. This study was conducted to fill this knowledge gap.

Methods: We analyzed data from patients with SLE who received follow-up care at St. Luke's International Hospital between April 2006 and February 2023, excluding those with missing diagnosis date information. Patients were stratified based on the timing and their age at the onset of their disease. We utilized Gray's test to examine differences in mortality rates and the prevalence of lupus nephritis among the groups.

Results: We included a total of 501 SLE patients in the study. The median age at diagnosis was 31.0 years [21.0, 43.0], with approximately 90% of the patients being Japanese. Biopsy-proven lupus nephritis and class III lupus nephritis were observed in 24% and 16.4% of the patients, respectively. chronic kidney disease (CKD) stage 4 or 5 was noted in 2.5% of the patients, while 2.7% died during the follow-up period. When patients were segregated according to the calendar year of diagnosis, lower cumulative incidence of biopsy-proven lupus nephritis, class III/IV lupus nephritis, and mortality was noted in those diagnosed in the 2010s and 2020s, as compared to those diagnosed in the 2000s and prior. Additionally,

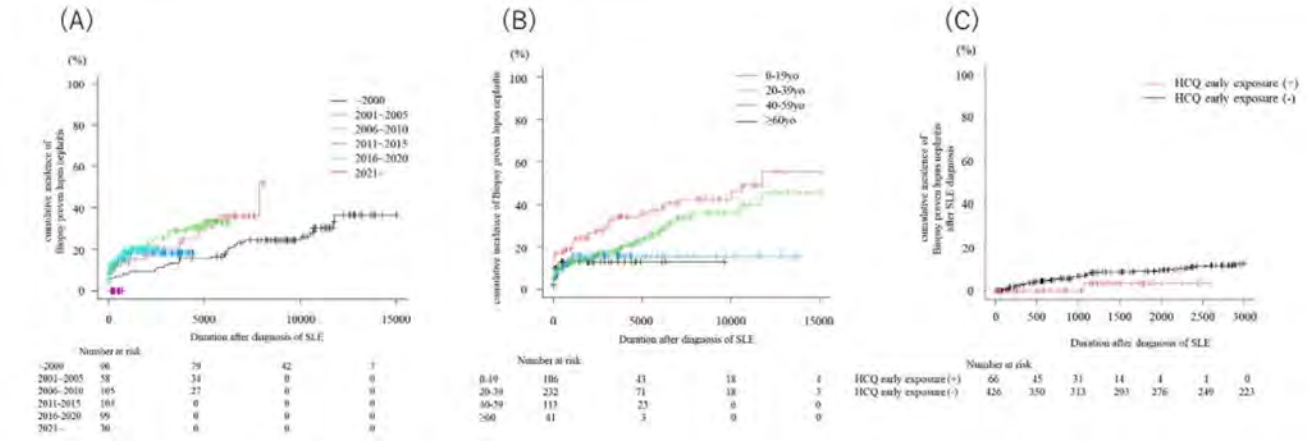


Figure 1: cumulative incidence of biopsy proven lupus nephritis A) Change in the cumulative incidence of lupus nephritis according to the year of diagnosis B) Change in the cumulative incidence of lupus nephritis according to the age of diagnosis C) Change in the cumulative incidence of lupus nephritis after the diagnosis of SLE according to the early exposure (<3m of onset) to hydroxychloroquine

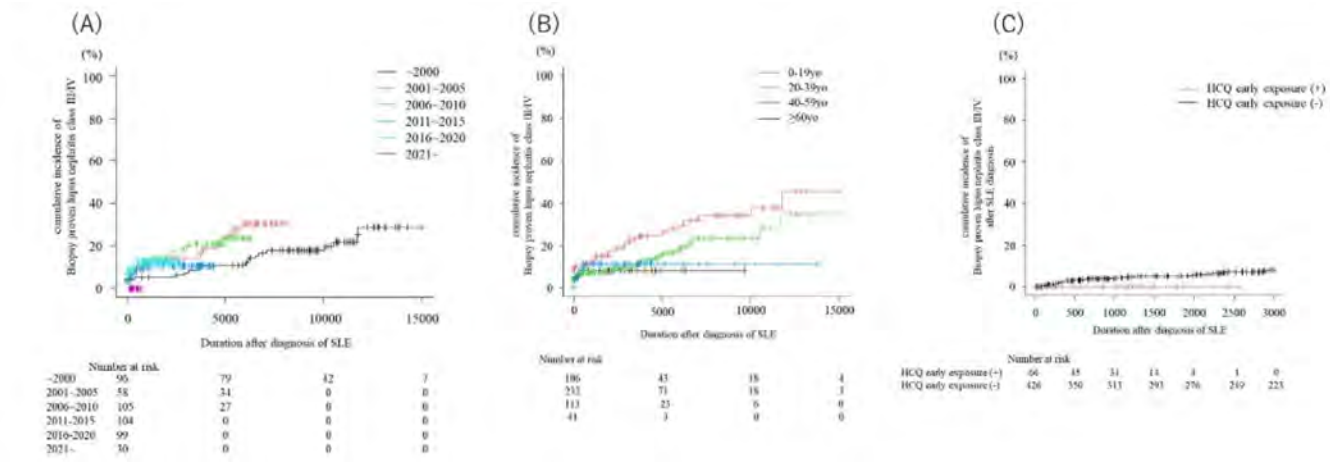


Figure 2: cumulative incidence of biopsy proven lupus nephritis class III/IV A) Change in the cumulative incidence of lupus nephritis class III/IV according to the year of diagnosis B) Change in the cumulative incidence of lupus nephritis class III/IV according to the age of diagnosis C) Change in the cumulative incidence of lupus nephritis class III/IV after the diagnosis of SLE according to the early exposure (<3m of onset) to hydroxychloroquine

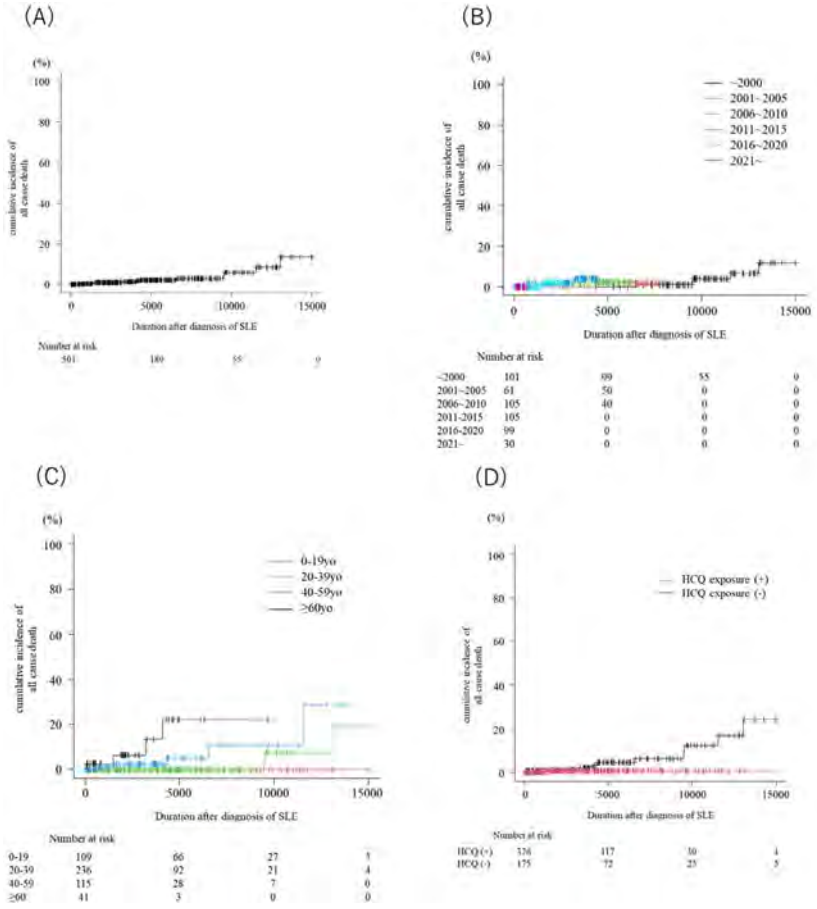


Figure 3: cumulative incidence of all cause death A) Change in the cumulative incidence of all cause death B) Change in the cumulative incidence of all cause death according to the year of diagnosis C) Change in the cumulative incidence of all cause death according to the age of diagnosis D) Change in the cumulative incidence of all cause death after the diagnosis of SLE according to the exposure to hydroxychloroquine

the incidence of new lupus nephritis and class III/IV lupus nephritis was lower among patients who initiated HCQ at diagnosis. HCQ was demonstrated to be a protective factor against the development of CKD stage 4 or 5 and all-cause mortality (CKD stage 4 or 5: Hazard Ratio [HR] 0.22, 95% Confidence Interval [CI] 0.06-0.83, p=0.03; all-cause death: HR 0.124, 95% CI 0.03-0.56, p< 0.01). Furthermore, the prevalence of lupus nephritis and class III/IV lupus nephritis was higher among patients diagnosed with SLE before the age of 40, compared to those diagnosed at or after 40. However, even among this group, the mortality rate was lower.

Conclusion: Advancements in lupus treatment have considerably improved SLE mortality and the prevalence of lupus nephritis. Moreover, initiating treatment with hydroxychloroquine was found to be a significant factor in improving lupus outcomes.

Disclosure: T. Nakai: None; **S. Fukui**: None; **T. Asano**: None; **F. Iwata**: None; **H. Ozawa**: None; **S. Kawaai**: None; **Y. Ikeda**: None; **H. Yanaoka**: None; **H. Tamaki**: AbbVie, 6, Astellas Pharma, 6, Ayumi, 6, Chugai pharmaceutical, 6, Kyowa-Kirin, 6, Ono pharmaceutical, 6, Takeda Pharmaceutical, 6, Tanabe-Mitsubishi, 6; **M. Kishimoto**: AbbVie, 2, 6, Amgen, 2, 6, Asahi-Kasei Pharma, 2, 6, Astellas, 2, 6, Ayumi Pharma, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Chugai, 2, 6, Daiichi-Sankyo, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Ono Pharma, 2, 6, Pfizer, 2, 6, Tanabe-Mitsubishi, 2, 6, UCB, 2, 6; **K. YAMAGUCHI**: None; **M. Okada**: AbbVie/Abbott, 6, Eli Lilly, 6, Pfizer, 6.

Abstract Number: 1483

High Chronicity Index of the Modified NIH (National Institute of Health) Scoring System of Lupus Nephritis Is Associated with Increased Risk of End-stage Kidney Disease: A Retrospective Single-center Study

Shiori Nakagawa, Yasunori Iwata, Takahiro Yuasa, Keisuke Sako, Keisuke Horikoshi, Taichiro Minami, Megumi Oshima, Tadashi Toyama, Shinji Kitajima, Akinori Hara, Norihiko Sakai, Miho Shimizu and Takashi Wada, Department of Nephrology, Kanazawa University Hospital, Kanazawa, Japan

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis (LN) is a major manifestation which develops in more than 50% of patients with systemic lupus erythematosus (SLE), and is also a primary risk factor for morbidity and mortality in these patients. The revision of International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification guidelines for lupus nephritis (LN) was suggested by a working group, who recommended a modified National Institute of Health (NIH) activity and chronicity scoring system to evaluate active and chronic LN lesions. However, whether this approach was useful for estimating long-term prognosis for LN patients is unclear.

Methods: We conducted a retrospective cohort study in Japanese subjects with biopsy-proven LN, between 1977 and 2022. Pathologic lesions were evaluated based on ISN/RPS 2003 classifications and the modified NIH scoring system. Patients were grouped by activity index (low, 0–5; moderate, 6–11; high, 12–24), and chronicity index (low, 0–2; moderate, 3–5; high, 6–12). The primary outcome was a composite of end-stage kidney disease (ESKD) or all-cause death, and the secondary outcome was ESKD alone.

Results: Seventy subjects with a median age of 31 years were included. Median follow-up period was 11.3 years. For the activity index, Kaplan–Meier analysis showed that the survival rate of the primary outcome decreased with a higher activity index (log-rank trend p = 0.026) . Multivariable analysis, adjusted by age and serum creatinine, did not show any significant relationship to the activity index. For the chronicity index, Kaplan–Meier analysis showed that the survival rate of the primary outcome decreased with a higher chronicity index (log-rank trend p< 0.001). Multivariable analysis, adjusted by age and serum creatinine, revealed that moderate (HR 6.18, 95% CI 1.15 to 33.3; p = 0.034) and high chronicity indices (HR 20.33, 95% CI 1.14 to 360.50; p = 0.04) were significant risk factors for the primary outcome. Consistent results with the primary outcome were determined by Kaplan–Meier and univariable analysis.

Conclusion: Moderate and high chronicity indices were associated with an increased ESKD risk for LN. This modified NIH activity and chronicity scoring system may help physicians predict long-term prognosis for patients with LN.

Disclosure: S. Nakagawa: None; **Y. Iwata**: None; **T. Yuasa**: None; **K. Sako**: None; **K. Horikoshi**: None; **T. Minami**: None; **M. Oshima**: None; **T. Toyama**: None; **S. Kitajima**: None; **A. Hara**: None; **N. Sakai**: None; **M. Shimizu**: None; **T. Wada**: None.

Abstract Number: 1484

Ruminococcus Implicated in the Clinical Development of Lupus Nephritis: A Systematic Review of the Literature

Katarzyna Karpinska-Leydier[1], Arseni Khorochkov[2], Ambar Morales-Rodriguez[1], Nur Barlas[1], Sait Barlas[1], Abraham Bell[1], Magdy El-Din[3] and Shristi Basnyat[4], [1]Florida State University - Cape Coral Hospital, Cape Coral, FL, [2]Poznan University of Medical Sciences, Poznań, Poland, [3]Florida State University/Lee physicians group, Cape Coral, FL, [4]Florida State University/Lee physicians group, Fort Myers, FL

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis (LN) is a serious complication of systemic lupus erythematosus (SLE). Current investigations implicate microbiome changes in disease pathogenesis, particularly pathobiont expansions of *Ruminococcus gnavus* (RG) ranging from minor dysbiosis to extreme blooms. Transient spikes in RG communities in human and mouse models have been associated with disease activity.

Methods: A methodical search of MEDLINE, Science Direct, and EMBASE was conducted to evaluate the understanding of *Ruminococcus* involvement in LN up to May 28, 2023. Two reviewers independently assessed the literature for the inclusion and exclusion criteria methodically by title, abstract, and full text resulting in a cumulative 83 articles. Once screened for duplicates and open-access content on relevant primary literature, 13 remaining articles were identified.

Results: The 13 included articles commonly recognized RG population blooms in active SLE including LN, outnumbering other members of the genus. These blooms correlated with the presence of anti-native DNA autoantibodies. LN patients were found to have elevated fecal RG based on 16S rRNA amplicon analysis with serum IgG anti-RG Ab in concordance with anti-dsDNA. Furthermore, anti-RG Ab targeted to bacterial cell-wall lipoglycans correlated with SLE disease activity index indicating a disease model in which specific strains of gut commensal contribute to the immunopathogenesis of LN. Distorted tryptophan metabolism toward the kynurenine pathway is reported in SLE; differential microbial catabolism

has been implicated since tryptophan and the metabolite tryptamine increase pro-inflammatory T cell metabolism and mTOR activation thus promoting damage to renal tubular epithelial cells. RG expresses tryptophan decarboxylase necessary to synthesize tryptamine from tryptophan, contributing to elevated tryptamine levels in LN pathogenesis. The experimental administration of *Lactobacillus casei Zhang* shows evidence of delayed kidney disease in mice. Short-chain fatty acids and nicotinamide in these studies reduced renal inflammation, suggesting the commensal metabolic impact can mitigate or progress renal decline in mice models. Despite SLE disease heterogeneity, pathobiont blooms may impair gut barriers and fuel systemic inflammation. In another study, SLE mouse models given acidic pH water developed nephritis slower compared to those given neutral pH water. A higher level of circulating auto-Ab against plasma cells and nuclear antigen were found in the latter with notable variations in 16S rRNA gene-targeted sequencing of the gut microbiome and immune responses shifted to TH17 and Th9-associated factors. This suggests that dietary changes can influence SLE flares through the regulation of the microbiome.

Conclusion: The microbiomes of SLE patients show a decrease in species diversity; disease activity, including LN development, is associated with RG pathobiont blooms. Given the demonstrated association between the microbiome and immunomodulation, RG populations may be a novel therapeutic target in the treatment of patients with LN.

Disclosure: K. Karpinska-Leydier: None; **A. Khorochkov**: None; **A. Morales-Rodriguez**: None; **N. Barlas**: None; **S. Barlas**: None; **A. Bell**: None; **M. El-Din**: None; **S. Basnyat**: None.

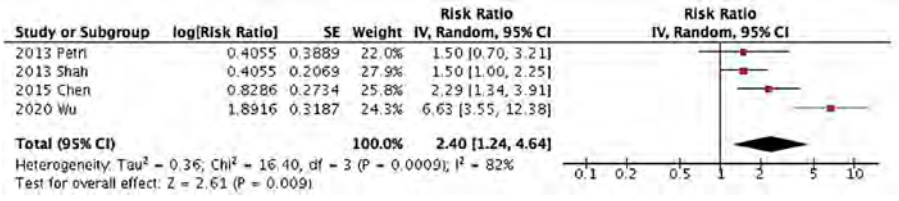
Abstract Number: 1485

Risk of Diabetes Mellitus in Systemic Lupus Erythematosus: Systematic Review and Meta-analysis

CLAUDIA MENDOZA PINTO[1], Pamela Munguía-Realpozo[1], Ivet Etchegaray-Morales[2], Mario García-Carrasco[2] and Socorro Méndez Martínez[1], [1]Instituto Mexicano del Seguro Socia, Puebla, Mexico, [2]Medicine School, Benemérita Universidad Autónoma de Puebla, Puebla, Mexico

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that increases the risk of severe clinical outcomes and mortality. However, the association between SLE and the risk of diabetes mellitus (DM) is unclear. Our study aimed to investigate the risk of DM and to evaluate the impact of SLE therapies on the risk of developing DM in patients with SLE.



Forest plot of DM risk in SLE patients treated with glucocorticoids

Methods: Electronic database searches of PubMed, Embase, Cochrane Library, and Web of Science, together with hand search, were performed from inception to February 2023. Studies analyzing the relationships between risk factors for DM in SLE patients in cohort or case-control were included. Data were pooled utilizing fixed- or random-effects metanalysis to estimate pooled relative risk (RR) and 95% confidence intervals (CIs). The study was registered with PROSPERO, CRD42023402774.

Results: A total of 36 studies (23 case-control and 13 cohort studies) involving 265,822 patients with SLE were included. In the pooled analysis from case-control studies, we found a greater risk (OR = 1.05, 95% CI 0.87-1.27; P = 0.63) of diabetes in patients with SLE compared with non-SLE controls. However, the pooled risk estimate of cohort studies did not show a significant risk of DM (RR= 1.32, 95% CI 0.93-1.87; P = 0.12). In a subgroup analysis, reduced risk of diabetes was reported with antimalarials (RR= 0.56, 95% CI 0.42-0.75; P < 0.001), while glucocorticoids use was associated with an increased risk of developing diabetes (RR= 1.45, 95% CI 1.20-1.76; P = 0.0002). Age, sex, hypertension, and immunosuppressants were not associated with DM in SLE patients.

Conclusion: Although there was not an increased risk of DM in overall SLE patients compared to controls, antimalarials users or adherents had a decreased risk, while GCT users had an increased risk.

Disclosure: C. MENDOZA PINTO: None; **P. Munguía-Realpozo**: None; **I. Etchegaray-Morales**: None; **M. García-Carrasco**: None; **S. Méndez Martínez**: None.

Abstract Number: 1486

Clinical Outcomes in Patients Admitted for ST-Elevation Myocardial Infarction with vs Without Systemic Lupus Erythematosus: An Analysis from National Inpatient Sample Database (2015-2018)

Hamza Liaqat[1], Muhammad Qureshi[2], Awais Farooq[3], **Mashal Awais**[2], Amar Patel[4] and Aisha Barlas[5], [1]Wah Medical College, Wah Cantt, Pakistan, [2]Southeast Health Internal Medicine Residency Prog., Dothan, AL, [3]University of Illinois Chicago, Chicago, IL, [4]Texas Tech University Health Sciences Center, El paso, TX, [5]Mercy Health, Rockford, IL

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Impact of systemic lupus erythematosus (SLE) on the clinical outcomes of patients admitted for ST-elevation myocardial infarction (STEMI).

Methods: Patient data was collected for years 2015-2018 from National Inpatient Sample using the International Classification Of Disease Revision Codes (ICD-10). We selected patients who were admitted with the diagnosis of STEMI. We then divided our patient population into two groups, those without SLE (STEMI group) and patients with an underlying diagnosis of SLE (STEMI/SLE group). Multivariate Logistic Regression and Mann-Whitney U testing were employed for this purpose.

Results: Our study included 1,009,407 patients with a primary diagnosis of STEMI. Of these patients, 4150 (0.41%) had an underlying diagnosis of SLE. The mean age of patients in the STEMI group was 67 years, compared to 61 years in the STEMI/SLE group. 61.8% were males in STEMI patients and female predominance was noted in STEMI/SLE group,

81.3%. The predominant race involved in both groups was noted to be Caucasian, 70.5% in the STEMI group vs 58.53% in STEMI/SLE group. In regards to mortality, we found that the underlying diagnosis of SLE in STEMI patients was associated with an increased risk of mortality, adjusted odds ratio of 1.278 (95% CI 1.09-1.48, p< 0.05). The length of stay in STEMI patients was 4.5 days, vs 4.7 days in the STEMI/SLE group. Hospitalization charges were noted to be $84522 and $82783 in STEMI and STEMI/SLE groups respectively.

Conclusion: This nationwide study showed that concomitant SLE in patients admitted with STEMI was associated with a statistically significant increase in inpatient mortality and length of stay. However, reduced cost of hospitalization was noted among STEMI/SLE patients.

Disclosure: H. Liaqat: None; **M. Qureshi**: None; **A. Farooq**: None; **M. Awais**: None; **A. Patel**: None; **A. Barlas**: None.

Abstract Number: 1487

Prevalence of Objectively Measured Sleep Disturbance in Systemic Lupus Erythematosus (SLE)

Patti Katz[1], Jinoos Yazdany[2] and Maria Dall'Era[3], [1]University of California San Francisco, San Rafael, CA, [2]University of California, General Department of Medicine, Division of Rheumatology, San Francisco, CA, [3]University of California San Francisco, San Francisco, CA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Self-reported poor sleep is common in SLE, but few studies have objectively measured sleep have been conducted. In general population studies, sleep disorders are associated with poor health outcomes relevant to SLE, including lower pain thresholds and higher rates of depression, cognitive impairment, systemic inflammation, and cardiovascular events. We report on the prevalence of objectively-measured sleep disturbances in an SLE cohort, examine whether patient-reported measures of sleep correspond with objective measures, and analyze the association of sleep disturbances with patient-reported outcomes.

Methods: All participants were drawn from the California Lupus Epidemiology Study (CLUES). A subset of CLUES participants (n = 61) who received their SLE care at our institution participated in a sleep study and underwent 7 nights of home sleep monitoring via actigraphy (GT9X, Actigraph Corp., Pensacola, FL), as well as concurrent interviews in which patient-reported outcome measures (PROMs) of sleep (PROMIS Sleep Disturbance and Sleep Impairment) and symptoms (pain rating 0-10, PROMIS Fatigue, and depressive symptoms [Patient Health Questionnaire, PHQ-8]) were collected. Actigraphs yielded estimates of time in bed, time asleep, and sleep efficiency (time asleep/time in bed).We examined 2 indicators of sleep disturbance: poor sleep efficiency and short sleep. Poor sleep efficiency was defined as < 85% (the standard criterion) and < 80%.Short sleep time was defined as < 7 hours (based on CDC guidance) and < 6 hours. Analyses examined differences in PROMs by each sleep disturbance indicator.

Results: Participant characteristics are shown in Table 1.Mean sleep efficiency was 79.4% ± 8.7%, 74% had sleep efficiency < 85%, and 39% had sleep efficiency < 80% (Table 2). Mean sleep time was 6.6 ± 1.0 hours, 66% had sleep time < 7 hours, and 23% had sleep time < 6 hours. Sleep PROM scores were generally within 0.5 SD of the population mean,

not reflecting the high prevalence of objective sleep disturbance in the sample. There were no significant differences in the sleep or symptom PROMs by any of the sleep disturbance indicators (Table 3).

Conclusion: Overall, objective sleep disturbances measured by actigraphy were common in this cohort. However, these results were discordant with self-reported sleep PROMs, which were similar to the general population. The lack of differences in sleep or symptom PROMs by sleep disturbance may be due to our relatively small sample. It is also possible that if sleep disturbances are of long duration, individuals' perceptions of the effects sleep disturbances may have normalized. If findings are replicated, research will be needed to identify more sensitive methods of measuring sleep disturbances in SLE by patient report.

Table 1. Characteristics of participants (n = 61)

	mean ± SD or % (n)
Sociodemographic	
Age	39.7 ± 12.7
Female	88.5 (54)
Race	
Asian	41.0 (25)
Black	6.6 (4)
White	36.1 (22)
Other	16.4 (10)
Hispanic	21.7
Health and SLE	
BMI	26.5 ± 5.6
SLE duration	15.0 ± 9.8
Current glucocorticoid use	50.8 (31)
High dose use (>7.5 mg)	21.3 (13)
Baseline Sleep PROs	
PROMIS Sleep Disturbance	52.0 ± 9.1
PROMIS Sleep Impairment	52.6 ± 9.2

Table 2. Results from Actigraph assessments

	Mean ± SD or % (n)
Sleep efficiency	
Mean	79.4 ± 8.7
<85%	73.8 (45)
<80%	39.3 (24)
Sleep time	
Mean	6.6 ± 1.0
<7 hours	65.6 (40)
<6 hours	223.0 (14)

Table 3. Differences in outcomes by the presence of sleep disturbances

Outcomes	Sleep Efficiency <85%			Sleep Efficiency <80%			Sleep time <7 hours			Sleep time <6 hours		
	No	Yes	P	No	Yes	P	No	Yes	P	No	Yes	P
Sleep measures												
PROMIS Sleep Disturbance	52.9 ± 8.2	51.7 ± 9.4	0.64	50.8 ± 9.5	5.7 ± 8.3	0.22	51.2 ± 9.3	52.4 ± 9.1	0.62	50.9 ± 9.5	55.6 ± 6.7	0.09
PROMIS Sleep Impairment	53.7 ± 8.3	52.3 ± 9.6	0.61	51.5 ± 9.8	54.4 ± 10.8	0.22	50.9 ± 9.3	53.5 ± 9.2	0.29	51.7 ± 9.5	55.6 ± 7.9	0.17
Symptom measures												
Pain, 0 – 10 rating	2.3 ± 2.6	2.6 ± 2.9	0.69	2.4 ± 3.0	2.7 ± 2.7	0.63	2.7 ± 2.8	2.4 ± 2.9	0.73	2.4 ± 2.8	2.7 ± 2.9	0.74
PROMIS Fatigue	5.6 ± 9.7	51.9 ± 10.1	0.13	52.2 ± 10.1	54.4 ± 10.2	0.42	52.1 ± 9.4	53.5 ± 10.6	0.62	52.2 ± 10.5	55.9 ± 8.5	0.24
PHQ-8 (depressive symptoms	5.8 ± 4.5	6.4 ± 5.0	0.71	5.5 ± 5.0	7.3 ± 4.5	0.18	6.8 ± 5.7	5.9 ± 4.4	0.49	5.7 ± 4.9	7.9 ± 4.7	0.17

Disclosure: P. Katz: None; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, Gilead, 5, Pfizer, 2; **M. Dall'Era**: Annexon Biosciences, 2, 5, AstraZeneca, 2, Aurinia, 2, Biogen, 2, GlaxoSmithKlein, 2, 5, Pfizer, 2.

Abstract Number: 1488

Association of Glucocorticoid Use with Patient-Reported Outcomes Among Persons with Systemic Lupus Erythematosus

Patti Katz[1], Sofia Pedro[2], Jiyoon Choi[3] and Kaleb Michaud[4], [1]University of California San Francisco, San Rafael, CA, [2]Forward, The National Databank for Rheumatic Diseases, Wichita, KS, [3]Bristol Myers Squibb, Lawrenceville, NJ, [4]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Glucocorticoids (GCs) have long been a mainstay of treatment for SLE. While GCs do provide benefit, there are potential side effects that increase with dose and duration and that have potential to affect quality of life negatively. In these analyses, we examine the association of GC use and patient-reported outcomes (PROs).

Methods: Data are from the FORWARD Databank questionnaires collected from participants with physician-diagnosed SLE at 6-month intervals from July 2015 – July 2020.Respondents provide comprehensive health information including GC use and dosage during the prior 6 months and complete PROs, including PROMIS Physical Function, Fatigue, Pain Interference, Sleep Disturbance, and Satisfaction with Social Roles; Systemic Lupus Activity Questionnaire (SLAQ); PHQ-8 (depressive symptoms); and a numeric rating scale of pain (0–10).Analyses examined PROs at baseline according to GC use/non-use. For GC users, baseline data were drawn from the questionnaire in which GCs were first reported during the analysis period. For non-users, baseline data were drawn from the first questionnaire completed during the observation period. Longitudinal logistic regression analyses used generalized estimating equation (GEE) models to estimate the likelihood of worsening in PROs from prior to current observation (by ≥0.5 standard deviation) based on increases in GC dose, addition of other medications, or both during the same period. Models controlled for age, sex, race, BMI, comorbidities, education level, smoking, SLE duration, self-reported lupus disease activity, and SLE organ damage measured by BILD (Brief Index of Lupus Damage).

Results: 512 participants qualified for the analysis; 46.3% reported GC use in at least one 6-month period (Table 1).GC users were less likely to be male or white, had more comorbidities, had longer SLE duration, were more likely to also be taking immunosuppressive medications, and reported more active SLE and greater disease damage. GC users had worse scores on all PROs at baseline (**Table 1**).Non-GC users rarely had medication changes (97% of observations, 89% of GC non-users; **Table 2**). The majority of GC users also had no medication changes (83% of observations, 53% of GC users).

Table 1. Participant characteristics and PROs at baseline

Variable	No GC use 53.7% (275)	GC use 46.3% (237)	p-value
Dose of GC		9.1 (12.2)	
0 – <5 mg)		9.5 (46)	
5 – <10 mg)		24.3 (118)	
≥ 10 mg		13.4 (65)	
Male sex	8.0 (22)	3.4 (8)	0.028
White, non-Hispanic ethnicity	88.4 (243)	78.1 (185)	0.002
Age, years	58.0 ± 13.0	59.6 ± 13.3	0.172
Education level, years	14.2 ± 2.7	14.5 ± 2.0	0.111
College graduate	48.0 (132)	47.7 (113)	0.942
General health characteristics			
RD Comorbidity Index (0-9)	2.4 ± 1.9	2.8 ± 1.9	0.024
BMI, kg/m²	29.2 ± 7.9	29.6 ± 9.3	0.561
Ever smoked	37.5 (103)	31.2 (74)	0.139
SLE characteristics			
SLE duration, years	23.6 ± 12.4	25.6 ± 13.1	0.083
How active is your lupus today (0 – 10 rating)	2.4 ± 2.5	3.33 ± 2.8	0.000
BILD Score	3.1 ± 2.1	4.00 ± 2.4	0.000
Medications			
Hydroxychloroquine	57.8 (159)	59.1 (140)	0.774
Immunosuppressives	19.6 (54)	43.0 (102)	0.000
Patient-Reported Outcomes (PROs)			
PROMIS Physical Function	44.5 ± 9.5	40.5 ± 9.4	0.000
PROMIS Fatigue †	54.5 ± 11.5	58.3 ± 10.7	0.001
PROMIS Pain Interference †	55.8 ± 10.1	58.1 ± 9.9	0.027
PROMIS Sleep Disturbance †	53.2 ± 9.1	56.0 ± 8.9	0.003
PROMIS Satisfaction Social Roles	49.3 ± 10.3	46.1 ± 10.1	0.002
SLAQ †	4.0 ± 3.9	5.6 ± 4.7	0.000
PHQ-8 †	5.5 ± 4.7	7.1 ± 5.7	0.004
Pain rating †	3.7 ± 2.9	4.3 ± 2.8	0.019

Tabled values are % (n) or mean ± SD
† Higher scores indicate worse status

Table 2. Observation time and frequency of medication changes

			Medication changes, % (n)			
	Observation time (years)		No change	Increase GC	Add other medications	Both
GC non-users	3.0 ± 2.3	N observations	97.2 (1803)	---	2.8 (51)	---
		N people	88.7 (293)	---	11.3 (37)	---
GC users	3.4 ± 2.2	N observations	83.0 (1342)	11.1 (180)	4.4 (71)	1.4 (23)
		N people	53.1 (126)	27.8 (66)	14.2 (34)	4.9 (12)

Table 3. Likelihood of worsening in PROs by medication changes

			Medication changes		
Patient-reported outcomes	N observations	N people	Increase GC	Add other medications	Both
PROMIS Physical Function	1984	355	0.8 (0.4, 1.6)	0.9 (0.4, 1.6)	2.3 (0.6, 7.9)
PROMIS Fatigue †	1988	355	0.9 (0.5, 1.5)	1.3 (0.8, 2.2)	1.6 (0.5, 5.8)
PROMIS Pain Interference †	1758	358	1.2 (0.7, 2.1)	0.9 (0.4, 1.8)	1.0 (0.2, 4.3)
PROMIS Sleep Disturbance †	1963	354	0.8 (0.4, 1.3)	1.3 (0.8, 2.1)	1.2 (0.3, 4.5)
PROMIS Satisfaction Social Roles	1973	357	1.3 (0.8, 2.1)	1.4 (0.7, 2.6)	2.0 (0.6, 7.0)
SLAQ †	2321	359	0.9 (0.6, 1.3)	1.0 (0.6, 1.7)	2.1 (0.6, 6.7)
PHQ-8 †	2576	400	1.4 (0.9, 2.1)	1.1 (0.6, 1.9)	**2.6 (1.2, 5.7)**
Pain rating †	2958	424	1.0 (0.6, 1.4)	1.0 (0.6, 1.7)	1.3 (0.4, 3.9)

However, increases in GC dose were noted in 11.1% of observations, other medications added in 4.4%, and both GC increases and medication additions in 1.4%.Increases in GC dose, addition of other medications, or the combination were not associated with PRO worsening (**Table 3**).The exception was PHQ, for which there was a significant likelihood of higher scores in the group with increase in GC plus addition of another medication.

Conclusion: GC use was associated worse with PROs at the baseline for these analyses. In this non-inception cohort with relatively long disease duration, however, PROs generally did not worsen over time with changes in GC dosage or other medications; i.e., the differences between GC users and non-users appeared to be static over time. Results suggest that despite potential side effects, patients tend to remain on relatively stable GC doses over time. Patients may be willing to risk negative side effects of GCs to avoid further worsening of symptoms such as pain and fatigue.

Disclosure: P. Katz: None; **S. Pedro**: None; **J. Choi**: Bristol Myers Squibb, 3; **K. Michaud**: None.

Abstract Number: 1489

Treatment with Upadacitinib in Patients with Systemic Lupus Erythematosus Results in the Inhibition of B-Cell–related Biomarkers: Analysis of the M19-130 (SLEek) Phase 2 Study

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: B-cell hyperactivity (1) is a hallmark of the disordered immunity of SLE, arising in the context of a complex array of innate and adaptive mediators. A phase 2 study (NCT03978520) in SLE of upadacitinib (UPA, Janus kinase inhibitor) administered alone or in combination (ABBV-599) with elsubrutinib (a Bruton's tyrosine kinase inhibitor). found significant improvement in disease activity, as measured by SLE Responder Index-4 (SRI-4) and BILAG-Based Combined Lupus Assessment, (BICLA) at weeks 24 and 48.

This analysis evaluates response to UPA and ABBV-599 of immunologic pathways associated with SLE pathogenesis.

Methods: Patients with SLE (n = 205) were randomized to placebo (PBO; n = 75), UPA 30 mg once daily (n = 62), or ABBV-599 (n = 68). At screening, patients were stratified by immunosuppressant use (Yes/No), corticosteroid dose (> 10-mg prednisone or not), IFN score (High/Low), and SLE Disease Activity Index 2000 score. Changes in biomarkers between treatment vs PBO were evaluated with a repeated mixed-linear model, with the Benjamini–Hochberg method used to correct for multiple testing. Total IgG and IgM and anti-dsDNA IgG were measured from serum using a commercially available immunoturbidimetric assay and enzyme linked immunosorbent assay. B-cell subsets and immune cell counts were identified using flow cytometry. Plasma samples were collected for proteomic analyses and assessed with a proximity-extension immunoassay.

Results: Flow cytometry analyses revealed an increase in absolute number of B cells in the peripheral blood of patients treated with UPA or ABBV-599, while the percentage of plasmablasts and plasma cells were reduced, corresponding to a decrease in total IgG and anti-dsDNA antibodies. Reduction in B-cell activation proteins in plasma such as CD72, CD22 and CD79b suggests a direct impact of UPA and ABBV-599 on B cells (**Figure 1**). The observed increase in total peripheral

Figure 1. B cell-related proteins. **$P < .01$; ***$P < .001$.

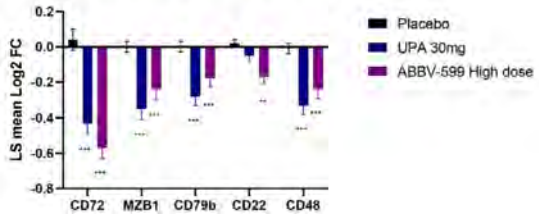
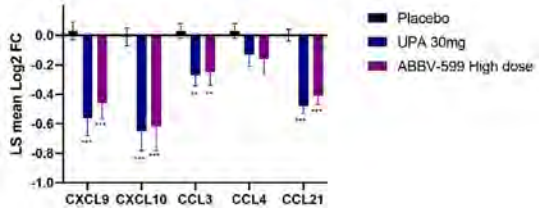


Figure 2. Chemokines. **$P < .01$; ***$P < .001$.



B cells could be explained by the marked reduction in chemokines induced by UPA or ABBV-599 including CXCL9, CXCL10, CCL3 and CCL21 (**Figure 2**). These effects were similar with UPA and ABBV-599, suggesting that the main impact on B cell and plasma cell activating pathways was due to activity of UPA.

Conclusion: These results suggest an association between clinical benefit seen with UPA and an impact on pathogenic B cells involved in SLE, with biomarker effects of both UPA and ABBV-599 apparently driven by UPA. These findings are consistent with our previous analysis in this population that showed treatment with UPA or ABBV-599 significantly reduced the IFN gene scores compared with PBO at weeks 4 and 24. (2)

1. Szelinski F, et al. Curr Opin Rheumatol. 2022;34(2):125-132. DOI: 10.1097/BOR.0000000000000865
2. Gaudreau M-C, et al. Abstract 4002. Presented at European Congress of Rheumatology (EULAR), 31 May–3 June 2023, Milan, Italy.

Disclosure: M. Gaudreau: AbbVie, 3, 11; **J. Fann**: AbbVie, 3, 11; **A. Friedman**: AbbVie, 3, 11; **T. Sornasse**: AbbVie, 3, 11; **J. Merrill**: AbbVie, 2, Alexion, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, Bristol Myers Squibb, 2, 5, EMD Serono, 2, Genentech, 2, Gilead, 2, GlaxoSmithKline, 2, 5, Lilly, 2, Merck, 2, Pfizer, 2, Provention, 2, Remegen, 2, Sanofi, 2, UCB Pharma, 2, Zenas, 2.

Abstract Number: 1490

Early Experience with SGLT2i in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis (LN) occurs in over 50% of the systemic lupus erythematosus (SLE) patients. It remains an independent risk factor for mortality, with deaths from LN increasing from 2015-2020. Progression to chronic kidney disease occurs from both lupus specific and non-specific factors, that are due to general mechanisms that occur in many types of chronic kidney disease. In patients with type 2 diabetes and albuminuric kidney disease the risk of kidney failure and cardiovascular events was lower with SGLT2 inhibitors (SGLT2i) than placebo after 2.6 years median follow up. We examined changes in trajectories of eGFR and proteinuria after starting SGLT2i among patients with SLE.

Methods: 45 SLE patients who started taking SGLT2i were included:87% female; 35.5% Caucasian, 55.5% African-American, 9% East Asian; mean age when started on SGLT2i was 47.2 ± 13.4 yrs (mean ± SD). SGLT2i was started for standard of care (diabetes mellitus, chronic kidney disease, or both). eGFR was calculated using the 2021 CKD-EPI creatinine equation. eGFR and Urine protein/creatine ratio were measured at every quarterly visit.The analysis was based on clinical visits up to three years prior to starting SGLT2i and all clinical visits after starting SGLT2i. The mean follow-up time prior to starting SGLT2i was 1.9 years with 5 patients contributing no pre-SGLT2i follow-up. The mean follow-up time after starting SGLT2i was 1.1 years with 2 patients contributing no post SGLT2i follow-up. For each outcome (GFR and urine protein), we estimated each person's trajectory before and after starting SGLT2i using a mixed effects longitudinal regression model with random person-specific slopes and intercepts.

Results: Prior to starting SGLT2i, the average annual change in eGFR was a decline of 3.1 (P=0.0014, Table 1). After starting SGLT2i, the average annual change in eGFR was estimated to be a decline of 0.9. The difference between these two degrees of decline did not reach statistical significance (p=0.27). Prior to starting SGLT2i, the average annual change in urine protein-creatinine ratio was estimated to be an increase of 0.40 (p=0.16, Table 2). However, after starting SGLT2i, the average annual change was estimated to be a decline of 0.37. Again, the difference between these two slopes was not statistically significant (p=0.18).

Conclusion: SLE patients were excluded from the canagliflozin CREDENCE trial (Perkovic V et al. NEJM 380:2295, 2019). Thus, there is a crucial need for data on SGLT2i use in SLE. Like the CREDENCE trial, we observed a reduction in decline in eGFR after starting SGLT2i, however, this reduction was not statistically significant. Similarly, like the CREDENCE trial, we observed an improvement in urine protein/creatinine ratio after starting SGLT2i, but again, our observed difference did not achieve statistical significance. In the CREDENCE trial, reduction in proteinuria was observed by 6 months, and then plateaued. Thus, early experience suggested marginal benefit of SGLT2i in SLE. Additional patients and longer follow-up are needed for a more definite conclusion regarding the value of SGLT2i in SLE.

Table1: Estimated impact of SGLT2i on trajectories of eGFR before and after starting SGLT2

Effect	Estimated average slope	95% CI	Estimated range of 95% of patient-specific slopes	P-value
Average annual slope in eGFR prior to starting SGLT2i	-3.1	-5.0, -1.2	-11.7, 5.53	0.0014
Average annual slope in eGFR after starting SGLT2i	-0.9	-3.6, 1.8	-7.7, 5.9	0.52
Difference between the two slopes	2.2	-1.7, 6.1	-11.6, 16.0	0.27

Table2: Estimated impact of SGLT2i on trend based in mean urine protein/creatinine ratio

Effect	Estimated average slope	95% CI	Estimated range of 95% of patient-specific slopes	P-value
Average annual slope in urine protein/creatinine ratio prior to starting SGLT2i	0.40	(-0.16, 0.97)	(-3.20, 4.0)	0.16
Average annual slope in urine protein/creatinine ratio after starting SGLT2i	-0.37	(-0.94, -0.20)	(-3.83, 3.09)	0.21
Difference between the two slopes	-0.77	(-1.90, 0.35)	-0.77 (-7.83, 6.29)	0.18

Disclosure: M. Petri: Alexion, 1, Amgen, 1, AnaptysBio, 1, Annexon Bio, 1, Argenx, 1, Arhros-Focus Med/Ed, 6, AstraZeneca, 1, 5, Aurinia, 1, 5, 6, Axdev, 1, Biogen, 1, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CVS Health, 1, Eli Lilly, 1, 5, Emergent Biosolutions, 1, Exagen, 5, Exo Therapeutics, 2, Gilead Biosciences, 2, GlaxoSmithKlein(GSK), 1, 5, 6, Horizon Therapeutics, 2, Idorsia Pharmaceuticals, 2, IQVIA, 1, Janssen, 1, 5, Kira Pharmaceuticals, 2, MedShr, 6, Merck/EMD Serono, 1, Momenta Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Proviant, 2, Sanofi, 2, Sinomab Biosciences, 2, Thermofisher, 5, UCB, 2; **D. Goldman**: None; **A. Fava**: Annexon Biosciences, 2, Sanofi, 1; **L. Magder**: None.

Abstract Number: 1491

Targeting the Mevalonate Pathway-dependent Protein Geranylgeranylation to Restrict Follicular Helper T Cell Differentiation for the Treatment of Systemic Lupus Erythematosus

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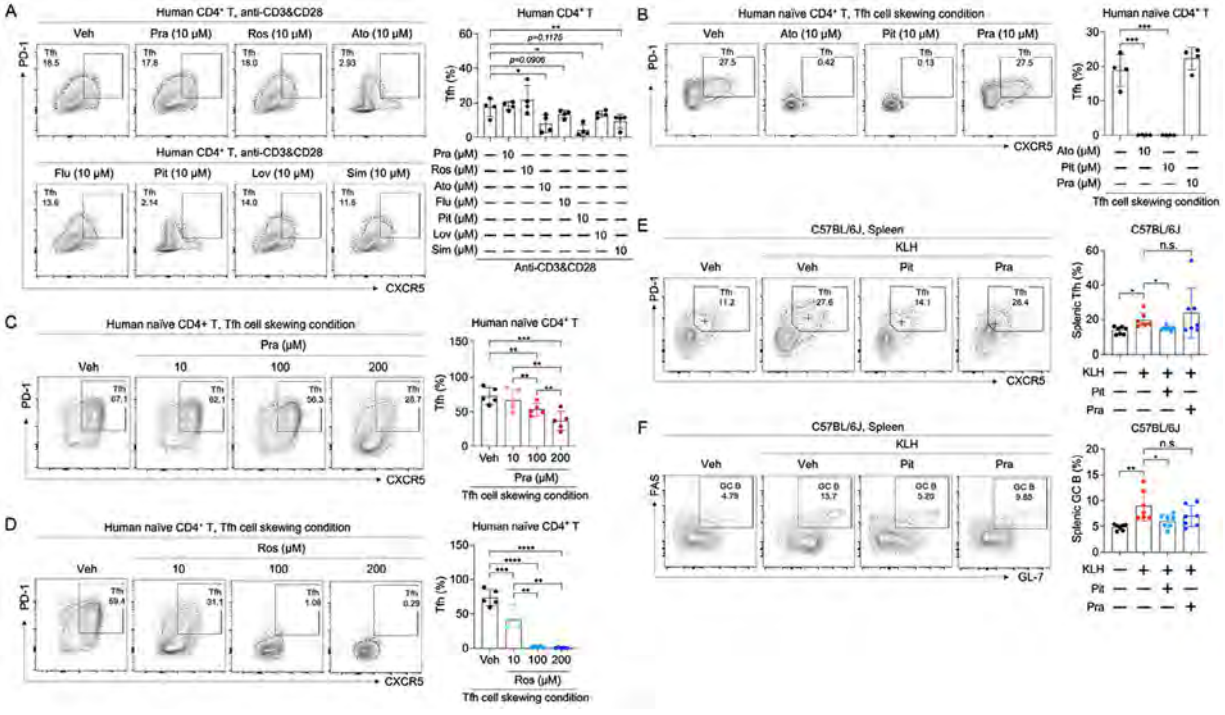
SESSION INFORMATION

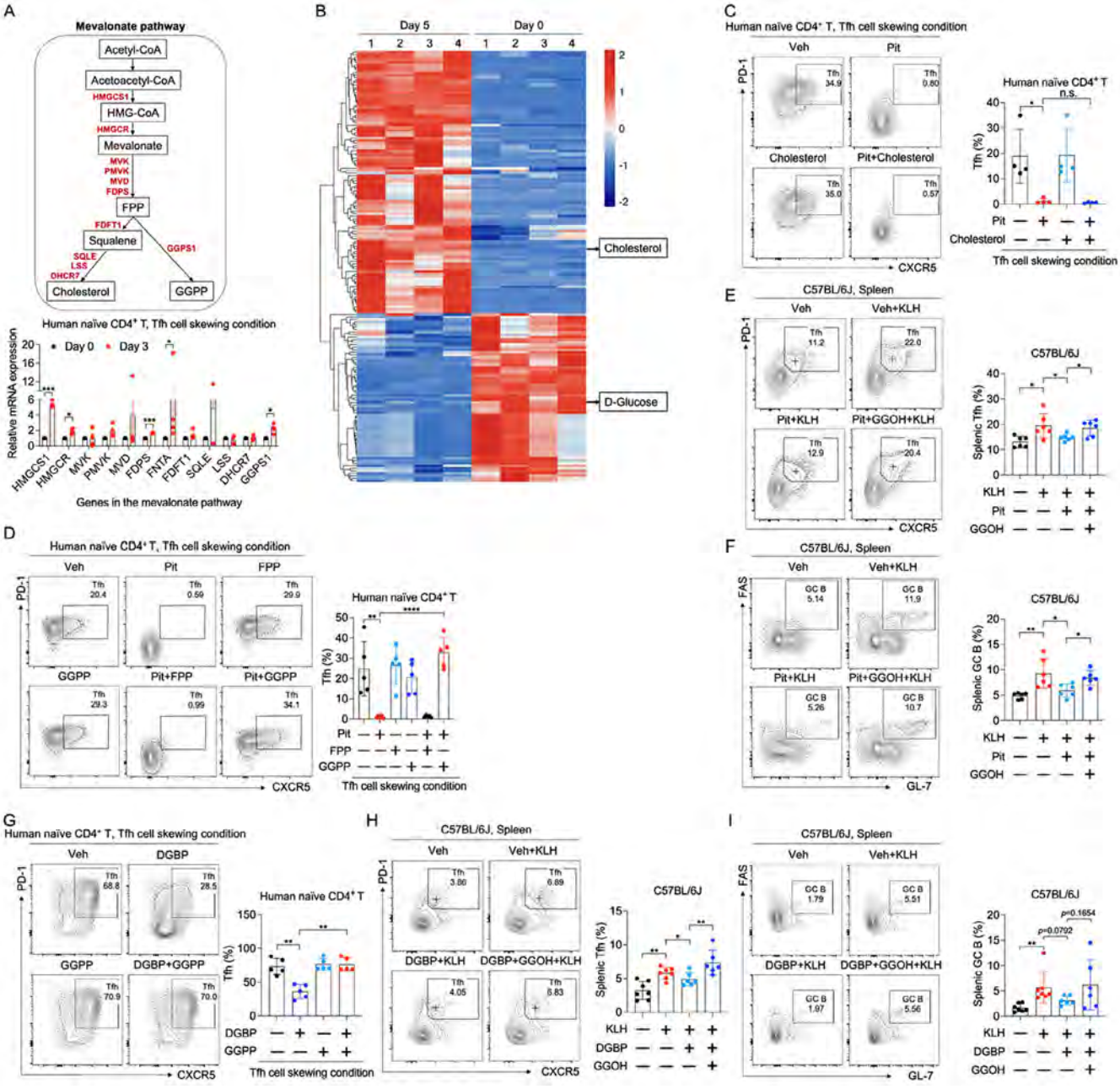
Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Recent research focusing on follicular helper T (Tfh) cells emphasizes its importance in autoimmune diseases, such as systemic lupus erythematosus (SLE). However, the mechanisms underlying Tfh cell differentiation remain largely unknown, and therapeutic strategies targeting Tfh cells for SLE are urgently needed.



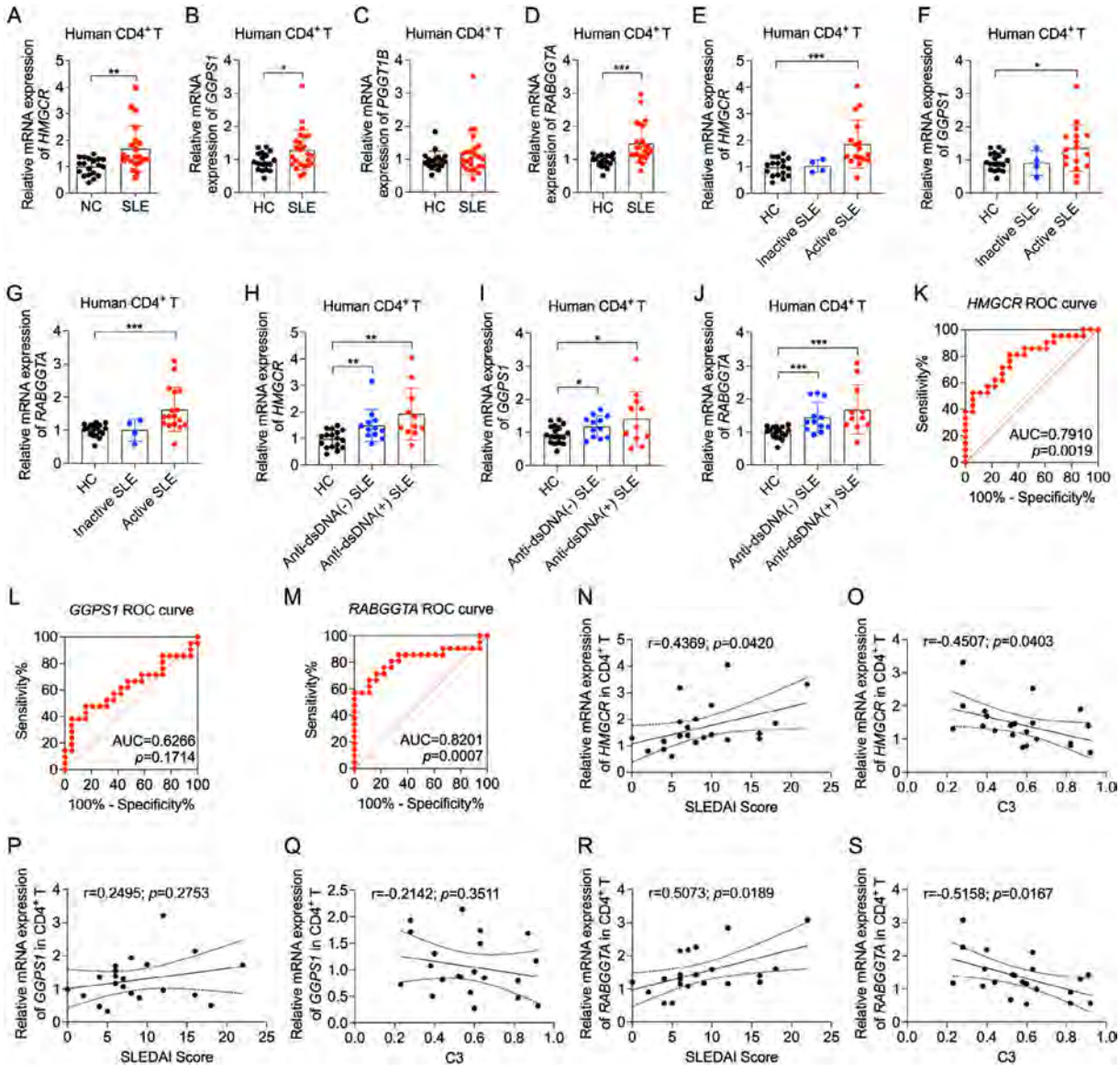
Lipophilic statins inhibited Tfh cell differentiation in vitro and in vivo.

Methods: The effects of seven clinically used statins on human CD4$^+$ T cell subsets were investigated and compared. Chemical and genetic approches were employed to investigate the role of the mevalonate pathway in Tfh cell differentiation and germinal center (GC) reactions *in vitro* and *in vivo*. Chemical and genetic approches were subsequently employed to investigate the role of GGPS1 and GTase II in Tfh cell differentiation and GC reactions *in vitro* and *in vivo*. Expression of the genes in the mevalonate pathway and the genes for protein geranylgeranylation in SLE CD4$^+$ T cells was detected by RT-qPCR and flow cytometry. The role of key genes in the mevalonate pathway and GGTase II in CD4$^+$ T cells in SLE pathogenesis was investigated in pristane-induced lupus-like mice. The effects of pitavastatin on SLE were evaluated in lupu prone MRL/lpr mice.



GGPP derived from the mevalonate pathway is essential for Tfh cell differentiation and GC reactions.

Results: Pharmacological and genetic inhibition of the mevalonate pathway leads to suppressed Tfh cell differentiation and impaired germinal center (GC) reactions. We identify geranylgeranyl pyrophosphate (GGPP) as the key intermediate metabolite derived from the mevalonate pathway driving Tfh cell differentiation. Further studies emphasize that geranylgeranyl transferase II (GGTase II) facilitates the membrane localization of CXCR5 by regulating the geranylgeranylation of RAB proteins, which transfers the effect of GGPP on Tfh cell differentiation. Conditional ablation of the specific subunit of GGTase II, *RABGGTA,* in $CD4^+$ T cells, leads to impaired Tfh cell differentiation and GC reactions. Moreover, the expression of key genes in the mevalonate pathway and *RABGGTA* is increased in SLE $CD4^+$ T cells and is positively correlated with SLE disease activity. Genetic ablation of key genes in the mevalonate pathway and *RABGGTA* postpones the pathological progression in pristane-induced lupus-like mice. Additionally, RAB35 is identified as the key RAB protein that upregulated in SLE $CD4^+$ T cells, and whose expression is positively correlated with SLE disease activity. Point mutation of the Cys sites for geranylgeranylation at the carboxyl terminus of RAB35 impedes the membrane localization of CXCR5 and restricts Tfh cell differentiation both *in vitro* and *in vivo*. Finally, lipophilic pitavastatin is effective in ameliorating SLE disease activity.



The mevalonate pathway was dysregulated in SLE CD4+ T cells and was positively associated with SLE disease activity.

Conclusion: In summary, our current study highlights the importance of geranylgeranylation of RAB proteins regulated by the mevalonate pathway in Tfh cell differentiation and SLE pathogenesis, and proposes pitvastatin as an adjuvant therapy for SLE.

Disclosure: L. Wang: None.

Abstract Number: 1492

Pre-treatment Differentially Expressed Metagenes Characterize Systemic Lupus Patients Who Subsequently Achieve Clinical Response to Belimumab

Miles Smith[1], Kevin Thomas[1], Nicolas Dominguez[1], Susan Macwana[1], Wade DeJager[1], Stan Kamp[1], Carla Guthridge[1], Bridget Parrish[1], Cristina Arriens[2], Judith James[1], Joan Merrill[1] and Joel Guthridge[1], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]Oklahoma Medical Research Foundation and University of Oklahoma Health Sciences Center, Department of Arthritis & Clinical Immunology, Oklahoma City, OK

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Belimumab, which targets the B Cell activator and survival factor BLyS, is an approved treatment for systemic lupus (SLE) and has demonstrated efficacy in multiple clinical trials around the world. Nevertheless, like other SLE treatments, belimumab can have disappointing results in a significant proportion of this heterogenous population, a problem further complicated by the unpredictable impact of various combination treatments used with belimumab in trials and clinical practice. Using gene expression variables, we aim to identify SLE patients prior to treatment who will respond favorably to belimumab treatment.

Methods: A prospective open-label study of belimumab was conducted in 24 SLE patients with active but non-organ threatening disease, who were required to withdraw other immune suppressants (only antimalarials or low dose steroids allowed). At baseline, after blood samples obtained, patients were given optional steroid injections for temporary relief, then

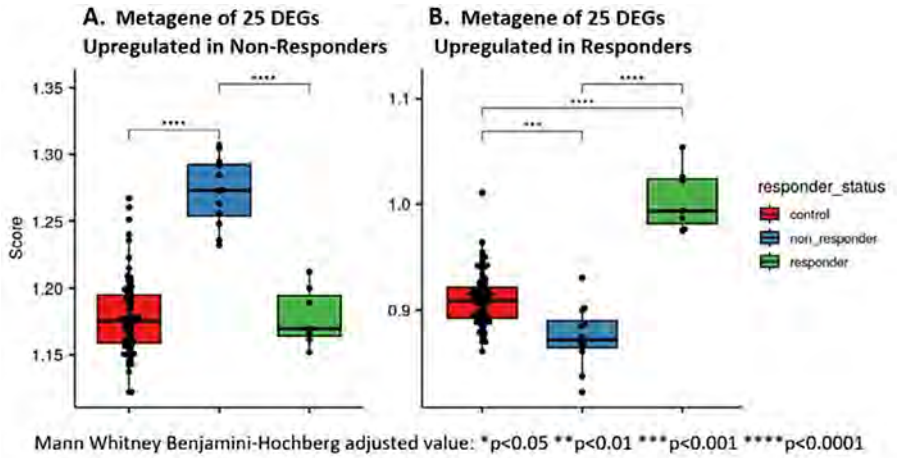


Figure: No overlap between pre-treatment metagene module scores In SLE patients who do vs do not respond to belimumab

followed for six months on intravenous belimumab (10 mg/kg). The primary endpoint was time to treatment failure (flare, treatment change or study withdrawal) compared to historical controls from the BOLD study[1] (same protocol but without treatment after initial steroids). Response was also evaluated at six months by the SLE Responder Index (SRI-4) or the BILAG-based Combined Lupus Assessment (BICLA). Before and during treatment, PAX gene tubes were collected, and RNA sequenced, using the same methods for healthy control samples. To maximally discriminate clinical responders from non-responders by baseline gene expression patterns in a small, heterogenous population, principal component analysis was conducted with modules (metagenes) comprised of differentially expressed genes (DEGs).

Results: Of 24 patients entering the study, 20 completed 6 months of treatment. The mean survival time without treatment failure was 18.4 weeks (CI 15.3-21.5) compared to the 41 BOLD participants with mean survival 9.829 weeks (CI 0.999-7.871) ($p< 0.001$ by log rank test). At 6 months, 14 patients who received belimumab (58%) and 1 from the BOLD study (2.4%) remained free of flare. The SRI-4 was met by 7 patients in this study (29.2%), the BICLA by 9 (37.5%). SRI-4 response was used as the basis for modeling two metagenes comprised of baseline expression of the 25 most upregulated genes in non-responders and the 25 most upregulated genes in responders with no overlap between metagene scores of responders vs non-responders (figure). After 3 months of treatment with belimumab the metagene scores corrected towards levels in healthy controls. The most discriminatory DEGs included protein transcription factors and long non-coding RNA (some being known transcription regulators).

Conclusion: When background immune suppressants are excluded, belimumab still achieves SRI 4 or BICLA response for a subset of patients, and most do not flare for at least six months. Preliminary identification of a composite metagene model as a potential predictor of belimumab response provides an intriguing model which will require testing in prospective confirmation studies. [1]Merrill, Arth Rheum 2017 69:1257

Disclosure: M. Smith: None; **K. Thomas**: None; **N. Dominguez**: None; **S. Macwana**: None; **W. DeJager**: None; **S. Kamp**: None; **C. Guthridge**: None; **B. Parrish**: None; **C. Arriens**: AstraZeneca, 1, 5, 6, Aurinia, 6, Bristol-Myers Squibb, 1, 5, Cabaletta, 1, GSK, 1, Kezar, 1, UCB, 1; **J. James**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 2, Novartis, 2, Progentec Biosciences, 5; **J. Merrill**: AbbVie, 2, Alexion, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, Bristol Myers Squibb, 2, 5, EMD Serono, 2, Genentech, 2, Gilead, 2, GlaxoSmithKline, 2, 5, Lilly, 2, Merck, 2, Pfizer, 2, Provention, 2, Remegen, 2, Sanofi, 2, UCB Pharma, 2, Zenas, 2; **J. Guthridge**: None.

Abstract Number: 1493

Novel BCMA-CD19 Compound CAR-T (cCAR) Targets B Cells and Plasma Cells Achieving Immune Reset and Eliminates All Autoantibodies in Systemic Lupus Erythematosus (SLE) and Lupus Nephritis (LN) Patients Resulting in Long-Term, Medication-Free Remission

Yong Yuan[1], Shanzhi He[1], Wenli Zhang[2], Hongyu Zhang[2], Vincent DeStefano[3], Masayuki Wada[3], Kevin Pinz[3], **Greg Deener**[3], Yu Ma[4], Min Wang[1], Fugui Li[1], Ming Hong[1], Chanjuan Zou[1], Mingxia Wang[1], Ling Ding[1], Yingwen Liang[1], Yupo Ma[3] and Weijia Wang[1], [1]Zhongshan People's Hospital, Zhongshan, China, [2]Peking University Shenzhen Hospital, Shenzhen, China, [3]iCell Gene Therapeutics Inc., Stony Brook, NY, [4]iCAR Bio Therapeutics Ltd, Zhongshan, China

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Evaluate cCAR safety in SLE, LN and autoimmune conditions. Determine whether a single dose eliminates autoantibodies with well tolerated long-term, medication-free remission in open label proof of concept.

Methods: BCMA-CD19 cCAR approved by Zhongshan People's Hospital and Peking University Shenzhen Hospital IRBs for autoimmune patients. Initially compassionate use in 2 lymphoma patients with 20-year history of SLE (Patient 1 Sept 2019). After initial SLE patients safely in remission, IRB approved cCAR for use in LN (11 LN patients June 22 to April 23). 18 patients in safety dataset (includes NMOSD, donor specific antibodies in transplant).

Lupus patients: After apheresis, prior to cyc/fludarabine conditioning all lupus medications discontinued. Patients dosed 1.5-3x10^6 cCAR cells/kg (LN target 3x10^6/kg) and then monitored, IVIG given PRN. LN: required to fail multiple lines of therapy, be refractory and active disease on kidney biopsy (class III to V). All LN, SLE patients met ACR criteria.

Baseline Characteristics: Lupus age range: 17-58. 10 of 13 female. SLEDAI-2K baseline mean = 10. All LN patients at screening treated with HCQ, glucocorticoids, immunosuppressant (MMF, CYC); majority with belimumab. At screening, mean 24-hour urine microprotein 1.7g and urine/creatine ratio 1.0. Patients avg 3.9 elevated autoantibodies (2.5 >3X ULN, many >20X ULN). Majority had low C3.

Results: Safety: cCAR well tolerated; no CRES/iCANs, no CRS >Grade 1, no fever >40^o C. All LN patients received target dose and only infection other than Covid was a Grade 1 UTI.8 patients tested positive for Covid (at time >80% local population tested positive), 3 hospitalized as precaution, none in ICU. No other URIs reported. No GI infections or diarrhea AEs suggesting no concerning IgA related AEs.

B cells/Ig: B cells eliminated in 1-10 days; IgM, IgA, IgG eliminated in 1-2 months. WBC normal in 7-21 days. B cells returned to normal in all patients (mean 90 days, range 40 to 150). All patients treated >150 days normal IgM. Flow cytometry, BCR sequences confirm immune reset achieved. Given B cells, IgM normal within 150 days, expect all patients to fully regain humoral immunity.

Efficacy: All elevated autoantibodies eliminated, including those derived from long-lived plasma cells, most in first month. All C3, C4 normal within 21 days. All patients had significant medication-free symptom improvement (11 of 13 in first month). All 3 patients at >1 year (up to 44 months) in medication-free remission (no symptoms). Renal function significantly improved in LN patients within first 6 months.

Conclusion: Proof of concept achieved. cCAR safely eliminated all autoantibodies, reset B cell and humoral immune system, and delivered long-term, medication-free remission in a single dose. Monitoring patients to ensure humoral immunity fully recovers. Will update with full dataset, further research is needed.

Acknowledgements: Patients and their families.

Disclosure: Y. Yuan: None; **S. He**: None; **W. Zhang**: None; **H. Zhang**: None; **V. DeStefano**: iCell Gene Therapeutics Inc., 3; **M. Wada**: iCell Gene Therapeutics Inc., 3; **K. Pinz**: iCell Gene Therapeutics Inc., 3; **G. Deener**: ICell Gene Therapeutics, 3, iCell Gene Therapeutics Inc., 3; **Y. Ma**: iCAR Bio Therapeutics Ltd, 3; **M. Wang**: None; **F. Li**: None; **M. Hong**: None; **C. Zou**: None; **M. Wang**: None; **L. Ding**: None; **Y. Liang**: None; **Y. Ma**: iCell Gene Therapeutics Inc., 3, 3; **W. Wang**: None.

Abstract Number: 1494

The Effect of Belimumab on Steroid Use in Patients with SLE: Results from a Retrospective Observational Study of Real-World Data from a US Rheumatology Provider Network

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: While oral CS (OCS) are the mainstay of SLE therapy, prolonged use is associated with organ damage and early mortality.[1,2] Minimizing OCS use is among SLE treatment goals.[1] The beneficial effect of belimumab (BEL) on OCS reduction was shown in two pooled analyses of five randomized clinical trials,[3] and six retrospective observational real-world studies.[4]

This study used real-world data from a large rheumatology provider network to compare OCS use in patients (pts) with SLE in the US before and after BEL initiation.

Methods: This retrospective cohort study (GSK Study 214140) utilized data from the Patient-Important Outcomes Data Repository (PIONEER)-Rheumatology database.[5] Eligible adults with SLE initiated BEL between Jan 1, 2012, and Jun 30, 2021, and had available data for ≥180 days before and ≥360 days post BEL initiation. The index was the date of BEL initiation. Primary objectives: proportion of pts receiving any OCS; mean total OCS dose per pt; mean total number of OCS days supplied per pt; mean daily OCS dose for days supplied per pt (in pts with ≥1 OCS prescription); proportion of pts with daily OCS dose of ≤5 mg and ≤7.5 mg for days supplied. A secondary objective was to describe pt clinical

Table 1. Change from P1 to P2 and P3 in OCS use among pts adherent to BEL treatment at 180 days (P1 vs P2) and 360 days (P1 vs P3) who were receiving OCS in P1. Note: Percentages for differences are shown after rounding to the nearest whole number. Distributions of differences between periods were assessed by Kolmogorov–Smirnov and Shapiro–Wilk tests and none of the measures were found to be normally distributed. Wilcoxon Signed Ranks test was used to generate p values. OCS dose=prednisone equivalent.

	P1 (N=342)	P2 (N=342)	P1 vs P2 difference, %	P1 vs P2 p value	P1 (N=268)	P3 (N=268)	P1 vs P3 difference, %	P1 vs P3 p value
Proportion of pts receiving OCS, n (%)	342 (100.0)	268 (78.4)	-22	<0.001	268 (100.0)	174 (64.9)	-35	<0.001
Mean total OCS dose per pt, mg	718.8	572.8	-20	<0.001	695.1	426.6	-39	<0.001
Mean total OCS days supplied per pt	64.1	59.6	-7	0.064	62.7	51.9	-17	<0.001
Mean OCS daily dose for days supplied, mg	12.3	10.4	-15	<0.001	11.7	9.4	-20	<0.001
Proportion of pts with OCS dose of ≤5 mg/day for days supplied, n (%)	85 (24.9)	163 (47.7)	92	<0.001	68 (25.4)	161 (60.1)	137	<0.001
Proportion of pts with OCS dose of ≤7.5 mg/day for days supplied, n (%)	121 (35.4)	196 (57.3)	62	<0.001	100 (37.3)	183 (68.3)	83	<0.001

characteristics during follow-up. Changes in OCS use were assessed between Period (P) 1 (180 days pre-index [–180 to –1 days]), P2 (first 6 months post index [0 to 180 days]), and P3 (second 6 months post index [180 to 360 days]) in ptswith OCS use in P1 who were adherent to BEL at each assessed period.

Results: Of the 14,439 pts with SLE in the database, 608 received BEL for >180 days (full analysis set, FAS; 92.8% female, 70.4% with moderate SLE) and were included; 492 pts adhered to 360 days of BEL. In P1, 56.3% of FAS pts and 54.5% of pts who adhered to 360 days of BEL were receiving OCS.

Improvements in OCS use were more pronounced in pts with OCS use in P1 (**Table 1**), compared with the FAS, which included pts with no OCS use in P1 (**Table 2**).

Table 2. Change from P1 to P2 and P3 in OCS use among pts adherent to BEL treatment at 180 days (P1 vs P2) and 360 days (P1 vs P3). Note: Percentages for differences are shown after rounding to the nearest whole number. Distributions of differences between periods were assessed by Kolmogorov–Smirnov and Shapiro–Wilk tests and none of the measures were found to be normally distributed. Wilcoxon Signed Ranks test was used to generate p values. OCS dose=prednisone equivalent.

	P1 (N=608)	P2 (N=608)	P1 vs P2 difference, %	P1 vs P2 p value	P1 (N=492)	P3 (N=492)	P1 vs P3 difference, %	P1 vs P3 p value
Proportion of pts receiving OCS, n (%)	342 (56.3)	335 (55.1)	−2	0.613	268 (54.5)	236 (48.0)	−12	0.013
Mean total OCS dose per pt, mg	404.3	377.1	−7	0.260	378.7	292.2	−23	0.004
Mean total OCS days supplied per pt	36.0	38.6	7	0.220	34.1	34.2	0	0.775
Mean OCS daily dose for days supplied, mg	12.3	11.0	−11	<0.001	11.7	10.4	−11	<0.001
Proportion of pts with OCS dose of ≤5 mg/day for days supplied, n (%)	351 (57.7)	377 (62.0)	7	0.048	292 (59.3)	337 (68.5)	15	0.001
Proportion of pts with OCS dose of ≤7.5 mg/day for days supplied, n (%)	387 (63.7)	417 (68.6)	8	0.022	324 (65.9)	368 (74.8)	14	0.001

Table 3. Changes from P1 to P2 and P3 in pt clinical characteristics among pts adherent to BEL treatment at 180 days (P1 vs P2) and 360 days (P1 vs P3). *Among pts with data available for the given period; data may not be for the same pts assessed in each period. IQR, interquartile range; SD, standard deviation.

	P1 (N=608)	P2 (N=608)	P1 (N=492)	P3 (N=492)
C3* (mg/dL)				
N	326	323	259	255
Mean (SD)	113.9 (34.7)	120.6 (33.3)	113.1 (34.8)	120.7 (33.3)
Median (IQR)	113.0 (86.0, 136.0)	119.0 (99.0, 145.0)	112.0 (85.0, 136.0)	117.0 (97.0, 146.0)
C4* (mg/dL)				
N	240	260	189	211
Mean (SD)	25.7 (8.9)	26.9 (9.4)	25.7 (8.9)	27.3 (9.9)
Median (IQR)	24.0 (19.0, 31.2)	25.0 (20.0, 31.9)	24.0 (19.0, 31.3)	25.6 (20.0, 31.5)
SLEDAI*				
N	34	30	28	23
Mean (SD)	12.5 (6.3)	9.6 (6.4)	12.7 (5.7)	11.6 (9.4)
Median (IQR)	11.5 (8.0, 16.0)	8.5 (6.0, 16.0)	12.0 (8.0, 16.5)	8.0 (4.0, 17.0)

Among pts receiving OCS in P1, significantly fewer received OCS in P2 and P3 versus P1 (**Table 1**). Significant reductions from P1 were observed in P2 and P3 for mean total OCS dose per pt, mean OCS daily dose for days supplied, and mean total OCS days supplied per pt in P3 only; significantly more pts received daily OCS dose of ≤5 mg and ≤7.5 mg in P2 and P3 versus P1 (**Table 1**).

Slight increases from P1 in C3 and C4 levels were observed in P2 and P3; mean SLEDAI scores (for pts with available data for the specified period) decreased from 12.5 in P1 to 9.6 in P2 in FAS pts and from 12.7 in P1 to 11.6 in P3 in pts who adhered to 360 days of BEL (**Table 3**).

Conclusion: This analysis of data from a large rheumatology database showed OCS dose and use reductions with BEL in pts receiving OCS before BEL initiation, providing more real-world evidence for the steroid-sparing effect of BEL in pts with SLE and baseline OCS use. The beneficial effect was more pronounced with longer duration of BEL treatment.

Funding: GSK

References

1 Fanouriakis A et al. *Ann Rheum Dis* 2019;78:736–45
2 Sheane BJ et al. *Arthritis Care Res* 2017;69:252–6
3 Costenbader K et al. *Arthritis Rheumatol* 2021;73 (suppl 9)
4 Collins CE et al. *Rheumatol Ther* 2020;7:946–65
5 Helfgott S et al. *Arthritis Rheumatol* 2022;74 (suppl 9)

Disclosure: K. Worley: GSK, 3, 11; **S. Milligan**: AbbVie, 5, Actelion Pharmaceuticals, 5, AstraZeneca, 5, Gilead Sciences, 5, GSK, 5, Horizon Pharma, 5, Johnson & Johnson, 5, Merck, 5, Pharming Healthcare, 5, Sanofi, 5, Takeda, 5, Trio Health Analytics, 3, UCB Biosciences, 5, ViiV Healthcare, 5; **B. Rubin**: GSK, 3, 11.

Abstract Number: 1495

Deep Serological Profiling of SLE Patients Treated with anti-CD19 CAR T Cells

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SESSION INFORMATION
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Background/Purpose: Anti-CD19 chimeric antigen receptor (CAR) T cell therapy is a ground-breaking emerging treatment modality for severe refractory systemic lupus erythematosus (SLE) and has shown early promise in other diseases.Initial clinical data demonstrate that adoptive transfer of anti-CD19 CAR T cells induce a durable long-term remission in SLE paitents. However, the mechanisms underlying remission are unclear. Our aim was to elucidate the serological factors that are associated with responses in SLE patients following treatment with anti-CD19 CAR T cells.

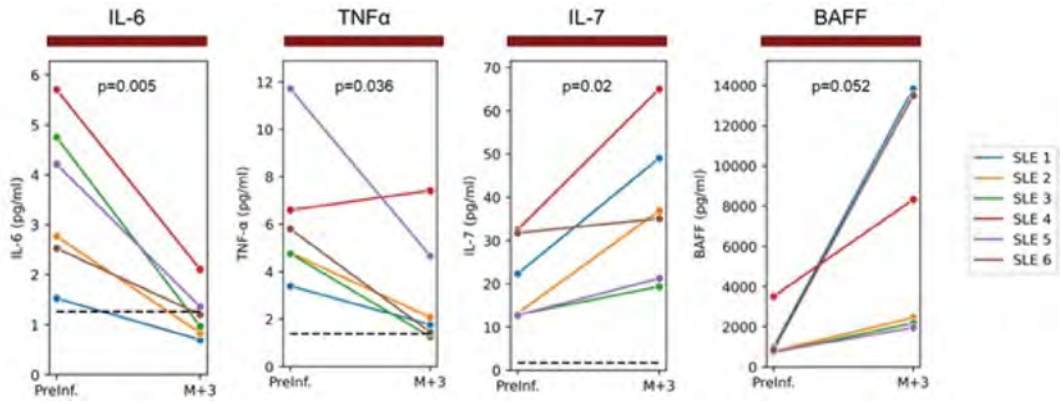

Figure 1. Changes in serum cytokines following CD19 CAR T cell infusion across 6 patients

Methods: Sera were collected from six severe refractory SLE patients prior to and 3 months following anti-CD19 CAR T cell therapy.All patients were in remission off-therapy at 3 months following adoptive T cell transfer. Sera were evaluated for 25 cytokines by electro-chemiluminescence immunoassay (MSD). Sera were also evaluated for 17 SLE-associated and 14 infectious disease-associated antibodies using a custom developed Luminex-based immunoassay.

Results: Serum levels of the inflammatory cytokines IL-6 and TNFα were decreased in SLE patients 3 months post-anti-CD19 CAR T cell infusion relative to pre-infusion (Figure 1).Over the same period, the B cell memory and homeostatic cytokines IL-7 and BAFF increased (Figure 1).SLE associated antibodies decreased dramatically in 5 out of 6 patients following anti-CD19 CAR T cell infusion.In 1 out of 6 patients, SLE associated antibodies either remained stable or increased mildly despite resolution of clinical disease. Infectious disease associated antibodies typically remained stable or changed minimally following anti-CD19 CAR T cell infusion. Lastly, circulating $CD19^+$ B cells were detected in all patients 3 months following anti-CD19 CAR T cell infusion.

Conclusion: We report on 6 SLE patients following anti-CD19 CAR T therapy showing sustained remission off-therapy. Serum cytokine data suggest that systemic inflammation is consistently decreased at three months post infusion. An expanded panel of SLE-associated antibodies shows a profound drop in SLE-associated antibodies observed in most patients supports the idea of an immune reset following CAR T therapy. These studies support the continued exploration of anti-CD19 CAR T cell therapy in SLE.

Disclosure: S. Basu: CabalettaBio, 3, 11; **D. Nunez**: CabalettaBio, 3, 11; **D. Patel**: CabalettaBio, 3, 11; **J. Volkov**: CabalettaBio, 3, 11; **Z. Vorndran**: CabalettaBio, 3, 11, 11; **S. Wong**: CabalettaBio, 3, 11; **A. Mackensen**: BioNTech, 1, Bristol-Myers Squibb(BMS), 1, KITE/Gilead, 1, 6, Kyverna, 5, Miltenyi Biotech, 5; **G. Schett**: None.

Abstract Number: 1496

Clinical Safety and Efficacy Results from EQUALISE Type B: A Phase 1b Open-label Clinical Study of Itolizumab, a Novel anti-CD6 Therapy, in Subjects with Active Proliferative Lupus Nephritis

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SESSION INFORMATION
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Background/Purpose: Itolizumab is a first-in-class, non-depleting, monoclonal antibody against the co-stimulatory receptor CD6 that blocks its interaction with ALCAM, to inhibit T_{eff} cell activity and trafficking. It is being evaluated to treat immunoinflammatory diseases where T cells play a central role, including active proliferative lupus nephritis (apLN). Here we present results from EQUALISE (Type B; NCT04128579), a Phase 1b study of itolizumab in subjects with apLN.

Methods: 17 adult subjects with apLN (ISN/RPS class III or IV with or without class V) were enrolled. All were treated with open-label itolizumab subcutaneously at 1.6 mg/kg Q2W for up to 13 doses in combination with mycophenolate mofetil (2-3 g/day) and systemic corticosteroids (methylprednisolone with rapid taper to prednisone < 10 mg/day by W10). Subjects were followed for 12 weeks after their last dose. Safety and efficacy measures were assessed.

Results: The median age of subjects was 34 years; 94% were female with 82% Asian; most subjects had ISN/RPS class IV +V disease (47%). Mean duration of LN was 5.4 years with Baseline mean 24 hour urine protein of 4.9 g and eGFR of 104 ml/min/1.73m2. Treatment was completed in 11 subjects with 4 discontinuing early (3 due to AEs and 1 due to physician decision) and 2 are still dosing.

88% of subjects experienced at least 1 adverse event (AE), most common were peripheral edema and lymphopenia. At least 1 low lymphocyte count was reported by 7 subjects (41%). Serious AEs occurred in 2 subjects (12%), including dehydration and COVID-19 infection, with none deemed related to study treatment.

Based on the 14 subjects that completed/terminated the study and had a post-baseline measure, there was a median 72% reduction in spot urine protein creatinine ratio (UPCR), resulting in high partial and complete response (PR and CR) rates (FIGURE). At Week 12, the overall response rate was 57% (n=14), and at Week 36 (n=12) was 83%. 2 subjects are still dosing, and 2 are in the follow up period. These responses occurred as early as Week 4 on study with steroids tapered to a median of prednisone 5 mg by Week 12.

Conclusion: EQUALISE Type B demonstrates that subjects with proteinuric apLN had high CR and PR rates with rapid and deep reduction in UPCR when itolizumab was added to mycophenolate mofetil and corticosteroids. Further controlled studies are warranted in this population at high risk of disease progression and end stage kidney disease.

EQUALISE Type B: % response at Week 12/EOS and Week 36/EOS

Disclosure: K. Kalunian: AbbVie/Abbott, 2, Amgen, 5, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EquilliumBio, 2, Genentech, 2, Gilead, 2, Janssen, 2, KezarBio, 1, Merck/MSD, 2, Novartis, 2, Pfizer, 2, Remegene, 2, Roche, 2, UCB, 5; **R. Levin**: AbbVie/Abbott, 2, 5, 6, Amgen, 5, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 2, 5, Eli Lilly, 5, Equillium, 5, Exagen, 2, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Novartis, 5, Sanofi, 6, Scipher,

2, 5, 6; **S. Parameswaran**: None; **n. kopyt**: AstraZeneca, 2, 6, Aurinia, 6, Bayer, 1, Bristol-Myers Squibb(BMS), 6, Opko, 6, otsuka, 2, 6, Vifor, 6; **S. Connelly**: None; **E. Sun**: Equillium Inc, 3, 11; **K. Kim**: None; **m. fung**: Equillium, 3; **M. Rathi**: None.

Abstract Number: 1497

Eltrombopag in SLE-Associated Thrombocytopenia: Treatment Response and Thrombotic Complications

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Background/Purpose: This study aimed to assess the efficacy of Eltrombopag, a medication used to treat thrombocytopenia, in patients with systemic lupus erythematosus (SLE)-associated thrombocytopenia. Additionally, we investigated the occurrence of thrombotic complications in these patients.

Methods: Nineteen SLE patients with thrombocytopenia were followed for two years or until Eltrombopag discontinuation. Data included medical history, examinations, labs, antiphospholipid serology, response rates, and complications

Results: All patients (12 females, mean age 33±12 years) fulfilled the SLICC criteria for SLE and presented with mucocutaneous bleeding. Antiphospholipid serology was positive in 11 patients, with two patients meeting the criteria for antiphospholipid syndrome due to a history of deep vein thrombosis. Six patients had a history of lupus nephritis. Eltrombopag was initiated after the failure of prior therapies. At the start of treatment, the mean platelet count was 12±13 x 109. A daily dose of 50mg of Eltrombopag was used, with one patient requiring 75mg. Twelve patients demonstrated a sustained response, and four patients were able to taper off corticosteroids. However, one patient did not respond to Eltrombopag. Six patients developed thrombotic complications, including deep vein thrombosis, pulmonary embolism, myocardial infarction, cavernous sinus thrombosis, stroke, and catastrophic antiphospholipid syndrome. The median time to thrombotic events was 5.5 months (range: 0.3-8) with a median platelet count of 170 x 10^9 (range: 68-330). These complications necessitated the discontinuation of Eltrombopag. Four out of the six patients with thrombotic events had positive antiphospholipid antibodies, and two had a history of lupus nephritis.

Conclusion: Our study demonstrates that Eltrombopag is effective in treating SLE-associated thrombocytopenia, with favorable treatment responses observed in the majority of patients, including steroid tapering. However, caution should be exercised regarding the development of thrombotic complications, especially in patients with positive antiphospholipid antibodies. Further research is warranted to identify risk factors and strategies for preventing these complications in this patient population.

Disclosure: A. Beltagy: None; **A. Abdelati**: None; **F. Fayed**: None; **N. Eshak**: None; **A. Elghandour**: None; **M. Halaby**: None.

Abstract Number: 1498

First-in-Human Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics Study of DS-7011a, an Anti-TLR7 Antagonistic Monoclonal Antibody for the Treatment of Systemic Lupus Erythematosus

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Toll-like receptor (TLR)7 is a pattern recognition receptor, whose ligands include nucleic acids and whose activation is part of the pathogenesis of systemic lupus erythematosus (SLE).In mice, TLR7 overexpression worsens lupus models, while TLR7 deficiency ameliorates them.In humans, TLR7 gain-of-function mutations confer susceptibility to SLE.DS-7011a is an anti-TLR7 monoclonal antibody (mAb), which prevents TLR7 from signaling.DS-7011a inhibits in vitro production of cytokines stimulated by TLR7.A surrogate anti-TLR7 mAb effectively treats mouse lupus models, improving survival and decreasing autoantibody production.The aim of this first-in-human, single ascending intravenous (IV) and

Baseline characteristics	Results
Total number of patients	19
Gender (female)	12 (63.2%)
Mean age (years)	33 ± 12 (range: 16-55)
SLICC criteria for SLE	All patients fulfilled the criteria
Presenting symptom	Mucocutaneous bleeding
Patients with positive serology for APS	11 (57.9%)
Patients fulfilling APS criteria	2 (10.5%)
Patients with a history of lupus nephritis	6 (31.6%)
Treatment and response	
Platelet count at time of Eltrombopag initiation (mean)	12 ± 13 x 10^3/L
Eltrombopag dosage	50 mg daily (one patient required 75 mg)
Sustained response to Eltrombopag	12 (63.2%)
Patients weaned off steroids	4 (21.1%)
No response	1 (5.3%)
Treatment discontinuation due to side effects (thrombosis)	6 (31.6%)
Complications n=6	
Patients with positive APS serology and complications	4/6 (66.6%)
Patients with lupus nephritis and complications	2/6 (33.3%)
Median time to thrombosis	5.5 months (range: 0.3-8)
Platelet count at the time of thrombosis	170 x 10^3/L (range: 68-330)
Thrombotic complications	Deep vein thrombosis, Pulmonary embolism, Myocardial infarction, Cavernous sinus thrombosis, Stroke, Catastrophic APS.

subcutaneous (SC) dose study was to evaluate the safety, pharmacokinetics (PK), and pharmacodynamics (PD) of DS-7011a in human volunteers (HV), including HV of Japanese descent [NCT05203692].

Methods: This study was a double-blind, randomized, and placebo-controlled trial. Eighty HV were enrolled in 3 stages and assigned to receive DS-7011a or placebo 6:2 in 10 cohorts of 8 each.Non-Japanese HV were enrolled in Stage 1 in 6 ascending IV dose (0.1, 0.3, 1, 3, 10, and 20 mg/kg) cohorts and in Stage 2 in 3 ascending SC dose (100, 300, and 600 mg) cohorts; Japanese HV were enrolled in Stage 3 in 1 IV dose (3 mg/kg) cohort.HV received a single DS-7011a dose on Day 1 and were followed for 8 weeks until Day 57 for safety, PK, and PD assessments. PK exposure was evaluated by measuring DS-7011a in plasma by ligand-binding assay.PD response was evaluated ex vivo in blood using TruCulture® tubes containing gardiquimod, which is a TLR7-specific stimulant, and measuring interleukin (IL)-6 by ligand-binding assay.

Results: DS-7011a was generally safe and well tolerated across all cohorts given by either IV (up to the dose of 20 mg/kg) or SC (up to the dose of 600 mg) administration to either non-Japanese or Japanese HV. The treatment emergent adverse events (TEAE) observed during the study were mostly mild in severity and not drug-related (one TEAE of hospitalization for bone fractures was considered severe and reported as serious but not drug-related).DS-7011a exposure (AUClast and Clast) generally increased with dose increment.PK linearity started at 3 mg/kg following IV administration and at 300 mg following SC, while the elimination of lower doses was noticeably accelerated probably by target-mediated disposition. Mean terminal half-life was about 17 days (within dose range of PK linearity) and mean Tmax upon SC administration was about 5 days. PK exposure in non-Japanese HV was slightly higher than Japanese, reflecting difference in body weight.DS-7011a showed ex vivo inhibition of TLR7-stimulated IL-6 production that was of large extent, early onset, and lasting duration.

Conclusion: DS-7011a, a mAb that specifically antagonizes TLR7, was generally safe and well tolerated and showed appealing PK and PD properties that support its development for the treatment of SLE.

Disclosure: G. Senaldi: Daiichi Sankyo, 3; **A. Mohan**: Daiichi Sankyo, 3; **L. Zhang**: Daiichi Sankyo, 3, Regeneron, 3; **J. Tanaka**: Daiichi Sankyo, 3, The Japan Agency for Medical Research and Development, 5; **G. Pandya**: Daiichi Sankyo, 3; **S. Grossman**: Daiichi Sankyo, 3; **S. Urbina**: None; **S. Reynolds**: None; **A. Hand**: None.

Abstract Number: 1499

Year-5 Follow-up of Belimumab Safety (mortality and Malignancies) in Patients with Systemic Lupus Erythematosus (SLE) Who Completed a Phase 4, 52-week, Randomized, Double-blind Placebo-controlled Safety Study

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Background/Purpose: Belimumab (BEL) is an approved treatment for active SLE and LN, in addition to standard therapy (ST). Despite BEL clinical studies demonstrating a favorable benefit–risk profile, varying incidence rates of mortality and adverse events of special interest, including malignancies, require further evaluation. This study aimed to assess the long-term safety of BEL therapy in patients with SLE.

Methods: This was a Year-5 post-treatment follow-up of the Phase 4, double-blind, placebo (PBO)-controlled Belimumab Assessment of Safety in SLE (BASE) study (GSK Study BEL115467; NCT01705977).[1] Overall, 4003 adults with active, autoantibody-positive SLE received BEL (10 mg/kg intravenously [IV]) or PBO, plus ST, for 48 weeks. Patients then entered a Year 2–5 follow-up period in which they received physician-directed ST. All patients were contacted annually by telephone, including patients who discontinued treatment in Year 1. Mortality and new primary malignancies (including nonmelanoma skin cancer) were the endpoints collected, and rates summarized. We present the final Year-5 follow-up data by treatment received during Year 1.

Results: Out of the Year-1 population, 77.0% (N=3081) were followed up through to Year 5 with a similar proportion of patients in each Year-1 treatment group. Baseline characteristics for the Year-5 follow-up population were similar to the Year-1 study population (N=4003). By the Year-5 follow-up, cumulatively 13.4% and 11.4% of patients in the BEL and PBO Year-1 treatment groups had received BEL as part of physician-directed care, respectively. Cumulative follow-up adjusted mortality rates were lower in the BEL vs PBO Year-1 treatment group by Years 2 to 5 (Year 5 BEL 0.61 vs PBO 0.96 per 100 patient-years; **Table**). Post hoc analyses of the Year 2–5 follow-up period showed that 96 patients (2.85%) died and the highest incidence of deaths by system organ class was infections and infestations (total 0.83%: BEL 0.83% and PBO 0.84%) and cardiac disorders (total 0.51%: BEL 0.29% and PBO 0.72%). Cumulative follow-up adjusted new

Table. Year 1 plus Years 2–5 post-treatment* follow-up mortality and new primary malignancy† rates by Year-1 study treatment. *Patients in the post-treatment follow-up period were no longer receiving study treatment; †includes nonmelanoma skin cancer.

	Patients with events per year, n (%)			Cumulative patient incidence rate per 100 patient-years, (%)		
	BEL	PBO	Total	BEL	PBO	Total
Year-1 (as-treated) population	**N=2002**	**N=2001**	**N=4003**	**N=2002**	**N=2001**	**N=4003**
Deaths	13 (0.65)	22 (1.10)	35 (0.87)	0.66 (0.65)	1.11 (1.10)	(0.87)
New primary malignancies	9 (0.45)	10 (0.50)	19 (0.47)	(0.45)	(0.50)	(0.47)
Year-2 (as-treated in Year-1) population	**N=1695**	**N=1670**	**N=3365**	**N=2002**	**N=2001**	**N=4003**
Deaths	9 (0.53)	21 (1.26)	30 (0.89)	0.60 (1.10)	1.18 (2.15)	0.89 (1.62)
New primary malignancies	3 (0.18)	7 (0.42)	10 (0.30)	0.34 (0.60)	0.48 (0.85)	0.41 (0.72)
Year-3 (as-treated in Year-1) population	**N=1658**	**N=1629**	**N=3287**	**N=2002**	**N=2001**	**N=4003**
Deaths	9 (0.54)	17 (1.04)	26 (0.79)	0.58 (1.55)	1.14 (3.00)	0.86 (2.27)
New primary malignancies	8 (0.48)	9 (0.55)	17 (0.52)	0.38 (1.00)	0.49 (1.25)	0.44 (1.12)
Year-4 (as-treated in Year-1) population	**N=1619**	**N=1583**	**N=3202**	**N=2002**	**N=2001**	**N=4003**
Deaths	14 (0.86)	13 (0.82)	27 (0.84)	0.65 (2.25)	1.07 (3.65)	0.86 (2.95)
New primary malignancies	10 (0.62)	5 (0.32)	15 (0.47)	0.44 (1.50)	0.44 (1.45)	0.44 (1.47)
Year-5 (as-treated in Year-1) population	**N=1555**	**N=1526**	**N=3081**	**N=2002**	**N=2001**	**N=4003**
Deaths	6 (0.39)	7 (0.46)	13 (0.42)	0.61 (2.55)	0.96 (4.00)	0.78 (3.27)
New primary malignancies	3 (0.19)	2 (0.13)	5 (0.16)	0.40 (1.65)	0.38 (1.55)	0.39 (1.60)

primary malignancy patient incidence rates were lower in the BEL vs PBO Year-1 treatment group by Years 2 and 3, but similar by Years 4 and 5 (Year 5 BEL 0.40 vs PBO 0.38 per 100 patient-years; **Table**). Post hoc analyses of the Year 2–5 follow-up period showed that 46 patients (1.37%) developed new primary malignancies (BEL 1.42% and PBO 1.32%). The area most affected by neoplasm was the breast (total 0.36%: BEL 0.35% and PBO 0.36%).

Conclusion: The Year-5 follow-up results of BASE, the largest double-blind, placebo-controlled clinical trial in patients with SLE to date, support the safety of BEL therapy with no new BEL safety concerns identified in this analysis.

Funding: GSK

Reference

1 Sheikh SZ et al. Lancet Rheum 2020;3:e122–30

Disclosure: S. Sheikh: AstraZeneca, 2, Aurinia Pharmaceuticals Inc., 2, Biogen, 2, GSK, 1, 1, 2, Lilly USA, 2, Pfizer, 5; **J. Wei**: Abbvie, 2, 5, 6, Amgen, 5, AstraZeneca, 6, BMS, 2, 5, 6, Celgene, 2, Chugai, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 5, 6, Gilead, 5, GSK, 2, 5, Janssen, 2, 5, 6, Novartis, 2, 5, Pfizer, 2, 5, 6, Sanofi-Aventis, 2, SUN pharma, 5, TSH Taiwan, 2, UCB pharma, 2, 5; **D. Tegzova**: None; **W. Stohl**: GSK, 5, Pfizer, 5; **R. Acayaba de Toledo**: AbbVie, 2, 5, 6, Celltrion, 6, Fresenius, 6, GSK, 5, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer, 5, UCB, 2; **T. Mucenic**: AbbVie, 6, BMS, 6, Eli Lilly, 5, Gilead, 6, GSK, 2, Janssen, 5, 6, Novartis, 6, Pfizer, 6, Roche, 5, UCB, 5; **M. Abello Banfi**: None; **K. Maksimowicz-McKinnon**: Chemocentryx, 5; **C. Abud-Mendoza**: GSK, 6, Lilly, 6, Pfizer, 6; **S. Navarra**: Astellas, 6, AstraZeneca, 6, Biogen, 2, Boehringer-Ingelheim, 2, GSK, 6, Novartis, 6, Pfizer, 6; **M. García**: GSK, 6, Janssen, 6, Pfizer, 6; **I. GARCÍA-DE LA TORRE**: None; **S. Fernandes**: GSK, 3, 12, Shareholder; **J. Harris**: GSK, 3, 11; **A. Roy**: GSK, 3; **J. Olaiz**: GSK, 3, 11; **P. WIlde**: GSK, 3, 11; **D. Roth**: GSK, 3, 12, Shareholder.

Abstract Number: 1500

Cumulative Infections by Week 52 Among Patients with SLE: A Summary of Data from Placebo-Controlled Belimumab Studies

Saira Sheikh[1], Kevin Withrop[2], Jinoos Yazdany[3], Sandra Navarra[4], Tatsuya Atsuma[5], Paula Curtis[6], Jose Miyar Olaiz[7], Christine Henning[8], Roger A. Levy[9], William Stohl[10] and Daniel Wallace[11], [1]University of North Carolina at Chapel Hill, Chapel Hill, NC, [2]Oregon Health & Science University, Schools of Medicine and Public Health, Portland, OR, [3]University of California, General Department of Medicine, Division of Rheumatology, San Francisco, CA, [4]University of Santo Tomas Hospital, Joint and Bone Center, Manila, Philippines, [5]Hokkaido University, Department of Rheumatology, Endocrinology and Nephrology, Sapporo, Japan, [6]GlaxoSmithKline, R&D Biostatistics, Brentford, United Kingdom, [7]GlaxoSmithKline, Safety Evaluation and Risk Management, Brentford, United Kingdom, [8]GlaxoSmithKline, US Medical Affairs, Durham, NC, [9]GlaxoSmithKline, Global Medical Affairs, Collegeville, PA, [10]University of Southern California Keck School of Medicine, Division of Rheumatology, Los Angeles, CA, [11]Cedars-Sinai Medical Center, Los Angeles, CA

SESSION INFORMATION

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Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with SLE have a high risk of infections, which remains a common cause of mortality in this population.[1] This infection risk can result from the pathophysiology of SLE itself, with corticosteroids and immunosuppressive therapy contributing to further infection risks.[1] Belimumab is an approved treatment for active SLE and LN, in addition to standard therapy.[2] To evaluate the incidence of infections onbelimumab treatment, we summarized 52-week infection data from placebo-controlled belimumab SLE studies.

Methods: Infection data were sourced from the Phase 4 Belimumab Assessment of Safety in SLE (BASE) study (GSK Study BEL115467)[3] and GSK Study BEL116559, a pooled post hoc analysis of 52-week safety data from six studies (BEL110751,[4] BEL110752,[5] BEL112341,[6] BEL113750,[7] BEL115471,[8] and LBSL02[9]). In BASE, 4003 adults with active, autoantibody-positive SLE (no criteria based on disease activity level) received belimumab (10 mg/kg/month intravenously [IV]) or placebo, plus standard therapy (ST), for 48 weeks. Only data for patients receiving marketed doses of belimumab (10 mg/kg/month IV or 200 mg/week subcutaneously) or placebo, plus ST are reported from BEL116559 integrated randomized controlled trials (RCTs) included in this analysis, with criteria to exclude patients with low disease activity at baseline. The number of serious infections and infections of special interest (opportunistic infections, active tuberculosis, herpes zoster, sepsis) through 52 weeks were summarized for belimumab and placebo treatment groups.

Results: The age and sex profile of patients in the BASE and integrated BEL116559 studies were similar; however, in BASE more patients were white, the median disease duration was longer, and disease activity and average doses of corticosteroids were lower than in BEL116559 (**Table 1**). Over 52 weeks, serious adverse events (SAEs) of infection and infestation occurred slightly more frequently with placebo than belimumab in both BASE and BEL116559 (**Table 2**). Infections of special interest were of a similar or higher incidence (such as with opportunistic infections and herpes zoster) in BEL116559 versus BASE and occurred more frequently with placebo than belimumab in both datasets (**Table 2**).

Table 1. Baseline patient characteristics for the BASE and BEL116559 datasets. *Baseline patient characteristics are presented for the intention-to-treat population; †patient characteristics for integrated randomized-controlled trials include patients on all doses of belimumab; this cohort is not limited to patients receiving marketed doses (10 mg/kg intravenous or 200 mg subcutaneous) of belimumab. IQR, interquartile range; SD, standard deviation; SELENA, Safety of Estrogens in Lupus Erythematosus National Assessment.

	BASE*		BEL116559 integrated RCTs*	
	Placebo (N=2002)	Belimumab (N=2001)	Placebo (N=1355)	Belimumab (N=2815)†
Female, n (%)	1853 (92.6)	1848 (92.4)	1268 (93.6)	2661 (94.5)
Age (years), mean (SD)	40.8 (12.7)	40.4 (12.8)	37.8 (12.0)	37.5 (11.5)
Race, n (%)				
White	1090 (54.4)	1096 (54.8)	516 (38.1)	1100 (39.1)
Asian	492 (24.6)	483 (24.1)	418 (30.8)	836 (29.7)
Black African ancestry	155 (7.7)	175 (8.7)	269 (19.9)	568 (20.2)
American Indian or Alaskan native	257 (12.8)	228 (11.4)	149 (11.0)	307 (10.9)
Native Hawaiian or other Pacific Islander	2 (<0.1)	5 (0.2)	3 (0.2)	4 (0.1)
Multiracial	14 (0.7)	19 (0.9)	16 (1.2)	26 (0.9)
Missing	6 (0.3)	14 (0.7)	0	0
SLE duration (years), median (IQR)	5.3 (1.8–11.2)	5.1 (1.6–10.6)	4.7 (1.7–9.9)	4.7 (1.7–9.7)
SELENA-SLEDAI score				
Mean (SD)	7.9 (4.5)	7.8 (4.7)	10.0 (3.8)	9.9 (3.7)
≤9, n (%)	1369 (68.4)	1363 (68.1)	612 (45.2)	1315 (46.7)
≥10, n (%)	633 (31.6)	638 (31.9)	743 (54.8)	1500 (53.3)
SLICC/ACR Damage Index score				
Mean (SD)	0.6 (1.2)	0.6 (1.2)	0.6 (1.1)	0.6 (1.1)
0, n (%)	1373 (68.6)	1361 (68.0)	780 (57.6)	1598 (56.8)
≥1, n (%)	626 (31.3)	637 (31.8)	462 (34.1)	878 (31.2)
Missing, n (%)	3 (0.1)	3 (0.1)	113 (8.3)	339 (12.0)
Average daily prednisone-equivalent dose, mg/day				
Mean (SD)	9.7 (10.8)	10.2 (11.9)	12.0 (9.7)	11.4 (9.6)
0, n (%)	363 (18.1)	339 (16.9)	171 (12.6)	411 (14.6)
>0 and ≤7.5, n (%)	649 (32.4)	676 (33.8)	351 (25.9)	719 (25.5)
>7.5, n (%)	990 (49.5)	986 (49.3)	833 (61.5)	1685 (59.9)

Table 2. Incidence of infection and infestation SAEs, and infections of special interest through Week 52 for the BASE and BEL116559 integrated RCT datasets. *BASE and BEL116559 safety data are shown for the on-treatment population, patient numbers vary between baseline data and Week 52 follow-up data, since patients could withdraw from study agent during Year 1 and continue on study, or could withdraw from Year 1 study visits and reconsent to a Week 52 follow-up; †this cohort is limited to patients receiving marketed doses (10 mg/kg intravenous or 200 mg subcutaneous) of belimumab; ‡data for the 4 most common individual SAEs for the BASE and BEL116559 datasets are shown, calculated as the total incidence across both treatment arms; §only treatment-emergent SAEs for the on-treatment period are summarized from patients who received ≥1 dose of belimumab or placebo; ||all infections of special interest are limited to opportunistic infections, active tuberculosis, herpes zoster, and sepsis; ¶per sponsor adjudication.

	BASE*		BEL116559 integrated RCTs*	
	Placebo (N=2001)	Belimumab (N=2002)	Placebo (N=1355)	Belimumab (N=2031)†
Infection and infestation SAEs,‡ n (%)	82 (4.1)§	75 (3.7)§	80 (5.9)	96 (4.7)
Pneumonia	21 (1.0)	17 (0.8)	18 (1.3)	14 (0.7)
Herpes zoster	5 (0.2)	0	4 (0.3)	9 (0.4)
Urinary tract infection	8 (0.4)	16 (0.8)	8 (0.6)	5 (0.2)
Cellulitis	6 (0.3)	6 (0.3)	5 (0.4)	6 (0.3)
Infections of special interest,‖ n (%)	50 (2.5)	36 (1.8)	97 (7.2)	122 (6.0)
Serious infections of special interest	17 (0.8)	17 (0.8)	17 (1.3)	29 (1.4)
Opportunistic infections¶	15 (0.7)	11 (0.5)	92 (6.8)	112 (5.5)
Active tuberculosis	4 (0.2)	4 (0.2)	5 (0.4)	4 (0.2)
Herpes zoster	36 (1.8)	18 (0.9)	59 (4.4)	77 (3.8)
Sepsis	7 (0.3)	10 (0.5)	10 (0.7)	14 (0.7)

Conclusion: Over 52 weeks, serious infections and infections of special interest occurred at a similar or higher incidence with placebo versus belimumab in the Phase 4 BASE safety study and the BEL116559 pooled analysis of safety RCT data. These data further support the favorable safety profile of belimumab for SLE treatment.

Funding: This analysis of the GSK Studies 115467 and 116559 was funded by GSK.

References:

1 Yuan Q et al. Semin Arthritis Rheum 2020;50(5):1022–39
2 GSK. Benlysta US prescribing information. 2023
3 Sheikh SZ et al. Lancet Rheum 2020;3:e122–30
4 Furie R et al. Arthritis Rheumatol 2011;63(12):3918–30
5 Navarra SV et al. Lancet 2011;377(9767):721–31
6 Stohl W et al. Arthritis Rheumatol 2017;69(5):1016–27
7 Zhang F et al. Ann Rheum Dis 2018;77(3):355–63
8 Ginzler E et al. Arthritis Rheumatol 2021; doi: 10.1002/art.41900
9 Wallace DJ et al. Arthritis Rheum 2009;61(9):1168–78

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Abstract Number: 1501

Lupus Low Disease Activity State (LLDAS) Achievement with Deucravacitinib, an Oral, Selective, Allosteric Tyrosine Kinase 2 Inhibitor, in a Phase 2 Trial in SLE

Eric Morand[1], Coburn Hobar[2], Samantha Pomponi[3], Ravi Koti[4], Thomas Wegman[5] and Ronald van Vollenhoven[6], [1]Monash University, Centre for Inflammatory Diseases, Melbourne, Australia, [2]Bristol Myers Squibb, Bradenton, FL, [3]Bristol Myers Squibb, Princeton, NJ, [4]Syneos Health, Morrisville, NC, [5]Bristol Myers Squibb, Beaver Falls, PA, [6]Amsterdam University Medical Centers, Amsterdam, Netherlands

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: SLE – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Deucravacitinib is a first-in-class, oral, selective, allosteric tyrosine kinase 2 inhibitor approved in multiple countries for the treatment of adults with plaque psoriasis. A 48-week, double-blind, phase 2 trial (NCT03252587) in patients with SLE showed that deucravacitinib demonstrated efficacy across multiple endpoints compared with placebo, including the primary endpoint of Systemic Lupus Erythematosus Responder Index 4 (SRI[4]) at week 32 and the secondary endpoint of LLDAS at week 48.[1] Achievement and maintenance of LLDAS is associated with reduced risk of SLE-associated organ damage and mortality.[2] Here, we further investigate LLDAS outcomes with deucravacitinib through post hoc analyses assessing time to first LLDAS response and cumulative time in LLDAS.

Methods: Patients with active SLE (N=363) were randomized 1:1:1:1 to placebo or deucravacitinib 3 mg twice daily (BID), 6 mg BID, or 12 mg once daily (QD). Exploratory outcomes included median time to first LLDAS response and the percentage of patients who achieved LLDAS for ≥ 3 or ≥ 5 consecutive visits and the percentage of patients who achieved LLDAS for ≥ 20% or ≥ 50% of the time through week 48, via logistic regression. Odds ratios and nominal *P* values for each treatment group compared with the placebo group were provided.

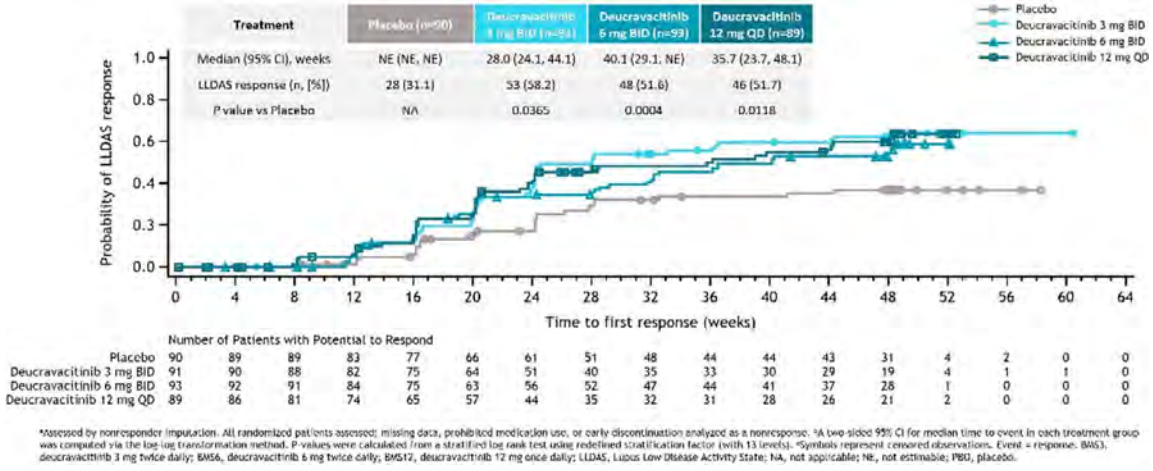
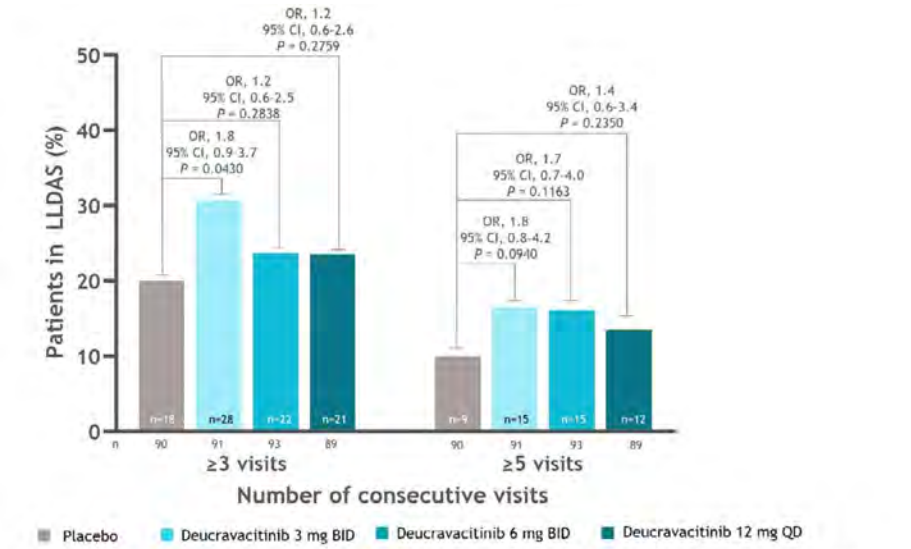
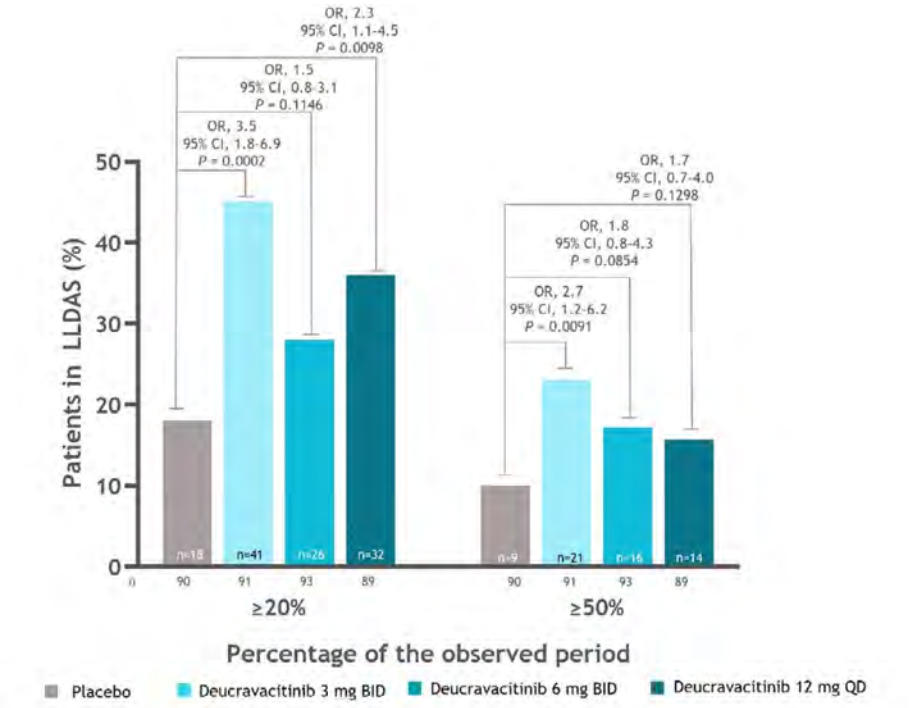


Figure 1. Time to first LLDAS response (a, b, c)



[a]Assessed by nonresponder imputation. All randomized patients assessed; missing data, prohibited medication use, or early discontinuation analyzed as a nonresponse. [b] Logistic regression with treatment group and redefined stratification factor as fixed factors; redefined stratification factor has 13 levels based on the combination of 3 factors: CS dose (≥10 mg QD or <10 mg QD), SLEDAI-2K score (≥10 or <10), and Region (North America, Latin America, Japan, and rest of world). CS dose and SLEDAI-2K score are not applied for stratification in Japan, therefore Japan is considered a separate stratum. In case the logistic regression model fit is not stable, the region stratification factor may be removed from the model (resulting in 5 stratification factors). One sided p-value was used for comparison vs placebo.
BID, twice daily; LLDAS, Lupus Low Disease Activity State; NA, not applicable; OR, odds ratio; QD, once daily.

Figure 2. Percentages of patients attaining LLDAS for ≥ 3 or ≥ 5 consecutive visits (a, b)



[a]Assessed by nonresponder imputation. All randomized patients assessed; missing data, prohibited medication use, or early discontinuation analyzed as a nonresponse. [b] Logistic regression with treatment group and redefined stratification factor as fixed factors; redefined stratification factor has 13 levels based on the combination of 3 factors: CS dose (≥10 mg QD or <10 mg QD), SLEDAI-2K score (≥10 or <10), and Region (North America, Latin America, Japan, and rest of world). CS dose and SLEDAI-2K score are not applied for stratification in Japan, therefore Japan is considered a separate stratum. In case the logistic regression model fit is not stable, the region stratification factor may be removed from the model (resulting in 5 stratification factors). One sided p-value was used for comparison vs placebo.
BID, twice daily; LLDAS, Lupus Low Disease Activity State; NA, not applicable; OR, odds ratio; QD, once daily.

Figure 3. Percentages of patients attaining LLDAS for ≥ 20% or ≥ 50% of observed time (a, b)

Results: Median time to first LLDAS response was significantly shorter in all deucravacitinib groups compared with the placebo group (3 mg BID, 28.0 weeks: P = 0.0365 vs placebo; 6 mg BID, 40.1 weeks: P = 0.0004 vs placebo; 12 mg QD, 35.7 weeks: P = 0.0118 vs placebo). Median time to first LLDAS response was not estimable in the placebo group because 50% of the patients had not yet achieved an LLDAS response **(Figure 1)**. The deucravacitinib 3 mg BID group had a significantly higher percentage of patients who achieved LLDAS for ≥ 3 visits compared with the placebo group (OR, 1.8; 95% CI, 0.9–3.7, P = 0.0430). A higher percentage of patients treated with any dose of deucravacitinib attained LLDAS for ≥ 3 or ≥ 5 visits compared with patients receiving placebo **(Figure 2)**. A higher percentage of patients treated with deucravacitinib attained LLDAS for ≥ 20% and ≥ 50% of cumulative observed time compared with patients receiving placebo **(Figure 3)**. The deucravacitinib 3 mg BID and 12 mg QD groups had significantly higher percentages of patients who achieved LLDAS for ≥ 20% of cumulative time compared with placebo (3 mg BID: OR, 3.5; 95% CI, 1.8–6.9; P = 0.0002; 12 mg QD: OR, 2.3; 95% CI, 1.1–4.5; P = 0.0098), and the 3 mg BID group also had a significantly higher percentage of patients who achieved LLDAS for ≥ 50% of cumulative time (3 mg BID: OR, 2.7; 95% CI, 1.2–6.2; P = 0.0091).

Conclusion: Patients treated with deucravacitinib achieved LLDAS response earlier and demonstrated more sustained and cumulative LLDAS responses compared with patients receiving placebo. Taken together, these data suggest that deucravacitinib may contribute to better long-term prospects for patients with SLE.

Reference:

1. Morand E, et al. *Arthritis Rheumatol* 2023;75:242–252.
2. Petri M, Magder LS. *Arthritis Rheumatol* 2018; 70(11); 1790–1795.

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Abstract Number: 1502

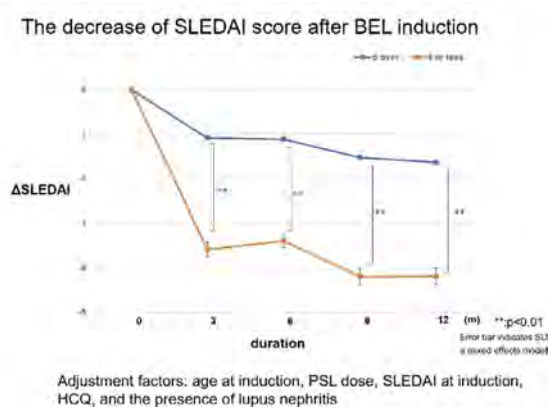
Introduction of Belimumab Within Five Years of the Onset of Systemic Lupus Erythematosus (SLE) Contributes to the Better Therapeutic Response; A Multi-center Retrospective Cohort Study

Kanako Kojima[1], Kunihiro Ichinose[1], Toshimasa Shimizu[1], Masataka Umeda[1], Takahisa Suzuki[2], Yoshikazu Nakashima[3], Akitomo Okada[4], Yoshiro Horai[5], Keita Fujikawa[6], Toshiyuki Aramaki[7], Taiichiro Miyashita[8], Masako Furuyama[3], Naoki Matsuoka[9] and Atsushi Kawakami[10], [1]Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, [2]Japanese Red Cross Nagasaki Genbaku Hospital, Nagasaki, Japan, [3]Nagasaki Kita Hospital, Nagasaki, Japan, [4]National Hospital Organization Nagasaki Medical Center, Omura, Japan, [5]Sasebo City General Hospital, Sasebo, Japan, [6]Japan Community Healthcare Organization, Isahaya General Hospital, Isahaya, Japan, [7]Sasebo Chuo Hospital, Sasebo, Japan, [8]Miyashita Rheumatology Clinic, Omura, Japan, [9]Nagasaki Medical Hospital of Rheumatology, Nagasaki, Japan, [10]Nagasaki University, Nagasaki, Japan

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Figure 1.



The decrease of SLEDAI score after BEL induction

Background/Purpose: Belimumab (BEL), B cell-targeted biologic agent for systemic lupus erythematosus (SLE), is cumulating evidence such as reducing glucocorticoids and preventing the progressionof organ damage. The BLISS-LN study evaluated the effect of BEL on lupus nephritis (LN) and found that BEL administered early in the course of LN improved proteinuria. There is ongoing debate regarding the optimal timing of administering BEL in the treatment of SLE in real-world settings. BAFF receptor expression decreases along with B cell differentiation, and the number of memory B cells is higher in SLE patients with longer disease duration. In addition, the shorter disease duration correlated with the higher blood BAFF concentration in SLE patients. Based on these reports, we hypothesized that BEL, which targeted BAFF, would be more effective in patients with shorter disease duration. In this study, we investigated whether the duration of SLE at the time of BEL introduction contributes to its treatment responsiveness.

Methods: Ninety-eight patients diagnosed with SLE according to the 1997 ACR Diagnostic Revision Criteria or 2012 SLICC Classification Criteria at Nagasaki University Hospital and its affiliated hospitals in Nagasaki Prefecture and who started BEL between December 2017 and August 2021 were included in the analysis. The primary objective of the study is to compare the decrease in SLEDAI scores after the introduction of BEL at different time points (3, 6, 9, and 12 months) between two groups categorized based on disease duration at BEL introduction (≤5 years and >5 years). The analysis will be adjusted using a mixed-effects model. Adjustment factors include age at induction, prednisolone (PSL) dose, SLEDAI at induction and hydroxychloroquine (HCQ), and the presence of lupus nephritis.

Results: In the overall patient population, the mean age at BEL introduction was 41 years, the mean SLEDAI score was 7, the mean dose of PSL was 9 mg/day, and HCQ was used in 50 patients (51%). The number of ≤5 years group was 20 patients and the number of >5 years was 78 patients. Both groups (≤5 years and >5 years) showed improvement in SLEDAI scores 3 months after the BEL introduction. In addition, the group receiving BEL at 5 years or less showed significantly greater improvement in SLEDAI than the group receiving BEL at more than 5 years at each evaluation time point after BEL introduction.

Conclusion: Our investigating headlights and earlier introduction of BEL in SLE patients may contribute to a more remarkable improvement in disease activity. This finding could potentially impact the clinical decision-making process regarding the implementation of a treat-to-target strategy for patients with SLE.

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Abstract Number: 1503

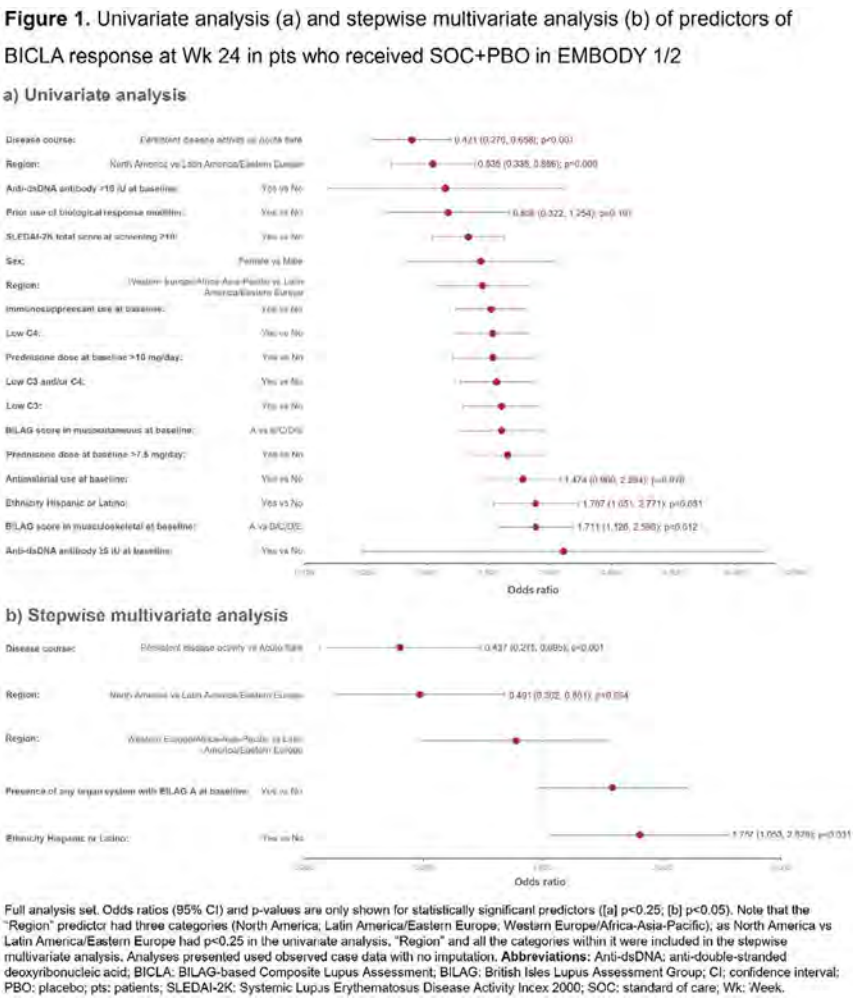
Disease Course and Complement as Predictors of Response to Standard of Care Plus Placebo in Patients with SLE: A Post Hoc Analysis of Dapirolizumab Pegol and Epratuzumab Clinical Trial Data

Christian Stach[1], Caroline Gordon[2], Vanessa Taieb[3], George Stojan[4] and **Joan Merrill**[5], [1]UCB Pharma, Monheim am Rheim, Germany, [2]Institute of Inflammation and Ageing, University of Birmingham, Birmingham, United Kingdom, [3]UCB Pharma, Colombes, France, [4]UCB, Baltimore, MD, [5]Oklahoma Medical Research Foundation, Oklahoma City, OK

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

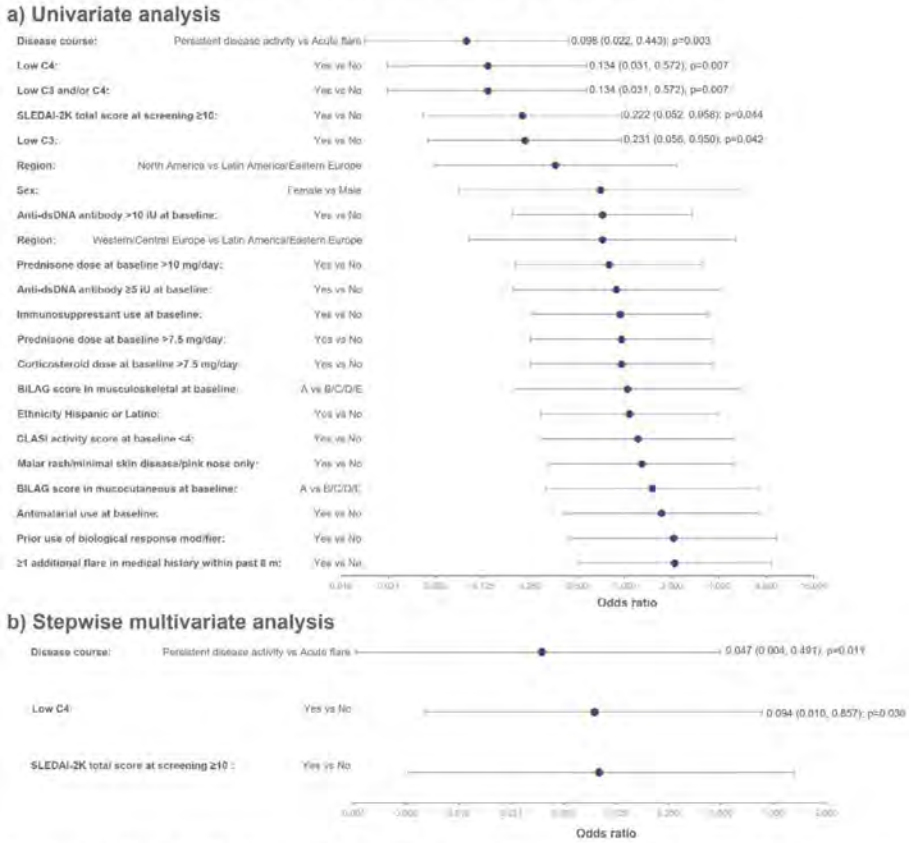
Background/Purpose: High placebo responses pose challenges to systemic lupus erythematosus (SLE) clinical trials.[1]This analysis aims to identify predictors of standard of care plus placebo (SOC+PBO) response using data from epratuzumab (Emab; a humanized anti-CD22 monoclonal antibody) and dapirolizumab pegol (DZP; a polyethylene glycol-conjugated antigen-binding fragment lacking a functional Fc domain that inhibits CD40L) trials.[2,3]

Figure 1. Univariate analysis (a) and stepwise multivariate analysis (b) of predictors of BICLA response at Wk 24 in pts who received SOC+PBO in EMBODY 1/2



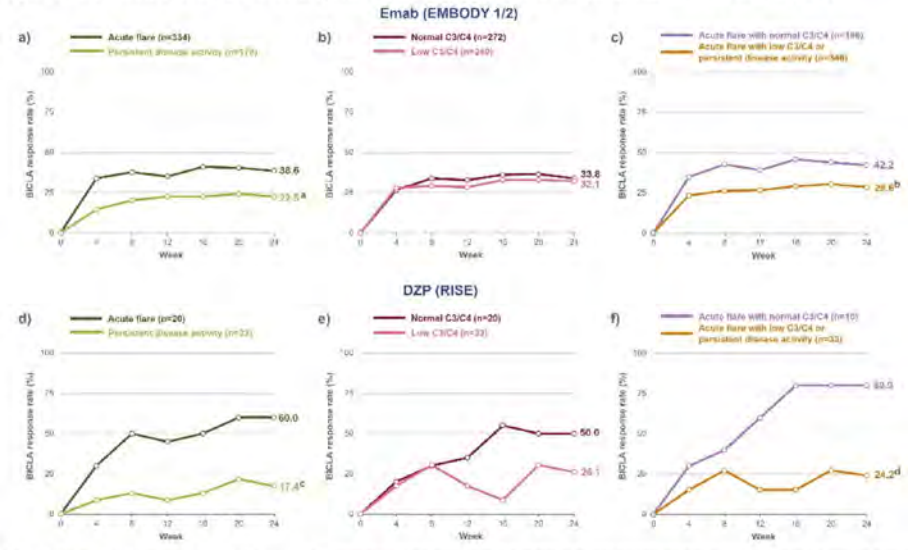
Full analysis set. Odds ratios (95% CI) and p-values are only shown for statistically significant predictors ([a] p<0.25; [b] p<0.05). Note that the "Region" predictor had three categories (North America; Latin America/Eastern Europe; Western Europe/Africa-Asia-Pacific), as North America vs Latin America/Eastern Europe had p<0.25 in the univariate analysis. "Region" and all the categories within it were included in the stepwise multivariate analysis. Analyses presented used observed case data with no imputation. **Abbreviations:** Anti-dsDNA: anti-double-stranded deoxyribonucleic acid; BICLA: BILAG-based Composite Lupus Assessment; BILAG: British Isles Lupus Assessment Group; CI: confidence interval; PBO: placebo; pts: patients; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000; SOC: standard of care; Wk: Week.

Figure 2. Univariate analysis (a) and stepwise multivariate analysis (b) of predictors of BICLA response at Wk 24 in pts who received SOC+PBO in RISE



Full analysis set. Odds ratios (95% CI) and p-values are only shown for statistically significant predictors ([a] p<0.25; [b] p<0.05). Analyses presented used observed case data with no imputation. **Abbreviations:** Anti-dsDNA: anti-double-stranded deoxyribonucleic acid; BICLA: BILAG-based Composite Lupus Assessment; BILAG: British Isles Lupus Assessment Group; CI: confidence interval; CLASI: Cutaneous Lupus Erythematosus Disease Area and Severity Index; m: months; PBO: placebo; pts: patients; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000; SOC: standard of care; Wk: Week.

Figure 3. BICLA response to Wk 24 by subgroups of pts receiving SOC+PBO in (a–c) EMBODY 1/2, and (d–f) RISE



Full analysis set. [a]p=0.0002 for the odds ratio (95% CI) of persistent disease activity vs acute flare (0.5 [0.3, 0.7]). [b]p=0.0023 for the odds ratio (95% CI) of acute flare with low C3/C4 or persistent disease activity vs acute flare with normal C3/C4 (1.8 [1.2, 2.7]). [c]p=0.0064 for the odds ratio (95% CI) of persistent disease activity vs acute flare (0.1 [0.0, 0.6]). [d]p=0.0050 for the odds ratio (95% CI) of acute flare with low C3/C4 or persistent disease activity vs acute flare with normal C3/C4 (0.1 [0.0, 0.5]). Only significant p values at Wk 24 are presented. Missing data were imputed using modified non-responder imputation. Low C3/C4 was defined as below the lower limit of normal (C3: <0.9 g/L; C4: <180 mg/L). **Abbreviations:** BICLA: British Isles Lupus Assessment Group-based Composite Lupus Assessment; CI: confidence interval; DZP: dapirolizumab pegol; Emab: opratuzumab; PBO: placebo; pts: patients; SOC: standard of care; Wk: Week.

Methods: Analyses were performed on the full analysis sets of the SOC+PBO arms of two phase 3 trials of Emab (EMBODY 1 [NCT01262365]; n=249, and EMBODY 2 [NCT01261793]; n=263) and the phase 2b trial of DZP (RISE [NCT02804763]; n=43) in SLE.[2,3] Response was assessed by British Isles Lupus Assessment Group (BILAG)-based Composite Lupus Assessment (BICLA) response at Week (Wk) 24.[4] Univariate/multivariate analyses were performed, with 18 and 22 potential predictors of SOC+PBO response evaluated in EMBODY 1/2 and RISE, respectively. Stepwise multivariate analysis included univariate predictors with $p< 0.25$, using $p\leq 0.1$ as entry/stay criteria. In subgroup analyses, disease course at screening was defined using BILAG 2004 item level scores as acute flare (worsening/new symptoms) or persistent disease (symptoms rated as the same) based on the past 4 wks compared with the 4 wks prior to those; low C3/C4 was defined as below the lower limit of normal at screening.

Results: Univariate and subsequent stepwise multivariate analysis found the following significant ($p < 0.05$) predictors of BICLA response at Wk 24 in EMBODY 1/2: acute flare (vs persistent disease activity; $p< 0.001$), Latin America/Eastern European (vs North America; p=0.004), and Hispanic or Latino (vs not; p=0.031; **Figure 1**). Significant ($p < 0.05$) predictors of BICLA response at Wk 24 in RISE following stepwise multivariate analysis were: acute flare (vs persistent disease activity; p=0.011) and normal C4 (vs low C4; p=0.036; **Figure 2**).

Focusing on disease characteristics, recent acute flares and normal complement were identified as predictors of SOC+PBO response. In all trials, a significantly higher proportion of patients (pts) with acute flare (vs persistent disease activity) achieved BICLA response (**Figure 3a& 3d**). In RISE, a significantly higher proportion of pts with normal C3/C4 (vs low C3/C4) achieved BICLA response (**Figure 3e**); this pattern was not observed in EMBODY 1/2 (**Figure 3b**). In all trials, when the subgroups were combined, a significantly higher proportion of pts with acute flare and normal C3/C4 (vs acute flare with low C3/C4 or persistent disease activity) achieved BICLA response (**Figure 3c & 3f**).

Conclusion: In both EMBODY 1/2 and RISE, acute flare predicted SOC+PBO response. In RISE, normal complement levels also predicted SOC+PBO response; low complement has been described as a predictor of increased treatment effect in previous studies.[5] Recent medical history of pts may have to be considered when defining SLE study populations.

References: 1. Durcan L. Lancet. 2023;S0140-6736(23)00342-2.**2.** Clowse ME. Arthritis Rheumatol. 2017;69(2):362–75. **3.** Furie RA. Rheumatology (Oxford). 2021;60:5397–407. **4.** Wallace D. Arthritis Rheum. 2011;63(Suppl 10):S885. **5.** van Vollenhoven RF. Ann Rheum Dis. 2012;71(8):1343–9.

Disclosure: C. Stach: UCB Pharma, 3, 11; **C. Gordon**: AbbVie, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, Sanofi, 2, UCB Pharma, 2; **V. Taieb**: UCB Pharma, 3, 11; **G. Stojan**: UCB Pharma, 3, 11; **J. Merrill**: AbbVie, 2, Alexion, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, Bristol Myers Squibb, 2, 5, EMD Serono, 2, Genentech, 2, Gilead, 2, GlaxoSmithKline, 2, 5, Lilly, 2, Merck, 2, Pfizer, 2, Provention, 2, Remegen, 2, Sanofi, 2, UCB Pharma, 2, Zenas, 2.

Abstract Number: 1504

Characteristics and Prior Treatment Journey of Systemic Lupus Erythematosus (SLE) Patients Who Were Prescribed Anifrolumab -- Observations from the American Rheumatology Network (ARN) in the U.S

Vasileios Kyttaris[1], Gelareh Atefi[2], Daniel Persons[3], Christopher S. Ambrose[4], Scott Milligan[5] and Sandra Wu[6], [1]BIDMC, Boston, MA, [2]BioPharmaceuticals Medical, AstraZeneca, Wilmington, DE, [3]Trio Health, Denver, CO, [4]AstraZeneca, Wilmington, DE, [5]Trio Health, Analytics, Louisville, CO, [6]AstraZeneca, Hockessin, DE

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: FDA-approved for moderate-severe SLE in August 2021, anifrolumab is a type I interferon (IFN) receptor antagonist that has been shown to decrease lupus flares and reduce corticosteroid use. Here we provide real world data describing its use in daily rheumatology practice, focusing on the clinical/laboratory characteristics and previous treatments of SLE patients who were prescribed anifrolumab for the first time.

TABLE 1: Study Population demographics and select baseline measures

CHARACTERISTIC	STUDY POPULATION (N=203)
AGE GROUP - NO. (%) PATIENTS	
19-34	30 (15%)
35-44	47 (23%)
45-54	43 (21%)
55-64	43 (21%)
65-74	32 (16%)
75+	8 (4%)
GENDER - NO. (%) PATIENTS	
F	189 (93%)
M	14 (7%)
PAYER - NO. (%) PATIENTS	
COMMERCIAL	103 (51%)
MEDICAID	12 (6%)
MEDICARE	56 (28%)
OTHER	28 (14%)
UNKNOWN	4 (2%)
RACE - NO. (%) PATIENTS	
BLACK	50 (25%)
OTHER	55 (27%)
WHITE	98 (48%)
US RESIDENCE - NO. (%) PATIENTS	
CENTRAL	2 (1%)
SOUTH	151 (74%)
WEST	50 (25%)
BASELINE MEASURES – MEAN [SD]	
SLEDAI	10.7 [5.9] (N=56)
PAIN SCORE (0-10)	5.4 [2.9] (N=125)
SWOLLEN JOINTS (0-28)	2.8 [4.8] (N=105)
TENDER JOINTS (0-28)	6.6 [7.0] (N=105)
BASELINE MEASURES - %	
POSITIVE ANTI-DS DNA	24 (27%)
LOW COMPLEMENT C3	13 (10%)
LOW COMPLEMENT C4	8 (7%)
BMI (CALCULATED) (N=198)	
OBESE (≥30)	95 (48%)
OVERWEIGHT (25-29.9)	52 (26%)
HEALTHY (18.5-24.9)	47 (24%)
UNDERWEIGHT (<18.5)	4 (2%)
SLE MANIFESTATIONS AND COMPLICATIONS	
AGE-RELATED OSTEOPOROSIS	28 (14%)
INFLAMMATORY POLYARTHROPATHY	32 (16%)
LUPUS NEPHRITIS	11 (5%)
OBESITY	78 (38%)
FATIGUE	41 (20%)
RASH	47 (23%)
RAYNAUD'S SYNDROME	21 (10%)
RENAL FAILURE	6 (3%)
SJOGREN'S SYNDROME	18 (9%)

TABLE 2: Treatment patterns and regimens prior to anifrolumab prescription

*LIMITED TO REGIMENS WITH ≥1% SHARE OF STUDY POPULATION

DRUG CLASSES RECEIVED AT ANY TIME PRIOR TO INDEX*	STUDY POPULATION (N=203)
ONLY ANTIMALARIALS	32 (16%)
ONLY BIOLOGICS	6 (3%)
ONLY IMMUNOSUPPRESSANTS	5 (2%)
ANTIMALARIALS, BIOLOGICS	39 (19%)
ANTIMALARIALS, IMMUNOSUPPRESSANTS	18 (9%)
BIOLOGICS, IMMUNOSUPPRESSANTS	11 (5%)
ANTIMALARIALS, BIOLOGICS, IMMUNOSUPPRESSANTS	87 (43%)
NO OBSERVED PRIOR ANTIMALARIALS, BIOLOGICS, IMMUNOSUPPRESSANTS	5 (2%)
DRUGS RECEIVED AT ANY TIME PRIOR TO INDEX*	**STUDY POPULATION (N=203)**
HYDROXYCHLOROQUINE	176 (87%)
ORAL CORTICOSTEROIDS	163 (80%)
BELIMUMAB	111 (55%)
MYCOPHENOLATE	75 (37%)
METHOTREXATE	71 (35%)
AZATHIOPRINE	59 (29%)
LEFLUNOMIDE	26 (13%)
RITUXIMAB	20 (10%)
ABATACEPT	9 (4%)
TACROLIMUS	9 (4%)
CYCLOSPORINE	6 (3%)
REGIMENS RECEIVED IMMEDIATELY PRIOR TO INDEX *	**STUDY POPULATION (N=203)**
ANTIMALARIAL-CONTAINING	154 (76%)
IMMUNOSUPPRESSANT-CONTAINING	105 (52%)
BIOLOGIC-CONTAINING	67 (33%)
BELIMUMAB-CONTAINING	62 (31%)
HYDROXYCHLOROQUINE	55 (27%)
BELIMUMAB + HYDROXYCHLOROQUINE	20 (10%)
HYDROXYCHLOROQUINE + MYCOPHENOLATE	16 (8%)
AZATHIOPRINE + HYDROXYCHLOROQUINE	15 (7%)
HYDROXYCHLOROQUINE + METHOTREXATE	15 (7%)
BELIMUMAB	10 (5%)
BELIMUMAB + HYDROXYCHLOROQUINE + MYCOPHENOLATE	7 (3%)
BELIMUMAB + HYDROXYCHLOROQUINE + METHOTREXATE	6 (3%)
MYCOPHENOLATE	6 (3%)
BELIMUMAB + MYCOPHENOLATE	5 (2%)
AZATHIOPRINE	4 (2%)
AZATHIOPRINE + BELIMUMAB + HYDROXYCHLOROQUINE	4 (2%)
BELIMUMAB + METHOTREXATE	4 (2%)
METHOTREXATE	3 (1%)
HYDROXYCHLOROQUINE + METHOTREXATE + MYCOPHENOLATE	2 (1%)
LEFLUNOMIDE	2 (1%)
DRUGS DISCONTINUED IN 90 DAYS PRIOR TO INDEX WITH DOCUMENTED DISCONTINUATION REASONS	**STUDY POPULATION (N=73)**
BELIMUMAB	57 (78%)
METHOTREXATE	6 (8%)
MYCOPHENOLATE	3 (4%)
AZATHIOPRINE	2 (3%)
HYDROXYCHLOROQUINE	2 (3%)
RITUXIMAB	2 (3%)
ABATACEPT	1 (1%)

Methods: Data were collected from patients under the care of ARN providers using PIONEER Rheumatology, an enhanced database combining fielded EMR data with extracted information from open text (office visits, infusion logs, and provider-patient communications). The study population consisted of adult (18+ years old) patients with documented diagnosis of SLE at least twice who were prescribed anifrolumab between August 1, 2021, to March 30, 2023. The index date for each patient was defined as the initial prescription date and baseline measures were those occurring within 365 days prior to the index date. Reasons for prior therapy discontinuation were extracted from office visit notes by clinically-trained scribes and categorized as lack/loss of efficacy, clinical reasons, or non-clinical reasons.

Results: 203 patients met study criteria [TABLE 1]; they were predominantly female (93%), commercially insured (51%), and in the Southern region of the U.S. (74%). At baseline, mean±SD SLEDAI was 10.7±5.9. Treatment history prior to anifrolumab prescription included oral corticosteroids (80%), hydroxychloroquine (87%), belimumab (55%), mycophenolate (37%), and methotrexate (35%). Patients' treatment regimen immediately prior to anifrolumab included belimumab (31%), antimalarials (76%), and immunosuppressants (52%) [TABLE 2]. 30% of patients who initiated anifrolumab were biologic-naïve. In 69/203 patients, anifrolumab substituted another medication in the treatment regimen, most notably belimumab. Therefore, we analyzed reasons behind discontinuation of belimumab prior to anifrolumab. Among the 57 patients who discontinued belimumab within 90 days of anifrolumab prescription, 49 (86%) indicated lack or loss of efficacy, 33 (58%) indicated a clinical reason, and 4 (7%) indicated a non-clinical reason [TABLE 3]. The top reasons for discontinuation from belimumab among the 57 patients included joint pain (47%), rash/pruritus/urticaria (46%), and fatigue (26%).

TABLE 3: Reasons* for discontinuation of the last regimen that a) contained belimumab and b) was stopped within 90d of anifrolumab prescription (n=57)

CATEGORY	%	SUBCATEGORY LEVEL 1	%	SUBCATEGORY LEVEL 2	%
LACK OF EFFICACY	86%	GENERAL	49%	CONTINUED DISEASE ACTIVITY (PHYSICIAN)	11 (19%)
				FATIGUE	15 (26%)
				FLARES	8 (14%)
				GENERAL OTHER	3 (5%)
				MALAISE	1 (2%)
		INFLAMMATION/SWELLING	19%	BACK INFLAMMATION	1 (2%)
				GENERAL BODY STIFFNESS	3 (5%)
				INFLAMMATION/SWELLING OTHER	1 (2%)
				JOINT INFLAMMATION	6 (11%)
				JOINT STIFFNESS	4 (7%)
				LEG INFLAMMATION	1 (2%)
				TIME STIFFNESS	2 (4%)
		LAB RESULT CHANGE	2%	INFLAMMATORY MARKERS/CRP	1 (2%)
		PAIN	54%	CHEST PAIN/TIGHTNESS	3 (5%)
				FOOT PAIN	4 (7%)
				JOINT PAIN	27 (47%)
				LEG PAIN	2 (4%)
				MUSCLE PAIN	1 (2%)
				PAIN OTHER	4 (7%)
		PATIENT REASONS	16%	CONTINUED DISEASE ACTIVITY (PATIENT)	9 (16%)
		SKIN/DERMATOLOGIC	49%	HAIR LOSS/ALOPECIA/HAIR THINNING	4 (7%)
				LESIONS/NODULES/PLAQUES	4 (7%)
				RASH/PRURITUS/URTICARIA	26 (46%)
CLINICAL REASON	58%	COMORBIDITY	2%	COMORBIDITY	1 (2%)
		OPHTHALMIC	5%	EYE INFLAMMATION	1 (2%)
				PHOTOSENSITIVITY/SENSITIVITY TO LIGHT	2 (4%)
		FLU/COLD SYMPTOMS	4%	FLU-LIKE SYMPTOMS	2 (4%)
		GENERAL	11%	GENERAL OTHER	3 (5%)
				MALAISE	2 (4%)
				SLEEPING DIFFICULTIES	1 (2%)
				WEAKNESS	1 (2%)
		HEART/CARDIAC	2%	PALPITATIONS	1 (2%)
		INFECTION	7%	GENERAL INFECTION	1 (2%)
				INFECTION OTHER	2 (4%)
				UTI	1 (2%)
		LAB RESULT CHANGE	12%	LAB RESULT CHANGE	4 (7%)
				LAB RESULT CHANGE OTHER	4 (7%)
		NEUROLOGIC	11%	BURNING SENSATION	1 (2%)
				COGNITIVE CHANGES/ISSUES	3 (5%)
				NEUROPATHY	1 (2%)
				VERTIGO	2 (4%)
		OTHER	2%	OTHER PHYSICAL/MEDICAL	1 (2%)
		PAIN	14%	BACK PAIN	3 (5%)
				DIFFUSE PAIN	2 (4%)
				HEADACHES	4 (7%)
				PAIN OTHER	1 (2%)
		PATIENT REASONS	2%	PATIENT CONCERNED ABOUT SIDE EFFECTS	1 (2%)
		PSYCHIATRIC/MOOD DISORDERS	4%	ANXIETY	1 (2%)
				DEPRESSION	1 (2%)
				PSYCHIATRIC/MOOD DISORDERS OTHER	2 (4%)
		REACTIONS	7%	ALLERGIC REACTION/ADR	3 (5%)
				REACTIONS OTHER	1 (2%)
		SKIN/DERMATOLOGIC	16%	BRUISING	1 (2%)
				SKIN/DERMATOLOGIC OTHER	5 (9%)
				SORES/ULCERS	4 (7%)
NON-CLINICAL REASON	7%	PATIENT REASONS	2%	PATIENT REASONS OTHER	1 (2%)
		PAYER PAYMENT ISSUES	2%	PAYER PAYMENT ISSUES	1 (2%)
		HOSPITALIZATION/ INJURY/ SURGERY	2%	HOSPITALIZATION/INJURY/SURGERY	1 (2%)
		OTHER	2%	OTHER EVENT	1 (2%)

*Patients may have more than 1 reason for discontinuation.

Conclusion: This is one of the first studies to characterize real-world utilization of anifrolumab in management of SLE patients in the US. The majority of patients receiving anifrolumab within ARN were DMARD-experienced. Lack or loss of efficacy of belimumab, most frequently associated with joint pain, skin rashes, or fatigue, was a common reason for switching to anifrolumab. These findings highlight a need to understand which patients will benefit from anifrolumab as an early-line biologic therapy.

Disclosure: V. Kyttaris: AbbVie/Abbott, 5, AstraZeneca, 2, Aurinia, 1, EMD Serono, 5, Exagen, 2, 5, Fresenius Kabi, 1, Horizon Pharmaceuticals, 1, Novartis, 5, Scipher, 1, Takeda, 5, Vertex, 2; **G. Atefi**: AstraZeneca, 3; **D. Persons**: AbbVie/Abbott, 5, Amgen, 5, AstraZeneca, 5, Gilead, 5, GlaxoSmithKlein(GSK), 5, Janssen, 5, Merck/MSD, 5, Scipher, 5, Trio Health Analytics, 3, UCB, 5; **C. Ambrose**: AstraZeneca, 3; **S. Milligan**: AbbVie, 5, Actelion Pharmaceuticals, 5, AstraZeneca, 5, Gilead Sciences, 5, GSK, 5, Horizon Pharma, 5, Johnson & Johnson, 5, Merck, 5, Pharming Healthcare, 5, Sanofi, 5, Takeda, 5, Trio Health Analytics, 3, UCB Biosciences, 5, ViiV Healthcare, 5; **S. Wu**: AstraZeneca, 3.

Abstract Number: 1505

Long-term Safety and Efficacy of Voclosporin in Black Patients with Lupus Nephritis: Results from the AURORA 1 and AURORA 2 Studies

Gabriel Contreras[1], Matt Baker[2], Lucy Hodge[2] and Ernie Yap[2], [1]University of Miami Health System, Miami, FL, [2]Aurinia Pharmaceuticals Inc., Edmonton, AB, Canada

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Black patients with lupus nephritis (LN) are reported to have more severe disease, are often refractory to treatment, and have worse long-term outcomes. Voclosporin in conjunction with low-dose glucocorticoids and mycophenolate mofetil (MMF) has shown significant benefit across ancestries and classes of LN. Here we report outcomes from up to three years of follow-up in patients identifying as Black and treated with voclosporin during the global Phase 3 AURORA studies.

Methods: Key inclusion criteria for the parent AURORA 1 study included biopsy-proven LN, urine protein creatinine ratio (UPCR) ≥1.5 g/g (≥2 g/g for Class V) and estimated glomerular filtration rate (eGFR) >45 mL/min/1.73 m^2. Patients completing AURORA 1 were eligible to enter the AURORA 2 continuation study on the same blinded therapy of voclosporin or placebo in combination with MMF and glucocorticoids for an additional two years. Programmed complete renal response (CRR; UPCR ≤0.5 g/g, stable eGFR, low-dose steroids, and no rescue medication), partial renal response (PRR; reduction in UPCR of ≥50% from baseline) and safety were assessed in patients self-identifying as Black or mixed Black.

Results: Twenty-six of 179 (14.5%) and 19 of 178 (10.6%) patients identified as Black or mixed Black in the voclosporin and control arms of AURORA 1. Baseline characteristics were similar between arms. Complete renal response rates at one year numerically favored voclosporin (46.2% vs 15.8%, Odds Ratio [OR] 3.92 [CI 0.95, >9.99] p=0.0597) as did PRR rates (69.2% vs 47.4%, OR 2.62 [CI 0.72, 9.45] p=0.1422).

Eighteen voclosporin-treated patients and seven control-treated patients in the Black subgroup continued into AURORA 2. Response rates at three years continued to numerically favor voclosporin (CRR, 44.4% vs. 14.3%, OR 4.17 [CI 0.41, >9.99] p=0.2276; PRR, 66.7% vs. 42.9%; OR 1.67 [CI 0.23, >9.99] p=0.6094). Greater reductions in mean UPCR were observed over the three-year period in the voclosporin arm (change from baseline -3.4 vs -1.5 g/g, p=0.0349). Mean eGFR levels remained stable and in the normal range over three years of treatment.

Conclusion: Black patients treated with a voclosporin-based regimen achieved higher rates of renal response than patients treated with MMF and glucocorticoids alone. For patients entering the continuation study, the response was largely durable for up to 3 years.

Disclosure: G. Contreras: None; **M. Baker**: Aurinia, 3; **L. Hodge**: Aurinia, 3, 11; **E. Yap**: Aurinia Pharmaceuticals, 3, 11.

Abstract Number: 1506

Prescribing Patterns in Lupus Nephritis: Analyzing Time from Proteinuria to Prescription of ACE/ARB

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Black patients with lupus nephritis have worse renal outcomes compared with their White counterparts. Currently, there is a paucity of data evaluating the use of angiotensin-converting enzyme inhibitors (ACE) and angiotensin receptor blockers (ARB) in lupus patients with proteinuria despite their well-established benefits. The objective of this study was to examine the prescribing patterns of ACE/ARB in lupus patients with laboratory evidence of proteinuria, focusing on demographic factors such as race/ethnicity, gender and age.

Methods: The study population comprised patients seen in an urban academic medical center from January 1, 2000 through September 12, 2020 with at least one ambulatory encounter and a diagnosis code associated with either lupus or lupus nephritis. Proteinuria was defined according to the American College of Rheumatology (ACR) definition of renal disease, which includes a urine protein 3+ or above (300 mg/dL or greater), a urine protein creatinine ratio > 0.5, a 24-hour urine protein excretion greater than 0.5g, or a urine microalbumin/creatinine ratio greater than 50. The time interval from the first laboratory result indicating proteinuria in patients naive to an ACE/ARB to the day of ACE/ARB prescription was measured in days.

Results: Data show 39% of lupus patients with laboratory evidence of proteinuria were prescribed an ACE/ARB during the study time frame. For those who received a prescription, the median time from the detection of proteinuria to the prescription of an ACE/ARB was 382 days. Non-White patients (Black, Hispanic, and Other) were more frequently prescribed an ACE or

Table 1. Cohort and Treatment Cohort Demographics

	Cohort Demographics (N=682)		Demographics of Proportion Given ACE/ARB (N=264)	
	No. of Patients	Percentage of Patients	Patients Given ACE/ARB	Percent Given ACE/ARB
Sex				
Female	427	62.6%	177	41.5%
Male	255	37.4%	87	34.1%*
Age				
18-40	269	44.0%	108	40.1%
40-65	343	56.0%	136	39.7%
>65	70	11.4%	20	28.6%**
Race				
Hispanic	197	28.9%	73	37.1%
Black	356	52.2%	156	43.8%
White	78	11.4%	18	23.1%***
Other	51	7.5%	17	33.3%
*p=0.06, **p=0.07, ***p=0.003				

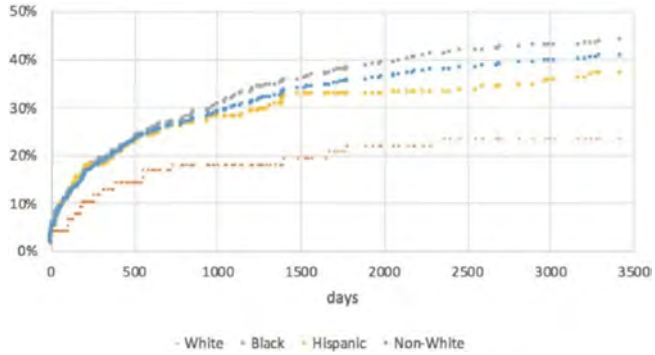


Figure 1. Percentage of Patients with Proteinuria Prescribed an ACE/ARB Over Time in Days

an ARB compared with White patients (p=0.005). There was also a trend indicating higher prescription rates for female patients compared with male patients (p=0.06). There was a non-statistically significant reduction in prescription of ACE/ARB in patients greater than 65 years old.

Conclusion: Our study reveals a pattern of incomplete and delayed treatment of proteinuria with an ACE/ARB in lupus patients with evidence of proteinuria. Less than half of lupus patients with proteinuria received an ACE/ARB during the study timeframe, with Non-White patients significantly more likely to receive an ACE/ARB than White patients. The median time to ACE/ARB initiation was greater than a year. We intend to conduct further analysis to investigate hypertension as a potential confounding factor in the earlier initiation of an ACE/ARB among Non-White patients. Additionally, we plan to examine the time elapsed from proteinuria diagnosis to the prescription of immunosuppressive medications. These additional analyses will provide insight into optimizing timely evidence-based management of lupus nephritis patients.

Disclosure: J. JANSZ: None; **W. GALLANTER**: None; **E. Adams**: None; **N. Sweiss**: None; **H. Chang**: None.

Abstract Number: 1507

Pharmacodynamic Changes in SLE Relevant Gene Expression Induced by Deucravacitinib in Patients Enrolled in the Phase 2 PAISLEY Trial

Chun Wu[1], Cristina Arriens[2], J. Michelle Kahlenberg[3], **Yanhua Hu**[1], Coburn Hobar[1], Adrian Coles[4] and Ian M. Catlett[5], [1]Bristol Myers Squibb, Princeton, NJ, [2]Oklahoma Medical Research Foundation and University of Oklahoma Health Sciences Center, Department of Arthritis & Clinical Immunology, Oklahoma City, OK, [3]University of Michigan, Ann Arbor, MI, [4]Bristol Myers Squibb, Lawrenceville, NJ, [5]Bristol Myers Squibb, Pennington, NJ

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Deucravacitinib (DEUC) is a first-in-class, oral, selective, allosteric inhibitor of TYK2. TYK2 is required for signal transduction downstream of cytokines implicated in SLE pathophysiology, including type I and III interferons (IFN), IL-12 and IL-23. In a phase 2 trial (NCT03252587), DEUC was effective vs placebo (PBO) in patients with SLE receiving standard background therapy. Lupus is a disease with activation of innate and adaptive arms of the immune system, including pathways driven by IFN and B cell activity. Inhibition of TYK2 is expected to reduce the activity of SLE (ie,

IFN-activation), however, the role of additional TYK2-regulated cytokines in SLE is not clear. We performed global transcriptomic analysis of patients treated with DEUC to further explore the mechanism of action (MOA) and effects of DEUC in SLE.

Methods: Blood samples (Paxgene RNA) were collected at baseline and multiple timepoints throughout the study following patient randomization (N=363). In a sub-study, samples (n=80) were collected 22-114 hours after the first dose. Global gene expression was assessed by RNA-sequencing and specific genes of interest were measured by endpoint PCR (Dxterity). Following quality control, 16,725 protein-coding genes were analyzed from 3,334 samples from patients with SLE. A set of demographically matched (sex and age) healthy control samples were collected to compare with study groups. Statistical analysis was conducted using Dream package in R. Differentially expressed genes from disease association and pharmacodynamic analyses were further characterized by pathway enrichment using standard databases.

Figure 1. 527 genes were significantly differentially expressed in patients with active SLE compared to healthy volunteers

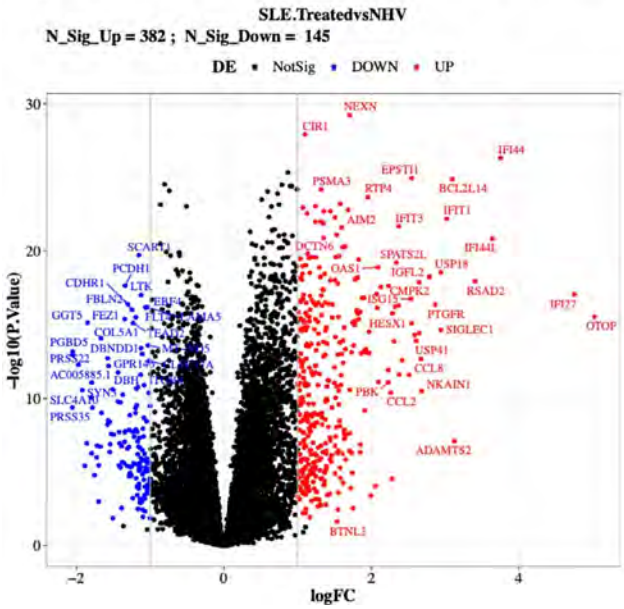
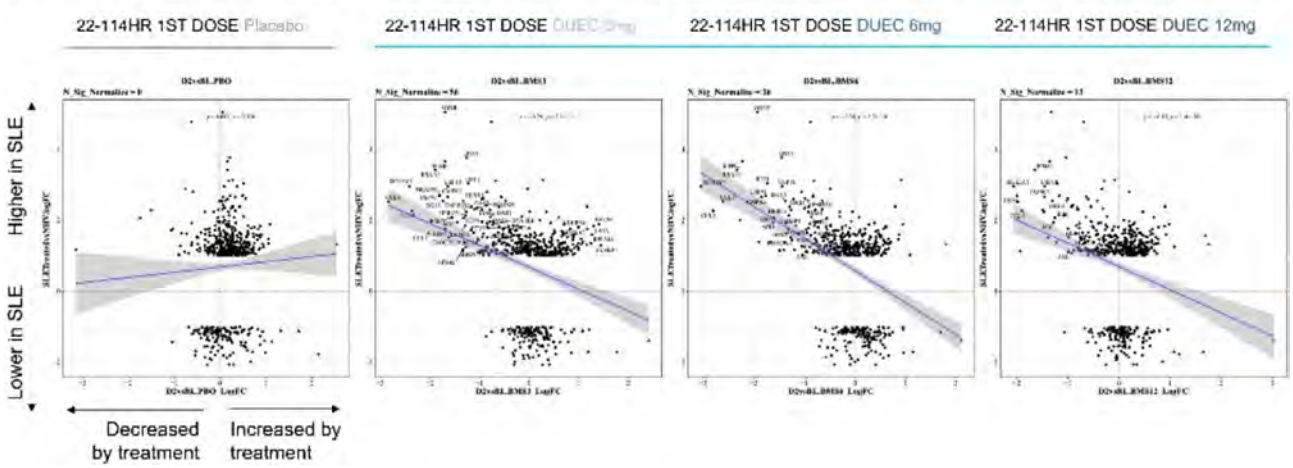


Figure 2. Deucravacitinib normalized the 527-gene SLE signature as early as 22-114 hours after the first dose



Results: 527 genes were significantly differentially expressed in subjects with active SLE compared to healthy volunteers with logFC >1 and adjusted P< 0.05 (Figure 1). The 527-gene signature was significantly enriched in 6 KEGG pathways, including "hsa05322-Systemic lupus erythematosus". IFN-regulated genes were overexpressed as expected for patients with SLE. No gene expression changes were observed in PBO patients, however, treatment with DEUC significantly normalized the 527-gene set of differentially regulated genes. In the sub-study, gene expression was normalized in DEUC treated patients as early as 22-114 hours after the first dose (Figure 2). At the primary clinical endpoint of week 32, patients treated with DEUC exhibited significantly modulated gene expression of 461, 833 and 2529 genes, in the 3 mg BID, 6 mg BID, and 12 mg QD groups respectively.

Conclusion: Moderate to severe SLE is characterized by significant elevation of IFN regulated gene expression and B cell autoimmunity gene expression pathways. DEUC treatment significantly reduced IFN-regulated gene expression. These findings are consistent with the expected MOA, which inhibits signaling at the type I and type III IFN receptors. These results support the anticipated MOA and novel inhibition of B cell autoreactivity pathways, increasing evidence of this therapeutic strategy in the treatment of SLE. Additional analyses will focus on additional SLE-specific pathways by deucravacitinib and whether data will support a wider array of indications.

Disclosure: C. Wu: Bristol Myers Squibb, 3; **C. Arriens**: AstraZeneca, 1, 5, 6, Aurinia, 6, Bristol-Myers Squibb, 1, 5, Cabaletta, 1, GSK, 1, Kezar, 1, UCB, 1; **J. Kahlenberg**: AstraZeneca, 1, Bristol-Myers Squibb(BMS), 2, 5, EMD Serano, 2, exo therapeutics, 2, Gilead, 2, GlaxoSmithKlein(GSK), 1, horizon Therapeutics, 2, Janssen, 5, Pfizer, 2, ROME Therapeutics, 2, 5, Rome Therapeutics, 5, Ventus Therapeutics, 2, 5; **Y. Hu**: BMS, 3, 12, BMS stock holder; **C. Hobar**: Bristol-Myers Squibb(BMS), 3; **A. Coles**: Bristol-Myers Squibb(BMS), 3; **I. Catlett**: Bristol Myers Squibb, 3, 8.

Abstract Number: 1508

Predicting in Virtual Patients the Efficacy of an Anti IFNa Mab in Cutaneous Lupus Erythematosus

Vincent Hurez[1], Krishnakant Dasika Dasika[1], Perrine Soret[2], Renee Myers[3], Katherine Kudrycki[1], Robert Sheehan[1], Christina Friedrich1[1], Sandra Hubert[2], Mike Reed[1], Emiko Desvaux[2], Audrey Aussy[2], Laurence Laigle[2], Loubna Chadli[2], Florian Chassereau[2], Sylvain Fouliard[2], Glenn Gauderat[2] and **Philippe Moingeon**[2], [1]Rosa and Co, San Carlos, CA, [2]Les Laboratoires Servier SAS, Suresnes, France, [3]Les Laboratoires Servier SAS, San Carlos, France

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a heterogeneous autoimmune disease that requires more specific treatments to target patient subsets. To support precision medicine approaches, we report herein on a molecular profiling approach to stratify SLE patients, as well as the creation of a cohort of virtual patients to predict the efficacy of an anti-interferon (IFN)-α monoclonal antibody in Cutaneous Lupus Erythematosus (CLE) across patient heterogeneity. Systemic Lupus Erythematosus (SLE) is a heterogeneous autoimmune disease that requires more specific treatments to target patient subsets. To support precision medicine approaches, we report herein on a molecular profiling approach to stratify SLE patients, as well as the creation of a cohort of virtual patients to predict the efficacy of an anti-interferon (IFN)-α monoclonal antibody in Cutaneous Lupus Erythematosus (CLE) across patient heterogeneity.

Methods: Multiomics profiling data from whole blood samples of 300 SLE patients and 330 matched healthy controls from the PRECISESADs cohort were used to stratify patients through hierarchical and k-means clustering. A quantitative systems pharmacology (QSP) mechanistic model recapitulating skin manifestations of CLE was developed using proprietary and public literature data, and qualified using the Rosa model qualification method [1]. This model was used to assess the efficacy of the pan-neutralizing anti-IFN-α S95021 monoclonal antibody .

Results: The integrated analysis of multiomics profiling data led to the identification of four clusters of SLE patients. Gene enrichment analyses confirmed the upregulation of the type I IFN pathway in a majority of SLE patients, while further revealing distinct patterns of immune dysregulation involving B lymphocytes and autoantibodies, as well as T and polymorphonuclear cells. The QSP model of CLE relates various cellular and soluble proinflammatory mediators in the blood, lymph nodes and skin to subcomponents of the cutaneous severity score (CLASI). The time-course of CLASI score responses simulated in the model matched published clinical trial data with the anti-type I IFN receptor anifrolumab. Additionally, it predicted the efficacy of the S95021 antibody at various doses in CLE. By varying the contribution of the different cell types and mediators to skin damage and inflammation in the model, a cohort of ∼700 virtual patients was generated, reflecting the heterogeneity observed across the various clusters of real patients from PRECISESADs. The analysis of predicted responders vs non responders using machine learning yielded biomarkers that could be used for the stratification of patients in subsequent clinical studies.

Table 1: CLASI score subcomponents and their mapping to QSP model species

CLASI score component	QSP model species
Erythema	Pro-inflammatory mediators Activated vasculature
Ulceration	Correlated with disease activity
Alopecia	Hair follicle damage Effector T cells Pro-inflammatory mediators
Scarring	Fixed value (no change with therapy)

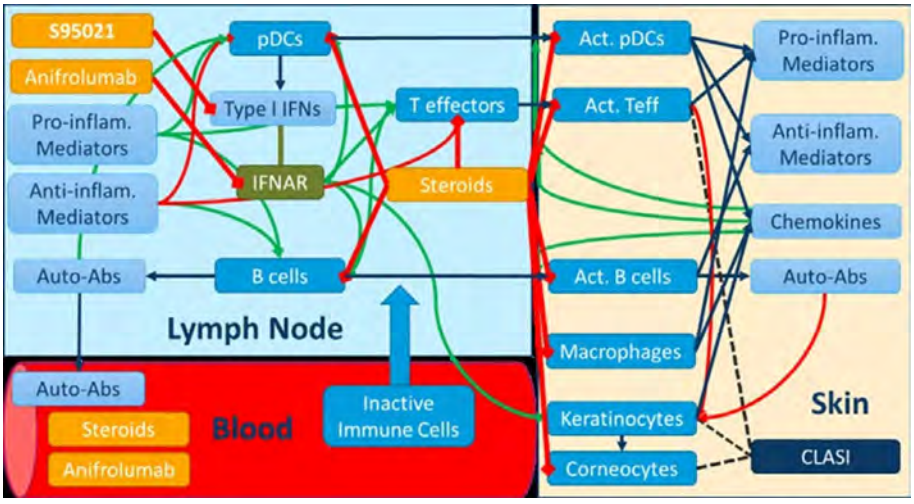


Figure 1: Overview of the mechanistic QSP model of Cutaneous Lupus

Conclusion: Combining molecular profiling of large cohorts of actual patients with QSP simulation encompassing hundreds of virtual patients is a powerful approach to document patient heterogeneity in a complex autoimmune disease. It also supports precision medicine strategies by enabling the creation of predictive models of drug response at an individual patient level. 1. Friedrich, C.M. et al, A model qualification method for mechanistic physiological QSP models. CPT Pharmacometrics Syst Pharmacol, 2016. 5: 43-53

Disclosure: V. Hurez: Rosa and Co, 3; **K. Dasika**: Rosa and Co, 3; **P. Soret**: Servier, 3; **R. Myers**: Rosa and Co, 3; **K. Kudrycki**: Rosa and Co, 3; **R. Sheehan**: Rosa and Co, 3; **C. Friedrich1**: Rosa and Co, 3; **S. Hubert**: Servier, 3; **M. Reed**: Rosa and Co, 3; **E. Desvaux**: Servier, 3; **A. Aussy**: Servier, 3; **L. Laigle**: Servier, 3; **L. Chadli**: Servier, 3; **F. Chassereau**: Servier, 3; **S. Fouliard**: Servier, 3; **G. Gauderat**: Servier, 3; **P. Moingeon**: Servier, 3.

Abstract Number: 1509

Calcineurin Inhibitors for Treatment of Lupus Nephritis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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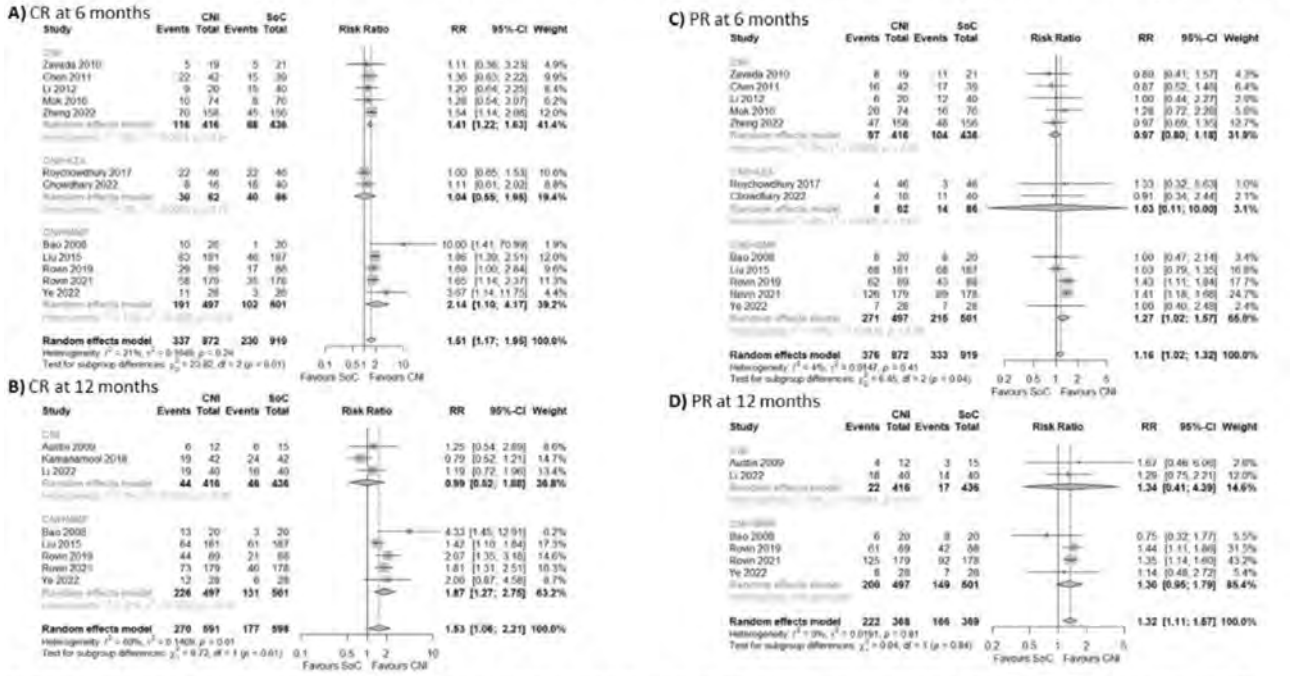
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The current recommendations for the treatment of LN consider as the standard of care (SoC) the use of MMF or CYC. Considering the expanding evidence for the use of calcineurin inhibitors (CNI) in patients with LN, we aimed to summarize and assess the efficacy and safety of CNI compared to the current SoC for the treatment of patients with LN.

Methods: We comprehensively searched MEDLINE, EMBASE, CENTRAL, and Scopus from each database's inception to January 19, 2023. Studies were eligible if they included (P) patients with biopsy-proven LN, (I) compared CNI (voclosporin, tacrolimus, and CSA) alone or in combination with other immunosuppressors against (C) the SoC (MMF or CYC), (O) for efficacy (complete and partial renal response [CR and PR, respectively]) and safety (death, infections, gastrointestinal adverse effects [GIAE], cytopenias). Exclusion criteria were patients with SLE without biopsy-proven LN, non-pharmacological interventions, observational studies, and non-RCTs. We used the revised Cochrane risk of bias tool for randomized trials 2. We expressed the results as relative risk (RR) with 95% confidence intervals (CI). We used random-effect models and assessed heterogeneity by visual inspection and by using the I^2 and Chi^2 tests. We performed subgroup analyses to test for interactions based on CNI and SoC.

Results: We included 1998 patients with LN (16 RCTs), 975 patients who received CNI, and 1023 patients who received SoC (433 MMF and 590 CYC). The overall risk of bias was low in nine studies, five studies showed some concerns, and two had a high risk of bias (**Table 1**). Patients with LN treated with CNI for induction of remission may be more likely to achieve CR at 6 (RR 1.51, 95% CI 1.17-1.95; I^2 = 21%; 12 RCTs; 1791 patients; **Figure 1A**) and 12 months (RR 1.53, 95% CI 1.06-2.21; I^2 = 60%; 8 RCTs; 1189 patients; **Figure 1B**) than those treated with the SoC. CNI alone (RR 1.41, 95% CI 1.22-1.63; I^2 = 0%; 5 RCTs; 852 patients) and CNI+MMF (RR 2.14, 95% CI 1.10-4.17; I^2 = 15%; 5 RCTs; 998 patients) were more likely to achieved CR at 6 months against the SoC. Only CNI+MMF was better than SoC at

Figure 1. Forest plots for efficacy of calcineurin inhibitors (CNI) versus the standard of care (SoC) at 6 and 12 months. Complete (CR) and partial (PR) renal response.



CR: Defined as a <0.5g/d and inactive urinary sediment; PR: Defined as a fall to <3.0g/d (if baseline ≥3.0g/d) or ≥50% reduction of urinary protein excretion from baseline and stabilization of serum creatinine ±25%.

12 months (RR 1.87, 95% CI 1.27-2.21; I^2 = 31%; 5 RCTs; 998 patients). CNI also showed a higher probability of achieving PR at 6 and 12 months compared with the SoC (**Figure 1C and 1D**). We did not find a difference in the risk of death between patients treated with CNI or SoC (RR 0.96, 95% CI 0.50-1.85; I^2 = 0%; 14 RCTs; 1826 patients; **Figure 2A**). Patients with LN treated with CNI showed a similar infection risk to those patients treated with the SoC (RR 0.86, 95% CI 0.66-1.22; I^2

Figure 2. Forest plots for safety outcomes of calcineurin inhibitors (CNI) versus standard of care (SoC).

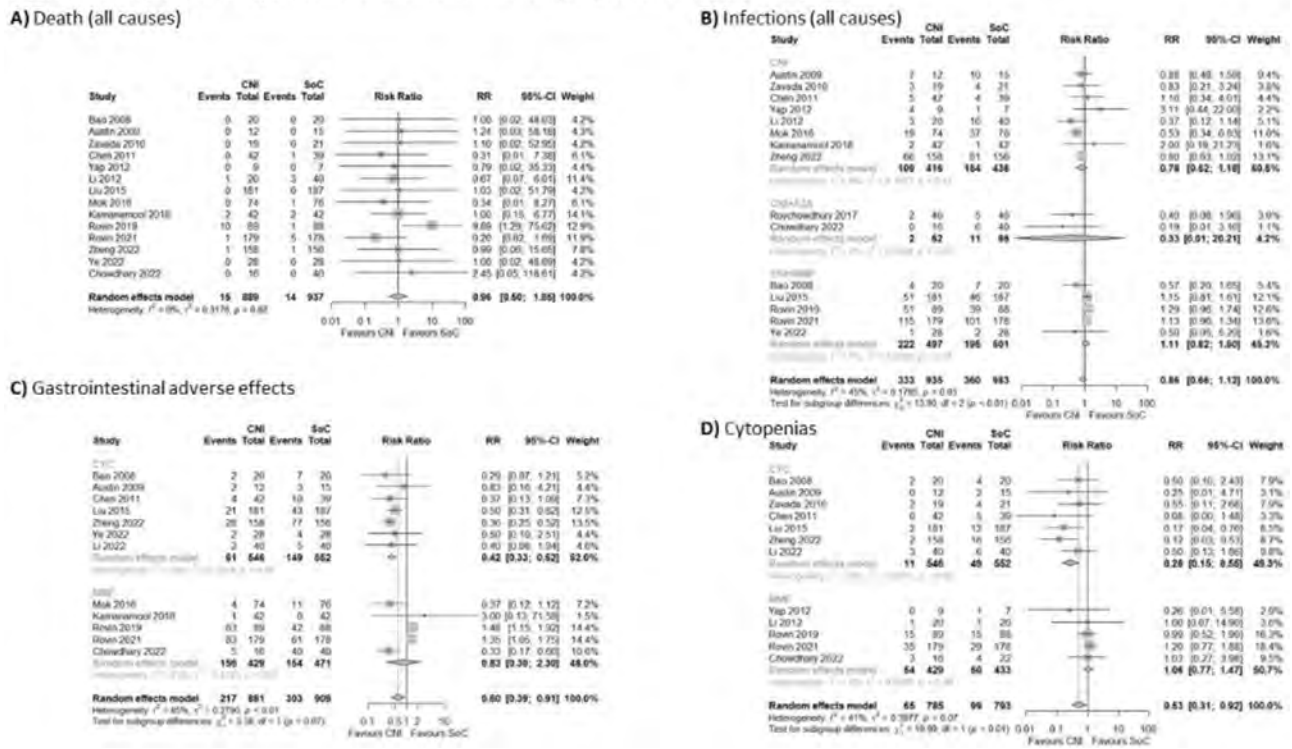


Table 1. Risk of bias assessment of included studies

Study	Randomization process	Deviations from interventions	Missing outcome data	Measurement of outcome	Selection of reported results	Overall risk of bias
Bao 2008	Low	Low	Low	Low	Low	Low risk
Austin 2009	Some concerns	Low	Low	Low	Low	Some concerns
Zavada 2010	Low	Low	Low	Low	Low	Low risk
Chen 2011	Low	Low	Low	Low	Low	Low risk
Yap 2012	Some concerns	Low	Low	Low	Low	Some concerns
Li 2012	Low	Low	Low	Low	Low	Low risk
Liu 2015	Low	Low	Low	Low	Low	Low risk
Mok 2016	Low	Low	Low	Low	Low	Low risk
Roychowdhury 2017	Some concerns	High	High	Some concerns	Some concerns	High risk
Kamanamool 2018	Low	Low	Low	Low	Low	Low risk
Rovin 2019	Low	Low	Low	Low	Low	Low risk
Rovin 2021	Low	Low	Low	Low	Low	Low risk
Zheng 2022	Low	Some concerns	Low	Low	Low	Some concerns
Ye 2022	Some concerns	Low	Low	Low	Low	Some concerns
Li 2022	Some concerns	High	Low	Low	Some concerns	High risk
Chowdhary 2022	Some concerns	Some concerns	Low	Low	Some concerns	Some concerns

= 45%; 15 RCTs, 1918 patients; **Figure 2B**). There was a difference given by the subgroups of CNI ($p< 0.01$), but not according to the SoC (p=0.99). We found a lower risk of GIAE (RR 0.6, 95% CI 0.39-0.91; I^2 = 85%; 12 RCTs; 1790 patients; **Figure 1C**) and cytopenias (RR 0.52, 95% CI 0.31-0.87; I^2 = 41%; 12 RCTs; 1616 patients; **Figure 1D**) among patients treated with CNI than those treated with the SoC.

Conclusion: Patients with LN treated with CNI for the induction of remission may have better response compared with MMF or CYC. CNI might be considered as equally safe in mortality and infections as the SoC. Possibly CNI might have less GIAE and cytopenias than the SoC, particularly compared with CYC.

Disclosure: G. Figueroa-Parra: None; **M. Cuellar-Gutierrez**: None; **M. Gonzalez-Trevino**: None; **L. Prokop**: None; **M. Murad**: None; **A. Duarte-Garcia**: None.

Abstract Number: 1510

Efficacy of Gonadotropin-releasing Hormone Agonist (GnRHa) in Ovarian Preservation in Women with Systemic Lupus Erythematosus (SLE) Receiving Cyclophosphamide (CYC)

Jun Chu[1], Dania Abid[2], Zerai Manna[1], Subrata Paul[3], Isabel Ochoa[3], Yalan Wu[3], Sonia Goyal[4], Syed Ali Abbas Naqvi[5], Lubna Hooda[3] and Sarfaraz Hasni[3], [1]Lupus Clinical Trials Unit, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health (NIH), Bethesda, MD, [2]Idaho College of Osteopathic Medicine, Meridian, ID, [3]National Institutes of Health, Bethesda, MD, [4]George Washington University, Washington, DC, [5]Jewish Hospital of Cincinnati, Cincinnati, OH

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE patients with life-threatening lupus manifestations are often treated with cyclophosphamide (CYC), which has known cytotoxic effects on ovarian reserve. Co-administration of Gonadotropin-releasing hormone agonist (GnRHa) is suggested to protect ovaries from the cytotoxic effects of CYC but there is lack of data to support its use. We administered a questionnaire evaluating ovarian function of a cohort of SLE patients who either received CYC alone or GnRHa+CYC.

Methods: The study was approved by the National Institutes of Health, Institutional Review Board. Female SLE patients < 40 years old at the time of IV CYC treatment were included in this study. Review of medical records resulted in: CYC only (n=20) =group 1, GnRHa+CYC (n=30) =group 2. These patients were age/gender matched with SLE patients not treated

with CYC (n=50) =group 3. Data about demographics, disease activity, damage accrual, and cumulative CYC dose were collected. Data from questionnaires assessed regularity, duration of menstrual cycles, and pregnancies, before and after CYC. Premature ovarian insufficiency (POI)was defined as menopause prior to 40 years. Fisher's exact test and one-way ANOVA were performed in R (version 4.2.2) for categorial and continuous variables, respectively.

Results: There were no significant differences in age, disease activity, damage accrual, mean cumulative CYC dose, and duration of follow-up (Table 1).However, age at diagnosis and consequently age at time of CYC infusion was higher in group 1 compared to group 2. There were more Hispanic patients in group 2 and 3. 88/100 patients completed the questionnaire (Group 1=20, Group 2=23, Group 3=43).Post-CYC, 40% of group 1 patients reported POI compared to 20% of group 2 and 16% group 3, calculated as total of all POI defined (Table 2). Length of menses was decreased by 1.4 days (p=0.083) in group 1 compared to 0.7 days (p=0.122) in group 2 (Figure 1). There was no statistical significance seen between regularity of menses between group 1 and 2 pre and post CYC treatment. Similar numbers of pregnancies and live birth were reported by all groups. Data concerning adverse events related to GnRHa were not collected.

Table 1. Baseline Demographics

Table 1. Baseline Demographics

Characteristic	Group1 (Only CYC[2]) N = 20[1]	Group2(GnRHa[3]+CYC) N = 23[1]	Group3(No CYC), N = 43[1]
Age at diagnosis (years)	27.00 (7.68)	23.32 (5.89)	24.79 (8.97)
Duration of SLE (years)	6.56 (6.64)	6.40 (4.24)	5.43 (4.32)
Race:			
African American	8	4	11
Asian	1	4	6
Caucasian	5	1	7
Hispanic	6	17	19
Age when IV CYC started (years)	32.22 (7.17)	29.18 (5.96)	N/A
Age at the time of self-reported questionnaire (years)	46.50 (6.95)	40.43 (6.56)	42.28 (7.51)
Cumulative CYC dose in mgs[4]	14,241.54 (9,421.69)	15,331.77 (7,785.67)	NA (NA)
SELENA-SLEDAI[5] score at the start of CYC treatment	6.8 (4.7)	8.7 (6.7)	6.2(5.7)
SLICC/ACRDI[6] score at the start of CYC treatment	1.6(2.3)	1.4(1.4)	1.2(1.4)

[1] Mean (SD). [2] CYC – Cytoxan. [3] GnRHa – gonadotropin-releasing hormone agonist.
[4] mgs= Milligrams. [5] SELENA-SLEDAI= Safety of Estrogens in Lupus Erythematosus National Assessment–SLE Disease Activity Index. [6] SLICC/ACRDI – Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index

Table 2. Premature Ovarian Insufficiency (POI)

Table 2. Premature Ovarian Insufficiency (POI)

Group	No	Yes	NA*	Percent
Group1(CYC Only)	9	6	5	40
Group2 (GnRha+CYC)	12	3	8	20
Group3 (SLE Controls)	21	4	18	16

*NA= Not applicable when POI is not definable if a patient is younger than 40 and was not diagnosed with menopause

Figure 1: Changes in menstrual cycle length before and after cyclophosphamide treatment

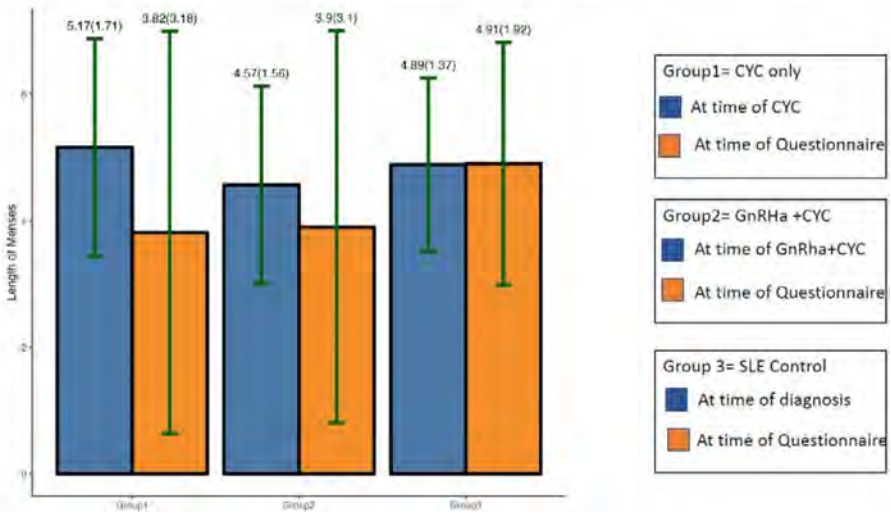


Figure 1: Changes in menstrual cycle length before and after cyclophosphamide treatment

Conclusion: Our study suggests that co-administration of GnRHa with CYC protects the ovary from its cytotoxic effects. Incidence of POI, and other markers of ovarian dysfunction such as length of menstrual cycle were significantly higher when CYC was administered alone. Larger, prospective studies are needed to establish role of GnRHa in preserving ovarian function in patients with SLE.

Disclosure: J. Chu: None; **D. Abid**: None; **Z. Manna**: None; **S. Paul**: None; **I. Ochoa**: None; **Y. Wu**: None; **S. Goyal**: None; **S. Naqvi**: None; **L. Hooda**: None; **S. Hasni**: None.

Abstract Number: 1511

B-Cell Recovery in a Randomized Controlled Trial of B-Cell Depletion with Obinutuzumab for the Treatment of Proliferative Lupus Nephritis

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SESSION INFORMATION

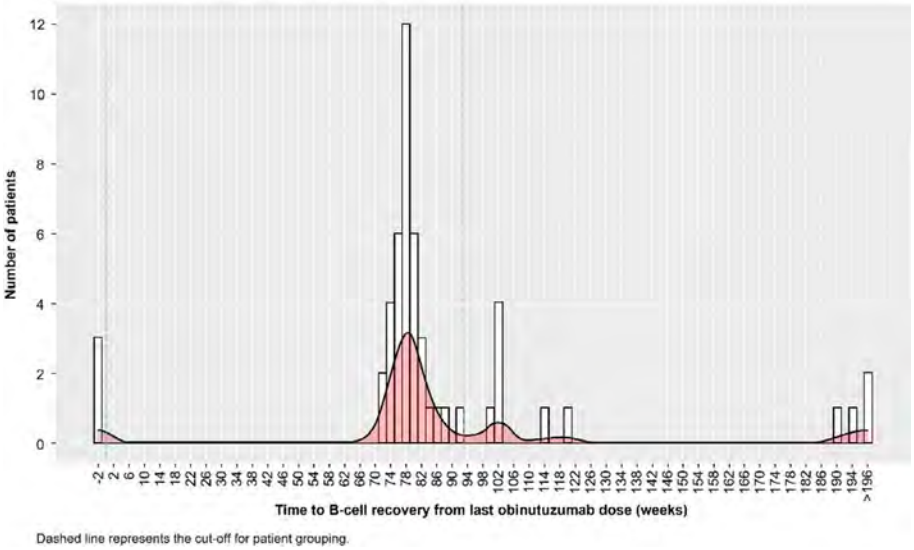
Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with LN who received obinutuzumab, a humanized type II anti-CD20 monoclonal antibody, with standard-of-care (MMF) immunosuppression (Phase II NOBILITY; NCT02550652; PMID 34615636) showed improved clinical responses through Week 104 versus those who received MMF alone. Sustained depletion up to Week 52 was associated with a better initial clinical response.[1] This analysis aims to characterize subsequent B-cell recovery after the last dose of obinutuzumab in NOBILITY and its impact on later response and safety.

Methods: 125 patients with active Class III/IV LN receiving MMF and corticosteroids were randomized and received either obinutuzumab 1000 mg (n=63) or placebo (n=62) on Day 1 and Weeks 2, 24 and 26, and followed through Week 104 or to B-cell recovery, whichever was longer. Blood B cells were measured using both a TBNK cell assay with a LLoQ of 10 $CD19^+$ cells/μL and a high-sensitivity minimal residual B-cell 1.1 assay with an LLoQ of 0.4 cells/μL. B-cell depletion was defined as ≤0.4 cells/μL, and recovery was defined as ≥20 cells/μL or the patient's predose baseline, whichever was lower. Time to peripheral B-cell recovery after the last dose of obinutuzumab, the relationship between time to recovery and efficacy at Week 104, and safety throughout the main study and follow-up period were evaluated (SAE and infectious SAE rates, adjusted for patient-years [PY] at risk).

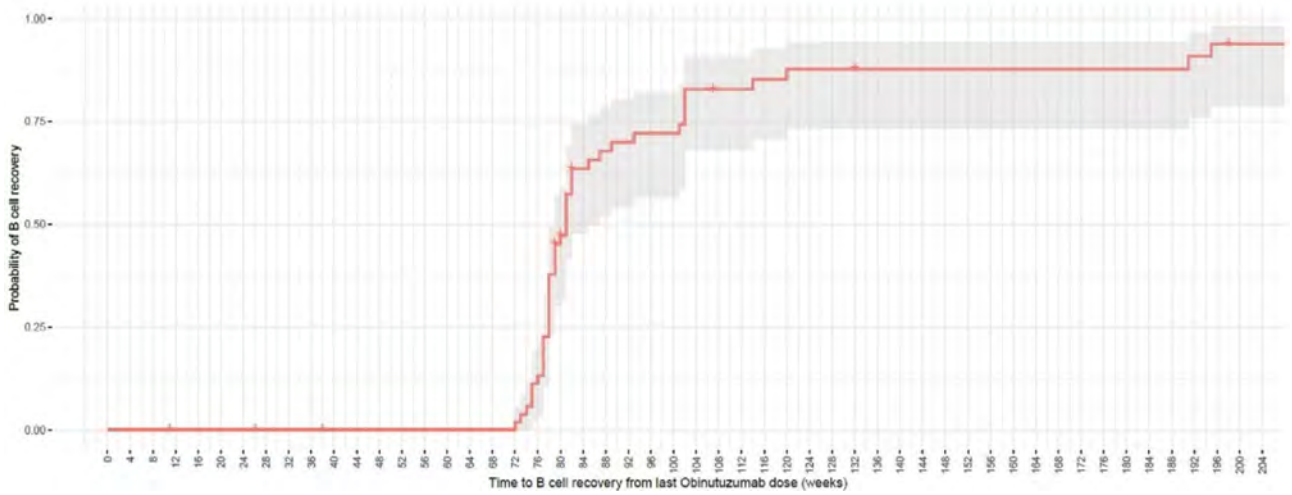
Results: Of 63 patients who received obinutuzumab, 4 did not achieve full B-cell depletion during the study. By Week 24, 59 patients (93.7%) achieved B-cell depletion (before obinutuzumab redosing); of those, 4 discontinued prior to B-cell recovery, and 4 completed the study at or after Week 104 but before achieving B-cell recovery. The remaining 51 patients comprised the analysis population, which was grouped based on the time to B-cell recovery distribution (**Figures 1 and 2**). Of the 51 patients, 3 (5.9%) recovered B cells before redosing at Week 26; 1/3 achieved CRR at Week 104. 37 patients (72.5%) attained B-cell recovery ≤93 weeks of their last dose of obinutuzumab (median, 78.1 weeks). 18/ 37 (48.6%) and 23/37 (62.2%) achieved CRR and overall renal response (ORR), respectively, at Week 104. In these 37 patients, SAE and infectious SAE rates per 100 PY were 13 and 8. 11 patients (21.6%) did not recover B cells by Week 93 after their last dose of obinutuzumab. 9/11 patients achieved B-cell recovery at a median of 102 weeks, and 2/11 had not yet achieved B-cell

Figure 1. Distribution of Time to B-Cell Recovery



Dashed line represents the cut-off for patient grouping.

Figure 2. Time to B-Cell Recovery From the Last Obinutuzumab Infusion (in Weeks)



recovery at the time of writing. 5/11 patients (45.5%) achieved CRR, and 8/ 11 (72.7%) achieved ORR at Week 104. In these 11 patients, SAE and infectious SAE rates per 100 PY were 10 and 0, respectively.

Conclusion: Most patients recovered peripheral B cells ≤93 weeks after the last obinutuzumab dose. Renal response rates at Week 104 were similar among patients who recovered B cells within 2 years of their final obinutuzumab infusion and those who recovered later or were still depleted, suggesting a greater clinical effect of early sustained depletion vs duration of depletion on clinical response.[1] Within the limitation of small sample size, the SAE and infectious SAE rates appeared similar regardless of the duration of B-cell depletion. 1. Vital E, et al. *Arthritis Rheumatol*. 2020;72 (suppl 10).

Disclosure: E. Vital: F. Hoffmann-La Roche Ltd, 2, Genentech, Inc., 2, Sandoz, 5; **D. Roccatello**: None; **D. Black**: F. Hoffmann-La Roche Ltd, 11, Genentech, Inc., 3; **R. Jacob-Moffatt**: F. Hoffmann-La Roche Ltd, 3; **C. Looney**: F. Hoffmann-La Roche Ltd, 3, 11; **E. Martins**: F. Hoffmann-La Roche Ltd, 3; **H. Mao**: F. Hoffmann-La Roche Ltd, 11, Hoffmann-La Roche Ltd, 3; **T. Schindler**: F. Hoffmann-La Roche Ltd, 3, 11; **H. Seghal**: F. Hoffmann-La Roche Ltd, 3; **J. Garg**: F. Hoffmann-La Roche Ltd, 11, Genentech, Inc., 3; **J. Ross Terres**: F. Hoffmann-La Roche Ltd, 11, Genentech, Inc., 3; **R. Furie**: Biogen, 2, 5.

Abstract Number: 1512

Rituximab Objective Outcome Measures Trial in SLE (ROOTS): Randomised and Rescue Therapy Outcomes from a Randomised Controlled Trial

Khaled Mahmoud, Michelle Wilson, Md Yuzaiful Md Yusof, Sarah Brown, Elizabeth Hensor and **Ed Vital**, University of Leeds, Leeds, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: SLE – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: New medicines in SLE have not met endpoints in placebo-controlled RCTs when other evidence indicates they are effective. Reasons suggested are inclusion of patients with inactive disease, inaccurate or subjective outcome measures that seek to address diverse manifestations, comparator arms that include excessive glucocorticoid dose and retention of patients.

Objectives: (i) To evaluate the feasibility of a novel trial design focusing on musculoskeletal SLE with objective eligibility criteria and endpoints and low-dose glucocorticoids (ii) To provide additional validation of LAMDA and ultrasound outcome measures (iii) To provide preliminary evidence for efficacy of rituximab

Methods: Adults with SLE were enrolled if they had clinical synovitis and/or ultrasound (US) tenosynovitis and/or positive power Doppler (PD) in >=1 joint despite stable background therapies including a maximum 10mg prednisolone. Patients were randomized to 1000mg rituximab (Rixathon, RTX) or placebo, on days 1 and 15. Blinded infusions were preceded by 100mg methylprednisolone. Outcome measures, including BILAG-2004, SLEDAI-2K, The Lupus Arthritis and Musculoskeletal Disease Activity Score (LAMDA), tender and swollen joint counts, physician global, patient MSK pain and global VAS, patient reported outcome measures, BICLA, SRI-4 were evaluated monthly. US of both hands and wrists was performed at 0 and 16 weeks. The primary endpoint was overall feasibility. The key efficacy timepoint was 16 weeks. After 16 weeks placebo patients with active disease were eligible for rescue rituximab with repeat follow up timepoints. US and LAMDA were validated against BILAG-MSK improvement at 16 weeks using regression models adjusted for baseline.

Results: 24/27 (89%) patients were female, 17/27 (63%) were white, 7/27 (26%) were South Asian. Mean (SD) age was 49.7 (12.7) and disease duration 6.7 (9.0). BILAG MSK domain at baseline was scored A in 7/27 (26%), B in 16/27 (59%) and C in 2/27 (7.4%). At 16 weeks, BILAG-MSK response was significantly associated with improvement in LAMDA (OR 0.48, 95% CI 0.18, 0.84); US joints grey-scale (OR 0.56, 95% CI 0.28, 0.85) and US tendons PD (OR 0.33, 95% CI 0.04, 1.01). No substantive difference between arms in efficacy variables was found at week 16. Unexpectedly, results suggested greater improvement in some outcomes in patients who received methylprednisolone and placebo compared to methylprednisolone and rituximab. These measures then converged by 16 weeks (Figure 1) Pooling all rituximab cycles administered (as initial therapy or as rescue) showed improvement in LAMDA (coefficient(95% CI) -2.68 (--4.02, -0.09)), number of joints with US-PD >0 (-0.59(-1.16, -0.02)), and number of joints with GS >1 (-2.68(-4.74, -0.62).

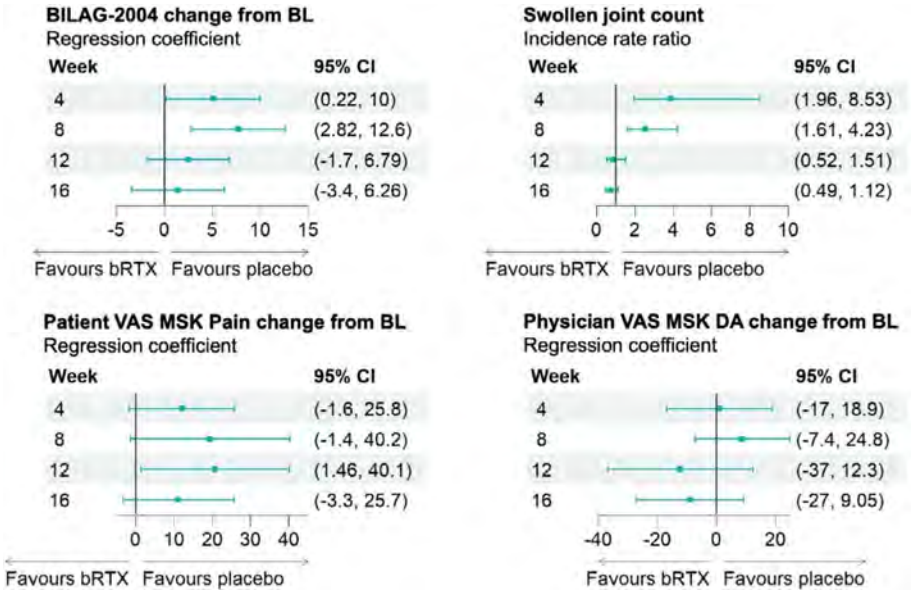


Figure 1

Conclusion: Clinical trials focused on a single feature of SLE (arthritis) are feasible and offer a homogenous trial population, control of standard of care and opportunities for objective imaging. The LAMDA is responsive and associates with validated outcome measures. ROOTS was not powered to measure efficacy but these data suggest potential worsening before benefit from rituximab. Detecting such signals may be enhanced by the greater sensitivity of this trial design.

Disclosure: K. Mahmoud: None; **M. Wilson**: None; **M. Md Yusof**: Novartis, 6, Roche, 6, UCB, 1; **S. Brown**: None; **E. Hensor**: None; **E. Vital**: F. Hoffmann-La Roche Ltd, 2, Genentech, Inc., 2, Sandoz, 5.

Abstract Number: 1513

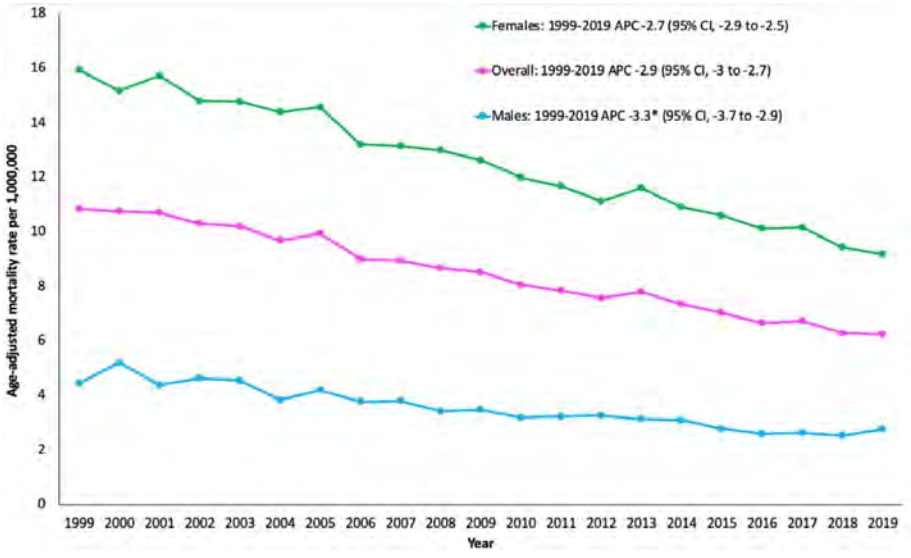
Trends in Systemic Sclerosis- related Mortality by Age, Sex and Race in the United States, 1999-2019

Anum Akhlaq[1], **Emily He**[2] and Risha Fayyaz[3], [1]University of Mississippi Medical Center, Jackson, MS, [2]Loma Linda University Health, Loma Linda, CA, [3]University of Mississippi Medical Center, Flowood, MS

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Sclerosis (SSc) is a rare chronic disease characterized by widespread vascular damage and tissue fibrosis of the skin and various internal organs, which is associated with high morbidity and mortality. National disparities in SSc- related deaths based on age, sex, and race have not been extensively studied. We examined the trends in SSc-related deaths in the United States from 1999-2019 stratified by age, sex, and race/ethnicity.

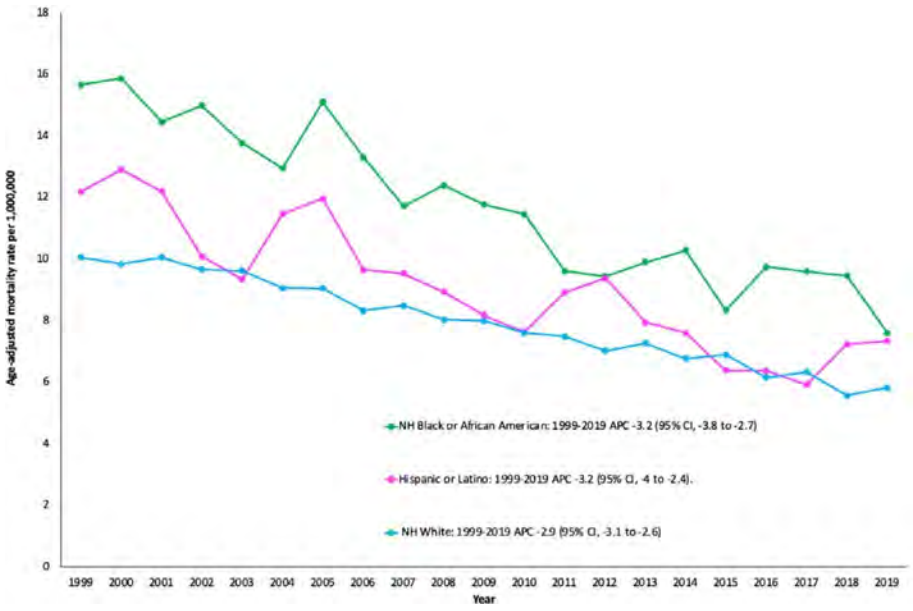
Methods: We used the Centers for Disease Control and Prevention Wide-Ranging OnLine Data for Epidemiologic Research (CDC WONDER) to access National Vital Statistics System data from 1999 to 2019. SSc-related deaths, age >/= 25 years were identified using the International Classification of Diseases, Tenth Revision, codes M34 from multiple causes of death



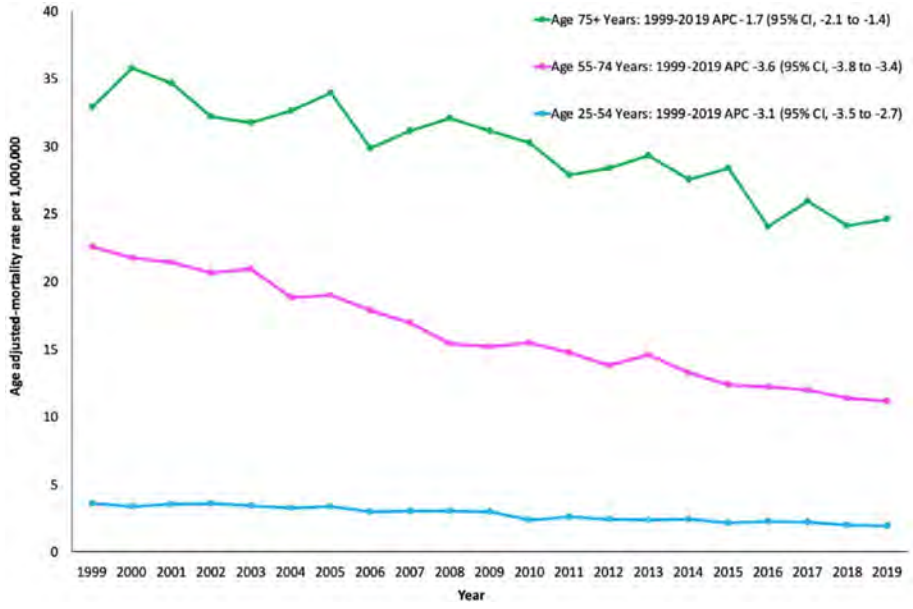
Trends in SSc related-mortality overall and stratified by sex

and were represented as age-adjusted mortality rates (AAMR) per 1,000,000 population. Joinpoint regression was used to examine changes in trend using annual percentage change (APC) in SSc-related deaths overall and stratified by age groups (25-54 years [young], 55-74 years [midlife], and >/=75 years [old]), sex, racial/ethnic groups (non-Hispanic whites (NHWs), non-Hispanic blacks or African Americans (NHB/AAs), and Hispanic or Latinos).

Results: There were a total of 37,594 SSc-related deaths during the study period. AAMR related to SSc decreased from 10.84 (95% CI, 10.35 to 11.32) in 1999 to 6.24 (95% CI, 5.93 to 6.55) in 2019 (APC -2.9 [95% CI, –3.0 to –2.7]). AAMR was higher in women (12.37) than men (3.49). Among the racial/ethnic groups, AAMR was highest in NHB/AAs (11.47) followed by Hispanic or Latinos (8.58), and lastly NHWs (7.86). AAMR was highest in old (29.76) followed by midlife (15.64) and young (2.83). From 1999-2019 APC in AAMR decreased in men (-3.3 [95% CI, -3.7 to -2.9]), women (-2.7 [95% CI, -2.9 to -2.5]), NHWs (-2.9 [95% CI, -3.1 to -2.6]), NHB/AAs -3.2 (95% [CI, -3.8 to -2.7]), Hispanic or Latinos (-3.2 [95% CI, -4 to



Trends in SSc related-mortality stratified by race/ethnicity



Trends in SSc related-mortality stratified by age

-2.4]), young (-3.1 (95% [CI, -3.5 to -2.7]) midlife (-3.6 [95% CI, -3.8 to -3.4] and old -1.7 [95% CI, -2.1 to -1.4]). AAMR related to SSc in 2020 was 6.28.

Conclusion: Our study showed a progressive decrease in SSc-related mortality throughout the study period regardless of gender, race, and age group. This could be due to early screening and management of life-threatening complications. Mortality was higher among females, NHBs, and older people. This could be due to higher SSc prevalence among these groups. Further research is required to understand the reasons for these disparities.

Disclosure: A. Akhlaq: None; **E. He**: None; **R. Fayyaz**: None.

Abstract Number: 1514

Phase I Study to Evaluate the Safety of Allogeneic Bone Marrow Derived Mesenchymal Stem Cells for Interstitial Lung Disease in Patients with Connective Tissue Disorders

Andy Abril[1], Isabel Mira-Avendano[2], Nisha Durand[1], Hassan Baig[1], augustine Lee[1], Meghan Baer[1] and Abba Zubair[1], [1]Mayo Clinic, Jacksonville, FL, [2]University of Texas, Houston, TX

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a leading cause of morbidity and mortality in connective tissue disorders (CTD) including rheumatoid arthritis, scleroderma and inflammatory myopathies. Conventional immunosuppressive therapies for CTDs are not always successful at preventing and treating pulmonary interstitial. Mesenchymal Stem Cells (MSC) have immunomodulating properties by blocking T cell proliferation, NK-Cell function and cytokine production. MSC have ability to induce tissue repair. Pulmonary fibrosis maybe the result of failed epithelial repair on stromal cells. Phase 1 trials in patients with post-transplant bronchiolitis obliterans, and idiopathic pulmonary fibrosis have shown MSCs are safe and patients showed stability. These characteristics suggest MSC may be an attractive therapeutic alternative in ILD associated with CTD. In this study, we assessed the safety of the adding allogeneic bone marrow derived mesenchymal stem cells to conventional pharmacological treatment in CTD patients who developed ILD.

Methods: Subjects with CTD who have developed ILD within the previous 2 years, were recruited from the clinical practice of the Pulmonary and Rheumatology clinics in Mayo Clinic Florida. Allogeneic MSC were manufactured at the Mayo Clinic Florida. 0.5 - 1 million MSC per Kg were infused IV. There were no adverse reactions reported during the infusions. Basic CBC and chemistries were obtained pre and post infusion, and on day1, 7, 30, 91 and 182. B, NK and T cell enumerations including T-reg cells, pro-inflammatory cytokines (TH1) and tolerogenic cytokines (TH2) levels as well as pro-angiogenic factors such as VEGF and iNOS were obtained prior to infusion. We assesed. Chest CT without contrast were obtained 1 to 7 days pre-infusion and day 182 post-infusion approximately. Spirometry was obtained at day 1, 7 and 30. Pulmonary function tests were obtained before the infusion, and at day 90 and 182

Results: Age ranged from 39-76 years, 7 patients were female and 3 were male.3 patient's had scleroderma, 3 rheumatoid arthritis, 2 anti synthetase syndrome, 1 polymyositis and 1 patient had interstitial pneumonia with autoimmune features (IPAF). 6 patients had a fibrotic NSIP (Nonspecific Interstitial Pneumonia) pattern, three patients UIP (Usual Interstitial

Table 1 : Demographic Characteristics of Study Subjects

Dosing	Age	Sex	Diagnosis	CT Pattern	PFT? FEV1	Time: Diagnosis to MSC infusion (years)
Group 1 0.5 x 10^6 MSC/Kg	65	F	Anti-synthetase	F-NSIP		
	39	F	Scleroderma	F-NSIP		
	47	F	OCTD(SSSA52kd)	F-NSIP		
	40	F	Anti-synthetase	F-OP		
	53	M	Polymyositis	F-NSIP		
Group 2 1.0 x 10^6 MSC/Kg	68	F	Scleroderma	F-NSIP		
	63	F	IPAF	F-NSIP		
	73	M	Rheumatoid arthritis	UIP		
	76	F	Rheumatoid arthritis	UIP		
	73	M	Rheumatoid arthritis	UIP		
Mean ± SD	59.7 ± 13.9					

Abbreviations: M-male, F-female, OCTD, MSC-mesenchymal stem/stromal cell, OCTD-overlap connective tissue disease, IPAF- interstitial pneumonia with autoimmune features, F-NSIP- fibrosing nonspecific interstitial pneumonia, F-OP-fibrosing organizing pneumonia, UIP-usual interstitial pneumonia

Characteristics of study subjects

Circulating Immune Cells

Follow-up Complete PFT Diffusion Capacity

	Event Name		
	visit_5_day_30_arm_1 (N=10)	visit_6_day_91_arm_1 (N=9)	visit_7_day_182_arm_1 (N=7)
Event Name, n (%)			
visit_5_day_30_arm_1	10 (100.0%)	0 (0.0%)	0 (0.0%)
visit_6_day_91_arm_1	0 (0.0%)	9 (100.0%)	0 (0.0%)
visit_7_day_182_arm_1	0 (0.0%)	0 (0.0%)	7 (100.0%)
DLCO_SB			
N	7	8	3
Median (Range)	8.1 (4.0, 12.8)	7.4 (1.5, 11.2)	9.7 (7.5, 12.6)
DLCO_SB (%PRED)			
N	7	8	3
Median (Range)	39.0 (20.0, 52.0)	36.5 (8.0, 54.0)	46.0 (32.0, 47.0)
DLCOcSB			
N	7	8	4
Median (Range)	7.9 (4.2, 12.5)	7.3 (1.8, 11.1)	11.0 (7.1, 14.5)
DLCOcSB (%PRED)			
N	7	8	4
Median (Range)	39.0 (21.0, 51.0)	36.5 (9.0, 53.0)	45.5 (30.0, 55.0)

Diffusion Capacity

Pneumonia) and 1 patient had fibrotic organizing pneumonia. There were no adverse events related to the MSC infusions. CT scans stable 6 months post-infusion, and in 1 patient the CT worsened. Pulmonary function tests were stable in 4 patients, 4 patients improved and 1 worsened at 6 months post infusion. The 6-minute walk testing showed improved oxygenation in 3 patients, stable numbers in 5 patients and worsening in 2 patients, overall there was a decline on the a distance walked at 6 months. There was a general trend towards improvement of the median diffusion capacity.

Conclusion: The results of our study suggest that MSCs are safe in patients with ILD associated with autoimmune rheumatologic disorders. There were no adverse events related to the infusion. Most patients achieved clinical stability regarding pulmonary function test and CT scan however future Phase II trials would be necessary to determine efficacy in this group of patients.

Disclosure: A. Abril: None; **I. Mira-Avendano**: None; **N. Durand**: None; **H. Baig**: None; **a. Lee**: None; **M. Baer**: None; **A. Zubair**: None.

Abstract Number: 1515

Performance of the Revised CRISS in a Phase 3 Trial of Early Systemic Sclerosis

Dinesh Khanna[1], Christopher Denton[2], Masataka Kuwana[3], Daniel Furst[4], Suiyuan Huang[1], Barbara White[5] and Robert Spiera[6], [1]University of Michigan, Ann Arbor, MI, [2]University College London, London, United Kingdom, [3]Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [4]University of California Los Angeles, Los Angeles, CA, [5]SFJ Pharmaceuticals, Towson, MD, [6]Hosptial for Special Surgery, New York, NY

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Revised CRISS has been proposed an approvable outcome measure in early diffuse cutaneous SSc (dcSSc)[1]. The index is undergoing the FDA review as part of the Drug Development Tool Clinical Outcomes Assessments Qualification Program. The Revised CRISS is a two-step process wherein trial patients are determined to have improved (responder) or not improved (non-responder). The first step of the Revised CRISS accounts for worsening or incident cases of any internal organ involvement. If the patient meets any of the Step 1 criteria, their percentage change is 0%, and they are considered a non-responder in a trial. Step 2 includes 5 core set measures. The FVC% is evaluated to see if the change is at least 5% The other 4 core set measures (mRSS, HAQ-DI, Patient (PGA) and Clinician global assessments (CGA)) are evaluated for change of at least 25% from baseline. A responder is a patient who has relative improvement on at least 2 of the 5 core set measures without worsening on more than 1 core set measure. The improvement or worsening must be at least 25% relative change from the baseline for 4 core set measures (or ≥5% for FVC%). Our objective was to assess the performance of Revised CRISS in a phase 3 clinical trial of lenabasum in early dcSSc at week 52[2].

Methods: The Phase 3 trial was not able to discriminate the active medication vs. placebo and the data was pooled together. Percentages of revised CRISS and corresponding group differences (95% CI) were reported for each factor we explored. Multiple imputation was used for missing data. The imputation model includes five core set measures and three non-missing variables: 1) treatment; 2) indicator of meeting the ACR CRISS step 1; 3) visit weeks. All Results were pooled from each imputed dataset using the Rubin's rule.

	% of patients achieving Revised CRISS	Group Differences (95% CI)
Revised CRISS, Overall, Completers only N=294 At least 2 improvements (25%/ 5% in FVC) and no more than 1 worsening	62.2	NA
Revised CRISS, Overall, Imputation only N=363 At least 2 improvements (25%/ 5% in FVC) and no more than 1 worsening	62.1	NA
Age, Median <52 years, N=178	58.5	-7.2 (-17.7, 3.3)
Age, Median ≥52 years, N=185	65.7	
Disease duration, Median <30 mths, N=181	62.5	0.8 (-9.8, 11.4)
Disease duration, Median ≥30 mths, N-182	61.8	
Female, N=275	62.4	0.9 (-11.3, 13.0)
Male, N= 88	61.5	
White, N=252	63.5	White - Asian 9.3 (-4.1, 22.7), White- Others -5.7 (-22.8, 11.4)
Asians, N=74	54.2	**Asians- Others -15.0 (-34.5, 4.5)**
Others, N=37	69.2	
ILD Present, N=249	63.2	3.4 (-8.0, 14.8)
ILD Absent, N= 114	59.8	
Anti-SCL-70, N =144	56.5	SCL-70- RNA Pol3 -7.5 (-19.7, 4.8) **SCL-70- Others -11.7 (-25.0, 1.6)**
Anti-RNA Pol 3, N=119	63.9	RNA Pol3- Others, -4.3 (-18.4, 9.9)
Others, N=100	68.2	
MMF, N=185	67.0	MMF- Other Immuno 8.3 (-3.2, 19.8) **MMF- No 13.3 (-1.4, 28.0)**
Other Immunosuppressives §, N=119	58.7	Others Immuno - No 5.0 (-10.7, 20.7)
No Immunosuppressives, N=59	53.7	
North America, N= 140**	68.5	**NA- Asia 15.2 (0.2, 30.2)**; NA- Others 8.4 (-3.1, 19.9)
Asia*+, N= 64	53.3	Asia- Others -6.8 (-21.9, 8.3)
Others, N= 159	60.1	

Results: Of 363 patients, 294 (81.0%) are completers, among which 9 (3.1%) met Step 1 (internal organ involvement). The overall response in the Revised CRISS was 62.1% in the imputed dataset. The different baseline factors influenced the response in the Revised CRISS (Table). Using a cutoff of 10% difference between the baseline factors (Table), the variables associated with lower Revised CRISS responses were being an Asian/ living in Asia, anti-SCL-70 antibody, and no background immunosuppressive therapy. Patients who lived in Asia had both lower prevalence of RNA pol3 + (23.4% in Asia vs. 47.9% in North America and 23.3% in Europe), and lower utilization of MMF (23.4% in Asia vs. 74.3% in North America and 41.5% in Europe).

The heatmap (Figure) visualizes the performance of the individual 5 core set measures and the Revised CRISS. There were large improvements in the mRSS followed by CGA that drove a high response in the RCT.

Conclusion: We propose a new preliminary definition of the Revised CRISS that is undergoing the FDA Qualification. The mRSS and CGA drove the Revised CRISS in this RCT, and the future trials should enrich for more severe skin involvement (progressive skin phenotype and less regressive disease) to limit improvement in mRSS (as part of the natural history). In addition, stratification by autoantibodies and background immunosuppressives may balance the Revised CRISS response.

[1]Khanna D. Ann Rheum Dis 2021 [2]Spiera R, et al Arthritis Rheumatol 2023

Disclosure: D. Khanna: AbbVie, 12, DSMB, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb, 2, 5, CSL Behring, 2, Genentech, 2, Horizon Therapeutics, 2, 5, Janssen, 2, 6, Pfizer, 5, Prometheus, 2; **C. Denton**: AbbVie, 2, Acceleron, 2, Arxx Therapeutics, 5, Bayer, 2, Boehringer-Ingelheim, 2, 6, Corbus, 2, 6, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Horizon Therapeutics, 2, Inventiva, 2, 5, Janssen, 6, Roche, 2, Sanofi, 2, Servier, 5; **M. Kuwana**: AbbVie/Abbott, 6, Asahi-Kasei, 5, 6, Astellas, 6, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, 6, Chugai, 2, 5, 6, Corbus, 2, Eisai, 6, GlaxoSmithKlein(GSK), 2, Horizon, 2, Janssen, 6, Kissei, 2, MBL, 2, 5, Mitsubishi Tanabe, 2, 5, 6, Mochida, 2, 6, Nippon Shinyaku, 6, Ono, 5, 6; **D. Furst**: Amgen, 2, 5, Corbus, 2, 5, CSL Behring, 5, Galapagos, 2, 5, Gilead, 5, GSK, 5, Horizon, 5, Novartis, 5, Pfizer, 5, Roche, 5; **S. Huang**: None; **B. White**: Corbus Pharmaceuticals, 12, Own stock; **R. Spiera**: AbbVie/Abbott, 2, 5, Amgen, 2, AstraZeneca, 5, chemocentryx, 5, corbus, 5, Formation Biologics, 5, GSK, 2, 5, Inflarx, 5, Kadmon, 5, Novartis, 2, 5, Principia, 5, Sanofi, 2.

Abstract Number: 1516

Systemic Sclerosis Gastrointestinal Tract Vascular Biomarkers of Symptomatic Disease Activity

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention

Session Type: Poster Session B

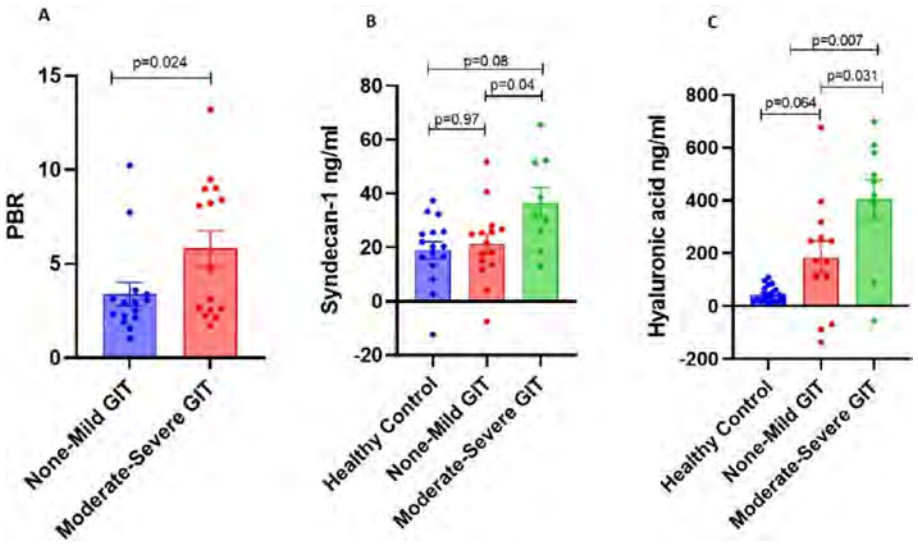
Session Time: 9:00AM–11:00AM

Background/Purpose: Gastrointestinal tract symptoms are common in systemic sclerosis (SSc). The Scleroderma Clinical Trials Consortium University of California Los Angeles Gastrointestinal Tract Questionnaire (GIT 2.0) is a validated, patient-reported outcome measure to assess gastrointestinal tract symptom severity in SSc. Intravital microscopy of the sublingual microcirculation can be used in SSc patient assessment for measurement of microvascular function and the glycocalyx, which is an indicator of endothelial dysfunction. In this study, biomarkers of endothelial dysfunction were examined in SSc patients by categorical GIT symptom severity.

Methods: SSc patients were enrolled at Vanderbilt University Medical Center and Tennessee Valley Healthcare System (IRB # 1618579).Enrolled patients who completed the GIT 2.0 and had same day sublingual microscopy measurement of glycocalyx penetrability by perfused boundary region [PBR]) in microvessel segments, and serum samples available for analysis were included. The PBR is scored as healthy (0-1.5), abnormal (1.6-3.5), or significantly elevated (3.6 and greater; indicative

Age (years), Mean (SD)	42 (11)
Sex: Female	23 (85%)
Race:	
• White	20 (71%)
• Black	5 (18%)
• Asian	2 (7%)
• Other	1 (4%)
Disease duration (years) for non-Raynaud's (SD)	8 (6)
Cutaneous Subset	
• Limited	17 (61%)
• Diffuse	11 (39%)
ANA positive	28 (100%)
Autoantibody Subset	
• Centromere	12 (43%)
• RNA polymerase III	6 (21%)
• Topoisomerase	3 (11%)
• PM-SCL	2 (7%)
Digital Ulcers	8 (29%)
Pulmonary Arterial Hypertension	2 (7%)
Scleroderma Renal Crisis	2 (7%)
Gastric Antrum Vascular Ectasia	3 (11%)

Clinical Features of SSc Patients (n=28)



Endothelial Biomarkers of Gastrointestinal Tract Symptoms in Systemic Sclerosis: A) Perfused Barrier Region (PBR), B) Syndecan-1, C) Hyaluronic Acid (HA)

of glycocalyx dysfunction). The plasma measurements of serum glycocalyx turnover (hyaluronic acid [HA] and syndecan-1) were determined by ELISA and compared to age- and sex- matched healthy controls. The endothelial biomarkers (PBR, HA, and syndecan-1) were analyzed by total GIT 2.0 severity: none-to-mild (0.49) and moderate-to-severe (0.5-3.00).

Results: The clinical features of 28 SSc patients that had same day acquisition of complete datasets are shown in Table 1. There were 15 SSc patients with mild GIT 2.0 and 13 SSc patients with moderate-to-severe GIT 2.0 symptoms, which were compared to 24 healthy control samples. The endothelial function biomarkers by GIT score category is shown in Figure 1. Only one patient had a healthy PBR measurement, 14 had an abnormal level, and 11 had an elevated PBR, which was significantly higher in patients with moderate-severe SSc-GIT symptoms (p=0.024). The syndecan -1 levels were significantly higher in SSc patients with moderate-severe GIT symptoms compared to patients with mild GIT symptoms (p=0.04), but not healthy controls. The HA levels were significantly higher in patients with moderate-severe SSc-GIT symptoms compared to both SSc mild GIT symptoms (p=0.031) and healthy controls (p=0.007).

Conclusion: This study supports that GIT symptoms in SSc may be due to endothelial dysfunction. The glycocalyx is a multifunctional and dynamic structure that participates in many vascular processes, including but not limited to vascular permeability, inflammation, thrombosis, mechano-transduction, and cytokine signaling. Sublingual estimates of endothelial glycocalyx health and serum measures of HA and syndecan-1 support the potential use of these biomarkers for objectively quantifying the role of vasculopathy in symptomatic SSc-GIT disease.

Disclosure: V. Gogulamudi: None; **S. Wood**: None; **E. Johnson**: None; **A. Petrey**: None; **A. Donato**: None; **T. Frech**: None.

Abstract Number: 1517

Comparing Deep Neural Network to Modified Rodnan Skin Score in a Trial for Belumosudil in Systemic Sclerosis Patients

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: We previously published a proof-of-principle study demonstrating the potential utility of computer vision (Deep Neural Network/DNN) methods applied to stained skin biopsy sections from patients with systemic sclerosis (SSc) as a novel skin outcome. The present study compared the 'DNN-Fibrosis Score' with histopathologic and modified Rodnan Skin Score (mRSS) changes for participants enrolled in a clinical trial.

a.

Stain	Visual Analog Scale
CD34 Alpha Smooth Muscle Actin	0= Normal Changes consistent with SSc 1= Mild 2= Moderate 3= Maximum
Hematoxylin & Eosin	1= Normal Changes consistent with SSc 2= Slight 3= Mild 4= Moderate 5= Marked 6= Maximum
Trichrome	1= Normal Changes consistent with SSc 2= Slight 3= Mild 4= Moderate 5= Maximum

b.

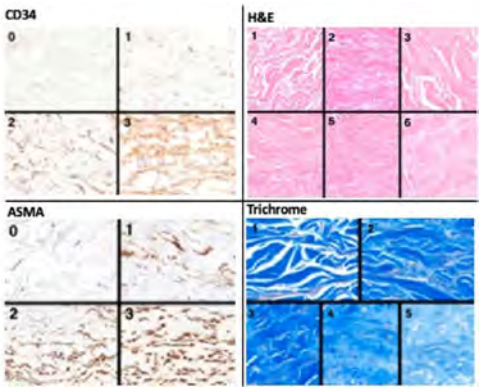


Figure 1. Histopathology assessment. a. Visual Analog Scale keys. b. Composite visual analog scales (from normal to maximum).

Methods: Ten adults with early (≤ 6 y) diffuse cutaneous SSc (15 ≤ mRSS ≤ 35) in an open-label belumosudil (ROCK2 inhibitor, 200 mg PO BID) trial had mRSS and two, 4mm, dorsal arm skin biopsies performed at weeks 0, 24, and 52. Biopsies were stained with CD34, CD3, CD8, alpha smooth muscle actin (ASMA), H&E, and trichrome. Two blinded dermatopathologists assessed biopsies for 16 histopathological parameters important in SSc (Van Praet JT et al., 2011). CD3+, CD8+ were counted, and visual analogue scales (VAS) were used to score CD34, ASMA, and relative SSc severity on H&E and

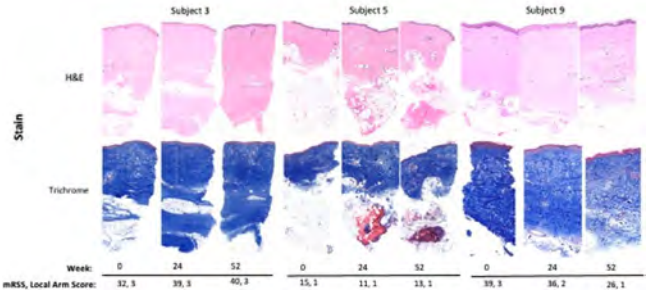
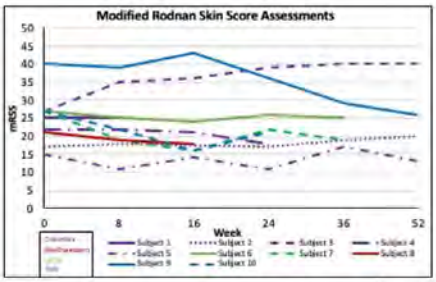
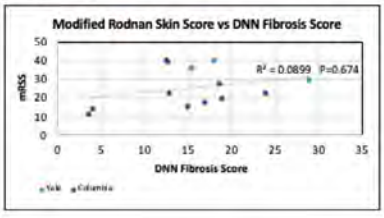


Figure 2. Stained sections from the 3 subjects with the largest mRSS changes between W0, 24 and 52 (40x).

a.



b.



c.

Ordinal Logistic Regression Analysis

Parameter	mRSS Parameter Odds Ratio (95% CI)	Parameter	Fibrosis Score Parameter Odds Ratio (95% CI)
Telangiectasia	2.01 (1.33 - 3.07)*	Eccrine entrapment	1.14 (1 - 1.31)*
Perivascular CD3+ lymphs	0.99 (0.97 - 1.02)*	Loss of subcutaneous fat/widened septum	1.47 (1.29 - 1.81)*
% of CD8+ among CD3+ cells	0.95 (0.89 - 1.01)*	Intima wall thicker than lumen deep arterioles	1.25 (1.05 - 1.38)*
ASMA	1.26 (1.17 - 1.35)	Hyalinized collagen	1.1 (1.04 - 1.16)*
Eccrine completely lost?	1.21 (0.92 - 1.59)	ASMA	1.37 (1.05 - 1.78)
Eccrine entrapment	1.2 (0.98 - 1.47)	% of CD8+ among CD3+ cells	1.13 (0.99 - 1.3)
Intima wall thicker than lumen deep arterioles	1.14 (1.03 - 1.27)	Pathology on trichrome	1.09 (1.01 - 1.18)
Loss of subcutaneous fat/widened septum	1.09 (0.93 - 1.28)	Telangiectasia	1.01 (0.87 - 1.16)
Mean epidermal thickness	1.07 (0.96 - 1.19)	Perivascular CD8+ lymphs	1 (0.81 - 1.23)
Pathology on trichrome	1.06 (0.95 - 1.19)	Mean epidermal thickness	0.94 (0.82 - 1.08)
Hyalinized collagen	1.04 (0.93 - 1.17)	Loss of epidermal papillae	0.93 (0.72 - 1.21)
Perivascular CD8+ lymphs	1.03 (1 - 1.06)	Eccrine completely lost?	0.91 (0.69 - 1.21)
Loss of follicle	1 (0.88 - 1.13)	Pathology on CD34	0.9 (0.78 - 1.03)
Pathology on CD34	0.93 (0.83 - 1.01)	Loss of follicle	0.89 (0.73 - 1.07)
Loss of epidermal papillae	0.9 (0.75 - 1.03)	Perivascular CD3+ lymphs	0.87 (0.68 - 1.11)
Calcification	N/A - All Values are 0	Calcification	N/A - All Values are 0

* denotes p<0.05

Figure 3. Belumosudil open-label trial results. a. Subject's mRSS W0 to last follow-up. b. Scatter plot of DNN Fibrosis Score and mRSS (p = 0.125). c. Ordinal logistic regression (95% CI) comparing DNN Fibrosis Score to 16 scored histologic parameters.

trichrome (**Fig. 1**). A previously developed DNN algorithm (AlexNet) was applied to trichrome-stained images to generate a 'DNN-Fibrosis Score' as previously reported. 'DNN-Fibrosis Scores' were compared to mRSS using a linear regression model and Spearman correlation. Histopathologic parameters were compared to mRSS or DNN Fibrosis-Scores using logistic regression models. A $p \leq 0.05$ was considered significant.

Results: Five patients had paired biopsies (**Fig. 2**). The median (interquartile range/IQR) mRSS change between 0 - 52W was -2.5 (-11 to 7.5) while the median (IQR) DNN-Fibrosis Score change (W0 - last follow-up) was -6 (-10.5 to 6.5) (**Fig. 3**). Of the histopathological scores, subcutaneous (SC) fat loss ($p = 0.012$), eccrine entrapment ($p = 0.008$), % CD8+ among CD3+ cells ($p = 0.006$) changed most during treatment. The correlation between mRSS and DNN-Fibrosis Score for the 5 paired biopsies was 0.18 [at higher mRSS, *i.e*. 25-51, the correlation was weaker] (**Fig. 3b**). Per 1-unit mRSS increase, the histopathological parameter odds ratios (OR); p-values were: telangiectasia =2.01; 0.001, perivascular CD3+ =1.03; 0.015, and % of CD8+ among CD3+ =1.08; 0.031 (**Fig. 3c**). Likewise, per 1-unit DNN Fibrosis-Score increase, OR; p-values for histopathological parameters were: hyalinized collagen =1.1; 0.00033, SC fat loss =1.47; 0.00033, intima wall =1.21; 0.005, and eccrine entrapment =1.14; 0.046 (**Fig. 3c**).

Conclusion: In this novel exploratory analysis, the DNN-Fibrosis Score exhibited sensitivity to histopathologic changes. The weak correlation between mRSS and DNN-Fibrosis Score contrasted with our previous findings. We note that predicted DNN-Fibrosis Scores tended to be lower for participants with higher mRSS (>25). We attribute this divergence to batch effects from staining protocols between our published and our current analysis which may be overcome with analyses of larger cohorts. However, despite the weak correlation with mRSS, the DNN-Fibrosis Score significantly correlated with a set of histopathological variables that were distinct from those correlated with mRSS, including hyalinized collagen, SC fat loss, intima wall thickness, and eccrine entrapment.

Disclosure: B. Gunes: None; **L. Duran Camacho**: None; **S. Cowper**: None; **G. Panse**: None; **E. Bundschuh**: None; **A. Williams**: None; **N. Page**: None; **M. Karns**: None; **K. Aren**: None; **N. Pradhan**: None; **E. Bernstein**: Boehringer Ingelheim, 2, 5, Kadmon, 5, Pfizer, 5; **S. Fantus**: None; **E. Volkmann**: Boehringer-Ingelheim, 2, 5, 6, CSL Behring, 2, GlaxoSmithKline, 2, Horizon, 5, Prometheus, 5, Roche, 2; **H. Bukiri**: None; **C. Correia**: None; **F. Wilson**: Amgen, 5, AstraZeneca, 5, Vifor Pharma, 5; **S. Mawe**: None; **J. Mahoney**: None; **M. Hinchcliff**: Boehringer-Ingelheim, 5, Kadmon, 5; **R. Wang**: None.

Abstract Number: 1518

Efficacy and Safety of Prostaglandins Analogues in Systemic Sclerosis-associated Raynaud's Phenomenon. a Systematic Review and Meta-Analysis

Hana Alahmari[1], Hila Jazayeri[2] and Sindhu Johnson[3], [1]Toronto Scleroderma Program, Mount Sinai Hospital, Toronto Western Hospital, Division of Rheumatology, Department of Medicine, University of Toronto, Toronto, ON, Canada, [2]University of Toronto, Toronto, ON, Canada, [3]Institute of Health Policy, Management, and Evaluation, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Raynaud's phenomenon (RP) is a vasculopathic manifestation of Systemic Sclerosis (SSc) that can lead to digital ulceration, gangrene, autoamputation, and hand disability. Prostaglandin analogs are prostacyclin-derived medications with potent vasodilatory properties. We conducted a systematic review and meta-analysis evaluating the efficacy and tolerability of prostaglandin analogs in controlling RP among SSc patients.

Methods: We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) of adults with SSc-associated RP with or without digital ulcers. The exposure was any prostaglandin compared to placebo or active control. The primary outcome was the effect on RP frequency. Secondary outcomes included RP severity, duration of RP attacks, healing of digital ulcers, development of new digital ulcers, change of capillary blood flow, impact on the patient's health-reported outcome, and tolerability. The time points were divided into short-term-follow (< 16 weeks) and long-term follow-up (≥ 16 weeks). The statistical analysis used RevMan software. Data were reported as pooled weighted mean difference (WMD) or odds ratio (OR) with 95% confidence intervals (95%CI). The study was compliant with PRISMA-S 2020 guidelines.

Results: Our search yielded 11 RCTs, of which ten were parallel, and 1 was crossover design. The studies were published between 1981 and 2017 and included five PGs (iloprost n=6, PGE1 n=2, baroprost n=1, trepinostil n=1, and selexipag n=1), often against a placebo. Most of the studies were conducted during winter to eliminate seasonal variability as a confounder. We performed meta-analyses using -effects models. PG significantly reduced RP severity in the short-term WMD -0.63 (95%CI -0.99, -0.27)]. In addition, there were trends for PG to reduce the frequency of RP attacks WMD -0.32 (95%CI -0.76, 1.13), and duration of attacks WMD -4.78 (95%CI -14.69, 5.14) but were not statistically significant. Withdrawal from trials due to adverse events was considered an indirect measure of drug intolerability. PGs increase the odds of withdrawal by 88%, OR 1.88 [95% CI 1.00, 3.55]. The most common adverse effects were postural hypotension, flushing, and headache. The quality of evidence ranged from moderate to low.

Conclusion: PGs can be beneficial in the short term to reduce the severity of SSc-associated RP. Therefore, PG may be considered a therapeutic option in people with SSc-associated RP.

Disclosure: H. Alahmari: None; **H. Jazayeri**: None; **S. Johnson**: None.

Abstract Number: 1519

Renal Complications Following Autologous Stem Cell Transplantation for Systemic Sclerosis

Malcolm MacKenzie[1], Harry Atkins[2] and Nancy Maltez[1], [1]The Ottawa Hospital, Ottawa, ON, Canada, [2]Ottawa Hospital Research Institute, Ottawa, ON, Canada

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rapidly progressive diffuse systemic sclerosis (SSc) is a devastating autoimmune disease with high morbidity and mortality. Autologous hematopoietic stem cell transplantation (AHSCT) is recognized as an effective treatment option with randomized controlled trials demonstrating long-term improvement in skin fibrosis, pulmonary function, and overall survival. Although the risk of renal complications following AHSCT for hemato-oncologic conditions has been well established, the risk in SSc remains unclear. In addition to acute kidney injury (AKI), this subset of patients with rapidly

progressive, severe SSc is particularly vulnerable to developing scleroderma renal crisis (SRC), a life-threatening complication of SSc characterized by malignant hypertension and AKI.

Methods: We conducted a retrospective review of all patients with SSc treated with AHSCT between 2001 and 2023 at The Ottawa Hospital. All patients satisfied the ACR classification criteria for SSc. Data was sought for baseline patient characteristics and the development of AKI and SRC as defined by the KDIGO 2012 definition or the International Scleroderma Renal Crisis Survey Criteria respectively, during the first 120 days following AHSCT.

Table 1. Demographic and clinical characteristics

	Total	Any renal* complication	No renal complication	SRC total
N—no. (%)	34	17 (50)	17 (50)	7 (21)
Mean age—yr	49.6 ±10.6	48.7 ±9.83	50.4 ±11.1	47.7 ±12.6
Female sex—no. (%)	17 (50)	11 (65)	6 (35)	5 (71)
Scl-70—no. (%)	11 (32)	5 (29)	6 (35)	1 (14)
RNA Polymerase III—no. (%)	7 (21)	4 (24)	3 (18)	2 (29)
Mean modified Rodnan skin score	25.7 ±10.3	26.4 ± 12.0	25.1 ± 8.78	32.5 ±7.68
Mean—FVC % of predicted value	79 ±22.0	71 ±23.0	86 ±19.0	71 ±24.2
Mean—DLCO % of predicted value	61 ±23.4	53 ±21.0	69 ± 23.0	55 ±32.2
Protocol: CTX + TBI + eATG	10**	3 (18)	7**	1 (14)
Protocol: CTX + rATG	26 (76)	14 (82)	12 (71)	6 (86)
ICU admission—no. (%)	7 (21)	7 (41)	0 (0)	4 (57)
Mortality—no. (%)	7 (21)	4 (24)	3 (18)	2 (29)

* Patient experienced scleroderma renal crisis or acute kidney injury or both

** Two patients underwent two AHSCT. CTX + rATG followed by CTX + TBI + eATG

± Denotes mean ±standard deviation

FVC, forced vital capacity; DLCO, diffusion capacity of the lung for carbon monoxide; ICU, intensive care unit, CTX, cyclophosphamide; rATG, rabbit anti-thymocyte globulin; eATG, equine anti-thymocyte immunoglobulin; TBI, total body irradiation; SRC, scleroderma renal crisis

Table 2. Characteristics of SRC patients (N=7)

Age (years)	47	53	56	46	21	52	59
Sex	Female	Female	Female	Male	Male	Female	Female
RNA polymerase III	-	+	+	-	-	-	-
Transplant protocol	CTX + rATG	CTX + TBI + eATG	CTX + rATG	CTX + rATG	CTX + rATG	CTX + rATG	CTX + rATG
Previous SRC	with mobilization	yes	no	yes	no	no	unknown
History of HTN	yes	no	no	yes	no	no	no
Proteinuria on admission	yes	no	yes	yes	yes	yes	unknown
History CKD prior to AHSCT	no	no	no	yes	no	no	yes
SRC meds stopped during AHSCT	no	yes	N/A	yes	N/A	N/A	N/A
Steroids at time of SRC	yes	yes	no	yes	yes	no	yes
AKI prior to SRC	no	no	no	no	no	yes	yes
AKI with SRC	yes	no	yes	yes	yes	yes	N/A on HD
SRC onset from AHSCT (days)	4	42	40	-1	27	109	30
BP on admission for AHSCT (mmHg)	103/67	96/59	115/61	112/73	98/67	134/97	unknown
Max recorded BP during SRC (mmHg)	193/119	172/84	176/101	198/110	149/100	177/106	unknown
Cr on mobilization	18	82	66	123	49	36	132
Max Cr post mobilization	23	87	66	127	60	38	175
Cr on admission for AHSCT	17	74	62	123	44	38	153
Max Cr over 120 days after AHSCT	112	111	158	199	115	425	484
LDH (99-186 U/L)	2792	522	1773	210	319	1115	395
Schistocytes	many	none	rare	few	rare	many	many
Haptoglobin (0.3-2 g/L)	<0.1	unknown	<0.1	unknown	unknown	unknown	unknown
Platelet count (130-380 x 10*9/L)	7**	96	60	<10**	90	13	47
ICU admission	yes	no	yes	no	no	yes	yes
ICU admission length (days)	61	N/A	3	N/A	N/A	18*	3*
RRT and type	none	none	none	none	none	SLED then HD	HD
Time on RRT	N/A	N/A	N/A	N/A	N/A	indefinite	indefinite
Treatment	captopril	captopril	captopril	captopril	captopril	perindopril	unknown
Renal outcome	normal GFR	normal GFR	CKD I	CKD 3B	normal GFR	permanent HD	permanent HD
Overall outcome	alive	alive	alive	alive	alive	died: scleroderma	died: colon cancer

*ICU admission prior to SRC development

**platelet count pre-engraftment

HTN, hypertension; CKD, chronic kidney disease; AHSCT, autologous hematopoietic stem cell transplantation; AKI, acute kidney injury; BP, blood pressure; Cr, creatinine, LDH, lactate dehydrogenase; ICU, intensive care unit; RRT, renal replacement therapy; SSA, anti-Sjögren's-syndrome-related antigen A autoantibodies; ANA, antinuclear antibody; GFR, glomerular filtration rate; CTX, cyclophosphamide; rATG, rabbit anti-thymocyte globulin; eATG, equine anti-thymocyte immunoglobulin; TBI, total body irradiation; SLED, sustained low-efficiency dialysis; N/A, not applicable

Results: 34 patients underwent AHSCT, the mean age was 49.6 years (21-65), 53% were female, 10 received cyclophosphamide (CTX), equine anti-thymocyte globulin (ATG), total body irradiation (TBI) conditioning and 26 received CTX, rabbit ATG conditioning. The mean modified Rodnan skin score (mRSS) was 25 (2-43), the mean FVC was 79% (37-119) and the mean DLCO was 61% (32-119) before AHSCT. The median follow-up time was 29.9 months (0-72). 50% (n=17) experienced renal complications following AHSCT with 29% (n=10) experiencing AKI alone, 20% (n=7) with SRC alone and 3% (n=1) having SRC without AKI. AKI occurred earlier with a mean of 18 days (-3 to 92) following AHSCT compared to SRC with a mean of 44 days (-1 to 109). 4 of the 7 patients with SRC required admission to the intensive care unit (ICU) and 2 required permanent hemodialysis. Of those with AKI only, 8 out of 10 were diagnosed with pre-renal AKIs and 2 had cardiorenal AKIs. Transient hemodialysis was required in 2 AKI patients. Among those with SRC, 5 patients were receiving steroids at the time of diagnosis. There was no statistically significant difference in overall survival associated with the development of renal complications post-AHSCT.

Conclusion: Although renal complications were common following AHSCT for SSc, affecting half of our cohort, there was no significant impact on survival observed with renal injury in our series. Nonetheless, given the frequency and often the severity of renal morbidity, close monitoring both before and after transplant is warranted as early intervention could be effective. Ideally, with much-needed prospective studies, high-risk patients may be identified prior to AHSCT and provided with pre-emptive supportive interventions to mitigate renal morbidity.

Disclosure: M. MacKenzie: None; **H. Atkins**: None; **N. Maltez**: None.

Abstract Number: 1520

Identifying Core Domains for Clinical Trials in Systemic Sclerosis-Associated Raynaud's Phenomenon and Digital Ulcers Using the Delphi Consensus Method

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: The OMERACT Scleroderma Vascular Disease Working Group sought to identify essential core outcome domains for inclusion in clinical trials focusing on Raynaud's phenomenon (RP) and digital ulcers (DUs) caused by systemic sclerosis (SSc). This effort aimed to gather insights from patients and other stakeholders, ensuring their perspectives are reflected in the development of a Core Outcome Set.

Methods: Candidate items identified from previous qualitative work and systematic literature reviews were included in separate Delphi surveys for RP and DUs. The surveys were in English and conducted in parallel. Participants were invited by email: patients through international patient advocacy groups, and other stakeholders, including physicians and others with experience

in treating patients with SSc-related RP and DUs and/or conducting clinical trials in these disorders. Patients completed the surveys for RP and DUs only if they had lived experience of RP and DUs, respectively. Core domains were defined as those reaching group consensus (≥70% ratings of 'critical' in both patient and other stakeholder groups) in the third/final Delphi exercise.

Results: The 3-round Delphi surveys were completed by 62 patients and 132 others from 39 countries for RP, and by 20 patients and 105 others from 36 countries for DUs.

For RP, group consensus for core domains was met for i) *pathophysiological manifestations core area*: severity and frequency of RP attacks; and ii) *life impact core area:* items grouped under the target domain of function, adaptation required to manage life with RP, and impact on health-related quality of life (HRQoL). Pain, duration of RP attacks, patient global assessment (PtGA), and need for hospitalization (*resource usecore area*) were considered critical by other stakeholders but not by patients. Conversely, patients but not other stakeholders considered coldness to be critical. Assessment of perfusion and temperature (*biomarkers* category) did not meet the threshold for inclusion by either group but assessment of microvasculature was raised for further consideration by the Working Group.

For DUs, group consensus for core domains was met for i) *pathophysiological manifestations core area*: pain, number, global burden, healing of DUs, and physician global assessment; and ii) *life impact core area:* items grouped under the target domain of function, adaptation required to manage life with DUs, and impact on HRQoL; and iii) *resource use core area:* items grouped under hospitalization or urgent intervention. Digital sensitivity, impact on emotional well-being, and assessment of microvasculature were considered critical by patients but not by other stakeholders. PtGA was considered critical by others but not patients.

Conclusion: Patients with SSc and clinicians identified core domains for use in clinical trials in SSc-associated RP and DUs, with several domains common to both manifestations of disease. These results will inform development of a final Core Domain Set for use in clinical trials.

Disclosure: S. Proudman: None; **M. Hughes**: Certa, 1, Eli Lilly, 6, Janssen, 5, 6, Pfizer, 6; **N. Maltez**: None; **E. Brown**: None; **V. Hickey**: None; **s. grosskleg**: None; **B. Shea**: None; **A. Herrick**: Arena, 2, Camurus, 2, Galderma, 2, Gesynta Pharma, 2, 5, Janssen, 6; **J. Pauling**: AstraZeneca, 2, Boehringer-Ingelheim, 2, IsoMab, 2, Janssen, 2, 6, Permeatus, 2, Sojournix Pharma, 2; **P. Merkel**: AbbVie/Abbott, 5, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos, 5, Electra, 5, Genentech, 5, GlaxoSmithKlein(GSK), 2, 5, HiBio, 2, InflaRx, 2, 5, Janssen, 2, Jubilant, 2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, Takeda, 2, 5, UpToDate, 9, Visterra, 2.

Abstract Number: 1521

Microvascular Remodeling After Autologous Stem Cell Transplant for Systemic Sclerosis

Lisa Balistreri[1], Megan Sullivan[1], Florentina Berianu[1], Ernesto Ayala[2] and Andy Abril[2], [1]Mayo Clinic Florida, Jacksonville, FL, [2]Mayo Clinic, Jacksonville, FL

SESSION INFORMATION

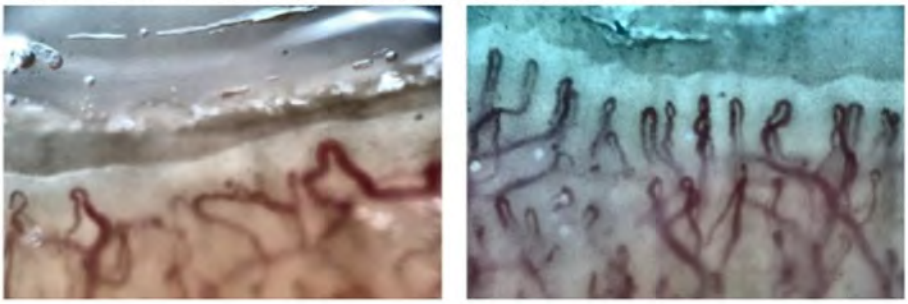
Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Figure 1: Nailfold video capillaroscopy images prior to HSCT and after HSCT



A B

A. NVC performed prior to HSCT shows low capillary density with disorganization of the normal capillary array B. NVC performed after HSCT shows increased capillary density to normal, hairpin-shaped capillaries, and absence of enlarged capillaries

Background/Purpose: Autologous hematopoietic stem cell therapy (HSCT) is an effective therapy for patients with rapidly progressive systemic sclerosis (SSc) refractory to standard therapies. The disease is characterized by microvascular damage and dysfunction which can be observed using nailfold video capillaroscopy (NVC). NVC can be useful to examine the severity, activity, and stage of microvascular damage. At this time, there are few reported cases of NVC improvement after HSCT. Other therapies for SSc have not been found to provide reversal of the capillary abnormalities. Our objective was to evaluate the effect of HSCT on nailfold capillary changes in SSc.

Methods: Prospective study in patients diagnosed with SSc followed at our institution who underwent treatment with HSCT and had NVC images available pre- and post- treatment. All patients met the ACR 2013 classification criteria for SSc. Demographics, clinical features, serologies, date of diagnosis, laboratory data, last follow-up, response to treatment, NVC, and outcome were recorded. NVC was performed on all eight nailbeds using the 2nd-5th digits of both hands. Capillary morphology, density, organization, microhemorrhages, and ramifications of each nailbed were compared to determine the degree of vascular remodeling pre and post HSCT.

Results: A total of 5 patients diagnosed with SSc underwent HSCT. Mean age was 43.75 years with 4 women (80%) and 1 man (20%). Post-treatment images were collected at a median of 2 months (range 1-3 months) after HSCT. From baseline to follow-up, 80% of HSCT patients showed significant improvement in parameters including density, architecture, and microhemorrhages. The change in capillary density and disorganization to the resemblance of a normal capillary was seen in most patients. The most notable improvement was seen in one patient with scleroderma overlap syndrome with normal capillary density noted as early as one month post transplant in most of the fingers corresponding with significant clinical improvement in the modified Rodnan skin score. NVC findings showed overall positive changes with increased capillary density, reduced capillary loss, and improved capillary morphology.

Conclusion: Our findings support reversibility of the NVC changes in patients with SSc in a short time interval post HSCT. Further research is warranted to determine if microvascular improvements post HSCT contribute to the improved mortality and quality of life previously reported in the literature.

Disclosure: L. Balistreri: None; **M. Sullivan**: None; **F. Berianu**: None; **E. Ayala**: None; **A. Abril**: None.

Abstract Number: 1522

Treatment of Pulmonary Arterial Hypertension in Patients with Connective Tissue Diseases: A Meta-analysis

Mustafa Erdogan[1], Sinem Nihal Esatoglu[2], Burcak Kilickiran Avci[3] and Gulen Hatemi[2], [1]Marmara University - Pendik Training and Research Hospital, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, [2]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, [3]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Department of Cardiology, Istanbul, Turkey

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Treatment options for pulmonary arterial hypertension (PAH) have expanded in the last two decades. However, evidence for the treatment of connective tissue disease-associated PAH (CTD-PAH) mostly depends on subgroup analysis of randomized controlled trials (RCTs). Thus, we performed a meta-analysis of the RCTs reporting outcomes for CTD-PAH.

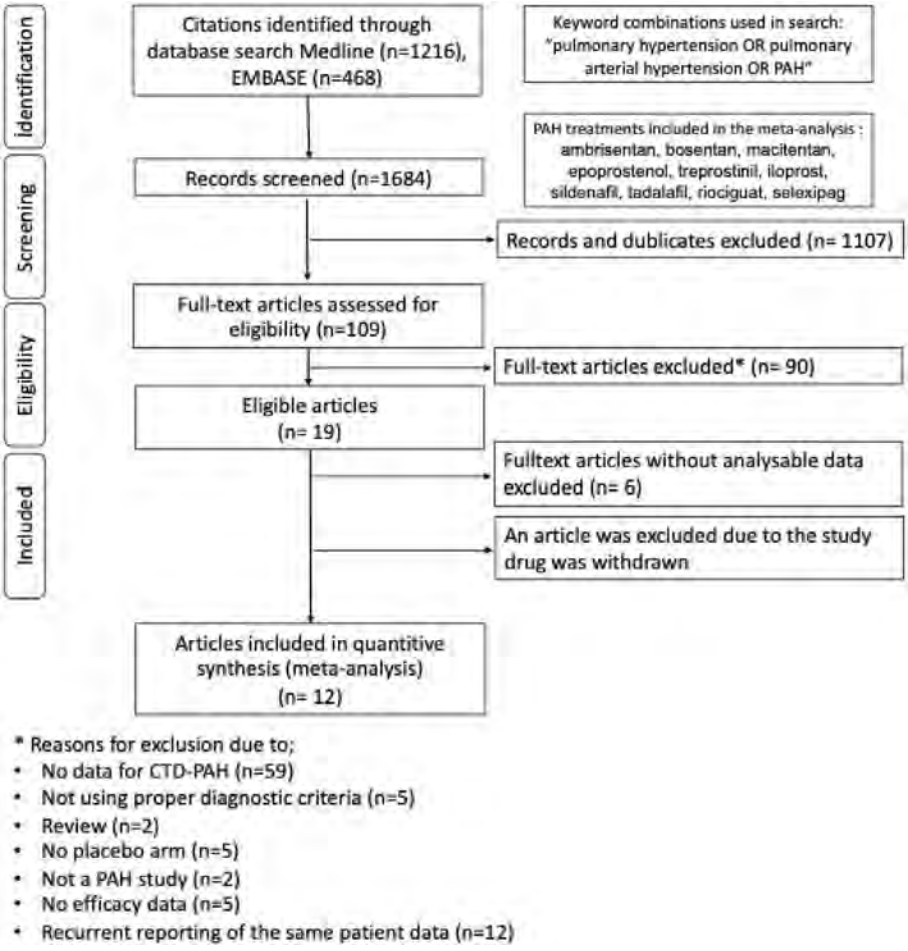


Figure 1. Flow chart of the study inclusion process

Methods: The search strategy was summarized in Figure 1. The outcomes selected for meta-analysis were functional class (FC) change, survival rates, six-minute walk distance (6-MWD), clinical worsening (CW), N-terminal prohormone BNP (NT-proBNP), pulmonary vascular resistance (PVR), mean pulmonary arterial pressure (mPAP), right atrial pressure (RAP), and cardiac index (CI). The systematic review and meta-analysis protocol was registered in PROSPERO (CRD42020153560).

Results: PubMed and Embase searches revealed 1216 and 468 articles, respectively. After excluding the irrelevant articles and studies without available data for meta-analysis, 12 RCTs, including 1837 patients, were selected (Figure 1). The diagnoses were SSc in 59%, SLE in 20%, and other CTDs in 21%. The follow-up duration of selected trials ranged between 12 weeks to 192 weeks. The pharmacological interventions were prostacyclin analogs in 3 studies (epoprostenol in 1 study and treprostinil in 2 studies), PDE-5 inhibitors in 2 studies (sildenafil and tadalafil in one study each), ERA in 4 studies (bosentan in 2 studies, macitentan and, ambrisentan in 1 study each), riociguat in 1 study, selexipag in 1 study and, ambrisentan and tadalafil combination in 1 study. There was a significant difference between the groups in FC, 6MWD, CW, PVR, RAP, and CI, favoring the intervention arms (Figure 2.) Our analysis showed a 30% reduction in the risk of CW with PAH treatment. The reduction was higher (46%) with combination therapies. However, short-term (24-26 weeks) survival and mean serum NT-proBNP level changes were similar between groups. The RoB of the studies were summarized in Figure 3.

Conclusion: Although treatment for CTD-PAH had favorable effects on many of the clinical and hemodynamic outcomes, the effect on survival and NT-proBNP levels were not significant. This is the first meta-analysis on CTD-PAH that reported the pooled analysis of change in functional class, hemodynamic measurements (RAP, PVR, CI), and NT-proBNP, some of which have important prognostic value for PAH. Improvement in exercise capacity and reduction in risk of CW in CTD-PAH patients were less pronounced compared to idiopathic PAH (IPAH). However, changes in hemodynamic parameters in patients with CTD-PAH in our meta-analysis were similar to those in patients with IPAH in the published RCTs.

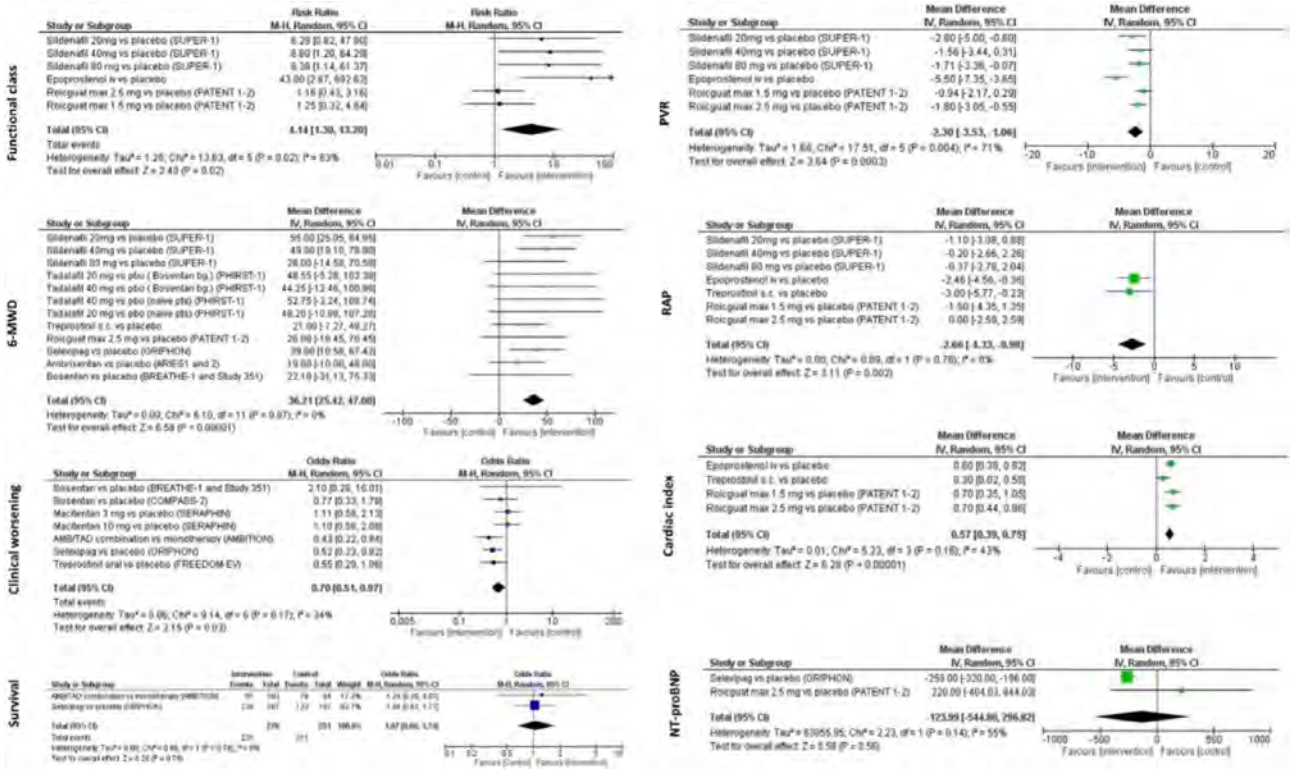


Figure 2. The results of the meta-analyses

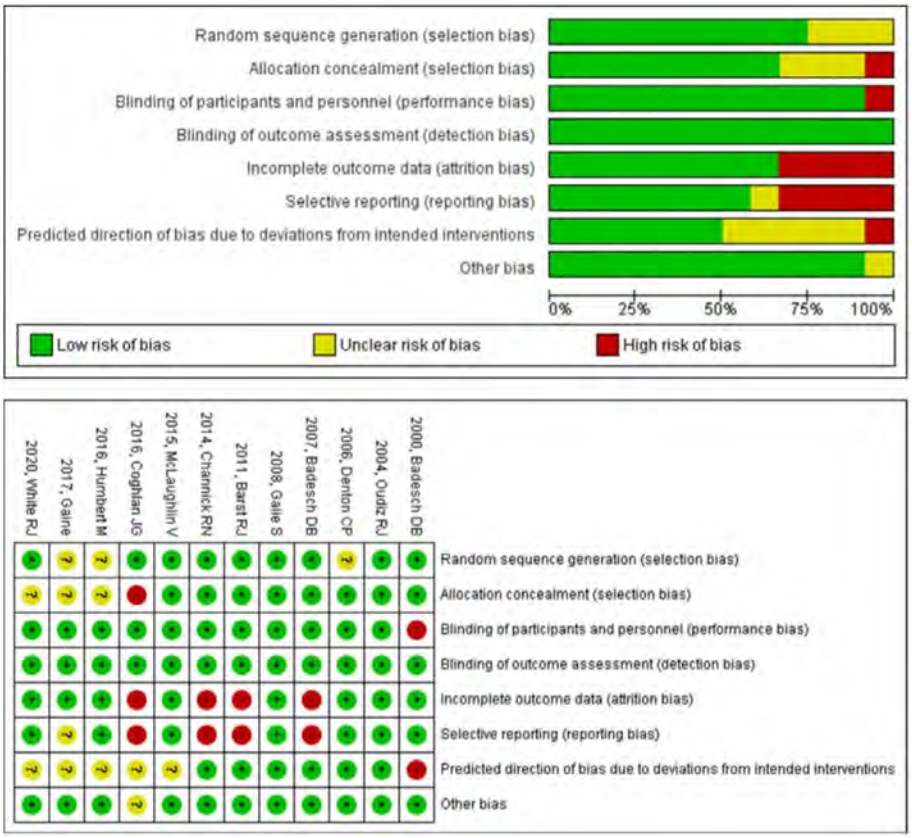


Figure 3. Risk of bias graph and summary: review authors' judgments about each risk of bias item for each included study

Disclosure: M. Erdogan: None; **S. Esatoglu**: None; **B. Kilickiran Avci**: None; **G. Hatemi**: None.

Abstract Number: 1523

The Risk of Scleroderma Renal Crisis from Intraarticular Corticosteroid Injection in Systemic Sclerosis

Muruganandam Maheswari, **Eyerusalem Akpan**, Matthew Mcelwee, Meredith Keller, Angie Ariza - Hutchinson, Rosemina Patel, Wilmer Sibbitt, Frank O'Sullivan, Sharon nunez, N. Suzanne Emil and Roderick Fields, University of New Mexico, Albuquerque, NM

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention

Session Type: Poster Session B

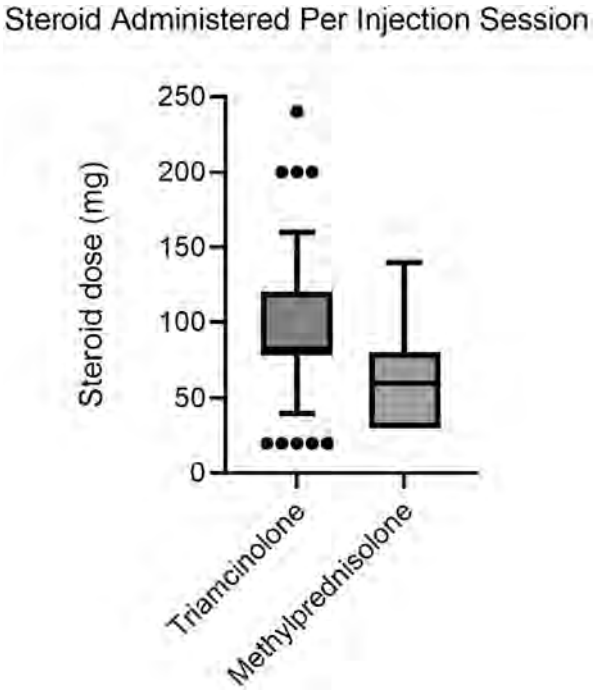
Session Time: 9:00AM–11:00AM

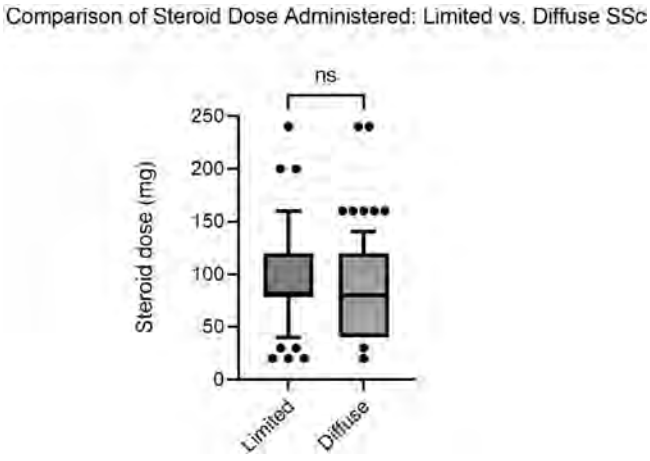
Background/Purpose: Scleroderma renal crisis (SRC) is a rare but a life-threatening complication of systemic sclerosis (SSc), affecting 2-15% of patients with SSc. SRC has been tied to the use of oral and intravenous corticosteroids in SSc. Due to this association, SSc patients with musculoskeletal complaints are often denied intraarticular (IA) corticosteroids when these therapies might otherwise benefit them. Although dose-dependent risk of oral corticosteroids in inducing SRC is well understood, the risk of IA corticosteroids for inducing scleroderma renal crisis has not been well studied. We

investigated the prevalence of SRC and other complications in patients with SSc following the injection of commonly used dosages of IA corticosteroids used to treat musculoskeletal complaints.

Methods: Under an IRB approved protocol, 136 patients with SSc followed in single university-based rheumatology clinic were retrospectively reviewed for receiving and complications subsequent to IA corticosteroid injections including: SRC, infection, hypertension, hyperglycemia, infection, tendon rupture and mortality. 46 of 136 SSc patients received IA steroids with a total 191 injection sessions (4.15± 4.04 injection sessions/subject). The mean steroid dose was 95.2± 44.2 mg/session. (Figure 1). Blood pressure, serum creatinine, and serum glucose were determined before and after the injection session (mean 5.9±4.8 weeks). Incidence of SRC, local infection, hypertension, hyperglycemia, infection, tendon rupture and mortality were assessed 12 months after the last injection session.

Results: The IA injection and control SSc subjects were similar in age (IA: 58.9±12.1 vs. 55.5±14.9 years), female gender (IA: 100% vs.89.9%, odds ratio (OR)=NA, p=0.02), antinuclear antibody (IA: 71.7% vs.81.1% OR=0.59, CI: 0.25-1.36, p=0.08), anti-centromere antibody (ACA) (IA: 47.8% vs.37.8%, OR=1.51, CI: 0.74-3.1, p=0.08), anti-topoisomerase





antibody (ATA) (IA: 26.1% vs. 26.7%, OR=0.97, CI: 0.43-2.18, p=0.16), antibody negative (negative for ACA/ATA or positive for RNA-polymerase III) (IA: 32.6% vs. 35.6%, OR=0.79, p=0.13). Additionally, there was not a difference in steroid dosing between limited and diffuse SSc patients(Figure 2). Outcome characteristics were very similar before and after the injections: systolic BP (before IA: 127±22 vs. after 127±21 mm Hg, p=1), diastolic BP (before IA: 71±13 vs. after 71±11 mm Hg, p=1), creatinine (before IA: 0.78±0.56 vs. after 0.76±0.20 mg/dL, p = 0.54), and blood glucose (before IA: 100±21 vs. after 99±24 mg/dL, p=0.57).One episode of SRC occurred in the control group. No episodes of SRC, serious local or systemic infection, tendon rupture, or death occurred in the IA injection group during the 12-month period after the 330 injections.

Conclusion: IA corticosteroid injections in patients with SSc does not appear to increase risk of SRC or other negative outcomes. These findings indicate that IA injections should not be denied to patients with systemic sclerosis if they are otherwise indicated.

Disclosure: M. Maheswari: None; **E. Akpan**: None; **M. Mcelwee**: None; **M. Keller**: None; **A. Ariza - Hutchinson**: None; **R. Patel**: None; **W. Sibbitt**: None; **F. O'Sullivan**: None; **S. nunez**: None; **N. Emil**: None; **R. Fields**: None.

Abstract Number: 1524

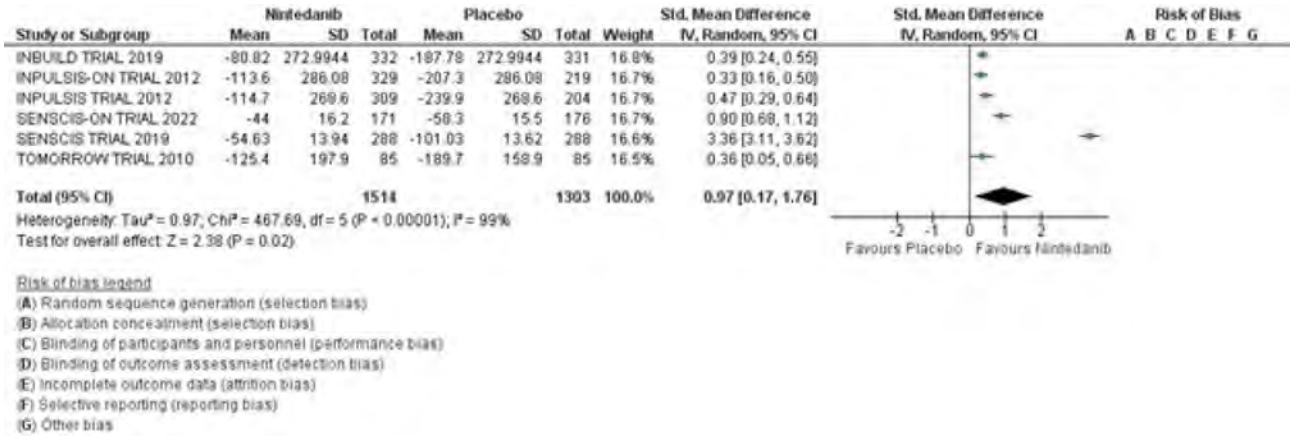
The Effectiveness of Nintedanib in Treating Fibrosing Interstitial Lung Disease in Both Scleroderma and Non-scleroderma Patients: A Systematic Review and Meta-analysis

Yasmin Khader, Fatima Rawish, Aya Abughrbyeh, Samantha Davis, Sabeen Sidiki, Pejma Safavi and Nezam Altorok, University of Toledo, Toledo, OH

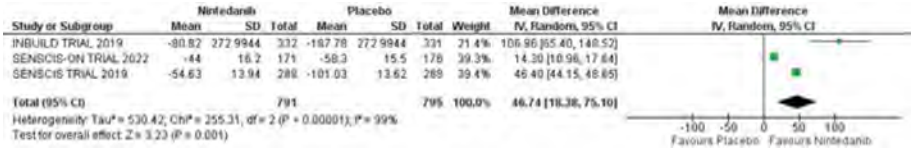
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Nintedanib, an intracellular inhibitor of tyrosine kinases, has shown promise in clinical trials by inhibiting key processes associated with the advancement of lung fibrosis. Its effectiveness has been demonstrated in treating idiopathic pulmonary fibrosis (IPF) as well as Systemic Sclerosis associated Interstitial Lung Disease (SSc-ILD). In this meta-analysis, we assessed the effectiveness of nintedanib in treating fibrosing interstitial lung diseases in both scleroderma and non-scleroderma patients.

Methods: We conducted a systematic review and meta-analysis of studies that investigated the effect of nintedanib on the annual decline of Forced Vital Capacity (FVC) in patients with fibrosing interstitial lung disease. We performed a comprehensive search in the databases of PubMed/MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials from inception through May 2023. We included all randomized controlled trials. We excluded observational studies, abstracts, animal studies, case reports, reviews, editorials, and letters to editors. From each study, we collected the rate of annual reduction of FVC in both treatment and control groups. The treatment group included patients with fibrosing lung disease treated with nintedanib. The primary outcome was the rate of annual reduction in FVC measured in millimeters per year assessed after 52 weeks of follow-up. The random-effects model was used to calculate the mean differences (MD), and confidence intervals (CI). A p value < 0.05 was considered statistically significant. Heterogeneity was assessed using the Higgins I^2 index.



Annual reduction rate in FVC (ml/year) in patients with fibrosing interstitial lung disease treated with nintedanib compared to placebo group



Annual reduction rate in FVC (ml/year) in patients with SSc-ILD treated with nintedanib compared to placebo group

Results: Five randomized controlled trials involving 2817 patients were included in the meta-analysis. Patients were randomized to treatment and placebo groups in almost 1:1 ratio. The rate of annual decline in FVC was significantly lower in all patients with fibrosing lung disease treated with nintedanib (MD 0.97, 95% CI 0.17-1.76, $p < 0.02$. $I^2 = 99\%$). Three of the five randomized trials included 1586 patients with known scleroderma associated interstitial lung disease. The annual reduction in the FVC was also significantly lower in scleroderma patients treated with nintedanib (MD 46.74, 95% CI 18.38-75.10, $p < 0.001$, $I^2 = 99\%$).

Conclusion: Our meta-analysis revealed that patients treated with nintedanib experienced a decelerated rate of interstitial lung disease progression compared to those who received a placebo, regardless of the underlying cause of the fibrosing interstitial lung disease.

Disclosure: Y. Khader: None; **F. Rawish**: None; **A. Abughrbyeh**: None; **S. Davis**: None; **S. Sidiki**: None; **P. Safavi**: None; **N. Altorok**: None.

Abstract Number: 1525

Chelation Therapy in the Management of Calcinosis Associated with Systemic Sclerosis

Alison Fernandes, Ashraf El-Meanawy and ME Csuka, Medical College of Wisconsin, Milwaukee, WI

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Calcinosis is a common complication of systemic sclerosis (SSc), though effective treatment options are limited. Of the several medical therapies that have been employed over the years, chelation with intravenous ethylenediaminetetraacetic acid (EDTA) has shown subjective and objective improvement, but its use has been limited by side effects, such as tetany, hypocalcemia, and kidney dysfunction. Using a slower rate of intravenous (IV) administration, toxicity was less frequently demonstrated in animal models. The objective of this project was to evaluate the safety and efficacy of EDTA in a case series of patients with SSc associated calcinosis.

Methods: Out of 34 identified patients with SSc associated calcinosis as defined by the 2013 ACR/EULAR classification criteria, three accepted the invitation to receive EDTA. These patients had clinical and radiographic evidence of one or more calcinotic deposits in either the trunk or the upper or lower extremities. Patients received EDTA chelation infusion (1.5gm EDTA in 500ml total volume IV) once weekly for total of 12 weeks. Radiographs of calcinotic burden were monitored prior to treatment and at 12 weeks. The primary endpoint was the percentage of patients without radiographic progression of calcinosis at 12 weeks. Key secondary endpoints included the completion of an unvalidated Mawdsley Calcinosis Questionnaire (MCQ) per permission of Dr. Saketkoo (1), and important safety signals, which included monitoring of renal function, and serum calcium.

Results: Three female patients with SSc were included, two limited cutaneous SSc and one diffuse cutaneous SSc. The median age was 63 years old. Two patients completed all 12 infusions and 1 patient discontinued therapy after 7 infusions due to financial constraints. No patient experienced clinical or radiographic progression while on therapy. The MCQ survey supported moderate disease burden. One patient reported subjective improvement which was reflected in the MCQ survey results at week 12. Increased 24hr urine calcium excretion was observed in one patient. Due to expected excretion of EDTA in the urine, the urinary calcium post infusion will be an under-estimate. A limitation of the study is that urinary calcium estimate using atomic emission was not done, which would avoid EDTA interference in assessing accurate total urinary calcium excretion. Other secondary endpoints revealed no adverse events occurred.

Conclusion: Low dose EDTA infused at a slow rate was well tolerated. No patients progressed on therapy, one patient reported subjective improvement, and measures of calcium excretion suggested successful chelation in one patient. Larger studies using higher dose of EDTA, are needed to determine the possible benefit of using EDTA to reduce the burden of calcinosis.

Disclosure: A. Fernandes: None; **A. El-Meanawy**: None; **M. Csuka**: None.

Abstract Number: 1526

Evusheld Efficacy and Safety in Autoimmune Rheumatic Diseases (AIRD) Treated by B Cell Depeting Therapy or Autologous Stem Cell Transplantation: A Prospective Observational Study

Lisa Kaly[1], mark Volevich[1], shiri keret[2], Abid Awisat[3], Aniela Shouval[1], Itzhak Rosner[4], Michel Rozenbaum[1], Nina Boulman[1] and Doron Rimar[1], [1]Bnai Zion Medical Center, Haifa, Israel, [2]Bnai Zion, Atlit, Israel, [3]Bney-Zion Medical Center, Baqa Elgharbiya, Israel, [4]Bnai Zion Medical Center/Technion, Haifa, Israel

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: B cell depleting therapy (rituximab) and Autologous Hematopoietic Stem Cell transplantation (AHSCT) result in impaired ability to mount a humoral immune response.

Evusheld (tixagevimab co-packaged with cilgavimab) is a passive vaccine against SARS-CoV-2.

The aim of our study was to evaluate prospectively the efficacy and safety of evusheld vaccine for preventing SARS-COV2 infection in patients with autoimmune rheumatic diseases (AIRD) treated with rituximab or AHSCT.

Methods: We compared rheumatoid arthritis and systemic sclerosis patients treated with rituximab or AHSCT, who agreed to receive evusheld, to patients who refused. The primary outcome was the risk of severe COVID19 infection (omicron variant) defined as pneumonia, hospitalization, or death. A secondary outcome was safety.

Table 1 - Clinical and epidemiological characteristics

		Evusheld injection		
Characteristic	N	No, N = 26[1]	Yes, N = 45[1]	p-value[2]
Gender(female)	71	20 (77%)	40 (89%)	0.2
Age	62	55 (15)	59 (12)	0.5
Autoimmun disease	70			0.5
RA		10 (38%)	18 (41%)	
SSC		9 (35%)	18 (41%)	
ANCA VASCULITIS		5 (19%)	3 (6.8%)	
OTHER		2 (7.7%)	5 (11%)	
Rituximab treatment	71	25 (96%)	45 (100%)	0.4
Bone marrow transplantation	71	1 (3.8%)	3 (6.7%)	>0.9
Weight (kg)	49	67 (11)	70 (17)	0.6
Globulin	33	2.84 (0.62)	2.75 (0.49)	0.4
Hypertension	37	4 (40%)	9 (33%)	0.7
Dyslipidemia	37	2 (20%)	5 (19%)	>0.9
Diabetes	37	0 (0%)	5 (19%)	0.3
Cardiovascular disease	35	1 (10%)	2 (8.0%)	>0.9
Smoker	33	0 (0%)	2 (8.3%)	>0.9
Malignancy	34	0 (0%)	2 (8.3%)	>0.9
Interstitial lung disease	37	6 (50%)	14 (56%)	0.7
Previous COVID infection	52	4 (36%)	20 (49%)	0.5
COVID current infection	68	12 (48%)	21 (49%)	>0.9
COVID severe infection	33	3 (33%)	1 (4.2%)	0.052
Mabthera (number of years)	39			0.5
<3		9 (82%)	19 (68%)	
>3		2 (18%)	9 (32%)	

[1] n (%); Mean (SD)

[2] Fisher's exact test; Wilcoxon rank sum test; Pearson's Chi-squared test

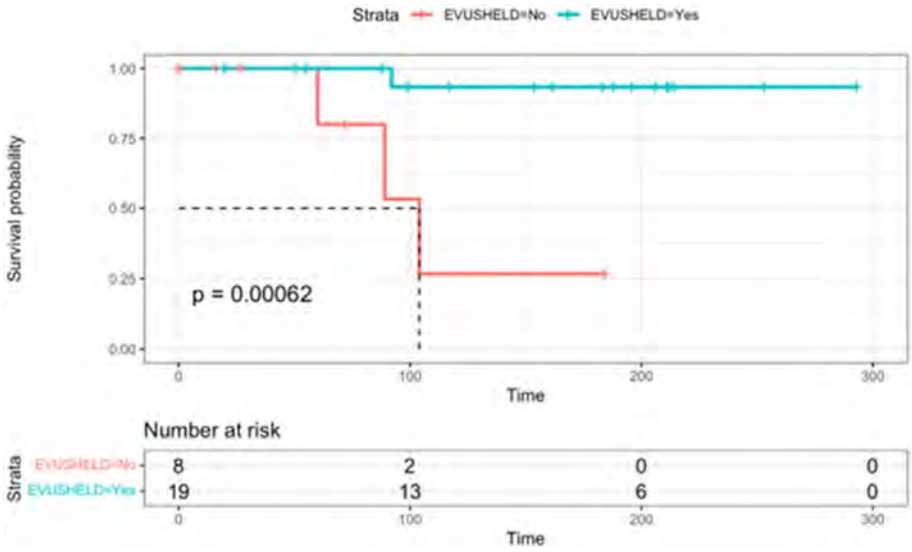


Figure 1 - The risk for severe COVID-19 infection - Kaplan-Meir Survival curve

Results: A total of 45 AIRD patients (41 treated by rituximab and 4 systemic sclerosis patients who underwent AHSCT) in the intervention group and 26 in the control group, were recruited. There was no difference between the groups with regard to sex, age, years of rituximab treatment, previous mRNA vaccination and serum immunoglobulins level (table1). No difference in the infection rate was found between intervention group and control group (21 (49%) versus 12 (48%) respectively). Four patients had a severe infection, 3 in the control group and 1 in the intervention group. Evusheld reduced the risk for severe infection by 94% (HR 0.06, 95% CI 0.01-0.76, p-value 0.017) (figure 1). There were no adverse events related to evusheld injection.

Conclusion: Evusheld decreased the risk for severe COVID19 infection in patients with AIRD treated with B-cell depleting therapy or after AHSCT in a period in which Omicron BA.5, BQ1 and BQ.1.1 variants were prevalent in Israel, with a favorable safety profile.

Disclosure: L. Kaly: None; **m. Volevich**: None; **s. keret**: None; **A. Awisat**: None; **A. Shouval**: None; **I. Rosner**: None; **M. Rozenbaum**: None; **N. Boulman**: None; **D. Rimar**: None.

Abstract Number: 1527

Acute Effects of Intravenous Iloprost on Finger Power Doppler Ultrasound in Scleroderma Patients

Sofia Testoni[1], **Luca Magnani**[2], Caterina Tomassini[3], Alessia Laneri[3], Carlo Salvarani[4] and PIERLUIGI MACCHIONI[2], [1]Università degli Studi di Modena e Reggio Emilia, San Giovanni in Persiceto, Italy, [2]Azienda USL -IRCCS di Reggio Emilia, Reggio Emilia, Italy, [3]Università degli Studi di Modena e Reggio Emilia, Modena, Italy, [4]Azienda USL -IRCCS di Reggio Emilia and Università di Modena e Reggio Emilia, Reggio Emilia, Italy

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: So far few studies explored ultrasound (US) as a tool to assess vascular subcutaneous involvement in patients affected by systemic sclerosis (SSc). We aim to evaluate the acute vascular effects of intravenous iloprost (ILO) infusion by power Doppler US (PDUS) examination at periungual (PU) and finger pulp (FP) subcutaneous areas in a consecutive series of SSc patients.

Table 1. Demographic, clinical and laboratory characteristics of the 38 patients. SD: standard deviation; ILD: interstitial lung disease; HAP: pulmonary arterial hypertension; ERA: endothelin receptors antagonists; CCB: calcium channel blockers; PDE5i: Phosphodiesterase type 5 inhibitors; ENA: extractable nuclear antigen; ACA: Anti-centromere antibody.

	number (%)	Mean ± SD	Median (range)
Disease Duration (years)		13.3±10.5	10 (1-40)
Age (years)		55.9±13.1	54.5 (31-78)
Female/male	35/3 (92/8%)		
Iloprost therapy duration (years)		6.4±5.9	4.0 (0.2-25.0)
Disease features			
Digital Ulcers	26 (68.4%)		
Calcinosis	12 (31.6%)		
Esophageal involvement	23 (60.5%)		
Arthritis	6 (15.8%)		
ILD	12 (31.6%)		
HAP	8 (21.1%)		
Concomitant vasoactive therapy			
ERA	16(42%)		
CCB	17 (44.7%)		
PDE5i	1 (2.6%)		
ENA antibodies			
Topoisomerase I	17 (44.7%)		
Negative	3 (7.9%)		
ACA	15 (39.5%)		
Other	7 (18.4%)		
Cutaneous subset of disease			
Diffuse	19 (50%)		
Limited	16 (42.1%)		
Other	3 (7.9%)		

Table 2. Values of Total PD score of the 77 observations before and after iloprost infusion. SRM = Standardized Response Mean (< 0.20 = trivial, 0.20-0.40 = small, 0.40-0.80 = moderate; > 0.80 = good).

	PD score T0	PD score T1	SRM*	p
Total PD score (TotS)	9.43±6.34	16.1±6.6	0.88	<0.001
Total Periungueal PD score (TotPU)	5.21±3.37	9.17±3.7	0.85	<0.001
Total Finger Pulp PD score (TotFP)	4.22±3.75	6.9±4.22	0.68	<0.001

Methods: Seventy-seven consecutive observations were done in 38 SSc patients (ACR/EULAR criteria). FP and PU vascularization of the 1st, 2nd, and 3rd finger of the dominant hand were evaluated before and after ILO infusion (dosage 0.5-2.0 ng/kg/min for 4-6 hours) using an Esaote MylabClassC, (Genoa, Italy) machine equipped with a 22-8 Mhz multifrequency linear probe. The image with the highest presence of PD signal at PU and FP for each finger was scored according to a semiquantitative 0-5 scale (0 = no signal, 5 = signal of healthy controls) and summed up to obtain a total patient PD score (TotS). Single finger PU PD scores were summed to obtain total PU PD score (TotPU). Single finger FP PD scores were summed to obtain total FP PD score (TotFP). Values before and after ILO treatment were compared by T-test for paired samples. No improvement in TotS was defined as a difference between T1 and T0 observation ≤ 0; improvement if the difference between T1 and T0 was 1. Clinical demographic and US data entered in a multivariate logistic regression analysis to evaluate factors predictive of TotS improvement.

Results: Clinical and laboratory features of the enrolled patients are reported in Table 1. The effects of ILO infusion on total PD scores are reported in Table 2. TotS was 9.43±6.34 at T0 and increased to 16.1±6.6 after treatment (**p= < 0.001**). TotS improved in 60 observations, while in 17 there was no variation or worsening. TotPU was 5.21±3.37 at T0 and increased to 9.17±3.7 after treatment (**p= < 0.001**). TotFP was 4.22±3.75 at T0 and increased to 6.9±4.22 at T1 (**p= < 0.001**). At multivariate logistic regression analysis concomitant therapy with calcium channel blockers (CCB) was predictive of PD total score improvement > 0 (**OR 4.53**; 95% CI 1.14-18.1 **p=0.032**) and concomitant pulmonary arterial hypertension (HAP) was associated to lack of response (**OR 0.27**; 95% CI 0.08-0.94 **p=0.04**).

Conclusion: PDUS examination of the PU and FP area can demonstrate an ILO acute vascular effect in SSc patients. Therapy with CCB and presence of HAP impact on PD score improvement.

Disclosure: S. Testoni: None; **L. Magnani**: None; **C. Tomassini**: None; **A. Laneri**: None; **C. Salvarani**: None; **P. MACCHIONI**: None.

Abstract Number: 1528

Intravenous or Subcutaneous Immunoglobulins as Potential Treatment for Gastrointestinal, Cutaneous and Vascular Involvement in Systemic Sclerosis: Data from an Italian Cohort of 65 Patients

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Treatment of systemic sclerosis (SSc) is challenging, and in the last 2 decades there has been an increasing interest for immunoglobulin (Igs) treatment as it exhibits both immunomodulatory and antifibrotic properties. Currently, its efficacy on gastrointestinal (GI), skin and muscle involvement has been described only in case series with limited numbers of patients. With this study we wanted to evaluate the efficacy of Ig therapy on GI, cutaneous, and vascular involvement of SSc.

Table 1. Variation trend and significancy of clinical items from BL to T12

	BL	T6	P value (BL-T6)	T12	P value (T6-T12)
GER, n (%)	59 (90.8)	31 (49.2)	**p<0.0001**	15 (25.9)	**p<0.001**
Diarrhea, n (%)	31 (49.2)	12 (19.4)	**p<0.0001**	4 (6.9)	0.0771
mRSS, median (min-max)	10 (0-50)	6 (0-34)	**p<0.0001**	3 (0-23)	**p<0.0001**
Digital edema, n (%)	50 (76.9)	28 (44.4)	**p<0.0001**	17 (30.9)	0.131
Digital ulcers, n (%)	25 (38.5)	9 (14.1)	**0.0022**	3 (5.3)	0.0736
VCP, n - Normal, n (%) - Early, n (%) - Active, n (%) - Late, n (%)	64 - 2 (3.1) - 14 (21.9) - 29 (45.3) - 19 (29.7)	45 - 7 (15.6) - 7 (15.6) - 16 (35.6) - 15 (33.3)	**0.00448**	42 - 8 (19.0) - 10 (23.8) - 12 (28.6) - 12 (28.6)	0.00596

Methods: A retrospective observational study was conducted enrolling patients with diagnosis of SSc (ACR/EULAR 2013) and that were treated with Ig (intravenously or subcutaneously) at a 2 gr/kg/month dosage for at least 6 months. Demographical data, antibodies positivity, associated therapies (vasoactive and immunosuppressants) and disease duration were

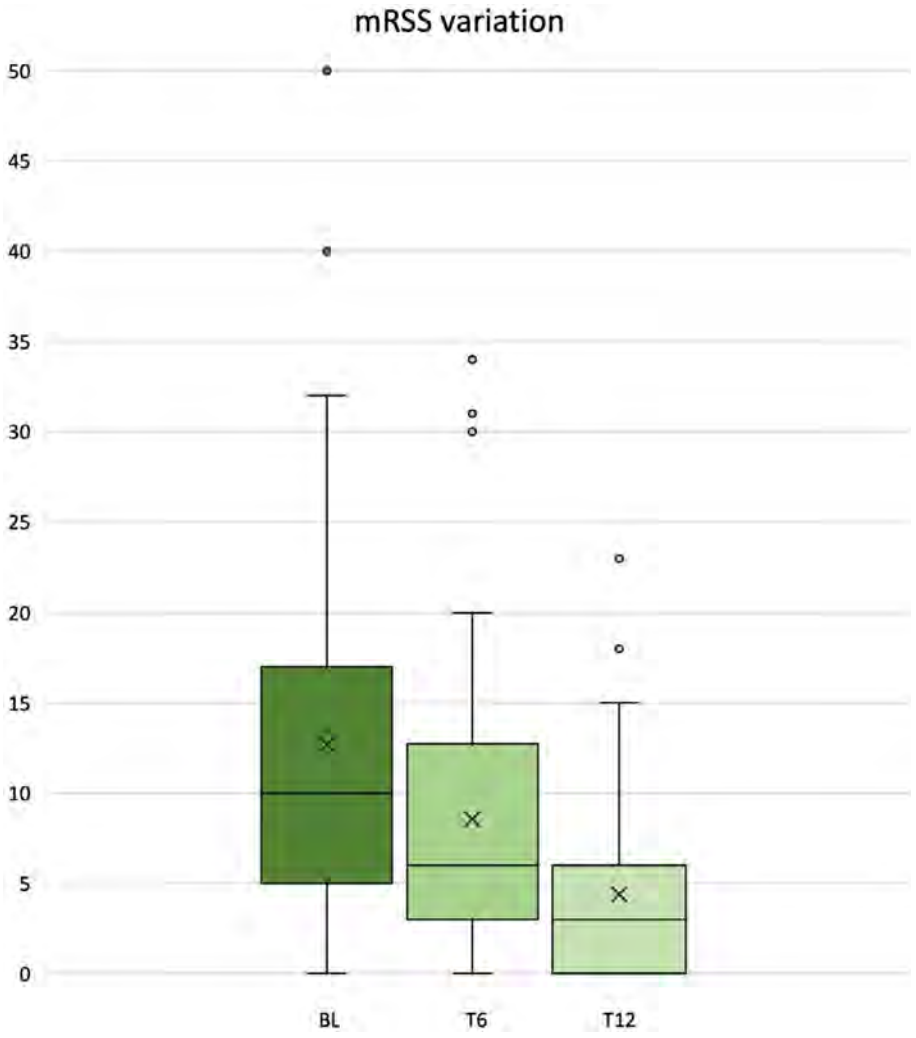

Figure 1. Variation of mRSS from BL to T12

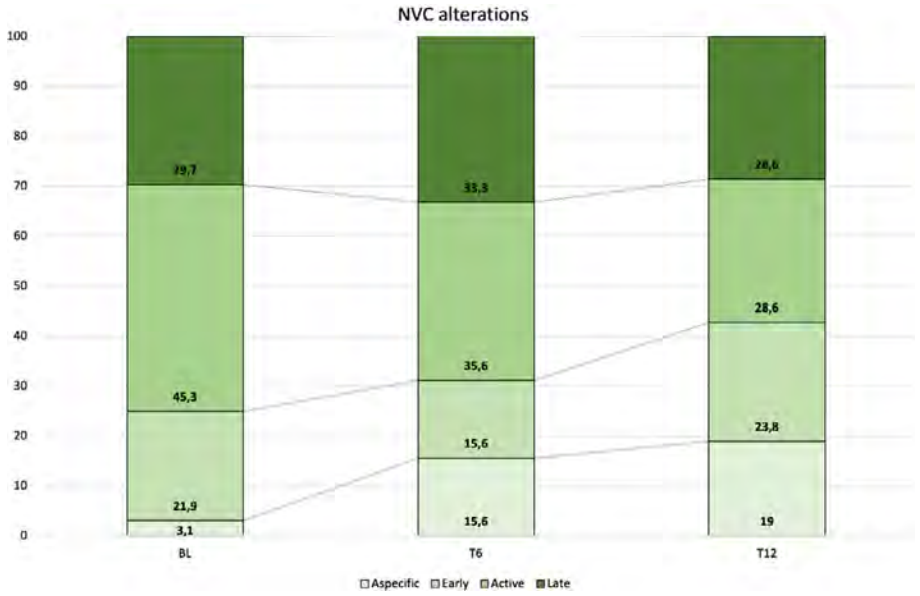

Figure 2. Variation of NVP from BL to T12

collected from clinical records. Moreover, the presence of diarrhea, gastroesophageal reflux (GER), digital edema, digital ulcers (DUs), as well as the modified Rodnan Skin Score (mRSS) and videocapillaroscopic pattern (VCP; normal, early, active, late) were assessed at baseline (BL) and after 6 (T6) and 12 (T12) months of Ig therapy. Variation of these items from BL to T6 and T12 was tested by Paired T Test, Mc Nemar test, Wilcoxon's signed rank test as appropriate. Regression analysis were than performed to assess influence of possible confounders variables (vasoactive and immunosuppressants drugs) on outcome variables (VCP, digital edema, DUs)

Results: Sixty-five patients were enrolled, and their clinical data were analyzed. Mean age was 56.18 (± 12.32) and median disease duration was 10.00 years (min-max 1.00-38.00). Sixty-three patients (96.9%) were ANA positive, with positivity for anti-centromeric antibodies in 23 (35.4%), Scl-70 in 27 (41.5%) and RNA polymerase III in 8 (12.3%) patients. Fifty-five patients received the treatment intravenously, the remaining subcutaneously. Table 1 summarizes the trend and significancy of clinical items from BL to T12. At BL, 49.2% of patients complained diarrhea, 90.8% GER, 76.9% digital edema; 38.5% DUs. VCP was normal in 3.1% of patients, early in 21.9%, active in 45.3%, and late in 29.7%. Also, median mRSS was 10 (min-max 0-50). At T6, median mRSS significantly improved [6 (min-max 0-34), $p< 0.0001$] together with VCP (normal in 15.6%, early in 15.6%, active in 35.6%, and late in 33.3%, $p=0.00448$). Moreover, a significant reduction of the prevalence of GER (49.2%, $p< 0.0001$), diarrhea (19.4%, $p< 0.0001$), digital edema (44.4%, $p< 0.0001$), DUs (14.1%, $p=0.0022$) was found. At T12, median mRSS improved even more [3 (min-max 0-23), $p< 0.0001$] along with VCP (normal in 19.0%, early in 23.8%, active in 28.6%, and late in 28.6%, $p=0.00596$). Also, the prevalence of GER was lower (25.9%, $p< 0.001$). Regression analysis did not evidence any influence of other treatments on the tested outcome variables.

Conclusion: Our data confirm the efficacy of Ig on GER and diarrhea and skin involvement and, for the first time, also a possible positive effect on VCP. Further studies on larger samples are required to confirm these findings.

Disclosure: F. Bonomi: None; **A. Damiani**: None; **C. Coccia**: None; **J. Levani**: None; **e. Fiorentini**: None; **s. peretti**: None; **G. Lepri**: None; **m. orlandi**: None; **f. bartoli**: None; **m. Matucci Cerinic**: accelerong, 2, 6, actelion, 2, 6, bayer, 2, 6, biogen, 2, 6, Boehringer-Ingelheim, 2, 6, Chemomab, 2, 6, corbus, 2, 6, CSL Behring, 2, 6, Eli Lilly, 2, 6, galapagos, 2, 6, Inventiva, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 6, Mitsubishi, 2, 6, Pfizer, 2, 6, regeneron, 2, 6, Roche, 2, 6, samsung, 2, 6; **s. bellando randone**: None; **s. guiducci**: None.

Abstract Number: 1529

Mycophenolate Mofetil Use in Clinical Practice: Persistence on Therapy and Long-term Adverse Events in a Multicentric Cohort of Scleroderma Patients

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention

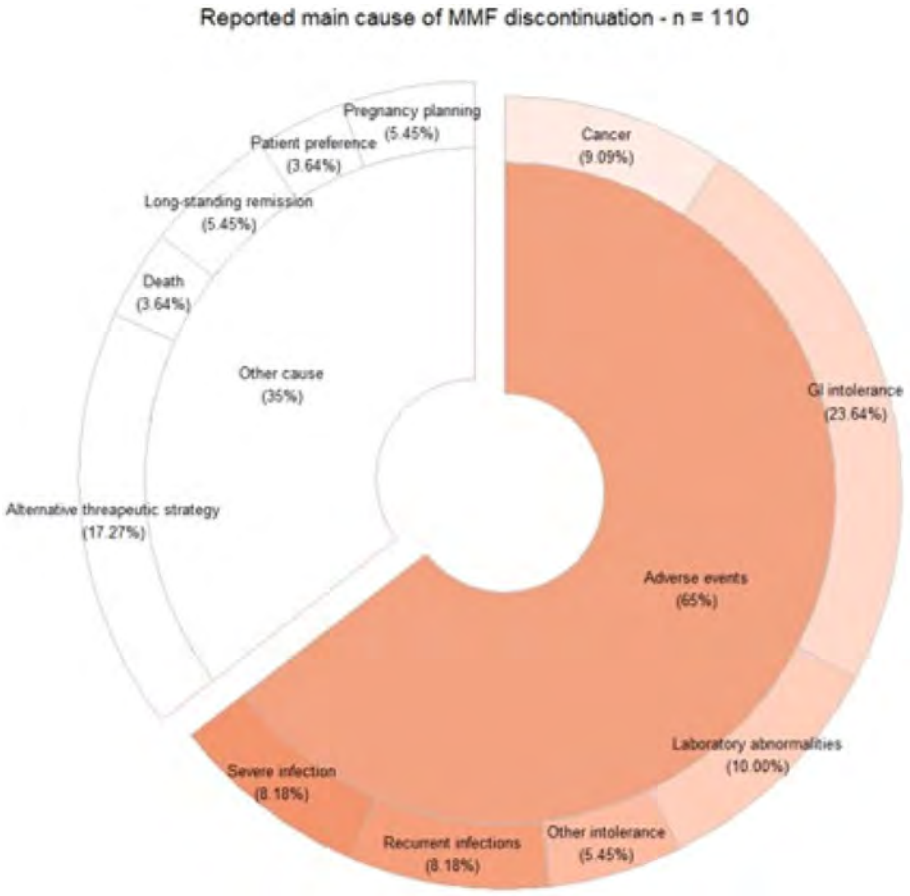
Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Mycophenolate mofetil (MMF) is a first-line immunosuppressant treatment for systemic sclerosis (SSc), particularly for patients with interstitial lung disease (ILD) and diffuse skin involvement. MMF persistence reflects its efficacy, the risk or occurrence of adverse events (AEs), the risk of relapse after discontinuation, and the availability of therapeutic alternatives. Real-life evidence about early and long-term adverse events (AEs) associated with the use of MMF in SSc is lacking, and predictors of drug discontinuation are not identified yet. We aimed to investigate a) the incidence and causes of MMF discontinuation due to AEs in SSc patients and b) the incidence and association of severe infections, lower airway infections, and unbearable gastrointestinal symptoms leading to MMF discontinuation.

Methods: Medical records of SSc patients treated with MMF from January 2012 to December 2021 and followed up in 9 tertiary centers were retrospectively collected and evaluated. Clinical and demographic data included AEs (i.e., infections, gastrointestinal (GI) intolerance, laboratory abnormalities, new cancer diagnosis) and reasons for dosage reduction or discontinuation. Infection severity was ranked according to the GREFIG study classification system. A competing risk analysis was performed to explore the association of AE-related MMF discontinuations with alternative causes of MMF discontinuation as a competing risk.

Results: Data from 545 SSc patients observed for 3.1 years (IQR 1.4-4.9) were analyzed. Combination therapy with steroids was recorded in 37.0% of patients, while in 14.7% of cases, MMF was associated with additional immunosuppressants. Almost 25% of patients did not tolerate the prescribed dose of MMF because of drug-related AEs. MMF discontinuation rate was 6.6/1000 patients-year (95% IC 5.3-8.0) with a 70.3% 5-year retention rate (95% IC 0.65-0.76). Gastrointestinal intolerance and infections (GREFIG grades 2-3) were the most common AEs leading to discontinuation with



different time patterns. Infection severity tended to increase over time. Respiratory infections were the most commonly reported infections. The risk of major infections (grades 2-3) was associated with male gender (HR 1.9, 95% IC 1.3-2.9), anti-centromere antibody (HR 1.7, 1.1-2,6), pulmonary hypertension (HR 2.0, 95% IC 1.3-3.0), late capillaroscopy pattern (HR 1.5, 95% IC 1.0-2.3), and concomitant COPD (HR 3.0, 95% IC 1.4-6.4) at univariate analysis.

Conclusion: One in four SSc patients had to reduce or discontinue MMF due to adverse events, primarily gastrointestinal intolerance and infections. Factors linked with microvascular impairment served as a risk factor for severe infections during MMF treatment.

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Abstract Number: 1530

Outcomes in Patients with Systemic Sclerosis Following Lung Transplantation: An Italian Multicentre Experience

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Lung transplantation (LT) is gaining ground in managing advanced ILD in SSc patients. However, concerns remain among surgeons due to SSc's complexity, multiorgan involvement (including oesophagus), and heightened risk of post-transplant complications. To date, outcomes focused on survival rates, lacking a comprehensive evaluation of how LT and immunosuppressive therapy affect SSc disease activity and progression. The aim of the study was to evaluate in a cohort of SSc patients, survival, complications, and post-LT outcomes regarding extra-pulmonary involvement, disease activity according to the EUSTAR activity index, and progression of lung scleroderma function

Methods: A retrospective analysis was conducted on SSc patients post-lung transplantation. Outcome variables (mRss, FVC, ulcers, EUSTAR activity, NVC) were evaluated at baseline, 6 months, 1 year, and 2 years. The study aimed to assess cutaneous involvement, lung function, ulcers, and disease activity in these patients

Results: We evaluated 11 patients, 9 with dcSSc and 2 lcSSc. M/F=8/3. Median disease duration: 10.33 yrs (IQR 9,42). Main reason for LT was ILD-related end-stage lung disease (11/11); 6/11 patients had concomitant PAH. NSIP pattern at HRTC scan was the most common one (9/11). Bilateral LT was performed in all patients but 1, who underwent unilateral procedure. Maintenance therapy with tacrolimus was the standard of care after LT and the mean dosage decreased from 4.31 mg at 6 months to 1.22 at 2 years. Perioperative complications included 4 acute rejects, with only 1 *exitus*. The survival at 1 and 2 years was of 100%, and 81,8% respectively. Mean value of FVC significantly increased from 42±10% at baseline, to 63.6±18% at 6 months, 69.8±22% at 1 year, and 76.6±6% at 2 years ($p< 0.001$ for all). Mean mRSS at baseline was 6.8 decreasing at 6 months (4.6), 1 yr (4.2) and 2yr (1.5) ($p< 0.0001$). 7 patients with active ulcers before transplantation experienced their resolutions after 6 months, with just one patient relapsing after 1 year, and another one after 2 years. In the same patients, the NVC features improved from late to active pattern. The EUSTAR activity index decreased progressively over time from 3.23 ±1.5 at baseline to 0,7 ±0.6 after 2 years ($p< 0.0001$)

Conclusion: To our knowledge this is the first study evaluating clinical outcomes and disease activity in SSc patients following LT. Previous studies have primarily focused on survival and post-transplant complications. The survival rate was 82% with no unexpected complications. Despite the underlying disease, we observed improvements in FVC, and disease activity scores consistently decreased after LT. These results were sustained throughout the follow-up period. Our findings confirm

Table 1: baseline characteristics of cohorts 1 & 2 after propensity matching

Table 1: baseline characteristics of cohorts 1 & 2 after propensity matching

Demographics						
Cohort		Mean ± SD	Patients	% of Cohort	P-Value	Std diff.
1	Current Age	66.1 +/- 9.8	92	100%	0.988	0.002
2		66.1 +/- 10.5	92	100%		
1	Age at Index	63.8 +/- 9.7	92	100%	0.971	0.005
2		63.8 +/- 10.5	92	100%		
1	White		83	90.2%	0.636	0.070
2			81	88.0%		
1	American Indian or		10	10.9%	1	<0.001
2	Alaska Native		10	10.9%		
1	Female		44	47.8%	0.658	0.065
2			47	51.1%		
1	Unknown Ethnicity		10	10.9%	1	<0.001
2			10	10.9%		
1	Not Hispanic or Latino		89	96.7%	0.700	0.057
2			88	95.7%		
1	Hispanic or Latino		10	10.9%	1	<0.001
2			10	10.9%		
1	Black or African		10	10.9%	1	<0.001
2	American		10	10.9%		
1	Male		48	52.2%	0.658	0.065
2			45	48.9%		
1	Unknown Race		10	10.9%	1	<0.001
2			10	10.9%		
1	Asian		0	0%	--	--
2			0	0%		

Table 2- Use of immunosuppressants in cohorts 1 & 2 after propensity matching

Table 2- Use of immunosuppressants in cohorts 1 & 2 after propensity matching both cohorts

Medication						
Cohort		Mean ± SD	Patients	% of Cohort	P-Value	Std diff.
1	mycophenolate mofetil		39	42.4%	0.365	0.134
2			33	35.9%		
1	rituximab		10	10.9%	1	<0.001
2			10	10.9%		
1	methotrexate		10	10.9%	1	<0.001
2			10	10.9%		
1	azathioprine		10	10.9%	1	<0.001
2			10	10.9%		
1	cyclophosphamide		10	10.9%	1	<0.001
2			10	10.9%		
1	tacrolimus		0	0%	--	--
2			0	0%		
1	tofacitinib		10	10.9%	0.001	0.494
2			0	0%		

that LT is a viable therapeutic option for progressive, end-stage lung disease in SSc. Prolonged immunosuppressive therapy and improved tissue perfusion may contribute to the persistent reduction in disease activity.

Disclosure: C. Iannone: None; **M. Pellico**: None; **L. Corinna Morlacchi**: None; **V. Rossetti**: None; **M. Vicenzi**: None; **P. Airò**: None; **M. Saracco**: None; **A. iagnocco**: None; **L. Beretta**: None; **A. Severino**: None; **E. Zaccara**: None; **p. Faggioli**: None; **F. Cacciapaglia**: None; **S. Stano**: None; **S. Cavalli**: None; **A. Minniti**: None; **g. Trignani**: None; **f. Blasi**: None; **R. Caporali**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celltrion, 2, 6, Fresenius Kabi, 2, Galapagos, 2, 6, Janssen, 2, 6, Lilly, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, Sandoz, 2, 6, UCB, 2, 6; **N. Del Papa**: None.

Abstract Number: 1531

A Retrospective Analysis of the Efficacy of Nintedanib in Connective Tissue Disease-Associated Interstitial Lung Disease (CTD-ILD): A TriNetX Database Study

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

<**Background/Purpose:** Connective tissue diseases such as scleroderma are frequently associated with interstitial lung disease (ILD). Detection of autoantibodies is crucial in characterizing disease phenotypes, but there remains a lack of substantial data on the association of some autoantibodies present in scleroderma patients with specific ILD patterns. We sought to investigate possible association, describe the phenotypes of scleroderma seen in our study cohort, and review findings from other studies.

Methods: The cohort included adults with scleroderma and ILD who were treated at Mayo Clinic between January 2011 and December 2021. Baseline demographic, serologic, and imaging data were extracted from the electronic medical record. Continuous variables were summarized with median and range, and categorical variables were summarized with frequency and percentage (%). The Kruskal-Wallis Rank Sum test was used for continuous measures and the Chi-square test was used for categorical measures. All tests were two-sided and p-values less than 0.95 were considered to be statistically significant. Analysis programming was performed by R-studio with R version 4.1.2.

Results: A total of 454 patients with both scleroderma and ILD were included in the study. The study cohort had a mean age of 62 years, and 103 patients (22.7%) were males. ILD patterns analyzed included NSIP (83.3%), UIP (11%), probable UIP (2.9%), indefinite UIP (2.9%), OP (1.5%) and LIP (2%). The antibody and symptoms were determined for patients with and without each of these ILD patterns. NSIP patients were more likely to have anti-Scl70 antibodies compared to patients without NSIP (p=0.01). OP patients were more likely to have anti-PM/Scl antibodies compared to patients without OP (p=0.006), and LIP patients were more likely to have anti-U1 snRNP antibodies compared to patients without LIP (p=0.002). LIP patients were significantly less likely to have antiScl70 antibodies than patients without LIP (p=0.025). Additionally, UIP patients were also less likely to have anti-Scl70 antibodies than patients without UIP (p=0.017). There were no

clinically significant findings of anti-centromere antibodies or anti-RNA Pol III antibodies in any of the ILD patterns. No symptoms had a clinically significant association with the ILD pattern groups.

Conclusion: Our study examined associations between serologic data and ILD patterns and demonstrated a statistically significant association of anti-Scl70 antibodies with NSIP and antiPM/Scl antibodies with OP. There also appears to be an association between anti-U1 snRNP antibodies and LIP, which has not been demonstrated in the literature thus far aside from another observational study. LIP and UIP patterns were significantly less likely to have association with anti-Scl70 antibodies. We did not find any statistically significant association between anticentromere antibodies and specific ILD patterns. Finally, our study suggests that antibodies may develop in scleroderma but are not necessarily associated with development of ILD. Autoantibodies offer an invaluable tool in predicting disease outcomes and further studies are needed to elucidate this, especially with regards to scleroderma-associated ILD.

Disclosure: J. Uppal: None; **K. Vadlamudi**: None; **S. Hasan**: None; **A. Kattubadi**: None; **M. Mishra**: None; **S. Umer**: None; **S. Hayat**: None; **K. Muzaffar**: None.

Abstract Number: 1532

Safety and Microvascular Effects of Long-term Treatment with Aminaphtone in Systemic Sclerosis Patients: A Retrospective Analysis

Alberto Sulli[1], Rosanna Campitiello[1], Emanuele Gotelli[1], Andrea Cere[1], Elvis Hysa[2], Tamara Vojinovic[2], Carlotta Schenone[1], Carmen Pizzorni[1], Sabrina Paolino[1], Elisa Alessandri[1], Vanessa Smith[3] and Maurizio Cutolo[4], [1]Laboratory of Experimental Rheumatology and Academic Division of Rheumatology, Department of Internal Medicine, University of Genoa, IRCCS San Martino Polyclinic Hospital, Genoa, Italy, [2]Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS San Martino Polyclinic Hospital, Genova, Italy, [3]Ghent University Hospital, Gent, Belgium, [4]Laboratory of Experimental Rheumatology, Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS San Martino Polyclinic, Genova, Italy

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: The progressive endothelial damage is one of the hallmarks of systemic sclerosis (SSc), an autoimmune connective tissue disease characterized by organ fibrotic involvement. Aminaphtone is a synthetic moleculeregistered for clinical use to treat microvascular disorders that interferes with the expression of vasoactive mediators released by activated endothelial cells [1,2].Nailfold videocapillaroscopy (NVC) is a reliable and non-invasive tool to assess microvascular damage and is considered a morphological biomarker for detection of disease progression in SSc [3].The aim of this retrospective study was to evaluate the safety data and the possible beneficial effects on microcirculation induced by aminaphtone when added to standard therapy (ST) in SSc patients during a four-year follow-up.

Methods: Seventy-five Caucasian SSc patients (7 males and 68 females, mean age 68±15 years; mean disease duration 13 ±7 years) (according to 2013 EULAR/ACR criteria) with secondary Raynaud's phenomenon (RP) started aminaphtone treatment (75 mg BID) in addition to ST. NVC was performed at baseline, after 1 year and 4 years of treatment, adopting the SSc-pattern classification (‘‘Early’’, ‘‘Active’’, ‘‘Late’’ NVC SSc-patterns) [4]. The timing of transition between capillaroscopic

patterns in SSc treated with aminaphtone and ST was compared to SSc patients only treated with ST [5]. The study was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice, and all patients provided written informed consent.

Results: No life-threatening side effects were reported in the SSc cohort during 4 years of treatment. However, 10% of patients discontinued aminaphtone treatment due to mild intolerance due to well-known adverse events (headache 2.7%, itching 1.3%, others 6%). NVC SSc-patterns in SSc patients treated with aminaphtone remained stable during the observational time frame in 72% of cases, in 8 of the patients (14.7%) was observed a dynamic transition from "Early" to "Active" or from "Active" to "Late" pattern (2.7% and 10.7%, respectively). Of note, SSc patients treated with aminaphtone showed a slower timing of transition between NVC patterns compared to the control group with ST alone (from "Early" to "Active" 57.6 ± 37.4 months vs 28 ± 20 months; P= 0.12 and from "Active" to "Late" 48± 1.0 months vs 36 ± 29 months; P =0.42), even if this difference was not statistically significant.

Conclusion: Aminaphtone seems to be a safe and well tolerated drug in SSc patients with secondary RP during long term treatment. NVC scleroderma-pattern stability over time suggests a possible additional therapeutical effect as a concomitant treatment to ST in SSc patients with RP, but the suggestion deserves further investigations.

1. Gotelli E et al. Pharmaceuticals (Basel) 2023;16(4):569.2. Ruaro B et al. Front Pharmacol 2019;10:293. 3. Cutolo M et al. Nat Rev Rheumatol 2010;6, 578–87. 4.Smith V et al. Autoimmun Rev. 2020;19(3):102458. 5. Sulli A, et al. Arthritis Rheum. 2012;64(3):821-25

Disclosure: A. Sulli: None; **R. Campitiello**: None; **E. Gotelli**: None; **A. Cere**: None; **E. Hysa**: None; **T. Vojinovic**: None; **C. Schenone**: None; **C. Pizzorni**: None; **S. Paolino**: None; **E. Alessandri**: None; **V. Smith**: Boehringer Ingelheim, 2, 5, 6, 12, Support for travel, Galapagos, 6, Janssen-Cilag, 1, 2, 5, 6; **M. Cutolo**: Amgen, 5, Boehringer Ingelheim, 5, Bristol-Myers Squibb, 5, Lab.Baldacci, 5.

Abstract Number: 1533

Long-term Use of Rituximab in Systemic Sclerosis: A Real-life Italian Multicentre Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II: Clinical Trial, Treatment & Intervention
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rituximab(RTX) has been used for the management of systemic sclerosis(SSc). Its efficacy has been recently confirmed in a phase III clinical trial with extension observation up to 48 weeks, but long term data are limited. We analyzed the real life long-term use of RTX in SSc Italian patients.

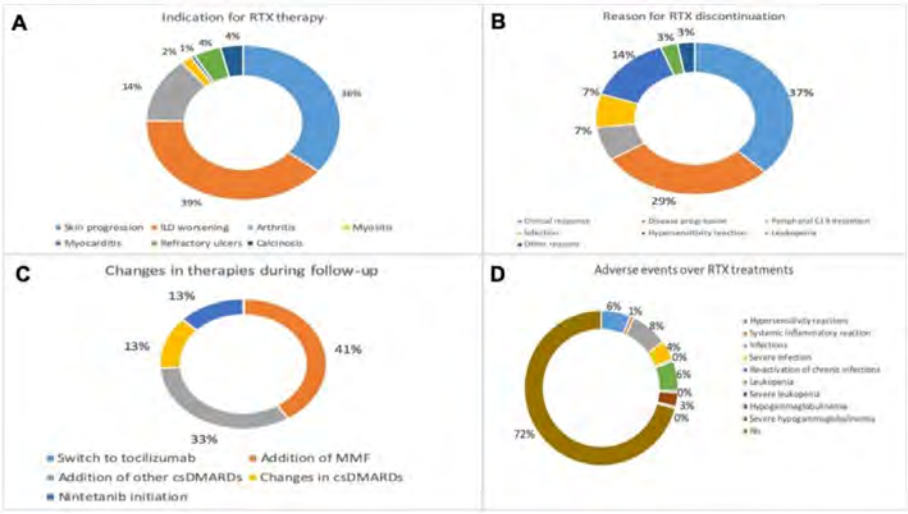
Methods: SSc patients treated with RTX and with a follow-up ^{3}36 months were included. Disease features at baseline, 6, 12, 24 months and latest available follow-up were analyzed. Persistence of RTX, reasons for RTX introduction and suspension, immunosuppressive therapy (ISTs) modifications, and RTX-related adverse events (AEs) were recorded.

Results: the main characteristics of SSc patients are presented in on Table 1 (median follow-up was 72(52-96) months). RTX was primarily started for lung (38.8%), skin (36.2%), or arthritis (13.8%) worsening (Figure 1A). Patients were treated with RTX for a median of 42.5(26.0-69.7) months: 138 patients(90.8%) were treated with ^{3}1 RTX course. In the entire cohort, mRSS significantly improved both at 6 months and at final follow- (mRSS: 11.9±8.0 and 8.3±7.4 vs 16.5±9.6) and in dcSSc patients with progressive skin involvement (mRSS: 15.6±9.6 and 9.2±7.9 vs 21.0±10.8)($p< 0.001$ for all). Mean predicted (%) FVC and DLCO remained stable at 6 months and at final follow-up, both in the entire cohort (FVC: 105.1±84.2 and 87.0±23.5 vs 91.1±49.3; DLCO: 69.4±23.2 and 63.0±26.5 vs 62.1±19.7) and in patients with ILD (FVC: 88.7±38.2 and 82.9±22.5 vs 89.0±54.8; DLCO: 63.8±18.0 and 56.9±18.8 vs 58.7±19.9)(p= ns for all). in 41 patients(27.0%) ILD worsened, defined as a decline in pFVC ≥5% or in pDLCO ≥10% at 12±3 months. During follow-up, in 26 patients (17.1%)

Table 1. Demographic and clinical characteristics

	Patients n=152
Age (years), mean ± SD	54.7 ± 12.3
Females, n (%)	121 (79.6)
Disease duration (months), mean ± SD	146.9 ± 79.2
Diffuse cutaneous disease, n (%)	118 (77.6)
Anti-topoisomerase I, n (%)	96 (63.2)
Anti-centromere, n (%)	25 (16.4)
Interstitial lung disease, n (%)	115 (75.7)
Gastrointestinal involvement, n (%)	96 (63.2)
History of digital ulcers, n (%)	91 (59.9)
Musculoskeletal involvement, n (%)	63 (41.4)
Myositis, n (%)	21 (13.8)
Calcinosis, n (%)	26 (17.1)
Pulmonary arterial hypertension, n (%)	21 (13.8)
Primary heart involvement, n (%)	18 (11.9)
Renal involvement, n (%)	2 (1.4)
Previous and concomitant therapies	
Previous csDMARDs therapy, n (%)	141 (92.8)
Concomitant csDMARDs, n (%)	107 (70.4)
Rituximab treatment*	
Rituximab started for multiple clinical indications, n (%)	41 (27.0)
Rituximab routinely planned every 6 months, n (%)*	78 (51.3)
Rituximab re-treatment based on clinical status, n (%)*	74 (48.7)
Rituximab discontinuation, n (%)	70 (46.0)

SD= standard deviasion; n= number; csDMARDs=conventional synthetic disease modifying anti-rheumatic drug. *RTX administered at 1 gr repeated after 15 days in 98.7% of cases.



RTX= rituximab; ILD=interstitial lung disease; MMF=mycophenolate mofetil; csDMARDs= conventional synthetic disease modifying anti-rheumatic drugs.

RTX was stopped for complete clinical response, especially in dSSc ($p< 0.001$); median time to discontinuation was 30.0 [24.0-48.0] months. RTX was stopped due to disease progression in 20 patients (13.2%) and due to infections in 5 (3.3%) (Figure 1B-C). AEs were recorded in 42 patients (27.6%)(Figure 1D). Discontinuation for both clinical remission or AEs was not influenced by indication for RTX, disease features or therapeutic scheme (p=ns).

Conclusion: our study shows that in Italian SSc patients, RTX is used as a long-term immunosuppressive drug due to its clinical effectiveness and satisfactory safety profile. The most common reason for RTX suspension was indeed clinical remission, whereas infectious concerns were only marginal.

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Abstract Number: 1534

ANCA-associated Vasculitis Incidence in a Norther Spanish Health Region

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV) includes granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA) or microscopic polyarteritis (MPA). Precise estimation of the incidence of AAV has been difficult due to the absence of reliable diagnostic criteria.

To estimate the incidence in a Northern Spanish population-based cohort.

Methods: Population-based study of 132 patients diagnosed with small vessel vasculitis between 1994 and 2022 in a tertiary hospital. Finally, 98 patients were included as AAV according to ACR/EULAR 2022 criteria (1). Incidence was estimated by gender, age, and year of diagnosis.

Results: AAV was diagnosed in 98 (49 women/ 49 men) patients: GPA (n=47, 48%) MPA (n=37,37.8%) and EGPA (n=14, 14.3%). Annual incidences were estimated in AAV (**Figure**). GPA annual incidence in our population area in the 1994-2022 period was 2.81 per 1,000,000 people, 95% CI: 3.77-1.85 (2.82 [4.35-1.29] in males and 2.80 [4.50-1.09] in females). An upward trend in annual incidence over time was observed with rates ranging from 1.88 in 1994 to 6.84 in 2022 (weak correlation; r^2=0.2729). On the other hand, MPA annual incidence was 2.23 per 1,000,000 people (1.92 [3.55-0.27] in males and 2.46 [4.07-0.85] in females). Rates ranged from 1.88 in 1994 to 1.71 in 2022 with an upward trend over time (very weak correlation; r^2=0.0746). In the case of GEPA, annual incidence was 0.83 per 1,000,000 people, 95% CI: 1.72-0.06 (1.22 [2.74-0.30] in males and 0.46 [2.29-1.37] in females). As in the other types of AAV, there was an upward trend over time with variations of from 1.88 in 1999 to 3.42 in 2022 (weak correlation; r^2=0.3335). A comparison between different geographical areas is summarized in **Table**. Wide variations in annual incidence per million were observed in all AAV (GPA 2.1-34; MPA 2.23-10.4; EGPA 0.64-2.7). The highest annual incidence of all AAV was observed in nordic countries and central Europe while the lowest in Southern Europe.

Conclusion: There seems to be a progressive increase in incidence of AAV over the years in the studied population. Annual incidence in our population was similar to that of other southern European countries.

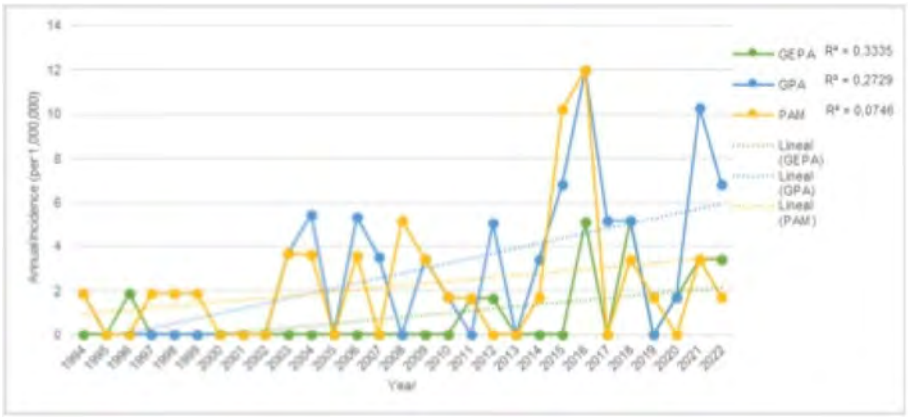

Figure . Annual incidence of AAV in 1994-2022.

Table. AAV incidence cases reported in the literature.

Study, year	Country, data source	Time period	Incident cases per million population GPA	Incident cases per million population MPA	Incident cases per million population EGPA
Pearce, F. A. et al. 2016	Nottingham, UK, population register	1656-1663	8.2	13.4	1.5
Nilsen, A. T. et al. 2020	Tromso, Norway, population register	1999-2013	15.6	10.4	2.7
Mohammad, A. J et al. 2009	Lund, South Sweden, population register	1997-2006	9.8	10.1	0.9
Takala, J. H et al. 2008	Finland, analysis national discharge data	1996-2000	9.3	NA	NA
Hellmich, B. et al. 2021	Germany, analysis insurance claims database	2013-2016	34	13	NA
Dadoniene, J. et al 2005	Vilnius, Lithuania, analysis hospital database	1990-1999	2.1	3	1.3
Panagiotakis, S. H. et al. 2009	Crete, Greece, analysis hospital database	1995-2003	6.6	10.2	NA
Romero-Gómez, C. et al. 2004	Malaga, Spain, retrospective population.	1994-2010	2.1	3.4	0.64
Catanaso, M. et al. 2014	Reggio Emilia, Italia, analysis hospital discharge database	2004-2009	3.4	NA	NA
Vinit, J. et al. 2006	Burgundy, France, analysis hospital discharge database	1998-2008	NA	NA	1.2
Kanecki, K. et al. 2018	Poland, analysis hospital discharge database	2008-2013	NA	NA	1.5
Kanecki, K. et al. 2018	Poland, analysis hospital discharge database	2011-2015	7.7	NA	NA
Present study, 2023	Northern Spain	1999-2022	2.81	2.23	0.83

Disclosure: S. Al Fazazi: None; **F. Benavides**: None; **A. Herrero-Morant**: None; **V. Calvo Río**: None; **m. renuncio garcia**: None; **c. escagedo Cagigas**: None; **m. rodriguez Vidriales**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, Astra-Zeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6.

Abstract Number: 1535

Epidemiology and Treatment Outcome of ANCA-associated Vasculitis in South Korea: A Nationwide, Population-based Cohort Study

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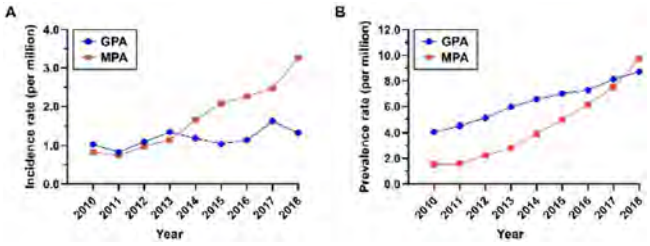
SESSION INFORMATION

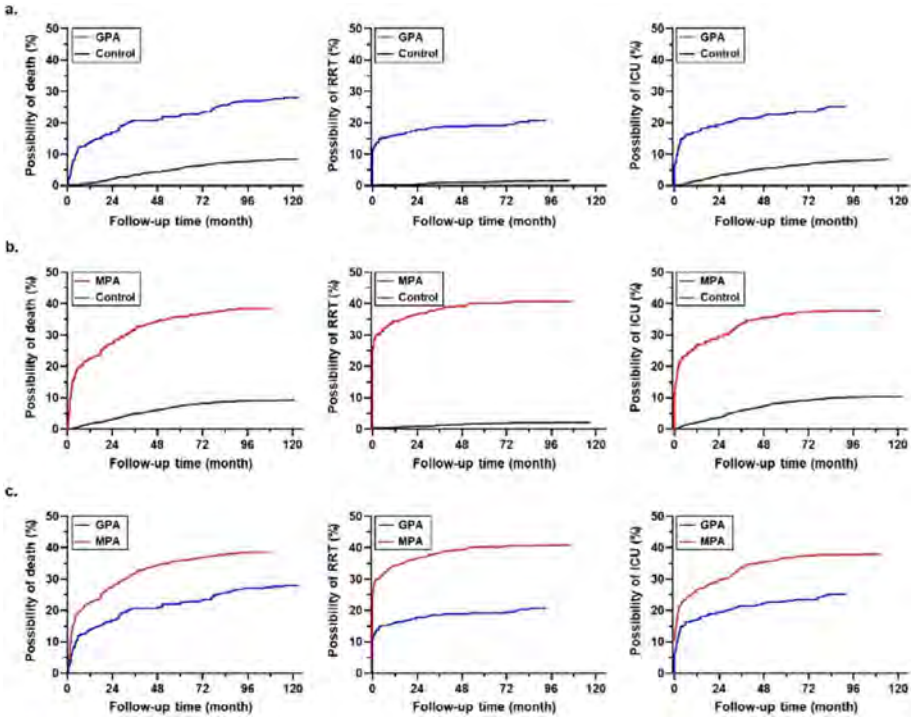
Session Date: Monday, November 13, 2023
Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies on AAV have shown that the epidemiology and clinical features of GPA and MPA differ among countries. Considering their high mortality and morbidity, establishing a national epidemiology for GPA and MPA is necessary for physicians and healthcare systems to estimate the impact and burden of AAV. In this study, we investigated the epidemiological features of granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) in South Korea.

Methods: We identified index cases of GPA and MPA using the 2010-2018 Korean National Health Insurance Service database and Rare Intractable Disease registry for the entire Korean population. Each disease's incidence and prevalence rates and trends over time were analysed. To assess the impact of disease on morbidity and mortality, a comparator group



Annual incidence (A) and prevalence (B) rates (per million) of GPA and MPA over time.



Kaplan-Meier curves indicating cumulative incidence of all-cause mortality, renal replacement therapy (RRT), and admission to intensive care unit (ICU) compared to the comparator group in patients with GPA (A) and MPA (B). Direct comparison of the incidence of these outcomes showed that all-cause mortality, RRT, and ICU care were more common in patients with MPA (C).

indicating the general population was established using nearest neighbourhood matching by age, sex, income, and comorbidity index, at a 5:1 ratio. Morbidity outcomes included the initiation of renal replacement therapy and admission to the intensive care unit (ICU).

Results: A total of 546 and 795 patients with GPA and MPA, respectively, were identified. The incidence rates of both diseases increased with age, and the peak incidence rate was observed in patients aged > 70 years. GPA and MPA showed different trends in incidence rates over time. In 2010, the annual incidence rates (per million) of GPA and MPA were 1.03 and 0.83, respectively. The incidence of MPA has continuously increased over time and increased to 3.26 in 2018. In contrast, the annual incidence of GPA did not significantly change during the observation period and was 1.33 in 2018 (Figure 1).

During the observation period, 90 (28.3%) and 187 (38.6%) patients in the GPA and MPA groups, respectively, died. Although all-cause mortality rates in the GPA and MPA group were significantly higher compared to that in each comparator group (adjusted HR 5.15 [3.21 to 8.38] and 8.62 [6.52 to 11.4], respectively), it was even higher in patients with MPA (adjusted HR 1.69 [1.31 to 2.18]). Patients in the GPA and MPA groups also showed a significantly higher risk of renal replacement therapy and ICU admission than those in the comparator population. In both groups, mortality and morbidity outcomes occurred mainly within the first year from the diagnosis of underlying vasculitis (Figure 2).

Conclusion: In South Korea, the incidence of MPA has increased over time. Although both GPA and MPA had high rates of mortality and morbidity, MPA has a poorer prognosis than GPA.

Disclosure: J. Jung: None; **J. Park**: None; **S. Jihun**: None; **S. Choi**: None; **S. Park**: None; **S. Park**: None; **E. Lee**: None.

Abstract Number: 1536

The Impact of COVID-19 Vaccination on ANCA Vasculitis Hospitalisations: A Perspective from Sydney Australia

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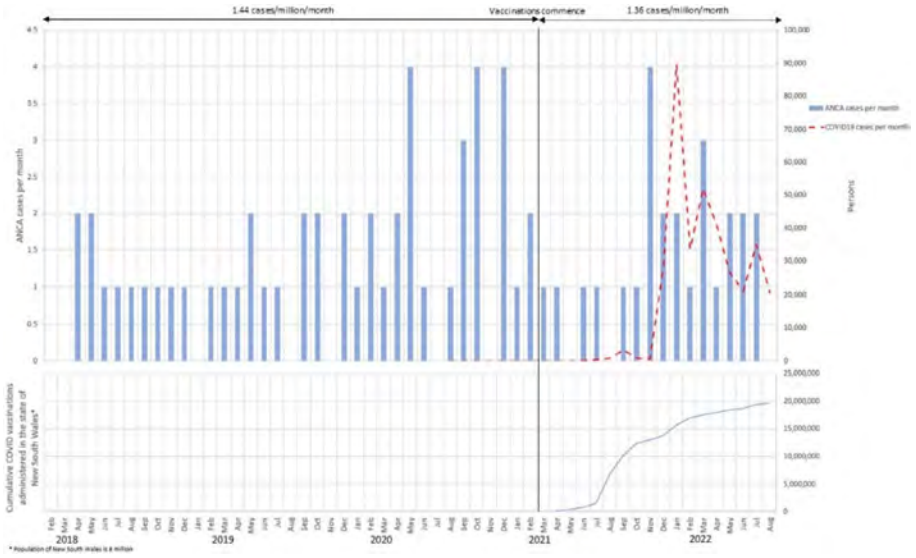
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose:

COVID-19 vaccination can trigger a range of inflammatory and auto-immune phenomena, potentially including AAV. There are several international case reports of de novo and relapsed AAV following primary and booster vaccines, though few reports from Australia. Our study assessed the rate of new-onset and relapses of ANCA-associated vasculitis following COVID-19 vaccination, within our Sydney Local Health District of approximately 1 million people.

Methods: All patients admitted between February 2018 and July 2022, with the diagnosis of AAV (Granulomatosis with Polyangiitis or Microscopic Polyangiitis) were included. Patients were classified as de novo if they fulfilled the 2022 American College of Rheumatology classification criteria. Patients were classified as relapsed if they presented with symptoms included in the Birmingham Vasculitis Activity Score (BVAS) and their dose of corticosteroids was increased. The pre-



AAV and COVID-19 cases between 2018 and 2022 within the South East Sydney Local Health District (SESLHD)

vaccination period was defined as February 2018 to February 2021 (37 months), the post-vaccination period was defined as March 2021 to August 2022 (18 months). The rate of AAV cases was calculated using the Poisson count method and adjusted for exposure time.

Results: There were 75 cases of AAV between February 2018 and August 2022, with 51 during the pre-vaccine period and 24 during the post-vaccine period. The case rate of AAV in the pre-vaccination period was 1.44 cases/million/month, and 1.36 cases/million/month in the post-vaccination period. The rate ratio was 0.95 (95% CI 0.56 to 1.57, p = 0.93). There was no significant difference between the characteristics of patients who presented with AAV within 4 weeks of vaccination.

Conclusion: There was no significant increase in the rate of AAV presentations following vaccination within our Sydney Local Health District.

Disclosure: D. Turner: None; **G. Luxton**: None; **K. Yong**: None; **A. Sammel**: None.

Abstract Number: 1537

Long-term Observational Study of Interstitial Lung Disease in ANCA-associated Vasculitis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: There is limited data on the epidemiology and long-term outcome of patients with Interstitial Lung Disease (ILD) in ANCA-associated Vasculitis (AAV) with conflicting results regarding the effectiveness of the immunosuppressive treatment.

Methods: We retrospectively reviewed 1,002 patients with AAV or ANCA associated ILD followed at a single academic medical centre. ILD patients were those with chest CTs showing UIP, NSIP, organising pneumonia or chronic hypersensitivity pneumonia. We compared the occurrence of ILD with the presence and histology of nephritis, focusing on fibrotic phenotypes and assessed the impact of immunosuppressive therapy on the rate of evolution of FVC% and TLCOc% between treatment initiation (T0) and 12(±3) months (T12).

Results: 54 had microscopic polyangiitis (MPA; AAV-ILD), 15 had granulomatosis with polyangiitis (GPA; AAV-ILD) and 20 had ANCA positive ILD without vasculitis (ANCA-ILD). The total prevalence of ILD was 8.9% (n=89) with mean age 69.2±10.8 years and MPO positivity in 82%. In MPO cohort the prevalence of ILD was 19.6% and these patients presented

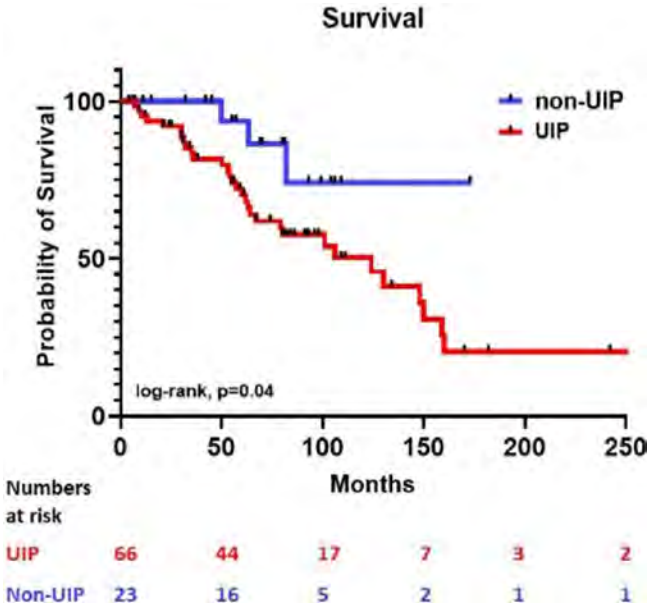

Figure 1. Kaplan Meir survival curve according to UIP and non-UIP ILD groups.

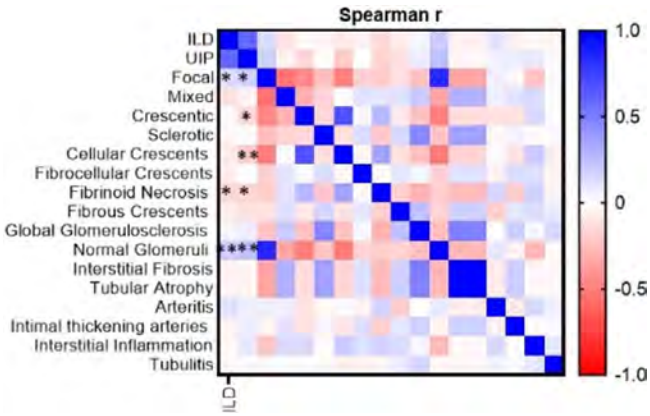

Figure 2. Correlative analysis among renal histopathological parameters shown by heatmap reflecting mean values of Spearman's r, asterisks indicate * $p < 0.05$, ** $p<0.01$.

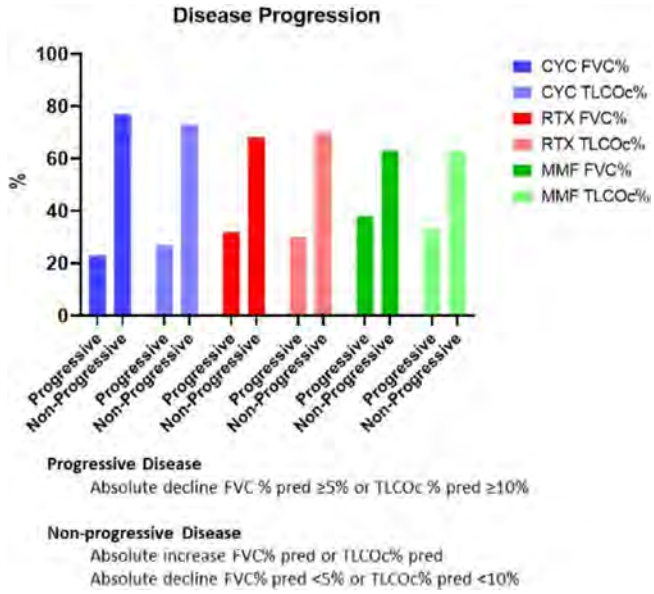

Figure 3. Column chart indicated the percentage of patients with progressive and non-progressive disease over 12 months, according to CYC, RTX and MMF-treated groups.

higher ANCA levels [81.5±50.8 (ILD) vs 59.9±51 (non-ILD), p=0.002]. The median survival was 10 years; the survival with UIP (n=66) was worse compared to non-UIP (n=23) (log-rank, p=0.04, figure 1). No difference in survival between AAV and ANCA-ILD was found. Patients with AAV-ILD and renal involvement (n=47) had better kidney function and lower proteinuria at diagnosis compared to those with nephritis without ILD (n=186) (mean eGFR 41.87 vs 29.6 ml/min/1.73m^2, p=0.007). The presence of ILD was also correlated with lower kidney histological activity (normal glomeruli r=0.193, cellular crescents r=-0.200, fibrinoid necrosis r=-0.151, all p< 0.05, figure 2), while the mixed class in ILD patients characterized with more interstitial fibrosis compared to mixed class in non-ILD (r=0.289, p=0.04) [total cohort 10y ESRD-free survival 91.3 (ILD) vs 82% (non-ILD)]. Median respiratory failure free-survival was 10 years and FVC% at baseline was an independent risk factor for respiratory failure (oxygen requirement) [HR 0.94 CI 95% (0.892-0.994), p=0.030]. When evaluating the impact of immunosuppression on lung progression over 12 months (cyclophosphamide, CYC, n=30; rituximab, RTX, n=25; mycophenolate, MMF, n=8) (figure 3), higher increase of FVC% and lower decline of TLOCc% were reported in the CYC compared to the RTX groups [mean difference: FVC%= -2.49, 95% CI (-10.06 to 5.07), TLCOc=-11.25, 95% CI (-33.08 to 10.58)].

Conclusion: We have reported the prevalence and long-term outcomes of AAV and ANCA associated ILD. Respiratory failure rates were similar between AAV-ILD and ANCA-ILD groups and dominated over ESKD in AAV-ILD. Kidney involvement in ILD presented with less glomerular abnormalities while the mixed class with more fibrotic features compared to patients without ILD. Within the limitations of this study, immunosuppressive treatment appeared to retard progression of lung disease in the short term.

Disclosure: a. chalkia: None; **D. Jones**: CSL Vifor, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Roche, 5, 6; **P. Sivasothy**: None; **D. Jayne**: AstraZeneca, 2, Aurinia, 4, Boehringer Ingelheim, 2, Chinook, 2, CSL Vifor, 2, Roche, 2.

Abstract Number: 1538

Large Vessel Involvement in Antineutrophil Cytoplasmic Antibody-Associated Vasculitis: A Single Center Experience over Two Decades

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV) is currently categorized under the small vessel vasculitides and includes granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA). There is limited knowledge about large vessel involvement in AAV (L-AAV), which is mainly described in case reports and small series. L-AAV can involve temporal arteries (TA-AAV), aorta (A-AAV), and periaortic soft tissue (PA-AAV). The objective of this study was to investigate the characteristics of L-AAV.

Methods: Patients older than 18 years at diagnosis of TA-AAV, A-AAV and PA-AAV seen at a single institution between January 1, 2000, and December 31, 2021, were identified through a proprietary medical text search algorithm. Patients were included if diagnosed with L-AAV by the treating physician, fulfilled 2022 American College of Rheumatology/ European Alliance of Associations for Rheumatology classification criteria for GPA, MPA or EGPA, had positive ANCA, and had more than one outpatient or inpatient visit. Arteritis of the temporal artery was based on histopathology whereas the diagnosis of aortitis and periaortitis could be either based on radiology or histopathology. Descriptive statistics were used to summarize patient characteristics and clinical manifestations. Survival rates were estimated using Kaplan-Meier methods. Overall observed survival was compared with lifetable rates from the US population. The standardized mortality ratio was estimated as the ratio of the observed and expected number of deaths.

Results: The study cohort consists of 36 patients with L-AAV. Of those, 23 had p-ANCA/ MPO-ANCA and 13 had c-ANCA/ PR3- ANCA. Mean (SD) age at AAV diagnosis was 63.4 (12.79); 20 (56%) were male. Seventeen patients had TA-AAV, 10 had A-AAV and 9 had PA-AAV (Table 1). Most of the patients (n=25, 69%) were diagnosed with large vessel involvement and AAV within a one-year timespan (Figure 1). Inflammatory markers were elevated at the time of diagnosis of large vessel involvement. Twenty-five (69%) patients had histopathologic confirmation of AAV diagnosis. There was no overlap between TA-AAV, A-AAV and PA-AAV groups. Of the 17 patients with TA-AAV, 6 had inflammation of a temporal artery branch vessel. The most frequent site of involvement in the A-AAV group was the ascending thoracic aorta, whereas in the PA-AAV group, the abdominal aorta was most frequently involved. Glucocorticoids (36/36), rituximab (19/36), and methotrexate (18/36) were the most frequent treatments. During the study period 8 patients died (4 in TA-AAV, 3 in A-AAV, and 1 in PAAAV). There was no difference in mortality between this cohort of L-AAV patients and the general population (standardized mortality ratio: 0.99; 95% CI, 0.43- 1.95) (Figure 2).

Conclusion: This is the largest single-center cohort of patients with L-AAV to date. Clinicians should consider L-AAV in the differential diagnosis of vasculitides especially in the context of positive ANCA and atypical organ manifestations.

Table 1. Features of the study cohort.

Characteristics	Arteritis of Temporal Artery (N=17)	Aortitis (N=10)	Periaortitis (N=9)	Total (N=36)
Demographics				
Mean (SD) age at AAV diagnosis	68.8 (7.07)	56.2 (16.64)	61.2 (13.05)	63.4 (12.79)
Sex, male n (%)	9 (53)	4 (40)	7 (78)	20 (56)
Race, white n (%)	17 (100)	9 (90)	7 (78)	33 (92)
Smoking status, ever n (%)	7 (41)	4 (40)	7 (78)	18 (50)
Duration of follow-up from AAV diagnosis years, median (IQR)	4.5 (0.1- 12.6)	9.5 (2.2 – 16.9)	4.7 (1.8 – 6.2)	4.7 (1.0 – 11.8)
AAV classification				
GPA, n (%)	3 (18)	6 (60)	6 (67)	15 (42)
MPA, n (%)	13 (76)	4 (40)	3 (33)	20 (56)
EGPA, n (%)	1 (6)	0 (0)	0 (0)	1 (3)
Histopathological confirmation of AAV, positive n (%) *	11 (65)	6 (60)	8 (89)	25 (69)
Diagnosis type of arteritis of temporal artery/ aortitis/periaortitis				
Histopathology, n (%)	17 (100)	3 (30)	5 (56)	25 (69)
Radiology, n (%)	0 (0)	7 (70)	9 (100)	16 (44)
Laboratory parameters at the time of diagnosis of arteritis of temporal artery/aortitis/ periaortitis				
Erythrocyte sedimentation rate mm/hour, median (IQR)	94.5 (79-109) (n=14)	74 (50-79) (n=10)	42.5 (29- 80) (n=6)	79 (47-99) (n=30)
C-reactive protein mg/l, median (IQR)	76.5 (37.5- 92.9) (n=10)	32.1 (23.7- 74.5) (n=9)	37.7 (8.5- 68.4) (n=4)	64 (21.2- 81.0) (n=23)
Clinical Manifestations before or at AAV diagnosis				
Constitutional symptoms, n (%)	16 (94)	6 (60)	7 (78)	29 (81)
ENT, n (%)	5 (29)	8 (80)	5 (56)	18 (50)
Pulmonary, n (%)	5 (29)	2 (20)	5 (56)	12 (33)
Renal, n (%)	6 (35)	0 (0)	4 (44)	10 (28)
Nervous system, n (%)	8 (47)	1 (10)	0 (0)	9 (25)
*Histological confirmation of AAV, other than large vessel pathology				

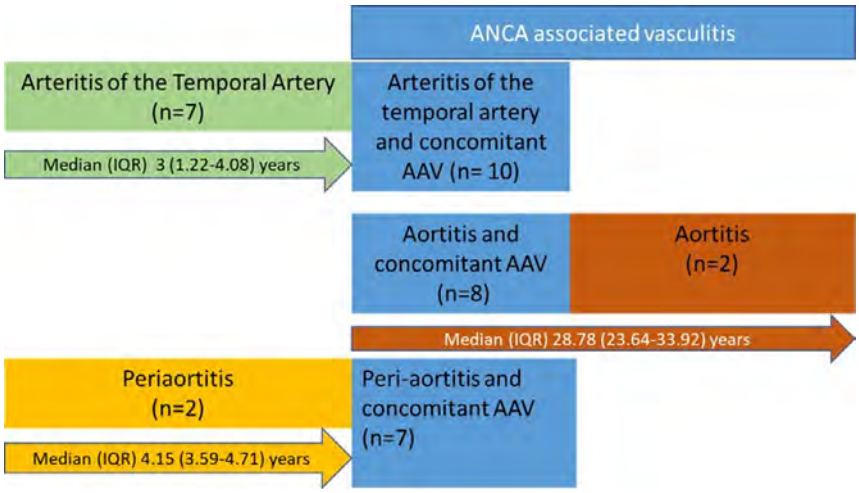

Figure 1. Timeline for the diagnosis of arteritis of temporal artery, aortitis, and periaortitis in relation to AAV diagnosis.

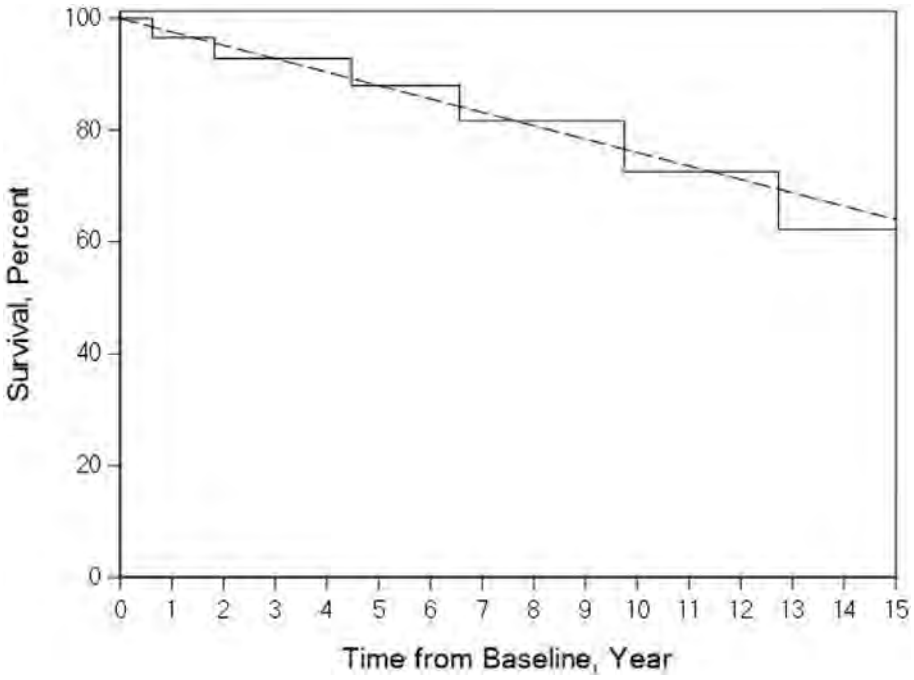

Figure 2. Overall survival of patients with L-AAV compared to expected rates from United States total lifetables (observed: solid line; expected: dashed line).

Disclosure: M. Kaymakci: None; **M. Elfishawi**: None; **H. Langenfeld**: None; **A. Hanson**: None; **C. Crowson**: None; **M. Bois**: None; **U. Ghaffar**: None; **U. Specks**: Amgen, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 5, ChemoCentryx, 2, Genentech, 5, GlaxoSmithKlein(GSK), 5; **M. Koster**: None; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Chemocentryx, 1, 6, Eli Lilly, 5, kiniksa, 5.

Abstract Number: 1539

Digital Ischemia, a Rare Manifestation in Anti-neutrophil Cytoplasmic Antibody (ANCA) Associated Vasculitis (AAV)

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Digital ischemia is a rare, yet severe manifestation observed in AAV. Despite gangrene being a major criterion in the Birmingham Vasculitis Activity Score, this clinical entity is not well described in the literature. We aimed to investigate digital ischemia in AAV.

Methods: This retrospective case series analyzed adult patients with a confirmed diagnosis of AAV and digital ischemia/gangrene, as determined by vasculitis specialists at Cleveland Clinic. Patients without digital ischemia, those diagnosed with a vasculitis other than AAV, and those with digital ischemia related to other causes were excluded from the study. Data collection spanned from January 2002 to January 2023 obtained by chart review.

Table 1. Baseline characteristics.

Table 1. Baseline characteristics

Variable	n=12
Diagnosis Age*	52.6 (18.2)
Gender	
Male	9 (75.0%)
Female	3 (25.0%)
Race	
White	12 (100%)
Active Smoker	4 (33.3%)
Anticoagulation therapy prior to diagnosis (Yes/No)	1 (8.3%)
Warfarin	1 (100%)
Antiplatelet therapy prior to diagnosis (Yes/No)	
No	12 (100%)
History of cardiovascular disease	
Hypertension	7 (58.3%)
Coronary artery disease	2 (16.7%)
Cerebrovascular accident	1 (8.3%)
Prior history of venous thromboembolism	1 (8.3%)
AAV-Disease Type	
GPA	12 (100%)
ANCA antibody	
c-ANCA	9 (75.0%)
p-ANCA	1 (8.3%)
Negative	2 (16.6%)
Antigen type	
Proteinase 3	9 (75.0%)
Myeloperoxidase	1 (8.3%)
Negative	2 (16.6%)
Laboratory findings	
Elevated acute phase reactants	12 (100%)
Anemia	7 (58.3%)
Thrombocytosis	8 (66.7%)
Positive cardiolipin antibodies	2 (16.7%)
Positive Lupus anticoagulant antibodies	3 (25.0%)
AAV organ involvement	
ENT (upper respiratory tract)	8 (66.7%)
Kidney	8 (66.7%)
Nervous system (central and/or peripheral)	5 (41.7%)
Pulmonary	9 (75.0%)
Cutaneous	7 (58.3%)
Mucous membrane/Eyes	2 (16.7%)
Cardiovascular	1 (8.33%)
Gastrointestinal	2 (16.7%)

Results: Twelve patients met the inclusion criteria. The mean age at diagnosis was 52.6 years (SD=18.2), with a male-to-female ratio of 3:1. 33.3% of the patients were active smokers. All patients were diagnosed with granulomatosis with polyangiitis (GPA) and the majority (75%) tested positive for c-ANCA antibodies and PR3 antigen. Other organ involvements at the time of digital ischemia presentation were pulmonary (75%), followed by upper respiratory tract (66.7%), and renal (66.7%) **(Table 1)**.

In terms of digital ischemia, 5 patients (41.6%) had isolated upper extremity involvement, 2 patients (16.6%) had isolated lower extremity involvement, and 5 patients (41.6%) had in both upper and lower extremities. The mean count of involved digits was 4.5 (SD=2.97). Doppler US was the most frequently employed vascular diagnostic modality (83.3%). The most frequently involved vessels were the digital arteries (33.3%). 75% of patients presented with digital ischemia leading to a new diagnosis of GPA, while 3 patients (25%) developed digital ischemia during a disease flare **(Table 2)**.

Table 2. Summary of digital ischemia features.

Table 2. Summary of digital ischemia features

Location	**n=12**
Upper extremity only	5 (41.6%)
Lower extremity only	2 (16.6%)
Both upper and lower extremities	5 (41.6%)
Involved digit count*	4.50 (2.97)
Available vascular diagnostic modalities	
Doppler Ultrasonography	10 (83.3%)
Computerized Tomography Angiography	2 (16.7%)
Invasive angiography	2 (16.7%)
Findings on imaging studies	
Stenosis	6 (50.0%)
Thrombosis	1 (8.3%)
Involved Vessels	
Digital artery	4 (33.3%)
Dorsalis pedal artery	2 (16.7%)
Ulnar artery	1 (8.3%)
Dorsal arch	1 (8.3%)
New GPA diagnosis with digital ischemia presentation	9 (75.0%)
Digital ischemia presentation during GPA flare	3 (25.0%)

Granulomatosis with polyangiitis (GPA)

*Digit count presented as Mean (SD) other variables presented as N (column %).

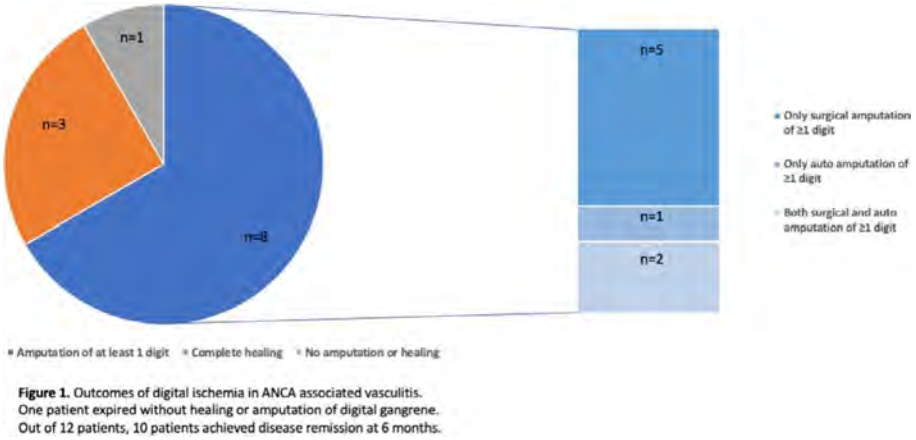

Figure 1. Outcomes of digital ischemia in ANCA associated vasculitis.
One patient expired without healing or amputation of digital gangrene.
Out of 12 patients, 10 patients achieved disease remission at 6 months.

Figure 1. Outcomes of digital ischemia in ANCA associated vasculitis.

Treatment strategies for induction therapy were cyclophosphamide CYC in 33.3%, and rituximab (RTX) in 50.0% of patients respectively in addition to glucocorticoids. Maintenance therapy predominantly consisted of RTX (41.7%). Following diagnosis, 66.7% of patients received anticoagulation therapy, primarily with warfarin (62.5%), and 41.7% received anti-platelet therapy **(Table 1)**.

At 6 months, remission was achieved in 10 patients **(Figure 1)**. Surgical amputation was required in 58.3% of patients, 25% experienced autoamputation, while only 25% of patients had complete healing of all digital gangrene. Among the 3 patients who had complete healing; 2 patients were on anticoagulation after developing digital ischemia for a treatment of deep venous thrombosis.

Conclusion: This study provides insights into AAV-associated digital ischemia which is a rare manifestation of this disease. When present, digital ischemia can be the initial presenting feature leading to GPA diagnosis and generally it occurs in conjunction with other organ involvement. Therefore, GPA should be on the differential diagnosis for patients presenting with digital ischemia. Despite most patients achieving remission, a high degree of morbidity occurred with surgical and/or autoamputation of single or multiple digits. Further research is needed to evaluate the role of adjunct treatments such as anticoagulation and anti-platelet for this rare manifestation.

Disclosure: A. Vural: None; **C. Zhang**: None; **K. Yaseen**: None.

Abstract Number: 1540

Evaluation of the Validity of the 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology Classification Criteria for Antineutrophil Cytoplasmic Antibody-associated Vasculitis for an Asian Population on the Basis of the Patterns of Organ Involvement

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The European Medicines Agency (EMA) algorithm has been widely accepted as a conventional and reliable method to diagnose ANCA-associated vasculitis (AAV). In 2022 the ACR/EULAR endorsed new classification criteria for three clinicopathological subtypes of AAV. Epidemiological studies revealed that MPO-ANCA-positive GPA patients are more common in Asia than in northern Europe and the United States. However, the new criteria assign greater importance to ANCA serology than histology and surrogate markers compared with the conventional method.

This study aimed to evaluate the reliability and validity of the new criteria when targeting AAV patients from an Asian background. The performance of the new criteria was assessed with a focus on the phenotypes of organ involvement, including histology and surrogate markers.

Methods: This study included a total of 432 patients diagnosed with MPA, GPA, and EGPA (147, 141, and 144, respectively) by the conventional method at three medical institutions in Japan between 2000 and 2023 (Table). Only Asians accounted for the whole population. Firstly, the distribution of each AAV subtype was examined before and after reclassification according to the new criteria. Secondly, the difference in the proportion of each AAV subtype per phenotype of organ involvement before and after reclassification.

Table. Clinical characteristics of patients diagnosed with MPA, GPA, and EGPA, according to the 2022 ACR/EULAR classification criteria for AAV.

		Total	The EMA algorithm-based diagnosis		
			MPA	GPA	EGPA
Total number of patients, n (%)		432 (100)	147 (100)	141 (100)	144 (100)
Female, n (%)		173 (40)	60 (41)	54 (38)	59 (41)
Age at diagnosis, mean (SD), years		64.3 (16.1)	71.1 (13.7)	65.9 (15.3)	55.8 (15.4)
Items related to the 2022 ACR/EULAR classification criteria for AAV					
Clinical manifestations, n (%)	Obstructive airway disease	129 (30)	2 (1)	0 (0)	127 (88)
	Nasal polyps	8 (2)	0 (0)	1 (1)	6 (4)
	Mononeuritis multiplex	188 (44)	60 (41)	22 (16)	106 (74)
	Nasal involvement (discharge, ulcers, crusting, congestion, septal defect/perforation)	159 (37)	0 (0)	88 (62)	70 (49)
	Cartilaginous involvement	64 (15)	0 (0)	63 (45)	1 (1)
	Conductive or sensorineural hearing loss	58 (13)	8 (5)	36 (26)	14 (10)
Laboratory/imaging/histological findings, n (%)	PR3-ANCA (or C-ANCA) positivity	64 (15)	9 (6)	48 (34)	7 (5)
	MPO-ANCA (or P-ANCA) positivity	277 (64)	144 (98)	83 (59)	50 (35)
	Serum eosinophil count ≥ $1x10^3$/liter	145 (34)	1 (1)	0 (0)	144 (100)
	Extravascular eosinophilic-predominant inflammation on biopsy	26 (6)	0 (0)	0 (0)	26 (18)
	Fibrosis or interstitial lung disease on chest imaging	161 (37)	85 (58)	36 (26)	41 (28)
	Pulmonary nodules, mass or cavitation on chest imaging	80 (19)	0 (0)	64 (45)	15 (10)
	Hematuria	207 (48)	113 (77)	64 (45)	29 (20)
	Pauci-immune glomerulonephritis on biopsy	126 (29)	77 (52)	40 (28)	8 (6)
	Nasal/paranasal sinusitis or mastoiditis on imaging	141 (33)	9 (6)	101 (72)	31 (22)
	Granuloma, granulomatous inflammation, or giant cell on biopsy	9 (2)	0 (0)	9 (6)	0 (0)
Organ involvement					
ENT, n (%)		207 (48)	8 (5)	117 (83)	80 (56)
	Chronic sinusitis	159 (37)	0 (0)	88 (62)	70 (49)
	Chronic otitis media	58 (13)	8 (5)	36 (26)	14 (10)
	Nasal polyps	8 (2)	0 (0)	1 (1)	6 (4)
	Subglottic stenosis	5 (1)	0 (0)	5 (4)	0 (0)
Eye and orbit, n (%)		32 (7)	0 (0)	29 (21)	3 (2)
	Retro-orbital mass	10 (2)	0 (0)	10 (7)	0 (0)
	Scleritis	16 (4)	0 (0)	16 (11)	0 (0)
	Retinal vasculitis	8 (2)	3 (2)	3 (2)	2 (1)
Central nervous system, n (%)		87 (20)	23 (16)	40 (28)	24 (17)
	Cerebrovascular disease	58 (13)	21 (14)	17 (12)	20 (14)
	Cerebral pachymeningitis	20 (5)	3 (2)	17 (12)	0 (0)
	Cerebral granulomatous lesions/cerebral nodules	3 (1)	0 (0)	3 (2)	0 (0)
	Cranial nerve palsy	6 (1)	0 (0)	2 (1)	4 (3)
	Pituitary gland enlargement	5 (1)	0 (0)	3 (2)	0 (0)
Peripheral nervous system, n (%)	Sensory/ motor peripheral neuropathy	188 (44)	60 (41)	22 (16)	106 (74)
Pulmonary, n (%)		301 (70)	88 (60)	88 (62)	125 (87)
	Obstructive airway disease	130 (30)	2 (1)	0 (0)	128 (89)
	Pulmonary nodules, mass or cavitation	80 (19)	0 (0)	64 (45)	15 (10)
	Fibrosis or interstitial lung disease	161 (37)	85 (58)	36 (26)	41 (28)
	Alveolar hemorrhage	14 (3)	13 (9)	0 (0)	1 (1)
	Endobronchial disease	13 (3)	2 (1)	9 (6)	2 (1)
	Pleural effusion	21 (5)	6 (4)	4 (3)	11 (8)
Renal, n (%)		207 (48)	114 (78)	65 (46)	28 (19)
	Pauci-immune glomerulonephritis on biopsy	126 (29)	77 (52)	40 (28)	8 (6)
	Hematuria	207 (48)	113 (77)	64 (45)	29 (20)
Cardiovascular, n (%)		27 (6)	4 (3)	8 (6)	15 (10)
Cutaneous, n (%)		97 (22)	26 (18)	13 (9)	58 (40)
	Purpura/ulcers	93 (22)	24 (16)	12 (9)	57 (40)
	Nodules	2 (0)	0 (0)	1 (1)	1 (1)
Gastrointestinal, n (%)		24 (6)	5 (3)	0 (0)	19 (13)

Results: The patients diagnosed with MPA and EGPA by the conventional method were significantly more likely to be reclassified as the same AAV subtype (146 out of 147 and 142 out of 144 patients [99 % and 98 %], respectively) (Figure 1). On the other hand, the patients diagnosed with GPA by the conventional method were less likely to be reclassified as the same AAV subtype (97 out of 141 patients [69%]). Figure 2 shows the proportion of each AAV subtype per phenotype of organ involvement before and after reclassification. (A and B, respectively). In the conventionally-diagnosed GPA population, those who presented with pulmonary nodules and sinusitis were partially reclassified as MPA, and most of them were MPO-ANCA-positive. Also, those who presented with chronic otitis media and interstitial lung disease were partially reclassified as MPA. However, those who presented with orbital and intracranial nodules were all reclassified as GPA as ever. In the conventionally-diagnosed MPA population, those who presented with alveolar hemorrhage and pauci-immune glomerulonephritis were mostly reclassified as MPA as ever, and most of them were MPO-ANCA-positive. In the conventionally-diagnosed EGPA population, there were almost no significant changes except for two PR3-ANCA-positive patients who were excluded from the diagnosis of EGPA after reclassification.

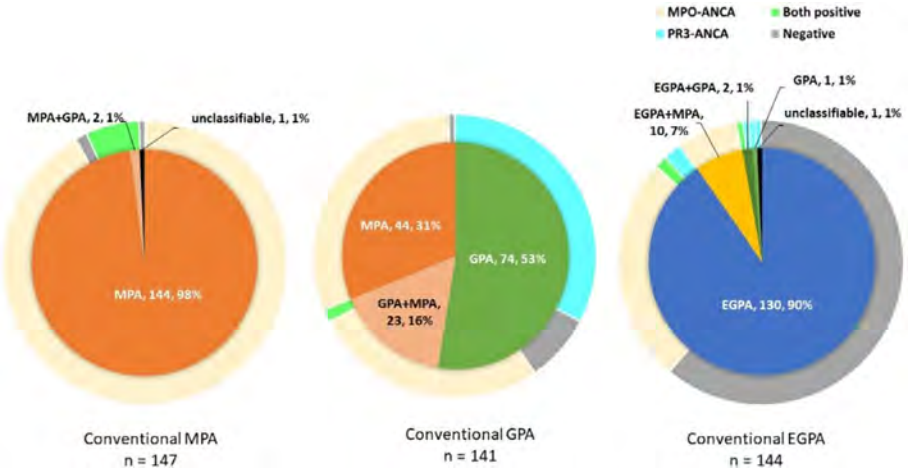

Figure 1. Reclassification of the patients diagnosed with MPA, GPA, and EGPA by the conventional method according to the 2022 ACR/EULAR classification criteria for AAV, including the distribution of ANCA serotypes.

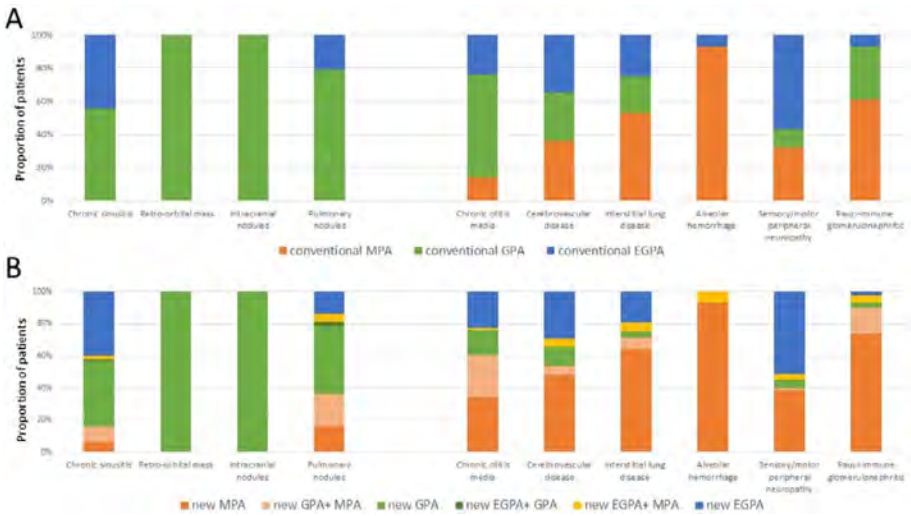

Figure 2.The proportion of patients with each AAV subtype before and after reclassification. (A) conventional criteria and (B) 2022 ACR/EULAR criteria.

Conclusion: The 2022 ACR/EULAR criteria were more likely to reclassify MPO-ANCA-positive patients diagnosed with GPA according to the EMA algorithm as MPA even in the presence of findings suggesting granulomatous inflammation, which led to a diagnostic contradiction. However, PR3-ANCA-positive patients diagnosed with GPA by the conventional method were likely to present with recurrent or severe organ involvement, including orbital and intracranial nodules, and the new criteria also reclassified these patients as GPA.

Disclosure: R. Kuwata: None; **Y. Shirota**: None; **T. Shirai**: None; **H. Yamashita**: None; **H. Sato**: None; **Y. Oka**: None; **T. Kodera**: None; **K. Motomura**: None; **H. Kaneko**: None; **J. Kameoka**: None; **H. Fujii**: None; **T. Ishii**: None.

Abstract Number: 1541

Neurologic Involvement Does Not Affect Cumulative Survival Rates in Patients with ANCA-associated Vasculitis and Is Less Commonly Associated with Rapidly Progressive Glomerulonephritis in Patients with GPA

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The aim of this study was to analyze the incidence of nervous system manifestations in a cohort of patients with Microscopic Polyangiitis (MPA) and Granulomatosis with Polyangiitis (GPA), and to identify if neurological manifestations influence the overall survival rates in these patients. We also evaluated how other clinical characteristics of AAV patients correlated with the neurologic involvement.

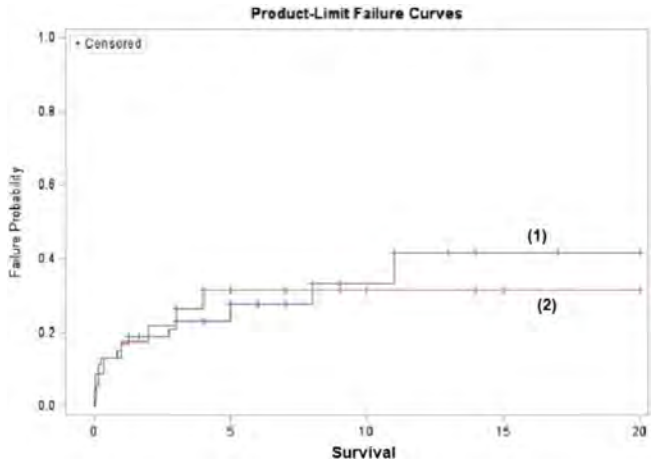


Fig. 1 : Microscopic Polyangiitis (MPA) Kaplan-Meyer's survival curves. (1) Represents those without neurologic involvement (2) Represents those with neurologic involvement

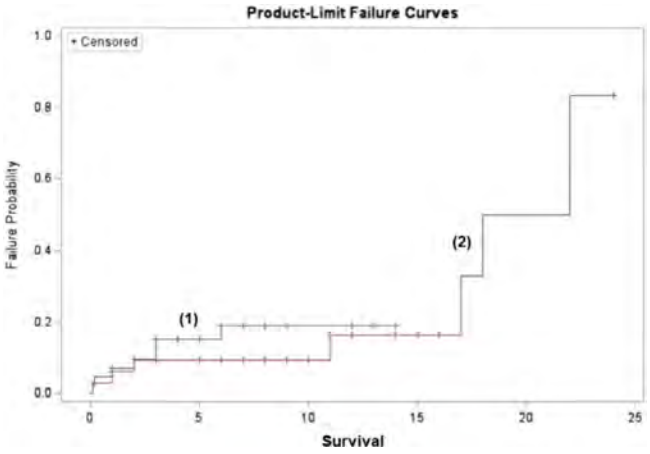


Fig. 2 : Granulomatosis with Polyangiitis (GPA) Kaplan-Meyer's survival curves. (1) Represents those without neurologic involvement (2) Represents those with neurologic involvement

Methods: This is a retrospective single-center cohort study of AAV patients. Medical records of all patients with ANCA-positive serology from 08/2/2014 to 8/7/2021 were analyzed. One hundred and fifty one patients met the 2022 ACR/EULAR classification criteria for either MPA or GPA. An additional 19 patients with limited GPA were diagnosed but not included in this analysis. Data were collected from medical records and analyzed for organ involvement, neurologic manifestations, laboratory findings, electrophysiology and imaging.

Results: One hundred and seventy patients with ANCA associated systemic vasculitis were identified. Of this number, 75 patients were diagnosed with MPA and 76 patients were diagnosed with GPA. The median duration of follow-up was 6.3 years. The majority of the MPA patients were female (60.5%) with a mean age of 58.0 years. GPA patients were mostly male (58.7%) with a mean age of 54.2 years. Each ANCA vasculitis group was analyzed separately as well as cumulative analysis was also completed. A total of 30.3% of MPA- and 44.0% of GPA-patients had neurological involvement. Peripheral neuropathy was the most common neurologic manifestation noted in 60.9% of those with evidence of neurologic involvement in the MPA group. On the contrary, the central nervous involvement was more common in the GPA group with 54.4% involvement. In the GPA cohort, the estimated cumulative survival at 1 year point in patients with neurological involvement was 82.6% in comparison to those without neurologic involvement (83.0%). In the MPA cohort, survival rate was 93.9% in those with neurologic involvement in comparison to those without neurologic involvement (92.9%). The 5-year survival in the MPA group was comparable between those with neurologic involvement (73.6%) and those without neurologic involvement (69.6%). Interestingly, patients with GPA showed a trend towards reduced overall 5-year survival rates in those without neurologic involvement (85.7%) to those that had neurologic involvement (90.9%). Analysis of secondary outcomes showed that the patients with peripheral neurologic involvement were statistically less likely to develop rapidly progressive renal disease, 29.4% vs 63.8% in the GPA group (p value=0.02) while this difference didn't reach statistical significance in the MPA group (50.0% vs 69.4%, p value=0.22).

Conclusion: Neurologic manifestations commonly accompany systemic vasculitis such as ANCA-associated vasculitis. Nervous system involvement causes increased morbidity and reduces the quality of life in patients with either MPA or GPA but does not affect the overall survival rate at either 1 year or 5-year point in these patients. Interestingly, GPA patients with peripheral nervous system involvement were less likely to develop rapidly progressive glomerulonephritis.

Disclosure: G. Gheriani: None; **P. Lenert**: None.

Abstract Number: 1542

The Burden of Multimorbidity in ANCA-Associated Vasculitis: A Cohort Study

Zachary Wallace[1], Xiaoqing Fu[2], Shruthi Srivatsan[2], Zachary Williams[2], Claire Cook[2], Jennifer Hanberg[2], John Stone[3], Hyon K. Choi[4] and Yuqing Zhang[5], [1]Massachusetts General Hospital, Newton, MA, [2]Massachusetts General Hospital, Boston, MA, [3]Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Concord, MA, [4]Massachusetts General Hospital and Harvard Medical School, Lexington, MA, [5]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, MA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: With improvements in the risks of relapse and mortality in ANCA-associated vasculitis (AAV), a better understanding of disease- and treatment-related complications is necessary to optimize outcomes and personalize care. Multimorbidity (MM) is a patient-centered approach to measuring complications and is associated with risk of death and quality of life in other conditions. It is defined as having multiple chronic conditions but remains poorly understood in AAV. We sought to determine the burden of multimorbidity in AAV.

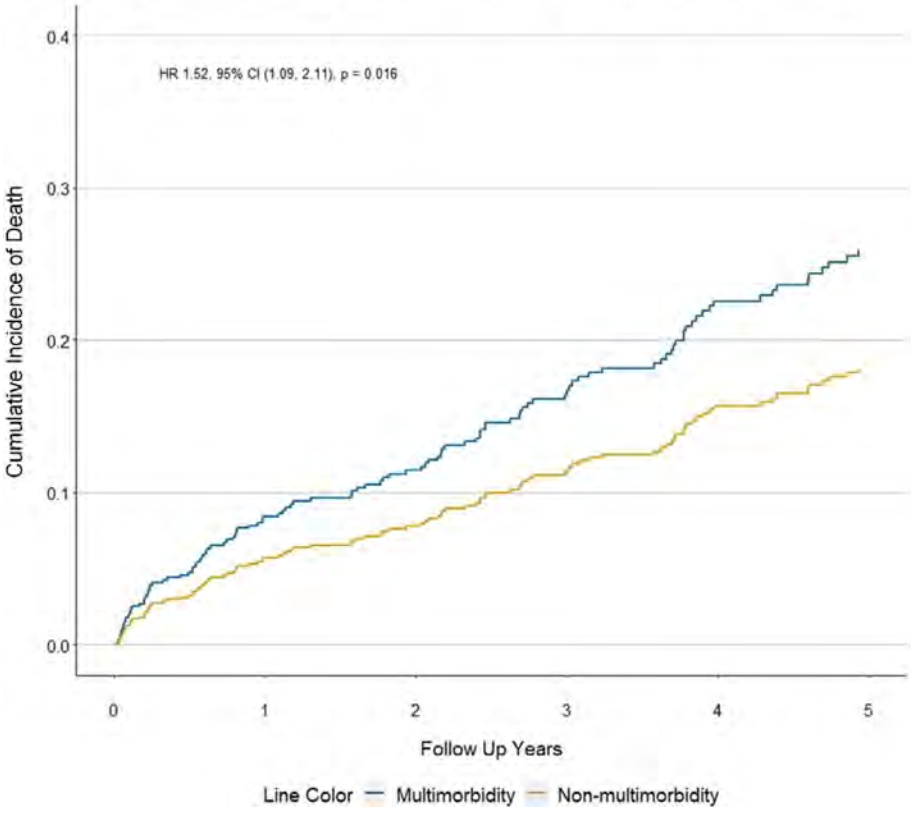
Methods: We used the 2002-2019 Mass General Brigham (MGB) AAV cohort: an inception cohort of consecutive MPO- or PR3-ANCA+ incident AAV cases at a multi-center healthcare system. Up to 10 comparators without systemic rheumatic disease were identified from MGB and matched to each case by encounter date, age, sex, and race. We adapted a definition of MM as the presence of ≥ 2 of 37 chronic conditions, identified by use of ICD-9/10 codes. Manifestations of AAV (e.g., kidney disease) were excluded from this definition. Pre-existing comorbidities were excluded. We determined the proportion of cases and comparators with MM using the Aalen-Johansen method, accounting for the competing risks of death and loss to follow up. We used Cox proportional hazard models to estimate the risk of MM in cases vs comparators and restricted mean survival time to estimate days free of MM. Among patients with AAV, we used latent class analysis to characterize clusters of morbidity among people with MM and time-varying multivariable-adjusted Cox proportional hazards models to assess the association of MM with mortality risk.

Table 1: Baseline Demographic Features	**AAV Cases**	**Comparators**
N	547	5259
Age (mean, SD)	59 (17)	59 (17)
Female (%)	39%	39%
Race		
White	88%	92%
Black/African American	2%	2%
Asian	1%	1%
Other	2%	2%
Unknown	3%	1%
BMI (mean, SD)	28.3 (6.9)	28.5 (7.3)
BVAS/WG (median, IQR)	4 [4, 6]	--
Renal Manifestation (n, %)	351 (64)	--
MPO-ANCA+	372 (68)	--
Initial Treatment		
Rituximab-Based	241 (44)	--
Cyclophosphamide-Based	227 (42)	--

Table 2: The Burden of Multimorbidity	**AAV Cases**	**Comparators**	**Difference in Days Free from Multimorbidity**
Primary Analysis: Proportion with Multimorbidity (>= 2 comorbid conditions)			
Year 1	32.9%	2.3%	
Year 2	44.7%	3.6%	
Year 3	47.6%	4.9%	
Year 4	53.2%	6.5%	
Year 5	57.4%	8.6%	
Primary Analysis: Days Free from Multimorbidity*			
Year 1	282	353	-71 (-81, -61)
Year 2	489	696	-207 (-230, -184)
Year 3	666	1028	-362 (-400, -324)
Year 4	823	1353	-530 (-582, -478)
Year 5	963	1671	-707 (-773, -641)
Sensitivity Analysis: Multimorbidity defined as >= 5 comorbid conditions			
Year 1	7.2%	0.03%	
Year 2	9.0%	0.03%	
Year 3	10.3%	0.03%	
Year 4	11.3%	0.04%	
Year 5	11.6%	0.04%	
Sensitivity Analysis: Annual proportion with multimorbidity, as assessed at each year of follow-up among those surviving and with >= 1 visit in previous 12 months**			
Year 1	27.6%	2.9%	
Year 2	14.6%	2.2%	
Year 3	10.6%	1.5%	
Year 4	14.2%	1.4%	
Year 5	13.1%	1.8%	

Multimorbidity is defined by the presence of at least 2 morbidities identified by ICD9/10 codes used at least twice at least 30 days apart; *Adjusted for age, sex, race, **Cases alive at each year of follow-up were matched to comparators who were alive and, to be eligible for inclusion, both cases and comparators had to have at least 1 visit in the preceding 12 months

Figure: The cumulative incidence of death among those with vs without multimorbidity



Results: There were 547 cases matched to 5,259 comparators (**Table 1**). AAV cases had nearly an 8-fold higher risk of MM vs comparators (**Table 2**, aHR 7.6, 95% CI 6.6-8.7). Over 5 years, each case had an average of 707 fewer days with MM than comparators (963.4 vs 1670.5 days, p< 0.001). At 1 year, two clusters of MM in AAV were identified: Clusters 1A (76%) and 1B (24%). Hypertension and hyperlipidemia were common in Cluster 1A; Cluster 1B was characterized by painful conditions (e.g., headache, back pain, GERD). At 2 years, two clusters were identified: Clusters 2A (82%) and 2B (18%). Cluster 2B was distinguished from 2A by a high burden of cardiovascular (CV) and pulmonary disease. At 5 years, three clusters were identified: Cluster 5A (81%), 5B (11%), and 5C (8%). Morbidities most common in Cluster 5A were hypertension and hyperlipidemia. Cluster 5B was distinguished by a high burden of CV and pulmonary disease; 5C had a high burden of glucocorticoid toxicities (e.g., osteoporosis, obesity, hypertension). Among AAV patients, developing MM is associated with a 52% higher risk of death than not having MM (**Figure**, age-, sex-, race-, and creatinine-adjusted HR 1.52, 95% CI 1.09-2.11).

Conclusion: AAV is associated with a high burden of MM and greater risk of MM than the general population. MM in AAV is characterized by clusters defined by morbidity burdens that vary over disease course and reflect a high impact of disease and its treatment. MM in AAV is associated with mortality risk. The development of interventions to prevent MM and minimize its impacts are needed.

Disclosure: Z. Wallace: BioCryst, 2, Bristol-Myers Squibb(BMS), 5, Horizon, 1, 2, 5, MedPace, 2, Novartis, 1, PPD, 2, Sanofi, 1, 5, Shionogi, 1, Visterra, 1, 2, Zenas, 1, 2; **X. Fu**: None; **S. Srivatsan**: None; **Z. Williams**: None; **C. Cook**: None; **J. Hanberg**: None; **J. Stone**: Abvie, 2, Amgen, 1, 2, Argenx, 2, Aztrazeneca, 2, Bristol Myers Squibb, 2, 5, Celgene, 2, Chemocentryx, 2, Chugai, 2, GSK, 2, Horizon Therapeutics, 1, 2, 5, InflaRx, 2, IQVIA, 1, 2, Kyverna, 2, Mirabio, 2, NIH, 5, Novartis, 2, PPD, 2, Prometheus, 2, Q32, 2, Regeneron, 2, Roche-Genentech, 2, Roivant, 2, Sanofi, 2, 5, Spruce Biosciences, 2, Star Therapeutics, 2, Steritas, 12, Chair, Scientific Advisory Board (no fiduciary responsibilities), ZenasBio, 2; **H. Choi**: Ani, 2, Horizon, 2, 5, LG, 2, Protalix, 2, Shanton, 2; **Y. Zhang**: None.

Abstract Number: 1543

The Association of Frailty with Outcomes in Patients with Vasculitis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Frailty is associated with poor health outcomes including increased risk of hospitalizations, infections, and fractures. In the baseline survey of the VascStrong study, we reported a high prevalence of frailty and pre-frailty in participants with multiple forms of vasculitis. The 1-year follow-up survey collected data on adverse health outcomes, patient-reported outcomes (PRO), and a reassessment of self-reported frailty.

Methods: VascStrong was a longitudinal study using the Vasculitis Patient-Powered Research Network (VPPRN), an internet-based prospective longitudinal cohort. All participants of the baseline survey were invited to participate in the 1-year follow-up survey.

Data elements collected included type of vasculitis, demographic, medications, and PROs that included a patient global assessment (PGA) and several domains of the Patient-Reported Outcomes Measurement Information System (PROMIS). Frailty was measured by the FRAIL scale, a self-reported tool, and patients were classified as robust, pre-frail, and frail based on meeting 0, 1-2, or ≥ 3 criteria, respectively.

Participants reported the occurrence over the prior year of hospitalizations, infections, fractures, and disease flares. Data were analyzed by frailty classification (baseline and follow-up).

Results: Between October 28, 2022 and January 26 2023, 272/328 participants (82.9%) responded to the follow-up survey. Most participants were female (71.0%) and non-Hispanic white, and the most common diagnosis was granulomatosis with polyangiitis (39.0%), followed by eosinophilic granulomatosis with polyangiitis (14.3%), and microscopic polyangiitis (12.9%). Mean age of participants was 62.5 years.

Prevalence of robustness, pre-frailty, and frailty was 47.1%, 33.8%, and 19.1%, respectively. PROs at follow-up showed similar associations to baseline with pre-frail and frail patients reporting worse pain (intensity and interference), fatigue, depression, and physical function (**Table 1**). The majority of participants were classified similarly to their baseline assessment (75%, 50.9%, and 66.1% for robust, pre-frailty, and frailty, respectively). However, transitions in frailty classification between consecutive states were observed from robust to pre-frail (21.2%), pre-frail to robust (38.9%), pre-frail to frail (10.2%), and frail to pre-frail (25%) (**Figure 1**). Transitions from frail to non-frail (8.9%) or non-frail to frail (3.7%) were rare.

Table 1. Patient-reported outcomes among patients with vasculitis by frailty classification Data presented as median (interquartile range). *Raw score, scale 0-10.

Table 1. Patient-reported outcomes among patients with vasculitis by frailty classification

	Robust (N = 128)	Pre-frail (N = 92)	Frail (N = 52)	p-value
Patient Global Assessment	2.0 (0.0, 5.0)	4.5 (1.0, 6.0)	6.0 (5.0, 8.0)	<0.0001
PROMIS-29 Pain intensity*	1.0 (0, 2.5)	3.0 (1.0, 5.0)	5.5 (4.0, 7.0)	<0.0001
PROMIS T-scores				
Anxiety	77.9 (71.2, 81.6)	73.3 (65.3, 81.6)	68.3 (63.4, 71.2)	<0.0001
Fatigue	48.6 (46.0, 53.1)	58.8 (51.0, 66.7)	64.6 (60.7, 69.0)	<0.0001
Depression	49.0 (41.0, 53.9)	52.9 (45.0, 58.9)	57.3 (49.0, 62.2)	<0.0001
Pain Interference	41.6 (41.6, 53.9)	55.6 (41.6, 61.2)	63.8 (58.5, 66.6)	<0.0001
Physical functioning	56.9 (45.3, 56.9)	41.8 (36.7, 48.0)	34.4 (32.1, 36.7)	<0.0001

Data presented as median (interquartile range). *Raw score, scale 0-10.

Table 2. Adverse health outcomes of patients with vasculitis at one-year follow-up based on baseline frailty classification *Severe infections were defined as infections requiring hospitalization. **Flares of disease that required changes in immunosuppressive treatment.

Table 2. Adverse health outcomes of patients with vasculitis at one-year follow-up based on baseline frailty classification

	Total	Non-frail	Pre-frail	Frail	p-value
Hospitalizations	51 (18.8%)	13 (12.0%)	20 (18.5%)	18 (32.1%)	0.0075
Infections	138 (50.7%)	48 (44.4%)	55 (50.9%)	35 (62.5%)	0.0134
Severe infections*	19 (13.8%)	7 (14.6%)	6 (10.9%)	6 (17.1%)	0.7045
Fractures	21 (17.7%)	6 (5.6%)	9 (8.3%)	6 (10.7%)	0.4911
Flares	66 (24.3%)	17 (15.7%)	26 (24.1%)	23 (41.1%)	0.0005
Flares requiring treatment**	45 (68.2%)	9 (52.9%)	20 (76.9%)	16 (69.6%)	0. 3698

*Severe infections were defined as infections requiring hospitalization.
**Flares of disease that required changes in immunosuppressive treatment.

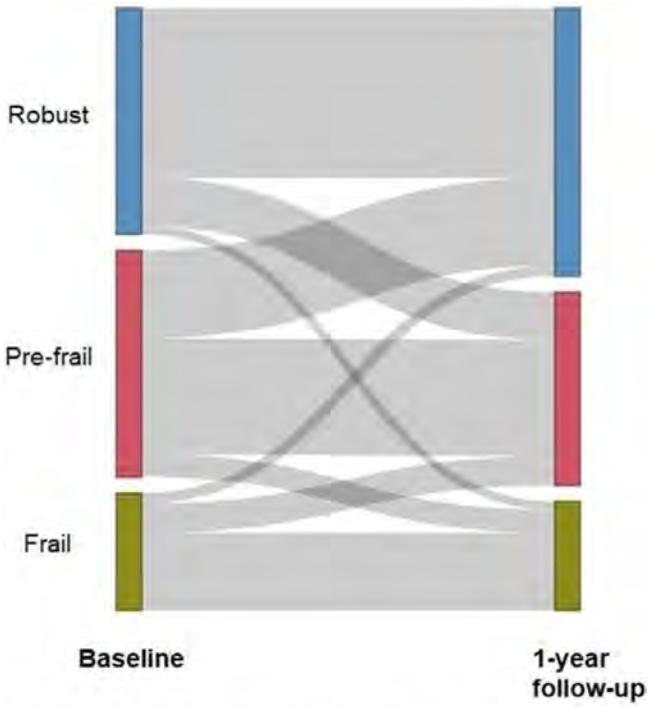

Figure 1. Changes in frailty status among patients with vasculitis at one-year follow-up

Figure 1. Changes in frailty status among patients with vasculitis at one-year follow-up

Hospitalizations, infections, and flares were most frequent in participants classified as frail at baseline (**Table 2**). Similar observations were made using follow-up frailty classification. No difference was observed in severe infections and fractures, that were overall uncommon in the cohort.

Conclusion: At 1-year follow-up, pre-frailty and frailty remained prevalent among patients with vasculitis and were associated with worse PROs. Transitions in frailty status were observed among participants, showing that amelioration of frailty is achievable in a subset of patients with vasculitis. Among patients with vasculitis, pre-frailty and frailty are associated with a substantial 1-year risk of hospitalizations, infections, and flares of disease.

Disclosure: S. Sattui: AstraZeneca, 5, Bristol Myers Squibb Foundation, 5, Rheumatology Research Foundation, 5, Sanofi, 2, 5; **J. Stadler**: None; **R. Borchin**: None; **C. Burroughs**: None; **C. Yeung**: None; **P. Merkel**: AbbVie/Abbott, 5, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos, 5, Electra, 5, Genentech, 5, GlaxoSmithKlein(GSK), 2, 5, HiBio, 2, InflaRx, 2, 5, Janssen, 2, Jubilant, 2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, Takeda, 2, 5, UpToDate, 9, Visterra, 2; **R. Spiera**: AbbVie/Abbott, 2, 5, Amgen, 2, AstraZeneca, 5, chemocentryx, 5, corbus, 5, Formation Biologics, 5, GSK, 2, 5, Inflarx, 5, Kadmon, 5, Novartis, 2, 5, Principia, 5, Sanofi, 2.

Abstract Number: 1544

Increased Risk of Severe Infection in Patients with Antineutrophil Cytoplasmic Antibody-associated Vasculitides: A Population-based Trend Analysis

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SESSION INFORMATION

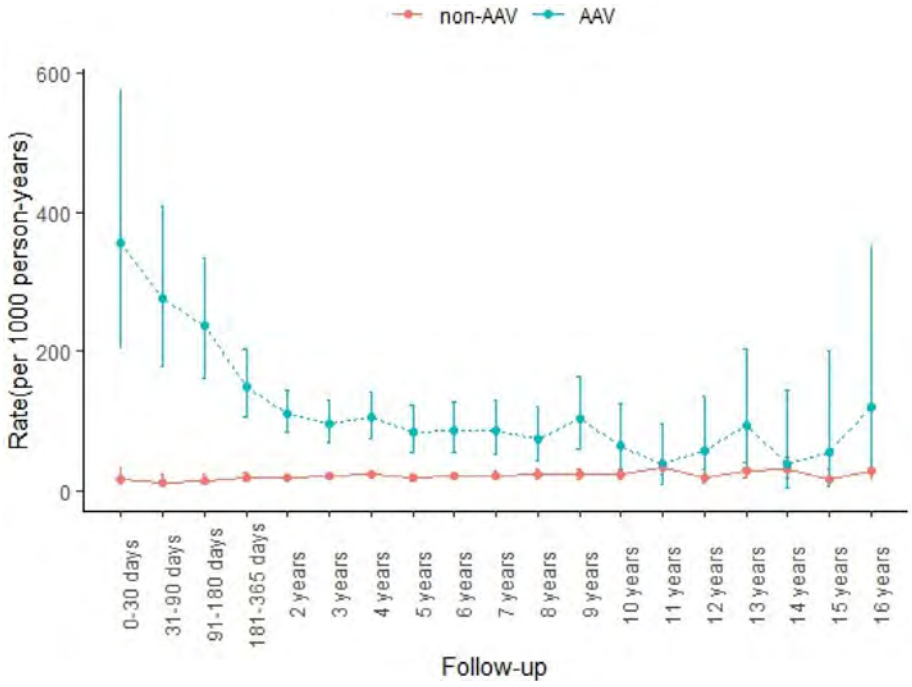
Session Date: Monday, November 13, 2023

Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAVs) are a group of multisystem inflammatory diseases. One of the most serious and common side-effects of GC and immunosuppressant drug use is infection. No studies have explained the change in risk over time. What's more, findings from previous studies may not accurately represent the risk of infection due to AAV as many studies are based on hospitalized patients, small sample sizes, prevalent cohorts, different approaches to defining AAV, and/or limited adjustment of potential confounders. To address these research gaps, we conducted a large population-based study of all patients with incident AAV. We aimed to answer three questions: a) what is the independent risk of first severe infection due to AAV, b) the trajectory of the risk for severe infection in AAV compared to the matched controls , and c) the trajectory of the rate of repeated severe infections in AAV compared to the matched controls.



Comparing secular trends in the rate of severe infections in AAV and non-AAV.

Cohorts	Mixed Logistic Part (No infection vs infection)			Mixed Poisson Part (Infection count)		
	OR	95% CI	P-value	RR	95% CI	P-value
	AAV onset					
AAV	0.00	0.003-0.37	0.01	0.00	0-0.001	<0.001
non-AAV	0.00	0-0.005	<0.001	0.00	0-0.001	<0.001
AAV vs non-AAV	77.01	11.66-508.51	<0.001	2.55	1.36-4.78	<0.001
	Before the 2nd year of AAV onset					
Secular trend in AAV	0.32	0.16-0.62	<0.001	0.97	0.79-1.20	0.79
Secular trend in non-AAV	1.08	0.76-1.53	0.66	1.08	0.89-1.31	0.46
Secular trend in AAV vs non-AAV	0.29	0.13-0.64	0.00	0.90	0.66-1.23	0.52
	After the 2nd year of AAV onset					
Secular trend in AAV	0.85	0.76-0.96	0.01	1.11	1.04-1.17	0.00
Secular trend in non-AAV	1.05	0.93-1.18	0.43	1.04	0.97-1.11	0.23
Secular trend in AAV vs non-AAV	0.81	0.68-0.97	0.02	1.06	0.96-1.18	0.23

Secular trend of infection count in AAV relative to the general population using ZIPMM spline model. Abbreviations: AAV, Antineutrophil cytoplasmic antibody-associated Vasculitis; OR = odds ratio. RR = Rate ratio; 95% CI = 95% confidence interval. RRs and 95% CI are individual-specific (or conditional) estimates.

Methods: We conducted an age- and sex-matched cohort study of all patients with incident AAV using administrative health data from British Columbia, Canada. The primary outcome was the first severe infection after AAV onset necessitating hospitalization or occurring during hospitalization. We used multivariate Cox proportional hazard models to compare time to the onset of infection and estimate hazard ratios. The secondary outcome was the longitudinal counts of severe infection. We used two-part zero-inflated Poisson mixed model (ZIPMM) with splines to assess the secular trend in the infection count.

Results: One in three patients with newly diagnosed AAV developed severe infection (3.8-fold when compared to non-AAV). AAV patients had the highest risk of severe infection during the first 30 days of diagnosis, which dropped at different rates before and after the second year. However, among those at risk for severe infections, the rate of repeated severe infections stayed the same over time within the first two years of AAV diagnosis and even increased over time afterward.

Conclusion: In summary, this is the first large comprehensive population-based study evaluating the risk of infection with incident AAV. Our study demonstrates that one in three AAV patients developed severe infections, demonstrating that the diagnosis of AAV is an independent risk factor for severe infection. ZIPMM spline model suggests that an AAV patient who has experienced infection should be treated differently and properly from one who experiences no infection. Having a more precise understanding of which individuals are likely to experience infection and develop repeated infections could help to ensure a more efficient use of healthcare dollars and perhaps a more accurate attribution of intervention effects. This research is a further step towards a deeper understanding of the prevention, screening and treatment of infection over time. We recommend a closer surveillance for severe infections in AAV patients and routine risk checks for severe infections for AAV patients after diagnosis. Further studies are also warranted to further clarify the relative contribution of inflammation and medication, and to identify modifiable risk factors for infections in AAV.

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Abstract Number: 1545

Validation of the 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology Classification Criteria in Patients with ANCA-associated Vasculitis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The early diagnosis of ANCA-associated vasculitis (AAV) and treatment initiation may prevent progression to end organ damage, particularly renal disease. Based on the Vasculitis Patient-Powered Research Network study, the delay with diagnosis of AAV draws up to 7 months and 73% of patients are misdiagnosed initially. Recently the American College of Rheumatology (ACR) and European Alliance of Associations for Rheumatology (EULAR) have proposed the new classification criteria for AAV, but they have not yet validated in a different external cohort. We aimed to validate the 2022 ACR/EULAR classification criteria in a Ukrainian patients with AAV.

Methods: The retrospective study included patients diagnosed between 2010 and 2022 with Granulomatosis with Polyangiitis (GPA), Eosinophilic Granulomatosis with Polyangiitis (EGPA) and Microscopic Polyangiitis (MPA) and undifferentiated vasculitis (UV) in two expert rheumatology centers. All patients have serology confirmation (positivity of antibodies against proteinase-3 and/or myeloperoxidase performed using the ELISA test) and surrogate clinical markers of vasculitis. The 1990 ACR criteria, the 2007 European Medicine Agency (EMA) algorithm and the new ACR/EULAR 2022 criteria were applied for all patients. The level of agreement was evaluated by Cohen's kappa coefficient with determination of sensitivity and specificity.

Results: A total of 42 patients (female: male ratio 1:0.6) diagnosed AAV with mean age at the time of diagnosis of 47.19 ±11.55 years were included. The distribution of AAV patients classified according to various classification criteria is shown in Fig 1. The established diagnosis simultaneously corresponded to the diagnosis according to the previous and new criteria

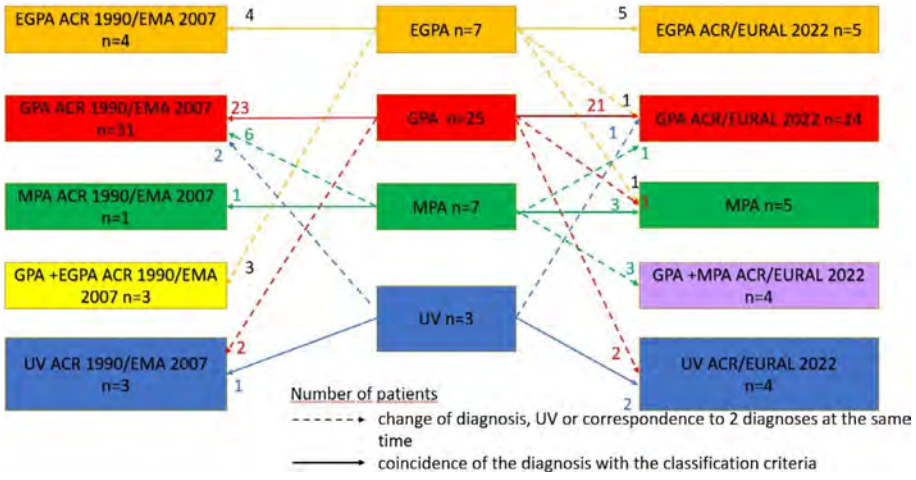


Figure 1. Distribution of patients with AAV according to various classification criteria

in 28 patients, only to the ACR/EULAR 2022 criteria in 8 patients (6 MPA, 1GPA, 1 UV), to the classification criteria of ACR 1990 and the EMA algorithm in 5 patients (3 EGPA, 1 UV, 1 GPA), and one patient has not met any criteria. The ACR/EULAR 2022 classification criteria compared to the previous ones demonstrated better agreement with the established diagnosis of GPA (k 0.6 vs 0.3, sensitivity 88.0% vs 92.0%, specificity 70.6% vs 35.3 %) and MPA (k 0.5 vs 0.2, sensitivity 71.4% vs 14.3%, specificity 88.6% vs 100%) but worse agreement with the diagnosis of EGPA (k 0.8 vs 1.0, sensitivity 71.4% vs 100%, specificity 100% vs 100%).

Conclusion: The ACR/EULAR 2022 classification criteria for AAV demonstrate a good accuracy in the Ukrainian patient population (for GPA, sensitivity - 88%, specificity - 71%, for MPA - 71% and 89%, respectively, and for EGPA - 71% and 100%, respectively) and an advantage compared to the previous classification criteria for GPA and MPA. However, about 10% of the patients are still unclassified and the same amount are matched two diagnoses with the ACR/EULAR 2022 criteria.

Disclosure: L. Petelytska: None; **V. Kravchenko**: None; **O. Iaremenko**: None.

Abstract Number: 1546

Eosinophilic Granulomatosis with Polyangiitis: Clinical Suspicion Red Flags Identification by a Systematic Literature Review and Multidisciplinary Expert Consensus

Ricardo Blanco[1], Iñigo Rúa-Figueroa[2], Roser Solans[3], Maria C Cid[4], Marina Blanco[5], Ismael Garcia Moguel[6], Francisco Perez Grimaldi[7], Ana Noblejas[8], Moises Labrador[3], Cristian Domingo[9], Georgina espigol[10], Fernando Sanchez Toril[11], Francisco Ortiz-Sanjuán[12], Ebymar Arismendi[13] and Jose María Alvaro-Gracias[14], [1]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain, [2]Rheumatology, Hospital de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain, [3]Internal Medicine Department, H. Universitari Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona, Spain, [4]Hospital Clinic Barcelona, Barcelona, Spain, [5]Pneumology Department, Hospital Universitario de A Coruña, Madrid, Spain, [6]Allergy Department, Hospital Universitario 12 de Octubre, Madrid, Spain; Instituto de Investigación Sanitaria Hospital 12 de Octubre (imas12), Madrid, Spain, [7]Pneumology Department, H. University of Jerez, Cádiz, Spain, [8]Internal Medicine Department, Hospital Universitario La Paz, Madrid, Spain, [9]Pneumology Department, Corporació Sanitaria Parc Taulí, Universitat Autònoma de Barcelona, Barcelona, Spain, [10]Autoimmune Diseases Department, Hospital Clínic, FCRB-IDIBAPS, Universitat de Barcelona, Barcelona, Spain, [11]Pneumology Department, Hospital Arnau Vilanova, Valencia, Spain;, Valencia, Spain, [12]Hospital Universitario y Politécnico La Fe, Valencia, Spain, [13]Pneumology Department, Hospital Clínic de Barcelona, Barcelona, Spain, Universitat de Barcelona, Spain and CIBERES, Barcelona, Spain, [14]Hospital General Universitario Gregorio Marañon, Madrid, Spain

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Eosinophilic Granulomatosis with Polyangiitis (EGPA) is a rare ANCA-associated vasculitis, characterized histologically by eosinophilic tissue infiltration, necrotizing vasculitis, and eosinophil-rich granulomatous inflammation.

The diagnosis of EGPA is often challenging due to its rarity, heterogeneous and multiorgan clinical presentation, and the overlapping with other vasculitis or eosinophilic disorders. The identification of suspicion signals of EGPA addresses a fundamental practical barrier in achieving timely diagnosis for patients with this rare but potentially devastating disease.

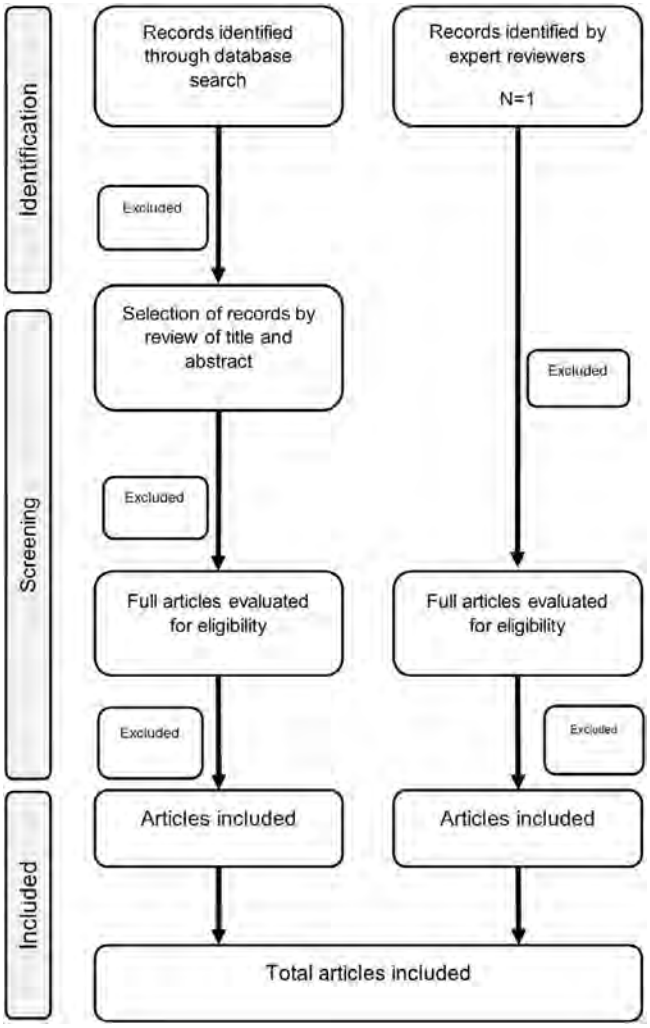


Figure 1. PRISMA flowchart for the systematic literature review.

Our purpose was to identify a comprehensive and evidence-based checklist of signs, symptoms and laboratory parameters reported to precede the diagnosis of EGPA that can be used as red flags, raising the suspicion and prompt the performance of appropriate confirmatory tests.

Methods: A systematic literature search strategy was developed to identify signs, symptoms and laboratory abnormalities that should raise the suspicion of a possible EGPA patient. GRADE (Grading of Recommendations, Assessment, Development and Evaluations) methodology was used to assess the quality of the scientific evidence supporting each criterion.

A multidisciplinary nominal group consensus approach (including rheumatologists, internal medicine specialists, pulmonologists, and allergists) was established for the development of the expert consensus.

Red flags identified as suspicion signals for EGPA were categorized by organ system, manifestation, and laboratory test to facilitate rational, evidence-based clinical review of patients presenting with eosinophilia.

Results: A total of 382 records were identified and reviewed, and 85 studies were included in the literature review (Figure 1). From these 85 publications a total of 214 items were assessed and 40 red flags were identified as relevant to raise a suspicion of EGPA. As the publications were derived from observational studies the GRADE level of evidence was low.

Blood eosinophil count. - levels of > 1000 cells /µL (>1 x 109/L) with no pharmacological treatment that could explain an alteration of this value - levels of > 500 cells /µL with a treatment that could decrease this value (such as glucocorticoids)			
	Red flag		**Red flag**
Respiratory		ENT	
	Asthma		Nasal polyps
	Lung infiltrates / nodules / alveolitis		Chronic media otitis
	Eosinophilic pleural effusion	Dermatological	
	Alveolar haemorrhage / haemoptysis		Palpable purpura
	Chronic cough over 8 weeks / wheezing (not explained by another cause)		Skin lesions such as ulcers, urticaria, nodules and papules (cannot be explained by another cause)
Histopathological		Neurological	
	Vasculitis on biopsy		Mononeuritis multiplex/polyneuropathy
	Biopsy with inflammatory infiltrate predominantly eosinophilic		Paraesthesia
Analytical marker-related			Cerebrovascular disease, other pathologies ruled out
	ANCA positive	Renal	
	Elevated creatinine (together with sediment alteration)		Glomerulonephritis
	Proteinuria (>500 mg)		Glomerular extra-capillary proliferation in renal biopsy
	Elevated troponin (cannot be explained by another cause)		Renal infarction
	High BNP (without any other apparent cause)	Gastrointestinal	
	Positive rheumatoid factor		Ischaemic injuries including intestinal ischaemia and perforation (gastric, oesophageal, and small intestine, unexplained by any other cause)
	High IgE		Recurrent abdominal pain ischemic in nature (cannot be explained by another cause)
Cardiac			Chronic diarrhoea, melena (not explained by another cause)
	Pericardial effusion / pericarditis	Musculoskeletal	
	Cardiomyopathy		Polyarthritis (no alternative explanation)
	Ischaemic heart disease /arterial occlusion / infarction in a patient under 45 years of age		Myositis / myopathy
	Cardiomegaly	Ophthalmological	
Vascular			Retinal vasculitis
	Digital ischaemia		Episclentis / scleritis
	Venous thrombosis (without any other factors)		Orbital inflammatory disease/ orbital pseudotumour
			Red eye (including conjunctivitis and keratitis)
Constitutional syndrome and/or fever (not attributable to any other cause)			
If a patient has the indicated levels of eosinophilia, the detection of any of the listed factors, with no other apparent cause, should alert to the possibility of EGPA. The presence of more than one factor will reinforce the suspicion of EGPA.			

TABLE 1. EGPA suspicion red flags

Using these 40 red flags, an evidence-based clinical checklist tool was developed for use in routine practice to raise EGPA suspicion in patients with eosinophilia (peripheral blood eosinophil count >1 x 10^9/L, with no treatment that could explain an alteration of this value) (Table 1).

Conclusion: Systematic literature review, multidisciplinary expert consensus rating and GRADE methodology has enabled, for the first time, the identification of a comprehensive set of red flags that could be used to raise a suspicion for EGPA, providing clinicians with an evidence-based checklist tool that can be integrated into their routine practice.

Disclosure: R. Blanco: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6; **I. Rúa-Figueroa**: AstraZeneca, 5, GSK, 1, 6; **R. Solans**: CSL-Vifor, 6, GSK, 1, 6; **M. Cid**: AbbVie/Abbott, 1, 2, 6, AstraZeneca, 1, GSK, 1, 2, 6, Kininksa Pharmaceutical, 5, SCL-Vifor, 2, 6; **M. Blanco**: None; **I. Garcia Moguel**: AstraZeneca, 1, 2, 5, 6, GSK, 1, 2, 5, 6, Sanofi, 1, 2, 5, 6, Teva Therapeutics, 1, 2, 5, 6; **F. Perez Grimaldi**: AstraZeneca, 6, Chiesi, 6, GSK, 6, Novartis, 6, Sanofi, 6, Teva Therapeutics, 6; **A. Noblejas**: CSL-Vifor, 6, GSK, 1, 6; **M. Labrador**: AstraZeneca, 6, GSK, 1, 6, Novartis, 6, Sanofi, 6; **C. Domingo**: ALK, 1, 2, 5, 6, AstraZeneca, 1, 2, 5, 6, Chiesi, 1, 2, 5, 6, GSK, 1, 2, 6, Menarini, 12, Travel fees, Novartis, 1, 2, 5, 6, Sanofi, 1, 2, 5, 6, Teva Therapeutics, 1, 2, 5, 6; **G. espigol**: CSl-Vifor, 1, GSK, 1; **F. Sanchez Toril**: None; **F. Ortiz-Sanjuán**: Eli Lilly, 6, Grunenthal, 2, GSK, 2; **E. Arismendi**: AstraZeneca, 6, GebroPharna, 6, GSK, 6, Merck/MSD,

6, Sanofi, 1; **J. Alvaro-Gracias**: Abbvie, 2, 6, AstraZeneca, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, GSK, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6.

Abstract Number: 1547

Disease Burden of Eosinophilic Granulomatosis with Polyangiitis (EGPA): A Retrospective Analysis of US Health Insurance Claims Data

Paul Dolin[1], Danuta Kielar[1], Anat Shavit[1], **Karina Keogh**[2], Jennifer Rowell[1], Chris Edmonds[3], Juliana Meyers[4], Elizabeth Esterberg[4], Tram Nham[4] and Stephanie Chen[5], [1]AstraZeneca, Cambridge, United Kingdom, [2]Mayo Clinic, Rochester, MN, [3]AstraZeneca, Gaithersburg, MD, [4]RTI Health Solutions, Research Triangle Park, NC, [5]BioPharmaceuticals Medical, AstraZeneca, Gaithersburg, MD

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare necrotizing small-to-medium vessel vasculitis with a relapsing-remitting course involving prodromal (various allergic reactions), eosinophilic (infiltration into organs), and vasculitic (widespread inflammation of small and medium blood vessels) phases, with symptoms depending on the affected organ. Using a retrospective analysis of US administrative health insurance claims data (Merative™ MarketScan® databases), we assessed the clinical burden of EGPA.

Methods: Patients with newly diagnosed EGPA from 2017 to 2021 with ≥12 months of continuous pre-diagnosis health plan enrollment and ≥1 inpatient or ≥2 outpatient EGPA-related diagnoses (≥90 days apart, ICD-10-CM code M30.1) were included. Follow-up was from date of first observed EGPA diagnosis (index date; ID) until health plan disenrollment or database end. Major and non-major coexisting conditions and symptoms were analyzed in patients with EGPA and in a general population cohort matched on demographic characteristics.

Results: In total, 236 patients with EGPA were identified ('EGPA cohort'); 88% had commercial insurance. At ID, mean (standard deviation [SD]) age was 50.4 (14.5) years, 88% were < 65 years, and 58% were female. Mean (SD) duration of follow-up from ID was 21.7 (14.6) months; 26% had ≥30 months' follow-up. Of these, 213 patients with EGPA ('matched EGPA cohort') were matched to a general population cohort ('matched general population cohort'; N=779; mean [SD] age 50.6 [13.7] years, 90% were < 65 years, 59% were female). The most common coexisting conditions at ID in the EGPA cohort were asthma (74% of patients), allergic rhinitis (57%), throat and chest pain (46%), and dyslipidemia (42%) (**Table 1**). After the ID, 79.2% of patients in the EGPA cohort reported ≥1 new EGPA symptom, with 31.4% experiencing a major symptom, of which the most common was hematuria (8.1%). At ID, in the matched EGPA cohort, 44% of patients had major symptoms, the most common of which were respiratory failure (19%), hematuria (9%), hemoptysis/alveolar hemorrhage (6%), and cardiomyopathy (6%). More patients in the matched EGPA cohort had a major symptom compared with the matched general population cohort at ID (prevalence ratio 8.0 [95% confidence interval (CI) 5.8–11.1]; p< 0.001) as well as new symptoms after ID (prevalence ratio 3.0 [95% CI 2.2–4.0]; p< 0.001) (**Table 2**). The symptoms with the three highest prevalence ratios in the matched EGPA cohort versus the matched general population cohort at ID were respiratory failure (73.1 [17.8–300.2]; p< 0.001), hemoptysis or alveolar hemorrhage (23.8 [5.4–104.5]; p< 0.001), and congestive heart failure (21.9 [4.9–97.3]; p< 0.001).

Table 1. History of coexisting conditions in the EGPA cohort at the index date

Coexisting condition*	EGPA cohort (n=236)
Asthma	174 (73.7%)
Severe persistent asthma	152 (64.4%)
Severe uncontrolled asthma	105 (44.5%)
Other eosinophilic conditions	
Atopic dermatitis/eczema	44 (18.6%)
Pulmonary eosinophilia	39 (16.5%)
Eosinophilic esophagitis	8 (3.4%)
Hypereosinophilic syndrome	5 (2.1%)
All malignancies	24 (10.2%)
Primary (essential) thrombocythemia	9 (3.8%)
Allergic rhinitis	134 (56.8%)
Throat and chest pain	109 (46.2%)
Dyslipidemia	98 (41.5%)
Gastro-esophageal reflux disease	90 (38.1%)
Back pain (dorsalgia)	77 (32.6%)
Nasal polyposis	66 (28.0%)
Vitamin D deficiency	60 (25.4%)
Obesity	59 (25.0%)
Anxiety	58 (24.6%)
Sleep disorder/Obstructive sleep apnea	46 (19.5%)
Arrhythmia	46 (19.5%)
Depression	45 (19.1%)
Ischemic heart disease	45 (19.1%)
Interstitial pulmonary disease	33 (14.0%)
Deep vein thromboembolism	11 (4.7%)
Hyperthyroidism	9 (3.8%)
Irritable bowel syndrome	8 (3.4%)
Arterial thrombosis	3 (1.3%)

*Before or at the index date.

Data are n (%).

EGPA, eosinophilic granulomatosis with polyangiitis.

Table 2. Prevalence of symptoms in the matched EGPA cohort versus matched general population cohort

Symptom	Existing symptoms at index date				New symptoms after index date			
	Matched EGPA cohort (N=213)	Matched general population cohort (N=779)	Comparison		Matched EGPA cohort (N=213)	Matched general population cohort (N=779)	Comparison	
	Prevalence (95% CI)		Prevalence ratio (95% CI)	p-value	Prevalence (95% CI)		Prevalence ratio (95% CI)	p-value
Major symptoms								
Any	44.1% (37.9–51.3)	5.5% (4.1–7.4)	8.0 (5.8–11.1)	<0.001	31.4% (25.8–38.4)	10.5% (8.6–12.9)	3.0 (2.2–4.0)	<0.001
GI infarction or ischemia	0	0.1% (0.0–0.4)			0	0		
Retinal change	1.9% (0.7–5.0)	0.3% (0.1–1.0)	7.3 (1.3–39.7)	0.021	2.3% (1.0–5.6)	0.9% (0.4–1.9)	2.6 (0.8–8.1)	0.098
Sensorineural hearing loss	3.8% (1.9–7.4)	1.2% (0.6–2.2)	3.3 (1.3–8.3)	0.014	6.1% (3.6–10.3)	2.6% (1.7–4.0)	2.4 (1.2–4.7)	0.013
Hemoptysis or alveolar hemorrhage	6.1% (3.6–10.3)	0.3% (0.1–1.0)	23.8 (5.4–104.5)	<0.001	1.4% (0.5–4.3)	0.3% (0.1–1.0)	5.5 (0.9–32.6)	0.061
Respiratory failure	18.8% (14.2–24.8)	0.3% (0.1–1.0)	73.1 (17.8–300.2)	<0.001	3.8% (1.9–7.4)	1.3% (0.7–2.4)	2.9 (1.2–7.3)	0.022
Ischemic cardiac pain	0.9% (0.2–3.7)	0.6% (0.3–1.5)	1.5 (0.3–7.5)	0.65	0.9% (0.2–3.7)	0.4% (0.1–1.2)	2.4 (0.4–14.5)	0.33
Cardiomyopathy	6.1% (3.6–10.3)	0.4% (0.1–1.2)	15.8 (4.6–55.1)	<0.001	3.3% (1.6–6.8)	0.5% (0.2–1.4)	6.4 (1.9–21.7)	0.003
Congestive heart failure	5.6% (3.3–9.6)	0.3% (0.1–1.0)	21.9 (4.9–97.3)	<0.001	7.0% (4.3–11.5)	1.4% (0.8–2.5)	5.0 (2.3–10.7)	<0.001
Hematuria	8.5% (5.4–13.1)	1.5% (0.9–2.7)	5.5 (2.7–11.2)	<0.001	8.0% (5.1–12.6)	3.2% (2.2–4.7)	2.5 (1.4–4.5)	0.003
Creatininemia/stage 4–5 CKD	2.3% (1.0–5.6)	0.1% (0.0–0.9)	18.3 (2.1–155.7)	0.008	1.4% (0.5–4.3)	0.3% (0.1–1.0)	5.5 (0.9–32.6)	0.061
Cerebrovascular accident	4.2% (2.2–8.0)	0.6% (0.3–1.5)	6.6 (2.2–19.4)	<0.001	2.3% (1.0–5.6)	1.2% (0.6–2.2)	2.0 (0.7–6.0)	0.20
Spinal cord lesion	0	0			0	0.1% (0.0–0.4)		
Cranial nerve palsy	0.9% (0.2–3.7)	0.1% (0.0–0.9)	7.3 (0.7–80.3)	0.10	0.5% (0.1–3.3)	0.3% (0.1–1.0)	1.8 (0.2–20.1)	0.62
Mononeuritis multiplex	3.8% (1.2–6.3)	0			3.3% (0.9–5.7)	0		
Non-major symptoms								
General	40.8% (34.7–48.0)	13.4% (11.2–16.0)	3.1 (2.4–3.9)	<0.001	30.0% (24.5–36.9)	24.8% (21.9–28.0)	1.2 (1.0–1.5)	0.11
Skin	19.7% (15.0–25.9)	2.1% (1.3–3.3)	9.6 (5.5–16.7)	<0.001	19.2% (14.5–25.3)	4.9% (3.6–6.7)	3.9 (2.6–6.0)	<0.001
Mucous membrane and eyes	12.2% (8.5–17.5)	3.0% (2.0–4.4)	4.1 (2.4–7.1)	<0.001	10.8% (7.3–15.9)	6.4% (4.9–8.4)	1.7 (1.1–2.7)	0.03
ENT	55.4% (48.1–62.5)	8.2% (6.5–10.4)	6.7 (5.2–8.6)	<0.001	20.7% (15.9–26.9)	15.4% (13.1–18.2)	1.3 (1.0–1.8)	0.064
Chest	39.4% (33.4–46.6)	1.9% (1.2–3.2)	20.5 (12.1–34.7)	<0.001	20.7% (15.9–26.9)	5.5% (4.1–7.4)	3.7 (2.5–5.5)	<0.001
Cardiovascular	12.7% (8.9–18.0)	1.4% (0.8–2.5)	9.0 (4.5–17.8)	<0.001	10.8% (7.3–15.9)	3.2% (2.2–4.7)	3.4 (1.9–5.8)	<0.001
Abdominal	0.5% (0.0–1.4)	0			0.5% (0.1–3.3)	0.4% (0.1–1.2)	1.2 (0.1–11.7)	0.86
Renal	36.2% (30.2–43.2)	21.1% (18.4–24.1)	1.7 (1.4–2.1)	<0.001	23.0% (18.0–29.4)	17.1% (14.6–19.9)	1.3 (1.0–1.8)	0.044
Nervous system	22.1% (17.1–28.4)	3.7% (2.6–5.3)	5.9 (3.8–9.2)	<0.001	18.8% (14.2–24.8)	10.1% (8.2–12.5)	1.9 (1.3–2.6)	<0.001

CI, confidence interval; CKD, chronic kidney disease; EGPA, eosinophilic granulomatosis with polyangiitis; ENT, ear, nose, and throat; GI, gastrointestinal.

Rate ratios and their corresponding confidence intervals and p-values were obtained using Zeger modified Poisson regression (Zou, G. Am J Epidemiol 2004;159:702–9).

Conclusion: At ID, over 40% of patients with EGPA had major symptoms. New major symptoms continued to occur after ID, with many occurring significantly more frequently than in a matched population without EGPA. These data highlight the substantial burden of EGPA, with a large portion of symptoms within the respiratory system. Greater awareness of EGPA symptoms is needed to ensure proper disease management between different specialties and multidisciplinary teams.

Disclosure: P. Dolin: AstraZeneca, 3, 11; **D. Kielar**: AstraZeneca, 3, 11; **A. Shavit**: AstraZeneca, 3, 11; **K. Keogh**: AstraZeneca, 12, site PI for an AstraZeneca pharmaceutical trial in asthma; **J. Rowell**: AstraZeneca, 3, 11; **C. Edmonds**: AstraZeneca, 3, 11; **J. Meyers**: AstraZeneca, 12, Employee of RTI Health Solutions, which received funding from AstraZeneca to conduct the study; **E. Esterberg**: AstraZeneca, 12, Employee of RTI Health Solutions, which received funding from AstraZeneca to conduct the study; **T. Nham**: AstraZeneca, 12, Employee of RTI Health Solutions, which received funding from AstraZeneca to conduct the study; **S. Chen**: AstraZeneca, 3, 11.

Abstract Number: 1548

Diagnosis Pathways in Patients with Eosinophilic Granulomatosis with Polyangiitis (EGPA): A Retrospective Analysis of US Health Insurance Claims Data

Paul Dolin[1], Danuta Kielar[1], Anat Shavit[1], **Karina Keogh**[2], Jennifer Rowell[1], Chris Edmonds[3], Juliana Meyers[4], Elizabeth Esterberg[4], Tram Nham[4] and Stephanie Chen[5], [1]AstraZeneca, Cambridge, United Kingdom, [2]Mayo Clinic, Rochester, MN, [3]AstraZeneca, Gaithersburg, MD, [4]RTI Health Solutions, Research Triangle Park, NC, [5]BioPharmaceuticals Medical, AstraZeneca, Gaithersburg, MD

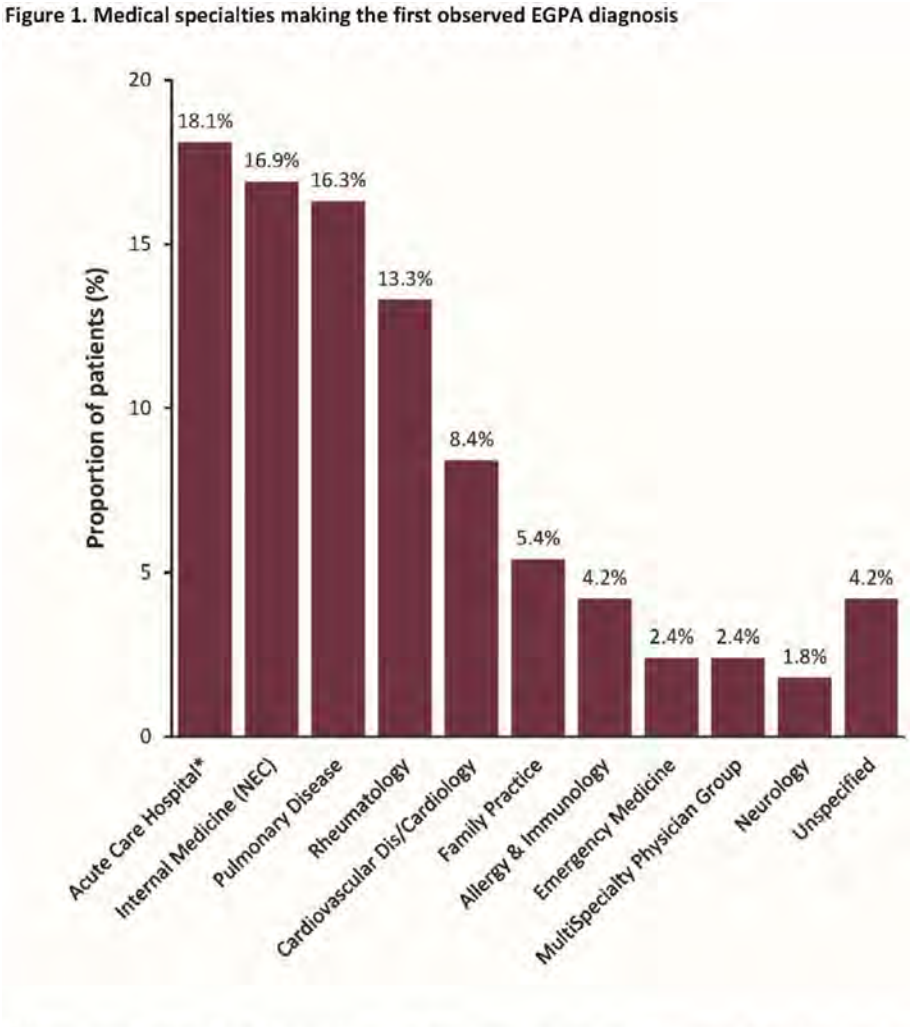
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Raising awareness of eosinophilic granulomatosis with polyangiitis (EGPA), a rare necrotizing small-to-medium vessel vasculitis, amongst clinicians is important to ensure timely diagnosis and treatment. EGPA is associated with substantial disease burden and impact on health-related quality of life, with patients often facing a long and complex pathway from symptom onset to diagnosis. We aimed to characterize the diagnostic journey of patients with EGPA using a retrospective analysis of US administrative health insurance claims (Merative™ MarketScan® databases).

Methods: Patients with newly diagnosed EGPA from 2017 to 2021 with ≥12 months of continuous pre-diagnosis health plan enrollment and ≥1 inpatient or ≥2 outpatient EGPA-related diagnoses (≥90 days apart, ICD-10-CM code M30.1) were included. Follow-up was from date of first observed EGPA diagnosis (index date; ID) until health plan disenrollment or database end. Drug therapies and outpatient visits prior to ID, specialties making incident EGPA diagnosis, time from first observed symptom to ID, and persistent vasculitic damage were analyzed.

Results: In total, 236 patients with incident EGPA were identified; 88% had commercial insurance. At ID, mean (standard deviation [SD]) age was 50.4 (14.5) years, 88% were < 65 years, and 58% were female. In the year before ID, 80% of patients were receiving systemic glucocorticoids, most commonly oral glucocorticoids (OGCs; 77%), 13.6% were receiving immunosuppressants, and 12.7% biologics. Among the 164 patients receiving prednisone, the mean (SD) daily dose was 28 (17) mg, for a mean (SD) of 3.2 (3.5) months. In the year before ID, 96% of patients had at least one outpatient visit; most frequently family practice (50%) and internal medicine (45%). The most frequent (mean [SD]) outpatient visits were to allergy and immunology (6.2 [8.0]), family practice (4.7 [4.2]), internal medicine (4.3 [3.6]), otolaryngology (3.7 [3.0]), and pulmonary

Figure 1. Medical specialties making the first observed EGPA diagnosis



*Most claims (93.6%) came from Outpatient Hospital - On Campus. Other places of service include Inpatient Hospital, Office, Emergency Room - Hospital, and Other/Unknown.
EGPA, eosinophilic granulomatosis with polyanglitis

disease (3.3 [4.4]). Overall, 31% and 70% of patients had their first observed EGPA diagnosis in an inpatient and/or outpatient setting, respectively, which were most commonly made by acute care hospital specialists, followed by internal medicine, and pulmonary disease specialists (**Figure 1**). The mean (SD) time from first observed EGPA symptom or organ damage in the claims record to first observed EGPA diagnosis was 25.0 (15.0) months, with >99% of patients experiencing symptoms or organ damage prior to their first observed diagnosis. At ID, 95% of patients had persistent damage to at least one organ. Most patients had pulmonary damage, followed by ear, nose, and throat, and cardiovascular damage (**Table 1**).

Conclusion: Prior to their first observed diagnosis, most patients with EGPA were prescribed OGCs and made frequent health care provider (HCP) visits. At the time of their first observed diagnosis, the vast majority of patients had already experienced an EGPA event/organ damage for >2 years.These data highlight that greater awareness of EGPA is needed amongst HCPs to facilitate more rapid diagnosis, minimize organ damage, reduce exposure to therapies with harmful side effects, and better enable a multidisciplinary approach.

Table 1. Cumulative incidence of persistent organ damage

Characteristic	n (%)
Persistent damage in ≥1 organ	224 (94.9)
Pulmonary	194 (82.2)
Ear, nose, and throat	120 (50.8)
Cardiovascular	101 (42.8)
Ocular	40 (16.9)
Endocrine	25 (10.6)
Peripheral vascular disease	13 (5.5)
Renal	12 (5.1)
Musculoskeletal	9 (3.8)
Neuropsychiatric	4 (1.7)
Skin	3 (1.3)
Bone marrow	3 (1.3)
Gastrointestinal	1 (0.4)

Disclosure: P. Dolin: AstraZeneca, 3, 11; **D. Kielar**: AstraZeneca, 3, 11; **A. Shavit**: AstraZeneca, 3, 11; **K. Keogh**: AstraZeneca, 12, site PI for an AstraZeneca pharmaceutical trial in asthma; **J. Rowell**: AstraZeneca, 3, 11; **C. Edmonds**: AstraZeneca, 3, 11; **J. Meyers**: AstraZeneca, 12, Employee of RTI Health Solutions, which received funding from AstraZeneca to conduct the study; **E. Esterberg**: AstraZeneca, 12, Employee of RTI Health Solutions, which received funding from AstraZeneca to conduct the study; **T. Nham**: AstraZeneca, 12, Employee of RTI Health Solutions, which received funding from AstraZeneca to conduct the study; **S. Chen**: AstraZeneca, 3, 11.

Abstract Number: 1549

Treatment Patterns for Eosinophilic Granulomatosis with Polyangiitis (EGPA): A Retrospective Analysis of US Health Insurance Claims Data

Paul Dolin[1], Danuta Kielar[1], Anat Shavit[1], Karina Keogh[2], Jennifer Rowell[1], Chris Edmonds[3], Juliana Meyers[4], Elizabeth Esterberg[4], Tram Nham[4] and **Stephanie Chen**[5], [1]AstraZeneca, Cambridge, United Kingdom, [2]Mayo Clinic, Rochester, MN, [3]AstraZeneca, Gaithersburg, MD, [4]RTI Health Solutions, Research Triangle Park, NC, [5]BioPharmaceuticals Medical, AstraZeneca, Gaithersburg, MD

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare, immune-inflammatory disorder characterized by asthma, eosinophilia, eosinophil-rich granulomatous inflammation, and chronic necrotizing vasculitis of small-to-medium-sized blood vessels. Systemic glucocorticoids (SGCs) and immunosuppressants remain the cornerstone of treatment, even though chronic SGC use increases the risk of side effects. This retrospective analysis of US administrative health insurance claims data (Merative™ MarketScan® databases) evaluated treatment patterns for patients with EGPA.

Methods: Patients with newly diagnosed EGPA from 2017 to 2021 with ≥12 months of continuous pre-diagnosis health plan enrolment and ≥1 inpatient or ≥2 outpatient EGPA-related diagnoses (≥90 days apart, ICD-10-CM code M30.1) were included. Follow-up was from date of first observed EGPA diagnosis (index date; ID) until health plan disenrollment or database end. Use of SGCs, immunosuppressants, and biologics was analyzed, including duration and dosages (for oral medications). Duration of drug therapy was the period of continuous use including the estimated duration of last fill/refill.

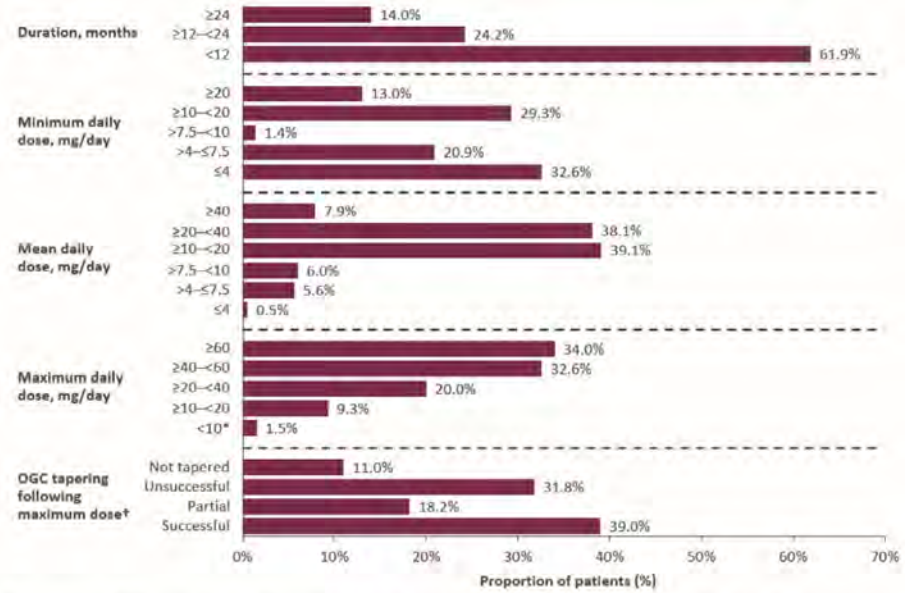
Results: 236 patients were included; 57.6% were female and mean (standard deviation [SD]) age at ID was 50.4 (14.5) years. Mean (SD) follow-up duration was 21.7 (14.6) months and 26.3% of patients had ≥30 months of follow up. In the 12 months before ID and at any time after ID, 92.4% of patients were prescribed a SGC (**Table**). Prednisone was used by 86.0% of patients, with a mean (SD) daily dose of 22.2 (12.7) mg and mean (SD) duration of 11.8 (11.5) months. Of the 236 patients, 91.1% received oral glucocorticoids (OGCs) either before or after ID, 14.0% had continuous use for ≥24 months, the mean (SD) average dose was 22.4 (13.7) mg/day, and 34.0% had a maximum dose ≥60 mg/day for a mean (SD) duration of 1.6 (1.6) months (**Figure**). Mean (SD) cumulative OGC dose was 6.3 (6.3) g with 25.6% of patients receiving ≥8 g. Among the 154 patients with at least one OGC dose >4 mg/day, OGC dose was tapered to ≤4 mg/day within 60 days of maximum dose and remained ≤4 mg/day for ≥60 days for 39.0% of patients, and OGC was tapered to >4 mg/day with ≥50% reduction in OGC dose and no subsequent increase in dose for ≥60 days for 18.2%; 11.0% did not attempt to taper their dose. Immunosuppressants were used by 40.3% of patients, most commonly azathioprine (18.2%), methotrexate (17.8%), and mycophenolate mofetil (8.1%). Mean (SD) daily dose and treatment duration were 112.4 (39.6) mg and 10.2 (11.2) months for azathioprine, 3.4 (5.5) mg and 15.5 (14.9) months for methotrexate, and 1,644.4 (749.1)

Table. Treatment patterns before and after the index date

	Patients, n (%) (N=236)		Daily dose (mg*), mean (SD)		Total duration of use (months†), mean (SD)	
	Post-index	Pre- and/or post-index	Post-index	Pre- and/or post-index	Post-index	Pre- and/or post-index
Any systemic glucocorticoids	188 (79.7)	218 (92.4)				
Oral glucocorticoids						
Any	197 (83.5)	215 (91.1)				
Prednisone	188 (79.7)	203 (86.0)	21.1 (12.5)	22.2 (12.7)	9.9 (10.0)	11.8 (11.5)
Methylprednisolone	44 (18.6)	93 (39.4)	13.9 (2.4)	13.8 (2.3)	1.3 (3.2)	1.0 (2.9)
IV glucocorticoids	65 (27.5)	95 (40.3)	N/A	N/A	3.7 (3.2)	3.5 (3.5)
Traditional immunosuppressants						
Any	90 (38.1)	95 (40.3)				
Methotrexate	39 (16.5)	42 (17.8)	3.6 (5.8)	3.4 (5.5)	14.2 (13.8)	15.5 (14.9)
Azathioprine	37 (15.7)	43 (18.2)	116.8 (38.7)	112.4 (39.6)	10.3 (10.8)	10.2 (11.2)
Mycophenolate mofetil	18 (7.6)	19 (8.1)	1,696.1 (734.8)	1,644.4 (749.1)	10.4 (10.0)	11.7 (11.5)
Cyclophosphamide (IV)	10 (4.2)	10 (4.2)	N/A	N/A	3.8 (1.6)	4.2 (1.8)
Cyclophosphamide (oral)	7 (3.0)	7 (3.0)	114.5 (50.0)	114.5 (50.0)	4.3 (2.7)	4.3 (2.7)
Cyclosporin	3 (1.3)	3 (1.3)	111.8 (10.6)	120.1 (23.1)	10.6 (4.3)	16.0 (1.1)
Biologic agents						
Any	88 (37.3)	91 (38.6)				
B-cell targeting						
Rituximab	36 (15.3)	37 (15.7)	N/A	N/A	13.3 (11.3)	14.1 (10.7)
Eosinophil/type 2 inflammation targeting						
Mepolizumab	42 (17.8)	44 (18.6)	N/A	N/A	11.4 (9.4)	11.7 (9.5)
Benralizumab	10 (4.2)	10 (4.2)	N/A	N/A	7.9 (4.3)	9.1 (4.9)
Omalizumab	8 (3.4)	13 (5.5)	N/A	N/A	9.1 (10.3)	9.9 (10.3)

The index date is the date of the first claim with a diagnosis of eosinophilic granulomatosis with polyangiitis between 2017 and 2021. The pre-index period is the 12 months prior to the index date.
*Calculated for oral tablet medications only. Methylprednisolone dose is reported as prednisone equivalent. †Total duration of drug therapy was calculated as the period of continuous use, including the estimated duration of the last fill or refill, and excluding any gaps due to discontinuation.
IV, intravenous; N/A, not applicable; SD, standard deviation.

Figure. Proportion of patients with eosinophilic granulomatosis with polyangiitis using oral glucocorticoids (N=215)



Data relate to OGC use during the 12 months before the index date, or at any time after the index date. Doses are prednisolone equivalent doses.
*Percentages for subcategories of maximum OGC were: 0.5% for ≤4 mg/day, 0.5% for >4.1–≤7.5 mg/day, and 0.5% for >7.5–<10 mg/day.
†Tapering data are for patients with ≥1 OGC dose >4 mg/day. Successfully tapered: within 60 days of the maximum dose, the OGC dose was tapered to ≤4 mg/day and remained ≤4 mg/day for ≥60 days. Partially tapered: within 60 days of the maximum dose, the OGC dose was tapered to >4 mg/day with ≥50% reduction in the OGC dose and subsequently no increase in dose for ≥60 days.
OGC, oral glucocorticoid.

mg and 11.7 (11.5) months for mycophenolate mofetil. Biologics were used by 38.6% of patients, with 15.7% using a B-cell targeting therapy (rituximab).

Conclusion: Despite the use of traditional immunosuppressants and biologics by more than one-third of patients with EGPA, the vast majority were prescribed glucocorticoids, with many receiving OGCs for long, continuous periods, and many with a maximum dose ≥60 mg/day. Most patients were unable to maintain reduced OGC doses during the follow-up period suggesting there is a need for better OGC-sparing therapies.

Disclosure: P. Dolin: AstraZeneca, 3, 11; **D. Kielar**: AstraZeneca, 3, 11; **A. Shavit**: AstraZeneca, 3, 11; **K. Keogh**: AstraZeneca, 12, site PI for an AstraZeneca pharmaceutical trial in asthma; **J. Rowell**: AstraZeneca, 3, 11; **C. Edmonds**: AstraZeneca, 3, 11; **J. Meyers**: AstraZeneca, 12, Employee of RTI Health Solutions, which received funding from AstraZeneca to conduct the study; **E. Esterberg**: AstraZeneca, 12, Employee of RTI Health Solutions, which received funding from AstraZeneca to conduct the study; **T. Nham**: AstraZeneca, 12, Employee of RTI Health Solutions, which received funding from AstraZeneca to conduct the study; **S. Chen**: AstraZeneca, 3, 11.

Abstract Number: 1550

Importance of Shared Decision-Making for Patients with ANCA-Associated Vasculitis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification

Session Type: Poster Session B

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Background/Purpose: ANCA-associated vasculitis (AAV) is a rare autoimmune disease associated with significant morbidity. It can present at any age and treatment needs change over time. Multimorbidity is common, leading to polypharmacy and increased treatment burden. Management is a complex balance of achieving effective disease control to prevent progressive organ damage and minimizing treatment-emergent toxicities with long-term health consequences. Revised EULAR recommendations in 2022 for the management of AAV recommend shared decision-making (SDM) between patient and specialist, acknowledging that involving patients in decision-making enables better understanding of patient needs and priorities and potential to improve treatment decisions. (1) As significant opportunity exists to enhance multidisciplinary care of AAV, this expert review aims to identify opportunities to support SDM across the care pathway.

Methods: Embase, Medline, and Cochrane Library were searched for relevant publications using terms and strategies including variations of ANCA-associated vasculitis plus shared decision-making in titles or abstracts. Extracted data are described without synthesis of quantitative data.

Results: Beyond the EULAR guidelines, few publications highlight the practice of, implementation of, or outcomes associated with SDM in AAV. Barriers to implementation include lack of sufficient knowledge and communication about the disease (owing to its rarity and few experts), uncertain prioritization of management goals, absence of proven initiatives in healthcare settings, lack of dedicated healthcare spaces, and poor patient health status. Central to SDM is discussion between patients and specialists on the benefits and harms of therapeutic options, leading to collaborative management decisions based on the best available evidence. Potential approaches to meet the challenges of practical implementation include sharing information on AAV management to help close knowledge gaps by broadening understanding of disease impact, key warning symptoms, and treatment-related toxicities. Support mechanisms for SDM in AAV include use of decision aids such as the three-talk model based on choice, option and decision talk stages to provide balanced information. Increasing use of patient-reported outcome measures may help evaluate the impact of symptoms and interventions on patient health-related quality of life (HRQoL), and should support the choice of treatment.

Conclusion: The implementation of SDM in AAV has the potential to increase knowledge about the disease and risks, give patients an active role allowing for a collaborative approach and enhance the responsiveness and confidence of patients and caregivers, supporting enhanced outcomes and improved patient HRQoL.

Disclosure: J. Robson: CSL Vifor, 2, 5, 6, Sanofi, 5, UKIVAS Registry, 12, Non profit organization Rheumatology Co-Chair; **M. Díaz Encarnación**: AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Novartis, 1; **P. Verhoeven**: None; **R. Olivenza**: CSL Vifor, 3; **M. Balcells**: Amgen, 12, RSU, CSL Vifor, 3; **S. Monti**: CSL Vifor, 6; **A. Kronbichler**: Catalyst Biosciences, 2, CSL Vifor, 2, Delta4, 2, GlaxoSmithKlein(GSK), 2, Otsuka, 2, Waiden Biosciences, 2.

Abstract Number: 1551

Measurement of Sinonasal Disease Activity in Granulomatosis with Polyangiitis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification
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Background/Purpose: In granulomatosis with polyangiitis (GPA), sinonasal inflammation can be severe and significantly impact quality of life. Little is known about the most effective local and systemic therapies for sinonasal disease in GPA, in part due to outcome measures which lack sensitivity to change. The Sino-Nasal Outcome Test-22 (SNOT22) is a patient-reported outcome measure validated in chronic rhinosinusitis but it has not been well-studied in GPA. This study measured sinonasal disease activity using the SNOT22 and the more widely-used Birmingham Vasculitis Activity Score for Wegener's Granulomatosis (BVAS/WG) in patients treated for active GPA.

Methods: This prospective, longitudinal cohort study included patients who met the 1990 ACR classification criteria for GPA. Patients with active disease during enrollment and at least one follow-up visit 3 or more months later were included. The following therapy initiations were examined: I) saline nasal rinses; II) topical nasal glucocorticoids; III) topical nasal antibiotics; and IV) rituximab (within the prior 6 months); patients could be in more than one group. Outcome measures included: (a) percent of patients achieving the minimal clinically important difference (MCID) for SNOT22 of 8 as determined for chronic rhinosinusitis; (b) percent change in SNOT22; and (c) percent of patients achieving BVAS/WG=0 for sinonasal items. For analysis of MCID, regression models adjusted for baseline SNOT22 score and predicted values were plotted. In secondary analyses models also adjusted for potential confounders, including prednisone, other concurrent treatments, and active sinus disease at relapse visit.

Results: The study included 52 flares in 42 patients with GPA. 35 (83%) patients had a prior history of sinonasal involvement, 28 (67%) were PR3-ANCA positive, and mean disease duration was 2 (0-5) years. At the active visit, 37 (70%) visits had active sinonasal involvement, and mean SNOT-22 score was 27 (IQR 4,15). New medications prescribed included: 30 (58%) saline nasal rinse, 9 (18%) topical nasal glucocorticoids, 4 (8%) topical nasal antibiotics, and 8 (15%) rituximab. For topical nasal glucocorticoids, new initiation vs. no initiation was associated with a greater probability of achieving an MCID for SNOT22 (OR 8.5 [95% CI 1.3, 55.6], P-value 0.026) **(Figure 1**). For saline nasal rinse, new initiation vs no initiation was associated with a greater percent change in SNOT22 (coefficient -0.60, [95% CI -1.17, -0.04], P= 0.037) (**Figure 2**). Results remain statistically significant even after adjusting for confounders. No significant changes were seen between any treatment groups when using the sinonasal items on BVAS/WG (**Figure 3**).

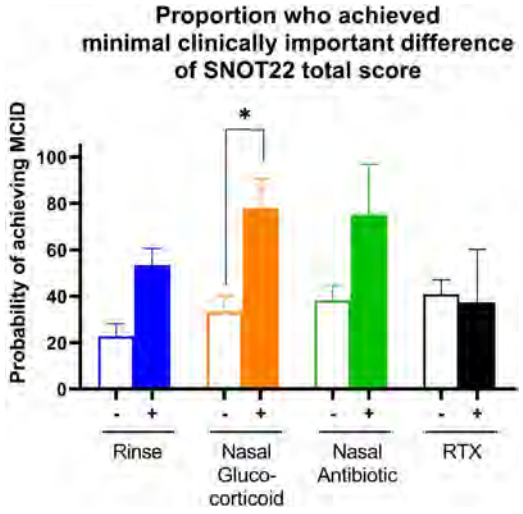

Figure 1: Proportion of patients with active GPA who achieved MCID of SNOT22 after new initiation of treatment. Bar graphs show mean (95% CI) of probability of achieving the minimal clinically important difference (MCID) of the Sino-Nasal Outcome Test 22 (SNOT22) score. Four treatments were analyzed separately so each patient contributed to each analysis and were categorized based on no initiation of treatment (-) vs initiation of treatment (+). Four medications were evaluated: saline nasal rinse (blue), topical nasal glucocorticoids (orange), topical nasal antibiotic (green), and rituximab within the prior 6 months (RTX; black). Logistic regression models adjusted for baseline SNOT22 score at time of active disease. * $P < 0.05$.

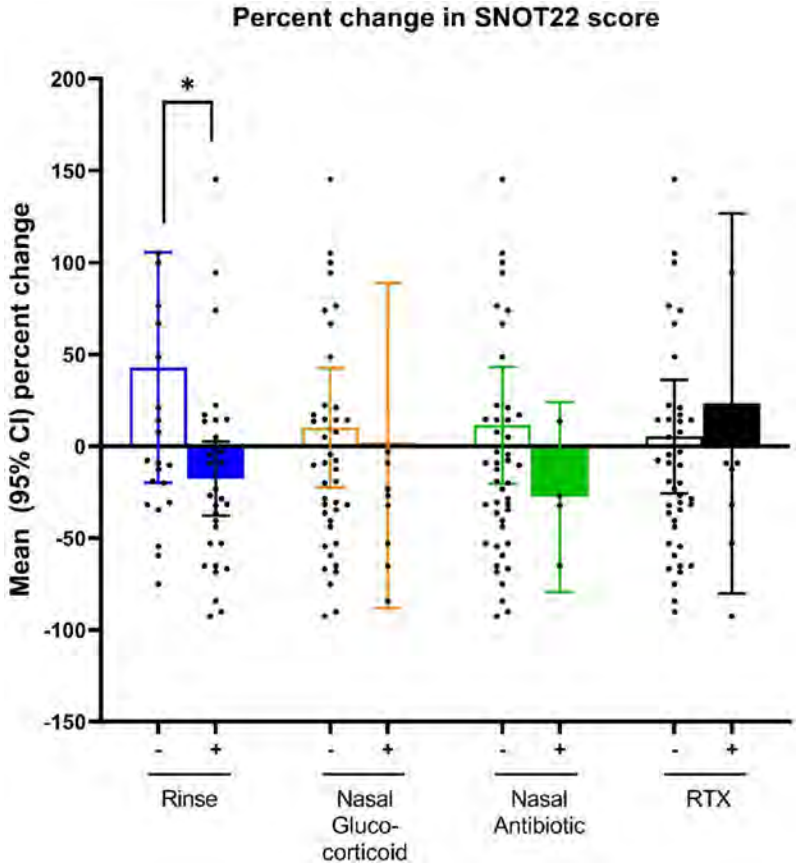

Figure 2: Percent change in SNOT22 score after initiation of new treatment for active granulomatosis with polyangiitis. Bar graphs show mean (95% CI) percent change in Sino-Nasal Outcome Test 22 (SNOT22) score between active and follow-up visits. Four different treatments were analyzed separately so each patient contributed to each analysis and were categorized based on no initiation of treatment (-) vs initiation of treatment (+). Four medications were evaluated: saline nasal rinse (blue), topical nasal glucocorticoids (orange), topical nasal antibiotic (green), and rituximab within past 6 months (RTX; black). * $P < 0.05$.

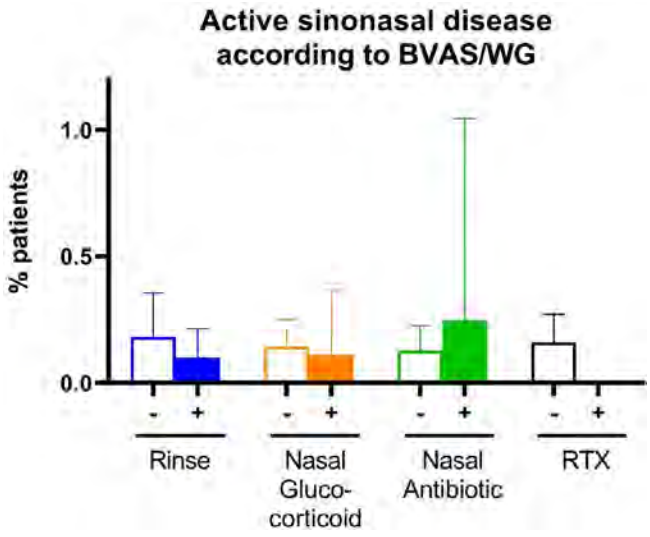

Figure 3: Proportion of patients with sinonasal disease activity according to BVAS/WG after initiation of new treatment for active granulomatosis with polyangiitis. Bar graphs show percentage (95% CI) of patients who had new/worsening or persistent sinonasal activity according to the BVAS/WG. Four different treatments were analyzed separately so each patient contributed to each analysis and were categorized based on no initiation of treatment (-) vs initiation of treatment (+).. Four medications were evaluated: saline nasal rinse (blue), topical nasal glucocorticoids (orange), topical nasal antibiotic (green), and rituximab within the prior 6 months (RTX; black). No statistically significant differences were found among the four treatment comparisons.

Conclusion: In GPA use of a patient-reported outcome measure of sinonasal symptoms (SNOT22) enabled detection of response to topical nasal therapies. Specifically, use of saline nasal rinse and topical nasal glucocorticoids were associated with improvement in sinonasal symptoms. In contrast, treatment response was not detected when using the BVAS/WG, suggesting that SNOT22 may have more responsiveness and convergent validity when assessing sinonasal disease in GPA.

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Abstract Number: 1552

Epidemiology and Outcome of Eosinophilic Granulomatosis with Polyangiitis in France

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

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Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA, formerly Churg-Strauss) belongs to the group of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV). There are no recent data on the epidemiology and outcome of EGPA in France.

Methods: Patients with EGPA were identified from 2013 to 2019 for the epidemiological objective and from 2012 to 2016 for the longitudinal analysis in the French National Health System database, which covers 98% of the French population. To be included, patients had to be affiliated to the general health insurance system and either have full coverage for EGPA (ICD-10 code M30 Polyarteritis nodosa and related conditions or M301 Periarteritis with pulmonary involvement [Churg-Strauss]) or have been hospitalised for EGPA (ICD-10 code M301 only). A sensitivity analysis was also performed on a population restricted to patients who had at least 3 courses of oral glucocorticoids in the year after diagnosis.

Results: There were 7,238 subjects in the main analysis and 3,328 subjects in the sensitivity analysis, corresponding to a prevalence of 85.3 cases/million and 38.4 cases/million, respectively. There were 1,650 and 1,035 new cases/year in the main and the sensitivity analysis, corresponding to an incidence of 3.5 and 2.1 cases/million/year, respectively. In the incident case population (main analysis), the mean age was 61.7 ± 17.4 years, with 57.1% of females; the mean duration of follow-up was 60.1 ± 22.3 months.

The mean duration of oral glucocorticoids was 45.6 months and 53.1 months in the main and sensitivity analyses, respectively. The mean monthly dose of glucocorticoids during the first 6 months was 449.5 mg (i.e. 15 mg/d) in the main analysis and 693.9 mg (i.e. 23.1 mg/d) in the sensitivity analysis, while it gradually decreased to reach a plateau from the 3rd year and until the 8th year of follow-up, with a mean monthly dose of glucocorticoids during these years of approximately 135 mg (or 4.5 mg/d) in the main analysis and 190 mg (or 6.3 mg/d) in the sensitivity analysis.

During follow-up, 62.6% of patients in the main analysis and 69.1% of patients in the sensitivity analysis had at least one complication or new comorbidity, the most common being osteoporosis (21.6% and 31.4%, respectively), followed by arterial hypertension (20.7% and 21.7%), arrhythmia (14.6% and 15.2%) and diabetes (10.9% and 12.2%).

The age- and sex-standardized mortality rate of EGPA was 11.3/1000 patients (main analysis) and 9.7/1000 (sensitivity analysis), compared with 9.2/1000 patients in the general population. At 5 years, the rate of hospitalization for asthma exacerbation was 10.2% (8.7-11.8), and the rate of EGPA relapse was 69.3% (66.9-71.6).

Conclusion: The incidence of EGPA estimated in a large population is consistent with previous estimates but prevalence seems to be higher. This comprehensive study of treatments and complications highlights the extensive and prolonged use of oral corticosteroid therapy. Complications are common and include osteoporosis, hypertension, cardiac arrhythmias, and diabetes. Overall survival of EGPA is excellent but relapses are still frequent, suggesting that the burden of disease remains high.

Disclosure: B. Terrier: AstraZeneca, 5, CSL Vifor, 2, GlaxoSmithKlein(GSK), 2; **C. Taillé**: AstraZeneca, 6, Chiesi, 5, 6, GSK, 5, 6, Novartis, 5, 6, Sanofi, 6; **A. Brouquet**: None; **S. Tauty**: None; **F. Bugnard**: None; **L. Guillevin**: None; **X. Puéchal**: None; **V. Cottin**: Boehringer Ingelheim, 2, 5, 6, 12, Support for attending meetings, Celgene/BMS, 1, 2, CSL Behring, 2, Ferrer, 2, 6, 12, Support for attending meetings, FibroGen, 1, Galapagos, 1, 2, Galecto, 1, GlaxoSmithKline, 2, Pliant, 2, Pure Tech, 2, Redx, 2, Roche, 1, 2, 6, 12, Support for attending meetings, Sanofi, 2, Shionogi, 2.

Abstract Number: 1553

Central Nervous System Involvement and Mimickers in ANCA Associated Vasculitis

Yeliz Yagiz Ozogul[1], **Sinem Nihal Esatoglu**[2], Murat Ozogul[3], Osman Kizilkilic[4], Yesim Ozguler[5], Ugur Uygunoglu[6], Vedat Hamuryudan[2] and Gulen Hatemi[2], [1]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Department of Internal Medicine, Istanbul, Turkey, [2]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, [3]Haydarpasa Numune Training and Research Hospital, Department of Radiology, Istanbul, Turkey, [4]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Department of Radiology, Istanbul, Turkey, [5]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Department of Internal Medicine, Division of Rheumatology, İstanbul, Turkey, [6]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Department of Neurology, Istanbul, Turkey

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Vasculitis – ANCA-Associated Poster II: Epidemiology, Outcomes, & Classification

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Central nervous system (CNS) involvement is rare in ANCA associated vasculitis (AAV). On the other hand, AAV patients may develop complications or other conditions that mimic CNS involvement. We aimed to present the clinical, laboratory and imaging features of our AAV patients with CNS involvement and conditions other than CNS involvement that caused neurologic symptoms.

Methods: We surveyed the charts of 430 AAV patients in order to identify patients who were evaluated for neurologic symptoms suggesting CNS involvement. We extracted data on their demographics, types of AAV, neurologic symptoms, final diagnoses after neurologic work-up and their outcome.

Results: Of 430 AAV patients, 61 patients (14%) (41 GPA, 11 MPA, 9 EGPA; 27 women, 34 men; mean age: 51.6±15.4) with neurologic symptoms were identified. Among these, the cause of neurologic symptoms was CNS involvement of AAV in 7 patients (data summarized in Table 1), other AAV manifestations in 30, and secondary complications mimicking CNS involvement in 15 patients, whereas neurologic work-up did not lead to an underlying condition in 9 (Table 2). Among the 61 AAV patients with neurologic symptoms, the most common neurologic symptom suggesting CNS involvement was headache (n=20), followed by muscle weakness (n=17), numbness (n=17), and visual impairment (n=16). At the time of the occurrence of neurologic symptoms, all patients had active disease [median (IQR) BVAS=11.9 (7-15)]. 14 patients (22.9%) had accompanying peripheral nervous system (PNS) involvement. Regarding the outcomes, 6 of the 7 patients with CNS involvement of AAV recovered with sequelae, whereas one patient completely recovered. Among the 30 patients with other AAV manifestations causing neurologic symptoms, 21 recovered without sequela while the remaining 9 recovered with sequela despite treatment. Finally, among the 15 patients with conditions mimicking CNS involvement of AAV, one patient with spondylodiscitiscomplicated with aortic pseudoaneurysm, one with septic emboli and one with diabetic ketoacidosis complicated with pneumosepsis had died, one patient withskull base osteomyelitis recovered with a sequela of blindness, and the remaining patients recovered without sequela.

Conclusion: CNS involvement was uncommon, observed in only 1.6% of our 430 AAV patients. AAV manifestations other than CNS involvement such as ocular, orbital and nasopharyngeal involvement, as well as complications like infections and cardiovascular disease, may mimic CNS involvement in patients with AAV. These non-CNS entities account for almost 75% of the causes for any neurological symptom among AAV patients.

Table 1. Demographic features of the patients and causes for neurologic sign or symptoms

Variable, n (%)	61 AAV patients
Male	34 (55.7)
Mean age, years	51.6±15.4
Type of AAV	
GPA	41 (67.2)
MPA	11 (18)
EGPA	9 (14.7)
CNS involvement of AAV	7 (11.4)
Meningeal involvement	3 (4.9)
Dural involvement and secondary parenchymal infarct	1 (1.6)
Meningeal, parenchymal involvement and syringomyelia	1 (1.6)
Dural involvement	1 (1.6)
Vascular involvement	2 (3.2)
Ischemic CVA	1 (1.6)
Ischemic CVA with hemorrhagic transformation	1 (1.6)
Intracranial hypertension	1 (1.6)
Cerebral venous sinus thrombosis	1 (1.6)
AAV manifestations other than CNS involvement	30 (49.1)
PNS involvement	8 (13.1)
Sinonasal involvement	4 (6.5)
Nasal involvement	2 (3.2)
Associated with disease activation	2 (3.2)
Orbital and paranasal involvement, seconder CNS paralysis and PNS	2 (3.2)
Orbital involvement	1 (1.6)
Ocular involvement	1 (1.6)
Facial paralysis due to facial nerve involvement	1 (1.6)
Facial paralysis due to orbital involvement	1 (1.6)
Facial paralysis due to parotid gland involvement	1 (1.6)
Associated with disease activation and PNS involvement	1 (1.6)
Associated with disease activation and cervical hernia	1 (1.6)
Retinal vasculitis	1 (1.6)
Nasopharyngeal mass and PNS involvement	1 (1.6)
Parotid gland involvement	1 (1.6)
Cardioembolic CVA associated with cardiac mass	1 (1.6)
Cardiac thrombus	1 (1.6)
Secondary complications	15 (24.5)
Atherosclerotic CVA	5 (8.1)
Drug side effect	2 (3.2)
Cardioembolic CVA associated with atrial fibrillation and PNS inv.	1 (1.6)
PRES	1 (1.6)
Hemorrhagic CVA secondary to hypertension	1 (1.6)
Spondylodiscitis complicated with aortic pseudoaneurysm	1 (1.6)
Heart failure	1 (1.6)
Skull base osteomyelitis	1 (1.6)
Septic cranial embolism	1 (1.6)
Ketoacidosis and sepsis	1 (1.6)

Table 2. Management and outcome of 7 AAV patients with CNS involvement

Type of CNS involvement	Type of AAV	Treatment	Outcome
Ischemic CVA with hemorrhagic transformation	EGPA	CYC, GC, anti-epileptic	Recovered without sequela
Intracranial hypertension	GPA	CYC, RTX, GC	Recovered with sequela
Ischemic CVA	GPA	CYC, GC	Recovered with sequela
Meningeal, parenchymal involvement and syringomyelia	GPA	RTX, AZA, GC	Recovered with sequela
Dural involvement and secondary parenchymal infarct	GPA	RTX, GC, anti-epileptic	Recovered with sequela
Dural involvement	GPA	IVIG	Recovered with sequela
Cerebral venous sinus thrombosis	MPA	RTX, AZA, GC	Recovered

CNS, Central Nervous System; GC, glucocorticoids; CYC, Cyclophosphamide; RTX, Rituximab; CVA, cerebrovascular accident; AZA, Azathioprine; IVIG, intravenous immunoglobulin

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Abstract Number: 1554

Therapeutic Approaches and Predictive Factors of Relapse in Severe Ocular Involvement in Behçet's Disease: A Multicentre Retrospective Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: The management of severe ocular involvement in Behçet's disease (BD) is an important issue with major functional implications due to the risk of blindness. In patients with severe ocular involvement, *TNF*-alpha blockers have been shown to be a rapid and effective therapeutic option for controlling the disease. Once complete remission of ocular involvement has been achieved, there is a risk of relapse and potential blindness. We aimed to describe the therapeutic strategies used and to identify factors associated with ocular relapse.

Methods: This French, multicenter, retrospective study was conducted using a standardized data collection form over a 2-year period and included adults with Behçet's disease presenting with severe ocular involvement (posterior uveitis, retinal vasculitis, macular involvement). Patients' systemic and ocular characteristics were compared using Student's t-tests, Chi-2 tests and Fischer tests, as appropriate. Variables associated with the risk of relapse were assessed using Cox proportional hazards models and adjusted for potential confounders.

Results: A total of 119 patients were included in this study (male/female ratio of 2.1, median age 34 (28-43) years). Severe ocular involvement was the first manifestation of BD in 101 (88%) patients. Fifty percent of patients were active smokers at the time of ocular involvement.

Severe ocular involvement consisted of posterior uveitis in 108 (91%) patients, retinal vasculitis in 86 (72%) cases, and macular involvement was found in 32 patients (34%).

Oral glucocorticoids therapy was initiated in 114 (97%) patients at a median dose of 60 mg per day (IQR 50-70), preceded by pulses of methylprednisolone in 54/110 (49%). In combination with systemic and/or topical corticosteroid therapy, 91 patients (76%) received at least one immunosuppressive and/or immunomodulatory treatment: azathioprine (n=62), *TNF*-alpha blockers (n=36), cyclophosphamide (n=13), mycophenolate mofetil (n=6), interferon-alpha (n=6) or methotrexate (n=5). Colchicine was prescribed in 85 patients (71%).

Characteristics and therapeutic management according to whether the presence or absence of macular involvement or the presence or absence of retinal vasculitis did not show any difference.

At the end of the first line of treatment, 99/119 patients (87%) achieved remission, and 52 of them (53%) relapsed during follow-up.

Remission and relapse rates were similar between patients with and without macular involvement and with and without retinal vasculitis. After achieving remission, the risk of relapse was significantly associated with active smoking (adjusted HR 1.92 (1.02-3.61)) and was lower in those who received prolonged glucocorticoids (adjusted HR 0.3 (0.16-0.55)), colchicine (adjusted HR 0.43 (0.22-0.83)), and anti-TNF-alpha (adjusted HR 0.5 (0.25-0.99)).

Conclusion: Among patients with Behçet's disease and severe ocular involvement, the risk of ocular relapse was reduced by prolonged glucocorticoid therapy, systematic use of colchicine, and TNF-alpha blockers. Active smoking was associated with an increased risk of relapse, supporting the need for tobacco cessation in patients with Behçet's disease and severe ocular involvement.

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Abstract Number: 1555

Axial Spondyloarthritis in Patients with Gastrointestinal Involvement of Behçet Syndrome

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Controlled studies have shown that radiographic sacroiliitis was not increased in Behçet syndrome (BS), compared to other inflammatory diseases. However, gastrointestinal involvement of Behçet syndrome (GIBS) shares common features with inflammatory bowel disease which, in turn, can be associated with spondyloarthritis (SpA). We wanted to see whether GIBS patients have an increased frequency of radiographic sacroiliitis or non-radiographic axial spondyloarthropathy (nr-AxSpA) compared to BS patients with only mucocutaneous and/or joint involvement with no major organ involvement.

Table. Demographics and clinical characteristics

	GIBS (n=71)	BS with only mucocutaneous and/or joint involvement (n=76)
Male	38 (53.5%)	23 (30%)
Mean (SD) age, years	45 ±12	42 ± 13
AxSpA according to ASAS criteria	5 (7%)	4 (5%)
Clinical arm	2	2
Imaging arm	3	2
Chronic back pain	30 (42%)	25 (33%)
Inflammatory back pain	17 (24%)	13 (17%)
SpA features among patients with chronic back pain		
Inflammatory back pain	17 (57%)	13 (52%)
HLA-B27	2 (7%)	3 (12%)
Arthritis	14 (47%)	11 (44%)
Enthesitis	11 (37%)	7 (28%)
Dactylitis	2	0
Psoriasis	1	1
Good response to NSAID	21 (70%)	16 (64%)
Family history for SpA	10 (33%)	6 (24%)
Elevated CRP	7 (23%)	3 (12%)

Methods: We included 71 GIBS patients and 76 consecutive BS patients without major organ involvement. Patients were screened for axial spondyloarthritis (axSpA) using the Assessment of Spondyloarthritis International Society (ASAS) criteria. First they were questioned for chronic back pain, defined by ASAS as the presence of chronic back pain for more than 3 months and an age at onset of < 45 years. Patients with chronic back pain were questioned for other spondyloarthritis features and tested for HLA-B27 status, CRP levels and X-ray and magnetic resonance imaging of the sacroiliac joints. All radiologic images were evaluated independently and blind bytwo radiologists.

Results: Chronic back pain was reported by 30 (42%) GIBS patients and 25 (33%) BS patients with only mucocutaneous and/or joint involvement (p=0.24). Five (7%) GIBS patients and 4 (5%) controls met ASAS criteria for axSpA (p=0.74). Only 1 GIBS patient had radiographic axSpA (also termed ankylosing spondylitis), whereas 4 GIBS patients and 4 patients among the controls had nr-AxSpA. HLA B27 was positive in 3 (4%) of the GIBS patients and in 5 (7%) of the controls (p=0.72). There were no significant differences between the groups regarding other SpA features of the ASAS criteria (Table).

Conclusion: The frequency of axSpA in GIBS patients was not found to be higher than that in BS patients who have only mucocutaneous and/or joint involvement. This finding further suggests that, despite certain clinical similarities between GIBS and Crohn's disease, different disease mechanisms may be involved.

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Abstract Number: 1556

Abdominal Surgical Interventions Among Patients with Gastrointestinal Involvement of Behçet Syndrome

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SESSION INFORMATION
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Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
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Session Time: 9:00AM–11:00AM

Background/Purpose: Gastrointestinal involvement of Behçet's syndrome (GIBS) may require surgery in up to one third of the patients. We aimed to investigate the clinical characteristics, treatments, and long-term prognosis of GIBS patients who underwent abdominal surgical interventions.

Methods: We conducted a retrospective chart review of all Behçet syndrome (BS) patients recorded between 1978 and 2022 to identify those with GIBS who had undergone abdominal surgery for GIBS. Data were collected regarding demographics, type of interventions, treatment, recurrences, and outcomes. Relapse was defined as the presence of endoscopic or clinical activity with a positive fecal calprotectin test following bowel resection.

Table. Demographic and characteristics of the patients

Variable	GIBS patients who underwent abdominal surgery (n=29)
Male, n (%)	19
Mean (SD) current age, years	49 ± 11
Juvenile onset, n (%)	4 (13%)
Mean (SD) age at BS diagnosis, years	28 ± 10
Mean (SD) age at GIBS diagnosis, years	34 ± 11
Patients fulfilling ISG criteria, n (%)	23 (79%)
Major organ involvement, n (%)	15 (51%)
Uveitis	11
Vascular	5
Central nervous system	2
Pathergy positivity , n/N (%)	13/27 (48%)
HLAB51 positivity, n/N (%)	12/18 (66%)
Reasons for surgery	
Perforation	18 (62%)
Massive hematochezia	6 (21%)
Ileus	2
Suspicion of acute abdomen	2
Refractory disease	1
Patients who were receiving immunosuppressive treatment at the time of surgery	3 (10%)

Results: Among our 11,200 BS patients, 119 (1%) had GIBS, and 27 (24%) of these GIBS patients (19 male, mean age: 49 ± 11 years) had undergone abdominal surgery (Table). BS was already diagnosed at the time of gastrointestinal involvement in 19 (65%) patients while 10 were diagnosed with BS with the development of gastrointestinal involvement. All except 1 patient who underwent ileocecal resection due to refractory disease, were diagnosed with GIBS following abdominal surgery. Perforation (n=18, 62%) and massive hematochezia (n=6, 21%) were the main reasons for surgery. The type of surgery

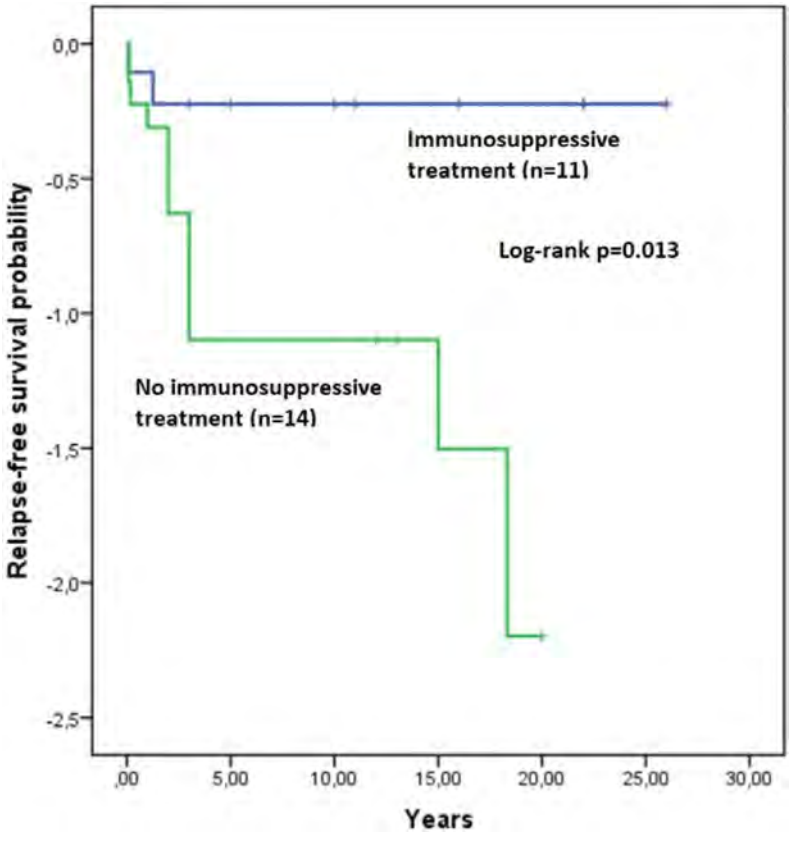

Figure. Relapse-free survival of patients who used postoperative immunosuppressive vs who did not

was bowel resection in 25 patients, primary closure in 2 and diagnostic laparotomy in 2 patients. Two patients with refractory GIBS had died due to extensive vascular involvement (n=1) and secondary amyloidosis (n=1). Among the 25 patients who underwent bowel resection, 14 (56%) experienced a relapse during a median follow-up of 24 (IQR: 1.75-36) months. Of these 14 patients, 12 had only one relapse. At the time of relapse, 4 (29%) patients required a reoperation. The remaining 11 patients did not experience any relapses during a median follow-up of 13 (IQR: 10-22) months. Postoperative azathioprine treatment was initiated in 11 patients, with 3 of them also receiving a TNF inhibitor. Three of these 11 patients experienced a relapse while among the 14 patients who did not receive postoperative immunosuppressive treatment, 11 had a relapse (27% vs 79%; p=0.01). The use of postoperative immunosuppressive treatment was associated with a reduced risk of relapse (OR: 0.10; 95% CI: 0.016-0.644). Moreover, time to relapse was significantly longer in patients who received postoperative immunosuppressive treatment compared to those who did not (p=0.013, log-rank test, Figure)

Conclusion: GIBS may presently acutely with perforation or severe bleeding requiring surgery, as the first manifestation. In this cohort 24% of GIBS patients required abdominal surgery and all except one were diagnosed with GIBS following the surgical procedure. Approximately 50% of the patients experienced a relapse, with most relapses occurring within 3 years. Among the patients who relapsed, 30% required reoperation. The use of immunosuppressive treatment after surgery showed a significant protective effect, reducing the risk of relapse by 90%.

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Abstract Number: 1557

De Novo Manifestations During Adalimumab Treatment in Behçet Syndrome

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SESSION INFORMATION

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Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

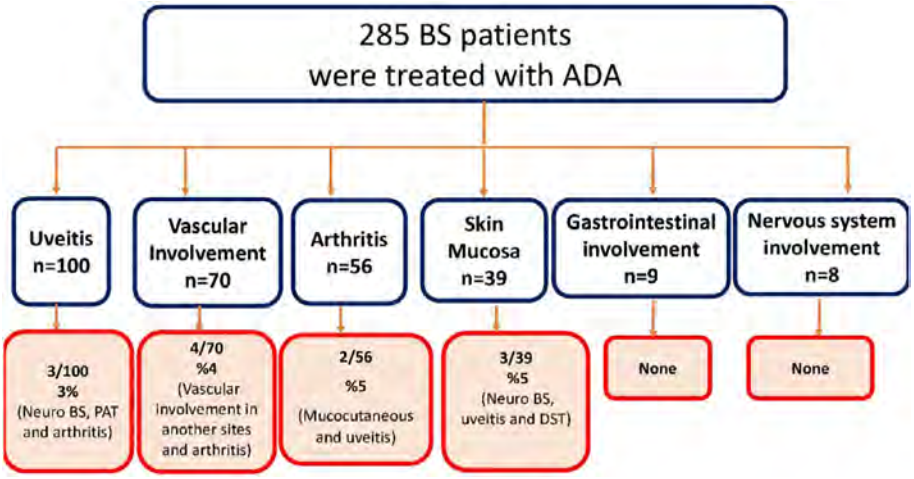
Background/Purpose: Monoclonal antibody tumor necrosis factor alpha inhibitors, particularly infliximab and adalimumab, are the most commonly used biological agents in the treatment of Behçet's syndrome (BS). Treatment response may show variability across organ manifestations of BS. We aimed to determine the frequency of de novo manifestations during adalimumab (ADA) treatment.

Methods: We conducted a chart review of 285 BS patients who received ADA in our Behçet Disease Research Center. Demographic data, reasons for initiating ADA, concurrent medications, previous treatments, and treatment outcomes were recorded. We defined de novo manifestations as new BS manifestations that had not manifested prior to the initiation of ADA treatment. For patients with vascular involvement, a new vascular event at another vessel was also considered as a de novo manifestation.

Age at ADA initiation, gender	BS manifestations	Main involvement requiring ADA	Previous drugs	Concomitant drugs	Time to de novo (months)	De novo manifestation	Treatment for de novo manifestation
24, M	O,G,J,E,U	MK	AZA,COL	AZA,COL	2	Arthritis	GC and IFX
51, M	O,G,J,EN,STM	Arthritis	SZP,MTX, ETA,IFN,AZA, COL	AZA,MTX	32	DST	ADA Intervals ↓
26,M	O,G,J,EN,U, Budd-Chiari, CT	MK	IFX,COL, AZA,CYC, MMF	COL,GC	35	Anterior uveitis	Topical steroid
26,M	O,G,P,DVT,DST ,PAT,VCI,CT	DVT	COL,AZA, CYC,IFN,IFX	COL,GC	3	DST	Pulse MP and AZA
39, W	O,G,EN,DVT	Lower extremity DVT	COL, AZA,CYC, IFN,IFX	AZA,GC	12	Upper extremity DVT	GC
44, M	O,G,U,DVT,PAT ,PAA,STM	PAI	IFX,AZA,CYC	AZA,GC	30	MVT and PVT	Pulse MP and ADA intervals ↓
34, M	O,G,P,EN,U,PA T,DVT	Uveitis	COL, CY-A,CYC,MMF,I FN,AZA	None	9	NBS	Pulse MP, IFX and MMF
51, M	O,P,EN,J,DVT, STM	DVT	AZA,COL	COL	18	Arthritis	GC
15, W	O,G,P,U,GIS,J	Arthritis	AZA,COL	AZA,COL	12	Anterior uveitis	Topical treatment
62, W	O,G,P,EN,J,U, NBS	Arthritis	COL,AZA, CY-A,IFN	AZA,COL, GC	26	NBS	Pulse MP, CZP
57, W	O,G,EN,J,U	Uveitis	COL,AZA, CY-A	AZA,GC	26	Arthritis	COL
25, M	O,G,P,EN,U,PA T	Uveitis	AZA,COL,GC	AZA,GC	14	PAT	ADA Intervals ↓

ADA: adalimumab; AZA: azathioprine; Cardiac Thrombus: CT;COL: colchicine; CSA: cyclosporine-A; CYC: cyclophosphamide; CZP: Certolizumab;DST: dural sinus thrombosis; DVT: deep vein thrombosis; EN: erythema nodosum; Epididymitis: E; genital ulcer:GC; glucocorticoid/prednisolone: GC;GIS: gastrointestinal:GIS; IFX: infliximab; INF: interferon alpha; IVC: inferior vena cava; J: joint; M: male; MMF: mycophenolate mofetil; MTX: methotrexate; MVT: Mesenteric Ven thrombosis;; NBS: Neuro-Behçet syndrome; O: oral ulcers; PAA: pulmonary artery aneurysm; PAI : pulmonary artery involvement; PAT: pulmonary artery thrombosis; Pulse MP: high-dose intravenous methylprednisolone (1 gr for 3 days); PVT: Portal Ven thrombosis; STM: superficial thrombophlebitis; U: uveitis; W: woman.

Demographics, characteristics, de novo manifestations and treatment of de novo manifestations of 12 patients



Results: The main reasons for ADA use among our 285 patients were uveitis in 100 patients (35%), vascular involvement in 70 (%25), arthritis in 56 (%20), mucocutaneous involvement in 39 (%14), parenchymal central nervous system involvement in 8 (%3), and gastrointestinal involvement in 9 (%3). Among these patients, 12 (4%) developed a de novo manifestation. De novo manifestations that occurred in 12 patients were vascular involvement in 5 patients, arthritis in 3, anterior uveitis in 2, and parenchymal central nervous system involvement in 2. The primary reasons for ADA treatment were vascular involvement in 3, arthritis in 3, uveitis in 3, and mucocutaneous involvement in 2 of these 12 patients. Among these 12 patients, 8 (61%) were using concomitant conventional immunosuppressive treatment at the time of occurrence of de novo manifestations.

Treatment with ADA was intensified in 3 patients by shortening the intervals to 1 week, along with the addition of high dose glucocorticoids in one patient. In the 3 patients, ADA was switched to another agent (infliximab in 2 patients, certolizumab in 1 patient). Only glucocorticoids were added in two patients, azathioprine along with high dose corticosteroids in one patient and colchicine in one patient. Two patients who had developed anterior uveitis were initiated topical treatment (Table).

Conclusion: De novo manifestations occurred in 4% of BS patients treated with adalimumab. Majority of these (75%) were major organ involvement, mainly vascular involement. None of the patients developed posterior uveitis, the 2 patients with uveitis developing during ADA had anterior uveitis that was controlled with topical agents.

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Abstract Number: 1558

Development of Posterior Uveitis in Behçet's Syndrome Patients with Vitreous Cells Without Any Other Posterior Involvement

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Background/Purpose: A considerable number of patients with Behçet's syndrome (BS) have vitreous cells (VC) on slit lamp examination at the time of diagnosis. However, the prognostic importance of VC and their association with the development of posterior uveitis (PU) requiring immunosuppressive treatment is unknown. We aimed to determine the prognostic importance of VC in BS patients.

Methods: The charts of 572 consecutive BS patients fulfilling ISG criteria who were registered between 2010 and 2012 were reviewed. At baseline visit 164 patients had VC in one or both eyes. Among the remaining patients, 229 had no eye involvement, 116 patients had bilateral pan or posterior uveitis, 14 had unilateral pan or posterior uveitis and no eye involvement in the other eye, 20 had isolated anterior uveitis, and 29 had insufficient data in their medical records. Among the 164 patients with VC, 110 patients with a follow-up of ≥2 years were included in this study (Figure).

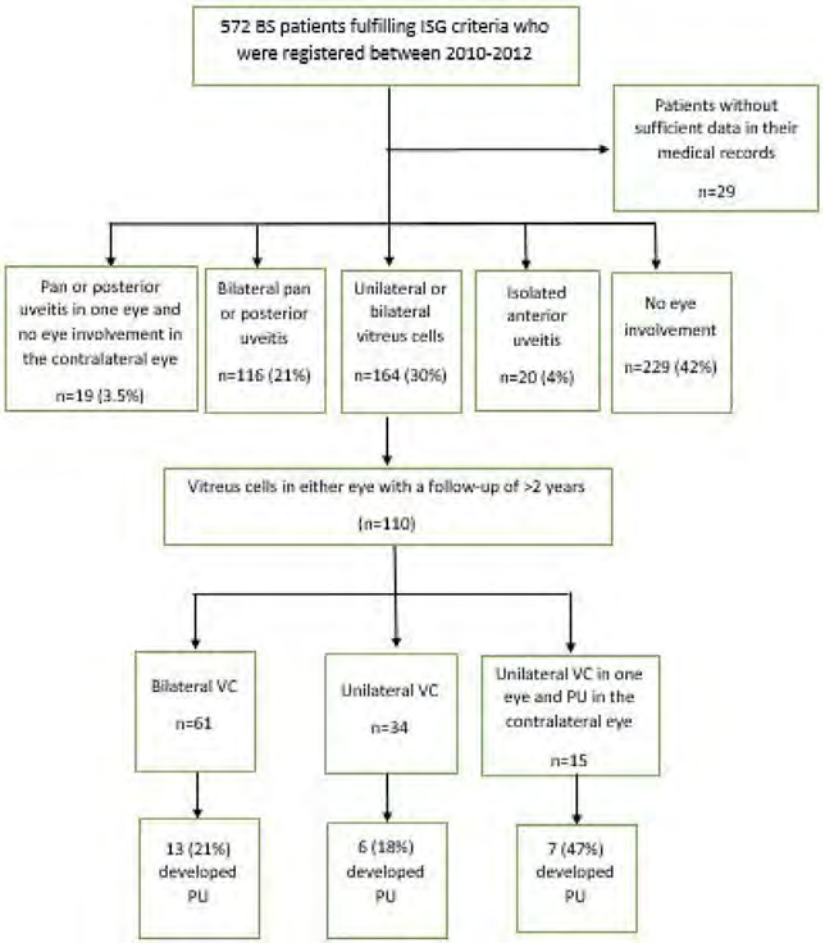

Figure. Flowchart of the patients

Results: At baseline, among the 110 included patients (68 men, mean ± SD age: 31±9 years), 61 had VC in both eyes, 34 had VC in only one eye, and 15 had VC in one eye and PU in the other eye. There was anterior uveitis (AU) in addition to VC in the same eye in 13 patients at baseline.

New PU developed in 26 (24%) patients during a mean follow-up of 1.9±1.1 years. Seven patients that developed PU in the eye with VC had had PU in the contralateral eye at baseline. This means 7 of 15 patients with VC in one eye and PU in the contralateral eye developed bilateral PU despite treatment. Two of these 7 patients had developed AU before they developed PU. Additionally, 6 patients that developed PU in the eye with VC had anterior uveitis in the same eye at baseline (Figure).

Multivariate logistic regression analysis showed that the presence of both VH and AU in the same eye at baseline (OR, 3.75, 95% CI; 1.07-13.18) and the presence of VH in one eye and PU in the other eye at baseline (OR, 3.86, 95% CI; 1.19-12.60) were the independent risk factors for the development of PU in patients with VH. Age at diagnosis, sex, and the use of immunosuppressive medications during the first 3 years of follow-up were not associated with the development of PU.

Conclusion: Careful follow-up is required for patients with VC since one quarter developed PU within 2 years. The presence of PU in the contralateral eye and AU in the same eye are risk factors for the development of PU in patients with VC.

Disclosure: D. Ucar: None; **B. Bircan**: None; **N. Rustamli**: None; **B. Batu Oto**: None; **V. Hamuryudan**: None; **S. Esatoglu**: None; **G. Hatemi**: None.

Abstract Number: 1559

Comparison of Treatment with Adalimumab, Infliximab and Certolizumab in Refractory Cystoid Macular Edema Due to Behçet Disease

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Cystoid macular edema (CME) is the leading cause of blindness in non-infectious uveitis. One of the most frequently associated conditions is Behçet's disease (BD) (1-3). The objective is to compare efficacy and safety of Adalimumab (ADA), Infliximab (IFX) and Certolizumab (CZP) in CME refractory due to BD.

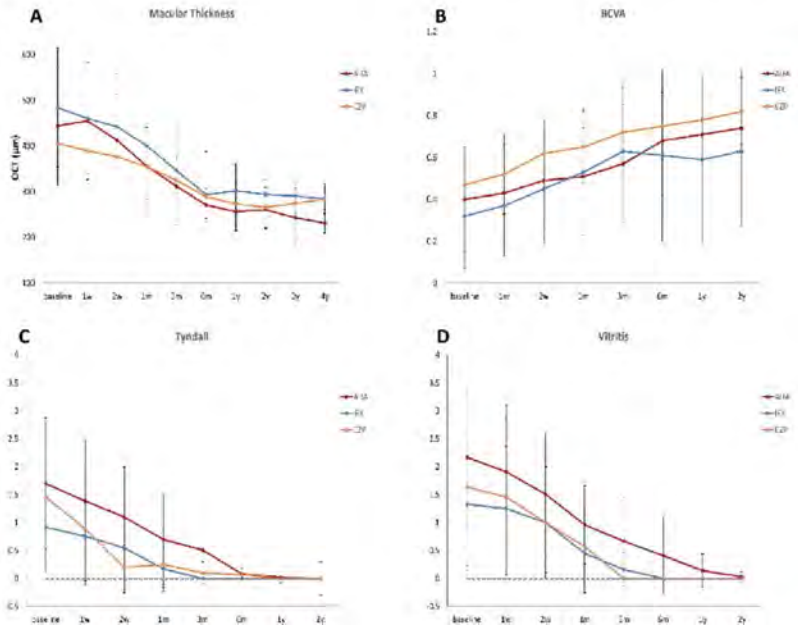
Methods: Multicenter study of patients with CME secondary to BD refractory to glucocorticoids (GC) and at least 1 conventional immunosuppressant. All patients had CME (OCT >300μ) at baseline. From baseline up to 2 years of follow-up, the evolution of macular thickness (μm), visual acuity (BCVA), anterior chamber (AC) cells, vitritis and GC-sparing effect was analyzed to assess the efficacy of ADA, IFX and CZP. Statistical analysis was performed with IBM SPSS Statistics v.23.

Results: Fifty patients (78 eyes) were evaluated. Twenty-five patients were treated with ADA, 15 with IFX and 10 patients received CZP. No significant differences in demographic parameters were identified in all groups. However, patients in the CZP group had a significantly longer time from diagnosis to drug initiation (75 [36-120] vs 30 [12-82] vs 15 [8-60] months; p=0.04) and had received a greater median [IQR] number of biological treatments (2 [0.75-3] vs 0 [0-0] vs 0 [0-0]) than the ADA and IFX groups. In CZP group, ADA and IFX were used previously in 7 patients. ADA was used in combined therapy in 64%, IFX in 66.7% and CZP in 70% of patients (p=0.94) (**TABLE**).

TABLE. Main general features of CME patients due to BD receiving adalimumab (ADA), infliximab (IFX) or Certolizumab Pegol (CZP).

	ADA *group* **(n=25)**	**IFX** *group* **(n=15)**	**CZP** *group* **(n=10)**	**P**
Age, mean (SD) years	41 (11)	38 (9)	36 (8)	0.34
Sex, men/women, n/n	12/13	7/8	3/7	0.61
HLA-B51 positive, n(%)	19 (76)	10 (67)	4 (40)	0.13
Duration of uveitis before treatment, median	30 [12-82]	15 [8-60]	75 [36-120]	**0.04**
Unilateral, n(%)	10 (40)	9 (60)	3 (30)	0.28
Pattern of uveitis, n(%)				
Anterior	0 (0)	0 (0)	2 (20)	-
Intermediate	0 (0)	0 (0)	1 (10)	0.13
Posterior	5 (20)	5 (33.3)	3 (30)	0.62
Panuveitis	20 (80)	10 (66.7)	4 (40)	0.07
Ocular outcomes at the time of anti-TNF beginning				
AC cells (Tyndall), median [IQR]	2 [1-3]	1 [0-1]	1 [0-2]	0.15
Vitritis, median [IQR]	3 [1-3]	1 [0-2]	1 [0-2]	**0.03**
BCVA, mean (SD)	0.41±0.24	0.33±0.22	0.48±0.18	0.17
Macular thickness, mean (SD)	431.9±117.6	483.4±126.1	380.7±96.5	0.08
Previous conventional treatment, n (%)				
IV pulses of MTP	13 (52)	9 (60)	5 (50)	0.85
Cyclosporine A	22 (88)	11 (73.3)	6 (60)	0.17
Azathioprine	14 (56)	8 (53.3)	4 (40)	0.69
Methotrexate	13 (52)	8 (53.3)	2 (20)	0.18
CFM	1 (4)	2 (13.3)	0 (0)	0.33
Previous biological treatment (BT), n (%)	0 (0)	0 (0)	8 (80)	-
Number of previous BT per patient, median [IQR]	0	0	2 [1-3]	-
Combined treatment, n (%)	16 (64)	10 (66.7)	7 (70)	0.94
Cyclosporine A	10 (40)	5 (33.3)	1 (10)	0.23
Azathioprine	4 (16)	3 (20)	2 (20)	0.34
Methotrexate	2 (8)	2 (13.3)	4 (40)	0.86
Prednisone dose (baseline)	45 [30-60]	30 [20-60]	8 [6-25]	**0.04**
Follow-up, median [IQR],	24 [18-45]	24 [3-36]	30 [24-60]	0.12
Remission, n (%)	19 (76)	9 (60)	7 (70)	0.58
per 100 patient-year	28.8	30	19.4	
Drug withdrawal, n (%)	8 (32)	8 (53.4)	2 (20)	0.20
per 100 patient-year	12.1	26.7	5.6	
Side-effects/toxicity, n (%)	1 (4)	0 (0)	0 (0)	-
per 100 patient-year	3	0	0	

FIGURE. Rapid and maintained improvement following the onset of ADA, IFX and CZP. **A.** Macular thickness (OCT); **B.** Best-corrected visual acuity (BCVA); **C.** Anterior Chamber (AC) cells – Tyndall; **D.** Vitritis.



Concerning efficacy outcomes, a rapid and maintained improvement in macular thickness was observed after 2 years of follow-up in three groups with no statistically significant differences between them (**FIGURE**). Improvement in BCVA, AC cells, vitritis and a GC-sparing effect was also noted. No serious adverse events were observed in IFX and CZP group. One case of pyelonephritis was reported in the ADA group.

Conclusion: ADA, IFX and CZP are effective and safe in refractory CME due to BD. CZP appears effective even in patients with inadequate response to ADA and/or IFX.

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Abstract Number: 1560

Decreased Level of Peripheral CLA$^+$ Treg Is a Protective Factor of Nervous System Involvement in Behcet's Syndrome: A Real-World Study in China

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SESSION INFORMATION
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Session Type: Poster Session B
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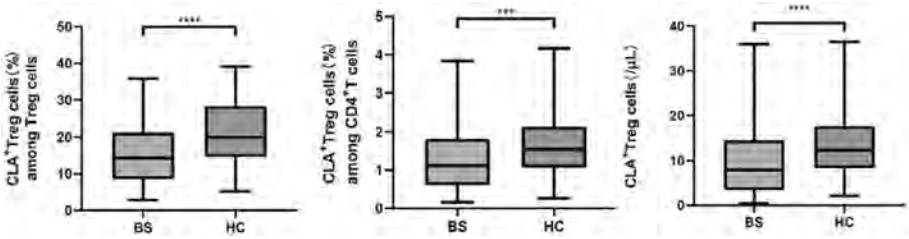
Background/Purpose: Behcet's syndrome (BS) is an autoimmune disease characterized by recurrent mucocutaneous ulcerations, vascular and nervous system involvement. While there have been a lot of researches proving that immune cells play a vital role in rheumatic disease, opinions on the effect of different immune cell subsets on BS is inconsistent. Therefore, we performed this real-world study to investigate the changes in the levels of several immune cell subsets in BS, and the correlation between the levels of different immune cell subsets and clinical features in patients with BS.

Methods: This is a retrospective, single-center study conducted in Beijing. We enrolled a total of 136 patients diagnosed with BS in rheumatology and immunology department of Peking University People's Hospital from 2018 to 2021 and 114 healthy controls (HCs) in this study. All patients met the International Criteria for Behcet's Disease (ICBD). The levels of peripheral immune cells, including CD4$^+$ T lymphocytes, CD8$^+$ T lymphocytes, B lymphocytes, NK lymphocytes, several subsets of CD4$^+$ T lymphocytes and several subsets of Treg cells were analyzed by flow cytometry. Wilcoxon rank test, student's t-test and Logistic regression analysis were used and a P-value < 0.05 was considered statistically significant.

Results: Compared with HCs, the absolutely numbers of CD4$^+$ T lymphocytes, B lymphocytes and NK lymphocytes were decreased in BS patients. Among CD4$^+$ T lymphocytes, the proportion of IFN-g, IL-2 and IL-4 producing lymphocytes, follicular helper T cells and Foxp3$^+$ Tregs were significantly elevated, while TNF-a producing lymphocytes, Naïve Th cells and T

	BS (136)	HC (114)	P
Total lymphocyte count (/ μ L)	1798.00 (1266.00, 2473.00)	2097.00 (1706.50, 2547.25)	0.003**
$CD4^+$T lymphocytes (/ μ L)	638.00 (501.00, 968.25)	812.00 (629.75, 1040.25)	0.004**
$CD8^+$T lymphocytes (/ μ L)	565.50 (398.00, 736.00)	510.00 (421.00, 665.00)	0.329
B lymphocytes (/ μ L)	194.00 (82.00, 286.75)	247.00 (198.25, 329.25)	<0.001***
NK lymphocytes (/ μ L)	175.50 (123.50, 328.00)	346.50 (220.25, 474.75)	<0.001***
Among $CD4^+$T lymphocytes			
TNF-α (%)	42.70 (34.20, 50.40)	48.67 (33.77, 60.75)	0.008**
IFN-γ (%)	16.00 (12.30, 20.60)	13.43 (10.15, 16.62)	<0.001***
IL-2 (%)	49.94±14.36	42.02±13.18	<0.001***
IL-4 (%)	1.72±0.82	1.13±0.50	<0.001***
IL-17 (%)	1.53 (1.01, 2.25)	1.64 (1.39, 2.00)	0.124
Treg (%)	8.30 (6.70, 10.75)	7.83 (6.99, 9.23)	0.083
Tfh (%)	2.10 (1.70, 3.10)	1.03 (0.71, 1.33)	<0.001***
Naïve Th cell (%)	28.11±13.15	33.19±13.22	0.004**
$Foxp3^+$Treg (%)	8.45 (6.52, 10.30)	7.59 (6.36, 8.76)	0.004**
Teff (%)	90.60 (88.33, 92.95)	91.95 (90.85, 93.23)	0.001**
Among Treg cell			
$CD161^+$Treg (%)	11.70 (8.95, 15.80)	11.10 (8.60, 14.23)	0.165
CLA^+Treg (%)	14.65 (8.93, 21.63)	20.55 (14.60, 28.43)	<0.001***

Comparation of different subsets of immune cells in BS patients and HCs



Comparison of CLA+Treg count, proportion of CLA+Treg among CD4+T cells and among Treg cells in BS patients and HCs

effectors were significantly decreased in BS patients. (P< 0.05) There was a significant decrease in the absolute number (7.91[3.69, 14.92] vs 12.56[8.39, 18.15], P< 0.001), proportion of CLA^+ Tregs among $CD4^+$ T lymphocytes (1.18[0.61, 1.91] vs 1.61[1.78, 2.15], P=0.001) and $CD4^+$ regulatory T cells (14.65[8.93, 21.63] vs 20.55[14.60, 28.43], P< 0.001) in BS patients. We observed that BS patients with arterial aneurysm had lower proportion of CLA^+ Treg among Tregs (10.67±5.92 vs 16.90±9.80, P=0.019) compared with those without arterial aneurysm and patients had nervous system involvement had higher proportion of CLA^+ Treg among Tregs (20.95[16.63, 26.85] vs 13.00[8.00, 20.60], P=0.001) than

Neurological subtype of Behcet's syndrome						
	β	SE	Wald	P	OR	95%CI
Age	-0.060	0.028	4.434	0.035	0.942	(0.891, 0.996)
Male	1.605	0.719	4.975	0.026	4.977	(1.215, 20.387)
Naïve Th (%)	-0.083	0.031	7.165	0.007	0.920	(0.866, 0.978)
CD161+Treg (%)	0.147	0.056	6.950	0.008	1.158	(1.038, 1.292)
CLA+Treg (%)	0.102	0.037	7.518	0.006	1.107	(1.029, 1.190)

Multivariate Logistic regression analysis of Neurological subtype Behcet's syndrome patients

patients without that manifestation. Multivariate Logistic regression analysis showed that decreased level proportion of CLA^+ Treg among Tregs was a protective factor of nervous system involvement in BS patients (b=0.102, SE=0.037, *Wald*=7.518, P=0.006, OR=1.107, 95%IC: [1.029, 1.190]). The proportion of CLA^+ Treg among Tregs in 11 BS patients of 14 was elevated after treatment of corticosteroids and immune suppressor.

Conclusion: BS patients have a decreased level of CLA^+ Treg than HCs. Decreased CLA^+ Treg may be a protective factor of nervous system involvement in BS patients. BS patients' level of CLA^+ Treg can be elevated after treatment.

Disclosure: J. Li: None; **F. Sun**: None; **W. Zhou**: None; **T. Liu**: None.

Abstract Number: 1561

Clinical Features and Quality of Life of Japanese Bechet's Disease Patients with Arthritis: A Japanese Monocentric Study

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Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Arthritis is positioned as one of the main symptoms in Behcet's disease (BD), and it is a relatively frequent symptom that is observed in about 57% of patients in Japan. Arthritis associated with BD is considered to be important domain affecting the patient's QOL same as oral ulcers. However, few reports have compared the clinical symptoms and QOL of BD patients with and without arthritis. This study aims to clarify the correlation between arthritis and other clinical manifestations of BD, which affect the patient's QOL in Japanese patients with BD.

Methods: Sixty-six BD patients treated at Kagawa University Hospital for more than 6 months and who visited the hospital from January to October 2022 were included in this retrospective study. We divided these patients into with (arthritis group) or without arthritis (non-arthritis group), and evaluated clinical symptoms, disease activity, and patient quality of life. Patient's global assessment(PGA), Evaluator's global assessment (EGA) and Behcet's disease current activity form (BDCAF) were used as indices of disease activity. Behcet's disease quality of life scale (BDQOL) was used to assess patient QOL. Statistical analysis was performed using JMP® Pro 16.1.0 software (SAS Institute, Cary, NC, USA).

Results: Arthritis was observed in 48.5% of patients. No significant difference in patient characteristics was observed between two groups. Activity of arthritis in arthritis group evaluated by SDAI, CDAI and DAS-28CRP was low to moderate (Table 1). The frequency of oral ulcers were significantly higher in arthritis group than in non-arthritis group. Although skin lesions tended to be detected in arthritis group more than non-arthritis group, there was no significant difference between two groups. Among the skin domain, papulopustular lesion tended to be observed more frequently in arthritis group (Table 2). EGA and BDCAF were significantly higher in arthritis group. Although PGA and BDQOL were higher in arthritis group, the difference was not significant between two groups (Figure 1).

Table.1 Characteristics of study participants

	Without arthritis	With arthritis	P-value
Number of cases	34	32	
Age, y	49.3 ± 14.8	47.8 ± 12.9	0.8022
Gender, Female, n(%)	21(61.8)	25(78.1)	0.1483
Disease duration, y	14.7 ± 11.7	11.3 ± 7.7	0.2973
HLA-B51 positive, n(%)	10(47.6), n=21	6(27.3), n=22	0.1677
HLA-A26 positive, n(%)	7(36.8), n=19	10(50.0), n=20	0.4075
Medication, n(%)			
NSAIDs	2 (6.1)	6 (19.4)	0.108
Corhitine	25 (73.5)	20 (64.5)	0.4316
Glucocorticoids	12 (35.3)	12 (38.7)	0.7756
dose, median(IQR), mg/d	2.5 (2.0,5.0)	2.3 (2.0,5.0)	0.789
Methotrexate	2 (5.9)	3 (9.7)	0.5663
Azathioprine	1 (2.9)	0 (0)	0.3359
Cyclosporine	1 (2.9)	0 (0)	0.3359
Mizoribine	0 (0)	1 (3.2)	0.2912
Tumor necrosis factor inhibitors	4 (11.8)	4 (12.9)	0.889
Apremilast	6 (17.7)	4 (12.9)	0.5965
5-aminosalicylic acid	0 (0)	3 (9.7)	0.0633
Arthritis activity			
SDAI, median(IQR)	-	10 [6.6-12.8]	-
CDAI, median(IQR)	-	9.7 [6.6-12]	-
DAS28-CRP, median(IQR)	-	2.8 [2.3-3.5]	-

P values were determined by the Mann–Whitney U test.
*Data were considered significant at P < 0.05.

Table.2 Association between arthritis and major lesions of Behcet's disease

	Without arthritis n=34	With arthritis n=32	P-value
Oral ulcer	17 (50.0%)	25 (78.1%)	0.0176*
Genital ulcer	6 (17.7%)	8 (25.0%)	0.4652
Skin lesion	6 (17.7%)	10 (31.3%)	0.1975
Erythema nodosum	3 (8.8%)	4 (12.5%)	0.6278
Thrombophlebitis	0 (0%)	0 (0%)	-
Papulopustular skin lesions	4 (11.8%)	7 (21.9%)	0.2707
Eye involvement	0 (0%)	1 (3.1%)	0.299
Epididymitis	1 (2.9%)	0 (0%)	0.3283
Gastrointestinal involvement	1 (2.9%)	0 (0%)	0.3283
Nervous system involvement	0 (0%)	0 (0%)	-
Vascular involvement	0 (0%)	0 (0%)	-

P values were determined by the Mann–Whitney U test.
*Data were considered significant at P < 0.05.

Conclusion: Japanese BD patients with arthritis tended to be complicated with mucocutaneous lesions. In addition, arthritis may affect overall disease activity and QOL in patients with BD, even if its activity is low to moderate. Because this study was a small, single-center, observational study, further research is needed to clarify the relationship between clinical feature and QOL in BD patients.

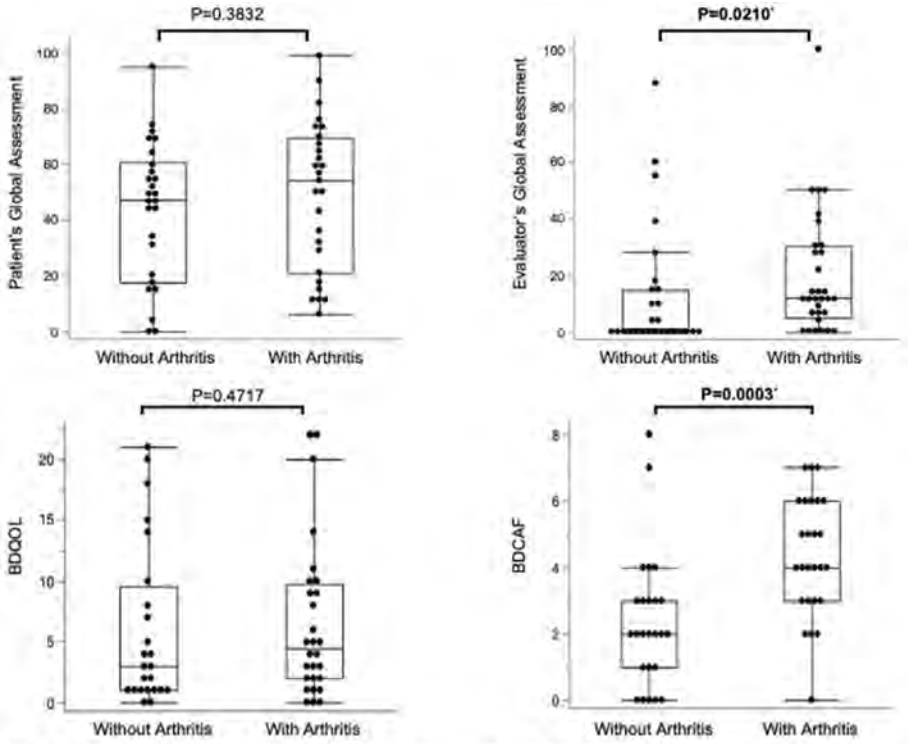

Figure 1. Comparison of disease activity and QOL of patients with Behcet's disease with and without arthritis. BDQOL = Behcet's disease quality of life scale; BDCAF = Behcet's disease current activity form. *Data were considered significant at P < 0.05.

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Abstract Number: 1562

Behcet's Disease Coagulopathy in a Racially Diverse Patient Population

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

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Session Time: 9:00AM–11:00AM

Background/Purpose: Behcet's disease (BD) is a vasculitis with both thrombotic and bleeding complications which can make management challenging. Thrombosis is due to direct vascular inflammation, and thus guidelines emphasize immunosuppression (IS) as the mainstay of treatment [1] rather than anticoagulation (AC). BD is most prevalent in the Mediterranean region and East Asia [2]. Countries may vary in management of BD coagulopathy, possibly due to differences in prevalence of BD [1]. Our study objective is to explore management of BD coagulopathy in a racially diverse population, and we compared clinical features of BD patients on anticoagulation to those not on anticoagulation.

Methods: After institutional review board (IRB) approval, we queried Montefiore Medical Center electronic medical record and the clinical looking glass databases to identify patients with a diagnosis of BD aged 16 years and older who met International Criteria for Behcet's Disease (ICBD). We performed a retrospective chart review and analyzed the results using two sample t-tests for continuous variables and Fisher's exact tests for categorical variables.

Results: We identified 26 patients with BD. Among them, 46% were Hispanic, 39% were Black, 8% were Asian, and 8% were Middle Eastern. A total of 10 patients had vascular manifestations of BD [Figure 1], out of which 8 had thrombosis. Of those patients with thrombosis, 7 were both on IS and AC, and 1 was on IS alone. Of the 7 patients who were on AC, 3 were on AC for less than 1 year, 4 were on AC for more than 1 year. Two patients suffered from both bleeding and thrombotic complications of BD. No patients were identified to have pulmonary artery aneurysm. Out of the 8 patients with thrombosis, 2 patients were noted to have hypercoagulable diseases– one had protein C and protein S deficiency, and another had protein S deficiency.

Table 1: Comparison of clinical features Behcet's disease patients on anticoagulation versus not on anticoagulation

Characteristic	Behcet's disease patient on anticoagulation (n=7)	Behcet's disease patient not on anticoagulation (n=19)	p-value
Age at diagnosis, mean (SD)	23 (6.35)	24 (9.61)	0.72
Male Female	5 (71.4%) 2 (28.6%)	7 (36.8%) 12 (63.2%)	0.19
Asian Black/African Hispanic Middle Eastern	0 (0%) 5 (71.4%) 2 (28.6%) 0 (0%)	2 (10.5%) 5 (26.3%) 10 (52.6%) 2 (10.5%)	0.27
Oral ulcers	7 (100%)	19 (100%)	<.0001
Genital ulcers	4 (57.1%)	14 (73.7%)	0.64
Vascular manifestation Thrombosis Stenosis Thrombophlebitis Aneurysm Arterial disease Venous disease	 7 (100%) 2 (28.6%) 1 (14.3%) 0 (0%) 3 (42.9%) 7 (100%)	 1 (5.3%) 1 (5.3%) 1 (5.3%) 1 (5.3%) 1 (5.3%) 2 (10.5%)	 <0.0001 0.17 0.47 1 0.05 <0.0001
Skin manifestation Erythema nodosum Folliculitis Acneiform rash Hidradenitis suppurativa Other rash	 2 (28.6) 0 (0%) 1 (14.3%) 2 (28.6%) 0 (0%)	 5 (26.3) 2 (10.5%) 1 (5.3%) 0 (0%) 1 (5.3%)	 0.19
Neurologic manifestation Sinus vein thrombosis White matter changes Brainstem lesion Carotid aneurysm Unspecified	 3 (42.9%) 0 (0%) 0 (0%) 0 (0%) 0 (0%)	 0 (0%) 1 (5.3%) 1 (5.3%) 1 (5.3%) 1 (5.3%)	 0.09
Ocular Anterior uveitis Pan uveitis Scleritis Keratitis	 1 (14.3%) 1 (14.3%) 0 (0%) 0 (0%)	 1 (5.3%) 3 (15.8%) 3 (15.8%) 1 (5.3%)	 0.86
Gastrointestinal manifestation Ulcers with GI bleed Ulcers without GI bleed	 1 (14.3%) 1 (14.3%)	 0 (0%) 1 (5.3%)	 0.82
Fever at time of diagnosis	4 (57.1%)	4 (21.1%)	0.04
Inflammatory arthritis Arthralgia	2 (28.6%) 5 (71.4%)	9 (47.4%) 6 (31.6%)	0.29
Gastrointestinal bleed identified	1 (14.3%)	0 (0%)	0.07
Hemorrhagic stroke identified	1 (14.3%)	0 (0%)	0.07
Both clotting and bleeding event	2 (28.6%)	0 (0%)	0.06

Table 2 - Management of Behcet's disease patients with thrombosis

Patient	Type of Thrombosis	On anticoagulation	On immuno-suppression	Bleeding complication	Gastrointestinal ulcer	Pulmonary Artery Aneurysm	Recurrence of thrombosis	Other hypercoagulable state
1	DVT	Yes (<1 year)	Yes	Yes (hemorrhagic stroke)	No	No	Yes	No
2	DVT	Yes (>1 year)	Yes	No	No	Not checked	Yes	Protein S deficiency
3	DVT	Yes (>1 year)	Yes	Yes (gastrointestinal bleed)	Yes	No	Yes	Protein C/S deficiency
4	DVT	No	Yes	No	No	No	No	No
5	DVT, IVC filter thrombosis	Yes (>1 year)	Yes	No	No	Not checked	Yes	No
6	Extensive DVT	Yes (>1 year)	Yes	No	No	Not checked	No	No
7	Tricuspid valve thrombus	Yes (<1 year)	Yes	No	No	No	No	No
8	Sinus vein thrombosis	Yes (<1 year)	Yes	No	No	No	No	No

* DVT = deep venous thrombosis

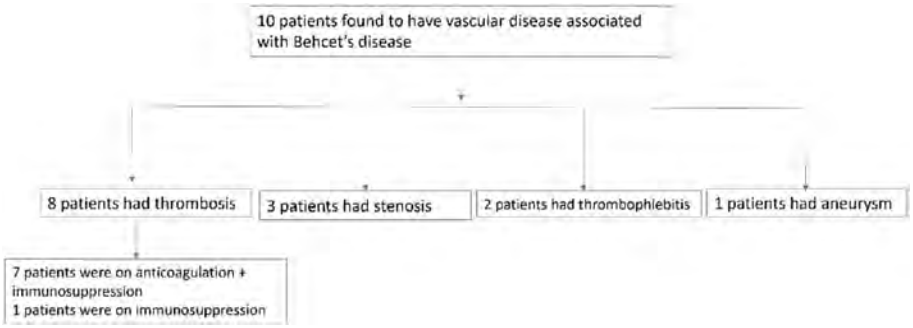

Figure 1: Vascular manifestations of Behcet's disease

Conclusion: We compared the clinical features of BD patients on anticoagulation to those not on anticoagulation, and we found that unless there was a thrombotic event, patients were not initiated on AC [p< 0.0001]. Among our patients, 31% experienced thrombosis, and 25% of these patients experienced a bleeding event related to BD. The majority of our patients with thrombosis were treated with both IS and AC, though one patient with thrombosis was given IS alone. We found decisions on AC use considered presence of other hypercoagulable disorders, severity and location of clot, clot recurrence, pulmonary artery aneurysm screening, and history of major bleed. Our study suggests that while the mainstay of treatment for BD coagulopathy remains IS, each individual's clotting and bleeding risk should be evaluated when considering AC. If patients have recurrent clotting despite IS, they should also be screened for hypercoagulable disorders and pulmonary artery aneurysms if AC is considered to avoid untoward outcomes.

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Abstract Number: 1563

Methotrexate: A Safe and Effective Therapeutic Alternative in Behçet´s Disease

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Behçet's disease (BD) is characterized by great clinical heterogeneity. The therapeutic strategy for BD could be tailored to the specific needs of the patient, based on clinical phenotypes, as we often find refractory cases with overlapping of different clinical manifestations. Eular recommendations on the management of BD were updated in 2018 and did not include methotrexate (MTX) as a therapeutic strategy, despite being a widely used drug in Rheumatology. OBJECTIVES: To describe the efficacy and safety of MTX treatment in patients diagnosed with BD.

Methods: We performed a multicentre retrospective observational study that included 68 BD patients (ICBD 2013) on MTX treatment. The indication of MTX was based on the criteria of the treating physician with the informed consent of the patient. Statistical analysis was performed by T-test and Fisher's exact test to compare quantitative and qualitative variables. Values of $p < 0.05$ were considered statistically significant.

Results: 68 patients diagnosed with BD and treated with MTX was evaluated, 53% women, 94% caucasians, with a median age of 39.7 (33.7-42.8) years and 3.6 (1.5-15.7) years of disease progression at MTX onset. Table I summarises the main general and clinical features at baseline. Previously to MTX, patients had received colchicine (95.6%), oral glucocorticoids (80.9%, maximum median dose of 20 [10-30] mg/day), hydroxychloroquine (17.7%) and csDMARDs (35.8%). In addition, 6 patients had received apremilast and 13 had received bDMARDs. MTX was started due to joint phenotype (54.4%), refractory oral and/or genital aphthosis (35.3%) and ocular involvement (8.8%). The mean dose of MTX was 12.6±3.6 mg/week. Survival at 3, 6 and 12 months was 94% (61/68), 84% (57/68) and 68% (42/68). The median duration of MTX was 26.8 (8-71.3) months, and treatment was discontinued in 43 patients (63.2%) (Table II).

To assess efficacy, patients who presented early intolerance or adverse effects (< 6 months) were eliminated (7/68).46% of patients (28/61) received MTX for joint involvement and 54% of patients (33/61) for other reasons. Those who received treatment for arthritis had a higher response rate (24/28) compared to those who received MTX for other clinical manifestations (19/33) (p=0.016). There were no significant differences between these two groups in terms of maximum dose of methotrexate or the use of concomitant biologic therapy.

Conclusion: Despite not being included as a therapeutic strategy in the latest Eular 2018 recommendations, methotrexate appears to be an effective treatment in patients with BD, especially against the articular phenotype, with a good safety profile.

1 Median (IQR), or number (%); 2 At the start of MTX; 3 Others: thalidomide, leflunomide, salazopyrin, dapsone.

Table I. Clinical characteristics of 68 patients with BD treated with MTX.

Clinical features[1]	n 68
Female sex	36 (53%)
Age[2]	39.7 (33.7-48.2)
Caucasian race	64 (94%)
HLAB51 positive (n 49)	20 (40.8%)
Duration of BD[2] **(years)**	3.6 (1.5-15.7)
Clinical phenotype (evolution)	
Oral ulcers	68 (100%)
Genital ulcers	51 (75%)
Cutaneous (erythema nodosum, pseudofolliculitis)	41 (60%)
Articular	12 (18%)
Gastrointestinal	42 (62%)
Vascular	4 (6%)
Neurological	12 (18%)
Ophthalmic	22 (32%)
Clinical phenotype of MTX onset[2]	
Articular	37 (54.4%)
Cutaneous	24 (35.3%)
Gastrointestinal	1 (1.5%)
Ocular	6 (8.8%)
Previous treatment	
Colchicine	65 (95.6%)
Oral glucocorticoids	55 (88.9%)
Hydroxychloroquine	12 (17.7%)
Azathioprine	5 (7%)
Cyclosporine	11 (20%)
Apremilast	6 (9%)
Anti-TNF	13 (19.1%)
IL-1 inhibitor	0
IL-6 Inhibitor	1 (1.5%)
Anti IL12/23	2 (2.9%)
Cyclophosphamide	5 (7.4%)
Other[3]	6 (8.8%)

Table II. Clinical evolution of 68 patients with BD treated with MTX[1].

	n 68
Dose of MTX (mg/week)	12.1±3.2
Duration of MTX (months)	26.8 (8-71.3)
Concomitant treatment	
csDMARDs	4 (5.9%)
Apremilast	1 (1%)
TNFi	26 (38%)
TCZ	2 (3%)
USK	3 (4%)
Drug withdrawal	
Inefficacy	14 (21%)
Side-effects	8 (12%)
Intolerance	9 (13%)
Clinical remission	7 (10%)
Others	5 (7%)

[1]Median (IQR), or number (%).

Disclosure: M. Retuerto-Guerrero: None; **E. Díez Álvarez**: None; **J. Narvaez**: None; **R. Fornons Servent**: None; **C. Moreno Vilchez**: None; **J. Graña Gil**: None; **U. Couto Lareo**: None; **C. San José-Méndez**: None; **C. Moriano Morales**: None.

Abstract Number: 1564

Common Femoral Vein Wall Thickness Measurement as a Diagnostic Test in Suspected Behçet's Disease

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

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Session Time: 9:00AM–11:00AM

Background/Purpose: The diagnosis of Behçet's disease (BD) is mainly based on multi-systemic clinical manifestations after ruling out other potential causes. There is no specific diagnostic feature for BD. Therefore, the diagnosis may be a challenge in patients especially those presenting with only major organ involvement. The development of other disease manifestations to make a definite diagnosis can sometimes take months and even years and disease can remain clinically limited lifelong in some patients. In this group of patients, the term incomplete or suspected BD was used especially in Japanese Criteria, also possible BD was defined in recent ICBD Classification Criteria. Diagnosis is made by 'expert opinion' according to the presence of specific clinical manifestations of BD. We recently published the first controlled Doppler US study showing increased venous wall thickness (VWT) of lower extremity veins in male BD patients, and suggested that the cut-off value

Table 1: Baseline characteristics of patients with suspected Behçet's Disease and healthy controls

	Suspected Behçet's Disease (n=51)	Healthy Controls (n=41)	p value
Age, mean (SD)	39.0 (10.9)	36.8 (8.3)	0.29
Sex, n (%)			
Male	26 (51)	21 (51.2)	0.98
Female	25(49)	20 (48.8)	
Age at Diagnosis (SD)	34.8 (11.2)		
Family History, n (%)	16 (31.4)		
Duration of disease (month), mean (SD)	60.3 (51.7)		
Pathergy, n (%)			
Positive	7 (13.7)		
Negative	43 (84.3)		
Unknown	1 (2)		
Follow up period (month), mean (SD)	38.6 (46.7)		
Mucocutaneous Involvement, n (%)	9 (17.6)		
Major Organ Involvement, n (%)	42 (82.4)		

SD, standard deviation

of≥0.5 mm for common femoral vein (CFV) thickness had a high specificity and sensitivity for the diagnosis of BD (>80%). We later assessed the diagnostic performance of CFV thickness measurement in BD compared to multiple disease control groups. We found that CFV thickness is a distinctive feature of BD, rarely present in other inflammatory or vascular diseases. Most recently, increased VWT was observed in childhood BD with and without vascular involvement, and suggested as a new criterion for the diagnosis in both definite and incomplete pediatric BD patients. In this study, we aimed to assess the diagnostic performance of CFV thickness measurement in patients with 'suspected' BD and compared it with healthy controls.

Table 2: Subgroup analysis of suspected Behçet's patients (BD) and healthy controls

	R-CFV, mean (SD),mm	L-CFV, mean (SD), mm
Suspected BD patients, all group	0.71 (0.16)	0.71 (0.15)
Healthy controls	0.18 (0.05)	0.19 (0.04)
Suspected BD patients with mucocutaneous involvement	0.68 (0.09)	0.70 (0.07)
Suspected BD patients with major organ involvement	0.72 (0.17)	0.71 (0.16)
Suspected BD patients with vascular involvement	0.72 (0.15)	0.73 (0.14)
Suspected BD patients only with ocular involvement	0.68 (0.12)	0.64 (0.14)
Suspected BD patients only with neurological involvement	0.75 (0.28)	0.73 (0.23)
Suspected BD patients non-vascular involvement	0.70 (0.17)	0.68 (0.19)

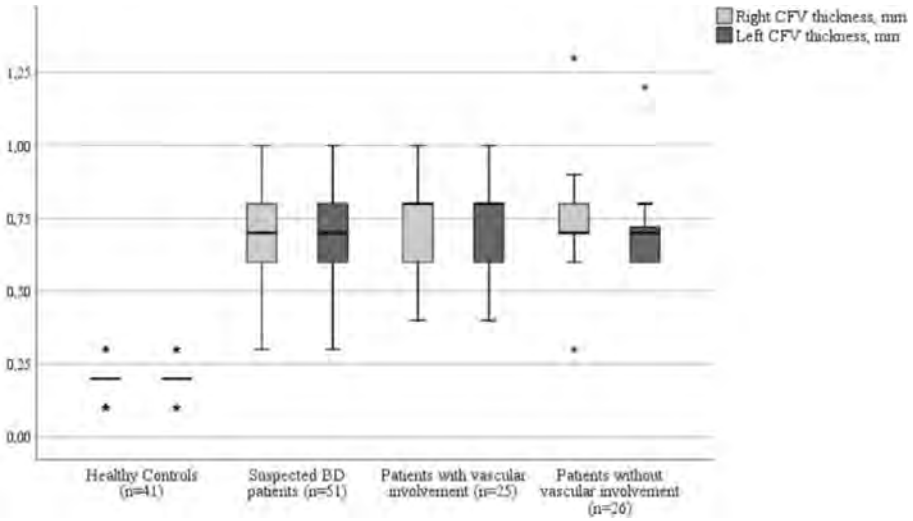

Figure 1: Distribution of common femoral vein (CFV) wall thicknesses in healthy controls and suspected Behçet's Disease (BD) according to organ involvements (The asterisk (*) symbols represent the extreme values)

Methods: Suspected BD was defined as limited manifestations not meeting ISG and Japan Research Committee Criteria, but diagnosed as BD by expert opinion. 51 patients were recruited from Behçet's Clinic of Marmara University. Bilateral CFV wall thickness was measured in the prone position from the posterior wall by an experienced radiologist blinded to the clinical data.

Results: The mean age of suspected BD patients was 39 years (SD: 10.9), and the mean disease duration was 60.3 (SD: 51.7) months *(Table 1)*. 42 (82.4%)had major organ involvement (20 vascular, 8 ocular, 8 neurological involvement). The mean right CFV (R-CFV) wall thickness was 0.71 (SD: 0.16) mm, the left CFV (L-CFV) wall thickness was 0.71 (SD: 0.15) mm in the study group. Bilateral CFV thickness was significantly higher than age-sex-matched healthy controls ($p< 0.001$ for both). There was no difference between patients with and without vascular involvement (*Table 2, Figure 1)*. 48 (94.1%) patients had CFV wall thickness above the cut-off value of ≥ 0.5 mm.

Conclusion: Our study shows that CFV thickness measurement can be helpful in daily practice for the differential diagnosis of BD in patients presenting with limited disease manifestations. Early diagnosis of BD is important, especially in cases presenting with venous thrombosis due to major treatment differences between thrombosis associated with BD and non-inflammatory thrombosis. Our results suggest that CFV thickness measurement is a noninvasive, and widely accessible diagnostic tool in suspected BD.

Disclosure: f. Alibaz-Öner: None; **R. Ergelen**: None; **S. Kutluğ Ağaçkıran**: None; **F. Temiz**: None; **T. Ergun**: None; **H. Direskeneli**: AbbVie/Abbott, 1, 5, 6, Amgen, 6, celltrione, 1, 6, Pfizer, 5, 6, Roche, 12, Educational, UCB, 5, 6, 12, Educational.

Abstract Number: 1565

Baseline Vascular Ultrasound of Polymyalgia Rheumatica Patients at Time of Diagnosis Predicts Clinical Outcomes at 3 Months

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Background/Purpose: It has been reported that up to a quarter of patients with polymyalgia rheumatica (PMR) have subclinical giant cell arteritis (GCA). It is currently uncertain if the presence of this finding may predict clinical outcomes in PMR.

Methods: 65 newly diagnosed PMR patients who met a clinical diagnosis for PMR were examined with ultrasound of their temporal and axillary arteries at time of diagnosis. US of all 6 branches of the superficial temporal arteries and both axillary arteries was performed using a GE P9 device. Sonographic abnormalities considered indicative of vasculitis in the temporal arteries included the halo sign and non-compressible arteries with a thickened intima-media complex. An intima-media thickness of 0.42mm for the common superficial temporal branch, 0.34mm for the frontal branch, and 0.29mm for the parietal branch was considered positive. In the axillary arteries, a halo sign, and an intima-media thickness of >1.0mm was considered positive. Halo scores were calculated for positive cases. Clinical, ultrasound and laboratory characteristics were recorded at baseline, 1 month and 3 months. Ultrasound findings were compared to a cohort of 48 GCA patients.

Baseline Characteristics	PMR (54)	PMR with subclinical GCA (11)	GCA (48)
Age (mean and range)	71.2 (51-89)	68.2 (53-78)	72.8 (56-92)
Female	32	3	17
Male	22	8	33
Mean baseline ESR (mm/hr)	41	51	57
Mean baseline CRP (mg/l)	38	36	53
Mean initial steroid dose (mg)	17.2	20.4	45.5
3 month outcomes			
Mean cumulative steroid at 3 months (mg) + SD	1336.8 ± 404.3	2051.5 ± 840.7	2411.3 ± 424.6
% of patients with relapse at 3 months	14.8%	36.6%	6%

Baseline Characteristics And Three-Month Outcomes:

Results: 65 patients with a clinical diagnosis of PMR and 48 patients with a diagnosis of GCA were included in the study. 58 (89%) of the PMR patients met the 2012 ACR/EULAR PMR classification criteria (those who did not meet this classification were primarily due to prior corticosteroid use in primary care resulting in normal ESR/CRP). All 48 GCA patients met the 2022 ACR/EULAR GCA classification criteria. 20.3% of patients with PMR had evidence of subclinical GCA on ultrasound of their temporal and axillary vessels. The mean initial prednisolone dose initiated for PMR was 17.2mg, while those with subclinical GCA in PMR were started on a mean of 20.4mg prednisolone and those with GCA were on average started on 45.5mg of prednisolone. The mean cumulative corticosteroid dose at 3 months was 1336.8mg ± 404.3mg for PMR, 2051.5mg ± 840.7mg for subclinical GCA in PMR and 2411.3 ± 424.6 in GCA. PMR with subclinical GCA had significantly more cumulative corticosteroid than those with pure PMR (p=0.0069). Patients with subclinical GCA in PMR were more likely than either those with PMR or GCA patients to experience a relapse, with 36.6% of patients having a minor relapse, compared to 14.8% of the PMR group and 6% of the GCA group having a minor relapse in the first three months of treatment.

Conclusion: The presence of subclinical GCA in PMR at baseline predicts increased cumulative steroid dose at three months compared with PMR alone. Patients with subclinical GCA in PMR are also more likely to have a clinical relapse in the first three months of treatment than those with either PMR or GCA.

Disclosure: S. Cowley: None; **C. Kirby**: None; **P. Harkins**: Janssen, 5; **R. Conway**: AbbVie/Abbott, 5, 6, Celltrion, 5, Fresenius Kabi, 6, Galapagos, 6, Janssen, 5, 6, Nordic Pharma, 5, Novartis, 5, UCB, 6, Viatris, 6; **D. Kane**: None.

Abstract Number: 1566

Exposure-Response Analysis of Sarilumab in Patients with Polymyalgia Rheumatica

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Sarilumab blocks interleukin-6 (IL-6) from binding to the membrane-bound and soluble IL-6 receptor-α subunit (IL-6Rα). Sarilumab is now approved for both rheumatoid arthritis (RA) and polymyalgia rheumatica (PMR) in adult patients. The objectives of the exposure-response (E-R) analyses presented here are to characterize the pharmacokinetic-pharmacodynamic (PK-PD) relationships of sarilumab exposure with key efficacy, and safety endpoints in patients with PMR.

Methods: The SAPHYR study (NCT03600818) assessed the efficacy and safety of sarilumab in patients with steroid resistant active PMR. Patients were randomized (1:1) to 52 weeks of treatment with sarilumab 200 mg every 2 weeks (q2w) + 14 weeks glucocorticoid (GC) tapering regimen or placebo q2w + 52 weeks GC tapering regimen. In the E-R analyses, the efficacy endpoints included the primary endpoint of the proportion of patients achieving sustained remission at Week 52 and the cumulative proportion (%) of patients who had rescue GC therapy during the 52-week treatment period; the safety endpoints included treatment-emergent adverse events (TEAEs), serious adverse events, adverse events of special interest, and absolute neutrophil count (ANC). PK-PD relationships were assessed using descriptive E-R analyses for the efficacy and safety endpoints and were explored graphically for biomarkers (IL-6, total soluble [s] IL-6Rα and C-reactive protein [CRP]) using the observed steady state trough concentrations (C_{trough}) of sarilumab at Week 24. Descriptive E-R analyses were conducted by tertiles of sarilumab steady-state C_{trough}. Results were compared with results in patients with RA when appropriate.

Results: Greater sarilumab C_{trough} in patients with PMR was associated with an increase in total sIL-6Rα and a decrease in CRP levels and was similar in patients with PMR and RA.

There was a slight increase in the proportion of patients achieving sustained remission from the low to the medium tertile. The treatment effect approached a plateau with increasing $C_{trough.}$ However, higher C_{trough} was not associated with decreased need for rescue therapy. No clear E-R relationships were observed between increasing sarilumab C_{trough} and a higher incidence of TEAEs. There was a greater ANC reduction with an increase in sarilumab C_{trough}; however, the effect appeared to reach a plateau at ~20 mg/L. In contrast, no higher proportion of patients with ANC < 1.0 Giga/L in patients with increasing sarilumab C_{trough} was observed. These results in patients with PMR were consistent with those observed in patients with RA.

Conclusion: The PK-PD relationship between sarilumab exposure and efficacy, and safety endpoints demonstrated that the pharmacodynamic effect of sarilumab appeared to reach a plateau at C_{trough} levels of 20 to 25 mg/L for target saturation, supporting a sarilumab dose of 200 mg q2w for the treatment of patients with PMR.

Disclosure: C. Xu: Sanofi, 3, 11; **Y. Liu**: Sanofi, 3, 11; **J. Sloane**: Sanofi, 3, 11; **R. Diab**: Sanofi, 3, 11; **H. van Hoogstraten**: Sanofi, 3, 11; **H. Abdallah**: Regeneron Pharmaceuticals, Inc., 3, 11; **S. Macha**: Sanofi, 3, 11; **B. Dasgupta**: AbbVie, 5, Cipla, 6, Roche Chugai, 2, 5, 6, Sanofi, 2, 5.

Abstract Number: 1567

Assessment of the Extent and Accrual of Damage in Takayasu's Arteritis

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SESSION INFORMATION
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Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Damage is the irreversible consequence of disease or its treatment**.** This study aimed to evaluate the accrual of damage in Takayasu's arteritis (TAK) using 2 currently-available indices of damage.

Methods: Patients with TAK enrolled in a multicenter, prospective, observational cohort from North America, and, a single-center in Turkey were included. Damage was assessed using the Vasculitis Damage Index (VDI) and the Large-Vessel Vasculitis Index of Damage (LVVID) at baseline and last visit.

Results: The study included 350 patients with TAK, mean±SD age 40.3 (13.4) years, 91% female, median (25^{th}, 75^{th} percentile) disease duration 69 (1.6, 274) weeks. 39% were enrolled ≤180 days from diagnosis. 313 (89%) had at least 1 follow-up visit, median (25^{th}, 75^{th}) duration 4.5 (2.1, 8.0) years. Damage was present at first visit in 83% on VDI, 89% on LVVID with median VDI (range) 3 (0, 10) and median (range) number of damage items on LVVID 3 (0, 13). Most items of damage at baseline visit were captured in the peripheral vascular (83% VDI, 89% LVVID) and cardiac (42% VDI, 44% LVVID) categories. At last follow-up, damage items were noted in 95% on VDI and 95% on LVVID mainly in the peripheral vascular (97% VDI, 89% LVVID) and cardiac (60% VDI, 59% LVVID) categories (**Table 1**). *New* damage was captured in 52% patients on VDI and 53% on LVVID. In patients with *new items,* median (range) number of *new* items was 1 (range 1, 13) on VDI and 2 (1, 17) on LVVID (**Table 1**). The majority of *new* items of damage were disease-related and were in the peripheral vascular (18% VDI), and cardiac (18% VDI) categories on VDI and cardiovascular category (37% total, 26% peripheral vascular, 20% cardiac) and "Other" (22%) categories on LVVID (**Table 1**). The most frequent items of damage at last visit in the most frequently affected categories, and, *new* items of damage at last visit are in **Table 2**. Damage captured on VDI but not LVVID included major vessel stenosis (83%), pulse loss (98%), elevated diastolic blood pressure (40%), second pulse loss (12%); items of damage captured on LVVID but not VDI included hypertension (40%), arterial thrombosis (41%), renal artery stenosis (28%), damage requiring vascular intervention (8% angioplasty alone, 20% angioplasty with stent), bypass surgery (22%), aortic aneurysms (14%). 12 of 64 items (19%) on VDI and 20 of 87 items (23%) on LVVID were never applicable to

Table 1: Total and new items of damage in 313 patients with Takayasu's arteritis at last visit, as recorded on the Vasculitis Damage Index and the Large-Vessel Vasculitis Index of Damage.

	VDI		LVVID	
Organ System	Follow-up, N (%)	New items, N (%)	Follow-up, N (%)	New items N (%)
Cardiovascular	N/A	N/A	285 (91)	119(38)
Peripheral vascular	304 (97)	55 (18)	280 (89)	83 (46)
Cardiac	190 (61)	58 (18)	186 (59)	63 (20)
Musculoskeletal	45 (14)	26 (8)	43 (14)	27 (9)
Ocular	50 (16)	37 (12)	44 (14)	37 (12)
Ear, Nose, and Throat	4 (1)	0 (0)	2 (0.6)	0 (0)
Gastrointestinal	8 (3)	3 (1)	5 (2)	2 (1)
Neuropsychiatric	39 (12)	12 (4)	38 (12)	12 (4)
Endocrine	N/A	N/A	22 (7)	15 (5)
Hematology/Oncology	N/A	N/A	15 (5)	8 (3)
Skin	20 (6)	7 (2)	22 (7)	13 (4)
Pulmonary	28 (9)	13 (4)	N/A	N/A
Renal	10 (3)	6 (2)	N/A	N/A
Other	55 (18)	34 (11)	129 (41)	70 (22)

VDI=Vasculitis Damage Index; LVVID=Large-Vessel Vasculitis Index of Damage
N=number, %=percent, N/A=not applicable

Table 2: Most frequent items of damage in 313 patients with Takayasu's arteritis ever (cumulative) and new items of damage at last visit during observation

	VDI		LVVID	
Organ System	**At last visit**	**New items**	**At last visit**	**New items**
Peripheral vascular, N (%)[a]	**304 (97)**	**55 (18)**	**280 (89)**	**83 (46)**
Claudication	211 (67)	22 (7)	---	---
Left arm claudication	---	---	147 (47)	17 (5)
Right arm claudication	---	---	110 (35)	10 (3)
Left leg claudication	---	---	44 (14)	4 (1)
Right leg claudication	---	---	43 (14)	4 (1)
Arterial thrombosis/occlusion	---	---	127 (41)	20 (6)
Renal artery stenosis	---	---	89 (28)	10 (3)
Pulse loss	310 (98)	15 (5)	---	---
Second episode absent pulse in one limb	38 (12)	11 (3)	---	---
Major vessel stenosis	261 (83)	16 (5)	---	---
Aortic aneurysm	---		45 (14)	11 (3)
Angioplasty alone	---		25 (8)	6 (2)
Angioplasty with stent	---		63 (20)	16 (5)
Bypass	---		70 (22)	10 (3)
Cardiac, N (%)[a]	**190 (61)**	**58 (18)**	**186 (59)**	**63 (20)**
Angina/Angioplasty	48 (15)	25 (8)	---	---
Hypertension	---		124 (40)	28 (9)
Diastolic blood pressure ≥95 mm Hg or requiring treatment	126 (40)	30 (10)	---	---
Coronary artery disease	---	---	46 (15)	7 (2)
Valvular disease	76 (24)	28 (9)	---	---
Aortic valve regurgitation	---	---	64 (20)	17 (5)
Tricuspid regurgitation	---	---	29 (9)	17 (5)
Mitral regurgitation	---	---	35 (11)	14 (4)
Other, N (%)	**55 (18)**	**34 (11)**	**129 (41)**	**70 (22)**
Weight gain >10 pounds	---	---	78 (25)	37 (12)
Damage requiring surgical intervention	---	---	57 (18)	22 (7)
Other (free texted)	33 (11)	13 (4)	24 (8)	8 (3)
Ocular	**50 (16)**	**37 (12)**	**44 (14)**	**37 (12)**
Left low vision	---	---	13 (4)	9 (3)
Right low vision	---	---	14 (4)	11 (3)
Left cataract	---	---	18 (6)	11 (3)
Right cataract	---	---	17 (5)	11 (3)
Visual Impairment	16 (5)	11 (3)	---	---
Cataract	19 (6)	14 (4)	---	---
Retinal change	21 (7)	16 (5)	---	---
Musculoskeletal, N (%)	**45 (14)**	**26 (8)**	**43 (14)**	**27 (9)**
Osteoporosis, vertebral collapse	29 (9)	13 (4)	30 (10)	13 (4)
Avascular necrosis	10 (3)	7 (2)	10 (3)	7 (2)
Neurologic, N (%)	**39 (12)**	**12 (4)**	**38 (12)**	**12 (4)**
Cerebrovascular accident	28 (9)	10 (3)	---	---
Cerebrovascular accident, ischemic	---	---	25 (8)	9 (3)
Cerebrovascular accident, hemorrhagic	---	---	5 (2)	2 (1)

N = number, % = percentage, VDI=Vasculitis Damage Index, LVVID=Large-Vessel Vasculitis Index of Damage, ---=Not applicable (i.e. item not queried on index), [a]Cardiovascular category on LVVID

any patient with TAK but 13 of the 20 (65%) items not used on LVVID were in the ocular category with manifestations that can occur in giant cell arteritis.

Conclusion: Damage is present in >80% of patients with TAK at first visit. During follow-up, new damage items, mostly disease related, are observed in 50% including new cardiovascular damage in nearly 40%. LVVID captures *new* damage items in the cardiovascular category more comprehensively than VDI but many damage items were captured in the "Other" category on both measures. Based on these results, LVVID can be modified and streamlined to more efficiently measure damage in TAK and perhaps be focused on disease-related damage. Disease-associated damage accrues in TAK despite treatment and assessment of damage should be included in therapeutic trials.

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Bristol Myers Squibb, 3; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Chemocentryx, 1, 6, Eli Lilly, 5, kiniksa, 5; **f. Alibaz-Öner**: None; **H. Direskeneli**: AbbVie/Abbott, 1, 5, 6, Amgen, 6, celltrione, 1, 6, Pfizer, 5, 6, Roche, 12, Educational, UCB, 5, 6, 12, Educational; **P. Merkel**: AbbVie/Abbott, 5, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos, 5, Electra, 5, Genentech, 5, GlaxoSmithKlein(GSK), 2, 5, HiBio, 2, InflaRx, 2, 5, Janssen, 2, Jubilant, 2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, Takeda, 2, 5, UpToDate, 9, Visterra, 2.

Abstract Number: 1568

Comparison of Methotrexate and Azathioprine as the First Steroid-Sparing Immunosuppressive Agent in Patients with Takayasu's Arteritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
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Background/Purpose: Conventional disease-modifying anti-rheumatic drugs (cDMARDs) are recommended in addition to glucocorticoids (GC) for all active Takayasu's arteritis (TAK) patients as the first-line therapy. However, there is limited data comparing cDMARDs as the first-line immunosuppressive (IS) treatment. In this study, we aimed to compare the outcomes of methotrexate (MTX) and azathioprine (AZA), which were used most frequently as the first-line cDMARDs, in TAK patients.

Methods: TAK patients who received cDMARDs in addition to GCs as the initial therapy were included in this multicenter retrospective cohort study. Clinical, laboratory and imaging data of the patients were assessed. In addition, a match analysis (cc match) using variables 'age', 'gender' and 'diffuse aortic involvement' was performed between patients who received MTX or AZA as first-line cDMARD treatment.

Results: We included 301 (F/M: 260/41, mean age: 42.2±13.3) patients from 10 centres in the study. As the first-line cDMARD, 204 (67.8%) patients received MTX and 77 (25.6%) patients received AZA. First cDMARD was cyclophosphamide in 17 (5.6%), leflunomide in 2 (0.5%) and mycophenolate mofetil in one patient. The remission, relapse and radiographic progression rates were similar between patients who received MTX and AZA as first-line cDMARDs. Vascular surgery rate was higher in the AZA (23% vs. 9%, p=0.001), whereas the frequency of patients receiving ≤5 mg/day GCs at the end of the follow-up was higher in the MTX group (76 vs 62%, p=0.034). Similarly, the rate of vascular surgery was higher and the GC dose reduction rate (≤5 mg) was lower in AZA group in match analysis. Drug survival was similar between

Table 1. Demographic and clinical characteristics of patients with Takayasu's arteritis

	Total group (n=301)	First-line methotrexate (n=204)	First-line azathioprine (n=77)	p
Age, mean±SD	42,2±13,3	43,5±13,3	40,4±13,2	0,08
Gender, female, n(%)	260 (86)	184 (90)	63 (82)	0,055
Duration of first cDMARD, months	35 (3-336)	35,5 (3-312)	35 (3-336)	0,64
Remission with first cDMARD, n(%)	193/296 (65)	138/199 (69)	50/77 (65)	0,48
Disease activity (baseline)				
PGA, active, n (%)	283/297 (95)	191/201 (95)	74/77 (96)	0,70
Kerr, active, n (%)	270/289 (93)	181/195 (93)	70/75 (93)	0,53
ITAS 2010	9 (2-20)	9 (0-19)	10 (3-21)	0,61
Disease activity (12th month)				
PGA, active, n (%)	53/118 (45)	33/76 (43)	18/39 (46)	0,78
Kerr, active, n (%)	32/120 (27)	24/79 (30)	6/38 (16)	0,26
ITAS 2010	1 (0-11)	1 (0-9)	1 (0-11)	0,48
Relapse rate, n(%)	95/192 (50)	68/138 (49)	24/49 (49)	0,97
Vascular surgery rate with first cDMARD, n(%)	40/291 (14)	17/196 (9)	18/77 (23)	**0,001**
GC dose reduction (?5 mg) or discontinuation with first cDMARD, n(%)	153/220 (70)	110/145 (76)	100/65 (62)	**0,034**
Radiographic progression, n(%)	75/142 (53)	48/98 (49)	22/39 (56)	0,43
CRP, baseline, mg/L	13 (0,4-235)	15,3 (0,5-280)	19,0 (0,4-145)	0,82
CRP, 12th month, mg/L	3 (0,8-130)	4,4 (0,2-200)	3,7(0,4-83)	0,90

PGA: Physician global assessment

MTX and AZA groups (median 48 months, MTX vs AZA: 32% vs 42%, p=0.34). IS therapy was discontinued in 18 (11 MTX, 7 AZA) patients during the follow-up period due to remission. In the IS discontinuation group 2 patients had a relapse at 2 and 6 months, while 16 patients were still on remission at the end of mean 69.4 (±50.9) months of follow-up.

Conclusion: Remission, relapse, radiographic progression and drug survival rates of azathioprine and methotrexate were similar in Takayasu's arteritis patients having the first-line of therapy. The rate of vascular surgery was higher and the rate of steroid dose reduction was lower with azathioprine compared to methotrexate at the end of the follow-up.

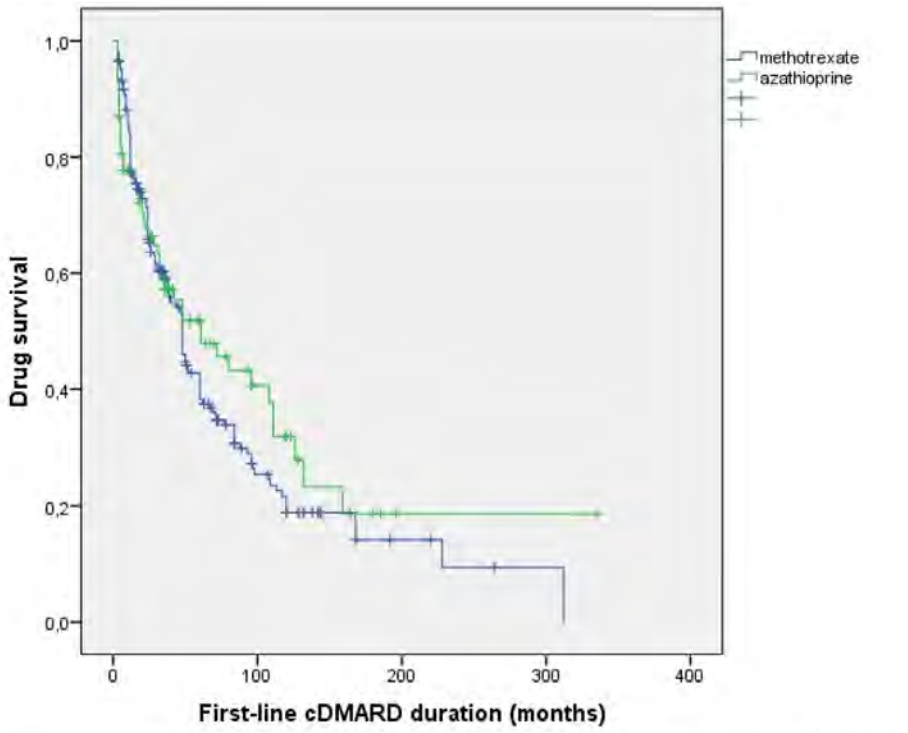

Figure 1. Drug survival for methotrexate and azathioprine treatments in TAK patients as first-line

Figure 1. Drug survival for methotrexate and azathioprine treatments in TAK patients as first-line cDMARD

Disclosure: S. Kaymaz-Tahra: None; **O. Bayindir Tsechelidis**: Janssen, 5; **B. Ince**: None; **O. Isik**: None; **M. Kutu**: None; **O. Karakas**: None; **T. Demirci Yildirim**: None; **Z. Ademoglu**: None; **E. Durak Ediboglu**: None; **B. Ekti Uludogan**: None; **C. Ilgin**: None; **S. Yasar Bilge**: None; **T. Kasifoğlu**: None; **S. Akar**: None; **H. Emmungil**: None; **F. Onen**: AbbVie/Abbott, 6, Amgen, 6, Novartis, 6, Pfizer, 6, UCB, 6; **A. Omma**: None; **N. Alpay Kanitez**: None; **A. Yazici**: None; **A. Cefle**: None; **M. Inanç**: Boehringer-Ingelheim, 6, Pfizer, 6, UCB, 6; **K. Aksu**: None; **G. Keser**: None; **H. Direskeneli**: AbbVie/Abbott, 1, 5, 6, Amgen, 6, celltrione, 1, 6, Pfizer, 5, 6, Roche, 12, Educational, UCB, 5, 6, 12, Educational; **f. Alibaz-Öner**: None.

Abstract Number: 1569

Efficacy and Safety of Tofacitinib and Tocilizumab in 84 Patients with Takayasu Arteritis: Single-Center Post-Hoc Analysis of a Prospective Study

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SESSION INFORMATION

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Background/Purpose: To compare the efficacy and safety of tofacitinib and tocilizumab in patients with Takayasu arteritis (TAK) in real world situation.

Methods: A post-hoc analysis was conducted in 84 patients with TAK registered in the Chinese Registry of Systemic Vasculitis (CRSV) cohort [median age 26 years (interquartile range 22-32), 76 (90%) females] were included (Figure 1). Patients who were treated with either tofacitinib (*n*=42) or tocilizumab (*n*=42) were followed up regularly according to the pre-set protocol. Complete response was defined as both clinically and imagine remission with the dosage of prednisone ≤ 10mg daily

Table 1 Baseline characteristics of patients with Takayasu's arteritis in tofacitinib and tocilizumab treatment groups

Characteristics	Total (N=84)	Tofacitinib (N=42)	Tocilizumab (N=42)	*P*-value
Age, years, median (IQR)	26 (22-32)	28 (23-33)	25 (21-31)	0.27
Female, *n* (%)	76 (90)	38 (90)	38 (90)	1.0
Disease duration, years, median (IQR)	4.1 (1.8-6.1)	4.7 (2.1-7.2)	3.3 (1.3-5.3)	0.08
Time from diagnosis to start of study medication, years, median (IQR)	2.9 (1.0-5.1)	3.2 (1.6-5.6)	2.1 (0.8-4.4)	0.06
Numano's classification of Takayasu's arteritis, *n* (%)				
I	16 (19)	8 (19)	8 (19)	0.93
IIa	8 (10)	5 (12)	3 (7)	
IIb	12 (14)	5 (12)	7 (17)	
III	0	0	0	
IV	2 (2)	1 (2)	1 (2)	
V	46 (55)	23 (55)	23 (55)	
Arterial hypertension, *n/N* (%)	18/82 (22)	9/42 (21)	9/42 (21)	1.0
Hyperlipidemia, *n/N* (%)	5/82 (6)	1/42 (2)	4/42 (10)	0.36
Diabetes, *n/N* (%)	1/82 (1)	1/42 (2)	0	-
Smoking, *n/N* (%)	3/82 (4)	1/42 (2)	2/42 (5)	1.0
Tuberculosis history, *n/N* (%)	2/82 (2)	2/42 (5)	0	-
Vascular signs, *n/N* (%)	43/81 (53)	24/42 (57)	19/39 (49)	0.45
Constitutional signs, *n/N* (%)	16/81 (20)	8/42 (19)	8/39 (21)	0.87
NIH score ≥2, *n/N* (%)	55/82 (67)	29/42 (69)	26/40 (65)	0.70
ESR, mm/hr, median (IQR)	27 (12-52)	20 (8-44)	31 (18-55)	0.06
CRP, mg/L, median (IQR)	25 (9-48)	17 (3-46)	33 (15-51)	0.06
Serum IL-6, pg/ml, median (IQR)	9.8 (5.2-36.9)	8.2 (4.0-24.9)	19.8 (6.2-56.0)	0.10
Serum TNF-α, pg/ml, median (IQR)	7.3 (4.7-12.5)	6.0 (4.5-9.3)	10.3 (6.1-28.1)	0.06
Glucocorticoid used, *n/N* (%)	81/84 (96)	39/42 (93)	42/42 (100)	0.24
Glucocorticoid dose, mg/day of prednisone or equivalent, median (IQR)	13 (10-20)	10 (10-18)	15 (10-21)	0.07
Concurrent immunosuppressive agent used, *n* (%)	77 (92)	37 (88)	40 (95)	0.43
Methotrexate (MTX), *n* (%)	49 (58)	26 (62)	23 (55)	0.51
Azathioprine (AZA), *n* (%)	13 (16)	5 (12)	8 (19)	0.37
Mycophenolate mofetil (MMF), *n* (%)	13 (16)	5 (12)	8 (19)	0.37
Cyclophosphamide (CYC), *n* (%)#	47 (56)	23 (55)	24 (57)	0.83
Leflunomide (LEF), *n* (%)	6 (7)	5 (12)	1 (2)	0.20
Hydroxychloroquine (HCQ), *n* (%)	9 (11)	6 (14)	3 (7)	0.48
Cyclosporin A (CsA), *n* (%)	2 (2)	1 (2)	1 (2)	1.0
Tacrolimus, *n* (%)	3 (4)	0	3 (7)	-
*Combinations, *n* (%)	25 (30)	10 (24)	15 (36)	0.23
Previous biologics, *n* (%)	28 (33)	20 (48)	8 (19)	0.005
TNF inhibitor	15 (18)	8 (19)	7 (17)	0.78
Tocilizumab	14 (17)	13 (31)	1 (2)	<0.001
Both	4 (5)	4 (10)	0	-

Note: IQR: interquartile range; NIH: National Institute of Health; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; IL-6: interleukin-6; TNF-a: tumor necrosis factor-a. * Combinations of immunosuppressive agents: MTX+MMF(7), MTX+AZA(2), MMF+HCQ(2), LEF+HCQ(2), MTX +TAC(1), MTX+LEF(1), MTX+HCQ(1), MTX+CTX(1), MTX+CsA(1), MTX+HCQ+CsA(1), MTX+HCQ+AZA(1), CTX+TAC(1), AZA+TAC(1), AZA +LEF(1), AZA+HCQ(1), AZA+CTX(1). # Number of patients who ever received cyclophosphamide.

and normal acute-phase reactant, while partial response were the same with complete response except that ESR was less than 40mm/h or hs-CRP (hypersensitive C reactive Protein) higher than 16mg/L or the acute-phase reactant decreased by more than 50% compared to the baseline.

Results: The baseline clinical features and demographic date were similar in these two groups (Table 1). Complete response at 6 months was found in 18/27 (67%) patients treated with tofacitinib and 22/32 (69%) with tocilizumab, and rates of overall response in intention-to-treat (ITT) populations were 43% and 52% respectively (P>0.05). At 12, 18 and 24 months, the rates of overall response in ITT population (41%, 24% and 14% *vs*. 41%, 36% and 29%) and in per-protocol (PP) population (77%, 71% and 75% *vs*.65%, 83% and 80%) were similar in patients treated with tofacitinib to those with tocilizumab (Table 2). There were no significant difference found in the changes of ESR, CRP, TNFa, dose of glucocorticoid, mural thickness and lumen diameters of common carotid and subclavian arteries in these two groups. And the cumulative incidences of relapse, treatment failure, and drug retention were similar, too (Figure 1). The drug retention rates at 6, 12, 18 and 24 months in patients treated with tofacitinib and tocilizumab were 64%, 52%, 33% and 19% *vs*. 76%, 60%, 43% and 36%, respectively.

Six (14%) adverse events occurred in the tofacitinib treatment group (including 3 patients with herpes zoster infection, 1 with pulmonary infection, 1 with headache and 1 with abdominal pain) and 6 (14%) occurred in the tocilizumab treatment group (including 2 patients with back pain, 1 with acute pancreatitis, 1 with pulmonary infection, 1 with vomiting and 1 with hepatic dysfunction).

Conclusion: Tofacitinib and tocilizumab are both effective for refractory TAK with similar response rates, cumulative incidences of relapse, treatment failure, and drug retention. Both medications may be effective alternatives for patients who failed to respond to traditional immunosuppressive agents.

Table 2 Response to treatment at 6, 12, 18 and 24 months by intention-to-treat analysis and per-protocol analysis among patients with Takayasu's arteritis in tofacitinib and tocilizumab treatment groups

Intention-to treat analysis	6 months			12 months			18 months			24 months		
	Tofacitinib (n=42)	Tocilizumab (n=42)	*P*-value	Tofacitinib (n=42)	Tocilizumab (n=42)	*P*-value	Tofacitinib (n=42)	Tocilizumab (n=42)	*P*-value	Tofacitinib (n=42)	Tocilizumab (n=42)	*P*-value
Overall response	18 (42.9%)	22 (52.4%)	0.382	17 (40.5%)	17 (40.5%)	1.0	10 (23.8%)	15 (35.7%)	0.233	6 (14.3%)	12 (28.6%)	0.111
Complete response	16 (38.1%)	22 (52.4%)	0.148	16 (38.1%)	15 (35.7%)	0.821	10 (23.8%)	15 (35.7%)	0.233	6 (14.3%)	12 (28.6%)	0.111
Partial response	2 (4.8%)	0 (0%)	-	1 (2.4%)	2 (4.8%)	1.0	0	0	-	0	0	-

Per-protocol analysis	6 months			12 months			18 months			24 months		
	Tofacitinib (n=27)	Tocilizumab (n=32)	*P*-value	Tofacitinib (n=22)	Tocilizumab (n=26)	*P*-value	Tofacitinib (n=14)	Tocilizumab (n=18)	*P*-value	Tofacitinib (n=8)	Tocilizumab (n=15)	*P*-value
Overall response	18 (66.7%)	22 (68.8%)	0.883	17 (77.3%)	17 (65.4%)	0.387	10 (71.4%)	15 (83.3%)	0.589	6 (75.0%)	12 (80.0%)	1.0
Complete response	16 (59.3%)	22 (68.8%)	0.518	16 (72.7%)	15 (57.7%)	0.278	10 (71.4%)	15 (83.3%)	0.589	6 (75.0%)	12 (80.0%)	1.0
Partial response	2 (7.4%)	0 (0%)		1 (4.5%)	2 (7.7%)	1.0	0	0		0	0	

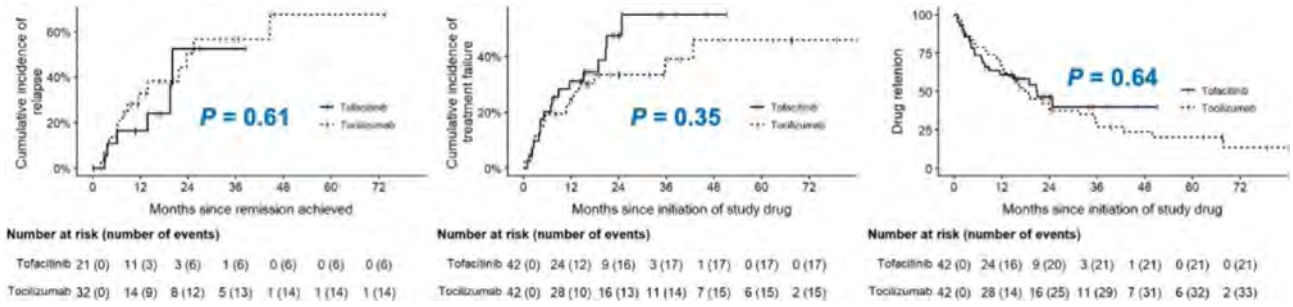

Figure 1 The cumulative incidences of relapse, treatment failure, and drug retention of patients treated with tofacitinib and tocilizumab were similar.

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Abstract Number: 1570

Prognostic Assessment of the 2022 ACR/EULAR Classification Criteria for Takayasu Arteritis: A Multi-centre International Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: The 2022 ACR/EULAR classification criteria for Takayasu arteritis (TAK) rely on a point-based clinical and imaging scoring system (from 0 to 22). The aim of this study is to investigate whether the baseline cumulative score and the fulfillment of each item included in the score correlate with the long-term prognosis of TAK patients.

Methods: Data of TAK patients from 4 centres (2 from Italy; 2 from India) were retrospectively reviewed. For each patient, the score provided by the 2022 classification criteria was calculated and the following outcomes were evaluated: glucocorticoid (GC) suspension, need of conventional and biologic DMARDs (cs- and bDMARDs) introduction, need of vascular procedures. Data on bDMARDs were retrieved only from the Italian cohorts. Correlation of these outcomes with the cumulative baseline score and with single item fulfillment was assessed. Additionally, the correlation between baseline ACR/EULAR 2022 score and disease activity indexes (i.e., DEI.Tak, ITAS2010) was evaluated. Univariate and multivariate logistic analyses and Spearman correlation analyses were performed as appropriate.

Table 1 legend. Univariate and multivariate logistic analyses evaluating the association of each item with different outcomes

	GC SUSPENSION						INTRODUCTION OF ≥1 csDMARD						INTRODUCTION OF ≥1 bDMARD						NEED OF ≥1 VASCULAR PROCEDURE					
	Univariable			Multivariable			Univariable			Multivariable			Univariable			Multivariable			Univariable			Multivariable		
	OR	CI	p-value	OR	CI	p-value	OR	CI	p-value	OR	CI	p-value	OR	CI	p-value	OR	CI	p-value	OR	CI	p-value	OR	CI	p-value
Female sex	1.366	0.783-2.440	0.294				0.997	0.541-1.838	0.992				1.314	0.535-3.259	0.556				1.342	0.735-2.580	0.356			
Angina/ischemic cardiac pain	0.573	0.201-1.381	0.167				0.850	0.391-2.231	0.769				1.020	0.293-3.888	0.978				2.092	1.126-5.424	**0.006**	2.662	1.313-6.479	**0.007**
Limb claudication	1.033	0.646-1.611	0.921				2.166	1.308-3.671	**0.009**	2.019	1.155-3.665	**0.014**	1.021	0.350-2.886	0.888				1.466	0.893-2.314	0.181			
Vascular bruits	0.593	0.362-0.971	**0.038**	0.810	0.473-1.395	0.446	1.552	0.925-2.609	0.062				1.869	0.915-3.694	0.059				0.925	0.565-1.543	0.758			
Reduced pulse	0.932	0.586-1.472	0.762				1.282	0.775-2.119	0.333				1.445	0.743-2.755	0.276				0.958	0.616-1.527	0.852			
Carotids abnormalities	0.935	0.591-1.474	0.766				2.595	1.591-4.164	**0.004**	2.121	1.184-3.798	**0.012**	1.074	0.526-2.217	0.840				0.427	0.268-0.680	**0.0002**	0.413	0.255-0.669	**<0.001**
Blood pressure difference ≥20	0.474	0.284-0.795	**0.002**	0.537	0.327-0.880	**0.014**	1.316	0.797-2.207	0.293				1.089	0.493-2.509	0.804				0.715	0.449-1.138	0.155			
1 artery involved	2.250	0.929-5.678	0.074				0.680	0.200-2.350	0.099				0.397	0.129-1.199	0.100				1.125	0.559-2.259	0.747			
2 arteries involved	1.973	0.836-5.061	0.160				0.862	0.401-1.606	0.533				1.264	0.511-3.080	0.621				1.508	0.829-2.825	0.174			
≥3 arteries involved	0.586	0.312-0.925	**0.024**	0.743	0.405-1.365	0.341	1.597	0.901-2.831	0.109				1.342	0.656-2.754	0.422				0.704	0.415-1.193	0.192			
Symmetric involvement	0.711	0.442-1.145	0.160				1.840	1.106-3.068	**0.019**	1.450	0.851-2.472	0.172	1.093	0.535-2.071	0.812				1.075	0.669-1.728	0.766			
Abd. aorta + renal/mesenteric involvement	0.479	0.293-0.782	**0.002**	0.577	0.341-0.976	**0.040**	0.790	0.472-1.329	0.358				1.233	0.592-2.569	0.576				1.074	0.670-1.699	0.761			

Results: We included 407 patients (163 from Italy; 244 from India) with a median follow-up of 80 (IQR, 37-143) months. Mean baseline score was 10.1 ± 3.5 and 378 (92.9%) patients were classified as TAK according to the 2022 ACR/EULAR criteria. GCs were started in 348 patients (85.5%) and suspended in 110 (31.6%) after a median of 43 (IQR, 23-87) months. csDMARDs were started in 331 patients (81.3%) after a median of 1 (IQR, 0-5) month. bDMARDs were started in 108 patients (66.3%) after a median of 16 (IQR 8.8-39) months. Vascular procedures were performed in 101 patients (24.8%). Mean baseline DEI.Tak and ITAS2010 scores were 8.8 ± 5.5 and 10.4 ± 6.6, respectively. A higher baseline cumulative score was negatively associated with GC suspension (OR 0.901 [95%CI 0.844-0.962], p=0.002) and positively associated with csDMARD introduction (OR 1.102 [95%CI 1.027-1.184] p=0.007). No correlation with bDMARD start and vascular procedures was found. **Table 1** shows the association of each item with different outcomes. At multivariate analysis, difference in blood pressure ≥20 mmHg and abdominal aorta + renal/mesenteric involvement were negative predictors of GC suspension; limb claudication and carotid abnormalities were predictors of csDMARD introduction. Angina/ischemic cardiac pain was predictor of need for vascular procedure, conversely to carotid abnormalities. Finally, a higher score strongly correlated with both baseline DEI.Tak (rho=0.549, p< 0.001) and ITAS2010 (rho=0.575, p< 0.001).

Conclusion: A higher baseline score obtained from the ACR/EULAR 2022 TAK classification criteria was associated with a more aggressive disease course. No specific item was associated with disease prognosis. At baseline, the ACR/EULAR 2022 score might be a surrogate of disease activity scores.

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Abstract Number: 1571

Tocilizumab in Pregnant Takayasu Arteritis - The Use of Tocilizumab at Conception and Throughout Pregnancy in Those with Takayasu Arteritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Takayasu arteritis (TA) is a large vessel vasculitis predominantly affecting female of reproductive age. Tocilizumab (TCZ) is frequently used in synthetic DMARD refractory cases. Preclinical animal studies and small case reports suggest potential teratogenicity of TCZ in pregnancy. The current ACR guidance is to continue TCZ at conception but to cease upon confirmation of pregnancy. Herein we describe the use of tocilizumab throughout pregnancy in those with TA.

Methods: A total of 160 cases of TA were identified from a single center in the United Kingdom from 2016-2023. Cases limited to female who received TCZ during pregnancy were screened. Data regarding disease, medications, and pregnancy outcomes; live birth, miscarriage, fetal abnormalities, and fetal anomalies were extracted from the database.

	CASE 1	CASE 2	CASE 3	CASE 4	CASE 5	CASE 6
Age at diagnosis	20	30	24	25	24	24
Age at delivery	28	32	33	33	30	32
Disease duration (yrs)	10	2	9	9	6	9
Angiographic classification	Type III : Thoracic Abdominal Renal, Mesenteric Celiac	Type IIb : Subclavian, Axillary, celiac	Type IIb : Subclavian Carotid Renal	Type IIa : Carotid, vertebral, subclavian	Type V : Carotid, Coeliac Mesenteric Renal	Type IIb: Subclavian Celiac
Complication	Refractory Hypertension Renal angioplasty	Nil	Cerebral Ischemia, Hypertension	Cerebral Ischemia	Hypertension	Nil
Significant history	Ectopic pregnancy (methotrexate)	Nil	Miscarriage x1	TOP(MMF-feticide)	Nil	2 sisters microcephaly
Disease activity (NIH)						
Pre pregnancy	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive
Post pregnancy	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive
Duration of Tocilizumab Usage (yrs)	2	2	4	5	4	1
Tocilizumab exposure during pregnancy	Stop at 3rd trimester	Throughout	Throughout	Stop at 3rd trimester	Throughout	Stop at early pregnancy
Concomitant medications	Prednisolone 5mg od Azathioprine 75mg od Amlodipine 10mg od Thyroxine 125mcg od Aspirin 150mg od	Prednisolone 3 mg od Nortriptyline 10mg od Aspirin 75mg od Dalteparin 5000u od	Azathioprine 100mg od Amlodipine 5mg od Bisoprolol 2.5mg od Aspirin 75mg od	Prednisolone 5mg Azathioprine 100mg Citalopram 20mg od Aspirin 300mg Rivaroxaban 20mg od	Prednisolone 1.5mg od Amlodipine 10mg od	Prednisolone 20mg on tapering Azathioprine 75mg od Acyclovir 75mg od

TOF – Termination of pregnancy , MMF -Mycophenolate mofetil
(note – concomitant medications listed exclude usual pregnancy supplements)

Baseline Characteristics

	CASE 1	CASE 2	CASE 3	CASE 4	CASE 5	CASE 6
Gestational age (weeks) at delivery	37	36	33	35	39	39
Live Birth	Yes	Yes	Yes	Yes	Yes	Yes
Miscarriage	No	No	No	No	No	No
Fetal abnormality	Nil	LBW(1.87kg) Pre-term (abruptio)	LBW(1.58kg) Pre-term (Fetal cardiac-trigeminy)	LBW Pre-term	Nil	Nil
Fetal anomalies	Nil	Nil	Nil	Nil	Nil	Nil

LBW -Low birth weight

Pregnancy Outcomes

Results: Out of 160 TA patients, 45 were on TCZ between 2016-2022. Six patients were identified to have concomitant use of TCZ during pregnancy, all received Tocilizumab 162mg subcutaneously per week. The baseline characteristic and pregnancy outcomes of each case are shown in Table 1 and 2 respectively. The age at delivery range between 28 to 33 years old with the mean duration of illness of 7.5 years. In 5/6 cases the risk of flare off tocilizumab was considered higher than the potential teratogenicity. Patients and obstetric physicians were involved in the decision making. In 2 of 6 cases TCZ was stopped prior to the active transport of the monoclonal antibody across the placenta from week 30 of gestation. In 3 cases risk of flare was considered so high that TCZ was continued throughout gestation. Live vaccination of the newborn was avoided in all cases. No teratogenicity was reported following TCZ usage in TA pregnancy. However, a high proportion (50%) of pre-term deliveries and low birth weight were observed.

Conclusion: The use of TCZ in TA is well established. TA is a disease predominantly in female of childbearing age. Often TCZ cannot be stop during pregnancy. We describe six successful pregnancies exposed to tocilizumab with good maternal and neonatal outcomes

Disclosure: N. Zakaria: None; **A. Porter**: None; **R. Maughan**: None; **C. Pericleous**: None; **J. Satara**: None; **M. Colquhoun**: Pfizer, 6; **P. Agrawal**: None; **j. Nouza**: None; **H. Wilson-Morkeh**: None; **T. Youngstein**: None; **J. Mason**: None.

Abstract Number: 1572

Long-term Efficacy and Retention Rate of Molecular Targeted Drugs in Takayasu Arteritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Takayasu arteritis (TAK) is a type of large-vessel vasculitis that predominantly affects young females. The relapse is frequent, accounting for 60% of cases, and molecular targeted drugs including tocilizumab (TCZ) and tumor necrosis factor inhibitor (TNFi) are used. Although the steroid-sparing effect of molecular targeted drugs has been reported in short period, information about the long-term efficacy and retention rate is scarce. The aim of this study is to investigate the long-term efficacy and retention rate of molecular targeted drugs in TAK.

Methods: 117 patients with TAK who satisfied the JCS or ACR classification criteria and visited Tohoku University Hospital during 2018 to 2022 were enrolled to this study. The use of molecular targeted drugs, clinical background, long-term efficacy and retention rate of the drugs were retrospectively evaluated.

Results: 45 of 117 patients (38.5 %) received molecular targeted drugs, and all were applied for the relapse of TAK. The clinical characteristics of patients required molecular targeted drugs included young age at onset and the presence of extra-arterial comorbidities. Eight and four patients required more than two and three molecular targeted drugs, respectively. The numbers of molecular targeted drugs used were as follows, TCZ, 35; TNFi, 12; JAK inhibitors, 2; abatacept, 1; rituximab, 1. During 45 months of median-follow up period after the initiation of molecular targeted drugs, the retention rate

was as follows; TCZ, 77.1 %, TNFi, 91.6 %. TCZ was discontinued in following cases; infection, 3; major relapse, 2; exacerbation of extra-arterial manifestation, 2; infusion reaction, 1. In four patients who discontinued TCZ, TNFi was used as the 2nd molecular targeted drug. Although the retention rate of TCZ was high, TCZ was not discontinued in following seven cases; worsening of vascular legion, 2; major relapse without vascular change, 2; minor relapse, 2; severe infection, 1. This was because there existed little evidences for the effectiveness of other molecular targeted drugs. The discontinuation of TCZ was frequent in patients receiving vascular surgery or complicating with extra-arterial comorbidities. Of note, severe colitis was observed in 8.8% of patients receiving TCZ, and infective endocarditis was also documented. The mean dose of prednisolone (PSL) was significantly reduced in patients receiving molecular targeted drugs, irrespective of drugs, as follows; before initiation, 10.1±3.9 mg/day; upon initiation 25.1±11.6mg/day; the most recent, 5.6±3.7 mg/day. PSL was discontinued in seven cases treated with TCZ, and six cases remained relapse-free.

Conclusion: The retention rate of molecular targeted drugs was high, and molecular targeted drugs were useful for the maintenance of remission and reducing the dose of corticosteroid in relapsed cases. Nevertheless, there existed patients who were not able to change TCZ due to insufficient evidences of other molecular targeted drugs in TAK.

Disclosure: T. Shirai: None; **H. Sato**: None; **T. Ishii**: None; **H. Fujii**: None.

Abstract Number: 1573

Inpatient Prevalence and Comorbidity of Takayasu's Arteritis: Nationwide Inpatient Sample 2016-2020

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session B
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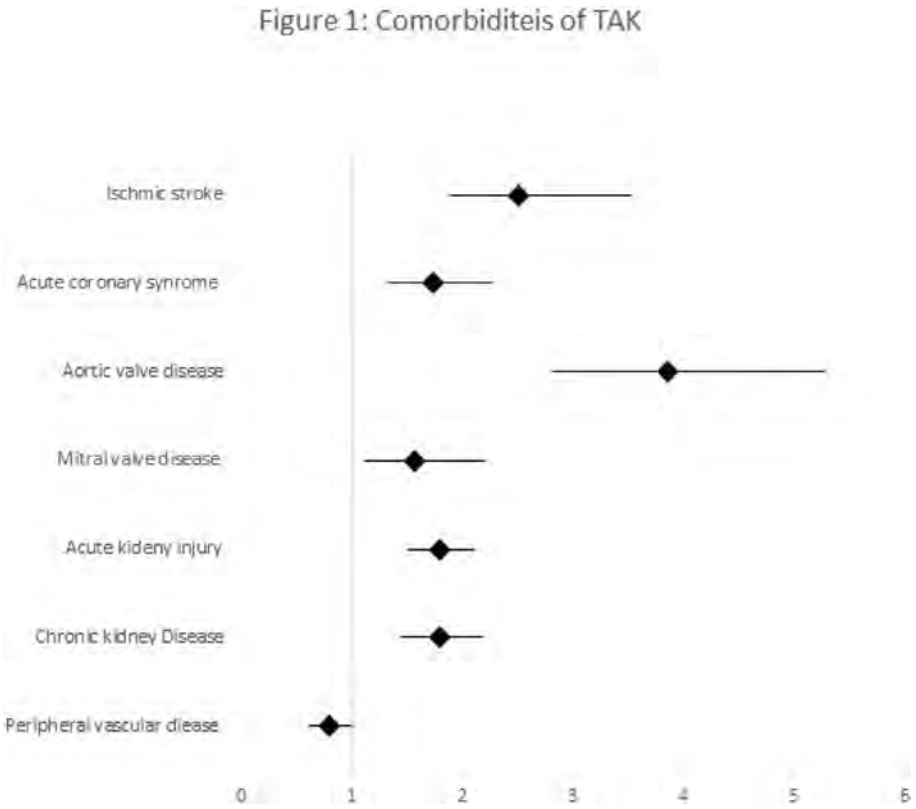
Background/Purpose: Takayasu's Arteritis (TAK) is a granulomatous large-vessel vasculitis that affects the aorta and its branches, and it is more commonly observed in women. We aimed to describe the prevalence, comorbidities, and burden of admitted TAK patients in the United States

Methods: The 2016-2020 National Inpatient Sample database (NIS) was analyzed to identify adult hospitalizations with TAK, using International Classification of Diseases – 10 Clinical Modification (ICD-10-CM) codes. The studied primary outcome was to assess TAK inpatient comorbidities. A multivariate logistic regression, and linear regression analyses were used to adjust for possible confounders.

Results: 5439 hospitalizations of TAK were analyzed. Of these, 4389 (80.69%) were females. The mean age was 52.2. Logistic regression analysis showed that patients had a higher risk of ischemic stroke (adjusted Odds Ratio [aOR] of 2.5, 95% Confidence Interval [CI] 1.89-3.53), acute coronary syndrome (aOR: 1.73, CI: 1.32-2.28), aortic valve disease (aOR: 3.86, CI: 2.81-5.28), mitral valve disease (aOR: 1.57, CI: 1.12-2.21), acute kidney injury (aOR: 1.79, CI: 1.51-2.11), and chronic kidney disease (aOR: 1.79, CI: 1.45-2.19). There was no statically significant difference in peripheral vascular disease (aOR: 0.79, CI: 0.62-1.02). Patients with TAK required the use of more expensive imaging modalities (aOR: 2.84, CI: 1.40-5.74). Figure 1 shows the Forrest plot for multivariate analysis of in hospital morbidities when adjusted for patient demographics, comorbidities, and hospital characteristics.



Comorbidities of TAK

Conclusion: Analysis of patients with TAK showed a higher risk of comorbidities including ischemic stroke, acute coronary syndrome, aortic valve disease, mitral valve disease, acute kidney injury, and chronic kidney disease.

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Abstract Number: 1574

The Role of ^{18}F-FDG PET/CT Scans in Takayasu Arteritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
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Background/Purpose: Takayasu arteritis (TA) is a large-vessel vasculitis which primarily affects the aorta and its main branches. Accurate assessment of disease activity has always been challenging and inadequate treatment may result in irreversible damage. The Indian Takayasu Clinical Arteritis Scores (ITAS 2010, ITAS.A) are validated and reliable measures of

disease activity. Positron-emission tomography (PET) and ^{18}F-FDG PET with computed tomography (PET/CT) are non-invasive metabolic imaging modalities that have been proposed as important tools to assess disease activity.

Methods: We retrospectively studied 26 TA patients between January 2008 – March 2023. The diagnosis was confirmed on clinical, laboratory and imaging criteria. Disease activity as assessed by the ITAS 2010, clinical, laboratory and imaging techniques (including magnetic resonance imaging, Doppler ultrasound and/or digital subtraction angiography) was compared with the results of the PET/CT scans.

Results: Median age at TA diagnosis was 33 years (13-57). There were 22 females (84.6%), 4 males and Caucasians (61.5%), Asians (30.8%) and Afro-Caribbean (7.7%). Median follow up was 156 months (20 – 444). Thirteen of 26 patients (50%) had positive antiphospholipid antibodies (aPL). Two of the patients were diagnosed with obstetric anti-phospholipid syndrome (APS) and 1 with both thrombotic and obstetric APS.

Of 26 patients, there were 43 PET/CT scans performed in 22 patients. Ten patients had a single scan and 12 patients had 2 or more scans (maximum 4 scans). Nine scans were done for diagnosis and 34 during follow up. Of the 9 diagnostic scans, all 9 had clinically active disease (ITAS score ≥ 2), 8 (88.9%) had raised inflammatory markers (median ESR 57 (20 -115), median CRP 46 (1-126)) and 7 (77.8%) had a positive PET scan (suggestive of active vasculitis). Of the 34 follow up scans, 27 scans (in 17 patients) had clinically active disease (ITAS score ≥ 2) and 7 scans (in 6 patients) were in remission (ITAS score 0). Of the 27 scans with clinically active disease, 12 scans were positive (44.4%). In the remaining 15 scans,

Table 1: Role of PET scan in Takayasu Arteritis (TA)

Groups	No. of scans (n)	Median ESR (range)	Median CRP (range)	ITAS ≥ 2 (n)	PET +ve (n)	%
1. Patients with active disease (symptomatic ± raised ESR/CRP)						
• For diagnosis	9	57 (20-115)	46 (1-126)	9	7	77.8%
• For flares	10	47 (11-118)	35 (8-48)	10	6	60%
2. Asymptomatic patients with raised ESR, CRP	2	65 (15-115)	18 (6-30)	0	0	-
3. Asymptomatic patients with radiological progression	7	15 (8-53)	9 (1-34)	7	2	28.6%
4. Symptomatic patients with normal ESR, CRP	10	5 (2-17)	1 (0-3)	10	4	40%
5. Patients in remission (normal ESR/CRP, asymptomatic)	5	6 (2-20)	2 (0-2)	0	0	-
Total	43					

11 (73.3%) were done while on steroids and/or immunosuppression (median prednisolone dose 5mg (2.5 - 10mg)). The 7 follow up scans in clinical remission and had no FDG uptake.

Conclusion: ^{18}F-FDG PET/CT scanning is helpful as a diagnostic and monitoring tool to assess disease activity in TA. PET scan imaging correlates with ITAS activity. Corticosteroid therapy may negatively impact the PET scan result and results should be correlated carefully with clinical, laboratory and other radiological assessments. It remains unclear whether presence of aPL/APS is a clinically important association.

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Abstract Number: 1575

Takayasu Arteritis Is Associated with Worse Fatigue Than Healthy Controls Which Persists over Time - A Longitudinal Cohort Study

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
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Background/Purpose: Few studies have assessed patient-reported outcome measures in Takayasu arteritis (TAK), a rare large vessel vasculitis. We prospectively analysed fatigue and fibromyalgia in TAK and its relationship with disease activity in a large cohort of TAK from India.

Methods: Patients with TAK satisfying ACR 1990 criteria or 2012 Chapel Hill consensus conference definition for TAK and age- and gender-similar healthy controls (HC) were enrolled after written informed consent. Disease activity scores (using DEI.TAK, ITAS2010 and NIH disease activity scores), fatigue [using Multidimensional Fatigue Inventory (MFI), FACIT Fatigue Scale (Version 4)] and fibromyalgia (using 2019 American College of Rheumatology diagnostic criteria for fibromyalgia) were assessed at baseline and 6 months.

TAK were compared with healthy controls using unpaired student's t-test or Chi squared test. Comparisons between TAK at baseline and at 6 months follow-up were performed using paired student's t-test or Chi squared test. Pearson's correlation coefficient was computed for the association of fatigue and fibromyalgia scores with disease activity scores. p values < 0.05 were considered as statistically significant.

Results: One hundred and two TAK patients (Females-73.5%, mean age-35.5 years, mean disease duration-94.4 months) and fifty healthy controls (Females-68%, mean age-31.4 years) were enrolled. Hata's Type V was the most common angiographic subtype (63.7%) and 17.6% had active disease as per physician global assessment. TAK had greater severity of fatigue than HC [MFI (p= 0.045), FACIT (p =< 0.001), *lower FACIT scores indicate greater fatigue*]. The prevalence of fibromyalgia was similar between TAK and HC (p=0.286) (Table 1). Active TAK had higher fatigue scores [MFI (p= 0.002), FACIT (p=0.033)] than inactive TAK (Table 2). At baseline, MFI had weak positive correlation (r=0.231, p=0.019) & FACIT score had weak negative correlation (r=-0.226, p =0.022) with NIH disease activity score but not with ITAS 2010 or DEI TAK. The

Table 1: Baseline characteristics of TAK patients and comparison with healthy controls

Parameter [mean (SD)]	TAK (N=102)	HC (N=50)	p value
Age (years)	35.5 (11.7)	31.4 (8.0)	
Gender (Females) (%)	75 (73.5)	34 (68)	
Duration of disease (months)	94.4 (81.7)		
Fatigue and Fibromyalgia scores			
MFI			
General fatigue	10.2(2.6)	9.7(2.7)	0.283
Physical fatigue	10(4.5)	8.5(3.7)	**0.041**
Reduced activity	10 (4.7)	8.2(3.9)	**0.023**
Reduced motivation	8.3(3.8)	7.4(2.8)	0.157
Mental fatigue	9.0(4.4)	7.8(4.4)	0.108
Total MFI score	47.7(17.6)	41.8(15.3)	**0.045**
FACIT score	35.04 (11.1)	44.40 (7.2)	**<0.001**
Number of items fulfilled on the 2019 ACR diagnostic criteria for fibromyalgia	5.29 (4.5)	1.64 (2.6)	**<0.001**
Proportion fulfilling 2019 ACR diagnostic criteria for fibromyalgia (%)	6 (5.8)	1 (2)	0.286

ACR- American College of Rheumatology, DEI.TAK- Disease Extent Index for Takayasu Arteritis, FACIT- The Functional Assessment of Chronic Illness Therapy, HC-Healthy Controls, MFI- Multidimensional Fatigue Inventory, NIH- National Institute of Health, SD- Standard deviation, TAK- Takayasu Arteritis,

Table 2- Comparison of fatigue and fibromyalgia between active and inactive TAK

Parameter [mean (SD)]	Active TAK * (N=18)	Inactive TAK* (N=84)	p value
Age	32.2 (8.4)	36.2 (12.2)	0.193
Duration of disease	81.7 (80.9)	97.1 (82.0)	0.470
MFI score			
General fatigue	11.5(2.4)	10(2.5)	**0.021**
Physical fatigue	13(4.4)	9.4(4.2)	**0.002**
Reduced activity	12.8(3.9)	9.4(4.6)	**0.004**
Reduced motivation	11.2(3.8)	7.7(3.5)	**<0.001**
Mental fatigue	10.7(3.5)	8.7(4.5)	0.074
Total MFI score	59.3(14.5)	45.2(17.2)	**0.002**
FACIT score	30.0 (10.4)	36.1 (11.0)	**0.033**
2019 ACR diagnostic criteria for fibromyalgia	7.4 (4.3)	4.8 (4.4)	**0.026**
ITAS2010	6.1 (5.7)	0.6 (1.2)	**<0.001**
ITAS-A-ESR	7.8 (6.0)	1.6 (1.6)	**<0.001**
ITAS-A-CRP	7.9 (6.1)	1.0 (1.7)	**<0.001**
DEI.TAK	5.6 (5.7)	0.5 (1.1)	**<0.001**
NIH disease activity score	2.2 (1)	0.6 (0.6)	**<0.001**
ESR (mm/hour)	45.3 (21.0)	32.0 (21.0)	**0.017**
CRP (mg/L)	19.7 (30.0)	6.1 (6.9)	**0.001**
Daily prednisolone dose (mg)	23.4 (14.2)	5.6 (9.8)	**<0.001**
Proportion fulfilling 2019 ACR diagnostic criteria for fibromyalgia (%)	2 (11)	4 (4.7)	0.299

*Active or inactive TAK as per physician global assessment.
ACR- American College of Rheumatology, CRP – C-reactive protein, , DEI.TAK- Disease Extent Index for Takayasu Arteritis, ESR – Erythrocyte sedimentation rate, FACIT- The Functional Assessment of Chronic Illness Therapy, ITAS2010- Indian Takayasu Clinical Activity Score 2010, , ITAS-A-CRP – ITAS2010 adjusted for CRP, ITAS-A-ESR – ITAS2010 adjusted for ESR, MFI- Multidimensional Fatigue Inventory, NIH- National Institute of Health, SD- standard deviation, TAK- Takayasu arteritis,

Table 3- Comparison of baseline and 6-month follow-up of 69 TAK patients

Parameter [mean (SD)]	Baseline (N=69)	Follow up (N=69)	p value
MFI score			
General fatigue	10.2(2.5)	10.4(2.3)	0.573
Physical fatigue	10.1(4.7)	10.1(4.0)	0.978
Reduced activity	10.1(5.0)	9.7(3.9)	0.455
Reduced motivation	8.4(4.0)	8.3(3.5)	0.772
Mental fatigue	9.2(4.7)	8.1(4.0)	**0.031**
Total MFI score	48.2(18.7)	46.7(15.5)	0.390
FACIT score	34.5 (11.0)	36.3 (10.8)	0.077
2019 ACR diagnostic criteria for fibromyalgia	5.5 (4.8)	5.6 (5.0)	0.901
ITAS2010	1.0 (2.0)	0.71 (1.2)	0.268
ITAS-A-ESR	2.2 (2.5)	1.9 (1.7)	0.269
ITAS-A-CRP	1.5 (2.5)	1.5 (1.6)	1.00
DEI.TAK	0.8 (1.6)	0.6 (0.9)	0.246
NIH disease activity score	0.8 (0.9)	0.8 (0.7)	0.905
ESR (mm/hour)	35.9 (19.4)	33.5 (17.6)	0.375
CRP mg/L	8.2 (10.0)	11.1 (12.5)	0.101
Daily prednisolone dose	7.8 (11.1)	2.6 (3.2)	**<0.001**

ACR- American College of Rheumatology, CRP – C-reactive protein, , DEI.TAK- Disease Extent Index for Takayasu Arteritis, ESR – Erythrocyte sedimentation rate, FACIT- The Functional Assessment of Chronic Illness Therapy, ITAS2010- Indian Takayasu Clinical Activity Score 2010, , ITAS-A-CRP – ITAS2010 adjusted for CRP, ITAS-A-ESR – ITAS2010 adjusted for ESR, MFI- Multidimensional Fatigue Inventory, NIH- National Institute of Health, SD- standard deviation, TAK- Takayasu arteritis,

number of items on the 2019 ACR diagnostic criteria for fibromyalgia showed a weak positive correlation with ITAS 2010 (r=0.230, p=0.020), DEI TAK (r=0.227, p=0.022), and NIH disease activity score (r=0.285, p=0.004). No difference was observed in fatigue or fibromyalgia scores at six months of follow-up (Table 3).

Conclusion: Fatigue was more prevalent in TAK than in healthy controls, and correlated with TAK disease activity. Fibromyalgia did not differ between TAK and controls. Fatigue and fibromyalgia remained similar in TAK over time.

Disclosure: D. Thakare: None; **U. Rathore**: None; **K. Singh**: None; **V. Agarwal**: None; **D. Misra**: None.

Abstract Number: 1576

Application of the 2022 ACR/EULAR Criteria for Takayasu Arteritis to Previously Diagnosed Patients Based on the 1990 ACR Criteria

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

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Table 1. Comparisons of the results of the application of the 2022 ACR/EULAR criteria to patients with previously diagnosed TAK according to the imaging modalities

Table 1. Comparisons of the results of the application of the 2022 ACR/EULAR criteria to patients with previously diagnosed TAK according to the imaging modalities

Variables		Conventional angiography (N=75)	CT angiography (N=97)	FDG-PET (N=84)	MR angiography (N=6)
At the time of diagnosis	Score	Values	Values	Values	Values
Absolute requirements					
Age ≤ 60 years		66 (88.0)	85 (87.6)	72 (85.7)	6 (100.0)
Evidence of vasculitis on imaging		75 (100.0)	95 (97.9)	55 (65.5)	6 (100.0)
Additional clinical criteria		**N=66**	**N=83**	**N=48**	**N=6**
Female sex	1	57 (86.4)	74 (89.2)	39 (81.3)	3 (50.0)
Angina or ischemic cardiac pain	2	4 (6.1)	9 (10.8)	5 (10.4)	0 (0.0)
Arm or leg claudication	2	12 (18.2)	26 (31.3)	14 (29.2)	2 (33.3)
Vascular bruit	2	46 (69.7)	70 (84.3)	37 (77.1)	4 (66.7)
Reduced pulse in upper extremities	2	32 (48.5)	57 (68.7)	29 (60.4)	4 (66.7)
Carotid artery abnormality	2	34 (51.5)	52 (62.7)	32 (66.7)	5 (83.3)
Systolic blood pressure difference in arms ≥ 20mmHg	1	57 (86.4)	79 (95.2)	46 (95.8)	6 (100.0)
Additional imaging criteria					
Number of affected arteries (aorta or its primary branches)					
One artery	1	17 (25.8)	11 (13.3)	24 (50.0)	3 (50.0)
Two arteries	2	21 (31.8)	33 (39.8)	10 (20.8)	2 (33.3)
Three or more arteries	3	28 (42.4)	39 (47.0)	14 (29.2)	1 (16.7)
Symmetric involvement of paired arteries	1	29 (43.9)	52 (58.6)	16 (38.1)	2 (33.3)
Abdominal aorta involvement with renal or mesenteric involvement	3	12 (18.2)	10 (12.0)	0 (0.0)	1 (16.7)
The total score		9.0 (3.3)	10.0 (3.0)	9.0 (4.0)	9.5 (4.3)
Patients with the total score of ≥ 5 (N (%))		**N=75**	**N=97**	**N=84**	**N=6**
Among patients undergoing the corresponding imaging modality		63/75 (84.0)	83/97 (85.6)	46/84 (54.8)	5/6 (83.3)

Values are expressed as number (percentage) or median (quartile).
ACR: the American College of Rheumatology; EULAR: the European Alliance of Associations for Rheumatology; TAK: Takayasu arteritis; CT: computed tomography, FDG-PET: fluorodeoxyglucose-positron emission tomography, MR: magnetic resonance.

Background/Purpose: Recently, a joint group of the American College of Rheumatology (ACR) and the European Alliance of Associations for Rheumatology (EULAR) proposed new criteria for Takayasu arteritis (TAK) (the 2022 ACR/EULAR criteria). This study applied the 2022 ACR/EULAR criteria to patients with previously diagnosed TAK based on the 1990 ACR criteria and investigated the concordance rate between the two criteria according to the four imaging modalities.

Table 2. Comparison of the results of the application of the 2022 ACR/EULAR criteria to patients with previously diagnosed TAK (CT angiography and FDG-PET performed simultaneously) (N=61)

Table 2. Comparison of the results of the application of the 2022 ACR/EULAR criteria to patients with previously diagnosed TAK (CT angiography and FDG-PET performed simultaneously) (N=61)

At the time of diagnosis		CT angiography	FDG-PET	Both CT angiography and FDG-PET
	Score	Values	Values	Values
Absolute requirements				
Age ≤ 60 years		54 (88.5)	54 (88.5)	54 (88.5)
Evidence of vasculitis on imaging		61 (100.0)	61 (100.0)	61 (100.0)
Additional clinical criteria		**N=54**	**N=54**	**N=54**
Female sex	1	48 (88.9)	48 (88.9)	48 (88.9)
Angina or ischemic cardiac pain	2	8 (14.8)	8 (14.8)	8 (14.8)
Arm or leg claudication	2	16 (29.6)	16 (29.6)	16 (29.6)
Vascular bruit	2	46 (85.2)	46 (85.2)	46 (85.2)
Reduced pulse in upper extremities	2	35 (64.8)	35 (64.8)	35 (64.8)
Carotid artery abnormality	2	37 (68.5)	37 (68.5)	37 (68.5)
Systolic blood pressure difference in arms ≥ 20mmHg	1	52 (96.3)	52 (96.3)	52 (96.3)
Additional imaging criteria				
Number of affected arteries (aorta or its primary branches)				
None	0	2 (3.7)	20 (37.0)	0 (0.0)
One artery	1	7 (13.0)	15 (27.8)	9 (16.7)
Two arteries	2	21 (38.9)	8 (14.8)	19 (35.2)
Three or more arteries	3	24 (44.4)	11 (20.4)	26 (48.1)
Symmetric involvement of paired arteries	1	19 (35.2)	13 (24.1)	25 (46.3)
Abdominal aorta involvement with renal or mesenteric involvement	3	5 (9.3)	0 (0.0)	5 (9.3)
The total score		10.0 (3.0)	8.0 (3.3)	10.5 (4.0)
Patients with the total score of ≥ 5 (N (%))		**N=61**	**N=61**	**N=61**
Among patients undergoing the corresponding imaging modality		52/61 (85.2)	52/61 (85.2)	53/61 (86.9)

Values are expressed as number (percentage) or median (quartile).
ACR: the American College of Rheumatology; EULAR: the European Alliance of Associations for Rheumatology; TAK: Takayasu arteritis; CT: computed tomography, FDG-PET: fluorodeoxyglucose-positron emission tomography, MR: magnetic resonance.

Table 3. Comparisons of the results of the application of the 2022 ACR/EULAR criteria to patients with previously diagnosed TAK according to an age of 60 years

Table 3. Comparisons of the results of the application of the 2022 ACR/EULAR criteria to patients with previously diagnosed TAK according to an age of 60 years

At the time of diagnosis	Score	Age ≤ 60 years (N=156)	Age > 60 years (N=23)	P-value
Absolute requirements				
Age ≤ 60 years		156 (100)	0 (0)	
Evidence of vasculitis on imaging		156 (100)	23 (100)	
Additional clinical criteria				
Female sex	1	135 (86.5)	19 (82.6)	0.535
Angina or ischemic cardiac pain	2	14 (9)	4 (17.4)	0.257
Arm or leg claudication	2	41 (26.3)	6 (26.1)	0.984
Vascular bruit	2	122 (78.2)	15 (65.2)	0.170
Reduced pulse in upper extremities	2	94 (60.3)	18 (78.3)	0.096
Carotid artery abnormality	2	90 (57.7)	11 (47.8)	0.373
Systolic blood pressure difference in arms ≥ 20mmHg	1	143 (91.7)	22 (95.7)	1.000
Additional imaging criteria				
Number of affected arteries (aorta or its primary branches)				
One artery	1	33 (21.2)	6 (26.1)	0.575
Two arteries	2	53 (34.0)	9 (39.1)	
Three or more arteries	3	70 (44.9)	8 (34.8)	
Symmetric involvement of paired arteries	1	69 (44.2)	7 (30.4)	0.211
Abdominal aorta involvement with renal or mesenteric involvement	3	21 (13.5)	1 (4.3)	0.316
The total score		10.0 (3.0)	9.0 (4.0)	0.354
Patients with total score ≥ 5 (N (%))		**N=156**	**N=23**	
Among patients undergoing at least one of the four imaging modalities		153/156 (98.1)	22/23 (95.7)	0.426

Values are expressed as number (percentage) or median (quartile).
ACR: the American College of Rheumatology; EULAR: the European Alliance of Associations for Rheumatology; TAK: Takayasu arteritis.

Methods: This study reviewed the medical records of 179 patients who met the 1990 ACR criteria for TAK. The imaging modalities included conventional angiography, computed tomography (CT) angiography, fluorodeoxyglucose-positron emission tomography (FDG-PET), and magnetic resonance (MR) angiography.

Results: Regardless of the imaging modalities, the concordance rate between the two criteria was 85.5% when including all patients, whereas, it increased to 98.1% when only patients aged ≤60 years were included. Among the four imaging modalities, CT angiography exhibited the highest concordance rate between the two criteria (85.6%). The concordance rate among patients aged >60 years was 95.7%. Only one patient aged 50—60 years was reclassified as having both TAK and giant cell arteritis (GCA).

Conclusion: The concordance rate was 85.5% regardless of the imaging modalities, and increased to 86.9% on simultaneous CT angiography and FDG-PET imaging. We suggest that the upward readjustment of the age requirement should be reconsidered not to miss patients with TAK over the age of 60.

Disclosure: J. Ha: None; **S. Ahn**: None; **J. Song**: None; **Y. Park**: None; **S. Lee**: None.

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Analysis of Takayasu's Arteritis as Risk Factor for Acute Coronary Syndrome

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SESSION INFORMATION

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Background/Purpose: Takayasu's arteritis (TAK) is an autoimmune disease that primarily affects the aorta and its major branches. It has an incidence of 1-3 per million people in the USA and Europe and is primarily seen in females between the ages of 10 – 40 years. Coronary artery involvement has been reported in TAK. This study aims to analyze TAK as a risk factor for acute coronary syndrome (ACS) in a US inpatient population.

Methods: We conducted a retrospective review of 2016-2020 National Inpatient Sample (NIS) database. All adult hospitalizations were selected as our study population and were subdivided into those with and without ACS (ICD-10 codes I20 and I21). For ACS risk factors, the following ICD-10 codes were used: diabetes (DM) code E08-E13, hypertension (HTN) code I10, hyperlipidemia (HLD) code E78, and obesity code E66. A univariable analysis was used to calculate unadjusted odds ratios (ORs) for ACS. All variables with p values ≤ 0.2 were included in a multivariable logistic regression model with p values < 0.05 considered to be significant.

Results: There were 148,767,786 adult hospitalizations in the 2016 to 2020 NIS database. Of those, 3,282,749 of those had a primary diagnosis of ACS. Compared to non-ACS hospitalizations (Table 1), the ACS group was older (median age 67 vs 61 years; p< 0.001), had less females (37.8% vs 57.8%; p< 0.001), more Whites (70.7% vs 65.8%; p< 0.001), less

Table 1: Descriptive Characteristics of Adult ACS Hospitalizations from the 2016 to 2020 National Inpatient Sample Database (n= 148,767,786)

Table 1: Descriptive Characteristics of Adult ACS Hospitalizations from the 2016 to 2020 National Inpatient Sample Database (n= 148,767,786)

Hospitalization Characteristics	ACS Hospitalizations (n=3,282,749)	Non-ACS Hospitalizations (n=145,485,037)	P-value
Age, median (IQR) in years	67 (57 - 77)	61 (40 - 74)	<0.001
Women (n, %)	1,241,200 (37.8%)	84,002,747 (57.8%)	<0.001
Race/Ethnicity (n, %)			
White	2,320,850 (70.7%)	94,331,899 (64.8%)	<0.001
African American	367,190 (11.2%)	21,721,366 (14.9%)	<0.001
Hispanic	281,715 (8.6%)	15,970,665 (11.0%)	<0.001
Asian/PI	88,885 (2.7%)	3,910,588 (2.7%)	0.641
Native American	18,680 (0.5%)	930,380 (0.6%)	<0.001
Other	96,455 (2.9%)	4,223,473 (2.9%)	0.490
CCI, median (IQR)	3 (2 - 4)	1 (0 - 3)	<0.001
Risk factors (n, %)			
DM	1,335,960 (40.7%)	39,248,260 (27.0%)	<0.001
Hypertension	1,416,260 (43.1%)	48,128,871 (33.1%)	<0.001
Hyperlipidemia	2,048,760 (62.4%)	42455973 (29.2%)	<0.001
Obesity	666,980 (20.3%)	23,995,676 (16.5%)	<0.001
Nicotine	842,740 (25.7%)	25,068,460 (17.2%)	<0.001
Takayasu Arteritis	180 (0.005%)	6,055 (0.004%)	0.102
Median Household Income			
Q1	30.3%	29.9%	0.019
Q2	27.1%	25.9%	<0.001
Q3	22.9%	23.2%	0.002
Q4	17.9%	19.2%	<0.001
LOS, median (IQR)	3 (2 - 5)	3 (2 - 5)	<0.001
Total charges median (IQR)	66,803 (36,697 – 116,752)	32,167 (17,243 – 62,122)	<0.001
In-Hospital Mortality (n, %)	150,145 (4.6%)	3,433,974 (2.4%)	<0.001

Abbreviations: ACS= Acute Coronary Syndrome; CCI= Charlson Comorbidity Index, DM=Diabetes; IQR=interquartile range, n=number, PI=Pacific Islander, LOS=Length of Stay

Table 2: Univariable and Multivariable Analysis for ACS from NIS 2016-2020

Table 2: Univariable and Multivariable Analysis for ACS from NIS 2016-2020

Variable	Univariable Analysis			Multivariable Analysis		
	OR	P-value	95% C.I.	OR	P-value	95% CI
Age	1.02	<0.001	1.0242-1.0246	1.02	<0.001	1.0168-1.0173
Female	0.44	<0.001	0.4417-0.4480	0.55	<0.001	0.5453-0.5520
White	1.31	<0.001	1.2908-1.3262	0.84	<0.001	0.8262-0.8628
African American	0.72	<0.001	0.7068-0.7285	0.68	<0.001	0.6615-0.6938
Hispanic	0.76	<0.001	0.7446-0.7783	0.82	<0.001	0.8003-0.8433
Asian/PI	1.01	0.641	0.9763-1.0400			
Native American	0.89	<0.001	0.8433-0.9376	0.85	<0.001	0.8025-0.8919
Other Race	1.01	0.490	0.9774-1.0488			
Income Q1	1.02	0.019	1.0029-1.0329	1.03	0.007	1.0093-1.0607
Income Q2	1.07	<0.001	1.0548-1.0774	1.02	0.224	0.9907-1.0406
Income Q3	0.98	0.002	0.9734-0.9942	0.96	0.001	0.9358-0.9836
Income Q4	0.92	<0.001	0.9012-0.9306	0.91	<0.001	0.8839-0.9330
DM	1.86	<0.001	1.8443-1.8708	1.19	<0.001	1.1786-1.1944
Hypertension	1.53	<0.001	1.5223-1.5476	1.06	<0.001	1.0558-1.0715
Hyperlipidemia	4.03	<0.001	3.9918-4.0666	2.94	<0.001	2.9090-2.9666
Nicotine	1.66	<0.001	1.6447-1.6735	1.96	<0.001	1.9430-1.9717
Obesity	1.29	<0.001	1.2783-1.3038	1.21	<0.001	1.1981-1.2210
Takayasu Arteritis	1.32	0.103	0.9457-1.8354	1.78	0.001	1.2702-2.4976

Abbreviations: ACS= Acute Coronary Syndrome; CCI= Charlson Comorbidity Index; C.I.=Confidence Interval; DM=Diabetes; NIS= National Inpatient Sample; OR=Odds Ratio; PI=Pacific Islander; Q= Quartile

Table 3: Descriptive Characteristics of Adult ACS Hospitalizations with and without Takayasu Vasculitis from the 2016 to 2020 National Inpatient Sample (n= 3,282,749)

Table 3: Descriptive Characteristics of Adult ACS Hospitalizations with and without Takayasu Vasculitis from the 2016 to 2020 National Inpatient Sample (n= 3,282,749)

Hospitalization characteristics	ACS with Takayasu (n=180)	ACS without Takayasu (n=3,282,569)	P-value
Age, median (IQR) in years	61 (53 - 72)	67 (57 - 77)	0.063
Women	155 (86.1%)	1,241,045 (37.8%)	<0.001
Race/Ethnicity (n, %)			
White	130 (72.2%)	2,320,720 (70.7%)	0.841
African American	≤10*	367,185 (11.2%)	0.110
Hispanic	25 (13.9%)	281,690 (8.6%)	0.255
Asian/ PI	≤10*	88,875 (2.7%)	0.292
Native American	0	18,680 (0.6%)	---
Other race	0	96,455 (2.9%)	---
CCI, median (IQR)	3 (1 - 4)	3 (2 - 4)	0.374
Household Income (%)			
Q1	22.2%	30.3%	0.293
Q2	30.6%	27.1%	0.643
Q3	30.6%	22.9%	0.277
Q4	13.9%	17.9%	0.531
LOS, median (IQR)	2 (1 - 4.5)	3 (2 - 5)	0.716
Total charges median (IQR)	$70,319 (32,179 – 135,036)	$66,803 (36,697 – 116,752)	0.617
In-Hospital Mortality (n, %)	15 (8.3%)	150,130 (4.6%)	0.281

Abbreviations: ACS= Acute Coronary Syndrome; IQR=interquartile range, n=number, CCI= Charlson Comorbidity Index, LOS=Length of Stay; *=Not reported as below permitted reporting threshold; PI=Pacific Islander,

African Americans (11.2% vs 14.9%; p< 0.001), less Hispanics (8.6% vs 11%; < 0.001), same Asian/Pacific Islander (2.7% vs 2.7%; p=0.641), less Native Americans (0.5% vs 0.6%; p< 0.001), higher CCI (3 vs 1; < 0.001), lower household income, higher median total hospital charges ($66,803 vs $32,167; p< 0.001) and higher in-hospital mortality (4.6% vs 2.4%; p< 0.001). LOS was similar between the ACS and non-ACS hospitalizations. Univariable analysis for the outcome of ACS showed that age, white race, lowest income quartile, DM, HTN, HLD, obesity, nicotine dependence/tobacco use and TAK were associated with higher odds of ACS (Table 2). Female, African American race, Hispanic race, Native American race and upper two income quartiles were associated with a lower odds of ACS. Multivariable analysis showed that age (OR 1.02; 95% C.I. 1.0168 – 1.0173), lowest income quartile (OR 1.03; 95% C.I. 1.0093 – 1.0607), DM (OR 1.19; 95% C.I. 1.1786 – 1.1944), HTN (OR 1.06; 95% C.I. 1.0558 – 1.0715), HLD (OR 2.94; 95% C.I. 2.9090 – 2.9666), obesity (OR 1.21; 95% C.I. 1.1981 – 1.2210), nicotine dependence/tobacco use (OR 1.96; 95% C.I. 1.9430 – 19717) and TAK (OR 1.78; 95% C.I. 1.2702 – 2.4976) were associated with higher odds of ACS (Table 2). In comparison to ACS without TAK, ACS with TAK group comprised of more females (86.1% vs 37.8%; p< 0.001) and showed a trend towards being younger (Table 3).

Conclusion: We performed an analysis of the 2016-2020 NIS database to better understand TAK as a risk factor for ACS. After controlling for traditional ACS risk factors, TAK was found to increase the odds of ACS by 1.78 times. Other significant ACS risk factors from the multivariable analysis included age, low income, DM, HTN, HLH, obesity, and nicotine dependence. This study emphasizes the importance of recognizing TAK as a risk factor for ACS especially in women and in the younger population.

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Abstract Number: 1578

Impact of Anxiety or Depression Status and Fibromyalgia on Adherence to Treatment of Patients with Takayasu Arteritis

Alejandra Espinosa-Orantes[1], David Vera-Bustamante[2], Jessica Roldan Ortega[3], Maria Mejia-Avila[4], Jose Raul Molina[5], Evelyn Aranda Cano[5], Adriana Miguel-Alvarez[5], Ismael Valenzuela[5], Viridiana Del Río-Guerrero[6], Paloma Rodriguez[5], Mauricio Mora-Ramirez[5], Nilda Espinola-Zavaleta[4], Luis H Silveira-torre[6], Angélica Vargas Guerrero[7] and Laura A Martínez-Martínez[8], [1]Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico, [2]BENEMERITA UNIVERSIDAD AUTONOMA DE PUEBLA, Mexico City, Mexico, [3]INSTITUTO NACIONAL DE CARDIOLOGIA, Ciudad de México, Mexico, [4]Instituto Nacional de Cardiologia Ignacio Chavez, Mexico City, Mexico, [5]Instituto Nacional de Cardiologia, Mexico City, Mexico, [6]Instituto Nacional de Cardiología, Mexico City, Mexico, [7]Instituto Nacional de Cardiología, Mexico City, Mexico, [8]Universidad Nacional Autónoma de México - Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Takayasu arteritis (TAK) is a chronic, granulomatous large-vessel vasculitis. As TAK has a chronic course, higher frequency rates of anxiety and depression are reported in these patients [Misra DP, et al. Rheumatol Ther. 2021 Sep;8(3):1073-93]. Fibromyalgia (FM) incidence in active TAK patients is higher [Alibaz-Oner F, et al. Intern Med. 2013;52(24):2739-42]. Data regarding the impact of anxiety, depression, and FM in adherence to treatment on TAK have not been previously reported. This study aimed to explore the impact of mental illness and fibromyalgia on adherence to treatment of TAK patients.

Methods: A cross-sectional study was designed for including patients who satisfy the 2022 ACR/ EULAR classification criteria for TAK. FM screening was made with the 2016FM criteria published by Wolfe. Patient Health Questionnaire-9 (PHQ-9) and General Anxiety Disorder-7 (GAD-7) were used to measure depression and anxiety severity. Impact on quality of life was measured by EuroQol-5D (EQ-5D) questionnaire. Patients completed the Morisky-Green Test (MGT) for treatment adherence. Disease activity was assessed by the National Institutes of Health (NIH) scale and the Indian Takayasu Clinical Activity Score (ITAS2010).

Data were described as percentages, mean ± standard deviation or median and interquartile range (IQR) according to its distribution. The assessment of normality was done by the Kolmogorov-Smirnov test. The Chi-square, Fisher test, Student's t-test, or Mann-Whitney U test were used for comparisons as required. The correlation between MGT values and PHQ-9 or GAD-7 was evaluated by Spearman's method. A value of $p < 0.05$ was considered statistically significant.

Results: Fifty-five TAK patients were invited. Two patients denied answering questionnaires, and one was excluded because of a lack of medical data therefore 52 patients were analyzed. Fifty (96%) female patients were included, and the mean age was 39±18. Remission was found in 28 (54%) patients, according to the rheumatology care provider. Activity according to NIH score was found in 16 (30%) patients and by ITAS2010 in 20 (38%) patients. Anxiety was found in 23 (44%) and depression in 30 (58%) patients. 16 (31%) patients have poor treatment adherence, 20 (38%) moderate, and 16 (31%) have high adherence rates. EQ-5D median score was 80 (67-90). 5 patients fulfilled FM 2016 criteria and all of them have depression or anxiety. There was a tendency for lesser MGT scores in mental illness-affected TAK patients [6 (5 -7) vs 7 (6.7-8), p=0.060]. Interestingly, a weak negative correlation between MGT and GAD7 score was found (Rho=-0.314, p=0.023). Higher treatment adherence has a positive significant correlation with better EQ-5D (Rho=0.357, p=0.009) and a negative correlation with the patient global assessment of disease activity (Rho= 0.311, p=0.025). Paresthesias are higher in patients with mental illness (46.9% vs 15%, p=0.018).

Conclusion: Higher treatment adherence scores were associated with a better quality of life and a better patient global assessment of disease activity. Despite anxiety and depression have a high prevalence, there was no great impact on the medication adherence rates. More studies regarding treatment adherence are needed.

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Abstract Number: 1579

Sodium-Glucose Co-transporter-2 Inhibitors and the Risk of Cardiac and Renal Outcomes in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Plenary II
Session Type: Plenary Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Sodium-glucose cotransporter-2 inhibitors (SGLT2) have benefits on kidney and cardiovascular (CV) outcomes that are largely independent of glycemic control. These benefits have been demonstrated in patients with type 2 diabetes, heart failure, and other causes of proteinuric kidney disease, but it is unknown whether SGLT2 have similar benefits in patients with SLE and lupus nephritis (LN).

Methods: We designed and emulated a pragmatic target trial to determine the impact of SGLT2 versus a comparator oral hypoglycemic agent, dipeptidyl peptidase 4 inhibitors (DPP4), on kidney and CV outcomes among patients with SLE and LN. Using a large US multi-center electronic health record-based SLE cohort (N=96,511), we identified all patients with incident prescriptions for SGLT2 or DPP4 after diagnosis with SLE from 3/2013 to 8/2021. We used propensity score overlap weighting to balance baseline covariates including demographics, geographic region, LN, comorbidities (e.g., CKD, diabetes, heart failure), tobacco use, diabetic complications, HbA1c, medication use including other hypoglycemic agents, angiotensin converting enzyme inhibitors (ACEi)/angiotensin receptor blockers (ARBs), glucocorticoids, hydroxychloroquine, and immunosuppressants, SLE severity index, and healthcare utilization. We assessed the outcomes of renal progression, defined by a decrease in eGFR by ≥30% or new onset end-stage renal disease, and major adverse cardiac events (MACE), defined by CV death or hospitalization for ischemic stroke, myocardial infarction, heart failure, or venous

Table 1. Baseline Characteristics of Patients Initiating SGLT2 Inhibitor Versus DPP4 Inhibitor Therapy

Characteristics	Before Propensity Score Overlap Weighting			After Propensity Score Overlap Weighting		
	SGLT2 (n=426)	DPP4 (n=865)	Std. Diff.	SGLT2	DPP4	Std. Diff.
Age, mean (SD)	56.8 (11.9)	58.2 (12.1)	0.1172	57.2	57.2	<0.001
Female, n (%)	371 (87.1)	790 (91.3)	0.1370	89.1	89.1	<0.001
Race, n (%)			0.1235			<0.001
Asian	5 (1.2)	14 (1.6)		1.4	1.4	
Hispanic	34 (8.0)	86 (9.9)		8.5	8.5	
Black	158 (37.1)	292 (33.8)		35.7	35.7	
White, Non-Hispanic	197 (46.2)	413 (47.7)		47.2	47.2	
Geographic Region, n (%)			0.0677			<0.001
East	72 (16.9)	163 (18.8)		17.8	17.8	
Midwest	78 (18.3)	143 (16.5)		16.9	16.9	
South	239 (56.1)	470 (54.3)		56.4	56.4	
West	37 (8.7)	89 (10.3)		8.9	8.9	
Lupus nephritis	154 (36.2)	270 (31.2)	0.1046	33.8	33.8	<0.001
Charlson Index, mean (SD)	1.7 (1.7)	1.7 (1.8)	0.0282	1.7	1.7	<0.001
Comorbidities, n (%)						
CKD stage ≥3	154 (36.2)	298 (34.5)	0.0356	34.9	34.9	<0.001
Heart Failure	123 (28.9)	149 (17.2)	0.2793	23.7	23.7	<0.001
CVD	115 (27.0)	208 (24.0)	0.0677	25.3	25.3	<0.001
Obesity	146 (34.3)	238 (27.5)	0.1466	31.9	31.9	<0.001
Diabetic complications:						
Diabetic nephropathy	60 (14.1)	130 (15.0)	0.0268	14.2	14.2	<0.001
Diabetic retinopathy	31 (7.3)	49 (5.7)	0.0656	6.6	6.6	<0.001
Diabetic neuropathy	103 (24.2)	182 (21.0)	0.0751	23.5	23.5	<0.001
Peripheral arterial disease	22 (5.2)	45 (5.2)	0.0017	5.2	5.2	<0.001
Hemoglobin A1c (%)	8.1 (4.0)	7.9 (3.9)	0.0589	8.0	8.0	<0.001
Tobacco use, n (%)	124 (29.1)	210 (24.3)	0.1094	27.1	27.1	<0.001
Medications						
Insulin use	149 (35.0)	269 (31.1)	0.0825	33.6	33.6	<0.001
Metformin	155 (36.4)	320 (37.0)	0.0126	37.0	37.0	<0.001
Sulfonylurea use	71 (16.7)	141 (16.3)	0.0099	16.7	16.7	<0.001
Other diabetic medication	13 (3.1)	25 (2.9)	0.0095	2.9	2.9	<0.001
ACEi or ARB	210 (49.3)	339 (39.2)	0.2045	45.2	45.2	<0.001
SLE Medications, n (%)						
Glucocorticoids	202 (47.4)	431 (49.8)	0.0482	48.1	48.1	<0.001
Hydroxychloroquine	156 (36.6)	308 (35.6)	0.0211	36.8	36.8	<0.001
Azathioprine	25 (5.9)	58 (6.7)	0.0345	6.1	6.1	<0.001
Methotrexate	35 (8.2)	70 (8.1)	0.0045	8.1	8.1	<0.001
Mycophenolate	45 (10.6)	95 (11.0)	0.0135	10.6	10.6	<0.001
SLE Severity Index, n (%)			0.1358			<0.001
Mild	123 (28.9)	299 (34.6)		30.7	30.7	
Moderate	182 (42.7)	351 (40.6)		42.8	42.8	
Severe	121 (28.4)	215 (24.9)		26.5	26.5	
Healthcare Utilization						
Outpatient visits, median (IQR)	7 (12)	7 (15)	0.0336	7	7	<0.001
ER/Inpatient visits, n (%)	178 (41.8)	354 (40.9)	0.0174	41.2	41.2	<0.001

CKD, chronic kidney disease; CVD, cardiovascular disease; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; ER, emergency room

thrombosis. We also assessed the safety outcome of genital infection and the control outcome of traumatic injury. We used Cox regression to assess the risk of each outcome, using an intention-to-treat analysis and a per-protocol analysis with censoring from deviation from treatment assignment.

Results: There were 426 and 865 incident users of SGLT2 and DPP4 with SLE. This included 154 and 270 patients with LN, respectively. After propensity score overlap weighting, all baseline covariates were balanced (**Table 1**). The mean age was 57 years; 89% were female. 36% were Black and 8% were Hispanic. 35% had CKD and 24% had heart failure. ACEi/ARBs were used by 45%. SGLT2 use was associated with a lower risk of MACE (HR 0.69 [95% CI 0.48-0.99]) and renal progression (HR 0.71 [95% CI 0.51-0.98]) than DPP4 use (**Table 2**). Among the subgroup with LN, the risk of MACE was also lower with SGLT2 use (HR 0.58 [95% CI 0.34-0.99]); there were numerical differences in renal progression but it did not reach statistical significance. SGLT2 us was associated with a higher risk of genital infections (**Table 3**). There was no difference in the risk of traumatic injury (HR 1.02 [0.80-1.29]) as expected.

Conclusion: In this cohort of patients with SLE who initiated SGLT2 or DPP4, we found a lower risk of MACE and renal progression associated with SLGT2i use, suggestive of cardiac and renal benefits as have been observed in other disease populations. Limitations include the small sample size and that patients in this study used SGLT2 for non-SLE indications. However, the findings indicate a potential role for SGLT2 for patients with SLE/LN and warrants further investigation in these populations.

Table 2. Cardiovascular and Renal Outcomes Associated with SGLT2 Inhibitors versus DPP4 Inhibitors Among People with Systemic Lupus Erythematosus and Lupus Nephritis

Outcomes	Events, n		Follow-up Time, years		Incidence Rate (per 100 PY)		Hazard Ratio (95% CI)
	SGLT2	DPP4	SGLT2	DPP4	SGLT2	DPP4	
All SLE							
Intention-to-treat							
MACE	36	61	1.7	2.4	7.6	9.4	0.74 (0.55-1.00)
Renal outcome	39	75	1.6	2.3	8.7	12.3	0.65 (0.49-0.87)
Per Protocol							
MACE	24	41	1.0	1.2	9.2	12.6	0.68 (0.48-0.98)
Renal outcome	30	51	0.9	1.2	11.9	16.3	0.71 (0.51-0.98)
Lupus Nephritis							
Intention-to-treat							
MACE	11	28	1.3	1.9	10.8	17.5	0.55 (0.33-0.90)
Renal outcome	18	31	1.2	1.8	18.2	21.1	0.76 (0.50-1.16)
Per Protocol							
MACE	9	20	0.8	1.1	14.1	21.9	0.58 (0.34-0.99)
Renal outcome	15	23	0.8	1.1	23.8	26.6	0.83 (0.52-1.32)

PY, person-years; SGLT2, sodium-glucose co-transporter 2 inhibitor; DPP4, Dipeptidyl peptidase-4 inhibitor; MACE, major adverse cardiac events. MACE outcome includes hospitalization for myocardial infarction, ischemic stroke, or heart failure, or cardiac death. Renal outcome includes a decrease in eGFR by ≥30% or new onset end-stage renal disease.

Table 3. Secondary Outcomes Associated with SGLT2 Inhibitors versus DPP4 Inhibitors Among Patients with Systemic Lupus Erythematosus

Outcomes	Events, n		Follow-up Time, years		Incidence Rate (per 100 PY)		Hazard Ratio (95% CI)
	SGLT2	DPP4	SGLT2	DPP4	SGLT2	DPP4	
Intention-to-treat							
Genital Infection	29	22	1.7	2.7	6.3	3.1	1.89 (1.29-2.75)
Traumatic Injury	63	80	1.5	2.0	16.0	14.5	1.02 (0.80-1.29)
Per Protocol							
Genital Infection	21	12	1.0	1.3	8.1	3.4	2.32 (1.45-3.72)
Traumatic Injury	46	56	0.8	1.1	20.7	19.1	1.02 (0.77-1.35)

PY, person-years; SGLT2, sodium-glucose co-transporter 2 inhibitor; DPP4, Dipeptidyl peptidase-4 inhibitor; GU, genitourinary. GU infection defined by ICD-9 599.0, 608.83 and ICD 10- N39.0, N49.3. Traumatic injury defined by ICD-9 codes 800-804, 810-812, 815-819, 823-826, 830-959 and ICD-10 codes S00-S59, S61, S67-S68, S82, S87-S88, S90-S99, and T15-T19.

Disclosure: A. Jorge: None; **B. Zhou**: None; **N. McCormick**: None; **C. Yokose**: None; **Y. Zhang**: None; **H. Choi**: Ani, 2, Horizon, 2, 5, LG, 2, Protalix, 2, Shanton, 2.

Abstract Number: 1580

CXCL13^{+} T Cell Differentiation in Systemic Lupus Erythematosus Is Controlled by Opposing Effects of Aryl Hydrocarbon Receptor and Type I Interferon

Calvin Law[1], Vanessa Wacleche[2], Ye Cao[3], Arundhati Pillai[1], Alice Horisberger[4], Sabrina Bracero[3], Viktoriya Skidanova[3], Zhihan Li[3], Ifeoluwakiisi Adejoorin[2], Isaac Benque[3], Diana Pena Nunez[3], Daimon Simmons[2], Joshua Keegan[4], Lin Chen[3], John Sowerby[3], Accelerating Medicines Partnership (AMP): RA/SLE[2], Elena Massarotti[2], Karen Costenbader[4], Michael Brenner[4], James Lederer[4], Judd Hultquist[1], Jaehyuk Choi[1] and Deepak Rao[2], [1]Northwestern University Feinberg School of Medicine, Chicago, IL, [2]Brigham and Women's Hospital, Boston, MA, [3]Brigham and Women's Hospital, Boston, MA, [4]Brigham and Women's Hospital and Harvard Medical School, Boston, MA

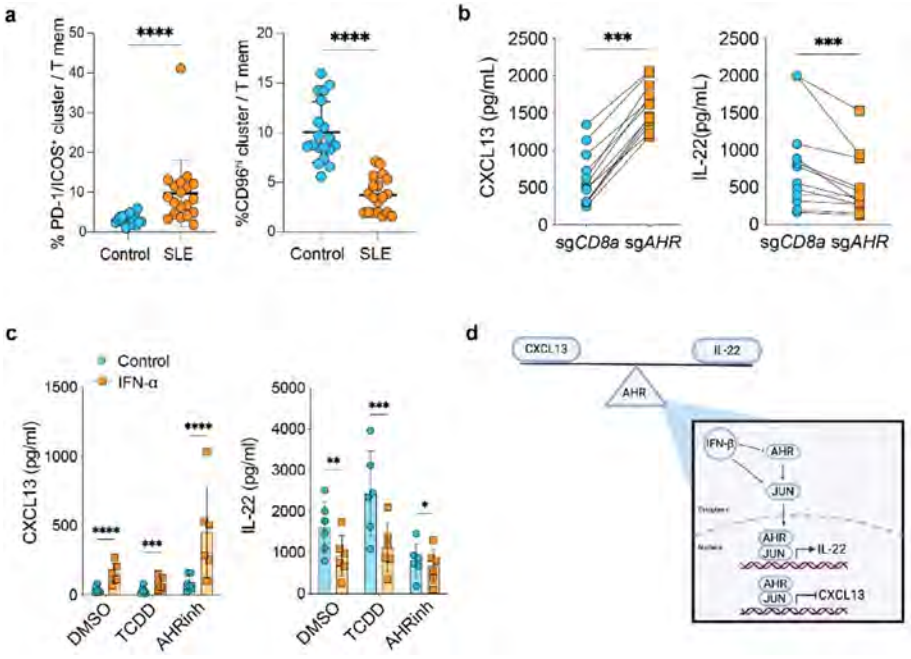
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Plenary II
Session Type: Plenary Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Expansion of B cell-helper T cells including T follicular helper (Tfh) and T peripheral helper (Tph) cells is a prominent feature of systemic lupus erythematosus (SLE). Tfh and Tph cells are marked by high production of the B cell chemoattractant CXCL13; however, regulation of T cell CXCL13 production and the relationship between a CXCL13^{+} state and other differentiated T cell states remain largely undefined.

Methods: We used mass cytometry to characterize CD4 T cell phenotypes of SLE patients (n=19) and controls (n=19). We used CRISPR screens of primary human CD4 T cells to identify transcription factors that drive core Tph phenotypes. We used transcriptomics (bulk RNA-Seq), epigenetics (ATAC-Seq and CUT&RUN), and functional studies (pharmacological modulators, lentiviral overexpression, reporter cell lines) to characterize mechanisms and pathways that influence CXCL13 production in disease relevant T cells.

Results: Mass cytometry immunophenotyping demonstrated a dramatic imbalance in CD4 T cell phenotypes in SLE patients, with expansion of PD-1^{+}/ICOS^{+} CXCL13^{+} T cells and reduction of CD96^{hi} IL-22^{+} T cells. An arrayed CRISPR screen targeting 80 transcription factors or signaling molecules revealed that deletion of the aryl hydrocarbon receptor (AHR) significantly increased T cell CXCL13 production. Validation experiments confirmed that AHR deletion or pharmacologic inhibition strongly induced T cell CXCL13 production and T cell acquisition of a transcriptomic and epigenetic signature of ex vivo Tph cells. Conversely, AHR activation inhibited a CXCL13 production and a Tph signature while promoting an IL-22^{+} Th22 cell signature. Luciferase reporter assay using AHR reporter cells show decreased luciferase activity from cells cultured with SLE serum in the presence of AHR agonist. Time coursed transcriptomic analyses of AHR-activated cells combined with unbiased analysis for transcription factor binding sites in AHR CUT&RUN peaks indicated AP-1 transcription factors and AHR co-regulate gene expression. A second CRISPR screen targeting AP-1 family members identified JUN as a potent negative regulator of CXCL13 production and a Tph signature. Further CUT&RUN analyses placed both JUN and AHR at the CXCL13 locus, suggesting direct inhibition of CXCL13 expression. Finally, type I interferon (IFN), a pathogenic driver of SLE, promoted T cell CXCL13 production and a Tph-associated epigenetic signature in part by inhibiting AHR activation and reducing JUN protein expression, while overexpression of JUN inhibited the ability of IFN to induce T cell CXCL13 production.

Conclusion: Our results identify AHR and JUN as potent inhibitors of a Tph cell fate and implicate type I IFN as a key signal in SLE that inhibits AHR and JUN to induce Tph cells.



a, Quantification of indicated clusters in SLE patients (n=19) and controls (n=19), P=6.32e-6 for PD-1/ICOS+, P=2.9e-9 for CD96hi. b, ELISA data for indicated cytokines in supernatants of memory CD4+ T cells nucleofected with sgAHR or sgCD8 control. All cells were cultured with TGF-beta, and each line represents a separate donor (n=12). For CXCL13 P=4.88e-4and IL-22 P=4.88e-4. c, ELISA for CXCL13 (left) and IL-22 (right) from memory CD4+ T cells stimulated with or without IFN-alpha for 24 hours prior to addition of AHR agonist/inhibitor or DMSO control as indicated (n=6). From left to right, P-value for CXCL13: 8.5e-5, 4.05e-4, 2.9e-5, and for IL-22: 2.35e-3, 8.76e-4, 0.0338. d, Graphical representation of proposed model in type I IFN regulation of AHR and JUN to promote Tph cells in SLE.

Disclosure: C. Law: None; **V. Wacleche**: None; **Y. Cao**: None; **A. Pillai**: None; **A. Horisberger**: None; **S. Bracero**: None; **V. Skidanova**: None; **Z. Li**: None; **I. Adejoorin**: None; **I. Benque**: None; **D. Pena Nunez**: None; **D. Simmons**: None; **J. Keegan**: None; **L. Chen**: None; **J. Sowerby**: None; **A. Medicines Partnership (AMP): RA/SLE**: None; **E. Massarotti**: None; **K. Costenbader**: Amgen, 2, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Eli Lilly, 2, Exagen Diagnostics, 5, Gilead, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5; **M. Brenner**: 4FO Ventures, 2, GlaxoSmithKlein(GSK), 2, Mestag Therapeutics, 2, 11, Third Rock Ventures, 2; **J. Lederer**: None; **J. Hultquist**: None; **J. Choi**: None; **D. Rao**: AstraZeneca, 2, Bristol-Myers Squibb, 2, 5, GlaxoSmithKlein(GSK), 2, Hifibio, 2, Janssen, 5, Merck, 5, Scipher Medicine, 2.

Abstract Number: 1581

Microbiome Transplantation Prevents Osteoarthritis in Mice and Is Associated with Immunophenotype Changes

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Plenary II

Session Type: Plenary Session

Session Time: 11:00AM–12:30PM

Background/Purpose: MRL/MpJ mice are protected from developing post-traumatic osteoarthritis (OA). We have previously shown transplantation prior to OA induction prevents OA development. We now extend this work to include measures of synovitis and osteophytes, transplantation after OA induction, transplantation breeding experiments, and peripheral blood immunoprofiling.

Methods: Adult male B6 and MRL mice were inoculated by oral gavage with diluted cecal contents from the opposite mouse strain or vehicle control. Adult male germ-free (GF) mice were inoculated with B6 or MRL cecal contents. A subset of male MRL-transplanted-B6 mice were bred to transplanted female mice and F1 and F2 generation mice were evaluated. Destabilization of the medial meniscus (DMM) surgery was then performed unilaterally to induce OA. Eight weeks after DMM, mice were sacrificed, knee joints fixed, paraffin-embedded, stained with Safranin-O and histologically graded for OARSI

Figure 1: OA outcomes in mice under various transplant conditions

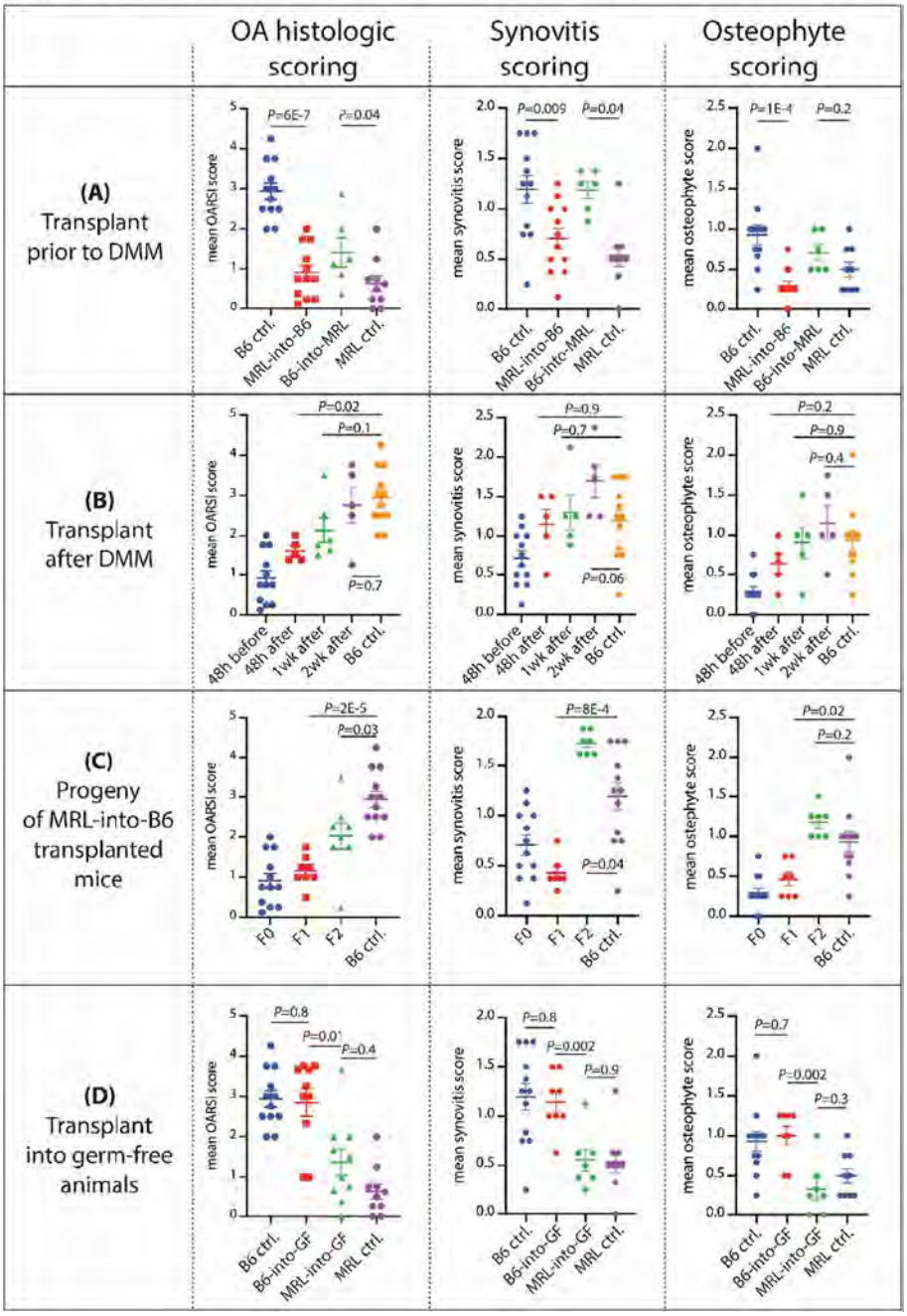
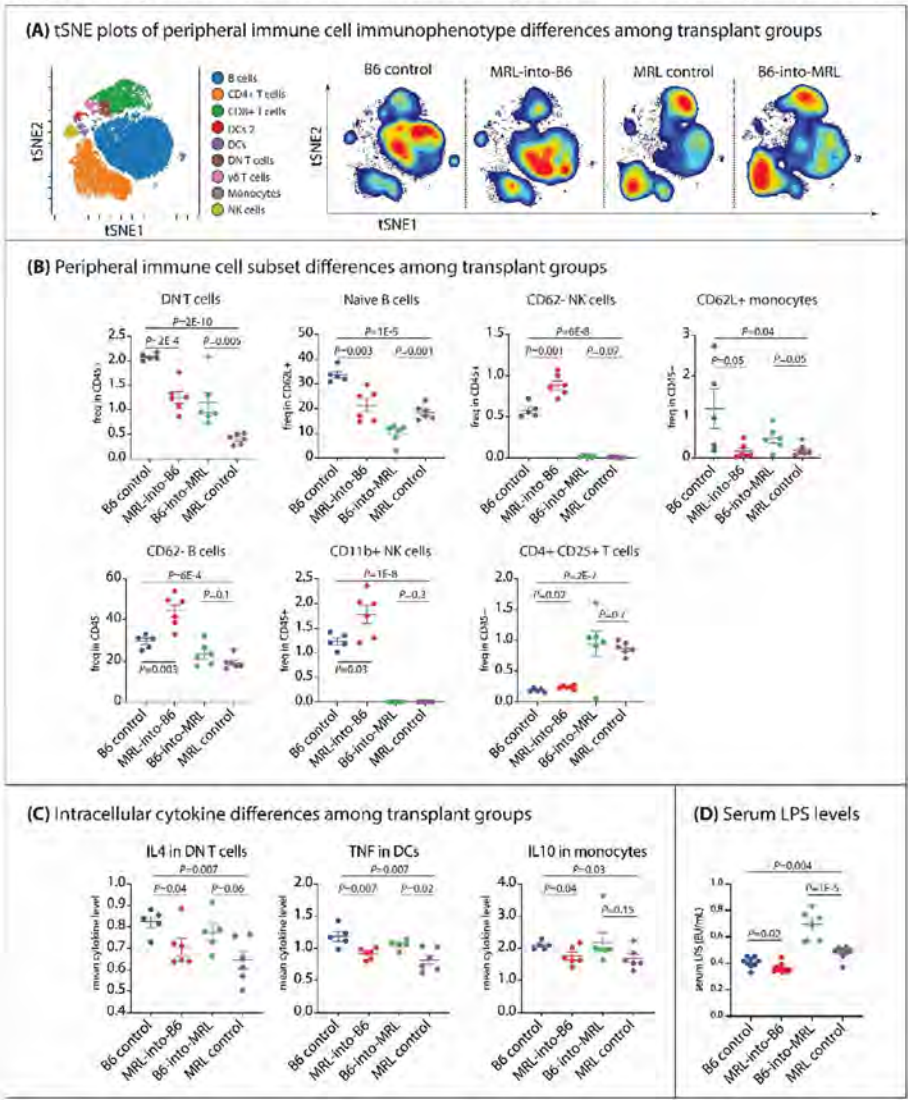


Figure 2: Peripheral blood immune cell subset analysis under various transplant conditions



score, synovitis, and osteophytes. Immunophenotyping of splenocytes was performed by mass cytometry (CyTOF). Seurm LPS was determined by chromogenic assay.

Results: Adult male MRL and MRL-transplanted B6 (48h prior to DMM) were protected from OA (Figure 1,OARSI: *P*=6.7E-7, 6.3E-7 respectively, synovitis: *P*=0.002, *P*=0.009; osteophytes: *P*=0.02, *P*=0.0001). Transplant 48h after DMM (*P*=0.002) but 1 week (*P*=0.1) and 2 weeks (*P*=0.7) after DMM were not effective. Synovitis and osteophytes were not improved by transplant after DMM. B6-into-MRL transplant worsened OA (OARSI: *P*=0.04, synovitis: *P*=0.04). F1 and F2 progeny of MRL-into-B6 mice were protected from OA (OARSI: *P*=2E-5, *P*=0.003 respectively). B6-into-GF mice developed OA similar to B6 controls (OARSI: *P*=0.8), whereas MRL-into-GF mice were protected from OA similar to MRL controls (OARSI: *P*=0.4). Five cecal microbiome clades were strongly correlated with OA outcome (*Lactobacillus* R=-0.32, *Akkermansia* R=-0.31, *Oscillospira* R=-.28, *Anaerostipes* R=0.35, *Christensenellaceae* R=0.37, *Rikenellaceae* R=0.43). Immunophenotyping revealed reduced DN T-cells, reduced naïve B cells, reduced CD26+ monocytes, and increased CD4+CD25+ regulatory T cells with transplantation and in MRL mice vs. B6 controls. LPS levels were reduced in MRL-into-B6 vs. B6 controls.

Conclusion: Gut microbiome transplantation from OA-protected MRL mice to OA-susceptible B6 mice 48h before or 48h after DMM prevents OA development. Specific microbiome clades associated with OA protection, and are associated with changes in circulating immunophenotypes.

Disclosure: G. Dyson: None; **M. Barrett**: None; **M. Khan**: None; **C. Miranda**: None; **N. Hanebutt**: None; **C. Dunn**: None; **M. Jeffries**: None.

Abstract Number: 1582

Non-TNFi b/tsDMARDs vs. TNFi in Rheumatoid Arthritis-Interstitial Lung Disease: An Active-Comparator, New-User, Propensity Score Matched Study Using National Veterans Affairs Data

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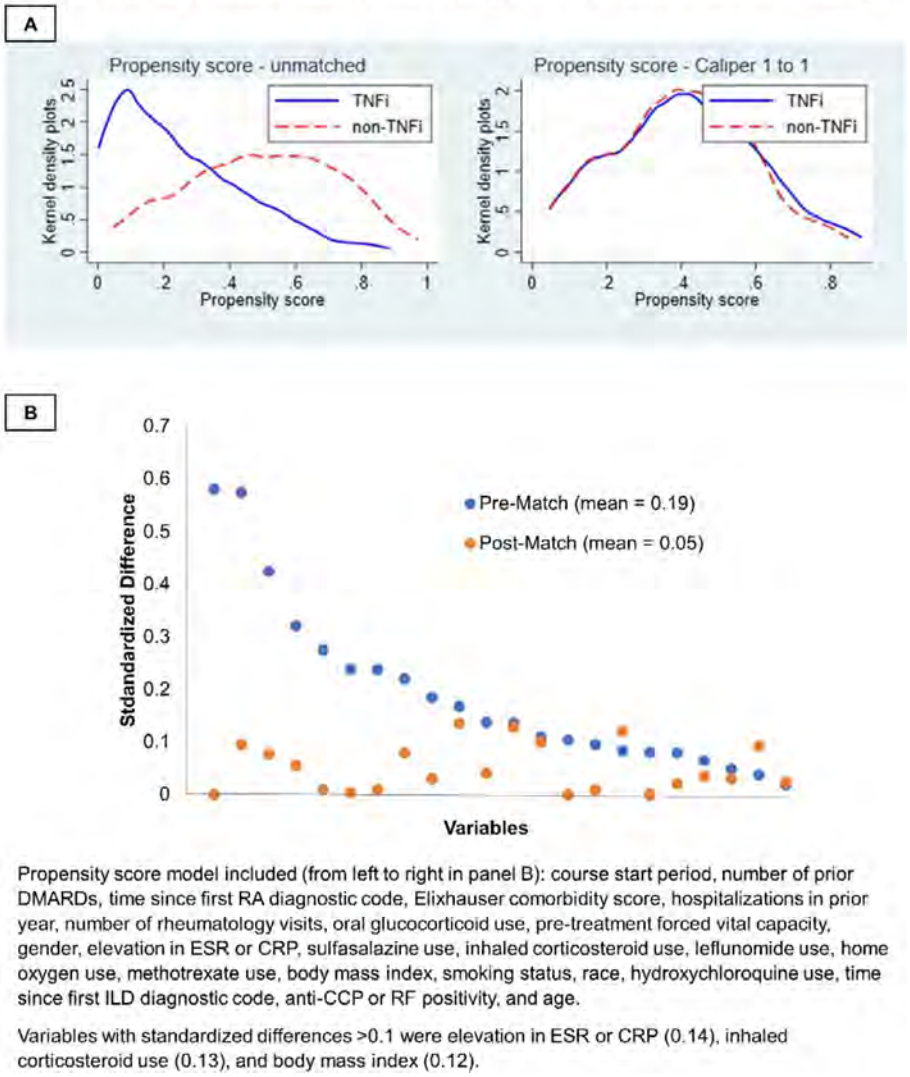
SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Plenary II
Session Type: Plenary Session
Session Time: 11:00AM–12:30PM

Background/Purpose: There is a paucity of data to guide biologic and JAKi DMARD selection in rheumatoid arthritis-interstitial lung disease (RA-ILD), with some reports of higher mortality with TNFi use in this population (Druce et al. *RMD Open*, 2017). We performed a real-world pharmacoepidemiologic study of non-TNFi/JAKi vs. TNFi in RA-ILD using the Target Trial Emulation framework (Hernan et al. *JAMA*, 2022).

Methods: We performed an active-comparator, new-user study of patients with RA-ILD initiating TNFi or non-TNFi biologic/JAKi in the Veterans Health Administration (VA) between 2006 and 2018. Receipt of ILD-focused therapies (e.g., mycophenolate, antifibrotics) was an exclusion. RA-ILD was identified using validated administrative algorithms requiring multiple RA and ILD diagnostic codes (PPV >70%). TNFi and non-TNFi/JAKi initiators were 1:1 propensity score (PS) caliper-matched using calendar time-specific PS models (2006-2010, 2011-2015, 2016-2018) that included demographics, healthcare utilization, comorbidities, and several RA- and ILD-related factors (including pre-treatment forced vital capacity [FVC]) obtained from EHR and administrative data (**Figure 1**). The primary outcome was a composite of time to respiratory-related hospitalization (by VA and Medicare data linkage) or death (by National Death Index linkage) using Cox regression models following an intention-to-treat analysis approach. Secondary outcomes were respiratory hospitalization and death (all-cause, respiratory). Outcomes were assessed over 3-year (primary) and 1-year (secondary) follow-up periods. Sensitivity analyses were performed among modified cohorts requiring: 1) prior biologic/JAKi treatment, 2) non-missing pre-treatment FVC values, or 3) additional ILD classification criteria.

Results: Among 1,046 RA-ILD patients fulfilling eligibility criteria (n=704 TNFi), 237 TNFi initiators were matched to 237 non-TNFi/JAKi initiators in the primary analyses (mean age 68 years, 92% male). Mean standardized differences of variables in the PS model improved from 0.19 to 0.05 after matching, though few variables remained modestly imbalanced (**Figure 1**). Adalimumab (51%) and etanercept (37%) were the most frequent TNFi while rituximab (53%) and abatacept (28%) were

Figure 1. Distribution of propensity scores (A) and standardized differences for variables (B) among RA-ILD patients initiating a non-TNFi/JAKi or TNFi before and after matching.



Propensity score model included (from left to right in panel B): course start period, number of prior DMARDs, time since first RA diagnostic code, Elixhauser comorbidity score, hospitalizations in prior year, number of rheumatology visits, oral glucocorticoid use, pre-treatment forced vital capacity, gender, elevation in ESR or CRP, sulfasalazine use, inhaled corticosteroid use, leflunomide use, home oxygen use, methotrexate use, body mass index, smoking status, race, hydroxychloroquine use, time since first ILD diagnostic code, anti-CCP or RF positivity, and age.

Variables with standardized differences >0.1 were elevation in ESR or CRP (0.14), inhaled corticosteroid use (0.13), and body mass index (0.12).

Figure 1. Distribution of propensity scores (A) and standardized differences for variables (B) among RA-ILD patients initiating a non-TNFi/JAKi or TNFi before and after matching.

the most frequent non-TNFi/JAKi. There was no significant difference in the primary outcome between non-TNFi/JAKi vs. TNFi (HR 1.19 [0.91, 1.56]; aHR 1.22 [0.92, 1.60]; **Table 1**). There were also no significant differences in respiratory hospitalization, all-cause mortality, or respiratory-related death (**Table 1**). In sensitivity analyses with modified cohort eligibility requirements, no significant differences in outcomes were observed between non-TNFi/JAKi and TNFi (**Figure 2**).

Conclusion: In this national VA, PS-matched study using the Target Trial Emulation framework, we did not observe significant differences in the risk of respiratory hospitalization or death between RA-ILD patients initiating non-TNFi/JAKi vs. TNFi. Our findings do not support systematic avoidance of TNFi in RA-ILD. Comparative data from clinical trials are needed to further guide these routine clinical decisions.

Table 1. Comparative risk of Non-TNFi/JAKi vs .TNFi in RA-ILD.

Table 1. Comparative risk of Non-TNFi/JAKi vs. TNFi in RA-ILD.

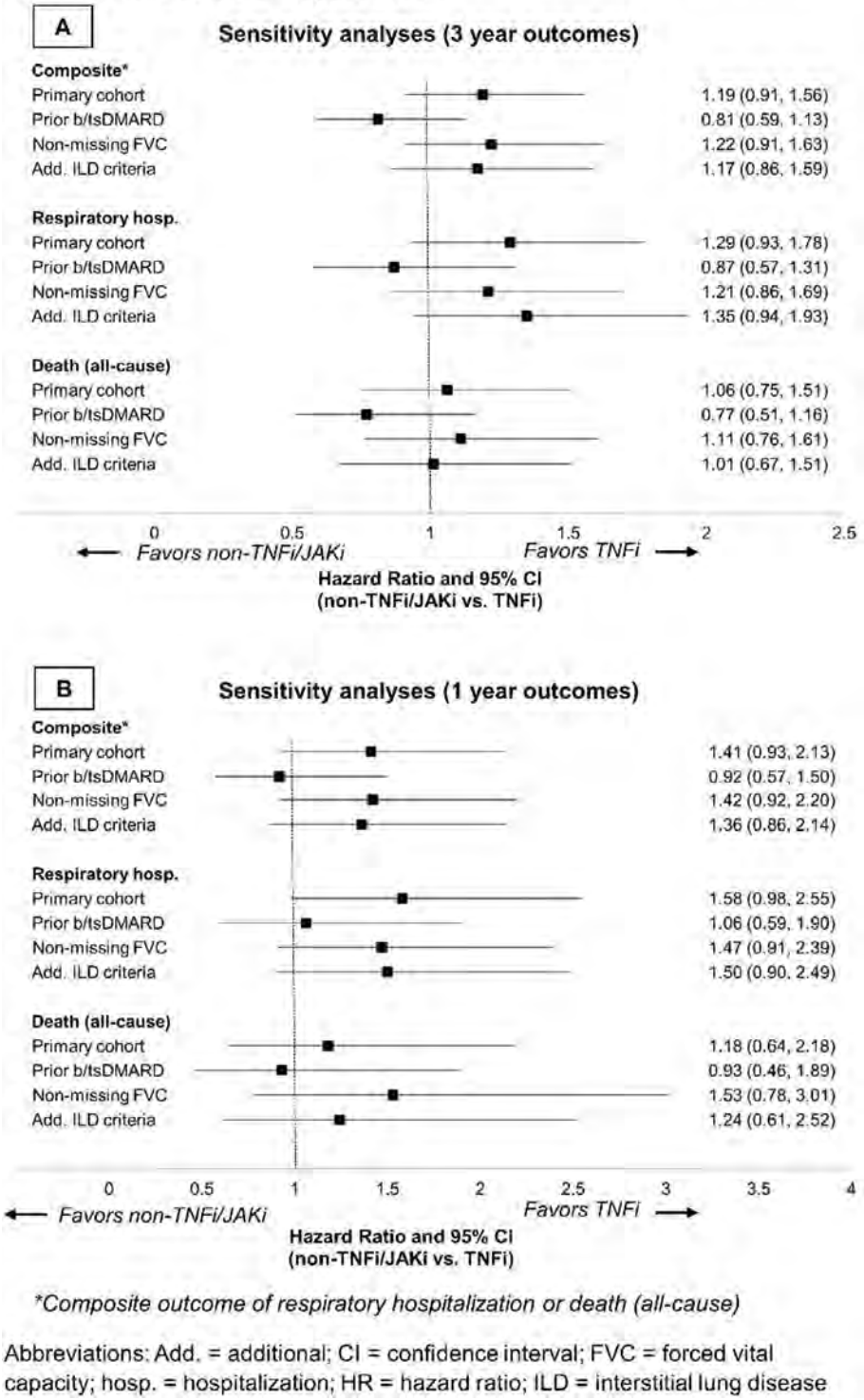
	Events	PY	IR (95% CI) /100PY	HR (95% CI)	aHR (95%CI)*
Primary Outcome					
Composite of respiratory hospitalization or death (all-causes), 3 years					
TNFi	98	550.6	17.8 (14.6, 21.7)	Ref	Ref
Non-TNFi/JAKi	108	508.4	21.2 (17.6, 25.7)	1.19 (0.91, 1.56)	1.22 (0.92, 1.60)
Secondary Outcomes					
3-year outcomes					
Respiratory hospitalization					
TNFi	67	550.6	12.2 (9.6, 15.5)	Ref	Ref
Non-TNFi/JAKi	80	508.4	15.7 (12.6, 19.6)	1.29 (0.93, 1.78)	1.28 (0.92, 1.77)
Death (all-causes)					
TNFi	62	624.3	9.9 (7.7, 12.7)	Ref	Ref
Non-TNFi/JAKi	64	606.8	10.5 (8.3, 13.5)	1.06 (0.75, 1.51)	1.12 (0.79, 1.59)
Respiratory-related death					
TNFi	20	624.3	3.2 (2.1, 5.0)	Ref	Ref
Non-TNFi	25	606.8	4.1 (2.8, 6.1)	1.29 (0.71, 2.31)	1.36 (0.75, 2.46)
1-year outcomes					
Composite of respiratory hospitalization or death (all-causes)					
TNFi	39	218.5	17.9 (13.0, 24.4)	Ref	Ref
Non-TNFi/JAKi	52	206.5	25.2 (19.2, 33.0)	1.41 (0.93, 2.13)	1.41 (0.93, 2.13)
Respiratory hospitalization					
TNFi	28	218.5	12.8 (8.8, 18.6)	Ref	Ref
Non-TNFi/JAKi	42	206.5	20.3 (15.0, 27.5)	1.58 (0.98, 2.55)	1.52 (0.94, 2.47)
Death (all-causes)					
TNFi	19	229.9	8.3 (5.3, 13.0)	Ref	Ref
Non-TNFi/JAKi	22	226.0	9.7 (6.4, 14.8)	1.18 (0.64, 2.18)	1.25 (0.67, 2.31)
Respiratory-related death					
TNFi	8	229.9	3.5 (1.7, 7.0)	Ref	Ref
Non-TNFi	8	226.0	3.5 (1.8, 7.1)	1.02 (0.38, 2.71)	1.05 (0.39, 2.81)

Hazard ratio (HR) for study outcomes in RA-ILD evaluated using Cox regression models among N=237 TNFi new-users 1:1 propensity score matched to n=237 non-TNFi/JAKi new-users.

*Adjusted for calendar year, elevated ESR or CRP, body mass index, and inhaled corticosteroid use.

Abbreviations: aHR = adjusted hazard ratio; CI = confidence interval; JAKi = Janus kinase inhibitor; HR = hazard ratio; IR = incidence rate; PY = person-years; TNFi = tumor necrosis factor inhibitor.

Figure 2. Sensitivity analyses comparing Non-TNFi/JAKi vs. TNFi in cohorts with additional requirements.



*Composite outcome of respiratory hospitalization or death (all-cause)

Abbreviations: Add. = additional; CI = confidence interval; FVC = forced vital capacity; hosp. = hospitalization; HR = hazard ratio; ILD = interstitial lung disease

Figure 2. Sensitivity analyses comparing Non-TNFi/JAKi vs. TNFi in cohorts with additional requirements.

Disclosure: B. England: Boehringer-Ingelheim, 2, 5; **J. Baker**: CorEvitas, 2, Cumberland Pharma, 2, Horizon Pharmaceuticals, 5; **M. George**: AbbVie/Abbott, 2, GlaxoSmithKlein(GSK), 5, Janssen, 5; **T. Johnson**: None; **Y. Yang**: None; **P. Roul**: None; **H. Sayles**: None; **F. Yu**: None; **J. Rojas Jr**: None; **B. Sauer**: None; **G. Cannon**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, BMS, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Genentech, 2, 5, Janssen, 2, 5, Pfizer, 2, 5, Roche, 2, 5,

UCB Pharma, 2, 5; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9.

Abstract Number: 1583

Comparison of Two Dosing Schedules for Oral Methotrexate (Split-Dose versus Single-Dose) Once Weekly in Patients with Active Rheumatoid Arthritis: A Multicenter, Open Label, Parallel Group, Randomized Controlled Trial (SMART Study)

Chandra Bhushan Prasad[1], **Varun Dhir**[2], Ranjan Gupta[3], Koshy Nithin Thomas[4], Devarasetti phani kumar[5], VENKATESH S PAI[6], Avinash Jain[7], Shankar Naidu[8], Priya Saini[8], Leishangthem Bidyalaxmi[8], AASTHA KHULLAR[8], Ramesh Manthri[9], Shefali Sharma[10], Aman Sharma[11], Amita Aggarwal[4] and Sanjay Jain[8], [1]Healthway Hospital, Goa, Zuarinagar, India, [2]PGIMER, CHD, INDIA, Chandigarh, India, [3]All India Institute of Medical Sciences, New Delhi, India, [4]Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow, India, [5]Nizams Institute of Medical Sciences, Hyderabad, India, [6]AIIMS RISHIKESH, Rishikesh, India, [7]SMS Medical College, Lucknow, India, [8]PGIMER, Chandigarh, India, [9]Department of Clinical Immunology and Rheumatology, Nizams Institute of Medical Sciences, Hyderabad, India, [10]PGIMER< Chandigarh, Chandigarh, India, [11]PGIMER, Chandigarh, India, Chandigarh, India

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Plenary II
Session Type: Plenary Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Methotrexate (MTX), the anchor drug for rheumatoid arthritis (RA), has limited bioavailability above an oral dose of 15 mg. Split-dose oral MTX (morning, evening same day) has been shown to lead to higher blood levels compared to single-dose, however, its effect on clinical efficacy is unknown. Thus, we planned to compare the efficacy, safety and tolerability of oral split-dose to single-dose MTX once a week in RA.

Methods: This multicenter (six centers), open-label (assessor blinded) RCT recruited patients with Rheumatoid arthritis (2010 ACR/EULAR), 18-60 years of age, seropositive (RF or ACPA), disease duration < 5 years, not on DMARDs (except hydroxychloroquine and/or low-dose prednisolone) but with active disease (TJC28 ≥4 and SJC28 ≥2). Patients were randomized 1:1 (online generator) and allocated (concealed using SNOOSE) into either single dose (25 mg) or split-dose (10 mg morning, 15 mg evening, same day) once weekly MTX for 24 weeks. Disease activity was assessed by DAS28 (ESR) at 16 and 24 weeks. At 16 weeks, either leflunomide or sulfasalazine could be added if DASS28≥3.2. (Figure 1) Primary outcome was EULAR good response at 24 weeks, and secondary outcomes were EULAR response at 16 weeks, DAS28, ACR20, 50, 70 and HAQ at 16 and 24 weeks. Safety outcomes included laboratory abnormalities. Intolerance to methotrexate was assessed using MISA score. Analysis was by intention-to-treat and missing data was accounted by last-observation-carried-forward (locf), and non-response was imputed for categorical variables.

Trial registration CTRI/2021/02/03136

Results: 253 patients (females 83%), with age and disease duration (mean ± SD) of 42.2±10.4 and 2.1±1.5 years, were randomized to split-dose (n=128) and single-dose (n=125) group. Baseline DAS28 was comparable, 6.5±1.0 and 6.6±1.0 (p=0.554), but after 16 weeks of MTX monotherapy, DAS28 was significantly lower in split-dose (4.4±1.4) than single-dose (5.1±1.5, p< 0.001) group. At 16 weeks, there was significantly higher EULAR good response (difference 12.3%, CI 12.4 to 66); ACR20 (difference 24.6%, CI 13.1 to 36), ACR50 (difference 19.5%, CI 7.5 to 31.5%) and ACR70 (difference 12.2%, CI 2.5 to 28.9) in split versus single-dose group. Fewer patients in the split-dose (35%) compared to single-dose (54.5%,

Table 1: Efficacy measures

Table 1: Efficacy measures between the two groups at 16 and 24 weeks (intention-to-treat).

Parameters	Split Dose (n=128)	Single Dose (n=125)	p-value
16 weeks (MTX monotherapy phase)			
EULAR good response, n(%)	28 (21.9)	12 (9.6)	
EULAR moderate response, n(%)	69 (53.9)	61 (48.8)	} **0.002***
EULAR no response, n(%)	31 (24.2)	52 (41.6)	
ACR20, n(%)	98 (76.6)	65 (52)	**<0.001***
ACR50, n(%)	70 (54.7)	44 (35.2)	**0.002***
ACR70, n(%)	33 (25.8)	17 (13.6)	**0.02***
Additional csDMARDs at 16wk, n(%)	41 (36)	60 (54.5)	**0.005***
24 weeks (After additional csDMARD)			
EULAR good response, n(%)	37 (28.9)	28 (22.4)	
EULAR moderate response, n(%)	66 (51.6)	68 (54.4)	} 0.46
EULAR no response, n(%)	25 (19.5)	29 (25.2)	
ACR20, n(%)	88 (68.8)	89 (71.2)	0.67
ACR50, n(%)	71 (55.5)	62 (49.6)	0.35
ACR70, n(%)	48 (37.5)	39 (31.2)	0.29

Table 2: Laboratory abnormalities and intolerance between the two groups

Table 2: Laboratory abnormalities and symptoms of intolerance between the two groups

Parameters	Split Dose (n=128)	Single Dose (n=125)	p-value
Transaminitis[1]			
8 weeks, n (%)	33 (27.5)	23 (20.3)	0.190
16 weeks, n (%)	38 (33)	18 (20)	**0.010***
24 weeks, n (%)	44 (39.3)	32 (28.8)	0.100
Persistent[2], n(%)	42 (38)	28 (25.7)	**0.047***
Low WBC (<4 x 10^9/L)			
8 weeks, n	5	2	0.280
16 weeks, n	3	1	0.622
24 weeks, n	0	8	**0.004***
Low platelets (<100 x 10^9/L)			
8 weeks	0	1	0.310
16 weeks	0	1	0.310
24 weeks	0	2	0.152
Any intolerance[3]			
8 weeks	54 (44.6)	41 (36)	0.176
16 weeks	57 (49.1)	49 (44.1)	0.451
24 weeks	59 (53.1)	50 (45)	0.227
Ever	82 (67.8)	67 (58.8)	0.152

[1] Either ALT or AST above 40 IU/L

[2] Persistent implies on atleast two visits out of 4, 8, 16 and 24 weeks

[3] Methotrexate intolerance score in adults score >=1, consists of nausea, vomiting, stomach discomfort, fever, diarrhea, fatigue, anticipatory nausea, oral ulcers (Ref Int J Rheum Dis 2021;24:1294-1301)

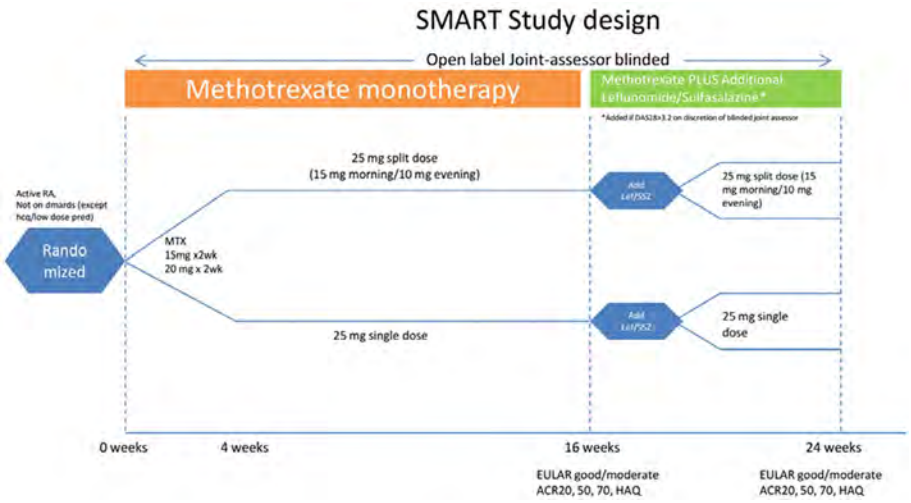


Figure 1: Study design

p=0.005) group were started on additional DMARD at 16 weeks; leflunomide was started in 34 (30%) and 54 (49%), and sulfasalazine in 6 each. At 24 weeks, there was significantly lower DAS28 in split-dose (4.1±1.5) compared to single-dose (4.5 ±1.5, p=0.03) group, however, no difference in other efficacy measures (Table 1). There was no difference in HAQ scores at 16 or 24 weeks. There was no major AE, but significantly higher frequency of transaminitis at 16 weeks and persistent transaminitis in split-dose group. Frequency of leucopenia was higher in single-dose group at 24 weeks (Table 2). No significant difference in symptoms of intolerance between groups. (Table 2)

Conclusion: Oral split-dose MTX given once weekly in RA patients had significantly higher efficacy and reduced the need for additional DMARDs, compared to single-dose MTX given once a week. There was no major AE, but slight increase in frequency of persistent transaminitis in split-dose group.

Disclosure: C. Prasad: None; **V. Dhir**: None; **R. Gupta**: None; **K. Thomas**: None; **D. phani kumar**: None; **V. PAI**: None; **A. Jain**: None; **S. Naidu**: None; **P. Saini**: None; **L. Bidyalaxmi**: None; **A. KHULLAR**: None; **R. Manthri**: None; **S. Sharma**: None; **A. Sharma**: None; **A. Aggarwal**: None; **S. Jain**: None.

Abstract Number: 1584

Effect of Trimethoprim Sulfamethoxazole Prophylaxis on Infections During Treatment of Granulomatosis with Polyangiitis with Rituximab: A Population-Based Study

Arielle Mendel[1], Hassan Behlouli[2], Evelyne Vinet[1], Jeffrey Curtis[3] and Sasha Bernatsky[2], [1]McGill University Health Centre, Montréal, QC, Canada, [2]Research Institute of the McGill University Health Centre, Montreal, QC, Canada, [3]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Plenary II
Session Type: Plenary Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Infections during treatment of ANCA-associated vasculitis (AAV) lead to excess mortality. Trimethoprim sulfamethoxazole (TMP-SMX), recommended for pneumocystis jirovecii pneumonia (PJP) prophylaxis, has broad antimicrobial activity. We assessed associations between TMP-SMX prophylaxis and subsequent infections within a United States population sample of granulomatosis with polyangiitis (GPA) treated with rituximab (RTX).

Methods: We included adults with GPA within the Merative™ Marketscan® Research Databases who had a minimum 6 months of insurance enrolment prior to a first (index) RTX treatment (2011-2020). Baseline TMP-SMX prophylaxis was defined as a >=28-day prescription dispensed within 30 days (before/after) RTX initiation. We defined serious infections as an inpatient ICD-9 or -10 primary diagnostic code for infection following the index date (excluding viral and mycobacterial codes). Secondary outcomes were outpatient infections (for the same codes), and PJP. Subjects were followed until end of insurance enrolment or Dec 31, 2020. Multivariable Cox proportional hazards regression assessed the association of baseline and time-dependent TMP-SMX with serious infection. Models were adjusted for age, sex, prednisone (>=20 mg/day dispensed < 30 days prior to index RTX), hospitalization and/or serious infection in the 6 months prior to index RTX, and having any of of the following: interstitial or obstructive lung disease, diabetes, chronic kidney disease, or dialysis. As a sensitivity analysis, we assessed the association between TMP-SMX prophylaxis and a "control" infection, herpes

Table 1 Baseline cohort characteristics, overall and according to trimethoprim sulfamethoxazole (TMP-SMX) use

Characteristic at time of first rituximab treatment	Overall cohort (N=919)	Baseline TMP-SMX (n=281)	No baseline TMP-SMX (n=638)
Age, mean (SD)	52.1 (16.1)	**49.8 (15.5)**	**53.1 (16.2)**
Female n (%)	488 (53)	**118 (42)**	**370 (58)**
Insurance type, n (%)			
Commercial	688 (75)	**230 (82)**	**458 (72)**
Medicare	162 (18)	**33 (12)**	**129 (20)**
Medicaid	69 (8)	18 (6)	51 (8)
Index RTX treatment, n (%) Induction Maintenance	 679 (74) 240 (26)	 **220 (78)** **61 (21)**	 **459 (72)** **179 (28)**
Healthcare use in prior 6 months			
Hospital admission, n (%)	489 (53)	**197 (70)**	**292 (46)**
Intensive care unit admission, n (%)	210 (23)	**84 (30)**	**126 (20)**
Serious infection	108 (12)	39 (14)	69 (11)
Disease features and/or co-morbidities, n (%)			
Sinusitis	306 (33)	89 (32)	217 (34)
Obstructive lung disease	233 (25)	71 (25)	162 (25)
Interstitial lung disease	56 (6)	14 (5)	42 (7)
Glomerulonephritis	138 (15)	38 (14)	100 (16)
Chronic kidney disease	248 (27)	67 (24)	181 (28)
Dialysis	99 (11)	34 (12)	65 (10)
Diabetes	161 (18)	45 (16)	116 (18)
Prior medication use, n (%)			
Prednisone 1-19 mg/day [b]	108 (12)	31 (11)	77 (12)
Prednisone ≥20 mg/day[b]	445 (48)	**180 (64)**	**265 (42)**
Oral or IV cyclophosphamide[b]	39 (4)	12 (4)	27 (4)
Azathioprine[c]	49 (5)	13 (5)	36 (6)
Methotrexate[c]	113 (12)	38 (14)	75 (12)

[a] bold denotes that the 95% CI for the difference in mean or proportion between TMP-SMX exposed and unexposed groups excludes the null value
[b] at least one prescription dispensed in the month prior to rituximab
[c] at least one prescription in the 6 months prior to rituximab

Table 2. Cox proportional hazards regression of factors associated with time to serious infection, considering baseline and time-dependent (TD) TMP-SMX exposure (n=917, 104 events)

Covariate	Univariable	Multivariable	Multivariable (TD)
	HR (95% CI)	HR (95% CI)	HR (95% CI)
TMP-SMX use	**0.58 (0.34-0.92)**	**0.49 (0.30-0.79)**	**0.49 (0.28-0.87)**
Age (years)	1.02 (1.01-1.03)	1.01 (0.99-1.02)	1.01 (0.99-1.02)
Female sex (vs male)	**0.67 (0.45-0.98)**	0.69 (0.46-1.02)	0.73 (0.49-1.08)
Prednisone ≥20 mg/day	1.12 (0.76-1.64)	0.94 (0.63-1.40)	0.92 (0.62-1.38)
Induction RTX	0.67 (0.45-1.02)	-	-
Other immunosuppressant in the prior 6 months	0.87 (0.51-1.49)	-	-
Hospitalization prior 6 months	**2.42 (1.59-3.71)**	**1.93 (1.19-3.11)**	**1.79 (1.11-2.88)**
Serious infection prior 6 months	**3.01 (1.96-4.63)**	**2.35 (1.47-3.77)**	**2.36 (1.47-3.78)**
Chronic obstructive pulmonary disease	1.48 (0.99-2.22)	-	-
Interstitial lung disease	1.78 (0.90-3.54)	-	-
Diabetes	1.55 (0.99-2.42)	-	-
Chronic kidney disease	**1.98 (1.34-2.92)**	-	-
Dialysis	**2.72 (1.69-4.36)**	-	-
≥1 of above comorbidities	**2.50 (1.6-3.90)**	**2.20 (1.38-3.51)**	**2.33 (1.46-3.69)**

zoster (HZ). Finally, we determined rates of adverse events potentially attributable to TMP-SMX during person-time exposed and unexposed to TMP-SMX.

Results: The cohort included 919 RTX-treated individuals with GPA, of which 53% were female, mean age 52 years (SD 16). TMP-SMX was dispensed to 281 (31%) at the time of index RTX (and to 40% on prednisone >=20 mg/day). Over a median (IQR) follow-up of 496 (138, 979) days, the rates of serious infection, outpatient infection, and PJP per 100-person years were 6.1 (95% confidence interval, CI 5-7), 28.7 (95% CI 26-32), and 0.7 (0.4-1.2), respectively. Serious infections were primarily pulmonary (36%) or general sepsis (45%). In multivariable analyses, TMP-SMX was negatively associated with serious infections, considering baseline (adjusted HR 0.5; 95% CI 0.3-0.8) and time-varying TMP-SMX exposure (aHR 0.5; 95% CI 0.3-0.9). Prophylaxis was also negatively associated with outpatient infections (aHR 0.7; 95% CI 0.5-0.9). Thirteen PJP infections occurred, all in TMP-SMX unexposed subjects. TMP-SMX was not associated with reduced HZ (aHR; 1.6, 95% CI 0.6-3.2). Rates for adverse events potentially attributable to TMP-SMX per 100 person-years were 29.6 (95% CI, 22-39) during periods of TMP-SMX exposure and 13.4 (95% CI, 11-16) during periods without TMP-SMX exposure.

Conclusion: TMP-SMX prophylaxis was associated with subsequent reduced serious and overall infections in RTX-treated GPA. Further study is needed to determine how to balance potential benefits and harms from prophylaxis in individual patients, and determine optimal prophylaxis duration.

Disclosure: A. Mendel: None; **H. Behlouli**: None; **E. Vinet**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, CorEvitas, 2, 5, Eli Lilly and Company, 2, 5, Janssen, 2, 5, Myriad, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **S. Bernatsky**: None.

Abstract Number: 1585

Defining Neutrophil-Mediated Renal Damage Triggered by Ultraviolet (UV) Skin Exposure

Angelique Cortez[1], Lindsay Mendyka[2], Fred Kolling[3], Michael Whitfield[1] and Sladjana Skopelja-Gardner[4], [1]Dartmouth College, Hanover, NH, [2]Dartmouth Hitchcock, Lebanon, NH, [3]Geisel School of Medicine at Dartmouth, Hanover, NH, [4]Dartmouth-Hitchcock, Lebanon, NH

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Innate Immunity
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Lupus (SLE) is one of the leading causes of death in young women in the United States. Roughly ~80% of SLE patients experience sensitivity to ultraviolet light (UV), which leads to local and systemic inflammation and can trigger nephritis flares. While we previously showed skin exposure to UV leads to neutrophil-mediated kidney damage, the exact mechanisms are unknown. We use scRNA-Seq to characterize kidney injury pathways resulting from skin UV exposure.

Methods: B6 female mice (3-mo) were exposed to UVB (1x500mJ/cm^2). On day 2 (D2) or No UV, cardiac perfusion was performed with Dynabeads for glomerular magnetic isolation. Glomeruli were digested (Col IV, Pronase I, DNase I) following Col. I kidney digest and scRNA-seq performed by 10X Genomics. Glomeruli from anti-GCSF and IgG D2 UV-exposed mice were digested and sent for 10X Genomics scRNA-seq. Neutrophils were enriched from digested skin, lungs, and kidney by Ly6G magnetic beads and sorted for >90% purity. Single Cell clustering and differential gene expression (DGE) analyses were performed using Seurat 4.1.1 R package. Gene ontology pathway analysis was performed using clusterProfiler. Ligand-receptor analysis was performed using CellChat. Injury scores created using DGE from D2-UV renal structural cells.

Results: ScRNAseq analysis of kidney structural cells revealed endothelial, stromal, podocyte and distal tubular cell (DTC) injury on D2 after skin UV exposure. Pathway analysis showed downregulation of actin filament organization in podocytes and ion transport in DTCs (Fig 1B-C). Type I interferon pathway was upregulated in stromal cells, while angiogenic and cell

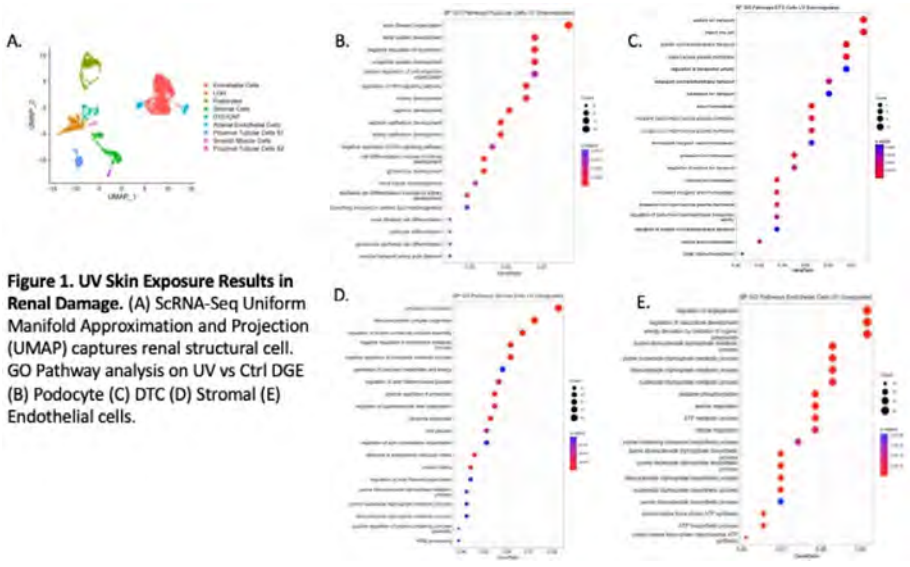


Figure 1. UV Skin Exposure Results in Renal Damage. (A) ScRNA-Seq Uniform Manifold Approximation and Projection (UMAP) captures renal structural cell. GO Pathway analysis on UV vs Ctrl DGE (B) Podocyte (C) DTC (D) Stromal (E) Endothelial cells.

Figure 1. UV Skin Exposure Results in Renal Damage.

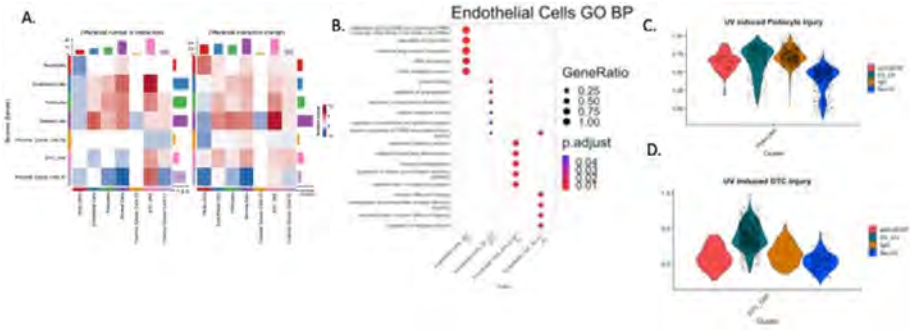


Figure 2. UV skin exposure triggers neutrophil-mediated damage. (A) Ligand-receptor interaction performed using CellChat shows altered number and interaction strength in D2 UV exposed cells compared to No-UV. (B) GO Pathway analysis on Endothelial D2-UV, No-UV, Anti-GCSF IgG, & Ctrl IgG DGE. UV-exposed Injury Score on anti-GCSF, D2-UV, Ctrl IgG, & No-UV in (C) podocyte cells & (D) DTCs

Figure 2. UV skin exposure triggers neutrophil-mediated damage.

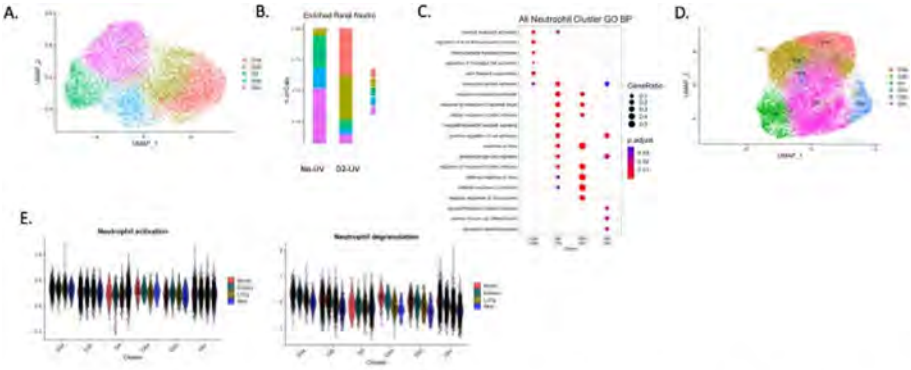


Figure 2. UV skin exposure triggers neutrophil heterogeneity. (A) UMAP of enriched neutrophils from D2-UV and No-UV exposed mice. (B) Stacked bar plot of enriched neutrophils separated by D2-UV and No-UV . (C) UV-exposed Injury (D) UMAP of enriched neutrophils from lung, skin, blood & kidney. (E) Neutrophil activation and Neutrophil degranulation scores on different clusters from lung, skin, blood & kidney.

Figure 3. UV skin exposure triggers neutrophil heterogeneity.

stress pathways were increased in renal endothelial cells (Fig 1D-E). Kidney-infiltrating neutrophils showed an increased number and strength of interactions with stromal, endothelial, and DT cells (Fig 2A). Preventing neutrophil recruitment by anti-GCSF IgG abolished endothelial injury pathways (Fig 2B) and decreased injury scores in podocytes and DTCs (Fig2C-D). Five distinct neutrophil clusters (G3a, G3b, G4, G5b, & G5c) were identified in the kidney, though activated immature G3a and G3b neutrophil clusters were only present after UV (Fig3A-B). Pathway analysis showed G3a was enriched for myeloid leukocyte activation and actin regulation pathways (Fig3C). ScRNA-Seq analysis revealed neutrophil heterogeneity at the local site of injury (skin) vs. the distal organs (kidney, lung, & blood) (Fig3D). Kidney infiltrating neutrophils had increased degranulation and activation scores in the kidney vs. the lung or skin (Fig3E).

Conclusion: We identified that neutrophils primarily cause endothelial renal injury but also contribute to podocyte and DTC damage after skin UV exposure. The increased number and strength of podocyte and stromal interactions indicates UV skin exposure triggers injury to the glomerular filtration barrier, supporting our previous findings of UV triggered proteinuria. Altered neutrophil heterogeneity at the local site of injury and distal organs demonstrates tissue specificity in the skin-kidney pathogenic axis.

Disclosure: A. Cortez: None; **L. Mendyka**: None; **F. Kolling**: None; **M. Whitfield**: None; **S. Skopelja-Gardner**: None.

Abstract Number: 1586

Keratinocyte VISTA Suppresses Skin IFN-I Production by Regulating DNA Damage Repair and Cytosolic DNA Sensing

Zachary Peters[1], Lindsay Mendyka[2], Sicong Shan[1], William Rigby[3], Christopher Burns[4], Randolph Noelle[5] and Sladjana Skopelja-Gardner[4], [1]Dartmouth College, Hanover, NH, [2]Dartmouth Hitchcock, Lebanon, NH, [3]Dartmouth-Hitchcock, Norwich, VT, [4]Dartmouth Hitchcock Medical Center, Lebanon, NH, [5]Geisel School of Medicine at Dartmouth, Hanover, NH

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Innate Immunity

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Persistent production of type I interferons (IFN-Is) is one of the hallmarks of lupus skin disease that is exacerbated by ultraviolet (UV) light. We previously showed IFN-I induction by UV occurs in a cGAS-STING-dependent manner, but the IFN-I signature returns to baseline levels in healthy skin, unlike in lupus. Here, we propose that the immune checkpoint VISTA is a regulator of skin IFN-I production in keratinocytes of therapeutic relevance to lupus.

Methods: Skin biopsies from B6, B6.*Vsir*-/- (VISTA-deficient), B6.*Vsir-/-Sting-/-*, KRT14^{cre}*Vsir*$^{fl/fl}$ (*Vsir*-/- in keratinocytes), and cre-*Vsir*$^{fl/fl}$ female mice (3 mo) were collected prior to, 3 and 24h after UVB (500mJ/cm^2). Gene expression was quantified by RNA-seq (Rosalind). Skin infiltrating cells were quantified by flow cytometry. Human keratinocytes were isolated from healthy skin and *cultured in vitro*. Cells were treated with agonistic anti-VISTA (803) or isotype IgG2a (20ug/ml) prior to UVB (50mJ/cm^2), in the presence or absence of IFNa (100U). Expression of IFN-Is and IFN-I stimulated genes (ISGs) were quantified by qPCR (4hr after UV) and IFN-I score derived.

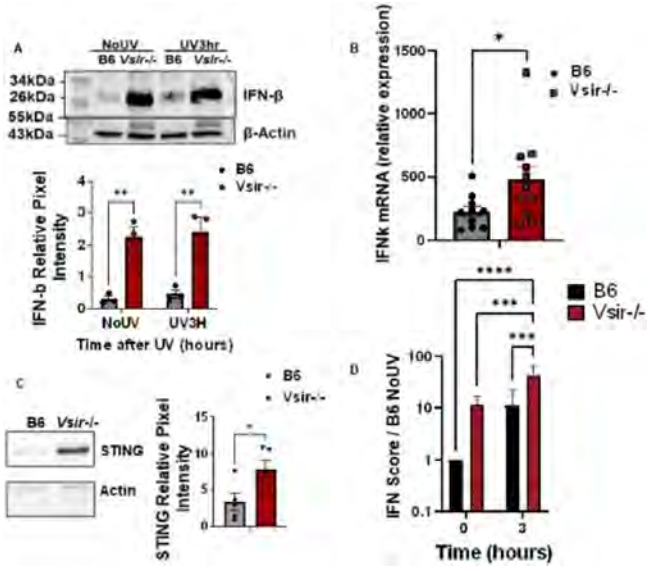


Figure 1. Elevated skin IFN-I production in the absence of VISTA. A. IFN-β immunoblot of B6 and B6.Vsir-/- skin lysates; levels normalized to β-actin (ImageJ). B. IFN-k gene expression in B6 and Vsir-/- whole skin measured by qPCR. C. STING immunoblot of B6 and B6.vsir-/- skin lysates. D. Skin IFN score in B6 and Vsir-/- mice, before and after UVB exposure (1x500mJ/cm2). Differences in gene expression determined relative to baseline B6 and all statistical significance determined by two-way ANOVA (A,D) or Student's T test(B,C) (n=5, *p<0.05, **p<0.01, ***p<0.005, ****p<0.00001). IFN-I score calculated as sum normalized expression of 6 ISGs relative to baseline B6 (ISGs: IRF7, IFIT1, IFIT3, ISG15, IFI27La, Mx1) and normalized to 18s.

Results: At baseline, B6.*Vsir-/-* skin had increased IFN-k mRNA, IFN-b protein, as well as total STING protein levels (Fig. 1A-C). RNA-seq revealed increased expression of *Sting* and upstream cytosolic DNA sensors in VISTA-deficient mouse skin before and after UV. B6.*Vsir-/-* mice exhibited a 5-fold higher skin IFN-I score after UV compared to B6 mice (Fig.1D). Higher baseline and UV-induced IFN-I response in VISTA-deficient skin was suppressed in the absence of STING (*Vsir-/-Sting-/-* mice). Moreover, fewer skin-infiltrating neutrophils and inflammatory monocytes were recruited to *Vsir-/-Sting-/-* vs. STING-sufficient *Vsir-/-* skin post UV. RNAseq also revealed decreased expression of DNA repair genes like *Ogg1, Xpd and Pole* in *B6.Vsir-/-* skin, which are essential for repair of UV-induced DNA damage. VISTA deficient mouse keratinocytes produced 2-fold higher IFN-k at baseline *ex vivo* and accumulated higher levels of oxidized DNA (8-OHdG) compared

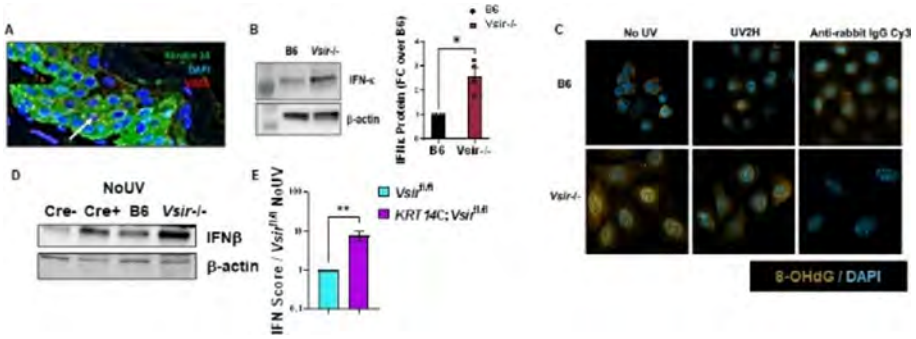


Figure 2. VISTA regulates IFN-I production in keratinocytes. A. Mouse epidermis stained for VISTA (red), Keratin-14 (green), and DAPI (blue). B. Baseline IFN-κ protein in B6 and Vsir-/- keratinocyte lysates after 6 days in culture, quantified relative to B-actin. C. Mouse keratinocytes stained for 8-hydroxyguanosine (yellow) and DAPI (blue). D. IFN-b immunoblot of skin lysates from B6, B6.Vsir-/-, Vsirfl/fl and KRT14Cre:Vsirfl/fl mice. E. Baseline skin IFN-I score of Vsirfl/fl and KRT14Cre:Vsirfl/fl mice. Significance determined by two-way ANOVA (A). (n=3, * p<0.05, p<0.01). Differences in gene expression relative to Vsirfl/fl control and statistical significance determined by T test (n=4).

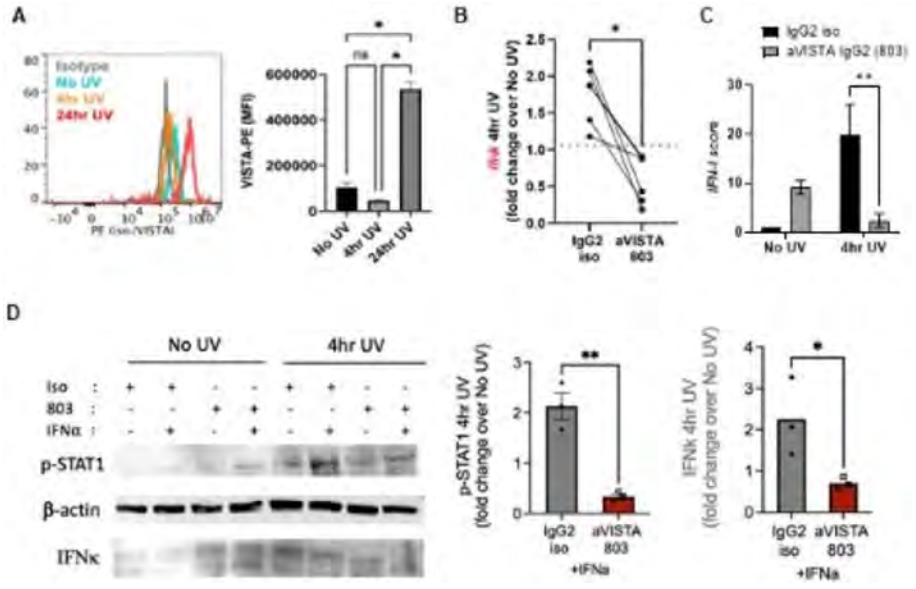


Figure 3. Anti-VISTA agonistic IgG suppresses UV-induced IFN-I signature in human keratinocytes. A. VISTA surface expression on primary human keratinocytes measured by flow cytometry, without UV, 4 and 24hr after UVB (50mJ/cm2). B. IFN-k gene expression in human keratinocytes pre-treated with either anti-VISTA INX803 IgG2 or isotype control IgG2 antibody. C. IFN-I scores of human keratinocytes pre-treated with 803 or isotype control IgG2 before and after UV exposure were derived as the sum of normalized expression levels of 9 interferon-stimulated genes (CXCL10, BST2, ifitm3, ifi27, isg15, ifit1, mx1, Ly6E, irf7). D. Immunoblot of phosphorylated STAT1 and IFN-k in human keratinocyte lysates from cells before and after UVB exposure, in the absence or presence of IFNα (100U, 24hr prior to UV exposure) and pre-treated with anti-VISTA 803 or isotype control IgG2 antibody. Pixel intensity calculated relative to b-actin (ImageJ) and fold change of P-STAT1 and IFN-k in the presence of IFNa calculated relative to baseline NoUV. Statistical significance was determined by two-way ANOVA(A,C) and Student's t-test (B,D); *p<0.05, **p<0.01, ns= not significant.

with B6 cells (Fig. 2B-C).Mice with a conditional VISTA deletion only in keratinocytes exhibited a 10-fold higher baseline IFN-I signature and increased IFN-b protein levels compared to controls (Fig. 2D-E). Expression of VISTA on human keratinocytes decreased 4 hr after UV, but increased 5-fold 24 hr after UV(Fig. 3A).Pre-treatment of human keratinocytes with an agonistic anti-VISTA antibody (803) suppressed UV-induced IFN-k, Stat1 phosphorylation and IFN-I score, even in keratinocytes with a pre-existing IFN-I signature (Fig. 3C-D).

Conclusion: These studies identify VISTA as a suppressor of IFN-I production in keratinocytes and demonstrate STING-dependent IFN-I production in the absence of VISTA. As oxidized DNA is resistant to degradation in the cytosol where it can serve as a potent trigger of cGAS-STING, VISTA promotion of DNA repair may indirectly suppress STING signals. Antibody-mediated activation of VISTA in keratinocytes demonstrates its potential as a target to suppress IFN-I production in the context of photosensitivity and lupus.

Disclosure: Z. Peters: None; **L. Mendyka**: None; **S. Shan**: None; **W. Rigby**: None; **C. Burns**: None; **R. Noelle**: None; **S. Skopelja-Gardner**: None.

Abstract Number: 1587

Mitochondrial Z-DNA and ZBP1 Drive Autoimmune Photosensitivity

Benjamin Klein, Mack Reynolds, Bin Xu, Mehrnaz Gharaee-Kermani, Amanda Victory, Shannon Loftus, Mary O'Riordan and J. Michelle Kahlenberg, University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Innate Immunity
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Autoimmune photosensitivity is observed in type I Interferon (IFN) mediated diseases such as systemic and cutaneous lupus erythematosus (SLE/CLE) and dermatomyositis. Type I IFN has been described as an activator of UV-induced immune responses, but how a chronic IFN-high environment drives photosensitivity is not understood. Mitochondrial DNA has been identified as a source of IFN responses via activation of cGAS-STING in diverse cells of SLE. Here, we investigated how UV light and type I IFN exposure impact mitochondrial stress and Z-DNA formation, a left-handed dsDNA primarily localized in mitochondria which leads to type I IFN production through activation of cGAS.

Methods: Confocal microscopy of primary keratinocytes (KCs) from healthy controls and SLE patients and N/TERT immortalized KCs was performed to assess mitochondrial dynamics and cytosolic Z-DNA formation after UV exposure and IFN-α treatment. qPCR and single cell RNA sequencing was used to assess gene expression. Tissue immunofluorescence was used for protein expression of ZBP1. shRNA-mediated knockdown of ZBP1 was performed in NTERTs.

Results: After UV light exposure, NTERTs showed significantly upregulated gene expression of *IFNB, IFNK, IFNL, MX1* and *OASL*. This upregulation was significantly inhibited by preincubation with the mitochondrially-targeted antioxidant mito-TEMPO (MT), indicating mitochondrial reactive oxygen species-dependent IFN responses. Additionally, mitochondria showed significant fragmentation after UV light that was associated with cytosolic Z-DNA accumulation. Strikingly, this accumulation was enhanced with IFN incubation leading to large Z-DNA puncta within the cytosol. Primary SLE KCs exhibit cytosolic Z-DNA at baseline and showed strong cytosolic Z-DNA accumulation after UV exposure. Cytosolic Z-DNA accumulation and UV-induced ISG expression was prevented by MT in SLE KCs. Importantly, ZBP1, the cytosolic sensor of Z-DNA, is induced by IFN-α and upregulated in nonlesional and lesional SLE and dermatomyositis skin biopsies but is

not detectable in healthy control biopsies. Confocal analysis showed colocalization of Z-DNA with ZBP1 and cGAS after IFN +UVB exposure. Knockdown of ZBP1 in NTERTs attenuated ISG expression after UVB in an IFN-high environment.

Conclusion: Our data indicate that type I IFN priming, coupled with UV light exposure, results in mitochondrial stress that leads to increased mitochondrial Z-DNA formation and cytoplasmic release. Cytosolic Z-DNA interacts with ZBP1 and cGAS to activate IFN upregulation. Collectively, we describe a new pathway of mitochondrial Z-DNA sensing by ZBP1 that drives and sustains IFN responses in KCs, giving further insight into autoimmune photosensitivity.

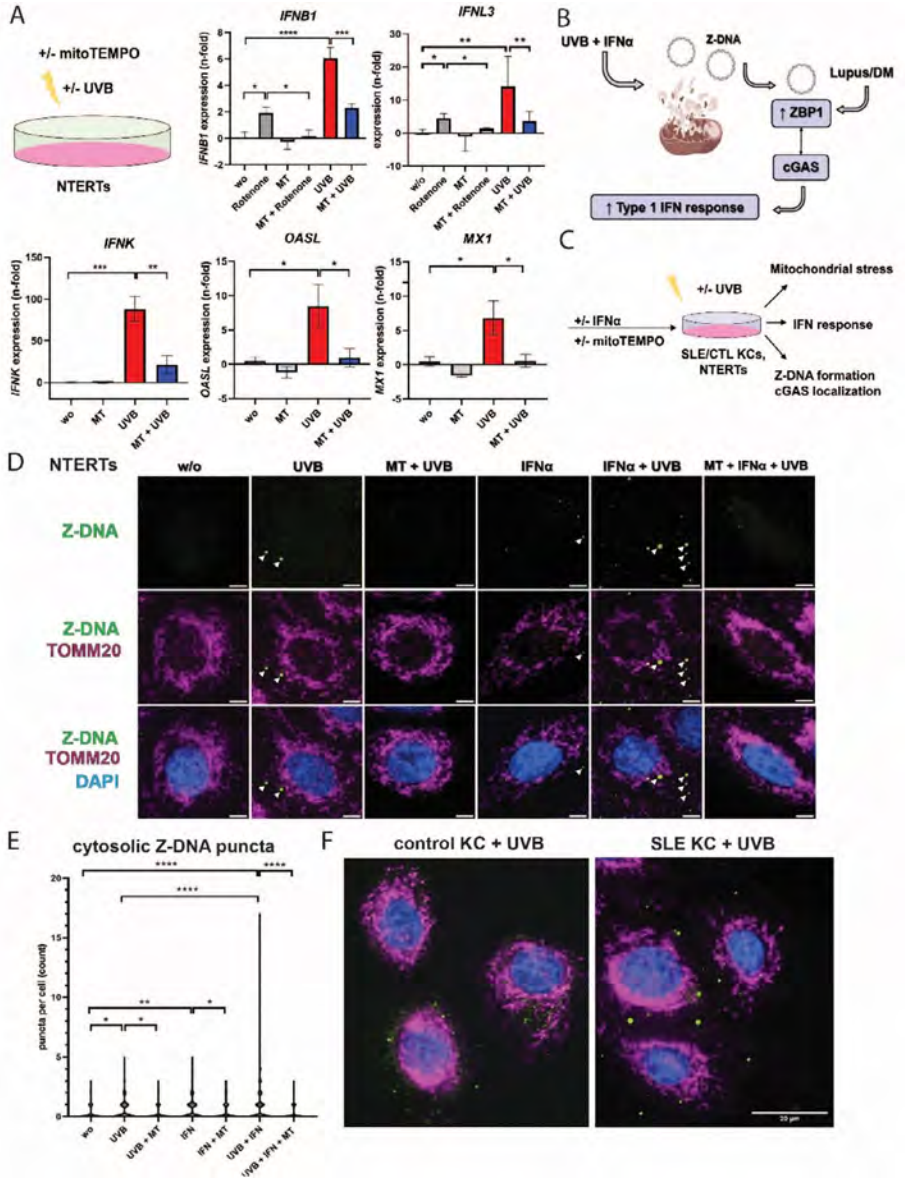


Figure 1. UVB leads to mitochondrial ROS-dependent IFN upregulation and cytoplasmic release of Z-DNA in keratinocytes (KCs). A) Expression of interferon genes in NTERTs +/- UVB exposure and +/- preincubation with mitochondrial targeted antioxidant mitoTEMPO (n=4). B) Schematic of Z-DNA release: Upon mitochondrial damage by UVB and IFN-α, Z-DNA is released into the cytosol and bound by ZBP1 which is overexpressed in the epidermis of lupus and dermatomyositis patients. ZBP1 can interact with cGAS to sustain IFN responses in KCs. C) Methodology to assess mitochondrial stress and Z-DNA formation in KCs. D) Immunofluorescence (IF) staining of NTERTs identifies mitochondrial-derived cytoplasmic Z-DNA release upon UVB exposure resulting in large Z-DNA puncta after IFN-α treatment (n=4). E) Quantification of cytoplasmic Z-DNA by automatic image analysis using CellProfiler software. F) IF of control KCs (n=3) and SLE KCs (n=2) for Z-DNA after UVB exposure identifies large Z-DNA puncta in SLE KCs.

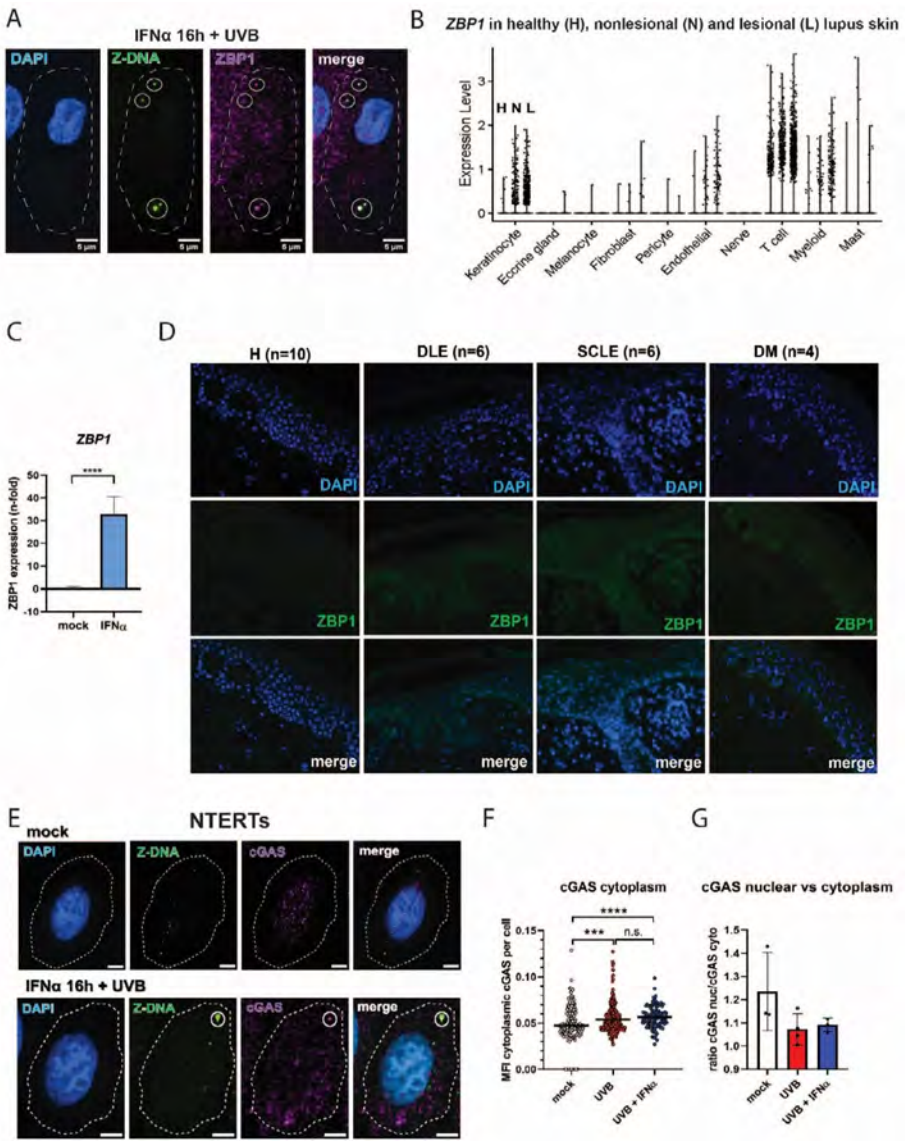


Figure 2. ZBP1 interacts with Z-DNA and is upregulated in autoimmune photosensitivity disorders. A) IF staining of Z-DNA and ZBP1 in NTERTs reveals colocalization of large cytoplasmic Z-DNA puncta with ZBP1. B) Violin plots showing expression levels of ZBP1 in different cell types of healthy control (HC, n=14), nonlesional (n=7) and lesional (n=7) lupus skin. C) ZBP1 is induced by IFN-α incubation in NTERTs (n=4). D) IF staining of HC, discoid lupus (DLE), subacute cutaneous lupus (SCLE), and dermatomyositis (DM) identifies increased epidermal ZBP1 expression in autoimmune photosensitive disorders compared to HC. E) IF staining of cGAS in NTERTs reveals colocalization of cGAS with large Z-DNA puncta after UVB exposure and IFN-α treatment (n=3). F) Quantification of cGAS staining shows cytoplasmic shift of cGAS after UVB exposure. G) Ratio of nuclear and cytoplasmic cGAS after UVB and IFN-α treatment.

Disclosure: B. Klein: None; **M. Reynolds**: None; **B. Xu**: None; **M. Gharaee-Kermani**: Rome Therapeutics, 5; **A. Victory**: None; **S. Loftus**: None; **M. O'Riordan**: None; **J. Kahlenberg**: AstraZeneca, 1, Bristol-Myers Squibb(BMS), 2, 5, EMD Serano, 2, exo therapeutics, 2, Gilead, 2, GlaxoSmithKlein(GSK), 1, horizon Therapeutics, 2, Janssen, 5, Pfizer, 2, ROME Therapeutics, 2, 5, Rome Therapeutics, 5, Ventus Therapeutics, 2, 5.

Abstract Number: 1588

Monocyte-derived Macrophages Accumulate in the Lungs in anti-MDA5+ Dermatomyositis with RP-ILD: Proinflammatory and Profibrotic Phenotype Revealed by Single-cell RNA Sequencing

Xiaoya Pei[1], **Jia Shi**[2], Yangzhong Zhou[2], Xiao Zhang[2], Xiaoman Wang[1], Mingwei Tang[2], Shuang Zhou[2], chanyuan wu[2], Jinmin Peng[3], Mengtao Li[4], xiaofeng Zeng[2], Jun Liu[5], Houzao Chen[1] and Qian Wang[2], [1]State Key Laboratory of Medical Molecular Biology, Department of Biochemistry and Molecular Biology, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China, [2]Department of Rheumatology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China, [3]Medical Intensive Care Unit, State Key Laboratory of Complex Severe and Rare Diseases, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing, China, [4]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China, [5]State Key Laboratory of Protein and Plant Gene Research, School of Life Sciences, Peking-Tsinghua Center for Life Sciences, Peking University, Beijing, China

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Innate Immunity

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Anti-melanoma differentiation-associated gene 5-positive dermatomyositis (anti-MDA5+ DM) is a rare inflammatory autoimmune disease with impressively life-threatening rapid progressive interstitial lung disease (RP-ILD). The mechanism that leads to immune dysfunction and lung injury remains elusive.

Methods: We applied single-cell RNA sequencing to the peripheral blood mononuclear cells (PBMCs) from three anti-MDA5+ DM patients and cells in paired broncho-alveolar lavage fluid (BALF). The datasets of healthy controls are from GSE158055 (PBMC) and GSE14592 (BALF). Flow cytometry and Luminex assay were further applied to validate the results.

Results: A high-quality scRNA-seq dataset composed of 64,565 cells were generated from three anti-MDA5+ DM patients, revealing profound aberrations of various immune compartments and distinct immune responses both in peripheral blood and lungs. We found increased monocytes resembling myeloid-derived suppressor cells (MDSCs), which correlated with inflammatory markers in the blood ofanti-MDA5+ DM patients. While those MDSC-like monocytes showed enhanced activation of type I interferon signaling pathway, they were immune-paralyzed, with downregulation of cytokines and inflammatory gene expressions. In contrast, the lung microenvironmentofanti-MDA5+ DM exhibited overactivation of immune responses, with monocyte-macrophages in BALFs producing massive amounts of cytokines and chemokines. To be more specific, monocyte-derived alveolar macrophages (Mo-AMs) might be the major source triggering the cytokine storm in the lung, with cell ratios and inflammatory expression both significantly elevated inanti-MDA5+ DM patients. The prominent expression of chemokines of Mo-AMs suggested a feed forward loop of immune cell recruitment and inflammatory cascade. Besides, pseudo-time trajectory analysis revealed that recruited Mo-AMs adopt a fibrosis-associated phenotype during the process of differentiation.

Conclusion: Our study comprehensively depicts the dysregulated peripheral and lung immune landscape inanti-MDA5+ DM, and highlights the proinflammatory and profibrotic role of Mo-AMs in the pathogenesis and progression ofanti-MDA5+ DM with RP-ILD, implying that targeting Mo-AMs or blockade of monocyte influx to lung may present an effective strategy.

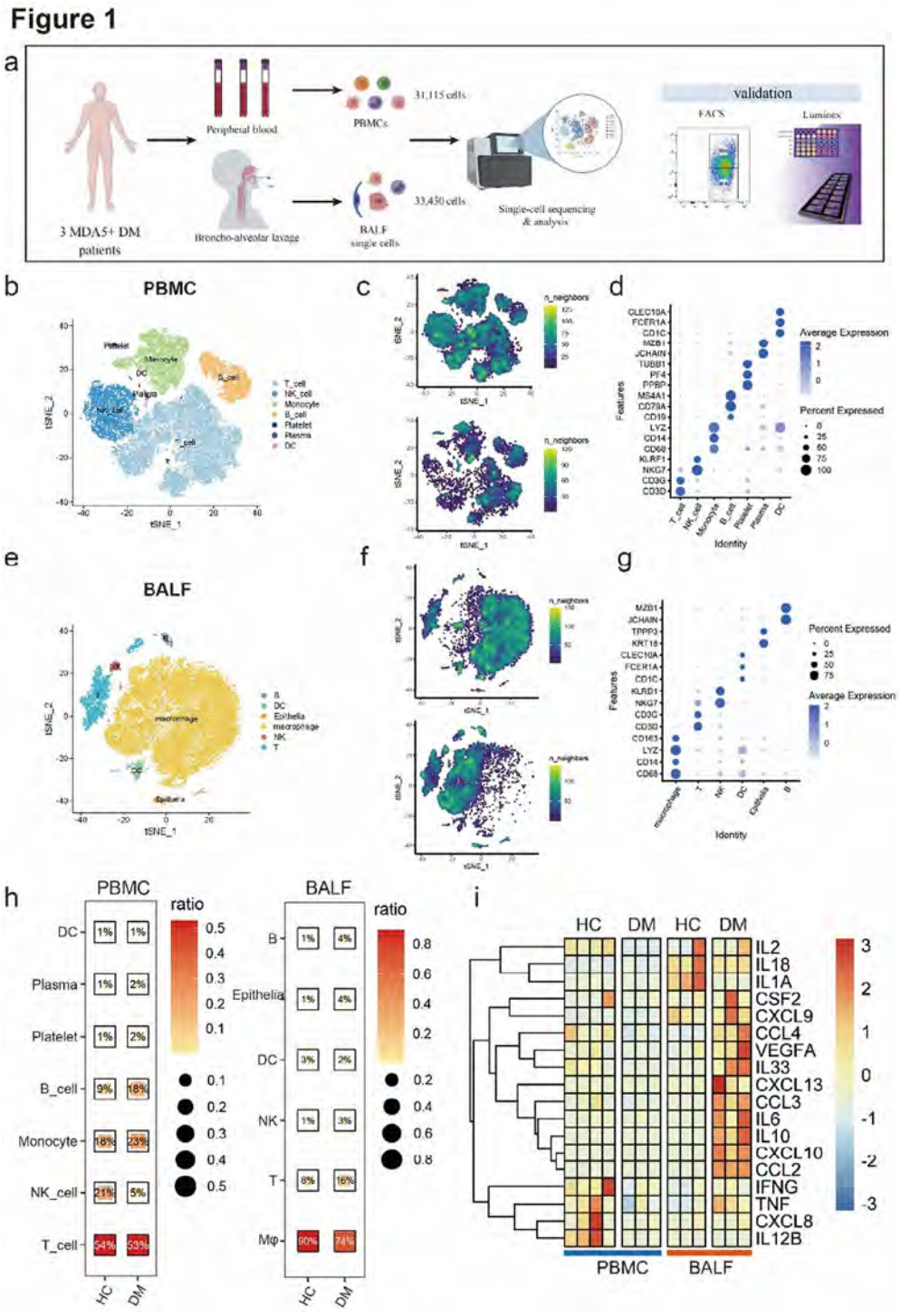


Figure 1. (a) Flowchart depicting the overall experimental design of this study. (b&e) t-SNE plot showing the overview of cell clusters in the integrated single-cell transcriptomes of PBMCs and BALFs from anti-MDA5+ DM patients and healthy controls (HCs). (c&f) t-SNE plots showing the single-cell transcriptomes of PBMCs and BALFs from HCs (top) and anti-MDA5+ DM patients (bottom) respectively. (d&g)The specific markers for identifying each immune cell types in b&e are indicated. (h)The ratios of each cell cluster in PBMCs and BALFs from anti-MDA5+ DM patients and HCs. (i) Heatmap showing the expressions of key cytokines and chemokines involved in cytokine strom of PBMCs and BALFs from HCs and patients.

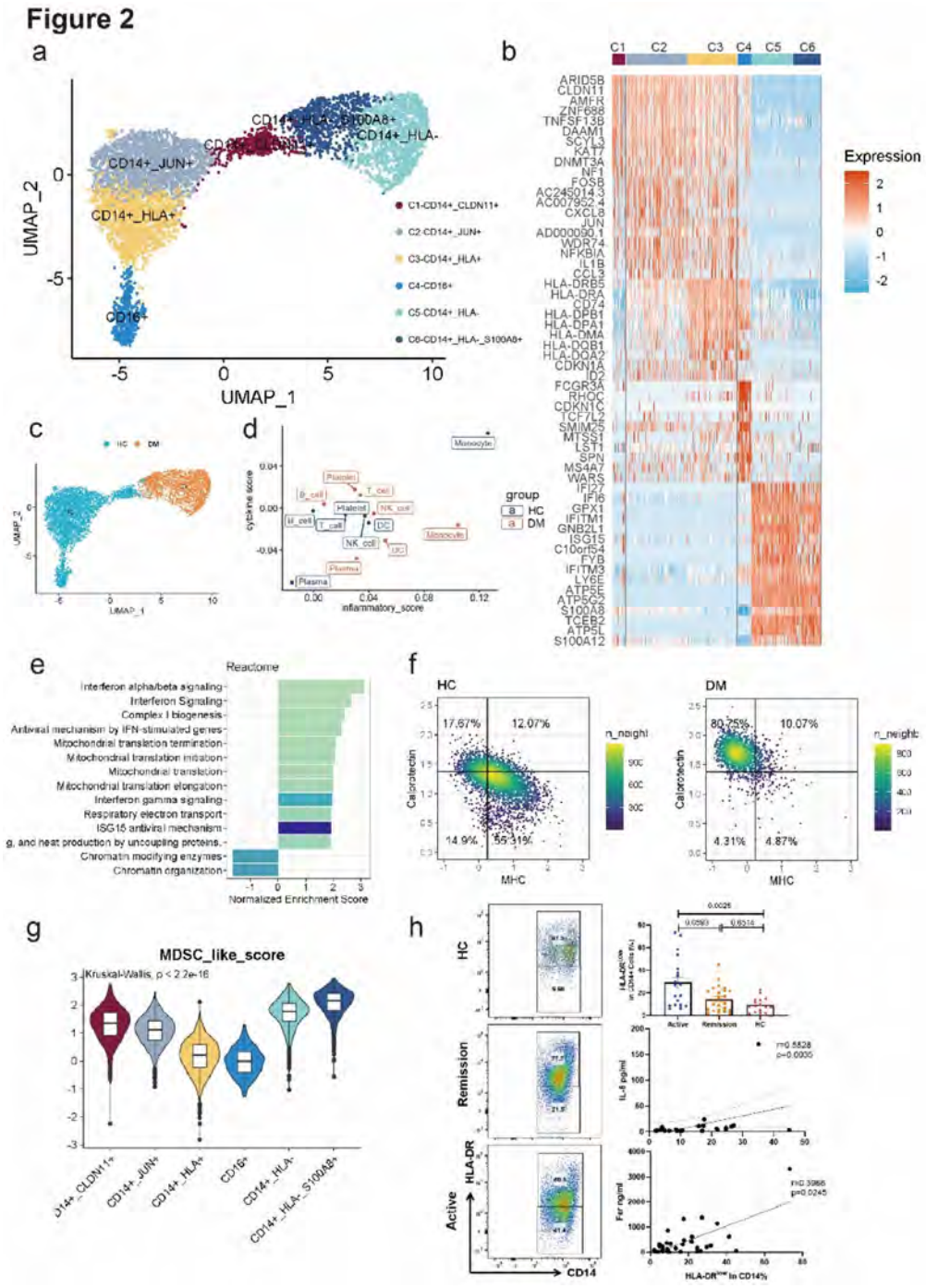


Figure 2. (a) UMAP plot of six cell clusters of monocytes in PBMCs. (b) Heatmap showing top 10 marker genes for each cluster. (c) UMAP plot showing monocytes across HCs and patients. (d) Inflammatory scores and cytokine scores of PBMC cell clusters. (e) Bar plot showing the pathways enriched in the anti-MDA5+ DM group across monocytes. (f) Density plots show the composite MHC II signature scores and calprotectin signature scores of peripheral CD14+ monocytes in 2D maps. The horizontal and vertical lines separating the four quadrants represent the median scores of all CD14+ monocytes. The percentages of cells in each quadrant are indicated. (g) Violin plot showing the MDSC-like score of each monocyte cluster. (h) Left panel shows the representative flow cytometric data of HLA-DR expression on CD14+ PBMCs. Right top plot shows the percentage of HLA-DRLow cells in CD14+ PBMCs among anti-MDA5+ DM-active group, anti-MDA5+ DM-remission group and HC group. The middle and bottom plot on the right shows the Spearman correlation of HLA-DRLow% and IL-6, and ferritin levels.

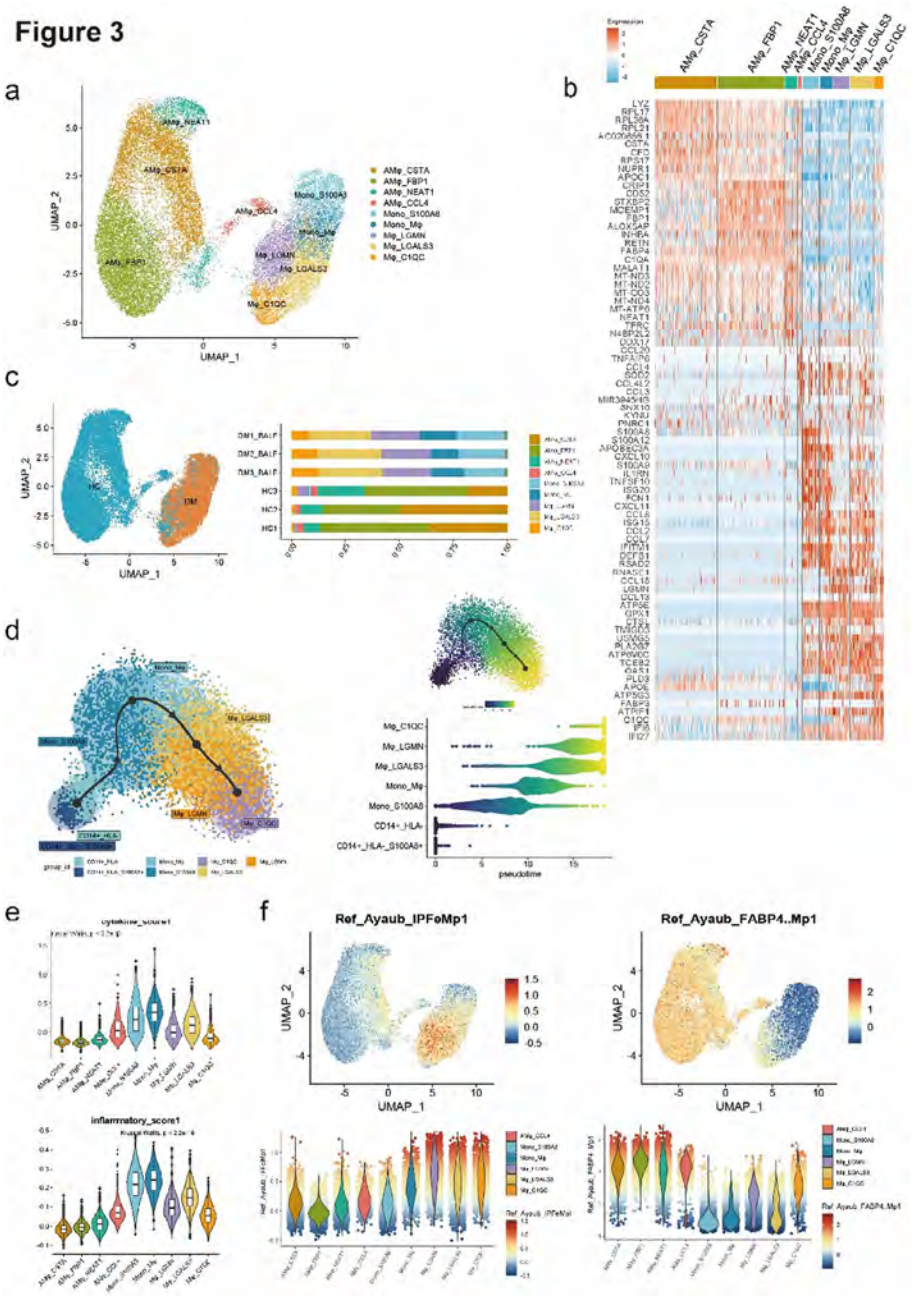


Figure 3. (a) UMAP plot of nine cell clusters of monocyte-macrophage in BALFs. (b) Heatmap showing top 10 marker genes for each cluster. (c) UMAP plot showing monocyte-macrophages across HCs and anti-MDA5+ DM patients. Bar plot showing the proportions of each monocyte-macrophage cluster in BALFs from individual subjects. (d) Pseudotime trajectory analysis of monocyte-macrophages in anti-MDA5+ DM patients. (e) Violin plots showing the cytokine scores and inflammatory scores of each monocyte-macrophage cluster. (f) Gene set module score of 'IPF-expanded macrophages' (IPFe-Mp) and alveolar FABP4+Mp (Ayaub et al., 2021), calculated based on single transcriptomes. Projected onto the UMAP embedding (top) and plotted as violin plots (bottom) across the monocyte-macrophage clusters. Dot color indicates signature module score. Violin colors show cluster identity.

Disclosure: X. Pei: None; **J. Shi**: None; **Y. Zhou**: None; **X. Zhang**: None; **X. Wang**: None; **M. Tang**: None; **S. Zhou**: None; **c. wu**: None; **J. Peng**: None; **M. Li**: None; **x. Zeng**: None; **J. Liu**: None; **H. Chen**: None; **Q. Wang**: None.

Abstract Number: 1589

Epigenetic Regulation of DNMT3A by TFEB and DOT1L Through AMPK Signalling Orchestrates the Lysosomal Response of Macrophages During Gout and Clonal Hematopoiesis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Innate Immunity
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Gout is the most common form of inflammatory arthritis worldwide, which is characterised by the deposition of monosodium urate crystals (MSUc) in the joints that leads to lysosomal damage and triggers the activation of the inflammasome leading to acute episodes of inflammation. **Clonal hematopoiesis** of indeterminate potential (CHIP) is defined as a common, age-related disorder marked by the expansion of blood-cell clones by somatic mutations, mainly in *DNMT3A* or *TET2*. Interestingly, individuals with CHIP have a higher risk of developing gout. In line with this, activating similar inflammatory programs raises the question of what epigenetic molecular mechanisms underlying the association between gout and CHIP are.

Methods: We performed ATAC-Seq, ChIP-Seq, RNA-Seq, Western Blot, RT-qPCR, ChIP-qPCR, LysoTracker staining, in murine bone marrow-derived macrophages and human monocyte-derived macrophages stimulated with MSUc for 5h. Tfeb KO, Dnmt3a KO and Tfeb overexpressing macrophages (Tfeb-Tg) were used. AMPK activators Metformin or A766992 and DOT1L inhibitor SGC0946 (DOT1Li) were used.

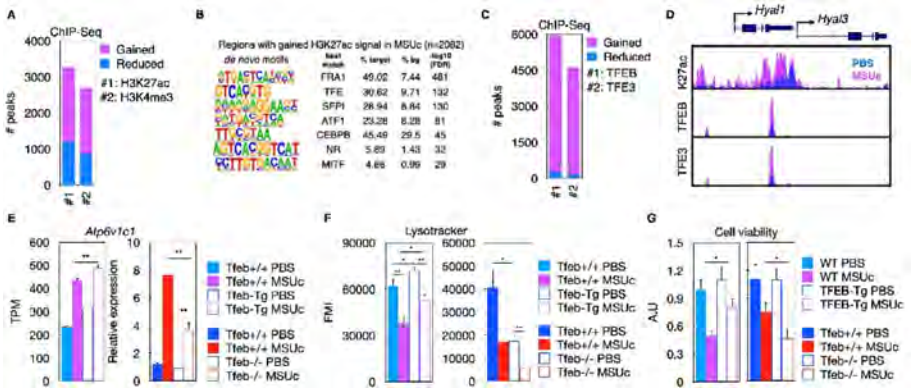

Figure 1. MSUc leads to an altered histone landscape with increased TFEB, which is required to activate the lysosomal program during gouty inflammation. (A) ChIP-Seq of H3K27ac and H3K4me3 in macrophages by MSUc. (B) Motif analysis of regions with gained H3K27ac signal. (C) ChIP-Seq of TFEB and TFE3 after stimulation with MSUc. (D) UCSC Browser composite of H3K27ac (K27ac), TFEB and TFE3 ChIP-Seq. (E-G) Analysis of Atp6v1c1 expression (E), LysoTracker staining (F) or cell viability (G) of macrophages over-expressing Tfeb (Tfeb-Tg) or Tfeb KO. TPM=transcripts per million reads. FMI=fluorescence mean intensity. N>3/experiment. Except for RNA-Seq experiments, Student T-test was used to calculate statistical significance.

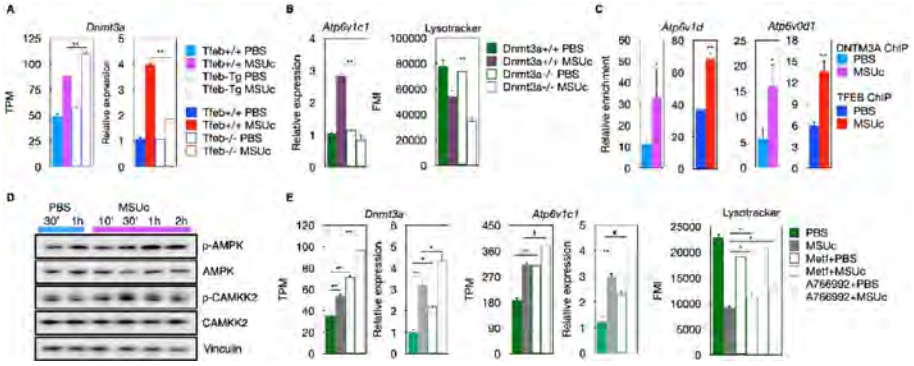

Figure 2. Upregulation of DNMT3A by TFEB through AMPK signaling is required to activate the lysosomal gene expression program by MSUc. (A) Expression analysis of Dnmt3a of macrophages over-expressing Tfeb (Tfeb-Tg) or Tfeb. (B) Expression of Atp6v1c1 (left) or LysoTracker staining (right) of wild type or Dnmt3a KO macrophages stimulated with MSUc. (C) Chromatin Immunoprecipitation of TFEB and DNTM3A over the promoter of Atp6v1d and Atp6v0d1. (D) Protein analysis by Western blot of AMPK signaling components. (E) Expression analysis of Dnmt3a (left), Atp6v1c1 (center) or LysoTracker staining (right) of macrophages incubated with Metformin (Metf) or A766992 prior to stimulation with MSUc. TPM=transcripts per million reads. FMI=fluorescence mean intensity. N>3/experiment. Except for RNA-Seq experiments, Student T-test was used to calculate statistical significance.

Results: We found over 2000 genomic regions with increased H3K27ac or H3K4me3 signal **(Figure 1A)**. These genomic regions are enriched in binding sequences for MITF/TFE transcription factors **(Figure 1B)** which are master regulators of lysosomal biogenesis. Interestingly, we found that stimulation by MSUc leads to an increased binding of TFEB and TFE3 over 4000 genomic regions **(Figure 1C)** associated with the promoter of lysosomal genes *Hyal1* and *Hyal3* **(Figure 1D)**. Moreover, whereas genetic overexpression of *Tfeb* (Tfeb-Tg) leads to increased expression of lysosomal genes including *Atp6v1c1*, higher LysoTracker staining and improved cell viability **(Figure 1E-G, left panel)**, the opposite is observed for Tfeb knock-out macrophages **(Figure 1E-G, right panel)**. In addition, we found that TFEB regulates *Dnmt3a* upregulation

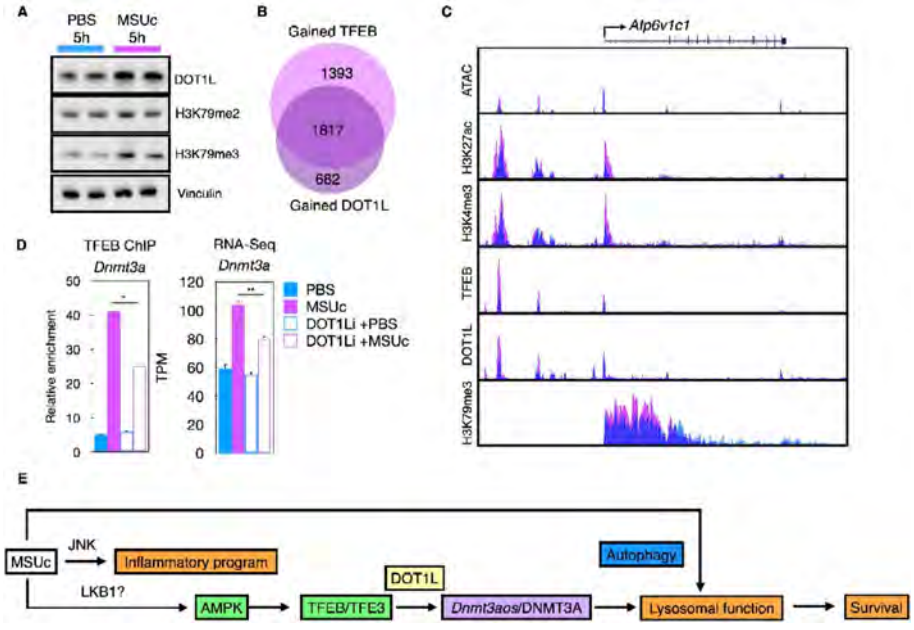

Figure 3. DOT1L is a TFEB binding partners that regulate Dnmt3a and lysosomal gene expression during gouty inflammation. (A) Protein analysis by Western blot for DOT1L and its downstream modified histone products. (B) Overlap between genes associated to increased TFEB and increased DOT1L signal by MSUc. (C) UCSC browser composite. (D) Chromatin immunoprecipitation of TFEB over the promoter of Dnmt3a (left) or Dnmt3a expression analysis (right) of macrophages incubated with DOT1L inhibitors prior to stimulation with MSUc. (E) Schematic summary of the response of macrophages to MSUc . TPM=transcripts per million reads. FMI=fluorescence mean intensity. N>3/experiment. Except for RNA-Seq experiments, Student T-test was used to calculate statistical significance.

by MSUc **(Figure 2A)** and that *Dnmt3a* deletion leads to downregulation of lysosomal gene expression and LysoTracker staining **(Figure 2B)**.

Moreover, we found that DNMT3A co-binds with TFEB over the promoter of *Atp6v1d*, and *Atp6v0d1* **(Figure 2C)**, indicating that TFEB and DNMT3A are part of the same genomic network. We also found that MSUc leads to activation of AMPK signaling **(Figure 2D)** and that treatment with AMPK activators Metformin or A766992 induces *Dnmt3a* and lysosomal gene expression and increases the LysoTracker staining by MSUc **(Figure 2E)**. Furthermore, we found that the histone-methyl transferase DOT1L is upregulated by MSUc **(Figure 3A)** and co-bind with TFEB **(Figure 3B)** and DNMT3A over the promoter of lysosomal genes such as *Atp6v1c1***(Figure 3C)**. Treatment with DOT1L inhibitor reduces the recruitment of TFEB to the promoter of *Dnmt3a*, thereby, downregulating *Dnmt3a* expression **(Figure 3D)**.

Conclusion: Our data indicate that DNMT3A cooperates with TFEB and DOT1L for the required regulation of lysosomal gene expression during gout flares by MSUc and provides a mechanistic explanation as to why patients with clonal hematopoiesis by *DNMT3A* mutations are at higher risk of developing more severe gout **(Figure 3E)**. Our data opens novel therapeutic possibilities for patients with clonal hematopoiesis and gout.

Disclosure: I. Cobo: None; **J. Murillo-Saich**: None; **M. Alishala**: None; **S. Calderon**: None; **R. Coras**: None; **N. Spann**: None; **A. Cheng**: None; **T. Prohaska**: ; **B. Razani**: None; **R. Terkeltaub**: atom biosciences, 2, dyve, 2, fortress, 2, generate biosciencez, 2; **B. Ebert**: Calico, 5, Exo Therapeutics, 1, 8, Neomorph, 12, Founder, SAB member, stockholder, Novartis, 5, Skyhawk Therapeutics, 1, 8, TenSixteen Bio, 12, Founder, SAB member, stockholder; **R. Liu Bryan**: None; **M. Guma**: Genentech, 5, Gilead, 5, Novartis, 5, Pfizer, 5; **C. glass**: None.

Abstract Number: 1590

Autoimmune Pathway Blockade by a Potent Orally Bioavailable STING Antagonist

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Innate Immunity
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: The cyclic GMP-AMP synthase (cGAS)-stimulator of interferon genes (STING) pathway has emerged as a key innate immune mediator of autoimmune and inflammatory diseases. However, the development of a drug-like STING antagonist remains challenging. Here, we report the discovery and characterization of RGT-118, a highly potent, selective and orally bioavailable small molecule STING antagonist for autoimmune disorders in preclinical models.

Methods: By leveraging the Computer Accelerated Rational Design (rCARD^{TM}) platform, we designed and synthesized a small molecule STING antagonist RGT-118. Cellular potency was measured in cGAMP stimulated THP-1 cells with IFN-b secretion as a readout. The absorption (MDCK based permeability assay and kinetic solubility), distribution (free fraction in plasma), and metabolism (liver microsomes, hepatocytes, plasma and blood stability) were characterized in *in vitro* assays. The pharmacokinetic (PK) study was performed in preclinical species to evaluate the exposure and bioavailability. Proof-of-mechanism (POM) studies were also performed using a mouse model in which the inhibition of RGT-118 on the

production of IFN-a, IFN-b, IL-6 and TNF-a was measured after being challenged with cGAMP. Trex1$^{-/-}$ mouse model was used to investigate the mechanistic activity of RGT-118. In addition, imiquimod-induced psoriasis model was used to evaluate the efficacy of RGT-118 in inhibiting disease development. Furthermore, to explore the therapeutic window of RGT-118, rat and dog 14-day dose-range finding (DRF) exploratory toxicity studies were performed.

Results: RGT-118 covalently binds to cysteine residue 91 in transmembrane domain, which blocks the activation induced palmitoylation of STING. The downstream pathways (i.e. type I IFN and NF-kB) mediated by cGAS-STING were attenuated by RGT-118 in a dose-dependent manner in both cellular assay and *in vivo* POM study. RGT-118 demonstrated good permeability and solubility *in vitro*. Furthermore, it showed good oral bioavailability and drug exposure *in vivo* in rat and dog. In Trex1$^{-/-}$ mice, treatment of RGT-118 significantly increased body weight and decreased ISGs and NF-kB related cytokines. Additionally, it showed comparable therapeutic effect in IMQ-induced psoriasis model with head-to-head comparison of PDE4i and anti-IL-17 treatment. Moreover, no severe toxicological signs were observed in both rat and dog 14-day dose-range finding studies and the no-observed-adverse-effect-level (NOAEL) of this compound was determined to be 200 mg/kg/day.

Conclusion: RGT-118 is a highly potent, selective and orally bioavailable small molecule STING antagonist with demonstrated efficacy in several preclinical animal models. With a favorable therapeutic window, RGT-118 provides therapeutic opportunities in multiple autoimmune and inflammatory diseases.

Disclosure: M. Yang: None; **H. Li**: None; **y. liu**: None; **l. yao**: None; **J. Lin**: None; **Z. xie**: None; **W. zhong**: None.

Abstract Number: 1591

Complement Factor D/Adipsin Knockout Mice Demonstrate Disparate Pain and Structural Damage Phenotypes in Obesity-induced Post Traumatic Osteoarthritis

Kelsey Collins[1], Kristin Lenz[2], Arin Oestreich[2], Luke Springer[2], Antonina Akk[2], Huimin Yan[2], Xiaobo Wu[2], John Atkinson[3], Christine Pham[4] and Farshid Guilak[4], [1]University of California San Francisco, San Francisco, CA, [2]Washington University in St. Louis, St. Louis, MO, [3]Washington University School of Medicine, St. Louis, MO, [4]Washington University, St. Louis, MO

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Osteoarthritis & Joint Biology – Basic Science
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Osteoarthritis (OA) is the leading cause of musculoskeletal pain, which is a primary driver of care-seeking behavior. There is lack of mechanistic information detailing the interface between OA pain and structural damage. Understanding pain signals independent of structural damage has been difficult using existing pre-clinical models. We have identified a mouse model that displays discordant knee pain and structural damage, which provides a unique opportunity to explore pain independently of structural changes. Mice that lack fat-derived adipsin (also known as complement factor D, FD) are protected from cartilage damage induced by the destabilization of the medial meniscus (DMM) but demonstrate increased sensitivity to pressure-pain hyperalgesia. The goal of this study is to determine the mechanism by which FD modulates pain in OA.

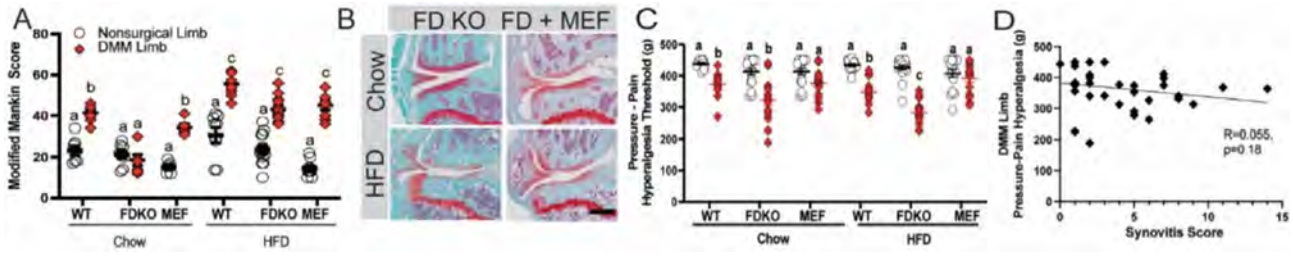

Figure 1. Modified Mankin Score (A), red diamonds indicate limbs challenged with destabilization of the medial meniscus (DMM), circles contralateral limbs, Mouse Embryonic Fibroblast (MEF) indicates FD KO + MEF; (B) Medial tibial plateau Safranin-O/Fast Green histology sections of DMM limbs (black bar indicates 100μm); (C) pressure-pain hyperalgesia measured by SMALGO on DMM (red diamonds) and nonsurgical (circles) limbs; (D) relationship between synovitis score and DMM-limb pressure-pain hyperalgesia is not significant (p=0.18), indicating that the hyperalgesia phenotype is not explained by synovitis. Different letters indicate $p<0.05$ by ANOVA, data are shown as mean ± standard error.

Methods: FD KO mice and WT controls (7-12/group) were fed chow (10% kcal fat) or high-fat diet (HFD, 60% kcal fat). To restore circulating FD, FD KO mice were transplanted with mouse embryonic fibroblast (MEF)-derived fat implants. At 16-weeks, mice underwent destabilization of the medial meniscus (DMM) unilaterally to induce OA. At 26-weeks, forelimb grip strength, knee hyperalgesia (via small animal algometer) and tactile allodynia (Electronic von Frey) were assessed. Knee joints were evaluated using a Modified Mankin Score and immunohistochemistry for C3 and C5-9. Bulk RNA sequencing was performed on L3-L5 dorsal root ganglia (DRG). Data were analyzed by repeated measures of ANOVA (genotype, limb, diet) and post hoc testing.

Results: Chow-fed FD KO mice were protected from DMM-induced structural OA (Fig. 1a,b) but not from increased synovitis, osteophyte formation, or pain in the DMM limb (Fig. 1c). Specifically, chow-fed FD KO mice demonstrated reduced pressure-pain thresholds and increased tactile allodynia when compared to WT DMM limb. Protection against DMM-induced cartilage damage was reversed in HFD FD KO mice (Fig.1a). There was no evidence of an alternative pathway (AP) bypass mechanism to explain this reversal in phenotype suggesting that complement is dispensable for structural damage under HFD conditions. However, HFD FD KO mice demonstrated lower pressure-pain threshold, or increased hyperalgesia at the knee (Fig. 1c), despite having a similar Modified Mankin Score to HFD WT DMM limbs (Fig. 1a,b). Restoration of AP activity using MEF transplantation in both diet groups induced a reversal of pain thresholds in FD KO to corresponding WT DMM limb levels, suggesting a role for FD in joint pain (Fig. 1c). Gene ontology (GO) analysis of DRG from FD KO mice revealed differentially expressed genes associated with neutrophil infiltration and histone modifications. Lastly, no significant relationship was found between pain and synovitis (Fig. 1d).

Conclusion: We observed paradoxically heightened pain phenotype in the FD KO mice post DMM suggesting that this model can be used to dissect the clinical discordance between subjective pain and objective joint structural damage. Understanding the mechanism by which FD modulates the DRG neuroimmune profile in regulating OA pain may inform whether therapeutic targeting of complement activity will be beneficial in OA treatment.

Disclosure: K. Collins: None; **K. Lenz**: None; **A. Oestreich**: Agathos Biologics, 10; **L. Springer**: None; **A. Akk**: None; **H. Yan**: None; **X. Wu**: None; **J. Atkinson**: Alexion Pharmaceuticals, 2, Alnylam Pharmaceuticals, 2, Celldex Therapeutics, 2, Genentech, 2, Idera Pharmaceuticals, 2, Kereos Inc, 2; **C. Pham**: Insmed, 1, 9; **F. Guilak**: None.

Abstract Number: 1592

Memantine Attenuates the Development of Osteoarthritis by Blocking NMDA Receptor Mediated Calcium Overload and Chondrocyte Senescence

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Osteoarthritis & Joint Biology – Basic Science

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Memantine is an FDA proved drug utilized for the treatment of dementia and exerts its function by blocking the NMDA (N-methyl-D-aspartate) receptor, a calcium permeable ion channel that reduces cytotoxic calcium overload. Chondrocyte senescence is a crucial cellular event that contributes to articular cartilage degeneration during osteoarthritis (OA) development. However, little information has been reported regarding the effects of memantine and its downstream NMDA receptor on chondrocyte senescence and OA.

Methods: The protein levels of the NMDA receptor and its agonistic ligand, glutamate, were compared in OA and normal chondrocytes. The amount of intracellular calcium ions and mitochondrial damage were evaluated using specific fluorescent probes and transmission electron microscopy (TEM). Senescence-associated β-galactosidase (SA-β-gal) staining and $p16^{INK4a}$ were analyzed to assess chondrocyte senescence. The function of the NMDA receptor in chondrocyte senescence and OA were tested through agonists activation and gene knockout experiments. The therapeutic effects of memantine on OA were tested both in vitro and in vivo. Additionally, to verify the findings from animal samples, a propensity score matched human cohort study using the IQVIA Medical Research Data primary care database in the UK was conducted to compare the risk of OA associated joint replacement (the clinically relevant endpoint of OA) in memantine initiators with initiators of active comparator, i.e., acetylcholinesterase (AchE), among patients with dementia.

Results: The protein expression of the NMDA receptor and the secretion of glutamate were both significantly higher in OA chondrocytes. Activation of the NMDA receptor stimulated chondrocyte calcium overload, which resulted in mitochondrial fragmentation and chondrocyte senescence. Inhibiting the NMDA receptor by memantine and knockout NR1, the gene encoding NMDA receptor, resulted in reduced calcium influx, mitochondrial fragmentation as well as cellular senescence in OA chondrocyte. In addition, intra-articular injection of memantine in OA mice model exhibited protective effects on cartilage degeneration. What's more, in the 1:5 propensity-score matched cohort study consisted of 6,218 patients (n=1,435 in memantine cohort; n=4,783 in AchE cohort), memantine initiators was associated with a lower risk of OA-associated joint replacement compared with AchE initiators (hazard ratio=0.57, 95% confidence interval: 0.34 to 0.99).

Conclusion: As a clinically licensed drug used for dementia, memantine shows promising therapeutic effects on OA. Mechanistically, it blocks NMDA receptor-mediated chondrocyte senescence. The protective effects of memantine on OA were verified not only through in vitro and in vivo experiments but also via a propensity-score matched human cohort study. These findings present robust evidence for repurposing memantine for the treatment of OA.

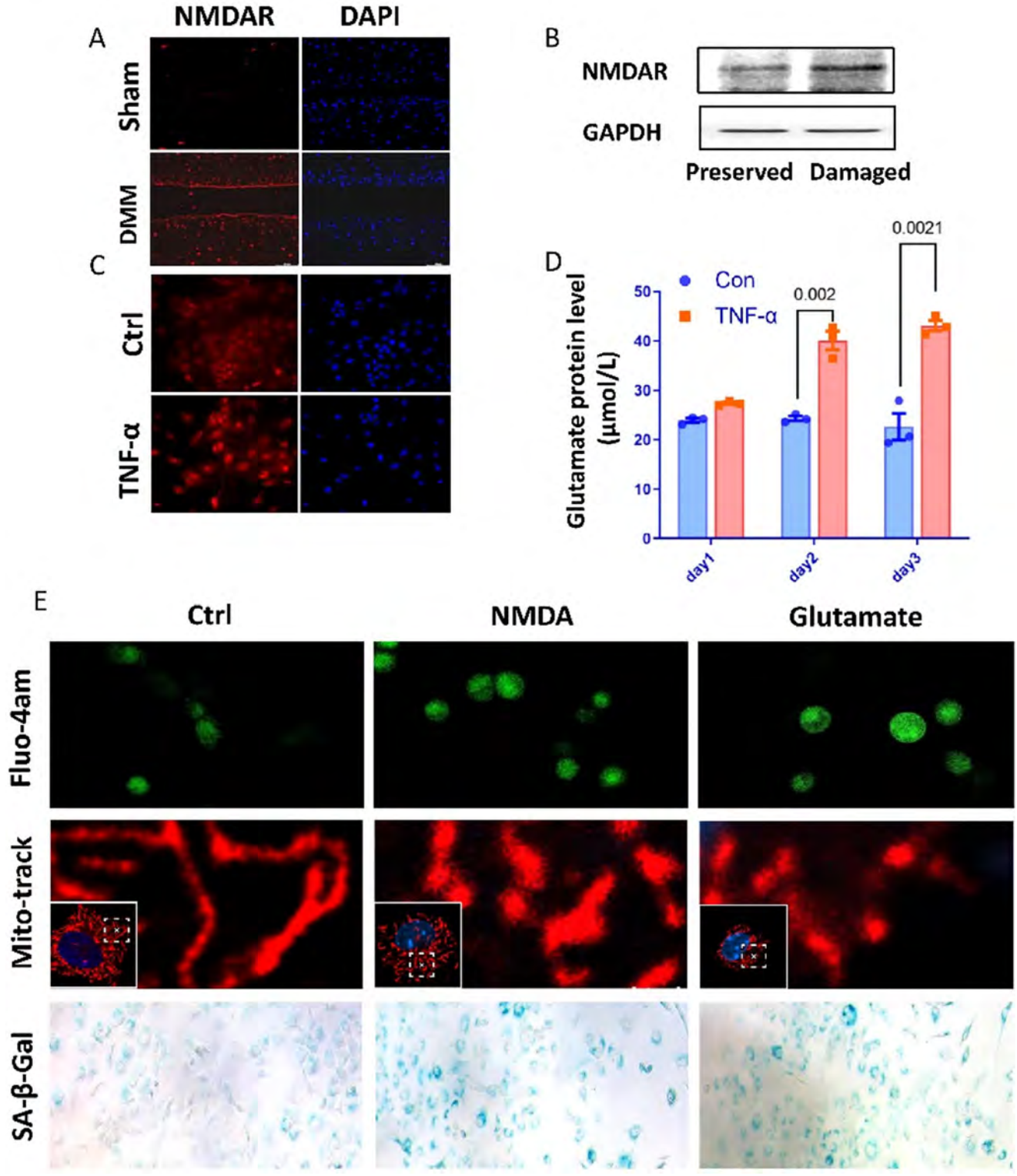

Figure 1. OA progression accompanied by highly expressed and activated levels of NMDA receptor that led to mitochondrial fragmentation and chondrocyte senescence. Immunostaining was used to analyze the level of NMDA receptor in the destabilization of the medial meniscus (DMM) surgery-induced OA mice knee joint (A), as well as the inflammatory-induced OA chondrocyte (C). The protein level of NMDA receptor in preserved and damaged cartilage from OA patients (B). The secretion of glutamate from OA chondrocytes in cell culture medium (D). The calcium probe Fluo-4am, the mitochondrial probe mito-tracker, and the SA-β-gal staining were used for chondrocytes stimulated with NMDA or glutamate (E).

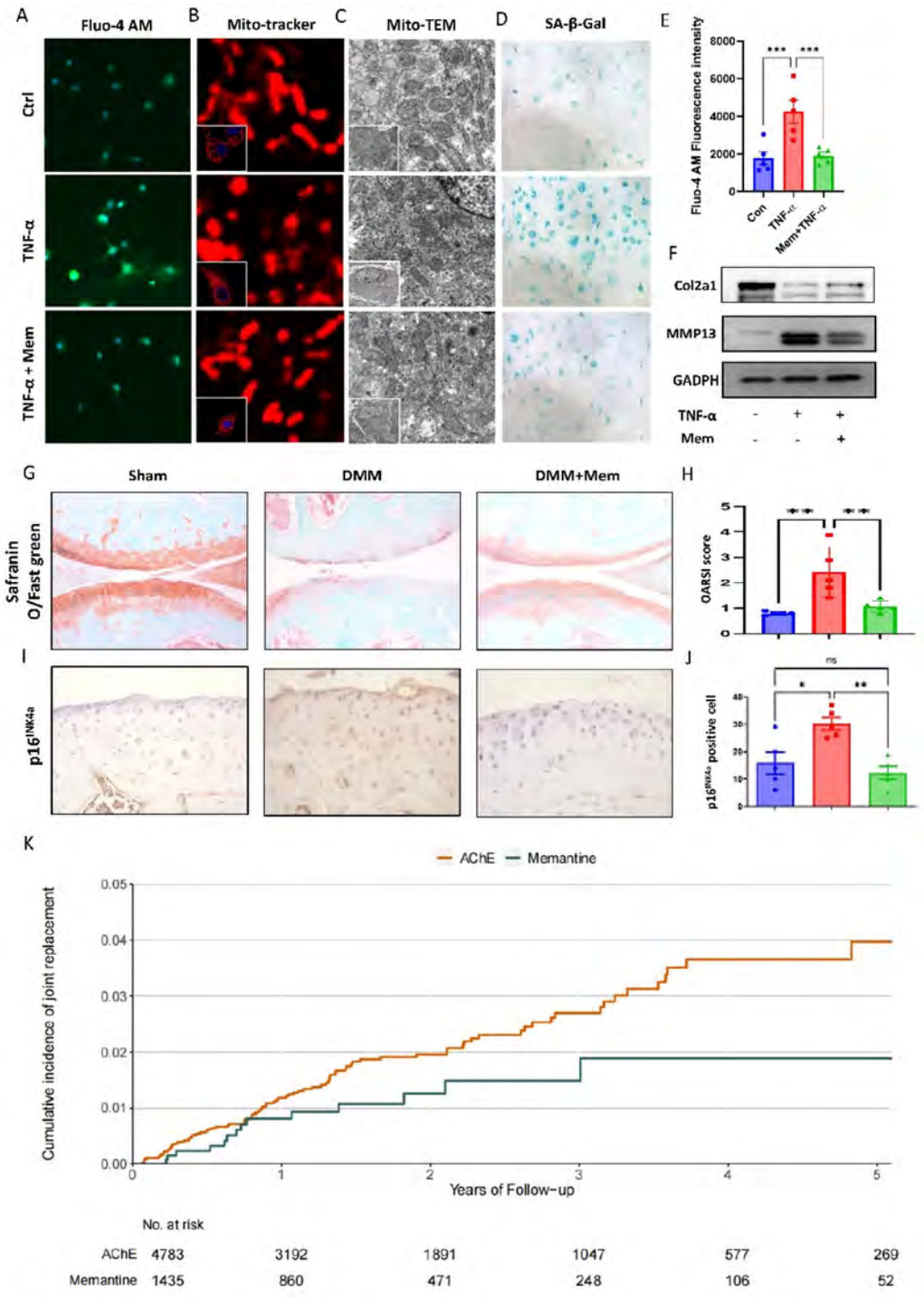

Figure 2. Memantine protects against OA and is associated with reduced risk of knee or hip OA-associated joint replacement among patients with dementia. The Fluo-4am (A), mito-tracker (B), TEM (C), and SA-β-gal staining (D) were used for OA chondrocytes stimulated with Memantine or not. Semi-quantification of calcium overload based on the staining (E). Protein levels of Col2a1 and MMP13 were detected (F). Safranin O/Fast green staining (G) and OARSI score (H), p16INK4a immunohistochemistry staining (I), and semi-quantification (J) for DMM-induced OA model. Cumulative incidence of knee or hip osteoarthritis-associated joint replacement in 1,435 memantine users and 4,783 AchE users (K), matched by propensity score.

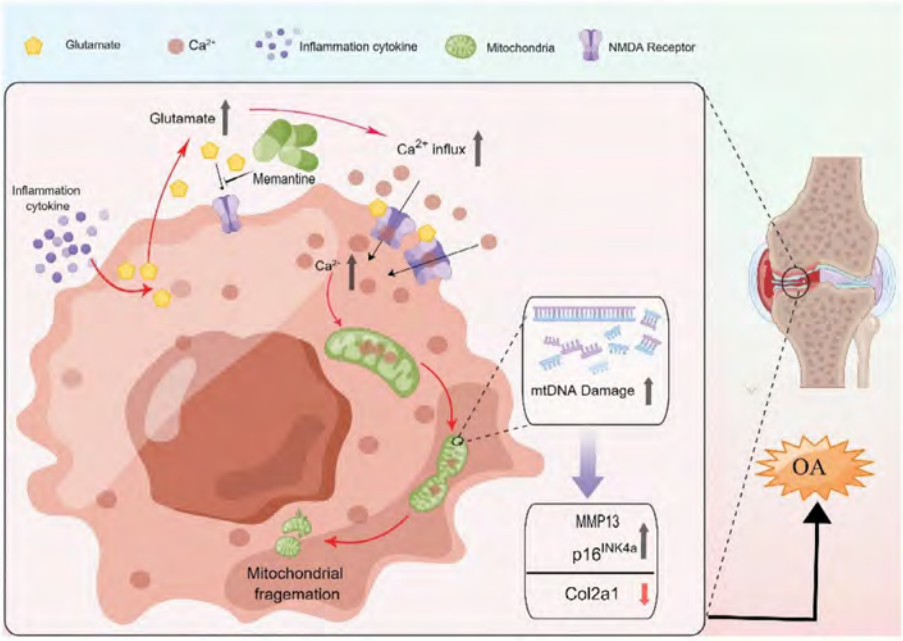

Figure 3. The mechanistic diagram of memantine as a potential chondroprotective drug for OA.

Disclosure: N. Wang: None; **Q. Cheng**: None; **X. Li**: None; **k. he**: None; **J. Zhu**: None; **H. Li**: None; **J. Wei**: None.

Abstract Number: 1593

Combining Single-cell RNA Sequencing and Population-based Studies Reveals Hand Osteoarthritis-associated Chondrocyte Subpopulations and Pathways

Hui Li[1], Xiaofeng Jiang[1], Yongbing Xiao[1], Yuqing Zhang[2], Weiya Zhang[3], Michael Doherty[3], Jacquelyn Nestor[4], Changjun Li[5], Jing Ye[1], Tingting Sha[6], Houchen Lyu[1], Jie Wei[7], Chao Zeng[1] and Guanghua Lei[1], [1]Department of Orthopaedics, Xiangya Hospital, Central South University, Changsha, China, [2]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, MA, [3]Academic Rheumatology, Clinical Sciences Building, University of Nottingham, City Hospital, Nottingham, United Kingdom, [4]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, [5]National Clinical Research Center for Geriatric Disorders, Xiangya Hospital, Central South University, Changsha, China, [6]Hunan Key Laboratory of Joint Degeneration and Injury, Changsha, China, [7]Health Management Center, Xiangya Hospital Central South University, Changsha, China

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Osteoarthritis & Joint Biology – Basic Science

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Hand osteoarthritis (OA) is a common heterogeneous joint disorder with differences in etiology and pathophysiology from the large weight-bearing knee or hip OA. Its pathophysiological mechanism remains largely unexplored, partially because of limited access to clinical sample tissues and lack of animal models. To date, there is no known cure for hand OA, indicating an urgent need for better understanding of the underlying mechanisms to develop appropriate treatment strategies. Here, we aimed to identify hand joint chondrocyte subpopulations and investigate the molecular

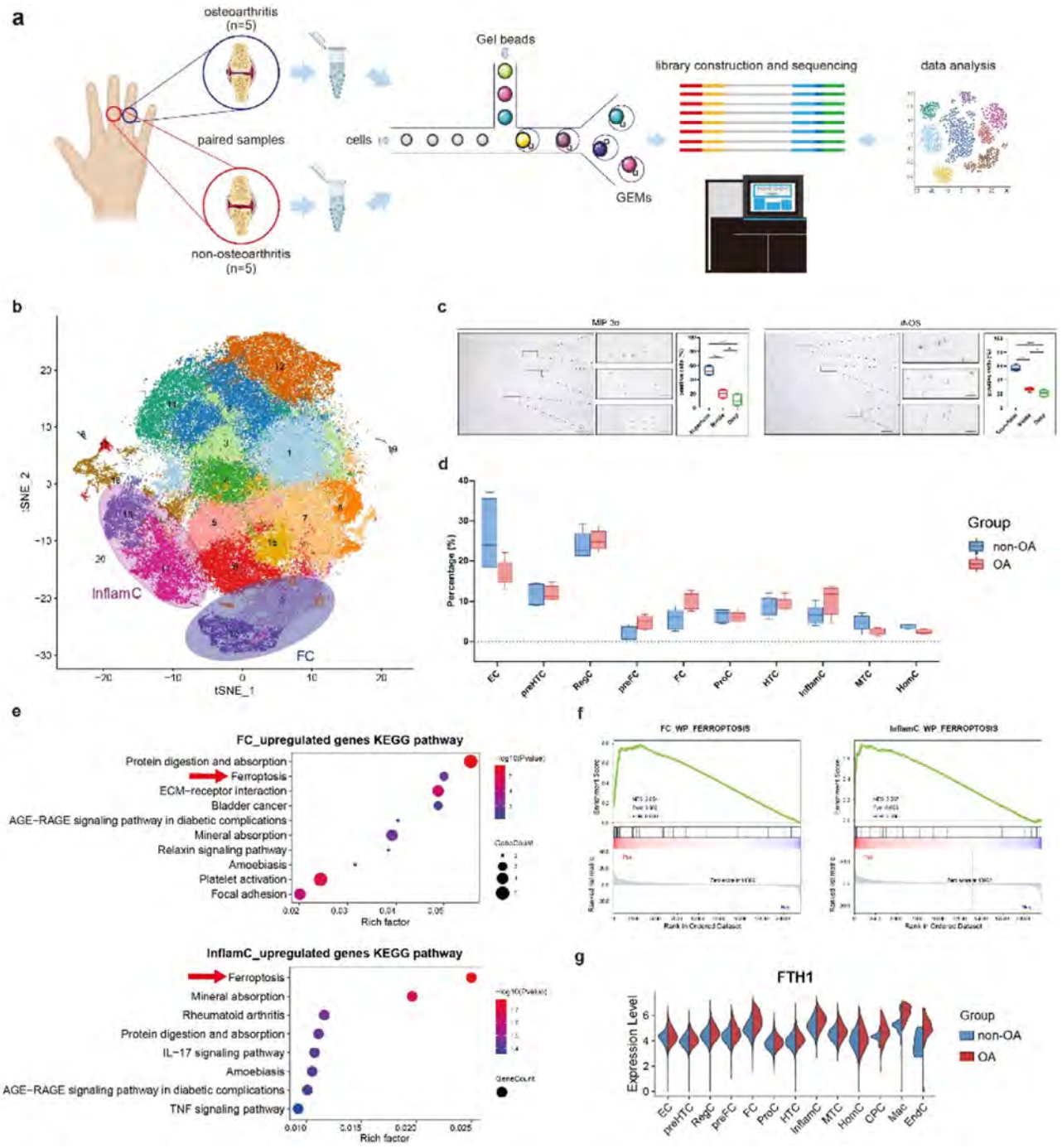

Figure 1. ScRNA-seq analysis of human hand OA and non-OA articular cartilage (a) Schematic workflow of single-cell RNA sequencing. (b) t-SNE embedding plot for 105,142 cells, derived from paired articular cartilage samples of five donors. (c) Representative immunohistochemistry (IHC) staining for MIP-3α and iNOS in hand articular cartilage tissues (n=4). Scale bar, left, 100 μm; right, 20 μm. ***P<0.001, ****P<0.0001. (d) Differential analysis of subpopulation abundance between osteoarthritic and non-osteoarthritic cartilage. Wilcoxon matched-pairs signed rank test was used for analysis. (e) KEGG enrichment analysis of the upregulated genes of FC and InflamC in hand OA. Arrows indicate ferroptosis enriched in the upregulated genes in osteoarthritic FC and InflamC. (f) GSEA analysis showing extensive enrichment of ferroptosis in the osteoarthritic FC and InflamC. (g) Violin plot showing the differential expression of FTH1 in all subpopulations between OA and non-OA cartilage. OA, osteoarthritis; FC, fibrocartilage chondrocytes; InflamC, inflammatory chondrocytes; KEGG, Kyoto Encyclopedia of Genes and Genomes; GSEA, gene set enrichment analysis.

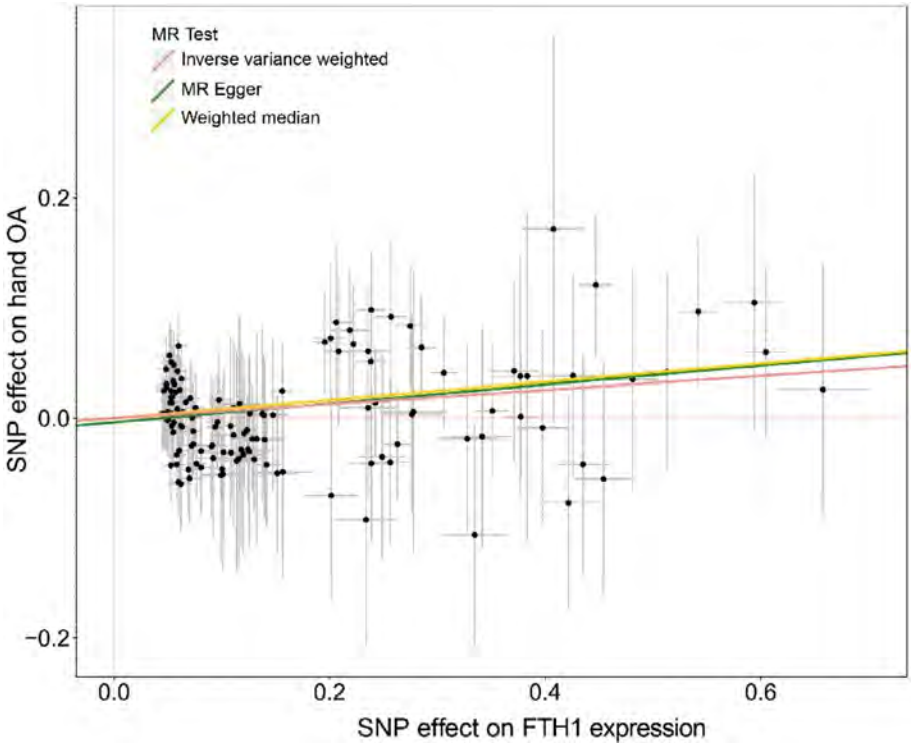

Figure 2. Mendelian randomization analysis of the causal association between FTH1 mRNA expression and risk of hand OA

mechanism of hand OA by performing single-cell RNA sequencing (scRNA-seq) analysis, and verify the findings in two large independent population-based studies.

Table 1. Association between serum ferritin levels and prevalence of hand OA

	Quintiles of serum ferritin, μg/L					*P*-for-trend
	Q1	Q2	Q3	Q4	Q5	
Hand (n)*	495	496	491	494	487	
Median of serum ferritin levels, μg/L	75.0	138.5	213.0	308.0	564.0	
Number of hand OA (%)	99 (20.0)	105 (21.2)	104 (21.2)	119 (24.1)	136 (27.9)	
Crude OR (95% CI)	1.00 (Ref)	1.07 (0.74-1.56)	1.07 (0.74-1.56)	1.27 (0.88-1.84)	1.55 (1.08-2.22)	0.037
Age-sex-BMI adjusted OR (95% CI)	1.00 (Ref)	1.31 (0.89-1.93)	1.23 (0.83-1.83)	1.46 (0.97-2.22)	1.69 (1.13-2.52)	0.005

OA, osteoarthritis; Q, quantile; n, number; OR, odds ratio; CI, confidence interval; BMI, body mass index; Ref, reference.
*The association between serum ferritin levels and hand osteoarthritis was evaluated by logistic regression model using generalised estimating equations (hand specific analysis).

Methods: We obtained hand interphalangeal joints from five donors who had destructive forearm injury. Using scRNA-seq analysis, we analyzed the cellular composition and subpopulation-specific gene expression of hand articular cartilage, and then compared these features between cartilages from joints with macroscopically confirmed OA (n=5) and those without OA (n=5). We further conducted: (1) a Mendelian randomization study using data from the UK Biobank to investigate the causal association between the key differentially expressed gene and hand OA; and (2) a cross-sectional study using data collected from a community-based observational study, i.e., the Xiangya OA (XO) Study, to examine the association between a serum biomarker (encoded by the key gene) and hand OA.

Results: Of 105,142 cells we identified 13 subpopulations, including a novel inflammatory chondrocyte subpopulation that specifically expressed genes related to inflammatory and immune response. Fibrocartilage chondrocytes represented a major source of OA-related proteases and exhibited an extensive alteration of gene expression patterns in OA cartilage compared with non-OA cartilage. Both inflammatory chondrocytes and fibrocartilage chondrocytes showed a trend towards increased numbers in hand OA cartilage. In these two subpopulations from OA cartilage, the ferroptosis pathway was enriched, in which the expression of iron overload-related genes, e.g., *FTH1*, was elevated. These findings are further validated by two independent population-based studies. Among participants (n=332,668) in the UK Biobank, genetic predisposition to higher expression of *FTH1* mRNA significantly increased the risk of hand OA (OR=1.07, 95%CI:1.02-1.11). Among participants (n=1,241) from the XO Study, high levels of serum ferritin (encoded by *FTH1*), a biomarker of body iron overload, were significantly associated with a high prevalence of hand OA (*P*-for-trend=0.037).

Conclusion: Our datasets will be valuable as a rich resource and open new possibilities for the research of molecular mechanism, drug development and precise treatment for hand OA. Inflammatory and fibrocartilage chondrocytes are key subpopulations and ferroptosis may be a key pathway in hand OA. Markers of these chondrocyte subpopulations, as well as ferroptosis inhibitors or iron chelators, could be focus of attention in future studies.

Disclosure: H. Li: None; **X. Jiang**: None; **Y. Xiao**: None; **Y. Zhang**: None; **W. Zhang**: None; **M. Doherty**: None; **J. Nestor**: None; **C. Li**: None; **J. Ye**: None; **T. Sha**: None; **H. Lyu**: None; **J. Wei**: None; **C. Zeng**: None; **G. Lei**: None.

Abstract Number: 1594

Oral Delivery of $\triangle^9$-Tetrahydrocannabinol Provides Symptom and Disease Modification in a Mouse Model of Knee Osteoarthritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Osteoarthritis & Joint Biology – Basic Science

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

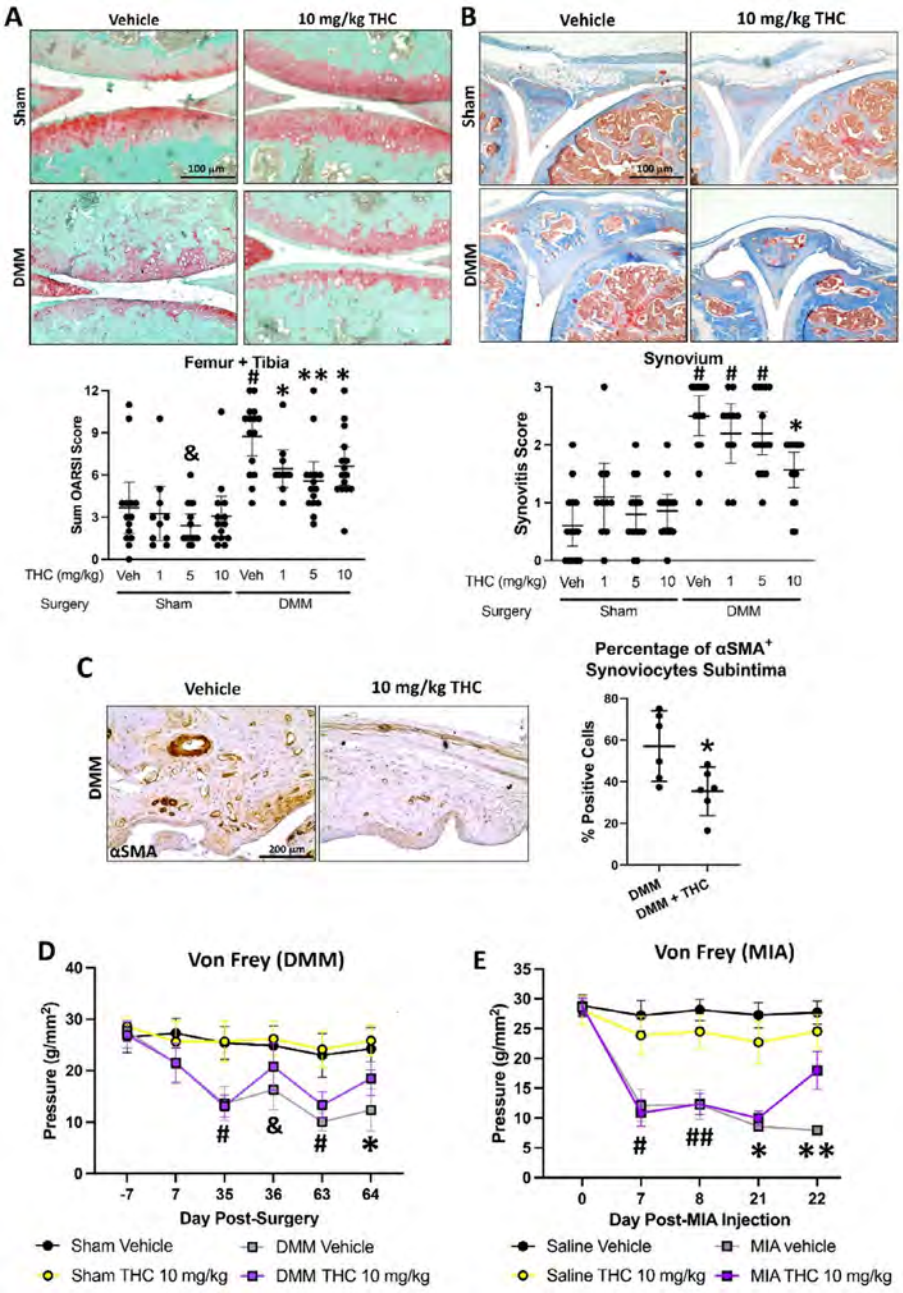

Fig 1. Oral administration of THC attenuates modifies disease progression and pain in OA-induced mice. Sham or DMM mice received treatment by oral gavage 5 days/week with vehicle [veh; medium chain triglyceride (MCT)] or THC (1, 5, 10 mg/kg) for 9 weeks. Knee joints were collected at 10 weeks post-surgery and stained with (A) Safranin O for OARSI scoring of cartilage degeneration and (B) Masson's Trichrome for synovitis, respectively (n=10-15/group). Data was analyzed by Kruskal-Wallis tests followed by Mann-Whitney post-hoc tests corrected for multiple comparisons using the method of Benjamini, Kreiger and Yekutieli using R v 3.5.03 with coin package v 1.3-24 to account for ties.*, &, or #, $q < 0.05$ compared to all other comparison groups with different or no symbols. (C) Representative images and quantification of synovial subintima IHC staining for αSMA in knee joint synovium collected from DMM mice given MCT or 10mg/kg THC treatment by oral gavage for 9 weeks (n=6/group). Data was log transformed prior to analysis by Student's two-tailed t-tests with Welch's correction. *, $p < 0.05$. (D) Sham and DMM-surgical mice (n=10-15/group) or (E) saline and MIA-injected mice (n=10-25/group) were administered vehicle (MCT) or 10 mg/kg THC by oral gavage and were evaluated for mechanical allodynia using the von Frey test. (D & E) Data was log-transformed prior to analysis by repeated measures two-way ANOVA followed by multiple comparison's tests using the method of Benjamini, Kreiger and Yekutieli to correct for false-discovery rate. (D) #, $q < 0.0001$ in DMM groups vs Sham groups. &, $q < 0.01$ for DMM + vehicle compared to Sham + vehicle or Sham + THC groups. *, $p < 0.05$ for all comparisons except between sham groups. (E)#, $p < 0.05$ for all comparisons except for MIA + saline vs. MIA + THC. ##, $p < 0.01$ for all comparisons except for MIA + saline vs. MIA + THC. *, $p < 0.05$ for all comparisons. **, $q < 0.05$ for all comparison and $q < 0.0001$ between MIA + vehicle and MIA + THC.

Background/Purpose: Osteoarthritis (OA) results in joint pain, cartilage degeneration, and synovitis. Recent studies suggest that some OA patients are self-medicating with cannabis. Δ^9-tetrahydrocannabinol (THC) is a prominent psychoactive phytocannabinoid in cannabis that can signal in joint cells, including chondrocytes and fibroblast-like synoviocytes (FLS). Currently, no studies link THC to disease modification in OA. We investigated effects and mechanisms of action of THC on pain and disease modification in pre-clinical models of knee OA.

Methods: OA was induced in male C57BL/6 mice by destabilization of the medial meniscus (DMM) or monosodium iodoacetate (MIA; 0.5 mg) and mice were administered THC (0, 1, 5 or 10 mg/kg) orally 5 days/week for 9 or 3 weeks, respectively. Von Frey tests were used to evaluate mechanical allodynia (pain) and open field tests were used to evaluate locomotion and anxiety. DMM knee joints were evaluated for cartilage degeneration/synovitis (OARSI scoring) and Ki67, αSMA, and collagen degradation (C2C) expression (immunohistochemistry). Human FLS and chondrocytes were cultured with 1 mM THC for 48h. RNA was sequenced to determine differentially expressed genes (DEGs; FDR-adjusted $p< 0.05$; absolute FC≥1.5) and DEG-enriched pathways. Pathway and transcription factor enrichment analyses were used to determine putative cellular mechanisms and transcriptional regulators modified by THC.

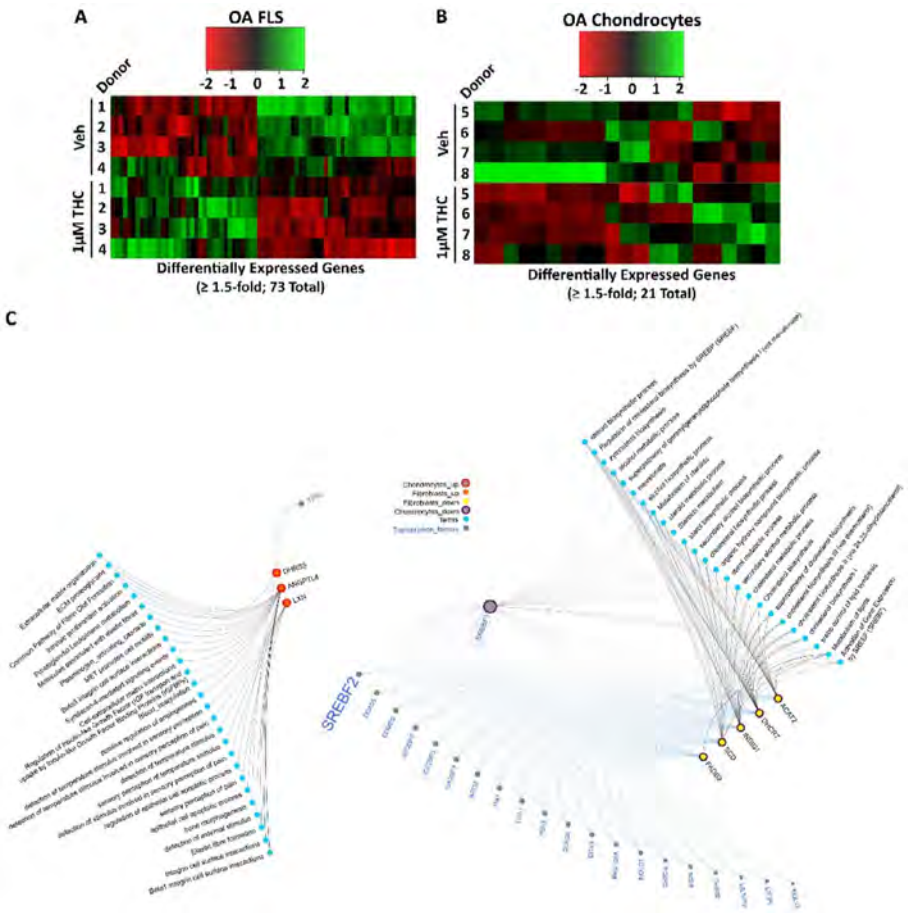

Fig 2. RNA Sequencing of THC-treated human OA fibroblast-like synoviocytes (FLS) or chondrocytes identifies differentially expressed genes (DEGs) associated with ECM and lipid metabolism pathways. Human OA FLS and chondrocytes were treated with 1 μM THC and was isolated after 48h and subjected to RNA sequencing. (A) Heat map shows the 73 DEGs from human OA FLS and (B) 21 DEGs from human OA chondrocytes stimulated with 1μM THC compared to vehicle-treated controls (veh; 0.5% DMSO) (n=4/group). (C) Network analysis shows combined transcription factors [determined by analysis through Catrin (http://ophid.utoronto.ca/Catrin/index.jsp] and protein-protein interactions (PPIs) with the overlapping DEGs and linked pathways [identified through analysis using pathdip (http://ophid.utoronto.ca/pathDIP/) and Gene Ontology Annotation analysis] in FLS and chondrocytes after THC treatment compared to vehicle-treated cells. Red nodes with red outlines represent upregulated genes and yellow nodes with purple outlines represent the downregulated genes in both FLS and chondrocytes after THC treatment. Grey lines connect genes to interacting pathways (blue nodes) and blue lines connect genes to predicted upstream TFs (grey nodes). Note SREBF2 is a putitive upstream regulator of common genes downregulated in both OA FLS and chondrocytes.

Results: In DMM mice, all THC doses reduced cartilage degeneration. 10 mg/kg THC also reduced synovitis (n=14-15/group) and synovial αSMA expression, but not Ki67 or C2C expression (n=6/group). Administration of 5 or 10 mg/kg THC in DMM (n=14-15/group) or MIA (n=10 25/group) mice reduced pain, particularly with 10 mg/kg administration (Fig. 1). Locomotion or anxiety were not modified longitudinally by THC administration. In cultured OA FLS (n=4), RNA sequencing identified 73 DEGs (35 up, 38 down) after treatment with 1 mM THC for 48h compared to vehicle. In cultured OA chondrocytes (n=4), 21 DEGs (9 up, 12 down) were identified after treatment with 1 mM THC compared to vehicle. Computational biology analyses found extracellular matrix (ECM)-related pathways were enriched in the upregulated DEGs in both fibroblasts and chondrocytes, while lipid/steroid/cholesterol-related pathways were enriched in the downregulated DEGs in both cell types. Three genes were commonly upregulated while 5 genes were commonly downregulated in FLS and chondrocytes by THC treatment. From FLS and chondrocyte downregulated DEGs, 22 common putative transcription factors were identified as potential regulators, with SREBF2 as a candidate of interest (Fig. 2).

Conclusion: Oral administration of 10 mg/kg THC reduced cartilage degeneration synovitis and synovial αSMA expression in DMM mouse knee joints, and modified pain in both DMM and MIA OA models. THC treatment of human OA FLS or chondrocytes modified expression of genes associated with ECM and lipid-based pathways, with common genes and putative regulatory transcription factors identified, including SREBF2. We are currently investigating contributions of SREBF2 to effects of THC on joint cells in vitro and mechanisms of pain in vivo.

Disclosure: J. rockel: None; **A. Maglaviceanu**: None; **H. Fetter Filippini**: None; **E. Wasilewski**: None; **M. Lewis-Bakker**: None; **S. Gabrial**: None; **E. Rossomacha**: None; **J. Garcia**: None; **N. Mahomed**: AIC, 4, ARTHUR HEALTH CORP, 3; **T. Leroux**: Depuy Synthes, 2, Smith and Nephew, 2, Stryker, 2; **H. Clarke**: AbbVie/Abbott, 6, Managing Life, 2, Master Clinician Alliance, 6, Ontario Ministry of Health and Long Term Care, 5, Shoppers Drug Mart, 5; **R. Bonin**: None; **L. Kotra**: None; **M. Kapoor**: None.

Abstract Number: 1595

Pharmacological Modulation of Krüppel-like Factor 4 Reduces the Severity of Experimental Osteoarthritis via Tissue Protection and Regeneration

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Osteoarthritis & Joint Biology – Basic Science
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Krüppel-like factors (KLFs) are members of the zinc finger family of transcription factors, which includes 17 members in mammals. We found that expression of KLF4 is dysregulated with progression of osteoarthritis (OA) in human and mouse knee cartilage. Further, we identified KLF4 as a new central transcription factor that regulates protective and regenerative functions in joint tissue cells. We hypothesized that molecules that increase KLF4 expression would be novel therapeutic candidates for OA.

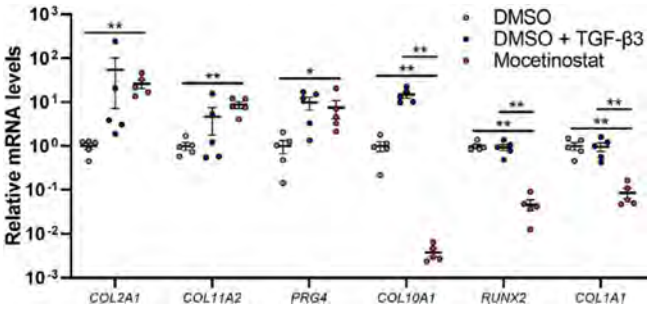


Figure 1. Regulation of chondrogenic and hypertrophic genes by mocetinostat in human BMSC pellets. Human BSMCs were cultured in pellets, and were treated with mocetinostat, or DMSO + TGF-b3. RNA was collected one week after pellet culture. mRA levels are expressed as means +SE, relative to DMSO (n=5 donors). *P<0.05, **P<0.01, Dunnett's test versus mocetinostat.

Methods: We performed high throughput drug screening (HTS) using the Repurposing, Focused Rescue, and Accelerated Medchem (ReFRAME) library with 11,948 clinical-stage molecules. Hit compounds were tested in joint tissue cells The lead compound was tested in the surgical destabilization of the medial meniscus (DMM) model of OA. As mechanistic studies included transcriptomic and proteomic profiling.

Results: Fifty-one hit compounds were identified in the HTS, and 18 compounds were confirmed in a secondary screen. We validated the 18 hits using SW1353 cells and human chondrocytes, and found that mocetinostat, a class I histone deacetylase (HDAC) inhibitor, had the best profile of biological activities. While mocetinostat upregulated KLF4, KLF2, FOXO1 and cartilage signature genes such as COL2A1, COL11A2, SOX9 and PRG4 in human chondrocytes, meniscal cells and pellet-cultured BMSCs, it down-regulated hypertrophic and catabolic genes, including COL10A1, RUNX2, ADAMTS5 and IL6 (Figure 1 for pellet-cultured BMSCs). Mocetinostat enhanced protective functions in human chondrocytes and synoviocytes through down-regulation of inflammatory and catabolic genes. Intraperitoneal administration of mocetinostat into mice after surgical OA induction significantly improved pain behaviors and reduced the severity of OA histopathological changes

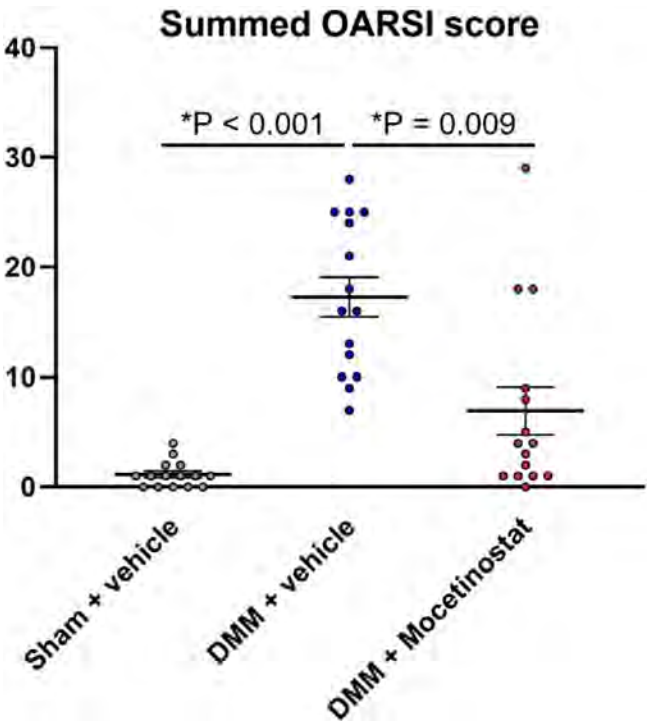


Figure 2. Therapeutic effects of OA by mocetinostat. Summed OARSI scores for the medial femoral condyle and the tibial plateau are expressed as means +SE (n=15 for each group). *P<0.05 versus DMM + vehicle, Dunn's test.

in cartilage, meniscus, and synovium (Figure 2 for the summed OARSI scores). We performed RNA-seq and TMT mass spectrometry analysis using mocetinostat-treated TC28a2 cells. While the significantly upregulated genes and proteins showed enrichment of Rap1 signaling pathway and ECM-receptor interaction previously shown to be modulated by KLF4, several unique pathways and terms were also enriched such as PPAR signaling pathway, suggesting novel regulatory mechanisms of HDAC inhibitors.

Conclusion: The class I HDAC inhibitor mocetinostat was identified through the HTS of compounds activating endogenous expression of KLF4. Mocetinostat increased protective and regenerative functions in joint tissue cells and reduced the severity of experimental OA in mice, qualifying it as a novel potential therapeutic candidate for OA.

Disclosure: M. Kawata: None; **M. Olmer**: None; **K. Johnson**: None; **M. Lotz**: None.

Abstract Number: 1596

A Cell and Transcriptomic Atlas of the Infrapatellar Fat Pad from Patients with Knee Osteoarthritis: Identification of an Obesity-Associated Transcriptomic Signature

Hayley Peters[1], Pratibha Potla[1], Jason Rockel[1], Keemo Delos Santos[1], Shabana Vohra[1], starlee lively[2], Kim Perry[3], Anthony Perruccio[1], Nizar Mahomed[4], Raja Rampersaud[1], Rajiv Gandhi[5] and **Mohit Kapoor**[6], [1]Schroeder Arthritis Institute, Toronto, ON, Canada, [2]University Health Network, Toronto, ON, Canada, [3]Schroeder Arthritis Institute, University Health Network, Toronto, ON, Canada, [4]Division of Orthopaedics, Osteoarthritis Research Program, Schroeder Arthritis Institute, Krembil Research Institute, and Toronto Western Hospital, University Health Network, Toronto, ON, Canada, [5]Schroeder Arthritis Institute, Krembil Research Institute, University Health Network and Division of Orthopaedics, Department of Surgery, University of Toronto, Toronto, ON, Canada, [6]Schroeder Arthritis Institute, University Health Network and Department of Surgery, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Osteoarthritis & Joint Biology – Basic Science

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Knee osteoarthritis (KOA) is the most common form of arthritis that affects multiple knee joint tissues. The infrapatellar fat pad is the largest fat pad in the knee; however, its cell composition, including associated transcriptomic profiles, during KOA are not well described. Defining these cellular and transcriptomic profiles is crucial to defining the role of the infrapatellar fat pad in KOA pathogenesis. In this study, we subjected infrapatellar fat pad from KOA patients to high throughput single nuclei RNA sequencing (snRNAseq) and advanced bioinformatics to identify and define the cellular and transcriptomic atlas of KOA fat pad. Furthermore, we investigated transcriptomic differences in cell subsets identified in the fat pad of obese BMI patients compared to normal BMI patients with KOA.

Methods: Infrapatellar fat pad was obtained from late-stage KOA patients [KL grades III/IV; n=15; 53% females, 47% obese, BMI 30-40 and 53% non-obese, BMI 18.5-25] undergoing total knee arthroplasty and subjected to snRNAseq. Nuclei were sequenced on an Illumina NextSeq 550 using the 150bp high output sequencing kit. Cluster analysis, advanced bioinformatics and pathway analyses were employed to identify key cell types, cell subsets, cell transcriptomic profiles and biological pathways.

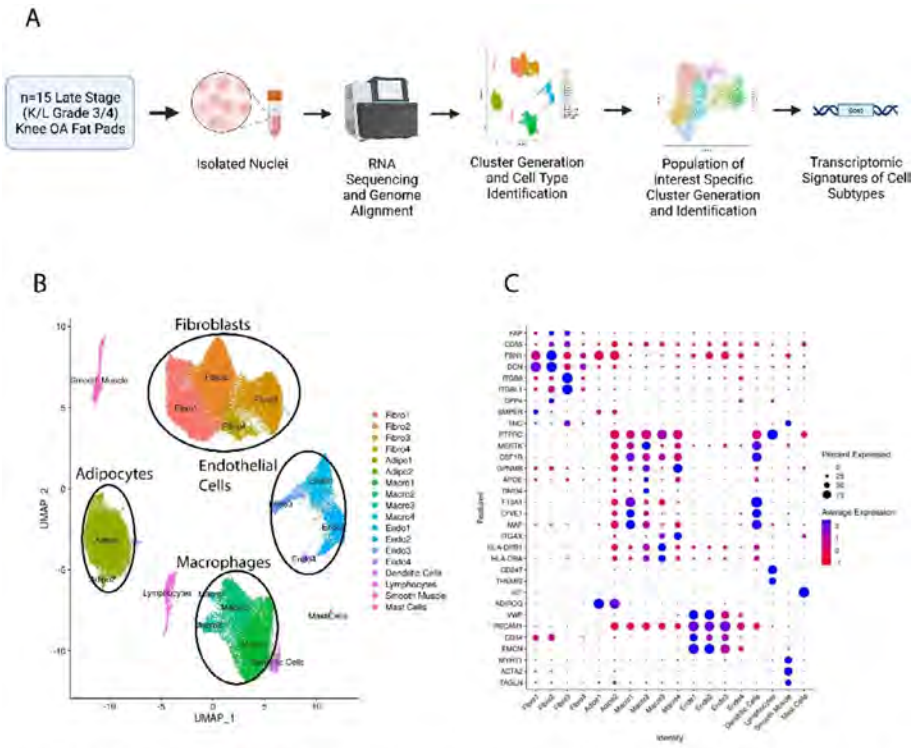


Figure 1: Infrapatellar Fat Pad Cell Populations A) Schematic workflow to identify cell subtypes and their functions within a fat pad. B) Uniform manifold approximation and projection (UMAP) of snRNA seq data of eight normal BMI (18.5 – 25) and seven obese BMI (30 – 40) fat pad samples with late-stage knee OA. C) Dot plot with the average expression of canonical cell surface markers for each cell population.

Results: Clustering analysis of snRNAseq data identified multiple cell populations based on canonical cell surface markers (Fig 1). The major cell types observed within the fat pad include fibroblasts (43.3%), macrophages (20.8%), adipocytes (18.5%), and endothelial cells (11.6%) (Fig 1). Interestingly, each major cell population identified had multiple cell subsets with unique transcriptomic profiles. Specifically, we identified nine distinct fibroblast cell subsets, four macrophage subsets, two adipocyte subsets and six endothelial subsets, each with unique transcriptomic profiles of highly expressed genes (Fig 2). We did not identify any differences in the proportions of fibroblast subsets when comparing normal BMI and obese BMI fat pads; however, we did identify a distinct transcriptomic signature with uniquely upregulated and downregulated genes in fibroblasts of the fat pad from obese BMI KOA patients compared to normal BMI KOA patients (Fig 3). We are now employing computational analyses of identified transcriptomic signatures and functional assays using primary fat pad fibroblasts of KOA patients to elucidate the mechanisms associated with the transcriptomic differences in obese BMI versus normal BMI KOA patients.

Conclusion: Using snRNAseq, we have generated a KOA fat pad transcriptomic and cell atlas. We have identified distinct cell subsets and transcriptomic profiles of fibroblasts, adipocytes, macrophages, and endothelial cells in the fat pad of patients with KOA. We also uncovered differences in transcriptomic profiles within fat pad fibroblasts of obese BMI KOA patients compared to normal BMI KOA patients. Further investigations regarding the contributions of these transcriptomic profiles and their function within the OA fat pad are currently underway.

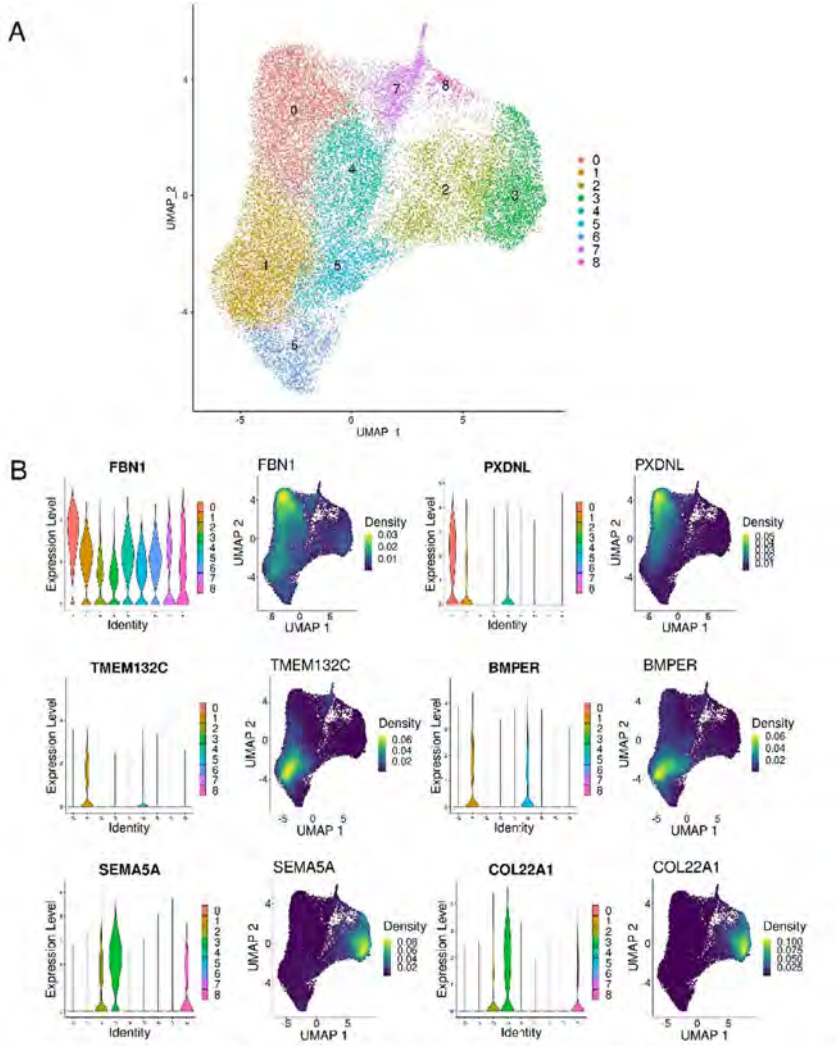


Figure 2: Fibroblast Subsets Present within Infrapatellar Fat Pad A) Projection of fibroblast subsets only from snRNA seq data of the 15 sequenced fat pad samples with late-stage knee OA. B) Violin plots and nebulosa plots displaying the expression of the top two significantly differentially expressed genes within the major fibroblast subsets 0, 1 and 3. Nebulosa plots display expression density from dark purple (low) to yellow (high).

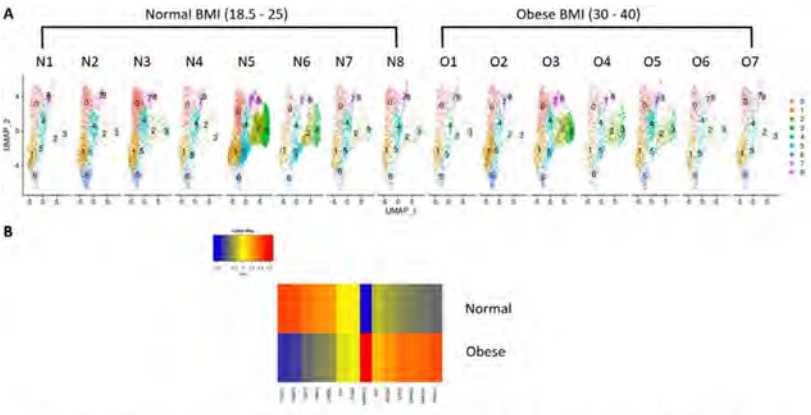


Figure 5: Transcriptomic Differences in Fibroblast Subsets Based on BMI A) Cell projections showing the contribution of fibroblast subsets within each sample from snRNA seq data. The left seven samples have a normal BMI (18.5 – 25) while the right eight samples have an obese BMI (30 – 40). B) Heat map showing the level of expression of significant differentially expressed genes within obese BMI fat pad compared to normal BMI fat pad with KOA. Expression levels range from blue (highly downregulated) to red (highly upregulated).

Disclosure: H. Peters: None; **P. Potla**: None; **J. Rockel**: None; **K. Delos Santos**: None; **S. Vohra**: None; **s. lively**: None; **K. Perry**: None; **A. Perruccio**: None; **N. Mahomed**: AIC, 4, ARTHUR HEALTH CORP, 3; **R. Rampersaud**: None; **R. Gandhi**: None; **M. Kapoor**: None.

Abstract Number: 1597

Staphylococcus Aureus Peptidoglycan Induces Pathogenic Autoantibody Production via Autoreactive B Cell Receptor Clonal Selection, Implications in Systemic Lupus Erythematosus

Wangbin Ning, Gary Gilkeson and **Wei Jiang**, Medical University of South Carolina, Charleston, SC

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: SLE – Etiology & Pathogenesis
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: There is an intricate interplay between the microbiome and the immune response impacting the development of normal immunity and autoimmunity. However, we do not fully understand how the microbiome affects the production of natural-like and pathogenic autoantibodies. Peptidoglycan (PGN) is a component of the bacterial cell wall that is highly antigenic. PGNs from different bacteria can differ in their immune regulatory activities.

Methods: Female C57BL/6 and MRL/lpr mice were intraperitoneally injected (i.p.) with PBS, *Staphylococcus aureus* PGN, or *Bacillus subtilis* PGN (100 μg/time). C57BL/6 mice (6-week-old) were treated with PGNs and PBS twice per week for 8 weeks; then the treatment was stopped for another 8 weeks. MRL/lpr lupus-prone mice (6-week-old) were treated with PBS and PGNs twice per week for 12 weeks. Spleen anti-double-stranded DNA (dsDNA) IgG+ B cells were sorted for B-cell receptor sequencing. Serum autoantibody levels and kidney damage were analyzed.

In a human study, we recruited unrelated controls (n = 25) or lupus patients (n = 32) as defined by the updated American College of Rheumatology classification criteria. All participants were premenopausal females (age ≥18 years). Pregnant or breastfeeding, recent severe illness, contraindications for blood withdrawals, or received antibiotics within the past 90 days were excluded. The method for determining plasma S. aureus DNA levels was evaluated by qPCR usingprimersfor *S. aureus* were forward:5′-TTCGCTACTAGTTGCTTA-3′ and reverse: 5′-GCACTATATACTGTTGGATC-3′.

We applied non-parametric Mann-Whitney U tests to compare differences between two groups, and Spearman's correlation tests to evaluate associations. All tests were two-sided, and $P \leq 0.05$ was considered significant.

Results: Administration of B. subtilis PGN-induced natural-like anti-dsDNA autoantibodies (e.g., IgM, short-lived IgG response, and no tissue damage), whereas S. aureus PGN-induced pathogenic anti-dsDNA autoantibodies (e.g., prolonged IgG production, low IgM, autoantibody-mediated kidney damage) in C57BL/6 and/or MRL/lpr mice (Figures 1-2, $P < 0.05$, non-parametric MannWhitney U tests). However, serum total IgG did not differ ($P > 0.05$, Figure 1B). S. aureus PGN drives specific clonal expansion, somatic hypermutation of IGHV3-74, and TLR2-dependent Class switch recombination in splenic anti-dsDNA autoreactive B cells ($P < 0.05$, Figure 2). In women with SLE, plasma S. aureus DNA levels were increased compared to control women ($P < 0.05$, Figure 3) and plasma S. aureus DNA levels were correlated with levels of lupus-related autoantibodies and renal involvement ($P < 0.05$, Spearman Correlation tests, Figure 3).

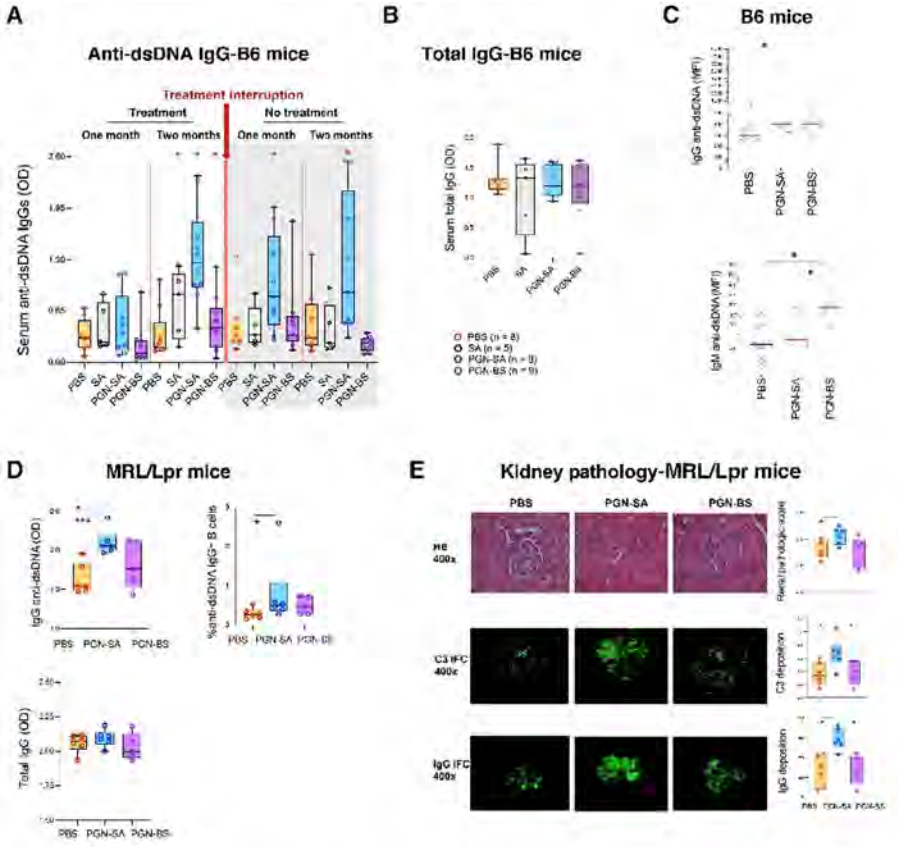


Figure 1. Administration of *B. subtilis* PGN induced natural-like anti-dsDNA autoantibodies (e.g., IgM, short lived IgG response, and no tissue damage), whereas *S. aureus* PGN induced pathogenic anti-dsDNA autoantibodies (e.g., prolonged IgG production, low IgM, autoantibody-mediated kidney damage) in C57BL/6 and/or MRL/lpr mice. (A-C) C57/B6 mice were treated with PBS (0.2 mL), *S. aureus* or *B. subtilis PGN* (100 µg/mouse/injection), or whole inactivated *S. aureus* ($5x10^7$ CFU/mouse/injection) via i.p. injection twice per week for 8 weeks. Then treatment was stopped for 8 weeks. (A) Serum levels of IgG anti-dsDNA and (B) endpoint serum levels of total IgG. Median ± Interquartile range. $^*P < 0.05$ compared to the PBS group. (C) Heatmaps show the relative levels of IgG or IgM autoantibodies in mouse serum after 8 weeks of treatment with PGNs or PBS (red color represents higher level and green color represents lower level). Mean fluorescent intensity (MFI) of IgG or IgM anti-dsDNA. (D-E) MRL/Lpr mice were treated with PBS, *S. aureus* PGN, or B. subtili PGN (100 µg/mouse/injection) via i.p. injection twice per week for 12 weeks. (D) Serum levels of IgG anti-dsDNA, percent of anti-dsDNA IgG+ B cells in spleen (gating on B cells), and serum levels of total IgG at the end of the study. (E) Representative kidney H&E imaging and collective glomerular lesion index. Representative kidney C3 and total IgG staining and collective quantification of C3 and IgG deposition. Statistical analysis involved non-parametric Mann-Whitney U tests.

Figure 1. Administration of B. subtilis PGN induced natural-like anti-dsDNA autoantibodies (e.g., IgM, short lived IgG response, and no tissue damage), whereas S. aureus PGN induced pathogenic anti-dsDNA autoantibodies (e.g., prolonged IgG production, low IgM, autoantibody-mediated kidney damage) in C57BL/6 and MRL/lpr mice.

Conclusion: *S. aureus* PGN induces pathogenic autoantibody production, whereas *B. subtilis* PGN drives the production of natural nonpathogenic autoantibodies. The higher plasma S. aureus DNA in patients, we postulate, is one factor that induces autoantibody production and disease development in susceptible individuals. Therapeutics aimed at blocking TLR2 or *Staphylococcus* colonization may have a role in treating lupus.

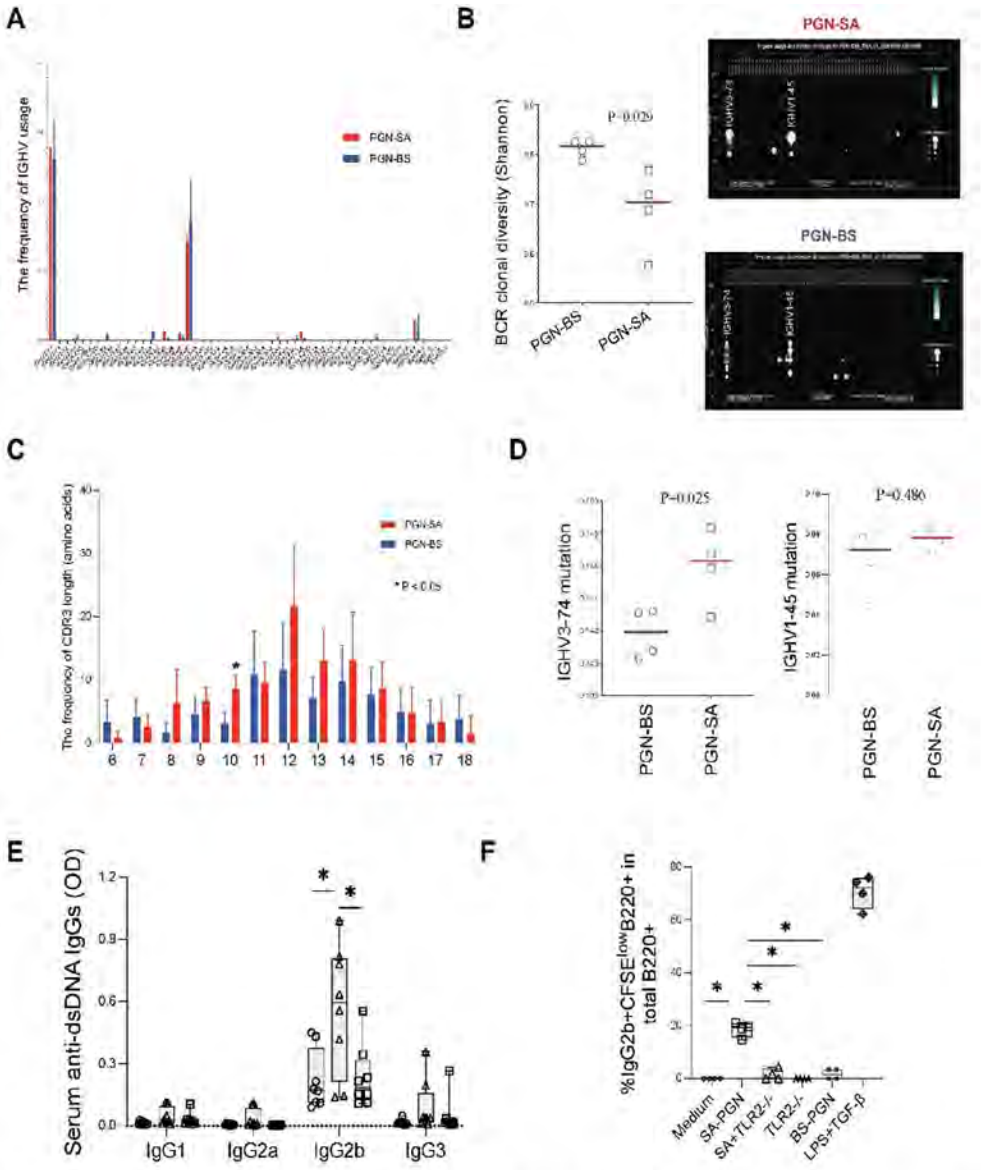
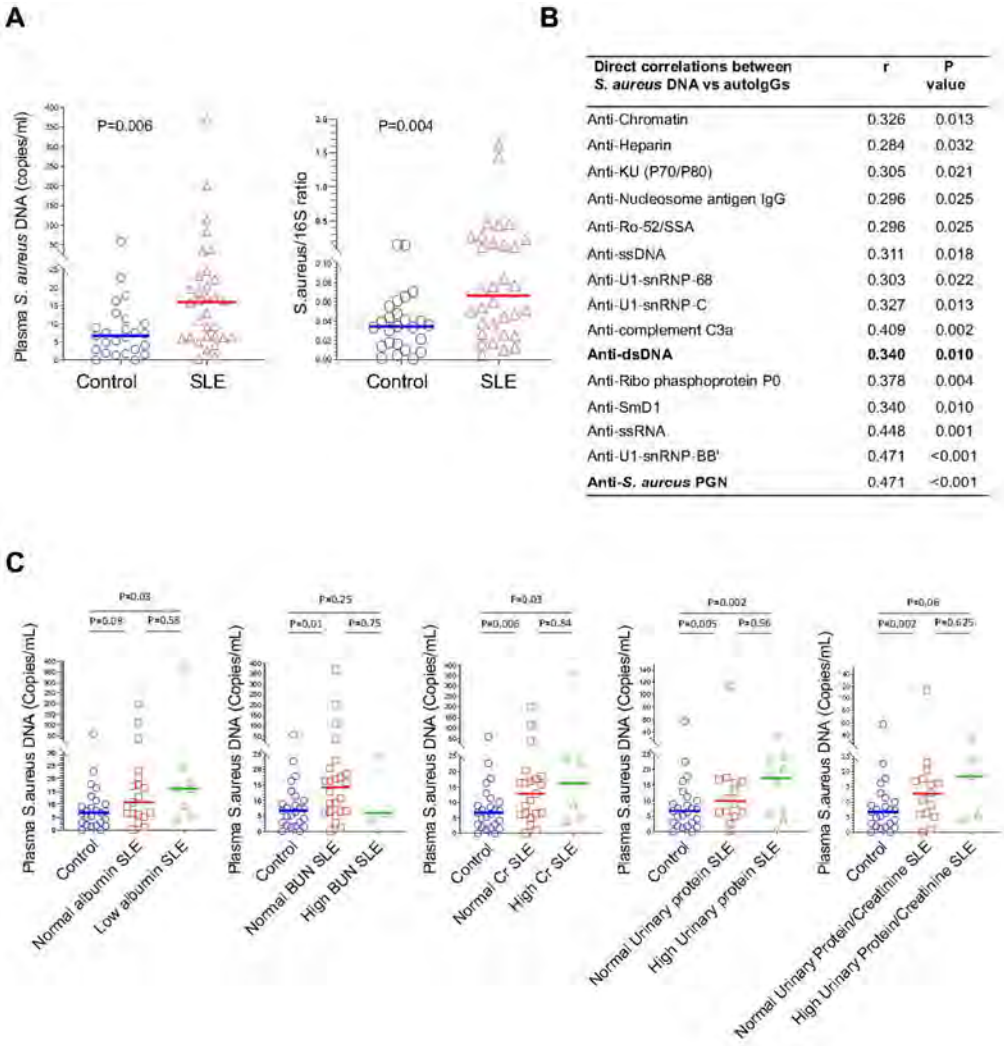


Figure 2. Characteristics of BCR repertoire from anti-dsDNA IgG+ B cells from spleen; Class switch recombination in response to *S. aureus* PGN. C57/B6 mice were treated with *S. aureus* or *B. subtilis* PGNs via i.p. injection twice per week for 8 weeks. At the end of study, B cells were isolated from spleen and anti-dsDNA IgG+ B cells were sorted using flow cytometry. RNA was extracted, and BCR sequencing was conducted. BCR clonality was analyzed in C57/B6 mice treated with *S. aureus (SA) and* B. subtilis (BS) PGN (n = 4 per group). (A) The frequency of IGHV usage. (B) BCR clonal diversity. (C) The frequency of CDR3 length. (D) Somatic mutation of IGHV3-74 and IGHV1-45. (E) Subclasses of serum anti-dsDNA IgG at the end of the study in vivo. (F) B cells were isolated from spleen of untreated C57/B6 mice, cultured with basal medium (control), LPS plus TGF-β1 (a positive control), *S. aureus* (SA) or *B. subtilis* (BS) PGN for 72 hours in vitro. The percentages of proliferating IgG2b+ B cells (%$CFSE^{low}$IgG2b+ in B220+ cells) were calculated. Statistical analysis used non-parametric Mann-Whitney U tests.

Figure 2. Characteristics of BCR repertoire from anti-dsDNA IgG+ B cells from spleen and class switch recombination in response to S. aureus PGN in B6 mice.



Direct correlations between *S. aureus* DNA vs autoIgGs	r	P value
Anti-Chromatin	0.326	0.013
Anti-Heparin	0.284	0.032
Anti-KU (P70/P80)	0.305	0.021
Anti-Nucleosome antigen IgG	0.296	0.025
Anti-Ro-52/SSA	0.296	0.025
Anti-ssDNA	0.311	0.018
Anti-U1-snRNP-68	0.303	0.022
Anti-U1-snRNP-C	0.327	0.013
Anti-complement C3a	0.409	0.002
Anti-dsDNA	**0.340**	**0.010**
Anti-Ribo phasphoprotein P0	0.378	0.004
Anti-SmD1	0.340	0.010
Anti-ssRNA	0.448	0.001
Anti-U1-snRNP-BB'	0.471	<0.001
Anti-*S. aureus* PGN	0.471	<0.001

Figure 3. Increased *S. aureus* DNA translocation in patients with SLE and its correlation with lupus disease pathogenesis. (A) Translocation of plasma *S. aureus* DNA (absolute copy number per mL blood or ratio of *S. aureus* DNA versus total 16S rDNA) measured by qPCR in extracted microbial DNA from plasma samples of patients with SLE (n = 32) and healthy controls (n = 25). (B) Spearman correlation coefficient (r) and *P* values of *S. aureus* DNA copy number per mL blood and levels of each lupus-related autoantibody. Autoantibody levels were evaluated in plasma samples with ELISA. (C) Translocation of *S. aureus* DNA in different patients with SLE based on levels of serum albumin, BUN, creatinine, urinary protein, and ratio of urinary protein versus creatine. Spearman Correlation tests.

Figure 3. Increased S. aureus DNA translocation in patients with SLE and its correlation with lupus disease pathogenesis.

Disclosure: W. Ning: None; **G. Gilkeson**: None; **W. Jiang**: None.

Abstract Number: 1598

Single-cell Spatial Proteomics Identifies Intraglomerular Myeloid Cells in Membranous Lupus Nephritis

Chen-Yu Lee[1], Caleb Marlin[2], Xiaoping Yang[1], Tayte Stephens[2], Alessandra Ida Celia[3], Jeff Hodgin[4], Peter Izmirly[5], H Michael Belmont[6], Jill Buyon[7], Chaim Putterman[8], Judith James[2], the Accelerating Medicines Partnership in RA/SLE[9], Michelle Petri[10], Joel Guthridge[2], Avi Rosenberg[11] and **Andrea Fava**[1], [1]Johns Hopkins University, Baltimore, MD, [2]Oklahoma Medical Research Foundation, Oklahoma City, OK, [3]John Hopkins University of Medicine, Rome, Italy, [4]University of Michigan, Ann Arbor, MI, [5]New York University School of Medicine, New York, NY, [6]NYU School of Medicine, New York, NY, [7]NYU Grossman School of Medicine, New York, NY, [8]Albert Einstein College of Medicine, Bronx, NY, [9]Multiple, Multiple, [10]Department of Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Timonium, MD, [11]Department of Pathology, The Johns Hopkins University School of Medicine, Baltimore, MD

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: SLE – Etiology & Pathogenesis
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Lupus nephritis (LN) leads to end-stage kidney disease (ESKD) in more than 20% of patients despite optimal treatment. Up to 30% of LN patients have membranous LN which is characterized by subepithelial immune deposits without immune infiltration in the glomeruli. Despite its association with ESKD, membranous LN is considered a milder type of LN with no consensus on the optimal use of immunosuppression. To develop mechanistic hypotheses of disease, we analyzed kidney samples from patients with LN using a whole slide spatially resolved proteomic approach as part of the Accelerating Medicines Partnership in RA/SLE. We report here the initial analysis.

Methods: We developed a serial immunohistochemistry (sIHC) staining workflow to stain for 18 antibodies, DNA, and PAS to be visualized on a single section via a cycle of staining, imaging, and destaining. This included incubation of FFPE slides with primary antibody, secondary HRP reagents, AEC-Red Chromogen, and Hematoxylin. Image processing was performed using HALO (Indica Labs) and included deconvolution of single-color channels, registration, fusion, cell segmentation, and automated tissue classification (glomeruli, tubulointerstitium, connective tissue, vasculature, background, and biopsy edges). To minimize batch effect, the analytical pipeline included within sample CLR-normalization and scaling, followed by harmonization (Harmony).

Results: In this initial analysis, we included 29 clinically indicated kidney biopsies classified as LN (13 pure proliferative, 10 pure membranous, 5 mixed, and 1 ISN class II). Patients were 79% female, 34% White, 31% Black, 10% Asian, and 24% identified with Other race/ethnicity. We detected 182,783 CD45+ cells out of 1,913,845 cell objects. Our analysis identified 10 immune cell clusters at low resolution (**Figure 1A**). **Figure 1B** displays the tissue distribution of each cell subset. B and T lymphocytes dominated the tubulointerstitium. The CD68+ myeloid subsets were the predominant cell type in the glomeruli (**Figure 2**). More than half of CD68+ cells expressed Ki67 indicating active proliferation. Surprisingly, we identified intraglomerular CD68+ cells (including endocapillary) also in patients with pure membranous LN, but at a lower tissue density than proliferative LN (**Figure 2**). **Figure 3** demonstrates intraglomerular CD68+ cells in a biopsy classified as pure membranous LN by two experienced renal pathologists.

Conclusion: sIHC can be successfully employed to perform multiplexed whole slide analysis harnessing both the subcellular resolution (brightfield) and the reliability of IHC. Our analysis revealed intraglomerular CD68+ myeloid cells in pure membranous LN. By traditional clinical pathology, intraglomerular / endocapillary immune cells characterize proliferative LN and are

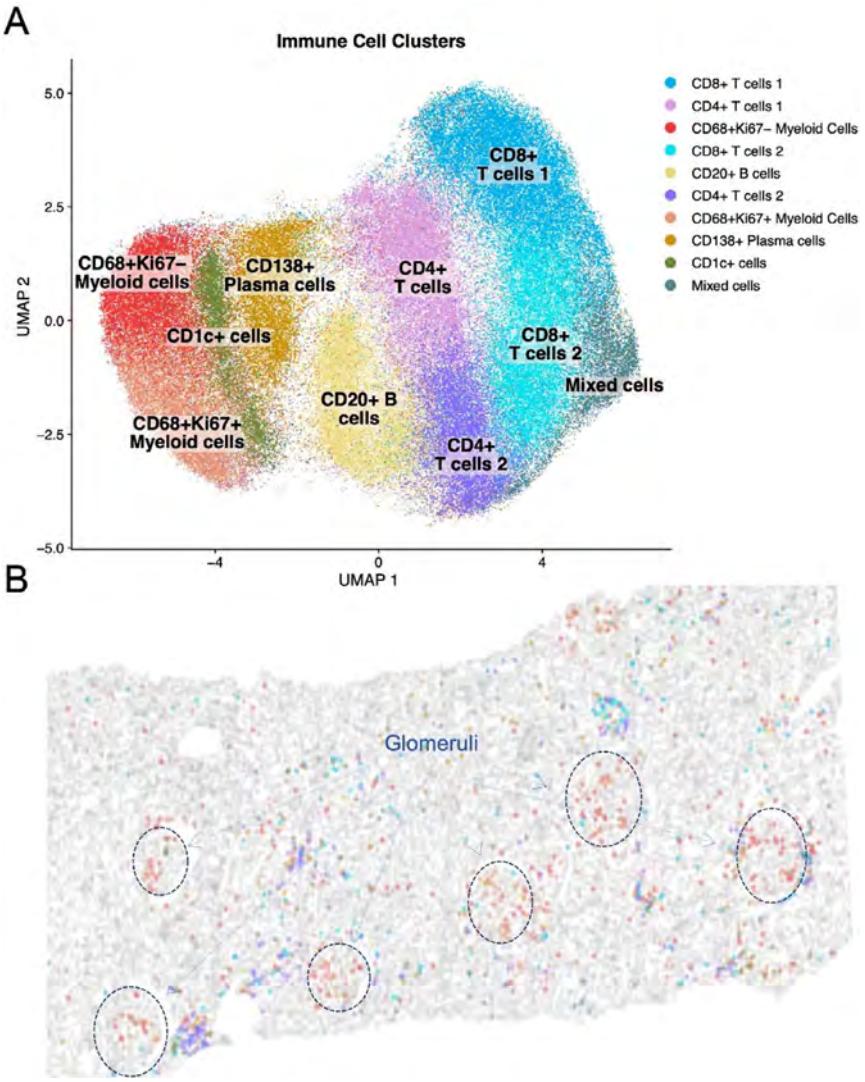


Figure 1. Phenotype and spatial distribution of intrarenal immune cells. (A) UMAP of CD45+ cells (n=182,783, 29 patients) indicating the low-resolution cluster annotation. (B) Digital reproduction of a representative biopsy displaying the distribution of the cells clusters (colors matching panel A). The biopsy in panel B was classified as ISN class III, NIH Activity Index 6, NIH Chronicity Index 3.

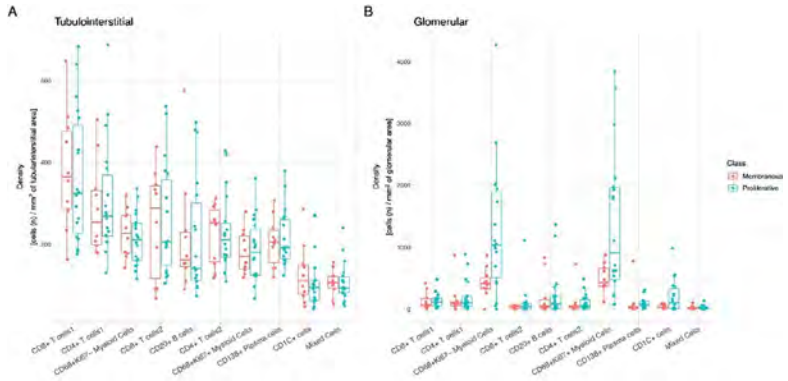


Figure 2. Myeloid cells dominate intraglomerular inflammation, including membranous LN. Box plots displaying the density (cells / area) of the immune cell clusters in the tubulointerstitium (A) and glomeruli (B) according to ISN class group. Both CD68+ myeloid cell clusters showed a statistically significant higher intraglomerular density compared to all other clusters in both proliferative and membranous LN ($p<0.05$, Wilcoxon test). Proliferative LN includes ISN class III and IV +/- V (n=18); membranous LN indicate pure ISN class V (n=10).

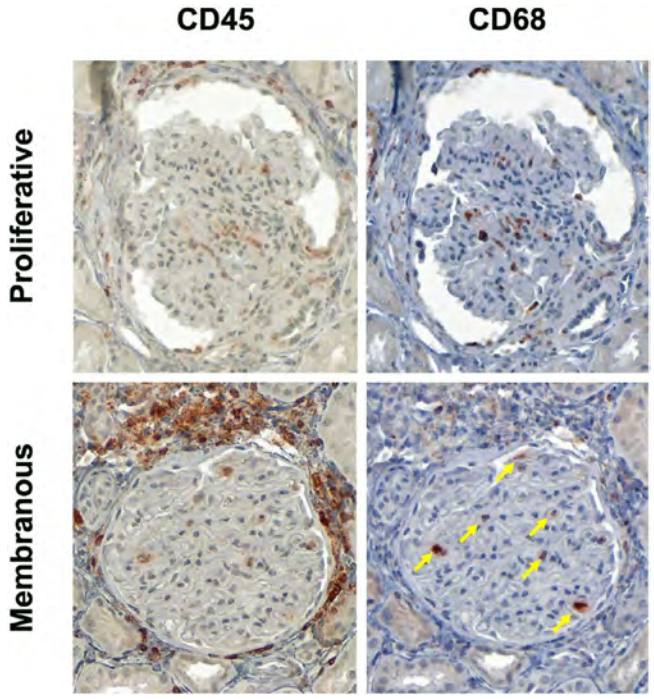


Figure 3. Intraglomerular CD68+ monocyte/macrophages in proliferative and membranous LN. Immunohistochemistry images displaying the expression of CD45 and CD68 in a representative glomerulus from a patient with proliferative LN (upper panels) and a patient with pure membranous LN (lower panels). The yellow arrows indicate intraglomerular CD68+ cells in membranous LN.

not consistent with pure membranous LN. These findings implicate macrophages/monocytes in the glomerular disease in membranous LN with therapeutic implications. The analysis of 90 additional biopsies and a myeloid-focused panel is underway to validate and extend these findings.

Disclosure: C. Lee: None; **C. Marlin**: None; **X. Yang**: None; **T. Stephens**: None; **A. Celia**: None; **J. Hodgin**: AstraZeneca, 5, 6, Eli Lilly, 5, Gilead, 5, Janssen, 5, Moderna, 5, Novo Nordisk, 5, Regeneron, 5; **P. Izmirly**: None; **H. Belmont**: Alexion, 6, Aurinia, 6; **J. Buyon**: Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, Related Sciences, 1; **C. Putterman**: Equillium, 2, KidneyCure, 1, Progentec, 2; **J. James**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(-GSK), 2, Novartis, 2, Progentec Biosciences, 5; **t. Accelerating Medicines Partnership in RA/SLE**: None; **M. Petri**: Alexion, 1, Amgen, 1, AnaptysBio, 1, Annexon Bio, 1, Argenx, 1, Arhros-Focus Med/Ed, 6, AstraZeneca, 1, 5, Aurinia, 1, 5, 6, Axdev, 1, Biogen, 1, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CVS Health, 1, Eli Lilly, 1, 5, Emergent Biosolutions, 1, Exagen, 5, Exo Therapeutics, 2, Gilead Biosciences, 2, GlaxoSmithKlein(GSK), 1, 5, 6, Horizon Therapeutics, 2, Idorsia Pharmaceuticals, 2, IQVIA, 1, Janssen, 1, 5, Kira Pharmaceuticals, 2, MedShr, 6, Merck/EMD Serono, 1, Momenta Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Proviant, 2, Sanofi, 2, Sinomab Biosciences, 2, Thermofisher, 5, UCB, 2; **J. Guthridge**: None; **A. Rosenberg**: None; **A. Fava**: Annexon Biosciences, 2, Sanofi, 1.

Abstract Number: 1599

Single-Cell RNA Sequencing Reveals Cellular Drivers of UV-mediated Skin Injury in Cutaneous Lupus

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: SLE – Etiology & Pathogenesis
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Ultraviolet light (UV) is a known trigger of cutaneous lupus erythematosus (CLE) flares in systemic lupus erythematosus (SLE) patients, yet cell populations and mechanisms driving UV-induced skin inflammation are poorly understood. In this study, we use single-cell RNA sequencing of skin from healthy control (HC) and SLE patients with a history CLE to identify differences in SLE UV responses that serve as novel mediators of UV injury.

Methods: Seven HC and eight SLE patients were recruited. Biopsies were taken from the upper thigh 24 hours after treatment with 1x minimal erythema dose or from unexposed skin. Cells were processed via 10x pipelines, RNA was sequenced with an average of 10,000 reads per cell, and DEGs were analyzed and compared between HC and SLE patients.

Results: Globally, an increase in type I IFN regulated gene expression was seen in SLE >HC across all cell populations after UV exposure. In the epidermis, UV exposure led to differential gene expression in basal keratinocytes (KCs) where stress responses such as S100 proteins were noted in HC, while chemokines and IFN responses were noted in SLE KC, particularly in spinous and basal inflammatory KCs. Subclustering of fibroblast (FB) populations revealed two subpopulations that increase in proportion following UV exposure in both SLE and HC, identified as IFN-FBs and IL6+ FBs. CellphoneDB analysis revealed significant crosstalk between basal and spinous inflammatory KCs and IFN- and IL6+- FBs in SLE skin, suggesting that basal and spinous inflammatory KCs represent critical mediators of UV signal between the epidermis and dermis in lupus. Analysis of the myeloid compartment did not support an influx of pDCs into the skin at our selected timepoint. However, recruitment of myeloid dendritic cells (moDCs) was robust in both SLE and HC skin. Compared with HC skin, moDCs from SLE patients engaged in greater crosstalk with IL-6- and IFN-fibroblasts through CXCL12, a myeloid chemoattractant. Additionally, lupus moDCs engaged in crosstalk with TREM2+ macrophages, a lupus-specific skin resident population, through chemoattractant proteins.

Conclusion: We thus propose that in SLE skin, UV light induces unique inflammatory keratinocyte responses that educate fibroblasts and resident myeloid cells to recruit inflammatory myeloid dendritic cells, which may contribute to inflammatory cytokine production and downstream adaptive immune cell activation in SLE. Targeting of these pathways may be beneficial for prevention of photosensitive responses.

Disclosure: M. Maz: None; **F. Ma**: None; **M. Gharaee-Kermani**: Rome Therapeutics, 5; **A. Victory**: None; **A. Hurst**: None; **J. Gudjonsson**: Abbvie, 2, 5, Almirall, 2, 5, AnaptysBio, 2, Boehringer Ingelheim, 2, Celgene/BMS, 2, 5, Eli Lilly, 2, 5, Galderma, 2, Janssen, 2, 5, Kyowa Kirin, 5, MiRagen, 2, Novartis, 2, Prometheus Biosciences, 5, Sanofi, 2, SunPharma, 5, TimberPharma, 5; **J. Kahlenberg**: AstraZeneca, 1, Bristol-Myers Squibb(BMS), 2, 5, EMD Serano, 2, exo therapeutics, 2, Gilead, 2, GlaxoSmithKlein(GSK), 1, horizon Therapeutics, 2, Janssen, 5, Pfizer, 2, ROME Therapeutics, 2, 5, Rome Therapeutics, 5, Ventus Therapeutics, 2, 5.

Abstract Number: 1600

Transcriptomic Characterization of Class II Lupus Nephritis and Outcomes

Jasmine Shwetar[1], Katie Preisinger[1], Devyn Zaminski[2], Philip Carlucci[1], Kristina Deonaraine[1], Qian Xiao[3], Joseph Mears[4], Siddarth Gurajala[3], Izmirly peter[5], Judith James[6], Joel Guthridge[6], Andrea Fava[7], Brad Rovin[8], Wade DeJager[6], Ming Wu[9], Deepak Rao[10], Chaim Putterman[11], Betty Diamond[12], Derek Fine[13], Jose Monroy-Trujillo[13], Kristin Haag[14], H Michael Belmont[2], William Apruzzese[10], Anne Davidson[12], Fernanda Payan-Schober[15], Richard Furie[16], Paul Hoover[10], Celine Berthier[17], Maria Dall'Era[18], Kerry Cho[19], Diane L. Kamen[20], Kenneth Kalunian[21], Jennifer Anolik[22], Soumya Raychaudhuri[10], Nir Hacohen[23], Michelle Petri[24], Robert Clancy[25], David Wofsy[18], Arnon Arazi[26], Kelly Ruggles[9], Jill Buyon[25] and The Accelerating Medicines Partnership SLE/RA[27], [1]New York University School of Medicine, New York, NY, [2]NYU School of Medicine, New York, NY, [3]Harvard Medical School, Boston, MA, [4]Michigan University, Ann Arbor, MI, [5]NYU, New York, NY, [6]Oklahoma Medical Research Foundation, Oklahoma City, OK, [7]Johns Hopkins University, Baltimore, MD, [8]Ohio State University, Columbus, OH, [9]NYU Langone, New York, NY, [10]Brigham and Women's Hospital, Boston, MA, [11]Albert Einstein College of Medicine, Bronx, NY, [12]Feinstein Institutes for Medical Research, Manhasset, NY, [13]Johns Hopkins School of Medicine, Baltimore, MD, [14]Thomas Jefferson University, Philadelphia, PA, [15]Texas Tech University Health Sciences Center, El Paso, TX, [16]Northwell Health, Manhasset, NY, [17]University of Michigan, Ann Arbor, MI, [18]University of California San Francisco, San Francisco, CA, [19]UCSF Health, San Francisco, CA, [20]Medical University of South Carolina, Charleston, SC, [21]University of California San Diego, La Jolla, CA, [22]University of Rochester Medical Center, Rochester, NY, [23]Broad Institute of MIT and Harvard, Cambridge, MA, [24]Department of Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Timonium, MD, [25]NYU Grossman School of Medicine, New York, NY, [26]Broad Institute of MIT and Harvard, Melrose, MA, [27]University of Colorado Anschutz Medical Campus, Aurora, CO

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Abstracts: SLE – Etiology & Pathogenesis
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Lupus Nephritis (LN) significantly reduces the survival and life expectancy of patients with SLE. Given this, considerable effort has gone into characterizing the histologic classes that confer the highest standardized mortality ratios. Although Class II LN is considered a milder form of disease which often requires less aggressive treatment, a growing body of clinical evidence suggests that these patients can progress to more advanced LN classes. Accordingly, this

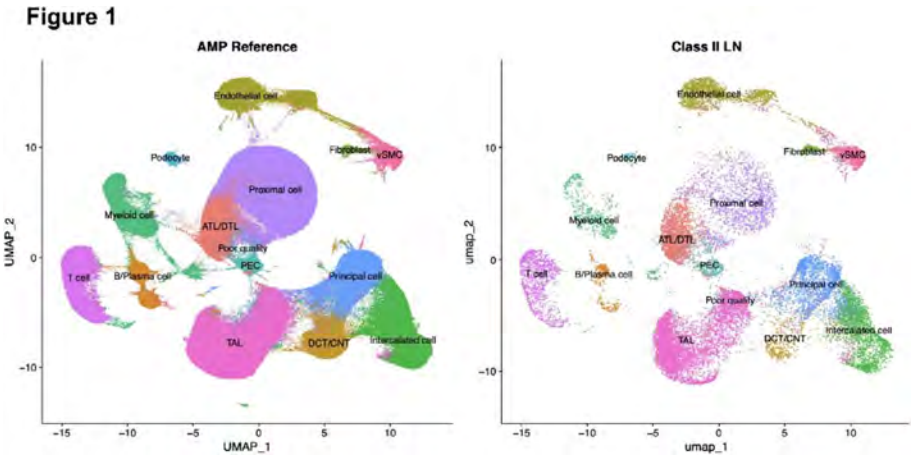

Figure 1: UMAP representation of all cells in AMP dataset from control and membranous, proliferative, and mixed LN biopsies (left); UMAP representation generated by Symphony reference mapping of all cells from Class II LN biopsies (right).

study leveraged the multi-center LN Accelerating Medicine Partnership (AMP) Network to focus on the transcriptome of Class II kidney biopsies with comparison to other histologic classes to provide insights into the molecular underpinnings of early disease and potential drivers of progression.

Methods: LN patients were enrolled in AMP at the time of a clinically indicated kidney biopsy and followed for one year. scRNA-seq was performed using the 10x genomics sequencing platform and quality control was performed to retain high-quality cells. Using the AMP consortium dataset which includes patients with membranous, mixed and proliferative LN, a reference-based mapping approach was employed to identify shared cell states and insights into Class II pathogenesis and outcomes.

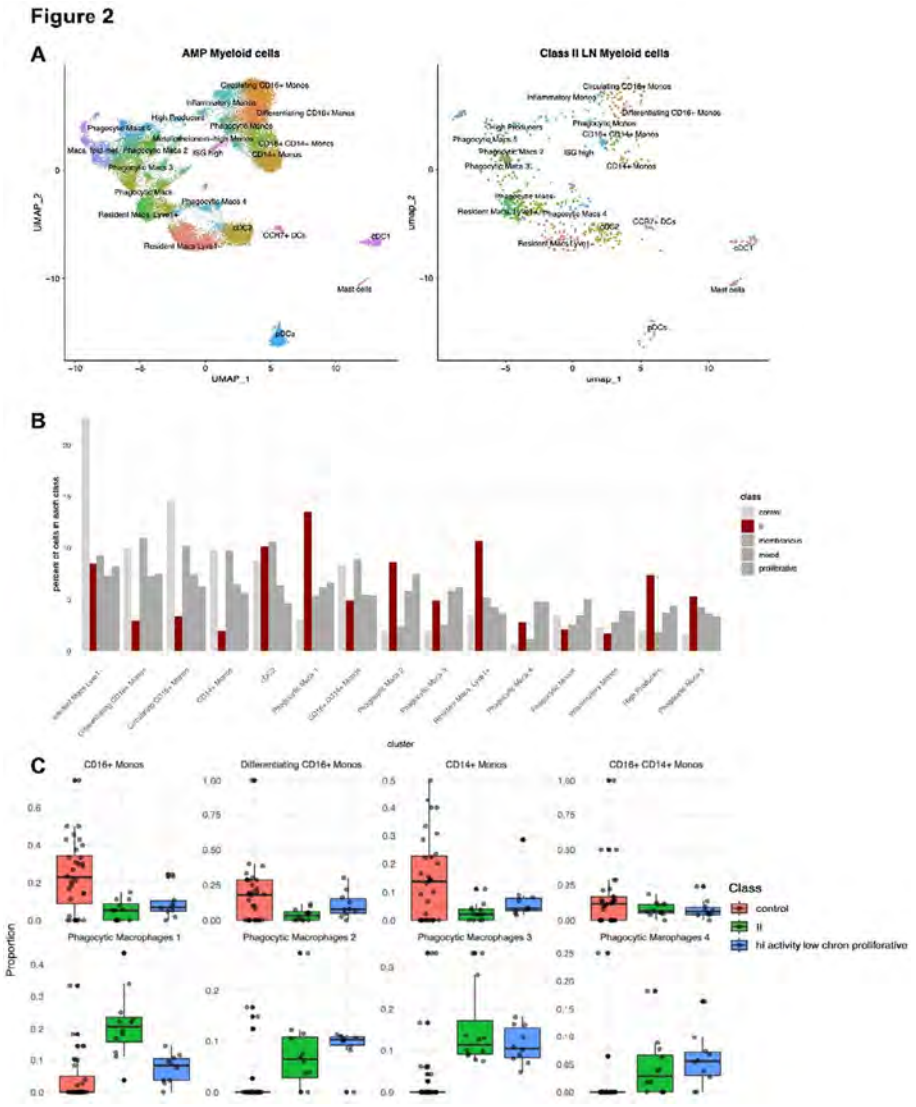

Figure 2: (A) UMAP representation of myeloid cells in AMP (left); UMAP representation generated by Symphony reference mapping of Class II myeloid cells (right). (B) Per disease condition proportion of cells in each myeloid subcluster (control = light gray; proliferative, membranous or mixed LN = dark gray; Class II LN = red) (C) Per sample proportion of cells in various monocyte (top) and macrophage (bottom) subclusters. All comparisons of the median proportion of cells in Class II LN versus control were significant ($p<0.05$) using Mann-U Whitney test. When comparing Class II LN with high activity low chronicity proliferative LN, only the porportion of differentiating CD16+ Monocytes and Phagocytic macrophages were found to be significant ($p = 0.033$, 0.003 respectively). Control = red; Class II LN = green; High activity low chronicity proliferative LN = blue.

Results: scRNA-Seq from 12 patients with Class II LN biopsies yielded 25,483 high-quality cells comprised of 11 parenchymal and three immune cell types (Fig 1). Reference mapping identified B, T and myeloid cells which are infrequently found in Class II LN by conventional microscopy (Fig 2A). In the myeloid compartment, cell type proportion analysis revealed a distinct signature with fewer monocytes and a greater number of differentiated and phagocytic macrophages in Class II compared to control and other LN classes (Fig 2B). This distinct myeloid signature was also identified in proliferative LN samples with high activity and low chronicity (activity index >= 4, chronicity index = 0). In both Class II and proliferative LN with high activity, monocytes and phagocytic macrophage subtypes were contracted and expanded relative to biopsies from healthy donors, respectively (Fig. 2C). The stromal compartment of Class II unexpectedly had a higher proportion of fibroblasts and myofibroblasts compared to all other classes (3A-B). These myofibroblasts were characterized by high expression of canonical markers, such as ACTA2 as well as markers of immune activation such as CTGF, CCL19, and CCL21 (3C). The proportion

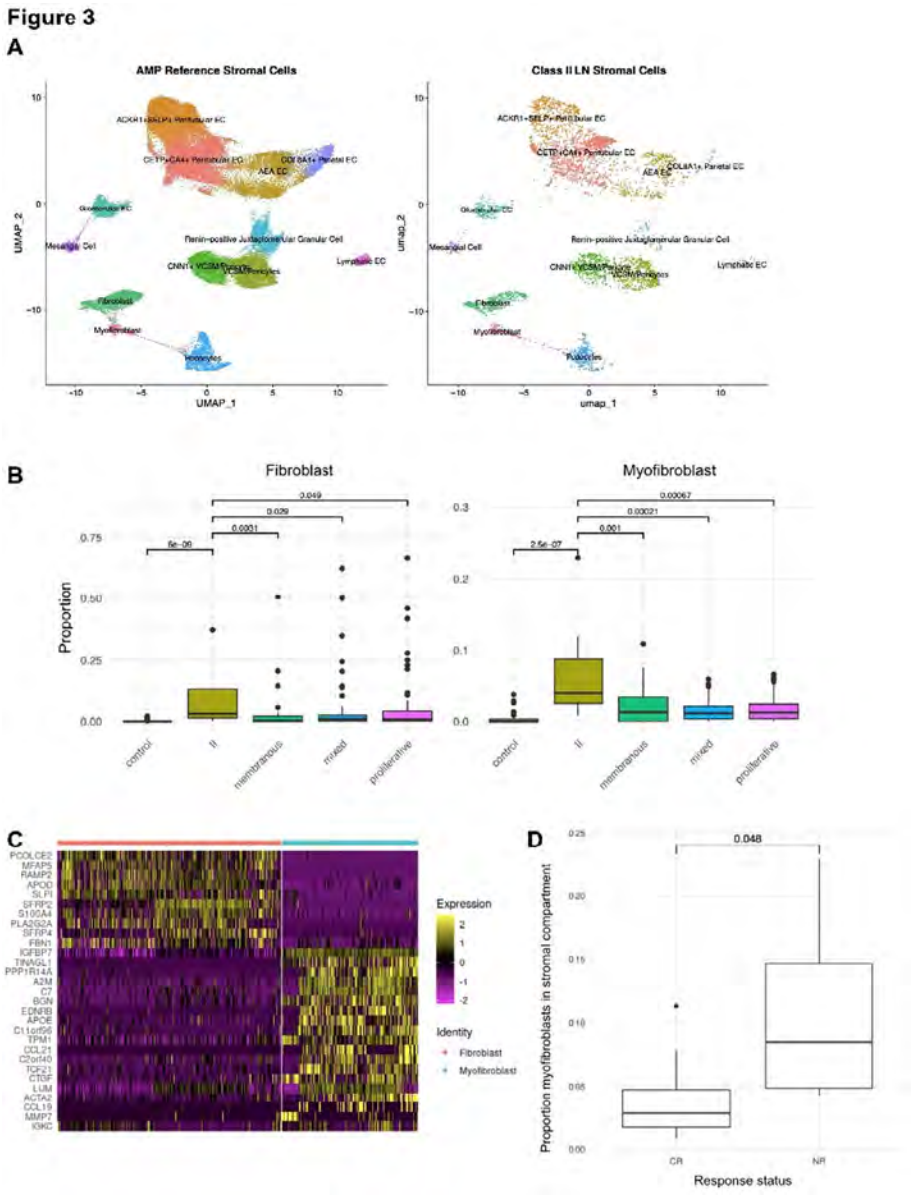

Figure 3: (A) UMAP representation of stromal cells in AMP dataset (left); UMAP representation generated by Symphony reference mapping of Class II stromal cells (right). (B) Proportion of fibroblast and myofibroblast cells in each disease class. P-values calculated using Mann-U Whitney test. (C) Heatmap of markers in Class II fibroblasts (red) and myofibroblasts (blue). (D) Proportion of myofibroblasts in Class II LN patients that were complete responders to treatment (CR) and non-responders to treatment (NR). P-value comparing median myofibroblast proportion using Mann-U Whitney test.

of myofibroblasts was higher in Class II patients whose UPCR fell below 0.5 and creatinine remained normal or did not exceed 125% of baseline compared to Class II patients considered non-responders at 52 weeks (3D, p = 0.048).

Conclusion: These data support that histology provides an incomplete picture of the molecular and cellular landscape in Class II LN. Increased phagocytic macrophage activity and immune-induced myofibroblast differentiation were associated with higher disease activity, highlighting these cellular composition changes as potential drivers of non-responsiveness and progression.

Disclosure: J. Shwetar: None; **K. Preisinger**: None; **D. Zaminski**: None; **P. Carlucci**: None; **K. Deonaraine**: None; **Q. Xiao**: None; **J. Mears**: None; **S. Gurajala**: None; **I. peter**: None; **J. James**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 2, Novartis, 2, Progentec Biosciences, 5; **J. Guthridge**: None; **A. Fava**: Annexon Biosciences, 2, Sanofi, 1; **B. Rovin**: AstraZeneca, 2, 5, Aurinia, 2, 5, Biogen, 2, F. Hoffmann-La Roche Ltd, 2, Genentech, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **W. DeJager**: None; **M. Wu**: None; **D. Rao**: AstraZeneca, 2, Bristol-Myers Squibb, 2, 5, GlaxoSmithKlein(GSK), 2, Hifibio, 2, Janssen, 5, Merck, 5, Scipher Medicine, 2; **C. Putterman**: Equillium, 2, KidneyCure, 1, Progentec, 2; **B. Diamond**: Alpine, 12, DSMB, DBV, 2, 2, IMT, 2, Kyverna, 2, Nighthawk, 2, ONO, 2; **D. Fine**: None; **J. Monroy-Trujillo**: None; **K. Haag**: None; **H. Belmont**: Alexion, 6, Aurinia, 6; **W. Apruzzese**: None; **A. Davidson**: None; **F. Payan-Schober**: None; **R. Furie**: Biogen, 2, 5; **P. Hoover**: None; **C. Berthier**: None; **M. Dall'Era**: Annexon Biosciences, 2, 5, AstraZeneca, 2, Aurinia, 2, Biogen, 2, GlaxoSmithKlein, 2, 5, Pfizer, 2; **K. Cho**: None; **D. Kamen**: None; **K. Kalunian**: AbbVie/Abbott, 2, Amgen, 5, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EquilliumBio, 2, Genentech, 2, Gilead, 2, Janssen, 2, KezarBio, 1, Merck/MSD, 2, Novartis, 2, Pfizer, 2, Remegene, 2, Roche, 2, UCB, 5; **J. Anolik**: None; **S. Raychaudhuri**: AbbVie, 6, Janssen, 1, Mestag, Inc, 2, 8, Pfizer, 1, Sanofi, 1, Sonoma, 1, 8; **N. Hacohen**: None; **M. Petri**: Alexion, 1, Amgen, 1, AnaptysBio, 1, Annexon Bio, 1, Argenx, 1, Arhros-Focus Med/Ed, 6, AstraZeneca, 1, 5, Aurinia, 1, 5, 6, Axdev, 1, Biogen, 1, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CVS Health, 1, Eli Lilly, 1, 5, Emergent Biosolutions, 1, Exagen, 5, Exo Therapeutics, 2, Gilead Biosciences, 2, GlaxoSmithKlein(GSK), 1, 5, 6, Horizon Therapeutics, 2, Idorsia Pharmaceuticals, 2, IQVIA, 1, Janssen, 1, 5, Kira Pharmaceuticals, 2, MedShr, 6, Merck/EMD Serono, 1, Momenta Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Proviant, 2, Sanofi, 2, Sinomab Biosciences, 2, Thermofisher, 5, UCB, 2; **R. Clancy**: None; **D. Wofsy**: Amgen, 7, Novartis, 7; **A. Arazi**: None; **K. Ruggles**: None; **J. Buyon**: Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, Related Sciences, 1; **T. SLE/RA**: None.

Abstract Number: 1601

Interleukin-6 Disrupts Blood-cerebrospinal Fluid Barrier Permeability in Murine Neuropsychiatric Lupus

Joshua Reynolds[1], Lola Torz[2], Natalia Petersen[2], Ayal Ben-Zvi[3] and **Chaim Putterman**[1], [1]Albert Einstein College of Medicine, Bronx, NY, [2]Novo Nordic, Global Obesity Research, Malov, Denmark, [3]Hebrew University of Jerusalem, Jerusalem, Israel

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: SLE – Etiology & Pathogenesis
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: In exploring the pathogenic mechanisms underlying neuropsychiatric lupus (NPSLE), it was discovered that cerebrospinal fluid (CSF) from lupus patients often contains neurotoxic antibodies, cytokines, and metabolites. Disruption of the blood-CSF barrier (B-CSFB), formed by choroid plexus (CP) epithelia, could explain these abnormalities. In

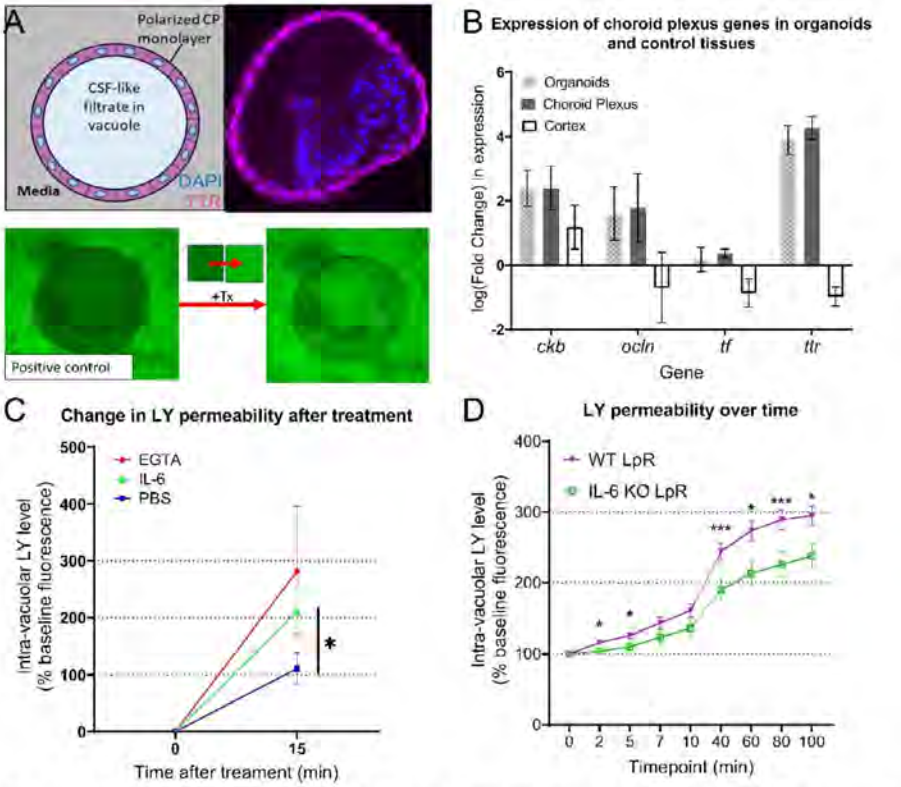

Figure 1. Choroid plexus organoids faithfully replicate in-vivo characteristics of CP tissue and demonstrate IL-6's impact on permeability. To directly assess lupus-related changes in blood-cerebrospinal fluid barrier (B-CSFB) permeability, spherical organoids were grown from 16+ week-old, female MRL/lpr lupus mouse choroid plexus (CP), the tissue forming the B-CSFB. In all groups, CP explants from 2 to 5 mice were pooled, mechanically digested, plated in an extracellular matrix, and cultured in epithelia-specific media for 2 weeks before experiments. A) Top: Schematic of a single CP explant organoid (left) and a representative immunofluorescent image of an actual organoid (right). TTR = transthyretin, a canonical CP marker; DAPI = 4',6-diamidino-2-phenylindole, a nuclear stain. Bottom: A representative permeability experiment wherein fluorescence intensity within the organoid's central vacuole ("intra-vacuolar") rapidly increases following administration of a permeabilizing agent. This exemplar color change reflects increasing permeability to a tracer. B) Real-time qPCR measurement of key CP gene expression in organoids, control CP tissue, and cortex tissue (all from MRL/lpr mice). C) Change in permeability to lucifer yellow (LY) tracer over 15 minutes following organoid treatment with positive control EGTA (egtazic acid; tight-junction disruption; n=20), 10 ng/mL IL-6 (n=39), or PBS (n=40). The IL-6 group had higher LY permeability at the 15-minute time point (p=0.0141). D) To determine if IL-6 is necessary for increased permeability, organoids were generated from either IL-6 knockout (KO) MRL/lpr mice or wildtype (WT) MRL/lpr as described. Permeability to LY was significantly lower in IL-6 KO organoids (n= 31) compared to WT ones (n= 27) at almost all timepoints. * $p < 0.05$, *** $p < 0.01$.

Figure 1. Choroid plexus organoids faithfully replicate in-vivo characteristics of CP tissue and demonstrate IL-6's impact on permeability. To directly assess lupus-related changes in blood-cerebrospinal fluid barrier (B-CSFB) permeability, spherical organoids were grown from 16+ week-old, female MRL/lpr lupus mouse choroid plexus (CP), the tissue forming the B-CSFB. In all groups, CP explants from 2 to 5 mice were pooled, mechanically digested, plated in an extracellular matrix, and cultured in epithelia-specific media for 2 weeks before experiments. A) Top: Schematic of a single CP explant organoid (left) and a representative immunofluorescent image of an actual organoid (right). TTR = transthyretin, a canonical CP marker; DAPI = 4′,6-diamidino-2-phenylindole, a nuclear stain. Bottom: A representative permeability experiment wherein fluorescence intensity within the organoid's central vacuole ("intra-vacuolar") rapidly increases following administration of a permeabilizing agent. This exemplar color change reflects increasing permeability to a tracer. B) Real-time qPCR measurement of key CP gene expression in organoids, control CP tissue, and cortex tissue (all from MRL/lpr mice). C) Change in permeability to lucifer yellow (LY) tracer over 15 minutes following organoid treatment with positive control EGTA (egtazic acid; tight-junction disruption; n=20), 10 ng/mL IL-6 (n=39), or PBS (n=40). The IL-6 group had higher LY permeability at the 15-minute time point (p=0.0141). D) To determine if IL-6 is necessary for increased permeability, organoids were generated from either IL-6 knockout (KO) MRL/lpr mice or wildtype (WT) MRL/lpr as described. Permeability to LY was significantly lower in IL-6 KO organoids (n= 31) compared to WT ones (n= 27) at almost all timepoints. * $p < 0.05$, *** $p < 0.01$.

both NPSLE patients and lupus mouse models, immune cells infiltrate the CP and can alter normal epithelial functions through extensive cytokine signaling. Interleukin-6 (IL-6) is elevated in the serum and CSF of both NPSLE patients and lupus mice. ATP-binding cassette (ABC) transporter function in the CP, including P-gp, MRP1, and BCRP, is fundamental to the

clearance of neurotoxic substrates from the CSF. In this study, we assessed the effects of IL-6 on lupus mouse derived CP organoids to investigate the integrity of the B-CSFB in NPSLE.

Methods: CP tissue from 2-5 female MRL/lpr (WT) or IL-6 knockout (KO) mice of at least 16 weeks of age were pooled and cultured for two weeks to generate CP organoids for each experiment, as described (Petersen et al, 2020). Organoid morphology was confirmed using whole-mount immunostaining and electron microscopy. Gene expression was measured by

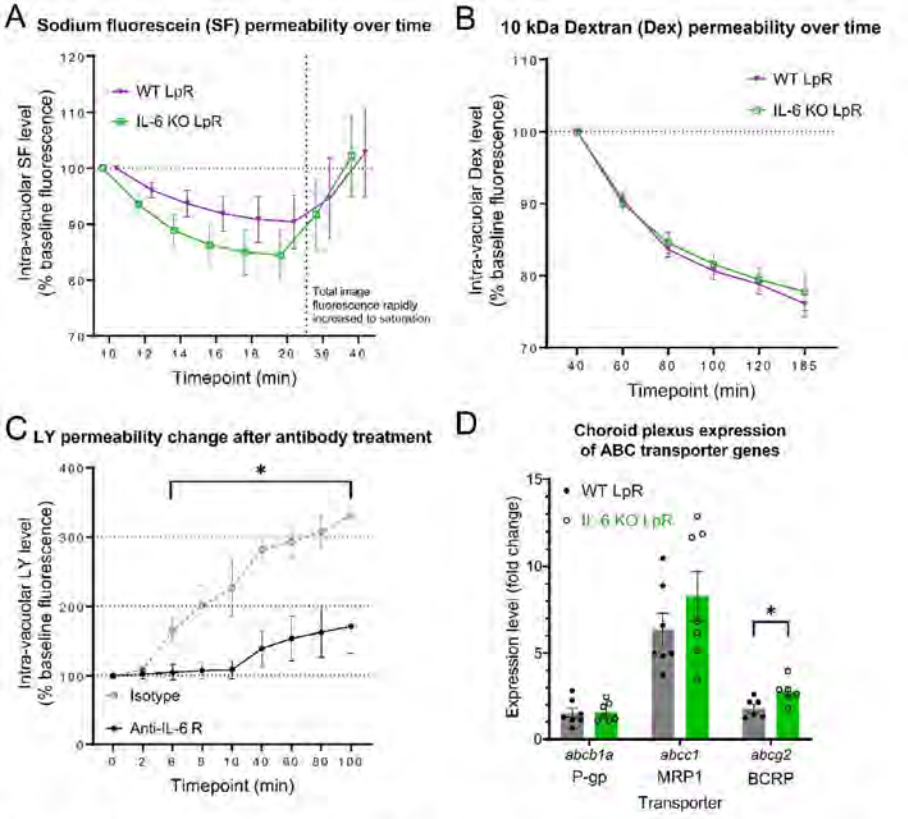

Figure 2. IL-6 signaling selectively alters LY permeability and alters BCRP transporter expression. Given the observed increased LY permeability with IL-6 supplementation and decreased LY permeability when IL-6 is knocked out, we assessed this IL-6 effect on other tracer molecules. A) Permeability to sodium fluorescein (SF), a small molecule like LY but which is not affected by ATP-binding cassette transporters, was measured over 40 minutes in IL-6 KO and WT MRL/lpr organoids but no differences were apparent. The parabolic shape of each curve is due to shifting pH over the observation window increasing fluorescence to saturation. B) Permeability to 10 kDa Dextran, a large molecule tracer, was measured over three hours to assess possible transcytotic differences (which were not observed). C) To determine if IL-6 signaling is responsible for the observed knockout effect on LY permeability, organoids were treated with anti-IL-6 receptor blocking (n= 8) or isotype control antibodies (n= 3). All timepoints after 2 minutes showed reduced permeability in the anti-IL-6 receptor antibody treated group. D) Real-time qPCR measurement of ABC transporter gene expression within the CP of IL-6 KO or WT MRL/lpr mice to elucidate possible mediators of the IL-6 effect on LY permeability. BCRP expression was significantly increased in IL-6 KO mice (p=0.0259) * $p < 0.05$.

Figure 2. IL-6 signaling selectively alters LY permeability and alters BCRP transporter expression. Given the observed increased LY permeability with IL-6 supplementation and decreased LY permeability when IL-6 is knocked out, we assessed this IL-6 effect on other tracer molecules. A) Permeability to sodium fluorescein (SF), a small molecule like LY but which is not affected by ATP-binding cassette transporters, was measured over 40 minutes in IL-6 KO and WT MRL/lpr organoids but no differences were apparent. The parabolic shape of each curve is due to shifting pH over the observation window increasing fluorescence to saturation. B) Permeability to 10 kDa Dextran, a large molecule tracer, was measured over three hours to assess possible transcytotic differences (which were not observed). C) To determine if IL-6 signaling is responsible for the observed knockout effect on LY permeability, organoids were treated with anti-IL-6 receptor blocking (n= 8) or isotype control antibodies (n= 3). All timepoints after 2 minutes showed reduced permeability in the anti-IL-6 receptor antibody treated group. D) Real-time qPCR measurement of ABC transporter gene expression within the CP of IL-6 KO or WT MRL/lpr mice to elucidate possible mediators of the IL-6 effect on LY permeability. BCRP expression was significantly increased in IL-6 KO mice (p=0.0259) * $p < 0.05$.

real-time qPCR. A standard time-lapse permeability assay which quantified tracer fluorescence within each organoid's central vacuole was performed under various conditions. We assessed organoid permeability to tracer in the presence of supplemental IL-6 (10 ng/mL) or anti-IL-6 receptor antibodies (1 ug/mL). We also assessed inherent tracer permeability differences between IL-6 competent WT and IL-6 KO MRL/lpr-derived organoids. The fluorescent tracers used included two small dyes, lucifer yellow (LY) and sodium fluorescein (SF), and a larger 10 kDa dextran molecule (Dex). Importantly, LY but not SF is transported by ABC transporters. Two-tail Mann-Whitney u tests compared differences between groups.

Results: MRL/lpr-derived organoids replicated the *in-vivo* morphology and gene expression of the CP (Fig 1A-B). IL-6 rapidly increased MRL/lpr organoid permeability to LY (IL-6: n=39, 174.4+/- 37.91; PBS: n=40, 76.1+/-27.1; p=0.014; Fig 1C). IL-6 KO organoids demonstrated consistently reduced permeability to LY compared to WT (KO: n=31; WT: n=27; p<< 0.05; Fig 1D). No permeability differences between IL-6 KO (n=19) and WT (n=19) organoids were seen for SF (Fig 2A) or Dex (Fig 2B). Incubation with an anti-IL-6 receptor antibody (n=8) significantly decreased LY permeability relative to an isotype control (n=3; Fig 2C). *In-vivo* expression of *abcg2*, a constituent of BCRP, was increased in IL-6 KO MRL/lpr mice (KO: n=6, 8.83+/-0.84; WT: n=4.17+/-0.61; p=0.026; Fig 2D).

Conclusion: In the first application of a novel CP organoid model to study lupus, we found that IL-6 signaling appears sufficient and necessary to increase permeability to LY, but not other tracers studied. Changes in BCRP, which effluxes only LY, could explain this accumulation of LY within organoids. Therefore, the high IL-6 environment of SLE could interfere with BCRP function and hinder the CP's ability to clear potentially neurotoxic metabolites, and thus contribute to the pathogenesis of NPSLE.

Disclosure: J. Reynolds: None; **L. Torz**: None; **N. Petersen**: None; **A. Ben-Zvi**: None; **C. Putterman**: Equillium, 2, KidneyCure, 1, Progentec, 2.

Abstract Number: 1602

NADPH Oxidase Exerts a B Cell-intrinsic Contribution to Lupus Risk by Modulating Endosomal Toll-like Receptor (TLR) Signals

Shuozhi Liu[1], Natali Shumlak[1], Andrea Largent[1], Sebastien Lewis[1], Mridu Acharya[1] and **Shaun Jackson**[2], [1]Seattle Children's Research Institute, Seattle, WA, [2]Seattle Children's Research Institute / University of Washington, Seattle, WA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: SLE – Etiology & Pathogenesis
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Genome-wide association studies in systemic lupus erythematosus (SLE) have linked loss-of-function mutations in phagocytic NADPH oxidase complex (NOX2) genes, including *NCF1* and *NCF2*, to disease pathogenesis. The prevailing model holds that reduced NOX2 activity promotes SLE via defective efferocytosis, the immunologically silent clearance of apoptotic cells. However, we previously showed that B cell-intrinsic Toll-like receptor (TLR) signaling is modulated by endolysosomal trafficking, such that dysregulated endosomal flux can drive breaks in B cell tolerance. Since NCF1/NCF2 are known regulators of endosomal trafficking in myeloid lineages, we hypothesized that a parallel B cell-intrinsic mechanism contributes to lupus risk.

Methods: We tested the impact of NOX2 family gene deletion on B cell TLR signaling using in vivo animal models, primary murine B cells, NCF1-null human B cell lymphoma lines, and CRISPR-edited primary human B cells

Results: We show that NOX2-deficient mice exhibited increased humoral responses to nucleic acid-containing antigens, findings which correlate with enhanced B cell signals downstream of endosomal TLRs. In keeping with important roles for B cell TLRs in lupus pathogenesis, B cell-intrinsic NADPH oxidase deletion promoted murine humoral autoimmunity

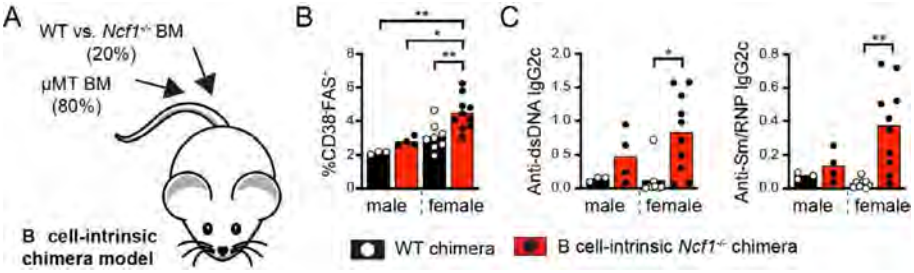

Figure 1: (A) Bone marrow chimeras with B cell-intrinsic Ncf1-/- deletion exhibit spontaneous germinal centers (B) and class-switched auto-antibodies (C).

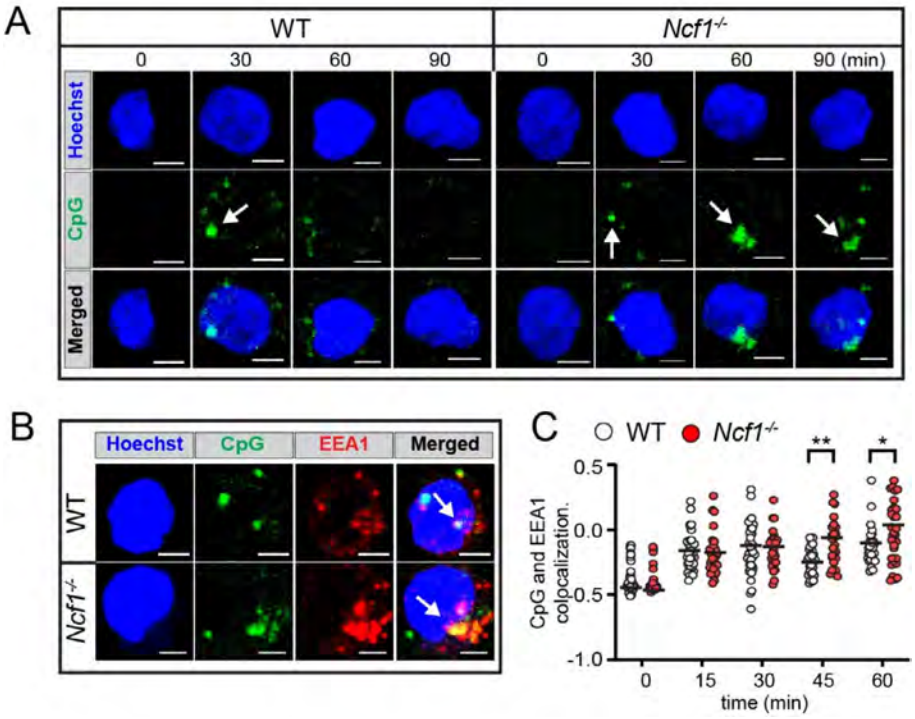

Figure 2: Delayed endolysosomal trafficking of CpG in NCF1-/- B cells. (A) NCF1-/- B cells exhibit prolonged retention of fluorescent CpG in EEA1 early endosomes (B, C).

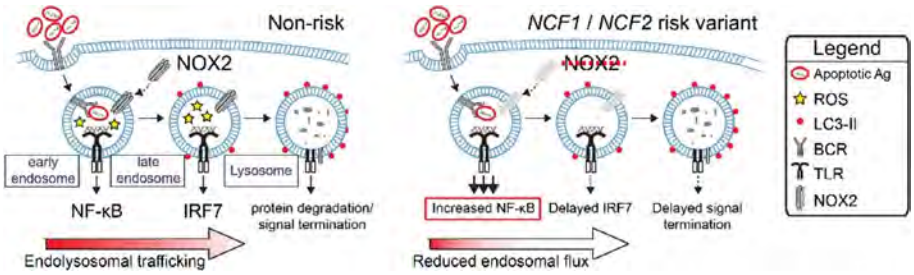

Figure 3: Disease model showing impact of NOX2 loss-of-function on B cell-intrinsic Toll-like receptor signaling. NOX2 deletion promotes dysregulated endolysosomal trafficking, resulting in delayed signal termination and increased TLR signaling thresholds.

(Figure 1). To understand the underlying mechanisms, we quantified TLR-induced intracellular trafficking in B cells using live cell microscopy. Following CpG stimulation, NADPH oxidase activation facilitated trafficking of TLR-containing endosomes to lysosomes, resulting in TLR signal termination. Whereas initial uptake and aggregation of fluorescent CpG in early endosomes was preserved in NCF1-null B cell, loss of NADPH oxidase activity limited signal degradation resulting in enhanced downstream NFkB activation (Figure 2). Finally, CRISPR-mediated disruption of NCF1 in primary human B cells confirmed a direct role for NOX2 in regulating endosomal TLR signaling in B cells. In response to in vitro TLR9 activation, NCF1-deficient human B cells exhibited increased differentiation into IgM- and IgG-producing plasma cells, supporting a mechanistic link between B cell NADPH oxidase activity and human lupus pathogenesis.

Conclusion: Together, these data highlight a new B cell-specific mechanism contributing to autoimmune risk in *NCF1* and *NCF2*variant carriers. We show that loss of NADPH oxidase results in disruption of B cell endolysosomal trafficking, thereby lowering endosomal TLR signaling thresholds and promoting B cell-intrinsic breaks in tolerance (disease model shown in Figure 3).

Disclosure: S. Liu: None; **N. Shumlak**: None; **A. Largent**: None; **S. Lewis**: None; **M. Acharya**: None; **S. Jackson**: None.

Abstract Number: 1603

Infection-Associated Antiphospholipid Antibodies and Their Potential Role in Sepsis Outcomes

Katarina Kmetova, Emily Chong, NaveenKumar K. Somanathapura, Sherwin Navaz, Lyndsay Kluge, Srilakshmi Yalavarthi, Jason Knight, Michael Maile and Yu Zuo, University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Antiphospholipid Syndrome
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Antiphospholipid syndrome (**APS**) is an acquired autoimmune thrombophilia characterized by circulating antiphospholipid antibodies (**aPL**). While the association between aPL and infection has long been recognized, the factors that trigger the production of aPL during infection are largely unknown, and the clinical significance of those infection-associated aPL continues to be debated. Here, we endeavored to comprehensively evaluate the presence of aPL in a large cohort of critically ill sepsis patients and non-sepsis intensive care unit controls. We further investigated whether purified IgG fraction from APS patients with high anti-phosphatidylserine/prothrombin (**aPS/PT**) IgG can modulate neutrophil activation and neutrophil extracellular traps (**NETs**) formation in the mouse sepsis model.

Methods: Plasma from 231 critically ill sepsis and 94 non-sepsis patients were evaluated for eight different types of aPL: anticardiolipin (**aCL**) IgG/IgM/IgA, anti-beta-2 glycoprotein I (**aβ2GPI**) IgG/IgM/IgA, aPS/PT IgG/IgM with ELISA kits (Werfen), Human E-Selectin/CD62E and BAFF/BLyS/TNFSF13B DuoSet ELISA (R&D Systems). An intranasal *Klebsiella pneumonia*-induced mouse sepsis model was used to evaluate the potential role of patient-derived aPL in sepsis outcomes.

Results: We found that 23% of critically ill sepsis patients had at least 1 positive aPL, as compared with 9.6% of non-sepsis patients. The most prevalent aPL found among sepsis patients was aPS/PT IgM (16%), followed by aCL IgM (8.2%), and aβ2GPI IgM (3.5%). When considering only aPL at moderate-to-high titer, 16% of critically ill sepsis patients had at least 1 positive aPL compared to 5.3% of non-sepsis patients (**Table 1**). High aPL levels, such as aPS/PT IgM demonstrated a

Table 1. Prevalence of antiphospholipid antibodies in critically ill sepsis patients (n=231) and critically ill non-sepsis patients (n=94)

aPL	Number positive (manufacturer's threshold)	%	Number positive (≥40 U)	%	Number positive (manufacturer's threshold)	%	Number positive (≥40 U)	%
	Sepsis patients (n=231)				Non-sepsis patients (n=94)			
aCL IgG*	0	0.0%	0	0.0%	1	1.1%	1	1.1%
aCL IgM*	19	8.2%	2	0.9%	3	3.2%	1	1.1%
aCL IgA	2	0.9%	1	0.4%	0	0.0%	0	0.0%
aβ2GPI IgG*	3	1.3%	2	0.9%	0	0.0%	0	0.0%
aβ2GPI IgM*	8	3.5%	1	0.4%	0	0.0%	0	0.0%
aβ2GPI IgA	4	1.7%	3	1.3%	0	0.0%	0	0.0%
aPS/PT IgG	3	1.3%	1	0.4%	1	1.1%	1	1.1%
aPS/PT IgM	36	16%	31	13%	4	4.3%	2	2.1%
Any positive	54	23%	37	16%	9	9.6%	5	5.3%

*Antiphospholipid antibodies that are part of current APS classification criteria. Others are characterized as "non-criteria" aPL.
aPL=antiphospholipid antibodies; aCL=anticardiolipin; $aβ_2$GPI=anti-beta-2 glycoprotein I; aPS/PT=anti-phosphatidylserine/prothrombin; Manufacturer's thresholds:
- aCL IgG/M/A=20 GPL/MPL/APL
- $aβ_2$GPI IgG/M/A=20 SGU/SMU/SAU
- aPS/PT IgG/IgM=30 units

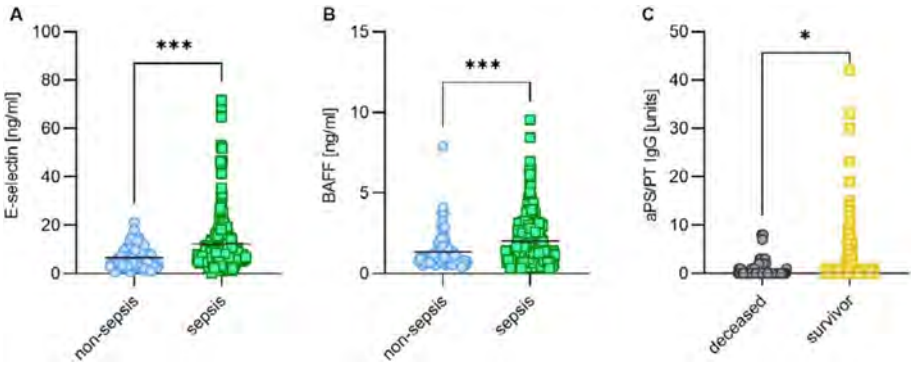

Figure 1: A, Circulating levels of E-selectin were compared between critically ill sepsis patients and non-sepsis patients. B, Circulating levels of BAFF were compared between critically ill sepsis patients and non-sepsis patients. C, Levels of aPS/PT IgG were compared between sepsis survivors and those who died. For statistical analyses, the Mann-Whitney test was used. * - $p<0.05$; *** - $p<0.00$; aPS/PT – anti-phosphatidylserine/prothrombin

positive correlation with soluble E-selectin ($r=0.21$, $p=0.039$), a marker of endothelial cell activation. Higher levels of E-selectin were found in critically ill sepsis patients compared to non-sepsis patients (**Fig 1A**). To evaluate a potential trigger of infection-associated aPL, we measured BAFF, a B cell-activating factor that promotes the differentiation of autoantibody-secreting cells. We found markedly elevated BAFF among critically ill sepsis patients (**Fig 1B**). Interestingly, patients who survived sepsis were more likely to have elevated aPS/PT IgG as compared to those who did not (**Fig 1C**). To evaluate the extent to which aPL may improve sepsis outcomes, we set up an intranasal *Klebsiella pneumoniae* mouse sepsis model (**Fig 2A**). Our data suggest that the administration of IgG purified from patients with high-titer anti-PS/PT antibodies to septic mice led to a strong trend toward improved survival while ameliorating infection-associated weight loss and sepsis severity (**Fig 2B-D**). Interestingly, aPL treatment also attenuated in situ neutrophil activation and NET formation, which are well-known orchestrators of sepsis hyper-inflammation (**Fig 2E-G**).

Conclusion: Our study suggests that many critically ill sepsis patients can develop aPL, potentially driven by heightened B-cell stimulating signals. While further mechanistic studies are warranted, some aPL may contribute to improved sepsis survival.

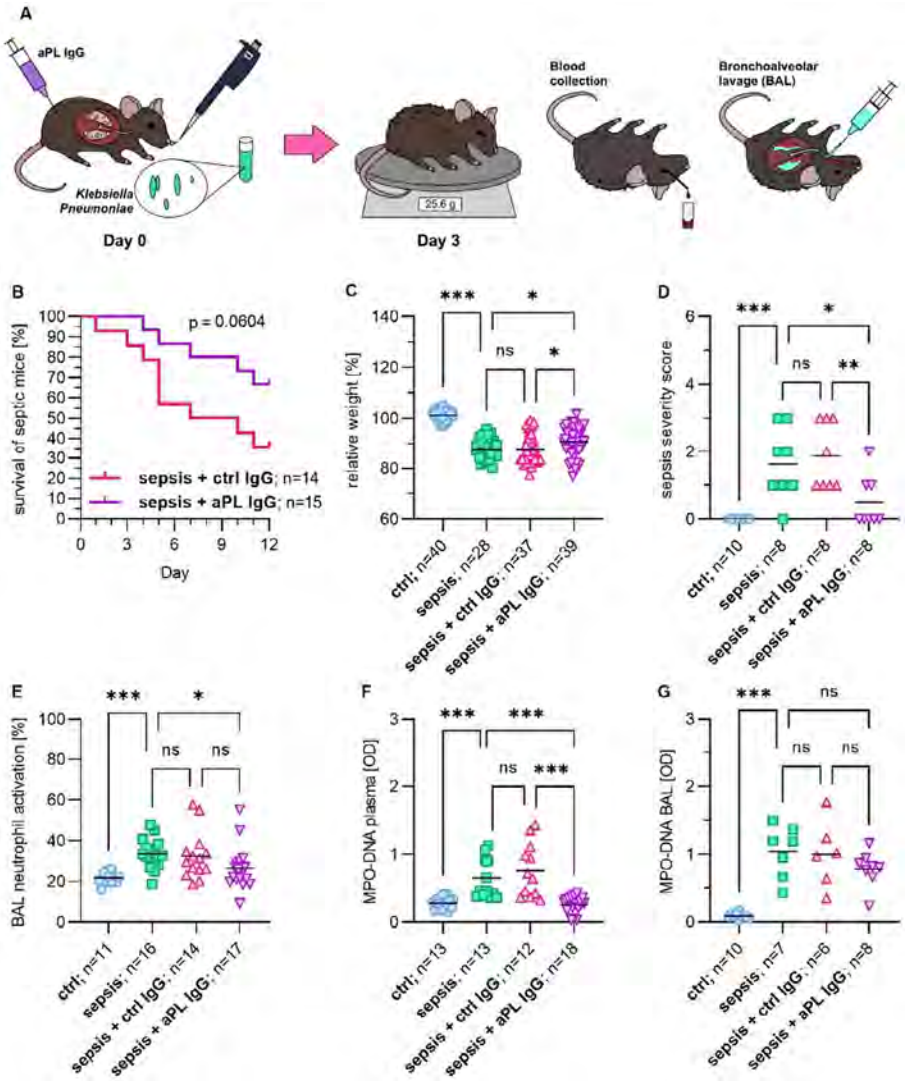

Figure 2: A, Schematic of Klebsiella pneumoniae sepsis mouse model. Mice were infected intranasally with Klebsiella pneumoniae. After 3 days, mice were sacrificed, and plasma and bronchoalveolar lavage fluid (BAL) were collected. B, Survival curves were compared between aPL and control (ctrl) IgG-treated mice by the Gehan-Breslow-Wilcoxon test. C, % weight change relative to day 0 was determined and compared between groups. D, Sepsis severity score was assessed based on observation of mice's piloerection, hunching, and movement and compared between groups. E, Activation of BAL neutrophils determined by flow cytometry based on CD63 positivity. F, circulating MPO-DNA complexes were measured in mouse plasma and compared between groups. G, MPO-DNA complexes were measured in BAL and compared between groups. We used the Kruskal-Wallis test with Dunn's correction to determine differences between groups. * - p<0.05; ** - p<0.01; *** - p<0.001; aPL – antiphospholipid antibodies MPO – myeloperoxidase; OD – optical density

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Abstract Number: 1604

First and Recurrent Thrombosis Risk After 4,454 Patient-Years of Follow-Up: Prospective Results from the AntiPhospholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking (APS ACTION) Clinical Database and Repository (“Registry”)

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Antiphospholipid Syndrome

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: The APS ACTION Registry was created to study the natural course of disease over 10 years in persistently antiphospholipid antibody (aPL)-positive patients with or without other systemic autoimmune diseases (SAID). The primary objective of this study was to update the incident first and recurrent thrombosis risk in registry-enrolled patients, previously reported in 2021 as 1.02 and 2.09 per 100 pt-y, respectively (*Arthritis Rheumatol*.2021;73[suppl 9]).

Methods: A web-based data capturing system is used to store patient demographics, history, and medications. The inclusion criteria are positive aPL according to the Updated Sapporo Classification Criteria, tested within one year prior to enrollment. Follow-up occurs every 12±3m with clinical data and blood collection. In this prospective analysis, based on patients who completed 1- to 10-year follow-up visits, we report the incident thrombosis risk in persistently aPL-positive patients with and without a history of thrombosis. Secondarily, we compare baseline clinical and laboratory characteristics of patients with vs without new thrombosis.

Results: As of April 2023, 1,166 patients were enrolled; 22 patients with a prior history of transient ischemic attack and no prior imaging-confirmed thrombosis were excluded. Five other patients were excluded due to incomplete data. Of the remaining 1,139 patients; a) 606 had aPL/APS without SAID, including aPL without APS classification (n=125), thrombotic

Table 1: Frequencies and Types of New Thrombotic Events Since the Inception of APS ACTION Registry

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	First Events (n = 14)	Recurrent Events (n = 88 in 65 patients)
Venous Thrombosis	6 (43%)	39 (44%)
Arterial Thrombosis	7 (50%)	44 (50%)
Catastrophic APS	0 (0%)	1 (1%)
Microthrombosis*	1 (7%)	4 (5%)

*Includes diffuse alveolar hemorrhage (3), aPL-nephropathy (2), cutaneous ulceration (1), and adrenal infarction with hemorrhage (1). Lung, kidney, and skin involvement occurred concurrently in one patient and were thus counted as a single small vessel event.

APS (TAPS, n=357), obstetric APS (OAPS, n=57), and TAPS+OAPS (n=67); and b) 533 patients had aPL/APS associated with SAID, including aPL without APS (n=164), TAPS (n=269), OAPS (n=35), and TAPS+OAPS (n=65). Mean follow-up (enrollment to first new thrombosis or most recent follow-up) was 3.67 years (1401 pt-y) and 4.03 years (3053 pt-y) for those

Table 2: Baseline Clinical and Laboratory Characteristics of Patients With vs Without Thrombosis Since the Inception of APS ACTION Registry

Table 2: Baseline Clinical and Laboratory Characteristics of Patients With vs Without Thrombosis Since the Inception of APS ACTION Registry

	aPL-positive Patients with First Events n = 14	aPL-positive Patients without First Events n = 368	APS Patients with Recurrent Events n = 65	APS Patients without Recurrent Events n = 692
Mean age +/- SD (registry entry)	41.86 +/- 13.5	44.83 +/- 13.0	44.08 +/- 14.6	47.13 +/- 13.7
Female	12 (86%)	315 (86%)	43 (66%)	472 (68%)
Systemic Autoimmune Disease	8 (57%)	192 (52%)	22 (34%)	311 (45%)
aPL Profile				
Triple aPL-positive	2 (14%)	119 (32%)	31 (48%)	247 (36%)
Double aPL-positive	4 (29%)	104 (28%)	14 (22%)	198 (29%)
Single aPL positive (aCL or aB2GPI)	2 (14%)	54 (15%)	4 (6%)	77 (11%)
single aPL positive (LA)	6 (43%)	91 (25%)	16 (25%)	170 (25%)
LA-positive with/without aCL/aB2GPI	12 (86%)	260 (71%)	55 (85%)	542 (78%)
Antiplatelet and Anticoagulant Medications				
VKA* Only	2 (14%)	14 (4%)	33 (51%)	366 (53%)
LMWH** Only	0 (0%)	4 (1%)	4 (6%)	24 (3%)
VKA + Antiplatelet Agent	0 (0%)	9 (2%)	12 (19%)	159 (23%)
LMWH + Antiplatelet Agent	0 (0%)	9 (2%)	1 (2%)	19 (3%)
Antiplatelet Agent only	7 (47%)	229 (62%)	5 (8%)	92 (13%)
Direct Oral Anticoagulants	0 (0%)	2 (1%)	8 (13%)	30 (4%)
None	5 (33%)	101 (27%)	4 (6%)	16 (2%)
Other Medications				
Hydroxychloroquine	6 (40%)	184 (49%)	29 (45%)	308 (45%)
Statin	2 (13%)	43 (12%)	14 (22%)	211 (30%)
Non-aPL Risk Factors				
≥ 1 CVD Risk Factor***	10 (71%)	225 (60%)	52 (80%)	515 (74%)
Hypertension	2 (14%)	75 (20%)	20 (31%)	270 (39%)
Diabetes	1 (7%)	17 (5%)	6 (9%)	48 (7%)
Hyperlipidemia on Medication	1 (7%)	43 (12%)	14 (22%)	209 (30%)
Family History of Early CVD	3 (20%)	39 (10%)	12 (19%)	86 (12%)
Obesity	2 (13%)	85 (23%)	26 (41%)	182 (26%)
Renal Failure	0 (0%)	5 (1%)	8 (12%)	33 (5%)
Smoking History (any)	8 (53%)	119 (32%)	22 (34%)	248 (36%)

*Vitamin K antagonist; **Low molecular weight heparin; ***CVD risk factors include hypertension, hyperlipidemia, diabetes mellitus, renal failure (GFR < 60), obesity (BMI > 30), history of smoking, family history of early cardiovascular disease (myocardial infarction in a first-degree relative before age 55 in men or age 65 in women).

Table 3: Clinical and Laboratory Characteristics of Patients (at the time of events) with First and Recurrent Thrombotic Events Since the Inception of APS ACTION Registry

Table 3: Clinical and Laboratory Characteristics of Patients (at the time of events) with First and Recurrent Thrombotic Events Since the Inception of APS ACTION Registry

	Patients with First Events (n = 14)	Patients with Recurrent Events (n = 65)*
Antiplatelet and Anticoagulant Medications		
VKA** only	2 (14%)	31 (48%)
LMWH*** only	0 (0%)	5 (8%)
VKA + Antiplatelet Agent	0 (0%)	11 (17%)
LMWH + Antiplatelet Agent	0 (0%)	1 (2%)
Antiplatelet Agent only	7 (50%)	6 (9%)
Direct Oral Anticoagulants	0 (0%)	9 (14%)
None	5 (36%)	4 (6%)
Other Medications		
Hydroxychloroquine	6 (43%)	32 (49%)
Statin	2 (14%)	14 (22%)
Non-aPL Risk Factors		
Sub-therapeutic INR (< 2)	--	19/42 (45%)
Recent Vascular Procedure	3 (21%)	2 (3%)
Prolonged Immobilization/Surgery/Travel	3 (21%)	8 (12%)
Active Malignancy	0 (0%)	2 (3%)
≥ 1 CVD Risk Factor****	10 (71%)	52 (80%)
Hypertension	2 (14%)	31 (48%)
Diabetes	1 (7%)	10 (15%)
Hyperlipidemia on Medication	3 (21%)	21 (32%)
Obesity	2 (14%)	28 (43%)
Renal Failure	0 (0%)	12 (18%)

*Among APS patients with multiple recurrent events during follow-up, characteristics from the time of the first recurrent event were analyzed; **Vitamin K antagonist; ***Low molecular weight heparin; ****CVD risk factors include hypertension, hyperlipidemia, diabetes mellitus, renal failure (GFR < 60), obesity (BMI > 30), history of smoking, family history of early cardiovascular disease (myocardial infarction in a first-degree relative before age 55 in men or age 65 in women).

without and with a history of thrombosis, respectively. Based on *14 first events in 14 patients,* and *88 recurrent events in 65 patients* (Table 1), the incident thrombosis risk was 1.00 and 2.13 per 100 pt-y in patients without and with a history of thrombosis, respectively. Baseline characteristics were similar between aPL-positive patients with (n=14) or without (n=368) first thrombosis, and between APS patients with (n=65) or without (n=692) recurrent thrombosis, except: a) obesity, renal failure, and direct oral anticoagulant use were more common in APS patients with recurrent thrombosis than in those without (p=0.02, 0.01, and 0.005, respectively); and b) smoking history was more common in patients with first thrombosis than in those without (p=0.05) (Table 2). Table 3 describes patient characteristics at the time of new events.

Conclusion: Based on 4,454 pt-y of follow-up, the incident thrombosis risk in persistently aPL-positive patients remains relatively low. Secondary analysis revealed possible differences in medications and cardiovascular risk factors at enrollment between patients with and without thrombosis during follow-up, but these results should be interpreted with caution given the large number of covariates analyzed (multiplicity). Future Cox proportional hazards analysis will help better define the risk and protective factors for thrombosis in persistently aPL-positive patients.

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AbbVie, 1, AstraZeneca, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Roche-Genentech, 1; **D. WAHL**: None; **M. Gerosa**: None; **G. De Jesús**: GlaxoSmithKlein(GSK), 5, UCB, 1; **Z. Zhang**: None; **T. Atsuma**: AbbVie, 5, 6, Alexion, 5, 6, Astellas, 5, 6, Boehringer-Ingelheim, 2, Bristol-Myers Squibb, 6, Chugai, 5, 6, Daiichi Sankyo, 5, 6, Eisai, 5, 6, Eli Lilly, 5, 6, Gilead, 5, 6, GSK, 2, 5, Merck Sharp & Dohme, 2, 6, Mitsubishi Tanabe Pharma, 5, 6, Otsuka, 5, 6, Pfizer, 5, 6, Sanofi/Genzyme, 2, 6, Takeda, 5, 6, UCB, 5, 6; **M. Efthymiou**: Alexion, 1, Immune Tolerance Network (ITN), 1; **D. Branch**: UCB Pharmaceuticals, 5; **L. Andreoli**: None; **E. Rodriguez almaraz**: None; **M. Petri**: Alexion, 1, Amgen, 1, AnaptysBio, 1, Annexon Bio, 1, Argenx, 1, Arhros-Focus Med/Ed, 6, AstraZeneca, 1, 5, Aurinia, 1, 5, 6, Axdev, 1, Biogen, 1, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CVS Health, 1, Eli Lilly, 1, 5, Emergent Biosolutions, 1, Exagen, 5, Exo Therapeutics, 2, Gilead Biosciences, 2, GlaxoSmithKlein(GSK), 1, 5, 6, Horizon Therapeutics, 2, Idorsia Pharmaceuticals, 2, IQVIA, 1, Janssen, 1, 5, Kira Pharmaceuticals, 2, MedShr, 6, Merck/EMD Serono, 1, Momenta Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Proviant, 2, Sanofi, 2, Sinomab Biosciences, 2, Thermofisher, 5, UCB, 2; **G. Pazzola**: None; **R. Cervera**: None; **B. Artim Esen**: None; **H. Shi**: None; **J. Knight**: Jazz Pharmaceuticals, 2; **G. Pons-Estel**: GlaxoSmithKlein(GSK), 1, 5, 6, Janssen, 1, 5, 6, Novartis, 1, 6, Pfizer, 5, 6, Werfen/Inova, 5, 6; **R. Willis**: None; **A. Duarte-Garcia**: None; **M. Bertolaccini**: None; **H. Cohen**: argenx, 1, Roche, 1, Technoclone (paid to University College London Hospital (UCLH) Charity), 6, UCB Biopharma (paid to UCLH Charity), 2; **D. Erkan**: Abbvie, 1, ACR/EULAR, 5, APS ACTION, 12, Executive Committee Co-chair, Argenx, 1, Aurinia, 6, Chugai, 1, Exagen, 5, GSK, 5, 6, NIH-NIAID, 5, Up-To-Date, 9; **O. Of APS ACTION**: None.

Abstract Number: 1605

Complement Activation as a Marker of Thrombosis Risk in Antiphospholipid Antibody Positive Patients: Prospective Results from AntiPhospholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking (APS ACTION) Clinical Database and Repository (''Registry'')

Cecile Yelnik[1], Shruti Chaturvedi[2], Julien Labreuche[1], Xiang-Zuo Pan[3], H Michael Belmont[4], Kello Nina[5], Paul R. Fortin[6], D. Ware Branch[7], Yu Zuo[8], Rohan Willis[9], Robert Brodsky[10], Jane Salmon[11], Maria Laura Bertolaccini[12], Hannah Cohen[13], Michelle Petri[14], Doruk Erkan[11] and On Behalf Of APS ACTION[15], [1]University of Lille, Lille, France, [2]Johns Hopkins University School of Medicine, Baltimore, MD, [3]John Hopkins University, Baltimore, MD, [4]NYU School of Medicine, New York, NY, [5]Northwell Health, Brooklyn, NY, [6]Centre ARThrite - CHU de Québec - Université Laval, Quebec City, QC, Canada, [7]University of Utah, Salt Lake City, UT, [8]University of Michigan, Ann Arbor, MI, [9]University of Texas Medical Branch, Galveston, TX, [10]Johns Hopkins University, Baltimore, MD, [11]Hospital for Special Surgery, New York, NY, [12]King's College London, London, United Kingdom, [13]University College London Hospitals NHS Foundation Trust, London, United Kingdom, [14]Department of Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Timonium, MD, [15]on behalf of APS ACTION, New York, NY

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Antiphospholipid Syndrome

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Recent studies implicate complement activation in the pathophysiology of antiphospholipid syndrome (APS), especially in patients with severe manifestations, such as catastrophic APS (CAPS). This study aimed to prospectively evaluate whether complement activation biomarkers are associated with new (first or recurrent) thrombosis in antiphospholipid antibody (aPL)-positive patients.

Methods: APS ACTION registry inclusion criteria are positive aPL based on the updated Sapporo APS Classification Criteria, tested at least twice within one year prior to enrollment. Patients are prospectively followed every 12±3m with clinical data and blood collection. We identified patients with new thrombosis during follow-up, and controls without new

Table 1: Baseline Characteristics of Antiphospholipid Antibody (aPL)-positive Patients with or without New Thrombosis During the Follow-up

Characteristics	Total (n=52)	New Thrombosis (n=27)	No New Thrombosis (n=25)	p-value
Age at Registry Entry, years	53 (±15)	52 (±15)	53 (±14)	0.75
Female	36 (69)	18 (67)	18 (72)	0.68
Associated-SAID	40 (77)	20 (74)	20 (80)	0.61
SLE	18 (35)	9 (33)	9 (36)	0.84
aPL with no APS Classification	4 (8)	2 (7)	2 (8)	0.94
Thrombotic APS	45 (87)	22 (82)	23 (92)	0.27
- Venous thrombosis	31 (60)	18 (67)	13 (52)	0.28
- Arterial thrombosis	18 (35)	9 (33)	9 (36)	0.84
- Both	6 (12)	6 (22)	0 (0)	0.02
Obstetric APS	3 (6)	3 (6)	0 (0)	NA
Microvascular APS	12 (23)	6 (22)	6 (24)	0.88
- aPL nephropathy	3 (6)	3 (11)	0 (0)	0.24
- Diffuse Alveolar Hemorrhage	3 (6)	1 (4)	2 (8)	0.60
- Other	8 (15)	4 (15)	4 (16)	1.00
Non-criteria manifestation				
- Livedo reticularis/racemosa	4 (8)	3 (11)	1 (4)	0.61
- Thrombocytopenia	5 (10)	4 (15)	1 (4)	0.35
- Cardiac valve disease	3 (6)	1 (4)	2 (9)	0.61
Body Mass Index	29 (±10)	32 (±11)	28 (±8)	0.03
Baseline aPL profile				
-LA positive	42 (88)	24 (96)	18 (78)	0.09
-aCL IgG/IgM positive	38 (73)	21 (78)	17 (68)	0.43
-aβ_2GPI IgG/IgM positive	35 (67)	18 (67)	17 (71)	0.75
-Triple aPL positivity	25 (48)	16 (59)	9 (36)	0.09
-Double aPL positivity	15 (29)	5 (19)	10 (40)	0.09
-Single aPL positivity	10 (19)	5 (19)	5 (20)	1.00
Antiplatelet therapy	22 (42)	10 (37)	12 (48)	0.42
Anticoagulant therapy	35 (67)	16 (59)	19 (76)	0.20
Hydroxychloroquine	32 (62)	15 (56)	17 (68)	0.36
Statins	10 (19)	5 (19)	5 (20)	1.00
Duration between historical thrombosis and first blood sample, months	77 (±102)	53 (±71)	110 (±118)	0.04

- Data are expressed as number (percentage of the total), mean (±standard deviation), or median (±interquartile range). Comparisons between groups were performed using T-test or Mann Whitney U test for continuous variables and Chi-square or Fisher's exact test for categorical variables. Statistical significance $p<0.05$.
- APS= antiphospholipid syndrome, SAID= systemic autoimmune disease, SLE= systemic lupus erythematosus, LA= lupus anticoagulant, aCL= anticardiolipin antibody, aβ_2GPI= anti-β_2-glycoprotein-I antibody

thrombosis, matched (1:1) for gender, age (±5 years), history of thrombosis, and associated autoimmune disease. Complement activation was evaluated by plasma levels of soluble C5b-9 (sC5b-9), C4d, and Bb fragment (commercial ELISA), and the modified HAM (mHAM) assay that measures complement-dependent cell killing. For each patient, two annual follow-up samples were evaluated (first available and most recent prior to event; or first two available in those without new thrombosis). If available, a third "acute" sample within three months of the new thrombosis was also studied.

Results: As of May 2022, 365 aPL-positive patients from North American centers were included in the registry; 27 (7%) patients had a new thrombosis during the prospective follow-up and were matched with 25 patients without new thrombosis. Baseline characteristics were similar, except those with new thrombosis were more likely to have a history of both arterial and venous thromboses ($p=0.02$), a higher body mass index ($p=0.03$), and a trend towards triple aPL positivity ($p=0.09$) (Table 1). After a median follow-up of 4.6 years (±IQR, 5.6), 13 patients had new arterial thrombosis, 12 venous, and two microvascular. In patients with new thrombosis, compared to those with no new thrombosis: a) C4d level was significantly elevated (median level 4.22 (±IQR, 3.39) μg/ml versus 3.33 (±IQR, 2.56) μg/ml; $p=0.041$); b) the number of patients with positive mHAM test was significantly higher (8 [30%)]versus 1 [4%]; $p=0.026$); and c) there was no significant difference in

Table 2: Complement Activation Biomarkers in Antiphospholipid Antibody-positive Patients with or without New Thrombosis During the Follow-up

Complement Biomarkers	Total (n=52)	New Thrombosis (n=27)	No New Thrombosis (n=25)	p-value
Elevated sC5b-9 (# patients (%))	44/50 (88)	23/26 (89)	21/24 (88)	1.00
sC5b-9 level, ng/ml (median (±IQR))	412 (±307)	491 (±367)	346 (±308)	0.20
sC5b-9 in acute* samples, ng/ml		482 (±295)		
Elevated C4d	NA	NA	NA	NA
C4d levels, µg/ml (median (±IQR))	3.63 (±3.18)	4.21 (±3.39)	2.87 (±2.56)	**0.041**
C4d in acute* samples, µg/ml		4.27 (3.7)		
Elevated Bb (# patients (%))	15/50 (30)	10/26 (39)	5/24 (21)	0.17
Bb level, µg/ml (median (±IQR))	1.06 (±0.59)	1.03 (±0.77)	1.16 (±0.53)	0.71
Bb in acute* samples, µg/ml		1.41 (±1.54)		
Positive mHAM (# of patients)	9/51 (18)	8/27 (30)	1/24 (4)	**0.026**

- Data are expressed as number (percentage of the total), or median (±interquartile range). Comparisons between groups were performed using Mann Whitney U test for continuous variables and Chi-square or Fisher's exact test for categorical variables. Statistical significance $p<0.05$
- Elevated levels were defined based on manufacturer 's normal range values, which were available for soluble C5b-9 (sC5b-9) (normal: (≤219 ng/ml) and Bb (normal: ≤1.42 µg/ml), but not for C4d. Positive modified HAM (mHAM) test was based on >20% cell non-viability.
- sC5b-9, C4d, and Bb values were expressed as the mean of the two values obtained from samples before the new thrombosis (no significant changes in results if analyzed based on the first or second sample – data not shown). * within three months of acute thrombosis.

sC5b-9 and Bb levels despite a trend toward a higher number of elevated Bb in patients with new thrombosis (Table 2). In nine patients with "acute" samples obtained within three months of new thrombosis, sC5b-9 was elevated in all, Bb fragment in four (44%), and mHAM test was positive in three (33%).

Conclusion: Based on the analysis of our multi-center prospective cohort of persistently aPL-positive patients, our preliminary findings suggest that markers of complement activation, specifically elevated C4d levels and positive mHAM test, are associated with a higher risk of thrombosis, which might be a useful tool to aid risk-stratification.

Disclosure: C. Yelnik: None; **S. Chaturvedi**: AstraZeneca, 1, sanofi, 2, Sobi, 1, 2, takeda, 1, 2; **J. Labreuche**: None; **X. Pan**: None; **H. Belmont**: Alexion, 6, Aurinia, 6; **K. Nina**: None; **P. Fortin**: AbbVie, 1, AstraZeneca, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Roche-Genentech, 1; **D. Branch**: UCB Pharmaceuticals, 5; **Y. Zuo**: None; **R. Willis**: None; **R. Brodsky**: None; **J. Salmon**: None; **M. Bertolaccini**: None; **H. Cohen**: argenx, 1, Roche, 1, Technoclone (paid to University College London Hospital (UCLH) Charity), 6, UCB Biopharma (paid to UCLH Charity), 2; **M. Petri**: Alexion, 1, Amgen, 1, AnaptysBio, 1, Annexon Bio, 1, Argenx, 1, Arhros-Focus Med/Ed, 6, AstraZeneca, 1, 5, Aurinia, 1, 5, 6, Axdev, 1, Biogen, 1, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CVS Health, 1, Eli Lilly, 1, 5, Emergent Biosolutions, 1, Exagen, 5, Exo Therapeutics, 2, Gilead Biosciences, 2, GlaxoSmithKlein(GSK), 1, 5, 6, Horizon Therapeutics, 2, Idorsia Pharmaceuticals, 2, IQVIA, 1, Janssen, 1, 5, Kira Pharmaceuticals, 2, MedShr, 6, Merck/EMD Serono, 1, Momenta Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Proviant, 2, Sanofi, 2, Sinomab Biosciences, 2, Thermofisher, 5, UCB, 2; **D. Erkan**: Abbvie, 1, ACR/EULAR, 5, APS ACTION, 12, Executive Committee Co-chair, Argenx, 1, Aurinia, 6, Chugai, 1, Exagen, 5, GSK, 5, 6, NIH-NIAID, 5, Up-To-Date, 9; **O. Of APS ACTION**: None.

Abstract Number: 1606

Purinergic Signaling as a Potential Therapeutic Target for APS Thromboinflammation

NaveenKumar K. Somanathapura, Claire Hoy, Srilakshmi Yalavarthi, Cyrus Sarosh, Bruna De Moraes Mazetto Fonseca, Caroline Ranger, Christine Rysenga, Ajay Tambralli, Jacqueline Madison, Yu Zuo and Jason Knight, University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Antiphospholipid Syndrome
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: In first responding cells such as neutrophils and platelets, extracellular ATP released from activated or dying cells engages cell-surface receptors to launch proinflammatory and prothrombotic signals. As a counterpoint to this thromboinflammatory purinergic signaling, the surface ectonucleotidases CD39 (ATP to AMP) and CD73 (AMP to adenosine) convert ATP into homeostatic adenosine. Adenosine then activates G protein-coupled receptors to increase

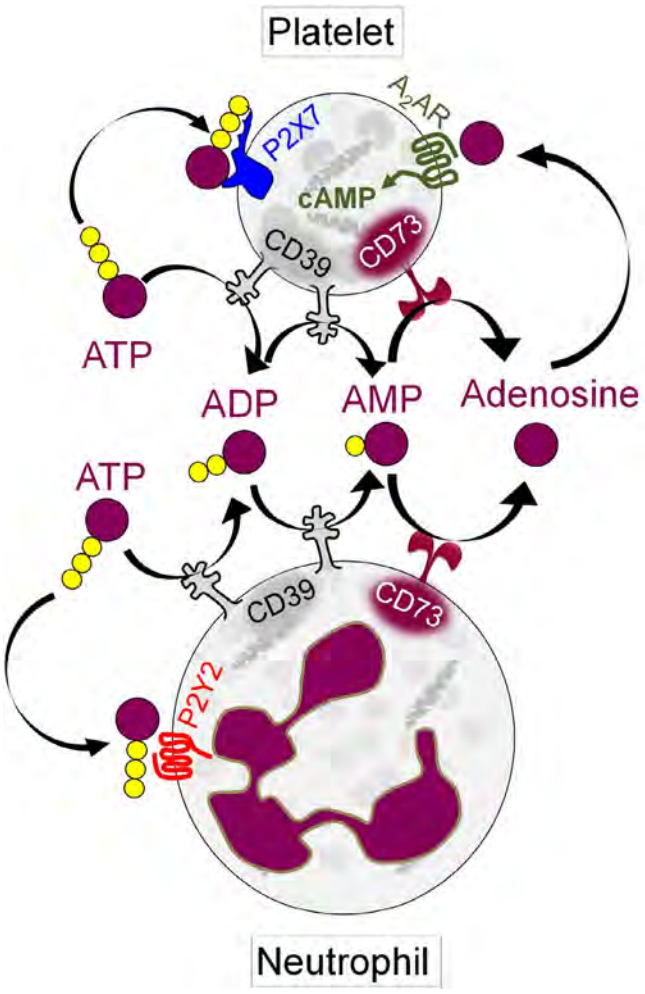

Figure 1: Schematic representation of purinergic signaling in platelets and neutrophils.

intracellular cyclic AMP (**cAMP**), thereby blunting inflammation and thrombosis. Here, we aimed to understand the potential relationship between the CD39/CD73 axis, neutrophils, and platelets in antiphospholipid syndrome (**APS**).

Methods: Neutrophil-platelet aggregates (**NPAs**) and platelet P-selectin (CD62P) were assessed in the blood of patients with primary APS by flow cytometry. In parallel, CD39 and CD73 activities on both neutrophils and platelets were measured by a standard malachite green assay. Levels of adenosine generation and intracellular cAMP were estimated using standard kits. In some experiments, healthy neutrophils and platelets were treated with APS IgG, specific CD39/CD73 activity inhibitors (ARL 67156, PSB 12379), or inhibitors of various surface receptors.

Results: As compared with healthy controls (n=48), patients with primary APS (n=55) showed at least a 50% reduction in median activities of neutrophil CD39 ($p< 0.0001$), neutrophil CD73 ($p< 0.0001$), platelet CD39 ($p< 0.0001$), and platelet CD73 ($p< 0.0004$). These changes were negatively correlated with significant increases in both NPAs (up to 80%, $p< 0.0001$) and platelet activation as defined by CD62P expression ($p< 0.002$). The levels of NPAs were higher in patients with APS who had a history of thrombosis than those without. When healthy neutrophils and platelets were cultured with either APS IgG or a CD39 inhibitor, there was a dose-dependent increase in NPA formation (from baseline 15% to 70%), and this phenotype was substantially blocked by inhibition of either the neutrophil P2Y2 receptor or the platelet P2X7 receptor. Focusing further on APS platelets, we found a significant decrease in their ability to generate adenosine ($p< 0.01$), as well as in their accumulation of intracellular cAMP ($p< 0.001$). Notably, CD62P expression was inversely correlated with platelet cAMP levels in patients ($r=-0.52$, $p=0.007$). Exposure of healthy platelets to APS IgG induced AKT phosphorylation (ser473) followed by downstream activation of GSK3β (ser9). This pro-activation signaling was efficiently blunted by agents that either activated adenosine receptors or directly boosted intracellular cAMP.

Conclusion: In primary APS, deficiency of CD39 and CD73 on both neutrophils and platelets potentiates pro-thrombotic platelet activation and NPA formation. By interrogating the downstream mechanisms, we identified several potential therapeutic targets including neutrophil P2Y2 and platelet P2X7 (**Figure 1**). Adenosine receptor agonists might be a strategy for restoring platelet homeostasis in APS. Overall, we speculate that a subset of patients with APS would benefit from therapies that modulate extracellular purinergic signaling.

Disclosure: N. Somanathapura: None; **C. Hoy**: None; **S. Yalavarthi**: None; **C. Sarosh**: None; **B. De Moraes Mazetto Fonseca**: None; **C. Ranger**: None; **C. Rysenga**: None; **A. Tambralli**: None; **J. Madison**: None; **Y. Zuo**: None; **J. Knight**: Jazz Pharmaceuticals, 2.

Abstract Number: 1607

Autoantibodies to Transcription Factor a Mitochondria Link Mitochondrial Damage and Thrombosis in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Antiphospholipid Syndrome

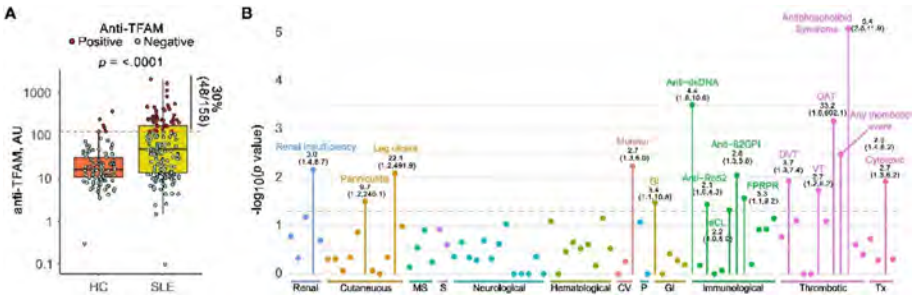
Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

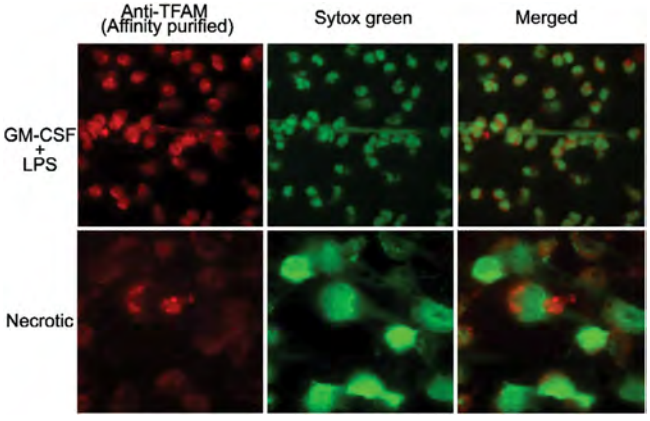
Background/Purpose: Upon activation with interferon (IFN) and RNP-immune complexes, defective mitophagy in neutrophils results in the release of mtDNA in complex with transcription factor A mitochondria (TFAM), leading to immune activation in SLE. TFAM is a member of the high-mobility group (HMG) family of DNA-binding proteins, which is essential for mtDNA transcription and for packaging mtDNA into nucleoids. Extracellular TFAM released from necrotic cells is also a DAMP. While characterizing novel autoantigens expressed by neutrophils, we identified TFAM as a target of antibodies in SLE. The purpose of this study was to investigate the relationship between anti-TFAM antibodies and clinical and transcriptional markers of disease activity in SLE

Methods: Anti-neutrophil antibodies in SLE sera were detected by indirect immunofluorescence (IIF). Anti-TFAM antibodies were screened by ELISA in sera from 98 healthy controls and 158 SLE patients from the "Study of biological Pathways, Disease Activity and Response markers in patients with Systemic Lupus Erythematosus" (SPARE). SPARE is a 2-year prospective cohort of adult patients for which extensive clinical, serologic, and whole blood transcriptional data is available. Binding of anti-TFAM antibodies to activated (GM-CSF + LPS) and necrotic neutrophils was determined by IIF.

Results: A subset of antibodies in SLE serum co-localizes with TFAM in neutrophils. The existence of anti-TFAM antibodies in SLE was confirmed by ELISA and immunoblotting. Thirty percent (48/158) of SLE patients were positive for anti-TFAM antibodies (Fig. 1A). Anti-TFAM antibodies were significantly associated with antibodies to dsDNA, cardiolipin (aCL), and β2-glycoprotein I (β2GPI) (Fig 1B). Anti-TFAM antibodies were strongly associated with history of thrombotic events, OR (95% CI) 2.9 (1.4,6.2), and secondary antiphospholipid syndrome (APS), OR (95% CI) 5.4 (2.5,11.9), independently of



Anti-TFAM antibodies are associated with thrombosis and APS in SLE. (A) Serum levels of anti-TFAM antibodies in patients with SLE (n=158) and Healthy controls (HC, n-98). Dots in red represent subjects positive for anti-TFAM. (B) Clinical and serological associations of anti-TFAM antibodies in SLE. Each dot represents the p value for the indicated SLE feature. Only features with a p value < 0.05 are labeled. P values were obtained with Fisher's exact test. Odds ratios and 95% CI, OR (95%CI), are indicated below each label.



Anti-TFAM antibodies recognize extracellular TFAM from GM-CSF + LPS activated (upper row) and necrotic neutrophils (lower row). Anti-TFAM antibodies (red) were purified by affinity chromatography, using recombinant TFAM, from a pool (n=3) of anti-TFAM positive SLE sera. DNA was stained using Sytox Green (Green channel).

aCL and anti- β2GPI (Fig. 1B). Unlike antibodies to dsDNA and RNPs, anti-TFAM antibodies were not associated with blood transcriptional markers of SLE disease activity, including the IFN signature, supporting a primary role of anti-TFAM antibodies in thrombosis rather than disease flaring. Anti-TFAM antibodies bind to TFAM-decorated DNA released from activated and necrotic neutrophils (Fig. 2), which is a mechanism that may contribute to thrombosis.

Conclusion: TFAM is novel autoantigen in SLE, which is associated with thrombosis and APS independently of aCL in SLE. These data support a link between mitochondrial damage and thrombosis in SLE.

Disclosure: E. Gomez-Banuelos: None; **A. Celia**: None; **M. Trejo Zambrano**: None; **M. Paz**: None; **E. Darrah**: None; **D. Goldman**: None; **M. Petri**: Alexion, 1, Amgen, 1, AnaptysBio, 1, Annexon Bio, 1, Argenx, 1, Arhros-Focus Med/Ed, 6, AstraZeneca, 1, 5, Aurinia, 1, 5, 6, Axdev, 1, Biogen, 1, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CVS Health, 1, Eli Lilly, 1, 5, Emergent Biosolutions, 1, Exagen, 5, Exo Therapeutics, 2, Gilead Biosciences, 2, GlaxoSmithKlein(GSK), 1, 5, 6, Horizon Therapeutics, 2, Idorsia Pharmaceuticals, 2, IQVIA, 1, Janssen, 1, 5, Kira Pharmaceuticals, 2, MedShr, 6, Merck/EMD Serono, 1, Momenta Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Proviant, 2, Sanofi, 2, Sinomab Biosciences, 2, Thermofisher, 5, UCB, 2; **F. Andrade**: None.

Abstract Number: 1608

Plasma Proteomic Profiling in Antiphospholipid Antibody-positive Patients with Different Clinical Phenotypes: Results from the Antiphospholipid Syndrome Alliance for Clinical Trials and International Networking (APS ACTION) Registry

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Abstracts: Antiphospholipid Syndrome
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Antiphospholipid syndrome (APS) is an autoimmune disease with thrombotic and obstetric complications arising via a model of immunothrombosis. Patients may present with a spectrum of phenotypes, including thrombotic (tAPS), obstetric (oAPS), or catastrophic/microvascular APS (C/MAPS), while others may have antiphospholipid antibodies (aPL) without disease manifestations. Mechanisms underlying the development of these diverse phenotypes remain uncertain. Proteomic profiling was used in other thrombotic and microvascular disorders to highlight potential mechanisms of disease pathogenesis and may have a role in understanding the pathophysiology of APS.

We performed multiplex plasma proteomic profiling in aPL-positive patients with different clinical phenotypes to gain a greater understanding of potential immunothrombotic mechanisms in the pathogenesis of APS.

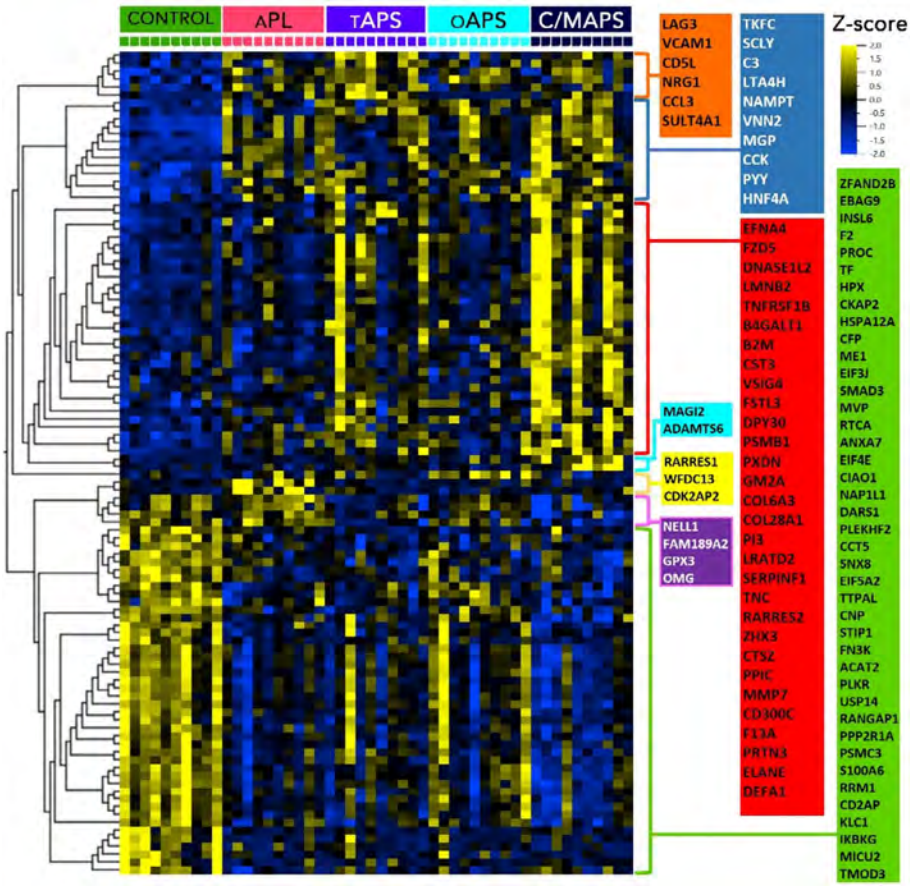

Figure A. Differentially abundant proteins by APS types and control subjects; APL, non-thrombotic APS (antibodies only); TAPS, thrombotic APS; OAPS, obstetric APS; CAPS/MV, catastrophic /microvascular APS. ANOVA on log-normalized data ($p<0.0007$, FDR $q<0.05$). FDR, false discovery rate.

Methods: A web-based data capturing system was used to store patient demographics, history, and medications. The inclusion criteria were positive aPL per Updated Sapporo Classification Criteria tested within 1 year prior to enrollment. Multiplex proteomic profiling measuring approximately 7,000 unique proteins (SomaLogic; Boulder, CO, USA) was performed

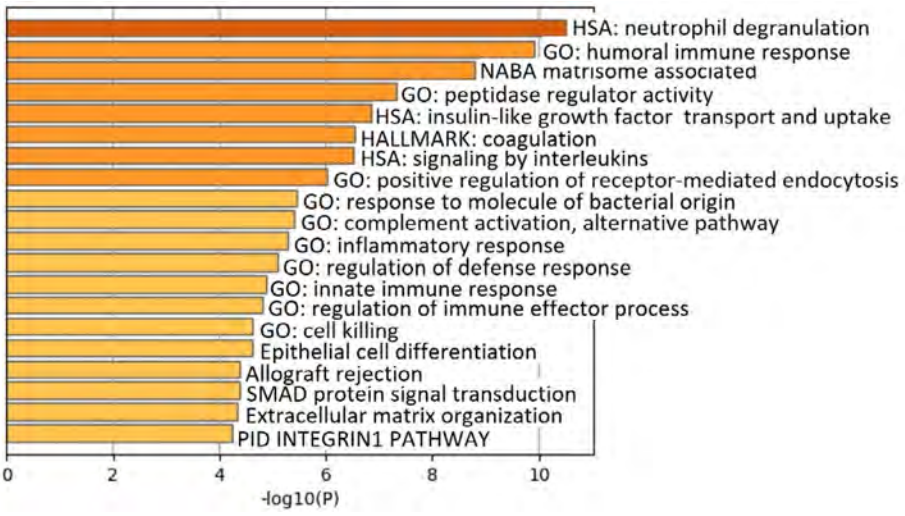

Figure B. Pathways enrichment analysis of proteins from Figure A.

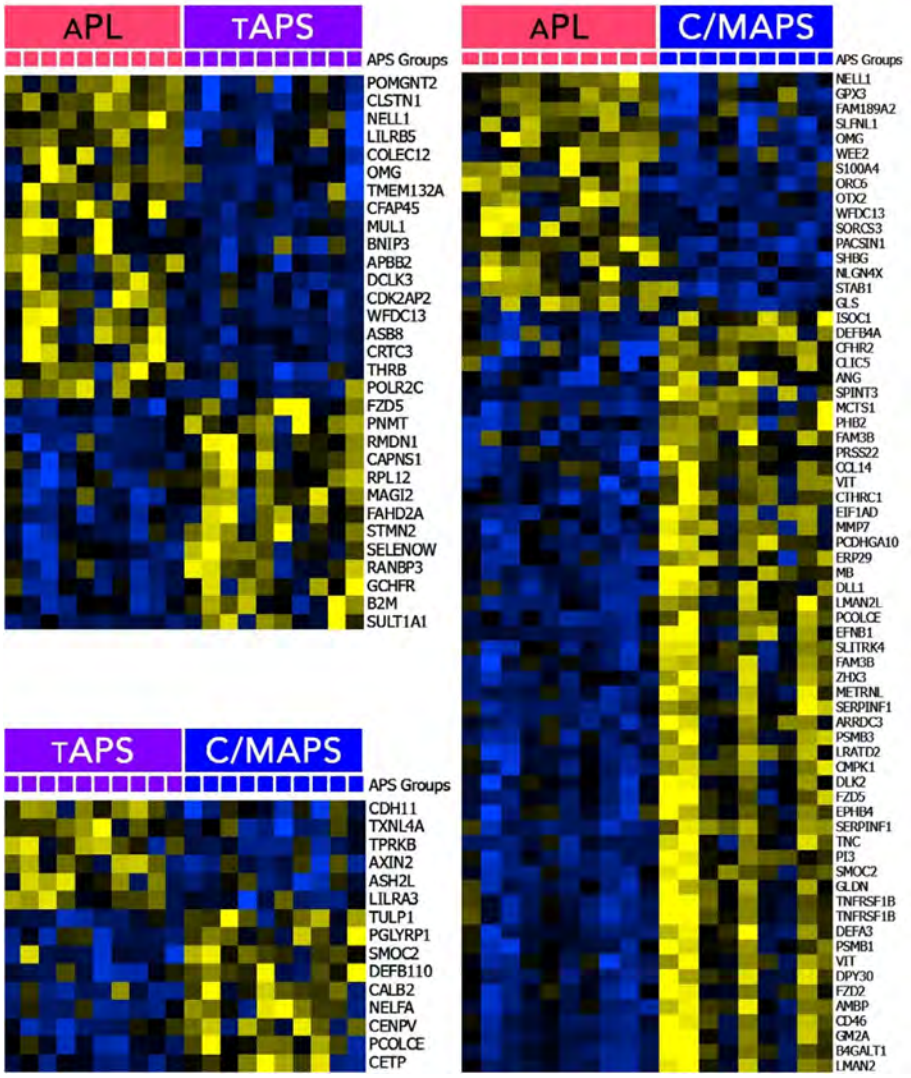

Figure C. Differentially abundant proteins by APS in pairwise comparisons between APS types; APL (non-thrombotic APS, antibodies only), p<0.01; TAPS (thrombotic APS), p<0.01; CAPS/MV (catastrophic /microvascular APS), p<0.005. T-tests on log-normalized data.

on 40 primary aPL-positive patient plasma samples from APS ACTION Registry (10 each of tAPS with/without oAPS, oAPS only, C/MAPS, and positive aPL without APS classification), and 10 of healthy controls. Differentially abundant proteins among all phenotypic groups and in pairwise comparisons were determined by applying ANOVA and t-tests to log-normalized data, respectively, with $p < 0.05$ considered statistically significant. Tests were adjusted for false discovery to minimize the likelihood of false positives.

Results: The median age of patients was 48 years; 30% were men, 70% had triple aPL-positivity, and no one had a concurrent diagnosis of lupus. A set of concordant and differentially abundant proteins clustered patients with 4 APS clinical phenotypes and controls (Figure A) with a high statistical significance ($p < 0.0007$) and a high false discovery confidence ($q < 0.05$). Pathway enrichment analysis of proteins in the identified set revealed involvement of several pathways such as neutrophil degranulation ($p < 10^{-10}$), humoral immune response ($p < 10^{-9}$), coagulation ($p < 10^{-6}$), alternative complement ($p < 10^{-5}$) and others (Figure B). Pairwise analyses of APS subtypes revealed increasing abnormalities in these pathways with worsening APS severity, but distinctly in cellular processes such as endocytosis/vesicle-mediated transport, receptor signaling, signal transduction and cellular differentiation (Figure C). This was particularly striking in C/MAPS subtype, with members of negative regulation of inflammatory response and cellular differentiation processes being the only distinction between tAPS and C/MAPS.

Conclusion: Plasma proteome of several APS subtypes is characterized by alteration in peripheral blood cellular processes, particularly receptor signaling, signal transduction and regulation of cellular differentiation, in addition to significant neutrophil, complement, coagulation and cytokine activation notable in all aPL-positive patients.

Disclosure: A. Butt: None; **R. Garcia Milian**: None; **G. Goshua**: None; **S. Gu**: None; **E. Chock**: None; **V. Restrepo**: None; **J. Hwa**: None; **H. Chun**: None; **H. Belmont**: Alexion, 6, Aurinia, 6; **K. Nina**: None; **D. Branch**: UCB Pharmaceuticals, 5; **M. Petri**: Alexion, 1, Amgen, 1, AnaptysBio, 1, Annexon Bio, 1, Argenx, 1, Arhros-Focus Med/Ed, 6, AstraZeneca, 1, 5, Aurinia, 1, 5, 6, Axdev, 1, Biogen, 1, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CVS Health, 1, Eli Lilly, 1, 5, Emergent Biosolutions, 1, Exagen, 5, Exo Therapeutics, 2, Gilead Biosciences, 2, GlaxoSmithKlein(-GSK), 1, 5, 6, Horizon Therapeutics, 2, Idorsia Pharmaceuticals, 2, IQVIA, 1, Janssen, 1, 5, Kira Pharmaceuticals, 2, MedShr, 6, Merck/EMD Serono, 1, Momenta Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Proviant, 2, Sanofi, 2, Sinomab Biosciences, 2, Thermofisher, 5, UCB, 2; **J. Knight**: Jazz Pharmaceuticals, 2; **R. Willis**: None; **M. Bertolaccini**: None; **D. Erkan**: Abbvie, 1, ACR/EULAR, 5, APS ACTION, 12, Executive Committee Co-chair, Argenx, 1, Aurinia, 6, Chugai, 1, Exagen, 5, GSK, 5, 6, NIH-NIAID, 5, Up-To-Date, 9; **A. Iee**: None; **A. Sharda**: None; **A. Pine**: None.

Abstract Number: 1609

Associations Between SARS-Cov-2 Infection and Neuropathic Pain in Fibromyalgia Patients: A Cohort Study

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Fibromyalgia & Other Clinical Pain Syndromes
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: SARS-CoV-2 infection has been increasingly recognized for its potential neurological manifestations. Fibromyalgia (FM) patients, who already experience neuropathic pain, may be particularly vulnerable to the impact of COVID-19 on their symptoms.

This study aims to investigate the specific influence of SARS-CoV-2 infection on the neuropathic component of pain in Fibromyalgia patients, shedding light on potential interactions between COVID-19 and FM.

Methods: We conducted a prospective cohort study enrolling FM patients who met the ACR 2016. The cohort was divided into two groups: patients who tested positive for SARS-CoV-2 infection and a matched cohort of uninfected FM patients. Neuropathic pain was assessed using the PainDetect Questionnaire (PDQ) at baseline (t0) and after six months (t1). Prevalence, incidence, and worsening of neuropathic pain were evaluated in both groups. Patients were considered to have neuropathic pain if the PDQ score was > 20, and data were analyzed by Chi-Square and paired T student test as appropriate

Results: We conducted a cohort study involving 58 FM patients (median age: 47 years; 2 males, 56 females). All patients were receiving treatment with SNRI antidepressants and Pregabalin, except for one patient who solely underwent physical therapy. At baseline, there were no significant differences in clinical or demographic characteristics between the infected and uninfected groups (table 1).

Baseline characteristics	COVID-19 Group	Uninfected Group	*p value*
Sex n (% of Female)	29 (96.5%)	29 (96.5%)	
Age Median years (SD)	52,07 (11.53)	55,72 (8.73)	*0,179*
BMI Kg/m2 (SD)	26,59 (9.45)	26,38 (5.41)	*0,2781*

As assessed by PDQ, the prevalence of neuropathic pain did not differ significantly between the two groups at baseline (36.21% vs 27.59%, p=0.17). However, patients who experienced SARS-CoV-2 infection had a significantly higher incidence of neuropathic pain at the six-month follow-up compared to the uninfected controls (46.55% vs. 31.03%, p=0.004, Relative Risk 5.5, 95% CI [1.5;21.1]).

When analyzing the sequential changes in PDQ scores, we found no statistically significant alteration in neuropathic pain severity over the six-month observation period among the uninfected group (t0 PDQ mean 20,1 (SD 6.7) vs. t1 20.72 (SD 7.4), p =0.37). Conversely, the infected group demonstrated a significant worsening of neuropathic pain at six months post-infection, as indicated by higher mean PDQ scores (t0 21.1 (SD 5.8) vs. t1 26.9 (SD 5.3) $p < 0.0005$).

Conclusion: This study indicates a potential link between infections and chronic pain in FM patients, as evidenced by the associations observed between SARS-CoV-2 infection and increased incidence and worsening of neuropathic pain. Further research is required to confirm these findings and explore potential interventions for FM patients.

Disclosure: D. Perretta: None; **D. Mauro**: None; **f. riccio**: None; **v. marino**: None; **e. scoppetta**: None; **F. ciccia**: None; **r. tirri**: None.

Abstract Number: 1610

Digital Acceptance and Commitment Therapy Improves Fibromyalgia Outcomes: Results from a Pivotal, Multi-center, Randomized Controlled Trial

Michael Gendreau[1], Andrea Chadwick[2], Lance McCracken[3], David Williams[4], Daniel Clauw[5], Juan Luciano[6], Yifei Dai[7], Nicolette Vega[8], Zunera Ghalib[8], Kristen Guthrie[8], Allison Kraus[8], Michael Rosenbluth[8], Jennifer Zomnir[9], Dana Reddy[10] and Lesley arnold[11], [1]Gendreau Consulting, LLC, Poway, CA, [2]Department of Anesthesiology, Pain, and Perioperative Medicine, University of Kansas School of Medicine, Kansas City, KS, [3]Department of Psychology, Uppsala University, Uppsala, Sweden, [4]Chronic Pain and Fatigue Research Center, Department of Anesthesiology, University of Michigan, Ann Arbor, MI, [5]Department of Anesthesiology, University of Michigan, Ann Arbor, MI, [6]Department of Clinical and Health Psychology, Universitat Autónoma de Barcelona, Barcelona, Spain, [7]Swing Therapeutics, Gainesville, FL, [8]Swing Therapeutics, San Francisco, CA, [9]DelRicht Resesarch, Mckinney, TX, [10]Curavit, Scarsdale, NY, [11]Department of Psychiatry and Behavioral Neuroscience, University of Cincinnati, Cincinnati, OH

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Fibromyalgia & Other Clinical Pain Syndromes

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Acceptance and Commitment Therapy (ACT), a form of guideline-recommended Cognitive Behavioral Therapy (CBT), has been empirically validated as a non-drug treatment for fibromyalgia (FM). However, clinical adoption of the therapy has been limited partly due to availability of qualified providers as a major barrier.

A smartphone-based, prescription digital application (FM-ACT) that has been recently cleared by the FDA helps address the access barrier by delivering self-guided ACT for treatment of FM symptoms. Its preliminary clinical benefits have been demonstrated in a pilot RCT.[1] This report presents the results from PROSPER-FM (NCT05243511), a pivotal, prospective, multicenter, randomized controlled trial (RCT).

Methods: Individuals meeting 2016 FM diagnostic criteria were randomized to receive 12 weeks of FM-ACT or a digital symptom tracker control (ST) while remaining stable on any ongoing FM treatment(s). The FM-ACT intervention consists of 42 daily structured ACT lessons, mindfulness practices, and activities to encourage paced exercise and behavior change. The ST program offers daily symptom tracking and access to FM education materials. Participants were informed they would receive one of two potentially beneficial treatments that were being evaluated for clinical effectiveness.

The primary endpoint was Patient Global Impression of Change (PGIC). Secondary endpoints included the Revised Fibromyalgia Impact Questionnaire (FIQ-R), pain intensity, pain interference, and sleep interference. Endpoints were collected weekly through electronic patient-reported outcomes (ePROs).

Results: A total of 275 participants were randomized (Fig 1, Table 1). Analysis results are summarized in Table 2. At week 12, 70.6% of the FM-ACT participants reported an improvement on PGIC, which was significantly greater than that reported by ST participants (22.2%) ($p < 0.001$). The FM-ACT arm exhibited a significantly greater post-treatment reduction on the

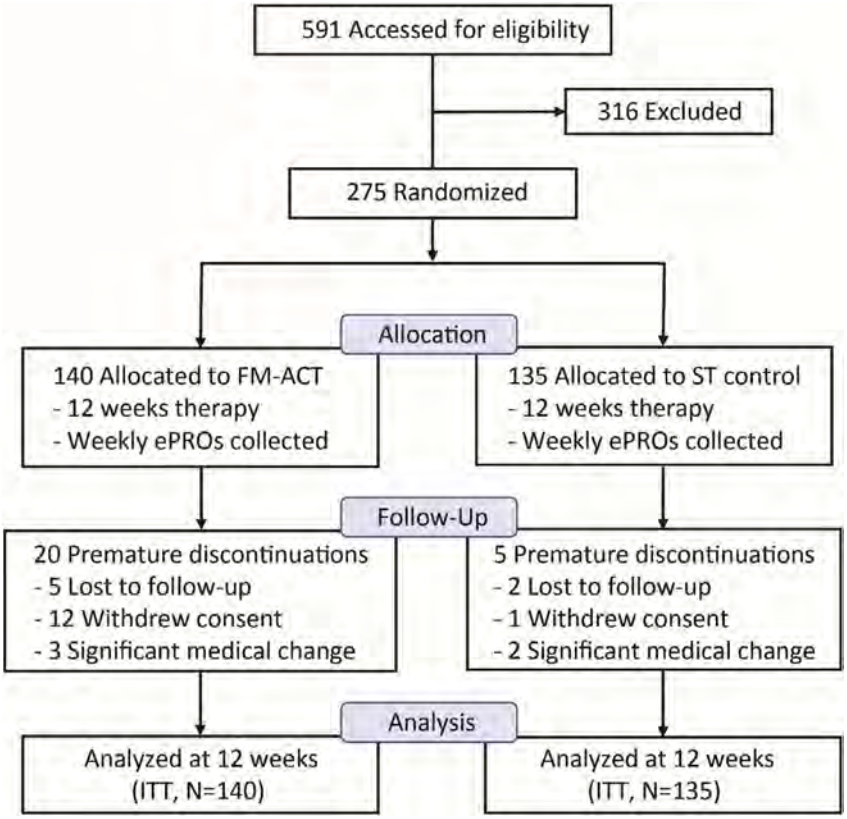

Figure 1. Consolidated Standard of Reporting Trials (CONSORT) diagram. Screening and enrollment were conducted between February 2022 and February 2023. ePROs, electronic patient reported outcomes; ITT, intention to treat.

FIQ-R total score as compared to the ST arm ($p < 0.001$, Effect Size = 0.65). FM-ACT was statistically superior to the control treatment on virtually all measures, including FIQ-R (total and domain-level scores), PGIC, pain intensity and interference, PROMIS Fatigue and Sleep Disturbance, Beck Depression Inventory II (BDI II), Psychological Inflexibility in Pain Scale (PIPS), and committed action (CAQ-8). No treatment related adverse events were observed.

Table 1. Participant demographic and baseline characteristics by treatment arm (ITT).

Characteristic	FM-ACT (N = 140)	ST (N = 135)
Age, years, mean (SD)	49.3 (12.5)	49.4 (11.0)
Female, n (%)	132 (94.3%)	125 (92.6%)
Race, n (%)		
American Indian or Alaska Native	2 (1.4%)	5 (3.6%)
Asian	2 (1.4%)	3 (2.2%)
Black or African American	16 (11.4%)	10 (7.4%)
Native Hawaiian or other Pacific Islander	0 (0.0%)	1 (0.7%)
Other	3 (2.1%)	4 (3.0%)
White	117 (83.6%)	112 (83.0%)
Ethnicity, n (%)		
Hispanic or Latino	16 (11.4%)	19 (14.1%)
Not Hispanic or Latino	123 (87.9%)	115 (85.2%)
Unknown	1 (0.7%)	1 (0.7%)
Education, College degree attained, n (%)	82 (58.6%)	69 (51.1%)
Employment status, Employed, n (%)	92 (65.7%)	95 (70.4%)
Years since FM diagnosis, mean (SD)	9.9 (9.7)	9.1 (9.0)
FM characteristics		
Widespread pain index, mean (SD)	13.3 (3.0)	13.6 (3.2)
Symptom severity score, mean (SD)	8.3 (1.8)	8.7 (1.7)
Fatigue, moderate or greater, n (%)	133 (95.0%)	132 (97.8%)
Waking unrefreshed, moderate or greater, n (%)	130 (92.9%)	127 (94.1%)
Cognitive symptoms, moderate or greater, n (%)	86 (61.4%)	100 (74.1%)
Concurrent FDA approved FM medications, n (%)		
Duloxetine	30 (21.4%)	20 (14.8%)
Pregabalin	11 (7.9%)	13 (9.6%)
Milnacipran	0 (0.0%)	3 (2.2%)
Baseline FIQ-R, mean (SD)		
Total score	54.5 (10.2)	56.8 (11.0)
Physical function	15.7 (4.6)	16.8 (4.1)
Overall impact	11.1 (3.1)	11.7 (3.6)
Severity of symptoms	27.8 (4.7)	28.2 (5.5)
Baseline Weekly Pain Intensity NRS, mean (SD)	6.4 (1.1)	6.6 (1.2)
Baseline Weekly Pain Interference NRS, mean (SD)	6.4 (1.2)	6.7 (1.4)
Baseline Weekly Sleep Interference NRS, mean (SD)	6.6 (1.8)	6.9 (1.5)
Baseline PROMIS Fatigue T-score, mean (SD)	63.8 (5.3)	64.6 (4.9)
Baseline PROMIS Sleep Disturbance T-score, mean (SD)	60.5(5.9)	61.0 (5.3)
Baseline BDI II, mean (SD)	11.6 (6.4)	13.9 (7.1)
Baseline PIPS, mean (SD)	51.9 (9.5)	53.9 (9.3)
Baseline CAQ-8, mean (SD)	31.9 (6.0)	32.0 (5.5)

BDI II: Beck Depression Inventory II; CAQ-8: Committed Action Questionnaire; FIQ-R: Revised Fibromyalgia Impact Questionnaire; NRS: numerical rating scale; PROMIS: Patient-Reported Outcomes Measurement Information System; PIPS: Psychological Inflexibility in Pain Scale. The NRS scores range from 0 (worst outcome) to 10 (best outcome). Percentages may not total 100 due to rounding.

Table 2. Analysis of efficacy endpoints by treatment arm (ITT).

Measure	FM-ACT (N = 140)	ST (N = 135)	P-value	Effect size
PGIC Responders at Week 12				
Any improvement as responder, %	70.6%	22.2%	***< 0.001***	-
Difference in proportions (95% CI)	48.4% (37.9%, 58.9%)			
Much or Very Much Improved as responder, %	25.9%	4.5%	***< 0.001***	-
Difference in proportions (95% CI)	21.4% (13.0%, 29.8%)			
FIQ-R Total at Week 12				
LS mean CFB to week 12 (SE)	-9.1 (1.2)	-1.1 (1.2)	***< 0.001***	0.65
Difference in LS means from ST arm (SE)	-8.0 (1.5)			
95% CI for difference in LS means	-11.0 to -5.1			
FIQ-R Physical Function Domain at Week 12				
LS mean CFB (SE)	-2.7 (0.4)	-0.9 (0.4)	***< 0.001***	0.40
Difference in LS means from ST arm (SE)	-1.8 (0.5)			
95% CI for difference in LS means	-2.9 to -0.8			
FIQ-R Overall Impact Domain at Week 12				
LS mean CFB (SE)	-3.1 (0.4)	-0.6 (0.4)	***< 0.001***	0.59
Difference in LS means from ST arm (SE)	-2.5 (0.5)			
95% CI for difference in LS means	-3.5 to -1.5			
FIQ-R severity of Symptoms Domain at Week 12				
LS mean CFB (SE)	-4.4 (0.5)	-0.7 (0.5)	***< 0.001***	0.62
Difference in LS means from ST arm (SE)	-3.7 (0.7)			
95% CI for difference in LS means	-5.1 to -2.4			
Weekly Pain Intensity NRS at Week 12				
LS mean CFB (SE)	-1.1 (0.2)	-0.4 (0.1)	***< 0.001***	0.40
Difference in LS means from ST arm (SE)	-0.7 (0.2)			
95% CI for difference in LS means	-1.1 to -0.3			
Weekly Pain Interference NRS at Week 12				
LS mean CFB (SE)	-1.3 (0.2)	-0.6 (0.2)	***0.001***	0.39
Difference in LS means from ST arm (SE)	-0.7 (0.2)			
95% CI for difference in LS means	-1.2 to -0.3			
Weekly Sleep Interference NRS at Week 12				
LS mean CFB (SE)	-1.0 (0.2)	-0.5 (0.2)	0.047	0.24
Difference in LS means from ST arm (SE)	-0.5 (0.2)			
95% CI for difference in LS means	-1.0 to 0.0			
PROMIS Fatigue T-score at Week 12				
LS mean CFB (SE)	-4.2 (0.6)	-1.0 (0.6)	***<0.001***	0.51
Difference in LS means from ST arm (SE)	-3.2 (0.7)			
95% CI for difference in LS means	-4.7 to -1.7			
PROMIS Sleep Disturbance T-score at Week 12				
LS mean CFB (SE)	-2.7 (0.5)	-0.7 (0.5)	***0.004***	0.35
Difference in LS means from ST arm (SE)	-2.0 (0.7)			
95% CI for difference in LS means	-3.4 to -0.7			
BDI II at Week 12				
LS mean CFB (SE)	-3.6 (0.6)	-0.1 (0.6)	***<0.001***	0.55
Difference in LS means from ST arm (SE)	-3.5 (0.8)			
95% CI for difference in LS means	-5.0 to -2.0			
PIPS at Week 12				
LS mean CFB (SE)	7.8 (0.8)	-3.1 (0.8)	***<0.001***	0.54
Difference in LS means from ST arm (SE)	-4.7 (1.0)			
95% CI for difference in LS means	-6.7 to -2.7			
CAQ-8 at Week 12				
LS mean CFB (SE)	1.5 (0.4)	-0.4 (0.4)	***<0.001***	0.40
Difference in LS means from ST arm (SE)	1.9 (0.6)			
95% CI for difference in LS means	0.8 to 3.0			

BDI II: Beck Depression Inventory II; CAQ-8: Committed Action Questionnaire; CFB: Change from baseline; CI: confidence interval; FIQ-R: Revised Fibromyalgia Impact Questionnaire; LS mean: least-square mean; NRS: numerical rating scale; PGIC: Patient Global Impression of Change; PIPS: Psychological Inflexibility in Pain Scale; PROMIS: Patient-Reported Outcomes Measurement Information System; SE: standard error. The NRS scores range from 0 (worst outcome) to 10 (best outcome).

Conclusion: Analysis of the PROSPER-FM pivotal trial supports the clinical benefits of FM-ACT in managing FM. This smartphone based digital therapeutic demonstrated statistical superiority over the control on patients' wellbeing, FM symptoms, impact, and function, as well as common disorders associated with FM.

Validated digital ACT therapy provided by FM-ACT, combined with the low-risk safety profile of this device-based intervention, offers an important step forward in reaching and benefiting the broader FM population with a non-drug therapy.

References

1. Catella et al. J Behav Med. Accepted for publication.

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Abstract Number: 1611

Mitochondrial Structural Alterations in Fibromyalgia - A Pilot Electron Microscopy Study

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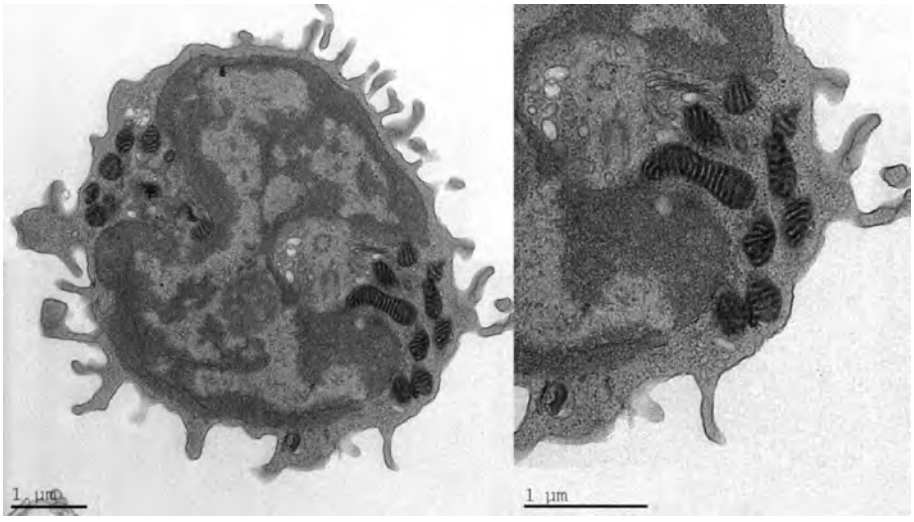
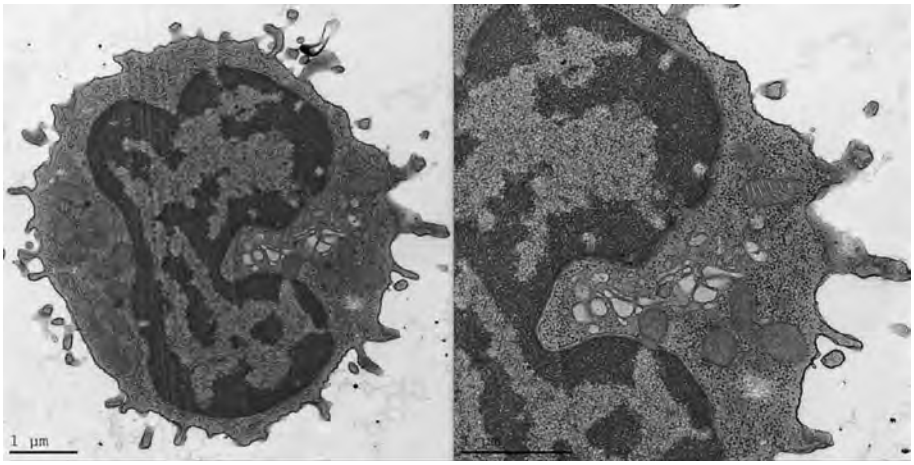
SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Abstracts: Fibromyalgia & Other Clinical Pain Syndromes
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Fibromyalgia (FM) is among the most common chronic pain conditions, clinically characterized by widespread pain and fatigue. FM pathogenesis remains unknown, leading to challenges in diagnosis and treatment. Mitochondria are the headquarters of cellular energy metabolism and their malfunction has been proposed to contribute to both

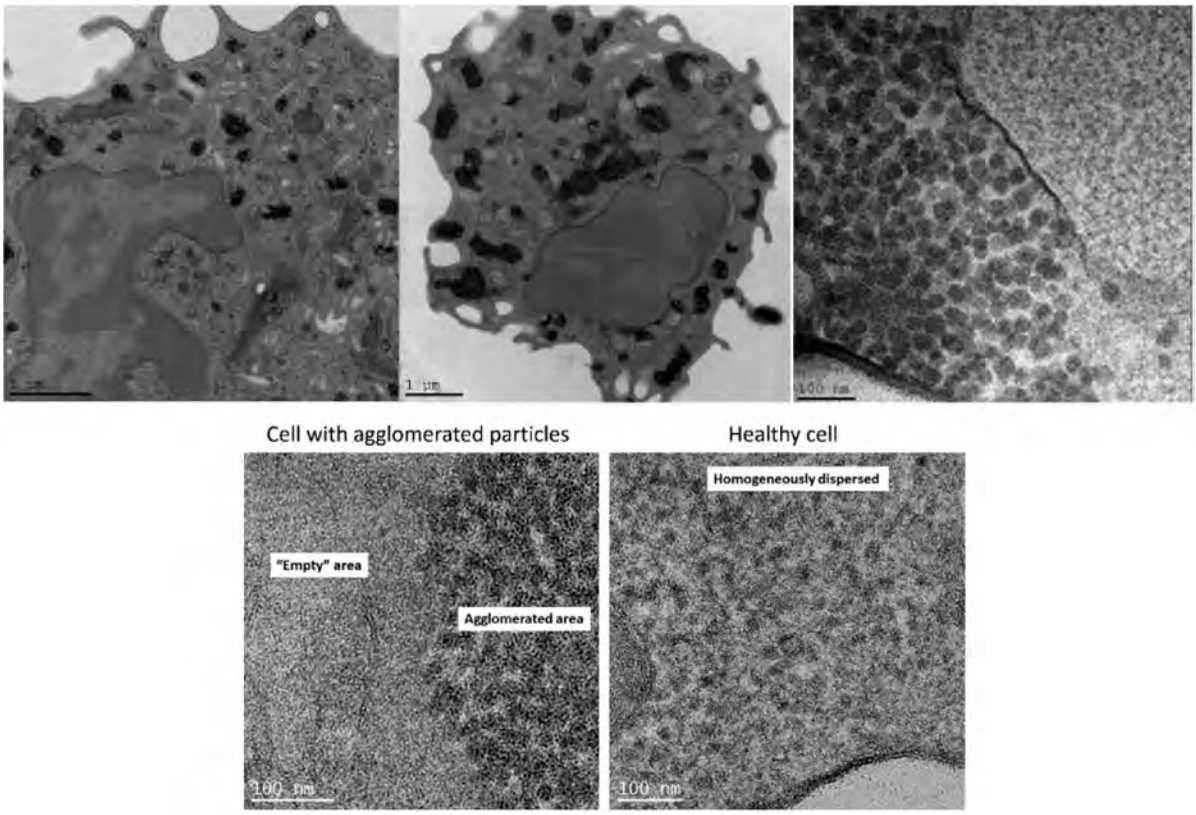


TEM of PBMCs, Healthy controls, showing normal mitochondrial crista (A) vs. FM with partial or complete loss of crista (B).



fibromyalgia and chronic fatigue. Thus, the aim of the current study was to detect structural changes in mitochondria of peripheral blood mononuclear cells (PBMCs) of FM patients, using transmission electron microscopy (TEM).

Methods: To detect mitochondrial structural alterations in FM patients, we analyzed PBMCs from seven FM patients and seven healthy controls using TEM. Patients were recruited from a specialized fibromyalgia clinic at a tertiary hospital. After providing informed consent, patients responded to questionnaires, including the Widespraede Pain Index (WPI) and the symptom severity Scale (SSS), to verify a diagnosis of FM according to ACR criteria. Subsequently, blood samples were drawn and PBMCs were collected for EM analysis.



TEM from FM patient PBMCs, showing stages of accumulation of "black particles (Size bars = 1 m). Right: high magnification of the particles (100 m).

Results: TEM analysis of PBMCs showed several distinct mitochondrial patterns, including total loss of normal crista in FM patients (Fig. 1). The number of mitochondria with intact crista morphology was reduced in FM patients and the percentage of mitochondria that completely lacked crista was significantly increased. These results correlated with WPI severity. Moreover, in FM patient samples we observed a high percentage of cells containing "black-particles" (Fig. 2), which may represent ribosomal aggregates. Crista loss and possible ribosome aggregation were intercorrelated, and thus may represent reactions to a shared cellular stress condition. These changes may indicate an adaptive hypometabolic "hibernation-like" state to a stressful event, similar to hibernation in some mammalian species. The changes in mitochondria morphology suggest that mitochondrial dysfunction, resulting in inefficient respiration, Reactive Oxygen Species generation, etc., may play a pathogenetic role in FM.

Conclusion: We here describe novel morphological changes in mitochondria of FM patients, including loss of mitochondrial crista. While these observations cannot determine whether the changes are pathogenetically primary, or represent an epiphenomenon, they highlight the possibility that mitochondrial malfunction may play a causative role in the cascade of events leading to chronic pain and fatigue in FM. Moreover, the results offer the possibility of utilizing changes in mitochondrial morphology as an objective biomarker in FM. Further understanding the connection between FM and mitochondria morphology, function, and turnover (biogenesis/mitophagy), may assist in developing both novel diagnostic tools as well as specific treatments for FM.

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Abstract Number: 1612

Design and Validation of a Comparator for Randomized Controlled Trials of a Digital Cognitive Behavioral Therapy

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Fibromyalgia & Other Clinical Pain Syndromes
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: The use of a control arm (comparator) in randomized controlled trials (RCTs) is considered the gold standard for trial conduct and interpretation. Choosing an appropriate control for RCTs evaluating Cognitive Behavioral Therapy (CBT) interventions is particularly challenging, as it is not feasible to develop a blinded sham behavioral treatment. Pilot and pivotal RCTs were performed to evaluate the efficacy of a smartphone based digital therapeutic app (FM-ACT), which delivers self-guided Acceptance and Commitment Therapy (ACT) for treatment of fibromyalgia symptoms. For the control arm of these RCTs, a digital comparator app was developed. The comparator app was designed to offer similar participant engagement and usability to control for potential study biases. This report presents the approach and validation of the novel comparator design.

Methods: In both RCTs, participants meeting 2016 diagnostic criteria for fibromyalgia were randomized to receive 12 weeks of FM-ACT or the digital symptom tracker (ST) comparator. The FM-ACT intervention consists of 42 daily sessions of structured ACT lessons, mindfulness practices, and activities to encourage paced exercise and behavior change. The ST

app was developed as an alternative intervention consisting of two common pain management components: 1) patient education on FM and general health; and 2) daily symptom and function tracking with progress reports available to the participant. During consent, participants were informed that they would be evaluating one of two potentially effective digital treatments. Participant engagement (number of sessions completed during the study) and usability factors were assessed to compare the performance of this novel control strategy.

Results: The pilot RCT data demonstrated a similar number of completed sessions between the FM-ACT and ST comparator arms, which was further supported by the results from the pivotal RCT (Fig. 1). Usability assessment from the pivotal trial showed more participants reported "good" to "excellent" usability comparing the ST arm to FM-ACT (Fig. 2).

Participants from both arms reported high rates of satisfaction with their app experience (proportion of satisfied participants: FM-ACT 80%, ST: 85%). Similar proportion of participants from both arms reported that they would use the app again (FM-ACT 80%, ST 79%).

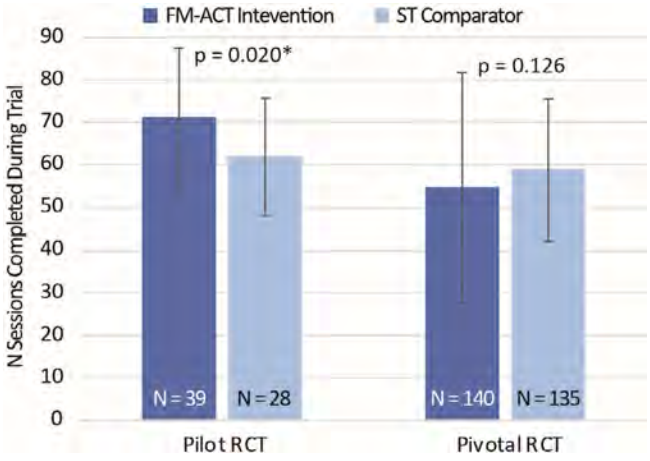

Figure 1. Comparison of participant app engagement between the FM-ACT intervention and the ST comparator arms from the pilot and pivotal RCTs. *Although statistical significance was found in the pilot RCT, both arms exhibited high app engagement with 97.3% and 92.6% of the participants completed ≥ 42 sessions (corresponding to the core therapy content) in the FM-ACT and ST arm, respectively.

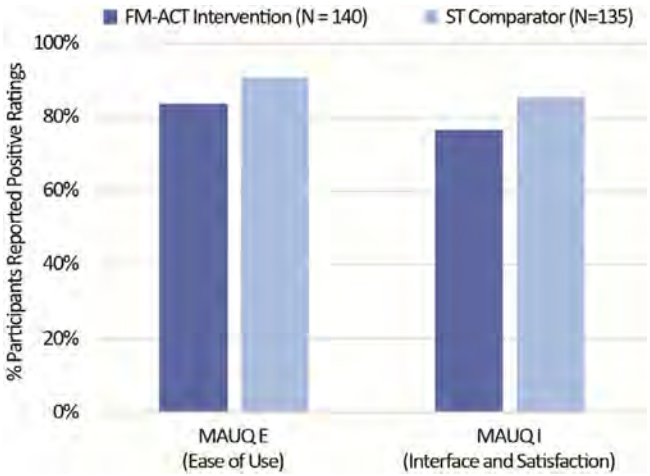

Figure 2. Participants reported "Good" to "Excellent" app experience from the pivotal RCT, measured by the mHealth App Usability Questionnaire (MAUQ), Domains: E – "Ease of Use" and I – "Interface and Satisfaction".

Conclusion: Participants randomized to the ST comparator arm engaged with the app at rates equal to or exceeding FM-ACT engagement rates and had similar usability ratings. The evidence suggests that the ST design may minimize participant bias towards a perceived inferior therapy. This approach may provide a basis for comparator strategies for RCTs of behavioral health interventions.

Disclosure: M. Gendreau: Swing Therapeutics, 2, 11; **Y. Dai**: Swing Therapeutics, 3, 11; **M. Rosenbluth**: Swing Therapeutics, 4, 11; **D. Williams**: Swing Therapeutics, 2; **D. Clauw**: AbbVie, 2, Allergan, 2, Aptinyx, 2, Eli Lilly, 2, Fasken Martineau DuMoulin LLP, 6, H. Lundbeck A/S, 2, Heron Therapeutics, Inc, 2, Kellogg, Hansen, Todd, Figel & Frederick, 6, Marks & Clerk Law LLP, 6, Neumentum, Inc., 2, Nix Patterson LLP, 6, Pfizer, 2, 6, Regeneron Pharmaceuticals, Inc., 2, Samumed, LLC, 2, Swing Therapeutics Inc, 2, Tonix Pharmaceuticals, Inc., 2, Virios Therapeutics, Inc., 2, Zuber Lawler & Del Duca LLP, 6.

Abstract Number: 1613

Tetrodotoxin Sensitive $Na_v1.7$ Sodium Channel SCN9A Gene Polymorphism rs6754031(T >G) Is Associated with Fibromyalgia

Koshy Nithin Thomas, Shivika Guleria, Amita Aggarwal and Able Lawrence, Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow, India

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Fibromyalgia & Other Clinical Pain Syndromes
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: SCN9A gene encodes a tetrodotoxin sensitive $Na_v1.7$ Sodium channel expressed in dorsal root ganglia, peripheral nerves, olfactory nerves and inner ear. Rare Mutations in SCN9A are associated with a spectrum of pain disorders from erythromelalgia (gain of function) to congenital insensitivity to pain. We planned a case control study to explore the association of intronic SNPs rs6754031(T >G) and rs6746030 (G >A) of which rs6754031 minor allele (GG) was previously associated with Fibromyalgia.

Methods: Patients diagnosed as Fibromyalgia using ACR1990 and/or ACR2016 criteria and consenting to genetic study were included. Healthy controls with no widespread pain or connective tissue disease or medical comorbidity were included. Although a sample size of 250 each was targeted, study was terminated due to slow recruitment during covid pandemic. DNA was extracted by phenol-chloroform method. Genotyping was done by real time PCR. All continuous variables among baseline characteristics are expressed in mean (SD) and comparison by one way ANOVA while Fisher's exact test was used for frequency tables. Odds Ratios and confidence intervals were estimated using Logistic Regression using a recessive minor allele (G) model using STATA14.

Results: A total of 118 FMS patients (88% female) of mean age of onset 35 (±9.6) years and 118 healthy controls (78% female) of age 34.7 (±10.9) years were included. Clinical features and comorbidities of patients are given in Table 1. SCN9A polymorphism rs6754031 was in Hardy Weinberg equilibrium among controls (P=0.83) while SNP rs6746030 was not (P=0.002). The two SNPs were independent of each other consistent with genomic distance and lack of linkage. Genotyping results are given in Table 2. Of the 118 patients, 74 were classified Fibromyalgia by both ACR2016 and ACR1990 criteria while 33 and 11 subjects were classified by ACR2016 and ACR1990 alone respectively. Minor allele of rs6754031 (GG versus TT/TG) was associated with Fibromyalgia **OR=2.62 (1.15-6.00)** and diagnosis of Fibromyalgia by ACR2016

Table 1. Clinical features of FMS cohort

Table 1. Clinical features of FMS cohort					
Clinical feature	FMS (n-118)	1990 ACR (n-11)	1990 + 2016 ACR (n-74)	2016 ACR (n-33)	p-value
Female	104 (88%)	11 (100%)	64 (86%)	29 (87%)	0.6
Age (years)	40.6 (±10.3)	40 (±11.8)	39.7 (±10.4)	42.9 (±9.4)	0.3
Age at onset (years)	35 (±9.6)	34 (±10)	34.3 (±9.8)	36.9 (±9)	0.4
WPI	14.6 (±3.6)	12.9 (±4.6)	15.5 (±3)	12.9 (±3.6)	<0.01
SSS	7.8 (±2.5)	2.7 (±1.4)	8.6 (±2.1)	7.9 (±1.7)	<0.01
TP	12.3 (±5)	13.6 (±2)	15.1 (±2.3)	5.5 (±3.4)	<0.01
Obese (≥25 kg/m^2)	70 (67%)	5 (45%)	46 (62%)	19 (57%)	0.4
Prediabetes (HbA1c 5.7 – 6.4)	26 (22%)	0	20 (27%)	6 (18%)	0.2
Diabetes (HbA1c ≥ 6.5)	15 (12%)	1 (9%)	13 (17%)	1 (3%)	0.1
Hypertension	47 (39%)	7 (63%)	28 (37%)	12 (36%)	0.3
OSA	38 (32%)	1 (9%)	23 (31%)	14 (42%)	0.1
CFS	44 (37%)	1 (9%)	33 (44%)	10 (30%)	0.06
PTSD	19 (16%)	0	15 (20%)	4 (12%)	0.2
RLS	13 (11%)	0	8 (10%)	5 (15%)	0.4

WPI widespread index; SSS symptom severity score; TP tender point count; OSA obstructive sleep apnoea (intermediate/high risk by STOP BANG questionnaire); CFS chronic fatigue syndrome; PTSD post traumatic stress disorder; RLS restless leg syndrome

Table 2. SCN9A genotypes in Fibromyalgia and Controls

Table 2. SCN9A genotypes in Fibromyalgia and Controls									
	rs6754031 (Minor allele freq 29.7% in controls)				rs6746030 (Minor allele freq 20.5% in controls)				
P=0.056	TT	TG	GG	Groups		GG	GA	AA	P=NS
	57	52	**9**	Controls (118)	Controls (117)	80	26	11	
	54	43	**21**	Fibromyalgia (118)		76	29	13	
P=NS	11	13	9	FMS 2016 only (33)		25	5	3	P=NS
	36	26	12	FMS Both (74)		42	22	10	
	7	4	0	FMS 1990 only (11)		9	2	0	

Table 3. SCN9A gene polymorphism rs6754031 association in recessive (G) model

Table 3. SCN9A gene polymorphism rs6754031 association in recessive (G) model			
	rs6754031 (TT/TG)	**rs6754031 (GG)**	
Fibromyalgia (N=118)	**97**	**21**	**P=0.03 OR=2.62 (1.15-6.00)**
Controls (N=118)	**109**	**9**	
	N=206	N=30	
Fibromyalgia by ACR2016 (N=107)	86	21	**P=0.005 OR=3.26 (1.42-7.46)**
No Fibromyalgia by ACR2016 (N=129)	120	9	
	N=206	N=30	
Fibromyalgia by ACR1990 (N=85)	73	12	P=0.685 OR=1.21 (0.55-2.66)
No Fibromyalgia by ACR1990 (N=151)	133	18	
	N=206	N=30	
Multivariate Analysis with ACR2016 (OR 5.05 CI 1.90-13.45 P<0.001) and ACR1990 (OR 0.47 CI 0.18-1.20 P=0.113)			

OR=3.26 (1.42-7.46) but not with ACR1990 OR=1.21 (0.55-2.66) using a recessive model (Table 3). On multivariate analysis, association of rs6754031 GG with ACR2016 (**OR 5.05 CI 1.90-13.45 P< 0.001**) strengthened while ACR1990 (OR 0.47 CI 0.18-1.20 P=0.113) showed a negative trend. Among core Fibromyalgia features, rs6754031(GG) was associated with non-restorative sleep (waking unrefreshed) **OR=1.61(1.00-2.57) P=0.048**.

Conclusion: Our study supports previously reported association of rs6754031 GG with Fibromyalgia with a differential association between ACR2016 and ACR1990 underscoring the heterogeneity of Fibromyalgia.

Disclosure: K. Thomas: None; **S. Guleria**: None; **A. Aggarwal**: None; **A. Lawrence**: None.

Abstract Number: 1614

Therapy Combining Millimeter Wave-based Neuromodulation with Coaching for the Improvement in Quality of Life of Patients with Fibromyalgia: A Prospective, Multicenter, Randomized, Controlled Trial

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Fibromyalgia & Other Clinical Pain Syndromes
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Fibromyalgia is a chronic syndrome with symptoms of moderate to severe intensity, including diffuse pain, fatigue, sleep disturbance, and cognitive impairment. While first-line recommendation for this pathology is non-drug therapies (Macfarlane et al., 2017), namely physical therapy, symptoms often prevent patients from exercising. Therapies that rely on the body's endogenous opioid system thus present an interesting non-pharmacological method of helping patients. The objective of this trial was to assess the efficacy of an intervention combining a millimeter-wave emitting wristband (MMW) and a coaching program. Exposure of the peripheral nervous system to MMW has been shown to provide a neuromodulating effect, mediated by the release of various neurotransmitters, including endorphins. Endorphins have pain relief and parasympathetic modulation properties that can alleviate the symptoms of fibromyalgia patients. Coaching aims to improve treatment adherence and efficacy.

Methods: In a multicenter, randomized, controlled trial (ClinicalTrials.gov NCT05058092), 170 fibromyalgia patients (ACR 2016 criteria, Wolfe et al., 2016)) with moderate or severe Fibromyalgia Impact Questionnaire score (FIQ, Bennett et al., 2009, score ≥ 39/100) were divided into 2 groups of immediate (IG) or delayed (DG) intervention. The IG (N=84) received the intervention immediately after groups were assigned, in addition to their usual care (UC). The DG (N=86) received the intervention with a delay of 3 months, intervention starting after assessment of the primary endpoint (M3). In both groups, patients first received MMW wristband treatment and coaching for 3 months, then wristband treatment alone for 3 months. The intervention consisted of using the wristband for three 30-minute sessions a day and receiving 4 coaching sessions including educational content on the intervention and training in the use of the device (D0), a usability assessment (D7) and a benefit assessment (M1 and M2). In the event of low benefit at M1 or M2, the wristband's stimulation mode (power &

duration) could be adapted. Efficacy of intervention was assessed by comparing the number of patients in both groups whose quality of life measurement on the FIQ significantly improved between inclusion and M3. A decrease in FIQ score of ≥14% is considered clinically significant (Bennett et al., 2009). FIQ scores of the 2 groups were also measured at 6 months (M6).

Results: At M3, 55.1% patients of IG improved their quality of life beyond 14%, compared with 35.9% in the DG, and this difference between the groups was statistically significant (p=0.021). On average, patients in the IG improved their FIQ score by 21.7%, versus 7.2% in the DG. Benefits observed in the IG were preserved at M6, patients in this group having used their device autonomously between M3 & M6.

Conclusion: The combination of MMW and coaching led to improvements in the quality of life of fibromyalgia patients superior to those obtained with UC after M3. This improvement was maintained at M6, while patients were using their wristband autonomously. This non-pharmaceutical therapy offers patients a therapy they can use independently and on an outpatient basis.

Disclosure: C. Maindet: None; **A. Dumolard**: None; **M. Veloso**: None; **M. Barmaki**: None; **R. Deleens**: None; **R. Gonon-Demoulian**: None; **A. Lorenzi-Pernot**: None; **M. Michel-Cherqui**: None; **A. Serrie**: None; **S. Velliet**: None; **J. Bosson**: None.

Abstract Number: 1615

Therapeutic Hydroxychloroquine Blood Levels Are Cost Effective and May Reduce Health Disparities by Reducing Lupus Hospitalizations

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Health Services Research II
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Studies show factors including daily hydroxychloroquine (HCQ) dosing or nonadherence affect blood concentrations risking 6-fold higher lupus (or SLE) flares requiring hospitalization. Given disparities in nonadherence resulting in more hospitalizations, measuring HCQ levels in blood could guide clinicians to tailor HCQ dosing to maximize efficacy and improve adherence at the individual patient level. Yet, HCQ blood level monitoring is *not* routinely done due to cost, coverage, and unclear clinical standardization. Thus, we aimed to examine the cost effectiveness of HCQ blood level monitoring by measuring: 1) risk of lupus-related acute care utilization (Hospital or Emergency Room (ER) visits) by HCQ blood levels overall and in patients of Black race or Hispanic ethnicity; 2) the cost of lupus-related acute care visits vs. HCQ blood level monitoring.

Methods: We measured HCQ blood levels during 167 consecutive visits of unique patients using liquid chromatography mass spectrometry. HCQ blood levels were categorized as: a) subtherapeutic (< 750 ng/ml), b) therapeutic (750-1100 ng/ml), or c) supratherapeutic (>1100 ng/ml) per our prior findings. All lupus-related acute care (hospital/ER) visits from the clinic visit until next follow-up visit were manually abstracted. Covariates included socio-demographics, SLE disease

activity score, SLE damage index, kidney function (eGFR), steroid and HCQ doses. Using Cox hazard models, we examined associations between HCQ blood levels and time to first acute care visit after the index clinic visit. We compared published data (Kan, 2013) on the cost of lupus-related acute care visits to HCQ blood level monitoring in our cohort.

Results: Table 1 shows characteristics of 167 patients included in this study by: subtherapeutic (n=74), therapeutic (n=50), supratherapeutic (n=43) HCQ blood levels. A total of 31 lupus-related acute care visits were observed during the study period. Patients of Black race or Hispanic ethnicity and those with public insurance had 3-fold higher acute care utilization risk (Adjusted HR 3.3 & HR 3.6; Fig. 1 & Table 2A). A 71% lower acute care utilization risk was seen in patients with therapeutic HCQ blood levels, 750-1100 ng/ml, compared to those with subtherapeutic levels, < 750 ng/ml (Fig. 1 & Table 2A; p=0.029).

In a subgroup analysis among patients of Black race or Hispanic ethnicity (n=51), we noted that public insurance predicted 5-fold higher acute care utilization risk (Table 2B). Therapeutic HCQ blood levels were associated with 94% lower acute care utilization (Table 2B).

Using published costs of $562 per SLE ER visit and $11,716 per SLE hospitalization, 28 ER visits and 3 hospitalizations cost approximately $50,584 in our study. At a cost of $50 per HCQ blood level measurement, monitoring HCQ blood levels for 167 draws costs $8,350. Thereby, preventing one ER visit could cover the cost of up to 11 HCQ blood level draws per year.

Table 1. Baseline characteristics and hospital visits after index visit by HCQ blood level categories

Table 1. Baseline characteristics and hospital visits after index visit by HCQ blood level categories

	Subtherapeutic levels (<750 ng/ml) n=74	Therapeutic levels (750-1100 ng/ml) n=50	Supratherapeutic levels (>1100 ng/ml) n=43	
Variables at HCQ blood level draw visit	Mean±SD or n (%)	Mean±SD or n (%)	Mean±SD or n (%)	p
Age (years)	45±17	47±16	47±17	0.58
Female	67 (91%)	47 (94%)	36 (88%)	0.18
Black Race or Hispanic Ethnicity	26 (35%)	13 (26%)	12 (28%)	0.55
Public insurance	20 (27%)	10 (20%)	13 (30%)	0.53
Current smoker	25 (34%)	16 (32%)	10 (23%)	0.54
eGFR (ml/min/m^2)	96±25	89±25	88±31	0.08*
Body weight (kg)	77±21	84±21	78±19	0.61
SLE disease activity index	**3.7±5.6**	**2.9±3.6**	**1.9±3.0**	**0.04**
SLE damage index	0.78±1.1	0.59±0.84	0.90±1.1	0.71
Guidelines recommended HCQ dose, ≤5mg/kg/d	68 (92%)	44 (88%)	39 (91%)	0.75
HCQ dose				
300 mg	**20 (27%)**	**15 (30%)**	**14 (33%)**	**0.0003**
400 mg	**25 (34%)**	**30 (60%)**	**25 (58%)**	
Steroid dose (mg)	5±13	2.4±5.1	3.5±6.3	0.36
Outcomes				
Acute care visits	20 (27%)	5 (10%)	4 (9%)	0.09*
Visit type				
ER visit	17 (85%)	5 (100%)	4 (100%)	
Hospital admission	3 (15%)	-	-	
Total Cost[1]	$44,972	$2,810	$2,284	
Flares leading to ER visits ($562/visit)[1]	$9,554	$2,810	$2,284	
Flares leading to hospital admissions ($11,716/visit)[1]	$35,418	-	-	

*[1]Kahn et al. 2013; HCQ=Hydroxychloroquine; ER=Emergency Room; eGFR=Glomerular Filtration Rate. p-values are calculated using univariable chi-square test or fisher's test for categorical variables and ANOVA for quantitative variables. *Trend towards significance. [1]Kan. Biomed Res Int. 2013*

Table 2. Multivariable Cox model showing risk factors for hospitalization after index patient-visit

Table 2. Multivariable Cox model showing risk factors for hospitalization after index patient-visit

A. All patients with lupus (n=167)		
Variables at index patient-visit	Adjusted HR (95% CIs)	p-value
Age per 10 years	0.98 (0.96, 1.01)	0.21
Female	3.5 (0.38, 32)	0.25
Black Race or Hispanic Ethnicity	**3.3 (1.3, 8.5)**	**0.011**
Public insurance	**3.6 (1.4, 8.1)**	**0.007**
eGFR per 10 ml/min/m^2 increase	1.003 (0.98, 1.02)	0.76
SLE disease activity index per 1 point increase	0.97 (0.82, 1.1)	0.70
SLE damage index per 1 point increase	1.1 (0.69, 1.8)	0.65
Guideline-recommended HCQ dose ≤5mg/kg/d	1.4 (0.28, 6.9)	0.69
HCQ daily dose		
300 mg	0.98 (0.32, 3.0)	0.97
400 mg	1.7 (0.57, 4.9)	0.36
HCQ blood levels categories		
Therapeutic levels (750-1100 ng/ml)	**0.26 (0.08, 0.87)**	**0.029**
Supratherapeutic levels (>1100 ng/ml)	**0.26 (0.08, 0.85)**	**0.026**
B. Patients of Black Race or Hispanic Ethnicity (n=51)		
Variables at index patient-visit	Adjusted HR (95% CIs)	p-value
Age per 10 years	0.99 (0.93, 1.04)	0.63
Female	4.4 (0.30, 66)	0.28
Public insurance	**5.2 (1.4, 20)**	**0.015**
eGFR per 10 ml/min/m^2 increase	1.0 (0.97, 1.03)	0.96
SLE disease activity index per 1 point increase	1.1 (0.83, 1.4)	0.11
SLE damage index per 1 point increase	0.64 (0.32, 1.3)	0.58
Guideline-recommended HCQ dose ≤5mg/kg/d	0.89 (0.11, 7.3)	0.90
HCQ daily dose		
300 mg	0.50 (0.08, 3.2)	0.43
400 mg	2.3 (0.49, 10)	0.29
HCQ blood levels categories		
Therapeutic levels (750-1100 ng/ml)	**0.06 (0.01, 0.52)**	**0.011**
Supratherapeutic levels (>1100 ng/ml)	0.23 (0.05, 1.4)	0.12

Multivariable model includes all variables with p-value <0.1 in univariable analysis, socio-demographics, and other factors that can impact lupus hospitalization risk, such as SLE disease activity index. Significant p-values in bold font. HCQ=Hydroxychloroquine.

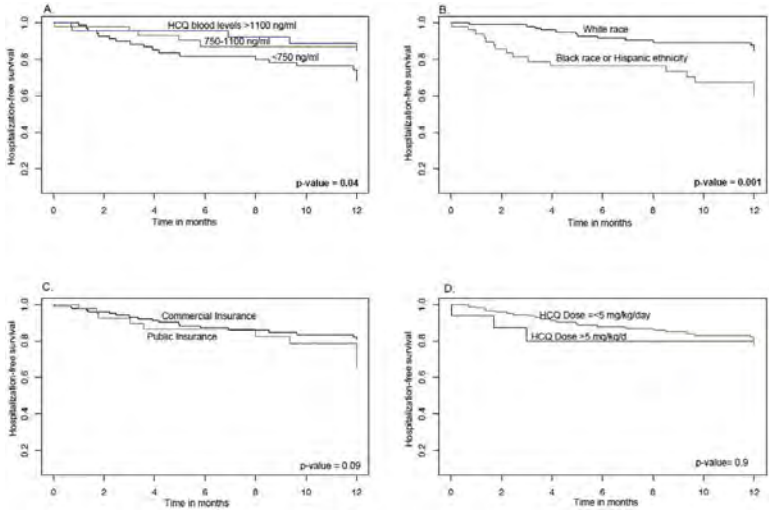

Fig 1. Kaplan Meier curves showing hospitalization-free survival by: A. HCQ blood level categories; B. Insurance; C. Race; D. HCQ dose

Conclusion: Therapeutic HCQ blood levels (750-1100 ng/ml) were associated with 94% lower acute care utilization risk among patients of Black race or Hispanic ethnicity. Routine HCQ blood level monitoring could cost effectively reduce acute care utilization and health disparities in lupus.

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Abstract Number: 1616

Geographic and Demographic Representation in Industry-sponsored, US-based Clinical Trials of Systemic Lupus Erythematosus Therapies

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Health Services Research II
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Clinical trials of systemic lupus erythematosus (SLE) therapies have increased over the last decade, driven by evolving knowledge of targetable pathways. However, these trials are often small, leading to evidentiary gaps over which patients benefit from new therapies. Racially minoritized populations, which disproportionately experience severe disease, are underrepresented in published SLE trials, but little is known specifically about trials supporting drug development, including where enrollment sites are located and whether enrollment is representative of the US population with SLE. Our objective was to assess geographic and demographic enrollment patterns for registered SLE clinical trials.

Methods: Industry-sponsored clinical trials investigating small molecules and biologics for use in SLE or lupus nephritis with at least 1 US site were identified from ClinicalTrials.gov; cutaneous lupus trials were excluded. Study characteristics were abstracted from trial registrations. US sites were characterized at the county level using the National Center for Health

Table 1: Characteristics of US enrollment sites for industry-sponsored SLE clinical trials.

Table 1: Characteristics of US enrollment sites for industry-sponsored SLE clinical trials.

		Clinical trials (No.)	US enrollment sites					
			Sites (No.)	Enrollment site designations (No., %)[c]				Medically underserved area (No., %)[d]
				Large metropolitan	Medium metropolitan	Small metropolitan	Non-metropolitan	
All trials		144	3454	2565 (74)	652 (19)	201 (6)	36 (1)	164 (5)
Year of study start	2002 – 2009	29	621	445 (72)	135 (22)	38 (6)	3 (0)	17 (3)
	2010 – 2017	59	1534	1130 (74)	294 (19)	96 (6)	14 (1)	82 (5)
	2018 – 2024[a]	56	1299	990 (76)	223 (17)	67 (5)	19 (1)	65 (5)
Study indication	SLE	107	2827	2090 (74)	523 (19)	179 (6)	35 (1)	146 (5)
	LN	37	627	475 (76)	129 (21)	22 (4)	1 (0)	18 (3)
Therapeutic type	Small molecule	37	922	697 (76)	168 (18)	43 (5)	14 (2)	45 (5)
	Biologic	107	2532	1868 (74)	484 (19)	158 (6)	22 (1)	119 (5)
Primary efficacy endpoint	Yes	102	2945	2191 (74)	576 (20)	147 (5)	31 (1)	125 (4)
	No	42	509	374 (73)	76 (15)	54 (11)	5 (1)	39 (8)
Enrollment sites	US only	28	271	209 (77)	39 (14)	23 (8)	0 (0)	16 (6)
	Multi-national	116	3183	2356 (74)	613 (19)	178 (6)	36 (1)	148 (5)
Trial status	Completed or terminated	99	2590	1888 (73)	510 (20)	165 (6)	27 (1)	123 (5)
	Other[b]	45	864	677 (78)	142 (16)	36 (4)	9 (1)	41 (5)

Abbreviations: SLE, systemic lupus erythematosus; LN, lupus nephritis.
[a] Includes 4 clinical trials registered prior to, but started after, January 01, 2023.
[b] Includes clinical trials that are not yet recruiting, recruiting or enrolling by invitation, active (not recruiting), withdrawn, or with unknown status.
[c] Based on National Center for Health Statistics Urban-Rural Classification, last updated 2013. "Large metropolitan" includes large central and fringe metros. "Non-metropolitan" includes micropolitan and noncore areas.
[d] Based on Health Resources and Services Administration designation of "medically underserved areas" lacking access to primary care services at the county level, last updated 2023.

Table 2: Enrollment demographics for completed and terminated, industry-sponsored SLE clinical trials.

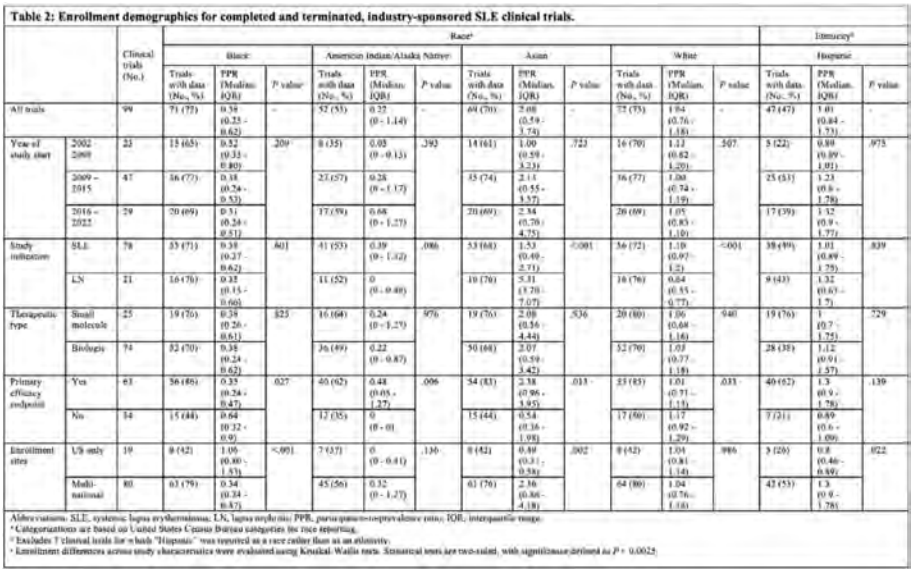

Table 2: Enrollment demographics for completed and terminated, industry-sponsored SLE clinical trials.

		Clinical trials (No.)	Race[a]												Ethnicity[b]		
			Black			American Indian/Alaska Native			Asian			White			Hispanic		
			Trials with data (No., %)	PPR (Median, IQR)	P value	Trials with data (No., %)	PPR (Median, IQR)	P value	Trials with data (No., %)	PPR (Median, IQR)	P value	Trials with data (No., %)	PPR (Median, IQR)	P value	Trials with data (No., %)	PPR (Median, IQR)	P value
All trials		99	71 (72)	0.38 (0.25 - 0.62)	-	52 (53)	0.22 (0 - 1.14)	-	69 (70)	2.08 (0.59 - 3.74)	-	72 (73)	1.04 (0.76 - 1.18)	-	47 (47)	1.01 (0.84 - 1.73)	-
Year of study start	2002 - 2008	22	15 (65)	0.52 (0.33 - 0.80)	.209	8 (35)	0.03 (0 - 0.13)	.392	14 (61)	1.09 (0.59 - 3.23)	.723	16 (70)	1.12 (0.82 - 1.20)	.507	5 (22)	0.88 (0.09 - 1.91)	.975
	2009 - 2015	47	36 (77)	0.38 (0.24 - 0.52)		23 (57)	0.28 (0 - 1.17)		35 (74)	2.14 (0.55 - 3.57)		36 (77)	1.00 (0.74 - 1.19)		25 (53)	1.23 (0.8 - 1.78)	
	2016 - 2022	29	20 (69)	0.51 (0.24 - 0.51)		17 (59)	0.68 (0 - 1.27)		20 (69)	2.34 (0.78 - 4.75)		20 (69)	1.05 (0.85 - 1.10)		17 (59)	1.52 (0.9 - 1.77)	
Study indication	SLE	78	55 (71)	0.38 (0.27 - 0.62)	.601	41 (53)	0.39 (0 - 1.32)	.086	53 (68)	1.53 (0.49 - 2.71)	<.001	56 (72)	1.10 (0.97 - 1.2)	<.001	38 (49)	1.01 (0.89 - 1.75)	.839
	LN	21	16 (76)	0.35 (0.15 - 0.66)		11 (52)	0 (0 - 0.48)		16 (76)	5.31 (3.78 - 7.07)		16 (76)	0.64 (0.55 - 0.77)		9 (43)	1.32 (0.63 - 1.7)	
Therapeutic type	Small molecule	25	19 (76)	0.39 (0.26 - 0.61)	.825	16 (64)	0.24 (0 - 1.27)	.976	19 (76)	2.08 (0.56 - 4.44)	.536	20 (80)	1.06 (0.68 - 1.16)	.940	19 (76)	1 (0.7 - 1.75)	.729
	Biologic	74	52 (70)	0.38 (0.24 - 0.62)		36 (49)	0.22 (0 - 0.87)		50 (68)	2.07 (0.59 - 3.42)		52 (70)	1.03 (0.77 - 1.18)		28 (38)	1.12 (0.91 - 1.57)	
Primary efficacy endpoint	Yes	63	36 (86)	0.35 (0.24 - 0.47)	.027	40 (62)	0.48 (0.05 - 1.27)	.006	54 (83)	2.38 (0.96 - 3.95)	.033	53 (85)	1.01 (0.71 - 1.15)	.033	40 (62)	1.3 (0.9 - 1.78)	.139
	No	14	15 (44)	0.64 (0.32 - 0.9)		12 (35)	0 (0 - 0)		15 (44)	0.54 (0.36 - 1.95)		17 (50)	1.17 (0.92 - 1.29)		7 (21)	0.89 (0.6 - 1.09)	
Enrollment sites	US only	19	8 (42)	1.06 (0.80 - 1.83)	<.001	7 (37)	0 (0 - 0.61)	.136	8 (42)	0.89 (0.31 - 0.98)	.002	8 (42)	1.04 (0.81 - 1.14)	.986	3 (16)	0.8 (0.46 - 0.89)	.022
	Multi-national	80	63 (79)	0.34 (0.24 - 0.47)		45 (56)	0.32 (0 - 1.27)		61 (76)	2.36 (0.86 - 4.18)		64 (80)	1.04 (0.76 - 1.18)		42 (53)	1.3 (0.9 - 1.78)	

Abbreviations: SLE, systemic lupus erythematosus; LN, lupus nephritis; PPR, participation-to-prevalence ratio; IQR, interquartile range.
[a] Categorizations are based on United States Census Bureau categories for race reporting.
[b] Excludes 7 clinical trials for which "Hispanic" was reported as a race rather than an ethnicity.
[c] Enrollment differences across study characteristics were evaluated using Kruskal-Wallis tests. Statistical tests are two-sided, with significance defined as $P < 0.0025$.

Statistics Urban-Rural Classification Scheme and Health Resources and Services Administration Medically Underserved Area designation. For completed and terminated trials with results, participation-to-prevalence ratios (PPRs) were calculated by dividing proportions of participants by sex, ethnicity, and race by US population proportions across Centers for Disease Control and Prevention SLE registries; PPRs from 0.80 to 1.20 indicated adequate representation. Enrollment differences across study characteristics were evaluated using Kruskal-Wallis tests.

Results: Among 144 industry-sponsored SLE clinical trials, 3454 US sites were reported, including 2565 (74%) in large metropolitan counties and 237 (7%) in small- or non-metropolitan counties (**Table 1**). Only 164 sites (5%) were in medically underserved counties. Female participants were adequately represented relative to the US population with SLE (median PPR 1.03, IQR 0.99-1.05) in 81 trials reporting enrollment by sex (**Table 2**). Among 72 trials reporting enrollment for at least 1 race, representation was inadequate for Black (median PPR 0.38, IQR 0.25-0.62) and American Indian/Alaska Native participants (median PPR 0.22, IQR 0-1.14), and adequate for White participants (median PPR 1.04, IQR 0.76-1.18). Asian participants were overrepresented in trials overall (median PPR 2.08, IQR 0.59-3.74), but underrepresented in trials with US sites only. Among 47 trials reporting ethnicity data, Hispanic participants were adequately represented (median PPR 1.01, IQR 0.84-1.73).

Conclusion: Among registered industry-sponsored clinical trials of SLE therapies, US enrollment sites were concentrated in metropolitan areas; only 5% were in medically underserved counties. Female, White, Asian, and Hispanic participants were adequately represented in trials overall, but Black and American Indian/Alaska Native participants were underrepresented relative to the US population with SLE. Future analyses are needed to further characterize regional enrollment, and to assess the alignment of research practices with the needs of clinicians seeking new therapies for SLE.

Disclosure: J. Skydel: None; **R. Ramachandran**: None; **S. Suttiratana**: Rezolut, Inc., 3; **J. Ross**: Janssen Pharmaceuticals, 5; **J. Wallach**: Johnson & Johnson, 12, I receive support from Johnson & Johnson through the Yale Open Data Access (YODA) Project to review requests for data.; **C. Burns**: None.

Abstract Number: 1617

Comparing Uptake of Biosimilar Infliximab Among Patients with Medicare, Medicaid and Private Insurance in U.S. Rheumatology Practices 2016-2022

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Health Services Research II
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: The first infliximab biosimilar (infliximab-dybb) entered the U.S. market in 2016, and two additional products have subsequently been introduced (infliximab-axxq (2017) and infliximab-abda (2020)). Biosimilars have significant potential to slow drug spending; however, uptake in the U.S. has lagged behind other countries. We compared rates of biosimilar uptake for Medicare, Medicaid, and private insurance after each infliximab biosimilar approval from 2016 to 2022.

Methods: Data from RISE, a national registry with electronic health records from one-third of U.S. rheumatology practices, was used. We examined all bio-originator or biosimilar infliximab administrations for users ≥ 18 years from the release of -dybb (biosimilar #1) in November 2016 through March 2022 regardless of diagnosis among participants with Medicare, Medicaid or private insurance. Dual Medicare-Medicaid patients were assigned to Medicaid. We modeled the log odds of receiving a biosimilar as a function of a three-way interaction between time (month), time-window (windows between

Table 1. Demographic characteristics of infliximab bio-originator or biosimilar recipients in RISE registry between April 2016 and March 2022.

	Overall (n= 422388)	
	n	%
Biosimilar	40401	9.56
Age group		
18-30	8034	1.90
31-50	63502	15.03
51-64	113856	26.96
65+	236996	56.11
Sex		
Women	285571	67.61
Men	136811	32.39
Race-ethnicity		
White	318426	75.39
Black	27869	6.60
Hispanic	15214	3.60
Asian	5072	1.20
Other/mixed	2271	0.54
Insurance		
Medicare	232722	55.10
Medicaid	16502	3.91
Private	173164	41.00

*Numbers may sum to less than 422388 due to missing values.

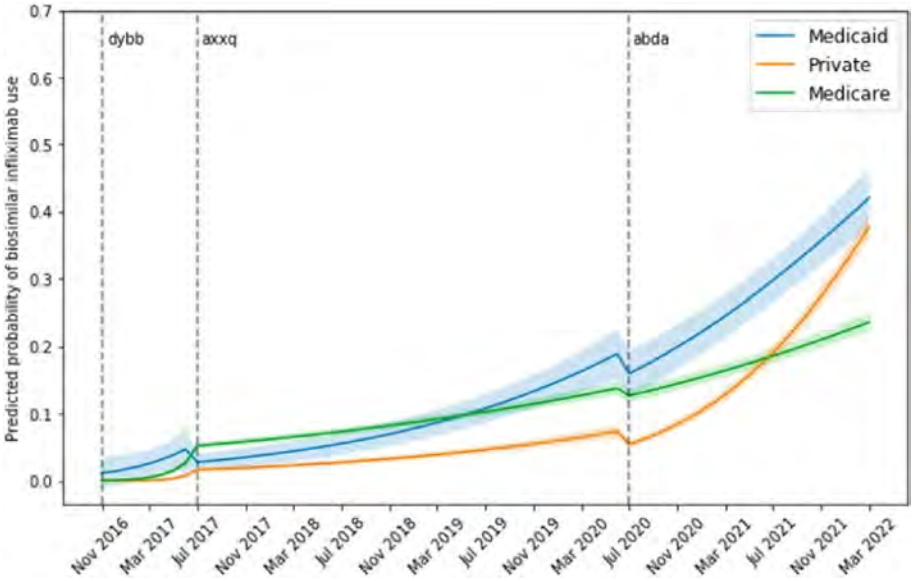

Figure 1. Predicted probability and 95% confidence interval of receiving biosimilar infliximab over time by insurance type

biosimilar market introductions), and insurance (Medicare, Medicaid, Private) adjusting for age, sex, race or ethnicity, and socioeconomic status (as measured by Area Deprivation Index (ADI)). We used cluster robust standard errors to account for repeated measures on patients. We reported patient demographics, and adjusted predicted probabilities of receiving a biosimilar by insurance type over time.

Results: Among 33,751 distinct patients, there were 422,388 administrations of infliximab products in RISE between November 2016 and March 2022, 40,401 (9.6%) of which were for a biosimilar. Overall, 56.1% of patients were ≥65 years; 67.6% were women; 75.4% white; 55.1% had Medicare, 3.9% had Medicaid, and 41% had private insurance (Table 1). Figure 1 depicts the predicted probability of receiving biosimilar infliximab over time by time-window and insurance. After -dyyb (biosimilar #1) came out, uptake for all insurances remained low at less than 10%. With -axxq (biosimilar #2) release, Medicaid was the only insurance to show rapid increase in uptake reaching 19% over 3 years (4 times increase) versus 14% and 7% for Medicare and private insurance. However, after -adba (biosimilar #3) release, both Medicaid and private insurance uptake skyrocketed, reaching similar rates around 40%. Meanwhile, Medicare uptake continued to remain modest at 24%.

Conclusion: Adoption of biosimilar infliximab was quickest for Medicaid, with private insurance catching up after the release of a third biosimilar. Medicare uptake lagged significantly. To reduce drug spending, efforts are needed to understand poor Medicare uptake of biosimilars such as manufacturer rebates for biologics, and lack of financial incentives to switch to biosimilars.

Disclosure: E. Roberts: None; **J. Li**: None; **N. Bansback**: None; **C. Tseng**: Hawaii Medical Services Association Endowed Chair, 5, www.enavvi.com, 1; **S. Shiboski**: None; **G. Schmajuk**: None; **J. Yazdany**: Astra Zeneca, 2, 5, Aurinia, 5, Gilead, 5, Pfizer, 2.

Abstract Number: 1618

Intervention to Improve Medication Adherence Among Patients with SLE

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Health Services Research II
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Medication nonadherence is common and is associated with increased disease activity, morbidity, and mortality in SLE. To optimize medication adherence and SLE outcomes, we developed a simple clinician-led adherence intervention that involves clinicians reviewing real-time pharmacy refill data during the encounter and using effective communication techniques with patients to collaboratively overcome adherence barriers (Figure 1). Prior pilot testing demonstrated intervention feasibility, acceptability, and preliminary effect on adherence. In this study, we aimed to examine how the intervention is performed in practice and identify areas for improvement to inform future implementation.

Methods: We audio recorded clinic encounters between clinicians and patients seen at an academic lupus clinic. Patients were included if they had 90-day medication possession ratio (MPR) < 80% for SLE-specific medications. We coded which intervention components clinicians performed, quality of patient-clinician communication, and time spent discussing adherence. Following the intervention encounter, we also conducted audio-recorded semi-structured interviews with patients and

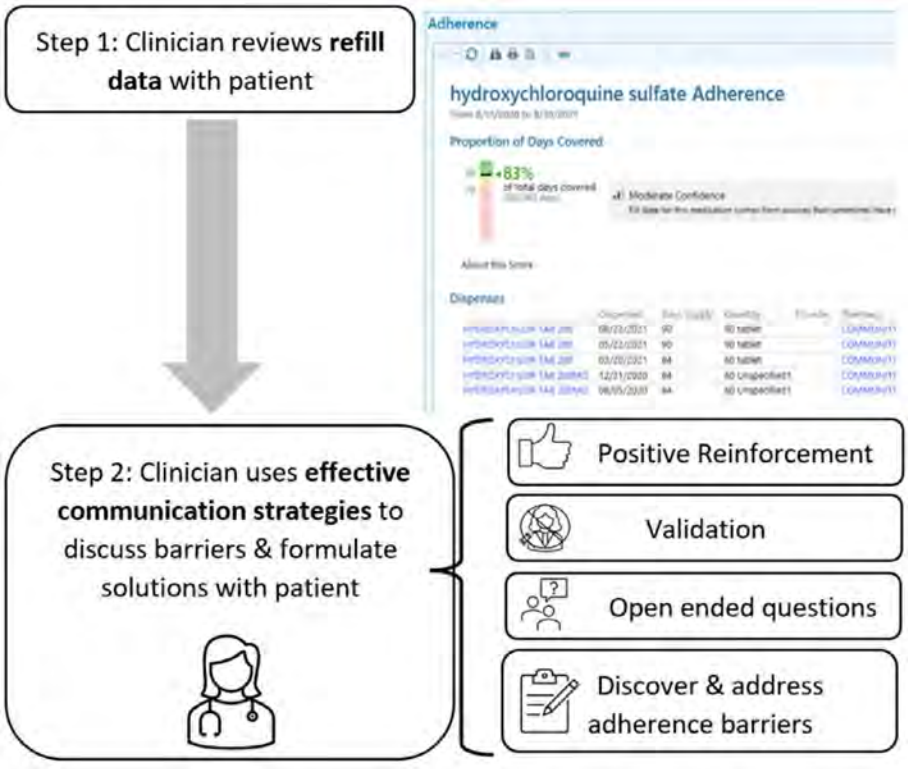


Figure 1. Adherence intervention steps.

Table 1. Intervention components performed during 25 recordings of the adherence intervention.

Intervention components	Definition	N=25 (% yes)
Reviewed refills	Clinician reviewed pharmacy refill data with patient during the visit	88%
Positive Reinforcement	Clinician praised patient for good behavior observed related to adherence, e.g., refilling regularly, being honest about nonadherence	88%
Validation	Clinician made statement to normalize missing doses and difficulties patients face in taking medications consistently	84%
Open-ended questions	Clinician asked a question about adherence that cannot be answered with yes or no or a finite number of answers	52%
Identified barriers	Clinician and patients discussed reasons for missing refills	76%
Addressed barriers	Clinician made suggestions about how to improve adherence	68%

clinicians about their experiences with the intervention and analyzed the data using applied thematic analysis. Lastly, we assessed change in 90-day MPR after the intervention visit and considered a 20% increase as major improvement.

Results: We recorded and analyzed 25 patient encounters (median age 39, 100% female, 72% Black) among 6 clinicians. Clinicians performed the majority of intervention components in most of encounters, suggesting fidelity (Table 1). Global communication scores and rates of active patient participation were high, suggesting excellent communication. Adherence discussions took on average 3.8 minutes.

Nineteen patients and 5 clinicians completed in-depth interviews. Nearly all participants felt the time spent discussing adherence was just right and necessary. Almost all patients felt the intervention was useful. Many patients described feeling heard and valued, being more honest about nonadherence, and being more knowledgeable and motivated to take SLE medications. Clinicians described less judgmental adherence discussions as a result of the intervention. To improve the intervention, patients emphasized better patient-clinician communication and wanted help problem solving financial and logistical barriers. Clinicians suggested additional resources and training to improve adherence conversations and utilizing peer support and other staff in the intervention.

Table 2. Quality of patient-clinician communication during the adherence intervention.

Global score category	Definition	Median score
Attentive	How engaged was the clinician	4.0/5.0
Concerns	How well did clinician address and anticipate patient concerns	5.0/5.0
Flow	Ease of flow of the conversation between clinician and patient	4.5/5.0
Respect	How much respect clinician conveyed to patient	5.0/5.0
Warmth	Warmth of the clinician	5.0/5.0
Active patient participatory behavior		**% of encounters, n/visit**
Asking questions	Seeking information and clarification related to medical encounter	88%, 3/visit
Assertive responses	Offering opinions, making requests, introducing new topics, stating preferences, making recommendations, disagreeing, clarifying, or interruption	88%, 2/visit

Following the intervention visit, almost half (48%) of patients had a major improvement (>20% increase) in MPR.

Conclusion: Our findings suggest that this intervention can be performed with high fidelity in a short amount of time. It encouraged high quality communication and improved adherence. Both patients and clinicians described positive experiences with the intervention. Future work will focus on optimizing clinician training, exploring ways to increase the intervention's efficiency and effectiveness, and testing the intervention in a larger controlled setting.

Disclosure: K. Sun: AstraZeneca, 6; **N. Molokwu**: None; **E. Hanlen**: None; **A. Corneli**: None; **K. Pollak**: None; **J. Rogers**: Amgen, 2, Ampel Biosolutions, 1, AstraZeneca, 6, Aurinia, 1, Eli Lilly, 1, Exagen, 5, GlaxoSmithKlein(GSK), 2, Immunovant, 2, 5; **R. Sadun**: None; **L. Criscione-Schreiber**: GlaxoSmithKlein(GSK), 5, UCB, 5; **J. Doss**: None; **H. Bosworth**: None; **M. Clowse**: Exagen, 5, GlaxoSmithKlein(GSK), 2, 5, Immunovant, 5, UCB, 2, 5.

Abstract Number: 1619

Receipt of Antimicrobial Prophylaxis in U.S. Medicare Beneficiaries Initiating Immunosuppressive Medications for ANCA Vasculitis

Carolyn Thorpe, Ryan Hickson, Sherrie Aspinall, Vimal Derebail, Xinhua Zhao, Joshua Thorpe, Binxin Cao, Alexa Ehlert, Ronald Falk and Susan Hogan, University of North Carolina, Chapel Hill, NC

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Health Services Research II
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Infections are the leading cause of hospitalization and mortality in patients with ANCA vasculitis (AV). Multiple AV treatment guidelines recommend antimicrobial prophylaxis during treatment with rituximab or cyclophosphamide, with agents that target prevention of *Pneumocystis jirovecii*pneumonia (PJP), but vary in recommendations for AV patients on other immunosuppressant (IS) medications. Providers may also initiate prophylaxis with other antimicrobials to prevent non-PJP infections. To address a gap in knowledge regarding real-world patterns of prophylaxis in AV, we characterized receipt, type, and duration of antimicrobial prophylaxis in U.S. Medicare beneficiaries initiating IS medication over 2016-18.

Methods: Using Medicare fee-for-service claims and a 90-day washout, we identified a national, retrospective cohort of new IS treatment episodes in 2016-18, including rituximab (RTX), cyclophosphamide (CYC), methotrexate, azathioprine, mycophenolate, leflunomide, mepolizumab, reslizumab, benralizumab, dupilumab, and/or corticosteroids (CS) at >10 mg/day prednisone equivalents. Episodes were restricted to adults with ≥1 diagnosis code for granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), or eosinophilic granulomatosis with polyangiitis (EGPA) in the prior year. IS regimens were classified as having either a strong indication for prophylaxis (regimens containing RTX, CYC, or CS of >20 mg/day in combination with another IS) or weaker indication (all other regimens). Prophylaxis was defined as ≥14 days' supply of a qualifying antimicrobial overlapping the first 30 days of IS treatment. Antimicrobials included PJP prevention (trimethoprim-sulfamethoxazole, pentamidine, dapsone, atovaquone), other antibacterials (azithromycin, doxycycline, fluoroquinolones), and antifungals (azole or mold-active). We calculated descriptive statistics overall and by IS regimen. We estimated Aalen-Johansen cumulative incidence of prophylaxis discontinuation over one year of follow-up, with death as a competing risk.

Results: Among 14,798 new AV IS treatment episodes (Table 1), 35% involved regimens with a stronger indication for prophylaxis. Overall, 21% received prophylaxis in the 30 days following IS initiation (Table 2). PJP prophylaxis was most frequent (16%), followed by other antibacterials (7%) and antifungals (2%). IS regimens with a stronger vs. weaker indication

Table 1. Characteristics of fee-for-service Medicare enrollees initiating a new course of immunosuppressive medication for ANCA vasculitis (AV) over 2016-2018 (n=14,798 treatment episodes; 8,446 unique patients)

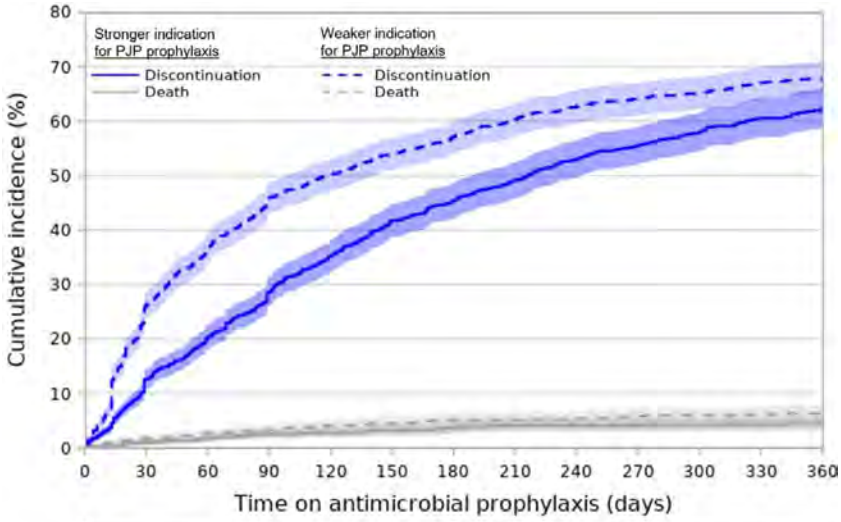
	%
Age Group (as of immunosuppressant episode start date)	
<65	21.2%
65 to <70	20.6%
70 to <75	23.2%
75 to <80	17.8%
>=80	17.2%
Female	62.9%
Race/Ethnicity	
Non-Hispanic White	82.8%
Black	5.3%
Hispanic	6.9%
Asian	1.9%
Native American	0.9%
Other/unknown	2.2%
Type of ANCA vasculitis (most recent AV code on/before index date)	
Granulomatosis with polyangiitis (M31.30 or M31.31 or 446.4)	72.9%
Microscopic polyangiitis (M31.7)	16.1%
Eosinophilic granulomatosis with polyangiitis (M30.1)	10.0%
Multiple types	1.0%
Immunosuppressive medication regimen	
RTX and/or CYC with any dose of corticosteroids[1]	26.0%
RTX and/or CYC without any corticosteroids[1]	7.8%
Other IS[3] plus corticosteroid dose of >20 mg prednisone equivalents[1]	1.6%
Other IS[3] alone or with corticosteroid dose of <=20 mg prednisone equivalents[2]	10.7%
Corticosteroids alone at >10 mg/day prednisone equivalents[2]	54.0%

[1]Regimen with Stronger Indication for PJP Prophylaxis; [2]Regimen with Weaker Indication for PJP Prophylaxis. [3]Other IS=methotrexate, azathioprine, mycophenolate, leflunomide, mepolizumab, reslizumab, benralizumab, or dupilumab. RTX=rituximab; CYC= cyclophosphamide.

for prophylaxis more often involved any prophylaxis (29% vs. 16%) and PJP prophylaxis (26% vs. 11%), but less often involved other antibacterials (5.5% vs. 7.4%). The cumulative incidence of antimicrobial discontinuation was 51.3% (95% CI=49.1, 53.7) at 180 days after IS initiation and 65.1% (95% CI=62.6-67.5) at 360 days, and was higher for regimens with a weaker indication for prophylaxis (360-day RD=5.6%, 95% CI=0.9-9.9; Figure 1).

Table 2. Use of antimicrobial prophylaxis in the 30 days following the start of a new immunosuppressant treatment episode.

	Full Sample (n=14,798)	Regimen with Stronger Indication for PJP Prophylaxis (n=5,228)	Regimen with Weaker Indication for PJP Prophylaxis (n=9,570)
	%	%	%
Receipt of any type of prophylaxis	20.7%	29.0%	16.1%
Type of Prophylaxis Received			
PJP Prevention	16.3%	26.4%	10.8%
Trimethoprim-sulfamethoxazole (TMP/SMX)	14.3%	22.7%	9.8%
Atovaquone, dapsone, or inhaled pentamidine	2.2%	4.1%	1.1%
Other Antibacterials	6.7%	5.5%	7.4%
Fluoroquinolones	3.5%	2.5%	4.0%
Azithromycin	2.3%	1.8%	2.5%
Doxycycline	2.1%	1.6%	2.3%
Antifungal	1.5%	1.1%	1.7%
Number of Antimicrobial Classes Used			
1 classes	16.4%	25.0%	11.7%
2 or more classes	4.3%	4.0%	4.4%



Follow-up time	IS Regimen: Indication for PJP Prophylaxis	Discontinuation: Risk % (95% CI)	Risk Difference % (95% CI)
180 days	Stronger	45.4 (42.2, 48.7)	–
	Weaker	57.2 (54.2, 60.1)	11.8 (7.7, 15.7)
360 days	Stronger	62.3 (58.9, 66.1)	–
	Weaker	67.9 (64.9, 70.9)	5.6% (0.9, 9.9)

Conclusion: Despite high infection risk, most AV patients initiating IS did not receive antimicrobials for prevention of PJP or other infections and a majority discontinued within 6 months. This discordance with AV treatment guidelines highlights the need to further investigate barriers and outcomes associated with prophylaxis in this population.

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Abstract Number: 1620

Cardiovascular Risk and Fracture Risk Among Women Initiating Treatment with Romosozumab or Denosumab

Ye Liu[1], Tarun Arora[2], S. Bobo Tanner[3] and **Jeffrey Curtis**[1], [1]University of Alabama at Birmingham, Birmingham, AL, [2]Foundation for Advancing Science, Technology, Education, and Research, Birmingham, AL, [3]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Abstracts: Health Services Research II
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

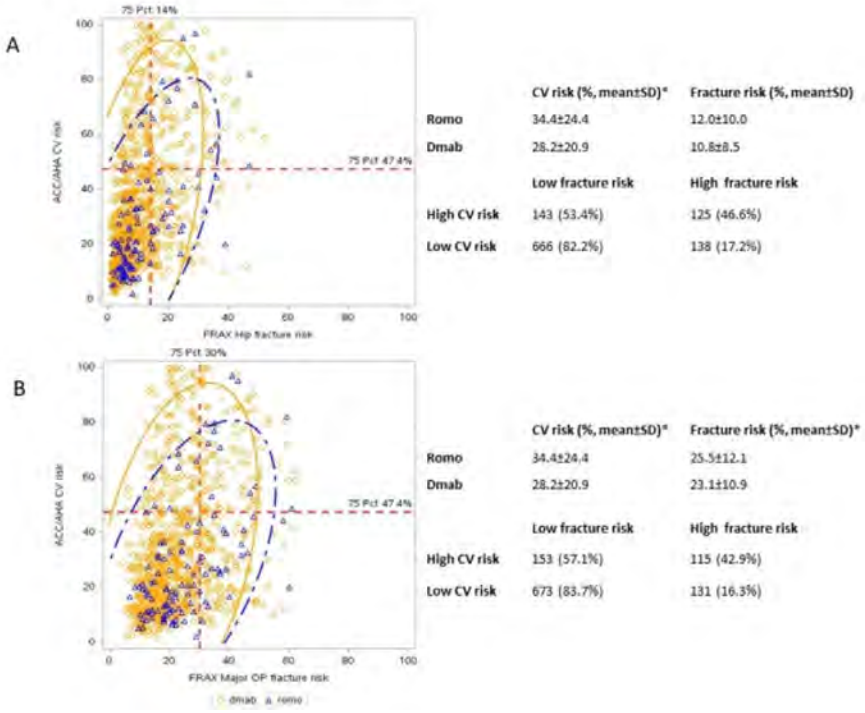
Background/Purpose: Romosozumab (romo) and denosumab (dmab) are recommended for postmenopausal women with osteoporosis (OP) at high risk of fracture. The U.S. prescribing information includes a boxed warning that romo should not be initiated in patients with prior myocardial infarction or stroke in the prior year. Forall other patients without recent MI or

Figure 1. Scatter plots with 95% prediction ellipse between ACC/AHA CV risk and fracture risk for romosozumab or denosumab new users (n=1072).

A: Hip fracture

B: Major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture)

*: p<0.05 between romo and dmab users



	CV risk (%, mean±SD)*	Fracture risk (%, mean±SD)
Romo	34.4±24.4	12.0±10.0
Dmab	28.2±20.9	10.8±8.5
	Low fracture risk	**High fracture risk**
High CV risk	143 (53.4%)	125 (46.6%)
Low CV risk	666 (82.2%)	138 (17.2%)

	CV risk (%, mean±SD)*	Fracture risk (%, mean±SD)*
Romo	34.4±24.4	25.5±12.1
Dmab	28.2±20.9	23.1±10.9
	Low fracture risk	**High fracture risk**
High CV risk	153 (57.1%)	115 (42.9%)
Low CV risk	673 (83.7%)	131 (16.3%)

stroke, the warning recommends to consider whether the benefits of romo outweigh its risks. This study evaluated CV and fracture risks among patients who initiated romo referent to dmab users.

Methods: We used Medicare data from 1/1/2017 to 9/30/2021 to identify women age ≥55 newly initiating romo or dmab after 4/1/2019.Claims data was linked to electronic medical record (EMR) data from multiple PCORNet Clinical Research Networks. Comorbidities and medical history were identified from claims while biometric data and lipid test results were obtained from the EMR. The ACC/AHA pooled cohort risk equation was used to calculate the 10-year CV risk. The FRAX algorithm was used to calculate 10-year risk of hip and major fracture (clinical spine, forearm, hip, or shoulder). We set the 75 percentile of each risk score as the cut-off for high CV and fracture risk. A scatter plot with 95% prediction ellipse was used to illustrate the relationship between CV risk versus the risk of fractures (Figure 1) at a patient level and to compare the cohort of romo vs. dmab patients. Multivariable logistic regression was used to evaluate the relationship between high CV or fracture risk and medication initiation.

Results: A total of 197,515 new users of romo(n=14,596)or dmab (n=182,919) were eligible for analysis and 1072 were linked to PCORNet data. Figure 1 showed romo users had lower CV risk but comparable or higher risk for hip or major fracture compared with dmab users. Romo was more likely to be prescribed to patients with higher fracture risk but lower CV risk, compared with dmab. The odds ratios (95% CI) for initiating romo vs. dmab for high CV risk, hip fracture risk, and major fracture risk were 0.46 (0.26, 0.80), 0.97 (0.47, 2.01), and 1.83 (0.89, 3.75), respectively.

Conclusion: In this cohort of older women with claims data linked to EHR data, patients with high CV risk were less likely to be given romo compared with dmab. These data suggest that the boxed warning regarding CV risk for romo appropriately influences clinical decision making of physicians when prescribing anabolic medications for osteoporosis patients.

Disclosure: Y. Liu: None; **T. Arora**: Amgen, 5; **S. Tanner**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, 5, CorEvitas, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 1621

Maxillofacial MRI Augments Detection of Non-CNS Abnormalities in Pediatric Craniofacial Scleroderma

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Pediatric Rheumatology – Clinical II: Connective Tissue Disease

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Craniofacial scleroderma is a rare subtype of linear scleroderma affecting the head and neck. Up to 40% of patients experience extracutaneous manifestations (ECMs), but radiographic characterization of non-CNS involvement is not well described. Existing clinical assessment rubrics prioritize cutaneous changes, likely underestimating the extent of disease-related manifestations. We sought to categorize and quantify the incidence of non-CNS ECMs detected

Table 1. Demographics and craniofacial scleroderma characteristics (N=37)

Table 1. Demographics and craniofacial scleroderma characteristics (N=37)

Demographics	
Female, n (%)	20 (46)
Age, median (IQR)	10.5 (8.3 - 14.3)
Craniofacial Scleroderma Subtype	**n (%)**
Parry-Romberg Syndrome (PRS)	9 (24)
En coup de sabre (ECDS)	18 (49)
Overlap (PRS + ECDS)	10 (27)
Clinical features	
Disease Duration, Months, median (IQR)	66.5 (29.5 - 91.8)
mLoSDI, median (IQR)	5 (3 - 6)
mLoSSI , median (IQR)	0 (0 - 0)
Medication History	**n (%)**
Prior or Current Treatment	28 (76)
Methotrexate	16 (43)
Mycophenolate Mofetil	13 (35)
Steroids	12 (32)
Abatacept	2 (5)
Hydroxychloroquine	3 (8)
Topicals	8 (22)
Tacrolimus	3 (8)
Calcipotriene	2 (5)
Topical Corticosteroids	3 (8)
No Treatment	9 (24)

*mLoSDI = modified Localized Scleroderma Damage Index, mLoSSI = modified Localized Skin Severity Index

on maxillofacial MRI in a prospective cohort of patients with craniofacial scleroderma. We hypothesize that maxillofacial MRI would identify facial involvement beyond standard clinical examination.

Methods: We performed retrospective review of 120 patients with Craniofacial Scleroderma enrolled in the prospective National Registry of Childhood Onset Scleroderma (IRB #19080297). Inclusion criteria included baseline maxillofacial MRI with concurrent clinical 3D image.

Laterality of visible facial involvement (left, right, midline) and superior to inferior facial lesion distribution (top, middle, bottom thirds) were recorded from review of 3-dimensional digital facial images. Top third was defined as the area between horizontal lines drawn through trichion and glabella, middle third between glabella and subnasale, and bottom third between subnasale and mention. Evaluation of bone, soft tissue, fat, glands, and muscles were categorized as atrophy, edema, or abnormal enhancement.

Table 2. Structural abnormalities identified on maxillofacial MRI

Table 2. Structural abnormalities identified on maxillofacial MRI

Anatomic Structure	Overall Affected N=37 n, (%)	Atrophy		Enhancement		Edema	
		Count	Percent	Count	Percent	Count	Percent
Bone	18 (49)						
Calvarium		11/35	31%	2/24	8%	6/35	17%
Orbit		3/37	8%	1/26	4%	1/36	3%
Maxilla		5/37	14%	0/24	-	0/34	
Mandible		2/34	6%	0/23	-	0/31	
TMJ		5/37	14%	0/27	-	0/36	
Soft Tissue	27 (73)						
Skin & Subcutaneous	27 (73)	27/36	75%	3/21	14%	NR	NR
Orbit	9 (24)						
Preseptal		9/37	24%	NR	NR	NR	NR
Postseptal		7/37	19%	NR	NR	NR	NR
Enophthalmos	4 (11)	NR	NR	NR	NR	NR	NR
Adipose Tissue	21 (57)						
Parapharyngeal Fat		10/37	27%	NR	NR	NR	NR
Premaxillary Fat		18/37	49%	NR	NR	NR	NR
Glandular Tissue*	21 (57)						
Parotid		9/37	24%	9/25	36%	4/36	11%
Submandibular		6/34	18%	6/23	26%	5/33	15%
Sublingual		6/33	18%	0/22	-	0/32	-
Lacrimal		3/37	8%	8/28	29%	NR	NR
Muscle	26 (74)						
Orbit	5 (14)						
Extraocular		4/37	11%	3/28	11%	NR	NR
Muscles of Mastication	15 (41)						
Temporalis		7/37	19%	1/27	4%	NR	NR
Masseter		10/37	27%	1/27	4%	NR	NR
Lateral pterygoid		2/37	5%	0/27	-	NR	NR
Medial pterygoid		2/37	5%	0/27	-	NR	NR
Intrinsic Tongue		2/37	5%	0/27	-	NR	NR
Extrinsic Tongue		0/37	-	0/27	-	NR	NR
Sup. Pharyngeal Constrictor		5/36	14%	0/24	-	NR	NR
Oropharynx		2/37	5%	0/26	-	NR	NR
Muscles of Facial Expression	20 (54)						
Orbicularis oculi		5/37	14%	0/27	-	NR	NR
Mentalis		3/28	11%	1/19	5%	NR	NR
Orbicularis oris		6/32	19%	2/21	10%	NR	NR
Depressor labii inf.		4/28	14%	0/18	-	NR	NR
Depressor anguli oris		5/30	17%	1/19	5%	NR	NR
Levator labii sup.		7/37	19%	2/26	8%	NR	NR
Levator anguli oris		6/31	19%	1/22	5%	NR	NR
Zygomaticus major		7/31	19%	5/26	19%	NR	NR
Buccinator		6/32	19%	1/21	5%	NR	NR
Platysma		4/32	13%	0/23	-	NR	NR

*Two patients experienced duct dilations: one in parotid gland and one in submandibular gland. NR = not recorded

Table 3. Clinical and radiographic analysis of facial-thirds involvement (N=37)

Table 3. Clinical and Radiographic Analysis of Facial-Thirds Involvement (N=37)

	Upper Third		Middle Third		Lower Third	
	Count	Percent	Count	Percent	Count	Percent
Clinical Findings	28	76%	35	95%	24	65%
Radiographic Findings	31	84%	28	84%	29	78%
Bone	15	41%	7	19%	6	16%
Soft Tissue	26	70%	1	3%	4	11%
Adipose Tissue	8	22%	17	46%	10	27%
Glandular Tissue	9	24%	0	-	19	51%
Muscle	10	27%	18	49%	17	46%
	Right		**Left**		**Bilateral**	
Clinical Sidedness	14	38%	22	59%	1	3%
Radiographic Sidedness	14	38%	14	38%	9	24%

Results: Thirty-seven patients met imaging criteria for inclusion, (age range 4-20 years, median age 10.5 years) (Table 1). Overall, structural abnormalities were frequently detected on maxillofacial MRI (bone=49%, soft tissue=73%, adipose=57%, gland=57% and muscle=74%) (Table 2). Atrophy was the most common finding, particularly in the skin/subcutis (75%) and adipose tissues (57%). Enhancement was frequently observed in glandular tissues (parotid 36%, lacrimal 29%) as well as in the muscles of facial expression. MRI demonstrated increased frequency of bilateral involvement compared to clinical assessment (24% vs 3%). Radiographic changes were more frequently seen compared to clinical abnormalities in the upper-third (84% vs 76%) and lower-third (78% vs 65%) (Table 3). Frequencies of radiographic abnormalities differed across facial thirds, with soft tissue changes most frequent in the upper third (70%), muscle changes in the middle third (49%), and glandular changes in the lower third (51%).

Conclusion: Our study demonstrated an overall high incidence of facial bone, soft tissue, glandular, and muscle involvement in craniofacial scleroderma. Clinical examination and radiographic review frequently demonstrated discordant results. Therefore, we recommended baseline maxillofacial MRI in addition to brain MRI to better delineate the full extent of disease involvement in craniofacial scleroderma patients. Future work should assess evolution of these findings over time, response to immunomodulatory treatment, and development of multi-modal assessment rubrics.

Disclosure: D. Glaser: None; **A. Metry**: None; **E. DeRosas**: None; **S. Subramanian**: None; **K. Torok**: None.

Abstract Number: 1622

Myositis-associated Autoantibodies in Juvenile Myositis Are Associated with Severe Disease Features and Mortality

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Pediatric Rheumatology – Clinical II: Connective Tissue Disease

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Background/Purpose: Myositis-associated autoantibodies (MAAs), such as anti-Ro52 autoantibodies (Abs), have been found to be associated with interstitial lung disease (ILD) and worse prognosis in the idiopathic inflammatory myopathies. MAAs remain largely uncharacterized in juvenile-onset myositis. Moreover, MAAs often co-exist and it is unknown whether the number of MAA specificities may be associated with increased disease severity.

Methods: Patients with juvenile myositis enrolled in cross-sectional NIH myositis natural history studies who underwent testing for myositis Abs were included. Demographics, clinical manifestations, treatments, and outcomes of those with and without MAAs were compared using Chi-squared, Fisher's exact test, or Wilcoxon rank-sum test. Multivariable logistic regression with adjustment for year of diagnosis and myositis autoantibodies was performed for statistically significant variables from the univariable analyses. Multivariable logistic regression was also used to determine whether the number of MAA specificities is predictive of severe disease features. A two-sided $p< 0.05$ was considered significant.

Results: MAAs were present in 36% of this North American cohort of 551 juvenile myositis patients and were found across serologic subgroups (**Figure 1**). Among patients with any MAA, there was a higher frequency of juvenile connective tissue myositis (JCTM) (18% vs 5.9%, $p< 0.001$) and lower frequency of juvenile dermatomyositis (JDM) (74% vs 88%, $p< 0.001$) (**Table 1**). Anti-synthetase Abs (9.1% vs 1.7%, $p< 0.001$) were more frequent and anti-NXP2 Abs (18% vs

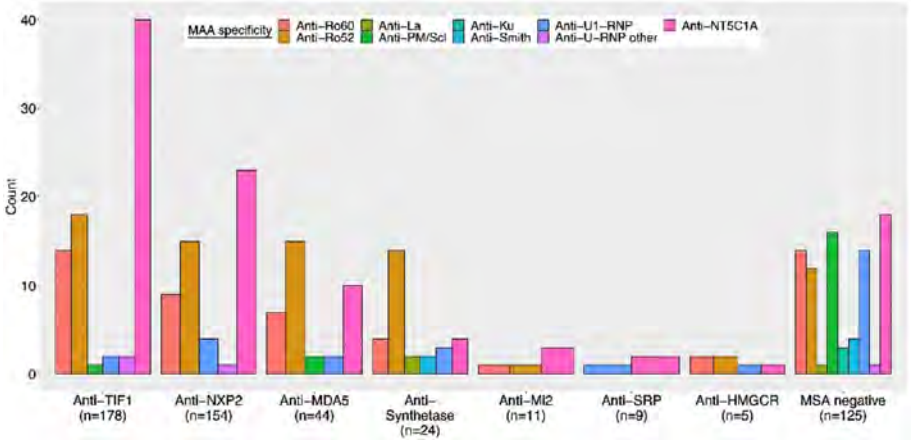

FIGURE 1: Myositis-associated autoantibodies among juvenile myositis serologic subgroups

Characteristic	Any MAA positive, N = 198	Any MAA negative, N = 353	p-value
Demographics			
Female	71% (140 / 198)	70% (247 / 353)	0.9
Caucasian	69% (136 / 198)	69% (245 / 353)	0.9
Black	13% (26 / 198)	12% (44 / 353)	0.8
Hispanic	5.1% (10 / 198)	6.5% (23 / 353)	0.5
Asian	2.0% (4 / 198)	2.5% (9 / 353)	0.8
Other	11% (22 / 198)	9.1% (32 / 353)	0.4
Age at diagnosis (years)	9.2 (5.8, 13.2)	7.1 (5.1, 10.8)	**<0.001**
Duration from diagnosis to enrollment (years)	1.2 (0.4, 3.0)	2.0 (0.5, 4.0)	**0.008**
Clinical Subgroups			
JDM	74% (147 / 198)	88% (310 / 353)	**<0.001**
JPM	7.6% (15 / 198)	6.2% (22 / 353)	0.5
JCTM	18% (36 / 198)	5.9% (21 / 353)	**<0.001**
Juvenile myositis with SLE	7.1% (14 / 198)	0.9% (3 / 350)	**<0.001**
Juvenile myositis with SSc	3.5% (7 / 198)	0% (0 / 350)	**<0.001**
Juvenile myositis with SjS	1.5% (3 / 198)	0% (0 / 350)	**0.047**
Serologic Subgroups			
Positive MSA	73% (144 / 198)	80% (282 / 353)	0.054
Anti-TIF1	31% (62 / 197)	33% (116 / 353)	0.7
Anti-NXP2	18% (35 / 197)	34% (119 / 353)	**<0.001**
Anti-MDA5	9.7% (19 / 196)	7.2% (25 / 345)	0.3
Anti-Synthetase	9.1% (18 / 198)	1.7% (6 / 353)	**<0.001**
Anti-Mi2	2.0% (4 / 198)	2.0% (7 / 353)	>0.9
Anti-SRP	1.0% (2 / 198)	2.0% (7 / 353)	0.5
Anti-HMGCR	1.9% (3 / 160)	0.7% (2 / 271)	0.4

TABLE 1: Demographics and clinicoserologic subgroups among juvenile myositis patients with and without myositis-associated autoantibodies. Abbreviations: JCTM, juvenile connective tissue myositis; JDM, juvenile dermatomyositis; JPM, juvenile polymyositis; MAA, myositis-associated autoantibody; MSA, myositis-specific autoantibody; SjS, Sjogren's syndrome; SLE, systemic lupus erythematosus; SSc, systemic sclerosis.

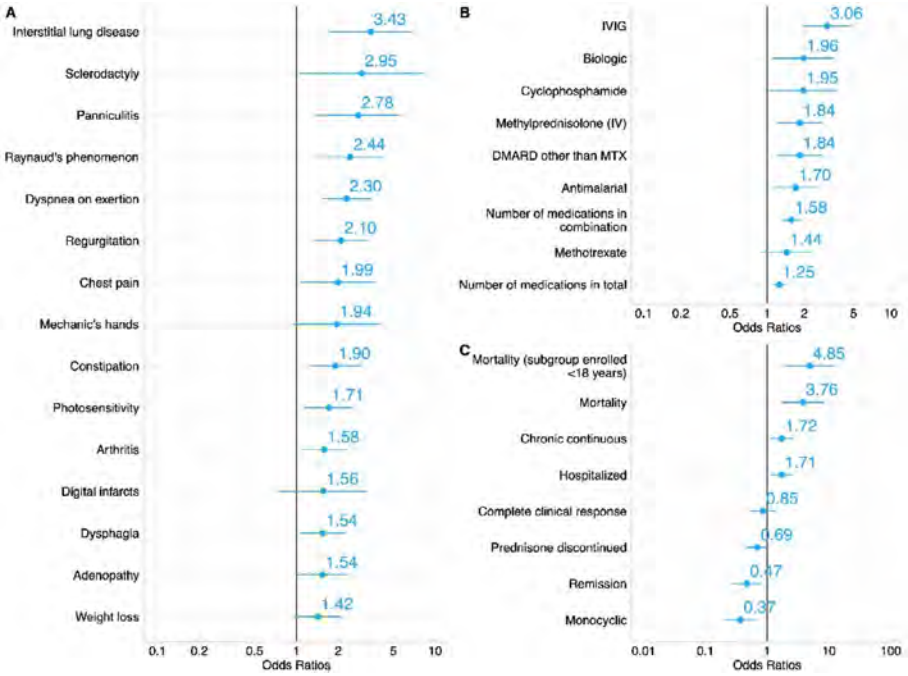

FIGURE 2: Disease features (A), medications received (B), and outcomes (C) among juvenile myositis patients with and without myositis-associated autoantibodies. Abbreviations: DMARD, disease-modifying antirheumatic drug; IV, intravenous; IVIG, intravenous immunoglobulin; MTX, methotrexate.

34%, p< 0.001) less frequent among those with an MAA. The presence of an MAA was associated with certain clinical manifestations, such as ILD (OR 3.43; 95% CI 1.75-6.96), Raynaud's phenomenon (OR 2.44; 95% CI 1.41-4.28), and arthritis (OR 1.58; 95% CI 1.07-2.34) (**Figure 2**). The presence of any MAA was associated with increased treatment burden, including a greater odds of receiving IVIG (OR 3.06; 95% CI 1.98-4.76), IV methylprednisolone (OR 1.84; 95% CI 1.21-2.83), and a greater number of major medications in combination (OR 1.58; 95% CI 1.33-1.88). Positivity for any MAA was also associated with worse outcomes, including higher odds of mortality (OR 3.76; 95% CI 1.72-8.43) and a chronic continuous disease course (OR 1.72; 95% CI 1.10-2.72) and lower odds of a monocyclic disease course (OR 0.37; 95% CI 0.19-0.67) and achievement of remission (OR 0.47; 95% CI 0.26-0.82). Moreover, the number of MAA specificities was predictive of mortality (OR 1.83; 95% CI 1.16-2.86).

Conclusion: MAAs were prevalent in this large cohort of patients with juvenile myositis and were associated with severe disease features, more refractory disease, and mortality. Future prospective studies are needed to determine whether early detection of MAAs may improve outcomes for patients with juvenile myositis.

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Abstract Number: 1623

Diffuse Juvenile Systemic Sclerosis Patients Show Distinct Organ Involvement, Antibody Pattern and Have More Severe Disease in the Largest jSSc Cohort of the World. Results from the Juvenile Scleroderma Inception Cohort

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SESSION INFORMATION

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Background/Purpose: Juvenile systemic sclerosis (jSSc) is an orphan disease with a prevalence of 3 in 1,000,000 children. In adult patients there are significant differences between clinical presentation of cutaneous diffuse (djSSc) and cutaneous limited phenotypes(ljSSc).

Methods: We reviewed the baseline clinical characteristics of the patients, who were recruited to the jSScC prior to April 2023. jSScC is a prospective cohort of jSSc patients, who developed the first non-Raynaud´s symptom before the age of 16 years and were under the age of 18 years at the time of inclusion.

Results: The jSScC included 238 patients, 69% (n=164) had cutaneous diffuse subtype. The median age at onset of Raynaud's phenomenon was 10.4 years (7.3-12.9) and the median age at the first non-Raynaud's symptom was 10.9 years (7.3-13.0). Median disease duration was 2.5 years (1.0-4.7). The female/male ratio was not significantly lower in the djSSc subtype (3.3:1 versus 4.7:1, p=0.611). Antibody profile was similar, with the exception of a significantly higher number of anticentromere positive patients in the ljSSc (10% versus 2%, p=0.019). Patients with djSSc had significantly higher modified Rodnan Skin Score (17 versus 4, p=0.011), more frequently sclerodactyly (85% versus 56%, p< 0.001), Gottron

Table 1. Characteristics of patients with diffuse and limited subtype

Comparison diff/lim at time of inclusion in the cohort	Whole Group N=238	Diffuse Subtype N=164	Limited Subtype N=74	P value
Female to Male Ratio	3.7:1 (187/51)	3.3:1 (122/37)	4.7:1 (61/13)	0.611
Cutaneous subtype				
Diffuse subtype	69% (164)	164	0	
Limited subtype	31% (74)	0	74	
Median Disease duration (years), IQR	2.5 (1 – 4.7)	2.6 (1.3 – 4.7)	2.0 (0.6 – 4.5)	0.831
Median age at onset of Raynaud's (years), IQR	10.4 (7.3 – 13.0)	10.1 (7.5 – 12.5)	11.8 (7 – 13.7)	0.617
Median age at onset of non-Raynaud's (years), IQR	10.9 (7.4 – 13.4)	10.5 (7.4 – 12.5)	12.0 (7.3 – 14.4)	0.397
Autoantibody positivity:				
ANA	92% (209/227)	92% (144/156)	93% (64/69)	0.907
Anti-scl 70	33% (74/225)	37% (57/155)	26% (17/66)	0.112
Anti-centromere	5% (8/164)	2% (2/110)	10% (5/50)	0.019
Anti-PMScl	18% (18/101)	14% (9/63)	24% (9/37)	0.207
Cutaneous:				
MRSS, median (IQR)	10 (4 – 20)	17 (8 - 27)	4 (0 – 8)	0.011
Gottron Papules	26% (61/234)	31% (50/160)	15% (11/74)	0.008
Sclerodactylie	76% (170/225)	85% (131/155)	56% (39/70)	<0.001
Vascular:				
Telangiectasia	37% (80/215)	45% (65/146)	22% (15/69)	0.001
History of ulceration	51% (121/235)	61% (100/163)	29% (21/72)	<0.001
Active ulceration	17% (39/235)	20% (33/163)	8% (6/72)	0.024
Cardiac Involvement:				
Only Cardiac Involvement	5% (12/238)	2% (4/164)	11% (8/74)	0.006
Gastrointestinal Involvement:				
BMI ≤ - 2 z score	15% (33/220)	19% (29/151)	6% (4/69)	0.010
Musculoskeletal:				
Presence of joints with decreased range	59% (139/237)	64% (104/163)	47% (35/74)	0.017
Patient Reported Outcomes				
Patient global disease activity	40 (20 – 50) n=184	40 (20 – 50) n=134	30 (15 – 54) n=50	0.041
Patient global disease damage	30 (13 – 55) n=183	40 (20 – 60) n=133	25 (6 – 54) n=50	0.001
Patient Raynaud activity	30 (10 – 60) n=208	30 (10 – 60) n=150	18 (0 – 54) n=58	0.025
Physician Reported outcomes				
Physician global disease activity	30 (20 – 45) n=202	35 (20– 50) n=143	20 (10 – 30) n=59	0.034
Physician global disease damage	28 (15 – 40) n=200	30 (20 – 45) n=143	20 (5 – 30) n=57	0.011

papules (31% versus 15%, p=0.008), a history of digital ulceration (61% versus 29%, p< 0.001), active ulceration (20% versus 8%, p=0.024),telangiectasia (45% versus 22%, p=0.001), a decreased Body Mass Index (BMI) z score ≤ -2 (19% versus 6%, p=0.010) and decreased joint range of motion (64% versus 47%, p=0.017). Patients with ljSSc had significantly higher rate of cardiac involvement (11% versus 2%, p=0.006). There was no difference between the groups regarding sicca symptoms, pulmonary involvement assessed by FVC, DLCO and high resolution lung CT; renal involvement; gastrointestinal involvement beside decreased BMI < -2 z score; and muscle weakness.

Regarding patient related outcomes assessed by visual analogue scales (VAS0 to 100), djSSc patients had more severe disease related to patient reported global disease activity (40 versus 30, p=0.041), patient reported global disease damage (40 versus 25, p=0.001), and patient reported Raynaud activity by(30 versus 18, p=0.025). Additionally, physician related outcomes assessed by visual analogue scales (VAS), the physician reported global disease activity (35 versus 20, p=0.034), and physician reported global disease damage (30 versus 20, p=0.011), were significantly higher in djSSc patients.

Conclusion: In the largest jSSc cohort in the world, djSSc patients have significantly more severe disease according to patient and physician related outcomes than ljSSc patients. Patients with djSSc also had more cutaneous, vascular, and musculoskeletal involvements and patients with ljSSc had more cardiac involvement. Interestingly, we found no significant differences regarding interstitial lung disease, pulmonary hypertension or gastrointestinal involvement, although the number of patients with decreased BMI ≤-2 z score was significantly higher in the djSSc patients.

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Racial Disparities Impact Achieving LLDAS and Glucocorticoid Use in Pediatric Lupus: A CARRA Registry Study

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SESSION INFORMATION

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Session Title: Abstracts: Pediatric Rheumatology – Clinical II: Connective Tissue Disease

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Background/Purpose: Social determinants of health (SDoH) contribute to disparate outcomes in both adult and pediatric systemic lupus erythematosus (pSLE), including length of hospitalization, mortality, and risk of severe sequelae, such as renal damage. Differential disease control may drive racial and ethnic disparities in disease damage and mortality. Therefore, we sought to determine how race associates with achievement of low lupus disease activity state (LLDAS), a clinically relevant disease activity target associated with higher health-related quality of life and less disease damage. We hypothesized that minoritized race would associate with lower rates of achieving LLDAS in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry cohort of children with pSLE.

Table 1: Demographic and clinical characteristics of children with pSLE in the CARRA Registry (between March 2017-December 2021)

Table 1: Demographic and clinical characteristics of children with pSLE in the CARRA Registry (between March 2017-December 2021)

	Total N=540	White	Black	Latino(a)	Asian	More than one race	Other race
Age at enrollment, (years) median (IQR)	15 (12, 16)	15 (13, 16)	15 (13, 17)	15 (12,16)	15 (12, 16)	14 (11, 16)	15 (12, 16)
Age at diagnosis, years) median (IQR)	14 (12, 16)	14 (12, 16)	14 (12, 16)	15 (12, 16)	14 (11, 16)	14 (11, 15)	15 (12, 15
Sex – Female, N (%)	487 (87)	119 (88)	127 (87)	107 (88)	41 (81)	42(89)	25(83)
Insurance, N (%)							
Private	257 (46)	90 (67)	50 (35)	32 (26)	40 (69)	27 (58)	18 (60)
Public	248 (45)	35 (26)	92 (63)	77 (62)	16 (27)	16 (34)	12(40)
Other/Non-U.S	19 (3)	8 (5)	2 (1)	6 (5)	1 (2)	2 (4)	0 (0)
None	18 (3)	2 (1)	2 (1)	9 (7)	1 (2)	2 (4)	0 (0)
Area Deprivation Index[1] (ADI), N (%)							
0-25%ile	169 (31)	45 (33)	16 (12)	38 (31)	37 (64)	17 (36)	14 (47)
26-50%ile	144 (27)	39 (29)	29 (20)	38 (30)	17 (29)	15 (32)	6 (20)
51-75%ile	114 (21)	30 (22)	39 (27)	29 (23)	3 (5)	7 (15)	7 (23)
76-100%ile	113 (21)	21 (16)	60 (41)	20 (16)	1 (2)	8 (17)	3 (10)
Major Organ Involvement, N (%)							
CNS	78 (14)	11 (8)	26 (18)	13 (11)	6 (10)	13 (28)	9 (30)
Renal	277 (51)	98 (50)	83 (57)	61 (49)	24 (41)	25 (53)	16 (53)
CV/Pulm	152 (28)	32 (24)	56 (39)	35 (28)	12 (21)	12 (27)	5 (17)
Baseline Medication, N (%)							
Adjunctive DMARD[2]	43 (8)	9 (7)	20 (14)	5 (4)	3 (5)	4 (9)	2 (7)
Conventional DMARD[3]	462 (86)	115 (85)	125 (89)	102 (82)	53 (91)	39 (83)	28 (93)
Rituximab or CYC[4]	169 (30)	27 (20)	59 (40)	34 (27)	13 (22)	20 (43)	10 (33)
Anti-malarial	523 (97)	129 (96)	144 (98)	120 (97)	54 (93)	46 (98)	30 (100)
Achievement of LLDAS, N[5] (%)	337 (63)	99 (74)	170 (39)	226 (74)	139 (39)	67 (24)	57 (32)
Time adjusted mean prednisone dose in milligrams (IQR)	6.6 (1.7, 12.6)	6.4 (0.2, 11.4)	8.3 (3.5, 19.0)	6.5 (1.8, 12.5)	4.1 (0, 7.4)	6.5 (1.4, 13.5)	5.8 (2.5, 9.8)
Any prednisone restarts or increases during study period, N (%)	169 (57)	43 (32)	86 (45)	42 (34)	19 (33)	16 (34)	13 (43)
Any secondary rheumatologic disease, N (%)	63 (12)	16 (12)	22 (15)	9 (7)	6 (10)	9 (19)	4 (13)
Time from diagnosis to enrollment (years), median (IQR)	0.4 (0.1, 1.2)	0.4 (0.1, 1.2)	0.4 (0.1, 1.4)	0.9 (0.1, 0.8)	0.8 (0.1, 2.0)	0.3 (0.1, 1.2)	0.9 (0.1, 1.6)
Duration of follow up time (years), median (IQR)	2.1 (1.3, 2.9)	2.2 (1.3, 2.9)	1.9 (1.0, 2.7)	2.1 (1.3, 2.7)	2.4 (1.5, 2.9)	2.0 (1.1, 3.0)	2.1 (1.5, 2.7)

[1] Area Deprivation Index (ADI) is a national measure of neighborhood socioeconomic disadvantage at the level of census block group, developed by U.S. Census data including American Community Survey (ACS) data. Higher scores suggest more disadvantaged areas.
[2] Adjunctive DMARDs include azathioprine, methotrexate, mycophenolate mofetil, leflunomide, and tacrolimus.
[3] Conventional DMARDs include antimalarials, azathioprine, methotrexate, mycophenolate mofetil, leflunomide, and tacrolimus.
[4] Cyclophosphamide (CYC).
[5] Total 2048 encounters where LLDAS was assessed across all subjects. See Table 2 for more.

Table 2: Mixed effects models to estimate the effect of race or ethnicity, insurance status, and area deprivation index (ADI) on achievement of LLDAS in children with pSLE in the CARRA Registry

Table 2: Mixed effects models to estimate the effect of race or ethnicity, insurance status, and area deprivation index (ADI) on achievement of LLDAS in children with pSLE in the CARRA Registry

	Univariate ‡ OR (95% CI), p-value	Multivariable * OR (95% CI), p-value
Race or ethnicity		
White	Reference	Reference
Black	**0.47 (0.33, 0.69), <0.001**	**0.56 (0.38, 0.82), 0.003**
Latino/a	0.83 (0.57, 1.20), 0.312	0.87 (0.60, 1.30), 0.459
Asian	1.30 (0.85, 2.10), 0.206	1.10 (0.69, 1.70), 0.729
More than one	**0.51 (0.30, 0.86), 0.011**	**0.51 (0.31, 0.86), 0.011**
Other	0.94 (0.52, 1.70), 0.0014	0.90 (0.51, 1.60), 0.712
Insurance		
Private	Reference	Reference
Public	**0.74 (0.56, 0.97), 0.032**	0.88 (0.66, 1.20), 0.385
Other/Non-U.S.	0.79 (0.37, 1.70), 0.557	0.81 (0.39, 1.70), 0.584
None	0.63 (0.28, 1.40), 0.266	0.79 (0.35, 1.80), 0.560
Area Deprivation Index		
0-25%ile	Reference	Reference
26-50%ile	0.87 (0.62, 1.20), 0.445	1.1 (0.79, 1.50), 0.560
51-75%ile	0.74 (0.51, 1.10), 0.109	1.0 (0.70, 1.50), 0.911
76-100%ile	**0.53 (0.36, 0.78), 0.001**	0.9 (0.51, 1.60), 0.712

‡ All univariate models include time.
* Adjusted for age at enrollment, sex, major organ involvement, medication type, disease duration at enrollment, and presence of any secondary rheumatologic disease

Table 3: Logistic regression models to estimate the effect of race or ethnicity, insurance status, and area deprivation index (ADI) on any prednisone restarts or increases between Registry visits in children with pSLE in the CARRA Registry

Table 3: Logistic regression models to estimate the effect of race or ethnicity, insurance status, and area deprivation index (ADI) on any prednisone restarts or increases between Registry visits in children with pSLE in the CARRA Registry

	Univariate ‡ OR (95% CI), p-value	Multivariable * OR (95% CI), p-value
Race or ethnicity		
White	Reference	Reference
Black	**1.80 (1.10, 2.90), 0.022**	1.7 (0.99, 3.10), 0.055
Latino/a	1.10 (0.65, 1.80), 0.730	1.2 (0.68, 2.20), 0.500
Asian	1.00 (0.53, 2.00), 0.902	1.1 (0.55, 2.30), 0.724
More than one	1.10 (0.54, 2.20), 0.782	1.1 (0.51, 2.40), 0.774
Other	1.60 (0.72, 3.70), 0.232	1.7 (0.70, 4.10), 0.232
Insurance		
Private	Reference	Reference
Public	1.00 (0.73, 1.50), 0.823	0.98 (0.63, 1.50), 0.926
Other/Non-U.S.	0.59 (0.19, 1.60), 0.324	0.55 (0.17, 1.70), 0.346
None	**0.11 (0.01, 0.56), 0.034**	**0.08 (0.00, 0.43), 0.017**
Area Deprivation Index		
0-25%ile	Reference	Reference
26-50%ile	1.40 (0.85, 2.20), 0.196	1.40 (0.82, 2.30), 0.231
51-75%ile	1.00 (0.60, 1.70), 0.988	0.87 (0.48, 1.50), 0.633
76-100%ile	**1.60 (1.00, 2.70), 0.047**	1.40 (0.76, 2.50), 0.284

‡ All univariate models include time.
* Adjusted for age at enrollment, sex, major organ involvement, medication type, disease duration at enrollment, and presence of any secondary rheumatologic disease

Methods: This was a cohort study of children with pSLE enrolled in the CARRA Registry between March 2017-December 2021 with baseline and at least one follow-up visit and a valid U.S. zip code. The primary exposure was self-identified race or ethnicity. SDoH of interest were insurance status and area deprivation index (ADI). The primary outcomes were 1) LLDAS and 2) occurrence of prednisone restarts or dose escalation between visits. Associations between race and/or ethnicity and the outcomes were examined using univariate and multivariable logistic regression models, adjusted for covariates (insurance status, ADI, age at enrollment, sex, major organ involvement, medication use, disease duration at enrollment, and secondary rheumatologic disease). Random effect was included in the LLDAS model to account for repeated measures.

Results: A racially diverse cohort of 540 children with pSLE self-identified as 27% Black, 23% Latino/a, 25% White, 11% Asian, 5% Other, and 9% more than one race. 87% were female with a median age of 14.2 years at diagnosis (IQR 3.2-19.0). 48% were privately insured and 46% publicly insured. Black participants were more likely to be publicly insured, live in areas with higher social deprivation (ADI), and have renal disease (Table 1). In both unadjusted and adjusted analyses, Black race and more than one race were significantly associated with lower odds of achieving LLDAS (Table 2: adjusted OR 0.56, 95% CI: 0.38-0.82; OR 0.51, 95% CI: 0.31-0.86, respectively). In unadjusted analyses, Black race also associated with higher odds of prednisone dose increases or restarts. The adjusted estimate was similar, though not statistically significant at the 0.05 level (Table 3: OR: 1.7, 95% CI: 0.99-3.1, p=0.055).

Conclusion: Children with pSLE in the CARRA Registry identifying as Black or more than one race had significantly lower odds of achieving LLDAS. Black participants were more likely to be publicly insured and live in areas of higher social deprivation. Black race remained strongly associated with lower achievement of LLDAS despite adjustment for SDoH and disease characteristics. This suggests there are unmeasured factors driving the disparities, which may include other influences of structural racism, such as the experience of racial discrimination. Strategies to address these root causes will be important components of treat-to-target interventions designed to mitigate racial disparities in achievement of LLDAS.

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Abstract Number: 1625

Identifying Potential Neuroimaging Biomarkers of Neuropsychiatric Lupus in Children Using Deep Learning

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Pediatric Rheumatology – Clinical II: Connective Tissue Disease
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic, multisystem, autoimmune disease. Childhood-onset SLE (cSLE) is characterised by a higher frequency of nervous system involvement, known as neuropsychiatric SLE (NPSLE). Biomarkers for NPSLE are lacking, posing challenges for clinical diagnosis and management. The existence of neuropsychiatric manifestations in patients without a definite NPSLE diagnosis, as well as normal conventional magnetic

resonance imaging (MRI) findings in patients with NPSLE, allude to suboptimal diagnostic protocols. To identify potential biomarkers of NPSLE, we aimed to develop a deep learning model capable of identifying structural brain image features of patients with cSLE.

Methods: This retrospective study involved a binary classification task between cSLE and non-cSLE patients. Searching all clinically-obtained brain MRIs for cSLE patients from 2000-2021, we retrieved 233 T1-weighted images of sufficient quality for analysis. We then matched these images by age and sex to an existing set of T1-weighted images (n=233) from non-cSLE patients with clinical MRIs (primarily for indication of headache; normal conventional read), obtained from 2000-2020. A chart review was conducted to extract clinical data for cSLE patients, including history of NPSLE diagnosis and SLEDAI scores. Deep learning models consisted of a 3D image feature extractor and a linear prediction layer. The data was split into 70% for training, 15% for validation, and 15% for testing. Learning was performed on the training set. We used classification performance, measured via the ROC AUC score, on the validation set to find the best model configuration.

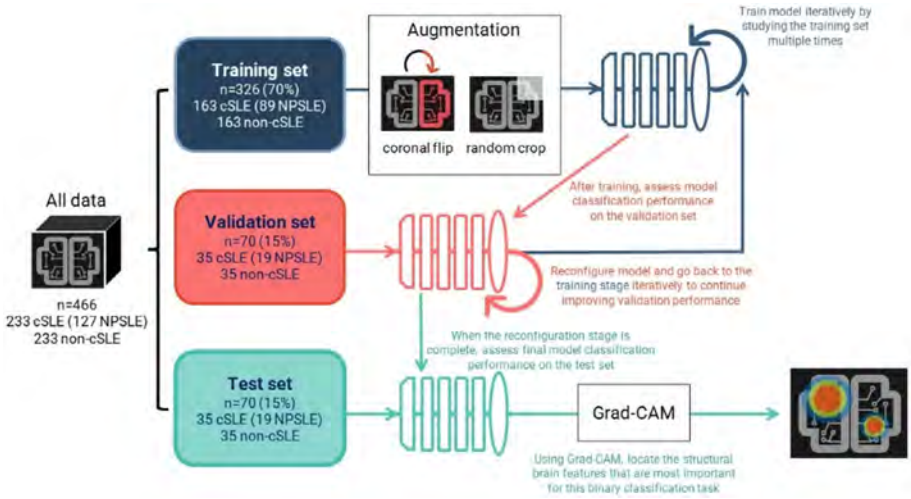

Figure 1. Methods summary for model training, configuration, evaluation, and interpretation. Grad-CAM stands for Gradient-weighted Class Activation Maps, a technique commonly used to interpret computer vision models.

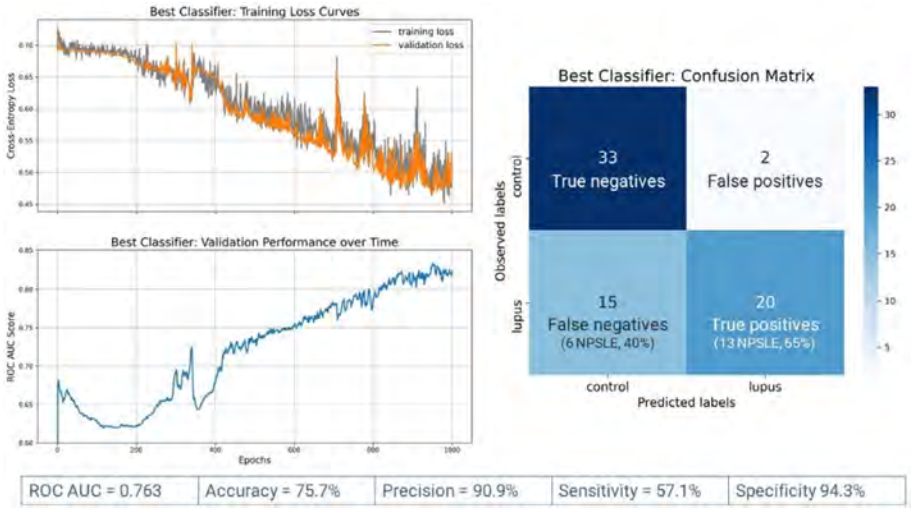

Figure 2. Learning behaviour and final classification performance of the best model. The left panel illustrates normal learning behaviour through decreasing loss curves and increasing performance over time. The right panel contains a confusion matrix illustrating the classification performance of the model on a held-out test set at an optimal classification threshold of 0.60. The bottom table summarises final model performance through 5 different classification metrics.

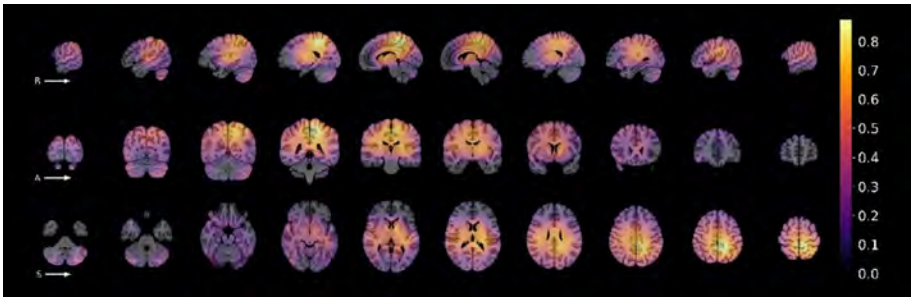

Figure 3. A standard MNI brain overlaid with the average class activation map for the correctly classified cSLE test samples (n=20). Yellow and orange colours highlight image features of the brain that were consistently used to correctly classify samples as cSLE. The top row shows sagittal slices (left -> right); middle row shows coronal slices (anterior -> posterior), and bottom row shows axial slices (inferior -> superior).

Using the test set and the best model configuration, we assessed final model performance (Fig. 1). Interpretability analyses allowed for the identification of brain image features that were most informative for this binary classification task.

Results: Of all 233 cSLE images (133 patients), 127 (55%) were obtained from 57 patients with NPSLE. Most cSLE patients had mild/moderate disease activity at the time of scan (SLEDAI < = 10, n=153, 69.96%). When distinguishing cSLE vs non-cSLE, we achieved acceptable final classification performance with ROC AUC score = 0.763. From the 70 test samples (35 cSLE, 35 control), 20/35 of cSLE were correctly classified (true positives) (Fig. 2). The proportion of NPSLE samples in the true positives was 65%, and that in the false negatives, 40%. The difference between these proportions was not significant (z-score=1.47, p=0.07). The most important brain image features for this classification task were found in intra-ventricular, peri-ventricular, and left medial parietal regions.

Conclusion: The resulting model was effective in capturing structural brain MRI features distinguishing cSLE, with and without NPSLE, from non-cSLE patients. Our findings suggest the presence of regional brain abnormalities in cSLE patients without an NPSLE diagnosis. This model may serve as a novel diagnostic tool prototype, and as a hypothesis generating tool in future NPSLE biomarker research. Further study is needed to characterise brain image features for each type of NP manifestation observed in cSLE.

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Abstract Number: 1626

Clinical Presentation, Disease Course and 12-month Outcomes in Childhood Polyarteritis Nodosa: A PedVas Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Pediatric Rheumatology – Clinical II: Connective Tissue Disease

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Childhood polyarteritis nodosa (PAN) is a systemic vasculitis with necrotizing inflammation that typically affects small and medium-sized arteries. The clinical presentation is variable; it can either be cutaneous or systemic and can present with mild predominantly skin disease versus severe disease with multi-organ involvement. Since it is rare in children, the data are limited. The aims of this study are to characterize the clinical presentation, disease course and outcomes in childhood polyarthritis nodosa in an international cohort.

Table 1. Presenting clinical features in the 55 patients with PAN

Presenting features	No. (%) of patients (n= 55)
Mucocutaneous involvement	47 (85)
Livedo Reticularis	21 (38)
Polymorphous exanthema	7 (13)
Panniculitis	10 (18)
Purpura	23 (42)
Skin nodules	32 (58)
Nail edge lesion	0 (0)
Splinter hemorrhage	6 (11)
Skin ulcers	3 (5.5)
Gangrene	2 (3.6)
Skin vasculitis	0 (0)
Mouth ulcers/ granulomata	7 (13)
Genital ulcers	0 (0)
Constitutional	39 (71)
Arthralgia	34 (62)
Fever	22 (40)
Weight loss > 5% of body weight	21 (38)
Myalgia	19 (35)
Renal involvement	16 (29)
Proteinuria (>0.3 g/24h)	4 (7.3)
>20mg/mmol Creatinine	6 (11)
Haematuria >= 2+ or 5 RBC/HPF or Red cells casts	8 (15)
GFR 50-80ml/min/1.73 m2	3 (5.5)
GFR 15-49 ml/min/1.73 m2	0 (0)
GFR < 15 ml/min/1.73m2	1 (1.8)
Rise in creatinine > 10% or Creatinine Clearance (GFR) fall > 25%	1 (1.8)
Neurological involvement	15 (27.3)
Headache	9 (16)
Meningitis/ encephalitis	0 (0)
Organic confusion/cognitive dysfunction	0 (0)
Seizures	1 (1.8)
Stroke	4 (7.3)
Cord lesion	0 (0)
Cranial nerve palsy	1 (1.8)
Sensory peripheral neuropathy	2 (3.6)
Motor mononeuritis multiplex	3 (5.5)
Gastrointestinal involvement	15 (27.3)
Abdominal pain	18 (33)
Peritonitis	0 (0)
Bloody diarrhea or blood in stools	0 (0)
Bowel ischemia	4 (73)
ENT involvement	5 (9)
Cardiac involvement	3 (5.5)
Pulmonary involvement	1 (1.8)

Methods: A multicenter ambispective study was conducted of children diagnosed with polyarteritis nodosa (PAN) using data collected in PedVas. PedVas is a multi-center, international study that is currently collecting clinical and biological data from children with chronic vasculitis. Eligible patients had an MD diagnosis of PAN and were < 18 years of age at time of diagnosis (TOD). Both systemic and cutaneous PAN subtypes were included. The primary outcome was the rate of inactive disease (Pediatric Vasculitis Activity Score [PVAS] of < =1) at 12 months. Secondary outcomes included rates of inactive disease at post induction (4–6 months after diagnosis), improvement rate in the PVAS at post induction (defined as a 50% reduction in PVAS), presence of damage at 12 months (measured by the Pediatric Vasculitis Damage Index [PVDI]) and relapse rates post induction.

Results: 55 children with PAN were included in the study; 19 were male, and the median age was 11 years (IQR 7-14.5). 25 of these patients were diagnosed as cutaneous PAN. 18 (33%) were Caucasian, 11 (20%) were East Asian, and 8 (14.5%) were South Asian. The most common presenting features were: mucocutaneous disease (85%), constitutional symptoms (71%), renal involvement (29%), gastrointestinal involvement (27.3%) and neurological involvement (27.3%). See Table 1. Corticosteroids were used in (80%) and cyclophosphamide in (26%). Other less frequently used agents included IVIG, methotrexate, azathioprine, other DMARDs, and biologic agents. An improvement in the PVAS score of more than 50% from TOD to post induction was seen in 79% of systemic PAN patients, and in 72% of cutaneous PAN. Rates of inactive disease at post induction and at 12 months in cutaneous PAN were 72%, and 74% respectively, and in systemic PAN were 63% and 67%, respectively. Relapses occurred in 2 (5%) of 39 patients after inactive disease had been achieved post-induction. 40 patients had completed PVDI scores at 12-months. The median PVDI score at 12 months was 0 in both cutaneous and systemic subgroups. 26 out of 40 patients (65%) had a PVDI score of 0, 14 (35%) had a PVDI score of 1 or more. There were no deaths.

Conclusion: This study describes the clinical course and outcomes of one of the largest cohorts of childhood PAN to date. The results show that the majority of patients have a reduction in disease activity by post-induction, and at least two-thirds of patients achieved inactive disease by 12-months. Disease relapse was rare in our cohort; however, one-third of patients have evidence of damage at 12-months. Further studies to evaluate predictors of treatment response and damage will help inform prognosis and guide treatment.

Disclosure: S. Alzaabi: None; **E. Bosman**: None; **D. Cabral**: None; **K. Morishita**: None; **P. Investigators Network**: None.

Abstract Number: 1627

Methotrexate Use Associates with Ischemic Cardiovascular Risk Reduction in Males but Not Females with Rheumatoid Arthritis

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Sciences (SGPGIMS), Lucknow, India, [17]The Dudley Group NHS Foundation Trust, Birmingham, United Kingdom, [18]Aarhus University Hospital, Aarhus, Denmark

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes II: Comorbidities
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Patients with rheumatoid arthritis (RA) experience higher cardiovascular risk compared to non-inflammatory disease controls. Methotrexate (MTX) may decrease cardiovascular risk in patients with RA. It is, however, unclear whether sex differentially impacts cardiovascular risk in MTX users and non-users and whether men and women derive equal benefit from methotrexate use. We here explored the influence of sex on cardiovascular risk in MTX nonusers and users. We further evaluated the effect of MTX treatment on cardiovascular risk in males and females with RA.

Methods: We evaluated 4362 patients and no cardiovascular disease prospectively included in an observational cohort [*A*n I*nternationa*l *C*ardiovascular *C*onsortium for people with *RA* (ATACC-RA)]. Outcomes were (a) major adverse cardiovascular events (MACE) defined as cardiovascular death, non-fatal myocardial infarction or stroke and (b) any ischemic cardiovascular events (CVE) including MACE, stable angina, coronary revascularization, transient ischemic attack and peripheral arterial disease with or without revascularization. Missing data were imputed using multiple imputation with 10 repetitions. Multivariable Cox models stratified by center evaluated the impact of sex, baseline MTX use and their interaction on event risk after adjusting for age, hypertension, diabetes, family history, smoking, total cholesterol to high-density lipoprotein cholesterol ratio, disease duration, and activity score (DAS28 ESR). Two sensitivity analyses were conducted; The first used inverse probability of treatment weights to balance differences in MTX treated and untreated patients. The second included patients enrolled in the cohort on or after January 1, 2000, when MTX use became more prevalent.

Figure 1 Impact of sex in methotrexate nonusers and users and effect of methotrexate treatment for females and males

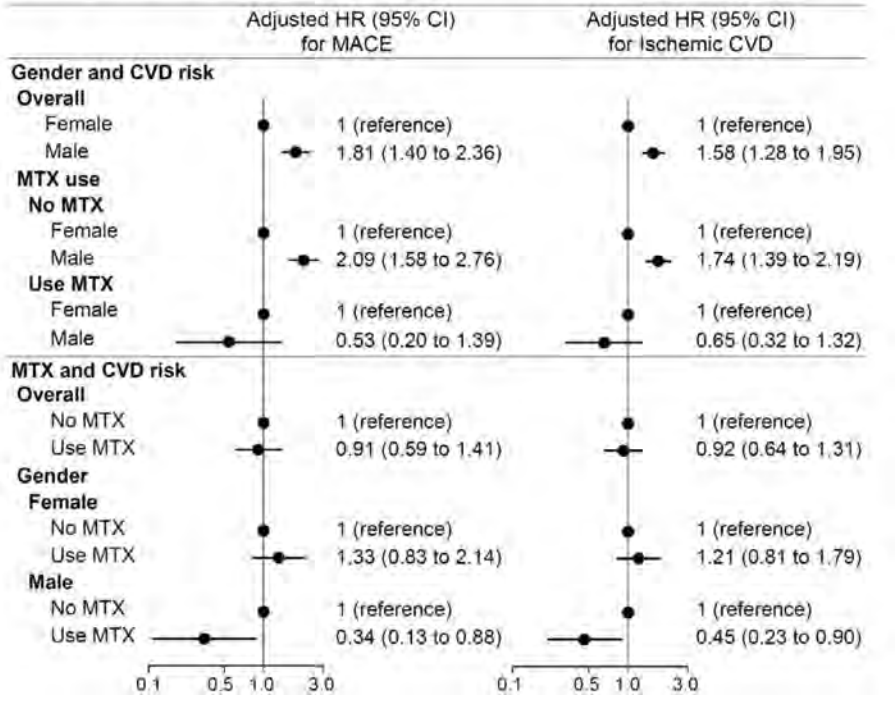
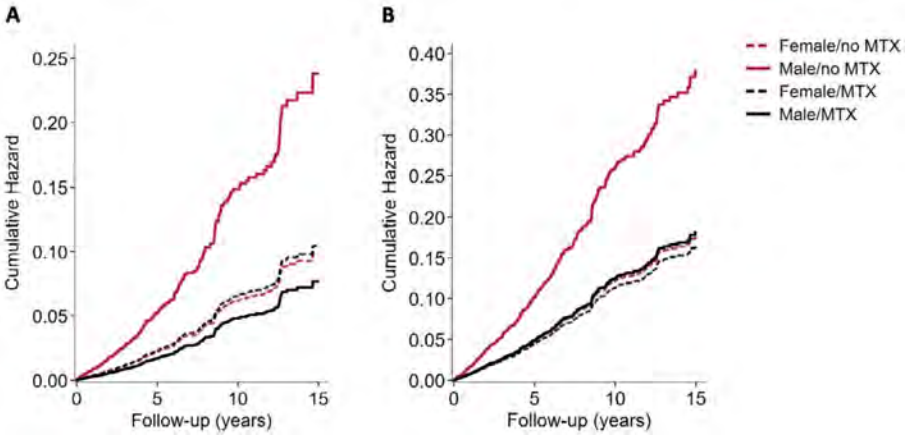


Figure 2 Risk of (A) MACE or (B) any ischemic cardiovascular event in males and females who use or do not use methotrexate



Results: There were 237 first MACE and 358 total ischemic CVE during follow-up. Male sex associated with an 81% and 58% greater risk of MACE and any ischemic CVE respectively (Figure 1). Among MTX nonusers, incidence of MACE and any ischemic CVE was higher in males [17.6 (95% CI 14.4-21.3) and 24.5 (20.7-28.9) events/1000PY] compared to females [6.9 (5.7-8.4) and 11.4 (9.8-13.3) events/1000PY, all p for difference < 0.001]. In adjusted Cox models, male nonusers had a 2.09-fold and 74% higher risk of MACE and any ischemic CVE compared to female nonusers (both p< 0.001, Figures 1 and 2). In contrast, among users, incidence of MACE and any ischemic CVE was not different in males [4.2 (1.7-10.0) and 7.6 (4.0-14.6) events/1000PY] versus females [6.4 (4.4-9.2) and 9.4 (6.9-12.8) events/1000PY] and sex was not associated with event risk in MTX users. Among males, MTX use associated with a 66% and 55% lower risk of MACE and any ischemic CVE (p=0.026 and 0.024). In contrast, MTX use was not associated with MACE or any ischemic CVE in females [adjusted HR 1.33 (0.83-2.14) and 1.21 (0.81-1.79)]. Both sensitivity analyses yielded similar results.

Conclusion: RA males not using MTX exhibit higher risk of MACE and any ischemic CVE compared to female nonusers, while no differences were observed between male and female users. Baseline MTX use associated with lower risk of MACE and all ischemic CVE in males but not females.

Disclosure: G. Karpouzas: Janssen, 1, Pfizer, 5, Scipher, 1; **S. Ormseth**: None; **P. Van Riel**: None; **E. Myasoedova**: None; **M. Gonzalez-Gay**: AbbVie/Abbott, 5, 6, Amgen, 5, 6, Pfizer, 5, 6; **A. Corrales**: None; **S. Rantapää-Dahlqvist**: None; **P. Sfikakis**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Boehringer-Ingelheim, 2, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5; **P. Dessein**: None; **L. Tsang**: None; **C. Hitchon**: Astra Zeneca, 1, Pfizer, 5; **H. El Gabalawi**: None; **V. Pascual Ramos**: None; **I. Contreras Yañez**: None; **I. Colunga**: None; **D. Galarza-Delgado**: None; **J. Azpiri-López**: None; **S. Rolefstad**: None; **A. Semb**: None; **D. Misra**: None; **G. KITAS**: None; **E. Hauge**: AbbVie/Abbott, 5, 6, Galapagos, 5, Novartis, 6, Novo Nordic Foundation, 5, 6, Sanofi, 6, Sobi, 6.

Abstract Number: 1628

The Impact of Cardiovascular and Cerebrovascular Disease on the Risk of Dementia in Rheumatoid Arthritis. a Mediation Analysis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes II: Comorbidities
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Alzheimer's disease and related dementias have an immense disease burden, with predicted continuous increase in incidence and prevalence. Systemic inflammation plays a major role in dementia, as well as in cardiovascular and cerebrovascular disease (CVD). Both RA and CVD have been reported to independently increase the risk of dementia, but little is known on the interplay between them on cognitive decline.

Methods: In this retrospective population-based study, patients with incident RA after age 50 who met 1987 classification criteria between 1980-2014, with no previous diagnosis of dementia prior to index date were included. RA cases were matched 1:1 with non-RA controls on age, sex and calendar year of index.

Data on CVD risk factors (i.e., hypertension, diabetes mellitus, hyperlipidemia, body mass index [BMI]) and CVD were abstracted from the medical records at baseline and throughout the follow-up. CVD was defined as coronary heart disease (including angina pectoris, coronary artery disease, myocardial infarction, coronary revascularization procedures), heart failure, cerebrovascular accident or transient ischemic attack. Dementia was defined as two relevant ICD-9/ICD-10 codes at least 30 days apart. Mediation analysis was carried out with RA as the exposure, CVD as a mediator, and dementia as the outcome. Models for both baseline mediation and time-dependent mediation were constructed.

Cox proportional-hazards models were used to estimate the adjusted hazard ratio (aHR) between RA and CVD along with the direct association between RA and dementia, with age, sex, education, hypertension, hyperlipidemia, and diabetes as covariates.

Results: 1,754 patients were included (877 RA cases and 877 non-RA controls). Mean age at index date was 64.7 years, with 65% females in both groups. At baseline, hypertension, hyperlipidemia, and diabetes were more prevalent in the RA cohort, with mean BMI similar in both cohorts. Prevalence of any CVD at baseline was not significantly different between the two groups (20.3% in RA vs 21.4% in non-RA, p=0.56). Mediation analysis with CVD at baseline as the mediator showed no significant mediated effect between the two cohorts.

During follow-up, 139 patients with RA and 125 individuals without RA developed dementia and 444 and 375, respectively, had any CVD. There was a significant association between RA and dementia both without (aHR 1.35, 95% CI 1.05-1.75) and with (aHR 1.33, 95% CI 1.04-1.72) CVD as a time-dependent mediator. There was a significant association between CVD on follow-up (aHR 2.02, 95% CI 1.53-2.67) with dementia risk. Yet, the mediation effect of any CVD on dementia was non-significant (p=0.69). There was a significant interaction between RA and CVD during the follow-up on dementia (aHR 1.89, 95% CI 1.12, 3.21; p=0.017).

Conclusion: Patients with RA are at a 35% increased risk of dementia, rising to 89% for patients who have both RA and CVD. We found no significant evidence that CVD acts as a mediator for the risk of dementia in RA. Yet, there is a significant synergistic effect of RA and CVD on dementia risk. This re-enforces the need for robust CVD prevention and dementia screening, along with optimization of disease activity in individuals with RA.

Disclosure: E. Lovering: None; **C. Kodishala**: None; **R. Kumar**: None; **C. Crowson**: None; **R. Lennon**: None; **J. Davis**: Girihlet, 9, Pfizer, 5, Remission Medical, 9; **E. Myasoedova**: None.

Abstract Number: 1629

Persons with Rheumatoid Arthritis and Long COVID Had Worse Pre-COVID RA Symptoms and Worse Non-RA Symptoms, as Well as Higher Rates of Fibromyalgia Compared with COVID Infected Long COVID Negative

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes II: Comorbidities
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Long COVID, also known as Post COVID syndrome or postacute sequelae of SARS-CoV-2 infection, refers to the development of persistent or new symptoms lasting for weeks or longer in individuals who have recovered from SARS-CoV-2 infection. Symptoms include breathlessness, cough, chest tightness, palpitations, fatigue, myalgia, and difficulty concentrating. Estimates of 30% who contracted COVID-19 may experience Long COVID and 10% remain positive after 6 months post infection. Recent studies showed increased odds of Long COVID in RA though uncertainty remains on whether this was due to a direct response to infection or the natural RA symptom course. We set out to examine if characteristics and symptoms of those receiving Long COVID diagnosis appeared before COVID infection.

Methods: Data are from the FORWARD, The National Databank for Rheumatic Diseases, through comprehensive questionnaires collected from participants with physician-diagnosed RA and self-reported COVID infections at 6-month intervals through April 2023. Study inclusion required a response to the following Long COVID item: "Have you EVER been told by a healthcare provider that you have Long COVID?" first available July 2022. Baseline was defined as the survey closest to and before initial COVID infection or initial Long COVID if no prior COVID infection was reported. Respondents provided health information including socioeconomic status, treatments, symptoms, hospitalizations, and several PROs including HAQ, Fatigue, Pain, Sleep Problem, Health Satisfaction, PHQ-8 (depressive symptoms), GAD2 (anxiety symptoms), WPI, SSS, and fibromyalgia 2016 criteria. Descriptive analyses examined PROs at baseline according to future Long COVID status. A Lasso approach was used for variable selection in a multivariate logistic model with Long COVID as the outcome (presented using OR 95%CI).

Results: There were 667 participants with RA, COVID infection, and who responded to the Long COVID item with 15% Long COVID positive. Those with Long COVID were older, less likely to be white, lower socioeconomic status, had more comorbidities, had worse RA PROs, more depression, more likely to meet fibromyalgia 2016 criteria, yet had no differences in DMARD use (Table 1). Fibromyalgia was ~3 times more common among those who would report Long COVID (13 vs 41%). Long COVID+ had more severe COVID infections with greater use of IV antibiotics (23% vs 9%) and hospitalizations for COVID (18 vs 5%). Multivariable logistic model had ten items after Lasso selection with several overlapping patient reported outcomes around pain and symptoms (Table 2).

Conclusion: Persons with RA who reported Long COVID in the past year had many symptoms of Long COVID prior to the development of a COVID infection. They had increases in many variables associated with RA severity and psychosocial distress. A Long COVID diagnosis may reflect preexisting illness, which may not be possible to separate. Our observations are limited by self-report and by not having official criteria for Long COVID diagnosis for healthcare providers. Future work will

Table 1

Table 1. RA participant characteristics and PROs at baseline, the observation before COVID infection, by future Long COVID status.

Variable	Long COVID– 85.5% (n=570)	Long COVID+ 14.5% (n=97)	p-value
Time before Long COVID item, yrs	1.65 (0.72)	1.40 (0.93)	0.014
Age, years	65.4 (11.3)	68.2 (12.4)	0.026
Male sex	12.8 (73)	10.3 (10)	0.491
White, non-Hispanic	94.7 (540)	88.7 (86)	0.021
Education level, years	14.9 (2.3)	14.1 (2.6)	0.003
Employed	38.6 (220)	26.8 (26)	0.026
General health characteristics			
RD Comorbidity Index (0-9)	1.7 (1.6)	2.6 (1.8)	0.000
Depression diagnosis	14.4 (81)	25.3 (24)	0.007
BMI, kg/m^2	28.3 (7.0)	29.4 (6.7)	0.160
Ever smoked	32.6 (186)	33.0 (32)	0.945
RA characteristics			
RA duration, years	25.3 (13.0)	26.0 (14.6)	0.615
Glucocorticoid use	21.6 (123)	19.6 (19)	0.652
csDMARD use	61.9 (353)	62.9 (61)	0.858
Biologic use	53.9 (307)	47.4 (46)	0.240
Patient-Reported Outcomes (PROs)			
Patient global assessment (0-10)	3.0 (2.3)	4.5 (2.4)	0.000
PAS (0-10)	3.1 (2.0)	4.5 (2.1)	0.000
HAQ (0-3)	0.94 (0.70)	1.17 (0.65)	0.002
Fatigue (0-10)	3.7 (2.9)	5.2 (3.0)	0.000
Pain (0-10)	3.0 (2.5)	5.0 (2.7)	0.000
Sleep disturbance (0-10)	3.3 (2.9)	4.0 (3.2)	0.028
Health satisfaction (0-5)	1.5 (1.2)	2.0 (1.2)	0.000
Fibromyalgia 2016 criteria	12.8 (54)	41.1 (23)	0.000
Polysymptomatic distress (PSD, 0-29)	8.2 (5.9)	13.4 (7.4)	0.000
Symptom severity scale (SSS, 0-12)	3.5 (2.5)	5.1 (2.8)	0.000
Widespread Pain Index (WPI, 0-19)	4.8 (4.4)	8.5 (5.8)	0.000
PHQ-8 (depression) (0-24)	3.9 (4.1)	6.8 (5.6)	0.000
GAD2 (anxiety) (0-6)	0.71 (1.31)	1.20 (1.40)	0.001

Values are % (n) or mean (SD)

examine how well recent criteria identify Long COVID in our cohort, including those without COVID, and rates of Long COVID diagnosis termination.

Table 2

Table 2. Multivariable Logistic Regression Model for Long COVID Outcome

Variable	OR	95% CI	p-value
Age, years	1.03	1.01, 1.06	0.010
White, non-Hispanic	0.32	0.12, 0.85	0.022
Ever smoked	0.64	0.35, 1.16	0.141
Glucocorticoid use	0.52	0.27, 1.02	0.058
Time before Long COVID item, yrs	0.67	0.42, 1.07	0.097
COVID infections, No.	0.33	0.18, 0.60	0.000
Pain (0-10)	1.20	1.06, 1.36	0.004
Widespread Pain Index (WPI, 0-19)	1.13	1.07, 1.20	0.000
Fibromyalgia 2016 criteria	1.40	0.51, 3.84	0.518
PHQ-8 (depression) (0-24)	2.56	1.19, 5.52	0.016

Disclosure: K. Michaud: None; **S. Pedro**: None; **S. Gandhi**: None; **F. Wolfe**: None.

Abstract Number: 1630

Patient-Reported Fatigue Associated with Joint Histopathology in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes II: Comorbidities

Session Type: Abstract Session

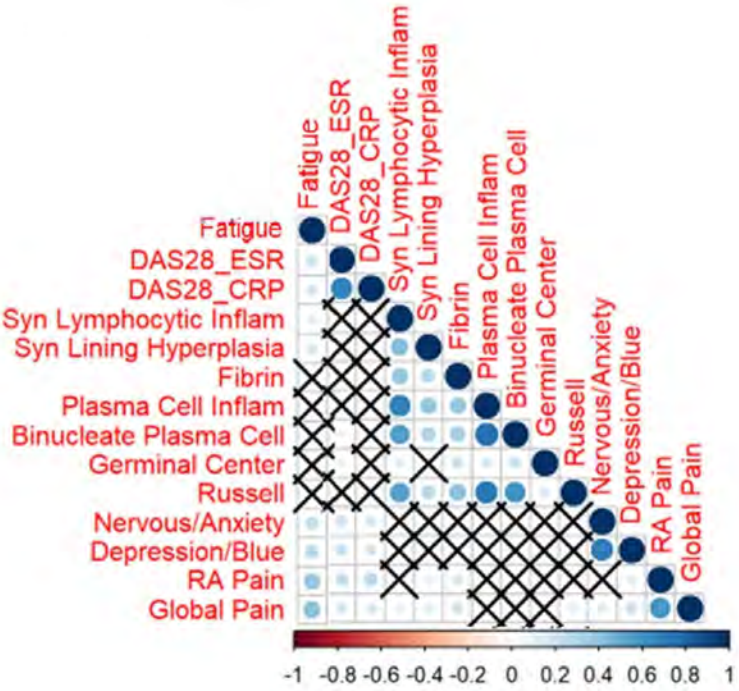
Session Time: 2:00PM–3:30PM

Background/Purpose: Fatigue or tiredness is an important symptom for patients with rheumatoid arthritis (RA), yet the factors associated with fatigue are poorly understood and may differ between patients with low vs. high disease activity. We sought to explore whether patient-reported fatigue is associated with histologic changes in the synovium in both low and high disease activity patients.

Table 1. Demographics and disease characteristics stratified by fatigue.

	Total (N=152)	Mild (N=43)	Moderate (N=60)	Severe (N=49)	p-value
Age[1]	62.70 (11.39)	65.80 [56.40, 71.50]	61.70 [53.60, 73.47]	63.50 [55.80, 68.00]	0.60
Sex, Female[2]	**131 (86.2)**	**33 (76.7)**	**51 (85.0)**	**47 (95.9)**	**0.03**
Race, Black[2]	35 (23.0)	10 (23.3)	11 (18.3)	14 (28.6)	0.45
BMI[1]	29.17 (7.19)	27.50 [23.30, 33.65]	28.05 [24.23, 32.82]	29.30 [23.70, 34.80]	0.58
Criteria[2]					0.07
Both	82 (53.9)	20 (46.5)	35 (58.3)	27 (55.1)	
1987	22 (14.5)	5 (11.6)	13 (21.7)	4 (8.2)	
2010	48 (31.6)	18 (41.9)	12 (20.0)	18 (36.7)	
DAS28[3]	**3.87 (1.30)**	**3.52 (1.48)**	**3.80 (1.21)**	**4.26 (1.17)**	**0.02**
ESR[1]	21.65 (18.59)	16.00 [8.50, 44.00]	13.00 [6.75, 28.25]	17.00 [9.00, 31.00]	0.30
CRP[1]	1.82 (2.75)	1.10 [0.00, 2.15]	1.20 [0.00, 2.40]	1.00 [0.00, 1.90]	0.92
RA Pain[1]	**5.84 (2.79)**	**4.00 [2.00, 6.00]**	**6.00 [4.00, 7.00]**	**8.00 [6.00, 9.00]**	**<0.0001**
Recent anxiety[1*]					**0.05**
0	66 (43.4)	25 (58.1)	27 (45.0)	14 (28.6)	
1	62 (40.8)	13 (30.2)	26 (43.3)	23 (46.9)	
2	22 (14.5)	4 (9.3)	7 (11.7)	11 (22.4)	
3	2 (1.3)	1 (2.3)	0 (0.0)	1 (2.0)	
Recent depression[1*]					**0.0014**
0	79 (52.0)	31 (72.1)	31 (51.7)	17 (34.7)	
1	63 (41.4)	9 (20.9)	28 (46.7)	26 (53.1)	
2	8 (5.3)	2 (4.7)	1 (1.7)	5 (10.2)	
3	2 (1.3)	1 (2.3)	0 (0.0)	1 (2.0)	
Synovial Lymphocytic Inflammation[2]					0.41
None	28 (18.4)	11 (25.6)	10 (16.7)	7 (14.3)	
Mild	48 (31.6)	16 (37.2)	20 (33.3)	12 (24.5)	
Moderate	32 (21.1)	6 (14.0)	11 (18.3)	15 (30.6)	
Marked	26 (17.1)	7 (16.3)	12 (20.0)	7 (14.3)	
Band-like	18 (11.8)	3 (7.0)	7 (11.7)	8 (16.3)	
Plasma Cell Inflammation[2]					0.26
<10%	92 (60.5)	29 (67.4)	35 (58.3)	28 (57.1)	
<50%	27 (17.8)	4 (9.3)	15 (25.0)	8 (16.3)	
>50%	33 (21.7)	10 (23.3)	10 (16.7)	13 (26.5)	
Synovial Lining Hyperplasia[2]					0.063
Normal	5 (3.3)	4 (9.3)	0 (0.0)	1 (2.0)	
1-3 cells	69 (45.4)	21 (48.8)	31 (51.7)	17 (34.7)	
3-4 cells	38 (25.0)	11 (25.6)	14 (23.3)	13 (26.5)	
>4 cells	40 (26.3)	7 (16.3)	15 (25.0)	18 (36.7)	
History of back pain[2]	**46 (30.3)**	**6 (14.0)**	**17 (28.3)**	**23 (46.9)**	**0.003**
History of fibromyalgia[2]	7 (4.6)	2 (4.7)	2 (3.3)	3 (6.1)	0.89

Figure 1. Correlation plot of patient fatigue with histological features, RA disease activity, and clinical characteristics.



Size/color of circle indicates strength of association between 2 variables using Kendall's tau, with significance set at P<0.1, otherwise "X" added

Table 2: Multivariable model predicting fatigue in patients with low or high disease activity using backwards stepwise selection to create the models.

Predicting Fatigue in patients with Low disease activity (DAS28 ≤ 3.2)			
Variable	Odds	Confidence Interval	P Value
Sex	**5.77**	**1.35, 29.27**	**0.017**
Synovial Lymphocytic Inflammation	**1.92**	**1.09, 3.57**	**0.024**
DAS28	**3.89**	**1.46, 11.96**	**0.006**
DAS28 = disease activity score in 28 joints Removed from the model as insignificant(P>0.1): recent anxiety, recent depression, synovial lining hyperplasia, RA pain			
Predicting Fatigue in Patients with High Disease Activity (DAS28 ≥ 3.2)			
Variable	Odds	Confidence Interval	P Value
Sex	**3.68**	**1.06, 13.63**	**0.04**
Anxiety/Nervousness	**2.08**	**1.26, 3.52**	**0.004**
Synovial Lining Hyperplasia	**1.57**	**1.01, 2.5**	**0.047**
DAS28 = disease activity score in 28 joints Removed from the model as insignificant (P>0.1): recent depression, synovial lymphocytic inflammation, RA pain			

Methods: 152 patients meeting ACR/EULAR 1987 and/or 2010 RA criteria were recruited prior to elective total joint replacement. At a pre-operative visit, patients were given questionnaires to assess global function and RA disease activity. Patient reported fatigue ("How much of a problem has unusual FATIGUE or TIREDNESS been for you in the PAST WEEK?") was rated by patients on a 0-10 scale and stratified into mild (0-3), moderate (4-7), or severe (8-10). Patients were also asked how they dealt with depression/feeling blue and nervousness/anxiety over the last week through the Multi-Dimensional Health Assessment Questionnaire (MDHAQ). Demographics, RA characteristics, tender and swollen joints to measure disease activity, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were collected. Hematoxylin and eosin (H&E) stains were prepared from the synovium of the operative joint and 10 characteristics were systematically scored by a pathologist as previously described. Relationships between patient fatigue and studied variables were measured with Kendall's Tau and compared in patients with high (DAS28$\geq$3.2) vs low (DAS28< 3.2) disease activity. Backward stepwise selection and multivariable ordered logistic regression were used to study the association of patient fatigue with other variables.

Results: Of the 152 patients in the study, 86.2% were women, with age 62.7 (±11.4) (mean±SD) years old, disease duration 14.75 (±12.4) years, and DAS28 3.87 (±1.30), indicating overall moderate disease activity. Among mild, moderate, and severe fatigue groups, there were no differences in comorbidities, such as history of diagnosed mental illness, anemia, fibromyalgia, thyroid disease, and cancer (Table 1). However, patients with higher fatigue reported higher recent anxiety and depression. Fatigue was correlated with DAS28, synovial lymphocytic inflammation (SLI), synovial lining hyperplasia, recent anxiety, recent depression, RA pain, and global pain (Figure 1). Of the patients with low disease activity, 46.5% had moderate, marked, or band-like SLI. In multivariable models, fatigue was significantly associated with SLI in low diseases activity patients (1.92[1.09,3.57]; p=0.024) but not with recent anxiety or depression. In high disease activity patients, fatigue was associated with anxiety and synovial lining hyperplasia (1.57[1.01,2.5]; p=0.047) but no other synovial histopathologic features.

Conclusion: In patients with low disease activity, fatigue is associated with chronic lymphocytic joint inflammation but not with anxiety or depression, suggesting an association with subclinical synovitis. In contrast, in RA patients with high disease activity, fatigue is associated with anxiety and synovial lining hyperplasia but not chronic lymphocytic inflammation.

1 = median(IQR); 2=n(%); 3=mean(SD) **Questions from the Multi-Dimensional Health Assessment Questionnaire: Over the last week, were you able to: Deal with feelings of anxiety or being nervous? Deal with feelings of depression or feeling blue? 0, Without any difficulty | 1, With some difficulty | 2, With much difficulty | 3, Unable to do BMI = body mass index; DAS28 = disease activity score using 28 joints; RF = rheumatoid factor; CCP = cyclic citrullinated protein; ESR=erythrocyte sedimentation rate; CRP=C Reactive Protein; Bolded values significant p<0.05

Disclosure: D. Fisher: None; **D. Orange**: AstraZeneca, 2, Pfizer, 2; **M. Smith**: None; **B. Mehta**: Janssen, 1, Novartis, 5; **E. Spolaore**: None; **E. DiCarlo**: None; **D. Sun**: None; **L. Donlin**: Bristol-Myers Squibb(BMS), 2, Stryker, 2; **S. Goodman**: NIH, 5, Novartis, 5.

Abstract Number: 1631

Comparison of Peripheral Biomarker Profiles Across Unique Multimorbidity Patterns in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes II: Comorbidities
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Rheumatoid arthritis (RA) predisposes affected individuals to develop multiple chronic conditions (i.e., multimorbidity). Mechanisms underlying multimorbidity onset in RA are incompletely understood, particularly for different multimorbidity patterns. We examined how peripheral biomarker profiles encompassing pro-inflammatory, autoantibody, tissue remodeling, and metabolic measures are associated with the clinical expression of distinct multimorbidity patterns.

Methods: From a multicenter, prospective cohort of U.S. Veterans with RA fulfilling ACR classification criteria (Veterans Affairs Rheumatoid Arthritis registry), we measured 61 peripheral biomarkers including 37 pro-inflammatory cytokines/chemokines, 4 matrix metalloproteinases, rheumatoid factor (RF), anti-CCP antibody, 12 antibodies to malondialdehyde-acetaldehyde (MAA), 3 adipokines, and 3 alarmins by the MesoScale platform, ELISA, or nephelometry on serum or plasma from registry enrollment. Principal component analysis (PCA) was performed to generate distinct biomarker profiles (PCs)

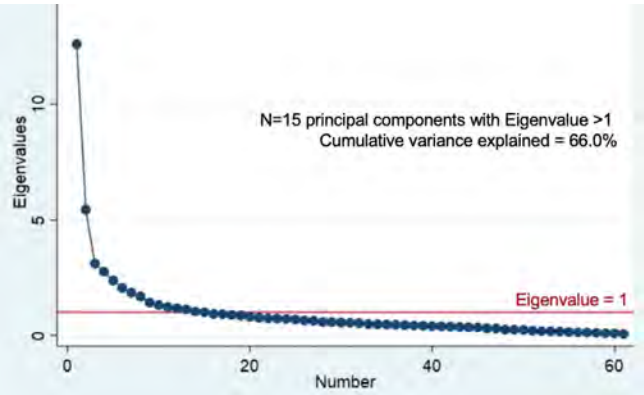

Figure 1. Scree plot from principal component analysis of 61 pro-inflammatory, autoantibody, tissue remodeling, and metabolic measures.

Table 1. Associations of peripheral biomarker profiles with multimorbidity patterns in rheumatoid arthritis. Values shown are odds ratios, with 95% confidence intervals, per 1-unit change in principal component (PC) score from logistic regression models adjusting for age, sex, race, and smoking status. Biomarkers listed are those with significant loadings (>0.3) onto the PC. P < 0.05 indicated in bold. Positive associations indicated in red and negative associations indicated in green with color gradient based on effect size.

		Multimorbidity Patterns			
	Biomarkers	Mental health & substance abuse	Metabolic	Cardiovascular	Chronic pain
PC1	IL-7, IL-16, IL-27, MCP1, MCP4, MDC, TARC	**0.95 (0.94, 0.96)**	**0.95 (0.94, 0.96)**	**0.98 (0.97, 0.99)**	**0.97 (0.96, 0.97)**
PC2	IL-1 alpha, IL-1 beta, IL-4, IL-6	**0.98 (0.97, 0.99)**	**0.98 (0.97, 0.99)**	**0.90 (0.88, 0.92)**	**0.97 (0.96, 0.98)**
PC3	IL-15, IL-3, IL-5, INF alfa-2a	1.00 (0.98, 1.02)	**1.03 (1.02, 1.05)**	**0.97 (0.94, 0.99)**	**1.10 (1.08, 1.12)**
PC4	anti-MAA albumin IgG, IgM, IgA	**0.94 (0.92, 0.95)**	**0.91 (0.89, 0.93)**	1.02 (0.99, 1.04)	**0.93 (0.92, 0.95)**
PC5	IL-12/IL-23p40, IL-17a	**1.05 (1.03, 1.08)**	**1.11 (1.09, 1.12)**	**1.20 (1.17, 1.23)**	**1.04 (1.02, 1.05)**
PC6	anti-CCP, RF	**0.86 (0.84, 0.88)**	**0.85 (0.83, 0.86)**	**0.88 (0.86, 0.91)**	**0.85 (0.83, 0.86)**
PC7	anti-MAA col, fib, and vim IgM; anti-MAA fib IgA	**1.05 (1.03, 1.07)**	**1.08 (1.06, 1.10)**	**1.09 (1.06, 1.12)**	**1.05 (1.03, 1.06)**
PC8	FGF-21, FLT3L, fractalkine, leptin	**1.26 (1.23, 1.29)**	**1.35 (1.31, 1.37)**	**1.35 (1.31, 1.39)**	**1.25 (1.23, 1.27)**
PC9	anti-MAA col, fib, and vim IgG	**1.06 (1.04, 1.09)**	**1.03 (1.01, 1.05)**	**1.04 (1.01, 1.07)**	**1.04 (1.02, 1.06)**
PC10	IL-17e, IL-25, TSLP	0.98 (0.96, 1.00)	**0.93 (0.91, 0.94)**	**0.88 (0.85, 0.91)**	**0.97 (0.96, 0.99)**
PC11	MMP3, MMP7	1.00 (0.98, 1.03)	1.01 (0.99, 1.03)	**1.42 (1.37, 1.46)**	**0.92 (0.91, 0.94)**
PC12	IL-8, MMP9	**1.05 (1.03, 1.08)**	**1.05 (1.03, 1.07)**	**1.05 (1.03, 1.08)**	**0.97 (0.95, 0.98)**
PC13	anti-MAA collagen IgG and IgA, adiponectin	0.99 (0.97, 1.01)	**1.09 (1.07, 1.11)**	0.99 (0.96, 1.02)	**1.03 (1.01, 1.05)**
PC14	IL-33	**0.97 (0.95, 0.99)**	**0.90 (0.88, 0.92)**	**1.03 (1.00, 1.07)**	**0.95 (0.93, 0.97)**
PC15	IL-23, anti-MAA vimentin IgA	1.01 (0.99, 1.04)	1.00 (0.98, 1.02)	**0.87 (0.85, 0.90)**	**0.97 (0.96, 0.99)**

from log-transformed and normalized analyte concentrations. The presence of forty-four pre-defined conditions at enrollment was determined using diagnostic codes from outpatient and inpatient encounters within linked administrative claims. Four previously developed multimorbidity patterns were then applied (mental health and substance abuse; metabolic; cardiovascular; chronic pain; England et al. Arthritis Care Res, 2023). Cross-sectional associations of PC scores with multimorbidity patterns were assessed using multivariable logistic regression models adjusting for age, sex, race, and smoking status.

Results: Among 2,007 participants with RA (89% male, mean age 64 years), 64% had metabolic, 47% had chronic pain, 21% had mental health and substance abuse, and 13% had cardiovascular multimorbidity. PCA identified15 unique peripheral biomarker PCs with Eigenvalues >1 that together explained 66% of the variance (Figure 1). PC8 scores, primarily characterized by adipokines (FGF-21, FLT3L, fractalkine, leptin), were positively associated with all multimorbidity patterns (aORs range: 1.25-1.35). In contrast, PC6 scores (anti-CCP and RF) were negatively associated with all multimorbidity patterns (aORs range: 0.85-0.88). Cardiovascular multimorbidity was positively associated with PC5 (IL12/IL-23p40, IL-17a) and PC11 (MMP3 and MMP7), but negatively associated with PC10 (IL-17e, IL-25, TSLP) and PC15 (IL-23, anti-MAA vimentin IgA). Several additional associations of smaller magnitude were observed between other PCs and multimorbidity patterns (Table 1).

Conclusion: Biomarker profiles consisting of cytokines/chemokines, MMPs, RA autoantibodies, adipokines, and alarmins were differentially associated with multimorbidity patterns in a large, RA cohort. These findings may indicate shared pathophysiologic mechanisms underlying multimorbidity in RA, such as obesity, metabolic dysfunction, and tissue remodeling. Further, they highlight pathways that could potentially be targeted to reduce multimorbidity burden or prevent its onset.

Disclosure: C. Peyton: None; **T. Johnson**: None; **J. Baker**: CorEvitas, 2, Cumberland Pharma, 2, Horizon Pharmaceuticals, 5; **Y. Yang**: None; **P. Roul**: None; **M. Duryee**: None; **J. Poole**: AstraZeneca, 12, I have received no monies. I received anti-IL-33 monoclonal antibody from AstraZeneca for animal research sutdies.; **G. Thiele**: None; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **B. England**: Boehringer-Ingelheim, 2, 5.

Abstract Number: 1632

Incident Malignancies in Patients with Rheumatoid Arthritis in Daily Rheumatological Care

Martin Schaefer[1], Yvette Meissner[1], Bernhard Manger[2], Sylvia Berger[3], Karin Rockwitz[4], Anne Regierer[5] and Anja Strangfeld[1], [1]German Rheumatism Research Center, Berlin, Germany, [2]Department of Internal Medicine 3, Friedrich-Alexander University (FAU) Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Germany, [3]Rheumatologist, Naunhof, Germany, [4]Rheumatologist, Goslar, Germany, [5]Deutsches Rheuma-Forschungszentrum Berlin, Berlin, Germany

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes II: Comorbidities

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: In 2021, the European and US-American regulatory agencies EMA and FDA issued warnings about malignancy risk associated with the Janus kinase inhibitor (JAKi) tofacitinib and required changes in labelling. These actions were based on results of the post-authorisation safety trial Oral Surveillance (OST)[1]. We aimed to analyse incident malignancies under treatment with JAKi, tumour necrosis factor inhibitors (TNFi), abatacept (ABA), rituximab (RTX), interleukin

6 inhibitors (IL6i) or conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs - bionaive) in patients with rheumatoid arthritis (RA) observed in daily rheumatological care.

Methods: Data from patients without cancer history enrolled in the biologics register RABBIT and initiating any DMARD treatment between 01/2017 - 04/2022 were included. Incidence rates (IR) of malignancies (without non melanoma skin cancer) per 1000 patient-years (PY) with 95% confidence intervals (CI) and adjusted hazard ratios (HR) were calculated for all and for selected patients according to OST inclusion criteria (age ≥ 50 years and ≥ 1 cardiovascular (CV) risk factor) to compare treatment groups to the reference (TNFi). Andersen-Gill regression analysis was used with a 6-months risk window, adjusted via stabilized and winsorized inverse probability of treatment weights taking into account age, sex, smoking, disease activity, prior therapies, comorbidities, and type of enrolling institution (clinic vs. private practice) as covariates. Multiple imputation of missing data was applied.

Results: 2763 JAKi, 3403 TNFi, 744 ABA, 834 RTX, 1125 IL6i and 1130 csDMARD initiations were documented. Patients with a JAKi start were less often men and (with exception of RTX) slightly older and had a longer RA disease duration (table). The proportion with positive autoantibodies and the number of previous treatments with biological (b) or targeted

Table: Patient characteristics at the start of a JAKi, TNFi, ABA, RTX, IL6i or csDMARD episode.

ALL PATIENTS	**JAKi** n=2763	**TNFi** n=3403	**ABA** n=744	**RTX** n=834	**IL6i** n=1125	**csDMARD** n=1130
Age	59.9	57.3	59.6	61.5	58.6	59.6
Men	24%	26%	25.	30%	25%	27%
Disease duration	12.5	9.4	12.0	15.6	11.1	5.9
Seropositivity	79%	74%	81%	92%	79%	67%
# previous b/tsDMARDs	2.7	1.0	2.7	5.1	2.5	0
DAS28-ESR	4.2	4.3	4.4	3.7	4.3	4.2
% of full physical function	65.2	69.3	63.0	64.4	65.5	72.8
# comorbidities	2.2	1.8	2.4	2.5	2.0	1.5
Current smokers	26%	26%	27%	22%	26%	30%
SELECTED PATIENTS*	**JAKi** n=1665	**TNFi** n=1810	**ABA** n=444	**RTX** n=490	**IL6i** n=623	**csDMARD** n=645
Age	64.5	63.7	64.9	66.0	63.5	64.7
Men	27%	30%	29%	36%	28%	30%
Disease duration	13.5	10.2	13.1	16.0	11.9	6.4
Seropositivity	79%	73%	81%	90%	78%	67%
# previous b/tsDMARDs	2.8	1.0	2.7	5.2	2.5	0
DAS28-ESR	4.3	4.5	4.5	3.8	4.4	4.3
% of full physical function	61.5	64.7	59.5	61.7	61.2	70.3
# comorbidities	3.0	2.6	3.2	3.4	2.9	2.2
Current smokers	34%	37%	35%	28%	35%	38%

*Values are given as mean or percentage. *Age ≥50 years and ≥ 1 CV risk factor (hypertension, coronary heart disease, diabetes, hyperlipoproteinaemia, current smoking)*

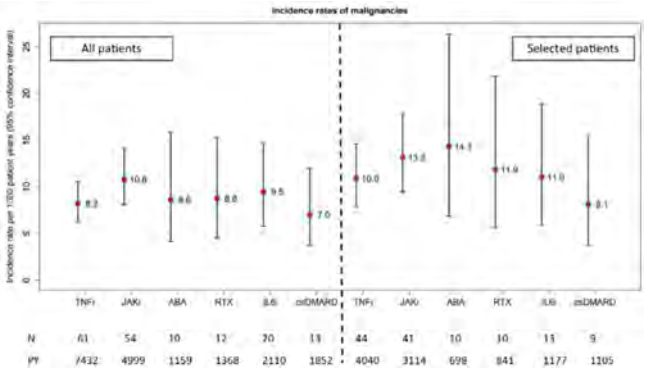

Figure: Incidence rates of malignancies (without non-melanoma skin cancer) per 1000 patient years by treatment group, for all patients (left) and selected patients only (right).

(ts) synthetic DMARDs was higher than in the TNFi and csDMARD group, but lower than in the ABA and RTX groups.

151 incident malignancies were reported. Across treatments, patients showed comparable IRs between 7 and 11 events per 1000 PY (10.8 events per 1000 PY in JAKi patients, 95% CI: 8.1 – 14.1, see figure). Among selected patients IRs were higher (13.2 events per 1000 PY in JAKi patients, 95% CI: 9.5 – 17.9). In adjusted analyses, neither JAKi (HR 1.07, 95% CI: 0.71 - 1.62), ABA (HR 0.73, 0.38 - 1.40), RTX (HR 0.86, 0.42 - 1.75), IL6i (HR 0.79, 0.44 - 1.40) nor csDMARDs (HR 2.07, 0.87 - 4.94) showed a significantly altered risk for malignancies compared with TNFi in unselected patients, with similar results in selected patients.

Conclusion: IR of malignancies in selected patients receiving JAKi in a real-world setting was numerically higher than the IR reported for tofacitinib in the Oral Surveillance study. However, we found no statistical evidence of an increased risk of malignancies with JAKi compared to TNFi, although patients on JAKi were older and had longer disease duration and more previous b/tsDMARDs treatments. Further analyses assessing exposure in terms of treatment duration are needed.

References:

[1] PMID: 35081280

Disclosure: M. Schaefer: None; **Y. Meissner**: Eli Lilly, 6, Pfizer, 6; **B. Manger**: AbbVie/Abbott, 6, Alexion, 6, Celgene, 6, Eli Lilly, 6, EUSA, 6, Gilead, 6, Janssen, 6, Merck/MSD, 6, Pfizer, 6, Roche, 6, Sanofi, 6; **S. Berger**: None; **K. Rockwitz**: None; **A. Regierer**: Novartis, 6, Pfizer, 6, Roche, 6; **A. Strangfeld**: AbbVie/Abbott, 6, Amgen, 6, Bristol-Myers Squibb(BMS), 6, Celltrion, 6, Eli Lilly, 6, Janssen, 6, Pfizer, 6, Roche, 6, Sanofi, 6, UCB, 6.

Abstract Number: 1633

Dose Dependent Modulation of a B Cell Protein Signature by Ianalumab in Patients with Sjögren's Disease

Stephanie Finzel[1], Andrea Grioni[2], Benjamin A Fisher[3], Athena S Papas[4], Alexandre Avrameas[2], Danny Tuckwell[2], Jonas Zierer[2], Celine Rauld[2], Valeria De Luca[2], Enrico Ferrero[2], Andre Nogueira da Costa[2], Rainer Hillenbrand[2], Isabelle Isnardi[2] and Wolfgang Hueber[2], [1]Department of Rheumatology and Clinical Immunology, University Medical Center Freiburg, University of Freiburg, Freiburg, Germany, [2]Novartis Pharma AG, Basel, Switzerland, [3]University of Birmingham, Birmingham, United Kingdom, [4]Division of Oral Medicine, Tufts School of Dental Medicine, Boston, MA

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Sjögren's Syndrome – Basic & Clinical Science
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Ianalumab (VAY736) is an afuscosylated monoclonal antibody targeting the B cell activating factor receptor (BAFFR) that depletes B cells via enhanced antibody dependent cellular cytotoxicity with concurrent blockade of BAFF:BAFFR mediated survival signals. Sjögren's disease (SjD) is an autoimmune disorder which primarily affects exocrine glands along with diverse systemic manifestations. It is characterized by elevated BAFF levels, hypergammaglobulinemia and autoantibodies to nuclear autoantigens. A phase 2b dose finding trial of ianalumab (NCT02962895) in 191 patients with active SjD met its primary endpoint, identifying 300 mg as the most clinically efficacious dose, despite a similar reduction in blood B cells as seen with 50 mg. We explored the changes in autoantibody and proteomic signatures of patients with SjD pre- and post-treatment with ianalumab to characterize pharmacodynamic and biological biomarkers associated with disease activity and clinical response.

Methods: Patients with active SjD (N=191) were randomly assigned 1:1:1:1 to receive placebo or one of three different doses of ianalumab (5 mg, 50 mg, or 300 mg). Serum samples were collected at baseline and Week 24. Serum protein profiling was performed using the SomaScan(R) v4.1 platform measuring >7000 aptamers. The interferon protein signature (IFNPS) was derived from the SomaScan data. Autoantibodies and BAFF levels were assessed by Luminex-based and ELISA assays. A linear mixed effect model was used to identify longitudinal changes in protein concentration at Week 24 versus baseline, and proteins with FDR < 0.05 and log fc >0.1 were selected for further analysis. Results were visualized using heatmaps and hierarchical clustering based on protein expression patterns.

Results: A cluster analysis performed on autoantibodies and proteins, including IFNPS at baseline did not reveal significant correlations between ESSDAI scores (including subdomains) and levels of autoantibodies or proteins of interest **(Fig 1)**. Administration of ianalumab led to marked changes in autoantibody and serum protein levels. The 300 mg dose group showed an increased number of significantly modulated serum proteins (42), versus the 5 mg (9) and 50 mg (20) dose groups, along with a more pronounced modulation of their expression **(Fig 2)**. Several B cell surface proteins were consistently downregulated by ianalumab, including F_CRL4, expressed by B cells hypothesized to be involved in the pathogenicity of SjD. The 50 mg and 300 mg doses induced the downregulation of additional proteins such as BCMA, specifically expressed by antibody producing cells, or the chemokines CXCL13 and CCL21, associated with immune infiltration of glandular tissues in patients with SjD. Although statistically non-significant, a downregulation of IFNPS was also seen with 50 mg and 300 mg doses.

Conclusion: No differential proteomic signatures related to baseline disease activity were identified. The dose response in clinical efficacy of ianalumab in treating patients with SjD as observed in the phase 2b trial is reflected at the protein level, with increased depth and breadth of proteomic changes by Week 24 correlating with increasing dose.

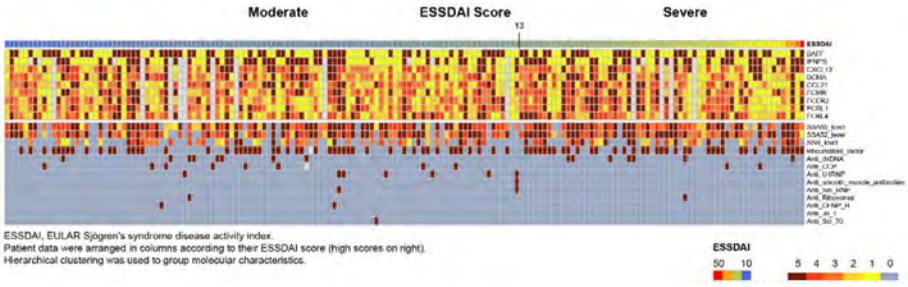

Fig 1. Baseline molecular characteristics of patients with Sjögren's disease

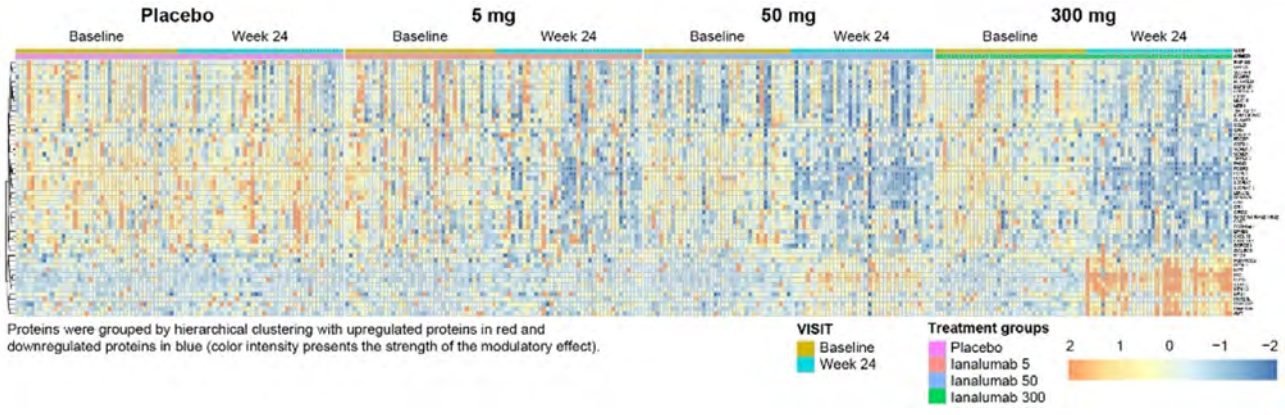

Fig 2. Heatmap illustrating the modulatory effect of ianalumab over time across different treatment groups

Disclosure: S. Finzel: AbbVie, 6, AstraZeneca, 2, 6, Chugai, 6, Galapagos, 2, 6, Novartis, 2, Novo Nordisk, 2, UCB, 6; **A. Grioni**: Novartis, 3, 11; **B. A Fisher**: Bristol-Myers Squibb(BMS), 2, Celgene, 5, Galapagos, 2, 5, Janssen, 2, 5, Novartis, 2, Roche, 2, Sanofi, 2, Servier, 2, 5, UCB, 2; **A. S Papas**: Novartis, 1, 5; **A. Avrameas**: Novartis, 3, 11; **D. Tuckwell**: Novartis, 3; **J. Zierer**: Novartis, 3, 11; **C. Rauld**: Novartis, 3, 11; **V. De Luca**: Novartis, 3, 11; **E. Ferrero**: Novartis, 3, 11; **A. Nogueira da Costa**: Novartis, 3, 11; **R. Hillenbrand**: Novartis, 3, 11; **I. Isnardi**: Novartis, 3, 11; **W. Hueber**: Novartis, 3, 11.

Abstract Number: 1634

Iscalimab (CFZ533) in Patients with Sjögren's Disease: Week 24 Efficacy and Safety Results of a Randomized, Placebo-controlled, Phase 2b Dose-ranging Study

Benjamin A Fisher[1], Xavier Mariette[2], Athena S Papas[3], Thomas Grader-Beck[4], Hendrika Bootsma[5], Wan-Fai Ng[6], Paul Van Daele[7], Stephanie Finzel[8], Sergio Elgueta[9], Josef Hermann[10], Sara McCoy[11], Arthur Bookman[12], Monika Sopala[13], Wen-Lin Luo[14], Cornelia Scheurer[13] and Wolfgang Hueber[13], [1]University of Birmingham, Birmingham, United Kingdom, [2]Université Paris-Saclay, Le Kremlin-Bicêtre, France, [3]Division of Oral Medicine, Tufts School of Dental Medicine, Boston, MA, [4]Division of Rheumatology, Johns Hopkins School of Medicine, Baltimore, MD, [5]Department of Rheumatology, University Medical Centre Groningen, Groningen, Netherlands, [6]NIHR Newcastle Clinical Research Facility, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, United Kingdom, [7]Department of internal medicine, Erasmus MC, Rotterdam, Netherlands, [8]Department of Rheumatology and Clinical Immunology, University Medical Center Freiburg, University of Freiburg, Freiburg, Germany, [9]Clinical Research Chile SpA, Biomedical Research Centre, Valdivia, Chile, [10]Division of Rheumatology and Immunology, Department of Internal Medicine, Medical University Graz, Graz, Austria, [11]University of Wisconsin School of Medicine and Public Health, Middleton, WI, [12]Toronto Western Hospital, Toronto, ON, Canada, [13]Novartis Pharma AG, Basel, Switzerland, [14]Novartis Pharmaceuticals Corporation, East Hanover, NJ

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Sjögren's Syndrome – Basic & Clinical Science

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Sjögren's disease (SjD) is an autoimmune disease affecting secretory glands and other organs with no approved systemic treatments. Iscalimab (CFZ533) is a mAb directed against CD40, a novel way to target underlying disease pathophysiology. TWINSS is an ongoing phase 2b dose-ranging trial assessing safety and efficacy of multiple CFZ533 doses in two distinct patient (pt) populations with SjD of moderate/severe systemic disease (Cohort 1/C1) and of low systemic disease and high symptom burden (Cohort 2/C2). We report Week 24 primary results from both cohorts (N=273).

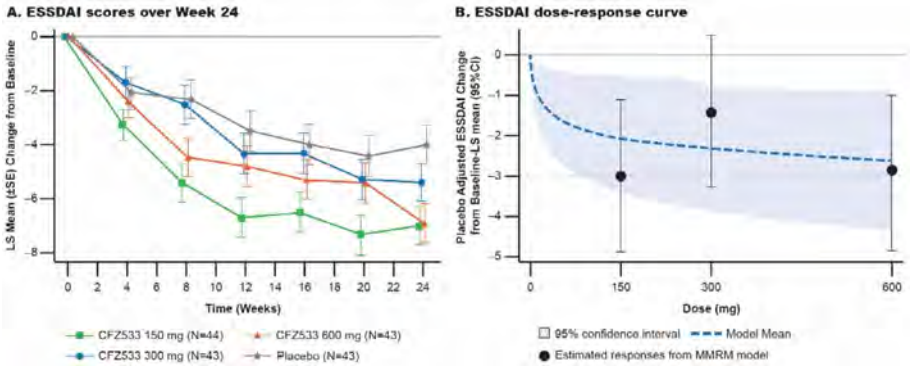

Figure 1: Least-square mean of change from baseline in ESSDAI scores over time up to Week 24 and estimated dose-response curve in Cohort 1

Methods: In C1, 173 pts were randomized (1:1:1:1) to CFZ533 150 mg or 300 mg or 600 mg s.c. q2w or placebo (PBO). In C2, 100 pts were assigned (1:1) to CFZ533 600 mg or PBO. Key inclusion criteria were: fulfilled ACR/EULAR 2016 classification criteria; stimulated salivary flow rates of ≥0.1 mL/min; anti-Ro/SSA positivity; **C1**: EULAR Sjögren's Syndrome (SS) Disease Activity Index (ESSDAI) ≥5 (on 8 selected domains), EULAR SS Patient Reported Index (ESSPRI) ≥5; and **C2**: ESSDAI < 5 with presence of activity in biologic domain (>0), ESSPRI (fatigue or dryness ≥5, impact of dry eye on everyday life [IDEEL] ≥30). Statistical methods included Multiple Comparison Procedure – Modelling methodology to assess the dose response of the ESSDAI change from baseline (C1) and mixed model for repeated measures to estimate the adjusted mean change from baseline and difference vs PBO (C1 and C2). Similar methods were applied to all other endpoints including ESSPRI.

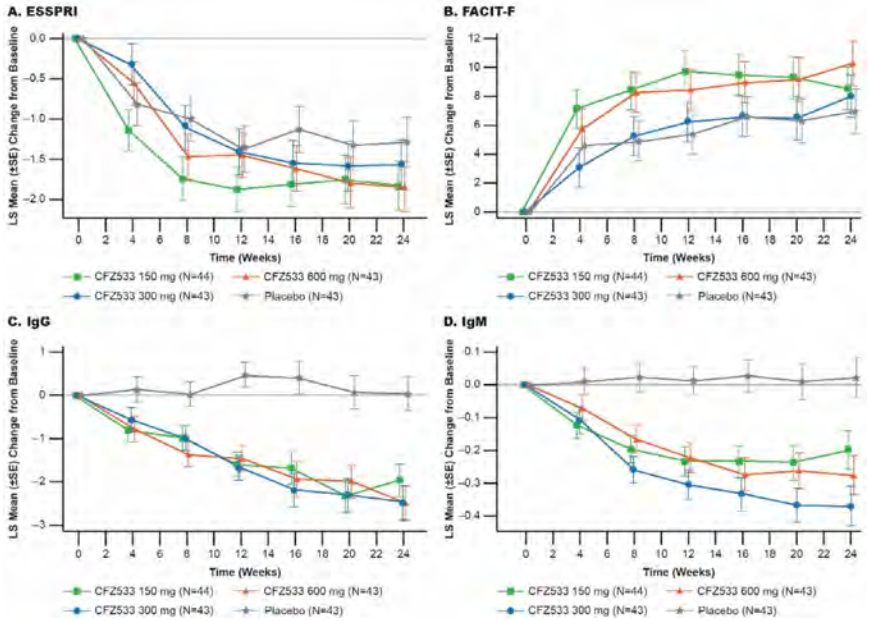

Figure 2: Least-square mean of change from baseline in patient-reported outcomes (secondary outcome measures) and pharmacodynamic markers up to Week 24 in Cohort 1

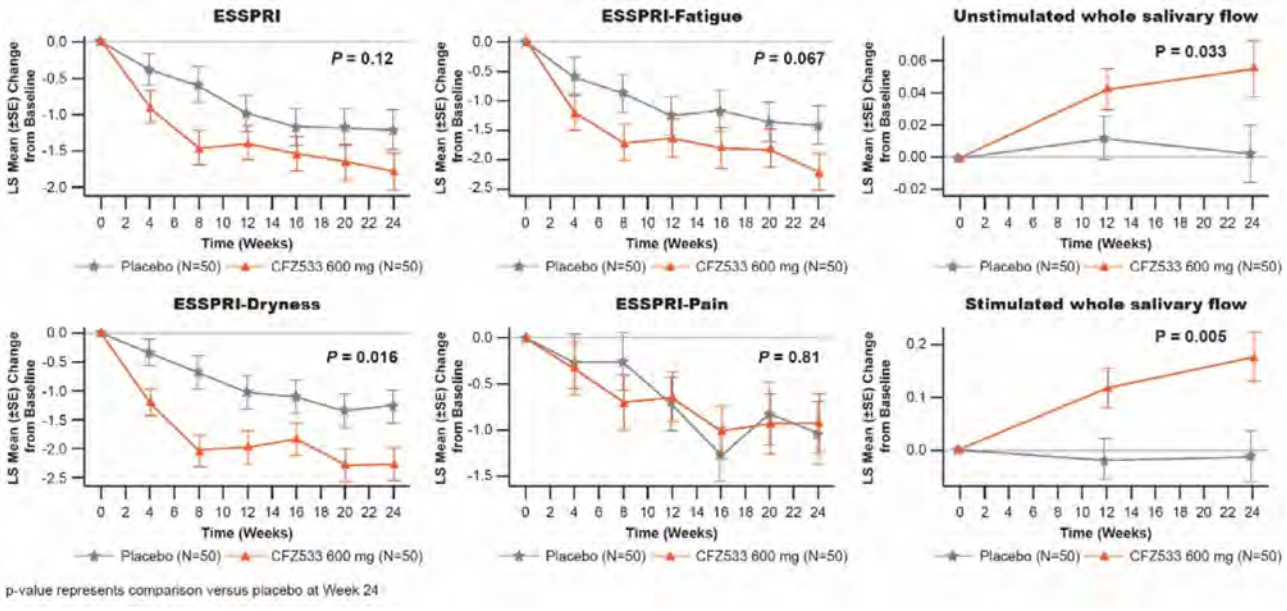

Figure 3. Least-square mean of change from baseline in ESSPRI and its subdomains and whole salivary flow up to Week 24 in Cohort 2

Results: Baseline characteristics were balanced across treatments except in C1 where more pts on iscalimab 300 mg had severe disease activity (ESSDAI >13; 44%) and used HCQ (70%), compared to the other treatment arms (ESSDAI >13, 19-28% and HCQ, 47-64%, respectively).

In **C1**, ESSDAI change from baseline at Week 24 showed statistically significant improvements compared to PBO for CFZ533 150 and 600 mg (least square mean difference (Δ) = –3.0 and –2.9; $p < 0.005$), and 300-mg dose showed a similar trend (Δ= –1.4; $p = 0.16$) (**Fig 1**). Primary objective of significant dose response of ESSDAI change from baseline at Week 24 ($p = 0.004$) with a log-linear dose-response was met. Predicted dose-response curve suggested that the drug effect plateaued at ≥150 mg. ESSPRI, FACIT-F **(Fig 2)**, tear flow, and salivary flow (SF) rates showed numerical trends for improvement with active treatment. By Week 24, IgG/IgM as objective pharmacodynamic markers showed significant and similar plateaus of reduction for all doses of CFZ533 compared to PBO. In **C2**, the primary objective of ESSPRI change from baseline showed a strong trend (Δ = –0.57; $p = 0.12$) toward improvement with dryness (Δ = –1.0; $p = 0.016$) and fatigue (Δ = –0.8; $p = 0.067$) as the response drivers **(Fig 3**). For exploratory outcomes, statistically significant increases in SF were seen.

At Week 24, SAE rates in **C1** (PBO, CFZ533 150 mg, 300 mg, 600 mg) were 2.3%, 2.3%, 7.1%, and 9.1%, respectively, in **C2** (PBO or CFZ533 600mg) 4% each. Infection rates in C1 were 39.5%, 45.5%, 26.2%, and 43.2%; and in C2 42.0% and 56.0%, respectively.

Conclusion: Iscalimab showed a clinically important improvement over placebo in 2 distinct populations of SjD patients and was well tolerated without obvious safety signals.

Disclosure: B. A Fisher: Bristol-Myers Squibb(BMS), 2, Celgene, 5, Galapagos, 2, 5, Janssen, 2, 5, Novartis, 2, Roche, 2, Sanofi, 2, Servier, 2, 5, UCB, 2; **X. Mariette**: AstraZeneca, 2, 6, BMS, 2, 6, Galapagos, 2, 6, GSK, 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **A. S Papas**: Novartis, 1, 5; **T. Grader-Beck**: IQVIA, 2, Novartis, 2; **H. Bootsma**: None; **W. Ng**: AbbVie, 12, Research Collaboration, Argenx, 2, GlaxoSmithKlein(GSK), 12, Research Collaboration, Janssen, 2, Novartis, 2, Resolve Therapeutics, 2, Sanofi, 2; **P. Van Daele**: None; **S. Finzel**: AbbVie, 6, AstraZeneca, 2, 6, Chugai, 6, Galapagos, 2, 6, Novartis, 2, Novo Nordisk, 2, UCB, 6; **S. Elgueta**: None; **J. Hermann**: None; **S. McCoy**: Bristol-Myers Squibb(BMS), 2, Horizon, 2, Kiniksa, 2, Novartis, 2, Otsuka/Visterra, 2, Target RWE, 2; **A. Bookman**: GlaxoSmithKline(GSK), 12, Regional Principal Investigator, Novartis, 12, Regional Principal Investigator, VIELA BIO, 12, Regional Principal Investigator; **M. Sopala**: Novartis, 3; **W. Luo**: Novartis, 3; **C. Scheurer**: Novartis, 3; **W. Hueber**: Novartis, 3, 11.

Abstract Number: 1635

Deep Learning Accurately Predicts Focus Score and Diagnosis of Primary Sjögren Syndrome Using Labial Salivary Gland Biopsies

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Sjögren's Syndrome – Basic & Clinical Science
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Primary Sjögren Syndrome (pSS) diagnosis relies on the weighted sum of three EULAR/ACR 2016 criteria: i) quantification of lymphocyte infiltration in labial salivary gland (LSG) biopsies, ii) autoantibody status and iii) objective quantification of eye and mouth dryness. Diagnosing pSS is highly challenging and the histological interpretation of LSG tissue requires specific expertise. It poses a challenge to non-specialized centers as highlighted by Vivino et al. [1] who show up to 53% of diagnosis reclassification after expert center rescoring. This analysis is critical and involves the determination of the focus score (FS), where a score ≥1 confirms the histological criteria for pSS. With mounting evidence underlining the potential of artificial intelligence in assisting pathologists, we aimed to develop two deep learning models using LSG biopsies only: one to automatically assess the FS (≥ 1 or < 1), and one to predict pSS diagnosis. Furthermore, we put effort in implementing explainable models highlighting the subregions of the biopsy leveraged for the prediction.

Methods: Deep learning models were developed using digitalized LSG slides from patients from three European expert centers taking part in the NECESSITY consortium, a European H2020 IMI2 project. Three patient groups were included: sicca patients with a FS < 1, pSS patients with a FS ≥ 1, and pSS patients with a FS < 1. All pSS diagnoses were confirmed by rheumatologists from expert centers and satisfied the EULAR/ACR 2016 classification criteria. Models were trained on 70% of the patients and validated on the remaining 30%. Algorithm performance was measured using the area under the receiver operating characteristic curve (AUROC), positive and negative predictive values (PPV and NPV), specificity and sensitivity. The models provide risk scores for each biopsy subregion, these scores explain how predictions of FS and pSS are computed.

Results: The dataset included a total of 325 patients: 145 from Paris-Saclay University (Bicêtre Hospital), 71 from Queen Mary University of London and 109 from the University of Birmingham. In the validation set, the model achieved an AUROC of 0.88 (95% CI 0.85 to 0.90) for binary assessment of the FS (≥ 1 or < 1); and 0.84 (95% CI 0.83 to 0.86) for predicting pSS

Table 1: Detailed performance results on the validation set of the models predicting the FS (≥ 1 or < 1) and pSS diagnosis (PPV: positive predictive value, NPV: negative predictive value, mean confidence interval (CI)).

Task	AUROC	PPV	NPV	Specificity	Sensitivity
FS≥1/<1 prediction	**0.88** (0.85, 0.90)	**0.77** (0.74, 0.80)	**0.83** (0.79, 0.87)	**0.79** (0.77, 0.82)	**0.81** (0.76,0.87)
pSS+/- prediction	**0.84** (0.83, 0.86)	**0.83** (0.81, 0.84)	**0.67** (0.63, 0.71)	**0.64** (0.60, 0.67)	**0.84** (0.81, 0.87)

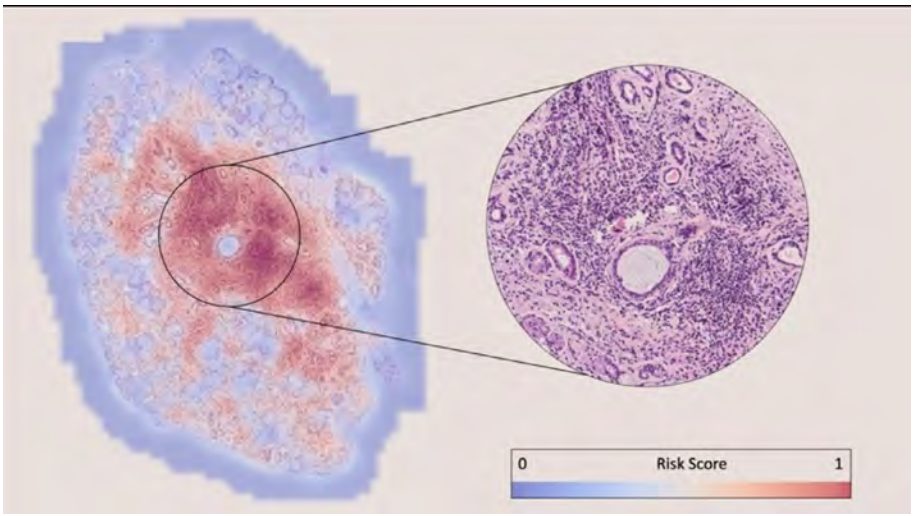


Figure 1: LSG biopsy with computed FS ≥ 1 probability (blue is low, red is high). Note that subregions with high-risk score (red; left) highlight lymphocytes aggregates (right).

diagnosis. Analysis of histological subregions selected by the model determining the FS unsurprisingly revealed regions with a high concentration of lymphocytes (Figure 1). Detailed performance results for both models are available in Table 1.

Conclusion: Deep learning can predict both the FS and pSS diagnosis with high accuracy using digitalized LSG slides only. The FS model could serve as a valuable tool to assist pathologists who may not specialize in oral pathology, reducing their reliance on reference centers. Furthermore, this study paves the way for a better understanding of pSS physiopathology: the determination of the regions selected by the algorithm for the diagnosis of pSS in FS negative patients is in progress, with up to now a highlight on lympho-epithelial lesions.

[1] Vivino FB et al. Change in final diagnosis on second evaluation of labial minor salivary gland biopsies. J Rheumatol. 2002 May;29(5):938-44. PMID: 12022353.

Disclosure: L. Basseto: None; **J. Duquesne**: None; **M. Barnes**: Servier, 2; **E. Pontarini**: None; **A. Gallagher-Syed**: None; **M. Bombardieri**: None; **B. A Fisher**: Bristol-Myers Squibb(BMS), 2, Celgene, 5, Galapagos, 2, 5, Janssen, 2, 5, Novartis, 2, Roche, 2, Sanofi, 2, Servier, 2, 5, UCB, 2; **S. Nayar**: None; **C. Adam**: None; **T. Lazure**: None; **X. Mariette**: AstraZeneca, 2, 6, BMS, 2, 6, Galapagos, 2, 6, GSK, 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **S. Bitoun**: None; **V. Bouget**: None.

Abstract Number: 1636

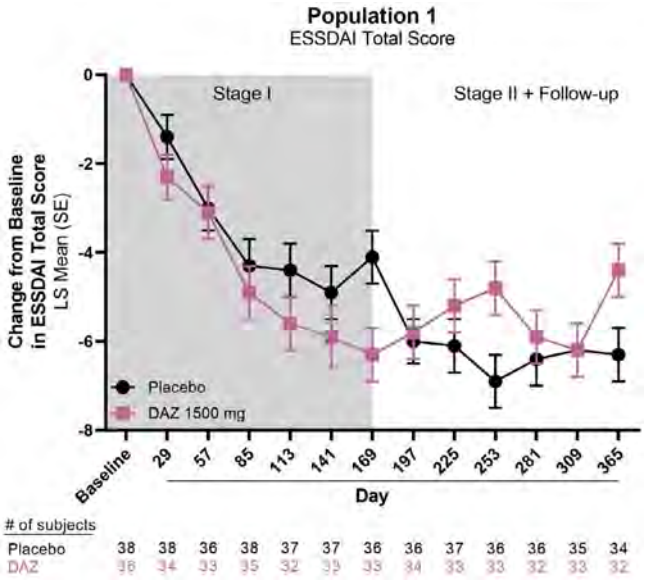
Dazodalibep, a CD40L Antagonist, in Subjects with Sjögren's Having Moderate-to-Severe Systemic Disease Activity: Full Crossover Results from a Phase 2, Randomized, Double-Blind, Placebo-Controlled, Proof of Concept Study

E. William St. Clair[1], Liangwei Wang[2], Ilias Alevizos[2], William A. Rees[2], Alan Baer[3], Wan-Fai Ng[4], Ghaith Noaiseh[5] and Chiara Baldini[6], [1]Duke University Medical Center, Durham, NC, [2]Horizon Therapeutics, Rockville, MD, [3]Johns Hopkins University School of Medicine, Baltimore, MD, [4]NIHR Newcastle Clinical Research Facility, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, United Kingdom, [5]University of Kansas Medical Center, Kansas City, KS, [6]University of Pisa, Pisa, Italy

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Sjögren's Syndrome – Basic & Clinical Science
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Dazodalibep (DAZ) is a non-antibody fusion protein that acts as a CD40L antagonist and blocks costimulatory signals between immune cells, including T cells, B cells, and antigen-presenting cells. Previously, we reported that the primary endpoint, the change from baseline to Day 169 in the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI), was achieved in the population of subjects with moderate-to-severe systemic disease activity (NCT04129164).[1] Here, we evaluated the efficacy and safety of DAZ therapy in this population through the crossover period of the study.

Methods: We performed a randomized, double-blind, placebo-controlled, crossover study to evaluate DAZ therapy in adult subjects with Sjögren's having moderate-to-severe systemic disease activity, as defined by an ESSDAI ≥ 5. Eligible subjects were randomized 1:1 to receive intravenous DAZ 1500 mg or PBO Q2W x 3 doses, and then Q4W x 4 additional doses (Stage I). Starting on Day 169, subjects initially randomized to DAZ transitioned to PBO Q4W x 5 doses (DAZ-PBO) and subjects randomized to PBO were switched to DAZ Q4W x 5 doses (PBO-DAZ); all were then followed for 12 weeks (Stage II).



Adjusted mean change from baseline in ESSDAI total score. DAZ, dazodalibep; ESSDAI, EULAR Sjögren's Syndrome Disease Activity Index; LS, least squares; SE, standard error.

Results: A total of 74 eligible subjects were randomized (DAZ, N=36; PBO, N=38) and received study medication, with 71 (95.9%) completing Stage I and 67 (90.5%) completing Stage II. In the PBO-DAZ group (N=37), the change in ESSDAI score improved from baseline to −4.1 ± 0.6 at Day 169 and to −6.3 ± 0.6 at Day 365 in Stage II. In the DAZ-PBO group (N=34), the change in ESSDAI score was −6.3 ± 0.6 at Day 169 and −4.4 ± 0.6 at Day 365. The proportions of subjects achieving ESSDAI responses (3- or 4-point improvements from baseline) at Day 365 were greater in the PBO-DAZ group compared with the DAZ-PBO group (ESSDAI [3]: 66.7% [24/36] vs 55.9% [19/34]; ESSDAI [4]: 66.7% [24/36] vs 52.9% [18/34]). During Stage II, the PBO-DAZ group showed greater improvement in the EULAR Sjögren's Syndrome Patient Reported Index, Functional Assessment of Chronic Illness Therapy-Fatigue, and Ocular Surface Disease Index relative to DAZ-PBO group.

Treatment-emergent AEs in Stage II Preferred term, n (%)	PBO-DAZ N=37	DAZ-PBO N=34
COVID-19	6 (16.2)	6 (17.6)
Upper respiratory tract infection	5 (13.5)	5 (14.7)
Diarrhea	2 (5.4)	3 (8.8)
Arthralgia	3 (8.1)	2 (5.9)
Blood creatinine increased	0	2 (5.9)
Chronic gastritis	0	2 (5.9)
Constipation	0	2 (5.9)
Enteritis	0	2 (5.9)
Headache	4 (10.8)	2 (5.9)
Nausea	1 (2.7)	2 (5.9)
Rash macular	0	2 (5.9)
Urinary tract infection	2 (5.4)	2 (5.9)

Most frequently reported treatment-emergent AEs occurring in ≥5% of subjects in Stage II. The PBO-DAZ group received PBO in Stage I and transitioned to DAZ in Stage II. The DAZ-PBO group received DAZ in Stage I and transitioned to PBO in Stage II. AE, adverse event; DAZ, dazodalibep; PBO, placebo.

In Stage II, 53 of 71 subjects reported an AE (DAZ-PBO: 25 [73.5%]; PBO-DAZ: 28 [75.7%]) and the majority were mild/moderate in severity. Four SAEs were reported in three subjects in the DAZ-PBO group (drug-induced liver injury and deep vein thrombosis [DVT; also captured as an AESI] in one subject, multiple injuries, and cervical dysplasia). The subject with a lower extremity DVT also had acute liver injury, with onset of SAEs occurring 180 days after the final dose of DAZ. One SAE was reported in the PBO-DAZ group (chronic cholecystitis). One subject in the DAZ-PBO group discontinued the study during Stage II due to an AE (COVID-19) compared to none in the PBO-DAZ group.

Conclusion: The results during Stage II provide further evidence of DAZ clinical efficacy in Sjögren's disease and support the primary endpoint result. DAZ was generally safe and well tolerated in Stage II, although larger trials of DAZ therapy for this indication are warranted to further explore its safety profile and confirm its clinical efficacy.

References:

1. St. Clair EW et al. *Ann Rheum Dis* 2023; 82(Suppl 1):95.

Disclosure: E. St. Clair: Bristol-Myers Squibb(BMS), 2, CSL Behring, 2, Horizon Therapeutics, 2, Resolve Therapeutics, 2, Sonoma Biotherapeutics, 2, UpToDate, 9; **L. Wang**: Horizon Therapeutics, 3, 11; **I. Alevizos**: Horizon Therapeutics, 3, 11; **W. Rees**: Horizon Therapeutics, 3, 11; **A. Baer**: Bristol-Myers Squibb(BMS), 2; **W. Ng**: AbbVie, 12, Research Collaboration, Argenx, 2, GlaxoSmithKlein(GSK), 12, Research Collaboration, Janssen, 2, Novartis, 2, Resolve Therapeutics, 2, Sanofi, 2; **G. Noaiseh**: Novartis, 2; **C. Baldini**: GlaxoSmithKlein(GSK), 6, Horizon, 6, Sanofi, 6.

Abstract Number: 1637

IgG-Fc-N-Sialylation and -Galactosylation in Primary Sjögren's Syndrome (Pss) in Its Potential as Marker of Disease State and Disease Activity

Helena Achten[1], Liselotte Deroo[2], Kristel De Boeck[3], Matthias Jarlborg[1], Tine Decruy[1], Joke Deprez[1], Emilie Dumas[1], Dirk Elewaut[4] and isabelle peene[5], [1]Ghent University, Ghent, Belgium, [2]Ghent University, Gent, Belgium, [3]Ghent University Hospital, Ghent, Belgium, [4]Ghent University and VIB Center for Inflammation Research, Ghent, Belgium, [5]University Hospital Ghent, Ghent, Belgium

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Sjögren's Syndrome – Basic & Clinical Science
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Loss of galactose and sialic acid structures attached to the IgG-Fc-fragment switches the antibody effector function from anti-inflammatory to pro-inflammatory[1]. This study investigated the IgG- Fc-N-glycosylation profiles in patients from the *Belgian Sjögren's Syndrome Transition Trial* (BeSSTT) in relation to disease state, salivary gland ultrasonography SGUS) and histopathology, and autoantibodies against SSA (Ro52/Ro60) and SSB.

Methods: The relative amount of N-sialylated and N-galactosylated IgG was determined by capillary electrophoresis after using the endo-S glycosidase based assay. 300 serum samples of patients of the BeSSTT, an observational cohort of patients with definite pSS (n=177), fulfilling the 2016 ACR/EULAR classification criteria, and of patients with suspected pSS (n=111) due to presence of either objective sicca or one immunological criterion, were investigated. Groups were made based on the presence or absence of sicca complaints, objective sicca, anti-SSA reactivity and histopathology focus score. SGUS was assessed by Hocevar Score, categorized in negative (0-14), low positive (15-26) and high positive (27-48)[2].

Table 1. Relative amount of Fc-N-sialylated and Fc-N-galactosylated IgG in relation to disease state, salivary gland damage (SGUS and histopathology) and autoantibody profile.

	Number	IgG-Fc-sialylation Median (IQR)	IgG-Fc-galactosylation Median (IQR)
Disease state	288	P <0.001	P <0.001
Sicca complaint	22	0,096 (0,017)	0,599 (0,089)
Sicca	53	0,083 (0,027)	0,552 (0,130)
Probable pSS	36	0,090 (0,034)	0,584 (0,137)
Definite pSS	177	0,068 (0,030)	0,472 (0,150)
SGUS	300	P<0.001	P<0.001
Negative Hocevar (0-14)	149	0,077 (0.033)	0,539 (0.143)
Low positive Hocevar (15-26)	71	0,081 (0.026)	0,540 (0.116)
High positive Hocevar (27-48)	80	0,061 (0.027)	0,439 (0.145)
Histopathology FS	119	P<0.05	P<0.01
FS <1	75	0,082 (0.026)	0,549 (0.121)
FS≥1	44	0,070 (0.034)	0,481 (0.122)
Autoantibody profile	288	P<0.001	P<0.001
anti-SSA-	97	0,086 (0,027)	0,553 (0.129)
mono anti-Ro52+	24	0,067 (0,026)	0,484 (0.151)
mono anti-Ro60+	30	0,086 (0,037)	0,571 (0.133)
double anti-Ro52+Ro60+	77	0,071 (0.036)	0,481 (0.136)
triple anti-Ro52+Ro60+ SSB+	60	0,064 (0.028)	0,460 (0.137)

Differences in levels of IgG-Fc-N-sialylation and -galactosylation were determined using Kruskal-Wallis testing. *P*-values ≤0.05 were considered statistically significant. Bonferroni correction was applied for post-hoc analyses.

Results: IgG-Fc-N-sialylation and -galactosylation were significantly lower in definite pSS than in patients with sicca complaints, objective sicca or anti-SSA/SSB reactivity only (probable pSS) (Fig 1). Besides, IgG-Fc-N-sialylation and IgG-Fc-N-galactosylation were significantly lower in high positive SGUS- versus low positive and negative SGUS-scores and in positive versus negative focus scores. IgG-Fc-N-sialylation and -galactosylation were significantly lower in anti-Ro52+Ro60+SSB+,

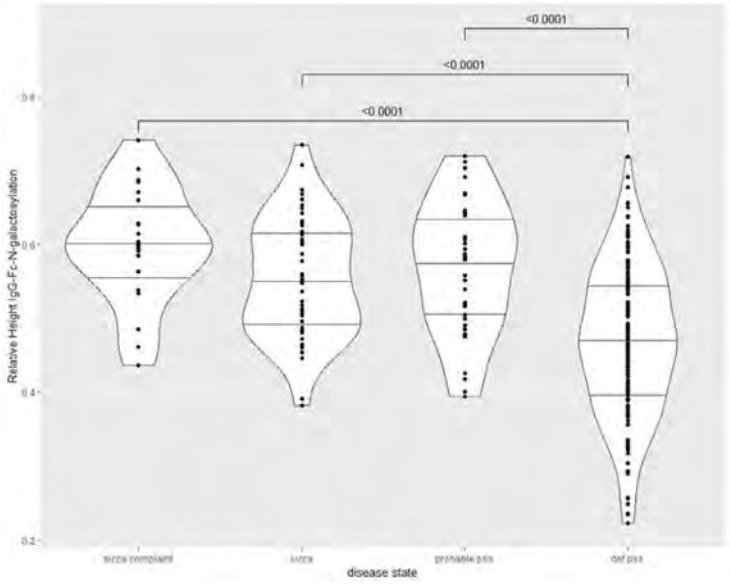


Figure 1. IgG- Fc-N-galactosylation in function of disease state

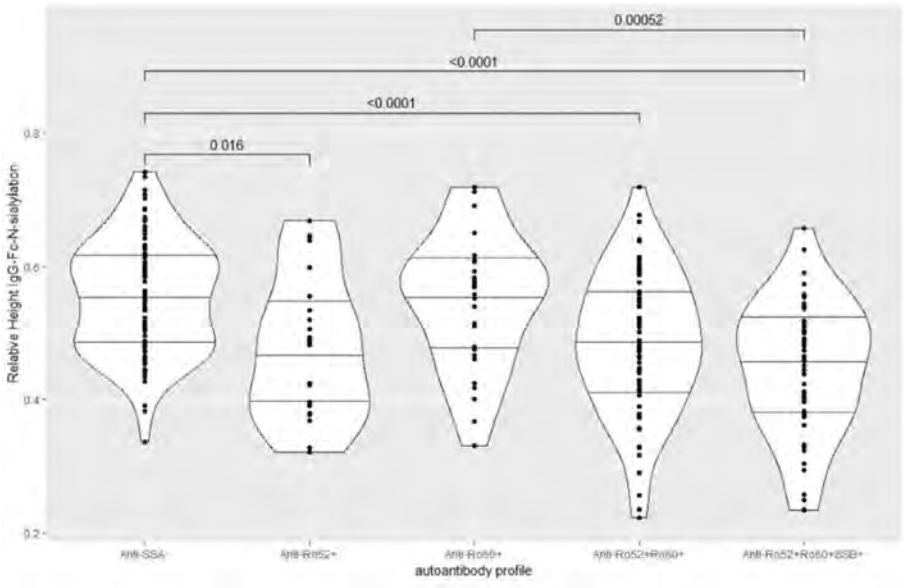


Figure 2. IgG-Fc-N-galactosylation level in function of autoantibody profile

anti-Ro52+Ro60+ and anti-Ro52+ patients than in anti-SSA-/SSB- patients. Strikingly, IgG-Fc-N-sialylation and -galactosylation were also significantly higher in anti-Ro52+60+ and anti-Ro52+Ro60+SSB+patients than in anti-Ro60+ patients (Fig 2). Results are shown in Table 1.

Conclusion: There was a gradual loss of IgG-Fc-N-sialic acid and IgG-Fc-N-galactose as the disease became more prominent, as observed from sicca and probable pSS to definite pSS. The IgG-Fc-N-glycosylation profile was associated with the degree of salivary gland damage in pSS. Anti-Ro52+Ro60+SSB+, Anti-Ro52+Ro60+ and Anti-Ro52+ patients had a more pro-inflammatory IgG-Fc-N-glycosylation profile than anti-SSA- and strikingly also than anti-Ro60+ patients.

Disclosure: H. Achten: None; **L. Deroo**: None; **K. De Boeck**: None; **M. Jarlborg**: None; **T. Decruy**: None; **J. Deprez**: None; **E. Dumas**: None; **D. Elewaut**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 2, galapagos, 5, Janssen, 6; **i. peene**: argenx, 1, Eli Lilly, 6, Janssen, 6.

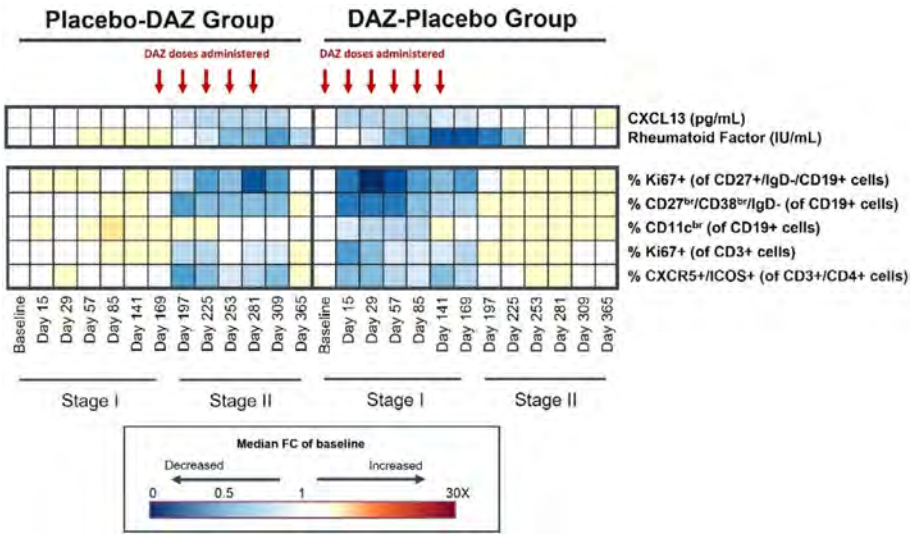
Abstract Number: 1638

CD40L Inhibition with Dazodalibep Rapidly Reduces Blood Biomarkers of T and B Cell Costimulation in Subjects with Sjögren's Having High Disease Activity or High Symptom Burden

Tuyet-Hang Pham[1], Michael A. Smith[1], Nannette Mittereder[1], William A. Rees[2], Ilias Alevizos[2], E. William St. Clair[3] and Claire Emson[1], [1]Horizon Therapeutics plc, Rockville, MD, [2]Horizon Therapeutics, Rockville, MD, [3]Duke University Medical Center, Durham, NC

SESSION INFORMATION

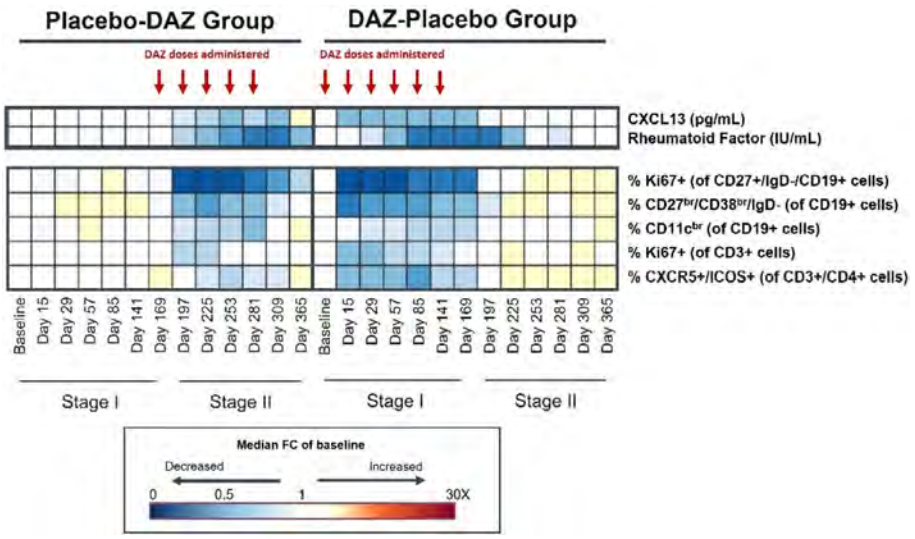
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Sjögren's Syndrome – Basic & Clinical Science
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM



Impact of dazodalibep on blood biomarkers of T and B cell costimulation in Population 1: Subjects with moderate-to-severe systemic disease activity. DAZ, dazodalibep; FC, fold-change.

Background/Purpose: Dazodalibep (DAZ) is a non-antibody fusion protein that acts as a CD40L antagonist and blocks costimulatory signals between immune cells, including T cells, B cells, and antigen-presenting cells. CD40L inhibition disrupts costimulatory signals that lead to activation of germinal centers (GC), pathogenic B cells, plasma cells, and autoantibodies that are hallmarks of Sjögren's disease. Among the previously studied biomarkers in Sjögren's, CXCL13 is produced by activated T Follicular Helper (Tfh) cells and is essential for GC formation and activity.

Methods: This study enrolled two distinct populations of subjects with Sjögren's (NCT04129164). Population 1 (Pop1) included 74 pts with moderate-to-severe systemic disease activity as defined by a EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) ≥ 5. Population 2 (Pop2) consisted of 109 pts with unacceptable symptom burden and limited extraglandular systemic involvement as defined by a EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) ≥ 5 and ESSDAI < 5. Eligible subjects were randomized 1:1 to receive intravenous DAZ 1500 mg or placebo (PBO) Q2W x 3 doses, then Q4W x 4 additional doses (Stage I). Starting on Day 169, subjects initially randomized to DAZ transitioned to PBO Q4W x



Impact of dazodalibep on blood biomarkers of T and B cell costimulation in Population 2: Subjects with an unacceptable symptom burden, and limited extraglandular systemic organ involvement. DAZ, dazodalibep; FC, fold-change.

5 doses and those initially randomized to PBO were switched to DAZ Q4W x 5 doses and then followed for 12 weeks (Stage II). B and T cell subsets (Ki67+ post-switch memory B cells [of CD27+/IgD-/CD19+ cells], $CD27^{br}/CD38^{br}$/Ig D- plasmablasts, $CD11c^{br}$ atypical memory cells, CXCR5+/ICOS+ TfH, and Ki67+ T cells) were immunophenotyped using flow cytometry. Serum levels of CXCL13 and rheumatoid factor (RF) autoantibodies were assessed by immunoassay and nephelometry, respectively.

Results: Baseline immune profiles of the subjects in Pop1 and Pop2 revealed similar levels of autoantibodies and CXCL13. Baseline levels of $CD27^{br}/CD38^{br}$/Ig D- plasmablasts, and $CD11c^{br}$ atypical memory cells were higher in Pop2 than Pop1, while composition of other blood immune cell phenotypes remained similar. In Pop2, compared with the PBO group, DAZ treatment produced significant and rapid reductions from Day 15 onwards in the percentage of Ki67+ post-switch memory B cells, $CD27^{br}/CD38^{br}$/Ig D- plasmablasts, $CD11c^{br}$ atypical memory cells, and CXCR5+/ICOS+ TfH cells, as well as decreases in the serum levels of CXCL13 and RF. These results were similar to those previously observed in Pop1 Stage I. In Stage II, when PBO-treated subjects transitioned to DAZ treatment, there were similar sustained reductions in these biomarkers. In DAZ-treated subjects that transitioned to PBO in Stage II, these biomarkers returned to baseline values.

Conclusion: DAZ-mediated CD40-CD40L blockade in subjects with Sjögren's disease reduced biomarkers by inhibiting T/B cell costimulation and downstream biomarkers of GC formation, activity, and autoantibody production. These findings demonstrate the biological impact of DAZ in subjects with Sjogren's across populations with either moderate-to-severe systemic disease activity or unacceptable symptom burden.

Disclosure: T. Pham: Horizon Therapeutics, 3, 11; **M. Smith**: Horizon Therapeutics, 3, 11; **N. Mittereder**: Horizon Therapeutics, 3, 11; **W. Rees**: Horizon Therapeutics, 3, 11; **I. Alevizos**: Horizon Therapeutics, 3, 11; **E. St. Clair**: Bristol-Myers Squibb(BMS), 2, CSL Behring, 2, Horizon Therapeutics, 2, Resolve Therapeutics, 2, Sonoma Biotherapeutics, 2, UpToDate, 9; **C. Emson**: Horizon Therapeutics, 3, 11.

Abstract Number: 1639

PsA Patients of Diverse Ethnic and Racial Backgrounds Experience More Skin Psoriasis, Increased Pain, and Higher Rates of Radiographic Axial Disease

Rebecca Haberman[1], Tasneem Ahmed[2], Seungha Um[1], Ying Yin Zhou[1], Sydney Catron[1], Kathryn Jano[1], Sarah Moussavi[1], Eileen Lydon[2], Alexandra Rice[1], Andrea Neimann[1], Soumya Reddy[3], Samrachana Adhikari[1] and Jose Scher[4], [1]NYU Grossman School of Medicine, New York, NY, [2]New York University, New York, NY, [3]NYU School of Medicine, New York, NY, [4]New York University School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes II: Psoriatic Arthritis

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Individuals of diverse ethnic and racial backgrounds are generally underrepresented in psoriatic arthritis (PsA) research and clinical trials, despite evidence that their disease presentation, severity and course may be distinct. Here we aimed to characterize a cohort of patients with PsA to evaluate how race, ethnicity, and sex may inform features of clinical presentation, comorbidities, disease course and outcomes.

Table 1. Baseline Characteristics by Race and Ethnicity

Characteristics	All (n=817)	Non-Hispanic, white (n=632)	White Hispanic + Nonwhite (n=185)	p-value
Age- mean (SD)	46.47 (14.42)	47.16 (14.73)	44.1 (13.06)	**0.007**
Female- n (%)	398 (48.71)	307 (48.58)	91 (49.19)	0.883
Race/Ethnicity- n (%)*				0.000
White	632 (77.4)	632 (100.00)	--	
Black	15 (1.84)	--	15 (8.11)	
Asian	58 (7.10)	--	58 (31.35)	
Other	81 (9.92)	--	81 (43.78)	
Hispanic	93 (11.38)	--	93 (50.27)	
Body Mass Index- mean (SD)	27.75 (6.69)	27.61 (6.59)	28.28 (7.05)	0.296
Comorbidities- n (%)				
Depression	182 (22.36)	150 (23.73)	32 (17.30)	0.072
Anxiety	166 (20.32)	141 (22.31)	25 (13.51)	**0.009**
Cardiovascular disease	313 (38.31)	239 (37.82)	74 (40.00)	0.591
Metabolic disease	132 (16.16)	90 (14.24)	42 (22.70)	**0.006**
Diabetes	69 (8.45)	45 (7.12)	24 (12.97)	**0.012**
Current smoker	63 (7.71)	43 (6.80)	20 (10.81)	0.072
Disease involvement—n (%)				
Axial disease	179 (21.91)	129 (20.41)	50 (27.03)	0.056
Axial (radiographic)	150 (18.36)	103 (16.30)	47 (25.41)	**0.005**
Axial (non-radiographic)	29 (3.55)	26 (4.11)	3 (1.62)	0.107
Enthesitis	274 (33.54)	211 (33.39)	63 (34.05)	0.866
Dactylitis	263 (32.19)	208 (32.91)	55 (29.73)	0.415
Nail disease	467 (57.16)	360 (56.96)	107 (57.84)	0.832
Skin disease	807 (98.78)	622 (98.42)	185 (100.00)	0.085
Radiographic erosion	227 (27.78)	171 (27.06)	56 (30.27)	0.391
Medication use—n (%)				
Any	610 (74.66)	479 (75.79)	131 (70.81)	0.171
Biologic	354 (46.15)	273 (46.19)	81 (46.02)	0.968

* Patients may identify as more than one race/ethnicity.

Methods: 817 consecutive patients with PsA from a large, diverse metropolitan area (NYU Psoriatic Arthritis Center, New York) were enrolled in an observational, longitudinal registry. Demographics, medical history, medication use, and psoriatic disease phenotype and activity were all recorded and analyzed.

Results: The population was 77.4% non-Hispanic, White, 7.1% Asian, 1.8% Black, with 9.9% identified as other races or multiracial, and 11.8% identified as Hispanic (Table 1). Non-white individuals (include white Hispanic participants) were younger, more likely to have concomitant metabolic disease and diabetes, and less likely to have anxiety compared to non-Hispanic white individuals. Phenotypically, they were also more likely to have radiographic axial disease (p=0.005). Non-white individuals had higher tender joint counts (4.0 vs. 3.0, p=0.03) with similar swollen joint counts (2.2 vs. 1.8, p= 0.31) and proportion of individuals receiving PsA medication (70.8% vs. 75.8%, p=0.17) (Figure 1). Even when adjusting for age, sex, and medication use, the tender joint count of non-white individuals was estimated to be 1.03 joints more than white individuals (Figure 2). In the subgroup of medication naïve patients (n=207), non-white individuals also had significantly higher precent body surface area (BSA) affected by psoriasis (5.4% vs. 2.2%, p=0.02). Hispanic individuals were significantly more likely to have higher tender joint counts (4.4 vs. 3.0, p=0.03), higher RAPID3 scores (14.6 vs. 10.3, p=0.004), and moderate-severe psoriasis (30.7% vs. 17.5%, p=0.01) compared to non-Hispanic white individuals. Compared to men, women demonstrated higher RAPID3 scores (11.5 vs. 9.8, p=0.011), despite similar tender and swollen joint counts (3.5 vs. 3.0, p=0.27 and 1.8 vs. 2.0, p= 0.29 respectively) and skin involvement (3.5% BSA vs. 2.9%, p=0.37). Women continued to have higher estimated RAPID3 scores when adjusting for race/ethnicity, age, and medication use (mean difference 1.66 points higher, 95% CI 0.4-2.9, p=0.01).

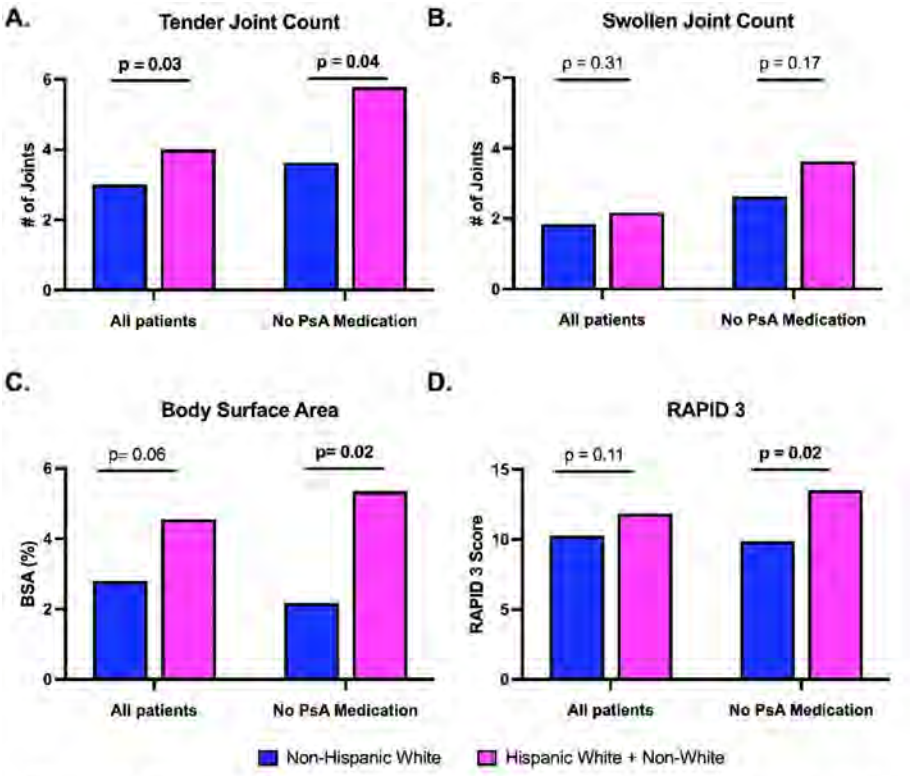


Figure 1. Disease activity measures by race and ethnicity. Unadjusted activity measures for tender joint count (A), swollen joint count (B), percent body surface area (BSA) covered by psoriasis (C) and RAPID 3 score (D). Left side of each graph shows all participants (n= 817) and right side shows only those patient naive to immunomodulatory treatment (n=207, right). Blue represents non-Hispanic White individuals and pink represents non-White individuals (including those identifying as Hispanic and White).

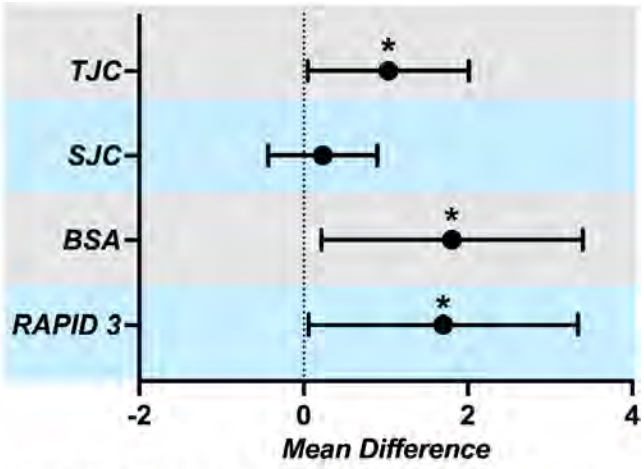


Figure 2. Estimated mean differences based on regression model analysis adjusted for age, sex, and medication use. Mean difference represents non-White and Hispanic White patients as compared to non-Hispanic White individuals as the reference.

Conclusion: We describe the NYU Psoriatic Arthritis Cohort, a relatively more diverse cohort compared to other registries and clinical trials, which includes 22.6% non-white individuals, mostly identifying as Asian or Hispanic. Non-white individuals had higher tender joint counts compared to white individuals despite similar swollen joint counts and medication use. Unexpectedly, they also had higher rates of radiographic axial disease. Additionally, women had higher RAPID 3 scores despite similar joint and disease measures. These findings may reflect differences in PsA presentation and outcomes as experienced by racial, ethnic, and sex groups, which need to be taken into consideration in clinical care and research design.

Disclosure: R. Haberman: Janssen, 1, 5, UCB, 1; **T. Ahmed**: None; **S. Um**: None; **Y. Zhou**: None; **S. Catron**: None; **K. Jano**: None; **S. Moussavi**: None; **E. Lydon**: Aurinia, 1, GlaxoSmithKlein(GSK), 1, UCB, 1; **A. Rice**: None; **A. Neimann**: Sun Pharma, 1, UCB, 1; **S. Reddy**: AbbVie, 2, Amgen, 2, Fresenius Kabi, 2, Janssen, 2, Novartis, 2, UCB, 2; **S. Adhikari**: None; **J. Scher**: AbbVie, 2, Janssen, 2, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 2, UCB, 2.

Abstract Number: 1640

Psoriatic Disease Associated with Neuroconnectivity Alterations in the Default Mode Network

Rebecca Haberman[1], Sydney Catron[1], Yu Veronica Sui[1], Sarah Moussavi[1], Soumya Reddy[2], Eileen Lydon[3], Andrea Neimann[1], Alexis R Ogdie[4], Mariana Lazar[1] and Jose Scher[5], [1]NYU Grossman School of Medicine, New York, NY, [2]NYU School of Medicine, New York, NY, [3]New York University, New York, NY, [4]University of Pennsylvania, Philadelphia, PA, [5]New York University School of Medicine, New York, NY

SESSION INFORMATION
Session Date: Monday, November 13, 2023
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Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Despite significant advances in psoriatic disease (PsD) therapeutics, treatment response remains suboptimal. Even in patients with psoriatic arthritis (PSA) that achieve seemingly controlled inflammation, up to half continue to experience residual symptoms, notably pain and fatigue, which can prevent meaningful improvement in symptoms and quality of life. However, the pathophysiology and effectors of residual pain are not well understood. Functional brain MRI

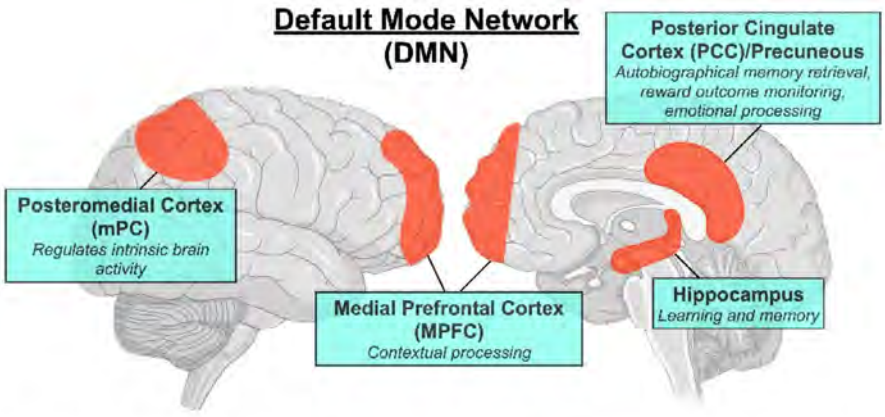

Figure 1. The Default Mode Network (DMN) is often altered in chronic pain states. The main structures include the posteromedial cortex (mPC), the medial prefrontal cortex (MPFC), the posterior cingulate cortex (PCC), the precuneous, and the hippocampus.

(fMRI) can be used to identify alterations in brain connectivity as a possible basis for residual pain and have the potential to discern inflammatory driven pain from centrally-provoked pain. Here we describe pilot fMRI data showing neuroconnectivity changes in those with PsD.

Methods: Seven patients with PsD were enrolled from the NYU Psoriatic Arthritis Center (PAC). Patients on psychotropic medications were excluded. Demographics, medical history, and medication use were recorded and focused musculoskeletal and skin exams were performed. Participants completed patient reported outcomes including the SF-36, Beck Depression Index, fatigue numeric rating score, and RAPID 3. Four healthy controls were used as a comparison group. fMRI sequences were obtained in all participants at both rest and with a fatigue inducing task (Paced Auditory Serial Addition Test) using a 3 Tesla Siemens Prisma scanner. fMRI time series were analyzed using the independent component analysis, with a focus on connectivity within the default mode network (DMN, Figure 1) which has been previously implicated in depression and chronic pain states such as fibromyalgia.

Results: Compared to healthy controls, those with PsD had decreased connectivity between the DMN's posteromedial cortex node and the superior parietal lobule ($p = < 0.05$ FDR-corrected at cluster level) (Figure 2). Additionally, for the 7 participants with PsD, levels of pain, depression, and fatigue all correlated with strength of connectivity in pathways of the DMN (Figure 3).

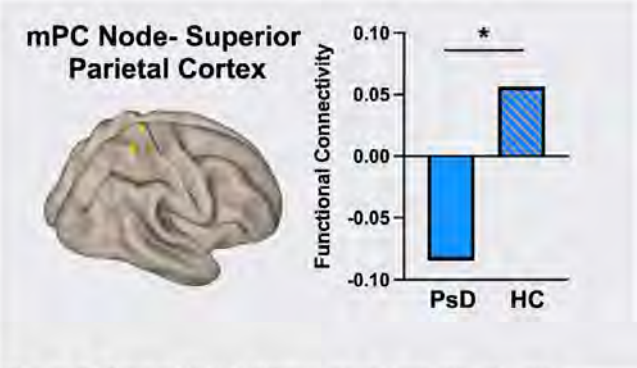

Figure 2. Connectivity differences in individuals with psoriatic disease (PsD) and healthy controls (HC). The posteromedial cortex (mPC) is involved in intrinsic brain activity and the superior parietal lobule in cognitive function, attention, and higher order thinking. *p < 0.05

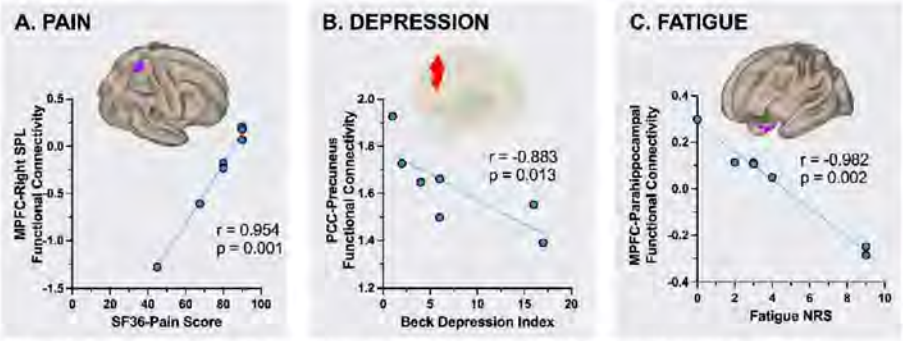

Figure 3. Functional connectivity patterns in the DMN (default mode network) correlate with pain, depression, and fatigue. (A) Standard Form (SF)-36 Pain Subscale (higher number indicating less pain) correlates with activity of the medial prefrontal cortex (MPFC, creating active associations within a contextual frame to generate predictions and expectations of what will be encountered next in the environment) to right superior parietal lobule (SPL, cognitive function, attention, and higher order thinking). (B) Beck depression index (higher number indicating higher level of depression) correlates with activity of the posterior cingulate cortex (PCC) to precuneus (memory retrieval, reward out coming monitoring, and emotional processing). (C) Fatigue numerical rating scale (NRS, 0-10 with higher number indicating less fatigue) correlates with activity of the MPFC to parahippocampus (contextual processing).

Conclusion: This initial data demonstrates the feasibility and acceptability of using fMRI to characterize neuroconnectivity in patients with PsD. We observed differences in functional connectivity between healthy participants and patients with PsD, even with well controlled disease. Furthermore, identifying networks and connections associated with pain, depression, and fatigue may ultimately help in identifying and characterizing residual pain that contributes to worse clinical outcomes. Future studies will confirm and further characterize these findings using larger sample sizes.

Disclosure: R. Haberman: Janssen, 1, 5, UCB, 1; **S. Catron**: None; **Y. Sui**: None; **S. Moussavi**: None; **S. Reddy**: AbbVie, 2, Amgen, 2, Fresenius Kabi, 2, Janssen, 2, Novartis, 2, UCB, 2; **E. Lydon**: Aurinia, 1, GlaxoSmithKlein(GSK), 1, UCB, 1; **A. Neimann**: Sun Pharma, 1, UCB, 1; **A. Ogdie**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, UCB, 2; **M. Lazar**: None; **J. Scher**: AbbVie, 2, Janssen, 2, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 2, UCB, 2.

Abstract Number: 1641

The Window of Opportunity in Psoriatic Arthritis: Similar to Rheumatoid Arthritis?

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Background/Purpose: In rheumatoid arthritis (RA), initiation of treatment within the window of opportunity, i.e. 12 weeks after symptom onset, results in higher remission rates, and less radiographic progression and functional impairment. In contrast, in psoriatic arthritis (PsA) a diagnostic delay of 1-2 years is still common. PsA guidelines state that DMARDs should be started early, with a maximum delay of 1 year. However, it is unknown whether a shorter delay of 12 weeks yields better clinical outcomes. We aimed to investigate what the window of opportunity is in PsA.

Methods: All newly diagnosed, DMARD naïve PsA patients who participated in the Dutch southwest Early PsA cohort (DEPAR) were included (n=855). First, we calculated total delay, and then split this into patient and general practitioner (GP) delays to assess where potential gains could be made. Thereafter, patients were categorized in 3 groups, based upon total delay:

1. < 12 weeks delay (early diagnosis)
2. 12-52 weeks delay (late diagnosis)
3. > 52 weeks delay

Aforementioned groups were compared on their probability of achieving Minimal Disease Activity (MDA) and Disease Activity in PSoriatic Arthritis (DAPSA) remission, defined as DAPSA < 5. We also assessed differences in radiographic progression and functional impairment. Radiographic progression is measured with the modified Sharp van der Heijde score (mTSS), while functional impairment is measured with the Health Assessment Questionnaire–Disability Index (HAQ-DI). Mixed models were used to compare outcomes over time (3 years).

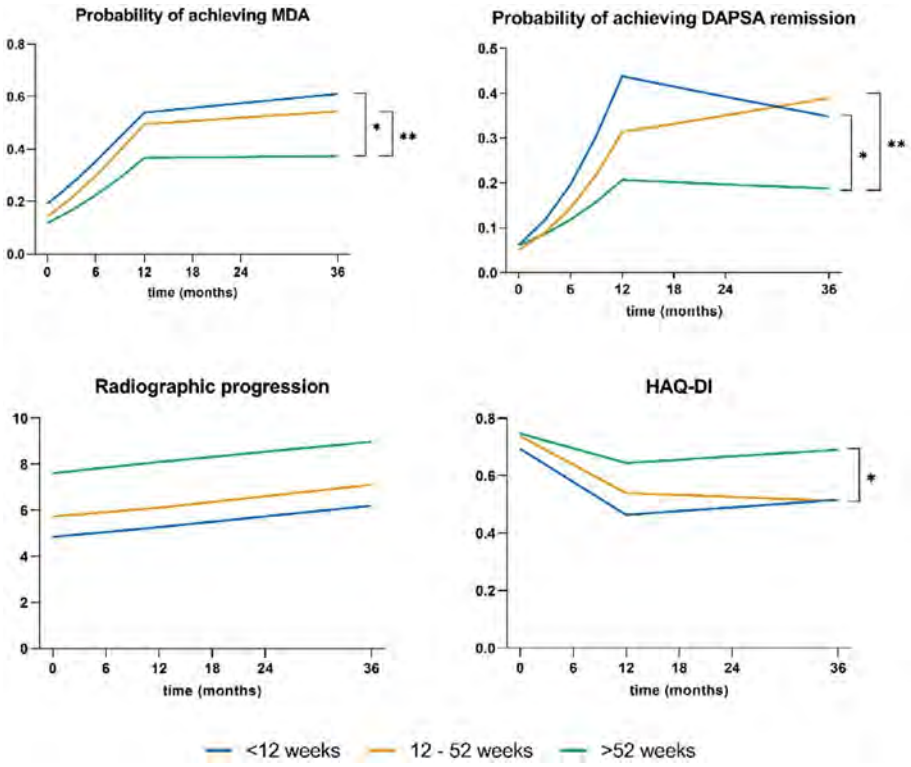

Figure 1. Probability of achieving MDA and DAPSA remission, and radiographic progression and functional ability over 3 years. *Indicates a significant difference between the >52 weeks delay and early diagnosis group, ** indicates a significant difference between the >52 weeks delay and late diagnosis group.

Results: Median total delay was 42.0 weeks. Patient and GP delay were 4.4 and 18.0 weeks, respectively. PsA patients with > 52 weeks delay were more often female, had less swollen joints and lower CRP and ESR. They also more often had enthesitis. In contrast, no baseline differences were found between early and late diagnosis groups, respectively < 12 weeks and 12-52 weeks. The group with > 52 weeks delay was significantly less likely to achieve MDA and DAPSA remission over 3 years of follow-up compared to both the early and late diagnosis groups (**Figure 1**). The > 52 weeks delay group also scored significantly worse on HAQ-DI than the early diagnosis group. Radiographic progression did not differ significantly between groups. Although all outcomes were numerically better in PsA patients who were diagnosed within 12 weeks compared to those with a diagnosis within 52 weeks, no significant differences were found (**Figure 1**).

Conclusion: Early referral and diagnosis is associated with better clinical outcomes. Therefore, disease outcomes of PsA patients may improve with timely referral to a rheumatologist.

Disclosure: S. Snoeck Henkemans: None; **P. de Jong**: None; **J. Luime**: None; **M. Kok**: None; **i. Tchetverikov**: None; **A. van der Helm-van Mil**: None; **m. vis**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Dutch Arthritis Foundation, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 1642

Identifying Distinct Phenotypes in Psoriatic Arthritis: A Study from the Psoriatic Arthritis Research Consortium (PARC) Cohort

Paras Karmacharya[1], Daniel W. Byrne[2], Alisa Stephens-Shields[3], Leslie Crofford[4], M. Elaine Husni[5], Jose Scher[6], Ethan Craig[3], Robert Fitzsimmons[3], Soumya Reddy[7], Marina Nighat Magrey[8], Jessica A Walsh[9] and Alexis R Ogdie[3], [1]Vanderbilt University, Nashville, TN, [2]Vanderbilt University Medical Center, Nashville, TN, [3]University of Pennsylvania, Philadelphia, PA, [4]Vanderbilt University Medical Center, Melbourne, AR, [5]Cleveland Clinic / Department of Rheumatic and Immunologic Diseases, Cleveland, OH, [6]New York University School of Medicine, New York, NY, [7]NYU School of Medicine, New York, NY, [8]Case Western Reserve University, University Hospitals, Cleveland, OH, [9]Salt Lake City Veterans Affairs Health and University of Utah Health, Division of Rheumatology, Salt Lake City, UT

SESSION INFORMATION

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Background/Purpose: Despite an increasing number of therapeutic options, less than one-third of patients with PsA achieve remission. A major cause of non-response is that PsA is studied and managed as if it were a single disease, without accounting for heterogeneity in disease presentation and prognosis. Understanding heterogeneity better can improve

Table 1. Baseline characteristics overall and by psoriatic arthritis phenotypes in the PARC cohort. SD, Standard Deviation; N (%), Number of patients (Percentage); BMI, body mass index; TJC, total joint count; SJC, swollen joint count; BSA, body surface area involved by psoriasis; Pt, patient; PsO, psoriasis; IBD, inflammatory bowel disease; CRP, C-reactive protein †p-values from Kruskal-Wallis and Fisher's exact test for continuous and categorical variables respectively *From the BASDAI questionnaire Missing variables: race, 47 and ethnicity, 85

Baseline characteristics	Overall (N=529)	Cluster 1 (N=265)	Cluster 2 (N=195)	Cluster 3 (N=27)	Cluster 4 (N=2)	Cluster 5 (N=40)	†p-value
Age	50.17 (13.69)	50.19 (14.49)	51.10 (12.73)	45.55 (14.24)	47.50 (9.19)	48.63 (12.38)	0.327
Female	282 (56.29%)	120 (47.81%)	128 (68.45%)	10 (41.67%)	2 (100.00%)	22 (59.46%)	<0.0001
Race							0.011
White	444 (92.12%)	226 (91.87%)	171 (95.00%)	22 (95.65%)	2 (100.00%)	23 (74.19%)	
Other	38 (7.88%)	20 (8.13%)	9 (5.00%)	1 (4.35%)	0 (0.00%)	8 (25.81%)	
Ethnicity							0.019
Not Hispanic/Latino	404 (76.37%)	208 (78.49%)	152 (77.95%)	21 (77.78%)	1 (50.00%)	22 (55.00%)	
Hispanic/Latino	28 (5.29%)	8 (3.02%)	14 (7.18%)	0 (0.00%)	0 (0.00%)	6 (15.00%)	
Other	12 (2.27%)	6 (2.26%)	5 (2.56%)	1 (3.70%)	0 (0.00%)	0 (0.00%)	
Clustering variables							
BMI	30.3 (7.3)	28.58 (6.19)	32.42 (7.77)	32.44 (9.64)	28.60 (8.26)	29.36 (6.61)	<0.0001
TJC	5.7 (8.3)	2.05 (3.10)	6.38 (6.90)	8.70 (10.21)	1.50 (2.12)	24.25 (10.90)	<0.0001
SJC	3.3 (5.5)	1.10 (2.21)	3.30 (3.74)	4.15 (4.22)	1.50 (0.71)	16.88 (8.58)	<0.0001
BSA	2.5 (6.8)	1.20 (3.17)	1.99 (4.03)	4.70 (7.02)	2.50 (3.54)	12.52 (18.24)	<0.0001
Enthesitis count	0.7 (1.2)	0.30 (0.70)	0.97 (1.31)	0.93 (1.30)	1.00 (1.41)	1.82 (1.82)	<0.0001
Dactylitis count	0.3 (1.3)	0.13 (0.48)	0.29 (0.93)	0.26 (0.59)	6.50 (9.19)	1.62 (3.49)	<0.0001
Pt pain	4.4 (2.9)	2.30 (1.77)	6.33 (2.03)	4.59 (2.44)	7.00 (4.24)	8.06 (2.29)	<0.0001
Pt global	3.9 (2.8)	1.89 (1.58)	5.80 (1.94)	4.07 (2.64)	6.75 (3.18)	7.29 (2.19)	<0.0001
Pt fatigue*	5.2 (2.7)	3.49 (2.25)	7.06 (1.87)	5.56 (2.26)	6.50 (2.12)	7.47 (2.15)	<0.0001
Axial disease	122 (23.1%)	62 (23.40%)	37 (18.97%)	7 (25.93%)	1 (50.00%)	15 (37.50%)	0.0857
Plaque PsO	225 (42.5%)	104 (39.25%)	76 (38.97%)	17 (62.96%)	1 (50.00%)	27 (67.50%)	0.0011
Inverse PsO	18 (3.4%)	0 (0.00%)	0 (0.00%)	16 (59.26%)	0 (0.00%)	2 (5.00%)	<0.0001
Guttate PsO	8 (1.5%)	1 (0.38%)	0 (0.00%)	7 (25.93%)	0 (0.00%)	0 (0.00%)	<0.0001
Palmoplantar PsO	19 (3.6%)	8 (3.02%)	8 (4.10%)	2 (7.41%)	0 (0.00%)	1 (2.50%)	0.5741
Genital PsO	7 (1.3%)	0 (0.00%)	0 (0.00%)	7 (25.93%)	0 (0.00%)	0 (0.00%)	<0.0001
Pustular PsO	2 (0.4%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (100.00%)	0 (0.00%)	<0.0001
Nail PsO	147 (27.8%)	60 (22.64%)	44 (22.56%)	16 (59.26%)	0 (0.00%)	27 (67.50%)	<0.0001
Uveitis	30 (5.7%)	19 (7.17%)	6 (3.08%)	0 (0.00%)	0 (0.00%)	5 (12.50%)	0.0614
IBD	8 (1.5%)	3 (1.13%)	0 (0.00%)	3 (11.11%)	1 (50.00%)	1 (2.50%)	0.0001
Prior biologic use	206 (38.9%)	86 (32.45%)	82 (42.05%)	11 (40.74%)	1 (50.00%)	26 (65.00%)	0.0011
Elevated CRP	144 (27.2%)	38 (14.34%)	75 (38.46%)	7 (25.93%)	1 (50.00%)	23 (57.50%)	<0.0001

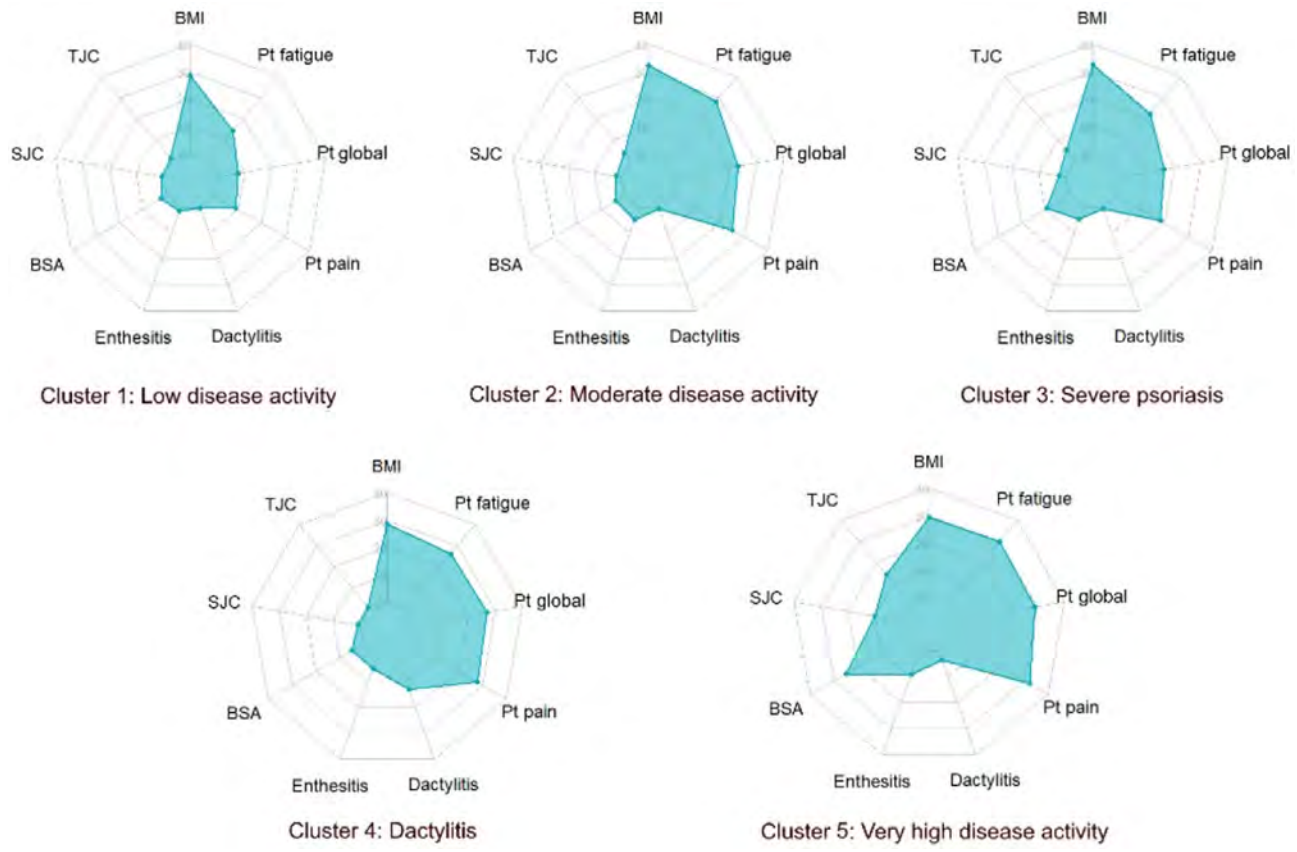

Figure 1. Radar chart comparison of the mean values of the continuous variables across the five phenotypic clusters of psoriatic arthritis in the PARC cohort (n=529). Note: The variables are not standardized for better interpretability and hence on different scales plotted from 0 (lowest at the center) to maximum value for the variable (highest at the outside). Maximum value for the different variables is as follows: BMI 40, TJC 68, SJC 66, BSA 20, Enthesitis count 8 (Leeds enthesitis index + proximal plantar fascia), Dactylitis count 20, Pt pain 10, Pt global 10, and Pt fatigue 10. Abbreviations: BMI, body mass index; TJC, total joint count; SJC, swollen joint count; BSA, body surface area involved by psoriasis; Pt, patient

treatment selection, shorten exposure to suboptimal therapies, reduce potential for side effects, and improve long-term outcomes. The objective of this study was therefore to identify distinct phenotypes in PsA using the PsA Research Consortium (PARC) cohort.

Methods: Baseline disease characteristics from the multicenter PsA Research Consortium (PARC) study was used to cluster PsA patients. Variable selection was performed by clinical relevance and continuous variables were standardized. Multiple Imputation by Chained Equations (MICE) was used to impute missing values. Factor analysis of mixed data (FAMD) was applied for dimensionality and collinearity reduction, followed by hierarchical clustering on the principal components to group similar patient phenotypes. The optimal number of clusters was determined by evaluating the balance between within-cluster variance reduction and between-cluster variance reduction for each level of the hierarchical clustering tree (tree method). Kruskal-Wallis and Fisher's exact tests were performed to examine differences in continuous and categorical variables respectively across the clusters.

Results: In this analysis of 21 clinical variables from 529 PsA patients, five distinct phenotypic clusters were identified. The baseline characteristics of the cohort are presented in **Table 1**. Cluster 1 (50.09%) represented patients with low disease activity, joint counts, and PROs. Cluster 2 (36.86%) displayed moderate disease activity with higher BMI and joint counts compared to Cluster 1. Cluster 3 (5.10%) was characterized by severe psoriasis, higher guttate, palmoplantar, inverse, genital psoriasis, nail dystrophy (59.26%), and the highest mean BMI (32.44 kg/m^2). Cluster 4 (0.37%) exhibited dactylitis with relatively low joint counts, but worse patient-reported outcomes (PROs). Cluster 5 (7.56%) represented very high disease

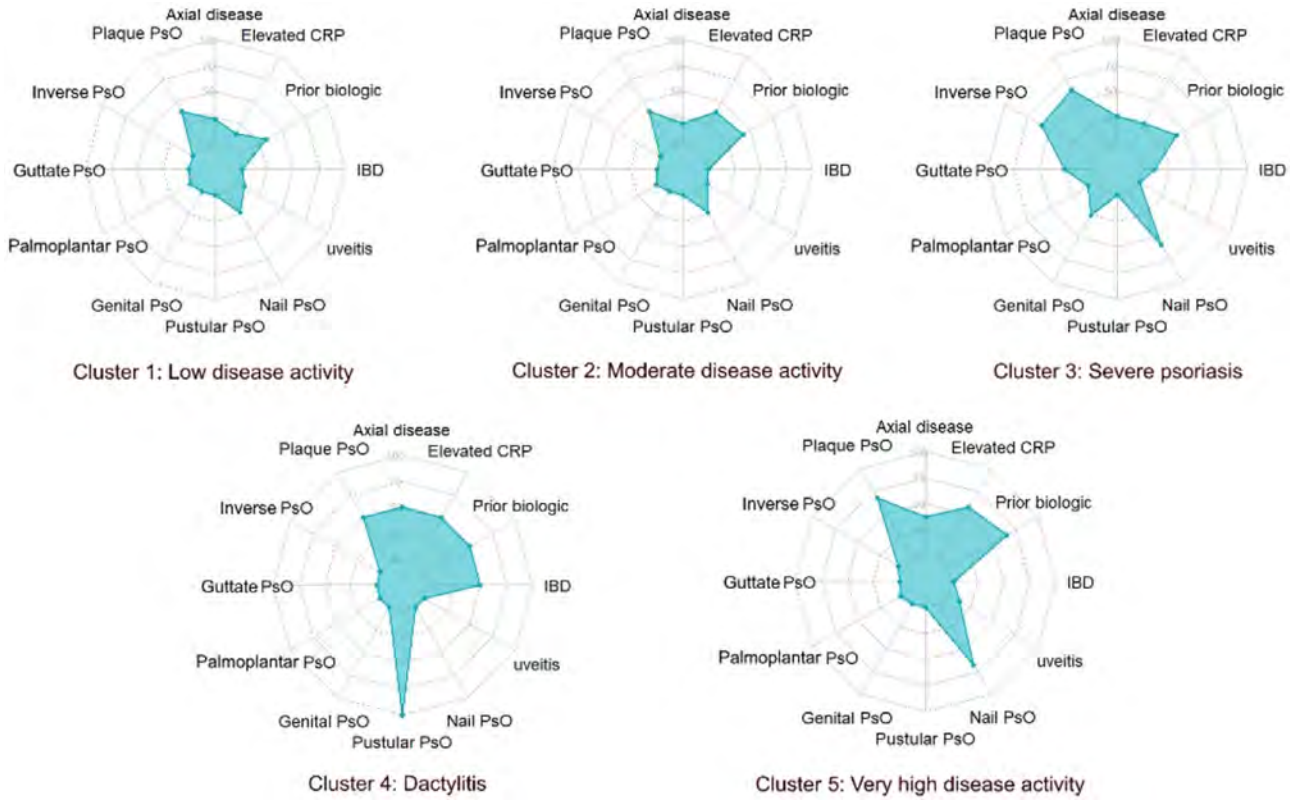

Figure 2. Radar chart comparison of the mean percentages of the categorical variables across the five phenotypic clusters of psoriatic arthritis in the PARC cohort (n=529). Note: The variables are plotted from 0 (lowest at the center) to 100 percent (highest at the outside). Abbreviations: PsO, psoriasis; IBD, inflammatory bowel disease; CRP, C-reactive protein

activity patients with the highest joint counts, BSA, and PROs (**Figures 1 & 2**). The proportion of females was significantly higher in the moderate/high disease activity clusters and all patients in the dactylitis cluster were females. The very high disease activity cluster had a significantly higher proportion of non-white population (15%) compared to other clusters although overall numbers were small. The clusters were significantly different across all clustering variables except axial disease, uveitis, and palmoplantar psoriasis ($p > 0.05$).

Conclusion: The data-driven clusters identified in this real-world study highlight the extensive heterogeneity in PsA. The variability in clinical parameters across clusters underscores the need for personalized treatment approaches in PsA, accounting for unique disease features. Future studies should focus on validating these clusters in different cohorts and exploring their application in precision medicine to transform PsA treatment paradigms.

Disclosure: P. Karmacharya: None; **D. Byrne**: None; **A. Stephens-Shields**: None; **L. Crofford**: None; **M. Husni**: AbbVie, 1, 2, Amgen, 1, 2, Bristol-Myers Squibb, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, UCB, 1, 2; **J. Scher**: AbbVie, 2, Janssen, 2, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **E. Craig**: None; **R. Fitzsimmons**: None; **S. Reddy**: AbbVie, 2, Amgen, 2, Fresenius Kabi, 2, Janssen, 2, Novartis, 2, UCB, 2; **M. Magrey**: AbbVie, 2, Bristol Myers Squibb, 2, Eli Lilly, 2, Novartis, 2, Pfizer Inc, 2, UCB, 5; **J. Walsh**: AbbVie, 5, Amgen, 2, Eli Lilly, 2, Janssen, 2, Merck, 5, Novartis, 2, Pfizer, 2, 5, UCB Pharma, 2; **A. Ogdie**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, UCB, 2.

Abstract Number: 1643

Exploring the Serum Metabolome for Potential Diagnostic Markers of Psoriatic Arthritis

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Background/Purpose: Psoriatic arthritis (PsA) is an inflammatory immune-mediated musculoskeletal skin disease that affects approximately 25% of psoriasis patients causing progressive disability. As a heterogeneous disease, with sometimes subtle manifestation, accurate assessment of PsA is difficult. As such, there is a need for early detection diagnostic tests for PsA. A liquid chromatography – high resolution mass spectrometry (LC-HRMS) general untargeted metabolomics analysis following solid phase microextraction (SPME) was applied to serum samples collected from patients with PsA and psoriasis without PsA (PsC), to perform discovery analysis to investigate potential diagnostic markers of PsA.

Methods: Serum samples were obtained from a biobank of carefully phenotyped PsC (n=100) and PsA (n = 101) patients who had no history of cancer, had no active infection nor received previous treatment with biologics. Novel high throughput technique – SPME – was used to prepare all samples simultaneously followed by LC-HRMS analysis.

Data (pre)processing and feature identification was performed using 2 workflows - Compound Discoverer 3.3 and an independent Rscript. Supervised multivariate analysis and various Machine Learning (ML) algorithms including logitboost, adaptive boosting, support vector machine (SVM), logistic regression, and random forest (RF), were used for predictive feature analysis. Area Under the Receiver Operating Characteristic (AUROC) was then used to evaluate the performance of these features. Only features in models with an area under the curve (AUC) of 0.85 or greater were considered as candidate biomarkers.

Results: Table 1 provides the demographic and disease characteristics of the included subjects. Table 2 provides a summary of the results from predictive feature analyses. A minimum of ten features and a maximum of eighty features from the adaptive boost models produced an AUC of 0.896 and 0.921 respectively. All other models with feature numbers ranging

Table 1: Summary of patient demographics and disease characteristics

Patient category	Total No. of patients	Gender	Age (median) (yrs)	BMI	Avg. Ps. Dur. (yrs)	Avg. PsA Dur. (yrs)
PsC	101	Males (54), Females (47)	19-73 (42)	27.5	16.8	-
PsA	102	Males (55), Females (47)	19-70 (46)	27.8	15.5	1.9

Table 2: Confirmed and tentatively identified features of statistical significance. These features were implicated in a cross validated PLS-DA model. Features containing a (*) were also found to perform well (>0.85) using Area Under the Receiver Operating Characteristic (AUROC).

Feature No.	m/z	Ret. time (min)	Calculated Molec. Weight	Adduct	VIP score	Identification
Confirmed features using MS level 2 spectral matching						
2044	*348.2741	13.8	330.2406	$[M+NH_4]^+$	3.8	9,12,13-TriHOME: a trihydroxyoctadecenoic acid
3828	*470.3684	15.8	469.359	$[M+H]^+$	2.6	N-nervonoyl cysteine
1898	149.0596	8.5	148.0524	$[M+H]^+$	2.2	(2E)-3-(3-Hydroxyphenyl)acrylaldehyde: p-Coumaraldehyde
2241	166.0861	8.5	165.0790	$[M+H]^+$	2.0	Phenylalanine (Found in both positive and negative mode)
353	363.216	12.5	362.2093	$[M+H]^+$	1.9	Cortisol
18	361.2005	13.0	360.1937	$[M+H]^+$	1.7	Cortisone
5056	568.3394	18.0 (18.1)	567.3325	$[M+H]^+$	1.0	1-(4Z,7Z,10Z,13Z,16Z,19Z-docosahexaenoyl)-sn-glycero-3-phosphocholine
918	165.0914	16.1	166.0994	$[M-H]^-$	1.8	TBHQ
450	279.2334	21.6	280.2402	$[M-H]^-$	2.7	linoleic acid
472	284.0892	7.1	285.0961	$[M-H]^-$	1.5	N4-acetylcytidine
149, 747	165.0411	7.0	166.0486	$[M-H]^-$	1.0	Methylxanthine
Tentatively identified features using MS level 1 exact m/z matching						
4827	*203.1834	8.5	202.1755	$[M+H]^+$	3.9	1-dodecanethiol; 24 other hits
2188	*320.2429	9.2	302.2093	$[M+NH_4]^+$	3.8	Hydroxyhexadecanedioic acid; 3 drug metabolites
3146	*784.5516	18.05	783.5414	$[M+H]^+$	2.4	2) PC(20:4(5Z,7E,11Z,14Z)-OH(9)/15:0);
6149	*521.384	17.7	520.3764	$[M+H]^+$	2.3	DG(20:4(5Z,7E,11Z,14Z)-OH(9)/0:0/8:0)
6176	*913.6059	16.9	985.5727	$[M+NH_4]^+$	2.2	PC(22:5(4Z,7Z,10Z,13Z,19Z)-O(16,17)/22:5(7Z,10Z,13Z,16Z,19Z))
5871	*703.4923	17.8	702.4836	$[M+H]^+$	2.2	PA(18:1(9Z)-O(12,13)/i-17:0)
5628	555.3918	18.0	554.3819	$[M+H]^+$	2.1	DG(PGD1/0:0/8:0)

between twenty to eighty produced AUC between 0.891 and 0.915. Several small molecules could be validated via MS Level 2 spectral database matching. Trihydroxyoctadecenoic acid and N-nervonoyl cysteine contributed significantly to the multivariate supervised analysis and performed well according to high AUROC scores. Interestingly, lipids such as docosahexanoyl-sn-gylcerophosphocholine were identified via MS level 2, but there were several other features that were found to be significant that could only be tentatively identified as glycero-lipids and fatty acids. Results from this metabolomics workflow were integrated with top-down multi-omics data for the same patients. Data integration revealed that confirmed and tentatively identified features like glycero- and phospholipids overlapped differentially expressed pathways from the transcriptome.

Conclusion: SPME-LC-HRMS based untargeted metabolomic analyses have identified small molecules (lipids) with excellent discriminative ability between PsA and PsC. Thus, the development of quantitative targeted assays for these metabolites and subsequent validation may provide diagnostic markers for PsA.

Disclosure: N. Looby: None; **M. Kotlyar**: None; **C. Pastrello**: None; **D. Ganatra**: None; **V. Kulasingam**: None; **I. Jurisica**: None; **V. Chandran**: AbbVie, 1, 5, 6, Amgen, 1, 5, 6, AstraZeneca, 3, Bristol-Myers Squibb (BMS), 1, 6, Eli Lilly, 1, 5, 6, Janssen, 1, 6, Novartis, 1, 1, 6, UCB, 1, 2.

Abstract Number: 1644

The EISER Study: Identifying Microbial Factors Associated with Subclinical Gut Inflammation in Spondyloarthritis Patients

Alba Boix-Amorós[1], Rebecca Blank[2], Adam Cantor[1], Jesus Sanz[3], Ana Gutiérrez-Casbas[4], Jordi Gratacos Masmitja[5], Iago Rodríguez -Lago[6], Elisa Trujillo[7], Ignacio Marin-Jimenez[8], Zulema Plaza[9], Marta Domínguez[10], Jose Federico Diaz-Gonzalez[11], Juan D Canete[12], Jose Scher[13] and Jose Clemente[1], [1]Icahn School of Medicine, New York, NY, [2]New York University, New York, NY, [3]Hospital Universitario Puerta de Hierro, Majadahonda, Spain, [4]Hospital General Universitario Dr. Balmis, Alicante, Spain, [5]University Hospital Parc Taulí, Sabadell, Spain, [6]Gastroenterology department Hospital Galdakao, Galdakao, Spain, [7]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [8]Public Health System, Madrid, Spain, [9]Universidad Autónoma de Madrid, Madrid, Spain, [10]Sociedad Española de Reumatología, Madrid, Spain, [11]Hospital Universitario de Canarias, La Laguna, Spain, [12]Hospital Clinic an IDIBAPS, Barcelona, Spain, [13]New York University School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes II: Psoriatic Arthritis

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Nearly 8% of patients with spondyloarthritis (SpA) manifest symptoms that are compatible with active inflammatory bowel disease (IBD), despite not having any previous diagnosis of chronic intestinal pathologies. It is well established that the microbiome plays an important role in immunity, and there is growing evidence showing that intestinal dysbiosis of microbial communities is associated with different immune-mediated diseases. This association is particularly notable in IBD, which is characterized by aberrant microbiome communities and can also be treated by restoring homeostasis through fecal microbiota transplants. We therefore hypothesize that the gut microbiome could be a determining factor in the etiology of psoriatic arthritis (PsA), a type of SpA, and a potential modulator of co-occurrence with intestinal inflammation.

Methods: As part of the EISER study, we selected a subset of 196 subjects diagnosed with with axial, periferic or mixed forms of PsA, who had no prior diagnosis of IBD or other chronic intestinal pathologies. The presence of subclinical and clinical IBD was evaluated at time of enrollment. Subjects with fecal calprotectin (CP) levels less than 80μg/g of fecal matter were considered negative for IBD. For patients with CP levels of 80 μg/g or higher, IBD was diagnosed based on colonoscopy and histological analysis of biopsies collected during the procedure. Capsule endoscopy was performed on those patients with a negative colonoscopy result for additional confirmation. Stool samples were collected from all participants, and microbial DNA was extracted for shotgun metagenomic sequencing using the Illumina HiSeq platform. Sequenced data was processed using MetaPhlAn 4 to estimate microbial composition and HUMAnN 2 to annotate bacterial pathways.

Results: Twenty-five out of 196 subjects in our cohort (12.75%) had subclinical IBD (sIBD), two of whom (1.02% of total) were confirmed to have clinical IBD (cIBD). The use of proton-pump inhibitors (PPI) resulted in significant differences in overall beta diversity (PERMANOVA, $p < 0.008$). The levels of fecal CP were significantly correlated with the abundance of multiple species within the *Streptococcus* genus and with *Rothia mucilaginosa*. Patients with sIBD had lower abundance of *Dialister,Barnesiella spp* and *Eubacterium rectale,* and higher abundance of taxa including *Blautia* spp, *Prevotella copri and Roseburia* compared with non sIBD patients. These findings were further confirmed in the two cIBD patients.

Conclusion: Microbiome composition was impacted by the use of PPIs, in agreement with previous reports. Bacteria typically found in the oral cavity were significantly correlated with CP levels, suggesting a potential role for oral taxa in pro-inflammatory responses in PsA patients. We identified taxa differentially enriched in sIBD patients consistent with patterns observed in the two patients with confirmed IBD diagnosis, suggesting a potential role for these taxa as biomarkers. Further

analysis will evaluate differences in microbial pathways associated with disease groups and medications, as well as the relation between gut microbiome composition, function and blood proteomic biomarkers.

Disclosure: A. Boix-Amorós: None; **R. Blank**: None; **A. Cantor**: None; **J. Sanz**: AbbVie/Abbott, 1, 6, Janssen, 1, 5, 6, Novartis, 6, UCB, 1, 5, 6; **A. Gutiérrez-Casbas**: None; **J. Gratacos Masmitja**: AbbVie/Abbott, 1, 6, Amgen, 6, AstraZeneca, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 1, 6, Janssen, 1, 6, Novartis, 1, 6, Pfizer, 1, 6, UCB, 1, 6; **I. Rodríguez-Lago**: None; **E. Trujillo**: None; **I. Marin-Jimenez**: None; **Z. Plaza**: None; **M. Domínguez**: None; **J. Diaz-Gonzalez**: None; **J. Canete**: None; **J. Scher**: AbbVie, 2, Janssen, 2, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **J. Clemente**: None.

Abstract Number: 1645

Aortic Dilatation and PET/CT Vascular Activity at Diagnosis and 5 Years in an Inception Giant Cell Arteritis (GCA) Cohort

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders I: Imaging

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Aortic dilatation is typically a late complication of giant cell arteritis (GCA) but there are no tools to risk stratify patients at the time of diagnosis. We assessed the prevalence of aortic dilatation at 5 years in an inception giant cell arteritis cohort and assessed the relationship with FDG-PET/CT detected vascular activity at diagnosis, 6 months and 5 years.

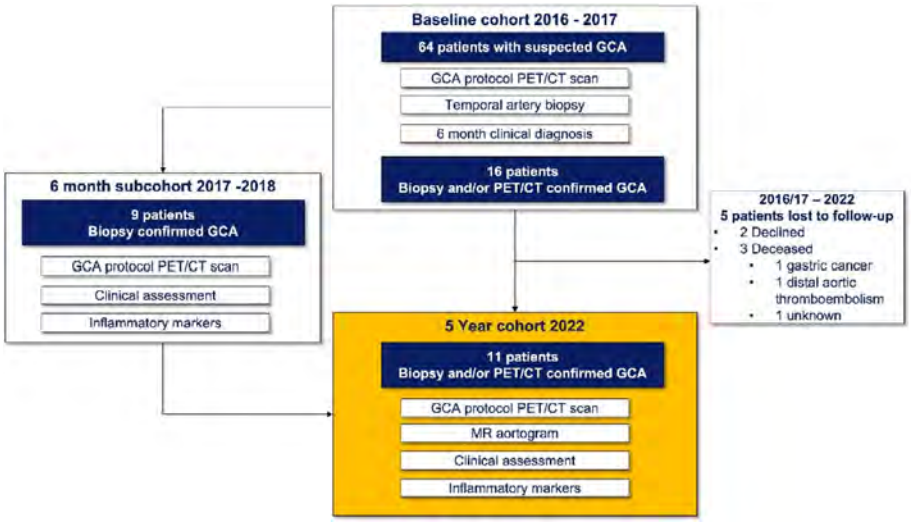

Figure 1: Patient flow

Methods: Patients were eligible for this 5-year study if they had been enrolled in the Giant Cell Arteritis and PET Scan (GAPS) cohort in 2016 or 2017, had a clinical diagnosis of GCA and a positive temporal artery biopsy (TAB) and/or a positive FDG-PET/CT scan at diagnosis. Patients underwent an FDG-PET/CT scan including assessment of cranial and large vessels, non-contrast MRI of the aorta, trans-thoracic echocardiogram (TTE) of the ascending aorta, blood collection and clinical assessment. PET/CT scans were dual reported by 2 blinded nuclear medicine physicians. Scans were reported overall positive or negative for disease activity and a visual grading of FDG avidity in each vascular territory was made with comparison to blood pool. MRI was reported by a single blinded cardiovascular radiologist and thoracic aortic dilatation was defined as external diameter >= 40 mm in ascending or >= 30 mm in the descending aorta.

Results: 16 of the original 64 "suspected GCA" patients in the GAPS cohort met inclusion criteria and 11 participated in the 5-year study (3/16 deceased, 2/16 declined). The median age was 75, 73% were female and all were in clinical and serological remission with a median CRP of 1 (range 1 - 8). 4/11 (36%) patients had aortic dilatation (range 40 - 43mm) and 5/11 (45%) had globally active FDG-PET/CT scans. There was a trend towards a higher median aortic diameter in those with positive scans at 5 years (42 mm vs 35 mm, p=0.08) but aortic avidity at diagnosis did not predict 5-year dilatation. The distribution of FDG-PET/CT detected activity changed from a mix of cranial and large vessel disease at diagnosis to exclusively large vessel disease at 5-years. Aortitis developed in 4 patients who previously had inactive aortas. All 6 patients with inactive scans were taking an immunosuppressive agent (methotrexate, leflunomide, azathioprine or tocilizumab) at 5 years while all patients with active scans were not on therapy (p=0.02). TTE had excellent correlation with MRI for maximum aortic diameter (Pearson's correlation coefficient 0.91).

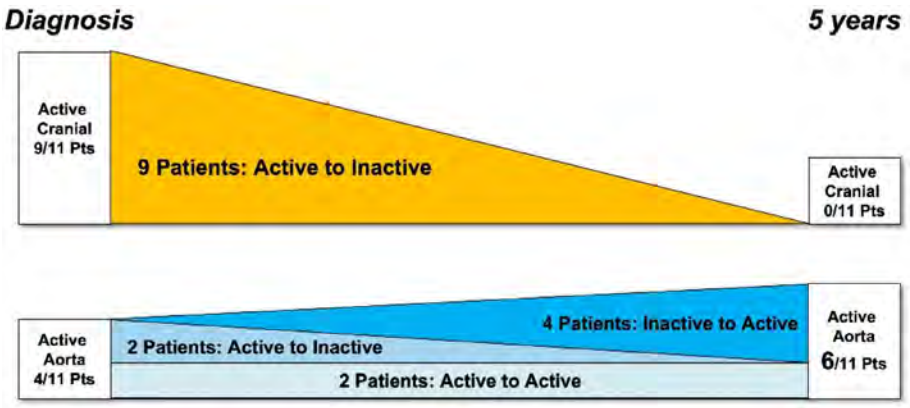

Figure 2: FDG-PET/CT activity by vascular region at diagnosis and 5 years

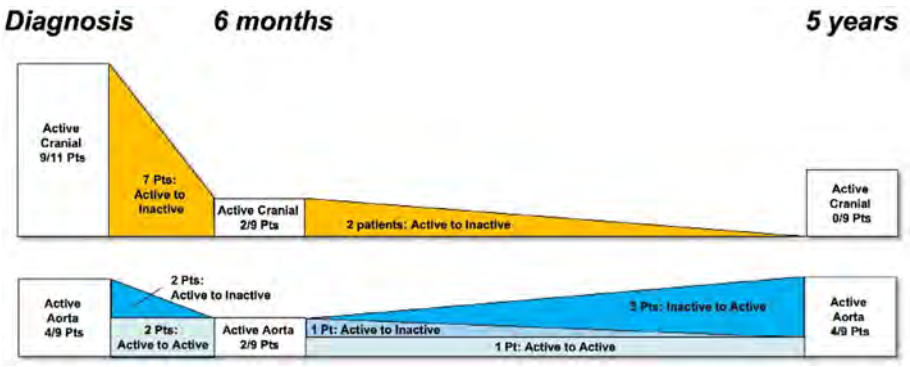

Figure 3: FDG-PET/CT activity by vascular region at diagnosis, 6 months and 5 years (subcohort who underwent 6 month scans)

Conclusion: Aortic dilatation was present in 36% GCA patients at 5 years. The distribution of FDG PET-CT detected avidity changed from predominantly cranial to exclusively large vessel disease and this may explain the lack of association between aortic avidity at diagnosis and dilatation at 5 years. Long-term use of steroid sparing agents may protect against subclinical vascular disease activity. TTE was a reliable screening modality for late aortic dilatation.

Disclosure: A. Sammel: None; **I. Ho Shon**: None; **D. Moses**: None; **F. Stacey**: None; **G. Mathur**: None; **C. Hillenbrand**: None; **E. Hsiao**: None; **S. Geoffrey**: None; **R. Laurent**: None; **E. Wegner**: None.

Abstract Number: 1646

The Real-World Experience of Combined Cranial and Large Vessel FDG-PET/CT in the Investigation of Giant Cell Arteritis

Keren Port[1], Ivan Ho Shon[1], Sally Ayesa[1], Rachel Langford[1], Olivia Bennett[1], Andrew Csillag[1], Stacey Fredericks[1], Luz Palacios-Derflingher[2], Eva Wegner[1] and Anthony Sammel[1], [1]The Prince of Wales Hospital, Sydney, Australia, [2]University of New South Wales, Sydney, Australia

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders I: Imaging
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: GCA is a systemic medium-large vessel vasculitis (M-LVV) involving the cranial arteries, aorta and its major branches. Recent studies have shown that PET/CT including the cranial and large vessels offers high diagnostic accuracy for GCA in research settings. At our institution in Sydney, Australia, PET/CT is the protocolized first-line investigation for GCA, and here we report its diagnostic performance in this "all comer" real world setting.

Methods: We audited all inpatients and outpatients investigated with PET/CT for suspected new onset GCA between July 2019 and March 2022. Patients were scanned from vertex to thighs with arms by their side, 90 minutes post-fluorodeoxyglucose (FDG) administration. Patients completed a self-reported questionnaire at the time of scan. Scans were reported by the experienced nuclear medicine physician of the day as overall positive, equivocal or negative for M-LVV. FDG uptake by vascular region was also reported. The gold standard comparator was the treating clinician's diagnosis of active M-LVV at a minimum of 6 months post the time of the scan. Active M-LVV included diagnoses of GCA, large vessel vasculitis and aortitis. Temporal artery biopsy (TAB) and vascular US results conducted within 4 weeks of scan were recorded.

Results: 135 patients underwent PET/CT for suspected new onset GCA, with a median age of 73 years (range 48-98), 70% were female. 86 (63.7%) patients were taking glucocorticoids at the time of scan. 44 (32.6%) patients had a final clinical diagnosis of active M-LVV. 35 (25.9%) scans were reported as positive, 27 (20%) equivocal and 73 (54.1%) negative for M-LVV. The likelihood ratio for a diagnosis of active M-LVV with a positive scan was 70.3, equivocal scan 0.59, and a negative scan 0.12. Sensitivity (Sn) and specificity (Sp) of PET/CT was dependent on treatment of equivocal scans in the binary analysis. If equivocal scans were excluded, Sn was 89.5% and Sp 98.6%. If equivocal scans were considered positive, Sn was 90.9% and Sp 75.8%. If equivocal scans were considered negative, Sn was 77.3% and Sp 98.9%. 55/135 (40.7%) patients underwent TAB and/or US (27 TAB, 33 US, 5 both TAB and US) as an additional investigation to PET/CT. 13/55 (23.6%) in this cohort had equivocal PET/CT scans, and 11/13 of the additional test (TAB/US) results matched the clinical diagnosis. In the total cohort, TAB had a Sn of 42.9% and Sp of 100%, and US had a Sn range of 53.3% to 66.7% (dependent on

Table 1: Patient baseline characteristics Values are number (%) of patients, except where indicated otherwise PMR = polymyalgia rheumatica TAB = temporal artery biopsy US = vascular ultrasound temporal +/- axillary arteries High dose glucocorticoid use = prednisone ≥40mg oral daily or methylprednisolone ≥500mg IV daily M-LVV = medium-large vessel vasculitis

Baseline characteristic	All patients at time of PET/CT (N=135)	In patients with final clinician diagnosis M-LVV (N=44)
Age median (range), years	73 (48-98)	74.5 (61-90)
Sex, female	95 (70.4%)	29 (65.9%)
Headache	94 (69.6%)	32 (72.7%)
Visual disturbance	67 (49.6%)	17 (38.6%)
Fevers	39 (28.9%)	11 (25.0%)
PMR symptoms	51 (37.8%)	20 (45.5%)
Jaw claudication	26 (19.3%)	14 (31.8%)
Scalp tenderness	43 (31.9%)	17 (38.6%)
Glucocorticoid use	86 (63.7%)	33 (75.0%)
High dose glucocorticoid use	50 (37.0%)	23 (52.3%)
TAB within 4 weeks of PET/CT	27 (20.0%)	7 (15.9%)
US within 4 weeks of PET/CT	33 (24.4%)	15 (34.1%)

Table 2: Overall interpretation of PET/CT compared to clinician final diagnosis

Overall PET/CT interpretation for M-LVV	Clinician final diagnosis M-LVV	Clinician final diagnosis not M-LVV	Total	Post-test probability	Likelihood ratio
Positive	34 (77.3%)	1 (1.1%)	35 (25.9%)	97.1%	70.32
Equivocal	6 (13.6%)	21 (23.1%)	27 (20.0%)	22.2%	0.59
Negative	4 (9.1%)	69 (75.8%)	73 (54.1%)	5.5%	0.12
Total	44 (32.6%)	91 (67.4%)	135		

treatment of the 2 equivocal US) and Sp of 88.9%. For the 34 patients with positive PET/CT scans and a clinical diagnosis of M-LVV, significant FDG uptake was most commonly reported in the supra-aortic (88.2%), followed by cranial (55.9%), aortic (52.9%) and infra-aortic (23.5%) regions.

Table 3: PET/CT performance analysis for clinician final diagnosis of M-LVV, M-LVV = medium-large vessel vasculitis PPV = positive predictive value NPV = negative predictive value CI = confidence interval AUC = area under the receiver operating curve

PET/CT cohort	Total # scans	Sensitivity - 95% CI (%)	Specificity - 95% CI (%)	PPV (%) - 95% CI	NPV (%) - 95% CI	AUC
Equivocal overall scans excluded	108	89.5 (75.2-97.1)	98.6 (92.3-100)	97.1 (85.1-99.9)	94.5 (86.6-98.5)	0.940
Equivocal overall scans included as 'positive for M-LVV'	135	90.9 (78.3-97.5)	75.8 (65.7-84.2)	64.5 (51.3-76.3)	94.5 (86.6-98.5)	0.834
Equivocal overall scans included as 'negative for M-LVV'	135	77.3 (62.2-88.5)	98.9 (94.0-100)	97.1 (85.1-99.9)	90.0 (82.4-95.1)	0.881

Conclusion: This is the largest real-world study of combined cranial and large vessel PET/CT as a first-line test for GCA. PET/CT had good diagnostic performance with sensitivity ranging from 77.3 to 90.9%, and specificity 75.8 to 98.9% for a clinician diagnosis of active M-LVV, dependent on treatment of equivocal scans. TAB and/or US can be used as ancillary tests to help confirm a diagnosis when PET/CT is indeterminate or discordant with the clinical presentation.

Disclosure: K. Port: None; **I. Ho Shon**: None; **S. Ayesa**: None; **R. Langford**: None; **O. Bennett**: None; **A. Csillag**: None; **S. Fredericks**: None; **L. Palacios-Derflingher**: None; **E. Wegner**: None; **A. Sammel**: None.

Abstract Number: 1647

Association Between Vascular FDG Uptake at Diagnosis and Evolution in Aortic Dimensions in Giant Cell Arteritis: A Prospective Study

Lien Moreel[1], Walter Coudyzer[2], Lennert Boeckxstaens[3], Albrecht Betrains[1], Geert Molenberghs[4], Steven Vanderschueren[1], Eveline Claus[2], Koen Van Laere[5] and **Daniel Blockmans**[1], [1]Department of General Internal Medicine, University Hospitals Leuven, Department of Microbiology, Immunology, and Transplantation, KU Leuven, Leuven, Belgium, [2]Department of Radiology, University Hospitals Leuven, Leuven, Belgium, [3]Department of Nuclear Medicine, University Hospitals Leuven, Leuven, Belgium, [4]Interuniversity Institute for Biostatistics and Statistical Bioinformatics (I-BioStat), University of Leuven and Hasselt University, Leuven, Belgium, [5]Department of Nuclear Medicine, University Hospitals Leuven,Department of Imaging and Pathology, Nuclear Medicine and Molecular Imaging, KU Leuven, Leuven, Belgium

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders I: Imaging

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Patients with giant cell arteritis (GCA) have an increased risk of developing thoracic aortic aneurysms. Retrospective studies have shown that ^{18}F-fluorodeoxyglucose (FDG) uptake in large vessels at diagnosis increases the risk of developing aortic complications during follow-up. The aim of this study was to prospectively evaluate the association between FDG uptake in large vessels at diagnosis and the evolution of aortic diameter and volume in GCA patients.

Methods: GCA patients who have had FDG positron emission tomography (PET) imaging at diagnosis ≤3 days after initiation of glucocorticoids and who were prospectively followed for ≥2 years were included. PET scans were semi quantitatively scored (0-3) at 7 vascular areas and a total vascular score (TVS) was calculated, ranging from 0 to 21. PET scans were

Table 1: Evolution of the aortic diameters (in mm) and volumes (in cm^3) in 5 years in patients with (PET positive) and without (PET negative) FDG uptake ≥ grade 2 in any large vessel. The linear mixed models were adjusted for age, sex, AORTA score, CT or PET/CT scan, and intravenous contrast. Abbreviations: 95% CI, 95% confidence interval; CT, computed tomography; FDG, fluorodeoxyglucose; PET, positron emission tomography

	5-year progression (95% CI)		Difference in 5-year progression (95% CI)	P-value
	PET negative	PET positive		
Volume of thoracic aorta	12.59 (-1.44-26.61)	32.88 (24.34-41.47)	20.29 (4.07-36.57)	0.01
Volume of abdominal aorta	0.97 (-2.80-4.81)	0.94 (-1.25-3.19)	-0.04 (-4.35-4.26)	0.99
Diameter of thoracic aorta				
○ **Ascending aorta**	0.45 (-0.56-1.45)	1.98 (1.36-2.60)	1.53 (0.36-2.70)	0.01
○ **Aortic arch**	1.02 (0.25-1.79)	1.75 (1.28-2.23)	0.73 (-0.15-1.62)	0.11
○ **Descending aorta**	0.50 (-0.31-1.31)	1.72 (1.23-2.22)	1.22 (0.28-2.16)	0.01
Diameter of abdominal aorta				
○ **Suprarenal aorta**	0.13 (-0.36-0.64)	0.57 (0.28-0.88)	0.44 (-0.13-1.01)	0.13
○ **Juxtarenal aorta**	0.60 (0.05-1.15)	0.65 (0.31-0.98)	0.04 (-0.59-0.68)	0.89
○ **Infrarenal aorta**	0.68 (0.30-1.07)	0.35 (0.13-0.58)	-0.33 (-0.77-0.11)	0.14

considered positive in case of FDG uptake ≥ grade 2 in any large vessel. Patients underwent computed tomography (CT) imaging at diagnosis and yearly thereafter for a maximum of 10 years. The association between vascular FDG uptake and aortic dimensions was estimated by linear mixed effect models with random intercept and slope in time adjusted for age, sex, AORTA score, CT or PET/CT scan and intravenous contrast. The ascending aorta, aortic arch, and descending aorta were considered aneurysmatic when the diameter was ≥45, ≥40, and ≥35 mm, respectively.

Results: Hundred patients (mean age 70 years, 68% females) were included, of which 74 (74%) had FDG uptake ≥ grade 2 in any large vessel. The 2022 ACR/EULAR GCA criteria were fulfilled in 89 (89%) patients. Median follow-up was 80 months (IQR 47-110). The increase in ascending and descending aortic diameter and in thoracic aortic volume was higher in patients with a positive PET scan compared to those without (difference in 5-year progression 1.53 mm [95%CI 0.36-2.70 mm],

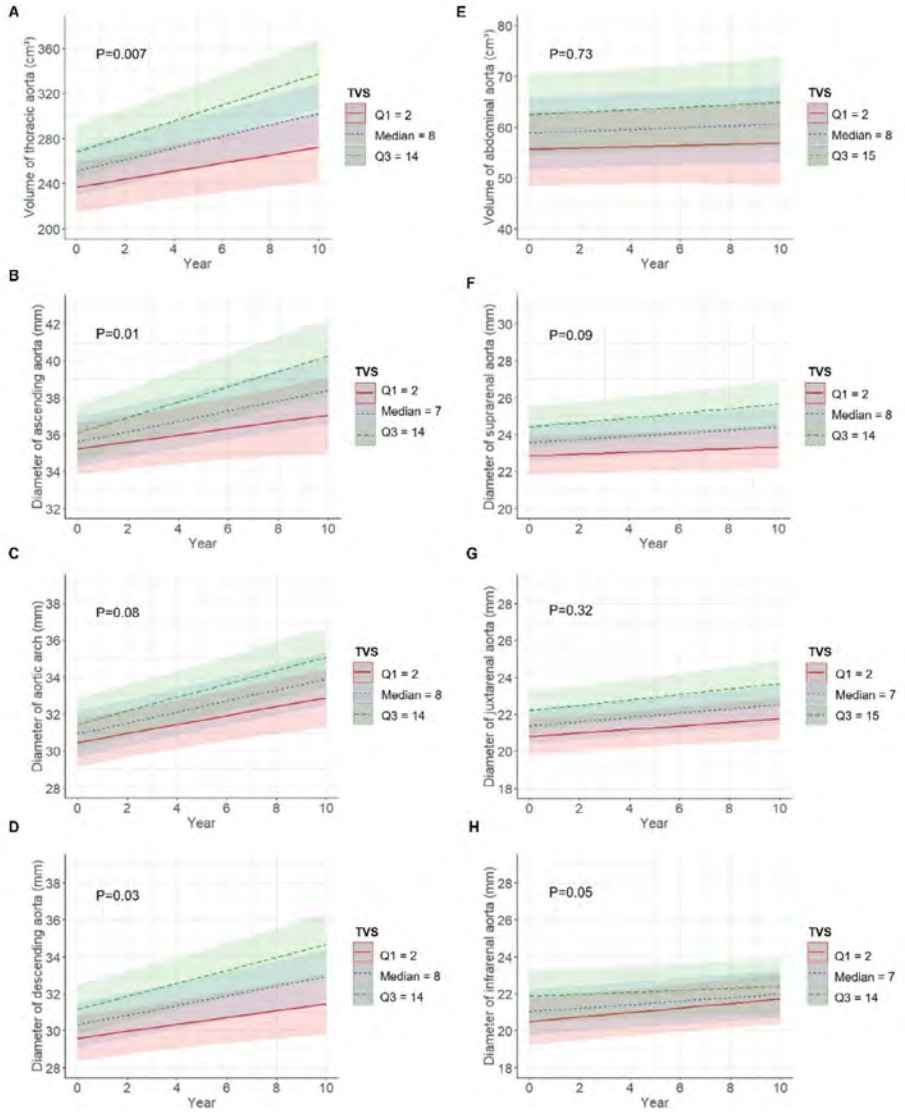

Figure 1: Linear mixed model analysis of the association between the total vascular score and the evolution in aortic dimensions. The x-axis represents the time (in years) since the diagnosis. The y-axis represents the size of the aorta: A. volume of thoracic aorta (in cm^3), B. diameter of ascending aorta (in mm), C. diameter of aortic arch (in mm), D. diameter of descending aorta (in mm), E. volume of abdominal aorta (in cm^3), F. diameter of suprarenal aorta (in mm), G. diameter of juxtarenal aorta (in mm), and H. diameter of infrarenal aorta (in mm). The lines and bands represent the mean trajectory and 95% confidence interval of each subgroup. The red solid line represents the first quartile of the total vascular score, the blue dotted line the median and the green dashed line the third quartile. The linear mixed models were adjusted for age, sex, AORTA score, CT or PET/CT scan, and intravenous contrast. Abbreviations: CT, computed tomography; PET, positron emission tomography; TVS, total vascular score

1.22 mm [95%CI 0.28-2.16 mm] and 20.29 cm^3 [95%CI 4.07-36.57 cm^3], respectively) (**Table 1**). These thoracic aortic dimensions were also significantly associated with TVS (**Figure 1**). FDG uptake was not associated with an increase in abdominal aortic diameters nor volume. Patients with a positive PET scan had a higher risk of developing thoracic aortic aneurysms (aHR 13.61, 95%CI 1.63-113.50) with a median time since diagnosis of 40 months (IQR 18-61). Thoracic aortic aneurysm developed in 13 of the 15 (87%) patients in a region with elevated FDG uptake at diagnosis. Two patients with high TVS (15 and 16) needed surgery for ascending aortic aneurysm.

Conclusion: Higher TVS was associated with greater yearly increase in thoracic aortic dimensions. Vascular FDG uptake at diagnosis was an independent risk factor for developing thoracic aortic aneurysm in GCA patients. Performing PET imaging at diagnosis may help to estimate the future risk of aortic aneurysm formation. Follow-up of aortic dimensions may be warranted in patients with thoracic aortic FDG uptake or high TVS.

Disclosure: L. Moreel: None; **W. Coudyzer**: None; **L. Boeckxstaens**: None; **A. Betrains**: None; **G. Molenberghs**: None; **S. Vanderschueren**: None; **E. Claus**: None; **K. Van Laere**: None; **D. Blockmans**: None.

Abstract Number: 1648

EULAR Recommendations for the Use of Imaging in Large Vessel Vasculitis in Clinical Practice: 2023 Update

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SESSION INFORMATION

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Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders I: Imaging

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Table 1. Recommendations for the use of imaging in large vessel vasculitis in clinical practice

Overarching principles
A. In patients with suspected GCA, an early imaging test is recommended to support the clinical diagnosis of GCA, assuming high expertise and prompt availability of the imaging technique. Imaging should not delay initiation of treatment.
B. Imaging examination should be done by a trained specialist using appropriate equipment, standardized operational procedures and settings.
C. In patients in whom there is a high clinical suspicion of GCA and a positive imaging result, the diagnosis of GCA may be made without an additional test (biopsy or further imaging). In patients with a low clinical probability and a negative imaging result, the diagnosis of GCA can be considered unlikely. In all other situations (including the case of an inconclusive imaging result), additional efforts towards a diagnosis are necessary.
Recommendations
1. Ultrasound of temporal and axillary arteries should be considered as the first imaging modality to investigate mural inflammatory changes in patients with suspected GCA.
2. High resolution MRI or FDG-PET can be used as alternatives to ultrasound for the assessment of cranial arteries in patients with suspected GCA.
3. FDG-PET, alternatively MRI or CT, can be used for the detection of mural inflammation or luminal changes of extracranial arteries in patients with suspected GCA.
4. In patients with suspected TAK, MRI to investigate mural inflammation or luminal changes should be used as the first imaging test to make a diagnosis of TAK.
5. FDG-PET, CT or ultrasound may be used as alternative imaging modalities in patients with suspected TAK. Ultrasound is of limited value for assessment of the thoracic aorta.
6. Conventional angiography is not recommended for the diagnosis of GCA or TAK as it has been superseded by the previously mentioned imaging modalities.
7. In case of a suspected relapse of GCA or TAK, particularly when laboratory markers of disease activity are unreliable, ultrasound, FDG-PET or alternatively MRI may be considered for the assessment of vessel abnormalities. Imaging is not routinely recommended for patients in clinical and biochemical remission.
8. In patients with GCA or TAK, MRA, CTA or ultrasound of extracranial vessels may be used for long-term monitoring of structural damage, particularly at sites of preceding vascular inflammation. The frequency of screening as well as the imaging method applied should be decided on an individual basis.

Background/Purpose: Imaging recommendations for primary large vessel vasculitis (LVV) were developed in 2018. Several new studies have emerged since then, and an update of the original statements was required. The objective of this project was to update the recommendations for the use of imaging in LVV.

Methods: A systematic literature review update was performed to retrieve new evidence on ultrasound (US), magnetic resonance imaging (MRI), computed tomography (CT) and [18F]-fluorodeoxyglucose positron emission tomography (FDG-PET) for diagnosis, monitoring and outcome prediction in LVV. The task force consisted of 24 physicians, health professionals and patients from 14 countries.

Results: Three overarching principles and eight recommendations were agreed (Table 1). Compared to the 2018 version, US is now recommended as first line imaging test in all patients with suspected GCA, and axillary arteries should be included in the standard examination. As an alternative to US, cranial and extracranial arteries can be examined by FDG-PET or MRI. For Takayasu arteritis, MRI is the preferred imaging modality; CT or FDG-PET are alternatives. Although imaging is not routinely recommended for follow-up, US, FDG-PET or MRI may be used for assessing vessel abnormalities in LVV patients with suspected relapse, particularly when laboratory markers of inflammation are unreliable. MRA, CTA or US may be used for long-term monitoring of structural damage, particularly at sites of preceding vascular inflammation.

Conclusion: The 2023 recommendations provide up-to-date guidance for the role of imaging in the diagnosis and assessment of patients with (suspected) LVV.

Disclosure: C. Dejaco: AbbVie/Abbott, 2, 5, 6, Amgen, 6, Eli Lilly, 2, 6, Galapagos Pharma, 2, 6, Janssen, 1, Novartis, 2, 5, 6, Pfizer, 6, Sparrow, 2; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, Galapagos, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, UCB Pharma, 2, 5; **M. Bond**: AbbVie/Abbott, 5; **P. Bosch**: Janssen, 6, 12, Congress fees, Pfizer, 5; **C. Ponte**: None; **S. Mackie**: AbbVie/Abbott, 2, AstraZeneca, 2, GlaxoSmithKlein(GSK), 3, 12, Investigator, National Institute for Health and Care Research, 5, 12, investigator on STERLING-PMR trial, funded by NIHR; patron of the charity PMRGCAuk, Pfizer, 2, 6, Roche, 2, 6, 12, Support from Roche/Chugai to attend EULAR2019 in person, Sanofi, 2, 12, Investigator, Sparrow, 12, Investigator, UCB and Novartis, 6, Vifor, 6; **T. Bley**: None; **D. Blockmans**: None; **S. Brolin**: Novartis, 5; **E. Bolek**: None; **R. Cassie**: None; **M. Cid**: AbbVie/Abbott, 1, 2, 6, AstraZeneca, 1, GSK, 1, 2, 6, Kininksa

Pharmaceutical, 5, SCL-Vifor, 2, 6; **J. Molina-Collada**: None; **B. Dasgupta**: AbbVie/Abbott, 2, 5, Chugai, 2, 5, Novartis, 2, 5, Roche, 2, 5, Sanofi, 2, 5; **B. Dalsgaard Nielsen**: None; **E. De Miguel**: None; **H. Direskeneli**: AbbVie/Abbott, 1, 5, 6, Amgen, 6, celltrione, 1, 6, Pfizer, 5, 6, Roche, 12, Educational, UCB, 5, 6, 12, Educational; **C. Duftner**: Abbvie, 2, 6, AOP Orphan, 2, 6, AstraZeneca, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 5, 6, Galapagos Pharma, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 5, 6, Roche, 2, 6, Sandoz, 2, 6, UCB, 2, 5, 6, Vifor, 2, 6; **A. Hocevar**: None; **A. Molto**: None; **V. Schäfer**: None; **L. Seitz**: None; **R. Slart**: None; **W. Schmidt**: AbbVie/Abbott, 1, 5, 6, Amgen, 1, 6, Bristol-Myers Squibb(BMS), 6, Chugai, 6, GlaxoSmithKlein(GSK), 1, 5, 6, Janssen, 6, Medac, 6, Novartis, 1, 5, 6, Roche, 6, UCB, 6.

Abstract Number: 1649

Follow-up Ultrasound Examination in Patients with Newly Diagnosed Giant Cell Arteritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders I: Imaging

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: In recent years, ultrasound has become a standard tool in the diagnosis of giant cell arteritis (GCA). Typical findings are increased intima media thickness (IMT) of the temporal and other arteries, caused by inflammation. To date, only few studies evaluated the role of ultrasound in follow-up and monitoring of GCA. [1,2] The purpose of this study was to prospectively evaluate changes of IMT of cranial and extra-cranial arteries during a 12-month follow-up of newly diagnosed GCA patients.

Methods: We prospectively enrolled patients with a new diagnosis of GCA who received glucocorticoid (GC) therapy up to seven days. Patients underwent ultrasound examinations of the axillary, carotid, vertebral, facial, and temporal arteries. IMT, total number of affected arteries, and the Omeract GCA ultrasonography score (OGUS)[3], alongside laboratory parameters, current GC dose, and GCA symptoms were evaluated at baseline, after three, six, nine and 12 months. Additionally, a

Table 1. reduction of intima media thicknesses (IMT) over the follow-up time compared to baseline IMT

	Axillary artery		Carotid artery		Vertebral artery		Common temporal artery		Frontal temporal artery		Parietal temporal artery		Facial artery	
	ß	p	ß	p	ß	p	ß	p	ß	p	ß	p	ß	p
Baseline	1.11		1.18		0.83		0.54		0.39		0.40		0.48	
After 3 months	-0.18	<0.001	-0.17	<0.001	-0.32	<0.001	-0.11	<0.001	-0.07	<0.001	-0.09	<0.001	-0.10	<0.001
After 6 months	-0.26	<0.001	-0.21	<0.001	-0.34	<0.001	-0.17	<0.001	-0.11	<0.001	-0.13	<0.001	-0.13	<0.001
After 9 months	-0.23	<0.001	-0.20	<0.001	-0.35	<0.001	-0.18	<0.001	-0.11	<0.001	-0.12	<0.001	-0.14	<0.001
After 12 months	-0.18	<0.001	-0.19	<0.001	-0.36	<0.001	-0.21	<0.001	-0.13	<0.001	-0.14	<0.001	-0.15	<0.001

IMT: intima media thickness

p: p-value, values<0.05 indicates significant changes in IMT compared to baseline

ß: absolute reduction in IMT compared to baseline

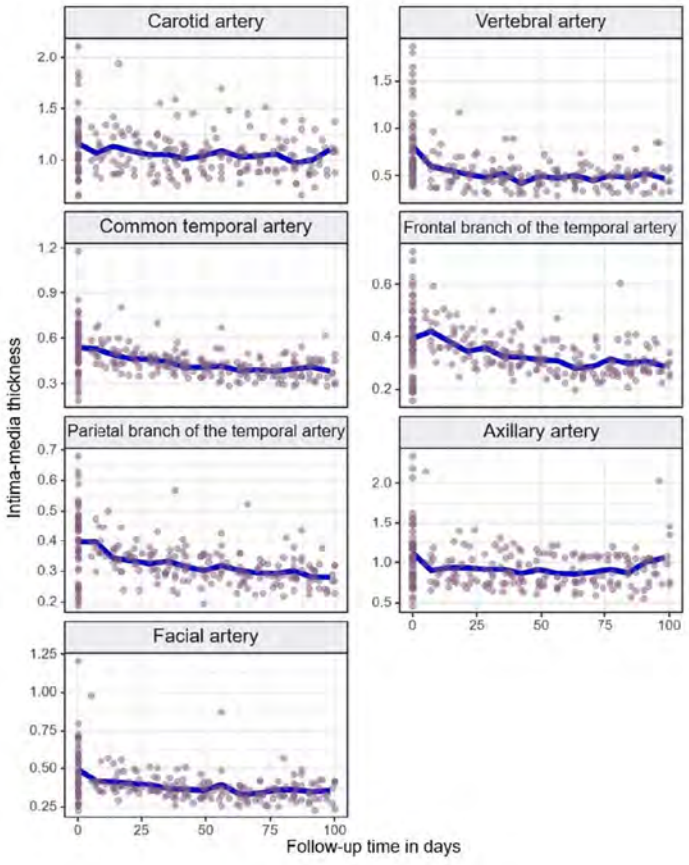
Table 2. Changes in number of affected arteries and in provisional OMERACT GCA ultrasonography score (OGUS) at respective follow-up time compared to baseline

	Mean number of all affected arteries		Mean number of large affected arteries		Mean number of medium-sized affected arteries		OGUS	
	N	p	n	p	n	p	n	p
Baseline	8.5		7.9		7.7		1.27	
After 3 months	5.1	<0.001	4.7	<0.001	4.6	<0.001	1.01	<0.001
After 6 months	3.2	<0.001	2.9	<0.001	2.9	<0.001	0.91	<0.001
After 9 months	2.9	<0.001	2.6	<0.001	2.6	<0.001	0.91	<0.001
After 12 months	2	<0.001	1.8	<0.001	1.8	<0.001	0,87	<0.001

GCA: giant cell arteritis; OGUS: provisional OMERACT GCA ultrasonography score; p: p-value, values<0.05 are statistically significant; n: number of affected arteries/ OGUS at respective follow-up time; OGUS: provisional OMERACT GCA ultrasonography score; Large arteries: axillary artery, carotid artery, vertebral artery; Medium-sized arteries: superficial temporal artery with parietal and frontal branch, facial artery

subgroup of patients underwent weekly exams during the first 100 days. We conducted further sub-analyses to compare ultrasound findings between patients with GCA versus GCA plus polymyalgia rheumatica (PMR), and between patients receiving GC therapy only and those receiving GC plus tocilizumab.

Figure 1. Changes in intima media thickness (IMT) within the first 100 days



Vertical: Intima-media thickness (IMT), horizontal: follow-up time in days, the blue line indicates the mean values that were observed for each time point. Each point indicates one examination.

Results: Fifty patients were enrolled, 36 completed the 12-months follow-up. The cohort consisted of 23 (46%) females at a mean age of 73.6 years (SD ±8.3). The mean GC intake at baseline was 130 mg (SD ±266) at a mean of 1.7 days (SD ±2.5). In 18 patients, up to weekly exams were performed. Figure 1 displays the changes in mean IMT of all examined arteries in the first 100 days. The mean IMT of the axillary and temporal artery were normal after seven and 50 days, respectively. After six months, mean IMT of all examined arteries and OGUS were below published cut-off values.[3,4,5] During the follow-up period, we observed a significant and consistent decrease in mean IMT, total number of affected arteries and OGUS (Table 1 and 2). After termination of GC therapy, follow-up visits were continued and no increase of ultrasound parameters was observed. Additionally, we found no significant differences in the reduction of these parameters between patients with GCA only and those with GCA and polymyalgia rheumatica (PMR), as well as between patients receiving GC therapy only and those receiving additional tocilizumab therapy.

Conclusion: IMT, OGUS and the total number of affected arteries decreased significantly over a 12-months follow-up period under GC with/without immunosuppressive treatment. In the first 100 days, the mean IMT of the axillary artery was found to decrease the fastest, while the mean IMT of the temporal artery was elevated for up to 50 days. Especially, the parameters did not increase after end of GC therapy. Our study underlines the important role of ultrasound examinations in monitoring of GCA.

References:

1. Bosch P et al., Therapeutic advances in musculoskeletal disease 2021; 13:1759720X21998505.
2. Ponte C et al., Ann Rheum Dis 2021; 80(11):1475–82.
3. Dejaco C et al., Ann Rheum Dis 2022.
4. Schäfer VS et al., Rheumatology (Oxford) 2017; 56(9):1479–83.
5. Ješe R et al., Rheumatology (Oxford) 2021; 60(3):1346–52.

Disclosure: L. Burg: None; **C. Dejaco**: AbbVie/Abbott, 1, 5, 6, Eli Lilly, 6, Galapagos Pharma, 1, 6, Janssen, 1, 6, Novartis, 1, 6, Pfizer, 6, Sparrow, 1; **P. Karakostas**: None; **C. Behning**: None; **P. Brossart**: None; **V. Schäfer**: None.

Abstract Number: 1650

Optic Nerve Sheath Measurement as a Disease Activity Biomarker in Giant Cell Arteritis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders I: Imaging
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Recently, optic nerve sheath (ONS) enhancement using contrast-enhanced magnetic resonance imaging of the brain and orbits was observed in most patients with biopsy-proven GCA. In addition, we recently showed that ONS diameter (ONSD) and ONS thickness (ONST) measured by ultrasound are increased in patients with new-onset, active GCA. The objective of this study is to assess whether ONSD and ONST measurements improve when clinical remission is achieved in patients with GCA.

Table 1 – Clinical features and treatments at diagnosis (active GCA) and month 3 (clinical remission) of 9 patients with new-onset GCA.

GCA features	Diagnosis (month 0)	Follow-up (month 3)
Symptoms, n (%)		
Headache	7 (78)	0 (0)
Scalp tenderness	4 (44)	0 (0)
Constitutional symptoms	4 (44)	1 (11)
Jaw claudication	5 (56)	0 (0)
PMR	3 (33)	0 (0)
Diplopia	1 (11)	0 (0)
Amaurosis fugax	1 (11)	0 (0)
Complete vision loss	4 (44)	3 (33)
Physical examination, n (%)		
Abnormal temporal artery exam	5 (56)	0
AION	4 (66.7)	N/A
Inflammatory markers, median (IQR)		
C-reactive protein (mg/L)	60 (41 – 88)	4 (3 – 23)
ESR (mm/h)	62.5 (58 – 64)	21 (13 – 32)
GC dosage (prednisone equivalent)		
Days on GC prior to assessment, median (IQR)	5 (2 – 6)	106 (98 – 107)
GC dose at assessment (mg), median (IQR)	50 (50 – 50)	15 (10 – 25)
Intravenous methylprednisolone, n (%)	5 (56)	N/A
Immunosuppressive therapies, n (%)		
Tocilizumab	0	5 (56)
Methotrexate	0	0
Leflunomide	0	1 (11)

GCA: Giant cell arteritis, PMR: polymyalgia rheumatica, AION: anterior ischemic optic neuropathy, N/A: not applicable, IQR: interquartile range, ESR: erythrocyte sedimentation rate, GC: glucocorticoid

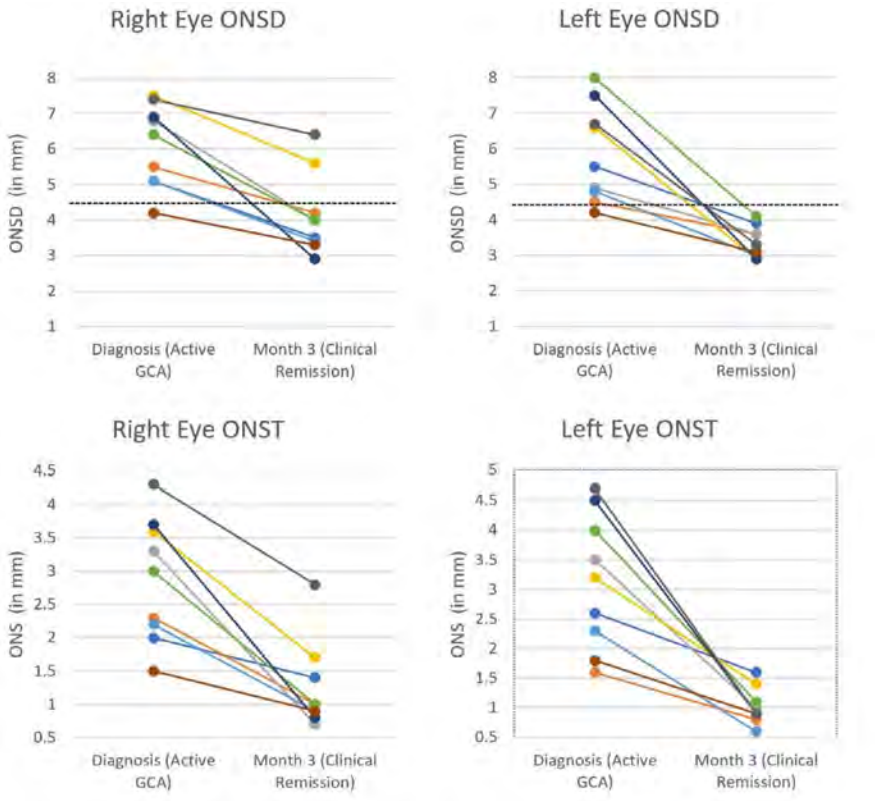
Methods: A prospective inception cohort study was conducted at the vasculitis clinic of Sacre-Coeur Hospital, in Montreal, Canada, from June 2022 to January 2023. Patients who had an optic nerve (ON) ultrasound at GCA diagnosis as part of a previous cross-sectional study were approached. Participants in clinical remission after 3 months of therapy were included if (1) ON ultrasound had successfully been performed at the time of GCA diagnosis, (2) GCA was confirmed on color doppler ultrasound (CDUS) of temporal/axillary arteries, (3) they satisfied the 2022 ACR/EULAR classification criteria for GCA.

At month 3, a standardized clinical assessment, bloodwork, CDUS of temporal/axillary arteries and ON ultrasound were performed. ON ultrasound was performed by the same investigator at diagnosis and month 3, unblinded to clinical information. Ultrasound measurements were performed for both eyes, 3mm distal to the posterior aspect of the ocular globe. Optic nerve sheath diameter (ONSD, includes ON and its sheath) and optic nerve diameter (OND) were measured. Optic nerve sheath thickness (ONST) was obtained by subtracting OND from ONSD.

Table 2 – Comparison of Optic Nerve Measurements on ultrasound at diagnosis (active GCA) and month 3 (clinical remission) in 9 patients with new-onset GCA.

Measurements (in mm), mean (SD)	Diagnosis (month 0)	Follow-up (month 3)	Mean difference (M0-M3)	95% CI	*P* value
Right ONSD	6.10 (1.16)	4.14 (1.14)	1.96 (0.98)	1.20 – 2.71	< 0.001
Left ONSD	5.86 (1.38)	3.38 (0.44)	2.48 (1.41)	1.39 – 3.56	< 0.001
Right OND	3.22 (0.35)	2.90 (0.66)	0.32 (0.50)	-0.06 – 0.70	0.09
Left OND	2.72 (0.76)	2.37 (0.43)	0.36 (0.89)	-0.33 – 1.04	0.26
Right ONST	2.88 (0.93)	1.24 (0.66)	1.63 (0.80)	1.02 – 2.25	< 0.001
Left ONST	3.13 (1.14)	1.02 (0.31)	2.11 (1.15)	1.23 – 2.99	< 0.001

GCA: Giant cell arteritis, CI: confidence interval, SD: Standard deviation, ONSD: Optic nerve sheath diameter, OND: Optic nerve diameter, ONST: Optic nerve sheath thickness



Dotted line: threshold of ONSD ≤ 4.5mm is considered normal in healthy adults.
ONSD: optic nerve sheath diameter, ONST: optic nerve sheath thickness, GCA: giant cell arteritis

Figure 1. Evolution of ONSD and ONST Measurements on Ultrasound from diagnosis (active GCA) to Month 3 (clinical remission) in 9 patients with new-onset GCA.

Descriptive statistics for baseline characteristics and paired sample t-test were performed to assess the mean difference in OND, ONSD, and ONST between diagnosis and month 3. One-Way ANOVA was used to explore the association between clinically persistent vision defect at month 3 and ON ultrasound measurements.

Results: Nine patients with a diagnosis of GCA were included in our study. The median age at disease onset was 79 years (interquartile range (IQR) of 79 – 82 years) and 7 patients were males. All patients were in clinical remission at month 3. GCA characteristics and therapy at diagnosis and month 3 are presented in table 1.

There was strong evidence that the mean ONSD and ONST measured in millimeters were lower at month 3 (clinical remission) than at diagnosis (active GCA) for both eyes (table 2, figure 1). Furthermore, in 7/9 patients, ONSD decreased below 4.5mm (considered normal in healthy adults). As anticipated, OND measurements did not vary between diagnosis and month 3. There was no evidence of an association between persistent vision defect at month 3 and mean difference in ONSD and ONST measurements.

Conclusion: In patients with active, new-onset GCA, we demonstrated that ONSD and ONST measured on ultrasound improved with therapy. Thus, ONSD and ONST may be dynamic biomarkers in GCA and allow detection of disease relapse. These findings and hypothesis will be addressed in a larger, longer prospective trial (ClinicalTrials.gov id: NCT05749094).

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Abstract Number: 1651

Beneficial Effect of Temporary Methotrexate Interruption on B and T Cell Responses upon SARSCoV-2 Vaccination in Patients with Rheumatoid Arthritis or Psoriatic Arthritis

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SESSION INFORMATION

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Session Title: Abstracts: Interprofessional Exemplary

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Background/Purpose: Previous published works have raised the concern that methotrexate (MTX) might have a negative effect on immune response upon vaccine administration. At the beginning of the COVID-19 vaccination campaigns, there were controversial opinions regarding the possibility of temporary interrupting immunomodulatory treatments in rheumatic patients.

The objective of this study was to evaluate B and T cell responses in patients with rheumatoid arthritis (RA) or psoriatic arthritis (PsA) after 1 or 2 weeks of MTX withdrawal following each COVID-19 vaccine dose and compare them with that of those who maintained MTX unchanged.

Methods: This is a single-centre, randomised, prospective study. Adult RA and PsA patients treated with MTX were recruited and randomly assigned to 3 groups: MTX-maintenance (n=72), MTX-withdrawal for 1 week (n=71) or MTX-withdrawal for 2 weeks (n=73) after each vaccine dose. Samples were collected before and 30 days after complete vaccination in 2021. Multi-antigen cytometric bead array assays to detect specific antibodies to several SARS-CoV-2 antigens and ELISPOT assays measuring interferon (IFN)-γ and interleukin (IL)-21 were performed. Multivariable analyses were used to control the effect of possible confounding variables.

Results: The study population consisted of 216 patients (178 RA and 38 PsA), of which 47 had COVID-19 before vaccination. Participants were vaccinated with BNT162b2 (71%), ChadOX-1-S (14%), mRNA-1273 (6%) and Ad26.COV2.S (9%). Population characteristic are shown in Table 1. The types of COVID vaccines, the vaccine protocols and the occurrence of COVID, prior and after vaccination, as well as the differences of these variables across groups are shown in Table 2. MTX withdrawal in patients without previous COVID-19 was associated with higher levels of anti-RBD IgG (p=0.01) and neutralising antibodies (p=0.004), especially in the 2-week withdrawal group and with higher IFN-γ secretion upon stimulation with pools of SARS-CoV-2 S peptides (p< 0.001). Interestingly, no significant differences in the number of RA/PsA relapses were detected across groups (Table 2).

Conclusion: Our data indicate that a brief MTX interruption following COVID-19 vaccination doses in patients with RA or PsA improves humoral and cellular immune responses, without significant increase of relapses, especially in patients without previous infection.

	MTX-m	MTX-1ww	MTX-2ww	
POPULATION CHARACTERISTICS	n= 72	n= 71	n= 73	p-value
Age	57 (48-63)	57 (45-67)	56 (47-69)	0.79
Sex (female)	57 (79.2)	58 (81.7)	58 (79.5)	0.92
Ethnicity (Caucasian)#	64 (88.9)	63 (88.7)	57 (78.1)	0.24
Rheumatoid arthritis	59 (81.9)	58 (81.7)	61 (83.6)	0.13
Psoriatic Arthritis	13 (18.1)	13 (18.3)	12 (16.4)	0.95
MTX dose (mg/week)	15 (10-17.5)	15 (10-15)	15 (10-17.5)	0.71
DAS28	2.3 (1.7-3.2)	2.1 (1.5-3)	2.3 (1.6-3.1)	0.58
CRP (mg/dL)	0.2 (0.1-0.4)	0.2 (0.1-0.3)	0.2 (0.1-0.5)	0.12
Lymphocyte count (10^3/mm^3)	1865 (1465-2440)	2020 (1520-2440)	2010 (1595-2315)	0.70
Biologic DMARDs	19 (26.4)	22 (31)	26 (35.6)	0.49
TNF inhibitors	16 (22.2)	20 (28.2)	19 (26)	__
IL-6 inhibitors	2 (2.8)	2 (2.8)	5 (6.8)	__
IL-17 inhibitors	1 (1.4)	1 (1.4)	1 (1.4)	__
Rituximab	0 (0)	0 (0)	1 (1.4)	__
Other csDMARDs	12 (16.7)	12 (16.9)	13 (17.8)	0.95
Hydroxycloroquine	5 (6.9)	3 (4.2)	3 (4.1)	__
Sulphasalazine	3 (4.2)	4 (5.6)	3 (4.1)	__
Leflunomide	4 (5.6)	5 (7)	7 (9.9)	__
tsDMARDs	4 (5.6)	3 (4.2)	2 (2.7)	0.65
Tofacitinib	0 (0)	2 (2.8)	0 (0)	__
Baricitinib	4 (5.6)	1 (1.4)	1 (1.4)	__
Upadacitinib	0 (0)	0 (0)	1 (1.4)	__
Glucocorticoids	7 (9.7)	9 (12.7)	13 (17.8)	0.40
Average dose of GC (mg/day)	5 (2.5-10)	3.8 (2.5-6.2)	3.8 (2.5-5.0)	0.70

All categorical variables are expressed as absolute count (percentage) and quantitative variables as median (IQR). Statistical significance was determined by using ANOVA or Kruskal Wallis for quantitative and chi-square or Fisher exact test for qualitative variables. #Other non-Caucasian ethnicities included: Hispanic, Arabian and 1 Afro-American. MTX, methotrexate; ; MTX-m, methotrexate maintenance; MTW-1ww, 1 week of MTX withdrawal; MTX-2ww, 2 weeks of MTX withdrawal; DAS28, disease activity score in 28 joints; CRP, C-reactive protein; DMARDs, disease-modifying antirheumatic drugs; csDMARDs, conventional synthetic DMARDs; tsDMARDs, targeted synthetic DMARDs; GC, glucocorticoids; COVID-19, coronavirus disease 2019 caused by the SARS-CoV-2 virus; RA, rheumatoid arthritis; PsA, psoriatic arthritis.

	MTX-m	MTX-1ww	MTX-2ww	
COVID VACCINES	n= 72	n= 71	n= 73	p-value
Type of vaccine				0.15
One dose of BNT162b2	4 (5.6)	3 (4.2)	8 (11)	__
Two doses of BNT162b2	47 (65.3)	44 (62)	47 (64.4)	__
One dose of ChAdOx-1-S	1 (1.4)	0 (0)	0 (0)	__
Two doses of ChAdOx-1-S	11 (15.3)	13 (18.3)	5 (6.8)	__
One dose of mRNA-1273	0 (0)	1 (1.4)	1 (1.4)	__
Two doses of mRNA-1273	5 (6.9)	1 (1.4)	6 (8.2)	__
One dose of Ad26.COV2.S	4 (5.6)	9 (12.7)	6 (8.2)	__
Days between vaccine doses	21 (21-29)	21 (21-28)	21 (21-25)	0.91
Days post-vaccination	28 (28-35)	29 (28-35)	29 (28-35)	0.85
COVID-19				
COVID-19 pre-vaccination, n (%)	18 (25)	10 (14.1)	12 (16.4)	0.21
COVID-19 after 1st dose, n (%)	3 (4.2)	1 (1.4)	3 (4.1)	__
DISEASE RELAPSE AFTER COVID VACCINE				
RA/PsA relapse, n (%)	7 (9.7)	8 (11.3)	11 (15.1)	0.60
Mild	5 (7)	5 (7)	8 (11)	__
Moderate	2 (2.8)	3 (4.2)	3 (4.1)	__

All categorical variables are expressed as absolute count (percentage) and quantitative variables as median (IQR). Statistical significance was determined by using ANOVA or Kruskal Wallis for quantitative and chi-square or Fisher exact test for qualitative variables. MTX, methotrexate; MTX-m, methotrexate maintenance; MTW-1ww, 1 week of MTX withdrawal; MTX-2ww, 2 weeks of MTX withdrawal; RA, rheumatoid arthritis; PsA, psoriatic arthritis.

Disclosure: E. Vicente Rabaneda: None; **P. Martínez-Fleta**: None; **A. Triguero-Martínez**: None; **E. Roy**: None; **M. Uriarte-Ecenarro**: None; **F. Gutiérrez-Rodríguez**: None; **P. Quiroga**: None; **A. Romero**: None; **N. Montes**: None; **L. Esparcia Pinedo**: None; **M. Alfranca**: None; **R. Garcia-Vicuna**: None; **F. Sánchez-Madrid**: None; **I. González-Álvaro**: None; **S. Castañeda**: None.

Abstract Number: 1652

Lupus Research Action Network: Increasing Minority Clinical Trial Participation Through Peer Leaders

Melicent Miller[1], Stephanie Slan[1], Rosalind Ramsey-Goldman[2], Rodlescia Sneed[3], Candace Feldman[4], Patrick Wildman[1], Tori Justin[5], Lydia Oberholtzer[5] and Joy Buie[6], [1]Lupus Foundation of America, Washington, DC, [2]Northwestern University, Chicago, IL, [3]Wayne State University, Detroit, MI, [4]Brigham and Women's Hospital, Boston, MA, [5]Sharp Insight, LLC, Montgomery County, MD, [6]Lupus Foundation of America, York, SC

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Interprofessional Exemplary

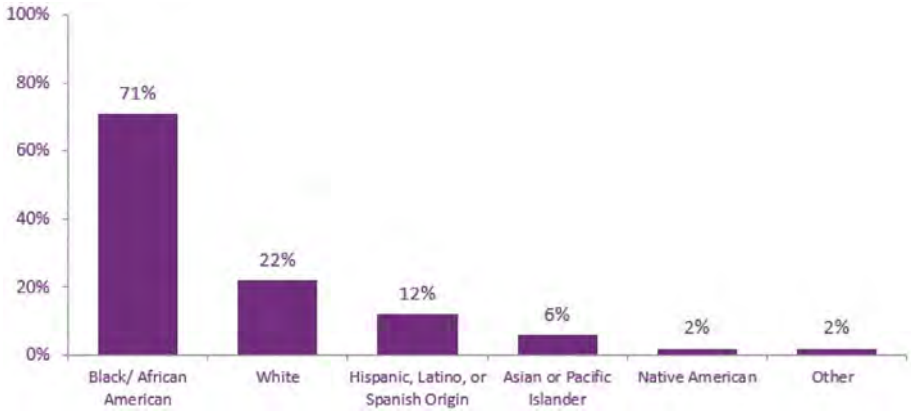
Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

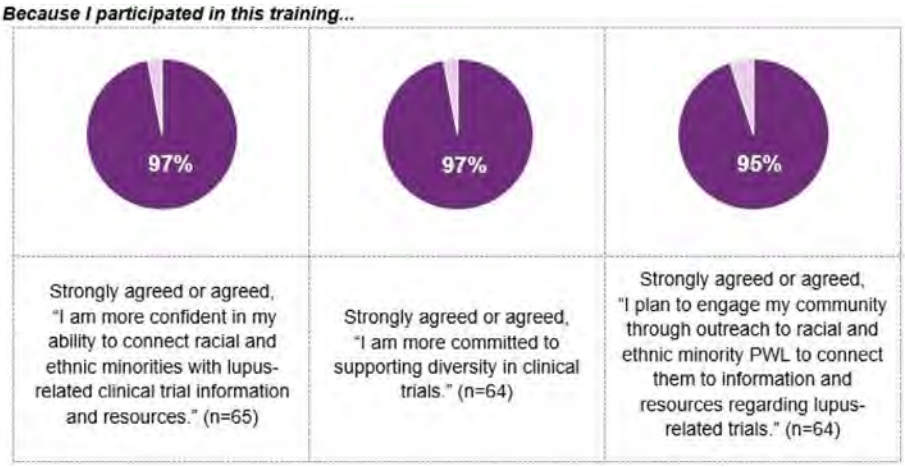
Background/Purpose: Black/African American people with lupus (PWL) experience greater disease prevalence and severity than White PWL. The need for more racial and ethnic diversity amongst lupus clinical trial (CT) participants is needed as there continues to be a high level of unmet medical need within this population. Lack of trust has been found to negatively influence Black/African American participation in CT that contributes to higher perceptions of bias and racism among this population. Peer-to-peer models such as CDC's Popular Opinion Leader (POL) has been shown to be effective in building trust and confidence within the community while empowering PWL to take leadership roles in communicating the importance of diversifying CT participation.

Methods: The Lupus Conversations Program, an evidence-based curriculum based on the POL model, aims to improve the awareness of lupus CT, increase knowledge of the CT process as well as addressing barriers, facilitators, and mediators to CT participation such as structural racism in research among Black/African American PWL. This model was adapted and employed through virtual and in-person training sessions for Lupus Research Action Network (LRAN) members with goals of increasing knowledge, confidence, and intent to engage in peer-to-peer outreach opportunities to discuss the importance of participation in lupus CT among Black/African American PWL. A retrospective pre-post survey was developed to assess participant demographics and increases in CT knowledge and awareness of trials, self-efficacy, and confidence to share CT information with peers, and examine training satisfaction.

Results: LRAN members participated in one of two trainings in September 2022 (n=40) and April 2023 (n= 27). Almost all LRAN survey respondents identified as female. The average age of participants was 42 (n=63). Over two-thirds of the training participants identified as Black/African American. Almost a quarter identified as White, 12% as Hispanic, Latino or



Race and Ethnicity of LRAN Training Participants



Changes in confidence, commitment, and behavioral intentions for diversifying minority participation in CT

Spanish origin, 6% as Asian or Pacific Islander, and 2% as Native American. LRAN members resided in 12 states. Over 90% of LRAN members reported satisfaction with LRAN training content, facilitation, and engagement. Sixty percent reported an increased understanding of CT needs and barriers to enrollment among racial and ethnic minority PWL. Eight out of ten increased their understanding of CT and racism and increased their awareness of lupus CT and outreach markets. Nearly all participants increased their commitment to diversifying CT participation for PWL, confidence in connecting target population with lupus CT information and resources, and behavioral intention to engage their community through outreach to racial and ethnic minority PWL to connect them to information and resources related to lupus CT.

Performance Measure: Evidence of program participant satisfaction	
●	**94-97%** LRAN trainees will report satisfaction with the Lupus Conversation program content, facilitation, and engagement. *Target = 75%*
Performance Measure: Evidence of increased understanding, commitment, self-efficacy, and behavioral intentions among LRAN participants related to racial and ethnic minority PWL in lupus clinical trials	
●	**80%** Increased understanding (knowledge areas) of clinical trials and racism among LRAN participants. *Target=75%*
●	**76%** Increased awareness of lupus clinical trials and outreach markets among LRAN training participants. *Target=60%*
●	**97%** Increased commitment to diversifying clinical trials for PWL among LRAN training participants. *Target=50%*
●	**97%** Increased confidence in connecting target population with lupus-related clinical trial information and resources in LRAN training participants. *Target=50%*
●	**95%** Increased behavioral intention of LRAN training participants to engage their community through outreach to racial and ethnic minority PWL to connect them to information and resources related to lupus-related clinical trials. *Target=50%*
○	**60%** Increased understanding of clinical trial needs and barriers to enrollment among racial and ethnic minority PWL in LRAN training participants. *Target=75%*
Performance Measure: Evidence of program participation	
●	**67** By the end of the grant period, at least 50 people with lupus (PWL) will attend an LRAN training that incorporates Lupus Conversations. *Target=50 PWL*

● Met ○ Not Met -- Data Not Available

Overall LRAN Training Performance Measures

Conclusion: An adapted, community-based POL model can be used to increase awareness of and commitment to diversifying participation in lupus CT among Black/African American PWL. Further research is needed to determine the degree to which a peer-to-peer education module may reduce disparities in CT participation among Black/African American PWL. Existing level of CT knowledge must be considered when developing patient-centered content.

Disclosure: M. Miller: None; **S. Slan**: None; **R. Ramsey-Goldman**: Ampel Solutions, 2, Calabetta, 2, Exagen, 2, Immunocor, 6; **R. Sneed**: None; **C. Feldman**: BMS Foundation, 5, Curio Bioscience, 12, My husband is one of the founders and will receive equity (but has not received anything to date)., OM1, Inc., 2, Pfizer, 5; **P. Wildman**: None; **T. Justin**: None; **L. Oberholtzer**: None; **J. Buie**: None.

Abstract Number: 1653

Up or Down: Does Direction of Stair Climbing Difficulty Matter for Incident Functional Limitation and Knee Replacement in Knee Osteoarthritis?

Jason Jakiela[1], Thomas Bye[1], Sydney Liles[2] and Daniel White[1], [1]University of Delaware, Newark, DE, [2]University of Delaware, Elkton, MD

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Interprofessional Exemplary
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Knee osteoarthritis (OA) is a leading cause of functional limitation (FL) in older adults, with difficulty climbing stairs often the first-reported limitation. Overall increased difficulty with stair climbing is associated with greater risk of developing FL and receiving a knee replacement (KR). However, little is known about the relation of the direction of stair climbing difficulty (ascending or descending) with the development of knee OA-related outcomes. Therefore, the purpose of this study was to examine the relationship of difficulty ascending and descending the stairs with incident FL and KR in adults with or at high risk for knee OA.

Methods: We used data from the Osteoarthritis Initiative (OAI). Stair climbing difficulty was assessed at baseline (BL) using two questions from the WOMAC: 1.) What degree of difficulty do you have with ascending stairs? and 2.) What degree of difficulty do you have with descending stairs? Choices included: none, mild, moderate, severe, extreme. A 4-level exposure

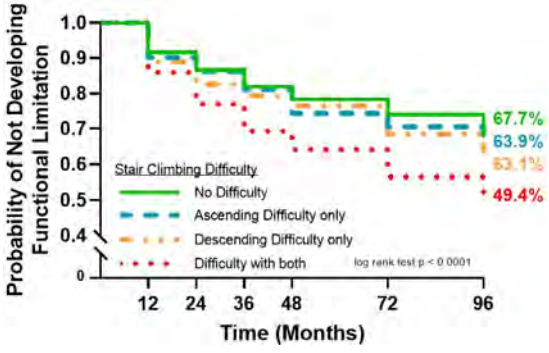


Figure 1: Kaplan-Meier survival curves for functional limitation by stair climbing difficulty group.

combining difficulty with ascending and descending stairs was created: no difficulty with either, difficulty with ascending only, difficulty with descending only, difficulty with both ascending and descending. FL was defined as walking speed < 1.22 m/s over 20 meters and was collected at BL, 12-, 24-, 36-, 48-, 72-, and 96-month follow-up. 1.22 m/s has been previously used to represent poor function. KR was defined as any type of KR and was collected from the BL visit until 10 years later. Separate analytic samples were used for each outcome and only included those without the outcomes at BL. We produced Kaplan-Meier survival curves for cumulative incidence of FL and KR and used Cox proportional hazards regression to calculate hazard ratios (HR) and 95% confidence intervals (CI), adjusted for age, sex, BMI, race, radiographic knee OA, VAS pain, and presence of comorbidity.

Results: 2866 participants (mean age = 60.3 years old, 53.8% female, mean BMI = 28.1 kg/m^2) were included in the FL sample and 4523 participants (mean age = 61.3 years old, 58.3% female, BMI = 28.7 kg/m^2) were included in the KR sample. 957 participants developed FL (Figure 1) and 438 participants received a KR (Figure 2) during follow-up. Compared to those without any difficulty ascending and descending stairs, those with difficulty in both ascending and descending stairs were at a 44% greater hazard of FL and a 132% greater hazard of KR, those with only difficulty ascending but not descending stairs were at a 7% greater hazard of FL and a 64% greater hazard of KR, and those with only difficulty descending but not ascending stairs were at a 10% greater hazard of FL and a 40% greater hazard of KR (Table 1).

Conclusion: Adults with knee OA who have any amount of difficulty with both ascending and descending stairs are at greater risk of developing both walking speed FL and receiving a KR compared to those with no difficulty. Self-reported stair climbing difficulty may be useful as a functional vital sign for identifying those at early risk for FL and KR and in need of further evaluation and treatment.

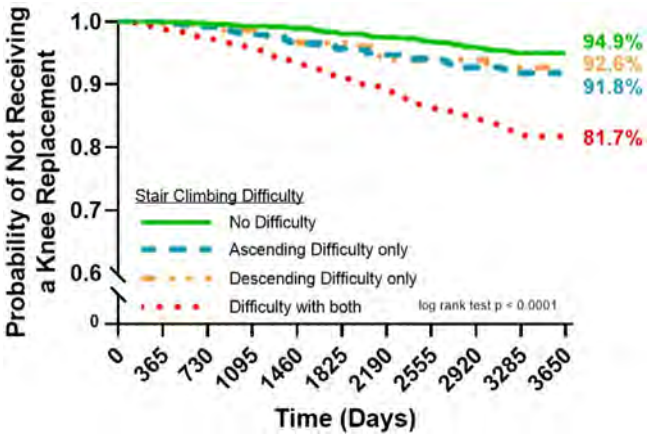


Figure 2: Kaplan-Meier survival curves for knee replacement by stair climbing difficulty group.

Table 1: Hazard ratios (HRs) & 95% confidence intervals (95% CIs) for walking speed functional limitation and knee replacement by stair climbing difficulty group.

Stairs Difficulty	Functional Limitation n/N (%)	HR [95% CI] (adjusted)	Knee Replacement n/N (%)	HR [95% CI] (adjusted)
No difficulty	348 / 1284 (27.1%)	1.0 [REF]	75 / 1728 (4.3%)	1.0 [REF]
Ascending only	92 / 310 (29.7%)	1.07 [0.85, 1.36]	31 / 445 (7.0%)	1.64 [1.07, 2.52]
Descending only	44 / 143 (30.8%)	1.10 [0.79, 1.52]	14 / 212 (6.6%)	1.40 [0.79, 2.50]
Difficulty with both	473 / 1129 (41.9%)	1.44 [1.23, 1.70]	318 / 2138 (14.9%)	2.32 [1.75, 3.08]

Note: adjusted for age, sex, BMI, race, radiographic knee OA, VAS pain, and presence of comorbidity

Disclosure: J. Jakiela: None; **T. Bye**: None; **S. Liles**: None; **D. White**: Viatris, 6.

Abstract Number: 1654

A Peer Health Coached Resilience-Based Energy Management Program Was Effective in Improving Fatigue and Other Outcomes in People with Systemic Sclerosis: Results of a Randomized Controlled Trial

Susan Murphy[1], Yen Chen[2], Mary Alore[2], Sheri Hicks[2], Adam Pape[2], Afton Hassett[2], Anna Kratz[2], Daniel Whibley[2], Alexandra Harper[3], Suiyuan Huang[2], Gina Jay[2], Shannen Bolde[2] and Dinesh Khanna[2], [1]University of Michigan, Plymouth, MI, [2]University of Michigan, Ann Arbor, MI, [3]University of Michigan, Ypsilanti Charter Twp, MI

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Interprofessional Exemplary

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Systemic sclerosis (SSc), a rare autoimmune condition, has a high chronic symptom burden that can have dramatic, life-altering effects on function and quality of life. Fatigue is one of the most problematic symptoms. Pain, depression, and social isolation are also potential contributors to fatigue and reduced quality of life. Our team developed a

Table 1. Baseline Characteristics of the Study Participants (N = 173)

Table 1. Baseline characteristics of the study participants (N = 173)

Variable	Total	Control group (n = 58)	RENEW group (n = 115)
Demographics			
Age, mean (SD), years	54.5 (11.7)	55.1 (12.5)	54.1 (11.3)
Sex, n (%)			
Female	161 (93.1)	54 (33.5)	107 (66.5)
Male	12 (6.9)	4 (33.3)	8 (66.7)
Race, n (%)			
White	144 (85.2)	51 (35.4)	93 (64.6)
African American	16 (9.5)	2 (12.5)	14 (87.5)
Asian and other	9 (5.3)	2 (22.2)	7 (77.8)
Education status, n (%)			
High school/GED	14 (8.3)	7 (50.0)	7 (50.0)
Some college	54 (32.1)	14 (25.9)	40 (74.1)
College degree	50 (29.8)	19 (38.0)	31 (62.0)
Master's or advanced degree	50 (29.8)	15 (30.0)	35 (70.0)
Work status, n (%)			
Full-time employed	54 (32.0)	14 (25.9)	40 (74.1)
Part-time employed	20 (11.8)	8 (40.0)	12 (60.0)
Homemaker	11 (6.5)	4 (36.4)	7 (63.6)
Retired	40 (23.7)	14 (35.0)	26 (65.0)
On disability	44 (26.0)	14 (31.8)	30 (68.2)
Marital status, n (%)			
Not married	56 (33.1)	19 (33.9)	37 (66.1)
Married	113 (66.9)	36 (31.9)	77 (68.1)
SSc characteristics			
SSc subtype, n (%)			
Diffuse	82 (47.1)	32 (39.0)	50 (61.0)
Limited	61 (35.1)	16 (26.2)	45 (73.8)
Overlap	22 (12.6)	8 (36.4)	14 (63.6)
Unspecified/other (e.g., SINE)	8 (5.2)	2 (25.0)	6 (75.0)
Disease duration, mean (SD), years	8.1 (9.2)	9.6 (10.5)	7.4 (8.4)
0 – 1 years, n (%)	40 (23.1)	13 (32.5)	27 (67.5)
2 – 5 years, n (%)	59 (34.1)	17 (28.8)	42 (71.2)
5+ years, n (%)	74 (42.8)	28 (37.8)	46 (62.2)
Fatigue Severity Scale, score, mean (SD)	5.6 (0.7)	5.7 (0.8)	5.5 (0.7)
PROMIS FACIT Fatigue, T score, mean (SD)	63.2 (5.7)	64.4 (6.3)	62.6 (5.3)
PROMIS Pain interference, T score, mean (SD)	60.5 (8.4)	61.6 (8.5)	59.9 (8.3)
PROMIS Depressed mood, T score, mean (SD)	54.7 (7.6)	54.9 (7.6)	54.6 (7.6)
Resilience, score, mean (SD)	26.2 (6.5)	26.1 (5.6)	26.3 (6.9)

T-scores are compared to a US normative population in which 50 is the mean and SD is 10. Fatigue Severity Scale is a 9-item questionnaire that assesses perceived fatigue on a 7-point Likert scale (1 = strongly disagree to 5 = strongly agree). Eligible participants had an average score of at least 4 on Fatigue Severity Scale. Abbreviations: SSc, systemic sclerosis; PROMIS, Patient Reported Outcomes Measurement Information System; FACIT, functional assessment of chronic illness therapy.

resilience-based energy management program (called RENEW) designed to be delivered through a website or app. Trained peer health coaches, who also have SSc, provided health coaching during regular online sessions over a 12-week period. This study examined whether participants in the RENEW program had clinically important improvements in fatigue, pain interference, depressive symptoms, and resilience.

Methods: In this randomized controlled trial (NCT04908943), participants were assigned to either RENEW or a wait list control group in a 2:1 ratio. Participants were ≥18 years old with doctor-diagnosed SSc of any subtype. Eligible participants had moderate to severe fatigue (≥4 on the Fatigue Severity Scale). The RENEW program included a comprehensive educational website and app with instructions for goal setting around specific topics plus 9 one-on-one health coaching sessions via Zoom over 12 weeks. The primary outcome was fatigue (assessed by PROMIS FACIT-Fatigue). Secondary outcomes were PROMIS measures of pain interference and depressive symptoms, and Connor-Davidson Resilience Scale. Outcomes were assessed at baseline, 6 weeks, and 12 weeks. Intent-to-treat linear mixed models were used to assess group differences over time, controlling for age, sex, race, SSc subtype, SSc duration, and baseline values of each outcome. A three-way interaction with group, time, and SSc duration was examined in each model.

Results: Among 173 participants (mean age 54.5 years ± 11.7), most were female (93%) and White (85%). 47% had diffuse SSc, and 57% had early SSc duration (≤5 years diagnosed) (Table 1). At 12 weeks, participants in RENEW had significantly reduced fatigue compared to controls (β=-5.1, 95% CI: -7.2 to -2.9; $p < 0.001$), which was considered clinically meaningful (>3 point change). Participants also had significantly improved pain interference (β=-2.6, 95% CI -4.9 to -0.4; $p = 0.021$), depressive symptoms (β=-3.8, 95% CI: -6.2 to -1.5; $p = 0.002$), and resilience (β=2.9, 95% CI: 1.2 to 4.5; $p < 0.001$) compared to controls (Figures 1 & 2). Within the RENEW group, fatigue and pain at 12 weeks were found to be significantly moderated by SSc

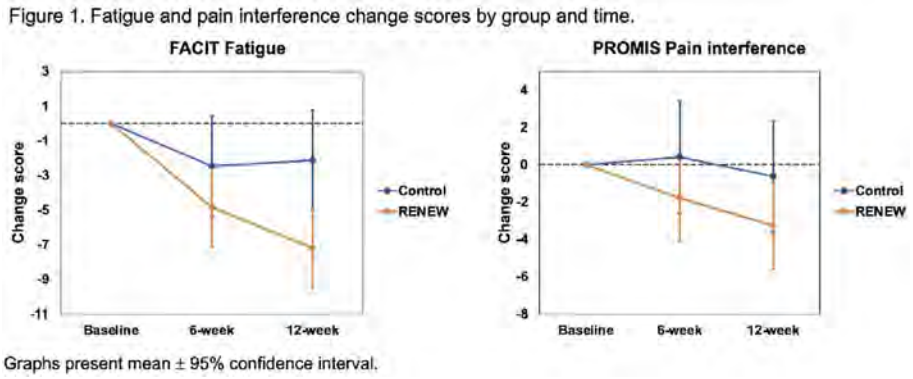


Figure 1. Fatigue and Pain Interference Change Scores by Group

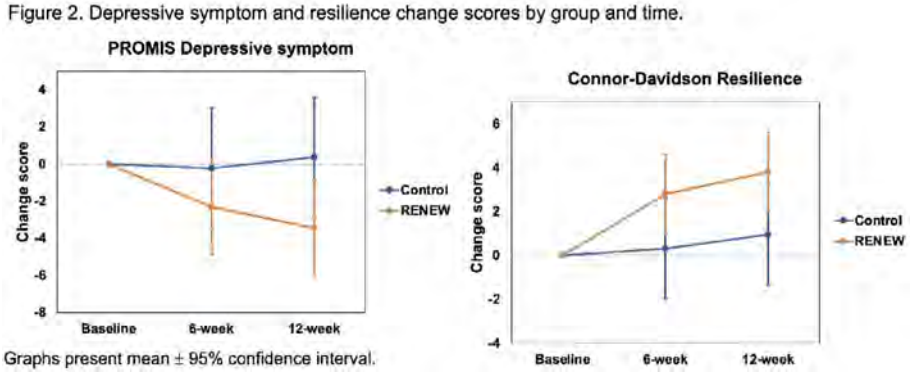


Figure 2. Depressive Symptoms and Resilience Change Scores by Group

duration. Participants with ≤ 1 year SSc duration had significantly reduced fatigue compared to those with >5 year SSc duration (β=-3.1, 95% CI: -5.9 to -0.3; p = 0.032). Participants with 2-5- year SSc duration had significantly reduced pain compared to those with >5 year SSc duration (β=-4.2, 95% CI: -7.0 to -1.4; p = 0.004). No other three-way interaction effects were found.

Conclusion: A remotely-delivered, peer health coached energy management program had positive effects on fatigue and other outcomes, particularly in early diagnosed patients. This program has the potential for broad scalability to assist with SSc symptom management.

Disclosure: S. Murphy: None; **Y. Chen**: None; **M. Alore**: None; **S. Hicks**: None; **A. Pape**: None; **A. Hassett**: None; **A. Kratz**: American Psychological Association, 12, Editor, Happify/Twill, 2; **D. Whibley**: None; **A. Harper**: None; **S. Huang**: None; **G. Jay**: None; **S. Bolde**: None; **D. Khanna**: AbbVie, 12, DSMB, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb, 2, 5, CSL Behring, 2, Genentech, 2, Horizon Therapeutics, 2, 5, Janssen, 2, 6, Pfizer, 5, Prometheus, 2.

Abstract Number: 1655

Usability Testing of JIActiv, an Instagram-Based Program Promoting Engagement in Physical Activity Among Young People Living with Juvenile Idiopathic Arthritis

Zeinab Ahmadian Sangkar[1], Fatou Bagayogo[2], Karina Cristea[2], Ciaran Duffy[3], Jennifer Stinson[4], Karine Toupin April[3], Michele Gibbon[5], Marianne Boulet[1], Élodie Bolduc[1], Aymane Alilou[6], Sara Ahmed[7], Claudine Auger[1], Laurie Proulx[8], Alexandra Sirois[9] and Sabrina Cavallo[10], [1]University of Montreal, Montreal, QC, Canada, [2]CRIR, Montreal, QC, Canada, [3]University of Ottawa, Ottawa, ON, Canada, [4]The Hospital for Sick Children, Toronto, ON, Canada, [5]Children's Hospital of Eastern Ontario RI, Ottawa, ON, Canada, [6]Unviersity of Montreal, Montreal, QC, Canada, [7]McGill University, Montreal, QC, Canada, [8]Canadian Arthritis Patient Alliance, Ottawa, ON, Canada, [9]CARRA, Outremont, QC, Canada, [10]University of Montreal, Montréal, QC, Canada

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Interprofessional Exemplary
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: This study evaluated the usability (user performance and satisfaction) of an Instagram-based educational and interactive program promoting physical activity among young people living with juvenile idiopathic arthritis (JIA).

Methods: A descriptive qualitative study design was used. A convenience sample of adolescents and young adults (13 to 25 years) with JIA (n = 28; mean age = 18.69, SD=± 2.28 years) was recruited from arthritis-patient organizations, rehabilitation, and hospital centers to participate in two iterative cycles of online (Zoom platform) semi-structured interviews. The audio recordings of the interviews were transcribed verbatim, sorted, organized, and coded using the MAXQDA 11 software. The interview questions were grouped into 10 main categories including: 1. Privacy and Safety, 2. Design Aesthetics, 3. Functionalities, 4. Organization of the program, 5. Content of page, 6. Motivating factors, 7. Willingness to follow the program, 8. Language display (preferences),9. Suggestions for improvement to the JIActiv program and 10. Willingness to recommend the program.

Results: All participants used a computer, a smartphone or a tablet to access and navigate the JIActiv program. Overall, participants did not report any significant concerns about privacy and safety while using the JIActiv program. Participants provided positive feedback regarding the program's user-friendly navigation and appealing visual design. Most participants

reported that the featured information was relevant and of good quality. They appreciated the structure of the intervention program (overall length of the program, frequency of posts and weekly time requirements). The interactive features supporting group-based activities were highly appreciated as they offered opportunities to communicate and share information and experiences with peers. Peer interactions and the opportunity to communicate with healthcare providers were identified as motivating factors to use the JIActiv program. Some participants suggested shortening the videos length and presenting English and French content on separate Instagram pages, however this was not identified as a barrier to the use of the program. Participants suggested some minor modifications to the program. Based on these, modifications were implemented after each cycle if semi-structured interviews including edits to the informational videos to facilitate navigation.

Conclusion: Findings showed that the JIActiv program demonstrated good usability. This testing has allowed us to optimize end users' (young people with JIA) ability to access, to navigate, to understand and to implement the informational content and practical strategies featured through this program in a culturally competent, efficient and satisfying manner.

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Abstract Number: 1656

Nothing About Us Without Us: Top 10 Research Priorities from Patients - A James Lind Alliance Project for Public and Patient Involvement (PPI)

anna Fryxelius[1], Amy Martinsen[2], Ida Løchting[3], Linda Aimee Hartford Kvæl[4], Astrid Lunestad[2], Astrid Bergland[4] and Kjersti Storheim[2], [1]Norwegian Rheumatism Association / REMEDY - Center for Treatment of Rheumatic and Musculoskeletal Diseases, Oslo, Norway, [2]Oslo University Hospital, Oslo, Norway, [3]REMEDY - Center for Treatment of Rheumatic and Musculoskeletal Diseases, Oslo, Norway, [4]OsloMET, Oslo, Norway

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Interprofessional Exemplary
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Patient and public involvement (PPI) is gaining increasing recognition as important to ensure research is relevant and to reduce avoidable research waste. Active collaboration between patients and researchers in development and implementation of scientific projects is important to ensure a good match between patient's priorities and the scientific focus in research, contribute to more patient-oriented medical research agendas, enhance patient friendly design of research projects, and creating support for implementation. Bemden et al. in BMJ Rheumatology - states that "Patient and public involvement in rheumatic and musculoskeletal research is an idea whose time has firmly come" (2023) 7:12.

Interest in improved PPI also stems from knowledge that 85% of all research funds are avoidably wasted (Chalmers, Glasziou, Lancet 2009). Identifying knowledge gaps in partnership with end users of medical research, in this case both clinicians and patients, can help reduce research waste.

PPI can be most effective when used to identify and prioritise knowledge gaps for producing new research projects - so that patients are effectively involved in the early planning stages of new projects, but this process can be time consuming and complicated.

Table: Top ten research priorities for RMDs

Top ten research priorities for RMDs
1. Which interventions can prevent persistent RMDs?
2. How is overall health affected by living with persistent musculoskeletal pain?
3. Are there higher rates of gastrointestinal issues in people with RMDs?
4. Why do symptoms fluctuate and flare unpredictably?
5. Are different RMDs connected to one another?
6. Which criteria should be used for the diagnosis of RMDs?
7. What kind of rehabilitation is best for treating RMDs?
8. What does personalised medicine mean for people with RMDs?
9. What treatments are effective against fatigue?
10. How should healthcare services be organised to best meet the needs of people with RMDs?

Organising effective PPI processes to ensure value for all parties and increase effectiveness of research funds, requires new systems and structures to be developed and tested. The James Lind Alliance initiative has developed methods for Priority Setting Partnerships that ensure real engagement.

Methods: To identify key questions most relevant for patients with RMDs, a priority-setting project was conducted using methods established by the James Lind Alliance (JLA)[4]. A steering group comprised of patients and multidisciplinary clinicians led the process. 239 questions were first gathered from patients living with RMDS who were members of five collaborating RMD patient organisations. The questions covered six broad themes including diagnosis, treatment, aetiology, symptoms and comorbidities, healthcare systems and daily life.

After rejecting out-of-scope submissions, removing duplicates, and merging similar questions, 56 questions remained and were included in a web-based ranking survey distributed to more than 40,000 patient organisation members.

5346 individuals responded to the survey, the results of which were used to generate a shortlist of 20 questions in line with the James Lind Alliance methodology. Fourteen patient representatives from all 5 organisations were then brought together for a final prioritising workshop in Oslo, Norway September 2022.

Results: The result of the workshop was a consensus on a final ranked list of questions, including the top ten priorities for future research.

The top ten identified priorities (panel) reflect patients' leading concerns around uncertainties in the field of RMDs. These concerns were thematically focused primarily on understanding symptoms and improving treatments.

Conclusion: The identified priorities are intended to provide a platform for ensuring responsiveness of future research activity and funding to questions that are most important for people living with RMDs.

Disclosure: a. Fryxelius: None; **A. Martinsen**: None; **I. Løchting**: None; **L. Hartford Kvæl**: None; **A. Lunestad**: None; **A. Bergland**: None; **K. Storheim**: None.

Abstract Number: 1657

Mapping the Network of Coordinated Immune Dysregulation in Juvenile Dermatomyositis at Single-cell Resolution

Gabrielle Rabadam[1], Camilla Wibrand[2], Emily Flynn[1], George Hartoularos[1], Yang Sun[1], Susan Kim[3], Chun Jimmie Ye[1], Zev Gartner[1], Marina Sirota[4] and Jessica Neely[1], [1]University of California San Francisco, San Francisco, CA, [2]Aarhus University, Aarhus, Denmark, and University of California San Francisco, San Francisco, CA, [3]UCSF Benioff Children's Hospital, San Francisco, CA, [4]Bakar Computational Health Sciences Institute, University of California San Francisco, San Francisco, CA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

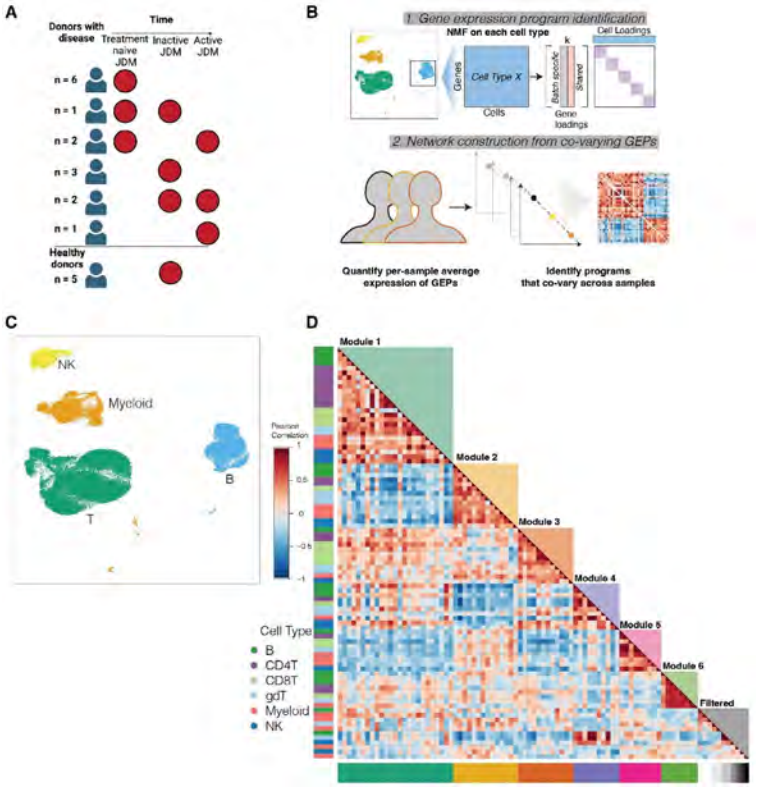
Session Title: Abstracts: Pediatric Rheumatology – Basic Science

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Juvenile Dermatomyositis (JDM) is a rare multisystem autoimmune condition that involves complex immune responses in both innate and adaptive compartments. Currently, we have a limited systems-level understanding of how cellular immunophenotypes functionally cooperate and are dysregulated in JDM. Increasing knowledge of

Fig. 1: A) Table showing samples included from JDM donors (n=15) and HCs. Some patients with JDM have longitudinal samples with a change in disease activity level included. B) UMAP reduction showing major immune cell types in peripheral blood samples annotated based on canonical markers. C) Overview of the DECIPHERseq workflow. Briefly, major cell types are subsetted and reduced via non-negative matrix factorization (NMF) into a set of GEPs defined by gene loadings quantifying the contribution of individual genes to that GEP and cell loadings quantifying how strongly expressed that GEP is in each cell. Cell loadings are averaged per PBMC sample and pairwise correlations are calculated between all the programs to identify co-varying GEPs. D) Heatmap showing 6 "blocks" (Modules 1-6) identified by DECIPHERseq from all pairwise correlations of GEPs across 6 major cell types. GEPs are clustered into modules using a Constant Potts Model for community detection, with isolated GEPs filtered out (greyscale).



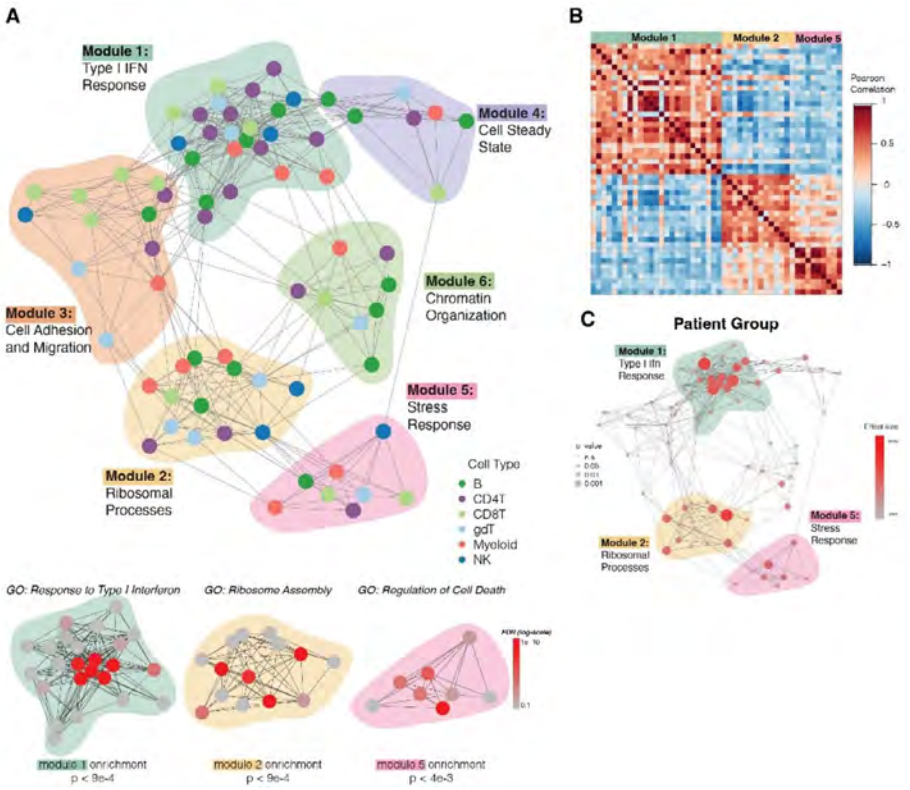


Fig. 2: A) Force-directed network graph (top) constructed from correlated GEPs in PBMCs from JDM patients and healthy controls, where strongly positively correlated programs appear closer and strongly anti-correlated programs appear further apart. Nodes represent biological activity programs in the given cell types and plotted edges represent significantly positively correlated activity programs (Pearson, $p<0.05$). Modules were identified using a Constant Potts Model for community detection. Module labels were annotated from the top 20 gene sets significantly enriched for each module relative to the rest of the network (module enrichment $p < 0.05$). Selected network modules (bottom) are colored by FDR of enrichment for indicated gene ontology set. B) Subsetted heatmap highlighting the negative correlations between Module 1 and Modules 2 and 5. C) Network graph of activity programs in PBMCs, colored by the relative effect size (linear scale) calculated by 4 group ANOVA of disease activity categorized by TN-JDM, active JDM, inactive JDM, and HCs. Significance level is indicated by node size.

the immune regulatory networks associated with JDM could lead to identification of precision treatment strategies and biomarkers.

Methods: We used multiplexed single cell RNA sequencing to profile 27 peripheral blood samples from JDM patients (n=15, samples=22) and healthy pediatric controls (n=5, HCs). We performed standard processing, dimensional reduction, and clustering steps to identify 6 major cell types (B, CD4T, CD8T, gdT, NK & Myeloid). We applied an unsupervised network inference method, DECIPHERseq, which uses non-negative matrix factorization to identify coordinated regulatory networks of functional gene expression programs (GEPs) across cell types and community detection to identify hubs or 'modules' of GEPs. The network was annotated using 1) gene set enrichment analysis to identify pathways overrepresented in each program and 2) the DECIPHERseq enrichment method, which relies on resampling to identify gene sets enriched within modules compared to the rest of the network. To determine JDM disease activity-associated changes in network structure, we performed ANOVA on mean patient expression of GEPs between treatment-naive (TN), active, and inactive JDM, and HC samples.

Results: We analyzed ~110,000 cells. DECIPHERseq inferred a network of 76 activity programs that formed 6 modules. All modules contained multiple cell types, highlighting that biological processes are coordinated across many cell types in JDM. Module enrichment analysis revealed consensus biological themes for each GEP hub. Module 1 was enriched in type I IFN responses and many programs in this module were increased in TN-JDM, as expected. Several disease-associated programs were highly correlated to this central IFN hub suggesting these cell-specific responses may be either up or downstream of IFN signaling. These included NK12, a proliferative NK program *(MKI67, HIST1H1B)*; gdT4, a cytotoxic Th1

polarized gdT program *(GZMB, CX3CR1, TBX21)*; CD4T10, an activated and proliferative Treg program *(FOXP3, IL2RA, PRDM1, MKI67)*; and B9, an immature naïve B cell program *(CD9, TCL1A, CD24)*, all of which were expressed higher in TN-JDM. Module 2, enriched in ribosomal processes, and Module 5, enriched in stress responses and regulation of cell death, were negatively correlated with Module 1.Several programs within Modules 2 and 5 were expressed significantly lower in TN-JDM suggesting dysfunction of these cellular processes in new-onset disease.

Conclusion: By employing unsupervised network analyses, we identified a central IFN hub highly correlated with novel cell-specific GEPs as well as dysfunction of ribosome and cell stress responses across many cell types in TNJDM. This systems-level perspective highlights coordinated peripheral immune responses that are both over- and underactive in JDM providing a foundation for future work to identify therapies to reprogram this dysregulation.

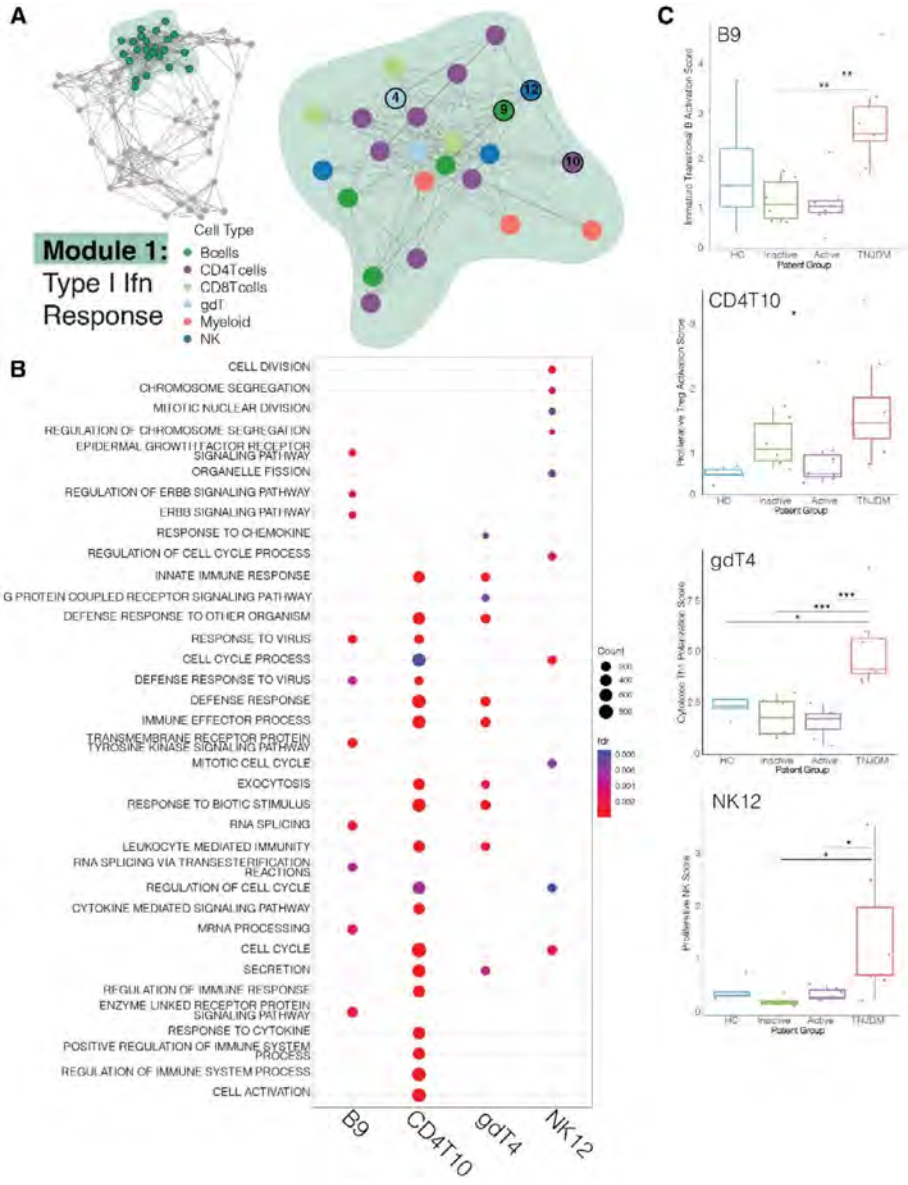


Fig. 3: A) Diagram showing GEPs in Module 1, indicating IFN hub-associated programs B9, CD4T10, gdT4, and NK10. B) Dotplot comparing top 10 enriched gene ontology (GO) sets for each program (FDR < 0.01). C) Boxplots for indicated disease-associated programs (4 group ANOVA, $p < 0.05$). Significant post-hoc pairwise comparisons between groups (Tukey HSD) are shown as * $p<0.05$, ** $p<0.01$, ***<0.001 (BH adjusted p value).

Disclosure: G. Rabadam: 23andMe, 7; **C. Wibrand**: AMBU, 11, GenMab, 11, Lundbeck, 11, NovoNordisk, 11; **E. Flynn**: None; **G. Hartoularos**: None; **Y. Sun**: None; **S. Kim**: None; **C. Ye**: Chan Zuckerberg Initiative, 5, Genentech, 5, ImmunAI, 1, 8, Maze Therapeutics, 2, 8, Related Sciences, 1, 8, TReX Bio, 2; **Z. Gartner**: Scribe Biosciences, 1, 8, Serotiny, 1, 8; **M. Sirota**: Exxagen, 1; **J. Neely**: None.

Abstract Number: 1658

Title: Inflammatory Arthritis Across the Age-Spectrum: Single-Cell Profiling of the Inflamed Synovium in Children with Juvenile Idiopathic Arthritis

Chrissy Bolton[1], Christopher Mahony[2], Charlotte Smith[2], Vicky Alexiou[3], Huong Nguyen[3], Patricia Reis-Nisa[2], Søren Lomholt[4], Annie Hackland[2], Sugrah Sultan[5], Klaudia Kupiec[3], Sunit Davda[6], Charlene Foley[6], Calliope Dendrou[1], Elizabeth C Rosser[7], Accelerating Medicines Partnership Program RA SLE Network[8], Anna Helena Jonsson[9], Fan Zhang[10], Michael Brenner[11], Soumya Raychaudhuri[9], Christopher Buckley[1], Manigandan Thyagarajan[5], Zishan Shiekh[5], Sandrine Compeyrot-Lacassagne[6], Samantha Chippington[6], Mark Coles[1], Eslam Al-Abadi[5], Andrew Filer[2], Tissue Research in Childhood Onset Inflammatory Arthritis (TRICIA) Consortium[12], Lucy R Wedderburn[3] and Adam Croft[2], [1]University of Oxford, Oxford, United Kingdom, [2]University of Birmingham, Birmingham, United Kingdom, [3]UCL Great Ormond Street Institute of Child Health, London, United Kingdom, [4]Aarhus University, Aarhus, Denmark, [5]Birmingham Women's and Children's NHS Foundation Trust, Birmingham, United Kingdom, [6]Great Ormond Street Hospital, London, United Kingdom, [7]University College London, London, United Kingdom, [8]Cedars-Sinai Medical Center, Los Angeles, CA, [9]Brigham and Women's Hospital, Boston, MA, [10]University of Colorado, Aurora, CO, [11]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [12]MRC, Birmingham, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Pediatric Rheumatology – Basic Science

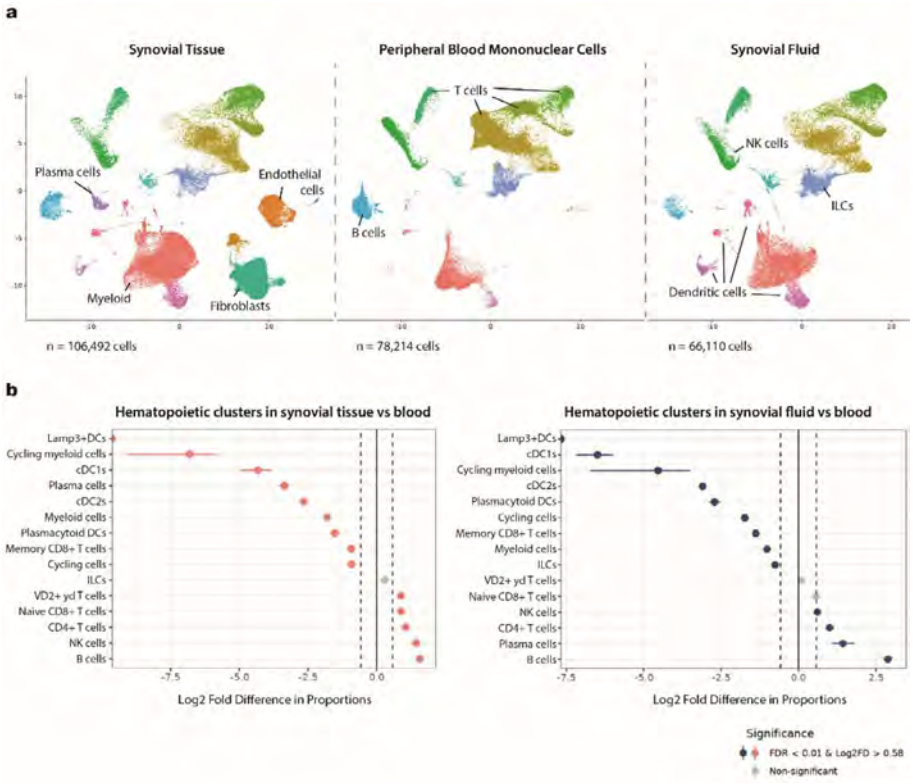
Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Understanding the unique and shared pathogenic processes between childhood-onset and adult-onset inflammatory arthritides is needed to guide more effective drug development and their application to different age groups. Difficulties in accessing samples from the inflamed tissue site in children has limited our understanding of disease mechanisms that operate locally in the joint. As part of the Tissue Research in Childhood Onset Inflammatory Arthritis (TRICIA) Consortium, we have established the first single cell multi-omic atlas of the inflamed joint in Juvenile Idiopathic Arthritis (JIA).

Methods: Ultrasound-guided needle biopsies of synovial tissue, with matched synovial fluid and peripheral blood mononuclear cell samples were obtained from n=12 pediatric patients with JIA, who were naïve to disease-modifying anti-rheumatic drugs. Multimodal single-cell characterisation of cells (n = 250, 816 cells, with scRNA-seq, VDJ-sequencing and TotalSeq surface assays) and multiplexed imaging of synovial tissue fragments were performed.

Results: Transcriptomic profiles of hematopoietic cells at a global level of clustering revealed that synovial tissue and synovial fluid were proportionally enriched in the same cellular subtypes (dendritic cell subsets, myeloid and memory CD8+ T cells) compared to blood (> 0.58 log2 fold difference, FDR < 0.01, Fig 1). Core tissue-enriched populations identified in adult rheumatoid arthritis (Zhang *et al*., 2022, the AMP RA/SLE network) were also prominent in pediatric synovial tissue samples, including *GZMK*+ memory *CD8*+ T cells, *CXCL13*+ *CD4*+ T peripheral helper cells and *NR4A*+ germinal centre-like B cells. Evidence for a distinct immune environment of the synovial fluid cavity relative to synovial tissue included upregulation of interferon-response genes, greater proportions of dendritic cells (Fig 1), less diversity of αβ T cell receptors on CD8+ T cells



Comparative analysis highlights conserved proportions of hematopoietic cells between synovial tissue and fluid in children with Juvenile Idiopathic Arthritis a) Integrated scRNA-seq global UMAP of major cellular clusters and their b) proportional difference between different specimen types, with bootstrap confidence intervals shown (10,000 permutations).

(P = 0.02) and more hyperexpanded CD8+ T cell clones: 13.6% of total T cells in synovial fluid had the same clonotype in ≥ 20 cells, compared to 3.8% in synovial tissue (n = 8091 and 7039 cells respectively).

Conclusion: Our work implicates the synovial fluid cavity in disease pathogenesis, with synovial fluid providing a reservoir of free-flowing activated cells as barrier integrity breaks down. Despite distinct disease features and physiology, our analysis identifies shared cellular phenotypes within inflamed synovium between children and adults. This suggests that certain pathogenic mechanisms extend across the age-spectrum in inflammatory arthritis, enabling a more informed approach to clinical trials in children in the future.

References*: Zhang, F. et al. (2022) 'Cellular deconstruction of inflamed synovium defines diverse inflammatory phenotypes in rheumatoid arthritis'. bioRxiv, p. 2022.02.25.481990. Available at: https://doi.org/10.1101/2022.02.25.481990*.

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Abstract Number: 1659

Cellular Deconstruction of Stromal and Myeloid Cell Compartments in the Inflamed Synovium of Juvenile Idiopathic Arthritis

Christopher Mahony[1], Chrissy Bolton[2], Charlotte Smith[1], Vicky Alexiou[3], Huong Nguyen[3], Patricia Reis-Nisa[1], Søren Lomholt[4], Annie Hackland[1], Sunit Davda[5], Sugrah Sultan[6], Charlene Foley[5], Catherine Cotter[6], Klaudia Kupiec[3], Calliope Dendrou[2], Elizabeth C Rosser[7], Accelerating Medicines Partnership (AMP): RA/SLE[8], Fan Zhang[9], Soumya Raychaudhuri[8], Michael Brenner[10], Christopher Buckley[2], Manigandan Thyagarajan[6], Accelerating Medicines Partnership Program RA SLE Network[11], Zishan Shiekh[6], Sandrine Compeyrot-Lacassagne[5], Samantha Chippington[5], Mark Coles[2], Eslam Al-Abadi[6], Andrew Filer[1], Tissue Research in Childhood Onset Inflammatory Arthritis (TRICIA) Consortium[12], Lucy R Wedderburn[3] and Adam Croft[1], [1]University of Birmingham, Birmingham, United Kingdom, [2]University of Oxford, Oxford, United Kingdom, [3]UCL Great Ormond Street Institute of Child Health, London, United Kingdom, [4]Aarhus University, Aarhus, Denmark, [5]Great Ormond Street Hospital, London, United Kingdom, [6]Birmingham Women's and Children's NHS Foundation Trust, Birmingham, United Kingdom, [7]University College London, London, United Kingdom, [8]Brigham and Women's Hospital, Boston, MA, [9]University of Colorado, Aurora, CO, [10]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [11]Cedars-Sinai Medical Center, Los Angeles, CA, [12]MRC, Birmingham, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Pediatric Rheumatology – Basic Science

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: The synovial membrane is the primary target tissue during the effector phase of inflammatory arthritis in children and young people with Juvenile Idiopathic Arthritis (JIA). However, due to difficulties accessing synovial tissue in children, little is known of the disease mechanisms that operate locally in the synovium. As part of the UK Tissue Research in Childhood Arthritis Consortium we have generated the first single cell multiomic atlas of the inflamed synovium in JIA.

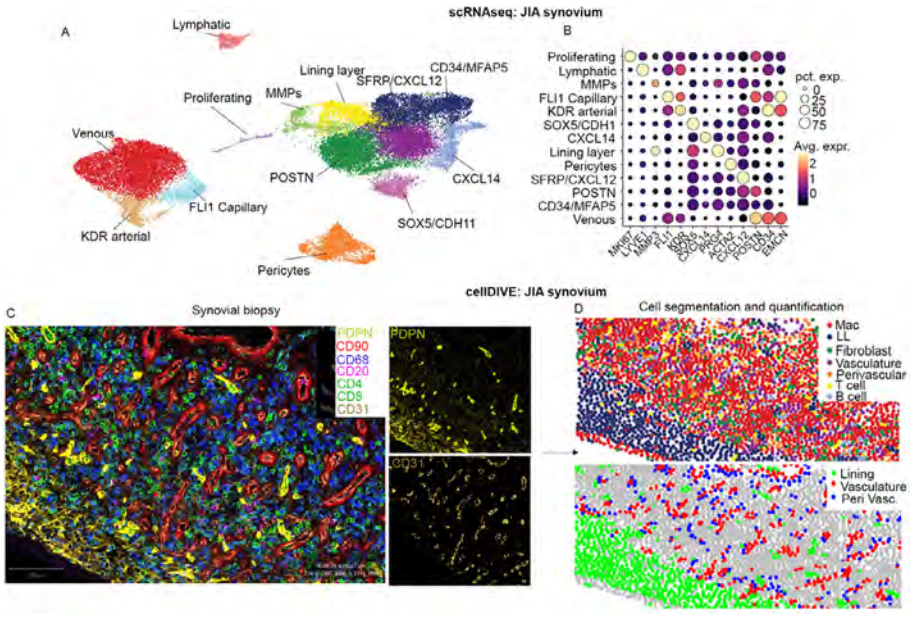

Figure 1. Multiomic characterisation of JIA inflamed synovium. (A) scRNAseq of stromal cells and assigned clusters. (B) Dotplot of key marker genes defining stromal cell subpopulations. (C) example of multiplex cellDIVE imagines. (D) analysis cellDIVE pipeline whereby cells are segmented and fluorescence quantified.

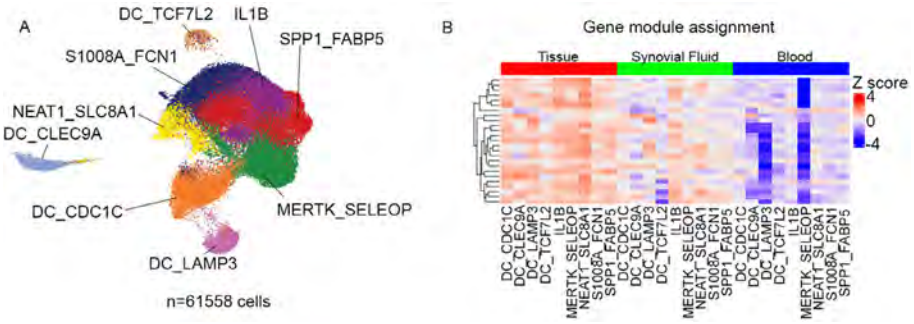

Figure 2. Transcriptional characterisation of JIA myeloid cells. (A) scRNAseq of myeloid cells and assigned clusters. (B) gene module assignment based on co-expression of top 10,000 highly variable genes.

Methods: Synovial tissues were obtained from inflamed knee joints of 12 children with JIA, who were naïve to disease modifying anti-rheumatic drugs using minimally invasive ultrasound guided biopsy procedures refined for use in children. Where possible, matched synovial fluid and peripheral blood samples were obtained from the same children at the time of the procedure. Tissues were cryopreserved, thawed and disaggregated and viable cells from each sample sorted for single-cell (sc) RNAseq. Multiplex imaging of matched synovial tissue sections (GE Cell Dive) and spatial transcriptomics were performed to generate the first synovial tissue atlas of JIA.

Results: We profiled 250,816 cells from matched tissue, blood and synovial fluid samples in children with newly diagnosed JIA using scRNA sequencing. We resolved 11 major cell types, including stromal (endothelial, pericytes, fibroblasts, lymphatic) and myeloid cells. Analysis of stromal cells revealed 7 transcriptionally distinct fibroblast clusters (Fig. 1A, B). One fibroblast cluster highly expressing Sox5 and Cadherin-11 (and devoid of endothelial/pericyte/lining layer markers) was enriched in JIA synovium when compared to adult synovium of patients with rheumatoid arthritis (RA - analysis from the Accelerated Medicines Partnership (AMP) network, Zhang et al., BioRxiv, 2022). This cluster expresses several transcription factors (Fig. 1B) and ongoing neighbourhood analysis of spatial data will determine the location of these cells in synovial tissue (Fig. 1C,D). Myeloid cells were resolved into 9 clusters that are transcriptionally conserved compared to myeloid cells from adult RA inflamed synovium (AMP: Zhang et al., BioRxiv, 2022, Fig. 2A). Differential gene expression showed heterogeneity of myeloid cells between blood, tissue, and synovial fluid (Figure 2B).

Conclusion: We have generated the first single cell atlas of the inflamed synovium in children with JIA. Through a comparative analysis with adult RA synovium, we have identified a distinct fibroblast subcluster that expresses Sox5 and Cadherin-11 and is enriched in JIA synovial tissue. It is not yet known if this fibroblast subtype represents an age, developmental or disease specific transcriptional program that drives JIA pathology. Fully mapping and characterising the inflamed synovium in children is critical in understanding the cellular pathogenesis of JIA.

References: Zhang, F. et al. (2022) 'Cellular deconstruction of inflamed synovium defines diverse inflammatory phenotypes in rheumatoid arthritis'. bioRxiv, p. 2022.02.25.481990. Available at: https://doi.org/10.1101/2022.02.25.481990

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A. Filer: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 5, Janssen, 5, Nascient, 5, Sonoma Biotherapeutics, 2; **T. Inflammatory Arthritis (TRICIA) Consortium**: None; **L. Wedderburn**: AbbVie/Abbott, 5, GlaxoSmithKlein(GSK), 5, Pfizer, 1, SOBI, 5, UCB, 5; **A. Croft**: None.

Abstract Number: 1660

Still's Disease Patients with High Interferon-stimulated Gene Expression Have Enrichment of Rare, *de Novo* and Recessive Protein Altering Variants in Innate Immune Pathways

Mariana Correia Marques[1], Zuoming Deng[2], Navid Chowdhury[2], Elizabeth Schmitz[3], Alana Platukus[4], Stephen Brooks[5], Carol Lake[2], Ly-Lan Bergeron[2], Michelle Millwood[2] and **Michael Ombrello**[6], [1]National Institute of Arthritis & Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [2]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [3]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), St. Louis, MO, [4]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Philadelphia, PA, [5]Biodata Mining and Discovery Section, National Institute of Arthritis and Musculoskeletal and Skins Diseases, National Institutes of Health, Bethesda, MD, [6]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), North Bethesda, MD

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Pediatric Rheumatology – Basic Science

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Still's disease (systemic juvenile idiopathic arthritis in children, adult-onset Still's disease in adults) is an enigmatic inflammatory condition that affects people of all ages. It is characterized by inflammasome activation and pyroptosis, and is often punctuated by striking elevation of IL-18. Increased interferon (IFN) signaling, which promotes pyroptosis, has been described in Still's disease complicated by either macrophage activation syndrome (MAS) or an emergent form of lung disease (LD) with drug-induced hypersensitivity reaction (DHR), but it is unclear whether IFN signaling is an active participant or is epiphenomenal. Here, we explore the relationship between genetic variation and IFN signaling in Still's disease.

Methods: We examined consecutive Still's disease patients enrolled in an IRB approved research study at the NIH Clinical Center. Whole blood expression of 28 IFN-stimulated genes (ISG) was quantified with custom NanoString arrays and expressed as a normalized score. Trio whole exome sequencing (WES) was performed in 41 probands and candidate causative variant lists (protein-altering *de novo,* recessive, or X-linked variants of canonical transcripts; popfreqmax frequency < 0.01) were generated. Lists of genes containing candidate causative variants were compiled for individuals with the highest or lowest ISG scores and subjected to pathway over-representation analysis (ORA) and network topology analysis (NTA) using the Web-based Gene Set Analysis Toolkit (webgestalt.org).

Results: ISG scores among 59 Still's patients were negatively skewed and the upper quartile included 15 people (Figure 1). DHR was more common in the top quartile than in the bottom quartile (0.6, 0.13; p = 0.02), while rates of active disease, IL-18 > 15K, use of IL-1 directed therapy, HLA-DRB1*15 carriage and history of MAS did not differ between the groups (Table 1). Trio WES identified 83 candidate genes among the top ISG quartile. ORA of these 83 candidate genes revealed enrichment in the macrophage activation (ratio = 21.7, p = 3.4E-7, FDR = 0.0055), type I IFN biosynthetic process (ratio = 77.9, p = 6.7E-6, FDR = 0.03) and myeloid leukocyte activation (ratio = 5.0, p = 1.9E-5, FDR = 0.039) pathways. Most people in the top ISG quartile (11/15) had candidate causative variation within these 3 pathways. Chemokine production, regulation of IL-18 production, and NF-KB signaling also had evidence of over-representation (p < 0.0005, FDR > 0.05). NTA also demonstrated enriched pathways, including the MyD88-dependent TLR signaling pathway (corrected

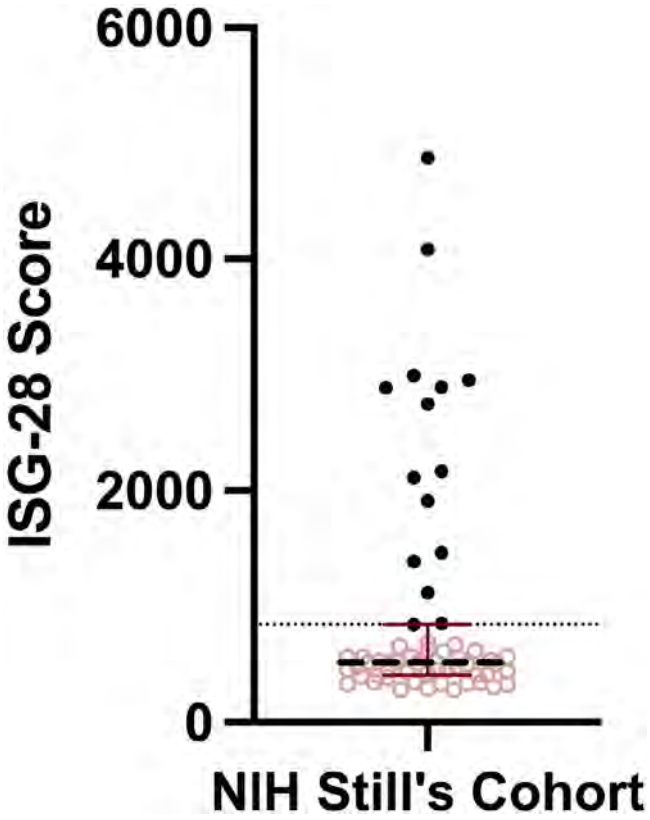

Figure 1. Scatter plot of interferon stimulated gene (ISG) scores from 59 Still's disease patients. The median and interquartile range are show by the error bars. The 75th percentile is marked by a dashed horizontal line. People in the top quartile are shown as solid circles, while all others are shown as open circles.

Table 1. Clinical characteristics of Still's patients in the top and bottom quartile of ISG scores. Active disease is defined as sJADAS > 3.

	Proportion with Characteristic		
Clinical Characteristic	**Top ISG Quartile**	**Bottom ISG Quartile**	**p-value**
Drug hypersensitivity reaction	0.60	0.13	0.02
DHR with lung disease	0.40	0.13	
DHR without lung disease	0.20	0.00	
Active disease	0.67	0.80	
History of MAS	0.40	0.27	
IL-18 > 15K pg/ml	0.40	0.20	
Current IL-1 directed therapy	0.60	0.40	
HLA-DRB1*15 positive	0.47	0.20	

p = 0.0045). ORA/NTA of 81 candidate genes from 15 subjects with the lowest ISG scores did not reveal enrichment of any pathway.

Conclusion: In our Still's cohort, high ISG score was associated with the presence of DHR but not MAS. Unbiased analysis of trio WES revealed that people with high ISG scores had specific enrichment of potentially causative variation in overlapping innate immune pathways, notably type I IFN production, MyD88/TLR signaling, and macrophage/myeloid leukocyte activation. This suggests that rare *de novo* or recessive variation contributes to the pathophysiology of Still's disease, where it promotes enhanced IFN signaling and may predispose to LD/DHR.

Disclosure: M. Correia Marques: None; **Z. Deng**: None; **N. Chowdhury**: None; **E. Schmitz**: None; **A. Platukus**: None; **S. Brooks**: None; **C. Lake**: None; **L. Bergeron**: None; **M. Millwood**: None; **M. Ombrello**: None.

Abstract Number: 1661

Spatial Transcriptional Alterations in the Cellular Landscape of Pediatric Scleroderma Skin

Kathryn Torok[1], Ying-Ju Lai[2], Zhongli Xu[3], Anwesha Sanyal[3], Giffin Werner[3], Theresa Hutchins[3], Claire Cheng[3] and Wei Chen[3], [1]University of Pittsburgh, University of Pittsburgh Medical Center, Pittsburgh, PA, [2]University of Pittbsurgh, Pittsburgh, PA, [3]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Pediatric Rheumatology – Basic Science

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Recent single-cell RNA sequencing (scRNA seq) data has been generated across several tissues in autoimmune diseases, helping to understand the cellular and molecular underpinnings of disease. However, the location of cells or interest identified and their proximity to important structure in the tissues, has not been as well described. Pairing spatial transcriptomics (ST) with scRNA seq data would add the much needed in situ spatial context of cellular and extracellular matrix tissue deposition, provide detail to characterize ligand-receptor and cell-cell interaction patterns and has the potential for biomarker discovery for rare diseases like scleroderma. Our scleroderma cohort, both localized scleroderma (LS) and systemic sclerosis (SSc) patients, have two 4mm skin punch biopsies collected in tandem from same site, one sample processed with scRNAseq and the other formalin-fixed paraffin-embedded (FFPE) available for spatial transcriptomics application.

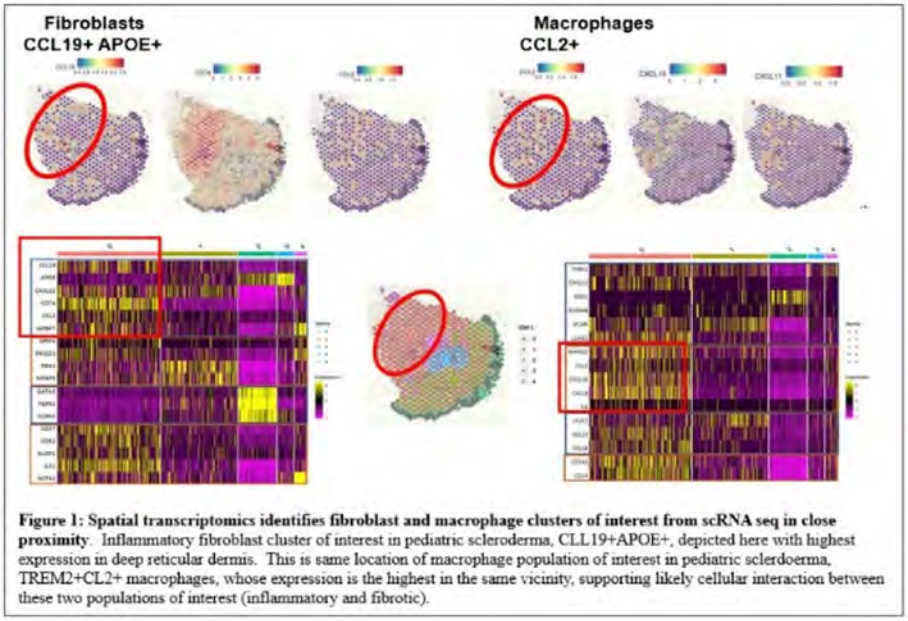

Figure 1: Spatial transcriptomics identifies fibroblast and macrophage clusters of interest from scRNA seq in close proximity. Inflammatory fibroblast cluster of interest in pediatric scleroderma, CLL19+APOE+, depicted here with highest expression in deep reticular dermis. This is same location of macrophage population of interest in pediatric sclerdoerma, TREM2+CL2+ macrophages, whose expression is the highest in the same vicinity, supporting likely cellular interaction between these two populations of interest (inflammatory and fibrotic).

Figure 1: Spatial transcriptomics identifies fibroblast and macrophage clusters of interest from scRNA seq in close proximity. Inflammatory fibroblast cluster of interest in pediatric scleroderma, CLL19+APOE+, depicted here with highest expression in deep reticular dermis. This is same location of macrophage population of interest in pediatric scleroderma, TREM2+CL2+ macrophages, whose expression is the highest in the same vicinity, supporting likely cellular interaction between these two populations of interest (inflammatory and fibrotic).

Methods: To preserve both the cellular location and architecture of the tissue while also gathering a large quantity of information about the cellular phenotypes of cells, we applied an innovative technology, VisiumSpatialGeneExpression(10XGenomics), Visium CytAssist for formalin-fixed paraffin-embedded (FFPE), which captures transcripts on spatially barcoded slide with a probe panel targeting 18,085 human protein coding genes. After sequencing, barcode information was used to determine the transcriptional profile (cellular representation) of each spot within the spatial context of the entire tissue(SpaceRanger, 10x Genomics). A novel integrative analyses approach was then applied that combines scRNA seq with spatial location of cells with in the tissue, Robust Cell-type Decomposition, which is an optimized deconvolution pipeline to decipher specific cell-type composition by anatomic location and can obtain details to the individual cell level.

Results: We performed a pilot study on 4 skin FFPE samples, 3 from pediatric LS and 1 from pediatric SSc patients using the Visium 10X CytAssist for FFPE platform. We obtained an average of a total number of 566 spots under tissue section (4 mm x 4mm) with mean reads per spot 257,119, with 96% reads mapped to probe set, with 2,896 median genes detected per spot, and a total number of 18,029 genes detected. Transcriptomic expression using either marker genes or unbiased clustering was able to distinguish epidermis, dermis, and inflammatory regions. We also investigated some of the cell subsets and upregulated genes in those clusters from our scRNA seq data and observed the co-localization of an inflammatory fibroblast (CL19+APOE+) and a macrophage population (CCL2+TREM2+) that highly expresses IL-β in pediatric scleroderma together in the deep reticular dermis (**Figure 1**).

Conclusion: Using an innovative bioinformatic approach coupling scRNA seq and ST from paired tissue samples, we are able to identify dysregulated genes of interest, cells expressing these genes and their location within the skin and surrounding cells. To our knowledge, this would be the first study to employ spatial transcriptomics in localized scleroderma and systemic sclerosis skin.

Disclosure: K. Torok: None; **Y. Lai**: None; **Z. Xu**: None; **A. Sanyal**: None; **G. Werner**: None; **T. Hutchins**: None; **C. Cheng**: None; **W. Chen**: None.

Abstract Number: 1662

Chronic Excess IL-18 Induces NK Deficiency, but Drives Hyperinflammation via CD8 T-cell Cytokine Overproduction and Selective Immunodeficiency

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Pediatric Rheumatology – Basic Science
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Systemic Juvenile Idiopathic Arthritis (SJIA) and Macrophage Activation Syndrome (MAS) are associated with highly elevated peripheral blood levels of the inflammasome-activated cytokine IL-18 and chronic exposure to free IL-18. IL-18 canonically acts on NK and activated T-cells in concert with other signals, like T-cell receptor engagement or IL-12 signaling, to amplify Interferon gamma (IFNg) production and cytotoxicity. We sought to determine the mechanisms by which excess IL-18 drives systemic hyperinflammation.

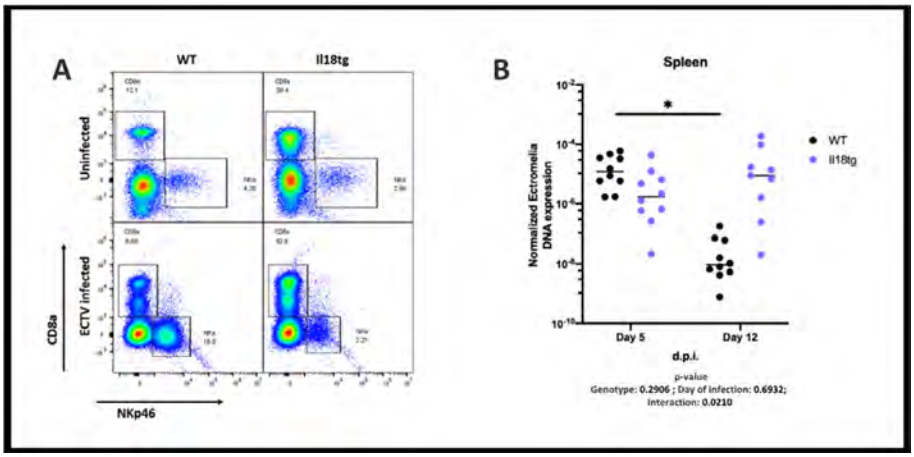

Figure 1. (A) Representative flow plots of live liver immune cells from uninfected mice or at day 5 post-infection showing sustained NK deficiency and increased CD8 T-cells. (B) 18s rRNA normalized ectromelia viral DNA (Evm003) from spleen at the indicated timepoints. Significance was analyzed with a two-way ANOVA.

Methods: We assessed lymphocyte phenotypes, distribution, and function via flow cytometry and RNAseq in mice with transgenic expression of mature, secretable IL-18 (Il18tg) and relevant controls. Lymphocytic Choriomeningitis Virus (LCMV) Armstrong strain and ectromelia virus (ECTV) were injected intraperitoneally and via footpad, respectively. Cytokines were measured by bead array and viral quantitation by quantitative PCR. Data were analyzed using descriptive statistics.

Results: Like SJIA/MAS patients, Il18tg mice demonstrated decreased numbers of NK cells and a concomitant increase in activated CD8 T-cells in peripheral blood, spleen, and liver. Splenic and hepatic NK cells from Il18tg mice showed decreased IL-18 receptor expression, and were enriched for cell cycle and gene transcription programs, suggesting rapid cellular turnover possibly due to activation-induced cell death. Il18tg mice cleared (non-lytic) LCMV infection similarly to WT, but thereafter developed CD8 T-cell and IFNg-mediated immunopathology reminiscent of MAS. To directly challenge NK function in vivo, We infected Il18tg mice with ectromelia, which causes severe viral immunopathology in NK-depleted mice. In contrast to WT, NK cells from infected Il18tg mice neither expand nor upregulated activation markers. However, Il18tg mice managed virus similarly to WT mice at early timepoints. NK depletion impaired viral clearance in WT, but not Il18tg mice. As with LCMV, Il18tg mice developed MAS at 8-12 days post-infection, the peak of the CD8 T-cell response. As expected, WT mice largely cleared ectromelia between days 5 and 12. Il18tg mice showed robust CD8 T-cell expansion and activation, but nevertheless failed to significantly decrease ectromelia DNA (Fig. 1).

Conclusion: Thus, though chronic excess IL-18 both impairs NK cell numbers and IL-18 responsiveness, NK dysfunction appears irrelevant for the development of virus-triggered MAS. Chronic IL-18 excess may overcome NK dysfunction by "pre-priming" CD8 T-cell responses at early timepoints. However, excess IL-18 induced hyperinflammation to a variety of triggers, but only with the lytic ectromelia virus did excess IL-18 also causean unexpected, selective immunodeficiency most evident at the peak of CD8 T-cell expansion. Together, this suggests IL-18 may promote MAS by both CD8 T-cell cytokine amplification and an unexpected impairment of viral clearance.

Disclosure: J. Varghese: None; **S. Canna**: Apollo Therapeutics, 2, Novartis, 12, Site PI for industry-sponsored trial, PracticePoint CME, 6, Simcha Therapeutics, 2, Sobi, 6; **E. Landy**: None; **L. Eisenlohr**: None; **E. Peauroi**: None; **V. Dang**: None; **A. Frank-Kamenetskii**: None; **J. Morrissette**: None.

Abstract Number: 1663

Clinically Severe Systemic Sclerosis Skin Harbors Inflammatory Fibroblasts Associated with Lymphocytes and Plasmacytoid Dendritic Cells

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Basic Science

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: We have previously shown that skin fibroblast activation is related to clinical severity and resolves with improvement in diffuse systemic sclerosis (dcSSc). The immune cells that associate with fibroblast activation are not fully characterized. The purpose of this study was to evaluate associations between immune cells and fibroblasts of varying stages of activation in dcSSc skin.

Methods: Histology of 137 forearm skin biopsies from 105 dcSSc patients were scored for fibroblast markers (CD34, alpha smooth muscle actin (aSMA); semiquantitative), and immune cells (B cells (CD20+), T cells (CD3+) and plasmacytoid dendritic cells (pDCs; CD123+); count per 5 HPF). 79 samples were also stained for MxA, a type 1 interferon (IFN)-related protein, scored present or absent. Non-inflammatory fibroblast pattern was defined by $CD34^{high}$/$aSMA^{low}$ scores. Inflammatory fibroblast pattern was defined as $aSMA^{high}$ and/or $CD34^{low}$ scores. Clinical variables and cell counts were compared between fibroblast immunophenotypes using Fisher's exact, t-test, or Wilcoxon rank-sum. Spearman correlation was used to assess the association between histologic features. Imaging mass cytometry (IMC) was used to visualize immune-stromal cell spatial interactions. Gene expression was analyzed by microarray for all samples. GSEA was performed using hallmark gene sets between fibroblast groups. Average expression of genes in selected pathways were ranked, and a loess curve was fit to each fibroblast group (bands represent 0.99 confidence interval).

Results: Inflammatory (vs. non-inflammatory) fibroblast samples (66 of 137, 48%) had worse clinical severity (modified Rodnan skin score ($p< 0.001$), HAQ ($p=0.012$), Patient Global ($p=0.036$) and Physician Global ($p< 0.001$)) (Table 1A) and higher median CD20+ ($p< 0.001$), CD3+ ($p=0.003$) and CD123+ cell count ($p=0.028$) (Table 1B). CD34 (key marker of non-inflammatory fibroblasts) correlated negatively with CD20 (r_s=-0.315, $p=0.0002$), CD123 (r_s=-0.281, $p=0.0009$), and CD3 (rs=-0.236, $p=0.0058$), while aSMA (key marker of inflammatory fibroblasts) correlated positively with CD20 (r_s=0.415, $p< 0.00001$) and CD3 (r_s=0.212, $p=0.0135$). Samples with detectable MxA protein expression had higher median CD123+ cells (5 vs. 1, $p=0.001$). IMC in a representative sample revealed infiltrating pDC adjacent to B cells and local interactions between these cells and aSMA+ fibroblasts (Fig. 1). Gene expression analysis demonstrated upregulation of IFN-alpha, TGF-beta, and inflammatory response as well as epithelial-mesenchymal transition among samples with inflammatory vs. non-inflammatory fibroblasts (Fig. 2).

Conclusion: Inflammatory fibroblasts in clinically severe SSc skin are associated with hallmark inflammatory response, IFN-alpha response, and TGF-beta signaling, as well as T cell, B cell, and pDC infiltration. Inflammatory fibroblasts are physically associated with B cells and pDCs in SSc skin. These data are relevant to SSc trials targeting B cell and IFN pathways. To our

Table 1. Clinical and molecular characteristics by skin fibroblast immunophenotype

	Non-inflammatory Fibroblasts[a] (n=71)	Inflammatory, Fibroblasts[a] (n=66)	p-value
A. Clinical			
Age, mean (SD)	50.2 (14.2)	51.5 (13.8)	0.60
Sex, n (%)	16 (23%)	19 (29%)	0.44
Race, n (%)			0.28
White	48 (68%)	53 (80%)	
Black	8 (11%)	7 (11%)	
Asian	12 (17%)	5 (8%)	
Other	3 (4%)	1 (2%)	
Disease duration, n (%)			**0.006**
< 2 years	32 (45%)	47 (71%)	
2-3 years	24 (34%)	10 (15%)	
>3 to 6 years	15 (21%)	9 (14%)	
Autoantibody profile, n (%)			
Scl-70, positive	28 (39%)	16 (24%)	0.068
RNA polymerase III, positive	29 (45%)	39 (60%)	0.11
Centromere, positive	3 (4%)	4 (6%)	0.72
Antinuclear antibody, positive	66 (93%)	62 (94%)	1.00
Interstitial lung disease, present, n (%)	28 (39%)	21 (32%)	0.37
HAQ, median (IQR)	0.8 (0.2, 1.2)	1.1 (0.6, 1.6)	**0.012**
MRSS, total, median (IQR)	20 (14, 25)	26 (21, 33)	**<0.001**
Physician Global (VAS, 0-10), mean (SD)	4.3 (1.6)	5.5 (1.7)	**<0.001**
Patient Global (VAS, 0-10), median (IQR)	3.0 (1.9, 5.0)	4.8 (2.6, 6.0)	**0.036**
B. Histology			
CD20 (B cells)[+], median (IQR), n=136	0 (0, 1)	2 (0, 10)	**<0.001**
CD3 (T cells)[+], median (IQR), n=135	60 (40, 90)	80 (50, 120)	**0.015**
CD123 (pDC)[+], median (IQR), n=136	2 (1, 8)	5 (2, 10)	**0.028**
MxA (IFN response)[*]) n (%), n=79	10 (21%)	7 (22%)	1.00

[a]Non-Inflammatory fibroblasts were defined as samples with $CD34^{high}/aSMA^{low}$ immunohistochemical scores. Inflammatory fibroblasts had low CD34 and/or high aSMA scores. [+]immune cells were counted by examining total biopsy slide and counting cells within the 5 most populated high-power field (HPF); [*]MxA staining was scored as present or absent. MRSS=modified Rodnan skin score; HAQ=health assessment questionnaire; VAS=visual analogue scale.

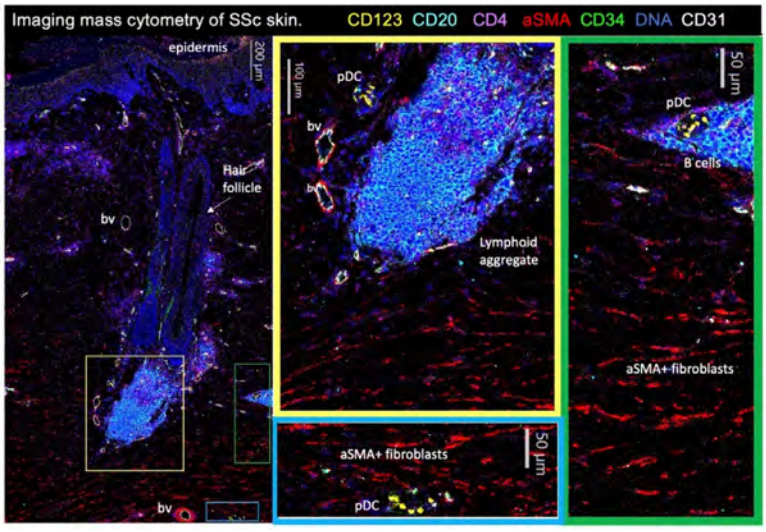

Figure 1. The use of imaging mass cytometry (Hyperion) to visualize pDCs, B cell, T cells, and fibroblasts in the skin of an individual with early, severe diffuse systemic sclerosis (modified Rodnan skin score (MRSS) 32, local (biopsy-site) MRSS 3).

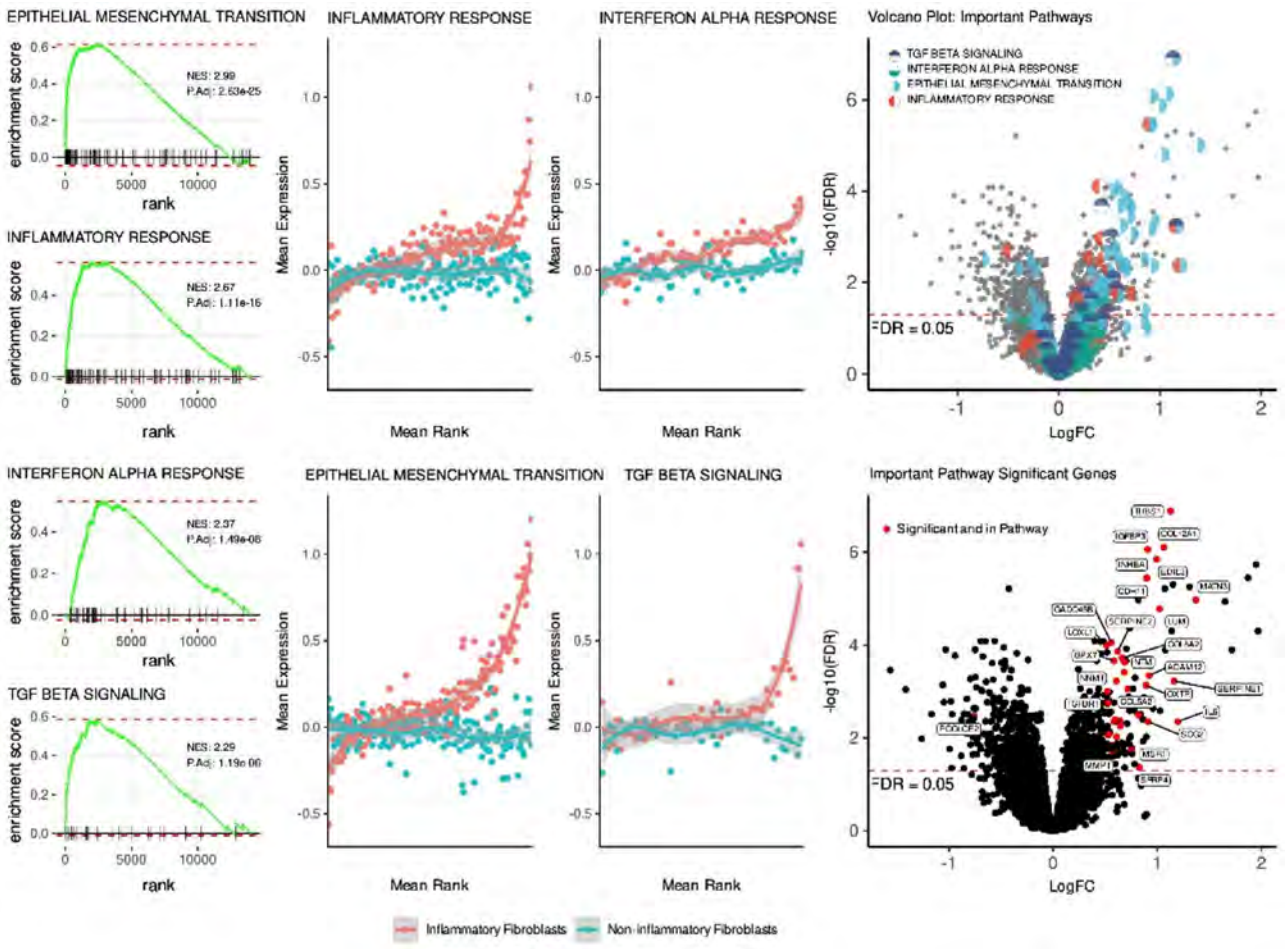

Figure 2. Genes related to interferon-alpha response, TGF-beta signaling, and hallmark inflammatory response as well as epithelial-mesenchymal transition are upregulated among samples characterized by inflammatory versus non-inflammatory fibroblasts. (Left Panel) Gene Set Enrichment Analysis for selected pathways according to fibroblast group. (Center Panel) Average expression of individual genes included in each pathway according to inflammatory vs. non-inflammatory fibroblast samples. (Right Panel) Volcano plot of relevant genes between inflammatory vs. non-inflammatory fibroblast samples.

knowledge, this is the first report using IMC to visualize immune-stromal cell spatial interactions in dcSSc skin. Future work quantifying IMC data will further characterize these associations in a larger sample.

Disclosure: K. Lakin: None; **R. Spiera**: AbbVie/Abbott, 2, 5, Amgen, 2, AstraZeneca, 5, chemocentryx, 5, corbus, 5, Formation Biologics, 5, GSK, 2, 5, Inflarx, 5, Kadmon, 5, Novartis, 2, 5, Principia, 5, Sanofi, 2; **Y. Zhang**: None; **D. Oliver**: None; **A. Bloostein**: None; **H. Ravichandran**: None; **N. Anandasabapathy**: 23&me, 2, Immunitas, 2, Janssen, 1, Leo pharma, 1, Shennon Pharma, 1; **F. Barrat**: AstraZeneca, 2, Boehringer-Ingelheim, 2, Colton Center - NYU, 1, IpiNovyx Bio, 2, 5, 8, 10; **J. Gordon**: Cumberland Pharmaceuticals, 5, Prometheus Pharmaceuticals, 5; **D. Orange**: AstraZeneca, 2, Pfizer, 2.

Abstract Number: 1664

Fibroblast Specific Interferon Regulatory Factor 7 (IRF7) Expression Is a Key Link Between Type I Interferon Activation and the Exaggerated Dermal and Pulmonary Fibrosis in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Basic Science

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: A prominent interferon (IFN) activation signature has been observed at the peripheral blood and end-organ levels in systemic sclerosis (SSc). However, the mechanisms by which the IFN pathway leads to the exaggerated fibrotic response in fibroblasts is not well-understood. Interferon Regulator Factor 7 (IRF7), a key transcription factor in the IFN pathway, has been identified as one of the top predicted upstream regulators of SSc transcript profile in skin bulk sequencing and SSc enriched fibroblast subpopulations in single-RNA sequencing. Herein, we investigated the role of IRF7 in fibroblasts in linking type I IFN activation to fibrosis.

Methods: Skin IRF7 expression and its clinical correlates were examined in 113 SSc patients and 44 matched healthy controls. SSc and healthy control dermal fibroblasts were treated with IFNα and nine prominent Th1, Th2, or Th17 cytokines, as well as with IFN inhibitors. *Col1a2-Cre/Irf7$^{f/f}$* fibroblast specific conditional knockout (KO) mice and *Col1a2-Cre* control mice

Figure.1

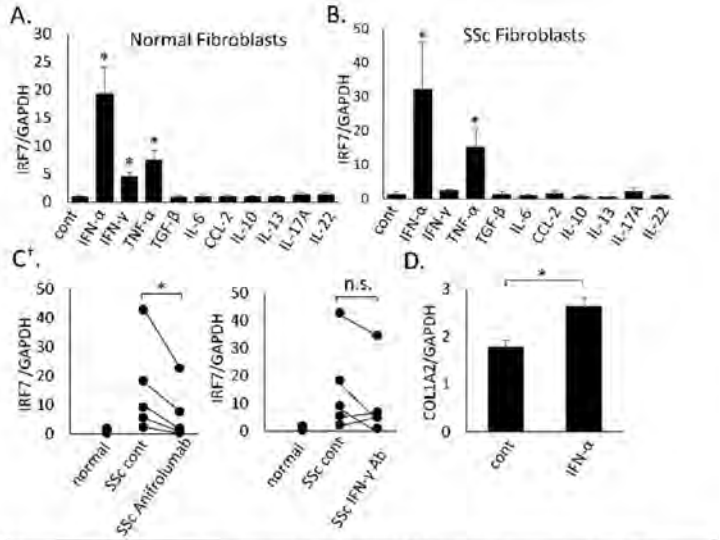

Figure 1. IFN-α induced IRF7 expression in normal and SSc dermal fibroblasts and anti-IFN treatment attenuated IRF7 expression in SSc fibroblasts: A, B. Healthy control or SSc skin fibroblasts were treated with indicated cytokines for 24 hrs and total RNA was extracted for qRT-PCR analysis. *p<0.05. **C.** Human skin fibroblasts treated with anti-type I IFN receptor antibody (Anifrolumab) or anti-IFN-γ antibody for 24 hrs. Total RNA was extracted for qRT-PCR. All results from **A,B,C** were normalized to GAPDH and present fold induction compared to controls. n=5. *p<0.05. **D.** SSc fibroblasts were stimulated with IFN-α for 72 hrs and RNA extracted for qRT-PCR analysis. n=5, *p<0.05.† Results of the same experiment shown in two panels in order to depict treatment related changes.

Figure.2

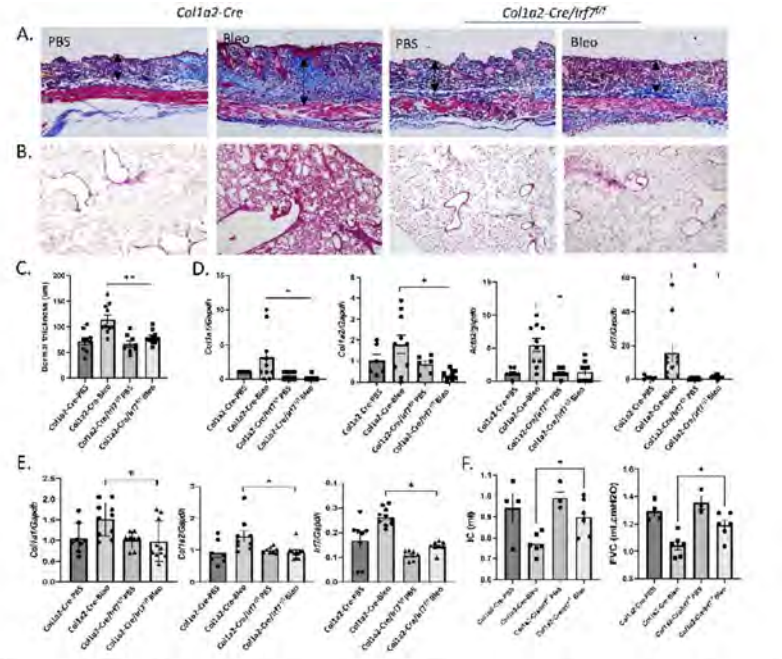

Figure 2. *Irf7* knock down in fibroblasts attenuated skin & lung fibrosis in bleomycin induced fibrosis mouse models: A. Masson & Trichrome stain is showing dermal collagen deposition in different treatment groups. **B.** H&E stain in lung tissues with i.p. bleomycin model. **C.** Dermal thickness measurements. (n=10). **D.(skin)& E.(lung).** qRT-PCR showing attenuated *Col1a1*,*Col1a2*, *Acta2* and *Irf7* mRNA expression in *Col1a2-cre-Irf7*$^{f/f}$ mice. n=6-10 per group.*p<0.05. **F.** Lung function test showing attenuated IC and FVC. N=4-6. .*p<0.05.

(n=10 per experimental group) were treated either with daily subcutaneous or intraperitoneal (i.p.) bleomycin injections for 28 days to induce dermal and pulmonary fibrosis, respectively. Furthermore, *Col1a2-Cre/irf7*$^{f/f}$*Tsk*+ triple congenic mice and *Col1a2-Cre/Tsk*+ control mice received tamoxifen injections for Cre activation and were examined for hypodermal fibrosis.

Results: Skin IRF7 mRNA levels were higher in SSc patients than in healthy controls (p=0.0009). Moreover, skin IRF7 mRNA levels correlated significantly with modified Rodnan Skin Score (r=0.42, p< 0.0001) and were higher in patients with early diffuse SSc (disease duration < 3 years) than in the remainder of patients(p=0.006). In vitro study (Figure 1), IFNα stimulation resulted in the highest IRF7 expression levels among all examined cytokines in SSc and control fibroblasts. Moreover, treatment with an inhibitory antibody against type I IFN receptor (anifrolumab) consistently led to decreased IRF7 expression in unstimulated cultured SSc fibroblasts while a similar effect was not observed with IFNγ blockade. Linking type I IFN

Figure.3

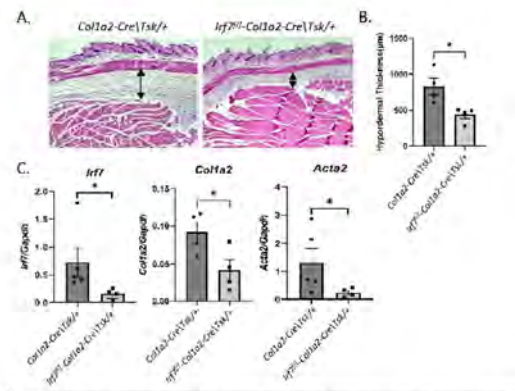

Figure 3. Knock down *Irf7* in fibroblasts attenuated skin fibrosis in *Tsk/+* mouse model: **A.** H&E stain in skin from *Irf7*$^{f/f}$*/Col1a2-Cre\Tsk/+* mice. **B.** Quantitation of hypodermal thickness. **C.** Downregulation of Irf7, Col1a2 and Acta2 mRNA expression in the skin of *Irf7*$^{f/f}$*-Col1a2-cre\Tsk/+* mice. n=4-5 per group. *p<0.05.

activation to the fibrotic response, IFNα stimulation also led to increased collagen expression in SSc dermal fibroblasts. As shown in Figure 2, in the bleomycin induced dermal fibrosis model, tamoxifen injected *Col1a2-Cre/Irf7$^{f/f}$* mice had markedly attenuated dermal fibrosis based on histology and mRNA levels. In i.p. bleomycin lung fibrosis model, tamoxifen injected *Col1a2-Cre/irf7$^{f/f}$* mice showed attenuated pulmonary fibrosis based on histology, mRNA, and lung function. In the *Col1a2-cre/irf7$^{f/f}$\Tsk+* triple congenic mice, fibroblast specific *Irf7* knock-down led to reduced hypodermal thickness, *Col1a2* and *Acta2* mRNA levels compared to control *Col1a2-Cre/Tsk+* mice after *Cre* activation (Figure 3).

Conclusion: IRF7 is upregulated in SSc skin and correlates with the severity of skin disease. Its expression in fibroblasts is induced by Type I IFN, and fibroblast-specific deletion of IRF7 abrogated skin and lung fibrosis.IRF7 therefore provides a pathologic bridge between type I IFN signaling and the fibrotic response in fibroblasts.

Disclosure: M. Wu: Boehringer-Ingelheim, 5, Janssen, 5, Prometheus Biosciences, 5; **J. Alonso**: None; **J. charles**: None; **B. Skaug**: None; **T. Mills**: None; **M. Mayes**: Boehringer Ingelheim, 1, 5, British Medical Journal, 9, Corbus, 5, EICOS, 1, 5, Horizon Pharma, 5, Medtelligence, 6, Mitsubishi Tanabe, 1, 5, Oxford University Press, 9, Prometheus, 5, Springer International Publishing, 9; **S. Assassi**: AstraZeneca, 2, aTyr, 2, Boehringer Ingelheim, 2, 5, CSL Behring, 2, Janssen, 5, Merck, 2, Momenta, 5, TeneoFour, 2.

Abstract Number: 1665

Endothelial Response to Type I Interferon Contributes to Vasculopathy and Fibrosis and Predicts Disease Progression of Systemic Sclerosis

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Basic Science
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Type I interferon (IFN-1) signature is a hallmark of patients with systemic sclerosis (SSc). However, its significance in clinical stratification and contribution to deterioration still need to be better understood.

Methods: For hypothesis generation, we performed single-cell RNA sequencing (scRNAseq) on skin biopsies (SSc=4, control =2) using the BD Rhapsody platform. Two publicly available datasets of skin scRNAseq were used for validation (GSE138669: dcSSc=12, control=10; GSE195452: dcSSc=52, lcSSc=41, control =54). IFN-1 signature was mapped, functionally investigated in a bleomycin plus IFNα2-adeno-associated virus (IFNA2-AAV) induced model, and verified in an SSc cohort (n=61).

Results: The discovery and validation datasets shared findings. The endothelial cells (EC) had the most prominent IFN-1 response among dermal non-immune cells. EC IFN-1 signature was increased both in SSc vs. control and in dcSSc vs. lcSSc. Among EC subclusters, the elevation of IFN-1 signature in dcSSc patients compared to control was still true in capillary, post-capillary venule, and venule ECs in all datasets. Endothelial-to-mesenchymal transition (EndoMT) scores increased in parallel. IFNA2-AAV deteriorated bleomycin-induced dermal fibrosis, EndoMT, and perivascular fibrosis and caused blood vessel loss with EC apoptosis. Vascular MX1, an IFN-1 response protein, was significantly increased both in

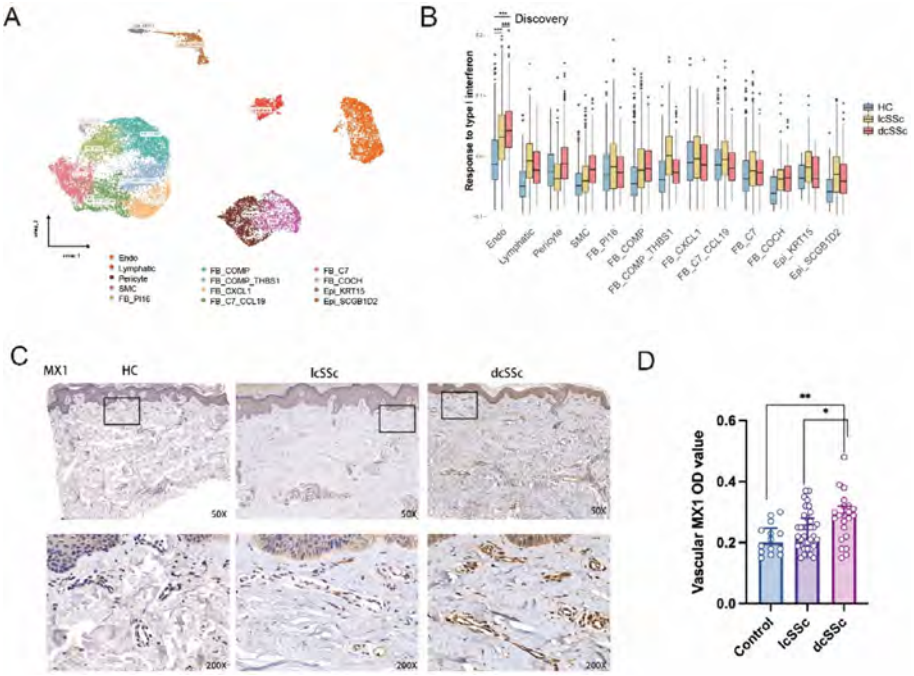

Figure1 (A)Umap plot exhibiting the identified 13 clusters in dermal stromal cells. (B)Response to type I interferon scores calculated by GSVA method in each celltype. (C)Immunohistochemical staining of MX1 in dcSSc, lcSSc, and HC skin. (D)Qualification of vascular MX1 OD value.

total SSc skin and in dcSSc vs. lcSSc. To predict disease progression in 6-34 months, the baseline vascular MX1 performed similarly to skin score in total SSc and was superior in the dcSSc subpopulation.

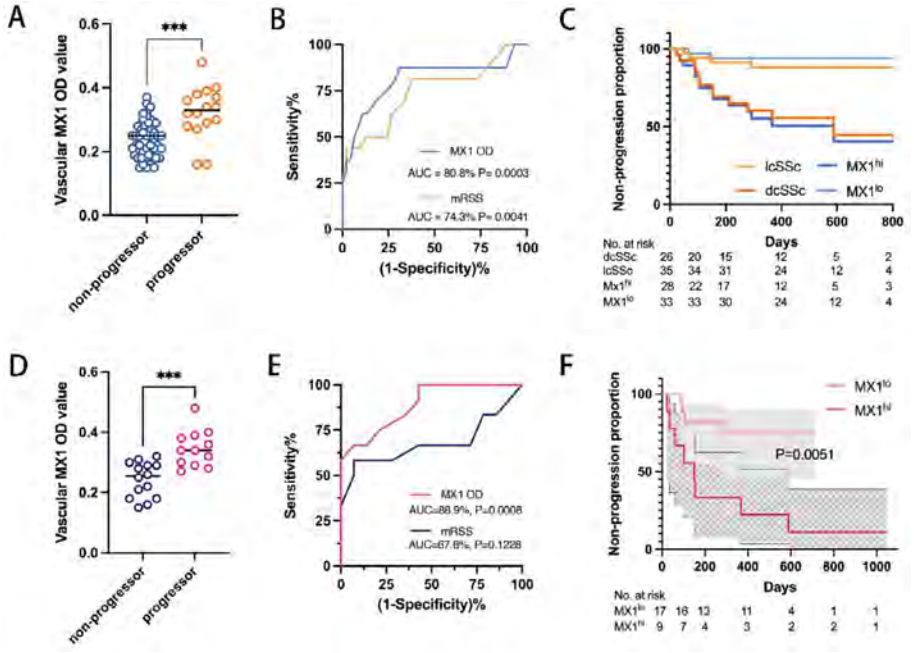

Figure2: Vascular MX1 is predictive of disease progression in SSc. (A)Vascular MX1 OD value in progressor and non-progressor among all SSc patients. (B)ROC curves of the predictive values for vascular MX1 OD value (blue) and mRSS (yellow) in all SSc patients. (C)Kaplan–Meier analysis of non-progression in patients with low and high vascular MX1 expression as well as patients with lcSSc and dcSSc . (D)Vascular MX1 OD value in progressor and non-progressor among dcSSc patients. (E)ROC curves of the predictive values for vascular MX1 OD value (red) and mRSS (purple) in dcSSc group. (F)Vascular MX1 distinguished disease worsening eddectively in Cox regression for dcSSc.

Conclusion: The EC IFN-1 signature distinguished SSc skin subtypes and disease progression and may contribute to vasculopathy and fibrosis.

Disclosure: H. Yin: None; **O. Distler**: 4P-Pharma, 2, 5, 6, AbbVie, 2, 5, 6, Acceleron, 2, 5, 6, Alcimed, 2, 5, 6, Altavant Sciences, 2, 5, 6, Amgen, 2, 5, 6, AnaMar, 2, 5, 6, Arxx, 2, 5, 6, AstraZeneca, 2, 5, 6, Bayer, 2, 5, 6, Blade Therapeutics, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Citus AG, 12, Co-Founder, Corbus Pharmaceuticals, 2, 5, 6, CSL Behring, 2, 5, 6, Galapagos, 2, 5, 6, Galderma, 2, 5, 6, Glenmark, 2, 5, 6, Gossamer, 2, 5, 6, Horizon Therapeutics, 2, 5, 6, Janssen, 2, 5, 6, Kymera, 2, 5, 6, Lupin, 2, 5, 6, Medscape, 2, 5, 6, Miltenyi Biotec, 2, 5, 6, Mitsubishi Tanabe, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143), 10, Prometheus Biosciences, 2, 5, 6, Redx Pharma, 2, 5, 6, Roivant, 2, 5, 6, Topadur, 2, 5, 6; **B. Li**: None; **Q. Yan**: None; **L. Lu**: None.

Abstract Number: 1666

TNF-mediated Pulmonary Hypertension Is Marked by Aberrant Bone Morphogenic Protein (BMP) and Integrin/Basement Membrane Ligand-Receptor Signaling

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Basic Science
Session Type: Abstract Session
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Background/Purpose: : We recently described TNF-transgenic mice as a novel model of pulmonary hypertension (PH) and have shown that they express altered endothelial and mesenchymal cell populations by single-cell RNA sequencing. Mutations in BMPR2 are known to cause genetic pulmonary arterial hypertension (PAH), and loss of BMPR2 function is seen in idiopathic forms of PAH, but the role of BMP signaling in inflammatory PH has not been well characterized.

Methods: Endothelial and mesenchymal cells were isolated from lungs from TNF transgenic mice and littermate controls at 8, 14, and 20 weeks of age (n=3-5 mice per timepoint and genotype).6000-8000 cells were used for droplet-based single cell capture (10X Genomics) and RNA sequencing. Data were analyzed using multinichenetr to assess for ligand-receptor (L:R) interactions between cell types in each condition. Putative L:R interactions were confirmed using immunostaining including stains for BMPR2, BMPR1a, BMP2, BMP4, Noggin, COL4A1, and ITGA2.Representative images were taken at both central/peribronchiolar areas and peripheral lung areas. aSMA was utilized to visualize vessels and as an anatomical landmark in other immunofluorescent stains BMPR2/Nog/aSMA, BMPR1a/Nog/aSMA, BMP4/Nog/aSMA, and Bmp2/Hjv/aSMA.

Results: Ligand-receptor analysis demonstrated an impaired interaction ofBMPR2 with BMP ligands (BMP4, BM6, and BMP7) in TNF-Tg PAH lungs, leading to the establishment of an alternative maladaptive BMP signaling cascade dominated by the interaction of BMP2 with BMPR1a and HJV (Figure 1 A-D).Immunofluorescence confirmed down-regulation of BMPR2 and BMP4 in TNF-Tg relative to WT littermates and up-regulation of BMPR1a, HJV, BMP2, and Noggin in TNF-Tg lungs (Figure 1E-H). L:R interactions between basement membrane proteins (COL4A1, HSPG2), TGF-beta family

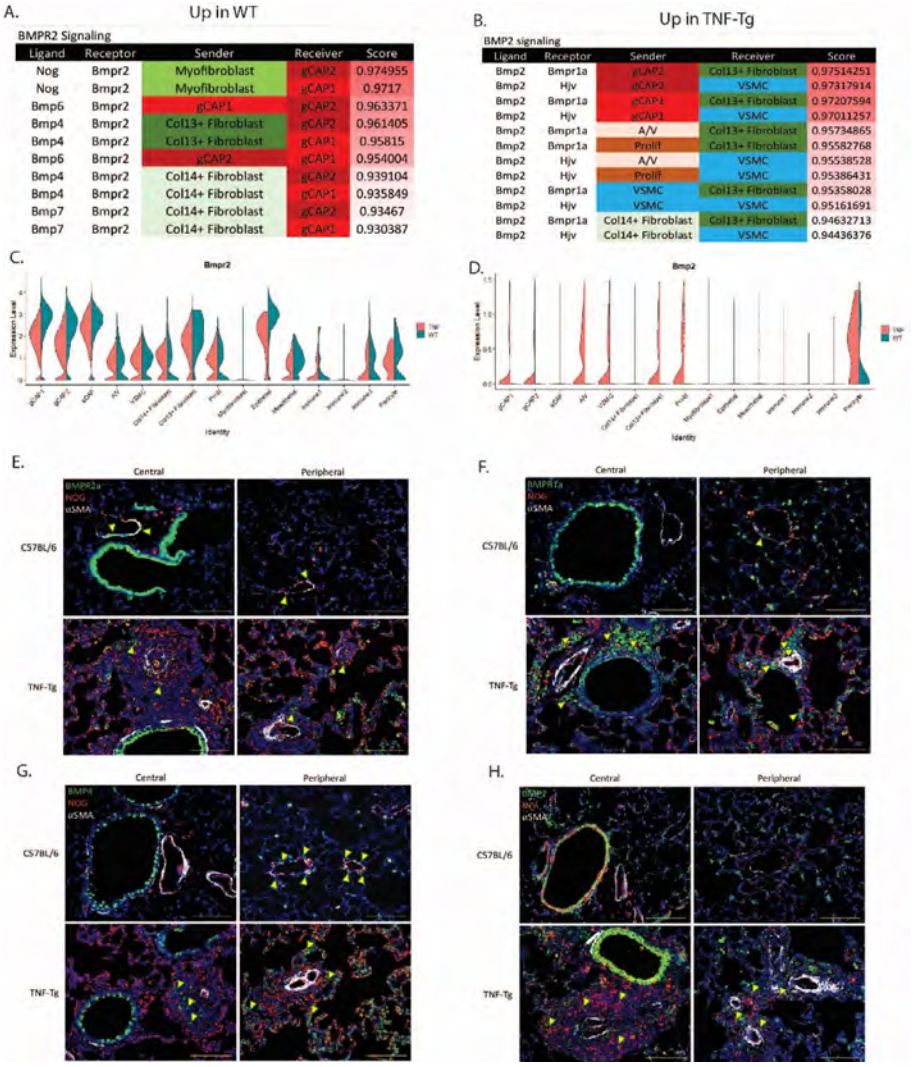

Figure 1. Altered BMP signaling in TNF-Tg lungs is a hallmark of pulmonary hypertension. A. Ligands, receptors, cells sending and receiving signals, and the strength of the predicted interaction in WT mice. Note that BMPR2 signaling has the strongest ligand-receptor interactions in WT mice. B. Ligands, receptors, cells sending and receiving signals, and the strength of the predicted interaction in TNF-Tg mice. Note that BMP2 signals through BMPR1a and HJV but the absence of BMPR2 signaling is absent in TNF Tg lungs. C. Violin plot showing differential expression of BMPR2 in endothelial and mesenchymal cell populations. Note that BMPR2 loss is most prominent in TNF-Tg gCAP cells . D. Violin plot demonstrating differential expression of BMP2 in endothelial and mesenchymal cell populations. Note that BMP2 is over-expressed in most cell types and that it is only expressed in TNF-Tg lungs in some cells. E. Representative immunofluorescence for BMPR2, Noggin, and aSMA. F. Immunostaining for BMP1a, Noggin, and aSMA. G. Immunostaining of BMP4, Noggin, and aSMA. H. Immunostaining for BMP2, Hjv, and aSMA.

proteins, and integrins increased, while a decrease in pro-angiogenic signaling was observed in TNF-Tg mice (Figure 2). Circos plot and network analysis confirmed the centrality of altered BMP signaling in TNF-mediated PH pathogenesis (Figure 3).

Conclusion: Constitutive activation of TNF leads to loss of BMPR2 signaling and formation of an alternate weaker BMP signaling profile associated with increased TGF-beta/integrin and basement membrane protein expression in the PH cellular niche. Given the centrality of BMP signaling in PAH, this suggests that TNF is a key upstream mediator of pulmonary vascular disease and might represent an essential target for modulating PAH induced by inflammation and autoimmunity.

Disclosure: J. Rangel-Moreno: None; **M. Garcia-Hernandez**: None; **Q. Xu**: None; **B. Korman**: Teneofour, Inc, 2.

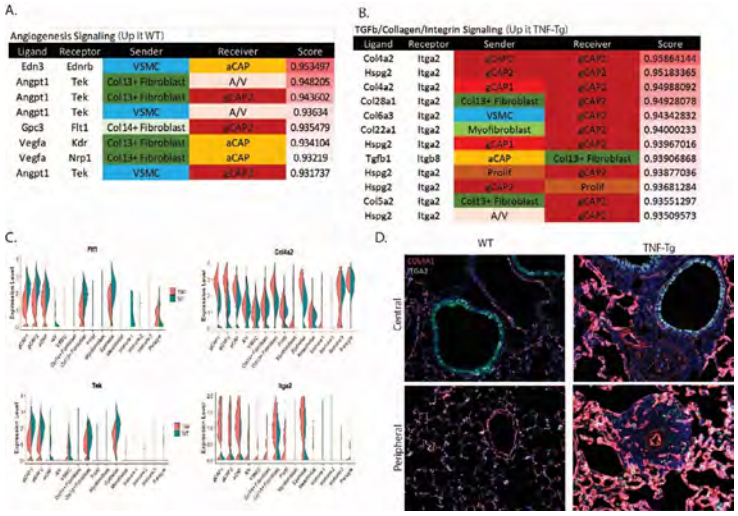

Figure 2. TNF-Tg pulmonary hypertension is associated with increased integrin/basement membrane and impaired angiogenesis signaling. A. Ligand:receptor pairs and strength of the predicted interaction in WT mice support the presence of an angiogenesis signature which is prominent in WT and not TNF-Tg mice. B. Ligand:receptor pairs and strength of the predicted interaction in TNF-Tg mice indicate over-expression of collagens and basement membrane proteins interacting with integrins. C. Violin plots demonstrating differential expression of Flt1, Tek, Col4A2, and Itga2 in endothelial and mesenchymal cell populations. D. Immunofluorescence for Col4a1 and Itga2 demonstrates significant up-regulation of these proteins in TNF-Tg lungs.

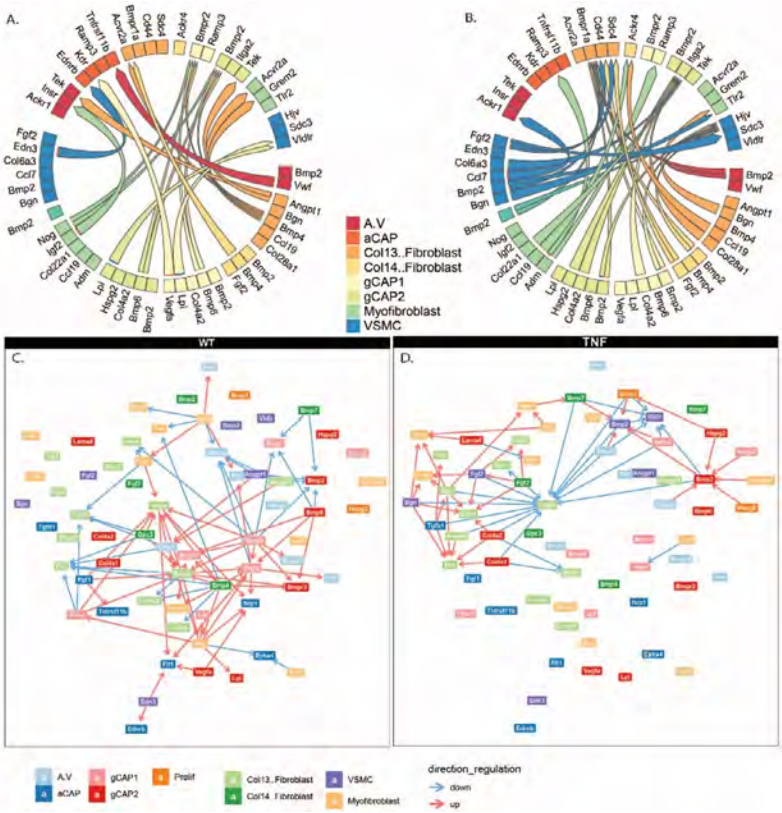

Figure 3. Network analysis demonstrates centrality of BMP signaling in TNF-mediated pulmonary hypertension. A-B. Circos plots displaying most differentially regulated ligand/receptor pairs ascertained by multinichenetr in WT lungs (A) and TNF (B) lungs; sender cells are listed on the bottom while arrows point to receiver cells on the top. C-D. Network diagram showing the gene regulatory links between ligands from sender cell types to their induced ligands/receptors in receiver cell types in WT (C) and TNF (D) conditions. Lines show if the ligand/receptor in the receiver is a potential downstream target of the ligand based on literature/database knowledge and correlation in expression across samples.

Abstract Number: 1667

Characterization of the Vascular Niches in Systemic Sclerosis (SSc) as a Prototypical Immune-mediated Fibrotic Disease with Prominent Vasculopathy Using Imaging Mass Cytometry

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Basic Science
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Systemic sclerosis (SSc) is a prototypical collagen-vascular disease with prominent vasculopathy. Although microvascular changes are the earliest histopathologic manifestation of SSc, the vascular dysregulation and immune environment of vascular niche in SSc are largely unknown. Here, we applied Imaging Mass Cytometry (IMC) as a spatial proteomic approach to deconvolute the heterogeneity of vascular cells at single-cell level *in situ* and to characterize cellular alterations of the vascular niches of SSc patients.IMC is a multiplex imaging technique that detects metal isotope-labelled antibodies in tissues using localization-specific laser mediated ablation coupled with mass-spectrometry.

Methods: Skin biopsies collected from 19 SSc patients and 14 matched healthy individuals were analyzed by IMC, yielding a total of90,755 cells including 8,865 vascular cells and 4,096 immune cells. Single cells were clustered according to marker expression, referred back to the tissue, quantified and correlated with clinical disease outcomes. Direct cellular interactions and accumulation of immune cells in the local vascular niches of specific endothelial cell subsets were analyzed.

Results: Our analyses revealed microvascular rarefaction with significant reductions in blood vessels and lymphatic vessels in SSc. However, we showed that increase in the number of apoptotic and proliferating ECs in SSc was restricted to blood vessels and was not observed in lymphatic vessels. We identified seven different subpopulations of blood endothelial cells (BECs), two subpopulations of lymphatic endothelial cells (LECs) and three subpopulations of pericytes by unsupervised clustering. A novel population of $CD34^+$;αSMA^+;$CD31^+$ BECs was more common in SSc, whereas numbers of endothelial precursor cells (EPCs) were decreased. EPCs displayed significant changes in cellular turnover in SSc patients. The micro-environment of $CD34^+$;αSMA^+;$CD31^+$ BECs, but not of EPCs, was enriched for immune cells and myofibroblasts. Monocytes, $CD4^+$ T cells, dendritic cells (DCs), classically activated macrophages (CAMs), and alternatively activated macrophages (AAMs) were found to be enriched numerically in the niche of $CD34^+$;αSMA^+;$CD31^+$ BECs, but with differential proximity in the inner niche and in the outer niche determined by distance measurement. Consistent with the expression of αSMA as a marker of myofibroblasts, the density of $CD34^+$;αSMA^+;$CD31^+$ BECs was associated with clinical markers of progression of fibrotic remodeling in SSc patients.

Conclusion: We unraveled the heterogeneity of vascular cells in healthy individuals and SSc patients using IMC. We identified $CD34^+$;αSMA^+;$CD31^+$ BECs as a novel EC population that is increased in SSc patients, and is located in close proximity to immune cells and myofibroblasts. $CD34^+$;αSMA^+;$CD31^+$ BEC counts were associated with clinical outcomes of progressive fibrotic remodeling, thus providing a novel cellular correlate for the crosstalk of vasculopathy and fibrotic remodeling.

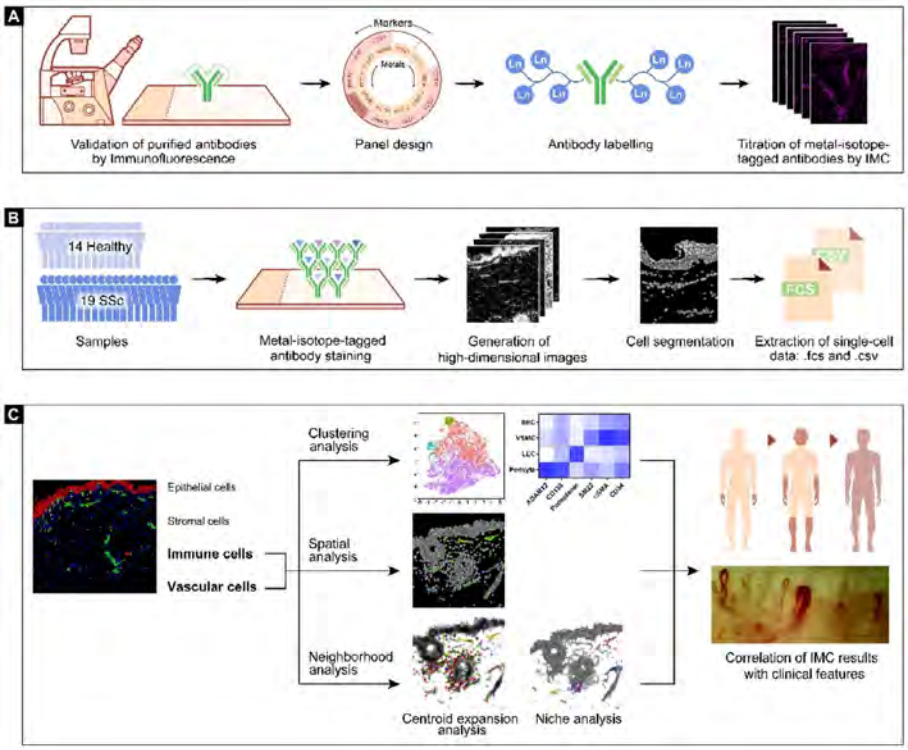

Figure 1. Schematic representation of the experimental workflow. (A) All purified antibodies were first tested by standard immunofluorescence staining. Each antibody was assigned to one channel according to its signal intensity and predicted spillover. After validation by immunofluorescence, the purified antibodies were labeled with lanthanide metal epitopes and further tested at different dilutions by IMC. (B) A total of 33 skin biopsies, 14 healthy controls and 19 SSc patients were stained with a panel of 38 metal-labelled antibodies as well as Iridium 193 and 191 isotopes, and further processed with the Hyperion IMC device. After generation of high-dimensional images and cell segmentation, the single-cell data with spatial information were generated by convertion from 40-channel stacked .tiff to .csv and .fcs files. (C) Major clusters of epithelial cells, vascular cells, immune cells and stromal cells were gated according to the specific cell markers. Populations of interest were selected and clustered using an unsupervised analysis pipeline, which was validated spatially by visualization in segmented map. Centroid expansion analysis and niche analysis were applied to describe neighborhood associations, including direct cell-cell contact and composition of the vascular niche. The above results were compared between healthy subjects and SSc patients and correlated with clinical phenotypes of SSc patients.

Disclosure: M. Liang: None; **A. Rius Rigau**: None; **y. Li**: None; **J. Distler**: 4D Science and FibroCure, 8, 11, AbbVie, Active Biotech, Anamar, ARXX, AstraZeneca, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, Genentech, GSK, Inventiva, Janssen, Novarti, 2, Anamar, Argenx, ARXX, BMS, Bayer Pharma, Boehringer Ingelheim, Cantargia, Celgene, CSL Behring, Galapagos, GSK, 5, Inventiva, Kiniksa, Lassen, Sanofi-Aventis, RedX, UCB, 5.

Abstract Number: 1668

Cell Specific Molecular Profiling of Scleroderma Associated Interstitial Lung Disease Subtypes

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Basic Science

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Interstitial lung disease (ILD) is present in up to 90% of patients with systemic sclerosis (SSc) and the leading cause of SSc-related mortality. SSc-ILD is categorized radiographically and pathologically in two subtypes: non-specific interstitial pneumonia (NSIP) and usual interstitial pneumonia (UIP). Epidemiologic studies show SSc-UIP has a significantly worse prognosis than SSc-NISP and does not respond to immunomodulating therapy. However, despite these clinical differences, little is known regarding the molecular profiles of the two SSc-ILD subtypes, making biomarker discovery and treatment development challenging. The objective of this study is to define the cellular and molecular profiles underpinning SSc-NSIP and SSc-UIP compared to idiopathic pulmonary fibrosis (IPF).

Methods: Single nuclei RNA sequencing (snRNAseq) was performed on frozen explanted lung tissue of 20 age and sex matched individuals including 10 SSc (5 NSIP and 5 UIP), 5 IPF, and 5 healthy controls (HC). Nuclei were isolated, multiplexed, and sequenced using the 10x genomics 3' v3 platform. Data were processed using standard CellRanger and Seurat pipelines and SoupX, Harmony, and Demuxlet. Cell proportions between conditions were compared using Kruskall Wallis

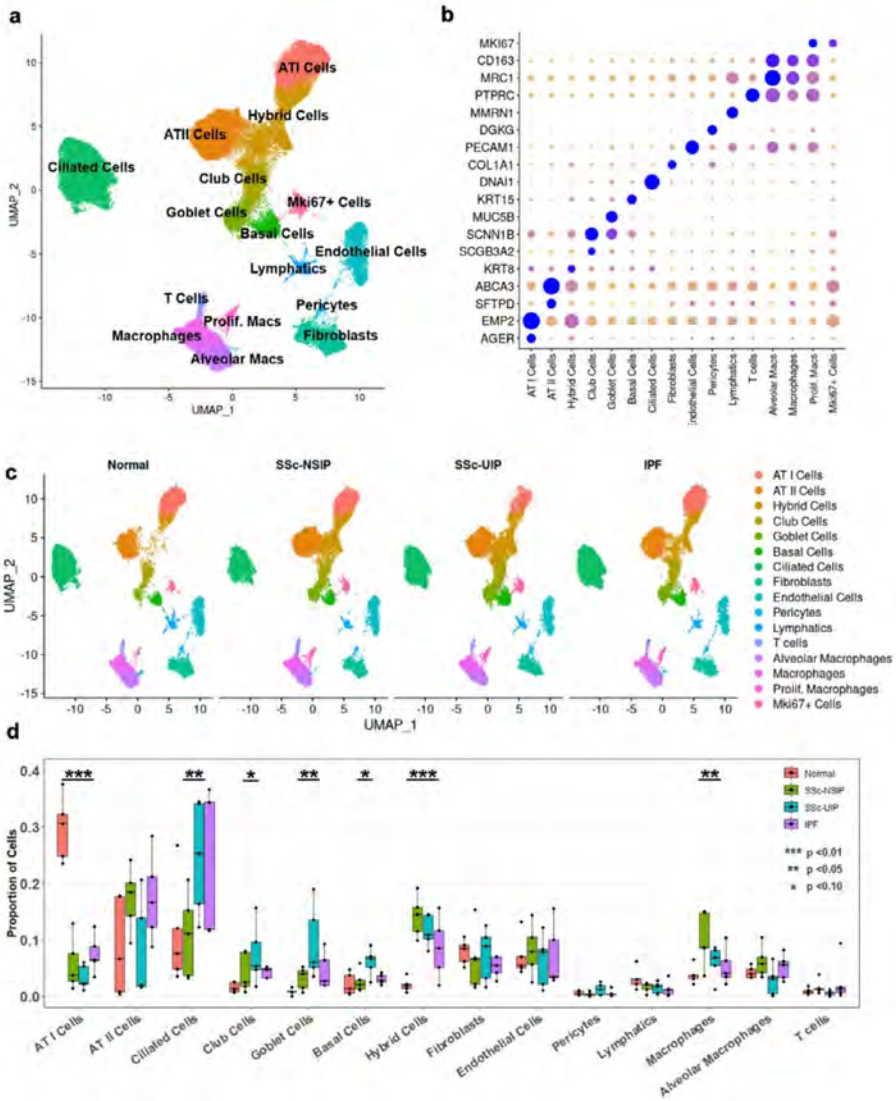

Figure 1: Profiling SSc-ILD subtypes with snRNA-seq. (a) UMAP of 92,128 nuclei from 5 SSc-NSIP, 5 SSc-UIP, 5 IPF and 5 healthy lungs demonstrates 16 distinct cell types. (b) Dot plot of gene markers for all 16 identified cell types. (c) UMAP by condition demonstrates visual differences in cell proportions and (d) compositional analysis confirms significant differences in cell proportions in AT I cells, ciliated cells, goblet cells, hybrid cells and macrophages ($p<0.05$).

test and differential expression was performed using DESeq2. Unsupervised hierarchical clustering of DEGs was used to examine similarities and differences between SSc-ILD subtypes within cell subsets.

Results: Following QC filtering, a total of 92,128 nuclei, including 20,738 SSc-NSIP, 24,012 SSc-UIP, 21,122 IPF, and 26,256 healthy nuclei, were used in downstream analysis. Clustering revealed 16 distinct cell types (Fig 1a) labeled using canonical gene markers (Fib 1b). Cell composition analysis revealed a profound loss of ATI cells in the diseased lungs compared to HC ($p < 0.01$) and an enrichment of other epithelial cells including ciliated and goblet cells in SSc-UIP and IPF. Macrophages were uniquely enriched in SSc-NSIP (Fig 1c-d). A "Hybrid" epithelial cell was identified that was unique to diseased lung and significantly increased in both SSc-ILD subtypes. DEG analysis of this cell group revealed 133 genes of which some were shared with other epithelial cells, such as ATI and ATII, while others were unique to the population (Fig 2a). Notable genes included markers of cellular senescence, i.e., GDF15 and CCND2, and previously described markers of "aberrant cells" in IPF, i.e., PLD5 and CPA6 (Fib 2b). Pathway analysis revealed upregulation of extracellular matrix organization and cell adhesion and migration processes. Comparing SSc-ILD subtypes, epithelial cells demonstrated a distinct expression pattern between SSc-NSIP and SSc-UIP which was redemonstrated in ATI cells, Club cells, and Basal Cells, while other epithelial subsets showed a more similar pattern of expression between the SSc-ILD subtypes.

Conclusion: This study provides novel insight to the molecular makeup of the SSc-ILD subtypes and demonstrates that SSc-NSIP and SSc-UIP have differing cell compositions but have both shared and distinct molecular pathways that also overlap with IPF. Ongoing analyses will further elucidate the molecular profiles underpinning the SSc-ILD subtypes.

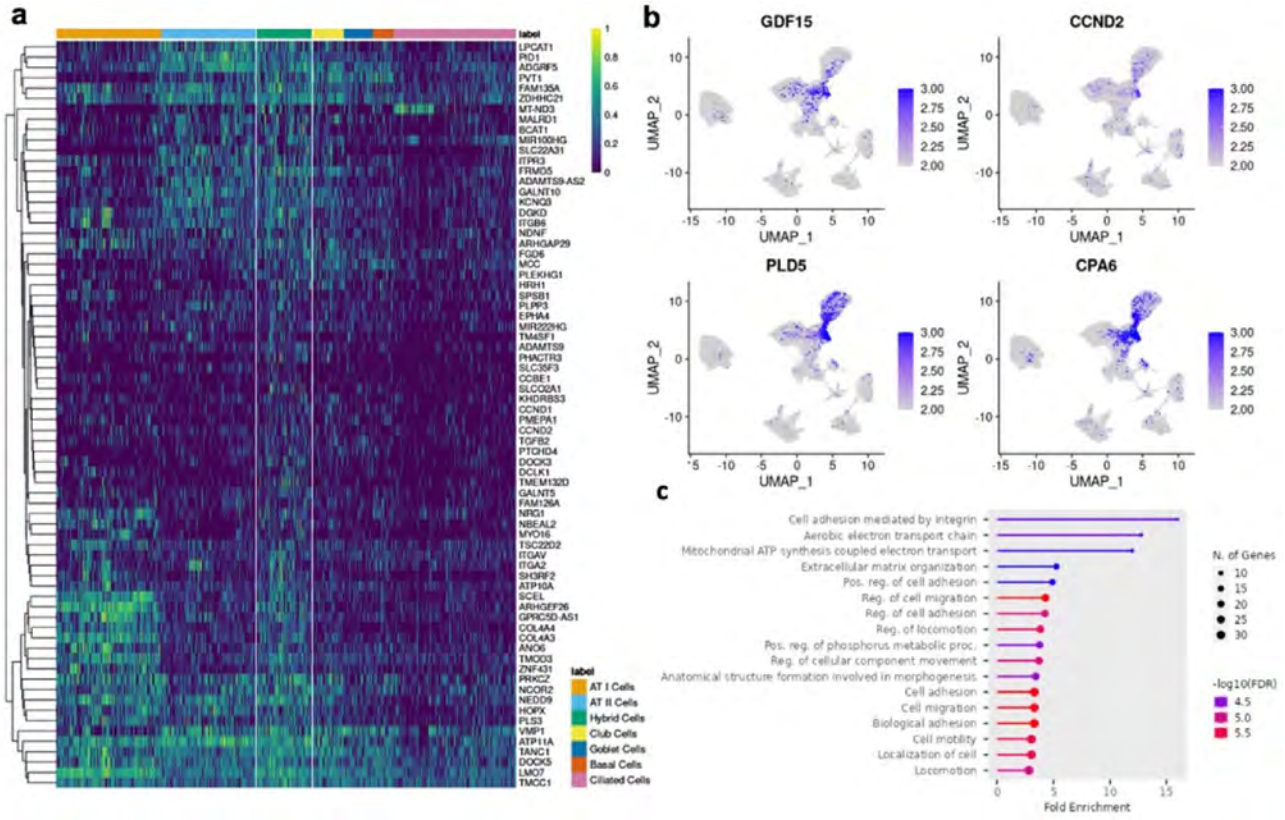

Figure 2: Identification of 'Hybrid' epithelial cell population unique to SSc-ILD and IPF. (a) Heatmap of differentially expressed genes demonstrates both shared markers across epithelial cells as well as uniquely expressed markers. (b) Feature plots of notable uniquely expressed 'Hybrid' cell markers including GDF15 and CCND2, markers of cellular senescence, and PLD5 and CPA6, markers expressed in aberrant cells in IPF. (c) Pathway analysis demonstrates enrichment of extracellular matrix organization and cell adhesion and migration.

Disclosure: M. Yang: None; **F. Deiter**: None; **E. Flynn**: None; **J. Neely**: None; **S. Lee**: None; **J. Greenland**: None; **M. Sirota**: Exxagen, 1; **P. Wolters**: None.

Abstract Number: 1669

High Incidence of Immune-mediated Inflammatory Diseases in Sepsis Survivors: A Nationwide Exposed-non-exposed Epidemiological Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Infection-related Rheumatic Disease

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. Previous studies have shown that immune dysregulation associated with severe infection persists after discharge in two-thirds of surviving patients and is associated with worse long-term outcome. Hypothesizing that persistent immune dysregulation associated with sepsis may be involved in immune-mediated inflammatory diseases **(**IMIDs), we used a nationwide database to analyze the incidence of IMIDs after sepsis. We aim to analyze the incidence of IMIDs in patients who survived sepsis.

Table 1 Characteristics of the matched populations

	Sepsis	Myocardial infarction	Absolute SMD
	n = 62,257	n = 62,257	
Age, years, mean (std) §	62.8 (14.0)	62.8 (14.0)	0.004
Gender, female, n (%) §	19,968 (32.1)	19,968 (32.1)	0.000
Event-associated hospital stay			
Duration of stay, days, median (Q1-Q3)	11 (6-18)	5 (3-7)	0.767
Intensive care unit admission, n (%)	47,135 (75.7)	21,756 (34.9)	0.900
SAPS-II score, mean (std) *	39.5 (22.1)	29.3 (20.3)	0.480
Organ failure associated procedures			
- Mechanical ventilation, n (%)	12,075 (19.4)	1,687 (2.7)	0.552
- Noninvasive ventilation, n (%)	10,091 (16.2)	715 (1.2)	0.552
- Hemodialysis for AKI, n (%)	2,216 (3.6)	160 (0.3)	0.243
- Pressor amine use, n (%)	10,288 (16.5)	1,697 (2.7)	0.481
Death during index hospital stay	7,525 (12.1)	2,813 (4.5)	0.277
Pathogens involved			
Bacteria, n (%)	22,207 (35.7)	NA	
Viruses, n (%)	35,248 (56.6)	NA	
- SARS-CoV2, n (%)	22,185 (35.6)	NA	
Other, n (%)	7,657 (12.3)	NA	
Unidentified, n (%)	27,284 (43.8)	NA	
Comorbidities/medical history			
CCI, mean (std)	3.2 (2.4)	2.2 (1.8)	0.472
Modified CCI, mean (std)	2.9 (2.1)	2.1 (1.7)	0.392
Obesity, n (%) †	6,683 (10.7)	4,938 (7.9)	0.100
Hypertension, n (%)	23,499 (37.8)	11,468 (18.4)	0.440
Diabetes mellitus, n (%)	10,481 (16.8)	4,510 (7.2)	0.298
Ischemic cardiopathy, n (%)	10,633 (17.1)	NA	0.457
Congestive heart failure, n (%)	9,664 (15.5)	1,684 (2.7)	0.642
Stroke or transient ischemic attack, n (%),	5,153 (8.3)	1,925 (3.1)	0.224
Chronic kidney disease, n (%)	3,973 (6.4)	989 (1.6)	0.247
- End-stage renal disease, n (%)	8864 (1.4)	259 (0.4)	0.103
HIV infection, n (%) §	189 (0.3)	189 (0.3)	0.000
Chronic pulmonary disease, n (%)	6,913 (11.1)	2,123 (3.4)	0.300
Active cancer, n (%) §	1,272 (2.0)	1,2172 (2.0)	0.000
Active malignant hemopathy, n (%) §	229 (0.4)	229 (0.4)	0.000
Hepatopathy, n (%)	3,370 (5.4)	641 (1.0)	0.250
Organ transplantation, n (%) §	25 (0.1)	25 (0.1)	0.000

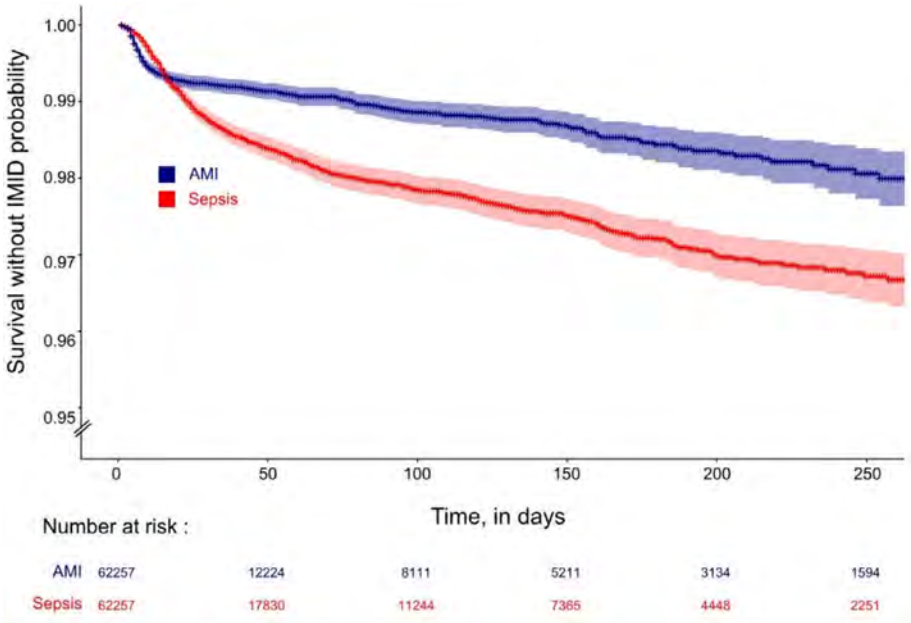

Figure 1 Survival without IMIDs among matched populations

Methods: Comprehensive data on all exposed and non-exposed patients admitted to all French hospitals from January 2011 to November 2020 were collected from the national medical-administrative database, the PMSI (*Programme de Médicalisation des Systèmes d'Information,* Information system medicalization program). The PMSI provides a summary of diagnoses, procedures, and individual medical conditions at discharge from all French healthcare facilities. All data on adult patients admitted for sepsis between January to November 2020, in any of the French healthcare facilities were retrieved from the database. Exposure was sepsis requiring hospitalization. Sepsis was defined by the combination of at least one code of infection and one code referring to an organ failure diagnosis or procedure. Patients with a first sepsis

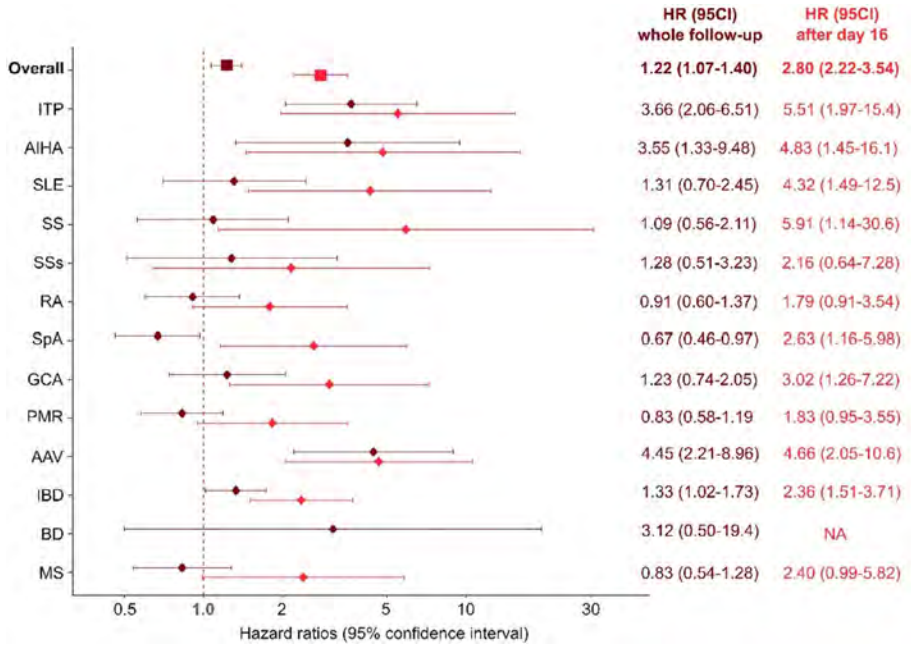

Figure 2 Risk for IMIDs onset after sepsis IMIDs, immune-mediated inflammatory diseases; ITP, immune thrombocytopenia; AIHA, autoimmune hemolytic anemia; SLE, systemic lupus erythematosus; SS, Sjögren's syndrome; SSs, systemic sclerosis; RA, rheumatoid arthritis; GCA, giant cell arteritis; PMR, polymyalgia rheumatica; AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; IBD, inflammatory bowel disease; UC, ulcerative colitis; MS, multiple sclerosis.

(i.e. exposed) diagnosed in a French hospital in 2020 were randomly matched (ratio 1/1) with patients admitted during the same period for acute myocardial infarction (i.e. non-exposed). An exact matching procedure taking age ±2 years, gender, and comorbidities as matching variables was performed. The main outcome was a diagnosis of IMID based on specific ICD-10 codes during a 9-month follow up. Only patients with i) a first diagnosis of sepsis (exposed) or AMI (non-exposed) in 2020 and ii) no history of IMIDs reported in PMSI between January 1, 2010 and the index stay were included.

Results: In France, the incidence rate of IMIDs after a sepsis in 2020 - analyzed in 62,257 patients – was of 7,956 [95CI 7,392-8,520] per 100,000 patient-years. As compared to the non-exposed admitted population (Table 1), the IMID-free survival analysis showed an increased risk for IMIDs of 2.80 (HR; 95%CI [2.22-3.54]) starting from day 16 after admission (Figure 1). Risk of IMIDs following severe infection differed according to the nature of the autoimmune disease and were higher for immune thrombocytopenia (5.51 [1.97-15.4]), autoimmune hemolytic anemia (4.83 [1.45-16.1]) and ANCA associated vasculitis (4.66 [2.05-10.6]) (Figure 2).

Conclusion: Our study shows an intriguing and extremely high incidence of IMIDs among survivors of severe infections.

Disclosure: A. Mageau: None; **A. Helary**: None; **S. Ruckly**: None; **A. Strukov**: None; **T. Papo**: None; **J. Timsit**: None; **K. Sacre**: None.

Abstract Number: 1670

Exacerbation of Immune-mediated Inflammatory Diseases in COVID19 Sequelae

CAMILA CAETANO[1], Tamiris Azamor[1], Nikki M. Meyer[1], Cassandra Calabrese[2], Leonard Calabrese[2], Nicolas Piuzzi[3], M. Elaine Husni[2], Suan-Sin Foo[1] and Weiqiang Chen[1], [1]Cleveland Clinic / Infection Biology Program, Global Center for Pathogen Research and Human Health, Lerner Research Institute, Cleveland, OH, [2]Cleveland Clinic / Department of Rheumatic and Immunologic Diseases, Cleveland, OH, [3]Cleveland Clinic / Department of Orthopedic Surgery, Cleveland, OH

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Infection-related Rheumatic Disease
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Patients with underlying immune-mediated inflammatory diseases (IMIDs), such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), have a higher susceptibility to severe COVID19 and adverse IMID outcomes. While there is growing evidence of SARS-CoV-2 infection triggering preexisting arthritic conditions, the mechanism underlying this phenomenon remains ill-defined. Indeed, the SARS-CoV-2 accessory protein, ORF8, shares similarities with the human inflammatory cytokine IL-17. In light of the potential association between inflammatory arthritis and ORF8-mediated IL-17 signaling, our objectives are to (i) characterize immune alterations, and (ii) determine the role of ORF8 in COVID19-mediated disease exacerbation in patients with preexisting IMIDs.

Methods: Using a retrospective Cleveland Clinic COVID19 biobank cohort, we obtained 74 plasma specimens collected from four groups of patients: (i) Healthy ($COVID^{Neg}IMID^{Neg}$; n=20); (ii) IMID only ($COVID^{Neg}IMID^{Pos}$; n=20); (iii) COVID19 only ($COVID^{Pos}$ $IMID^{Neg}$; n=20) and (iv) COVID19+IMID ($COVID^{Pos}$ $IMID^{Pos}$; n=14). All $COVID^{Pos}$ samples were obtained within 10-17 days post-COVID19 diagnosis. We employed aptamer-based SomaScan technology to profile 1500 protein biomarkers in plasma, focusing on the levels of circulating plasma ORF8. Next, primary human osteoblast (OBs) cells derived

from a healthy control and an RA patient, were treated with 20ng/ml of ORF8 protein for 2 and 4 days. Supernatants and cells were collected at each time point to evaluate inflammatory (IL-17A, IL-17F, CCL2, IL-6) and bone-resorption (RANKL:OPG, CTSK, PTH1R, TPP1) markers by ELISA and real-time PCR analyses, respectively.

Results: Comparative analysis of four patient groups revealed 154 specific biomarkers associated with COVID19+IMID patients. Specifically, 74 upregulated plasma proteins were found to be indicative of augmented bone resorption process, with elevated levels of the inflammatory IL-17F and bone resorptive biomarkers – RANKL: OPG, CTSK, PTH1R and TPP1. Immunoglobulin was predicted as an upstream regulator of both the IMID only and COVID19+IMID groups, suggestive of autoimmune-dominant IMID condition. Indeed, among both groups of patients with IMIDs (n=34), RA and SLE were most commonly reported, with 15% of the IMID only patients and 17% of COVID19+IMID patients diagnosed for each condition. High circulating ORF8 levels were detected in COVID19+IMID patients, but not seen in the COVID19 only group. Intriguingly, treatment of RA OBs with ORF8 resulted in significantly higher expression of inflammatory markers (IL-17A, IL-17F, CCL2, IL-6) and bone resorption markers: (RANKL: OPG) compared to healthyOB controls, suggesting IL-17-driven inflammation and bone resorption.

Conclusion: We identified an augmented IL-17-mediated inflammatory bone resorption in COVID-19 patients with preexisting IMIDs, which is uniquely driven by SARS-CoV-2 ORF8. The predicted immune pathways identified here provide insights into unique biomarkers and potential therapeutic targets for COVID19-mediated inflammatory "flares" in IMID patients.

Disclosure: C. CAETANO: None; **T. Azamor**: None; **N. Meyer**: None; **C. Calabrese**: AstraZeneca, 2, Eli Lilly, 2, Pfizer, 2, Sanofi, 2, 6; **L. Calabrese**: AstraZeneca, 6, Bristol-Myers Squibb(BMS), 2, Galvani, 2, Genentech, 2, GlaxoSmithKlein(GSK), 2, sanofi, 2, 6; **N. Piuzzi**: None; **M. Husni**: AbbVie, 1, 2, Amgen, 1, 2, Bristol-Myers Squibb, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, UCB, 1, 2; **S. Foo**: None; **W. Chen**: None.

Abstract Number: 1671

Use of Metagenomic Microbial Plasma Cell-Free DNA Next-Generation Sequencing Assay in Outpatient Rheumatology Practice

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Infection-related Rheumatic Disease
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Metagenomic next-generation sequencing (mNGS) of microbial cell-free DNA (mcfDNA) allows for non-invasive broad-range pathogen detection from plasma. The Karius test (KT) is a commercially available mNGS mcfDNA technology able to evaluate over 1000 pathogens on a single blood draw. Patients presenting with inflammatory syndromes often have overlapping clinical features and in some circumstances, differentiation between autoimmune disease and indolent infection can be challenging. This is of particular importance in patients where infection needs to be excluded prior to the initiation or escalation of immunosuppression. The purpose of this study was to describe the clinical utility of KT in a tertiary outpatient rheumatology practice.

Methods: All patients for which a KT was ordered by a rheumatology provider during outpatient evaluation at Mayo Clinic, Rochester, MN between 7/1/2021 and 12/31/2022 were identified. Demographics, symptoms, and laboratory parameters at time of KT draw were abstracted. Reason for testing was categorized as fever of unknown origin (FUO), atypical

Table 1. Baseline characteristics of Karius testing groups

Characteristic, n (%)	Clinically Relevant Organism[a]	Sex, female	Age, years[b]	Fever of unclear source[c]	Atypical RD[c]	Flare RD vs infection[c]	ESR (mm/Hr)[b]	CRP (mg/L)[b]	WBC (10³/L)[b]	Hg (g/dL)[b]
All patients N=150		79 (53)	52.0	5 (3.3)	120 (80.0)	25 (16.7)	31.5	20.1	8.7	12.8
Karius Result										
Negative N=121	No	65 (54)	51.8	5 (4.1)	98 (81.0)	18 (14.9)	28.0	18.5	8.7	13.1
Negative N=5	Yes	2 (40)	43.6	0 (0)	4 (80.0)	1 (20.0)	44.3	9.2	6.9	12.6
Positive N=18	No	10 (59)	54.4	0 (0)	13 (76.5)	4 (23.5)	43.4	23.8	9.8	11.6
Positive N=6	Yes	1 (17)	53.7	0 (0)	4 (66.6)	2 (33.3)	55.8	53.0	8.7	10.9

RD, rheumatic disease; ESR, erythrocyte sedimentation rate; CRP, c-reactive protein; WBC, white blood cell; Hg, hemoglobin
[a]Organism detected on Karius test correlated clinically with the ongoing presenting syndrome
[b] mean
[c]reason for ordering Karius test

Table 2: Organisms identified among patients with clinically relevant and non-clinically relevant positive Karius test results

Karius Result	Clinically relevant organism[a]	Patient ID	Detected Organisms
Positive	Y	4	*Haemophilus influenza and Streptococcus pneumoniae*
		17	*Borrelia burgdorferi (associated with inflammatory arthritis)*
		65	*Coxiella burnetii (endocarditis)*
		92	*Ebstein Barr Virus (associated with lymphoproliferative disorder)*
		97	*Tropheryma whipplei (arthritis, pericarditis, serositis, gastroenteritis)*
		150	*Mycobacterium haemophilum (disseminated – skin, joint, tendon)*
Positive	N	1	*Burkholderia cepacia*
		2	*Burkholderia cepacia*
		9	*Escherichia coli, Enterobacter cloacae Herpes simplex virus 1*
		10	*Staphylococcus cohnii*
		12	*Burkholderia cepacia*
		27	*Human herpes virus - 6*
		30	*Cytomegalovirus*
		38	*Helicobacter pylori Kaposi-sarcoma associated herpes virus*
		49	*Human Herpes Virus – 7 Legionella*
		56	*Klebsiella pneumoniae Human Herpes Virus - 7*
		68	*Klebsiella quasipneumoniae*
		87	*Escherichia coli , Herpes simplex virus - 1*
		91	*Epstein Barr Virus*
		123	*Human herpes virus – 7*
		125	*Klebsiella pneumoniae, Escherichia coli, Phocaelcola vulgatus*
		128	*Klebsiella pneumoniae*
		129	*Helicobacter cinaedi, Adenovirus*
		137	*Terrisporobacter othiniensis, Fusobacterium mortiferum*

[a]clinical relevance was assessed based on whether the listed pathogen was considered associated with the clinical presentation for which the KT was drawn and/or resulted in initiation (or modification) of anti-microbial therapy to address the detected organism

Table 3: Organisms detected by other methodology in patients with negative Karius test

Karius Result	Clinically relevant organism	Patient ID	Organism identified by method other than Karius Test	Test/method of organism detection	Prednisone	Immuno-suppression	Antibiotic within past 1 month
Negative	Y	14	*Actinomyces odontolyticus*	Laryngeal tissue culture, surgical biopsy	No	No	No
		78	*Tropheryma whipplei*	Synovial fluid aspirate PCR	No	Methotrexate Golimumab	No
		79	*Mycobacterium marinum*	Soft tissue, tendon, culture, surgical biopsy	Yes 7.5mg/day	Methotrexate Adalimumab	No
		80	*Staphylococcus lugdunensis*	Surgical culture, joint	No	No	No
		118	*Strongyloides*	Serology	No	Certolizumab	No

presentation of possible rheumatic disease (RD) or assessment of RD flare versus infection. Results were considered negative (-) if no pathogen was listed as above KT threshold for positive. Among positive tests, determination of an organism's clinical relevance was assessed based on whether the listed pathogen was considered associated with the clinical presentation for which the KT was drawn and/or resulted in initiation (or modification) of anti-microbial therapy to address the detected organism. Records of patients with (-) KT were reviewed for a minimum of 3 months after KT draw to determine if patients with a (-) KT had subsequent identification of pathologic organism by another testing method.

Results: 150 patients with an outpatient KT were identified, 53% female, mean age of 52 years. Reasons for KT were atypical presentation of possible RD (80%), evaluation for flare of RD vs infection (16.7%) and FUO (3.3%). In total 24 (16%) patients had at least one organism listed as detected, among which 25% (6/24) were considered clinically relevant and altered final diagnosis and treatment (Table 2). 126 (84%) patients had a (-) KT of which 5 (4%) were subsequently found to have a clinically relevant infection by other testing (Table 3). Among the 121 patients with (-) KT for which alternative organism was not seen, 55 started and 11 increased immunosuppression after (-) KT; none of which were diagnosed with an infection associated with initial presentation within the subsequent 3 months after the KT test.

Conclusion: This study describes the first large series of mNGS mcfDNA in outpatient rheumatology. Six patients were found to have systemic infections which altered diagnosis and treatment. KT false (-) rate was only 4% and 3 of the 5 cases with false (-) KT required surgical biopsy for organism confirmation. Over 50% of patients with negative KT were started on immunosuppression without subsequent infection identified. Determining which patients best benefit from KT use in rheumatology practice remains to be defined. Further research is needed prior to consideration of widespread use.

Disclosure: R. Jenkins: None; **M. Samec**: None; **C. Arment**: None; **M. Koster**: None.

Abstract Number: 1672

Association of COVID-19 Vaccinations with Flares of Systemic Rheumatic Disease: A Case-Crossover Study

Genna Braverman[1], Medha Barbhaiya[2], Minerva Nong[1], Vivian Bykerk[3], Nathaniel Hupert[4], Colby Lewis V[4] and Lisa Mandl[2], [1]Hospital for Special Surgery, New York, NY, [2]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [3]Department of Rheumatology, Hospital for Special Surgery, New York, NY, [4]Weill Cornell Medicine, New York, NY

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Infection-related Rheumatic Disease

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Fear of flare contributes to COVID-19 vaccine hesitancy in patients with systemic rheumatic diseases (SRD). Accurately ascertaining post-vaccine SRD flares and differentiating them from routine vaccine side effects is difficult. We evaluated the association of COVID-19 vaccination with SRD flares using a case-crossover design, which is ideal for studying outcomes triggered by transient within-person exposures with short windows of time-to-effect.

Methods: Adults ≥18 years enrolled in a COVID-19 Rheumatology Registry at a tertiary center were invited to participate in this study assessing SRD flares. COVID-19 vaccine dates and brands were obtained from self-report and electronic health records. International Classification of Disease-10 algorithms identified SRD diagnoses. Subjects with rheumatoid arthritis (RA), psoriatic arthritis (PsA), systemic lupus erythematosus (SLE) and scleroderma (SSc) had their diagnoses validated by classification criteria; 138 (31.8%), 55 (12.7%), 44 (10.1%) and 15 (3.5%) of 434 participants met criteria for RA, PsA, SLE and SSc, respectively. Participants self-reported both SRD flares and SRD quiescence. "Hazard periods" were defined as time before self-reported flares, and "control periods" as time before self-report of no flare. We used univariate conditional logistic regression, stratified by participant with a log likelihood equivalent Cox proportional hazards model, to evaluate for an association between flare and vaccination in the preceding 2, 7 and 14 days. (Figure 1). Subgroup analyses were performed.

Results: Of 9361 Registry participants, 1797 opted into the SRD flare study and 434 (24.2%) subjects (mean age 59 years [±13], 84.1% female, 81.9% White) contributed both hazard and control periods between 3/5/21 and 9/6/22. Most had an inflammatory arthritis or a connective tissue disease (Table 1). 96.1% of subjects received at least 1 dose of a COVID-19 vaccine and 93.1% received at least 2 doses. Of the 1316 COVID-19 immunizations received during the study, 31.7% were 1st doses, 30.7% 2nd doses and the remainder ≥ 3rd doses; 58.5% were Pfizer-BioNTech, 39.5% were Moderna and 1.4% were Johnson & Johnson. 997 flares were reported. There was no association between COVID-19 vaccination and SRD flares using lookback windows of 2, 7 or 14 days (OR 1.46 [95% CI, 0.86-2.46], OR 1.09 [95% CI, 0.76-1.55], OR 0.85 [95% CI, 0.64-1.13] respectively; p=NS for all) (Table 3). Subanalyses stratified on sex, age, SRD subtype and vaccine brand similarly showed no association with flare. Information on vaccine side effects was available for 897/1316 (68.2%) doses; 468 (52.2%) and 491 (54.7%) of 897 doses were complicated by CDC-defined local and systemic vaccine side effects, respectively. There was no association between reporting a vaccine side effect and reporting an SRD flare (p=0.09). Information on whether reported flares were consistent with a subject's "typical" flare was available for 813/997 (81.5%) flares, of which 664/813 (81.7%) were typical.

Conclusion: In this cohort of participants with SRD and high vaccine uptake, COVID-19 vaccination was not associated with SRD flares. These data are reassuring and can inform shared decision-making on COVID-19 immunization.

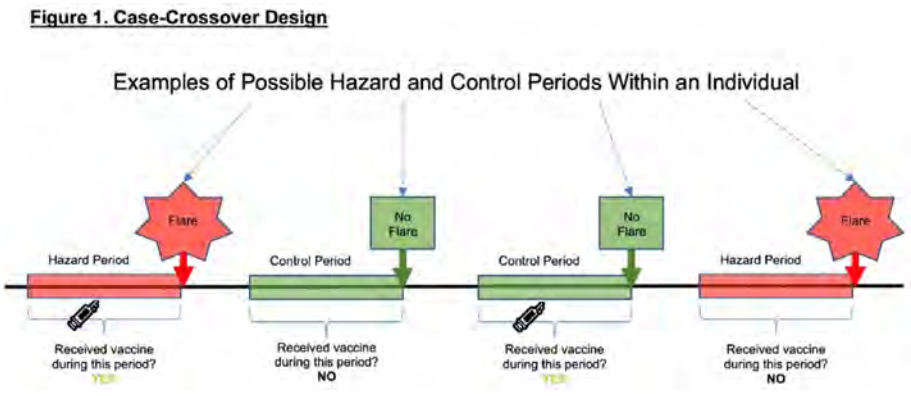

Figure 1. Case-Crossover Design

Table 1. Study Participant Demographics at Time of Registry Enrollment

Table 1. Study Participant Demographics at Time of Registry Enrollment (N=434)	
Age in years, mean (SD)	59 (±13)
Sex, N (%)	
Female	365 (84.1%)
Male	67 (15.4%)
Prefer not to answer/other	2 (0.5%)
Race, N (%)	
White	355 (81.8%)
Black or African American	18 (4.1%)
Asian or Indian Subcontinent	10 (2.3%)
Multiracial	31 (7.1%)
Other	7 (1.6%)
Prefer not to answer	13 (3.0%)
Insurance, N (%)	
Commercial only	256 (59.0%)
Medicare¥ (excluding Medicaid)	153 (35.3%)
Self-pay/uninsured	12 (2.8%)
Medicaid#	11 (2.5%)
Unknown/missing	2 (0.5%)
SRD Categories: ICD-10 Algorithms##, N (%)	
Inflammatory arthritis*	280 (64.5%)
Connective tissue disease**	117 (27%)
Other***	23 (5.3%)
More than one category	14 (3.2%)
Select SRD: Classification Criteria, N (%)	
RA	138 (31.8%)
PsA	55 (12.7%)
SLE	44 (10.1%)
SSc	15 (3.5%)
##≥2 instances of same ICD-10 code from a comprehensive list of SRD diagnosis codes, ≥14 days apart entered by rheumatologist within the division	
*Ankylosing spondylitis, enteropathic arthritis, juvenile idiopathic arthritis, palindromic rheumatism, polymyalgia rheumatica, polyarthritis, psoriatic arthritis, rheumatoid arthritis and spondyloarthritis **Secondary antiphospholipid syndrome [APS], eosinophilic fasciitis, mixed connective tissue disease [MCTD], myositis, overlap connective tissue disease, Sjogren's/sicca, SLE, systemic sclerosis and undifferentiated connective tissue disease [UCTD] ***Any vasculitis, autoinflammatory syndromes, primary APS, Behcet's, IgG4-related disease, relapsing polychondritis and sarcoidosis	
¥ alone or in combination with another non-Medicaid plan # alone or in combination with other insurance	

Table 2. Case-Crossover Analysis: Association of COVID-19 Vaccination with SRD Flares

Table 2. Case-Crossover Analysis: Association of COVID-19 Vaccination with SRD Flares				
COVID-19 Vaccination	Hazard Periods (N)	Control Periods (N)	OR (95% CI)	P value
2-day lookback				
Yes	44	31	1.46 (0.86, 2.46)	0.16
No	953	1145		
7-day lookback				
Yes	91	77	1.09 (0.76, 1.55)	0.65
No	906	1099		
14-day lookback				
Yes	135	153	0.85 (0.64, 1.13)	0.27
No	862	1023		

Disclosure: G. Braverman: None; **M. Barbhaiya**: None; **M. Nong**: None; **V. Bykerk**: AbbVie, 2, Bristol Myers Squibb, 1, 2, 5, Pfizer, 1, 2; **N. Hupert**: None; **C. Lewis V**: None; **L. Mandl**: Annals of Internal Medicine, 12, Associate Editor, Regeneron Pharmaceuticals, 5, Up-to-Date, 9.

Abstract Number: 1673

Immunomodulatory Treatment and Autoimmune Patient Responses to COVID-19 Booster Shots: Results from the Covid-19 VaccinE Response in Rheumatology Patients (COVER) Study

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Infection-related Rheumatic Disease

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Given an increased risk of COVID-19 in patients with autoimmune conditions, we must better understand the immunogenicity and safety of SARS-CoV-2 vaccines in people living with rheumatic disease. We conducted the Covid VaccinE Response (COVER) trial, a multicenter, randomized controlled trial to assess the response to the SARS-CoV-2 booster in rheumatology patients on immunomodulatory therapies. A primary goal was to assess whether patients randomized to hold therapy for 2 weeks after a booster dose had improved vaccine response compared to those who continued therapy.

Methods: The COVER trial enrolled patients with rheumatoid arthritis (RA) or spondylarthritis (SpA) and was conducted in the Excellence Network in RheumatoloGY (ENRGY), a large practice-based research network (PBRN) of US rheumatologists. Participants were randomized to continue or hold current medication, abatacept (ABA) or tumor necrosis factor inhibitors (TNFi), for 2 weeks following a booster dose of COVID-19 vaccine. All patients had received primary vaccination against COVID-19 with an mRNA vaccine. LabCorp Cov2Quant IgG™ Spike assay measured levels of anti-Receptor Binding Domain (RBD) IgG antibodies prior to and following the booster dose. For each medication group (ABA or TNFi), we looked at the mean log-transformed difference pre- and post-booster and used linear regression to compare the two groups with respect to change in COVID-19 RBD antibody levels, adjusting for age, sex, BMI, methotrexate use, and number of prior vaccine doses.

Results: Within both the abatacept (n=142) and TNFi (n=121) medication groups, there were no significant baseline differences in demographics or clinical characteristics (Table 1). Combining both groups, the population was 76% female, 92% white, 17% Hispanic, with mean (SD) age of 61.1 (13.5) years, and mean (SD) BMI of 31.2 (8.2) kg/m^2. The ABA group was significantly older than the TNF group: 64.8 (11.7) vs 57.1 (14.3), p< 0.0001). Following the COVID booster vaccine, RBD antibody titers increased significantly in both ABA (p=0.0029 for holding; p=0.03604 for continuing) and TNF ($p < 0.0001$ for both arms) patients (Figure 1). Patients who continued their ABA had a numerically lower increase in anti-RBD antibody titers compared to those who held it for two weeks. However, in linear regression analysis, the mean increase in the holding arm compared to the continuing arm was not significantly different for either drug group in unadjusted analysis or after adjusting for demographic and clinical factors (a significant effect was seen for BMI (β=0.04, p=0.03) in the ABA

Table 1: Patient Demographics and Clinical Characteristics by Drug Group and Intervention

	Abatacept (n=142)			Tumor Necrosis Factor Inhibitors (n=121)		
	Holding (n=60)	Continuing (n=82)	p-value	Holding (n=64)	Continuing (n=57)	p-va
Age, Years, Mean (SD)	63.8 (11.5)	64.8 (12.3)	0.6236	56.1 (13.8)	58.5 (14.8)	0.35
BMI, Mean (SD)	30.6 (6.9)	31.7 (7.8)	0.4077	32.1 (9.6)	30.2 (7.1)	0.26
Female, N (%)	46 (77)	68 (83)	0.3544	49 (77)	38 (67)	0.22
Race, N (%)						
White	55 (92)	73 (89)	0.1111	57 (89)	52 (91)	0.11
Black / African American	4 (7)	2 (2)		6 (9)	1 (2)	
Other	1 (2)	7 (9)		1 (2)	4 (7)	
Ethnicity, N (%)						
Not Hispanic or Latino	52 (87)	67 (82)	0.6324	51 (80)	46 (81)	0.73
Hispanic or Latino	8 (13)	13 (16)		13 (20)	10 (18)	
Unknown	0	2 (2)		0	1 (2)	
Autoimmune Disease, N (%)						
RA	59 (98)	78 (95)	0.3051	43 (67)	41 (72)	0.57
SpA	1 (2)	4 (5)		21 (33)	16 (28)	
Concomitant Med, N (%)						
Methotrexate	18 (30)	23 (28)	0.1480	21 (33)	18 (32)	0.88
Prednisone	11 (18)	16 (20)	0.8596	12 (19)	9 (16)	0.66
Hydroxychloroquine	7 (12)	15 (18)	0.3510	8 (13)	6 (11)	0.78
Leflunomide	7 (12)	9 (11)	1.0000	6 (9)	3 (5)	0.49
Nucleocapsid Status Positive, N (%)	20 (35)	24 (30)	0.7137	25 (39)	20 (35)	0.70
Self-Reported COVID-19 Positive, N (%)	21 (35)	26 (32)	0.7202	22 (34)	17 (30)	0.69
Anti-RBD IgG antibodies specific to SARS-CoV-2 at Pre-Booster Visit, Mean (SD)	106.3 (248.4)	89.9 (202.1)	0.6655	186.2 (283.8)	116.3 (171.4)	0.10
Anti-RBD IgG antibodies specific to SARS-CoV-2 at Post-Booster Visit, Mean (SD)	256.1 (537.7)	156.1 (213.4)	0.1710	296.9 (415.1)	195.9 (196.4)	0.09

Figure 1: Mean Pre-Booster Visit to Post-Booster Visit anti-RBD IgG Difference by Drug Group and Intervention

analysis and MTX use (β=0.63, p=0.02) in TNFs). There was no significant interaction in the effect of holding or continuing medication between the ABA and TNFi groups (interaction p-value = 0.55).

Conclusion: RA and SpA patients receiving abatacept and tumor necrosis factor inhibitors had a significant increase in antibody response after receiving a COVID-19 booster. There was a weak and non-significant trend toward improved response in the group that held ABA for up to 2 weeks post-booster that was not significant. Based on these results, briefly interrupting ABA or TNFi at the time of COVID boosting may not appear warranted.

Disclosure: A. Mudano: None; **G. Cutter**: AI therapeutics, 1, Alexion, 2, AMO Pharma, 1, Antisense Therapeutics, 2, Applied Therapeutics, 1, Astra-Zeneca, 1, Avexis Pharmaceuticals, 1, Avotres, 2, Biogen, 2, Bristol Meyers Squibb/Celgene, 1, Clene Nanomedicine, 2, Clinical Trial Solutions LLC, 2, CSL Behring, 1, Entelexo Biotherapeutics, 2, Genentech, 2, Genzyme, 2, GW Pharmaceuticals, 2, Horizon Pharmaceuticals, 1, Hoya Corporation, 2, Immunic, 1, 2, Immunosis Pty Ltd, 2, Karuna Therapeutics, 1, Kezar Life Sciences, 1, Klein-Buendel Incorporated, 2, linical, 2, Mapi Pharmaceuticals L, 1, Merck, 1, Merck/Serono, 2, Mitsubishi Tanabe Pharma Hold, 1, Novartis, 2, Novartis, 1, Opko Biologics, 1, Perception Neurosciences, 2, Protalix Biotherapeutics, 2, Prothena Biosciences, 1, Pythagoras, Inc, 8, Reata Pharmaceuticals, 1, Regeneron, 1, 2, Roche, 2, SAB Biotherapeutics, 2, Sanofi-Aventis, 1, Teva Pharmaceuticals, 1, Visioneering Technologies, Inc, 1; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **G. Thiele**: None; **E. Holladay**: None; **K. Withrop**: AbbVie, 2, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GSK, 2, Novartis, 2, Pfizer, 2, 5, Regeneron, 2, Roche, 2, Sanofi, 2, UCB, 2; **M. Law**: None; **B. Hamilton**: None; **M. Bastidas**: None; **M. Zikry**: None; **K. Chun**: None; **M. George**: AbbVie/Abbott, 2, GlaxoSmithKlein(GSK), 5, Janssen, 5; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, 5, CorEvitas, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 1674

Severe Infections in Patients with VEXAS Syndrome: A Study from the French VEXAS Group

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Infection-related Rheumatic Disease

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: VEXAS (Vacuoles, E1 Enzyme, X-Linked, Autoinflammatory, Somatic) syndrome is an autoinflammatory monogenic disease caused by inactivating somatic mutations in the UBA1 gene and characterized by heterogenous systemic auto-inflammation and progressive hematologic manifestations. Its management is not consensual but often include biologic DMARDs or azacytidine in case of association with myelodysplastic syndrome. Prognosis appears to be poor, with substantial morbidity and mortality mainly caused by infection. The aim of this study was to describe the spectrum of infectious complications and their risk factors in VEXAS patients.

Methods: Retrospective multicenter study including patients with genetically proven VEXAS syndrome, with at least one episode of severe infection (defined as an infection leading to hospitalization and/or intravenous infectious treatments and/or death). These patients were compared to a cohort of 50 VEXAS patients without severe infection after at least one year of follow-up since diagnosis. Risk factors of infections were assessed with multivariate Cox proportional hazard ratios models.

Results: Seventy-four patients (99% male, median [IQR] age at VEXAS onset of 68 [63-75] years) with 133 severe infections were included. Infections occurred despite anti-infective prophylaxis in 46% of cases. The main immunosuppressive drugs received at the time of infection were JAK inhibitors (29%), biologics (21%) and azacitidine (11%), while 16% of infections occurred without treatment (no immunosuppressant or corticosteroids ≤ 10 mg/d). Most frequent infection localizations

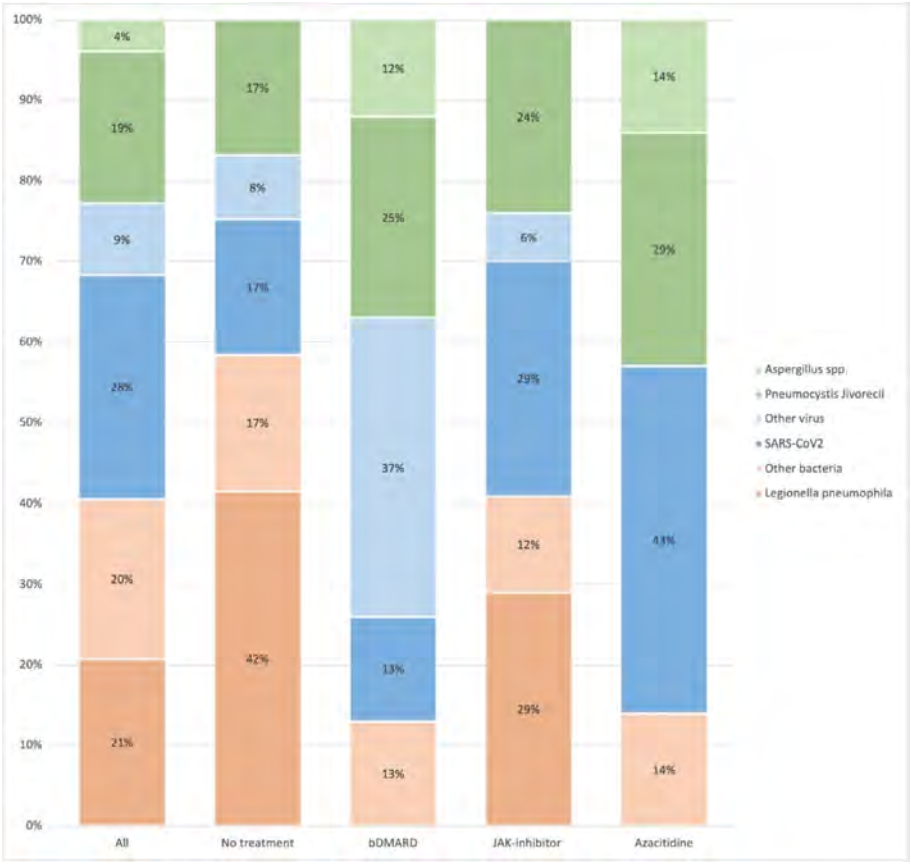

Figure 1: Distribution of infectious agents in pulmonary infections

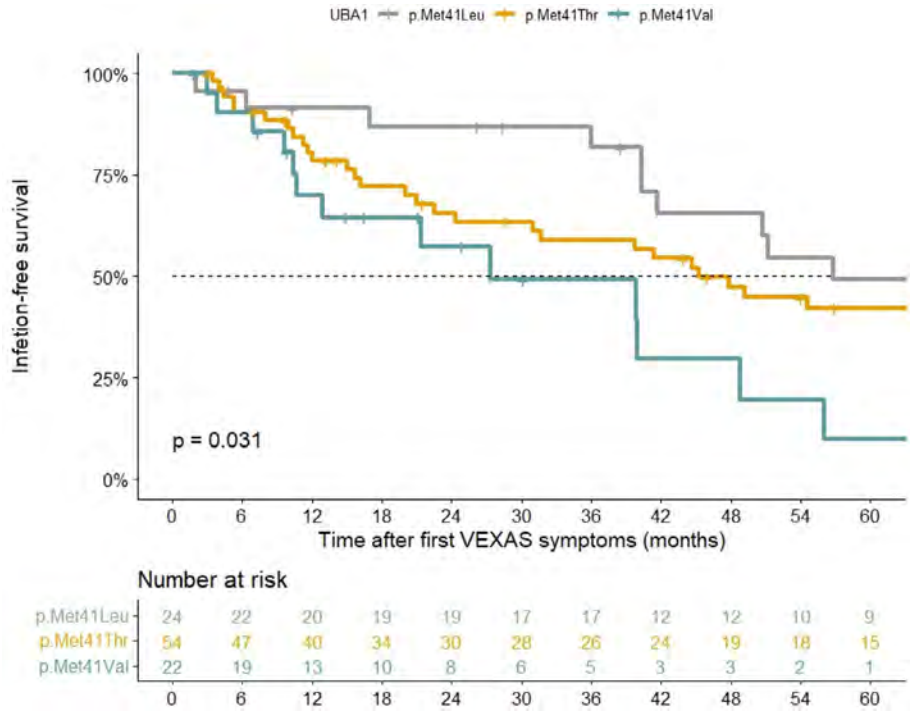

Figure 2: Kaplan-Meier curves for infection-free survival according to the type of UBA1 mutation

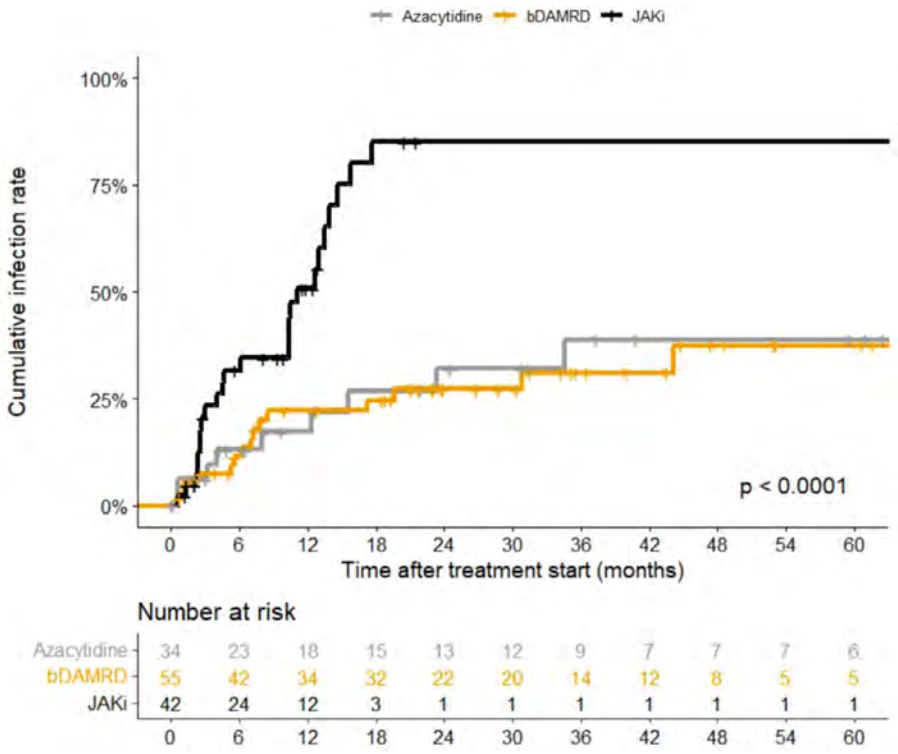

Figure 3: Cumulative incidence of severe infections according to the type of treatment received

were the lung (59%), skin (10%) and urinary tract (9%). The most commonly found infectious agents were SARS-CoV-2, Legionella pneumophila and Pneumocystis jivoreci in 28%, 21% and 19% of pulmonary infections, respectively (figure 1). Invasive fungal infections accounted for 11% of all infections. Nearly 20% of pulmonary infections occurred in the absence of treatment with a high prevalence of L. pneumophila (42%) and P. jivoreci (17%) infections.

In multivariate analysis, factors significantly associated with severe infection were p.Met41Val mutation (figure 2) (HR 2.44 [1.05-5.63], p=0.037), age at symptom onset >75 years (HR 1.91 [1.05-3.47], p=0.034) and arthralgia (HR 2.03 [1.16-3.56], p=0.013) whereas leukopenia was a protective factor (HR 0.58 [0.34-0.99], p=0.046). Among treated patients, cumulative infection rate was significantly higher with JAK inhibitors (multivariate HR 3.90 [1.78-8.55], p=0.001) compared to biologic DMARDs and azacitidine, with a median time to infection of 12 months (figure 3). After a median follow-up of 4.4 [2.5–7.7] years, 27 (36%) patients died including 15 (56%) due to severe infection.

Conclusion: VEXAS syndrome is associated with a high incidence of severe infections especially in patients carrying the p.-Met41Val mutation. The high frequency of atypical infections such as legionellosis and invasive fungal infections in patient without immunosuppressive treatment might suggest an intrinsic immunodeficiency of the disease. JAK inhibitors, used as first-line treatment, are particularly at risk of severe infections occurring early after initiation.

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Abstract Number: 1675

Survival in Patients with Rheumatoid Arthritis and Early Breast Cancer Treated with Tumor Necrosis Factor Inhibitors

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: RA – Treatments II: RA Treatment Safety
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: There have been concerns about the use of tumor necrosis factor inhibitors (TNFi) in patients with rheumatoid arthritis (RA) and concomitant cancer. Few studies have examined cancer outcomes in these patients, and they have mostly included long-term survivors, rather than patients with early cancer. Therefore, the safety of TNFi in patients with recent cancer is unknown. Our aim was to examine the survival of patients with RA recently diagnosed with early-stage breast cancer (BC), who received TNFi in the first year after BC diagnosis.

Methods: We conducted a retrospective cohort study of patients with RA diagnosed with BC and RA identified in two databases from 2008 onwards: Optum's de-identified Clinformatics® Data Mart Database, and the combined Surveillance, Epidemiology, and End Results Program (SEER) and Texas Cancer Registry (TCR) – Medicare linked databases. Early BC was ascertained in Clinformatics by surgical claims codes and in SEER/TCR by stage (excluding distant BC). Use of disease modifying antirheumatic drugs (DMARDs) and glucocorticoids in the year after BC diagnosis was identified from claims and prescriptions files. Outcomes were overall survival (OS) and BC-specific survival (BCSS; only in SEER/TCR-Medicare) defined as the time from BC diagnosis to death from all causes or from BC. Survival was truncated at 5 years. We compared patients who received TNFi with those who received conventional cDMARDs, or no DMARDs, during the first year after BC diagnosis. We estimated a propensity score for use of TNFi through a logistic regression model. We conducted multivariate Cox proportional hazards regression, controlling for various covariates and for the propensity score.

Results: We identified 970 patients with RA and early-stage BC in Clinformatics (mean age 67 years, SD 10.6) and 1,246 in SEER/TCR-Medicare (mean age 74 years, SD 6). In the first year after BC diagnosis 165 (17%) received TNFi in the Clinformatics cohort, and 201 (16.1%) in the SEER/TCR-Medicare cohort. After multivariate and propensity score adjustment, no significant differences in OS were observed between patients treated with TNFi (alone or with cDMARDs) and patients treated with cDMARDs alone in Clinformatics (hazard ratio, HR=0.75 95% CI 0.41-1.37), or in SEER/TCR-Medicare (HR=0.86 95%CI 0.55-1.34). BCSS was only available for SEER/TCR-Medicare and was significantly better in patients receiving TNFi than in those receiving cDMARDs (HR=0.29 95%CI 0.09-0.98). No significant differences in OS or BCSS were observed when comparing patients who did not receive any DMARDs to those receiving TNFi. Patients receiving prednisone-equivalent doses of ^{3} 7.5mg/day had worse survival than those who did not receive glucocorticoids in Clinformatics, HR=2.51, 95%CI 1.32-4.76; in SEER/TCR-Medicare, HR=1.63, 95%CI 0.93-2.87.

Conclusion: TNFi therapy in patients with RA during the first year after early-stage BC diagnosis did not have a detrimental effect on survival. Glucocorticoids were associated with a significant increase in overall mortality in one of the databases. Additional studies are needed to determine the effects of other biologics on cancer outcomes, and of TNFi in patients with other cancer types.

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Abstract Number: 1676

Tofacitinib Accelerates in Vitro Clot Formation and Delays Clot Lysis in Rheumatoid Arthritis Blood by Enhancement of Macrophage TLR4 Mediated Cytokine Responses- a New Angle on Thrombosis with JAKi in Rheumatology

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: RA – Treatments II: RA Treatment Safety

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Rheumatoid Arthritis (RA) patients treated with Janus Kinase inhibitors (JAKi) have reportedly higher venous thromboembolism (VTE) risk and atherosclerotic-related complications including myocardial infarction (1).Although underappreciated by Rheumatologists, in certain experimental situations JAK inhibition has been linked to increased pro-inflammatory cytokine production by myeloid cells(2,3). Thus, we hypothesized that JAK inhibition-related pro-inflammatory

Figure 1: Effect of tofacitinib on immunothrombotic cytokine secretion following TLR4 stimulation.

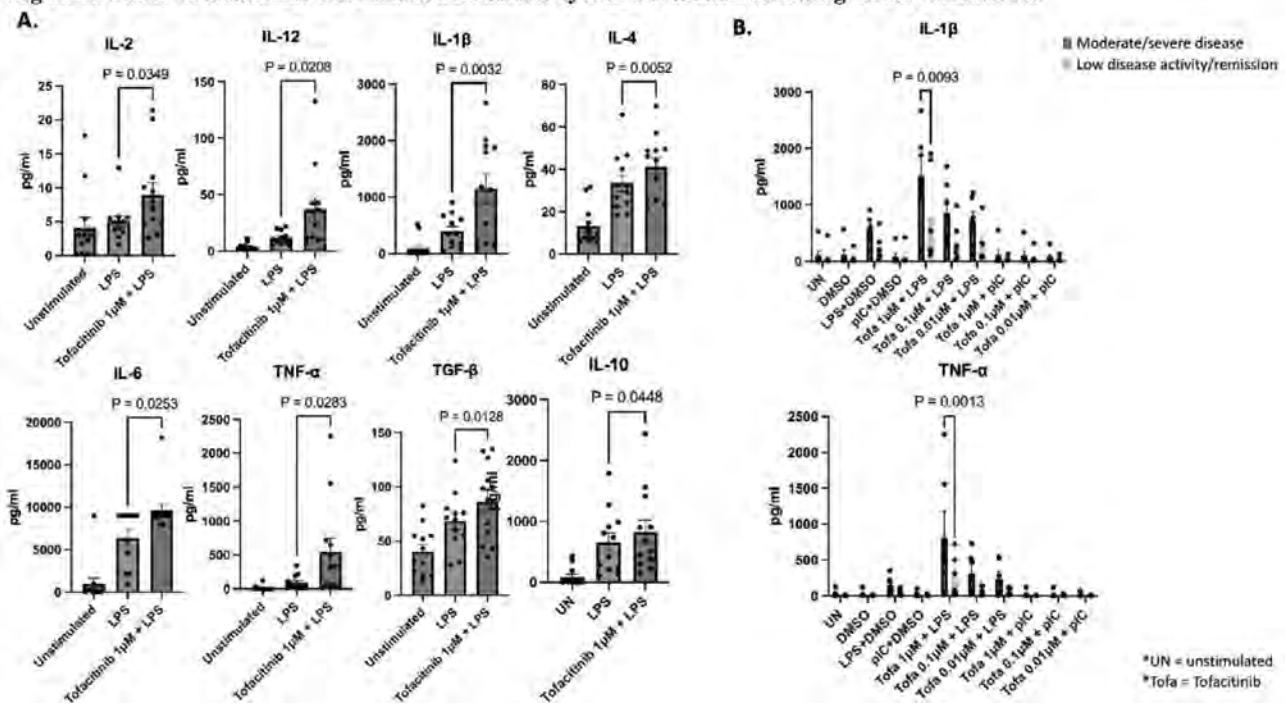
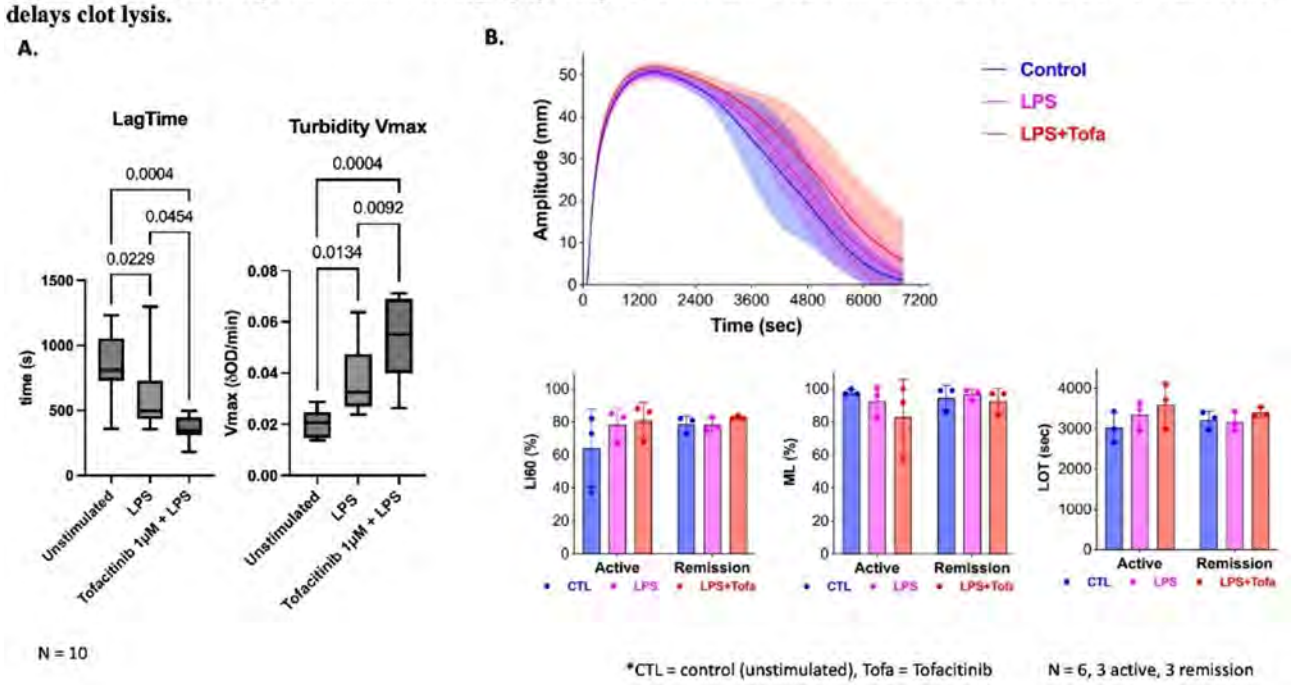


Figure 2: Fibrin turbidity and thromboelastography assays demonstrate tofacitinib accelerates in vitro clot formation and delays clot lysis.



A. LagTime is the time it takes for the protofibrils to start aggregating into fibres, and Vmax is the clotting rate at the steepest point of the turbidity curve. The graphs show that the clot formation rate is faster with Tofacitinib. B. Lysis index at 60 minutes (LI60) indicates how much of the clot is remaining at 60min. So clearly there is less degradation with Tofacitinib. Maximum lysis (ML) indicates how much of the clot is lysed at the end of the run (2hrs). This shows that less clot has been lysed over the duration of the assay. Lysis onset time (LOT) represents how long it takes for the lysis to kick-in. So here, it takes longer for the lysis to start.

cytokine dysregulation with tofacitinib (JAKi) might actually drive "immunothrombosis" in both normal and RA blood.We thus investigated the circumstances where JAK inhibition may drive innate immune-mediated immunothrombosis

Methods: Blood was obtained from RA patients (n=12) under any treatment except JAKi and divided into two groups: remission/low disease activity (DAS-28-CRP < 3.2, n=6) or moderate/active disease activity (DAS-28-CRP ^{3} 3.2, n=6). Experiments were also performed on peripheral blood mononuclear cells (PBMCs) from healthy donors (n= 12) including other JAKi.Leukocytes were isolated using ammonium chloride and stimulated with TLR4 (lipopolysaccharide, LPS) and TLR3 (Polyinosinic:polycytidylic acid) agonists with and without tofacitinib at three pharmacologically relevant concentrations. Bulk RNA sequencing of stimulated cells, ELISA and Legendplex kits were used to assess cell responses to tofacitinib. Plasma turbidity assays of clot formation and fibrinolysis and thromboelastography assays were used to assess the dynamics of in-vitro clotting. Results were analyzed with GraphPad Prism software.

Results: In both RA and healthy blood, LPS-activated leukocytes treated with tofacitinib at therapeutically relevant concentrations (1 mM, 0.1 mM and 0.01 mM) further increased cytokines associated with immunothrombosis, including TNF-α, IL-1β, IL-12, IL-4, IL-6 and TGF-b (Fig 1A). This effect was absent with TLR3 agonists (not shown), and more evident in active RA when compared to remission (Fig 1B) despite similar baseline cytokine levels. Bulk RNA sequencing data showed multiple pathways whereby tofacitinib augmented LPS-treated macrophage inflammatory signatures including the NF-kB pathway, IL-12, and IL-23 pathway, and suggested disruption of immunoregulatory interferon- and IL-10-induced pathways**.**In turbidity and lysis analysis, all LPS-activated cell supernatants induced faster clot formation than the buffer control. However, clot formation rate was further increased significantly when tofacitinib was added in combination with LPS (Fig 2A).Thromboelastography showed delayed clot lysis in active RA patients' blood treated with LPS/tofacitinib, but not in remission/low disease activity subjects (Fig 2B).

Conclusion: TLR4, but not TLR3, activated myeloid cells treated with JAKi exhibited accelerated clot formation and delayed thrombolysis in RA blood samples in-vitro. This work offers novel insights into how venous and arterial immunothrombosis might occur in RA, especially in the context of bacterial challenge in active RA on JAKi therapy.

References

1 Molander V et al. Ann Rheum Dis. 2022
2 Pattison MJ et al. The Journal of Immunology. 2012
3 Chen F et al. J Immunol. 2016

Disclosure: P. David: None; **T. Macleod**: None; **Y. Shi**: None; **P. Ganguly**: None; **C. Duval**: None; **M. Harland**: None; **C. Wong**: None; **B. Saleem**: None; **D. McGonagle**: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Janssen, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 1677

Two-week Break in Methotrexate Treatment and COVID-19 Vaccine Response. Results of the Vaccine Response on off Methotrexate (VROOM) Study, an Open Label, Prospective, Two-arm Parallel-group, Multi-center, Superiority, Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Abstracts: RA – Treatments II: RA Treatment Safety
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Immunosuppressive treatments inhibit vaccine-induced immunity. We evaluated if a two-week interruption of methotrexate treatment immediately after COVID-19 booster improved antibody response against spike protein of the receptor binding domain (S1-RBD) and live virus neutralization (ancestral Wuhan and Omicron BA.1) in patients with immune mediated inflammatory diseases (IMIDs).

Methods: We conducted an open-label, prospective, parallel-group, randomized controlled, superiority trial in 26 UK hospitals. Adults attending Rheumatology and Dermatology clinics taking methotrexate (≤25mg/week) for ≥3 month for inflammatory conditions were randomly assigned 1:1 using minimization to suspend or continue methotrexate treatment for two-weeks immediately after their COVID-19 booster. Data were analyzed using an intention to treat approach.

Results: 383 participants (mean age 59.0 years, 61% female) were randomized to either suspend or continue methotrexate arms. 61.4% (n=235) were female, 54.3% (n=208) had RA, 31.9% (n=122) psoriasis with/without arthritis. The median methotrexate dose was 20 mg/week. 94.5% (n=362) received a mRNA vaccine booster, mean 178 days after the second

Serological outcomes at primary and secondary endpoints

	Continue Methotrexate		Suspend Methotrexate		Mixed effects model:	
	N	Geometric mean (95% CIs)	N	Geometric mean (95% CIs)	geometric mean ratio (95% CI)[1]	p-value
S1-RBD antibody						
Baseline	191	948 (711, 1263)	189	881 (670, 1159)	-	-
4 Weeks	187	12326 (10538, 14418)	180	25413 (22227, 29056)	2.08 (1.59, 2.70)	< 0.001
12 Weeks	183	8973 (7493, 10745)	179	17131 (14882, 19721)	1.88 (1.44, 2.46)	< 0.001
26 Weeks	151	9971 (8050, 12350)	137	15318 (12430, 18878)	1.50 (1.12, 2.01)	0.006
Neutralization of live SARS-CoV-2 virus						
Baseline						
Wuhan Hu-1 IC50	50	2229 (1096, 4531)	50	1524 (736, 3155)	-	-
Omicron BA.1 IC50	50	157 (103, 239)	50	122 (80, 185)	-	-
4 Weeks						
Wuhan Hu-1 IC50	50	18342 (9059, 37139)	50	35919 (17628, 73191)	2.56 (1.21, 5.44)	-
Omicron BA.1 IC50	50	339 (220, 522)	50	724 (426, 1230)	2.42 (1.45, 4.05)	-
12 Weeks						
Wuhan Hu-1 IC50	50	21879 (11084, 43187)	50	22150 (10874, 45119)	1.32 (0.62, 2.81)	-
Omicron BA.1 IC50	50	280 (172, 454)	50	274 (170, 443)	1.11 (0.67, 1.86)	-
26 Weeks						
Wuhan Hu-1 IC50	29	11161 (4517, 27578)	28	25613 (9865, 66500)	3.50 (1.34, 9.18)	-
Omicron BA.1 IC50[2]	29	881 (399, 1946)	28	1001 (370, 2703)	1.50 (0.69, 3.29)	-

[1]Mixed effects model, adjusted by baseline value, randomization factors (age, inflammatory condition, vaccine platform), prior infection, booster platform, and included time by treatment interaction. [2]Participants got vaccinated against Covid-19 in this period using a bivalent vaccine including Omicron and this explains a higher neutralization titre at week 26 than at week 12

Serological outcomes at primary and secondary endpoints

Self-reported clinical outcomes at primary and secondary endpoints

	Continue with Methotrexate	Suspend Methotrexate	Treatment effect (95% CI)[1]
EQ-5D Utility Scores, mean (SD)			
4 Weeks	0.769 (0.181)	0.743 (0.213)	-0.024 (-0.063, 0.015)
12 Weeks	0.763 (0.191)	0.745 (0.220)	-0.014 (-0.052, 0.025)
26 Weeks	0.787 (0.183)	0.756 (0.201)	-0.032 (-0.072, 0.009)
EQ VAS, mean (SD)			
4 Weeks	77.0 (16.5)	73.6 (19.4)	-3.090 (-6.687, 0.508)
12 Weeks	75.3 (17.9)	72.0 (20.2)	-2.786 (-6.382, 0.810)
26 Weeks	77.9 (16.7)	75.1 (19.4)	-2.257 (-6.075, 1.562)
Patient assessment of disease, mean (SD)			
2 Weeks	7.3 (1.7)	6.8 (2.2)	-0.437 (-1.226, 0.353)
4 Weeks	7.4 (1.9)	6.9 (2.2)	-0.462 (-1.254, 0.331)
12 Weeks	7.2 (2.0)	7.0 (2.1)	-0.177 (-0.966, 0.612)
26 Weeks	7.5 (1.9)	7.0 (2.1)	-0.475 (-1.292, 0.342)
Participants with at least one flare-up, N (%)[2]			
0-4 Weeks	63 (32.8)	102 (53.4)	2.280 (1.723, 3.655)
0-12 Weeks	89 (46.4)	124 (64.9)	1.982 (1.334, 2.901)
0-26 Weeks	117 (60.9)	132 (69.1)	1.371 (0.721, 2.165)

[1] Mixed effects model for EQ-5D, patient assessment of disease outcomes, and flares adjusted by baseline value, randomization factors (age, inflammatory condition, vaccine platform), prior infection, booster platform, and included time by treatment interaction. [2]OR for participants with at least one flare-up.

Self-reported clinical outcomes

dose of the primary vaccination. Adherence to the intervention was high with 96.3% (n=184) and 97.4% (n=187) self-reported adherence with allocation in the suspend and continue methotrexate groups respectively.

At four-weeks, the geometric mean (95% confidence interval (CI)) S1-RBD antibody level was 25,413(22,227-29,056) and 12,326(10,538-14418) U/mL in suspend and continue treatment groups respectively, with geometric mean ratio (GMR) (95%CI) 2.08(1.59-2.70), p< 0.0001, mixed-effects model. The increase in antibody response was consistent across age-groups, methotrexate doses, route, IMIDs, primary vaccination platform, and prior SARS-CoV-2 infection. Enhanced antibody responses were sustained at 12 and 26 weeks with GMR(95%CI) 1.88(1.44-2.46) and 1.50(1.12-2.01) respectively. Planned exploratory subgroup analyses suggested a greater treatment effect at higher methotrexate dose (Interaction GMR effect (95% CI) 0.67(0.47, 0.96) at 4-weeks and 0.64(0.420.96) at 12-weeks).

The Wuhan Hu-1 IC50 neutralizing antibody titer was higher in the methotrexate suspend group compared to the continue treatment group at four and 26-weeks. In a mixed-effect model, the GMR (95% CI) for Wuhan Hu-1 IC50 neutralizing antibody titer on suspending methotrexate for two-weeks was 2.56 (1.21-5.44) at 4 weeks, and 3.50 (1.34-9.18) at 26-weeks. The Omicron BA.1 IC50 cross neutralizing antibody titer was higher in the methotrexate suspend group compared to the continue treatment group at 4-weeks with GMR (95% CI) 2.42 (1.45-4.05).

There were no differences in quality of life. Self-reported disease activity deteriorated slightly at 4-weeks in the suspend methotrexate group, but normalized by week-12.

Conclusion: Two-week interruption of methotrexate treatment for IMIDs enhanced boosting of antibody responses after COVID-19 vaccination that were sustained at 12 and 26 weeks. *(Trial registration:* ISRCTN11442263)

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Abstract Number: 1678

Comparative Safety of Biologic and Targeted Synthetic Disease Modifying Anti-Rheumatic Drugs for Cancer in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Abstracts: RA – Treatments II: RA Treatment Safety
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: In the ORAL Surveillance trial, cancer risk was higher among patients with rheumatoid arthritis (RA) on tofacitinib, a Janus kinase inhibitor (JAKi), compared to tumor necrosis factor inhibitors (TNFi), in a population enriched for cardiovascular disease risk [1]. However, less is known regarding the comparative safety of non-TNFi biologics relative to TNFi. We assessed the comparative safety of individual non-TNFi and JAKi relative to TNFi for the risk of incident cancer in patients with RA.

Methods: We performed a cohort study using Merative MarketScan databases (2012-2021) of patients with RA identified using ≥1 ICD9/10 codes, age 18-64 years, who initiated treatment with TNFi, non-TNFi (rituximab, abatacept, tocilizumab and sarilumab), or JAKi (tofacitinib, baricitinib) on or after November 2012. Patients with past cancer diagnoses were excluded. We used Cox proportional hazard models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for developing incident cancer (excluding non-melanoma skin cancer) within 2 years of treatment initiation in patients on non-TNFi or JAKi relative to TNFi, adjusting for potential confounders, including demographics, geographic region, year of initiating a biologic, Charlson Comorbidity Index, frailty status measured using claims-based frailty index (2), healthcare utilization within 12 months prior to starting treatment, and proxies for RA severity. Cancer diagnoses were identified using validated administrative algorithms [3]. Patients were allowed to switch from one drug class to the other, allowing a single patient to contribute person-time over different drug classes. Patients were censored if they did fill of a prescription of any of these drugs for >90 days (>180 days for rituximab), or end of study period (12/31/2021).

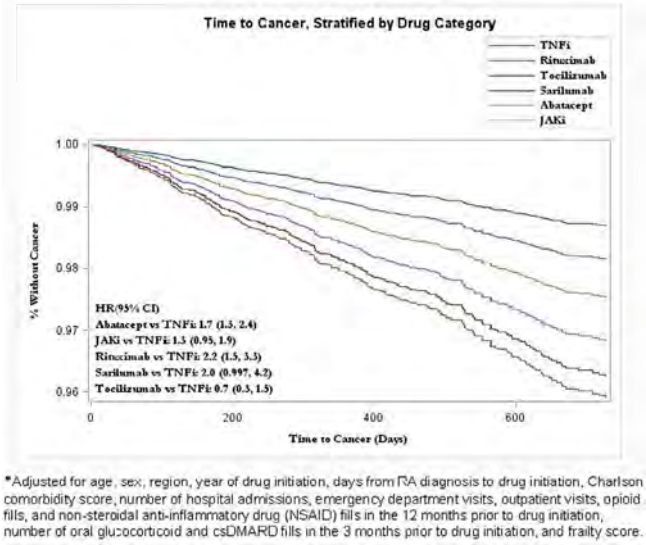
Table 1. Baseline characteristics of the cohort stratified by drug initiation.

Variable	TNFi n=29,286 (72%)	Rituximab n=1857 (5%)	Tocilizumab n=1279 (3%)	Sarilumab n=868 (2%)	Abatacept n=3139 (8%)	JAKi n=3991 (10%)
Age in years (Median, IQR)	49 (41, 55)	49 (41, 56)	50 (42, 56)	52 (45, 57)	50 (43, 56)	50 (43, 56)
Female, n (%)	22,705 (78)	1468 (79)	1011 (79)	631 (73)	2639 (84)	3206 (80)
US geographic region, n (%)						
Northeast	4136 (14)	314 (18)	201 (16)	147 (17)	468 (16)	636 (16)
Central	5812 (20)	358 (20)	240 (19)	188 (22)	586 (19)	723 (18)
South	14,444 (50)	852 (46)	592 (47)	438 (50)	1562 (50)	2050 (51)
West	4456 (15)	308 (17)	227 (18)	94 (11)	477 (15)	562 (14)
Year of Initiating Biologic Drug (Median, IQR)	2016 (2014, 2018)	2016 (2014, 2018)	2016 (2014, 2018)	2018 (2015, 2020)	2016 (2014, 2019)	2019 (2016, 2020)
Days from RA diagnosis to Initiating Biologic Drug (Median, IQR)	420 (190, 900)	590 (250, 1170)	600 (290, 1060)	720 (350, 1480)	620 (360, 1170)	640 (350, 1230)
Charlson Comorbidity Score						
1-2	25,796 (88)	1364 (73)	1069 (84)	650 (75)	2610 (83)	3466 (87)
3-4	2796 (10)	361 (19)	166 (13)	141 (16)	398 (13)	413 (10)
5+	694 (2)	132 (7)	44 (3)	77 (9)	131 (4)	112 (3)
Frailty Score@, Median (IQR)	0.13 (0.12, 0.16)	0.15 (0.12, 0.18)	0.14 (0.12, 0.17)	0.15 (0.12, 0.18)	0.15 (0.12, 0.16)	0.14 (0.12, 0.16)
Utilization in prior 12 months						
Any Hospital Admissions (n (%))	2416 (8)	477 (26)	143 (11)	107 (12)	300 (10)	314 (8)
Any Emergency Department Visits, n (%)	7903 (27)	822 (44)	425 (33)	295 (34)	935 (30)	974 (24)
Any Opioid Prescription Fills (n (%))	11,333 (39)	687 (37)	527 (41)	319 (37)	1251 (40)	1399 (35)
Any NSAID Prescription Fills (n (%))	16,340 (56)	642 (35)	594 (46)	418 (48)	1567 (50)	2244 (56)
Concomitant csDMARDs, n (%)	20,245 (69)	763 (41)	667 (52)	246 (28)	1871 (60)	2601 (65)
Any Fills of Glucocorticoids in 3 Months Prior (n (%))	13,493 (46)	903 (49)	614 (48)	237 (27)	1366 (44)	1671 (42)

@Frailty score: 0 indicates non-frail and ≥0.2 indicates frail
Abbreviations: csDMARD: conventional synthetic disease modifying anti-rheumatic drug; IQR: Interquartile range; NSAID: Non-steroid anti-inflammatory drug; TNF: Tumor necrosis factor

Table 2. Number of cancer outcomes (95% confidence intervals) within 2 years of initiating biologic drug per 10,000 person-years at risk, stratified by drug category that the patient initiated.

	Median (IQR) days to cancer diagnosis (among those with cancer)	Raw n of cancer diagnoses	# of cancer diagnoses/10,000 person-years (95% confidence interval)
TNF alpha	173 (91, 371)	248 (0.9%)	102 (90, 115)
Rituximab	147 (37, 246)	31 (1.7%)	264 (180, 373)
Tocilizumab	212 (189, 280)	<10 (0.6%)	76 (31, 156)
Sarilumab	146 (57, 299)	<10 (0.9%)	243 (106, 474)
Abatacept	194 (98, 359)	45 (1.4%)	188 (137, 250)
JAKi	120 (52, 292)	40 (1.0%)	143 (102, 194)



*Adjusted for age, sex, region, year of drug initiation, days from RA diagnosis to drug initiation, Charlson comorbidity score, number of hospital admissions, emergency department visits, outpatient visits, opioid fills, and non-steroidal anti-inflammatory drug (NSAID) fills in the 12 months prior to drug initiation, number of oral glucocorticoid and csDMARD fills in the 3 months prior to drug initiation, and frailty score.

Figure 1. Kaplan-Meier curves showing the adjusted hazard ratio* for incident cancer per drug exposures.

Results: We included 37,026 patients involving 78% female patients with a mean age of 47.6 ± 10.3 years, of whom 72% initiated TNFi, 10% JAKi, 8% abatacept, 5% rituximab, 3% tocilizumab, and 2% sarilumab (**Table 1**). The mean follow-up time was 360 days for TNFi, 250 days for non-TNFi, and 280 days for JAKi. There were 379 incident cancers observed during follow-up (**Table 2**). In multivariable models, exposure to rituximab or abatacept had a significantly higher risk of incident cancer (HR 2.2, 95% CI 1.5, 3.3; HR 1.7, 95% CI 1.3-2.4, respectively), compared with exposure to TNFi (**Figure 1**). While the hazard ratio for incident cancer was higher with exposure to JAKi compared with TNFi, this difference was not statistically significant (HR 1.3; 95% CI 0.9-1.9).

Conclusion: While we observed a lower hazard ratio for incident cancer with exposure to TNFi compared to non-TNFi and possibly JAKi in this generally younger and predominantly female population, potential for residual confounding by indication and the small number of outcomes per drug class limit interpretation of these results. Larger studies with longer follow-up are needed for better comparison of cancer risk between these drug classes.

References:

1. Ytterberg SR, *et al*: *N Engl J Med* 2022
2. Kim DH, et al: *J Gerontol A Biol Sci Med Sci* 2018
3. Setoguchi S, et al: *Cancer causes & control : CCC* 2007

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Abstract Number: 1679

Effects of Janus Kinase Inhibitor on TNF-a and IL-6-Induced Osteoclasts and RANKL-Induced Osteoclasts in Peripheral Blood Monocytes from Patients with Rheumatoid Arthritis

Kazuhiro Yokota[1], Yoshimi Aizaki[2], Takuma Tsuzuki Wada[1], Hiroshi Kajiyama[1], Yasuto Araki[2], Hiroaki Yazawa[2], Yuji Akiyama[2] and Toshihide Mimura[1], [1]Department of Rheumatology and Applied Immunology, Faculty of Medicine, Saitama Medical University, Iruma-gun, Japan, [2]Department of Rheumatology and Applied Immunology, Faculty of Medicine, Saitama Medical University, Saitama, Japan

SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: RA – Treatments II: RA Treatment Safety
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: We have previously demonstrated that a combination of TNF-a and IL-6 induces mouse osteoclast-like cells with bone resorption activity both *in vitro* and *in vivo* [Arthritis & Rheumatology (A&R), 2014]. Recently, we have shown that the combination of TNF-a and IL-6 induces osteoclasts (OCs) derived from human peripheral blood monocytes (PBMs) via RANKL-independent pathways *in vitro*. In particular, the number of TNF-a and IL-6-induced OCs differentiated from peripheral blood mononuclear cells in patients with RA had a significant positive correlation with the modified total Sharp score. On the other hand, the number of RANKL-induced OCs had a significant negative correlation with whole-body bone mineral density (A&R, 2021). We undertook the present study to clarify the effects of Janus kinase (JAK) inhibitor on TNF-a and IL-6-induced OCs and RANKL-induced OCs in PBMs derived from patients with RA or healthy donors (HDs).

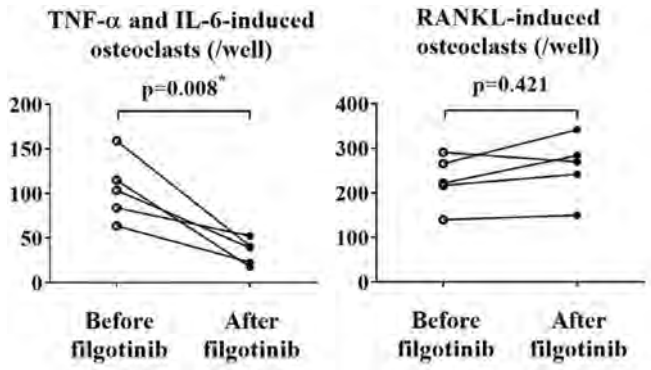

Figure. Administration of filgotinib, a JAK inhibitor, for six months inhibits the differentiation of TNF-α and IL-6-induced osteoclasts in peripheral blood monocytes from patients with RA. Left; Six months after treatment with filgotinib, the number of TNF-α and IL-6-induced osteoclasts differentiated from peripheral blood monocytes was significantly decreased compared with those of before the treatment. Right; No significant change in the number of RANKL-induced osteoclasts was observed in the same patients (each n = 5). * = $p < 0.05$ between groups, Wilcoxon's signed rank test.

Methods: PBMs derived from 5 RA patients and HDs were stimulated by TNF-α and IL-6 or RANKL with or without 100-1000 nM filgotinib, a JAK inhibitor. The number of tartrate-resistant acid phosphatase-positive multinucleated cells and bone resorption activity using a pit formation assay were assessed. Quantitative RT-PCR was used to measure the mRNA expression levels of *IL-1b* and *IL-8*. Furthermore, the number of TNF-α and IL-6-induced or RANKL-induced OCs differentiated from PBMs in RA patients before and 6 months after treatment with filgotinib was examined.

Results: The number of TNF-α and IL-6-induced OCs and RANKL-induced OCs derived from PBMs in RA patients was significantly increased compared to that in HDs (each n=5, $p< 0.05$). Filgotinib significantly inhibited the differentiation of TNF-α and IL-6-induced OCs derived from PBMs of RA patients in a dose-dependent manner (n=4, all $p< 0.05$). On the other hand, the same concentrations of filgotinib did not inhibit osteoclastogenesis induce by RANKL (n=4, all $p >0.05$). Resorption pits generated by TNF-α and IL-6-induced OCs derived from HDs in the presence of filgotinib was reduced comparing with those without filgotinib. In contrast, filgotinib did not inhibit generation of resorption pits by RANKL-induced OCs (n=4). Levels of *IL-1b* and *IL-8* mRNA expressed by TNF-α and IL-6-induced OCs from RA patients, but not RANKL-induced OCs, were significantly reduced by filgotinib (each n=3, $p< 0.05$). Six months after treatment with filgotinib, the number of TNF-α and IL-6-induced OCs differentiated from PBMs was significantly decreased compared with those of before the treatment (n=5, p=0.008) (Figure). In contrast, no significant change in the number of RANKL-induced OCs by the six-months administration of the JAK inhibitor was observed in the same patients (n = 5, p=0.421).

Conclusion: Filgotinib inhibits TNF-α and IL-6-induced osteoclast differentiation *in vitro*. Administration of filgotinib reduces differentiation potential of TNF-α and IL-6-induced OCs in PBMs from RA patients. Our results suggest that the inhibitory mechanism of filgotinib on joint destruction in RA may be related to its inhibition of TNF-α and IL-6-induced OCs, presumed pathogenic OCs.

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Abstract Number: 1680

What Trade-offs Are Acceptable to Rheumatoid Arthritis Patients During Treatment Selection?

Rieke Alten[1], Juan carlos Nieto-Gonzalez[2], Peggy Jacques[3], Carlomaurizio Montecucco[4], Robert Moots[5], Helga Radner[6], Sebastian Heidenreich[7], Chiara Whichello[7], Nicolas Krucien[7], Monia Zignani[8], Harald Vonkeman[9] and Katrien Van Beneden[10], [1]Department of Internal Medicine and Rheumatology, Schlosspark Klinik, University Medicine Berlin, Berlin, Germany, [2]Servicio de Reumatología, Hospital General Universitario Gregorio Marañón, Madrid, Spain, [3]Department of Rheumatology and VIB Inflammation Research Center, University Hospital Ghent, Ghent, Belgium, [4]Division of Rheumatology, University of Pavia and Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, [5]Department of Rheumatology, Aintree University Hospital, Liverpool, United Kingdom, [6]Department of Internal Medicine III, Division of Rheumatology, Medical University Vienna, Vienna, Austria, [7]Patient-centred Research, Evidera Inc., London, United Kingdom, [8]Medical Affairs, Galapagos GmbH, Basel, Switzerland, [9]Department of Rheumatology, Medisch Spectrum Twente and University of Twente, Enschede, Netherlands, [10]Medical Safety, Galapagos NV, Mechelen, Belgium

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: RA – Treatments II: RA Treatment Safety

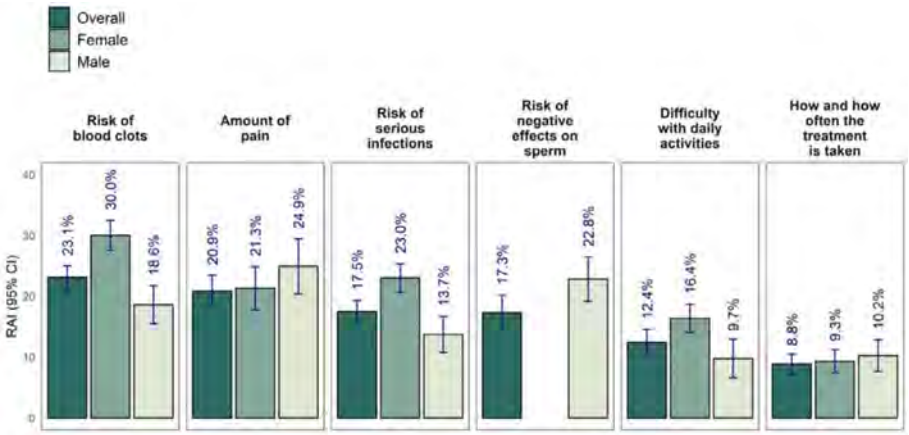
Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Multiple RA therapies are available that differ in attributes such as mode of administration and benefit-risk profile. Challenging trade-offs are made during treatment selection to accommodate patients' circumstances and ensure comprehensive disease management. EULAR recommendations for RA management emphasize the need to recognize patient preferences in shared decision-making (SDM). This study elicited trade-offs that RA patients were willing to make during treatment selection, accounting for preference heterogeneity.

Methods: An online discrete choice experiment was conducted from Sep–Oct 2021; RA patients were required to elicit their preferences for RA treatment attributes (**Figure**) and make trade-offs between them. Attributes were chosen based on literature review and qualitative patient interviews; these were tested in a quantitative pilot. Main data collection was via an online survey which asked participants to choose between hypothetical treatments. Patients were ≥18 years old, diagnosed with RA, currently received systemic DMARD therapy for RA, and resident in France, Germany, Italy, Spain, United Kingdom, or United States. Male patients were oversampled to support subgroup analysis of preferences for effects on sperm parameters. Data were analyzed using a correlated mixed logit model; differences in preferences by sex and age were explored. Relative attribute importance (RAI) scores and maximum acceptable risk (MAR) measures were derived.

Results: In total, 2,090 patients participated; 42% were female with predefined oversampling of males; mean age was 45.2 years (range 18–83). Estimated effects were significant for all attributes ($p < 0.001$), implying that they all influenced treatment choice and that preferences differed between participants. RAI scores revealed different priorities between males and females (**Figure**). Reducing pain and negative effect on semen parameters was most important to males; females were most concerned by risk of blood clots and serious infections. Remaining attributes were of lower importance. No single



Preference drivers: males – pain, blood clots; females – blood clots, infections, pain. Sperm risk data are based on male responses only.

Figure. RAI overall and by sex

Table. Benefit-risk trade-offs: willingness to accept extra risk

Attribute	Oral pill every day vs injection once a week		Reducing pain from 30% to 10%	
	Male	Female	Male	Female
Acceptable increased risk of blood clots	1.8%	0.8%	2.3%	1.2%
Acceptable increased risk of serious infections	2.5%	1.0%	3.2%	1.6%
Acceptable increased risk of negative effects on sperm (males only)	7.4%	-	10.4%	-

attribute explained treatment preferences by more than 30%. Patients aged 18-44 years placed less importance on frequency and mode of treatment administration than older patients. Patients accepted extra risks of blood clots, serious infections, or negative effects on sperm for an oral pill every day vs injection once a week, and for reducing amount of pain from 30% to 10% (**Table**). Similar observations were made for improved performance of daily activities. Acceptable trade-offs varied between patients.

Conclusion: Preferences of RA patients were driven by benefits and risks of RA treatments, with no single attribute dominating the decision making. Patients were willing to accept higher risk of serious infections and blood clots in exchange for improvements in pain, daily activities, or administration convenience. These findings emphasize the importance of considering the entire treatment profile, including benefits, risks, and administration to support SDM between providers and patients.

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Abstract Number: 1681

Tacrolimus Use in SLE Pregnancy and Its Effect on Pregnancy Outcomes: Retrospective Study in Two Japanese Tertiary Referral Centers

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Reproductive Issues in Rheumatic Disorders
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Tacrolimus is one of the major treatment options of systemic lupus erythematosus (SLE) and is thought to be pregnancy compatible medication. Since little is known on tacrolimus use during pregnancy complicated by SLE, we conducted this study.

Methods: We included pregnant patients with SLE who were followed up at two Japanese tertiary referral centres. The pregnant patients with tacrolimus exposure and those without it were propensity score matched in a ratio of one-to-two to minimise difference in disease severity. Thereafter, we compared adverse pregnancy outcome (APO) ratio according to tacrolimus exposure.

Results: Of the 124 pregnancies, 29 were exposed to tacrolimus. The pregnant patients with tacrolimus exposure tended to suffer from lupus nephritis than did those without exposure (51.7% versus 17.9%, p< 0.01) . Moreover, they tended to be treated with hydroxychloroquine/higher dose of glucocorticoid and experienced lupus flare at conception compared with those without exposure (hydroxychloroquine: 69.9% versus 28.4%, p< 0.01; glucocorticoid dosage: 5.00 [5.00, 10.00] versus 5.00 [1.00, 7.75] mg/day, p=0.03; lupus flare: 19.2% versus 1.4%, p< 0.01).

After propensity score matching, group difference in the baseline characteristics including SLE severity diminished. In addition, no statistical differences were also noted in the APO ratio; blood pressure; and estimated glomerular filtration rate during pregnancy and after delivery between the groups. (overall APO: 47.1% versus 47.1%, p=1.0; maternal APO: 29.4% versus 26.5%, p=1.0; neonatal APO: 58.8% versus 41.2%, p=0.25; PROMISSE APO: 17.6% versus 17.6%, p=1.0; hypertensive disorders of pregnancy: 17.6% versus 14.7%, p=1.0; preeclampsia: 5.9% versus 5.9%, p=1.0)

Table 1: prevalence of adverse pregnancy outcome according to the use of tacrolimus

	Tacrolimus exposure (before PS matching)			Tacrolimus exposure (after PS matching)			Logistic regression model		
Factor	(-)	(+)	p value	(-)	(+)	P value	OR	95% CI	P value
Number of patients	95	29		34	17				
Overall APO (%)	46 (48.4)	16 (55.2)	0.67	16 (47.1)	8 (47.1)	1.0	1.0	0.31-3.21	1.0
Maternal APO (%)	**23 (24.2)**	**13 (44.8)**	**0.04**	9 (26.5)	5 (29.4)	1.0	1.16	0.32-4.21	0.82
Neonatal APO (%)	42 (44.2)	14 (48.3)	0.83	14 (41.2)	10 (58.8)	0.25	2.04	0.63-6.56	0.24
PROMISSE APO (%)	24 (25.3)	5 (17.2)	0.46	6 (17.6)	3 (17.6)	1.0	1.0	0.22-4.61	1.0
Flare during pregnancy (%)	**8 (8.4)**	**8 (27.6)**	**0.01**	3 (8.8)	4 (23.5)	0.20	3.18	0.62-16.2	0.17
Flare after delivery (%)	3 (3.4)	2 (8.7)	0.27	1 (3.1)	0 (0.0)	1.0	NA	NA	NA
Hypertensive Disorders of Pregnancy (%)	13 (13.7)	7 (24.1)	0.25	5 (14.7)	3 (17.6)	1.0	1.24	0.26-5.96	0.79
Preeclampsia (%)	5 (5.3)	3 (10.3)	0.39	2 (5.9)	1 (5.9)	1.0	1.0	0.08-11.9	1.0
HELLP syndrome (%)	2 (2.1)	0 (0.0)	1	0 (0.0)	0 (0.0)	NA	NA	NA	NA
Gestational DM (%)	8 (8.4)	6 (20.7)	0.09	3 (8.8)	3 (17.6)	0.39	2.21	0.40-12.4	0.37
Oligohydramnios (%)	8 (8.4)	1 (3.4)	0.68	1 (3.0)	1 (5.9)	1.0	2.0	0.12-34.1	0.63
Maternal death (%)	0 (0.0)	0 (0.0)	NA	0 (0.0)	0 (0.0)	NA	NA	NA	NA
Live birth (%)	88 (92.6)	23 (79.3)	0.08	32 (94.1)	13 (76.5)	0.09	0.20	0.03-1.25	0.09
Total duration of gestation (days)	267.0 [257.5, 275.0]	266.0 [213.0, 273.0]	0.17	266.5 [260.3, 271.8]	263.0 [166.0, 267.0]	0.14	NA	NA	NA
Preterm birth (%)	16 (17.8)	5 (20.0)	0.78	6 (18.8)	3 (21.4)	1.0	1.18	0.25-5.6	0.83
Spontaneous abortion (%)	1 (1.1)	2 (7.4)	0.12	0 (0.0)	2 (12.5)	0.10	NA	NA	NA
Missed abortion (%)	3 (3.2)	1 (3.7)	1.0	0 (0.0)	0 (0.0)	NA	NA	NA	NA
Iatrogenic abortion (%)	4 (4.2)	3 (10.3)	0.35	2 (5.9)	2 (11.8)	0.59	2.13	0.27-16.6	0.47
Still birth (%)	0 (0.0)	0 (0.0)	NA	0 (0.0)	0 (0.0)	NA	NA	NA	NA
Planned C section (%)	14 (15.7)	3 (13.0)	1.0	6 (18.8)	2 (15.4)	1.0	1.0	0.14-4.53	0.79
Emergency C section (%)	**28 (31.5)**	**13 (56.5)**	**0.03**	9 (28.1)	6 (46.2)	0.30	2.19	0.58-8.33	0.25
Height at birth (cm)	47.2 [46.0, 49.0]	47.0 [43.5, 50.0]	0.94	47.3 [46.0, 49.0]	46.0 [44.0, 48.0]	0.24	NA	NA	NA
Weight at birth (g)	2709 [2411, 3016]	2812.00 [2165, 2943]	0.57	2731.0 [2465.5, 2951.5]	2532.0 [2080.0, 2896.0]	0.22	NA	NA	NA
Low birth weight (%)	31 (35.2)	8 (34.8)	1.0	10 (31.2)	6 (46.2)	0.49	1.89	0.50-7.07	0.35
Small for gestational age (%)	15 (17.0)	4 (17.4)	1.0	2 (6.2)	2 (15.4)	0.57	2.73	0.34-21.8	0.34
Apgar score (1min)	8.00 [8.00, 8.00]	8.00 [8.00, 8.00]	0.29	8.00 [8.00, 8.00]	8.00 [8.00, 8.00]	0.47	NA	NA	NA
Apgar score (5min)	9.00 [9.00, 9.00]	9.00 [9.00, 9.00]	0.92	9.00 [9.00, 9.00]	9.00 [9.00, 9.00]	0.48	NA	NA	NA
Apgar score≥7 (1min) (%)	85 (96.6)	21 (91.3)	0.28	31 (96.9)	12 (92.3)	0.50	0.39	0.02-6.7	0.51
Apgar score≥7 (5min) (%)	87 (98.9)	22 (95.7)	0.37	32 (100.0)	12 (92.3)	0.29	NA	NA	NA

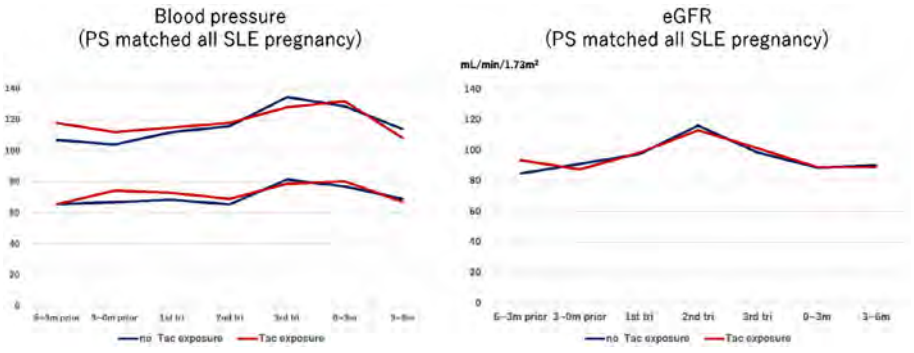

Figure 1: change in the blood pressure before and during pregnancy and after delivery

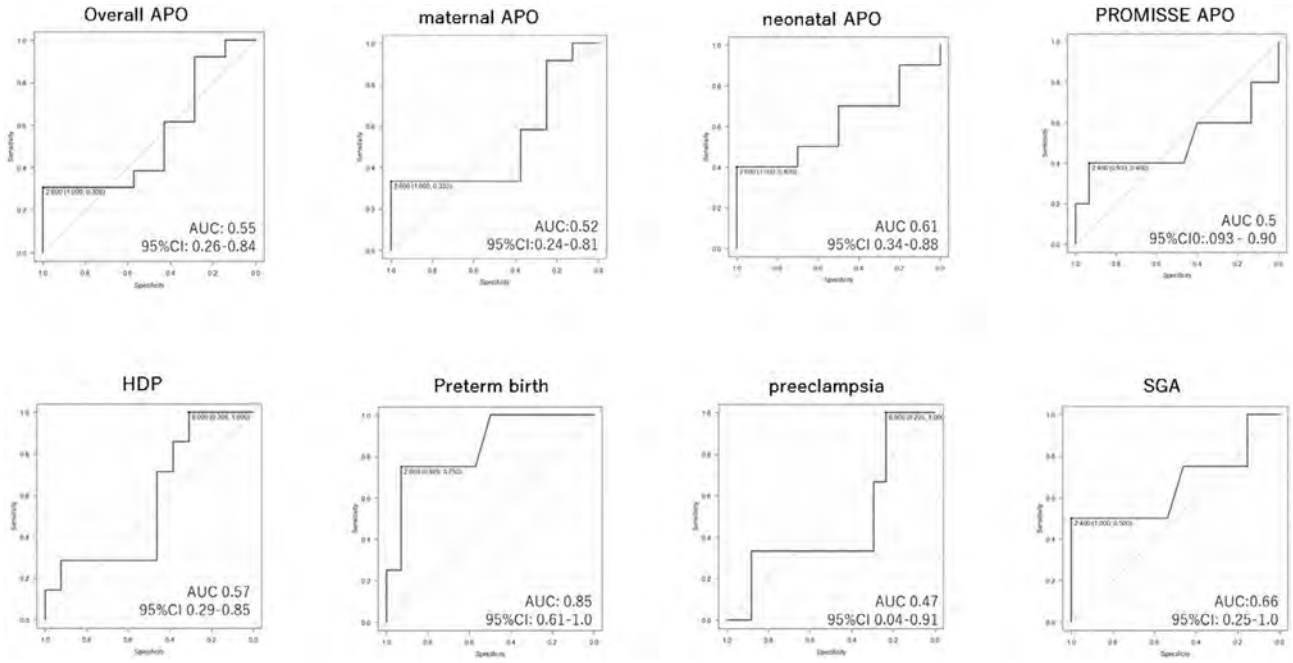

Figure 2 ROC curve for the maximum tacrolimus concentration during pregnancy and each adverse pregnancy outcome

Furthermore, receiver operating characteristic curve showed that tacrolimus concentration >2.6ng/ml was related to reduced preterm birth rate.

Conclusion: Tacrolimus use during pregnancy showed no significant impact on APO ratio, blood pressure, or renal function. Therefore, tacrolimus use might be acceptable to control lupus activity during pregnancy.

In addition, when administering tacrolimus during pregnancy, it is advisable to maintain its concentration ≥2.6 ng/ml in order to reduce the risk for preterm birth while paying careful attention to possible maternal side effects of tacrolimus.

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Abstract Number: 1682

Prospective Evaluation of Anti-SSA/Ro Pregnancies Supports the Utility of High Titer Antibodies and Fetal Home Monitoring for the Detection of Fetal Atrioventricular Block

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Reproductive Issues in Rheumatic Disorders

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: The management of fetuses exposed to maternal anti-SSA/Ro autoantibodies is challenging as the clinician weighs the rarity of fetal atrioventricular block (AVB) against the burden of serial surveillance. Antibody titer should be an important contributor to risk assessment and pathogenesis of disease since placental transport of maternal IgG via FcRn expressed on syncytiotrophoblast cells is less efficient during the second trimester with fetal IgG concentrations only about 10% of the maternal levels at weeks 17 – 22, the vulnerable period for AVB detection. Accordingly, we leveraged prospective data from the large multi-racial national study of pregnant women, **S**urveillance **ToP**revent AV **B**lock **L**ikely to **O**ccur **Q**uickly (STOP BLOQ), to address the impact of anti-Ro titers and utility of frequent ambulatory monitoring on outcomes in women with no previously affected children and those at risk for recurrence.

Methods: Women with positive anti-Ro autoantibodies by commercial CLIA testing from 21 sites across the U.S. were risk stratified into high and low anti-Ro60 and anti-Ro52 titers based on previous ELISA cutoff data demonstrating that women with titers < 1000 arbitrary units per mL were not at risk for fetal AVB. Those with low titers had echocardiograms only and EKGs at birth. Women exceeding this threshold for either anti-Ro60 or 52 performed fetal heart rate monitoring (FHRM)

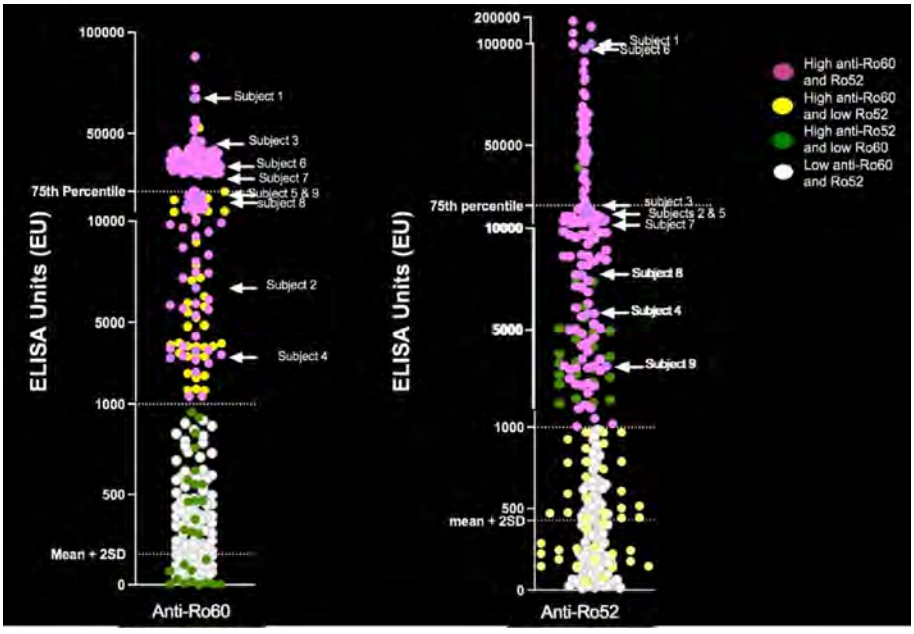

Figure 1. Titers of anti-Ro60 and Ro52 in the women enrolled in STOP BLOQ. Top quartile for anti-Ro60 > 21,336 and for anti-Ro52 > 20,420.

Table 1: Frequency of AVB in STOP BLOQ women who have completed FHRM and >26 weeks gestation.

	Overall		Previous AVB (recurrence)		No Prior AVB	
Step 1 + 2	9/381	(2.4%)	2/32	(6.3%)	7/349	(2.0%)
Step 2	9/241	(3.7%)	2/32	(6.3%)	7/209	(3.3%)
Top quartile anti-Ro60	4/58	(6.9%)	2/9	(22.2%)	2/49	(4.1%)
Top quartile anti-Ro52	2/60	(3.3%)	0/14	(0.0%)	2/46	(4.3%)
Top quartile anti-Ro60/52	2/28	(7.1%)	0/4	(0.0%)	2/24	(8.3%)

Table 2: Titers of anti-Ro60 and 52 in 4 women obtained during a prior pregnancy with AVB and a healthy pregnancy in STOP BLOQ.

	Pregnancy Outcome	Anti-Ro60	Anti-Ro52
Pair 1	AVB	5398	5116
	Healthy (STOP BLOQ)	8498	6120
Pair 2	AVB	3156	1053
	Healthy (STOP BLOQ)	3675	889
Pair 3	AVB	4406	52252
	Healthy (STOP BLOQ)	5198	49007
Pair 4	AVB	12590	102058
	Healthy (STOP BLOQ)	12003	70063

thrice daily in addition to weekly or biweekly fetal echocardiography from 18 – 26 weeks. Abnormal FHRM prompted urgent echocardiography to identify AVB.

Results: To date, 405 women have been enrolled (**Fig 1, titers**). Of these, 150 (37%) had low titers of both anti-Ro60 and 52.None of 140 pregnancies past 26 weeks resulted in AVB. Of the 255 women with titers above the threshold for either antibody, 241 completed surveillance. FHRM (performed 44,187 times) was considered abnormal in 37 audios, 9 of which were confirmed AVB by urgent echo (7 were 2nd degree AVB). Surveillance echocardiogram (performed 1871 times) detected no AVB when the FHRM was normal. Of the 9 AVB, 2/32 (6.25%) were recurrences and 7/209 (3.3%) were first time AVB (**Table 1**). Independent of previous AVB status, comparing titers for the non AVB vs AVB in the high titer group, anti-Ro60 was 16155 $\pm$ 19821 SD and 25133 $\pm$ 21494 SD (P= 0.11) and anti-Ro52 was 21194 $\pm$ 36165 SD and 32310 $\pm$ 38871 SD (P = 0.04), respectively. AVB risk increased with titers **(Table 1)**. For women within the top quartile for both anti-Ro60 and 52, the rate of AVB was 7.1% overall, and 8.3% for those never having AVB. Albeit limited numbers, having anti-Ro60 antibodies in the top quartile and a previous child with AVB conferred the highest risk of AVB, at 22%. High titer anti-Ro antibodies are necessary, but not sufficient for fetal AVB since 4 women with a prior pregnancy complicated by fetal AVB but without AVB in the current pregnancy had titers equivalent to those detected during their affected pregnancies (**Table 2**).

Conclusion: FHRM identifies early AVB, supporting this approach in the management of anti-Ro exposed pregnancies. To date, low titer anti-Ro confers no risk of AVB. While the titer of anti-Ro60 and 52 increases risk, as does previous AVB, additional factors beyond antibodies are likely.

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Abstract Number: 1683

Moving the ACR's Reproductive Health Guidelines into Practice: Assessment of a Novel Reproductive Rheumatology ECHO

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Reproductive Issues in Rheumatic Disorders
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Project ECHO™ in an education model that links experts with community providers through a series of video teleconferences. Each conference involves a brief didactic session followed by a discussion of real patient cases. We piloted the first ECHO in reproductive rheumatology to increase rheumatologists' knowledge and self-efficacy in providing reproductive health care.

Methods: The Project ECHO guides informed ReproRheum ECHO curriculum development, provider recruitment, logistics, and assessment. All ACR RISE Registry providers received email invitations. The ECHO was evaluated using interviews and pre/post surveys to assess provider knowledge, self-efficacy, and to identify program strengths, weaknesses, and solicit suggestions. Self-efficacy was assessed using a modified validated Self-Efficacy 12 survey.

Results: A total of 12 providers, 8 rheumatology providers (4 MD, 2 NP, 2 fellows) and 4 experts (2 reproductive rheumatologists, 2 MFM), participated in the ReproRheum ECHO's 6, 1-hour sessions from January-March 2023. Feasibility was demonstrated: all but one provider attended all sessions.

Knowledge of the rate of birth defects after exposure to azathioprine and mycophenolate both significantly increased. Provider self-efficacy increased significantly (6.8 +/- 1.2 pre-ECHO to 8.1 +/- 0.5 post-ECHO, p=0.03). All participants 'agreed' or 'strongly agreed' that they had increased confidence in their ability to answer colleagues' questions and guide patients' choices in contraception and medication in pregnancy.

In interviews, providers described the didactic and case discussion sections as being the most valuable, noting the combination allowed them to apply the knowledge in clinical care. They expressed appreciating the diversity of perspectives and experiences of rheumatologists from across the US and the inclusion of MFM experts. Providers said they were satisfied with the amount of facts and experienced very few barriers to attendance. Providers shared they had increased knowledge, comfort and confidence in speaking with patients about reproductive health. Providers who were not recording reproductive health information routinely before the ECHO said that they had added pregnancy counseling sections to their notes. Nearly all providers viewed the LupusPregnancy.org and ReproRheum.Duke.edu handouts as useful during patient discussions. Some providers said they shared handouts with patients, while others had verbally reviewed them together. Nearly all

providers said they would definitely attend future ECHO sessions and that they would definitely recommend the ECHO to other rheumatologists and midlevel providers.

Suggestions for improvement included having patients share their perspective, role-playing patient counseling, and enhancing curricula with articles and summary sheets.

Conclusion: The pilot ReproRheum ECHO was feasible and improved knowledge and self-efficacy among rheumatologists in reproductive health. We hope to expand to multiple audiences using tailored content, including fellows, rural providers and advanced practice providers. This model is a promising approach to improving reproductive health care for women with rheumatic disease.

Disclosure: M. Clowse: Exagen, 5, GlaxoSmithKlein(GSK), 2, 5, Immunovant, 5, UCB, 2, 5; **T. Swezey**: None; **J. Federspiel**: Hemosquid, 2; **C. Sims**: UCB, 5; **A. Snyderman**: GSK, 5, UCB, 5; **A. Corneli**: None; **S. Wheeler**: None; **J. Zell**: None.

Abstract Number: 1684

The Impact of Pregnancy Timing on Outcomes in SLE

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Abstracts: Reproductive Issues in Rheumatic Disorders
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: To minimize risk of poor pregnancy outcomes, the ACR Reproductive Health Guideline recommends women conceive when SLE is well controlled and treated with pregnancy-compatible medications. In addition to SLE disease activity and medications, social determinants of health can impact pregnancy outcomes. We studied the association between pregnancy timing, social determinants of health, and pregnancy outcomes.

Table 1. Patient demographics based on whether pregnancy was medically optimized, intended, or both.

	Medically Optimized Pregnancies* n=115		Intended Pregnancies° n=108		Well-Timed Pregnancies§ n=109	
	Yes n=78 (68%)	No n=37 (32%)	Yes n=68 (63%)	No n=40 (37%)	Yes n=54 (50%)	No n=55 (50%)
Age, years (mean +/- SD)	30.7 (5.1)	27.8 (4.1)[1]	31.0 (4.3)	27.7 (5.5)[2]	31.5 (4.4)	28.1 (5.0)[3]
Race	Black 37% Other 13% White 50%	Black 47% Other 28% White 25%[1]	Black 34% Other 18% White 48%	Black 55% Other 15% White 30%	Black 35% Other 13% White 52%	Black 50% Other 20% White 30%
Hispanic Ethnicity	4 (5%)	9 (24%)[1]	4 (6%)	5 (13%)	1 (2%)	8 (15%)
Marital Status: Single	6 (8%)	18 (50%)[1]	6 (9%)	17 (43%)[2]	3 (6%)	20 (37%)[3]
Living without Adults	2 (3%)	7 (19%)[1]	4 (6%)	5 (13%)	1 (2%)	8 (15%)[3]
Less than College Degree	24 (32%)	18 (50%)	16 (24%)	24 (60%)[2]	11 (20%)	29 (54%)[3]
Annual Income < $50,000	22 (31%)	24 (69%)[1]	17 (27%)	28 (70%)[2]	10 (20%)	35 (66%)[3]
Medicaid or Medicare	17 (23%)	22 (61%)[1]	15 (22%)	24 (60%)[2]	7 (13%)	32 (59%)[3]

*Medically optimized for pregnancy if they met all three of the following criteria: urine protein:creatinine ratio (UPC) measured ≤ 6 months prior to conception or during the first trimester with < 1g proteinuria, not prescribed a teratogen at conception, and continued pregnancy compatible SLE medications after conception.
°Intended pregnancies were defined as London Measure of Unplanned Pregnancy with a score ≥ 10 at study entry.
§Well-timed pregnancies met criteria for both Medically Optimized and Intended.
[1]Comparison of data between medically optimized and not medically optimized pregnancies resulted in a p value < 0.05
[2]Comparison of data between intended and unintended pregnancies resulted in a p value < 0.05
[3]Comparison of data between well-timed and not well-timed pregnancies resulted in a p-value < 0.05

Table 2. SLE characteristics, treatment, and activity based on whether pregnancy was medically optimized, intended, or both.

	Medically Optimized Pregnancies* n=115		Intended Pregnancies° n=108		Well-timed Pregnancies§ n=109	
	Yes n=78 (68%)	No n=37 (32%)	Yes n=68 (63%)	No n=40 (37%)	Yes n=54 (50%)	No n=55 (50%)
SLE Characteristics						
History of Lupus Nephritis	16 (21%)	21 (57%)[1]	18 (26%)	18 (45%)	11 (20%)	26 (47%)[3]
Antiphospholipid Syndrome	5 (6%)	0 (0%)	2 (3%)	1 (3%)	2 (4%)	1 (2%)
SLE Medications at Registry Enrollment						
Mycophenolate Exposure[4]	0 (0%)	8 (22%)[1]	2 (3%)	6 (15%)[2]	0 (0%)	8 (15%)[3]
Hydroxychloroquine	75 (96%)	16 (43%)[1]	58 (85%)	27 (68%)[2]	52 (96%)	34 (62%)[3]
Azathioprine	32 (41%)	6 (16%)[1]	30 (44%)	8 (20%)[2]	26 (48%)	12 (22%)[3]
Prednisone	25 (32%)	16 (43%)	23 (34%)	16 (40%)	17 (31%)	23 (42%)
SLE Activity						
Patient Reported (0-10)	3.1 (2.8)	3.6 (3.1)	2.7 (2.9)	4.3 (2.6)[2]	2.5 (2.7)	4.1 (2.8)[3]
Physician Global Assessment (0-3)	0.3 (0.4)	0.8 (0.7)[1]	0.4 (0.5)	0.7 (0.7)[2]	0.3 (0.4)	0.7 (0.7)[3]

*Medically optimized for pregnancy if they met all three of the following criteria: urine protein:creatinine ratio (UPC) measured ≤ 6 months prior to conception or during the first trimester with < 1g proteinuria, not prescribed a teratogen at conception, and continued pregnancy compatible SLE medications after conception.
°Intended pregnancies were defined as London Measure of Unplanned Pregnancy with a score ≥ 10 at study entry.
§Well-timed pregnancies met criteria for both Medically Optimized and Intended.
[1]Comparison of data between medically optimized and not medically optimized pregnancies resulted in a p value < 0.05
[2]Comparison of data between intended and unintended pregnancies resulted in a p value < 0.05
[3]Comparison of data between well-timed and not well-timed pregnancies resulted in a p-value < 0.05
[4]All patients stopped after conception but prior to registry enrollment

Methods: All study participants met SLICC criteria for SLE, were pregnant, and enrolled in a prospective registry. At baseline, patients reported social determinants of health and SLE activity; medications, laboratory results, and physician-assessments of SLE activity were also recorded. Pregnancy timing was defined in 3 ways based on whether the woman was medically optimized, the woman intended to become pregnant, or both. "Medically optimized" pregnancies met the following criteria: no teratogen use, continued pregnancy-compatible SLE medications, and urine protein:creatinine ratio (UPC) < 1g in the 6 months prior to or during the first trimester. "Intended" pregnancies were defined using the London Measure of Unplanned Pregnancy (LMUP), a validated, 6-question self-reported survey assessing the extent that the woman intended to become pregnant. Well-timed pregnancies were both medically optimized and intended; ill-timed were either not medically optimized and/or intended. Statistical analyses compared differences in outcomes by our three definitions of pregnancy timing.

Results: A total of 115 women were enrolled, with half of pregnancies both intended and medically optimized, 20% neither intended nor medically optimized, 17% not intended but medically optimized, and 13% intended but not medically optimized. Ill-timed pregnancies were more likely to be conceived by women who were single, identify as Black or Hispanic, receive Medicaid or Medicare, have a lower income and level of education (Table 1). Additionally, women with ill-timed

Table 3. Pregnancy outcomes based on whether pregnancy medically was optimized, intended, or both.

	Medically Optimized Pregnancies* n=98		Intended Pregnancies° n=92		Well Timed Pregnancies§ n=92	
	Yes n=65 (66%)	No n=33 (34%)	Yes n=58 (63%)	No n=34 (37%)	Yes n=46 (50%)	No n=46 (50%)
Pregnancy Loss < 20 Weeks						
Pregnancy Loss All Cause	10 (15%)	7 (21%)	7 (12%)	10 (29%)[2]	6 (13%)	11 (24%)
Termination	2 (3%)	0 (0%)	1 (2%)	1 (3%)	1 (2%)	1 (2%)
Miscarriage (< 20 weeks)	7 (11%)	3 (9%)	5 (9%)	5 (15%)	4 (9%)	6 (13%)
Outcomes in Pregnancies > 20 Weeks						
Stillbirth	1 (2%)	4 (12%)	1 (2%)	4 (12%)	1 (2%)	4 (9%)
Gestational Weeks at Delivery	37.0 (3.0)	34.3 (5.5)[1]	36.6 (3.3)	34.8 (5.6)	36.7 (3.5)	35.2 (5.0)
Preterm Delivery (< 37 weeks)	12 (21%)	12 (41%)	14 (24%)	9 (32%)	11 (27%)	12 (32%)
Preeclampsia	8 (16%)	11 (41%)[1]	8 (17%)	11 (44%)[2]	6 (16%)	13 (37%)

*Medically optimized for pregnancy if they met all three of the following criteria: urine protein:creatinine ratio (UPC) measured ≤ 6 months prior to conception or during the first trimester with < 1g proteinuria, not prescribed a teratogen at conception, and continued pregnancy compatible SLE medications after conception.
°Intended pregnancies were defined as London Measure of Unplanned Pregnancy with a score ≥ 10 at study entry.
§Well-timed pregnancies met criteria for both Medically Optimized and Intended.
[1]Comparison of data between medically optimized and not medically optimized pregnancies resulted in a p value < 0.05
[2]Comparison of data between intended and unintended pregnancies resulted in a p value < 0.05

pregnancy had higher physician-reported SLE disease activity, were less likely to be taking pregnancy-compatible medications at their initial pregnancy visit and more likely to be taking mycophenolate at conception (Table 2). Ill-timed pregnancies were more likely to end with preeclampsia and early delivery (Table 3). In pregnancies that were not medically optimized, when adjusted for marital status, low income, Medicaid or Medicare, the risk of preterm birth and preeclampsia was three times higher than in medially optimized pregnancies (AOR: 3.33; 95% CI: 1.06, 10 for preterm birth and AOR: 3.0; 95% CI: 0.95, 10 for preeclampsia). These pregnancies were, on average, more than two weeks shorter (adjusted β: -2.38; 95% CI: -4.42, -0.34).

Conclusion: In this cohort of pregnant patients with SLE, women with ill-timed pregnancies, whether because she didn't intend to be pregnant or was not medically optimized for pregnancy, had multiple factors contributing to their higher risk for poor pregnancy outcomes, including social disadvantage, increased lupus activity, and inappropriate medication use. In order to improve outcomes in SLE, we need to target specific interventions to this particularly vulnerable population.

Disclosure: C. Sims: None; **A. Eudy**: Amgen, 2, Exagen, 5, GlaxoSmithKlein(GSK), 5, Immunovant, 5, Pfizer, 5; **C. Harding**: None; **C. Edens**: None; **M. Birru Talabi**: None; **R. Ramsey-Goldman**: Ampel Solutions, 2, Calabetta, 2, Exagen, 2, Immunocor, 6; **L. Neil**: None; **M. Clowse**: Exagen, 5, GlaxoSmithKlein(GSK), 2, 5, Immunovant, 5, UCB, 2, 5.

Abstract Number: 1685

SLE Disease Activity Is a More Important Risk Factor Than Immunosuppression for Acquiring Human Papillomavirus (HPV) Infection in Systemic Lupus Erythematosus Patients

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Reproductive Issues in Rheumatic Disorders
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: SLE patients have increased rates of HPV infection and cervical cancer. Although some factors are recognized for HPV infection in SLE, the relationship with SLE disease activity is not well studied. Here, we studied the association between SLE activity and HPV infection in a time adjusted manner.

Methods: We studied patients visiting lupus clinic between May 2020 and May 2022. We included females between 21 to 65 years who had at least 1 pap smear after SLE diagnosis. Patients who had hysterectomy were excluded. We collected HPV vaccination data, HPV results, disease activity and exposure to immunosuppression since 2011.

SLE Disease Activity Index 2000 (SLEDAI-2K) and prednisone doses were recorded for each visit. Time adjusted SLEDAI (TAS) and time adjusted prednisone dose (TAP) were determined by calculating the area under the curve of over time. Data for 3 consecutive clinic visits were used.

Immunosuppressive drugs were divided into 3 groups: Conventional: Methotrexate; nonbiologic: Azathioprine, Mycophenolate mofetil, Tacrolimus, Voclosporin, Cyclophosphamide; and biologic: Belimumab, Rituximab or Abatacept.

Descriptive statistics, univariate and multivariate logistic regression were performed.

Results: We studied 74 female SLE patients (61% Hispanic, 24% African American, and 15% Caucasian) who had no history of prior HPV. Only 3 patients had received HPV vaccine. The mean ± SD age was 41 ±11 years. The mean ± SD of SLE disease duration was 7.9 ± 4.3 years. The mean number of pap smears per patient was 2.6.HPV testing was performed on 68 patients and 19 patients were HPV positive. In 6 patients, HPV testing was not performed due to HPV screening guidelines. The average time between visits was 3.7 months. The mean ± SD TAS and TAP were 4.2± 3.7 and 7.7 ± 13.1 mg, respectively.

Table 1a: Univariate factors associated with incident HPV infection

Risk factor	HPV negative (n=49)	HPV positive (n=19)	P value
Age (years)	45.6 ± 1.45	34.47 ± 2.33	0.0001
Average Number of pap smears(n)	2.45	3.47	0.03
Time Adjusted SLEDAI (months)	2.97 ±0.55	7.37 ±0.84	0.0012
Time adjusted prednisone dose (mg)	4.4	16.6	0.0023
Conventional drug exposure (%)	18.4	21.1	0.800
Non-biologic drug exposure (%)	63.3	68.4	0.689
Biologic drug exposure (%)	18.4	5.3	0.171

Table 1b: Multivariate logistic regression with acquiring HPV infection as dependent variable.

Risk factor	Odds ratio (CI)	P value
Age	0.86 (0.75-0.99)	0.032
Average Number of pap smears	2.14 (1.16-3.96)	0.015
Time adjusted prednisone dose	1.02 (0.96-1.09)	0.533
Time adjusted SLEDAI	1.43 (1.03-1.99)	0.033

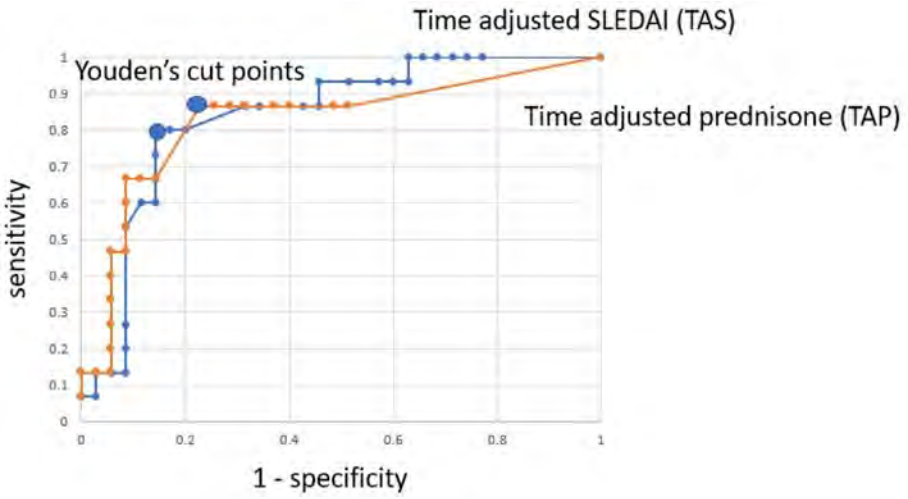

Figure 1: ROC curves of the association of HPV infection with time adjusted SLEDAI (TAS) (area under the curve 0.80) and time adjusted prednisone (TAP) (area under the curve 0.79)

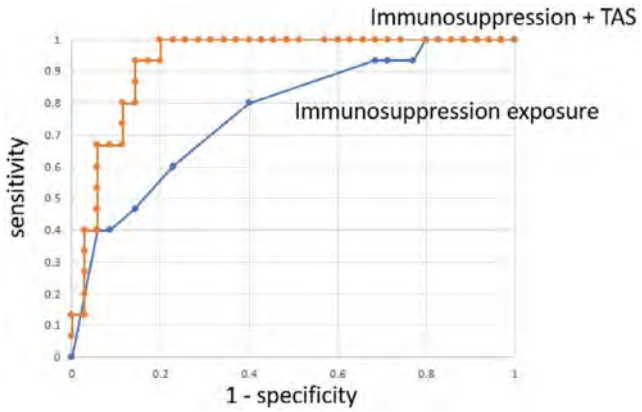

Figure 2: ROC curves of the association of HPV infection with time adjusted SLEDAI (TAS) and immunosuppression exposure (p = 0.019)

In univariate analysis, the risk of acquiring HPV was associated with younger age, higher number of pap smears, greater TAP dose, and higher TAS (Table 1a).The odds of acquiring HPV increase by 7.5% for 1 mg increase of TAP (OR 1.07, 95% CI: 1.01- 1.14). Ethnicity, SLE disease duration, alcohol use, hormonal contraception use and prior immunosuppression exposure were not associated HPV (p >0.05).

In multivariable logistic regression, age, number of pap smears and TAS were independently associated with HPV (p< 0.05 for all), but TAP was not (Table 1b). Patients were stratified into 3 TAS categories: mild < 3, moderate 3-6 and severe >6. Patients with severe SLE activity had 22.0 times higher odds of having HPV than those with mild activity (OR 22.0, 95% CI: 3.6-132.7, p 0.0007).

The cut point that better discriminated the risk of HPV infection for TAS was >5 (OR 24.0, 95% CI: 4.9-116.5) and for TAP was >15 mg (OR 16.0, 95% CI 3.5-72.6) (Figure 1). TAS increased the accuracy of immunosuppression exposure to detect HPV infection (Figure 2).

Conclusion: Our findings suggest that SLE disease activity is an independent risk factor for HPV infection, which has not been previously recognized. Reducing disease activity rather than immunosuppression may be the clinical approach to lower the risk for HPV infection. The biological basis for this association represents an important area for future study as is the role of disease activity in other infections among SLE patients.

Disclosure: Z. Kazmi: None; **C. Lorenzo**: None; **A. Escalante**: None.

Abstract Number: 1686

Adolescent and Young Adult Rheumatology Patient Reports of Reproductive Health Screening and Counseling in the Clinical Setting

Brittany Huynh[1], Mary Ott[1] and Stacey Tarvin[2], [1]Indiana University School of Medicine, Indianapolis, IN, [2]Riley Hospital for Children at Indiana University Health, Indianapolis, IN

SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Abstracts: Reproductive Issues in Rheumatic Disorders
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Adolescents and young adults (AYAs) with rheumatic disease are at high risk of poor reproductive health outcomes due to disease-related risks and teratogen use. We describe patient reported counseling on sexual and reproductive health (SRH) related to rheumatic disease among an AYA population.

Methods: AYAs ages 14-26 years and assigned female at birth were recruited from pediatric rheumatology clinics at a Midwest tertiary care center. Participants completed a one-time online survey assessing SRH behaviors and counseling. Diagnosis and medication were extracted from the EMR. Data were analyzed using descriptive statistics.

Results: The 108 participants were 14-23 years old (mean 16.7 +/- 2.0). 24% reported ever having sex. 36% were on a teratogen (excluding NSAIDs). (Table 1)

Among all participants, we found low rates of reported screening for sexual activity by pediatric rheumatologists (38%). Few reported discussions regarding pregnancy prevention (17%) or emergency contraception (EC, 6%); more participants reported counseling by any provider (56% and 20% respectively, Table 2). Sexual activity screening was associated with

Table 1. Participant characteristics, N=108

Age (years)	Mean (SD)
Mean	16.7 (2.0)
	n (Percent)
Race/Ethnicity	
White	82 (76%)
Black	11 (10%)
Latinx	9 (8%)
Asian	3 (3%)
American Indian/Alaska Native	1 (1%)
Prefer not to answer	2 (2%)
Rheumatic diagnosis	
Juvenile idiopathic arthritis	56 (52%)
Systemic lupus erythematosus	17 (16%)
Primary raynauds	6 (6%)
Juvenile dermatomyositis	5 (5%)
Scleroderma	5 (5%)
Vasculitis	5 (5%)
Idiopathic uveitis	4 (4%)
MCTD/UCTD*	4 (4%)
Chronic recurrent multifocal osteomyelitis	2 (2%)
Antiphospholipid antibody syndrome	1 (1%)
Sjogrens syndrome	3 (3%)
Current Teratogen Use	39 (36%)
Methotrexate	28 (26%)
Mycophenolate	11 (10%)
Cyclophosphamide	1 (1%)
Leflunomide	1 (1%)
Ever sex	26 (24%)
Currently sexually active	15 (14%)
Current effective hormonal contraceptive use**	26 (24%)
Current LARC use***	5 (5%)

*Mixed connective tissue disease/undifferentiated connective tissue disease

**Includes non-LARC hormonal contraception (progestin-only pills, combined oral contraceptives, Depo provera, etc.)

† Current contraceptive use did not align with sexual experience

***Long-acting reversible contraception

Table 2. Participant self-report of reproductive health screening and counseling by healthcare providers; knowledge of teratogenicity of current medication

		Current Teratogen Use			
	Overall (N=108)	Teratogen (n=39)	None (n=69)	Test Statistics	
Reproductive Health Screening/Counseling (Has provider ever…)	n (Percent)	n (Percent)		χ^2	p-value
Pediatric Rheumatologist:					
Asked about sexual activity	41 (38%)	21 (54%)	20 (29%)	6.539	0.014
Counseled risk of disease or medication on health of fetus	35 (32%)	20 (51%)	15 (22%)	9.928	0.003
Told should not get pregnant due to medication for rheumatic disease	29 (27%)	17 (44%)	12 (17%)	8.707	0.006
Talked about how to prevent pregnancy	18 (17%)	9 (23%)	9 (13%)	1.806	0.191
Talked about how to get or use emergency contraception	6 (6%)	3 (8%)	3 (4%)	0.531	0.665
Any Provider:					
Asked about sexual activity	89 (82%)	33 (85%)	56 (81%)	0.205	0.794
Counseled risk of disease or medication on health of fetus	38 (35%)	21 (54%)	17 (25%)	10.406	0.006
Told should not get pregnant due to medication for rheumatic disease	30 (28%)	17 (44%)	13 (19%)	10.906	0.004
Talked about how to prevent pregnancy	60 (56%)	23 (59%)	37 (54%)	0.719	0.698
Talked about how to get or use emergency contraception	22 (20%)	11 (28%)	11 (16%)	2.580	0.275
Key Knowledge Assessment					
"The medicine I am on for my rheumatic disease could be bad for my baby if I were to become pregnant"					
Yes		24 (62%)	22 (32%)		
No		3 (8%)	6 (9%)	9.342	0.009
Unsure		12 (31%)	41 (59%)		

current teratogen use (X^2=6.539, p< 0.05). EC counseling was associated with older age (18.3+/-2.7 vs 16.6+/-2.0 years, p< 0.05) but not teratogen use or sexual activity. Pregnancy prevention counseling was associated with none of these factors.

Among AYAs on teratogens, 54% reported screening for sexual activity by pediatric rheumatologists. Only 51% reported receipt of counseling regarding the risk of their disease or medication on the health of a fetus if they were to get pregnant, and 44% regarding counseling to avoid pregnancy due to their medication. We found similar rates when asked regarding counseling by any provider. We found gaps in counseling of patients on teratogens regarding pregnancy prevention and EC, which they largely received from non-rheumatology providers. (Table 2)

Table 3. Participant rated importance of reproductive health counseling and preferences regarding education

	n (Percent)
Report to be moderately or extremely important to know*	
Effects of medication on pregnancy	100 (93%)
Birth control	92 (85%)
Emergency contraception	91 (84%)
Report personal concern about topic in the 3 months prior to survey	
Effects of medication on pregnancy	34 (32%)
Birth control	41 (38%)
Emergency contraception	15 (14%)
Preferred method of receiving information on these topics	
Talk to a healthcare provider**	62 (57%)
Rheumatologist	52/62 (84%)
Primary care provider	41/62 (66%)
OB/GYN or Adolescent medicine	41/62 (66%)
Email	50 (46%)
Website	42 (39%)
Report it is important to talk to their rheumatologist about these topics	
Yes	88 (82%)
No	5 (5%)
Unsure	15 (14%)

*For people their age with a rheumatic disease

**Select all that apply

Notably, among those on teratogens only 62% knew their medication was teratogenic. Those not on teratogens were largely unsure of the teratogenicity of their medications, and 9% inappropriately reported that their medications were teratogenic. (Table 2)

AYAs reported these topics of high importance for young people with rheumatic disease to know, and many reported recent concerns on these topics. They preferred to receive information in person from their rheumatologist, and 82% agreed it is important to talk to their rheumatologist regarding these topics. (Table 3)

Conclusion: AYAs with rheumatic disease report low levels of reproductive health screening and counseling by their rheumatologist yet report these topics are important and want to discuss them. Gaps in knowledge were identified among teratogen users. This study identifies a need for improved communication with AYAs regarding their sexual and reproductive health.

Disclosure: B. Huynh: None; **M. Ott**: Eli Lilly, 3, 11; **S. Tarvin**: Pfizer, 5, Roche, 5, UCB, 5.

Abstract Number: 1687

Sex of the Patient Affects Response to Advanced Therapies in Psoriatic Arthritis: Meta-analysis of Data from Randomized Controlled Trials

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment II: PsA
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Limited information exists on participation and study outcomes by sex in randomized controlled trials (RCTs) among patients with psoriatic arthritis (PsA). Through a systematic literature review and meta-analysis, we aimed to compare patient characteristics and efficacy and safety of advanced therapies between male and female patients with PsA participating in RCT.

Methods: We performed a systematic literature search of Medline, Embase and Central databases, and conference abstract archives from January 1, 2000 to June 30, 2022. RCTs that assessed the efficacy of an advanced therapy (biologic or targeted synthetic) in adult participants with PsA were included. Among studies that reported sex-disaggregated results, we extracted information on participants' baseline characteristics and proportion of participants achieving minimal disease activity (MDA), or meeting the American College of Rheumatology 20 (ACR20) and ACR50 response criteria at the primary endpoint of the study by sex. Random-effect models were used to calculate pooled effects for response in males vs. females for the different classes of advanced therapies.

Results: A total of 52 trials (21,769 participants) were included. The average percentage of male and female participants enrolled was 50.2% and 49.8%, respectively. Only 9 studies (17.3%) reported sex-disaggregated baseline characteristics, 16 studies (30.7%) reported sex-disaggregated efficacy endpoints and 2 studies (3.8%) reported sex-disaggregated safety endpoints.

Female patients had significantly higher baseline tender joint count, Health Assessment Questionnaire Disability Index, physician and patient global assessment and pain scores. Male patients had significantly higher baseline psoriasis area and severity index and CRP [**Table 1**].

Differences in pooled estimates of efficacy endpoints were seen for male and female patients across the different classes of advanced therapies. The probability of achieving MDA was significantly higher in males in the following classes of advanced therapies [**Fig. 1**]: IL-17 inhibitors (i) (OR 1.99), IL-23i (OR 1.79), TNFi (OR 2.62) and JAKi (OR 1.77). The probability was also higher in IL-12/23i and methotrexate, but not statistically significant.

Table 1 - Summary results of random effects meta-analysis of baseline patient characteristics by sex

Table 1 – Summary results of random effects meta-analysis of baseline patient characteristics by sex

Variable	Number of trials	Number of Males/Females	Mean difference (Male-Female) (95% CI)	Heterogeneity (I^2)
Tender joint count (0-68)	9	2156/2312	-3.01 (-3.83, -2.18)	0%
Swollen joint count (0-66)	9	2156/2312	-0.30 (-0.80, 0.20)	0%
PASI (0-72)	6	900/1004	1.95 (0.78, 3.11)	48%
CRP (mg/L)	5	1498/1704	2.57 (0.40, 4.74)	58%
Physician global assessment (0-100)	8	2034/2189	-1.34 (-2.08, -0.08)	16%
Patient global assessment (0-100)	9	2156/2312	-3.22 (-5.27, -1.17)	62%
Pain score (0-100)	9	2154/2312	-4.58 (-6.86, -2.30)	70%
HAQ-DI (0-3)	9	2156/2312	-0.28 (-0.33, -0.24)	61%
Variable	**Number of trials**	**Number of Males/Females**	**Odds Ratio (Male vs. Female) (95% CI)**	**Heterogeneity (I^2)**
Presence of dactylitis (yes)	3	470/512	1.92 (1.00, 3.70)	58%
Presence of enthesitis (yes)	5	1029/1051	0.67 (0.55, 0.83)	12%

CRP-C-reactive protein; HAQ-DI – health assessment questionnaire disability index; PASI- psoriasis area and severity index;

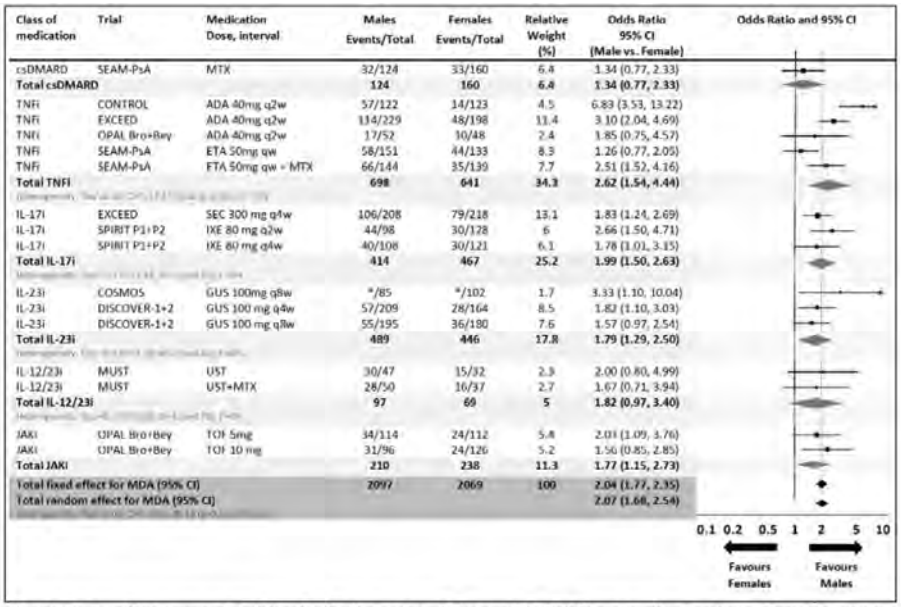

Figure 1. Random-effects meta-analysis of the odds of achieving **minimal disease activity (MDA)** in male vs. female patients with psoriatic arthritis.
CI, confidence interval; ADA, Adalimumab; DEUC, Deucravacitinib; CER, Certolizumab; csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; ETA, etanercept; GUS, Guselkumab; IL-17i, interleukin-17 inhibitor; IL-12/23i, interleukin-12/23 inhibitor; IL-23i, interleukin-23 inhibitor; IXE, Ixekizumab; JAKi, janus kinase inhibitor; MTX, methotrexate; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; Q8W, every 8 weeks; RIS, Risankizumab; SEC, secukinumab; TOF, Tofacitinib, TNFi, tumour necrosis factor inhibitor; UPA, Upadacitinib; UST, Ustekinumab.

Figure 1. Random-effects meta-analysis of the odds of achieving minimal disease activity (MDA) in male vs. female patients with psoriatic arthritis.

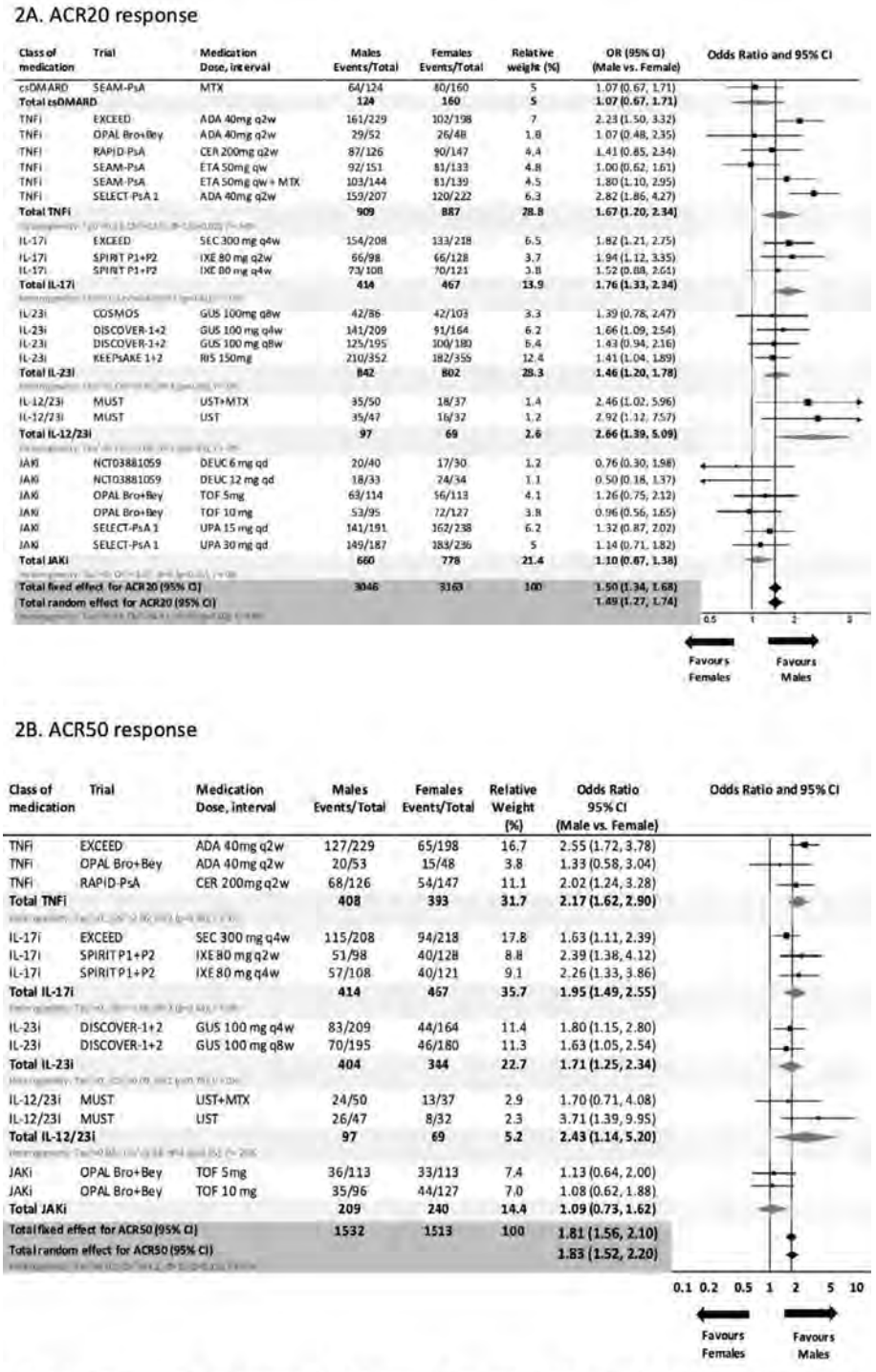

Figure 2. Random-effects meta-analysis of the efficacy of advanced therapies, by **(A) ACR20, (B) ACR50 response** between male and female patients with psoriatic arthritis.

CI, confidence interval; ACR, American College of Rheumatology; ADA, Adalimumab; DEUC, Deucravacitinib; CER, Certolizumab; csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; ETA, etacercept; GUS, Guselkumab; IL-17i, interleukin-17 inhibitor; IL-12/23i, interleukin-12/23 inhibitor; IL-23i, interleukin-23 inhibitor; IXE, Ixekizumab; JAKi, janus kinase inhibitor; MTX, methotrexate; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; Q8W, every 8 weeks; RIS, Risankizumab; SEC, secukinumab; TOF, Tofacitinib, TNFi, tumour necrosis factor inhibitor; UPA, Upadacitinib; UST, Ustekinumab.

Figure 2. Random-effects meta-analysis of the efficacy of advanced therapies, by (A) ACR20, (B) ACR50 response between male and female patients with psoriatic arthritis.

In contrast, variability was seen in the probability of achieving ACR response by sex across classes of advanced therapies. The probability of achieving ACR20 response was significantly higher in male vs. female patients for IL-17i (OR 1.76), IL-23i (OR 1.46), IL-12/23i (OR 2.66) and TNFi (OR 1.67), but significantly different for JAKi (OR 1.10). [**Fig. 2A**]. Similarly, the probability of achieving ACR50 response was significantly higher in males vs. females in all advanced therapies, and not significantly different for JAKi (OR 1.09) **[Fig 2B]**. Male and female patients had a similar probability of achieving ACR20 response when using placebo (OR 1.04, 95% CI 0.86, 1.27).

Conclusion: Female patients participating in RCTs are less likely to achieve efficacy end points for most classes of advanced therapies. Some differences in response outcomes were found across classes of advanced therapies. Future studies should report disaggregated sex data for baseline and end-points.

Disclosure: L. Eder: AbbVie, 2, 5, Eli Lilly, 2, 5, Fresenius Kabi, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Sandoz, 5, UCB, 2, 5; **S. Mylvaganam**: None; **J. Pardo Pardo**: None; **J. Petkovic**: None; **V. Strand**: Abbvie, 2, Alpine Immune Sciences, 2, Amgen, 2, Arena, 2, AstraZeneca, 2, Bayer, 2, Biosplice, 2, Bioventus, 2, Blackrock, 2, 2, BMS, 2, Boehringer Ingelheim, 2, Celltrion, 2, Chemocentryx, 2, EMD Serono, 2, Equillium, 2, Ermium, 2, Eupraxia Pharmaceuticals, 2, Flexion, 2, Galapagos, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon, 2, Ichnos, 2, Inmedix, 2, Janssen, 2, Kiniksa, 2, 2, Kypha, 2, Lilly, 2, Merck, 2, MiMedx, 2, Novartis, 2, Omeros, 2, Pfizer, 2, Regeneron, 2, Rheos, 2, R-Pharm, 2, Samsung, 2, Sandoz, 2, Sanofi, 2, Scipher, 2, Setpoint, 2, Sorrento, 2, Spherix, 2, Tonix, 2, UCB, 2, Urica, 2; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2; **K. Colaco**: None.

Abstract Number: 1688

Izokibep Demonstrates Major Disease Control on ACR70, PASI100 and Enthesitis Resolution in Patients with Active Psoriatic Arthritis Treated Through 46 Weeks

Philip J. Mease[1], Peter C. Taylor[2], Kurt de Vlam[3], Paul M. Peloso[4], Apinya Lertratanakul[5], Dieter Wetzel[6], Nikolai Brun[7], Brian Wiens[8], Jan Brandt-Juergens[9], Edit Drescher[10], Eva Dokoupilova[11], Anna Rowińska-Osuch[12], Nadia Abdel-Kader Martin[13] and Frank Behrens[14], [1]Swedish Medical Center/Providence St. Joseph Health and University of Washington School of Medicine, Seattle, WA, [2]Nuffield Department of Orthopedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom, [3]University Hospitals Leuven, Leuven, Belgium, [4]ACELYRIN, INC., Naples, FL, [5]ACELYRIN, Chicago, IL, [6]toclinco GmbH, Freiburg im Breisgau, Germany, [7]Affibody AB, Solna, Sweden, [8]ACELYRIN, Inc., Half Moon Bay, CA, [9]rheumatologische Schwerpunktpraxis, Berlin, Germany, [10]Csolnoky Ferenc Hospital / Vital Medical Center Private Clinci, Veszprém, Hungary, [11]Masaryk University, Faculty of Pharmacy, Department of Pharmaceutical Technology; MEDICAL PLUS sro, Brno, Czech Republic, [12]ETG Warszawa, Warsaw, Poland, [13]Hospital Quironsalud Infanta Luisa, Sevilla, Spain, [14]Goethe University, Division of Rheumatology, University Hospital and Fraunhofer Institute for Translational Medicine & Pharmacology, Frankfurt, Germany

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment II: PsA

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: IL-17 inhibition demonstrates efficacy in multiple disease domains in psoriatic arthritis. Izokibep is a unique IL-17A inhibitor with high IL-17A binding affinity (K_D= 0.3 pM), small molecular size (18.6 kDa), and an albumin attachment site. Week 16 data showed ACR50 of 52% and enthesitis resolution rates of 88%. We report data from baseline to 46 weeks in this phase 2 PsA trial[1] on arthritis and skin composite efficacy endpoints and longer-term safety.

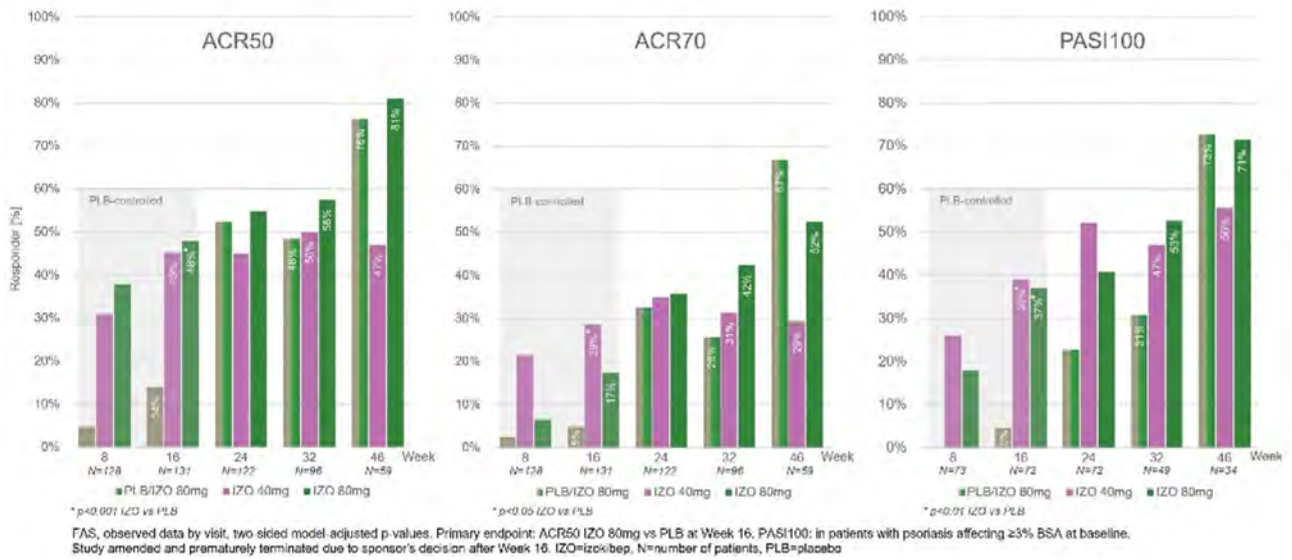

Figure 1. High Levels of ACR50, ACR70, and PASI100 Scores Obtained at Week 46

Table. Majority of Patients Achieve DAPSA LDA/Remission and Minimal Disease Activity at Week 46

	DAPSA LDA and Remission (≤14)*			MDA		
	PLB/IZO 80 mg %	IZO 40 mg %	IZO 80 mg %	PLB/IZO 80 mg %	IZO 40 mg %	IZO 80 mg %
Week 16 N=129/131	14	43	46	5	38	35
Week 24 N=121/122	58	58	51	35	45	36
Week 32 N=96/96	55	59	55	32	44	49
Week 46 N=58/59	71	53	65	67	29	57

FAS, observed data by visit *post-hoc analysis
IZO=izokibep, N=number of patients, PLB=placebo

Methods: Izokibep doses of 80 mg Q2W or 40 mg Q2W were evaluated to 46 weeks or study termination. The original placebo arm switched to 80 mg Q2W at week 16 in this multicenter trial (NCT04713072). Once week 16 data were available, this trial was terminated to further examine the effective dose range of izokibep in a next P2b/3 trial. The results include as observed analysis. Eligible patients met CASPAR criteria, with ≥3 swollen and ≥3 tender joints, and prior failure/insufficient response to NSAIDs, csDMARDs or TNF inhibitors.

Results: 135 patients were randomized 1:1:1: 44 to 40 mg Q2W, 47 to 80 mg Q2W, 44 to placebo later switched to 80 mg Q2W at week 16. At week 32, 96 of 102 eligible patients had measured results and at week 46, 59 of 62 patients did. Baseline mean age was 49 (SD 12), BMI 29 (5), PsA duration 7 (8) years, SJC 10 (7) and TJC 17 (10), DAPSA 47 (22), and PsAID-9 5.9 (1.8). Mean PASI was 10 (6) in those patients with BSA >3%, and in those with enthesitis, mean LEI was 1.5 (0.5) and SPARCC was 3.4 (2.8). 13% used prior TNF inhibitors.

Beyond week 16, the 80 mg groups continued to improve, while the 40 mg group remained largely stable (Figure 1).

Most patients in the 80 mg group and the placebo/80 mg switchers achieved DAPSA low disease activity/remission and minimal disease activity (MDA) thresholds through week 46 (Table).

High LEI enthesitis resolution rates on 80 mg until week 16 were maintained while SPARCC enthesitis resolution progressed through week 46 (Figure 2). Mean PsAID-9 scores improved to week 46, to a mean 2.3 (2.0) on 80 mg, 2.2 (2.1) in the placebo/80 mg switchers and remained largely stable on 40 mg after 16 weeks, with mean 3.2 (2.5).

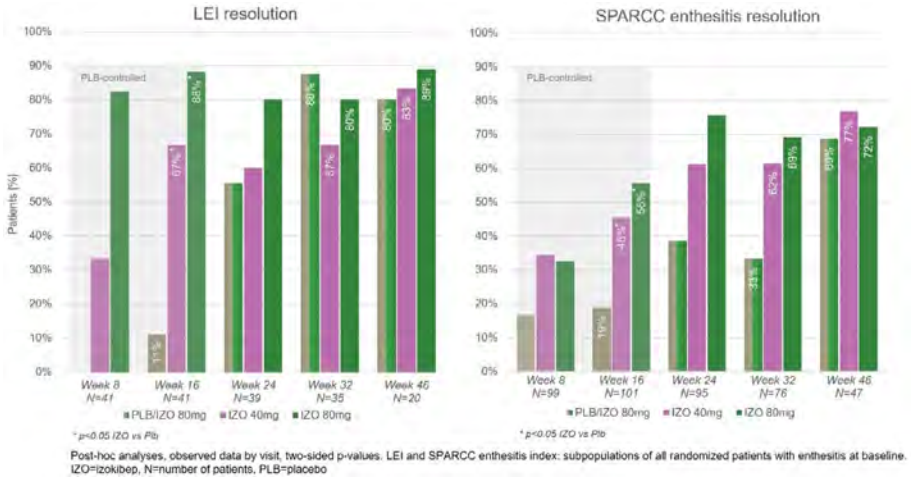

Figure 2. High Rates of LEI and SPARCC Enthesitis Complete Resolution to Week 46

Safety over the interval from week 16 to 46 remained unchanged. The most frequent adverse events were injection site reactions (14.5%) and injection site erythema (12.2%), with 1 patient discontinuing for ISR. Nasopharyngitis occurred in 6.9%, and headache and backpain occurred in 5.3% each. AEs were mostly mild and balanced across treatment groups. No Candida or fungal infections were observed from weeks 16 to 46.

Conclusion: Izokibep 80 mg demonstrated high levels of disease control with ACR70 in 52%, PASI100 in 71% and enthesitis complete resolution in 89% at week 46. Izokibep remained well tolerated, with no dose related adverse events and a safety profile generally consistent with approved IL-17A inhibitors.

References

[1]Behrens, F et al. ACR 2022. Abstract 1597. Arthritis Rheumatol. 2022; 74 (suppl 9).

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2; **P. Taylor**: AbbVie, 2, Biogen, 2, Eli Lilly, 2, Fresenius, 2, Galapagos, 2, 5, Gilead Sciences, 2, GSK, 2, Janssen, 2, Nordic Pharma, 2, Pfizer Inc, 2, Sanofi, 2, UCB, 2; **K. de Vlam**: AbbVie, 2, Amgen, 2, Celgene, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, 5, 6, Novartis, 2, 6, UCB, 2, 6; **P. Peloso**: ACELYRIN, 3, 8, 11; **A. Lertratanakul**: AbbVie, 11, ACELYRIN, 3, 11; **D. Wetzel**: ACELYRIN, 2, Affibody, 2; **N. Brun**: Affibody, 3, 8, 11; **B. Wiens**: ACELYRIN, 3, 8, 11, Horizon Therapeutics, 8; **J. Brandt-Juergens**: AbbVie/Abbott, 2, 6, Affibody, 2, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Gilead, 2, Janssen, 2, 6, Medac, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **E. Drescher**: None; **E. Dokoupilova**: AbbVie/Abbott, 5, Eli Lilly, 5, Galapagos NV, 5, Gilead, 5, GlaxoSmithKlein(GSK), 5, Hexal, 5, Janssen, 5, Novartis, 5, Pfizer, 5, Samsung Bioepis, 5, Sanofi, 5, UCB, 5; **A. Rowińska-Osuch**: None; **N. Abdel-Kader Martin**: None; **F. Behrens**: AbbVie, 2, 6, Affibody, 2, Amgen, 6, Boehringer-Ingelheim, 2, Celgene, 5, Chugai, 5, Eli Lilly, 6, Genzyme, 6, Gilead Sciences, 2, GSK, 2, 6, Janssen, 2, 5, MoonLake, 2, 6, MSD, 2, 6, Novartis, 6, Pfizer, 2, 5, 6, Roche, 5, Sandoz, 2, 6, Sanofi, 2, 6.

Abstract Number: 1689

Deep Cellular Immune Profiling in Psoriatic Arthritis Correlates with Imaging Phenotypes and Response to Targeted Advanced Therapy

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment II: PsA

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: To characterize the relationships between peripheral blood immune cell profiles in patients with psoriatic arthritis (PsA) and (1) baseline clinical and imaging disease features; (2) response to targeted advanced therapies at 3 months.

Methods: Patients with PsA who were initiating treatment with advanced therapies for active peripheral musculoskeletal disease were recruited. Patients were examined and ultrasound was performed to assess the level of inflammation in various PsA domains at baseline and after 3 months of treatment. Mass cytometry (CyTOF) was performed to characterize immune cell populations in whole blood. The frequencies of 16 immune cell populations (among CD3+ positive cells) were

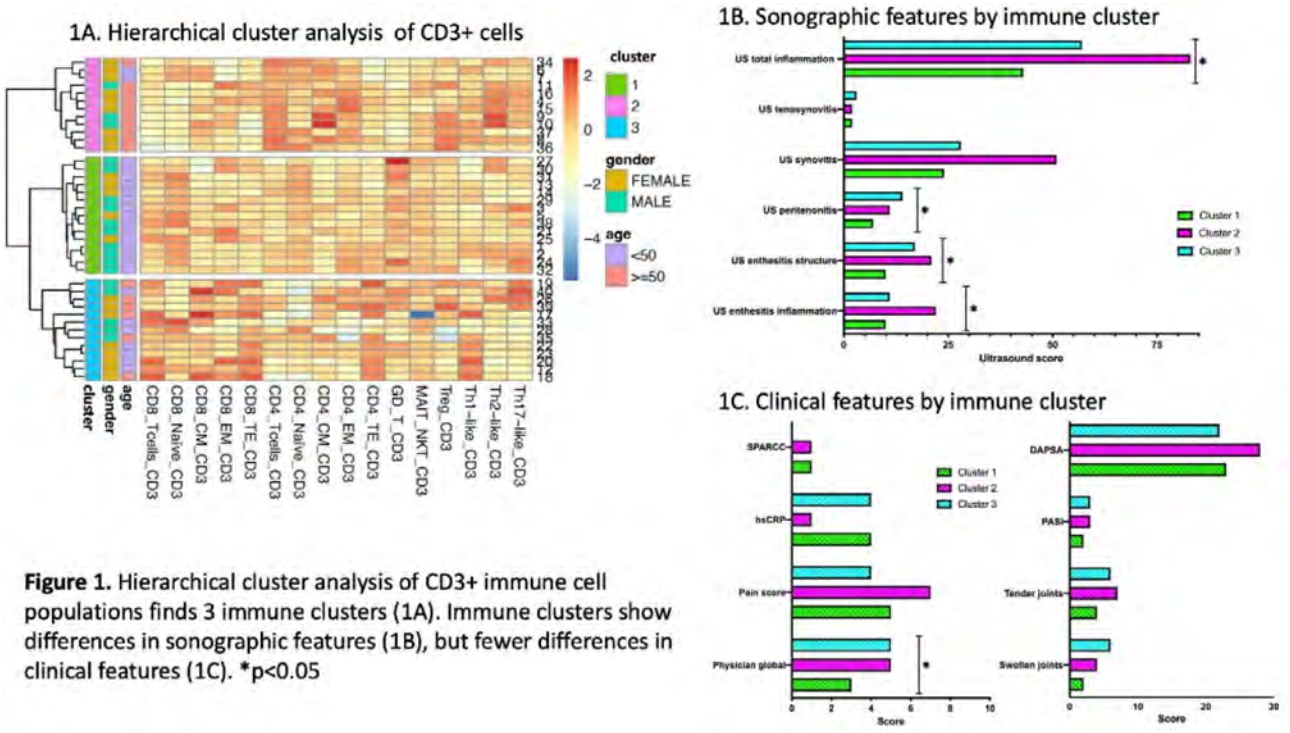

Figure 1. Hierarchical cluster analysis of CD3+ immune cell populations finds 3 immune clusters (1A). Immune clusters show differences in sonographic features (1B), but fewer differences in clinical features (1C). *p<0.05

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Table 1: The association between baseline immune profile* and clinical response to targeted advanced therapies at 3 months - GEE regression model (N=40)

Table 1: The association between baseline immune profile* and clinical response to targeted advanced therapies at 3 months - GEE regression model (N=40)

	ACR20 response (24 events)		DAPSA change**	
Immune cell population	**Odds Ratio (95% CI)**	**P value**	**β coefficient (95% CI)**	**P value**
Cluster 2 vs. Cluster 1	**0.15 (0.02, 0.93)**	**0.04**	**12.28 (5.69, 18.86)**	**<0.001**
Cluster 2 vs. Cluster 3	**0.09 (0.01, 0.68)**	**0.02**	**13.85 (7.73, 19.97)**	**<0.001**
CD8+ T cells	6.85 (0.65, 71.62)	0.10	**-13.2 (-20.6, -5.7)**	**<0.001**
CD8+ naïve T cells	1.43 (0.52, 3.92)	0.47	**-5.07 (-9.73, -0.40)**	**0.03**
CD8+ CM T cells	0.72 (0.25, 2.09)	0.54	-0.20 (-6.80, 6.40)	0.95
CD8+ EM T cells	2.98 (0.58, 15.41)	0.18	-2.52 (-18.52, 13.48)	0.75
CD8+ TE T cells	1.68 (0.77, 3.67)	0.18	-4.18 (-8.60, 0.25)	0.06
CD4+ T cells	0.002 (0.000, 2.40)	0.08	**31.05 (13.47, 48.64)**	**<0.001**
CD4+ Naïve T cells	**0.23 (0.05, 0.97)**	**0.04**	**11.64 (3.36, 19.93)**	**0.004**
CD4+ CM T cells	0.38 (0.03, 4.35)	0.42	**15.60 (5.79, 25.42)**	**0.001**
CD4+ EM T cells	0.14 (0.02, 1.29)	0.07	**12.01 (4.62, 19.39)**	**0.001**
CD4+ TE T cells	1.47 (0.51, 4.24)	0.46	1.30 (-6.88, 9.49)	0.99
γδ T cells	**2.92 (1.02, 8.35)**	**0.04**	1.30 (-6.88, 9.49)	0.75
MAIT NKT cells	1.98 (0.97, 4.06)	0.05	-2.47 (-5.00, 0.06)	0.047
Regulatory T cells	0.90 (0.20, 4.14)	0.89	6.25 (-0.42, 12.92)	0.06
Th1 cells	**0.20 (0.04, 0.86)**	**0.03**	14.20 (-7.19, 35.58)	0.18
Th2 cells	1.31 (0.30, 5.82)	0.71	8.51 (-38.04, 55.06)	0.71
Th17 cells	1.73 (0.43, 6.86)	0.42	1.83 (-5.32, 8.97)	0.60

*cell count/CD3+ cells; **difference in baseline-follow up DAPSA score adjusted for DAPSA score at baseline; CM- central memory; DAPSA – disease activity in psoriatic arthritis; EM – effector memory; MAIT NKT – mucosal associated T and Natural Killer T; TE-terminal effector; Th – T helper

automatically quantified using Probability State Modelling algorithms. Hierarchical clustering was performed using immune cell population data. The association between the 3 identified immune cell clusters and baseline characteristics, as well as clinical and sonographic response to treatment, was assessed using GEE regression models.

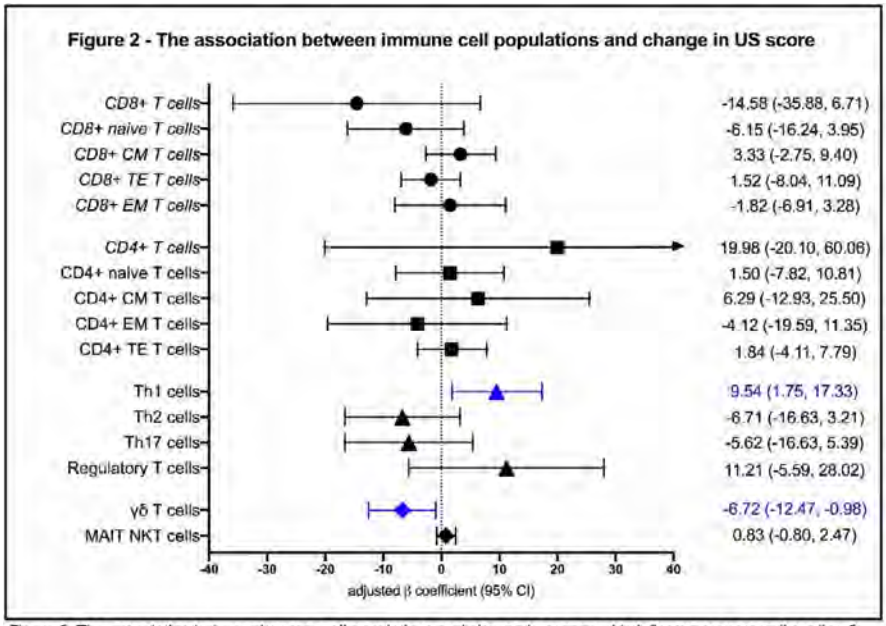

Figure 2: The association between immune cell populations and change in sonographic inflammatory score (baseline-3 months) adjusted for baseline sonographic score by GEE linear regression models. Blue lines=significant association (p<0.05)

Figure 2 - The association between immune cell populations and change in sonographic inflammation score by GEE model adjusted for baseline sonographic score

Results: 40 treatment periods involving 34 patients were analyzed (21 IL-17i; 16 TNFi; 3 JAKi). 60% of patients achieved ACR20 response. Cluster analysis identified 3 immune clusters (Figure 1). **Cluster 1** (γδT cells and CD8+ naïve predominant) was associated with lower sonographic inflammation, lower physician global assessment and younger age. **Cluster 2** (Central Memory (CM) and Effector Memory (EM) CD4+ T cells predominant) was associated with the highest levels of sonographic inflammation, in particular synovitis and enthesitis scores, and older age. **Cluster 3** (CD4+ and CD8+ Terminal Effector (TE) T cells and Th1 predominant) was associated with highest levels of peritenon inflammation (Figure 1B-C). Immune cell profiles were associated with clinical and sonographic response to therapy. Being in Cluster 2 was associated with a lower probability of achieving ACR20 response and with an increase in Disease Activity index for PsA (DAPSA) score compared to clusters 1 and 3 (Table 1). Among individual cell populations, higher levels of CD8+ cells, in particular naïve cells, was associated with reduction in DAPSA. Higher levels of γδT cells was associated with higher chances of achieving ACR20 response, while higher levels of naïve EM and CM CD4+ and Th1 cells were associated with lower treatment response (Table 1). The levels of Th1 and γδT cells also predicted change in sonographic inflammatory score (Figure 2).

Conclusion: Immune cell profiling can improve PsA phenotyping. CD4+ memory and Th1cells correlated with more severe synovitis and enthesitis and poor response to advanced therapies, while γδT cells and CD8+ naïve cells were associated with milder disease phenotype and improved treatment response.

Disclosure: L. Eder: AbbVie, 2, 5, Eli Lilly, 2, 5, Fresenius Kabi, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Sandoz, 5, UCB, 2, 5; **X. Li**: None; **S. Thib**: None; **D. Ganatra**: None; **L. Diao**: None; **V. Chandran**: AbbVie, 1, 5, 6, Amgen, 1, 5, 6, AstraZeneca, 3, Bristol-Myers Squibb (BMS), 1, 6, Eli Lilly, 1, 5, 6, Janssen, 1, 6, Novartis, 1, 1, 6, UCB, 1, 2.

Abstract Number: 1690

Apremilast Reduces Inflammation as Measured by MRI of the Hand in Patients with Psoriatic Arthritis: Primary Results from the Phase 4 MOSAIC Study

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SESSION INFORMATION

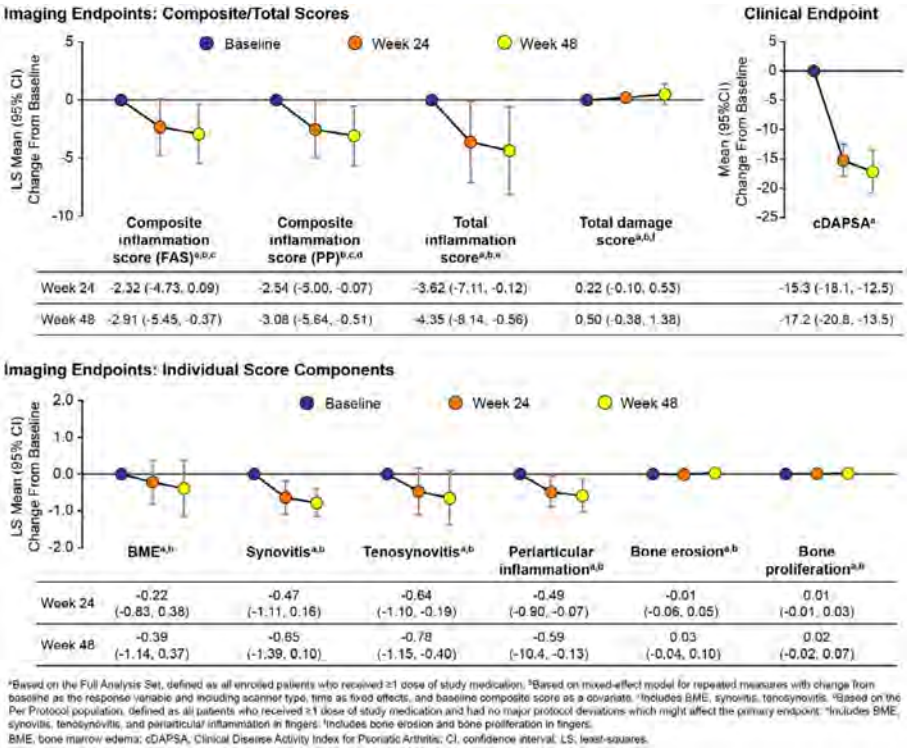
Session Date: Monday, November 13, 2023

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment II: PsA

Session Type: Abstract Session

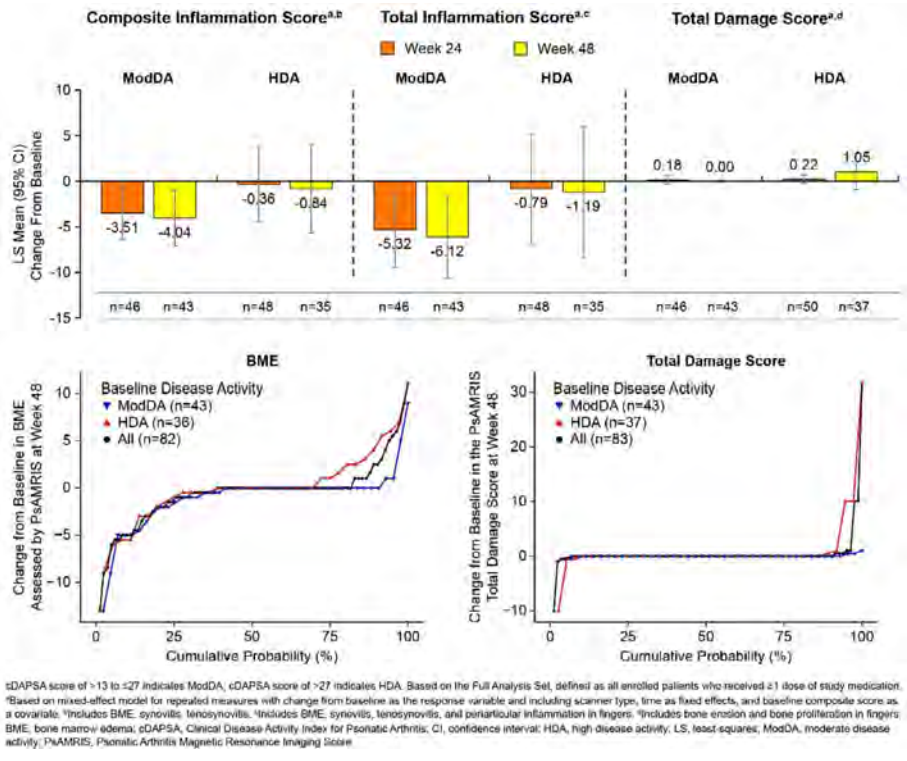
Session Time: 4:00PM–5:30PM

Background/Purpose: PsA is characterized by inflammatory arthritis, enthesitis, dactylitis, and spondylitis. Apremilast (APR) is an oral immunomodulating phosphodiesterase-4 inhibitor approved for the treatment of PsA. Here, we evaluate the efficacy of APR 30 mg BID on inflammation measured by a dedicated MRI of the hand.



Change From Baseline in Imaging and Clinical Efficacy Endpoints Following Treatment With Apremilast

Methods: MOSAIC (NCT03783026) was a phase 4, multicenter, single-arm, open-label study in patients (pts) with active PsA (≥3 months but ≤5 years since diagnosis, meeting CASPAR criteria) evaluating APR as monotherapy or in combination with stable MTX. Pts were treated with APR for 48 weeks (wk) and had contrast-enhanced MRI of the hand performed at



cDAPSA score of >13 to ≤27 indicates ModDA, cDAPSA score of >27 indicates HDA. Based on the Full Analysis Set, defined as all enrolled patients who received ≥1 dose of study medication. [a]Based on mixed-effect model for repeated measures with change from baseline as the response variable and including scanner type, time as fixed effects, and baseline composite score as a covariate. [b]Includes BME, synovitis, tenosynovitis. [c]Includes BME, synovitis, tenosynovitis, and periarticular inflammation in fingers. [d]Includes bone erosion and bone proliferation in fingers.
BME, bone marrow edema; cDAPSA, Clinical Disease Activity Index for Psoriatic Arthritis; CI, confidence interval; HDA, high disease activity; LS, least-squares; ModDA, moderate disease activity; PsAMRIS, Psoriatic Arthritis Magnetic Resonance Imaging Score.

Change From Baseline in Imaging Endpoints by Disease Activity Status at Baseline (Subgroup Analyses)

baseline (BL), Wk 24, and Wk 48. All images were read and adjudicated by 2 experienced readers blinded to clinical information and time of acquisition. The primary endpoint was change from BL in the composite score of hand bone marrow edema (BME), synovitis, and tenosynovitis in fingers 2–5, as assessed by the PsA MRI Score (PsAMRIS) at Wk 24. Total inflammation score, comprised of BME, synovitis, tenosynovitis, and periarticular inflammation in fingers, was also assessed. Structural progression determined by bone erosion and proliferation in fingers 2–5 was assessed by the total hand damage score. Subgroup analyses based on BL disease activity as measured by Clinical Disease Activity Index for PsA (cDAPSA) were performed for key endpoints.

Results: A total of 122 pts enrolled and received APR (mean age, 47 y; 55% female; and mean PsA duration, 1.9 y). The Full Analysis Set (FAS) included 98 pts evaluable for the primary endpoint and 94 were included in the per protocol (PP) set. The least-squares (LS) mean (95% CI) change from BL in the PsAMRIS (FAS) was -2.32 (-4.73, 0.09) at Wk 24 and -2.91 (-5.45, -0.37) at Wk 48 (**Figure 1**). In the PP set, the LS mean (95% CI) change from BL in the PsAMRIS at Wks 24 and 48 showed a significant reduction of disease activity (**Figure 1**). Significant improvements from BL were seen in total inflammation scores in the FAS (**Figure 1**). The total hand damage score showed no significant change from BL to Wk 48 (**Figure 1**). Pts also experienced significant improvements from BL in cDAPSA at Wks 24 and 48 (**Figure 1**). Subgroup analyses based on BL disease activity showed significant improvements from BL in inflammation in pts with moderate disease activity (ModDA; cDAPSA >13 to ≤27) and no significant change from BL in total damage. Though it was insignificant, pts with high disease activity (HDA; cDAPSA >27) did have improvement from BL in inflammation indices (**Figure 2**). No new safety signals were identified.

Conclusion: Pts with PsA treated with APR had improvements in both clinical indices and objective MRI indices of inflammation assessed by PsAMRIS in the target hand at Wk 24 and Wk 48, confirming an effect of APR on clinical and inflammatory manifestations of PsA. Pts with ModDA seemed to have greater improvement from BL in MRI inflammation scores than pts with HDA. No significant structural progression was observed. These results offer important insights on the effect of APR in PsA and highlight the value of using MRI and PsAMRIS as measures of inflammatory disease activity and change following treatment.

Disclosure: M. Østergaard: AbbVie, 2, 5, 6, Amgen, 5, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Hospira, 2, 6, Janssen, 2, 6, MEDAC, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Novo Nordisk, 2, 6, Orion, 2, 6, Pfizer, 2, 6, Regeneron, 2, 6, Roche, 2, 6, Sandoz, 2, 6, Sanofi, 2, 6, UCB, 2, 6; **W. Maksymowych**: AbbVie, 2, 5, 6, BMS, 2, 6, Boehringer-Ingelheim, 2, CARE Arthritis Ltd, 4, CARE Arthritis Ltd., 4, Celgene, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **M. Boesen**: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 6, Image Analysis Group, 2, 6, 11, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6; **R. Lambert**: Calyx, 2, CARE Arthritis Limited, 2, Image Analysis Group, 2; **G. Valenzuela**: AbbVie, 2, Bristol-Myers Squibb, 12, Investigator, Celgene, 2, Eli Lilly, 2, Genentech, 2, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, Merck, 2, MLKCDT, 12, Investigator, Novartis, 2, Pfizer, 2, Regeneron, 2, Sanofi, 2, UCB, 2; **M. Bubb**: Amgen, 5, Bristol-Myers Squibb, 5, Eli Lilly, 5, Gilead, 5, GlaxoSmithKline, 5, Janssen, 5, Novartis, 5, Pfizer, 5, UCB, 5; **O. Kubassova**: Image Analysis Group, 3, 11; **J. Reddy**: Amgen, 3, 11; **S. Colgan**: Amgen, 3, 11; **Y. Klyachkin**: Amgen, 3, 11; **C. Deignan**: Amgen, 3, 11; **L. Tang**: Amgen, 3, 11; **M. Paris**: Amgen, 3, 11; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2.

Abstract Number: 1691

16-Week Results from FOREMOST, a Placebo-Controlled Study Involving Oligoarticular Psoriatic Arthritis Treated with Apremilast

Philip J. Mease[1], Dafna Gladman[2], Laura Coates[3], Jacob Aelion[4], Jitendra Vasandani[5], Arthur Kavanaugh[6], Joseph F. Merola[7], Jyotsna Reddy[8], Rebecca Wang[8], Michele Brunori[8], Stephen Colgan[9] and Laure Gossec[10], [1]Swedish Medical Center/Providence St. Joseph Health and University of Washington School of Medicine, Seattle, WA, [2]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Department of Medicine, University of Toronto, Toronto, ON, Canada, [3]University of Oxford, Oxford, United Kingdom, [4]West Tennessee Research Institute, Jackson, TN, [5]West Texas Clinical Research, Lubbock, TX, [6]University of California San Diego, School of Medicine, Riverside, CA, [7]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [8]Amgen, Inc., Thousand Oaks, CA, [9]Amgen, Inc., Halton Hills, ON, Canada, [10]Sorbonne Université and Pitié Salpêtrière Hospital, Paris, France

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Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Oligoarticular PsA can be associated with significant impact on quality of life, despite limited joint involvement. The phase 4 FOREMOST study evaluated the efficacy of apremilast (APR) in patients (pts) with limited joint involvement (defined as 2–4 swollen and 2–4 tender joints [2–8 active joints]) using a modified minimal disease activity score (MDA-Joints).

Table 1. Clinical and Quality-of-Life Outcomes at Week 16

	Sentinel[a] Joints			All Joints (Exploratory Analysis)		
	PBO n=105	APR n=203	Difference (95% CI)	PBO n=105	APR n=203	Difference (95% CI)
Primary endpoint						
MDA-Joints[b], n (%)	16.8 (16.0)	68.8 (33.9)	18.5% (8.9, 28.1) *P*=0.0008	8.3 (7.9)	43.2 (21.3)	13.6% (5.9, 21.4) *P*=0.0028[d]
Secondary endpoints						
cDAPSA REM/LDA[c], n (%)	54.4 (51.8)	142.6 (70.2)	18.6% (7.0, 30.2) *P*=0.0017	40.0 (38.0)	122.5 (60.3)	22.5% (10.7, 34.3) *P*=0.0004[d]
PASDAS Good/ Moderate Response, n (%)	43.9 (41.8)	123.8 (61.0)	19.7% (7.7, 31.8) *P*=0.0016[d]	42.8 (40.8)	120.3 (59.3)	19.0% (7.0, 31.1) *P*=0.0023[d]
PsAID-12, LS mean (SE) change from baseline				-0.4 (0.2)	-1.5 (0.2)	-1.0 (-1.5, -0.6) *P*<0.0001[d]
PtGA ≤20, n (%)				20.1 (19.1)	61.7 (30.4)	11.8% (1.7, 22.0) *P*=0.0286[d]

Percentages are based on the number of patients in the Full Analysis Set.
[a]Sentinel joints defined as joints affected at baseline. [b]MDA-Joints is a composite of TJC ≤1 and SJC ≤1 plus achieving 3 of the following: psoriasis BSA ≤3%, patient assessment of pain VAS (0–100-mm) ≤15, PtGA (0–100-mm) ≤20, HAQ-DI ≤0.5, and LEI ≤1. [c]REM: ≤4, LDA: >4 but ≤13. [d]Nominal *P*-value.
APR, apremilast; BSA, body surface area; cDAPSA, clinical disease activity index for psoriatic arthritis; CI, confidence interval; HAQ-DI, health assessment questionnaire disability index; LDA, low disease activity; LEI, Leeds enthesitis index; MDA, Minimal Disease Activity; PASDAS (0–10), PsA Disease Activity Score; PBO, placebo; PsAID-12 (0–10), PsA Impact of Disease; PtGA, Pt Global Assessment of Disease activity (0–100 mm VAS); REM, remission; SJC, swollen joint count; TJC, tender joint count; VAS, visual analog scale.

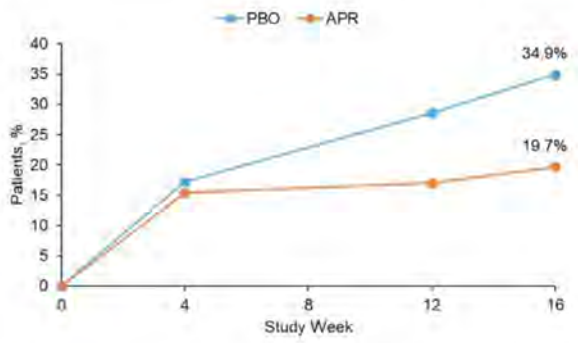
Table 2. Baseline Demographics and Clinical Characteristics by Baseline Joint Count

	SJC or TJC ≤4		SJC or TJC >4	
	PBO (n=92)	APR (n=176)	PBO (n=13)	APR (n=27)
Age, mean (SD), years	49.4 (12.6)	50.9 (12.2)	56.2 (14.9)	53.9 (12.7)
Male, n (%)	47 (51.1)	73 (41.5)	7 (53.8)	12 (44.4)
Race, white, n (%)	86 (93.5)	167 (94.9)	13 (100.0)	25 (92.6)
Duration of PsA, mean (SD), months	10.3 (11.2)	10.0 (10.3)	7.3 (4.9)	8.2 (7.9)
Prior use of csDMARDs, n (%)	62 (67.4)	120 (68.2)	7 (53.8)	15 (55.6)
SJC (0–66), mean (SD)	2.5 (0.6)	2.6 (0.7)	3.2 (0.8)	3.1 (0.8)
TJC (0–68), mean (SD)	3.1 (0.8)	3.2 (0.8)	3.8 (0.4)	3.6 (0.7)
BSA, mean (SD), %	6.0 (8.5)	7.5 (13.0)	8.9 (21.6)	3.1 (5.2)
Patient's Assessment of Pain (0–100 mm VAS), mean (SD)	49.6 (23.0)	52.5 (21.8)	61.4 (18.4)	50.9 (23.2)
PtGA (0–100 mm VAS), mean (SD)	49.4 (21.1)	51.2 (22.0)	58.2 (16.1)	54.3 (22.2)
HAQ-DI, mean (SD)	1.0 (0.7)	1.0 (0.6)	1.2 (0.5)	1.0 (0.6)
LEI[a], mean (SD)	2.4 (1.5)	2.4 (1.4)	3.4 (2.0)	2.5 (1.8)
cDAPSA, mean (SD)	15.5 (4.5)	16.2 (4.3)	19.0 (2.9)	17.2 (4.2)
PASDAS, mean (SD)	4.8 (1.1)	4.9 (1.1)	5.3 (0.7)	5.2 (1.2)

[a]In patients with pre-existing enthesopathy.
APR, apremilast; BSA, body surface area; cDAPSA, clinical disease activity index for psoriatic arthritis; HAQ-DI, health assessment questionnaire disability index; LEI, Leeds enthesitis index; PASDAS (0–10), PsA Disease Activity Score; PBO, placebo; PsAID-12 (0–10), PsA Impact of Disease; PtGA, Pt Global Assessment of Disease activity (0–100 mm VAS); SJC, swollen joint count; TJC, tender joint count; VAS, visual analog scale.

Methods: FOREMOST (NCT03747939) is a phase 4, multicenter, randomized, double-blind, placebo (PBO)-controlled, parallel-group study. Eligible pts had early disease (PsA duration ≤5 years) and limited joint involvement (>1 but ≤4 swollen and >1 but ≤4 tender joint count [SJC and TJC] of 66–68 joints assessed). Joints affected at baseline (BL) were defined as sentinel joints. Pts were randomized 2:1 to APR or PBO for 24 weeks, with an early escape at Week 16. The primary

Figure 1. Percentage of Patients Shifting From Baseline Joint Count ≤4 to Joint Count >4 Through Week 16



Percentages are calculated based on non-missing observed data at each timepoint. APR, apremilast; BL, baseline; PBO, placebo.

endpoint was the proportion of pts at Week 16 who achieved MDA-Joints (mandating SJC ≤1 and TJC ≤1 and 3/5 alternate items). Secondary endpoints assessed at Week 16 included the proportion of pts achieving Clinical Disease Activity in Psoriatic Arthritis (cDAPSA) remission (REM, ≤4) or low disease activity (LDA, >4 to ≤13), Patient's Global Assessment of Disease Activity (PtGA) ≤20, patient assessment of pain ≤15, Psoriatic Arthritis Disease Activity Score (PASDAS) good or moderate response, and change from BL in Psoriatic Arthritis Impact of Disease 12-item (PsAID-12). Exploratory analyses were performed for all joints and posthoc analyses were conducted in pts with 2–4 sentinel joints. The proportions of pts with SJC or TJC >4 over time were also assessed by pts with a BL joint count of 2–4.

Results: Of 308 pts randomized (APR: n=203; PBO: n=105), mean PsA duration was 9.9 (SD 10.2) months, mean age was 50.9 (SD 12.5) years, and 39.9% of pts were using a csDMARD. In the overall population, MDA-Joints response (primary endpoint, based on sentinel joints) was achieved by significantly more pts with APR (33.9%) vs PBO (16.0%) at Week 16 (P=0.0008) (**Table 1**). Additionally, significantly greater proportions of pts achieved secondary endpoints with APR vs PBO at Week 16 (**Table 1**). Clinical characteristics were similar between pts with ≤4 joints and >4 joints involved at BL (**-Table 2**). A total of 268 (87%) patients had ≤4 active joints at BL. In a post hoc analysis, similar MDA-Joints response rates were seen in pts with 2–4 joints (APR: 34.4%, PBO: 17.2%) vs the overall study population at Week 16. In pts with 2–4 joints involved at BL, there was an increase in the proportions of pts who switched to a joint count >4 through Week 16 among those receiving PBO but not among those receiving APR (**Figure 1**). No new safety signals were identified.

Conclusion: FOREMOST is the first global randomized controlled trial studying early oligoarticular PsA. In this study, better disease control is achievable with APR, with twice the MDA-Joint response compared with PBO at 16 weeks. A higher percentage of pts with BL joint count ≤4 shifted to a joint count of >4 with PBO vs APR.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, Gilead Sciences, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, Bristol Myers Squibb, 2, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead Sciences, 2, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake, 2, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **J. Aelion**: AbbVie, 5, 6, Acceleron, 5, Acelyrin, 5, Aclaris Therapeutics, 5, Alpine Immune Sciences, 5, Amgen, 2, 5, AstraZeneca, 5, Biogen, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 5, Galapagos, 5, GlaxoSmithKline, 5, Horizon, 5, Janssen, 2, 5, Novartis, 2, 5, Roche, 5, Selecta, 5, UCB, 5, Ventyx, 5; **J. Vasandani**: None; **A. Kavanaugh**: AbbVie, 1, 2, Amgen, 1, 2, BMS, 1, 2, Eli Lilly, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, UCB, 1, 2; **J. Merola**: AbbVie, 12, Consultant and/or investigator, Amgen, 2, Biogen, 12, Consultant and/or investigator, Bristol Myers Squibb, 2, Dermavant, 12, Consultant and/or investigator, Eli Lilly, 12, Consultant and/or investigator, Janssen, 12, Consultant and/or investigator, LEO Pharma, 12, Consultant and/or investigator, Novartis, 12, Consultant and/or investigator, Pfizer, 12, Consultant and/or investigator, Regeneron, 12, Consultant and/or investigator, Sanofi, 12, Consultant and/or investigator, Sun Pharmaceuticals, 12, Consultant and/or investigator, UCB Pharma, 12, Consultant and/or investigator; **J. Reddy**: Amgen, 3, 11; **R. Wang**: Amgen Inc., 3, 8; **M. Brunori**: Amgen Inc., 3, 11; **S. Colgan**: Amgen, 3, 11; **L. Gossec**: AbbVie, 2, 12, Personal fees, Amgen, 2, Biogen, 5, BMS, 12, Personal fees, Celltrion, 12, Personal fees, Eli Lilly, 5, 12, Personal fees, Galapagos, 12, Personal fees, Janssen, 12, Personal fees, MSD, 12, Personal fees, Novartis, 5, 12, Personal fees, Pfizer, 12, Personal fees, Sandoz, 5, 12, Personal fees, UCB Pharma, 5, 12, Personal fees.

Abstract Number: 1692

Insights on the Use of JAK-inhibitors in Patients with Psoriatic Arthritis in an International Collaboration of Registers (the "JAK-pot" Study)

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment II: PsA

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: JAK-inhibitors (JAKi) are increasingly being prescribed to treat various inflammatory conditions, including psoriatic arthritis (PsA). While the understanding of JAKi efficacy and safety in rheumatoid arthritis is progressing, it remains less developed for PsA. The purpose of this study was to evaluate the profile of PsA patients to whom JAKi are prescribed, in a large multi-country real-world collaboration (JAK-pot).

Methods: Patients with a diagnosis of PsA, treated with either JAKi, TNF-inhibitors (TNFi) or bDMARDs with other modes of action (OMA) were included from 10 registers in which JAKi were prescribed for PsA. Treatment-courses were included only since JAKi became available in each country. We used standard descriptive statistics to evaluate patient-, disease-, and treatment characteristics across treatment groups, and across registers for JAKi only. We plotted crude retention rates for each treatment group.

Results: Among the 11,939 treatment courses considered (Table 1), 582 were JAKi, mainly tofacitinib (67%) and upadacitinib (27%), and to a lesser extent baricitinib (6%). Patients initiating JAKi tended to have more difficult to treat disease, defined as longer disease duration (> 9 years), older age, more prior bDMARD experience (52% with 3 or more previous bDMARDs), and more concomitant glucocorticoids. JAKi patient characteristics were consistent across countries (Table 2), despite varying use of specific JAKi agents, tofacitinib use ranging from 36 to 100% and upadacitinib from 0 to 64%. Crude drug retention at 1 year was 65% for JAKi was (Figure 1), which was significantly lower than for OMA (74%) and TNFi (77%).

Table1: Baseline characteristics across treatment groups

	JAKi n = 582	OMA n = 4,383	TNFi n = 6,974
Treatment duration (median [IQR])	0.8 [0.3, 1.7]	1.3 [0.5, 2.7]	1.4 [0.5, 3.0]
Age (mean (SD))	53.8 (11.1)	53.5 (11.7)	51.1 (12.5)
Female (%)	375 (64.4)	2515 (57.4)	3971 (56.9)
Disease duration (median [IQR])	9.6 [4.9, 16.4]	8.2 [3.6, 15.0]	6.6 [2.7, 13.0]
Previous b/tsDMARD (%)			
0	90 (15.6)	1006 (23.3)	2932 (42.7)
1	90 (15.6)	1298 (30.1)	1973 (28.7)
2	95 (16.5)	777 (18.0)	1104 (16.1)
3 or more	302 (52.3)	1230 (28.5)	855 (12.5)
Concomitant csDMARD (%)			
MTX	99 (17.0)	717 (16.4)	1303 (18.7)
MTX + other	41 (7.0)	252 (5.7)	736 (10.6)
none	373 (64.1)	3054 (69.7)	4261 (61.1)
other	69 (11.9)	360 (8.2)	674 (9.7)
Glucorticoids (%)	199 (36.2)	950 (22.6)	1461 (21.7)
CRP (mean (SD))	11.5 (21.1)	10.0 (27.8)	10.0 (27.5)
CDAI (mean (SD))	22.1 (11.9)	16.5 (10.0)	16.0 (10.4)
DAS28 (mean (SD))	4.3 (1.5)	3.9 (1.4)	3.7 (1.4)
HAQ (mean (SD))	1.1 (0.7)	0.9 (0.7)	0.8 (0.7)
DAPSA28 (mean (SD))	31.2 (18.2)	23.1 (14.6)	22.4 (15.2)
cDAPSA28 (mean (SD))	30.2 (17.5)	22.1 (14.2)	21.4 (14.6)

JAKi: JAK-inhibitor, MTX: methotrexate, OMA: biologics with other mode of action, TNF: TNF-inhibitor

Table 2: Baseline characteristics for JAK inhibitors across countries

	AU n = 49	CA n = 58	CZ n = 11	FI n = 73	IT n = 99	PT n = 70	RO n = 5	SI n = 41	SP n = 166	TR n = 6
Generic name (%)										
baricitinib	5 (10.2)	2 (3.4)	0 (0.0)	4 (5.5)	14 (14.1)	0 (0.0)	0 (0.0)	1 (2.4)	6 (3.6)	0 (0.0)
tofacitinib	18 (36.7)	33 (56.9)	4 (36.4)	69 (94.5)	38 (38.4)	65 (92.9)	5 (100.0)	32 (78.0)	117 (70.5)	6 (100.0)
upadacitinib	26 (53.1)	23 (39.7)	7 (63.6)	0 (0.0)	47 (47.5)	5 (7.1)	0 (0.0)	8 (19.5)	43 (25.9)	0 (0.0)
Treatment duration (median [IQR])	0.8 [0.4, 1.5]	1.0 [0.4, 1.4]	0.3 [0.3, 0.9]	2.6 [0.6, 3.8]	0.3 [0.1, 0.5]	1.0 [0.5, 1.5]	1.1 [0.5, 1.3]	1.4 [0.5, 2.7]	0.9 [0.4, 1.5]	0.3 [0.0, 1.3]
Age (mean (SD))	57.7 (9.5)	54.2 (11.1)	52.5 (11.2)	53.4 (12.5)	54.7 (11.8)	51.8 (11.7)	49.2 (11.7)	54.6 (12.1)	52.8 (9.9)	50.4 (8.5)
Female (%)	24 (49.0)	35 (60.3)	3 (27.3)	44 (60.3)	69 (69.7)	43 (61.4)	2 (40.0)	26 (63.4)	120 (72.3)	5 (83.3)
Disease duration (median [IQR])	12.8 [6.9, 20.5]	9.1 [4.5, 14.1]	23.5 [11.7, 27.2]	9.1 [5.0, 22.5]	9.3 [5.2, 14.8]	12.9 [6.7, 16.3]	9.3 [3.1, 19.2]	9.4 [3.6, 16.4]	7.7 [4.3, 14.8]	13.2 [10.3, 14.0]
Previous b/tsDMARD (%)										
0	0 (0.0)	8 (13.8)	0 (0.0)	16 (21.9)	10 (10.6)	25 (35.7)	3 (60.0)	1 (2.4)	26 (15.7)	1 (16.7)
1	10 (20.4)	9 (15.5)	1 (9.1)	10 (13.7)	13 (13.8)	13 (18.6)	0 (0.0)	9 (22.0)	24 (14.5)	1 (16.7)
2	5 (10.2)	9 (15.5)	5 (45.5)	14 (19.2)	12 (12.8)	10 (14.3)	1 (20.0)	12 (29.3)	25 (15.1)	1 (16.7)
3 or more	34 (69.4)	32 (55.2)	5 (45.5)	33 (45.2)	59 (62.8)	22 (31.4)	1 (20.0)	19 (46.3)	91 (54.8)	3 (50.0)
Concomitant csDMARD (%)										
MTX	7 (14.3)	9 (15.5)	5 (45.5)	23 (31.5)	1 (1.0)	0 (0.0)	1 (20.0)	9 (22.0)	43 (25.9)	1 (16.7)
MTX + other	0 (0.0)	4 (6.9)	1 (9.1)	9 (12.3)	0 (0.0)	25 (35.7)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)
none	42 (85.7)	39 (67.2)	4 (36.4)	28 (38.4)	96 (97.0)	38 (54.3)	4 (80.0)	27 (65.9)	88 (53.0)	4 (66.7)
other	0 (0.0)	6 (10.3)	1 (9.1)	13 (17.8)	2 (2.0)	7 (10.0)	0 (0.0)	5 (12.2)	33 (19.9)	1 (16.7)
Glucocorticoids (%)	9 (31.0)	10 (19.2)	5 (50.0)	24 (33.3)	39 (39.4)	28 (40.6)	0 (0.0)	4 (9.8)	79 (47.6)	0 (0.0)
CRP (mean (SD))	8.0 (13.2)	4.0 (NA)	10.2 (12.9)	12.7 (21.2)	10.1 (22.5)	11.0 (16.2)	9.8 (9.5)	21.1 (38.6)	10.2 (15.8)	5.8 (8.0)
CDAI (mean (SD))	NaN (NA)	27.5 (16.6)	28.3 (17.6)	19.2 (9.5)	20.2 (10.9)	24.4 (11.1)	16.0 (NA)	23.4 (12.9)	NaN (NA)	NaN (NA)
DAS28 (mean (SD))	NaN (NA)	NaN (NA)	4.6 (1.7)	4.2 (1.2)	4.2 (1.4)	4.7 (1.5)	3.3 (NA)	4.9 (1.6)	4.1 (1.6)	2.6 (1.7)
HAQ (mean (SD))	0.8 (0.6)	1.0 (0.5)	1.3 (0.6)	1.2 (0.7)	1.1 (0.6)	1.1 (0.6)	NaN (NA)	1.1 (0.8)	NaN (NA)	0.5 (0.4)
DAPSA28 (mean (SD))	NaN (NA)	NaN (NA)	40.5 (25.4)	28.2 (13.9)	27.3 (15.8)	33.3 (18.3)	16.3 (NA)	36.9 (20.9)	NaN (NA)	NaN (NA)
cDAPSA28 (mean (SD))	NaN (NA)	35.7 (20.6)	39.4 (25.7)	26.6 (13.8)	26.5 (15.3)	32.7 (17.2)	16.0 (NA)	34.7 (19.5)	NaN (NA)	NaN (NA)

AU : Austria, CA : Canada, CZ : Czech Republic, FI : Finland, IT : Italy, PT : Portugal, RO : Romania, SI : Slovenia, SP : Spain, TR : Turkey

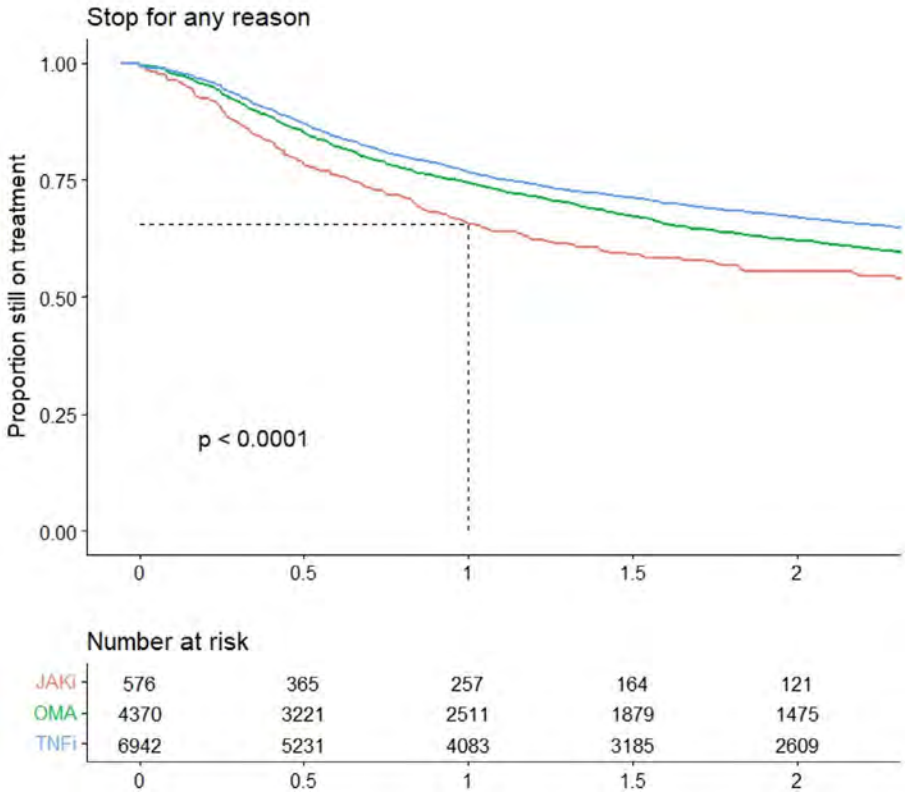

Figure 1: Crude drug retention rates

Conclusion: Unadjusted drug retention rates for second line therapies in PsA patients suggest lower drug maintenance of JAKi compared to OMA and TNFi. However, it is likely that these results are largely driven by the severity of the disease of patients on JAKi compared to patients on other treatments. Adjusted analyses are needed when evaluating the real-life effectiveness and safety of JAKi for PsA patients.

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Abstract Number: 1693

Blood Immunophenotyping Distinguishes Three Subgroups of Lupus Nephritis Patients with Distinct Kidney Infiltrates and Interferon Signatures

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes II: Omics

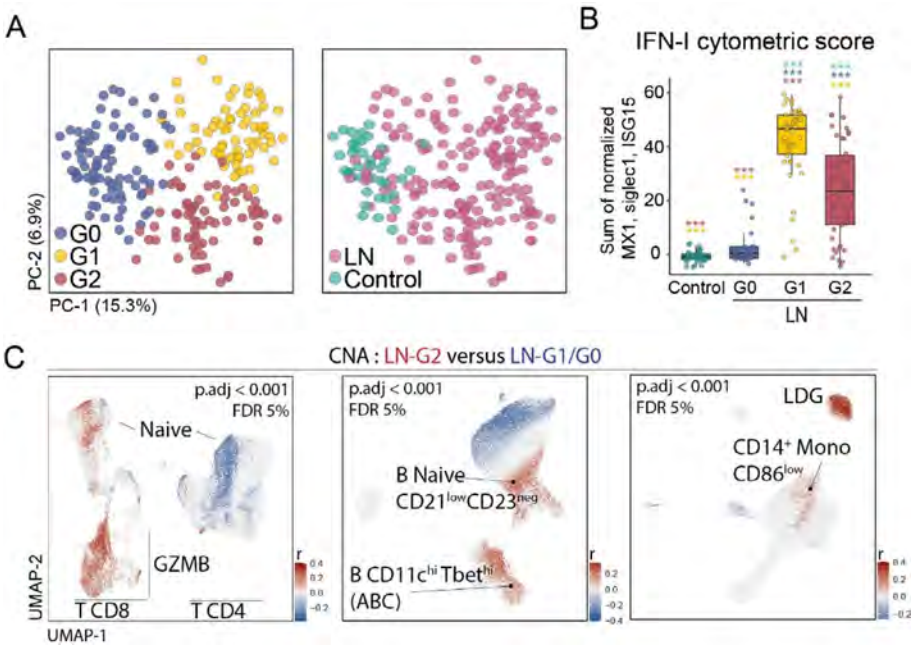
Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

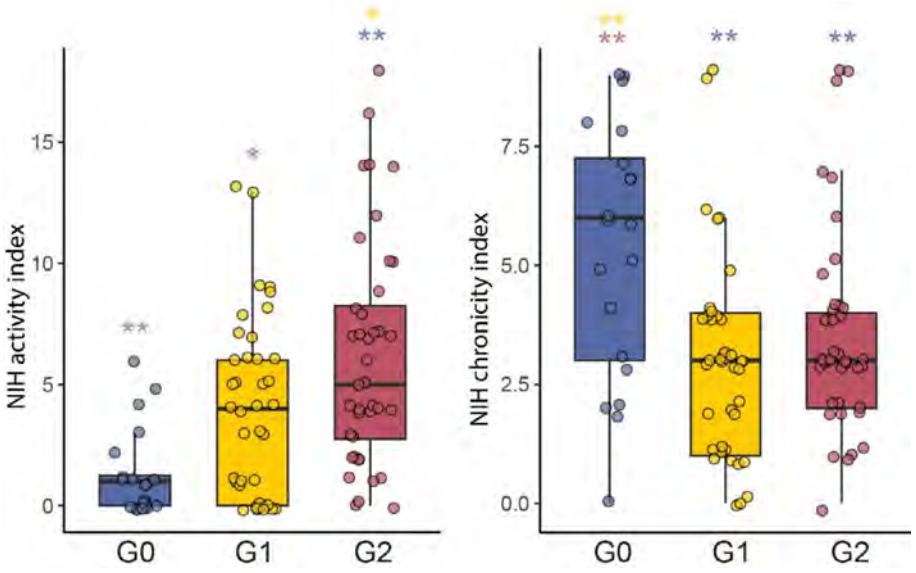
Background/Purpose: Patients with lupus nephritis (LN) have variable responses to standard-of-care therapy, and a third of patients with class III, IV, or V show a progressive decline in kidney function. Identifying distinct inflammatory processes associated with LN using non-invasive tools may improve treatment targeting. Here, we aimed to identify subgroups of LN patients that differ in systemic immune activity and to evaluate their relationship to kidney pathology.

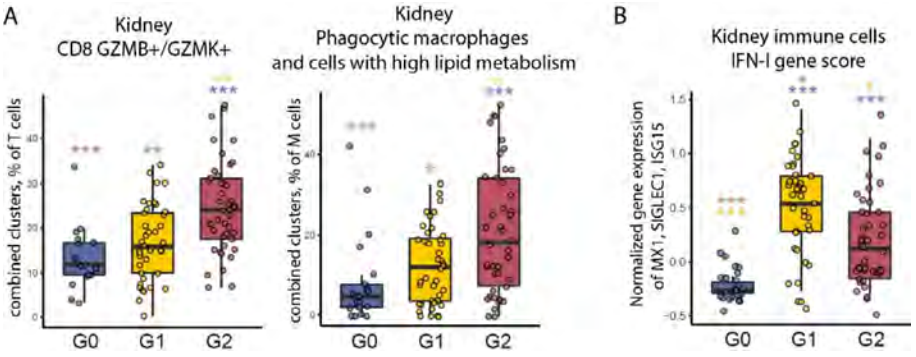
Methods: Mass cytometry using four 48-marker panels was applied to characterize peripheral blood mononuclear cells from 140 patients with active, biopsy-proven proliferative (class III or IV +/- V, n=98) or membranous (class V, n=42) nephritis and 40 healthy controls in the Accelerated Medicine Partnership RA/SLE Network Phase II study. K-means clustering was used to stratify patients based on the proportions of 55 immune cell subsets defined using B cell-, T cell-, myeloid cell-, and NK cell-focused panels.

Results: Unsupervised analysis of all samples identified 3 patient subgroups based on blood immunophenotypes (Figure 1A). The first group (G0) included all controls and 20% LN patients; the two others (G1, G2) included only LN patients. A cytometric IFN-I score, based on MX1, siglec1 and ISG15 expression, was significantly different between the three groups; G0-LN patients had comparable scores to controls and G1 displayed the highest values (Figure 1B). G2 membership was driven by an increased proportion of $GZMB^{+}$ $GZMK^{+/-}$ CD8 T cells, plus increased $CD86^{dim}$ monocytes and



activated B cells including CD11c^{hi} cells (Figure 1C). G2 was associated with higher histologic activity scores, whereas G0 had higher chronicity scores, even after controlling for race, corticoid dose, immunosuppressant use, and previous history of renal biopsy (Figure 2). Complete renal response (CR), determined at 1 year in patients with baseline urine protein-creatinine ratio $\geq$ 1, was more frequent in G2 than in G0/G1 LN patients, independently of history of previous renal biopsy (CR in G2 = 15 [41%] vs others = 9 [18%]; OR [95%CI] = 3.9 [1.3,12.5]; p.adj = 0.02). Finally, we asked whether the composition of immune cell infiltrates in the kidney, evaluated by scRNA-seq of kidney biopsies, differed between the 3 blood-defined subgroups. G2 patients had kidney T cell infiltrates enriched in GZMB^{+}/GZMK^{+} CD8 T cell subsets and in myeloid cells with an activated and phagocytic profile compared to G0/G1 patients. In contrast, G1 patients showed the highest expression of IFN-I gene signature across the groups, consistent with the pattern seen in blood (Figure 3).





Conclusion: Blood immunophenotyping identified 3 groups of LN patients with different patterns of immune cell infiltration and likelihood of response to treatment. Cytometric profiles distinguished patients with a signature involving activated CD8 T cells, CD11c^{hi} B cells and activated myeloid cells (G2) from those with the highest IFN scores (G1). Patients with increased blood and kidney CD8 GZMB^{+}GZMK$^{+/-}$ cells (G2) had increased renal activity scores at baseline and a higher likelihood of response at 1 year.

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Abstract Number: 1694

Transcriptomic Analysis of the Impact of Iberdomide on Patients with SLE

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SESSION INFORMATION
Session Date: Monday, November 13, 2023
Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes II: Omics
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Iberdomide is a high affinity cereblon ligand that promotes ubiquitylation and proteasomal degradation of Ikaros (IKZF1) and Aiolos (IKZF3) transcription factors and, thereby altering specific aspects of immune responsiveness. Iberdomide has been shown to be efficacious in a randomized controlled trial in patients with generalized SLE (NCT03161483) and to be specifically effective in patients with high baseline expression of the interferon gene signature (IGS)[1,2]. The current analysis sought to identify the profile of gene expression abnormalities in SLE patients responsive to iberdomide and the impact of the agent on gene expression abnormalities.

Methods: Baseline whole blood samples from 276 female SLE patients from the phase 2b iberdomide trial were utilized for this analysis. These patients had a >/= 6 month history of SLE and disease activity determined by SLEDAI-2K >/=6. Patients were randomized to placebo, or one of three doses of iberdomide (0.15, 0.3 or 0.45 mg once daily). Clinical response was determined by the SLE Responder Index 4 (SRI-4) at 24 weeks. RNAseq was performed and analyzed by Gene Set Variation Analysis (GSVA) using 32 informative gene modules and K-means clustering.

Results: Whole blood K-means clustering of the GSVA scores yielded 5 subsets of patients (Figure 1). Subset A had the fewest molecular abnormalities, whereas Subset E had the most disturbances in immune function, including enrichments in the IGS, immunoproteasome, IL-1/ inflammasome pathway, and neutrophil/granulocyte genes and lymphopenia. Clusters B-D had intermediate degrees of abnormal enrichment in specific gene modules. Cluster C had high IGS, immunoproteasome, plasma cells/Ig chains, and IL-23 complex genes, but no lymphopenia. No differences were noted between the

Figure1: KMeans clustering of GSVA scores from baseline gene expression profiles effectively identifies 5 subsets of SLE patients.

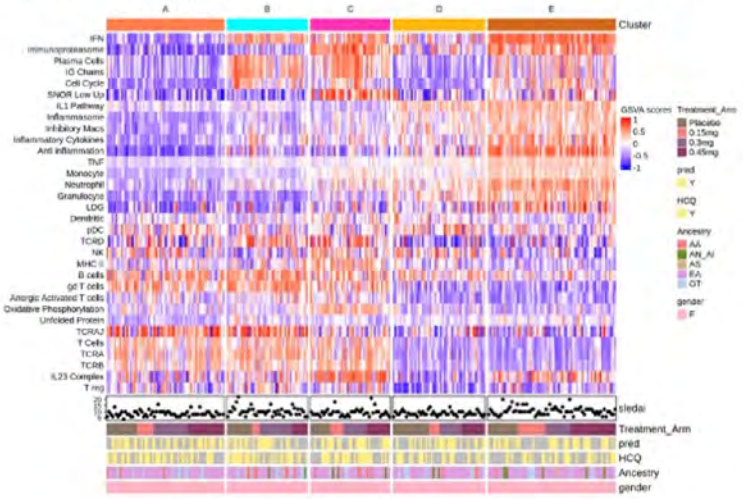
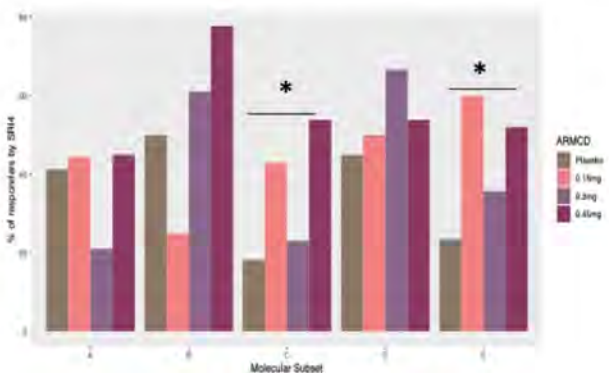


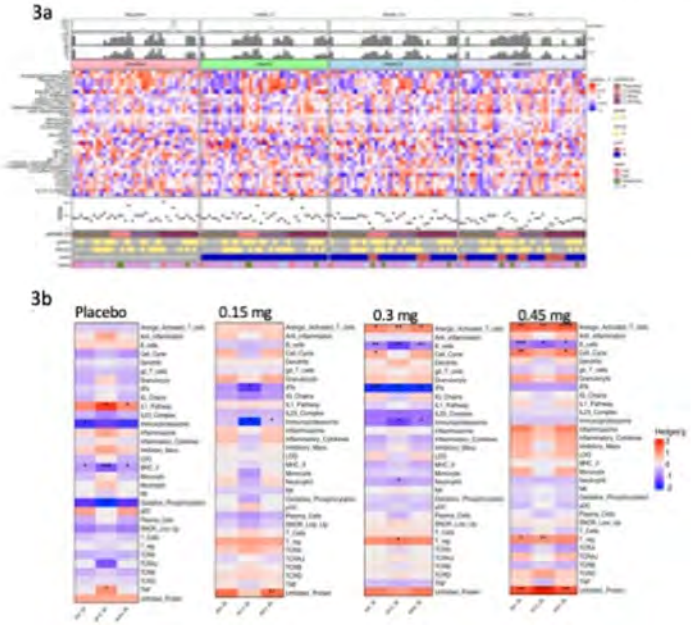
Figure 2. Clinical responses of patients in subsets defined by gene expression profiles. Responses to Iberdomide are significantly different from those to placebo in subsets C and E (p=0.002, Fishers Exact test).



subsets with regard to steroid or hydroxychloroquine use, and differed only modestly in disease activity as measured by SLEDAI-2K, anti-DNA and Compelemnt C3and C4. Significant clinical responses to iberdomide were confined to subsets C and E (Figure 2). Effect sizes of responses in these groups ranged between 20-30%. Other subsets had higher placebo responses and no additional response to iberdomide. Treatment with iberdomide resulted in significant decreases in the B cell, plasma cell and interferon signatures and increases in the Treg signature (Figure 3).

Conclusion: K-means clustering of GSVA scores from baseline samples of the iberdomide trial successfully clustered patients into subsets that exhibited differences in response to iberdomide treatment, with the greatest responses observed in patients with the highest IGS, immunoproteasome, plasma cell, inflammasome, and IL-23 pathways. Treatment with iberdomide altered gene expression profiles in a manner consistent with the known action of the agent. Gene expression based subsetting may be useful to enrich trials for responsive patients and monitor the impact of therapy.

Figure3. Longitudinal analysis of lupus samples in subset C reveals significant decrease in IFN, B cells, Immunoproteasome and an increase in T reg and Unfolded Protein Response signatures. 3a) GSVA scores of lupus samples from subset C across baseline, week4, week12, and week24 were visualized using ComplexHeatmap in R.3b) Hedges' g effect sizes of process and cellular gene modules for week4, week12, and week24 compared to baseline in patients treated with Placebo, and three doses of Iberdomide were calculated. The heatmap visualizes the increased gene expression (> 0) in red and decreased gene expression (< 0) in blue. Welch's t-test p values are referred by * p < 0.05, ** p < 0.01, *** p < 0.001, **** p < 0.0001



Disclosure: P. Bachali: None; **S. Korish**: BMS, 3; **Y. Hu**: BMS, 3, 12, BMS stock holder; **P. Schafer**: Bristol Myers Squibb, 3, 10, 11; **A. Grammer**: None; **P. Lipsky**: None.

Abstract Number: 1695

Single Cell Transcriptomics in Kidney Tissue from African American Patients Enrolled in the Accelerating Medicines Partnership (AMP) Implicates Tubular Cells in the Pathogenesis of APOL1 Associated Lupus Nephritis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes II: Omics

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: The G1 and G2 risk variants (RVs) in Apolipoprotein L1 (APOL1) associate with CKD and may contribute to poorer outcomes for African American (AA) patients with lupus nephritis (LN). While the pathogenetic mechanism for APOL1 related CKD remains unknown, most studies focus on glomerular injury. This study leveraged the multi-center LN AMP to evaluate APOL1 RV associated clinical phenotypes and identify whether these genetic variants influence the transcriptomic landscape in kidney cells.

Methods: LN patients were consecutively enrolled in AMP at the time of a clinically indicated renal biopsy and followed for one year. Dissociated biopsies were passed through a droplet-based single-cell RNA sequencing (scRNAseq) pipeline that included quality control of sequenced libraries. Genotypes for APOL1 RVs were identified by sanger sequencing for all AA patients enrolled with available DNA.

Results: In total, 104 AA patients were genotyped; 47 (45.2%) carried zero APOL1 RVs, 45 (43.3%) one RV, and 12 (11.5%) two RVs. RVs did not associate with baseline anti-dsDNA or complement levels, biopsy class/activity/chronicity, GFR or proteinuria (Fig. 1A-G). While there was a trend toward decreased GFR at one year by gene variant dosage, there was no association with changes in proteinuria (Fig. 1F-H). ScRNAseq yielded 88383 high quality cells in patients with zero RVs (n=30), 72288 one RV (n=28), and 28694 two RVs (n=11) spanning nine parenchymal cluster types (Fig. 2A). Independent of

genotype, APOL1 expression was highest in podocyte, endothelial and ascending thin limb (ATL) cells (Fig. 2B). Median APOL1 expression was significantly higher in cells with one or two RVs in the ATL cluster but this association was not seen in podocytes or endothelial cells (Fig. 2C). Single cell pathway analysis revealed that the ATL cluster demonstrated greater pathway level variation between cells with two RVs vs zero than any other cluster, with the most distinguishing related to interferon signaling (increased), antigen presentation (increased), and mitochondrial function (decreased) (Fig. 2D). The ATL damage associated gene, lipocalin-2 (LCN2), was expressed at significantly higher levels in cells carrying two RVs (Fig. 2E). Likewise, the proportion of ATL cells double positive for APOL1 and LCN2 was higher in patients with two RVs (Fig. 2F). While it did not reach significance, the percentage of ATL cells expressing APOL1 more strongly correlated with eGFR and tubular atrophy on biopsy histology among patients with two RVs compared to those carrying zero or one RV (Fig. 3A-F).

A

Genetic Risk	Lupus Nephritis N (%)
G1/G2 Risk Variant Number	
0	47 (45.2)
1	45 (43.3)
2	12 (11.5)
APOL1 Genotype	
G0G0	47 (45.2)
G0G1	30 (28.8)
G0G2	15 (14.4)
G1G1	1 (0.96)
G1G2	10 (9.6)
G2G2	1 (0.96)

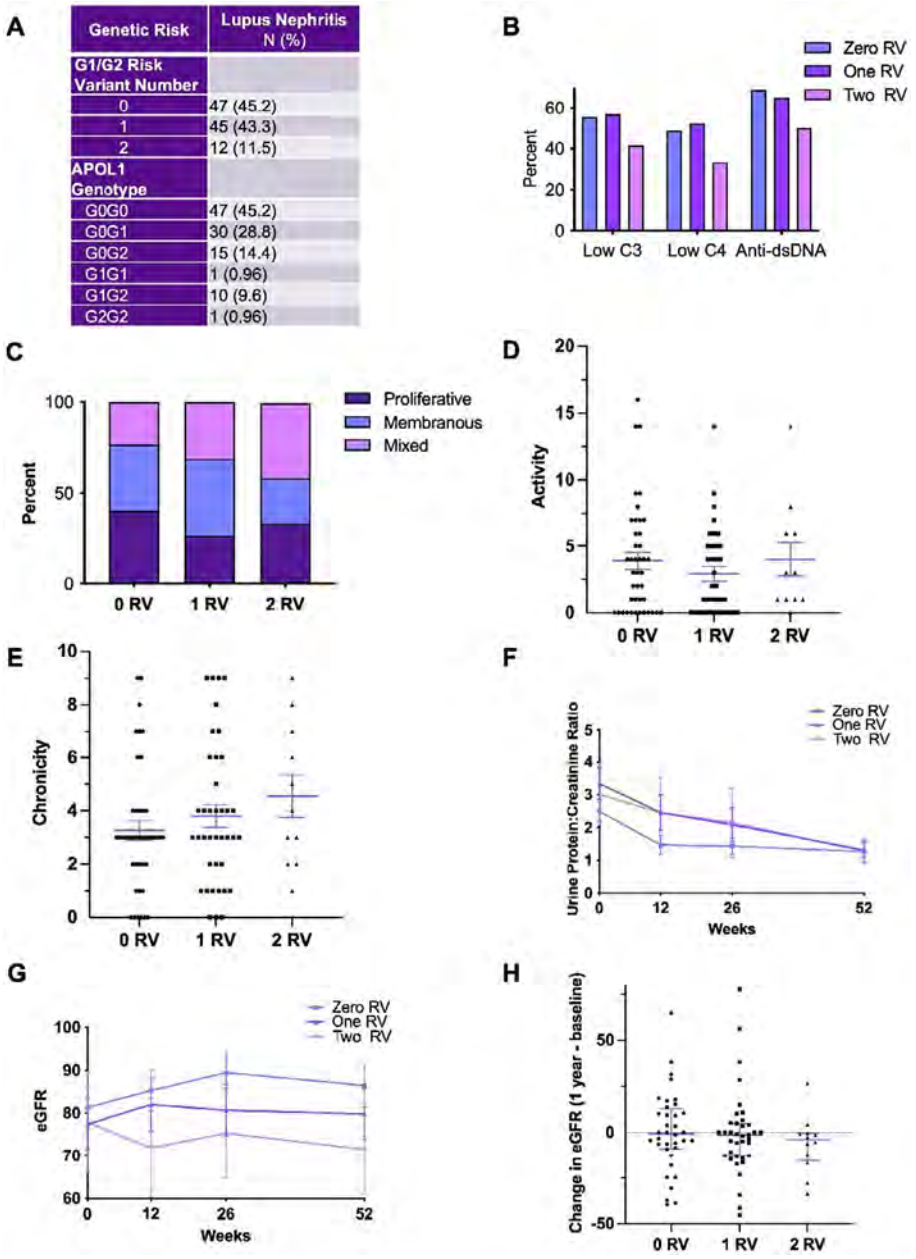
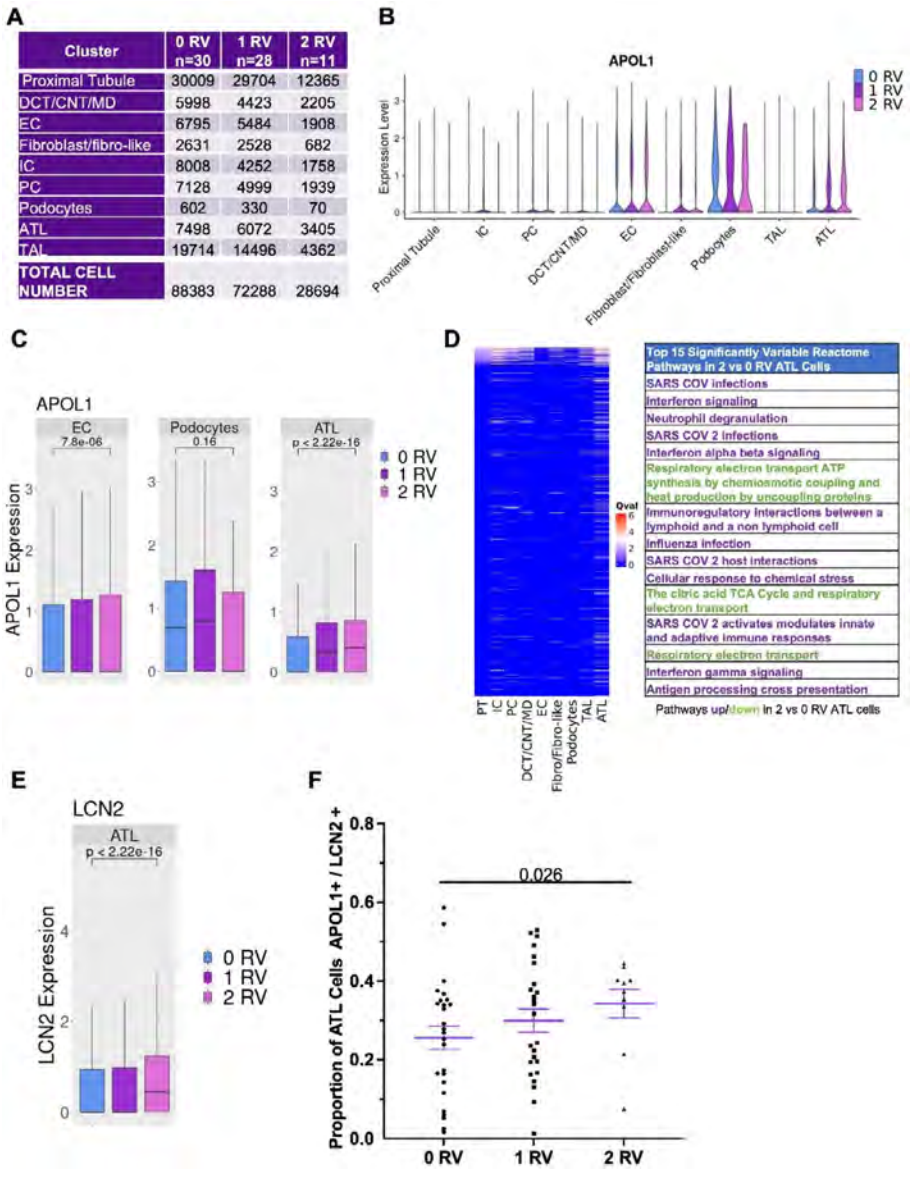


Figure 1: (A) Frequency of patients with zero, one, or two APOL1 risk variants and APOL1 genotypes. (B) Percent of patients with low C3, low C4, and positive anti-dsDNA by RV number. (C) Stacked barplot showing percent of patients with proliferative, membranous, or mixed biopsy class by RV number. (D) NIH biopsy activity index by RV number. (E) NIH biopsy chronicity index by RV number. (F) Urine protein:creatinine ratio by RV number at 0, 12, 26, and 52 weeks. (G) Estimated glomerular filtration rate (eGFR) by RV number at 0, 12, 26 and 52 weeks. (H) Change in eGFR (1 year -baseline) by RV number.

Conclusion: APOL1 RVs associated with decreased GFR but not proteinuria suggesting that current clinical indicators of LN severity may not appropriately prognosticate patients carrying APOL1 RVs and that the use of routine genotyping in the clinical setting may better risk stratify AA patients with LN. The scRNAseq data revealed that ATL cells likely express APOL1 and that this may be relevant to progressive kidney dysfunction over time. This highlights the potential for a previously unrecognized extraglomerular injury in AA SLE patients carrying APOL1 RVs providing a novel future direction for understanding APOL1 toxicity and translation to clinical trials.



Cluster	0 RV n=30	1 RV n=28	2 RV n=11
Proximal Tubule	30009	29704	12365
DCT/CNT/MD	5998	4423	2205
EC	6795	5484	1908
Fibroblast/fibro-like	2631	2528	682
IC	8008	4252	1758
PC	7128	4999	1939
Podocytes	602	330	70
ATL	7498	6072	3405
TAL	19714	14496	4362
TOTAL CELL NUMBER	88383	72288	28694

Figure 2: (A) Total number of single cells in each identified cluster type included in analyses by RV number. (B) Violin plot showing log normalized expression of APOL1 in each cluster by RV number. (C) Boxplot showing APOL1 log normalized expression in endothelial cells (EC), podocytes, and ascending thin limb (ATL) cells by RV number. P-values compare 0 vs 2 RV using Wilcoxon rank-sum test. (D) Heatmap with rows representing q-values (measure of variability) for each Reactome pathway resulting from differential pathway expression using Single Cell Pathway Analysis (Biby et al. Cell Reports, 2022) comparing cells with 2 vs 0 RVs within each cluster type. The table displays the top 15 significantly different pathways within ATL cluster between cells with 2 vs 0 RVs(pathways in purple are up in 2RV and pathways in green are down in 2RV). (E) Boxplot showing log normalized LCN2 expression in ATL cells by RV number. P-value compares 0 vs 2 RV using Wilcoxon rank-sum test. (F) Proportion of ATL cells that were double positive for APOL1 and LCN2 (log normalized expression greater than 0 for both genes) by RV number; patients with less than 20 total ATL cells were excluded. P-value compares 0 vs 2 RV using student's two-tailed t-test. Abbreviations: DCT/CNT/MD: distal convoluted tubule, connecting tubule, macula densa. EC: endothelial cell. IC: intercalated cell. PC: principal cell. ATL: ascending thin limb. TAL: thick ascending limb.

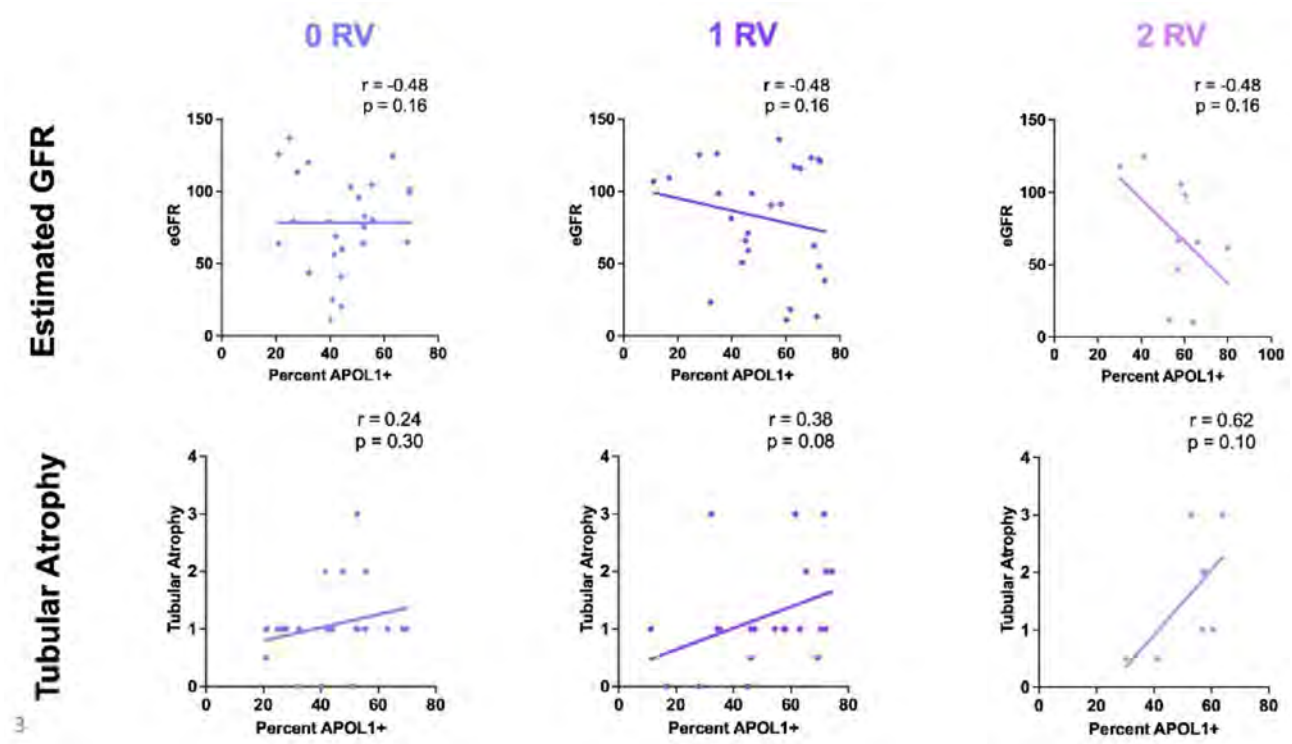


Figure 3: (A-C) Pearson correlation between percent of ATL cells positive for APOL1 (log normalized expression greater than 0) and baseline estimated glomerular filtration rate (eGFR) among patients with 0 (A), 1 (B), or 2 (C) RVs. (D-F) Pearson correlation between percent of ATL cells positive for APOL1 (log normalized expression greater than 0) and tubular atrophy on biopsy histology among patients with 0 (D), 1 (E), or 2 (F) RVs. Patients with less than 20 total ATL cells were excluded.

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Abstract Number: 1696

Multi-Omic Profiling Reveals Immune Cell Priming Signature Linked to Systemic Lupus Erythematosus Prognosis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes II: Omics

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Much of our understanding of systemic lupus erythematosus (SLE) immunopathogenesis is derived from gene profiling studies, where core pathways such as neutrophil dysregulation and uncontrolled type I interferon (IFN) production by plasmacytoid dendritic cells (pDCs) have been identified. However, gene signatures found in whole blood may not reflect those in the tissues, thus potentially overlooking key drivers of disease activity and pathogenesis. While gene expression is commonly used as a proxy for protein abundance, significant discordance can exist between transcript and protein levels. We hypothesized that multidimensional blood profiling could identify new biology and reveal key molecular signatures that underlie distinct SLE pathologies.

Methods: Whole blood samples from 87 patients with mild to moderate SLE and 48 matched healthy controls were analyzed (discovery cohort). To ensure robustness of data, samples from an independent cohort of 43 patients and 52 healthy cohorts were also analyzed (validation cohort). All samples and data were collected after obtaining informed consent. Whole blood gene expression, serum proteins, autoantibodies, and immune cell assessments were collected with longitudinal clinical data. Statistical analyses were carried out in R v. 3.5.1. All data were made available in an interactive SLE Immune Atlas.

Results: We identified three protein signatures relating to interferon (IFN) signaling, granulocyte activation, and immune cell priming (IAI, GRN, and ICP) that significantly associated with disease status and unique organ-specific manifestations in SLE patients. Type I IFN activity (21-IFNGS) was present in 69.0% of patients, the IAI, GRN, and ICP signatures were present in 52.9%, 35.6%, and 42.5% of patients, respectively. While the IAI and GRN signatures correlated with transcripts, no strong gene correlates of the ICP signature were found. The ICP signature featured proteins associated with antigen presenting cells and kidney injury and correlated with proteinuria ($p=1.1E^{-3}$), decreased GFR (p=5.0E–7), and active nephritis (p=0.044). The ICP signature was predictive of damage accrual as measured by the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) over a 6-year follow-up (RR= 1.92, 95% CI 1.41–2.67). The ICP-positive patients were more likely to exhibit worsening in the renal, pulmonary, ocular and skin domains of SDI.

Conclusion: Our analyses identified a previously uncharacterized ICP protein signature enriched in patients with renal involvement, predictive of disease worsening and organ damage over time. Prospective studies would be useful to confirm the ability of the ICP signature to identify patients in need of therapeutic intervention to prevent increased risk for damage accrual.

Disclosure: M. Smith: AstraZeneca, 3, 11, Horizon Therapeutics, 3, 11; **D. Sinibaldi**: AstraZeneca, 3, Neuraly, 3; **S. Rahman**: Sanofi, 3; **C. Chiang**: AstraZeneca, 3; **A. Hansen**: AstraZeneca, 3; **J. Henault**: None; **C. Roca**: AstraZeneca, 3, CSL Behring, 3; **S. Wang**: Horizon Therapeutics, 3; **K. Zerrouki**: None; **R. Filippi**: AstraZeneca, 3; **C. Groves**: Q Squared Solutions, 3; **Z. Manna**: None; **J. Chu**: None; **M. Davis**: None; **s. gupta**: None; **C. Morehouse**: None; **M. De los Reyes**: AstraZeneca, 11; **R. Ettinger**: AstraZeneca, 3, 11, Horizon Therapeutics, 3, 11, VielaBio, 3, 11; **R. Kolbeck**: None; **M. Kaplan**: AstraZeneca, 5, Bristol Myers Squibb, 5, Cytrill, 2, Neutrolis, 2; **M. Sanjuan**: AstraZeneca, 3; **R. Siegel**: Novartis, 3, 11; **s. Hasni**: AstraZeneca, 5; **K. Casey**: AstraZeneca, 3, 11, Regeneron, 3, 11.

Abstract Number: 1697

Molecular Characterisation of Remission and Lupus Low Disease Activity State (LLDAS) by Whole-Blood Transcriptome-Based Pathways in a Pan-European Systemic Lupus Erythematosus Cohort

Ioannis Parodis[1], Julius Lindblom[1], Guillermo Barturen[2], Rafaela Ortega Castro[3], Ricard Cervera[4], Jacques-Olivier Pers[5], Fernanda Genre Romero[6], Falk Hiepe[7], Maria Gerosa[8], Laszlo Kovacs[9], Ellen De Langhe[10], Silvia Piantoni[11], Georg Stummvoll[12], Carlos Vasconcelos[13], Barbara Vigone[14], Torsten Witte[15], Marta Alarcon-Riquelme[16] and Lorenzo Beretta[17], [1]Karolinska Institutet, Stockholm, Sweden, [2]Center for Genomics and Oncological Research (GENYO), Andalusia, Spain, [3]Hospital Reina Sofía, Cordoba, Spain, [4]Hospital Clínic de Barcelona, Barcelona, Spain, [5]Centre Hospitalier Universitaire de Brest, Hospital de la Cavale Blanche, Brest, France, [6]IDIVAL, Santander, Spain, [7]Charité Universitatsmedizine - Berlin, Berlin, Germany, [8]University of Milan, Milano, Italy, [9]University of Szeged, Szeged, Hungary, [10]Katholieke Universiteit Leuven and Universitair Ziekenhuis Leuven, Leuven, Belgium, [11]ASST Spedali Civili and University of Brescia, Brescia, Italy, [12]Medical University Vienna, Baden, Austria, [13]Centro Hospitalar do Porto, Porto, Portugal, [14]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy, [15]Dept of Immunology and Rheumatology, Hannover, Germany, [16]Center for Genomics and Oncological Research (GENYO), Granada, Spain, [17]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di MIlano, Milan, Italy

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes II: Omics

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

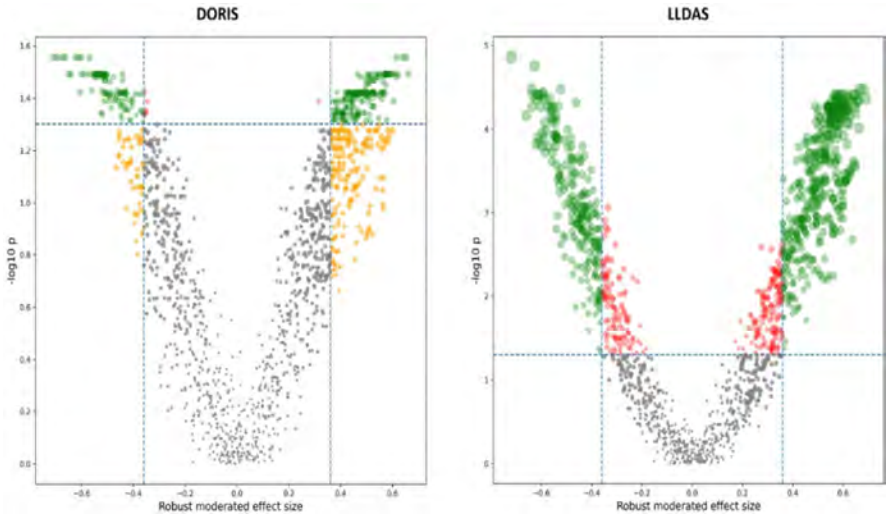

Figure 1. Volcano plot in DORIS and LLDAS subjects. Volcano plot of Reactome pathways in DORIS (left panel) or LLDAS patients (right panel). The horizontal dashed line indicates the log-transformed false-discovery rate probability threshold (q=0.05) for the moderated t-test statistic; the vertical dashed lines indicate the moderated robust effect size threshold (|dr|=0.36). Significant pathways for both conditions are highlighted in green. DORIS, definition of remission in systemic lupus erythematosus; LLDAS, lupus low disease activity state.

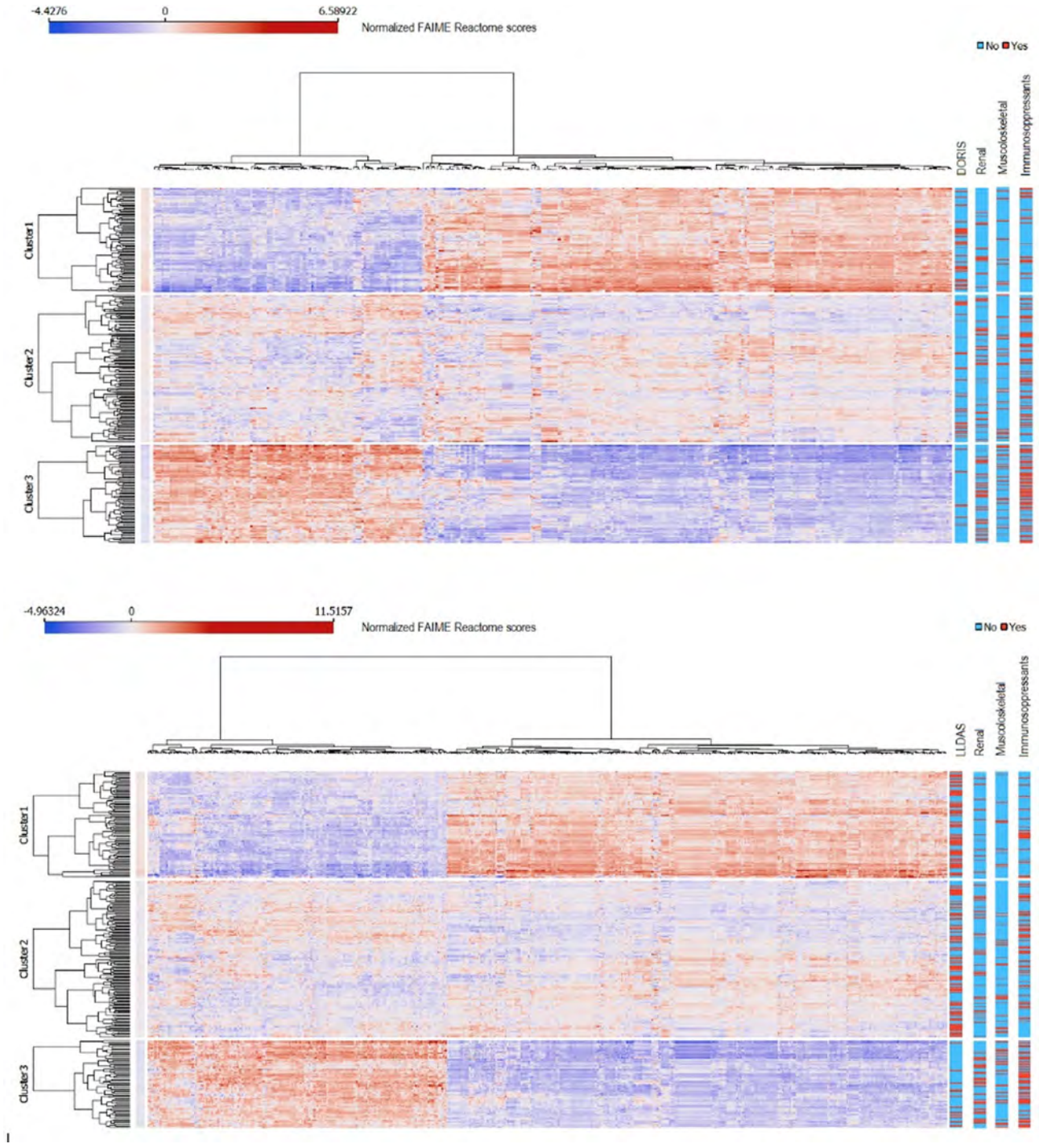

Figure 2. Clusters of Reactome individualized pathways. Individualized Reactome pathways after clustering of selected features associated with DORIS remission (top panel) or LLDAS (bottom panel). The bars to the right illustrate the distribution of relevant clinical features across clusters. DORIS, definitions of remission in systemic lupus erythematosus; LLDAS, lupus low disease activity state. Cluster1, DORIS/LLDAS cluster; Cluster2, mixed cluster; Cluster3, non-remission/non-LLDAS cluster.

Background/Purpose: Treating to remission or lupus low disease activity state (LLDAS) are conceptual frameworks for the management of SLE, but the biological milieus underlying these states have yet to be explored. We aimed at determining differentially expressed pathways (DEPs) between remission and non-remission state as well as between LLDAS and non-LLDAS.

Methods: Patients with SLE from the PRECISESADS project (NTC02890121) were stratified into patients fulfilling and not fulfilling the criteria of (i) DORIS remission, (ii) LLDAS, and (iii) LLDAS after exclusion of remission attainers. None of the patients had been treated with cyclophosphamide within 6 months or depletive therapies within 12 months from baseline.

Results: We had available data from 321 patients; 17.4% were in DORIS remission and 40.8% were in LLDAS; 28.3% of non-remission patients were in LLDAS. A total of 1465 unique Reactome pathways were selected for analysis. Overall, 288 pathways differed significantly between DORIS remitters and non-remitters with an FDR-corrected p (q)< 0.05 and a

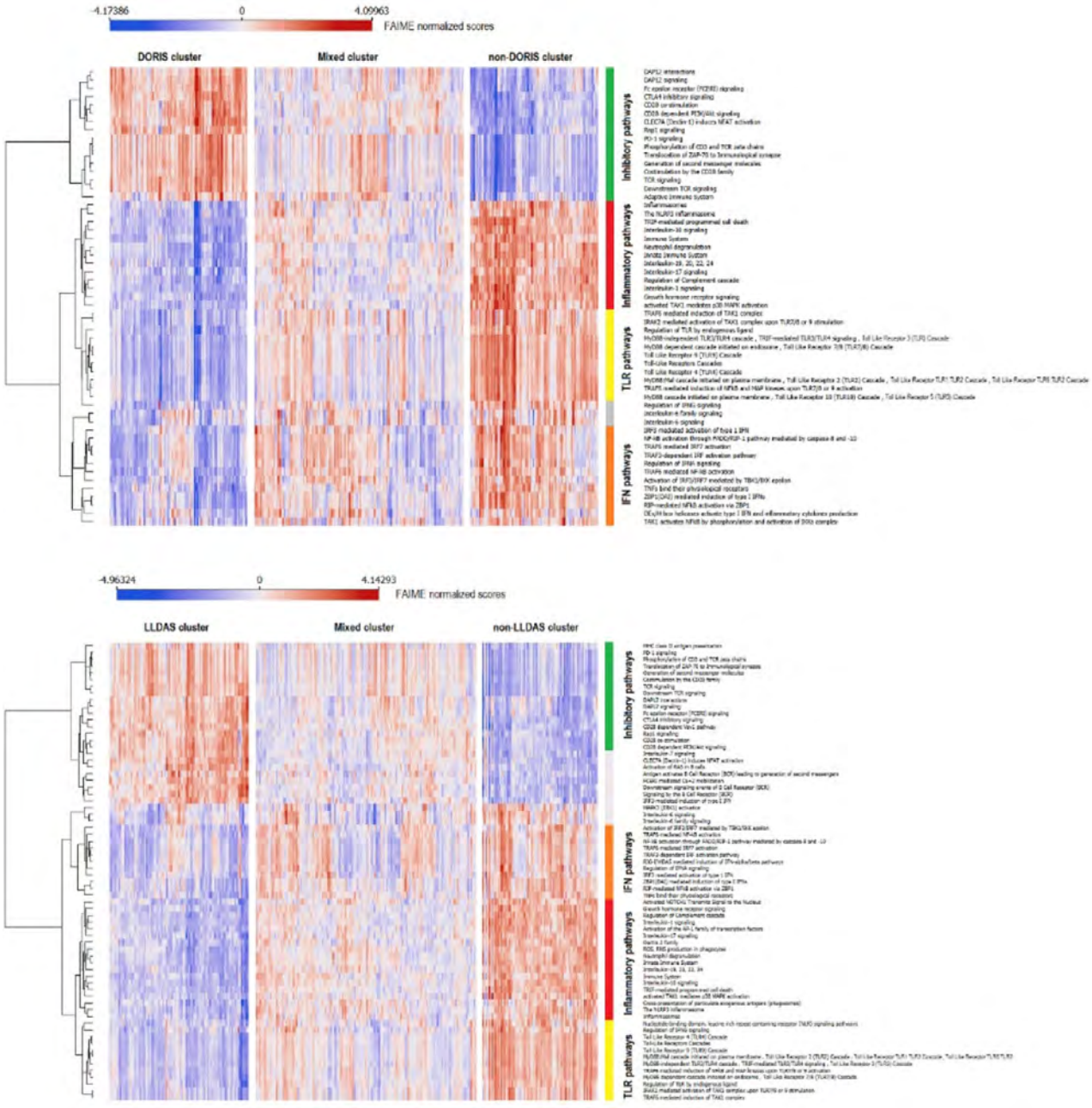

Figure 3. Immune system Rectome pathways according to biological clusters and main function. Distribution of individualized immune system Rectome pathways in DORIS (top panel) and LLDAS (bottom panel). The colored bars represent manual annotation according to the main functions of each pathway cluster, with green denoting pathways with inhibitory function on the immune system, red denoting inflammasome/inflammatory pathways enriched in cytokines, yellow denoting toll-like receptor (TLR) and related functions, orange denoting interferon (IFN) pathways, and grey denoting mixed, interleukin (IL)-6, B cells, or other pathways. DORIS, definitions of remission in systemic lupus erythematosus; LLDAS, lupus low disease activity state.

robust effect size (*dr*)≥0.36; of those, 97 were downregulated and 191 upregulated in DORIS remitters. Clustering of significant pathways yielded 3 distinct groups of patients. Accordingly, 604 pathways differed significantly ($q< 0.05$ and $dr\geq 0.36$) in LLDAS vs. non-LLDAS patients; 226 pathways were downregulated and 378 upregulated in patients in LLDAS. After clustering, 3 distinct groups could be identified (separation of classes among clusters, $\chi^2=25.3$; $p< 0.001$). In both cases, the 3 clusters were characterized by differential serological, musculoskeletal and renal activity, as well as use of immunosuppressants. Analysis of adjacent levels of disease activity using forward difference coding in linear regression models showed no DEPs between patients in DORIS remission compared with patients in LLDAS after suppression of the remitting patients. By contrast, 662 DEPs were documented between patients in LLDAS after suppression of the remitting patients and non-LLDAS patients.

Conclusion: We demonstrated for the first time molecular signaling pathways distinguishing remission/LLDAS from active SLE. Remission/LLDAS was associated with reversal of biological processes related to SLE pathogenesis, and processes linked to specific clinical manifestations. While DEP clustering by DORIS remission better grouped patients than clustering by LLDAS, substantiating the conceptual testimonial of remission being the ultimate treatment goal in SLE, the lack of substantial pathway differentiation between the two states justifies LLDAS as an acceptable goal from a biological perspective when remission is not achievable. The study revealed potentiality of existing drugs that could be repurposed to treat SLE and important pathways underlying active SLE whose modulation could aid attainment of remission. Among those, TLR cascades, BTK activity, the CTLA-4-related inhibitory signaling, and the NLRP3 inflammasome pathway were of particular interest.

Disclosure: I. Parodis: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia Pharmaceuticals, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Elli Lilly and Company, 5, 6, F. Hoffmann-La Roche AG, 5, 6, Gilead Sciences, 5, 6, GSK, 5, 6, Janssen Pharmaceuticals, 5, 6, Novartis, 5, 6, Otsuka Pharmaceutical, 5, 6; **J. Lindblom**: None; **G. Barturen**: None; **R. Ortega Castro**: None; **R. Cervera**: None; **J. Pers**: None; **F. Genre Romero**: None; **F. Hiepe**: None; **M. Gerosa**: None; **L. Kovacs**: None; **E. De Langhe**: None; **S. Piantoni**: None; **G. Stummvoll**: None; **C. Vasconcelos**: None; **B. Vigone**: None; **T. Witte**: None; **M. Alarcon-Riquelme**: None; **L. Beretta**: None.

Abstract Number: 1698

High-throughput Proteomics Identities a Spectrum of Novel Serum Biomarkers of Lupus Nephritis

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SESSION INFORMATION
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Background/Purpose: Navigating the molecular complexity of lupus nephritis (LN), a heterogeneous autoimmune disorder, poses challenges to biomarker discovery. This study addresses these challenges through an integrative approach, combining high-throughput proteomics and curated clinical samples from diverse LN states and subtypes. Our goal is to identify novel biomarkers, enhancing our understanding of LN and informing personalized treatments.

Methods: Proximity extension immunoassay (PEA, Olink) was used to evaluate the serum levels of inflammation related proteins using Explore 384-plex panel in the cohort of 80 SLE patients, including 64 active LN patients with concurrent renal biopsies and 16 active SLE patients without renal involvement at the baseline, as well as 8 age-and sex- matched healthy

controls (HCs) (Table 1). Ontological and interrelationship analyses between proteins were performed by GEO, KEGG and String analyses, to interpret the high-throughput proteomic data.

Results: Among the 368 molecules analyzed, 193 differentially expressed serum protein signatures were identified by the comparative analysis between SLE patients and HCs including 144 increased and 49 decreased molecules in SLE patients compared to HCs **(Figure 1A-E)**. The Gene Ontology (GO) analysis was performed to enrich the primary biological processes **(Figure 1F)**. Further comparative analysis was performed in the 80 SLE patients to identify novel biomarkers for kidney damage. There were 130 differentially expressed proteins between LN patients and non-LN SLE patients **(Figure 1G-I)**. The top biological processes were enriched in cytokine-mediated signaling pathway, cellular response to cytokine stimulus, response to cytokine and cell surface receptor signaling pathway **(Figure 1J)**. MCODE module screening using String software identified two clusters among the differential expressed proteins **(Figure 1K)**. Importantly, for the 64 biopsy-proven LN patients, 30 circulating proteins were found significantly altered between proliferative LN (III±V and IV±V) and membranous LN (V) patients **(Figure 1L-N)**. The GO analysis demonstrated osteoclast differentiation, collagen-activated signaling pathway, myeloid cell differentiation and hemopoiesis were enriched in the differential proteins **(Figure 1O)**. Venn diagram was performed to illustrate the distribution of total differential expressed proteins of the three comparasion sets **(Figure 1P)**.

Table 1. Demographic and clinical characteristics of study subjects (n=88).

	SLE			HC
	LN-biopsy	SLE without LN		
		Progress to LN	Non-progress	
N	64	8	8	8
Age (mean ± SD)	32.1 ± 10.3	25.6 ± 2.9	30.4 ± 5.9	28.7 ± 2.5
Gender (Female, %)	60 (93.8)	8 (100)	8 (100)	8 (100)
SLE duration (years)	5.1 ± 5.4	1.4 ± 1.2	1.1 ± 0.9	/
LN duration (months)	21 ± 35	/	/	/
dsDNA (IU/mL), median (IQR)	62 (70)	100 (0)	56 (66)	/
ANA, median (IQR)	640 (960)	1280 (160)	960 (640)	/
C3 (g/L), median (IQR)	0.49 (0.25)	0.30 (0.19)	0.66 (0.25)	/
C4 (g/L), median (IQR)	0.07 (0.06)	0.03 (0.05)	0.10 (0.04)	/
eGFR-EPI, median (IQR)	113 (49)	132 (26)	126 (17)	/
Cr (ummol/L), median (IQR)	60.5 (33.5)	46.5 (18.0)	52.0 (13.6)	/
SLEDAI	10 (4)	10 (2.5)	10.5 (4)	/
rSLEDAI	4 (4)	/	/	/
Treatment, n (%)				/
Prednisone	59 (92)	5 (63)	2 (25)	/
Hydroxychloroquine	29 (45)	3 (38)	1 (13)	/
Immunosuppressor	32 (50)	0 (0)	0 (0)	/
Cyclophosphamide	4 (6.3)	0 (0)	0 (0)	/
Mycophenolate mofetil	12 (18.8)	0 (0)	0 (0)	/
Tacrolimus	4 (6.3)	0 (0)	0 (0)	/
Methotrexate	1 (1.6)	0 (0)	0 (0)	/
Leflunomide	6 (9.4)	0 (0)	0 (0)	/
Methotrexate	1 (1.6)	0 (0)	0 (0)	/
ISN/RPS classification, n (%)				/
II	0 (0)	/	/	/
III	11 (17.2)	/	/	/
IV	24 (37.5)	/	/	/
III+V	5 (7.8)	/	/	/
IV+V	14 (21.9)	/	/	/
V	10 (15.6)	/	/	/
Proliferative	54 (84.4)	/	/	/
Membranous	10 (15.6)	/	/	/
Therapy response at 6 ms, n (%)				
CR	27 (42.2)	/	/	/
PR	13 (20.3)	/	/	/
NR	24 (37.5)	/	/	/
Therapy response at 12 ms, n (%)				
CR	26 (40.6)	/	/	/
PR	14 (21.9)	/	/	/
NR	22 (34.4)	/	/	/
NA	2 (3)	/	/	/

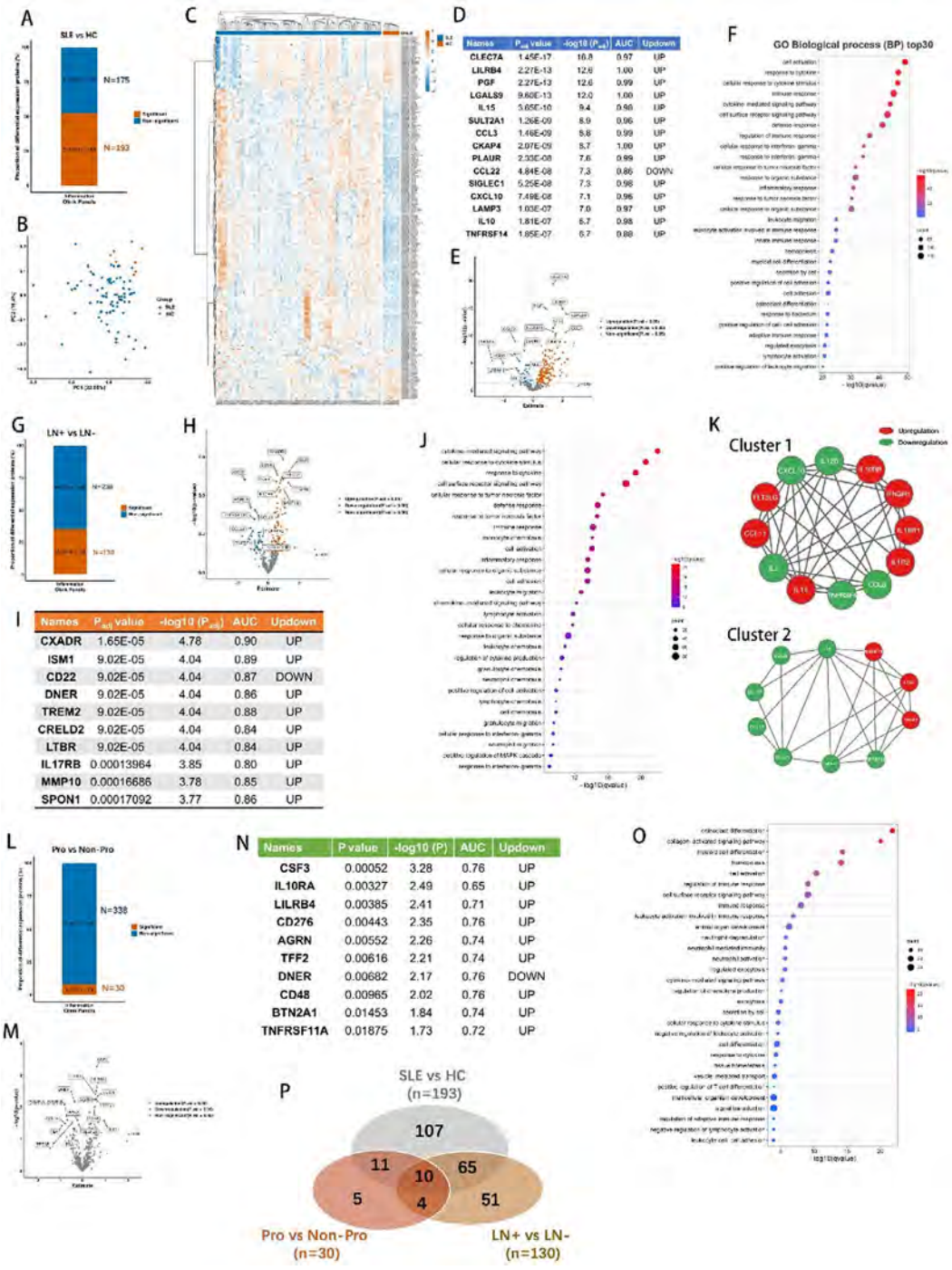

Figure 1: (A-F) Comparison of protein expression between SLE patients and healthy controls (HC). (A) There were 193 differentially expressed proteins including 144 increased and 49 decreased molecules in SLE compared to HCs; (B) PCA analysis revealed the distinctive distribution for the two groups; (C) Heat map of protein expression profiles in SLE and HCs; (D-E) The top 15 differentially expressed proteins were listed and plotted; (F) The Gene Ontology (GO) analysis was performed to identify the top biological processes for the SLE vs HC set. (G-K) Comparison of protein expression between LN patients and non-LN SLE patients; (G) There were 130 differentially expressed proteins in LN patients compared to non-LN patients. (H-I) The top 10 differentially expressed proteins were listed and plotted. (J) The Gene Ontology (GO) analysis was performed to identify the top biological processes for the LN vs Non-LN set. (K) The MCODE module screening were performed identifying two clusters using the differentially expressed proteins in the String software. (L-O) Comparison of protein expression between proliferative LN (III±V and IV±V) and membranous (V) LN patients. (L-M) There were 30 differentially expressed proteins in the proliferative LN compared to membranous LN groups; (N) The top 10 differentially expressed proteins were listed; (O) The Gene Ontology (GO) analysis was performed to identify the top biological processes for the proliferative vs membranous LN set. (P) Venn plot illustrated the distribution of the total differentially expressed proteins in three comparison sets.

Conclusion: The combination of high-throughput proteomics and well-structured clinical samples provides the foundation to dissect the molecular complexity of LN, potentially leading to the discovery and validation of effective biomarkers for this challenging disease.

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Abstract Number: 1699

Immunosuppression with Targeted Therapies Reduces Morbidity and Mortality in Pre-Capillary Pulmonary Hypertension Associated with Systemic Sclerosis: A EUSTAR Analysis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Systemic Sclerosis & Related Disorders II: Clinical Research

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Systemic sclerosis (SSc) associated pre-capillary pulmonary hypertension (precapPH) is a severe condition that requires prompt treatment. Although immunosuppressants (IMS) are standard of care for treating interstitial lung disease (ILD) and diffuse skin fibrosis (dcSSc), their effect on SSc-precapPH remains unclear. We aimed to test whether IMS affect morbidity and mortality in SSc-precapPH in the EUSTAR cohort.

Table 1. Characteristics of the study population and divided according to exposure to immunosuppressants (IMS)

	ALL (n=755)	IMS no (n=377)	IMS yes (n=378)
Age, years	63 ± 11	66 ± 10	61 ± 12
Diffuse SSc, n (%)	223 (29)	67 (18)	156 (41)
Digital ulcers history, n (%)	285 (38)	146 (39)	139 (37)
Renal crisis history, n (%)	24 (3)	9 (2)	15 (4)
Muscle weakness, n (%)	120 (16)	38 (10)	82 (22)
Arthritis, n (%)	85 (11)	26 (7)	60 (16)
ILD on HRCT, n (%)	456 (60)	162 (43)	294 (78)
DLCO%	42 ± 15	44 ± 15	39 ± 15
FVC%	83 ± 23	91 ± 22	75 ± 13
LVEF%	60 ± 7	61 ± 6	60 ± 7
NYHA>2, n (%)	388 (51)	178 (47)	210 (56)
mPAP on RHC, mmHg	35 ± 11	35 ± 11	35 ± 11
Cardiac index on RHC<2.5, n (%)	269 (36)	140 (37)	129 (34)
Increased BNP/NTproBNP, n (%)	516 (68)	364 (70)	252 (67)
6MWD<440 m, n(%)	635 (84)	318 (84)	317 (84)
PrecapPH profile [group 1, mild group 3, severe group 3], n (%)	299 (39) 262 (35) 194 (26)	215 (57) 123 (33) 39 (10)	84 (22) 139 (37) 155 (41)
Any csDMARD	356 (47)		356 (94)
Mycofelolate mofetil, n(%)	187 (25)		187 (50)
Any targeted therapy	68 (9)		68 (18)
Rituximab, n(%)	52 (7)		52 (14)
Tocilizuman, n(%)	21 (3)		21 (6)
ANY PAH medication	642 (85)	321 (85)	321 (85)
Follow up duration	2.9 (1.2-5.4)	2.9 (1.2-5.4)	2.9 (1.2-5.5)
Morbidity-Mortality, n(%)	546 (72)	261 (69)	285 (75)
Death, n(%)	307 (41)	148 (39)	159 (42)
PrecapPH worsening, n(%)	387 (54)	177 (48)	210 (58)

Methods: SSc-precapPH patients (mPAP≥ 21 mmHg, PWP≤15 mmHg, PVR≥2 WU) with at least 3 months follow-up were eligible. IMS included csDMARDS (prednisone ≥10 mg/day, cyclophosphamide, mycophenolate mofetil, azathioprine, methotrexate) and targeted therapies (abatacept, rituximab, tocilizumab, TNFi, JAKi), administered after the diagnostic right heart catheterization. The WHO precapPH class was categorized into WHO group 1 (no ILD), mild WHO group 3 (ILD and forced vital capacity – FVC ≥70%) and severe WHO group 3 (ILD and FVC< 70%).

The morbidity-mortality outcome was defined by the occurrence of either death or precapPH worsening (one of 6MWD decrease≥15%, worsening of NYHA class, onset of right heart failure, additional PAH medication, starting iv/sc prostanoids, lung transplantation, atrial septostomy). Death and precapPH worsening were also separate secondary outcomes.

We evaluated the association between IMS and time to first event with a multiple Cox regression model. Baseline covariates were chosen by expert opinion, including the WHO precapPH class, SSc-related risk factors for mortality (e.g., sex, age, dcSSc, renal crisis, digital ulcers), reasons for IMS use (e.g., muscle weakness, joint synovitis), and PAH parameters for risk

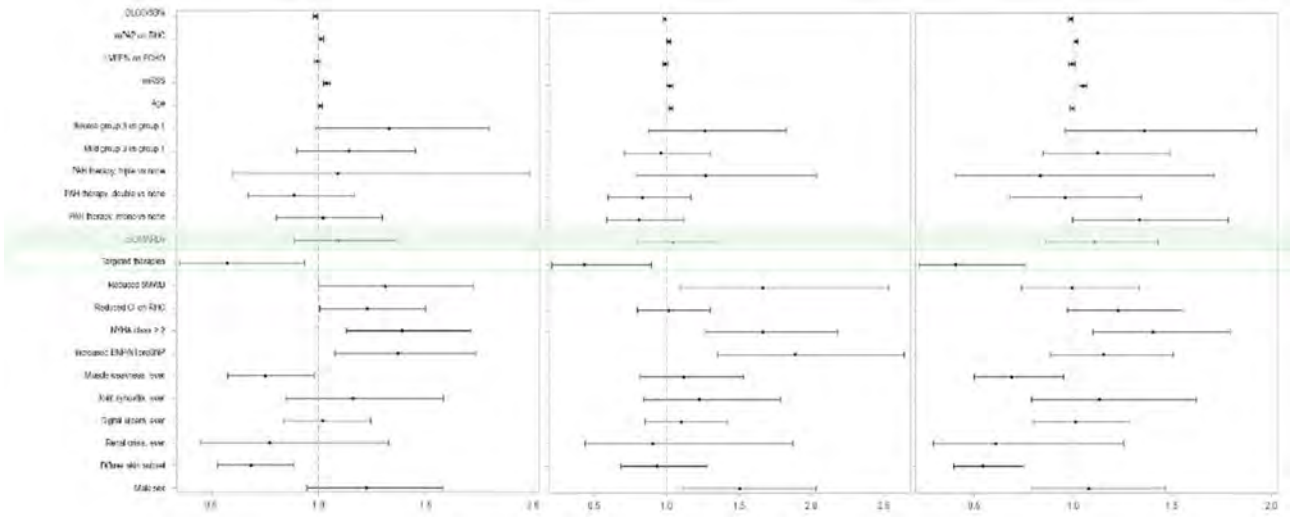

Figure 1. Effect of targeted therapies and csDMARDS on risk of morbidity-mortaliy (left panel), only death (central panel) and only worsening of precapPH (right panel).

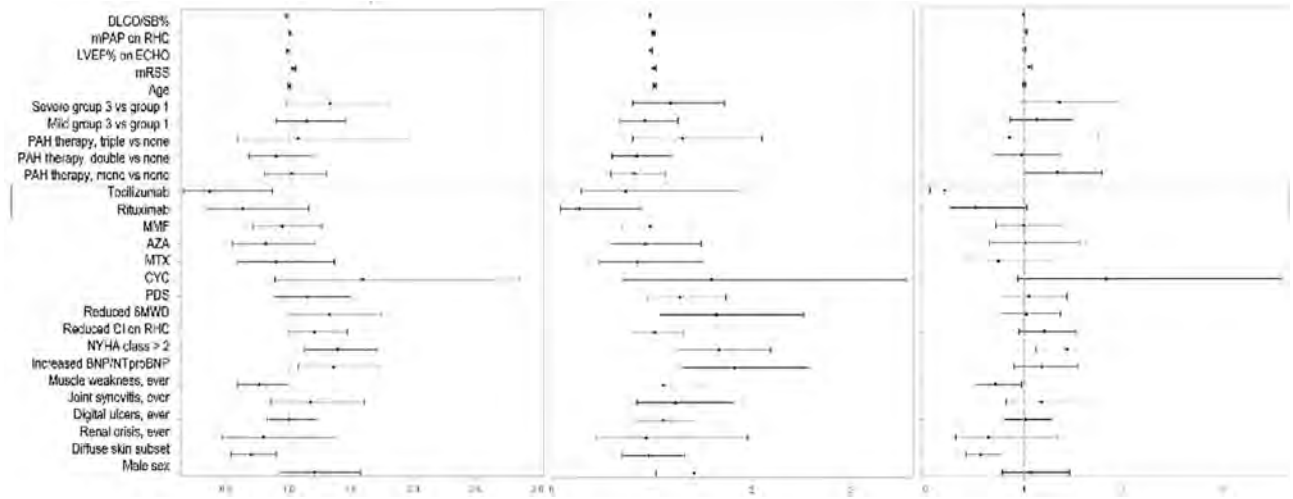

Figure 1. Effect of specific immunosuppressive compounds on risk of morbidity-mortaliy (left panel), only death (central panel) and only worsening of precapPH (right panel).

stratification (mPAP, BNP/NTproBNP, NYHA class, cardiac index, 6MWD). IMS and pulmonary arterial hypertension (PAH) drugs were treated as time-dependent variables.

Results: 755 SSc-precapPH patients were included (18% males, age 63±11 years, disease duration 11±9 years, 29% dcSSc, 60% ILD on HRCT). 377 (50%) received IMS [365 (47%) csDMARDs, 68 (9%) targeted therapies]. Patients receiving IMS had more frequently ILD, dcSSc, joint and muscle involvement (Table 1).

In median follow-up of 2.9 years, 70% of patients developed a morbidity-mortality event. While overall IMS exposure did not associate with outcomes, targeted therapies were associated with reduced risk of morbidity-mortality [HR 0.58, 95% CI 0.35-0.95, p=0.03] and both secondary outcomes [death, HR 0.43, 95% CI 0.21-0.89, p=0.02; precapPH worsening, HR 0.41, 95% CI 0.22-0.78, p< 0.01] – Figure 1.

When looking at specific targeted therapies, tocilizumab showed a risk reduction for morbidity-mortality and precapPH worsening (HR 0.37, 95% CI 0.17-0.81, p=0.02 and HR 0.19, 95% CI 0.05-0.78, p=0.02, respectively), while rituximab for death (HR 0.28, 95% CI 0.08-0.93, p=0.04) with a trend for precapPH worsening (HR 0.51, 95% CI 0.25-1.04, p=0.06) – Figure 2.

Conclusion: In this large EUSTAR SSc-precapPH cohort, targeted therapies are associated with reduced risk of mortality and precapPH worsening, which is independent from WHO group and other confounders. The impact of targeted therapies on long-term outcomes should be further explored in RCTs.

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Abstract Number: 1700

Incidence and Risk Factors for New Onset of Interstitial Lung Disease in Systemic Sclerosis: A EUSTAR Analysis

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SESSION INFORMATION

Session Date: Monday, November 13, 2023
Session Title: Abstracts: Systemic Sclerosis & Related Disorders II: Clinical Research
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Although prevalence of interstitial lung disease (ILD) in systemic sclerosis (SSc) and associated risk factors are established, less is known about its incidence and the risk factors associated with new onset of ILD following a negative baseline. We aimed to (1) estimate the annual incidence of ILD and (2) identify risk factors for new onset of ILD in baseline negative patients.

Methods: SSc patients classified according to the 2013 ACR/EULAR criteria from the EUSTAR database, with absence of ILD on high resolution computed tomography (HRCT) at baseline and having at least 1 follow-up visit were included. Patients with pulmonary arterial hypertension diagnosed by right heart catheterization were excluded. Based on follow-up HRCT, our population was divided into patients with new onset of ILD (incident group) and patients who remained ILD negative (negative group). Incidence of SSc-ILD was calculated as rate per 1000 person-years and presented starting from the first visit at the center. Prediction models were built to identify risk factors for ILD onset, with logistic regression for the 1-year and Cox regression for the long-term observation. Known predictors of new onset of ILD were chosen as covariates from previous literature and based on expert opinion.

Results: We identified 5336 ILD negative patients at baseline. New onset of ILD occurred in 1080 (20.2%) cases with median of 3.8 (IQR 1.6-7.3) years follow-up.

Table 1. Baseline characteristics of SSc patients according to the ILD onset at follow up.

	Incident ILD group (n=1080)	Negative ILD group (n=4256)	P value between groups
Age, years, mean±SD	52±14	53±14	**<0.01**
Male sex, n (%)	194 (18.1)	546 (12.8)	**<0.01**
Disease duration, years, mean±SD	6±7	7±7	**<0.01**
Caucasian, n (%)	1013 (93.8)	4057 (95.3)	**<0.05**
Smoking, ever, n (%)	68 (6.3)	409 (9.6)	**<0.01**
Diffuse SSc, n (%)	486 (45)	1023 (24)	**<0.01**
Modified Rodnan skin score, median (IQR)	7 (4-13)	4 (2-9)	**<0.01**
Digital ulcers, ever, n (%)	180 (16.7)	577 (13.6)	0.17
Pitting scars on fingertips, n (%)	351 (32.5)	1184 (27.8)	**<0.01**
Arthritis, ever, n (%)	19 (1.8)	133 (3.1)	**<0.01**
Tendon friction rubs, n (%)	74 (6.9)	192 (4.5)	**<0.01**
Muscle weakness, n (%)	167 (15.5)	503 (11.8)	**<0.01**
Esophageal symptoms, n (%)	650 (60.2)	2521 (59.2)	0.21
Dyspnea NYHA stage≥2, n (%)	357 (33.1)	1258 (29.6)	**0.02**
Scleroderma pattern on NVC, n (%)	1020 (94.6)	3915 (92)	**0.06**
DLCO/SB, % predicted, mean±SD	71±18	75±17	**<0.01**
FVC, % predicted, mean±SD	94±18	99±18	**<0.01**
Anticentromere/ Anti-topoisomerase I/ Anti-RNApolymerase III/ Anti-Pm-Scl / none of above or other, n (%)	339 (31.4) / 497 (46.0) / 32 (3) / 12 (1.1) 200 (18.5)	2459 (57.8) / 780 (18.3) / 170 (4) / 40 (0.9) / 807 (19)	**<0.01**
Increased inflammatory markers, n (%)	186 (17.2)	495 (11.6)	**<0.01**
Haemoglobin, g/dl, mean±SD	12.3±1.5	12.5±2.5	0.61
Immunosuppressants ever, n (%)	267/373 (71.6)	796/1221 (65.2)	**0.02**

The overall ILD incidence rate was 74.0 (95% CI: 68.5-79.5) per 1000 person-years. There was a continuous detection of new onset of ILD during the longitudinal observation, up to 10 years from baseline (incidence rate 54.5-82.9 per 1000 person-years; Figure 1). The baseline characteristics of incident and negative groups are shown in Table 1.

In the analysis of long-term incidence, new onset of ILD was independently predicted by dyspnea NYHA stage≥2 (HR 1.23, 95% CI1.08-1.40), male sex (HR 1.28, 95% CI1.10-1.50), age (HR 1.02, 95% CI 1.01-1.02), DLCO/SB% (HR 0.99, 95% CI 0.98-0.99), elevated inflammatory markers (HR 1.59, 95% CI 1.35-1.87), haemoglobin level (HR 0.94, 95% CI: 0.90-0.98), anti-topoisomerase I antibody (HR 2.15, 95% CI 1.82-2.53), anti-centromere antibody (HR 0.47, 95% CI0.39-0.56,) and digital ulcers ever (HR1.77, 95% CI: 1.49-2.08) (Figure 2 A). Surprisingly, the incidence of new onset of ILD was independent from disease duration.

The analysis for 1-year incidence included 13339 yearly follow-ups from 4067 baseline negative patients. All risk factors of new onset of ILD identified in the analysis of long-term incidence analysis, except for digital ulcers ever, were confirmed (Figure 2B).

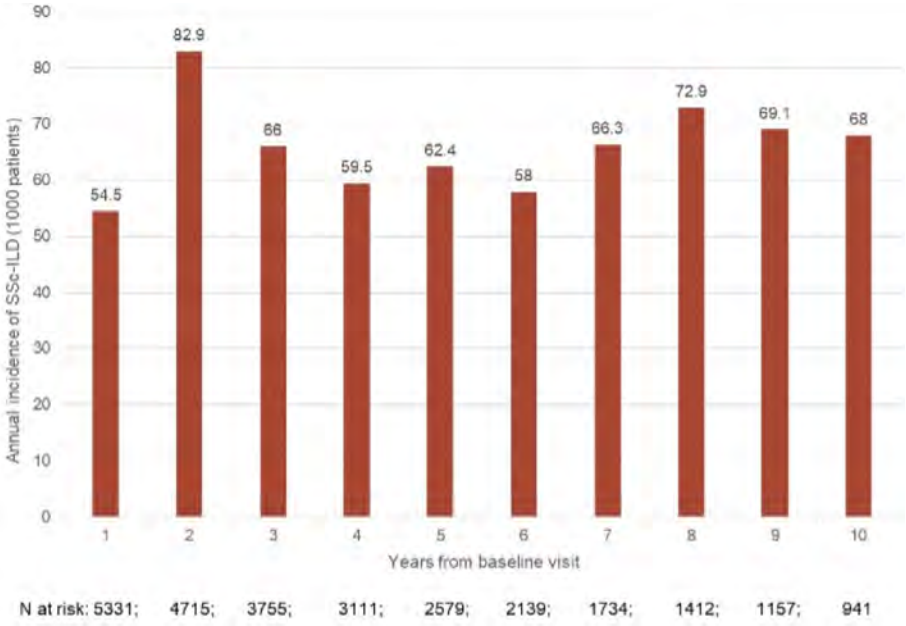

Figure 1. Annual incidence rate of new onset of ILD per 1000 patients from the baseline visit.

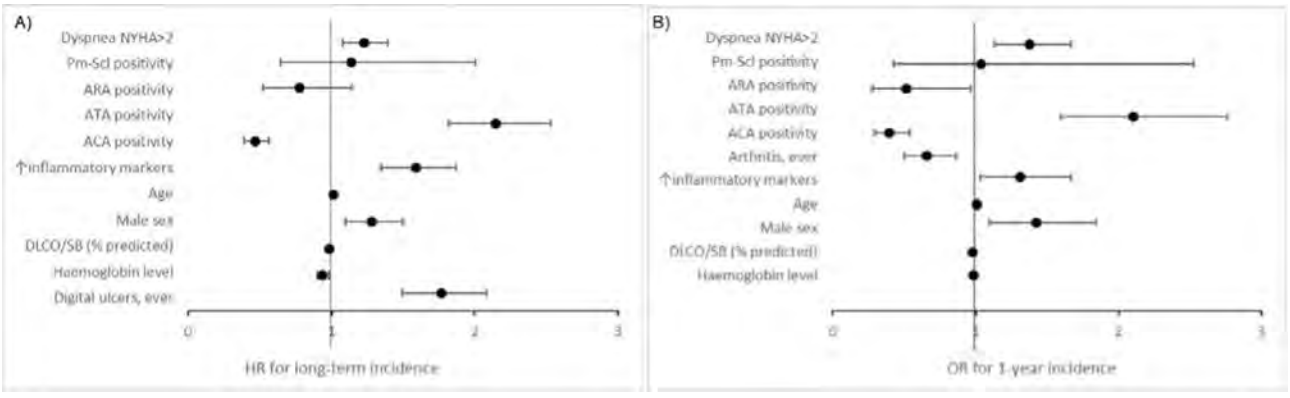

Figure 2. Prediction models of new onset of ILD for long-term (A) and 1-year observation (B).

When exposure to immunosuppressants was forced into the two models, this was not retained as a protective factor.

Conclusion: ILD can appear at any time after SSc diagnosis, with similar incidence during the disease course. We identified risk factors for new onset of ILD both at 1-year and long-term follow-up. Therefore, SSc patients should be screened following a negative baseline HRCT.

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Abstract Number: 1701

Treatment Regimens and Mortality in Systemic Sclerosis-associated Pulmonary Arterial Hypertension in Light of the 2022 ESC/ERS Guidelines

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Systemic Sclerosis & Related Disorders II: Clinical Research

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: The 2022 ESC/ERS Guidelines recommend upfront combination therapy for low- and intermediate-risk, and triple therapy for high-risk patients with systemic sclerosis (SSc)-associated pulmonary arterial hypertension (PAH).[1] There is no treatment recommendation for patients with mean pulmonary arterial pressure (mPAP) 21-24 mmHg and pulmonary vascular resistance (PVR) 2-3 WU. We aimed to assess treatment regimens, risk stratification, and mortality according to mPAP and PVR thresholds.

Table: Demographic and clinical characteristics by mPAP and PVR thresholds

	All PAH, n=367	mPAP 21-24 mmHg and/or PVR 2-3 WU, n=109	mPAP ≥25 mmHg and PVR ≥3 WU, n=258
Age, years (SD)	66±11	66±11	65±11
Female sex, n (%)	318 (87)	95 (87)	223 (86)
Time non-Raynaud to RHC, years (Q1-Q3)	9.5 (3.3-16.3)	12.5 (4.3-20.4)	8.5 (2.7-14.9)
Limited cutaneous subtype, n (%)	297 (83)	83 (77)	214 (86)
Anti-centromere Ab,n (%)	234 (64)	63 (58)	171 (67)
Digital ulcers, n (%)	146 (40)	45 (42)	101 (31)
Limited ILD<20%, n (%)	164 (45)	44 (40)	120 (47)
WHO-FC III and IV, n (%)	180 (50)	30 (28)	150 (59)
6MWD, meters (SD)	343±128	400±110	321±128
NT-proBNP, ng/L (Q1-Q3)	567 (207-1485)	275 (136-569)	880 (286-2120)
FVC, % (SD)	91±21	95±20	89±21
DLCO, % (SD)	45±15	53±15	42±13
mPAP, mmHg (SD)	35±12	24±3	40±11
PAWP, mmHg (SD)	9±3	10±3	9±3
PVR, WU (SD)	6.3±4.3	2.9±1.2	7.7±4.4
Risk groups			
• Low risk, n (%)	62 (24)	34 (44)	28 (16)
• Intermediate-low risk, n (%)	82 (32)	30 (38)	52 (29)
• Intermediate-high risk, n (%)	78 (31)	11 (14)	67 (38)
• High risk, n (%)	33 (13)	3 (4)	30 (17)
Treatment-naïve status, n (%)	306 (86)	87 (87)	219 (86)
Upfront therapy			
1) Monotherapy	140 (39)	28 (27)	112 (44)
2) Combination therapy	77 (21)	5 (5)	72 (28)
• Dual	67 (18)	4 (4)	63 (25)
• Triple	10 (3)	1 (1)	9 (3)
3) None	143 (40)	70 (68)	73 (28)
1-, 3- and 5-year survival	92% / 79% / 66%	98% / 91% / 83%	90% / 74% / 60%

Methods: We included SSc patients from the EUSTAR database who were diagnosed with PAH by right heart catheterization (RHC) between 2001-2021 (Project Number: CP122). PAH was defined as mPAP >20 mmHg, pulmonary artery wedge pressure ≤15 mmHg, and PVR >2 WU. We excluded patients with previous PAH-specific treatment and meaningful interstitial lung disease (ILD), defined as an extent of ILD >20% on HRCT or FVC < 70% in patients with missing quantification. We stratified patients into four risk groups based on WHO-functional class (FC), six-minute walk distance (6MWD), and NT-proBNP applying the COMPERA 2.0 risk stratification.[2] Initial treatment regimens were defined as (1) upfront monotherapy with endothelin receptor antagonists, phosphodiesterase-5 inhibitors, or prostanoids; (2) upfront combination therapy; or (3) no therapy.

Survival was evaluated using Kaplan–Meier analysis and log-rank test. We assessed treatment regimens segregated by mPAP and PVR thresholds (lower thresholds: mPAP 21-24 mmHg and/or PVR 2-3 WU vs. higher thresholds: mPAP ≥25 mmHg and PVR ≥3 WU) and by risk stratification. We assessed the impact of initial treatment regimens on mortality using Cox regression adjusted for age, male sex, DLCO, mPAP and PVR thresholds, treatment-naïve status, and risk stratification.

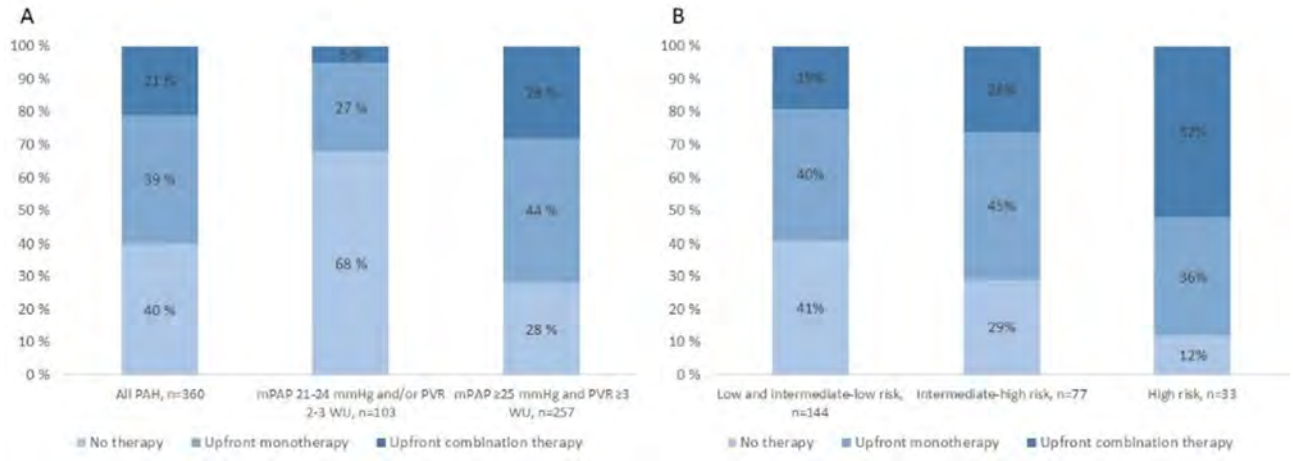

Figure 1: Proportion of patients starting upfront monotherapy, upfront combination therapy or none segregated by (A) mPAP and PVR thresholds, and (B) risk stratification

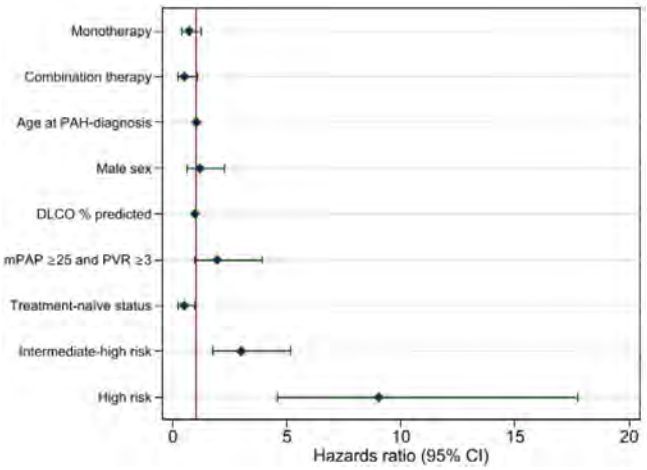

Figure 2: Impact of upfront mono- or combination therapy on mortality compared with no treatment adjusted for other risk factors in multivariable Cox regression model

Results: Of 890 patients who had RHC, 367 were eligible (table). Survival was significantly lower in the group with higher mPAP and PVR thresholds (p< 0.001) (table). The 5-year survival according to risk stratification for low-, intermediate-low, intermediate-high, and high risk was 85%, 86%, 60% and 25%, respectively.

Upfront combination therapy was used more frequently in patients with mPAP ≥25 mmHg and PVR ≥3 WU (p< 0.001) and in patients in the high-risk group (p=0.002) (fig. 1 a-b). Despite at high risk and higher thresholds, 40% of these patients did not receive any treatment (fig. 1a). In multivariable Cox regression analysis, upfront combination therapy was numerically associated with reduced mortality compared with no treatment (HR 0.50, 95% CI (0.23 - 1.09), p=0.08) (fig. 2).

Conclusion: Our study shows that survival is impaired in SSc-PAH regardless mPAP and PVR thresholds, particularly in patients at intermediate-high and high risk. Current results show a trend toward reduced mortality for upfront combination therapy, and that many patients are not treated according to guideline recommendations. We suggest considering treatment in patients with lower mPAP and PVR thresholds and a more aggressive treatment approach in patients at intermediate-high risk to increase survival over time.

References:

[1]Humbert, Eur Heart J, 2022
[2]Hoeper, Eur Respir J, 2022

Disclosure: H. Jenssen Bjørkekjær: Janssen, 5; **C. Bruni**: AbbVie/Abbott, 5, Boehringer-Ingelheim, 2, 12, Travel Support, Eli Lilly, 6; **C. Brunborg**: None; **P. Carreira**: None; **P. Airò**: Boehringer-Ingelheim, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, CSL Behring, 2, 5, 6, Janssen-Cilag, 2, 5, 6, Novartis, 2, 5, 6, Roche, 2, 5, 6; **C. Simeon-Aznar**: None; **M. Truchetet**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Gilead, 5, 6, Merck/MSD, 6, UCB, 6, 12, support for conferences; **A. Giollo**: Eli Lilly, 6, Galapagos, 2, 6, Novartis, 2, Sandoz, 2; **A. Balbir-Gurman**: None; **M. Martin**: Boehringer-Ingelheim, 6, GlaxoSmithKlein(GSK), 6; **C. Denton**: AbbVie, 2, Acceleron, 2, Arxx Therapeutics, 5, Bayer, 2, Boehringer-Ingelheim, 2, 6, Corbus, 2, 6, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Horizon Therapeutics, 2, Inventiva, 2, 5, Janssen, 6, Roche, 2, Sanofi, 2, Servier, 5; **A. Gabrielli**: Boehringer-Ingelheim, 12, Educational Grants, Janssen, 12, Educational Grants, Roche, 12, Educational Grants; **H. Fretheim**: actelion, 5, bayer, 2, Boehringer-Ingelheim, 6, GlaxoSmithKlein(GSK), 5; **I. Barua**: None; **H. Bitter**: Boehringer-Ingelheim, 6; **O. Midtvedt**: None; **T. Garen**: None; **K. Broch**: Amgen, 2, 6, AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, Novartis, 2, 6, Orion Pharma, 2, 6, Pfizer, 2, 6, Pharmacosmos, 2, 6; **A. Andreassen**: Amgen, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Orion Pharma, 2, 6, Pfizer, 2, 6; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer-Ingelheim, 6, Chugai, 5, 6, Eisai, 5, 6, Eli Lilly, 6, Gilead, 6, GSK, 6, Mitsubishi-Tanabe, 5, Pfizer, 6, Taiho, 6, Taisho, 5, 6; **G. Riemekasten**: None; **U. Müller-Ladner**: None; **m. Matucci Cerinic**: accelerong, 2, 6, actelion, 2, 6, bayer, 2, 6, biogen, 2, 6, Boehringer-Ingelheim, 2, 6, Chemomab, 2, 6, corbus, 2, 6, CSL Behring, 2, 6, Eli Lilly, 2, 6, galapagos, 2, 6, Inventiva, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 6, Mitsubishi, 2, 6, Pfizer, 2, 6, regeneron, 2, 6, Roche, 2, 6, samsung, 2, 6; **I. Castellvi**: None; **E. Siegert**: None; **E. Hachulla**: Bayer, 2, CSL Behring, 5, GlaxoSmithKlein(GSK), 2, 5, 6, johnson&Johnson, 2, 5, 6, Novartis, 2, 5, Otsuka, 6, Roche-Chugai, 2, 5, 6, sanofi-genzyme, 2, 5, Sobi, 5; **O. Distler**: 4P-Pharma, 2, 5, 6, AbbVie, 2, 5, 6, Acceleron, 2, 5, 6, Alcimed, 2, 5, 6, Altavant Sciences, 2, 5, 6, Amgen, 2, 5, 6, AnaMar, 2, 5, 6, Arxx, 2, 5, 6, AstraZeneca, 2, 5, 6, Bayer, 2, 5, 6, Blade Therapeutics, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Citus AG, 12, Co-Founder, Corbus Pharmaceuticals, 2, 5, 6, CSL Behring, 2, 5, 6, Galapagos, 2, 5, 6, Galderma, 2, 5, 6, Glenmark, 2, 5, 6, Gossamer, 2, 5, 6, Horizon Therapeutics, 2, 5, 6, Janssen, 2, 5, 6, Kymera, 2, 5, 6, Lupin, 2, 5, 6, Medscape, 2, 5, 6, Miltenyi Biotec, 2, 5, 6, Mitsubishi Tanabe, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Patent issued ‘‘mir-29 for the treatment of systemic sclerosis’’ (US8247389, EP2331143), 10, Prometheus Biosciences, 2, 5, 6, Redx Pharma, 2, 5, 6, Roivant, 2, 5, 6, Topadur, 2, 5, 6; **A. Hoffmann-Vold**: Arxx Therapeutics, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Support for travel, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, 12, Support for travel, Roche, 2, 6, 12, Support for travel.

Abstract Number: 1702

Outcomes in Systemic Sclerosis Patients Treated with Rituximab and Mycophenolate Mofetil Combination Therapy Compared to Autologous Hematological Stem Cell Transplantation

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Systemic Sclerosis & Related Disorders II: Clinical Research

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

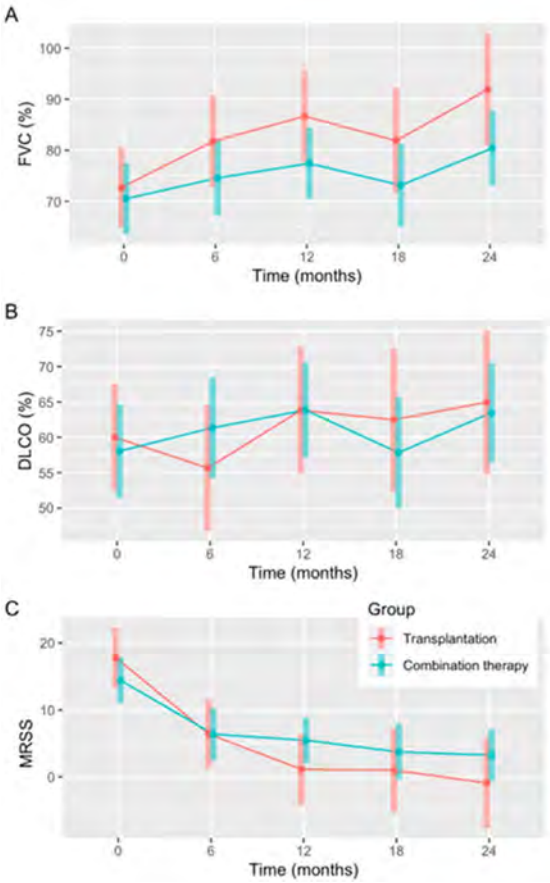
Background/Purpose: Autologous hematological stem cell transplantation (AHSCT) is a grade A therapy for early diffuse progressive systemic sclerosis (SSc), that has been validated in three randomized controlled trials (RCT) compared to cyclophosphamide (CYC). CYC, however, is no longer considered the gold standard therapy for SSc and does not provide long-term benefit. The efficacy of rituximab on skin and lung involvement in SSc has recently been demonstrated in an RCT, the DESIRES study. The combination of rituximab with mycophenolate mofetil (MMF) is a potential potent regimen for progressive SSc, that has not been evaluated compared to AHSCT. We retrospectively compared the outcomes of SSc patients in our cohort, fulfilling eligibility criteria for AHSCT studies, who received a combination therapy of MMF and rituximab, with patients who underwent AHSCT.

Methods: Repeated longitudinal assessments at baseline and every 6 months for 24 months, including modified Rodnan Skin Score (mRSS), forced vital capacity (FVC), and diffusing capacity of the lung for carbon monoxide (DLCO) values, were compared between groups using a linear mixed model regression. Clinical improvement (CI) was defined as a decrease in mRSS by more than 25% or an increase in FVC by more than 10%. Event-free survival (EFS) was defined as the occurrence of death or the development of persistent major organ failure (heart, lung, kidney). Hazard ratios (HRs) and 95% CIs were calculated by Cox regression.

Results: Twenty-one SSc patients in the combination group were compared to sixteen in the AHSCT group. There were no significant differences in the demographic or clinical variables, except for Nintedanib treatment (Table 1). CI at 12 months was seen in 86% of patients in the combination group, compared to 81% in the AHSCT group (p=0.7). The hazard ratio (HR) for EFS at 24 months favored the combination group (HR=0.09, 95% CI 0.009 to 0.9; P =0.04). In both groups, a statistically significant and similar increase in FVC values, but not in DLCO, was demonstrated at each time point during follow-up. The inclusion of Nintedanib usage in the mixed model did not influence these results. In both groups, there was a significant and similar reduction in mRSS at 12 and 24 months compared to baseline (figure 1).

Conclusion: In our cohort, combination therapy of MMF and rituximab compared to AHSCT in SSc patients eligible for AHSCT, resulted in similar skin and lung clinical improvement with a better safety profile after 24 months.

1Mean (SD); n (%) 2Wilcoxon rank sum test; Fisher's exact test



A linear mixed model of the forced vital capacity (FVC) (1A), diffusing capacity of the lung for carbon monoxide (DLCO) (1B), and modified Rodnan Skin Score (mRSS) (1C) values at follow-up in the two groups

Variable	Transplantation, N = 16[1]	Combination therapy, N = 21[1]
Age at treatment initiation (years)	48 (9)	49 (15)
Gender (female)	13 (81%)	15 (71%)
Autoantibodies		
SCL70	8 (50%)	9 (45%)
RNA POL3	7 (44%)	6 (30%)
Negative/other	1 (6.2%)	5 (25%)
Disease duration		
< 5 years	14 (88%)	19 (90%)
≥ 5 years	2 (12%)	2 (9.5%)
Scleroderma subtype		
diffuse	15 (94%)	13 (62%)
limited	1 (6.2%)	8 (38%)
Lung fibrosis > 10% on lung CT	13 (81%)	16 (76%)
Nintedanib (yes)	0 (0%)	9 (43%)
Smoking (yes)	3 (19%)	6 (29%)
Event free survival	13 (81%)	21 (100%)
Baseline FVC %	73 (16)	70 (15)
Baseline DLCO %	60 (13)	58 (15)
Baseline MRSS	23 (9)	16 (14)

[1]Mean (SD); n (%)

[2]Wilcoxon rank sum test; Fisher's exact test

Disclosure: s. keret: None; **L. Kaly**: None; **A. Shouval**: None; **T. Zuckerman**: None; **I. Henig**: None; **A. Awisat**: None; **I. Rosner**: None; **M. Rozenbaum**: None; **N. Boulman**: None; **Y. Molad**: None; **a. Dortort Lazar**: None; **G. Slobodin**: None; **D. Rimar**: None.

Abstract Number: 1703

Increased Mortality and Cardiovascular Events in Male Patients with Systemic Sclerosis: Left Ventricular Global Longitudinal Strain as Possible Screening Tool

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SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Systemic Sclerosis & Related Disorders II: Clinical Research

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Systemic sclerosis (SSc) is less frequent in males, but the risk of severe outcomes is higher in males than in females(1). Seven to 30% of SSc patients have cardiovascular involvement, which is associated with poor prognosis. Cardiovascular events are reported to be more frequent in male SSc patients(2). However, the cause of this sex-specific cardiovascular risk in SSc is unknown, and commonly available screening tools including echocardiography and ECG are not sensitive to detect early cardiac dysfunction in SSc(3). Objective of this longitudinal prospective study was to assess sex differences in echocardiographic characteristics. We specifically analysed whether a difference in left ventricular global longitudinal strain (LV GLS) can explain sex difference in cardiovascular outcomes in SSc, and can be applied as prognostic screening tool for cardiovascular events in SSc.

Methods: A total of 746 SSc patients from four SSc expert centers, including 628 (84%,54±13 years) women and 118 (16%,55±15 years) men, were evaluated with standard and advanced echocardiographic examinations. The independent association of the echocardiographic parameters with the combined endpoint of cardiovascular events-hospitalization/death was evaluated.

Results: Men and women with SSc showed significant differences in disease characteristics and cardiac function. After adjusting for the most important clinical characteristics (age, disease duration since Raynaud, skin involvement, interstitial lung disease (ILD), DLCO-SB % predicted, smoking), LV ejection fraction (LVEF) and diastolic function were not significantly different anymore. However, men still presented with more impaired LV GLS as compared to women (-19% (IQR-20%-[-17%]) vs.-21%(IQR:-22%-[-19%]),p< 0.001). After median follow-up of 48 months (IQR:26–80), the combined endpoint occurred in 182 patients (24%). Kaplan-Meier survival curves showed that men experienced higher cumulative rates of

Table 1. Baseline clinical characteristic in the overall population and for male and female patients

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Baseline clinical Characteristics				
	Total (N=746)	Men (N=118)	Women (N=628)	P-value
Age Yr, mean ± SD	55±14	54 ±13	55 ±14	0.337
Diffuse cutaneous SSc, n (%)	192 (30)	52 (48)	140 (26)	<0.001
Time since Raynaud Yr median (IQR)-till 1st echo	10 (4-19)	7 (3-14)	10 (4-19)	0.006
Time since non-Raynaud Yr median (IQR)-till 1st echo	5 (2-10)	4 (1-9)	5 (2-13)	0.059
Disease characteristics, n (%)				
mRSS>15	94 (16)	26(26)	68 (13)	0.002
Digital ulcers	226 (31)	39 (34)	187 (31)	0.259
Myositis	12 (3)	7(13)	5(2)	<0.001
Lung fibrosis	332 (49)	67 (63)	265 (46)	0.002
Medical history & Cardiovascular risk factors, n (%)				
Hypertension	153 (21)	24 (21)	129 (21)	0.925
Diabetes	18(4)	4 (6)	14 (4)	0.429
(History of) smoking	348 (50)	76 (66)	272 (47)	<0.001
Coronary artery disease	68 (9)	14 (12)	54(9)	0.282
Prior/current pericarditis	55 (7)	9 (8)	46 (7)	0.888
Holter ECG abnormalities (prior or current arrhythmias)	126 (31)	25 (40)	101(89)	0.073
History of renal crisis	17 (4)	1 (2)	16 (4)	0.280
Laboratory tests				
Creatine Phosphokinase U/L, median (IQR)	84 (61–120)	115 (80 – 200)	79 (58–110)	<0.001
eGFR ml/min/1.73m2, mean ± SD	89 ±27	103 ±31	87±26	<0.001
NT-proBNP ng/L, median (IQR)	80 (20 –143)	37(11 – 97)	62 (25– 150)	0.004
Pulmonary function tests, mean ± SD				
FVC % of predicted	96±23	86±20	98±22	<0.001
FEV1 % of predicted	90 ±20	82±20	91± 20	<0.001
DLCO-SB % of predicted	67±20	60±23	67±20	0.001

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor antagonist; DLCO-SB, diffusing capacity for carbon monoxide single breath; eGFR estimated Glomerular Filtration Rate; ESR, erythrocyte Sedimentation Rate; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; mRSS, modified rodnan skin score; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; VO2max, maximal oxygen uptake

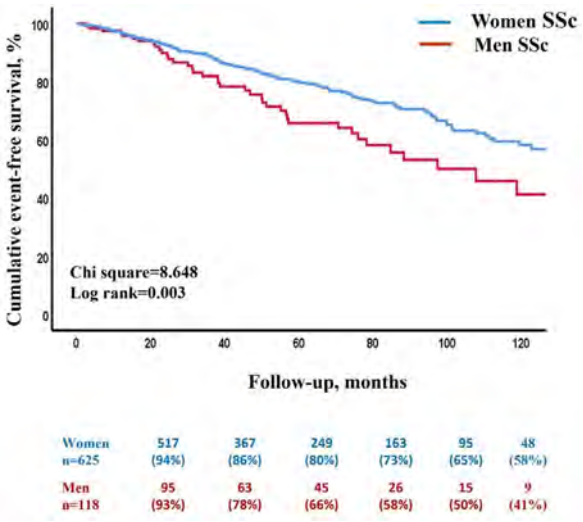

Figure 1. Survival function (for cardiovascular hospitalization/death) in women and men patients with systemic sclerosis (SSc).

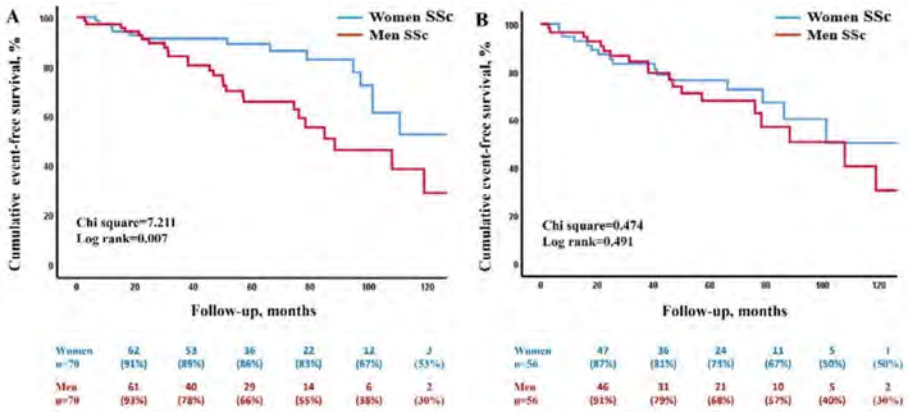

Figure 2. Survival function in women and men patients with SSc in Panel A after adjusting for age, disease duration (since Raynaud), type of SSc, lung fibrosis, DLCO-SB and NT-proBNP, in Panel B after adjusting for age, disease duration (since Raynaud), type of SSc, lung fibrosis, DLCO-SB, NT-proBNP and LV GLS.

cardiovascular events-hospitalization/death as compared to women (Chi-square 8.648; Log rank 0.003. Figure 1). When using propensity score matching to match men and women according to clinical characteristics (age, disease duration since Raynaud, subtype of SSc, ILD, DLCO-SB% predicted and NT-proBNP, n=140 patients), men still experienced higher cumulative rates of cardiovascular events/death as compared to women (Chi-square 7.211; Log rank 0.007. Figure 2A). Sex-difference in outcome disappeared when matching the groups according to the LV GLS on top of the abovementioned clinical characteristics (n=112 patients, Chi-square 0.474; Log rank 0.491, Figure 2B).

Conclusion: In SSc patients, male sex is associated with worse cardiovascular outcomes after adjusting for important clinical characteristics. LV GLS was more impaired in men as compared to women and potentially explains the sex difference in cardiovascular outcomes. Using LV GLS for early assessment of myocardial involvement may improve risk stratification and surveillance in SSc patients for both sexes.

1. Ann Rheum Dis; 2010; 69 (10): 1809.
2. Ann Rheum Dis; 2017; 76 (11): 1897.
3. JACC Cardiovacs Im. 2019; 12 (11 Pt 1): 2273.

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Abstract Number: 1704

Esophageal Mucosal Erosions Can Predict the Deterioration of Lung Function over a Four-year Follow-up Period and Long-term Mortality in Patients with Interstitial Lung Disease Associated with Scleroderma

gerlando Natalello[1], enrico De Lorenzis[1], Ludovica Berardini[2], lucrezia verardi[1], pier giacomo Cerasuolo[1], Alfredo Papa[3], Italo De Vitis[3], Francesco Varone[2], Luca Richeldi[2], Maria Antonietta D'Agostino[1] and Silvia Bosello[1], [1]Division of Rheumatology - Catholic University of the Sacred Heart, Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy, [2]Division of Pulmonology - Catholic University of the Sacred Heart, Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy, [3]Division of Gastroenterology - Catholic University of the Sacred Heart, Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy

SESSION INFORMATION

Session Date: Monday, November 13, 2023

Session Title: Abstracts: Systemic Sclerosis & Related Disorders II: Clinical Research

Session Type: Abstract Session

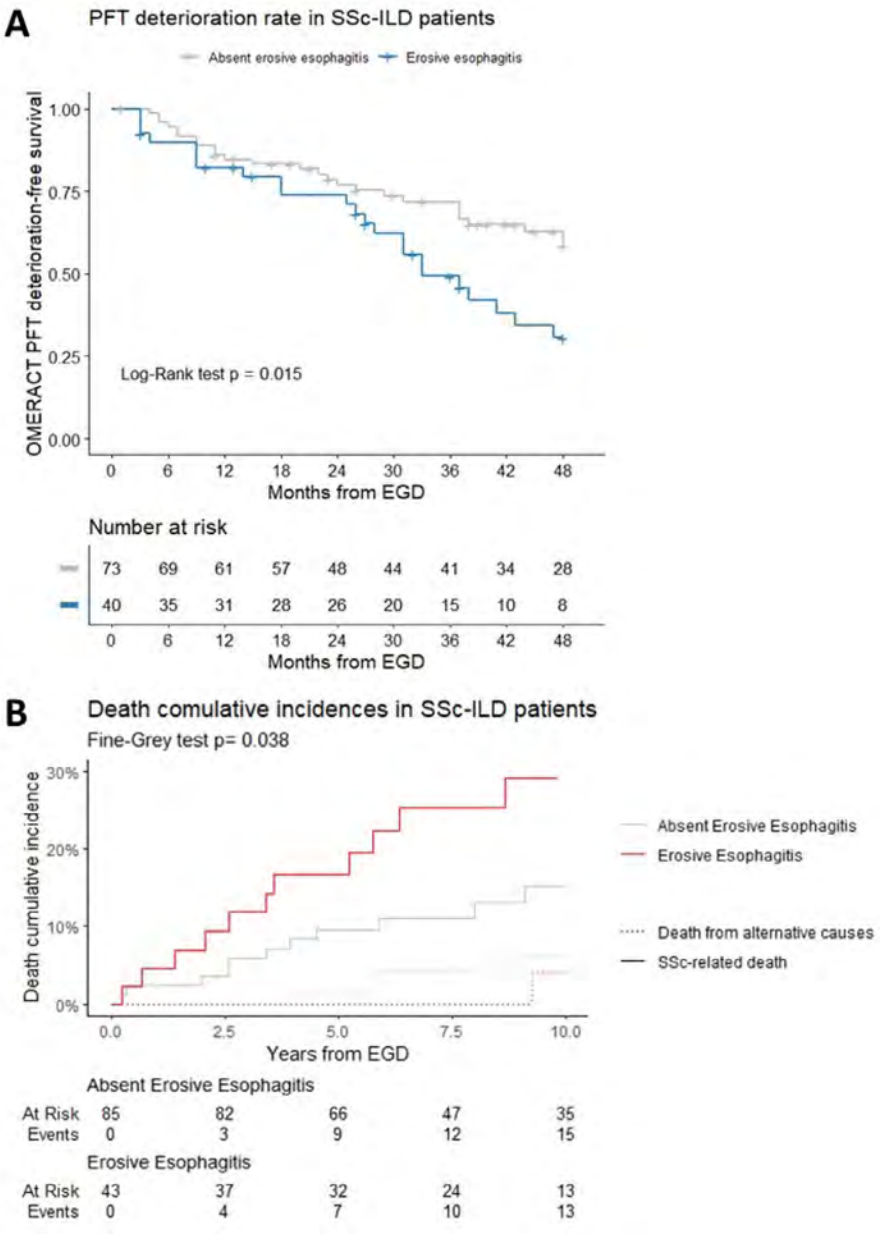
Session Time: 4:00PM–5:30PM

Background/Purpose: Interstitial lung disease (ILD) is a major cause of morbidity and disease-related death in systemic sclerosis (SSc). Esophageal disease is common in SSc, and micro-aspiration of gastroesophageal reflux may contribute to the pathogenesis of ILD. The aim of this study is to explore the association of erosive esophagitis (EE) determined by esophagogastroduodenoscopy (EGD) with lung function deterioration and survival in patients with SSc.

Methods: Consecutive patients presenting with symptoms of gastro-esophageal involvement who underwent EGD from 2005 to 2015 were characterized based on the occurrence of EE, following the Los Angeles criteria[1], and longitudinally evaluated. Patients with SSc-ILD were assessed over a 48-month period for pulmonary function test deterioration according to OMERACT criteria[2]. Both raw and SSc-associated mortality were documented over a ten-year period for the entire cohort. SSc patients, with or without EE, were compared though survival analysis. A competing risk survival analysis was specifically performed to investigate the association of EE with SSc-related mortality with death due to alternative causes as competing event.

Results: Of the 214 SSc patients studied, 9.8% were male, the mean age was 58.8±13.5 years, the median disease duration was 5.0 years (IQR 1.0-9.0), and the diffuse variant was present in 36.9%. Out of these patients, 33.6% had EE and 59.8% had ILD and no association was found between these two disease characteristics. Forty-nine SSc-ILD patients experienced OMERACT deterioration. EE was associated with a reduced OMERACT progression-free survival (Log-Rank p=0.015) (Fig.A) and an independently doubled risk of progression (HR 1.97, 95% CI 1.09-3.55 adjusted for age, gender, digital ulcers, disease duration, p=0.025). In the overall cohort, fifty-one deaths were reported, 37 of which were SSc-related. In the ILD group, there were a total of 27 deaths due to any cause, with 23 specifically due to SSc. EE was associated with the risk of SSc-related death in the ILD group (HR 2.08, 95% CI 1.05-5.28, Fine-Gray p=0.038) (Fig.B), but not in SSc patients without ILD.

Conclusion: In our cohort, EE represents a risk factor for functional deterioration and SSc-related long-term mortality specifically in SSc patients with ILD, supporting a detrimental role of gastro-esophageal micro-aspiration in exacerbating lung fibrosis.



Disclosure: g. Natalello: None; **e. De Lorenzis**: None; **L. Berardini**: None; **I. verardi**: None; **p. Cerasuolo**: None; **A. Papa**: None; **I. De Vitis**: None; **F. Varone**: None; **L. Richeldi**: None; **M. D'Agostino**: AbbVie/Abbott, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **S. Bosello**: None.

Abstract Number: 1705

Reduced DNASE1L3 Activity and Increased Anti-NET Protective Antibodies Contributes to Accumulation of Neutrophil Extracellular Traps in Pediatric SLE Patients

Betsy Barnes[1], Lydia Thomas[2], Jenna Battaglia Battaglia[3], Kim Simpfendorfer[3], Joyce Hui-Yuen[4], Vinay Sharma[5] and **Bharati Matta**[6], [1]Northwell Health, Manhasset, NY, [2]Northwell Health - Cohen Children's Medical Center, Lake Success, NY, [3]Feinstein Institutes for Medical Research, Northwell Health, Manhasset, NY, [4]North Shore LIJ Health System, Great Neck, NY, [5]Amity Institute of Biotechnology, Amity University Rajasthan, Jaipur, India, [6]The Feinstein Institutes for Medical Research, Northwell Health, Manhasset, NY and Amity Institute of Biotechnology, Amity University Rajasthan, Jaipur, NY

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Pediatric Rheumatology – Basic Science Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Pediatric systemic lupus erythematosus (pSLE) is a multisystemic chronic autoimmune disease with high renal involvement. In SLE, neutrophil extracellular traps (NETs) are considered a potential source of antigen, leading to autoantibody production. NETs activate plasmacytoid dendritic cells to produce high levels of interferon-α, a known driver of lupus pathogenesis. NETs have also been shown to play a role in kidney pathology leading to lupus nephritis (LN).Also, low DNase activity and mutations in *DNASEIL3* have been associated with lupus. We hypothesized that NETs will be elevated in pediatric lupus and our study aims to investigate levels of circulating NETs in pSLE as compared to healthy children (pHC) and further elucidate mechanisms contributing to NET accumulation.

Methods: Plasma was obtained from 13 pSLE patients who were either treatment-naïve or not on corticosteroids at the time of enrollment and 12 pHC. Lupus disease activity was measured using SELENA-SLEDAI. ELISA and smear assay were used to detect NETs in plasma samples. DNASE1L3 concentration was measured using ELISA and DNase1L3 enzymatic activity was assayed by digestion of chromatin in purified nuclei. The ability of plasma to degrade NETs was measured using NET degradation assay.

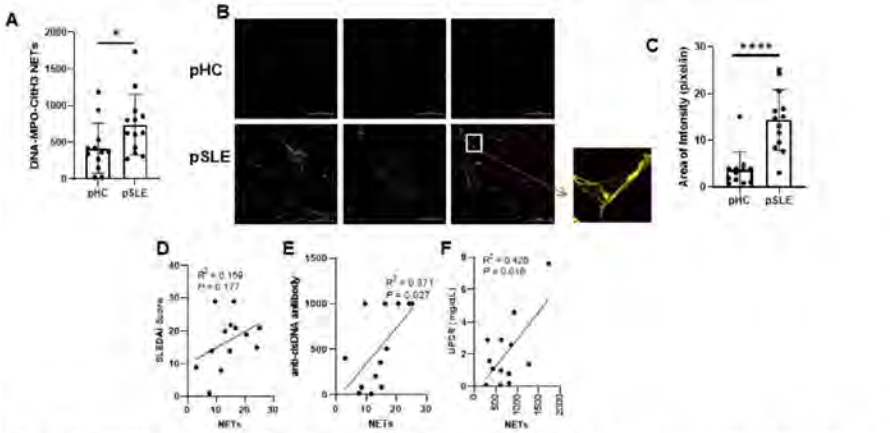


Figure 1. Increased NETs in pSLE plasma correlate with markers of disease activity. (A) ELISA detecting higher MPO-CitH3-DNA NETs in plasma of pSLE (n=13) compared to pHC (n=12). **(B)** Representative images of 3 healthy children and 3 pSLE patient plasma smears stained for MPO (green, AF488), CitH3 (red, AF594) and DAPI (blue) showing higher NETs in pSLE. **(C)** Plasma smear quantification of pHC (N=12) and pSLE (N=13) samples using ImageJ. **(D)** SELENA-SLEDAI scores demonstrated a positive slope with level of circulating NETs as detected by smear assay. Other makers of disease activity including anti-dsDNA antibody level **(E)** and UPCR **(F)** showed a strong positive correlation with circulating NETs in pSLE patients (n=13) detected by ELISA. Data are presented as mean ±SD. Statistical significance tested by unpaired parametric t test (A,C). Individual merged images represent separate donors (B). All images were taken on ZEISS Confocal M880 at 20x objective. Set scale 200 µm (B). A two-tailed correlation analysis was performed using Pearson correlation coefficients assuming Gaussian distribution (D-F).

Results: 10/13 of pSLE patients were female, with a mean of 13±4.4years, and a mean SLEDAI score of 13.8±8.1. 7/13 patients had biopsy-proven proliferative LN. Significantly higher levels of circulating NETs were found in pSLE plasma which positively correlated with measures of disease activity and anti-ds DNA titers (Figure 1). Plasma from pSLE failed to degrade NETs efficiently. Although DNASE1L3 levels were higher in pSLE patients, DNASE1L3 activity was reduced, as compared to healthy children. Moreover, higher anti-NET protective antibodies were found in pSLE plasma.

Conclusion: These data suggest that defective functional DNASE1L3 activity and increased anti-NET protective antibodies could lead to delayed clearance and accumulation of NETs in pSLE plasma.

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Abstract Number: 1706

Autoreactive B Cell Responses Are Enriched in Early-onset Oligoarticular Juvenile Idiopathic Arthritis

Claudia Harris[1], Maria Taylor[2], Ki Pui Lam[2], Indu Raman[3], Chengsong Zhu[3], Pui Lee[1], Peter Nigrovic[4], Erin Janssen[5], Jing Cui[6] and Lauren Henderson[4], [1]Division of Immunology, Boston Children's Hospital, Boston, MA, [2]Division of Immunology, Boston Children's Hospital, Boston, MA, [3]Department of Immunology, Microarray & Immune Phenotyping Core Facility, University of Texas, Southwestern Medical Center, Dallas, TX, [4]Boston Children's Hospital, Boston, MA, [5]Department of Pediatrics, Michigan Medicine, Ann Arbor, MI, [6]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: A subset of children with oligoarticular juvenile idiopathic arthritis (oligo JIA) who are anti-nuclear antibody (ANA) positive are known to have dysregulated T cell-B cell interactions in affected joints. In these patients, clonally expanded T peripheral helper (Tph) cells are enriched in the synovial fluid (SF), overexpress factors associated with B cell help, and promote the differentiation of antibody-producing plasmablasts. To further evaluate B cell responses in oligo JIA, we characterized the autoantibody profile of these patients.

Methods: Paired blood and SF samples were obtained from oligo JIA patients, defined by ILAR criteria. Blood samples were also collected from pediatric controls. Plasma and SF supernatant were inputted into an autoantigen microarray platform to screen for 120 IgG and IgA autoantibodies. The net fluorescence intensity (NFI) for each antigen was calculated by subtracting the background signal. The NFI was normalized to control antibodies spiked into the arrays. Autoantigens with low signal-to-noise ratio (SNR) were excluded. The autoantibody score (Ab-score) for each autoantigen was generated by a log2 transformation using NFI and SNR. Oligo JIA patients were stratified into 3 groups based on age of disease onset and ANA status: ≤6 years, ANA+; ≤6 years, ANA-; and >6 years. ANOVA with correction for multiple comparisons was used to compare the Ab-score for each autoantigen across the study groups. R was used to generate heat maps, and statistical analysis software (SAS) was used for the statistical analysis.

Results: 23 oligo JIA and 15 pediatric controls were studied (Table 1). After quality control, results from 97 and 88 autoantigens on the IgG and IgA arrays, respectively, were retained for analysis. Compared to the plasma of controls, 57 IgG and 49 IgA autoantibodies were significantly elevated in the SF of all 3 strata of oligo JIA patients. An additional 19 IgG and

Table 1. Clinical Characteristics of the Study Subjects

	Oligo JIA ANA+; ≤6 yrs N=9	Oligo JIA ANA-; ≤6 yrs N=7	Oligo JIA >6 yrs N=7	Pediatric Controls N=15
Age at Disease Onset* (median yrs, range)	2, 2-4	4, 3-6	11, 9-13	n/a
Age at Sample (median yrs, range)	2.9, 2.4-9.5	5.2, 4.2-8.8	11.8, 10.0-15.6	6.2, 4.0-11.8
Female Sex (n, %)	9, 100%	6, 86%	5, 71%	8, 53%
Race (n, %)				
American Indian	0, 0%	0, 0%	0, 0%	0, 0%
Asian	1, 11%	1, 14%	0, 0%	0, 0%
Black	0, 0%	0, 0%	0, 0%	0, 0%
Other	2, 22%	0, 0%	0, 0%	0, 0%
Undisclosed	1, 11%	2, 29%	2, 29%	12, 80%
White	5, 56%	4, 57%	5, 71%	3, 20%
Hispanic Ethnicity (n, %)				
Hispanic	3, 33%	1, 14%	0, 0%	0, 0%
Non-hispanic	5, 56%	4, 57%	5, 71%	3, 20%
Undisclosed	1, 11%	2, 29%	2, 29%	12, 80%
Immunomodulatory Treatment (n, %)	0, 0%	0, 0%	0, 0%	0, 0%

32 IgA autoantibodies were significantly increased in the SF of oligo JIA patients with disease onset ≤6 years, regardless of ANA status. Fewer autoantibodies were significantly elevated in oligo JIA plasma vs. control plasma (14 IgG; 8 IgA autoantibodies), most in the ≤6 year groups. After setting a false discovery rate (FDR) of 5% to account for testing multiple autoantigens, 72 IgG and 82 IgA autoantibodies remained significantly different across the study groups. Heat maps showed that autoantibody reactivity was highest in the SF of children with early-onset disease (Figures 1-2). Directly comparing oligo JIA patients with disease onset ≤6 years (regardless of ANA status) to those who were older at initial presentation confirmed that all differentially expressed autoantibodies were higher in the patients with early-onset disease (35 IgG; 53 IgA autoantibodies in SF and 8 IgG; 36 IgA autoantibodies in plasma).

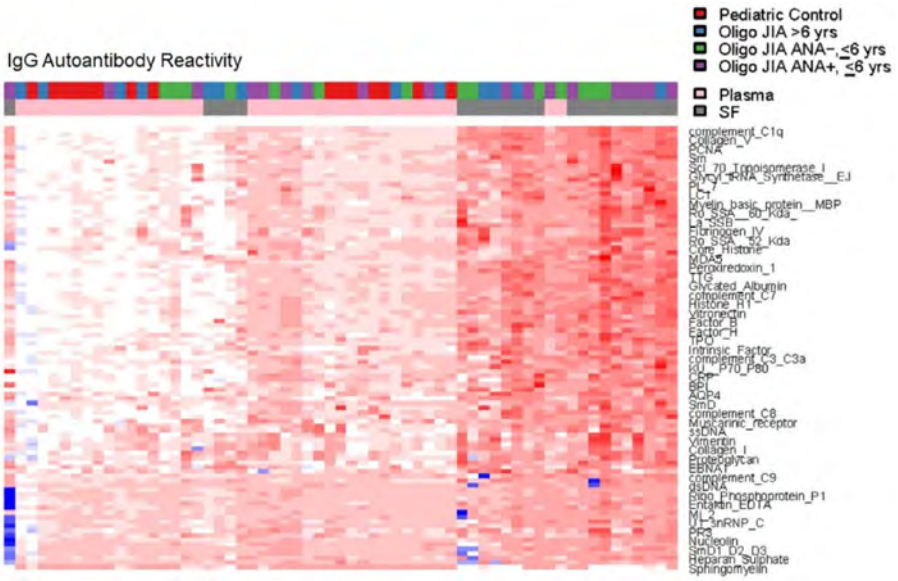

Figure 1. Heat map showing IgG Autoantibody Reactivity. Plasma and SF samples from pediatric controls and oligo JIA patients were evaluated with an autoantigen microarray. The most differentially expressed autoantibodies are depicted in the heat map. The color represents distance in standard deviations from the mean of the controls with red indicating an increase in reactivity above controls and blue indicating a decrease in reactivity compared to controls. Oligo JIA, oligoarticular juvenile idiopathic arthritis; ANA, anti-nuclear antibody; yrs, years

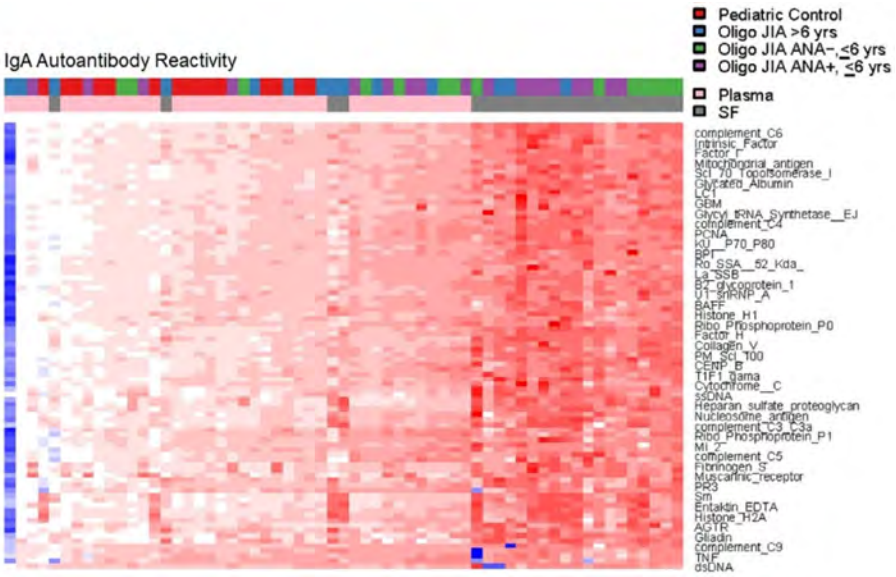

Figure 2. Heat map showing IgA Autoantibody Reactivity. Plasma and SF samples from pediatric controls and oligo JIA patients were evaluated with an autoantigen microarray. The most differentially expressed autoantibodies are depicted in the heat map. The color represents distance in standard deviations from the mean of the controls with red indicating an increase in reactivity above controls and blue indicating a decrease in reactivity compared to controls. Oligo JIA, oligoarticular juvenile idiopathic arthritis; ANA, anti-nuclear antibody; yrs, years

Conclusion: A broad array of autoantibodies were detected in the SF of oligo JIA patients. Early age at disease onset, not ANA status, was the factor most associated with the high levels of autoantibodies in SF. These findings suggest that dysregulated B cell responses in the arthritic joint are particularly prominent in oligo JIA patients who develop disease at a young age.

*Age patient/family reported onset of symptoms, rounded to the nearest year. Oligo JIA, oligoarticular juvenile idiopathic arthritis; ANA, anti-nuclear antibody; yrs, years; n/a, not available

Disclosure: C. Harris: None; **M. Taylor**: None; **K. Lam**: None; **I. Raman**: None; **C. Zhu**: None; **P. Lee**: None; **P. Nigrovic**: None; **E. Janssen**: None; **J. Cui**: None; **L. Henderson**: Adaptive Biotechnologies, 2, 5, Bristol-Myers Squibb(BMS), 5, Pfizer, 2, Sobi, 1, 2, 5.

Abstract Number: 1707

PD1-Expressing Regulatory T Cells Found in Inflamed Joints Suppress Tph Cell-B Cell Interactions

Ki Pui Lam[1], Amélie M Julé[1], Claudia Harris[2], Maria Taylor[1], Maryrose Hahn[2], Laurie A Ohlms[3], Pui Lee[2], Margaret Chang[4], Talal Chatila[5], Peter Nigrovic[4] and Lauren Henderson[4], [1]Division of Immunology, Boston Children's Hospital, Boston, MA, [2]Division of Immunology, Boston Children's Hospital, Boston, MA, [3]Department of Otolaryngology & Communication Enhancement, Boston Children's Hospital, Boston, MA, [4]Boston Children's Hospital, Boston, MA, [5]Division of Immunology, Boston Children's Hospital, Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Pediatric Rheumatology – Basic Science Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Table 1. Clinical characteristics of the study subjects.

	Healthy Controls* (N=10)	JIA Patients (N=10)
Age at sampling (median, 25th-75th percentile)	26, 22.3-31.0	14, 6.6-17.0
Female (n, %)	4, 40%	8, 80%
Age at disease onset (median, IQR)	-	5, 2.9-10.3
JIA Diagnosis		6 oligo JIA 4 seroneg poly JIA
ANA+ (n, %)	-	7, 70%
Active joints at sampling (median, 25th-75th percentile)	-	2, 1-3
Immunomodulatory medication at sampling	-	1 systemic steroid, 3 MTX
Samples collected	Peripheral blood	Synovial fluid

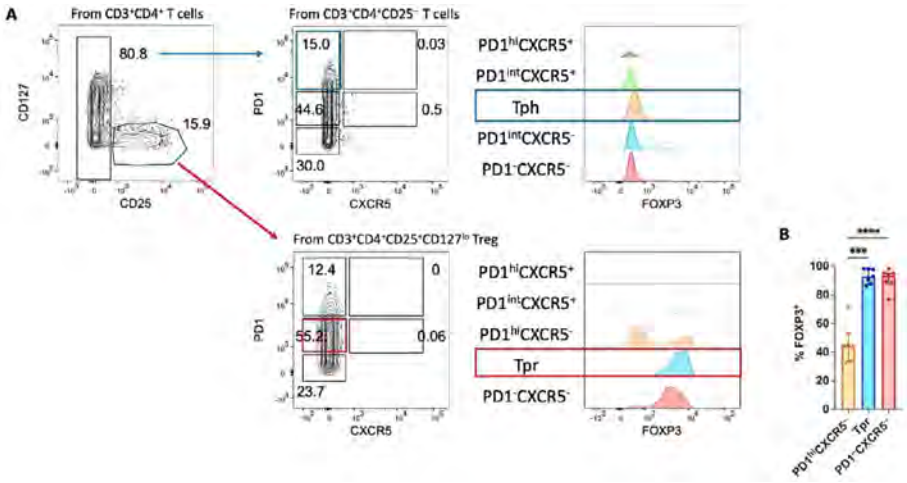

Figure 1. Gating strategy for Tph/Tpr cells from JIA synovial fluid. A) Representative dot plots showing flow cytometry gating strategy and Tph/Tpr cells from JIA SF. Histogram overlay showing % of maximum FOXP3 expression in each T cell subset. B) Summary data showing % FOXP3+ cells in each T cell subset, gated on CD4+CD25+CD127lo cells (n=7). SF Tph: CD4+CD25-PD1hiCXCR5-; SF Tpr: CD4+CD25+-CD127loPD1intCXCR5-. Statistical analysis: paired, one-way ANOVA. ***, P≤0.001; ****, P≤0.0001. JIA, juvenile idiopathic arthritis; SF, synovial fluid.

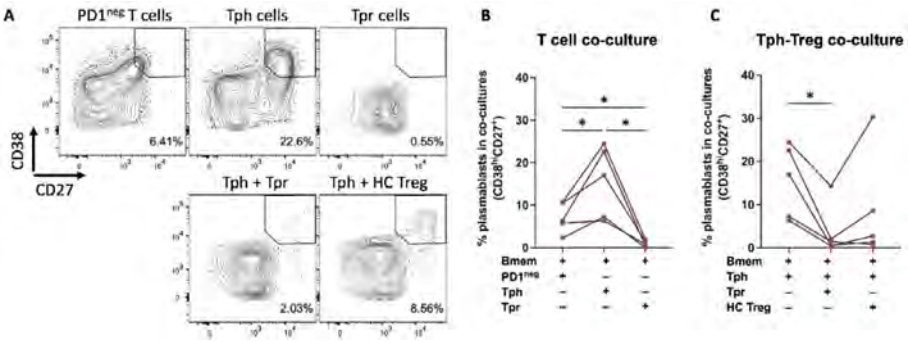

Figure 2. Tpr cells suppressed plasmablast differentiation in Tph cell-B cell co-cultures. A) Representative flow cytometry dot plots showing % plasmablast (CD38hiCD27+) of alive CD19+ B cells after co-culture of the indicated population(s) of T cells with Bmem cells from the peripheral blood (PB) of a healthy donor. B) Summary data showing % plasmablast in co-culture conditions of Bmem cells with the indicated single population of T cells and C) co-culture conditions of Bmem cells plus Tph cells with autologous Tpr cells or bulk Treg from PB of a healthy donor. SF from 5 ANA+ JIA patients. JIA SF Tph: CD4+CD25-PD1hiCXCR5-; JIA SF Tpr: CD4+CD25+CD127loPD1intCXCR5-; HC Treg (PB): CD4+CD25+-CD127lo. Statistical analysis: paired, one-way ANOVA. *, P≤0.05. SF, synovial fluid; ANA, anti-nuclear antibody; JIA, juvenile idiopathic arthritis; HC, healthy control.

Background/Purpose: T peripheral helper (Tph) cells promote B cell maturation and the generation of antibodies in the inflamed joints of adults with seropositive rheumatoid arthritis (RA) and children withanti-nuclear antibody(ANA) positive oligoarticular juvenile idiopathic arthritis (oligo JIA). We recently identified a population of T cells in the synovial fluid (SF) of patients with oligo JIA that express both regulatory T (Treg) cell (FOXP3, CTLA4, GITR) and B cell-helper T cell factors (PD1, ICOS, CXCL13), which we term T peripheral regulatory (Tpr cells). We sought to determine if Tpr cells are a suppressive T cell population that may have the capacity to restrain Tph cell-B cell interactions in peripheral tissues.

Methods: Children with oligo or the closely related seronegative polyarticular JIA (ILAR criteria) provided SF samples. Healthy adults provided peripheral blood (PB) samples. PB mononuclear cells (MCs) and SFMCs were isolated by Ficoll density gradient centrifugation. Cells were stained for surface markers and then fixed and permeabilized for FOXP3 staining. Flow cytometry was used to measure FOXP3 expression in various T cell populations. For T cell-B cell co-cultures, memory B cells (Bmem; $CD19^{+}CD27^{+}IgD^{-}$) were sorted from leukocollars obtained from controls. Bmem were co-cultured with various effector T cell populations from ANA^{+}JIA patients at a ratio of 10:1 for 5 days in the presence of staphylococcal enterotoxin B (SEB). These T cell-B cell co-cultures were also performed with the addition of PB Treg cells from controls ($CD4^{+}CD25^{+}CD127^{lo}$) or autologous Tpr cells from SF ($CD4^{+}$ $CD25^{+}CD127^{lo}PD1^{int}CXCR5^{-}$) at a ratio of 1:1. After 5 days of incubation, cells were harvested and stained to determine the frequency of plasmablasts ($CD19^{+}CD27^{+}CD38^{hi}$) in the co-cultures. Study subjects with co-cultures of Tph cells and Bmem cells with less than 10% of cells in the lymphocyte gate and/or without visible lymphocyte proliferation in the FSC/SSC gate were excluded. GraphPad Prism was used for statistical analysis.

Results: 10 JIA and 10 healthy controls were studied (Table 1). FOXP3, the Treg lineage defining transcription factor, was measured in $PD1^{+}$ T cells from JIA SF by flow cytometry (Figure 1). FOXP3 levels were highest in $CD4^{+}CD25^{+}CD127^{lo}$ Treg cells with intermediate PD1 ($PD1^{int}$) expression. Thus, we identified cell surface markers to isolate viable Tpr cells ($CD4^{+}CD25^{+}CD127^{lo}PD1^{int}CXCR5^{-}$) for functional assays. To evaluate T cell-B cell interactions, we used our co-culture system to study SF samples from 5 ANA^{+} JIA patients (Figure 2). As expected, co-culture of Bmem with Tph cells ($CD4^{+}CD25^{-}PD1^{hi}CXCR5^{-}$) from JIA SF induced the production of plasmablasts. In contrast, co-culture of Bmem with Tpr cells resulted in essentially no plasmablast differentiation. Once Tpr cells were added to co-cultures of Tph and Bmem cells, they significantly reduced the frequency of plasmablasts while bulk Treg cells from control blood did not.

Conclusion: We identified a novel Treg population present in inflamed joints that expresses B cell-help factors and restrains Tph cell-B cell interactions. Further work is needed to define the effector functions of Tpr cells and determine their role in regulating inflammation in tissues.

*PBMCs from 5/10 healthy adult controls were isolated from leukocollars obtained at our institution's blood bank. Per IRB regulations, no clinical information on these individuals could be shared. JIA, juvenile idiopathic arthritis; oligo, oligoarticular; seroneg, seronegative; poly, polyarticular; ANA, anti-nuclear antibody; MTX, methotrexate; PBMCs, peripheral blood mononuclear cells; IRB, institutional review board.

Disclosure: K. Lam: None; **A. Julé**: None; **C. Harris**: None; **M. Taylor**: None; **M. Hahn**: None; **L. Ohlms**: None; **P. Lee**: None; **M. Chang**: None; **T. Chatila**: None; **P. Nigrovic**: None; **L. Henderson**: Adaptive Biotechnologies, 2, 5, Bristol-Myers Squibb(BMS), 5, Pfizer, 2, Sobi, 1, 2, 5.

Abstract Number: 1708

In Cis SOCS1 Variants Illustrate the Precise Regulation of Interferon Signaling Needed to Prevent Autoimmunity

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic autoimmunity can be driven by monogenic or polygenic risk variants. We aimed to characterize the genetic basis of disease in a family with early-onset autoimmune manifestations including systemic lupus erythematosus (SLE), discoid lupus, and immune thrombocytopenia.

Methods: Whole exome sequencing (WES) was conducted to identify candidate variants. The impact of the identified variants was analyzed by flow cytometry, immunoprecipitation, and luciferase reporter assay in transfected 293T cells. Gene expression in peripheral blood mononuclear cells was profiled by bulk RNA sequencing and plasma cytokines were measured by proximity extension assay.

Results: We studied two siblings with early-onset systemic lupus erythematosus and immune thrombocytopenia. Mother of the probands had a history of discoid lupus and positive antinuclear antibody test. WES identified maternally inherited in cis variants (p. Pro50Leu and p.Ala76Gly) in *Suppressor of cytokine signaling 1 (SOCS1)* flanking the kinase inhibitory domain (Figure 1A). Both variants are predicted to be benign by in silico algorithms and neither variant alone affected the ability of SOCS1 to inhibit JAK-STAT1 signaling by luciferase reporter assay and flow cytometry quantification of STAT1 phosphorylation (Figure 1B,C). Immunoprecipitation studies showed that when both variants were expressed in cis, the mutant SOCS1 protein displayed decreased binding to JAK1 and reduced capacity to inhibit IFN-I signaling by ~25% compared to wildtype protein (Figure 1D,E).

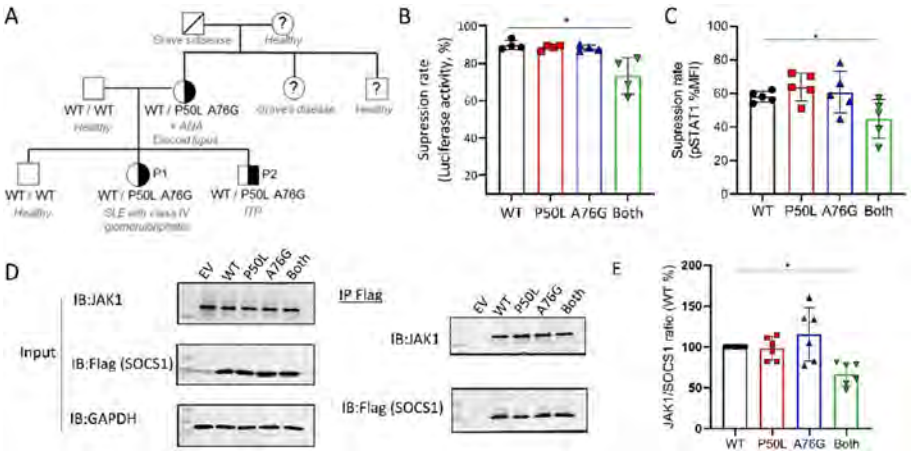

Figure 1. A) in cis SOCS1 variants in a family with multiple autoimmune manifestations. B). Suppression of IFNα2-induced luciferase activity in ISRE-luc reporter cells by ectopic expression of wildtype and mutant SOCS1. Luciferase was measured 24 hours after IFN stimulation. C) Suppression of IFNα2-induced STAT1 phosphorylation in 293T cells by ectopic expression of wildtype and mutant SOCS1. Flow cytometry for phospho-STAT1 was performed 5 minutes after IFN stimulation. D) Assessment of SOCS1-JAK1 interaction by immunoprecipitation of Flag-tagged SOCS1 and JAK1. E) Densitometry analysis of JAK1/SOCS1 ratio from 6 independent immunoprecipitation studies. * $p < 0.05$.

Supporting defective regulation of IFN-I, transcriptomic and cytokine analysis of both siblings and their mother showed increased expression of interferon-inducible genes compared to healthy controls, but less striking compared to patients with SOCS1 haploinsufficiency due to loss-of-function variants (Figure 2A,B). Peripheral blood monocytes from all three subjects further displayed increased CD169 expression and STAT1 phosphorylation upon IFN-I stimulation (Figure 2C,D).

Conclusion: Our work illustrates the critical fine-turning of IFN-I signaling by SOCS1 to prevent autoimmunity and demonstrates that a combination of variants that are individually benign may have deleterious consequences.

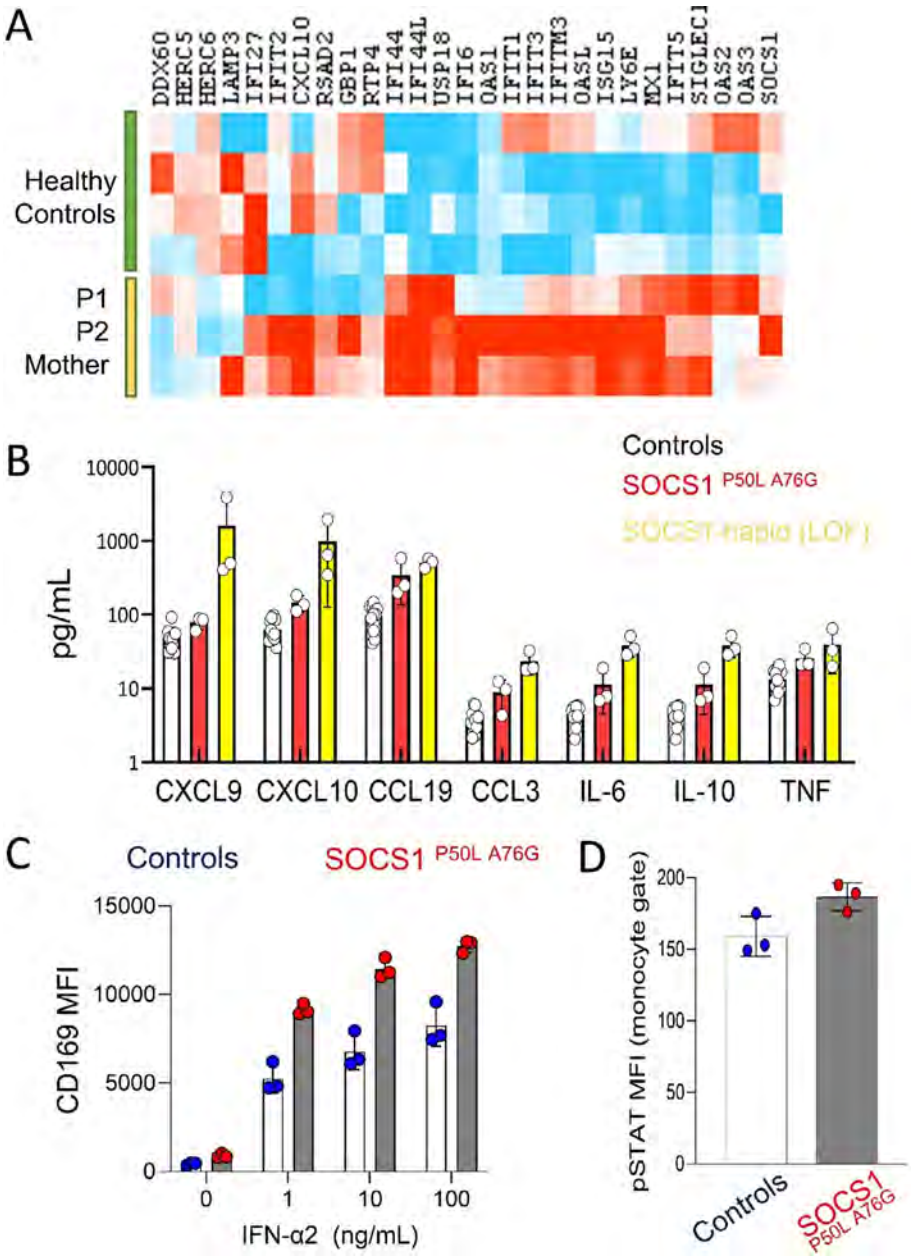

Figure 2. A) Heatmap display of IFN-inducible genes from bulk RNAseq of PBMCs from the healthy controls, probands and their mother. B) Quantification of cytokine and chemokine levels in the plasma of healthy controls, SOCS1 mutant family and SOCS1-haplosufficiency patient by Olink proximity extension assay. C) CD169 expression on CD14+ monocytes 24 hours after stimulation with IFN-2. Three individuals with SOCS1 haploinsufficiency with confirmed loss-of-function variants were included as controls. D) Flow cytometry quantification of phospho-STAT1 in CD14+ monocytes 5 minutes after IFN-2 stimulation.

Disclosure: Y. Du: None; **E. Hsu**: None; **K. Brodeur**: None; **M. Liu**: None; **M. Lo**: None; **C. Platt**: None; **P. Lee**: None.

Abstract Number: 1709

Tape Stripping Expression Signatures Identify Biologically Unique Juvenile Dermatomyositis Patient Subgroup Characterized by Increased Mitochondrial Dysfunction

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Pediatric Rheumatology – Basic Science Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Skin inflammation in juvenile dermatomyositis (JDM) can signal disease onset or flare and prevent complete disease remission. The study of cutaneous expression signatures holds the potential to reveal novel mechanisms underlying disease heterogeneity and organ-specific inflammation. The objectives in this study were to 1) analyze skin tape stripping (TS) transcriptional profiles to identify JDM disease endotypes and 2) compare skin and blood expression signatures.

Methods: We performed TS on non-lesional +/- lesional skin in a JDM cohort (n=28, n=16 with longitudinal sampling, n=77 TS samples). All JDM patients met 2017 EULAR/ACR classification criteria and had standardized clinical disease activity assessments. Paired blood was collected in PAXgene tubes. mRNA was isolated from TS and blood followed by RNAseq. Unsupervised hierarchical clustering was performed to determine molecular JDM subgroups. Differentially expressed genes (DEGs; q-value< 0.01 and absolute log2 fold-change ≥ 1) between subgroups were extracted using TIGR-MeV. Literature-based pathways were explored using Ingenuity Pathway Analysis (IPA). Pathway-based expression scores in skin and blood

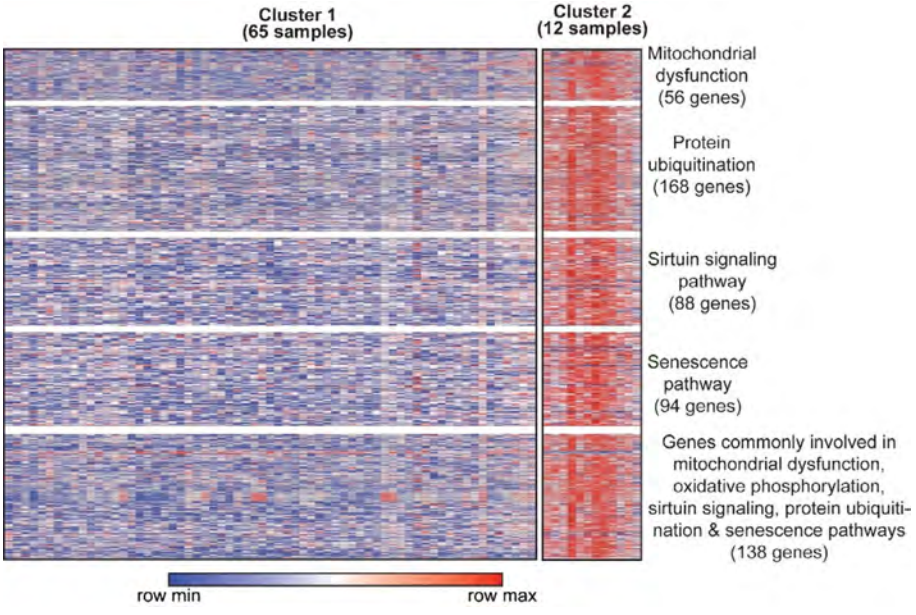

Figure 1. Heatmap of DEGs from top pathways differentiating the two JDM subgroups upon clustering of tape stripping expression profiles.

were calculated (PMID ref: 16947629) and compared between subgroups (t-test; p-value< 0.05). Cell type enrichment analysis was performed using xCell.

Results: We identified two JDM subgroups with distinct TS expression profiles (corresponding to 65 samples (28 patients) in cluster 1 and 12 samples (8 patients) in cluster 2). The two subgroups did not separate by lesional/non-lesional skin, disease duration or activity. However, subgroup 2 represented patients with a higher frequency of chronic disease and more likely to be on steroids. The 6,773 DEGs distinguishing the two subgroups represented pathways involving mitochondrial dysfunction, sirtuin signaling, oxidative phosphorylation, protein ubiquitination and senescence (p-value< 0.0001) (**Figure 1**). *NFE2L2*, a transcription factor involved in response to oxidative stress and innate immune signaling, was the top upstream regulator activated in subgroup 2 (IPA Z-score = 10.74, enrichment p-value = 6.1 E-14). Subgroup 2 demonstrated higher skin-directed interferon, mitochondrial/oxidative phosphorylation dysfunction, angiogenesis and innate immune scores in skin compared to subgroup 1 and controls (**Figure 2, top panel**). Blood as compared to skin-derived pathway scores did not as effectively highlight biological differences in subgroup 2 (**Figure 2, lower panel**). Subgroup 2 also differed from subgroup 1 in potential immune cell populations present in skin, notably with higher xCell scores from CD4 T-cells in subgroup 2 and from B-cells in subgroup 1.

Conclusion: We identified a unique JDM subgroup based on TS expression signatures, with upregulation of genes involved in mitochondrial dysfunction, sirtuin signaling and protein ubiquitination. Interestingly, TS JDM subgroups were distinguished by metabolic in addition to traditional inflammatory pathways. TS performed better than blood in differentiating

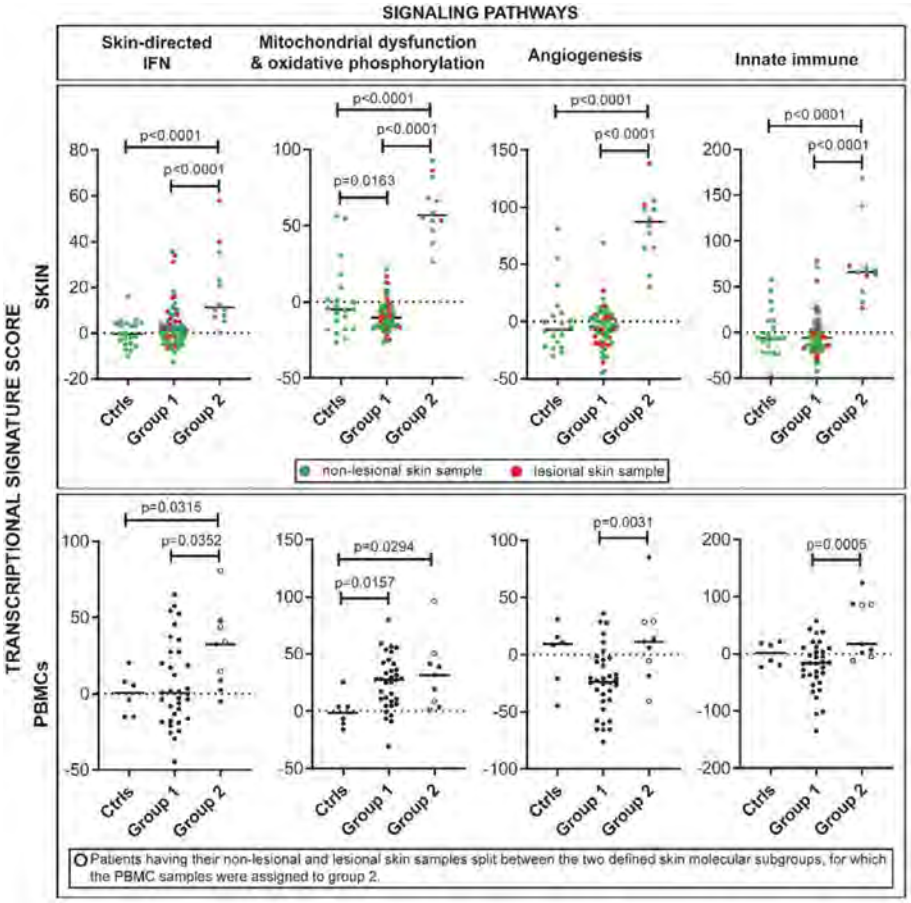

Figure 2. Skin tape stripping (top panel) and blood (lower panel) gene expression scores from selected pathways. Filled green circles represent non-lesional skin samples; filled red circles represent lesional skin samples (top panel); black open circles represent patients with non-lesional and lesional skin samples split between the two defined skin molecular subgroups, for which blood samples were assigned to group 2 (lower panel).

possible mechanisms underlying JDM disease endotypes. Skin-specific transcriptomic signatures may be able to lend insight into precision medicine care in JDM.

Disclosure: J. Turnier: None; **C. Berthier**: None; **S. Vandenbergen**: None; **C. Goudsmit**: None; **M. McClune**: None; **J. Gudjonsson**: Abbvie, 2, 5, Almirall, 2, 5, AnaptysBio, 2, Boehringer Ingelheim, 2, Celgene/BMS, 2, 5, Eli Lilly, 2, 5, Galderma, 2, Janssen, 2, 5, Kyowa Kirin, 5, MiRagen, 2, Novartis, 2, Prometheus Biosciences, 5, Sanofi, 2, SunPharma, 5, TimberPharma, 5; **L. Tsoi**: None; **J. Kahlenberg**: AstraZeneca, 1, Bristol-Myers Squibb(BMS), 2, 5, EMD Serano, 2, exo therapeutics, 2, Gilead, 2, GlaxoSmithKlein(GSK), 1, horizon Therapeutics, 2, Janssen, 5, Pfizer, 2, ROME Therapeutics, 2, 5, Rome Therapeutics, 5, Ventus Therapeutics, 2, 5.

Abstract Number: 1710

Genetic Associations in Juvenile Idiopathic Arthritis Determined with an Electronic Health Record Based Approach

Elizabeth Jasper, Srushti Gangireddy, Henry Ong, Jacklyn Hellwege, Todd Edwards, Digna Velez Edwards, Wei-Qi Wei and **Anna Patrick**, Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile idiopathic arthritis (JIA) encompasses multiple forms of pediatric autoimmune arthritis. Research studies in JIA are complicated by disease heterogeneity and difficulties gathering large numbers of patients for longitudinal studies. Electronic health records (EHRs) store nearly all clinical data in one central location, are used widely across institutions, and are becoming a major source of data for studying diseases in a real-world population with longitudinal data. In this study, we use an algorithm to accurately identify a JIA cohort from an EHR linked to a DNA biobank and perform genetic studies. The goal of this work is to establish a cost-effective method for performing JIA studies in a cohort with longitudinal clinical data.

Methods: A portable algorithm was used to identify JIA patients using a combination of ICD-9-CM and ICD-10-CM codes, age criteria, and exclusion of ICD codes associated with connective tissue disease. Classification of JIA status by the algorithm was compared to true cases as determined by a rheumatology clinic note documenting JIA before 20 years old. Individuals with ICD-9-CM and ICD-10-CM codes for well child visits and without JIA-associated ICD codes or use of disease-modifying and biologic medications used to treat JIA were classified as controls. Identified cases and controls with existing genotype data from a Multi-Ethnic Genotyping Array (MEGA-ex) were included. A genome-wide association study (GWAS), adjusted for 10 principal components, was performed. S-PrediXcan was used to assess associations between JIA and genetically predicted gene expression in placenta and 48 GTEx (v7) tissues. Functional Mapping and Annotation (FUMA) of GWAS was used for annotation of single-nucleotide polymorphisms (SNPs) and to test for enrichment of predefined biological pathways. Significance was determined by a Bonferroni corrected p-value.

Results: The JIA algorithm identified 1,379 cases with a positive predictive value of 0.98 from a cohort of over 3.5 million records. There were 229 cases and 2,798 controls with genotype data. Cases were 68% female and 84% white while controls were 58% female and 48% white. GWAS identified numerous significant SNPs, the majority of which were on chromosome 6. Significant results of note include SNPs previously associated with JIA (rs2395148, rs7775055) (Figure 1). FUMA

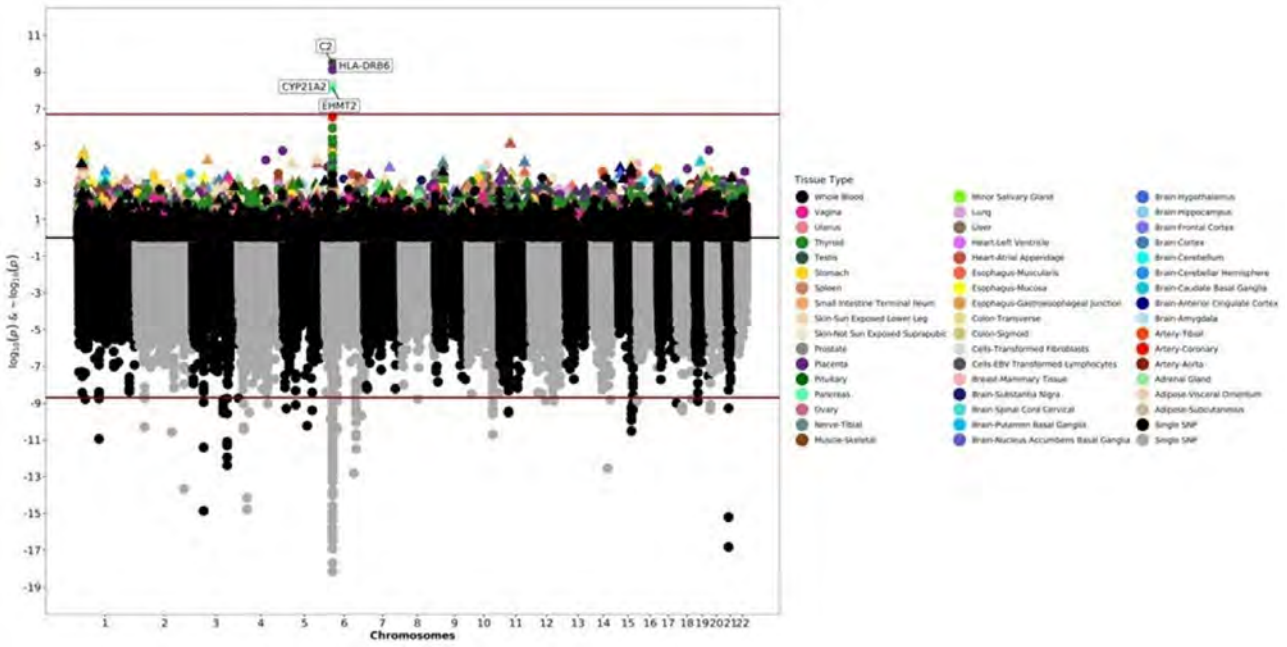

Figure 1. Juvenile Idiopathic Arthritis Miami Plot. The bottom of the graphic is a Manhattan plot which displays significant SNPs from GWAS. The top of the graphic is the results from S-PrediXcan, with symbols now representing entire genes and their genetically determined expression levels. The x-axis are chromosomes. The y-axis is log and negative log p-values from the GWAS and S-PrediXcan analyses. Colors correspond to specific tissues.

analysis identified 29 genomic risk loci and 33 lead SNPs. Canonical pathways, GO biological processes, and GO molecular functions were enriched for important processes in the immune system. S-PrediXcan identified 4 genes (*C2*, *HLA-DRB6*, *CYP21A2*, and *EHMT2*) predicted to be differentially expressed in JIA (Figure 1).

Conclusion: A portable algorithm can identify JIA patients in a real-world cohort with longitudinal clinical data. This phenotype is highly accurate and leads to biologically plausible genetic associations with JIA. This is a cost-effective method for studying JIA and its genetic associations. This approach can be expanded to generate larger cohorts across multiple institutions.

Disclosure: E. Jasper: None; **S. Gangireddy**: None; **H. Ong**: None; **J. Hellwege**: None; **T. Edwards**: None; **D. Velez Edwards**: None; **W. Wei**: None; **A. Patrick**: None.

Abstract Number: 1711

CD14+ Monocytes Demonstrate a Unique Transcriptional Signature in Macrophage Activation Syndrome, Highlighting a Role for Interferons and Identifying Putative Hemophagocytes in Circulation

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SESSION INFORMATION
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Session Title: Pediatric Rheumatology – Basic Science Poster
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Background/Purpose: Macrophage activation syndrome (MAS) is a potentially fatal complication of rheumatic diseases. MAS is characterized by a dysfunctional hyperinflammatory response in which there is abnormal activation of lymphocytes and phagocytes, leading to an overproduction of inflammatory cytokines and damage to host tissues. Circulating monocytes are highly responsive to their surrounding environment, are known to exhibit phenotypic and functional changes during inflammation, and can give rise to macrophages that phagocytose immune cells. However, monocytes and macrophages have not been well-studied in MAS. MAS is most commonly associated with systemic juvenile idiopathic arthritis (sJIA). At least 10% of sJIA patients will experience an overt episode of MAS with up to 50% exhibiting signs of subclinical inflammation.

Methods: We analyzed classical CD14+ monocytes from children with active MAS (6 subjects) compared to individuals with sJIA without MAS (4 subjects) and age/sex/race-matched healthy children (8 subjects) by flow cytometry and RNA sequencing (RNA-Seq). Seven MAS subjects and four age/sex/race-matched healthy controls were analyzed by single cell RNA sequencing (scRNA-Seq). Subjects with MAS were defined based on the 2016 classification criteria by Ravelli and colleagues as well as the ratio of ferritin to ESR.

Results: We found significant upregulation of CD16 surface expression during active MAS using flow cytometry (n=4-8 per group, $p < 0.001$). Our bulk RNA-Seq data show broad transcriptional changes in CD14+ monocytes from children with active MAS, including upregulation of RNase 2 (involved in processing RNAs for the innate immune sensor TLR8) and SLAMF7 (associated with monocyte/macrophage hyperinflammation in response to interferon gamma). scRNA-Seq analyses of myeloid cells from subjects with active MAS revealed a strong interferon signature in MAS monocytes with enrichment of interferon stimulated genes and alarmins. We identified hemoglobin transcripts in monocytes cells from MAS subjects by scRNA-Seq. Cells containing hemoglobin transcripts were also enriched for platelet associated genes (PF4, PPBP, GP9) and genes involved in motility, suggesting the detection of hemophagocytes in circulation.

Conclusion: These data confirm an important role for cytokines, specifically interferons, in driving gene expression in monocytes during MAS and suggest potential targets for future therapies. Together, our data show that CD14+ monocytes have a unique transcriptional signature in MAS and identify putative hemophagocytes in circulation during MAS.

Disclosure: S. Canny: None; **H. DeBerg**: None; **G. Gessay**: None; **A. Lu**: None; **M. Eckert**: None; **A. La Bella**: None; **S. Shenoi**: None; **J. Hui-Yuen**: None; **B. Barnes**: None; **J. Hamerman**: None.

Abstract Number: 1712

Identification and Functional Characterization of Eight CANDLE/PRAAS Causing Proteasome Variants in Five Unrelated Patients

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Pediatric Rheumatology – Basic Science Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Mutations in genes coding for 20S proteasome subunits or proteasome assembly helpers cause chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperatures (CANDLE) or proteasome-associated autoinflammatory syndromes (PRAAS). Patients with CANDLE/PRAAS present with chronically elevated type I interferon scores as consequence of increased proteotoxic stress by mechanisms that are only partially characterized. The purpose of this study is to report and functionally characterize eight disease-causing variants, six of which are novel variants, in four proteasome genes (*PSMA5, PSMC5,PSMB10* and *PSMB8*) in five unrelated patients with CANDLE/PRAAS.

Methods: All patients (Pts) were enrolled into an IRB-approved protocol (NCT02974595). Whole exome sequencing was performed in all patients. Peripheral blood interferon response gene signature was determined by NanoString. The effects of the proteasome variants were investigated by transfection studies in HeLa cells.

Results: The five Pts presented in the first month of life with fever, systemic inflammation, and nodular or annular rash. Skin biopsies showed a neutrophilic dermatosis (Pts1, 2, 4 and 5) or a perivascular lymphocytic infiltrate (Pt3). One patient (Pt1) had additive loss-of-function variants in *PSMB8/*β5i (c.224C >T, p.T75M), and in 2 previously not disease-associated genes, *PSMA5/*α5 (c.502C >T, p.R168*, de novo), and *PSMC5/*Rtp6 (c.1080+1_1080+10del). Four patients had novel compound heterozygous variants in 2 known CANDLE/PRAAS-associated genes, *PSMB8/*β5i *and PSMB10/*β2i. Three Brazilian patients, Pts2-4, had the same *PSMB10/*β2i variant,c.40_42del, p.F14del, in combination with a different variant, c.500G >A p.G167D (Pt2); c.247_248insT, p.C83Lfs*123 (Pt3), and c.710+1G >C (Pt4). Pt5 was compound heterozygous for *PSMB8/*β5i variants c.163C >T, p.Q55* and c.352T >C, p.S118P. Pt1 is in clinical remission on treatment with tofacitinib in combination with tocilizumab; Pt2 responded partially and Pt5 responded fully to tofacitinib; and Pts3 and 4 are in clinical remission on baricitinib. All five patients had a high type I interferon signature in peripheral blood. Transient transfection of mutant constructs *PSMA5/*α5 p.R168*, *PSMB8/*β5i p.Q55* or *PSMB10/*β2i p.C83Lfs*123 into HeLa cells result in mRNA nonsense mediated decay and no protein production, and mutant constructs *PSMB10/*β2i p.G167AD and p.F14del, and *PSMB8/*β5i p.S118P impair cleavage of the pro-peptide and prevent incorporation of the mutant proteasome component. *PSMB10/*β2i c.710+1G >C leads to exon skipping with no incorporation of the mutant protein. All but the *PSMC5/*Rtp6 variant were shown to substantially impact the steady-state expression of the affected proteasome subunits and/or their incorporation into mature 20S and/or 26S proteasomes.

Conclusion: Our observations expand the spectrum of CANDLE/PRAAS-causing genetic variants and will improve molecular diagnosis and genetic counseling of patients with autoinflammation.

This study was supported in part by the Intramural Research Program of NIAID, NIH.

Disclosure: A. Almeida de Jesus: None; **J. Papendorf**: None; **F. Ebstein**: None; **S. Alehashemi**: None; **D. Pioto**: None; **A. Kozlova**: None; **M. TErreri**: None; **A. Shcherbina**: None; **A. Rastegar**: None; **M. Rodrigues**: None; **R. Pereira**: None; **S. Park**: None; **B. Lin**: None; **K. Uss**: None; **A. da Silva Pina**: None; **F. SZTAJNBOK**: None; **S. Torreggiani**: None; **J. Stoddard**: None; **J. Niemela**: None; **S. Rosenzweig**: None; **A. Fonseca**: None; **M. De Guzman**: None; **N. Micheloni**: None; **M. Fraga**: None; **S. Perazzio**: None; **R. Goldbach-Mansky**: None; **E. Krueger**: None.

Abstract Number: 1713

Prevention of Arthritis Development by Mechanical Unloading Through Inhibition of CCL2 and YAP-mediated Inflammation in the Rat Adjuvant-induced Arthritis Model

Elisa Dalix[1], Mathieu Maalouf[1], Robin Caire[2], Guillaume Courbon[1], Virginie Dumas[3], Sylvie Peyroche[1], Marie-Thérèse Linossier[1], Mireille Thomas[1], Charles-Antoine Arthaud[1], Arnaud Vanden-Bossche[1] and Hubert Marotte[4], [1]Université Jean Monnet Saint-Étienne, Mines Saint-Etienne, INSERM, Saint-Etienne, France, [2]Department of Molecular Medicine, University of Padua School of Medicine, Padua, Italy, [3]Laboratory of Tribology and Systems Dynamics, Ecole Nationale d'Ingénieurs de Saint Etienne, Ecole Centrale de Lyon, University of Lyon, Saint-Etienne, France, [4]CHU Saint-Etienne, Saint-Etienne, France

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

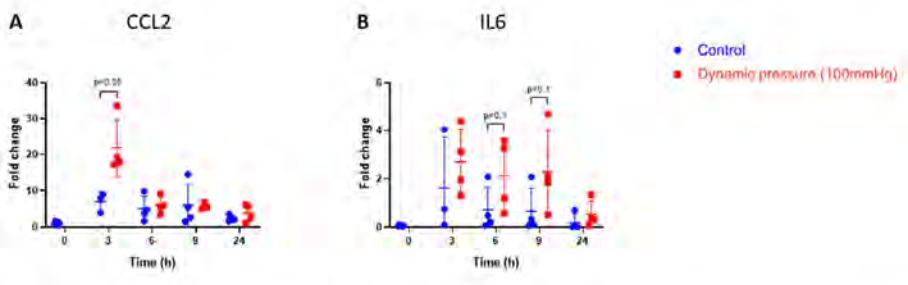
Session Title: RA – Animal Models Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

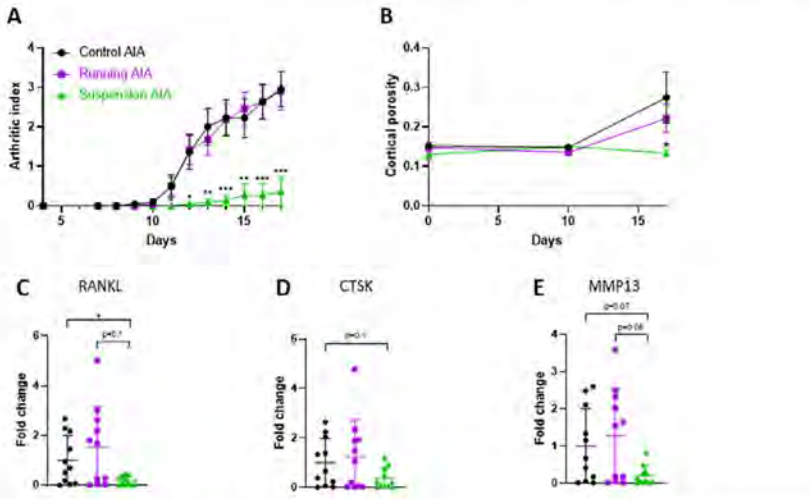
Background/Purpose: Rheumatoid arthritis (RA) is the most common chronic inflammatory rheumatic disease, characterized by synovitis associated with progressive bone loss and joint degradation. The adjuvant-induced arthritis (AIA) model mimics the pathophysiological features of RA, with high prevalence and reproducibility. Yes-associated protein (YAP) is a transcription factor involved in inflammatory signaling and arthritis progression, especially by driving the RA fibroblast-like synoviocyte (FLS) phenotype. Beyond inflammation sensing, YAP responds to mechanical stimuli. The inhibition of YAP transcriptional activity decreases arthritis in the AIA model. The objective of this study was then to investigate the effect of mechanical loading or unloading on arthritis.

Figure 1. Mechanical stress induced expression of pro-inflammatory mediators in RA organoids.



RA organoids (n=3-4 patients) were submitted to a continuous dynamic compressive force (100 mmHg) or not (control) at different times (0, 3, 6, 9 and 24h). CCL2 (A) and IL6 (B) expression were normalized by HPRT and by average of control group at 0h. Wilcoxon's tests showed no significant difference between control and dynamic pressure groups.

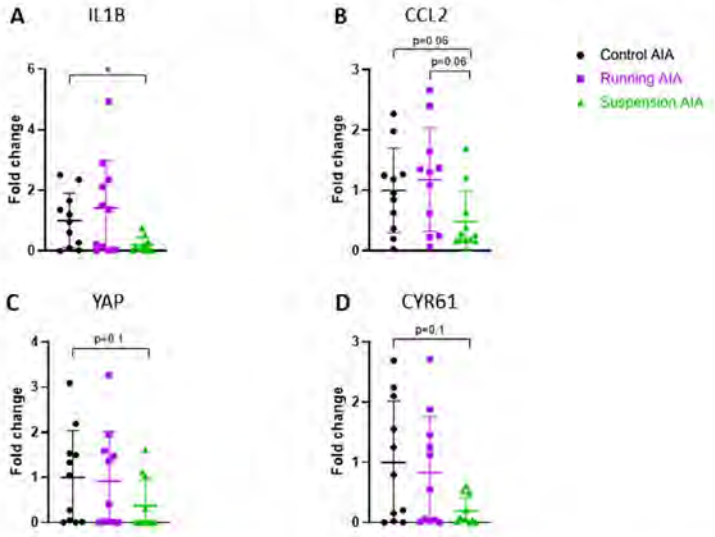
Figure 2. Mechanical unloading decreased arthritis severity and bone loss in AIA model.



Progression of arthritic index (A) and cortical porosity of the navicular bone (B) over time. Expression of RANKL (C), CTSK (D) and MMP13 (E) in the ankle of control, running and suspended AIA rats at day 17. Wilcoxon's tests were performed: *p<0.05 **p<0.01,***p<0.001. *RANKL: RANK ligand, CTSK: Cathepsin K.*

Methods: For *in vitro* studies, a compressive dynamic pressure (100mmHg) was applied on RA FLS organoids. For *in vivo* studies, mechanical loading (voluntary running), unloading (tail suspension) or no mechanical stress (control) was applied in AIA rats (n=11/group), from arthritis induction (day[D]0) until D17. Running rats only ran (1.5km/day) from D0 to D10, which is the arthritis onset in the AIA model. Daily clinical monitoring was assessed to follow the severity of arthritis. *In vivo* μ-computed tomography was realized to follow arthritis-induced bone loss.At D10 or D17, the ankles of the rats were collected to perform RT-qPCR. At D17, blood samples were collected to perform protein dosages.

Figure 3. Mechanical unloading decreased inflammation and YAP activity in AIA model.



Expression of IL1B (A), CCL2 (B), YAP (C), and CYR61 (D) in the ankle of control, running and suspended rats at day 17. were normalized by HPRT and by average of control group. Wilcoxon's tests were performed. *YAP: Yes-associated protein.*

Results: In RA organoids, mechanical stress was able to induce inflammation by increasing IL6 and CCL2 expression (Figure 1). Surprisingly, YAP transcriptional activity remained unchanged in response to mechanical stress in RA organoids. In AIA rats, CCL2 expression is increased before arthritis onset, but also during and after the peak of inflammation (D17), independently from YAP activity. In AIA rats, the control and running groups displayed the same disease onset (D10) and progression, with similar arthritis index and ankle circumference over time (Figure 2). No difference in expression of bone degradation markers (RANK ligand, Cathepsin K, MMP9, and MMP13) was observed in joint at D17 between the control and running groups (Figure 2) and pro-inflammatory mediators (IL6, IL1B, TNF, and CCL2) (Figure 3). However, the expression of pro-inflammatory mediators and bone degradation markers trended to increase in the running AIA rats joint at D10. The suspension prevented arthritis development with a decreased expression of bone degradation markers (Figure 2) and pro-inflammatory mediators in the joint at D17 (Figure 3). Moreover, arthritis-induced bone loss was inhibited in the suspension group, where cortical porosity and trabecular volume remained similar to baseline.YAP transcriptional activity also trended to decrease.

Conclusion: In conclusion, two independent mechanisms could be involved in arthritis in response to mechanical stress, one mediated by YAP and the other involving CCL2. Mechanical unloading might then prevent arthritis by decreasing YAP activity and CCL2 production. A high level of CCL2 might then increase arthritis severity by inducing inflammation at arthritis onset, leading to an increase in YAP activity and joint degradation.

Disclosure: E. Dalix: None; **M. Maalouf**: None; **R. Caire**: None; **G. Courbon**: None; **V. Dumas**: None; **S. Peyroche**: None; **M. Linossier**: None; **M. Thomas**: None; **C. Arthaud**: None; **A. Vanden-Bossche**: None; **H. Marotte**: None.

Abstract Number: 1714

Aberrant Myeloid Populations in the TNF-Transgenic Model of Pulmonary Hypertension Overexpress Interferon Pathways and Are Driven by TNFR1 Signaling

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Animal Models Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Pulmonary hypertension (PH) is a severe, progressive disorder characterized by elevated pulmonary artery pressures, right ventricular hypertrophy, and increased mortality. We previously demonstrated that TNF-transgenic (TNF-Tg) mice develop a severe PH phenotype and that deficiency of TNFR1 reversed this pathology. To explore the roles of immune cells contributing to PAH in TNF-Tg mouse model, we assessed single-cell RNA expression of immune cells in TNF-Tg mice crossed with mice lacking TNFR1 or TNFR2.Because we saw dramatic shifts in myeloid populations, we focused on characterizing the abnormal monocytes and macrophages present in TNF lungs.

Methods: TNF-Tg mice were crossed with mice deficient in either TNFR1(TNFR1KO) or TNFR2 (TNFR2KO). Lungs from wild type, TNF-Tg, TNF-Tg-TNFR1KO and TNF-Tg-TNFR2KO mice (n = 5–6) at 4.5 months of age were harvested and digested to a single cell suspension for single cell RNA sequencing (scRNAseq). The library was prepared using 10X Genomics Chromium instrument and sequencing was performed on Illumina NovaSeq6000. scRNAseq reads were examined for

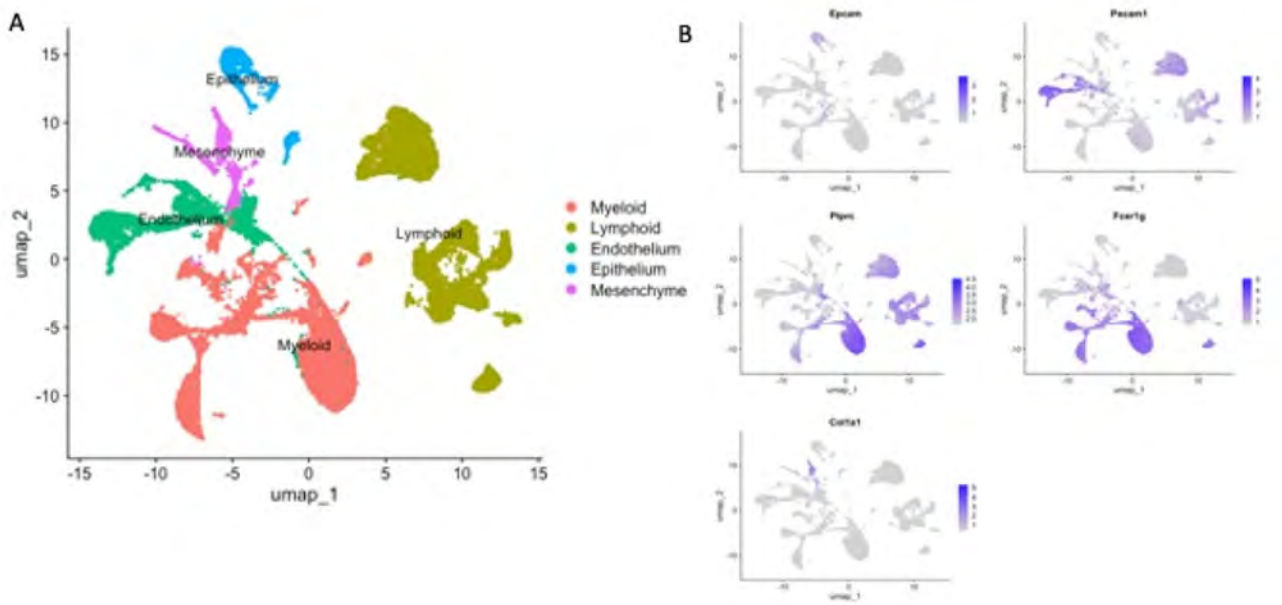

Figure 1. Cellular composition of major cell types in mouse lung. A. UMAP projection of all scRNA-seq data, showing 5 major cell groups that were identified. B. Feature plots identifying canonical markers of epithelial (Epcam), endothelial (Pecam1), mesenchymal (Col1a1), myeloid (Ptprc, Fcer1g) and lymphoid (Ptprc+, Fcer1g-) cells populations.

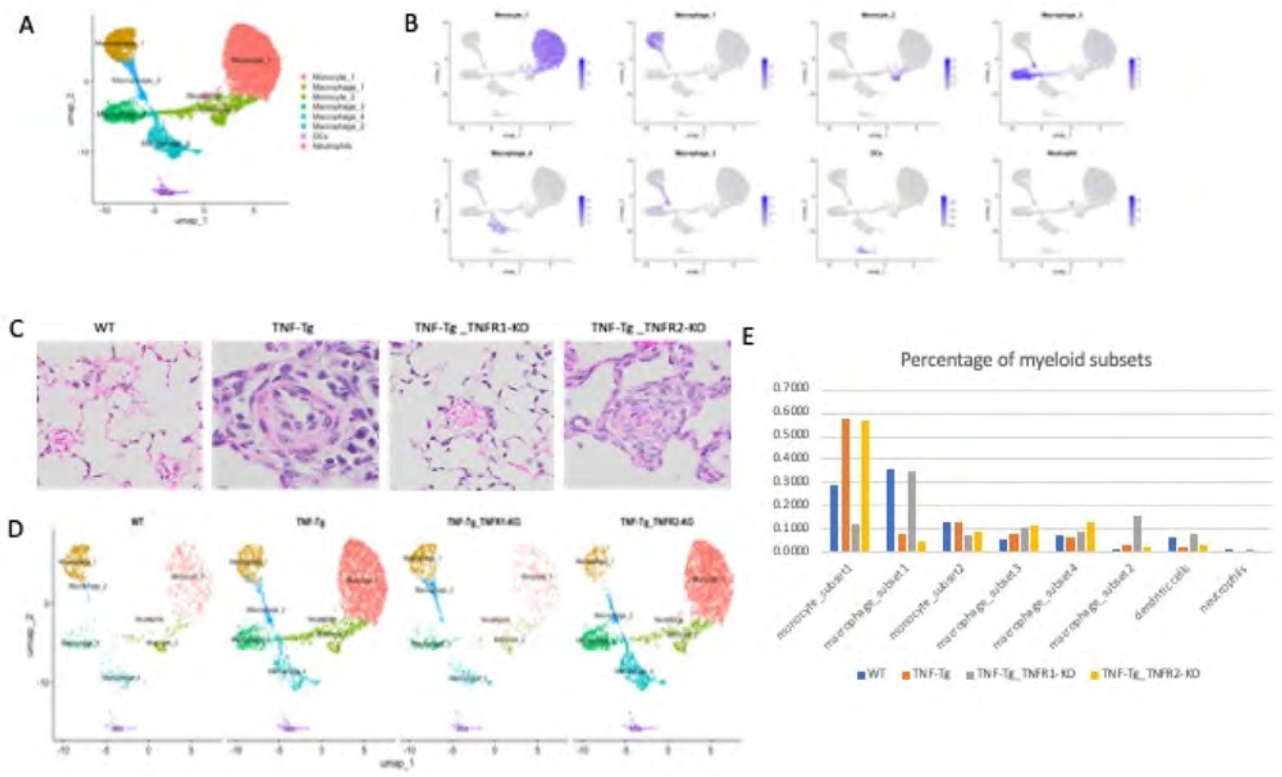

Figure 2. Cellular composition of myeloid cells identified in mouse lung from TNF-Tg and TNF receptor deficient mice. A. A total of eight clusters of myeloid cells were identified from mice across all genotypes. Cell populations are colored as indicated by legend. B. Feature plots showing expression of principal identifiers of different myeloid cell types. C. Lung histology images demonstrated that TNF-Tg and TNF-Tg_TNFR2-KO mice, but not WT and TNF-Tg_TNFR1-KO mice have pulmonary inflammation and vascular occlusion. D. UMAP plots myeloid subsets in TNF-Tg mice with and without TNF receptor deficiency. Cell populations are colored as indicated by legend. E. Proportion of myeloid subsets across genotypes.

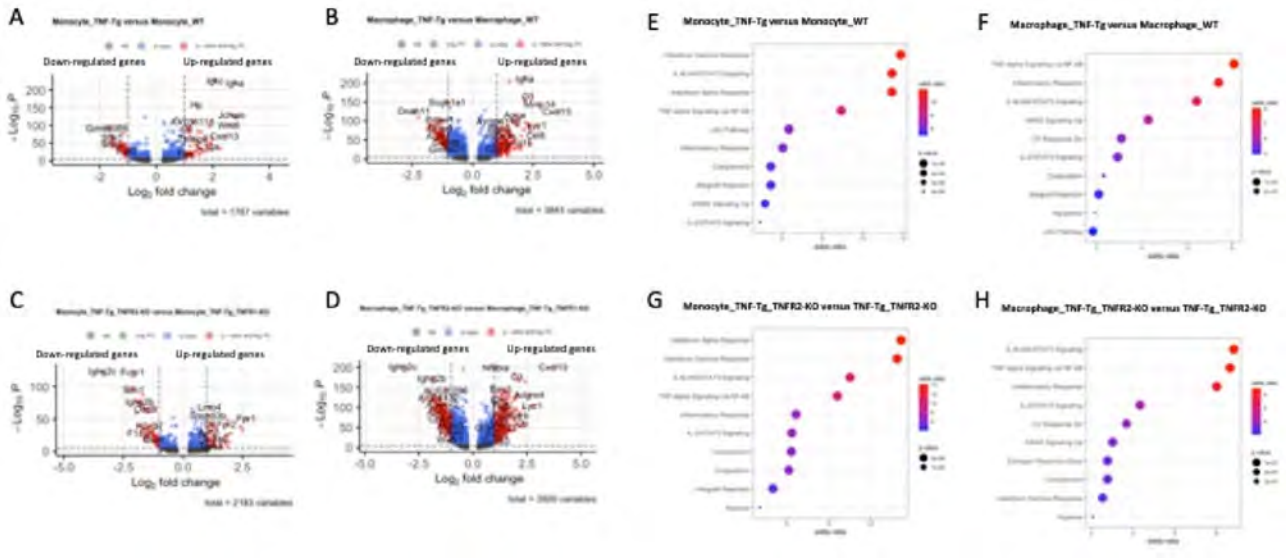

Figure 3. Differential expression (DE) analysis of genes and pathways in monocytes and macrophages. A-B. Volcano plot showing the differentially expressed genes in monocytes and macrophage between TNF-Tg and WT mice. C-D. Volcano plot showing the differentially expressed genes in monocytes and macrophage between TNF-Tg_TNFR2-KO and TNF-Tg_TNFR1-KO mice. E-F. Pathway analysis in monocytes. G-H. Pathway analysis in macrophages. MSigDB_Hallmark_2020 database was used for analysis. Dot plots identify pathways in descending significance of p-value (dot size) and odds-ration (color).

quality and mapped to reference mouse genome. The resulting scRNAseq data was analyzed with Seurat v.4.9. Differential expression and pathways analysis were performed and visualized using Seurat and R packages enrichR and Enhanced Volcano.

Results: Cells were clustered based on their expression profiles and cell types were annotated based on established cell markers from Lung Map and the published literature. A total of 40 clusters were identified, corresponding to 5 major cell groups (Fig 1.A-B): epithelial (*Epcam*$^{+}$), endothelial (*Pecam1*$^{+}$), mesenchymal (*Col1a1*$^{+}$), lymphoid (*Ptprc*$^{+}$), and myeloid (*Ptprc*$^{+}$ and *Fcer1g*$^{+}$). We observed dramatic changes in cellular composition of myeloid cells between WT and TNF-Tg, and TNF-Tg_TNFR1-KO and TNF-Tg_TNFR2-KO. We focused on myeloid cells and re-clustered these cells to identify 7 myeloid cell types (2 monocytes subsets, 4 macrophage subsets, neutrophils, and dendritic cells) were identified (Fig 2. A-B). Among the myeloid cells, monocytes and macrophages account for the dramatic changes in cellular composition. Moreover, WT and TNF-Tg-TNFR1KO mice shared the similar cellular composition, and TNF-Tg and TNF-Tg-TNFR2KO mice shared the similar cellular composition (Fig 2.D), which was consistent with the whole cellular composition in 4 mouse groups and lung histology (Fig 2.C). We next performed differential expression analysis in monocytes and macrophages (Fig 3. A-D). In monocytes, interferon responses and complement signaling were significantly differentially expressed in both TNF-Tg and TNF-Tg_TNFR2-KO mice. In macrophages, a majority of pathways related to TNF-mediated NK-kB signaling pathways and JAK/STAT signaling in TNF-Tg and TNF-Tg_TNFR2-KO mice (Fig 3. E-H).

Conclusion: Overexpression of TNF results in significant shifts in cellular composition of pulmonary myeloid cells. TNFR1 signaling is primarily responsible for these changes. Pathway analysis suggests that lung monocyte-mediated interferon responses contribute to the pathogenesis of PH.

Disclosure: G. Wang: None; **Q. Xu**: None; **S. Duemmel**: None; **B. Korman**: Teneofour, Inc, 2.

Abstract Number: 1715

Androgen Treatment Exhibits a Protective Role Against Focal Erosions in TNF-Induced Inflammatory Arthritis in Mice

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Animal Models Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is characterized by chronic joint inflammation and bone erosion and is female predominant. The TNF-transgenic (TNF-Tg) murine model of RA develops inflammatory erosive arthritis and displays a sex difference in disease severity, with females having worse disease than males (1). Studies suggest androgens provide a protective effect against joint disease and TNF-mediated bone erosion (2). We have previously shown that the removal of endogenous sex hormones in TNF-Tg males significantly worsens their inflammatory erosive disease. Here, we investigated whether treatment of TNF-Tg mice with exogenous androgen ameliorates erosive disease.

Methods: TNF-Tg male mice were orchiectomized followed by subcutaneous implantation of either 5α-dihydrotestosterone (DHT) or placebo pellet at 1-month old (n = 3/group). Pellets released 1.5mg of DHT or placebo for 60 days (0.025mg/day). Micro-computed tomography (μCT) scans of hindpaws were taken at 3-months old and compared with μCT data of same age intact TNF-Tg males (n = 4-6 paws/group). The total bone volumes (mm^3) of the cuboid, talus, navicular and lateral intermediate cuneiform, and periarticular metatarsals were compared between groups. Deformation scores of the paws and weights were taken weekly from 1 to 3 months old. Same age sham TNF-Tg male mice weekly weights were compared between orchiectomized groups. Serum and paws were obtained for analysis and histology. Values are reported as the mean +/- standard deviation.

Results: Segmented hindpaw images showed bone erosion occurring in the periarticular regions of the metatarsals (Fig 1 A-C). Placebo-treated orchiectomized mice had significantly more bone volume loss than DHT-treated orchiectomized mice and intact mice in the cuboid (0.34 ± 0.03 Orchiectomized + Placebo; 0.43 ± 0.02 Orchiectomized + DHT; 0.43 ± 0.06 Intact), talus (0.97 ± 0.09 Orchiectomized + Placebo; 1.10 ±0.06 Orchiectomized + DHT; 1.21 ± 0.07 Intact), navicular and lateral intermediate cuneiform (0.78 ± 0.04 Orchiectomized + Placebo; 0.87 ± 0.03 Orchiectomized + DHT; 0.94 ± 0.04 Intact), and distal metatarsals (0.23 ± 0.05 Orchiectomized + Placebo; 0.28 ± 0.07 Orchiectomized + DHT; 0.27 ±0.07 Intact) (Fig 1D-H). Orchiectomized mice with placebo had significantly higher mean deformation scores at 4 weeks post-surgery (p = 0.03) (Fig 2A). Orchiectomized mice also gained significantly less weight than sham TNF-Tg mice by 6 weeks post-surgery (p = 0.03). DHT treatment of orchiectomized mice resolves that weight loss over time (Fig 2B).

Conclusion: Androgen treated orchiectomized arthritic mice had significantly improved bone volumes, limiting bone erosion even in the presence of ongoing inflammation**.** Clinical measures of weight loss and arthritis also improve with androgen treatment. These finding suggests sex hormones have a relationship with the immune system in inflammatory-erosive disease that warrants further study. Histological analysis of the paws and osteoclastogenic cultures of bone marrow are ongoing to delineate the mechanism of androgen effects on inflammation.

1. Bell R.D. et al. *Arthritis Rheumatol* 71(9): 1512-1523. 2019. 2. Traish A et al. *J Clin Med* 7(12): 549. 2018.

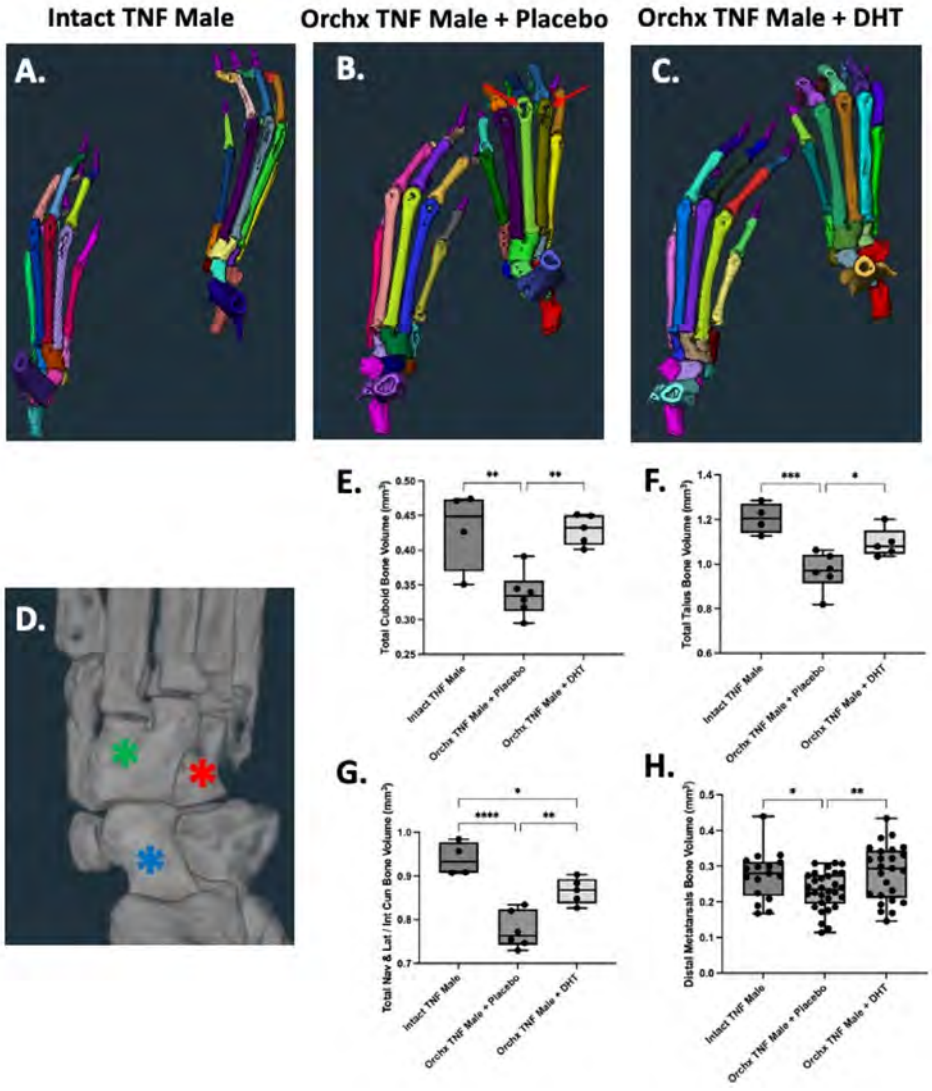

Figure 1. DHT Decreases Bone Erosions in Orchiectomized TNF-Tg Mice. μCT imaged hindpaw bones were segmented using Amira to determine total bone volume (mm3). Mice were divided into three groups (n = 4-6 paws/group), intact mice (A), orchiectomized (orchx) mice treated with placebo (B) and orchx mice treated with DHT (C). The cuboid (D, red asterisk), talus (D, blue asterisk), and navicular and lateral intermediate cuneiform (D, green asterisk) bone volumes were compared between groups. Orchiectomized mice treated with placebo were found to have significantly greater bone loss due to bone erosion in the cuboid (E), talus (F), navicular and lateral intermediate cuneiform (G) compared to the other cohorts. Placebo treated orchiectomized mice also had significantly less bone volume in the distal ends of the metatarsals that showed periarticular erosions reminiscent of erosions seen in RA patients (B, arrows; H). Orchiectomized mice treated with DHT had significantly greater bone volumes than orchiectomized mice treated with placebo, exhibiting that DHT treatment decreases bone erosion. Mid-hindpaw bone volume analysis was performed using a one-way ANOVA with Tukey's multiple comparisons. Metatarsal bone volume analysis was performed using a one-way ANOVA with Fisher's LSD test. * = $p<0.05$; ** = $p<0.01$; *** = $p<0.001$; **** = $p<0.0001$.

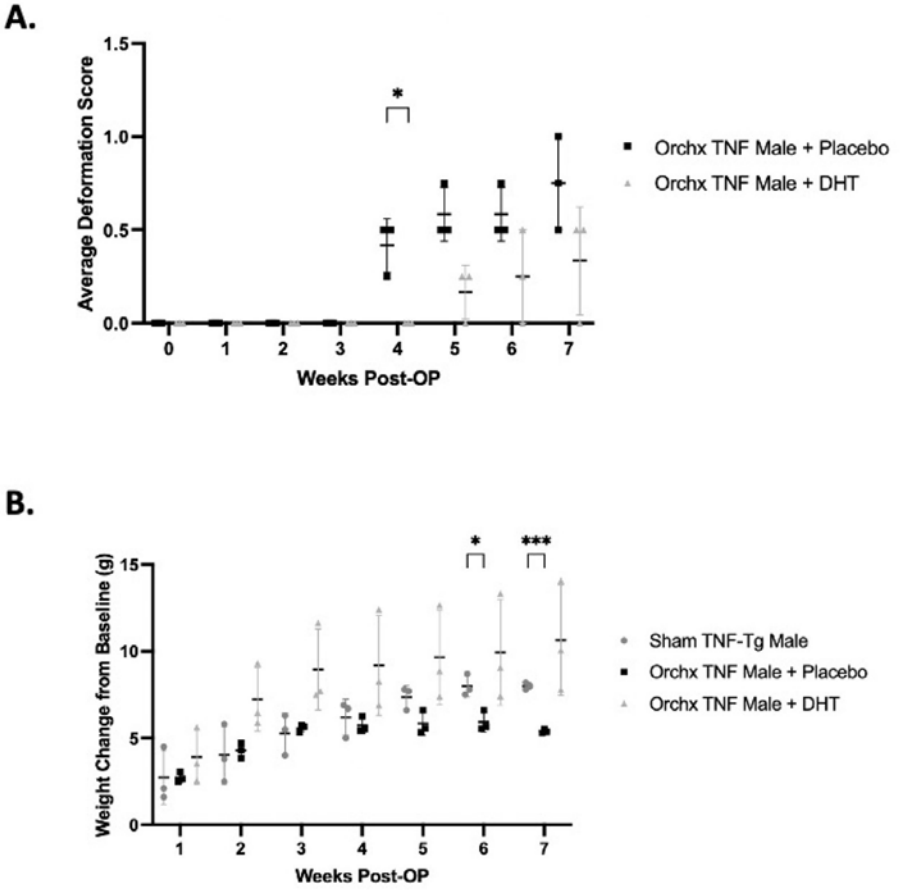

Figure 2. DHT-Treated Orchiectomized TNF-Tg Mice have Improved Clinical Measures of Disease. Orchiectomized mice treated with placebo and orchiectomized mice treated with DHT had weekly deformation scoring of their paws after surgery (n = 3 mice/cohort) (A). There was a significant difference in the average deformation score at week 4 post-op, signifying that orchiectomized mice treated with placebo displayed paw inflammation earlier than mice treated with DHT. Orchiectomized TNF-Tg mice treated with placebo, orchiectomized TNF-Tg mice treated with DHT, and sham TNF-Tg mice were also weighed weekly after surgery. The weight change from the baseline week (week 0) was compared between cohorts (B). Orchiectomized mice has significantly less weight gain than sham TNF-Tg mice by week 6 post-op. DHT treatment of orchiectomized mice ameliorates this weight loss over time. Average deformation score analysis was performed with multiple unpaired t-tests. Weight analysis was performed with a two-way ANOVA with Tukey's multiple comparisons. * = $p<0.05$, *** = $p<0.001$.

Disclosure: K. Chen: None; **A. Weidner**: None; **O. Astapova**: None; **E. Schwarz**: None; **H. Rahimi**: None.

Abstract Number: 1716

High-Throughput Semi-Automated Micro-CT Analysis Identifies the Cuboid Bone as a Sex-Dependent Biomarker of Inflammatory-Erosive Arthritis in TNF-Tg Mice

H. Mark Kenney[1], Kiana Chen[2], Lindsay Schnur[3], Jeffrey Fox[3], Ronald Wood[3], Lianping Xing[4], Christopher T Ritchlin[5], Homaira Rahimi[6], Edward Schwarz[6] and Hani Awad[3], [1]University of Rochester School of Medicine and Dentistry, Henrietta, NY, [2]University of Rochester School of Medicine and Dentistry, Rochester, NY, [3]University of Rochester Medical Center, Rochester, NY, [4]University of Rochester Medical Center, Webster, NY, [5]University of Rochester Medical School, Allergy, Immunology & Rheumatology Division, Canandaigua, NY, [6]University of Rochester, Rochester, NY

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Animal Models Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Development of reliable disease activity biomarkers is critical for diagnostics, prognostics, and novel drug development. In the case of preclinical models of inflammatory-erosive arthritis, such as sexually dimorphic tumor necrosis factor transgenic (TNF-Tg) mice (1), disease severity is routinely quantified in the ankle through manual segmentation of the talus or small regions of adjacent bones primarily due to the ease in measurement (2,3). Herein, we sought to determine the particular hindpaw bones that represent reliable biomarkers of sex-dependent disease progression to guide future investigation and analysis.

Methods: Hindpaw micro-computed tomography (μCT) was performed on wild-type (n=4 male, n=4 female) and TNF-Tg (n=4 male, n=7 female) mice at monthly intervals from 2-5 (females) and 2-8-months (males) of age, where female TNF-Tg mice exhibit early mortality from cardiopulmonary disease at approximately 5-6-months (1). For image analysis, we utilized our recently developed high-throughput and semi-automated segmentation strategy in Amira software (v2020.2) (4). Synovial (H&E-OG) and osteoclast (TRAP) areas of ankle joints were quantified using Visiopharm (v2021.07).

Results: First, we demonstrated our analysis method had comparable automated segmentation accuracy in wild-type and TNF-Tg hindpaws before correction (79.2±8.9% vs 80.1±5.1%, *p=0.52*), determined through analysis of ~9000 individual bones by a single user, with representative μCT (left) and bone segmentation (right) provided **(Fig. 1A-D)**. Compared to other bone compartments, the tarsal region demonstrated a sudden, specific, and significant bone volume reduction in female TNF-Tg mice by 5-months **(Fig. 1E-J)**. This sexual dimorphism was associated with unique bone-specific changes across time, as the cuboid at 4-months of age showed significantly reduced bone volumes compared to all other tarsals. In contrast, TNF-Tg male mice exhibited no difference between individual bone volumes at this timepoint **(Fig. 2A-F)**. Compared to bones with limited erosions (i.e., tibiale), the cuboid showed a corresponding increased synovial and TRAP area **(Fig. 2G-P)**. At 5-months of age, additional bones localized to the antero-lateral region of the ankle were also responsible for the dramatic erosions in the tarsal region of females **(Fig. 3A-F**, red stars), coinciding with increased $TRAP^{+}$ osteoclasts in female vs male TNF-Tg mice **(Fig. 3G-K)**.

Conclusion: Taken together, here we demonstrated that sexual dimorphism of arthritis in TNF-Tg mice is bone-specific, where the cuboid serves as a reliable biomarker of erosive arthritis with the greatest sensitivity to early and consistent bone loss related to enhanced osteoclast numbers. Ongoing work will further investigate the cellular mechanisms of these bone-specific erosions in mice and evaluate the translational potential of these biomarkers in arthritis patients through our segmentation model. 1. Bell et al. *Arthritis Rheumatol*. 71(9):1512-1523. 2019. 2. Proulx et al. *Arthritis Rheumatol*. 56(12):4024-4037. 2007. 3. Cambre et al. *Nat Commun*. 9(1):4613. 2018. 4. Kenney et al. *Bone Rep*. 16(101167). 2022.

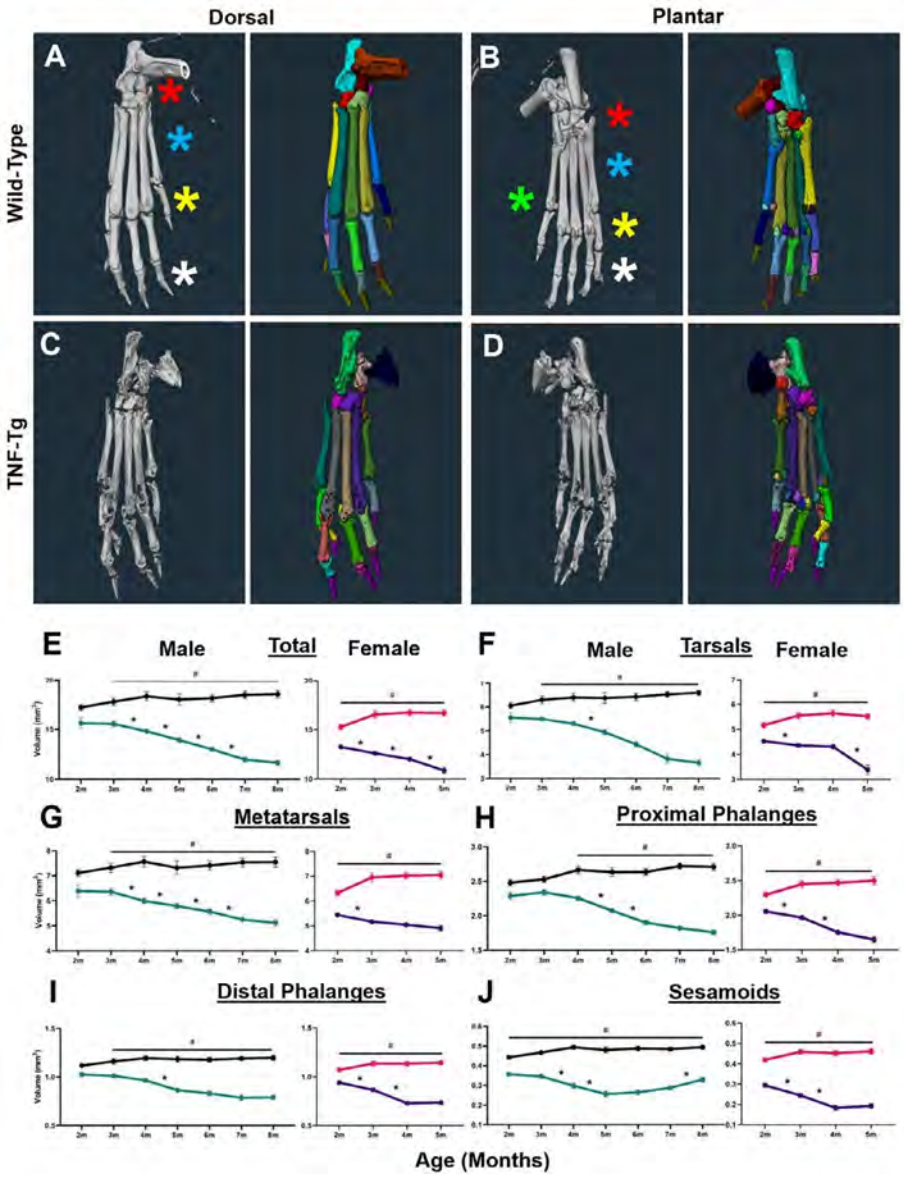

Figure 1. Semi-automated segmentation of TNF-Tg hindpaws reveals unique temporal patterns of erosions by bone compartment in female mice. To evaluate bone-specific erosions in the TNF-Tg mouse model of inflammatory-erosive arthritis, we utilized our recently published high-throughput semi-automated hindpaw segmentation protocol (4). Representative images of the dorsal and plantar surfaces of hindpaw micro-CT images (left) and the segmentation of each bone indicated by unique colors (right) are provided for wild-type (A, B) and TNF-Tg (C, D) male mice at 8-months of age. Without user intervention, the semi-automated protocol produced accurate segmentations of approximately 80% of bones in wild-type datasets (error rate ~20%), which remarkably remains consistent, and potentially improved due to reduced variance, for TNF-Tg mice with bone erosions. Patterns of bone loss in hindpaw compartments (shown in A, B: tarsals, red star; metatarsals, blue; proximal phalanges, yellow; distal phalanges, white; and sesamoids, green) were analyzed for temporal and genotype effects. Although both TNF-Tg males and females exhibited consistent bone loss across time (E, *$p<0.05$), TNF-Tg females showed unique time-dependent erosions by particular compartments. For TNF-Tg females, there was a dramatic decrease in the bone volume of the tarsals between 4-5-months of age (F) that was preceded by early erosions starting at 2-months of age in the bones associated with the phalanges that was not sustained past 4-months (G-J). In contrast, males showed relatively slow progression of erosions with limited statistical change for particular compartments at monthly intervals, except for the metatarsals (F-J). Also note the "U"-shaped progression of bone volumes in the TNF-Tg male sesamoids, likely representing reactive bone remodeling following an initial period of erosions (J). Compared to wild-type, both TNF-Tg male and female mice showed significantly reduced bone volumes in all compartments starting at 3-months and 2-months of age, respectively (#$p<0.05$). Statistics: 2-way ANOVA (males) and mixed-effects analysis (females) with Tukey's multiple comparisons (E-J).

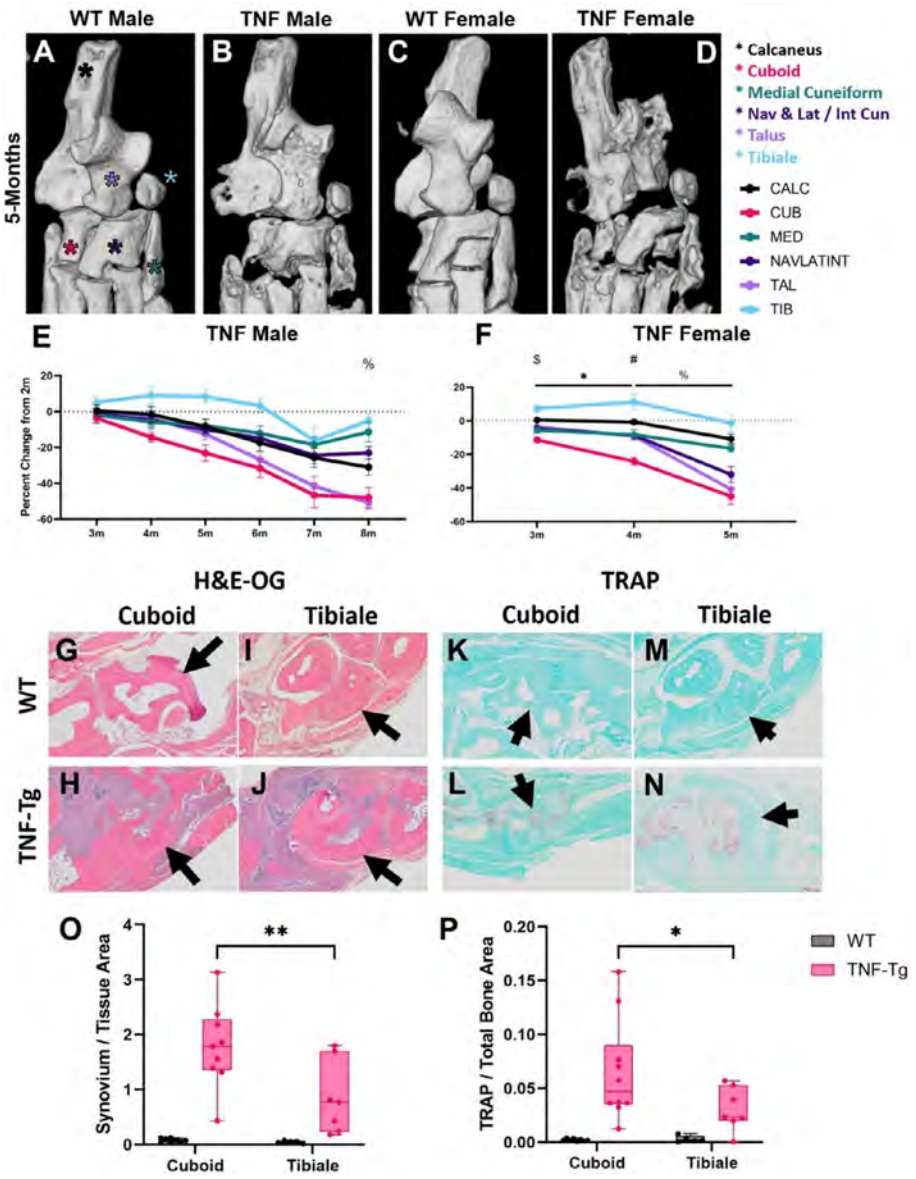

Figure 2. The cuboid is an early biomarker of erosive arthritis in TNF-Tg female mice. To further elucidate the dynamic sex-dependent, bone-specific, and temporal changes in the tarsals of TNF-Tg mice, we directly compared erosive activity between each tarsal bone to determine their biomarker potential during progression of inflammatory arthritis. High-magnification images of the tarsal compartment at 5-months of age, with the individual bones indicated by stars (calcaneus, black; cuboid, pink; medial cuneiform, green; fused navicular, lateral and intermediate cuneiform [a known C57BL/6 murine variant (4)], dark purple; talus, light purple; and tibiale, blue), are shown for each group (A-D). In order to compare the individual bones, percent change in bone volume from their baseline at 2-months was calculated to control for the differences in bone size. TNF-Tg males exhibited no significant difference in erosions between individual bones in the tarsal region, except for the tibiale, which showed a resistance to erosions compared to all other bones, except the medial cuneiform (% $p<0.05$) (E). In contrast, TNF-Tg females exhibited early erosive activity localized specifically to the cuboid bone with significantly reduced bone volumes compared to the other bones in the tarsal region by 3- and 4-months of age ($ cuboid vs all bones except medial cuneiform, # cuboid vs all bones, $p<0.05$). In addition, significant decreases in bone volume over time from 3- to 4-months of age were noted only in the cuboid and fused navicular, lateral cuneiform and intermediate cuneiform (* $p<0.05$). All bones, except for the tibiale, showed significantly reduced bone volumes from 4- to 5-months of age (% $p<0.05$), explaining the time-dependent erosions of the tarsal compartment during this timeframe, noted in Fig. 1 (F). To understand the cellular mechanisms mediating resistance (i.e., tibiale) and susceptibility (i.e., cuboid) to erosions, we histologically assessed and quantified the amount of synovium (H&E-OG) and osteoclasts (TRAP) surrounding these particular bones (arrows). Compared to the tibiale, the cuboid exhibited both increased synovial infiltrate (G-J, purple) and TRAP+ osteoclasts (K-N, red), likely involved in mediating the bone-specific erosions (G-P). Statistics: 2-way ANOVA (E, O, P) and mixed effects analysis (F) with Tukey's multiple comparisons.

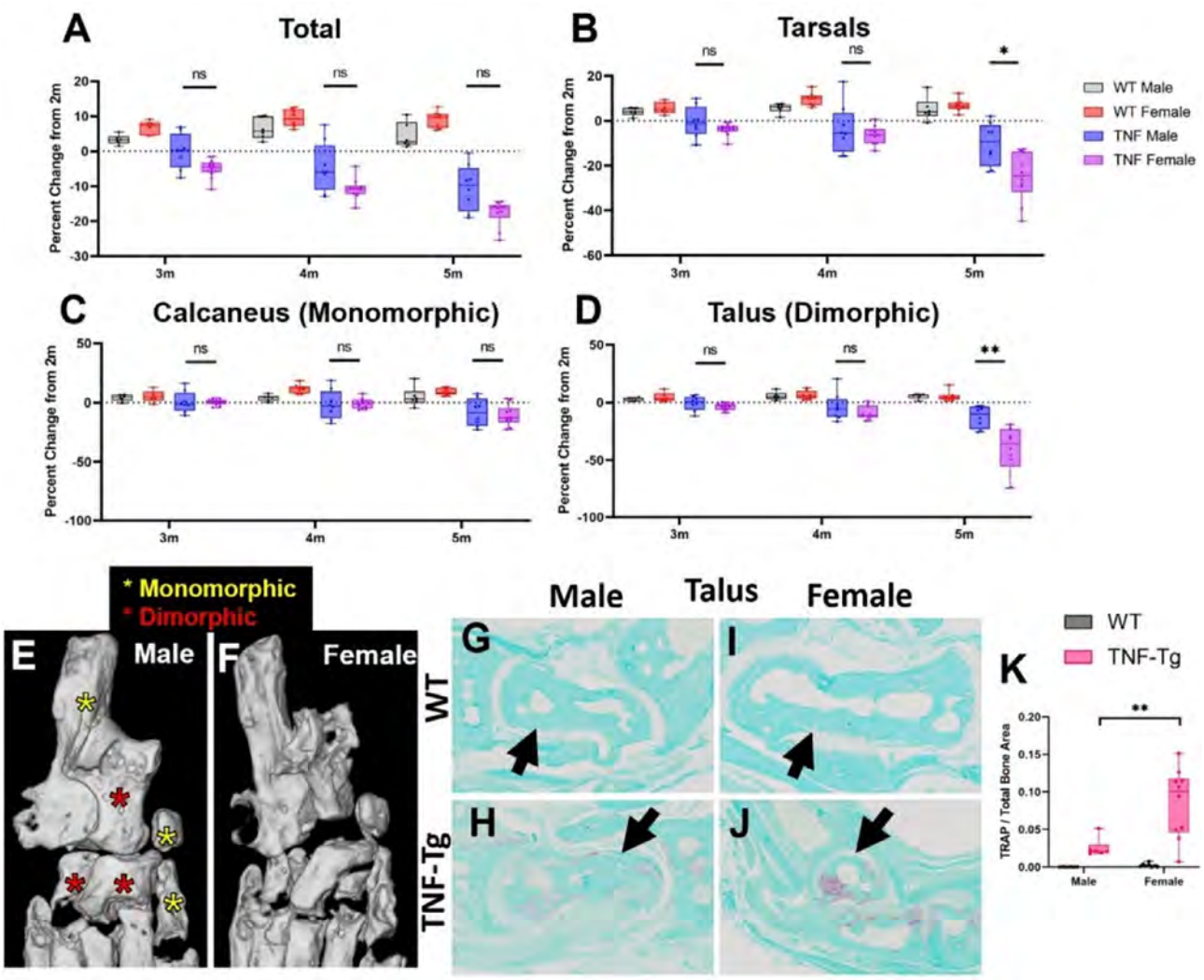

Figure 3. Anterolateral tarsal bones show severe female-specific erosions in TNF-Tg mice. Sex-dependent differences in bone erosions within the tarsal compartment were evaluated using percent change in bone volumes to normalize for animal size between groups. While total bone volume showed no significant changes between TNF-Tg males and females (A), the tarsal compartment exhibited reduced bone volumes in females compared to males at 5-months of age (B). Interestingly, for bones such as the calcaneus (C), there were no changes noted between the sexes. The significant reduction in tarsal bone volume in females was instead driven by sex-specific erosive activity in bones such as the talus (D). The particular bones associated with erosion of the tarsals in females are notably localized to the anterolateral region of the ankle (red stars), while those without sexual dimorphism are oriented posteromedially (yellow stars). Representative micro-CT images of male (E) and female (F) TNF-Tg mice at 5-months of age exhibit the lateralization of the sexually dimorphic effects (reproduced from Fig. 2 for convenience). Corresponding with these bone-specific changes, histologic evaluation revealed significantly increased TRAP+ osteoclasts (red) around the talus in TNF-Tg females vs males at 5-months of age (G-K). Statistics: Mixed effects analysis (A-D) and 2-way ANOVA (K) with Tukey's multiple comparisons; *p<0.05, **p<0.01.

Disclosure: H. Kenney: None; **K. Chen**: None; **L. Schnur**: None; **J. Fox**: None; **R. Wood**: None; **L. Xing**: None; **C. Ritchlin**: AbbVie, 2, 5, 6, Amgen, 2, BMS, 2, Eli Lilly, 2, Gilead, 2, Janssen, 2, Novartis, 2, Pfizer, 2, 5, 6, UCB, 2, 6; **H. Rahimi**: None; **E. Schwarz**: None; **H. Awad**: None.

Abstract Number: 1717

Endothelial Cell Sphingosine 1-Phophate Receptor 1 Restrains VE-cadherin Cleavage and Attenuates Experimental Inflammatory Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Animal Models Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In rheumatoid arthritis, inflammatory mediators extravasate from blood into joints via gaps between endothelial cells (EC), but the contribution of ECs to inflammatory arthritis is not known. Sphingosine 1-phosphate receptor-1 (S1PR1), widely expressed on ECs, plays critical roles in EC barrier function and vascular health. Mice with an inducible EC-specific KO of S1PR1 (S1PR1 ECKO) had increased injury in response to SIA. Blockade of EC S1PR1 induced metalloproteinase-dependent cleavage of VE-cadherin in vitro. These data suggested that vascular leakage associated with S1PR1 inhibition, potentially a consequence of shedding of VE-cadherin, contributed to inflammatory injury. Therefore, we studied mice with highly stabilized EC junctions (VE-cad-α-cat mice) to test whether they resisted vascular permeability in the face of S1PR1 blockade and whether they would resist SIA. We also asked whether patients with active RA have dysregulated S1P/S1PR1 axis favoring vascular leakage.

Methods: VE-cad-α-cat mice were treated with the S1PR1 antagonist NIBR-0213 (30 mg/kg IM) for 3 hours. We measured vascular leak and sVE-cad in bronchoalveolar fluids (BAL) with BCA assay and ELISA, respectively.VE-cad-α-cat, S1PR1 ECKO, and control mice were subjected to SIA (75 ul on days 0 and 2) and clinical scores were measured in a blinded fashion. For human studies, sera from 20 patients with RA and 20 age and sex matched patients with OA were analyzed for S1P and Sa1P by mass spectroscopy. Synovial EC S1PR1 was analyzed by single cell RNA seq in 3 data sets: (1) RA subjects in Accelerating Medicines Partnership Rheumatoid Arthritis / Systemic Lupus Erythematosus (AMP RA/SLE) Network, https://www.biorxiv.org/content/10.1101/2022.02.25.481990v1, (2) RA subjects from the The Roche Network for RA, and (3) healthy controls from Faust et al (https://doi.org/10.1101/2023.05.16.540975). Data sets were integrated and clusters of endothelial subtypes were identified using the top 10 marker genes for each cluster. Capillaries were subsetted for downstream visualization of S1PR1 expression. P-values were calculated using Wilcoxon rank-sum tests across RA statuses.

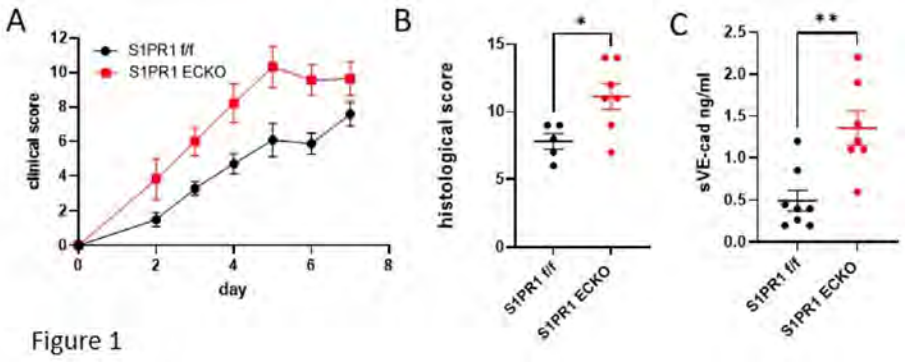

Figure 1

S1PR1 ECKO mice have increased K/BxN serum induced arthritis with evidence of increased soluble VE-cadherin (sVE-cad) in synovial fluids (SF) in early disease. (A) Clinical scores, (B) Histological scores, (C) sVE-cad in SFs on day 2-3 after SIA. *p<0.05; **p<0.01

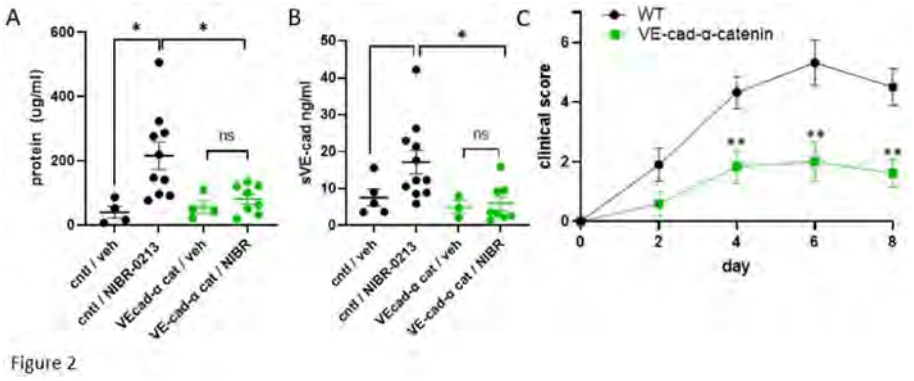

Figure 2

VE-cad-alpha-cat mice demonstrate decreased vascular leakage and soluble VE-cadherin in BAL fluids after challenge with S1PR1 antagonist NIBR-0213 and they resist SIA. Mice were treated with NIBR-0213 for 3 hours before isolation of BAL fluids. (A) BAL protein concentrations, (B) BAL sVE-cad, and (C) clinical scores after SIA. *p<0.05; **p<0.01

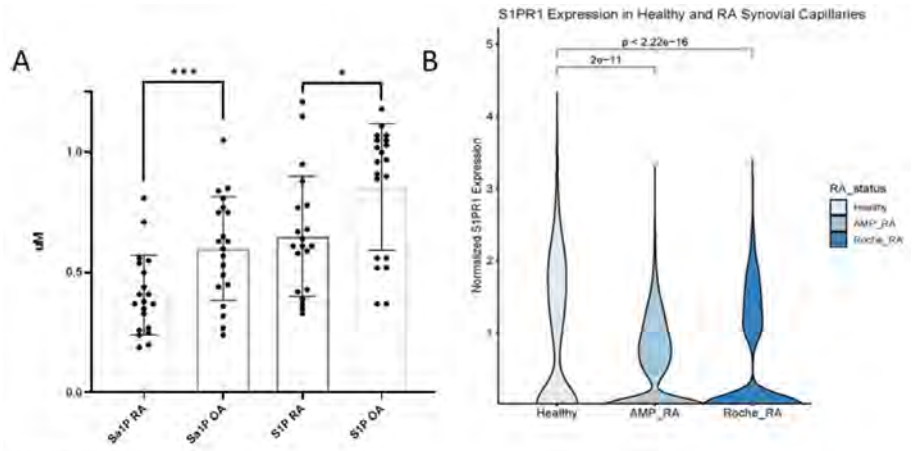

Figure 3

Patients with RA have decreased serum S1P and Sa1P and decreased S1PR1 expression in synovial capillaries compared to controls. (A) S1P and Sa1P levels in active RA vs age and sex matched OA controls. (B) Violin plots indicating S1PR1 expression in capillary ECs from RA and healthy synovial tissues as determined by single cell RNA seq; * p≤ 0.05; *** p≤ 0.001 or as indicated on graph.

Results: S1PR1 ECKO mice had more severe SIA than littermate controls (Fig 1 A,B) along with increased extravascular sVE-cadherin in synovial tissues (Fig 1C). S1PR1 blockade induced less vascular leakage and extravascular VE-cadherin in the BAL in VE-cad-α cat mice compared to controls (Fig 2 A,B).VE-cad-α-cat mice were significantly protected from SIA (Fig 2C). Patients with active rheumatoid arthritis have decreased circulating S1P and Sa1P (Fig 3A), and their synovial microvascular ECs showed decreased expression of S1PR1 (Fig 3B) suggesting dysregulated S1P/S1PR1 axis in favor of vascular permeability and vulnerability.

Conclusion: We present a model in which EC S1PR1 signaling restrains the shedding of VE-cadherin to maintain homeostatic vascular barrier function and curb inflammation in experimental arthritis. Our hypothesis that vascular permeability is a clinical target in RA is supported by evidence that patients have dysregulated S1P/ S1PR1. We identify the microvascular barrier as a potential therapeutic target in inflammatory arthritis.

Disclosure: N. Burg: None; **M. Tran**: None; **K. Wei**: 10X Genomics, 5, capital one, 6, Gilead sciences, 5, horizon therapeutics, 6, Mestag, 2; **C. Blobel**: None; **J. Salmon**: None.

Abstract Number: 1718

Longitudinal Quantification of Bone Erosions, Pulmonary Disease, Pain, Gait and Sarcopenia to Holistically Assess Decreased *Ad Libitum* Physical Activity and Effects of Exercise in the TNF-Transgenic Murine Model of Rheumatoid Arthritis

Calvin Cole[1], H. Mark Kenney[2], Zachary Sechrist[1], Yue Peng[1], Kiana Chen[3], Megan Falsetta[1], Ronald Wood[1], Homaira Rahimi[4], Christopher T Ritchlin[5] and Edward Schwarz[4], [1]University of Rochester Medical Center, Rochester, NY, [2]University of Rochester School of Medicine and Dentistry, Henrietta, NY, [3]University of Rochester School of Medicine and Dentistry, Rochester, NY, [4]University of Rochester, Rochester, NY, [5]University of Rochester Medical School, Allergy, Immunology & Rheumatology Division, Canandaigua, NY

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Animal Models Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by pain, swelling, and joint destruction that decreases mobility.RA patients also suffer from pulmonary disease (PD) and sarcopenia, which decrease strength and endurance for physical activity (PA).Remarkably, the ACR just released its first guidelines on exercises in conjunction with medications as an integrative management approach for RA.[1]However, the risk:benefit ratio of exercise on inflamed joints remains a major concern, although the most recent clinical studies demonstrate long-term benefits.[2]In the tumor necrosis factor transgenic (TNF-Tg) mouse model of RA, which displays joint and extra-articular sequelae of RA in a sexually dimorphic manner, we showed that voluntary wheel running is effective in improving PD, but also exacerbated joint degeneration, correlating with activity output.[3, 4]Coinciding with the multifactorial disease phenotype in TNF-Tg mice, running activity (distance, rate, length, and number of run bouts) significantly declined during disease progression vs. WT littermates through multiple potential contributing features, including joint degeneration, PD, pain, gait deficiency, and sarcopenia, which have not been holistically studied in RA mouse models.

Methods: To address this deficiency, we developed an automated, *ad libitum* wheel running tracking system to examine disease outcomes related to PA and the relationship with features of RA disease outcomes in TNF-Tg mice.To holistically quantify the independent disease variables associated with PA outcomes, we developed longitudinal outcome measures of bone erosion and PD (micro-CT),[3] pain (semiautomated von Frey with the Topcat EVF system), gait (TreadScan^{Tm}), and sarcopenia (DEXA), and evaluated 8 groups of mice: male and female TNF-Tg running vs. sedentary controls, and their WT littermates.

Results: Evaluation of PD revealed that running males and females increased their aerated lung volumes, which was positively correlated with running distance and rate in WT and TNF-Tg female mice,[3] confirming the known efficacy of exercise on cardiopulmonary disease.[5] In contrast, talus bone volumes were significantly reduced in running vs. sedentary males, and negatively correlated with running distance and rate in both male and female TNF-Tg mice.[3]We also found that TNF-Tg mice have reduced sensitivity thresholds indicative of pain (**Figure 1**, $p< 0.05$), decreased stride length, and reduced lean mass (**Figure 2**, $p< 0.05$) vs. WT littermates.

Conclusion: Taken together, these results demonstrate the feasibility of holistically assessing the relationship between PA and independent disease variables in murine models of arthritis. Ongoing studies will evaluate the effects of regimented exercise on the onset and progression of these various manifestations in RA towards strategic refinement and integration of non-

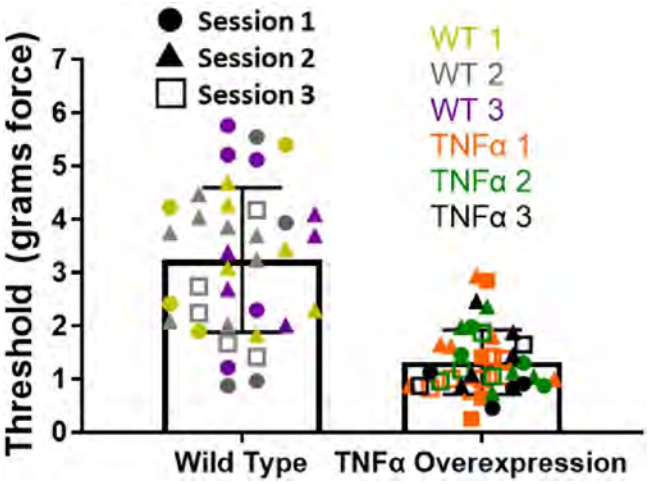

Figure 1. Automated pain assessment of mice with chronic arthritis. 4-month-old male WT and TNF-Tg mice, denoted by color, were evaluated for touch sensitivity in the modified Topcat EVF system. Values were averaged from 3 testing sessions 3 days apart denoted by symbol (n=3; p=0.0002 via t-test).

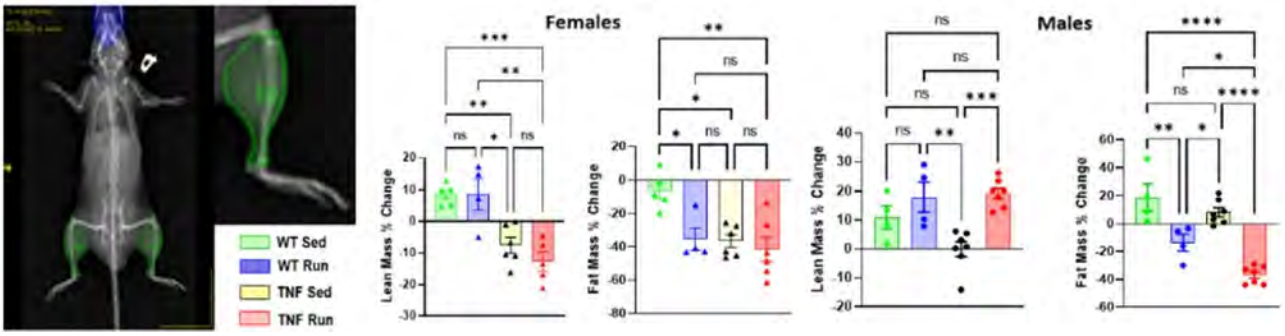

Figure 2. Ad libitum wheel running alters body composition of mice in a sexually dimorphic manner. A representative scout view of a DEXA scan of a mouse is shown to illustrate segmentation of the lower hind-limb soft tissue region of interest (ROI) used for body composition studies. DEXA analyses of the % change in lean mass (muscle) and fat mass composition of WT and TNF-Tg mice from 2 to 5.5 months of age ± ad libitum wheel running are shown. Data are presented for each mouse with mean ± SD (*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001, two-way ANOVA with Tukey's multiple comparisons).

pharmacologic treatment approaches. 1. England et al. *Arthritis Rheumatol*. 2023 2. Azeez et al. *Clin Rheumatol*. 39(6):1783-92. 2020. 3. Kenney et al. *Arthr Res & Ther*. 25(1):17. 2023. 4. Bell et al. *Arthritis Rheumatol*. 71(9):1512-23. 2019. 5. Baillet et al. Arthritis Care Res. 62(7):984-92. 2010.

Disclosure: C. Cole: None; **H. Kenney**: None; **Z. Sechrist**: None; **Y. Peng**: None; **K. Chen**: None; **M. Falsetta**: None; **R. Wood**: None; **H. Rahimi**: None; **C. Ritchlin**: AbbVie, 2, 5, 6, Amgen, 2, BMS, 2, Eli Lilly, 2, Gilead, 2, Janssen, 2, Novartis, 2, Pfizer, 2, 5, 6, UCB, 2, 6; **E. Schwarz**: None.

Abstract Number: 1719

Exploring the Link Between Osteitis and Bone Microstructure Changes in Rheumatoid Arthritis: Role of JAK-STAT Signaling Pathway

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Animal Models Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Osteitis on MRI and bone microstructure changes (BMC) on high-resolution peripheral quantitative CT are the earliest signs of arthritis, preceding the development of bone erosion in rheumatoid arthritis (RA). Recently, a JAK inhibitor, Baricitinib (BAR), was shown to inhibit these early changes. This study aimed to elucidate the underlying molecular mechanism of osteitis and BMC, including the role of JAK-STAT cytokines, using SKG mice, an animal model of RA with a ZAP70 gene point mutation.

Methods: Osteitis was assessed by an increase in the femur/gastrocnemius muscle (F/G) ratio in fat-suppressed T2-weighted images on MRI. BMC was evaluated by a decrease in bone volume/tissue volume (BV/TV) ratio on micro CT. Arthritis was induced by intraperitoneal injection of zymosan. BAR or a vehicle was orally administered in the early or late phases during arthritis development. Flow cytometry was used to analyze the bone marrow (BM) cells, including granulocyte-monocyte (GM) progenitor cells, granulocytes, and monocytes. Immunohistochemistry (IHC) was performed

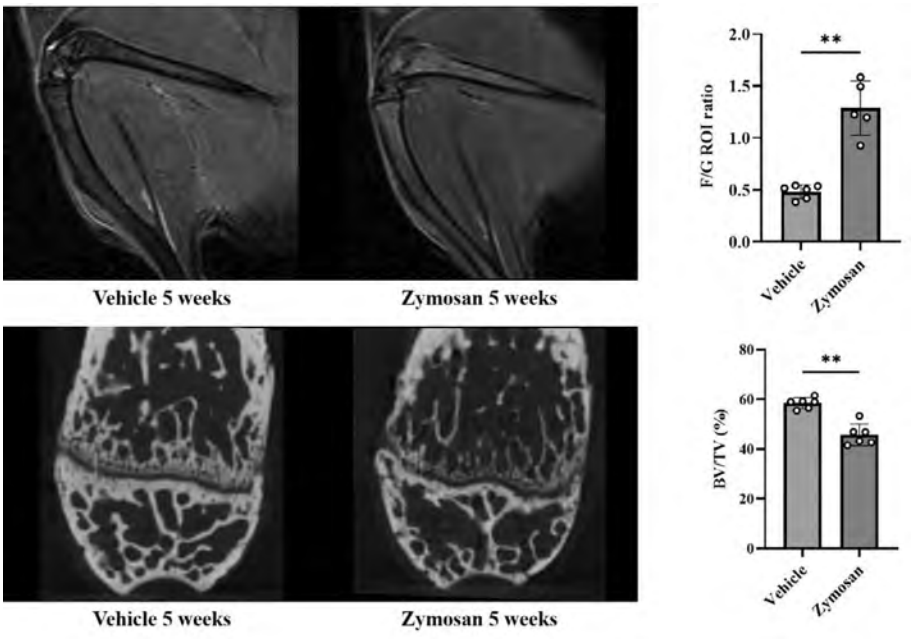


Figure: Osteitis and bone microstructure changes after arthritis induction in SKG mice BV/TV: Bone volume/Tissue volume, F/G: Femur/Gastrocnemius muscle Mann-Whitney test, ** $p < 0.01$

to identify the distribution of tartrate-resistant acid phosphatase (TRAP)-positive cells in the BM. The role of JAK-STAT cytokines was investigated by examining the expression of JAK-STAT cytokines in the BM or by supplementing recombinant (r-) GM-CSF or IL-6 to *in vivo* arthritis model or *in vitro* RANKL-mediated osteoclast differentiation assay.

Results: Osteitis developed earlier (at 2 weeks) than BMC (at 5 weeks) during arthritis development. Osteitis scores on MRI well correlated with BMC scores on micro CT (ρ=-0.58, p=0.03). Following zymosan injection, GM progenitor cells, granulocytes, and monocytes were increased in the BM. The number of monocytes significantly correlated with osteitis scores (ρ=0.77, p=0.0008). Monocytes were further subdivided into three populations (Ly6C high CD11b low, Ly6C high CD11b high, and Ly6C mid CD11b+), and TRAP-positive osteoclasts were preferentially differentiated from the Ly6C high CD11b low population (osteoclast precursor cells) *in vitro*. IHC revealed increased TRAP-positive cells at the edges of bone surfaces in the BM where BMC was observed. BAR effectively suppressed osteitis (F/G ratio: 1.44 in vehicle group vs. 1.17 in BAR group, p=0.0379) and BMC (BV/TV ratio: 37.3 % in vehicle group vs. 46.3 % in BAR group, p=0.0052). BAR reduced the number of GM progenitor cells, monocytes, and osteoclast precursor cells. Among JAK-STAT cytokines, GM-CSF and IL-6 were highly expressed in the BM after zymosan injection. *In vivo* administration of rGM-CSF to SKG mice promoted osteitis, especially when administered in the late phase of arthritis. *In vitro* addition of rGM-CSF to osteoclast differentiation assay markedly increased the number and size of osteoclasts, especially when added in the late phase of osteoclast differentiation, which was inhibited by further addition of BAR.

Conclusion: During arthritis progression, osteitis precedes BMC. The increase of GM-lineage cells in the BM induces osteitis, while proliferation and subsequent differentiation of osteoclast precursors contribute to BMC. JAK-STAT cytokines, especially GM-CSF, play a crucial role in these processes.

Disclosure: T. Yoshida: None; **Y. Nakayama**: None; **M. Katsushima**: None; **Y. Nishida**: None; **M. Shirakashi**: None; **R. Nakashima**: None; **R. Watanabe**: AbbVie, 5, Asahi Kasei, 6, Chugai, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Sanofi, 6; **K. Murakami**: None; **H. Yoshifuji**: None; **A. Morinobu**: None; **M. Hashimoto**: Abbvie, 5, 6, Asahi Kasei, 5, 6, Astellas, 5, 6, Ayumi, 5, 6, Brystol Meyers, 5, 6, Chugai, 5, 6, Daiichi Sankyo, 5, 6, EA Pharma, 5, 6, Eisai, 5, 6, Eli Lilly, 5, 6, Novartis Pharma, 5, 6, Taisho Toyama, 5, 6, Tanabe Mitsubishi, 5, 6.

Abstract Number: 1720

Successful Treatment of Rheumatoid Arthritis in Mice Using Cenerimod, a Selective Modulator of the S1P1 Receptor, Demonstrates the Potential Benefits of S1P1 Receptor Immunomodulation for Rheumatic Diseases

Thomas Hoyler, Maxime Bulle, Conrad Wyss, Jeremy Scherer, Sylvie Froidevaux and Marianne Martinic, Idorsia Pharmaceuticals Ltd., Allschwil, Switzerland

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Animal Models Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Discovery of the essential role of S1P signaling in regulating lymphocyte trafficking led to the development of S1P receptor modulators for the treatment of autoimmune disorders such as multiple sclerosis and ulcerative colitis. Cenerimod, a selective S1P1 receptor modulator, has shown positive results in preclinical models of SLE, systemic sclerosis, and Sjögren's syndrome[1-3] and two phase 2 trials in SLE. Recruitment is ongoing for two Phase 3 clinical trials

investigating 4 mg cenerimod for the treatment of adults with SLE (OPUS; NCT05648500 & NCT05672576). We examined the potential of cenerimod to modulate the progression of rheumatoid arthritis (RA) in multiple preclinical murine models.[4]

Methods: Cenerimod was orally administered as therapeutic or prophylactic treatment in RA rodent models. In the mBSA-DTH model, C57BL6/J mice were immunized with mBSA/CFA before antigen challenge. Pristane-induced arthritis (PIA) and adjuvant-induced arthritis (AIA) were induced in rats by CFA or pristane challenge, respectively. Disease development was monitored by measuring edema formation. Relevant biomarkers such as cellular changes, autoantibody development, and chemokine secretion were measured in plasma, inflamed tissue, and draining lymph nodes.

Results: In the mBSA-DTH model, cenerimod significantly reduced joint swelling and limited the production of autoantibodies and pro-inflammatory chemokines in the joints. Furthermore, analysis of the draining lymph nodes revealed a novel effect of cenerimod treatment in mitigating the migration of dendritic cells. Similarly, proliferation and cytokine secretion by effector T cells were blunted by S1P1 receptor modulation, which may be a direct consequence of reduced dendritic cell lymph node homing and hence, antigen presentation. In the rat PIA model, therapeutic cenerimod treatment decreased paw inflammation by inhibiting leukocyte influx to the site of inflammation. In the AIA model, low-dose cenerimod treatment limited joint inflammation to the same degree as low-dose corticosteroid treatment with dexamethasone, without displaying negative effects on body weight.

Conclusion: Cenerimod is highly efficacious in several murine RA models by preventing antigen transport, by reducing the release of pro-inflammatory cytokines & chemokines, and by inhibiting lymphocyte egress to the circulation. In particular, the reduction of dendritic cell migration suggests cenerimod may modulate antigen presentation, which could have implications for the treatment of autoimmune diseases. Our findings suggest that cenerimod can effectively disrupt multiple nodes of a vicious circle of pathogenesis associated with rheumatic diseases like RA. Combining these novel results with published data, we propose that S1P1 receptor modulation has potential to provide clinical benefit to patients with arthritis who currently lack satisfactory treatment options.

REFERENCES 1. Strasser DS et al. RMD Open 2020;6(2):e001261. 2. Kano M et al. Sci Rep 2019;9:658. 3. Gerossier E et al. Arthritis Res Ther 2021;23:289. 4. Hoyler T et al. Doi: 10.1136/annrheumdis-2023-eular.879

Disclosure: T. Hoyler: Idorsia Pharmaceuticals Ltd, 3, 11; **M. Bulle**: Idorsia Pharmaceuticals Ltd., 3, 11; **C. Wyss**: Idorsia Pharmaceuticals Ltd., 3; **J. Scherer**: Idorsia Pharmaceuticals Ltd., 3, 11; **S. Froidevaux**: None; **M. Martinic**: Idorsia Pharmaceuticals Ltd., 3, 11.

Abstract Number: 1721

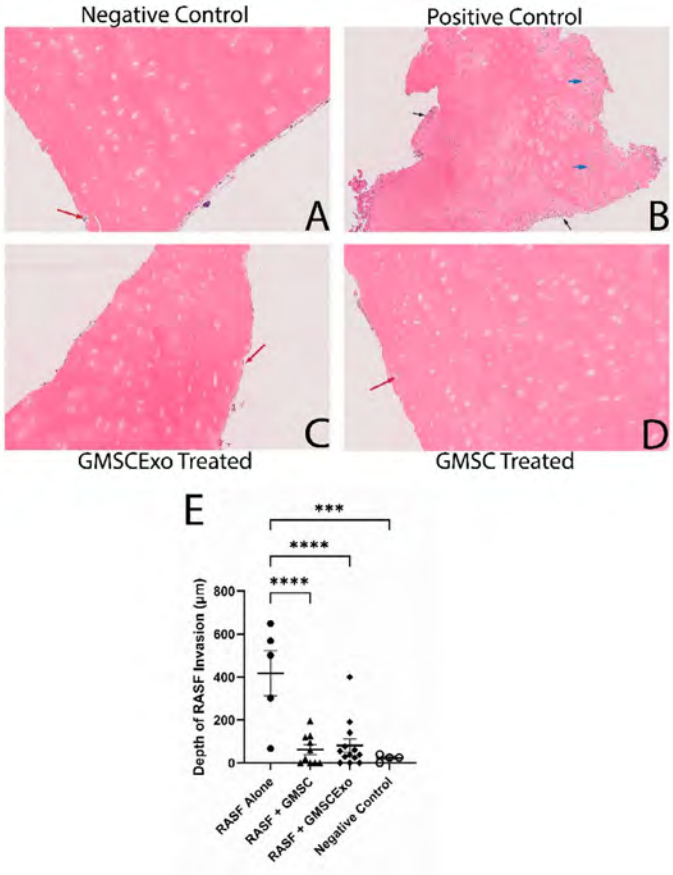
The Therapeutic Effects of Gingival Mesenchymal Stem Cells and Their Exosomes in a Chimeric Model of Rheumatoid Arthritis

shane Bruckner[1], Braden Zeno[2], Vittoria Capria[1], William Willis[3], Latha Prabha Ganesan[1] and wael Jarjour[1], [1]Ohio State University, Columbus, OH, [2]Ohio State University, Upper Arlington, OH, [3]Ohio State University, Reynoldsburg, OH

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Animal Models Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease that leads to progressive joint destruction involving multiple joints. There is a large body of evidence that suggests a crucial role for activated synovial fibroblasts in mediating both direct tissue injury and perpetuation of the complex disease process in RA (1). Synovial fibroblasts derived from RA patients (RASF) are able to attach to articular cartilage and deeply invade and degrade the cartilage matrix (2) and have been shown to migrate to secondary joint locations *in vivo* and invade and degrade cartilage similarly to the primary site (3). Human gingival-derived mesenchymal stem cells (GMSC) are promising therapeutic cell treatments for autoimmune diseases due to their immunomodulatory capacity (4). Others have demonstrated the ability of GMSC, and exosomes derived from GMSCs (GMSCExo) to suppress the deleterious *in vivo* effects of the collagen induced arthritis model in mice (5). Our aim was to test whether the destructive invasive effects of RASF in an *in vivo* chimeric mouse model of RA could be modulated by the presence of GMSC or GMSCExo. In addition, we analyzed the effects of both GMSC and GMSCExo on the ability of RASF to migrate to secondary locations. Mechanistic studies were done to understand how the GMSC were inhibiting the invasiveness of the RASF.

Methods: A chimeric human/mouse model of synovitis was created by surgically implanting SCID mice with a small piece of human articular cartilage surrounded by RASF. Each mouse received two implants; the primary implant on the right flank of the mouse contained RASF, the secondary implant contained no RASF. Mice were retro-orbitally injected once with either GMSC or GMSCExo at 5-7 days post-implantation. The implants were removed after 60 days for evaluation. Histology and IHC were used to assess RASF invasion of the cartilage. Flow cytometry was used to understand the homing ability of GMSC *in vivo,* the incidence of apoptosis of RASF and the exchange of exosomes *in vitro*.



GMSC and GMSC Derived Exosomes Block RASF Cartilage Degradation. (A) Untreated cartilage showing no RASF invasion (B) RASF treated cartilage showing perichondrocytic invasion, blue arrows, and pannus like invasive structures degrading the cartilage (C) RASF treated followed by GMSCExo treatment blocks RASF invasion and degradation (D) RASF treated followed by GMSC treatment blocks RASF invasion and degradation (E) GMSCExo and GMSC both block RASF cartilage invasion

Results: We demonstrate that both GMSC and GMSCExo are potent inhibitors of the deleterious effects of RASF. Both treatments were effective in inhibiting the invasive destructive properties of RASF as well as the potential of these cells to migrate to secondary locations and attack the cartilage there. We also present evidence that GMSC home to the site of the implant and induce programmed cell death of the RASF through the direct transfer of exosomes.

Conclusion: Our results indicate that both GMSC and GMSCExo can block the pathological effects of RASF in this chimeric model of RA. A single dose of either GMSC or GMSCExo can inhibit the deleterious effects of RASF. These treatments can also block the invasive migration of the RASF, suggesting that they can inhibit the spread of RA to other joints. Because the gingival tissue is harvested with little difficulty, relatively small amounts of tissue are required to expand the cells, the fairly simple *in vitro* expansion process, and the increasing technological advances in the production of therapeutic exosomes, we believe that GMSC and GMSCExo are excellent candidates as a treatment for RA.

Disclosure: s. Bruckner: None; **B. Zeno**: None; **V. Capria**: None; **W. Willis**: None; **L. Ganesan**: None; **w. Jarjour**: None.

Abstract Number: 1722

Fate-mapping of Synovial Monocytes and Macrophages

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Animal Models Poster
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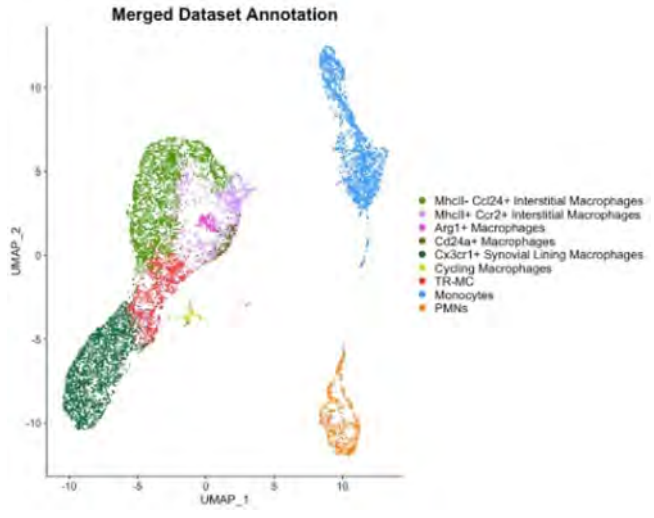
Session Time: 9:00AM–11:00AM

Background/Purpose: Synovial monocytes and macrophages are heterogenous populations. These populations play diverse roles in the development of arthritis in humans and mice. In recent years, our laboratory identified a new synovial cell type we named tissue-resident monocyte-lineage cells (TR-MCs), which are are necessary for the development of



The annotation of the merged CITE-seq datasets of synovial macrophages and monocytes.

inflammatory arthritis in mice. Although TR-MCs are CD64 negative and transcriptionally distinct from circulating monocytes and DCs, the current lack of targeted mouse models limit our ability to study this critical population and differentiate from other synovial monocyte and macrophage populations.

Methods: To study each synovial monocyte and macrophage population, we performed fate-mapping with 7 reporter models including *Cx3cr1*-ERcre-Ai3-YFP, *Cx3cr1*-Cre-Ai3-YFP, *Ms4a3*-cre-*Ai3*-YFP, *P2ry12*-ERcre-*Ai3*-YFP, *Tmem119*-GFP, *Cd68*-eGFP, and *Csf1r*-cre-*Ai3*-YFP in 8–12-week-old C57BL/6 mice. We also further characterized synovial monocyte and macrophage cells by performing cellular indexing of transcriptomes and epitopes (CITE-seq) on synovial macrophages (CD45+CD11b+CD4-CD8-Ly6G-SiglecF-NK1.1-CD64+) and monocytes (CD45+CD11b+CD4-CD8-Ly6G-SiglecF-NK1.1-MHCII-CD64-).

Results: Although 90% of synovial macrophages, 82% NCM and 76% TR-MC are derived from *Cx3cr1*-positive progenitor cells, only 41%, 91%, 27% of them express *Cx3cr1 at 8-12 week-old*. Although high percentages of Csf1r-expression were found in almost all synovial cell types, synovial macrophages express the highest intensity of *Csf1r*. Similarly, *Ms4a3* was expressed at a high percentage in both granulocytes and monocyte-lineage cell, but the intensity of Ms4a3 is more than 2 times higher in macrophages than other cell types. *P2ry12* was expressed in synovial macrophages and TR-MC with 20% positivity. The expression of CD68 and Tmem119 are same in all synovial myeloid cell types. To develop specific reporter models of synovial monocyte and macrophage subpopulations, we characterize them by merging the 2 CITE-seq datasets and identified 5 synovial macrophages subpopulations - MHCII+ CCL24+ interstitial macrophages, MHCII-CCR2+ interstitial macrophages, Arg1+ macrophages, CD24a+ macrophages and CX3CR1+ synovial lining macrophages as well as TR-MCs, monocyte-lineage cells and polymorphonuclear leukocytes (PMNs). MHCII- CCL24+ interstitial macrophages specifically expressed Cd209d and Ccl24 genes. Arg1+ macrophages exclusively expressed Arg1 and Flt1 genes. The differentially expressed genes of CX3CR1+ synovial lining macrophages are aligned with the CX3XR1+ lining macrophages published by Culemann S, et. al. CD24a+ macrophages highly expressed Tnip3 and Anxa8 genes as well as CD11c surface marker.

Conclusion: Our results currently showed that Cx3cr1, Csf1r, Ms4a3 and P2ry12 may have the ability of tracing one or more synovial monocyte and macrophage populations. The gene and surface markers identified in each synovial monocyte, macrophage and TR-MC population will help develop better tools to trace and delete them. Future studies will also focus on determining the spatial topology of each synovial monocyte and macrophage population to better define their role in joint health.

Disclosure: Y. Wang: None; **C. Cuda**: None; **D. Winter**: Pfizer, 2; **H. Perlman**: None.

Abstract Number: 1723

3,3-dimethyl-1-butanol and Its Metabolite 3,3-dimethylbutyrate Ameliorate Arthritis Severity in CIA Independent of Choline TMA Lyase Activity

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
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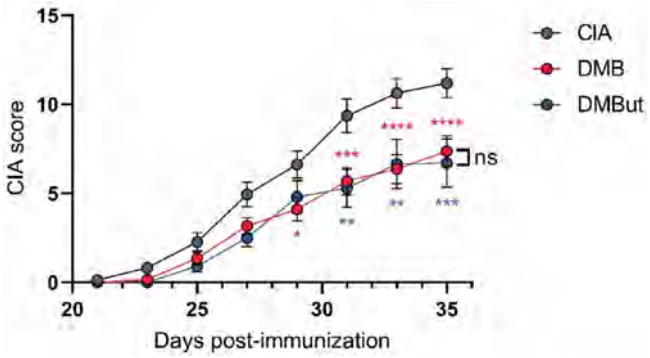
Session Time: 9:00AM–11:00AM

Background/Purpose: Both human and animal studies associate specific microbiota and microbial metabolic pathways with the development of RA and autoimmune arthritis, thereby providing a novel target for next-generation therapeutic development. Notably, carnitine and choline metabolism are associated with RA in humans and autoimmune arthritis in the collagen-induced arthritis (CIA) mouse model. Further, specific bacteria linked to disease in RA and CIA can metabolize dietary carnitine and choline to drive production of trimethylamine-N-oxide (TMAO). TMAO is implicated in the pathogenesis of inflammatory diseases, such as atherosclerosis, whose underlying disease processes mirror that of RA and CIA. Thus, we investigated modulation of TMAO production as a therapeutic target in CIA using the choline TMA lyase inhibitors 3,3-diemthyl-1-butanol (DMB) and fluoromethylcholine (FMC).

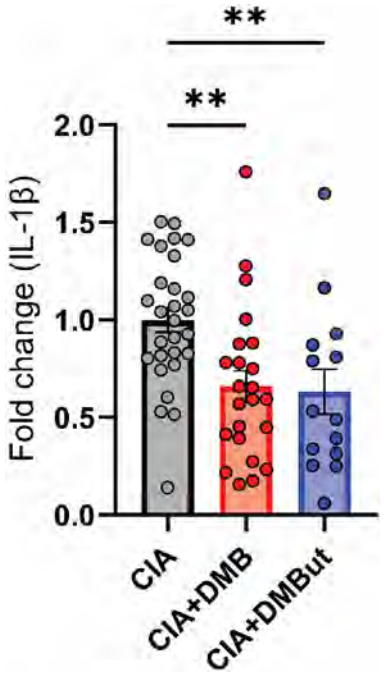
Methods: 6-week-old male DBA/1j mice were immunized at days 0 and 21 with bovine type II collagen (CII) in complete Freund's adjuvant and either left untreated or treated with 1% (vol/vol) DMB, 1% (vol/vol) 3,3-dimethylbutyrate (DMBut), or 100mg/kg FMC. Mice were assessed for disease severity using established metrics until 35 days post-initial immunization. On day 35, mice were sacrificed and tissues were harvested for analysis. Multiplex serum cytokine immunoassays; serum anti-CII ELISAs; fecal 16S sequencing; serum and liver metabolomics; flow cytometry of splenocytes and inguinal lymph node lymphocytes; and cytokine ELISAs of bone marrow-derived macrophage (BMDM) supernatants were performed.

Results: Mice given DMB showed significant reduction (>50%) in disease severity relative to untreated mice with CIA, while mice given FMC did not show reduced disease. FMC but not DMB significantly reduced cecal TMA and serum TMAO concentrations compared to untreated CIA mice. Fecal bacterial communities were not significantly altered by treatment with either FMC or DMB. DMB and its predicted metabolite, DMBut, were detected in the liver and serum, suggesting systemic effects, and both significantly reduced arthritis severity and circulating IL-1β and IL-6, but not circulating anti-CII antibodies, compared to untreated CIA mice. Splenic Th17 populations were significantly increased with DMBut treatment, but Th1, Tfh, and Treg populations were unchanged with DMB and DMBut treatment. Stimulation of BMDMs with LPS in the presence of DMB or DMBut significantly reduced secretion of IL-1β and IL-6.

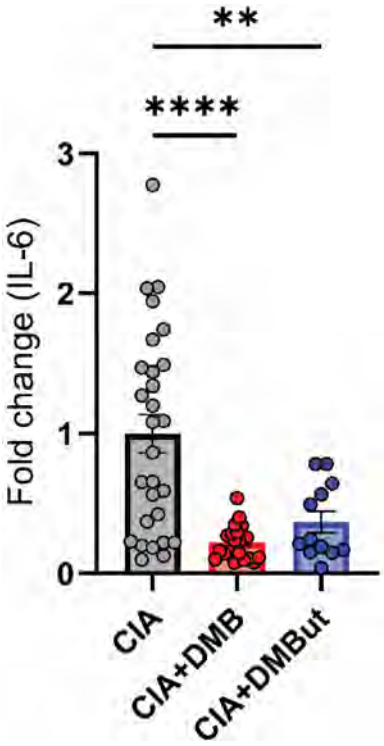
Conclusion: We found that inhibition of microbial TMA/TMAO production using FMC does not reduce arthritis severity in CIA, while treatment with DMB ameliorates CIA seemingly independent of TMA/TMAO production or microbiome effects. Moreover, DMB and a product of its metabolism in the host, DMBut, both significantly reduce disease severity and pro-inflammatory cytokines in CIA and stimulated BMDMs, suggesting that DMB and/or its metabolites have anti-inflammatory effects on monocytes. Elucidating the mechanism by which these small molecules modulate disease may provide directions for developing future RA therapies.



CIA was induced in 6-week-old male DBA/1j mice. On day 21 post-initial immunization, mice were left untreated (CIA), treated with 1% (v/v) DMB in drinking water (DMB), or treated with 1% (v/v) DMBut in drinking water (DMBut). N=24 (CIA), N=23-25 (DMB), and N=10 (DMBut) per group pooled from 5 individual experiments. Data are reported as mean ± SEM. *, p<0.05; **, p<0.01; ***, p<0.001; ****, p<0.0001; ns, non-significant as determined by two-way ANOVA with Bonferroni correction for multiple comparisons.



Serum was harvested from male DBA/1j mice at day 35 post-initial immunization and analyzed for IL-1B by a 6-plex immunoassay (Mesoscale). N=24-29 (CIA), N=27 (CIA+DMB), and N=14 (CIA+DMBut) per group pooled from 6 individual experiments. Data are reported as fold change normalized to the cytokine concentrations in the CIA group (symbols) and group mean ± SEM. **, p<0.01 as determined by one-way ANOVA with Dunnett's correction for multiple comparisons.



Serum was harvested from male DBA/1j mice at day 35 post-initial immunization and analyzed for IL-6 by a 6-plex immunoassay (Mesoscale). N=24-29 (CIA), N=27 (CIA+DMB), and N=14 (CIA+DMBut) per group pooled from 6 individual experiments. Data are reported as fold change normalized to the cytokine concentrations in the CIA group (symbols) and group mean ± SEM. **, p<0.01; ****, p<0.0001 as determined by one-way ANOVA with Dunnett's correction for multiple comparisons.

Disclosure: B. Allen: None; **S. Fechtner**: None; **M. Chriswell**: None; **W. Jubair**: None; **M. Vrolijk**: None; **V. Holers**: None; **k. Kuhn**: pfizer, 5, ucb, 2.

Abstract Number: 1724

Human Embryonic Stem Cell-derived Mesenchymal Stem Cells Attenuates Experimental Pulmonary Fibrosis Through Mitochondria Transfer Mediated Anti-apoptotic and Immunomodulatory Effects

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a serious condition characterized by inflammation and fibrosis in the lung interstitium. The important subtypes of ILD include idiopathic pulmonary fibrosis (IPF) and connective tissue disease-associated ILD (CTD-ILD). The main histopathological pattern observed in IPF and Rheumatoid arthritis-ILD (RA-ILD) is usual interstitial pneumonia (UIP), and if left untreated, the prognosis is unfavorable. Recently, cell-based mesenchymal stem cells (MSCs) can improve lung fibrosis through anti-apoptotic effect by immunomodulation, protein expression regulation, and mitochondria transfer. However, this ability decreases with passage in adult tissue-derived MSC. But Embryonic stem cell, called DW-MSCs, maintains a constant their ability even after repeated passage culture. Therefore, we evaluated whether DW-MSC can improve lung fibrosis in IPF and RA-ILD, and to identify the mechanism of improvement.

Methods: A total of 1.0 x 10^6 DW-MSCs were injected into mice via the tail vein either 4 or 7 days after intratracheal administration of bleomycin and collagen induction. The therapeutic effect was analyzed by evaluation the lung tissue fibrosis scores, and α-SMA expression through western blot and immunohistochemistry. The immune cell modulation of DW-MSCs was evaluated by analyzing immune cells in lung tissue using flow cytometry analysis. The Damaged AECs protection of DW-MSCs was investigated by inducing apoptosis in A549 cells with $CoCl_2$ and confirming trough TUNEL assay, cell viability and the expression level of Bcl-2 and Bcl-2 associated X (Bax) through western blot. Lastly, we co-cultured DW-MSCs and hypoxia-induced AECs to confirm the transfer of mitochondria through tunneling nanotubes (TNTs) of DW-MSCs using fluorescence microscopy.

Results: DW-MSCs attenuates Bleomycin-induced and Collagen-induced pulmonary fibrosis. The therapeutic efficacy of DW-MSCs was found to be comparable to Nintedanib. DW-MSCs showed improvements in the fibrosis score, reduced α-SMA expression, and regulated fibrosis relate gene expression. Furthermore, DW-MSCs exhibited immunomodulatory effects by influencing B cells during the early phase and promoting an increase in regulatory T cells while decreasing Th17 cells during the late phase. Additionally, DW-MSCs demonstrated the ability to inhibit apoptosis in damaged AECs and down-regulate apoptosis-related proteins. Moreover, DW-MSCs enhanced cell viability and mitochondrial respiration in damaged epithelial cells by facilitating the transfer of mitochondria through tunneling nanotubes.

Conclusion: Our study provides compelling evidence for the therapeutic potential of DW-MSCs in improving IPF and RA-ILD. A single administration, DW-MSCs exhibit beneficial effects on AECs injury, inflammation, and fibrosis. These effects are achieved through the protection of AECs by inhibiting apoptosis, facilitating mitochondrial transfer, and exerting

immunomodulatory and anti-fibrotic effects. Additionally, their high clinical applicability is an added advantage as their efficacy remains constant across various passages. Therefore, DW-MSCs can be considered an ideal candidate for ILD treatment in the future.

Disclosure: H. Lee: None; **S. Kim**: None; **M. Kim**: None; **O. Jeong**: None; **S. Lee**: None.

Abstract Number: 1725

Distinct Perivascular and Intravascular Lymphatic Mast Cells and Their Role in Lymphatic Clearance, Joint Inflammation, and Bone Erosion in the TNF-Transgenic Murine Arthritis Model

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Animal Models Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammatory-erosive arthritis is exacerbated by lymphatic dysfunction (1), and mast cells (MCs) regulate lymphatic vessel contractions via release of inflammatory and vasoactive mediators (2). In studies to directly assess this relationship, we identified a novel population of intravascular MCs embedded in the cellular architecture of murine joint-draining popliteal lymphatic vessels (PLVs) (3), along with perivascular MCs surrounding the PLV. Here, we investigated the phenotypic differences between PLV perivascular and intravascular MCs to elucidate their respective roles in regulating lymphatic function and inflammatory-erosive arthritis through genetic ablation and pharmacologic inhibition of MCs.

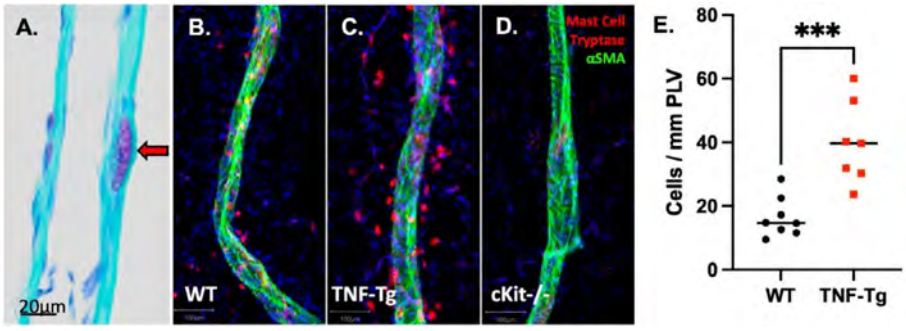

Figure 1. Identification of intravascular MCs and increased numbers of MCT+ perivascular MCs in TNF-Tg mice. Longitudinal sections of PLVs obtained from WT mice were subjected to toluidine blue staining, and a 200x micrograph is shown highlighting a novel intravascular MC embedded within the lymphatic vessel wall (red arrow), situated between the layers of lymphatic endothelial and lymphatic muscle cells (A) (3). PLVs were harvested for WMIFM of αSMA (green) and MCT (red), and representative 200x images are shown for WT (B),TNF-Tg (C), cKit-/-(D) mice, which demonstrated a complete absence of MCT+ MCs in cKit-/- as confirmation of the genetic ablation in this model. Quantification of perivascular MCT+ cells showed a significant increase in MCs surrounding inflamed TNF-Tg PLVs, normalized to vessel length (E, n=8). Statistics: Unpaired Mann Whitney test (E); ***$p < 0.001$.

Methods: PLVs from WT, TNF-Tg, and *Kit*$^{W\text{-}sh/W\text{-}sh}$ (cKit$^{-/-}$) mice (4), which have a selective hematopoietic deficit in MCs, were harvested for whole mount immunofluorescent microscopy (WMIFM) and toluidine blue histochemistry to identify MCs. *In silico* analyses were performed on single-cell RNA sequencing (scRNAseq) datasets of PLV MCs (5) vs MC populations identified in the Mouse Cell Atlas (6). Near-infrared indocyanine green (NIR-ICG) imaging quantified lymphatic clearance function. Longitudinal micro-computed tomography (μCT) assessed bone erosions, while H&E and TRAP histology evaluated synovitis and osteoclasts of the afferent ankle. MC deficiency was studied in cKit$^{-/-}$ x TNF-Tg mice (n=3), while MC inhibition was investigated in TNF-Tg mice treated with cromolyn sodium (CS; 3.15mg/g/day/i.p., n=6) vssaline (n=5) for 3 weeks.

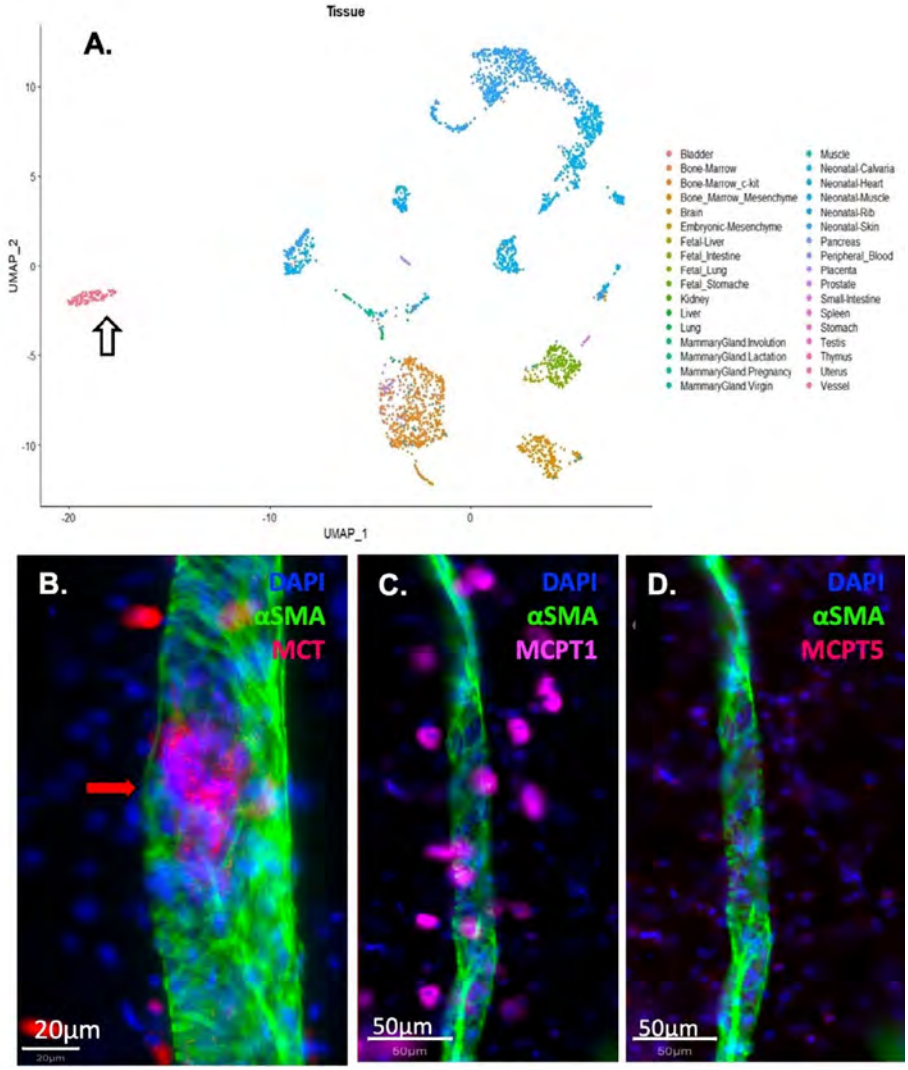

Figure 2. Identification of a unique MCT+/MCTP1-/MCPT5- PLV intravascular MC population. In silico datasets were used to extract MCs from a comprehensive scRNAseq dataset of 242k cells encompassing various organs in the Mouse Cell Atlas (6). The extraction was performed based on the expression of MC marker genes (Mcpt4, Cma1, Cpa3, Tpsb2, Kit, Fcer1a, Gata2) to subset MCs from other cell types. These MCs were subsequently integrated with the MCs from our previously published scRNAseq dataset of PLV tissue (5), reclustered, and shown as a UMAP. Notably, the PLV MCs (arrow) exhibited a distinct transcriptional pattern distinct from other MCs identified in the Mouse Cell Atlas (A). WMIFM was performed on PLVs for αSMA, MCT, MCPT1, and MCPT5, as described in Figure 1. A 400x image highlights the MCT+ intravascular MC (B, red arrow) embedded in gaps between αSMA+ lymphatic muscle cells, while a 200x image with 400x inset (white box) exhibits the MCPT1+ perivascular MC (pink arrow) and MCPT1- intravascular MC (white arrow) that exists within the αSMA- void (C). A 200x image with 400x inset (white box) demonstrates that both perivascular (red arrow) and intravascular (white arrow) MCs are MCPT5-negative (D).

Results: WMIFM of MC-tryptase (MCT) confirmed increased numbers of perivascular MCs in TNF-Tg mice, and their complete absence in cKit$^{-/-}$mice **(Fig. 1).** *In silico* scRNAseq analysis revealed a distinct population of PLV MCs vs known MCs in other mouse organs. WMIFM further demonstrated unique molecular signatures of perivascular (MCT^{+}/MCTP1^{+}/MCTP5^{-}) vs intravascular (MCT^{+}/MCTP1^{-}/MCPT5^{-}) MCs **(Fig. 2).** Remarkably, both CS treatment and cKit$^{-/-}$ x TNF-Tg mice exhibited decreased ICG clearance corresponding with increased bone erosions and synovitis vs their TNF-Tg controls **(Fig. 3)**.

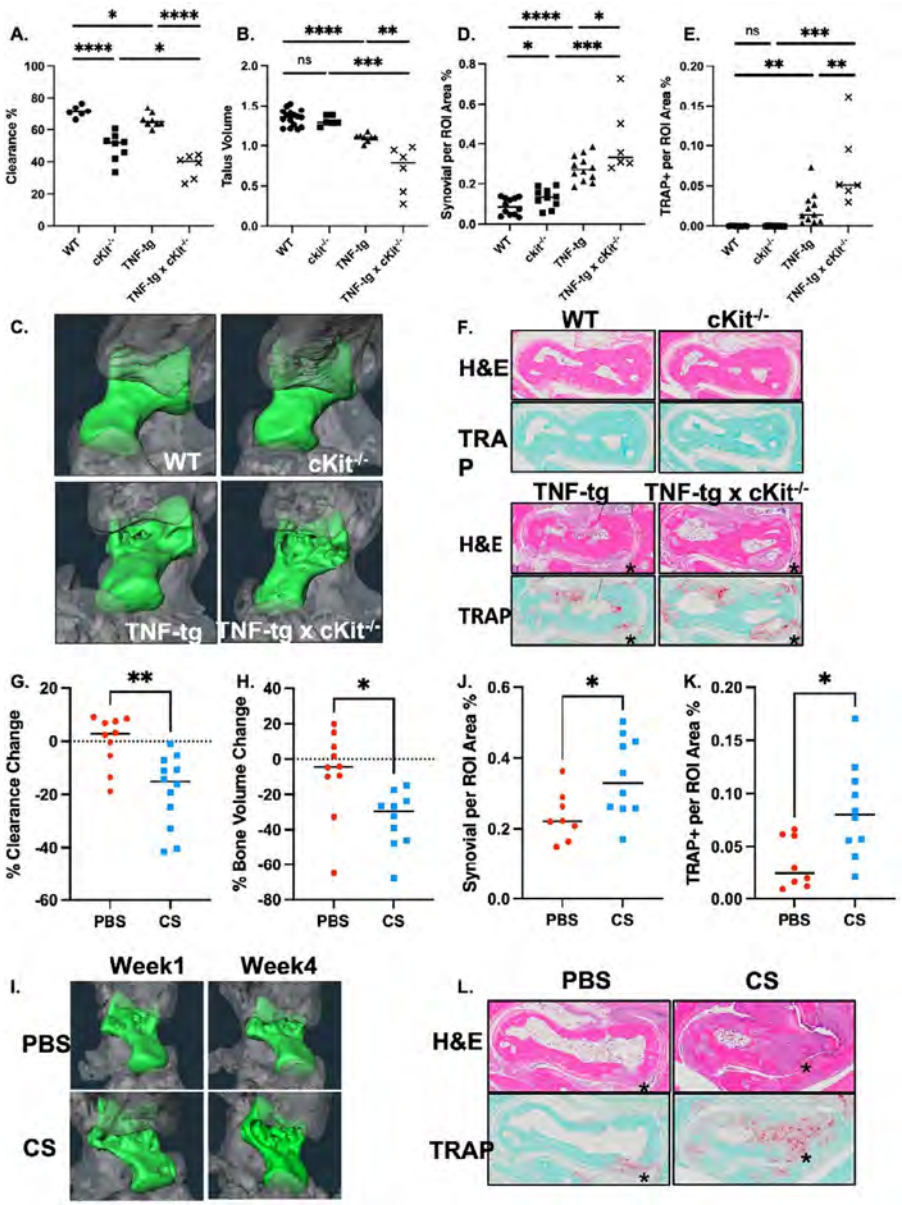

Figure 3. Global MC deletion and inhibition with cromolyn sodium decrease lymphatic clearance and exacerbate inflammatory-erosive arthritis in TNF-Tg mice. KitW-sh/W-sh (cKit-/-) and TNF-Tg mice were crossed to generate TNF-Tg x cKit-/- cohorts (both C57BL/6 background). Male mice at 4.5 months of age underwent NIR-ICG imaging, which demonstrated a combinatorial reduction of lymphatic function in the setting of inflammation (TNF-Tg) and MC ablation (cKit-/-) (A). In TNF-Tg mice, the enhanced lymphatic deficiency with MC deletion was associated with increased bone erosions in the talus (green bone) of the afferent ankle joint, quantified by micro-CT with represented images provided (B, C). Histomorphometric analysis revealed a corresponding increase in synovial inflammation (D, H&E) and number of osteoclasts (E, TRAP) in the talus region of MC deficient TNF-Tg x cKit-/- mice, as shown by representative images (F). To evaluate the effects of MC inhibition, 4-month-old female TNF-Tg mice (n=10) were randomized to 3-weeks of placebo (PBS) or cromolyn sodium (CS) treatment (n = 5 mice/group; 10 limbs) based on baseline lymphatic clearance by NIR-ICG imaging. Terminal NIR-ICG and micro-CT imaging revealed significantly reduced lymphatic clearance (G) and midfoot bone volumes (H, I; green talus as representative image) with CS, respectively. Coinciding with the increased bone erosions, histomorphometry also showed increased synovial (J) and TRAP+ osteoclast area (K) with representative images provided (L). Statistics: unpaired t-test; *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

Conclusion: In this work, we characterized unique intravascular MCTP1$^-$ MCs in a cellular niche within the tissue structure [BK1] of murine joint-draining PLVs. These intravascular MCs are distinct from known MC subtypes, including perivascular MCTP1$^+$ MCs, which are increased in TNF-Tg and absent in cKit$^{-/-}$ mice. Interestingly, both global MC deletion and inhibition decreased lymphatic function and exacerbated joint disease in TNF-Tg mice. These findings suggest subtype-specific MC regulation of lymphatic function through distinct cellular phenotypes, where MCTP1$^-$ intravascular MCs provide a protective role and selective deletion of MCTP1$^+$ perivascular MCs restored lymphatic drainage and ameliorated inflammatory-erosive arthritis.

Disclosure: Y. Peng: None; **H. Kenney**: None; **K. Bentley**: None; **L. Xing**: None; **C. Ritchlin**: AbbVie, 2, 5, 6, Amgen, 2, BMS, 2, Eli Lilly, 2, Gilead, 2, Janssen, 2, Novartis, 2, Pfizer, 2, 5, 6, UCB, 2, 6; **E. Schwarz**: None.

Abstract Number: 1726

Therapeutic Effect of ICAM-1 Mimic on Experimental Axial Spondyloarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Animal Models Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Axial Spondyloarthritis (AxSpA) is a chronic inflammatory arthritis primarily affecting the axial skeleton and commonly coexists with gut and skin inflammation. Currently, patients with axSpA require lifelong treatment. Current biologics (TNFi, IL-17i, JAKi)improve symptoms but are not curative and cannot prevent disease progression.

With the help of AI technology highlighting several unique small molecules with the potential efficacy in axSpA, it was possible to identify a potential small molecule that acts on the binding site of lymphocyte function-associated antigen-1 (LFA-1) and intercellular adhesion molecule-1 (ICAM-1). The LFA-1/ICAM-1 interaction is known to enable both T-cell activation and pro-inflammatory cytokine release. Through previously associated work with computational science and a preclinical in vivo model using DBA/1 collagen induced arthritis model, we have seen significant effects, resulting in decreased arthritis score and paw thickness. It is with this ICAM-1-mimicing small molecule compound that this study reports on the effect blocking this interaction has on an axSpA murine model.

Table 1:

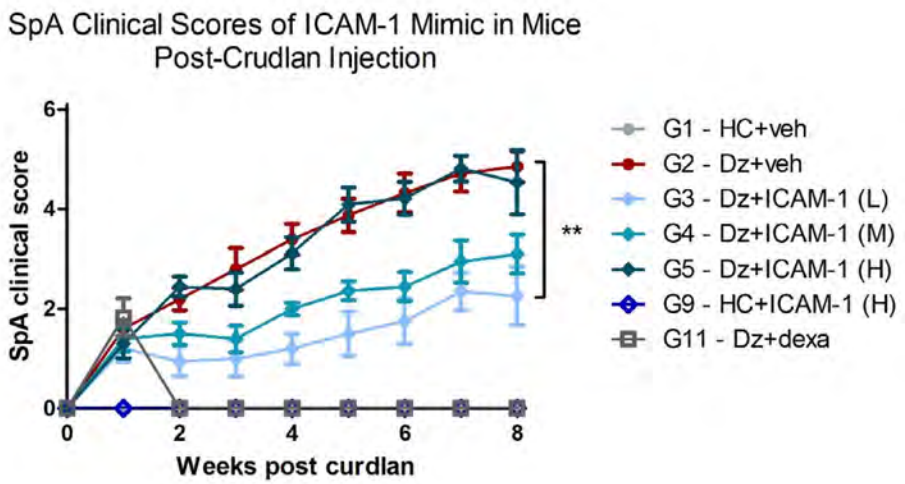
Group	Treatment	Dose (mg/kg)
G1	Healthy, no disease	0
G2	Disease + vehicle	0
G3	Disease + ICAM-1 mimic (low dose)	3
G4	Disease + ICAM-1 mimic (mid)	10
G5	Disease + ICAM-1 mimic (high)	20
G9	Healthy + ICAM-1 mimic (high)	20
G11	Disease + Dexamethasone	10

Breakdown of the treatment groups of the SKG mice for the experiment. Three different treatment doses were examined, along with control groups (healthy, diseased, dexamethasone-treated)

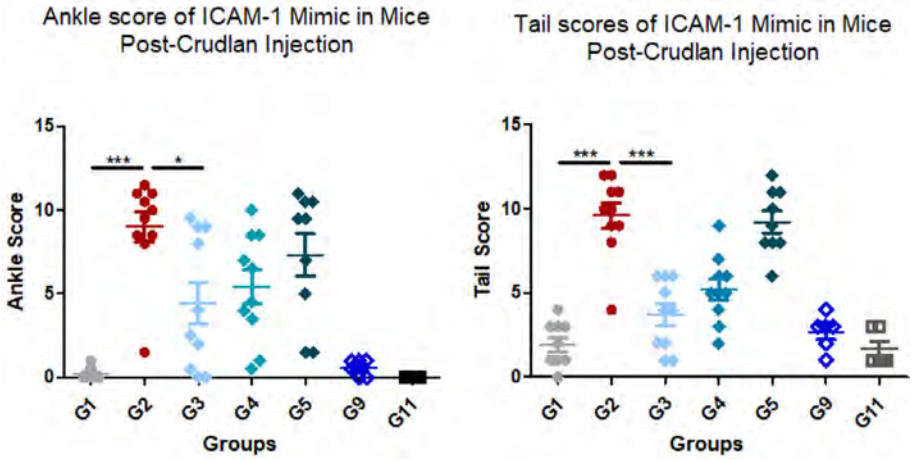
Methods: We employed the use of the SKG mouse, an IL-23- and IL17-dependent model leading to disease resembling human axSpA. SKG mice given a single dose 3mg curdlan (intraperitoneal) developed skin inflammation in ears and tail, blepharitis, and swelling of ankles and wrists and digits. Therapeutic intervention began one week post-curdlan disease induction. These mice were treated with varying doses of the ICAM-1 mimic via daily intraperitoneal (IP) injections and monitored for 8weeks.

Results: With the SKG mice, theICAM-1 mimic showed excellent tolerability and showed a significant decrease in clinical scores, which was most pronounced in the low dose treatment group (G3 in Fig 1). Histological analysis with H&E staining indicated that animals treated with the compound had significantly reduced histological scores of tails, skin, ankle, and gut for the low dose treatment group (G3).

Conclusion: This small molecule ICAM-1 mimic, identified by an axSpA drug discovery approach, shows efficacy in this preclinical model. Follow-up studies will examine pharmacokinetics and pharmacodynamics of the compound. This is promising data for application of this ICAM-1 mimic as a new therapeutic option for axSpA.



Clinical scores of the treatment groups with significance seen between the disease group (G2) and low dose (G3) treatment group.



Histological analysis H&E staining of joints. Left panel shows the ankle scores with significance seen between the disease (G2) and low dose (G3) groups. Right panel shows the ankle score with significance seen between the same two groups.

Disclosure: M. Lim: Aria Pharmaceuticals, 5; **S. Foroozan**: None; **Z. Qaiyum**: None; **M. Tang**: None; **E. Yau**: None; **R. Inman**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Sandoz, 2.

Abstract Number: 1727

Arthritogenicity of Homocitrullinated Peptides in HLA-DRB1 Transgenic Mice

Sheri Saunders, Garth Blackler, Patti Kiser, Ewa Cairns and **Lillian Barra**, Western University, London, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Animal Models Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Most rheumatoid arthritis (RA) patients express autoantibodies to post-translationally modified antigens, including citrullinated and homocitrullinated (also known as carbamylated) peptides. Homocitrulline and citrulline are structurally similar and immune responses to peptides containing either of these modifications are cross-reactive. Citrullinated peptides bind strongly to MHCII molecules containing a consensus sequence called the Shared Epitope (encoded by HLA-DRB1 alleles, the strongest genetic risk factor for RA). The relationship between homocitrullinated peptides and the Shared Epitope remains unclear. The aim of this study is to determine whether homocitrullinated peptides induce arthritis in a humanized mouse model of RA expressing the Shared Epitope.

Methods: Male and female HLA-DRB1*04:01-transgenic (DR4tg) mice and wild-type C57Bl/6 (B6) mice were immunized with a synthetic homocitrullinated peptide (HomoCitJED) or PBS and then received intra-articular (i.a.) HomoCitJED in one knee and PBS in the other knee. Immune responses in these mice were measured serially for serum autoantibody production by ELISA to the following antigens: HomoCitJED, CitJED (a synthetic citrullinated peptide that contains the same backbone as HomoCitJED), homocitrullinated fibrinogen (HomoCitFib), citrullinated fibrinogen (CitFib), fibrinogen (Fib) and cyclic citrullinated protein/peptide 2 (CCP2).Arthritis was assessed by serial measurements of joint swelling with calipers and by histopathology at sacrifice (day 137 post-primary immunization) using a standardized scoring system.

Results: After immunization with HomoCitJED, all DR4tg mice (14/14) developed IgG anti-HomoCitJED and anti-HomoCitFib antibodies, compared to 4/6 and 3/6 B6 mice, respectively. A small number of mice developed antibodies to CitJED (4/14 DR4tg and 1/6 B6). Anti-CCP2 was detected in 8/14 DR4tg and 4/6 B6 mice. None of the mice had detectable antibodies to Fib or CitFib. Antibody levels did not change significantly after i.a. injections and over time. PBS immunized mice did not have detectable immune responses or arthritis. After day 78 post-immunization, significant joint swelling was observed in the knees of HomoCitJED injected DR4tg mice with an arthritis score of 3.92 (SD 2.90)/12 versus 1.18 (SD 1.08)/12 in HomoCitJED-injected B6 wild-type mice; p=0.0016. Histopathologic findings included synovial thickening and pannus, hypervascularity, cartilage destruction and bone erosions.

Conclusion: Mice expressing human Shared Epitope developed immune responses to homocitrullinated and citrullinated antigens and RA-like arthritis. These findings support an arthritogenic role for homocitrullinated antigens that is enhanced by the Shared Epitope.

Disclosure: S. Saunders: None; **G. Blackler**: None; **P. Kiser**: None; **E. Cairns**: None; **L. Barra**: AstraZeneca, 1, GlaxoSmithKlein(GSK), 1, 6, Otsuka, 1, 5, 6, Pfizer, 1, 5, 6.

Abstract Number: 1728

A Novel Animal Model for Investigating the Effect of HLA-DRB1 on Atherosclerosis

Garth Blackler, James Akingbasote, Patti Kiser, Christopher Howlett, Ewa Cairns and **Lillian Barra**, Western University, London, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Animal Models Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: HLA-DRB1 alleles are associated with various autoimmune and inflammatory conditions, including rheumatoid arthritis, polymyalgia rheumatica, giant cell arteritis, systemic lupus erythematosus, diabetes and atherosclerotic cardiovascular disease. In rheumatoid arthritis, patients expressing HLA-DRB1 have a high risk for cardiovascular mortality. This study aimed to create and characterize a novel animal model to better understand the role of HLA-DRB1 in the pathogenesis of atherosclerosis.

Methods: Mice transgenic for HLA-DRB1*04:01 (DR4tg) were crossed with an established mouse model of atherosclerosis, low density lipoprotein receptor knock-out (*Ldlr*-/-) mice. DR4tg*Ldlr*-/- (n=48), *Ldlr*-/- (n=24), DR4tg (n=24), and C57Bl/6 (B6) background (n=24) mice were fed a high fat, high cholesterol (HFHC) or regular diet (RD) for 12 weeks. Serum lipoproteins were measured using a colorimetric assay. C-reactive protein (CRP), anti-cyclic citrullinated protein/peptide antibodies2 (anti-CCP2) and oxidized LDL (OxLDL) were measured using ELISA. Atherosclerosis in whole aortas was assessed using the lipid stain, Sudan IV. The presence of citrulline in atherosclerotic plaque from aortic sinus sections was determined by immunohistochemistry. Mice were monitored for arthritis by measuring knee and ankle swelling and by histopathology.

Results: DR4tg*Ldlr*-/- had a similar degree of atherosclerotic plaque burden compared to *Ldlr*-/-, despite having lower sera low-density lipoprotein cholesterol (LDL-C) levels; p=0.0056. Levels of the more pro-atherogenic lipoprotein, OxLDL was higher in DR4tg*Ldlr*-/- than *Ldlr*-/-mice; p=0.0017. Male *Ldlr*-/- mice had worse atherosclerosis than females, but there were no sex differences in DR4tg*Ldlr*-/-. CRP was elevated in all mice fed a HFHC diet, most pronounced for DR4tg*Ldlr*-/-; p=0.0009. B6 and DR4tg mice did not have significant elevations in serum cholesterol levels and did not develop atherosclerosis. None of the mice developed antibodies to citrullinated antigens or spontaneous inflammatory arthritis.

Conclusion: HLA-DRB1 expression in a mouse model of atherosclerosis resulted in an elevation of oxidized LDL and a reduction in the male bias for atherosclerosis, mimicking what is observed in rheumatoid arthritis.

Disclosure: G. Blackler: None; **J. Akingbasote**: None; **P. Kiser**: None; **C. Howlett**: None; **E. Cairns**: None; **L. Barra**: AstraZeneca, 1, GlaxoSmithKlein(GSK), 1, 6, Otsuka, 1, 5, 6, Pfizer, 1, 5, 6.

Abstract Number: 1729

An Antibody-drug Conjugate of Anti-TNFα Antibody and a Novel Glucocorticoid Molecule Exerts Synergistic Anti-inflammatory Effects for Treatment of Autoimmune Diseases

Yuhao Qin[1], **Wenming Ren**[2], Liangqin Tong[3], lu su[3] and cheng liao[3], [1]Jiangsu Hengrui Pharmaceuticals Co., Ltd, Shanghai, China, [2]Jiangsu Hengrui Pharmaceuticals Co., Ltd., Pudong New District, China, [3]Jiangsu Hengrui Pharmaceuticals Co., Ltd., Shanghai, China

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Animal Models Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Tumor necrosis factor α (TNFα) is a pivotal pro-inflammatory cytokine. And TNF inhibitors are the most successful anti-rheumatic drugs for the treatment of autoimmune diseases such as rheumatic arthritis. However, many patients respond poorly or lose response gradually to anti-TNF therapies. Glucocorticoids (GCs), which exert extensive immunosuppressive effects by inhibiting the nuclear factor kappa-B signaling pathway, have been the most powerful and basic/standard treatment for many autoimmune diseases, while their long-term usage is strictly limited due to the adverse effects. Here, we describe the preclinical characterization of an anti-TNF conjugate which is consisted of an anti-TNFα antibody and a novel GC molecule with high potency.

Methods: The glucocorticoid receptor (GR) binding activity of the GC molecule was measured in a GR biochemical assay. The binding affinity of the anti-TNF conjugate with TNFα were assessed by surface plasmon resonance assay. The TNF inhibitory activities of the anti-TNF conjugate were evaluated in LPS-induced monocyte IL-6 release assay and TNFα-induced L929 cytotoxicity assay. And the *in vivo* efficacy of the anti-TNF conjugate was determined in dinitrofluorobenzene-induced delayed-type hypersensitivity (DTH) mouse model and the collagen antibody-induced arthritis (CAIA) mouse model. In addition, a 4-week GLP repeated-dose toxicity study in cynomolgus monkeys was conducted to evaluate the safety profiles.

Results: The novel GC molecule was a high potent short-acting glucocorticoid. And the anti-TNF conjugate showed similar TNFα binding affinity and TNFα-induced cytotoxic inhibitory activity to the anti-TNFα antibody. The anti-TNF conjugate could block the pro-inflammatory pathways by neutralizing soluble TNFα, and deliver the GC molecule specifically to pathogenic immune cells by binding to the transmembrane TNFα, which exerts synergistic anti-inflammatory effects and reduces the systemic exposure and side effects of GC. We proved that the anti-TNF conjugate inhibited LPS-induced IL-6 secretion in monocytes more potently than the anti-TNFα antibody. In DTH mouse model, the anti-TNF conjugate demonstrated better ear swelling remission than anti-TNFα antibody. In hTNFα-transgenic CAIA mice model, the disease severity score and histopathology were also significantly improved at a relatively low dose of the anti-TNF conjugate. Furthermore, the GLP repeated-dose toxicity study in cynomolgus monkeys showed the anti-TNF conjugate was well tolerated and no changes in cortisol were observed at doses up to 50 mg/kg. Our results showed the anti-TNF conjugate has a better efficacy than anti-TNFα antibody and has superiority in safety and tolerance compared to GCs.

Conclusion: Our data provides strong evidence that the anti-TNF conjugate is a potent anti-rheumatic drug with good safety profile, which support its further clinical application in autoimmune diseases including rheumatic arthritis and ulcerative enteritis.

Disclosure: Y. Qin: Jiangsu Hengrui Pharmaceuticals Co., Ltd., 3; **W. Ren**: Jiangsu Hengrui Pharmaceuticals Co., Ltd., 3; **L. Tong**: Jiangsu Hengrui Pharmaceuticals Co., Ltd., 3; **l. su**: Jiangsu Hengrui Pharmaceuticals Co., Ltd., 3; **c. liao**: Jiangsu Hengrui Pharmaceuticals Co., Ltd., 3.

Abstract Number: 1730

Gut Microbiota Dysbiosis Impact Autonomic Function in Rheumatoid Arthritis Patients

Rachel AUDO[1], Jérome Thireau[2], Louis Rauzier[3], Marie Barozet[1], JACQUES MOREL[4], Patrice Bideaux[3], alain Lacampagne[2] and **Claire Daien**[5], [1]CHU Montpellier, Montpellier, France, [2]PhyMedExp INSERM U1046, Montpellier, France, [3]PhyMedExp U1046, Montpellier, France, [4]Protocole thérapeutique immuno-rhumatologie, Montpellier, France, [5]University Hospital, Montpellier, France

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Animal Models Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is associated with a high risk of cardiovascular (CV) risks, including accelerated atherosclerosis, left ventricular hypertrophy and decreased heart rate variability (HRV). HRV decrease reflects the inability of the autonomic nervous system (ANS) to adapt cardiac function and lower HRV is associated with a higher risk of CV events. Autonomic dysfunction is observed in RA with a prevalence as high as 60–80% and precedes apparition of symptoms. Given that gut microbiota (GM) dysbiosis also occurs before disease and inflammation in subjects who will develop RA, and that activity of vagus nerve can be modulated by the GM, we hypothesized that GM impairs the ANS balance in RA.

Methods: we investigated whether fecal microbiota transplantation (FMT) of RA patients modulates the electrocardiographic profile, the HRV and cardiac function (echocardiography) compared to FMT of healthy subjects (age-and-sex-matched controls). Using electrocardiogram (ECG) acquired by telemetry, we characterized the impact of FMT on sympathetic and/or vagal outflow using temporal- and spectral-domain analyses of HRV. High resolution echocardiography allowed us to assess both cardiac structural and contractile function. In parallel, FMT consequences on intestinal barrier permeability, the pro- or anti-inflammatory immune cells and early markers of atherosclerosis were evaluated to related potential modification to inflammatory profile.

Results: Heart Rate Variability (HRV) analysis showed that FMT from RA patients altered the ANS activity in mice, reproducing a defect of vagal tone. Indeed, in mice with fecal transfer of RA microbiota (RA-FMT), we observed an increase of heart rate, only during resting time (444.82(±20.07) bpm vs 477.12(±30), p=0.0001, n=34/group). This tachycardia results from a reduction of HRV reflecting altered ANS activity with a decrease in SDNN index (SDNN 23.88±9.97 vs 10.22±4.05 ms, p< 0.0001, n=34/group). Time domain and spectral domain analyses of HRV confirmed a decrease in the parasympathetic activity resulting in a drop of sympathovagal balance. These alterations are independent of cardiac structural, of contractile modifications and of any remodeling of cardiac muscarinic or adrenergic signaling pathway. In addition, this vagal tone dysfunction was independent of inflammation as RA FMT did not induce major immune dysfunction or change in the aortic expression of early markers of atherosclerosis (VCAM and ICAM).

Conclusion: We demonstrated that for the first time that the MI of RA patients contributes to autonomic dysfunction, independently of the inflammatory status, and without structural or contractile modification of the heart. This opens new therapeutic perspectives, such as dietary modifications, for example with the addition of fibre or the use of probiotics, to prevent autonomic dysfunction and CV risk in RA.

Disclosure: R. AUDO: None; **J. Thireau**: None; **L. Rauzier**: None; **M. Barozet**: None; **J. MOREL**: None; **P. Bideaux**: None; **a. Lacampagne**: None; **C. Daien**: None.

Abstract Number: 1731

A Competitive Inhibitor of MOART Showed Potent Therapeutic Effects in a Mouse Model of Collagen-induced Arthritis

Sujin Park[1], DongWoo Kang[2], Haein An[1], Eunji Hong[1], Kwiyeom Yoon[2], MinWoo Kim[2], Hwajung Kim[2] and **Seong Jin Kim**[2], [1]GILO Institute, GILO Foundation, Seoul, South Korea, [2]Medpacto Inc., Seoul, South Korea

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Animal Models Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite tumor necrosis factor (TNF) inhibitors and Jak kinase inhibitors (JKI) have shown a significant advance in the treatment of rheumatoid arthritis (RA) however, only 20 to 30% of patients experience remission. Recently, we identified that *moart*, whose expression is markedly elevated at a late phase of osteoclast differentiation, is a keymembrane organizer of osteoclast multinucleation. Knockout mice lacking the entire *moart* gene dramatically reduced a bone loss in an ovariectomized mouse model. In this study, we investigated the therapeutic effects of MP2021, a competitive inhibitor of MOART, in a mouse model of collagen-induced arthritis (CIA).

Methods: To induce CIA, DBA/1J mice (n = 10 per group) were immunized subcutaneously at the tail with chicken type II collagen on days 0 and 14. Mouse MP2021, human MP2021, control IgG-Fc or TNFR2-Fc fusion protein (etanercept) were injected subcutaneously twice a week after the onset of CIA (therapeutic treatment). Clinical arthritis scores were measured by summing the scores of all four paws. Disease progression was monitored daily, and cytokines and histologic analysis (synovial inflammation, joint damage, and bone loss) were measured by ELISA, IHC, and microCT at the end of the study.

Results: Clinical arthritis scores and morphological signs of bone destruction improved in the mMP2021-treated group compared to IgG-Fc. Expression levels of IL-1b, IL-6, TNFa, COMP, MMP-3, and MMP-13 were significantly reduced in the articular bones of mice treated with mMP2021. Histologic analysis also showed that mMP2021 inhibited bone damage by inhibiting synovitis, synovial formation, and chondrolysis, and significantly reduced the number of tartrate-resistant acid phosphatase (TRAP)-positive osteoclasts. hMP2021 administered subcutaneously to CIA mice also showed more inhibitory effects on clinical arthritis scores than etanercept. The hMP2021 showed equivalent effects when administered intravenously or subcutaneously, which is a promising result for the clinical application of this molecule.

Conclusion: We found that human MP2021 as well as mouse MP2021 significantly inhibited cartilage damage and bone erosion in established mouse CIA models, along with a reduction in multinucleated osteoclasts. These findings suggest that MP2021 has potential as a novel therapeutic agent that can be effectively applied to various bone and joint diseases, including rheumatoid arthritis.

Disclosure: S. Park: None; **D. Kang**: None; **H. An**: None; **E. Hong**: None; **K. Yoon**: None; **M. Kim**: None; **H. Kim**: None; **S. Kim**: None.

Abstract Number: 1732

Immunopathogenesis and Preclinical Trials in a Humanized Mouse Model of Rheumatoid Arthritis(RA)

Huiyi Wang[1], Kangkang Luo[1], Shuxin Xu[1], Jiayin Zhou[1], Santi Chen[2], Jun wang[2], Wenzhao Li[2], Jing Zhao[1] and Cunxiang Ju[1], [1]GemPharmatech CO., Ltd., Nanjing, China, [2]GemPharmatech LLC, La Jolla, CA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Animal Models Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The differences between human and mouse immune systems make it challenging to accurately reflect the immunopathogenesis of autoimmune diseases in patients. Therefore, translational research needs to shift focus from mouse immunology to human immunology. In addressing these challenges, the HSC-NCG-M mice have emerged as a valuable model. Gempharmatech developed the HSC-NCG-M mouse model to support the development of human T, B, NK, and myeloid cells more effectively. The HSC-NCG-M mouse model is genetically engineered on the severe immunodeficient NCG strain and produces human granulocyte/macrophage colony-stimulating factor 2 (GM-CSF, also known as CSF2), interleukin-3 (IL-3), and stem cell factor (SCF, also known as KITLG).

Methods: This study describes the construction process of the RA model in HSC-NCG-M mice. Female NCG-M mice (4-6 weeks old) were engrafted with $CD34^+$ HSC after irradiation. The RA model was induced by injecting Complete Freund's Adjuvant (CFA) into the foot pads of the hind limbs. The body weight, graft-versus-host disease (GvHD) score and the development of arthritis in the hind limbs of the mice were monitored three times a week. The arthritis score for each mouse was obtained by summing the scores for both hind limbs. The volume of the left and right hind limbs, including the joint of the paw and ankle, was measured three times a week using a claw measuring instrument until the end of the experiment.

Results: In the CFA-induced RA model based on HSC-NCG-M mice, there was an increasing number of human CD4+ T lymphocytes, Th17, Treg, and monocytes in peripheral blood, along with elevated IL-6 levels, which closely resembled clinical phenotypes of RA patients. Compared to the control group, HSC-NCG-M mice injected with CFA in the foot pads showed increased arthritis scores and swelling thickness in the hind limbs.

Conclusion: This model develop a fully functional human immune system capable of innate and adaptive immune responses. The CFA-induced RA model primarily involves the human immune system and closely resembles human RA patients. Therefore, the HSC-NCG-M mouse model is an appropriate model for studying RA, as it involves the engagement of the human immune system.

Disclosure: H. Wang: None; **K. Luo**: None; **S. Xu**: None; **J. Zhou**: None; **S. Chen**: None; **J. wang**: None; **W. Li**: None; **J. Zhao**: None; **C. Ju**: None.

Abstract Number: 1733

Platelet-Derived Growth Factor Is a Mediator of Disease in an Animal Model of Rheumatoid-Associated Interstitial Lung Disease

Nozima Aripova[1], Michael Duryee[1], Amy Nelson[1], Carlos Hunter[1], Breanna Butler[1], Bryant England[1], Jill Poole[1], Geoffrey Thiele[1] and Ted R Mikuls[2], [1]University of Nebraska Medical Center, Omaha, NE, [2]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Animal Models Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis-associated interstitial lung disease (RA-ILD) is a leading cause of mortality in RA with limited treatment options as well as lack of available animal modeling systems for preclinical investigations. We previously demonstrated that co-exposure of the collagen induced arthritis (CIA) with repetitive airborne lipopolysaccharide (LPS) exposure leads to increased autoimmunity, arthritis, and pro-fibrotic/pro-inflammatory lung disease. In addition to recapitulating important histopathologic features of RA-ILD, this model demonstrates more severe arthritis and lung manifestations in male mice. Platelet-derived growth factor (PDGF)-BB and its receptor (PDGFR) are important cellular proliferation and growth with dysregulation associated with cancers and tissue fibrosis, with limited and conflicting studies in RA. In the present study, we leveraged our novel mouse preclinical animal modeling system to investigate the potential role of PDGF-BB/PDGFR, in RA-associated lung disease.

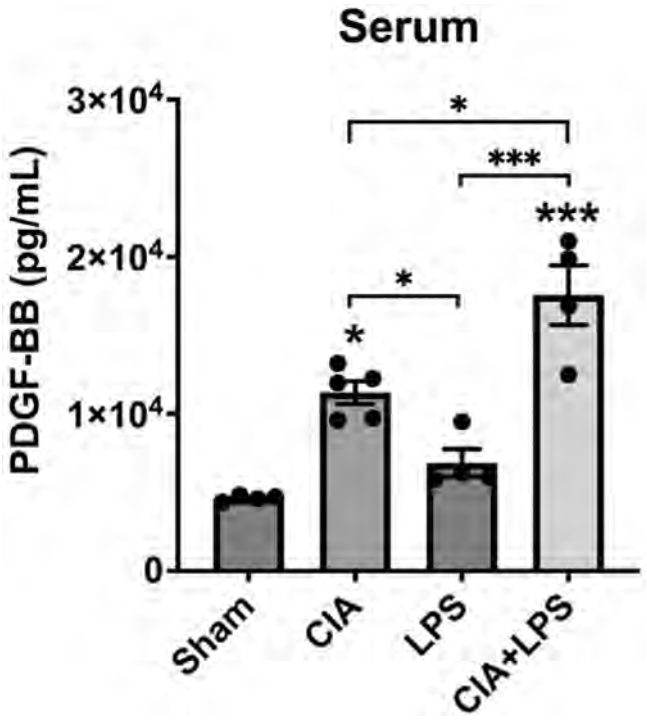


Figure 1. PDGF-BB levels in the serum of DBA mice. Mice were treated with/without CIA and with/without LPS inhalation. Scatter dot plots represent mean±SEM of platelet-derived growth factor (PDGF) levels (pg/mL). Comparisons made to Sham are illustrated above each bar: ***p<0.001, *p<0.05, n=4. Tukey's post-hoc test comparisons are illustrated between treatment groups, and only significant differences are illustrated: ***p<0.001, *p<0.05. Abbreviations: CIA, collagen-induced arthritis; LPS, lipopolysaccharide.

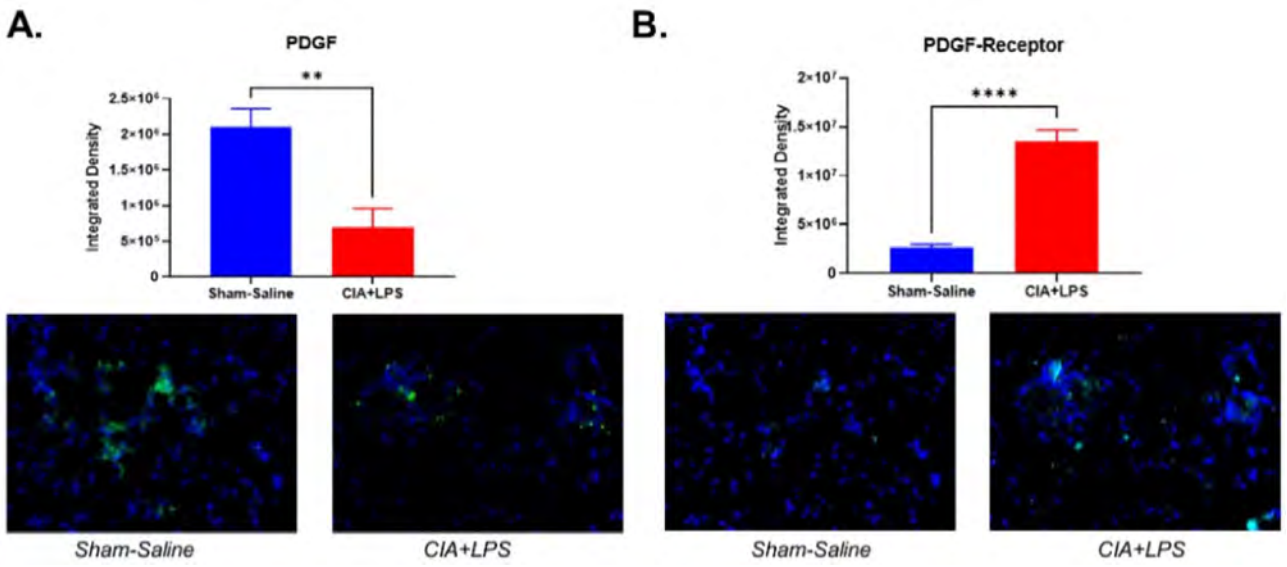


Figure 2. IHC Staining of Lung Tissue from DBA mice. Mice were treated with CIA+LPS or Sham-Saline. Lung tissues were stained for: (A) PDGF; and (B) PDGF-receptor. The data is represented as a mean of integrated density with SEM. Comparisons between the two groups were made using t-test: **p<0.01. Abbreviations: CIA, collagen-induced arthritis; LPS, lipopolysaccharide; PDGF, platelet-derived growth factor.

Methods: Arthritis-prone male (DBA/1J) mice (n=5/group) received either: Sham (saline injection/inhalation), CIA (CIA on day 1 and 21/saline inhalation), LPS (saline injection/ LPS 100ng inhalation), or CIA+LPS (CIA injection/LPS inhalation) for 5 weeks. At week 5, serum was collected for quantification of PDGF-BB using ELISA in all 4 groups. Based on marked serum differences observed between CIA+LPS and Sham, lung tissues were isolated for quantification of PDGF-BB and PDGF-receptor expression using fluorescent immunohistochemistry (IHC) in these two treatment groups. Serum PDGF-BB levels were compared using one-way ANOVA and Bonferroni multiple comparison tests across the 4 treatment groups. Fluorescent IHC, expressed in mean pixel density, was quantified and compared in CIA+LPS vs. Sham-treated mice using a t-test.

Results: Serum PDGF-BB concentrations (pg/ml mean ± SEM) were the highest in the CIA+LPS group ($1.6x10^4 \pm 1.2x10^3$; $p< 0.05$ vs. all others) (**Figure 1**). Also, serum PDGF-BB levels were significantly increased in CIA group ($1.1x10^4 \pm 5.5x10^2$) compared to Sham ($4.7x10^3 \pm 1.1x10^2$; $p< 0.05$) and LPS ($6.9x10^3 \pm 8.8x10^2$; $p< 0.05$) groups. Staining of lung tissues demonstrated that PDGF-BB expression was decreased significantly in CIA+LPS compared to Sham ($p< 0.01$) (**Figure 2**). In contrast, PDGF-receptor expression was increased significantly in CIA+LPS ($p< 0.0001$) compared to Sham.

Conclusion: Co-exposure of mice to CIA+LPS profoundly increased circulating PDGF-BB concentrations. In the corresponding lung tissues of CIA+LPS mice, PDGF-BB expression was strikingly reduced while PDGF-receptor expression was increased. These findings imply that dual exposure modulate the PDGF-BB/PDGFR pathway that release and/or production of PDGF is altered. Moreover, these observations suggest that PDGF-BB may serve as an important mediator of the inflammatory and fibrotic processes underlying RA-ILD pathogenesis and could represent a potential novel target for treatment.

Disclosure: N. Aripova: None; **M. Duryee**: None; **A. Nelson**: None; **C. Hunter**: None; **B. Butler**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **J. Poole**: AstraZeneca, 12, I have received no monies. I received anti-IL-33 monoclonal antibody from AstraZeneca for animal research sutdies.; **G. Thiele**: None; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9.

Abstract Number: 1734

Serum PDGF-BB Levels Correlate with Lung Fibrosis in Mice Injected with Malondialdehyde-Acetaldehyde and/or Citrulline Modified Vimentin

Nozima Aripova[1], Michael Duryee[1], Carlos Hunter[1], Amy Nelson[1], Breanna Butler[1], Jill Poole[1], Bryant England[1], Geoffrey Thiele[1] and Ted R Mikuls[2], [1]University of Nebraska Medical Center, Omaha, NE, [2]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Pulmonary manifestations of rheumatoid arthritis (RA), such as interstitial lung disease (RA-ILD), are a major contributor to morbidity and mortality. The mechanism of pulmonary fibrosis occurring in RA-ILD is not well understood. Lung tissues from patients with RA-ILD show increased expression of vimentin (VIM) and co-localization of citrulline (CIT) and malondialdehyde-acetaldehyde (MAA) modifications. Fibrotic lung disease such as RA-ILD involves increased cellular proliferation and excessive production of extracellular matrix proteins. Such cellular responses in fibrotic lung disease are modulated by a variety of cytokines, chemokines, and growth factors. One such growth factor, platelet-derived growth factor (PDGF)-BB has been strongly associated with tissue fibrosis but has been the subject of limited studies in RA-ILD. Therefore, the current study aimed to determine whether arthritis-prone (DBA/1J) mice immunized with MAA- and/or CIT-modified VIM develop pro-fibrotic responses in the lungs and altered PDGF-BB levels in the lungs or serum.

Methods: Arthritis-prone male (DBA/1J) mice (n=5/group) were given weekly subcutaneous injections at 25μg/mL (for VIM antigens)with a) saline, b) native VIM, c) MAA-modified VIM (VIM-MAA), d) CIT-modified VIM (VIM-CIT), or e) both (VIM-MAA-CIT) for 5 weeks. At week 6, mice were euthanized, and lung tissues were stained with trichrome for collagen deposition to assess fibrotic lung responses. Additionally, serum and lung tissue homogenates were collected for quantification of PDGF-BB levels using ELISA. Group differences were compared using one-way ANOVA and Bonferroni multiple comparison test.

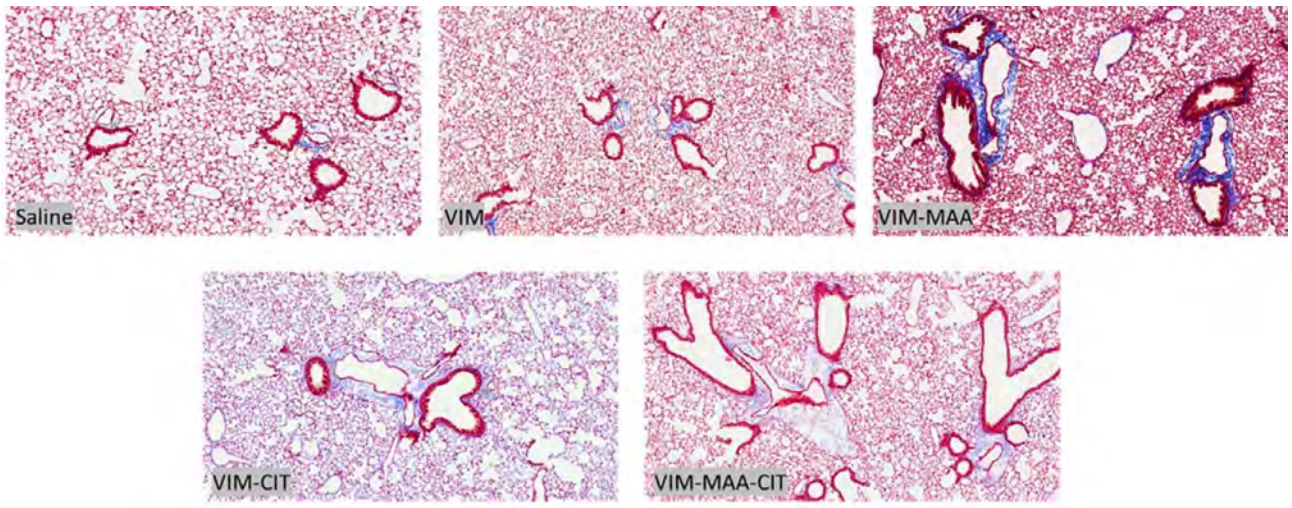


Figure 1. Trichrome staining of lung tissue in the DBA mice immunized with native and modified vimentin. Mice were immunized with saline, native VIM, VIM-MAA, VIM-CIT, and VIM-MAA-CIT.

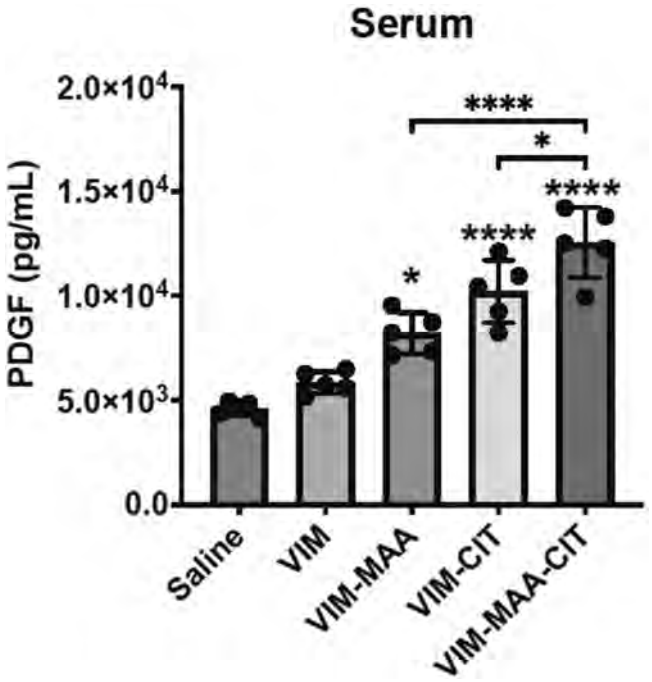


Figure 2. PDGF levels in serum of DBA mice immunized with native and modified vimentin. Mice were immunized with saline, native VIM, VIM-MAA, VIM-CIT, and VIM-MAA-CIT. The data is represented as a mean PDGF concentration (pg/mL) and reported with SEM. Comparisons made to Saline are illustrated above each bar: ****p<0.0001, *p<0.05, n≥4. Only significant differences between groups are illustrated: ****p<0.0001, *p<0.05.

Results: Trichrome staining of lungs demonstrated increased collagen deposition in mice immunized with modified VIM vs. native VIM (**Fig.1**). Serum PDGF-BB levels (mean±SEM) were highest in VIM-MAA-CIT injected group ($1.3x10^4 \pm 1.1x10^3$; $p < 0.05$ vs. others), and significantly higher than in mice immunized with VIM-CIT ($p < 0.0001$) or VIM-

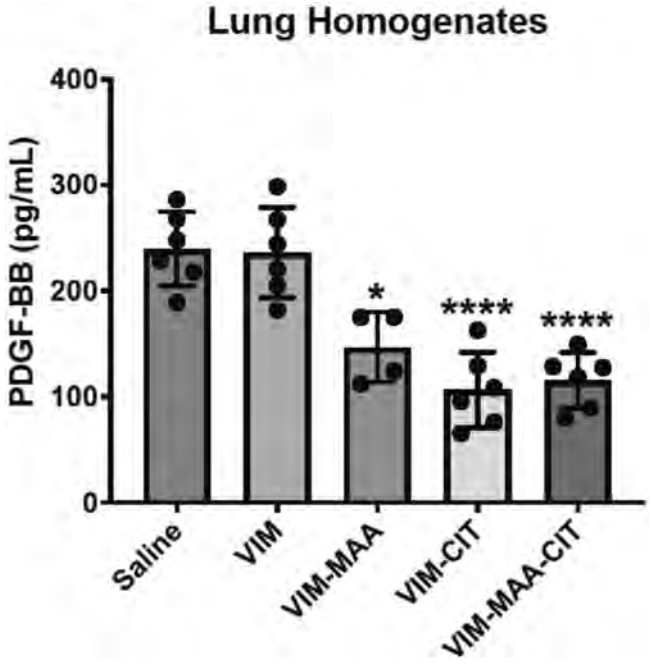


Figure 3. PDGF levels in lung homogenates of DBA mice immunized with native and modified vimentin. Mice were immunized with saline, native VIM, VIM-MAA, VIM-CIT, and VIM-MAA-CIT. The data is represented as a mean PDGF concentration (pg/mL) and reported with SEM. Comparisons made to Saline are illustrated above each bar: ****p<0.0001, *p<0.05, n≥4.

MAA ($p< 0.05$) alone (**Fig.2**). In the lung homogenates, PDGF-BB levels were decreased significantly in VIM-MAA-CIT (115.3 ±10.8; $p< 0.0001$ vs. VIM), VIM-CIT (106±14.6; $p< 0.0001$), and VIM-MAA (146.5±16.4; $p< 0.05$) compared to VIM and no significant differences between treatment groups were detected (**Fig.3**).

Conclusion: Immunization of arthritis-prone mice with modified vimentin leads to collagen deposition in lung tissues, suggesting that systemic immune reactivity to these antigens could a play in the pathogenesis of pulmonary fibrosis. In addition to generating collagen deposition, immunization of mice with dually-modified vimentin demonstrated the highest serum PDGF-BB levels compared to either single modification. In contrast, lung homogenates of mice immunized with modified vimentin showed a reduction in PDGF-BB levels compared to native vimentin. These findings suggest that PDGF-BB is either released into the circulation resulting in increased serum levels or consumed/bound by fibroblasts in the lungs of mice immunized with modified vimentin. Thus, PDGF-BB may serve as an important mediator between post-translational modifications of vimentin and fibrotic lung disease (i.e. RA-ILD).

Disclosure: N. Aripova: None; **M. Duryee**: None; **C. Hunter**: None; **A. Nelson**: None; **B. Butler**: None; **J. Poole**: AstraZeneca, 12, I have received no monies. I received anti-IL-33 monoclonal antibody from AstraZeneca for animal research sutdies.; **B. England**: Boehringer-Ingelheim, 2, 5; **G. Thiele**: None; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9.

Abstract Number: 1735

An Unorthodox HLA-DR^{hi}CD15^{+} 'Hybrid' Population in Rheumatoid Arthritis Characterized Using Spectral Cytometry

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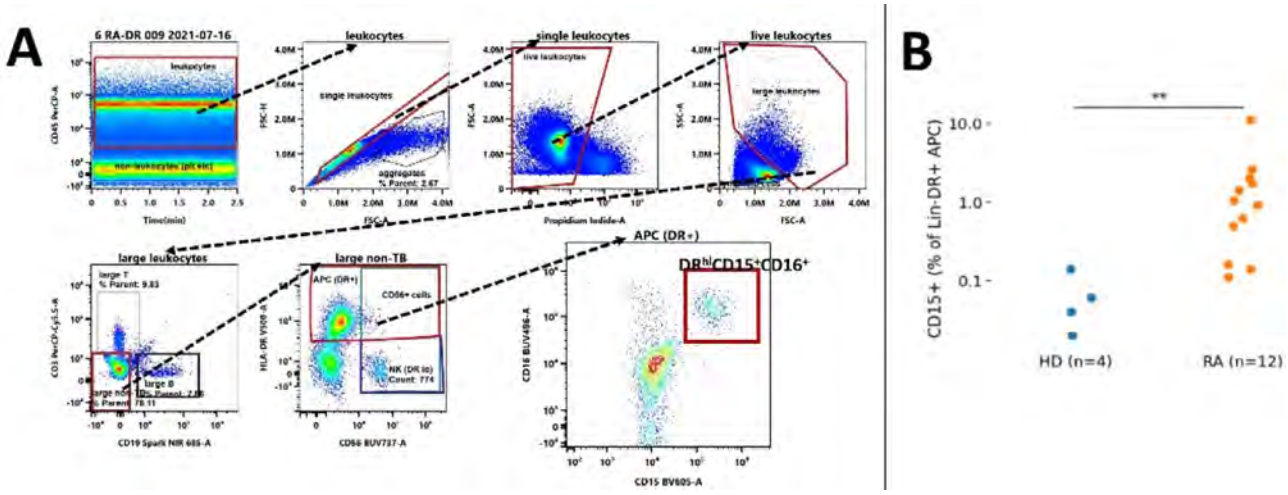
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

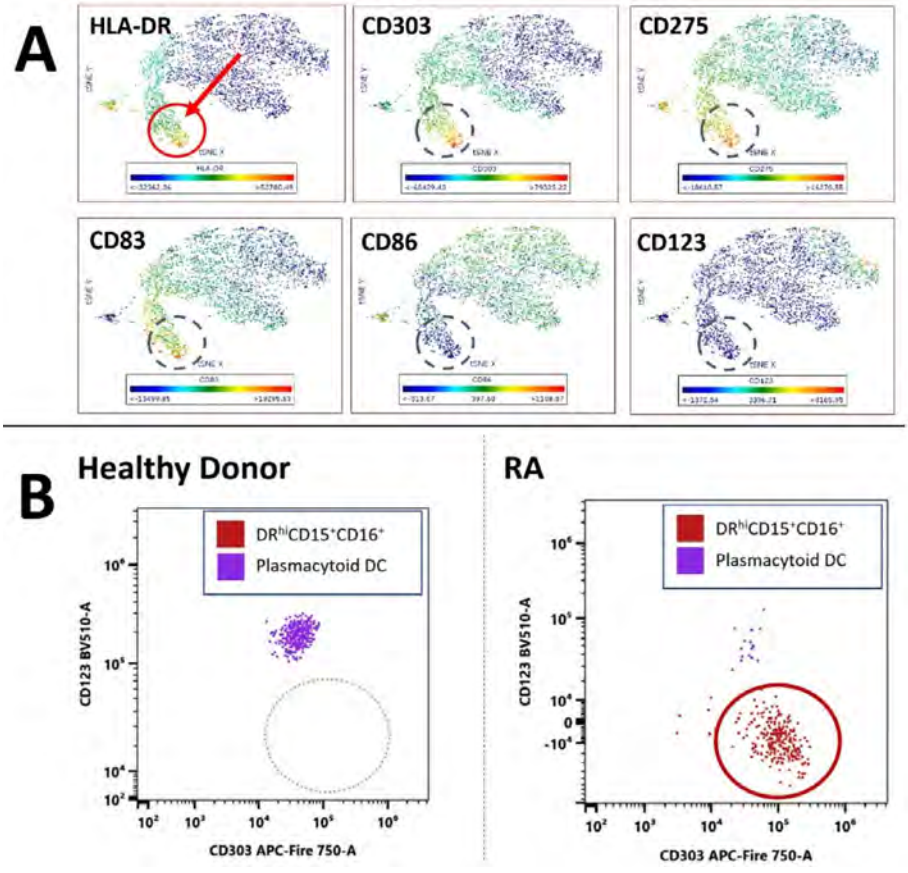
Background/Purpose: A variant of HLA-DR confers the strongest genetic risk for rheumatoid arthritis (RA) suggesting that DR^{hi} cells are important in RA. We previously found that RA blood contains 'unorthodox' DR^{hi} immune cells (non-lymphoid cells that do not conform to *bona fide* definitions of monocytesnor dendritic cells).The purpose of the study was to determine whether DR^{hi} immune cells expressing granulocyte associated molecules (CD15, CCR3)contribute to these alterations of the DR^{hi} pool in RA.

Methods: We studied RA patients (n=12) satisfying the 2010 ACR classification criteria and matched healthy donors by flow cytometry. PBMC and other low-density cells were isolated from blood by Ficoll density gradient centrifugation. To gate non-lymphoid DR^{hi} cells we excluded lymphocytes and non-viable cells based onforward and side scatter, CD3/CD19 dump and viability gates (Fig. 1A). We quantified the contribution of CD15^{+} cells to the non-lymphoid DR^{hi} pool and their expression (MFI) of co-stimulatory and co-inhibitory molecules. We used t-SNE on index patients (debilitating polyarticular synovitis)to clarify the higher-dimensional structure of the CD15positive DR^{hi} subpopulation followed by bi-axial gating to validate anyt-SNE guided observation and quantify distinctive features of DR^{hi}CD15^{+}. Kruskal-Wallis testing with a threshold of $p< 0.05$ was performed to assess for significant differences.



Flow cytometry and quantification of non-lymphoid DRhiCD15+ in RA. A) Gating strategy, patient with severe RA shown. B) DRhiCD15+ quantification in healthy donors (HD; blue) and RA (orange) and as percentage of non-lymphoid DRhi, logarithmic scale. Kruskal-Wallis Test ** p=0.0063

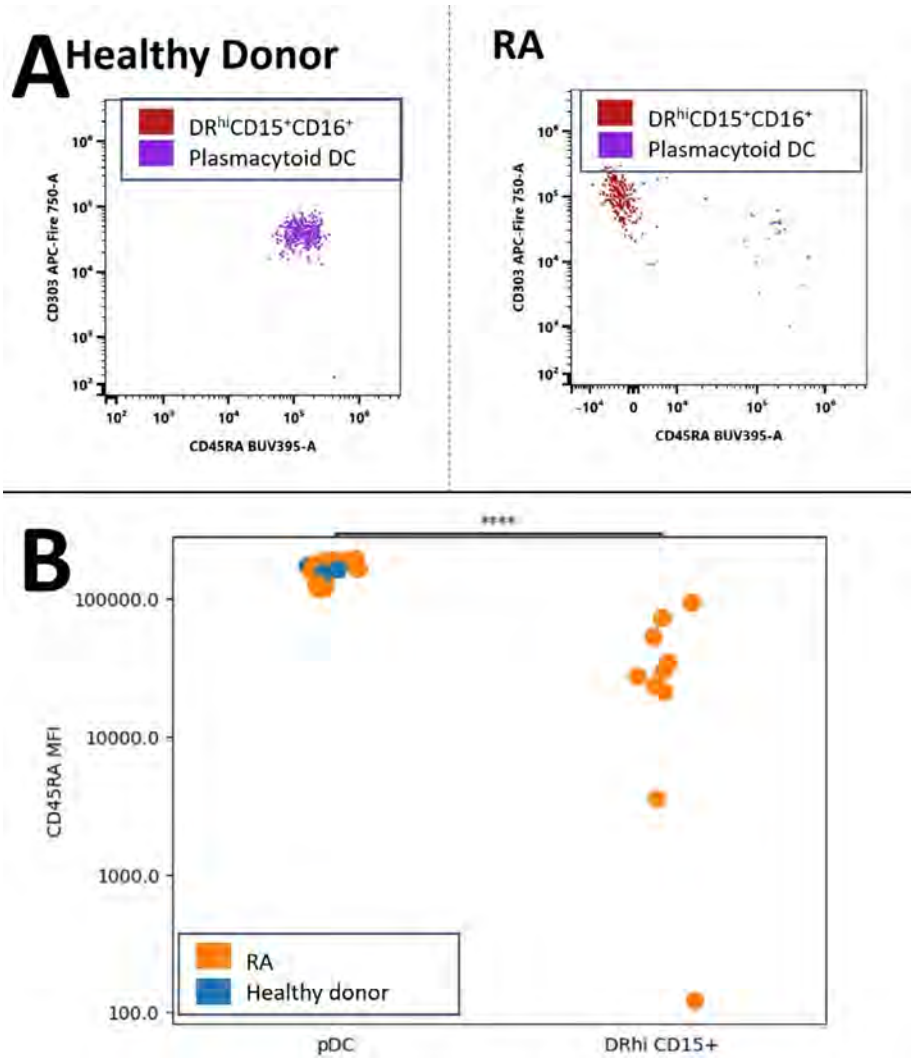
Results: In RA we found a non-lymphoid DR^{hi} $CD15^{+}$ population that was virtually absent in healthy donors (HD)(RA 0.98% vs. HD 0.05% of non-lymphoid DR^{hi}; p<0.01, Fig. 1B, 2B); these cells have near uniform CD16 co-expression (Fig 1A, gated in last plot).DR^{hi} $CD15^{+}$ showed—as expected from granulocytic cells — high side scatter but differed from granulocytes by a striking co-expression of plasma cytoid (pDC) marker CD303 (Fig. 2A, B; circled);CD123, highly expressed by pDC, was



Non-lymphoid DRhiCD15+CD16+. A) t-SNE from an RA patient with debilitating polyarthritis population (red circle and arrow) highlighting co-expression of CD303, CD83, CD275; lack of CD123. Red: high expression. Blue: low expression. B) Bi-axial gating of DRhiCD15+CD16+ and pDC reference populations. CD303 x-axis, CD123 y-axis. Left plot: healthy donor Right plot: RA patient.

not expressed. Given the shared features with both granulocytes and pDC we refer to this population as DR^{hi} 'Hybrid' cells. DR^{hi} Hybrids formed a separate cluster in RA which, along with CD303, co-expressed CD83 and CD275 (ICOS-L) (Fig. 2A, circled population).Lack of CD45RAseparatedCD303^{+}DR^{hi} Hybrids from their apparent *bone fide* CD303^{+} CD45RA^{int} pDC counterparts (Fig. 3A and B, p< 0.001), CD45RA expression of RA pDC and HD pDC did not differ (Fig 3B, left). CCR3 expression within non-lymphoid DR^{hi} was negligible (not shown).

Conclusion: RA blood contains DR^{hi}CD15^{+} cells, contributing to the non-lymphoid DR^{hi} pool in RA. Because these low-density cells share features with both granulocytes and pDCs we refer to them as DR^{hi} Hybrids; their expression of CD303 challenges the notion that this molecule is specific for plasmacytoid DC. Co-expression of CD83, CD275 suggests an inflammatory potential whereas their lack of CD45RA (as opposed to CD303^{+}pDCs) is reminiscent of the altered CD45RA expression we found previously in a DC2-like DR^{hi} subset. Joint expression of CD303 and DR suggests that DR^{hi} Hybrids maybe functionally involved in the capture and ultimate presentation of RA self-peptides to T lymphocytes. These apparently new DR^{hi} Hybrids and other unorthodox DR^{hi} populations are potential treatment targets in RA.



Comparison of CD303+ DRhiHybrids with CD303+ plasmacytoid DC. A) CD45RA and CD303 expression in healthy donor plasmacytoid DC (left; purple) and RA (with presence of DRhi hybrids) B) Quantification of CD45RA MFI of CD303+ pDC from RA (orange) and HD (blue) and CD303+ DRhi Hybrids. logarithmic scale. Kruskal-Wallis Test **** p=0.0008324

Disclosure: C. Geier: None; **H. Qudsi**: None; **J. BenGabr**: None; **R. Winchester**: None; **A. Perl**: None.

Abstract Number: 1736

The Effect of Resolvin E1 and Resolvin D1 Specialised Pro-resolving Mediators on the Inhibition of Osteoclastogenesis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
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Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoclasts (OCs) are multinucleated bone-resorbing cells playing a key role in rheumatoid arthritis (RA). Under physiological conditions, OCs are in balance with bone-forming osteoblasts, whilst in RA homeostasis is disrupted, leading to excessive bone resorption. Specialised pro-resolving mediators (SPMs), a group of lipids biosynthesised from fatty acids, have been shown to resolve inflammation and play a role in bone remodelling. Notably, the SPM Resolvin E1 (RvE1) was shown to inhibit OC differentiation and bone resorption using the RAW264.7 cell line and murine models. However, the effect of RvE1 on primary human cells and its mechanism-of-action in OCs remain unknown. Another SPM, Resolvin D1 (RvD1), has also been associated with reduced bone resorption in human OCs. Thus, this study aimed to evaluate the effects of SPMs on OCs (and their pre-cursors) differentiated from primary human cells derived from healthy individuals and those with RA; while also investigating the expression of proposed SPM receptors.

Methods: Peripheral blood mononuclear cells (PBMCs) were obtained from RA patients with active disease (DAS28 >2.8) and treated with conventional DMARDs or healthy controls (HC). $CD14^+$ monocytes were isolated from PBMCs and differentiated either into macrophages with 25 ng/ml of M-CSF or into OCs with 25 ng/ml of M-CSF and RANKL. The effect of various SPMs, namely RvD1, RvE1, 17-HDHA, Maresin 1, and their combination was tested in the presence or absence of TNF to mimic inflammatory environment. The impact of SPMs on osteoclastogenesis, bone resorption, ATP production, and mitochondrial superoxide levels was assessed. SPM receptor expression was analysed by RNA sequencing and protein expression was determined by western blot (WB).

Results: Exposure of TNF-stimulated OC pre-cursors to RvE1 resulted in inhibition of osteoclastogenesis in HC individuals (15±6.7% inhibition) but not in RA. In contrast, RvD1 inhibited osteoclastogenesis under the same conditions in RA patients (16±2.4% inhibition) but not in HC. Notably, OC inhibition was associated with the presence of numerous mono- and binuclear pre-cursors, which failed to differentiate into multinucleated mature OCs. The inhibition of OC differentiation by RvE1 and RvD1 was associated with reduced superoxide production in HC and RA OCs, respectively. Transcriptional profiling of human monocytes and OCs revealed that LTB4R, CMKLR1, FPR2, and GPR18 SPM receptors were expressed in both cell types. Validation of the selected SPM receptors via WB, demonstrated that LTB4R was significantly higher in HC monocytes and OCs than in RA, while CMKLR1 and FPR2 were similarly expressed.

Conclusion: In summary, this study highlights the capacity of RvE1 and RvD1 to specifically modulate OC differentiation in primary human cells in either health or RA. Combined, these findings suggest a potential for SPMs as novel treatment for RA.

Disclosure: P. Riedlova: None; **K. Woolcock**: None; **C. Ansalone**: None; **C. Goodyear**: Abbvie, 6, AstraZeneca, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 5, Eli Lilly, 5, Galvani, 2, 5, GlaxoSmithKlein(GSK), 5, Istesso, 5, Janssen, 5, MedAnnex, 2, 5, Medincell, 2, MiroBio, 5, Revolo, 5, UCB, 5, 6.

Abstract Number: 1737

ACPA, Anti-CarP and AAPA Can Be Detected in Saliva, but Not in Feces of Seropositive Rheumatoid Arthritis Patients – Support for Mucosal Involvement in Specific Locations in RA

Veerle Derksen[1], Klara Martinsson[2], René Toes[1], Daniel Sjöberg[3], Thomas Huizinga[1], Alf Kastbom[4], Anna Svärd[3] and Diane van der Woude[1], [1]Leiden University Medical Center, Leiden, Netherlands, [2]Linköping University, Linköping, Sweden, [3]Centre for Clinical Research Dalarna, Uppsala, Sweden, [4]Linköping University, Stockholm, Sweden

SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) patients harbor antibodies against several post-translational modifications (AMPA), for example anti-citrullinated protein antibodies (ACPA), anti-carbamylated antibodies (anti-CarP) and anti-acetylated protein antibodies (AAPA). The exact mechanism underlying the development of these autoantibodies is currently unclear. Remarkably, ACPA IgA have been detected in sputum and saliva of seropositive RA patients, suggesting local production of autoantibodies. This raises two questions: 1) Can other AMPA besides ACPA also be produced at mucosal surfaces and 2) Which mucosal sites can be involved in AMPA production? The intestines are an interesting site to investigate, as microbiome dysbiosis has been described in RA patients, and intestinal content may represent a source of post-translationally modified antigens which could trigger autoantibody formation.

Methods: Paired feces, saliva and serum samples of 36 ACPA IgG-positive RA patients, 11 ACPA IgG-negative RA patients and 21 healthy volunteers were collected. Saliva was collected via passive drooling. Feces was self-collected by participants and immediately frozen. To substantiate our findings regarding the lower intestinal tract, ileal wash fluid samples were used of 20 ACPA IgG-positive RA patients and 10 healthy donors, collected in an independent cohortvia colonoscopy. All patients fulfilled the ACR/EULAR 2010 criteria. Total IgA, anti-E. Coli IgA and ACPA, anti-CarP and AAPA IgA (serum, saliva) or Ig (feces) were detected using in-house ELISA. Samples were considered AMPA positive when the value of the modified peptide was above the cut-off (mean + 2 times SD of healthy donors) and the signal measured on the modified peptide was >2 times higher than on the unmodified peptide.

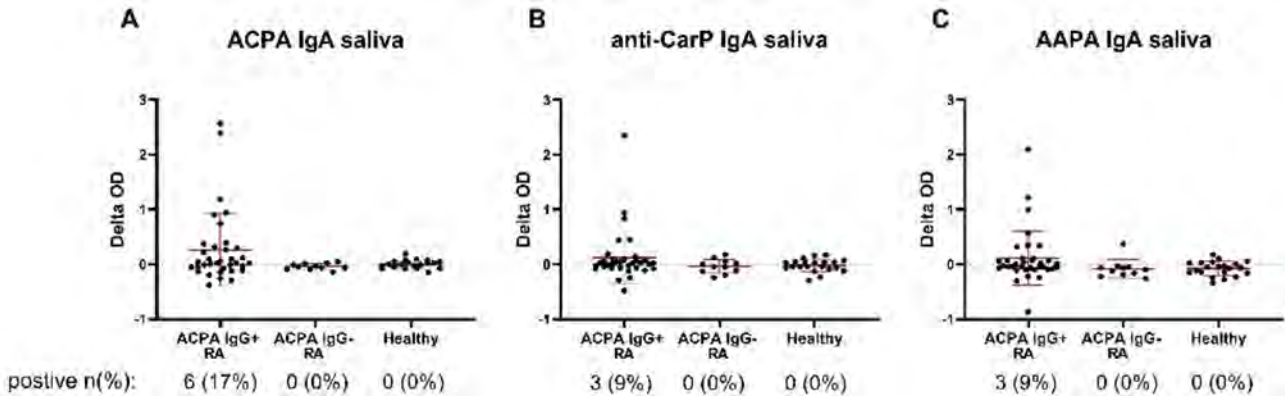

Figure 1: Autoantibody measurements in saliva. Delta OD (optical density): difference in OD between the modified peptide and the unmodified peptide. The groups on the X-axis are based on seropositivity. The number (%) of positive patients for that specific autoantibody is given. Red bars depict mean with standard deviation.

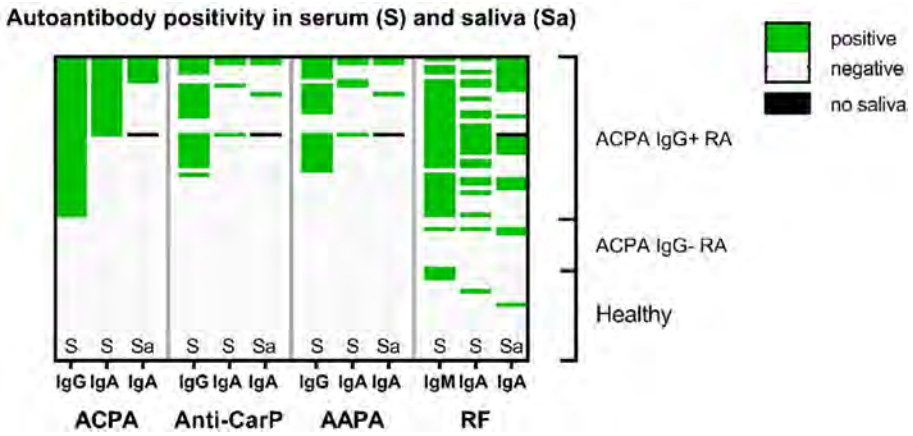

Figure 2: Positivity for the different AMPA in serum (S) and saliva (Sa). Each row depicts a study participant. The black box means no saliva available due to hyposalivation.

Results: ACPA, anti-CarP and AAPA IgA can all be detected in saliva of seropositive RA patients with differences in optical density (OD) between the modified and the unmodified peptide being clearly higher than in ACPA-negative patients and healthy controls, although the number of positive patients was low (Figure 1). When present, the saliva autoantibody profile reflects the breadth of the serum autoantibody response (Figure 2). However, AMPA Ig could not be detected in any of the fecal supernatants (Figure 3). Also in the ileal wash fluid samples no ACPA was found. Even in ACPA-positive RA patients OD-differences between the modified and unmodified peptide were consistently close to 0. Other intact IgA was present in feces, since the samples contained on average 76 μg/ml total IgA and anti-E.Coli IgA was detectable in feces of 12/36 ACPA-positive RA patients (Figure 3).

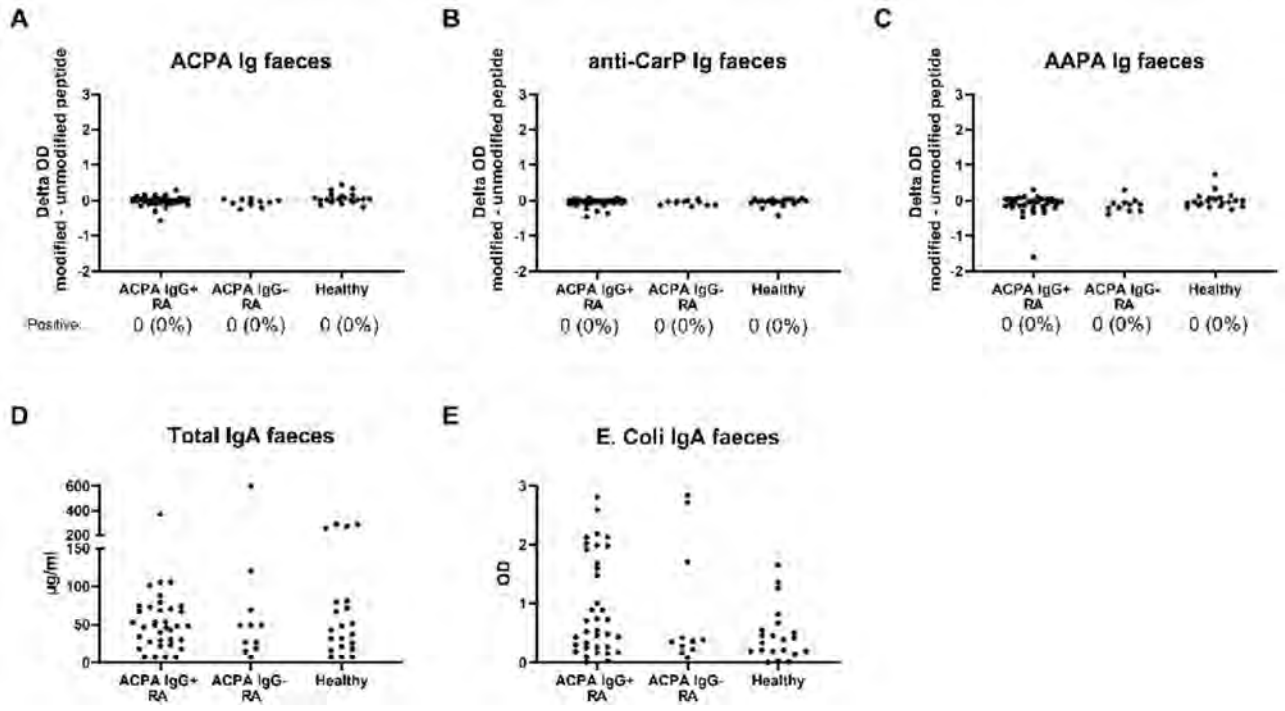

Figure 3: AMPA in feces of RA patients. A-C) ACPA, anti-CarP and AAPA Ig respectively. The groups on the X-axis are based on seropositivity. For AMPA, the number (%) of positive patients is given. On the Y-axis the difference in OD between the modified and unmodified peptide is depicted. D) Total IgA levels in μg/ml, E) OD on the anti-E. Coli IgA ELISA in the same feces samples.

Conclusion: ACPA, anti-CarP and AAPA can all be present in saliva of ACPA-positive RA patients. However, AMPA could not be detected in feces of these patients. Also in ileal wash fluid, collected in an independent cohort of ACPA-positive RA patients, no ACPA was present. Other (antigen-specific) antibodies were present in feces, indicating that the absence of an AMPA signal is not due to methodological issues. These findings suggest that the lower gastro-intestinal tract is not a main site of AMPA production in RA patients, but the oral mucosa might play a role in the AMPA response.

Disclosure: V. Derksen: None; **K. Martinsson**: None; **R. Toes**: Bristol-Myers Squibb(BMS), 5; **D. Sjöberg**: None; **T. Huizinga**: None; **A. Kastbom**: None; **A. Svärd**: None; **D. van der Woude**: None.

Abstract Number: 1738

Identification of Homeostatic and Inflammatory Synovial Fibroblast Signatures in Synovial Tissue Biopsies of Healthy Controls and Patients with Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Recent literature has identified different synovial fibroblast (FLS) populations within RA synovium with distinct inflammatory profiles. Despite current advances in classifying heterogeneity of FLS subsets, understanding of the FLS landscape in healthy synovial tissue is limited. We aim to identify homeostatic vs pro-inflammatory FLS signatures in synovial tissue biopsies obtained from healthy controls (HC) and RA patients and identify conversion triggers and activated signalling pathways.

Methods: Single cell (Sc) RNAseq was performed on 21,759 FLS derived from intact synovial biopsies from 5 HC and 4 RA. Subsequently, multiparametric flow cytometric analysis (22 markers) was performed on digested synovial biopsies from HC subjects and RA patients (further stratified between ACPA+/-) to identify FLS subsets and characterize functional phenotypes.

Results: ScRNAseq identified 14 FLS clusters which broadly aligned to 4 main subsets: CD55+THY1(CD90)-FAP+, CD55-THY1+FAP+, CD55+THY1+FAP+, and CD55-THY1-FAP+. Subsequent analysis showed clusters generally fall into lining/sublining layer, immunoregulatory, and regulatory/homeostatic functional FLS subsets. Six clusters showed higher frequency in RA synovium and eight had higher frequencies in HC. Three of the clusters had lining layer markers including

THY1-, CD55+, etc. and were enriched for invasive genes (MMP1, MMP3) and chemokines (CXCL1, CXCL8). Five clusters compose the THY1+ sublining layer fibroblasts and included a perivascular subset expressing NOTCH3, TAGLN, and ACTA2, in addition to enrichment of collagen and ECM genes. Two additional clusters sharing lining layer markers are immunoregulatory demonstrating enrichment of HLA-DR genes and genes involved in a chronic inflammatory response (IL7R, IL32, TGFB1). Of the homeostatic/regulatory subsets, two were enriched with transcription factors (TF), specifically those in the AP-1 TF family and mRNA splicing/ lipid homeostasis genes, while the two other clusters showed enrichment of genes involved in metabolic regulation and angiogenic function.

Flow cytometric analysis showed significantly higher frequencies of CD45-CD146-CD31-PDPN+ FLS in RA synovium compared to HC synovium. PDPN+ populations, both lining and sublining (based on the markers of the 4 main populations observed in the ScRNAseq) displayed higher frequency in RA synovium compared to HC. When stratified for ACPA positivity an increased frequency in sublining FLS population was demonstrated in ACPA+ RA compared to ACPA-, in contrast ACPA- RA had higher frequency of lining layer FLS. This suggests that differential FLS subsets are associated with the RA synovium vs with HC, in addition to possibly differentiating between ACPA status.

Conclusion: Identification of differential FLS subsets and their associated function in the RA vs HC synovium will better facilitate our understanding of their contribution to disease pathogenesis in RA. Furthermore, by stratifying RA patients between ACPA+ and ACPA- we can understand differences of these disease states and better tailor treatments.

Disclosure: B. Barker: None; **Ó. Tynan**: None; **C. Smith**: None; **D. Anton**: None; **C. Orr**: None; **M. Canavan**: None; **D. Veale**: None; **U. Fearon**: None.

Abstract Number: 1739

Mass Spectrometry Identified Rheumatoid Arthritis-Specific Modified Proteins and the Discovery of Antigen-Specific Hidden Autoantibodies

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SESSION INFORMATION
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Session Type: Poster Session C
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Background/Purpose: Rheumatoid arthritis (RA) is a chronic and systemic autoimmune disease characterized by synovial inflammation and progressive joint destruction. Given the presumed pathophysiologic role of anti-modified protein autoantibodies (AMPAs) in RA, it is important to obtain a comprehensive overview of the post-translational modified (PTM) proteins present in SF and serum of RA in order to reveal those autoantigens that might promote the expansion of autoreactive B cells. Therefore, mass spectrometry was used to identify citrullinated, carbamylated and acetylated proteins present within monomeric and IC (immune complexes) of synovial fluid (SF) and serum of RA, and serum of healthy donors (HD), which served as a control.

Methods: This study included 42 RA patients fulfilling the 2010 ACR/EULAR classification criteria, 44 patients with other arthritic diseases who served as the control group, and 47 HD. Proteins isolated from SF and serum were fractionated by sucrose gradient centrifugation and monomeric and IC IgG were isolated from the respective fractions according to protein markers. Mass spectrometry was used to identify PTMs within monomeric and IC IgG fractions. Rheumatoid factor (RF), anti-citrullinated, anti-carbamylated, and anti-acetylated antigen antibodies were analyzed by ELISA.

Results: In SF and serum of RA, positivity to anti-acetylated and anti-carbamylated IgG was restricted to samples positive for anti-cyclic citrullinated peptide (CCP) IgG. Anti- citrullinated IgG antibodies differentiated between RA and CG in serum and SF, while anti-acetylated IgG reactivities were significantly increased in RA-SF compared with CG. Monomeric and IC IgG isolated from formally seronegative RA patients showed very strong reactivity mainly against citrullinated peptides, indicating a "hidden" antibody response. Although mass spectrometry analysis identified citrullinated, carbamylated and acetylated proteins in all samples tested - SF from RA and serum from RA and HD - quality analysis revealed modified autoantigens unique to RA, and many were found in double or even triple modified isoforms. The frequency of modified carbamylated and acetylated proteins was significantly higher in RA than in HD.

Conclusion: Many RA-related autoantigens underwent single as well as multifold-modifications were identified within monomeric and IC of RA patients. Carbamylated and acetylated proteins distinguish between RA and HD. Monomers and IC isolated from formally seronegative patients showed hidden anti-citrullinated reactivities undetectable by conventional assays.

Disclosure: K. Ghannam: None; **M. Kirchner**: None; **H. Bang**: Orgentec Diagnostika GmbH, 3; **T. Häupl**: None; **S. Ohrndorf**: None; **J. Zernicke**: None; **U. Kuckelkorn**: None; **P. Mertins**: None; **E. Feist**: AbbVie, 12, has received honoraria and research grants, BMS, 12, has received honoraria and research grants, Galapagos, 12, has received honoraria and research grants, Lilly, 12, has received honoraria and research grants, MSD, 12, has received honoraria and research grants, Novartis, 12, has received honoraria and research grants, Pfizer, 12, has received honoraria and research grants, Roche, 12, has received honoraria and research grants, Sobi, 12, has received honoraria and research grants; **G. Burmester**: AbbVie, 2, 6, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Chugai, 6, Galapagos, 2, 6, Lilly, 2, 6, Pfizer, 2, 6, Sanofi, 2, 6.

Abstract Number: 1740

Exploring Disease-Associated DNA Methylome Alterations in Rheumatoid Arthritis: Potential Diagnostic and Prognostic Biomarkers

Arkaitz Mucientes[1], Martín-Núñez Gracia María[2], José Lisbona-Montañez[3], Patricia Ruiz-Limon[4], Rocío Redondo-Rodríguez[5], SARA MANRIQUE[6], Inmaculada Ureña[5], Laura Cano-García[5], Isabel Moreno-Indias[1], Natalia Mena Vazquez[7] and Antonio Fernandez-Nebro[8], [1]IBIMA Plataforma BIONAND, Málaga, Spain, [2]Universidad de Málaga, Departamento de Medicina y Dermatología, Málaga, Spain, [3]Universidad de Málaga, Departamento de Medicina y Dermatología, Moclinejo, Spain, [4]IBIMA Plataforma BIONAND, Cordoba, Spain, [5]Division of Rheumatology, Hospital Regional Universitario Carlos Haya, Málaga, Spain, [6]Division of Rheumatology, Hospital Regional Universitario Carlos Haya, Malaga, Spain, [7]IBIMA, Málaga, Spain, [8]Hospital Regional Universitario de Málaga, Malaga, Spain

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The etiology of rheumatoid arthritis (RA) is not fully understood. It is accepted that RA results from the interplay of genetic and environmental factors. Epigenetic modifications could serve as a bridge between genetic and environmental factors, potentially influencing the onset and progression of RA.

Purpose:to identify differential DNA methylation patterns across the entire genome in patients with RA compared to healthy controls, and to explore epigenetic alterations that couldbe predictors of increased disease severity.

Methods: In a cross-sectional study of a prospective cohort, we examined 64 subjects, including 16 with severe RA, 16 with non-severe RA, and 32 healthy controls. The severity phenotype was determined based on the average of moderate-to-high inflammatory activity, defined by an accumulated Disease Activity Score(DAS28-ESR) ≥3.2, positivity for rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA), as well as elevated levels of *Collinsella aerofaciens* (OTU ≥0.15). DNA methylation analysis was performed using the Infinium Methylation EPIC BeadChip (Illumina, San Diego, CA, USA), and the methylation level of each cytosine was expressed as a β-value. Descriptive analysis, ANOVA, and bivariate analysis were conducted for statistical comparisons among groups. Additionally, two multivariate logistic regression models were employed to identify factors associated with RA and the severe RA phenotype.

Table 1: Demographic and clinical features of the cohort

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	RA patients (n=32)		Healthy controls (n=32)	*p*-value
Caucasian (%)	32 (100%)		32 (100%)	1.000
Women (%)	24 (75%)		24 (75%)	1.000
Age (years, mean±SD)	57.6±9.4		57.1±9.4	0.370
Smoking habits (%)	62.5%		40.7%	0.015
Obesity (%)	53.1%		28.1%	0.012
	Severe RA (n=16)	Non-severe RA (n=16)		
DAS28-ESR (mean±SD)	3.9±0.6	3.3±0.2	-	0.001
RF>10 (%)	14 (87.5%)	13 (81.3%)	-	<0.001
Elevated ACPA>340 U/mL (%)	11 (68.8%)	5 (31.1%)	-	0.034
Mean HAQ (median, IQR)	1.1 (0.7)	0.9 (0.5)	-	0.098
Erosions (frequency,%)	93.8%	50.0%	-	0.006
Biological therapy (%)	56.3%	12.5%	-	0.009
Glucocorticoids (%)	3 (18.8%)	0 (0.0%)	-	0.069
Collinsella (median, IQR)	0.3 (0.1-1.7)	0.1 (0.0-0.4)	-	0.003

Table 2: CpG sites selected as possible potential biomarkers

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Site ID	Region	Gene	Relation to Island	Gene related to RA	Multivariate Logistic Regression
					Model 1 (R^2=0.618)
cg16474696	Promoter	*MRI1*	N_Shore	No	OR: 1.04, 95%CI (1.00-1.07), p=0.034
cg15741931	Promoter	*UBAP2L*	N_Shore	No	OR: 1.12, 95%CI (1.04-1.21), p=0.003
cg06508795	Gene Body	*DCC*	OpenSea	Yes	OR: 1.05, 95%CI (1.00-1.07), p=0.012
cg05510714	Gene Body	*KYNU*	OpenSea	Yes	OR: 0.94, 95%CI (0.89-0.98), p=0.026
cg06166490	Promoter	*HOXA2*	Island	No	OR: 1.23, 95%CI (1.07-1.41), p=0.003
					Model 2 (R^2=0.381)
cg08586441	Gene Body	*TEC*	OpenSea	Yes	OR: 1.07, 95%CI (1.00-1.15), p=0.037
cg14435720	Gene Body	*MIR126*	Island	Yes	
cg19405177	Gene Body	*PLEC1*	Island	No	
cg09497409	Promoter	*LASS4*	S_Shore	No	OR: 1.17, 95%CI (1.02-1.35), p=0.019
cg25251562	Promoter	*ALLC*	OpenSea	No	

Model 1: Dependent variable: Patients (1) vs. Controls (0). Model 2: Dependent variable: severe RA (1) vs. Non-severe RA (0). Age and sex were variables included in both models.

Results: Table 1 shows the main demographic characteristics. The majority (75%) were female, with a mean age of 57.6 ± 9.4 years. RA patients, in comparison with the controls, presented higher smoking habits (62.5% vs 40.7%; p=0.015) and obesity (53.1% vs 28.1%; p=0.012). Among patients, subjects with severe RA compared with non-severe had a higher mean DAS28-ESR (3.9 ± 0.6 vs. 3.3 ± 0.2 mg/L, p=0.001), higher median (IQR) abundance in *Collinsella*(0.3 [0.1-1.7] vs. 0.1[0.0-0.4] mg/L, p=0.003), higher frequency of erosions (93.8% vs 50.0%; p=0.006), elevated ACPA (68.8% vs 31.1%; p=0.034) and treatment with biological therapy (56.3% vs 12.5%, p=0.009). Regarding the methylation analysis, among all the differentially methylated CpGs, only those CpGs associated with genes or pseudogenes, exhibiting a minimum β value change of ± 0.10 between groups and a p-value ≤ 0.01, were selected;thus, 7 CpG sites differentially methylated between RA and controls and 14 CpG sites differentially methylated between severe RA and non-severe RA were selected (Figure 1). The CpG sites described in each gene, located in differentially methylated regions, together with other CpGs, were proposed as possible biomarkers (Table 1). In addition, cg06166490 was considered since it is located in a differentially methylated region (adjusted$p$-value < 0.00001). Of these CpGs, 5 CpG sites were associated with the presence of RA in multivariate model 1 and 2 CpG sites with disease severity in multivariate model 2 (Table 2).

Conclusion: DNA methylation levels at specific CpG sites are associated with RA. The present study identified epigenome marks related to RA and possible disease severity, which warrant further investigation and could be useful in the diagnosis and management of the disease.

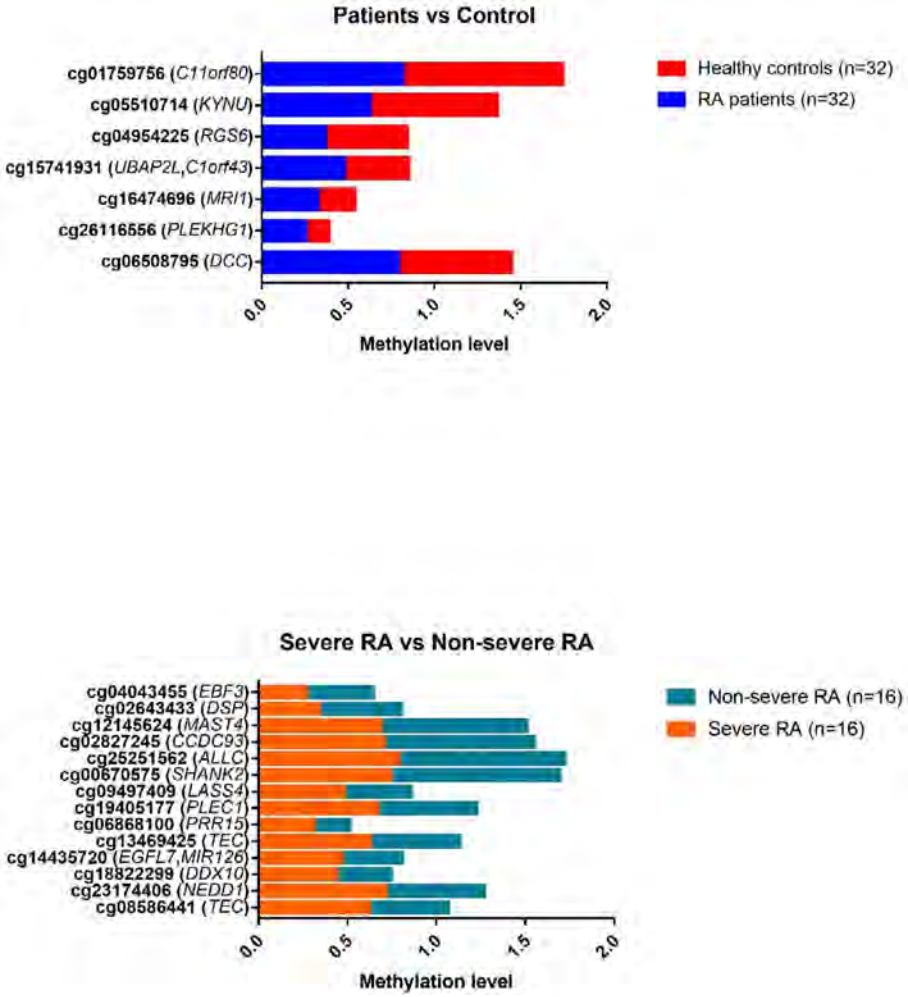

Figure 1: CpG sites with significantly differential methylation between patients with rheumatoid arthritis (RA) and healthy controls (upper panel), as well as between severe and non-severe RA patients (lower panel). The gene symbol is indicated in parentheses for each CpG site.

Disclosure: A. Mucientes: None; **M. Gracia María**: None; **J. Lisbona-Montañez**: None; **P. Ruiz-Limon**: None; **R. Redondo-Rodríguez**: None; **S. MANRIQUE**: None; **I. Ureña**: None; **L. Cano-García**: None; **I. Moreno-Indias**: None; **N. Mena Vazquez**: None; **A. Fernandez-Nebro**: None.

Abstract Number: 1741

The Occurrence and Phenotype of Autoreactive T Cells in the At-Risk Phase of Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Etiology and Pathogenesis Poster

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Background/Purpose: CD4+ T cells recognizing citrullinated epitopes are present in peripheral blood of anti-citrulline protein antibody (ACPA) positive rheumatoid arthritis (RA) patients at time of diagnosis and during the disease course. However, it has not priorly been known if these rare cells also can be found preceding disease onset. The aim of this study was thus to investigate the presence of such autoreactive CD4+ T cells, in the at-risk phase of RA, in combination with deep T cell phenotyping.

Methods: Twenty individuals from the Karolinska Risk-RA cohort carrying the genetic risk allele, HLA-DRB1*04:01, were included in the study. At baseline, all individuals had musculoskeletal symptoms, concomitant anti-CCP-positivity, but no clinical or ultrasound signs of synovitis. Ten of these individuals progressed to arthritis (over a median period of 13 months following inclusion) and were matched to individuals that had not progressed during a median follow-up period of 53 months. Peripheral blood mononuclear cells (PBMC), from up to three sample timepoints during one year of risk phase, were assessed using HLA-class II tetramers with twelve different citrullinated candidate autoantigens (originating from tenascin-C, α-enolase, fibrinogen-β, vimentin and cartilage intermediate layer protein) and a viral influenza peptide as positive control, combined with multiparameter phenotyping using a 20-color spectral flow-cytometry panel.

Results: Overall, the baseline CD4+ phenotype was similar in individuals who progressed to arthritis and those who did not when studying markers associated with Th1, Th17, T-peripheral helper and T-regulatory cells as well as with cell activation. The memory T cell compartment was predominantly of effector memory phenotype. When looking at antigen specific T cells, all individuals had similar levels of influenza specific CD4+ T cells irrespectively of disease progression status. CD4+ T cells recognizing pools of citrullinated antigens were also present in both groups but at significantly higher frequency in the non-progressors, particularly those with reactivity towards citrullinated fibrinogen-β/vimentin. Within the arthritis progressor group, CD4+ T cells specific for citrullinated tenascin-C were the most frequently observed, with their frequencies diminishing during follow-up time points leading up to arthritis onset. These cit-tenascin-C reactive CD4+ T cells displayed phenotypes of both activation and regulatory function.

Conclusion: Autoreactive CD4+ T cells recognizing citrullinated antigens are present in the circulation before disease onset in ACPA-positive individuals with arthralgia carrying HLA-DRB1*04:01. Lower frequency of circulating citrulline specific cells in arthritis progressor individuals may suggest an ongoing homing of these cells to the joints.

Disclosure: S. Turcinov: None; **C. de Vries**: None; **R. Kumar Sharma**: None; **C. Gerstner**: None; **B. Raposo**: None; **A. Dubnovitsky**: None; **W. Kwok**: None; **K. Chemin**: Janssen, 5; **V. Malmström**: Eli Lilly, 1, Janssen, 5, ONO, 1, Pfizer, 5; **A. Hensvold**: None.

Abstract Number: 1742

Sputum Citrullinated Proteins and Sputum Anti-Cit-S100A8/A9 IgG Antibodies Are Increased in Serum Anti-CCP-IgG Positive Individuals Who Developed RA

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SESSION INFORMATION
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Background/Purpose: The presence of anti-CCP-IgG in the blood identifies individuals who are "at-risk" of developing RA. Our group has reported that in a cohort of serum anti-CCP-IgG positive at-risk individuals, 27% developed RA within 3 years. Remarkably, the rate of incident RA increased to 57% in at-risk individuals who were also sputum anti-CCP positive. Because anti-CCP detects ACPA directed to joint-based citrullinated (cit) proteins/peptides, we explored the presence of lung-based cit-proteins and associated ACPA in sputum from at-risk individuals who did or did not later develop RA.

Methods: We performed a two-step study using stored baseline sputum from a cohort of serum anti-CCP-IgGpositive at-risk individuals categorized as having 'developed RA' or 'did not develop RA' within 3 years of longitudinal follow-up. In Step 1, we determined presence of cit-proteins using pooled sputum from nine at-risk individuals who developed RA and nine

Table 1. Baseline characteristics of study participant*

	Step 1 – Characterization of sputum citrullinome		Step 2- Sputum ACPA responses to cit-proteins identified in Step 1	
	At-Risk Developed RA (N=9)	At-Risk Did not develop RA (N=9)	At-Risk Developed RA (N=16)**	At-Risk Did not develop RA (N=49)**
Age	63 (43-70)	63 (36-73)	55 (44-65)	64 (49-71)
Female sex	7 (78%)	7 (78%)	12 (75%)	33 (67%)
Ever smoker	3 (33%)	2 (22%)	9 (56%)	15 (31%)
≥1 Shared epitope allele***	6 (67%)	6 (67%)	7 (44%)	19 (41%)
Sputum anti-CCP-IgG or sputum anti-CCP-IgA positive****	5 (56%)	0 (0%)	9 (56%)	12 (24%)
Median time to RA (month)	17 (9-30)	-	19 (10-24)	-
Median time of follow-up	-	33 (22-35)	-	32 (20-39)

Results are reported in median (IQR) or N (%)
* All at-risk participants were serum anti-CCP-IgG based on CCP3 ELISA (Werfern) at baseline
** Includes 6 of 9 from Step 1 who develop RA and 8 of 9 from Step 1 who did not develop RA. Samples included in Step 1 that were not included in Step 2 were not included due to lack of remaining sputum sample available to test
*** SE tested available on 46/49 who did not develop RA
**** As previously reported, serum anti-CCP-IgG+ individuals who later developed RA were more likely to have sputum anti-CCP positivity (In Step 2 cohort, 56% vs. 24%, p=0.02).

Table 2. Sputum citrullinated proteins identified in serum anti-CCP-IgG positive individuals who developed RA

Identified Proteins	p-value	Log2 Fold Change	Identified Proteins	p-value	Log2 Fold Change
Glyceraldehyde-3-phosphate dehydrogenase*	0.0034	5.03	Fibrinogen alpha chain*	**<0.0001**	4.70
Haptoglobin	**<0.0001**	4.37	Complement C4A*	**<0.0001**	3.86
Gamma-A of Fibrinogen gamma chain	0.0013	3.85	Alpha-2-macroglobulin	**<0.0001**	3.62
Aldehyde dehydrogenase family 3 member B1	0.0047	3.60	Alpha-1-antitrypsin*	**<0.0001**	3.49
Clusterin	0.0007	3.46	Pulmonary surfactant-associated protein B	0.0027	3.45
Cathepsin G*	0.0210	3.40	Hemopexin	**<0.0001**	3.35
Gelsolin	**<0.0001**	3.17	Fibrinogen beta chain	**0.0001**	3.13
Alpha-1-antichymotrypsin*	0.0069	3.10	Glucose-6-phosphate isomerase	0.0022	3.09
Heat shock protein beta-1	0.0320	3.06	Plastin-2*	**0.0004**	3.00
Tubulin beta-4B chain	**0.0001**	2.99	Mucin-5AC	**<0.0001**	2.97
14-3-3 protein zeta/delta*	0.0380	2.96	Myeloperoxidase*	0.0001	2.87
Alpha-actinin-1*	0.0019	2.84	Annexin A1	**<0.0001**	2.81
Myeloid cell nuclear differentiation antigen*	0.0043	2.80	Pyruvate kinase	0.0025	2.77
Serum albumin	**<0.0001**	2.69	Leukocyte elastase inhibitor*	0.1000	2.65
Mucin-5B	**<0.0001**	2.62	Neutrophil defensin 1*	0.0023	2.62
Serotransferrin	**<0.0001**	2.57	IgGFc-binding protein	**<0.0001**	2.54
CXCL17	0.0130	2.52	Protein S100-A8*	**0.0006**	2.46
Complement C3*	**<0.0001**	2.44	L-lactate dehydrogenase A chain	0.0690	2.40
Fructose-bisphosphate aldolase A*	**<0.0001**	2.37	Neutrophil elastase*	0.0320	2.23
Histone H4*	0.0170	2.18	Histone H2A type 1-B/E*	0.3500	2.13
Complement factor H*	0.3000	1.88	Ig heavy constant gamma 1	**0.0005**	1.84
BPI fold-containing family B member 1*	**0.0005**	1.84	Sulfhydryl oxidase 1	0.4000	1.73
Ig alpha-2 heavy chain	0.0095	1.65	Ceruloplasmin*	**0.0003**	1.65
Lactotransferrin	**<0.0001**	1.61	Ig heavy variable 3-7	0.5900	1.60
Beta-2-microglobulin*	0.0920	1.33	Zymogen granule protein 16 homolog B	0.2100	1.13
Actin, cytoplasmic 1	0.0072	1.13	Ezrin*	0.0190	1.10
Transketolase*	0.0250	1.09	Galectin-3-binding protein	0.0710	0.81
Carbonic anhydrase 6	0.4200	0.49	Ig heavy constant mu	0.3900	0.26
Immunoglobulin J chain	0.9900	0.15	Lysozyme C*	0.8900	0.10
Protein S100-A9*	0.5200	0.08	Ig kappa constant	0.9200	0.07
Ig heavy variable 3-74	1.0000	0.00	Zinc-alpha-2-glycoprotein	0.9600	-0.04
Ig lambda constant 2	0.6500	-0.09	Deleted in malignant brain tumors-1 protein	0.5700	-0.32
Alpha-amylase 1	0.3000	-0.36	Ig heavy constant alpha 1	0.4000	-0.48
Polymeric Ig receptor	0.1100	-0.60	Desmin	0.0004	-0.62
Lactoperoxidase	0.0120	-1.14	Prolactin-inducible protein	0.1800	-1.13
Protein LEG1	0.1500	-1.57	BPI fold-containing family B member 2	0.0160	-1.65
Cystatin-S	0.0019	-2.69	Lipocalin-1	0.0017	-2.90

Log2 fold change between those who developed incident RA (n=9) and those who did not (n=9) (i.e., Developed RA/Did Not Develop RA; positive values = higher in those who developed incident RA; negative values = lower in those who developed incident RA).
Bold = significantly different between groups after accounting for multiple comparisons (Bonferroni correction, p<0.0007 significant)
* Citrullinated proteins included in antigen microarray testing

matched individuals who did not develop RA. Cit-proteins were enriched using biotin labeled phenylglyoxal (chemically binds all citrulline) followed by streptavidin enrichment. Three replicates were tested for each group and cit-protein levels were compared between groups using Reductive Dimethylation based quantitative proteomics. In Step 2, we quantified ACPAs

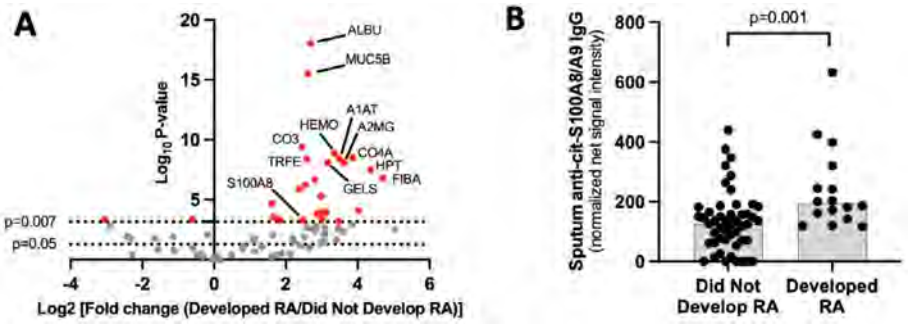

Figure 1. Sputum citrullinated proteins and sputum anti-cit-S100A8/A9 IgG antibody levels in serum an-ti-CCP-IgG positive at-risk individuals. Panel A depicts a volcano plot with the log2 (fold change) for ratios in (developed RA/did not develop RA) on the x-axis and log10 p-values on the y-axis. As such, cit-proteins to the right are increased in individuals who developed RA compared to individuals who did not develop RA. Lines correspond to a p-value of 0.05 and 0.007 (p<0.007 was significant after accounting for multiple com-parisons). Panel B depicts sputum anti-cit-S100A8/A9 IgG levels stratified by those who developed RA and those who did not develop RA within 3 years. P-values calculated based on Wilcoxon rank sum test and ac-counting for multiple comparisons (Bonferroni correction, p<0.002 significant). Abbreviations for selected proteins in Panel A: ALBU=serum albumin, MUC5B=mucin 5B, S100A8=S100-A8 protein, TRFE=lactotransferrin, CO3=complement C3, HEMO=-Hemopexin, A1AT=alpha-1 antitrypsin, A2MG=alpha-2 macroglobulin, CO4A=complement C4A, HPT=haptoglobin, FIBA=fibrinogen alpha chain, GELS=gelsolin.

directed to a subset of the cit-proteins identified in Step 1 using baseline sputum from an expanded cohort (n=65, 16 who developed RA and 49 who did not develop RA) and using a customized antigen microarray containing native and citrullinated whole proteins (GeneCopoeia OmicsArray). Cit-specific IgG and IgA reactivity was quantified by net signal intensity (background signal subtracted) normalized to internal Ig controls and subtracting native protein from cit-protein reactivity. Sputum anti-CCP-IgG and anti-CCP-IgA were quantified by ELISA and positive cut-off level established in a non-diseased control group.

Results: The cohort characteristics are described in Table 1. In Step 1, we identified 74 distinct cit-proteins in sputum (Table 2, Figure 1). Of those, 23 were significantly increased in those who developed incident RA (Table 2). In step 2, 27 of the 74 cit-proteins identified in Step 1 were tested for sputum antibody reactivity. Only sputum levels of anti-cit-S100A8/A9 IgG were significantly higher in individuals who developed RA (Figure 1). Within individuals who developed RA, sputum anti-cit-S100A8/A9 IgG correlated with sputum anti-CCP-IgG (r=0.53, p=0.03) but not sputum anti-CCP-IgA levels (p=0.12).

Conclusion: Our findings demonstrate the sputum citrullinome in serum anti-CCP-IgG positive at-risk individuals for the first time. We identified 23 sputum cit-proteins that were increased in at-risk individuals who later developed RA. Of note, multiple cit-proteins were present in sputum, and sputum antibody reactivity was detectable at some level to many of these cit-proteins. However, only sputum anti-cit-S100A8/A9 (i.e. calprotectin) IgG was significantly higher in at-risk individuals who later developed RA. This supports future studies to understand the effect of this ACPA in RA development and to understand the effects of citrullination on protein function in the lung during RA development.

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Abstract Number: 1743

Individuals At-risk for and with Rheumatoid Arthritis Have Elevated Fecal Concentrations of Arthritogenic *Subdoligranulum didolesgii* Correlating with CCP3 Antibodies

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Background/Purpose: Our prior investigation identified a specific strain of *Subdoligranulum didolesgii*, *S. dido*7, to which dual IgA/IgG family plasmablast-derived monoclonal autoantibodies from individuals at-risk for RA show cross-reactivity with RA-relevant autoantigens. *S. dido*7 stimulated CD4+ T cell activation in individuals with RA. Also, it led to inflammatory arthritis (IA) in mono-colonized germ-free mice and Th17 cell expansion, RA-relevant IgG autoantibody production and colon-isolated lymphoid follicle abundance [1]. In this study, we sought to assess the prevalence and compare the fecal concentration of *S. dido*7 among healthy controls vs. individuals at-risk and with early RA and its association with CCP3 antibodies and biomarkers of intestinal permeability, zonulin and soluble CD14.

Methods: Stool and sera were prospectively collected from 3 groups: 1) 'At-Risk' individuals, defined as those with positive CCP3 with no history of nor current IA (n=54), 2) individuals with CCP3(+) RA based on 2010 ACR/EULAR criteria within 12 months of diagnosis (n=5) and 3) controls without IA or RF/CCP3 positivity (n=32). Exclusion criteria included antibiotics in the 3 months prior to sample collection. Fecal DNA was extracted using a commercial kit (Qiagen). Quantitative PCR was used to create a standard curve using known concentrations of *S. dido*7 to allow for calculation of strain-specific fecal levels in individual samples. Serum CCP3 ELISA (Werfen) was used to measure CCP IgG. Serum ELISAs (Cusabio) were used to quantitate serum zonulin and soluble CD14.

Results: Demographics are summarized in Table 1. There were no significant differences across the groups apart from age. Fecal concentration of *S. dido*7 was 2.5-fold higher in At-Risk individuals and 3.1-fold higher in early RA compared to controls (p=0.02; Figure 1). Higher serum CCP3 levels significantly correlated with higher fecal *S. dido* 7 concentration (p=0.005; Table 2). Serum CD14 but not zonulin was significantly lower in At-Risk individuals and early RA (p=0.008; Table 1). Higher zonulin significantly correlated with lower fecal *S. dido*7 concentration (p=0.002; Table 2). There was no significant correlation between fecal *S. dido*7 and serum soluble CD14 or age (Table 2).

Table 1: Characteristics and Comparisons Among Healthy Controls, Individuals At-Risk for RA, and Individuals with Early RA

Variable[a]	Healthy Controls	At-Risk CCP+	CCP+ RA	P-value (All 3)	P-value (Controls vs At-Risk)
N	32	54	5		
Age (years)	49 (35.25, 60.75)	62.5 (48.25, 72.25)	57 (48, 67)	0.007	0.002
Sex (% female)	62.5	75.9	100	0.15	0.22
Shared epitope[b] (% positive)	45.2	37.5	66.7	0.55	0.63
Ever smoker (% yes)	21.9	33.3	40.0	0.46	0.33
Current smoker (% yes)	0	5.6	0	0.37	0.29
Race/Ethnicity (% NHW[c])	84.4	75.9	80.0	0.65	0.42
Rheumatoid Factor + (% yes)	0	44.4	60.0	<0.0001	<0.0001
BMI (kg/m^2)	25.71 (21.12, 30.13)	27.48 (23.05, 30.78)	25.73 (22.62, 32.45)	0.72	0.44
Fecal concentration of S. dido 7 (ng/μL)	0.002342 (0.001249, 0.005118)	0.005869 (0.002903, 0.01531)	0.007254 (0.003072, 0.06260)	0.02	0.008
Serum zonulin (ng/mL)	96.71 (33.24, 343.6)	65.81 (20.72, 220.9)	101.7 (78.72, 422.1)	0.15	0.11
Serum soluble CD14 (ng/mL)	405.8 (291.8, 506.1)	292.8 (209.3, 386.6)	248.2 (88.24, 580.9)	0.008	0.004

[a] Continuous variables presented as median (interquartile range)
[b] Defined as 1 or more HLA-DR4 alleles
[c] NHW, Non-Hispanic White

Kruskal-Wallis and Mann-Whitney tests were used for 3- and 2-way comparisons of continuous data, respectively. Categorical data comparisons were performed using Chi-square or Fisher's exact test. Correlations were performed using Spearman's rank correlation coefficient.

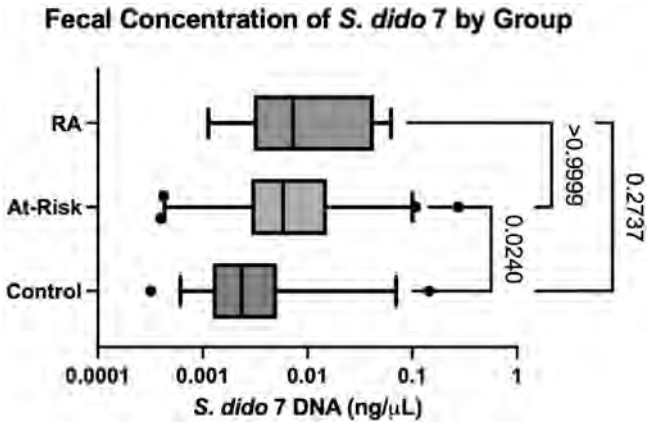

Figure 1: Fecal concentration of S. dido 7 in ng/L significantly differed across the three groups by Kruskal-Wallis test (p=0.02). After adjustment for multiple comparisons, the At-Risk group had a significantly higher fecal concentration of S. dido 7 compared to the control group by Mann-Whitney test (p=0.024).

Table 2: Spearman correlations with fecal concentration of *S. dido* 7		
Variable	**Spearman r (95% CI)**	**P value**
Serum CCP3	0.2921 (0.08551, 0.4746)	0.005
Serum zonulin	-0.3204 (-0.4984, -0.1165)	0.002
Serum soluble CD14	-0.1837 (-0.3807, 0.02933)	0.0814
Age	-0.03834 (-0.4018, 0.1555)	0.7183
BMI	-0.1310 (-0.3405, 0.09079)	0.2319

Conclusion: These data, along with prior data demonstrating arthritogenic potential of this bacterial strain, suggest*S. dido*7 may play an important mechanistic role in a subset of individuals during development of CCP autoantibodies and subsequent RA. Our data do not agree with others' findings of impaired intestinal permeability that we hypothesized as a potential mechanism by which*S. dido*7 may trigger autoimmunity. Future study is needed to address limitations, including validation of intestinal permeability studies and improvement in age- and sex-matching, as well as to evaluate*S. dido*7 in seronegative RA and its associations with clinical and biomarker features before and after arthritis development.

[1] Chriswell ME, Lefferts AR, Clay MR, et al. Clonal IgA and IgG autoantibodies from individuals at risk for rheumatoid arthritis identify an arthritogenic strain of Subdoligranulum. Sci Transl Med. 2022 Oct 26;14(668):eabn5166. doi: 10.1126/scitranslmed.abn5166. Epub 2022 Oct 26.

Disclosure: L. Cole: Appleton Medical Services, 12, Spouse is an employee for Appleton Medical (sales representative); **S. Liu**: None; **B. Allen**: None; **M. Feser**: None; **K. Demoruelle**: Boehringer-Ingelheim, 5, Gilead, 5, Pfizer, 5; **k. Deane**: Bristol-Myers Squibb(BMS), 1, Gilead, 5, Janssen, 5, Werfen, 1, 12, Biomarker kits; **M. Holer**: None; **k. Kuhn**: pfizer, 5, ucb, 2.

Abstract Number: 1744

Histological and Molecular Comparison in the Synovial Tissue of Patients with Active Rheumatoid Arthritis to Remission

Selina Ohl[1], Klaus Frommer[1], Markus Rickert[2], Stefan Rehart[3], **Ulf Müller-Ladner**[1] and Elena Neumann[1], [1]Justus Liebig University Gießen, Campus Kerckhoff, Bad Nauheim, Germany, [2]Dept. of Orthopaedics and Orthopaedic Surgery, University Hospital Giessen and Marburg, Giessen, Germany, [3]Dept. of Orthopaedics and Trauma Surgery, Agaplesion Markus Hospital Frankfurt, Frankfurt, Germany

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease which leads to local and systemic manifestations. Subsequently, the inflamed synovium drives the destruction of cartilage and bone in the affected joints. Until now, remission has been considered the therapeutic goal of the disease, as RA cannot be cured. However, as the prognostic outcomes of patients vary significantly, a better understanding of remission is required.

Objectives: To characterize remission in RA comparing histological and molecular features of active RA patients to those in remission in the synovium.

Methods: RA patients (35-82 years) were classified as active or remission after joint replacement surgery based on clinical (e.g. painful joints, pain degree, medication) and laboratory (e.g. ESR, CRP, leucocytes) parameters. To characterize synovitis, the Krenn score was used, and immunofluorescence with CD90 and podoplanin antibodies was performed. On RNA

level, RNA sequencing of RA synovial fibroblasts (RASF) was performed, which were previously stimulated with IL-1ß for 24 hours. Differentially expressed genes (DEGs) were analysed based on a combination of absolute expression, divergence and significance. To identify enriched gene sets and pathways, a gene set enrichment analysis of DEGs was performed.

Results: 64 RA patients (29 active, 35 in remission) were included in the Krenn score analysis. Reduced values especially for hyperplasia (p=0.001) as well as for infiltrates (p=0.0001) and the general degree of inflammation (p < 0.0001) was observed in the remission group. Subanalyses of medication (e.g. biologicals, DMARDs, NSAIDs, glucocorticoids) confirmed differences between remission and active RA for all drugs and indicated an overall reduction of hyperplasia observed most strongly in the biologics group (p=0.0008). The fibroblast markers podoplanin (marker for fibroblasts located mainly in the lining) and CD90 (marker for fibroblasts located mainly in the sublining) showed the greatest differences indicating patients in remission have fewer numbers of fibroblasts in both, the lining and the sublining layer. Patients in remission showed several differentially expressed genes that were lower in remission compared to active RA patients, including e.g. IL-36ß and its corresponding receptor antagonist. As those cytokines play a role in chronic inflammatory processes and the progression of RA, the impact of these factors on RASF of patients in remission compared to active RA are of especial interest.

Conclusion: The characterization of synovium after joint replacement surgery was used to compare histological and molecular differences that may help to characterize remission in RA. The histology showed a lower degree of inflammation and, most prominent, hyperplasia for patients in remission, specifically in patients receiving biologics. RNAseq identified several genes showing altered expression pattern related to the pro-inflammatory and destructive processes during RA which gives insight into the molecular characteristics.

Disclosure: S. Ohl: None; **K. Frommer**: None; **M. Rickert**: None; **S. Rehart**: None; **U. Müller-Ladner**: None; **E. Neumann**: None.

Abstract Number: 1745

Chronic Inflammation and Collagen IV Fragment Canstatin Influence Rheumatoid Arthritis Synovial Fibroblast and Endothelial Cell Interactions in Vitro and in Vivo

Corinna Heck[1], Sophie Haun[1], Daria Kürsammer[1], Klaus Frommer[1], Mona Arnold[1], Markus Rickert[2], Katrin Susanne Lips[3], Stefan Rehart[4], **Ulf Müller-Ladner**[1] and Elena Neumann[1], [1]Justus Liebig University Gießen, Campus Kerckhoff, Bad Nauheim, Germany, [2]Dept. of Orthopaedics and Orthopaedic Surgery, University Hospital Giessen and Marburg, Giessen, Germany, [3]Justus Liebig University Gießen, Department of Experimental Trauma Surgery, Giessen, Germany, [4]Dept. of Orthopaedics and Trauma Surgery, Agaplesion Markus Hospital Frankfurt, Frankfurt, Germany

SESSION INFORMATION
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Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In the inflamed synovium of RA patients, increased and altered angiogenesis is a pathological feature. Key players are chronically activated RA synovial fibroblasts (RASF), which promote synovial angiogenesis and matrix degradation. Canstatin is a matrix-derived anti-angiogenic collagen IV fragment that blocks the angiopoietin (ANGPT)/Tie2 pathway in endothelial cells (EC).

Objective: To analyse the effects of repetitively stimulated RASF and canstatin on vessel formation in the tube formation assay, the SCID-mouse model of RA and synovial tissue of RA patients with respect to ANGPT2 expression and RASF-EC interactions.

Methods: RASF were repetitively stimulated thrice every 24h with 0.05ng/ml IL-1ß. 2D tube formation assay was performed using HUVEC (+/- prestimulation with 0.2µg/ml canstatin for 20h) and 15%RASF seeded on Matrigel®. RASF/HUVEC were treated with 0.5µg/ml canstatin. Tube thickness and the area covered by the formed cellular network were measured. Supernatants were measured by ELISA. Cartilage was subcutaneously co-implanted with RASF alone or with 0.5µg/ml canstatin into SCID mice. Contralaterally, cartilage without RASF but with canstatin was implanted. Vessel formation and RASF-invasion were evaluated after 3-45 days.

Results: RASF or HUVEC stimulated once showed a significant IL-6 increase compared to unstimulated controls. Subsequent repetitive stimulation resulted in a significant IL-6 decrease compared to 1st stimulation in RASF (1st vs. 3rd: $p< 0.0001$) or HUVEC (1st vs. 3rd: $p=0.041$). The same effect was observed for IL-11 and CXCL2 in RASF (1st: vs. 3rd: $p< 0.0001$). In contrast, repetitive stimulation of HUVEC+15%RASF resulted in a significant IL-6 increase for each subsequent stimulation (1st vs. 3rd: $p=0.02$). Regarding tube formation, RASF significantly reduced tube thickness ($p=0.01$) and cell network area ($p < 0.0001$). RASF stimulated only once further reduced the network area ($p=0.04$), while repetitive stimulation significantly attenuated the proinflammatory effect ($p=0.03$). Stimulation of pre-treated HUVEC and unstimulated RASF with canstatin led to disturbed tube formation with reduced tube thickness ($p=0.01$). Co-culture of RASF with pre-treated HUVEC with canstatin further increased the RASF-mediated effect by reducing tube thickness ($p < 0.001$). In SCID mice, RASF-mediated helix-like vessel formation started at day 3. Number of helix-like vessels was significantly increased ipsilaterally compared to contralateral implants on day 3 and 30 ($p=0.04$). In contrast, number of helix-like vessels was significantly reduced ipsilaterally in implants containing canstatin on day 3 and 30 ($p=0.03$ both). In human RA synovium, the pathological vessel regulator ANGPT2 was significantly upregulated in vessels compared to OA tissue.

Conclusion: RASF-mediated effects on EC were detectable in the tube formation assay, since RASF and canstatin both specifically reduced tube thickness. RASF specifically altered neovascularization in SCID mice by promoting the formation of helix-like vessels. Human synovial tissue of RA patients showed significantly upregulated ANGPT2 expression compared to OA patients showing the effects on vessel formation in RA.

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Abstract Number: 1746

Smoking as a Risk Factor for Rheumatoid Arthritis: Exclusive Association with IgA Autoantibodies

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is characterized by autoantibodies to anti-modified protein autoantibodies (AMPAs) like anti-citrullinated protein antibodies (ACPA) and anti-acetylated protein antibodies (AAPA). Smoking is the most important environmental risk factor in autoantibody-positive RA and has been described to be specifically associated with AMPA-IgG. However, although smoking exerts its effect in the lungs, it is unknown whether smoking is preferentially associated with specific autoantibody isotypes, such as IgA, which would suggest a mucosal origin. Therefore, we set out to investigate if smoking is associated with AMPA of the IgA isotype in RA.

Methods: 618 RA patients from the Leiden Early Arthritis Cohort, of whom data were available on the presence of ACPA and AAPA -IgG and -IgA, and smoking were included. Current versus ever smoking data were collected at baseline using a questionnaire. The association between smoking and autoantibodies was assessed by logistic regression analysis. Next, a meta-analyses on results from systemic literature review on the association of smoking with ACPA-IgG and ACPA-IgA was performed.

Results: In univariate analysis, smoking was associated with various autoantibodies of different isotypes (ACPA-IgG, ACPA-IgA, AAPA-IgA, RF-IgM and RF-IgA), but since isotypes often co-occur, this precluded firm conclusions. Upon examining the exact autoantibody isotype composition, smoking was only associated with AMPA-positive RA in double-positive patients, i.e. patients who harbored both IgG ánd IgA-AMPA (figure 1A and 1B). Since smoking is also associated with autoantibody levels, we then corrected the isotype-smoking associations for these levels. Strikingly, after correction for IgA, the association between AMPA-IgG and smoking was lost (Figure 1C and 1D). However, after correction for IgG, AMPA-IgA were still associated with smoking (Figure 1C and 1D).Next, a meta-analysis was performed of all publications investigating the association of smoking with ACPA-IgG and ACPA-IgA and the current data. This confirmed that smoking was associated with ACPA-IgA but not with ACPA-IgG (figure 2). Interaction analysis of shared epitope and smoking revealed that interaction was only seen in patients that were ACPA-IgG and ACPA-IgA positive, but not in patients that were only positive for ACPA-IgG (figure 3A and 3B). This indicates that the presence of ACPA-IgA is necessary for the interaction effect.

Conclusion: In RA, smoking is exclusively associated with IgA autoantibodies against post-translationally modified proteins (AMPA), and not with AMPA IgG (figure 3C). Interaction between shared epitope and smoking is also solely found in patients positive for both IgG and IgA-ACPA. These findings support the hypothesis that smoking may exert its effect by the induction of local (auto)immune responses at mucosal sites.

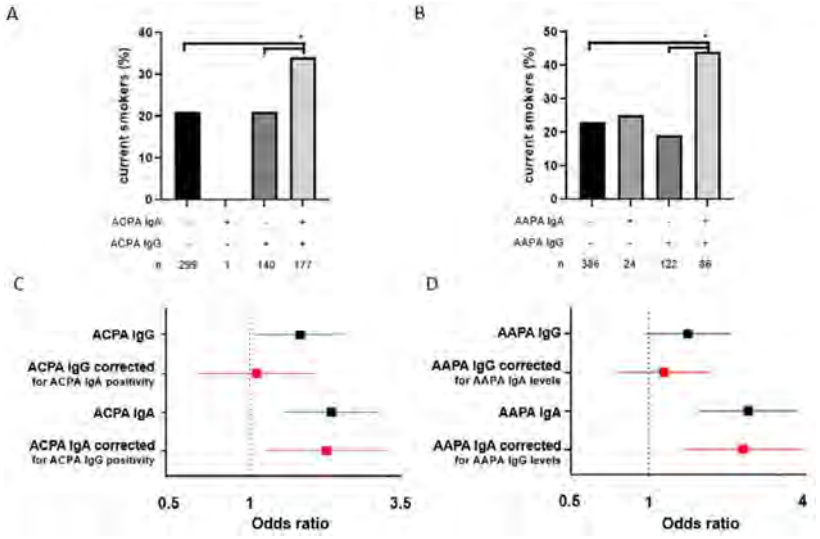

Figure 1. Association of smoking with anti-citrullinated protein antibodies (ACPA) and anti-acetylated protein antibodies (AAPA). A. Association of smoking with ACPA IgA & ACPA IgG. B Association of smoking with AAPA IgA & AAPA IgG. C. Association of smoking with ACPA IgA and ACPA IgG corrected for respectively ACPA IgG levels and ACPA IgA levels D. Association of smoking with AAPA IgA and AAPA IgG corrected for respectively AAPA IgG positivity and AAPA IgA positivity

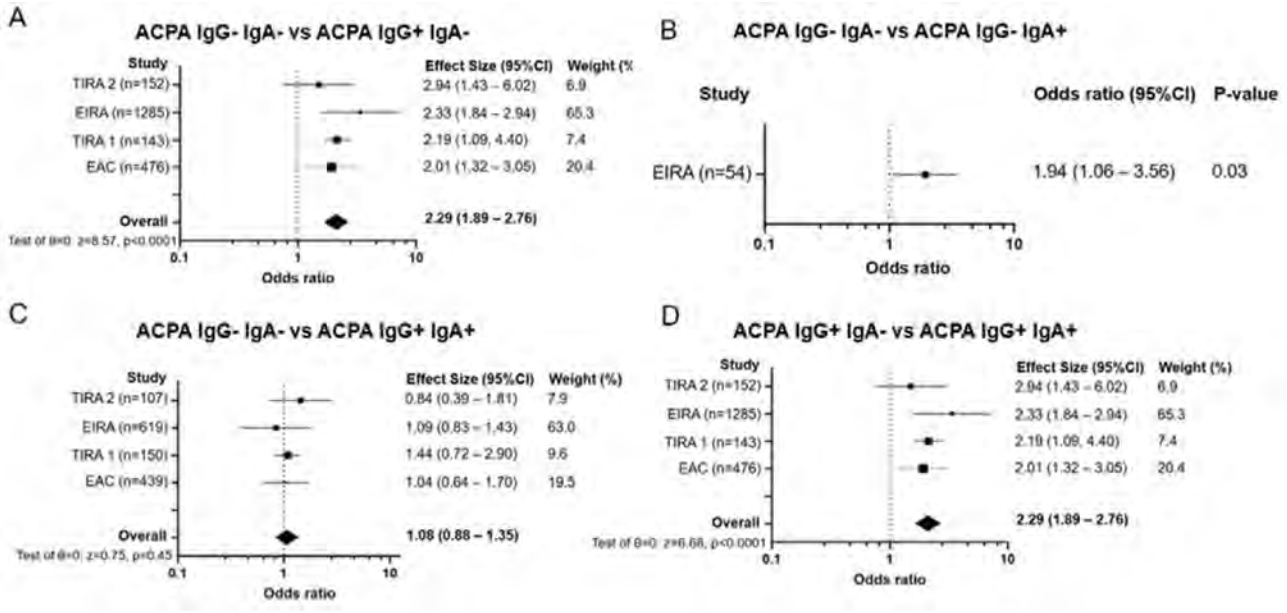

Figure 2. Meta-analysis for the association of smoking with anti-citrullinated protein antibodies (ACPA) IgG and ACPA IgA A. Meta-analysis for the association of smoking: ACPA IgG- ACPA IgA- versus ACPA IgG+ ACPA IgA- B. Association of smoking: ACPA IgG- ACPA IgA- versus ACPA IgG- ACPA IgA+ (no meta-analysis possible since this was examined in one study) C Meta-analysis for the association of smoking: ACPA IgG- ACPA IgA- versus ACPA IgG+ ACPA IgA+ D Meta-analysis for the association of smoking: ACPA IgG+ ACPA IgA- versus ACPA IgG+ ACPA IgA+

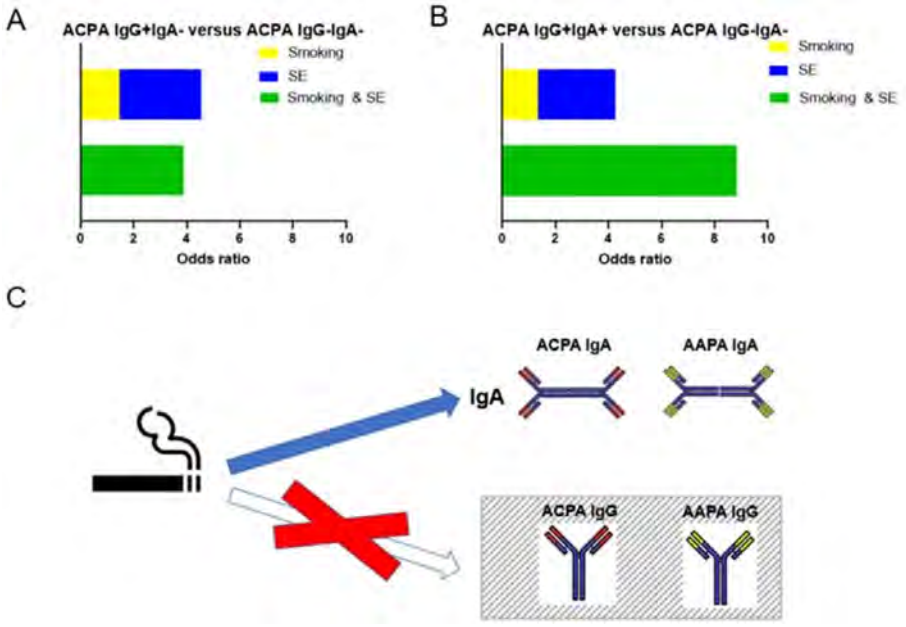

Figure 3. Interaction of shared epitiope (SE) and smoking with ACPA A. Interaction of smoking and SE in ACPA IgG+IGA- versus ACPA IgG-IgA- patients B. Interaction of smoking and SE in ACPA IgG+IGA+ versus ACPA IgG-IgA- patients. C. schematic representation of the association of smoking with autoantibodies in rheumatoid arthritis.

Disclosure: T. van Wesemael: None; **A. Svärd**: None; **A. Dorjee**: None; **T. Huizinga**: None; **R. Toes**: Bristol-Myers Squibb(BMS), 5; **D. van der Woude**: None.

Abstract Number: 1747

A Newly Described Cytokine interleukin-40 Is Increased in the Serum of Individuals At-risk of Rheumatoid Arthritis and Induces an Inflammatory Response in Mononuclear Cells

Adela Navratilova[1], Klára Prajzlerová[2], Nora Růžičková[3], Karel Pavelka[4], Jiri Vencovsky[5], Ladislav Senolt[6], Maria Filkova[3] and Lucie Andrés Cerezo[3], [1]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Hlavní město Praha, Czech Republic, [2]Institute of Rheumatology, Prague, Czech Republic, [3]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic, [4]Institut of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Praha, Czech Republic, [5]Institute of Rheumatology, Prague, Czech Republic, Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, [6]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Praha, Czech Republic

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Interleukin-40 (IL-40) is a newly described cytokine related to malignancies and immunity function. We have previously shown that IL-40 is up-regulated in early stages of rheumatoid arthritis (RA) and associates with processes that are thought to fuel the immune response. As the period preceding clinically apparent RA has not yet been fully described with respect to clinical biomarkers, we aimed to investigate IL-40 in individuals at-risk of RA development and its involvement in immune regulation in peripheral blood mononuclear cells (PBMCs).

Methods: IL-40 was analysed in the serum of individuals at-risk of RA (n=179, defined as patients with arthralgia with no clinical arthritis who are either carriers of anti-citrullinated protein antibodies, ACPA, or meeting the EULAR definition of clinically suspect arthralgia at baseline) and at the time of arthritis manifestation in patients who progressed to clinical arthritis (n=25). IL-40 was determined in the serum of age and sex-matched healthy controls (n=60). *In vitro* experiments were performed on PBMCs from at-risk individuals (n=10). Levels of IL-40 and IL-6 were measured by commercially available ELISA kits.

Results: IL-40 is up-regulated in at-risk individuals compared to healthy controls($p< 0.0001$) and the levels of IL-40 are higher in the serum of double-positive (ACPA/rheumatoid factor) compared to double-negative at-risk individuals ($p< 0.05$). Out of 175 at-risk individuals, 25 developed clinical arthritis (with median 8.17 months of follow up); however, we have not found a significant difference in the levels of IL-40 at baseline, and at the time of arthritis manifestation. *In vitro*, PBMCs from at-risk individuals exposed to recombinant IL-40 strongly enhance the secretion of IL-6 in a dose-dependent manner when compared to unstimulated cells (IL-40: 10 ng/ml, $p< 0.05$; 50, 100, 250 ng/ml, $p< 0.01$). Furthermore, the application of NFkB inhibitor to the PBMCs prior to the exposure to IL-40 significantly reduced the secretion of IL-6 when compared to IL-40 treated cells without inhibition ($p=0.004$).

Conclusion: Here we show for the first time that IL-40 is elevated in the serum of individuals at-risk of RA. Moreover, results imply that systemically elevated IL-40 induces the pro-inflammatory response in PBMCs at-risk individuals via NFkB dependent pathway.

Disclosure: A. Navratilova: None; **K. Prajzlerová**: None; **N. Růžičková**: None; **K. Pavelka**: Abbvie, 2, 6, Amgen, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Egis, 2, 6, MSD, 2, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 6; **J. Vencovsky**: Argenx, 2, Eli Lilly, 6, Galapagos, 2, Horizon, 2, Merck, 2; **L. Senolt**: None; **M. Filkova**: None; **L. Andrés Cerezo**: None.

Abstract Number: 1748

Macrophage Extracellular Traps Require Peptidylarginine Deiminase 2 and 4 and Are a Source of Citrullinated Antigens Bound by Rheumatoid Arthritis Autoantibodies

S Janna Bashar, Caitlyn Holmes and Miriam Shelef, University of Wisconsin, Madison, WI

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-citrullinated protein antibodies (ACPAs) are a hallmark of rheumatoid arthritis, but the sources of citrullinated antigens as well as which peptidylarginine deiminases (PADs) are required for their production remain incompletely defined. Neutrophil extracellular traps (NETs) appear to be a source of citrullinated antigens bound by ACPAs, but they may not be the only source. Macrophages also generate extracellular traps (METs), but their role in rheumatoid arthritis is still emerging. The purpose of this study was to determine if METs could be a source of citrullinated proteins bound by ACPAs, and if their formation requires PAD2 or PAD4.

Methods: Thioglycolate-elicited peritoneal macrophages were isolated from wildtype, PAD2$^{-/-}$, and PAD4$^{-/-}$ mice and were left untreated or were treated with ionomycin, monosodium urate (MSU) crystals, platelet activation factor, tumor necrosis factor alpha, lipopolysaccharide, phorbol myristate acetate, or heat killed *Candida albicans*. Macrophages were fixed and incubated with DAPI and either anti-citrullinated histone H4 antibody or sera from five ACPA+ or ACPA- rheumatoid arthritis subjects. Five predetermined areas of each coverslip were visualized by immunofluorescence at 400x, and METs (decondensed structures determined to be extracellular by DNase degradation studies) were counted by eye in a blinded manner. The percentage of macrophages that were METs, citrullinated METs, and ACPA-bound METs were compared between wildtype and PAD-deficient macrophages by paired t-test with $p< 0.05$ considered significant.

Results: Ionomycin and MSU crystals reliably induced METs with citrullinated histones. In the absence of PAD2 or PAD4, citrullinated METs were reduced, with a complete absence of citrullinated METs in PAD4-deficient macrophages. Also, IgG from ACPA+, but not ACPA- sera, bound METs. Finally, in the absence of PAD2 or PAD4, ACPA-bound METs were lost.

Conclusion: In response to ionomycin and MSU, macrophages generate citrullinated extracellular traps in a PAD4- and PAD2-dependent manner.Furthermore, ACPA+ sera can bind METs, suggesting that METs may contribute to the generation of citrullinated antigens targeted by ACPAs in rheumatoid arthritis in a PAD2- and PAD4-dependent manner.

Disclosure: S. Bashar: None; **C. Holmes**: None; **M. Shelef**: None.

Abstract Number: 1749

Fatty Acid Synthase Is a Critical Repressor of Ferroptosis in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a systemic autoimmune disease with synovial inflammation as the main pathological feature, and can eventually lead to irreversible joint or organ damage. Recently, several studies have reported that ferroptosis was involved in the pathogenesis of RA. However, the role of ferroptosis in abnormal activation of RA synovial fibroblasts (RASFs) is poorly understood. The purpose of our study was to explore the effect of fatty acid synthase (FASN) on ferroptosis in RASFs.

Methods: FASN expression was assessed by quantitative polymerase chain reaction (qPCR), western blotting and immunohistochemistry in synovial tissues and SFs from RA patients, osteoarthritis (OA) patients and collagen induced arthritis (CIA) mice. SF activation was evaluated by qPCR, CCK-8 and wound healing assay. Lipid peroxidation was detected by MDA levels and C11-BODIPY 581/591 fluorescence intensity. and transient small interfering RNA knockdown were performed to examine expression of SLC7A11 and signaling pathway protein.

Results: FASN was found to be significantly higher expressed in synovial tissue and SF from RA patients and CIA mice (Figure 1). Silencing of FASN by siRNA in RASFs reduced expression of FASN, SLC7A11, inflammatory cytokines (IL-1β, TNF-α and SDF-1), level of lipid and cell viability, and enhanced the expression of PTGS2 and level of lipid peroxidation,

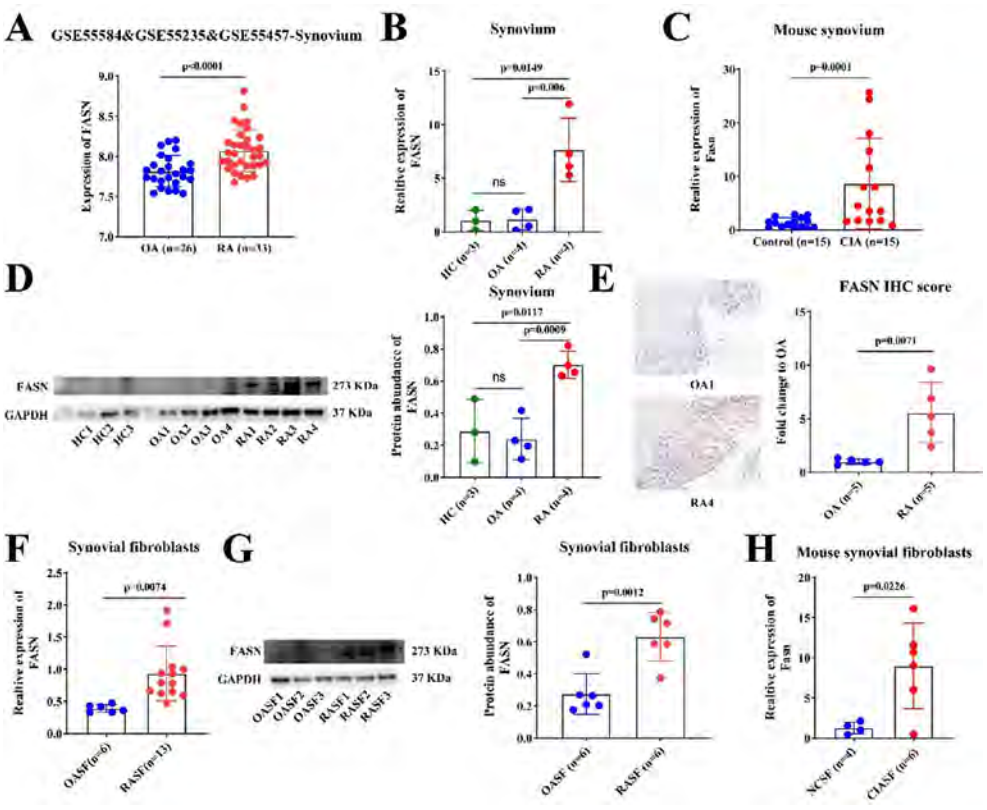

Figure 1 Expression of FASN in synovial tissues and synovial fibroblasts extracted from RA patients and CIA model mice. A. Expression of FASN in 33 RA and 26 OA synovial tissues from GSE55584&GSE55325&GSE55457 dataset. B-C. Expression of FASN in synovial tissues extracted from RA patients (B) and CIA model mice (C). D. FASN was detected by western blot in synovial tissues from 3 HC, 4 OA and 4 RA patients. E. FASN was detected by immunohistochemistry in synovial tissues from 5 OA and 5 RA patients. F-G, FASN was detected by PCR (F) and western blot (G) in SFs. H. Fasn was detected by PCR in mouse SFs. Values of $P < 0.05$ were considered significant. SFs, synovial fibroblasts. RA, rheumatoid arthritis; OA, osteoarthritis; SFs, synovial fibroblasts.

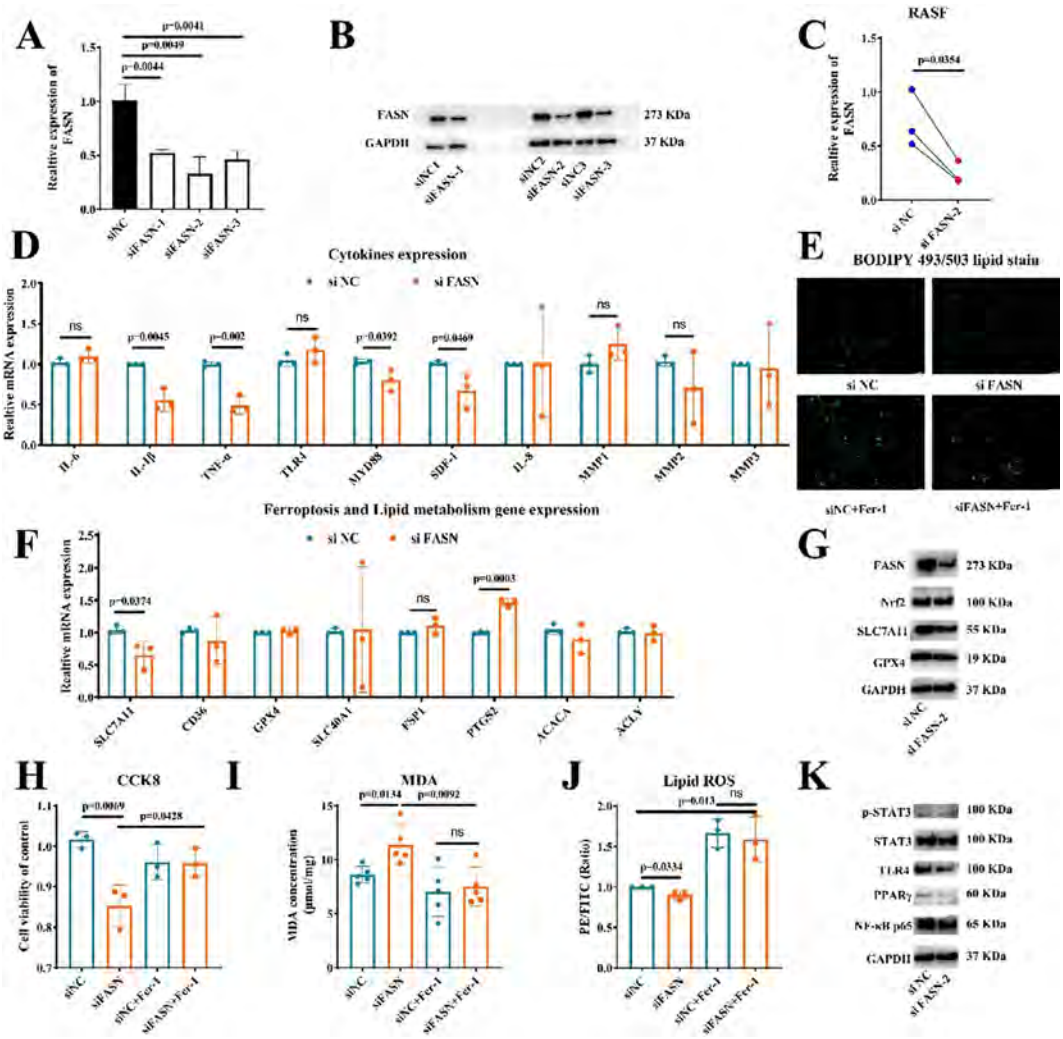

Figure 2 The role of FASN in production of inflammatory cytokines, lipid and regulation of ferroptosis on RASFs. A-B. Silencing efficiency of siRNA targeting FASN (siFASN) was detected by qPCR (A) and Western blot (B). C. mRNA level of FASN in 3 SFs after knockdown by siRNA. D. Expression of cytokines in SFs after transfection of siRNA to knockdown FASN. E. Representative fluorescent images of BIOIPY 493/503 lipid statin. F. Expression of ferroptosis and lipid genes in SFs after transfection of siRNA to knockdown FASN. G. Protein abundance of FASN, SLC7A11, Nrf2 and GPX4 in SFs after transfection of siRNA to knockdown FASN. H. Cell viability of SFs detected by a Cell Counting Kit-8. I. Intracellular MDA levels in SFs detected by a Lipid Oxidation (MDA) Assay Kit SFs. J. Fluorescence intensity of C11-BODIPY 581/591 in SFs detected by flow cytometry. K. Protein abundance of p-STAT3, STAT3, TLR4, PPARγ and NF-κB p65 in SFs after transfection of siRNA to knockdown FASN. Values of $P < 0.05$ were considered significant.

but not affected the expression of other ferroptosis (SLC40A1, FSP1 and GPX4) and lipid (ACACA, ACLY and CD36) genes (Figure 2A-2J). Moreover, treatment with the ferroptosis inhibitor, Ferrostatin-1 (Fer-1) could reverse the effect of FASN knockdown on lipid synthesis, cell viability and ferroptosis in RASFs (Figure 2E-2J). Mechanistically, FASN may promote inflammatory cytokines expression by TLR4/MYD88/NF-κ B signaling pathway, and enhance SLC7A11 expression by phosphorylating the STAT3 signal to suppress ferroptosis of RASFs (Figure 2K).

Conclusion: Our study found that FASN was a ferroptosis suppressor in RASFs. Silencing of FASN inhibited the abnormal activation of RASFs by suppressing STAT3/SLC7A11 axis and the TLR4/MYD88/NF-κB signaling pathway. Target FASN and ferroptosis may serve as a promising novel therapeutic strategy for RA.

Disclosure: Q. Cheng: None; **M. chen**: None; **X. chen**: None; **Y. Xie**: None; **Y. Du**: None; **H. wu**: None.

Abstract Number: 1750

Dysregulated NUB1 and Neddylation Enhances Rheumatoid Arthritis Fibroblast-Like Synoviocyte Inflammatory Responses

Sho Sendo[1], Camilla R. L. Machado[2], Robert Benschop[3], Narayanan B. Perumal[4], Eunice Choi[5], David Boyle[5], Wei Wang[5] and Gary Firestein[2], [1]Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe, Japan, [2]University of California San Diego, San Diego, CA, [3]Eli Lilly and Company, Indianapolis, IN, [4]Eli Lilly and Company, San Diego, CA, [5]University of California San Diego, La Jolla, CA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Etiology and Pathogenesis Poster

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Background/Purpose: Fibroblast-like synoviocytes (FLS) contribute to the pathogenesis of rheumatoid arthritis (RA), especially cartilage damage and cytokine production. These cells display an aggressive phenotype in RA. Activation of the transcription factor NF-κB, which is mediated by proteasome degradation of its inhibitor IκB, is a hallmark of RA. We evaluated gene expression and the epigenetic marks of genes involved with ubiquitination in RA FLS. This process is, in part, regulated by neddylation, which conjugates NEDD8 to the cullin (CUL)-ring E3 ubiquitin ligases (CRLs). We hypothesized that dysregulated neddylation in RA FLS contributes to the RA FLS behavior.

Methods: RA or osteoarthritis (OA) FLS lines were obtained from synovial tissues at arthroplasty and used at passage 4-8. Analysis of ubiquitination pathway epigenetic marks in RA and OA FLS was performed using public ChIPseq data. RT-qPCR and Western blot analysis were used to assess gene and protein expression, respectively. NUB1 was overexpressed using an expression vector encoding *NUB1* isoform 2 with a CMV promoter. NF-κB activation was assessed *in vitro* by stimulating FLS with IL-1β (IκBα degradation, NF-κB (p65) translocation, NF-κBreporter assay and *IL6* gene expression). MLN4924 (a neddylation inhibitor) and bortezomib (a proteasome inhibitor) were used to evaluate the neddylation, NF-κB activation in RA FLS and its migration (wound healing assay). *In vivo* effect of MLN4924 was evaluated in the K/BxN serum transfer arthritis model.

Results: Epigenetic analysis identified an enhanced H3K27ac and H3K27me3 peaks in the promoter region of *NUB1,* a protein that inhibits neddylation, in OA FLS vs RA FLS, which indicates a poised region in the former. NUB1 was constitutively expressed by FLS and induction by IL-1β was greater in OA than RA FLS (6.6±0.5 fold and 3.4±0.8-fold increase for OA and RA, respectively; $p< 0.0001$). We then explored the neddylation pathway in FLS. The ratio of neddylated CUL1 (N8-CUL1) to non-neddylated CUL1 was lower in OA FLS than RA FLS in non-stimulated condition (0.30±0.04 and 0.40±0.09, respectively, $p=0.02$). NUB1 overexpression (NUB1 OE) decreased the neddylation ratio in non-stimulated RA FLS (56% decrease, $p=0.02$), decreased NF-κB nuclear translocation (30% inhibition, $p=0.04$), and IL-6 mRNA (58% inhibition, $p=0.0007$) in IL-1β stimulated RA FLS. MLN4924 decreased the neddylation ratio of CUL1 (55% inhibition, $p=0.03$), NF-κB nuclear translocation (65% inhibition, $p=0.04$) and IL-6 mRNA (99 % inhibition, $p=0.002$) in IL-1β stimulated RA FLS. Administration of MLN4924 (20 mg/kg) decreased the arthritis scores in K/BxN serum-transfer arthritis by 34% compared to vehicle alone ($p\leq0.0002$).

Conclusion: We identified differential regulation of a novel gene, NUB1, in RA FLS after cytokine stimulation. Resultant abnormalities in ubiquitination, NF-κB activation, and cytokine expression in RA FLS suggest that neddylation system contributes to the pathogenesis of RA and regulation of neddylation could be a novel therapeutic approach.

Disclosure: S. Sendo: Eli Lilly, 5; **C. R. L. Machado**: Eli Lilly, 5; **R. Benschop**: Eli Lilly, 3; **N. B. Perumal**: Eli Lilly, 3; **E. Choi**: None; **D. Boyle**: None; **W. Wang**: None; **G. Firestein**: Eli Lilly, 5.

Abstract Number: 1751

Profiling of Anti-PAD IgG and IgA in Patients from the Head-to-head Adalimumab vs Abatacept Rheumatoid Arthritis AMPLE Trial and Matched Healthy Controls

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: A hallmark of rheumatoid arthritis (RA) is the presence of anti-citrullinated protein antibodies (ACPA) targeting neoantigens which are generated by a family of enzymes called protein-arginine deiminases (PAD). Among the five members of the PAD family (PAD1, PAD2, PAD3, PAD4 and PAD6), PAD4 has been reported to play a key role in RA pathogenesis. Besides ACPA, about 25-35% of RA patients express anti-PAD4 IgG of which about 20-40% cross-react between PAD3/PAD4 and have the potential to enhance PAD4 activity leading to more erosive disease. Although several studies have been published on cross-sectional RA cohorts and controls, limited data is available from controlled clinical trials. Consequently, the aim of this study was to evaluate the prevalence of anti-PAD2, anti-PAD3 and anti-PAD4 IgG and IgA in a cohort of established RA patients, and the impact of treatment on antibody (Ab) levels, in the adalimumab vs. abatacept head-to-head active RA AMPLE study (NCT00929864).

Methods: Sera from RA patients enrolled in the AMPLE trial [at baseline (n=498), and 1 year after treatment initiation (n=218)] and from age- and sex-matched healthy controls (n=129) were tested for ACPA IgG (ImmunoscanCCPlus, Svar, Malmö, Sweden), anti-PAD2, anti-PAD3 and anti-PAD4 IgG/IgA by a novel particle-based multi-analyte technology [PMAT, research use only (RUO), Werfen, San Diego, US]. The manufacturer cut-off was used for ACPA, and preliminary cut-offs determined with internal disease and healthy controls were used for the anti-PAD Abs. Joint erosion (JE) data as measured by van der Heijde modified Total Sharp Score were compared with the Ab levels by Spearman's correlation. Anti-PAD4 IgG results were normalized to total IgG levels for analysis of changes with treatment by t-test.

Results: Profiling of Abs to PAD2, PAD3 and PAD4 using the preliminary cut-offs identified both IgG and IgA in RA patients (Table 1). Except for anti-PAD2 and anti-PAD3 IgA, all other PAD autoantibodies were more prevalent in RA patients vs. the matched controls. At baseline, the highest prevalence of Abs was found for PAD4 IgA followed by PAD4 IgG, PAD2 IgG, PAD3 IgA, PAD3 IgG and PAD2 IgA. Twenty nine percent (145/498) of RA patients were anti-PAD4 IgG+ *vs*. 2/129 (1.6%) of controls ($p < 0.0001$). The presence of anti-PAD4 IgG was significantly higher in ACPA+ RA patients [139/387 (35.9%)] compared to the ACPA- group [6/117 (5.1%)] ($p < 0.001$, Fisher exact test). A weak correlation was observed when comparing anti-PAD4 IgG titers with JE and disease duration ($\rho = 0.13$ and 0.18, $p=0.0045$ and 5.1×10^{-5}, respectively). Positivity for anti-PAD2, anti-PAD3 or anti-PAD4 IgG or IgA did not predict response to either adalimumab or abatacept. Anti-PAD4 IgG levels were generally stable at 1 year of both treatments, with a slight observed reduction in the adalimumab group when normalized to total IgG.

Table 1. Frequency of anti-PAD IgG/IgA antibodies on the RA AMPLE trial cohort and healthy controls. * Fisher exact test, A p-value of <0.05 is considered significant; n.s.: not significant

Antibody	Number (%) positive in RA patients at baseline (n=498)	Number (%) positive in RA patients at 1 year follow-up (n=218)	Number (%) positive in controls (n=129)	RA baseline vs. controls *p* values *
PAD2 IgG	75 (15.1)	20 (9.2)	2 (1.6)	p<0.0001
PAD2 IgA	29 (5.8)	15 (6.9)	4 (3.1)	n.s.
PAD3 IgG	35 (7.0)	12 (5.5)	0 (0.0)	p=0.0004
PAD3 IgA	40 (8.0)	14 (6.4)	9 (7.0)	n.s.
PAD4 IgG	145 (29.1)	52 (23.9)	2 (1.6)	p<0.0001
PAD4 IgA	154 (30.9)	63 (28.9)	9 (7.0)	p<0.0001

Conclusion: In the head-to-head adalimumab vs abatacept trial, anti-PAD4 IgG were weakly associated with JE and longer disease duration in active RA patients, which is consistent with previous reports. Anti-PAD IgG or IgA status did not predict response to treatment, and treatments had little to no impact on titers after 1 year.

Disclosure: N. Kumar: None; **X. Chen**: Bristol-Myers Squibb(BMS), 3; **M. Aure**: Werfen Autoimmunity, 3, 3; **A. Ishii**: None; **L. Martinez-Prat**: Werfen, 3, 10; **c. Bentow**: Werfen, 3; **J. Saini**: Bristol-Myers Squibb(BMS), 3; **M. Mahler**: Werfen, 3; **L. Menard**: Bristol-Myers Squibb(BMS), 3, 10, 11.

Abstract Number: 1752

Fibroblast Expression of Neurotransmitter Receptor HTR2A Associates with Inflammation in Rheumatoid Arthritis Joint

Chunyan Xiang[1], Soomin Hong[1], Bingjiao Zhao[2], Hui Pi[3], Fang Du[4], Xingyu Lu[5], Yuanjia Tang[1], Nan Shen[6], Chunxi Yang[7] and Runci Wang[8], [1]Shanghai Institute of Rheumatology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University (SJTUSM), Shanghai, China, [2]Department of Orthodontics, Shanghai Stomatological Hospital & School of Stomatology, Fudan University, Shanghai, China, [3]Jiangxi Provincial People's Hospital, The First Affiliated Hospital of Nanchang Medical College, Nanchang, China, [4]Department of Rheumatology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University (SJTUSM), Shanghai, China, [5]Department of Endocrinology, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, [6]Shanghai Jiao Tong University School of Medicine, Shanghai, China, [7]Department of Orthopedics, Renji Hospital, School of Medicine, Shanghai Jiao Tong University (SJTUSM), Shanghai, China, [8]Renji hospital, Shanghai Jiaotong University, Pudong Xinqu, China

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Peripheral neuroimmune crosstalk plays a crucial role in the inflammatory process and bone metabolism in joint. Serotonin receptor HTR2A was reported to be expressed on immune cells, of which gene polymorphisms are associated with an increased risk of developing RA and other autoimmune disease. However, the expression and regulation of HTR2A in arthritis synovium remain poorly understood.

Methods: Differential expression of neurotransmitter receptors (NTRs) and their correlated inflammatory molecules was identified in RA and OA synovium from public scRNA-seq dataset[1]. IHC staining of synovial tissue from RA and OA patients was performed for validation. Expression of miRNAs potentially targeting HTR2A carried by synovial fluid extracellular vesicles (EVs) was screened in low- and high-grade inflammation RA from public dataset[2] and validated by qPCR.

Results: HTR2A was expressed by 34.3% and 42.1% of fibroblasts in OA and RA synovium, while barely expressed by synovial leukocytes. Higher level of IL-6, IFN-γ, IFN stimulated genes, chemokines including CCL2, CCL8, CCL13, CXCL9, and CXCL12, and MMPs and VEGFB were observed on all cell types in RA joint, indicating a highly inflammatory microenvironment in RA. (Fig.1).

Correlation analysis showed positive correlation of HTR2A with IL6, CCL5, CXCL12, TNFSF11 and VEGFC expression in fibroblast specifically as well as in all synovial cells. The strongest correlation was found between HTR2A and CXCL12 (R=0.45). Transcriptomic findings above were confirmed on the protein level with IHC staining of RA and OA synovial tissue

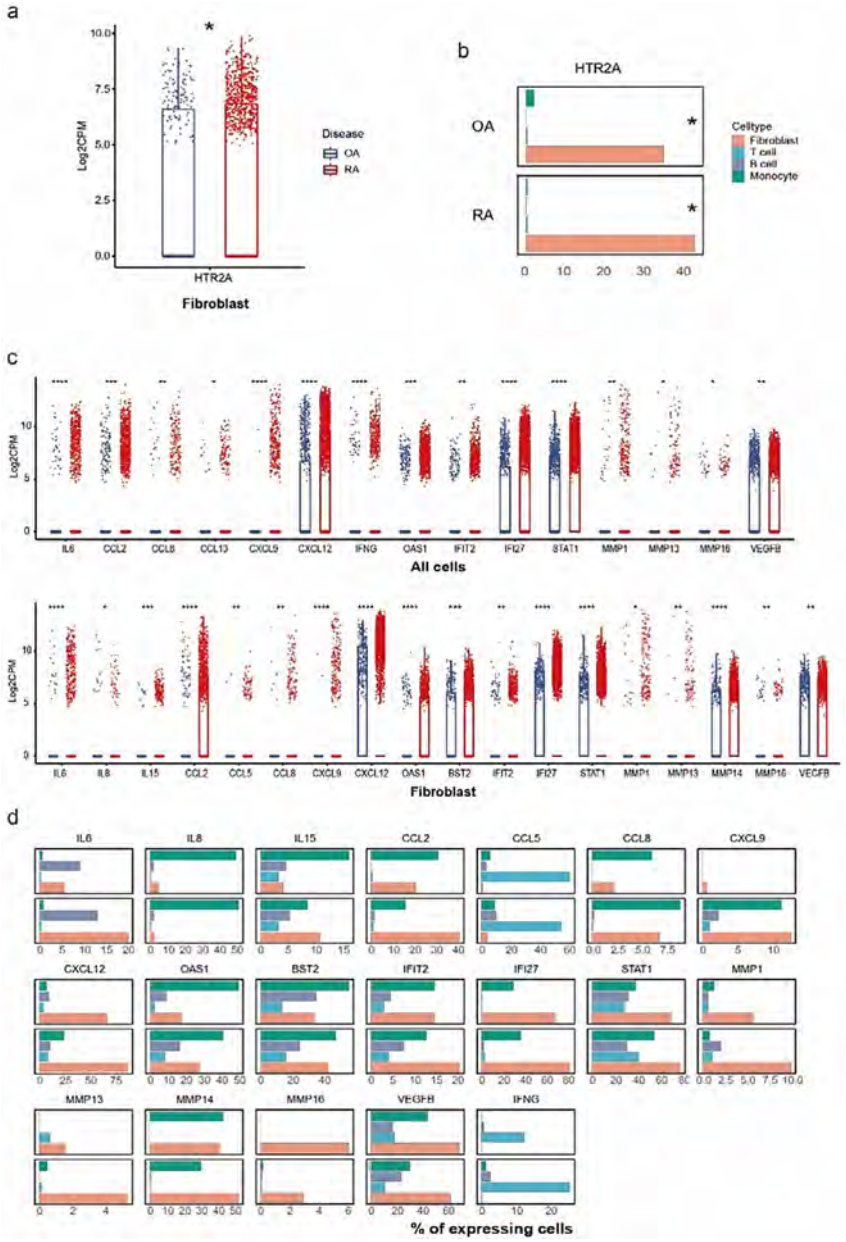

Figure 1. HTR2A and effectors expression pattern in joint synovial tissue of RA and OA patients. (a) Expression level and (b) positive percentage of HTR2A in RA and OA synovial fibroblast, (c) expression level and (d) positive percentage of inflammatory molecules in RA and OA synovium. Statistical test by Mann–Whitney U test in (a) and (c), *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001. Statistical test by Chi-square or Fisher's exact test in (b) and (d), *p < 0.05.

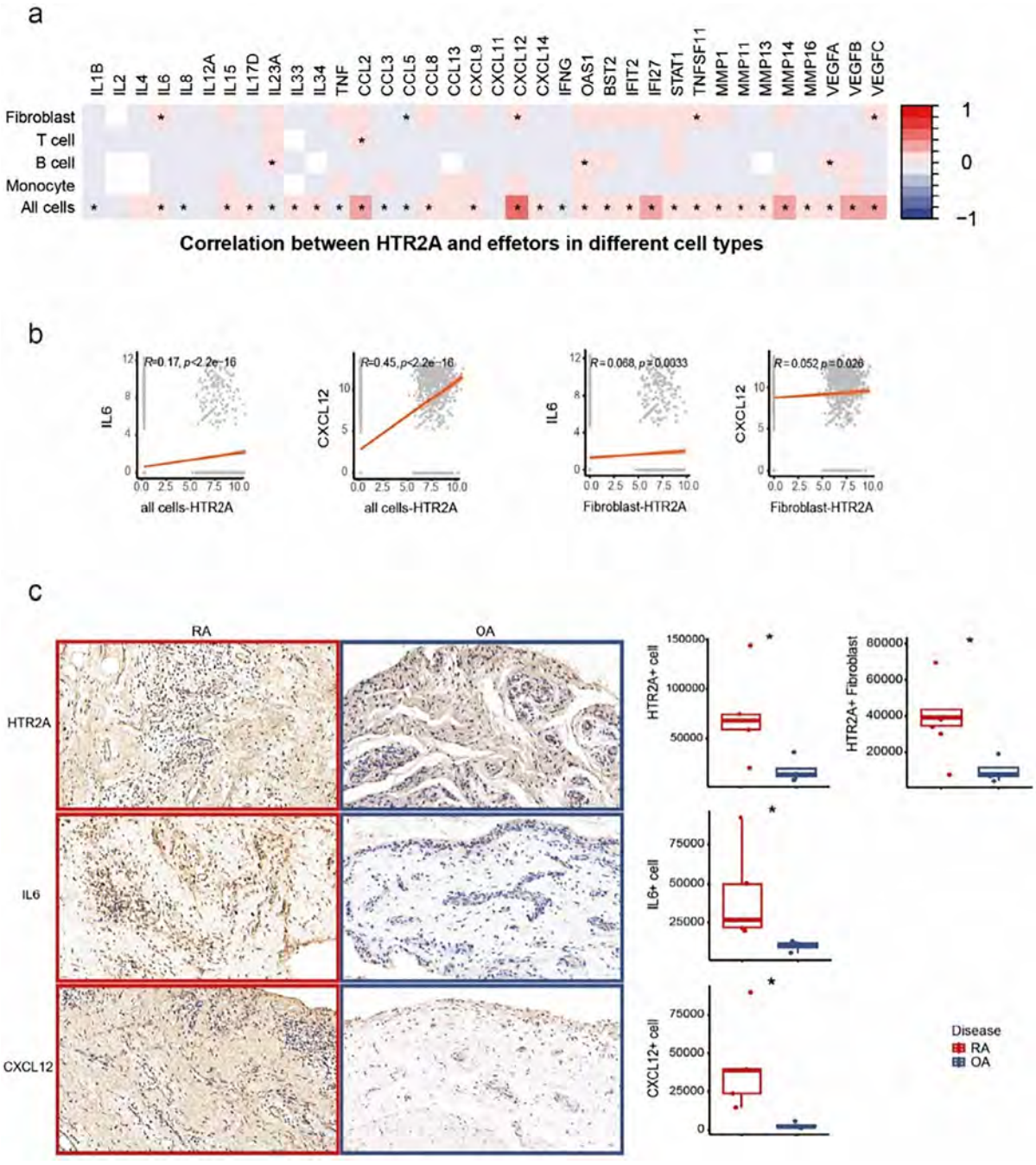

Figure 2. Inflammatory correlation and miRNA regulation of HTR2A in arthritis joints. (a) Heatmap showing correlation between HTR2A and inflammatory molecules using Pearson correlation. (b) Significant correlation plot between HTR2A and representative inflammatory molecules in fibroblast or all synovial cells. (c) 40x field view and quantification of immunohistochemical staining of HTR2A, IL6 and CXCL12 in synovial tissue of RA (n=5) and OA (n=4) patients, p values were calculated by Mann–Whitney U test, *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001.

from patients. There was significantly upregulated expression of HTR2A on RA whole synovial tissue level and fibroblast level. Increased expression of IL-6 and CXCL12 was also found in RA synovial tissue (Fig.2).

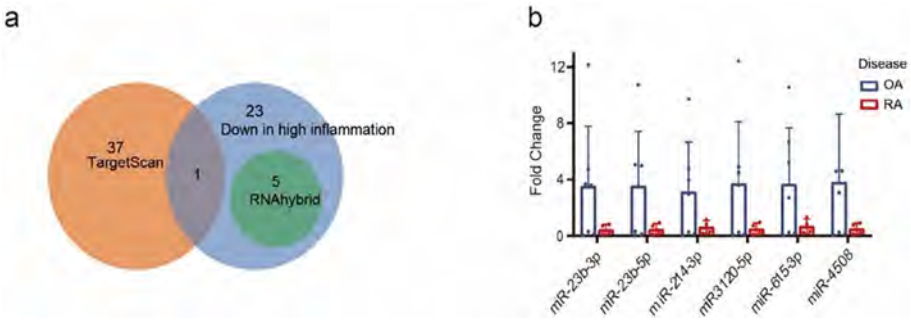

Figure 3. miRNAs targeting HTR2A carried by synovial fluid EVs. (a) Venn diagram of miRNAs targeting HTR2A. miRNAs predicted by TargetScan (orange) and RNAhybrid (green) databases, and miRNAs lowly expressed in high-inflammation RA synovial fluid EVs (blue). (b) miRNAs were extracted from OA(n=7) and RA(n=4) synovial fluid EVs, and the expression of 6 miRNAs targeting for HTR2A were validated by qPCR. p values were calculated by t-test. *p < 0.05, **p < 0.01, ***p < 0.001.

To investigate what could regulate the different HTR2A expression in RA and OA, we examined the content of EVs derived from RA and OA synovial fluid. Integrated with public RNAseq data, TargetScan and RNAhybrid prediction, 6 miRNAs predicted to regulate HTR2A expression, miRNA-23b-3p, miR-23b-5p, miR-214-3p, miR-3120-5P, miR-615-3p, and miR-4508, were significantly lower in RA EVs. A trend of lower expression of these 6 miRNAs was demonstrated by qPCR (Fig.3).

Conclusion: A neurotransmitter receptor of serotonin, HTR2A, was enriched in rheumatoid arthritis (RA) synovial fibroblast and positively correlated with inflammation. 6 miRNAs targeting HTR2A were decreased in RA synovial fluid EVs comparing to osteoarthritis. HTR2A may contribute to inflammation and RA pathogenesis, and miRNAs targeting HTR2A might offer new therapeutic strategies to alleviate inflammation in RA.

Disclosure: C. Xiang: None; **S. Hong**: None; **B. Zhao**: None; **H. Pi**: None; **F. Du**: None; **X. Lu**: None; **Y. Tang**: None; **N. Shen**: None; **C. Yang**: None; **R. Wang**: None.

Abstract Number: 1753

Acylcarnitine Enrichment Is a Characteristic of Rheumatoid Arthritis Fibroblast-Like Synoviocyte Metabolic Fingerprint

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Several metabolic pathways have been implicated in rheumatoid arthritis fibroblast-like synoviocytes (RA FLS) aggressive phenotype[1,2]. Here, we aimed to analyse the full spectrum of metabolic alterations associated with RA by performing untargeted metabolomics using mass spectrometry in RA FLS vs. non-inflamed (NI) FLS.

Methods: Ten RA FLS were obtained from synovial tissue specimens from patients with RA undergoing joint replacement surgery. Seven NI FLS were obtained from patients with no previous history of arthritis, undergoing diagnostic arthroscopy due to previous injury that occurred over 2 months prior to the operation. We collected primary RA and NI FLS culture extracts and untargeted annotated metabolomics were performed using liquid chromatography coupled to quadrupole time-of-flight mass spectrometry (Figure 1A).

Results: Peak intensities of 138 annotated metabolites were acquired. Metabolomics analysis revealed a distinct metabolic fingerprint between RA and NI FLS as illustrated by hierarchical clustering shown as heatmap, and partial least squares - discriminant analysis (Figure 1B, C). A volcano plot combining fold change analysis and Mann-Whitney test revealed

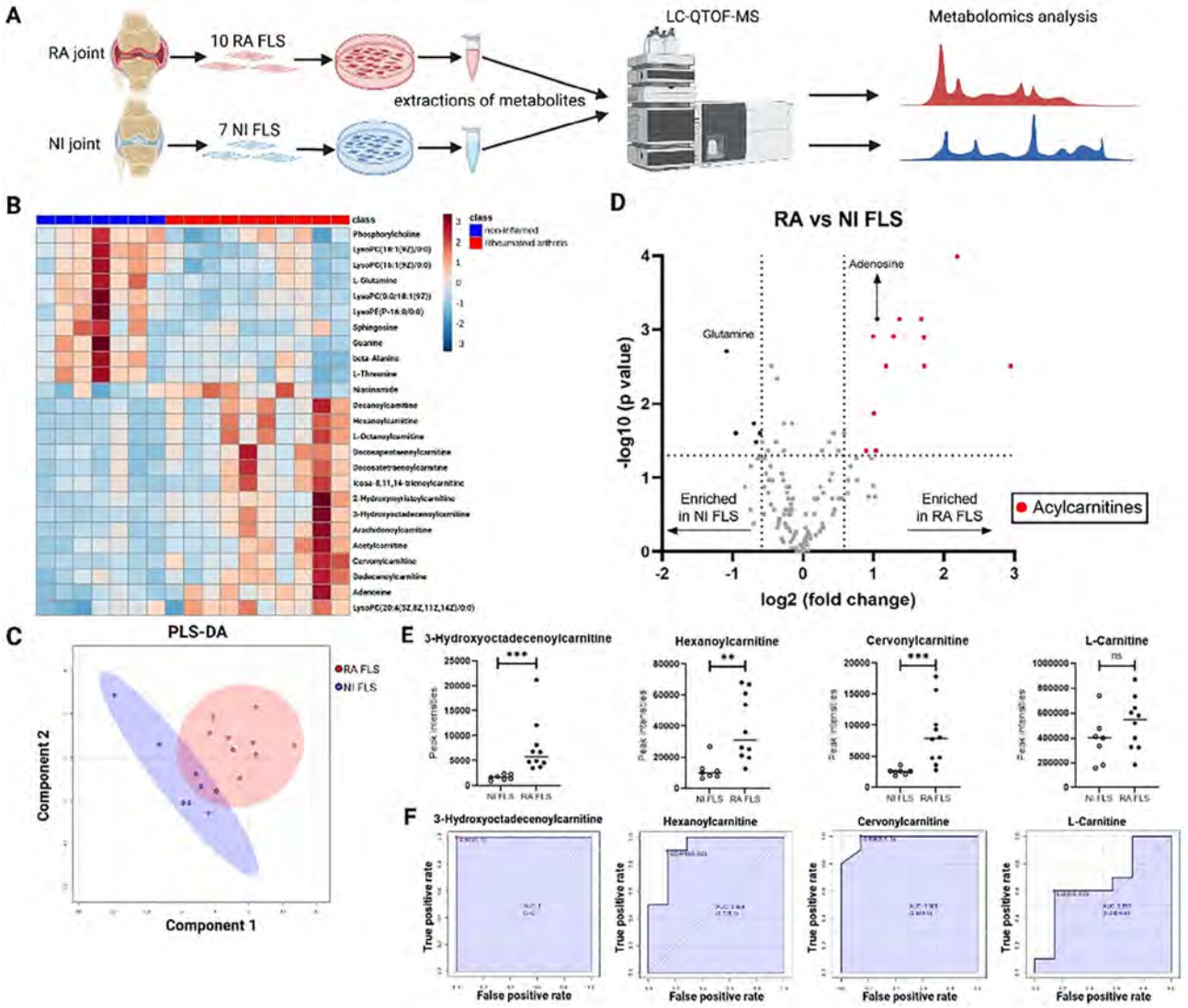

Figure 1: FLS metabolomics analysis. A. Experimental set up overview. B. Clustering result shown as heatmap. Distance measure using Euclidean distance, and clustering algorithm using Ward's linkage. Samples are shown on the x axis, while metabolites are shown on the y axis. C. Partial least squares - discriminant analysis showing the 2-D scores plot between principal component 1 and 2. Each dot represents a sample. The cycles show the 95% confidence interval. D. Enriched metabolites by volcano plot defined as fold change (x) ≥1.5 and Mann-Whitney test p-value (y) <0.05. The red dots represent acylcarnitines. E. Dot plots of the peak intensities of three selected acylcarnitines and L-carnitine in NI RA FLS. Mann-Whitney test was performed. $p<0.05$ was signified with *, $p<0.01$ with **, and $p<0.001$ with ***. F. ROC curves of three selected acylcarnitines and L-carnitine. Sensitivity is on the y-axis, and the specificity on the x-axis. Abbreviations: RA, rheumatoid arthritis; NI, non-inflamed; FLS, fibroblast-like synoviocytes; LC-QTOF-MS, liquid chromatography coupled to quadrupole time-of-flight mass spectrometry; PLS-DA, partial least squares - discriminant analysis; AUC, area-under-the-curve.

18 metabolites having different levels in RA and NI FLS; 13 were enriched in RA FLS, while five were enriched in NI FLS (Figure 1D). Of the 13 metabolites enriched in RA FLS, 12 were acylcarnitines (Figure 1E, F).

Conclusion: RA FLS show an accumulation of acylcarnitines compared to NI FLS, which suggests an involvement of lipid metabolism in RA pathophysiology. Further studies are needed to understand this phenomenon and to determine if acylcarnitine accumulation in FLS contributes to FLS dysfunction in RA.

Disclosure: G. Vasileiadis: None; **A. Hultgård Ekwall**: AbbVie/Abbott, 1, 2, Boehringer-Ingelheim, 6, Pfizer, 1; **R. Sureshkumar**: None; **M. Guma**: Genentech, 5, Gilead, 5, Novartis, 5, Pfizer, 5; **A. Rudin**: AstraZeneca, 12, financial support; **Y. Zhang**: None; **C. Maglio**: None.

Abstract Number: 1754

Novel and Unique Rheumatoid Factors Cross-React with Viral Epitopes in COVID-19

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SESSION INFORMATION
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Background/Purpose: Rheumatoid factors (RFs), polyreactive antibodies canonically known to bind two conformational epitopes of IgG, are a hallmark of rheumatoid arthritis but also can arise in other inflammatory conditions and infections. In turn, infections, such as respiratory infections, correlate with rheumatoid arthritis development, but the mechanisms are unclear. Recently, RF reactivity in rheumatoid arthritis, and not in other autoimmune diseases, was found to include citrullinated and homocitrullinated IgG epitopes as well as thousands of citrullinated and homocitrullinated antigens targeted by anti-citrullinated protein antibodies. Specific epitopes recognized by infection-induced RFs remain undefined. The purpose of this study was to evaluate the reactivity of RFs induced in a primary immune response in adults to better understand how a viral infection might lead to loss of immune tolerance and rheumatoid arthritis.

Methods: Clinical data and sera were obtained from adults five weeks post-COVID-19 (positive SARS-CoV-2 test in the spring of 2020) or the following subjects with no past COVID-19: rheumatoid arthritis, Sjögren's disease, lupus, smokers, and age- and sex-matched controls. Sera were used in a high density peptide array to evaluate IgA, IgM, and IgG binding to all possible 16 amino acid peptides derived from human IgG1-4 and the proteomes and proteins of several viruses including SARS-CoV-2 with results confirmed by ELISA. Antibodies were purified to evaluate cross-reactivity by ELISA. Data were analyzed by Kruskal-Wallis with Dunn's multiple comparisons tests, Mann-Whitney test, Wilcoxon matched-pairs signed rank test, and MixTwice.

Results: We identified three novel IgG epitopes (IgG1-131, IgG1-238, IgG1-293) bound by antibodies in COVID-19 but not rheumatoid arthritis, Sjögren's disease, lupus, smokers, or controls. In contrast, a hinge peptide, IgG1-104, was recognized by rheumatoid arthritis and Sjögren's disease antibodies. A polyreactive IgM-RF bound IgG1-131, IgG1-238, and many viral peptides with a tripeptide motif, as well as IgG Fc and SARS-CoV-2 spike proteins. In contrast, a previously identified rheumatoid arthritis-specific RF that binds homocitrullinated IgG1-219 recognized IgG Fc, but not motif-containing peptides or spike.

Conclusion: RFs are not a single entity in multiple diseases, but rather have disease-specific IgG reactivity and unique polyreactivities that reflect the broader immune response. Moreover, virus-induced, motif-driven polyreactivity, as opposed to molecular mimicry among a small number of antigens, can drive autoreactivity against IgG. These findings provide new insights into how viral infection may trigger immune tolerance loss with potential implications for rheumatoid arthritis and millions of people post-COVID-19.

Disclosure: M. Amjadi: None; **M. Parker**: JangoBio, 3; **Z. Zheng**: Google, 3; **A. Robbins**: None; **M. Denny**: None; **S. McCoy**: Bristol-Myers Squibb(BMS), 2, Horizon, 2, Kiniksa, 2, Novartis, 2, Otsuka/Visterra, 2, Target RWE, 2; **I. Ong**: None; **M. Shelef**: None.

Abstract Number: 1755

Unique Pattern of Cadherin 6 Localization in Fibroblast-Like Synoviocytes

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: The synovial lining of rheumatoid arthritis (RA) is formed by a network of fibroblast-like synoviocytes (FLS). Cadherins are type I transmembrane proteins and participate in FLS cell-to-cell contacts, particularly cadherin 11. Unbiased profiling of cadherin expression in FLS using epigenetic data identified cadherin 6 (CDH6) as a gene of interest in RA FLS. CDH6, which is a type II cadherin, has mainly been studied in oncology where high expression is associated with cancer progression and invasion. CDH6 in FLS could regulate similar functions in RA. To understand the diverse functions of CDH6 in FLS, we analyzed its cellular distribution in synovial tissue.

Methods: RA and osteoarthritis (OA) synovial tissue (n=6 each) were obtained at arthroplasty. RA FLS and OA FLS lines (n=6 each) were derived from enzymatically dispersed synovial tissue and used from passages 5-7. Western blot analysis was used for protein quantification with anti-CDH6 antibody and was normalized to GAPDH. The distribution of CDH6 in FLS and synovial tissue was evaluated by immunofluorescence and confocal microscopy.

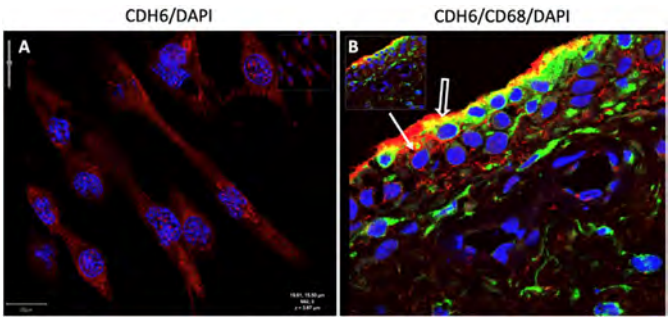

Figure 1. CDH6 expression in RA FLS and RA synovium. We performed confocal microscopy to determine if CDH6 is present in the synovial lining and its distribution in RA FLS. A) Representative image of RA FLS with anti-CDH6 (red) and DAPI (blue). CDH6 is found in the cytoplasm, perinuclear regions, nucleus, and the cell membrane. B) Representative image of RA synovium with anti-CDH6 (red) and -CD68 (green) (macrophage) antibodies show lining and sublining expression of CDH6, most likely in FLS (solid white arrow) and lining macrophages (open white arrow).

Results: Initial immunofluorescence studies of RA synovial tissue revealed abundant CDH6 in the intimal lining. Using anti-CD68 and anti-CDH6 antibodies in double stained tissues, we observed CDH6 expression in lining macrophages and fibroblasts. CDH6 was also expressed to a lesser degree in the sublining, particularly in the perivascular regions and included macrophages and non-macrophages (Figure 1). A similar distribution of CDH6 protein was observed in OA synovium and suggests that CDH6 is an important component in the synovial architecture. Because FLS reside in the intimal lining and were strongly CDH6 positive, we explored the expression and distribution of CDH6 in cultured FLS. Western blots showed that expression is higher in RA than OA FLS (1.2±0.01 vs 0.1±0.01 OD, p=0.03; n=4 each). Using immunostaining, expression was higher in FLS cultured at higher cell density and was ~2-fold higher in confluent vs. non-confluent cultures. Thus, CDH6 might be regulated, in part, by cell-cell contact. More intriguing, confocal microscopy showed significant expression of CDH6 protein in the cytoplasm, peri-nuclear regions, and nucleus in addition to the cell membrane.

Conclusion: CDH6 is expressed in synovial lining and sublining fibroblasts and macrophages. The striking intracellular distribution suggests additional functions beyond adhesion and homotypic aggregation, such as signalling and regulation of gene transcription. Thus, CDH6 has similarities to E-Cadherin, which also localizes to intracellular structures and participates in biologic functions. Our data suggest for the first time that CDH6 might have multiple functions in FLS that contribute to its pathogenic behaviour.

Disclosure: C. R. L. Machado: Eli Lilly, 5; **D. Boyle**: None; **N. B. Perumal**: Eli Lilly, 3; **R. J. Benschop**: Eli Lilly and Company, 3, 11; **G. Firestein**: Eli Lilly, 5.

Abstract Number: 1756

Circulating CD4+CD25+CD127-FoxP3+CD39+ T Cells Predict the Response to Methotrexate Across Basal Disease Activity Strata in Early Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: A subset of human FoxP3+ regulatory T (Treg) cells expresses CD39 (Treg39+) and hydrolyses pro-inflammatory adenine nucleotides released at inflammatory foci, rendering the antiinflamatory adenosine. Methotrexate (MTX), inhibiting AICAR transformylase, enhances the extracellular release of adenine nucleotides and may cooperate with Treg39+ cells to control inflammation. Therefore we examined whether Treg cells may help predict the response to MTX independently of clinical parameters.

Methods: PBMCs from 82 ERA patients (duration < 24 weeks) and 82 healthy controls (HCs) were examined by cytometry to assess the frequency of CD4+CD25+CD127-FopxP3+ [total circulating Treg (cTreg)] and CD4+CD27+CD127-FoxP3+-CD39+ Treg [circulating Treg39+ (cTreg39+)]. PBMCs from 40 patients were reexamined 12 months (12m) after initiating

MTX. Disease activity was assessed by DAS28-ESR. High, moderate or low disease activity (HDA, MDA, LDA) were defined as a DAS28>5.1, >3.2 and ≤ 5.1, or DAS28 ≤ 3.2, respectively.

Results: As compared with HC, ERA patients showed an increased baseline (0 months, 0m) frequency (fr.) of cTreg with increased proportions of cTreg39+ cells. Patients who attained LDA 12m after initiating MTX had significantly higher 0m fr. of cTreg [logistic regression OR 7.18 (95% CI, 3.26-21.75); ROC AUC 0.93 (0.87-0.99), p< 0.0001] and cTreg39+ cells [OR 1.55 (1.29-2.10); AUC 0.97 (0.95-1.0), p< 0.0001], as compared with those who did not; multiple regression indicated that this was independent of age, 0m disease activity, RF or ACPA titres. The baseline cutoff fr. for 12m LDA was cTreg >7.8% [sensitivity (S) 0.82, specificity (Sp) 0.91%] and cTreg39+ > 42.0% (S 90.4, Sp 96.8%). We next analyzed separately patients who had presented with 0m-HDA (n=44), 0m-MDA (n=34) or 0m-LDA (n=4). The number of patients who attained 12m LDA was 23 (52%) in the 0m-HDA, 24 (71%) in the 0m-MDA and 4 (100%) in the 0m-LDA group. Interestingly, in either the 0m-HDA or the 0m-MDA group, the basal Treg and Treg39+ cell fr. significantly correlated with the ΔDAS28, and were good predictors of 12m-LDA [Treg OR for 0m-HDA = 2.60 (1.50-5.35), AUC 0.81 (0.68-0.94), p< 0.0005; Treg OR for 0m-MDA = 3.03 (1.55-8.50), AUC 0.88 (0.77-0.99), p< 0.0005; Treg39+ OR for 0m-HDA = 1.79 (1.27-3.90), AUC 0.97 (0.91-1.0), p< 0.0001; Treg39+ OR for 0m-MDA = 1.49 (1.18-2.31), AUC 0.95 (0.87-1.0), p< 0.0001]. After removing the seronegative patients from the 0m-HDA (n=9, 20%) or the 0m-MDA (n=6, 18%) groups, the relation of the basal Treg or Treg39+ cell fr. with the response to MTX did not vary. The small number of patients who presented with 0m-LDA (n=4) did not allow further analysis of this group. At 12m, patients demonstrated a significant reduction of cTreg and cTreg39+ with no variation observed in HC, and differences between HC and ERA were no longer apparent, likely reflecting the 0m upregulation of the genetically determined CD39 expression levels; of note, the 12m cTreg [OR 3.19 (1.68-8.0)] and cTreg39+ [OR 1.31 (1.13-1.80)] cell fr. remained associated with LDA.

Conclusion: The baseline cTreg39+ fr. in untreated ERA predicts the clinical response to MTX across baseline disease activity strata, and facilitates the development of precision medicine strategies.

Disclosure: M. Miranda-Carus: Bristol-Myers Squibb(BMS), 5, Gebro Pharma, 5; **B. Nieto-Carvalhal**: None; **A. Villalba**: None; **L. Nuño**: None; **M. Benito-Miguel**: None; **M. Novella-Navarro**: Galapagos, 6, Janssen, 5, 6, Lilly, 5, 6, UCB, 5, 6; **I. Monjo**: Amgen, 6, Gedeon Richter, 6, Janssen, 6, Novartis, 6, Roche, 6, UCB, 6; **D. Peiteado**: None; **S. García-Carazo**: None; **A. Balsa**: AbbVie/Abbott, 1, 2, 5, 6, Bristol-Myers Squibb(BMS), 1, 5, Eli Lilly, 1, 5, 6, Merck/MSD, 1, 5, Novartis, 5, Pfizer, 1, 5, 6, UCB, 1, 5, 6.

Abstract Number: 1757

Quantitative Assessment of Synovial Vascularity Using Power Doppler Index in Rheumatoid Arthritis and Psoriatic Arthritis Patients with High Disease Activity

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Usefulness of quantitative assessment of synovial vascularity in ultrasound (US) imaging in patients with active RA and PsA (peripheral arthritis). Additionally the assessment of vascularity index (INDEX%) dependency on immunological markers such as rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) were assessed.The last aim of the study was to examine whether patients with high active peripheral PsA differ in the severity of synovial congestion from patients with high RA activity.

Methods: A total of n=80 patients were included into the study, n=60 with RA and n=20 PsA. Majority of them (for both group) were female (n=53.66.25%). Laboratory variables were assessed: RF (IU/ML units), ACPA (U/ML), ESR (mm/hour) and C-reactive protein (CRP;MG/L); disease activity were assessed by DAS 28(ESR) and simplified disease activity score (SDAI). The power doppler US (PDUS) was performed with assessment of a) the degree of the synovial membrane vascularization (from 0 to 4 grade); the following scores were used in the assessment: 0- no signs of synovial flow, 1- isolated signals in hypertrophied synovium, 2-vessels occupy less than 50% of hypertrophied membrane area synovitis, 3- inflammation affects over 50% of the examined area; b) vascularity index measured by PDUS index (INDEX%) in the ROI (region of interest) frame (figure 1). All patients underwent examination using the same US machine and by the same specialist in radiology and imaging diagnostics.

Results: Disease activity for RA and PsA patients was between 4.8- 8.3 with DAS28 and 23-183 with SDAI. The hypothesis of a positive correlation between the concentration of ACPA and INDEX% in RA group was confirmed however it was a week positivity(r=0.26) but such correlation between RF and INDEX% was not confirmed (r=0.03). ESR, CRP, DAS 28(ESR) and SDAI did not correlate significantly with the value of INDEX%. What was expected the strong positivity (r=0.56) was between SDAI and DAS28 results. Interestingly there was no correlation between DAS 28, SDAI and INDEX %, probably because all of patients from both groups had high disease activity.

Conclusion: Positive correlation between the concentration of ACPA and INDEX% value indicating that ACPA may be a prognostic factor for vascularization of the synovial membrane in patients with RA. No such correlation was confirmed for RF. Taken together obtained results pointed to ACPA as more important for synovial inflammatory activity in RA. Vascularity of synovial membrane assesed by INDEX %compared between RA and PsA group was equally high, despite the difference in RF and ACPA indicating that the presence of other cytokines is more involved in the development of synovial inflammation in PsA. The quantitative US assessment of synovial vascularity is a useful tool in comparative studies and may have a significant advantage over a qualitative study after expanding the study groups with different degrees of inflammatory activity in the synovium.

Synovial membrane with active inflammation (vascularization) and region of interest frame indicated.

Disclosure: M. Jakubaszek: None; **M. Maślińska**: None; **B. Kwiatkowska**: None.

Abstract Number: 1758

Identification of Circulating Autoantibodies Associated with ACPA Status in Early Rheumatoid Arthritis

Lucía Lourido[1], Vijay Joshua[2], Monika Hansson[3], Ronald Sjöberg[4], Elisa Pin[4], Cristina Ruiz-Romero[5], Peter Nilsson[4], Lars Klareskog[2] and Francisco J. Blanco[6], [1]Unidad de Proteómica. Grupo de Investigación de Reumatología (GIR). Instituto de Investigación Biomédica de A Coruña (INIBIC), Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC). C/ As Xubias de Arriba 84, 15006, A Coruña, Spain, [2]Karolinska Institutet, Stockholm, Sweden, [3]Division for Rheumatology, Department of Medicine (Solna) Karolinska Institutet, Stockholm, Sweden, [4]Department of Protein Science, SciLifelab, KTH Royal Institute of Technology, Stockholm, Sweden, [5]1) Unidad de Proteómica. Grupo de Investigación de Reumatología (GIR). Instituto de Investigación Biomédica de A Coruña (INIBIC), Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC). C/ As Xubias de Arriba 84, 15006, A Coruña, España. 4) Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN). Av. Monforte de Lemos, 3-5. Pabellón 11,28029, Madrid, Spain, [6]Rheumatology department, Complexo Hospitalario Universitario A Coruña (CHUAC). Instituto de Investigación Biomédica A Coruña (INIBIC), A Coruña, Spain

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Etiology and Pathogenesis Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is associated with the presence of autoantibodies being the anti-citrullinated protein antibodies (ACPAs) the hallmark as they are present in almost 70% of patients with established RA. However, despite the high diagnostic value of ACPA, the sensitivity in early RA of the most common tests used in clinics is between 60-70% in newly diagnosed RA. Besides, ACPA-negative patients, who constitute up to one-third of patients with RA, entails a challenge for early diagnosis. The fact that not all RA patients are ACPA-positive means that there is a need for additional biomarkers including autoantibodies that may help to diagnose RA patients at an early stage.

Interestingly, ACPA-positive RA patients also display a different etiology and disease course compared to ACPA-negative patients. Therefore, an increased knowledge about the presence of other circulating autoantibodies related with early RA is needed to improve its diagnosis, specifically for ACPA-negative patients, and to better understand the pathogenic mechanisms underlying the different RA subsets.

Herein we aimed to search for plasma autoantibodies associated with ACPA status that could be useful to define clinical phenotypes in early RA.

Methods: The autoantibody repertoire of 80 ACPA-negative and 80 ACPA-positive early RA subjects from the Swedish population-based Epidemiological Investigation of RA (EIRA) cohort was screened using a targeted suspension bead array built on protein fragments earlier described as autoimmunity targets. Four autoantibodies were validated in another set of EIRA samples containing 317 ACPA-positive, 302 ACPA-negative and 372 age- and sex-matched controls. The relationship between the four autoantibodies and lung abnormalities on high-resolution computed tomography was also examined in 93 early RA patients. Association between the autoantibodies and clinical features was assessed by logistic regression analysis.

Results: IgG autoantibody levels towards anosmin-1 (ANOS-1) and towards muscle related coiled-coil protein (MURC) were significantly increased in ACPA-positive subjects compared to ACPA-negative and controls, and associated with ACPA status (OR=3.02; 95% CI 1.86 to 4.89; and OR=1.86; 95% CI 1.16 to 2.97, respectively). IgG autoantibody levels towards dual

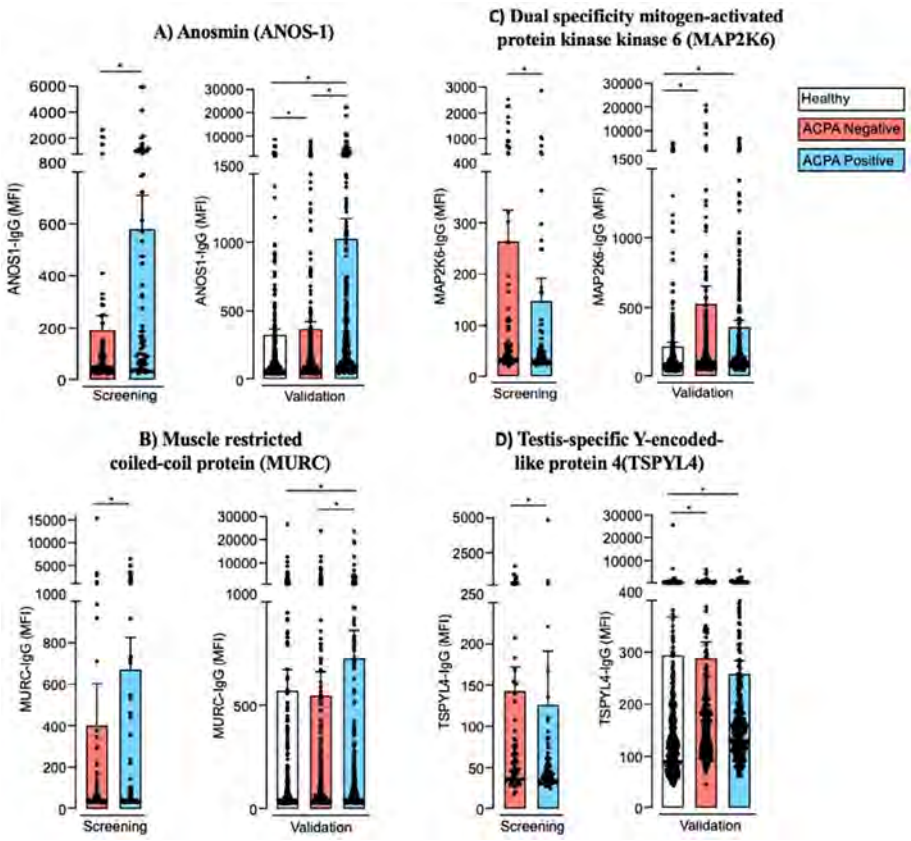

Figure 1. IgG immunoreactivity to Anosmin-1 (panel A), Muscle restricted coiled-coil protein (MURC) (panel B), Dual specificity mitogen-activated protein kinase kinase 6 (MAP2K6) (panel C) and Testis-specific Y-encoded-like protein 4 (TSPYL4) (panel D) in the screening sample set and in the validation sample set. Bar plots represent mean and standard deviation of the levels of autoantibodies measured in median fluorescence intensity (MFI).

specificity mitogen-activated protein kinase kinase 6 (MAP2K6), and testis-specific Y-encoded-like protein 4 (TSPYL4) were increased in the ACPA-negative subjects compared to ACPA-positive and controls. IgG anti-TSPYL4 was also significantly associated with ACPA-negative status (OR=0.41;95%CI 0.19 to 0.89). IgG anti-ANOS1 was associated with the smoking habit (OR=2.11;95% CI 1.22 to 3.67) and IgG anti-MURC with the presence of the shared-epitope (OR=1.95;95% CI 1.11 to 3.46). Regarding lung abnormalities, the presence of IgG anti-TSPYL4 was associated with a less prevalence of infiltrates (OR=0.11;95% CI 0.01 to 0.86), and IgG anti-MAP2K6 with less fibrosis (RR=0.85;95% CI 0.77 to 0.94).

Conclusion: Our data suggest that these four autoantibodies may be potentially useful to define clinical phenotypes of RA. Validation in other early RA sample cohorts is needed.

Disclosure: L. Lourido: None; **V. Joshua**: None; **M. Hansson**: None; **R. Sjöberg**: None; **E. Pin**: None; **C. Ruiz-Romero**: None; **P. Nilsson**: None; **L. Klareskog**: None; **F. Blanco**: None.

Abstract Number: 1759

Runx1 Is a Key Transcription Factor That Drives Synovial Fibroblast Pathogenicity in Rheumatoid Arthritis

Christopher Mahony[1], Samuel Kemble[2], Paulynn Chin[1], Cesar Prada[3], Annie Hackland[1], Patricia Reis-Nisa[1], Lucy-Jayne Marsh[1], Peter Keane[1], Constanze Bonifer[1], Christopher Buckley[4], Stevephen Sansom[5], Mark Coles[4] and Adam Croft[1], [1]University of Birmingham, Birmingham, United Kingdom, [2]University Birmingham, Rugeley, United Kingdom, [3]The Kennedy Institute, Oxford, United Kingdom, [4]University of Oxford, Oxford, United Kingdom, [5]Kennedy Institute of Rheumatology, Oxford, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Etiology and Pathogenesis Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Fibroblasts are key effector cells in rheumatoid arthritis (RA) underpinning joint inflammation and damage. Synovial tissue fibroblasts are heterogenous and acquire pathogenic cell states that either drive inflammation or tissue damage. However, the molecular mechanisms underpinning fibroblast heterogeneity and pathogenicity are poorly understood.

Methods: To identify key regulators of fibroblast behaviour, we performed combined scRNAseq and scATACseq analysis of synovial fibroblasts from the serum transfer induced arthritis model in mice and compared these data to additional scRNA-seq data from collagen induced arthritis and antigen induces arthritis models. Ongoing validation is being performed using multiplex imaging, spatial transcriptomics (10x Visium platform), conditionally inactivating *Runx1* in murine fibroblasts, lentiviral gain of function, pharmacologicalinhibition and ChIP-Seq.

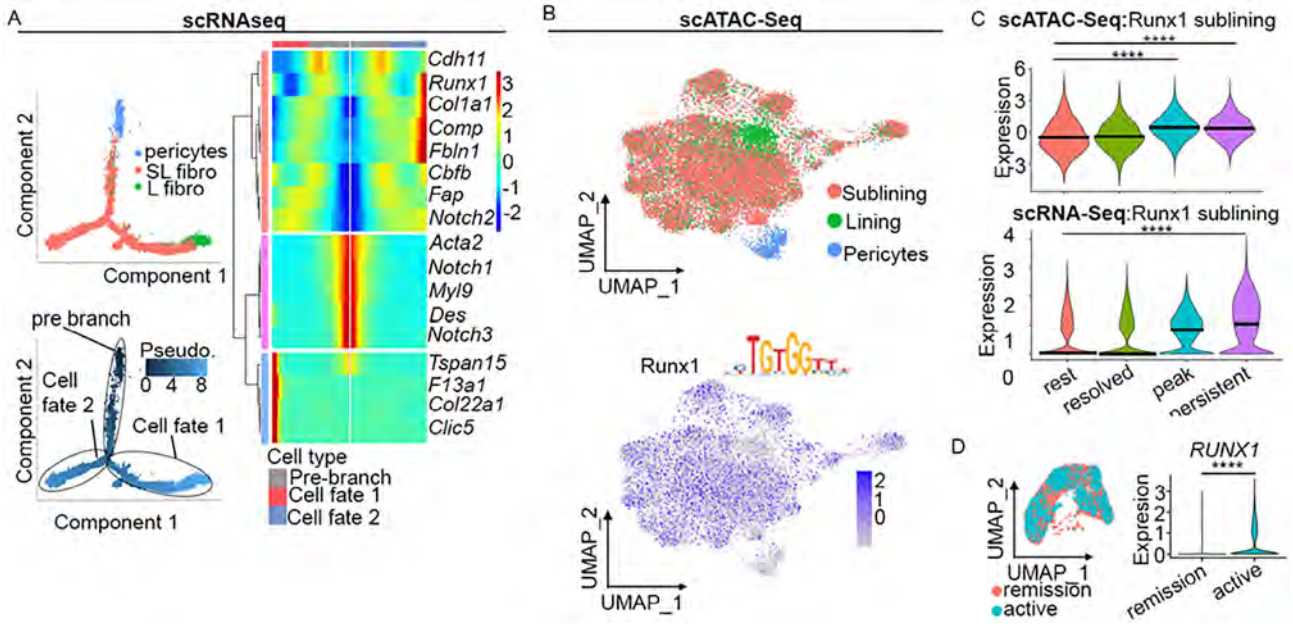

Figure 1. Runx1 expression is associated with sublining synovial fibroblast pathogenicity. (A) scRNAseq pseudotime trajectory of murine synovial fibroblasts (pericytes, sublining fibroblasts and lining layer fibroblasts). (B) scATACseq annotation and Runx1 motif activity in synovial fibroblasts. (C) scATACseq Runx1 motif activity and scRNAseq Runx1 expression across STIA (serum transfer induced arthritis) timepoints. (D) Runx1 expression in remission and active RA patients (Data from Alivernini et al., 2020).

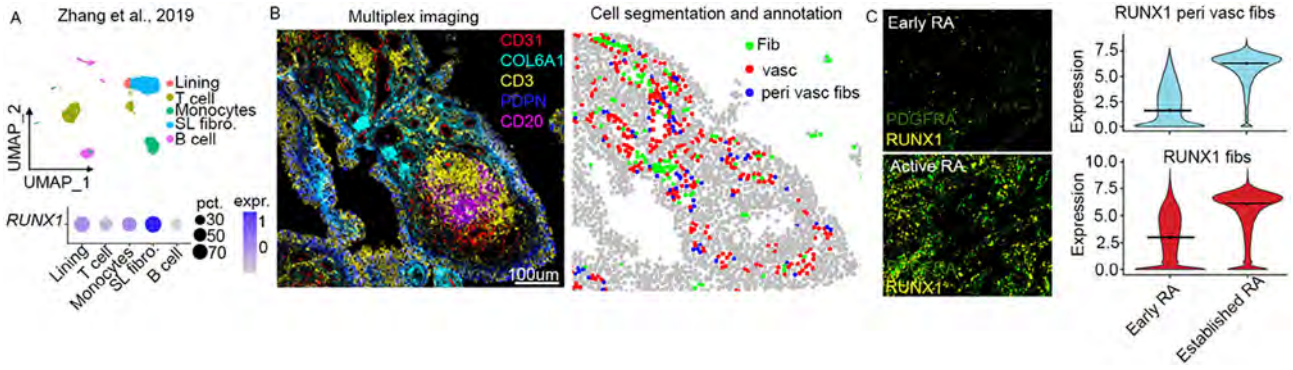

Figure 2. RUNX1 expression is associated with sublining synovial fibroblasts and is increased in active RA. (A) RUNX1 expression across synovial cells (Data from Zhang et al., 2019). SL fibro: sublining fibroblast. (B) Examples of multiplexed immunofluorescence images of synovial tissue and cellular segmentation to quantify fluorescence. Fib: fibroblasts; vasc: vasculature; peri vasc fibroblasts: perivascular fibroblasts. (C) Immunofluorescence staining and quantification of PDGFRA and RUNX1 expression on synovial tissue from early and established RA patients in perivascular and interstitial fibroblasts.

Results: We identified**Runt-related transcription factor 1**(*Runx1)* expression (scRNAseq) and motif activity (scATACseq) to be highly specific to sub-lining synovial fibroblasts which have been implicated in driving synovial inflammation (Fig. 1A, B). *Runx1* motif activity and gene expression were also found to be upregulated during joint inflammation in mice and in patients with RA and active joint inflammation, compared to those patients in clinical remission (Fig. 1C, D). Further analysis of publicly available data from RA synovium showed robust *RUNX1* expression in synovial fibroblasts (Fig. 2A). Multiplex imaging showed *RUNX1* to be enriched in perivascular fibroblasts compared to interstitial fibroblasts. Furthermore, *RUNX1* expression was increased in perivascular fibroblasts in active RA compared to early RA (Fig. 2B, C). We next confirmed that *RUNX1* expression in synovial fibroblasts is controlled by inflammatory stimuli using confocal imaging and analysis of publicly available Hi-C data. Examining publicly available ATAC-Seq data as well as coexpression analysis using spatial transcriptomics and scRNAseq data from murine models of arthritis highlighted several direct *RUNX1* target genes. We are now performing functional experiments to validate *RUNX1* targets to explore how *RUNX1* regulates fibroblast pathogenicity.

Conclusion: Our analysis identifies *RUNX1* as a novel regulator of disease associated, synovial fibroblast behaviour in inflammatory arthritis and a potential novel therapeutic target to modulate fibroblast-driven pathology in RA.

References: Zhang F et al. Nat Immunol. 2019. PMCID: PMC6602051. Alivernini S et al. Nat Med. 2020 Aug. PMID: 32601335.

Disclosure: C. Mahony: None; **S. Kemble**: None; **P. Chin**: None; **C. Prada**: Novo nordisk, 3; **A. Hackland**: None; **P. Reis-Nisa**: None; **L. Marsh**: None; **P. Keane**: None; **C. Bonifer**: None; **C. Buckley**: Bristol-Myers Squibb(BMS), 5, Mestag, 11; **S. Sansom**: None; **M. Coles**: None; **A. Croft**: None.

Abstract Number: 1760

Methotrexate Augments the Release of Granulocyte-macrophage Colony-stimulating Factor from Activated Rheumatoid Arthritis Fibroblast-like Synoviocytes - Possible Consequences for Persistence of Joint Inflammation

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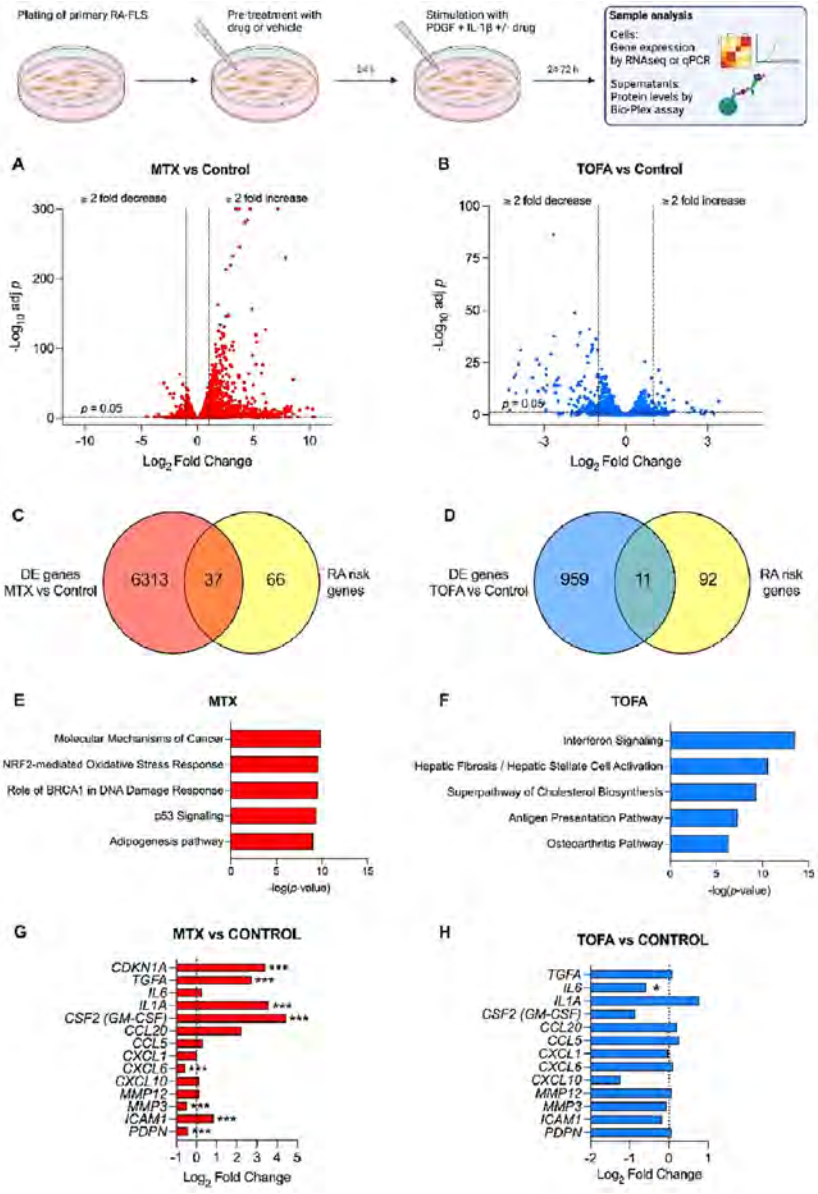
SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Activated fibroblast-like synoviocytes (FLS) are important mediators of synovitis and structural damage in rheumatoid arthritis (RA)[1]. Granulocyte-macrophage colony-stimulating factor (GM-CSF, encoded by the *CSF2* gene) is released from activated RA-FLS and promotes the production of pro-inflammatory cytokines from macrophages,

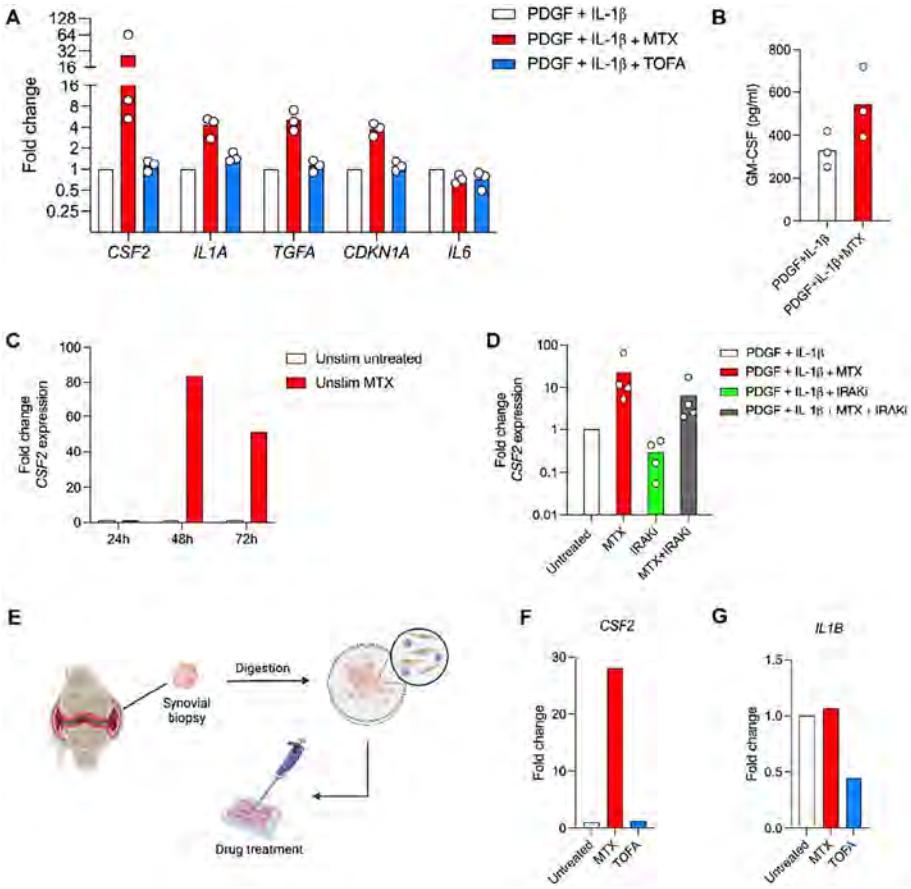


Primary RA-FLS were pre-treated with MTX, TOFA, or vehicle at 1-2,5 uM for 24 hours followed by stimulation with 20 ng/mL PDGF-BB and 2 ng/mL IL-1beta in medium with the drug or vehicle for 48 hours and finally processed for RNAseq. Vulcano plots show significantly DE genes by DESeq2 ($p \leq 0.05$) for MTX (A) and TOFA (B) vs untreated control. Venn diagram demonstrate effects of MTX (C) and TOFA (D) on RA risk genes identified by Genome wide association studies. Ingenuity Pathway Analysis revealed the five most significant pathways for MTX (E) and TOFA (F). Effects of MTX and TOFA on a core set of RA-associated FLS-expressed genes are demonstrated in G and H respectively. *Adjusted $p \leq 0.05$, **$p \leq 0.01$, ***$p \leq 0.001$ (Benjamini-Hochberg).

which in turn activates FLS creating a viscous cycle[2]. We investigated the effects of anti-rheumatic drugs on gene expression, in particular RA risk genes such as *CSF2*, in activated RA-FLS, and on cytokine release from RA synoviocyte cultures.

Methods: Primary FLS were established from synovial tissue collected from patients with RA undergoing arthroplasty or synovial biopsy. FLS were pre-treated with methotrexate (MTX), tofacitinib (TOFA, janus kinase inhibitor), zimlovisertib (IRAK4 inhibitor) or vehicle followed by stimulation with platelet-derived growth factor (PDGF) and interleukin-1β (IL-1β) for 24-72 hours (Fig.1, top). An RA *ex-vivo* synovial bioassay was performed according to Kuo et al.[3]. Cells were collected for RNAseq or qPCR, and supernatants were analyzed for protein concentrations using Bio-Plex assay.

Results: MTX demonstrated an overall activation of gene expression in PDGF+IL-1β stimulated RA-FLS compared to untreated (6350 differentially expressed (DE) genes), and to TOFA treated (970 DE genes) samples (Fig. 1A-B). MTX had a greater effect on RA risk genes (35 % DE in MTX vs CON) compared to TOFA (10 % DE in TOFA vs CON) (Fig.1C-D). Pathway analysis showed largest effects on *Molecular mechanisms of cancer* (MTX) and *Interferon signaling* (TOFA) respectively (Fig. 1E-F). Targeted analysis revealed that MTX in addition to the known induction of *CDKN1A* (p21)[4], profoundly increased *CSF2*, *IL1A* and *TGFA* expression compared to control treated activated FLS (Fig.1G). TOFA reduced *IL6* and *CXCL10* expression as expected (Fig.1H). RNAseq data were confirmed by qPCR and on protein level in FLS supernatants (Fig.2A-B). Furthermore, MTX induced *CSF2* expression also in unstimulated RA-FLS (Fig.2C). IRAK4i could not prevent the



Primary RA-FLS were pre-treated, stimulated and treated as outlined according to experimental design in figure 1. Graphs show fold change to untreated control by qPCR. A) Expression of RA-associated genes in stimulated RA-FLS treated with MTX (red bars) and TOFA (blue bars). B) GM-CSF concentration by Bio-Plex assay in supernatants of cells in A). C) Time course of CSF2 expression in MTX treated unstimulated RA-FLS. D) CSF2 expression in MTX, zimlovisertib (IRAK4i) or combination treated stimulated RA-FLS. E) Work flow of RA ex-vivo synovial bioassay. F) Induction of CSF2 expression by MTX and G) expression of IL-1beta in synoviocyte cultures (Bio-Assay) treated with MTX (red) and TOFA (blue).

increased GM-CSF expression by MTX in stimulated RA-FLS (Fig.2D). MTX induced *CSF2* expression in RA *ex-vivo* synovial cultures (Fig. 2E-F) and failed to reduce IL-1β expression as opposed to TOFA (Fig.2G).

Conclusion: Methotrexate treatment augments the release of GM-CSF from RA-FLS and leads to sustained cytokine production from synoviocytes. This off-target effect might contribute to the persistence of synovitis.

Disclosure: B. Bergström: None; **T. Selldén**: None; **M. Bollmann**: None; **M. Svensson**: None; **A. Hultgård Ekwall**: AbbVie/Abbott, 1, 2, Boehringer-Ingelheim, 6, Pfizer, 1.

Abstract Number: 1761

JAK/STAT Inhibition Modifies the Innate Lymphoid Cells 1 Immune Response in Patients with Rheumatoid Arthritis

Lidia La Barbera[1], Marianna Lo Pizzo[1], Chiara Rizzo[1], Leila Mohammadnezhad[1], federica Camarda[1], Francesco Ciccia[2] and Giuliana Guggino[1], [1]University of Palermo, Palermo, Italy, [2]University of Campania - Luigi Vanvitelli, Naples, Italy

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Recent evidence suggests that innate lymphoid cells (ILCs) might be involved in rheumatoid arthritis (RA) pathogenesis and individuals at risk of RA exhibited an increased frequency of ILC1 (Rodríguez-Carrio J, Arthritis Rheumatol. 2017). JAK3 participates in ILC1 and ILC3 differentiation. Tofacitinib and JAK3 inhibitor, PF-06651600, impair the ability of human intraepithelial ILC1 to produce IFN-γ and the proliferation of ILC1 and ILC3 (Robinette ML, Mucosal immunology. 2018). Our study aims to evaluate the effects of tofacitinib on ILC1 and ILC3 expansion and function in RA.

Methods: Twenty RA patients, who fulfilled the ACR/EULAR RA classification criteria, with active disease, naive to biological agents, were enrolled and started tofacitinib. The study was complied with the Declaration of Helsinki and was approved by the local Ethical Committee. Ten healthy donors (HD) matched for age and sex were also enrolled. Peripheral blood

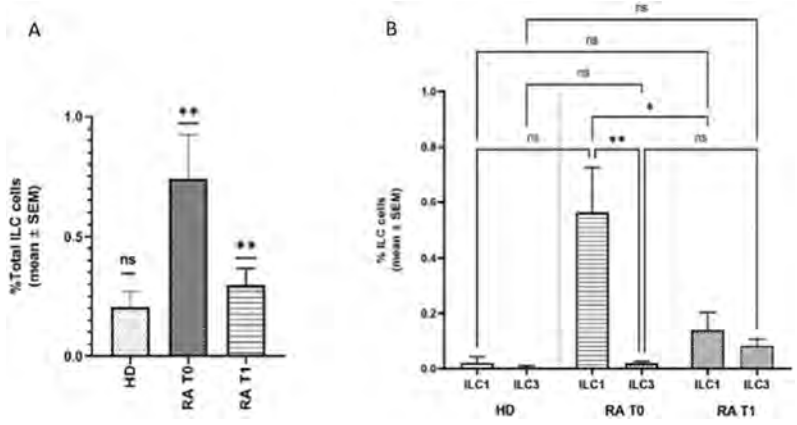


Figure 1: ILCs, ILC1, ILC3 frequencies at T0 and T1 A. Peripheral total ILCs frequency in HD and RA patients at T0 and T1; **p <0,01. B. Frequency of ILC1 and ILC3 in HD and RA patients at T0 and T1; **p <0,01, *p <0,05.

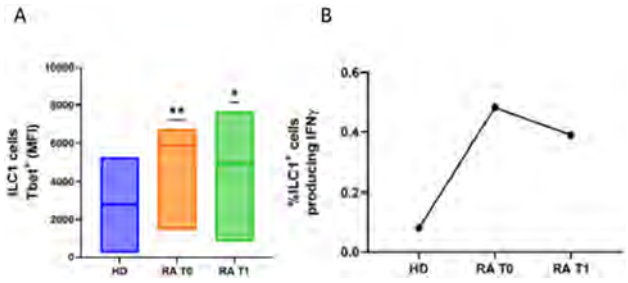


Figure 2: ILC1 functional activity at T0 and T1 A. Box plot showing comparison between median values of T-bet MFI for HD and RA patients at T0 and T1; **p <0,01, *p <0,05. B. IFNγ production by ILC1s in HD and RA patients at T0 and T1.

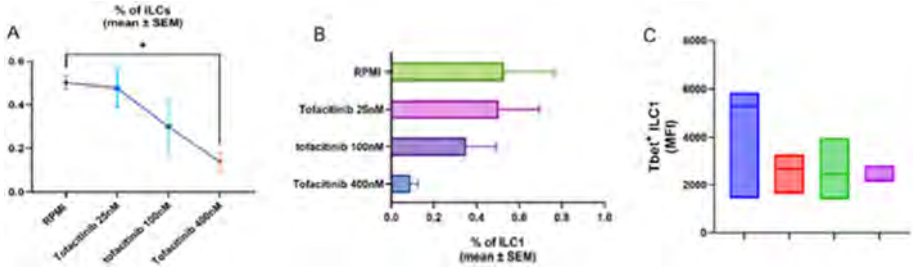


Figure 3: Effects on ILCs frequency of in vitro tofacitinib treatment A. Total ILCs frequency B. Frequency of ILC1 C. Box plot showing MFI expression of Tbet on ILC1s

mononuclear cells (PBMCs) collected before (T0) and three months after therapy (T1), were cultured to evaluate ILC1 and ILC3 frequencies and the respective production of IFN-γ and IL-17 by flow cytometry analysis. PBMCs of RA patients were *in vitro* cultured for 48 hours with tofacitinib at increasing concentrations (25nM, 100nMand 400nM) to evaluate the dose effects of tofacitinib on ILCs frequencies. Role of the Study Sponsor: Research was supported by an unrestricted grant by Pfizer.

Results: At T0, RA patients showed a significant expansion of peripheral total ILCs and ILC1 (Lin^-, $CD127^+$, $CD117^-$, $Tbet^+$) but not ILC3 (Lin^-, $CD127^+$, $CD117^+$, RoR γt^+), compared to HD. After three months of therapy the overall ILCsfrequency was significantly reduced in RA (Figure 1). Specifically, ILC1 frequency was significantly decreased in association with the reduction of transcriptional factor T-bet expression as well as the ILC1 ability to release IFN-γ (Figure 2). Instead, for ILC3 not significant modifications in frequency, RoR γt expression andIL-17 production were detected at T1. *In vitro* treatment of PBMCs with increasing concentrations of tofacitinib demonstrated a dose-dependent reduction in the frequency of ILCs compared to untreated cells. In particular, ILC1s resulted more affected, by the *in vitro* treatment, both in terms of frequency and transcription factors expressioncompared to ILC3, supporting our *ex vivo* results (Figure 3).

Conclusion: Our preliminary results demonstrate that tofacitinib modulates the innate immune response by reducing the frequency of ILC1 cells and their production of IFN- γ.

Disclosure: L. La Barbera: None; **M. Lo Pizzo**: None; **C. Rizzo**: None; **L. Mohammadnezhad**: None; **f. Camarda**: None; **F. Ciccia**: None; **G. Guggino**: None.

Abstract Number: 1762

Single-cell RNA Sequencing Analysis and Immune Profiling of Antigen-specific T Cells in Patients with Rheumatoid Arthritis and Healthy Controls

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Single-cell analysis has emerged as a powerful tool for investigating the transcriptomics and T-cell receptor (TCR) diversity in patients with rheumatoid arthritis (RA). However, there is limited information on the specificities, immunophenotype, and TCR diversity of antigen-specific T cells in RA using single-cell RNA sequencing (scRNA-seq). To address this knowledge gap, we conducted a pilot study to demonstrate the applicability of 10x single-cell sequencing for studying antigen-specific T cells.

Methods: Peripheral blood mononuclear cells (PBMC) were from patients with seropositive RA (n=3) and healthy control (HC) subjects (n=2). All individuals were HLA DRB1*0401 or 0404. Using an activation-induced marker (AIM) assay, PBMC were stimulated overnight with a pool of peptides derived from RA antigens (Table 1) or a peptide pool for viral antigens (CFEX). CD4+CD154+ and CD8+CD137+ cells were isolated to obtain paired scRNA-seq, cellular indexing of transcriptomes and epitopes by sequencing (CITE-seq), and TCR repertoire data. Specifically, we isolated RA antigen-specific T

Table1 RA peptide pool.

Peptide	number
cit-Tenascin	101
arg-Tenascin	182
cit-Aggrecan	47
arg-Aggrecan	81
cit-Enolase	10
arg-Enolase	26
cit-Fibrinogen	41
arg-Fibrinogen	100
cit-Vimentin	19
arg-Vimentin	27
DR0401/DR0404 cit	21
Total Peptides	655

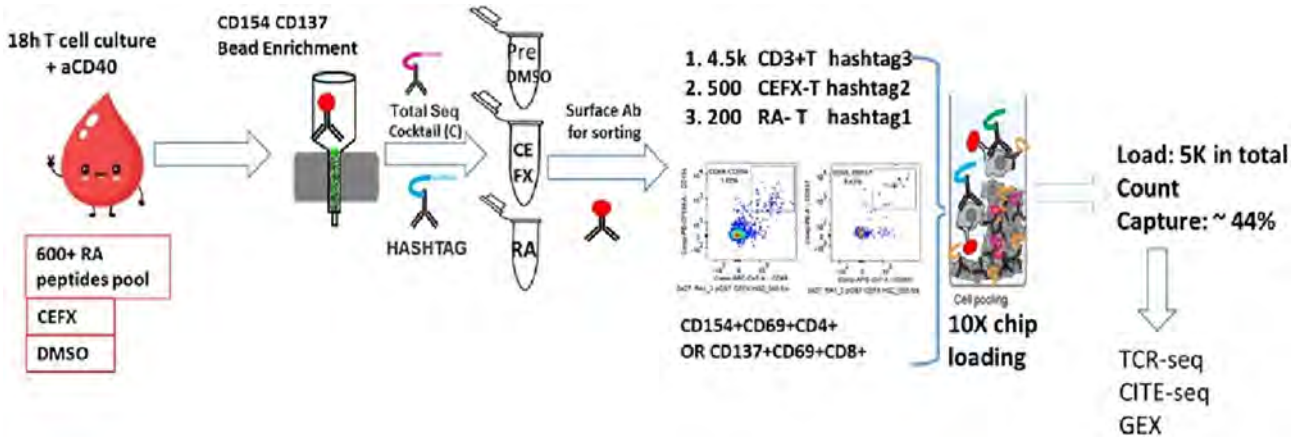

Figure 1. Experimental design of 10X single cell RNA sequence using an AIM assay.

cells, CEFX antigen-specific T cells, and general CD3 T cells from the same subjects (Figure 1). The sorted cells were stained with the TotalSeq Human Universal Cocktail (BioLegend), hashtagged, and the captured single cells sequenced using the droplet-based 10x Chromium platform. Cell projection and graph-based clustering were performed using the Seurat package.

Results: A total of 11,053 cells, 6464 from RA and 4589 from HC subjects, were subjected to high-quality scRNA-seq analysis. Utilizing a graph-based clustering approach, we identified seven distinct clusters of cells, representing both RA and HC, which were visualized through integrated UMAPs< ![if !supportAnnotations] >[VG1]< ![endif] > combining multimodal data. Overlaying hashtags to the UMAP suggests that RA and CEFX T cells mostly mapped to cluster 4. Differential gene expression analysis and antibody expression of established lineage markers revealed that cells in cluster 4 express high levels of activation markers including CD71, CD28, CD38, HLA-DR and KLRG1, transcription factors including NR4A1, HLA-A, HLA-B and IFNG, and translation initiation factorEIF5A and EIF1. We applied a similar graph-based clustering method to RA and CEFX antigen-reactive T cells, leading to the identification of four major clusters: a cytotoxic CD8+ T cells (cluster 0), exhausted CD8+ T cells (cluster 1), activated CD4+ T cells (cluster 2), and IFN I signature CD4+ T cells (cluster 3). We observed high-quality TCR sequences in over 90% of the captured cells from each subject and significant private clonal expansions, with CD8 RA antigen-specific T cells displaying a higher degree of clonotypic expansion compared to CD4 populations. We also identified clonal sharing between RA antigen-specific T cells and the non-selected CD3 T cells in each subject.

Conclusion: Our findings highlight the power of multimodal single cell analysis to identify clonally expanded T cells in RA, characterize their phenotypic features at rest and upon activation, which may provide valuable insights into the antigen-specific T-cell responses and TCR dynamics associated with RA pathology.

Disclosure: J. SONG: None; **C. Rims**: None; **M. Dufort**: None; **P. Linsley**: None; **E. James**: Bristol-Myers Squibb(BMS), 5, Janssen, 5, Novartis, 5, Provention Bio, 5; **J. Buckner**: Bristol-Myers Squibb(BMS), 2, gentibio, 1, 10, 11, hotspot therapeutics, 2, Janssen, 2.

Abstract Number: 1763

Asthma Severity Is Associated Increased Serum Anti-cyclic Antibody Level at Baseline and in Increase During Longitudinal Follow-up

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The lung airways have been implicated in the pathogenesis of RA. RA-associated autoantibodies, including anti-cyclic citrullinated peptide (anti-CCP) antibodies are found to be generated in the lung using induced sputum. Epidemiologic studies have identified that the presence of airways diseases, such as asthma, increase incident RA compared to healthy cohorts. However, it remains unclear how this relationship between asthma and RAdevelops. The aim of our study was to investigate the relationship between asthma severity and serumanti-CCP in cross-section andover time.

Methods: Our prospective cohort study included patients with mild, moderate, and severe asthma. One-hundred forty-four patients were included in this study. Serum anti-CCP-IgG (CCP3, Werfen) and anti-CCP-IgA (research modification of CCP3.1, Werfen) levels were measured in by ELISA in banked serum obtained at baseline and at a longitudinal visit, which was separated by four years. Cut off levels for anti-CCP positivity was determined based on 3 standard deviations above the mean level in a separate cohort of 100 non-RA controls. Comparison between anti-CCP titers across asthma severity groups were carried out via t-test where appropriate. Each participant was determined to have mild, moderate or severe asthma at their baseline visit based on previously published expert guidelines (1).

Results: Thirty-four of 144 (23.6%) were positive for anti-CCP-IgA and 2 were positive for anti-CCP-IgG (1.3%). Baseline serum anti-CCP-IgA levels were higher in patients with moderate or severe asthma compared to the mild asthma group (p=0.022, Figure 1), which remained significantly different at follow-up (p = 0.01).Both groups had an increase in mean anti-CCP-IgA levels at follow-up, although the moderate or severe group had a numerically higher increase that did not reach

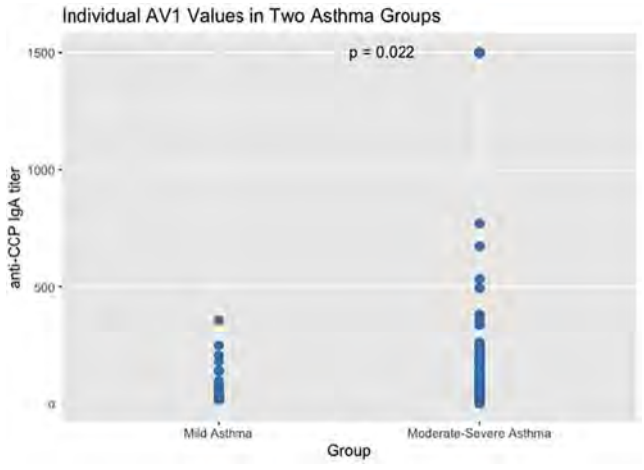

Fig1: Anti-CCP-IgA levels for each subject represented by each dot separated by asthma severity (mild vs moderate or severe)

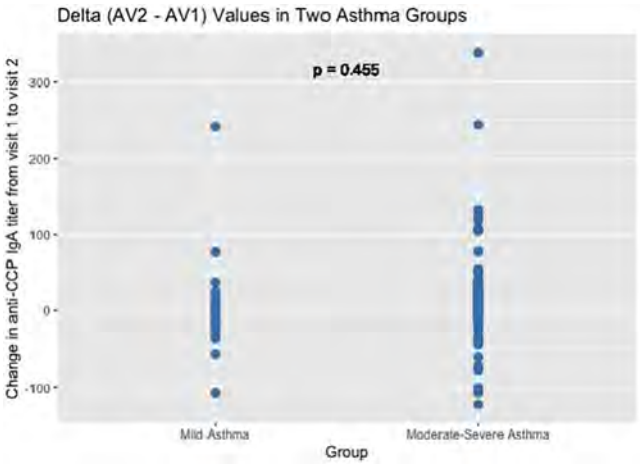

Fig 2: Each dot represents the delta in anti-CCP-IgA level from baseline to the longitudinal visit at year 4. Dots below zero represent subjects whose anti-CCP level decreased at follow-up, groups are separated by asthma severity level

statistical significance (p = 0.46, Figure 2) There was no difference in serum anti-CCP-IgG levels based on asthma disease severity at baseline or follow-up (p = 0.69 and p = 0.18 respectively).

Conclusion: We found serumanti-CCP-IgA antibodies in a modest number of asthma patients. Interestingly, there was a significant association between asthma severity and anti-CCP-IgA level, suggesting a potential relationship between airways inflammation and development of anti-CCP antibodies in these individuals. Additionally, worse baseline asthma severity (mild vs moderate/severe) had a numerically higher anti-CCP increase which did not reach statistical significance but may support the role of airway disease severity in anti-CCP generation. There was no association with anti-CCP-IgG titers which supports the role of lung mucosa in the development of this relationship.

Disclosure: D. Rorah: None; **L. Ngo**: None; **M. Castro**: None; **K. Demoruelle**: Boehringer-Ingelheim, 5, Gilead, 5, Pfizer, 5; **S. Matson**: None.

Abstract Number: 1764

Antibody Responses to Citrullinated Type II Collagen and Vimentin Modified with Malondialdehyde-Acetaldehyde Differ in Rheumatoid Arthritis and Rheumatoid Arthritis-Interstitial Lung Disease

Breanna Butler[1], Jill Poole[1], Michael Duryee[1], Nozima Aripova[1], Carlos Hunter[1], Bridget Kramer[1], James O'Dell[1], Geoffrey Thiele[1], Bryant England[1] and Ted R Mikuls[2], [1]University of Nebraska Medical Center, Omaha, NE, [2]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) causes significant complications and mortality in patients with rheumatoid arthritis (RA). We have previously shown that patients with RA-ILD had increased levels of serum IgA and IgM antibodies against human serum albumin modified with malondialdehyde-acetaldehyde (MAA) in addition to having higher levels of

ACPA. Moreover, lung tissues from RA-ILD patients demonstrated increased levels of MAA antigen that co-localized with citrullinated (CIT) proteins, Type II Collagen (CII) and Vimentin (VIM), suggesting that MAA may act as a cofactor that increases the immunogenicity of CIT proteins in RA-ILD patients. Therefore, antibody responses to dually modified (MAA and CIT) VIM or CII were evaluated as biomarker(s) to differentiate RA-ILD from RA and idiopathic pulmonary fibrosis (IPF), a condition with marked histopathologic similarities to RA-ILD.

Methods: Serum was collected from patients with RA, RA-ILD, or IPF (n=15 for each group). All patients with RA fulfilled the 1987 ACR classification criteria. The presence of RA-ILD was confirmed by a board-certified subspecialist (pulmonologist or rheumatologist) and the presence of supportive chest computed tomography (CT) findings. Patients were defined as having RA without ILD in the absence of a clinical diagnosis of ILD or past chest imaging findings suggestive of ILD. All patients with IPF without underlying autoimmune disease were diagnosed by a board-certified pulmonologist and had confirmatory findings of usual interstitial pneumonia (UIP) by chest CT imaging. Samples were assessed for CCP and relative units of IgG, IgM, and IgA antibody levels to CII-MAA-CIT and VIM-MAA-CIT via ELISA. Data was analyzed using a one-way ANOVA with Tukey's multiple comparison test.

Results: Participant characteristics were similar across groups: overall mean age 73 years, 90% male, 87% reporting White race and 68.9% current or former smokers. There was no difference in CCP positivity between RA and RA-ILD patients. Serum IgG antibodies to CII-MAA-CIT were significantly increased in RA-ILD patients compared to RA patients (4-fold higher, $p<0.05$) and IPF patients (42.5-fold higher, $p<0.01$) (**Fig. 1A**). Serum IgM (**Fig. 1B**) and IgA (**Fig. 1C**) antibodies to CII-MAA-CIT showed similar trends with IgG anti-CII-MAA-CIT, but only differences in RA-ILD vs. IPF reached statistical significance ($p<0.05$). In contrast, serum IgG antibodies to VIM-MAA-CIT were significantly increased in patients with RA patients when compared to those with RA-ILD (2-fold higher, $p<0.05$) and 2 IPF patients (2.1-fold higher, $p<0.05$) (**Fig. 1D**).Serum IgM (**Fig. 1E**) and IgA (**Fig. 1F**) antibodies to VIM-MAA-CIT showed a similar pattern to IgG anti-VIM-MAA-CIT, but again only differences between RA and IPF reached significance ($p<0.05$).

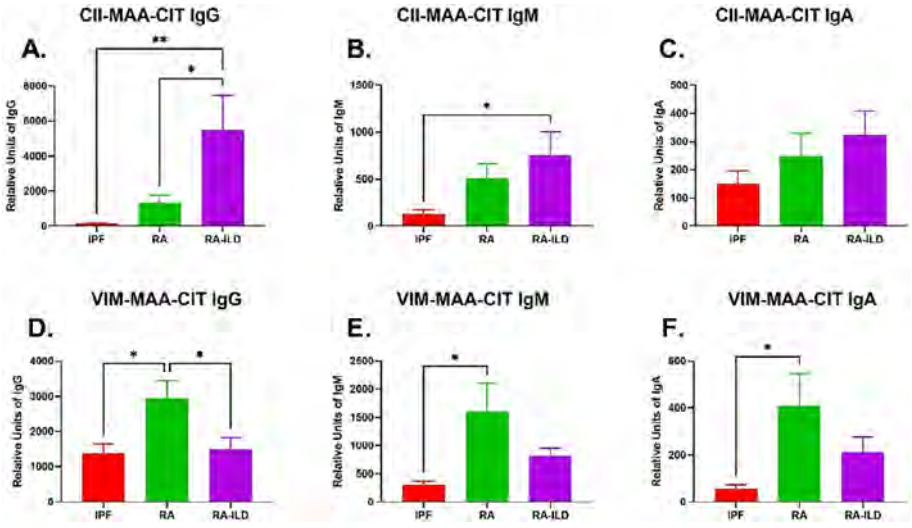

Figure 1. Serum IgG Antibody Levels to Dually Modified Type II Collagen or Vimentin. Serum samples from RA, RA-ILD, and IPF patients were incubated with native Type II Collagen and Collagen dually modified with MAA and CIT or native Vimentin and Vimentin dually modified with MAA and CIT. These samples were assayed by ELISA for (A,D) human IgG (B,E) human IgM (C,F) human IgA. Antibodies to native Collagen and Vimentin were subtracted from MAA-CIT responses. Serum IgG antibodies to CII-MAA-CIT were significantly increased in RA-ILD patients compared to RA patients (*$p<0.05$) and IPF patients (**$p<0.01$). Similar trends were observed with IgM and IgA antibodies to CII-MAA-CIT, but only IgM in RA-ILD compared to IPF was significantly increased (*$p<0.05$). Serum IgG antibodies to VIM-MAA-CIT were significantly increased in RA patients compared to both RA-ILD and IPF patients (*$p<0.05$). Similar trends were observed with IgM and IgA antibodies to VIM-MAA-CIT, but only RA compared to IPF patients had significantly increased IgM and IgA antibodies (*$p<0.05$). N=15 for IPF patients, N=15 for RA patients, and N=15 for RA-ILD patients.

Conclusion: Serum IgG antibody levels to dually-modified CII-MAA-CIT and VIM-MAA-CIT differ between patients with RA and RA-ILD. These findings suggest that dual modifications of type II collagen, but not vimentin, generate autoimmune responses that are substantially enhanced in RA-ILD and that could play a role in the pathogenesis of this extra-articular complication.

Disclosure: B. Butler: None; **J. Poole**: AstraZeneca, 12, I have received no monies. I received anti-IL-33 monoclonal antibody from AstraZeneca for animal research sutdies.; **M. Duryee**: None; **N. Aripova**: None; **C. Hunter**: None; **B. Kramer**: None; **J. O'Dell**: None; **G. Thiele**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9.

Abstract Number: 1765

Persistent Cigarette Smoking Is Associated with Rheumatoid Arthritis Onset and Neutrophil Activation in a Prospective Study of At-risk First-Degree Relatives

Jeba Maisha, Xiaobo Meng, Hani El-Gabalawy and Liam O'Neil, University of Manitoba, Winnipeg, MB, Canada

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Cigarette smoking (CS) is a major environmental risk factor for the development of Rheumatoid Arthritis (RA), and is associated with the development of RA autoantibodies, such as anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF). However, it remains unclear what role(s) smoking has in the pathogenesis of RA, particularly during the pre-clinical stage. Using clinical, proteomic and in-vitro approaches, we sought to better understand the relationship between CS and RA onset in a large, prospective cohort of unaffected First-Degree Relatives (FDR) of RA patients, some of whom progressed to develop RA (Progressors).

Methods: Over the past 15 years, we established a longitudinal cohort of FDR of RA patients with a view to detect and predict incident RA. At baseline, and at each subsequent study visit, a CS questionnaire was administered, which included questions regarding past and current CS, and CS intensity. Based on these data, longitudinal CS patterns were extracted and related to demographics and autoantibody profiles. A previously published (32770634) discovery serum proteomic dataset (SOMAscan, 1288 proteins) was analyzed to explore the potential effect of smoking on the proteome of FDR. Neutrophils from healthy donors were stimulated with CS extract (CSE) and analyzed by flow cytometry, enzymatic profiling, immunofluorescence, protein citrullination and extracellular DNA release (SYTOX green).

Results: In total, we were able to analyze CS patterns on 569 FDR, 19 of whom were Progressors. At baseline, current (79.6%) and ever (85.0%) CS rates were high in the study population, though neither was clearly associated with ACPA and/or RF seropositivity. Furthermore, baseline CS parameters did not predict future development of RA in the Progressors (n = 19). However, longitudinal CS patterns were strongly associated with Progression (Figure 1A, p = 0.009), with higher rates of persistent smoking in Progressors (90.0% vs 60.2%). In a logistic regression model, both persistent smoking (OR 8.0, 1.7 - 37.7) and ACPA positivity (15.9, 5.7 - 44.5) were independently associated with Progression (Figure 1B, C). Proteomic analysis and pathway enrichment suggested an upregulation of neutrophil proteins (Figure 2A) and *neutrophil degranulation* ($p=5.2E^{-18}$, Figure 2B) in active smokers. Neutrophils cultured *in-vitro* with CSE (20%) skewed neutrophils

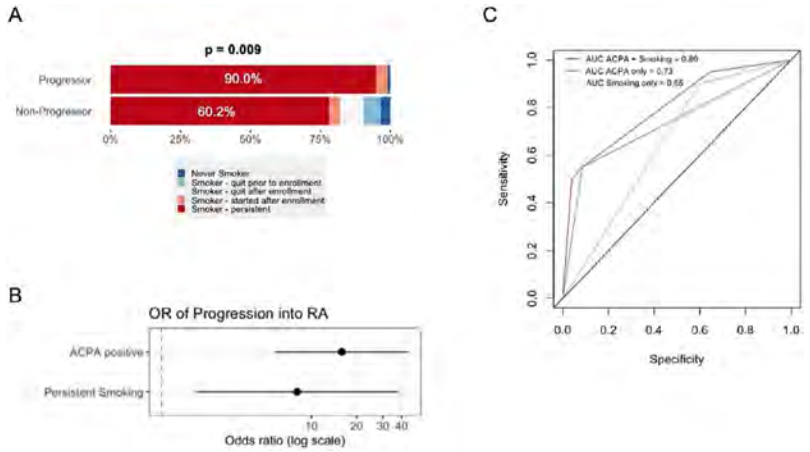

Figure 1: Persistent cigarette smoking is associated with Rheumatoid Arthritis (RA) development in at-risk First-Degree Relatives (FDR). (A) Longitudinal rates of smoking persistence, cessation and abstinence in Progressor and Non-Progressor FDR. Analyzed as an ordinal variable with Wilcoxon Rank-Sum test. (B) Odds Ratio (OR) of anti-citrullinated protein antibody positivity (ACPA) and smoking persistence for Progression into RA. (C) Area under the curve (AUC) for Smoking (teal), ACPA (blue) and Both (red) for RA Progression.

away from degranulation (Figure 3A, B) and toward neutrophil extracellular trap (NET) formation, leading to the release of neutrophil proteases, extracellular DNA and citrullinated proteins (Figure 3C, D, E).

Conclusion: We show that persistent CS rather than incident CS was associated with RA development in a cohort of at-risk FDR of RA patients. Serum proteomics suggested that neutrophils are activated in smokers and neutrophils treated with CSE release NETs, but do not degranulate. These data suggest a potential mechanism by which smoking may stimulate

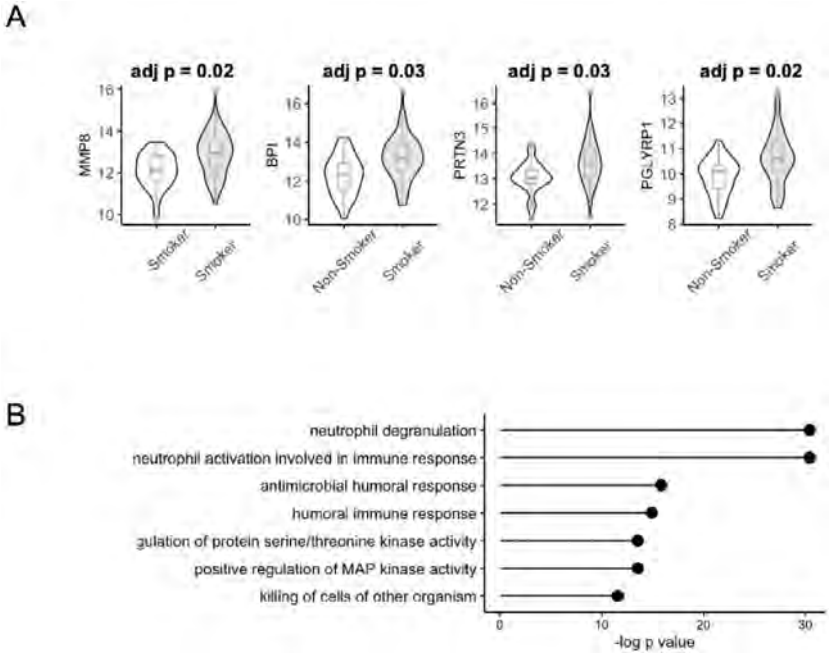

Figure 2: Smoking in at-risk First-Degree Relatives (FDR) of Rheumatoid Arthritis (RA) patients is associated with neutrophil activation. (A) Serum protein expression (SOMAscan) of matrix metalloproteinase-8 (MMP8 aka. neutrophil collagenase), bactericidal/permeability-increasing protein (BPI), proteinase-3 (PRTN3), and peptidoglycan recognition protein 1 (PGLYRP1). (B) Gene ontology enrichment scores ordered by -log p-value for significant ($p < 0.05$) upregulated proteins in smokers (FC > 1) compared to non-smokers.

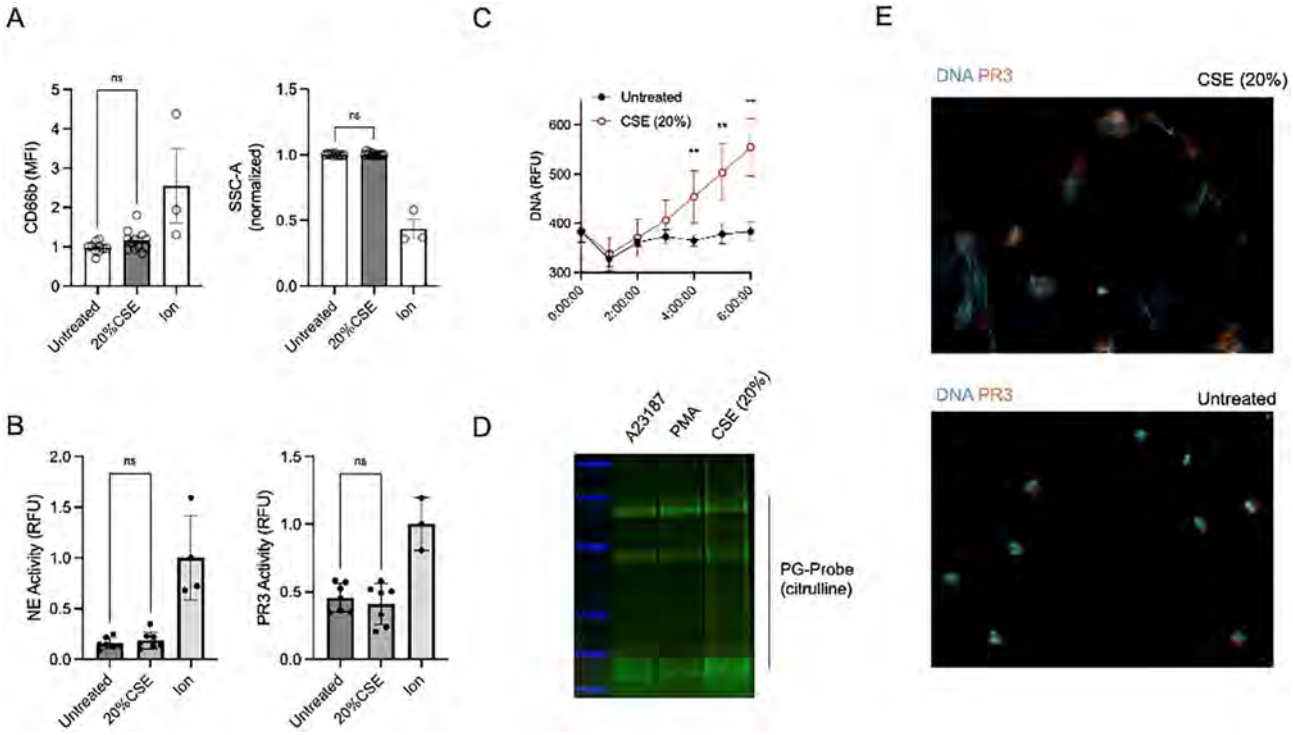

Figure 3: Neutrophils treated with cigarette smoke extract (CSE) skew towards neutrophil extracellular trap (NET) formation. (A) Neutrophils treated with CSE (20%) for 60 minutes do not upregulate CD66b (left, normalized) or display reduced side scatter (SSC, right), both surrogate markers of degranulation. Ion = A23187 (B) Protease activity for Proteinase-3 (PR3) and neutrophil elastase (NE) measured by enzyme kinetics by fluorescence in cell culture supernatant (60 minutes). Measured by Wilcox Rank-Sum Test (C) Cell-free DNA release over time measured by fluorescence (SYTOX green 0.2 μM), analyzed by multiple Mann-Whitney tests (** $p < 0.01$). (D) Protein citrullination in NETs (isolated after 4 hours in culture) measured by labeling with a Phenylglyoxal probe (PG) and in-gel fluorescent imaging. A23187 = Calcium Ionophore, PMA = phorbol myristate acetate (E) Immunofluorescence of images of CSE and untreated cells (4 hours) and stained for DNA (Hoescht, blue) and PR3 (orange).

neutrophils to undergo NET formation, and release citrullinated antigens and inflammatory proteins, which may in turn increase the risk of progression to clinically detectable RA.

Disclosure: J. Maisha: None; **X. Meng**: None; **H. El-Gabalawy**: None; **L. O'Neil**: None.

Abstract Number: 1766

Inflammatory Priming of the Joints via Pre-activation of Macrophages by Anti-MAA Antibodies in Rheumatoid Arthritis

Marcelo Afonso[1], Jitong Sun[1], Koji Sakuraba[1], Anca Catrina[1], Aase Hensvold[2], Caroline Grönwall[1] and Bence Réthi[1], [1]Karolinska Institutet, Stockholm, Sweden, [2]Division of Rheumatology, Department of Medicine Solna, Center for Molecular Medicine, Karolinska University Hospital, Karolinska Institutet. Center for Rheumatology, Academic Specialist Center, Stockholm, Sweden

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Etiology and Pathogenesis Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: We have previously shown that certain malondialdehyde/acetaldehyde modified protein binding autoantibodies (anti-MAA), obtained from the inflamed joints of rheumatoid arthritis (RA) patients, induced osteoclast differentiation *in vitro* and bone loss *in vivo* via an FcγR-mediated mechanism (1). In the present work we studied the effect of these antibodies on joint inflammation and, more specifically, on the function of macrophages.

Methods: We analysed global gene expression, by RNAseq, in the ankle joints of mice injected with patient-derived anti-MAA monoclonal antibodies, in the presence or absence of intraperitoneally injected LPS, which mimicked systemic inflammation. We have also analysed gene expression changes and cytokine production in anti-MAA treated macrophage cultures.

Results: Intravenous injection of anti-MAA antibodies led to subtle changes in the gene expression of the joints, with altered expression of several genes involved in immune responses and cell signalling. Intraperitoneally injected LPS induced robust gene expression changes in the ankles, with several cytokine and other immune mediators expressed at slightly higher level in the anti-MAA pretreated group. Anti-MAA pretreatment could also induce a more inflammatory macrophage phenotype *in vitro*, in response to a subsequent LPS activation. Similarly to the previously described osteoclast stimulatory effect, the inflammatory priming of macrophages was induced by several but not all of the tested anti-MAA monoclonal antibodies, and the effect was mediated via FcγR-transmitted signals.

Conclusion: Class-switched anti-MAA autoantibodies are typically associated with high disease activity in RA, but such antibodies have also been detected in some of the healthy donors and in individuals at risk of RA (2 and our unpublished data). Our results indicated that certain anti-MAA IgG autoantibody clones may contribute to an inflammatory priming of the joint tissues prior to the onset of systemic inflammation. FcγR-mediated pre-activation of macrophages could play an important role in this effect, by setting the stage for augmented responses to subsequent inflammatory stimuli.

1. Sakuraba et al. J Autoimmun 2022
2. Grönwall et al. Front Immunol 2021

Disclosure: M. Afonso: None; **J. Sun**: None; **K. Sakuraba**: None; **A. Catrina**: None; **A. Hensvold**: None; **C. Grönwall**: None; **B. Réthi**: None.

Abstract Number: 1767

TNF-α Utilizes the TWEAK/Fn-14 Axis in Human Rheumatoid Arthritis Synovial Fibroblasts to Induce Inflammation

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Tumor necrosis factor-alpha (TNF)-α is a proinflammatory cytokine in rheumatoid arthritis that transduces intracellular signal transduction pathways through specific receptors, TNF-R1, and TNF-R2. The anti-TNF therapy has been a primary approach in the management of RA, yet most of the patients fall into low- and non-responder groups with unclear reasons. TNF-like weak inducer of apoptosis (TWEAK), another TNF-superfamily member, is a pleiotropic cytokine that similar to TNF-α regulates inflammatory activity, angiogenesis, cell proliferation, and tissue remodeling by binding to its receptor, fibroblast growth factor-inducible 14 (Fn-14). As TNF-α and TWEAK activate common signaling pathways, we

investigated the crosstalk between TWEAK and TNF-α in human rheumatoid arthritis synovial fibroblasts (RASFs) and studied the role of Fn-14 receptor knockdown on TNF-α-mediated inflammation.

Methods: Human RASFs were serum-starved overnight followed by treatment with different concentrations of TWEAK (50, 100, 200, 400, and 800 ng/mL) and TNF-α (5, 10, 20, 40, and 80 ng/mL) alone and in combination for 24 hrs. The secretion of chemokines MCP-1/CCL2, RANTES/CCL5, and MMP-1 was analyzed using ELISA, and synergy was studied using CompuSyn Software. Fn-14 siRNA knockdown in RASFs was done followed by TNF-α stimulation for 24 hrs. Global effects of Fn-14 gene knockdown were studied using an RNA sequencing (RNA-seq) array. Differentially expressed genes (DEGs) were analyzed using GraphPad and Metascape tools. Interactions between Fn-14 and TNF-R1 receptors were studied using the immunoprecipitation (IP) method followed by Western blot analysis. The experiments were performed in at least three patient cell lines and the statistical value of $p< 0.05$ was considered significant.

Results: TNF-α in combination with TWEAK resulted in greater secretion of both MCP-1 and RANTES compared to each cytokine alone. The synergy was more remarkable at the low combinations of cytokines (5 ng/mL of TNF-α + 50 ng/mL of TWEAK) for MCP-1, RANTES, and MMP-1 with a combination index < 1. RNA-seq data showed that one-third of the genes were differentially expressed in RASFs when stimulated with TNF-α. Out of the 1,389 genes that were 2-fold upregulated by TNF-α, the knockdown of Fn-14 significantly suppressed 168 genes when compared to TNF-α with NCsi treatment. In addition, out of the 2,186 genes 2-fold downregulated by TNF-α, 32 genes were restored in the absence of Fn-14. Gene Ontology analysis of the RNA-seq data suggests that Fn-14-knockdown-associated genes are involved in processes like-regulation of intrinsic apoptosis, regulation of innate immunity, and sensory perception of pain. Furthermore, our IP results with TNF-R1 pull-down showed the presence of Fn-14 indicating the interaction between these two receptors, which requires further experimental investigation.

Conclusion: Our findings suggest that low-dose TNF-α synergizes with TWEAK to induce inflammation and also demonstrate the ability of TNF-α to potentially exploit the Fn-14 receptor to transduce non-canonical signaling in RASFs. This indicates that the pharmacological inhibition of Fn-14 may provide an effective adjunct therapy to anti-TNF therapy.

Disclosure: F. Shaikh: None; **A. Singh**: None; **P. Panipinto**: Regeneron, 3; **S. Ahmed**: None.

Abstract Number: 1768

The Dynamics of the Gut Microbiome in Rheumatoid Arthritis Susceptibility: A Cross-Sectional and Longitudinal Observational Study

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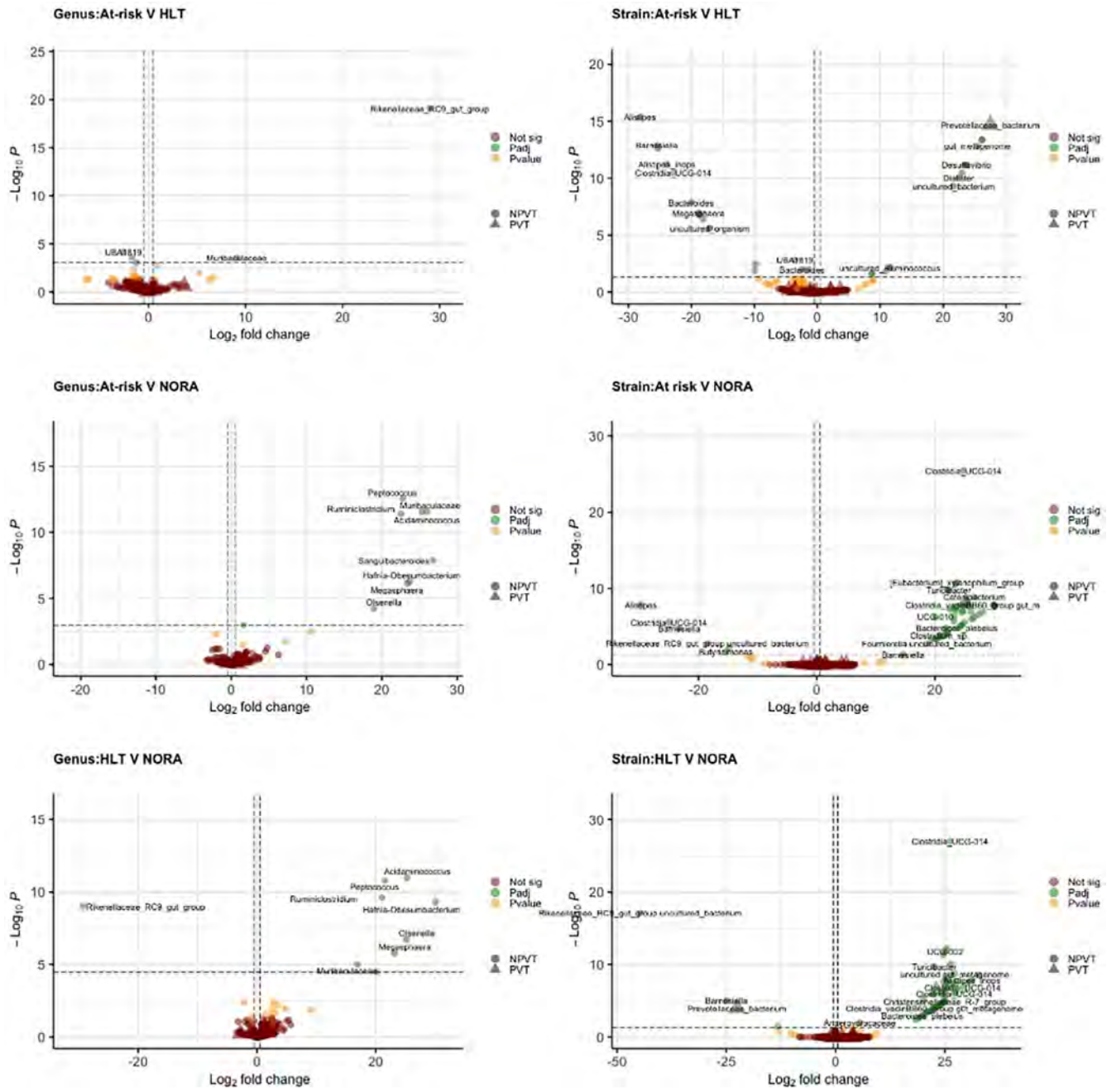
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

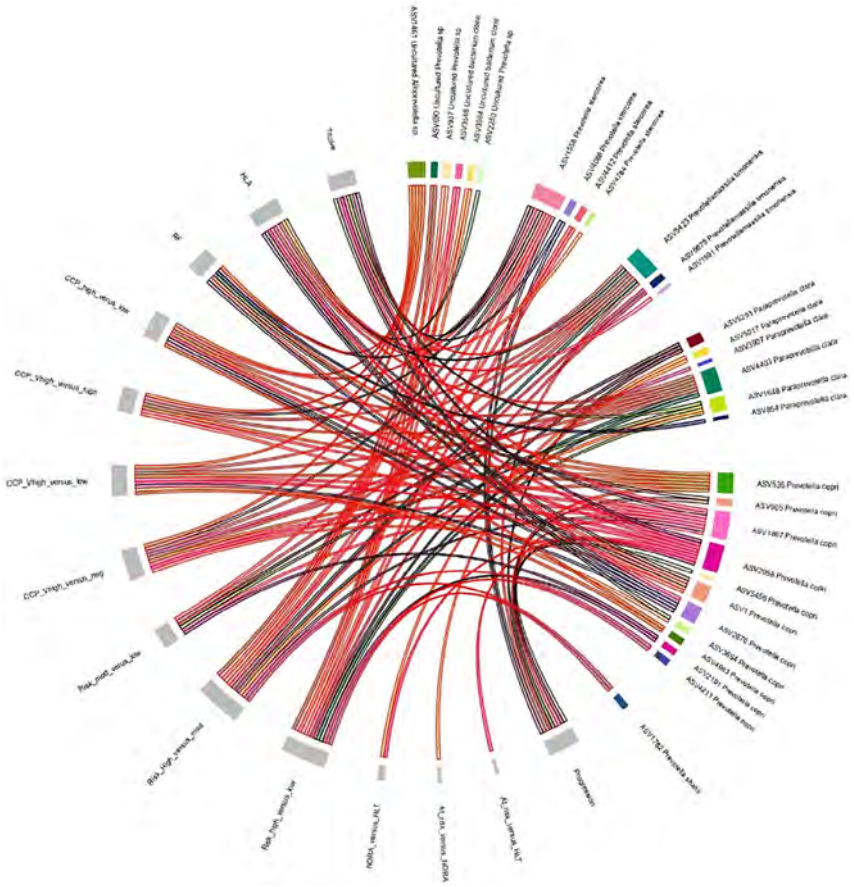
Background/Purpose: Multiple compositional shifts of gut microbiota have been identified within the rheumatoid arthritis (RA) disease continuum, encompassing both established RA and at-risk individuals (including those with pre-clinical RA). Subsequently, a variety of gut bacteria have been implicated as a potential impetus in the development of RA, none more



Differentially abundant taxa between groups. Pairwise volcano plots of at-risk individuals, NORA and healthy controls, plotting Log2 fold change against -Log10 P value, coloured according to significance. Vertical line denotes adjusted P value threshold, horizontal line denotes 0.5 Log2 fold change. Shape denotes Prevotellaceae (PVT) or not Prevotellaceae (NPVT) taxa.

so than Prevotella copri. Using a comprehensively phenotyped prospective cohort of individuals at-risk of RA this work investigates whether P. copri overabundance is ubiquitous within the pre-clinical phases of RA, establishes microbiota associations with traditional RA risk factors and hypothesizes a timeline for microbial action within RA development.

Methods: Individuals at-risk of RA were defined by the presence of anti-cyclic citrullinated protein (anti-CCP) antibodies and new musculoskeletal symptoms without clinical synovitis. Individuals were sampled at baseline (n =124 participants, 30 of whom progressed to RA), and longitudinally (n = 19 participants, 5 RA progressors) at 5 time points over 15 months. At-risk

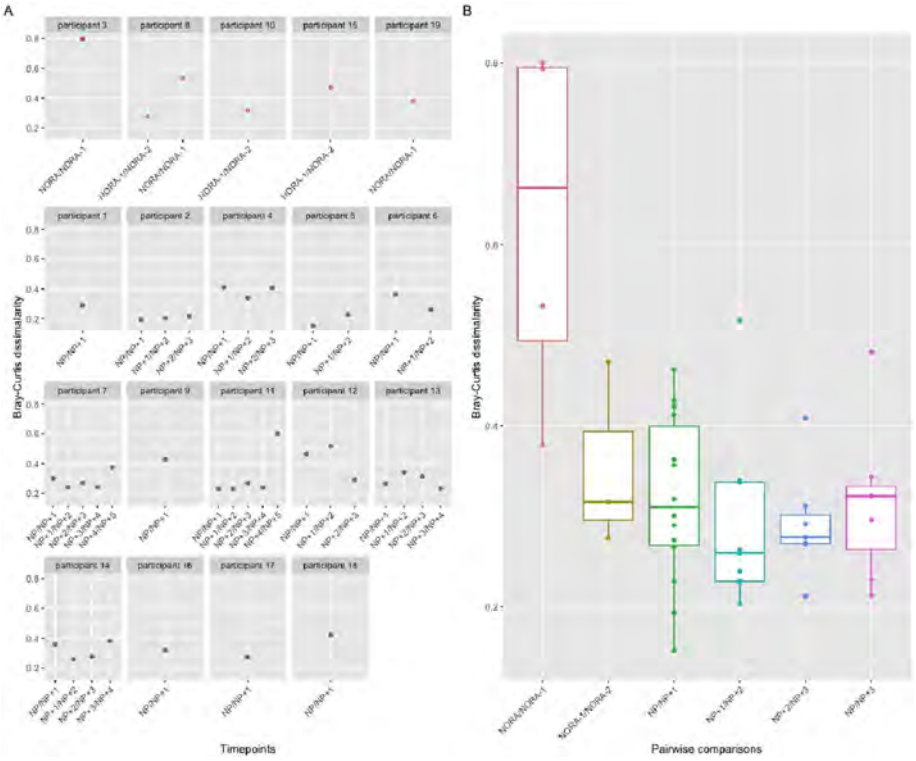


Prevotellaceae chord plot. Associations of Prevotellaceae strains reaching nominal significant from adjusted DESeq2 models. Metadata variables in grey and strains designated by colour. Outer border denotes direction of association, increased abundance in red or decreased abundance in black.

individuals were compared to healthy controls (n = 22) and to individuals with new onset RA (n = 7). Taxonomic alterations of the gut microbiome were investigated using 16S rRNA amplicon sequencing, at both strain and genus level and confirmed using shotgun metagenomic DNA sequencing.

Results: RA progression at genus level was associated with modest changes in the gut microbiome, mainly affecting the Firmicutes and Proteobacteria phyla. A single Prevotellaceae strain was enriched in at-risk individuals compared to healthy controls (fig 1). P. copri strains demonstrate overall increased abundance with increasing anti-CCP levels and risk of progression (score based on symptomatology, HLA status, anti-CCP level and ultrasound findings), but display strain specific fluctuations with respect to early immune dysregulation, intestinal permeability, genetic risk and rheumatoid factor positivity (fig 2). Time series analysis suggests RA progression involves the development of an unstable low diversity microbiome that is characterised by the accumulation of RA associated pathobionts within the 10 months preceding RA (fig 3), which includes, but is not limited to P. copri. Functional analysis shows the NORA gut microbiome has increased abundance of pathways associated with amino acid metabolism. Healthy controls had decreased ornithine production, a precursor for citrulline.

Conclusion: These results confirm and expand the bacterial associations linked to RA progression, which involves multiple taxa at both genus and strain level and is associated with the underlying risk profile of an individual. As with previous literature, an overabundance of Prevotellaceae was identified in those at-risk of RA compared to healthy controls. Strain specific fluctuations appears to be the hallmark of Prevotellaceae associations within the RA at-risk phase. Future work will investigate how niche bacterial specialisation to the underlying risk profile may subsequently affect the abundance threshold required for a bacterial impetus in RA related autoimmunity.



Pairwise Bray-Curtis dissimilarity boxplots. (A) Boxplots of individual Bray-Curtis dissimilarities between gut microbiome sampling. Individuals progressing to RA plotted in the first row, with Bray-Curtis dissimilarity index coloured in red. Note, participant 3, has two points plotted which overlap significantly. (B) Boxplot of pairwise Bray-Curtis dissimilarities grouped according to time to new onset RA (NORA), or time from baseline non-progression (NP) sample.

Disclosure: C. Rooney: None; **I. Jeffery**: 4D Pharma plc, 3; **K. Mankia**: Abbvie, 6, Eli Lilly, 5, Galapagos, 6, Gilead, 5, Serac Lifesciences, 6; **M. Wilcox**: None; **P. Emery**: Boehringer Ingelheim, 2, Eli Lilly, 2, Novartis, 2.

Abstract Number: 1769

TNF-Stimulated Production of IL-15 by Fibroblast-Like Synoviocytes Mediates Human Resident Memory T Cells Development in Synovial Organoid Model

Margaret Chang[1], Maryrose Hahn[2], Madison Mangin[1], Brian Wauford[1], Rachel Blaustein[3], Lauren Henderson[1], Kevin Wei[4] and Peter Nigrovic[1], [1]Boston Children's Hospital, Boston, MA, [2]Division of Immunology, Boston Children's Hospital, Boston, MA, [3]Brigham and Women's Hospital, Boston, MA, [4]Brigham and Women's Hospital and Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA) are chronic autoimmune diseases that tend to flare repeatedly in the same joints, displaying joint-specific memory. We have identified CD8+ tissue resident memory T cells (TRM) in human arthritic joints and demonstrated in murine models that these long-lived TRM remain in synovium

during remission and act as key mediators of arthritis flares. However, the factors that drive TRM formation in the synovium have not been characterized. IL-15 supports CD8 T cell activation and TRM development in other tissues. It is also elevated in synovial fluid and is expressed in the synovium in RA. Here, we explored the inflammatory drivers of IL-15 production by synovial stromal cells and investigated the role of IL-15 in synovial TRM development.

Methods: Fibroblast-like synoviocytes (FLS) isolated from human RA synovium and human umbilical vein endothelial cells (HUVEC) were grown in tissue culture and stimulated with TNF, IL-1beta, IL-6 or IFNgamma for 48 hours. Cells were collected, and IL-15 mRNA expression was assessed by quantitative PCR. To study human synovial TRM development, we developed a 3D synovial organoid that recapitulates the synovial stromal structure utilizing FLS and HUVEC encapsulated in Matrigel. CD8 memory T cells were isolated from peripheral blood of healthy donors and co-cultured with the synovial organoid for 2-3 weeks to generate TRM. TRM development was validated by cell surface markers, gene expression profile, free fatty acid uptake and migratory response to tissue egress signals. TNF was added to the culture media for 3-5 days to simulate inflammation, then removed for the duration in culture. IL-15 receptor alpha (IL-15Ra) or CD122 blocking antibodies were added to T cells 30 minutes prior to the formation of organoids, and they were replenished twice a week to inhibit IL-15 activity. After 3 weeks, cells were dissociated from the organoids and assayed for TRM surface phenotype by flow cytometry.

Results: TNF stimulation dramatically increased IL-15 gene expression in FLS by 30-fold, while it had a smaller effect on HUVEC (5-fold). IL-1beta also induced a 6-fold change in IL-15 expression in FLS, but IL-6 and IFNgamma did not. Culturing CD8 memory T cells in synovial organoids, particularly with TNF, supported the development of cells with TRM surface phenotype (CD45RO+CD62L-CCR7-HLADR-CD25-CD103+CD49a+) and TRM gene expression patterns. These TRM also had enhanced free fatty acid uptake, and they did not migrate across a transwell membrane in response to CCL21, further confirming TRM functionality. Inhibition of IL-15 activity with IL-15Ra or CD122 blocking antibodies reduced TRM development.

Conclusion: We developed a novel model for studying human synovial TRM by differentiating TRM within 3D synovial organoids composed of stromal cells from human RA synovium. We show that TNF preferentially induces FLS to produce IL-15 and demonstrate that IL-15 activity mediates TRM development in this synovial organoid system. As synovial TRM facilitate arthritis flares, effective methods to impede synovial TRM development may be valuable for durable disease control.

Disclosure: M. Chang: None; **M. Hahn**: None; **M. Mangin**: None; **B. Wauford**: None; **R. Blaustein**: None; **L. Henderson**: Adaptive Biotechnologies, 2, 5, Bristol-Myers Squibb(BMS), 5, Pfizer, 2, Sobi, 1, 2, 5; **K. Wei**: 10X Genomics, 5, capital one, 6, Gilead sciences, 5, horizon therapeutics, 6, Mestag, 2; **P. Nigrovic**: None.

Abstract Number: 1770

Dual Inhibition of TNF-α and OX40L on Synovial Inflammation and Osteoclastogenesis in Rheumatoid Arthritis

Hee Sung Kwon[1], Mi Hyeon Kim[2], Jeoung Yeon Kim[2], Seon Uk Kim[2], Hae Rim Kang[1], Seo Yoon Ban[3], Gyong Sik Ha[4], Chung Min Lee[4], Jeong Seok Lee[5] and Eun Young Lee[2], [1]Interdisciplinary Program in Cancer Biology, Integrated Major in Innovative Medical Science, Seoul National University, Seoul, South Korea, [2]Seoul National University College of Medicine, Seoul, South Korea, [3]Department of Cancer biology, Graduate School of College of Medicine, Seoul National University, Seoul, South Korea, [4]Research institute, IMBiologics Corp, Suwon, South Korea, [5]Graduate School of Medical Science and Engineering, Korea Advanced Institute of Science and Technology, Seoul, South Korea

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic, inflammatory disease that leads to progressive cartilage and bone destruction. TNF superfamily member OX40 ligand (OX40L; CD252) is expressed specifically to synovial tissue and OX40/OX40L interaction is contributed to the development of T-cell mediated immunity in RA. In collagen-induced arthritis mouse model, it was demonstrated that blockade of TNF-α or OX40L significantly ameliorated disease activity. We present targeting both TNF-α and OX40L is superior to single treatment in fibroblast-like synoviocytes (FLS) invasiveness and osteoclast activation which are crucial RA pathology.

Methods: RA FLS were used from passage 4-6. FLS were stimulated with TNF-α (10ng/ml) for 2h and then treated with single TNF-α inhibitor (50nM), OX40L inhibitor (50nM) or IMB-101, a TNF-α/OX40L bispecific antibody (50nM) for 24hrs. Differential expression of RA FLS genes were analyzed by RT-PCR. For osteoclast differentiation assay, FLS were stimulated with TNF-α (10ng/ml) for 3 days, after which CD14+ monocytes were co-cultured with the IMB-101 (50nM) in the presence of M-CSF (20ng/ml) for 3 weeks. Osteoclasts were evaluated by tartrate-resistant acid phosphatase (TRAP) staining.

Results: OX40L was increased in TNF- α induced RA FLS compared to unstimulated RA FLS ($p< 0.05$) (n=7). RT-PCR analysis revealed significant reduction of IL-6, IL-1β, CCL2, CX3CL1, MMP-1, MMP-3, ICAM-1, RANKL, VEGF and HIF1-α in TNF-α stimulated RA FLS after IMB-101 or anti TNF treatment (n=4). Among these genes, MMP-3, RANKL and VEGF were significantly reduced in dual inhibition of TNF-α and OX40L than single target therapies. In co-culture system of RA FLS and CD14+ monocytes for osteoclast formation, IMB-101 decrease the number of TRAP-positive multinucleated cells over TNF-α inhibitor.

Conclusion: These results indicated that dual inhibition of TNF-α and OX40L axis simultaneously are associated with reduction of invasiveness in synovial fibroblast and joint destruction in RA.

Disclosure: H. Kwon: None; **M. Kim**: None; **J. Kim**: None; **S. Kim**: None; **H. Kang**: None; **S. Ban**: None; **G. Ha**: None; **C. Lee**: None; **J. Lee**: None; **E. Lee**: None.

Abstract Number: 1771

Role of Periostin in the Pathophysiology and Accurate Diagnosis of Interstitial Lung Disease Associated with Autoimmune Diseases

Verónica Pulito-Cueto[1], David Iturbe-Fernández[2], Victor Mora-Cuesta[2], Joao Carlos Batista-Liz[1], Belén Atienza-Mateo[3], María Sebastián-Mora[1], Virginia Portilla[1], Alfonso Corrales[1], Miguel A Gonzalez-Gay[4], Jose Cifrian[5], Ricardo Blanco[1] and Raquel López-Mejías[1], [1]Rheumatology Department, Immunopathology Group, Hospital Universitario Marqués de Valdecilla-IDIVAL, Santander, Spain, [2]Immunopathology Group, Marqués de Valdecilla University Hospital-IDIVAL; Department of Pneumology, Marqués de Valdecilla University Hospital, Santander, Spain, [3]Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain, [4]IDIVAL and School of Medicine, UC, Santander; Department of Rheumatology, IIS-Fundación Jiménez Díaz, Madrid, Santander, Spain, [5]Immunopathology Group, Marqués de Valdecilla University Hospital-IDIVAL; Department of Pneumology, Marqués de Valdecilla University Hospital; School of Medicine, Cantabria University, Santander, Spain

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Periostin is an extracellular matrix protein that contributes to the development and repair of lung tissue [1]. Previous works have described periostin as a key factor in the aberrant evolution of the airways and parenchymal fibrosis, being involved in the pathophysiology of different chronic lung diseases such as interstitial lung diseases (ILD)

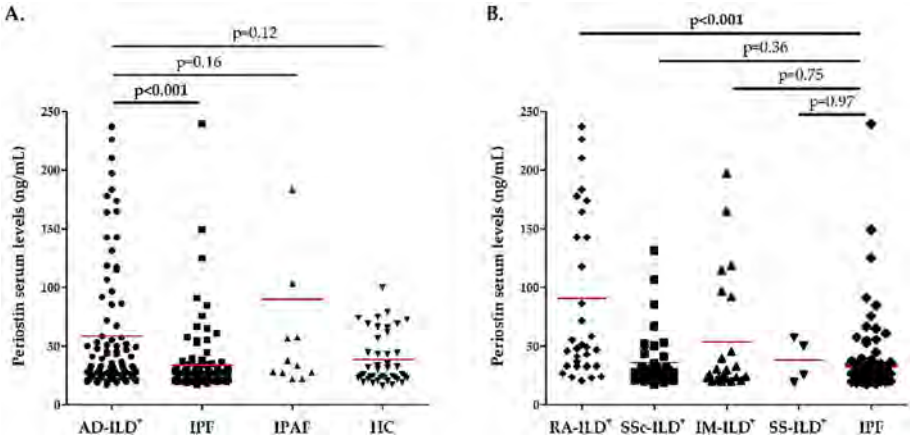

Figure 1. Role of periostin in the accurate diagnosis of AD-ILD+. A. Differences in periostin serum levels between patients with AD-ILD+ and those with IPF and IPAF, as well as HC; B. Differences in periostin serum levels between patients with AD-ILD+ stratified by the underlying AD and those with IPF. AD: autoimmune diseases; ILD: interstitial lung disease; IPF: idiopathic pulmonary fibrosis; IPAF: interstitial pneumonia with autoimmune features; HC: healthy controls; RA: rheumatoid arthritis; SSc: systemic sclerosis; IM: inflammatory myopathies; SS: sjögren syndrome. Significant results are highlighted in bold.

[1-3]. In this sense, ILD is one of the most frequent manifestations and the main cause of death in patients with autoimmune disease (AD), particularly in rheumatoid arthritis (RA), systemic sclerosis (SSc), inflammatory myopathies (IM) and Sjogren's syndrome (SS) [4]. However, the accurate diagnosis of AD-ILD$^+$ often remains a challenge due partially to the similarity with other diseases such as idiopathic pulmonary fibrosis (IPF) and interstitial pneumonia with autoimmune features (IPAF) [4]. Accordingly, this work aimed to elucidate the role of periostin in the accurate diagnosis of AD-ILD$^+$, as well as its relationship with molecules involved in the pathological process of vasculopathy and fibrosis typical of AD-ILD$^+$.

Methods: Peripheral venous blood was collected from a total of 98 patients with AD-ILD$^+$, a group composed of patients with RA-ILD$^+$ (n=33), SSc-ILD$^+$ (n=38), IM- ILD$^+$ (n=23) and SS-ILD$^+$ (n=4). Moreover, we recruited different comparative groups: 105 IPF patients, 11 IPAF patients and 43 healthy controls (HC). Serum levels of periostin were measured by enzyme-linked immunosorbent assay (ELISA). Additionally, serum levels of Krebs von den Lungen 6 (KL-6); interleukin 6 (IL-6); endothelin-1 (ET-1); vascular endothelial growth factor (VEGF) and intercellular adhesion molecule 1 (ICAM-1) were measured by ELISA.

Table 1. Relationship in AD-ILD$^+$ patients of serum levels of periostin with other relevant molecules involved in AD-ILD$^+$ pathophysiology.

	Periostin (ng/mL)	
Variable	*r*	*p*
KL-6 (U/mL)	0.10	0.55
IL-6 (pg/mL)	0.05	0.65
ET-1 (pg/mL)	0.13	0.31
VEGF (pg/mL)	**0.28**	**0.01**
ICAM-1 (ng/mL)	-0.07	0.57

AD: autoimmune diseases; ILD: interstitial lung disease; KL-6: Krebs von den Lungen 6; IL-6: interleukin 6; ET-1: endothelin-1; vascular endothelial growth factor; ICAM-1: intercellular adhesion molecule 1. Significant results are highlighted in **bold**.

Results: Patients with AD-ILD$^+$ exhibited significantly higher periostin serum levels than IPF patients ($p< 0.001$, **Figure 1A**), whereas no difference was observed in relation to IPAF patients and HC (**Figure 1A**). Specifically, RA-ILD$^+$ patients showed increased levels of periostin in relation to IPF patients ($p< 0.001$, **Figure 1B**). However, similar levels of periostin were found in patients with SSc-ILD$^+$, IM-ILD$^+$ as well as SS-ILD$^+$ and those with IPF (**Figure 1B**). Furthermore, a positive correlation was discovered between periostin serum levels and VEGF serum concentrations in AD-ILD$^+$ patients ($p=0.01$, **Table 1**). Nevertheless, periostin serum levels did not correlate with KL-6, IL-6, ET-1 and ICAM-1 levels in AD-ILD$^+$ patients (**Table 1**).

Conclusion: Our findings suggest that circulating periostin could be considered a useful biomarker to discriminate RA-ILD$^+$ from IPF, contributing to the accurate diagnosis of RA-ILD$^+$. Furthermore, this work indicates a relationship of periostin with vascular dysfunction in AD-ILD$^+$. **References**: [1] Cell Mol Life Sci.2017;74(23):4305-4314; [2] Respir Investig.2015;53 (2):73-81; [3] PLoS One.2017;12(3):e0174547; [4] Expert Rev Clin Immunol.2018;14(1):69-82. *Personal funds, VP-C: PI18/00042(ISCIII-ERDF); JB-L:FI22/00020(ISCIII-ESF); MSM-G:TRANSVAL22/01(IDIVAL); RL-M: CPII21/00004 (ISCIII-ESF)*.

Disclosure: V. Pulito-Cueto: None; **D. Iturbe-Fernández**: None; **V. Mora-Cuesta**: None; **J. Batista-Liz**: None; **B. Atienza-Mateo**: None; **M. Sebastián-Mora**: None; **V. Portilla**: None; **A. Corrales**: None; **M. Gonzalez-Gay**: AbbVie/Abbott, 5, 6, Amgen, 5, 6, Pfizer, 5, 6; **J. Cifrian**: None; **R. Blanco**: AbbVie/Abbott, 5, 6, Amgen, 6, AstraZeneca, 2, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, Merck/MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6; **R. López-Mejías**: None.

Abstract Number: 1772

Rheumatoid Arthritis-Specific Rheumatoid Factors Develop in Some COVID-19 Patients

Adam Titi[1], Ryan Adyniec[2], Nat Murren[1] and Miriam Shelef[1], [1]University of Wisconsin, Madison, WI, [2]University of Wisconsin-Madison, Madison, WI

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid factors (RFs), antibodies canonically known to bind two conformational epitopes of IgG Fc, are a hallmark of rheumatoid arthritis (RA) but also can arise in other inflammatory conditions and infections. In turn, infections, such as respiratory infections, correlate with RA development. Recently, RFs with reactivity to citrullinated and homocitrullinated IgG peptides were discovered in RA, but were not found in other autoimmune diseases. Similar to other infections, RFs have been reported in COVID-19, but RA-specific RFs, which perhaps could suggest a greater risk for RA, have not been evaluated. The purpose of this study was to determine if RA-specific RFs develop post-COVID-19.

Methods: Sera from adults with COVID-19 (~5 weeks post-symptom resolution), with seropositive RA, and age- and sex-matched controls (n=20) were used in ELISA to evaluate IgA, IgM, and IgG binding to the native, citrullinated (B), and homocitrullinated (J) forms of peptides beginning at amino acid positions 11, 80, 167, 202, 219, and 289 of IgG1 (Uniprot P01857) with results compared to controls by Kruskal-Wallis with Dunn's multiple comparisons tests. Also, using a threshold based on the highest control subject Ig binding signal, the percent positive for each antibody/peptide combination was compared by Fisher's exact test for RA and COVID-19 versus controls. $P< 0.05$ was considered significant.

Results: As expected, IgG binding to 75% of the citrulline- or homocitrulline-containing peptides and IgA binding to 50% of these peptides was increased in RA compared to controls. No peptides had increased IgM binding in RA. Also, no peptides had increased IgA, IgM, or IgG binding in COVID-19, although there was a trend towards increased IgG binding to IgG1-80J in COVID-19 (p=0.056). When analyzed based on percent positivity, significantly more COVID-19 subjects were positive for IgG binding to IgG1-80J and IgG1-219J compared to controls (45% and 30% vs. 0%, respectively). Also, significantly more COVID-19 subjects were positive for IgA binding to IgG1-11, IgG1-167, and IgG1-167J compared to controls (30%, 25%, and 25% vs 0% respectively). Many of these IgA and IgG binding values were minimally elevated in COVID-19, but some COVID-19 subjects had Ig binding >10x higher than controls for these peptides.

Conclusion: While RFs that bind to citrulline- and homocitrulline-containing IgG epitopes are primarily restricted to RA, some COVID-19 patients generate antibodies that bind to a few of these epitopes in the native or homocitrullinated form. Longitudinally evaluating reactivity against these IgG and related epitopes, as well as joint symptoms, could provide important insights into how immune tolerance is regained or further lost on a path towards RA following a viral infection.

Disclosure: A. Titi: None; **R. Adyniec**: Labcorp Drug Development, 3; **N. Murren**: None; **M. Shelef**: None.

Abstract Number: 1773

Integrated Analysis of Rheumatoid Arthritis (RA) Fibroblast-like Synoviocytes (FLS) Transcriptome and Chromatin Accessibility Identifies Mechanisms Associated with Location-specific Disease Severity

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Mechanisms responsible for the distribution and severity of joint involvement in RA are not known. To explore whether site-specific FLS biology might contribute to location-specific synovitis and explain the predilection for hand (wrist/metacarpal phalangeal joints) in RA, we generated transcriptomic and chromatin accessibility data from FLS to define the transcription factors (TFs) and pathways unique to each location.

Methods: FLS were derived from hand, knee and hip surgical samples. Whole genome ATAC-seq and RNA-seq were obtained from 10 hand, 10 hip, and 10 knee FLS under unstimulated (unstim) or stimulated conditions (TNF [50 ng/ml for 6 h]). Differentially expressed genes (DEGs) were identified using the Wilcoxon test. TF motifs were queried within promoter/enhancer open chromatin. The assays were integrated using Taiji (Nat Commun 2022;13:6221) and Personalized PageRanks were quantified. Cell growth was assayed using MTT in medium and PDGF-stimulated FLS on day 7.

Results: Multiple DEGs between joints were identified in their respective FLS (Table 1A). Hand vs knee or hand vs hip FLS comparisons revealed increased expression of genes associated with proliferation/inflammation (eg, *TLR2, VCAM1, MMP13*) and decreased cell-cycle inhibitors (eg, *CDKN1A, CDKN1C, CDKN2D*) in hand. Pathway analysis revealed greatest enrichment for hand vs hip and included proinflammatory (eg, TNFs bind physiological receptors) and proliferative (eg, Integrin cell surface interactions) pathways (Table 1A). Taiji distinguished joint-specific TFs and identified greater PageRanks

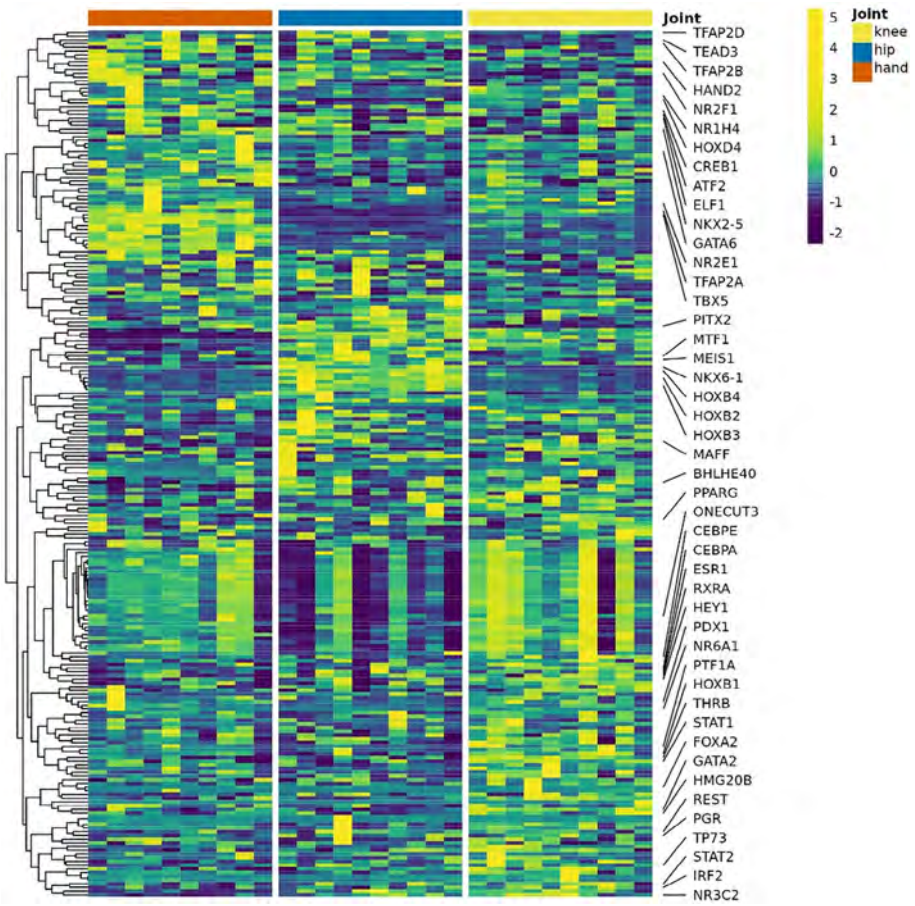


Fig 1. PageRanks of top differential TFs (Wilcoxon, top TFs selected by p-value for each pairwise comparison) for hand, knee and hip joint-derived FLS cultured in medium. Columns are colored by joint annotation. TF PageRank patterns are distinct for the 3 joint locations and involve key regulators of growth, differentiation and inflammation. Labeled TFs are TFs enriched in Reactome or Gene Ontology (GO) pathways. Unlabeled rows are not pathway enriched.

for key TFs (eg, *ATF2, CREB1*) in hand (Fig 1, Table 1A). Pathway analysis revealed greatest enrichment for hand vs hip and included proliferation/inflammation pathways (eg, MAPK activation, PIP3 activates AKT signaling) (Table 1A). The predicted differences in proliferation were confirmed in a cell growth assay showing that hand FLS proliferation was greater than hip or knee after PDGF-stim (Hand/knee or hip ratio=1.4; P< 0.001). The joint-specific transcriptome differences for hand vs hip

Table 1 A. Pairwise (hand vs hip, hand vs knee, hip vs knee) DEGs (Wilcoxon, p<0.05, abs log2FC > 0.58) were identified. Reactome and GO identified significantly enriched pathways using differentially expressed genes (p<0.05). Pairwise differential TFs were identified using the TF PageRank scores (Wilcoxon, p<0.05). Pathway enrichment for differential TFs were conducted as for the transcriptome. B. Responses to TNF stimulation were evaluated for each joint location and compared TNF-stim to unstim. DEGs between unstim and TNF-stim FLS for a particular joint location were identified (Wilcoxon, p<0.05, abs log2FC > 0.58). A similar process identified TNF-stim vs unstim differential TFs using the TF PageRank scores (Wilcoxon, p<0.05). Pathway enrichment for DEGs and differential TFs were conducted as part A.

A.	Between joint location comparisons (unstim)				B.	Within joint location comparisons (unstim vs TNF-stim)			
	#DEGs	#DEG-pathways	#TFs	#TF-pathways		#DEGs	#DEG-pathways	#TFs	#TF-pathways
Hand vs Hip	868	53	115	40	Hand	2171	103	107	89
Hand vs Knee	1539	36	73	13	Knee	2902	82	127	85
Hip vs Knee	973	3	140	13	Hip	2289	70	102	52

and knee were enhanced by TNF-stim. DEGs within a particular joint between unstim vs TNF-stim revealed greatest pathway enrichment in hand (Table 1B). TNF-stim hand FLS had unique induction of proliferation/inflammation genes (eg, *TANK, KSR1, CDC14A*) and pathways (eg, Diseases of signal transduction by growth factor receptors/second messengers, Regulation of necroptotic cell death), and these pathways were not observed in TNF-stim hip or knee. TNF-stim in hand FLS had increased PageRanks of key inflammatory TFs (eg, *RELA, STAT3*) and pathways (eg, MAPK activation, Signaling by ALK in cancer) that were not observed for hip/knee.

Conclusion: Integrated analysis of FLS identified joint-specific patterns of gene expression and TFs, including pathway enrichment in hand FLS associated with inflammation and proliferation. These differences are more prominent after TNF stimulation. Hand joints are commonly earlier and are more severe in RA. Distinctive joint-specific FLS biology associated with hand-specific pathways might explain the distribution and severity of joints involved in RA.

Disclosure: E. Choi: None; **C. R. L. Machado**: Eli Lilly, 5; **D. Boyle**: None; **W. Wang**: None; **G. Firestein**: Eli Lilly, 5.

Abstract Number: 1774

Gut Microbiota and Permeability Biomarkers for Diagnosis and Prognosis in Rheumatoid Arthritis Associated Interstitial Lung Disease

José Lisbona-Montañez[1], Patricia Ruiz-Limon[2], Arkaitz Mucientes[3], Natalia Mena Vazquez[4], Isabel Moreno-Indias[3], SARA MANRIQUE[5], Laura Cano-García[6], Rocío Redondo-Rodríguez[6], Francisco J tinahones[3] and Antonio Fernandez-Nebro[7], [1]Universidad de Málaga, Departamento de Medicina y Dermatología, Moclinejo, Spain, [2]IBIMA Plataforma BIONAND, Cordoba, Spain, [3]IBIMA Plataforma BIONAND, Málaga, Spain, [4]IBIMA, Málaga, Spain, [5]Division of Rheumatology, Hospital Regional Universitario Carlos Haya, Malaga, Spain, [6]Division of Rheumatology, Hospital Regional Universitario Carlos Haya, Málaga, Spain, [7]Hospital Regional Universitario de Málaga, Malaga, Spain

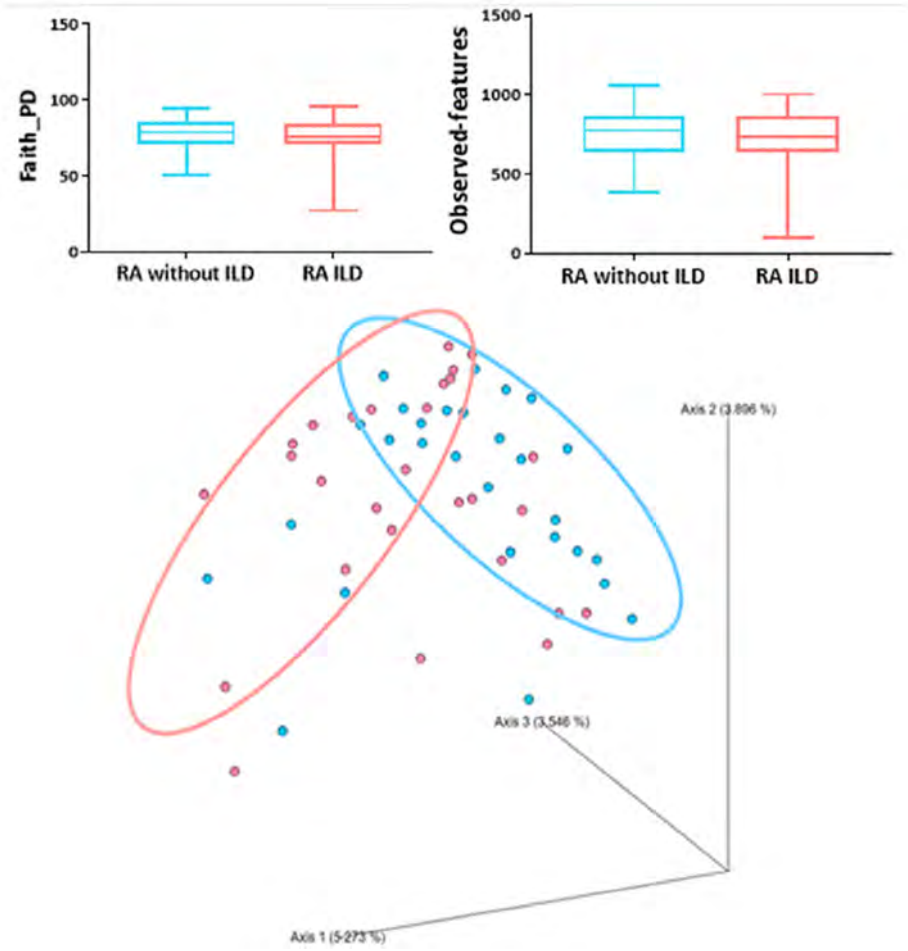
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Gut microbiota has been related to rheumatoid arthritis (RA), inflammation, and it's severity. Interstitial lung disease (ILD) is the most frequent non-pleural pulmonary manifestation and causes high morbidity and mortality in RA patients. However, the association between gut microbiota and RA associated ILD (RA-ILD) is still unknown. In the same way, there are currently no useful biomarkers for the diagnosis and prognosis of RA-ILD. Therefore, the objective of the present study is to analyze gut microbiota and permeability in RA-ILD patients and evaluate it´s association with RA-ILD and pulmonary progression.

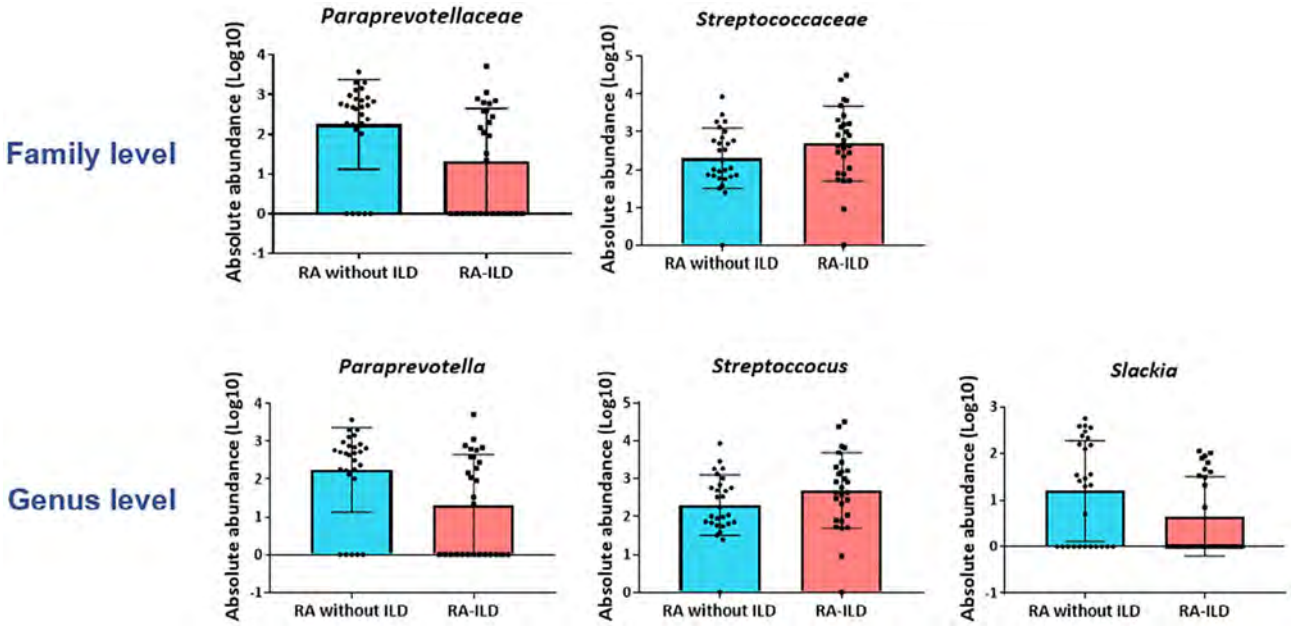
Methods: Nested case-cohort study of 2 prospective cohorts of patients with RA with and without ILD. The cohorts were matched for age, sex, and time of RA evolution. All cases systematically underwent high-resolution computed tomography (HRCT) and pulmonary function testing (PFT) on the diagnosis of ILD. ILD was defined according to lung biopsy or HRCT based on the standard criteria of the American Thoracic Society/European Respiratory Society. Pulmonary progression was defined as the worsening of the FVC > 10% or DLCO > 15%. Gut microbiota was measured by the 16S rRNA gene and the sequences were processed using the Quantitative Insights into Microbial Ecology (QIIME2). Serum lipopolysaccharide-binding protein (LBP) and lipopolysaccharide (LPS) were measured as markers of gut permeability. Demographic, clinical, laboratory, and treatment-related data were recorded. Disease activity was measured by Disease

VARIABLE	RA-ILD n=35	RA without ILD n=35	P-value
Age in years, mean (SD)	69.7 (9.3)	66.6 (7.0)	0.130
Male; n (%)	20 (57.1)	20 (57.1)	1.000
Smoking			0.760
Never smoked, n (%)	17 (48.6)	18 (51.4)	
Ex-smoker, n (%)	10 (28.6)	8 (22.9)	
Active smoker, n (%)	8 (22.9)	9 (25.7)	
Time since diagnosis RA, months, median (IQR)	149.8 (93.3-245.5)	133.7 (67.8-204.2)	0.384
Time since diagnosis of ILD, mean (SD)	66.1 (47.2)	-	-
FR+ (>10), n (%)	33 (94.3)	31 (88.6)	0.393
ACPA+ (>20), n (%)	32 (91.4)	31 (88.6)	0.690
Erosions, n (%)	21 (60.0)	19 (55.6)	0.705
DAS28-ESR, mean (SD)	3.1 (0.9)	2.6 (0.9)	**0.032**
HAQ, mean (SD)	1.2 (0.6)	0.8 (0.6)	**0.003**
FVC mean (SD)	63.0 (17.1)	83.4 (4.4)	**<0.001**
DLCO, mean (SD)	61.0 (15.2)	85.9 (7.9)	**<0.001**
UIP, n (%)	29 (82.9)	0 (0.0)	**<0.001**
NSIP, n (%)	6 (17.1)	0 (0.0)	**<0.001**

Clinical and demographic characteristics: Abbreviations. ACPA: anticitrullinated peptide antibody; DAS28: Disease activity score; DLCO: diffusing capacity of the lung for carbon monoxide; DMARDs: disease-modifying antirheumatic drug; ESR: erythrocyte sedimentation rate; FEV1: forced expiratory volume in the first second; FVC: forced vital capacity; HAQ: Health Assessment Questionnaire; HCRT: high-resolution computed tomography; NSIP: nonspecific interstitial pneumonia; RF: rheumatoid factor; SD: standard deviation; UIP: usual interstitial pneumonia.



Microbiota analysis: Alpha diversity (above) and Beta diversity (bottom). To compare the populations of both groups, the Jaccard similarity index was used and significant differences (p=0.017) were observed between both groups. Blue dots: RA without ILD; Pink dots: RA-ILD.



Gut microbiota profile: Graphs represent the families and genera with statistically significant differences. At the family level, Paraprevotellaceae (p=0.007) was significantly decreased, while Streptococcaceae (p=0.050) was significantly increased in RA-ILD patients compared to RA patients without ILD. At the genus level, Paraprevotella (p=0.007) and Slackia (p=0.041) were significantly decreased, while Streptococcus (p=0.050) was significantly increased in RA-ILD patients compared to RA patients without ILD.

Activity Score-28 with Erythrocyte Sedimentation Rate (DAS28-ESR), and the function using the Health Assessment Questionnaire (HAQ). We performed a descriptive analysis and Cox regression analysis to identify factors associated with ILD.

Results: 35 RA-ILD and 35 RA without ILD patients were included. After a mean (SD) period of 66,1 (47,2) months, pulmonary progression criteria was observed in 13 patients (37.1%). Compared with controls, RA-ILD had greater values of DAS28-ESR (p=0.032) and higher HAQ scores (p=0.003). They also had higher levels of serum LPS (p = 0.007) and more abundance of *Streptococcus* genus (p = 0.087), as well as a lower abundance of *Slackia* (p = 0.022) and *Paraprevotella* genera (p = 0.082*)*. RA-ILD patients with pulmonary progression had a higher abundance of *Streptococcus* genus (p = 0.090) and a lower abundance of *Slackia* genus. In Cox regression analysis, the moderate-high activity of DAS28-ESR (HR [IC 95%], 3.53 [1.20-6.98]; p=0.017), LPS (HR [IC 95%], 1.12 [1.02-1.23]; p=0.018) and the *Slackia* genus (HR [IC 95%], 0.98 [0.97-0.99]; p=0.010) were associated with RA-ILD.

Conclusion: RA-ILD patients showed increased gut permeability and also displayed a different pattern of gut microbiota associated with ILD diagnosis and prognosis. These findings may enable the discovery of potential RA-ILD biomarkers.

Disclosure: J. Lisbona-Montañez: None; **P. Ruiz-Limon**: None; **A. Mucientes**: None; **N. Mena Vazquez**: None; **I. Moreno-Indias**: None; **S. MANRIQUE**: None; **L. Cano-García**: None; **R. Redondo-Rodríguez**: None; **F. tinahones**: None; **A. Fernandez-Nebro**: None.

Abstract Number: 1775

The Peptidyl Arginine Deiminase Inhibitor BB-CLA Decreases the Inflammatory and Fibrotic Responses in Macrophages and Rheumatoid Arthritis Synovial Fibroblasts Exposed to Fibrinogen Modified with Malondialdehyde-Acetaldehyde Adduct and Citrulline

Jack Mordeson[1], Nozima Aripova[1], Michael Duryee[1], James O'Dell[1], Bryant England[1], Daniel Anderson[1], Ted R Mikuls[2] and Geoffrey Thiele[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Etiology and Pathogenesis Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Peptide citrullination and adduction with malondialdehyde-acetaldehyde adduct (MAA) are post-translational modifications involved in the pathogenesis of rheumatoid arthritis (RA). Anti-cyclic-citrullinated peptide antibodies are >90% specific for the diagnosis of RA. Our laboratory has shown co-localization of MAA with citrullinated proteins in RA synovial fluid, elevated anti-MAA antibodies in RA patients, and pro-inflammatory and pro-fibrotic responses to MAA-modified antigens by macrophages *in vitro*. In addition, macrophages demonstrate increased expression of peptidyl arginine deiminase-2 (PAD2), an isozyme of PAD, in response to these MAA-adducted and citrullinated proteins. PAD catalyzes protein citrullination and may mediate the immunogenic transformation of synovial proteins and subsequent auto-antibody formation in

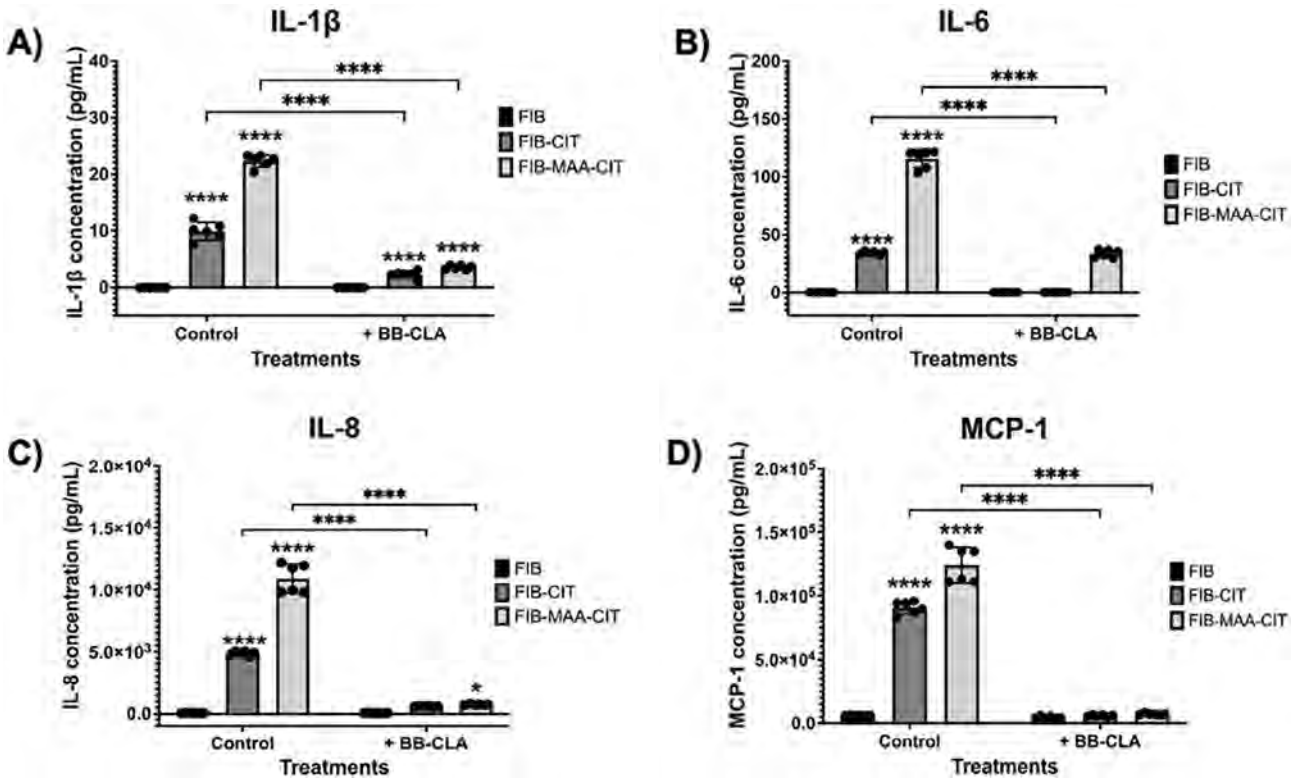


Figure 1. Inflammatory cytokines from stimulated U-937 cells. U-937 cells were stimulated with native and modified fibrinogen for 48 hours in the presence and absence of BB-CLA. IL-1β (A), IL-6 (B), IL-8 (C), and MCP-1 (D) levels were measured via ELISA. ****p<0.001.

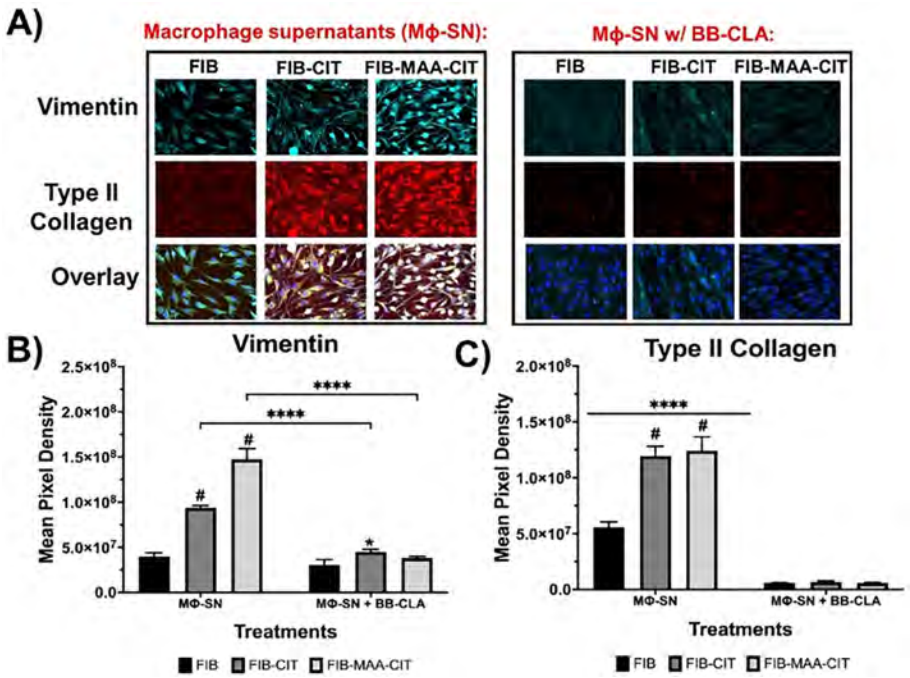


Figure 2. Fibrotic markers from stimulated HFLS-RA cells. U-937 supernatants were utilized for stimulation of HFLS-RA cells. Images were recorded following immunofluorescent staining with anti-vimentin and anti-type II collagen antibodies. ****p<0.001, #p<0.05.

RA. Here, we determine whether inhibition of PAD effects inflammatory and fibrotic markers in macrophages and RA human fibroblast-like synoviocytes (HFLS-RA) in response to stimulation with MAA and citrulline (CIT)-modified fibrinogen (FIB).

Methods: U-937 monocyte cell line was differentiated into activated macrophages by exposure to LPS, and subsequently stimulated with; unmodified FIB, FIB-CIT, or FIB-MAA-CIT in the presence (treatment group) and absence (control group) of BB-CLA (a general PAD inhibitor; PADi) for 48 hours. Supernatants collected from the media were assessed by ELISA for the pro-inflammatory cytokines; interleukin-1b (IL-1b), interleukin-6 (IL-6), interleukin-8 (IL-8), and monocyte chemoattractant protein-1 (MCP-1). HFLS from RA patients were stimulated with treatment and control supernatants from the antigen-stimulated macrophage cultures and assessed via immunofluorescent staining for the fibrotic markers vimentin and type II collagen.

Results: As previously reported, the modification of FIB with CIT and or MAA-CIT statistically increases the concentrations of the pro-inflammatory cytokines measured (Figure 1 A-D, Control). The effect of PAD inhibition on the inflammatory cytokine levels was a decrease in the secretion by stimulated macrophages of these cytokines (Figure 1 A-D, +BB-CLA) back to almost baseline levels. Examination of the HFLS cells stimulated with supernatants from macrophages activated with FIB-CIT or FIB-MAA-CIT showed an increase in both vimentin and Type II Collagen production that was significantly elevated when compared to FIB supernatant stimulation (Figure 2 A-C).

Conclusion: This study provides insight into the degree to which inflammatory and fibrotic responses from macrophages and HFLS to CIT and MAA-CIT modified fibrinogen may be PAD-mediated. Therefore, these observations strongly suggest that CIT and MAA-CIT modification of proteins play a role in the inflammatory and fibrotic responses observed in cells associated with RA development and/or progression. Additionally, they suggest that PAD inhibition is an obvious target for therapeutic intervention.

Disclosure: J. Mordeson: None; **N. Aripova**: None; **M. Duryee**: None; **J. O'Dell**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **D. Anderson**: None; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **G. Thiele**: None.

Abstract Number: 1776

Macrophage Migration Inhibitory Factor May Help Maintain Tight Junctions in the Gut by Enhancing Occludin Expression

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Axial Spondyloarthritis (AxSpA) is a chronic inflammatory disease with multifactorial origins, primarily affecting the musculoskeletal system. Gut inflammation is seen in the majority of AxSpA patients, with 60% having microscopic changes and 10% with overt Inflammatory Bowel Disease (IBD). Over the years many pathways and cell populations have been linked to the pathogenesis of gut inflammation in AxSpA. Macrophage migration inhibitory factor (MIF) plays a critical role in the pathogenesis of AxSpA. Over-expression of MIF in a mouse model of SpA (SKG mice) causes major clinical features of AxSpA while blocking or depletion of MIF significantly suppresses these symptoms. However, the role of MIF in gut inflammation in AxSpA is unknown. We hypothesized that MIF is a key player driving gut inflammation in AxSPA.

To study the effect of MIF on gut homeostasis and inflammation in the SKG mouse model of spondyloarthritis

Methods: A total of 12 SKG control mice, 11 SKG mice treated with curdlan, 9 SKG-MIF Knock Out (KO), and 6 SKG-MIFKO mice treated with curdlan that were all 16 weeks old were used for this study. H&E slides were prepared for histopathology assessment on formalin-fixed paraffin-embedded (FFPE) blocks of ileum tissue (2 individuals scored the samples independently and were blinded to the group). Immunohistochemistry (IHC) was performed for occludin and MPO antibody was used to assess neutrophil (a major source of MIF) infiltration. Kruskal–Wallis test was used to analyze the difference between the 4 groups.

Results: We observed significantly increased inflammation levels in the ileum of SKG+curdlan mice compared to SKG control mice (Fig1a). SKG-MIFKO+curdlan mice did not have a significant benefit of reduction in inflammation levels. Interestingly, even without curdlan treatment, MIFKO mice showed inflammation in the gut. SKG-MIFKO mice (with and without curdlan) developed a disruption of ileal epithelium. There was a significant reduction in occludin expression compared to SKG control mice, suggesting a disruption of tight junctions (Fig1b). MPO expression was significantly elevated in SKG+curdlan and SKG-MIFKO+curdlan groups. However, although not significant, it seems that the MPO expression is lower in the SKG-MIFKO+curdlan compared to SKG+curdlan mice.

Conclusion: Knocking out MIF in SKG mice has shown improvement in AxSpA symptoms. However, based on our findings, MIF seems to have a protective role in the gut of SKG mice unlike what we see in joints. The absence of MIF leads to decreased expression of occludin. These findings together suggest that MIF is essential for the integrity of the gut epithelial barrier in the SKG mouse model of SpA. If this effect on the tight junction is directly related to MIF or through changes in type 3 immune response needs to be investigated.

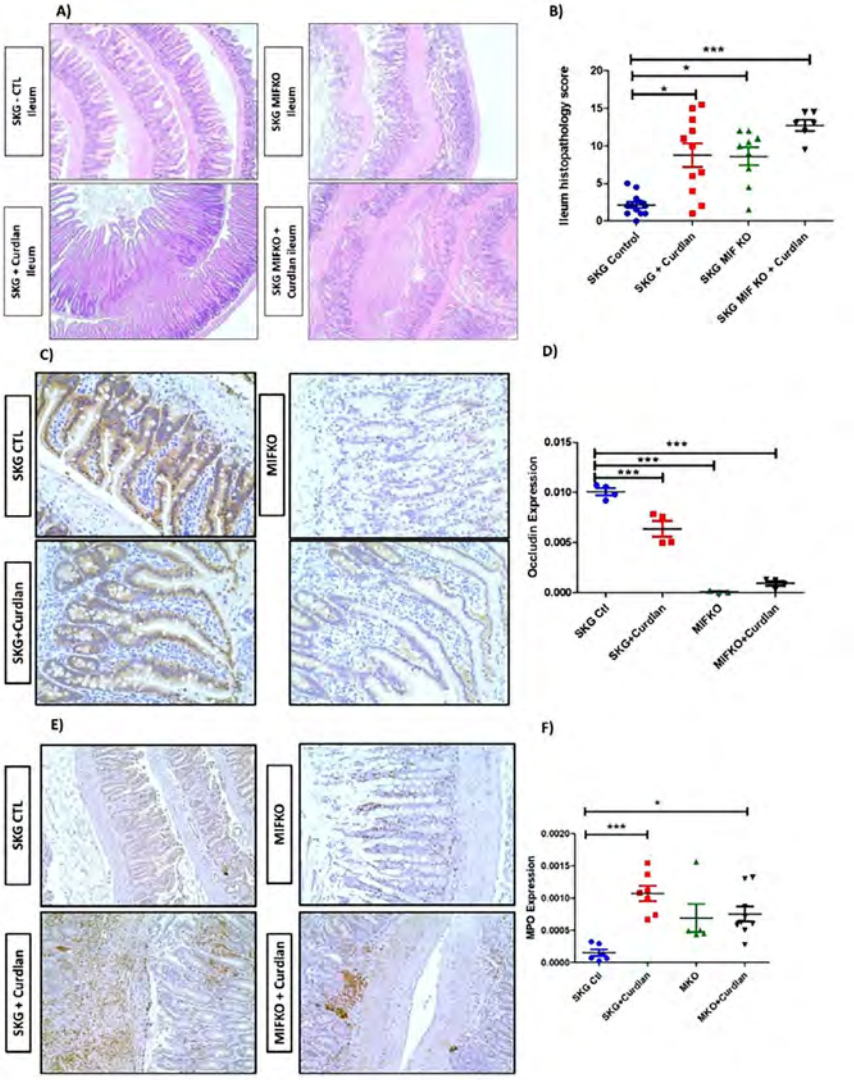

Figure1. A&B) Histopathology of ileum from SKG, SKG+Curdlan, SKG-MIFKO and SKG-MIFKO+Curdlan. C&D) IHC staining for occludin. E&F) IHC staining for MPO.

Disclosure: S. Foroozan: None; **N. Haroon**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, UCB Pharma, 2.

Abstract Number: 1777

The Effect of the Inflamed Joint Microenvironment on Endothelial Cell Function

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: While common pathogenic mechanisms exist between PsA and RA, distinct vascular morphology has been observed, with PsA displaying a tortuous, dilated, irregular shaped morphology compared to a straight regular branching pattern observed in RA. The aim of this study is to examine the effect of the PsA and RA joint microenvironment on endothelial cell function.

Methods: PsA and RA patients underwent key-hole joint arthroscopy and synovial biopsies were obtained. PsA and RA synovial fibroblasts (FLS) were isolated and grown to passage 1-5. PsA and RA FLS supernatants were harvested and referred to as conditioned media (CM). Endothelial cells (EC) were cocultured with PsA FLS/RA FLS or PsA CM/RA CM, and pro-inflammatory mediators (cytokines, matrix-metalloproteinases, angiogenic growth factors, chemokines and adhesion molecules) were quantified by ELISA, real-time PCR and flow cytometry.

Results: Co-culture of PsA and RA FLS with EC induced IL-6 secretion, with no effect observed for MCP-1 or Ang2. PsA FLS CM induced MCP-1, Ang2, ICAM-1, MMP2 and MMP3 expression in EC, with only MMP-2 increasing in response to RA FLS CM. Both PsA FLS CM and RA FLS CM decreased VCAM-1 expression, an effect that was more pronounced for RA FLS CM. Either co-culture of PsA FLS/RA FLS or PsA FLS CM/RA FLS CM with EC induced the frequency and/or MFI of key chemokine receptors CXCR3 and CXCR4 on EC, an effect that was more pronounced for FLS CM vs FLS co-culture, particularly for PsA CM. Both PsA FLS/RA FLS coculture or PsA/RA CM decreased the frequency of CXCR5, however induced CXCR5 MFI. Only co-culture with PsA FLS and RA FLS induced the expression of ICAM-1, with no effect observed for PsA or RA FLS CM. No effect was observed for VCAM-1 expression. In contrast, the effect of coculture on FLS led to a reduction in the expression of ICAM-1 on both PsA and RA FLS, with increased expression of VCAM-1 observed for PsA FLS. No effect was observed for chemokine receptor expression on either PsA FLS or RA FLS when co-cultured with EC.

Conclusion: PsA and RA FLS/CM induce angiogenic, chemokine and adhesion molecule expression on EC, with differential effects for some mediators observed in response to PsA vs RA joint microenvironments. Furthermore, differences were observed between EC-FLS cocultures vs EC FLS CM co-cultures, suggesting cell-cell contact and soluble mediators both influence the EC pathogenic phenotype.

Disclosure: A. Brugman: None; **Ó. Tynan**: None; **D. Anton**: None; **C. Orr**: None; **V. Marzaioli**: None; **D. Veale**: None; **U. Fearon**: None.

Abstract Number: 1778

Role of GITR/GITRL Interaction in Modulating T Helper 9, T Helper 17 and T Regulatory Response in Psoriatic Arthritis

Chiara Rizzo[1], Lidia La Barbera[1], Marianna Lo Pizzo[1], Leila Mohammadnezhad[1], federica Camarda[1], Francesco Dieli[1], Francesco Ciccia[2] and Giuliana Guggino[1], [1]University of Palermo, Palermo, Italy, [2]University of Campania - Luigi Vanvitelli, Naples, Italy

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The inflammatory process characterizing Psoriatic Arthritis (PsA) is mainly driven by interleukin (IL)-23/IL-17 axis and IL-9 overexpression, in presence of T helper (Th)17 and Th9 expansion (Veale DJ, The Lancet. 2018). Recently, a correlation between IL-9 and Glucocorticoid-induced Tumor Necrosis Factor-related receptor (GITR), whose ligand (GITRL) is expressed on antigen presenting cells, was described. Specifically, the activation of GITR/GITRL promotes Th9 and Th17 differentiation and alters Treg functions fueling inflammation (Tian J, Front Immunol. 2020). Considering the role of Th9 and Th17 in PsA and the proinflammatory function of GITR, we aimed to study the effects of GITR/GITRL interaction in PsA.

Methods: Eighteen patients fulfilling the 2006 classification criteria for PsA (CASPAR) and 10 healthy controls (HC) were enrolled in this study; all gave their informed written consent to participate. The study complied with the Declaration of Helsinki and was approved by the local Ethics Committee. Patients had an active disease and were naïve to biologicdisease modifying antirheumatic drug (bDMARDs). Blood samples were collected from all participants. Peripheral blood mononuclear cells were isolated and GITR/GITRL expression was determined by flow-cytometry in different cell subsets. An *in vitro* functional assay with a recombinant GITR agonist was performed to assess the effect of GITR activation on Th9 and Th17 expansion and Treg functions. Cells were stimulated with anti-CD3-CD28 monoclonal antibodies (mAb) too. The frequency of T cells was studied by flow-cytometry while the expression of cytokines and transcription factors was

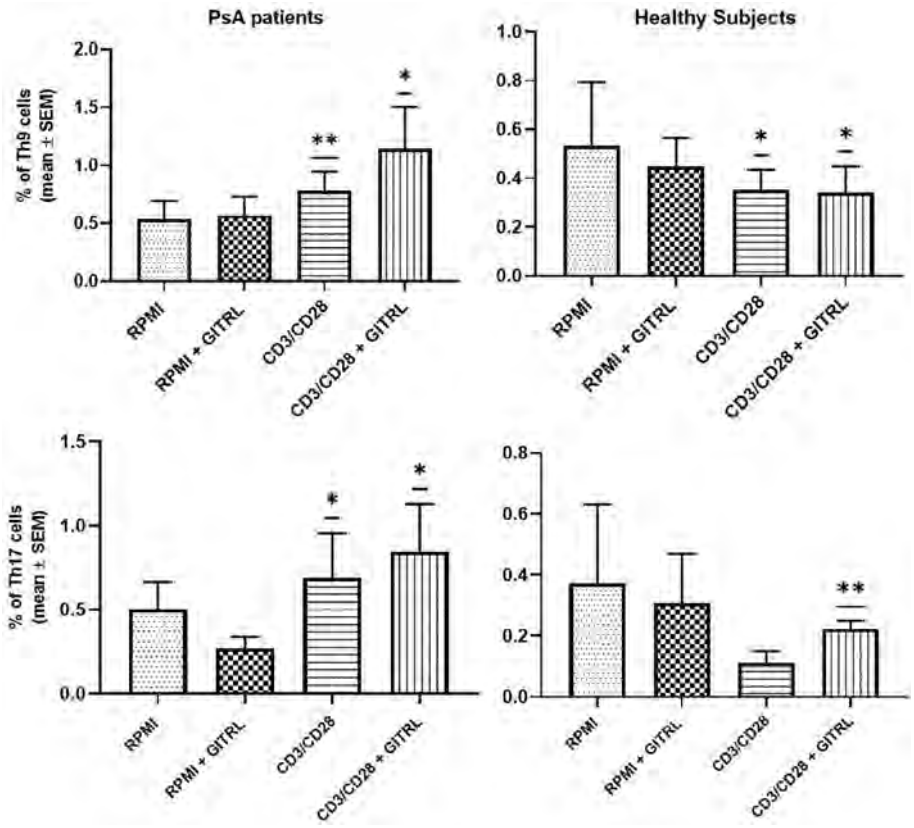

Figure 1. Recombinant GITRL effect on Th9 and Th17 frequency. Frequency of Th9 and Th17 analysed in four different conditions: RPMI, RPMI + GITRL, CD23/CD28 activation beads, CD3/CD28 + GITRL in PsA patients (left panel of the figure) and in healthy controls (right panel of the figure), respectively. *p<0.05

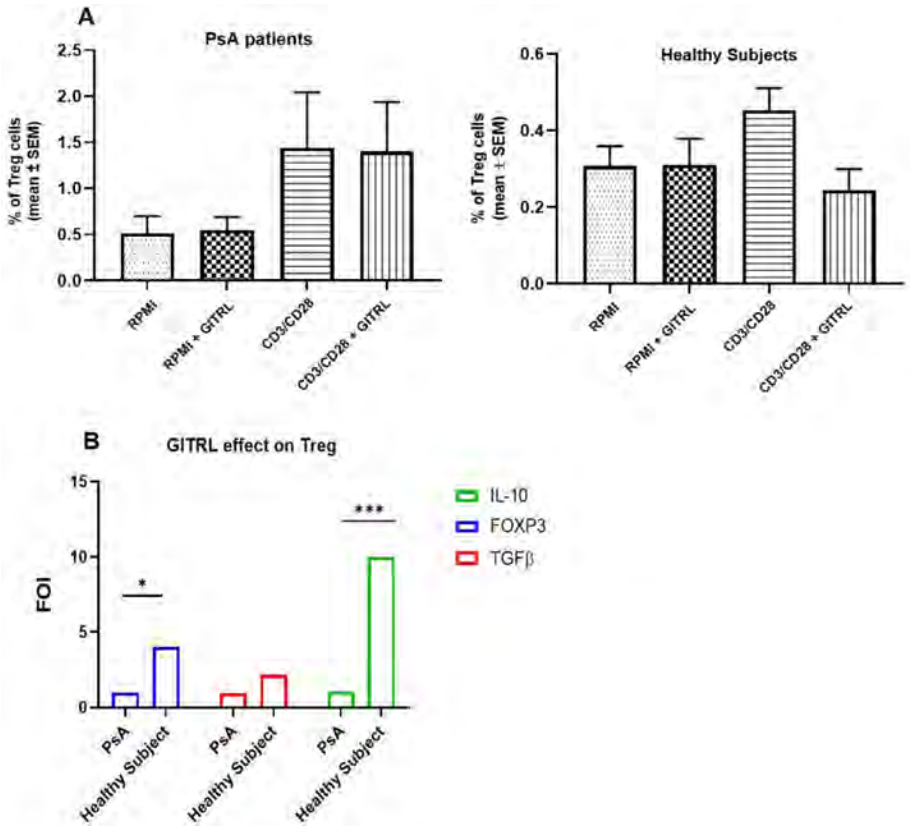

Figure 2. Recombinant GITRL effect on Treg frequency and function. A. Frequency of Treg analysed in four different conditions: RPMI, RPMI + GITRL, CD23/CD28 activation beads, CD3/CD28 + GITRL in PsA patients (on the left) and in healthy controls (on the right), respectively. B. mRNA expression of IL-10, FOXP3 and TGFβ after GITRL stimulation in PsA patients and healthy subjects analyzed by qRT-PCR. *p<0.05

assessed by qRT-PCR. Data were analyzed using GraphPad Prism version 8.0.1; p values < 0.05 were considered statistically significant.

Results: An enhanced expression of GITR among $CD4^+$ T cells was detected both pre and after *in vitro* stimulation with anti-CD3-CD28 mAb. In particular, although not statistically significant, Th17 and Th9 demonstrated an increased GITR expression after stimulation. GITRL was found upregulated on monocytes ($CD14^+$), dendritic cells ($CD11c^+$) and B cells ($CD19^+$) in PsA patients, even if no differences in cell frequency were detected between PsA and HC. The expression of HLA-DR was assessed as a positive control without evidencing any difference between PsA and HC. An expansion of both Th9 and Th17 was found after stimulation with anti-CD3-CD28 ($p< 0.05$); the proliferation of these subsets was further increased in presence of recombinant GITR agonist ($p< 0.05$) (Figure 1). Treg from PsA were expanded compared with HC after stimulation with anti-CD3-CD28 mAb. The addition of GITRL did not further modulate Treg proliferation. However, in presence of GITR agonist the mRNA expression of NF-kB, FOXP3, TGFb and IL-10 was reduced in Treg from PsA patients, with a statistically significant difference for both IL-10 and FOXP3 ($p< 0.05$) (Figure 2).

Conclusion: Our data support a novel role for GITR/GITRL axis in modulating the inflammatory process behind PsA through the expansion of Th9 and Th17 and the simultaneous suppression of Treg functions, unravelling a possible future target of therapy in PsA.

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Abstract Number: 1779

A Novel Inhibitory Pathway of Synovial Inflammation Exerted by Glucocorticoids and TNF Inhibitors Through LAG-3 Up-Regulation

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic immune-mediated condition that results in systemic musculoskeletal (MSK) inflammation, including peripheral synovitis, enthesitis and axial involvement. Glucocorticoids (GCs) are indicated for local control of synovitis by intra articular injection. We hypothesized that GCs may promote suppressive activity through up-regulation of lymphocyte-activation gene-3 (LAG-3), a regulatory molecule that can be modulated by different drugs. In this study, we investigated the effects of GCs and other anti-rheumatic drugs on modulation of LAG-3 and of an additional regulatory molecule co-expressed with LAG-3, programmed cell death receptor-1 (PD-1), in synovial cells ex-vivo.

Methods: Synovial fluid mononuclear cells (SFMCs) derived from PsA patients were co-cultured with GCs [betamethasone (BET) and methylprednisolone acetate (MPA))], TNF inhibitor (i) (infliximab, IFX), IL-17Ai (secukinumab, SEC), IL-12/23i (ustekinumab, UST)] and methotrexate (MTX) or with medium alone for 5 days. Cells were analyzed for CD45 and LAG-3 by flow cytometry and all drugs were used in their therapeutic concentrations. To identify the drugs' impact on cell growth and regulatory molecules, total SFMCs cell growth and expression of LAG-3 and PD-1 on CD3 and CD14 cells were analyzed.

Results: SFMCs derived from 11 PsA patients co-cultured with GCs showed a significant increase in %LAG-3$^+$CD45$^+$ cells (BET 1mg/ml, 6.8±1.3; BET 10mg/ml, 7.1±1.4; MPA 1mg/ml, 6.7±1.3; and MPA 10mg/ml, 9.4±2.0, $p< 0.001$, respectively) as compared to medium (1.0±0.3). Likewise, IFX also increased this cell population (2.0±0.3, $p= 0.005$) as compared to the medium (1.0±0.3), but to a lesser extent than GCs. In contrast, SEC, UST, and MTX had no effect on %LAG-3$^+$CD45$^+$ cells as compared to the medium, (1.0±0.2, 0.8±0.2, and 0.9±0.2, respectively) (Figure 1A). GCs (MPA) and IFX reduced the total SFMCs cell count/well but this change was statistically significant only for GCs (21±5.1X10^5/well, $p< 0.01$ and 41±5.1X10^5/well, respectively), while MTX had no effect compared to the medium (49±4.8X10^5/well and 51±5.1X10^5/well, respectively) (Figure 1B). In the same co-culture setting, the proportion of LAG-3$^+$CD3$^+$ T cells was low for all experimental groups (Figure 1C), whereas %LAG-3$^+$CD14$^+$ monocytes were markedly up-regulated by GCs (12.8±2.1, $p< 0.001$) compared to the medium (0.9±0.4) (Figure 1 D and F). The proportion of PD-1$^+$CD14$^+$ monocyteswas not significantly increased by GCs and other drugs (Figure 1E).

Conclusion: Our data show that GCs immunosuppressive activity is mediated through up-regulation of LAG-3 in SFMCs. Within the tested anti-rheumatic drugs, this activity was exclusively mediated by GCs and to a lesser extent by a TNF inhibitor. GCs reduced the total SFMCs cell growth in culture and concomitantly up-regulated LAG-3, mainly on monocytes. This study proposes that synovial monocytes expressing LAG-3 are potential mediators of the GCs immunosuppressive effect. Further investigation into the precise involvement of LAG-3 in inhibition of synovial inflammation is required.

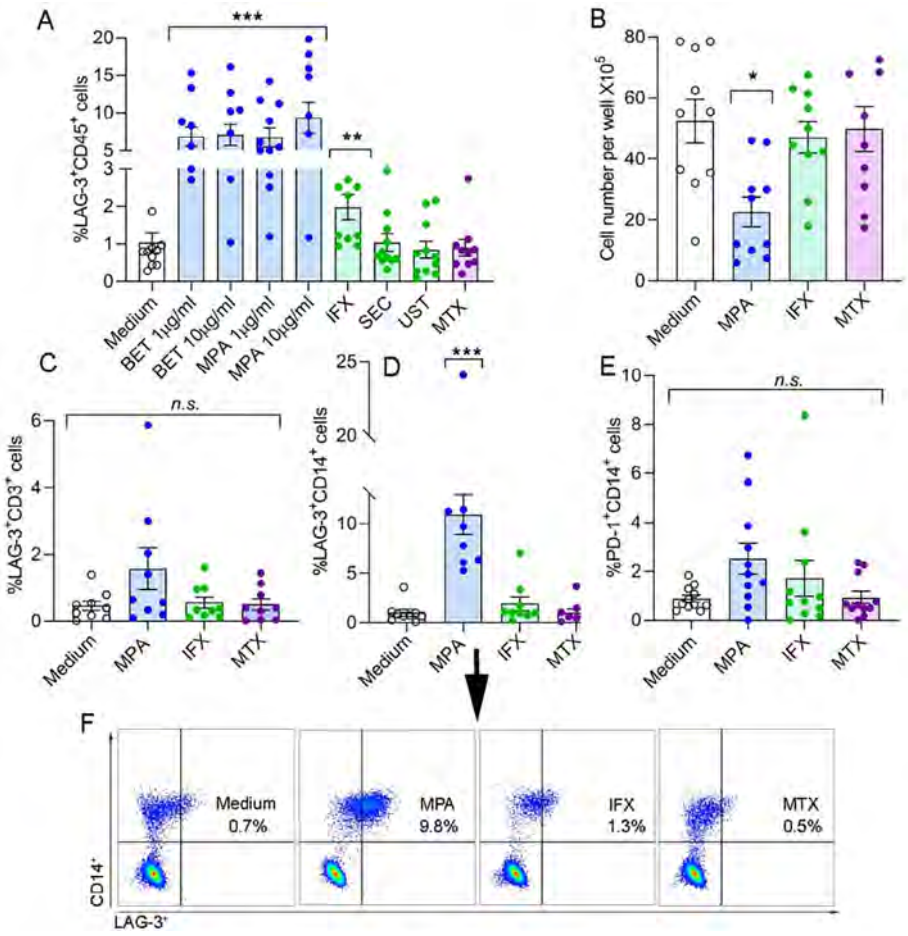

Figure 1. GCs and to a lesser extent TNF inhibitor up-regulate LAG-3 in SFMCs ex-vivo. (A) SFMCs derived from PsA patients (n=11) were cultured ex-vivo with betamethasone (BET), methylprednisolone acetate (MPA), infliximab (IFX), secukinumab (SEC), ustekinumab (UST), and methotrexate (MTX) and analyzed for %LAG-3+CD45+ cells using flow cytometry. (B) Total SFMCs cell count/well analysis was performed after 5 days in culture with the indicated drugs: MPA, IFX and MTX. In same co-culture setting: (C) %LAG-3+CD3+, (D) %+LAG-3+CD14+ and (E) %PD-1+CD14+ cells were analyzed using flow cytometry (F) Representative images of SFMCs derived from PsA patient stained for CD14 and LAG-3 after 5 days in culture with medium or with the therapeutics indicated. Positive staining is presented in the right upper quadrant of each plot with the percentage indicated. Statistical analysis calculated by the non-parametric one-way ANOVA Kruskal-Wallis test and Dunn's multiple comparison test, *$p < 0.01$, **$p < 0.005$, ***$p < 0.001$, n.s., non-significant.

Disclosure: S. Gertel: None; **V. Furer**: None; **A. Polachek**: None; **O. Elkayam**: None.

Abstract Number: 1780

Biomarkers Predicting Structural Progression of Axial Spondyloarthritis: A Pilot Study

Jiri Baloun[1], Kristyna Bubova[1], Aneta Pekacova[2], Lucia Ondrejcakova[3], Vladimir Cervenak[4], Monika Gregova[5], Sarka Forejtova[5], Jana Horinkova[1], Jindriska Gatterova[6], Michal Tomcik[7], Jiri Vencovsky[7], Karel Pavelka[8] and Ladislav Senolt[9], [1]Institute of Rheumatology, Prague, Czech Republic, [2]First faculty of medicine, Charles University, Prague, Czech Republic, [3]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic, [4]Department of Medical Imaging, St Anne's University Hospital, and Faculty of Medicine, Masaryk University, Brno, Czech Republic, [5]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Prague, Czech Republic, [6]Rheumatology Institute, Prague, Czech Republic, [7]Institute of Rheumatology, Prague, Czech Republic, Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, [8]Institut of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthritis (AxSpA) is a frequent inflammatory disease with a significant impact on a patient's quality of life. Therefore, early diagnosis and recognition of patients with rapid structural progression are of great importance. This pilot study aimed to profile the plasma proteome and disclose candidate biomarkers differentiating patients with structural radiographic progression after two years.

Methods: Twenty patients with ax-SpA fulfilling the ASAS classification criteria were selected according to an increase in the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) after a 2-year follow-up into radiographic progressors (ΔmSASSS ≥2) and non-progressors (ΔmSASSS = 0). Patients' disease activity was determined using C-reactive protein (CRP), Erythrocyte Sedimentation Rate (ESR), Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Activity Disease Activity Index (BASDAI) and physician global assessment (MDGA). The plasma proteome was profiled using the mass spectrometry method and statistical analysis was adjusted for CRP. All patients were naïve to b/ts DMARDs during the 2-year follow-up.

Results: Our cohort included ten patients without radiographic spinal progression (non-progressors) and ten patients who developed significant progression after two years (progressors) (mean±SD ΔmSASSS 9.88±5.1). All demographic and clinical characteristics are provided in Table 1. The profiling of plasma proteome revealed 489 quantifiable proteins, out of which 21 proteins were different between patient groups (ANOVA-computed $p < 0.05$ for all). The follow-up pairwise comparison revealed five promising biomarkers, out of which clusterin (1.20-fold, p=0.011), serum amyloid P-component (SAP) (1.43-fold, $p < 0.004$), retinol-binding protein 4 (RPB4) (1.28-fold, p=0.027), and fetuin-B (1.52-fold, p=0.051) were upregulated, while gelsolin (1.16-fold, p = 0.015) was downregulated in patients with mSASSS progression compared to those without progression (Fig. 1). Out of these proteins, gelsolin, RBP4, fetuin-B, and SAP significantly correlated with mSASSS, CRP or ASDAS (Fig. 2). All candidate proteins have previously been associated with rheumatic diseases.

Table 1 – Demographic and clinical characteristics of patients with axSpA at baseline. CRP - C-reactive protein, ESR - Erythrocyte Sedimentation Rate, ASDAS - Ankylosing Spondylitis Disease Activity Score, BASFI -Bath Ankylosing Spondylitis Functional Index, BASDAI - Bath Ankylosing Spondylitis Activity Disease Activity Index, MDGA - physician global assessment, mSASSS - modified Stoke Ankylosing Spondylitis Spinal Score, csDMARDs - conventional synthetic Disease-Modifying AntiRheumatic Drugs, MASES - Maastricht Ankylosing Spondylitis Enthesitis Score

	Non-progressors N = 10	Progressors N = 10	p-value[3]
Age [yrs]	38 (14)[2]	41 (11)[2]	0.2
Sex - male	6 (60%)[1]	6 (60%)[1]	>0.9
Duration from the first symptom [yrs]	12 (7)[2]	11 (9)[2]	0.8
CRP [mg/L]	1 (2)[2]	6 (10)[2]	0.019
ESR [mm/hr]	8 (11)[2]	19 (22)[2]	0.058
mSASSS	0 (0)[2]	4 (11)[2]	0.006
Radiographic axSpA	7 (70%)[1]	7 (70%)[1]	>0.9
ASDAS	1.69 (1.51)[2]	2.39 (0.92)[2]	0.2
BASDAI	2.14 (3.74)[2]	2.04 (1.64)[2]	>0.9
MASES	0.00 (1.75)[2]	0.00 (3.25)[2]	>0.9
MDGA	20 (24)[2]	15 (16)[2]	>0.9
csDMARDs	1 (10%)[1]	2 (20%)[1]	>0.9

[1] n (%); [2] Median (IQR)
[3] Fisher's exact test; Wilcoxon rank sum test; Wilcoxon rank sum exact test

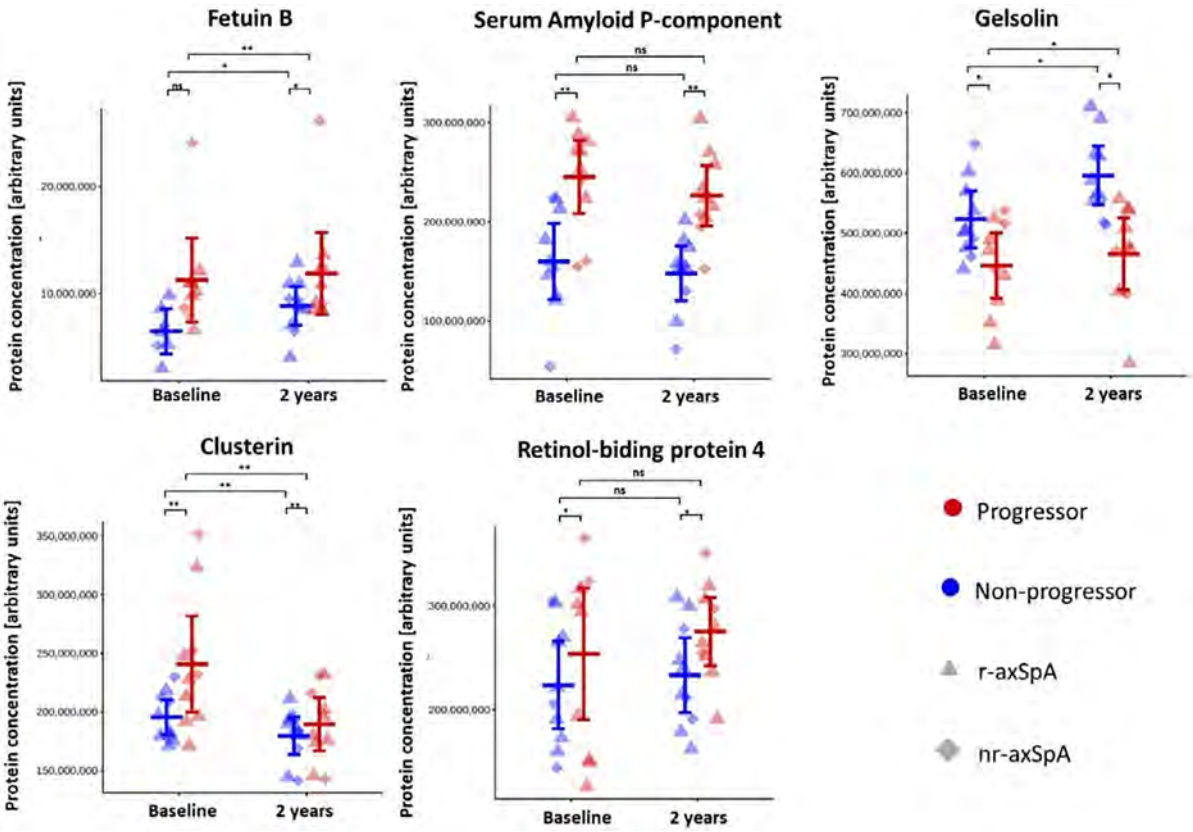

Figure 1 – Five candidate proteins with the potential to predict radiographic progression in axSpA. The error bars represent 95% confidence intervals with the mean for patients with or without mSASSS progression. p-values show statistical significance between depicted pairwise comparisons computed from linear mixed-effect models and adjusted for CRP. (***, $p < 0.001$; *, $p < 0.05$; ns, non-significant). Patients with and without mSASSS progression are coloured in red and blue, respectively, and radiographic (r-) and non-radiographic (nr-) axSpA patients are depicted as triangles and diamonds, respectively.

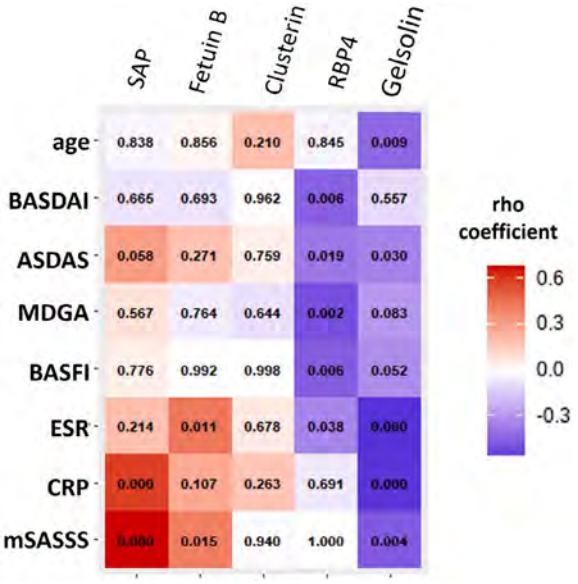

Figure 2 – Correlation matrix of five candidate proteins and selected clinical parameters. The matrix includes p-values and the colour indicates the strength and direction of Spearman's coefficient (rho).

Conclusion: This pilot study revealed five plasma proteins, which are likely to predict the structural progression of axSpA after two years. These data will be validated in an extended larger cohort.

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Disclosure: J. Baloun: None; **K. Bubova**: None; **A. Pekacova**: None; **L. Ondrejcakova**: None; **V. Cervenak**: None; **M. Gregova**: None; **S. Forejtova**: None; **J. Horinkova**: None; **J. Gatterova**: None; **M. Tomcik**: None; **J. Vencovsky**: Argenx, 2, Eli Lilly, 6, Galapagos, 2, Horizon, 2, Merck, 2; **K. Pavelka**: Abbvie, 2, 6, Amgen, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Egis, 2, 6, MSD, 2, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 6; **L. Senolt**: None.

Abstract Number: 1781

TNF Induces Neutrophil Elastase/Gasdermin D-mediated Neutrophil Extracellular Traps in Axial Spondyloarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Emerging studies have shown that neutrophil extracellular traps (NETs) are increased and associated with the disease activity in patients with axial spondyloarthritis (axSpA). However, the molecular mechanism underlying the release of NETs remains unclear in axSpA. In this study, we aimed to investigate the role of TNF/neutrophil elastase (NE)/Gasdermin D (GSDMD) in the release of NETs in axSpA.

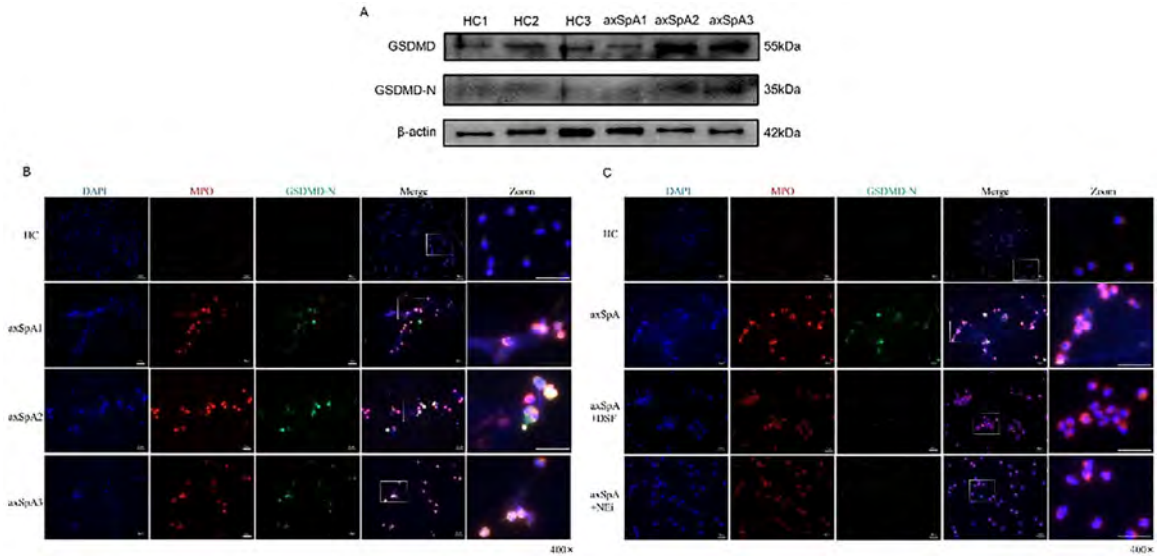

Figure 1 Increased expression of GSDMD in the neutrophils of axSpA patients and associates with NETs release. A. Western blot shows that the expressions of GSDMD and GSDMD-N were increased in the neutrophils of axSpA patients. B. Immunofluorescence images show that higher expression of GSDMD-N was found to be associated with the increased NETs structures in axSpA patients. C. Immunofluorescence images show that GSDMD inhibitor (disulfiram, DSF) or NE inhibitor (NEi) inhibited the NETs release and NEi inhibited the expression of GSDMD-N in axSpA patients.

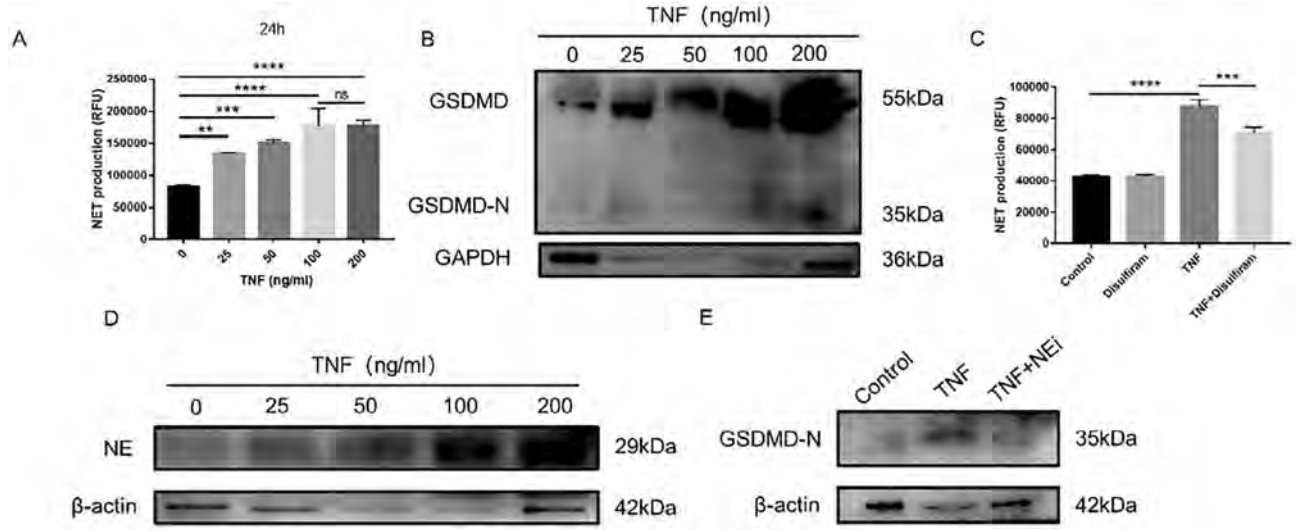

Figure 2 TNF induced the release of NETs through the NE/GSDMD pathway. A. Western blot shows that TNF induced the NETs release dose-dependently. B. Western blot shows that TNF stimulation increased the expression of GSDMD and GSDMD-N. C. GSDMD inhibitor disulfiram inhibited TNF-induced NETs release. D. Western blot shows that TNF stimulation increased the expression of NE. E. Western blot shows that NE inhibitor (NEi) inhibited TNF-induced GSDMD-N expression.

Methods: The expression of GSDMD in the neutrophils of axSpA patients was analyzed by Western blot and immunofluorescence. The role of NE/GSDMD in the NETs release of axSpA patients was tested. Furthermore, the effect of TNF on NE/GSDMD-mediated NETs was analyzed.

Results: Compared with the healthy controls, increased expression of GSDMD and the N-terminal fragment of GSDMD (GSDMD-N) were detected in the neutrophils of axSpA patients. In addition, higher expression of GSDMD-N was found to be associated with the increased NETs structures in axSpA, which was blocked by either GSDMD or NE inhibitor. Furthermore, TNF induced the release of NETs through the NE/GSDMD pathway.

Conclusion: These results demonstrated that TNF/NE/GSDMD pathway plays a critical role in the NETs release in axSpA, which reveals that NE/GSDMD may serve as novel potential targets for inhibiting NETs to treat axSpA.

Disclosure: Y. Li: None; **X. Peng**: None.

Abstract Number: 1782

The Stromal-cell Derived Cytokine interleukin-17D Attenuates Joint Inflammation

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

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Session Time: 9:00AM–11:00AM

Background/Purpose: The interleukin-17 (IL-17) family of cytokines consists of 6 evolutionarily conserved cytokines, IL-17A-F. Of these, IL-17A, B, C, and F play diverse roles in homeostasis and inflammation. IL-17A plays a critical pro-inflammatory role in inflammatory arthritis, particularly in the spondyloarthritis (SpA) spectrum of disease. IL-17D is an understudied member of the IL-17 family of cytokines and its function appears to be context dependent. We sought to identify the role of IL-17D in inflammatory arthritis.

Methods: We utilized two models of inflammatory arthritis: the SKG model and the serum transfer arthritis (STA) model. We tested the effect of recombinant IL-17D treatment on arthritis development in both the STA and SKG models of arthritis and assessed clinical inflammation and expression of pro-inflammatory factors in the paws by qPCR. We induced STA in *Il17d-deficient* mice and controls, performed histology and assessed cytokines by Luminex.

To identify the cell types expressing IL-17D in inflamed synovial tissues from patients with SpA and RA, we analyzed single-cell sequencing data from the Accelerating Medicines Partnership (AMP I) database, and performed RNAscope and immunofluorescence (IF). Finally, we performed *in vitro* stimulation experiments using primary human cells and cell lines.

Results: We have previously reported that IL-17D is the most highly expressed IL-17 family member in synovial tissue at the transcriptional level in patients with SpA and its expression correlates inversely with inflammation. *Il17d*-deficient mice develop more severe arthritis than littermate controls. We now show that treatment of arthritic mice with recombinant IL-17D protein attenuates inflammation in both the STA and SKG murine models of inflammatory arthritis, accompanied by downregulation of pro-inflammatory cytokines. In inflamed human synovial tissues, *IL-17D* mRNA is most highly expressed in CD34+ Fibroblast-like synoviocytes (FLS) that also express markers of stromal cell progenitors. Single-cell analysis and IF revealed the presence of one previously identified receptor for IL-17D, CD93, in inflamed synovial tissues.

Conclusion: IL-17D and the CD93 receptor are expressed in inflamed synovial tissues. IL-17D expression is localized to CD34+ FLS. In contrast to other IL-17 family cytokines that are pro-inflammatory, IL-17D attenuates inflammation in two animal models of arthritis. This finding is confirmed in the IL-17D-deficient setting. These data support an anti-inflammatory role for IL-17D in inflammatory arthritis. Further studies are ongoing to define the mechanism by which the IL-17D pathway impacts inflammation.

Disclosure: J. Chen: None; **C. Manning**: None; **N. Yeremenko**: None; **J. Shim**: AAVAA, 2, 5, 8; **D. Montoro**: TenSixty Biosciences, 3; **D. Baeten**: UCB, 3; **E. Gravallese**: Associate Editor, New England Journal of Medicine, 3, Co-editor of the textbook Rheumatology, 9, UptoDate, 9.

Abstract Number: 1783

Integrative Functional Genomics Points to Natural Killer Cells as Key Drivers in the Pathogenesis of Ankylosing Spondylitis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Multiple lines of evidence indicate that ankylosing spondylitis (AS) is a lymphocyte-driven disease. However, which lymphocyte populations are critical in AS pathogenesis is not known. AS is a highly heritable disease, with estimates of the genetic contribution to AS ranging from 69 to 90%. Genome-wide association studies (GWAS) have identified >100 loci associated with AS, with the vast majority of likely causal variants being non-coding. In this study, we aimed to identify the key cell types mediating the genetic risk in AS using an unbiased multi-omics approach.

Methods: We integrated GWAS data with epigenomic and transcriptomic datasets in human lymphocytes to identify key cell subsets mediating genetic susceptibility to AS. We used public ATAC-seq on sorted peripheral immune cell subsets of healthy subjects, low-input RNA-seq on 7 sorted lymphocyte populations of healthy subjects, and single-cell RNA-seq from the human gut single-cell atlas. To link cell type-specific open chromatin regions or gene expression with GWAS we used 3 published methods: Linkage Disequilibrium Score-regression in Specifically Expressed Genes (LDSC-seg), SNPsea, and single-cell disease-relevance score (scDRS). We validated that these methods could identify T-cells as the main drivers of Rheumatoid Arthritis. Additionally, we performed co-localization analyses between GWAS loci and genetic variants associated with gene expression (eQTL) to find putative target genes of AS risk variants.

Results: LDSC-seg revealed that NK-specific open chromatin regions are significantly enriched in heritability for AS, while this was not the case for other cell types such as T cells, B cells, and monocytes. This finding was consistent between two AS GWAS, one using the ImmunoChip, and the other (UK biobank) using a genome-wide chip. Applying SNPsea to RNA-seq data, we validated that genes in AS risk loci are enriched in NK cell-specific gene expression, compared to 6 T cell subsets (CD4+ T, CD8+ T, MAIT, iNKT, and two gamma delta T cell subsets). Gene expression levels of AS-associated genes, such as RUNX3, TNFRSF1A, and NPEPPS, were found to be highest in NK cells. Additionally, scDRS analysis using the human gut single-cell atlas revealed significant upregulation of AS-associated genes predominantly in NK cells. With co-localization analyses using a large-scale NK cell transcriptomic study with genotyped subjects, we found putative target genes for AS risk variants, including the widely studied ERAP1, previously reported as likely target gene TNFRSF1A and two new understudied target genes.

Conclusion: Using a variety of published datasets and complementary analytical approaches, we consistently identified NK cells as the primary cell type with gene expression and open chromatin enriched in genetic risk variants for AS. These findings point to NK cells as key mediators of the genetic susceptibility to AS.

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Abstract Number: 1784

Dendritic Cell-specific TNFR2 Depletion Reduces Psoriatic Arthritis-like Disease in a Mouse Model

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic, progressive autoimmune condition that affects both the skin and joints. It is characterized by increased levels of the proinflammatory cytokine tumor necrosis factor-alpha (TNF-α) (Guttman-Yassky et al., 2011). TNF signals via two receptors, TNFR1 and TNFR2. Recently, our lab discovered that globally deleting the TNFR2 gene, while keeping TNFR1 intact, can reduce psoriasis-like inflammation in mice (Chandrasekharan et al., 2022). Mechanistically, we found that TNFR2 plays a crucial role in the dendritic cell (DC)-dependent production of IL-23 and polarization of TH17 cells. In psoriasis, DCs are known to be involved in capturing self-antigens from abnormal skin cell growth, presenting them to T cells, and initiating an immune response (Kamata and Tada, 2022). The current research sheds light on the critical role of TNFR2 in DC activation and the development of PsA, offering potential avenues for targeted therapeutic therapies. In this study, we are testing if targeting TNFR2 specifically in DCs using conditional knock-out mice can alleviate PsA.

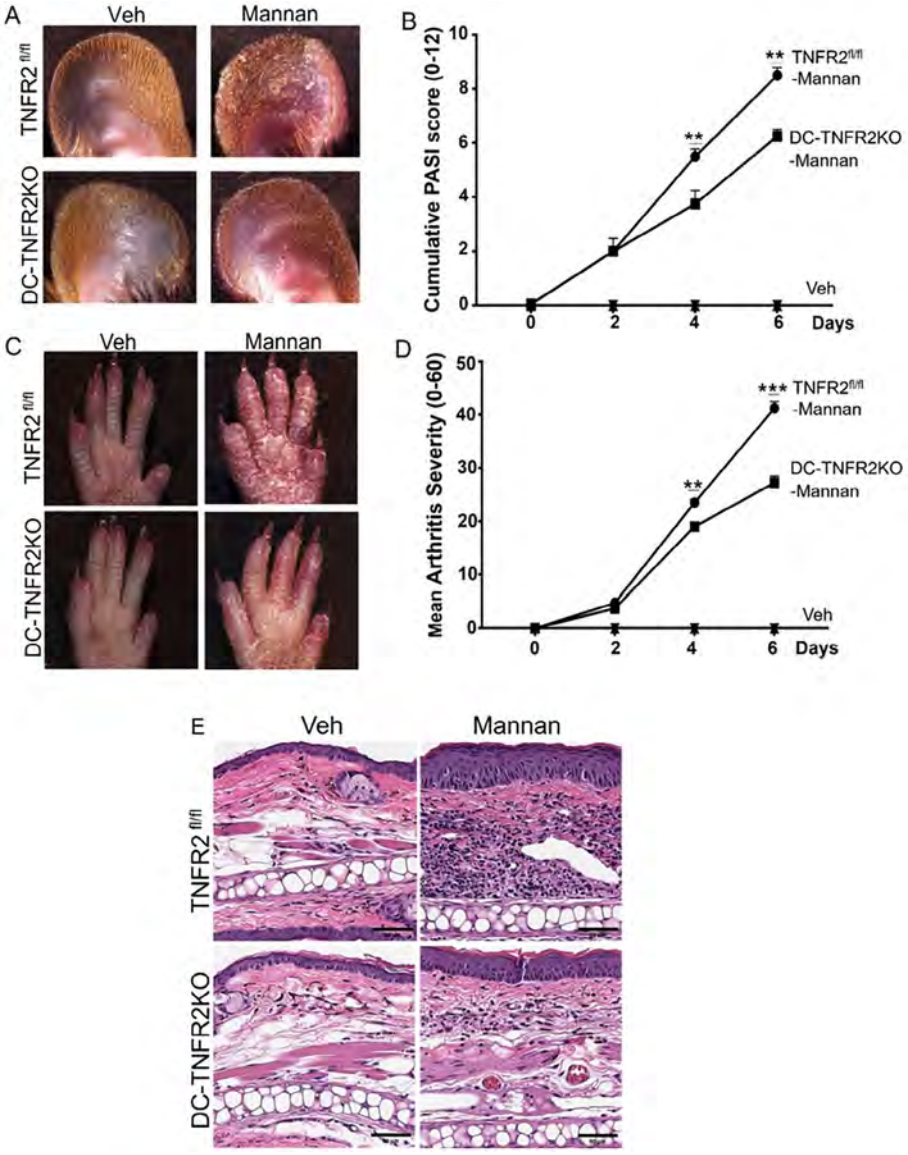

Figure 1: DC-TNFR2KO mice show reduced PsA-like disease development induced by Mannan: A. Psoriasis-like skin scaling in diseased TNFR2 fl/fl and DC-TNFR2KO mice compared with vehicle-treated mouse ear; B. PASI score of the ear; C. The arthritic phenotype (swelling and redness) and Psoriasis-like skin lesions in the hind paws of TNFR2 fl/fl and DC-TNFR2KO mice; D. Mean arthritis severity score of paws; E. Representative H &E staining of ear tissue from control and diseased TNFR2 fl/fl and DC-TNFR2KO mice; (n=6 each, ** represents p value <0.01; *** represents p value <0.001).

Methods: We investigated the impact of DC-specific TNFR2 knockout (DC-TNFR2KO) on skin lesions and joint inflammation in a mouse model of psoriatic arthritis induced by Mannan (Khmaladze et al., 2014). Psoriasis Area and Severity Index (PASI) Score and arthritis severity score calculations were performed on $TNFR2^{fl/fl}$ (control) and DC-TNFR2KO mice ($TNFR2^{fl/fl}$-CD11cCre). Histological evaluations were performed on ear skin and paw samples using H&E staining and safranin staining, respectively. Histopathological analyses and scoring were conducted in a blinded manner by independent investigators. Additionally, ELISA was used to determine whether DC-dependent cytokine production was altered in DC-TNFR2KO mice in response to Mannan treatment. Statistical analyses were performed with the SPSS version and Prism (GraphPad Software, San Diego, CA).

Results: Following Mannan injection $TNFR2^{fl/fl}$ mice developed PsA-like skin lesions and joint inflammation, while DC-TNFR2KO mice exhibited minimal symptoms (**Figure 1A-B**). The cumulative PASI score was significantly lower in DC-TNFR2KO mice compared to $TNFR2^{fl/fl}$ mice at days 4 and 6 after Mannan injection ($p < 0.01$, each). The mean arthritis severity score was also lower in DC-TNFR2KO mice ($p < 0.01$; $p < 0.001$) (**Figure 1 C-D**). Histological examination revealed that $TNFR2^{fl/fl}$ mice had significantly increased epidermal thickness (**Figure 1E**) and leukocyte infiltration compared to DC-TNFR2KO mice after Mannan injection ($p < 0.001$; $p < 0.01$). Safranin O staining showed cartilage loss in both $TNFR2^{fl/fl}$ and DC-TNFR2KO mice, however, it was less in TNFR2KO compared to $TNFR2^{fl/fl}$ mice ($p< 0.05$). Furthermore, we found diminished levels of IL-12, IFN-γ and TNF-α in the serum of DC-TNFR2KO mice compared to $TNFR2^{fl/fl}$ mice, post Mannan treatment ($p< 0.0001$; $p< 0.001$; $p< 0.01$ respectively).

Conclusion: Targeting TNFR2 specifically in dendritic cells can alleviate skin and joint inflammation in a mouse model of PsA. This study provides insights into the mechanistic role of TNFR2 in PsA pathogenesis and may contribute to the development of novel therapies for this debilitating disease.

Disclosure: R. Kaur: None; **M. Husni**: AbbVie, 1, 2, Amgen, 1, 2, Bristol-Myers Squibb, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, UCB, 1, 2; **U. Chandrasekharan**: None; **R. Brambilla**: None.

Abstract Number: 1785

Machine Learning Models Identify Gut Microbiota That Predict Chronicity in Reactive Arthritis

Prakashini MV[1], Soumendu Mahapatra[2], Krushna Chandra Murmu[2], Rasmita Mishra[2], Prasanta Padhan[1], Punit Prasad[2], Ramnath Misra[3] and Sakir Ahmed[4], [1]Kalinga Institute of Medical Sciences, KIIT University, Bhubaneswar, India, [2]Institute of Life Sciences, Bhubaneswar, India, [3]Kalinga Institute of Medical Sciences, KIIT University, Lucknow, India, [4]Kalinga Institute of Medical Sciences, Bhubaneswar, India

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Reactive arthritis (ReA) is the unique infection-triggered spondyloarthritis (SpA). Undifferentiated peripheral SpA (UpSpA) is similar but without previous infection, or psoriasis or inflammatory bowel disease. Around 50-70% of these remit spontaneously while the rest become chronic. There are no known markers of chronicity. We have previously described novel gut-microbiota associated with ReA/UpSpA[1]. Now, we have attempted to use these microbiota to predict which of these patients would develop chronicity.

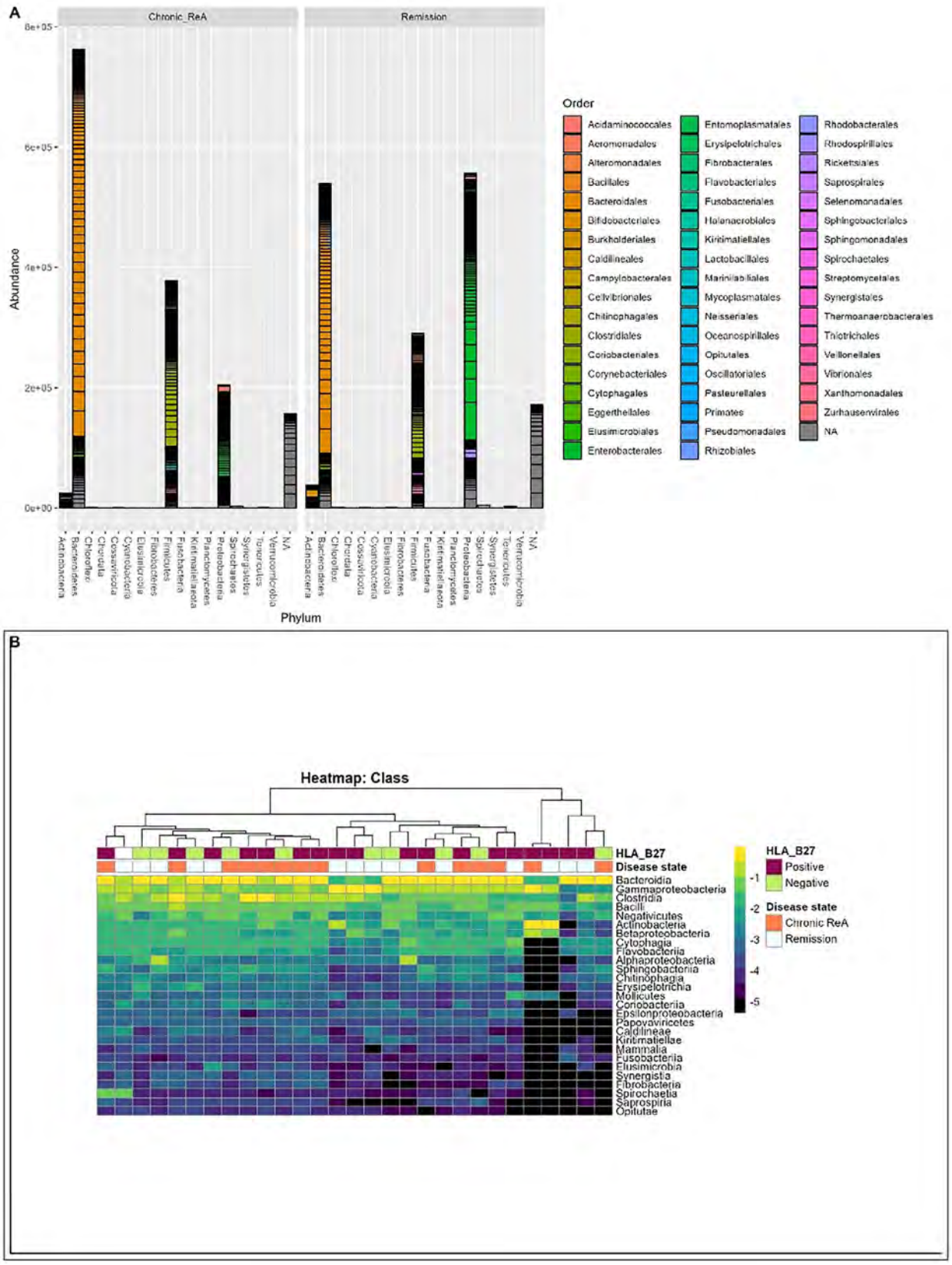

Figure 1: A – Differential abundance shown at phylum level. The Bacteroidetes to Firmicutes ratio is higher in the Chronic ReA group, as compared to Remission group; B – Heatmap visualizing the differential abundance at class level with dendrogram showing the phylogenetic relationship between different samples.

Methods: ReA and UpSpA recruited in the previous study[1] were followed up at 3 years after the initial recruitment. They were classified as having "Chronic ReA" (still on DMARDs or having symptoms of SpA) or in "Remission" (drug-free and without any symptoms in the last 12 months). A standard pipeline was used to analyze differentially abundant microbiota

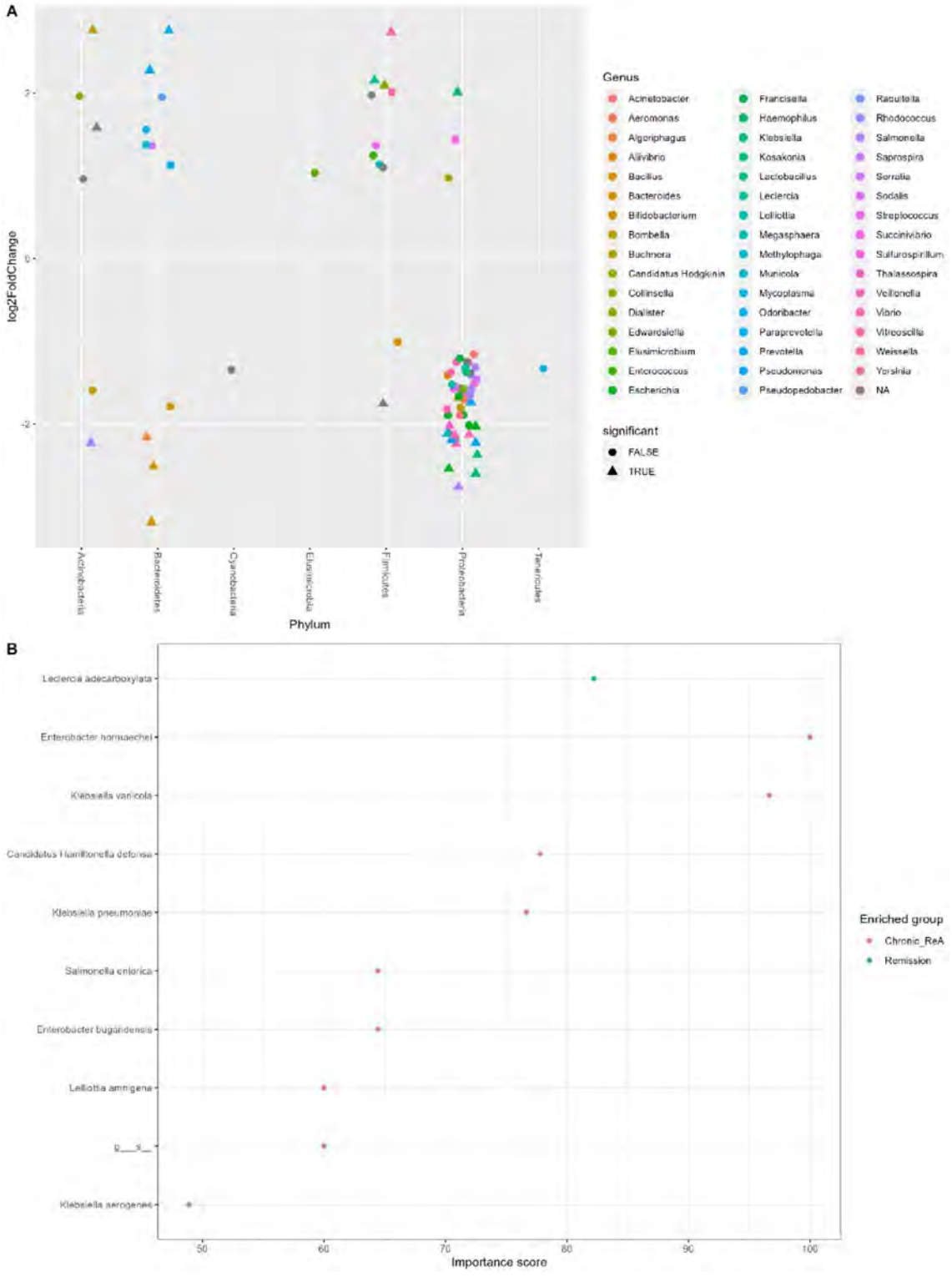

Figure 2: A – Microbiota that are at least 2-log-fold change different between chronic reactive arthritis and remission groups, stratified by Phylum. Statistically different genera (False Discovery Rate <0.05) are shown as triangles. B – Species that are most important for predicting chronicity of Reactive Arthritis as per Linear Regression Machine learning model.

between Chronic ReA and Remission groups. Further, the groups were randomly divided into training (80% data) and validation (20% data) sets. Clinical features (disease duration, DMARD use, HLA-B27 status) and microbiota of differential abundant families were analyzed by supervised machine learning algorithms (Support Vector Machine: SVM and Linear Regression: LR) to build models that could predict the development of chronicity of ReA.

Table 1: Clinical characteristics ReA – Reactive Arthritis; IQR – Interquartile range; NA – Not applicable; DMARD – Disease modifying anti-rheumatic drugs; VAS – Visual analogue score; HAQ-DI – Health assessment questionnaire-disability index; HLA – Human leukocyte antigen. *p<0.05

Table 1: Clinical characteristics

Characteristics	Chronic ReA (N=14)	Remission (N=15)	p-value
Male: Female	9:5	10:5	0.9
Median age (IQR) in years	29.5 (25.7-37.2)	29 (24-35)	0.62
Axial involvement	4 (28.5%)	0	NA
Uveitis	1	0	NA
Duration of DMARD exposure (IQR) in weeks	170 (147.7-183.4)	27 (24-35.7)	0.01*
Number of patients who received DMARDs ever	7 (50%)	4 (26.7%)	0.2
DMARDs used (ever):			NA
Methotrexate	0	2	
Sulfasalazine	5	0	
Tofacitinib	2	0	
Etanercept	0	1	
HLA-B27	10 (71.4%)	4 (26.7%)	0.015*
Pain-VAS at baseline (Median with IQR)	7.4 (5.5-9.1)	7.6 (4.4-8.4)	0.47
HAQ-DI at baseline (Median with IQR)	0.5 (0.38-0.8)	0.5 (0.3-0.5)	0.58

ReA – Reactive Arthritis; IQR – Interquartile range; NA – Not applicable; DMARD – Disease modifying anti-rheumatic drugs; VAS – Visual analogue score; HAQ-DI – Health assessment questionnaire-disability index; HLA – Human leukocyte antigen.

*p<0.05

Results: Out of the initial 55 cohort, 29 patients consented for the follow-up. 14 (48.3%) patients had chronic ReA. The clinical features are summarized in Table 1. The baseline microbiome data showed that alpha diversity (Observed, Shannon, Simpson, Fisher, InvSimpson) as well as Beta diversity (Bray-Curtis and Unweighted UniFrac) was similar between the two groups. After applying stringency filters (excluding OTUs that did not appear more than 5 times in least half the samples), the differential abundance is shown at the Phylum (Figure 1A) and Class levels (Figure 1B). Amongst microbiota whose abundance was at least log-2-fold different between Chronic ReA and Remission groups, we could identify 29 OTUs (Figure 2A) that were significantly different (FDR< 0.05). The maximum difference was seen for *Bacteroides ovatus* (log2fd=3.19), *Salmonella sp*. HNK130(2.76), *Escherichia coli* (2.54), *Bacteroides fragilis* (2.51) that were more abundant in the Chronic ReA group while *Veillonella parvula* (-2.74), *Prevotella dentalis* (-2.76), and *Bifidobacterium adolescentis* (-2.76) were more abundant in the Remission group. In the SVM model, the most accurate model was the one incorporating HLA-B27, the use of methotrexate and of sulfasalazine, and the families Enterobacteriaceae and Bifidobacteriaceae. The validation cohort showed an accuracy of 83% (95% CI: 0.36-0.99). Figure 2B summarizes the species most important for prediction in the LR model.

Conclusion: We have identified microbiota that can predict the chronicity of ReA. However, the accuracy of the prediction can be improved upon with larger cohorts with prospective validation. **Reference:** < 1. Ahmed S, Mishra R, Mahapatra S, Murmu KC, Padhan P,Prasad P, Punit and Misra R. 16S Metagenomics Reveals Unique Diversity and Novel Gut Microbiota Associated with Reactive Arthritis. Available at: ssrn.com/abstract=4455358.

Disclosure: P. MV: None; **S. Mahapatra**: None; **K. Murmu**: None; **R. Mishra**: None; **P. Padhan**: None; **P. Prasad**: None; **R. Misra**: None; **S. Ahmed**: Cipla, 6, DrReddy's, 6, Janssen, 6, Novartis, 6, Pfizer, 6.

Abstract Number: 1786

Newly Identified Gut Commensal *Clostridium Fessum* AM100 for Treating Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing spondylitis (AS) is an inflammatory disease of the spinal joints leading to progressive loss of spinal mobility and chronic pain. Gutdysbiosis has been reported implicated in the pathogenesis of AS, however,the functionally relevant microbial changes and the underlying molecular mechanisms remain unclear. The object of this study is to determine the key microbes in AS by meta-analysis of the metagenomic data and to examine the underlying mechanism in a proteoglycan-induced spondylitis (PGISp) mouse model of AS.

Methods: For human cohorts, meta-analysis of the fecal metagenomic data from three published cohorts was performed. Raw FASTQ files were downloaded from the ENA and NCBI Sequence Read Archive. Taxonomic profiles were generated with the mOTU profiler v.2.5.1. *Clostridium fessum*AM100 was isolated from the fecal sample of a healthy donor. The PGISp model was established to examine the effect of the strain. PGISp mice were orally inoculated daily with 10^8CFU of live AM100 diluted in 200ul PBS. The administration of AM100 was sustained across the entire time course of the experiment.

Clinical and histological analysis were performed based on the standard scoring system. Plasma IL-17A and colon lamina propria Th17 levels were assessed using ELISA and flow cytometry, respectively. New bone formation of the mouse spine was examined by micro-CT at week 20.

Results: We foundan as-yet-uncharacterized species *Clostridialesspecies*[meta_12476] with the most pronounced change between AS and the control group (FDR_{Total}= 6.95×10^{-7}), whichwas decreased in the fecalsamples from AS patients. The downregulation ofthe specieswas only found in AS patients, but not in RA patients. Next, we isolated this bacterial strain from the stool sample of a healthy male and named it*Clostridium fessum*AM100 (Figure 1).

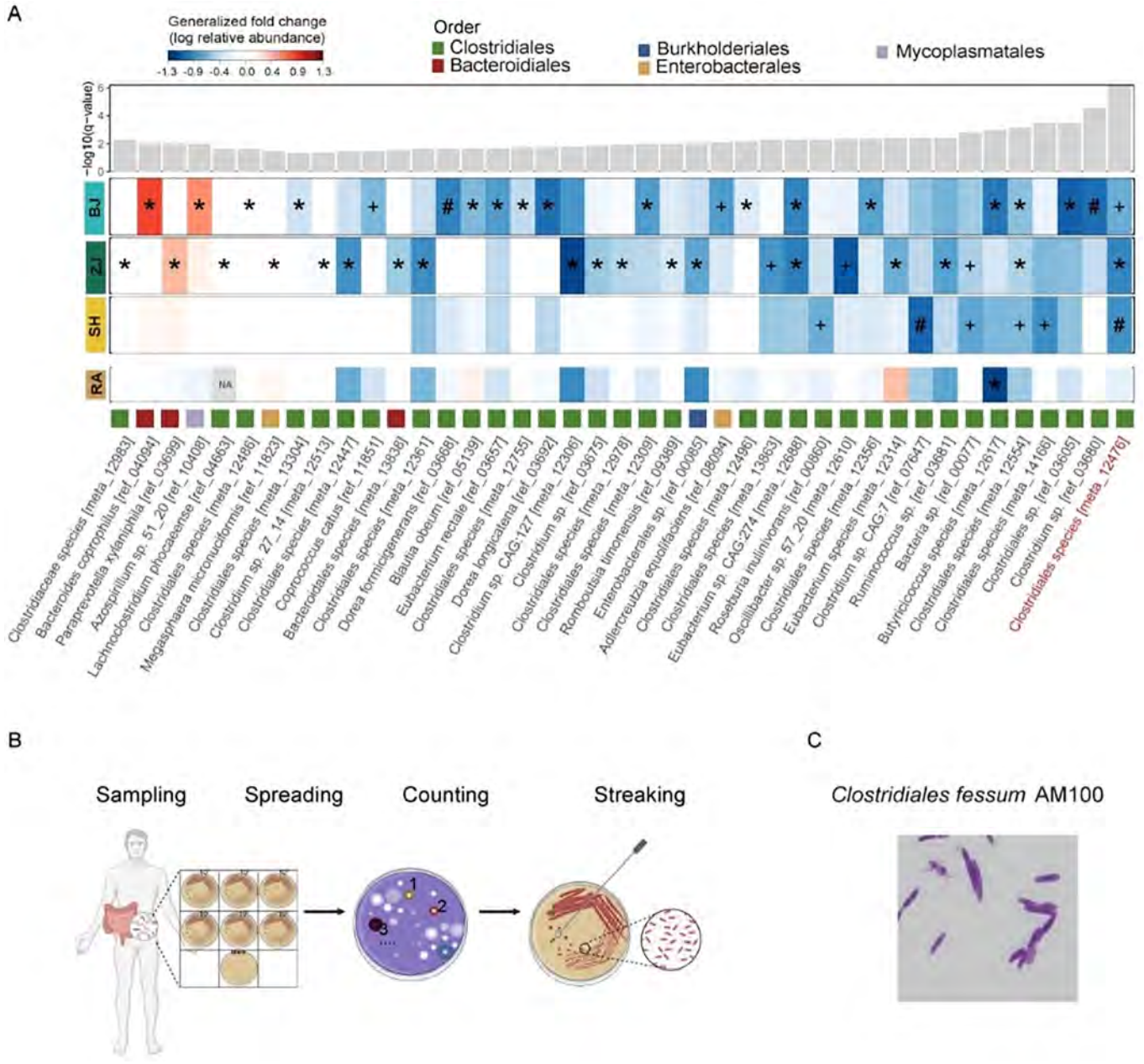


Figure 1. Gut microbial differences between AS patients and controls. (A) Heatmaps in gray and in colors showing the species-level significance, as calculated with a two-sided Wilcoxon test (FDR corrected P value), and the generalized fold change within individual studies. (B) The workflow of isolating C.fessum AM100 from male human feces. (C) Micrograph showing strain C.fessum AM100 after gram staining.

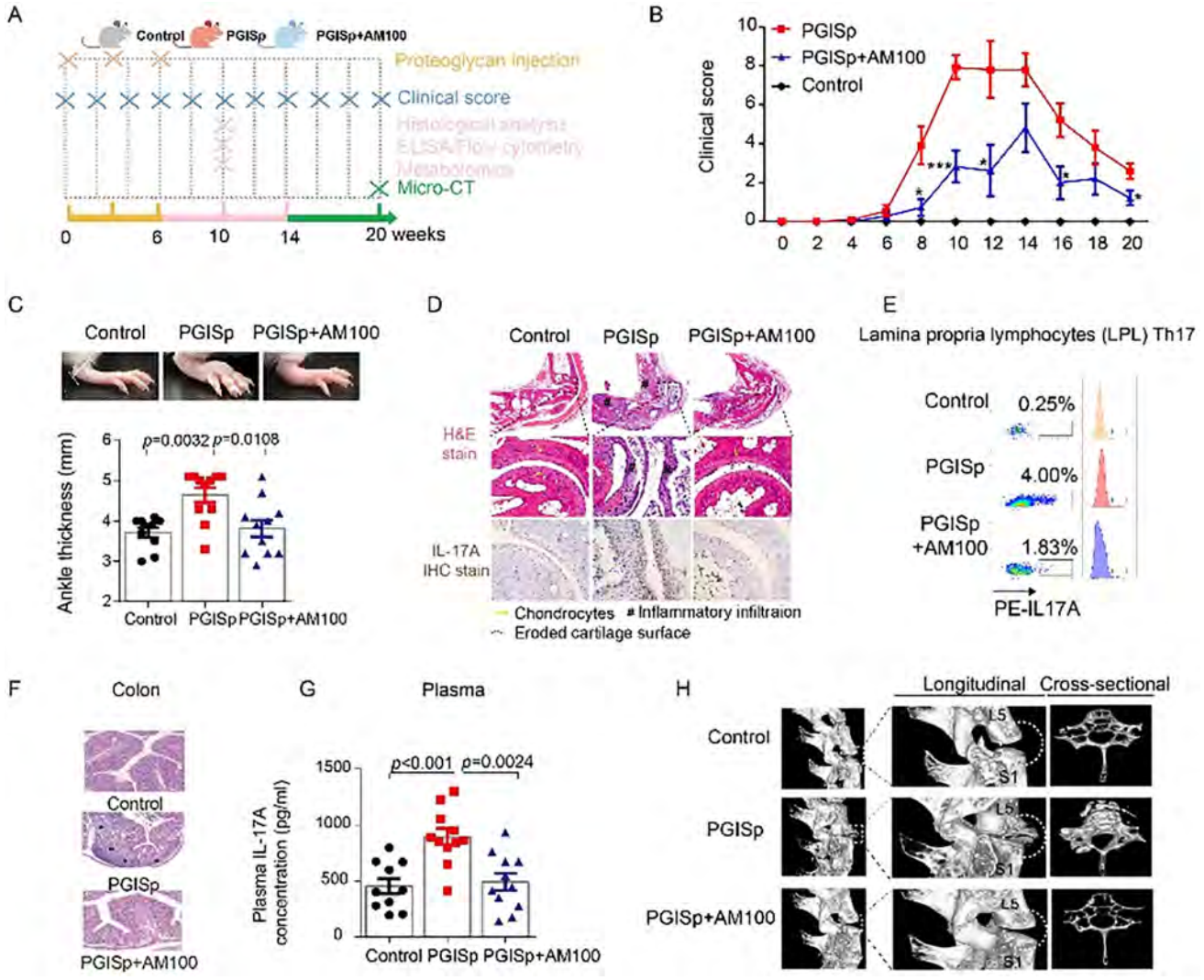


Figure 2. C.fessum AM100 ameliorates proteoglycan-induced spondyloarthritis (PGISp) in mice. (A) Schematic diagram showing the experimental design. (B) Clinical scores in control (n=10), PGISp (n=11), and PGISp mice with AM100 treatment (n=11). (C) Representative photographs of hind paws and ankle thickness. (D) Hematoxylin-eosin staining (H&E), and IL-17A immunochemistry staining images. (E) Flow cytometry analysis of Th17 cells in the LPLs. (F) Histological analysis of distal colon of mice. (G) Serum concentration of IL-17A. (H) Representative micro-CT images showing the lumbar spines and sacroiliac joints (L5-S1) at week 20.

Oral administration of *C.fessum*AM100 alleviated the AS symptoms in PGISp mice in terms of arthritis clinical score and hind paw ankle thickness. The inflammatory infiltration and synovial erosion were improved by *C.fessum*AM100. Compared with PGISp mice, AM100 treatment considerably decreased the percentage of Th17 cells among colonic lamina propria lymphocytes (cLPL), accompanied by the alleviation of colitis. AM100 significantly suppressed the cytokine production of IL17A in the plasma at week 10. At the advanced phase, AM100 delayed syndesmophyte formation in the PGISp mice (Figure 2). Metabolome analysis revealed that putrescine and γ-aminobutyric acid (GABA) were enriched in AM100 fermentation supernatant. Also, putrescine and GABA displayed anti-inflammatory effectsin vivo (Figure 3).

Conclusion: We demonstrated the key microbe *Clostridium fessum*AM100, significantly depleted in the feces of AS patients, can suppress the IL-17A-related inflammation and delay new syndesmophytes formation in the PGISp model of AS. Putrescine and GABA can mimic the beneficial effects of *C.fessum* AM100. This study suggests that *C. fessum*AM100 might serve as an attractive probiotic for the treatment of AS patients.

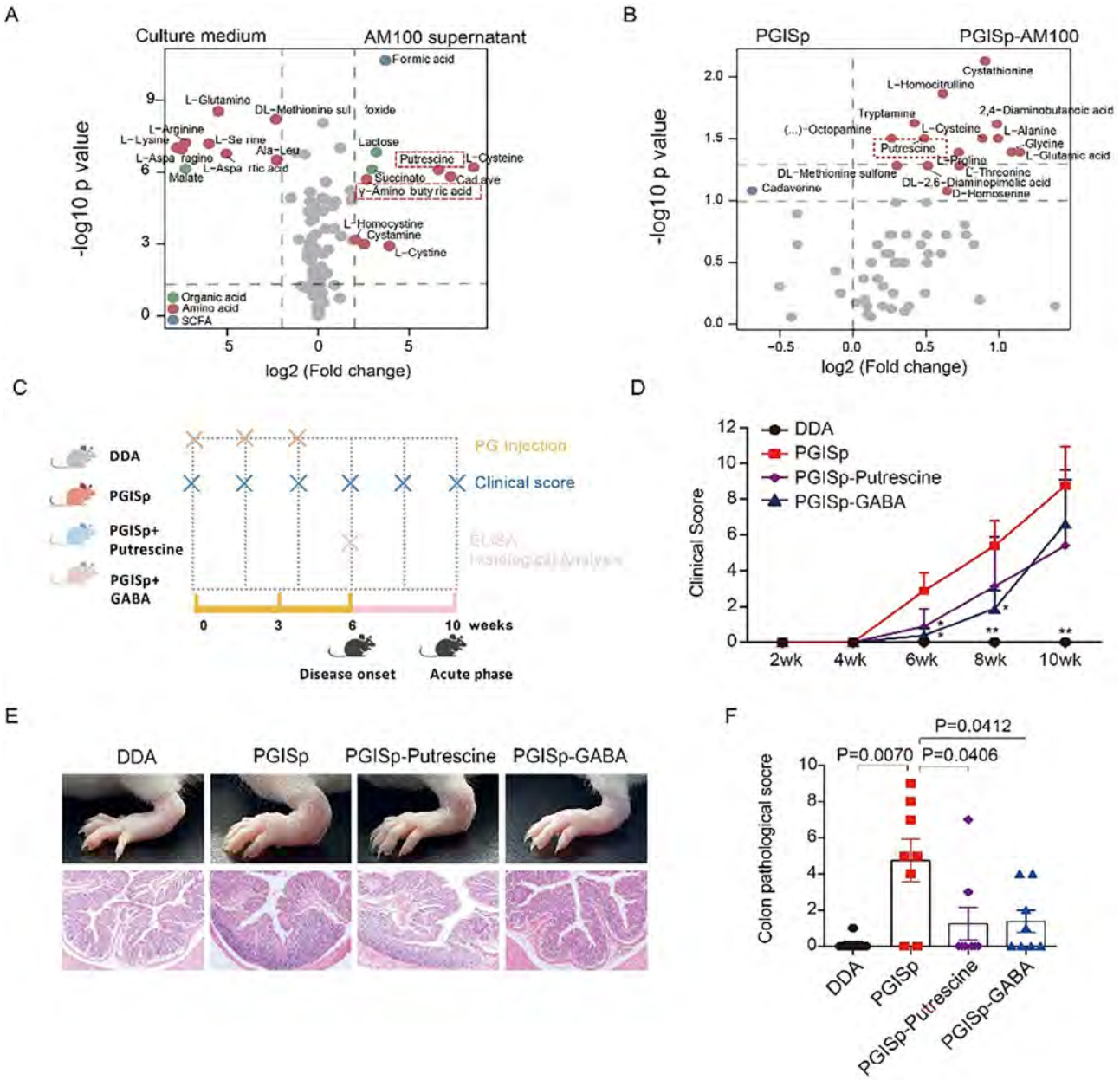


Figure 3. C.fessum AM100 ameliorates disease symptoms in mice by producing putrescine and GABA. (A) Targeted Metabolomics analysis revealed the significantly altered metabolites in AM100 fermentation supernatant vs. Culture medium, and (B) the feces of AM100-treated PGISp mice vs. PGISp mice. (C) Schematic diagram showing the experimental design. (D) Clinical scores in control, PGISp, and PGISp mice with putrescine and GABA treatment (n=8 for each group). (E) Representative photographs of hind paws and Hematoxylin-eosin (H&E) staining of the distal colon of mice. (F) Pathological severity of the colon was scored based on the severity of inflammation, damage of the crypt, and extension of lesions.

Disclosure: L. Bai: None; **C. Zhu**: None; **Y. Xu**: None; **K. Tang**: None; **D. Zhuo**: None; **Q. Zhang**: None; **C. Geng**: None; **W. Xu**: None; **H. Wu**: None; **X. Chen**: None; **J. Wang**: None.

Abstract Number: 1787

Regulatory Role of JAK-1/TYK2 Signaling on the Pannus Formation: Novel Mechanisms for JAK Inhibitors in Psoriatic Disease

Siba Raychaudhuri[1], Christine Abria[2] and Smriti K Raychaudhuri[2], [1]UC Davis, School of Medicine/ VA Medical Center, Sacramento, Davis, CA, [2]VA Sacramento Medical Center, Mather, CA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In psoriatic arthritis (PsA) aberrant activation/migration of specific T cell subpopulations (Th17/Th9/MAIT cells) in the joint synovium induce synovial inflammation and pannus formation. Several T cell cytokines such as IL-9, IL-17A/IL-17F, IL-22 and IL-23 play critical roles in the pathogenesis of PsA. IL-23 does not have any biological effect on synovial cells (FLS) and IL-17 does not activate the JAK/STAT signaling system. IL-9 and IL-22 have regulatory roles on proliferation of FLS; and as well JAK-1 and 3 are activated by IL-9; and JAK1/TYK2 by IL-22. Here to determine the functional significance of these signaling proteins on pannus formation we hypothesized that IL-9/IL22 induced JAK/STAT signaling regulates the proliferative cascades of FLS in PsA. We studied the regulatory role IL-9 induced JAK-1,3 and IL-22 induced JAK1/TYK2 on FLS biology.

Methods: FLS from PsA (n=10) were cultured as per our standardized protocol (Cytokine.2012;60:38-42) with rIL-9 (10ng/ml) and rIL-22 (100ng/ml). Proliferation was measured by MTT assay and CFSE dilution assay. IL-6, IL-8 and MMP3 levels were determined by ELISA. Immunoblot studies were done to assess JAK1/pJAK1, TYK2/pTYK2, STAT1/pSTAT1, STAT3/pSTAT3. Further to determine the molecular mechanisms of JAK inhibitors (JAKi) these experiments were done in the presence or absence of specific JAKi (JAK-inhibitor, Upadacitinib).

Figure 1

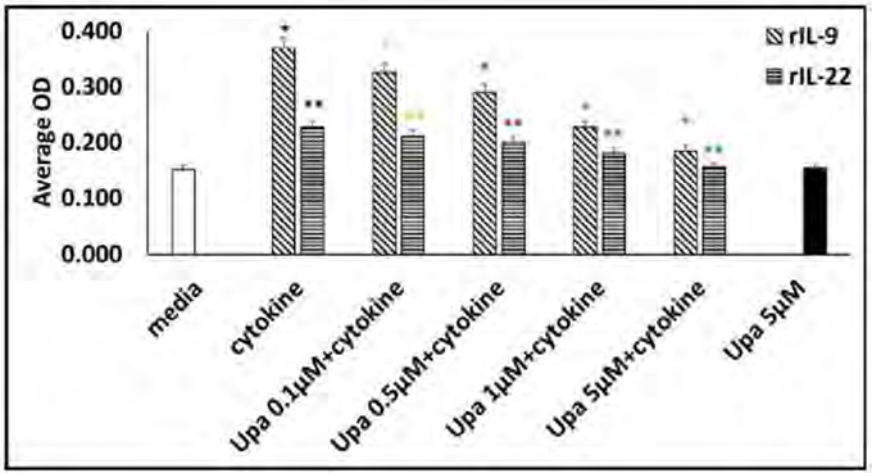


Figure 1: JAK-1 regulates rIL-9/rIL-22 induced proliferation of FLS. MTT assay results show that rIL-9/rIL-22 induced proliferation of FLS is inhibited by a specific JAK-1 inhibitor (upadacitinib). IL-9 and IL-22 increases FLS proliferation significantly compared to culture media ($p<.001$, t-test). Upadacitinib at several concentrations show significant inhibition of IL-9/IL-22 induced FLS proliferation compared to IL-9/IL-22 induced proliferation ($p<.001$).

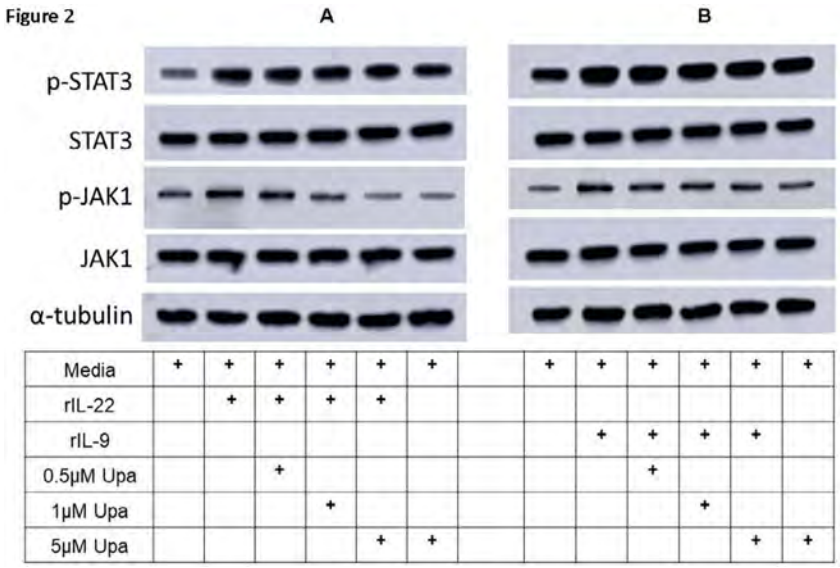


Figure-2: (A) immunoblot study of FLS demonstrates that rIL-22 induced phosphorylation of JAK-1 and STAT-3 were inhibited by specific JAK-1 inhibitor, upadacitinib. (B) immunoblot study of FLS demonstrates that rIL-9 induced phosphorylation of JAK-1 and STAT-3 were inhibited by specific JAK-1 inhibitor, upadacitinib.

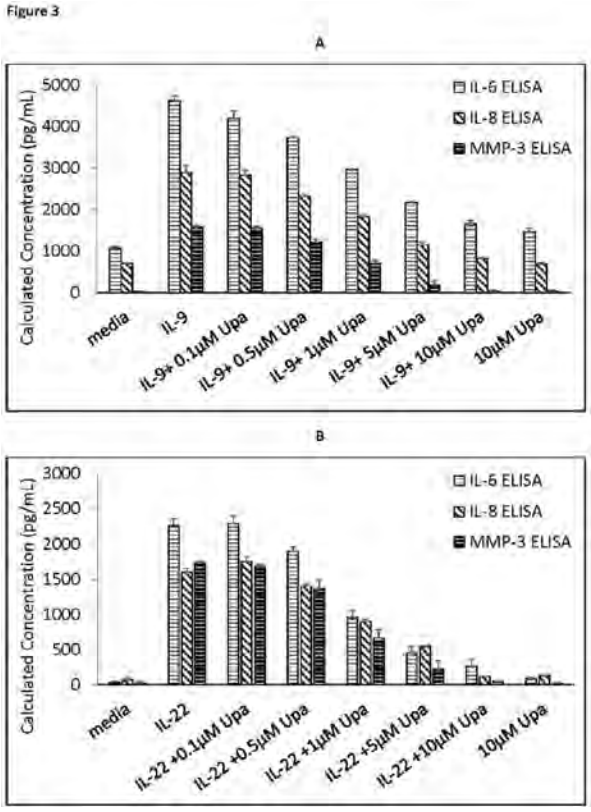


Figure 3: (A) rIL-9 induced IL-6, IL-8, MMP3 secretion by FLS was inhibited by JAK-1 inhibitor, upadacitinib. FLS were cultured with rIL-9 and several doses of upadacitinib. ELISA assay of culture supernatants showed significant inhibition of IL-6, IL-8 and MMP3 levels. (B) rIL-22 induced IL-6, IL-8, MMP3 secretion by FLS was inhibited by JAK-1 inhibitor, upadacitinib. FLS were cultured with rIL-22 and several doses of upadacitinib. ELISA assay of culture supernatants showed significant inhibition of IL-6, IL-8 and MMP3 levels.

Results: In cultured FLS we observed that rIL-22 and rIL-9 induced increased phosphorylation of JAK1/TYK2 and JAK1/JAK3 respectively compared to the culture media only, ($p< 0.01$). rIL9/rIL22 also phosphorylated STAT3/RORγt. We observed that the critical events in PsA such as (i) proliferation of FLS (ii) IL-6, IL-8 and MMP-3 production by FLS are induced by rIL-22 and rIL-9 and those were regulated by JAK1/TYK2 and JAK-1,3 respectively. Further pan-JAK inhibitors and other specific JAK-1 and TYK2 inhibitors blocked these effects significantly ($p< 0.01$). Details of some these observations on the regulatory role of JAK-1 are shown in the Figure 1. Figure-1 demonstrates that rIL-9r/rIL-22 induced proliferation of FLS could be inhibited by blocking JAK-1 with JAKi (upadacitinib) by MTT assay; Figure-2 shows the regulatory role of rIL-22 on JAK/STAT phosphorylation in FLS and Figure-3 demonstrates regulatory role of JAK-1 on FLS in respect to local cytokine and metalloproteinase production.

Conclusion: JAK/STAT signaling system of T cells and its regulatory role in the pathogenesis of psoriatic disease is well established.This study provides a novel insight about the role for JAK-1 and TYK2 signaling on pannus formation and demonstrates novel therapeutic targets for treatment of psoriatic disease.

Disclosure: S. Raychaudhuri: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, SUN Pharma, 2, 5, 6, UCB, 2, 5, 6; **C. Abria**: None; **S. Raychaudhuri**: None.

Abstract Number: 1788

The Emerging Mechanism of TNF&IL-17A/WNT5a/ROR2 Axis in Pathological Bone Formation of Ankylosing Spondylitis

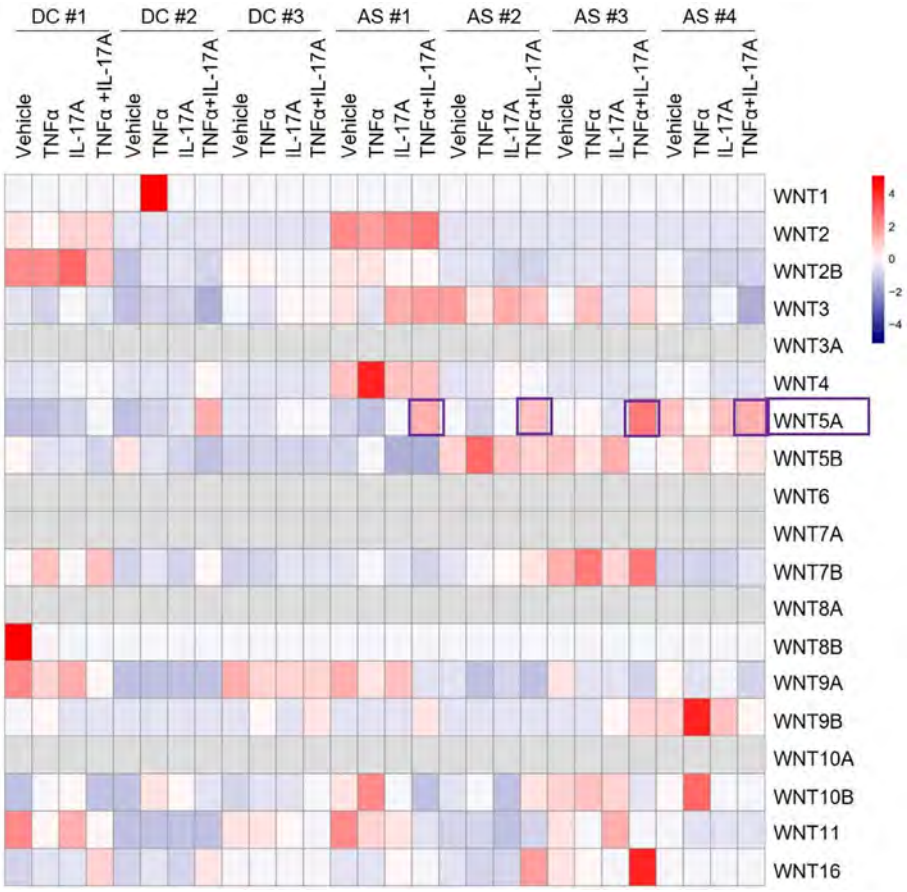
Sungsin Jo[1], Seung Hoon Lee[1], Chanhyeok Jeon[1], Sung Hoon Choi[2], Ye-Soo Park[3] and Tae-Hwan Kim[4], [1]Hanyang University Institute for Rheumatology Research, Seoul, South Korea, [2]Hanyang University Seoul Hospital, Seoul, South Korea, [3]Hanyang University College of Medicine, Guri, South Korea, [4]Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, South Korea

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

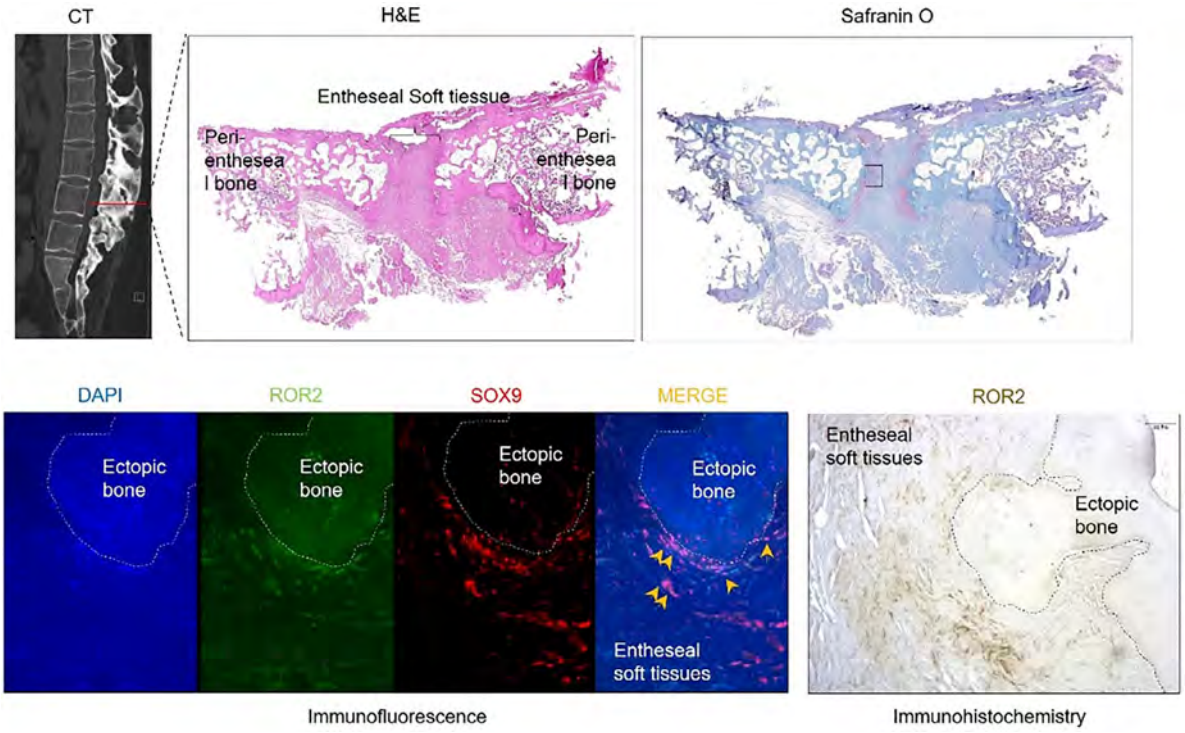
Background/Purpose: Enthesitis is one of the most distinctive features and signs of ectopic bone formation in ankylosing spondylitis (AS). The Wnt/β-catenin pathway and Th17 cells are closely associated with pathological bone formation in AS, but their association has not been fully understood.

Methods: Twenty-five healthy control (HC) and seventy AS sera was subjected to ELISA for human TNF, IL-17A, and WNT5a. Ten PBMC (three HC and seven AS) and seven enthesis cells (three control- and four AS-enthesis) were conducted to RNA-sequencing. WNT5a and Receptor tyrosine kinase like orphan receptor 2 (ROR2) expression in enthesis were validated by immunohistochemistry analysis in five diseases control and seven AS patients. Next, overexpression or knockdown of ROR2 in primary enthesis was assessed bone-forming activity in the presence or absence of WNT5a treatment. Finally, enthesitis and ectopic bone formation at the ankle were evaluated in treatment with Ror2 mouse shRNA lentiviral particle in curdlan-injected SKG mice.

Results: TNF, IL-17A and Wnt5a in AS sera were significantly increased and positively correlated with mSASSS. Co-treatment with TNF and IL-17A dramatically increased WNT5a expression in AS-enthesis cells, as evaluated by RNA-sequencing, RT-qPCR, immunoblotting, and ELISA. Also, co-treatment with TNF and IL-17A augmented the bone-forming



We found that co-treatment with TNF and IL-17A dramatically increased WNT5 expression in AS-enthesis.



We found that ROR2 is highly expressed in the ectopic bone of the human AS spinous process.

activity, bone-related gene expressions (ALP, RUNX2, and OCN), and WNT5A in AS-enthesis cells accompanied as compared to diseases control. Moreover, WNT5A treatment not only upregulated RUNX2 and CTCF expression in AS-enthesis cells via ROR2, but also showed excessive bone-forming activity under osteogenic stimulation. Intriguingly, an increase ROR2 expression in AS enthesis was revealed by RNA sequencing and validated at ectopic bone in spinal enthesis tissues from AS patients. Overexpression of ROR2 in enthesis had an accelerating bone-forming effect in Wnt5a treatment, whereas the knockdown of ROR2 in enthesis had shown the delaying bone-forming activity of AS enthesis in WNT5a treatment. Finally, treatment of Ror2 mouse shRNA lentiviral particle in curdlan-injected SKG mice exhibited a significant decrease in enthesitis and ectopic bone formation at the ankle.

Conclusion: We found that synergism of TNF and IL-17A triggers acceleration of bone mineralization and new bone formation in enthesis via WNT5/ROR2 axis. TNF&IL-17A/WNT5a/ROR2 axis may play a crucial role in pathological new bone formation in AS.

Disclosure: S. Jo: None; **S. Lee**: None; **C. Jeon**: None; **S. Choi**: None; **Y. Park**: None; **T. Kim**: None.

Abstract Number: 1789

Microtrauma Exacerbates Arthritis and Enthesitis in Curdlan-administered SKG Mice by Inducing FGF16 Expresssion

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Microtrauma might be considered a crucial of various environmental factors in AS, but there is still unknown whether microtrauma has a direct/indirect role in the pathogenesis of AS.

Methods: To induce microtrauma injuries, right hindlimb of male SKG mouse was immobilized by a surgical sticking plaster and pipette tip for a week. After this period, the fixed tip was removed from ankle and the mouse was intraperitoneally injected with 3 mg curdlan. Left and Right ankles were considered microtraumatized and non-microtraumatized group, respectively. We monitored clinical arthritis to score it every week for 5 weeks. At 6 weeks, the physical changes in ankles and sacroiliac joints were evaluated by histological and micro-CT analysis. Primary muscle cells were induced by shear stress for a day to mimic microtrauma and conducted RNA-sequencing.

Results: After curdlan injection in SKG mice, the left ankle was microtraumatized and showed an increase in frequency and severity of arthritis and enthesitis when compared to the non-microtraumatized right ankle. Also, as revealed by micro-CT analysis, the inflamed bone volume was decreased in the heel of non-microtraumatized right ankle, whereas dramatically increased in heel of microtraumatized left ankle. Moreover, TNFa expression in enthesis and arthritis of ankle using IHC were much higher in microtraumatized left ankle than non-microtraumatized right ankle. Intriguingly, the SI joints of the left hip were shown cartilage fusion in the microtraumatized left as compared to the non-microtraumatized right. When RNA-sequencing data of shear stress was compared to non-stress groups, we found that the FGF16 gene is a top rank in the stress group. The expression of FGF16 was significantly elevated in the femur muscle of microtraumatized left ankle.

Conclusion: Here we showed that microtrauma at ankle using immobilization contributes to severity arthritis and enthesitis at ankle and induction of FGF16 in muscle of curdlan-injected SKG mice.

Disclosure: S. Lee: None; **C. Jeon**: None; **S. Jo**: None; **T. Kim**: None.

Abstract Number: 1790

Expansion of CD8+ TCRVβ9+ T Cells in the Peripheral Blood of HLA-B27+ Patients with Axial Spondyloarthritis

Caroline Bauchiero[1], Micah Lefton[1], Stephanie Sinnappan[2], Jeffrey Sparks[3] and Joerg Ermann[4], [1]Brigham and Women's Hospital, Boston, MA, [2]Columbia University, New York, NY, [3]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [4]Division of Rheumatology, Inflammation and Immunity, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

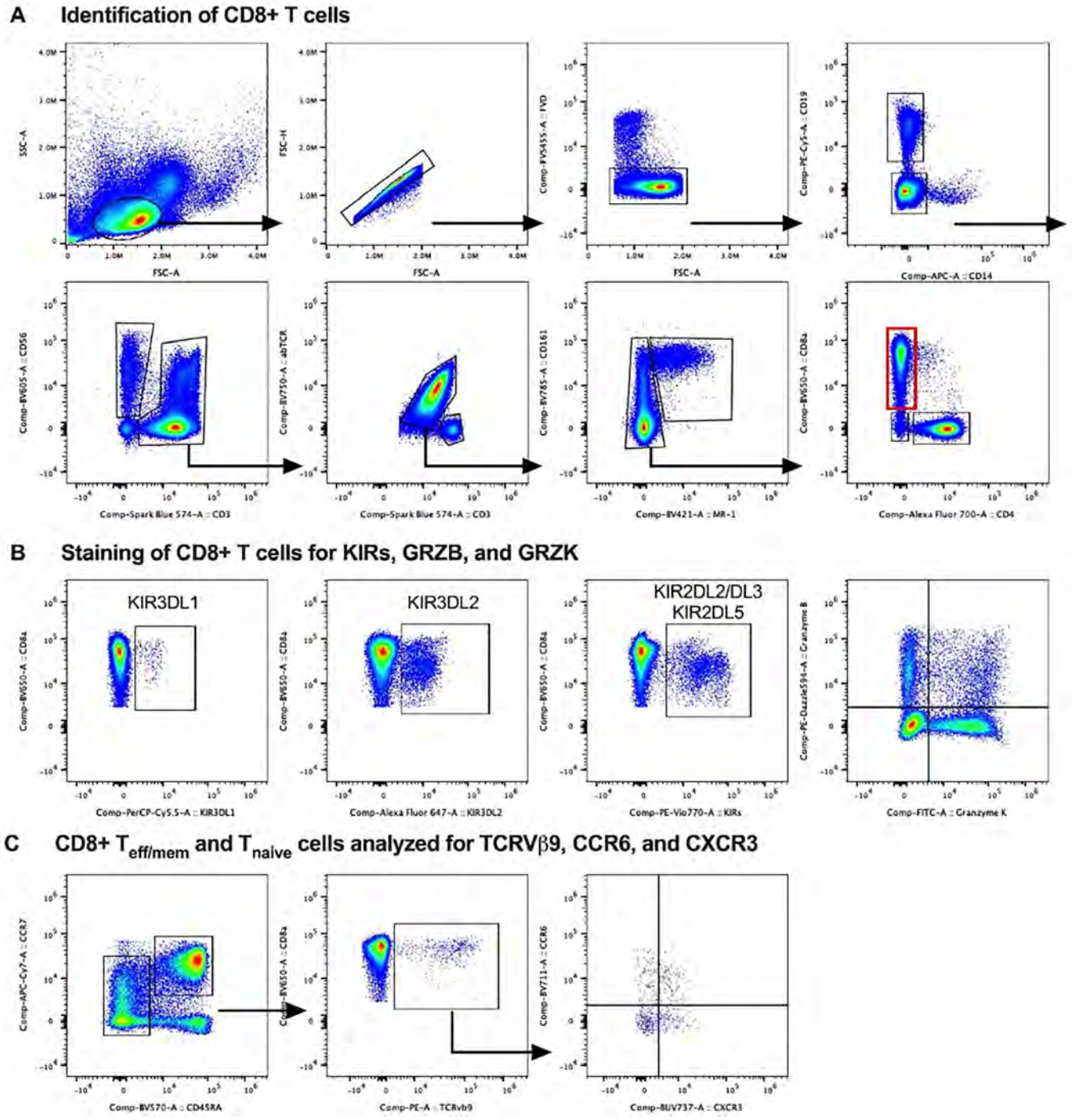
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Studies in human HLA-B27 transgenic rats largely discredited the idea that CD8+ T cells are key drivers of disease in axial spondyloarthritis (axSpA). However, recent studies in humans have revived interest in the role of CD8+ T cells in axSpA including the description of relevant CD8+ T cell subsets in a number of rheumatic disease settings (CD103+CD49a+ InEx cells, regulatory CD8+KIR+ T cells, Granzyme B and K expressing CD8+ T cell subsets) and the demonstration of expanded TCR clonotypes in the joints and eyes of HLA-B27+ SpA patients. In this study, we used state-of-the-art flow cytometry to search for diagnostic cellular biomarkers in axSpA reporting results for CD8+ T cells.

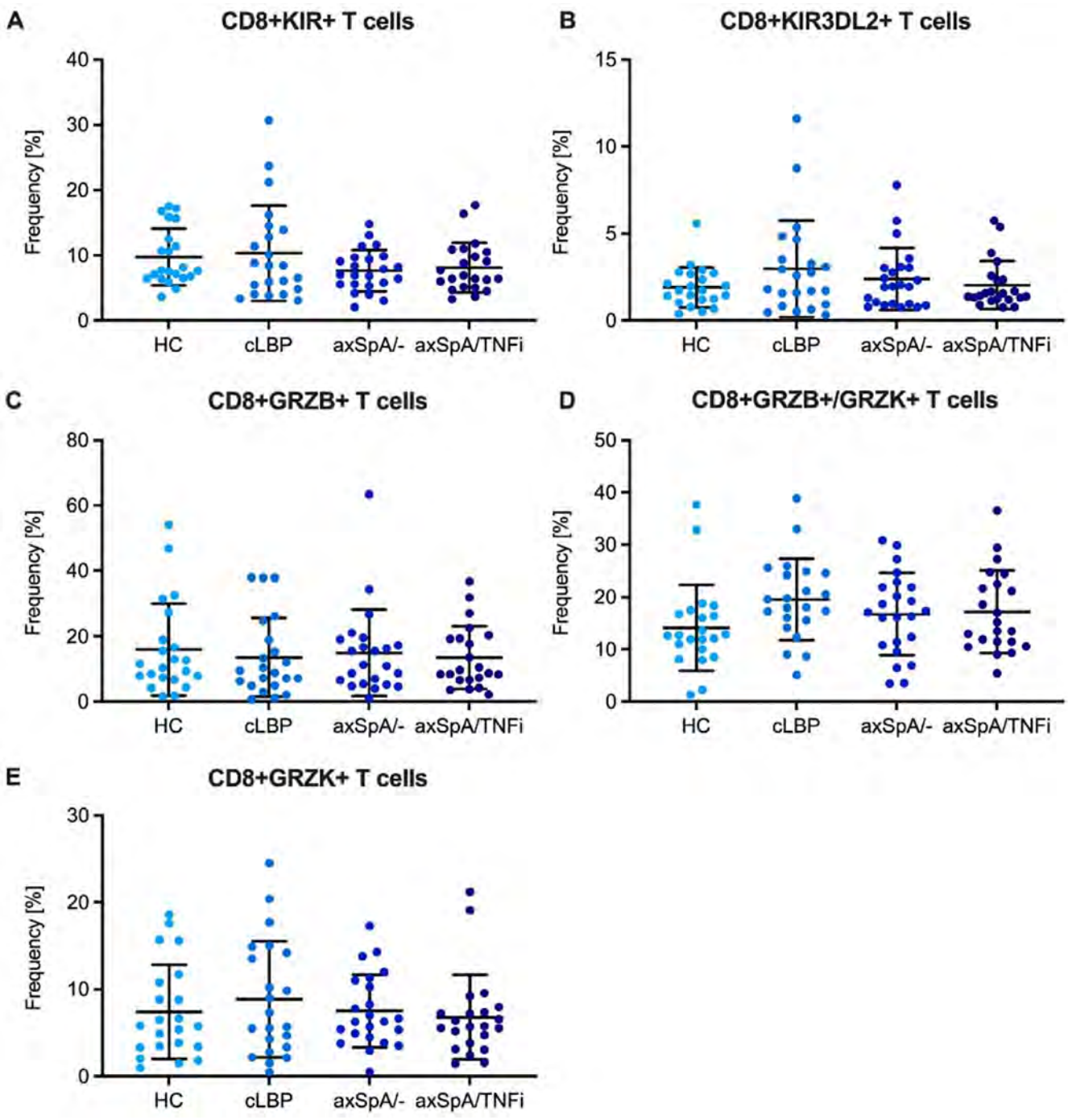
Methods: Study subjects were recruited from our hospital's Orthopedic and Arthritis Center. Four groups were compared: healthy controls (HC), patients with chronic low back pain without axSpA (cLBP), axSpA patients not on a biologic (axSpA/-), and axSpA patients treated with a TNF inhibitor (axSpA/TNFi). Groups (n=22-23 each) were matched for age, sex and genotyped for HLA-B27. All axSpA patients fulfilled modified New York criteria for ankylosing spondylitis or the 2009 ASAS criteria for axSpA. PBMCs were analyzed in two batches on a CYTEK Aurora spectral flow cytometer. Our customized 30-parameter staining panel included major lineage markers, lymphocyte differentiation and activation markers and functional markers for cytotoxicity, homing, and cytokine production potential. We included antibodies for KIR3DL1 (DX9), KIR3DL2 (DX31), KIR2DL2/L3 (DX27) and KIR2DL5 (UP-R1) as well as TCRVβ9+ (MKB1). Cells were further stained intracellularly for GRZB (GB11) and GRZK (GM26E7). FlowJo was used for quality control and analysis (see gating strategy in Fig. 1).

Results: There were no differences in the frequency of CD8+ T cells expressing any KIR or CD8+ T cells expressing the HLA-B27 binding KIR3DL2 between HC, cLBP, axSpA/- and axSpA/TNFi subjects (Fig. 2A,B). There were also no differences in the frequency of CD8+ T cell subsets distinguished by expression of GRZB and GRZK (Fig. 2C-E). About 2% of CD8+CD45RA^{lo}T$_{eff/mem}$ and CD8+CD45RA^{hi}CCR7+ T$_{naive}$ cells were TCRVβ9 positive without differences between groups. However, when only HLA-B27+ individuals were analyzed, we noticed an expansion of TCRVβ9+ cells amongst CD8+ T$_{eff/mem}$ cells in axSpA/- and axSpA/TNFi subjects, which was not seen in CD8+ T$_{naïve}$ cells or in the respective CD4+ T cell subsets (Fig. 3). Compared with control subjects, CD8+TCRVβ9+ T$_{eff/mem}$ cells in axSpA patients showed increased expression of CCR6 suggesting a Tc17 phenotype.

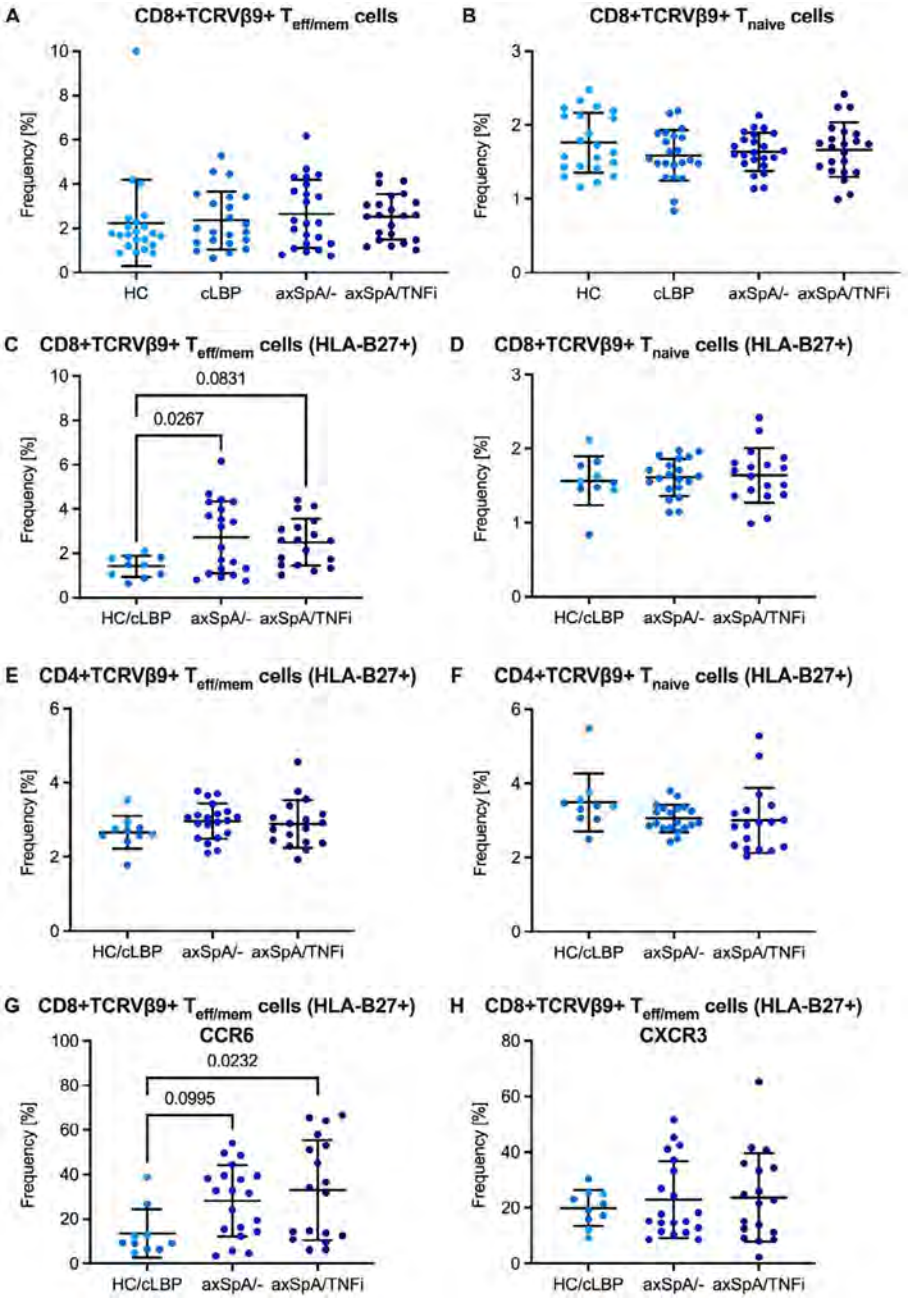
Conclusion: The observed expansion of CD8+Vβ9+ $T_{eff/mem}$ cells in the peripheral blood of HLA-B27+ patients with axSpA is consistent with the previously reported expansion of TRBV9–CDR3–TRBJ2.3 clonotypes in tissues and supports the peptide hypothesis for the HLA-B27 association with axSpA. The in-depth characterization of the CD8+TCRVβ9+ $T_{eff/mem}$ population using additional markers included in the staining panel is ongoing.



Gating strategy. (A) Identification of CD8+ T cells by hierarchical gating. (B) Staining of CD8+ T cells for expression of KIR3DL1, KIR3DL2, KIR2DL2/L3+KIR2DL5, and GRZB vs. GRZK. CD8+ T cells expressing any KIR were identified by Boolean gating (logic OR gate) in FlowJo. (C) CD45RA and CCR7 were used to identify CD8+ Teff/mem and Tnaive cells, which were then analyzed for expression of TCRVb9, CCR6 and CXCR3



(A) Expression of KIRs on total CD8+ T cells. Depicted is the fraction of CD8+ T cells that express any of the following KIRs: KIR3DL1, KIR3DL2, KIR2DL2/L3, KIR2DL5 (B) Fraction of KIR3DL2+ CD8+ T cells. (C-E) Fraction of CD8+ T cells expressing GRZB alone, GRZB and GRZK, or GRZK alone. Bars represent means and SD deviation. There were no significant differences between groups by one-way ANOVA.



(A, B) Fraction of TCRVb9+ cells amongst CD8+ Teff/mem cells and CD8+ Tnaive cells, respectively. (C, D) Fraction of TCRVb9+ cells amongst CD8+ Teff/mem cells and CD8+ Tnaive cells in HLA-B27+ individuals. HC (n=4) and cLBP (n=6) were pooled. (E, F) Fraction of TCRVb9+ cells amongst CD4+ Teff/mem cells and CD4+ Tnaive cells in HLA-B27+ individuals. (G, H) Fraction of CCR6+ and CXCR3+ cells amongst CD8+-TCRVb9+ Teff/mem cells in HLA-B27+ individuals. Bars represent means and SD deviation. P values were calculated by one-way ANOVA with post hoc Tukey's.

Disclosure: C. Bauchiero: None; **M. Lefton**: None; **S. Sinnappan**: None; **J. Sparks**: AbbVie, 2, Amgen, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, 5, Gilead, 2, Inova Diagnostics, 2, Janssen, 2, Optum, 2, Pfizer, 2, ReCor, 2; **J. Ermann**: AbbVie, 2, 5, Boehringer Ingelheim, 5, Janssen, 2, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, UCB Pharma, 2.

Abstract Number: 1791

Exploring the Mechanism of Anti-TNFα Therapy Non-response in Psoriatic Arthritis: The Role of TNF Receptor 2 Polymorphisms rs1061622

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite the widespread use of anti-TNFα therapy in psoriatic arthritis (PsA), a significant proportion of patients fail to achieve a complete treatment response. There are no predictive markers for response to TNFα blockade. Rs1061622 polymorphisms (T/T, T/G, or G/G genotypes) corresponds to a methionine with T allele or arginine with G allele at amino acid position 196 of TNFα receptor 2 (TNFR2). These polymorphisms in TNFR2 have been associated with treatment response in rheumatoid arthritis and PsA, with the G/G genotype being less likely to respond to anti-TNFα therapy compared to the T/T genotype. However, the underlying molecular mechanism explaining this association remains unknown. This study aimed to investigate the signaling differences between TNFR2 variants associated with rs1061622 polymorphisms carrying the T allele (TNFR2-196M) and G allele (TNFR2-196R), which could potentially elucidate the differential responsiveness to anti-TNFα therapy in PsA patients.

Methods: Gene expression studies were conducted in Jurkat T cells and primary human endothelial cells. Recombinant TNFR2-196M or TNFR2-196R were expressed in both cell types using a lentiviral approach. Cells were treated with TNFα alone (2 ng/mL) or TNFα in the presence of a TNFα neutralizing antibody. The expression of, ICAM-1, a TNFR2-dependent proinflammatory gene, was assessed using quantitative RT-PCR. These findings were further validated using human umbilical vein endothelial cells (HUVEC) with rs1061622 polymorphisms. The polymorphisms were determined

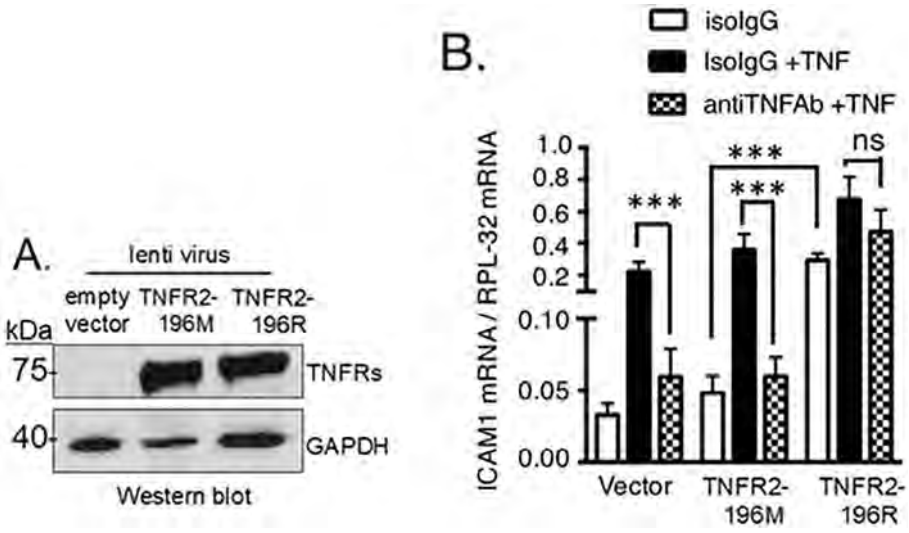

Figure 1. TNFR2-196R expressing Jurkat T cells show increased expression of ICAM-1 in the absence of TNFα. A) Western blot showing TNFR2-196M or TNFR2-196R protein expression using lentiviral approach. B) Using RTqPCR basal ICAM-1 mRNA abundance is significantly increased in TNFR2-196R over-expressing cells using lentiviral approach compared to control (vector) or TNFR2-196M over-expressing cells via lentiviral approach (white bars). This constitutive TNFR2-196R activity is not inhibited after treatment with anti-TNFα monoclonal antibody.

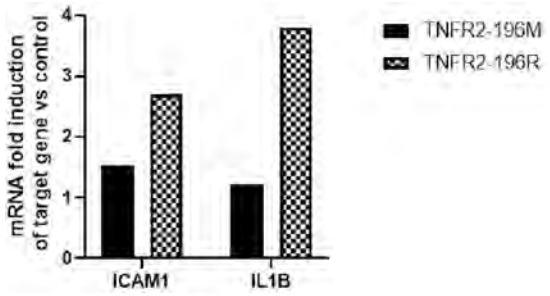

Figure 2. TNFR2-196R expressing HUVEC show increased expression of ICAM-1 and IL-1β in the absence of TNFα. Using RTqPCR basal ICAM-1 and IL-1β mRNA abundance is significantly increased in TNFR2-196R over-expressing cells via lentiviral approach (checkered) compared to uninfected HUVEC (normalized) or TNFR2-196M over-expressing cells via lentiviral approach (grey bars). Results are the average of two independent experiments.

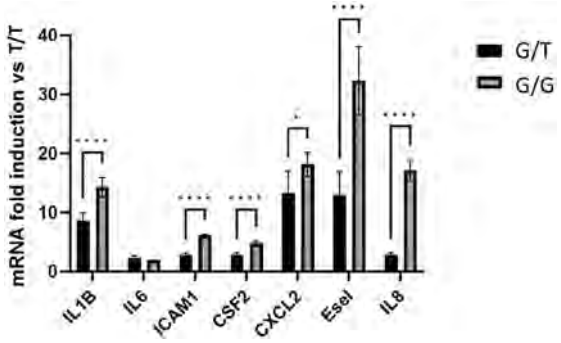

Figure 3. TNFα independent constitutive inflammatory activity in HUVEC expressing at least one G allele. Total RNA was extracted from HUVEC with T/T, T/G, or G/G genotypes. mRNA of indicated genes were quantified using RTqPCR after normalizing with mRNA levels of RPL-32, a housekeeping gene not induced by cytokines, including TNFα.

by genotyping (T/T, T/G, and G/G) discarded umbilical cord tissues prior to isolating and culturing the endothelial cells. Signaling pathways through TNFR2 were assessed using RTqPCR and Western blot analysis.

Results: In Jurkat T cells, successful expression of TNFR2-196M and TNFR2-196R was achieved (Figure 1A). Cells expressing TNFR2-196R exhibited increased basal expression of ICAM-1 compared to TNFR2-196M (Figure 1B). Importantly, treatment with a TNFα neutralizing antibody did not affect basal ICAM-1. Similarly, HUVEC cells over TNFR2-196R expressing (by lentiviral approach) showed increased ICAM-1 and IL-1β mRNA levels, while TNFR2-196M did not exhibit this effect (Figure 2). Furthermore, HUVEC isolated from subjects with G allele demonstrated higher basal expression of pro-inflammatory genes (IL-1β, IL-6, ICAM-1, GM-CSF2, CXCL2, E-selectin, Il-8) in the absence of TNFα (Figure 3). Notably, the TNFR2-independent gene P-selectin, did not show an increase in basal activity in cells expressing TNFR2-196R.

Conclusion: Our findings suggest that at least one G allele for the TNFR2 rs1061622 polymorphisms (TNFR-196R) confers a TNFα independent proinflammatory activity. These results may provide insights into a potential underlying mechanism for the association between rs1061622 polymorphisms and likelihood of response to anti-TNFα treatment in PsA. Further understanding of these signaling differences may contribute to the development of personalized treatment strategies for PsA patients based on their genetic profiles.

Disclosure: J. Sullivan: None; **V. Rai**: None; **J. Harvey**: None; **V. Del Signore**: None; **U. Chandrasekharan**: None; **M. Husni**: AbbVie, 1, 2, Amgen, 1, 2, Bristol-Myers Squibb, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, UCB, 1, 2.

Abstract Number: 1792

Identifying Synovial Fluid Micro-RNA Signature That Distinguishes Psoriatic Arthritis from Osteoarthritis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic Arthritis (PsA) is an inflammatory arthritis and shares several clinical features with Osteoarthritis (OA), the most common form of arthritis. This often leads to challenges in correctly diagnosing these diseases. Synovial Fluid (SF) from joints of arthritis patients contain a rich population of pathogenic modulators, such as microRNAs (miRNAs), making it a good source to study disease biomarkers. In this study, we aimed to 1) identify differentially expressed miRNA in SF of PsA and OA patients, and 2) identify differentially expressed miRNA driven pathways.

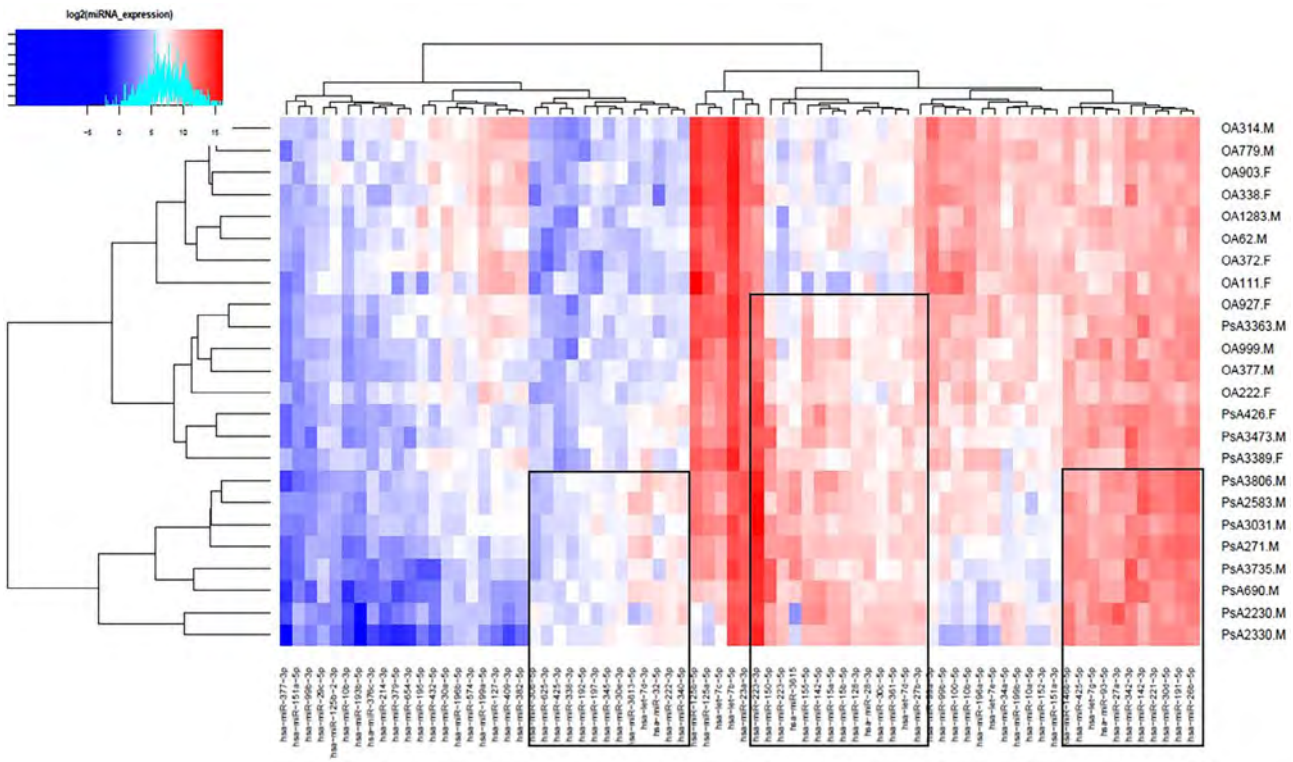

Figure. 1. Heatmap showing expression of miRNAs with Q<0.05 and fold change >1.5 in PsA and OA samples. Clusters of miRNAs that were relatively upregulated in PsA samples are indicated by the black rectangles.

Figure 2. Signaling cascades that include genes targeted by miRNAs upregulated in PsA and OA. Contextually relevant pathways were selected by applying filters for the synovium. Larger texts corresponds to highly enriched pathways.

Methods: Synovial fluid aspirated from knees of 12 PsA (sex: 8M, 4F; age (years): (median, range) = (45 (19-64)) and 12 OA patients (sex: 6M, 6F, age: (median, range) = (60 (43-74)) was used for miRNA sequencing using Illumina NextSeq 550. Linear modelling with empirical Bayes moderation (using the Limma R package) was used for assessing differential expression of miRNAs. Gene targets and enriched pathways targeted by significant miRNAs were identified by using integrative tools miRDIP and pathDIP set to a very high confidence class. For validation, SF samples from additional 35 PsA and 37 OA patients were retrieved. Total RNA including miRNA was extracted from these samples, and 5 selected candidate miRNAs were validated using quantitative RT-PCR. $\Delta\Delta$Ct method was used to calculate fold change. Differentially expressed miRNAs were defined as those with a two-fold change in expression ($-1.0 \geq \log2FC \geq 1.0$; p-value < 0.05).

Results: After miRNA sequencing, 51 miRNAs were found to be significantly differentially expressed between PsA and OA (FDR adjusted p-value less than 0.05) (Fig. 1). *QKI* (RNA binding protein), *OTUD4* (TLR signalling regulator), and *NFAT5* (osmotic stress response regulator) in PsA, and, *CELF2* (mRNA processor), *NFAT5*, and *ACVR2B* (TGFβ receptor) in OA, were the highest ranked gene targets of significant miRNAs.Figure 2 shows the signalling cascade that include genes targeted by miRNAs upregulated in PsA and OA. Pathways such as mitogen-activated protein kinase (MAPK), and WNT

Table 1. Enriched Pathways of gene targets of significant miRNAs with very high confidence of 1% and q-value <0.05. a) Enriched pathways of genes targeted by miR-27b-3p, b) Enriched pathways of genes targeted by miR-223-3p

Table 1a. Enriched Pathways of gene targets of miR-27b-3p with very high confidence of 1% and q-value <0.05 (9 of 114 shown)

Pathway	P-value	Q-value
Acute Myeloid Leukemia (AML)	4.40974e-06	2.24309e-03
Nuclear Receptors	4.39932e-06	3.35668e-03
Epidermal Growth Factor (EGF) Signaling	1.53324e-05	3.89954e-03
RUNX1 regulation involved in IL signaling	1.48978e-05	4.54681e-03
Adipogenesis	1.27126e-05	4.84986e-03
PI3K/AKT/mTOR Signaling	4.04984e-05	5.15005e-03
BDNF-TrkB signaling	3.53413e-05	5.39308e-03
IL-6 signaling	1.30613e-04	8.66589e-03
Mitogen-Activated Protein Kinase (MAPK) Pathway	1.28515e-04	8.91427e-03

Table 1b. Enriched Pathways of gene targets of miR-223-3p with very high confidence of 1% and q-value <0.05

Pathway	P-value	Q-value
Adenoid Cystic Carcinoma	1.91224e-05	1.12121e-02
Epithelial-Mesenchymal Transition (EMT) Regulators	1.49086e-05	1.31121e-02
Signaling pathways regulating pluripotency of stem cells	1.13908e-05	2.00364e-02
Regulation of nuclear SMAD2/3 signaling	5.80453e-05	2.04203e-02
Copper Homeostasis	5.76724e-05	2.53614e-02
RUNX1 Interaction with cofactors	9.05970e-05	2.65600e-02
Cholecystokinin Receptor (CCKR) Signaling	1.17513e-04	2.95293e-02
Longevity Regulating Pathway	1.40378e-04	3.08656e-02
Leptin	1.40378e-04	3.08656e-02

signalling were included which have also been previously demonstrated to be associated with PsA and OA. On qRT-PCR, 2 out of 5 miRNAs; miR-27b-3p (log2FC= -2.391, p-value < 0.05), and miR-223-3p (log2FC= 2.830, p-value < 0.05), were significantly dysregulated in SF of PsA patients compared to OA patients. Analysis using miRDIP and pathDIP revealed 195 gene targets and 114 enriched pathways for miR-27b-3p (Table 1a), and 223 gene targets and 9 enriched pathways for miR-223-3p (Table 1b).

Conclusion: Several miRNAs are deregulated between PsA and OA. miR-27b-3p, and miR-223-3p were validated in an independent cohort of patients. Identification of gene targets and enriched pathways further support the validated findings. Additional analysis of the remaining significant miRNAs will provide valuable pathogenetic insights and may identify diagnostic signature of PsA vs OA.

Disclosure: D. Ganatra: None; **A. Samman**: None; **D. Nasri**: None; **S. Rahmati**: None; **O. Cruz Correa**: None; **R. Machhar**: None; **R. Gandhi**: None; **M. Kapoor**: None; **V. Chandran**: AbbVie, 1, 5, 6, Amgen, 1, 5, 6, AstraZeneca, 3, Bristol-Myers Squibb (BMS), 1, 6, Eli Lilly, 1, 5, 6, Janssen, 1, 6, Novartis, 1, 1, 6, UCB, 1, 2.

Abstract Number: 1793

Goblet Cell Specific Anti-Apoptotic Role of Interleukin-24 in Spondyloarthritis-Associated Ileitis

Amy Cameron[1], Rabina Giri[2], Jakob Begun[2], Timothy Wells[1], Ranjeny Thomas[3] and Anne-Sophie Bergot[1], [1]Frazer Institute, The University of Queensland, Woolloongabba, Australia, [2]Mater Research Institute-UQ, Woolloongabba, Australia, [3]Frazer Institute, The University of Queensland, Brisbane, Australia

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The loss of intestinal barrier integrity is a key contributor to gut inflammation, however the mechanism behind this dysregulation is not well understood. The ZAP-70^{W163C} BALB/c (SKG) mouse model of Spondyloarthritis (SpA) develops IL-23-dependent Crohn's-like ileitis after systemic curdlan administration, with fecal dysbiosis, ileal goblet cell depletion and ER stress. IL-24 is associated with ER stress and apoptosis and increased levels were observed in inflammatory bowel disease (IBD) and SpA. To help elucidate the mechanism behind intestinal barrier dysfunction and goblet cell depletion in IBD, we assessed the role of IL-24 in ileal ER stress-mediated apoptosis in SKG mice.

Methods: SKG and control BALB/c ileum was analysed by histology and immunofluorescence (IF). Ileal epithelial cells were analysed by flow cytometry. ER stress was induced with thapsigargin in the MUC2^{hi} human colonic epithelial cell line LS174T in the presence of IL-24 or control siRNA. Gene expression was analysed by RT-qPCR and protein by flow cytometry.

Results: Naïve SKG ileum has fecal dysbiosis. In SKG ileum, expression of Il24 and ER stress marker transcripts were increased relative to BALB/c ileum. By IF, IL-24 localised to the ileal goblet cells. UEA-1 expression in Ep-CAM+ intestinal epithelial cells was significantly increased, indicating increased mucin production in SKG mice compared to BALB/c. IL-24 knockdown in LS174T epithelial cells *in vitro* increased ER stress and apoptosis including increased *CHOP*, *DR5* and active caspase-3 expression.

Conclusion: IL-24, a goblet cell-specific cytokine in small intestine mitigates ER stress-induced apoptosis in mucin-producing epithelial cells. This suggests that ER stress-associated IL-24 in SKG ileum is insufficient to prevent the cascade to IBD that commences with goblet cell apoptosis and epithelial barrier breakdown.

Disclosure: A. Cameron: None; **R. Giri**: None; **J. Begun**: None; **T. Wells**: None; **R. Thomas**: CSL, 2, 5, Janssen-Cilag, 6, Sandoz, 6; **A. Bergot**: None.

Abstract Number: 1794

The Role of the Deubiquitinase *ZRANB1*/TRABID in Inflammation and Bone Formation in Spondyloarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammation and new bone formation are important disease mediators in ankylosing spondylitis (AS). Recent studies in mice show that the deubiquitinase molecule TRABID epigenetically controls the expression of IL12/23 through JMJD2D (Jumonji Domain-Containing Protein 2D). Furthermore, TRABID also upregulates EZH2 (Enhancer of zeste homolog 2), a molecule that has been implicated in pro-osteogenic pathways. This study aims to study the functional and clinical relevance of TRABID in AS pathogenesis.

Methods:

1. TRABID, EZH2 and JMJD2D protein and gene expression was evaluated in AS and healthy control tissue by immunohistochemistry/immunofluorescence and qPCR respectively.
2. THP-1 cells (monocyte cell line) and splenocytes from 16-week-old SKG mice were incubated with lipopolysaccharide (LPS) to stimulate cytokine production and varying concentrations of NSC112200, a small molecule inhibitor of TRABID. Enzyme-linked immunosorbent assay (ELISA) was used to detect IL23, TNFa and IL1b production after 24 hours in the supernatant. Finally, western blot was used to evaluate expression of EZH2 and JMJD2D.
3. TRABID was knocked down in Saos-2 cells (osteoblast cell line) using siRNAs. Cells were then incubated in an osteogenic induction media for 14 days. RNA was extracted every 3 days to evaluate osteogenic gene expression by qPCR and RNA sequencing. At day 14, calcium mineralization levels were evaluated by Alizarin Red staining.

Results:

1. Our results showed that TRABID is significantly upregulated in human and mouse AS tissue (Figure 3). TRABID+ cells and gene expression were found to be upregulated in AS gut (n=20/group, $p< 0.0001$), bone marrow (n=5/group, $p< 0.0001$) and synovium (n=10/group, $p< 0.0001$). TRABID was found to be preferentially expressed by CD68+ macrophages in the synovial lining. EZH2 and JMJD2D were also found to be significantly upregulated in the inflamed synovium.
2. THP-1 cells treated with NSC112200 and LPS together showed a marked dose dependent inhibition of IL23 production when compared with cells treated with only LPS (n=6, $p >0.0001$). Furthermore, TRABID inhibition showed a significant downregulation of both JMJD2D and EZH2 protein levels (Figure 2).

3. SKG mouse splenocytes incubated with NSC112200 dose dependently showed decreased levels of TNFa when compared with cells treated with LPS alone after 24 hours (n=3, p=0.0043).
4. TRABID knockdown by siRNA showed significant suppression of pro-osteogenic genes like SP7, Runx2 and alkaline phosphatase. Moreover, osteoblasts knocked down for TRABID failed to mineralize as evidenced by diminished alizarin red staining. RNA sequencing confirmed pathways related to TGFb signaling, bone remodeling and endochondral ossification were suppressed while negative regulation of the immune system was upregulated (Figure 1). Lastly, osteogenic induction media significantly upregulated TRABID expression over time, compared with cells treated with unconditioned growth media (p=0.0027)

Conclusion: Our results show a role for TRABID in both cytokine production and osteogenesis. Future work will address both downstream mechanisms of TRABID in these processes and evaluate TRABID inhibition in animal models of AS.

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Abstract Number: 1795

Multi-Omics Analyses Identify Metabolic Pathways That Differentiate Psoriatic Arthritis from Psoriasis

Chiara Pastrello[1], Darshini Ganatra[2], Max Kotlyar[1], Nikita Looby[2], Quan Li[3], Lihi Eder[4], Dafna Gladman[5], Proton Rahman[3], Igor Jurisica[6] and **Vinod Chandran**[7], [1]Osteoarthritis Research Program, Division of Orthopaedic Surgery, Schroeder Arthritis Institute and Data Science Discovery Centre for Chronic diseases, Krembil Research Institute, Toronto, ON, Canada, [2]Schroeder Arthritis Institute, Krembil Research Institute, University Health Network, Toronto, ON, Canada, [3]Craig Dobbin Research Institute, Memorial University, St. John's, NL, Canada, [4]Women's College Research Institute, Division of Rheumatology, University of Toronto, Toronto, ON, Canada, [5]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Department of Medicine, University of Toronto, Toronto, ON, Canada, [6]Schroeder Arthritis Institute, Krembil Research Institute and Departments of Medical Biophysics and Computer Science and Faculty of Dentistry, University of Toronto and Institute of Neuroimmunology, Slovak Academy of Sciences, Bratislava, Slovakia, [7]Schroeder Arthritis Institute, Krembil Research Institute, University Health Network and Division of Rheumatology, Department of Medicine, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a form of inflammatory arthritis that occurs in patients with cutaneous psoriasis. Due to the lack of clinically useful diagnostic biomarkers or full understanding of pathways distinguishing PsA from psoriasis without PsA (PsC), we aimed to conduct integrated multiomics analyses using data from previously identified panel of SNPs and proteins, peripheral blood bulk RNA sequencing, miRNA sequencing and serum metabolomics obtained from carefully phenotyped individuals with psoriatic disease to identify pathways that differentiate PsA from PsC.

Methods: Serum, RNA and DNA from 102 PsA and 100 PsC patients were retrieved from a biobank of patients with psoriatic disease. Serum samples were used for miRNA sequencing, ELISA of 15 proteins (TNFSF14, S100A8/9, COMP, CRP, M2BP, OPG, DEFA, ITGB5, RANKL, CXCL10, Leptin, MMP3, OPN, Periostin, and SOST) and liquid chromatography-high resolution mass spectrometry (LC-HRMS) for metabolites, RNA for RNAseq and DNA for genotyping 42 SNPs of 19 'PsA weighted' genes. Resulting molecular data were combined with clinical data to identify the best set of biomarkers able to discriminate between PsA and PsC. A random forest model was developed to identify the best combination of diagnostic biomarkers. Further bioinformatics analysis was conducted using mirDIP 4.1[1] with threshold "very high" to identify biomarker

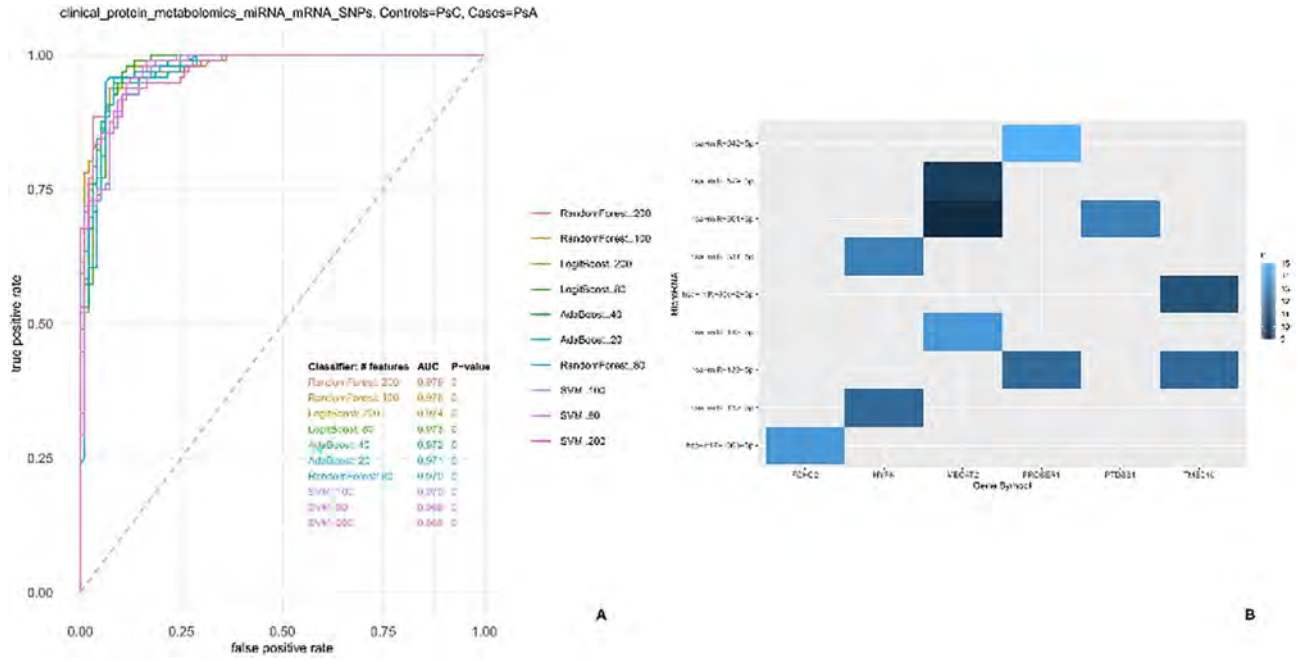

Figure 1. A) Analysis of the molecular and clinical features to identify the best biomarkers for PsA discrimination. B) miRNA to mRNA targeting using molecules from the 200 biomarkers and threshold "very high" from mirDIP 4.1.

mRNAs targeted by biomarker miRNA, and pathDIP 4[2] was used to perform pathway enrichment analysis for such mRNAs, while clusterProfiler 4.8.0[3] was used to perform Gene Ontology enrichment analysis. Analyses and visualization were performed in R 4.3.0.

Results: The random forest model identified 200 biomarkers, comprising 97 metabolites, 77 miRNAs, and 26 mRNAs, as the best performers to discriminate between PsA and PsC (Figure 1A, AUROC of 0.979, p-value < 0.001).Among the 77 miRNAs, 9 target 6 of the 26 mRNAs present in the 200 biomarkers (Figure 1B).Pathway and Gene Ontology enrichment analyses performed on the 6 genes identified several terms linked to phospho- and glycerophospholipid metabolism (Figure 2).Interestingly, of the 97 biomarker metabolites, 40 were mapped to known metabolites. Of these, 12 (30%) were either glycero- or phospholipids. Differences in phospholipid profiles between PsA and PsC have been described in [4], where a link to the immune system has also been proposed. Further validation is undergoing to confirm the diagnostic value of the 200 biomarkers and the role of the phospholipidic pathways in PsC progression to PsA.

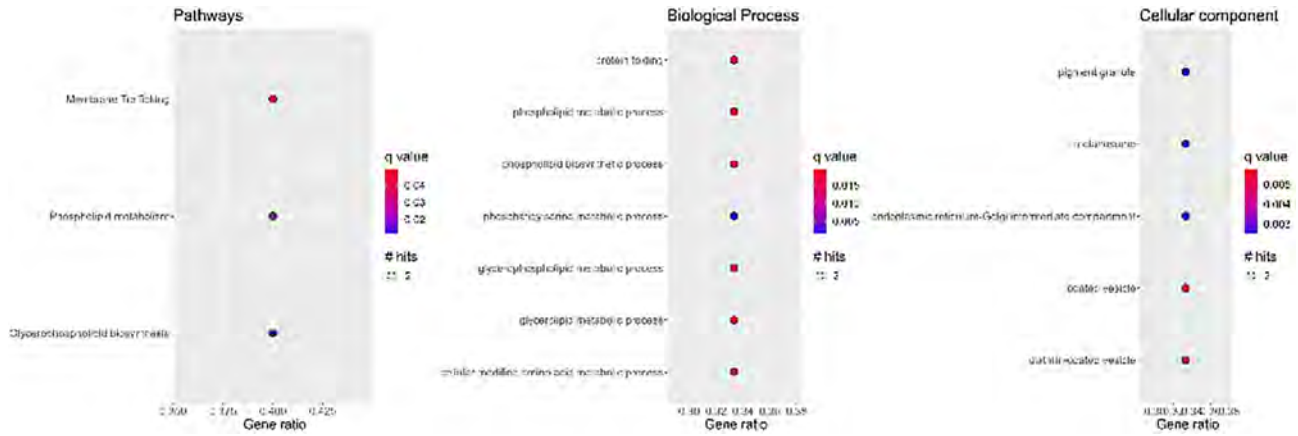

Figure 2. Pathway and Gene Ontology enrichment analysis results for the 6 genes from the 200 biomarkers identified as targets of 9 miRNAs from the same 200 biomarkers.

Conclusion: Our study highlights the importance of integrating multiple types of data to characterize different and complementary pieces of the molecular landscape that differentiate PsA and PsC. Our preliminary analysis shows that metabolic pathways can have a central role in the development and differentiation of PsA, a signal identified at the genetic level and confirmed through metabolomics analysis.

References: 1. Tokar, T. *et al. Nucleic Acids Res* **46**, D360 (2018). 2. Rahmati, S. *et al. Nucleic Acids Res* **48**, D479–D488 (2019). 3. Wu, T. *et al. Innovation (Cambridge (Mass.))* **2**, 100141 (2021). 4. Wójcik, P. *et al. Int J Mol Sci* **20**, (2019).

Disclosure: C. Pastrello: None; **D. Ganatra**: None; **M. Kotlyar**: None; **N. Looby**: None; **Q. Li**: None; **L. Eder**: AbbVie, 2, 5, Eli Lilly, 2, 5, Fresenius Kabi, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Sandoz, 5, UCB, 2, 5; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, Gilead Sciences, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5; **P. Rahman**: AbbVie, 2, Amgen, 2, Bristol Myers Squibb, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, UCB, 2; **I. Jurisica**: None; **V. Chandran**: AbbVie, 1, 5, 6, Amgen, 1, 5, 6, AstraZeneca, 3, Bristol-Myers Squibb (BMS), 1, 6, Eli Lilly, 1, 5, 6, Janssen, 1, 6, Novartis, 1, 1, 6, UCB, 1, 2.

Abstract Number: 1796

Safety & ImmUnogenicity of COVID-19 VaCcines in SystEmic immunE Mediated Inflammatory Diseases (SUCCEED)

Olga Tsyruk[1], **Vinod Chandran**[2], Carol Hitchon[3], J. Antonio Avina-Zubieta[4], Ines Colmegna[5], Paul R. Fortin[6], Maggie Larche[7], Gilles Boire[8], Luck Lukusa[1], Dawn Bowish[7], Gilaad G Kaplan[9], Daniel Pereira[10], Roaya Dayam[11], Jennifer LF Lee[1], Elizabeth Turnbull[1], Valeria Valerio[12], Laurie Proulx[13], Janet Gunderson[14], Anne-Claude Gingras[11] and Sasha Bernatsky[12], [1]RI-MUHC, Montreal, QC, Canada, [2]Schroeder Arthritis Institute, Krembil Research Institute, University Health Network and Division of Rheumatology, Department of Medicine, University of Toronto, Toronto, ON, Canada, [3]University of Manitoba, Winnipeg, MB, Canada, [4]Arthritis Research Canada, Vancouver, BC, Canada, [5]The Research Institute of the McGill University Health Centre, Montréal, QC, Canada, [6]Centre ARThrite - CHU de Québec - Université Laval, Quebec City, QC, Canada, [7]McMaster University, Hamilton, ON, Canada, [8]Université de Sherbrooke, Sherbrooke, QC, Canada, [9]University of Calgary, Calgary, AB, Canada, [10]University Health Network, Toronto, ON, Canada, [11]Lunenfeld-Tanenbaum Research Institute at Mount Sinai Hospital Sinai Health, Toronto, ON, Canada, [12]Research Institute of the McGill University Health Centre, Montreal, QC, Canada, [13]Canadian Arthritis Patient Alliance, Ottawa, ON, Canada, [14]Canadian Arthritis Patient Alliance, Saskatoon, SK, Canada

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The Canadian government's COVID Immunity Task Force funded SUCCEED to study COVID vaccination responses in immune-mediated inflammatory disease(IMID). We describe how drugs, clinical factors, and vaccine history influence serological response to vaccination, summarize safety, and describe breakthrough infections.

Methods: From Vancouver, Calgary, Winnipeg, Montreal, Quebec City, Sherbrooke, Toronto, and Hamilton, data and dried blood spots/sera post-COVID vaccination were collected from adults with rheumatoid arthritis, inflammatory bowel disease, SLE, ankylosing spondylitis/spondyloarthritis and psoriasis/psoriatic arthritis, with the first sample at enrolment and then 3, 6, and 12 months after latest vaccine dose. We evaluated anti-spike(S) trimer and anti-receptor-binding domain(RBD) IgG (indicating successful serologic response to vaccine) and anti-nucleocapsid (N) IgG (indicating recent infection, cross-referenced with self-report). Multivariate generalized estimating equation regressions (accounting for repeated measures) were used to evaluate serologic response, based on log-transformed anti-RBD titres.

Results: Baseline characteristics of 1556 participants are shown in Table 1. Table 2 shows crude and adjusted odds ratios(OR). Positive associations for anti-RBD/anti-S serologic responses were seenwithfemale sex, number of vaccine doses and infections in 2021-2022. Negative associations were seen with prednisone, anti-TNF agents and rituximab. Diminution of response was clearly seen even for daily prednisone doses of 1-10 mg (adjusted OR 0.73 95%CI 0.58-0.91) and 11-20 mg (aOR 0.62 95%CI 0.43-0.90). Methotrexate and other immunosuppressants were associated with reduced response only in univariate analyses. Time since last vaccination was negatively associated with serologic response; rate of decrease was similar during the period 15-120 days since last vaccine (OR 0.75 95%CI 0.64,0.87) and 121-210 days post-last vaccine (OR 0.79 95%CI 0.67,0.92) but worse after >210 days (OR 0.53 95%CI 0.43,0.66).

Table 1. Baseline characteristics

	RBD and SmT1 negative* N=172	RBD and/or SmT1 positive N=1384	Overall N=1556
Female sex, N (%)	99 (57.6)	879 (63.5)	978 (62.9)
Mean age, (SD)	56.1 (15.3)	52.1 (15.7)	52.5 (15.7)
Mean Disease duration, (SD)	19.7 (13.8)	16.9 (13.3)	17.1 (13.4)
White Race/ethnicity	151 (87.8)	1192 (86.1)	1343 (86.3)
Current smoker, N (%)	9 (5.3)	69 (5.5)	78 (5.5)
Disease, N (%)			
IBD	112 (65.1)	651 (47.0)	763 (49.0)
PsA	8 (4.7)	215 (15.5)	223 (14.3)
RA	48 (27.9)	378 (27.3)	426 (27.4)
SpA	4 (2.3)	78 (5.6)	82 (5.3)
SLE	0 (0.0)	62 (4.5)	62 (4.0)
Anti-N positivity	3 (1.7)	149 (10.8)	152 (9.8)
Self-reported infection, N (%)			
2020	1 (0.6)	39 (3.1)	40 (2.8)
2021	14 (8.1)	93 (7.4)	107 (7.5)
2022	64 (37.2)	558 (44.5)	622 (43.6)
Self-reported infection in the 3 months before sample N (%)	4 (2.3)	186 (14.4)	190 (13.0)
Current prednisone use, N (%)	37 (21.5)	271 (19.6)	308 (19.8)
Current biologic, N (%)*			
Current anti-TNF	96 (55.8)	455 (32.9)	551 (35.4)
Current rituximab	10 (5.8)	7 (0.5)	17 (1.1)
Current other biologic	43 (25.0)	292 (21.1)	335 (21.5)
None	23 (13.4)	464 (33.5)	496 (31.9)
Missing	0 (0.0)	166 (12.0)	166 (10.7)
Non-biologic therapy, N (%)			
Current jak-inhibitor	9 (5.2)	77 (5.6)	86 (5.5)
Current methotrexate	58 (33.7)	381 (27.5)	439 (28.2)
Current hydroxychloroquine	24 (14.0)	210 (15.2)	234 (15.0)
Current other	45 (26.2)	184 (13.3)	229 (14.7)
None	36 (20.9)	532 (38.4)	568 (36.5)
Number vaccine doses, N (%)			
One dose	9 (5.2)	34 (2.5)	43 (2.8)
Two doses	30 (17.4)	193 (13.9)	223 (14.3)
Three doses	74 (43.0)	601 (43.4)	675 (43.4)
Four doses	59 (34.3)	472 (34.1)	531 (34.1)
Five doses	0 (0.0)	84 (6.1)	84 (5.4)
Vaccine type, N (%)			
BNT-162b2 only	119 (69.2)	899 (65.0)	1018 (65.4)
mRNA1273 only	16 (9.3)	207 (15.0)	223 (14.3)
Mixed BNT-162b2/ mRNA1273	16 (9.3)	246 (17.8)	262 (16.8)
Other[a]	21 (12.2)	32 (2.3)	53 (3.4)

[a]One or more dose of AstraZeneca or Johnson & Johnson **Alberta patients did not have any anti-RBD serology evaluated.

Table 2: Odds ratios (OR) and 95% confidence intervals for the effects of demographics, clinical exposures, and vaccination history on anti-RBD serology

Characteristics	Crude OR (95% CI)	Adjusted OR (95% CI)[a]
Age (continuous) in years	0.97 (0.92, 1.02)	1.01 (0.96, 1.06)
Female sex	1.04 (0.92, 1.16)	**1.17 (1.05, 1.31)**
IMID		
Other (SpA and PsA)	Reference	Reference
IBD	1.32 (1.20, 1.46)	1.54 (1.34, 1.79)
RA	0.88 (0.79, 0.99)	0.95 (0.83, 1.09)
SLE	0.98 (0.84, 1.14)	0.85 (0.70, 1.05)
Current prednisone	**0.71 (0.62, 0.82)**	**0.78 (0.68, 0.90)**
Current biologic		
None	**Reference**	**Reference**
Anti-Tumor Necrosis Factor	**0.76 (0.68, 0.84)**	**0.67 (0.60, 0.75)**
Rituximab	**0.16 (0.07, 0.33)**	**0.19 (0.08, 0.42)**
Other biologic	1.46 (1.31, 1.65)	1.06 (0.91, 1.22)
Immunomodulators		
None	Reference	Reference
Methotrexate,	0.79 (0.71, 0.88)	0.90 (0.80, 1.02)
Hydroxychloroquine	0.80 (0.71, 0.90)	0.98 (0.84, 1.15)
JAK-inhibitors,	0.94 (0.65, 1.36)	0.97 (0.63, 1.49)
Other immunosuppressants	0.79 (0.68, 0.91)	0.87 (0.76, 1.00)
Vaccine type		
Other (Pfizer only, Moderna only and other)	Reference	Reference
Mixed	1.31 (1.15, 1.48)	1.05 (0.93, 1.17)
Number of prior vaccine doses		
Two	Reference	Reference
Three	**1.80 (1.67, 1.97)**	**1.86 (1.72, 2.03)**
Four	**1.75 (1.52, 2.03)**	**1.86 (1.62, 2.12)**
Time since last vaccine (continuous) in days	**0.88 (0.84, 0.91)**	**0.87 (0.84, 0.90)**
Self-reported infection		
None	Reference	Reference
In 2020	1.15 (0.81, 1.63)	1.26 (0.90, 1.77)
In 2021	**1.41 (1.15, 1.73)**	**1.43 (1.19, 1.75)**
In 2022	**1.00 (0.90, 1.11)**	**1.13 (1.02, 1.25)**

[a] Adjusted for all variables shown

Self-reported post-vaccine adverse events leading to emergency department(ED) visits or hospitalizations occurred in only 1.5% of participants. Bell's Palsy represented one ED visit, with no confirmed Guillain-Barre or transverse myelitis in our preliminary analyses. Over 2021-2022, anti-N positivity (indicating recent infection) was present in 9.8% of samples; most (85%) were associated with a self-reported infection. Anti-N positivity was lowest in the summer of 2021 and highest post-Omicron (fall 2022).

Conclusion: Past infections and number of COVID-19 vaccine doses were positively associated with serologic response. Time since vaccination, particularly >210 days, was negatively associated with response. Anti-TNF agents, rituximab, and prednisone were associated with less immunogenicity. Few vaccine-related adverse events led to ED or hospitalization. Ours is the first assessment of drugs, vaccine history, and other factors on serologic COVID vaccine response in a large, pan-Canadian IMID sample. These findings may help patients, clinicians, and other stakeholders make personalized decisions about vaccination in 2023-2024 and beyond.

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Roche-Genentech, 1; **M. Larche**: None; **G. Boire**: Eli Lilly, 1, Janssen, 6, Organon, 1, Orimed Pharma, 1, 6, Otsuka, 1, Pfizer, 1, 5, Sandoz, 1, Teva, 1, Viatris, 1, 6; **L. Lukusa**: None; **D. Bowish**: AstraZeneca, 2; **G. Kaplan**: AbbVie, 6, Ferring, 5, Janssen, 6, Pfizer, 6; **D. Pereira**: None; **R. Dayam**: None; **J. Lee**: None; **E. Turnbull**: None; **V. Valerio**: None; **L. Proulx**: AbbVie/Abbott, 5, ESDC, 5, IMC, 5; **J. Gunderson**: None; **A. Gingras**: ChairCIHR Institute of Genetics Advisory Board, and SAB of the National Research Council of Canada Human Health Therapeutics Board, 4, Participates in the COVID-19 Immunity Task Force (CITF) Immune Science and Testing working party, 2, Research funds from a research contract with Providence Therapeutics Holdings, Inc for other projects, 5; **S. Bernatsky**: None.

Abstract Number: 1797

Factors Associated with Distress Related to Perceived Dignity in Patients with Rheumatic Diseases

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: From the Human rights approach, dignity is accepted as a universal need, required for the well-being of every individual. It is an irrevocable feature of personhood that does not depend on or varies according to circumstances. However, in the medical context, what dignity entails in practice will also depend on patients´ perception of themselves, how others see them, and how the nature of the illness in question affects the person's life and identity. It evokes the patient's sense of autonomy and control. The loss of perceived dignity is an existential source of Human suffering rarely explored among patients with rheumatic diseases (RMDs), which contrasts with their observations that dignity, identity, and Quality of Life (QoL) are essential areas for research focus. We recently observed that distress related to perceived dignity (DPD) was present in 26.9% of Mexican outpatients with different RMDs.

The current study complements the research on the topic and investigates the factors associated with DPD in primary outpatients with different RMDs.

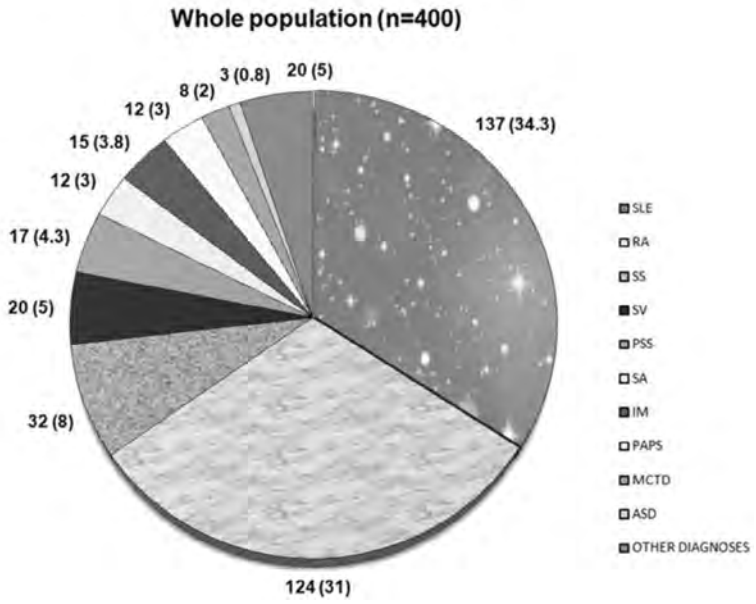
Methods: This cross-sectional study was performed in February-September 2022. Consecutive primarily outpatients with RMDs completed patient-reported outcomes (PROs) (to assess mental health [DASS-21], disease activity/severity [RAPID3], disability [HAQ-DI], fatigue [FACIT], QoL [WHOQOL-BREF], satisfaction with medical care [locally adapted questionnaire], resilience [brief-resilient coping scale] and family function [family APGAR]) and had a rheumatic evaluation to assess disease activity status and comorbidity (Rheumatic Disease Comorbidity Index). Sociodemographic variables and disease-related and treatment-related variables were retrieved with standardized formats. DPD was defined based on a score ≥ 54.5 (min 25-max 125) on the previously adapted and validated Mexican version of the Patient Dignity Inventory (PDI-Mx). Multivariate regression analysis was used to identify factors associated with DPD (the dependent variable). We estimated a sample size of 334 patients (considering 20% of losses for non-analyzable data) to achieve the objective described.

Table. Description of the population's characteristics and the comparison between patients with DPD and their counterparts.

	Overall population n=400	Patients with DPD n=107	Patients without DPD n=243	p
Socio-demographic characteristics				
Age, years	46 (33.3-57)	44 (34-54)	47 (33.58)	0.275
Females*	330 (82.5)	92 (86)	238 (81.2)	0.301
Years of scholarship	12 (9-16)	12 (9-16)	12 (11-16)	**0.031**
Living together*	201 (50.2)	56 (32.3)	145 (49.5)	0.400
Formal and non-formal job*	197 (49.3)	45 (42.5)	152 (51.9)	0.113
Access to Social Security benefits*	126 (31.5)	31 (29)	95 (32.4)	0.654
Middle-low socioeconomic level*	346 (86.5)	95 (88.8)	251 (86)	0.510
Religious beliefs*	306 (76.5)	74 (69.2)	232 (79.2)	0.319
Rheumatic disease characteristics				
SLE diagnosis*	137 (34.3)	41 (38.3)	96 (32.8)	0.439
RA diagnosis*	124 (31)	31 (29)	93 (31.7)	0.439
Disease duration, years	10 (5-19)	10 (5-20)	10 (5-18)	0.859
Rheumatic Diseases Comorbidity Index score	0 (0-1)	0 (0-1)	0 (0-1)	0.537
One year-previous hospitalization*	111 (27.8)	44 (41.4)	67 (22.9)	**0.001**
Adequate control of the rheumatic disease*	345 (88.5)	89 (84)	256 (90.1)	0.163
Immunosuppressive treatment*	287 (71.8)	82 (88.2)	205 (85.1)	0.599
N° of immunosuppressive drugs/patient[1]	1 (1-2)	1 (1-2)	1 (1-2)	**0.006**
Corticosteroids use*	159 (40.8)	53 (51.5)	106 (36.9)	**0.014**
Mental health-related variables				
Previous mental health-related comorbidity*	91 (22.8)	45 (42.1)	46 (15.7)	**≤0.0001**
DASS21 score of ≥moderate severity[2] *Depression* *Anxiety* *Stress*	 97 (19.3) 142 (35.5) 88 (22)	 61 (57) 84 (78.5) 66 (61.7)	 16 (5,5) 58 (19.8) 22 (7.3)	**≤0.0001**
PROs				
RAPID-3 score (0-30)	8 (2-14.8)	15.8 (9.4-20.7)	5.7 (1.4-11.5)	**≤0.0001**
HAD-DI score (0-3 scale)	0.3 (0-1)	1.1 (0.5-2.1)	0.1 (0-0.6)	**≤0.0001**
Patients with disability (HAQ-DI score >0.5)*	182 (45.6)	82 (76.6)	100 (34.2)	**≤0.0001**
FACIT score (0-52)	14 (10-23)	24 (17-30)	12 (9-18)	**≤0.0001**
Physical health dimension score (0-100) (WHOQOL-BREF)	50 (39.3-60.7)	35.7 (21.4-42.8)	57 (46.4-67.9)	**≤0.0001**
Psychological health dimension score (0-100) (WHOQOL-BREF)	50.3 (45.8-70.8)	41.7 (29.2-50)	64.6 (54.2-75)	**≤0.0001**
Social relationships dimension score (0-100) (WHOQOL-BREF)	50 (41.7-66.7)	41.7 (25-50)	58.3 (50-75)	**≤0.0001**
Environment dimension score (0-100) (WHOQOL-BREF)	53 (43.8-62.5)	43.8 (34.4-53)	56.3 (47-65.6)	**≤0.0001**
SMC score	77 (71.5-80)	74.3 (68-79.8)	77.5 (73-80)	**0.002**
Family APGAR score (0-10 scale)	9 (8-10)	9 (7-10)	9 (9-10)	**≤0.0001**
Patients with normal family function*	348 (87.2)	82 (77)	266 (90.8)	**0.001**
Brief Resilient Coping Scale score (4-20 scale)	15 (12-18)	13 (10-16)	16 (13-18)	**≤0.0001**
PDI-Mx (25-125)	40 (30-54.5)	70 (61-83)	34 (28-41.5)	**≤0.0001**

Data presented as median (IQR) or otherwise indicated. *Number (%) of patients.1Among those who met the characteristic. APGAR= Adaptation, Partnership, Growth, Affection, and Resolve. SLE=Systemic Lupus Erythematosus. RA=Rheumatoid Arthritis. DASS21=Depression, Anxiety, and Stress scale. RAPID-3= Routine Assessment of Patient Index Data. HAQ-DI=Health Assessment Questionnaire Disability Index. FACIT=Fatigue scale. WHOQOL-BREF=World Health Organization Quality of Life-Brief Questionnaire. SMC=Satisfaction with medical care. 2According to Lovibond SH, Lovibond PF. Manual for the Depression Anxiety and Stress Scales. 2nd ed. Sydney: Psychology Foundation;1995.

Figure 1. Diagnoses distribution.

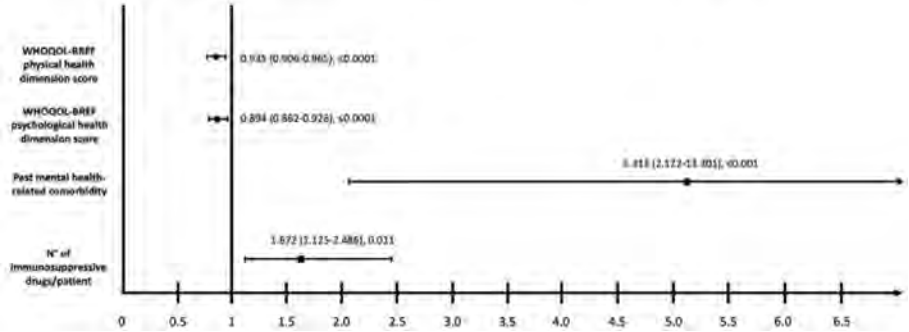


Data presented as number (%). SLE=Systemic Lupus Erythematosus. RA=Rheumatoid Arthritis. SS=Systemic Sclerosis. SV= Systemic Vasculitis. PSS=Primary Sjögren Syndrome. SA=Spondyloartrhitis. IM= Inflammatory Myopathies. PAPS= Primary Anti-phospholopid Syndrome. MCTD= Mixed Connective Tissue Disease. ASD= Adult Onset-Still Disease.

Results: Four hundred patients were included (February-September 2022), representing patients with RMDs and the most frequent rheumatic diagnoses in our outpatient clinic (**Figure 1**). One hundred and seven patients (26.8%) had DPD. They differed from their counterparts (less educated, with intensive treatment, mental health comorbidity, and worse PROMs) (**Table**). Past mental health-related comorbidity, the number of immunosuppressive drugs/patient, the physical health dimension score of the WHOLQOL-BREF, and the emotional health dimension score of the WHOLQOL-BREF were associated with DPD (**Figure 2**).

Conclusion: We observed that DRPD was present in a substantial proportion of patients with RMDs and was associated with previous mental health comorbidity, intensive treatment of the underlying RMD, and the patient QoL. Recognizing factors associated with DPD is an essential step in the right direction toward understanding the impact of RMDs in patients' lives and preventing poorer prognoses.

Figure 2. Results from multivariate regression analysis to identify factors associated with DPD.



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Abstract Number: 1798

Association Between Knee Osteoarthritis and Mortality: A Serial Propensity Score-matched Cohort Study

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The association between symptomatic knee osteoarthritis (OA) and higher cardiovascular disease (CVD) mortality is well established; however, findings from previous studies that utilized regression analysis were limited, attributed to the strong association between OA and metabolic risk factors. This study aimed to evaluate the association between knee OA and mortality through propensity score matching.

Methods: This was a cohort study including Korean National Health and Nutrition Examination Survey (2010–2013) participants aged ≥50 years who had undergone screening knee radiographs (N=13087). By linking the survey data to Cause of Death data (through 2019) from Statistics Korea, mortality and cause-specific mortality data were obtained. Radiographic knee OA (ROA) was defined as bilateral Kellgren-Lawrence grade ≥2.Propensity score matching (1:1) was conducted between asymptomatic ROA, knee pain (without ROA), and symptomatic ROA groups and normal groups, balancing

Table 1 Risk for all-cause and cause-specific death in knee state groups[a]

	Normal	Asymptomatic ROA	Normal	Knee pain	Normal	Symptomatic ROA
All-cause mortality						
N of deaths	229	234	59	71	140	160
Rate of death (per 1000 person-years)	1.06	1.09	0.72	0.87	1.14	1.29
HR (95% CI)	Ref.	1.03 (0.86–1.24)	Ref.	1.21 (0.86–1.71)	Ref.	1.13 (0.90–1.42)
HR (95% CI)[b]	Ref.	1.04 (0.86-1.25)	Ref.	1.22 (0.86-1.74)	Ref.	1.19 (0.94-1.50)
Cardiovascular disease mortality						
N of deaths	50	56	15	9	33	47
Rate of death (per 1000 person-years)	0.23	0.26	0.18	0.11	0.27	0.38
HR (95% CI)	Ref.	1.12 (0.77–1.65)	Ref.	0.61 (0.27–1.38)	Ref.	1.39 (0.89–2.17)
HR (95% CI)[b]	Ref.	1.13 (0.76-1.68)	Ref.	0.58 (0.24-1.38)	Ref.	1.48 (0.94-2.33)
Cancer mortality						
N of deaths	89	85	21	27	52	54
Rate of death (per 1000 person-years)	0.41	0.40	0.26	0.33	0.42	0.44
HR (95% CI)	Ref.	0.96 (0.72–1.30)	Ref.	1.30 (0.73–2.29)	Ref.	1.03 (0.70–1.51)
HR (95% CI)[b]	Ref.	0.96 (0.71-1.31)	Ref.	1.30 (0.73-2.29)	Ref.	1.09 (0.74-1.62)

a. ROA radiographic knee osteoarthritis defined as bilateral Kellgren-Lawrence grade of 2 or higher.

b. Results of the sensitivity analysis in which death in a year after observation was excluded.

confounding factors (age, sex, obesity, hypertension, diabetes, total cholesterol, household income, history of stroke, history of MI). Time to death was analyzed using Cox Proportional hazard modeling. Sensitivity analysis was performed excluding those who died in a year of the observation period.

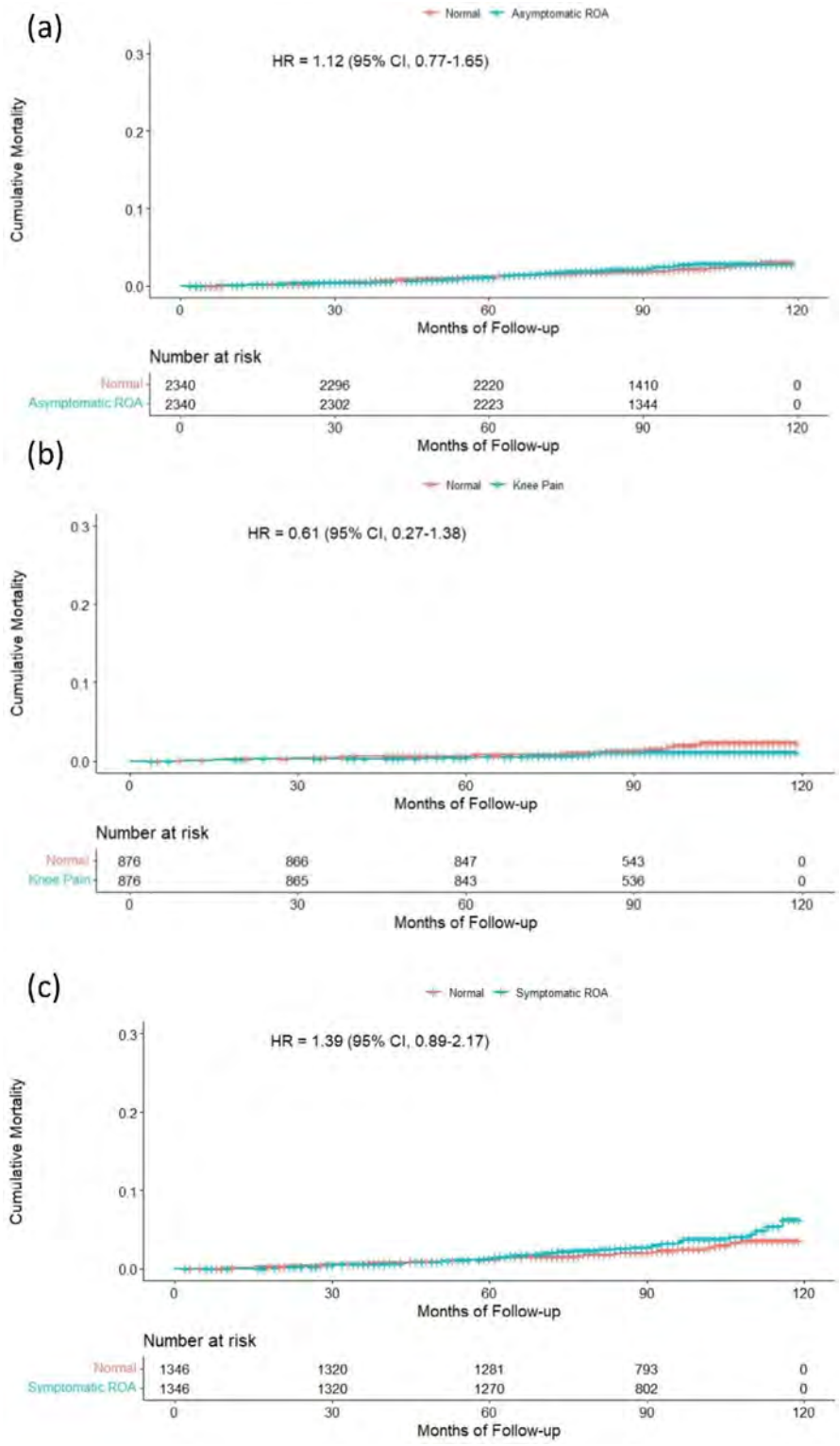

Figure 1. Kaplan–Meier plot of cumulative mortality from cardiovascular disease up to 10 years for propensity score-matched participants with (a) asymptomatic ROA, (b) knee pain without ROA, and (c) symptomatic ROA. ROA, radiographic knee osteoarthritis.

Results: The median and range of follow-up duration was 95 (0-124) months, and the total observation period was 103,330 person-years. There were 1128 deaths in the observation period. Crude mortality rates were higher in the ROA groups. All-cause mortality rate was 0.87, 1.32, 1.08, and 1.48 per 1000 patient-year in the reference, asymptomatic ROA, knee pain, and symptomatic ROA group, respectively. After matching there was a trend for higher CVD mortality in symptomatic ROA group, but not in other groups (Table 1 and Figure 1); the risk estimates were asymptomatic ROA HR 1.12 (95% CI 0.77–1.65), knee pain 0.61 (0.27–1.38), and symptomatic ROA 1.39 (0.89–2.17). There was no association between all-cause/cancer mortality and any group. In sensitivity analysis, there was a closer trend for higher CVD mortality in symptomatic ROA group (Table 1). The risk estimate was HR 1.48 (0.94–2.33).

Conclusion: When propensity score matching controls risk factor imbalances, the association between symptomatic knee OA and higher CVD-mortality was weaker compared with results of prior studies that used regression adjustment, and knee pain without radiographic OA was not associated with CVD mortality. Assuming that matching is a stronger method to control confounding variables and bias, the results may be more precise estimates of the total risk of knee OA for mortality, especially in East Asian population. Mediating effects by metabolic dysregulation merits further research.

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Abstract Number: 1799

Association of Pregabalin vs Gabapentin with Incident Congestive Heart Failure in Patients with Non-Cancer Pain

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SESSION INFORMATION
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Background/Purpose: Chronic pain affects 30% of all patients in developed countries, accounting for up to 35% of prescriptions in acute care settings. Non-opioid pain medications are widely utilized for treatment of non-cancer chronic pain. Among these, pregabalin is a commonly prescribed anticonvulsant, which works by antagonizing L-type calcium channels, decreasing the release of neurotransmitters . Pregabalin use has been associated with reports of congestive heart failure (CHF), including peripheral and pulmonary edema. However, the relationship between CHF incidence and pregabalin use among patients at the highest risk of adverse reactions (i.e., senior patients with various co-morbidities) remains unclear. The purpose of this study was to compare incident CHF among new users of pregabalin versus gabapentin (the active comparator) in Medicare beneficiaries treated for non-cancer chronic pain.

Methods: This was a retrospective cohort study among Medicare beneficiaries aged 65-89 years old with chronic non-cancer pain, without prior history of CHF. Patients who were newly prescribed users of pregabalin or gabapentin were followed up between 2015-2018. The outcome was incident CHF, ascertained by hospital admissions or emergency room visits with ICD 9 and 10 codes in the first position codes. Inverse probability of treatment weighting was used to account for differences between pregabalin and gabapentin users in a time-dependent analysis (i.e., Cox proportional-hazards

Table 1. Participant Demographics, Medical History/Diagnoses, and Medications

Table 1. Participant Demographics, Medical History/Diagnoses, and Medications

Characteristic/Covariates	Weighted		
	Gabapentin	Pregabalin	Standardized Difference
No of participants	221,053	17,756	...
Age on Day, mean (SD)	73	73	-0.002
Men n (%)	33.3	33.1	-0.003
Pain diagnoses			
Chronic Pain: Arthralgia	48.1	48.3	0.004
Chronic Pain: Back pain/degenerative back disorders	67.5	67.3	-0.004
Chronic Pain: Headache, including migraine	14.3	14.6	0.008
Chronic Pain: Fibromyalgia	13.7	14.4	0.019
Chronic Pain: Neuropathic	60.6	60.5	-0.002
Pain Medication History			
Coxibs	5.21	5.35	0.006
Cyclobenzaprine	5.67	5.81	0.006
NSAIDs, non-selective	35.9	36.0	0.001
Systemic oral corticosteroids	30.6	30.9	0.006
Anticonvulsants, Primary Use Pain	0.57	0.61	0.006
CV Diagnosis			
Diabetes (neuropathy)	11.6	11.9	0.009
Ischemic or unspecified stroke	9.75	9.94	0.006
Hyperlipidemia	73.9	73.9	0
Hypertension, benign or unspecified	79.0	79.2	0.005
Myocardial infarction	3.35	3.44	0.005
CV Medication History			
Angiotensin converting enzyme inhibitors	29.6	29.6	0
Angiotensin receptor blocker	25.9	26.1	0.004
Anti-arrhythmics	6.43	6.55	0.005
Beta-blockers	34.9	35.1	0.004
Calcium channel blockers	27.8	27.9	0.002
Diuretics, Potassium Sparing (and with hydrochlorothiazide)	5.93	5.95	0.001

regressions). A total of 318 covariates were selected for propensity scoring based on prior knowledge and literature review, and included categories such as concurrent baseline cardiovascular, neurologic, pain, and psychiatric diagnoses and corresponding medications including opioids and antipsychotics. Non-diagnostic covariates were included, as well as demographics, socioeconomic status, and indicators/metrics of health care utilization.

Results: Patient demographics and characteristics are summarized in *Table 1*. A total of 17,756 new users of pregabalin and 221,053 new users of gabapentin were included. The cohort was predominantly female sex (66.7%) and non-Hispanic White (79.9%), with a median age of 73 years. During 110,439 person-years (PY) of follow-up, 1,428 patients were hospitalized for CHF. The rate for CHF hospitalization was 18.7 per 1000 PY for pregabalin vs 12.6 per 1000 PY for gabapentin (adjusted HR 1.48 (95% CI 1.20-1.81)) (*Figure 1*). Stratified by cardiovascular disease (CVD), the rate of CHF hospitalization was 42.9 for pregabalin vs 23.4 for gabapentin (adjusted HR 1.87 (95% CI 1.40-2.60)) (*Figure 1*).

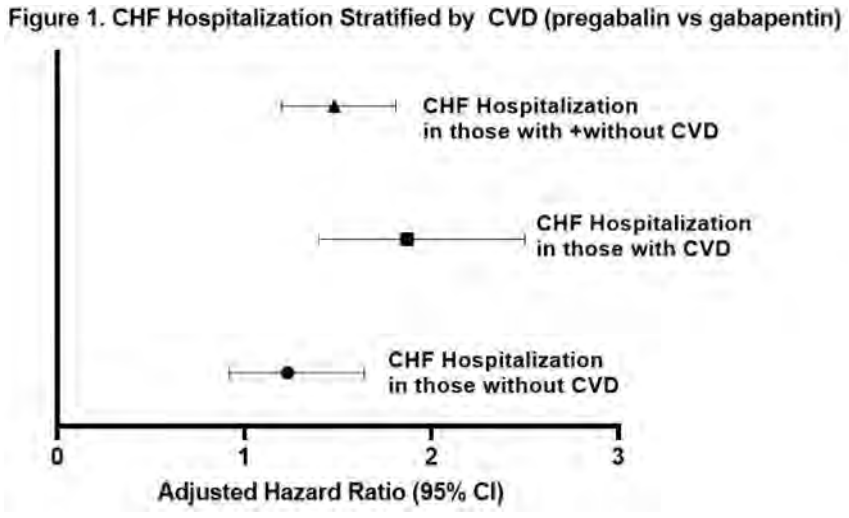

Figure 1. CHF Hospitalization Stratified by CVD (pregabalin vs gabapentin)

Conclusion: In this retrospective study of Medicare beneficiaries aged 65-89 years with chronic non-cancer pain, new users of pregabalin had higher rates of incident CHF hospitalizations or emergency room visits compared to new users of gabapentin.

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Abstract Number: 1800

Factors Associated with an Electronic Health Record-Based Definition of Post-Acute Sequelae of COVID-19 in Patients with Systemic Autoimmune Rheumatic Diseases

Naomi Patel[1], Xiaosong Wang[2], Yumeko Kawano[2], Abigail Schiff[2], Rathnam Venkat[2], Claire Cook[1], Kathleen Vanni[2], Grace Qian[2], Katarina Bade[2], Shruthi Srivatsan[1], Krishan Guzzo[1], Zachary Williams[1], Emily Kowalski[2], Alene Saavedra[2], Jeffrey Sparks[3] and Zachary Wallace[4], [1]Massachusetts General Hospital, Boston, MA, [2]Brigham and Women's Hospital, Boston, MA, [3]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [4]Massachusetts General Hospital, Newton, MA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Immunosuppression for treatment of systemic autoimmune rheumatic diseases (SARDs) is associated with increased risk of severe acute COVID-19 due to blunted vaccine responses and impaired immune response to infection. Whether immunosuppression may also alter the risk for post-acute sequelae of COVID-19 (PASC), or "long COVID," is unclear. Previous studies (Al-Aly *et al*, *Nature Medicine,* 2022) have developed electronic health record (EHR)-based definitions of PASC that have the benefit of including all COVID-19 survivors, rather than relying on prospective studies that may have selection bias, but have not been performed among SARD patients. We evaluated baseline demographic and disease factors associated with PASC in a large EHR-based cohort of patients with SARDs.

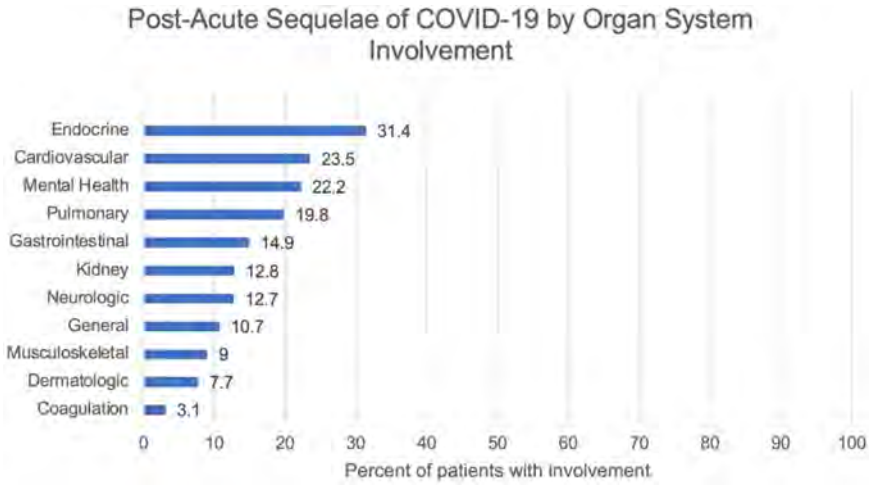

Figure. Proportion of patients who developed Post-Acute Sequelae of COVID-19 during the study period by organ system involvement

Methods: We systematically identified patients with SARDs and confirmed COVID-19 in a large healthcare system (up to 1/18/2023). We required patients to have baseline data in the EHR prior to the index date, defined as initial COVID-19 infection. Patients who survived COVID-19 were followed from 30 days after the index date until the development of any incident PASC feature, repeat COVID-19 infection, 1 year of follow-up, death, or until 4/14/2023. We evaluated the proportion with incident PASC features, defined by incident ICD codes, relevant vital signs or labs, and/or medications, extracted from the EHR. We estimated the association of baseline characteristics with the risk of PASC using multivariable Cox regression.

Table 1. Demographics and rheumatic disease characteristics of patients with history of COVID-19 infection

Characteristic	n (%) (n=2459)
Age at time of COVID-19, mean ± SD	57.38 (16.57)
Female, n (%)	1878 (76.4%)
Race, n (%)	
White	1862 (75.7%)
Black	212 (8.6%)
Asian	84 (3.4%)
Other	228 (9.3%)
Unknown	73 (3.0%)
Hispanic or Latinx ethnicity	73 (3.1%)
Rheumatic disease category	
Rheumatoid arthritis	815 (33.1%)
Other inflammatory arthritis	561 (22.8%)
Systemic lupus erythematosus	268 (10.9%)
Giant cell arteritis and/or polymyalgia rheumatica	157 (6.4%)
ANCA-associated vasculitis and other vasculitis	134 (5.5%)
Other rheumatic disease	379 (15.4%)
Multiple diagnoses	145 (5.9%)
Immunomodulatory medications at COVID-19 diagnosis	
Any DMARDs	1916 (77.9%)
Conventional synthetic DMARDs	1226 (49.9%)
Methotrexate	591 (24.0%)
Antimalarial	540 (22.0%)
Mycophenolate mofetil/mycophenolic acid	152 (6.2%)
Other csDMARD	187 (7.6%)
Targeted synthetic DMARD (JAK inhibitors)	84 (3.4%)
Biologic DMARDs	1014 (41.2%)
TNF inhibitors	556 (22.6%)
CD20 inhibitors	174 (7.1%)
IL-6 receptor inhibitors	96 (3.9%)
CTLA-4 Ig	58 (2.4%)
IL-17, IL-12/23, or IL-23 inhibitors	85 (3.5%)
Other biologic DMARD	
Baseline glucocorticoid use at COVID-19 diagnosis	577 (23.5%)
Dose (prednisone-equivalent, daily mg), median [IQR]	5 (4, 10)
Charlson Comorbidity Index, median (IQR)	1 (1, 3)
Calendar time of COVID-19 infection	
Mar 1, 2020 - June 30, 2021	834 (33.9%)
July 1, 2021 - December 16, 2021	179 (7.3%)
December 17, 2021 - January 18, 2023	1446 (58.8%)
Hospitalized for acute COVID-19	356 (14.5%)

Results: We identified 2,459 patients with SARDs and confirmed COVID-19 (76% female, mean age 57 years, **Table 1**)**.** The majority of patients (1566; 64%) had at least one incident feature of PASC. The most common incident PASC features were hyperlipidemia (561; 23%), anxiety (419; 17%), dyspnea (303; 12%), fatigue (263; 11%), and chest pain (246; 10%) (**Figure**). Compared to antimalarial monotherapy, TNF inhibitors were associated with lower PASC risk (aHR 0.78, 95% CI 0.64-0.94) and CD20 inhibitors were associated with higher PASC risk (aHR 1.27, 95% CI 1.02-1.59) (**Table 2**)**.** Glucocorticoid use (vs. non-use) was associated with higher PASC risk (aHR 1.15, 95% CI 1.02-1.29). Compared to those with COVID-19 infection early in the pandemic, those with infection during the Delta wave (aHR 0.59, 95% CI 0.46-0.76) and Omicron era (aHR 0.51, 95% CI 0.41-0.63) had a lower risk of PASC. Older age, Black race, increased comorbidity burden, hospitalization for acute COVID-19 infection, and diagnosis of SLE or ANCA-associated vasculitis (compared to RA) were also associated with higher PASC risk.

Table 2. Selected baseline factors at the time of COVID-19 infection and their associations with Post-Acute Sequelae of COVID-19.

Variable	PASC cases (N=1566)	Unadjusted hazard ratio	Adjusted hazard ratio*
Age (per 10 years)	1566	**1.11 (1.08, 1.14)**	**1.05 (1.02, 1.09)**
Sex			
Female	1208	1.0 (ref)	1.0 (ref)
Male	358	0.92 (0.82, 1.03)	0.92 (0.82, 1.03)
Race			
White	1127	1.0 (ref)	1.0 (ref)
Asian	47	0.88 (0.66, 1.17)	0.91 (0.68, 1.22)
Black	169	**1.55 (1.32, 1.81)**	**1.27 (1.08, 1.51)**
Other	178	**1.60 (1.36, 1.88)**	**1.44 (1.21, 1.70)**
Missing	45	0.96 (0.73, 1.26)	0.96 (0.75, 1.24)
Hispanic			
No	1504	1.0 (ref)	1.0 (ref)
Yes	62	**1.43 (1.10, 1.85)**	1.18 (0.91, 1.53)
CCI (per unit)	1566	**1.12 (1.10, 1.14)**	**1.11 (1.09, 1.13)**
Immunomodulatory medication or category**			
Antimalarial monotherapy	180	1.0 (ref)	1.0 (ref)
Methotrexate	204	0.85 (0.69, 1.04)	0.82 (0.67, 1.01)
Mycophenolate mofetil or mycophenolic acid	91	1.18 (0.92, 1.52)	1.05 (0.82, 1.36)
Other csDMARD	62	1.17 (0.87, 1.56)	0.92 (0.67, 1.26)
tsDMARD/JAK inhibitors	51	0.87 (0.63, 1.18)	0.91 (0.66, 1.24)
CD20 inhibitors	135	**1.29 (1.03, 1.60)**	**1.27 (1.02, 1.59)**
TNF inhibitors	290	**0.68 (0.57, 0.82)**	**0.78 (0.64, 0.94)**
IL-6 receptor inhibitors	54	0.79 (0.59, 1.05)	0.83 (0.62, 1.10)
CTLA-4 Ig	30	0.73 (0.51, 1.06)	**0.67 (0.45, 0.98)**
IL-17, IL-12/23, or IL-23 inhibitors	48	0.82 (0.60, 1.13)	0.90 (0.66, 1.24)
Other bDMARD	32	1.03 (0.69, 1.54)	1.09 (0.74, 1.60)
Systemic glucocorticoids			
No	1155	1.0 (ref)	1.0 (ref)
Yes	411	**1.34 (1.20, 1.50)**	**1.15 (1.02, 1.29)**
Rheumatic disease/category			
Rheumatoid arthritis	501	1.0 (ref)	1.0 (ref)
Other inflammatory arthritis	316	0.87 (0.76, 0.995)	1.04 (0.90, 1.21)
Giant cell arteritis and/or polymyalgia rheumatica	109	**1.34 (1.09, 1.63)**	1.12 (0.91, 1.38)
Systemic lupus erythematosus	197	**1.40 (1.19, 1.66)**	**1.50 (1.26, 1.78)**
ANCA-associated vasculitis and other vasculitides	97	**1.36 (1.10, 1.68)**	**1.34 (1.07, 1.68)**
Other rheumatic disease	247	1.12 (0.96, 1.30)	**1.20 (1.02, 1.41)**
Multiple rheumatic diseases	99	1.22 (0.97, 1.55)	1.23 (0.98, 1.55)
Calendar time			
Mar 1, 2020 to Jun 30, 2021 (early pandemic)	693	1.0 (ref)	1.0 (ref)
Jul 1 to Dec 16, 2021 (Delta wave)	111	0.56 (0.46, 0.68)	**0.59 (0.46, 0.76)**
Dec 17, 202 to Jan 18, 2023 (Omicron era)	762	0.51 (0.46, 0.56)	**0.51 (0.41, 0.63)**
Hospitalization for acute COVID-19 infection			
No	1259	1.0 (ref)	1.0 (ref)
Yes	307	**1.99 (1.75, 2.26)**	**1.25 (1.08, 1.45)**

*Multivariable model is adjusted for age, sex, CCI, vaccination status (unvaccinated or partially vaccinated, vaccinated with initial series, or additional vaccines), and calendar time
**DMARDs are mutually exclusive variables using hierarchical categories.

Conclusion: Among patients with SARDs, CD20 inhibitor users had a higher PASC risk while TNF inhibitor users had a lower PASC risk following COVID-19 infection, suggesting that baseline immunosuppression may alter the post-acute COVID-19 course. Other factors associated with PASC included SLE or ANCA-associated vasculitis, as well as general population risk factors including calendar time (as a marker of SARS-CoV-2 variant and available treatments), older age, race, and hospitalization for acute COVID-19. These findings emphasize the potentially large burden of PASC among patients with SARDs.

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Abstract Number: 1801

Tixagevimab/Cilgavimab for the Prevention of COVID-19 in Vaccine-refractory Patients with Autoimmune Diseases: A Prospective Cohort Study

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SESSION INFORMATION
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Session Title: Epidemiology & Public Health Poster III
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Background/Purpose: Patients with immune-mediated inflammatory diseases (IMIDs) and particularly those treated with B-cell-depleting agents frequently fail to develop humoral responses to SARS-CoV-2 vaccinations and have an increased risk of breakthrough infections and severe COVID-19 (Simon D, Arthritis Rheum (2022); Avouac J, Lancet Rheum (2022)). Passive immunization with monoclonal antibodies such as the FDA- and EMA-approved combination tixagevimab/cilgavimab could be an alternative option for this frail population. However, despite promising results from trials on healthy individuals (Levin MJ, NEJM (2022)), efficacy data on IMIDs are scarce. With our study, we aimed to investigate the effect of a pre-exposure prophylaxis (PrEP) with tixagevimab/cilgavimab on the humoral responses and on the prevention of symptomatic COVID-19 in vaccine-refractory IMID patients.

Methods: A prospective interventional cohort study was performed on a cohort of high-risk vaccine-refractory IMID patients undergoing B-cell depletion and/or with primary immunodeficiencies that received PrEP with a single dose of subcutaneous tixagevimab/cilgavimab (150mg/150mg). COVID-19 outcomes and serum anti-SARS-CoV-2 IgG were assessed at baseline, day 1, day 14, day 28, month 3, and after at least 6 months. Standardised incidence ratios (SIR) of COVID-19 were compared to (i) a control group of other vaccine-refractory IMID and primary immunodeficiency patients who did not receive

Table 1. Demographic and clinical characteristics of the treated cohort and control group.

	Controls, N = 114	PrEP-treated, N = 38
Age (years), Mean (SD)	62.7 (13.39)	62.1 (14.17)
Sex, n / N (%)		
female	77 / 114 (67.6%)	22 / 38 (57.9%)
male	37 / 114 (32.4%)	16 / 38 (42.1%)
BMI (kg/m^2), Mean (SD)	29.5 (14.4)	26.4 (5.4)
Smoking, n / N (%)	8 / 78 (10.3%)	3 / 38 (7.9%)
Comorbidities, n / N (%)		
Diabetes	10 / 114 (8.8%)	3 / 38 (7.9%)
Chronic pulmonary disease	16 / 114 (14.0%)	11 / 38 (28.9%)
Hypertension	45 / 114 (39.5%)	18 / 38 (47.4%)
Diagnosis, n / N (%)		
Rheumatoid arthritis	50 / 114 (43.9%)	13 / 38 (34.2%)
ANCA-associated vasculitis	10 / 114 (8.8%)	11 / 38 (28.9%)
Psoriatic arthritis	9 / 114 (7.8%)	0 / 38 (0.0%)
Axial spondylarthritis	8 / 114 (7.0%)	0 / 38 (0.0%)
Systemic sclerosis	8 / 114 (7.0%)	3 / 38 (7.9%)
Sarcoidosis	5 / 114 (4.4%)	0 / 38 (0.0%)
Systemic lupus erythematosus	5 / 114 (4.4%)	2 / 38 (5.3%)
Common variable immunodeficiency	4 / 114 (3.5%)	5 / 38 (13.2%)
Other	15 / 114 (13.2%)	5 / 38 (13.2%)
Treatment, n / N (%)		
Rituximab	41 / 114 (36.0%)	33 / 38 (86.8%)
csDMARDs		
Methotrexate	46 / 114 (40.4%)	9 / 38 (23.7%)
Mycophenolate	8 / 114 (7.0%)	1 / 38 (2.6%)
Azathioprine	3 / 114 (2.6%)	0 / 38 (0.0%)
Leflunomid	3 / 114 (2.6%)	0 / 38 (0.0%)
b/tsDMARDs		
JAKi	16 / 114 (14.0%)	0 / 38 (0.0%)
TNFi	13 / 114 (11.4%)	1 / 38 (2.6%)
IL17i	6 / 114 (5.3%)	0 / 38 (0.0%)
IL6i	6 / 114 (5.3%)	0 / 38 (0.0%)
Abatacept	5 / 114 (4.4%)	0 / 38 (0.0%)
IL12/23i	4 / 114 (3.5%)	0 / 38 (0.0%)
Belimumab	3 / 114 (2.6%)	0 / 38 (0.0%)
IVIG	2 / 114 (1.8%)	6 / 38 (15.8%)
PDE4i	4 / 114 (3.5%)	0 / 38 (0.0%)
Vaccination		
Number of vaccinations, n / N (%)		
1 dose	0 / 114 (0.0%)	0 / 38 (0.0%)
2 doses	0 / 114 (0.0%)	0 / 38 (0.0%)
3 doses	86 / 114 (75.5%)	19 / 38 (50.0%)
4 doses	24 / 114 (21.0%)	18 / 38 (47.0%)
5 doses	4 / 114 (3.5%)	1 / 38 (2.6%)

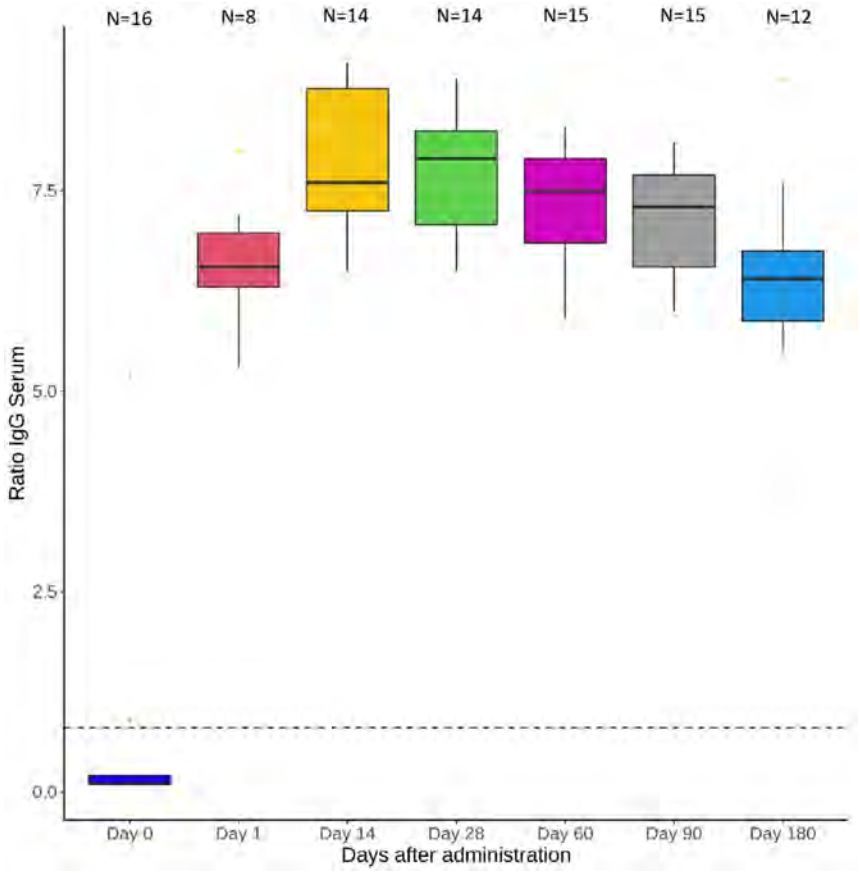

Figure 1. Box and whiskers plot of the levels of serum anti-SARS-CoV-2 spike IgG antibodies before and after 1 day, 14 days, 28 days, 60 days, and 90 days from tixagevimab/cilgavimab treatment. The dashed horizontal line represents the cut-off value of 0.8 optical density ratio (anti-SARS-CoV-2 IgG negative/positive).

prophylactic treatment with tixagevimab/cilgavimab and (ii) the local general population to assess the risk of symptomatic COVID-19. All included patients were attending the outpatient clinic of the Department of Medicine 3 (Rheumatology and Immunology) of the University Clinic Erlangen between March and September 2022. Ethical approval (#157_20 B) to conduct this analysis was granted by the institutional review board of the University Clinic of Erlangen.

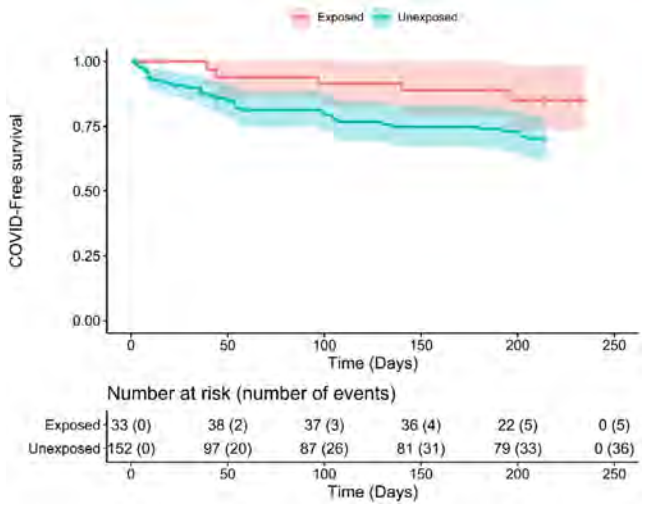

Figure 2. Kaplan-Meier curve of COVID-free survival for the treated group (red line) and the untreated vaccine-refractory controls (blue line).

Results: A total of 38 high-risk IMID patients received tixagevimab/cilgavimab and were compared with 114 untreated high-risk IMID controls. Clinical and demographic characteristics are shown in Table 1. Serum anti-Spike IgG increased to 6.6 OD (SD: ±0.8) at day one and remained positive up to month 6 (6.3±1.4 OD) (Figure 1). Compared to the general population, the SIR of COVID-19 in treated patients was 0.76 (95% CI: 0.24-1.58) despite the increased risk profile and more frequent use of B-cell-depleting therapies. The SIR of the untreated control group was 1.51 (1.07-2.02), corresponding to a significantly increased incidence of COVID-19. A Kaplan-Meyer curve of infection-free survival throughout the 6-month follow-up period is shown in figure 2.

Conclusion: Passive immunization with tixagevimab/cilgavimab is safe and effective in quicklly inducing anti-SARS-CoV-2 humoral immunity and potentially in preventing COVID-19 in high-risk vaccine-refractory IMID patients. These data provide a proof of concept for the use of monoclonal antibodies as a preventative strategy against SARS-CoV-2 in vulnerable populations such as those with inadequate vaccine responses. Thus, the development of new neutralizing antibodies to protect this frail population remains critical.

Disclosure: I. Minopoulou: AbbVie/Abbott, 6; **K. Tascilar**: None; **G. Corte**: None; **M. Yalcin Mutlu**: None; **K. Schmidt**: None; **D. Bohr**: None; **F. Hartmann**: None; **B. Manger**: AbbVie/Abbott, 6, Alexion, 6, Celgene, 6, Eli Lilly, 6, EUSA, 6, Gilead, 6, Janssen, 6, Merck/MSD, 6, Pfizer, 6, Roche, 6, Sanofi, 6; **A. Kleyer**: None; **D. Simon**: Janssen, 5; **T. Harrer**: None; **G. Schett**: None; **F. Fagni**: Eli Lilly, 6, Galapagos, 6, Novartis, 6.

Abstract Number: 1802

Rheumatologic Disorder Diagnostic Testing Patterns:Real World Evidence from a National Laboratory Database

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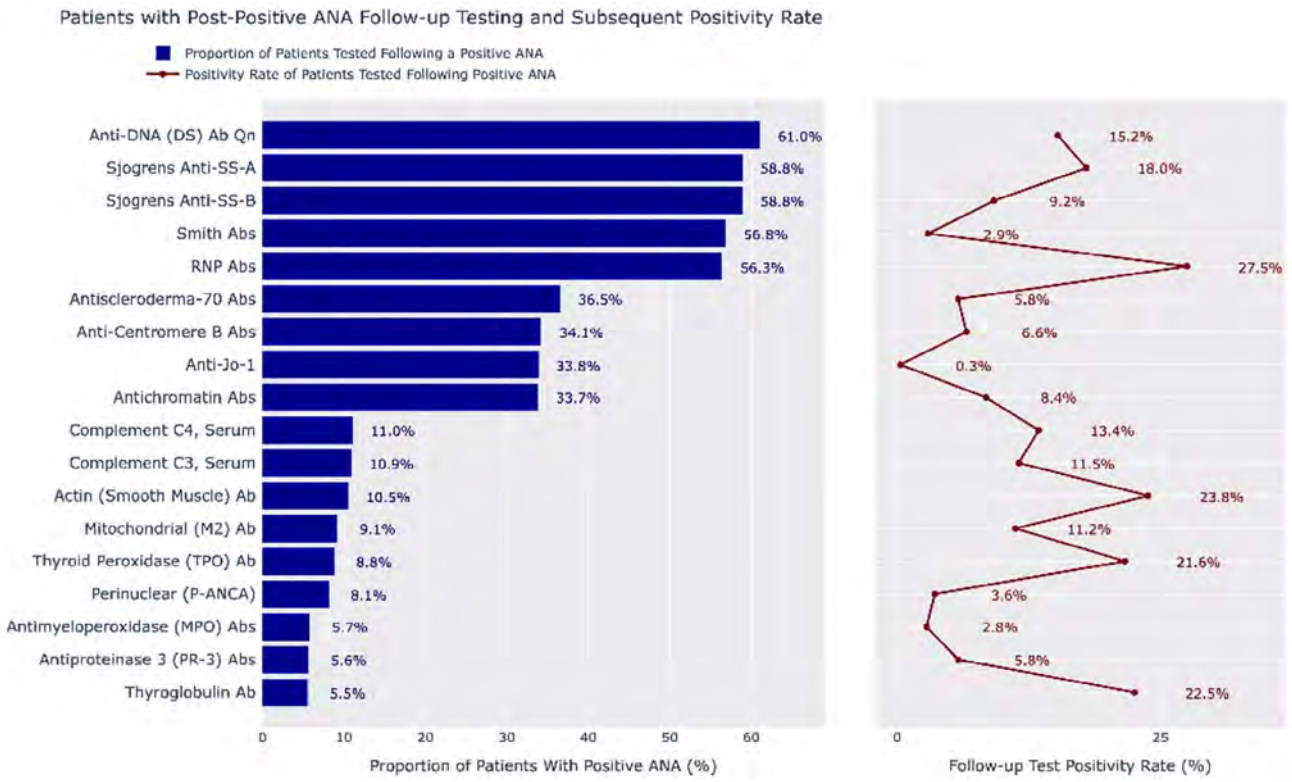
Background/Purpose: Rheumatologic disorders can take years to diagnose. Diagnosis often requires a combination of specific symptoms, examination findings and laboratory testing, rather than a single test. Additionally, symptoms presenting in rheumatologic processes are often present in other common conditions, making diagnosis challenging. A common starting point is an antinuclear antibody (ANA) test, often ordered by a non-rheumatology provider, followed by a wide range of further antibody testing to narrow disorders. Here, we sought to examine patterns of post-ANA testing using real world evidence to inform order guidance opportunities and help advance diagnosis.

Methods: De-identified data from the Labcorp® testing databasewere queried for all ANA orders (both individual and panel testing) between 2011 and 2022. Any ANA order placed by a rheumatologist was excluded. Follow-up antibody testing (such as Anti-Smith, Anti-dsDNA antibodies, etc.) within 365 days post-positive ANA result (1:80 or higher) and respective positivity rates were examined. Reason for ANA ordering was evaluated via ICD-10 codes associated with the original order where the ANA was the only test run on an individual specimen to remove any conflicting ICD codes with other tests.



Patients with Post-Positive ANA Follow-up Testing and Subsequent Positivity Rate

Results: A total of 1,834,048 distinct ANA tests were ordered by a non-rheumatology provider between 2011 and 2022 and had positive results. Of these tests, 49.7% (n=910,683) were ordered by primary care and only 11.2% of the total sample (n=204,608) were associated with patients who had any order placed by a rheumatologist within a year of the ANA. Anti-dsDNA, anti-SSA, anti-SSB, Smith and RNP antibodies were the most frequently ordered autoimmune-specific follow-up tests performed by non-rheumatologists, each representing just over 50% of the sample. Of these, RNP antibodies had the highest positivity rate (27.5%), and Smith antibodies the lowest (2.9%). Thyroglobulin antibodies were the least ordered tests (5.5% of cohort) but had one of the highest positivity rates (22.5%). Of specimens with only an ANA ordered (n=148,882), M25.50 (pain in unspecified joint, 12.6% of the cohort), R76.8 (other abnormal findings in serum, 6.7%) and R53.83 (other fatigue, 5.3%), I10 (essential primary hypertension, 3.8%) and E55.9 (Vitamin D deficiency, 3.1%) were the most frequent ICD-10s ordered but together represented only 8.1% of the total cohort.

Top 10 Most Frequently Used ICD-10s with ANA orders

Conclusion: There does not appear to be a clear ordering pattern of follow-up testing within a year of a positive ANA test. While more than half of the cohort received some common antibody tests like Anti-dsDNA, positivity rates were low. Interestingly, approximately 10% of the cohort had an order from a rheumatologist within a year, suggesting the majority of diagnostic workup is being done by primary care. Ordering ICD-10 codes represent suspicion for a rheumatologic process and symptoms, such as joint pain, but the frequency of hypertension and Vitamin D deficiency codes do not readily explain a reason for ordering. Results suggest the need for a guideline approach for rheumatologic disorder testing evaluation and education in the non-rheumatologic setting.

Disclosure: D. Alfego: None; **Q. Hlatky**: Labcorp, 3; **S. Naides**: Laboratory Corporation of America Holdings (Labcorp), 3; **K. Lee**: None; **J. Ennis**: Labcorp, 3, 11; **K. Clark**: Labcorp, 3.

Abstract Number: 1803

Perceived Dignity in Patients with Rheumatic Diseases: An Unrecognized Source of Emotional Distress

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Background/Purpose: Dignity is generally considered a fundamental feature of human individuals, related to human rationality and morality. This connotation of dignity is recognized as intrinsic dignity. However, in the clinical setting, the notion of dignity evokes how patients see themselves and are seen by others and how the nature of the illness in question affects the person's life and identity. Perceived dignity is a recognized source of multifaceted distress in cancer patients, which has been associated with the medical care environment, and patients feel a diminished sense of worth or value and a burden to others. The spectrum of rheumatic diseases' clinical expression provides evidence that a significant percentage of the patients might present with progressive health decline, disability, distressing symptoms affecting their capacity to continue with usual activities and roles, and limited autonomy, all of which threaten patients' perceived dignity.

The study's primary objective was to determine distress related to perceived dignity (DPD) among Mexican patients with RMDs. The rationale and methods for adapting and validating the Mexican version of the Patient Dignity Inventory (PDI-Mx) in the population are additionally described.

Methods: This cross-sectional study was developed in 2 phases (January 2022-July 2022). Three convenience samples of different patients were used, and quotes were considered to represent the ten most frequent local RMDs-related diagnoses (**Figure 1**). Phase 1 consisted of pilot testing and questionnaire feasibility (n=50 patients, *Sample 1*), and the PDI-Mx content validity (judgment experts' agreement), construct validity (exploratory factor analysis), criterion validity (Spearman correlations), and reliability (internal consistency and temporal stability) in 220 outpatients (*Sample 2*), among whom 30 underwent test-retest. Phase 2 consisted of DPD quantification in 290 outpatients with RMDs (*Sample 3*). Receiving Operating Curve

Table. Strength of the association between the PDI-Mx score, the DASS21 score, the HAQ-DI score, the family APGAR score, and the Brief Resilient Coping Scale score.

	DASS21 *Anxiety*	DASS21 *Depression*	DASS21 *Stress*	HAQ-DI	Family APGAR	BRCS
PDI-Mx global	0.673	0.754	0.692	0.549	-0.286	-0.285
Dimension I	0.677	0.758	0.670	0.507	-0.301	-0.292
Dimension II	0.631	0.688	0.694	0.448	-0.234	-0.253
Dimension III	0.495	0.492	0.448	0.628	NS	-0.149*
Dimension IV	0.503	0.574	0.521	0.417	-0.431	-0.173

DASS21=Depression, Anxiety, and Stress Scale. HAQ-DI=Health Assessment Questionnaire Disability Index. APGAR=Adaptation Partnership Growth Affection Resolve. BRCS= Brief Resilient Coping Scale. PDI-Mx= Perceived Dignity Inventory (Mexican version). NS=Not Significant. Dimension I=Loss of meaning in Life. Dimension II=Discomfort and uncertainty. Dimension III=Loss of Independence. Dimension IV=Loss of Social support.

was used to define the best PDI-Mx cut-off for DPD (≥54.5, min-max:25-125, higher scores indicating more DPD) with the gold standard defined according to DASS21 scores of at least moderate severity for anxiety and depression and a psychiatric interview that confirmed clinically relevant symptoms of emotional distress.

Figure 1. Diagnoses distribution in the 3 samples used.

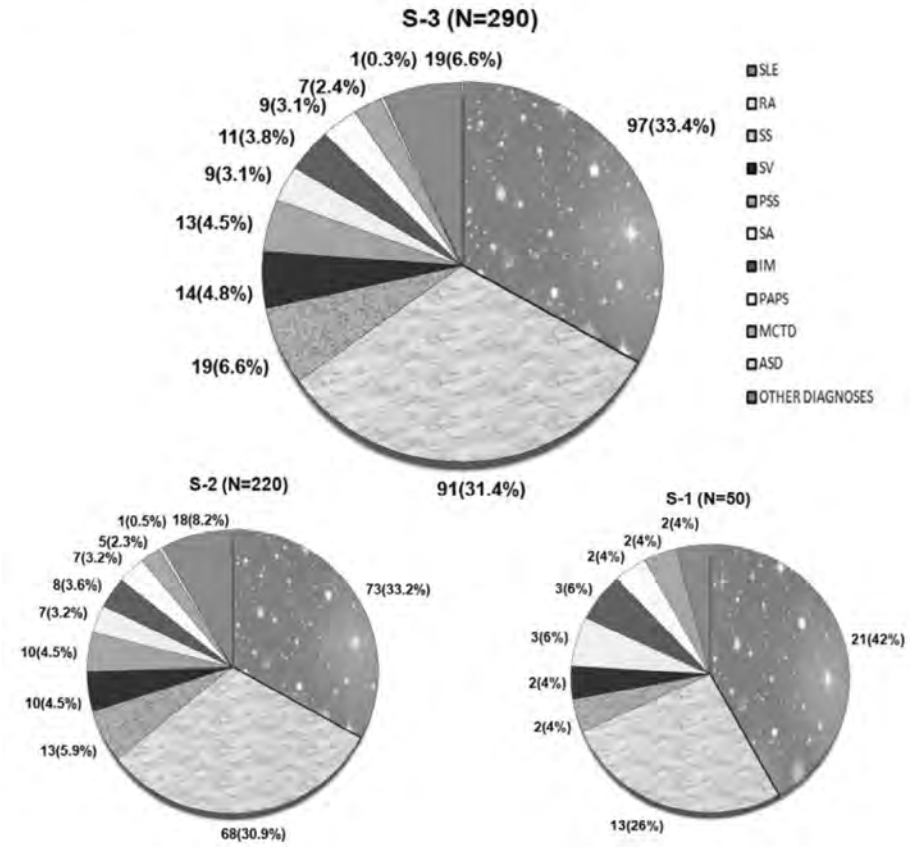

Figure 2. PDI-Mx structure pre and post-factorial analysis.

Results: Overall, patients were representative of typical outpatients with RMDs from a National tertiary care level center, and the most frequent diagnoses were Systemic Lupus Erythematosus and Rheumatoid arthritis (**Figure 1**). DPD was present in 78 patients (26.9%). The 25-item PDI-Mx was found feasible, valid (experts' agreement ≥82%; a 4-factor structure accounted for 68.7% of the total variance; moderate to high correlations between the PDI-Mx and questionnaires summarized in the **Table**) and reliable (Cronbach's α=0.962, ICC=0.939 [95%CI=0.913-0.961]). The structure of the PDI-Mx underwent mild modifications after factorial analysis (**Figure 2**).

Conclusion: DPD was homogeneously present in up to 27% of Mexican patients with different RMDs. The PDI-Mx process validation was rigorous, and its critical quality indicators were validity, reliability, and feasibility.

Disclosure: V. Pascual Ramos: None; **G. Guaracha Basañez**: None; **I. Contreras Yañez**: None; **M. Cuevas Montoya**: None; **O. Rodríguez Mayoral**: None; **H. Chochinov**: None; **M. García Alanís**: None.

Abstract Number: 1804

Plant-based Diet Quality and the Risk of Gout: Results from Two Prospective Cohort Studies of US Men and Women

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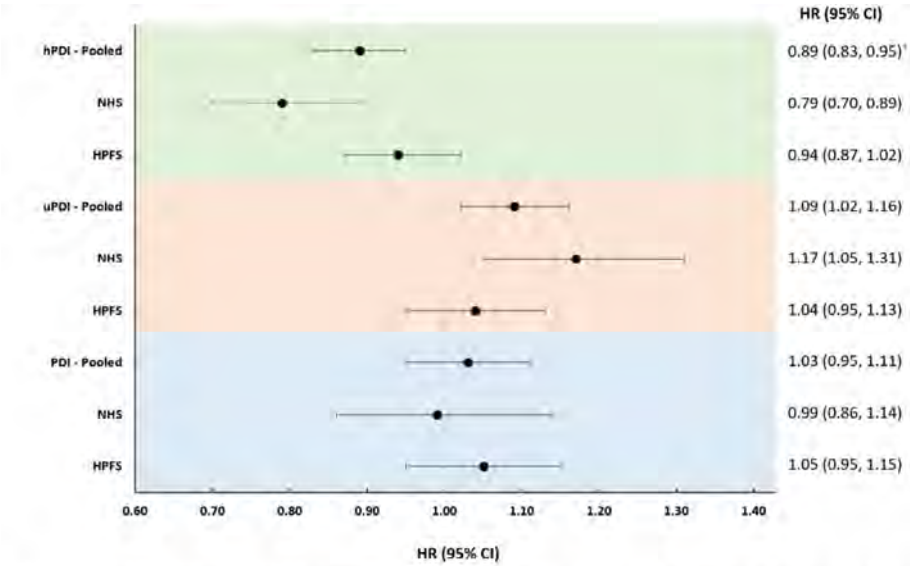
Background/Purpose: Plant-based diets are growing in popularity due to their health benefits for selected cardiometabolic diseases as well as favorable environmental impact. However, the limited prior studies of gout simply dichotomized plant-based diets as "vegetarian" vs. "meat-containing" and did not differentiate between the quality of plant foods. Therefore, we examined associations between adherence to a plant-based diet (including healthy and unhealthy versions of this diet), as well as its 18 individual food group components, and incident gout.

Methods: We analyzed data from 123,014 men and women in the Health Professionals Follow-up Study and Nurses' Health Study who were free of gout at baseline. We constructed an overall plant-based diet index (PDI) as well as healthy (hPDI) and unhealthy (uPDI) versions of this index that emphasize healthy and less healthy plant-based foods, respectively. These diet indices were comprised of 18 food groups which were assessed using a validated semi-quantitative food frequency questionnaire, with possible scores ranging from 18 (lowest) to 90 (highest). Participants reported a new diagnosis of gout on biennial questionnaires. We defined incident cases of gout as those that were confirmed with a supplementary questionnaire to meet the preliminary American College of Rheumatology survey criteria for gout (Wallace et al., 1977). We used Cox proportional hazards regression models to evaluate multivariable-adjusted associations between all three PDIs and incident gout.

Results: The hPDI was inversely associated with incident gout (pooled HR per 10-unit increase 0.89 [0.83, 0.95]), while the uPDI was positively associated (pooled HR per 10-unit increase 1.09 [1.02, 1.16]) **(Figure)**. Similar associations were observed in strata defined by hypertension status, overweight, dairy intake, fiber intake, and menopausal status with no evidence of statistically significant effect modification. However, for hPDI (not but uPDI), the inverse association with gout persisted among those who were less physically active (i.e., below the median level of physical activity; pooled HR comparing extreme quintiles 0.68 [0.56, 0.82]) but was no longer significant among those who were more physically active (0.94 [0.76, 1.16]) (P for interaction=0.01). Finally, the overall PDI (emphasizing intakes of all plant foods) was not associated with gout risk **(Figure)**. Among individual food groups, higher intakes of certain healthy plant foods such as whole grain foods (pooled HR per additional daily serving, 0.93 [0.89, 0.97]) and tea/coffee (0.95 [0.92, 0.97]) were independently associated with a lower risk of gout, while selected unhealthy plant foods such as fruit juice (1.07 [1.01, 1.13]) and sugar-sweetened beverages (1.17 [1.07, 1.27]) were positively associated with gout.



*Models were age and calendar time stratified and adjusted for energy intake (quintiles), body mass index (<21, 21-22.9, 23-24.9, 25-26.9, 27-28.9, 29-30.9, 31-32.9, 33-34.9, ≥35 kg/m², missing), history of hypertension, history of renal failure (men only), diuretic use, physical activity (quintiles or missing), and alcohol intake (0, 1-5, 6-10, 11-15, 16-30, >30 g/day). Among women, the model was additionally adjusted for oral contraceptive use and menopausal status/postmenopausal hormone use (premenopausal, postmenopausal never, current, or past users, or missing).
†P-value for *Q*-statistic <0.05, indicating statistically significant heterogeneity among the two cohorts.

Conclusion: In conclusion, we found evidence for an inverse association between a healthy plant-based diet and incident gout, and a positive association between an unhealthy plant-based diet and gout. Our findings support current dietary recommendations to increase consumption of healthy plant foods while lowering intake of unhealthy plant foods to mitigate gout risk.

Disclosure: S. Rai: None; **F. Hu**: None; **M. Wang**: None; **H. Choi**: Ani, 2, Horizon, 2, 5, LG, 2, Protalix, 2, Shanton, 2; **Q. Sun**: None.

Abstract Number: 1805

Longitudinal Changes in Serum Urate Associate Minimally with Changes in Daily Alcohol Intake

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Background/Purpose: Cross-sectional epidemiologic studies support a direct relationship between alcohol intake and serum urate (SU). These observations are parts of the basis for gout recommendations suggesting limiting alcohol intake. However, it is unknown whether reductions in alcohol intake over time are associated with reductions in SU. Hence, we evaluated the relationship between changes in daily alcohol intake and changes in SU levels.

Methods: This longitudinal observational study used prospectively collected annual medical checkup data at a large medical checkup center in Japan. At each visit, daily alcohol intake information was collected using a standardized collection tool, and SU was routinely measured. We included consecutive participants with at least two visits from Oct 2012 to Oct 2022. Participants who received treatment for hyperuricemia or gout during the study period were excluded. The outcome was a change in SU between two visits, and exposures of interest were changes in total daily alcohol intake and in specific types of alcoholic beverage intake (e.g., beer, whiskey, wine, sake, shochu, and others). We used a linear mixed-effect model with random intercepts to take longitudinal intrapersonal correlations into account. We adjusted for SU and alcohol consumption at a prior visit. In addition, age, sex, body mass index, eGFR, medication use, smoking status, daily activity level, exercise level, and results of dietary questionnaires measured at prior visits were adjusted for in primary analyses. In secondary analyses, covariates measured at subsequent visits were also included. As well, we examined the associations in people who fully discontinued alcohol consumption and in sub-groups.

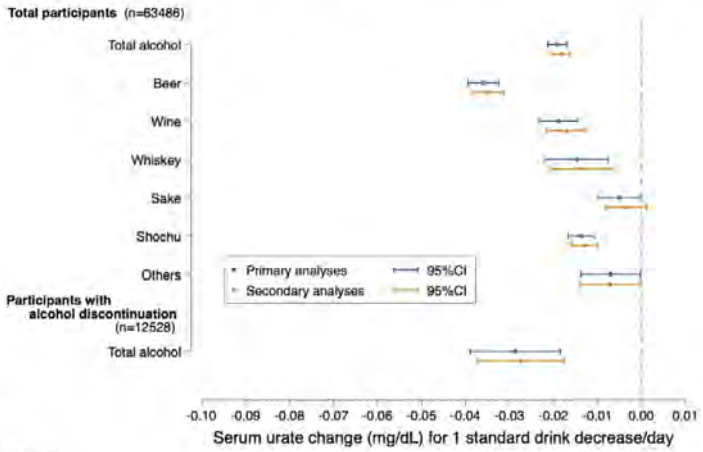
Results: A total of 63,486 participants with 370,572 visits were included in the analyses. The mean (standard deviation) age was 48.0 (12.9) years, and 28,578 (45.0%) were male. 37,199 (58.6%) were regular alcohol drinkers with a median alcohol intake of 1.4 drink/day. The mean interval between visits was 1.3 years. There were 149,441 episodes of changing daily alcohol intake in 41,661 participants (Table 1). The primary analysis showed a significant but very small association between one alcoholic drink decrease and SU (SU change -0.019 [-0.021, -0.017] mg/dL; $p< 0.001$); the association varied based on the type of alcohol consumed. The extents of the associations were almost the same in secondary analyses and when we

Table 1. Baseline characteristics of participants in the medical checkup

	Total participants N=63,486
Age	47.9 (12.9)
Sex Male	28,578 (45.0%)
Female	34,908 (55.0%)
Body Mass Index	22.2 (3.4)
The number of visit	5.0 (3.0, 9.0)
Total follow up, year	5.5 (2.7-8.8)
Interval between visits, year	1.3 (0.8)
Serum urate, mg/dL	5.4 (1.3)
eGFR	78.2 (16.1)
Medication use	
Hypertension	5,618 (8.8%)
Diabetes	1,426 (2.2%)
Dyslipidemia	4,058 (6.4%)
Ischemic heart disease	499 (0.8%)
Cerebrovascular diseases	294 (0.5%)
Baseline alcohol data	
Alcohol drinker	37,199 (58.6%)
Total alcohol intake (Standard drink/day)	1.40 (0.60, 2.91)
Beer drinker	26,694 (42.0%)
Daily intake (Standard drink/day)	1.09 (0.56, 1.67)
Wine drinker	10,298 (16.2%)
Daily intake (Standard drink/day)	0.99 (0.49, 1.97)
Whiskey drinker	2,107 (3.3%)
Daily intake (Standard drink/day)	1.10 (0.69, 1.92)
Sake drinker	3,128 (4.9%)
Daily intake (Standard drink/day)	1.85 (1.23, 3.09)
Shochu drinker	5,693 (9.0%)
Daily intake (Standard drink/day)	2.29 (1.43, 4.00)
Others drinker	1,084 (1.7%)
Daily intake (Standard drink/day)	0.84 (0.56, 1.96)
The number of participants who changed their daily alcohol intake at least once during the study period.	41,661 (65.6%) (149, 441 visits)
The number of participants who discontinued alcohol intake	12,528 (19.7%)

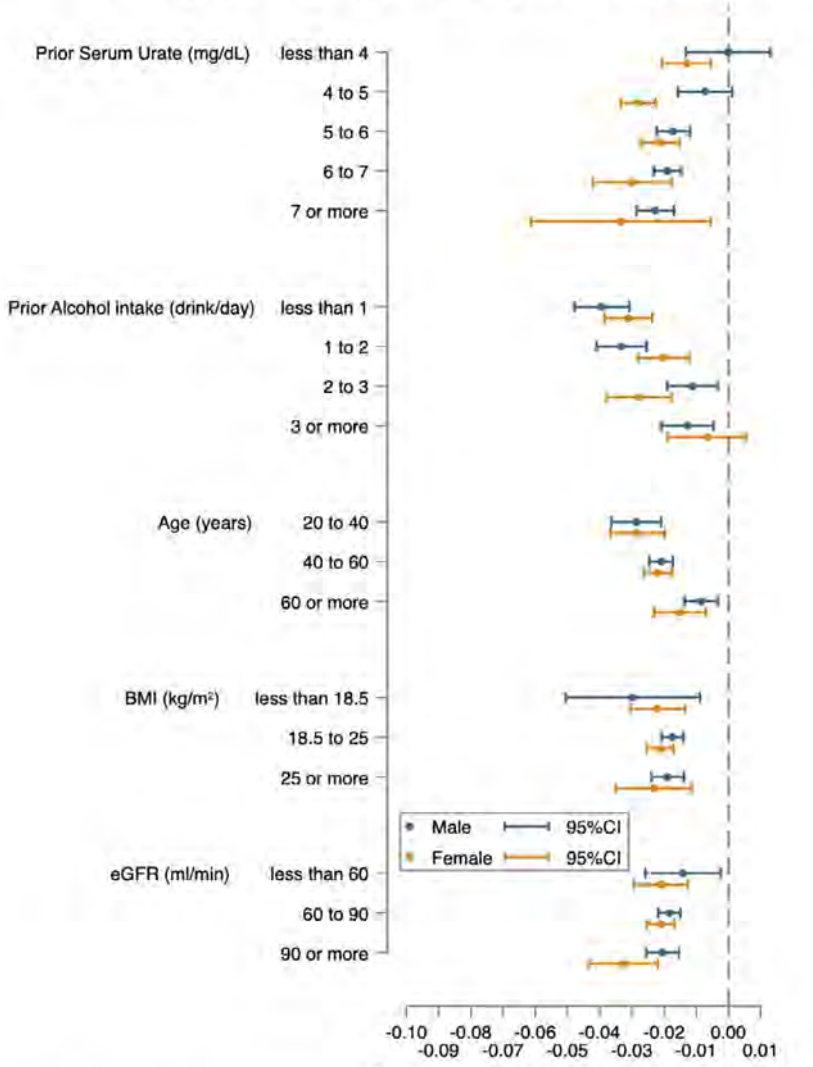
Continuous variables are presented as mean (standard deviation) or median (interquartile range) based on their distribution

Figure 1. The association of changes in serum urate levels (mg/dL) with one unit decrease in daily alcohol intake (standard drink/day)



NOTES:
Sake: Japanese rice wine, Shochu: Japanese spirit.
Total alcohol included beer, wine, whiskey, sake, shochu, and other alcoholic beverages.
SU and alcohol consumption at a prior visit were adjusted for in all analyses. In primary analyses, we adjusted for other covariates measured at prior visits. In secondary analyses, we additionally adjusted for covariates measured at subsequent visits
Other covariates included age, sex, body mass index, eGFR, medication use, smoking status, daily activity level, exercise level, and results of dietary questionnaires.

Figure 2. Results of stratified subgroup analyses for the association of changes in serum urate levels (mg/dL) with one unit decrease in daily alcohol intake (standard drink/day)



NOTES:
Results were adjusted for SU, alcohol consumption, age, body mass index, eGFR, medication use, smoking status, daily activity level, exercise level, and results of dietary questionnaires measured at prior visits.

focused on the visits where participants fully discontinued regular alcohol intake (Figure 1). In stratified sub-group analyses, larger but still small changes in SU were observed in younger participants, lighter drinkers, and those with higher initial SU levels. (Figure 2).

Conclusion: Although alcohol intake is associated with acute gout events, this study found that longitudinal changes in daily alcohol consumption did not result in clinically relevant changes in chronic SU levels. Reducing alcohol intake alone is unlikely to be a major driver of reductions in chronic SU in the general population.

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Kasei Pharma, 2, 6, Astellas, 2, 6, Ayumi Pharma, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Chugai, 2, 6, Daiichi-Sankyo, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Ono Pharma, 2, 6, Pfizer, 2, 6, Tanabe-Mitsubishi, 2, 6, UCB, 2, 6; **H. Hasegawa**: None; **T. Matsuda**: None; **J. Marrugo**: None; **S. Tedeschi**: Novartis, 2; **D. Solomon**: CorEvitas, 5, Janssen, 5, Moderna, 5, Novartis, 5.

Abstract Number: 1806

The Prevalence of Cardiac Sarcoidosis – A Systemic Review and Meta-Analysis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiac sarcoidosis (CS) results from granulomatous infiltrating of the myocardium and manifests as an extended clinical spectrum from silence to conduction disturbances, ventricular tachyarrhythmias, heart failure, and sudden cardiac death. Despite the various presentations, there is a dearth of cumulative evidence of CS prevalence, and the current knowledge is mainly based on studies with small sample sizes or performed in selected countries. This study aimed to use a systematic review and meta-analysis methodology to explore the CS prevalence among population subgroups worldwide and patients with different cardiac abnormalities.

Methods: A literature search was conducted in the PubMed and EMBASE databases until September 8, 2022. Methodological quality assessment of non-randomized studies was performed with high-quality studies included. The statistical analysis included meta-analysis using a random-effects model to estimate pooled CS prevalence and accounting for variations in the study populations, the timing of CS diagnosis, and the length of follow-up between studies in the subgroup analyses.

Results: The prevalence of CS was reported in 172 studies conducted in 28 countries across five WHO regions, with a significant proportion of research originating from the United States (37%) and Japan (21%) and a cumulative total of 122,535 individuals (Figure 1). The prevalence of definite CS among patients with systemic sarcoidosis, extracardiac sarcoidosis being screened for CS, and patients with clinical signs of CS was 11% (9%-14%), 27% (18-37%), and 43% (36%-50%), respectively. Besides patients with suspicions of CS, a higher pooled prevalence was also found in patients with an initial diagnosis of giant cell myocarditis (59%) and deceased sarcoidosis patients undergoing autopsy (36%). Among the organ-specific sarcoidosis cohort, cardiac involvement was diagnosed in 20% of pulmonary sarcoidosis patients, 6% of renal sarcoidosis patients, and 4% of ocular sarcoidosis patients. Seven studies showed that the prevalence of sarcoidosis with cardiac involvement only (isolated cardiac sarcoidosis, ICS) was 13% (4%-26%). Regarding subgroups of cardiac manifestations, 11% of patients with unexplained conduction block and 6% with ventricular arrhythmia or unexplained cardiomyopathy/structural abnormalities were diagnosed with CS. In comparison, CS was identified in 2% of patients who had succumbed to sudden cardiac arrest or death and 2% of patients eligible for or undergoing heart transplantation (Figure 2).

Conclusion: This systematic review and meta-analysis is the first study to provide an overview of CS prevalence among large-scale populations worldwide and introduces important epidemiologic data at population and organ-specific levels. Essential gaps in current epidemiology research of CS were also identified. We encourage and advocate for further global research efforts with the inclusion of currently underrepresented populations to better understand CS.

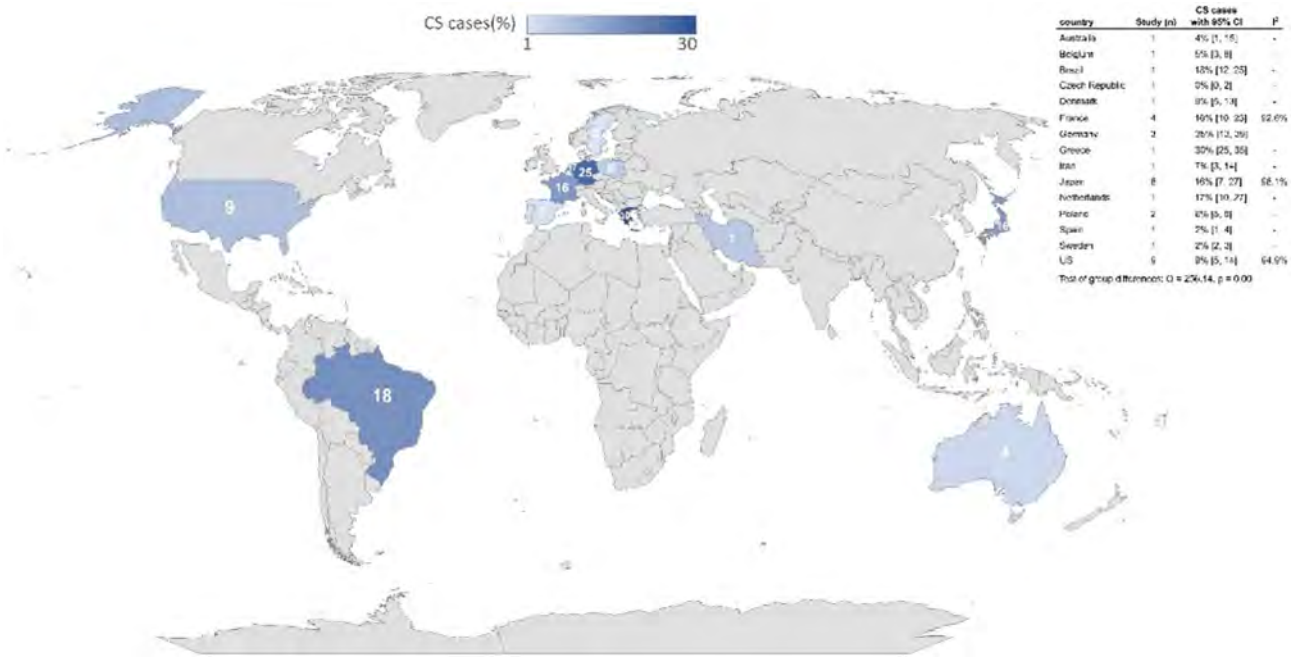

Figure 1. World map demonstrating the prevalence of cardiac sarcoidosis (CS) cases within systemic sarcoidosis subgroups by country. Country-specific studies on CS prevalence are present on the right with 95% confidence intervals (CIs), derived from meta-analysis (random-effects model). Significant differences were detected, p<0.001

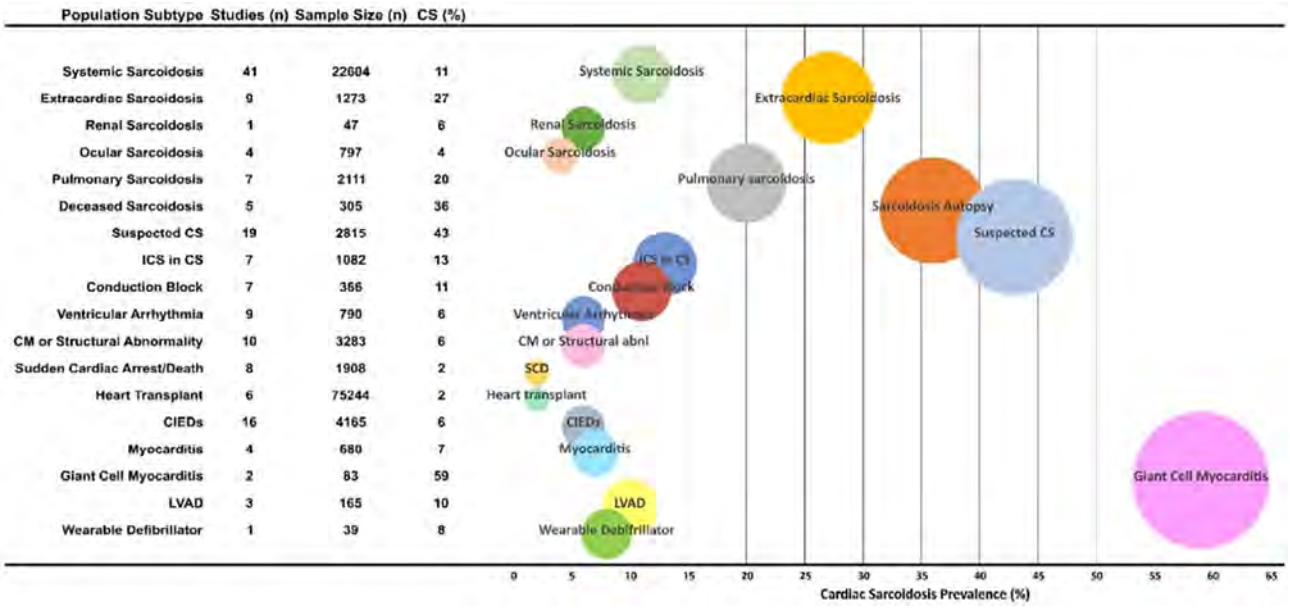

Figure 2. The prevalence of cardiac sarcoidosis (CS) in various populations. The bubble plot shows the prevalence of CS on the x-axis, with each bubble size corresponding to the CS prevalence. ICS, isolated cardiac sarcoidosis; CM, cardiomyopathy; CIED, cardiac implantable electronic device; LVAD, left ventricular assist devices; SCD, sudden cardiac death.

Disclosure: D. Shao: None; **J. Seo**: None; **S. Mangeshkar**: None; **N. Nazarenko**: None; **S. Esagian**: None; **L. Palaiodimos**: None; **D. Kokkinidis**: None.

Abstract Number: 1807

Hypothyroidism Impacts Clinical and Healthcare Utilization Outcomes After Primary Total Hip Arthroplasty

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Most data on the effect of comorbidities on primary total hip arthroplasty (THA) outcomes is focused on conditions that directly impact joint health, or on one underlying cause, such as osteoarthritis (OA), but there is little comparison between underlying causes of THA. This study aimed to assess the association of hypothyroidism with outcomes of primary THA, stratified by the primary underlying cause.

Methods: We identified all patients undergoing primary THA in the 2019 national inpatient sample. These patients were stratified based on primary diagnoses into hip OA (N=405691), avascular necrosis (AVN; N=17060), fracture (N=104265), inflammatory arthritis (IA; N=5720), and "other" (N=59155). We identified hypothyroidism and complications using secondary diagnoses. Complications codes were specified to be initial encounters, when possible. We performed multivariable-adjusted regression analyses adjusted for race, age, sex, hospital bed size, census region and teaching status with clinical and healthcare utilization outcomes as endpoints.

Results: Total cohort population was 591,891. Mean age was 68.8, mean length of stay (LOS) was 2.7 days, and 58.2% were female. Overall, hypothyroidism was significantly associated with increased LOS, non-routine discharge, acute renal failure (ARF), and anemia ($p \leq 0.003$ for each), and decreased risk of pneumonia ($p=0.031$). In the OA cohort, hypothyroidism was associated with increased LOS, non-routine discharge, anemia, and ARF ($p \leq 0.008$ for each). Hypothyroidism was associated with increased blood transfusion ($p=0.049$) in the AVN cohort. In the fracture cohort, hypothyroidism was associated with increased odds of non-routine discharge, and anemia ($p \leq 0.020$ for each), but decreased odds of deep veinous thrombosis ($p=0.034$).

Conclusion: Hypothyroidism was associated with clinical and healthcare utilization outcomes in a nationally representative sample of patients who underwent primary THA, especially in OA, AVN, and fracture cohorts. Interventions of tailored patient management strategies for hypothyroidism in THA peri-operative period should be tested for their efficacy to improve peri-operative outcomes.

Table-1: Baseline Hospital and Patient Characteristics with hypothyroidism who underwent primary total hip arthroplasty (THA) in the National Inpatient Sample (2019, N=591,891)

Variable	No Hypothyroidism (N=496,735; 83.9%)	Hypothyroidism (N=95,155; 16.1%)	Overall (N=591,891)	p value
Age (mean ± SD years)	68.01 ± 0.087	72.62 ± 0.112	68.75 ± 0.086	<.001
Length of Stay (mean ± SD days)	2.67 ± 0.026	3.05 ± 0.035	2.73 ± 0.026	<.001
Total Charges (mean ± SD dollars)	81,846.23 ± 962.114	73,614.63 ± 986.461	72130.27 ± 952.765	<.001
In-hospital mortality	1430 (0.3%)	415 (0.4%)	1845 (0.3%)	<.001
Underlying Condition (N,%)				<.001
Osteoarthritis	346045 (69.7%)	59645 (62.7%)	405691 (68.5%)	
Avascular necrosis	15185 (3.1%)	1875 (2.0%)	17060 (2.9%)	
Hip fracture	82230 (16.6%)	22035 (23.2%)	104265 (17.6%)	
Inflammatory arthritis[1]	4525 (0.9%)	1195 (1.3%)	5720 (1.0%)	
Other	48750 (9.8%)	10405 (10.9%)	59155 (10.0%)	
Sex (N,%)				<.001
Male	227795 (45.9%)	19660 (20.7%)	247455 (41.8%)	
Female	268935 (54.1%)	75495 (79.3%)	344430 (58.2%)	
Number of Obese Patients	104125 (21.0%)	19855 (20.9%)	123980 (20.9%)	0.788
Number of Morbidly Obese Patients	22835 (4.6%)	4895 (5.1%)	27730 (4.7%)	0.002
Race (N,%)				<.001
White	411720 (85.1%)	84920 (91.7%)	496641 (86.1%)	
Black	39180 (8.1%)	2775 (3.0%)	41955 (7.3%)	
Hispanic	17680 (3.7%)	2565 (2.8%)	20245 (3.5%)	
Asian or Pacific Islander	5750 (1.2%)	720 (0.8%)	6470 (1.1%)	
Native American	7800 (1.6%)	1340 (1.4%)	9140 (1.6%)	
Other	1790 (0.4%)	300 (0.3%)	2090 (0.4%)	
Charlson Comorbidity (N,%)				<.001
0	269310 (54.2%)	42835 (45.0%)	312145 (52.7%)	
1	128040 (25.8%)	27555 (29.0%)	155595 (26.3%)	
2	45155 (9.1%)	11215 (11.8%)	56370 (9.5%)	
3	22295 (4.5%)	5510 (5.8%)	27805 (4.7%)	
4	9550 (1.9%)	2470 (2.6%)	12020 (2.0%)	
≥5	22385 (4.5%)	5570 (5.9%)	27955 (4.7%)	
Insurance Type (N,%)				<.001
Medicare	301680 (60.8%)	70960 (74.7%)	372640 (63.0%)	
Medicaid	25230 (5.1%)	2340 (2.5%)	27570 (4.7%)	
Private Insurance	151460 (30.5%)	19800 (20.8%)	171260 (29.0%)	
Self-Pay	4765 (1.0%)	560 (0.6%)	5325 (0.9%)	
No Charge	200 (0.0%)	15 (0.0%)	215 (0.0%)	
Other	12855 (2.6%)	1380 (1.5%)	14235 (2.4%)	
Patient Disposition (N,%)				<.001
Routine	185590 (37.4%)	28235 (29.7%)	213825 (36.1%)	
Transfer to Short-term Hospital	1435 (0.3%)	330 (0.3%)	1765 (0.3%)	
Transfer Other[2]	124670 (25.1%)	34745 (36.5%)	159415 (26.9%)	
Home Health Care (HHC)	183150 (36.9%)	31340 (32.9%)	214490 (36.2%)	
Against Medical Advice (AMA)	400 (0.1%)	75 (0.1%)	475 (0.1%)	
Died	1430 (0.3%)	415 (0.4%)	1845 (0.3%)	
Median Household Income for ZIP Code (N,%)				<.001
0-25th percentile	106125 (21.7%)	18985 (20.2%)	125110 (21.4%)	
26th-50th percentile (median)	122220 (25.0%)	24355 (25.9%)	146575 (25.1%)	
51st to 75th percentile	132495 (27.1%)	26035 (27.7%)	158530 (27.2%)	
76th to 100th percentile	128715 (26.3%)	24630 (26.2%)	153345 (26.3%)	
Census Division of Hospital (N,%)				<.001
New England	28320 (5.7%)	4500 (4.7%)	32820 (5.5%)	
Middle Atlantic	66075 (13.3%)	12090 (12.7%)	78165 (13.2%)	
East North Central	83265 (16.8%)	16045 (16.9%)	99310 (16.8%)	
West North Central	40000 (8.1%)	8210 (8.6%)	48210 (8.1%)	
South Atlantic	99050 (19.9%)	18555 (19.5%)	117605 (19.9%)	
East South Central	32790 (6.6%)	6350 (6.7%)	39140 (6.6%)	
West South Central	45660 (9.2%)	9720 (10.2%)	55380 (9.4%)	
Mountain	37430 (7.5%)	8355 (8.8%)	45785 (7.7%)	
Pacific	64145 (12.9%)	11330 (11.9%)	75475 (12.8%)	
Location/teaching status of hospital (N,%)				0.481
Rural	43455 (8.7%)	8595 (9.0%)	52050 (8.8%)	
Urban nonteaching	107110 (21.6%)	20260 (21.3%)	127370 (21.5%)	
Urban teaching	346170 (69.7%)	66300 (69.7%)	412470 (69.7%)	
Complications (Post-operative)[3]				
Need for blood transfusion	724 (0.1%)	215 (0.2%)	865 (0.1%)	<.001
Prosthetic complications	282 (0.0%)	105 (0.1%)	320 (0.0%)	<.001
Post-procedural infection	82 (0.0%)	36 (0.0%)	92 (0.0%)	0.626
Complications (Cumulative)[4]				
Acute renal failure	22535 (4.5%)	6025 (6.3%)	28560 (4.8%)	<.001
Myocardial infarction	104 (0.0%)	53 (0.1%)	119 (0.0%)	<.001
Pulmonary embolism	76 (0.0%)	35 (0.0%)	83 (0.0%)	0.313
Deep vein thrombosis	119 (0.0%)	45 (0.0%)	131 (0.0%)	0.782
Anemia	2919 (0.5%)	692 (0.6%)	3516 (0.5%)	<.001
Pneumonia	135 (0.0%)	60 (0.1%)	151 (0.0%)	0.131

[1]Includes rheumatoid arthritis, spondylarthritis, ankylosing spondylitis and psoriatic arthritis

[2]Includes Skilled Nursing Facility (SNF), Intermediate Care Facility (ICF), Another Type of Facility

ICD-10 CM codes: Acute Renal Failure (N17.x), Myocardial Infarction (I21.x), Anemia (D62), Pneumonia (J18.9, J15.9, J22.x), Pulmonary Embolism (I26.x), Deep Venous Thrombosis (DVT; I82.x), Prosthetic Complication (T84.010A, T84.012A, T84.012A, T84.013A, T84.018A, T84.019A, T84.020A, T82.021A, T84.022A, T84.023A, T84.028A, T84.029A, T84.090A, T84.091A, T84.092A, T84.093A, T84.098A, T84.099A, M96.65, M96.661,M96.662, M96.669, M96.671, M96.672, M96.69, M97.02XA, M97.11X1, M97.12XA), Post-Procedural Infection (T84.50XA, T84.51XA, T84.52XA, T84.54XA, T84.59XA, T81.4)

ICD-10 PCS codes: Blood Transfusion (302*)

[3]Only initial encounter ICD-10 codes selected

Table-2: Multivariable-adjusted association of hypothyroidism with clinical outcomes of patients who underwent primary total hip arthroplasty (THA), stratified by underlying diagnosis

	Osteoarthritis (N=405691; 68.5%)		Avascular necrosis (N=17060; 2.9%)		Hip fracture (N=104265; 17.6%)		Inflammatory arthritis[1] (N=5720; 1.0%)		Other (N=59155; 10.0%)		Total (N=591891)	
Variable	aOR (95% CI)	p	aOR (95% CI)	p	aOR (95% CI)	p	aOR (95% CI)	p	aOR (95% CI)	p	aOR (95% CI)	p
Length of Stay (> 2 days)	1.144 (1.082-1.210)	<.001	0.924 (0.692-1.234)	0.593	1.042 (0.895-1.214)	0.595	0.978 (0.610-1.568)	0.927	1.140 (1.002-1.296)	0.046	1.075 (1.030-1.121)	<.001
Total Cost (Charges above median)	1.015 (0.965-1.068)	0.568	1.146 (0.888-1.479)	0.296	1.078 (0.999-1.163)	0.053	0.826 (0.578-1.179)	0.292	1.027 (0.914-1.155)	0.655	1.028 (0.987-1.070)	0.183
Mortality	1.497 (0.498-4.500)	0.473	*		1.225 (0.903-1.661)	0.193	0.592 (0.170-2.066)	0.411	0.702 (0.397-1.239)	0.222	1.062 (0.818-1.380)	0.651
Non-routine discharge	1.078 (1.027-1.131)	0.002	1.242 (0.956-1.614)	0.104	1.343 (1.139-1.583)	<.001	0.891 (0.511-1.553)	0.684	1.148 (0.988-1.334)	0.072	1.097 (1.051-1.146)	<0.001
Complications (Post-operative)[2]												
Need for blood transfusion	1.013 (0.885-1.159)	0.853	1.630 (1.002-2.653)	0.049	1.026 (0.910-1.158)	0.673	1.300 (0.888-1.903)	0.177	1.025 (0.879-1.196)	0.751	1.040 (0.966-1.119)	0.296
Prosthetic complications	1.055 (0.845-1.317)	0.637	0.697 (0.244-1.991)	0.5	1.100 (0.849-1.425)	0.47	1.248 (0.800-1.946)	0.329	0.946 (0.879-1.134)	0.546	1.021 (0.910-1.147)	0.72
Post-procedural infection	0.432 (0.062-2.995)	0.395	4.471 (0.183-109.531)	0.358	0.868 (0.346-2.181)	0.764	*		1.130 (0.795-1.607)	0.497	1.062 (0.777-1.453)	0.706
Complications (Cumulative)[3]												
Acute renal failure	1.250 (1.078-1.449)	0.003	0.798 (0.392-1.623)	0.534	1.090 (0.985-1.207)	0.094	1.451 (0.915-2.299)	0.113	1.093 (0.917-1.302)	0.321	1.138 (1.057-1.225)	<.001
Pneumonia	0.638 (0.312-1.304)	0.218	*		0.879 (0.702-1.100)	0.261	1.405 (0.552-3.571)	0.475	0.674 (0.419-1.083)	0.103	0.831 (0.673-0.982)	0.031
Pulmonary embolism	1.004 (0.421-2.395)	0.992	*		0.860 (0.551-1.343)	0.507	*		1.020 (0.536-1.942)	0.951	0.847 (0.605-1.185)	0.332
Deep vein thrombosis	1.428 (0.915-2.231)	0.117	*		0.645 (0.430-0.968)	0.034	0.419 (0.048-3.637)	0.43	0.747 (0.455-1.225)	0.247	0.822 (0.635-1.064)	0.136
Myocardial infarction	0.900 (0.460-1.761)	0.758	1.500 (0.362-6.210)	0.576	1.053 (0.806-1.374)	0.707	0.673 (0.180-2.515)	0.556	0.668 (0.373-1.195)	0.174	0.952 (0.763-1.188)	0.665
Anemia	1.081 (1.020-1.145)	0.008	1.172 (0.876-1.567)	0.285	1.097 (1.015-1.186)	0.02	1.132 (0.812-1.579)	0.465	0.937 (0.839-1.046)	0.247	1.066 (1.022 - 1.112)	0.003

[1] includes rheumatoid arthritis, spondylarthritis, ankylosing spondylitis and psoriatic arthritis

*removed from multivariate regression due to quasi-complete separation

ICD-10 CM codes: Acute Renal Failure (N17.x), Myocardial infarction (I21.x), Anemia (D62), Pneumonia (J18.9, J15.9, J22.x), Pulmonary Embolism (I26.x), Deep Venous Thrombosis (DVT; I82.x), Prosthetic Complication (T84.010A, T84.012A, T84.012A, T84.013A, T84.018A, T84.019A, T84.020A, T82.021A, T84.022A, T84.023A, T84.028A, T84.029A, T84.090A, T84.091A, T84.092A, T84.093A, T84.098A, T84.099A, M96.65, M96.661,M96.662, M96.669, M96.671, M96.672, M96.69, M97.02XA, M97.11X1, M97.12XA), Post-Procedural Infection (T84.50XA, T84.51XA, T84.52XA, T84.54XA, T84.59XA, T81.4)
ICD-10 PCS codes: Blood Transfusion (302*)

[2] Only initial encounter ICD-10 codes selected

[3] Complications may include pre-operative conditions

Disclosure: S. Chandrupatla: None; **K. Rumalla**: None; **J. Singh**: Other, 2, 6, 11, 11, 12, Adaptimmune Therapeutics, GeoVax Labs, Pieris Pharmaceuticals, Enzolytics Inc., Seres Therapeutics, Tonix, Charlotte's Web, 12, Atai life sciences, kintara therapeutics, Intelligent Biosolutions, Acumen pharmaceutical, TPT Global Tech, Vaxart pharmaceuticals, Atyu biopharma, 12, speaker's bureau of Simply Speaking, other, 12, received institutional research support from Zimmer Biomet Holdings. JAS received food and beverage payments from Intuitive Surgical Inc./Philips Elec, Other, 12, Schipher, Crealta/Horizon, Medisys, Fidia, PK Med, Two labs Inc., Adept Field Solutions, Clinical Care options, Clearview healthcare partners, Putnam.

Abstract Number: 1808

Tobacco Smoking Reduces the Incidence and Delays the Progression of Knee Osteoarthritis: 10-year Retrospective Cohort Study Based on Korea National Health Insurance Service-Health Screening Database

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Epidemiology & Public Health Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: There are conflicting results about relationship between smoking and incidence of knee osteoarthritis (OA). The effect of smoking to preexisting knee OA has also not been addressed in detail. To address these issues, we designed a retrospective cohort study to investigate the relationship between smoking and knee OA, based on a large-scale claim database from Korea.

Methods: The Korea National Health Insurance Service-Health Screening database is registered with 98% of Koreans and includes all insurance claims. From this database, two retrospective cohort study were conducted. The operational definition of diagnosis of knee osteoarthritis was knee osteoarthritis code (M17) or any site of osteoarthritis code (M15 to M19) along with a knee x-ray (G720, G721). In OA incidence study, the diagnosis of knee osteoarthritis was set as a primary endpoint on OA-naïve people. In OA progression study, we hypothesized that knee replacement surgery is a surrogate marker for progression of knee OA. Thus in OA progression study, the primary endpoint was set as knee replacement surgery (N2072, N2077, N2712, N2717) among previously diagnosed knee OA patients. The study populations were followed from the day of health screening at index year to primary endpoint, the date of death, or December 31, 2019, whichever comes first.

Table 1. Baseline characteristics of knee OA incidence study population

All subjects (n = 316,387)	Non-smoker group (n = 187,116)	Ex-smoker group (n = 65,290)	Smoker group (n = 63,981)	P-value
Demographics				
Age (years)	58.8 ± 9.0	58.2 ± 8.5	56.5 ± 7.8	< 0.001
Income level (%)				< 0.001
1st quartile	28,637 (15.3)	6,903 (10.6)	8,726 (13.6)	
2nd quartile	40,708 (21.8)	11,247 (17.2)	13,650 (21.3)	
3rd quartile	53,301 (28.5)	18,643 (28.6)	19,972 (31.2)	
4th quartile	64,470 (34.5)	28,497 (43.6)	21,633 (33.8)	
Health screening				
Body mass index (kg/m^2)	23.7 ± 2.9	24.3 ± 2.7	23.6 ± 2.9	< 0.001
Systolic blood pressure (mmHg)	124.7 ± 15.6	126.7 ± 14.5	125.2 ± 15.2	< 0.001
Diastolic blood pressure (mmHg)	77.0 ± 10.1	78.9 ± 9.8	78.3 ± 10.1	< 0.001
Fasting glucose (mg/dL)	100.0 ± 24.8	104.2 ± 26.6	104.4 ± 30.3	< 0.001
Total cholesterol (mg/dL)	200.7 ± 37.8	195.9 ± 36.8	197.5 ± 38.0	< 0.001
Smoking history (pack-years)	0.0	18.6 ± 15.8	24.3 ± 15.1	< 0.001
Regular exercise (%)	8,512 (4.5)	3,744 (5.7)	2,510 (3.9)	< 0.001
Underlying disease				
Hypertension (%)	60,840 (32.5)	20,466 (31.3)	17,488 (27.3)	< 0.001
Diabetes (%)	21,154 (11.3)	9,170 (14.0)	9,353 (14.6)	< 0.001
Dyslipidemia (%)	42,002 (22.4)	11,838 (18.1)	11,247 (17.6)	< 0.001
Outcome				
Knee osteoarthritis (%)	72,778 (38.9)	16,963 (26.0)	14,715 (23.0)	< 0.001

Table 2. Baseline characteristics of knee OA progression study population

All subjects (n = 37,795)	Non-smoker group (n = 26,494)	Ex-smoker group (n = 6,789)	Smoker group (n = 4,512)	P-value
Demographics				
Age (years)	61.7 ± 8.6	61.4 ± 8.3	59.9 ± 7.8	< 0.001
Health screening				
Body mass index (kg/m^2)	24.2 ± 3.0	24.6 ± 2.7	23.9 ± 2.9	0.16
Smoking history (pack-years)	0.0	20.0 ± 17.2	24.2 ± 16.1	< 0.001
Underlying disease				
Hypertension (%)	13,462 (50.8)	3,807 (56.1)	2,221 (49.2)	< 0.001
Diabetes (%)	3,894 (14.7)	1,311 (19.3)	910 (20.2)	< 0.001
Dyslipidemia (%)	8,668 (32.7)	2,151 (31.7)	1,306 (28.9)	< 0.001
Charlson comorbidity index	3.7 ± 2.5	3.7 ± 2.6	3.3 ± 2.4	< 0.001
Outcome				
Knee operation (%)	1,412 (5.3)	158 (2.3)	96 (2.1)	< 0.001

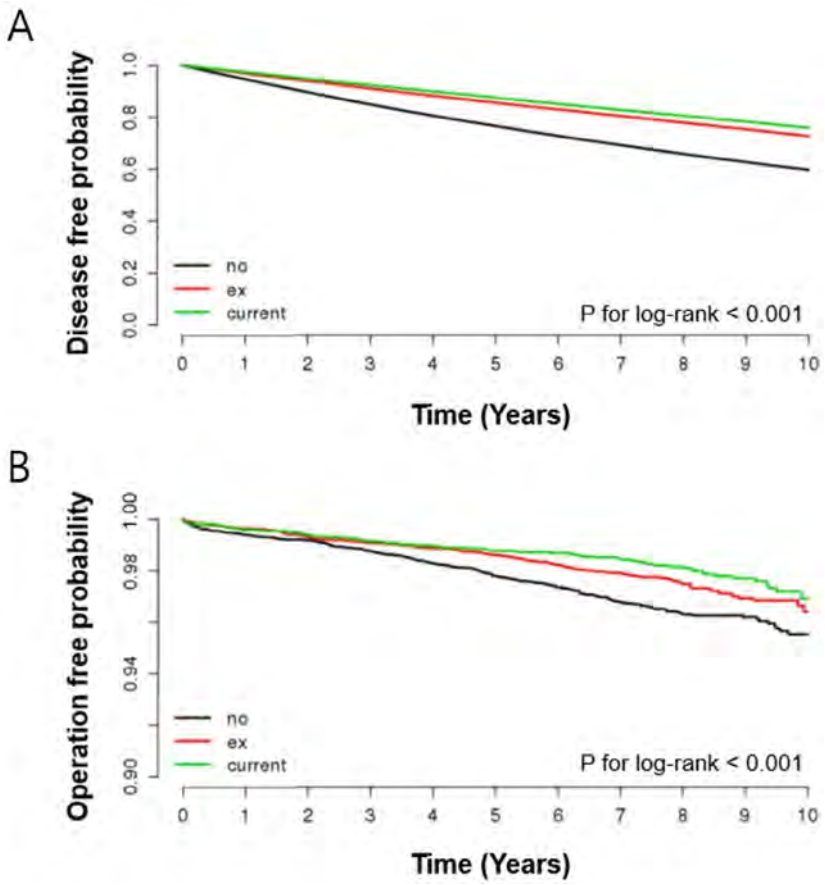

Figure 1. The Kaplan Meyer(K-M) curve of each studies. (A) K-M curve of knee OA incidence study. (B) K-M curve of knee OA progression study.

Results: The patient group was classified into non-smoker, ex-smoker, and smoker groups according to the responses to the health examination questionnaire. The baseline characteristics of each group in incidence study and progression study are included in Table 1 and Table 2. The incidence of knee OA was 38.9%, 26%, and 23% in each group of non-smoker, ex-smoker, and smoker group with statistical significance (P-value < 0.001). When the disease-free probability for knee OA was presented using the Kaplan-Meier curve, the risk of knee OA incidence was significantly different between the non-smoker group and the smoker group over time (Figure 1A). The hazard ratio of ex-smoker to non-smoker were 0.95 (0.83-0.97), and those of smoker to non-smoker were 0.89 (0.87-0.91). In knee OA progression study, the frequency of knee replacement surgery due to OA was 5.3% among non-smokers, 2.3% among ex-smokers, and 2.1% among smokers. The Kaplan-Meier curve of knee OA progression study showed that the knee replacement surgery in non-smoker group was more frequent than ex-smoker group and non-smoker group as time passed (Figure 1B). The adjusted hazard ratio of ex-smoker to non-smoker were 0.81 (0.66-0.99, p=0.04) and those of smoker to non-smoker were 0.76 (0.61-0.96, p=0.02).

Conclusion: This large-scale retrospective cohort study revealed that both incidence and frequency of knee replacement surgery, one of the indicators of progression of knee osteoarthritis, was lower in smoker group and ex-smoker group than in non-smoker group. Further studies on exact mechanism of smoking and osteoarthritis are required.

Disclosure: J. Park: None; **M. Son**: None; **S. Lee**: None; **W. Chung**: None; **S. Lee**: None.

Abstract Number: 1809

Clinical Outcome and Antibody Responses Following the Surge of SARS-CoV-2 Omicron Infection Among Patients with Systemic Autoimmune Diseases

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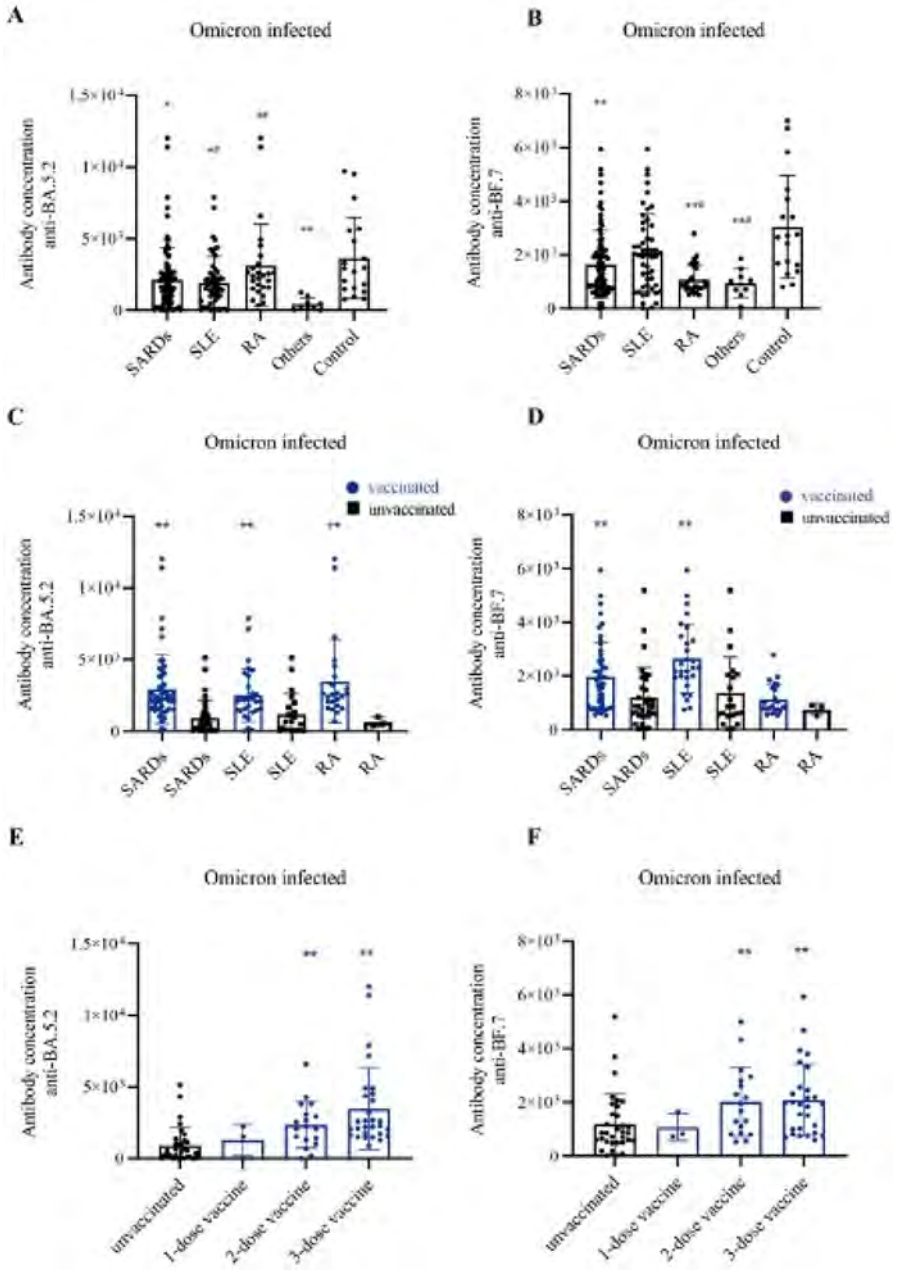
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The surge of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant Omicron infections has affected most Chinese residents at the end of 2022, including a number of patients with systemic autoimmune rheumatic diseases (SARDs). The aim of this study was to investigate clinical outcomes and the antibody level of the Omicron variant in SARDs patients after SARS-CoV-2 Omicron infection.

Methods: A total of 682 SARDs patients were surveyed. The type of SARDs, demographics, concurrent treatment, SARS-CoV-2 vaccination history, and clinical outcomes were recorded. Among these patients, we tested BA.5.2 and BF.7 Omicron variant IgG antibody level using enzyme-linked immunosorbent assay (ELISA) from the collected blood samples from 102 SARDs patients and 19 healthy controls (HCs).

Results: 604 (88.6%) SARD patients were infected with SARS-CoV-2 during the pandemic, with the most common symptoms including fever (79.3%), cough (70.1%), malaise (39.1%), expectoration (31.0%), sore throat (28.7%), and ageusia (25.3%). The majority of patients (78.6%) had mild symptoms after SARS-CoV-2 Omicron infection. A total of 102 SARDs

patients (mean age, 40.3 years, 89.2% female), including 60 SLE, 32 RA and 10 other SARDs, were tested for the antibodies against omicron variant IgG. We found that the BA.5.2 antibody level of infected SARDs patients was lower than that of HCs ($P< 0.05$), and a similar alteration was also observed in the antibody level of the BF.7 variant. Notably, the vaccinated SARDs group had notably higher levels of BA.5.2 and BF.7 antibodies than the unvaccinated group. Although the use of glucocorticoids (GC) does not affect the antibody levels, the level of BA.5.2 antibody was significantly decreased in SLE patients



The antibody concentrations in SARDs patients and controls infected with SARS-CoV-2 Omicron (A). Quantitative analysis of RBD antibody titers against the Omicron BA.5.2 variant calculated by ELISA. Compared with control, *P<0.05, ** P<0.01; compared with other SARDs group, #P<0.05, ## P<0.01. (B). Quantitative analysis of RBD antibody titers against the Omicron BF.7 variant calculated by ELISA. Compared with control, *P<0.05, ** P<0.01; compared with SLE group, #P<0.05. (C-D). Quantitative analysis of RBD antibody titers against the Omicron BA.5.2 (C) and BF.7 (D) variants calculated by ELISA between the vaccinated group and unvaccinated group, *P<0.05, ** P<0.01. (E-F). Quantitative analysis of RBD antibody titers against the Omicron BA.5.2 (E) and BF.7 (F) variants calculated by ELISA in SARDs patients with different vaccine doses, *P<0.05, ** P<0.01.

treated with bDMARDs compared with those treated with GCs and/or HCQ ($P< 0.05$). No significant difference in BF.7 antibody levels was found in SLE patients with different DMARDs use.

Conclusion: During the SARS-CoV-2 wave in China, in which the Omicron sublineages BA.5.2 and BF.7 were dominant, unvaccinated SARDs patients had lower antibody production, suggesting the need for valuable prevention and management strategies.

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Abstract Number: 1810

Alcohol Consumption Amount, Type of Beverage, and Gender, All Matters to Serum Uric Acid Levels

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
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Background/Purpose: Alcohol intake has been known to be interrelated with hyperuricemia and gout. However, the results of its influence are conflicting on serum uric acid (SUA) levels in terms of the beverage types and drinking amount. The study aimed to assess the impact of alcohol on SUA levels concerning the types of beverages and the drinking amount and habits in a large number of Korean populations.

Methods: We evaluated 17,011 adults who underwent comprehensive health examinations between 2011 and 2016. A standard drink unit for alcohol intake in Korea is defined as 8g based on the WHO definition. The dominant beverage was defined as the type of alcoholic beverage that was taken up more than 75% of total alcohol intake among beer, soju (Korean traditional liquor), and wine. Drinking habits were compared using the proportion within the same group of dominant liquor. Alcohol intake was categorized into six groups: none (0), almost none (0.01–0.49), little (0.50–0.99), light (1.00–1.99), moderate (2.00–3.99) and heavy (≥4.00) in the standard drink unit. The effect of alcohol consumption on SUA levels was investigated using linear regression models. Interaction effects were investigated in the subgroup analyses of sex and BMI.

Table 1. Associations between SUA levels and alcohol intakes of dominant groups in total. † Adjusted for other alcoholic beverages, age, sex, BMI, creatinine, LDL-C, hypertension, DM, alcohol-free calorie intake, and total protein intake ‡ Adjusted for age, sex, BMI, creatinine, LDL-C, hypertension, DM, alcohol-free calorie intake, and total protein intake

	SUA levels (mg/dL) according to the category of alcohol intakes						*P* for trend
	None	Almost none	Little	Light	Moderate	Heavy	
Beer effects	(n = 5,166)	(n = 863)	(n = 107)	(n = 103)	(n = 64)	(n = 50)	
Mean (S.E.)	4.52 (0.02)	4.57 (0.04)	4.62 (0.13)	4.88 (0.12)	5.16 (0.17)	5.77 (0.20)	-
Multivariable (95% C.I.)†	*(reference)*	-0.01 (-0.08, 0.06)	0.16 (-0.02, 0.35)	0.19 (-0.02, 0.39)	0.26 (0.02, 0.50)	0.64 (0.32, 0.96)	0.0007
Soju effects	(n = 5,166)	(n = 350)	(n = 357)	(n = 552)	(n = 662)	(n = 757)	
Mean (S.E.)	4.52 (0.02)	5.02 (0.06)	5.63 (0.07)	5.76 (0.06)	5.91 (0.05)	6.04 (0.05)	-
Multivariable (95% C.I.)†	*(reference)*	0.03 (-0.07, 0.14)	0.20 (0.08, 0.31)	0.19 (0.09, 0.30)	0.24 (0.14, 0.35)	0.32 (0.20, 0.43)	< 0.0001
Wine effects	(n = 5,166)	(n = 836)	(n = 108)	(n = 33)	(n = 47)	(n = 6)	
Mean (S.E.)	4.52 (0.02)	4.38 (0.04)	4.71 (0.12)	4.92 (0.21)	5.66 (0.19)	5.55 (0.63)	-
Multivariable (95% C.I.)†	*(reference)*	-0.00 (-0.07, 0.07)	-0.02 (-0.20, 0.17)	0.07 (-0.25, 0.39)	0.39 (0.10, 0.68)	-0.00 (-0.77, 0.76)	0.0400
Mixed alcohol effects	(n = 5,166)	(n = 1,266)	(n = 945)	(n = 1,182)	(n = 1,585)	(n = 1,650)	
Mean (S.E.)	4.52 (0.02)	4.77 (0.03)	5.08 (0.04)	5.44 (0.04)	5.82 (0.03)	6.01 (0.03)	-
Multivariable (95% C.I.)‡	*(reference)*	-0.02 (-0.08, 0.04)	-0.01 (-0.08, 0.06)	0.05 (-0.02, 0.12)	0.15 (0.08, 0.21)	0.25 (0.18, 0.32)	< 0.0001

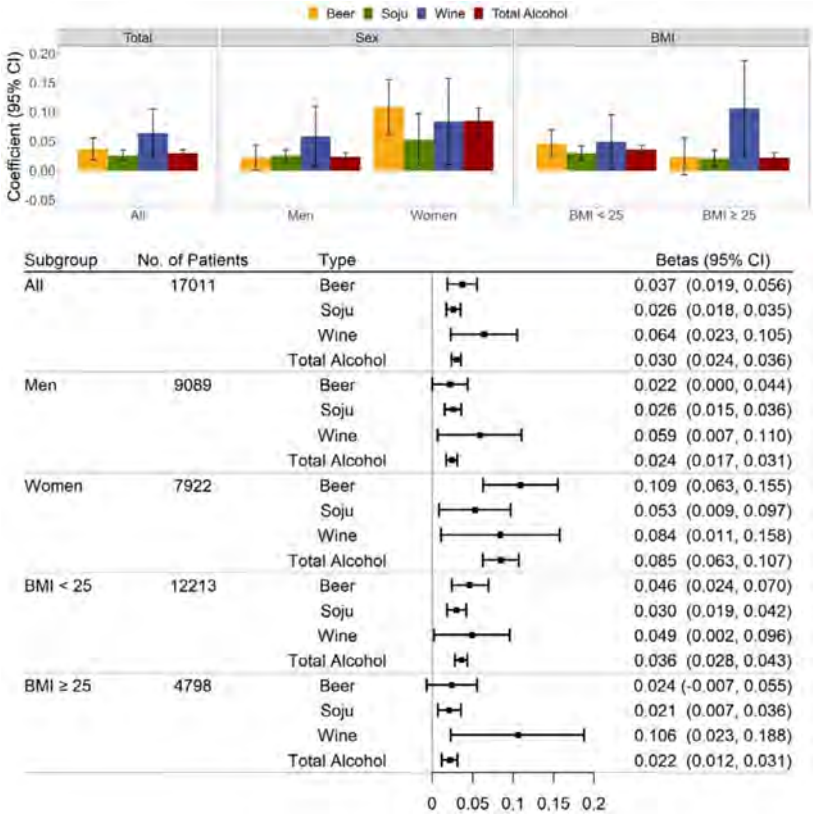

Figure 1. Associations between SUA levels and alcohol intakes in the sex and BMI subgroups. Interactions were significant for intake of beer, soju and total alcohol in the BMI subgroup, and for intake of beer and total alcohol in the sex subgroup (P values for interaction < 0.05). All other P values for interaction were greater than 0.05. Error bars represent 95% confidence intervals.

Results: The mean age of participants was 51.67±7.10 years, with 53.4% of men, and 69.6% of drinkers. The mean SUA level was 5.12±1.36 mg/dL and drinkers had significantly higher SUA, BMI, creatinine, low-density lipoprotein cholesterol, energy intake, and total protein intake ($p< 0.05$). Men's dominant beverage was soju, within which the proportion of heavy and mixed intake was noticeably higher. Women's dominant beverage was beer, within which the proportion of almost non-drinking was remarkable. SUA levels according to the six categories of alcohol intake were positively associated in a dose-dependent manner (p for trend< 0.001) irrespective of the beverage types and the association of beer and wine was weakened but still significant after adjusting in multivariable models. The total alcohol effect on SUA levels was greater in women compared to men: 0.26 [95% CI, 0.15-0.38] vs. 0.10 [0.01-0.18] mg/dL for the moderate drinking category and 0.53 [0.34-0.71] vs. 0.19 [0.11-0.27] mg/dL for the heavy drinking category (women vs. men). A significant change in SUA levels attributable to an association with alcohol intake was observed in beer, soju, and wine (0.039 [95% CI, 0.020-0.057], 0.028 [0.019-0.037], and 0.068 [0.027-0.108] mg/dL per standard drink unit per day). This effect on SUA levels differed in regard to the types of dominant beverages in men and women. Both sex and BMI had significant interactions with the alcohol effect on SUA levels. The modifying effects of alcohol intake were higher in women than those in men regardless of the beverage types. The interactions were also higher in subjects with BMI < 25 than in those with BMI ≥ 25, consistently across all types of beverages except wine.

Conclusion: Alcohol intake could have a significant dose-dependent association with SUA levels in both men and women, irrespective of the beverage types of alcohol and drinking habits. These findings may support healthcare providers to guide and educate subjects having hyperuricemia and gout in terms of alcohol intake.

Disclosure: J. Hwang: None; **S. Hong**: None; **K. Kim**: None; **J. Hur**: None; **Y. Chang**: None; **J. Ahn**: None; **M. Kang**: None.

Abstract Number: 1811

Strong Relationships Between Body Component Changes and Serum Uric Acid Variability

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Obesity has a well-known relationship with higher serum uric acid (SUA) levels. Skeletal muscles are another site for producing uric acid as the endogenous pool of purine. However, the actual influence of muscle mass on SUA levels was occasionally investigated.The study aimed to evaluate the impact of changing body components on SUA levels in a large number of Korean healthy populations.

Methods: We investigated 39,505 examinees from health check-up programs between 2015 and 2017. Analysis was separately conducted in men (n = 24,623) and pre- and post-menopausal women (n = 14,810 and n = 702, respectively). Body components including waist-hip ratio (WHR) were assessed using the bioimpedance method. We adopted skeletal muscle

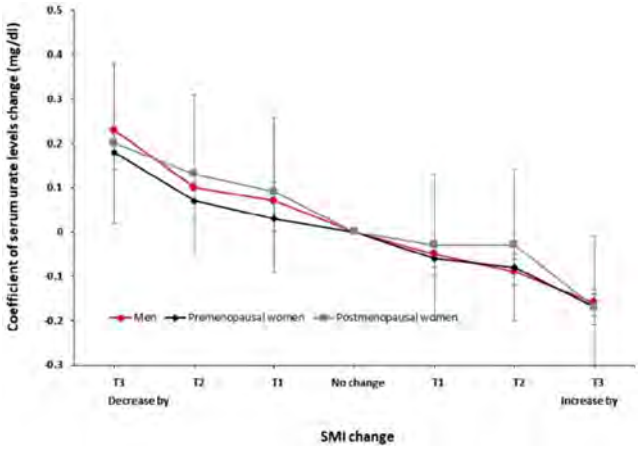

Figure 1. Association between SUA levels and SMI changes. The association was significantly strong and clearly dose-dependent along with the serial adjustment of covariates in the regression model.

mass index (SMI) and fat mass index (FMI) based on body weight (kg). Each study population was categorized into seven groups according to the changes of body components over two years as tertiles of increase and decrease: T3 (the most), T2, and T1 (the least) of increase, no change, and T3 (the most), T2, and T1 (the least) of decrease. Hyperuricemia was defined as SUA ≥ 7mg/dL in men and SUA ≥ 6 mg/dL in women. We analyzed odds ratios (ORs) for achieving the target SUA level (< 6mg/dL) and coefficients for the association with SUA level according to the changes in body components over two years.

Results: The mean age was 38.6 ± 6.5 years in men, 37.2 ± 5.4 years in premenopausal women, and 46.1 ± 8.2 years in postmenopausal women. The mean SUA level was 6.25 ± 1.21 mg/dL in men, 4.23 ± 0.88 mg/dL in premenopausal women, and 4.34 ± 0.91 mg/dL in postmenopausal women. Hyperuricemia was most common in men (26.08%), followed by postmenopausal women (4.42%) and premenopausal women (3.22%). Over two years, the change in muscle mass was mostly within ± 2.5kg and muscle mass decreased more frequently than increased in both men and women. The impact of SMI seemed dose-dependent; the ORs (95% CI) of target attainment for T1, T2, and T3 of SMI increase were 1.10 (1.00-1.20), 1.10 (1.01-1.21), and 1.45 (1.32-1.59) in men and 1.16 (0.82-1.65), 1.48 (1.02-2.15), and 1.48 (1.06-2.06) in premenopausal women whereas the ORs for T1, T2, and T3 of SMI decrease were 1.02 (0.93-1.12), 0.92 (0.84-1.00), and 0.85 (0.77-0.93) in men and 1.18 (0.84-1.65), 0.73 (0.55-0.98), and 0.67 (0.51-0.88) in premenopausal women as compared with the reference group. Of FMI and WHR, the impact seemed inverse. The relationship between the changes

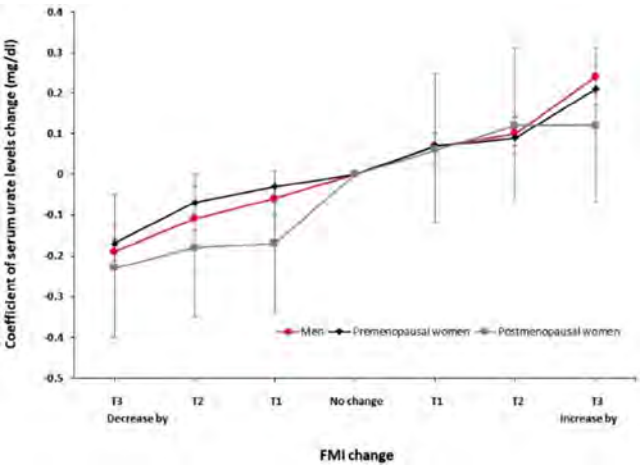

Figure 2. Association between SUA levels and FMI changes. The association was significantly strong and clearly dose-dependent along with the serial adjustment of covariates in the regression model.

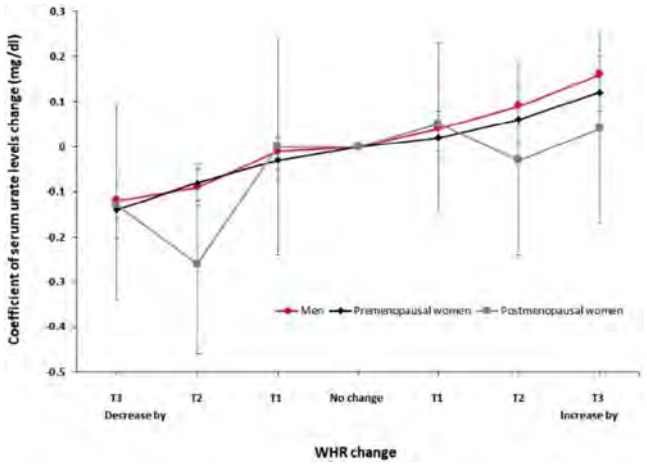

Figure 3. Association between SUA levels and WHR changes. The association was significantly strong and clearly dose-dependent along with the serial adjustment of covariates in the regression model.

in body components and SUA variability was strong and clearly dose-dependent in men and premenopausal women. However, the direction of SUA level changes was not the same among the relationship with body component changes: a positive relationship with FMI and WHR changes while a negative relationship with SMI changes.

Conclusion: We demonstrated that the changes in SMI, FMI, and WHR had a significant impact on achieving the target SUA level and the strong relationship with SUA level variability. Our results could boost the practical advice in clinics regarding physical fitness training for subjects with hyperuricemia and gout.

Disclosure: J. Hwang: None; **M. Lee**: None; **Y. Eun**: None; **J. Ahn**: None.

Abstract Number: 1812

Duloxetine and the Risk for Cardiovascular Events in US Veterans with Non-Cancer Pain

Laura Daniel[1], Alyson Dickson[2], Puran Nepal[1], Otis Wilson[3], Adriana Hung[2], Dale Plummer[3], William Dupont[3], Katherine Murray[3], C. Michael Stein[2], Wayne Ray[3] and Cecilia Chung[4], [1]University of Miami, Nashville, TN, [2]Vanderbilt University Medical Center, Nashville, TN, [3]Vanderbilt University, Nashville, TN, [4]University of Miami, Miami, FL

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
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Background/Purpose: Duloxetine is a serotonin-norepinephrine reuptake inhibitor approved by the FDA for the treatment of different forms of chronic pain. Because of its adrenergic activity, duloxetine could increase the risk for cardiovascular events, but conversely, given its antiplatelet activity, duloxetine may decrease cardiovascular risk. Therefore, there is a need to define duloxetine's comparative safety relative to other non-opioid medications used to treat chronic pain. We aimed to compare rates of a composite cardiovascular outcome among new users of duloxetine with rates among new users of the active comparator gabapentin in US Veterans with non-cancer chronic pain.

Methods: This is a retrospective cohort study among Veterans with chronic pain who received new prescriptions for one of the study drugs: duloxetine or gabapentin. The cohorts were assembled using the VA Informatics and Computing Infrastructure (VINCI). We excluded Veterans with cancer or other life-threatening diagnoses in the year prior to their first prescription of the study drugs. The primary outcome was a composite cardiovascular disease outcome including acute myocardial infarction (AMI), stroke, or out-of-hospital death. We calculated time-dependent propensity scores and used inverse probability weighting analysis to compare the risk of cardiovascular disease between the study drugs and adjust for confounding.

Results: The study included new users of duloxetine and gabapentin. At baseline, the groups had similar rates of cardiovascular comorbidities and medications. However, before inverse probability weighting, the groups differed in some baseline characteristics. In particular, fewer users of duloxetine had a diagnosis of diabetes neuropathy compared to gabapentin users (5.2% vs. 11.2%). During 288,430 person-years, the rate of cardiovascular events among new users of duloxetine was 11.5/1,000 person-years compared to 17.5/1,000 person-years among new users of gabapentin [unadjusted HR=0.66 (95% CI=0.60-0.73)]. However, after inverse probability weighting adjustment, the risk for cardiovascular events in new users of duloxetine was not statistically different than in new users of gabapentin [aHR=1.07 (95%CI: 0.94-1.21)].

Conclusion: In this large-scale retrospective study of VA patients who received treatment for non-cancer pain, new users of duloxetine and gabapentin had similar risks of cardiovascular events.

Disclosure: L. Daniel: None; **A. Dickson**: None; **P. Nepal**: None; **O. Wilson**: None; **A. Hung**: None; **D. Plummer**: None; **W. Dupont**: None; **K. Murray**: None; **C. Stein**: None; **W. Ray**: None; **C. Chung**: None.

Abstract Number: 1813

Assessing Immunogenicity of SARS-CoV-2 Vaccine Neoantigen S1 in Autoimmune Rheumatic Disease Patients: A Study on Cellular and Humoral Responses

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Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Data on cellular and humoral immunogenicity triggered by SARS-CoV-2 vaccines in patients with autoimmune rheumatic diseases (ARD) are limited. While current vaccine efforts have focused on the induction of neutralizing antibodies against SARS-CoV-2, T-cell immunity may also provide protection against infection. Experimental data suggest that CD8+ T cell responses may have a protective role in the presence of decreasing or sub protective antibody titers.

The aim of this project is to describe the serological and T cell responses to the third dose of vaccine (either with BNT162b2 mRNA or ChAdOx1 nCoV-19 replication-deficient adenoviral vector vaccines) in a cohort of patients with ARD (rheumatoid arthritis and spondyloarthropathies) treated with biologic therapies, to describe the impact of these treatments on vaccine

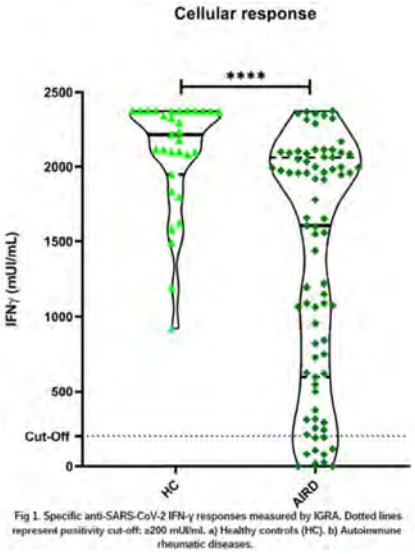

Fig 1. Specific anti-SARS-CoV-2 IFN-γ responses measured by IGRA. Dotted lines represent positivity cut-off: ≥200 mUI/ml. a) Healthy controls (HC). b) Autoimmune rheumatic diseases.

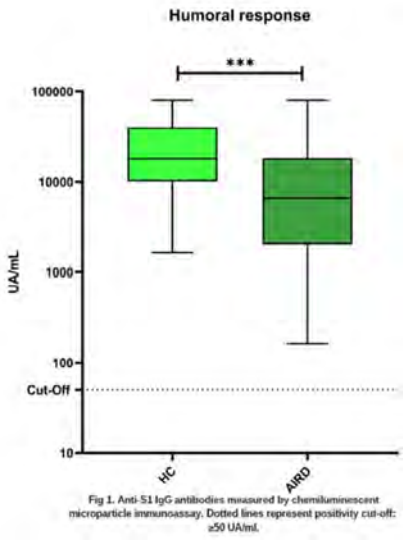

Fig 1. Anti-S1 IgG antibodies measured by chemiluminescent microparticle immunoassay. Dotted lines represent positivity cut-off: ≥50 UA/ml.

response in this patient population. As a second objective, we will describe the characteristics of patients who did not present an adequate immunogenic response.

Methods: Case-control study. We studied in 79 patients with ARD and in 31 healthy controls, anti-SARS-CoV-2 specific interferon-gamma (IFN-γ) production measured by IGRA between 8-12 weeks after the third dose of anti-SARS-CoV-2 vaccine. In addition, humoral response was measured by anti-S1 IgG antibody production measured by chemiluminescent microparticle immunoassay. Statistical comparison between categorical variables was performed by Fisher's or $\chi 2$ test. For quantitative variables by Kruskal-Wallis test or Mann-Whitney test.

Results: 79 patients with ARD (48 women, 31 men; mean age 58±11.4) 43 (54%), with rheumatoid arthritis and 36 (45.6%) with spondyloarthropathies. 32 (49.5%) of them were on glucocorticoid treatment (mean dose 4.92 mg/day), 25 (31.6%) on methotrexate and 56 (70.9%) on anti-TNF. Post-vaccination results showed positive T-cell immune responses in 68 of 79 (86.1%) ARD patients with mean IFN- γ anti-SARS-CoV-2 titers of 1,606.85 mUI/ml. 7 (8.9%) of ARD patients showed negative IFN-γ SARS-CoV-2 levels, while 4 (5%) had borderline titers. 100% of patients with previous COVID 19 disease had positive cellular responses. Within the group of negative or borderline cellular responses, 7 of 10 were men (70%), with no significant differences in terms of diagnosis, comorbidities or immunosuppressive treatments used. In the control group, 100% presented positive cellular responses. Anti-Spike IgG antibodies were detectable in all patients with ARD as in the control group.

Conclusion: Our preliminary data show that most patients with ARD were able to generate an adequate specific cellular response after vaccination against SARS-CoV-2, emphasizing the relevance of vaccination in this group. Specific antibody responses secondary to anti-SARS-CoV-2 vaccination were detected in all patients with ARD. Our data could support the relevance of these immune responses to personalize prevention, vaccination decision-making and treatment in this subgroup of patients.

Disclosure: I. Pérez Sancristóbal: None; **M. Alvarez Hernandez**: None; **k. Mohamed Mohamed**: None; **M. Rodriguez Laguna**: None; **C. Martinez**: None; **E. Toledano**: None; **D. Freites**: None; **B. Fernandez**: None; **M. Rodero**: None; **C. Bravo**: None; **A. Rodrígez de la Peña**: None; **S. Sanchez - Ramon**: None; **G. mato Chain**: None; **G. Candelas**: None.

Abstract Number: 1814

Silica and Other Exposures from Jobs and Hobbies Are Associated with Myositis Phenotype in a National Myositis Registry

Christine Parks[1], Jesse Wilkerson[2], Payam Noroozi Farhad[3], Nastaran Bayat[4], Adam Schiffenbauer[5], Hermine Brunner[6], Robert Goldberg[7], Frederick Miller[8] and Lisa Rider[5], [1]Epidemiology Branch, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, [2]NIEHS/NIH, Durham, NC, [3]Environmental Autoimmunity Group, National Institute of Environmental Health Sciences, National Institutes of Health, Bethesda, MD, [4]Social Scientific Systems, DLH Holdings Corp, Silver Spring, MD, [5]NIEHS, NIH, Bethesda, MD, [6]Cincinnati Children's Hospital Medical Center, Division of Rheumatology, Cincinnati, OH, [7]Myositis Foundation, Alexandria, VA, [8]NIH, NIEHS, Chapel Hill, NC

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Epidemiology & Public Health Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Growing evidence suggests that environmental factors may contribute to disease phenotype among patients diagnosed with the idiopathic inflammatory myopathies (IIM), dermatomyositis (DM), polymyositis (PM), and inclusion body myositis (IBM), as well as the anti-synthetase syndrome (SYN)-associated lung disease (LD). Occupational exposures, includingrespirable silica dust, have been associated with some systemic autoimmune diseases and lung disease, but associations with IIM phenotype are not well understood.

Methods: We analyzed data from 1390 adult IIM patients (ages 18-65) in a national patient registry (including 658 dermatomyositis [DM], 451 polymyositis [PM], and 309 inclusion body myositis [IBM]) diagnosed through 2011. Other phenotype data included self-reported lung involvement, fever, arthritis, and reported diagnosis of other autoimmune rheumatic

Table 1. Frequency and association of occupational exposures to silica, solvents, and metals in relation to DM and PM compared to IBM myositis phenotype

Exposure		IBM* N (%)	DM N (%)	Odds Ratio‡ (95% CI)	PM N (%)	Odds Ratio‡ (95% CI)
Silica						
	High	86 (22)	107 (18)	2.02 (1.18-3.46)	82 (20)	1.58 (0.92-2.70)
	Moderate	93 (24)	140 (23)	1.50 (0.90-2.50)	83 (20)	1.04 (0.62-1.75)
	Low	138 (36)	227 (38)	1.15 (0.72-1.82)	147 (36)	0.92 (0.57-1.47)
	No	66 (17)	124 (21)	1.00 (REF)	97 (24)	1.00 (REF)
	Total	383	598		409	
	Trend p-value			*0.004*		*0.077*
Solvents						
	High	86 (22)	97 (16)	0.90 (0.55-1.48)	90 (22)	1.10 (0.67-1.80)
	Moderate	167 (44)	262 (44)	1.17 (0.76-1.79)	145 (35)	0.86 (0.55-1.34)
	Low	58 (15)	70 (12)	0.58 (0.34-1.00)	59 (14)	0.68 (0.39-1.18)
	No	72 (19)	169 (28)	1.00 (REF)	115 (28)	1.00 (REF)
	Total	383	598		409	
	Trend p-value			*0.577*		*0.685*
Heavy Metals						
	High/Moderate	174 (45)	190 (32)	1.31 (0.82-2.09)	135 (33)	1.09 (0.68-1.76)
	Low	147 (38)	269 (45)	1.13 (0.72-1.79)	176 (43)	1.01 (0.64-1.62)
	No	62 (16)	139 (23)	1.00 (REF)	98 (24)	1.00 (REF)
	Total	383	598		409	
	Trend p-value			*0.248*		*0.695*

Abbreviations: IBM, Inclusion Body Myositis; DM, Dermatomyositis; PM, Polymyositis; CI, confidence interval*IBM is used as the reference group comparison to DM and PM; ‡Adjusted for age and gender.

Table 2. Occupational Exposures, the SYN phenotype, and ARD overlap

Table 2. Silica, solvents, and heavy metals associated with anti-synthetase syndrome phenotype and autoimmune rheumatic disease overlap

Exposure	Anti-synthetase syndrome*			Autoimmune Rheumatic Disease*		
	No N (%)	Yes N (%)	Odds Ratio‡ (95% CI)	No N (%)	Yes N (%)	Odds Ratio‡ (95% CI)
Silica						
High	197 (19)	53 (24)	1.75 (1.10-2.78)	241 (20)	34 (20)	2.07 (1.19-3.61)
Moderate	224 (22)	50 (23)	1.21 (0.77-1.90)	279 (23)	37 (22)	1.51 (0.89-2.57)
Low	394 (38)	68 (31)	0.86 (0.56-1.30)	445 (36)	67 (40)	1.55 (0.96-2.51)
No	213 (21)	47 (22)	1.00 (REF)	259 (21)	28 (17)	1.00 (REF)
Total	1,028	218		1,224	166	
Trend p-value			*0.005*			*0.020*
Solvents						
High	192 (19)	47 (22)	1.49 (0.96-2.32)	250 (20)	23 (14)	0.81 (0.47-1.39)
Moderate	421 (41)	90 (41)	1.24 (0.85-1.81)	501 (41)	73 (44)	1.25 (0.83-1.87)
Low	142 (14)	26 (12)	1.02 (0.61-1.70)	162 (13)	25 (15)	1.23 (0.72-2.09)
No	273 (27)	55 (25)	1.00 (REF)	311 (25)	45 (27)	1.00 (REF)
Total	1,028	218		1,224	166	
Trend p-value			*0.062*			*0.844*
Heavy Metals						
High/Mod	353 (34)	88 (40)	1.49 (1.00-2.24)	440 (36)	59 (36)	1.59 (0.99-2.55)
Low	454 (44)	78 (36)	0.81 (0.55-1.21)	519 (42)	73 (44)	1.23 (0.79-1.92)
No	221 (21)	52 (24)	1.00 (REF)	265 (22)	34 (20)	1.00 (REF)
Total	1,028	218		1,224	166	
Trend p-value			*0.026*			*0.051*

*Anti-synthetase syndrome phenotype included lung disease with arthritis or fever; Autoimmune rheumatic disease includes rheumatoid arthritis/juvenile rheumatoid arthritis, systemic lupus erythematosus, scleroderma; ‡Odds ratios and 95% Confidence Intervals (CI) adjusted for age and gender; referent group for anti-synthetase syndrome phenotype excludes those with lung disease the absence of fever or arthritis (n=144).

diseases (ARD). A self-administered questionnaire asked about specific jobs, hobbies, longest held job (year started/stopped), and exposures prior to diagnosis. Responses were evaluated in a blinded expert review and rules-based assessment to assign exposure intensity with certainty ratings forrespirable silica dust (derived from quartz in rock, sand, or soil), solvents, and heavy metals prior to diagnosis. We examined exposure associations with (1) DM or PM vs. IBM, (2) LD+ fever or arthritis (SYN phenotype; N=218; 16%) vs. no LD (N=1028) and (3) comparing those with overlapping ARD (N=166; 12%) vs. no ARD (N=1224). We calculated odds ratios (OR) and 95% confidence intervals (CI) in logistic regression models adjusted for age and gender.

Results: High silica exposure was associated with increased odds of DM compared to IBM (OR 2.02; 95%CI 1.18, 3.46; p-trend=0.004 vs. unexposed), and the SYN phenotype (1.71; 1.07, 2.74; p-trend=0.005), which was also associated with high or moderate exposure to heavy metals (1.49; 1.00, 2.14; p-trend=0.026). High silica exposure was also associated with the ARD-overlap phenotype (2.07; 1.19, 3.61; p-trend=0.02) and the OR was elevated for high or moderate heavy metal exposure (1.59; 0.99, 2.55, p-trend=0.051). Associations limited to high certainty exposures were stronger for silica exposure and the DM, SYN, and ARD phenotypes, and for heavy metals and the SYN phenotype, and results were similar when limited to female participants.Solvent exposure was not associated with DM or PM (vs. IBM), or the SYN or ARD-overlap phenotypes.

Conclusion: These findings suggest that intense occupational exposure to respirable silica dust and exposure to heavy metals may contribute to distinctive disease phenotypes in adult IIM patients, including lung involvement, one of the more severe manifestations of IIM, and overlap with other ARD. Larger clinical studies, including rigorous exposure assessment, are warranted to identify high risk patients and investigate potential etiologies.

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Abstract Number: 1815

The Association of Body Mass Index with SARS-CoV-2 Infection (COVID-19) in Patients with Inflammatory Arthritis on Biologic Disease Modifying Anti-Rheumatic Drugs: Results from the Singapore National Biologics Register

Preeti Dhanasekaran[1], Margaret Ma[2], Manjari Lahiri[2], Li Wearn Koh[3], Stanley Angkodjojo[4], Andrew Yu Keat Khor[5], James Jiaqi Liu[6], Stephanie Wong[7] and Siaw Ing Yeo[6], [1]National University of Singapore, Singapore, Singapore, [2]National University Hospital, Singapore, Singapore, [3]Tan Tock Seng Hospital, Braddell Heights, Singapore, [4]Sengkang General Hospital / Singhealth, Singapore, Singapore, [5]Changi General Hospital, Singapore, Singapore, [6]Singapore General Hospital, Singapore, Singapore, [7]Tan Tock Seng Hospital, Singapore, Singapore

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: To determine the association of body mass index (BMI) with incident COVID-19 infection in patients with inflammatory arthritis (IA) using biologic disease-modifying anti-rheumatic drugs (bDMARDs) and describe the demographic and clinical characteristics of patients with severe COVID-19.

Methods: This was a prospective inception cohort study of IA patients ≥ 21 years old initiating a bDMARD after July 2016 across 6 public-sector hospitals in Singapore. Data were collected via face-to-face questionnaires and abstracted from electronic medical records. Baseline characteristics were compared using chi-square test for categorical variables; and t-test and Mann-Whitney U test for continuous variables for normal and non-normal distributions respectively. The association of BMI with COVID-19 infection was analyzed using multivariate logistic regression, adjusting for demographics and other baseline characteristics.

Results: 477 patients (60.0% female, 69.4% Chinese) with median (IQR) age of 49.0 (38.0, 58.0)years were included. 39.8% had rheumatoid arthritis, 27.0% had psoriatic arthritis and 33.1% had a spondyloarthropathy. The majority of patients (67.1%) were on tumor necrosis factor inhibitors (TNFi). 148 (31.0%) patients had incident SARS-CoV-2 infection. Compared to patients not infected with COVID-19, those who contracted COVID-19 had a higher BMI (24.9 vs 26.4 kg/m^2, p = 0.03) (Table 1). Having a BMI of ≥ 25 kg/m^2 (odds ratio [OR] 1.75; 95% CI (1.09, 2.81), p = 0.02) was independently associated with COVID-19 infection, after adjusting for age, sex, race, smoking status and co-morbidities (Table 2). Severe COVID-19 was defined as infections resulting in hospitalization and/or death. Three (2.0%) of 148 patients had severe COVID-19 infection requiring hospitalization. All were male and two were Chinese. Two had rheumatoid arthritis while one had axial spondyloarthritis. All three had co-morbidities of hypertension and hyperlipidemia, and two had diabetes mellitus. At the time of severe COVID-19 infection, the patients were respectively on golimumab, tofacitinib and adalimumab biosimilar (Amgevita®).

Table 1: Summary of Baseline Characteristics*

Variable	Total (N = 477)	Non-covid (N = 365)	Covid (N = 112)	p-value
Age, years (median, IQR)	49.0 (38.0, 58.0)	49.0 (38.0, 58.0)	49.5 (38.0, 57.8)	0.92
Female, no. (%)	286 (60.0)	214 (58.6)	72 (64.3)	0.10
Race, no. (%)				0.64
Chinese	331 (69.4)	251 (68.8)	80 (71.4)	
Malay	55 (11.5)	40 (11.0)	15 (13.4)	
Indian	65 (13.6)	53 (14.5)	12 (10.7)	
Others	26 (5.5)	21 (5.8)	5 (4.5)	
Body mass index, BMI, kg/m² (median, IQR)	25.2 (22.0, 29.1)	24.9 (21.8, 28.9)	26.4 (23.0, 29.5)	0.03
Normal or underweight, < 25kg/m², no. (%)	226 (47.4)	183 (50.8)	43 (38.7)	0.03
Overweight or obese, ≥ 25kg/m², no. (%)	245 (51.4)	177 (49.2)	68 (61.3)	
Married, no. (%)	339 (69.2)	247 (68.0)	83 (74.1)	0.22
Ever-smoker, no. (%)	112 (23.5)	88 (24.3)	24 (21.4)	0.53
Clinical diagnosis, no. (%)				0.41
Rheumatoid Arthritis	190 (39.8)	148 (40.5)	42 (37.5)	
Axial Spondyloarthritis	128 (26.8)	97 (26.6)	31 (27.7)	
Psoriatic Arthritis	129 (27.0)	94 (25.8)	35 (31.2)	
Other Spondyloarthropathy	30 (6.3)	26 (7.1)	4 (3.6)	
Co-morbidities, no. (%)				
Hypertension	144 (30.2)	102 (28.3)	42 (37.5)	0.07
Diabetes Mellitus	63 (13.2)	49 (13.6)	14 (12.5)	0.76
Hyperlipidemia	199 (41.7)	147 (40.8)	52 (46.4)	0.29
Type of bDAMRDs, no. (%)				0.85
TNFi	320 (67.1)	241 (66.0)	79 (70.5)	
IL-17i	63 (13.2)	48 (13.2)	15 (13.4)	
JAKi	47 (9.9)	38 (10.4)	9 (8.0)	
Anti-CD20	13 (2.7)	11 (3.0)	2 (1.8)	
Others	34 (7.1)	27 (7.4)	7 (6.2)	

*Missing values – 6 (BMI), 3 (Smoking), 5 (Hypertension), 5 (Hyperlipidemia), 5 (Diabetes Mellitus). P-values denote statistical differences between the two groups of non-covid and covid-infected. Chi-square test was used for categorical variables, independent samples t-test for normally distributed continuous variables and Mann-Whitney U test for non-normally distributed continuous variables; to calculate p-values. bDMARD: biological disease modifying anti-rheumatic drug TNFi, Tumor necrosis factor inhibitors – adalimumab (Humira®), golimumab, infliximab, etanercept, adalimumab biosimilar (Amgevita®) and infliximab biosimilar (Remsima®); IL-17i, Interleukin-17 inhibitor – secukinumab, ixekizumab; JAKi, Janus kinase inhibitor – tofacitinib, baricitinib; Anti-CD20 – rituximab, rituximab biosimilar (Truxima®); Others include tocilizumab (Interleukin (IL)-6 inhibitor), gulselkumab and ustekinumab (IL-12/23 inhibitors) and abatacept (Cytotoxic T lymphocyte-associated antigen 4-immunoglobulin (CTLA4-Ig)).

Table 2: Odds Ratio of COVID-19 Infection in Inflammatory Arthritis Patients using bDMARDs*

	Univariable		Multivariable	
Variable	OR (95% CI)	p-value	OR (95% CI)	p-value
Age, years †	1.00 (0.99, 1.02)	0.68	0.99 (0.97, 1.01)	0.61
Gender †				
Male	1 (ref)	-	1 (ref)	-
Female	1.27 (0.82, 1.97)	0.29	1.12 (0.66, 1.89)	0.67
Race †				
Chinese	1 (ref)	-	1 (ref)	
Malay	1.18 (0.62, 2.24)	0.62	0.92 (0.46, 1.85)	0.82
Indian	0.71 (0.36, 1.40)	0.32	0.65 (0.32, 1.33)	0.24
Others	0.75 (0.27, 2.05)	0.57	0.75 (0.27, 2.12)	0.59
Body mass index, BMI				
Normal or underweight, < 25kg/m²	1 (ref)	-	1 (ref)	-
Overweight or obese , ≥ 25kg/m²	1.64 (1.06, 2.52)	0.03	1.75 (1.09, 2.81)	0.02
Married (vs not married)	1.34 (0.83, 2.16)	0.22	-	-
Ever-smoker (vs non-smoker) †	0.85 (0.51, 1.42)	0.53	0.84 (0.47, 1.53)	0.58
Clinical diagnosis			-	-
Rheumatoid Arthritis	1 (ref)	-		
Axial spondyloarthritis	1.13 (0.66, 1.91)	0.66		
Psoriatic Arthritis	1.31 (0.78, 2.20)	0.30		
Other Spondyloarthropathy	0.54 (1.18, 1.64)	0.28		
Comorbidities				
Hypertension †	1.51 (0.97, 2.37)	0.07	1.38 (0.78, 2.45)	0.26
Diabetes Mellitus	0.91 (0.48, 1.71)	0.76		-
Hyperlipidemia †	1.26 (0.82, 1.92)	0.29	1.04 (0.61, 1.76)	0.89
Type of bDAMRDs			-	-
TNFi	1 (ref)	-		
IL-17i	0.95 (0.51, 1.79)	0.88		
JAKi	0.72 (0.33, 1.56)	0.41		
Anti-CD20	0.55 (0.12, 2.56)	0.45		
Others	0.79 (0.33, 1.89)	0.60		

bDMARD: biological disease modifying anti-rheumatic drug * Variables were included in the multivariable model if they were significant at P ≤ 0.2 on univariate analysis. † Included in the multivariable model despite not statistically significant in the univariable analysis due to significant correlation with BMI and need to be adjusted for. TNFi, Tumor necrosis factor inhibitors – adalimumab (Humira®), golimumab, infliximab, etanercept, adalimumab biosimilar (Amgevita®) and infliximab biosimilar (Remsima®); IL-17i, Interleukin-17 inhibitor – secukinumab, ixekizumab; JAKi, Janus kinase inhibitor – tofacitinib, baricitinib; Anti-CD20 – rituximab, rituximab biosimilar (Truxima®); Others include tocilizumab (IL-6 inhibitor), gulselkumab and ustekinumab (IL-12/23 inhibitors) and abatacept (Cytotoxic T lymphocyte-associated antigen 4-immunoglobulin (CTLA4-Ig)).

Conclusion: Higher BMI was associated with incident COVID-19 infection in this cohort. This could be due to upregulation of angiotensin-converting enzyme 2 (ACE2) receptors found in adipose tissues and impaired viral elimination as a result of disease-related and/ or obesity-induced blunted immune response and chronic inflammation [1]. Severe SARS-CoV-2 infections in this cohort were rare.Optimization of BMI may contribute to reducing risk and severity of COVID-19 infection.

[1] Demeulemeester, F., de Punder, K., van Heijningen, M., & van Doesburg, F. (2021). Obesity as a Risk Factor for Severe COVID-19 and Complications: A Review.*Cells*,*10*(4), 933. https://doi.org/10.3390/cells10040933

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Abstract Number: 1816

Hyperuricemia – Especially "Metabolic Hyperuricemia" – Is Independently Associated with Higher Risk of Fatty Liver

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
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Session Time: 9:00AM–11:00AM

Background/Purpose: Elevated serum uric acid (SUA) level is rather prevalent in the general population, and it is associated with numerous comorbidities and mortality. Etiology of hyperuricemia seems to play a role in hyperuricemia-associated morbidity and mortality risk. Metabolic hyperuricemia (elevated SUA mainly due to urate overproduction) is found to be more dangerous than renal hyperuricemia (elevated SUA due to renal underexcretion of uric acid).[1] There has however been only few studies done on the association between hyperuricemia and fatty liver and it is not known if the different types of hyperuricemia affect the fatty liver risk differently.

Methods: We used data from GOAL (Good Ageing in Lahti region) study – a prospective, population-based study of elderly Northern European individuals (52–76 years). Data of SUA levels and other laboratory parameters, comorbidities, lifestyle habits and socioeconomic factors were collected. Persons with SUA values of >410 μmol/L (≈6.9 mg/dL; 75th percentile) are represented as clearly hyperuricemic. In those that are clearly hyperuricemia, we defined hyperuricaemia renal if estimated glomerular filtration rate (eGFR) was ≤67 ml/min (25th percentile) and metabolic if eGFR was >67 ml/min. Glomerulal filtration rate was calculated using CKD-EPI creatinine-cystatin C equation. Fatty liver index (FLI) is an accurate predictor of hepatic steatosis and it was calculated from body mass index, waist circumference, triglyceride, and gamma-glutamyl transferase data.[2] Persons with FLI ≥80 (75th percentile) are represented as having a very high probability of fatty liver. The results for mortality in the 15-year follow-up period were adjusted for age, sex, education, smoking status, alcohol consumption, body mass index, hypertension, dyslipidemia, and diabetes.

Results: There is a clear correlation between FLI and SUA in both women [r=0.47 (95% CI =0.43-0.51)]and men [r=0.37 (95% CI =0.32-0.42)], see figure 1. Mortality was higher in individuals with FLI ≥80 than in those with FLI < 80 both in clearly hyperuricemic and slightly hyperuricemic/normouricemic persons. When compared to individuals with SUA ≤410 μmol/L

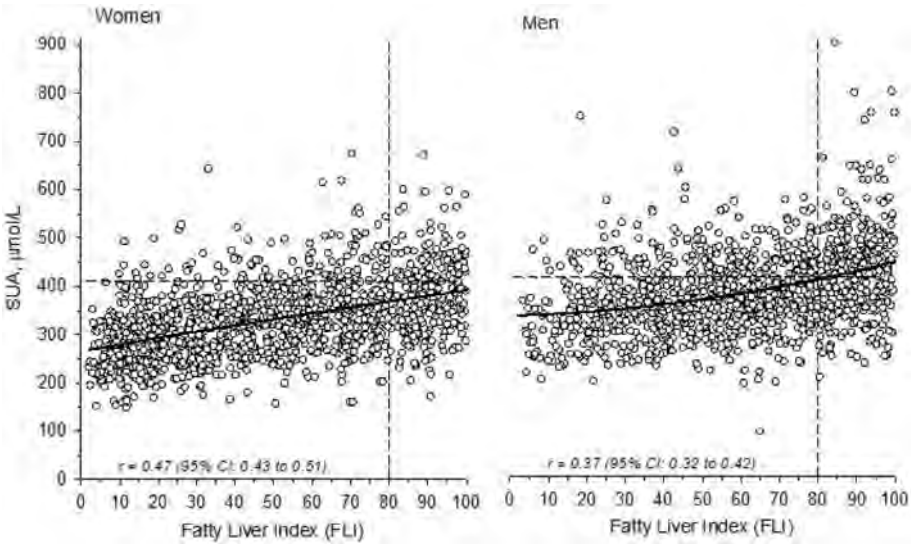


Figure 1. Correlation between fatty liver index (FLI) and serum uric acid (SUA) in women and men. The bold line indicates a trendline. Dashed lines indicate the 75th percentile of SUA (410 µmol/L (≈ 6.9 mg/dL)) and 25th percentile of estimated glomerular filtration rate (eGFR; 67 ml/min) of the study population. Models included quadratic terms for FLI.

Table 1. Adjusted hazard ratio (HR) for all-cause mortality in persons with fatty liver index (FLI) of ≥ 80 and < 80 and clearly elevated serum uric acid (SUA) level or slightly elevated/normal SUA level. Persons with FLI < 80 and SUA < 410 µmol/L (≈ 6.9 mg/dL) shown as reference.

	SUA < 410 µmol/L (≈ 6.9 mg/dL) HR (95% CI)	SUA ≥ 410 µmol/L (≈ 6.9 mg/dL) HR (95% CI)
FLI <80	1.00 (Reference)*	1.16 (0.95 to 1.40)
FLI ≥80	1.34 (1.06 to 1.70)	1.76 (1.39 to 2.23)

*Denominator of Hazard ratios.

(≈6.9 mg/dL) and FLI < 80 the hazard ratio (HR) for all-cause mortality was 1.76 (95% CI: 1.39 to 2.23) in clearly hyperuricemic persons with FLI ≥80, 1.16 (95% CI: 0.95 to 1.40) in clearly hyperuricemic persons with FLI < 80 and 1.34 (95% CI: 1.06 to 1.70) in persons with SUA ≤ 410 µmol/L (≈6.9 mg/dL) and FLI ≥80 (table 1). Individuals with metabolic hyperuricemia had a statistically significantly higher FLI than individuals with renal hyperuricemia: mean (SD)=73.4 (12.2) and 69.6 (22.5), respectively, p=0.015 after adjusting for sex and diabetes.

Conclusion: Fatty liver positively correlates with serum uric acid level. Both fatty liver and hyperuricaemia increase mortality and the most dangerous is a combination of both conditions. Regarding development of fatty liver "metabolic hyperuricemia" appears to be more hazardous than "renalhyperuricemia" since it associates with higher FLI.

[1]Timsans J, et al. Annals of the Rheumatic Diseases 2023;82:2067-2068.

[2]Bedogni G, et al. BMC Gastroenterol. 2006;6:33.

Disclosure: J. Timsans: None; **J. Kauppi**: None; **H. Kautiainen**: None; **M. Kauppi**: None.

Abstract Number: 1817

Geographic Variability of Inflammatory Bowel Disease Related Mortality, 1999-2019; CDC WONDER

Saleha Aziz[1], Anum Akhlaq[1], **Sana Gurz**[2] and Yousaf Zafar[1], [1]University of Mississippi Medical Center, Jackson, MS, [2]University of Nevada, Las Vegas, NV

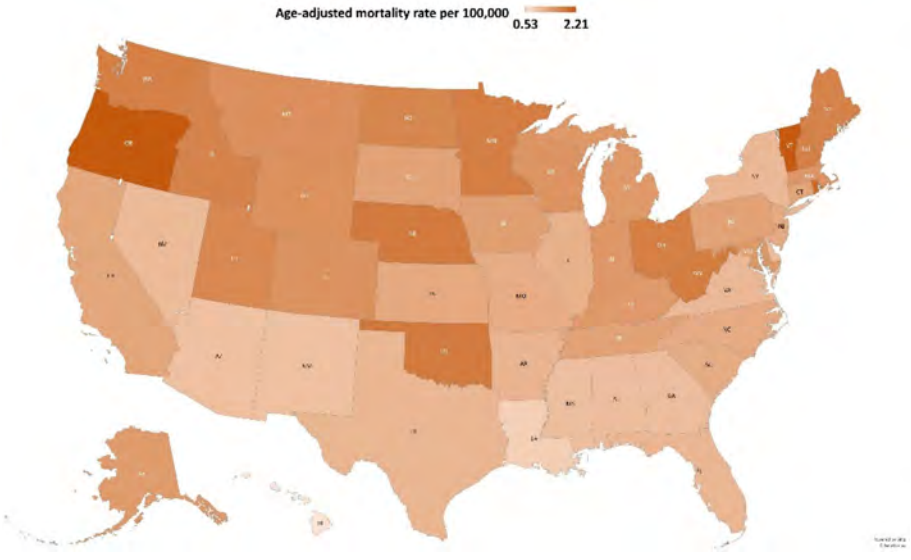
SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

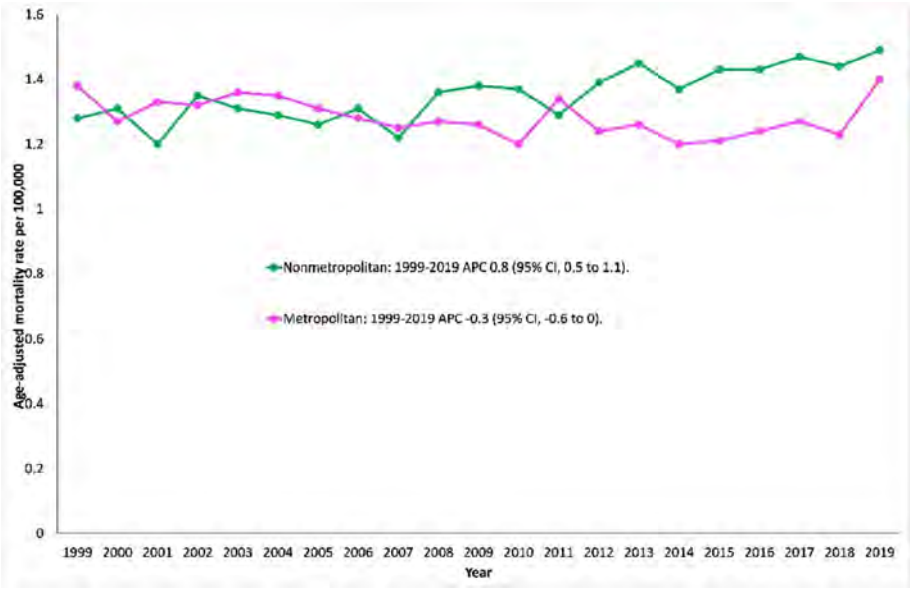
Background/Purpose: The United States makes a significant contribution to Inflammatory Bowel Disease (IBD) related disease burden worldwide. However, data on geographic variability of IBD related mortality within the United States is scarce. Our study assessed the trends in IBD related mortality stratified by geographic pattern through states and metropolitan-nonmetropolitan designation from 1999 to 2019.

Methods: We used Centers for Disease Control and Prevention Wide-Ranging OnLine Data for Epidemiologic Research (CDC WONDER) to access National Vital Statistics System data from 1999 to 2019. IBD related deaths, age >/=25 years were identified from multiple causes of death and were represented as age-adjusted mortality rates (AAMR) per 100,000 population. AAMR was stratified by states and metropolitan-nonmetropolitan designation. Annual percentage changes (APC) were calculated to examine changes in trends using joinpoint regression.

Results: The AAMR per 100,000 population from 1999 to 2019 was 1.29. Crohn's Disease had a higher AAMR compared with Ulcerative Colitis, (0.83 vs 0.53, respectively). The states with the highest AAMR included Oregon (2.21), Vermont (2.19), Rhode Island (1.98), Nebraska (1.81), and Oklahoma (1.78). The lowest AAMRs were seen in Hawaii (0.53), Louisiana (0.8), District of Columbia (0.97), New Mexico (0.98) and Arizona (0.98). Non-metropolitan areas had a higher AAMR compared with metropolitan areas from 1999 to 2019 (1.37 vs 1.28, respectively). Amongst non-metropolitan designations,



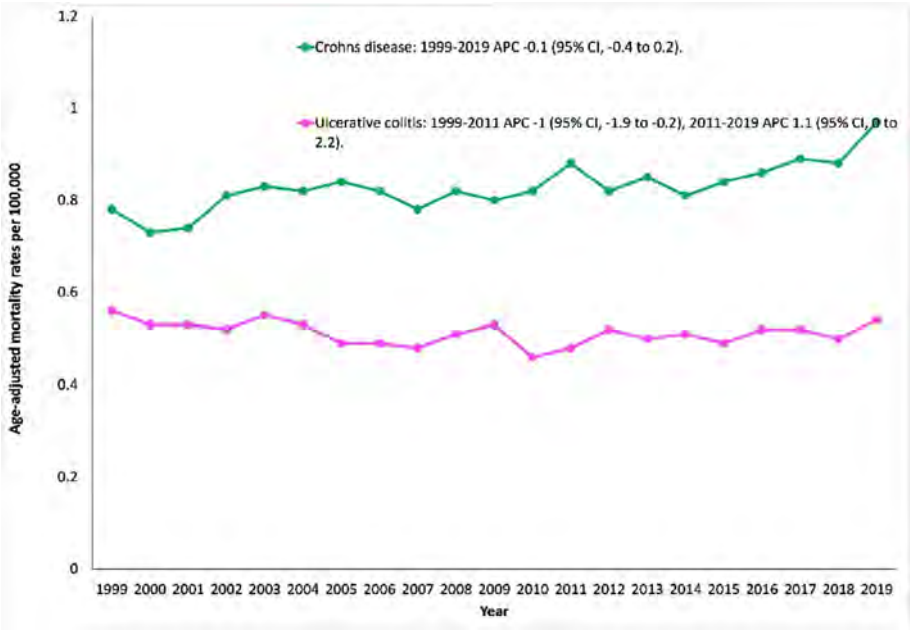
State-level Inflammatory Bowel Disease–related age-adjusted mortality rates per 100,000 people in the United States, 1999 to 2019.



Inflammatory Bowel Disease–related mortality rates stratified by Urban-Rural classification in the United States, 1999 to 2019.

there was a rise in AAMR (1.28 vs 1.49) from 1999 to 2019 (APC 0.8 [95% CI, 0.5 to 1.1]), whereas in metropolitan counties AAMR decreased from 1999 to 2019 (APC -0.3 [95% CI, -0.6 to 0.0]).

Conclusion: Our study demonstrated considerable geographic variation in regards to IBD-related mortality. Overall higher mortality rates were seen in non-metropolitan versus metropolitan areas, along with a rise in mortality trends within non-metropolitan areas. The geographic disparity in mortality determined by our study highlights the need for robust monitoring of patients in these locations, reevaluation of state level health policies, as well as investigation of risk factors leading to these discrepancies.



Inflammatory Bowel Disease–related mortality rates stratified by disease categories in the United States, 1999 to 2019.

Disclosure: S. Aziz: None; **A. Akhlaq**: None; **S. Gurz**: None; **Y. Zafar**: None.

Abstract Number: 1818

Compliance with Romosozumab and Fracture Risk Among Postmenopausal Women in the U.S

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
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Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Romosozumab (romo) is a newly approved osteoporosis (OP) medicine for women with postmenopausal OP at high risk of fracture. The utilization pattern of romo has not been well described. This study aimed to evaluate the association between treatment compliance and baseline fracture risk among new users of romo.

Methods: Using fee-for-service Medicare data, women age ≥65 years newly initiating romo between 4/1/2019 and 6/30/2021 were identified. Claims data was linked to electronic medical record (EMR) data obtained from 9 data marts of 3 PCORNet Clinical Research Networks to obtain the needed covariates to estimate a FRAX score (with Body Mass Index).Comorbidities and medical history were identified from claims while biometric data were obtained from the EMR. The FRAX algorithm was used to calculate 10-year risk of hip and major fracture (clinical spine, forearm, hip, or shoulder) upon romo initiation. We set the median of FRAX (BMI) hip and major fracture risk as the cut-off for higher fracture risk. Treatment adherence (measured by the proportion of days covered [PDC]) and discontinuation rate (defined as gap > 30 days after the expected date of the next romo administration) were calculated. Kaplan-Meier method was used to estimate the discontinuation rate and 95% confidence interval [CI]. A Cox proportional hazard model was used to evaluate the association between baseline fracture risk and discontinuation, controlling for demographics and Charlson score.

Results: There were 12,216 romo new users identified and among them, 559 were linked with PCORNet EMR data. Across PCORNet data marts, the proportion of women who linked ranged from 82% - 98%.The median (IQR) 10-year hip and major fracture risks estimated by FRAX were 11.0 (6.4, 19.0) and 26.0 (18.0, 35.0), respectively. Romo users with higher baseline fracture risk were older, had more history of fractures, were more likely to receive prior OP treatment, compared with those with lower risk (Table 1). They also had higher rate of romo discontinuation (Table 1, Figure 1). Cox regression showed that, after adjusting for age, race, geographic region, and Charlson comorbidity score, the HR (95% CI)for discontinuation associated with higher(above the median) hip and major OP fracture risk was 1.39 (1.01 - 1.91. p=0.043) and 1.51 (1.11 - 2.06. p=0.009), respectively.

Conclusion: In this cohort of women with high fracture risk and using administrative claims data linked to EHR data, romo users who had baseline higher fracture risk had poorer treatment compliance. These data suggest that physician should focus more on improving treatment adherence when prescribing new therapy such as romo for vulnerable patients with higher fracture risk.

Table 1: Baseline characteristics and romosozumab treatment compliance for the Medicare-PCORnet linked romosozumab new user cohort.

	Higher hip fracture risk [b] (n=278)	Lower hip fracture risk (n=281)	Higher major fracture risk (n=292)	Lower major fracture risk (n=267)
Selected Baseline factors [a]				
Age in years, %				
65-74	66 (23.7%)	194 (69.0%)	99 (33.9%)	200 (74.9%)
>=75	212 (76.3%)	87 (31.0%)	193 (74.9%)	67 (25.1%)
White	270 (97.1)	243 (86.5%)	259 (97.0)	254 (87.0%)
Charlson comorbidity score				
0	26 (9.4%)	61 (21.7%)	23 (8.6%)	64 (21.9%)
1-2	143 (51.4%)	158 (56.2%)	135 (50.6%)	166 (56.8%)
>=3	109 (39.2%)	62 (22.1%)	109 (40.8%)	62 (21.2%)
Prior fracture history (any site)	163 (58.6%)	63 (22.4%)	176 (65.9%)	50 (17.1%)
History of osteoporosis medication [c]	189 (68.0%)	162 (57.6%)	179 (67.0%)	172 (58.9%)
Utilization pattern				
Adherence (PDC, %)				
By the end of the 3th month				
Mean (SD)	86.8 (19.3)	90.5 (16.2)	86.7 (19.3)	90.4 (16.3)
PDC >=80%	73.6%	83.2%	73.2%	83.2%
By the end of the 6th month				
Mean (SD)	79.6 (23.9)	85.3 (20.8)	78.9 (24.1)	85.6 (20.6)
PDC >=80%	68.1%	75.6%	66.0%	77.2%
By the end of the 12th month				
Mean (SD)	72.4 (27.0)	79.2 (23.9)	71.4 (27.3)	79.8 (23.4)
PDC >=80%	55.2%	66.9%	53.8%	67.7%
Discontinuation rate [d]				
By the end of the 3th month	22.07 [15.08, 31.64]	13.57 [8.20, 22.02]	22.61 [15.40, 32.48]	13.40 [8.16, 21.58]
By the end of the 6th month	32.76 [24.28, 43.24]	22.70 [15.56, 32.43]	34.10 [25.31, 44.89]	21.89 [15.00, 31.29]
By the end of the 12th month	55.66 [41.78, 70.56]	51.77 [35.82, 69.84]	54.55 [41.97, 68.10]	54.20 [36.57, 73.80]

PDC: proportion of days covered. SD: standard deviation.

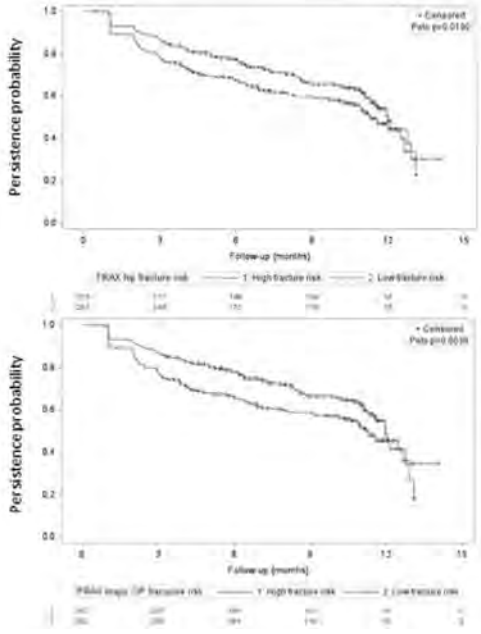
a: p<0.05 for all comparisons for all listed baseline characteristics.

b: Higher and lower risks were classified by the median risk among the linked cohort. Major fracture includes clinical spine, forearm, hip, or shoulder fractures

c: Osteoporosis medication include bisphosphonates, PTH analogues, and denosumab.

d: p<0.05 for both comparisons (Peto's test for Kaplan-Meier curve)

Figure 1. Kaplan-Meier plot for discontinuation between romo users with higher vs. lower baseline fracture risk [A: hip fracture risk. B: major osteoporosis fracture risk (clinical spine, forearm, hip, or shoulder). Peto's test p<0.05 for both comparisons]



A: Kaplan-Meier plot for discontinuation between romo users with higher vs. lower baseline hip fracture risk

B: Kaplan-Meier plot for discontinuation between romo users with higher vs. lower baseline major OP fracture risk

Disclosure: Y. Liu: None; **T. Arora**: Amgen, 5; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, 5, CorEvitas, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **J. Zhang**: None.

Abstract Number: 1819

Clinical Indications Associated with New Opioid Use for Pain Management in the United Kingdom Using National Primary Care Data

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Prescription opioids for non-cancer pain in the UK have increased considerably over the past two decades, alongside a rise in associated harms. Despite the high prevalence of opioid use, there are limited data on the specific indications for prescribing opioids for non-cancer pain. By understanding the reasons for opioid initiation and relative contribution of systems and specific conditions, the opioid burden in patient subgroups can be assessed to develop tailored interventions, policies, and additional support as appropriate. The aim was to evaluate indications associated with new opioid initiation in non-cancer pain using nationally representative UK data.

Methods: Data from the Clinical Practice Research Datalink (CPRD) AURUM were used, a nationally representative database of anonymised electronic health records from General Practices across the UK, between 1/1/06 to 31/09/21. People ≥18 years who were new users of opioids were included. Exclusion criteria included a cancer diagnosis five years prior to first opioid prescription (index date) and methadone users. SNOMED-CT code lists were derived for conditions associated with opioid use following consultation with GPs, rheumatologists, pharmacists, and chronic pain specialists. These were applied to a period one-year prior to index date for surgical indication and five years prior for chronic conditions. Descriptive statistics were used to analyse the data using STATA v13.1, allowing for overlap between indications.

Results: A total of 3,032,185 patients classed as new opioid users over the ~15-year study window were identified. Opioids were initiated more commonly in women (60.7%), people aged 45-64 (40.0%) and ≥65 years (37.0%). We identified 9 systems associated with initiating opioids. The most common were musculoskeletal (73.2%), respiratory (53.1%), infections (25.7%), trauma/injury (16.1%), neurology (16.0%), gastrointestinal (4.2%) and post-surgical (3.9%) (Table 1). Musculoskeletal (MSK) conditions that were most frequently associated with opioid use were osteoarthritis (n=1,536,437, 50.7%), low back pain (1,094,225, 36.1%), other non-inflammatory MSK conditions (e.g. rotator cuff tears), rheumatoid arthritis (63,367, 2.2%) and fibromyalgia (56,038, 1.9%). Post-surgical indications one year prior to index date were associated with 3.9% of all prescriptions. Orthopaedic surgeries were the most common and contributed to 42.1% all post-surgical indications (Table 1). This included total knee replacements (n= 31,944; 27.6%) and total hip replacements (n=17,865; 14.5%) of all post-surgical indications.

Conclusion: This is the first study in the UK evaluating large scale national data to assess indications associated with opioid initiation. Almost three quarters of the new prescriptions of opioids for non-cancer pain were in people with a diagnosis of a MSK condition. Orthopaedic surgeries contributed to a third of all post-surgical indications. These findings could help

Table 1: Clinical indications associated with new opioid use with different look back periods (overlapping totals) – systems ordered by percentages.

System	n (%)	Indications	n (%)
Musculoskeletal	2,244,444 (74.0%)	Osteoarthritis	1,536,437 (50.7%)
		Low back pain	1,094,225 (36.1%)
		MSK (non-inflammatory) bursitis, rotator cuff, tendonitis	344,347 (11.4%)
		Rheumatoid Arthritis	63,367 (2.1%)
		Fibromyalgia	56,038 (1.9 %)
		Psoriatic arthritis	13,829 (0.5%)
		Systemic lupus erythematosus	8,348 (0.3%)
		Ankylosing spondylitis	8,037 (0.3%)
		Gout	107,596 (3.6%)
Respiratory	1,610,327 (53.1%)	Respiratory infections	1,222,277 (40.3%)
		Respiratory (non-infective)	127,509 (4.2%)
		Cough	903,417 (29.8%)
Infections	778,832 (25.7%)	Infections (most commonly prescribed antibiotics – UTI/cellulitis/otitis media)	777,206 (25.6%)
		HIV	2,147 (0.1%)
Trauma/ injury	488,195 (16.1%)	Trauma (including sprains, sprains and dislocations)	264,790 (8.7%)
		Fractures	251,903 (8.3%)
Neurology	485,233 (16.0%)	Headaches	456,458 (15.1%)
		Neuropathic pain	37,773 (1.25%)
		Somatoform	201 (0.01%)
Major Surgery (top 10 presented)	115,669 (3.9%)	Total Knee Replacement	31,944 (1.1%)
		Total Hip Replacement	17,865 (0.6%)
		Hernia Repair	12,375 (0.4%)
		Hysterectomy	11,139 (0.4%)
		Cholecystectomy	8,003 (0.3%)
		Caesarean Section	9,641 (0.3%)
		Vasectomy	4,070 (0.1%)
		CABG	5,962 (0.2%)
		Appendectomy	3,524 (0.1%)
		Laparoscopy	2,173 (0.1%)
Gastrointestinal	126,939 (4.2%)	IBS	104,551 (3.5%)
		IBD	22,145 (0.7%)
		Chronic Pancreatitis	1,600 (0.1%)
Gynaecological reasons	39,434 (1.3%)		39,434 (1.3%)
Dental	38,706 (1.3%)		38,706 (1.3%)

prioritise efforts for targeted interventions in opioid prescribing, clinical vigilance and future policy to support non-pharmacological interventions.

Disclosure: M. Lyon: None; **C. Ramirez Medina**: None; **E. Davies**: None; **M. Jani**: None.

Abstract Number: 1820

Statewide Burden of Osteoarthritis in United States Between 1990-2019: A Systematic and Comparative Benchmarking Study

Dhruvkumar Gadhiya[1], Utsav Patel[2], Hiren Chhayani[3], Krushi Shah[3], Sneh Patel[3], Victor Adedara[4], Divya Patel[3], Hardik Desai[5] and Swetha Chittipolu[6], [1]St.Luke's University Health, Anderson Campus, Easton, PA, [2]Tulane University, New Orleans, LA, [3]G.M.E.R.S. Medical College, Gandhinagar, Gandhinagar, India, [4]St George's University SOM, True Blue Greneda, True Blue, Grenada, [5]Gujarat Adani Institute of Medical Sciences, Bhuj, India., Bhuj, India, [6]North Mississippi Medical Center, Tupelo, MS

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Epidemiology & Public Health Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is a prevalent and debilitating musculoskeletal condition that has imposed a significant burden on the United States (US) healthcare system. This study aims to explore the burden and trends of osteoarthritis in the US from 1990 to 2019.

Methods: Using the Global Burden of Disease methodology, this analysis presents a comprehensive overview of the Prevalence, Incidence, Disability adjusted life year (DALYs), Years lived with Disability (YLDs) by age, sex, year across the US from 1990-2019. All estimates were presented as total counts and age-standardized rates per 100 000 population, with uncertainty intervals (UIs).

Results: The prevalence cases of total osteoarthritis in the US nearly doubled from 28,873,208 (95%UIs: 25,939,261-32,228,468) in 1990 to 51,865,888 (46,804,271-57,860,984) in 2019. Similarly, the incidence of osteoarthritis increased from 1,990,039 (1,789,372-2,247,569) in 1990 to 3,462,236 (3,060,905-3,923,793) in 2019. The YLDs due to osteoarthritis also saw an upward trend, rising from 1,087,979 (556,601-2,194,304) in 1990 to 1,986,342 (1,023,960-3,964,292) in 2019. The annual percentage change (APC) in DALYs increased by 83% (75%-91%) from 1990 to 2019, indicating a substantial rise in the burden of osteoarthritis. The APC of age-standardized incidence rate (ASIR) increased by 6% (3%-10%), suggesting a steady growth in the occurrence of new cases. Among the states, Massachusetts experienced the highest incidence APC (13%), followed by California (12%) and Minnesota (10%) from 1990 to 2019. Interestingly, North Dakota was the only state that reported a decrease in the APC of ASIR by 2%. When analyzing the age-

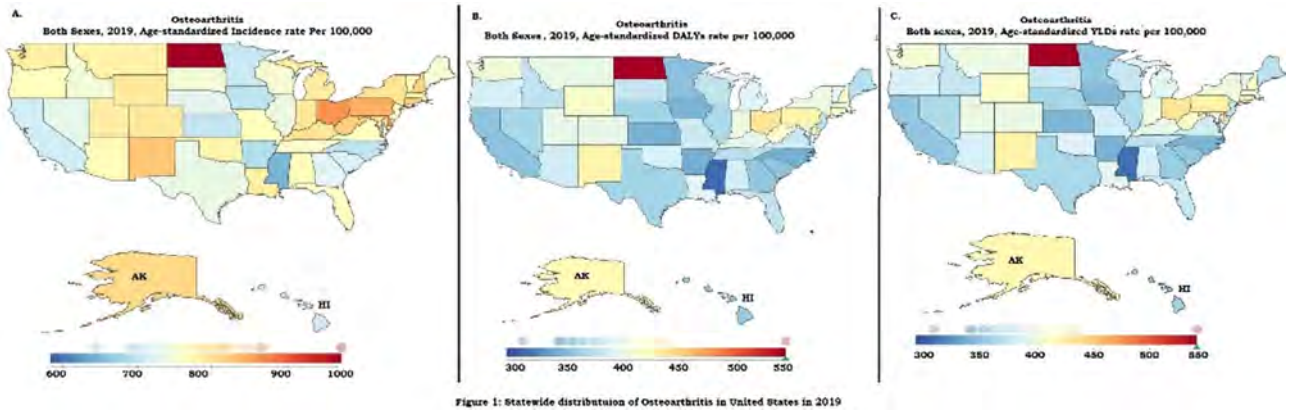

Figure 1: Statewide distribution of Osteoarthritis in United States in 2019

Statewide distribution of Osteoarthritis in United States in 2019.

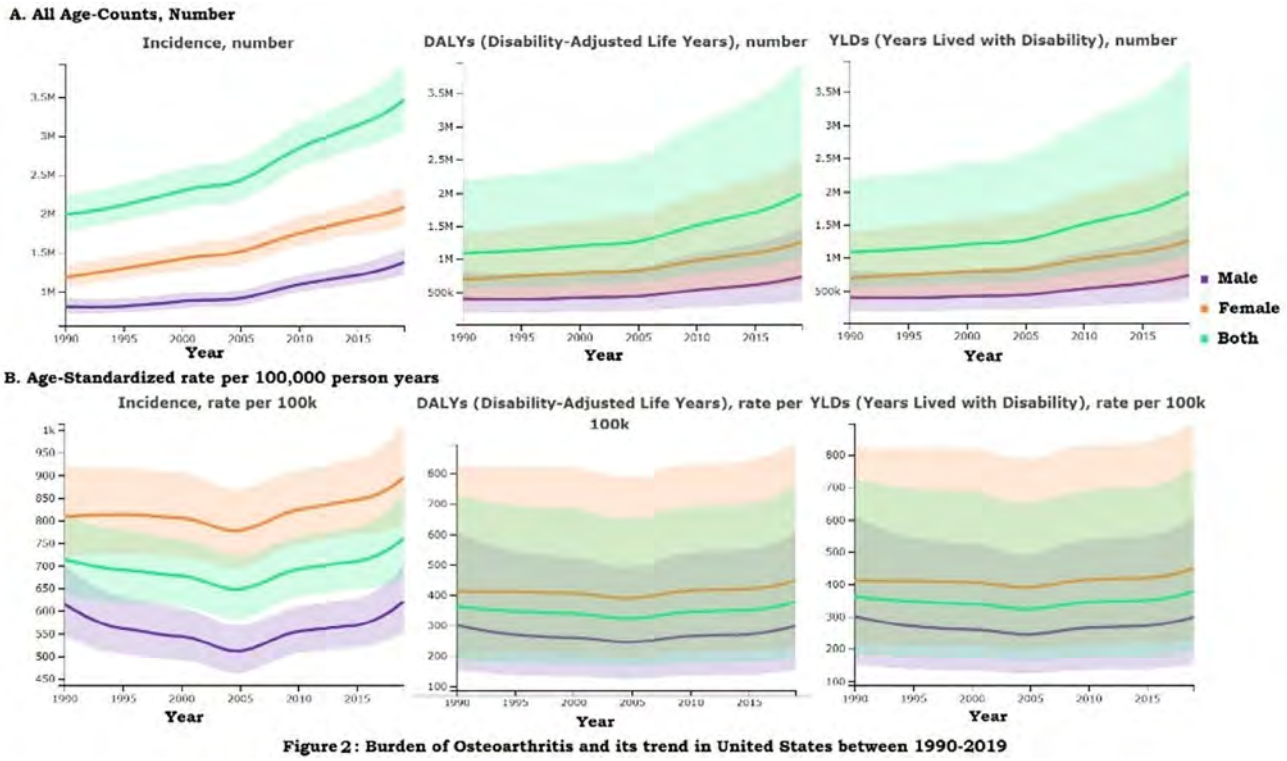

Figure 2: Burden of Osteoarthritis and its trend in United States between 1990-2019

Burden of Osteoarthritis and its trend in United States between 1990-2019.

standardized DALYs rate (ASDALR), California exhibited the highest APC (12%), followed by Massachusetts (10%). Nevada had the highest APC in total incidence cases (226%), with Arizona closely behind at 158%. In contrast, the District of Columbia had the lowest APC in total incidence cases (23%) from 1990 to 2019. Regarding gender differences, females had a higher total number of incidence cases in the APC analysis (76% vs. 70%), while the increase in DALYs was similar for both males and females. Looking at specific age groups, Nevada and Alaska had the highest APC increase in incidence among individuals aged 95 and above, while North Dakota had the lowest APC in the 40-44 age group for females. For males,

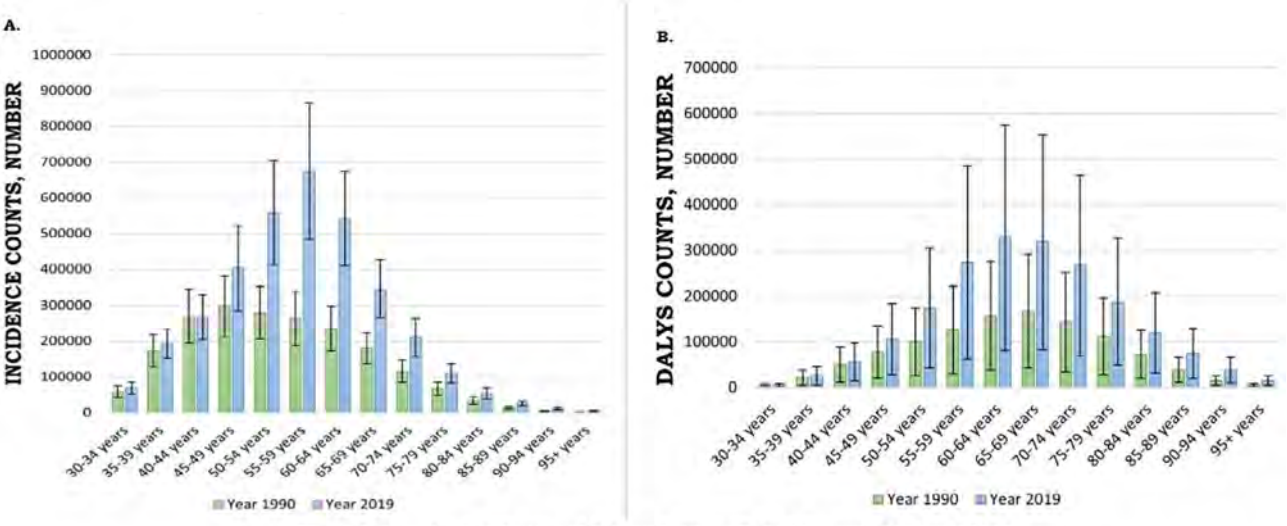

Figure 3: Age-wise distribution of Osteoarthritis in United States in 1990 and 2019.

Age-wise distribution of Osteoarthritis in United States in 1990 and 2019.

Nevada and Alaska had the highest APC increase in incidence among aged 95 and above, while Vermont had the lowest in the 40-44 age group.

Conclusion: In the US, the overall burden of osteoarthritis has steadily increased over the past three decades, with a notable variation in burden observed across different states. It is crucial to prioritize public health initiatives that promote healthy aging, early detection, and appropriate interventions. This includes raising awareness about the risk factors associated with osteoarthritis, implementing strategies to promote physical activity and healthy lifestyles, and ensuring equitable access to effective treatments and therapies.

Disclosure: D. Gadhiya: None; **U. Patel**: None; **H. Chhayani**: None; **K. Shah**: None; **S. Patel**: None; **V. Adedara**: None; **D. Patel**: None; **H. Desai**: None; **S. Chittipolu**: None.

Abstract Number: 1821

The "Weekend Effect" and Rheumatological Association in Patients with Diffuse Alveolar Haemorrhage

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Diffuse alveolar hemorrhage (DAH) is a life-threatening pulmonary complication commonly associated with autoimmune disorders. Limited treatment options are available for DAH, and time to initiating treatment is critical. The day of admission may be an important predictor of patient outcomes. The "weekend effect", which results from low staff availability over weekends, has been reported to have a number of negative outcomes. (1) However, there is limited evidence on the weekend effect on DAH, and in particular DAH association with rheumatologic disease. This study assesses the impact of the "weekend effect" inpatient mortality and outcomes in patients with DAH) and rheumatologic conditions.

Methods: This study utilized the National Inpatient Sample (NIS) database for 2020, which contains data on over seven million unweighted hospitalizations, to identify patients with DAH and rheumatological conditions. The patients were classified based on admission on a weekday or a weekend, and confounding variables were accounted for using multivariable logistic regression models. The primary outcome was inpatient mortality, and secondary outcomes included intubation, non-invasive ventilation, bronchoscopy, invasive ventilation, length of hospital stay, and total hospitalization charges.

Results: The study included 515 patients with primary diagnosis of DAH. Patients with lupus, systemic sclerosis, sjogren's syndrome, Granulomatosis with polyangitis, vasculitis had a significance association with DAH $p< 0.0001$. Overall, DAH had 17.8% mortality on weekends vs 9.30% on weekdays with an OR 4.1(0.63-27.3), p=0.139, and greater likelihood of intubation OR 2.81(1.08-7.33) p= 0.034. Patients admitted on weekends had higher length of stay (LOS) 5.28 vs 4.52 days, p = 0.024 and higher total cost of stay; $171,101 vs $83,867 vs., p=0.026. Use on non-invasive ventilation, invasive ventilation, and bronchoscopy had similar odds in both groups. Those admitted on the weekends were more often in the lowest income quartile, 42.86% vs 23.29%.

Table 2. Primary and Secondary Outcomes				
	Total	Weekend	Weekday	P Value
Total inpatient mortality (%)	60 (11.6%)	17.80%	9.30%	0.23
Intubation (%)	24.27%	39.29%	18.67%	**0.029**
Non-invasive ventilation (%)	5.80%	7.14%	5.30%	0.0726
Invasive ventilation (%)	27%	42.86%	21.33%	**0.028**
Bronchoscopy (%)	3.80%	7.14%	2.67%	0.295
Length of stay (d)	6.89	10.5	5.25	
Total charge ($)	110,256	171,101	87,233	
%- Percent $- Cost in US Dollar				
	Crude OR	P value	Adjusted OR	P value
Total inpatient mortality (%)	2.11 (0.606-7.35)	0.24	4.1 (0.63-27.3)	0.139
Intubation (%)	2.81 (1.08-7.33)	0.034	2.76 (0.65-11.67)	0.167
Non-invasive ventilation (%)	1.36 (0.236-7.88)	0.728	8.09 (0.37-176.9)	0.184
Invasive ventilation (%)	2.76 (1.09-6.99)	0.032	3.22 (0.79-13.12)	0.102
Bronchoscopy (%)	2.80 (0.37-20.94)	0.314	-	-
Length of stay (d)	5.28 (0.70-9.86)	0.024	4.52 (0.22-8.81)	0.039
Total charge ($)	83,867 (10,217-157,517)	0.026	66,568 (-640-133,777)	0.05
%- Percent, $- Cost in US Dollar, OR- Odds Ratio.				

Primary vs Secondary Outcome in Patients with Diffuse Alveolar Hemorrhage

Rheumatological Variables	Total number (%)	OR	p-value
Rheumatoid Arthritis	215(2.08%)	1.36 (1.01-1.85)	0.042
Lupus	259(2.51%)	4.95 (3.76-6.52)	0.0001
Systemic Sclerosis	30(0.29%)	3.32 (1.49-7.41)	0.003
Sjogren	119(1.1%)	2.63 (1.76-3.94)	0.0001
Polymyositis	5(0.04%)	2.42 (.341-17.23)	0.376
GCA	10(.09%)	2 (0.5-8.01)	0.327
Wegener	350(3.3%)	106 (83-135)	0.0001
Ankylosing spondylitis	10(0.09%)	1.70 (0.42-6.81)	0.452
Vasculitis	10(0.09%)	9.92 (2.47-39.81)	0.001
ANCA Vasculitis	490(4.7%)	124(101.67-153.6)	0.0001
EGPA	5(0.04%)	10.87 (1.52 - 77.4)	0.017
MCTD	25 (0.2%)	17.9 (7.43 -43.2)	0.0001
COVID			
OR- Odds Ratio, %- percentage			

Rheumatological Associations with Diffuse Alveolar Hemorrhage

Conclusion: This study highlights the association between several rheumatological conditions and DAH. As well it illustrates the weekend effect on inpatient mortality from DAH, and other outcomes. It shows a rather large increase in mortality from DAH in patients admitted on the weekends, as well as higher cost and length of stay. Interestingly, those in the lowest income bracket were most likely to be admitted on a weekend. These findings can help inform clinical decision-making and resource allocation to improve the care of DAH patients, especially in those with rheumatologic disease.

(1)Bell CM, Redelmeier DA. Mortality among patients admitted to hospitals on weekends as compared with weekdays. N Engl J Med. 2001 Aug 30;345(9):663-8. doi: 10.1056/NEJMsa003376. PMID: 11547721.

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Abstract Number: 1822

The Food and Drug Administration's (FDA's) Safety Surveillance of Baricitinib and Tocilizumab for COVID-19 (Disclaimer: This Abstract Reflects the Views of the Authors and Not Necessarily Those of the US FDA)

Laura Kangas[1], Lisa Wolf[2], Maya Beganovic[3], Rachna Kapoor[4], James Kidd[4], Kate McCartan[4], Kim Swank[4] and Ida-Lina Diak[4], [1]Food and Drug Administration, Bethesda, MD, [2]Food and Drug Administration, Chevy Chase, MD, [3]Food and Drug Administration, Chicago, IL, [4]Food and Drug Administration, Silver Spring, MD

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Baricitinib, a Janus kinase inhibitor, and tocilizumab, an interleukin-6 receptor antagonist, are two products first approved for the treatment of rheumatoid arthritis. Notably, these products were authorized for emergency use for the treatment of COVID-19 and now are FDA-approved for this use in adults. As part of FDA's mission to protect the public health, FDA performed safety surveillance of products used, authorized, or approved for the treatment or prophylaxis of COVID-19. The purpose of this descriptive study is to describe the high-level findings from FDA's surveillance of adverse event (AE) reports with baricitinib and tocilizumab used for the treatment of COVID-19.

Methods: We conducted recurring daily searches of the FDA Adverse Event Reporting System, weekly searches of the medical literature, and reviewed cases submitted to the FDA-American College of Medical Toxicology COVID-19 Toxicology Investigators Consortium (FACT) Pharmacovigilance Project Sub-registry through April 24, 2023. We performed a high-level overview of the reports, summarizing information on age, sex, country of origin, AE seriousness, and top reported AEs. We focused on reports containing AEs of interest defined as unlabeled AEs with the potential for serious outcomes, labeled AEs with unexpected characteristics, and other important findings that inform product safety.

Results: We reviewed 935 reports with baricitinib and 1,963 reports with tocilizumab. Regarding baricitinib, most reports originated from foreign countries (77%). Of those reporting sex (868) and age (837), more involved males (67%) than females (33%) and the median age was 62 years (range 8-100 years). About 30% of reports had a fatal outcome, which includes

mortality from all causes (e.g., sequelae of COVID-19, comorbidities, indeterminate) and does not imply a causal relationship to the drug. We identified the following AEs of interest: thromboembolism, acute kidney injury, major adverse cardiovascular events, gastrointestinal (GI) perforation, rhabdomyolysis, hepatitis B reactivation, drug-induced liver injury, and posterior reversible encephalopathy syndrome (PRES). Regarding tocilizumab, most reports originated from foreign countries (67%). Of those reporting sex (1,193) and age (1,090), more involved males (71%) than females (29%) and the median age was 61 years (range 7 months-98 years). About 44% of reports had a fatal outcome, which includes mortality from all causes and does not imply a causal relationship to the biologic. We identified the following AEs of interest: GI perforation, cerebrovascular accident, intestinal pneumatosis, viral-induced hepatitis, and PRES.

Conclusion: FDA identified multiple AEs of interest with use of baricitinib and tocilizumab for COVID-19 requiring continued monitoring; these AEs were few in number, confounded by concomitant medications/diseases, and/or were unassessable because of limited information. The current Emergency Use Authorization Fact Sheets for pediatrics and approved product labeling for baricitinib and tocilizumab appropriately communicate the safety profiles of these products for the COVID-19 population.

Disclosure: L. Kangas: None; **L. Wolf**: None; **M. Beganovic**: None; **R. Kapoor**: None; **J. Kidd**: None; **K. McCartan**: None; **K. Swank**: None; **I. Diak**: None.

Abstract Number: 1823

Higher Body Mass Index and Older Age, Both of Which Are Linked to Immunothrombosis Are Associated with Improved Survival with Baricitinib Therapy in COVID-19 Pneumonia

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Immunothrombosis is a critical pathological feature of fulminant COVID-19 pneumonia in which immunosuppression with common immunomodulatory agents such as corticosteroids, IL-6 receptor blockers, and JAK inhibitors have shown benefit [1–4].The basis for the efficacy of immunomodulation in the face of potentially critical viral pneumonia remains poorly understood. This study ascertained the impact of age and obesity, both of which increase thrombotic tendencies, on survival following baricitinib therapy for severe COVID-19 in the Phase III COV-BARRIER 3 trial where baricitinib improved survival compared to placebo [4].

Methods: We performed a post-hoc analysis of the COV-BARRIER multicentre double-blind randomized study of baricitinib versus placebo with an assessment of 28-day mortality (a key secondary outcome in the trial) in 1525 hospitalized COVID-19 adult patients. Age was categorized into < 65 years and ≥65 years, and BMI was categorized d into < 25 kg/m^2 (normal), and ≥ 25 kg/m^2 (high). To assess the incidence rate ratios of mortality in the different subgroups, we employed the assumption of a Poisson distribution. All-cause mortality by day 28 was evaluated in a cox-regression analysis (adjusted to age) in three different groups according to BMI (< 25 kg/m^2, 25-30 kg/m^2, and > 30 kg/m^2).

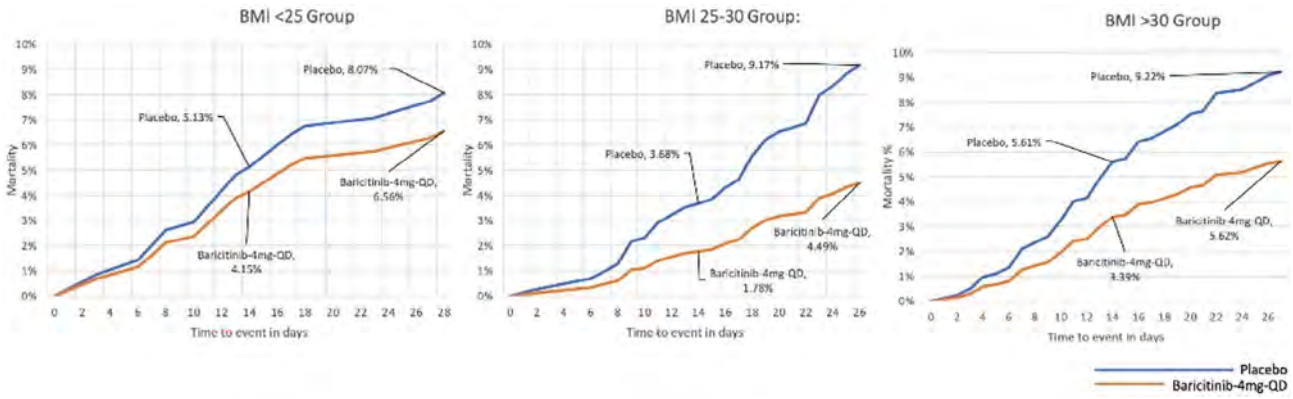

Figure 1. Twenty-eight-day-all-cause mortality in Placebo and Baricitinib arms according to different BMI groups (adjusted to age)

Results: As reported in COV-BARRIER 3 data [4], all-cause mortality by day 28, a key-secondary endpoint, was 8% (n=62) in the baricitinib arm and 13% (n=100) for placebo (PBO), HR 0.57 [95% CI 0.41-0.78].However, we found that in the normal BMI group, irrespective of age, baricitinib therapy did not show a significant survival advantage when compared to PBO [IRR of 1.89 (95% CI: 0.49 to 7.28) and 0.95 (95% CI: 0.46 to 1.99) for < 65yo and ≥ 65yo respectively]. In patients with high BMI, mortality in the baricitinib group was 5.3% (22/418) in < 65 years old (yo) and 20.0% (40/200) in ≥ 65yo. For PBO, mortality rates were 9.9% (43/435) in < 65yo and 30.5% (53/174) in ≥ 65yo. The Incidence rate ratio (IRR) was 0.53 (95% CI: 0.32 to 0.87) and 0.66 (95% CI: 0.46 to 0.94) for the respective age categories. The 28-all-cause-mortality for BMI over 30 was 9.22% for baricitinib and 5.62% for PBO [HR= 0.6, (5.6%vs 9.2%), $p< 0.05$], while for BMI < 25, the difference between 28-all-cause-mortality between baricitinib and PBO arms was not significant [(6.6% vs 8.1), $p>0.05$] (Figure 1).

Conclusion: Baricitinib was associated with significantly lower mortality in patients with high BMI and older subjects. Both BMI and age are associated with immunothrombosis, and the protective effect of JAK inhibition in such groups is remarkable given the reports of thrombosis with JAK inhibition in rheumatoid arthritis.

References:

1- Nicolai L, Leunig A, Brambs S, *et al. Journal of Thrombosis and Haemostasis* 2021;**19**:574–81.
2- Ranucci M, Ballotta A, di Dedda U, *et al*. *Journal of Thrombosis and Haemostasis* 2020;**18**:1747–51.
3- Kalil AC, Patterson TF, Mehta AK, *et al. New England Journal of Medicine* 2021;**384**:795–807.
4- Marconi VC, Ramanan A V., de Bono S, *et al. Lancet Respir Med* 2021;**9**:1407–18.

Disclosure: P. David: None; **N. Ben-Shabbat**: None; **O. Hen**: None; **H. Amital**: None; **A. watad**: None; **D. McGonagle**: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Janssen, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 1824

Breakthrough COVID-19 and Severity After Vaccination Among Pregnant Persons with Rheumatic Diseases

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose:

Acknowledgment: Contributed on behalf of the National COVID Cohort Collaborative (N3C) Consortium

Individuals with rheumatologic diseases (RD) are at higher risk for severe COVID-19 compared to their healthy counterparts. ACR recommendations for COVID-19 vaccination of patients with RD was issued at nearly the same time as CDC recommendations for vaccination during pregnancy, in late July 2021. However, limited data to date exists on vaccination effectiveness among pregnant patients with RD. The aim of this study was to assess the incidence and severity of breakthrough COVID-19 post-vaccination in pregnant patients with RD.

Table 1: Characteristics of unvaccinated and vaccinated pregnant persons within the N3C cohort, December 10, 2020 to May 28, 2022

Table 1: Characteristics of unvaccinated and vaccinated pregnant persons within the N3C cohort, December 10, 2020 to May 28, 2022

	Non-vaccinated pregnant persons	Pregnant persons vaccinated during pregnancy	Pregnant persons vaccinated prior to pregnancy
	N=2795	N=466	N=565
Rheumatic Disease			
RA	1034 (37.0%)	163 (34.9%)	227 (4.01%)
SLE	1001 (30.7%)	175 (37.6%)	174 (30.8%
Spondyloarthritis	427 (15.3%)	92 (19.7%)	116 (20.5%)
Overlapping	253 (9.1%)	36 (7.7%)	48 (8.5%)
Age in years			
Mean(sd)	34.1 (8.8)	34.6 (8.2)	35.4 (7.6)
Age groups			
25-35	377 (13.5%)	50 (10.7%)	33(5.8%)
25-35	1348(48.2%)	219 (47.0%)	260 (46.0%)
35-55	1070 (38.3%)	197 (42.3%)	272 (48.1%)
Race/Ethnicity			
White/non-Latinx	1678 (60.0%)	280 (63.1%)	361 (66.7%)
Black/non-Latinx	451 (16.1%)	72 (16.2%)	75 (13.9%)
Latinx	349 (12.5%)	69 (15.5%)	77 (14.2%)
Asian	67 (2.4%)	23 (5.2%)	<20
Other	32 (1.1%)	<20	<20
Missing	218 (7.8%)	<20	28 (5.2%)
Vaccination status			
Fully	N/A	364 (80.5%)	583 (89.8%)
Partially	N/A	88 (19.5%)	66 (10.2%)
Manufacturer of first vaccine	N/A		
Pfizer/BionTech		338 (75.8%)	404 (71.6%)
Moderna		<110	132 (23.4%)
Janssen		<20	28 (5.0%)
Comorbidities			
Asthma	617 (22.1%)	93 (20.0%)	131 (23.2%)
Current or past Smoking	889 (31.6%)	152 (32.6%)	162 (28.7%)
Cardiovascular Disease	724 (25.9%)	103 (22.1%)	140 (24.8%)
Type II diabetes	300 (10.7%)	50 (10.7%)	53 (9.4%)
Modified CCI Index*			
mCCI=0	1518 (54.3%)	261 (56.0%)	318 (56.3%)
mCCI=1	554 (19.8%)	99 (21.2%)	116 (20.5%)
mCCI=2+	723 (25.9%)	106 (22.7%)	131 (23.2%)
Insurance Type			
Private	468 (16.7%)	93 (20.5%)	112 (20.4%)
Medicare/Medicaid	309 (11.1%)	50 (11.0%)	57 (10.8%)
Missing	1982 (70.9%)	311 (68.5%)	380 (69.2%)
COVID-19 Severity			
Hospitalization(any)	137 (4.9%)	<20	<20
Hospitalization COVID-19 related	67 (2.4%)	<20	<20

*mCCI: Charlson Comorbidity Index with weighting for rheumatic disease removed

Methods: Using a retrospective cohort analysis of the National Covid Cohort Collaborative (N3C), a nationally sampled and prospectively collected electronic health records repository, we analyzed incident and severe COVID-19 in pregnant patients with RD who were fully vaccinated or additionally vaccinated as defined by CDC recommendations before or during their pregnancy compared to non-vaccinated pregnant persons with RD from December 10, 2020, through May 28, 2022. Pregnant persons were identified using the HIPPS algorithm developed and validated for this purpose for N3C data. Within this group, those with RD were identified using diagnostic codes for the most prevalent RDs, namely SLE, RA, or spondyloarthritis. Incident breakthrough infection was defined as any COVID-19 positivity via laboratory or diagnostic criteria at least 14 days after full vaccination. To evaluate the severity of COVID-19, we identified incidences of hospitalization (all-cause) and hospitalization for COVID-19. We estimated adjusted hazard ratios using Cox proportional hazard models, adjusting for age, race/ethnicity, comorbidities, and data partner site.

Results: Of the 3826 pregnant persons with RD included in our cohort, 466 (12.2%) were vaccinated during and 565 (14.8%) prior to pregnancy, with the remaining 2795 (73.0%) having no reported COVID-19 vaccine. Baseline characteristics of the cohort are shown in Table 1. Compared to unvaccinated pregnant persons, we found an adjusted hazard ratio (aHR) of incident COVID-19 of 1.26 (95%CI: 0.88, 1.78) for fully vaccinated, either before or during pregnancy, pregnant persons (Table 2). Compared to unvaccinated pregnant persons, the risk of severe COVID-19 was lower for fully vaccinated, either before or during pregnancy. The aHR for COVID-19 related hospitalization was 0.31 (95%CI: 0.10, 0.93) when comparing those who were fully vaccinated prior to pregnancy with unvaccinated individuals (Table 3).

Table 2: COVID-19 incidence and breakthrough among pregnant persons with rheumatic disease by vaccination status within the N3C cohort, December 10, 2020 to May 28, 2022

Table 2: COVID-19 incidence and breakthrough among pregnant persons with rheumatic disease by vaccination status

	Number of events	Events/100 person-months	Unadjusted HR (95%CI)	Partially adjusted HR (95%CI)*	Fully adjusted HR (95%CI)**
Unvaccinated pregnant persons (n=2795)	456	1.7	Ref	Ref	Ref
Fully vaccinated pregnant persons (n=879)	117	1.7	1.25 (0.87, 1.78)	1.26 (0.88, 1.81)	1.26 (0.88, 1.78)
Fully vaccinated pregnant persons compared to partially vaccinated pregnant persons					
Partially vaccinated pregnant persons (n=152)	22	2.5	Ref	Ref	Ref
Fully vaccinated pregnant persons (n=879)	117	1.7	0.70 (0.41, 1.21)	0.69 (0.41, 1.15)	0.69 (0.42, 1.13)
Received first vaccine during pregnancy					
Unvaccinated pregnant persons (n=2795)	456	1.7	Ref	Ref	Ref
Fully vaccinated pregnant persons vaccinated during pregnancy (n=317)	49	1.7	1.10 (0.77, 1.56)	1.14 (0.89, 1.64)	1.13 (0.79, 1.62)
Received first vaccine prior to pregnancy					
Unvaccinated pregnant persons (n=2795)	456	1.7	Ref	Ref	Ref
Fully vaccinated pregnant persons vaccinated prior to pregnancy n=(562)	68	1.7	1.14 (0.68, 1.89)	1.15 (0.69, 1.90)	1.14 (0.70, 1.86)

*adjusted for age, race/ethnicity, and data partner site

**adjusted for age, race/ethnicity, modified CCI, and data partner site

Table 3: Hospitalizations among pregnant persons with rheumatic disease by COVID-19 vaccination status within the N3C cohort, December 10, 2020 to May 28, 2022

	Events/100 person-months	Unadjusted HR (95%CI)	Partially adjusted HR (95%CI)*	Fully adjusted HR (95%CI)**
Any cause hospitalization				
Unvaccinated pregnant persons (n=2795)	0.50	Ref	Ref	Ref
Fully vaccinated pregnant persons (n=879)	0.34	0.73 (0.49, 1.09)	0.81 (0.53, 1.24)	0.83 (0.55, 1.26)
Hospitalization for COVID-19				
Unvaccinated pregnant persons (n=2795)	0.24	Ref	Ref	Ref
Fully vaccinated pregnant persons (n=879)	0.09	0.45 (0.22, 0.92)	0.47 (0.24, 0.96)	0.51 (0.26, 1.02)
Fully vaccinated pregnant persons compared to partially vaccinated pregnant persons				
Any cause hospitalization				
Partially vaccinated pregnant persons (n=152)	0.57	Ref	Ref	Ref
Fully vaccinated pregnant persons (n=879)	0.34	0.57 (0.13, 2.55)	0.61 (0.12, 3.09)	0.61 (0.12, 3.07)
Hospitalization for COVID-19				
Partially vaccinated pregnant persons (n=152)	0.46	Ref	Ref	Ref
Fully vaccinated pregnant persons (n=879)	0.09	0.21 (0.03, 1.37)	0.20 (0.03, 1.35)	0.23 (0.04, 1.56)
Received first vaccine during pregnancy				
Any cause hospitalization				
Unvaccinated pregnant persons (n=2795)	0.50	Ref	Ref	Ref
Fully vaccinated pregnant persons vaccinated during pregnancy (n=317)	0.39	0.76 (0.40, 1.43)	0.86 (0.45, 1.63)	0.88 (0.47, 1.67)
Hospitalization for COVID-19				
Unvaccinated pregnant persons (n=2795)	0.24	Ref	Ref	Ref
Fully vaccinated pregnant persons vaccinated during pregnancy (n=317)	0.11	0.44 (0.20, 0.96)	0.47 (0.22, 1.00)	0.51 (0.23, 1.16)
Received first vaccine prior to pregnancy				
Any cause hospitalization				
Unvaccinated pregnant persons (n=2795)	0.50	Ref	Ref	Ref
Fully vaccinated pregnant persons vaccinated prior to pregnancy n=(562)	0.30	0.53 (0.25, 1.09)	0.59 (0.28, 1.23)	0.60 (0.29, 1.25)
Hospitalization for COVID-19				
Unvaccinated pregnant persons (n=2795)	0.24	Ref	Ref	Ref
Fully vaccinated pregnant persons vaccinated prior to pregnancy n=(562)	0.08	0.27 (0.09, 0.84)	0.28 (0.09, 0.87)	0.31 (0.10, 0.93)

*adjusted for age, race/ethnicity, and data partner site

**adjusted for age, race/ethnicity, modified CCI, and data partner site

Conclusion: While our analysis did not identify a statistically significant protection from COVID-19 initial vaccinations for incident infections among pregnant persons with RD, our data suggests a clear benefit associated with vaccination and prevention of severe COVID-19. While the overall rates of these severe COVID-19 outcomes were rare, the positive signal suggests pregnant persons with RD should continue to be prioritized for booster vaccinations.

Disclosure: A. Sutton: None; **C. Hilliard**: None; **Q. Qin**: None; **A. Anzalone**: None; **M. Toth**: None; **R. Patel**: Gilead, 5, Merck/MSD, 5; **N. Singh**: None.

Abstract Number: 1825

Exploring the Health and Cannabis Use Among Young and Middle-Aged Adults with Rheumatologic Conditions in Alberta, Canada

Elaine Yacyshyn, Simran Gulati, Samuel Lowe, Allyson Jones, Tarek Turk, Shelby Yamamoto, Kali Gregg, Linda Kolewaski, Joanne Olson, Pauline Paul and Cheryl Sadowski, University of Alberta, Edmonton, AB, Canada

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Interest in using cannabis for the management of pain and associated symptoms of rheumatic diseases is rapidly rising in young adults. This, in turn, has heightened the pressure on healthcare providers and scientists to provide evidence-based answers on the role of cannabis in rheumatic diseases in a timely manner. To establish a foundation for care, we aim to contextualize the demand for cannabis. In this study, we assess the health profiles and cannabis use patterns among young and middle-aged (18-45) adult rheumatology patients in Alberta, Canada.

Methods: Adults in Alberta were contacted for recruitment through Alberta Health Services, the sole provincial-level administrative health authority, if they had one or more diagnostic code for rheumatologic conditions and had at least one billing code related to health system use in the past year. Data were collected between March and November 2022 from participants using an online survey designed to capture a broad range of sociodemographic, lifetime cannabis use, and health factors. Descriptive statistics were used to explore the health and cannabis use characteristics of survey respondents. Bivariate methods were used to investigate potential differences in self-rated pain and wellbeing scores, as well as reasons for using cannabis, between cannabis use groups.

Results: Our sample included 193 respondents between the ages of 18 and 45 (mean age=36.1, SD=6.5) and consisted of largely of Caucasian (80.3%, n=155) female (60.0%, n=108) respondents. Majority of respondents had used cannabis, with 94 (48.7%) current users, 59 (38.6%) past users, and 40 (20.7%) never users. The most prevalent rheumatologic conditions reported were rheumatoid arthritis (16.6%, n=32), osteoarthritis (15.5%, n=30), and fibromyalgia (7.8%, n=15) with 27 (14.0%) respondents having reported two or more rheumatologic conditions. A 101 (52.3%) and 111 (57.5%) respondents reported experiencing mental and physical comorbidities, respectively. When comparing self-rated health profiles, the proportion of respondents with high pain scores (47.0% vs. 23.1%, p=0.007) and low wellbeing scores (55.0% vs. 27.0%) were significantly higher for cannabis users (current and past users) compared to never users. Among cannabis users (n=153), the proportion of respondents with high pain scores (53.2% vs. 36.7%, p=0.047) was significantly higher among current users versus past users, with no significant difference in low wellbeing scores between groups (58.1% vs. 50.0%, p=0.338). A higher proportion of current-cannabis users report using cannabis to address rheumatologic pain (54.3% vs. 30.5%, p=0.004) and stress (64.9% vs. 17.0%) compared to past users.

Conclusion: Young adult and middle-aged rheumatology patients experiencing high pain and poor well-being might be more likely to use cannabis, with pain and stress management being common reasons for current use. Further work is needed to determine if cannabis use relates to changes in pain and well-being over time.

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Abstract Number: 1826

Investigating the Health Profiles and the Prevalence and Correlates of Cannabis Use Among Patients Accessing Rheumatologic Care in Alberta, Canada

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Implications of using cannabis as therapeutics in a growing number of diseases coupled with increasing public awareness are leading to an increase in patient interest to use cannabis for the treatment of rheumatic conditions. Nevertheless, its legalization and widespread availability have made it difficult for providers to attain a true understanding of its current uptake and demand. Through this study, we aim to delineate the prevalence of cannabis use as well as identify the health profiles and correlates of cannabis use among patients with rheumatic disease in Alberta.

Methods: Adults in Alberta were contacted for recruitment through Alberta Health Services, the sole provincial-level administrative health authority, if they had one or more diagnostic code for rheumatologic conditions and at least one billing code related to health system use in the past year. Data were collected between March and November 2022 from participants using an online survey designed to capture a broad range of factors including sociodemographics, rheumatologic diagnoses and therapeutics, medical history and comorbidities, patterns of cannabis use, and lifestyle factors. Descriptive statistics were used to assess the prevalence and patterns of rheumatologic conditions and cannabis use among our sample. Logistic regression modelling was used to investigate the factors associated with cannabis use among respondents that had ever used cannabis.

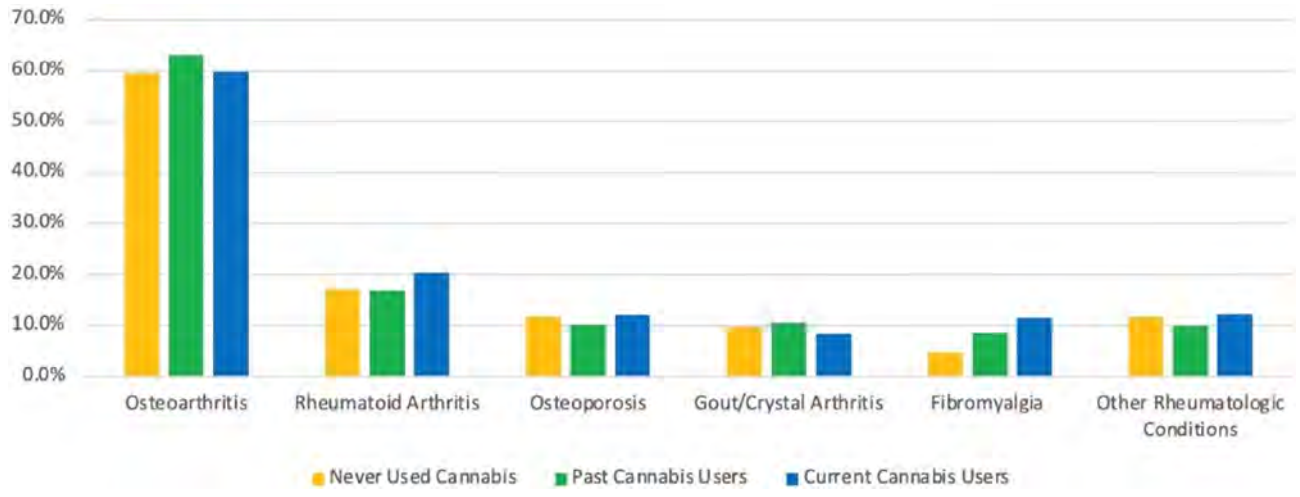

Figure 1: Distribution by percentage of current + past users of cannabis for treatment among various rheumatic conditions.

Results: Our sample of 2,932 respondents consisted largely of female (54.1%, n=1,588), Caucasian (92.5%, n=2,711), and older (mean age=66.7 years, SD=12.2 years, range=18-98 years) respondents, with 730 (24.9%) current cannabis users, 851 (29.0%) past users, and 1,351 (46.1%) never users. The most prevalent rheumatic conditions among respondents were osteoarthritis (60.6%, n=1,776), rheumatoid arthritis (17.9%, n=526), and osteoporosis (11.4%, n=335), with 614 respondents (20.9%) reporting two rheumatologic conditions and 200 respondents (6.8%) reporting three or more conditions. 535 (18.2%) and 2,334 (79.6%) respondents experienced at least one mental and physical comorbid condition, respectively. Logistic regression model estimates indicate that individuals with increased odds of using cannabis were those who were younger, male, experienced mental illness, and sleep disturbances, reported high levels of pain, lacked health insurance, were previous or current smokers, and consumed four or more alcoholic drinks per week.

Conclusion: This study highlights rheumatology patients are using cannabis and identifies factors associated with its use. Our results provide foundational context for ongoing work focused on better understanding the role of cannabis use as a therapeutic tool for rheumatology patients. Future work includes the development and implementation of a tool designed to inform the use of cannabis in managing rheumatologic conditions.

Disclosure: E. Yacyshyn: None; **S. Gulati**: None; **S. Lowe**: None; **A. Jones**: None; **T. Turk**: None; **S. Yamamoto**: None; **K. Gregg**: None; **L. Kolewaski**: None; **J. Olson**: None; **P. Paul**: None; **C. Sadowski**: None.

Abstract Number: 1827

Revolutionizing Fibromyalgia Treatment: Exploring the Efficacy of a New FDA Cleared Photoceutical Device

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Fibromyalgia syndrome effects 2-8% of the general population and is characterized by specific tender points. FM annual economic impact $12-$14 billion.Current treatments are only effective in 10% of patients.There is a need to develop alternative treatment methods. Photobiomodulation therapy (PBMT is an electrophysical agent that utilizes non-ionizing forms of light that can be used alone or associated to static magnetic field (PBMT-sMF) to promote analgesia in several health conditions. Evidence of the effects of PBMT alone and PBMT-sMF in FM patients is conflicting.We investigated the efficacy of a new PBMT-sMF device versus placebo on FM.

Methods: A randomized placebo-controlled trial, with blinded patients, therapists, and assessors was performed. 90 female (age= 46 years) patients that met ACR FM diagnostic criteria were randomized into either PBMT-sMF (n=45) or placebo (n=45) groups. Patients from both groups received 9 treatment sessions, 3 times a week, for 3 weeks. PBMT-sMF treatment consisted of 60 J per active tender point during each session, Placebo treatment was 0 J per active tender point. Clinical outcomes were collected at baseline, after the 9th treatment (PostTx) and at 4 weeks follow-up post-treatment. Outcome measures included Tender Point Count (TCP); Impact of FM on their life using Fibromyalgia Impact Questionnaire (FIQ); and Pain Intensity (PI) measured with a 0-100 Visual Analog Scale (VAS).A Fischer's Exact Test for two independent

Table 1. Mean and standard deviation (absolute values) for the outcomes of the study (n =90).

Outcomes	PBMT-sMF (n = 45)	Placebo (n = 45)
Tender Point Count (TPC)		
Baseline	15.29 (3.08)	15.20 (2.69)
End of treatment	7.29 (3.99)****	12.49 (3.92)
Follow-up	6.22 (4.25)****	10.13 (4.66)
Impact of fibromyalgia (FIQ 0-100)		
Baseline	79.68 (11.05)	77.54 (11.57)
End of treatment	43.89 (22.34)**	56.71 (18.63)
Follow-up	41.64 (25.86)*	52.61 (21.57)
Pain intensity (VAS 0-100)		
Baseline	80.64 (13.99)	74.89 (13.54)
End of treatment	37.80 (23.31)****	56.91 (20.31)
Follow-up	34.47 (26.34)**	49.58 (26.21)

Difference of placebo: ****p<0.0001; **p<0.01; *p<0.05.
PBMT-sMF, photobiomodulation therapy combined with static magnetic field.

groups was used to compare proportion of successes between groups and an Unpair T-test was used to analyze pain intensity.Patient satisfaction was measured using a Likert scale.

Results: Baseline outcomes measures were equal between groups.PBMT-sMF group reported lower TCP ((p< 0.0001), FIQ score (p< 0.01), and Pain intensity (p< 0.0001) than placebo post treatment.The lower outcomes remained at the 4-week follow-up (TCP p< 0,0001; FIQ p< 0.01; Pain Intensity (p< 0.01)).Table 1 summarizes data and significant differences.TCP decreased 52% Post Tx in PBMT-sMF group versus 18% in Placebo.Additionally, PBMT-sMF group FIQ and Pain intensity decreased 45% and 53% respectively.Placebo FIQ and Pain intensity on decreased 27% and 18% respectively.98% of PBMT-sMF group were somewhat satisfied or satisfied with their outcomes Post-treatment and 91% at the follow-up and the Placebo group were 71% and 73% at same time points.

Conclusion: PBMT-sMF is superior to placebo in decreasing TPC, improving function (decreased FIQ) and overall pain intensity.This study supports using PBMT-sMF to treat patients with fibromyalgia. PBMT-sMF might be considered an important adjuvant to the treatment of patients with fibromyalgia.

Disclosure: T. Demchak: Graston Technique LLC, 7, Multi Radiance Medical, 1, 5, 6; **E. Leal-Junior**: Multi Radiance Medical, 1, 5, 6; **N. Ribeiro**: None; **H. Casalechi**: None; **D. Johnson**: Multi Radiance Medical, 3; **S. Tomazoni**: Multi Radiance Medical, 2, 5.

Abstract Number: 1828

Positive Screening for Fibromyalgia or Depression on Validated MDHAQ Indices Is Seen in 56-71% of Rheumatoid Arthritis Patients with High DAS28 or CDAI, 40-47% with Moderate, 2-42% with Low, and 0-21% with DAS28 or CDAI Remission

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: DAS28 (disease activity score 28) and CDAI (clinical disease activity index) are prominent indices to assess patients with rheumatoid arthritis (RA) quantitatively, for which disease activity is classified into 4 categories of high, moderate, low, and remission. Both DAS28 and CDAI may be elevated by non-inflammatory comorbid fibromyalgia (FM) and depression (DEP), unrelated to disease activity.Prospective systematic comparison of the number of patients in different DAS28 and CDAI activity categories who screen positive for FM and/or DEP has not been reported. Feasible screening for FM and DEP is available using MDHAQ (multidimensional health assessment questionnaire) indices for FM FAST4 (FM assessment screening tool) and DEP MDS2 (MDHAQ depression screen), which agree more than 80% with reference standards and require a single MDHAQ completed by most patients in 5-10 minutes.

Methods: Across-sectional study at a routine care visit included collection of DAS28 and CDAI.Patients completed an MDHAQ to record global assessment (PaGA), pain, and fatigue on 0-10 visual numeric scales (VNS), a 0-3 DEP query, 0-54 self-report RADAI painful joint count, 60-symptom checklist including DEP, and medical history queries. A FAST4 FM screen is positive if 3/4 are met: pain VNS≥6/10, fatigue VNS≥6/10, RADAI ≥16/54, symptom checklist≥16/60. An MDS2 DEP screen is positive if 0-3.3 DEP response is ≥2.2 OR positive DEP on the symptom checklist. Patients were classified into 4 DAS28-ESR and CDAI activity categories: high (>5.1/28 & >22/76), moderate (3.2-5.1 & 10.1-22), low (2.6-3.2 & 2.9-10), and remission (≤2.6 & 2.8), respectively. The median swollen and tender joint counts (SJC and TJC) and proportions of FAST4 and MDS2 patients in each category were compared using chi-square analyses.

Table: Median (interquartile range interquartile range IQR) values for swollen joint count (SJC) and tender joint count (TJC) according to each of 4 “activity" categories for DAS28 and CDAI and and number of patients (percent) in each "activity” category

Table: Median (interquartile range interquartile range IQR) values for swollen joint count (SJC) and tender joint count (TJC) according to each of 4 “activity" categories for DAS28 and CDAI and and number of patients (percent) in each "activity” category

Measure (Range or units)	All Patients Median (IQR) or Number (%) pos	Remission Median IQR	Low Median IQR	Moderate Median IQR	High Median IQR
DAS28-ESR	2.9 (2.2-3.7)	<2.6	2.6-3.2	3.2-5.1	>5.1
Number of pts (%)	128	57	19	43	9
Median (IQR) values for swollen joint count (SJC) and tender joint count (TJC)					
SJC (0-28)	0 (0-2)	0 (0-1)	0 (0-1)	1 (0-4)	6 (3-11)
TJC (0-28)	2 (0-5)	0 (0-1)	2 (0-4)	5 (2-8)	14 (13-18)
Number of patients (% positive for FAST4 (FM screening tool) or MDS2 (MDHAQ depression screen)					
FAST4 (% pos FM)	36 (28%)	8 (14%)	4 (21%)	18 (42%)	6 (67%)
MDS2 (% pos DEP)	45 (35%)	12 (21%)	8 (42%)	20 (47%)	5 (56%)
CDAI	11.5 (5-18.5)	<2.8	2.9-10	10.1-22	>22
Number of pts (%)	140	17	44	55	24
Median (IQR) values for swollen joint count (SJC) and tender joint count (TJC) SJC and TJC					
SJC (0-28)	0 (0-2)	0 (0-0)	0 (0-1)	0 (0-3)	5 (1-8)
TJC (0-28)	2 (0-5)	0 (0-0)	1 (0-2)	3 (1-5)	13 (8-18)
Number of patients (% positive for FAST4 (FM screening tool) or MDS2 (MDHAQ depression screen)					
FAST4 (% pos FM)	40 (29%)	0 (0%)	1 (2%)	22 (40%)	17 (71%)
MDS2 (% pos DEP)	52 (37%)	1 (5.9%)	10 (23%)	24 (44%)	17 (71%)

Results: Among 128 patients for DAS28 and 140 for CDAI (12 were missing ESR), categories of remission, low, moderate, and high activity, respectively, included 44%, 15% 34%, and 7% by DAS28-ESR, and 13%, 31%, 39% and 16% by CDAI. Median SJC was 0, 0, 2 and 4 for patients in DAS28-ESR and 0, 0, 0 and 4 for patients in CDAI categories. Median TJC was 0, 2, 5 and 5 in 4 DAS28-ESR categories, and 0, 1, 3 and 14 in 4 CDAI categories, respectively (Table). Positive FAST4 FM screen was seen in 28-29% and MDS2 screen in 35-37% of all patients.Positive FAST4 screen was seen in 13%, 22%, 44% and 67% in 4 DAS28-ESR categories of remission, low, moderate, and high activity, respectively, and 0%, 2.6%, 38%, and 80% in the 4 CDAI categories, respectively. Positive MDS2 DEP was seen in 20%, 44%, 46% and 56% in 4 DAS28-ESR categories, and 6%, 24%, 40% and 70% in 4 CDAI categories, respectively.

Conclusion: Among RA patients classified as in high DAS28-ESR or CDAI activity, more than 50% screened positive for FM or DEP, compared to lower proportions for more favorable categories, including fewer than 21% for those in DAS28-ESR or CDAI remission.These phenomena may affect treat-to-target and other aspects of RA management. Feasible screening for FM and DEP is available according to valid MDHAQ FAST4 and MDS2 indices, as well as RAPID3 (routine assessment of patient index data), requiring only a single questionnaire which is completed by most patients in 5-10 minutes.

Disclosure: T. Pincus: None; **R. Hunter**: None; **N. Rodwell**: None.

Abstract Number: 1829

Blood-derived Extracellular Vesicles as Potential Diagnostic Biomarker in Fibromyalgia Syndrome

Gilad Halpert, Daniel Yechiali, liel Katbi, Eri Govrin, Boris Guilbord, Ori Segal and Howard AMITAL, Sheba Medical Center, Ramat Gan, Israel

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The Fibromyalgia syndrome (FMS) is a global chronic pain condition, which affects approximately 2–6% of the population. The underlying mechanism of FMS is unclear and there is no specific lab test to confirm the diagnosis of FMS. There is an unmet need regarding the development of a precise diagnostic marker for FMS. Previous studies had demonstrated that small extracellular vesicles (sEVs), are involved in: intercellular communications and in the pathogenesis of inflammatory/autoimmune diseases. Recently, an autoimmune origin had been suggested for the development of FMS. In the current study, we aimed to characterize sEVs derived from blood of FMS patients and to explore a potential change in the expression of key proteins in these vesicles as compared to healthy controls.

Methods: sEVs have been isolated from the plasma of women diagnosed with primary FMS (n=9) vs. Age matched healthy women (n=9), using size exclusion chromatography technique. Characterization of these sEVs have been conducted using nanoparticle tracking analysis, transition electron microscopy and western blot analysis. The protein profile of these sEVs have been explored using proteomics analysis.

Results: We found changes in the expression of various proteins in sEVs derived from plasma of FMS as compared to healthy controls (Figure 1), among them: immunological- (e.g. Complement component 1q), neurological- (e.g. Cofilin-1), ribosomal protein assembly- (e.g. Nucleophosmin) and oxidative stress- (e.g. Superoxide dismutase) related proteins.

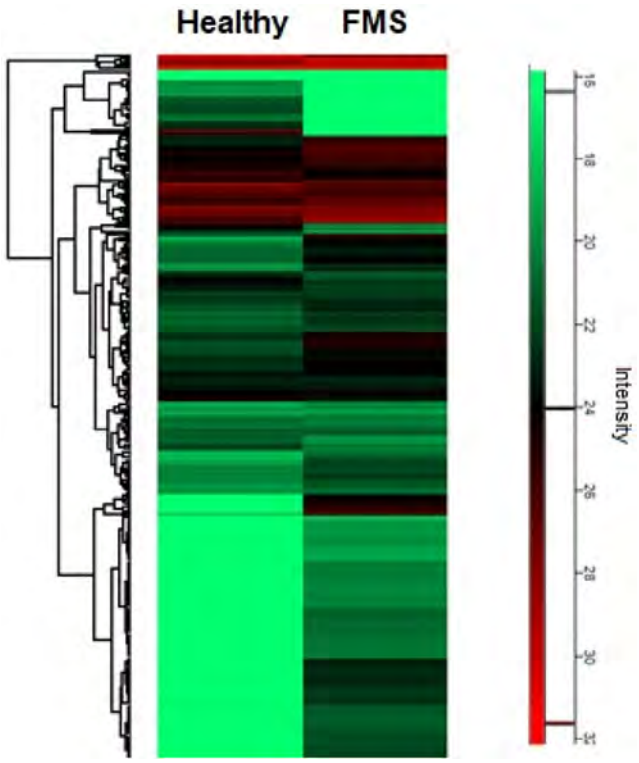

Figure 1: Heatmap visualization of protein expression profiles, in blood-derived small extracellular vesicles (sEVs) isolated from FMS patients vs. healthy controls, identified by proteomics analysis.

Conclusion: Our results potentially shed a light on the importance of sEVs in the pathophysiology of FMS and their potential to serve as a new diagnostic biomarker candidate in FMS.

Disclosure: G. Halpert: None; **D. Yechiali**: None; **I. Katbi**: None; **E. Govrin**: None; **B. Guilbord**: None; **O. Segal**: None; **H. AMITAL**: Janssen, 5.

Abstract Number: 1830

Exploring Psychosocial Characteristics of Youth with Chronic Pain Across Gender Identities

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Pediatric chronic pain is a common, significant public health concern leading to decreased quality of life for youth and burden on the healthcare system[1]. While there is research highlighting the benefit of a biopsychosocial model to treat chronic pain, there are disparities in access to evidence-based care[2]. Anecdotally, youth who identify with transgender or non-binary gender identities may not be referred to interdisciplinary pediatric chronic pain programs as often

as cis-gender youth. The current study aimed to explore baseline characteristics of youth referred to an outpatient interdisciplinary pediatric chronic pain program at an East Coast children's hospital across gender identity.

Methods: Youth completed questionnaires electronically as part of the initial evaluation within an outpatient interdisciplinary pediatric chronic pain program. From February 2020-April 2023, 335 youth completed questionnaires including the Chronic Pain Acceptance Questionnaire, PROMIS Pain Interference, and PROMIS Anxiety. Of these, 248 identified as cisgender female, 48 identified as cisgender male, 25 identified as non-binary, and 4 identified as transgender.

Results: Overall, 8.7% of the sample identified as gender diverse, which is a higher percentage as compared to national rates in the US for young adults (5.1%)[6]. Average age of the sample was 14 years old. Youth were predominately Non-Hispanic (92.7%) and White (83%). Youth who identified as transgender reported the highest pain acceptance scores. Cisgender males reported the least anxiety. Youth with non-binary gender identity reported the lowest pain acceptance, highest pain interference, and highest levels of anxiety. There were no statically significant differences in pain inference between cisgender and nonbinary youth.

Conclusion: These data represent a first look at exploring characteristics of youth and gender identity for patients entering a pediatric chronic pain program. Interestingly, youth with nonbinary gender identity did not differ in functional impairment, but appeared to experience higher levels of self-reported anxiety and lower acceptance of pain. This suggests these youth may have a decreased willingness to engage in activities in the face of pain or experience pain generally. Awareness of a patient's gender identity may be beneficial in understanding the impact of pain and highlights the need for a biopsychosocial model approach to pain management. This study was limited by relatively small numbers and does include youth already referred to a pain program. More research is needed to explore the role of gender identity as it relates to pain management, and referral patterns.

References

1. King, S., Chambers, C. T., Huguet, A., MacNevin, R. C., McGrath, P. J., Parker, L., & MacDonald, A. J. (2011). The epidemiology of chronic pain in children and adolescents revisited: a systematic review. Pain, 152(12), 2729-2738.
2. Jay, M. A., & Howard, R. F. (2016). Inequalities in access to a tertiary children's chronic pain service: a cross-sectional study. Archives of Disease in Childhood, 101(7), 657–661. doi: 10.1136/archdischild-2015-310280

Disclosure: E. Mulvihill: None; **L. Courtney**: None; **A. Rando**: None; **K. Salamon**: None.

Abstract Number: 1831

Effect of the COVID-19 Pandemic on Health Status of Fibromyalgia

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Fibromyalgia (FM) symptoms fluctuate, with exacerbation commonly associated with stressors. The COVID-19 pandemic was a cause of prolonged stress due to factors such as restricted medical care, social isolation, actual COVID infection, and changes in activity or work status. Worsening of health status in FM could be anticipated. To

Table 1: Self-reported effects of COVID pandemic on personal life, health status and changes to regular medical treatment.

Table 1: Self-reported effects of COVID pandemic on personal life, health status and changes to regular medical treatment.

		FM (32)	HC (21)	adj p value
Diagnosed with COVID (%)		34%	14%	0.165
COVID complications (%)		9%	0%	1.000
changed work status during COVID (%)		56%	43%	0.055
stopped working (%)		13%	5%	0.849
Perceived change in pain	pain worsened	53%	5%	
	pain unchanged	31%	90%	
	pain improved	16%	5%	
sadness		4±2.7	2.9±2.5	1.000
worried		4.9±3	4.1±3.2	0.094
solitude		3.6±3	2±3	0.213
anger		4±2.7	2.9±2.5	0.066
powerlessness		3.6±3	2±3	0.910
anxiety		3.8±3.1	2.5±2.9	0.018
surprise		5±3.5	3.1±3.1	1.000
relief		4.2±3.2	3.3±3.1	0.574
hope		1.9±2.2	0.6±1.1	0.254

understand the impact of the pandemic on FM patients, this survey compared health status prior to and 2 ½ years into the pandemic.

Methods: A cohort of pre-pandemic highly characterized FM patients (FM) and healthy controls (HC) completed an on-line survey in August 2022. Data included: demographic information, symptom characteristics, perception of change in health status and emotional perceptions related to the pandemic, Fibromyalgia Impact Questionnaire (FIQ), the Brief Pain Inventory (BPI), the Patient Health Questionnaire (PHQ) for anxiety and depression, the Physical Activity Self-Administered

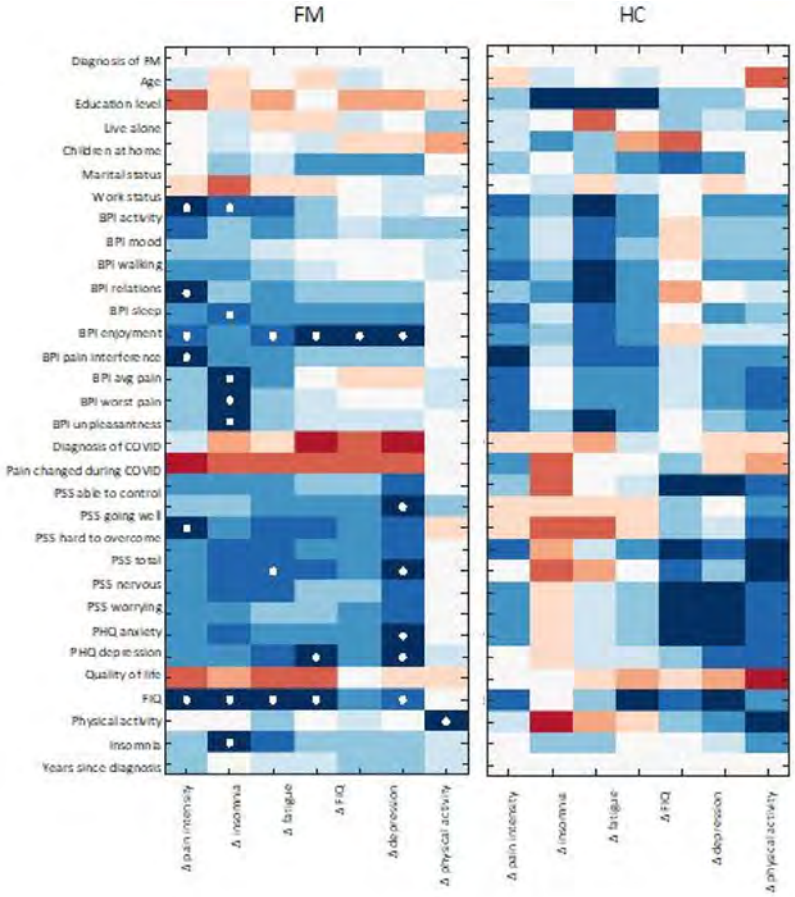
Table 2: Changes in clinical measures based on questionnaires for FM and HC in 2017 and in 2022.

Table 2: Changes in clinical measures based on questionnaires for FM and HC in 2017 and in 2022.

	FM (32)				HC (21)			
	before COVID	during COVID	change	adj p value	before COVID	during COVID	change	adj p value
pain intensity (mean±SD)	6.78±2.18	6.06±2.9	-0.72±3.19	0.455	0.52±1.08	0.95±1.91	0.43±1.83	0.693
fatigue (mean±SD)	7.66±2.13	7.22±2.66	-0.44±3.78	1.000	1.71±2.26	1.9±2.43	0.19±9.26	1.000
total FIQ score (mean±SD)	62.81±13.49	50.91±17.8	-11.91±21.78	**0.040**	7.63±9.26	25.04±11.93	17.41±6.6	**0.001**
insomnia severity index (mean±SD)	17.66±4.32	15.16±6.98	-2.5±7.97	0.100	5.88±6.6	6.05±5.57	0.17±5.84	1.000
anxiety (mean±SD)	5.97±2.46	5.03±2.96	-0.94±3.84	0.310	0.95±1.66	1.86±3	0.9±1.97	0.084
depression (mean±SD)	5.09±2.63	3.88±3.08	-1.22±4.02	0.134	0.38±0.86	1.52±2.6	1.14±2.43	0.062
physical activity score (mean±SD)	2.7±0.36	2.78±0.59	0.08±0.55	1.000	2.99±0.44	2.66±0.68	-0.33±0.6	**0.037**

Questionnaire (AQAP), the ED-5D-5L Quality of Life Questionnaire and pandemic-related emotions using the Perceived Stress Scale (PSS). Analyses included Fischer Exact test for dichotomous variables; Wilk-Shapiro test for normality of distribution for quantitative variables; ANOVA for normally distributed variables; the non-parametric Kruskal-Wallis test for non-normally distributed variables; adjustment for multiple comparisons using Benjamini-Hochberg correction; and correlation analysis using the non-parametric Kendall Tau test. Analyses were done on IBM SPSS version 28.

Results: Participants were FM (32) and HC (21), all female, predominantly white, and with significant differences in BMI (higher in FM), living alone and work status. COVID infection occurred in FM vs HC 34% vs. 14%. Emotions related to COVID were similar for both groups (**Table 1**). Treatment modifications for FM were non-pharmacological vs pharmacological by 47% vs 25% respectively. FM patients generally perceived worsening of pain, but without change on questionnaire-based measurement and greater COVID perceived anxiety, but without differences for numbers screened positive for anxiety and depression on PHQ. Quality of life was significantly improved for FM, with other questionnaires measures unchanged for



Heat map of a univariate Kendall correlation matrix based on a hierarchical clustering of clinical measure values. Blue shades indicate positive correlations while red shades indicate negative correlations (20.5,rho,0.5). Statistically significant correlations are marked by a white dot (Benjamini–Hochberg FDR corrected P , 0.05).

Legend: BPI – Brief Pain Inventory; PSS – Perceived Stress Scale; PHQ – Patient Health Questionnaire; FIQ – Fibromyalgia Impact Questionnaire.

Figure 1: Clinical measures vs. covariates for FM and HC

both groups (**Table 2**). Physical activity remained stable for FM but decreased for HC (**Table 2**). For FM, clinical measures did not correlate with demographic variables or subjective or measured change in pain, but did correlate with function, affective status and total FIQ, with no significant correlations among HC (**Figure 1**).

Conclusion: Contrary to expectations, FM status remained either stable or improved according to standard questionnaires, although there was a perception of increased pain. These observations could be explained by several putative explanations: 1) FM patients may have a resilience to prolonged compared to acute stressors; 2) Societal factors such as slower life pace related to the pandemic 3) as FM scored significantly higher than HC in all measures, changes during COVID pandemic may represent regression to the mean.

Disclosure: T. Sahar: None; **A. Minerbi**: None; **m. Verner**: None; **s. Mitrovic**: None; **y. Shir**: None; **G. Page**: None; **m. fitzcharles**: None.

Abstract Number: 1832

Prevalence of Musculoskeletal Manifestations in Post-acute COVID 19 Patients and Their Quality of Life at Kenyatta National Hospital

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Since its discovery in Wuhan, China, severe acute respiratory syndrome coronavirus 2 (*SARS CoV 2*) has ravaged the globe on an unprecedented scale. While coronavirus disease (COVID-19) was initially thought to be an *acute* disease only, protracted symptomatology led to the characterisation of post-acute COVID-19 syndrome (PACS). PACS is now recognised as a bonafide array of multi-systemic clinical manifestations 12 weeks beyond the onset of acute symptoms that is not attributable to alternative pre-covid diagnoses. The prevalence of musculoskeletal (MSK) manifestations in PACS has been demonstrated in different populations with Fibromyalgia (FM) in post-acute COVID-19 being identified as a new facet of PACS. MSK manifestations have decreased the quality of life (QoL) of patients affecting their self-care, mental health, work ethic and livelihood.

Our study set out to determine the prevalence of MSK manifestations in post-acute COVID-19 syndrome patients and their quality of life at Kenyatta National Hospital (KNH). We also set out to determine the prevalence of Fibromyalgia as a rheumatological diagnosis of interest in PACS.

Methods: A descriptive cross-sectional study conducted at KNH, a tertiary (Level 6) regional referral hospital in Nairobi, Kenya. We recruited 101 patients, randomly sampled from the inpatient COVID-19 database. Following screening for eligibility, contact via phone was established and patients who consented verbally were scheduled for physical participation where written consent was taken. A chart review was done prior to the PI-participant physical encounter. Study tools were filled by participants and a musculoskeletal examination was conducted by the Principal Investigator (PI). MSK manifestations were recorded accordingly. Diagnosis of Fibromyalgia was done using the American College of Rheumatology (ACR) criteria and assessment of QoL was done using the 36-item short form (SF 36) questionnaire.

Results: The prevalence of MSK manifestations in PACS was 57.4% (95% CI 47.5% - 66.3%), the most common being fatigue (65.5%), arthralgia (58.6%) and myalgia (53.4%). The prevalence of Fibromyalgia was documented at 10.9% (95% CI 5.9% - 17.8%). Patients with MSK manifestations were 6.8 times more likely to have poor QoL than those without MSK manifestations. All the 8 domains of the SF 36 were adversely impaired among PACS patients with MSK manifestations; physical health (mean score 5.3+/-4.5 SD) and emotional wellness (mean score 10.4+/-5.8 SD) being the most affected categories. PACS patients with MSK manifestations were more likely to be female, who had a high BMI and long duration of hospital stay where they were treated with steroids in the acute phase of COVID-19. Smokers were also more likely to develop MSK manifestations. We did not elicit presence of comorbidity, older age and positive vaccination status as independent associated factors.

Conclusion: MSK manifestations in PACS are significant clinical features affecting 57.4% of COVID-19 survivors, who are about 7 times more likely to have poor QoL, adversely influencing their productivity for work and livelihood.

Disclosure: M. Kiyiapi: None; **O. Oyoo**: Pfizer, 5; **P. Oyiro**: None; **F. Wangai**: None.

Abstract Number: 1833

Development of a Polygenic Risk Model for Therapeutic Response to Bedtime Sublingual Cyclobenzaprine (TNX-102 SL*) in Fibromyalgia Based on Polygenic Single Nucleotide Polymorphism (SNP)-Count Scores

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
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Session Type: Poster Session C
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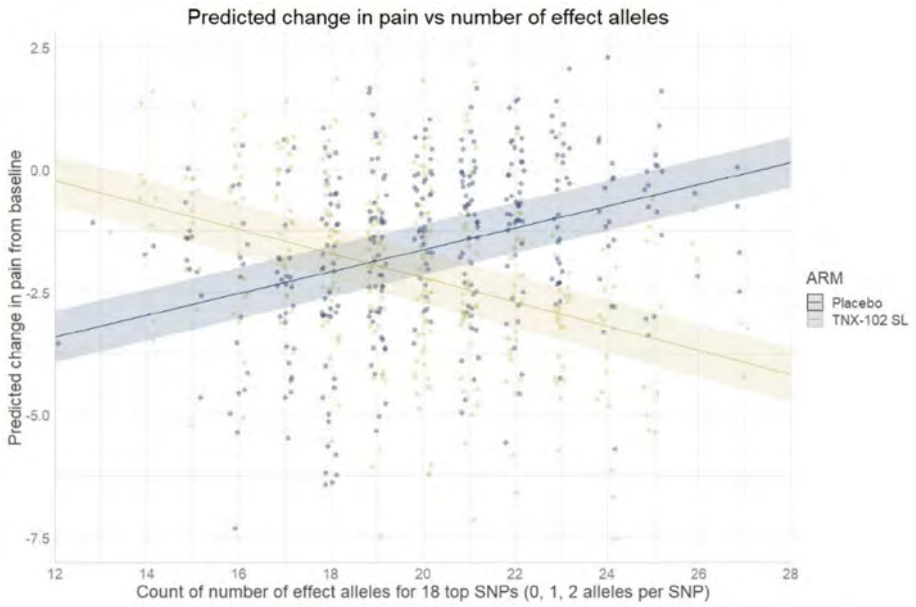
Background/Purpose: Fibromyalgia (FM) is characterized by widespread pain, non-restorative sleep, fatigue, and cognitive dysfunction. TNX-102 SL is a sublingual cyclobenzaprine tablet designed for daily use at bedtime. SNPs from participants in two Phase 3 trials were analyzed by an iterative genome-wide association study (GWAS) method to build a set of drug-response-related alleles that correlate with improvements in pain and sleep.

Methods: Whole exome sequencing (WES) was performed on peripheral blood from participants in two Phase 3 trials of TNX-102 SL 5.6 mg in FM. Markers were identified using a multi-loci mixed model (MLMM) extended to include a genome x treatment arm (G×T) term. A GWAS was run to test for each marker. First, a model was made using only the top marker. The GWAS was then repeated using the first marker as a co-variate to find the next top marker for the model. This procedure was iterated until an optimal model was constructed and a panel of best-performing loci was identified. A scoring system was developed that counted the number of favorable alleles (0-36) present in each patient. We examined the correlation of this count score with drug response on pain and sleep across both studies.

Results: In analyzing treatment responses in two Phase 3 FM studies, we identified 18 loci of interest. All of the markers in the final model had p-values $< e^{-4}$ which are individually of interest, but not genome-wide significant. However, when used together to generate a count score, substantially improved predictive power was observed. Sub-setting patients based on the count score resulted in increased effect sizes for the change in pain score and sleep score when comparing TNX-102 SL to placebo



The predicted change in pain for individuals across the 2 clinical trials as based on the number of positive drug response alleles

in each study separately. As the count scores increase, the effect size improves while the sample size decreases. For example, if patients with at least a count score of 20 are retrospectively grouped, the effect size for pain reduction in the group increases to 0.90, as compared to 0.26 in the unselected population. Of note, all of the drug-response-related SNPs were intronic.

Conclusion: Polygenic drug-response related SNP-counts have potential to identify patients with higher effect size on pain reduction from TNX-102 SL treatment compared to placebo, as first explored in a retrospective analysis of two Phase 3 FM studies. The use of this polygenic SNP-counting method has the potential to identify patients in future studies that are likely to benefit from TNX-102 SL treatment. The Whole Genome Sequencing of study participants has been completed and may reveal additional drug-response-related SNPs. The panel will be validated on a future trial of similar design.

Disclosure: J. Rosenfeld: Tonix Pharmaceuticals, 3; **G. Linse**: None; **S. Slipher**: None; **C. Flint**: Tonix Pharmaceuticals, 3; **A. Iserson**: Tonix Pharmaceuticals, 3; **H. Harris**: Tonix Pharmaceuticals, 3; **J. Engels**: Tonix Pharmaceuticals, 3; **G. Sullivan**: Tonix Pharmaceuticals, 3; **S. Lederman**: Tonix Pharmaceuticals, 3.

Abstract Number: 1834

Evaluation of Fibromyalgia, Clinical/Serologic Activity, and Patient Reported Outcomes in a Racially/Ethnically Diverse SLE Patient Cohort

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Session Time: 9:00AM–11:00AM

Background/Purpose: SLE patients have a higher prevalence of fibromyalgia (FM) than the general population. FM symptoms, such as nociplastic pain and fatigue, are known to cause discordance in how patients and physicians view well-controlled SLE, and these variables impact quality of life in ways not captured by traditional disease activity scores. There is a paucity of objective data surrounding the clinical interplay of these two diseases. Given this, and emerging evidence suggesting the contribution of autoimmunity to FM, this study evaluated FM clinically, serologically, and via patient reported outcomes in a multi-racial/ethnic SLE patient cohort.

Methods: Patients from an established lupus cohort were screened for FM using the 2016 FM classification criteria during an in-person rheumatologist visit. Hybrid SELENA-SLEDAI scores, SLE classification criteria, medications, and SLICC damage index were evaluated. A portion of the patients who reported any chronic pain also completed 8 PROMIS measures. Clinical and serologic activity was compared in patients with and without FM, as well as T-score means of PROMIS measures between FM and non-FM chronic pain patients. For T-score means significantly different between groups, linear regression models adjusting for age, race/ethnicity, SELENA-SLEDAI score, and steroid use were estimated.

Results: Of 316 SLE patients completing the FM questionnaire, 55 (17%) met criteria for FM, 57 (18%) reported chronic pain without FM, and 204 (65%) had no chronic pain. The racial/ethnic composition of the FM patients was 35% White, 27% Black, 6% Asian, and 31% Hispanic, which differed from those without FM (p=0.023), primarily due to a smaller proportion of Asian patients with FM. There was no significant difference in overall SELENA-SLEDAI score. However, there was more active arthritis in the FM group versus the non-FM group (Table 1). The widespread pain index (WPI) and symptom severity score (SSS) were not correlated with current degree of SLE activity in FM or in non-FM chronic pain patients (Figure 1). Of the SLE criteria, FM patients were less likely to have ever had lupus nephritis and more likely to have malar rash. The SLICC damage index did not differ between groups. Of the 112 patients with chronic pain (plus/minus FM), 70 completed at least one

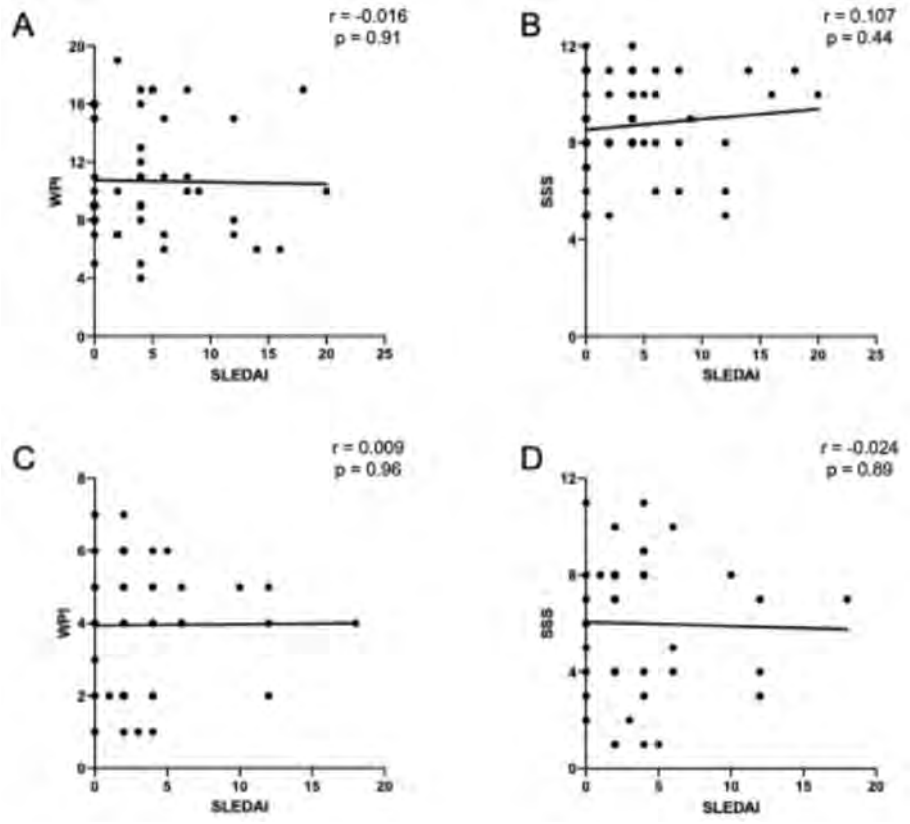

Figure 1. WPI and SSS do not correlate with SLEDAI in FM or non-FM chronic pain patients. A–B show the correlation between WPI (A) or SSS (B) and SLEDAI in FM patients and C–D show the correlation between WPI (C) or SSS (D) and SLEDAI in non-FM chronic pain patients.

PROMIS measure. Fatigue, sleep disturbance, and cognitive function were significantly worse in FM patients, whereas pain measures, depression, anxiety, and physical function did not differ between groups (Table 2). After adjusting for age, race (White/non-Hispanic), SELENA-SLEDAI score, and current steroid use, FM was associated with a 5-point increase in mean sleep disturbance and fatigue scores. Cognitive function, however, was no longer significantly associated with FM.

Table 1. Clinical and serologic profiling of SLE patients with FM compared to those without FM, n=316. Demographics, current SLE manifestations via SELENA-SLEDAI, SLE classification criteria and associated antibodies, and SLICC damage index are all shown. *N is specified where it differs from overall sample size.

	Non-FM n=261 n (%)	FM n=55 n (%)	P-value
Demographics			
Age (years), mean (SD)	41.7 (13.3)	40.5 (13.1)	0.531
SLE disease duration (years), mean (SD)	13.6 (10.4)	12.1 (7.9)	0.324
Female	176 (67.3)	53 (96.4)	
Male	31 (11.9)	2 (3.6)	0.068
Race			0.023
Asian	45 (17.2)	3 (5.5)	
Black	89 (34.1)	15 (27.3)	
White	79 (30.3)	19 (34.5)	
Other/Unknown	48 (18.4)	18 (32.7)	
Ethnicity			
Non-Hispanic	185 (70.8)	37 (67.3)	0.301
Hispanic	59 (22.6)	17 (30.9)	
Not specified	17 (6.5)	1 (1.8)	
Current SLE manifestations by SELENA-SLEDAI			
Rash	7 (2.7) n=259	4 (7.4) n=54	0.102
Alopecia	9 (3.4)	5 (9.1)	0.076
Arthritis	5 (1.9)	9 (16.4)	<0.001
Proteinuria	49 (19.6) n=250	8 (15.1) n=53	0.583
Pyuria	25 (10.0) n=250	4 (7.5) n=53	0.798
Hematuria	19 (7.6) n=250	4 (7.5) n=53	1
Leukopenia	13 (5.2) n=248	3 (5.5)	1
Thrombocytopenia	7 (2.8) n=248	1 (1.8)	1
Low complement	111 (44.4) n=250	23 (42.6) n=54	0.88
Increased dsDNA binding	135 (54.7) n=247	30 (55.6) n=54	1
SLE classification criteria and antibodies			
Malar Rash	87 (34.3) n=254	27 (50.9) n=53	0.026
Discoid Rash	41 (16.0) n=257	11 (20.0)	0.433
Photosensitivity	71 (27.6) n=257	22 (40.0)	0.075
Ulcers	45 (17.4) n=259	14 (25.5)	0.184
Serositis	77 (29.8) n=258	22 (41.5) n=53	0.107
Renal	142 (55.5) n=256	20 (36.4)	0.011
Neurologic	12 (4.7) n=256	5 (9.3) n=54	0.19
Anemia	25 (9.6)	3 (5.5)	0.439
Leukopenia	126 (49)	19 (35)	0.054
Lymphopenia	130 (50)	22 (41) n=54	0.235
Thrombocytopenia	56 (22)	7 (13)	0.193
Arthritis	174 (67)	44 (80)	0.055
Increased dsDNA binding	220 (84)	40 (73)	0.052
Low complement	188 (72)	33 (60)	0.105
Anti-Smith antibodies	115 (44)	21 (38)	0.457
Lupus Anticoagulant	49 (19)	10 (18)	1
Anticardiolipin antibodies	42 (16)	7 (13)	0.682
Anti-Beta-2 glycoprotein 1 antibodies	49 (19)	12 (22)	0.578
Anti-Ro antibodies	112 (43)	25 (46)	0.766
Anti-La antibodies	35 (13)	8 (15)	0.820
Anti-RNP antibodies	103 (40)	23 (43)	0.763
SLICC Damage Index			
Damage Index Score, median [IQR]	1 [0, 2]	1 [0,2]	0.753

Table 2. PROMIS measures assessed between groups, with "worse" quality of life represented by higher scores for symptoms and lower scores for function. PROMIS T score mean for the general United States population=50 (SD=10). Minimally important difference=2–3 for PROMIS measures in patients with lupus. Non-FM chronic pain patients had n=35 in the top 4 measures of the table and n=33 for the remaining 4 measures.

PROMIS Measure	FM (mean (SD)), n=35	Non-FM chronic pain (mean (SD)), n=35	p-value
Fatigue	67 (6.7)	61 (8.9)	0.006
Sleep disturbance 8b	62 (6.8)	57 (9.1)	0.01
Physical function	39 (5.6)	41 (6.1)	0.144
Pain intensity 3a	62 (7.1)	60 (6.0)	0.095
Pain Interference	63 (5.5)	61 (5.9)	0.054
Cognitive function abilities subset	41 (7.0)	46 (7.7)	0.005
Anxiety	62 (5.2)	61 (8.3)	0.911
Depression	58 (7.3)	55 (7.6)	0.162

Conclusion: These findings underscore that symptoms associated with FM in SLE patients can be independent of chronic pain, SLE disease activity and damage, and overall suggests the need for better understanding of the biology of this group.

Disclosure: K. Corbitt: None; **P. Carlucci**: None; **B. Cohen**: None; **M. Masson**: None; **H. Belmont**: Alexion, 6, Aurinia, 6; **A. Saxena**: AbbVie, 1, AstraZeneca, 1, GSK, 1; **C. Tseng**: None; **J. Wang**: None; **K. Barbour**: None; **J. Buyon**: Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, Related Sciences, 1; **P. Izmirly**: None; **H. Gold**: None.

Abstract Number: 1835

A Survey on Fibromyalgia-Related Knowledge Among Internal Medicine Residents

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Fibromyalgia is a chronic pain syndrome that commonly presents with fatigue, widespread musculoskeletal pain, and sleep disturbances. Patients can also have accompanying somatic and cognitive symptoms. According to National Fibromyalgia Association (NFA) it is estimated to affect around 10 million people every year in the U.S. It is more common in women (75-90%) but it can be seen in men and children as well. Fibromyalgia is usually under-recognized and the patients initially present to their primary care physicians when they start to develop symptoms. We did a cross-sectional survey to assess the knowledge of fibromyalgia diagnosis and management among Internal Medicine residents so that gaps can be identified, and intervention should be done through educational programs.

Methods: A 19-item questionnaire was prepared using current ACR and EULAR guidelines. A cross-sectional survey was conducted among residents from two residency programs in Chicago and Florida. The questionnaire included around 11 questions regarding the pathogenesis, diagnosis, and management of fibromyalgia. Other questions were mainly

focused on how comfortable the residents are with diagnosing and managing fibromyalgia patients and the educational training they have received so far. Residents with 70% or more correct answers were considered to have good knowledge. The correct answers were compared to the number of teaching sessions and if the residents are familiar with recent guidelines.

Results: A total of 64 (64%) residents out of 100 completed the survey, only 34% (22) got a score of 70% or more and 41% scored 50% or less. Only 15% of the responders felt that they were adequately taught on the subject. Less than 30% of the responders felt comfortable diagnosing and managing fibromyalgia and only 18.8% of the residents have read the guidelines regarding it. Around 53% of the residents reported that they have not attended any teaching sessions on fibromyalgia. It was also found on the survey that less than 15% of the residents are familiar with FDA-approved medications for the treatment of fibromyalgia and the recent advances in the subject. About 50% of the residents who read the guidelines scored 70% or more as compared to around 30% of the residents who did not indicating that many residents need to familiarize themselves with the recent guidelines which can aid in the appropriate management of fibromyalgia. Another interesting finding in the results was that around 38% of PGY-1 residents got 70% of the questions right compared to 14.3% of PGY-2 residents and 42% of PGY-3 residents.

Conclusion: Our survey results suggest that there is a lack of knowledge among residents regarding the diagnosis and management of fibromyalgia. Therefore, teaching sessions aiming at these knowledge gaps can help in early recognition and better initial management of these patients.

Disclosure: S. Afridi: None; **A. Raja**: None; **M. Daniyal**: None.

Abstract Number: 1836

Embracing a Biopsychosocial Approach to Fibromyalgia-like Symptoms in People with SLE: Insights from the Type 2 SLE Consortium

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Background/Purpose: Patients with SLE experience distressing fibromyalgia-like symptoms of fatigue, widespread pain, mood disturbance, and brain fog that negatively impact quality of life and are challenging to manage. These symptoms, termed Type 2 SLE, can be related to inflammatory and non-inflammatory etiologies. Studies of fibromyalgia suggest that addressing biopsychosocial factors can improve quality of life. A Type 2 SLE Consortium was created to bring together a multidisciplinary team of patients and clinicians to develop equitable, feasible, and potentially effective approaches to care for people living with Type 2 SLE.

Methods: The Type 2 SLE Consortium included patients meeting ACR/SLICC SLE classification criteria and clinicians who treat chronic pain, insomnia, and mood disorders. The consortium met in 3 group sessions; additionally, each consortium member was invited to complete an individual interview. The sessions were conducted virtually between August 2022-April 2023 and auto-recorded and then transcribed.

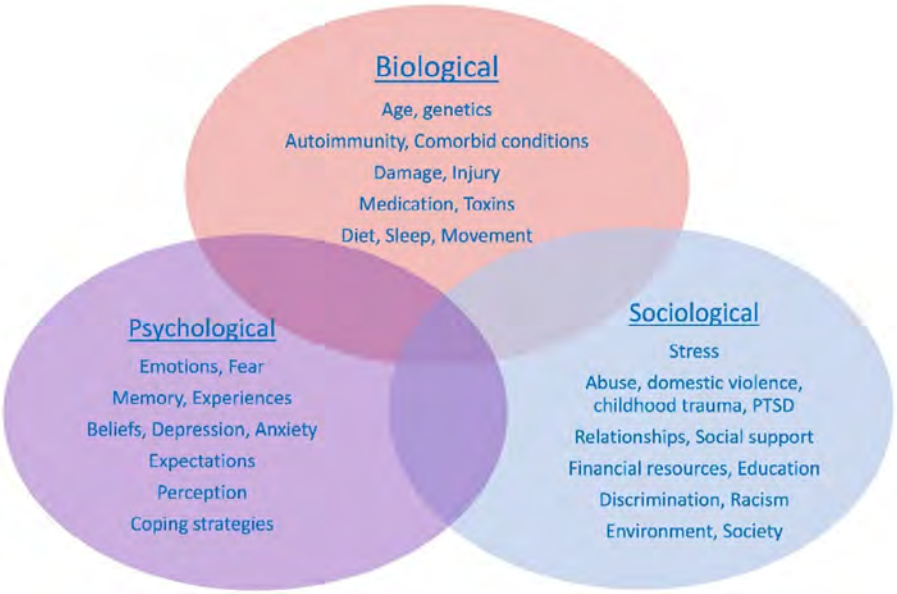

Figure 1. Biopsychosocial factors that contribute to fibromyalgia-like symptoms in SLE

Early sessions included a review of the Type 1 & 2 SLE Model, followed by suggestions from Consortium members about the possible etiology, contributing factors, and treatment approaches for fibromyalgia-like symptoms in people with SLE. Rapid qualitative evaluation identified key themes.

Table 2. Care delivery and treatment recommendations for clinicians and patients

Recommendations for clinicians	Recommendations for patients

• Meet the patient where they are
• Use motivational interviewing
• Build trust
  • "I'm here to work with you."
  • "How do we get you from here to a better place?"
• Be yourself, authentic, use humor
• Identify barriers and needs
• Set collaborative goals
• Explain symptoms and incorporate educational resources
• Set expectations
• Treat underlying mood disorders
• Refer to allied health professionals
• Minimize narcotics, benzodiazepines and sleep medications
• Explore alternative therapies and novel interventions
	• Reframe the relationship and emotions surrounding pain
	• Acceptance of situation
	• Manage expectations
	• Create personal goals
	• Pacing: adjust schedule and set limitations
	• Build self-efficacy → engage in healing
	• Practice mindfulness, distraction, relaxion techniques
	• Increase movement and exercise
	• Improve sleep hygiene
	• Use heating pads, soaks, topicals, massage
	• Plan for flares
	• Peer and social support
	• Have hope

Results: The Type 2 SLE Consortium included 2 women with SLE (both Black with SLE duration >15 years) and 18 health professionals (67% female, 89% academic). Expertise was gathered from adult and pediatric rheumatology, integrative medicine, neurology, psychiatry, psychology, palliative care, neuropsychology, medical weight management, sleep, pain, and stress management. The majority (83%) attended at least 1 group meeting and all but 1 member completed the individual session.

The Consortium identified a range of biopsychosocial factors that can predispose, precipitate, and perpetuate Type 2 symptoms such as fear, stress, and trauma (Figure 1).Two main categories of approaches to care were identified: one for providers and the other for patients (Table 2). Key themes consisted of building better therapeutic relationships, adjusting expectations, improving symptom understanding, lifestyle interventions, and multidisciplinary collaboration. Specific guidance for clinicians included active listening, validating symptoms, and using motivational interviewing. Patients with SLE would benefit from setting personal goals, building self-efficacy, pacing, identifying personal factors, and reframing their relationship with symptoms.

Conclusion: Key recommendations from this multi-disciplinary consortium were to individualize treatment based on the biopsychosocial underpinnings driving the symptom burden. The importance of communication, trust, education, and multidisciplinary collaboration was emphasized. Rheumatologists cannot be the sole providers to improve Type 2 SLE symptoms but can encourage patients to partner with others who can provide the necessary care. Our future studies will continue to develop and evaluate holistic approaches to SLE care.

Disclosure: J. Rogers: Amgen, 2, Ampel Biosolutions, 1, AstraZeneca, 6, Aurinia, 1, Eli Lilly, 1, Exagen, 5, GlaxoSmithKlein(GSK), 2, Immunovant, 2, 5; **M. Clowse**: Exagen, 5, GlaxoSmithKlein(GSK), 2, 5, Immunovant, 5, UCB, 2, 5; **A. Eudy**: Amgen, 2, Exagen, 5, GlaxoSmithKlein(GSK), 5, Immunovant, 5, Pfizer, 5.

Abstract Number: 1837

Depression and Suicide Attempt in Systemic Lupus Erythematosus with and Without Fibromyalgia

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
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Background/Purpose: Suicide and depression represent a high burden of morbidity and mortality worldwide. It is well known that fibromyalgia (FM) is associated with mood and behavioral disorders. FM is extremely common in patients with systemic lupus erythematosus (SLE) even though FM does not correlate with SLE activity. We investigate the rate of concomitant depressive disorder and suicide attempts in patients with SLE.

Methods: TrinetX, a global federated research network that provides a dataset of electronic medical records from different healthcare organizations (HCOs) was utilized. Initial query was made on June 6, 2023 from 1/1/2010 to 6/6/2023 to identify patients aged >18 with a diagnosis of "Systemic Lupus Erythematosus" (International Classification of Diseases, 10th version (ICD-10) Code M32). Two cohorts were made, on the basis of the presence of a diagnosis of "Fibromyalgia" (ICD-10

Table 1. Major Depressive Disorder and Suicide Attempts in Patients with SLE with and without FM

	FM	No FM	OR (95% CI)
	N=53,221	N=53,221	P Value
Major Depressive Disorder	5.864	2.255	2.799 (2.662-2.943)
			p<0.0001
Suicide Attempt	625	238	2.645 (2.277-3.073)
			p<0.0001

Abbreviations: CI, confidence interval; FM, Fibromyalgia; OR, odds ratio.

Code M79.7). Propensity score matching was carried out to match age, race , and gender. Compare outcome analytic function was utilized to map the correlation with "Suicide attempt" (ICD 10 Code T14.91) and "Major Depressive Disorder (MDD)" (ICD 10 Code F33), and prevalence Odds ratios (OR) were calculate

Results: We identified cohort 1 as patients with concomitant diagnoses of SLE and FM with a total of 55,350 patients. Cohort 2 as SLE patients without FM included 219,914 patients. Using propensity score matching, patients with SLE but without FM were matched 1:1 to 53,221 patients with both SLE and FM. Data demonstrated mean age of 55.6 years (SD 14.6). Percentage of females in cohort 1 was 93.978% and 93.969% in cohort 2 with the white race being the most prevalent followed by unknown ethnicity, African-American and Asian. A total of 5,864 patients with SLE and FM also had a diagnosis of "Major Depressive Disorder" (ICD 10 Code F33), compared to 2,255 patients without FM, with a 6.781% risk difference (95% CI - 6.465%-7.097%, $p < 0.0001$), and Odds ratio of 2.799 (2.662-2.943, $p< 0.0001$). In addition, 625 patients with SLE and FM also had a diagnosis of "Suicide Attempt" (ICD 10 Code T14.91), compared to 238 patients without FM, with 0.727% risk difference (95% CI - (0.619%,0.835%), $p < 0.0001$), and Odds ratio of 2.645 (2.277-3.073, $p< 0.0001$), see table 1. Similar results were identified before propensity score matching, with OR of concomitant MDD in patients with SLE and FM compared to the cohort without FM being 3.146 (3.037-3.258, $p< 0.0001$) and OR of Suicide Attempt being 2.653 (2.396-2.938, $p < 0.0001$.

Conclusion: In this real-world, real-time study, patients with SLE and concomitant fibromyalgia have increased risk of major depressive disorder and suicide attempt when compared with SLE patients without fibromyalgia.

Disclosure: I. Tskhakaia: None; **P. Khandwala**: None; **I. Tan**: None.

Abstract Number: 1838

The Burden of Dysautonomia in Patients Suffering from Pathologies Associated with Generalized Joint Hypermobility

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Background/Purpose: Hypermobility spectrum disorders (HSD) and hypermobile Ehlers Danlos syndrome (hEDS) are among the conditions associated with generalized joint hypermobility (GJH). Alongside myofascial and skeletal pain manifestations, other polymorphic co-morbid manifestations, often multiple, are linked to an autonomic dysregulation syndrome. The aim of this study was to characterize the impact of dysautonomia in patients suffering from joint hypermobility syndrome (HSD/hEDS).

Methods: Incident patients were recruited from consultations at the Center of Competence for Rare Diseases of Non-Vascular EDS. Inclusion criteria were GJH and clinical criteria for hEDS or HSD. Scores on the following questionnaires were collected : SCOPA-AUT (dysautonomia), Nijmegen (hyperventilation), HAD (anxiety, depression), Tampa (kinesiophobia), PSQI (sleep), Gastro-Intestinal Quality of Life Index (GIQLI), Pichot (fatigue), VAS physical pain and VAS psychological pain, VAS quality of life. A comparison of the 2 hEDS and HSD groups was carried out, followed by a principal component analysis (PCA). The search of homogeneous groups of patients was carried out using hierachical cluster analysis.

Results: 36 patients were included (18 hEDS, 18 HSD) with a significantly higher level of anxiety-depression in the hEDS group (25.33 vs 18.39, $p = 0.017$). The Nijmegen score was higher in the hEDS group (46.91 vs 38.94, $p = 0.016$). The mean SCOPA-AUT score was 37.08 ± 9.86 and did not differ significantly between the 2 groups; there was no statistically significant difference between the 2 groups for the other parameters studied. The level of dysautonomia was correlated with younger age, high Nijmegen score, kinesiophobia, fatigue, sleep disturbance, marked anxiety-depressive syndrome and poor GI QoL. PCA revealed a strong correlation between the level of dysautonomia and GI QoL. Two homogeneous groups of patients were identified : one of which ($n = 23$) was characterized by very high impairment of GI QoL and a high level of dysautonomia.

Conclusion: Our study illustrates the importance of dysautonomia as a major comorbidity in HSD/hEDS. Dysfunctional breathing seems almost constant, and dysautonomia is associated with a major impairment of GI QoL. An anxiety or depressive disorder is very common in these situations, and supports the recently put forward hypothesis of a neuroconnective phenotype. The polyvagal theory provides important physiological clues for understanding these pathologies and for their therapeutic management.

Disclosure: A. Perrein: None; **F. Pontille**: None; **P. Decker**: None; **d. Attali**: None; **T. Moulinet**: None; **R. Jaussaud**: None.

Abstract Number: 1839

Value of Small Fiber Neuropathy in Fibromyalgia Patients in a Rheumatological Setting

Styliani Tsiami[1], Elena Enax-Krumova[2], Dietrich Sturm[3], Matthias Vorgerd[2], Bjoern Buehring[4], Juergen Braun[5] and **Xenofon Baraliakos**[1], [1]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [2]Neurologische Klinik Universitätsklinikum Bergmannsheil Bochum, Ruhr-University Bochum, Bochum, Germany, [3]Agaplesion Bethesda - Krankenhaus, Wuppertal, Klinik für Neurologie, Wuppertal, Germany, [4]Krankenhaus St. Josef, Wuppertal, Klinik für Internistische Rheumatologie, Wuppertal, Germany, [5]Ruhr-Universität Bochum and Rheumazentrum Ruhrgebiet, Herne, Germany

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Small fiber neuropathy (SFN), a polyneuropathy (PNP) affecting A-delta and C-fibers has been described in patients with fibromyalgia (FM). Different patterns of small fiber damage may characterize distinct subtypes of FM. We aimed to investigate the value of detecting different degrees of SFN in patients diagnosed with FM.

Methods: Consecutive patients who were treated for pain exacerbation of FM at a university specialized tertiary center were included in the study after informed consent. Patients had to fulfil the 2016 ACR diagnostic criteria for FM and other inflammatory rheumatic musculoskeletal diseases (RMD) were excluded. The rheumatological therapy included pain pharmacotherapy, balneophysical treatment, physiotherapy and occupational therapy. All patients underwent a careful rheumatologic and neurologic physical clinical examination including a Schirmer-Test for dry eyes and were asked to fill out questionnaires, in which data on pain, depression, neuropathic symptoms, sleep quality, daytime sleepiness, fatigue, and quality of life were assessed. Thereafter small fiber tests were performed in the neurologic department including a skin punch biopsy on the upper and lower leg and a corneal confocal microscopy (CCM).

Results: Overall, 93 patients (86 females, 92.5%, mean age 54±10.1, mean disease duration 4.9±5.3 years) were included, 25 received anticonvulsants (26.9%) and 15 opioids (16.1%) for pain treatment. Intraepidermal nerve fiber density (IENFD) as detected by skin biopsy was reduced in 58 patients (62.4%), 43 of whom (74.1%) had reduced IENFD at both proximal and distal sites. CCM showed pathologic findings in 18 patients with reduced IENFD at any site (31%) and in 8 with normal IENFD (22.9%), with dry eyes being present in 13 (22.4%) and 6 (17.1%) of those patients, respectively. There was no difference in pain, depression, neuropathic symptoms, sleep quality, daytime sleepiness, fatigue, or quality of life scores between groups (Table).

Conclusion: In this FM population with high disease burden and indication for inpatient therapy, small fiber pathology as found by skin biopsies and CCM was present in more than two third of the FM patients suggesting that there are subgroups. However, there were no significant clinical differences between patients with and without SFN. Further analysis should explore, whether both subgroups differ in their long-term outcome after the inpatient treatment.

Table 1	normal IENFD	reduced IENFD at different biopsy sites	p-value	distally reduced IENFD	p-value	proximally reduced IENFD	p-value	generalized reduced IENFD	p-value
numerical pain scale	7.6±1.5	7.6±1.3	0.912	7.8±0.9	0.714	8.4±1.2	0.198	7.4±1.3	0.507
Fibromyalgia Impact Questionnaire (FIQ)	73.4±13.1	70.1±11.1	0.192	69.1±15.5	0.578	74.2±10.5	0.925	70.5±10.6	0.129
Widespread pain Index (WPI)*	94.3%	100%	0.067	100%	0.522	100%	0.494	100%	0.115
Neuropathic Pain Symptom Inventory	0.2±0.1	0.2±0.1	0.079	0.2±0.1	0.478	0.2±0.1	0.435	0.2±0.1	0.078
Ocular Surface Disease Index**	37.1%	27.6%	0.440	28.6%	0.548	32.5%	0.682	27.9%	0.504
Pittsburgh Sleep Quality Index	13.7±3.3	13.5±3.4	0.914	15.3±2.7	0.275	13.5±3.2	0.937	13.3±3.6	0.628

*criteria fulfilled. **normal

Disclosure: S. Tsiami: None; **E. Enax-Krumova**: None; **D. Sturm**: None; **M. Vorgerd**: None; **B. Buehring**: None; **J. Braun**: None; **X. Baraliakos**: AbbVie, 2, 6, BMS, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, 6, UCB, 2, 6.

Abstract Number: 1840

Value of Various Intra-Articular Injections for Knee Osteoarthritis Management

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Health Services Research Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Intra-articular injections (IAI) are commonly used to relieve pain and delay total knee replacement (TKR) in persons with knee OA. Despite higher costs and conflicting evidence of efficacy, utilization of hyaluronic acid (HA) and platelet rich plasma (PRP) IAIs have increased dramatically over the last decade.

Methods: We used the Osteoarthritis Policy (OAPol) Model, a widely published and validated microsimulation of knee OA, to assess the value of alternative IAIs. We considered 5 strategies: 1) no IAI, 2) saline (placebo), 3) corticosteroid (CS), 4) HA, and 5) PRP. We assumed that IAIs are offered to patients with inadequate pain control from NSAIDs. In the model, if and when IAIs do not provide adequate pain relief, OA care progresses to opioids and/or TKR. We used a random-effects meta-analysis to estimate IAI-specific pain reduction from high-quality (Jadad score 4+) RCTs. We analyzed data from 11 RCTs for saline, 12 for CS, 24 for HA, and 8 for PRP. We estimated pain reductions for one IAI series of -14 points for saline at 3 months, -22 for CS at 3 months, -22 for HA at 6 months, and -17 for PRP at 12 months. The cost of IAIs included the visit, IAI administration and medication costs. We derived the cost of CS ($315), HA ($795), and saline ($309) IAI from the Medicare Drug Fee Schedule and estimated the cost of PRP ($2586) from literature. In the base case analysis, based on the literature, we assumed that repeat CS injections increase the risk of OA progression (HR=3.02). We ran the model over the remaining lifetime of a cohort with average age 50 years at the start of simulation, pain 51 (WOMAC, 0-100, 100 worst), 50% KL3/50% KL2. We determined the value of specific IAIs using incremental cost-effectiveness ratios (ICERs), evaluated from the health care perspective and calculated as the ratio of the difference in lifetime costs to the difference in quality adjusted

Table 1. Costs, clinical benefits, and incremental cost effectiveness ratios for select intra-articular injections

Strategy	COST	QALYs	ICER
CS increases risk of OA progression:			
No Injection	$160,364	12.879	
Saline	$162,159	13.019	$12,900
CS	$162,626	13.033	$32,500
HA	$163,195	13.042	$62,100
PRP	$166,746	13.064	$159,400
CS does not increase risk of OA progression:			
No Injection	$160,364	12.879	
Saline	$162,159	13.019	d*
CS	$162,256	13.039	$11,800
HA	$163,195	13.042	d*
PRP	$166,746	13.064	$177,000

CS = Corticosteroid, HA = Hyaluronic Acid, PRP = Platelet Rich Plasma, QALY = Quality Adjusted Life Year, ICER = Incremental Cost-Effectiveness Ratio. ICERs were rounded to the nearest 100.

* Strategies that lead to greater ICER compared to the next strategy never represent an optimal use of resources. By convention, such strategies are labeled "extendedly dominated" and eliminated from consideration.

life years (QALYs) between two strategies. The IAI that maximizes QALYs with ICER< willingness to pay (WTP) threshold is considered the most cost-effective strategy.

Results: QALYs and costs for each strategy are presented in Table 1. Assuming CS does not increase the risk of OA progression, CS results in an ICER of $11,800/QALY compared to no injection, and PRP results in an ICER of $177,000/QALY compared to CS. Assuming CS does increase the risk of OA progression, the resultant ICERS are $12,900/QALY for saline compared to no injection, $32,500/QALY for CS compared to saline, $62,100/QALY for HA compared to CS, and $159,400/QALY for PRP compared to HA. If CS increased the risk of OA progression, PRP would achieve ICERs of $100K/QALY ($50K/QALY) at a price of $1,965 ($1,448). If CS did not increase risk of OA progression, even lower PRP prices ($1,655 and $1,086) would be required to attain these ICER thresholds.

Conclusion: For WTP thresholds between $11,800 and $62,100/QALY, CS is the preferred strategy, regardless of what we assume about their impact on OA progression. If CS has no impact on risk of OA progression, it remains the preferred strategy until WTP exceeds $177,000/QALY. If CS increases risk of OA progression, HA becomes preferred for WTP > $62,000.

Disclosure: H. Mass: None; **J. Collins**: None; **d. Hunter**: None; **C. Yang**: None; **M. Jones**: Biosplice, 1, 2, Pacira, 5, Regeneron, 1, 2; **S. Messier**: None; **T. Neogi**: None; **A. Paltiel**: None; **J. Katz**: Biosplice, 5; **E. Losina**: None.

Abstract Number: 1841

Clinical Trial Perceptions Among Male Patients with Systemic Lupus Erythematosus (SLE): Georgians Organized Against Lupus (GOAL) Cohort

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Health Services Research Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Minority patients are disproportionately affected by SLE. Yet, they are underrepresented in SLE clinical trials compared to White patients. Specifically, patients that identify as male and Black are significantly understudied. We explored racial and gender differences in clinical trial perceptions among a cohort of predominantly Black patients with SLE in Atlanta, Georgia.

Methods: Data from the Georgians Organized Against Lupus (GOAL) cohort were used for this analysis. The GOAL cohort consists of validated SLE patients living in Atlanta, Georgia. Since 2012, SLE patients have been surveyed annually regarding demographics, SLE natural history, treatment, healthcare utilization, and psychosocial factors. For this study, only male patients were assessed. The 2022 GOAL survey included ad-hoc questions that assessed clinical trial knowledge, willingness to participate, and hesitancy in clinical trial enrollment. The Systemic Lupus Activity Questionnaire (SLAQ), Self-administered Brief Index of Lupus Damage (SA-BILD), and self-efficacy, depression, and perceived stress measures were included in this study. Descriptive analysis was used for comparisons.

Results: A total of 47 males responded to the 2022 GOAL Survey; the majority were Black (79% Black, 19% White, 2% Asian) with a mean age 32 years (SD 11.8), mean education of 14 years (SD 2.3), and majority unemployed (59%). The mean disease duration was 16 years (SD 10.6), mean disease activity score was 11 (SD 7.3), and mean organ damage score was

			Clinical Trials-Comfortable Participating		
Characteristic	**Category**	**Overall (n= 47)**	**No (n=7)**	**Yes (n=22)**	**Unsure (n=18)**
Age at Diagnosis	Mean ± SD	31.8 ± 11.8	30.5 ± 15.7	31.6 ± 12.5	32.6 ± 9.9
Age at Survey	Mean ± SD	48.1 ± 13.3	49.4 ± 15.2	48.0 ± 12.3	47.7 ± 14.4
Disease Duration	Mean ± SD	16.3 ± 10.6	18.9 ± 2.9	16.4 ± 10.9	15.0 ± 12.4
Race	Asian	1 (2.1)			1 (5.6)
	Black	37 (78.7)	7 (100)	19 (86.4)	11 (61.1)
	White	9 (19.1)		3 (13.6)	6 (33.3)
Education (Years)	Mean ± SD	14.1 ± 2.3	14.1 ± 2.2	14.0 ± 2.5	14.2 ± 2.1
Work Status	Employed	18 (40.9)	1 (14.3)	9 (45.0)	8 (47.1)
	Off Workforce	11 (25.0)	2 (28.6)	4 (20.0)	5 (29.4)
	Unemployed/Disabled	15 (34.1)	4 (57.1)	7 (35.0)	4 (23.5)
Below 100% Poverty level	No	28 (66.7)	4 (57.1)	9 (50.0)	15 (88.2)
	Yes	14 (33.3)	3 (42.9)	9 (50.0)	2 (11.8)
Disease activity (SLAQ)	Mean ± SD	11.1 ± 7.3	4.7 ± 4.8	12.9 ± 7.6	11.4 ± 6.6
Organ damage (BILD)	Mean ± SD	5.0 ± 4.4	6.7 ± 3.2	5.8 ± 5.1	3.4 ± 3.6
PROMIS Emotional Support	Mean ± SD	52.5 ± 9.7	55.9 ± 11.6	50.2 ± 9.7	54.0 ± 8.9
PROMIS Informational Support	Mean ± SD	55.9 ± 11.3	58.6 ± 10.5	52.8 ± 12.1	58.6 ± 10.1
PROMIS Instrumental Support	Mean ± SD	53.5 ± 10.5	61.5 ± 4.9	50.8 ± 10.1	53.7 ± 11.4
PROMIS Self-Efficacy for Managing Medications and Treatments	Mean ± SD	48.6 ± 9.5	50.7 ± 15.9	49.0 ± 8.9	47.5 ± 7.3
PROMIS Self-Efficacy for Managing Symptoms	Mean ± SD	49.9 ± 9.7	49.0 ± 14.0	48.3 ± 9.2	52.2 ± 8.5
PROMIS Social Isolation	Mean ± SD	46.7 ± 11.3	39.2 ± 9.6	50.7 ± 11.4	45.0 ± 10.4
PROMIS Physical Function	Mean ± SD	42.0 ± 10.4	45.0 ± 11.5	40.7 ± 10.9	42.4 ± 9.5
PROMIS Depression	Mean ± SD	52.1 ± 11.6	47.0 ± 9.3	54.1 ± 12.5	51.6 ± 11.2
Perceived Stress Scale 10	Mean ± SD	16.3 ± 8.2	15.3 ± 3.9	17.6 ± 8.1	15.1 ± 9.4

PROMIS T-score rescales the raw score into a standardized score with a mean of 50 and a standard deviation of 10. Higher scores represent more of the concept measured. Values indicate the mean. Abbreviations: SA-BILD – Self-Administered-Brief Index of Lupus Damage, SLAQ – Systemic Lupus Activity Questionnaire

5 (SD 4.4). We found that 47% of male respondents (n=19 Black, n=3 White) were willing to participate in lupus clinical trials. In contrast, about 30% were unwilling to participate, and 38% were unsure if they would participate in a clinical trial. Male willingness to participate was associated with higher disease activity, living in poverty (50%), less instrumental support), and more social isolation, as compared to those unwilling or unsure (Table). Education, marital status, work status, insurance type, physical function, depression, and perceived stress were not associated with willingness to participate in clinical trials among male respondents.

Conclusion: Among a predominantly Black cohort of males with SLE**,** we found that respondents with more disease activity, fewer resources, and social support appeared more willing to participate in clinical trials. Further efforts are necessary to educate and provide social support to individuals with SLE that are unsure or resistant to clinical trial participation, especially among underrepresented groups, including males. Similar studies have found that clinical trial education, recruitment through lupus support groups, and diversity of clinical trial staff are potential ways to increase trial participation. Further studies of males with SLE are necessary to validate our study findings and provide more knowledge on factors associated with clinical trial hesitancy among this population.

Disclosure: H. Mozee: None; **C. Dunlop-Thomas**: None; **G. Bao**: None; **K. Schofield**: None; **J. Williams**: None; **S. Lim**: None.

Abstract Number: 1842

Reduction in the Concomitant Ordering of Erythrocyte Sedimentation Rate and C-Reactive Protein Within the Rheumatology Clinics at an Academic Medical Center

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Health Services Research Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: ESR and CRP are two laboratory values usedto assess inflammation. There is data to support that CRPis superior to ESR to detect/monitor inflammation or infection due to its better accuracy and reproducibility.Yet, they are often ordered on patients at the same time – essentially performing two separate tests to measure one biological process. This redundant laboratory testing is leading to higher costs to patients and the health systems, and contributes to excess phlebotomy, without any significant clinical benefits. The goal of this quality improvement project was to implement best practices to reduce ESR co-ordering with CRP within the rheumatologyclinics (one clinic in the university setting, 3 satellite clinics, and one safety net clinic)at an academic medical center.

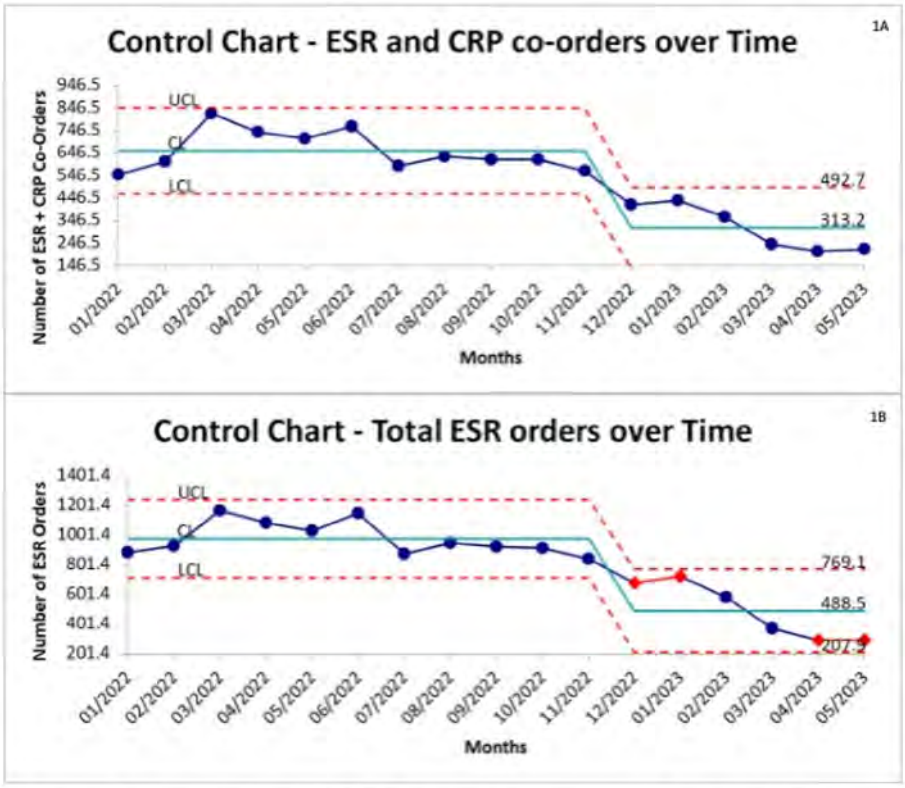

Figure 1: Control charts for ESR and CRP co-orders (1A) and Total ESR orders (1B) at university and satellite rheumatology clinics.

Control Charts for ESR and CRP co-orders and Total ESR orders at university and satellite rheumatology clinics.

Methods: We utilized the Plan, Do, Study, Act (PDSA) iterative methodology for continuous improvement.We collected and analyzed baseline information on CRP and ESR ordering at all 5 rheumatology clinics. Several interventions were implemented including general education to all rheumatology providers and clinic staff(February 2023), targeted education to a few providers with high ESR/CRP co-orders (March 2023), and removal of the ESR order from the rheumatology order set (March 2023) within the Electronic Health Record (EHR).At the safety net clinic, the ESR order had been deselected as a default order on their order set in March 2021. We monitored ESR and CRP co-ordersand total ESR orders to evaluate the impact of our interventions.

Results: Pre-intervention data analysis of CRP and ESR co-orders within the rheumatologyclinics showed that over 12 months, there were 2,392co-orders at the safety net clinic and 7,250co-orders at university clinics between 1/1/22-11/22/22.The primary reason for co-orders was high-risk medication monitoring for RA and SLE.At the university and satelliterheumatology clinics,the average number of total ESR orders decreased by 50% and the average number of ESR and CRP co-orders decreased by 52% between the time frames of 1/2022-11/2022 and 12/2022-5/2023with major changes in process seen around December 2022 and January 2023 (Figure 1).At the safety net clinic, the average number of ESR and CRP co-orders decreased by 65% and the average number of total ESR orders decreased by 64% between the time frames of 1/2022-9/2022 and 10/2022-5/2023 with major changes in process seen around October 2022 (Figure 2). Orders for CRP alone remained stable at all clinics.

Conclusion: It is feasible to reduce the unnecessary ordering of ESR tests through a systematic approach within the clinics in an academic setting.Educational and EHR interventions can be particularly effective interventions as demonstrated by the significant decrease in both ESR and CRP co-orders as well as total ESR orders.Changes seen prior to February 2023 may

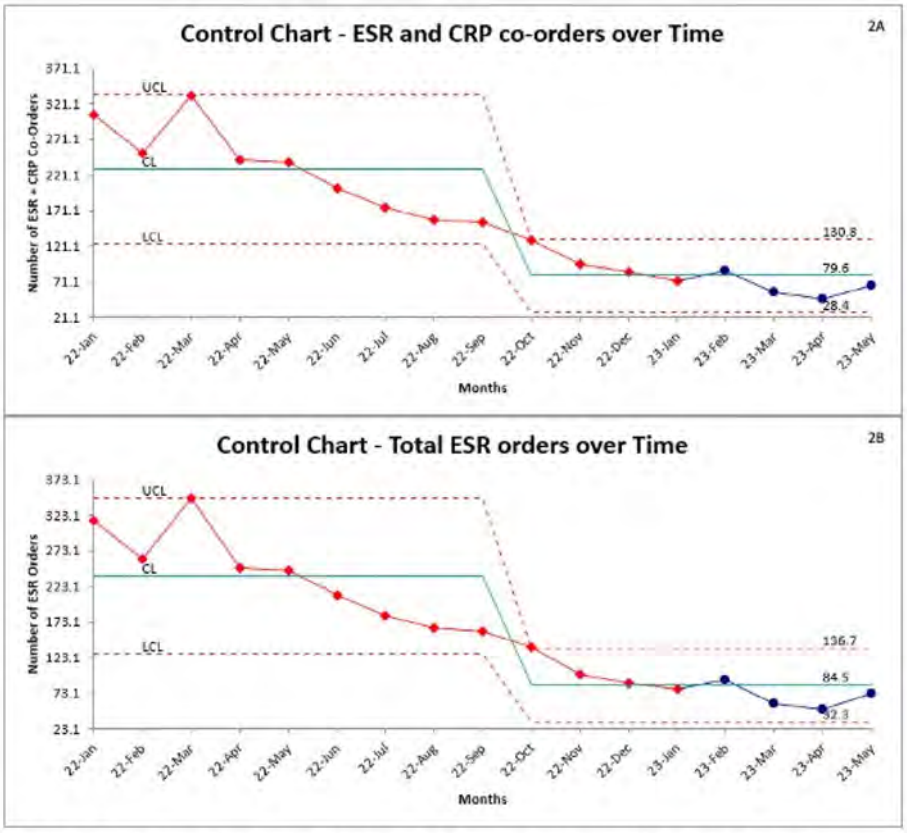

Figure 2: Control charts for ESR and CRP co-orders (2A) and Total ESR orders (2B) at the safety net clinic.

Control Charts for ESR and CRP co-orders and Total ESR orders at the safety net rheumatology clinic.

be due to the Hawthorne effect as rheumatology providers were aware that the department was investigating this topic. In the future, we plan to modify the ESR order with our EHR to implement changes throughout the health system covering all specialties.

Disclosure: R. Desai: None; **N. Shah**: None; **R. Zhang**: None; **M. Bacalao**: GlaxoSmithKlein(GSK), 1; **H. Galous**: None; **D. Karp**: Ampel Biosciences, 2, Biogen, 5, Bristol-Myers Squibb(BMS), 5, Celgene, 5, Eli Lilly, 5, Genentech, 5, Provention Bio, 1, Rilite, 5, UCB, 5; **P. Bajaj**: None.

Abstract Number: 1843

Detection of Clinically Relevant Subgroups in Patients Undergoing Knee Replacement Using Machine Learning

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Health Services Research Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In the US the lifetime risk for Knee Replacement surgery (KR) is 7% for men and 9.5% for women, and this accounts for substantial health care costs. The detection of distinct subgroups of patients among those who undergo KR would have substantial clinical benefits as the subgroups may help identify clinical phenotypes allowing more finely targeted treatment, potentially reducing costs and surgical burden. The purpose of this study is to use machine learning approaches to detect subgroups among the KR patients from the combined Osteoarthritis Initiative (OAI) and the Multi-Center Osteoarthritis Study (MOST) to determine clinical phenotypes.

Methods: We used data from the Osteoarthritis Initiative (OAI) and the Multicenter Osteoarthritis Study (MOST) for analysis. We took participants that underwent KR during follow-up and extracted demographic and clinical characteristics from the exam before a participant's first KR. These characteristics included age, sex, race and ethnicity, weight, height, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scales, Physical Activity Scale for the Elderly (PASE) score, Kellgren & Lawrence (KL) grade, education, depression status, Non-Steroidal Anti-inflammatory Drug (NSAID) use, opioid use and Charlson comorbidity index. For clustering, we used random forests analysis to determine nonparametric pairwise distances between participants, Principal Coordinates Analysis (PCoA) to place participants on a 2-dimensional grid best preserving pairwise distances, and Partitioning Around the Medoids (PAM) to group nearby participants on the grid into clusters. We prespecified use of the five cluster results to allow interpretability and clinical utility of resulting phenotypes. Continuous characteristics are compared between clusters by ANOVA F-tests and categorical characteristics by chi-square tests.

Results: We identified 1108 KR subjects; 412 (37%) from OAI and 696 (63%) from MOST. The 5-cluster results with participant positions on the 2-dimensional PCoA grid are shown in Figure 1 with plotting symbols indicating cohort (MOST vs. OAI) and color indicating cluster. Table 1 shows key characteristics by cluster membership. Cluster 1 is largest and most diverse, is majority female, with the highest percentage of depression and the greatest amount of WOMAC disability. Cluster 2 suggests post-traumatic osteoarthritis with physically active, younger men with a history of knee surgery or injury. Cluster 3 is older men with severe radiographic osteoarthritis. Cluster 4 is women with moderate levels of pain, activity and radiographic

Table 1: Key Characteristics by Cluster Membership

Table 1: Random Forest 5 Cluster Summary

	1 (N = 521)	2 (N = 154)	3 (N = 169)	4 (N = 159)	5 (N = 105)	P-value
Female, %	77.2	0.0	26.0	95.7	100.0	<0.001
Race, %						<0.001
White/Caucasian	82.7	93.5	85.8	87.4	96.2	
Black/African American	15.4	5.8	13.0	8.2	1.0	
Other	1.9	0.6	1.2	4.4	2.9	
Hispanic, %	0.6	0.6	0.0	1.9	1.9	0.229
Employed, %	57.8	83.1	60.9	56.6	39.0	<0.001
Highest Education Level, %						0.272
Graduate School	27.2	31.8	32.6	28.9	23.8	
College	45.9	42.2	40.8	45.3	40.0	
High School	26.9	26.0	26.6	25.8	36.2	
Depression, %	16.3	8.4	14.8	8.8	9.5	0.020
NSAID Use, %	59.7	39.6	52.7	60.4	77.4	<0.001
Opioid Use, %	45.7	26.0	34.9	44.7	59.0	<0.001
Surgery/Injury History, %	53.0	67.5	58.6	45.9	45.7	0.001
Kellgren-Lawrence Grade, %						0.007
0	3.6	3.9	3.0	3.8	1.0	
1	6.7	4.5	3.6	8.8	13.3	
2	15.7	7.8	17.2	14.5	9.5	
3	39.0	46.8	32.0	32.7	31.4	
4	34.9	37.0	44.4	40.3	44.8	
Age	65 ± 8	61 ± 7	64 ± 8	66 ± 8	71 ± 6	<0.001
PASE Score [0-400]	140 ± 76	194 ± 88	164 ± 82	149 ± 76	128 ± 58	<0.001
Maximum Adult Weight (Kg)	93 ± 12	118 ± 17	107 ± 17	75 ± 7	65 ± 6	<0.001
Minimum Adult Weight (Kg)	63 ± 8	88 ± 12	78 ± 9	55 ± 4	52 ± 5	<0.001
WOMAC Function [0-68]	27 ± 12	22 ± 11	24 ± 14	24 ± 12	22 ± 10	<0.001
WOMAC Pain [0-20]	8 ± 4	6 ± 4	8 ± 4	7 ± 4	7 ± 3	<0.001
WOMAC Stiffness [0-8]	4 ± 2	3 ± 3	4 ± 2	4 ± 2	3 ± 1	<0.001
Body Mass Index (BMI)	32 ± 5	35 ± 6	34 ± 8	27 ± 3	25 ± 3	<0.001
Height (mm)	1649 ± 70	1801 ± 52	1742 ± 66	1609 ± 57	1571 ± 56	<0.001
Weight (Kg)	88 ± 11	112 ± 17	102 ± 18	70 ± 6	62 ± 6	<0.001
Charlson Comorbidity [0-37]	1 ± 1	1 ± 1	1 ± 1	1 ± 1	0 ± 1	0.056
MOST Cohort, %	62.0	79.2	68.6	59.7	38.1	<0.001

Continous variables are summarized using the mean ± SD, while categorical variables are summarized using percentages.

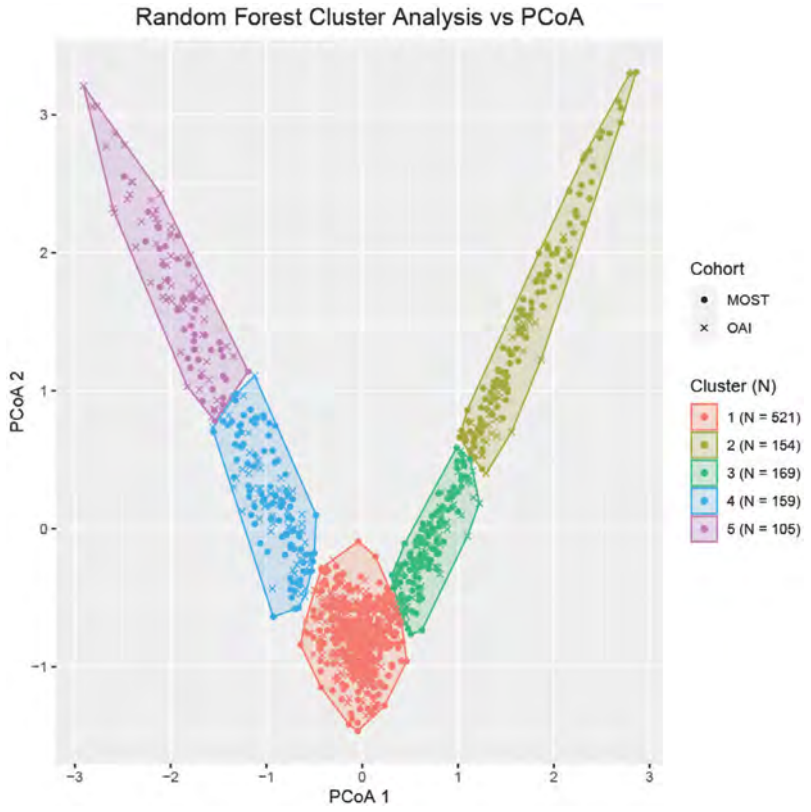

Figure 1: Participant Positions on PCoA Grid with Symbols for Cohort and Colors Indicating Clusters

involvement. Cluster 5 is older women with low levels of weight and physical activity, high NSAID and opioid use and severe radiographic osteoarthritis.

Conclusion: We found distinct clusters with differences in sex, age, radiographic OA severity, race, activity, disability, and depression among clusters. These clusters will be further validated and refined by comparison to sets of clusters generated using only participants from the Multicenter Osteoarthritis Study and only those from the Osteoarthritis Initiative.

Disclosure: B. McGinley: None; **G. Rabasa**: None; **J. Liew**: None; **T. Neogi**: None; **D. Felson**: None; **M. LaValley**: None.

Abstract Number: 1844

Are Patients with Inflammatory Rheumatic Diseases Ready for Studies with Medical Cannabis? – Results from a Digital Survey

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SESSION INFORMATION
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Session Title: Health Services Research Poster III
Session Type: Poster Session C
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Background/Purpose: There is an increasing demand from patients for medical cannabis in the German population [1]. Although medical cannabis might be used to treat pain and reduce inflammation in patients with inflammatory rheumatic diseases (IRD) in addition to the immunomodulatory therapy data regarding the prevalent use of and the interest in the treatment with medical cannabis is scarce. We investigated the knowledge of patients with IRD about medical cannabis and to evaluate patients' attitudes towards the use of medical cannabis in a clinical trial (CT). The analysis included whether attitudes towards medical cannabis depend e.g. on medication, treatment satisfaction, pain levels and health status.

Methods: A digital survey was conducted via an App from Asepha [2]. Our outpatients either filled out the questionnaire in the clinic using a clinic owned iPad (Version 9) or participated using a QR code handed out leading to the survey via their mobile device. Patients answered the questions anonymously. The survey included sociodemographic data, and current pain and immunosuppressive medication. Patients' willingness to consume medical cannabis in a CT was inquired. Concerns (e.g. fear of side effects, dependence on medical cannabis) that might prevent patients' from participating in a CT were assessed. Descriptive data and a penalized ordinal regression (POR) were performed using R. Ethical approval was obtained, DRKS registration number is DRKS00030875.

Results: Data were collected from 192 patients with IRD. Table 1 lists sociodemographic and clinical data. 70% were interested in the participation in a CT although of these 83% were satisfied with their current treatment. Mean number (± standard deviation) of taken pain medication was 0.8 (±0.9), mean number of taken herbal drugs was 0.6 (±1.0). Former recreational cannabis use increases the readiness to participate in a CT. Among those still undecided about taking medicinal cannabis in a CT, the main reason was the lack of sufficient information about cannabis (63%). Another relevant reason was

fear of side effects (40%) and fear of cannabis (16%). The POR depicted that current cs- resp. bDMARD therapy, former recreational cannabis use, number of already taken herbal drugs, lack of information on cannabis, and fear of cannabis but not pain or satisfaction with the current medication significantly influence patients' willingness to participate in a cannabis CT. Limitations in performing daily activities and patients global health status increase the willingness to participate in a cannabis CT, other OR are depicted in table2.

Conclusion: One third of IRD patients were interested in the participation in a CT with medical cannabis and additional 39% were potentially interested. Apart from current medication especially lack of information on cannabis and fear of cannabis were limiting factors. This demonstrates that patients' education about medical cannabis is highly necessary to increase its acceptance and thus willingness to participate in a related CT. Cannabis trials are widely and significantly accepted by patients with a history of recreational use.

Table 1: Sociodemographic and clinical data and willingness to take medical cannabis in a clinical trial (n.a. not applicable)

		Willing to take medical cannabis in a clinical trial		
	Total cohort n (%)	Yes n (%)	Undecided n (%)	No n (%)
	192 (100)	70 (37)	76 (39)	46 (24)
Female	126 (66)	49 (70)	48 (63)	29 (63)
Age in years				
18-39	36 (19)	12 (17)	15 (20)	9 (20)
40-65	113 (59)	42 (60)	47 (62)	24 (52)
>65	43 (22)	16(23)	14 (18)	13 (28)
IRD Diagnosis				
Rheumatoid arthritis	79 (41)	31 (44)	29 (38)	19 (41)
Spondyloarthritis	25 (13)	11 (16)	9 (12)	5 (11)
Connective tissue disease	50 (26)	16 (23)	24 (32)	10 (22)
Vasculitis	18 (9)	6 (9)	6 (8)	6 (13)
Others	20 (10)	6 (9)	8 (11)	6 (13)
Disease duration (in years)	7.8±10.8	8.7±9.9	7.3±11	7.1±12
Current DMARD medication				
csDMARD	88 (46)	33 (47)	38 (50)	17 (37)
bDMARD	58 (30)	28 (40)	16 (21)	14 (30)
tsDMARD	9 (5)	3 (4)	5 (7)	1 (2)
Number of currently taken pain medication (mean ± SD)	0.8±0.9	1 ± 0.9	0.8 ±0.9	0.6 ±0.7
Number of currently taken herbal drugs (mean ± SD)	0.6±1.0	0.9±1.2	0.5±0.8	0.4±0.7
Patient global health (visual analogue scale 0-10; mean ± SD)	4.8±2.4	5.1± 2.5	5.0±2.2	4.1 ± 2.3
Limitations in daily living activities (visual analogue scale 0-10, mean ± SD)	4.3±2.9	4.7± 2.9	4.4± 2.9	3.5±2.7
Former recreational cannabis use	29 (15)	20 (29)	7 (10)	2 (4)
Pain (visual analogue scale 0-10, grouped in 3 groups)				
No pain (0-3)	93 (48)	29 (41)	37 (49)	27 (59)
Moderate pain (4-6)	51 (27)	21 (30)	20 (26)	10 (22)
Severe pain (7-10)	48 (25)	20 (29)	19 (25)	9 (20)
Satisfied with current medication	164 (85)	58 (83)	65 (86)	41 (89)
Reasons for missing interest in a CT				
Not interested in studies	8 (4)	n.a.	1 (1)	7 (15)
Concerned of side effects	44 (23)	n.a.	30 (40)	14 (30)
Concerned of addiction	33 (17)	n.a.	24 (32)	9 (20)
Lack of information on cannabis	53 (28)	n.a.	48 (63)	5 (11)
Fear of cannabis	21 (11)	n.a.	12 (16)	9 (20)

Table 2 Relevant OR of a penalized ordinal regression (with lambda 0.013) (conventional synthetic (cs) disease modifying drug (DMARD), biological (b) DMARD)

Variable	OR
csDMARD	1.46
bDMARD	1.49
Disease duration	1.00
Patient global health	1.03
Limitations in daily living activities	1.12
Pain- Moderate vs. No	1.00
Pain- Severe vs. No	1.00
Satisfaction with current medication	1.00
Number of taken pain medication	1.05
Number of already taken herbal drugs	1.41
Recreational cannabis use	2.57
Lack of information on cannabis	0.48
Fear of cannabis	0.36

References [1] https://de.statista.com [2] https://www.asepha.com/

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Abstract Number: 1845

Development of a Scoring System for Accurate Lupus Nephritis Case Identification in Real-World Databases

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SESSION INFORMATION
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Session Title: Health Services Research Poster III
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Background/Purpose: Accurate identification of prevalent cases of lupus nephritis (LN) is essential for timely patient monitoring and treatment, advancing research, and informing public health initiatives for the management of LN. However, diagnosis codes for LN are generally underutilized, making identification of this patient population in real-world databases challenging. We developed a scoring system to quantify the probability of accurate LN case identification.

Table 1. Characteristics of the underlying population.

		Health system A N = 4,152	Health system B N = 370
Age, Mean (SD)		50.4 (18.6)	49.5 (15.5)
Sex, N (%)	Female	3,629 (87.4)	313 (84.6)
	Male	520 (12.5)	56 (15.1)
	Other or Unknown	3 (0.1)	1 (0.3)
Race/ethnicity, N (%)	Non-Hispanic White	1,534 (37.0)	35 (9.5)
	Non-Hispanic Black	473 (11.4)	76 (20.5)
	Asian	688 (16.6)	94 (25.4)
	Hispanic or Latino	802 (19.3)	122 (33.0)
	Other or Mixed	413 (10.0)	41 (11.1)
	Unknown	242 (5.8)	2 (0.5)

Methods: We used data from EHRs of two large health systems and included patients with ≥1 ICD9/10 codes for SLE from June 2012 to Jan 2022. Prevalent LN was defined as current active LN or a history of LN. We used regular expressions with negation to loosely tag LN within EHR notes, in a training set consisting of a balanced sample of 2038 patients from the larger health system. Testing sets included 100 patients randomly selected from each health system and were manually chart reviewed to classify patients as having 'no LN', 'definite LN' (biopsy report of Class III, IV or V LN), 'potential LN' (no biopsy report but physician diagnosed LN), and 'diagnostic uncertainty' (physician states LN is possible). A gradient boosting model (GBM) including 42 predictors that covered demographics, encounters, diagnosis and procedure codes, comorbidities, medications, and laboratory test results (e.g., serologies, urine studies, chemistries) was used for predictor selection. Predictive performance of a logit regression model (LRM) including key predictors from GBM was evaluated for identifying patients with a "strict" (definite LN) or an "inclusive" (definite LN, potential LN, or diagnostic uncertainty) definition of LN. A LRM-based scoring system was developed and calibrated.

Results: Table 1 includes demographics of the 4,522 patients meeting the eligibility criteria from both health systems. In addition to more specific diagnosis codes for LN, presence of diagnosis codes for acute or chronic kidney disease or proteinuria, younger age at first SLE diagnosis code, and use of mycophenolate mofetil or mycophenolic acid were identified as key predictors and included in the final LRM. Urine protein creatinine ratios (UPCR) >0.5, abnormal complement

Table 2. Performance of the final logit regression model including key predictors. LN: Lupus nephritis; AUC: area under the curve; PPV: positive predictive value; NPV: negative predictive value; Strict definition of LN: definite LN; Inclusive definition of LN: definite LN, potential LN, or diagnostic uncertainty.

Test set	Definition of LN	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy
Health system A	Strict	0.91	0.88	0.80	0.70	0.93	0.83
	Inclusive	0.93	0.88	0.88	0.84	0.91	0.88
Health system B (External set)	Strict	0.88	0.80	0.85	0.78	0.86	0.83
	Inclusive	0.87	0.74	0.87	0.83	0.80	0.81
Calibration							
Predicted probabilities		<50%	50-60%	60-70%	70-80%	80-90%	>90%
Observed probabilities (95% CI)		19% (17-21)	49% (40-58)	69% (55-81)	79% (69-86)	85% (81-89)	91% (86-95)

Table 3. The scoring system and interpretation. Diagnosis codes for lupus nephritis included ICD10 codes: M32.14 or M32.15, or ICD9 code 710.0 in combination with ICD9 codes 583.81, 581.81, or 583.89. Diagnosis codes for acute or chronic kidney disease or proteinuria included ICD10: N00-N08, N17-N19, and R80, or ICD9 codes 580-586, and 791.0.

Patient characteristic	Points *(add unless stated)*
One diagnosis code (ICD10) for lupus nephritis	35
Or	
Two or more diagnosis codes (ICD9 or ICD10) for lupus nephritis	115
One diagnosis code for acute or chronic kidney disease or proteinuria	70
Or	
Two or more diagnosis codes for acute or chronic kidney disease or proteinuria	95
Any use of mycophenolate mofetil or mycophenolic acid	45
Age (in years) at first systemic lupus erythematosus diagnosis code	Subtract age

Total Score	Predicted Probability
<80	<50%
80-110	50-60%
110-140	60-70%
140-175	70-80%
175-230	80-90%
>230	>90%

component 3 (C3) levels, any use of hydroxychloroquine, azathioprine, or rituximab, and glucocorticoid dose were also identified as important predictors but were omitted from the final LRM as their inclusion did not further improve performance. The final LRM had an area under the curve, sensitivity, and positive predictive value of 0.93, 0.88, and 0.84, respectively, for identifying LN using the inclusive definition, performed similarly with a strict LN definition, and had good external validity when tested in the second health system (Table 2). Predicted and observed probabilities had good calibration (Table 2).The scoring system was derived from this model (Table 3).

Conclusion: Prediction of prevalent LN using data elements available in EHR or claims data was feasible, had good accuracy and was validated externally. The scoring system has the potential to identify prevalent LN accurately across health systems.

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Abstract Number: 1846

A Longitudinal Study: The Benefits of Non-Pharmacological Approaches to Improve Self-Reported Pain, Stiffness, and Fatigue in Individuals with Musculoskeletal Disorders

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Health Services Research Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Musculoskeletal disorders are a leading cause of disability worldwide, with low back pain being one of the primary causes. The World Health Organization (WHO) reports that chronic musculoskeletal pain affects 20-33% of the global population, which amounts to a staggering 1.75 billion people. Chronic pain is often accompanied by persistent fatigue, a common complaint among individuals with musculoskeletal disorders such as osteoarthritis, rheumatoid arthritis, fibromyalgia, and low back pain. Stiffness is also a debilitating symptom that affects about half of those with chronic pain and musculoskeletal disorders. While medications can provide symptomatic relief to these conditions, non-pharmacological approaches reduce reliance on medications and address the underlying causes of musculoskeletal disorders. To optimize the quality of life of individuals with musculoskeletal disorders, the Education Institute at Hospital for Special Surgery (HSS) implemented non-pharmacological interventions.

Methods: These non-pharmacological interventions include 6-week virtual exercise classes, which encompass a variety of activities such as Pilates, Yoga, T'ai Chi Chih, mindfulness-based therapy, and relaxation techniques. These exercises are designed to be low-intensity, performed safely at home, and tailored to accommodate participants' diverse mobility levels. The virtual classes are led by certified instructors who specialize in working with individuals affected by musculoskeletal disorders. Moreover, these interventions are accessible to patients and the public using Zoom and phone as the platforms for delivery. Program effectiveness is measured using pre/post-online surveys assessing pain intensity, pain interference with seven aspects of daily living (ADL), stiffness, and fatigue. A longitudinal analysis is conducted using regression models.

Results: Since 2020, 366 participants have participated in our non-pharmacological interventions. Of those assessed (n=190), 70 participants self-reported having at least one musculoskeletal condition. Most were females (98%), ages ≥60 years (90%), Caucasian (91%), and non-Hispanic (98%). For every 6-week virtual physical activity program, participants reporting at least one musculoskeletal condition experienced statistically significant decreases in pain intensity ($p \leq 0.01$), stiffness ($p \leq 0.01$), and fatigue ($p \leq 0.05$). Decreased pain interference with seven ADL were seen but not at statistically significant levels. Also, most participants reported gaining knowledge (93%) and self-management skills (90%) to manage their condition.

Conclusion: Our findings support the benefits of non-pharmacological approaches in managing musculoskeletal disorders and their debilitating symptoms, offering a comprehensive approach that empowers individuals and promotes quality of life. Future research is needed in longitudinal studies to assess these interventions' sustainable benefits and long-term functional outcomes and examine the challenges and strategies for implementing these approaches within various healthcare settings, including community-based programs, which would help bridge the gap between research and practice.

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Abstract Number: 1847

Influence of Seasonal Changes on Adherence in Rheumatoid Arthritis Patients

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SESSION INFORMATION
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Background/Purpose: Rheumatoid arthritis (RA) symptoms are suspected to be linked with exposure to colder environments. Previous studies on RA and seasonality have focused on RA activity; however, none assess medication adherence. The objective of this study was to assess the impact of seasonal changes on medication adherence among patients beginning subcutaneous or oral RA treatment.

Methods: This is a retrospective cohort study of adult RA patients throughout the United States enrolled in a large health plan taking subcutaneous or oral RA medications between 3/1/2019 and 2/28/2021. Patients were included if they were newly diagnosed with RA (ICD-10 codes M05.X and M06.X). Medication adherence for these patients was tracked for 12 months after starting therapy. Medication classes included: TNF-αinhibitors, Janus Kinase inhibitors (JAK), Interleukin-6 (IL-6) inhibitors, a T-cell blocker, and folate analogs. Medication history was stratified into meteorological seasons for the northern hemisphere: spring (3/1-5/31), summer (6/1-8/31), fall (9/1-11/30), and winter (12/1-2/28). Monthly medication adherence was measured using proportion of days covered (PDC) between the first and last fill of the year. The effect of seasonality on monthly adherence was estimated using linear regression, controlling for age, gender, and other patient demographics. Predicted PDC was calculated using resultant equations; p-values < 0.05 were significant.

Results: In total, 3,710 patients were included in this study; adherence was captured for 39,628 member-months. The average age of the cohort was 56 years (standard deviation (sd) = 14); 2,797 (75%) identified as female. The average monthly PDC was 0.84. Predicted monthly PDC was highest in summer (0.85), followed by spring (0.85), fall (0.84) and lowest in the winter (0.83). Significant differences in PDC by season were found in winter ($p < 0.01$). Seasonality effects differed by drug class. For TNF-α inhibitors, spring ($p < 0.01$) and winter ($p < 0.01$) were associated with lower mean PDCs. None of the season coefficients were statistically significant for JAK inhibitors. Adherence for IL-6 inhibitors (p=0.04), T-Cell blockers ($p < 0.01$) and folate analog (p=0.01) were the most sensitive to winter seasonal changes. Subsampling by climate region revealed the negative impact of winter on medication adherence was limited to members residing in humid (p=0.00) or cold climates (p=0.01).

Conclusion: Medication adherence decreased in winter months, but the effect of seasonality depended on class and was drug specific. Seasonality influences adherence, but only for specific seasons.

Disclosure: C. Schmidt: CVS Health, 3, 11; **K. Patel**: CVS Health, 3, 11; **S. Delgado**: CVS Health, 3, 11; **G. Cozzi**: CVS Health, 3, 11; **E. Avalos-Reyes**: AstraZeneca, 11, CVS Health, 3, 11, GlaxoSmithKlein(GSK), 11, Haleon, 11, Johnson & Johnson, 11, Moderna, 11, Novavax, 11, Pfizer, 11, Viatris, 11; **W. Rutter**: CVS Health, 3, 11; **R. Grover**: CVS Health, 3, 11; **L. Feczko**: Baxter, 11, CVS Health, 3, 11; **W. Cavers**: Amedisys Inc, 11, Baxter, 11, Conmed Corp, 11, CVS Health, 3, 11; **K. Johnson**: CVS Health, 3, 4, 11, HC Technology Patent, 10.

Abstract Number: 1848

Demographic and Clinical Factors Associated with HPV Vaccination in Young Adults with Rheumatic Disease

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

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Session Time: 9:00AM–11:00AM

Background/Purpose: The HPV vaccine is safe and immunogenic in RD patients but uptake is suboptimal. We aimed to evaluate factors associated with HPV vaccination in individuals with RDs, including RD diagnosis and age at diagnosis. We hypothesized that being diagnosed with an RD around the age when HPV vaccine initiation is recommended could pose a barrier to vaccination.

Table 1. Demographic and Clinical Characteristics of Patients Aged 16-22 with Rheumatic Disease Stratified by HPV Vaccination Status

Variable	Unvaccinated (N=161)	Vaccinated (N=160)	p-value
Demographics			
Age, yrs – mean (SD)	19.5 (2.0)	19.6 (2.2)	0.66
Age at RD diagnosis, yrs – mean (SD)	14.9 (4.8)	15.0 (4.7)	0.92
Female	110 (68.3)	123 (76.9)	0.09
Race			*0.001*
• Asian	7 (4.3)	15 (9.4)	
• Black	7 (4.3)	22 (13.8)	
• White	114 (70.8)	81 (50.6)	
• Other	21 (13.0)	31 (19.4)	
• *Patient declined/Unavailable*	*12 (7.5)*	*11 (6.9)*	
Ethnicity			*0.005*
• Hispanic/Latino	30 (18.6)	45 (28.1)	
• Not Hispanic/Latino	121 (75.2)	114 (71.3)	
• *Patient refused/Unknown*	*10 (6.2)*	*1 (0.6)*	
Insurance type			*<0.001*
• Medicaid and/or Medicare	22 (13.7)	48 (30.0)	
• Private	134 (83.2)	112 (70.0)	
• *Unspecified*	*5 (3.1)*	*0 (0)*	
Clinical Information			
Rheumatic disease diagnosis			*0.007*
• Inflammatory arthritis	98 (60.9)	87 (54.4)	
• Connective tissue disease	34 (21.1)	60 (37.5)	
• Vasculitis	6 (3.7)	6 (3.8)	
• Chronic recurrent multifocal osteomyelitis	9 (5.6)	1 (0.6)	
• Localized scleroderma	6 (3.7)	2 (1.3)	
• Autoinflammatory disease	4 (2.5)	2 (1.3)	
• Other inflammatory disease	4 (2.5)	2 (1.3)	
Immunosuppressive medication use (at most recent visit)	95 (59.0)	106 (66.3)	0.26
Influenza vaccination (ever)	97 (60.2)	155 (96.9)	*<0.001*
COVID-19 vaccination			*<0.001*
• 0 doses	58 (36.0)	12 (7.5)	
• 1-2 doses	54 (33.5)	50 (31.2)	
• ≥3 doses	49 (30.4)	98 (61.3)	

Values are reported as N (%) unless otherwise indicated. A p-value <0.05 was considered statistically significant.

Methods: This retrospective study included individuals aged 16-22 seen by a rheumatologist in our academic center ≥2 times (2020-2022) who had an RD diagnosis and New York State (NYS) residence. We used chart review to ascertain demographics, immunization information (automatically pulled from the NYS Immunization Information System), RD diagnosis, and medications. We descriptively compared demographic and clinical variables between patients who had received 0-1 HPV vaccine doses ("unvaccinated") and those who had received 2-3 doses ("vaccinated") and performed multivariable logistic regression to assess the association between RD-related factors and HPV vaccination after adjusting for relevant demographic and clinical variables.

Results: Of 671 patients aged 16-22 seen by a rheumatologist ≥2 times in the study timeframe, 321 (47.8%) had an RD diagnosis and NYS residence. Mean age at most recent visit was 20 ± 2.1 years and at diagnosis was 14.9 ± 4.7 years, 233 (72.6%) were female, and 161 (50.2%) were unvaccinated. Compared to those who were vaccinated, unvaccinated individuals were more frequently White (70.8% vs 50.6%, p=0.001), non-Hispanic/Latino (75.2% vs. 71.3%, p=0.005), and privately insured (83.2% vs. 70.0%, p< 0.001). HPV vaccinated patients more frequently had received an influenza vaccine (96.9% vs. 60.2%, p< 0.001) or ≥3 COVID-19 vaccine doses (61.9% vs. 30.4%, p=0.003) compared to unvaccinated patients. RD diagnosis differed by HPV vaccine status (p=0.007): inflammatory arthritis (IA) was more common in unvaccinated vs. vaccinated patients (60.9% vs. 54.4%) and CTD was more common in vaccinated vs. unvaccinated patients (37.5% vs. 21.1%) [**Table 1**]. In multivariable analysis, Black vs. White patients with RD were more likely HPV vaccinated (OR 5.74, 95% CI [1.61-20.54], p=0.007) as well as those who had ever received an influenza vaccine vs. those who had not (OR 11.47, 95% CI [4.31-30-.51], p< 0.001); patients with "other" RD vs. IA were less likely HPV vaccinated (OR 0.20, 95% CI [0.08-0.52], p=0.001) [**Table 2**]. Age at RD diagnosis did not differ between groups and was not associated with HPV vaccination after adjustment.

Table 2. Logistic Regression Model Evaluating the Association Between Demographic and Clinical Characteristics and HPV Vaccination in Patients Aged 16-22 with Rheumatic Disease

Variable	Odds Ratio	95% Confidence Interval	p-value
Demographics			
Age	1.04	0.89 – 1.22	0.59
Sex			
• Male	*Referent*		
• Female	1.64	0.85 – 3.20	0.14
Race			
• White	*Referent*		
• Black	5.7	1.61 – 20.54	*0.01*
• Asian	2.76	0.79 – 9.62	0.11
• Other	2.62	1.02 – 6.78	0.05
Ethnicity			
• Hispanic/Latino	*Referent*		
• Not Hispanic/Latino	1.00	0.45 – 2.23	1.00
Insurance			
• Private	*Referent*		
• Medicaid and/or Medicare	1.72	0.77 – 3.88	0.19
Clinical Information			
Rheumatic disease diagnosis			
• Inflammatory arthritis	*Referent*		
• Connective tissue disease	0.64	0.30 – 1.36	0.25
• Other[1]	0.20	0.08 – 0.52	*0.001*
Age at diagnosis			
• <17 years	*Referent*		
• 17-22 years	1.34	0.65 – 2.73	0.43
Influenza vaccination (ever)			
• No	*Referent*		
• Yes	11.47	4.31 – 30.51	*<0.001*
COVID-19 vaccination			
• 0 doses	*Referent*		
• 1-2 doses	4.36	1.81 – 10.52	*0.001*
• ≥3 doses	8.00	3.37 – 19.00	*<0.001*

A p-value <0.05 was considered statistically significant.
1. Vasculitis, chronic recurrent multifocal osteomyelitis, localized scleroderma, autoinflammatory disease, and other inflammatory disease.

Conclusion: In a large sample of patients aged 16-22 with RD, half had not received ≥2 HPV vaccine doses. As has been demonstrated in the general population, White race, non-Hispanic/Latino ethnicity, and having private insurance were associated with decreased HPV vaccine uptake. HPV vaccination was associated with influenza and COVID-19 vaccination, suggesting that some factors driving elective vaccine uptake are independent of vaccine type. Unvaccinated individuals more commonly had IA whereas vaccinated individuals more commonly had CTD; age at diagnosis was not associated with HPV vaccination after adjustment. Further research is needed to identify and mitigate barriers to HPV vaccination in this high-risk group.

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Abstract Number: 1849

Impact of the First Three Waves of the Covid-19 Pandemic on Everyday Restrictions and Clinical Care of Patients with Spondyloarthritis Across Europe - Results from the EuroSpA Collaboration

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Health Services Research Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Table 1 Restrictions during the Covid-19 pandemic across European countries/registries

	First confirmed case of Covid-19	Nation-wide total lockdown *with* curfew	Nation-wide total lockdown *without* curfew	Other nation-wide curfew	Nation-wide curfew parts of the day	Mandatory use of facemask	Mandatory use of filtrating facemask	Mandatory distance in public (meter)	Recommended distance in public (meter)
Czech Republic	01.03.20	Yes	Yes	Yes	Yes	Yes	Yes	2	2
Denmark	26.02.20	No	Yes	Yes	No	Yes	No	1	2
Estonia	27.02.20	No	Yes	No	No	Yes	No	2	-
Finland	26.02.20	No	Yes	Yes	No	Yes	No	-	2
Iceland	28.02.20	No	No	Yes	No	Yes	No	1 and 2	2
Italy	01.02.20	Yes	Yes	No	No	Yes	Yes	1.5	1.5
Netherlands	27.02.20	Yes	Yes	Yes	Yes	Yes	No	1.5	1.5
Norway	26.02.20	No	Yes	Yes	No	Yes	No	1	1-2
Portugal	02.03.20	No	Yes	No	Yes	Yes	No	-	2
Romania	26.02.20	Yes	Yes	No	Yes	Yes	Yes	2	2
Slovenia	04.03.20	Yes	Yes	No	Yes	Yes	No	1.5	1.5
Spain	31.01.20	Yes	Yes	No	Yes	Yes	Yes*	1.5	1.5
Switzerland	25.02.20	No	Yes	No	No	Yes	No	1.5	1.5
Total	31.1.-4.3.20	6 Yes	12 Yes	6 Yes	6 Yes	13 Yes	4 Yes	1-2	1-2
*In hospitals									

Table 2 Routine care consultations in the registries before and during the Covid-19 pandemic

Types of *routine care* consultations in the countries/registries *before* the pandemic						
	In-person	**Phone**	**Video**	**Mobile app**	**E-mail**	**Other**
Czech Republic (ATTRA)	+	+	-	-	+	-
Denmark (DANBIO)	+	+	-	-	-	-
Estonia (ESRBTR)	+	-	-	-	-	-
Finland (ROB-FIN)	+	+	-	+	-	-
Iceland (ICEBIO)	+	-	-	-	-	-
Italy (GISEA)	+	-	-	-	-	-
Netherlands (ARC)	+	-	-	-	-	-
Norway (NOR-DMARD)	+	-	-	-	-	-
Portugal (Reuma.pt)	+	-	-	-	-	-
Romania (RRBR)	+	-	-	-	-	-
Slovenia (biorx.si)	+	-	-	-	-	-
Spain (BIOBADASER)	+	-	-	-	-	-
Switzerland (SCQM)	+	+	-	-	-	-
New modalities of *routine care* rheumatology consultations in the countries/registries *during* the pandemic						
	Any new modality	**Phone**	**Video**	**Mobile app**	**E-mail**	**Other**
Czech Republic (ATTRA)	-	NA	-	-	NA	-
Denmark (DANBIO)	+	NA	+	-	-	+
Estonia (ESRBTR)	-	-	-	-	-	-
Finland (ROB-FIN)	-	NA	-	NA	-	-
Iceland (ICEBIO)	+	+	-	-	-	-
Italy (GISEA)	+	+	-	+	+	-
Netherlands (ARC)	+	+	-	-	-	-
Norway (NOR-DMARD)	+	+	+	-	-	-
Portugal (Reuma.pt)	+	-	-	-	-	+
Romania (RRBR)	-	-	-	-	-	-
Slovenia (biorx.si)	+	+	-	-	-	-
Spain (BIOBADASER)	+	+	-	-	-	+
Switzerland (SCQM)	+	NA	+	-	-	-
NA, not applicable (already established option before the pandemic)						

Background/Purpose: The Covid-19 pandemic constituted major challenges for health-care services worldwide. We aimed to compare Covid-19 restrictions across Europe during the first three waves of the pandemic, as well as the consultation and follow-up practices of patients with spondyloarthritis before and during the pandemic.

Methods: Rheumatologists completed a Research Electronic Data Capture (REDCap) survey in 13 observational registries in the European Spondyloarthritis Research Collaboration Network (EuroSpA) between July 1st and October 27,th 2022: ATTRA (Czech Republic), DANBIO (Denmark), ESRBTR (Estonia), ROB-FIN (Finland), ICEBIO (Iceland), GISEA (Italy), ARC (Netherlands), NOR-DMARD (Norway), Reuma.pt (Portugal), RRBR (Romania), biorx.si (Slovenia), BIOBADASER (Spain), and SCQM (Switzerland), answering questions on Covid-19 restrictions in their individual countries and the impact of Covid-19 on consultation and follow-up of routine care patients with spondyloarthritis in their registries. The survey covered the period from the start of the pandemic in the different countries, until 1st of March, 2022.

Results: The first case of Covid-19 in each country was reported between 31st of January 2020 in Spain and 4th of March 2020 in Slovenia. Use of facemask in public was mandatory in all countries during the peak of the pandemic, but use of filtering facemask (type P2 or P3) only in four countries (Table 1). All countries except for Iceland had a

Table 3 Changes of follow-up and delays in the registries during the Covid-19 pandemic

Changes of follow-up during the first three waves of the pandemic as reported by rheumatologists in the individual countries/registries						
	The new modality of consultation* was mandatory	The new modality of consultation* was more often done by nurse	More patients were relocated from physical to remote consultations§	Relocation to remote consultations mainly applied to follow-up (FU) patients / new patients (NP)	Approximate proportion of patients assessed remotely at the peak of the pandemic	Information on type of consultation (physical/remote) for individual patients
Czech Republic (ATTRA)	NA	NA	+	FU	25-50%	-
Denmark (DANBIO)	-	-	+	FU	Unknown	-
Estonia (ESRBTR)	NA	NA	+	FU	Unknown	-
Finland (ROB-FIN)	NA	NA	+	FU, NP	>75%	Unknown
Iceland (ICEBIO)	-	+	+	FU, NP	>75%	-
Italy (GISEA)	-	-	+	FU	50-75%	-
Netherlands (ARC)	-	-	+	FU, NP	50-75%	-
Norway (NOR-DMARD)	-	-	+	FU	50-75%	-
Portugal (Reuma.pt)	-	Unknown	+	FU	Unknown	+ (from July 21)
Romania (RRBR)	NA	NA	+	FU	50-75%	-
Slovenia (biorx.si)	-	-	+	FU	>75%	-
Spain (BIOBADASER)	In some hospitals	Parts of the time	+	FU	50-75%	-
Switzerland (SCQM)	Parts of the time	-	+	FU	>75%	+ (from late 21)
Delays and cancellations during the first three waves of the pandemic as reported by rheumatologists in the individual countries/registries						
	More patients cancelled appointments themselves	Also more new patients cancelled their appointments	More cancellations by healthcare providers	More cancellations by healthcare providers also for new patients	Less follow-up visits than usual	Translocation of staff to other duties
Czech Republic (ATTRA)	+	+	+	+	Unknown	Unknown
Denmark (DANBIO)	+	Unknown	+	Unknown	+	+
Estonia (ESRBTR)	+	Unknown	+	+	+	+
Finland (ROB-FIN)	+	+	+	+	+	+
Iceland (ICEBIO)	+	+	+	Unknown	+	+
Italy (GISEA)	+	+	+	Unknown	+	+
Netherlands (ARC)	+	Unknown	+	Unknown	+	+
Norway (NOR-DMARD)	+	Unknown	+	-	+	+
Portugal (Reuma.pt)	+	+	+	+	+	Unknown
Romania (RRBR)	+	+	-	NA	+	+
Slovenia (biorx.si)	+	+	+	+	+	+
Spain (BIOBADASER)	+	+	+	+	+	+
Switzerland (SCQM)	+	+	+	+	+	+

*The new modalities of consultation referred to are listed in Table 2. §For Estonia and Romania this applied to routine care patients but not patients included in the respective registries +, Yes; -, No; FU, follow-up patients; NA, not applicable; NP, new patients

nationwide total lockdown. Most countries had nationwide curfews, which occasionally applied to specific periods throughout the day. All countries had social distancing varying between one and two meters from others in public. This was mandatory at some time-point during the pandemic in all countries, except in Finland and Portugal, where it was recommended.

Before the pandemic, only four countries/registries had alternative modes of consultation in addition to the usual routine care physical consultations (Table 2). However, during the pandemic, nine registries initiated other modes of routine care consultations, the most common being phone consultations. The new modalities of consultations were not mandatory in any registry, except for mandatory non-urgent remote consultations in Switzerland during the first wave of the pandemic (phone or video, Table 3). In addition, in Spain, phone consultations and consultations between primary care physicians and rheumatologists were mandatory at some hospitals.

In every registry, rheumatologists reported an increased patient relocation from physical to remote consultations during the pandemic. At the peak of the pandemic, most of the patients were assessed remotely; however, this mainly applied to follow-up patients. More patients and healthcare providers canceled appointments during the pandemic than before. Furthermore, in all registries, staff was translocated to other duties and patients had fewer follow-up consultations than usual.

Conclusion: The Covid-19 pandemic had far-reaching consequences across Europe, not only due to nationwide restrictions, but also as a result of its negative impact on the accessibility of rheumatological care and follow-up.

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Abstract Number: 1850

Long-term Glucocorticoid Use in a Cohort of Elderly Early Rheumatoid Arthritis Patients: A Joint Analysis of Medicare and the Rheumatology Informatics System for Effectiveness (RISE) Data

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SESSION INFORMATION

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Session Title: (1840–1861) Health Services Research Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: According to recent ACR and EULAR rheumatoid arthritis (RA) guidelines, glucocorticoids (GCs) should only be used for brief periods or not at all. Our aim was to investigate U.S. real-world GC usage patterns in elderly early RA patients, who are especially likely to suffer from adverse events, and assess the relationship between GC initiation, entrance into rheumatologic care, and subsequent, long-term GC use.

Methods: We joined data from the Rheumatology Informatics System for Effectiveness (RISE) with Medicare claims (2016-2018). Early RA patients were identified with a first RA ICD code in RISE between 01/01/2017 and 09/01/2018 (index date) plus a second code ≥30 days later. To ensure observability, we required continuous enrollment in Medicare in the year of their first RA code and the preceding year. To identify early RA patients, we required ≥18 months of observation in Medicare prior to the index date and no RA code for >12 months before the index date. Patients who received GCs before the index date from rheumatologists not participating in RISE were excluded. Patient characteristics were assessed during the six months following the index date. GC initiation for early RA was defined by a GC claim in Medicare between 3 months before to 6 months after the index date (**Figure**). Chronic use at 3, 6 and 12 months after initiation was defined by an active GC claim at each time point without a medication gap of >6 months. We used standardized mean differences to compare patient characteristics among GC initiators vs. non-initiators. Time between GC initiation and the start of rheumatology care was calculated as the difference between the GC initiation date and the index date. Mean GC doses during follow-up were

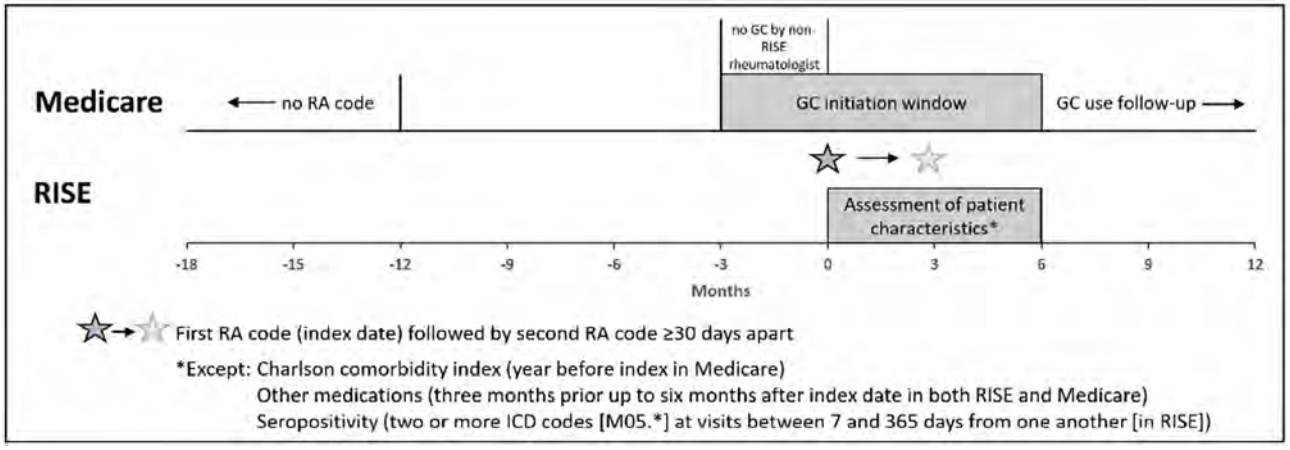

Figure 1. Study design. RA, rheumatoid arthritis; GC, glucocorticoid; RISE, Rheumatology Informatics System for Effectiveness; ICD, International Statistical Classification of Diseases and Related Health Problems.

Table 1. Baseline characteristics.

	GC initiation		
	No (n = 1091)	Yes (n = 763)	Standardized mean difference
Demographics			
Age, years	74.5 ± 8.1	75.6 ± 8.0	-0.13
Women	741 (67.9)	516 (67.6)	0.01
Race and ethnicity			
African American	89 (8.2)	44 (5.8)	
Asian	20 (1.8)	7 (0.9)	
Hispanic	53 (4.9)	42 (5.5)	0.16
Non-Hispanic white	788 (72.2)	583 (76.4)	
Other or multiracial	8 (0.7)	1 (0.1)	
Unknown	133 (12.2)	86 (11.3)	
National Area Deprivation Index* (n = 1710)	49.6 ± 25.6	48.9 ± 26.5	0.03
Clinical Characteristics			
Charlson Comorbidity Index (n = 1854)	2.36 ± 2.14	3.07 ± 2.08	-0.34
COPD (present)	248 (22.7)	240 (31.5)	0.20
BMI			
Underweight	13 (1.2)	7 (0.9)	
Healthy weight	247 (23.3)	194 (26.1)	
Overweight	339 (32)	263 (35.4)	0.14
Obese I	256 (24.2)	159 (21.4)	
Obese II	123 (11.6)	79 (10.6)	
Obese III	82 (7.7)	41 (5.5)	
Unknown	31 (2.8)	20 (2.6)	
Smoking status			
Ever	464 (42.5)	356 (46.7)	-0.08
Never	523 (47.9)	341 (44.7)	
Unknown	104 (9.5)	66 (8.7)	
Seropositivity			
Positive	436 (40)	322 (42.2)	0.05
Negative	637 (58.4)	427 (56)	
Unknown	18 (1.6)	14 (1.8)	
ESR, mm/h (n = 905)	24.3 ± 22.4	26.0 ± 25.5	-0.07
CRP, mg/l (n = 940)	12.8 ± 37.9	16.0 ± 30.9	-0.09
RA Outcome Measures			
Disease activity (RAPID 3)			
Unknown	802 (73.5)	553 (72.5)	
(Near) remission	41 (3.8)	36 (4.7)	0.10
Low	44 (4.0)	39 (5.1)	
Moderate	92 (8.4)	50 (6.6)	
High	112 (10.3)	85 (11.1)	
Disease activity (CDAI)			
Unknown	865 (79.3)	615 (80.6)	
Remission	41 (18.1)	28 (18.9)	0.11
Low	68 (30.1)	42 (28.4)	
Moderate	86 (38.1)	45 (30.4)	
High	31 (13.7)	33 (22.3)	
DMARDs (mutually exclusive categories)			
None	197 (18.1)	59 (7.7)	
Conventional regimens			
MTX only	247 (22.6)	213 (27.9)	
Other csDMARD only	265 (24.3)	192 (25.2)	
MTX and other csDMARD	135 (12.4)	119 (15.6)	0.34
Biologic / targeted synthetic DMARD (b/tsDMARD) regimens			
b/tsDMARD only	97 (8.9)	60 (7.9)	
b/tsDMARD and MTX	70 (6.4)	42 (5.5)	
b/tsDMARD and other csDMARD	46 (4.2)	44 (5.8)	
b/tsDMARD and MTX and other csDMARD	34 (3.1)	34 (4.5)	

Numbers are mean ± SD or n (%). Percentages of categorical variable levels are based on observed values. GCs, glucocorticoids; MTX, methotrexate; csDMARD, conventional synthetic disease-modifying antirheumatic drug; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; MDHAQ, Multidimensional Health Assessment Questionnaire; HAQ, Health Assessment Questionnaire.

*The Area Deprivation Index measures socioeconomic disadvantage in 9-digit zip codes based on neighborhood income, education, employment, and housing quality domains (ranging from 1-100 with higher scores indicating more deprivation).

Table 2. Time from first glucocorticoid claim to first rheumatologist rheumatoid arthritis code and average daily dose of continuous GC user groups at different time points.

	N (%)	Days between first GC claim to index date (mean ± standard deviation)	p	Average daily GC dose*	p
All GC initiators	763 (100%)	-16.2 ± 58.3	-	5.4 ± 4.6	-
Chronic GC users (mutually exclusive categories)					
<3 months after first GC claim	231 (30.3%)	10.9 ± 68.5	<0.01	8.0 ± 6.5	<0.01
≥3 to <6 months after first GC claim	150 (19.7%)	-11.3 ± 58.2		4.3 ± 2.8	
≥6 to <12 months after first GC claim	226 (29.6%)	-26.7 ± 47.5		4.1 ± 2.5	
≥12 months after first GC claim	156 (20.5%)	-45.8 ± 32.4		4.4 ± 2.9	

GC, glucocorticoid; RA, rheumatoid arthritis.

*Mg/d prednisone equivalent. Average daily dose estimated by summing all GC claims during follow-up divided by the number of days covered. Chronic use at 3, 6 and 12 months after initiation was defined by an active GC claim at each time point without a medication gap of >6 months.

estimated by summing total GC dose dispensed over total number of days covered. ANOVA was used to test differences in GC doses and time of GC initiation between patients with different durations of use.

Results: 1854 patients (68% female; mean [SD] age of 75 [8]) with early RA were included, of which 41% initiated GCs. GC initiators and non-initiators were similar in most baseline characteristics (**Table 1**), although data on disease activity was scarce. 65.1% of GC initiators had their first GC claim before the index date (mean [SD] time from first GC claim to index date: -16.2 [58.3] days). Of 497 patients with a GC claim before the index date, 63.6% received their first prescription from a non-rheumatologist. Among 763 GC initiators, 69.7%, 49.9%, and 20.5% became chronic GC users at 3, 6 and 12 months after their first GC claim. Longer duration of GC use was associated with a longer time between the first GC claim and the index date (**Table 2**). Mean GC doses during follow-up were less than 5 mg/d prednisone equivalent for chronic 6- and 12-month users.

Conclusion: Almost half of elderly early RA patients received GCs for their RA, most often prior to the first visit with a rheumatologist. Among patients who initiated GCs, 20% continued to receive them 12 months later. Most of the time doses were low. Initiatives to reduce GC exposure among patients with early RA will likely require close collaboration between rheumatologists and primary care to expedite referrals to rheumatology care.

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Abstract Number: 1851

Healthcare Providers' Experiences of a Mandatory Nationwide Transition to an Adalimumab Biosimilar

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1840–1861) Health Services Research Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Transitioning patients with rheumatic diseases to biosimilars has become common to reduce healthcare costs and improve patient access to biologic therapies. However, it is unclear how the transition process impacts healthcare providers at the frontline of the brand change. This study explores providers' experiences of a nationwide mandatory brand change to an adalimumab biosimilar.

Methods: A nationwide online survey was conducted in Aotearoa New Zealand with rheumatologists, rheumatology nurses, and pharmacists. The transition was the first large-scale nationwide brand change for biosimilars and was anticipated to benefit >700 patients in the first year and reduce administrative burdens by extending authorization renewal durations. The transition occurred between March and September 2022, with data collected between November 2022 and February 2023. Survey items assessed satisfaction with logistics and supply, information and education, support, and administrative workload, on a 0-10 scale, with 10 indicating high satisfaction. Open-ended questions explored changes to workload and what did and did not go well during the transition.

Results: The sample (N = 164) consisted of rheumatologists (n = 39), rheumatology nurses (n = 16), and pharmacists (n = 109), yielding a response rate of 61%, 62%, and 3% for each practicing workforce. The mean [SD] overall satisfaction score with the transition was 5.7 [2.6]. Providers were the least satisfied with training for the biosimilar device (mean [SD] 3.7 [2.8]), information from government agencies (4.4 [2.7]), and administrative workload (4.6 [2.9]) during the transition. Satisfaction with adalimumab safety, efficacy, quality of the device, and the provision of sharps bins, alcohol wipes, and patient support was lower following the transition ($p < .05$ for all). Satisfaction with administrative workload (B = .37, $p < .001$) and training for the device (B = .20, $p = .020$) predicted overall satisfaction. Providers' workload increased during the transition period due to additional patient counseling needs, navigating the initial authorization process, and sourcing resources and information. Participants reported that the transition was complicated by poorly implemented initial authorization processes and loss of the bio-originator patient support program. The citrate-free preservative and longer authorization duration after the transition were viewed positively.

Conclusion: Providers reported increased workload during the transition and less satisfaction with the biosimilar following the adalimumab transition. Provider experiences may be improved by ensuring training for the biosimilar device, maintaining a high-quality patient support program, and ensuring authorization processes function well throughout the transition period.

Disclosure: C. Gasteiger: None; **M. Lobo**: None; **L. Wong**: None; **R. Murdoch**: None; **N. Dalbeth**: Arthrosi, 2, AstraZeneca, 2, Dyve Biosciences, 2, Hikma, 6, Horizon, 2, JW Pharmaceutical Corporation, 2, LG, 2, Novartis, 6, Novotech, 5, PK Med, 2, Protalix, 2, PTC Therapeutics, 2, Selecta, 2, Unlocked Labs, 2.

Abstract Number: 1852

Human Papillomavirus Vaccine Uptakes in Ethnically Diverse Women Living with Systemic Lupus Erythematosus

Sebastian Bruera[1], Yinan Huang[2], Savannah Bowman[1], Maria Suarez-Almazor[3], Grace Lo[1], Maria A. Lopez-Olivo[4] and Sandeep Agarwal[1], [1]Baylor College of Medicine, Houston, TX, [2]Department of Pharmacy Administration, University of Mississippi School of Pharmacy, Oxford, MS, [3]MD Anderson Cancer Center, Houston, TX, [4]The University of Texas, MD Anderson Cancer Center, Houston, TX

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
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Session Time: 9:00AM–11:00AM

Background/Purpose: Women with systemic lupus erythematosus are at an increased risk of infections from the human papillomavirus (HPV) and subsequently HPV-mediated malignancies and genital warts. The HPV vaccine is an effective preventative strategy for these complications; however, the HPV vaccination rate has not been well described in a racially and ethnically diverse patient population in the United States.Furthermore, the attitudes, knowledge, and beliefs of patients towards HPV vaccination has not been described in women with SLE.

Methods: We performed a cross-sectional study in which we enrolled consecutive women with a diagnosis of SLE by 2019 ACR criteria. Eligible women were aged 21-45 years of age without a prior history of cervical cancer or hysterectomy. The Centers for Disease Control (CDC) recommends vaccination up to ages 45 for patients that are high risk for HPV infections. We collected demographics, clinical characteristics, constructs of the Health Belief Model (HBM) (susceptibility, severity, perceived barriers, benefits, cues to action, and self-efficacy). Patients answered questions according to the 5-point Likert Scale (1 – Strongly Agree to 5- Strongly Disagree). Answers were reversely coded when necessary and means with standard deviations were generated. Higher means showed an increased perception of an individual construct (i.e. a higher mean for barriers indicates women had perceived barriers for why they did not obtain the HPV vaccine, whereas a higher mean for severity indicates beliefs that there are less consequences from HPV infection). Our primary outcome was self-reported HPV vaccination, as there is currently no approved laboratory study to confirm vaccination status.

Results: We enrolled 75 women. The mean age was 33. Most patients were either black (27%) or Hispanic (44%). Our results showed that only 27% of patients had received HPV vaccination, whereas the remaining 73% either had not received the vaccine or were unsure. There were no associations between HPV vaccination and demographic variables (including race, ethnicity, marital status, insurance, education, and smoking status). With respect to HBM constructs where a value of 3 is neutral, women with SLE had increased perceived barriers (mean 4.0, SD 0.83) and decreased perceived severity (mean 3.25, SD 0.90). Women did not have an increase in the perceived susceptibility (mean 2.4, SD 0.63), benefits (mean 1.9, SD 0.81), self-efficacy (mean 1.96, SD 0.66), and cues to action (mean 1.9, SD 0.43). There were no statistically significant differences in the HBM constructs between vaccinated and non-vaccinated women.

Conclusion: Women with SLE that should consider HPV vaccination by the CDC guidelines are vaccinated at a low rate of 27%. Our HBM model shows that women had increased perceiver barriers to vaccination and had decreased perceived severity about HPV infection. This model suggests that strategies to target the constructs can be used to increase screening in this vulnerable patient population.

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Abstract Number: 1853

Each Joint in a 28 Joint Count Is More Likely to Be Affected by Deformity/Limited Motion Than by Swelling in Rheumatoid Arthritis Patients with Long Disease Duration: Deformity/Limited Motion Should Be Included in Joint Counts Performed in Routine Care

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Background/Purpose: The 28 joint count for rheumatoid arthritis (RA) was designed to recognize 3 abnormalities: swelling, (SWL), tenderness/pain on motion (TEN), and deformity/limited motion (DEF), recorded as total swollen joint count (SJC), tender/pain on motion joint count (TJC), and deformed/limited motion joint count (DJC). In clinical trials over 6-12 months, DJC generally is omitted, appropriately, as the aim is to assess reduction of inflammation by active vs control treatments in groups of selected patients. However, omission of DJC has been extended to most long-term routine care and longitudinal

Number of patients (total=104) with involvement of specific joints or joint groups included in the 28 joint count with swelling (SJC), tenderness/pain on motion (TJC), and/or deformity/limited motion (DJC)

Joint or joint group	SJC positive	TJC positive	DJC positive
Total mean	1.8	3.9	**5.5**
Total median	0	2	**4**
R mcp*	10	22	**52**
R pip*	21	30	**48**
L mcp*	21	32	**46**
L pip*	6	16	**27**
L wrist	32	40	**64**
R wrist	27	39	**67**
L shoulder	1	**32**	24
R shoulder	3	**38**	36
L elbow	7	**17**	10
R elbow	9	**21**	14
L knee	13	**40**	28
R knee	6	**37**	24
TOTAL			

Highest total in bold
*=Median of 5 joints

Number of patients (total=104) with involvement of specific joints or joint groups included in the 28 joint count with swelling (SJC), tenderness/pain on motion (TJC), and/or deformity/limited motion (DJC) Highest total in bold *=Median of 5 joints

databases, potentially underestimating the severity of patient status. We compared the likelihood of SWL, TEN and DEF in individual joints in 28 joint counts which were assessed in RA patients who had been treated over long periods.

Methods: A standard 28 joint count was performed at a routine care visit of 104 RA patients who had been treated over long periods, in which SWL, TEN and DEF were recorded for each joint. The total SJC, TJC, and DJC was recorded as totals of SWL, TEN and DEF in each of the 28 joints. The numbers of SWL, TEN and DEF of wrists, elbows, shoulders and knees were calculated for individual joints. Median values for 5 each of left (L) and right (R) interphalangeal (PIP) joints and metacarpophalangeal joints (MCP) were calculated to represent these joints.

Results: The study included 104 patients with mean and median age of 59.9 and 61.3 years and mean and median disease duration of 11.6 and 10.0 years, respectively. The mean and median total SJC was 1.8 and 0, TJC 3.9 and 2, and DJC 5.5 and 4, respectively (Table). The highest levels for all joint abnormalities were seen in wrists and lowest in elbows, although differences were not large. DEF was higher than SWL for all joints and joint groups included in the 28 joint count (Table). DEF was also higher than TEN for all 20 PIP and MCP joints (only 4 medians are included in the table) and wrists; TEN was marginally higher than DEF for shoulder, elbow, and knee joints.

Conclusion: Patients treated in the biological era with median disease duration of 10 years have low total SJC, reflecting excellent control of inflammation. However, joint deformity (and tenderness) are considerably more prevalent than swelling. Omission of deformity/limited motion, as is appropriately usual in clinical trials, in long-term care and longitudinal databases may give inappropriately favorable impressions of long-term RA outcomes. It is suggested that DJC be included in all formal joint counts in routine clinical care and long-term databases.

Disclosure: R. Hunter: None; **N. Rodwell**: None; **T. Pincus**: None.

Abstract Number: 1854

What Is Our Regional Delay to Diagnosis in Patients with Axial Spondyloarthropathy - Are We Hitting the Target? Data from a Multi-centre UK Patient Cohort

Gurdeep Dulay[1], Antoni Chan[2], Catherine Boys[3], Aisling Coy[4], Mary Devin[5], Leslie Goh[6], Arran McDougall[2], Kathryn Rigler[2], Jacqui Tomkins[7], Dinny Wallis[7] and Emma Williams[8], [1]Portsmouth Hospitals University NHS Trust, Portsmouth, United Kingdom, [2]Royal Berkshire NHS Foundation Trust, Reading, United Kingdom, [3]NHS, Basingstoke, United Kingdom, [4]Salisbury NHS Foundation Trust, Salisbury, United Kingdom, [5]Dorset County Hospital NHS, Dorchester, United Kingdom, [6]NHS, Portsmouth, United Kingdom, [7]NHS, Southampton, United Kingdom, [8]NHS, Winchester, United Kingdom

SESSION INFORMATION
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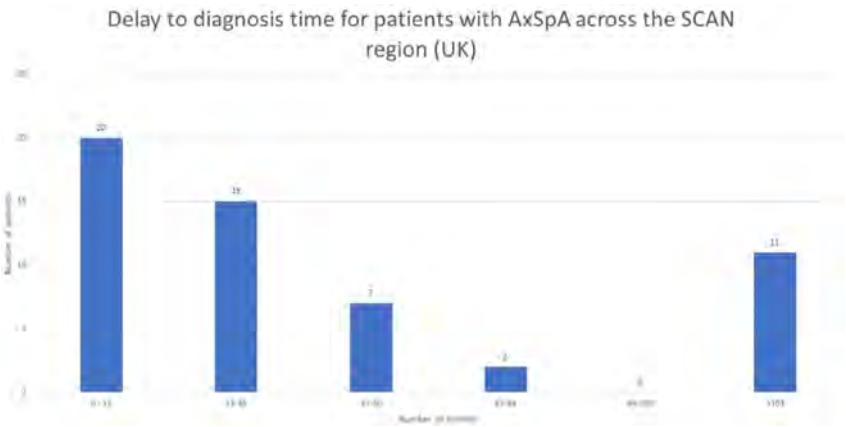
Background/Purpose: Due to the insidious onset of axial spondyloarthritis (AxSpA), there is often a significant delay to diagnosis. The average delay to diagnosis in the UK is 8.5 years. This is associated with several adverse sequelae including poor disease-related quality of life and worse overall health outcomes. In addition, there are substantial health-economic costs associated with this. Recent modelling data in the UK, commissioned by the National Axial Spondyloarthritis Society (NASS), demonstrated the average financial cost of this delay to be £196,000 ($243,000 US) per person affected. There is now a focus on reducing diagnostic delay for patients with AxSpA. The South Central Axial Spondyloarthritis Network



A summary of the length of time taken for patients to receive a diagnosis of AxSpA. 55 patients from 6 different hospitals across the SCAN region (UK).

(SCAN) is a network of NHS (National Health Service) Rheumatology departments in hospitals across south-central UK. The group is multidisciplinary.

Methods: We undertook a retrospective data collection of 5-10 sequential cases of newly diagnosed AxSpA from 6 different regional hospitals within the SCAN network. A total of 55 patient cases was included in this cohort. We categorised data in terms of length of delay to diagnosis from first symptom onset. A primary aim was to establish what proportion of our regional patient cohort received a diagnosis within 1 year of first symptom onset. This target aligns with the target set by NASS (UK) and represents the world's first gold standard time to diagnosis of 1 year. Data was also collected about gender and age at diagnosis.

Results: Based on this representative sample from our region, the gold standard time to diagnosis (within 1 year) is being acheived in 36% of our patient cohort. A further significant proportion of patients (27%) received a diagnosis between 13-36 months following first symptom onset. However, 20% of patients in our cohort are waiting longer than the national average of 8.5 years (or 103 weeks) before receiving a diagnosis of AxSpA.

One-third of our patient cohort (33%) were female. The average age of the patients at the time of diagnosis was 36.8 years.

Conclusion: Whilst acknowledging the relatively modest size of the sample, this regional multicentre dataset has allowed us to establish that 36% of our patient cohort achieved a gold standard time to diagnosis (within 1 year of first symptom onset). The majority of patients (63%) received a diagnosis within 36 months of first symptoms onset. it is important to also highlight that 20% of patients endured a longer than UK national average delay to diagnosis (>103 months/ >8.5 years).

We are aiming to improve our delay to diagnosis by introducing a standardised regional referral proforma for patients with suspected AxSpA. This can be used in primary care to guide clinicians and facilitate earlier referral to Rheumatology. The aims of this intervention would be to increase the proportion of patients achieving a gold standard time to diagnosis and reduce the proportion of patients in all the other time categories, especially those patients with the longest delay to diagnosis. By sharing this work we hope that other global colleagues may also review their own local data and consider service improvement initiatives to reduce delay to diagnosis for patients with AxSpA.

Disclosure: G. Dulay: AbbVie/Abbott, 6, Eli Lilly, 6, Janssen, 12, Advisory board meeting, Novartis, 6, UCB, 12, Fees paid to attend congress meetings; **A. Chan**: None; **C. Boys**: None; **A. Coy**: None; **M. Devin**: None; **L. Goh**: None; **A. McDougall**: None; **K. Rigler**: None; **J. Tomkins**: None; **D. Wallis**: None; **E. Williams**: Eli Lilly, 6, nordic pharma, 6, Novartis, 6.

Abstract Number: 1855

Using a Whole-population Approach to Help Design More Effective and Efficient Healthcare Services for People with Fibromyalgia

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SESSION INFORMATION
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Background/Purpose: A large body of evidence has informed, internationally, management recommendations for people with fibromyalgia. However there are very few studies which have examined how best to design services to deliver effective care. Much of the available evidence characterising the health and use of health services for people with fibromyalgia comes from small studies or in highly-selected groups. The use of routinely collected health data offers the possibility of large and unselected samples to better quantify the characteristics of people with fibromyalgia and their use of health services.

Methods: A case-control study of patients with fibromyalgia using deidentified National Health Service health and care data held in the Secured Anonymised Information Linkage (SAIL) databank for the whole population of Wales. Individuals ≥18 years and with a code present for fibromyalgia in their primary care records between 2004-18 formed the case group. Each case was matched with up to four controls: by sex, age; socio-economic status and with a code for any health care use within 30 days of the code date of the case. We analysed past events in their primary care record for cases and controls.

Results: 19,742 cases and 76,746 controls were included in this analysis. The vast majority of cases were female (89%) and had a median age of 48 years. The mean BMI was higher in cases (30.3 v. 28.8 kgm^{-2}) who were also more likely to have smoked (73 v. 68%), and have comorbidities (with the exception of cancer) (Table 1), specifically Inflammatory Arthritis (5.4 v. 2.2%) and Inflammatory Bowel Disease (1.9 v. 1.1%) . Depression/anxiety was recorded in 74% of cases, while sleep disorders were also common (24.8%). The use of anti-depressants was near universal in people with fibromyalgia (95%), opiates prescription common (82%), while gabapentin was used by 51% and steroids by 44%. Codes for tress and

Table 1: Prevalence of comorbidities in cases (fibromyalgia) and controls

	Cases (n= 19,742)	Controls (n= 76,746)	Difference (95% CI)
Hypertension	26.3%	25.0%	1.3% (0.6 to 2.0)
Hyperlipidaemia	12.3%	9.0%	3.4% (2.9 to 3.9)
Cardiovascular Disease	7.1%	5.6%	1.5% (1.1 to 1.9)
Diabetes	11.7%	10.0%	1.8% (1.3 to 2.3)
Cancer	9.0%	10.3%	-1.3% (-1.7 to -0.8)
Kidney disease	0.2%	0.1%	0.1% (0.02 to 0.2)
Digestive disorders (general)	77.6%	58.5%	19.0% (18.3 to 19.7)
Irritable bowel syndrome	23.7%	10.1%	13.6% (12.9 to 14.2)
Inflammatory bowel disease	1.9%	1.1%	0.8% (0.6 to 1.0)
Inflammatory arthritis	5.4%	2.2%	3.2% (2.9 to 3.6)
Respiratory conditions	12.5%	7.2%	5.3% (4.8 to 5.8)

Table 2: Referral to specialist outpatient one year pre-fibromyalgia diagnosis (cases) and index date (controls)

	Cases (%) (n = 19,742)	Controls (%) (n = 76,746)	Difference (%) 95% CI
Cardiology	19.1%	9.4%	9.7 (9.1 to 10.3)
Dermatology	23.8%	14.1%	9.7 (9.1 to 10.4)
Gastroenterology	17.8%	7.7%	10.1 (9.6 to 10.7)
Genitourinary Medicine	0.1%	0.1%	0.0 (-0.02 to 0.1)
Haematology	8.3%	4.9%	3.4 (3.0 to 3.9)
Renal medicine	1.9%	1.6%	0.3 (0.1 to 0.5)
Neurology	19.9%	6.6%	13.3 (12.8 to 13.9)
Neurophysiology	5.6%	1.7%	3.9 (3.6 to 4.3)
Oncology	0.7%	0.7%	0.0 (-0.1 to 0.2)
Ophthalmology	0.1%	0.1%	0.0 (-0.04 to 0.1)
Pain management	13.4%	2.1%	11.3 (10.7 to 11.7)
Physiotherapy	2.4%	1.6%	0.8 (0.5 to 1.0)
Psychotherapy	0.3%	0.1%	0.2 (0.1 to 0.3)
Radiology	1.5%	0.8%	0.7 (0.6 to 1.0)
Respiratory Medicine	10.3%	4.8%	5.5 (5.1 to 6.0)
Rehabilitation	6.6%	1.5%	5.1 (4.7 to 5.5)
Rheumatology	5.6 %	1.7%	3.9 (3.6 to 4.3)
General Surgery	47.0%	27.3%	19.7 (18.9 to 20.5)
Orthopaedics & trauma	49.2%	26.8%	22.4 (21.7 to 23.2)
Gynaecology (female patients)	46.8%	28.7%	18.1 (17.4 to 19.0)

bereavement (27.2 v. 17.6%) and specifically adverse life events (10.7% v. 8.8%) were significantly more common in cases. In the year prior to diagnosis referrals to 17 out of the 20 specialties examined were more common in cases – particularly for Gastroenterology, Neurology, Pain Management, General Surgery and Orthopaedics (Table 2). Only 1 in 20 of cases have been referred to Rheumatology prior to the first recording of fibromyalgia in their records, however almost half had been referred to each of General Surgery, Orthopaedics and Gynaecology.

Conclusion: This whole population approach has quantified the burden of comorbidities in people diagnosed with fibromyalgia, and highlighted the very common use of opiates whose use is recommended against. The previously reported role of adversity in the aetiology of the condition is replicated. This large unselected-sample approach offers potential for understanding interactions with healthcare of people before and after diagnosis of fibromyalgia (and relating to these to patient characteristics); investigating the opportunities for harm; and the design of more efficient and effective approaches to their care.

Disclosure: G. Macfarlane: None; **R. Cooksey**: None; **E. Choy**: AbbVie, 2, 6, Amgen, 2, 6, Bio-Cancer, 5, Biogen, 2, 5, Chugai Pharma, 2, 6, Eli Lilly, 2, 6, Fresenius Kabi, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Janssen, 2, Novartis, 5, Pfizer, 5, 6, R-Pharm, 2, Sanofi, 2, 5, 6, Sanofi-Genzyme, 2, UCB, 2; **R. Hollick**: CSL Vifor, 6.

Abstract Number: 1856

Improving Recombinant Zoster Vaccination Rates in Patients Receiving Immunosuppressive Therapy in the Rheumatology Clinic at the Orlando VA Healthcare System – a Quality Improvement Project

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SESSION INFORMATION

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Background/Purpose: Herpes zoster is a painful rash that involves one to three adjacent dermatomes, secondary to reactivation of latent varicella-zoster virus (VZV). About 95% of the U.S population has been exposed to VZV, and therefore are at risk of developing herpes zoster. Many patients with rheumatologic conditions are at higher risk for herpes zoster and related complications.

Since 2017, The Centers for Disease Control and Prevention has recommended the 2-dose series recombinant zoster vaccination (RZV) in all immunocompetent adults aged ≥50 years. In 2021, this recommendation was expanded to include adults aged ≥18 years who are or will be immunodeficient or immunosuppressed because of disease or therapy. This recommendation includes patients with rheumatologic conditions or patients on immunosuppressive medications. This Quality Improvement project was designed to increase the RZV vaccination rate to 50% in patients receiving immunosuppressive therapy in the rheumatology clinic at the Orlando VA Healthcare System.

Methods: We identified patients aged ≥18 years who were prescribed biologics, Janus Kinase (JAK) inhibitors and/or conventional synthetic disease modifying antirrheumatic drugs (csDMARDs), from 2/2021 until 2/2022, who had not received RZV vaccination. We conducted a root cause analysis to identify barriers for RZV vaccination. Our interventions included a visual aid in patient rooms encouraging patients to ask about RZV vaccination, pre-visit screening for RZV vaccination done by nurses and providers, set up a process on how to order RZV vaccine in satellite clinics, presentation to rheumatology faculty about baseline metrics, and providing education on the RZV vaccine at each clinic visit. We then obtained follow-up data from 5/2022 until 4/2023.

Results: A total of 808 patients aged ≥18 years who were prescribed immunosuppressive medications in the rheumatology clinics from 2/2021 until 2/2022 were identified. Of these patients, 67% (n=540) had not received RZV vaccination, and 418 of these patients were ≥50 years of age. Therefore, only 33% of our patients on immunosuppressive therapy have been appropriately vaccinated against VZV.

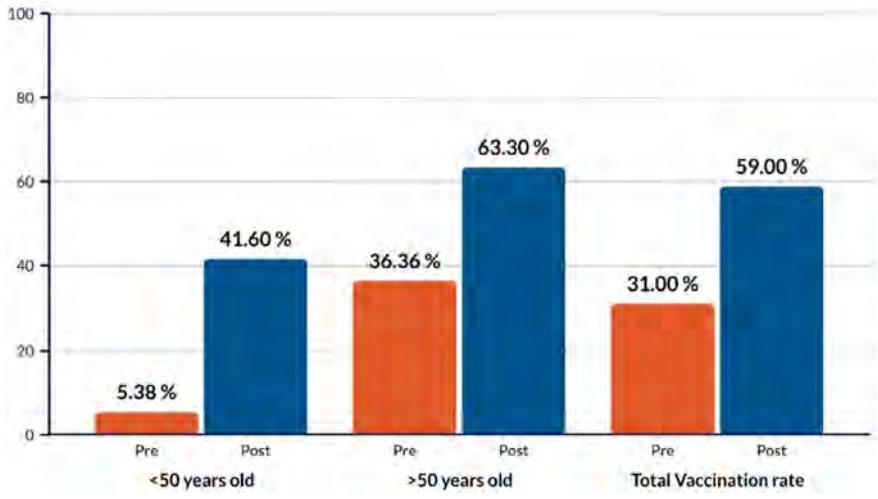

Figure 1. Percentage of RZV vaccination rate

After our intervention, we identified 761 patients aged ≥18 years who were prescribed biologics or JAK inhibitors from 5/2022 until 4/2023. Of these patients, 41% (n=309) had not received RZV vaccination and 229 of these patients were ≥50 years of age. Therefore, RZV vaccination rate increased from 33% to 59% (Figure 1).

There is a numerically increase of the percentage of immunosuppressed patients who have been appropriately vaccinated against VZV. The total of patients in the pre-intervention group is higher than post-intervention, and this could be related to changes in medication regimen or geographic relocation.

Conclusion: Results from our quality improvement project showed increase in the RZV vaccination rate in the rheumatology clinics at the Orlando VA Healthcare System. This initiative requires continuous awareness from the rheumatology providers and nurses to capture those patients that have not been vaccinated against RZV. Future directions include expanding this initiative to other departments that prescribe immunosuppressive therapy.

Disclosure: K. Camargo Macias: None; **R. Shahu Khal**: None; **A. Schmitz**: None; **K. McCabe**: None; **T. Kann**: None; **M. Mosquera**: None; **A. Komarla**: None.

Abstract Number: 1857

More Than 50% of Rheumatoid Arthritis (RA) Patients with High or Moderate CDAI (clinical Disease Activity Index) Screen Positive on MDHAQ (multidimensional Health Assessment Questionnaire) Indices for FAST4 (fibromyalgia Assessment Screening Tool) And/or MDS2 (MDHAQ Depression Screen)

Juan Schmukler and Theodore Pincus, Rush University Medical Center, Chicago, IL

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1840–1861) Health Services Research Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Treat to target in rheumatoid arthritis (RA) suggests escalation of therapy in patients whose scores are high or moderate on a disease activity index such as the Clinical Disease Activity index (CDAI), although exceptions are recognized according to shared decisions. Individual RA clinical core data set measures and indices may be elevated by non-inflammatory comorbidities such as fibromyalgia (FM) and depression (DEP), independent of disease activity (ACR Open Rheum. 2022. Semin Arth Rheum. 2023;58:152151).Most studies are retrospective using various patient questionnaires to recognize DEP or FM. A Multidimensional Health Assessment Questionnaire (MDHAQ) contains indices to screen for FM, Fibromyalgia Assessment Screening Tool (FAST4) and DEP, MDHAQ Depression Screen (MDS2-) on a single questionnaire, in addition to RAPID3 to assess clinial status. We performed a cross sectional study to analyze the prevalence of FM and DEP in RA patients in different CDAI categories.

Methods: A cross-sectional study was performed in unselected RA patients at a routine care visit. All patients completed an MDHAQ, which includes the FAST4 and MDS2 indices.A 28 swollen joint count (SJC), 28 tender joint count (TJC), 0-10 global assessments of patient (PaGA) and physician (PhGA) were assessed to calculate a 0-76 CDAI. The proportion of patients who screened positive (+) or negative (-) for FM on FAST4 and/or DEP on MDS2 were analyzed according to CDAI remission/low (R/L) vs moderate/high (M/H) categories. Chi-square tests were used to assess statistical significance.

CDAI n=104	FAST4 FM- MDS2 Dep- n (row%)	FAST4 FM+ and/or MDS2 Dep+ n (row%)	Total
Total	79	25	104
Remission/Low (R./L)	49 (96%)	2 (4%)	51
Moderate/High (M/L)	30 (57%)	23 (43%)	53
	p <0.0001		
Remission/Low SJC <2	47 (96%)	2 (4%)	49
Remission/Low SJC ≥2	2 (100%)	0	2
Moderate/High SJC <2	15 (52%)	14 (48%)	29
Moderate/High SJC ≥2	15 (63%)	9 (37%)	24
	p <0.0001	p=0.27	

Demographic and MDHAQ index data for anxiety, depression, fibromyalgia, and RAPID3 in routine care patients with osteoarthritis or rheumatoid arthritis

Results: The study included 104 RA patients, with median CDAI of 10.5 and interquartile range (IQR) 11.6, classified as moderate disease activity. Among the 104 patients 17 (16%) were FAST4+, 17 (16%) MDS2+, 9 (9%) were FAST4+ & MDS+ (8 each were FAST4+, MDS2- or FAST4-, MDS2+), and 79 (76%) were FAST4-,MDS2-.CDAI R/L activity was seen in 51 (49%) and M/H in 53 (51%) patients. Among the 51 in R/L, 49 (96%, 47% of all patients) were FAST4-,MDS2-, while 2 (4%, 2% of all patients) were FAST4-,MDS2+. Conversely, among the 53 patients in M/H activity, 30 (57%, 29% of all patients) were FAST4-,MDS2-, while 23 (43%, 22% of all patients) were FAST4+ or MDS2+ (or both FAST4+,MDS2+) ($p < 0.0001$) (Table). Further stratification of patients according to CDAI category, SJC of < 2 vs ≥2, and FAST4 and MDS2 status indicated that CDAI R/L patients included 47 FAST4-,MDS2- and with SJC< 2 vs 2 with SJC ≥2, compared to 15 CDAI M/H patients each with FAST4-,MDS2- or FAST4 or MDS2+ ($p < 0.0001$) (Table). By contrast, no significant differences in SJC vs CDAI categories were seen in FAST4+ or MDS2+ patients (p-0.27), although numbers are small.

Conclusion: About half of unselected RA patients seen in routine care who were in M/H CDAI activity screened positive for FM, DEP or both, in contrast to only 4% of those in R/L activity.FM or DEP were screened for on MDHAQ indices FAST4 and MDS2, with minimal extra time required for the physician.Patients in M/H CDAI activity did not differ significantly for SJC < 2 vs ≥2, regardless of FM or DEP status. These findings extend prior evidence that non-inflammatory comorbidities may elevate RA index levels, with implications for treat to target and general rheumatology care.

Disclosure: J. Schmukler: None; **T. Pincus**: None.

Abstract Number: 1858

How Did a Mandatory Switch Policy Influence the Uptake of Adalimumab Biosimilar and Other TNF Inhibitors?

Nick Bansback[1], Michael law[1], Fiona Clemont[2], Mina Tadrous[3], Sandra Blitz[1] and Mark Harrison[1], [1]University of British Columbia, Vancouver, BC, Canada, [2]University of Calgary, Calgary, AB, Canada, [3]University of Toronto, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1840–1861) Health Services Research Poster III
Session Type: Poster Session C
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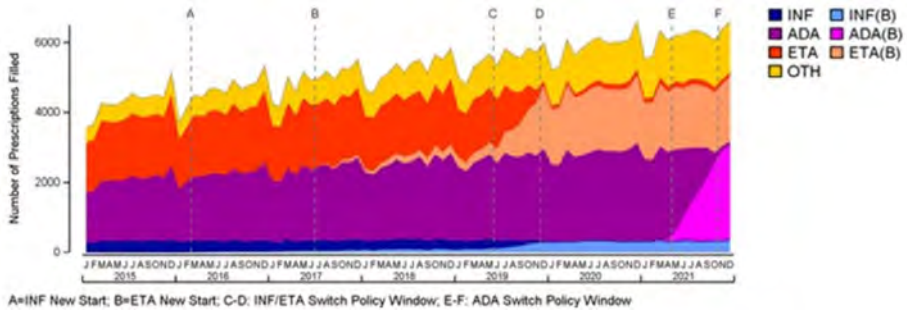
Background/Purpose: In response to the low uptake of biosimilars, British Columbia (BC) in Canada became the first jurisdiction in North America to require patients with inflammatory arthritis to switch to a biosimilar in order to maintain coverage. While the impact of this policy on etanercept (ETA) and infliximab (INF) has been previously reported, this study considered the impact of the policy on adalimumab (ADA) when the biosimilar became available in 2021.

Methods: We used administrative data from British Columbia (Population Data BC) to derive a cohort of patients with inflammatory arthritis being prescribed TNF inhibitor therapy before the policies were introduced. Previously established case definitions including ICD codes were used to establish patients with different inflammatory diseases. The data included both public and private coverage since commercial insurers providing supplementary drug coverage also aligned their policies with the BC Provincial government. Exceptional coverage for reference products was permitted under both biosimilar switching policies if medically necessary. We used descriptive statistics to analyze the trend of uptake pre and post the policy period, and a quasi-experimental interrupted time series analysis to consider the change in trends. We used interrupted time series analysis to estimate biosimilar uptake.

Results: The study identified 11,171 BC residents aged 18 years or older who were using a TNF inhibitor during the study period (01/2015-12/2021). The mean age of the cohort was 54 years and 59% were female. During the first switch policy that included mandatory switches for ETA and INF in 2019, biosimilar prescriptions increased from 7.9% to 35.0% of all TNF prescriptions. After the first switch period, there was a small but consistent decline in overall biosimilar use, with an increase in golimumab and certolizumab prescriptions. During the second switch policy in 2021 which focused on adalimumab, overall biosimilar prescriptions increased from 34% to 72% of all TNF inhibitor prescriptions. In December 2021, 96.4%, 93.0% and 92.0% of prescriptions for ADA, ETA and INF respectively were biosimilar products.

Conclusion: The study findings indicate that a mandatory switch policy for biosimilar adalimumab has been as successful as the policy for infliximab and etanercept achieving high biosimilar use in British Columbia. Prior to the policy, uptake was low indicating the need for such a policy to influence change. Further analysis will explore changes in other healthcare utilization and assess the long-term effects of these policies. These findings are particularly relevant to regions with concentrated insurance systems, as mandatory switching policies could yield greater cost savings.



Utilization of TNF inhibitors - originators and biosimilars - in patients with inflammatory disease over time

Disclosure: N. Bansback: None; **M. law**: None; **F. Clemont**: None; **M. Tadrous**: None; **S. Blitz**: None; **M. Harrison**: None.

Abstract Number: 1859

Examining Hydroxychloroquine Prescribing and SLE Damage in a Statewide Lupus Cohort

Jenna Cormier[1], Bryn Sutherland[1], Yiran Jiang[2], David Gazeley[3], Jonathan Katz[4], Shalvi Parikh[4], Carlos Torres[5], Eden Charles[5], Ang Yu[6], Felix Elwert[6] and Christie M. Bartels[7], [1]Medical College of Wisconsin, Milwaukee, WI, [2]Department of Medicine, Medical College of Wisconsin, Milwaukee, WI, [3]Medical College of Wisconsin, Wauwatosa, WI, [4]Department of Medicine, University of Wisconsin School of Medicine and Public Health, Madison, WI, [5]University of Wisconsin School of Medicine and Public Health, Madison, WI, [6]Department of Sociology, University of Wisconsin, Madison, WI, [7]University of Wisconsin, School of Medicine and Public Health, Madison, WI

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1840–1861) Health Services Research Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a heterogeneous disease that disproportionately affects women, racially and ethnically minoritized populations, and people of lower socioeconomic status (SES). Though SLE diagnosis and treatment have improved, United States health disparities persist. Our prior urban center study showed that living in disadvantaged neighborhoods was one of the strongest factors associated with fewer SLE visits and labs. The current study aimed to expand upon findings by examining SLE across rural, urban and suburban academic institutions in the state to identify care gaps and damage.

Methods: Our cohort included patients with prevalent SLE and at least one rheumatology and one primary care visit at one of three tertiary care centers in a Midwest state: urban, suburban, and rural populations. Process measures included receipt of any hydroxychloroquine (HCQ) (or documented contraindication or intolerance) and HCQ adherence defined as prescriptions covering >/=80% of calendar days (2014). Primary outcomes were time to new SLICC damage index (SDI) events or death 1/1/2015-12/31/2020. Processes and outcomes were reported by race, ethnicity, and Area Deprivation Index (ADI), a composite of 17 variables depicting neighborhood disadvantage. Data were analyzed using descriptive statistics and Cox proportional-hazards models.

Results: A total of 954 SLE patients were identified. Most were female (90.58%) and White (73.06% vs 21.28% Black; Table 1). Average age at SLE diagnosis was 43.38 (SD 14.92). Patients of Black race were diagnosed at an earlier age (38.23, SD 12.26 vs 45.37, 15.22 White). Most patients of Black race were from the urban site (73.89%). Black patients also had a much higher representation in the most disadvantaged ADI neighborhood quintile (42.25% vs 3.44% White). Antiphospholipid syndrome was more prevalent in White patients (15.20% vs. 9.5% Black); renal disease more prevalent in Black patients (59.61% vs. 29.12% White).

No statistically significant differences in HCQ use were noted by ADI or ethnicity, but compared to White patients, those of Black race had higher rates of prescription or contraindication for HCQ (97.38% vs 92.64 White%, p=0.002). Black patients had 9.37% lower adherence defined by prescriptions covering >/=80% of days (56.45% v. 65.82%, p=0.023). Yet, HCQ adherence did not predict SDI damage (38% with vs 33% without >/=80% HCQ days). Table 2 shows more damage in White and less disadvantaged. Limits include possible selection or follow up bias, and adherence by prescribing data.

Conclusion: SLE patients of Black race were much more likely to live in the most disadvantaged ADI quintile in this cohort. Black patients were more likely prescribed HCQ but less likely to have >/= 80% of days prescribed than White patients. In sum, data showed no significant disparities in HCQ use by neighborhood ADI or ethnicity at these tertiary centers, but did

Table 1. Statewide lupus cohort description (n=954 with complete data)

		Prevalent SLE (n=954) (%)	Black (n=203, 21.28%) (%)	White (n=697, 73.06%) (%)
SLE by ACR Criteria		93.29	93.10	93.26
SLE by SLICC Criteria		92.35	99.01	90.39
Age in 2013 (mean, SD)		47.70 (15.17)	42.45 (12.93)	49.79 (15.31)
Age at SLE diagnosis (mean, SD)		43.38 (14.92)	38.23 (12.26)	45.37 (15.22)
	Late onset (≥50)	31.34	16.75	36.44
SLE duration (median, IQR)		5.27 (5.40)	4.97 (5.66)	5.53 (5.32)
Sex	Female	90.58	91.41	89.90
	Male	9.42	8.59	10.10
Race	White	73.06		100.00
	Black	21.28	100.00	
	Asian	2.83		
	American Indian	0.84		
	Other/Unknown	1.99		
Ethnicity	Hispanic	4.19	1.00	2.87
Medicaid Ever		37.84	75.37	26.26
Payor type	Commercial	49.79	30.05	55.67
	Medicaid	17.71	39.41	10.76
	Medicare	24.32	25.62	24.68
	Other/Unknown	8.18	4.93	8.90
Area Deprivation Index (ADI) Quintile				
	1st (most disadvantaged)	12.47	42.25	3.44
	2nd	14.07	17.65	12.68
	3rd	20.94	12.83	23.32
	4th	32.49	16.58	37.56
	5th (least disadvantaged)	20.02	10.70	23.00
Rural-Urban Commuter Areas				
	Urban Core Area	70.41	98.03	62.36
	Suburban Area	12.59	0.00	16.24
	Large Town Area	9.02	1.48	11.35
	Small Town and Isolated Rural Areas	7.97	0.49	10.06
Rural Site		17.19	2.46	21.23
Suburban Site		42.56	23.65	48.35
Urban Site		40.25	73.89	30.42
Current Smoker		12.58	15.76	12.05
Charlson Comorbidity Index (mean SD)		1.665 (1.49)	1.98 (1.55)	1.57 (1.48)
Antiphospholipid syndrome		13.98	9.55	15.20
Renal disease		36.79	59.61	29.12

show lower prescribed days covered for Black patients possibly reflecting adherence or prescribing differences. No changes in subsequent damage correlated with HCQ prescribed coverage. Future larger studies should investigate long-term associations between damage and adherence and prescribing.

Table 2. Percent Retention & Treatment by ADI Quintile and Racial or Ethnic Group

2a. Retention & Treatment by Least and Most Disadvantaged ADI Quintile (n=284)

	ADI Least Disadvantaged	ADI Most Disadvantaged	p
Hydroxychloroquine (HCQ) Rx, contraind. or intolerance	97.06%	99.02%	0.230
HCQ prescribed	73.84%	75.47%	0.762
HCQ contraindicated	9.14%	6.42%	0.398
HCQ intolerance	11.43%	10.09%	0.723
HCQ adherence by 80% of prescribed days (n=278)	64.85%	59.41%	0.378
New SDI damage events	38.86%	21.10%	0.001

2b. Retention & Treatment by Race (n=900)

	White	Black	p
Hydroxychloroquine Rx, contraind. or intolerance	92.64%	97.38%	0.002
HCQ prescribed	70.53%	72.82%	0.529
HCQ contraindicated	7.17%	5.42%	0.348
HCQ intolerance	12.63%	13.79%	0.67
HCQ Adherence by 80% of prescribed days (n=845)	65.82%	56.45%	0.023
New SDI damage events	41.18%	19.21%	<0.001

2c. Retention & Treatment by Hispanic Ethnicity (n=954)

	Non-Hispanic	Hispanic	p
Hydroxychloroquine Rx, contraind. or intolerance	93.77%	97.37%	0.198
HCQ prescribed	71.16%	75.00%	0.591
HCQ contraindicated	6.67%	7.50%	0.849
HCQ intolerance	12.91%	10.00%	0.558
HCQ Adherence by 80% of prescribed days (n=898)	63.89%	59.46%	0.599
New SDI damage events	36.54%	27.50%	0.224

Abbreviations: ADI=Area Deprivation Index; HCQ=Hydroxychloroquine; Contraind.=contraindication as allergy, retinal toxicity, or cardiomyopathy; Rx=prescription. Intolerance included any other stated reason to not take HCQ.

Disclosure: J. Cormier: None; **B. Sutherland**: None; **Y. Jiang**: None; **D. Gazeley**: None; **J. Katz**: None; **S. Parikh**: None; **C. Torres**: None; **E. Charles**: None; **A. Yu**: None; **F. Elwert**: None; **C. Bartels**: Pfizer, 5.

Abstract Number: 1860

Evaluation of the Receipt of Adequate Pharmacological and Psychological Treatment for Incident Depression and Anxiety in Individuals Living with Inflammatory Arthritis

Alyssa Howren[1], Eric Sayre[2], J. Antonio Avina-Zubieta[3], Joseph Puyat[1], Deborah Da Costa[4], Hui Xie[5], Amit Gupta[1] and Mary De Vera[1], [1]University of British Columbia, Vancouver, BC, Canada, [2]British Columbia Centre on Substance Use, Vancouver, BC, Canada, [3]Arthritis Research Canada, Vancouver, BC, Canada, [4]McGill University, Pointe-Claire, QC, Canada, [5]Simon Fraser University, Richmond, BC, Canada

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: (1840–1861) Health Services Research Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: To describe patterns of pharmacological and psychological treatment and evaluate the receipt of minimally adequate treatment for incident depression and anxiety in individuals with inflammatory arthritis (IA), specifically ankylosing spondylitis (AS), psoriatic arthritis (PsA), and rheumatoid arthritis (RA).

Methods: Our cohort study used population-based linked administrative health databases from Population Data BC to identify individuals (≥18 years)with IA and IA-free controls matched on age, sex, and incident depression or anxiety. We assessed mental health treatment in the first year following incident depression or anxiety and pharmacological treatments were identified using Anatomical Therapeutic Chemical codes for antidepressants and anxiolytics. Psychological treatments were identified using fee-item codes that included publicly funded counselling, psychotherapy, and psychiatrist visits. We defined minimally adequate pharmacological treatment as antidepressant prescriptions filled with ≥84 days of supply. We defined minimally adequate psychological treatment as the receipt of ≥4 counselling/psychotherapy services. Multivariable logistic regression models, adjusted for age, sex, comorbidities, income, and residence, were used to evaluate the odds of individuals with IA receiving minimally adequate pharmacological or psychological care for their incident depression or anxiety as compared to IA-free controls.

Results: Cases of incident depression were identified in 6,951 individuals with IA (mean age 54.8 ± 18.3 years, 65.5% female) and 6,951 IA-free controls (mean age 54.8 ± 18.3 years, 65.5% female). Incident anxiety was identified among 3,701 with IA (mean age 52.9 ± 16.8 years, 74.3% female) and 3,701 IA-free controls (mean age 52.9 ± 16.8 years, 74.3% female) (**Table 1**). More than half of the IA and control study sample with depression had ≥1 antidepressant prescription filled (IA 64.3%; controls 61.4%). Fewer individuals with IA and comorbid anxiety had ≥1 antidepressant (IA 58.5%, controls 54.2%) or ≥1 anxiolytic (IA 46.8%, controls 40.1%) prescription dispensed. The receipt of minimally adequate pharmacological and psychological treatment for depression was observed in 50.5% and 19.6% of those with IA, respectively, with no significant difference compared to controls (pharmacological: adjusted odds ratio [aOR] 1.01, 95% confidence interval [CI] 0.90 to 1.13; psychological: aOR 0.96, 95% CI 0.88 to 1.05). The proportion receiving minimally adequate pharmacological (IA 46.9%, controls 44.1%) and psychological (IA 20.2%, controls 19.0%) treatment for anxiety was also similar between individuals with IA and controls (pharmacological: aOR 0.91, 95% CI 0.77 to 1.08; psychological: aOR 1.04, 95% CI 0.92 to 1.18).

Table 1. Characteristics of individuals with inflammatory arthritis (IA) and IA-free controls with incident depression or anxiety.

	Depression		Anxiety	
Characteristic	**IA (n=6,951)**	**IA-free Controls (n=6,951)**	**IA (n=3,701)**	**IA-free Controls (n=3,701)**
Age, mean (SD)	54.8 (18.3)	54.8 (18.3)	52.9 (16.8)	52.9 (16.8)
Female, n (%)	4555 (65.5)	4555 (65.5)	2751 (74.3)	2751 (74.3)
Charlson-Romano comorbidity index, mean (SD)	0.95 (1.09)	0.32 (0.99)	0.92 (1.03)	0.29 (0.85)
Neighbourhood income quintile, n (%)				
Quintile 1	1585 (22.8)	1495 (21.5)	830 (22.4)	786 (21.2)
Quintile 2	1454 (20.9)	1377 (19.8)	792 (21.4)	718 (19.4)
Quintile 3	1363 (19.6)	1337 (19.2)	697 (18.8)	736 (19.9)
Quintile 4	1349 (19.4)	1327 (19.1)	705 (19.1)	761 (20.6)
Quintile 5	1200 (17.3)	1415 (20.4)	677 (18.3)	700 (18.9)
Residence, n (%)				
Urban	5870 (84.5)	6101 (87.8)	3076 (83.1)	3201 (86.5)
Rural	1081 (15.6)	850 (12.2)	625 (16.9)	500 (13.5)

Descriptive statistics were determined for the year prior to IA index date.
Abbreviations: IA – inflammatory arthritis; SD – standard deviation

Conclusion: A large proportion of individuals with depression or anxiety were not receiving adequate care by means of medications and publicly funded mental health services, regardless of a comorbid IA diagnosis. Exploring methods for rheumatology to facilitate greater access to mental health care is imperative given the increased prevalence and negative impacts of depression and anxiety in this patient population.

Disclosure: A. Howren: None; **E. Sayre**: None; **J. Avina-Zubieta**: None; **J. Puyat**: None; **D. Da Costa**: None; **H. Xie**: None; **A. Gupta**: None; **M. De Vera**: None.

Abstract Number: 1861

Efficacy of Non-pharmacological Interventions: A Systematic Review Informing the 2023 EULAR Recommendations for the Management of Fatigue in People with Inflammatory Rheumatic and Musculoskeletal Diseases

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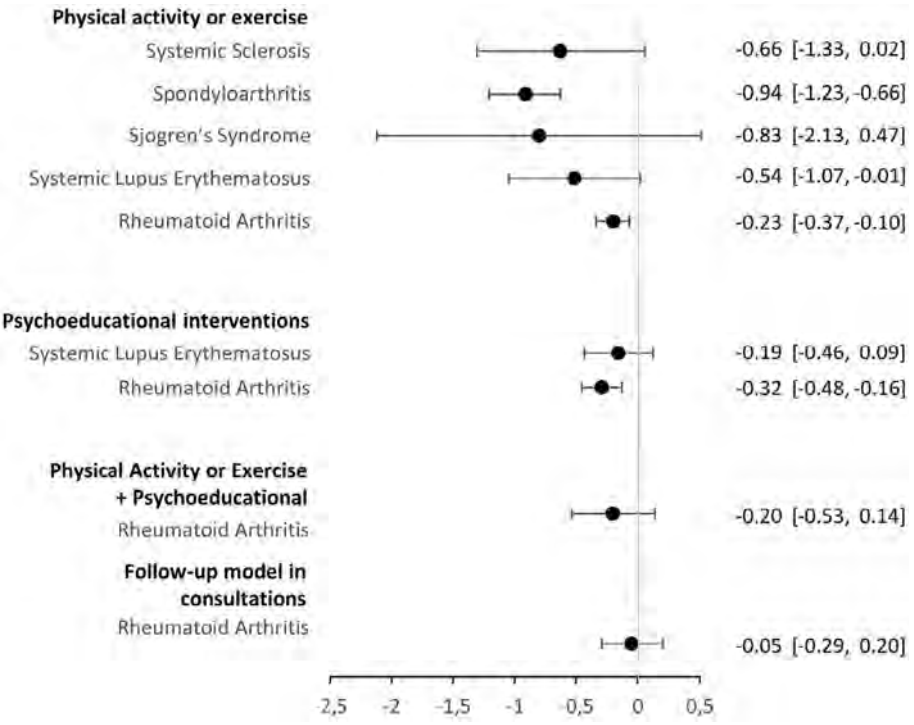
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1840–1861) Health Services Research Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: To identify the best evidence on the efficacy of non-pharmacological interventions in reducing fatigue in people with I-RMDs and to summarise their safety in the identified studies to inform EULAR recommendations for the management of fatigue in people with inflammatory rheumatic and musculoskeletal disease (I-RMD).

Methods: Systematic review of adults with I-RMD conducted according to the Cochrane Handbook. Search strategy ran in Medline, Embase, Cochrane Library, CINAHL Complete, PEDro, OTseeker and PsycINFO. Assessment of risk of bias, data extraction, and synthesis performed by two reviewers independently. Data pooled in statistical meta-analyses.

Results: From a total of 4,150 records, 454 were selected for full-text review, 82 fulfilled the inclusion criteria, and 55 RCTs were included in meta-analyses. Physical activity or exercise were efficacious in reducing fatigue in rheumatoid arthritis (RA) (SMD=-0.23, $p< 0.001$), systemic lupus erythematosus (SLE) (SMD=-0.54, $p=0.04$) and spondyloarthritis (SpA) (SMD=-0.94, $p< 0.001$). A reduction in fatigue was also observed in Sjögren's syndrome and systemic sclerosis, although not statistically significant (SMD=-0.83, $p=0.21$; SMD=-0.66, $p=0.06$, respectively). Psychoeducational interventions were efficacious in reducing fatigue in RA (SMD=-0.32, $p< 0.001$), but not in SLE (SMD=-0.19, $p=0.18$). Follow-up models in consultations and multicomponent interventions reduced fatigue in RA, although the effect was not statistically significant (SMD=-0.05, $p=0.71$; SMD=-0.20, $p=0.24$, respectively) (**Figure**). The narrative results of the RCTs not included in the meta-analysis indicated that several other non-pharmacological interventions were efficacious in reducing fatigue, with reassuring safety results.



Conclusion: Non-pharmacological interventions are efficacious and safe for the management of fatigue in people with I-RMD.

Disclosure: E. Santos: None; **B. Farisogullari**: None; **E. Dures**: None; **R. Geenen**: None; **P. Machado**: AbbVie/Abbott, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Orphazyme, 2, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 6.

Abstract Number: 1862

Significant Overlap of Inflammatory and Degenerative Features on Spinal Imaging Among Patients with Degenerative Spinal Disease, Diffuse Idiopathic Skeletal Hyperostosis and Radiographic Axial Spondyloarthritis

Nelly Ziade[1], Nikolaos Kougkas[2], Melanie Udod[3], Styliani Tsiami[4] and **Xenofon Baraliakos**[3], [1]Saint-Joseph University, Beirut, Lebanon, [2]4th Internal Department, Ippokratio Hospital, Aristotle University of Thesaaloniki, Thessaloniki, Greece, [3]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [4]Ruhr-Universität Bochum and Rheumazentrum Ruhrgebiet, Herne, Germany

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Table. Thoracic and Lumbar Spinal Imaging features in a cohort of 136 patients referred for low back pain.

	DISH	DEGENERATIVE	AS	All	p-value
Total number of patients	**38**	**71**	**27**	**136**	
Thoracic Spine Xray					
Presence of SpA changes, N patients/ All patients in the group (%)	10/36 (27.8)	5/66 (7.6)	3/26 (11.5)	18/128 (14.1)	0.024
Presence of degenerative changes, N patients/ All patients in the group (%)	36/36 (100)	58/66 (87.9)	25/26 (96.1)	119/128 (93.0)	0.055
Lumbar Spine Xray					
Presence of SpA changes, N patients/ All patients in the group (%)	7/32 (21.9)	14/62 (22.6)	11/22 (50.0)	32/116 (27.6)	0.034
Presence of degenerative changes, N patients/ All patients in the group (%)	30/32 (93.8)	58/62 (93.5)	21/22 (95.5)	109/116 (93.9)	1.000

Background/Purpose: Degenerative changes of the spine (DC), diffuse idiopathic skeletal hyperostosis (DISH) and radiographic axial Spondyloarthritis (r-axSpA) may present with overlapping inflammatory and degenerative findings on imaging, which, next to the general symptom of chronic back pain might, represent a challenge for an accurate diagnosis. We aimed to evaluate the distribution of spinal imaging features in a real-life cohort of patients with chronic back pain referred to a tertiary university rheumatology center and identify those associated with DC, DISH or r-axSpA.

Methods: In a cross-sectional analysis of patients with chronic low back pain, demographic and disease data were collected. Imaging of the spine (thoracic or lumbar) and sacroiliac joints was performed per the clinical indication. All images were evaluated by two independent trained readers including erosions, sclerosis, squaring, osteophytes and syndesmophytes on conventional radiographs (CR) and bone marrow edema (BME) or degenerative changes on magnetic resonance imaging (MRI). The final diagnosis made by the rheumatologist at discharge was the gold standard. Data were presented descriptively and compared among the three diagnosis groups (DC, DISH and axSpA).

Results: Among 136 referred patients, 71 had DC, 38 DISH, and 27 r-axSpA. Mean age was 63.2±11.4 (p=0.135 among the three groups), and 86 (63.2%) were males (88.9% in axSpA, p=0.003). Patients had high levels of comorbidities: 91 (72.8%) had hypertension (higher in the DC group, 52 (82.8%), p=0.04), 37 (27.6%) had diabetes (higher in DISH, 39.5%, p=0.012) and 31 (23.3%) were current smokers (higher in axSpA, 53.8%, p< 0.001). Although axSpA-related spinal changes on CR were expectedly more prevalent in the axSpA group (thoracic 14.1%, p=0.024; lumbar 93.9%, p=0.034), they were also present in DISH (27.8% and 21.9%) and DC (7.6% and 22.6%, respectively). DC were present in the three groups in 93.0% in the thoracic and in 93.9% in the lumbar spine, without a statistically significant differences (Table). Similarly, on thoracic and lumbar spine MRI, BME was present in DISH in 33.3% and 41.7% and in DC in 20.4% and 32.7% lumbar spines, respectively.

Conclusion: A significant overlap of inflammatory and degenerative features on spinal imaging among patients with DC, DISH or axSpA was found in this older group of patients. Particularly, r-axSpA-related spinal CR features were found in a fourth of patients with DISH, while MRI BME was found in a third of them.

Disclosure: N. Ziade: Abbvie, 6, Boehringer-Ingelheim, 6, Eli Lilly, 6, Janssen, 6, Newbridge, 6, Novartis, 6, Pfizer, 6, Pierre Fabre, 6, Roche, 6, sanofi, 6; **N. Kougkas**: None; **M. Udod**: None; **S. Tsiami**: None; **X. Baraliakos**: AbbVie, 2, 6, BMS, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, 6, UCB, 2, 6.

Abstract Number: 1863

Immune-mediated Hypertrophic Pachymeningitis: Focusing on the Localization and Volume of Thickened Dura Mater Lesion

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
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Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Hypertrophic pachymeningitis (HP) is a rare inflammatory neurological disorder characterized by the thickened dura mater with extensive tissue fibrosis and immune-mediated inflammation. Notably, headaches and cranial neuropathies are frequently observed in immune-mediated HP, which is attributed to antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis or IgG4-related disease as the common underlying diseases. However, it is still obscure how the volume and localization of HP lesions affect the development of the relevant neurological impairments. This study evaluated the quantification and localization of the thickened dura mater and analyzed their impact on clinical findings in immune-mediated HP.

Methods: We evaluated the volume of the contrast-enhanced dura mater on magnetic resonance imaging in 19 patients with HP, including 12 with ANCA-related, 4 with IgG4-related, and 3 with idiopathic HP, by the imaging feature quantification system. We enrolled 10 patients with multiple sclerosis (MS) as controls. In patients with HP, the impacts of HP volume on neurological symptoms and cerebrospinal fluid (CSF) laboratory markers were statistically analyzed. The receiver operating characteristic (ROC) curve analyses were also performed to detect the cut-off volume of the contrast-enhanced dura mater.

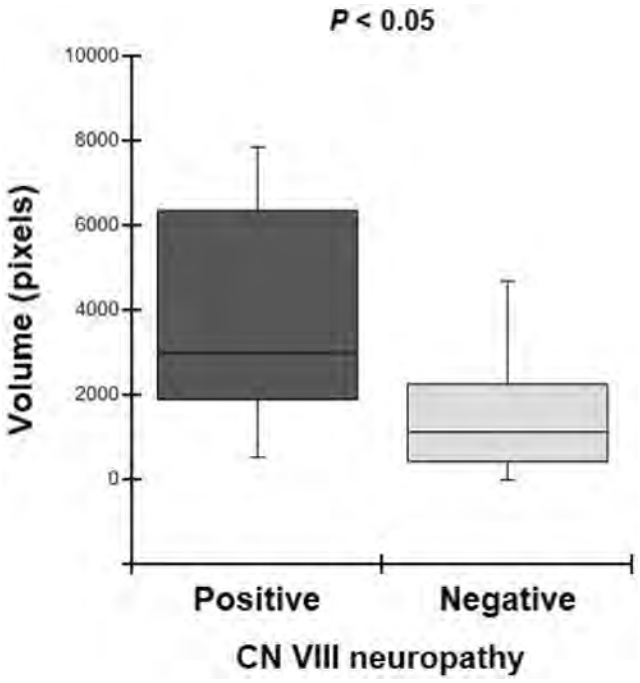

Figure 1: The volume of the thickened dura mater in the cranial fossa between patients with and without cranial nerve (CN) VIII neuropathy

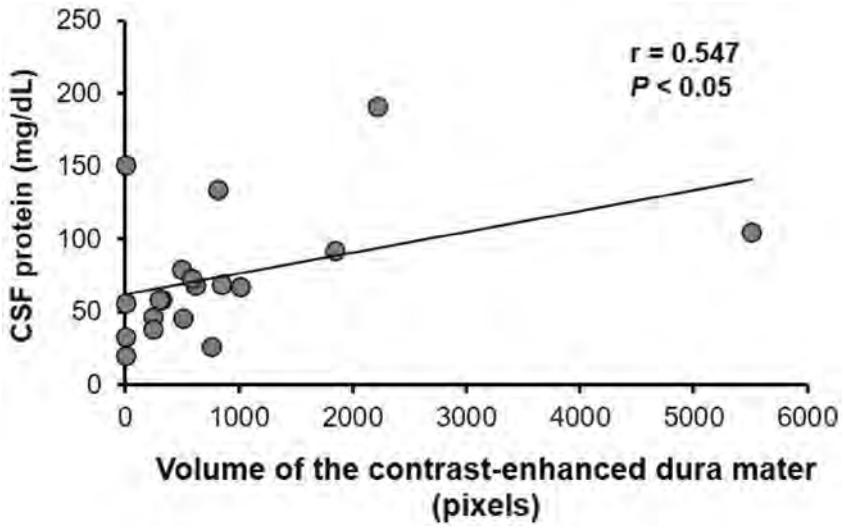

Figure 2: Correlation between the volume of the thickened dura mater in the tentorium cerebelli and cerebrospinal fluid (CSF) protein levels

Results: Patients with HP demonstrated significantly higher volumes of the contrast-enhanced dura mater in the convexity, cranial fossa, and tentorium cerebelli than those with MS ($P < 0.01$). Of the 19 patients with HP, more than the cut-off volume in the convexity, cranial fossa, and tentorium cerebelli was observed in 16 (84%), 12 (63%), and 15 (79%) patients, respectively. Meanwhile, the volume of the contrast-enhanced dura mater was not significantly different among patients with ANCA-related, IgG4-related, and idiopathic HP. In patients with HP, those with cranial nerve (CN) VIII neuropathy had a significantly higher volume of the contrast-enhanced dura mater in the cranial fossa than those without CN VIII neuropathy ($P < 0.05$) (**Fig. 1**). The cut-off volume in the cranial fossa was more frequently exceeded in patients with CN VIII neuropathy than in those without CN VIII neuropathy. A positive correlation between the volume of the contrast-enhanced dura mater in the tentorium cerebelli and CSF protein levels was significantly observed in patients with HP ($P < 0.05$) (**Fig. 2**).

Conclusion: HP lesions in the cranial fossa may be robustly implicated in impairing CN VIII. The enlargement of HP lesions in the tentorium cerebelli can increase CSF protein levels. This study suggests that quantification of the thickened dura mater is useful for elucidating the relationship with the clinical findings in immune-mediated HP.

Disclosure: Y. Shimojima: None; **J. Ikeda**: None; **Y. Sekijima**: None.

Abstract Number: 1864

Quantifying Inflammation: A Novel *In-Vivo* Total Body PET Imaging Tool to Determine the Kinetics of the Degree of Changes in Inflammation in Different Time Points

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Collagen-induced arthritis (CIA) mouse model is one of the best recognized animal model for autoimmune diseases. In this model clinical methods of evaluating inflammation and its severity are flawed due to observer bias; for histological studies mice need to be sacrificed so longitudinal studies in the same mouse cannot be performed. The hypothesis of our study was that as by PET imaging the degree of inflammation can be quantified so in a CIA mouse model by total body PET (TB-PET) imaging (i) we should be able to quantify the total inflammatory burden (SUVmax) to determine the kinetics of the degree of changes in inflammation with the progress of the disease (ii) this will allow to perform longitudinal studies to determine the efficacy of novel drugs within days.

Methods: Arthritis was induced using bovine type II collagen in DBA/1J mice (n=40) as per the standard protocol; mice developed arthritis around Day 28. The mice (n=10) had weekly PET imaging that is on day 28, day 35, day 42, and day 56. The maximum ^{18}F-FDG uptake (SUV score) was determined for the most severe joint in each mouse to generate a comprehensive**PET score (PS).** To further evaluate about applications of this model for quantitative longitudinal studies for therapeutic response 15 mice were treated with mouse anti-IL-23 mab; these mice received anti-IL23 mab weekly injections of 100ug/mouse for 4 weeks (Day35, Day42, Day49and Day56). Mice were scored clinically and scanned on these days and on day 63 one week after completion of the 4th dose. Mice (n=5) were additionally scanned on "day 5" and on "day 10" to determine early clinical response of IL-23p19 antibody.

Results: The clinical scores (CS) as well the **PET scores (PS)** for arthritis in the untreated mice gradually increased with time. The median clinical score**(CS)**increased with time to 2, 2.5, 3, 3.5 and 3 respectively on day 28, 35, 42 and 56. The PS SUV score (SUVmax) on Day 0 was 1.02. PS median values compared to the Day "0" increased to 1.52 on day 28 ($p< 0.05$), 3.5 on day 35 ($p< 0.05$),4.5 on day 42 ($p< 0.05$) and 3.5 on day 56 ($p< 0.05$). Our results confirm that the kinetics of the total inflammatory load can be quantified at different time points. The murine anti-IL-23 mAb treatment provided expected results, with time CS reduced from 7.3±1.8 (n=12) on day 35 to 2.8±1.1 (n=12) on day 63 ($p< 0.001$). Quantified *in vivo* PS median values as well showed improvement, PS (SUVmax) median values compared to the day 35 (before treatment) in this longitudinal study decreased with time: 2.0 on day 35 (before treatment), 1.8 on Day 40, 1.5 on Day 45 ($p< 0.05$), and 1.3 on day

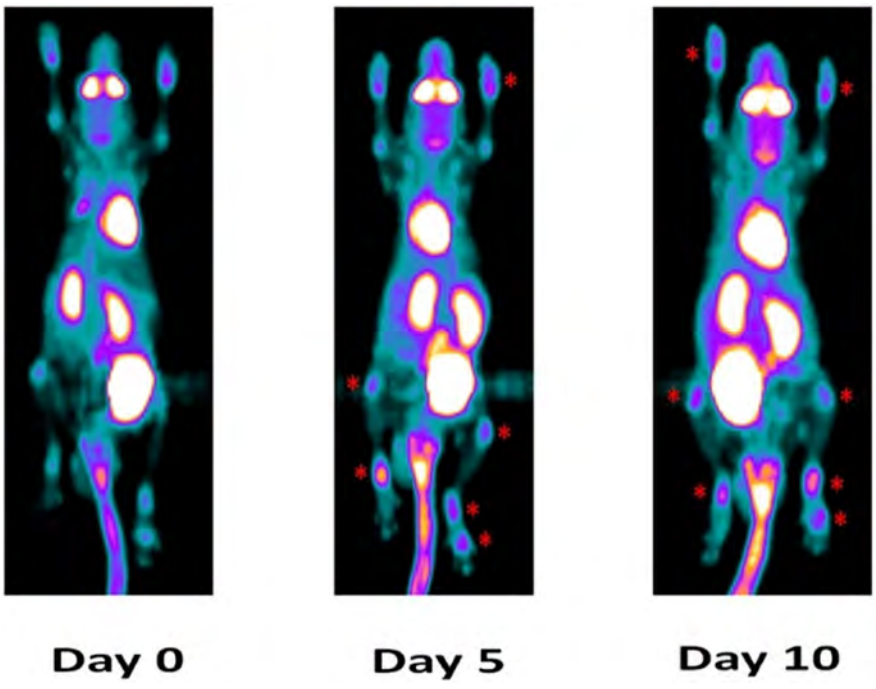

Figure 1. Untreated mice displayed increased inflammation on limb joints with increased PET signaling as marked by the red stars. This mouse not treated with anti-IL-23p19 mAb in longitudinal study by PET imaging demonstrated a progressive increase of PET signaling that is higher degree of inflammation on both fore and hind limb joints on Day 5 and Day 10.

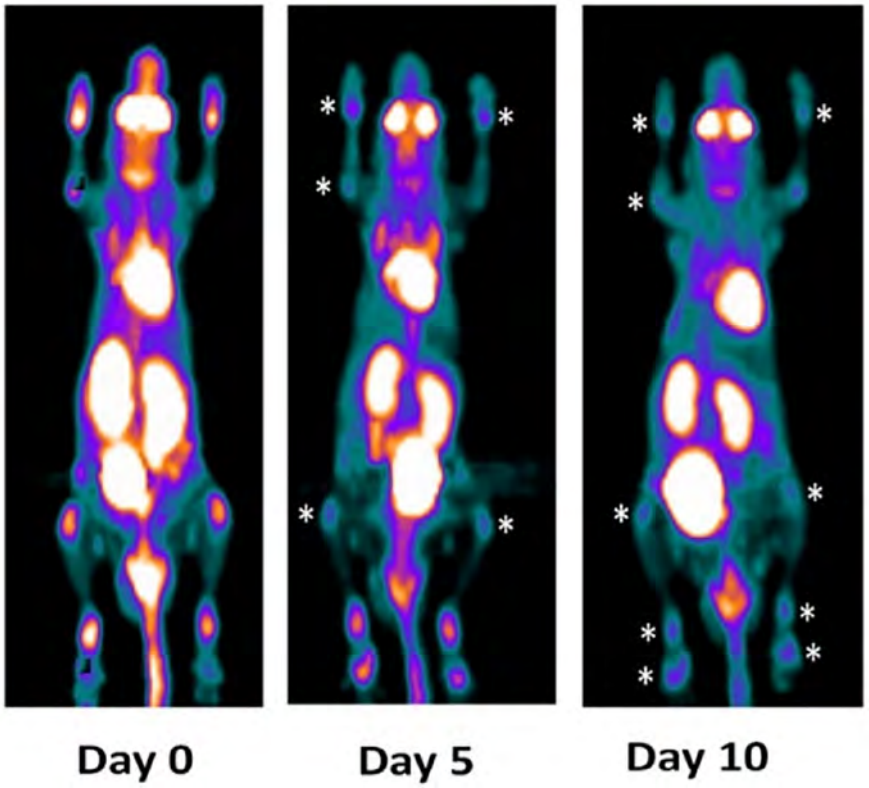

Figure 2. Efficacy of anti-IL23 mab could be identified as early as on the day 5 as identified by the white stars. This mouse treated with anti-IL-23 mAb in longitudinal study by PET imaging demonstrated progressive reduction of PET signaling that is the degree of inflammation on both fore and hind limb joints on Day 5 and Day 10.

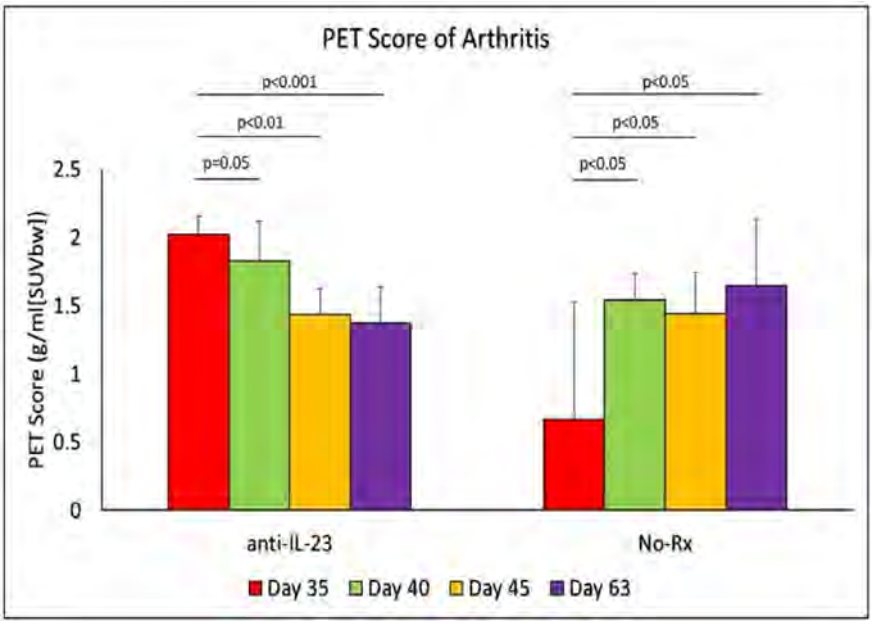

Figure 3. PET Score (SUVmax) of Arthritis with and without treatment: Change in PET Score (SUVmax) over the study to demonstrate the change in inflammation in treatment against the control group. Day 35 was the beginning of anti-IL23 antibody treatment and imaging, with further imaging on days 40, 45, and 63. Mice without any treatment showed significant increase in inflammation, while mice with anti-IL-23 antibody treatment demonstrated significant decrease of inflammation.

63 ($p < 0.05$) (Figure 1,2,3). These results demonstrated the unique quantifiable measures of therapeutic efficacy of anti-IL-23 mAb.

Conclusion: Our results demonstrate the quantification of the kinetics of degree of change in inflammation provided by the PET-CIA model; while the mice treated with mAb showed therapeutic efficacy as early as on the Day 5 (Figure 2,3). Thus, this model will be a novel tool for monitoring inflammatory load and a unique tool to evaluate efficacy or resistance to therapies during early stages of treatment. With time we are transferring these observations to quantify the degree of inflammation in human with RA and PsA.

Disclosure: S. Raychaudhuri: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, SUN Pharma, 2, 5, 6, UCB, 2, 5, 6; **S. Raychaudhuri**: None; **N. Chandrasekar**: None; **C. Abria**: None; **S. Banerjee**: None; **S. Raychaudhuri**: None; **A. Chaudhari**: None.

Abstract Number: 1865

Is Flexion Contracture in Knee Osteoarthritis Associated with MRI Pathologies over Time? Data from the Osteoarthritis Initiative

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SESSION INFORMATION
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Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Knee flexion contracture (FC) is associated with worse clinical outcomes in those with knee OA. Cross sectional data demonstrated that knee FC was associated with non-specific widespread MRI degenerative changes[1]. To our knowledge, there have been no longitudinal studies evaluating the association between knee FC and MRI-visualized OA-associated structural changes.

The purpose of this study is to determine whether baseline knee extension is associated with longitudinal knee structural changes on MRI, using data from the Osteoarthritis Initiative.

Methods: Retrospective cohort analysis using data from all 596 participants of the Foundation for the National Institutes of Health subset for whom knee extension and years 1 and 2 MRI data were available (1 knee/participant). MRIs were scored using the semi-quantitative MRI OA Knee Score (MOAKS). Participant demographics, body mass index (BMI), recruitment site, and baseline knee alignment and maximal extension were obtained. Baseline Kellgren Lawrence (KL) grade, and Western Ontario McMaster Osteoarthritis (WOMAC) Index score were also collected.

Univariate general linear model with analysis of covariance (ANCOVA) was performed to assess the association between baseline clinical knee extension (degrees) and MOAKS structural scoring at years 1 and 2, correcting for relevant clinical factors.

Results: Participant mean age was 61.5±8.9 years, BMI 30.7±4.9, mean KL grade 2.24 valgus 0.65, WOMAC total 12.7, with 58.7% being female. Max knee extension was 0.25±3.97°, alignment 0.34 valgus±3.68°.

Table 1. Associations between knee loss of extension and MOAKS ranked by effect size

Year 1		
Knee structure	**B [95% CI]**	**p-value[a]**
% BML - tibia medial posterior	-0.011 [-0.02,-0.002]	0.013
Osteophyte size - tibia medial	0.01 [0.002,0.018]	0.011
Osteophyte size - femur lateral anterior (trochlear)	0.009 [0.001,0.0017]	0.036
Osteophyte size - femur medial posterior	0.009 [0.001,0.017]	0.024
# BML lesions - tibia medial posterior	-0.004 [-0.007,-0.001]	0.02
Medial meniscal hypertrophy - posterior horn	-0.001 [-0.002,0]	0.005
Lateral meniscal extrusion - laterally	0.001 [9.35×10^{5},0.002]	0.03
Year 2		
Knee structure	**B [95% CI]**	**p-value[a]**
% BML - femur lateral posterior	-0.009 [-0.016,-0.001]	0.02
Osteophyte size - patella superior	0.009 [0.003,0.006]	0.031
Osteophyte size - femur lateral anterior (trochlear)	0.008 [0,0.016]	0.04
BML size - femur lateral posterior	-0.006 [-0.011,-0.001]	0.022
# BML lesions - femur lateral posterior	-0.005 [-0.009,-0.002]	0.003
Medial meniscal posterior root tear	0.003 [0,0.006]	0.025
Lateral meniscal extrusion - laterally	0.001 [4.39×10^{5},0.002]	0.039
Medial meniscal hypertrophy - posterior horn	-0.001 [-0.001,0]	0.006

[a] for knee extension association between MOAKS structure controlling for age, sex, BMI, recruitment site, knee alignment, baseline MOAKS for structure and site of interest, WOMAC score, and KL grade
CI: confidence interval
%BML: percent of bone marrow lesion comprised of edema
#BML: number of bone marrow lesions

Table 2. Associations between knee loss of extension and MOAKS by region

Year 1				
Region	***Tibia***		***Femur***	
	Medial	Lateral	Medial	Lateral
Anterior				*Osteophyte size*
Central	*Osteophyte size*	*Meniscal extrusion*		
Posterior	*% BML* *# BMLs* *Meniscal hypertrophy*		*Osteophyte size*	
Year 2				
Region	***Tibia***		***Femur***	
	Medial	*Lateral*	*Medial*	*Lateral*
Anterior				*Osteophyte size*
Central		*Meniscal extrusion*		
Posterior	*Meniscal hypertrophy* *Meniscal Tear*			*%BML* *BML size* *#BML*

[a] for knee extension association between MOAKS structure controlling for age, sex, BMI, recruitment site, knee alignment, baseline MOAKS for structure and site of interest, WOMAC score, and KL grade
CI: confidence interval
%BML: percent of bone marrow lesion comprised of edema
#BML: number of bone marrow lesions

Tables 1 and 2 summarize the associations between knee extension and MOAKSs pathologies by effect size and region at years 1 and 2.

Conclusion: Knee FC is associated with multiple OA structural pathologies at 1 and 2 years, with an anatomic predisposition to the posterior knee. At both years 1 and 2, osteophyte size at the lateral femur trochlea, lateral meniscal extrusion and medial meniscal posterior horn hypertrophy were consistently associated with baseline loss of knee extension. Further studies evaluating structural change mechanisms and potential early therapeutic interventions once a knee FC is detected are needed.

References

1. Campbell TM, Trudel G, Conaghan PG, Reilly K, Feibel RJ, McGonagle D. Flexion contracture is associated with knee joint degeneration on magnetic resonance imaging: data from the Osteoarthritis Initiative. Clin Exp Rheumatol. 2022 May;40(5):993-998. doi: 10.55563/clinexprheumatol/u8itzf. Epub 2021 Nov 3. PMID: 34796841.

Disclosure: D. Chan Chun Kong: None; **P. Conaghan**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, Genascense, 2, GlaxoSmithKlein(GSK), 2, Grunenthal, 2, Janssen, 2, Levicept, 2, Merck/MSD, 2, Moebius Medical, 2, Novartis, 2, 6, Stryker, 2, Takeda, 2, TrialSpark, 2; **M. Campbell**: None.

Abstract Number: 1866

MRI Confirms MRE Evidence of Sacroiliitis in Many with Crohn's Disease: A Prospective Study for the Screening of axSpA in High-risk Populations

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Sacroiliitis can be detected incidentally on magnetic resonance enterography (MRE) scans in Crohn's disease (CD) patients, obtained for CD assessment during clinical practice. However, the diagnostic accuracy of MRE-based sacroiliitis has not been studied for clinical relevance and applicability. The purpose of this study was to prospectively enroll CD patients with previously positive MRE-based sacroiliitis and examine them for signs of spondyloarthritis (SpA), undergo standardized MRI of sacroiliac joints (MRI-SIJ) and determine clinical significance of this finding by rheumatological assessment.

Methods: CD patients with evidence of sacroiliitis on routine MRE were prospectively enrolled from the NYU Inflammatory Bowel Disease (IBD) Center. All subjects underwent standard MRI-SIJ at time of follow-up. Data collected included history-related CD, joint symptoms, back pain, 66-68 joint count, enthesitis scores and Harvey Bradshaw Index (HBI, a measure of CD activity). Use of tumor necrosis factor-alpha inhibitors (TNFi) and non-TNFi therapies were recorded at the

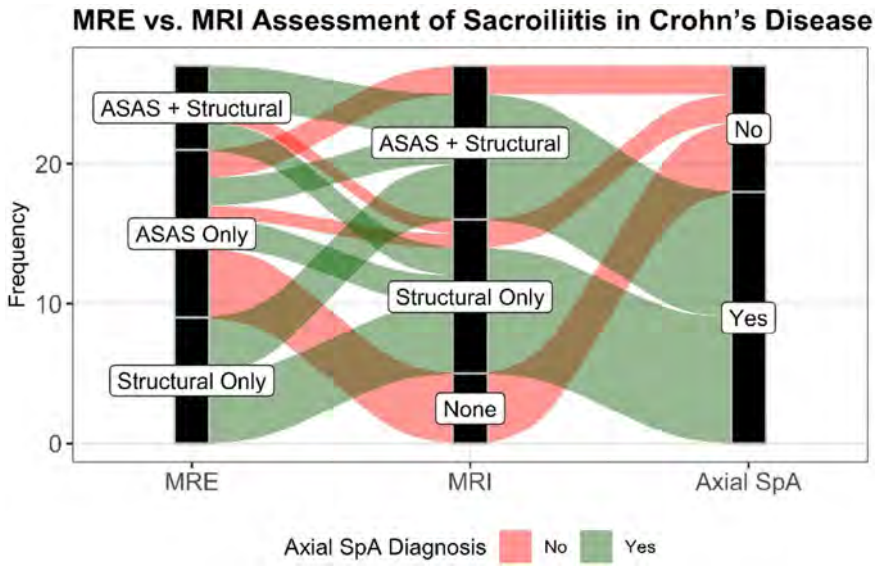

Figure: Alluvial plot showing evolution of sacroiliitis lesions between baseline MRE and follow up MRI and their relationship with axSpA diagnosis

time of MRE and MRI. MRI-SIJs were read by a blinded board-certified musculoskeletal radiologist. MRI was considered positive for sacroiliitis based on radiologist's global impression, Assessment of SpondyloArthritis International Society (ASAS) positivity and presence of structural lesions.

Results: 27 CD subjects with evidence of sacroiliitis on MRE were enrolled. 59.3% (n=16) were female, 88.9% (n=24) were white with a median age of 30 years [IQR: 27 – 43.5]. The median duration of CD was 3.2 years [IQR: 1.06 – 10.1] at the time MRE with a median HBI score of 4 [IQR: 1.5 – 7] consistent with mild CD activity. 37% of subjects were on TNFi and 14.8% were on non-TNFi therapy at the time of MRE. 66.6% (n=18) fulfilled ASAS positivity and 55.5% (n=15) with at least 1 structural lesion on MRE. The median duration between MRE and follow-up MRI was 2.13 years [IQR: 0.57 – 3.42]. 81.5% (n=22) of MRE-positive patients had evidence of sacroiliitis on the follow-up MRI, with 40.7% (n=11) fulfilling ASAS positivity. 23 subjects had back pain, and 15 subjects had inflammatory back pain (IBP) at the time of MRI. Of those with IBP, 93.3% (n=14) had MRI evidence of sacroiliitis. 66.7% (n=18) were determined to have Axial SpA (axSpA) by the assessing rheumatologist at the time of MRI. Median HBI was 3 [IQR: 2-6] at the time of MRI, suggesting remission. 48.1% and 33.3% of CD subjects were on TNFi and non-TNFi, respectively at the time of MRI. CD patients with structural lesions on the initial MRE were significantly more likely to have axSpA diagnosis on rheumatological assessment compared to those without (93.3% vs. 33.3%, p=0.003) (Figure 1).

Conclusion: Sequentially examined positive MRE scans in CD patients, obtained for standard of care, revealed a surprisingly high percentage of MRI-confirmed cases of sacroiliitis, many associated with clinical findings of axSpA. This study emphasizes the importance of MRE as a valuable screening tool to detect "hidden" sacroiliitis in CD patients, prompting rheumatological evaluation, which can impact therapeutic decision-making since only some of the currently available therapies for CD are effective in axSpA.

Disclosure: F. Malik: UCB, 2, 6; **S. Gyftopoulos**: None; **J. Axelrad**: AbbVie/Abbott, 2, Biofire Diagnostics, 5, Bristol-Myers Squibb(BMS), 2, Janssen, 2; **S. Chang**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 2, Pfizer, 2; **S. Hong**: bms, 2; **M. McAllister**: None; **M. Olateru Olagbegi**: None; **E. Alaia**: Biorez, 2; **W. Walter**: None; **A. RA SLE Network**: None; **D. Hudesman**: AbbVie/Abbott, 2, Janssen, 2, 5, Pfizer, 2, 5; **J. Scher**: AbbVie, 2, Janssen, 2, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 2, UCB, 2.

Abstract Number: 1867

Peripheral Volumetric Bone Mineral Density and Erosive Disease in Patients with Established Rheumatoid Arthritis: A Cross-Sectional Study Using High-Resolution Peripheral Quantitative Computed Tomography

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: High resolution peripheral quantitative computed tomography (HR-pQCT) is a promising imaging modality for assessing volumetric bone mineral density (BMD) in rheumatoid arthritis (RA), and has shown potential for use as an alternative to X-ray for detecting erosions in patients with RA. However, knowledge about the association between erosions and peripheral volumetric BMD is lacking. Thus, the aim of this study was to investigate the association between erosions and volumetric BMD in patients with RA.

Methods: In this cross-sectional study, 301 patients with established RA (disease duration > 5 years) according to the ACR/EULAR (2010) classification criteria were included. In total, 184 patients were imaged at the distal radius and 117 patients were imaged at the ultra-distal radius by HR-pQCT. All patients underwent radiographic examinations of the hands, wrists, and feet and were scored using the Sharp/Van der Heijde (SvH) method. Furthermore, the patients with RA imaged at the distal radius was matched by sex and age with a cohort of healthy controls (HC) with HR-pQCT of the distal radius (n =169).

Results: 301 patients with RA (median age 63.7 [55.1;70.8] years, 71 % women) were included in the study. The median disease duration was 14 [8;21] years. Compared with healthy controls, patients with RA had significantly lower total and cortical BMD at the distal radius (26.1%, $p < 0.0001$ & 13.0%, $p < 0.0001$), with no statistically significant difference in

Table 1: Results from HR-pQCT of the distal radius in patients with rheumatoid arthritis and healthy controls, matched by sex and age

	RA (n = 169)	HC (n = 169)	p
Tt. BMD (mg HA/cm³)	244.98 [63.35]	318.50 [76.43]	**<0.0001**
Ct. BMD (mg HA/cm³)	764.43 [104.34]	870.46 [68.31]	**<0.0001**
Tb. BMD (mg HA/cm³)	142.97 [44.04]	147.87 [46.17]	0.32
Ct. Th. (mm)	0.48 [0.20]	0.84 [0.23]	**<0.0001**
Tb. N. (1/mm)	2.03 [1.65;2.24]	1.95 [1.65;2.19]	0.28
Tb. Th. (mm)	0.060 [0.055;0.069]	0.063 [0.056;0.073]	**0.03**
Tb. Sp. (mm)	0.433 [0.374;0.533]	0.447 [0.389;0.547]	0.19
BV/TV	0.12 [0.04]	0.12 [0.04]	0.32

Tt. BMD = Total BMD, Ct. BMD = Cortical BMD, Ct. Th. = Cortical thickness, Tb. BMD = Trabecular BMD, Tb. N. = Trabecular number, Tb. Th. = Trabecular thickness, Tb. Sp. = Trabecular spacing, BV/TV = Bone volume/trabecular volume, HA = Hydroxyapatite.

Results are displayed as mean [SD] or median [IQR] and p-values are calculated according to distribution.

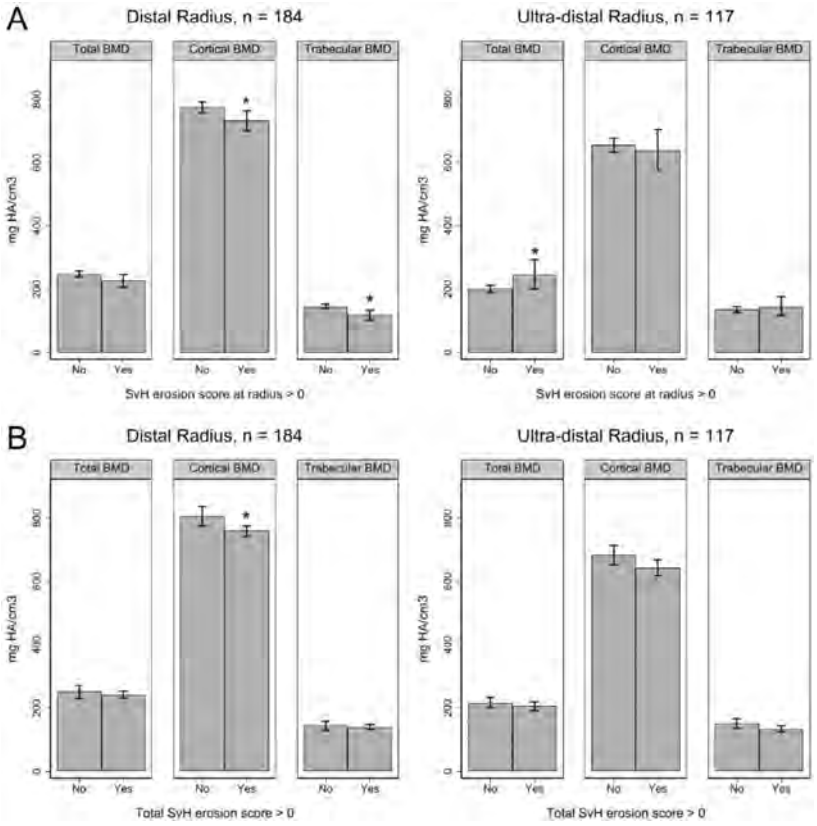

Figure 1: Mean and 95% confidence intervals for total, cortical and trabecular BMD at the distal and ultra-distal radius imaged by HR-pQCT (A): Stratified by Sharp/Van der Heijde erosion score at the radius. (B): Stratified by total Sharp/Van der Heijde erosion score. * = $p < 0.05$.

trabecular BMD. Furthermore, cortical and trabecular thickness was significantly lower in patients with RA compared to healthy controls (54.5%, $p < 0.0001$ & 4.9%, $p = 0.03$) (Table 1). Local erosions were associated with significantly decreased cortical and trabecular BMD at the distal radius ($p = 0.03$ & $p = 0.0008$), while at the ultra-distal radius, local erosions were associated with significantly higher total BMD ($p = 0.005$). Erosive disease in general was associated with significantly decreased cortical BMD at the distal radius ($p = 0.02$) with no statistically significant difference between the groups at the ultra-distal radius (Figure 1). At the distal radius, multivariate linear regression analyses showed a significant negative association between total SvH erosion score and trabecular BMD (coefficient = -0.28, $p = 0.001$) with no statistically significant associations between total and cortical BMD after adjusting for disease activity, sex, age, height, weight and tobacco pack years. At the ultra-distal radius, multivariate linear regression analyses showed a significant positive association between total SvH erosion score and total BMD (coefficient = 0.49, $p = 0.001$) with no statistically significant associations between total SvH erosion score and cortical and trabecular BMD.

Conclusion: Our results suggest that erosive disease in RA causes systemic bone changes resulting in decreased BMD at the cortical and/or trabecular bone compartment. This indicates that evaluation of erosive disease likely adds value to the assessment of systemic bone changes in patients with RA. Furthermore, it underlines the need for longitudinal studies investigating the changes in erosive status and BMD over time.

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Abstract Number: 1868

Long-term Efficacy of a 2-year MRI Treat-to-target Strategy on Radiographic Joint Damage Progression in Rheumatoid Arthritis Patients in Clinical Remission – Five Year Follow-up of the IMAGINE-RA Randomized Clinical Trial

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Radiographic joint damage progresses in 20-30% of rheumatoid arthritis (RA) patients despite fulfilling clinical remission criteria (1). Osteitis assessed on MRI is a well known predictor of subsequent radiographic bone damage progression (2). Therefore, targeting absence of osteitis combined with clinical remission may improve long-term radiographic outcomes. The purpose of the study was therefore: To investigate whether a 2-year MRI treat-to-target (MRI T2T) strategy targeting absence of osteitis combined with clinical remission, compared to a conventional T2T strategy targeting clinical remission only, could reduce radiographic joint damage progression over 5 years in RA patients.

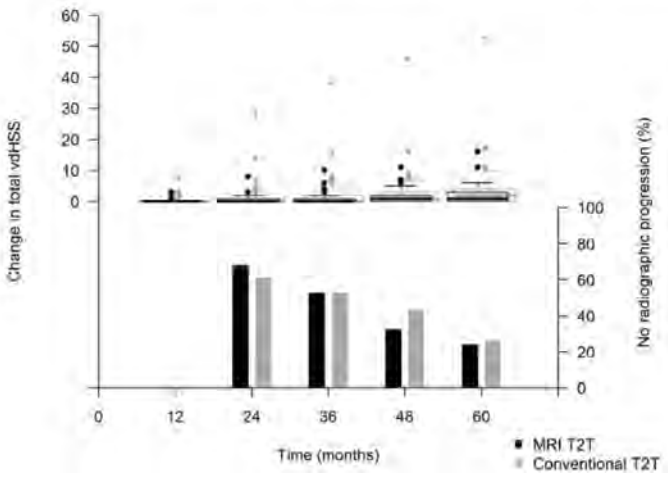
Methods: IMAGINE-more was designed as a 3-year observational extension study of the 2-year IMAGINE-RA randomized clinical trial (3). IMAGINE-RA included 200 RA patients in clinical remission (DAS28-CRP< 3.2 and no swollen joints), with erosive disease (bone erosion on conventional radiography),and treated with conventional synthetic DMARDs (csDMARDs).

TABLE: RADIOGRAPHIC ENDPOINTS AT 5 YEARS (CHANGE FROM BASELINE - YEAR 0)*

		MRI T2T		Conventional T2T	Difference between groups	P value
	n		n			
Primary endpoint						
No radiographic progression, No. (%)	59	14 (24%)	72	19 (26%)	OR=0.70 (0.28 to 1.71)	0.431
Key secondary endpoint						
Change in total vdHSS (0-448)	47	1.0 [0.0-3.0]	56	2.0 [0.0-4.0]	0.0 (-1.0 to 0.0)	0.515
Other secondary endpoints						
Change in erosion (0-280)	47	1.0 [0.0-2.0]	56	1.0 [0.0-3.0]	0.0 (0.0 to 0.0)	0.967
Change in JSN (0-168)	47	0.0 [0.0-0.5]	56	0.0 [0.0-1.3]	0.0 (0.0 to 0.0)	0.565

Group contrasts are presented as No. (%) for dichotomous data and medians [IQR] for continuous data. OR (95%CI) were estimated from logistic regression adjusted for a propensity score and with non-responder imputation. For endpoints with continuous data median differences (95%CI) were calculated based on the ITT population (no manual imputation) *In addition to the radiographic endpoints, the full IMAGINE-more study includes a clinical co-primary endpoint, and several secondary endpoints.

Figure: Changes from baseline to 5 years in total vdHSS (top) and proportions with no radiographic progression (bottom)



Illustrates the change in total vdHSS from baseline to 60 months (i.e., 5 years) based on the ITT population (no manual imputation done), as well as the proportions with no radiographic progression (delta total vdHSS<0) in each group from baseline to 60 months, with non-responder imputation.

The objective was to investigate whether a 2-year MRI T2T strategy targeting absence of osteitis combined with clinical remission (DAS28-CRP≤3.2 and no swollen joints) as compared to a conventional T2T strategy, targeting clinical remission only, could improve remission rates and prevent radiographic joint damage progression. If treatment target was not met, treatment was intensified stepwise starting with increment in csDMARDs and subsequently adding biologics. Participants in the IMAGINE-more extension study were managed in routine clinical practice in outpatient clinics. Clinical examinations and radiographs of hands and feet (also obtained at baseline, year 1 and 2 in IMAGINE-RA) were done year 3, 4 and 5. The primary endpoint was the proportion of patients with no radiographic progression (increase in total van der Heijde-modified Sharp score (vdHSS) ≤0) from baseline to year 5. Secondary endpoints were changes from baseline to 5 years in total vdHSS, vdHSS erosion and joint space narrowing (JSN) scores. Dichotomous endpoints were estimated by logistic regression, while median differences were calculated for the continuous outcome measures.

Results: Informed consent to participation in IMAGINE-more was obtained from 131 patients (59 from the originalMRI T2T group). Of these, 14 patients (24%) in the MRI T2T group and 19 patients (26%) in the conventional T2T group had no radiographic progression from baseline to year 5 (OR 0.70 [0.28 to 1.71]). As illustrated in the Table and Figure, the median progression in total vdHSS from baseline to 5 years was low, with no differences between treatment groups.

Conclusion: A 2-year combined MRI T2T and clinical T2T strategy, compared with a conventional clinical T2T strategy alone, did not result in reduced radiographic progression in the long term over 5 years in RA patients with erosive disease in clinical remission. In accordance with the primary results from the IMAGINE-RA trial, these findings do not support systematic use of MRI to guide treatment in RA patients in remission.

References: 1. Lillegraven et al. Ann Rheum Dis 2012 2. Brown et al. Arthritis Rheum 2008 3. Møller-Bisgaard et al. JAMA 2019

Disclosure: S. Møller-Bisgaard: None; **K. Hørslev-Petersen**: None; **L. Ørnbjerg**: Novartis, 5; **B. Ejbjerg**: None; **M. Hetland**: AbbVie/Abbott, 1, 5, Bristol-Myers Squibb(BMS), 5, Danbio, 12, MLH has chaired the steering committee of the Danish Rheumatology Quality Registry (DANBIO, DRQ), which receives public funding from the hospital owne, Eli Lilly, 5, MEDAC, 6, Novartis, 5, Pfizer, 5, 6, Sandoz, 5, 6; **J. Moeller**: None; **R. Christensen**: None; **S. Nielsen**: None; **D. Glinatsi**: Eli Lilly, 1, 6; **M. Boesen**: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 6, Image Analysis Group, 2, 6, 11, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6; **K. Stengaard-Pedersen**: None; **O. Madsen**: None; **B. Jensen**: None;

J. Villadsen: None; **E. Hauge**: AbbVie/Abbott, 2, 5, 6, Danish Regions Medicine Grants, 5, Danish Rheumatism Association, 5, Galapagos, 5, Novartis, 2, 6, Novo Nordic, 2, 5, 6, Sanofi, 2, 6, Sobi, 2, 6; **O. Hendricks**: AbbVie/Abbott, 4, 6, Eli Lilly, 6, Novartis, 6, Pfizer, 6; **H. Lindegaard**: None; **N. Krogh**: None; **A. Jurik**: None; **H. Thomsen**: None; **M. Østergaard**: AbbVie, 2, 5, 6, Amgen, 5, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Hospira, 2, 6, Janssen, 2, 6, MEDAC, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Novo Nordisk, 2, 6, Orion, 2, 6, Pfizer, 2, 6, Regeneron, 2, 6, Roche, 2, 6, Sandoz, 2, 6, Sanofi, 2, 6, UCB, 2, 6.

Abstract Number: 1869

FDG-PET/CT for Diagnosing Polymyalgia Rheumatica Before, During and After a Short-term Prednisolone Cessation – a Prospective Study of 101 Patients

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Polymyalgia rheumatica (PMR) can be challenging to diagnose since other diseases may present with similar symptoms. As a result, a significant number of patients are referred to rheumatologists for a second opinion. However, a notable proportion of patients are administered prednisolone prior to rheumatologic assessment, which can obscure the symptoms of PMR and important differential diagnoses. ^{18}F-fluorodeoxyglucose(FDG) positron emission tomography and computed tomography (PET/CT) has been suggested as a potential tool to aid the clinician diagnosing PMR, but it is unclear whether PET/CT can be used after the initiation of prednisolone. This study aimed to investigate the diagnostic utility of FDG-PET/CT in patients suspected of PMR, specifically evaluating the diagnostic accuracy before, during, and after a short-term taper of prednisolone.

Methods: This study included 101 patients who were suspected of having PMR. All patients were clinically diagnosed with PMR or non-PMR at a baseline visit and subsequently had a PET/CT performed. Patients diagnosed with PMR were administered prednisolone with a starting dose of 15 mg following the first PET/CT. After 8 weeks of treatment a second PET/CT was performed when prednisolone had been tapered to 10 mg, according to an algorithm reflecting routine care. Afterwards, prednisolone was tapered with complete cessation at week 9 followed by a third PET/CT at week 10. A PET/CT assessment of PMR or non-PMR was given utilizing the validated Leuven score (Figure 1) [1]. The final diagnosis for all patients was confirmed at a 1-year follow-up visit.

Results: Preliminary results of the first 79 patients have been obtained, and the baseline characteristics of the PMR and non-PMR group are outlined in table 1. A baseline PET/CT diagnosis showed a sensitivity of 88.7% and a specificity of 61.5% using a clinical diagnosis at 1 year as the reference standard (Figure 1). The low specificity was partially explained by a high rate of false positive patients with a final diagnosis of other inflammatory diseases, since 8 out of 10 non-PMR patients with a final diagnosis of rheumatoid arthritis or reactive diseases had a PET/CT indicating PMR according to the Leuven score. After 8 weeks of prednisolone treatment the Leuven score decreased significantly, but in 14/46 patients the PET/CT diagnosis remained positive for PMR (Figure 2). After prednisolone cessation the Leuven score increased significantly, with a positive PET/CT diagnosis of PMR in 25/37.

Table 1 – Baseline data of patients with a final diagnosis of PMR and non-PMR (control group) based on 1-year follow-up visit

Baseline characteristics	PMR group n=53	Control group n=26
Age, mean ±SD	72 ±7.3	69 ±8.8
Female sex, n(%)	25 (47%)	13 (50%)
Symptoms at diagnosis:		
Bilateral shoulder pain	50 (94%)	18 (69%)
Limited range of shoulder movement	42 (79%)	5 (19%)
Bilateral hip girdle pain	45 (85%)	17 (65%)
Limited range of hip movement	29 (55%)	8 (31%)
Absence of other joint pain	28 (53%)	11 (42%)
Morning stiffness >45 min	36 (69%)	11 (44%)
Weight loss >2 kg	10 (19%)	4 (15%)
Lab work		
C-reactive protein (mg/L), median (IQR)	39 (25-57)	12 (4-35)
Erythrocyte sedimentation rate, mm, median (IQR)	49 (30-64)	29 (18-42)
PMR activity		
Treating physician global VAS-score, mean ±SD	6.2 ±1.9	2.9 ±2.6
Patient reported pain VAS-score, mean ±SD	7.2 ±1.6	5.8 ±2.0
PMR activity score, mean ±SD	26.1 ±21.6	13.7 ±7.6

Conclusion: Initiation of prednisolone treatment prior to PET/CT significantly reduces the diagnostic accuracy for a PMR diagnosis. Therefore, a short-term prednisolone taper is advisable before using PET/CT to diagnose PMR in patients treated with a medium dosage of prednisolone. Furthermore, PET/CT utilizing the Leuven score may not be reliable for differentiating PMR from other inflammatory disorders during the initial evaluation.

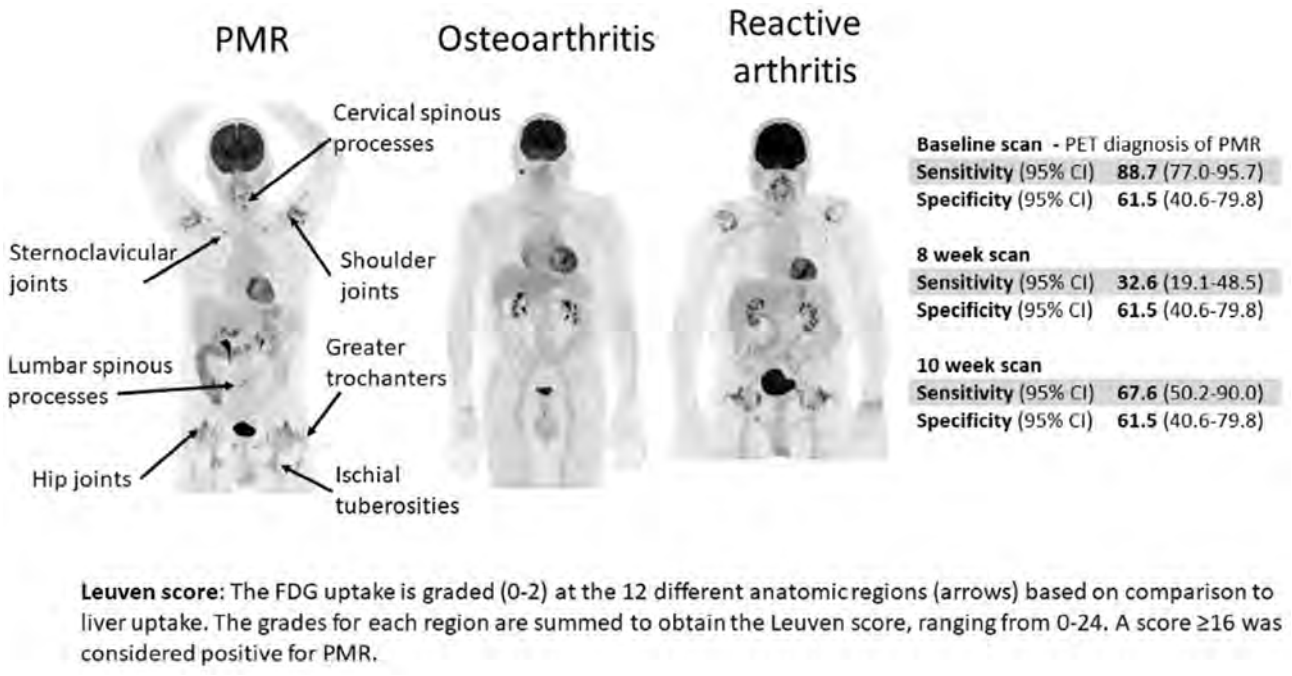

Figure 1 – PET/CT diagnosis of PMR at baseline, 8 weeks and 10 weeks using the Leuven score.

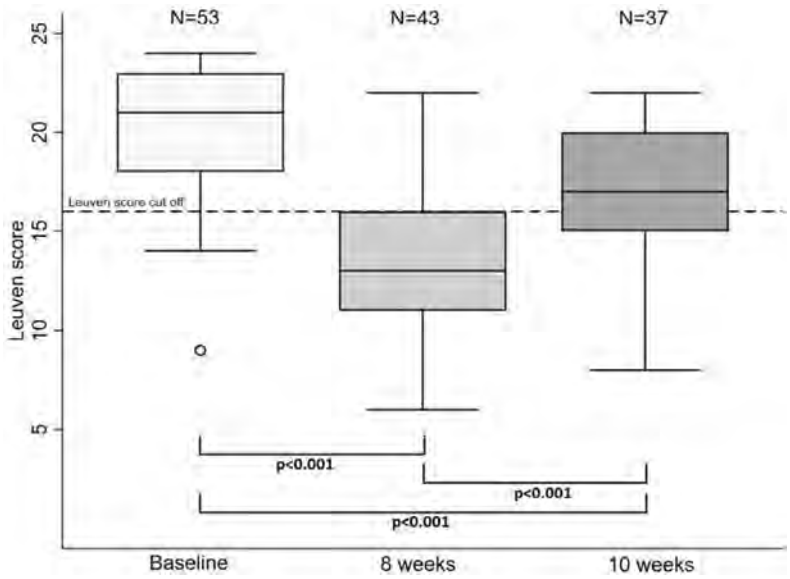

Figure 2 – Box plot of Leuven score at baseline, after 8 weeks of prednisolone treatment and at 10 weeks after a 2 week prednisolone taper.

References [1] Henckaerts L, Gheysens O, Vanderschueren S, Goffin K, Blockmans D. Use of 18F-fluorodeoxyglucose positron emission tomography in the diagnosis of polymyalgia rheumatica-A prospective study of 99 patients. Rheumatology (Oxford) 2018;57(11):1908-16.

Disclosure: A. Nielsen: None; **I. Hansen**: None; **B. Dalsgaard Nielsen**: None; **S. Kjær**: None; **J. Blegvad-Nissen**: None; **C. Sørensen**: None; **E. Hauge**: AbbVie/Abbott, 2, 5, 6, Danish Regions Medicine Grants, 5, Danish Rheumatism Association, 5, Galapagos, 5, Novartis, 2, 6, Novo Nordic, 2, 5, 6, Sanofi, 2, 6, Sobi, 2, 6; **L. Gormsen**: None; **K. Keller**: None.

Abstract Number: 1870

Assessing the Appropriateness of Imaging Modalities in Primary Care for Low Back Pain and Their Impact on Outcomes: A Retrospective Observational Study in a Single Center in Trenton

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Low back pain (LBP) is a leading cause of doctor visits and disability. The annual direct expenditures for LBP management exceed $80 billion, not including indirect costs associated with prolonged disability and lost worker productivity. Despite increasing expenses over time, patient outcomes have not improved, which may be due to overutilization of diagnostic imaging, invasive procedures, and unnecessary specialty referrals. Many providers investigate anatomic structures as an underlying etiology for back pain, which can lead to inappropriate, and even harmful low-validity

Table 1. Demographics

Table 2. Imaging findings

Characteristics	X-ray n (%)	CT scan n (%)	MRI n (%)	Total n (%)
Total number of imaging	41 (49%)	8 (9%)	34 (40%)	83 (100%)
Findings				
Normal or Nonspecific	18 (43%)	2 (25%)	6 (18)	26(31%)
DJD	22 (53%)	4 (50%)	25 (73%)	51(61%)
Spinal stenosis	2 (4%)	3 (37%)	11 (32%)	16 (19%)
Herniated disc	0 (0%)	4 (50%)	15 (44%)	19 (22%)
SI joint changes	1 (2%)	0 (0%)	4 (12%)	5 (6%)
Serious diagnosis	0 (0%)	0 (0%)	3 (8%)	3 (3%)

Table 2. Imaging findings

Table 1. Demographics

Characteristics	X-ray n (%)	CT scan n (%)	MRI n (%)	Total n (%)
Total number of imaging	41 (49%)	8 (9%)	34 (40%)	83 (100%)
Demographics				
Age mean	47.7	47.4	47.7	47.6
Gender (M/F)	24M/17F	5M/3F	13M/21F	42M/41F
BMI mean	29.6	29.4	29.7	29.6
Red flag symptoms	1 (2%)	1 (12%)	4 (12%)	6 (7%)
Duration of pain				
Acute <4 weeks	11 (26%)	6 (75%)	5 (15%)	22 (26%)
Subacute 4-12 weeks	3 (7%)	0 (0%)	3 (8%)	6 (7%)
Chronic >12 weeks	27 (65%)	2 (25%)	26 (76%)	56 (66.6%)
Treatment				
NSAIDs	32 (78%)	6 (75%)	32 (94)	70 (84%)
Muscle Relaxants	17 (41%)	4 (50%)	22 (64%)	43 (51%)
Opioids	2 (4%)	2 (25%)	10 (29%)	14 (16%)
Referral				
Spine surgery referral (Ortho or Neurosurgery)	1 (2%)	2 (25%)	18 (52%)	21 (25%)
Neurology	0 (0%)	0 (0%)	2 (6%)	2 (2%)
Rheumatology	4 (9%)	0 (0%)	4 (12%)	8 (9%)
CVIR	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Physical Therapy	27 (65%)	4 (50%)	24 (70%)	55 (66%)
Pain management	1 (2%)	0 (0%)	17 (50%)	18 (21%)
Counseling (including home physical therapy)	27 (65%)	3 (37%)	25 (73%)	55 (66%)
Opiod prescription	0 (0%)	0 (0%)	7 (20%)	7 (8%)
Disability application	1 (2%)	0 (0%)	2 (6%)	3 (3%)
Spinal Procedure performed	0 (0%)	0 (0%)	9 (26%)	9 (10%)

tests. Therefore, evidence-based clinical practice guidelines for optimal utilization of imaging are highly recommended. This study identifies our current practice for utilization of lumbar spine imaging in patients with LBP in our outpatient clinic and outcomes based on imaging findings.

Methods: We used the electronic medical record to generate a patient list, including those 18 years and older who were managed for LBP and referred for lumbar spine imaging between January 1, 2022, and December 31, 2022. Patient demographics, baseline clinical characteristics, and subsequent interventions, such as referrals, counseling, physical therapy, pain management, spinal procedures, opioid prescription, and disability application, were recorded and analyzed using descriptive statistics.

Results: 170 patients were diagnosed with LBP during the study period. Of these, 49% received imaging, with 49% having plain radiography, 9% CT scans, and 40% MRI. 17% of patients had more than one imaging study done, from which 71% had plain radiography followed by MRI. Notably, 82% of those who had plain radiography followed by MRI were done during the chronic course of LBP. Among patients who received imaging, 26% had acute pain, 7% had subacute pain, and 67% had chronic pain. Imaging showed that 43% of the X-ray group had normal or nonspecific results, 73% of the MRI group had degenerative diseases, 44% had herniated discs, and 32% had spinal stenosis. Overall, only 3% of patients had serious diagnoses. Sixty six percent (66%) had lifestyle counseling and referral to physical therapy, 25% of patients were referred to spine specialists, 9% to rheumatologists, and 21% to pain specialists. Half of patients with chronic LBP were treated with muscle relaxants. Only 3% were prescribed opioids and 10% had spinal procedures. Interestingly, 5 patients were referred to rheumatologists for sacroiliac (SI) joint changes.

Conclusion: Majority of LBP in the outpatient setting have an uncomplicated, nonspecific course that require no further diagnostic evaluation. MRI of the lumbar spine is the modality of choice for the majority of patients requiring imaging per ACR appropriateness criteria. Lumbar spine radiographs are of limited utility and are generally only indicated when fracture is a concern. Complete history and careful physical and neurologic examinations are always the cornerstones of LBP management. Our study identifies the current clinical practice for utilization of imaging for patients with LBP among providers in our outpatient clinic. The study recommends further projects to optimize LBP management in our clinic based on evidence-based guidelines.

Disclosure: D. Sereda: None; **C. Arcilla**: None; **K. Arslan**: None; **D. Goldsmith**: None.

Abstract Number: 1871

Utility of Infrared Thermography in Patients with Digital Gangrene

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

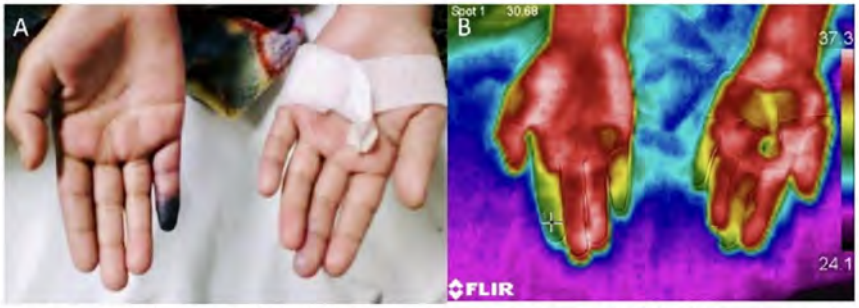
Background/Purpose: Digital gangrene has been described as a complication of several Autoimmune Inflammatory Rheumatic Diseases(AIIRD). Due to multiple underlying mechanisms causing digital gangrene in AIIRD patients, it is difficult clinically to determine the aetiology. Moreover, it is difficult to clinically assess and determine the progression of pregangrenous changes daily. In this study, we would like to assess the utility of infrared thermography in identifying the

Table 1: Baseline characteristics of patients with digital gangrene

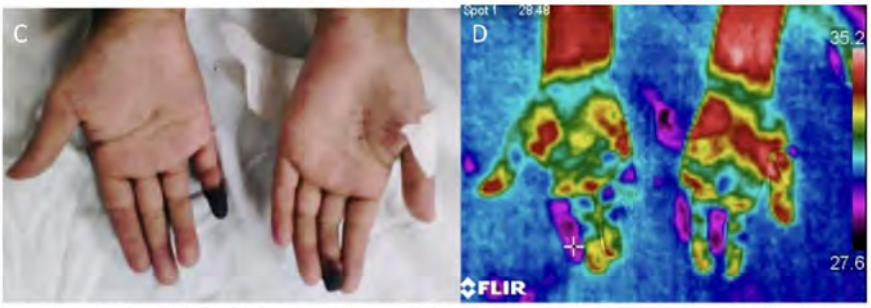
	All Patients (n=22)
Age (years)	29 ± 13.9
Females	16 (72.7%)
Etiology of gangrene at enrollment	
SLE vasculitis	9
RA vasculitis	2
Scleroderma	7
SLE vasculopathy	1
Mixed connective tissue disorder (MCTD)	1
Atherosclerosis	1
Buerger disease	1

aetiology of digital gangrene as well as assessing the daily progression of pregangrenous areas using infrared thermography principle.

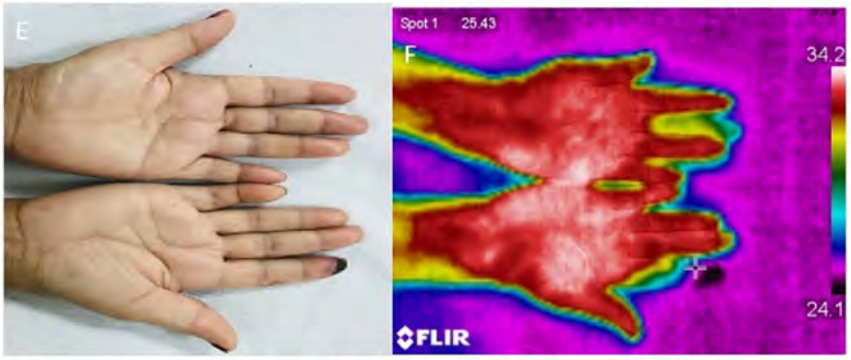
Methods: 22 patients with digital gangrene were included. Infrared thermography was done using compact thermal camera FLIR C5 which has a resolution of 19,200 pixels and an infrared sensor of 160*120 with thermal sensitivity of < 70 mK. Baseline thermography images will be taken on day 1 and will be repeated on daily basis till discharge to assess for daily



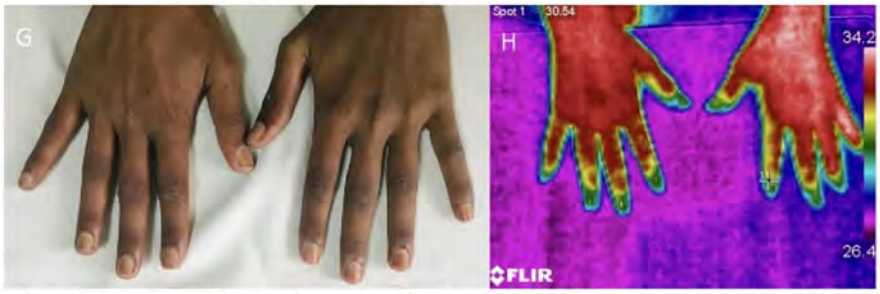
Panel A shows clinical image of a patient with gangrenous changes over right little finger. Panel B shows infrared thermography image of the same patient with reduced temperature over right index finger, little finger and left little finger and middle finger.



Panel C shows clinical image of the same patient on day 3 with new gangrenous change over left middle finger. Panel D shows infrared thermography image with reduced temperature over right index finger, little finger and left middle finger and little finger



Panel E shows clinical image of a patient with RA vasculitis with gangrenous change in right index finger. Panel F shows infrared thermography image of the same patient with reduced temperature in right index finger and left middle finger



Panel G shows clinical image of a patient with scleroderma with pregangrenous change in left index finger. Panel H shows infrared thermography image of the same patient with reduced temperature in all the fingers

progression of gangrene. Thermography images were correlated with clinical aetiology of gangrene to see for any specific pattern. Daily thermographic images were compared with clinical progression of gangrene to see if thermography could predict gangrene evolution.

Results: We found that infrared thermography was a useful tool for assessing pregangrenous lesion in patients presenting with digital gangrene. Out of 22 patients enrolled with digital gangrene, 3 had progressive gangrene in which infrared thermography image on day 1 showed reduced temperature of pregangrenous fingers which later became gangrenous. It was found that the mean temperature detected by using infrared thermography in gangrene due to vasculitis was 31.3 ±1.4°C whereas the mean temperature due to vasculopathic lesion was 27.8±1.6°C indicating that vasculopathic gangrene tend to be colder than vasculitic gangrene. Out of 9 patients who had vasculopathic gangrene, 7 had symmetrical reduction in temperature in both limbs which was clinically inapparent, indicating that infrared thermography could be used as a potential tool to detect vasculopathy. On monthly follow up of these patients, it was found that patients with vasculitic gangrene tend to have a better temperature response after treatment with immunosuppression when compared to vasculopathic gangrene indicating that infrared thermography could be utilised as a potential tool to assess treatment response in patients with vasculitis and vasculopathic gangrene.

Conclusion: Infrared thermography could be a utilized as a potential tool in assessing patients with digital gangrene especially in identifying pregangrenous lesions early, differentiating vasculitis and vasculopathic lesions and for assessing treatment response. Further studies are required to validate the use of infrared thermography in patients with digital gangrene.

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Abstract Number: 1872

Performance Analysis of a Deep Learning Algorithm to Detect Positive SIJ MRI According to the ASAS Definition in axSpA Patients

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II

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Background/Purpose: Magnetic resonance imaging (MRI) of the sacroiliac joints (SIJ) is an essential tool in the evaluation of patients with axial spondyloarthritis (axSpA). In-depth knowledge of characteristic MRI lesions and their definitions, as well as reliability of identification and scoring, varies amongst general radiologists and rheumatologists.[1] A deep learning algorithm was developed to detect the presence of inflammation in SIJ MRI (MRI+) scans with promising results.[2] The aim of this diagnostic performance study was to assess the ability of a deep learning algorithm to identify MRI+ scans in a study cohort of axSpA patients.

Methods: 731 baseline SIJ MRI scans were collected from two prospective randomized controlled trial cohorts in patients with non-radiographic (nr-) and radiographic (r-) axSpA (RAPID-axSpA [NCT01087762] and C-OPTIMISE [NCT02505542])[3,4] and were centrally evaluated by two expert readers (and adjudicator in case of disagreement) for the presence of inflammation by the 2009 Assessment in SpondyloArthritis international Society (ASAS) definition.[5] The MRI scans were processed by the previously trained deep learning algorithm,[2] blinded to clinical information and central expert

Table. Performance results comparing the algorithm and the human readers for the classification of MRI-SIJ scans. The metric values are point estimate (95% CI)

	All (N=731)	RAPID-axSpA (n=152)	C-OPTIMISE (n=579)
Central reading, MRI+; n (%)	436 (59.6%)	99 (65.1%)	337 (58.2%)
Sensitivity	0.70 (95% CI: 0.66–0.73)	0.66 (95% CI: 0.58–0.73)	0.71 (95% CI: 0.67–0.75)
Specificity	0.81 (95% CI: 0.78–0.84)	0.89 (95% CI: 0.82–0.95)	0.79 (95% CI: 0.75–0.83)
PPV	0.84 (95% CI: 0.82–0.87)	0.92 (95% CI: 0.87–0.96)	0.83 (95% CI: 0.79–0.86)
NPV	0.64 (95% CI: 0.61–0.68)	0.58 (95% CI: 0.50–0.67)	0.66 (95% CI: 0.62–0.70)
Cohen's kappa	0.49 (95% CI: 0.43–0.55)	0.48 (95% CI: 0.36–0.61)	0.49 (95% CI: 0.42–0.56)
Absolute agreement	0.74 (95% CI: 0.72–0.77)	0.74 (95% CI: 0.68–0.79)	0.74 (95% CI: 0.72–0.77)

CI: confidence interval; MRI: magnetic resonance imaging; NPV: negative predictive value; PPV: positive predictive value; SIJ: sacroiliac joints.

readings. Performance evaluation included sensitivity, specificity, positive and negative predictive values (PPV and NPV), Cohen's Kappa and the absolute agreement to assess the agreement between the deep learning algorithm and the human readers for the classification of MRI-SIJ scans. Bootstrapping was used to construct the 95% confidence interval (CI).

Results: Pooling the patients from RAPID-axSpA (n=152) and C-OPTIMISE (n=579) yielded a validation set of 731 patients (mean age: 34.2 years, SD: 8.6; 69.1% male) of which 44.6% were patients with nr-axSpA and 59.6% were MRI+ as per central readings. Comparing the trained algorithm with the human central readings for the classification of MRI+/MRI– on the pooled validation set yielded a sensitivity of 70% (95% CI: 66–73%), specificity of 81% (95% CI: 78–84%), PPV of 84% (95% CI: 82–87%), NPV of 64% (95% CI: 61–68%), Cohen's kappa of 0.49 (95% CI: 0.43–0.55), and absolute agreement of 74% (95% CI: 72–77%; **Table**).

Conclusion: A previously trained deep learning algorithm enabled acceptable detection of the presence of inflammation according to the 2009 ASAS MRI definition in axSpA patients from two clinical trials. This suggests that an MRI+ detection algorithm has the potential to support clinicians in identifying axSpA patients.

References: 1. Bennett AN. J Rheumatol 2017;44(6):780–5; **2.** Aouad T. Proc Int Conf Image Proc 2022;3351–5; **3.** van der Heijde. Rheumatology. 2017;56(9):1498–1509; **4**. Landewé RB. Ann Rheum Dis. 2020;79(7):920–28; **5**. Rudwaleit M. Ann Rheum Dis 2009;68(6):777–83.

Disclosure: J. Nicolaes: UCB Pharma, 3, 12, Shareholder; **E. Tselenti**: UCB Pharma, 2, Veramed, 3; **T. Aouad**: None; **C. López Medina**: AbbVie, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 6, MSD, 6, Novartis, 2, 5, 6, UCB Pharma, 2, 5, 6; **A. Feydy**: Guerbet, 2; **H. Talbot**: None; **B. Hoepken**: UCB Pharma, 3, 12, Shareholder; **N. De Peyrecave**: UCB Pharma, 3; **M. Dougados**: AbbVie, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Roche, 2, 5, UCB, 2, 5.

Abstract Number: 1873

Cervical Spine Involvement in Axial Spondyloarthritis. Radiographic Characteristics and Associated Factors

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SESSION INFORMATION
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Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The study of the cervical spine (CS) in axial spondyloarthritis (axSpA) and its radiographic characteristics including the zygapophyseal joints (ZJ) may be helpful for early diagnosis, establishing a prognosis and sharpening treatment choices.

The aim of this study is to describe the prevalence and characteristics of CS involvement in a cohort of patients with axSpA and its associated factors, who have been followed up in the Rheumatology Department of a third level university hospital.

Table 1. Characteristics of the CS and no CS group.

n=340			NoCS group (n=158)	CS group (n=182)	p-value
Sex	n (%)	Men	91 (57.6)	153 (84.1)	<0.001
		Women	67 (42.4)	29 (15.9)	
Age	Mean (SD)		49.9 (13.5)	63.9 (13.0)	<0.001
BMI	Mean (SD)		25.1 (3.8)	27.6 (4.4)	<0.001
Smoking	n (%)	Non smoker	74 (49.3)	66 (37.3)	0.001
		Ex smoker	36 (24.0)	77 (43.5)	
		Active smoker	40 (26.7)	34 (19.2)	
Age at the beggining of symptoms	Mean (SD)		27.6 (9.3)	26.4 (9.1)	0.238
Age at diagnosis	Mean (SD)		32.7 (10.5)	33.5 (11.9)	0.490
HLA B27	n (%)	negative	34 (21.8)	29 (15.9)	0.215
		positive	122 (78.2)	153 (84.1)	
Familiar history of SpA	n (%)		41 (25.9)	38 (20.9)	0.329
Uveitis	n (%)		40 (25.3)	39 (21.4)	0.473
Psoriasis	n (%)		15 (9.5)	9 (4.9)	0.155
IBD	n (%)		16 (10.1)	15 (8.2)	0.679
Arthritis	n (%)		42 (26.6)	59 (32.4)	0.291
Enthesitis (heel)	n (%)		27 (17.1)	41 (22.5)	0.265
Dactylitis	n (%)		6 (3.8)	2 (1.1)	0.152
axSpA type	n (%)	r-axSpA (AS)	114 (72.2)	166 (91.2)	<0.001
		EnA	13 (8.2)	10 (5.5)	
		Ps SpA	8 (5.1)	3 (1.6)	
		nr-axSpA	23 (14.6)	3 (1.6)	
BASDAI	Mean (SD)		3.3 (2.1)	3.8 (2.1)	0.036
BASFI	Mean (SD)		2.7 (2.3)	4.6 (2.7)	<0.001
ASDAS PCR	Mean (SD)		2.1 (1.0)	2.4 (1.0)	0.006
CS mobility	Mean (SD)		81.0 (11.3)	54.1 (24.6)	<0.001

Methods: Descriptive, retrospective and unicentric study. Patients with an axSpA diagnosis based on the ASAS classification criteria, from March 2011 to December 2022, retrieved from a dedicated axSpA database were included. Sociodemographic, clinical, radiographic and therapeutic variables were gathered. They were separated into two groups according to CS involvement; "CS group" as patients with BASRI≥2 in CS and/or a score ≥3 in ZJ measured by De Vlam method (1); and "no CS group" as controls.

Results: A total of 340 patients were included (71.8% men; mean age 57,4 ± 14,9 years). CS involvement is common among axSpA (n=182; 53,5%). ZJ involvement was observed in 99 patients (29,1%), and of those, 21 did not show concomitant structural damage in the vertebral bodies. A total of 83 patients (24,4%) had damage in the vertebral bodies

Schober 10	Mean (SD)		4.3 (1.2)	2.7 (1.7)	<0.001
Schober 15	Mean (SD)		6.4 (1.7)	4.2 (2.3)	<0.001
BASRI sacroiliac joints	n (%)	0	9 (5.7)	2 (1.1)	<0.001
		1	15 (9.5)	4 (2.2)	
		2	57 (36.1)	15 (8.2)	
		3	52 (32.9)	47 (25.8)	
		4	25 (15.8)	114 (62.6)	
BASRI coxofemoral joints	n (%)	0	126 (79.7)	55 (30.2)	<0.001
		1	15 (9.5)	36 (19.8)	
		2	11 (7.0)	65 (35.7)	
		3	3 (1.9)	10 (5.5)	
		4	3 (1.9)	16 (8.8)	
BASRI LS	n (%)	0	108 (68.4)	35 (19.3)	<0.001
		1	5 (3.2)	10 (5.5)	
		2	33 (20.9)	37 (20.4)	
		3	8 (5.1)	35 (19.3)	
		4	4 (2.5)	64 (35.4)	
LS facet joints	n (%)	0	121 (76.6)	40 (22.1)	<0.001
		1	32 (20.3)	58 (32.0)	
		2	5 (3.2)	83 (45.9)	
Use of NSAID	n (%)	None	35 (22.2)	63 (34.6)	0.019
		Punctual	41 (25.9)	30 (16.5)	
		3-4 days/week	39 (24.7)	51 (28.0)	
		Daily	43 (27.2)	38 (20.9)	
bDMARD	n (%)		52 (32.9)	75 (41.2)	0.143

BMI: Body Mass Index; SpA: Spondyloarthritis; CRP: C-Reactive Protein; IBD: Inflammatory Bowel Disease; r-axSpA: radiographic axial Spondyloarthritis; AS: Ankylosing Spondylitis; EnA: Entheropatic Arhtritis (IBD-Associated Spondyloarthritis); Ps SpA: Psoriasic Spondyloarthritis; nr-axSpA: non-radiographic Spondyloarthritis; NSAID: Non-steroidal anti-inflammatory drugs; bDMARD: *Biologic Disease-modifying Antirheumatic Drug*

exclusively, and 37 (10,9%) had CS involvement without radiographic involvement of the lumbar spine (LS) (29,7% women). Patients from the CS group were predominantly men, older, had a higher BMI and a higher prevalence of smoking (table 1). They also showed a higher disease activity (BASDAI and ASDAS-CRP), worse function (BASFI), worse mobility in CS and LS (Schober test), as well as more structural damage in both LS and sacroiliac joints. No differences were found between groups for HLA B27 positive, age at diagnosis, familiar history, presence of arthritis, enthesitis, dactylitis or extra musculo-skeletal manifestations (uveitis, psoriasis or IBD).

Conclusion: The radiographic evaluation of the CS is relevant in axSpA, and it should be performed routinely, as well as the evaluation of the ZJ, as they are commonly involved in axSpA and related to higher disease activity and worse function.

Disclosure: p. Maymó: None; **L. Berbel Arcobé**: None; **X. Michelena**: Pfizer, 5; **J. Narvaez**: None; **J. Nolla**: None; **L. Valencia**: None; **J. Palacios**: None; **X. Juanola Roura**: None.

Abstract Number: 1874

Cartilage Thickness Measures Are More Responsive Than Cartilage Area Loss Measures: A Comparison of Quantitative and Semi-quantitative Cartilage Assessments from the Osteoarthritis Initiative

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Cartilage loss in 1-2 year osteoarthritis clinical trials is often small, but a critical outcome measure. The aim of this study was to compare the cross-sectional relationship and longitudinal responsiveness of the semi-quantitative MRI Osteoarthritis Knee Score (MOAKS) with quantitative cartilage thickness measures.

Methods: Images and MOAKS scores from 297 participants with radiographic progression (groups 1 and 2) from the OAI FNIH sub-cohort were included. To facilitate direct comparison with MOAKS, novel quantitative measures of cartilage loss were matched to MOAKS regions (Q-MOAKS).Mean normative cartilage thickness was computed for each subregion (Figure 1) using FNIH controls (group 4). Q-MOAKS thickness loss score (tQCM) was based on the proportion of cartilage thickness over a subregion that was < 95% normative thickness and denudation score (dQCM) was based on < 5% normative thickness. Q-MOAKS area proportions (tQCMr) were compared for responsiveness. These were categorised into scores as for MOAKS for cross-sectional analysis. Quantitative cartilage thickness (ThCtAB) was also measured in the MOAKS subregions. We compared MOAKS against Q-MOAKS and ThCtAB. Cross-sectional relationships between measures were assessed using Spearman's rank correlation. Responsiveness was assessed at 1 and 2 years using standardised response means (SRM).

Results: Cross-sectionally, there was moderate correlation between MOAKS and Q-MOAKS denudation in the central medial femur (cMF *r*=0.42, (95%CI:0.32, 0.51)) and tibia (cMT *r*=0.51, (0.42, 0.59)). There was a poor correlation between MOAKS and Q-MOAKS thickness loss and denudation scores in all other regions. In the cMT region, 61% (96/159) of knees with MOAKS thickness loss tMCM = 2 (the 10-75% score) were also tQMC = 2 and 66% of MOAKS denudation dMCM = 2 were also dQCM = 2 (Figure 2). In the cMF region, the figures were 56% and 23%.MOAKS tMCM and dMCM were less responsive than Q-MOAKS tQCM and dQCM in most subregions (Table 1). MOAKS tMCM in cMT demonstrated the most

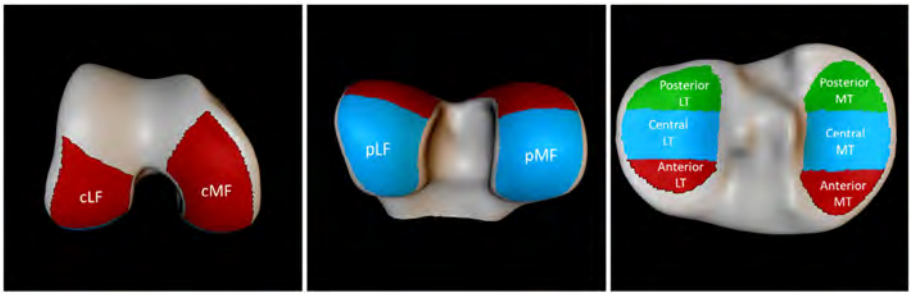

Figure 1: Cartilage regions defined for Q-MOAKS and ThCtAB. Cartilage regions definitions consisting of the medial and lateral central and posterior femur (cMF, cLF, pMF, pLF) subregions and the medial and lateral tibial anterior, central, posterior (aMT, cMT, pMT, aLT, cLT, pLT) subregions.

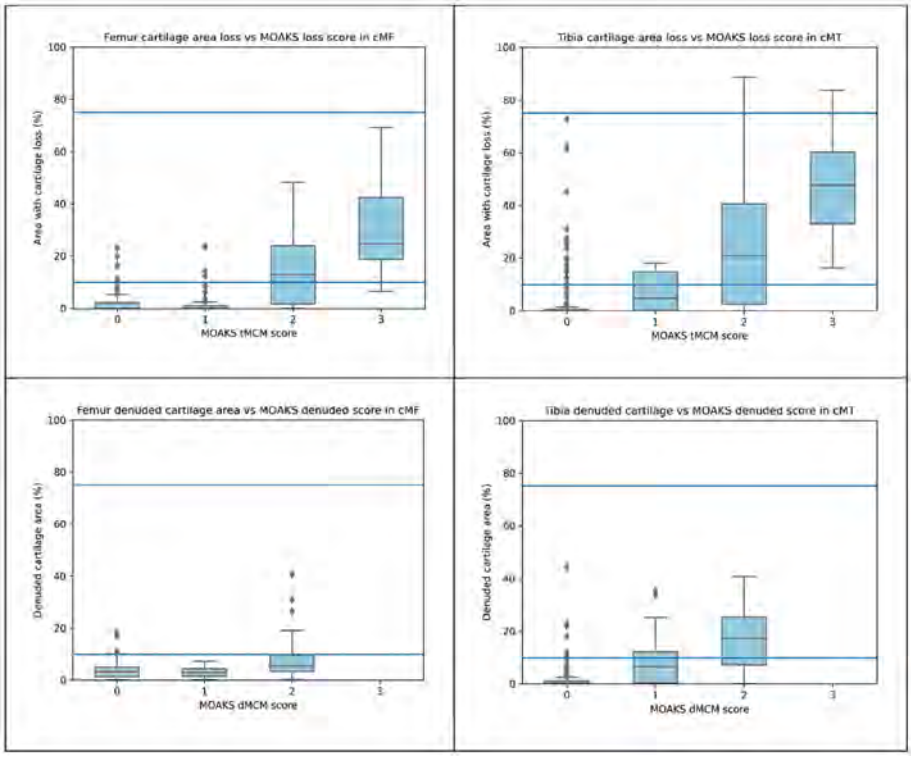

Figure 2: The association between 3D quantitative cartilage area percentage measures and MOAKS scores in the central medial femur and tibia. Top: comparison of cartilage thickness loss. Bottom: comparison of cartilage denudation. There were no MOAKS dMCM = 3 scores in this cohort. Horizontal blue lines indicate the MOAKS score definition thresholds (0: 0%, 1: 0-10%, 2: 10-75%, 3: >75%).

responsiveness for all the thickness loss scores (SRM=0.47, (95%CI:0.41, 0.54)). Quantitative cartilage thickness (ThCtAB) measures were most responsive.

Table 1: Responsiveness (SRM) of standard cartilage MOAKS scores, Q-MOAKS ratios and quantitative cartilage thickness at one-year and two-year follow-up.

	YEAR ONE			YEAR TWO		
			FEMUR			
	MOAKS tMCM	Q-MOAKS tQCMr	Thickness ThCtAB	MOAKS tMCM	Q-MOAKS tQCMr	Thickness ThCtAB
	0.15	0.36	-0.32	0.47	0.73	-0.84
	(0.02, 0.27)	(0.25, 0.47)	(-0.44, -0.20)	(0.41, 0.54)	(0.64, 0.83)	(-0.96, -0.73)
	0.00	0.09	-0.03	0.11	0.24	-0.22
	(-0.11, 0.12)	(-0.04, 0.18)	(-0.14, 0.08)	(0.00, 0.18)	(0.17, 0.31)	(-0.32, -0.11)
			TIBIA			
	MOAKS tMCM	Q-MOAKS tQCMr	Thickness ThCtAB	MOAKS tMCM	Q-MOAKS tQCMr	Thickness ThCtAB
	0.16	0.28	-0.40	0.39	0.49	-0.73
	(0.05, 0.26)	(0.18, 0.38)	(-0.52, -0.30)	(0.33, 0.45)	(0.38, 0.60)	(-0.85, -0.62)
	0.03	0.14	-0.23	0.19	0.22	-0.47
	(-0.07, 0.16)	(0.04, 0.24)	(-0.34, -0.13)	(0.14, 0.25)	(0.12, 0.32)	(-0.59, -0.36)

Conclusion: In the cross-sectional analysis, the concordance between MOAKS scores and the actual ratio of cartilage loss to subregion area was poor. MOAKS appeared to overestimate grades 2 and 3. Quantitative measures of thickness loss were almost twice as responsive as MOAKS, likely because thickness loss is a more responsive construct than area loss for cartilage assessment.

Disclosure: A. Ray: None; **A. Brett**: Stryker, 3, 8; **B. Dube**: None; **M. Bowes**: Stryker, 3, 8; **P. Conaghan**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, Genascense, 2, GlaxoSmithKlein(GSK), 2, Grunenthal, 2, Janssen, 2, Levicept, 2, Merck/MSD, 2, Moebius Medical, 2, Novartis, 2, 6, Stryker, 2, Takeda, 2, TrialSpark, 2.

Abstract Number: 1875

Inter and Intra-observer Reliability of Assessment for Nailfold Capillary Abnormalities in Rheumatic Patients with Raynaud's Phenomenon

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Background/Purpose: To investigate the consistency of rheumatologists' assessment of nailfold capillaroscopy images of patients with Raynaud's phenomenon (RP).

Methods: Nailfold video capillaroscopy(NVC), with a 200x magnification, was used to acquire images from6 digits (the second, third and fourth fingers of both hands) of patients with RP. According to the European League Against Rheumatism Study Group on Microcirculation in Rheumatic Diseases (EULAR SG MC/RD) standardized capillaroscopy evaluation chart, 5 trained rheumatologists classified all NVC images into five patterns: "normal", "non-specific", "early", "active" and "late", and their majority votes derived the gold standard. Two months later, one-fifth of these images were randomly selected for a second assessment by the same rheumatologists. Intra-class correlation coefficient (ICC) was used to analyze inter and intra-observer reliability, and Student's *t* test was used to compare ICC scores.

from

Results: We enrolled 302 participants with RP, 15 of them with primary and 287 with secondary RP. A total of 3805 high-resolution NVC images were obtained, with an average of 13.3 images per patient. The intra-observer reliability of assessment was higher than the inter- (ICC0.894 within and 0.645 between observers, p=0.001). There was poor reliability among rheumatologists for the evaluation of normal and non-specific patterns (inter-observer ICC 0.480 and 0.428 respectively). Agreement for the identification of active and late patterns (inter-observer ICC 0.508 and 0.513, respectively) is higher than for the early pattern (0.387, p=0.001).

Conclusion: Relatively low reliability between observers is one of the major problems in manual assessment of nailfold capillaries of RP patients. Methods to improve the consistency need to be proposed.

Disclosure: C. Wang: None; **H. Xu**: None; **X. Jiang**: None; **F. Jiang**: None; **Y. Zhuang**: None.

Abstract Number: 1876

A Deep Learning System for Automated Assessing Microcirculation Abnormalities in Nailfold Capillaroscopy Images of Systemic Sclerosis

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Session Time: 9:00AM–11:00AM

Background/Purpose: Detection of specific abnormalities in capillaries, named scleroderma patterns, by nailfold capillaroscopy (NFC) is one of the most important means to diagnose systemic sclerosis (SSc). In addition, different stages of the scleroderma pattern (the early, active, late stage) reflect the activity and severity of the disease. However, the reliability of the NFC images evaluated by rheumatologists was unsatisfactory. We aim to develop and validate a deep learning system for identifying scleroderma pattern from non-scleroderma patternand further classifying different stages of scleroderma pattern.

Methods: NFC with a 200x magnification was used to acquire images from the second, third and fourth fingers of both hands. Majority votes of three rheumatologists to judge the five NFC patterns (normal, non-specific, early, active and late pattern)derived ground-truth labels. NFC-captured images were randomly assigned to the train and validation sets in a 8:2

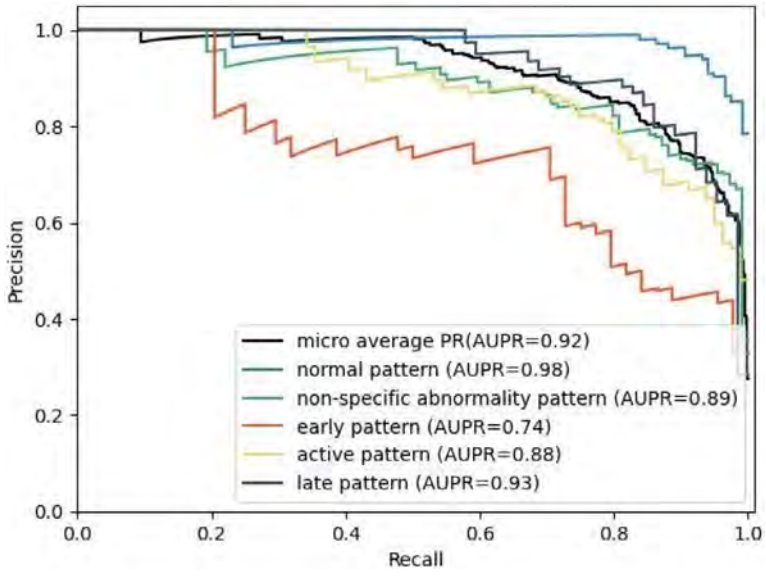

Figure 1. Precision Recall Curves on Validation Set. AUPR: Areas under the precision recall curve.

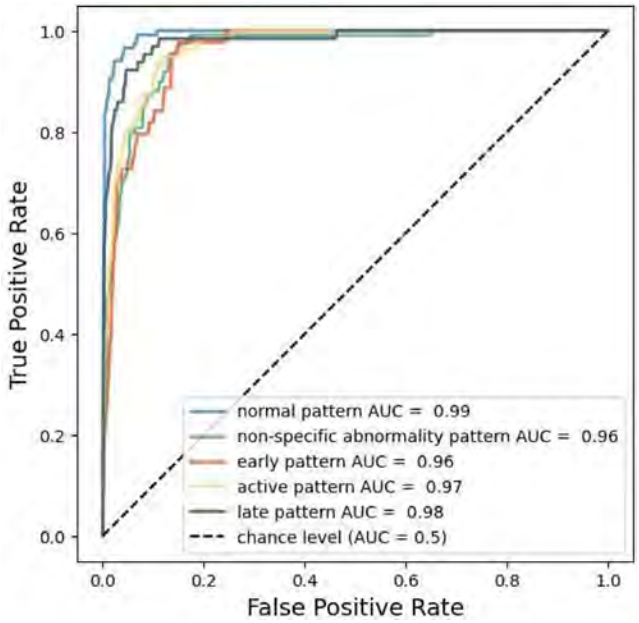

Figure 2. ROC Curves on Validation Set. AUC: Areas under the receiver operating characteristics curve.

ratio. Images analyzed using *ResNeXt*, a deep learning technique. The outcome investigated was the *ResNeXt*'s ability to identify different stages of NFC patterns. The performance of the model was assessed by estimating areas under the precision recall curvesand the receiver operating characteristics curves (ROCs).

Results: Nailfold capillaroscopy (NFC) was performed in 274 adult participants from two clinic medical centers, including 140 SSc and 134 controls (74 healthy controls, 27 with primary Raynaud's phenomenon, 48 with metabolic syndrome). A total of 2893 high-resolution NFC images were obtained, with an average of 10.6 images per participant. In the validation set, *ResNeXt* had good performance in identifying the different patterns in NFC images with areas under theprecision recall curves (AUPR) from 0.74 to 0.98, and with areas under the ROCs (AUC) from 0.96 to 0.99.

Conclusion: The *ResNeXt* is a well-performing tool for identifying scleroderma patterns in SSc from controls, and it may assist rheumatologistsin generating consistent and high-quality assessment of microcirculation abnormalities.

Disclosure: Y. Zhuang: None; **Z. Wang**: None; **J. Zhu**: None; **Y. Yu**: None; **Y. Liu**: None.

Abstract Number: 1877

Diagnostic Yield of ^{18}F-FDG PET-CT for Large Vessel Involvement in Patients with Suspected Giant Cell Arteritis and Negative Temporal Artery Biopsy

Javier Narvaez[1], Paula V. Estrada-Alarcón[2], Paola Vidal-Montal[3], Iván Sánchez-Rodriguez[4], Aida Sabate-Llobera[4], Montserrat Cortes-Romera[4] and Joan Miquel Nolla[5], [1]Hospital Universitario de Bellvitge, Barcelona, Spain, [2]Hospital de San Juan Despí Moisès Broggi, Barcelona, Spain, [3]Department of Rheumatology. Hospital Universitario de Bellvitge, Barcelona, Spain, [4]Department of Nuclear Medicine – PET IDI. Hospital Universitario de Bellvitge, Barcelona, Spain, [5]Department of Rheumatology, Hospital Universitario de Bellvitge, Barcelona, Spain

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II
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Background/Purpose: Every effort should be made to confirm a suspected diagnosis of giant cell arteritis (GCA). According to the 2018 update of the EULAR recommendations for the management of large vessel vasculitis, objective confirmation of the presence of vasculitis should always be obtained by histology (temporal artery biopsy [TAB]) or imaging, with color Doppler ultrasound (CDUS) of the temporal arteries being the most commonly used imaging method. However, in clinical practice, it is not uncommon to encounter patients with negative cranial studies, and this subgroup, remains the most challenging to diagnosis. The present study aimed to investigate the diagnostic performance of ^{18}F-FDG PET-CT for assessing large vessel involvement in patients with suspected GCA and a negative TAB.

Methods: We retrospectively reviewed our hospital databases to identify all patients with suspected GCA and a negative TAB who underwent an ^{18}F-FDG PET-CT in an attempt to confirm the diagnosis. The gold standard for GCA diagnosis was clinical confirmation after a follow-up period of at least 12 months.

Results: One hundred and twenty-seven patients were included. After a detailed review of the medical records, 73 patients were finally diagnosed has having GCA. Three of the remaining 54 subjects were diagnosed with other types of vasculitis, and 51 had other diagnoses. Among the 73 patients diagnosed with GCA, ^{18}F-FDG PET-CT was considered positive in 61 cases (83.5%). Nine of the 12 GCA patients with negative PET-CT had undergone previous glucocorticoid treatment. Of the 54 patients without ACG, FDG-PET was considered positive in only 8 (14.8%) (1 case of Erdheim-Chester disease, 3 IgG4-related disease, 1 case of sarcoidosis, and 3 clinically isolated aortitis). Overall, the diagnostic performance of ^{18}F-FDG PET-CT in assessing large vessel involvement in patients with suspected GCA and negative TAB yielded 83.5% sensitivity, 85.1% specificity, and a diagnostic accuracy of 84% with an area under the ROC curve of 0.844 (95% CI:0.752 to 0.936).

Conclusion: Our study confirms the usefulness of ^{18}F-FDG PET-CT when the GCA diagnosis is uncertain following a negative TAB result, by demonstrating the presence of large vessel vasculitis.

Disclosure: J. Narvaez: None; **P. Estrada-Alarcón**: None; **P. Vidal-Montal**: None; **I. Sánchez-Rodriguez**: None; **A. Sabate-Llobera**: None; **M. Cortes-Romera**: None; **J. Nolla**: None.

Abstract Number: 1878

MRI-determined Intramuscular Fat Changes During Oral Glucocorticoid Treatment: Findings from a Feasibility Study

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SESSION INFORMATION
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Background/Purpose: Oral glucocorticoid therapy has many adverse effects including insulin resistance and myopathy. Long-term glucocorticoid therapy causes a "sarcopenic obesity" phenotype of adiposity with muscle wasting. The type IIb ("fast twitch") muscle fibres affected by glucocorticoid myopathy make up a greater proportion of hamstrings than of quadriceps. Hamstring muscles also contains a higher proportion of intramuscular fat than quadriceps. In population studies intramuscular fat is a marker of "unhealthy aging" and is associated with elevated morbidity and mortality. We performed a study to determine the feasibility and sensitivity to change of various assessments of muscle for future research studies.

Methods: Modalities for assessment of muscles included MRI (using Siemens MAGNETOM Verio 3T MR Scanner) of proximal leg muscles(hamstrings; semitendinosus, semimembranosus, biceps femoris and quadriceps;rectus femoris, vastus lateralis, vastus medialis,vastus intermedius). A 40 slice volume interpolated breath-hold examination (VIBE), 2-point Dixon, image series was acquired with the inferior slice located at the insertion point of the distal rectus femoris muscle into the tendon. Muscle volume, and single slice intramuscular fat fraction estimates, were acquired from the same VIBE Dixon acquisition. Muscle strength was assessed by biodex/isokinetic dynamometry.Physical performance was assessed via an extended timed get up and go test. Feasibility was assessed in a group of patients treated with oral glucocorticoid therapy for various rheumatological indications and compared to data from age matched controls. Sensitivity to change was

A) Muscle Evaluation comparing baseline cases to controls (n=34 for cases and controls)			
	Case Mean (SD)	Control Mean (SD)	Unpaired T-test P-value
Muscle Imaging			
Muscle Volume [cm^3]	1130 (308)	1210 (298)	0.335
* Muscle Quality - Hamstring Fat Fraction [%]	8.93 (3.5)	7.26 (2.68)	0.028
Muscle Quality - Quadricep Fat Fraction [%]	4.57 (1.75)	4.84 (2.1)	0.559
Muscle Strength			
Time needed to complete extended time get up and go [s]	19.7 (10.8)	17.6 (3.64)	0.0845
* Hamstrings (Peak knee flexion [N.m])	31.2 (12.7)	47.0(21.8)	0.00155
Quadriceps (Peak knee extension [N.m])	89.1 (37.2)	77.1(34.4)	0.249
B) Longitudinal Muscle Evaluation comparing subset of baseline cases, to after 4-6 months of glucocorticoid use			
	Baseline Case Mean (SD)	Longitudinal Case Mean (SD)	Paired T-Test
Muscle Imaging (n=10)			
Muscle Volume [cm^3]	1130 (141)	1790 (158)	$t(9) = -2.09$, $p = 0.066$
*Muscle Quality - Hamstring Fat Fraction [%]	9.35 (4.81)	10.35 (5.65)	$t(9) = -2.97$, $p = 0.0157$
Muscle Quality - Quadricep Fat Fraction [%]	3.69 (1.07)	3.99 (1.36)	$t(9) = -1.92$, $p = 0.0868$
Muscle Strength (n=8)			
Time needed to complete extended time get up and go [s]	18.3 (3.94)	19.5 (6.37)	$t(7) = -1.04$, $p = 0.333$
Hamstrings (Peak knee flexion [N.m])	31.4(10.2)	31.0 (7.34)	$t(7) = 0.117$, $p = 0.910$
Quadriceps (Peak knee extension [N.m])	94.8 (31.5)	84.1(34.1)	$t(7) = 1.60$, $p = 0.154$

1a) Muscle Evaluation comparing baseline cases to controls (n=34 for cases and controls) 1b) Longitudinal Muscle Evaluation comparing subset of baseline cases, to after 4-6 months of glucocorticoid use

assessed in a subset of patients taking < 4 weeks glucocorticoid therapy at first assessment, by repeating the feasible measures after 4-6 months of glucocorticoid therapy.

Results: 34 glucocorticoid-treated patients (19 cases of polymyalgia rheumatica (PMR), 4 of giant cell arteritis (GCA), 5 of PMR and GCA, and 6 of other inflammatory conditions) were matched for age (range 45 to 86yrs) and sex (26/34 female) to 34 healthy controls. Compared to controls, patients treated with glucocorticoids had lower hamstring muscle strength and higher fat fraction, but similar muscle volume and physical performance (Table 1A). After 4-6 months of oral glucocorticoid therapy, there was a significant increase in hamstrings fat fraction compared to visit 1, and no significant change in the other measured variables (Table 1B).

Conclusion: Patients taking oral glucocorticoids for rheumatic diseases had greater hamstrings intramuscular fat than matched controls, and reduced hamstrings strength. These differences could have been due to the drug and/or the disease being treated. With increasing duration of glucocorticoid therapy there was a further increase in hamstring fat fraction despite no significant change in muscle strength. Intramuscular fat infiltration could be a sensitive modality for detecting metabolic alterations resulting from long-term glucocorticoid therapy. Further studies are needed to investigate the potential of MRI as a potential endpoint for clinical trials of glucocorticoid-sparing treatments.

Disclosure: T. Rajeswaran: None; **E. Harris**: None; **h. Mathieson**: None; **J. Biglands**: None; **P. Stewart**: Sparrow Therapeutics, 2; **A. Tan**: Abbvie, 1, 6, Gilead, 6, Janssen, 6, Lilly, 6, Novartis, 6, Pfizer, 6, UCB, 6; **S. Mackie**: AbbVie/Abbott, 2, AstraZeneca, 2, GlaxoSmithKlein(GSK), 3, 12, Investigator, National Institute for Health and Care Research, 5, 12, investigator on STERLING-PMR trial, funded by NIHR; patron of the charity PMRGCAuk, Pfizer, 2, 6, Roche, 2, 6, 12, Support from Roche/Chugai to attend EULAR2019 in person, Sanofi, 2, 12, Investigator, Sparrow, 12, Investigator, UCB and Novartis, 6, Vifor, 6.

Abstract Number: 1879

Artificial Intelligence for the Detection of Sacroiliitis on Magnetic Resonance Imaging in Patients with Axial Spondyloarthritis

Seulkee Lee[1], Uju Jeon[2], Ji Hyun Lee[3], Seonyoung Kang[1], Hyungjin Kim[1], Jaejoon Lee[1], Myung Jin Chung[2], Jinseok Kim[4], Eun-Mi Koh[5] and Hoon-Suk Cha[1], [1]Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea, [2]Medical AI Research Center, Samsung Medical Center, Seoul, South Korea, [3]Department of Radiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea, [4]Department of Rheumatology, Jeju National University Hospital, Jeju National University School of Medicine, Jeju-si, Jeju-do, South Korea, La Jolla, CA, South Korea, [5]Health Insurance Review and Assessment Service, Seoul, South Korea

SESSION INFORMATION

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Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II

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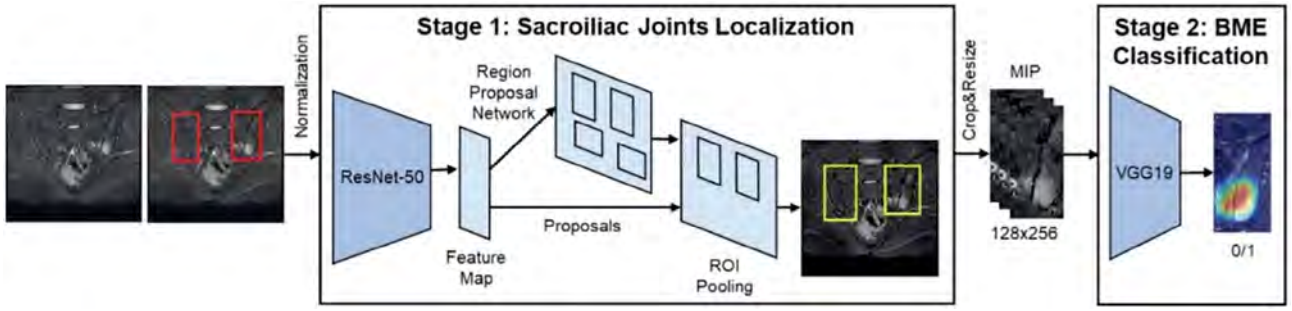
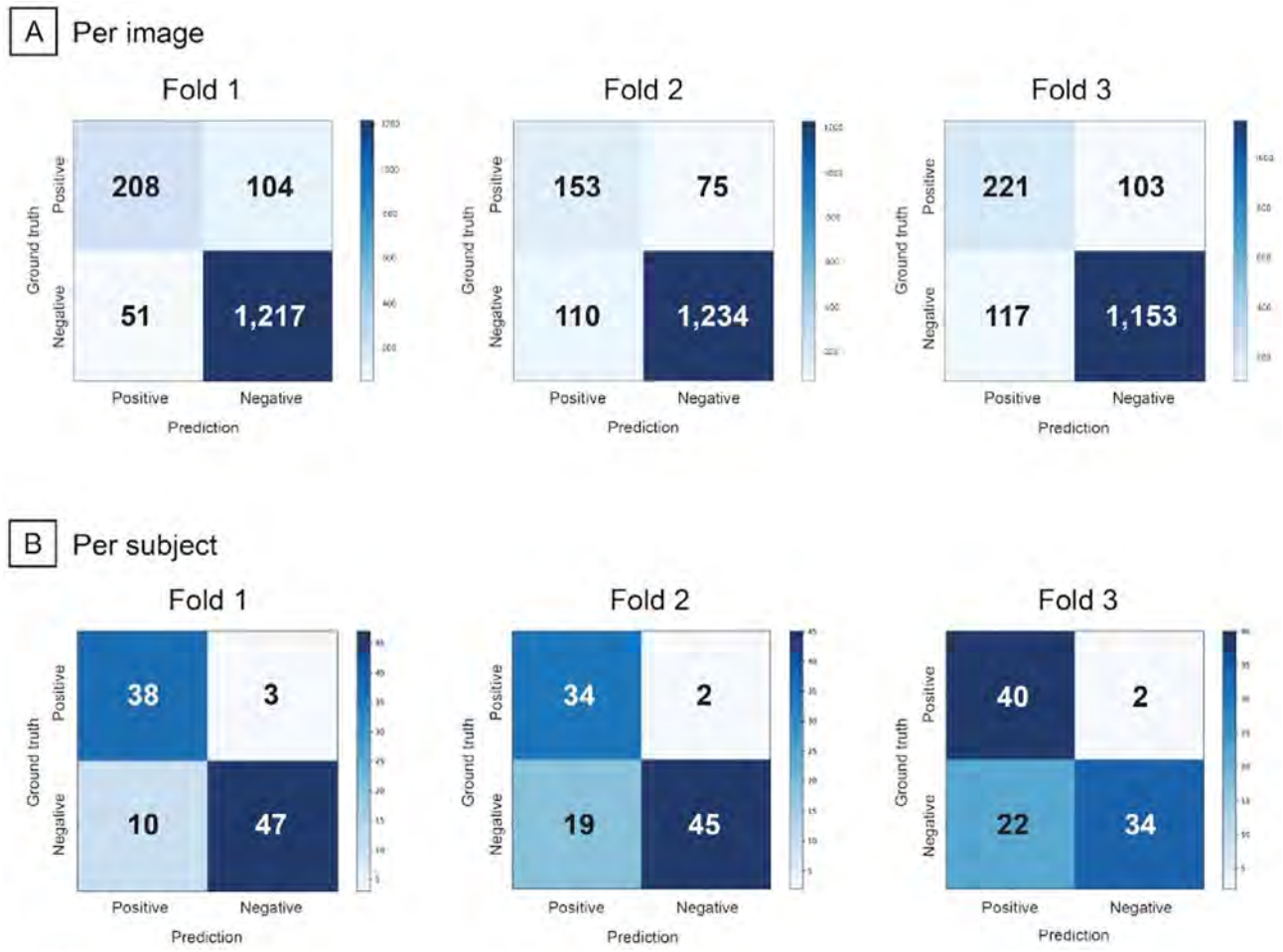
Session Time: 9:00AM–11:00AM

Background/Purpose: Magnetic resonance imaging (MRI) is important for the early detection of axial spondyloarthritis (axSpA). However, evaluation of sacroiliitis on MRI requires expertise because degenerative changes can mimic axSpA, and semiquantitative diagnosis remains subject to significant variation. Artificial intelligence (AI) has previously been applied to various MRI data including that of musculoskeletal system. Therefore, we developed an AI model for detecting in patients with axSpA, on MRI.

Methods: This study included MRI examinations of patients who underwent semi-coronal MRI scans of the sacroiliac joints owing to chronic back pain with short tau inversion recovery sequences between January 2010 and December 2021. Sacroiliitis was defined as a positive MRI finding according to the Assessment of Spondylo Arthritis international Society (ASAS) classification criteria for axSpA. The pipeline for the proposed automatic sacroiliitis classification method is shown in Figure 1. We developed a two-stage framework. First, the Faster R-CNN network extracted regions of interest (ROIs) to localize the sacroiliac joints. Maximum intensity projection (MIP) of three consecutive slices was used to mimic the reading



Artificial intelligence framework to detect sacroiliitis in accordance with the Assessment of SpondyloArthritis International Society criteria for axial spondyloarthritis.



Confusion matrices of the first-round cross-validation using the proposed method (Method C) for detecting sacroiliitis (A) for individual MRI slices; (B) for each subject.

Performances by individual MRI slices		
	Accuracy (95% CI), %	AUROC (95% CI)
Method A[a]	86.6 (85.4 to 87.8)	0.731 (0.681 to 0.780)
Method B[b]	86.5 (85.3 to 87.7)	0.747 (0.699 to 0.796)
Method C[c]	89.8 (88.8 to 90.8)	0.830 (0.792 to 0.868)
Performances by each patient		
	Accuracy	AUROC
Method A[a]	69.2 (62.7 to 75.6)	0.711 (0.660 to 0.763)
Method B[b]	69.9 (63.7 to 76.1)	0.722 (0.671 to 0.774)
Method C[c]	79.4 (73.9 to 84.9)	0.816 (0.776 to 0.856)

Abbreviation: AUROC, area under the receiver operating characteristic curve.

[a] Artificial intelligence model for the detection of sacroiliitis without augmentation and maximum intensity projection.

[b] Artificial intelligence model for the detection of sacroiliitis using augmentation without maximum intensity projection.

[c] Artificial intelligence model for the detection of sacroiliitis using both augmentation and maximum intensity projection.

Performances of artificial intelligence models for the detection of sacroiliitis compatible with the Assessment of SpondyloArthritis international Society definition.

of two adjacent slices. Second, the VGG-19 network determined the presence of sacroiliitis in localized ROIs. We augmented the positive dataset six-fold because of the smaller number of data points compared with the negative dataset. The sacroiliitis classification performance was measured using the accuracy and area under the receiver operating characteristic curve (AUROC). The prediction models were evaluated using three-round three-fold cross-validation.

Results: A total of 296 participants with 4,746 MRI slices were included. Sacroiliitis was identified in 864 MRI slices from 119 participants. The mean accuracy and AUROC for the detection of sacroiliitis were 89.8% (95% CI, 88.8%–90.8%) and 0.830 (95% CI, 0.792–0.868), respectively, at the image level and 79.4% (95% CI, 73.9%–84.9%) and 0.816 (95% CI, 0.776–0.856), respectively, at the patient level. The confusion matrices for the detection of sacroiliitis per image and subject are shown in Figure 2. In the original model, without using MIP and dataset augmentation, the mean accuracy and AUROC were 86.6% (95% CI, 85.4%–87.8%) and 0.731 (95% CI, 0.681–0.780), respectively, at the image level and 69.2% (95% CI, 62.7%–75.6%) and 0.711 (95% CI, 0.660–0.763), respectively, at the individual level (Table 1). Improved performances were observed compared with the original model.

Conclusion: An AI model was developed for the detection of sacroiliitis using MRI, compatible with the ASAS criteria for axSpA, with the potential to aid MRI application in a wider clinical setting.

Disclosure: S. Lee: None; **U. Jeon**: None; **J. Lee**: None; **S. Kang**: None; **H. Kim**: None; **J. Lee**: None; **M. Chung**: None; **J. Kim**: None; **E. Koh**: None; **H. Cha**: None.

Abstract Number: 1880

Performance of Machine Learning Algorithms in Discriminating Spondyloarthritis Features on Magnetic Resonance Imaging: A Systematic Review and Meta-analysis

Sun Jae Moon[1], **Seulkee Lee**[1], Seonyoung Kang[1], Hyungjin Kim[1], Jaejoon Lee[1], Jinseok kim[2], Eun-Mi Koh[3], Jinseub Hwang[4] and Hoon-Suk Cha[1], [1]Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea, [2]Division of Rheumatology, Department of Internal Medicine, Jeju National University Hospital, Jeju National University School of Medicine, Jeju, South Korea, [3]Health Insurance Review and Assessment Service, Seoul, South Korea, [4]Department of Data Science, Daegu University, Gyeongsan, South Korea

SESSION INFORMATION

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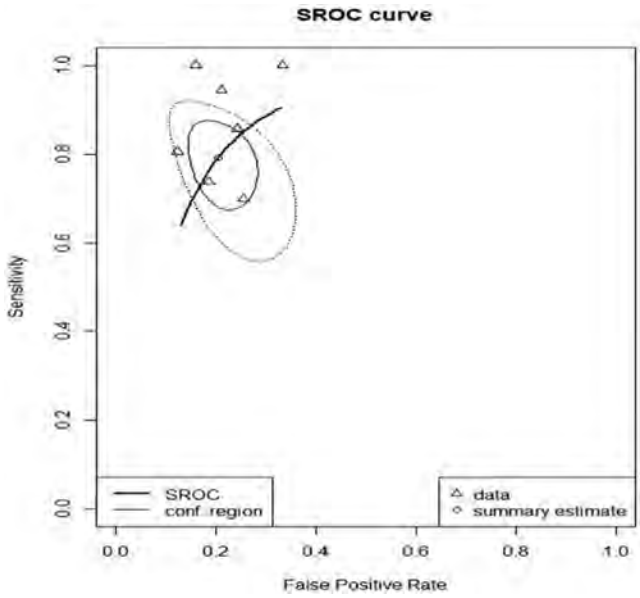
Background/Purpose: The diagnostic role of Magnetic Resonance Imaging (MRI) for axial spondyloarthritis(axSpA) has grown since introducing the ASAS criteria for axSpA. Recent advances in machine learning (ML) haveshown promisein MRI interpretation for sacroiliitis detection in axSpA. Thisstudy aims to provide a systemic review and a summary estimate ofperformance indices of MLalgorithms in discriminating sacroiliitis in accordance with axSpAon MRI.

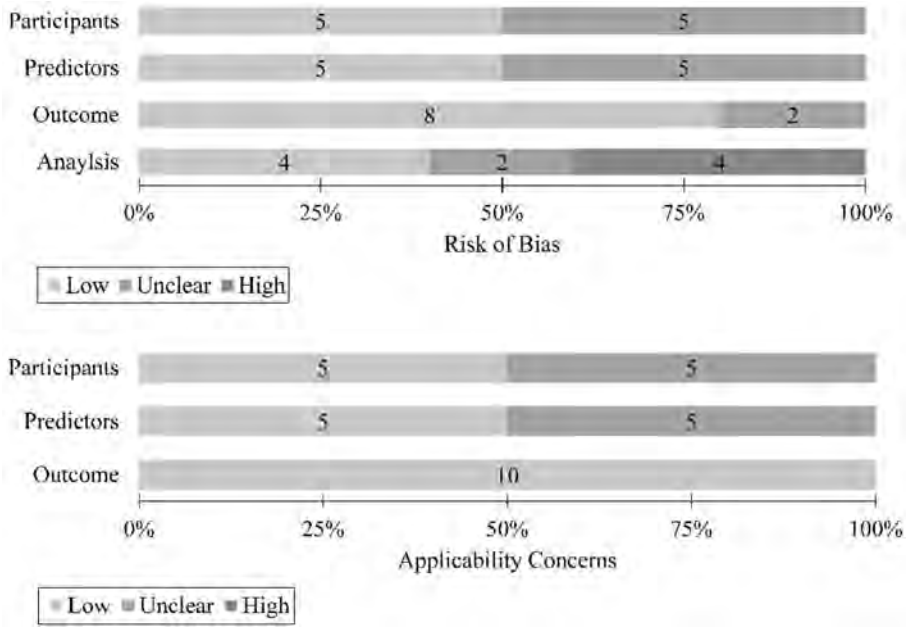
Methods: Embase, MEDLINE, CINAHL Complete, Web of Science, and IEEE Xplore Digital Library databases were used. The search was performed on 5 June 2023. Screening and extraction were performed independently by two authors according to the Checklist for Artificial Intelligence in Medical Imaging (CLAIM). To summarize sensitivity and specificity, a bivariate random effects model was employed. The Summary Receiver Operating Characteristics (SROC) curve derived from parameters extracted from a given model is presented with summary points defined by 95% confidence and prediction regions. This graph can also derive the partial Area Under the Curve (pAUC). Risk of bias was assessed by the checklist for



Summary Receiver Operating Characteristics (SROC) of seven studies, presented with the summary point of sensitivity and specificity defined by 95% confidence and 95% prediction regions

critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies (PROBAST). The protocol was registered before the review started (CRD42023415446).

Results: A total of 1,986 studies were searched. Following the selection process, ten and seven studies were used for qualitative assessment and meta-analysis, respectively. The majority of studies were original articles, predominantly from European and Asian regions, and based on hospital cohorts. Also, half of the 10 studiesutilized deep learning, and three studiesconducted external validation. Nine studies used the discrimination of radiologic SpA features of ASAS as the ground truth. Seven validation or test datasets (274 positive and 375 negative sacroiliitis patients) were included in the meta-analysis. Its pooled sensitivity, specificity, and pAUC were 79% (95% CI: 70-86%), 80% (73-85%), and 0.79 respectively (Figure 1). Two studies conducted external validation and comparison between machine and human doctors. The



Summary plot of the quality checklist for critical appraisal and data extraction for systematic reviews of prediction modeling studies (PROBAST) of 10 studies

	Machine learning vs human rater(s)	Sensitivity (95% CI)	Specificity (95% CI)	Accuracy (95% CI)
Bordner 2023 (n = 47)	Ensembling Mask Regions with convolutional neural network (RCNN)	56% (42% - 70%)	100% (100% - 100%)	92% (88% - 100%)
	Expert radiologist 1	100% (100% - 100%)*	100% (100% - 100%)	94% (87% - 98%)
	Expert radiologist 2	89% (80% - 98%)*	100% (100% - 100%)	98% (94% - 100%)
	Expert radiologist 3	67% (54% - 80%)	97% (92% - 100%)	92% (84% - 100%)
	Expert radiologist 4	100% (100% - 100%)*	95% (89% - 100%)	96% (90% - 100%)
	Expert radiologist 5	78% (66% - 90%)	100% (100% - 100%)	96% (90% - 100%)
	Expert radiologist 6	100% (100% - 100%)*	93% (86% - 100%)	94% (87% - 100%)
Bressem 2022 (n = 73)	Deep neural network (DNN)	86% (64% - 97%)	76% (68% - 86%)	78% (69% - 85%)
	Expert radiologist 1	71% (48% - 89%)	100% (97% - 100%)*	95% (89% - 98%)*
	Expert radiologist 2	100% (89% - 100%)	96% (90% - 99%)*	97% (91% - 99%)*
	Expert radiologist 3	90% (70% - 99%)	98% (93% - 100%)*	97% (91% - 99%)*
	Expert radiologist 4	95% (76% - 100%)	88% (80% - 94%)	90% (83% - 95%)
	Expert radiologist 5	67% (43% - 85%)	96% (90% - 99%)*	91% (84% - 95%)
	Expert radiologist 6	95% (76% - 100%)	89% (81% - 95%)	91% (84% - 95%)
	Average of experts	84% (64% - 98%)	95% (90% - 98%)*	94% (87% - 97%)*
	Non-expert radiologist 1	81% (58% - 95%)	84% (75% - 91%)	84% (76% - 90%)
	Non-expert radiologist 2	76% (53% - 92%)	87% (79% - 93%)	85% (78% - 91%)
	Non-expert radiologist 3	81% (58% - 95%)	91% (83% - 96%)	89% (82% - 94%)
	Average of non-experts	79% (56% - 93%)	87% (79% - 93%)	86% (79% - 92%)

Sensitivity, specificity and accuracy of two studies performed external validation and comparison between machine and human rater(s).

Ensembling Mask regions with convolutional neural network algorithm's accuracy achieved 92% (88-100%), and that of expert radiologists' showed a range of 92-98%. The deep neural network algorithm's accuracy from the other study showed 78% (69-85%), and that of expert and non-expert radiologists' were an average of 94% (87-97%) and 86% (79-92%) respectability (Table). The summary of the quality appraisal tool (PROBAST) showed that more than half of the studies (six of 10 studies) were unclear and had a high risk of bias in the analysis domain (Figure 2).

Conclusion: ML algorithms for discriminating SpAfeatures in MRI have acceptable pooled sensitivity and specificity (around 80%). However, there are potential bias concerns in the validation process, and the number of studies comparing the accuracy of human experts and machines was small, limiting interpretation. An accuracy issue of machine leaning algorithms inSpA can be concluded in the future if well-designed and transparent reports that follow a guideline become more widely available.

Disclosure: S. Moon: None; **S. Lee**: None; **S. Kang**: None; **H. Kim**: None; **J. Lee**: None; **J. kim**: None; **E. Koh**: None; **J. Hwang**: None; **H. Cha**: None.

Abstract Number: 1881

Deep Learning Approaches to Rheumatoid Arthritis Severity Prognosis

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SESSION INFORMATION
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Background/Purpose: Rheumatoid arthritis (RA) is the most common form of inflammatory arthritis affecting a large sector of the global population. The disease is associated with a high socio-economic burden owing to disability caused and costs of treatment. Conventional diagnostic methods rely on the skill of trained clinicians in interpreting and prognosing the severity of RA from X-ray images. This is slow, costly, and often error prone. We propose novel AI models that can perform an automatic quantification of X-Ray damage.

Methods: Data is retrieved from the Prince of Wales Hospital in Hong Kong. Patients diagnosed with RA were recruited with physician's diagnoses are recorded at the first clinic visit according to ICD9-CM. Inclusion criteria are 1) patients who carried the diagnosis code of RA (ICD9-CM: 714), 2) >= 1 follow up visit after disease onset, 3) serial XR hands available (>= 1 set) after disease onset, 4) age >=18 at disease onset, and 5) DAS28 < 5.1. The final dataset consists of a cohort of ∼600 X-ray images of hands and feet. Each X-ray image is labeled with a corresponding value for the van der Heijde Modified Sharp score (vdH score). Our trained deep learning model analyzes a typical X-ray image in two distinct ways:

1. Classification: we partition the dataset according to the vdH value into 11 disjoint sets. Each set corresponds to images with vdH score within a specific range. The classifier is then tasked with deciding the range of vdH values to be assigned to a typical X-ray image;

2. Regression: our trained model directly outputs a numerical value of the vdH score based on its analysis of a typical X-ray image. This task is computationally harder than classification as the model predicts continuous values and therefore can be used in disease progression analysis of X-rays collected over time.

These approaches are prefaced by preprocessing pipelines designed to take the intricacies of images into account. Our deep learning frameworks are based on the Visual Transformer (ViT) architecture. For regression, our framework can take prior information regarding RA severity into account, much in the same way that a physician performs annotation on an image. Prior information is integrated into the regression framework in the form of a trained shape model.

Results: We obtained accuracies between 70-75% on the validation dataset, for the 11-bin classification problem. We also computed the Area-Under-Curve score (AUC), which is a more accurate reflection on the robustness of our classification in the presence of imbalanced data. We obtained an AUC of 0.8. For the regression problem, we obtain relational errors of 0.25-0.3 (computed as fractional deviation of prediction from truths), competitive with a clinician.

Conclusion: We implement deep learning frameworks to automatically assign severity scores to X-rays of bones via classification or regression. With both frameworks we show that it is possible for deep learning prognostic pipelines to be robustly implemented and deployed for use in a conventional clinical workflow, thus paving the way for expedited prognosis and increased quality of care for RA patients.

Disclosure: Z. Lai: None; **A. Iyer**: None; **I. To**: None; **I. Lodato**: None; **S. Hiranandani**: None; **T. LAM**: None; **H. So**: None; **L. Tam**: AbbVie, 5, Amgen, 2, 5, Boehringer-Ingelheim, 2, 5, Eli Lilly, 2, GSK, 5, Janssen, 2, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 2.

Abstract Number: 1882

Imaging in Diagnosis, Monitoring and Outcome Prediction of Large Vessel Vasculitis: A Systematic Literature Review Informing the 2023 Update of the EULAR Recommendations

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Since the development of the EULAR recommendations for the use of imaging in large vessel vasculitis (LVV) in 2017, new data has emerged in the field of imaging techniques and their application in the diagnosis and follow-up of patients with giant cell arteritis (GCA) and Takayasu arteritis (TAK).The objective of this review was to summarize

Table 1. Pooled sensitivities and specificities of diagnostic studies on GCA with clinical diagnosis as reference standard GCA, giant cell arteritis; MRI, magnetic resonance imaging; PET-CT, positron emission tomography – computed tomography; US, ultrasound

	Index test	Number of studies	Pooled sensitivity (95%CI)	Pooled specificity (95%CI)
All studies	US	23	0.76 (0.66,0.83)	0.91 (0.86,0.94)
	MRI	8	0.82 (0.76,0.86)	0.92 (0.84,0.97)
	PET-CT	5	0.80 (0.70,0.87)	0.91 (0.67,0.98)
Low risk of bias studies	US	8	0.88 (0.83,0.92)	0.96 (0.86,0.99)
	MRI	3	0.81 (0.71,0.89)	0.98 (0.89,1.00)
	PET-CT	4	0.76 (0.67,0.83)	0.95 (0.71,0.99)

the evidence on different imaging techniques for diagnosis, monitoring, and outcome prediction in LVV in order to inform a EULAR task force updating the recommendations for imaging in LVV.

Methods: Systematic literature review (SLR) on studies published between 2017-2022 on ultrasound (US), magnetic resonance imaging (MRI), computed tomography (CT), positron emission tomography (PET)-CT/MRI and fluorescein angiography in patients with LVV (PROSPERO registration CRD42022360545). Eligible study designs included randomized controlled trials and observational studies but excluded case-controlled studies. Two reviewers independently performed data extraction, synthesis, and risk of bias assessment. For studies on diagnosis, meta-analyses were performed using data from both the original and updated SLR whenever possible. Pooled sensitivities and specificities were obtained by fitting random effects models for all studies and for studies with low risk of bias separately. Meta-analyses were performed in R version 4.2.1. using the "lme4" package. The description of observations without inferences and the heterogeneity of reported data precluded any meta-analysis for outcome prediction or monitoring.

Results: A total of 4696 references were identified. Thirty-eight studies on GCA (n=32), TAK (n=2), and GCA and TAK (n=4) were included through the update, adding up to eighty-one studies from both SLRs. Pooled sensitivities and specificities for US, MRI and PET-CT using a clinical diagnosis of GCA as the reference standard are depicted in table 1. No studies on the diagnostic value of imaging techniques were found for TAK. The US evaluation of patients with suspected GCA, including the assessment of both cranial and extracranial vessels, showed a higher pooled sensitivity (95%CI) (89% [73%-96%] vs 70% [59%-79%]) and similar specificity (95%CI) (91% [83%-95%] vs 91% [84%-94%]) compared to only including cranial vessels. Studies on outcome prediction (n=5) and monitoring (n=10) reported change of signs of vasculitis along with disease activity and proposed composite scores comprising several vessel territories for US, MRI and PET-CT.

Conclusion: US, MRI and PET-CT revealed a good performance for the diagnosis of GCA. Assessing both cranial and extracranial vessels with US leads to a higher pooled sensitivity with a similar pooled specificity compared to an assessment limited to cranial vessels.

Disclosure: P. Bosch: Janssen, 6, 12, Congress fees, Pfizer, 5; **M. Bond**: AbbVie/Abbott, 5; **C. Dejaco**: AbbVie/Abbott, 1, 5, 6, Eli Lilly, 6, Galapagos Pharma, 1, 6, Janssen, 1, 6, Novartis, 1, 6, Pfizer, 6, Sparrow, 1; **C. Ponte**: None; **S. Mackie**: AbbVie/Abbott, 2, AstraZeneca, 2, GlaxoSmithKlein(GSK), 3, 12, Investigator, National Institute for Health and Care Research, 5, 12, investigator on STERLING-PMR trial, funded by NIHR; patron of the charity PMRGCAuk, Pfizer, 2, 6, Roche, 2, 6, 12, Support from Roche/Chugai to attend EULAR2019 in person, Sanofi, 2, 12, Investigator, Sparrow, 12, Investigator, UCB and Novartis, 6, Vifor, 6; **L. Falzon**: None; **W. Schmidt**: AbbVie/Abbott, 2, 5, 6, Amgen, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Chugai, 2, 6, Eli Lilly, 2, GlaxoSmithKlein(GSK), 5, 6, Johnson & Johnson,

2, Medac, 2, Novartis, 2, 5, 6, Pfizer, 2, Roche, 2, 6, Sanofi, 2, 5, 6, UCB, 2; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, Galapagos, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, UCB Pharma, 2, 5.

Abstract Number: 1883

Thalamocortical Mechanisms of a Remote Mind-body Intervention for Knee Osteoarthritis Pain

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Studies found that individuals with pain exhibit altered thalamocortical rhythm, abnormal function, and structural connectivity within the network. Effective treatment may relieve pain by modulating the thalamocortical circuits. We examine how remote Tai Chi mind-body exercise modulates the static and dynamic resting state functional connectivity (rsFC) of thalamus subregions associated with movement, sensory and limbic systems.

Methods: Patients ≥ 50 years of age who met ACR criteria for symptomatic KOA were randomized to either a Tai Chi or Wellness Education and attended 12 weeks of biweekly remote sessions. The clinical outcomes included WOMAC, Anxiety and Depression, Self-efficacy and quality of life. Resting-state Functional magnetic resonance imaging (fMRI, using simultaneously multi-slice sequences) and high-resolution structure MRI scans were applied with a 3.0T Siemens scanner at baseline and after intervention. We applied theCONN toolbox for seed-based static and dynamic rsFC analysis. Three thalamus subregions (motor thalamus subregion, ventral posterolateral thalamus and mediodorsal thalamus) were used as seeds based on parcellation of the thalamic nuclei of AAL3. A threshold of $p < 0.005$ voxel-wise and $p < 0.05$ False Discovery Rate corrected at cluster level was applied for whole-brain analysis. Small volume correction was applied for pre-defined regions of interest (limbic system and prefrontal cortex).

Results: Thirty-four patients were randomized and 31 completed pre- and post-MRI scans. Mean age was 66 years, 65% female. At 12 weeks, compared to education, a significantly greater improvement in WOMAC pain score was found in the Tai Chi group ($p < 0.05$). No significant differences between groups were found for other clinical outcomes. *Static rsFC analysis* showed that compared to Wellness education, remote Tai Chi exercise increased 1) motor thalamus subregion static rsFC at the right cerebellum (lateral hemisphere); 2) ventral posterolateral thalamusstatic rsFC at the right cerebellum (medial and lateral hemisphere); 3) mediodorsal thalamus static rsFC at the bilateral cerebellum (medial and lateral hemisphere). Tai-Chi decreased 1) motor thalamus subregion static rsFC at the bilateral dorsal anterior cingulate cortex (dACC) and right amygdala/hippocampus; 2) ventral posterolateral thalamus static rsFC at the right lateral and orbital prefrontal cortex, bilateral dACC/mid-cingulate cortex, and right hippocampus; 3) mediodorsal thalamus static rsFC at bilateral temporal gyrus/uncus/amygdala/hippocampus. *Dynamic rsFC analysis* showed that compared to Wellness education, remote Tai Chi decreased 1) motor thalamus subregion dynamic rsFC at the left rACC/medial prefrontal cortex (mPFC), and bilateral cerebellum; 2) ventral posterolateral thalamus dynamic rsFC at the bilateral rACC/mPFC, primary motor and premotor cortex and middle temporal gyrus. No significant findings when using the mediodorsal thalamus as a seed.

Conclusion: Our results suggest that remote Tai Chi can modulate the functional connections between the thalamus-cerebellum and thalamus-limbic systems in individuals with KOA, and can reduce theconnectivityvariability betweenthese regions.

Disclosure: J. Kong: None; **V. Sacca**: None; **C. Wang**: None.

Abstract Number: 1884

Which Cell Pattern in Immunological Bronchoalveolar Lavage (BAL) Is Associated with a High-resolution Computer Tomography (HRCT) Pattern at the Onset of Inflammatory Rheumatic Disease with Interstitial Lung Disease?

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II
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Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammatory rheumatic diseases (IRD) are associated with interstitial lung disease (ILD). High-resolution Computer Tomography (HRCT) is recommended as goldstandard in the detection of IRD-ILD. The main HRCT-pattern included ground-glass opacities (GGO), non-specific interstitial pneumonia (NSIP), usual interstitial pneumonia (UIP), granuloma and cryptogenic organizing pneumonia (COP). Further, bronchoalveolar lavage (BAL) can be used to evaluate pulmonal cell pattern. The aim of this study was to evaluate HRCT pattern at the onset of IRD-ILD and to correlate the HRCT pattern to immunological BAL pattern.

Methods: The study includes 61 patients (connective tissue disease n=39, myositis n=9, vasculitis n=10 and rheumatoid arthritis n=3) with newly diagnosed IRD and evidence of ILD on HRCT. In addition to HRCT, immunological BAL was performed. The American Thoracic Society Clinical Practice Guideline were used to define BAL pattern with lymphocytic cellular pattern (>15% lymphocytes), neutrophilic cellular pattern (> 3% neutrophils), eosinophilic cellular pattern (>1% eosinophils) and unspecific cellular pattern. No patient received any immunosuppressive therapy.

Results: For the total study cohort, the main HRCT pattern were NSIP (44.3%) and GGO (31.3%), followed by UIP (14.8%), granuloma (4.9%) and COP (3.3%). BAL pattern showed the following distribution: 37.7% lymphocytic cellular pattern, 27.9% neutrophilic cellular pattern, 18.0% eosinophilic cellular pattern and 16.4% unspecific cellular pattern. Concerning GGO, the main BAL pattern was lymphocytic cellular pattern (47.4%), whereas neutrophilic cellular pattern (37.0%) and lymphocytic cellular pattern (25.9%) were the dominant pattern in NSIP. UIP revealed the following BAL pattern: lymphocytic cellular pattern 55.6%, neutrophilic cellular pattern 33.3% and unspecific cellular pattern 11.1%.

Conclusion: GGO in HRCT is associated with the occurrence of a lymphocytic pattern in BAL, whereas in NSIP and UIP pattern the lymphocytic and neutophilic pattern is equally expressed. Based on the data, a further leading evaluation should be made with regard to the therapeutic options (anti-inflammatory and / or anti-fibrotic therapy) as well as the prognosis of IRD-ILD.

Disclosure: t. Hoffmann: None; **M. Förster**: None; **P. Oelzner**: None; **C. Kroegel**: None; **U. Teichgräber**: None; **D. Renz**: None; **J. Böttcher**: None; **C. Schulze**: None; **G. Wolf**: None; **M. Franz**: None; **A. Pfeil**: None.

Abstract Number: 1885

The Frequency and Importance of Subchondral Radius Cysts in Rheumatoid Arthritis Patients Under B/tsDMARDs

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SESSION INFORMATION
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Background/Purpose: The presence of subchondral cysts in patients with rheumatoid arthritis (RA) has long been recognised. The concept of geodes used in geology would be the best terminology used to name the latter. In this asessment, we aimed to determine the frequency, distribution and characteristics of geodes in the radius in RA patients in a biologic disease modifying anti-rheumatic drug (bDMARD) cohort.

Methods: The HUR-BIO database was established in 2005, 2355 RA patients were registered as of January 2023. Anterior-posterior standard hand X-rays of the first 500 patients in HUR-BIO who had at least one hand X-ray were evaluated. The most recent hand X-ray of the patients was evaluated. From 500 patients in 28 (5.6%) patients, the presence or absence of subchondral cysts on radiographs could not be determined. 24 (4.8%) patients had cystic-erosive changes in the radius, but these patients were not included in the analysis because the bone integrity of the radius cortex was compromised. The localisation and size of the geodes, the distance from the distal part of the radius, the distance from the geodes to the radius, and the distance between the radius and the carpal bone were measured. The distance between the radius and scaphoid and the distance between the radius and lunate bone were measured at the narrowest point (Figure 1). Involvement of the carpal bones was evaluated according to the modified Larsen score. Demographic, clinic characteristtics were assessed and compared between patients with and without goedes.

Results: Goedes were found in 63/448(14.1%) of these patients. Mean (SD) years of age at the time of hand x-ray was 54.4 (12.4) and 51.1 (12.9) in with/out goedes, respectively In the comparison of patients with/out goedes, there were differences in terms of male gender and anti-CCP positivity and disease duration. Larsen score in carpal bones was worse in patients with subchondral cysts (Table 1). A total of 98 cysts were found in 63 patients; 8 (12.6%) unilateral single cyst 37 (58.7%), unilateral double cyst 14 (22.2%), bilateral 12 (19.0%). The dominant cyst on the right was found in 40 patients and the second cyst in 14 patients, while the dominant cyst on the left was found in 35 patients and the second cyst in 9 patients. The distribution of sclerosis around these cysts was as follows; absent 4 (4.1%), mild 59 (60.2%), moderate 33 (33.7%), marked 2 (2.0%). The mean (SD) distance between the upper end of the cyst and the radius was 1.7 (0.67) mm. In 26 patients with multiple cysts, anti-CCP antibody positivity was more frequent (90.0% vs 64.3%, p=0.043), and Larsen score of grade 2 or higher was more frequent (92.3% vs 67.6%, p=0.020) Patients with subchondral cysts larger than 50 mm2 were more frequently male (64.7% vs 21.7%, p=0.001), smoking was more frequent (76.5% vs 43.2%, p=0.020).(Table 2).

Conclusion: In a cohort of RA patients who were required to use bDMARD, geodes were found in the radius in 14% of patients. These cysts were, usually single but bilateral in one-fifth of the patients. The relation between the diameter and number of geodes, anti-CCP positivity and gender suggests that these patients may represent a subgroup with a more erosive course.

Table 1. Characteristics of patients with and without geodes in the radius

	Radius Subcondral cyst (+) n=63	Radius Subcondral cyst (-) n=385	p
Age at the time of , year, mean (SD)	54.4 (12.4)	51.1 (12.9)	0.073
Gender (Male), n(%)	21 (33.3)	82 (21.3)	**0.035**
Disease duration from diagnosis, year, median (IQR)	15 (13)	8 (9.8)	**<0.001**
Disease duration from symptom onset, year, median (IQR)	16 (10)	10 (10)	**<0.001**
Time between symptom onset-bDMARD start, year, mean (SD)	12.0 (7.0)	8.3 (7.6)	**<0.001**
Time between diagnosis bDMARD start, year, mean (SD)	11.5 (8.4)	6.4 (6.9)	**<0.001**
Anti-CCP positivity, n (%)	36/48 (75.0)	186/312 (59.6)	**0.041**
RF positivity, n (%)	44/62	247/379	0.37
Smoking, (Ever), n(%)	32/61	167/377	0.23
BMI, mean (SD)	29.2 (6.1)	29.4 (5.9)	0.84
DAS-28, mean (SD)	3.30 (1.48)	3.57 (2.05)	0.33
HAQ-DI, mean (SD)	0.73 (0.65)	0.87 (1.21)	0.41
Carpal bone involvement			
Grade 0	2 (3.2)	119 (30.9)	**<0.001**
Grade 1	12 (19.0)	157 (40.8)	
Grade 2	23 (36.5)	59 (15.3)	
Grade 3	21 (33.3)	41 (10.6)	
Grade 4	4 (6.3)	9 (2.3)	
SD: Standard deviation, IQR: Inter-quartile range, Anti CCP: anti- cyclic citrullinated peptide, RF:Rheumatoid factor, BMI: Body mass index, DAS 28: Disease Activity Score in 28 Joints			

Table 2. Differences in patient and clinical characteristics according to goedes count and size

	Number of goedes			Goedes area		
	One goede n=37	More than one goede n=26	p	≥ 50 mm² n=17	< 50 mm² n=46	p
Gender (Male), n(%)	12	9	0.85	11 (64.7)	10 (21.7)	**0.001**
Age at the time of X-ray year, mean (SD)	54.0 (12.2)	54.9 (12.8)	0.85	57.5 (13.0)	53.2 (12.0)	0.21
Time between the diagnosis and X-ray, year, mean (SD)	15.8 (9.4)	16.2 (7.3)	0.76	15.5 (7.2)	16.1 (9.0)	0.82
Anti-CCP positivity, n (%)	18/28	18/20 (90.0)	**0,043**	11/12	25/36	0.12
RF positivity, n (%)	23/36	21/26	0,14	11/16	33/46	0.82
Smoking, (Ever), n(%)	21/35	11/26	0,17	13/17 (76.5)	19/44 (43.2)	**0.020**
BMI, mean (SD)	29.8 (6.6)	28.4 (5.4)	0.45	32.1 (7.2)	28.0 (5.3)	**0.041**
DAS-28, mean (SD)	3.42 (1.59)	3.11 (1.30)	0.45	3.02 (1.46)	3.40 (1.49)	0.50
HAQ-DI, mean (SD)	0.78 (0.68)	0.67 (0.62)	0.54	0.73 (0.73)	0.73 (0.63)	0.99
Carpal bone involvement (≥ grade2), n(%)	25/37 (67.5)	24/26 (92.3)	**0,020**	11 (64.7)	38 (82.6)	0.13
Right RS distance (mm), mean (SD)	13.0 (7.7)	9.1 (5.7)	**0.031**	1.17 (0.53)	1.12 (0.77)	0.83
Right RL distance (mm), mean (SD)	12.1 (7.2)	9.3 (7.2)	0.14	1.19 (0.62)	1.06 (0.72)	0.54
Left RS distance (mm), mean (SD)	12.6 (7.2)	10.2 (7.9)	0.22	1.19 (0.55)	1.15 (0.82)	0.87
Left RL distance (mm), mean (SD)	12.4 (7.5)	9.3 (7.9)	0.11	1.08 (0.72)	1.12 (0.80)	0.84

SD: Standard deviation., Anti CCP: anti- cyclic citrullinated peptide, RF:Rheumatoid factor, BMI: Body mass index, DAS 28: Disease Activity Score in 28 Joints, RS:Radioscaphoid, RL:Radiolunate

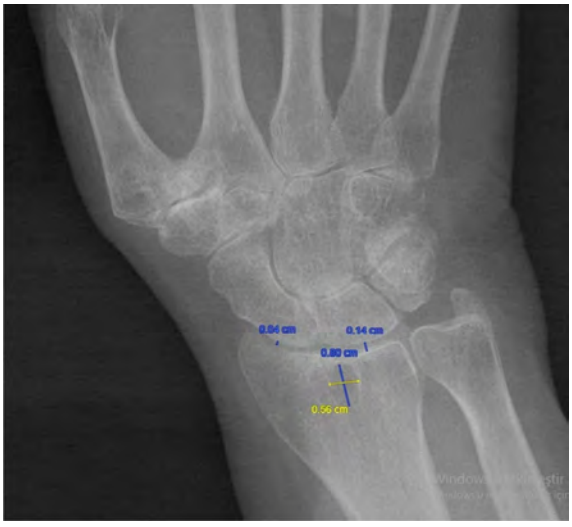

Figure. Schematic representation of measurements

Disclosure: U. Kalyoncu: None; **G. Ayan**: None.

Abstract Number: 1886

Costotransverse Joint Ankylosis and Association with Syndesmophyte Progression in Patients with Radiographic Axial Spondyloarthritis

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SESSION INFORMATION
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Background/Purpose: Costotransverse joint ankylosis in radiographic axial spondyloarthritis (r-axSpA) patients was measured. Furthermore, the association between syndesmophyte progression assessed by CT syndesmophyte score (CTSS) and facet, costovertebral, and costotransverse joints ankylosis were evaluated.

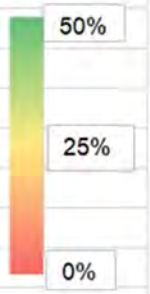
Methods: Whole spine CT images taken at baseline and at 2-year follow-up were used to calculate the CTSS of vertebral body. In addition, ankylosis of the facet/costovertebral/costotransverse joints was scored. CTSS (range, 0–552) and facet joint ankylosis (range, 0–46) were assessed at 23 vertebral units. Costovertebral joints at T1–T12 (range, 0–48) and costotransverse joints at T1–T10 (range, 0–20) were also assessed. Intraclass correlation coefficients (ICC) were calculated to determine inter-reader reliability. Odds ratios (OR) was calculated to identify associations between syndesmophyte progression and baseline status of other joints.

Results: Fifty patients with r-axSpA were included. Reader 1 identified C7–T3 (facet joints), T5–T7 and T12 (costovertebral joints), and T8–T9 (costotransverse joints), as common sites of ankylosis at baseline and at 2-year follow-up. The ICCs for facet, costovertebral, and costotransverse joints at baseline were 0.876 (95% confidence interval [CI] 0.782–0.930), 0.952 (95% CI, 0.915–0.973), and 0.753 (95% CI, 0.564–0.860), respectively. Multivariate logistic regression analysis revealed that the OR of baseline costovertebral and costotransverse joint ankylosis for predicting CTSS progression was 4.644 (95% CI, 2.295–9.398) and 1.524 (95% CI, 1.036–2.244), respectively.

Conclusion: Costotransverse joint ankylosis in r-axSpA patients can be measured semi-quantitatively on whole spine CT, and ankylosis of the costotransverse joints predicts progression of syndesmophytes.

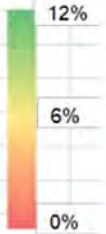
A

	Reader 1		Reader 2	
	Baseline	2 year follow-up	Baseline	2 year follow-up
C2 - C3	22	29	21	31
C3 - C4	18	27	20	32
C4 - C5	13	29	12	29
C5 - C6	8	12	9	17
C6 - C7	9	15	9	15
C7 - T1	23	25	25	37
T1 - T2	21	20	25	29
T2 -T3	42	48	23	26
T3 - T4	18	25	9	11
T4 - T5	6	10	2	6
T5 - T6	2	4	1	2
T6 - T7	0	3	0	2
T7 - T8	2	2	2	2
T8 -T9	0	0	0	0
T9 - T10	2	2	2	2
T10 - T11	2	1	0	0
T11 - T12	0	3	3	3
T12 - L1	3	2	2	2
L1 - L2	2	1	0	1
L2 - L3	0	0	0	0
L3 - L4	0	0	0	0
L4 - L5	2	2	0	0
L5 - S1	4	4	4	4



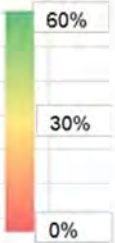
B

	Reader 1		Reader 2	
	Baseline	2 year follow-up	Baseline	2 year follow-up
T1	0	2	0	1
T2	2	2	2	3
T3	2	1	2	1
T4	4	5	3	4
T5	5	6	6	4
T6	8	9	3	5
T7	7	5	3	2
T8	1	3	3	6
T9	3	1	1	3
T10	1	3	3	6
T11	1	1	0	1
T12	9	12	7	8

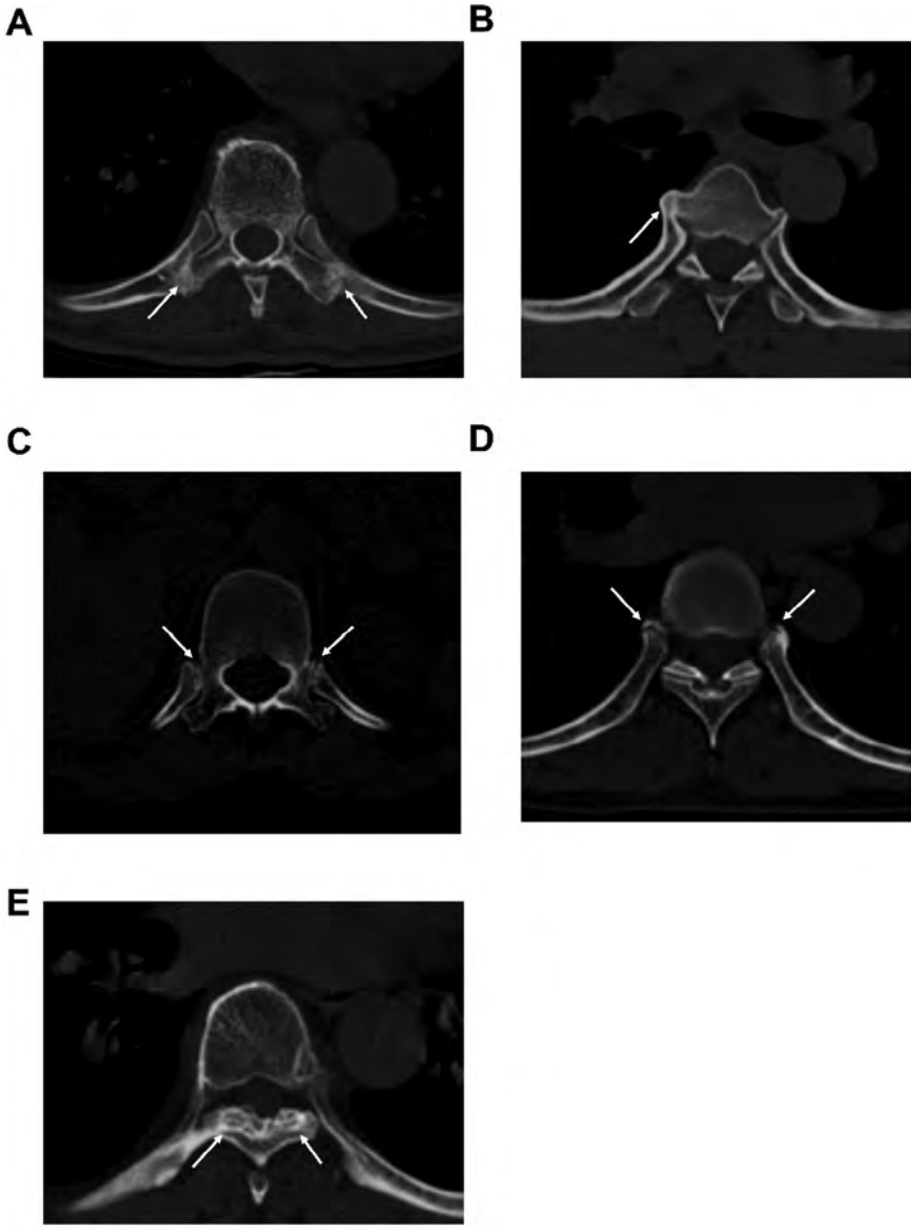


C

	Reader 1		Reader 2	
	Baseline	2 year follow-up	Baseline	2 year follow-up
T1	0	0	0	0
T2	1	2	2	2
T3	1	5	3	5
T4	4	5	8	11
T5	2	3	15	5
T6	3	5	15	16
T7	5	9	22	27
T8	17	27	40	56
T9	23	29	40	58
T10	9	13	20	24



Distribution of ankylosed facet joints (A), costovertebral joints (B), and costotransverse joints (C) at baseline and at the 2 year follow-up (the number inside each cell is a percentage).



Representative CT images showing costotransverse, costovertebral, and facet joint abnormalities. (A) Bilateral ankylosis of costotransverse joints (white arrow), (B) ankylosis of costovertebral joints on the right side (white arrow), (C) erosion of the bilateral costovertebral joints (white arrow), (D) syndesmophytes on the bilateral costovertebral joints (white arrow), (E) bilateral facet joint ankylosis.

Disclosure: H. Min: None; **S. Kim**: None; **H. Kim**: None; **S. Lee**: None; **S. Lee**: None.

Abstract Number: 1887

Total-body PET Quantitative Biomarkers Reveal Key Differences in Enthesitis Between Rheumatoid and Psoriatic Arthritis Patients

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate the ability of total-body PET (TB-PET) biomarkers to quantify enthesitis in Psoriatic (PsA) and Rheumatoid Arthritis (RA). We hypothesize that objective characterization of specific disease domains will allow PET to reliably distinguish between these two conditions and add to current understanding of their in-vivo pathologies.

Methods: As part of an ongoing study using TB-PET to study autoimmune inflammatory arthritis, we present results of 39 patients (N = 15 with RA and N = 24 with PsA). Participants underwent an ultra-low dose TB-PET/CT scan using the [18F]FDG radiotracer at a single timepoint. Thirty-eight entheses per participant were evaluated on PET images, matching those from the Leeds Enthesitis Index (LEI), Maastricht Ankylosing Spondylitis Enthesis Score (MASES), Spondyloarthritis Research Consortium of Canada (SPARCC), Berlin (Major), San Francisco, and 4-point enthesitis measures1.

Each enthesis was graded on a Likert scale (0-3) and the maximum Standardized Uptake Value (SUVmax) was recorded. Summed Likert scale scores and summed SUVmax across all entheses assessed and their average was used to compare between groups. The number of active entheses (scored 2 or more) were counted and compared between groups. Differences between groups were assessed via Mann Whitney U-tests. Receiver operating characteristic (ROC) curves were produced to assess the diagnostic potential of these metrics.

Results: The total number of PET-positive entheses was higher in participants with PsA (8.83 ± 5.1) compared to RA (4.25 ± 2.7, $p < 0.05$). Across all the 38 entheses sites, there was a significant difference in both summed Likert scale scores and summed SUVmax between groups ($p < 0.01$), as can be seen in Figure 1. The same metrics assessed for the LEI subset showed no difference between the groups. They did show significant differences for the MASES and SPARCC groupings of entheses ($p < 0.05$) (Table 1). ROC analysis showed that both summed scores for entheses can perform acceptably as binary classifiers. The best performing measures were those utilizing the San Francisco entheses sites and achieved AUC

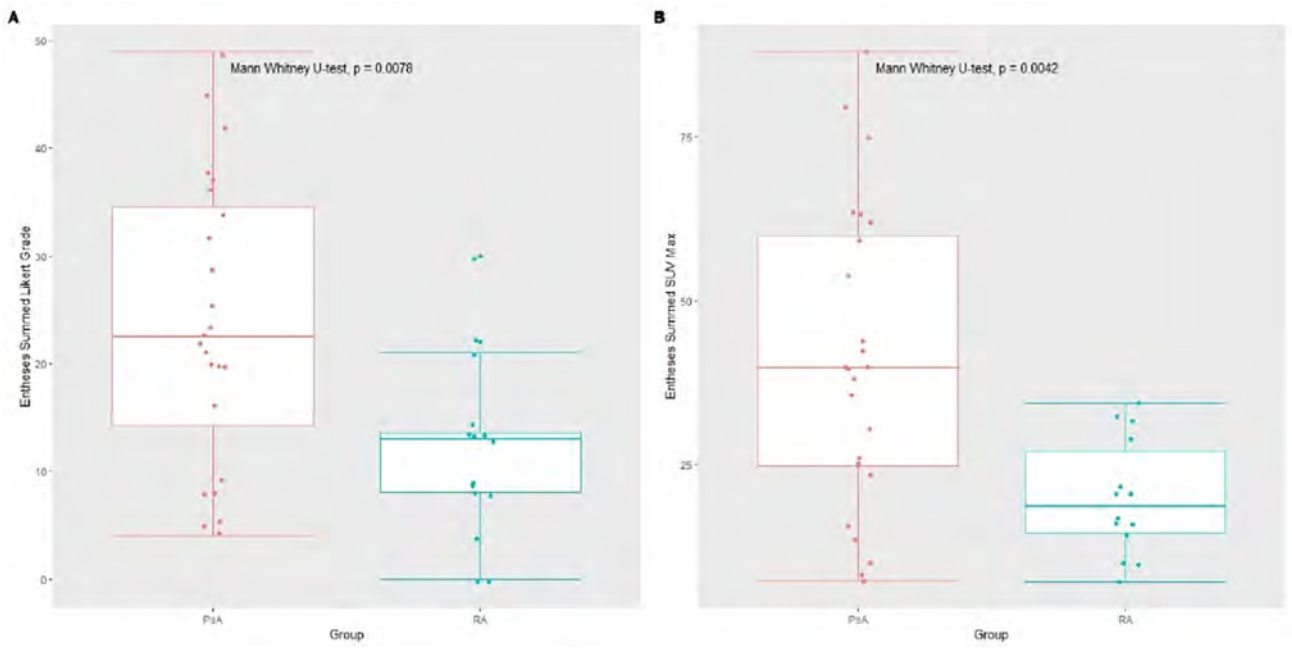

Figure 1: (A) Summed Likert grading of active entheses sites for PsA and RA participants; (B) Summed SUV max of active sites in PsA and RA participants.

Table 1: Summary of the differences in PET metrics between RA and PsA participants for each subset of entheses assessed. In all cases, PsA patients had higher average scores. Statistically significant results are shown in bold.

	Difference in PET positivity (p-value)	Difference in summed Likert score (p-value)	Difference in summed SUV max (p-value)
All 38 entheses sites	Yes **(0.01)**	Yes **(0.008)**	Yes **(0.004)**
LEI	Yes **(0.049)**	No (0.31)	No (0.39)
MASES	Yes **(0.02)**	Yes **(0.01)**	Yes **(0.01)**
SPARCC	No (0.07)	Yes **(0.03)**	Yes **(0.03)**
MAJOR	Yes **(0.04)**	Yes **(0.04)**	Yes **(0.02)**
San Francisco	Yes **(0.02)**	Yes **(0.007)**	Yes **(0.003)**
4-Point	Yes **(0.02)**	Yes **(0.04)**	Yes **(0.04)**

values of 0.76 (95% CI 0.63-0.90)and 0.79 (95% CI 0.63-0.91) for summed scores and summed SUV max, respectively, followed closely by all entheses sites (0.76, 0.78), MASES (0.74, 0.75), and SPARCC (0.71, 0.72). Summed Likert grades and summed SUVmax performed less well and poorly on the 4-point (0.69, 0.69) and LEI (0.56, 0.58) subsets, respectively.

Conclusion: Our results demonstrate that PET measures can be used to quantify and characterize specific disease domains in autoimmune arthritis. Higher and more frequent uptake in the entheses of PsA patients confirms enthesitis as a core feature of PsA that can potentially distinguish it from RA. Different performance of the various site groupings according to the established enthesitis measures highlight the need for in-depth evaluation of these measures against the standard clinical evaluation and possibly other imaging modalities.

Disclosure: D. Mazza: None; **S. Raychaudhuri**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, SUN Pharma, 2, 5, 6, UCB, 2, 5, 6; **Y. Abdelhafez**: None; **A. Chaudhari**: None.

Abstract Number: 1888

Solving the Final Puzzle of Gout Detection in DECT via Machine Learning-Based Mitigation of Pseudolesion-Related Challenges: Enhancing Diagnostic Accuracy

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In a recent study, the low specificity of Dual-Energy CT (DECT) has raised concerns due to the frequent occurrence of pseudo lesions, also referred to as clumpy artifacts, result in inaccurate discrimination from true monosodium urate (MSU) crystals due to their small size and overlapping image findings. This clinical impact is significant since a

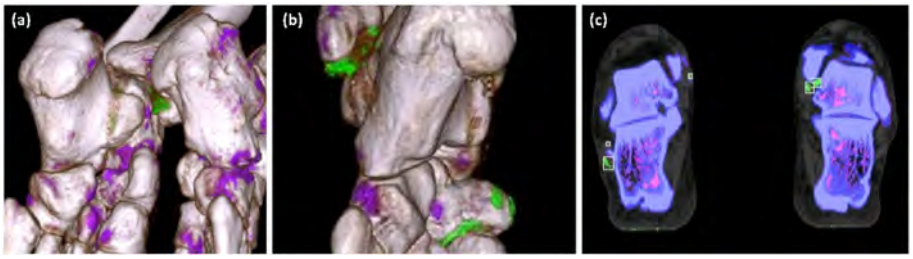

Figure 1. Applying deep learning to distinguish pseudo lesion and true monosodium urate (MSU) deposit. (a) In 3D DECT, there are pseudo lesions that appear as scattered green color foci at the hindfoot. Note that this patient obtains CT for fracture evaluation. (b) 3D DECT from gouty patients shows multiple patches of green color foci at the mid and hind foot. The green color from (a) and (b) are difficult to distinguish. (c) Final ROI labeling for deep learning.

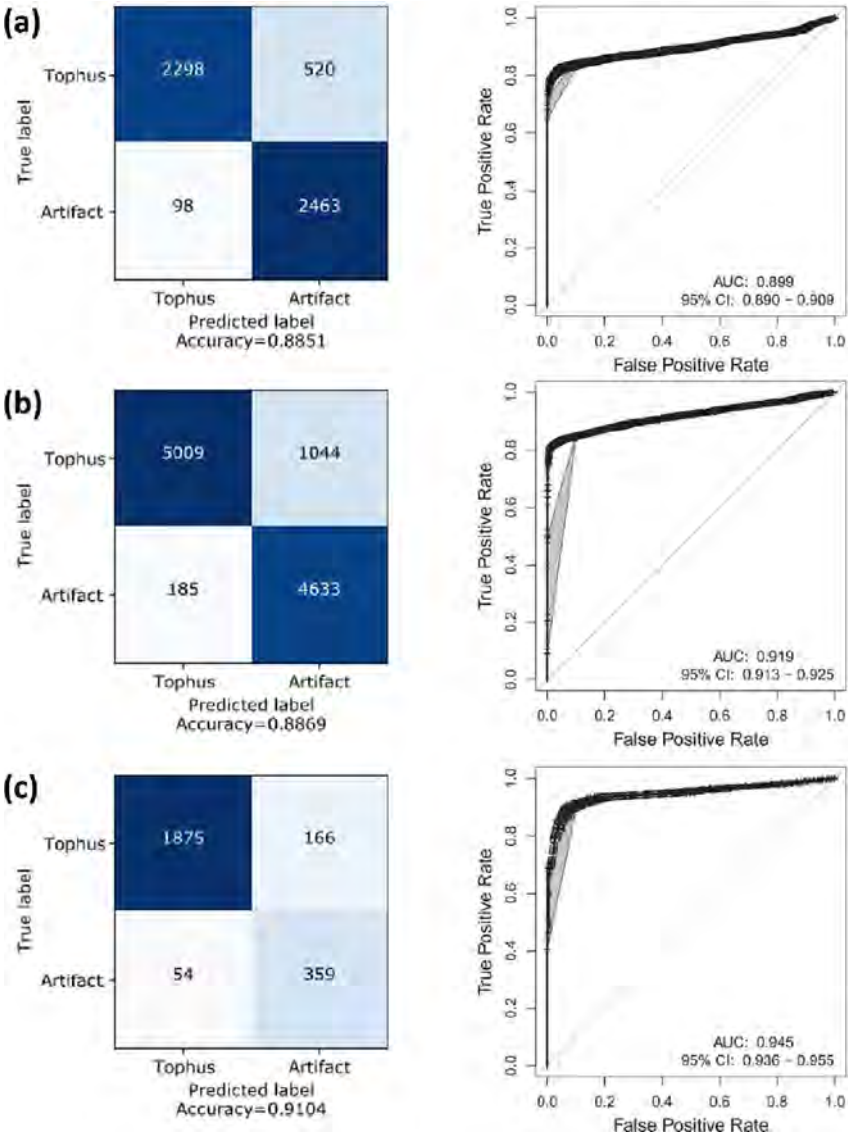

Figure 2. Confusion matrices and ROC curves of VGG16 architecture with Global Average Pooling (GAP) for differentiating between tophus and artifact instances on a per-region of interest (RoI) basis. The top pair (a) of matrices and curves corresponds to the classification model trained on the small-area dataset. The middle pair (b) represents the results for the medium-area dataset, while the bottom pair (c) displays the outcomes for the large-area dataset.

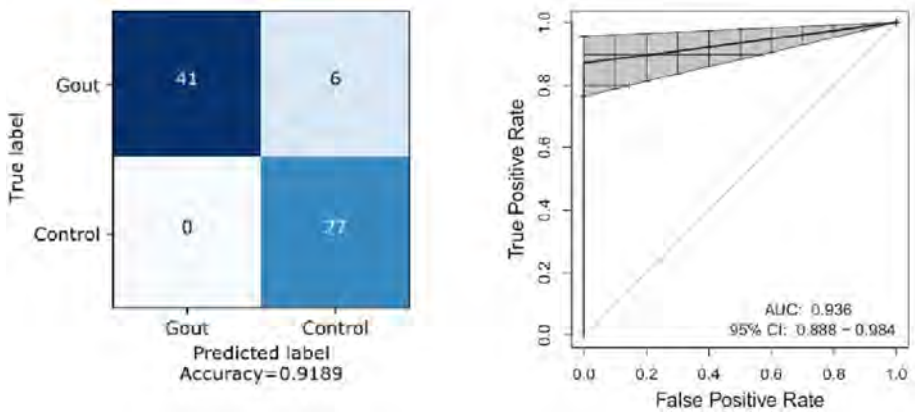

Figure 3. Confusion Matrix and ROC curve of Support Vector Machine (SVM) or distinguishing between gout and control cases on a per-patient basis

positive image finding on DECT is assigned a score of four, which accounts for half of the threshold according to the 2015 EULAR/ACR classification guideline.

The objective of this study is to assess the efficacy and accuracy of machine learning algorithms in distinguishing pseudo lesion from true MSU crystals in DECT imaging.

Methods: This study presents a comprehensive analysis of 18,958 regions of interest (ROIs) extracted from the green color foci of Dual-energy CT (DECT) scans obtained from 47 individuals diagnosed with gout and 27 gout-free controls. The ROIs were meticulously categorized into three size groups: small (n=4,911), medium (n=11,419), and large (n=2,628). As we conducted our analysis, we employed a two-step approach for the classification of tophus/artifacts, both on a per-lesion basis and on a per-patient basis. For the per-lesion classification, a convolutional neural network (CNN) model based on the VGG16 architecture with Global Average Pooling (GAP) was utilized. This model was trained using a 6-fold cross-validation scheme, where the dataset was divided into six subsets. To perform the classification on a per-patient basis, a Support Vector Machine (SVM) approach was employed and trained five times using cross-validation training folds. The performance of the models was evaluated using area under the receiver operating characteristic curve, sensitivity, specificity, positive predictive value, and negative predictive value.

Results: The sensitivity and specificity of the deep learning algorithm, VGG16 with GAP, for different sizes of ROIs were as follows: for small-sized ROIs, the sensitivity was 81.5% (95% CI, 95.3-96.8%) with a specificity of 96.1% (95% CI, 95.3-96.8%); for medium-sized ROIs, the sensitivity was 82.7% (95% CI, 81.7-83.7%) with a specificity of 96.1% (95% CI, 95.5-96.6%); and for large-sized ROIs, the sensitivity was 91.8% (95% CI, 90.6-93.0%) with a specificity of 86.9% (95% CI, 83.2-90.0%). The DL algorithm exhibited accuracies of 88.5% for small-sized ROIs, 88.6% for medium-sized ROIs, and 91.0% for large-sized ROIs. In the per-patient analysis, the SVM approach demonstrated a sensitivity of 87.2%, a specificity of 100%, and an accuracy of 91.8% (95% CI, 83.1-96.9%) in distinguishing between patients with gout and gout-free controls.

Conclusion: By applying deep learning algorithms, DECT shows impressive diagnostic performance by distinguishing the green color foci of DECT scans from pseudo lesions and tophi, leading to enhanced specificity even with small-sized green color lesions. Deep learning algorithms offer comprehensible and unequivocal approaches in DECT, allowing for precise and unmistakable diagnoses of gout.

Disclosure: W. Yoo: None; **E. Park**: None; **D. Lee**: None; **R. Casto-Zunti**: None; **Y. Choi**: None.

Abstract Number: 1889

Utility of a Diagnostic Algorithm in the Assessment of Large Vessel Vasculitis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Giant cell arteritis (GCA) is the most prevalent type of primary systemic vasculitis among individuals aged 50 and above. Imaging techniques such as ultrasound (US), magnetic resonance imaging (MRI), and {18F}-fluorodeoxyglucose positron emission tomography (PET-CT) have emerged as crucial diagnostic tools due to their non-invasive nature, higher sensitivity and availability compared to temporal artery biopsy (TAB) and angiography.

The purpose of this study is to evaluate the effectiveness of an algorithm based on imaging techniques in the diagnosis of GCA. Additionally, it seeks to assess the potential reduction in costs and unnecessary investigations during the diagnostic process.

Methods: The project consists of two phases. The first phase involved a retrospective analysis of a cohort suspected of having GCA, derived from outpatient consultations (OC) and hospitalizations in a tertiary hospital's Rheumatology department (February 2021-December 2022). A diagnostic evaluation was conducted using clinical criteria and imaging techniques

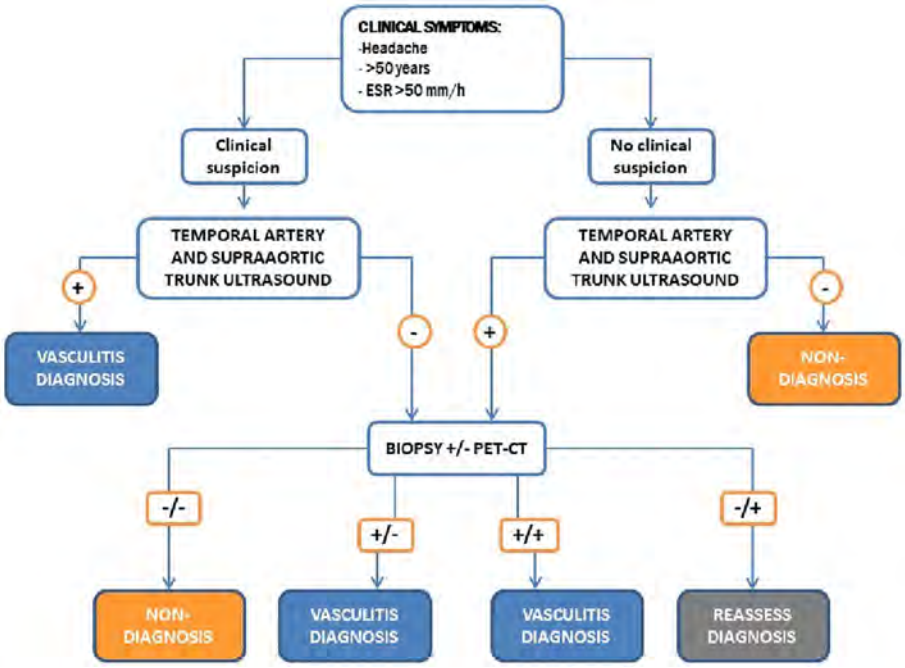

Figure 1. Proposed algorithm for the study of large vessels vasculitis

Table. Clinical variables, complementary tests, diagnosis and treatment. AION= Anterior ischemic optic neuritis; PET-CT= positron emission tomography; TAB= Temporal artery biopsy; US=ultrasound; GC=glucocorticoids

Variable	Hospitalized (n=6; 15%)	Outpatient Consultations (n=34; 85%)	Total (n=40; 100%)
SEX n, %			
Female	6 (15)	26 (65)	40
Male	0	8 (20)	
CLINIC n, %			
AION	5/6 (83)	0	5 (12.5)
NO AION	1/6 (26.6)	34/34 (100)	35 (87.5)
COMPLEMENTARY TESTS n, %			
Ultrasound performed	6/6 (100)	34/34 (100)	40 (100)
Ultrasound compatible	2	8	10 (25)
Cranial findings	2	2	4 (10)
Extracranial findings	0	5	5 (12.5)
Mixed findings	0	1	1 (2.5)
PET-CT performed	6/6 (100)	24/34 (70.58)	30 (75)
PET-CT compatible	3	10	13 (32.5)
TAB performed	4/6 (66.6)	5/34 (14.70)	9 (22.5)
TAB compatible	2	1	3 (7.5)
FINAL DIAGNOSIS PRE-ALGORITHM	5/6 (83.3)	11/34 (32.35)	16 (40)
Clinica + US	0	1/34 (2.94)	1/16 (6.25)
Clinic + US + PET-CT	1/6 (16.6)	7/34 (20.58)	8/16 (50)
Clinic + US + PET-CT + TAB	4/6 (66.6)	3/34 (8.82)	7/16 (43.75)
TREATMENT n, %			
GC prior complementary tests	5/6	5/34	10
Bolus of GC (500mg/day for 3 days)	5/6	0	5
Oral GC mean starting dose 50mg/day	0	11/34	11

(US, PET-CT, TAB). US examinations were performed according to a standardized protocol within the Rheumatology service. In the second phase, the proposed diagnostic algorithm (Figure) was retrospectively applied, and the results were compared with the pre-algorithm phase. All patients provided their consent for participation.

Results: The study included 40 patients (80% women, n=32; 20% men, n=8), with a mean age of 72.55. All patients had clinical suspicion and 100% underwent US examinations with findings suggestive of GCA in 10 individuals (25%). TAB was performed in 9 patients (22.5%) and 3 of them (7.5%) had compatible results. PET-CT was conducted in 30 (75%) with conclusive results observed in 13 cases (32.5%). A final diagnosis of GCA was established in 16 patients (40%): clinical criteria + US in 1 patient (6.25%); clinical criteria + US + PET-CT in 8 (50%); clinical criteria + US + PET-CT + TAB in 7 (43.75%) (Table). Notably, among the 6 patients admitted to the hospital, 5 presented with initial clinical manifestations of anterior ischemic optic neuritis (AION). Within the diagnosed group, 10 individuals received corticosteroid treatment for at least 5 days prior to undergoing imaging techniques. Retrospective application of the algorithm to 8 patients (20%) with compatible US findings indicated that no further investigations would have been necessary (TAB + PET-CT in 5 patients and PET-CT alone in 3). Consequently, a total of 13 unnecessary supplementary tests could have been avoided. The maximum cost per patient amounted to €1117 (PET-CT €997, US €70, TAB €50). Implementation of the algorithm could have resulted in cost savings of €8176 and reduced iatrogenesis in this subgroup.

Conclusion: The utilization of an algorithm represents a practical and applicable tool in the diagnostic process of GCA. US serves as a valuable screening method in the initial evaluation, effectively reducing costs and redundant investigations in patients with compatible results and a high clinical suspicion. In cases where both clinical criteria and US findings are negative, it aids in excluding GCA as a diagnosis.

Disclosure: H. AVALOS BOGADO: None; **G. AÑEZ STURCHIO**: None; **E. Trallero-Araguas**: None; **E. Espartal López**: Pfizer, 5; **s. Sandoval Moreno**: None; **d. Ulloa Navas**: None; **J. De Agustín De Oro**: None.

Abstract Number: 1890

Use of Artificial Intelligence to Diagnose Polymyalgia Rheumatica on ^{18}F-FDG Whole Body PET/CT in Patients with Atypical Clinical Features

Emily Martin[1], Christopher McMaster[1], Saskia Rowson[1], Victor Yang[1], Aurora Poon[1], Bonnia Liu[1], Jessica Leung[2], Andrew Scott[1], David Liew[1] and **Claire Owen**[3], [1]Austin Health, Heidelberg, Australia, [2]Austin Health, Preston, Australia, [3]Austin Health, Malvern East, Australia

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: PET/CT is a highly sensitive and specific test for diagnosing PMR.(1) This study investigated the utility of ^{18}F-FDG whole body PET/CT in patients presenting with atypical clinical features and tested the performance of a novel artificial intelligence (AI) algorithm to simplify PMR diagnosis.

Methods: PET/CT reports from January 2015 to current were searched for findings suggestive of PMR using natural language processing. The scanned medical record of each identified case was reviewed to determine the final clinical diagnosis. Required criteria per the 2012 EULAR/ACR PMR Classification Criteria(2) (age ≥50 years, bilateral shoulder aching and abnormal CRP +/ ESR) were recorded, with patients not meeting these considered "atypical". Qualitative and semi-

Table 1: Frequency and 18F-FDG avidity of key musculoskeletal site abnormalities in atypical compared with typical PMR patients.

Site	Atypical Frequency	Typical Frequency	Mean Atypical SUV_{max}	Mean Typical SUV_{max}
Peri-Articular Shoulder	17/17 (100%)	34/35 (97.1%)	2.44±0.76	3.27±1.34 *p=0.01*
Peri-Articular Hip	15/17 (88.2%)	33/35 (94.3%)	1.79±1.02	3.27±1.81 *p=0.001*
Interspinous Region	14/17 (82.3%)	31/35 (88.6%)	1.58±1.04	2.82±1.58 *p=0.003*
Adjacent to Ischial Tuberosities	17/17 (100%)	34/35 (97.1%)	2.32±0.63	3.48±1.42 *p=0.001*
Posteromedial Knee	12/15 (80%)	25/34 (73.5%)	1.59±1.03	2.70±1.04 *p=0.001*
Volar Hand	7/16 (43.7%)	12/34 (35.3%)	0.95±1.24	2.38±1.06 *p=0.001*

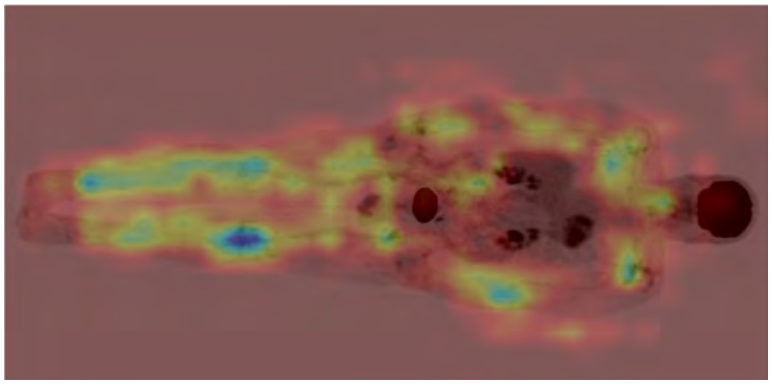

Figure 1: An example GradCam map highlights areas of the PET/CT image that contributed to a positive PMR diagnosis. This patient had bilateral shoulder and posteromedial knee symptoms – the GradCam map shows high intensity in these regions.

quantitative (SUV_{max}) PET/CT scores of steroid-naïve atypical PMR patients were compared with an existing typical steroid-naïve PMR population. Differences in ^{18}F-FDG avidity (mean SUV_{max}) were examined at key musculoskeletal sites. The performance of a ResNet50 AI model trained on PET/CT images of typical PMR and large joint arthritis patients was tested on the atypical PMR cohort. GradCam maps were employed to cross-check the AI's focus on characteristic PMR-involved anatomical regions.

Results: 225 PET/CT reports were retrieved from >38,000 scans, with 121 patients possessing a final clinical PMR diagnosis. 17 steroid-naïve atypical patients were compared with 35 steroid-naïve typical cases. Mean CRP (10.1±20.9 cf. 44.0 ±32.9 [p=0.0002]) and ESR (11.5±7.2 cf. 49.3±29.6 [p=0.0001]) were lower in the atypical group, but the frequency of abnormalities at key musculoskeletal sites was similar (Table 1). A statistically significant difference ($p < 0.05$) in mean SUV_{max} was detected between the groups at every musculoskeletal site analyzed. When the novel AI-trained model was tested on PET/CT images of atypical patients, 16/17 were identified as positive for a PMR diagnosis. Figure 1 provides a GradCam map example in an atypical PMR case.

Conclusion: PMR patients with atypical clinical features exhibit the same PET/CT abnormalities as typical cases, but affected musculoskeletal sites are less ^{18}F-FDG avid. This distinctive imaging pattern can be harnessed by AI technology to facilitate PMR diagnosis in challenging clinical scenarios.

References:

1. Owen CE, Poon AMT, Yang V, McMaster C, Lee ST, Liew DFL, et al. Abnormalities at three musculoskeletal sites on whole-body positron emission tomography/computed tomography can diagnose polymyalgia rheumatica with high sensitivity and specificity. Eur J Nucl Med Mol Imaging. 2020. 2. Dasgupta B, Cimmino MA, Kremers HM, Schmidt WA, Schirmer M, Salvarani C, et al. 2012 Provisional classification criteria for polymyalgia rheumatica: a European League Against Rheumatism/American College of Rheumatology collaborative initiative. Arthritis Rheumatol. 2012;64(4):943-54.

Disclosure: E. Martin: None; **C. McMaster**: None; **S. Rowson**: None; **V. Yang**: None; **A. Poon**: None; **B. Liu**: None; **J. Leung**: AbbVie, 1, 6, Eli Lilly, 1, 6, Novartis, 6; **A. Scott**: None; **D. Liew**: None; **C. Owen**: AbbVie/Abbott, 1, 6, Janssen, 6, Novartis, 6.

Abstract Number: 1891

Effect of Apremilast on Disease Interception in Patients with Psoriasis at Increased Risk of Developing PsA – Results of the Prospective Interventional Epos Trial

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Entheseal bone changes occur in a substantial proportion of psoriasis patients [1] and are associated with an increased risk of developing psoriatic arthritis (PsA) [2].Herein, we aimed to investigate the effect of phosphodiesterase-4 inhibition by apremilast on entheseal bone changes in psoriasis patients with a high-risk profile for developing PsA.

Table 1: Baseline and demographic characteristics. BSA: Body Surface Area; csDMARD: conventional synthetic Disease Modifying Antirheumatic Drug; PASI: Psoriasis Area and Severity Index; PhGA: Physician's Global Assessement of disease activity; SD: Standard deviation; SJC66: Swollen Joint Count 66; TJC68: Tender Joint Count 68; VAS: Visual Analogue Scale.

N	20
Age, mean (SD)	50 (11.6)
Female sex, N (%)	9 (45%)
Disease duration (years), mean (SD)	18.6 (12.8)
Smoking, N (%) Yes No	 3 (15%) 17 (85%)
Skin involvement, N (%) Face Scalp Genital Inverse Nail	 9 (45%) 19 (95%) 9 (45%) 9 (45%) 13 (65%)
PASI, mean (SD)	10.9 (6.7)
BSA, mean (SD)	18.8 (12.9)
Arthralgia VAS, mean (SD)	30.1 (23.3)
SJC66, mean (SD)	0.0 (0.0)
TJC68, mean (SD)	3.2 (3.4)
Tender enthesis count, mean (SD)	1.6 (2.7)
PhGA VAS, mean (SD)	37.6 (18.7)
Previous psoriasis treatment, N (%) csDMARD Combined topical treatment Corticosteroids Other topical treatment Phototherapy Vitamin-D3 Fumarate	 16 (80%) 10 (50%) 5 (25%) 5 (25%) 5 (25%) 5 (25%) 4 (20%)

Table 2: HR-pQCT and clinical outcomes at baseline and week 24. BSA: Body Surface Area; PASI: HR-pQCT: High-Resolution peripheral Quantitative Computed Tomography; Psoriasis Area and Severity Index; PhGA: Physician's Global Assessement of disease activity; SD: Standard Deviation; TJC68: Tender Joint Count 68; VAS: Visual Analogue Scale; vBMD: volumetric Bone Mineral Density.

	Baseline	Week 24	p-value
HR-pQCT (Entheseal Site)			
Cortical thickness (mm), mean (SD)	0.4 (0.1)	0.4 (0.1)	0.323
Cortical vBMD (mg HA/cm^3), mean (SD)	699.3 (92.7)	701.8 (97.6)	0.523
Clinical Outcomes			
PASI, mean (SD)	10.9 (6.7)	5.2 (6.6)	0.013
BSA, mean (SD)	18.8 (12.9)	8.6 (9.5)	0.022
Arthralgia VAS, mean (SD)	30.1 (23.3)	22.4 (26.7)	0.267
Tender enthesis count, mean (SD)	1.6 (2.7)	0.5 (0.9)	0.083
TJC68, mean (SD)	3.2 (3.4)	0.8 (1.8)	0.006
PhGA VAS, mean (SD)	37.6 (18.7)	21.8 (22.1)	0.046

Methods: Epos (Early PsA on treatment strategy) is a prospective, single-arm, interventional, open-label, single-center phase 4 trial (EUDRACT 2018-000335-27) in psoriasis patients with an increased risk of transition to psoriatic arthritis (PsA). Participants had to have (i) mild to moderate psoriasis, (ii) arthralgia and (iii) subclinical inflammatory changes assessed by hand MRI and/or high-resolution CT. Patients with any present or past signs of PsA (arthritis, dactylitis, enthesitis, axial involvement) as well as previous treatment with biological or targeted-synthetic DMARDs were not allowed to participate. Participants received apremilast 30 mg twice daily over 24 weeks. To assess the effect of apremilast on entheseal bone changes high-resolution CT scans of the entheseal areas of metacarpal finger joints were conducted at baseline and week 24. At the entheseal areas, peripheral volumetric bone mineral density (vBMD), bone microstructure and structural entheseal lesions were assessed. Clinical response and safety were monitored.

Results: 20 patients (50 [SD 11.6] years; 9 women) with a duration of skin psoriasis of 18.6 [SD 12.8] years were included (table 1). At week 24, skin disease significantly improved (Psoriasis Area and Severity Index: from 10.9±6.7 at baseline to 5.2±6.6 at week 24) as well as arthralgia (VAS: from 30.1±23.3 at baseline to 22.4±26.7 at week 24) (table 2). Tender joint count 68 and tender enthesis count also declined over 24 weeks of treatment (3.2±3.4 at baseline vs. 0.8±1.8 at week 24 and 1.6±2.7 at baseline vs. 0.5±0.9 at week 24, respectively) (table 2). No significant progress was found for entheseal cortical vBMD (baseline: 699.3±92.7 mg HA/cm^{3}vs. week 24: 701.8±97.6 mg HA/cm^3, p=0.523) and entheseal cortical thickness (0.4±0.1 mm vs. 0.4±0.1 mm, p=0.323) (table 2). Accordingly, no progression was detected in structural entheseal lesions. No new safety signals with apremilast treatment were observed.

Conclusion: Apremilast leads to early disease interception by improving skin disease and arthralgia and halting progression of entheseal bone changes in psoriasis patients at risk for the transition to PsA. Larger studies with longer follow-up periods are needed to validate these findings.

Disclosure: D. Simon: Janssen, 5; **I. Minopoulou**: AbbVie/Abbott, 6; **S. Bayat**: El Lilly, 5; **K. Tascilar**: None; **M. Yalcin Mutlu**: None; **F. Fagni**: Eli Lilly, 6, Galapagos, 6, Novartis, 6; **G. Schett**: None; **A. Kleyer**: None.

Abstract Number: 1892

Sacroiliac Bone Marrow Oedema on Postpartum MRI Does Not Result in Significant SpA-like Structural Lesions: Results of a 5-year Follow-up Study

De Meester Liesbet[1], **Gaelle Varkas**[2], Manouk de Hooge[3], Ann-Sophie De Craemer[4], Nele Herregods[5], Lennart Jans[5], Philippe Carron[6], Dirk Elewaut[7] and Filip Van den Bosch[8], [1]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium, [2]Dept. of Rheumatology, Ghent University Hospital, Ghent, Belgium, [3]Ghent University Hospital, Hesperange, Luxembourg, [4]Ghent University Hospital, Gent, Belgium, [5]Department of Radiology, Ghent University Hospital, Ghent, Belgium, [6]UZ Gent, Gent, Belgium, [7]Ghent University and VIB Center for Inflammation Research, Ghent, Belgium, [8]Department of Internal Medicine and Pediatrics, Ghent University and VIB Center for Inflammation Research, Ghent, Belgium

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Sacroiliac bone marrow oedema (BMO) on MRI, immediately after childbirth, has been observed in a large proportion of postpartum women and appears to be a transient phenomenon. Although generally attributed to mechanical stress, these postpartum BMO lesions bear a striking resemblance to the inflammatory lesions seen in axial spondyloarthritis (axSpA). In axSpA, active inflammatory lesions are likely to progress to structural lesions, particularly fat metaplasia and erosions. It is not known whether the same is true for mechanical stress-induced BMO. To assess the long-term evolution of postpartum BMO and the potential development of axSpA-like structural lesions, we performed a 5-year follow-up ofour prospective study on sacroiliac MRI lesions in healthy women following an uncomplicated vaginal delivery.

Methods: Seventeen (48.6%) of the original 35 participants underwent a new MRI of the sacroiliac joints (MRI-SIJ) approximately 5 years after delivery. Structural lesions (fat metaplasia, erosions, sclerosis, (partial) ankylosis) and BMO were scored by three well-trained, calibrated readers using the Spondyloarthritis Research Consortium of Canada (SPARCC) scoring system. Agreement with the Assessment of SpondyloArthritis international Society (ASAS) MRI definition of sacroiliitis was assessed. Baseline MRI images were re-evaluated, and compared with the 5-year follow-up MRI data. Demographic, clinical, and obstetric data were updated.

Results: The overall prevalence of fat metaplasia, erosions and sclerosis on baseline and 5-year MRI images was low. No ankylosis was found. Scores for fat metaplasia and erosions did not change significantly between the two time points. A numerical increase in sclerosis score at year 5 was seen in only3 of 17 subjects, all of whom had BMO after delivery. As expected, there was a significant decrease in BMO from baseline to year 5. Six of the 17 subjects (35%) still had BMO at the 5-year follow-up MRI-SIJ,3 of whom met the ASAS definition of sacroiliitis. No deep or intense BMO lesions were observed.

Conclusion: In postpartum women, nosignificant development of axSpA-like structural MRI lesions was observed 5 years after delivery. These results support the hypothesis that transient mechanical stress-induced sacroiliac BMO, while resembling axSpA on MRI,does not evolve into chronic structural lesions.

Disclosure: D. Liesbet: None; **G. Varkas**: AbbVie/Abbott, 1, 2, 5, 6, Eli Lilly, 6, Novartis, 6, UCB, 1, 2, 6; **M. de Hooge**: UCB, 6; **A. De Craemer**: None; **N. Herregods**: None; **L. Jans**: None; **P. Carron**: AbbVie/Abbott, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Merck/MSD, 2, 5, 6, Novartis, 2, 6, Pfizer, 2, 5, 6, UCB,

2, 5, 6; **D. Elewaut**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 2, galapagos, 5, Janssen, 6; **F. Van den Bosch**: AbbVie, 2, 6, Amgen, 2, BMS, 6, Celgene, 6, Eli Lilly, 2, Galapagos, 2, Janssen, 2, 6, Merck, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB Pharma, 2, 6.

Abstract Number: 1893

Abnormalities Detected with [^{18}F]-FDG-PET/CT Imaging in VEXAS Syndrome

Albrecht Betrains[1], Vincent Jachiet[2], Yannick Dieudonne[3], Jérémie Dion[4], Estibaliz Lazaro[5], Claire De Moreuil[6], Samuel Ardois[7], Sylvie Grosleron[8], Jean-benoit Arlet[9], Cécile-Audrey Durel[10], Laure Delaval[11], Sylvain Audia[12], Cécile Golden[13], Barbara Nicolas[13], Vincent Langlois[14], Antoinette Perlat[7], Frédéric Vandergheynst[15], Thomas Moulinet[16], Maxime Samson[17], **Daniel Blockmans**[1], Olivier Kosmider[18], Sophie Georgin-Lavialle[19], Arsène Mekinian[20] and Benjamin Terrier[21], [1]Department of General Internal Medicine, University Hospitals Leuven, Department of Microbiology, Immunology, and Transplantation, KU Leuven, Leuven, Belgium, [2]Service de médecine interne et Inflammation-Immunopathology-Biotherapy Department (DMU i3), Sorbonne Université, AP-HP, Hôpital Saint Antoine, Paris, France, [3]Department of Clinical Immunology and Internal Medicine, National Reference Centre for Systemic Autoimmune Diseases (CNR RESO), Strasbourg University Hospital, Strasbourg, France, [4]Internal Medicine Department, Toulouse University Hospital, Toulouse, France, [5]Bordeaux Hospital University, Pessac, France, [6]CHU de Brest, Brest, France, [7]CHU Rennes, Rennes, France, [8]CH Agen-Nérac, Agen, France, [9]Hôpital Georges-Pompidou APHP, Paris, France, [10]CHU Lyon, Lyon, France, [11]Hôpital Bichat APHP, Paris, France, [12]Department of Internal Medicine and Clinical Immunology, Dijon-Bourgogne University Hospital, Dijon, France, [13]CHU Dijon, Dijon, France, [14]Service de Médecine Interne, Hôpital Jacques Monod, Le Havre, France, [15]Université Libre de Bruxelles, Bruxelles, Belgium, [16]Department of Internal Medicine, Centre hospitalier universitaire de Nancy, Nancy, France, [17]Department of Internal Medicine and Clinical Immunology, Dijon University Hospital, Dijon, France, [18]Hôpital Cochin APHP, Paris, France, [19]AP-HP, Tenon hospital, Paris, France, [20]Department of Internal Medicine, Hôpital Saint-Antoine, AP-HP, Paris, France, [21]Department of Internal Medicine, Hôpital Cochin, AP-HP, Paris, France

SESSION INFORMATION

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Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: VEXAS syndrome (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) is anautoinflammatory syndrome caused by somatic mosaicism in the *UBA1* gene. [^{18}F]-FDG-PET/CT is often performed during the diagnostic workup of patients with VEXAS syndrome, but the abnormalities that may be detected with this imaging examination are not well described.

Methods: We performed a retrospective multicenter study in France and Belgium. Patients with confirmed VEXAS syndrome, defined by the presence of an autoinflammatory syndrome and detection of a pathogenic *UBA1*mutation, who underwent at least one [^{18}F]-FDG-PET/CT were considered eligible. Data on the clinical presentation, laboratory results, genetic analyses, and [^{18}F]-FDG-PET/CT imaging results were collected using a standardized form. In an exploratory analysis, the observed abnormalities were compared according to the clinical disease activity status and the VEXAS syndrome clusters as previously defined by Georgin-Lavialle et al. (Br J Dermatol 2022;186:564–74).

Results: A total of 106 [^{18}F]-FDG-PET/CT scans were performed in 57 VEXAS patients. All patients were male and had a median age of 71 (IQR, 66-76) years at symptom onset and 75 (IQR 69-79) years at diagnosis. The most frequent clinical manifestations included cutaneous lesions (86%), fever (79%), arthralgia or arthritis (68%), pulmonary manifestations (46%), ear or nose chondritis (37%), and venous thrombo-embolism (33%). Only 29% of scans were performed before treatment for VEXAS, as the majority of patients received corticosteroids (66%) and/or other immunosuppressive treatments (40%) at the time of imaging. Patients most commonly had increased FDG uptake in the bone marrow (82%), lymph nodes

(54%), lungs (37%), and spleen (30%). Less frequently, patients had hypermetabolism in the pleura (18%), nose or ear cartilage (9%), joints (5%), and pericardium (2%). Increased arterial FDG uptake was identified in 12% of patients, including aortic involvement (5%) and asymmetric artery involvement (9%). Significantly more abnormalities were detected by [^{18}F]-FDG-PET/CT in VEXAS patients with active disease (median 3 [IQR 2-4]) compared to those in clinical remission (median 1 [IQR 1-2]) ($P < 0.001$). However, abnormal FDG uptake often remained present in patients who were considered to be in clinical remission, particularly in the bone marrow (70%), lymph nodes (35%), lungs (20%), and arteries (10%). When comparing those with active disease according to the VEXAS syndrome clusters, we observed a trend towards more abnormalities in the inflammatory cluster (n=17; median 3 [IQR 2-5]) and the hematological/myelodysplasia cluster (n=24; median 3 [IQR 2-4]), compared to the mild-to-moderate cluster (n=7; median 1 [IQR 1-4]) (P=0.09).

Conclusion: We report on [^{18}F]-FDG-PET/CT imaging results among patients with VEXAS syndrome. Although zones of abnormal FDG uptake occurred frequently in VEXAS syndrome, the abnormalities were mostly non-specific. More abnormalities were detected among those with active disease, but bone marrow hypermetabolism in particular often persisted in those considered to be in remission, suggesting subclinical disease activity.

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Abstract Number: 1894

3-Dimensional Regional Variation in Inter-rater Reliability of Bone Marrow Lesion Scoring in the Knee

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1862–1894) Imaging of Rheumatic Diseases Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Bone marrow lesions (BML) are an important scoring feature on magnetic resonance imaging (MRI) of knee osteoarthritis (OA), and their presence in certain anatomical locations may be more closely related to various clinical measures than in others. At the same time, anatomical location may impact BML scoring reliability. The Knee Inflammation MRI Scoring System (KIMRISS) scores BML from fluid-sensitive sagittal MRI[1]. Readers place ready-made overlays onto scorable portions of the femur, tibia, and patella, demarcating medial, intercondylar, and lateral knee compartments. These overlays divide each scorable region into smaller grid squares which are evaluated for presence of BML on each slice. We aimed to evaluate 3-dimensional patterns of regional variation in inter-rater reliability for BML within these sagittally-placed KIMRISS grid elements when divided into subsections across the coronal plane. This granular analysis serves as a precursor to further study of the relationship of precise BML location to clinical measures and outcomes, as reliable data is required to ensure validity of such analyses.

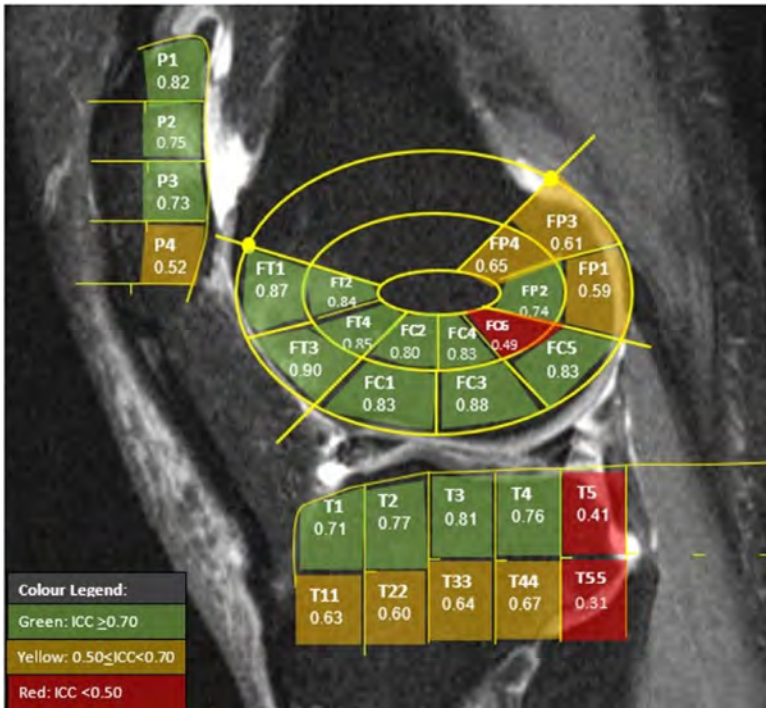

Figure 1. KIMRISS grid region labels with 8-reader mean ICC from baseline knee MRIs from the Osteoarthritis Initiative dataset (n=61).

Methods: MRI from 61 patients in the Osteoarthritis Initiative (OAI) dataset were scored by 8 trained readers using KIMRISS. Each grid overlay region in the femur and tibia (14 and 10 regions, respectively) was divided into 6 equal subregions medially to laterally, excluding the intercondylar region.We calculated an overall 8-reader interclass correlation coefficient (ICC) for each subregion and generated a 3D segmentation model of the knee to visualize variation in ICCs.

Results: Before any subdivision in the coronal plane, ICCs ≥ 0.70 were achieved in 61% of grid regions (Figure 1). Highest reliability was found trochlear region of the femur (ICCs 0.84-0.90), while lowest ICCs occurred in a small interior region of the femur [mean (SD) ICC=0.49 (0.26)] and the two posteriormost tibial regions [mean (SD) ICC=0.41 (0.26) and 0.31 (0.33)]. After further subdividing regions medially to laterally, highest overall reliability amongst all KIMRISS grid squares occurred in the central slices of the lateral compartment of the femur (median ICC=0.72) and the innermost slices of the medial compartment of the tibia (median ICC=0.42). (Figure 2, Table 1). Lowest overall reliability occurred in the central slices of the medial compartment of the femur (median ICC=0.15) and the medialmost slices of the medial compartment of the tibia (median ICC= 0.28)

Conclusion: While reduced ICCs are to be expected across the board in subdivided scoring regions compared to larger summed regions, this analysis highlights differences in inter-rater reliability over 3 dimensions of the knee. Any analysis of the relationship of clinical variables to precise BML location should consider the degree of scoring reliability at the scoring locations entered into the model. Certain regions may need to be excluded or enlarged to achieve inter-rater consistency.

Disclosure: S. Wichuk: None; **W. Maksymowych**: AbbVie, 2, 5, 6, BMS, 2, 6, Boehringer-Ingelheim, 2, CARE Arthritis Ltd, 4, CARE Arthritis Ltd., 4, Celgene, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **J. Paschke**: None; **A. Hareendranathan**: None; **J. Jaremko**: None.

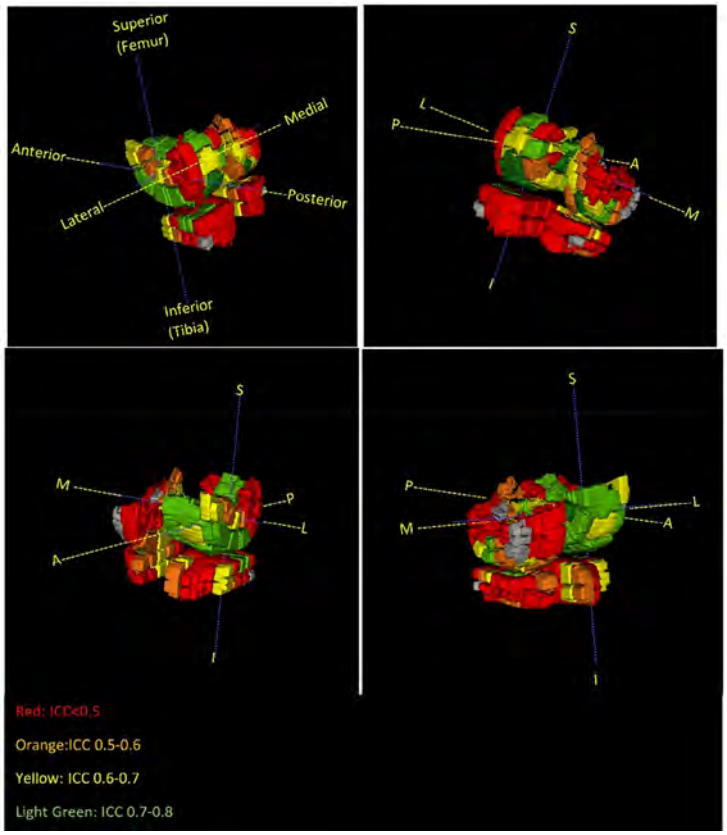

Figure 2. 3-D Heat Map of Femoral and Tibial BML scoring reliability in KIMRISS Grid squares when subdivided into 6 compartments laterally to medially, excluding intercondylar region.

Table 1. Median (IQR) 8-Reader ICC among all KIMRISS femoral and tibial subregions when divided into compartments in coronal plane.

	8-Reader ICC in individual KIMRISS Femoral subregions (n=14)			
Compartment	Median	IQR	Min	Max
All Lateral Slices	0.69	0.55 to 0.77	0	0.94
Lateral Lateral (3 most lateral slices)	0.55	0.10 to 0.68	0	0.75
Lateral mid	0.72	0.69 to 0.80	0.56	0.94
Lateral Inner (3 slices closest to intercondylar region)	0.68	0.55 to 0.79	0.07	0.92
All Medial Slices	0.33	0.060 to 0.59	-0.01	0.84
Medial Inner (3 slices closest to intercondylar region)	0.42	0.23 to 0.54	0	0.69
Medial mid	0.15	0.098 to 0.60	-0.01	0.84
Medial Medial (3 most medial slices)	0.38	0.00 to 0.60	0	0.76
	8-Reader ICC in individual KIMRISS Tibial subregions (n=10)			
Compartment	Median	IQR	Min	Max
All Lateral Slices	0.44	0.26 to 0.56	0	0.75
Lateral Lateral (3 most lateral slices)	0.54	0.29 to 0.69	0.1	0.75
Lateral mid	0.35	0.20 to 0.47	0	0.7
Lateral Inner (3 slices closest to intercondylar region)	0.46	0.26 to 0.53	0	0.62
All Medial Slices	0.42	0.27 to 0.58	0	0.76
Medial Inner (3 slices closest to intercondylar region)	0.54	0.34 to 0.60	0.24	0.67
Medial mid	0.46	0.28 to 0.59	0.05	0.76
Medial Medial (3 most medial slices)	0.29	0.16 to 0.49	0	0.65

Abstract Number: 1895

Comparative Analysis of Existing Tools in Assessing Cardiovascular Risk in Patients with Rheumatoid Arthritis: Exploring the Inadequacies

Pritee Shrestha[1], Peter Larsen[1] and Pablo Weilg Espejo[2], [1]Mercy One North Iowa Medical Center, Mason City, IA, [2]Boston Medical Center, Chelsea, MA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1895–1912) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with Rheumatoid Arthritis (RA) are at increased risk of cardiovascular disease (CVD). Despite multiple CVD risk tools available, reliability to RA population is limited as they might not fully incorporate the unique risk factors faced by this population cohort. Studies have shown a direct correlation between RA disease severity and increased prevalence of CVD risk factors like diabetes and arthrosclerosis. [1,2] Based on these findings, we can expect an adequate tool designed to assess the burden of cardiovascular disease risk should reflect the disease severity in patients

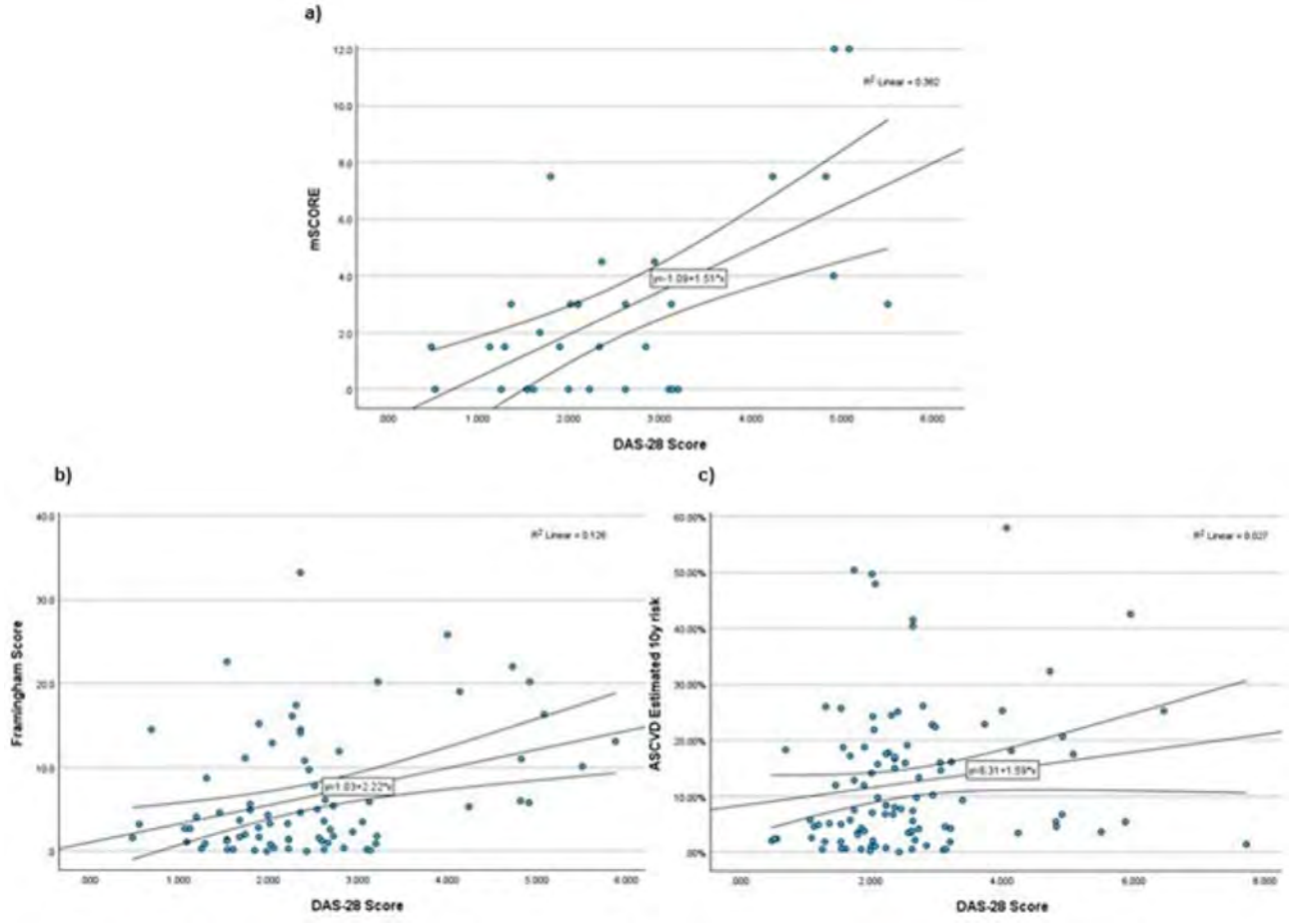

Figure 1. Scattered plot illustrating a) strongest correlation between mSCORE and DAS-28 scores suggesting that as RA disease activity increases, the cardiovascular risk per mSCORE calculation also increases. On the other hand, the b)Framingham score and c) ASCVD score shows weaker correlations with the DAS-28 score.

with RA. We aim to assess the reliability of current CVD assessment tools used in patients with RA by comparing the strength of correlation between these tools with the RA disease severity.

Methods: A single centered retrospective observational analysis was conducted. Medical records of 102 patients all of whom met 2010 ACR/EULAR criteria were included including the DAS-28 score calculated per rheumatologist. SPSS was utilized to assess the strength and direction of the relationship between each CVD assessment tool and RA disease activity. For the former, we employed ASCVD, Framingham and mSCORE. The mSCORE risk assessment tool was recommended by EULAR to access CVD risk in patients with RA. [1] Correlational analysis between CVD assessment tools and DAS-28 score was performed to evaluate the relationship between CVD risk and disease activity. Statin use in patients at risk as recommended by the AHA were reviewed.

Results: Results revealed the correlational coefficient for mSCORE, Framingham score and ASCVD score with DAS-28 score where 0.618, 0.355, 0.165 with P value of < 0.001, 0.001 and 0.098 respectively (Table 1). These findings suggest that mSCORE shows the strongest correlation with DAS-28 scores compared to ASCVD and Framingham score (Figure 1). Further, we identified the number of patients with moderate to high disease activity that are calculated to have a low CVD risk. Increased variability among the tools raises questions about the accuracy of these tools in reflecting the true risk. We found that 42% (n=8) patients and 21% (n=4) who had moderate to high risk were classified as low risk in ASCVD and Framingham score respectively. At the same time, for the mSCORE, none of the patients with moderate to high disease activity was classified as low risk(Table 2). These findings reinforce our previous result.

Table 1. Correlational analysis between the mSCORE, ASCVD score, Framingham score with DAS-28 score performed to evaluate the relationship between CVD risk and RA disease activity. The statistical significance for ASCVD likely impacted by a small sample size along with confounding variables such as age, sex, and other patient demographics. Overall, the higher correlational coefficient for mSCORE suggests that it may be a better predictor of cardiovascular risk in relation to disease activity in RA patients, compared to the Framingham and ASCVD scores.

Correlations				
		ASCVD Estimated 10y risk	Framingham Score of Individual (%)	mSCORE
DAS28	Pearson Correlation	.165	.355	.618
	Sig. (2-tailed)	.098	.001	< .001
	N	102	78	33

Table 2. Comparative analysis using crosstabulation to assess if the risk stratification categories calculated by each tool aligns with the severity category of the disease. 8 patients in ASCVD and 4 patients in Framingham score system who had moderate to high RA disease activity were classified to have a low risk of CVD using these risk assessment tools. Whereas none of the patients with moderate to high disease activities were classified to have a low CVD risk in mSCORE system.

		DAS-28 Severity Category	
Scoring Tool	Risk Category	high	moderate
ASCVD scale	High risk	2	5
	Intermediate risk	0	4
	Low risk	3	5
Framingham severity scale	*	3	3
	High risk	0	4
	Intermediate risk	2	3
	Low risk	0	4
mSCORE severity scale	*	4	9
	High risk	0	4
	Intermediate risk	1	1
	Low risk	0	0

* Population who did not meet criteria for the calculation of the associated CVD risk score

Conclusion: Being explicitly designed for RA patients, mSCORE is likely to capture the cardiovascular risk profile of these individuals better as it incorporates RA-specific factors. Although such RA-specific tools offer some improvement over general population-based tools, their practical application remains challenging due to several experimental limitations. As a result, providers often rely on general tools leaving a concern that these patients are not being appropriately treated. Moreover, we are observing treatment failures even with currently used general risk assessment tools. Approximately 32% (n=20) in our study, who warranted statin therapy based on their ASCVD risk were not receiving it. These findings draw attention to a significant gap in adequate management of cardiovascular health in this population.

Disclosure: P. Shrestha: None; **P. Larsen**: None; **P. Weilg Espejo**: None.

Abstract Number: 1896

Systematic Review and Analysis of Mobile Apps for Rheumatoid Arthritis Using the Mobile Application Rating Scale

Pamela Gonzalez Manrique[1], Vinit Gilvaz[2], Ravinder Kaler[3], Neha Batra[3] and Anthony Reginato[2], [1]Roger Williams Medical Center, North Providence, RI, [2]The Warren Alpert Medical School of Brown University, Providence, RI, [3]Roger Williams Medical Center, Providence, RI

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1895–1912) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis (RA) is a systemic autoimmune disease characterized by inflammatory polyarthritis with infrequent extra-articular involvement. The management of RA typically requires frequent clinic visits (approximately 7.2 visits/ year) to manage disease activity, as well as to monitor for the toxic effects of the medications prescribed. Evidence shows that mobile health (mHealth) apps, when implemented along with clinic visits, improve medication adherence, patient outcomes, in addition to decreasing health care costs in chronic diseases. The purpose of our study is to evaluate individual mHealth apps for RA from both the Android and Apple store. In addition to rating each app using the Mobile Application Rating Scale (MARS), we aim to assess the factual accuracy of the information provided, as well as the amount of medical and personal data collected by each app. We will also evaluate the 10 EULAR recommendations provided by the task force.

Methods: Each app will be rated by two physicians from the division of Rheumatology. The app searches will be done using Apple Store, and Google Play Store. The search will include the keywords: "arthritis", "RA", "rheumatoid arthritis". Inclusion criteria: 1) available for Android and iOS operating systems 2) in English 3) targets RA as subject matter 4) downloadable in the USA. Exclusion criteria: 1) not directed towards RA 2) explicitly only for physician use 3) inactive app 4) Duplicates 5) only available with an additional device. 6) All information with no data input option. Each mobile app will be rated on the MARS scale. The two physicians were trained prior. Additionally, we will evaluate if applications meet EULAR recommendations. We will compare and contrast the information gathered including demographic, insurance, provider information, and prescription data, as well as evaluate whether it is a pharmaceutical vs traditional app (Figure 1).

Results: Upon initial search, 133 applications were retrieved in the Apple Store and 178 in the Google App Store. Only 121 of the apps were in both stores, and only 10/121 met our inclusion and exclusion criteria. The mean score for MARS rating scare of our apps was 3.5 which indicates an acceptable quality. The lowest scores were found to be in the engagement sections with mean of 3.3, and the highest in functionality with mean of 3.87 (Fig 2a and 2b). Overall, it was found that the

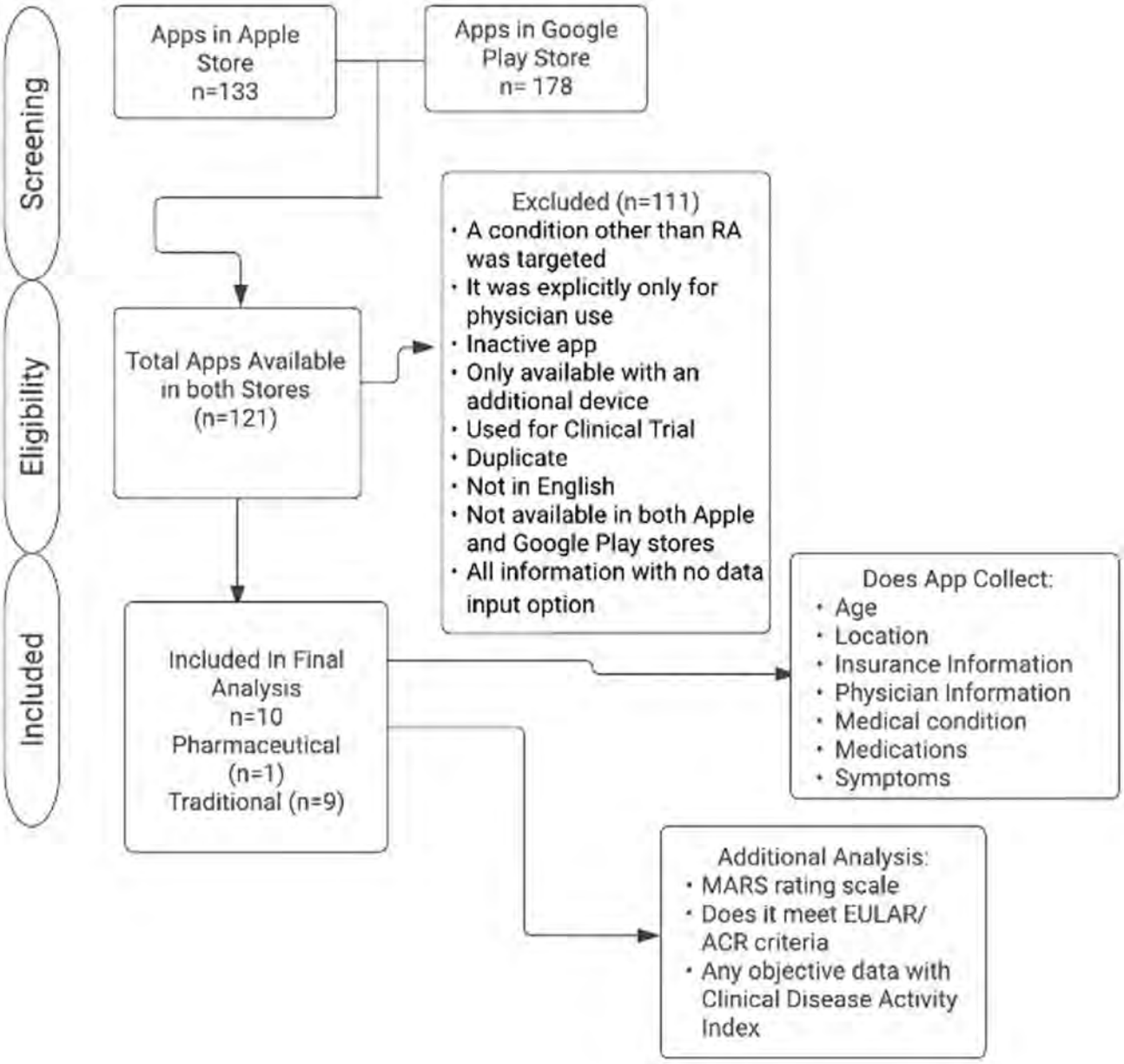

Figure 1: App Selection Process Flow Chart

best rated apps were those few that were designed by rheumatologists, and had arthritic patients involved. When looking at EULAR criteria, no application met all of them.

Conclusion: To our knowledge, this is the first study using both EULAR recommendations and MARS to systematically analyze RA apps. Mobile apps when used along with traditional visits can help foster compliance to medication, help disease modification and improve morbidity and mortality. Our study further illustrates that the applications that were designed by physicians did the best, which strengthen EULAR's recommendation. Overall, there are many applications in the app stores, however there are very few that are acceptable. More work and standardization needs to be done with these applications and we should look closer to EULAR guidelines to further optimize these applications.

Table 1: Characteristics of included rheumatology apps

App Name	Technical Aspects/Content	Privacy Policy Available	Ask for Insurance	Ask for Provider Information	Pharmaceutical Drug App	Price
Abbvie - Complete: Includes Humira, Skyrizi, Rinvoq	Injection reminder/ notification, nurse support, log symptoms/ medication side effects, Write down medications, Discounts/ savings, Age, sex, location; rheumatology condition but no other past medical history documented	Yes	Yes	No	Yes	Free
RA Monitor	Medication and symptoms tracker Daily functionality, mood and stress, Anonymous social networking with other people with RA. Can message provider. Updated news with rheumatology advancements, can share PDF files and upload. Location, age, sex	Yes	No	Yes	No	Free
RA Manager	Can upload pictures and share with provider, up-to date info on RA with reputable sources, HIPPA protected info, meds with reminders, sx, specific to RA, can share data with healthcare team, manage	Yes	No	Yes	No	Free
	medications, age, location, sex.					
Rheumatoid Arthritis Storylines	Medication, symptom and mood tracking. Health journal. Sync vital signs with wearable devices. Age, Sex.	Yes	No	No	No	Free
Rheumatoid Arthritis Diary	Symptom tracking. Gives you statistical % of triggers, including food, stress location, activity, weather patterns and sleep patterns. Keep track of your appointments, lab analyses, and medical records. how likely triggers are by finding patterns. Age, sex.	Yes	No	Yes	No	$4.99
Arthritis Tracker	Application mostly intended for teens and young adults with arthritis. Symptom tracking. Can track sleep, emotions, energy levels, medication side effects. There is an information section for advice and information. Age, Sex.	Yes	No	No	No	Free
ConnectPlus	For RA and other rheum conditions. Developed with pts and clinical teams across the NHS. Information about condition, symptom tracker, connect with specialists in	Yes	No	Yes	No	Free
	rheumatology. Medicine tracking, healthy lifestyle tips, they ask for sex, age, location.					
Arthritis + Patient	Made by rheumatologists and reviewed by a network of rheumatology peers. Development of the app was also done with consultation with arthritis patients. Information requested is past medical history, social history, age, sex, location, meds, homunculus, BASDAI, HAQ, BASFI. App also provides educational material. Also has features like speech to text widgets. Can take pictures to show progression or flares.	Yes	No	Yes	No	Free
My Arthritis	Ampersand Health in collaboration with King's College Hospital NHS Foundation and the National Rheumatoid Arthritis Society; sx tracking, courses for pts, connect to hospital, access medical records. Can also participate in research.	Yes	No	Yes	No	Free

Application Name	MARS Section	MARS Score
Abbvie - Complete: Includes Humira, Skyrizi, Rinvoq	Engagement	2
	Functionality	4
	Aesthetics	3.7
	Information	3.75
RA Monitor	Engagement	3.8
	Functionality	3.5
	Aesthetics	3.3
	Information	2.75
RA Manager	Engagement	3.8
	Functionality	4
	Aesthetics	3.7
	Information	4.5
Rheumatoid Arthritis Storylines	Engagement	2.2
	Functionality	3
	Aesthetics	2.3
	Information	1.75
Rheumatoid Arthritis Diary	Engagement	3.2
	Functionality	3
	Aesthetics	2
	Information	2.3
Arthritis Tracker	Engagement	3.6
	Functionality	4
	Aesthetics	4
	Information	4.5
ConnectPlus	Engagement	3.2
	Functionality	4
	Aesthetics	4
	Information	4
Arthritis + Patient	Engagement	4
	Functionality	4.25
	Aesthetics	4.7
	Information	4.5
My Arthritis	Engagement	3.6
	Functionality	4
	Aesthetics	4
	Information	4
Elsa- Paverka din reumatism-	Engagement	3.8
	Functionality	5
	Aesthetics	3.5
	Information	3.75

Figure 2 a: Mobile Application Rating Scale (MARS) section item scores by section and applications

MARS Section	Mean Score
Engagement	3.3
Functionality	3.87
Aesthetics	3.5
Information	3.58
Total mean	3.5

Figure 2 b) Mobile Application Rating Scale (MARS) section mean scores

Disclosure: P. Gonzalez Manrique: None; **V. Gilvaz**: None; **R. Kaler**: None; **N. Batra**: None; **A. Reginato**: None.

Abstract Number: 1897

In Pursuit of Excellence: Improving Systemic Sclerosis Quality of Care

Aos Aboabat[1], Samar Aboulenain[1], Zareen Ahmad[2], Medha Soowamber[3] and Sindhu Johnson[4], [1]University of Toronto, Toronto, ON, Canada, [2]Toronto Scleroderma Program, Mount Sinai Hospital, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, [3]Toronto Scleroderma Program, Mount Sinai Hospital, Toronto Western Hospital, University of Toronto, Woodbridge, ON, Canada, [4]Division of Rheumatology, Department of Medicine, Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western and Mount Sinai Hospitals; Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1895–1912) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a complex autoimmune disease with significant morbidity and mortality. Quality indicators (QIs) for SSc care, previously published, are essential tools to enhance patient outcomes. However, a gap in the implementation of these QIs in clinical practice has been observed. This quality improvement project was designed to enhance the application of SSc QIs. The objectives of this study were to identify the quality gap in systemic sclerosis (SSc) care through assessment of recommended QIs and to evaluate the impact of targeted interventions to improve their uptake.

Methods: We conducted an interrupted time series study at 4 Scleroderma clinics across 2 hospitals over 10 months. Using the model for improvement framework, we employed the Plan-Do-Study-Act (PDSA) methodology to implement sequential change ideas. Interventions were increasing knowledge and awareness among physicians, implementing standardized care processes, and ensuring the availability of necessary devices. Outcome measures were the rates of completion of suboptimal baseline and monitoring/treatment QIs among newly diagnosed and early SSc patients. Process measures were the rates of SpO2 documentation, completion of annual pulmonary function tests (PFTs), baseline creatinine kinase (CK) measurements, blood pressure (BP) self-measurement counseling, and referrals to a hand exercise program for patients with reduced hand function. Balancing measures were staff satisfaction (5-point Likert scale, 1-5 from strong dissatisfaction to strong satisfaction) and perceived workload related to interventions (increase in time per patient).

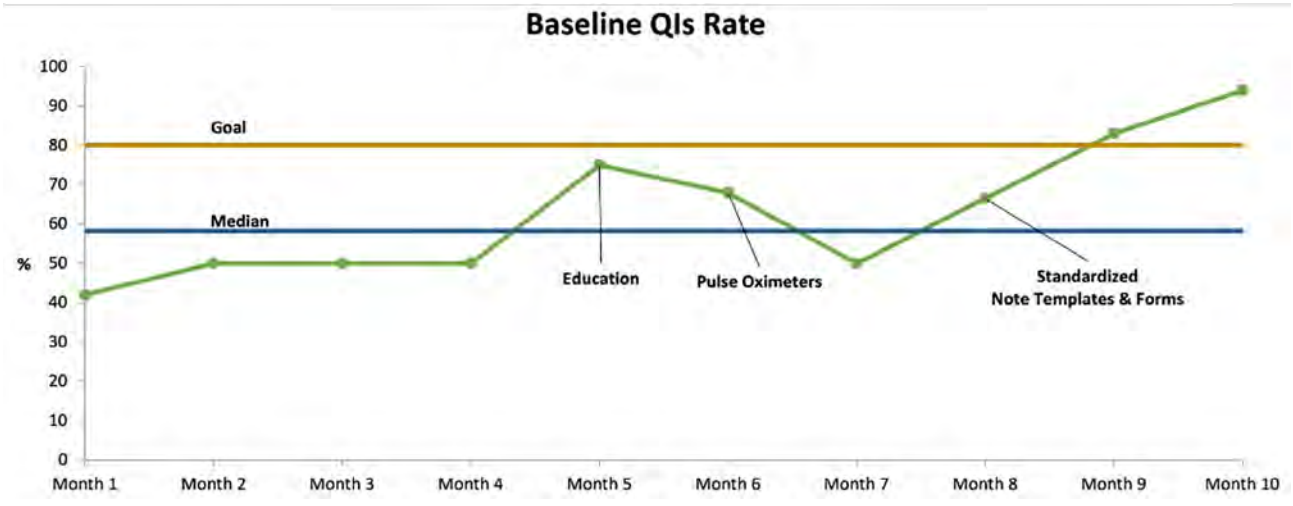

Figure 1

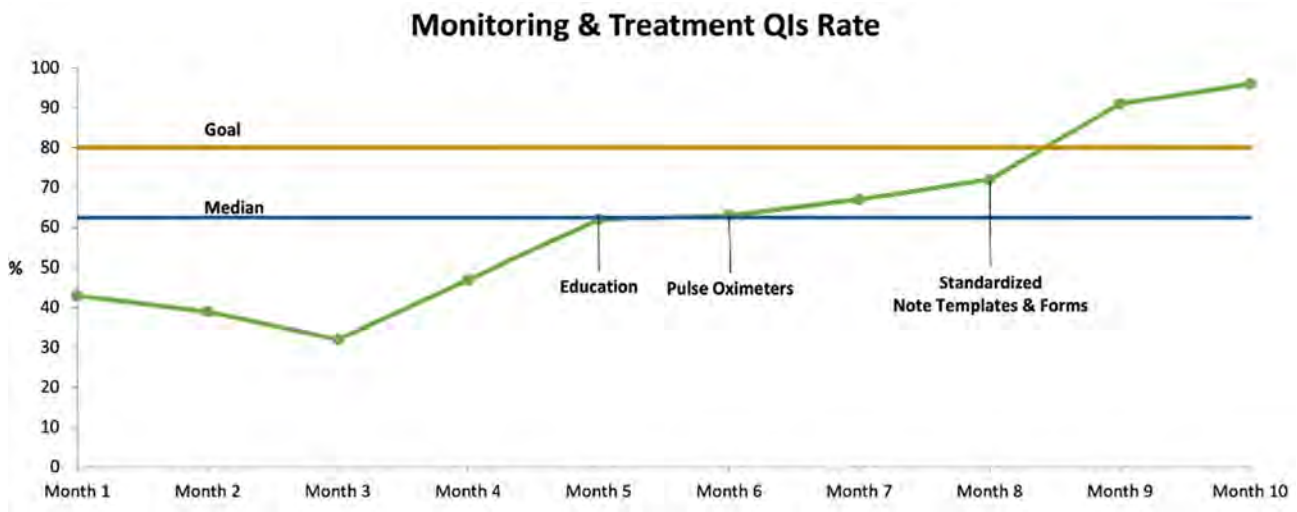

Figure 2

Results: The rate of baseline QIs among newly diagnosed SSc patients improved from 42% to 94% over 10 months (Figure. 1). The rate of monitoring and treatment QIs among early SSc patients improved from 43% to 96% (Figure. 2). Process measures including rates of SpO2 documentation during in-person visits (35.7% to 86%), completion of annual PFTs (64% to 100%), baseline CK measurements (33% to 100%), BP self-measurement counseling (0% to 100%), and referrals to a hand exercise program (33% to 100%) showed improvements. Balancing measures indicated stakeholder satisfaction (median rating 4) with the changes and no increased perceived workload (mean time increased by 2.5 minutes per patient).

Conclusion: The implementation of the interventions led to improvements in the rate of completion of QIs. Continuous monitoring through regular audits and the application of subsequent PDSA cycles as required is critical for sustaining these improvements. This initiative underscores the importance of systematic quality improvement in enhancing the management of complex autoimmune diseases like SSc.

Disclosure: A. Aboabat: None; **S. Aboulenain**: None; **Z. Ahmad**: None; **M. Soowamber**: None; **S. Johnson**: None.

Abstract Number: 1898

Patient After Visit Instructions at a University Rheumatology Outpatient Clinic: Do They Make a Difference?

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
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Background/Purpose: As low health literacy (HL) has been linked to poor health outcomes in rheumatic diseases, it is important to optimize organizational HL. One way of doing this might be through the delivery of after visit instructions (AVI) which are personalized instructions written by a provider & given to patients in the outpatient rheumatology setting. An initial needs assessment revealed that only 25% of patients received AVI at our institution. Herein, we aimed to evaluate the

effectiveness of two after visit interventions aimed at improving the delivery, comprehension, & retention of management plans for patients in an academic rheumatology clinic.

Methods: This was a prospective, randomized, proof-of-concept study. Patients scheduled for clinic visits were randomized into three groups: control group (standard of care), standardized AVI only (templated personalized AVI), & standardized AVI plus Teach back (TB). In TB, the patient repeats management changes to the provider in their own words. Patients completed an Arthritis Rapid Estimate of Adult Literacy in Medicine (A-REALM) questionnaire, to assess rheumatology health literacy. A telephone survey was conducted 1-2 weeks after their clinic visit to assess retention & comprehension in three categories: reason for visit, medication changes, & referrals/further testing. The primary outcome of the study was correspondence between patient responses & the plan outlined in the provider management plan. Patient satisfaction was assessed as a secondary outcome. AVI readability was evaluated using Flesch-Kincaid (FK) scores.

Table 1 Baseline demographics and characteristics

	Total (N=75) (%)
Mean Age Years (SD)	56.7 (14.5)
Gender	
Female	56 (75.7%)
Ethnicity	
Hispanic	13 (17.3)
Not Hispanic	62 (82.7)
Race	
White	27 (36)
Black	34 (45.3)
Asian	2 (2.7)
Other	11 (14.7)
New Patient	30 (40)
Mean Years of Education	15.08
Mean A-REALM*	61.83
Primary Rheumatological Diagnosis	
Inflammatory/Autoimmune	35 (47.3)
Non-inflammatory Conditions	36 (48.6)
Not Applicable	4 (5.3)
Study Arm	
Control	31 (41.3)
AVI only	19 (25.3)
AVI & TB	25 (33.3)
Change in Management During Visit	64 (85.3)
AVI Provided	57 (77)
AVI Provided in Control Group	14/31 (45.2%)
AVI Provided in Control Group w/ Change in Management	13/25 (52%)

*A-REALM is a screening instrument used to assess an adult's ability to read common rheumatology words. A score of >61 indicates a high school literacy level.

Table 2 Patients with Greater Than or Equal to 75% Concordance on the post-visit retention survey

	Control (N=31)	AVI Only (N=19)	AVI & TB (N=25)	Chi Squared P-Value
Reason for visit	18 (58.1%)	16 (84.2%)	18 (72%)	0.313
Medication changes/side effects	11 (35%)	7 (36%)	17 (68%)	0.207
Imaging, Diagnostics, Referrals	12 (38.7%)	10 (52.6%)	13 (52%)	0.631

Table 3 Satisfaction Survey Results of Patients that Answered Strongly Agree

	Control (N=22)	AVI only (N=14)	AVI & TB (N=18)	Chi Squared P-Value
Easy to Understand	21 (95.4%)	7 (50%)	16 (88.8%)	**.004**
Listened Carefully	18 (81.8%)	7 (50%)	16 (88.8%)	.139
Showed Respect	21 (95.4%)	10 (71.4%)	15 (83.3%)	**.025**
Spent Enough Time	18 (81.8%)	10 (71.4%)	16 (88.8%)	.557
Confident in Providers Ability	19 (86.3%)	7 (50%)	14 (77.8%)	.168

Results: 75 patients completed the study with 31 (41.3%) in the control group, 19 (25.3%) in the AVI only group, & 25 (33.3%) in the AVI w/ TB group. Demographics are shown in Table 1. Mean age was 56.7 years. The mean A-REALM was 61.83 which equated with a high school HL. Among the patients with >75% concordance between their responses & the provider's note, there was no difference across the three AVI groups in any of the categories evaluated: reason for visit, medication changes, & referrals (Table 2). Of the 54 patients that completed the satisfaction survey, more patients in the control group responded 'strongly agree' to "the doctor was easy to understand" & "the doctor spent enough time with me" (Table 3). The mean FK readability scores were significantly better in the control group than the intervention groups ($p < 0.001$). Of the patients that were provided personalized AVI only 55% acknowledged receiving them & of those 70% endorsed reading them.

Conclusion: Presence/type of AVI had no significant impact on patient's retention or comprehension regarding their disease or management.Unexpectedly, the readability of AVI & components of satisfaction were better among controls than the other two groups. This may potentially be attributed to more direct patient engagement, & the AVI being brief & simpler in the control group. Further research addressing the limitations of this study could allow us to understand the utility of these patient education strategies to optimize after visit processes.

Disclosure: D. Joseph: None; **R. Hu**: None; **R. Min**: None; **M. Jolly**: None; **S. Hassan**: None.

Abstract Number: 1899

Healthy People with Lupus 2030: Goals to Improve the Quality of Care and Health of All People with Lupus in the United States

Jinoos Yazdany[1], April Jorge[2], Claire Barber[3], April Barnado[4], Bonnie Bermas[5], Ali Duarte-Garcia[6], Amy Bennett[7], Candace Feldman[8], Shivani Garg[9], Leah Haseley[10], Shraddha Jatwani[11], Tracy Johansson[12], Alex Limanni[13], Wambui Machua[14], Wendy Rodgers[15], Brad Rovin[16], Yesenia Santiago-Casas[17], Lisa Suter[18], JoAnn Zell[19], Patti Katz[20] and Christie M. Bartels[21], [1]University of California, General Department of Medicine, Division of Rheumatology, San Francisco, CA, [2]Massachusetts General Hospital, Boston, MA, [3]University of Calgary, Calgary, AB, Canada, [4]Vanderbilt University Medical Center, Nashville, TN, [5]UT Southwestern, Dallas, TX, [6]Mayo Clinic, Rochester, MN, [7]ACR, Atlanta, GA, [8]Brigham and Women's Hospital, Boston, MA, [9]Department of Medicine, University of Wisconsin School of Medicine and Public Health, Madison, WI, [10]University of Washington, Seattle, WA, [11]Dignity Health-MMG Rheumatology, East Norriton, PA, [12]American College of Rheumatology, Atlanta, GA, [13]Self, Dallas, TX, [14]Piedmont Healthcare, Atlanta, GA, [15]Lupus Foundation of America, Los Angeles, CA, [16]Ohio State University, Columbus, OH, [17]Guillermo Valenzuela MD PA, Plantation, FL, [18]Yale School of Medicine, New Haven, CT, [19]University of Colorado Anschutz Medical Campus, Denver, CO, [20]University of California San Francisco, San Rafael, CA, [21]University of Wisconsin, School of Medicine and Public Health, Madison, WI

SESSION INFORMATION

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Background/Purpose: Collaborating with the Centers for Disease Control and Prevention (CDC), the ACR has developed new quality measures for lupus clinical care, including clinical and patient-reported outcome measures (PROMs), through a consensus-based process. Here we summarize the development of the 5 measures and introduce corresponding Healthy People with Lupus 2030 goals, which aim to guide the widespread adoption of these measures.

Methods: Two interdisciplinary workgroups, one focused on clinical process-of-care measures and one focused on PROMs, were convened. Both groups used literature reviews, modified Delphi procedures, and extensive patient input to arrive at lupus quality measures. For clinical measures, workgroup members extracted quality constructs from guidelines and rated them by importance and feasibility to generate evidence-based quality measure statements. In 3 Delphi sessions, a multidisciplinary panel voted on the importance to individual patients, feasibility of measurement, and public health impact of each statement. Measures with consensus on feasibility and importance were ranked to identify the top three. For PROMs, experts reviewed literature regarding quality-of-life domains in lupus and conducted focus groups with patients to prioritize domains and measures. A Delphi panel reviewed PROMs corresponding to priority domains for content validity, psychometric quality, feasibility of implementation, and importance for guiding patient-self management. The patient advisory panel reviewed PROMs in parallel and contributed to selecting final measures. Healthy People with Lupus 2030 goals were derived from the final clinical and PRO-based measures.

Results: For clinical process-of-care measures, review of guidelines and distillation of 57 quality constructs resulted in 15 quality measure statements. The 3 most highly ranked quality measures were 1) increasing hydroxychloroquine use, 2) avoiding glucocorticoid use >7.5 mg/day for >6 months, and 3) monitoring of kidney function and urine protein excretion at least every 6 months. For PROMs, literature review identified 12 domains. The workgroup and patient partners ranked depression, physical function, pain, cognition, and fatigue as high-priority domains. Delphi panel members and patient advisors recommended the 2 highest rated domains, physical function and depression, for annual measurement. PROMs recommended for depression were the Patient Health Questionnaire (PHQ) or Patient Reported Outcomes Measurement

Table. American College of Rheumatology/Centers for Disease Control and Prevention Quality Measures for Lupus and Corresponding Healthy People with Lupus 2030 Goals

Quality Measure	Healthy People with Lupus 2030 Goal	Potential Public Health Impact
IF a patient has lupus, THEN they should have a prescription for hydroxychloroquine on or after the date of the most recent rheumatology visit unless a contraindication or adverse event is documented in the medical record.	All eligible patients with lupus should take hydroxychloroquine	Reduce morbidity, decrease flares, reduce acute care use, and possibly improve mortality in SLE
IF a patient has lupus, THEN the glucocorticoid dose should not exceed 7.5 mg/day prednisone (or equivalent) for more than 6 months.	All people with lupus should avoid prednisone doses 7.5 mg/day (or equivalent) for longer than 6 months	Reduce glucocorticoid morbidity
IF a patient has lupus, THEN measurement of both kidney function and protein excretion (urinalysis and/or quantitative measurement) should be checked at least every 6 months.	All people with lupus should have twice yearly laboratory testing to screen for kidney disease and review these results with their lupus physician	Reduce morbidity by early identification of lupus nephritis, and reducing loss to follow-up
IF a patient has lupus, THEN functional status assessment using a standardized, validated measure (preferred: PROMIS PF10A or CAT; alternative: MDHAQ) should be performed at least once per year.	All people with lupus should complete a PROM evaluating functional status at least once per year	Reduce functional loss and disability
IF a patient has lupus, THEN depression assessment using a standardized, validated measure (preferred: PHQ-8; alternatives: PHQ-2, PHQ-9, PROMIS depression SF or CAT) should be performed at least once per year.	All people with lupus should complete a PROM evaluating depression at least once per year	Identify depression and reduce suicides

PROMIS, Patient Reported Outcomes Measurement Information System; PF10A, 10-item PROMIS physical function form; CAT, computerized adaptive testing; MDHAQ, Multi-Dimensional Health Assessment Questionnaire; PROM, patient-reported outcome measure; PHQ, Patient Health Questionnaire; SF, short form.

Healthy People with Lupus 2030: Goals to Improve the Quality of Care and Health of All People with Lupus in the United States

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Healthy People with Lupus 2030 Campaign

Information System (PROMIS) depression scales; PROMs recommended for physical function were the PROMIS physical function scales or the Multi-Dimensional Health Assessment Questionnaire (MDHAQ). The **Table** shows the final measures and corresponding Healthy People with Lupus 2030 goals.

Conclusion: Healthy People with Lupus 2030 provides a vision for improving clinical care for all people with lupus in the United States (**Figure**). Key priorities are increasing the use of hydroxychloroquine, reducing glucocorticoid exposure, regular monitoring for lupus nephritis (to prevent loss to follow-up and kidney failure), reducing disability, and reducing depression and suicide among people with lupus.

Disclosure: J. Yazdany: AstraZeneca, 2, 5, Aurinia, 5, Gilead, 5, Pfizer, 2; **A. Jorge**: None; **C. Barber**: None; **A. Barnado**: None; **B. Bermas**: None; **A. Duarte-Garcia**: None; **A. Bennett**: None; **C. Feldman**: BMS Foundation, 5, Curio Bioscience, 12, My husband is one of the founders and will receive equity (but has not received anything to date)., OM1, Inc., 2, Pfizer, 5; **S. Garg**: None; **L. Haseley**: None; **S. Jatwani**: None; **T. Johansson**: None; **A. Limanni**: None; **W. Machua**: None; **W. Rodgers**: None; **B. Rovin**: AstraZeneca, 2, 5, Aurinia, 2, 5, Biogen, 2, F. Hoffmann-La Roche Ltd, 2, Genentech, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **Y. Santiago-Casas**: None; **L. Suter**: Centers for Medicare Medicaid Services, 12, Salary support from unrelated CMS ontract, unrelated NIH grant to Elena Losina/ BWH, 1; **J. Zell**: None; **P. Katz**: None; **C. Bartels**: Pfizer, 5.

Abstract Number: 1900

Assessment of Hospitalist Confidence Levels in Management of Rheumatic Conditions to Identify Potential Knowledge Gaps

Lily Sung, Amber Young and Jiha Lee, University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1895–1912) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
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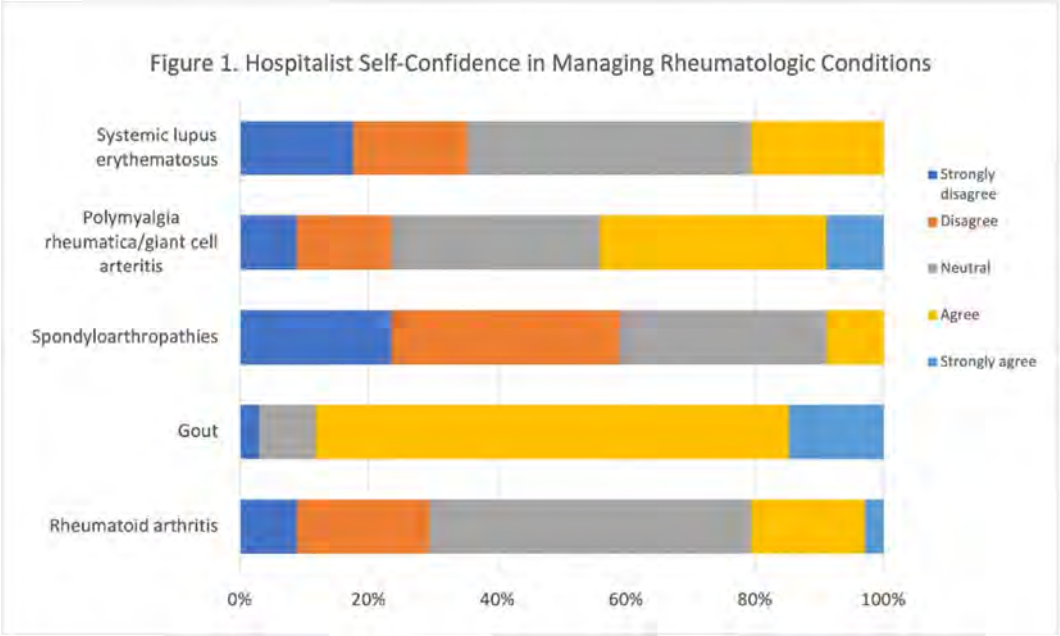
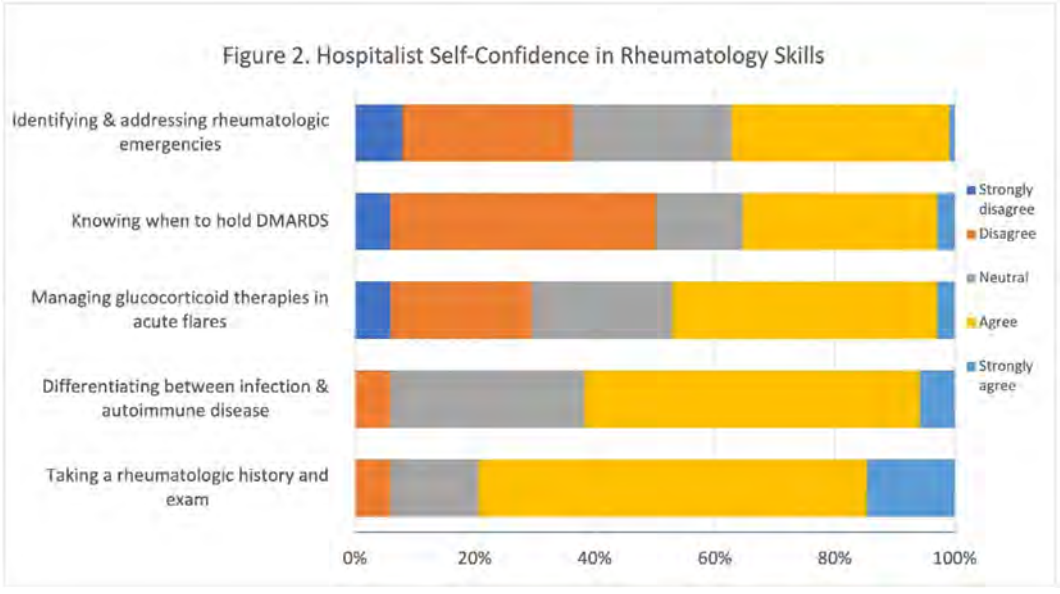
Background/Purpose: Healthcare utilization, including hospitalization, is high among patients with rheumatic musculoskeletal diseases (RMD). As the primary care providers during admission, hospitalists play a key role in improving care of RMD patients, and their role will be ever more important given the projected workforce shortage of rheumatologists, especially in resource limited and rural areas. We assessed academic hospitalists confidence levels, interests, and preferred method of learning to identify educational needs and opportunities to improve care of patients with RMD.

Methods: Hospitalists at a single large tertiary academic center participated in an online survey developed based on consensus between two rheumatologists and one hospitalist. Demographics of sex, years of experience, and exposure to rheumatology curriculum were obtained. Using a five-point Likert scale (1=strongly disagree, 5=strongly agree) hospitalists rated their level of confidence in managing five common RMD conditions: rheumatoid arthritis, gout, spondyloarthropathies, polymyalgia rheumatica/giant cell arteritis and lupus. They also rated confidence levels in five skills related to inpatient care of RMD patients: performing a rheumatologic history and exam, differentiating between acute infectious and autoimmune conditions, identifying rheumatologic emergencies, managing steroid therapy in acute rheumatic flares, and knowing when to hold DMARDs. We also asked open-ended questions to collect qualitative information on individual interest, perceived challenges, and preferred learning methods in rheumatology.

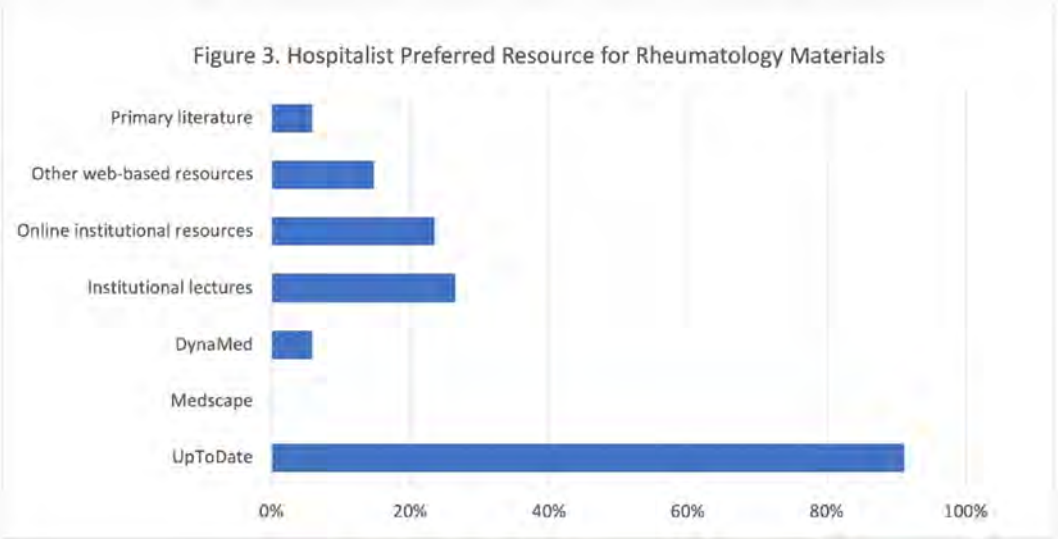
Results: This is an ongoing study, and we report preliminary data from 34 completed responses where the survey response rate was 26%. Half (53%) of the respondents had ≥ 5 years of experience working as hospitalists and 32% reported minimal training in rheumatology. Half reported caring for > 10 RMD patients on average each month. Hospitalist confidence in managing gout was highest, with 97% rating neutral or greater (Figure 1). Confidence in managing lupus and spondyloarthropathies were lowest, with 65% and 41% rating neutral or greater, respectively. Hospitalists were not confident in identifying rheumatologic emergencies or knowing when to hold DMARDs with 36% and 50% reporting less than neutral, respectively (Figure 2). Most were interested in learning about lupus and its complications, rheumatologic emergencies, and understanding appropriateness of rheumatology consultation. Almost all (n=31) hospitalists reported using UpToDate as their preferred resource for rheumatology (Figure 3).



Responses measured on a 5 point Likert scale (1: strongly disagree, 5: strongly agree), in response to statements regarding management of conditions listed.



Responses measured on a 5 point Likert scale (1: strongly disagree, 5: strongly agree), in response to statements regarding skill sets listed.



Respondents were able to select more than one option.

Conclusion: Hospitalists reported caring for a fair number of RMD patients, but they had minimal training and knowledge gaps in certain rheumatologic conditions and skills related to the care of hospitalized RMD patients. They expressed interest in rheumatologic learning opportunities and understanding how to best engage rheumatologists. Further studies are needed to develop educational resources and guide interdisciplinary collaboration between hospitalists and rheumatologists to improve the care of RMD patients in the inpatient setting.

Disclosure: L. Sung: None; **A. Young**: None; **J. Lee**: None.

Abstract Number: 1901

Which ASDAS-ESR Cut-offs for Disease Activity Correspond to ASDAS-CRP Cut-offs in Axial Spondyloarthritis? – Results from the EuroSpA Collaboration

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SESSION INFORMATION

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Background/Purpose: When assessing disease activity in patients with axial spondyloarthritis (axSpA), the Ankylosing Spondylitis Disease Activity Score with C-reactive protein (ASDAS-CRP) is recommended over ASDAS with erythrocyte sedimentation rate (ASDAS-ESR). Although ASDAS-CRP and ASDAS-ESR are not interchangeable, the same cut-offs are

Table 1. ASDAS-ESR cut-off estimation that corresponds to established ASDAS-CRP cut-offs

	n (P+N)	AUC	Sensitivity	Specificity	ASDAS-ESR cut-off
ASDAS-CRP<1.3	4,306 (1,255+3,051)	0.95	0.91	0.86	<1.3743
ASDAS-CRP<2.1	4,306 (2,566+1,740)	0.96	0.89	0.91	<1.8923
ASDAS-CRP>3.5	4,306 (2,209+2,097)	0.93	0.85	0.86	>3.3074

Optimal cut-off estimated by maximising the Youden index (=sensitivity+specificity-1). Selection of cut-offs relied on a single treatment course per patient with available baseline and at least one follow-up timepoint per patient, prioritising earlier TNFi (among the first three treatment courses) and timepoint (for follow-up data).

ASDAS: Ankylosing Spondylitis Disease Activity Score; ASDAS-CRP: ASDAS based on C Reactive Protein; ASDAS-ESR: ASDAS based on Erythrocyte Sedimentation Rate; AUC: area under the curve; n: number of patients; N: negative; P: positive.

Table 2. Statistical measures comparing ASDAS-ESR and ASDAS-CRP cut-offs for classifying patients in different disease activity states

A. Established ASDAS-ESR vs. ASDAS-CRP cut-offs							
Cut-offs between "inactive disease" and "low disease activity" (follow-up)							
N	ASDAS-ESR<1.3	ASDAS-CRP<1.3	Proportion of Discordance	Sensitivity	Specificity	BalAcc	κ
11,407	3,351/10,030 (33.4%)	3,041/10,238 (29.7%)	1,215/9,979 (12.2%)	0.86	0.89	0.87	0.72
Cut-offs between "low disease activity" and "high disease activity" (follow-up)							
N	ASDAS-ESR<2.1	ASDAS-CRP<2.1	Proportion of Discordance	Sensitivity	Specificity	BalAcc	κ
11,407	6,466/10,030 (64.5%)	6,237/10,238 (60.9%)	1,095/9,979 (11.0%)	0.94	0.82	0.88	0.77
Cut-offs between "high disease activity" and "very high disease activity" (baseline)							
N	ASDAS-ESR>3.5	ASDAS-CRP>3.5	Proportion of Discordance	Sensitivity	Specificity	BalAcc	κ
5,850	2,238/5,303 (42.2%)	2,637/5,352 (49.3%)	833/5,296 (15.7%)	0.77	0.92	0.84	0.68
B. Estimated ASDAS-ESR vs. ASDAS-CRP cut-offs							
Cut-offs between "inactive disease" and "low disease activity" (follow-up)							
N	ASDAS-ESR<1.4	ASDAS-CRP<1.3	Proportion of Discordance	Sensitivity	Specificity	BalAcc	κ
11,407	3,770/10,030 (37.6%)	3,041/10,238 (29.7%)	1,394/9,979 (14.0%)	0.90	0.84	0.87	0.69
Cut-offs between "low disease activity" and "high disease activity" (follow-up)							
N	ASDAS-ESR<1.9	ASDAS-CRP<2.1	Proportion of Discordance	Sensitivity	Specificity	BalAcc	κ
11,407	5,768/10,030 (57.5%)	6,237/10,238 (60.9%)	1,119/9,979 (11.2%)	0.88	0.90	0.89	0.77
Cut-offs between "high disease activity" and "very high disease activity" (baseline)							
N	ASDAS-ESR>3.3	ASDAS-CRP>3.5	Proportion of Discordance	Sensitivity	Specificity	BalAcc	κ
5,850	2,633/5,303 (49.7%)	2,637/5,352 (49.3%)	757/5,296 (14.3%)	0.86	0.86	0.86	0.71

Analyses were conducted on data from all available treatment courses, including up to 3 different follow-up timepoints per treatment course for each patient included in the study.

ASDAS: Ankylosing Spondylitis Disease Activity Score; ASDAS-CRP: ASDAS based on C-Reactive Protein; ASDAS-ESR: ASDAS based on Erythrocyte Sedimentation Rate; BalAcc: balanced accuracy (i.e., the average of sensitivity and specificity); N: number of observations; κ: Cohen's kappa coefficient.

used to classify patients into four distinct disease activity states: inactive disease (ID), low disease activity (LDA), high disease activity (HDA) and very high disease activity (VHDA). These cut-offs were developed based on ASDAS-CRP. We aimed to (i) estimate optimal ASDAS-ESR values corresponding to the established ASDAS-CRP cut-offs (< 1.3, < 2.1 and > 3.5), and (ii) investigate the improvement of level of agreement between ASDAS-ESR and ASDAS-CRP disease activity states when applying the estimated ASDAS-ESR cut-offs.

Methods: Prospectively collected real-world data from axSpA patients starting a 1st, 2nd or 3rd tumor necrosis factor inhibitor (TNFi) from 9 countries participating in the European Spondyloarthritis (EuroSpA) Research Collaboration Network were analysed. Data were collected at baseline and three follow-up visits (6, 12 and 24 months) per TNFi treatment course. To have the best representation of the disease activity states, aggregated follow-up data were used to evaluate the ASDAS-CRP cut-offs for ID and between LDA and HDA, while baseline data were used to assess the cut-off for VHDA. We performed receiver operating characteristic analyses using the Youden index to estimate the optimal ASDAS-ESR values corresponding to ASDAS-CRP cut-offs. The level of agreement between ASDAS-ESR and ASDAS-CRP disease activity states was also assessed.

Results: We analysed data from 4,306 patients with complete registration of ASDAS scores at baseline and at least one complete follow-up registration of ASDAS scores during the same TNFi treatment course. Mean (SD) ASDAS-CRP and ASDAS-ESR were 3.5 (1.0) and 2.0 (1.0) at baseline and 3.3 (1.0) and 1.9 (1.0) at follow-up, respectively. The estimated ASDAS-ESR cut-offs between ID and LDA, between LDA and HDA and between HDA and VHDA corresponding to ASDAS-CRP cut-offs were < 1.4, < 1.9 and > 3.3, respectively (Table 1). Good agreement was observed between disease activity states applying the established ASDAS-ESR and ASDAS-CRP cut-offs, although the VHDA cut-off showed slightly worse agreement than the other two cut-offs (Table 2, upper panel). The statistical measures comparing the estimated ASDAS-ESR (< 1.4, < 1.9 and > 3.3) and ASDAS-CRP (< 1.3, < 2.1 and > 3.5) cut-off values performed slightly better only for VHDA as compared to applying the same cut-offs for both ASDAS versions (Table 2, lower panel). However, the proportion of discordance for the cut-offs for ID and between LDA and HDA increased slightly with the estimated ASDAS-ESR cut-off values.

Conclusion: In a multi-national cohort, the estimated ASDAS-ESR cut-offs between disease activity states were < 1.4, < 1.9 and > 3.3. The original cut-offs overall performed similarly as the ones we estimated. Our findings did not provide sufficient evidence to reject the established ASDAS-ESR cut-offs.

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Abstract Number: 1902

Improving the Sharing of Information from Reviews of Measurement Properties: The OMERACT Summary of Measurement Properties (SOMP) Table

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1895–1912) Measures & Measurement of Healthcare Quality Poster II
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Background/Purpose: Systematic reviews of measurement properties of an outcome measurement instrument are fast becoming the evidence base for making decisions about the suitability of the instrument for a given application. Transparency in processes and decision-making at each step are important to allow consumers of the reviews to have a clear understanding of the results.At OMERACT (Outcome Measures in Rheumatology) we used an iterative process between methodologists and users for developing a summary of measurement properties table (SOMP) to use as a knowledge translation tool for communicating what was done, what was found, and what recommendations can be made from it.

Methods: Working with key stakeholders and end users, including patients, clinical trialists, clinicians and methodologists across several disease areas, the information that needed to be included in a SOMP was determined and initial designs laid out. Users provided feedback and revisions, which were integrated while ensuring the core elements were also being communicated.

Results: Several features emerged for inclusion in the SOMP.We wanted the SOMP to be a standalone resource so the name/version of the tool, the target population (if restricted in the review) and the target concept the reviewers are trying to measure with this instrument were all included at the top of the table. Further, we designed the SOMP to be assembled as teams moved through the review steps so that it was clear the level of detail that was going into any statement about an instrument, and it was transparent exactly which studies/primary resources were included in the review and how they were reviewed.

The SOMP (Figure 1) uses symbols (colour for critical appraisal of methods, +/- for comparison of results to psychometric standards) and algorithms (for making conclusions based on the results in the synthesis steps).Should steps not be done in a given review (i.e., no critical appraisal in a descriptive review) the absence of colours in the boxes would demonstrate this for the users. Rows within the table include evidence from each study included in decision-making.

Conclusion: The SOMP was designed to capture the measurement properties evidence and decision-making processes for the OMERACT community to agree on whether an instrument is good enough to be included to represent a domain for a core outcome set.Its iterative development within a multidisciplinary consensus-based organization has helped us develop a tool we are finding useful in the transparent communication about methods and decision-making made in a given review.Although our key target is regulatory approval and core outcome set development, we have learned about the importance of being transparent in how decisions were made about an instrument, and how to share the body of evidence with others, leading to broader applications of the evidence base.

EXAMPLE Completed Summary of Measurement Properties (SOMP) Table (fictitious)

Instrument: ABC Domain: Physical function					Date completed: 2021-02-11			
Population: rheumatoid arthritis	Intervention(s): drug		Control: placebo/drug			Type of studies: clinical trials		
Author/year	Truth	Feasibility	Truth		Discrimination			
	Domain match		Construct validity	Inter-method reliability	Test-retest reliability	Long'l construct validity	Clinical trial discrimination	Thresholds of meaning
Working Group Appraisal (n=20 including 7 PRPs)	+	+						
Tugwell 2005			+/–			+		
Shea 2004						+		+
Smith 1999								
Beaton 2015							+	
De Wit 2018							+	
Wells 2004			+					
March 2008							+	+/–
D'Agostino 2011						+/–		+
Bingham 2018			+		+/–			
Singh 2010			+					
Strand 2015			+/–					
Simon 2011						+		+/–
New data from Conaghan 2021					+			
Total available studies for each property	0	0	5	N/A	3	5	3	4
Total studies available for synthesis	0	0	5	N/A	2	4	3	4
Synthesis Rating	GREEN From Working group	GREEN From Working group	GREEN	N/A	AMBER	GREEN	GREEN	AMBER
OMERACT Endorsement	**Based on the OMERACT algorithm this instrument is:** **Provisionally endorsed** ***More work needed on test-retest reliability and thresholds of meaning.***							

OMERACT Summary of Measurement Properties (SOMP)

Disclosure: s. grosskleg: None; **l. maxwell**: None; **D. Beaton**: None; **B. Shea**: None; **P. Tugwell**: None.

Abstract Number: 1903

Assessing Disparities Through Missing Race and Ethnicity Data: Results from a Juvenile Arthritis Registry

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

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Background/Purpose: Research databases are missing 25-50% of race and ethnicity, typically related to Black and Hispanic data.[1,2]The absence of this data can lead to inaccurate assessment of patient outcomes by race.[1,3,4] Our aim is to assess the impact of missing race and ethnicity on outcome measures in a JIA registry (Pediatric Care Outcomes Improvement Network (PR-COIN)).

Methods: Descriptive analysis of demographic and clinical data from 9 PRCOIN centers was performed. Missing race and ethnicity data was quantified by site. Relative risk (RR) of moderate to severe clinical juvenile arthritis disease activity score (cJADAS ³5) at first visit after enrollment was compared across race (Black, White, other, missing) and ethnicity (Hispanic, non-Hispanic, missing).A RED Cap survey on data collection and entry was administered to each site.

Results: A total of 1,505 JIA patients from 9 (of 23) sites were included (Table 1). Race was missing for 24% and ethnicity was missing for 23% with missing data ranging from 0-100% (Table 2).

CJADAS score at first follow-up (2-6 months after enrollment) was high (³5) for 30% of White patients and 55% of Black patients with a RR of 1.84 (p=0.0001) of higher cJADAS in Black patients (Table 3). There was no difference in risk for patients of Other races, relative to White patients, RR 1.0 (p=0.99). For patients missing race, risk of high cJADAS at first follow-up was lower than for White patients, RR 0.88 (p=0.21). There was no difference in rates of high cJADAS at first follow

Table 1 Patient Characteristics

	n	%
Gender		
Female	1091	72.5
Male	414	27.5
Ethnicity		
Hispanic/Latino	160	10.6
Not Hispanic/Latino	1002	66.6
Missing	343	22.8
Race		
White	994	66
Black	40	2.7
Other	114	7.6
Missing	357	23.7
ILAR CODE (JIA subtype)		
Enthesitis Related Arthritis	28	1.9
Oligoarticular extended	190	12.6
Oligoarticular persistent	183	12.2
Polyarticular RF (+)	300	19.9
Polyarticular RF (-)	807	53.6
Psoriatic Arthritis	1059	70.4
Systemic JIA	1108	73.6
Undifferentiated Arthritis	1155	76.7
Missing	790	52.5

Table 2 Missing Data by Site		
	Missing race (%)	Missing ethnicity (%)
All sites	23.7	22.8
Site A	28.4	22.9
Site B	14.9	8.2
Site C	0.0	81.8
Site D	23.5	34.7
Site E	0.0	2.0
Site F	100.0	100.0
Site G	0.0	0.5
Site H	12.6	14.9
Site I	4.1	8.7

Table 3 cJADAS Outcomes by Race and Ethnicity			
	High cJADAS[1],n (%)	Low cJADAS, n (%)	Relative Risk of High cJADAS (p value)
RACE			
White	297 (30%)	697 (70%)	Reference
Black	22 (55%)	18 (45%)	1.84 (p=0.0001)
Other	34 (30%	80 (70%)	1.0 (p=0.9904)
Missing	94 (26%)	263 (74%)	0.88 (p=0.2106)
Ethnicity			
Hispanic	48 (30%)	112 (70%)	0.94 (p=0.6459)
Non-Hispanic	319 (32%)	683 (68%)	Reference
Missing	80 (23%)	263 (77%)	0.73 (p=0.0041)

(1) High cJADAS (score ≥5) at the first follow-up (2-6 months after enrollment)

up by Hispanic vs non-Hispanic ethnicity, RR 0.94 (p=0.65). For patients with missing ethnicity, risk of high cJADAS at first follow-up was 27% lower than non-Hispanic patients, RR 0.73 (p=0.0041).

Four of 9 sites completed a survey. Two sites are missing 0% of race and < 2% of ethnicity data. One is missing 12.6% race and 14.9% ethnicity. These 3 sites enter data manually. One is missing 100% of race and ethnicity data and uploads data via electronic data transfer (EDT).

Conclusion: Amount of missing race and ethnicity data is highly variable, ranging from 0-100%. Additional survey data is needed to understand the impact of data entry method on missingness. Preliminary, unadjusted analysis suggests RR of high cJADAS at first follow up is higher for Black compared to White patients in a setting of missing data. Patients with missing race had lower RR of high cJADAS at first follow up compared to White patients. This suggests that completion of missing race could change RR assessments. Next steps include multivariate analysis to adjust for confounding factors (age, gender, site, ILAR code, insurance status).It also includes interventions to complete missing data and reassessment of RR of high cJADAS.

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Abstract Number: 1904

Treat-to-Target in RA Clinical Practice: Global Evidence of Practice Gaps and Educational Needs

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SESSION INFORMATION

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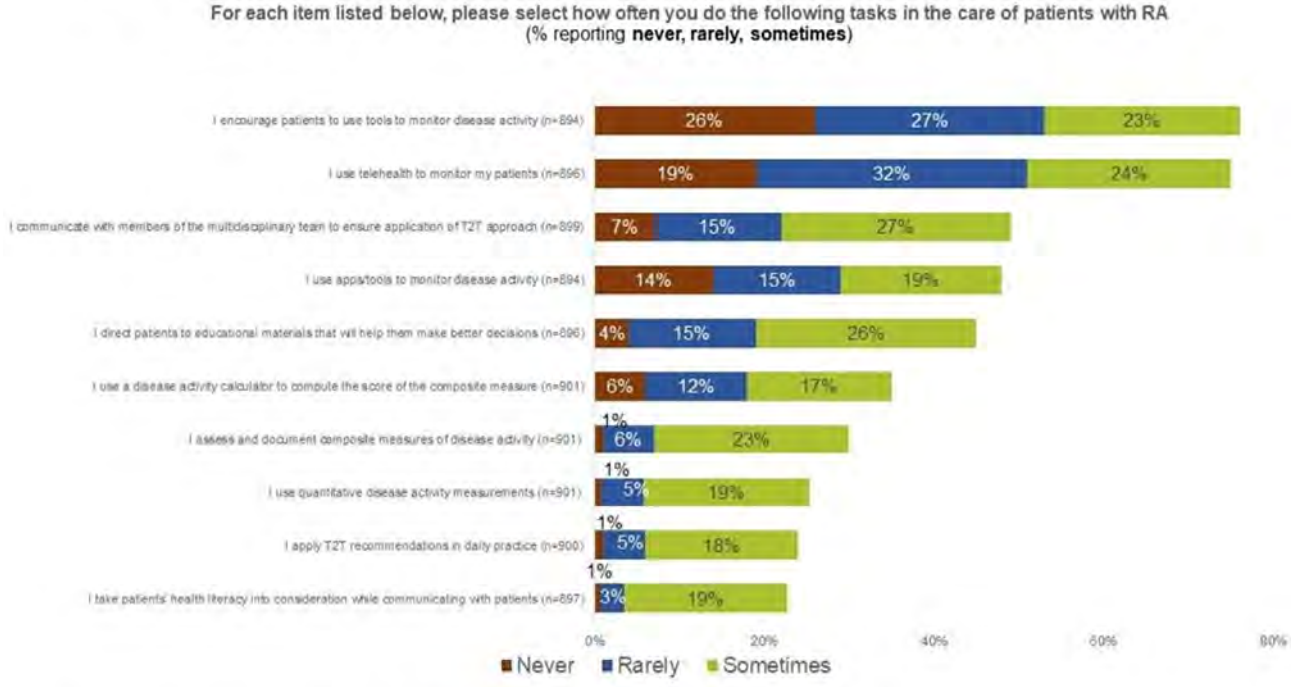
Session Time: 9:00AM–11:00AM

Background/Purpose: Treat-to-target (T2T) is a widely established and accepted approach in RA management, but its real-world implementation is suboptimal[1]. Further primary research is required to identify the most relevant barriers to, and facilitators of, real-world T2T implementation[2]. This survey assessed perceived barriers to, and facilitators of, T2T implementation among rheumatologists globally.

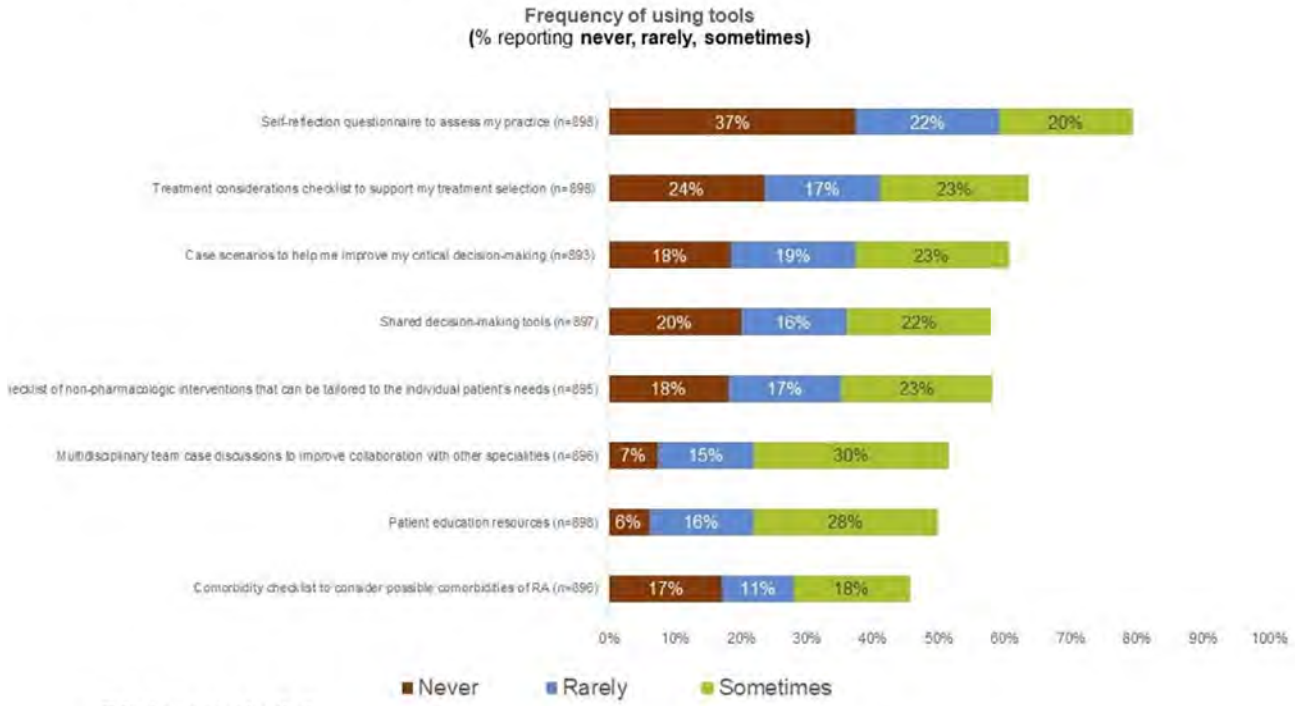
Methods: A non-remunerated quantitative survey was completed by eligible rheumatologists (≥2 years' practice experience, awareness of T2T approach, ≥10 patients with RA/year) between June 6 and Sep 30, 2022, in 35 ex-US countries. The survey was informed by a systematic literature review[2] and included 9 questions across 6 key areas of T2T

Figure 1. Least performed tasks by rheumatologists



RA, rheumatoid arthritis; T2T, treat-to-target.

Figure 2. Least frequently used tools by rheumatologists



RA, rheumatoid arthritis.

Table 1. Common gaps and barriers reported in the global survey that impact use of the T2T approach in RA

Key themes	Knowledge, skills, and confidence gaps	Clinical practice behaviors		System/contextual barriers
		Challenges/task performance	Use of tools	
Collaboration and communication with patients and colleagues	• Assessing health literacy levels of patients • Understanding patient goals and adapting language while communicating with patients	• Encouraging patients to use tools to monitor disease activity • Reconciling patient perspectives on successful treatment with their own perspectives • Directing patients to educational materials • Communicating with multidisciplinary teams to ensure application of T2T approach	• Limited use of shared decision-making tools	• Patients skipping too many appointments
Using PROs and considering patient preferences	• Using PROs to assess disease activity	• Identifying patient preferences to determine treatment target • Trusting patient-reported joint counts	• Limited use of treatment considerations checklist	• Contradictory assessments between PROs and composite measures
Adjusting treatment based on disease activity measures		• Interpretating disease activity measures, especially measures other than composite measures		• Electronic medical record not adapted to capture disease activity measures • Change in disease activity linked to patient non-adherence
Overall delivery of care		• Limited use, and confidence in use, of telehealth with patients with RA	• Limited use of self-reflection questionnaires	• Clinical processes limit full implementation of T2T approach

PRO, patient-reported outcome; RA, rheumatoid arthritis; T2T, treat-to-target.

implementation in RA: knowledge, skill, confidence, agreement (attitudes/context), contextual/systemic barriers, and behaviors. Knowledge, skill, and confidence were rated on a 5-point scale and reported as suboptimal (no/basic/intermediate knowledge or skill; not/slightly/somewhat confident) or optimal (advanced/expert knowledge or skill; confident/very confident). Agreement was rated on a 6-point scale (strongly disagree to strongly agree) and barriers on a 4-point scale (not at all to serious barrier). Behaviors were rated on a 5-point scale and reported as infrequent (never/rarely/sometimes) or frequent (often/always).

Results: Of 903 surveyed rheumatologists (Europe, n=297; Americas, n=293; Asia-Pacific, n=200; Middle East & Africa, n=113), 72% had ≥11 years of practice experience and 80% reported practicing T2T consistently or frequently. Despite awareness of the T2T approach, there was suboptimal knowledge, skill, and confidence in determining patient health literacy and adapting language while communicating with patients, considering patient goals, and using PROs to assess disease activity. At least 75% of rheumatologists never, rarely, or sometimes used telehealth or encouraged patients to use disease self-assessment tools (Figure 1). The least frequently used tools by rheumatologists were self-reflection questionnaires, treatment considerations checklists, case scenarios, and shared decision-making tools (Figure 2), primarily due to the perception these tools were time-consuming, not needed, or non-existent. Patient adherence-related issues were the top barriers to documenting disease activity, with the other barriers mostly related to healthcare system-related processes. Higher gaps were generally observed in rheumatologists who do not consistently or frequently practice T2T, or who had < 10 years of experience. Table 1 regroups the common gaps and barriers under 4 key themes.

Conclusion: These results highlight practice gaps and educational needs in rheumatologists that can inform educational programs and interventions to support T2T implementation. Based on these findings, recommended focus areas for improving T2T implementation include incorporating all components of T2T in practice, optimal use of telehealth in RA, patient education and shared decision-making, and the use of tools to enhance practice efficiency.

References:

1. Yu Z, et al. Arthritis Care Res 2018;70:801–6
2. Gossec L, et al. Ann Rheum Dis 2022;81:572 [POS0607]

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Abstract Number: 1905

Implementation of the Clinical Disease Activity Index to Optimize Treat-to-Target Management of Rheumatoid Arthritis at the University of North Carolina Hospitals Rheumatology Specialty Clinic

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SESSION INFORMATION

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Background/Purpose: The 2021 American College of Rheumatology (ACR) guidelines for the treatment of rheumatoid arthritis (RA) recommend a treat-to-target approach to optimize clinical outcomes. This approach requires frequent monitoring of disease activity using validated instruments and modification of treatment with the goal of reaching low disease activity or remission. The Centers for Medicare and Medicaid Services (CMS) and Rheumatology Informatics System for Effectiveness (RISE) registry have defined that patients with a diagnosis of RA should have an assessment using an ACR-preferred RA disease activity tool at ≥50% of encounters annually for the traditional Merit-based Incentive Payment System (MIPS). The University of North Carolina (UNC) Hospitals Rheumatology Specialty Clinic utilizes an electronic health record (EHR) with a flowsheet built to measure Clinical Disease Activity Index (CDAI); one such validated instrument. The purpose of this study was to understand use, limitations, and intervene to improve utilization of the CDAI among patients with RA.

Methods: Qualtrics™ surveys were distributed pre- and post-intervention to clinical care providers. Surveys queried knowledge of the ACR guidelines, CDAI implementation, and perceived barriers. Responses were anonymous and there was no identification if providers were trainees, faculty, or advance care partners. CDAI utilization was measured for the 6 months preceding the intervention and then 6 months post-intervention through the EHR. Interventions included 1) education to providers and care partners by a clinical pharmacist, 2) EHR daily reports for providers to capture relevant scheduled visits, 3) creation of a physical patient global assessment form, and 4) involvement of care partners in distributing and capturing the patient global assessment during patient triage. This project received IRB waiver as non-human subject research (UNC IRB 22-1967).

Results: On average, CDAI use in the 6 months prior to the intervention was 33%, improving to 58% post-intervention. We observed a slight lag for initial uptake as well as a plateau following intervention. Pre-intervention (n=17 providers) and post-intervention surveys (n=11 providers) indicated similar barriers, including: 1) lack of time during patient visit, 2) remembering

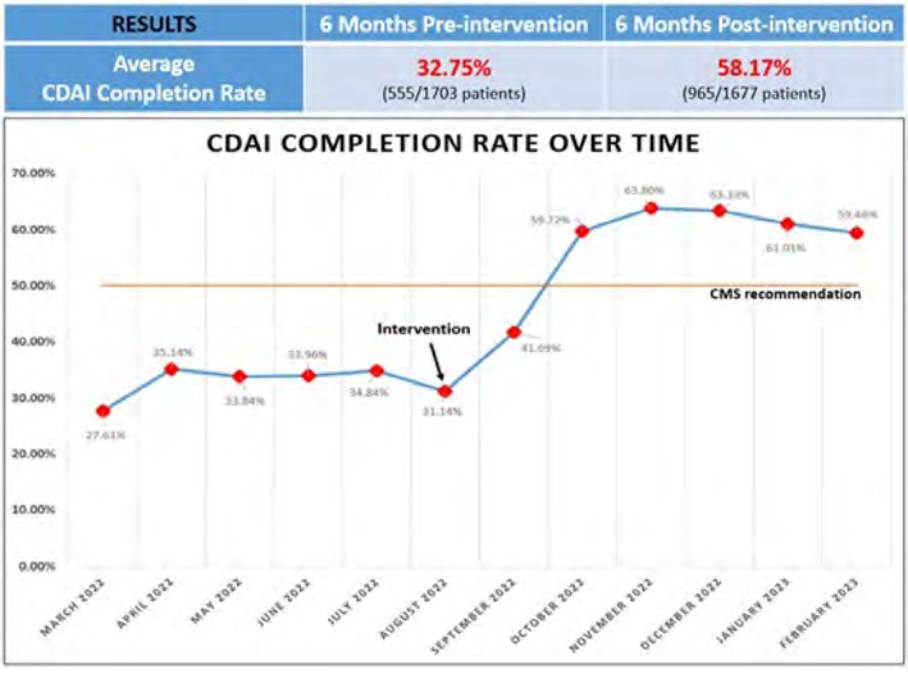

Figure 1. CDAI Completion Rate Over Time

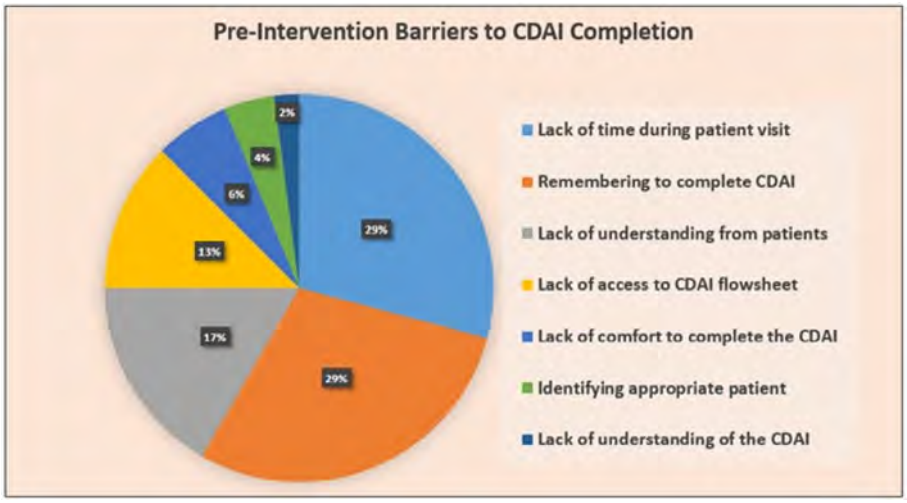

Figure 2a. Pre-Intervention Barriers to CDAI Completion

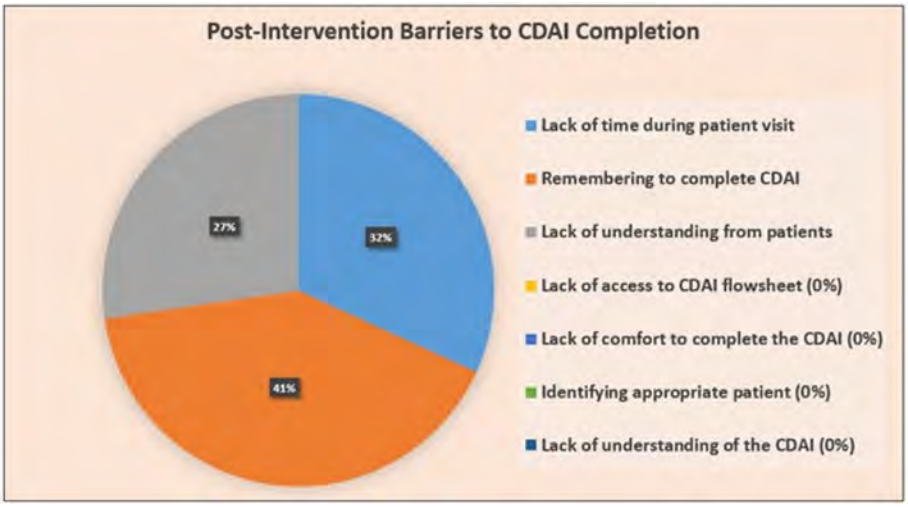

Figure 2b. Post-Intervention Barriers to CDAI Completion

to complete the CDAI, and 3) lack of understanding from patients to input CDAI global assessment. Following the intervention, provider barriers that were removed include: 1) lack of understanding of the CDAI, 2) lack of comfort in completing the CDAI, 3) access to the CDAI flowsheet in the EHR, and 4) identifying appropriate patients to complete the CDAI.

Conclusion: A simple educational intervention for both providers and care partners, as well as implementation of new workflow increased CDAI utilization in our clinic. Continuing assessment and repeated interventions are likely needed to optimize use. Identified barriers such as lack of time, remembering to complete CDAI, and patient understanding to complete global assessment are future targets for productive change.

Disclosure: R. Ishizawar: None; **T. Phan**: None; **S. Takacs**: None.

Abstract Number: 1906

Implementation Practices for the 2022 American College of Rheumatology Guidelines for Exercise, Rehabilitation, Diet, and Additional Integrative Interventions for Rheumatoid Arthritis

Laura Nichols[1], Meghan Scheibe[2], Ellen Erie[3], Austin Nickell[3] and Abe Sahmoun[3], [1]Sanford Health, Fargo, ND, [2]Sanford Health, West Fargo, ND, [3]University of North Dakota, Fargo, ND

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1895–1912) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In November 2022, the American College of Rheumatology (ACR) released the ACR Guidelines for Exercise, Rehabilitation, Diet, and Additional Integrative Interventions for Rheumatoid Arthritis with several lifestyle recommendations in dietary, exercise, rehabilitation categories as well as additional integrative and mental health guidance.Limited data on implementation practices post-guideline are published. Data were reviewed to determine rates of adherence to the guideline post-creation as well as referral patterns in the year prior to guideline release for both rheumatology and non-rheumatology clinicians.

Methods: We identified patients 18 and older with a primary diagnosis of rheumatoid arthritis seen within the rheumatology department at our institution between November 15, 2022 and February 15, 2023 utilizing an electronic medical record (EMR)-extracted report and manual chart review.Patients were excluded if they had expired within the study period or had an alternative primary rheumatologic diagnosis. IRB approval was obtained.

Results: Data were analyzed for 791 patients. Mean (SD) age was 62.3 (13.8), 77.6% of the patients were female, and 94.6% were white. Mean (SD) BMI was 31.3 (7.5) kg/m2. 394 (49.8%) were receiving biologic or synthetic targeted disease-modifying anti-rheumatic drug (DMARD) therapy (Table 1). 28 (3.5%) patients received a recommendation for an exercise regimen in the 3-month study period. 25 (3.2%), 4 (0.5%), and 4 (0.5%) patients received post-guideline referrals to physical therapy, occupational therapy, and dietary recommendation for the Mediterranean diet, respectively (Table 2). In the year prior to guideline release, 51 (6.4%) patients received physical therapy referrals from a rheumatologist and 109 (13.8%) from a non-rheumatologist. 3 (0.4%) patients received a weight loss clinic referral from a rheumatologist and 24 (3.0%) from a non-rheumatologist pre-guideline. 4 (0.5%) patients received dietician referral from a rheumatologist and 37 (4.7%) from a non-rheumatologist pre-guideline.

Conclusion: The adherence to the 2022 ACR lifestyle guidelines for RA was low. For interventions studied, there was no significant increase in referrals or recommendations post-guideline. Though there was significant obesity in the patient population with higher-than-average BMI (average BMI ∼26.5 in the United States), only a handful of patients received a dietary intervention from rheumatology.Dietary interventions were low for both rheumatology and non-rheumatology clinicians pre-guideline release. Study limitations include descriptive methods without comparisons for statistical analysis as well as short duration of follow up. Several factors such as patient preferences, workload and complex disease management, as well as the recency of the guideline release may offer explanations for low uptake of recommending lifestyle interventions. Future work is needed to create practical recommendations and measures of quality for lifestyle intervention in patients with rheumatoid arthritis that balance patient needs and provider workload.

Table 1: Patient characteristics

Total (n=791)		Value (n(%))
Age (mean)		62.3 (+/-13.8)
Sex	Female	614 (77.6)
	Male	177 (22.4)
Race	Caucasian/white	739 (94.6)
	Black/African American	6 (0.8)
	American Indian/Alaska Native	33 (4.23)
	Asian	3 (0.4)
Immunosuppressive Regimen	Biologic or Synthetic targeted DMARD	394 (49.8)
	Conventional DMARDs only	304 (38.4)
	Steroid only	18 (2.3)
	None	29 (3.7)
Disease control	Clinical remission	373 (47.2)
	Low disease activity	225 (28.4)
	Moderate to high disease activity	193 (24.4)
Comorbid conditions	Osteoarthritis	426 (53.9)
	Gout	40 (5.1)
	Psoriasis	27 (3.4)
	Type II Diabetes Mellitus	126 (15.9)
Body mass index (kg/m^2)	Mean	31.3 (+/- 7.5)
	Underweight (<18.5)	6 (0.8)
	Normal (18.5-24.9)	158 (20.0)
	Overweight (25-29.9)	207 (26.2)
	Obesity (30-39.9)	316 (39.9)
	Morbid Obesity (≥40)	92 (11.6)
	Missing	12 (1.5)

Table 2: Number and percentage of patients receiving lifestyle recommendations and referrals by rheumatology within 3 months post-guideline and referrals by rheumatology and non-rheumatology provider in the year prior to guideline release

Total=791	Rheumatology post-guideline n(%)	Rheumatology pre-guideline n(%)	Non-rheumatology pre-guideline n(%)
Exercise			
Any Exercise recommendation	28 (3.5)	N/A	N/A
Rehabilitation			
Physical Therapy Referral	25 (3.2)	51 (6.4)	109 (13.8)
Occupational Therapy Referral	4 (0.5)	20 (2.5)	45 (5.7)
Dietary			
Mediterranean Diet Recommendation	4 (0.5)	N/A	N/A
Dietician Referral	0	4 (0.5)	37 (4.7)
Weight Loss Clinic Referral	1 (0.1)	2 (0.3)	24 (3.0)
Additional			
Behavioral Health Referral	1 (0.13)	17 (2.3)	45 (5.7)

Disclosure: L. Nichols: None; **M. Scheibe**: None; **E. Erie**: None; **A. Nickell**: None; **A. Sahmoun**: None.

Abstract Number: 1907

Selection of a Candidate Instrument to Assess Flare in Osteoarthritis with Content Matching with Endorsed Domains

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1895–1912) Measures & Measurement of Healthcare Quality Poster II

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The Outcome Measures in Rheumatology group (OMERACT) developed methodological steps to select instrument(s) to assess content appropriateness of outcomes, as well as tools to accomplish this task. In this study we present the results obtained following these steps to select instrument(s) to assess flares in osteoarthritis, based on the associated domains

Methods: An update of a previous 2017 literature review was conducted in PubMed, Web of Science and Psych Info databases over the period from 2017 to 2021, with the primary goal of searching instruments associated with flare in knee and hip OA or their correlated characteristics. Using the OMERACT Handbook Filter 2.2[1], we evaluated the content of instruments included according to five core domains endorsed by OMERACT[2], and then classified into three categories: "sure match with domains of flare in OA"; "uncertain match with domains of flare in OA"; and "sure not match with domains of flare in OA". The instruments retained in the first two categories were analyzed by the experts of the working group (WG) Flares in OA, composed of patients, physicians, and researchers, in two rounds of Delphi survey using limesurvey. The goal was to identify among these five instruments which one best matches with the target domain (trust) and which one is more practical to use (feasibility). The final selection was obtained by a vote of the group.

Results: Initially 575 papers were filtered. After experts' analysis, 59 studies were included, and 44 instruments associated with flare in OA were identified. Most were studies about pain in knee or hip OA (35%), cultural adaptation of a measure (33%) or studies investigating psychometric properties of full (16%) or short form (4%) instruments. An international panel of 26 group members participated in the Delphi surveys. In Delphi Survey Round 1, we had 15 instruments flagged by experts with green, amber and red and we proposed: reject instrument with less than 50% in red flag, classify uncertain when they received between 50 and 70% in amber flag and keep instruments that received more than 70% in green flag. Five instruments were pre-selected: ICOAP, HOOS, KOOS, OAKHQOL and Flare-OA. WOMAC was clearly not focused on flare, and we decided to substitute the full length OAKHQOL with the short form Mini-OAKHQOL. For the Delphi Round 2, we set a unique threshold of 70% to make decision. The instruments obtained at least 75% in questions about trust and feasibility,which carried them all to the last phase, it means, to vote on the instrument. Only the Flare-OA questionnaire obtained 100% of votes in favor.

Conclusion: The OMERACT Handbook Filter 2.2 has proven helpful tool for selecting an instrument. The Flare-OA questionnaire was selected as the best matching and practical instrument to assess flare in lower limb osteoarthritis. References 1. Guillemin F, Ricatte C, Barcenilla-Wong A, et al. Developing a Preliminary Definition and Domains of Flare in Knee and Hip Osteoarthritis (OA): Consensus Building of the Flare-in-OA OMERACT Group. *J Rheumatol*. 2019;46(9):1188-1191.

doi:10.3899/jrheum.181085 2. Berton B, Maxwell L, Grosskleg S, et al. *THE OMERACT HANDBOOK*. Filter 2.2. The OMERACT Handbook © 2021 by OMERACT is licensed under CC BY-ND 4.0; 2021.

Disclosure: F. Queiroga: None; **M. Cross**: None; **L. Maxwell**: None; **L. Callahan**: None; **s. Cembalo**: None; **T. Buttel**: None; **C. Copenhaver**: None; **J. Epstein**: None; **d. Hunter**: None; **L. King**: None; **L. March**: None; **F. Guillemin**: None.

Abstract Number: 1908

Clinic Protocol Boosts Blood Pressure Confirmatory Readings and Accuracy in an Academic Medical Center

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1895–1912) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Hypertension is the most common modifiable risk factor for cardiovascular diseases among all adults. Studies have shown that single blood pressure (BP) measurements vary in an unpredictable way in clinics, and up to one-third of patients initially categorized with high BP were subsequently reclassified into lower BP categories upon confirmatory readings.

This quality improvement project aimed at improving the rate of checking BP a second time (confirmatory reading) if the initial BP was high (systolic ≥140 mmHg or diastolic ≥90 mmHg) by implementing a staff-driven workflow with a goal to improve accuracy of clinic BP values.

Methods: This study was conducted at a large quaternary care academic center.We included patients from internal medicine subspecialty clinics (IMSS), which includes rheumatology, seen between June 2022 and April 2023 with initial high BP (systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg). We created a new workflow (Figure 1) to standardize the process of obtaining confirmatory readings for initial high BP. Nurses and medical assistants (MAs) received education on accurate BP measurement techniques, the workflow, the importance of confirmatory readings and accurate documentation within EMR. Upon check-in, medical assistants escorted patients to the exam room, where they measured BP using proper techniques and recorded in the EMR. If the initial BP was high, the MAs flagged the patient's room accordingly. After the flagged patients were evaluated by the healthcare provider, MAs or nurses repeated the BP measurement using proper techniques and documented the results in the EMR. To collect and track the BP data, we developed a Tableau software dashboard that was updated monthly. The Department of Internal Medicine sent monthly quality improvement newsletter to all clinic leadership, serving as a reminder of clinic performance, which is then shared with the clinic staff to further reinforce adherence to the established workflow.

Results: Between June and December 2022, the IMSS clinics had a total of 18,390 encounters, of which 4,009 (21.8%) were eligible for confirmatory reading due to high initial readings. The confirmatory rate increased from a baseline of 38% between June 2021 to May 2022 to 55% between June to December 2022. In the rheumatology clinics, out of a total of 4,371 encounters, 1,073 (24.5%) were eligible for confirmatory reading. The clinic's confirmatory rate improved from a baseline of 17.6% between June 2021 to May 2022 to 48% between June to December 2022 as seen in the control charts

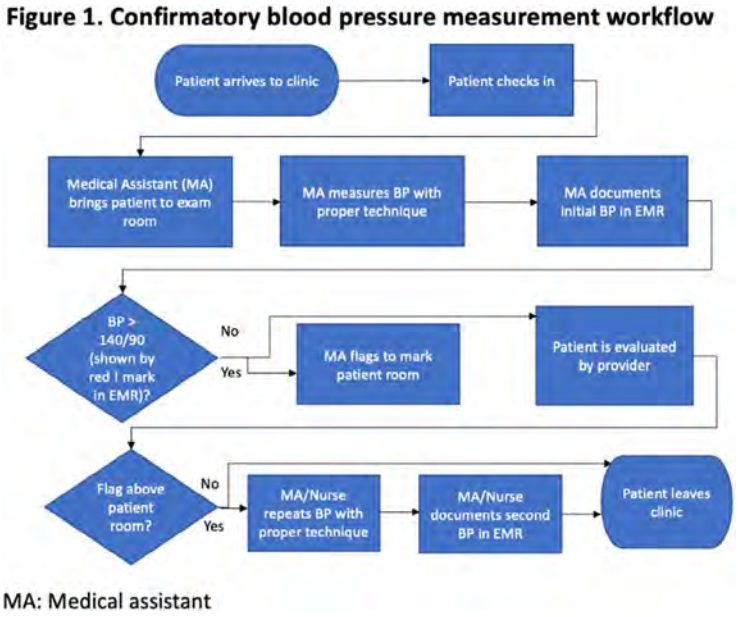

Figure 1. Confirmatory blood pressure measurement workflow

Figure 2.

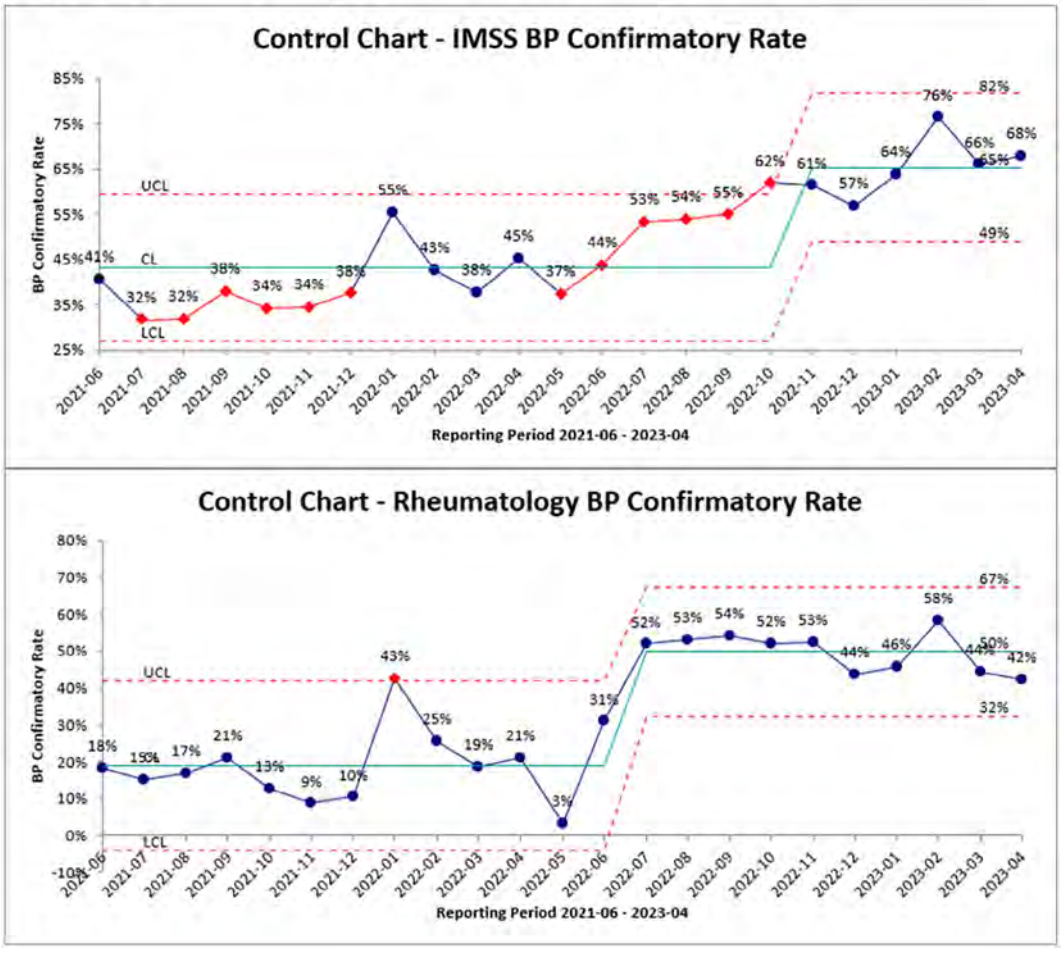

Figure 2. Control charts for confirmatory rates

Figure 3. The rate of blood pressure change from uncontrolled (≥ 140/90) to controlled (<140/90) after confirmatory reading

Figure 3. The rate of blood pressure change from uncontrolled (≥ 140/90) to controlled (<140/90) after confirmatory reading

(Figure 2). The confirmatory rate remained stable at 48% in the rheumatology clinics, while in the IMSS clinics, it improved to 60% by April 2023. Among patients who had confirmatory readings, 36% (Figure 3) showed an improvement in blood pressure to below 140/90 mmHg.

Conclusion: It is feasible to increase the rate of BP confirmatory readings within a clinic using a staff-driven workflow. We were able to improve the rate of confirmatory reading over 20% in the IMSS clinics and over 30% in the rheumatology clinics within eleven months. Additionally, 36% of the patient who underwent repeat BP checks had improved BP, underscoring the importance of confirmatory readings for accurate measurement.

Disclosure: K. Bugdayli: None; **A. Meyer**: None; **A. Keith**: None; **K. Dirisala**: None; **G. Quiceno**: None; **P. Bajaj**: None.

Abstract Number: 1909

Identifying and Addressing Suboptimal Urate Lowering Therapy in Gout Patients with Chronic Kidney Disease

Lena Eder[1] and David Leverenz[2], [1]Duke University, Chapel Hill, NC, [2]Duke University School of Medicine, Durham, NC

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1895–1912) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with gout and chronic kidney disease (CKD) are often not appropriately managed with goal-directed urate-lowering therapy (ULT). To address deficits in management of gout patients with CKD, we aimed to understand how their ULT was managed by primary care within an academic health system.

Methods: We used Slicer Dicer, an analytic tool within our electronic health record (EHR), to identify patients seen within the primary care health system associated with our academic medical center between 02/01/2022 and 02/01/2023 who also had an ICD-10 diagnosis code related to gout and CKD 3, 4, or 5. 121 charts were manually reviewed to determine patient's

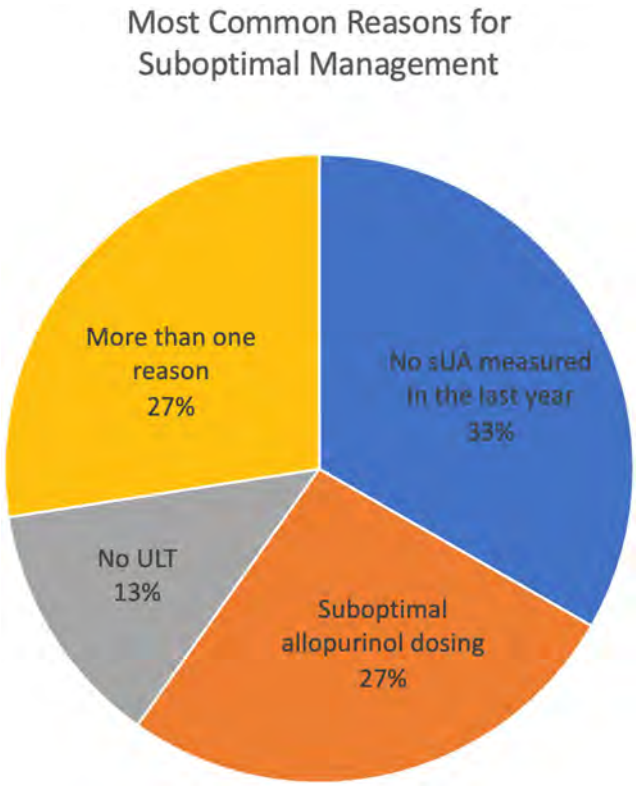

Figure 1. Most Common Reasons for Suboptimal Management of Gout Patients with CKD

glomerular filtration rate (GFR), stage of CKD, serum uric acid (and whether it was checked in the past year), urate-lowering therapy (and dose if applicable), and whether their gout was optimally managed according to the 2020 American College of Rheumatology Guideline for the Management of Gout. To address any seasonal factors, we reviewed charts of patients seen during the first weeks of April 2022, July 2022, October 2022, and January 2023.

Results: 3,371 gout patients with CKD were seen by a primary care provider between 02/01/2022 – 02/01/2023 in our health system. Of the 121 patients further analyzed, 40% had CKD 3, 35% had CKD 4, and 25% had CKD 5. The average GFR was 28.5. A total of 113 patients (93%) had a uric acid available to review. Among all patients, 52% (n = 63) had a serum uric acid checked within a year of their appointment, of which the mean serum uric acid was 7.8. 77% (n = 93) had an active prescription for allopurinol or febuxostat, and 96% (n = 116) were managed primarily by their PCP and had never seen a rheumatologist. Overall, 16% (n = 19) of all the patients reviewed had optimal management of their gout according to ACR guidelines. The most common reasons for suboptimal care were: no serum uric acid measured in the last year (33%, n = 34), suboptimal ULT dosing (27%, n = 27), no ULT prescribed (13%, n = 13), or a combination of these factors (27%, n = 28) (**Figure 1)**.

Conclusion: There are deficits in management of gout patients with a diagnosis of CKD which may lead to worsening morbidity and mortality. Many of these patients are not being treated to goal with suboptimal doses of urate-lowering therapy or no urate-lowering therapy at all. We speculate that this trend may be due to a number of reasons including gaps in knowledge by primary care regarding ULT in patients with a diagnosis of CKD and/or inaccurately in the "normal" range for serum uric acid in the EHR (abnormal is defined as 8 or above). Overall, these findings suggest the need for an educational initiative or health-systems based intervention to address the care of these patients.

Disclosure: L. Eder: None; **D. Leverenz**: Pfizer, 5, Rheumatology Research Foundation, 5, Sanofi, 2.

Abstract Number: 1910

Development of the American College of Rheumatology Toolkit for Implementation of Rheumatoid Arthritis Outcome Measures in Clinical Practice

Catherine Nasrallah[1], Lindsay Jacobsohn[1], Gabriela Schmajuk[2], Emma Kersey[1], Cammie Young[3], Cammie Young[3], Janell Martin[4], Lori Barber[5], Jennifer Barton[6], Puneet Bajaj[7], Christie M. Bartels[8], Sancia Ferguson[9], Elizabeth Wahl[10], Kimberly DeQuattro[11], Patti Katz[12], Maria I. (\"Maio\") Danila[13], Meera Subash[14], Christina Downey[15], JoAnn Zell[16], Kimberly Reiter[17], Elena Weinstein[18] and Jinoos Yazdany[1], [1]University of California San Francisco, San Francisco, CA, [2]UCSF / SFVA, San Francisco, CA, [3]University of California San Francisco, Oakland, CA, [4]American College of Rheumatology, Atlanta, GA, [5]ACR, Atlanta, GA, [6]VA Portland Health Care System/OHSU, Portland, OR, [7]UT Southwestern Medical Center, Dallas, TX, [8]University of Wisconsin, School of Medicine and Public Health, Madison, WI, [9]University of Wisconsin, Madison, WI, [10]VA Puget Sound Healthcare System, Seattle, WA, [11]University of Pennsylvania, Media, PA, [12]University of California San Francisco, San Rafael, CA, [13]University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL, [14]University of Texas Health Science Center at Houston, Houston, TX, [15]Loma Linda University Medical Center, Loma Linda, CA, [16]University of Colorado Anschutz Medical Campus, Denver, CO, [17]Albuquerque VA Medical Center, Albuquerque, NM, [18]University of Colorado, Englewood, CO

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1895–1912) Measures & Measurement of Healthcare Quality Poster II

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Despite significant interest in the scale and spread of rheumatoid arthritis (RA) outcome measures to facilitate a patient-centered, treat-to-target approach, use of these measures remains inconsistent among rheumatologists. We used the Consolidated Framework for Implementation Research (CFIR) to guide qualitative interviews with stakeholders about facilitators and barriers to RA outcome measurement in real-world rheumatology care, with the goal of disseminating best practices for implementation via an online toolkit

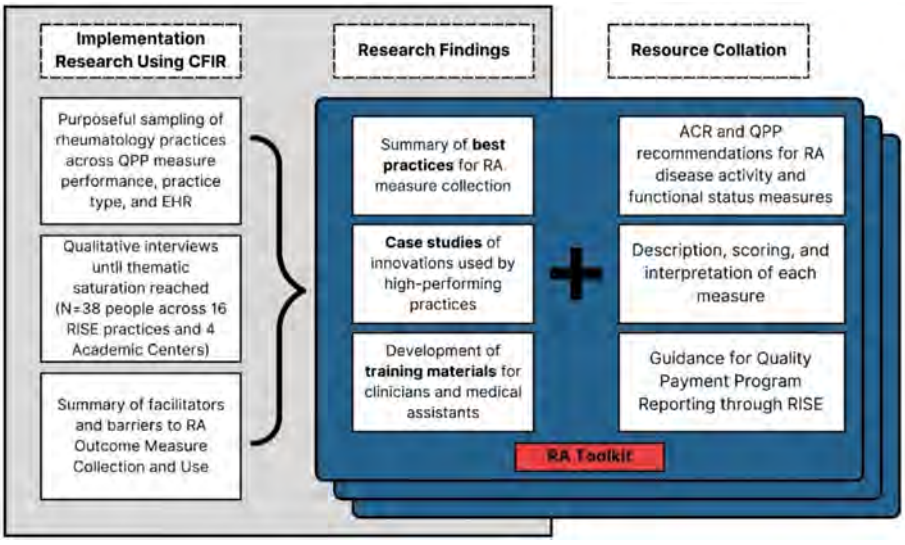

Figure 1: Methods for Developing the RA Outcome Measures Toolkit

Methods: Using RISE registry data, we invited 85 practices with high performance on RA disease activity (DA) measures (≥ 50% percentile on the Quality Payment Program (QPP) 177 periodic assessment of DA) and 54 practices with lower performance to participate. Because academic medical centers (AMCs) are under-represented in RISE, 4 AMCs were also invited to participate. Rheumatologists and key staff from each practice participated in virtual interviews. CFIR concepts were used to develop a semi-structured interview guide to understand workflows, facilitators, and barriers to RA outcome measure collection. Interview recordings were transcribed verbatim and analyzed thematically using deductive and inductive techniques to generate themes and subthemes. Collaborating with the ACR staff, we compiled information from these interviews to develop the online RA Toolkit, a comprehensive resource to facilitate RA outcome measurement in clinical practice (Figure 1).

Table 1: Summary of key findings from qualitative interviews about RA outcome measure collection with rheumatology practices

CFIR Framework Domain	Challenges Identified in Interviews	Solutions Implemented by High-Performing Practices
Outer setting	Incomplete capture of RA measure performance in RISE registry	Check performance on measures frequently. If performance measures are inaccurate, reach out to a representative of the registry for troubleshooting
Outer setting Inner setting	Financial limitations replacing older EHR systems with newer options dedicated to Rheumatology	Work within the range of capabilities in any EHR can help with the inability to migrate to a different, more expensive, system. (Example: customization and internal quality improvement techniques may result in more helpful outcomes than starting from scratch with a new EHR.
Inner setting	Challenges developing reliable workflows to administer patient-reported outcomes to only RA patients	Administer patient-reported outcomes to all rheumatology patients regardless of diagnosis
Inner setting	Time constraints with high patient volumes	Use quality improvement methods to reduce inefficiencies and optimize measure collection
Inner setting	Gaps in workflows that lead to missing RA outcome data in the EHR.	Checks and balances: Ensuring that workflows are consistent, efficient and engage practice staff and patients
Inner setting Individuals	Inadequate training for medical staff, particularly when there is high staff turnover	Ensure redundancy in workflows so that they are not dependent on a single staff member (or a limited number of staff)
Individuals	Patient survey fatigue	Review RA outcome measures regularly with patients to allow them to track their progress and facilitate shared decision-making, which motivates patients to fill out repeated RA outcome measures surveys
Individuals Characteristics	Language barriers and low health literacy	Have RA outcome measure forms available in multiple languages; visual scales for interpretation
Characteristics	Difficulty collecting RA outcome measures during telehealth visits	Administer questionnaires such as the RAPID-3 electronically through web-based applications
Implementation	Difficulty in keeping staff accountable to collect PROs, especially for in-person visits	Assign practice champions (physicians or staff) that regularly communicate importance of RA outcome measure performance and continually optimize workflows
Innovation	Difficulty collecting RA outcomes in structured data fields in the EHR	Use EHR software that facilitates RA outcome measure documentation, creating flowsheets, or investing in custom IT builds to permit reliable data capture

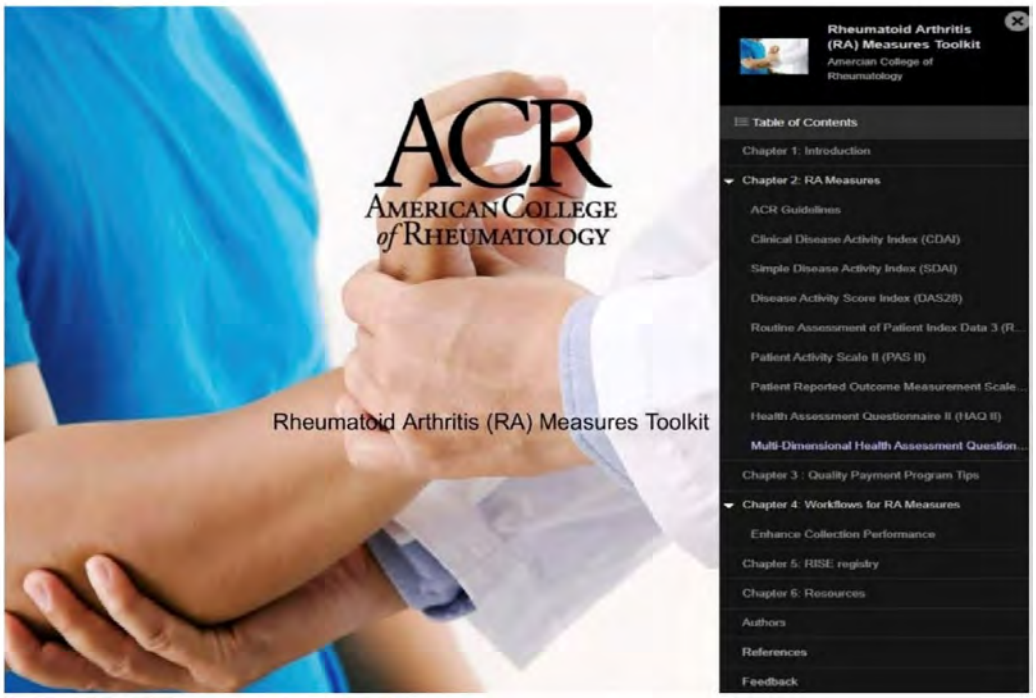

Figure 2: RA Measures toolkit: https://ratoolkit.kotobee.com/

Results: Interviews were conducted with invited practices until thematic saturation was reached (38 interviews across 16 RISE practices and 4 AMC). Participants included 21 rheumatologists, 8 medical assistants, 6 practice managers, 1 nurse practitioner, and 2 information technology specialists. Each interview highlighted unique innovations, resources, best practices, and challenges for collecting RA outcome measures (select findings summarized in Table 1). Results of the qualitative interviews, ACR guidelines regarding RA outcome measures, and other evidence-based resources were compiled in the RA Toolkit (available at RAToolkit.kotobee.com). The Toolkit is a multimedia online resource for RA outcome measure implementation geared toward use by clinicians and staff. Sections include text, videos, and downloadable forms that aid in understanding and using RA outcome measures in clinical practice, recommendations and best practices identified from high performers across diverse practice settings and EHRs, training resources for staff, and validated translations of available RA measures in Spanish and Chinese (Figure 2).

Conclusion: Qualitative interviews conducted with rheumatology teams laid the groundwork to develop a best practices implementation toolkit to disseminate innovations in RA measures collection. The ACR RA Toolkit is the first comprehensive, evidence-based, open-source resource available for rheumatologists and healthcare teams to guide effective implementation, collection, and use of RA outcome measures that promote quality and value-based patient-centered care.

Disclosure: C. Nasrallah: None; **L. Jacobsohn**: None; **G. Schmajuk**: None; **E. Kersey**: None; **C. Young**: None; **C. Young**: None; **J. Martin**: None; **L. Barber**: None; **J. Barton**: None; **P. Bajaj**: None; **C. Bartels**: Pfizer, 5; **S. Ferguson**: None; **E. Wahl**: None; **K. DeQuattro**: None; **P. Katz**: None; **M. Danila**: Horizon, 5, Pfizer, 5, RheumNow, 2, UCB, 2; **M. Subash**: None; **C. Downey**: None; **J. Zell**: None; **K. Reiter**: None; **E. Weinstein**: Priovant, 5; **J. Yazdany**: Astra Zeneca, 2, 5, Aurinia, 5, Gilead, 5, Pfizer, 2.

Abstract Number: 1911

Using the Technology Acceptance Model to Assess Physician Perceptions and Experiences Using the Rheumatoid Arthritis-Patient-Reported Outcomes Dashboard: Mixed-Methods Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1895–1912) Measures & Measurement of Healthcare Quality Poster II

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Improving shared decision-making using a treat-to-target approach, including the use of patient reported outcomes (PROs), is important to providing high quality care for rheumatoid arthritis (RA). We developed an EHR-integrated, patient-facing sidecar dashboard application that displays RA outcomes (disease activity (DA), functional status, pain scores), medications, and lab results for use during clinical visits (Figure 1). The purpose of this study was to assess physician perceptions and experiences using the dashboard in a university rheumatology clinic.

Methods: Data derived from focus group (FG) discussions and surveys with physicians who had access to the dashboard as part of a randomized, stepped-wedge pragmatic trial. FGs explored physician perceptions towards the usability, acceptability, and usefulness of the dashboard. FG data were analyzed thematically using deductive and inductive techniques; emerging themes were categorized according to the Technology Acceptance Model (TAM; Figure 2). Surveys, which were collected during consecutive visits in which the dashboard was not discussed with the patient, queried physicians' reasons for non-use. Survey data were summarized as proportions.

Results: 3 FGs included 12 rheumatologists and 102 surveys were collected from 14 physicians. Major themes that emerged from the FG analysis as barriers to using the dashboard included inconsistent collection of RA outcomes leading to sparse data in the dashboard and concerns about explaining RA outcomes, especially to patients with fibromyalgia (Table). Other challenges included time constraints and technical difficulties refreshing the dashboard to display real-time data. Nevertheless, physicians were enthusiastic about the dashboard and expressed the usefulness of visualizing RA outcome trajectories in a graphical format for motivating patients, enhancing patient understanding of their RA outcomes, and improving communication about medications. Methods for integrating the dashboard into the visit varied: some physicians used the dashboard at the beginning of the visit as they documented RA outcomes; others used it at the end to justify changes to therapy; and a few shared it only with stable patients. Survey results aligned with the themes identified in the FGs: the most reported reason for not using the dashboard was an assumption that the dashboard would not be useful for the patient (32%) (often because of low DA or comorbid conditions). Other reasons included forgetting to use the dashboard (19%), lack of patient data in the dashboard (12%), and time constraints (12%). Technical difficulties accounted for a small amount of non-use (6%).

Conclusion: We used a mixed-methods approach to assess physician perceptions of a novel EHR sidecar dashboard application that aims to improve the quality of care for RA patients. Despite enthusiasm for the value of this new technology, discomfort with discussing RA outcomes, inconsistent workflows for incorporating the dashboard into the visit, and incomplete EHR data were major reasons for not using the dashboard. Future work should address these barriers to improve uptake of the dashboard.

Figure 1: Screenshot of the Rheumatoid Arthritis-Patient-Reported Outcomes Dashboard (RA-PRO)

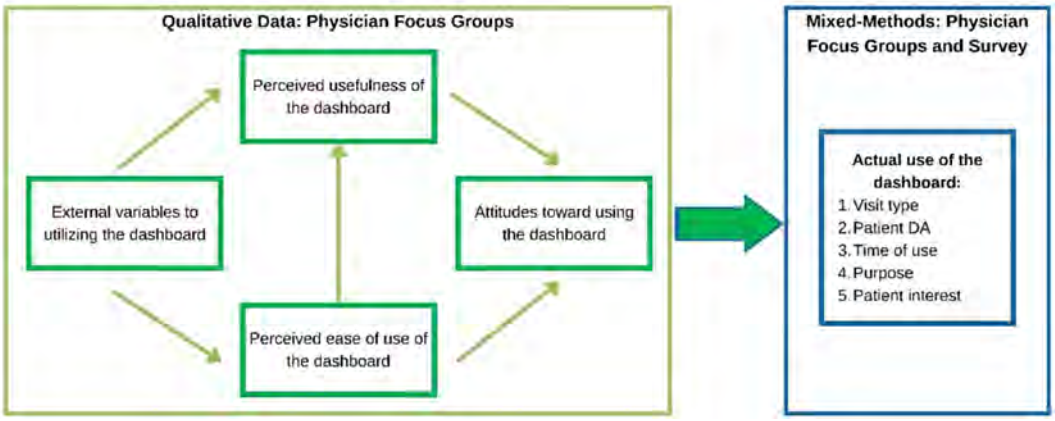

Figure 2: Physician Technology Acceptance Model (TAM) of the RA-PRO dashboard.

Table: Physician Perceptions of the RA-PRO dashboard sidecar application: Qualitative Results

TAM concept	Themes	Sample Quotes
External variables	Inconsistent collection of RA outcomes in the EHR	*"We have a lot of new staff, and they're not all up to speed with [collecting PROs] and gets dropped which I find it frustrating. But it's just all about training"*
	Patient Comorbidities	*"A patient who also has prominent fibromyalgia. There are challenges around that. How can I point out like discordance of patient global... I don't know how to use it in that context"*
	Patient interpretation of PRO questions	*"Patients don't always differentiate between the pain score and the global disease activity, some of them write different scores, [but] many of them write the same thing".*
	Limited knowledge about PRO scoring	*"I focus on the CDAI just because that's the easiest for me to explain. But I start to see the other ones like RIMIS. I'm not exactly sure how that's calculated"*
Perceived Usefulness	Initiating therapy	*"The patient had been off therapy for a long time, it was a good way to show her how severe her disease activity was, and she was open and starting treatment that day"*
	Changing medications	*"I've found it to be the most useful to convince patient to change their medications...I had a number of patients that I've been trying for several years to convince to change therapy and after a couple of visits with this dashboard they actually changed"*
	Discussing RA outcomes with patients	*"Patients asking questions about the numbers, what they are, what it means...They were surprised that we've been collecting and plotting the data for like so many years."*
	Visualizing disease trajectories	*"I think the visualization makes it easier for the patients to see as opposed to just looking at numbers across a chart and, I find that most of my patients really appreciate it"*
	Improving patient understanding of their disease	*"It's interesting to use it when patients feel like they're doing Ok, because say they're on prednisone and I don't think they're doing Ok...and when they actually see their score not being as good as it could be they actually sort of think twice."*
	Motivating patients about treat-to-target approach	*"What I find is that even in patients who are doing well, they like to see this positive feedback up during this green zone"*
Perceived Ease of Use	Lack of familiarity with dashboard content	*"I don't know how to talk about the dashboard. I just say, our goal is to get you up in the green zone, but I don't know what else to talk about"*
	Time constraints	*"I spend a lot of time listening to everything they recorded. At the end, I have to rush, explain the medications and follow up, so I think something additional is just a too much"*
	Technical difficulties	*"It just doesn't update and then you'll have their most recent CDAI, and you realize you're looking at the old CDAI, you have to refresh everything"*
	Virtual visits	*"I do a 28 joint count exam over video, and I walk the patients, through their exam."(O)* *"I have not been successful with that because I haven't figured out how to really assess the tender and swollen joint count numbers which is pretty significant for the CDAI" (C)*
	Design	*"It's a nice pictorial representation for the patients to see how they've been doing with their symptoms over time" (O)* *"I tend to discuss the DA and the PRO sort of separately, so I wish that the medications were closer to the CDAI" (C)*
	Collecting PROs	*"The best way to do it is to fill it out during the visit. It doesn't really take time and it makes the documentation and the homunculus better because I am doing it in real-time" (O)* *"it might be harder to remember to pause to do that with patients, we focus on other things" (C)*

*Challenges
*Opportunities
*Challenges for some and opportunities for others

Disclosure: C. Nasrallah: None; **C. Wilson**: None; **A. Hamblin**: None; **L. Jacobsohn**: None; **C. Young**: None; **C. Young**: None; **M. Nakamura**: None; **A. Gross**: None; **J. Ashouri**: None; **M. Matloubian**: None; **J. Yazdany**: Astra Zeneca, 2, 5, Aurinia, 5, Gilead, 5, Pfizer, 2; **G. Schmajuk**: None.

Abstract Number: 1912

Impact of Pharmacist-Led Specialty Medication Management Service on Time-to-Dispense for Specialty Rheumatologic Medications in a University Health System

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1895–1912) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Given the progressive joint damage and physical disability associated with uncontrolled Rheumatoid arthritis (RA), a treat-to target-strategy through the early utilization of disease-modifying antirheumatic drugs (DMARD) provides patients with the best opportunity to control their disease earlier. Biologic and targeted DMARDs are specialty medications, and while there is not a single defining aspect of specialty medications, most are high cost and involve complexity in storage requirements, handling and delivery, patient management and manufacturer restrictions. While specialty medications have brought successful treatment options to diseases that previously had limited options, they have also made the prior authorization system increasingly complex, often leading to a delay in treatment. Pharmacist-led specialty medication approval programs, such as Specialty Medication Services (SMS), complete prior authorizations, appeals, and aid in financial assistance for specialty medications. This study will examine the impact of a pharmacist-led SMS on time-to-dispense for DMARDs in patients with Rheumatoid Arthritis. The primary endpoint of this study will be to compare time-to-dispense for DMARDs before and after implementation of specialty medication services.

Methods: This study was conducted in a retrospective cohort manner, evaluating the time-to-dispense of specialty rheumatologic medications before and after implementation of SMS. Data was generated from the electronic medical record (EMR). Therapy initiation orders entered through the EMR for any of the included specialty medications prescribed by Rheumatology for the same 6-month period in April 2016- October 2016 (control group, pre-SMS), compared to April 2019-October 2019 (study group, post-SMS). Each patient's EMR was reviewed to collect information on dispensing pharmacy, prior authorization, indication for treatment, and if financial assistance was needed. A total of 100 patients were included in the study, 50 of whom underwent medication approval prior to the implementation of SMS (2016), and 50 of whom underwent medication approval after implementation of SMS (2019).

Results: Among the pre-SMS implementation group (2016), the mean time-to-dispense- was 14.7 days (SD +/- 24 days), while mean time-to-medication dispense for the post-SMS establishment group (2019) was 5 days (+/- 6.7 days). There is a statistically significant difference in days until medication dispensed ($p < 0.001$) for 2016 versus 2019. The two groups demographics and insurance carriers were comparable, though more patients had private insurance in the 2019 group (68%), as compared to the 2016 group (44%, Table 1)

Table 1: Characteristics of patients by Pharmacist access year.

	2016	2019	
Race/Ethnicity, n (%)			
Caucasian	30 (60.00)	31 (62.00)	
Hispanic	10 (20.00)	9 (18.00)	
African American	9 (18.00)	8 (16.00)	
Asian	-	1 (2.00)	
Other	1 (2.00)	1 (2.00)	
Gender, n (%)			
Female	46 (92.00)	40 (80.00)	
Male	4 (8.00)	10 (20.00)	
Insurance Type, n (%)			
Private	22 (44.00)	34 (68.00)	
Medicare	14 (28.00)	5 (10.00)	
Medicaid	14 (28.00)	11 (22.00)	
Biological Drug, n (%)			
Humira	20 (40.00)	15 (30.00)	
Enbrel	18 (36.00)	11 (22.00)	
Cimzia	3 (6.00)	4 (8.00)	
Xeljanz	2 (4.00)	7 (14.00)	
Orencia	7 (14.00)	7 (14.00)	
Abatacept	-	1 (2.00)	
Tofacitnib	-	2 (4.00)	
Tocilizumab	-	1 (2.00)	
Golilumab	-	2 (4.00)	
Age			
Mean (SD)	54.7 (12.3)	50.5 (13.1)	
*Significant at α = 0.05 level †Fisher's exact test p-value			

	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	P-VAL
Days until Approval	100	9.9 (18.2)	50	14.7 (24.0)	50	5.0 (6.7)	<.0001*

Conclusion: This study shows that the implementation of Pharmacist-led specialty medication approval programs, such as Specialty Medication Services, significantly reduced the number of days until specialty medications were dispensed in a university health system. While there is a difference in the average time to dispense with the utilization of Specialty Medication Services, further studies are needed to determine the impact of early medication approval and dispensing and how this corresponds to patient clinical outcomes.

Disclosure: K. Ahmadmehrabi: None; **N. Ravishankar**: None; **D. Mekhiel**: None; **Z. Aouhab**: None.

Abstract Number: 1913

Neurosarcoidosis Disease Epidemiology. University Hospital in Northern Spain 1999-2019

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Neurosarcoidosis (NS) is a serious and relative uncommon complication of sarcoidosis. Data on incidence is scarce and varies worldwide. Our objective is toestimate NS epidemiology in Northern Spain.

Methods: Patients diagnosed with sarcoidosis at a University hospital in Northern Spain, between January 1999 and December 2019 were assessed. Sarcoidosis diagnosis was established according to ATS/ERS/WASOG criteria as follows: compatible clinical and radiological presentation, histopathologic confirmation, and exclusion of other granulomatous diseases. NS was diagnosed according to the NS Consortium Consensus Group. Demographic and clinical data were collected. The incidence of sarcoidosis between 1999-2019 was estimated by gender, age, and year of diagnosis.

Results: NS was observed in 30 of 234 (12.8%) (19 women/ 11 men) (mean age: 55.0±15.8 years) patients with sarcoidosis. The underlying neurological manifestations were chronic headache (n=13, 43.4%), peripheral neuropathy (n=6, 20.0%), cranial neuropathy (n=5, 16.7%), spinal cord abnormalities (n=3, 10.0%) and aseptic meningitis (n=3, 10.0%). A comparison between different geographical areas is summarized in **Table 1**. There are wide variations in frequency (US:4.8% to France:33.9%), gender predominance and age at diagnosis (31 to 55 years) depending on the geographical area.

Author, year	Country	cases			Male n (%)		Age at onset years mean ± SD	
		S	NS	%	S	NS	S	NS
Gascón-Bayarri et. al., 2011	Spain	445	30	6.7	ND	10 (33.4)	ND	48.3±ND
Leonhard et. al, 2016	The Netherlands	ND	52	ND	ND	22 (48.0)	44±ND	43.0±ND
Joubert et. al, 2017	France	690	234	33.9	ND	117 (50.0)	ND	31.5±ND
Dorman et. al, 2019	USA	1706	82	4.8	691 (40.6)	43 (52.4)	49±10.8	45.0±11.4
Arun et. al, 2020	UK	ND	80	ND	ND	35 (44.0)	ND	47.8±ND
Goel et al., 2020	India	ND	12	ND	ND	4 (33.4)	ND	44.0± 9.2
Sambon et. al, 2022	Belgium	180	22	12.2	ND	14 (64.0)	ND	40.5±ND
Byg et al., 2022	Denmark	ND	20	ND	ND	11 (55.0)	ND	51.6±ND
Present study, 2023	Spain	234	30	12.8	105 (44.9)	11 (36.7)	48.4±14.8	55.0±15.8

Abbreviations: ND: non data, NS: neurosarcoidosis, S: Sarcoidosis

TABLE 1: Main clinical features and treatment of neurosarcoidosis in different geographical areas.

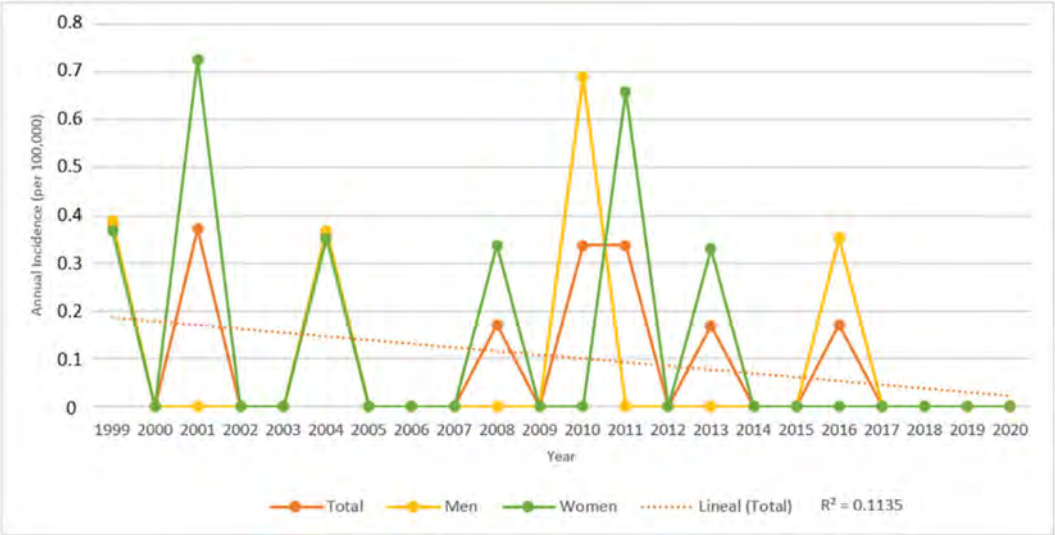

FIGURE 1: Trends in age at neurosarcoidosis diagnosis in Cantabria, Spain, in 1999-2019 by gender.

Nevertheless, most of the patients were diagnosed in the 5th decade of life. Annual incidence of NS in our population area in the 1999-2019 period was 0.11 per 100000 people, 95% (CI:0.11-0.26); 0.08 (0.07-0.24) in men, 0.13 (0.09-0.24) in women. There were variations in annual incidences, ranging from a minimum value of 0.08 in 2013-2014 to a maximum of 0.19/100000 population in 1999-2000. A downward trend in annual incidence over time was observed. Nevertheless, the correlation was weak(r^2=0.1135) (**Figure 1**).

Conclusion: The epidemiological characteristics of NS is very different in frequency. Frequency estimated in this study was similar to that of other countries.

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Abstract Number: 1914

Intravenous Immunoglobulins in the Treatment of Idiopathic Inflammatory Myopathies in a Region of Northern Spain: Analysis by Subtypes

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of diseases characterised mainly by the presence of inflammation and muscle weakness. The main subtypes of IIM are Dermatomyositis (DM), Polymyositis (PM), Inclusion body myositis (IBM), Immune-mediated necrotising myopathies (IMNM) and Anti-synthetase syndrome (ASS).

Currently the treatment of IIMs is not well established. Intravenous immunoglobulins (IVIG) are a therapeutic alternative for the treatment of IIM. Although their mechanism of action is not precisely known, several studies suggest that they are effective in the treatment of multiple rheumatological diseases, including IIM.

The main objective of this study is to describe the use of IVIG, as well as to determine its efficacy in different subtypes of IIM in a cohort of patients from northern Spain.

Methods: Observational study of patients with IIM who required at least one cycle of IVIG between January 2000 and December 2022. Patients with IIM who met a) EULAR/ACR 2017 criteria for DM and PM, b) European Neuromuscular International Workshop 2016 definition for MNIM and c) Connor's criteria in SAS were included.

Treatment efficacy was studied based on a) clinical variables (muscle weakness and skin involvement), b) analytical variables (Creatin Kinase CK) and c) corticosteroid sparing effect. All these factors were measured at 1 month, 3 months, 6 months, 1 year and 2 years after starting IVIG treatment.

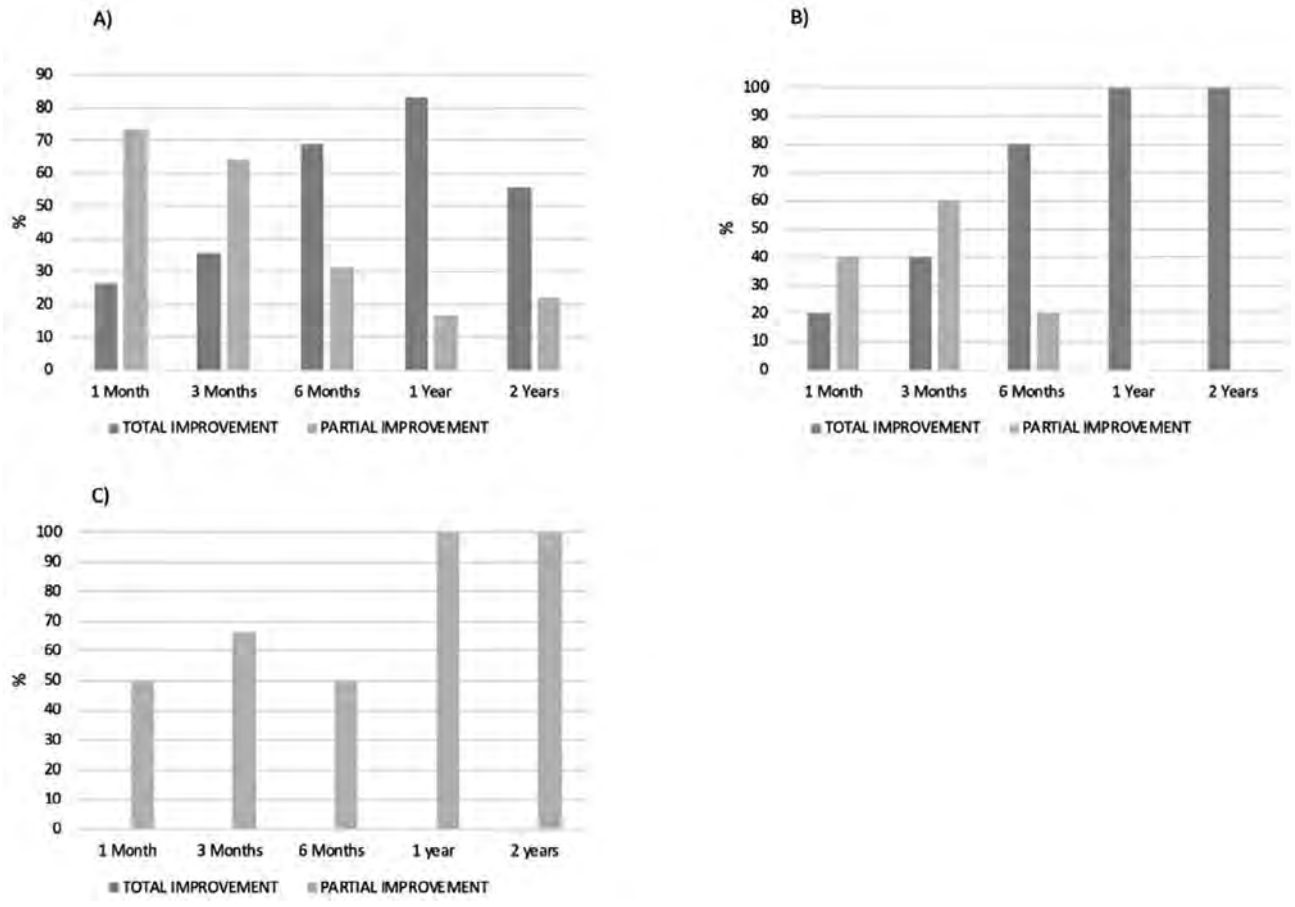

Figure 1. Muscle weakness improvement. a) Dermatomyositis b) Inmune-mediated necrotizing myopathies. c) Polymyositis

Muscle weakness was measured in 3 territories (upper limb, lower limb and neck flexor muscles) using the MRC (Medical Research Council Grading System) muscle strength scale.

The evolution of clinical parameters was classified into 3 categories: complete improvement (resolution), partial improvement and no improvement.

The IVIG treatment schedule used was 2g/kg spread over 2-5 days.

Results: A total of 37 patients with IIM were included, 29 females (78%) and 8 males (22%), with a mean age 47 ± 27 years. The most frequent group was DM (n=27; 73%), followed by IMNM (n=6; 16%), PM (n=3; 8%) and ASS (n=1; 3%).

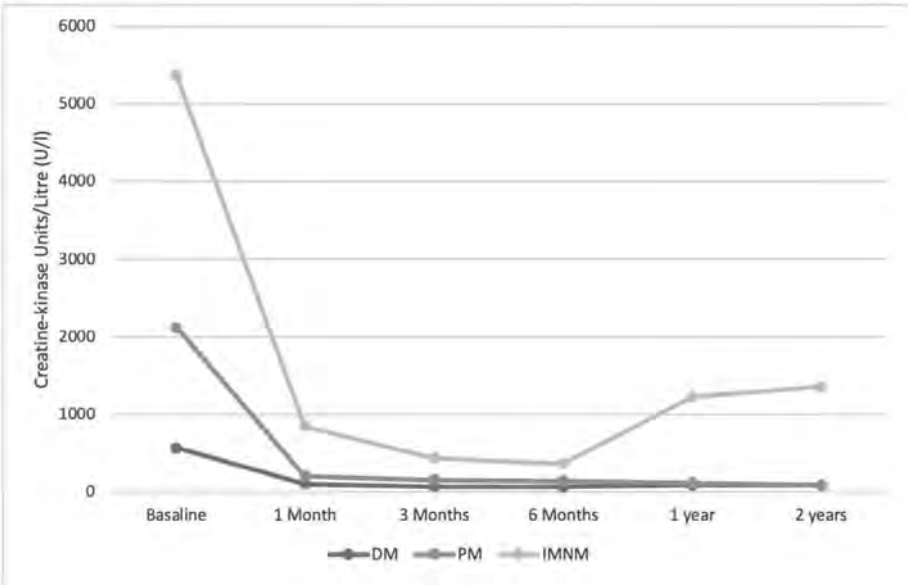

FIGURE 2. Creatine-Kinase evolution.

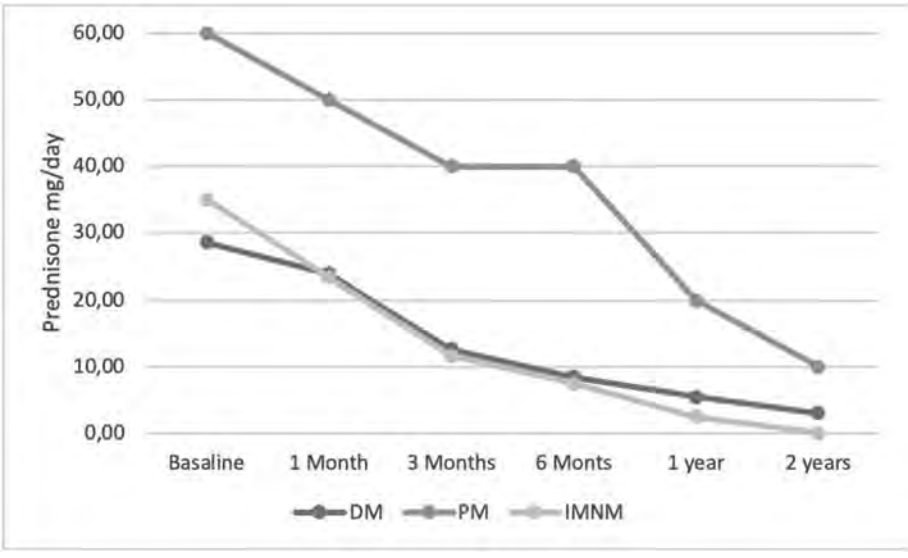

FIGURE 3. Corticosteroid sparing effect.

Eight (30%) patients with DM received IVIG as induction therapy associated with standard treatment, while 19 (70.37%) patients received IVIG after boluses of methylprednisolone (n=10; 53%), prednisone 45 mg/day (n=19; 100%), or associated with other immunosuppressants (IS) (methotrexate, azathioprine, cyclophosphamide or mycophenolate). The main indication for IVIG in this group was muscle weakness (n=19; 70%) and skin involvement (n=8; 30%). The main indication for IVIG in MD was muscle weakness (n=19; 70%) and skin involvement (n=8; 30%).

All PM patients (n=3) had received previous treatment with Prednisone 60mg/day. The main indication was muscle weakness (n=3, 100%).

Of the 6 patients with IMNM, 5 (67%) received IVIG as induction therapy and 1 patient (33%) after Prednisone 60 mg/day. In all of them the indication was muscle weakness.

Only one patient with ASS received IVIG treatment, due to interstitial lung involvement and muscle weakness.

An improvement in muscle weakness (total and/or partial) (Figure 1), CK levels (Figure 2) and a sparing glucocorticoid effectof IVIGwas observed in all IIM subtypes.(Figure 3)

Conclusion: IVIGs are effective in all 3 subtypes of IIM studied.

Disclosure: C. Corrales Selaya: None; **D. Martínez-Lopez**: None; **D. Prieto-Peña**: None; **F. Benavides**: None; **J. Martin-Varillas**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6.

Abstract Number: 1915

Scleritis and Development of Autoimmune Disease: A Case Series

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SESSION INFORMATION
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Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
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Session Time: 9:00AM–11:00AM

Background/Purpose: Scleritis involves inflammation of the sclera caused by trauma, infections, or autoimmune conditions. The purpose of our study was to understand the relationship between scleritis and the presence of autoimmune disease, including the temporal relationship, treatment course, recurrence, and associated serologies.Characterizing the relationship between scleritis and autoimmunity can help clinicians identify and treat conditions effectively.

Methods: We conducted a case series of 341 scleritis patients seen between January 1, 2005 and December 20, 2020. Demographics, treatment types, treatment failures, recurrence events, and serology data were compared among patients with and without autoimmune disorders. Autoimmune disorders were described by disease and by time course. American College of Rheumatology criteria were unable to be used to verify diagnoses for this study.

Results: Most patients with scleritis had an associated autoimmune disorder (n=196, 57%), and most patients developed their disorder before scleritis (62%). There were no significant differences in age, gender, ethnicity, or race among scleritis patients with and without autoimmune disorders. Most patients had recurrence of scleritis (54%), and patients with autoimmune disorders were more likely to have a recurrence (62% vs 48%, $p< 0.05$). The most common scleritis treatments were nonsteroidal anti-inflammatory drugs, topical and systemic prednisone. There were no differences in treatment failure rates based on having an autoimmune disorder. The most common autoimmune disorders associated with scleritis were rheumatoid arthritis (39%), vasculitis (21%), and inflammatory bowel disease (14%). The incidence of autoimmune disorders developed after scleritis for any condition was 0.84/100,000 person years, with 0.33/100,000 person years for vasculitis, and 0.23/100,000 person years for RA. Based on limited data, there were no relationships between RF and ACPA serologies

Table 1: Characteristics of scleritis patients

Category	Characteristic	Total		Those with associated AI disorder		Those without associated AI disorder		Measures of association	
		avg, SD	SD	avg, SD	SD	avg, SD	SD	T-test	Chi-sq
Age		51.3	16.1	51.8	14.7	50.2	17.0	-0.94	
		n	%	n	%	n	%		Chi-sq
Total		**341**		**145**		**196**			
Sex	Male	118	35%	51	35%	67	34%		0.04
	Female	223	65%	94	65%	129	66%		
Ethnicity	Hispanic	38	11%	16	11%	22	11%		0
	Not Hispanic	283	83%	120	83%	163	83%		
	Unknown	20	6%	9	6%	11	6%		0.24
Race	Asian	8	2%	4	3%	4	2%		1.39+
	Black	17	5%	7	5%	10	5%		0.05
	More than one race	4	1%	2	1%	2	1%		1.38+
	White	280	82%	117	81%	163	83%		0.01
	Unknown	32	9%	15	10%	17	9%		0.27
Treatment	NSAID	179	52%	66	46%	113	58%		6.05*
	NSAID failure	74	41%	32	48%	42	37%		2.2
	Topical prednisone	179	52%	80	55%	99	51%		0.73
	Topical prednisone failure	52	29%	28	35%	24	24%		2.48
	Systemic prednisone	216	63%	103	71%	113	58%		6.42*
	Systemic prednisone failure	51	24%	19	18%	32	28%		2.91
	Methotrexate	107	31%	67	46%	40	20%		25.76***
	Methotrexate failure	40	37%	23	34%	17	43%		0.71
Recurrence	Yes	183	54%	90	62%	95	48%		6.21*

+ Fisher's exact test used, reported as odd's ratio
*P<0.05
**P<0.01
***P<0.001

Table 2: Autoimmune conditions associated with scleritis and time course

Population	N	%	Incidence
Total patients	**341**		
Total patients with autoimmune conditions	**145**	**43%**	
RA	57	39%	
Vasculitis	31	21%	
IBD	21	14%	
SLE	7	5%	
Sarcoidosis	6	4%	
Other spondyloarthropathy	6	4%	
Relapsing polychondritis	6	4%	
Other	11	8%	
Autoimmunity before scleritis	**90**	**62%**	
RA	42	47%	
Vasculitis	8	9%	
IBD	17	19%	
SLE	6	7%	
Sarcoidosis	5	6%	
Other spondyloarthropathy	6	7%	
Relapsing polychondritis	2	2%	
Other	11	12%	
Autoimmunity at same time as scleritis	**19**	**13%**	
RA	5	26%	
Vasculitis	9	47%	
IBD	2	11%	
SLE	1	5%	
Sarcoidosis	0	0%	
Other spondyloarthropathy	0	0%	
Relapsing polychondritis	3	16%	
Other	1	5%	
Autoimmunity after scleritis	**36**	**25%**	5.7
RA	10	28%	5.3
Vasculitis	14	39%	0.67
IBD	2	6%	0.72
SLE	0	0%	0.00
Sarcoidosis	1	3%	0.33
Other spondyloarthropathy	3	8%	0.98
Relapsing polychondritis	1	3%	0.22
Other	5	14%	

Incidence reported as per 100,000 person years

Unclear date of rheumatologic diagnosis occurred in 21 of 90 patients with autoimmunity before scleritis

Table 3: RA serologies in scleritis patients by time period

Serology	AI then scleritis	Scleritis then AI	AI other than RA	AI	No AI	Total	AI vs no AI	Non-RA AI vs no AI	RA: AI then scleritis vs. Scleritis then AI
RF +	14	7	8	29	6	35	0.55	2.12	0.22
RF -	6	5	100	111	33	144			
ACPA +	10	6	2	18	1	19	30.41+***	4.83+	0.17
ACPA -	6	5	26	37	64	101			
RF + / ACPA -	1	1	5	7	3	10	4.35+*	4.49+*	0.82+
RF - / ACPA +	1	1	2	4	0	4	n/a	n/a	0.82+
RF + / ACPA +	7	5	0	12	1	13	22.1+***	n/a	1.11+
RF - / ACPA -	5	4	20	29	55	84	0.094+***	0.21+*	0.97+

+ Fisher's exact test used, reported as odd's ratio

*P<0.05

**P<0.01

***P<0.001

and time course of developing autoimmune disorders and scleritis. Dual-seropositive patients were more likely to have an autoimmune disorder compared to seronegative patients (72% vs 35%, p< 0.001), as were RF+/ACPA- patients (70% vs 35%,p< 0.05).

Conclusion: Scleritis is associated with autoimmune diseases, most commonly developed before scleritis. Scleritis among autoimmune patients is more likely to recur. Comparative studies are needed to identify individual risk factors associated with development of autoimmune disease among scleritis patients.

Disclosure: T. Morrison: None; **M. Gottman**: None; **M. Friedman**: None; **D. Ghetie**: None.

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Clinical Features of the Patients with *NLRP1* Gene Variants and a Systemic Autoinflammatory Phenotype

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
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Session Time: 9:00AM–11:00AM

Background/Purpose: Although *NLRP1* was the first identified member of the NOD-like receptors family, its role as a sensor of pathogen- or damage-associated signals and its connection with systemic autoinflammatory disorders (SAIDs) have not been clarified yet. Missense or non-sense variations of the NLRP1 gene have already been associated with some clinical phenotypes including dyskeratosis, arthritis, recurrent fever, chronic infections, recurrent acute phase response, recurrent respiratory papillomatosis, keratosis pilaris, palmoplantar wart-like hyperkeratotic papules, atrophoderma vermiculata, and familial keratosis lichenoides chronica. Some polymorphisms have also been associated with autoimmune disorders. We herein report the clinical findings of 5 patients with *NLRP1* variants.

Methods: The study group included the patients who were referred to our center with a potential diagnosis of SAID and screened for variants of 22 autoinflammatory genes. Those patients with NLRP3 variants were identified, and their clinical and laboratory findings were evaluated.

Results: A total of 146 cases with potential diagnosis of SAID were included, and their genetic analysis results were evaluated. *NLRP1* variants were identified in 5 (3.4 %) cases. All of the *NLRP1* gene variants were classified as variant of uncertain significance (VUS). All but one patients had additional variants in other autoinflammatory genes (Table 1). The most common clinical finding was recurrent urticaria (n=4). Case 1 had NLRP3-AID-like clinical phenotype in addition to Crohn's disease with sacroiliitis. Case 2 had scleritis attacks and had a combination of two gene variants. Case 3 had Behçet's disease-like phenotype with oral aphthous stomatitis, genital ulcers, and cerebrovascular event with VUS in both *NLRC4* and *NLRP1* genes. Case 4 had a TRAPS-like phenotype with serositis and periorbital edema with NLRP1 VUS and a pathogenic *MEFV*

variant. Case 5 had an FMF-like phenotype with VUS in the *NLRP1* VUS and a pathogenic variant in the *MEFV* genes along with five different gene variants. None of the patients had a family history for a phenotype compatible with SAIDs.

Table 1: Genotype and phenotypes of patients with NLRP1 variants. *: Pathogenic and likely pathogenic, †: VUS

Patient no	Sex	Current age	Age onset	Gene	Amino acid change	rs number	Frequency	Clinic	Treatment
1	F	32	4	NLRP1 †	p.Val939Met	rs61754791	0.016102	Fever attacks every two weeks with cold-induced urticarial rash, abdominal pain, nausea, elevated acute phase reactants, Crohn's disease and sacroiliitis, proteinuria (amyloidosis?)	Canakinumab
2	F	42	37	NLRP1 †	p.Val939Met	rs61754791	0.016102	Attacks of scleritis and urticarial rash with elevated acute phase reactants Skin biopsy: perivascular neutrophilic infiltrates without findings of vasculitis	Anakinra
				IL31RA †	p.Glu698Lys	-	-		
3	M	46	29	NLRP1 †	p.Val1235Ile	-	-	Attacks of fever, arthritis, urticarial rash, and abdominal pain lasting 2-3 days, aphthous stomatitis, genital ulcers, cerebrovascular event, elevated acute phase reactants, liver enzymes, and creatinine kinase.	Anakinra
				NLRC4 †	p.Ser572Asn	-	-		
4	F	41	30	NLRP1 †	p.Cys904Ter	-	-	Attacks of fever, serositis, urticarial rash, periorbital edema	Colchicine Canakinumab
				MEFV*	p.Val726Ala	rs28940579	0.001541		
					p.Arg761His	rs104895097	0.000199		
5	F	64	62	NLRP1 †	p.Val939Met	rs61754791	0.016102	Fever attacks lasting two weeks with elevated acute phase reactants, which started at the age of 62, exacerbation with COVID-19.	Colchicine Prednisolone
				MEFV*	p.Met694Val	rs61752717	0.000223		
				NLRP12 †	p.Thr260Met	rs150280940	0.000264		
				NLRP3 †	p.Gln705Lys	rs35829419	0.030266		
				CARD14 †	p.Lys284del	-	-		
				IKBKG †	p.Asp181Asn	-	-		
				LPIN2 †	p.Pro626Ser	rs150806357	0.000948		

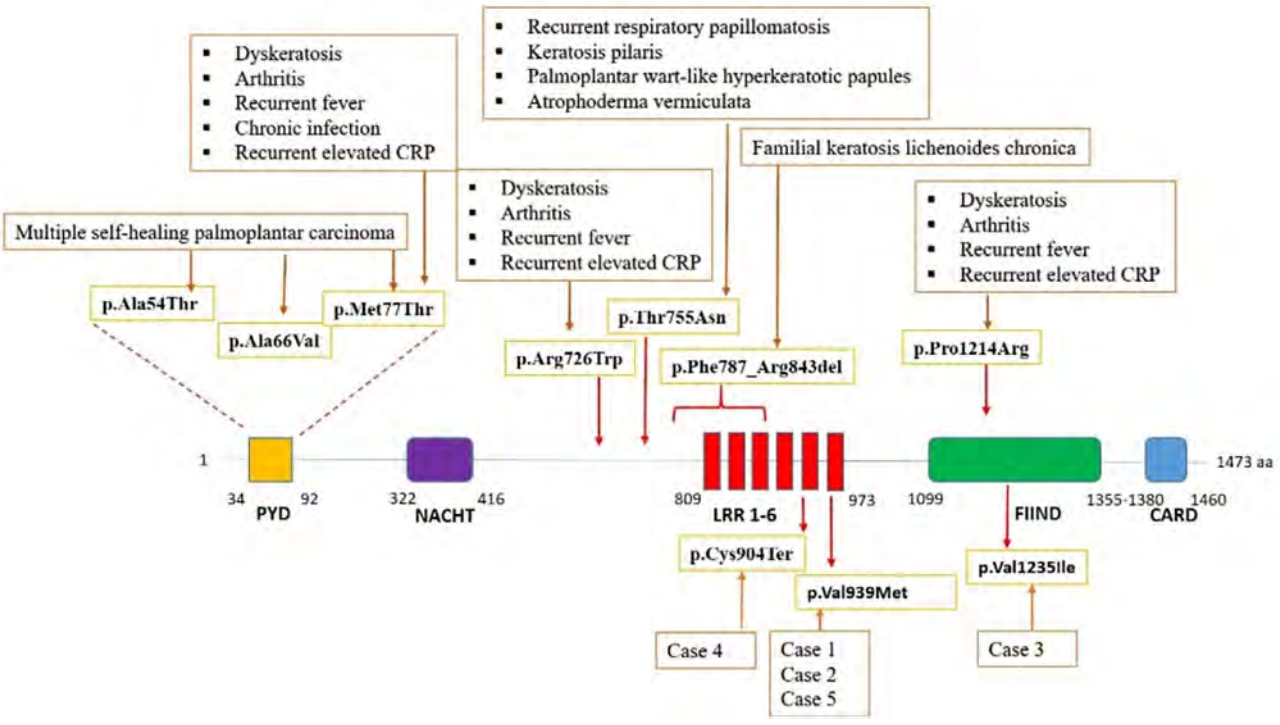

Figure 1: NLRP1 variants and phenotypic features of the reported patients (above the line) and our cases (below the line).

Conclusion: *NLRP1*-associated SAID has been emerging as a new entity, and the phenotypic features of the reported patients varied significantly according to the positions of the variants within the different domains of the gene (Figure 1). We herein report 4 patients with recurrent urticaria as the most common clinical feature in association with 3 different VUS in the *NLRP1* gene, and none of the accompanying genetic variants have not been related to urticaria below. The *NLRP1* gene p.Val939Met variant is a relatively common variant (allele frequency 0.01), but relatively frequent observation of this variant in the current patient group may suggest that it may have a functional role very similar to the relatively common variant of p.Gln703Lys in the NLRP3 gene. One of the remaining two variants (p.Val1235Ile) was not reported before, and the other one (p.Cys904Ter) was expected to have a pathogenic role due to early termination of the protein (Figure 1). Collection of more cases would help clarify the spectrum of clinical findings of the patients with NLRP1-AID.

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Reducing Inadvertent Antifilarial Antibody Testing at an Academic Medical Center: A Quality Improvement Project

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Background/Purpose: IgG4-Related Disease (IgG4-RD) is a fibroinflammatory autoimmune disease that can present with glandular swelling, chronic pancreatitis, sclerosing cholangitis, and retroperitoneal fibrosis, amongst others. Along with a supporting clinical history, diagnosis is typically established by biopsy of affected tissue showing hallmark histopathologic findings. Many patients demonstrate elevated serum IgG4 levels and checking levels is often part of the initial workup when considering IgG4-RD. At Atrium Health Wake Forest Baptist, IgG4 levels can be checked by ordering IgG subclass levels or IgG4 levels. However, we have frequently observed the filarial IgG4 antibody test erroneously ordered instead, even though the patient's symptoms are not suggestive of filariasis or other tropical infectious disease. Inadvertent ordering of filarial IgG4 consumes healthcare dollars and may lead to delay in diagnosis of potential IgG4-RD. Our goal was to quantify how prevalent this issue is over the last 5 years (March 2017-March 2022) and institute a quality improvement (QI) intervention to significantly reduce inadvertent filarial IgG4 testing.

Methods: Using SlicerDicer on EPIC, we determined the number of patients who had ≥ 1 filarial IgG4 level ordered (date range 3/22/2017-3/21/2022). Using the patient's medical record number (MRN), we individually reviewed the charts to determine whether such testing was indicated or done inadvertently while investigating a diagnosis of IgG4-RD. We designed a pop-up reminder that appears when a provider tries to order a filarial IgG4. The pop-up contained recommendations for alternative testing for IgG Subclass 4 or IgG Subclasses instead, and officially launched on 3/22/2022. To determine the efficacy of our intervention after a 1-year observation, we determined the number of patients who had ≥ 1 filarial IgG4 ordered between the dates 3/22/2022 and 3/21/2023.

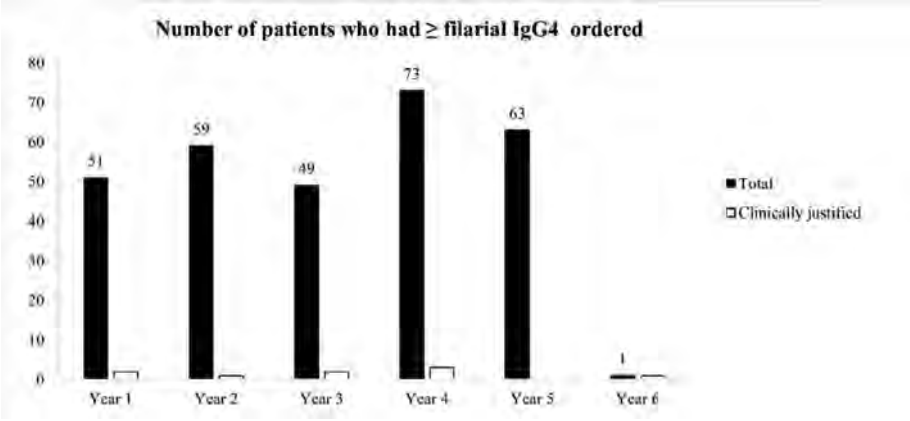

Figure 1

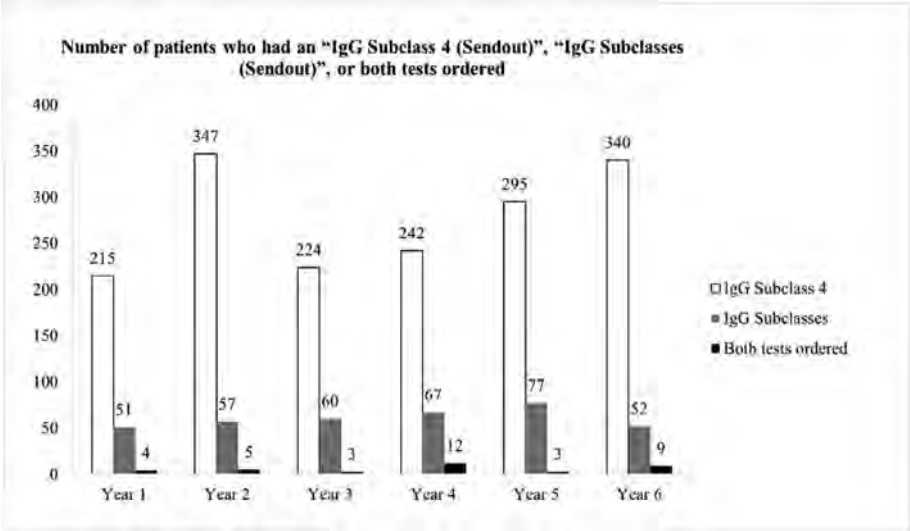

Figure 2

Results: 295 patients had ≥ 1 filarial IgG4 test ordered between 3/22/2017 and 3/21/2022 (average 59 patients per year). The vast majority of patients (97.3%) had unjustifiable reasons for ordering the test, after review of the patients' charts (**-Figure 1**) However, our pop-up intervention significantly reduced (100% reduction) inadvertent filarial IgG4 testing after a 1-year observation. Only 1 filarial IgG4 test was ordered during 3/22/2022-3/21/2023, and it was clinically indicated after chart review **(Figure 1)** Ordering of IgG4 Subclass 4 or IgG Subclasses was not negatively affected by the pop-up (**Figure 2**)

Conclusion: We instituted an effective QI intervention in the form of a pop-up reminder that effectively eliminated the inadvertent checking of filarial IgG4 when such testing was not justified.It was selective against filarial IgG4 orders, and did not create an undue burden on providers who tried to order potentially justifiable IgG4 or IgG subclass testing. Since each filarial IgG4 test costs $288.75 at Labcorp (821383), our intervention could potentially reduce health expenditures by $17,000 per year at our institution. This strategy could be applied at other medical centers if a similar problem with filarial IgG4 exists and can also be applied to other lab tests that are often checked inadvertently.

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Nationwide Analysis of Predictors of Sarcoid Inpatient Mortality

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Background/Purpose: Sarcoidosis is multisystem autoimmune disease characterized by noncaseating granulomas which can result in significant morbidity and mortality. This study aims to identify variables associated with in-hospital death for sarcoid patients on a national level.

Methods: We performed a retrospective study of adult sarcoid hospitalizations from 2016-2020 National Inpatient Sample (NIS) database. Diagnoses for each hospitalization were identified by ICD-10 codes. We sought to identify predictors of in-hospital death among sarcoid patients. Variables were selected from literature review and ranking of common diagnoses among sarcoid inpatients. Variables with a p value ≤ 0.2 in the univariable screen were included in a multivariable logistic regression model. P values ≤ 0.05 were considered significant in the multivariable analysis.

Results: There were 405,450 inpatient admissions with a diagnosis of sarcoidosis in the 2016-2020 NIS database. Of those, 10,210 (2.5%) died while in the hospital (table 1). The deceased group was older (median age 67 vs 61 years; p< 0.0001), had more males (41.7% vs 38.6%; p=0.0035), had longer median LOS (6 vs 4 days; p< 0.0001), had higher median total hospital charges ($78,507vs $37,333; p< 0.0001), and higher Charlson comorbidity index (CCI) (3 vs 2; p< 0.0001). Univariable analysis showed many variables associated with in-hospital death among sarcoid patients (table 2). Multivariable analysis showed the following variables were independently associated with a higher odds of in-hospital death: Age (OR 1.03; 95% CI 1.023 -1.032), CCI (OR 1.14; 95% CI 1.102-1.170), COVID-19 (OR 2.69; 95% CI 2.133-3.384), male gender (OR 1.16; 95% CI 1.047-1.290), other race (OR 1.79; 95% CI 1.275-2.505), acidosis (OR 2.46; 95% CI 2.190-2.755), Acute kidney failure (AKF) (OR 1.89; 95% CI 1.695-2.107), arrhythmia/heart blocks (OR 1.58; 95% CI 1.414-1.767), cerebral edema/brain compression (OR 8.29; 95% CI 6.177-11.115), disseminated intravascular coagulation (DIC) (OR 11.87; 95% CI 6.417-21.948), encephalopathy (OR 1.81; 95% CI 1.574-2.082), hepatic failure (OR 4.28; 95% CI 3.446-5.319), hemophagocytic lymphohistiocytosis (OR 5.43; 95% CI 1.269-23.212), aspiration pneumonia (OR 1.89; 95% CI 1.557-2.300), pulmonary embolus (OR 2.18; 95% CI 1.697-2.793), pulmonary hypertension (OR 1.22; 95% CI 1.079-1.383), respiratory failure (OR 6.70; 95% CI 5.911-7.592), and sepsis (OR 2.81; 95% CI 2.494-3.156) (table 3).

Conclusion: Our analysis showed that 2.5% of inpatient admissions carrying a sarcoid diagnosis ended in death. Demographic factors such as age, gender, other race, and CCI were independently associated with higher odds of mortality, while African American race and income quartile were not. Several comorbidities were independently associated with higher odds of in-hospital death: acidosis, acute kidney failure, arrhythmia/heart blocks, cerebral edema/brain compression, DIC, encephalopathy, hepatic failure, HLH, aspiration pneumonia, PE, pulmonary hypertension, respiratory failure, and sepsis. Clinicians should remain vigilant for these life-threatening complications since early recognition and intervention may improve inpatient sarcoid outcomes.

Table 1. Weighted Descriptive Characteristics of Adult Sarcoid Hospitalizations from the 2016 to 2020 National Inpatient Sample (n= 405,450)
Abbreviations: ACS=Acute Coronary Syndrome; CCI= Charlson Comorbidity Index; CKD=Chronic Kidney Disease; DIC=Disseminated Intravascular Coagulation; IQR=Interquartile Range; HF=Heart Failure; HLH= Hemophagocytic lymphohistiocytosis; HTN=Hypertension; n= number; PI=Pacific Islander; Q=Quartile

Hospitalization Characteristics	Discharge Alive (n=395,240)	In-Hospital Death (n=10,210)	P-value
Age, median (IQR) in years	61 (52-70)	67 (58-75)	<0.0001
Male	38.6%	41.7%	0.0035
Race (%)			
White	46.6%	44.9%	0.1516
African American	43.8%	44.9%	0.3234
Hispanic	4.0%	3.3%	0.1037
Asian or PI	0.7%	0.7%	0.9770
Native American	0.3%	0.1%	0.3242
Other Race	2.0%	2.8%	0.0204
Missing race data	2.6%	3.3%	0.1146
Length of Stay, median (IQR)	4 (2-7)	6 (2-12)	<0.0001
Total Charges, median (IQR)	$37,333 (20,667-69,943)	$78,507 (35,259- 175,992)	<0.0001
CCI, median (IQR)	2 (1-4)	3 (2-5)	<0.0001
Income Q1 (%)	34.6%	33.8%	0.4238
Income Q2 (%)	23.8%	25.1%	0.1580
Income Q3 (%)	21.9%	21.8%	0.9378
Income Q4 (%)	18.4%	18.2%	0.8306
Missing income data	1.3%%	1.1%	0.3466
Acidosis	7.8%	35.3%	<0.0001
Acute Kidney Disease	21.2%	53.9%	<0.0001
Arrhythmia/Heart Blocks	25.1%	45.6%	<0.0001
Cerebral Edema/Brain compression	0.6%	4.6%	<0.0001
Chronic Kidney disease	26.9%	36.4%	<0.0001
COVID-19	1.2%	6.3%	<0.0001
DIC	0.06%	3.4%	<0.0001
Encephalopathy	4.6%	20.8%	<0.0001
Hepatic failure	1.2%	11.3%	<0.0001
HF (Systolic or Diastolic)	29.5%	49.2%	<0.0001
HLH	0.02%	0.3%	<0.0001
Hypercalcemia	3.3%	3.3%	0.8801
Hypo-osmolality/hyponatremia	8.7%	16.0%	<0.0001
Ischemic Heart Disease/ACS	24.6%	34.2%	<0.0001
Interstitial Lung Disease	33.7%	43.4%	<0.0001
Myocarditis	2.2%	2.8%	0.0450
Myositis	0.2%	0.3%	0.4050
Pneumonia, Aspiration	1.6%	10.9%	<0.0001
Pneumonia, Bacterial or Viral	14.7%	36.5%	<0.0001
Pulmonary Embolus	2.0%	5.4%	<0.0001
Pulmonary HTN	12.3%	24.0%	<0.0001
Respiratory Failure	22.9%	79.0%	<0.0001
Sepsis	9.8%	44.4%	<0.0001

Table 2: Univariable Mortality Analysis for Sarcoid Inpatients, NIS 2016-2020 Abbreviations: ACS=Acute Coronary Syndrome; CCI= Charlson Comorbidity Index; DIC=Disseminated Intravascular Coagulation; HF=Heart Failure; HLH= Hemophagocytic Lymphohistiocytosis; HTN=Hypertension; NIS=National Inpatient Sample Database; PI=Pacific Islander; Q=Quartil

Variable	Odds Ratio	P-value	95% C.I.
Age	1.03	<0.001	1.031-1.038
CCI	1.22	<0.001	1.196-1.237
Male gender	1.14	0.004	1.044-1.247
White	0.94	0.152	0.854-1.025
AA	1.05	0.323	0.957-1.143
Hispanic	0.82	0.104	0.643-1.042
Asian/PI	0.99	0.977	0.597-1.650
Native American	0.61	0.329	0.230-1.636
Other Race	1.40	0.021	1.052-1.865
Income Q1	0.96	0.424	0.877-1.057
Income Q2	1.08	0.158	0.972-1.191
Income Q3	1.00	0.938	0.896-1.106
Income Q4	0.99	0.831	0.882-1.106
Acidosis	6.48	<0.001	5.902-7.122
Acute Kidney Disease	4.34	<0.001	3.975-4.737
Arrhythmia/Heart Blocks	2.50	<0.001	2.288-2.740
Cerebral Edema/Brain Compression	7.39	<0.001	5.932-9.212
Chronic Kidney Disease	1.56	<0.001	1.420-1.707
COVID-19	5.76	<0.001	4.726-7.015
DIC	50.23	<0.001	34.938-72.210
Encephalopathy	5.47	<0.001	4.890-6.108
Hepatic Failure	10.36	<0.001	8.877-12.101
HF (Systolic or Diastolic)	2.32	<0.001	2.127-2.530
HLH	11.64	<0.001	4.082-33.221
Hypercalcemia	1.02	0.880	0.798-1.301
Hypo-osmolality/Hyponatremia	2.01	<0.001	1.777-2.267
Ischemic Heart Disease/ACS	1.60	<0.001	1.453-1.751
Interstitial Lung Disease	1.51	<0.001	1.384-1.654
Myocarditis	1.30	0.046	1.005-1.670
Myositis	1.38	0.407	0.647-2.932
Pneumonia, Aspiration	7.60	<0.001	6.540-8.830
Pneumonia, Bacterial or Viral	3.34	<0.001	3.050-3.665
Pulmonary Embolus	2.74	<0.001	2.246-3.335
Pulmonary HTN	2.25	<0.001	2.022-2.493
Respiratory Failure	12.73	<0.001	11.440-14.164
Sepsis	7.37	<0.001	6.751-8.052

Table 3: Multivariable Mortality Analysis for Sarcoid Inpatients, NIS 2016-2020 Abbreviations: ACS=Acute Coronary Syndrome; CCI= Charlson Comorbidity Index; DIC=Disseminated Intravascular Coagulation; HF=Heart Failure; HLH= Hemophagocytic Lymphohistiocytosis; HTN=Hypertension; NIS=National Inpatient Sample Database

Variable	Odds Ratio	P-value	95% C.I.
Age	1.03	<0.001	1.023-1.032
CCI	1.14	<0.001	1.102-1.170
COVID 19	2.69	<0.001	2.133-3.384
Male gender	1.16	0.005	1.047-1.290
Hispanic	1.04	0.733	0.816-1.335
Other Race	1.79	0.001	1.275-2.505
Income Q2	1.12	0.056	0.997-1.257
Acidosis	2.46	<0.001	2.190-2.755
AKF	1.89	<0.001	1.695-2.107
Arrhythmia/Heart Blocks	1.58	<0.001	1.414-1.767
Cerebral Edema/Brain compression	8.29	<0.001	6.177-11.115
Chronic Kidney Disease	0.68	<0.001	0.590-0.779
DIC	11.87	<0.001	6.417-21.948
Encephalopathy	1.81	<0.001	1.574-2.082
Hepatic Failure	4.28	<0.001	3.446-5.319
HF (Systolic or Diastolic)	1.00	0.950	0.885-1.122
HLH	5.43	0.023	1.269-23.212
Hypoosmolality/Hyponatremia	1.04	0.629	0.898-1.195
Ischemic Heart Disease/ACS	1.00	0.998	0.894-1.119
Interstitial Lung Disease	1.05	0.309	0.953-1.166
Myocarditis	1.27	0.135	0.929-1.724
Pneumonia, Aspiration	1.89	<0.001	1.557-2.300
Pneumonia, Bacterial or Viral	1.11	0.078	0.988-1.255
Pulmonary Embolus	2.18	<0.001	1.697-2.793
Pulmonary HTN	1.22	0.002	1.079-1.383
Respiratory Failure	6.70	<0.001	5.911-7.592
Sepsis	2.81	<0.001	2.494-3.156

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Abstract Number: 1919

Arthroplasty Outcomes in Immune Checkpoint Inhibitor-Treated Patients: A Single Center Series

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitors (ICI) have changed the landscape of cancer treatment dramatically, but because of their mechanism of action they are also known to cause immune-related adverse events, including chronic inflammatory arthritis (ICI-IA) and osteoarthritis flares. Additionally, the safety of joint arthroplasty in such patients has not yet been described. We undertook this study to describe the histology and outcomes of hip and knee arthroplasty (THA and TKA) at our high-volume orthopedic hospital among patients who received ICI within one year of surgery.

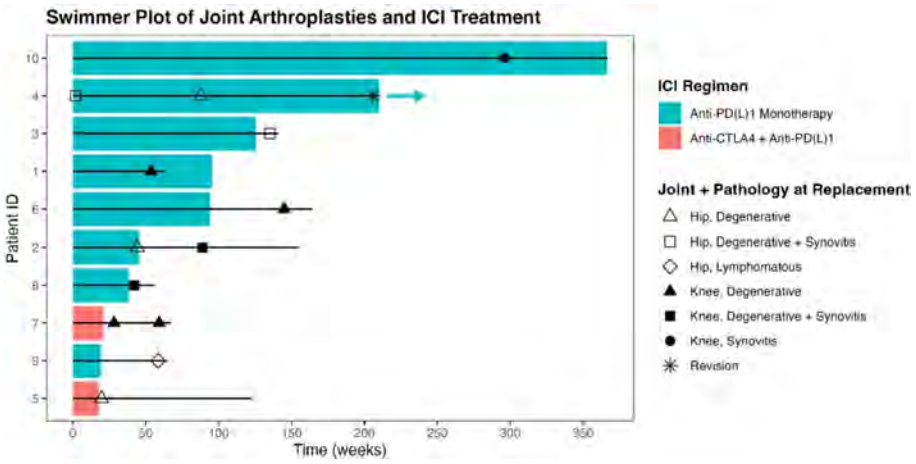

Figure 1. Swimmer's plot showing different checkpoint inhibitor regimens, joint replaced, and histology, plotted against time

Table 1. Patient characteristics. ICI = immune checkpoint inhibitor; ipi/nivo = ipilimumab/nivolumab

Patient	Age/Sex BMI	Cancer/Stage	ICI/Duration (months)	Time from last dose to surgery (days)	Joint	Charlson Comorbidity Index	Length of hospital stay (days)/discharge disposition	Complication	F/U Time (days)	Histology
1	68 M 30	Melanoma IV	Nivolumab 23	4	Right knee	8	2/home with services	None	65	Degenerative
2	79 M 25.9	Melanoma IIC	Nivolumab 10	27	Right hip	6	1/home	None	678	Degenerative
				305	Right knee	6	2/home with services	None	463	Degenerative with moderate synovial inflammation
3	67 F 20.3	Urothelial IV	Pembrolizumab 42	67	Right hip	8	1/home with services	None	39	Degenerative with moderate lymphoplasmacytic synovitis
4	67 F 23.3	NSCLC IV	Nivolumab 48	5	Right hip	8	2/home with services	Revision at 47 months	1458	Degenerative with chronic synovitis
				2	Left hip	8	3/home with services	None	855	Degenerative
5	87 M 25.1	Melanoma IV	Ipi/Nivo 4	14	Left hip	10	4/home with services	None	721	Degenerative
6	73 M 35	Prostate IV	Durvalumab 22	355	Right knee	10	1/home with services	None	134	Degenerative
7	66 M 29	Renal cell CA	Ipi/Nivo 5	50	Right knee	4	1/home with services	None	271	Degenerative
				267	Left knee	4	1/home with services	None	54	Degenerative
8	54 M 28.7	Esophageal IV	Pembrolizumab 14	27	Right knee	7	1/home	None	100	Degenerative with synovial hyperplasia
9	65 M 28.2	Lymphoma	Pembrolizumab 5	334	Right hip	4	1/home with services	None	47	Degenerative with lymphomatous involvement
10	69 M 29	Urothelial IV	Nivolumab 84	7	Right knee	8	2/home with services	None	492	Marked lymphoplasmacytic synovitis consistent with rheumatoid arthritis

Methods: We identified all ICI-treated patients who underwent joint arthroplasty at Hospital for Special Surgery (HSS) from 1/1/2018 to 12/31/2022, excluding patients whose last dose of ICI was >365 days prior to surgery. Clinical information was extracted retrospectively from the electronic medical record. The study was approved by the HSS IRB.

Results: Ten patients who had received ICI treatment underwent 13 native joint arthroplasties (**Table 1)**. Mean age was 70, mean BMI 27.45. Two patients had established ICI-IA. Median duration of ICI therapy was 18 months. Median time from the last dose of ICI to surgery was 27 days. Median duration of follow up was 271 days. There were 6 TKA, 1 unicompartmental knee replacement, and 6 THA (**Figure 1**). In 12/13, joint replacement surgery was indicated after failing conservative therapy for degenerative joint disease. There were no surgical site infections, wound healing issues, 30-day readmissions, cardiovascular events, or death. All patients were discharged home, most with services. Of the 2 patients with known ICI-IA, one (with known lymphoma) was found to have lymphomatous involvement of an otherwise degenerative hip; the other patient, who had monoarticular ICI-IA and for whom TKR was meant to be curative, had knee histology that showed marked lymphoplasmacytic inflammation resembling rheumatoid arthritis. All other joint explants had degenerative disease, 3 with mild-moderate synovitis. One patient had calcium pyrophosphate crystal deposits. One patient, who has remained on treatment from the time immediately preceding her first THA in 3/2019 until the present, required a revision THA 2/2023. The primary THA used a dual mobility prosthesis and modular dual mobility liner containing cobalt/chromium. Histology of the THA explant at the time of revision showed an immune-mediated inflammatory granulomatous reaction (adverse local tissue reaction), possibly from corrosion at the dual mobility liner, or from neck/stem incompatibility. Serum cobalt level was elevated at 2.7 ucg/L (nv 0.1-0.4). These reactions are uncommon; in one systematic review of arthroplasties using similar components, only 3% of patients had elevated ion levels.[1]

Conclusion: This single-center retrospective case series demonstrates the relative safety of performing joint arthroplasty in cancer patients treated with ICI. Most patients had degenerative changes with some mild to moderate reactive synovitis. One patient had an immune-mediated reaction leading to early revision; it is plausible that ICI treatment played a role in augmenting the immune response.

[1]Gkiatas I et al. *J Orthop*. 2020;21:432-437

Disclosure: Y. Elfarra: None; **E. DiCarlo**: None; **J. Vigdorchik**: None; **C. Aude**: None; **N. Ghosh**: None; **A. Bass**: None; **K. Chan**: None.

Abstract Number: 1920

A Phase Ib/II Randomized, Double-blind, Placebo-controlled Study of Novel anti-IL-17A Monoclonal Antibody JS005 in Patients with Moderate to Severe Psoriasis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
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Background/Purpose: JS005 is a novel anti-IL-17A monoclonal antibody with unique patented complementarity-determining region (CDR) sequences. This Phase Ib/II study (NCT05344248) aimed to evaluate the safety, tolerability, efficacy and pharmacokinetic characteristics of JS005 in patients with moderate to severe plaque psoriasis.

Methods: This study was composed of a dose-escalation phase Ib trial and a multicenter, double-blind, placebo-controlled phase II trial. Moderate to severe plaque psoriasis patients were enrolled to receive subcutaneous JS005 60mg (n=6), 150mg (n=9), 300mg (n=9), 600mg (n=6) and placebo (n=10) in the phase Ib trial. In the phase II trial, moderate to severe plaque psoriasis patients aged 18 to 75 years were randomized in a 1:1:1 ratio to receive subcutaneous JS005 at 150mg (n=48), 300mg (n=47) or placebo (n=48) once a week (QW) from Week 0 to Week 4, and once every 4 weeks (Q4W) from Week 5 to Week 12. Follow-up period was continued for 8 weeks after the last dose. The primary endpoint was the proportion of patients with at least 75% improvement in Psoriasis Area and Severity Index (PASI 75) from baseline at Week 12.

Results: A total of 40 and 143 patients were enrolled in this phase Ib and phase II trials, respectively. In the phase Ib trial, JS005 was well tolerated in moderate to severe plaque psoriasis patients, the incidence of Treatment Emergent Adverse Events (TEAEs) was similar across groups ($p > 0.05$). Results from full analysis set (FAS) showed significantly higher response rates of PASI 75 with JS005 60mg (50%, $p < 0.0001$), 150mg (100%, $p < 0.0001$), 300mg (100%, $p < 0.0001$) and 600mg (100%, $p < 0.0001$) than with placebo (0%) at Week 12 (Fig. 1). In the phase II trial, the proportions of patients achieved PASI 75 at week 12 were significantly higher in the JS005 150mg group (95.8%, $p < 0.0001$) and 300mg group (89.4%, $p < 0.0001$) than in the placebo group (8.3%) (Fig. 2). The incidence of TEAEs was 62.5%, 63.8%, and 64.6% in the JS005 150mg, 300mg and placebo groups, respectively. The severity of TEAEs in JS005 150mg and 300mg groups were all CTCAE grade 1 and Grade 2. The most common drug related TEAEs in JS005 group were hyperuricemia (6.3%), blood uric acid increase (5.3%), and hypertriglyceridemia (5.3%). There were no AEs that led to study withdrawal and permanent treatment discontinuation, and no serious AE or death events occurred.

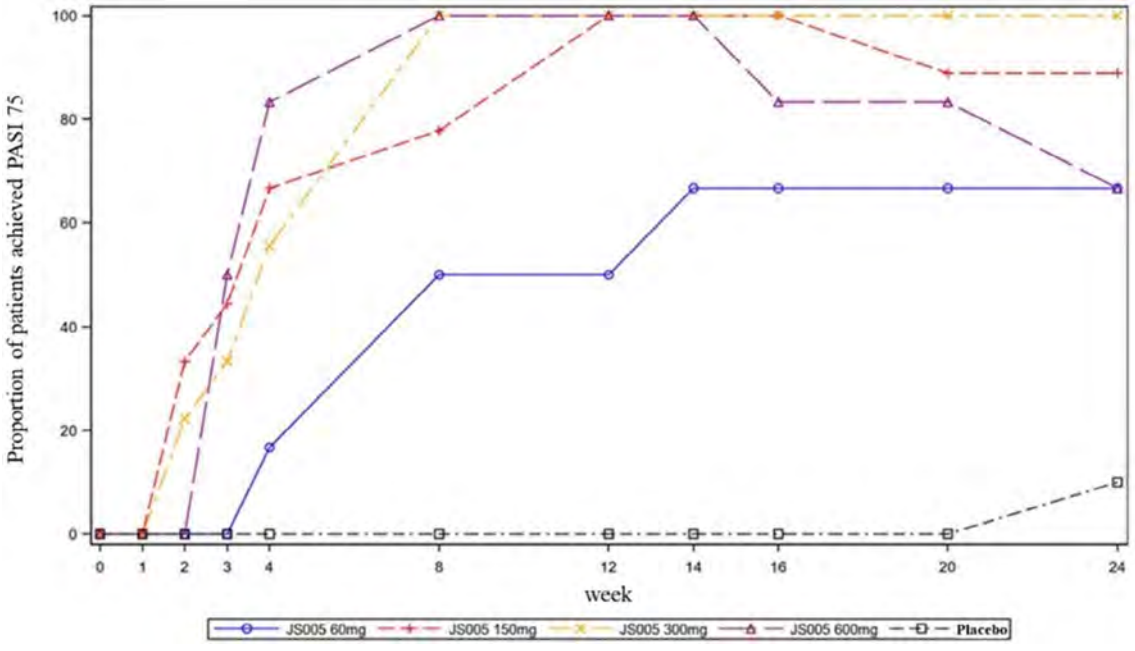

Figure 1 Proportion of patients achieving PASI 75 over 24 weeks in Phase Ib trial (full analysis set)

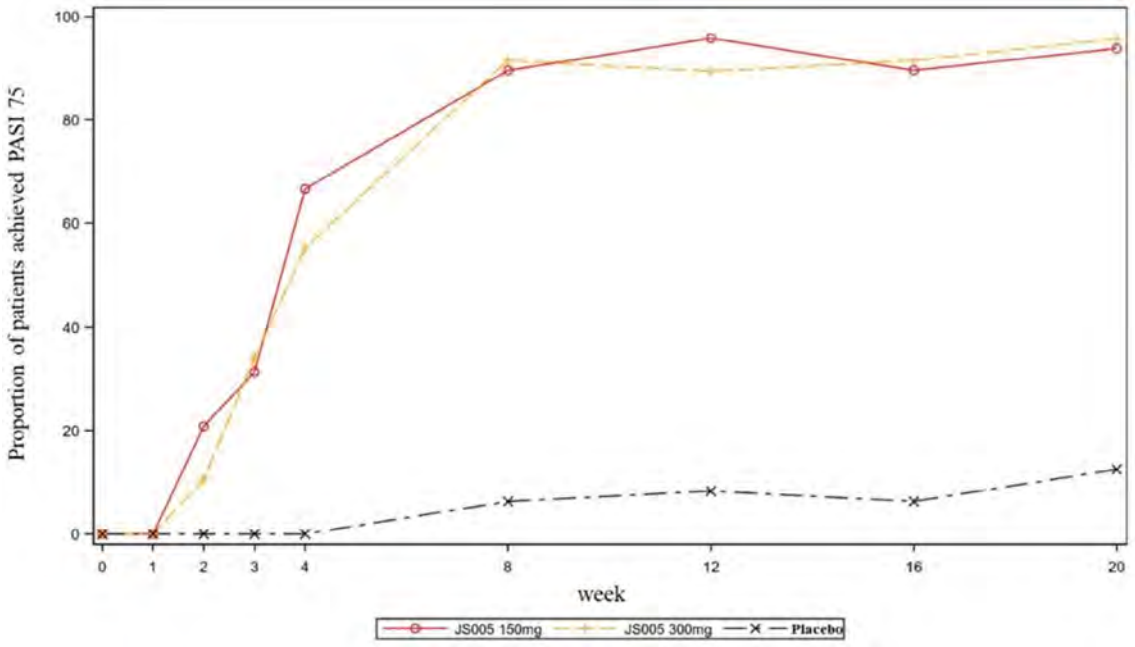

Figure 2 Proportion of patients achieving PASI 75 over 20 weeks in Phase II trial (full analysis set)

Conclusion: This phase Ib/II study demonstrated that JS005 was highly effective and well tolerated in moderate to severe plaque psoriasis.

Disclosure: L. Cai: None; **Z. Mu**: None; **X. Tao**: None; **L. Zhang**: None; **C. Zhang**: None; **Y. Li**: None; **G. Zhang**: None; **F. Zhang**: None; **X. Dong**: None; **C. Li**: None; **A. Chen**: None; **Z. Wu**: Shanghai Junshi Biosciences, 3; **Y. Zhu**: Shanghai Junshi Biosciences, 3; **M. Zhang**: Shanghai Junshi Biosciences, 3; **J. Liu**: Shanghai Junshi Biosciences, 3; **J. Zhang**: None.

Abstract Number: 1921

Clinical Spectrum of VEXAS Syndrome in a Rheumatology Department

Herman Mann[1], Blanka Stiburkova[2], Katerina Pavelcova[1], Monika Belickova[3], Cyril Salek[3], Jana Juhaszova[1] and Jiri Vencovsky[4], [1]Institute of Rheumatology, Praha 2, Czech Republic, [2]Institute of Rheumatology, Prague, Czech Republic, [3]Institute of Hematology and Blood Transfusion, Praha 2, Czech Republic, [4]Institute of Rheumatology, Prague, Czech Republic, Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
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Session Time: 9:00AM–11:00AM

Background/Purpose: VEXAS (vacuoles, E1 activating enzyme, X-linked, auto-inflammatory, somatic) syndrome is a clinically serious and potentially fatal adult-onset disease caused by somatic mutations in the *UBA1* (Ubiquitin-like modifier activating enzyme 1) gene in hematopoietic progenitor cells. VEXAS syndrome clinically presents with inflammatory and hematological symptoms in middle and older age, predominantly in males. Multisystem inflammation most commonly affects the skin, eyes, joints, blood vessels, cartilage, and lungs. Patients with VEXAS syndrome may meet diagnostic criteria

Table 1: Clinical characteristics of patients with VEXAS syndrome

Patient	UBA1 variant	Age at Sx onset (years)	Age at Dg (years)	Rheumatol. Dg	Previous Tx	CRP (mg/l)	HGB (g/l)	MCV (fl)	Fever	Weight loss	VTE	Inflammatory involvement							MDS
												Eyes	Arthritis	Skin	GI	Lungs	Chondritis	Vasculitis	
1	c.1221T>C	75	77	RA -	GC/MTX/AZA	58.0	79	103	-	-	-	-	+	+	-	-	-	-	-
2	c.122T>C	65	67	RPC	GC	9.2	121	106	+	-	-	+	-	+	-	-	-	-	-
3	c.121A>C	73	74	CTD	GC	43.0	82	101	-	-	+	-	-	+	-	-	-	-	+
4	c.1430G>C	56	60	RA-	GC/MTX/INF/ TOFA/TCZ	21.0	91	102	+	-	-	-	+	+	-	+	-	+	+
5	c.121A>C	57	67	Sweet's syndrome	GC/MTX/HCQ/ AZA/SAS	21.0	141	88	+	+	-	-	+	+	+	+	-	+	-
6	c.121A>G	68	73	CTD	GC	2.6	106	93	+		+	-	-	+	+	+	-	-	+

Abbreviations: AZA: azathioprine, GC: glucocorticoids, CTD: connective tissue disease, Dg: diagnosis, GI: gastrointestinal, HCQ: hydroxychloroquine, INF: infliximab, MDS: myelodysplastic syndrome, RA-: seronegative rheumatoid arthritis, RPC: relapsing polychondritis, SAS: sulfasalazine, Sx: symptoms, TCZ: tocilizumab, TOFA: tofacitinib, Tx: treatment, VTE: venous thromboembolism

for several rheumatic diseases and/or hematological disorders. Given its heterogeneous clinical manifestations a high degree of clinical suspicion is required for pursuing the diagnosis of VEXAS syndrome; therefore, clinicians must be aware of the clinical features of VEXAS syndrome. The purpose of this study is to describe a series of cases diagnosed in a rheumatology department.

Methods: Institute of Rheumatology is the largest tertiary academic center providing care for patients with all types of inflammatory rheumatic diseases in the Czech Republic. Patients with symptom onset at age ≥40 years with undiagnosed inflammatory conditions, chondritis, unclassified vasculitis, neutrophilic dermatosis and classifiable inflammatory rheumatic diseases, which were a) resistant to standard therapy, b) associated with hematologic disorders or c)associated with atypical inflammatory manifestations for given diagnosis were considered for *UBA1* testing. Retrospective chart review was performed to obtain pertinent demographic information and clinical data for patients with detected *UBA1* somatic mutations.

Results: We have tested 22 patients (17 males and 5 females) with suspicious clinical phenotype and were able to detect previously described somatic *UBA1* mutations in five of them. One additional patient with clonal cytopenia and multi-organ inflammatory features (patient 4) harbored a previously undescribed *UBA1* variant in exon 14, which proved pathogenic in enzymatic analyses (1). Clinical features of individual patients are summarized in Table 1. All patients were males with a median age at symptom onset 66.5 years (IQR 57, 73) and median duration of symptoms prior to VEXAS syndrome diagnosis 3 years (IQR 2, 5). All patients were treated for a presumptive rheumatologic diagnosis with glucocorticoids and three patients received various other immunosupressants prior to the diagnosis of VEXAS syndrome. Myelodysplastic syndrome was diagnosed based on bone marrow biopsy in three patients, two additional patients had macrocytic anemia. Notably no cytopenia and normal MCV were present in one patient with longstanding inflammatory symptoms.

Conclusion: VEXAS syndrome presents with heterogenous clinical manifestations and should be considered in rheumatology patients with corresponding inflammatory phenotype even in the absence of hematologic abnormalities. 1) Stiburkova B, et al.Novel Somatic UBA1 Variant in a Patient With VEXAS Syndrome. Arthritis Rheumatol. 2023 Feb 10. doi: 10.1002/art.42471. Epub ahead of print.

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Abstract Number: 1922

Use of Plasma with High Titer Neutralizing Autoantibodies to Type I Interferons in Patients with Severe Refractory Flare-up of Hidradenitis Suppurativa as Novel Passive Immunotherapy Approach: Trial Protocol

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

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Background/Purpose: Hidradenitis suppurativa (HS) is a multifactorial auto-inflammatory disorder with a prevalence of 1% in North American and European populations. HS may be associated with various systemic inflammatory conditions including arthritis. Transcriptome analyses of inflammatory pathways and single-cell RNA sequencing of injured skin found upregulation of type I interferon (IFN)-regulated genes (IFN signature). Plasma from healthy donors may contain autoantibodies (Abs) neutralizing type I IFN (alpha and/or omega). In patients with systemic lupus erythematosus (SLE), the presence of these antibodies has been associated with less severe disease. We hypothesize that these Abs provide a potential therapeutic strategy in patients with severe refractory flare-up of HS. Thus, we aim to evaluate the feasibility, safety, and to collect preliminary evidences of efficacy of plasma with neutralizing Abs to type I IFN in patients with severe refractory HS.

Methods: We propose a multicentre prospective phase I-II trial in adult patients with severe refractory flare-up of HS (Hurley stage III). This will be a two-level dose escalation (1 or 2 plasmas) trial combining safety (classic 3+3) and efficacy criteria (Fleming two-stage design), with priority given to safety. The total number of patients enrolled will range from 2 (if more than 1 severe adverse event) to 17 patients. Each patient will receive plasma from healthy donors identified as harboring high titers of neutralizing Abs against IFN. The primary endpoint will combine occurrence of serious adverse events and evidence of IFN alpha neutralization at Day 2 (D2) (> 90% neutralization of IFN alpha by the recipient's plasma). Secondary endpoints will be clinical response (defined as at least a 50% reduction in the abscess and inflammatory nodule count), disease activity score (HS-PGA, IHS4, HiSCR), pain intensity, health-related quality of Life (DLQI) and patient satisfaction (Patient Satisfaction Index and Treatment Satisfaction Questionnaire for Medication). IFN alpha neutralization will also be evaluated at hour 1 (after transfusion) and days 7, 14, 21 and 28. Other type I IFN-associated criteria, including anti-IFN alpha auto-Abs and IFN alpha levels at day 0 (pre-transfusion), hour 1 and days 2, 7 14, 21 and 28 will be part of secondary objectives and IFN signature will be assessed in biopsies of HS skin lesion, before and after transfusion.

Results: Expected results: plasma dose escalation will be based on the safety and the transient neutralization of circulating type I IFN. This neutralization is likely to impact the inflammatory response observed in these patients, as well as the associated lesions and pain.

Conclusion: To our knowledge, this will be the first trial assessing the potential for plasma with high titer neutralizing Abs to type I IFN to treat auto-inflammatory diseases. It may open opportunities for such passive immunotherapy in diseases characterized by interferon signature such as HS and SLE.

Disclosure: C. Vauchy: None; **M. Desmarets**: None; **P. Bastard**: None; **A. Puel**: None; **P. Richard**: None; **J. Casanova**: None; **P. Tiberghien**: None; **E. Toussirot**: None; **F. Aubin**: None.

Abstract Number: 1923

Prevalence and Patterns of Comorbidities in Different Rheumatic Diseases: A Study from Tertiary Healthcare Centre

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

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Session Time: 9:00AM–11:00AM

Background/Purpose: The prevalence of comorbidities in rheumatic diseases may vary by disease and geographic region. This study aimed to investigate the comorbidities associated with rheumatoid arthritis (RA), ankylosing spondylitis (AS), primary Sjögren's syndrome (PSS) and systemic lupus erythematosus (SLE).

Methods: Data from consecutive patients attending a tertiary care facility between 2020 and 2021 were analyzed. Patients diagnosed with RA, AS, PSS and SLE based on established criteria were included in the study

Table 1 Prevalence of comorbidities in inflammatory rheumatic patients

	Rheumatoid Arthritis	Ankylosing spondylitis	Primary Sjogren's (PSS)	Systemic lupus Erythematosus (SLE)	Total
Total number	N=1000	N=100	N=44	N=203	N=1347
F: M	880:120 (7:1)	27:73 (1:3)	42:2 (21:1)	191:12 (16:1)	1140:207 (6:1)
Age (mean + SD) years	47.68 ±11.46	37.2 ±14.06	47 ±11.00	34.17 ±11.30	41.51
ESR (mean) mm/ Hour	52.69 ± 26.8	31.21 ±16.12	41±26 mm/hour	21±26	38.23
Hypertension	11% (109/1000)	8% (8/100)	18.2% (8/44)	9.9 % (20/203)	10.7% 145/1347
Hypothyroidism	8.5% (85/1000)	10% (10/100)	15.9% (7/44)	27.1% (55/203)	11.6% (157/1347)
Diabetes	7% 70/1000	21% 21/100	6.8% (3/44)	4.4% (9/203)	7.6% (103/1347)
Skin	0.8% 8/1000	14 % (14/100)	4.6% (2/44)	1.5% (3/203)	2% (27/1347)
Ischemic heart Disease	0.1% 1/1000	0	0 % (0/44)	0.5% (1/203)	0.15% 2/1347
Osteoporosis	0.1 % (1/1000)	0	0% (0/44)	0% (0/203)	0.08% 1/1347
Surgery	2% 20/1000	9% (9/100)	2.3% (1/44)	0%	2.2% (30/1347)
Cancer	2/100 0.02%	2/100 (2%)	0%	0%	0.03% 4/1347
Tuberculosis	10 10/1000	2 2/100	1 1/47	0	0.09% 13/1347

Results: A total of 1347 patients (Table 1) were analyzed in this study. In patients with inflammatory rheumatic diseases (N=1347), hypertension (10.7%) and hypothyroidism (11.6%) were the most common comorbidities. When individually assessed for specific diseases, patients with rheumatoid arthritis (RA) (N=1000) had hypertension as the most common comorbidity (11%), followed by hypothyroidism (8.5%). Likewise, patients with ankylosing spondylitis (AS) (N=100) showed a similar pattern, with hypertension and hypothyroidism being the most common comorbidities. Patients with Sjögren's syndrome (N=44) showed a higher prevalence of hypertension (18.2%) and hypothyroidism (15.9%). In patients with systemic lupus erythematosus (SLE) (N=203), the prevalence of hypothyroidism (27.1%) and hypertension (9.9%) was higher, while diabetes was less common The overall prevalence of hypertension ranged from 8 to 12%, with the highest prevalence being found in primary Sjögren's syndrome (18.2%). SLE had the highest prevalence of hypothyroidism (27.1%), which was two to three times higher compared to other rheumatic diseases, likely reflecting the increased incidence of autoimmune thyroiditis in this population. In contrast, the prevalence of diabetes was lower in SLE, possibly reflecting the younger age of the patients. The relatively younger age group may also explain the lower prevalence of comorbidities such as cancer, osteoporosis, and ischemic heart disease in the study population Overall, the prevalence and pattern of comorbidities in this study were relatively lower compared to internationally published studies that included populations from different ethnic backgrounds. These findings underscore the distinct patterns of comorbidities among various rheumatic diseases, likely influenced by underlying disease characteristics. Additionally, the younger age group in the study population with fewer comorbidities emphasizes the importance of early diagnosis and optimal management of rheumatic diseases to prevent the development of comorbidities.

Conclusion: Prevalence and pattern of comorbidities in rheumatic diseases vary between different diseases and populations. Understanding these differences is crucial for tailoring treatment strategies and improving patient outcomes.

Disclosure: S. Ramteke: None; **s. Ramteke**: None; **S. Yadav**: None.

Abstract Number: 1924

Impact of the COVID-19 Pandemic on Clinical and Psychosocial Features of Patients with UCTD

Caroline Siegel[1], Lucy Masto[1], Amaya Smole[1], Bessie Stamm[1], JoAnn Vega[1], Dongmei Sun[1], Deanna Jannat-Khah[1], Michael Lockshin[2], Lisa Sammaritano[2] and Medha Barbhaiya[2], [1]Hospital for Special Surgery, New York, NY, [2]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
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Session Time: 9:00AM–11:00AM

Background/Purpose: The early COVID-19 pandemic led to physical and psychological burdens for patients with systemic rheumatic diseases, whether or not they had had COVID-19. To assess the impact of this public health crisis on people with UCTD, we compared demographic, clinical and psychosocial features between patients enrolled in our UCTD registry before versus after the initial wave of the COVID-19 pandemic in New York City.

Methods: This retrospective cohort study included patients enrolled in an academic hospital-based UCTD registry with positive ANA, ≥1 sign/symptom of a CTD, who do not meet ACR/EULAR-endorsed classification criteria for SLE, RA, SSc, Primary Sjögren's, Idiopathic Inflammatory Myopathy, or 2006 Revised Sapporo Criteria for APS. We collected demographic information from patients and clinical characteristics from chart review. Upon enrollment, participants completed the 36-Item Short Form Health Survey (SF-36) to assess health-related quality of life (HRQoL), General Anxiety Disorder-7

(GAD-7), Beck Depression Inventory (BDI), and Fatigue Severity Scale (FSS). We compared demographic, clinical, and psychosocial variables between participants enrolled April 2018-February 2020 ("pre-COVID-19") to those enrolled March 2020-May 2023 ("post-COVID-19"). We used multivariable linear regression to evaluate the association between enrollment date (before vs. after pandemic onset) and HRQoL (i.e. SF-36 physical component summary [PCS] and mental component summary [MCS] scores).

Results: There were 78 patients with UCTD: median age 49.5 years [IQR 34.3, 57.8], 96% female, 74% White race, 74% non-Hispanic/Latino ethnicity. There were no differences in demographics, CTD manifestations, comorbidities, or medications between groups [**Table 1**].

In the post-COVID-19 group, the SF-36 'social functioning' score was higher (i.e. better) than in the pre-COVID-19 group (median [IQR] 62.5 [50.0, 87.5] vs. 50.0 [37.5, 75.0], p=0.03). The post-COVID-19 PCS and MCS scores were numerically higher (PCS: 42.3 [32.3, 50.1] vs. 34.0 [27.3, 46.2], p=0.09; MCS: 45.9 [35.6, 52.8] vs. 44.1 [29.8, 46.6], p=0.06). The post-COVID-19 vs. pre-COVID-19 group had a higher frequency of BDI-defined mild depression and a lower frequency of moderate/severe depression (p=0.04); GAD-7 and FSS scores did not differ between groups [**Table 2**].

Table 1. Clinical Characteristics, COVID-19 Risk Factors, and Medication Use in "Pre-COVID-19" vs. "Post-COVID-19" UCTD Groups

Characteristic	Overall (N=78)	Pre-COVID-19 (N=41)	Post-COVID-19 (N=37)	p-values
Demographics				
Age	49.5 [34.3, 57.8]	51.0 [37.0, 58.0]	47.0 [33.0, 57.0]	0.59
Female Sex	75 (96.2)	40 (97.6)	35 (94.6)	0.93
Race (N=74)				0.13
• White	58 (74.4)	27 (65.9)	31 (83.8)	
• Non-White	16 (20.5)	12 (29.3)	4 (10.8)	
Ethnicity (N=77)				0.89
• Hispanic/Latino	19 (24.4)	10 (24.4)	9 (24.3)	
• Not Hispanic/Latino				
BMI	23.9 [21.3, 30.25]	25.6 [21.8, 32.3]	23.6 [21.0, 28.0]	0.20
CTD Manifestations[1]				
Arthralgia	69 (88.5)	37 (90.2)	32 (86.5)	0.87
Raynaud's	37 (47.4)	22 (53.7)	15 (40.5)	0.23
Nonspecific rash	31 (39.7)	15 (36.6)	16 (43.2)	0.71
Immunologic Disorder[2]	29 (37.2)	16 (39.0)	13 (35.1)	0.82
• Anti-dsDNA antibody	10 (12.8)	7 (17.1)	3 (8.1)	0.40
• Anti-Sm antibody	2 (2.6)	1 (2.4)	1 (2.7)	1
• aPL	22 (28.2)	11 (26.8)	11 (29.7)	0.81
Sicca symptoms	24 (30.8)	8 (19.5)	16 (43.2)	0.10
Myalgia	23 (29.5)	13 (31.7)	10 (27.0)	0.84
Alopecia	21 (26.9)	15 (36.6)	6 (16.2)	0.71
Hematologic Disorder	20 (25.6)	12 (29.3)	8 (21.6)	0.60
Nonerosive Arthritis	18 (23.1)	8 (19.5)	10 (27.0)	0.59
Photosensitivity	13 (16.7)	8 (19.5)	5 (13.5)	0.32
Pleuritis or Pericarditis	7 (9.0)	5 (12.2)	2 (5.4)	0.44
Malar Rash	4 (5.1)	1 (2.4)	3 (8.1)	0.34
Discoid Rash	2 (2.6)	1 (2.4)	1 (2.7)	1
Oral ulcers	2 (2.6)	2 (4.9)	0	0.52
COVID-19 Risk Factors				
Ever smoker (n=70)	19 (24.4)	12 (29.3)	7 (18.9)	0.57
Cardiac comorbidity[3]	13 (16.7)	6 (14.6)	7 (18.9)	0.84
Pulmonary comorbidity[4]	18 (23.1)	10 (24.4)	8 (21.6)	0.98
Medications (Active)				
Systemic corticosteroids	15 (19.2)	8 (19.5)	7 (18.9)	1
Antimalarial	19 (24.4)	9 (22.0)	10 (27.0)	0.79
Immunosuppressive	10 (12.8)	6 (14.6)	4 (10.8)	0.87
• Biologics, small molecules, IVIG	4 (5.1)	2 (4.9)	2 (5.4)	
• Disease-modifying antirheumatic drugs	6 (7.7)	4 (9.8)	2 (5.4)	

Data are represented by median [IQR] or n (%); p-values <0.05 was statistically significant.
1. All criteria-based manifestations defined as per 1997 ACR Classification Criteria for SLE.
2. Sub-categories not mutually exclusive.
3. Congestive heart failure, coronary artery disease, type 2 diabetes mellitus, hyperlipidemia, hypertension
4. Chronic obstructive pulmonary disease/asthma, interstitial lung disease

After adjustment, the post-COVID-19 group had slightly but not significantly increased PCS (Estimate: 3.32, 95% CI: -1.95 – 8.59, p=0.21) and MCS (Estimate:4.18, 95% CI -0.72 – 9.09, p=0.09) scores compared to the pre-COVID-19 group. BMI was inversely associated with PCS score (Estimate -0.46; 95% CI -0.87 – -0.05, p=0.03) [**Table 3**].

Conclusion: Comparing demographically and clinically similar patients with UCTD enrolled in our registry before and after March 2020, we found that those assessed after the onset of the COVID-19 pandemic had decreased moderate/severe depression and increased social functioning with a trend toward improved HRQoL. Our results suggest that circumstances

Table 2. Assessment of Health-Related Quality of Life, Anxiety, Depression, and Fatigue in "Pre-COVID-19" vs. "Post-COVID-19" UCTD Groups

Metric	Pre-COVID (N=41)	Post-COVID (N=37)	p-value
36-Item Short Form Health Survey (SF-36) – Range 1-100[1]			
Physical Component Summary	34.0 [27.3, 46.2]	42.3 [32.3, 50.1]	0.09
• Physical functioning	70.0 [40.0, 90.0]	80.0 [60.0, 95.0]	0.13
• Role-Physical	0 [0, 100]	25.0 [0, 100]	0.29
• Bodily Pain	42.0 [25.0, 62.0]	51.0 [41.0, 62.0]	0.26
• General Health	42.0 [25.0, 62.0]	52.0 [35.0, 70.0]	0.10
Mental Component Summary	44.1 [29.82, 46.6]	45.9 [35.6, 52.8]	0.06
• Vitality	35.0 [25.0, 50.0]	45.0 [25.0, 65.0]	0.16
• Social Functioning	50.0 [37.5, 75.0]	62.5 [50.0, 87.5]	*0.03*
• Role-Emotional	100 [0, 100]	100 [33.3, 100]	0.71
• Mental Health	68.0 [52.0, 80.0]	76.0 [60.0, 84.0]	0.18
Generalized Anxiety Disorder-7 (GAD-7) – Range 0-21[2]			0.27
• None [0-5]	18 (43.9)	22 (59.5)	
• Mild [6-10]	12 (29.3)	10 (27.0)	
• Moderate/Severe [11-21]	11 (26.8)	5 (13.5)	
Beck Depression Inventory (BDI) – Range 0-63[2]			*0.04*
• Minimal [0-13]	27 (65.9)	26 (70.3)	
• Mild [14-19]	6 (14.6)	10 (27.0)	
• Moderate/Severe [20-63]	8 (19.5)	1 (2.7)	
Fatigue Severity Scale (FSS) – Range 1-7[2]	4.6 [3.2, 6.0]	4.7 [3.0, 5.8]	0.94

Data are represented by median [IQR] or n (%); p-values <0.05 was statistically significant.
1. Higher score corresponds with better health state. 2. Higher score corresponds with worse health state.

Table 3. Linear Regression Models Evaluating the Association Between "Post-COVID-19" vs. "Pre-COVID-19" Groups, Demographics, and Health-related Quality of Life Summary Scores

Characteristic	Estimate	95% Confidence Interval	p-value
Model 1 Outcome: SF-36 Physical Component Summary Score[1]			
Date of Enrollment			0.21
• Pre-COVID-19	*Referent*		
• Post-COVID-19	3.32	-1.95 – 8.59	
Age	-0.03	-0.22 – 0.16	0.73
Race			0.85
• White	*Referent*		
• Non-white/Other	0.63	-5.92 – 7.18	
Ethnicity			0.51
• Not Hispanic/Latino	*Referent*		
• Hispanic/Latino	1.99	-4.05 – 8.04	
BMI	-0.46	-0.87 – -0.05	*0.03*
Model 2 Outcome: SF-36 Mental Component Summary Score[1]			
Date of Enrollment			0.09
• Pre-COVID-19	*Referent*		
• Post-COVID-19	4.18	-0.72 – 9.09	
Age	0.06	-0.12 – 0.24	0.51
Race			0.85
• White	*Referent*		
• Non-white/Other	2.32	-3.78 – 8.42	
Ethnicity			0.64
• Not Hispanic/Latino	*Referent*		
• Hispanic/Latino	-1.31	-6.9 – 4.31	
BMI	-0.35	-0.73 - 0.03	0.07

1. Scores range from 1-100; higher score corresponds with better health state.

of the "post-COVID-19" era may have contributed to unexpected improvement in some aspects of UCTD patients' well-being; further research with a larger sample is needed to confirm and elucidate these findings.

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Abstract Number: 1925

Importance of the Patient Pain Experience in Disease Activity Assessment in the Adult SAPHO and Chronic Nonbacterial Osteomyelitis Study

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SESSION INFORMATION
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Background/Purpose: Musculoskeletal pain is a key symptom experienced by patients with SAPHO and chronic nonbacterial osteomyelitis (SAPHO-CNO), yet its relation to disease activity assessment remains unknown. We sought to determine the relation between patient-reported outcome (PRO) measures for pain, and the physician and patient assessments of disease activity in adults with SAPHO-CNO.

Methods: Adults (≥18 years of age) with SAPHO-CNO enrolled in the SAPHO-CNO study (SCS), a prospective longitudinal observational study, completed 5 PRO instruments for the assessment of pain: 1) global pain in SAPHO-CNO by the numeric rating scale (NRS, 0-10); 2) pain scale of the Short Form 36-item survey (SF-36) (0-100); 3) Patient-Reported Outcomes Measurement Information System (PROMIS) pain interference short form (SF) (6a v1.1); 4) PROMIS nociceptive pain quality SF (5a v2.0); and 5) PROMIS neuropathic pain quality SF (5a v2.0). Subjects completed a patient global assessment (NRS, 0-10) for overall and musculoskeletal (MSK) disease activity in SAPHO-CNO. Physician-assessed disease activity was measured by the physician global scale (NRS, 0-10) for overall and MSK symptoms. Correlational analyses using Spearman's rank correlation coefficient (rho, *r*) were performed between 1) physician-assessed and patient-reported disease activity (for overall and MSK), and 2) disease activity (by physician and patient) and PRO pain measures. P-values less than 0.05 were considered significant.

Results: Fifty-eight subjects in the SCS completed their assessments at baseline and were included in this cross-sectional analysis. Baseline characteristics of the adult SAPHO-CNO cohort are summarized in Table 1. We observed weak correlation between physician-assessed and patient-reported overall ($r(56)$=0.37, p=0.005) and MSK ($r(56)$=0.34, p=0.009)

disease activity in SAPHO-CNO. Next, we observed a weak correlation for 4 out of 5 PRO pain measures and physician-assessed disease activity, except for PROMIS pain interference which showed moderate correlation (r ~0.44-0.46) with physician-assessed overall and MSK disease activity (Table 2). In contrast, there was moderate/good correlation for 3 out of 5 PRO pain measures, and strong correlation of pain by NRS with overall (r = 0.71) and MSK (r = 0.76) disease activity by the patient (Table 2). The PROMIS neuropathic scale showed weak correlation with patient-reported disease activity; additionally, this scale had a high floor effect (29.3% of subjects had the lowest score).

Conclusion: The physician global assessment of disease activity in adult SAPHO-CNO does not fully capture patient pain and likely misses important disease experiences from the patient perspective. For pain quality assessment, the PROMIS neuropathic pain scale may not be suitable. Incorporating patient-reported pain measures will be important for the development of a future composite disease activity index in adult SAPHO-CNO.

Table 1. Baseline demographics and disease characteristics of adults with SAPHO-CNO.

	Adults with SAPHO-CNO (n = 58)
Age, median (IQR), years	33 (24-49)
Gender, female (%)	52 (86.2)
Non-Hispanic (%)	56 (96.6)
White (%)	53 (91.4)
Time from diagnosis, median (IQR), years	5 (3-10)
MSK involvement, n (%)	58 (100)
Skin involvement, n (%)	
PPP	16 (27.6)
PSV	14 (24.1)
HS	6 (10.3)
Acne (severe)	7 (12.1)
Patient Global Assessment, median (IQR) (NRS, 0-10)	
Overall Disease Activity in SAPHO-CNO	3.5 (2.0-6.5)
MSK Disease Activity in SAPHO-CNO	3.5 (1.4-7.0)
Physician Global Assessment, median (IQR) (NRS, 0-10)	
Overall Disease Activity in SAPHO-CNO	3.0 (1.4-6.0)
MSK Disease Activity in SAPHO-CNO	2.8 (1.0-5.0)
Patient-reported Outcome Measures for Pain.	
Pain in SAPHO-CNO (NRS, 0-10)	5.0 (2.5-7.5)
SF-36 Pain Scale (0-100)	57.5 (45.0-71.9)
PROMIS Pain Interference	58.0 (53.3-65.1)
PROMIS Neuropathic Pain Quality	44.1 (37.2-48.2)
PROMIS Nociceptive Pain Quality	53.5 (44.6-58.0)

SAPHO: Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis; CNO: chronic nonbacterial osteomyelitis; IQR: interquartile range; MSK: musculoskeletal; PPP: palmo-plantar pustulosis, PSV: psoriasis vulgaris, HS: hidradenitis suppurativa, NRS: numeric rating scale; SF-36: Short Form 36-item survey; PROMIS: Patient-Reported Outcomes Measurement Information System. Scores are reported as median with interquartile range (IQR). For NRS, rating is from 0 (no active disease, no pain) to 10 (worst active disease, worst pain). All PROMIS measures are short forms.

Table 2. Correlations between physician- and patient-assessed disease activity with patient-reported measures of pain in adults with SAPHO-CNO.

	Physician Global Disease Activity		Patient Global Disease Activity	
	Overall	MSK	Overall	MSK
PRO Measure for Pain:	*r*	*r*	*r*	*r*
Pain in SAPHO-CNO (NRS)	0.30*	0.32*	0.71*	0.76*
SF-36 Pain Scale	-0.36*	-0.37*	-0.61*	-0.63*
PROMIS Pain Interference	0.46*	0.44*	0.61*	0.58*
PROMIS Neuropathic Pain Quality	0.23	0.14	0.30*	0.35*
PROMIS Nociceptive Pain Quality	0.30*	0.38*	0.55*	0.53*

SAPHO: Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis; CNO: chronic nonbacterial osteomyelitis; MSK: musculoskeletal; PRO: patient-reported outcome; *r*: Spearman's rank correlation coefficient; NRS: numeric rating scale; SF-36: Short Form 36-item survey; PROMIS: Patient-Reported Outcomes Measurement Information System. *p-value < 0.05.

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Abstract Number: 1926

Use of 18F-FDG PET in Assessing Response to Treatment in Adults with Pulmonary Sarcoidosis: A Systematic Literature Review

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

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Background/Purpose: Sarcoidosis is a chronic, multisystem, granulomatous disease commonly affecting the lungs. Immunosuppressants, particularly corticosteroids, are the mainstay of treatment. Symptoms, severity and response to treatment can follow a heterogenous pattern, presenting a clinical challenge. Positron Emission Tomography (PET) imaging with the use of Fludeoxyglucose F18 (18F-FDG) has been recommended by the American Thoracic Society guidelines in choosing an appropriate biopsy site.Use of 18F-FDG PET in disease monitoring remains uncertain. We undertook a systematic literature review (SLR) on the use of 18F-FDG PET in assessing response to treatment in adults with pulmonary sarcoidosis.

Methods: The protocol was registered on Prospero (CRD42023416412). All published articles discussing PET CT use in response to treatment in pulmonary sarcoidosis were included, until March 2023, in Medline, Embase, and Cochrane Databases. The search was restricted to English-language articles. All article types were eligible except opinion pieces, case reports, case series of ≤10 patients and reviews. Articles meeting inclusion criteria were examined by one author, with 20% validity screening. In addition to basic demographics, information was extracted on: Siltzbach classification of subjects; treatment; additional tests performed; time between baseline and follow-up PET CT.

Results: Initially, 1759 articles were retrieved with 8 ultimately included (4 prospective; 3 retrospective; 1 case-control). A pooled total of 260 patients with pulmonary sarcoidosis were included, 40.7% male, mean age 47.0 years (SD 3.4). Study populations were from France (n=1), China (n=1), The Netherlands (n=1), Turkey (n=1), India (n=2) and Serbia (n=2). Treatment for pulmonary sarcoidosis varied markedly amongst the included studies, including: infliximab (n=1) and systemic corticosteroids (n=3); treatment was unknown in 4 studies. All studies used 18F-FDG-PET, except one in which gallium-67 scintigraphy was also used. Time between baseline PET CT and follow-up scan ranged from 2.8 weeks to 12 months. Compared to clinical response, sensitivity of PET CT in determining response to treatment ranged from 56% to 100%, with mean sensitivity of 75.3% (SD 16.0). Additional tests performed across all studies included spirometry, chest radiograph, serum angiotensin-converting-enzyme levels, soluble interleukin-2 receptor levels. All studies concluded that PET CT correlates with clinical response to treatment and is useful for prognostication, aside from one study which concluded that metabolic response on PET CT can predict future risk of relapses but does not correlate with clinical response.

Conclusion: To our knowledge, this is the first SLR summarising the use of 18F-FDG PET in assessing response to treatment in adults with pulmonary sarcoidosis. 18F-FDG-PET is useful in determining response to treatment and prognosis in pulmonary sarcoidosis, and may have a role in predicting future response. Further work in greater patient numbers is required to confirm the utility of PET CT in the management of pulmonary sarcoidosis.

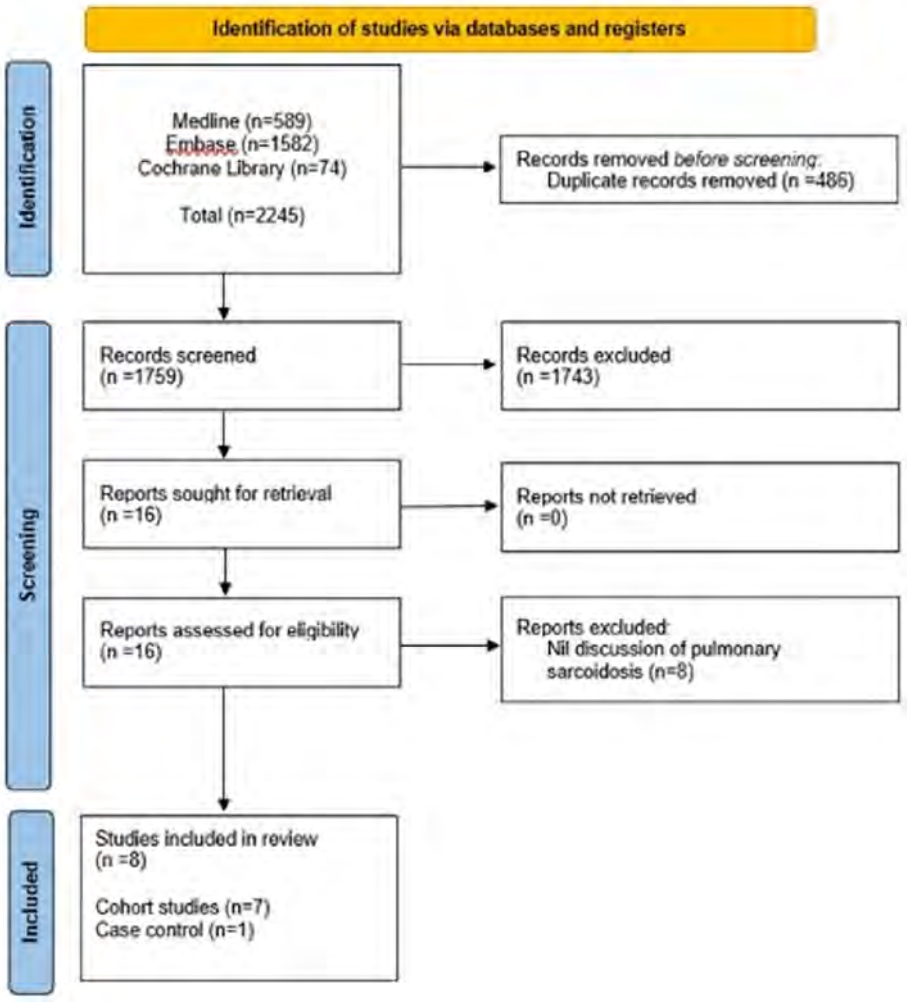

Figure 1: Flow diagram of stages of systematic literature review. Cochrane Library encompasses library of: systematic reviews; systematic review protocols; controlled clinical trials.

Disclosure: K. Kouranloo: None; **M. Krishnakumar**: None; **M. Dey**: None.

Abstract Number: 1927

Manifestations, Management and Outcomes of Interstitial Lung Disease Associated with Anti-synthetase Syndrome: A Systematic Literature Review

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Background/Purpose: Anti-synthetase syndrome (ASS) is a chronic autoimmune inflammatory condition, characterized by myositis, interstitial lung disease (ILD), arthritis, Raynaud's phenomenon and mechanic's hands. This systematic review (SR) aims to summarise the manifestations, management and outcomes of ILD associated with ASS (ASS-ILD).

Methods: The protocol was registered on Prospero (CRD42023416414). Articles discussing management and outcomes of ASS-ILD, published 1946 until April 2023, were included. Medline, Embase and Cochrane Databases were searched. Case reports, case series of < 10, reviews and conference abstracts were excluded. Articles meeting inclusion criteria were examined by two authors. Data on demographics, treatment, antibody serology, physiological and radiological findings at baseline and one-year were extracted.

Results: Initially, 451 articles were retrieved with 10 included (9 cohort, 1 case series; Figure 1). Risk of bias assessment established studies were of variable quality (Table 1). A total of 514 patients were included, 67.8% female, mean age 52.4 (SD 4.6) years at ILD induction therapy. Cohorts were from: Europe (n=5); North America (n=3); China (n=2). Patients had the following myositis-associated autoantibodies: Jo-1 (48%); PL7 (15.1%); PL12 (29.2%), EJ (15.9%); OJ (3.3%). In addition, 143 patients had anti-Ro52 positivity. Baseline high-resolution computed tomography (where available) showed: non-specific interstitial pneumonia (NSIP) (n=220; 42.8%); organising pneumonia (OP) (n=142; 27.6%); NSIP/OP overlap (n=51; 9.9%); nonspecific interstitial pneumonia (n=34; 6.6%). Of these, NSIP subtype was reported in 12 patients (6 fibrotic, 6 cellular). Pulmonary hypertension was discussed in 2 cohorts, with 6 patients having a confirmed diagnosis. Patients received the following drugs for induction (with glucocorticoids [GC]): cyclophosphamide (CYC) (n=136; 26.5%); rituximab (RTX) (n=88; 17.1%); calcineurin inhibitors (n=84; 16.3%); other disease-modifying anti-rheumatic drugs (n=183; 35.6%); intravenous immunoglobulin (IVIG; n=17; 3.3%); GC only (n=20; 3.9%). Overall median forced vital capacity (FVC) pre-treatment was 52.7% and 68.5% at one year. Overall median diffusion capacity of lungs for carbon monoxide (DLCO) pre-treatment was 44.5% and 49.1% at one year. Due to heterogeneity of methodology and cohorts, direct comparison was not possible for most drugs. Patients treated with RTX had an overall median 12.2% improvement in FVC and 2.9% increase in DLCO at one year. Patients treated with CYC had a 17% and 6.3% increase in FVC and DLCO respectively after one year. In patients receiving IVIG, 7/17 had >10% increase in FVC at one year. 5.4% (n=28) were reported to have died post-treatment due to: infection (n=8) including Pneumocystis [n=2, both post-rituximab]; malignancy (n=3); multiorgan failure (n=2). 15 patients had no reported cause of death.

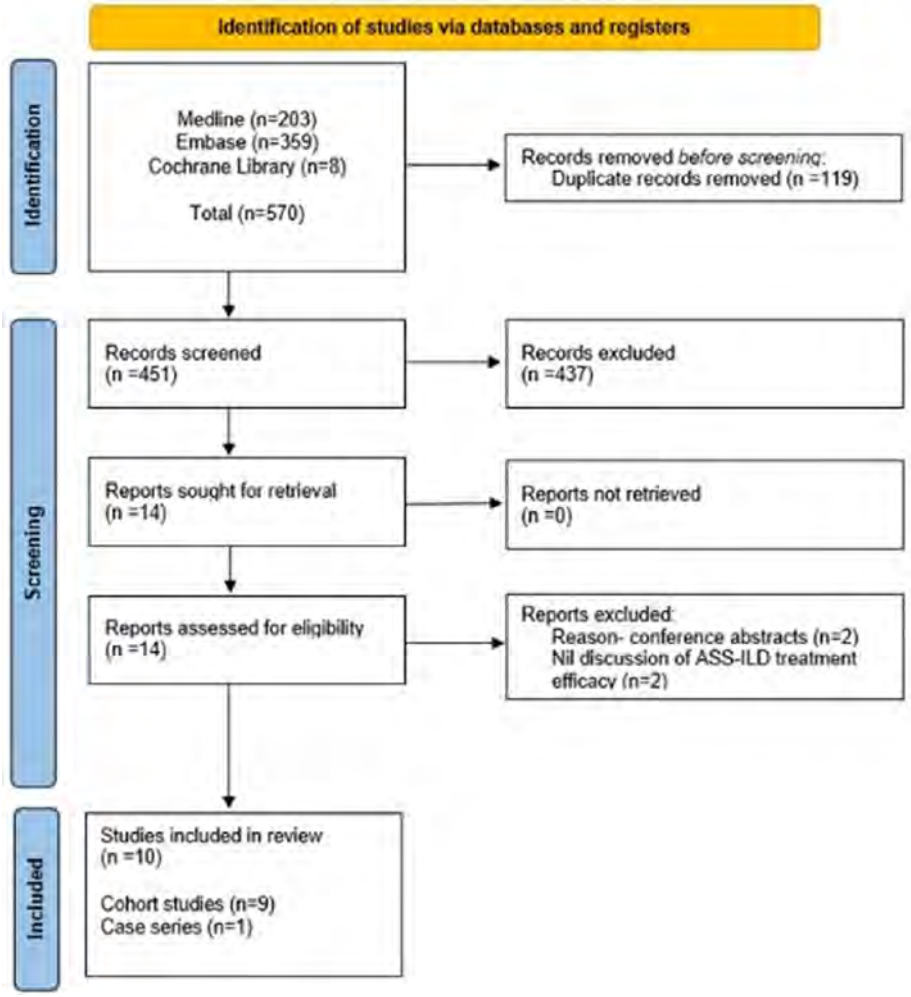

Figure 1: Flow diagram of stages of systematic literature review. Cochrane Library encompasses library of: systematic reviews; systematic review protocols; controlled clinical trials. ASS-ILD: interstitial lung disease associated with anti-synthetase syndrome.

Conclusion: This is the first SR summarising the management and outcomes of ASS-ILD. No significant difference was found between the effectiveness of treatments with regards to physiological respiratory function. More robust trials are required to reduce the morbidity and mortality resulting from ASS-ILD.

Disclosure: K. Kouranloo: None; **M. Dey**: None; **V. Yioe**: None; **L. Spencer**: None; **C. Cotton**: None.

Abstract Number: 1928

Response to Sars-Cov2 Vaccination in Rheumatic and Neurological Patients Treated with Different Immunosuppressive Therapies

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SESSION INFORMATION

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Background/Purpose: Vaccination against SARS-CoV2 has been the primary global strategy to prevent severe forms of this respiratory infection. However, multiple studies have shown that patients undergoing treatment with biological therapies, especially those targeting B lymphocytes, have a poorer response to vaccination. It should be taken into consideration that a lower IgG titer is associated with higher mortality from Covid-19. Objective: To describe the vaccine response rate in patients treated with rituximab (RTX), ocrelizumab (OCR), abatacept (ABT), belimumab (BEL), and compare the response between rheumatic and neurological patients.

Methods: Descriptive study. Rheumatic and neurological patients undergoing treatment with RTX, OCR, ABT, and BEL between January 2020 and July 2022 at the Germans Trias i Pujol Hospital were included. Immunoglobulin G (IgG) levels against the SARS-CoV2 spike protein were quantified, considering >260 BAU/mL as a positive response to vaccination. Variables such as age, vaccination schedule, recent infection, corticosteroid therapy, or synthetic DMARDs were analyzed. Additionally, clinical-demographic variables and risk factors for severe SARS-CoV2 infection were described.

Results: The study included 122 rheumatic patients, of whom 59 received RTX, 45 ABT, and 18 BEL, as well as 17 neurological patients undergoing treatment with OCR and 7 with RTX. The mean age was 51 years, and 72% were women. The most frequent rheumatic diagnoses were rheumatoid arthritis (55), systemic lupus erythematosus (31), small vessel vasculitis (8), among others. All neurological patients had demyelinating diseases such as multiple sclerosis. Concomitant DMARD therapy was received by 48% of the patients studied. 92% of the patients were fully vaccinated (3 or more doses), and 8% had experienced the infection in the previous 3 months. Corticosteroid therapy was received by 49% of the patients, with 92% receiving low-dose corticosteroids. 39% were on DMARDs, with hydroxychloroquine (27%) and methotrexate (19%) being the most common. In rheumatic patients, serology was negative in 40 patients treated with RTX (67%), and 8 with ABT (17%). No patient treated with BEL had negative serology. The median IgG level was 30 BAU/mL in patients undergoing treatment with RTX, 993 BAU/mL with ABT, and 1797 BAU/mL with BEL ($p < 0.001$) (Fig 1). Regarding negative serology, there were no differences in terms of age (RTX p=0.28, ABT p=0.71), corticosteroid use (RTX p=0.67, ABT p=0.25), or DMARDs (RTX p=0.06, ABT p=0.21). In neurological patients, the median IgG level with OCR was 504 BAU/mL, and with RTX it was 361 BAU/mL, compared to 30 BAU/mL in rheumatic patients with RTX (p 0.005) (Fig 2).

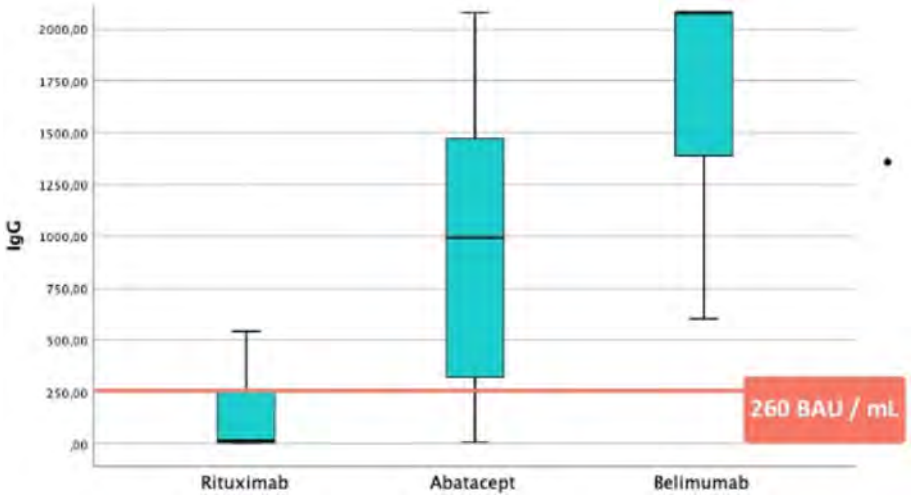

Figure 1. IgG levels aganist SARS-CoV2 spike protein in rheumatic patients treated with Rituximab, Abatacept and Belimumab.

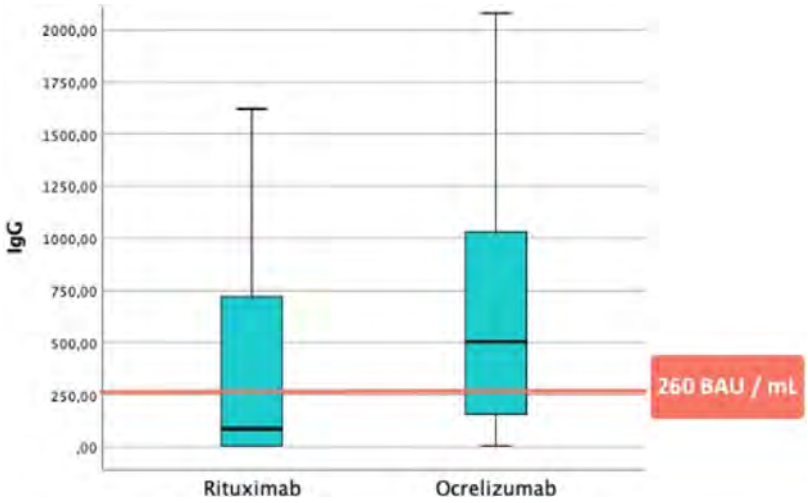

Figure 2. IgG levels aganist SARS-CoV2 spike protein in patients treated with Rituximab and Ocrelizumab.

Conclusion: In our cohort, not all patients undergoing biological treatment exhibit the same vaccine response to SARS-CoV2. Patients receiving RTX show the lowest response, followed by ABT. However, all patients treated with BEL had positive serology. Neurological patients treated with B lymphocyte-targeted therapies showed a greater vaccine response than rheumatic patients. No serological differences were observed depending on the use or non-use of DMARDs, age, or low-dose corticosteroid therapy.

Disclosure: C. Calomarde Gomez: None; **R. Ugena García**: None; **J. Valera**: None; **M. Mena**: None; **M. Esteve**: None; **I. Casas**: None; **j. Dominguez-Benitez**: None; **I. Carabias-Ane**: None; **i. Nuño-Ruiz**: None; **C. ramo-Tello**: None; **J. Santesmases**: None; **L. Mateo Soria**: None; **M. Martinez Morillo**: None.

Abstract Number: 1929

Anakinra Treatment in Idiopathic Recurrent Pericarditis: A Single-center Experience

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Idiopathic recurrent pericarditis (IRP) is defined by recurring episodes of pericardial inflammation without a known cause. This study investigates the safety and efficacy of anakinra, an interleukin-1 inhibitor, as an effective therapy for IRP in cases resistant to conventional therapy.

Methods: A retrospective evaluation of patients treated at our autoinflammatory center between 2011-2023 was conducted. Patient files were examined for demographic, clinical, and treatment response data, including non-steroid anti-inflammatory drugs (NSAIDs), corticosteroids, and colchicine. Monogenic autoinflammatory disease screening was

Table 1. Demographic data on all patients (N=21)

Female n (%)	9 (42.9%)
Male n (%)	12 (57.1%)
Age (mean ± standard deviation)	43.1±16.5
Recurrent Idiopathic Pericarditis n (%)	18 (85.7%)
Post COVID-19 Pericarditis n (%)	1 (4.8%)
Pericarditis Associated with Post COVID-19 Vaccination n (%)	2 (9.5%)

Table 2. Anakinra Treatment in IRP (N=21)

	(mean ± standard deviation)
Duration (months) of the treatment	28.1±28.1
Number of attacks before the treatment	5.57±3.49
The time (months) between the treatment and symptom onset	31,3±38.8
CRP levels before the treatment	196±67.8
CRP levels after the treatment*	2.6±3.15
Attacks during routine doses of anakinra	3 (14.3%)
	n (%)
Increased intervals between the anakinra administration	16 (76.1%)
Anakinra cessation without increasing intervals between administration	5 (23.8%)
Attacks during increasing intervals between administration	9 (56.3%)
Attempted anakinra dose reduction	14 (66.7%)
Attack after anakinra treatment reduction	8 (57.1%)
Anakinra cessation	9 (42.9%)
Side effects (injection site reaction)	4 (19.0%)

*$p<.001$

performed for MEFV, TRAPS, MVK, NLRP3, and NOD2. The study evaluated anakinra treatment in IRP patients unresponsive to conventional therapy. Patients who experienced multiple episodes of pericarditis were diagnosed with recurrent pericarditis.

Results: The study included 21 participants, with 9 (42.9%) female and 12 (57.1%) male patients. The average age of the participants was 43.1±16.5 years. Among the participants, 2 (9.5%) were diagnosed with pericarditis following the COVID-19 vaccine, 1 (4.8%) experienced pericarditis after a COVID-19 infection, and 18 (85.7%) had a diagnosis of IRP. The MEFV mutation analysis revealed that 2 (9.5%) had a mutation in Exon 10, and 4 (19.0%) had a mutation in Exon 2. MEFV mutation carriers did not exhibit typical symptoms of Familial Mediterranean Fever (FMF). Among the participants, 9 (56.3%) were classified as steroid-dependent, 5 (31.3%) were not treated with steroids, and 2 (12.5%) showed no response to steroid therapy. Successful steroid tapering was achieved in 12 (75%) out of 16 patients, and 2 (16.7%) experienced attacks after tapering. Out of 3 patients, 2 (66.6%) successfully discontinued hydroxychloroquine (HQ), while out of the 15 cases, 14 (93.3%) successfully discontinued NSAID treatment. Colchicine treatment was discontinued in 6 (28.6%) out of 21 patients. The participants experienced an average of 5.57±3.49 attacks of pericarditis before starting anakinra. The duration between symptom onset and anakinra treatment initiation was found to be an average of 31.3±38.8 months. The average duration of anakinra treatment was 28.1±28.1 months. In 16 patients (76.1%), the interval between the anakinra administration was increased, among which 9 (56.3%) experienced attacks during this period. An attempt to discontinue anakinra treatment was made in 14 (66.7%) cases, resulting in 8 (57.1%) participants experiencing attacks when anakinra was stopped, and complete discontinuation was achieved in 9 (42.9%) participants. The levels of C-reactive protein (CRP) before anakinra treatment were measured to be an average of 196±67.8, while after anakinra treatment, the average levels were 2.6±3.15. Four patients (19.0%) experienced injection site reactions.

Conclusion: In conclusion, the study adds to the growing body of evidence of the use of interleukin-1 inhibitors, such as anakinra, as a promising treatment modality for RIP in cases resistant to conventional therapy.

Disclosure: Z. Toker Dincer: None; **S. Karup**: None; **E. Yilmaz**: None; **O. Corbali**: None; **S. Ugurlu**: None.

Abstract Number: 1930

Blue Digit Syndrome as the Initial Presentation of Various Diseases: A Case Series

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
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Session Time: 9:00AM–11:00AM

Background/Purpose: Blue Digit Syndrome (BDS) represents the cutaneous manifestation of numerous diseases that cause blue discoloration in one or more fingers in the absence of trauma and with preserved pulses. The diagnosis of the underlying cause is crucial to preserve the affected extremity and treat the underlying disease. While it may not be the most common etiology, many systemic autoimmune and inflammatory diseases can present with cutaneous manifestations such as BDS. These conditions may include connective tissue diseases like systemic sclerosis (SSc), vasculitis, and other rheumatic disorders. Being sometimes the only exploratory finding, diagnosis may be challenging.

This study aimed to define the prevalence of different etiologies in patients with BDS. Additionally, the clinical characteristics, assessment findings, complementary investigations, and patient outcomes were described.

Methods: Ambispective cohort study. All patients admitted to the Rheumatology Department of Hospital Universitari Germans Trias i Pujol for blue digit syndrome between January 2017 and December 2022 were included.

Results: Forty-five patients (20 males and 25 females) were included with a mean age of 56.4 years. 46.7% were smokers. 48.9% had cardiovascular risk factors. The most frequent diagnoses were thromboangiitis obliterans (TAO) (22.2%) systemic sclerosis (SSc) (15.6%), severe atherosclerosis (8.9%), haematological disorder (8.9%) and cryoglobulinemia (8.9%). 10% of cases were considered idiopathic, and 12.5% were multifactorial. To be noted, a patient initially diagnosed of idiopathic blue finger syndrome was ultimately diagnosed with prostate cancer. Half of the cases presented with involvement limited to the upper extremities. 28.9% of patients had systemic symptoms. Examinations included autoimmunity tests, echocardiogram, arteriography, blood analysis among others. Skin biopsies were performed in 13 out of 40 patients, of which 2 out of 13 showed diagnostic findings of cholesterol emboli, 1 out of 13 showed calciphylaxis, 1 out of 13 showed vasculitis, and the remaining cases (9 out of 13) had no specific findings. 56% of the cases resolved with medical treatment. 8 patients (17.8) of patients required surgical amputation of the affected finger.

Conclusion: In our experience, the most common cause of BDS was TAO, followed by SSc. The differential diagnosis is broad and requires multiple complementary investigations, although some may have limited utility and carry the risk of iatrogenic harm. Therefore, a reasoned and systematic diagnostic approach based on initial suspicion is crucial.

Disclosure: R. Ugena García: None; **J. Lluch Galcerá**: None; **C. Calomarde Gomez**: None; **I. Casafont-Sole**: None; **L. Mateo Soria**: None.

Abstract Number: 1931

Anti-Ku Antibodies: A Case Series

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-Ku antibodies (Abs) were initially described in patients with polymyositis and scleroderma. Subsequently, an association has been demonstrated with other systemic autoimmune diseases (SADs), particularly overlap syndromes. However, controversies exist regarding their clinical significance and their relationship with SADs or some of their manifestations. Objective: To describe the clinical and immunological characteristics of a case series of patients with positive anti-Ku antibodies.

Methods: Descriptive study of a cohort of patients from a university hospital with positive anti-Ku antibodies between 2017 and 2022. Clinical variables (Raynaud's phenomenon, arthritis, arthralgia, myalgia, muscle weakness, dyspnea, dysphagia, diffuse interstitial lung disease (DILD)), complementary investigations (pulmonary function tests (PFTs), high-resolution computed tomography (HRCT), capillaroscopy), and autoimmune study (ANA ENA, anti-DNA, complement study, anti-PM scl 75 antibodies, anti-PM scl 100 antibodies, CENP-B, antiphospholipid antibodies, rheumatoid factor (RF), and anti-citrullinated peptide antibodies (ACPA)) were analyzed. Finally, clinical diagnostic orientation, diagnosis based on systemic autoimmune disease (SAD) criteria, or final diagnosis of non-SAD pathologies were recorded.

Results: A total of 17 patients positive for anti-Ku antibodies were identified, of whom 14 were women (82.4%) with a mean age of 57 years and a median follow-up of 43 months. The clinical manifestations presented were as follows: arthralgia (13; 76.5%), arthritis (8; 47.1%), myalgia (6; 35.3%), myositis (2; 11.8%), muscle weakness (2; 11.8%), dysphagia (1; 5.9%), dyspnea (4; 23.5%), and Raynaud's phenomenon (3; 17.6%). All patients had positive ANA, of which 8 cases (47.1%) exhibited a nucleolar pattern, 8 cases (47.1%) showed a fine speckled pattern, and only 1 case had a centromeric dot-like pattern. A total of 8 patients underwent high-resolution computed tomography (HRCT), of which 2 cases (25%) presented a ground-glass opacities pattern, 2 cases (25%) had pulmonary thromboembolism, and 2 cases (25%) had one or multiple neoplastic pulmonary nodules. Pulmonary function tests (PFTs) were performed in 7 cases, with 3 cases (42.9%) showing normal results, 2 cases (28.6%) displaying an obstructive pattern, and 2 cases (28.6%) demonstrating a restrictive pattern. Capillaroscopy was performed on 4 patients (3 normal results, 1 non-specific pattern). A diagnosis of neoplasia was established in 5 cases (29.4%). Only 6 patients (35.3%) met the criteria for systemic autoimmune disease (SAD), including 3 cases of systemic lupus erythematosus (one of them with associated antiphospholipid syndrome), 2 cases of Sjögren's syndrome, and 1 case of systemic sclerosis.

Conclusion: In our case series, the clinical and laboratory characteristics were highly heterogeneous. The presence of anti-Ku antibodies was associated with the diagnosis of a systemic autoimmune disease (SAD) in just over one-third of the cases.

Disclosure: R. Ugena García: None; **C. Calomarde Gomez**: None; **J. Climent**: None; **L. Mateo Soria**: None.

Abstract Number: 1932

The Association Between Initial Ferritin and Complications from Adults Onset Stills Disease and Intensive Care Unit Admission

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
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Session Time: 9:00AM–11:00AM

Background/Purpose: Adult Onset Still's Disease (AOSD) is an autoinflammatory disease characterized by quotidian fever, arthralgia, and a salmon colored rash. Due to its rarity, there is a dearth of knowledge regarding this patient population, clinical presentation, complications, and outcomes.

Methods: Data was collected retrospectively from the Hospital Corporation of America database from 2016 to 2021. Adult patients with a diagnosis of AOSD and without other autoimmune diseases were included in the study. On these subjects, characteristics such as gender and age were collected as well as clinical information such as presenting laboratory values, outcomes, and complications were analyzed.

Results: There were 185 subjects included in this study, 69.7% were women and 67.6% were white in race (Table 1). About 10% of subjects were on home biologic medications prior to presentation. Initial laboratory findings included mean white blood cell count of 12.84 +/- 6.91, ESR 55.60 +/- 39.26, CRP 16.66 +/- 42.77, ferritin 6,793.06 +/- 11,012.50, ALT 81.85 +/- 164.93, and AST 97.83 +/- 264.52 (Table 2). Forty-four subjects were admitted to the Intensive Care Unit (ICU). While there is no statistically significant difference in those who were admitted to the ICU and not admitted in initial CRP and ESR values, there is a statistically significant difference in initial ferritin. Those who had to be admitted to the ICU had an initial ferritin 5,974.597 units higher (p=0.048). Subjects who had hemophagocytic lymphohistiocytosis (HL) (p=0.001), disseminated intravascular coagulation (DIC) (p=0.013), pleural effusions (p < 0.001) had a statistically significant frequency

Table 1: Patient Demographics: including gender, race/ethnicity, and mean age.

		Number	Percentage
Gender	Male	56	30.3
	Female	129	69.7
Race/ethnicity	White	125	67.6
	Non-white*	60	32.4
Mean Age		47	

*The non-white groups were too small to further stratify

Table 2: Initial Laboratory Values: including liver enzymes, inflammatory markers, and complete blood count mean and standard deviations

		Mean	SD
Liver Enzymes	ALT	81.85	164.93
	AST	97.83	264.52
Inflammatory Markers	ESR	55.60	39.26
	CRP	16.66	42.77
	Ferritin	6,793.06	11,012.50
CBC	Hemoglobin	11.82	2.22
	WBC	12.84	6.91
	Platelet count	246.02	119.97

Table 3: Complications and Admission to ICU: list of different complications found in this sample with percent admitted to ICU. Some of the rates of admission to ICU are significant and listed below

	# of encounters	% admit to ICU
Hemophagocytic lymphohistiocytosis	9	67
Disseminated intravascular coagulation	2	100
Pleural effusion	8	75
Pulmonary hypertension	5	40
Pericardial effusion	7	43
Myocarditis	2	50
Cardiac tamponade	2	100
Hepatic failure	7	57
Significant	**P value**	**Not significant**
Hemophagocytic lymphohistiocytosis	0.001	Pericarditis
Disseminated intravascular coagulation	0.013	ARDS
Pleural effusions	<0.001	Hemolytic anemia

[a]ICU admission was used as a surrogate for mortality as mortality in this group was low
There were no patients with thrombotic thrombocytopenic purpura or interstitial pneumonitis

of being admitted to the ICU; whereas those with pericarditis, hemolytic anemia, and acute respiratory distress syndrome (ARDS) did not (Table 3).

Conclusion: The demographic results of white women being at highest risk for disease is consistent with current data. Similarly, the laboratory results of having leukocytosis, transaminitis, and elevated inflammatory markers are also consistent with prior studies. As only 6 subjects passed, admission to the intensive care unit (ICU) was used as a surrogate for morbidity from complications. Admission to the ICU was statistically associated with having a higher ferritin; however, ferritin was only collected in 92 subjects. While the average increase was about 6,000 units higher, this is likely an underestimate as the maximum laboratory value is 40,000. The complications of HL, DIC, and pleural effusions were associated with admission to the ICU, while pericarditis, hemolytic anemia, and ARDS were not. As those with AOSD tend to have delayed diagnosis and poor outcomes as a result, it is paramount that more studies are done to aid in management.

Disclosure: O. Yang: None; **C. Bui**: None; **S. Kubomoto**: None; **N. Ayutyanont**: None; **K. Vickery**: None; **K. Venkat**: None.

Abstract Number: 1933

Analysis of IgG4-Related Disease in a Diverse Long Island Population: Insights from the Rheumatology Clinic

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SESSION INFORMATION
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Background/Purpose: IgG4-related disease (IgG4RD) is an immune-mediated disease characterized by dense lymphoid-lymphoplasmacytic infiltrates with high IgG4-positive plasma cells with heterogeneous clinical manifestations. The data on IgG4-RD phenotypes variation is mounting but limited to Caucasian and Asian population. In our study we describe a IgG4-RD clinical and immunosuppressive (IS) treatment in four major ethnic groups.

Table 1. Demographic and clinical phenotypic IgG4RD variations between different ethnic groups.

	Caucasian (n = 25)	Asian (n = 15)	Black American (n = 9)	Hispanic (n = 7)	Total (n = 56)	P-value
Demographic						
Age (Mean ± SDV)	62±15	57±17	64±19	65±6	61±15	0.58
Male: Female	15:10	7:8	4:5	4:3	30:26	0.36
Diagnostic criteria met (% patients (n))						
Definite	32% (8)	40% (6)	33% (3)	29% (2)	34% (19)	0.44
Probable	40% (10)	40% (6)	60% (5)	29% (2)	41% (23)	0.66
Possible	20% (5)	7% (1)	0% (0)	42% (3)	16% (9)	0.16
Did not meet criteria	8% (2)	13% (2)	11% (1)	0% (0)	9% (5)	0.77
Clinical characteristics						
Organ involvement						
Pancreato-Biliary	5 (14%)	4 (18%)	3 (25%)	3 (25%)	15 (27%)	0.60
Retroperitoneal/Aortitis	9 (25%)	4 (18%)	1 (8%)	2 (17%)	16 (29%)	0.65
Head and Neck/ limited	9 (25%)	6 (27%)	3 (25%)	1(8%)	19 (34%)	0.40
Mikulicz/Systemic	13 (36%)	7 (32%)	5 (42%)	6 (50%)	31 (55%)	0.33
Serum IgG4						
Checked (% patients (n))	92% (23)	100% (15)	100% (9)	100% (7)	97% (54)	-
Elevated IgG4 (% patients (n))*	52% (13)	47% (7)	33% (3)	71% (5)	50% (28)	-
Mean serum IgG (mg/dL)	255 mg/dL	375 mg/dL	266 mg/dL	618 mg/dL	332 mg/dL	-
Biopsy						
Performed (% patients (n))	88% (22)	93% (14)	100% (9)	71% (5)	89% (50)	0.37
Met biopsy criteria	72% (18)	21% (12)	89% (8)	57% (4)	75% (42)	0.52
Pattern of organ involvement						
Pancreato-Biliary						
Pancreas	5 (20%)	3 (20%)	3 (33%)	3 (43%)	14 (25%)	0.98
Biliary tract	1 (4%)	2 (3%)	2 (22%)	1(14%)	6 (11%)	0.99
Liver	1 (4%)	1 (7%)	3 (33%)	0 (0%)	5 (9 %)	0.68
Retroperitoneal/Aortitis						
Pericardium	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-
Heart	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-
Aorta	4 (16%)	1 (7%)	0 (0%)	1 (14%)	6 (11%)	0.83
Retroperitoneum	6 (4%)	4 (27%)	1 (11%)	1 (14%)	9 (16%)	0.68
Mediastinum	1 (4%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	0.90
Head and Neck/ limited						
Orbits	4 (16%)	3 (20%)	2 (22%)	0 (0%)	9 (16%)	0.93
Meninges	0 (0%)	2 (13%)	0 (0%)	0 (0%)	2 (4%)	0.47
Ear	0 (0%)	1 (7%)	0 (0%)	0 (0%)	1 (2%)	0.93
Skull bones and sinuses	4 (16%)	3 (20%)	1 (11%)	1(14%)	9 (16%)	0.71
Thyroid	2 (8%)	1 (7%)	1 (11%)	0 (0%)	4 (8%)	0.96
Mikulicz/Systemic						
Lacrimal glands	3 (12%)	1 (7%)	1 (11%)	1 (14%)	6 (11%)	0.99
Salivary glands	4 (16%)	3 (20%)	2 (22%)	3 (43%)	12 (21%)	0.98
Lung	1 (4%)	0 (0%)	0 (0 %)	0 (0%)	1 (2%)	0.99
Pleural	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-
Kidney	2 (8%)	2 (13%)	0 (0%)	1 (14%)	5 (9%)	0.50
Lymph nodes	8 (32%)	4 (27%)	3 (33%)	2 (29%)	17 (30%)	0.40
Breast	0 (0%)	1 (5%)	0 (0%)	0 (0%)	1 (2%)	0.99
* IgG4 levels greater than 135 mg/dL.						

Methods: This is a retrospective analysis of IgG4-RD records from Northwell Health Rheumatology seen between 2011 and December 2023. Diagnosis of IgG4RD was confirmed by manual medical records review. Demographics data, disease characteristics, IgG4 serum level and pathology descriptors were recorded. Descriptive statistics were used for statistical analysis. We calculated the chi-square test statistic using the observed frequencies among the four ethnicities.

Results: 56 patients with diagnosis of IgG4RD were identified from the Rheumatology Northwell database. Demographic and clinical characteristics of the total cohort and ethnic subgroups in (**Table 1**). 45% (25/56) of patients were Caucasian, 27% (15/56) - Asian, 16% (9/56) - Black, and 13% (7/56) - Hispanic. 99% (51/56) met 2020 revised comprehensive diagnostic criteria for definite, probable, possible IgG4RD. 89% met pathologic criteria **(Table 1).** Clinical manifestations showed significant overlap of clinical clusters among the four ethnicities **(Figure 1).** The most prevalent manifestation was Mikulicz/systemic, observed in half of all patients, followed by 34% head and neck limited and 29% retroperitoneal. Retroperitoneal domain was more commonly recorded in Caucasians (36 % (9/25)) with 16 % of aortitis while frequency in Black patients was 11 % (1/9) and no aortitis was observed. Meningeal and ENT involvement was much more common in Asian subgroup (40%) compared to only 10 % in other ethnicities. The only case of breast IgG4RD was recorded in Asian subgroup. All patients across all ethnic groups received corticosteroids as initial therapy. 1st line immunosuppressive agent was used in more than 70% of all patients. Similar distribution was recorded for Caucasians, Asians, and Hispanics. Blacks were less likely (33%) to be on IS and none was on 2nd line IS therapy. Furthermore, 8-14% of Caucasians, Hispanics and Asian patients received rituximab, it was not used for Blacks patients (**Table 2**). No statistically significant evidence among the four ethnicities was found.

Conclusion: Significant overlap of clinical clusters was observed among the four ethnicities. Mikulicz /systemic pattern was highly predominant among entire cohort and all 4 ethnicities. Asian patients had more common ENT and meningeal involvement. The Blacks were less likely to be on IS agents and were not on rituximab. While this discrepancy with other ethnic groups could reflect more benign disease course, other factors should be investigated further. As New York is home to a highly diverse population, this study contributes important insights that can potentially be applicable to other regions with similar demographic characteristics.

Table 2. IgG4RD treatment variations between different ethnic groups

Treatment	Caucasian (n = 25)	Asian (n = 15)	Black American (n = 9)	Hispanic (n = 7)	Total (n = 56)	P-value
corticosteroids (% patients (n))	100 % (25)	100% (15)	100% (9)	100% (7)	100% (56)	-
past	72% (18)	87% (13)	56% (5)	100% (7)	77% (43)	0.19
current	28% (7)	13% (2)	44% (4)	0% (0)	23% (13)	0.06
1st IS treatment (% patients (n))	76% (19)	73% (11)	33% (3)	86% (6)	70% (39)	0.06
MMP, MTX, AZA	16% (4)	40% (6)	33% (3)	57% (4)	30% (17)	0.99
Cytoxan	4% (1)	0% (0)	0% (0)	0% (0)	2% (1)	0.99
Rituximab	53% (13)	33% (5)	0% (0)	29% (2)	36% (20)	0.06
Other biologics	4% (1)*	0% (0)	0% (0)	0% (0)	2% (1)	0.99
2nd IS treatment (% patients (n))	20% (5)	20% (3)	0% (0)	14% (1)	16% (9)	0.23
MMP, MTX, AZA	8% (2)	7% (1)	0% (0)	0% (0)	5% (3)	0.97
Cytoxan	0% (0)	0% (0)	0% (0)	0% (0)	0% (0)	-
Rituximab	8% (2)	13% (2)	0% (0)	14% (1)	9% (5)	0.72
Other biologics	4% (1) **	0% (0)	0% (0)	0% (0)	2% (1)	0.99
3rd IS treatment (% patients (n))	8% (2)	7% (1)	0% (0)	0% (0)	5% (3)	0.99
MMP, MTX, AZA	0% (0)	0% (0)	0% (0)	0% (0)	0% (0)	-
Cytoxan	0% (0)	0% (0)	0% (0)	0% (0)	0% (0)	-
Rituximab	8% (2)	7% (1)	0% (0)	0% (0)	5% (3)	0.98
Other biologics	0% (0)	0% (0)	0% (0)	0% (0)	0% (0)	-
4th IS treatment (% patients (n))	4% (1)	0% (0)	0% (0)	0% (0)	2% (1)	0.99
MMP, MTX, AZA	0% (0)	0% (0)	0% (0)	0% (0)	0% (0)	-
Cytoxan	4% (1)	0% (0)	0% (0)	0% (0)	0% (0)	0.99
Rituximab	0% (0)	0% (0)	0% (0)	0% (0)	0% (0)	-
Other biologics	0% (0)	0% (0)	0% (0)	0% (0)	0% (0)	-

*Mepolizumab
** Infliximab

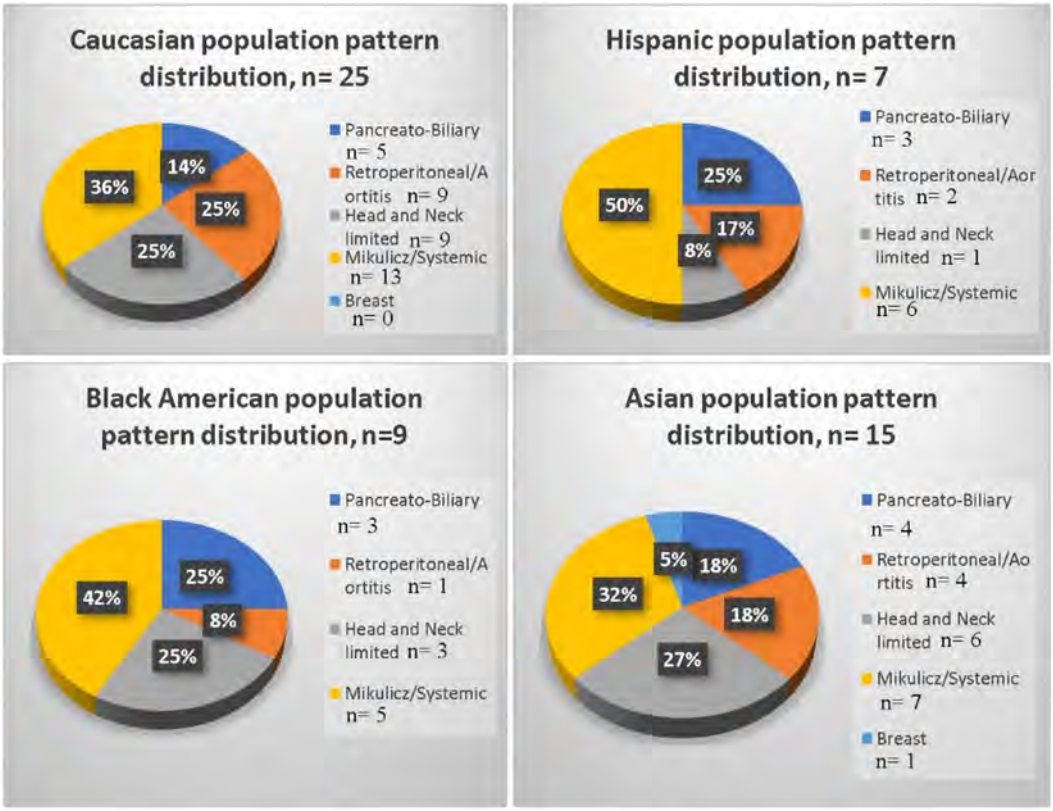

Figure 1. Percentage of distribution of organ involvement pattern per ethnicity.

Disclosure: Y. Cho: None; **G. Marder**: None; **K. Sangaraju**: None; **L. El Khoury**: None; **K. Shargani**: None; **J. Fragoso**: None.

Abstract Number: 1934

Pooled Safety Analysis from the VOLTAIRE Trials in Patients with Rheumatoid Arthritis, Crohn's Disease, and Chronic Plaque Psoriasis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The VOLTAIRE trials program compared the safety, efficacy, and immunogenicity of biosimilar BI 695501 with adalimumab reference product (RP) for indications including moderate-severe rheumatoid arthritis (RA), Crohn's disease (CD), and chronic plaque psoriasis (PsO),[1-4] and included a switching study to investigate interchangeability.[5] This analysis estimates the incidence of safety endpoints across 5 phase 3 randomized controlled clinical trials in patients with RA (VOLTAIRE-RA and VOLTAIRE-RAext), CD (VOLTAIRE-CD), and PsO (VOLTAIRE-PsO and VOLTAIRE-X) who received ≥1 dose of BI 695501 or adalimumab RP.

Methods: Safety endpoints included in this analysis were adverse events (AEs), serious adverse events (SAEs), discontinuations due to AEs, deaths, and adverse events of special interest (AESIs; specifically, serious infections, malignancies, and major adverse cardiovascular events [MACE; defined as non-fatal stroke, myocardial infarction, or fatal cardiovascular death]). Exposure-adjusted incidence rates (EAIR) were calculated per 100 patient-years. Incidence rates are reported by disease indication and treatment arm. For the at-risk person-years, the starting point was the first dose of BI 695501 or adalimumab RP, and the end point was 10 weeks after the last dose, the data cut-off date or the first safety event (whichever occurred first). Subgroup analyses by patient age and sex were also conducted.

Results: The mean age of patients with RA was higher than that of patients with CD or PsO, and a greater proportion of patients with RA were female. The mean length of follow up in this analysis was 62 weeks in patients with RA, 48 weeks in patients with CD, and 32 weeks in patients with PsO. Safety data are summarized in Table 1. Rates of SAEs and discontinuations due to AEs were similar among patients with RA and PsO, but slightly higher among those with CD. Overall incidence rates of AEs, SAEs, discontinuations due to AEs, deaths, and AESIs were consistent between the BI 695501 and adalimumab RP treatment arms within each indication. There were no cases of malignancies or MACE reported in patients with PsO or CD, while both were observed in patients with RA. Subgroup analyses of patients with RA by age and sex showed no between-group differences, and a similar trend was observed for patients with CD and PsO.

Conclusion: In patients with RA, CD and PsO, there were no differences between biosimilar BI 695501 or the adalimumab RP regarding the rate of AEs, SAEs, discontinuations due to AEs, deaths, or the AESIs of serious infections, cancer, or MACE. **Trial Registrations:** VOLTAIRE-RA, NCT02137226; VOLTAIRE-RAext, NCT02640612; VOLTAIRE-CD, NCT02871635; VOLTAIRE-PsO, NCT02850965

Table 1. Safety Data

	RA		CD		PsO	
	BI 695501 (N=324)	Adalimumab RP (N=321)	BI 695501 (N=72)	Adalimumab RP (N=75)	BI 695501 (N=159)	Adalimumab RP (N=417)
Mean age, years (SD)	53.2 (12.0)	53.1 (11.4)	37.4 (13.4)	33.2 (11.5)	42.1 (12.8)	44.9 (13.9)
n (%) female	267 (82.4)	269 (83.8)	33 (45.8)	31 (41.3)	58 (36.5)	56 (35.4)
Median follow-up, weeks (IQR)[a]	108.0 (58.1, 108.1)	25.7 (24.1, 50.1)	56.1 (48.2, 56.2)	56.1 (42.9, 56.3)	33.1 (33.1, 33.1)	33.1 (13.3, 45.3)
	IR per 100 PY (95% CI)					
AEs	81.6 (64.9, 101.4)	123.6 (102.7, 147.4)	198.5 (171.9, 228.2)	157.8 (134.1, 184.4)	99.1 (80.6, 120.7)	140.9 (118.6, 166.2)
SAEs	5.3 (1.8, 12.1)	10.6 (5.2, 19.2)	12.6 (6.7, 21.8)	23.1 (14.7, 34.7)	5.3 (1.8, 12.1)	6.8 (2.7, 14.2)
Discontinuations due to AEs	3.3 (0.8, 9.3)	5.4 (1.9, 12.2)	6.1 (2.3, 13.2)	10.3 (5.0, 18.8)	4.2 (1.2, 10.5)	3.2 (0.7, 9.0)
Deaths	0.2 (0.0, 4.1)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
AESIs						
Serious infections	0.6 (0.0, 4.8)	3.2 (0.7, 9.0)	0.0 (0.0)	0.0 (0.0)	1.0 (0.03, 5.6)	1.2 (0.1, 5.9)
Malignancies	0.4 (0.0, 4.4)	0.9 (0.02, 5.4)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
MACE	0.4 (0.0, 4.4)	0 (0.00)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.4 (0.0, 4.5)

IR per PY, incidence rate per 100 person-years; IQR, interquartile range

a. Total follow-up defined as number of years between i) first dose of BI 695501 or adalimumab RP, and ii) day on which new treatment began, 10 weeks beyond last dose of original treatment, or data cut-off date, whichever occurred first.

Disclosure: S. Cohen: AbbVie, 2, Amgen, 2, Boehringer Ingelheim, 2, Coherus, 2, Merck, 2, Pfizer, 2, Sandoz, 2; **S. Bender**: Boehringer Ingelheim, 3; **A. Shaberman**: Boehringer Ingelheim, 3; **R. Vinisko**: Boehringer Ingelheim, 3; **D. McCabe**: Boehringer Ingelheim, 3.

Abstract Number: 1935

Pre-exposure Prophylaxis with Tixegvimab/cilgavimab Is Effective in Limiting the Risk and Severity of COVID-19 in Patients with Auto Immune or Inflammatory Diseases at Increased Risk of Severe COVID-19

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

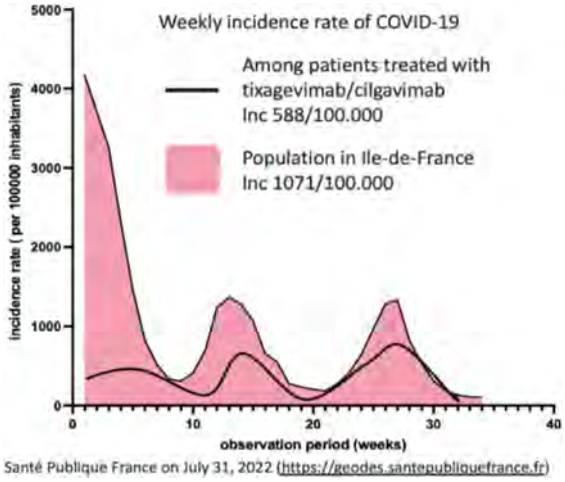
Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with autoimmune or inflammatory diseases treated with immunosuppressants such as anti-CD20 are at increased risk for severe COVID-19 and have a high probability of insufficient response to vaccination. The monoclonal antibody combination tixagevimab/cilgavimab has received early access approval to reduce the frequency of symptomatic COVID-19 in immunocompromised patients at risk for severe COVID-19 and unresponsive to vaccination. We aim to evaluate the clinical efficacy of tixagevimab/cilgavimab in pre-exposure prophylaxis in patients with increased risk of severe COVID-19 in rheumatology.

Methods: In this multicenter observational study conducted between December 2021 and August 2022, we included patients with autoimmune or inflammatory diseases who received at least one intramuscular injection of tixagevimab/cilgavimab as pre-exposure prophylaxis in 3 French rheumatology units. Occurrence of COVID-19 was assessed during usual follow-up or by phone call. The endpoint was the incidence of COVID-19 and its severity.



Results: Tixagevimab/cilgavimab was administered to 115 patients, median age 62 years (52-71), with chronic arthritis (n=53), connective tissue disease (n=38) or vasculitis (n=11). The main background immunosuppressants were rituximab (n=98), methotrexate (n=48), mycophenolate mofetil (n=19), cyclophosphamide (n=15), azathioprine (n=12), and corticosteroids (n=62, median dose 5 mg, CI95% 5-8). During a median follow-up of 128 days (93-173), COVID-19 occurred in 23/115 patients (20%) with Omicron identified for the 8 genotyped patients. During the study period, the average weekly incidence was 1071 per 100.000 inhabitants in Ile-de-France vs. 588 per 100.000 in our patients. Patients who received a 2-injections regimen had a lower risk of infection than patients with a single injection (16/49, 33%, vs. 5/64, 8%, p=0.0012). The COVID-19+ patients did not differ from uninfected patients in terms of age, comorbidities, type and duration of underlying disease, extra-articular organ involvement or background immunosuppressants. All COVID-19 cases were non-severe, there were no deaths. The tolerance of injections was excellent, with no side effects observed.

Conclusion: In a population with autoimmune or inflammatory diseases at increased risk of severe COVID-19 with a poor response to vaccination, pre-exposure prophylaxis by tixagevimab/cilgavimab limited the risk of infection and the severity of COVID-19. This study supports the use of COVID-19 serological tests in this patient population in order to detect those who do not respond adequately to vaccination since pre-exposure treatments and/or early treatments are available.

Disclosure: M. THOMAS: None; **M. MASSON**: None; **R. Seror**: None; **S. Bitoun**: None; **H. DUPUY**: None; **L. ESTIBALIZ**: None; **C. Richez**: AbbVie/Abbott, 2, 6, Amgen, 6, AstraZeneca, 2, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, 12, receipt of drugs, GlaxoSmithKlein(GSK), 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **Y. ALLANORE**: AbbVie/Abbott, 2, Alpine Immunoscience, 5, AstraZeneca, 2, Bayer, 2, Boehringer-Ingelheim, 2, Janssen, 2, Medsenic, 2, 5, Mylan, 2, OSE Immunotherapeutics, 5, Prometeus, 2, Roche, 2, Sanofi, 2; **J. AVOUAC**: AbbVie, 1, 2, 4, 6, BMS, 4, 5, 6, Fresenius Kabi, 4, 5, Galapagos, 1, 2, 4, 6, Lilly, 6, Novartis, 5, 6, Pfizer, 5, 6, Sanofi, 4, 6.

Abstract Number: 1936

Higher Rates of Disease Control During the Coronavirus Pandemic in Pediatric Patients with Autoinflammatory Periodic Diseases on Canakinumab Treatment – Interim Data from the RELIANCE Registry

Gerd Horneff[1], Norbert Blank[2], Jasmin B. Kuemmerle-Deschner[3], Joerg Henes[4], Birgit Kortus-Goetze[5], Prasad T. Oommen[6], Anne Pankow[7], Tobias Krickau[8], Catharina Schuetz[9], Ivan Foeldvari[10], Juergen Rech[11], Frank Weller-Heinemann[12], Ales Janda[13], Markus Hufnagel[14], Florian M. Meier[15], Frank Dressler[16], Michael Borte[17], Ioana Andreica[18], Peter Wasiliew[19], Michael Fiene[20], Daniel Windschall[21], Martin Krusche[22], Tania Kuempfel[23], Julia Weber-Arden[24] and Tilmann Kallinich[25], [1]Asklepios Klinik Sankt Augustin GmbH, Bonn, Germany, [2]University Hospital Heidelberg, Heidelberg, Germany, [3]med.uni-tuebingen, Tübingen, Germany, [4]University Hospital Tuebingen, Tuebingen, Germany, [5]Department of Internal Medicine, Division of Nephrology,University Hospital of Giessen and Marburg, Marburg, Germany, [6]Department of Pediatric Oncology, Hematology and Clinical Immunology, Center for Child and Adolescent Health,Medical Faculty Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany, [7]Department of Rheumatology and Clinical Immunology,Charité-Universitätsmedizin Berlin, Berlin, Germany, [8]Pediatrics, Friedrich-Alexander University Erlangen-Nuernberg (FAU), Erlangen, Germany, [9]Department of Pediatrics, Medizinische Fakultät Carl Gustav Carus,Technische Universität Dresden, Dresden, Germany, [10]Hamburger Zentrum für Kinder- und Jugendrheumatologie, Hamburg, Germany, [11]University Clinic Erlangen, Erlangen, Germany, [12]Division of Pediatric Rheumatology, Prof. Hess Children's Hospital, Bremen, Bremen, Germany, [13]Department of Pediatrics and Adolescent Medicine, University Medical Center Ulm, Ulm, Germany, [14]Division of Pediatric Infectious Diseases and Rheumatology, Department of Pediatrics and Adolescent Medicine, University Medical Center, Medical Faculty, University of Freiburg, Freiburg, Germany, [15]Department of General Pharmacology and Toxicology, Goethe University Hospital and Goethe University Frankfurt, Frankfurt am Main, Germany, [16]Department of Paediatric Pneumology, Allergology and Neonatology, Children's Hospital, Hannover Medical School, Hannover, Germany, [17]Hospital for Children & Adolescents, St. Georg Hospital, Leipzig, Germany, [18]Rheumazentrum Ruhrgebiet Herne, Herne, Germany, [19]Division of Pediatric Rheumatology and autoinflammation reference center Tuebingen, Department of Pediatrics, University Hospital Tuebingen, Tuebingen, Germany, [20]Rheumatology Center Greifswald, Greifswald, Germany, [21]Clinic of Paediatric and

Adolescent Rheumatology, St. Josef-Stift Sendenhorst, Northwest German Center for Rheumatology, Sendenhorst, Germany, [22]UKE, Hamburg, Germany, [23]Institute of Clinical Neuroimmunology, Biomedical Center and University Hospital, Ludwig-Maximilians Universität München, Muenchen, Germany, [24]Novartis Innovative Medicines, Nuernberg, Germany, [25]Department of Pediatric Respiratory Medicine, Immunology and Critical Care Medicine, Charité Universitätsmedizin Berlin, Nuremberg, Germany

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Pediatric patients with autoinflammatory diseases (AID) on Canakinumab (CAN) therapy have been affected by the coronavirus pandemic including SARS-CoV-2 infection, SARS-CoV-2 vaccination, and AID disease management. In the RELIANCE registry, severity of SARS-CoV-2 infection, safety of SARS-CoV-2 vaccination and comparison of disease management before and during pandemic in pediatric patients with cryopyrin-associated periodic syndromes (CAPS), familial Mediterranean fever (FMF), hyper-IgD syndrome/mevalonate kinase deficiency (HIDS/MKD) and tumor necrosis factor receptor-associated periodic syndrome (TRAPS) on CAN therapy was investigated in clinical practice.

Methods: The RELIANCE registry is a prospective, non-interventional, observational study in Germany enrolling pediatric (age ≥2 years) and adult patients with a clinically confirmed diagnosis of AID who routinely receive CAN. Efficacy and safety parameters are recorded at baseline and assessed at 6-month intervals.

Results: The present interim analysis includes data from n=101 pediatric patients with AID enrolled in the RELIANCE registry between October 2017 and December 2022. The median duration of CAN treatment before and during the study was 3.7 years (0-13.5 years).

During the study, 29 SARS-CoV-2 infections were reported for n=27 pediatric patients. 22 infections caused mild symptoms and 7 infections caused moderate symptoms. N=25 (24.8 %) of pediatric patients received at least one SARS-CoV-2 vaccination (15 Comirnaty, 13 not specified). Vaccination reactions (not further specified) were reported in n=3 patients. No reactions were classified as serious.

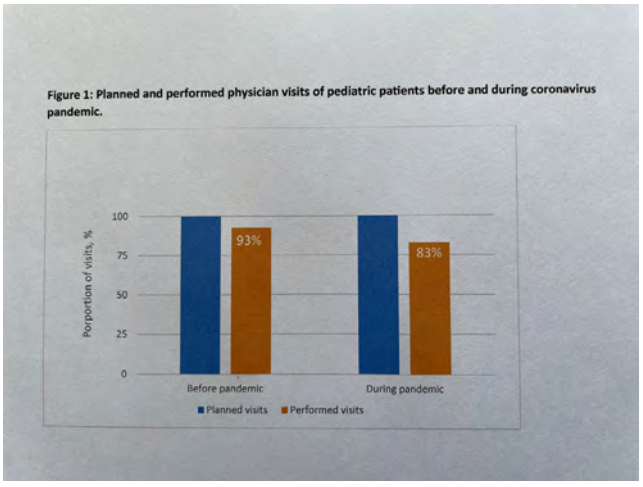


Figure 1: Planned and performed physician visits of pediatric patients before and during coronavirus pandemic.

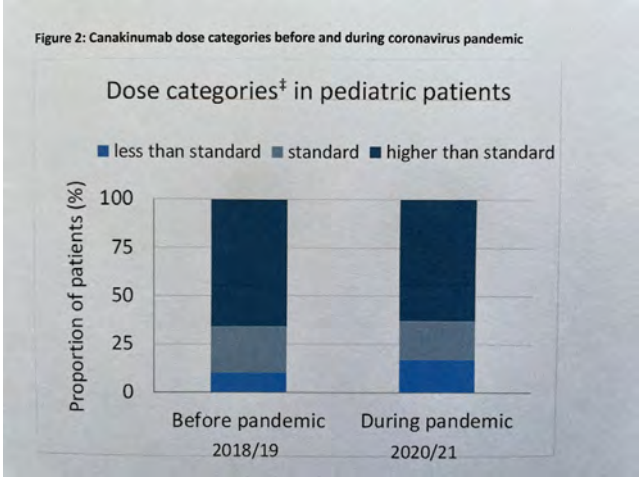


Figure 2: Canakinumab dose categories before and during coronavirus pandemic.

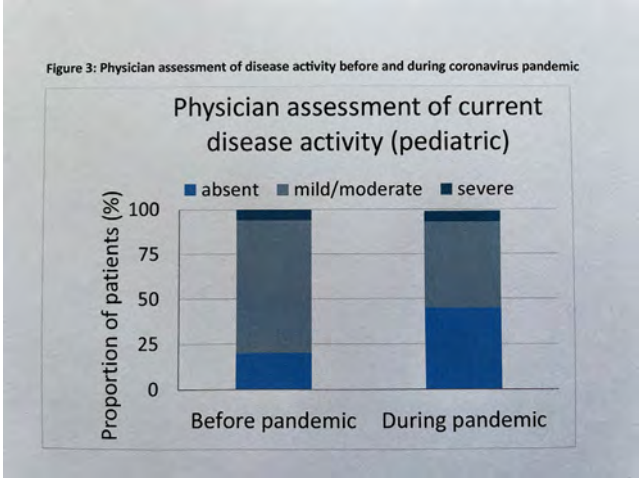


Figure 3: Physician assessment of disease activity before and during coronavirus pandemic.

During the COVID-19 pandemic in 2020 and 2021, only 83 % of regular patient visits were performed (Fig. 1). In addition, patients received slightly lower CAN dosing (20% standard dose CAN [SD], 17% lower than SD, and 63% higher than SD compared to 24% SD, 10% lower than SD, and 66% higher than SD before pandemic (Fig. 2). However, disease activity by patient rating (VAS score 1-10) improved from 3 before to 2 during the pandemic. By physician global assessment, the proportion of pediatric patients with no disease activity arose from 20% before to 45% during the pandemic (Fig. 3). In contrast: no major changes in disease activity were documented in adult patients.

Conclusion: Pediatric AID patients under long-term Canakinumab treatment experienced improved disease control during the Coronavirus pandemic.

Disclosure: G. Horneff: GSK, 6, Janssen, 6, MSD, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Roche, 5, 6, Sanofi, 6, Sobi, 6; **N. Blank**: Novartis, Sobi, 5, Novartis, Sobi, Lilly, Pfizer, Abbvie, BMS, MSD, Actelion, UCB, Boehringer-Ingelheim, Roche, 2; **J. Kuemmerle-Deschner**: Novartis, AbbVie, Sobi, 2, 5; **J. Henes**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, GlaxoSmithKlein(GSK), 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **B. Kortus-Goetze**: Novartis, 2; **P. Oommen**: Novartis, 5; **A. Pankow**: None; **T. Krickau**: Novartis,

2, 5, 6; **C. Schuetz**: Novartis, 5; **I. Foeldvari**: Novartis, 2; **J. Rech**: AbbVie, Biogen, BMS, Chugai, GSK, Janssen, Lilly, MSD; Mylan, Novartis, Roche, Sanofi, Sobi, UCB, 2, 6, Novartis, Sobi, 5; **F. Weller-Heinemann**: None; **A. Janda**: None; **M. Hufnagel**: Novartis, 5; **F. Meier**: Novartis, 6; **F. Dressler**: Abbvie, Mylan, Novartis, Pfizer, 2, Novartis, 5; **M. Borte**: Pfizer, Shire, 5; **I. Andreica**: AbbVie/Abbott, 1, 6, Amgen, 1, 6, AstraZeneca, 1, 6, Chugai, 6, Novartis, 1, 6, Sobi, 1, 6, UCB, 1, 6; **P. Wasiliew**: None; **M. Fiene**: None; **D. Windschall**: None; **M. Krusche**: Chugai, 2, 6; **T. Kuempfel**: None; **J. Weber-Arden**: Novartis, 3; **T. Kallinich**: Roche, 6.

Abstract Number: 1937

Efficacy of Different Treatment Approaches for Cardiac Sarcoidosis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: There is currently a lack of a consensus standardized guideline for the treatment of cardiac sarcoidosis (CS) because of its rarity, heterogeneity of disease manifestations, and challenges of long-term management. The purpose of this study is to evaluate the efficacy of different treatment regimens, including TNF-α inhibitors, on clinical outcomes. This is the most comprehensive and up to date analysis for CS patients treated at our tertiary care institution, and the continuity of longitudinal care highlights the nuances of treatment decisions made by our physicians to contribute to the standard of practice.

Methods: A monocentric retrospective study of 50 CS patients at our institution was conducted. 31 patients (62%) met World Association of Sarcoidosis and other Granulomatous Disorders (WASOG) and Health Rhythm Society (HRS) diagnostic criteria. The other 19 patients (38%) were clinically diagnosed without biopsy proven disease but fulfilled one of the WASOG probable cardiac characteristics. For clinical outcomes, worsening was defined by the onset of a new CS manifestation[1], stabilization as absence of a new CS manifestation and stable ejection fraction (EF) or PET myocardial uptake, and improvement as absence of a new CS manifestation, but with either a ≥ 10% increase in or normalization of EF or improvement in PET myocardial uptake. Generalized estimating equations (GEE) models with independent correlation structure and identity link were used to calculate p-values for comparisons of individual treatment regimens and outcomes.

1. Ballul T, et al. *Int J Cardiol*. 2019;276:208-211.

Results: Table 1 provides patient demographics and distribution of the different treatment combinations. Of the 50, there were 48 patients treated with at least one regimen, and 34 patients with at least one follow-up treatment for a total of 124 individual treatments.

Table 2 and 3 summarize the associations of each treatment with the overall clinical outcome defined as improved, stable, or worsened. 46.3% of treatment regimens showed clinical improvement and an additional 27.4% showed stabilization. Of these, 50% had clinical improvement with the first treatment as compared to 27.6% in follow-up treatments. In terms of the different regimens, 81% of regimens with steroids only had stable or improved clinical outcomes which was the highest percentage in the treatment groups. 60% of regimens with a TNF-α inhibitor had stable or improved clinical outcomes.

Table 1. Summary of Characteristics and Treatment Regimens

Patient Characteristics			
Age at Diagnosis in Years, Mean (SD)	55.3 (9.8)		
Male (%)	30 (62.5)		
Race			
White (%)	31 (64.6)		
Black (%)	11 (22.9)		
Other (%)	6 (12.5)		
Combination Groups	All treatments N = 124, n (%)	First Treatment N=48, n (%)	Follow-up Treatments N=76, n (%)
Steroids only	36 (29.0)	27 (56.3)	9 (11.8)
Methotrexate (w/ or w/o steroids)	37 (29.8)	12 (25.0)	25 (32.9)
Mycophenolate or Myfortic (w/ or w/o steroids)	16 (12.9)	4 (8.3)	12 (15.8)
Azathioprine (w/ or w/o steroids)	4 (3.2)	0 (0)	4 (5.3)
Hydroxychloroquine (w/ or w/o steroids)	3 (2.4)	0 (0)	3 (4.0)
Leflunomide (w/ or w/o steroids)	1 (0.8)	0 (0)	1 (1.3)
TNFi and TNFi + Methotrexate/Azathioprine (w/ or w/o steroids)	22 (17.7)	1 (2.1)	21 (27.6)
No Treatment/Regimens Not Included*	5 (4.0)	4 (8.3)	1 (1.3)

*Two patients on Tacrolimus and one patient on Rituxan were added to the 'No Treatment/Regimens Not Included' group as patients were not on these medications for cardiac sarcoidosis treatment

Table 2. Overall Clinical Outcomes for All, First, and Follow-up Treatments

Clinical Outcomes	All treatments N = 124, n (%)	First Treatment N=48, n (%)	Follow-up Treatments N=76, n (%)
Clinical Change			
Improve	45 (46.3)	24 (50.0)	21 (27.6)
Stable	34 (27.4)	9 (18.8)	25 (32.9)
Worsen	33 (26.6)	11 (22.9)	22 (29.0)
No TTE/PET for comparison	12 (9.7)	4 (8.3)	8 (10.5)
EF Overall			
Improve*	16 (12.9)	11 (22.9)	5 (6.6)
Stable	63 (50.8)	17 (35.4)	46 (60.5)
Worsen	9 (7.3)	5 (10.4)	4 (5.3)
No comparison	36 (29.0)	15 (31.3)	21 (27.6)
PET Overall			
Improve**	48 (38.7)	21 (43.8)	27 (35.5)
Stable	16 (12.9)	3 (6.3)	13 (17.1)
Worsen	12 (9.7)	4 (8.3)	8 (10.5)
No Comparison	48 (38.7)	20 (41.7)	28 (36.8)
Arrhythmias			
Either New or Recurrent arrhythmia***	26 (21.0)	9 (18.8)	17 (22.3)
New arrhythmia	14 (11.3)	6 (12.5)	8 (10.5)
Recurrent arrhythmia	14 (11.3)	3 (6.2)	11 (14.5)

*12 out of 16 'Improve' were 'Improved to Normal'
**26 out of the 49 'Improve' were to 'Complete Resolution'
***2 of the 26 had both types of arrhythmias

Conclusion: In our study, patients were more likely to see clinical improvement with initial treatment compared to subsequent regimens. This highlights the importance of early therapy as treatment later in the disease course will less likely lead to clinical improvement, possibly a reflection of scarring or irreversible pathology in later stages of the disease. Therefore, clinicians should consider an approach that is more proactive upfront to avoid this progression. In terms of a specific regimen, although our results do not show a superior treatment, the trend does show that regardless of the regimen, the majority of patients have clinical improvement with treatment.

Table 3. Clinical Outcomes of Individual Medications and Combination Treatments

Individual Medications	All Treatments N= 112, n (%)	Worse N=33, n (%)	Stable/ Improved N= 79, n (%)	P- value
Steroids	88 (79)	27 (31)	61 (69)	0.6328
TNFi	20 (18)	8 (40)	12 (60)	0.2576
Methotrexate	44 (39)	13 (30)	31 (70)	0.9873
Mycophenolate	15 (13)	5 (33)	10 (67)	0.7560
Azathioprine	6 (5)	1 (17)	5 (83)	0.3395
Hydroxychloroquine	4 (4)	2 (50)	2 (50)	0.2544
No treatment	5 (4)	1 (20)	4 (80)	0.5971
Combination Treatments				
Steroid Only	31 (28)	6 (19)	25 (81)	0.1640
Methotrexate (w/ or w/o steroids)	33 (29)	10 (30)	23 (70)	0.9074
Mycophenolate or Myfortic (w/ or w/o steroids)	15 (13)	5 (33)	10 (67)	0.7560
Azathioprine (w/ or w/o steroids)	4 (4)	1 (25)	3 (75)	0.8157
Hydroxychloroquine (w/ or w/o steroids)	3 (3)	1 (33)	2 (67)	0.8888
TNFi and TNFi + Methotrexate/Azathioprine (w/ or w/o steroids)	20 (18)	8 (40)	12 (60)	0.2576
No Treatment /Regimens Not Included	5 (4)	1 (20)	4 (80)	0.5971

Disclosure: F. Cai: None; **A. Paulson**: None; **A. Wozniak**: None; **E. Gilbert**: None; **R. Ostrowski**: None.

Abstract Number: 1938

Cranial Nerve Manifestations in Sarcoidosis Associated with Lymphoma, Non-facial Paralysis, and Other Neurologic Disorders

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Sarcoidosis is a systemic granulomatous inflammatory disease that affects multiple organ systems including the including the lungs, skin, skeletal, and nervous system. Cranial neuropathies (CN) involving the optic, facial, and oculovestibular nerves can be an isolated manifestation. Here, we aim to identify comorbidities in this subset of sarcoidosis patients to raise a higher suspicion for this diagnosis; thereby, avoiding a delay in appropriate management.

Methods: The National Inpatient Sample (NIS) from 2003 to 2014 was queried to identify patients diagnosed with sarcoidosis (ICD9: 135). Patients with sarcoidosis were categorized into two groups based on whether they had comorbid CN palsies and disorders (CN I-XII palsy, multiple CN palsies, optic neuritis, trigeminal neuralgia, and sensorineural hearing loss).Univariate and multivariate analyses were conducted to compare patient and hospital characteristics as well as Elixhauser comorbidities between the two groups.

Table 1			
	CN (n=1,314)	Non-CN (n=170,589)	p-value
Age, years	52.62 ± 15.19	56.15 ± 13.85	<.001
Sex			.002
Male	29.9%	34.1%	
Female	70.1%	65.9%	
Length of Stay (days)	5.91 ± 6.56	5.50 ± 6.82	0.030
Total Charges	$41,511 ± $55,206	$38,150 ± $62,345	0.053
Comorbidities	Odds Ratio (95% CI)		
Chronic pulmonary disease	0.634 (0.544-0.738)		<0.001
Congestive Heart Failure	0.528 (0.401-0.697)		<0.001
Lymphoma	2.271 (1.518-3.398)		<0.001
Other Neurological disorders	1.425 (1.155-1.758)		0.001
Paralysis	2.682 (2.037-3.531)		<0.001
Pulmonary circulation disorders	0.609 (0.423-0.876)		0.008
Renal Failure	0.649 (0.514-0.818)		<0.001

Results: Approximately 0.8% (n=1,314) of patients with sarcoidosis (n=173,236) had CN. Patients with CN were significantly younger (52.62 years±15.19 vs 56.15±13.85, p< 0.001) and female (70.1% vs 65.9%, p=0.002) compared to their non-CN counterparts. Although length of hospital stay (5.91days ± 6.56 vs 5.50±6.82, p=0.030) was significantly longer for sarcoidosis with CN, total hospital charges($41,511±$55,206 vs $38,150±$62,345, p=0.053)did not significantly differ between the groups. Patients were at significantly lower odds to develop CN if they had comorbid chronic pulmonary disease (OR [95% CI]:0.634 [0.544-0.738], p< 0.001),congestive heart failure (0.528 [0.401-0.697], p< 0.001), pulmonary circulation disorders (0.609 [0.423-0.876], p=0.008), or renal failure (0.649 [0.514-0.818], p< 0.001).Patients with lymphoma (2.271 [1.518-3.398], p< 0.001), other neurologic disorders (1.425 [1.155-1.758], p=0.001) and non-facial paralysis (2.682 [2.037-3.531], p< 0.001) had increased likelihood of developing CN. The presence of comorbid coagulopathy, iron deficiency anemia, diabetes, liver disease, or fluid/electrolyte disorders did not significantly impact the likelihood of developing CN (table 1).

Conclusion: Our analysis demonstrates greater odds of CN in sarcoidosis patients with comorbid lymphoma, other neurologic disorders, or non-facial paralysis. However, sarcoidosis patients with cardiopulmonary comorbidities or renal failure were less likely to have CN, suggesting that sarcoidosis patients with CN may somewhat spare other organs. Sarcoidosis patients who are relatively young, have other neurological disorders, non-facial paralysis, or lymphomas require a higher index of suspicion for CN.

Disclosure: M. Salim: None; **E. Kokush**: None; **E. Kalyoussef**: None; **E. Capitle**: None; **R. Khianey**: None.

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Sinonasal Sarcoidosis Associated with Chronic Pulmonary Disease, Deficiency Anemias, and Obesity

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Background/Purpose: Sarcoidosis is a systemic granulomatous inflammatory disease that can involve multiple organ systems. Rarely, sarcoidosis can involve the upper respiratory tract including the sinonasal region. Symptoms easily mimic those of allergic or atrophic rhinitis, bacterial sinusitis; therefore, commonly leading to misdiagnosis. Here, we aim to identify

Table 1			
	SN (n=5,127)	Non-SN (n=168,109)	p-value
Age, years	55.09 ± 13.45	56.15 ± 13.87	<.001
Sex			<.001
Male	29.5%	34.2%	
Female	70.5%	65.8%	
Length of Stay (days)	5.42 ± 6.71	5.51 ± 6.81	.357
Total Charges	$36,400 ± $52,672	$38,229 ± $62,562	.041
Comorbidities	Odds Ratio (95% CI)		
Chronic pulmonary disease	1.168 (1.093-1.249)		<0.001
Congestive Heart Failure	0.869 (0.785-0.963)		0.008
Deficiency anemia	1.171 (1.083-1.267)		<0.001
Diabetes, uncomplicated	0.872 (0.81-0.939)		<0.001
Diabetes, complicated	0.853 (0.743-0.979)		0.024
Obesity	1.228 (1.136-1.329)		<0.001
Renal Failure	0.833 (0.752-0.923)		<0.001
Death during admission	0.603 (.457-.795)		<0.001

comorbidities in this subset of sarcoidosis patients to raise a higher clinical suspicion for this diagnosis in a higher risk population; thereby, avoiding a delay in appropriate management.

Methods: The National Inpatient Sample (NIS) from 2003 to 2014 was queried to identify patients diagnosed with sarcoidosis (ICD-9: 135). Patients with sarcoidosis were categorized into two groups based on whether they had comorbid sinonasal diagnoses (including acute or chronic sinusitis, nasal polyps, deviated nasal septum, epistaxis, or nasal mucositis). Univariate and multivariate logistic analyses were conducted to compare patient and hospital characteristics as well as Elixhauser comorbidities between the two groups.

Results: A total of 173,236 sarcoidosis patients were included, 5,127 (3.0%) of whom had a comorbid SN diagnosis. Patients with SN involvement were younger (55.09 years ± 13.45 vs 56.15 ± 13.87, p< .001), more often female (70.5% vs 65.8%) than their non-SN counterparts. After accounting for demographics, patients who developed SN diagnoses were more likely to have chronic pulmonary disease (OR [95% CI]: 1.168 [1.093-1.249], p< 0.001), deficiency anemia (1.171 [1.083-1.267], p< 0.001), and be obese (1.228 [1.136-1.329], p< 0.001). However, those with congestive heart failure (0.869 [0.785-0.963], p=0.008), diabetes (0.872 [0.810-0.939], p< 0.001), or renal failure (0.833 [0.752-0.923], p< 0.001) were less likely to have a SN comorbidity. Patients with SN involvement had decreased hospital charges ($36,400 ± $52,672 vs $38,229 ± $62,562, p=0.041), but did not significantly differ on length of stay (5.42 ± 6.71 vs 5.51 ± 6.8, p=0.357) than those without a SN diagnosis. Patients with SN involvement of sarcoidosis were also less likely to die during their hospital admission than their non-SN counterparts (0.603[.457-.795], p< 0.001) (table 1).

Conclusion: Our findings suggest that the management of sarcoidosis patients with chronic pulmonary disease, deficiency anemia, or obesity should include a high index of suspicion for comorbid SN diagnoses. However, SN involvement does not increase sarcoid patients' risk for death, prolonged stay, or increased hospital charges. Further research is warranted to investigate underlying mechanisms and clinical implications of SN involvement in sarcoidosis.

Disclosure: E. Kokush: None; **M. Salim**: None; **E. Capitle**: None; **R. Khianey**: None; **E. Kalyoussef**: None.

Abstract Number: 1940

A Single-center, Observational, Retrospective, Case Control Study of Rituximab for the Treatment of Interstitial Pneumonia Associated with Autoimmune Features

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
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Background/Purpose: Patients with interstitial lung diseases (ILD) and clinical features of autoimmunity who do not satisfy the classification criteria for a specific autoimmune rheumatic disease are diagnosed with interstitial pneumonia with autoimmune features (IPAF). The treatment approach to ILD in this setting remains undefined. We conducted an observational retrospective study to examine the use of rituximab (RTX) in IPAF.

Methods: Patients from the Mount Sinai/National Jewish Respiratory Institute Patient Registry and Biorepository were included if they met the 2015 classification criteria for IPAF and were treated with RTX. Patients who met the criteria for another autoimmune disorder were excluded. Clinical improvement was defined as improvement in four domains after the use of RTX, including: pulmonary function tests (PFTs), CT chest findings, need for respiratory related hospitalization and survival.

Results: Of the 791 patients in the registry, 14 patients met the criteria for IPAF and received at least one dose of Rituximab. 19 patients were identified who met the criteria for IPAF and did not receive Rituximab to serve as the control group. There were no differences in the baseline demographics. Five patients (45.4%) in the RTX group were improved and 4 (36.3%) remained with stable FVC and DLCO. Accordingly, HRCT scan findings improved in 3 (33%) patients and remained stable

Table 1 Showing immunosuppressive use and the outcomes in the Rituximab and the control group

Immunosuppression and antifibrotic medication use			
	IPAF with Rituxan (N=14)	IPAF without Rituxan (N=19)	
Steroids	11 (78.6)	17 (89.5)	0.3
Cellcept	12 (85.7)	7 (36.8)	0.05
Imuran	3 (21.4)	0	0.067
Tacrolimus	3 (21.4)	0	0.067
Cytoxan	1 (7.1)	0	0.6
IVIG	4 (28.6)	0	0.024
Pirfenidone	1 (7.1)	1 (5.3)	0.6

Respiratory outcomes			
	Rituximab (n=14)	**Control group (n=19)**	**P value**
Need for supplemental oxygen	5 (35.7)	9 (47.4)	0.3
Incidence of infections	6 (42.9)	5 (26.3)	0.2
Respiratory related admissions	2 (14.3)	5 (26.3)	0.3
Mortality	1 (7.1)	1 (5.3)	0.5
Pulmonary Function Tests			
	Rituximab (n=11)	**Control group (n=15)**	P value
FVC improved	5 (45.4)	4 (26.6)	0.4
FVC remained stable	4 (36.3)	7 (46.6)	0.5
FVC worsened	2 (18.1)	4 (26.6)	0.7
First percent predicted FVC	72.4 + 18.2	69.6 + 18.7	0.68
Most recent percent predicted FVC	69.6 ± 15.7	73.4 ± 28.5	0.68
Percent predicted FVC delta	-2.57 ± 24	-0.68 ± 18.9	0.8
Median years between the PFTs	3.1	3.3	0.5
	Rituximab (n=10)	**Control group (n=15)**	P value
DLCO improved	3 (30)	4 (26.6)	0.63
DLCO stable	5 (50)	8 (53.3)	0.4
DLCO worsened	2 (20)	3 (20)	0.6
First percent predicted DLCO	51 + 17.3	54.6 ± 19.4	0.9
Most recent percent predicted DLCO	53.7 + 19.3	52.7 ± 25.9	0.7
Percent predicted DLCO delta	2.6 ± 13.2	-1.47 + 14.5	0.6

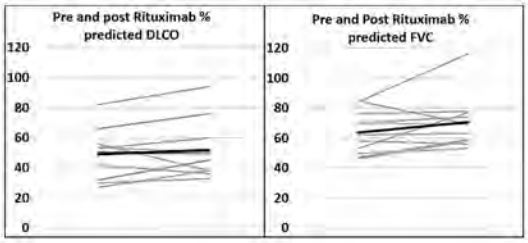

Figure 2. Line diagram showing the trend of the percent predicted DLCO and FVC before and after the Rituximab. Mean percent predicted DLCO and FVC values are represented by the solid black line.

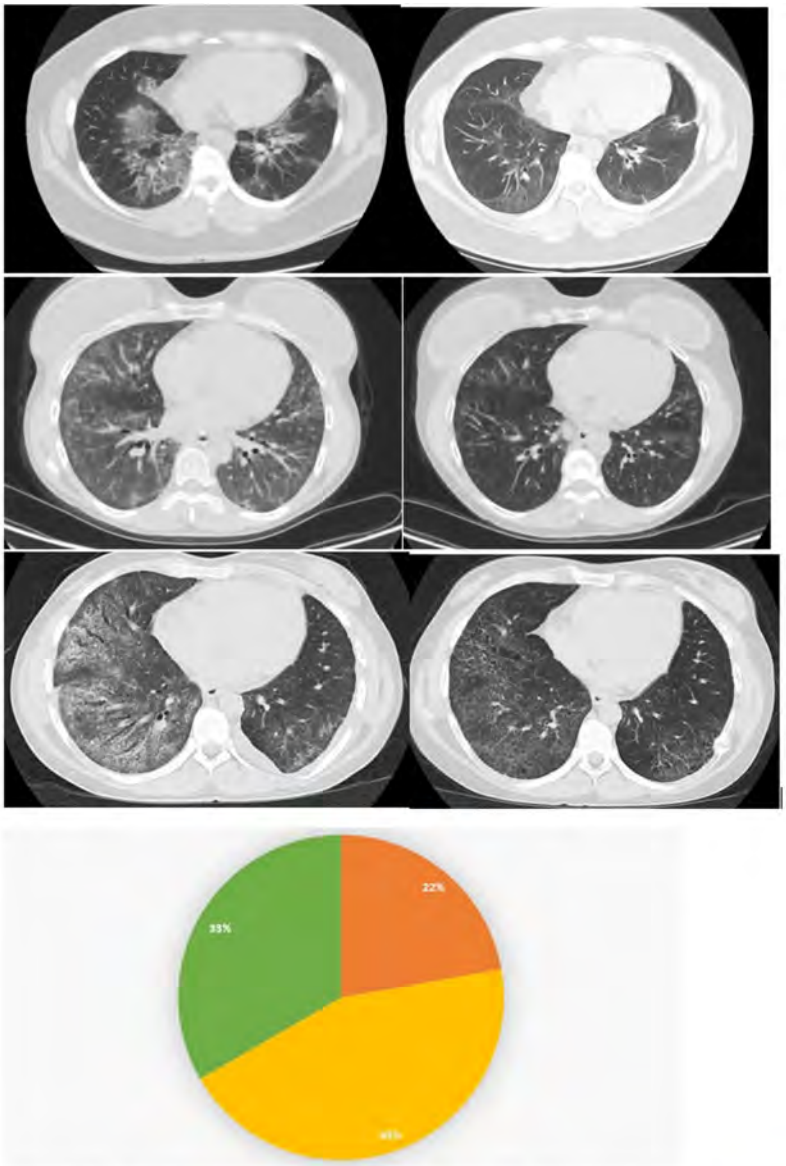

Figure 3: CT scan findings before (left) and after (right)the rituximab therapy showing improvement in three of the 9 patients who had repeat CT chests within two years of the Rituximab therapy. Pie chart (bottom) showing the percentage of patients with stable (yellow), improved (green) and worsened (orange) CT chest findings.

in 4 (45%), from 9 patients with available HRCT scans. Frequency of oxygen use, incidence of infection, respiratory related admissions and overall mortality was similar in both the groups.

Conclusion: The majority of patients with IPAF receiving rituximab showed improvement or stability in their pulmonary function. Although both the groups had similar outcomes, all patients in the RTX group had failed multiple immunosuppressive agents, suggesting refractory ILD. We propose RTX as an option for patients with moderate to severe IPAF who progress despite standard immunosuppressive therapy. Further prospective studies are needed to assess the benefit of RTX in this subset of patients with ILD.

Disclosure: T. Sandhu: None; **L. Meir**: None; **N. Ng**: None; **L. Klein**: None; **J. Zatakia**: None; **M. Padilla**: None; **I. Tassiulas**: None.

Abstract Number: 1941

Identification of VEXAS Syndrome in Mexican Patients with Inflammatory and Hematologic Manifestations

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SESSION INFORMATION
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Background/Purpose: There is limited information on VEXAS syndrome in the Latin-American population. We aimed to identify *UBA1* mutations causing VEXAS syndrome in Mexican patients presenting with inflammatory and hematologic manifestations.

Methods: We included patients who had (i) one or more inflammatory manifestations associated with VEXAS syndrome (e.g. chondritis, neutrophilic dermatoses, vasculitis, pneumonitis), and (ii) one or more chronic cytopenias, or isolated macrocytosis. Genomic DNA was extracted from peripheral blood or available biopsies (bone marrow or skin). To identify pathogenic *UBA1* mutations, Sanger sequencing of exons 3, 14, and 16 was performed. To identify variables associated with a positive result, we compared *UBA1*-positive and *UBA1*-negative patients. The *UBA1*-positive patients were compared with an external cohort comprising 20 patients with VEXAS syndrome from the USA.

Results: A total of 29 patients were tested, of whom 11 had a mutation in *UBA1* (positive detection rate: 37.9%). Eight were male (72.7%). The mean age at symptom onset was 59±17.2 years. The youngest patient was 23 y/o. Nine (81.8%) had the p.Met41Thr, and one each the p.Met41Val and p.Ser56Phe mutations. The clinical diagnoses (not mutually exclusive) were

Table 1. Clinical, genetic, and hematological characteristics of both VEXAS cohorts.

Table 1.	Mexican cohort N=11	External cohort N=20	P*
Male, n (%)	8 (72.7)	20 (100)	0.03
Age at symptom onset, years, mean (SD)	59 ± 17.2	61 ± 7	0.55
p.Met41Thr mutation, n (%)	9 (81.8)	13 (65)	0.32
p.Met41Val, mutation, n (%)	1 (9.1)	2 (10)	0.93
p.Met41Leu, mutation, n (%)	0	4 (20)	0.16
Relapsing polychondritis, n (%)	4 (36.4)	13 (65)	0.12
Sweet syndrome, n (%)	2 (18.2)	7 (35)	0.32
Undifferentiated autoinflammatory syndrome, n (%)	1 (9.1)	4 (20)	0.63
Myelodisplastic syndrome, n (%)	6 (54.5)	5 (25)	0.10
Fever, n (%)	6 (54.5)	17 (85)	0.06
Dermatological, n (%)	10 (90.9)	16 (80)	0.42
Inflammatory eye disease, n (%)	3 (27.3)	8 (40)	0.47
Periorbital edema, n (%)	2 (18.2)	12 (60)	0.02
Arthritis, n (%)	4 (36.4)	17 (85)	0.006
Pneumonitis, n (%)	2 (18.2)	13 (65)	0.01
Auricular chondritis, n (%)	5 (45.5)	14 (70)	0.17
Nasal chondritis, n (%)	3 (27.3)	11 (55)	0.13
Venous thrombosis, n (%)	2 (18.2)	10 (50)	0.08
Orchitis, n (%)	2/8 (25)	3 (15)	0.60
Macrocytic anemia, n (%)	8 (72.7)	10 (50)	0.22
Leukopenia, n (%)	6 (54.5)	4 (20)	0.04
Neutropenia, n (%)	5 (45.5)	0	0.003
Thrombocytopenia, n (%)	5 (45.5)	5 (25)	0.24
*Dichotomous variables were analysed with the Chi-square test or Fisher exact test. Comparison between means was made with Student's T-test			

myelodysplastic syndrome in 6 (54.5%), relapsing polychondritis in 4 (36.5%), Sweet syndrome in 2 (18.2%), and one each of polyarteritis nodosa, type I cryoglobulinemia, pyoderma gangrenosum, thyroid orbitopathy, undifferentiated autoinflammatory syndrome, multiple myeloma, and chronic myeloid leukemia.

Clinical and hematological manifestations are summarized in Table 1. Ten patients (90.9%) had hematological manifestations, with macrocytic anemia being the most common in 8 cases (72.7%), although most had macrocytosis (90.9%). Out of the 7 patients who underwent a bone marrow aspirate, 4 (57.1%) had vacuoles. Glucocorticoids and immunosuppressors were prescribed to 7 patients (58.3%), while chemotherapeutic regimens were used in 2 (18.2%). The median number of treatment lines was 1.5 (IQR: 1-2.5). With a median follow-up of 44 months (IQR 24-66), two patients had died.

The presence of macrocytosis (OR: 12.5, CI: 1.3-119.3) and macrocytic anemia (OR: 6.9, CI: 1.2-37.2) were associated with the presence of a pathogenic *UBA1* mutation. Conversely, having a clinical diagnosis other than the most reported in VEXAS syndrome exhibited a negative association with a positive *UBA1* mutation (OR: 0.064, CI: 0.007-0.612).

Compared to the external cohort, our patients showed higher frequencies of female patients, leukopenia, and neutropenia, but lower frequencies of fever, periorbital edema, arthritis, pneumonitis, and venous thrombosis (Table 1).

Conclusion: Patients with clinical diagnoses commonly associated with VEXAS syndrome, along with the presence of macrocytosis or macrocytic anemia, have an increased likelihood of harboring a pathogenic *UBA1* mutation. While our cohort displayed some distinct clinical and hematologic manifestations compared to the USA cohort, the type of *UBA1* mutations and clinical diagnoses were consistent. Noteworthy, our cohort included a higher proportion of female patients and one of the youngest ever reported cases of VEXAS.

Disclosure: E. Martin-Nares: None; **B. Sánchez-Hernández**: None; **P. Grayson**: None; **J. Crispin**: None; **D. Montante-Montes de Oca**: None; **A. Hinojosa-Azaola**: None; **G. Hernandez-Molina**: None; **E. Apodaca**: None; **E. Groarke**: None; **J. Delgado-de la Mora**: None; **S. Méndez-Flores**: None; **A. Gamboa-Domínguez**: None; **B. Patel**: None; **M. Ferrada**: None.

Abstract Number: 1942

Prevalence and Screening Strategy for Latent Tuberculosis Infection in Patients with Rheumatic Immune-Mediated Diseases

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SESSION INFORMATION

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Background/Purpose: Patients with rheumatic immune-mediated inflammatory diseases (rheumatic-IMID) with latent tuberculosis infection (LTBI) requiring biologic therapy (BT) are at anincreased risk of developing active tuberculosis (TB). Screening of LTBI with tuberculin skin test (TST) and/or interferon (IFN)-γ release assays (IGRA) is recommended before startingBT.

Methods: Cross-sectional single University hospital study including all patients diagnosedwith rheumatic-IMID who underwent a TST test and/or IGRA in a five-year period (2016-2020). TST was performed by a subcutaneous injection of 0.1 ml of purified proteinderivative (PPD) with a reading after 72 hours. TST was considered positive with aninduration of more than 5 mm of diameter. If the first TST was negative, a new TST (booster)was performed between 1 and 2 weeks after the first TST. The IGRA test used wasQuantiFERON®-TB Gold Plus (QFT-Plus). LTBI was diagnosed by a positive IGRA and/orTST and absence of active TB (normal chest X-ray). Concordance between IGRA and TSTwas studied using adjusted Cohen's kappa coefficient.

Results: Booster was positive in 66 patients (7.7%) out of 857 patients with a negative simple TST.TST (+ booster) was positive in 187 patients (22.9%) out of 817 with a negative orindeterminate IGRA test. IGRA test was positive in 30 (3.8%) out of 793 patients with anegative TST (+ booster), as is shown in **Figure 1 and 2.** Adjusted Cohen's Kappa coefficient between TST (+ booster) andIGRA (QFT-plus) was 0.62.

Figure 1. Increased sensitivity in detection of LTBI in patients with negative simple TST with additional booster TST and IGRA test.

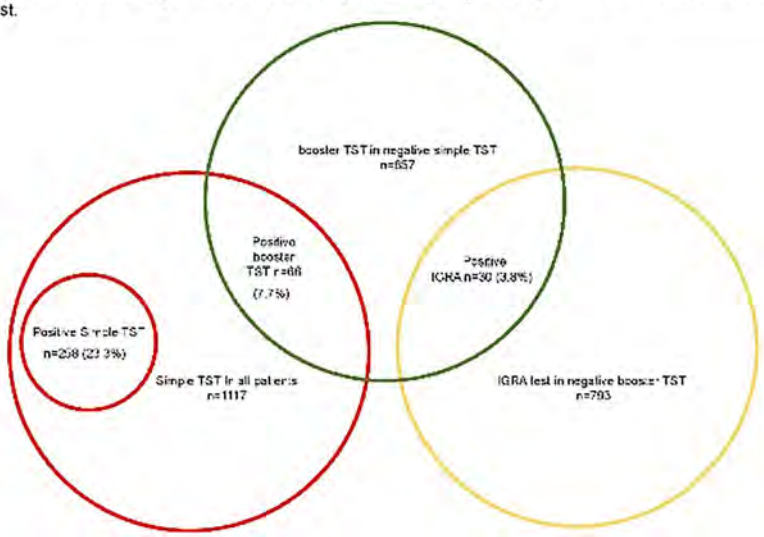
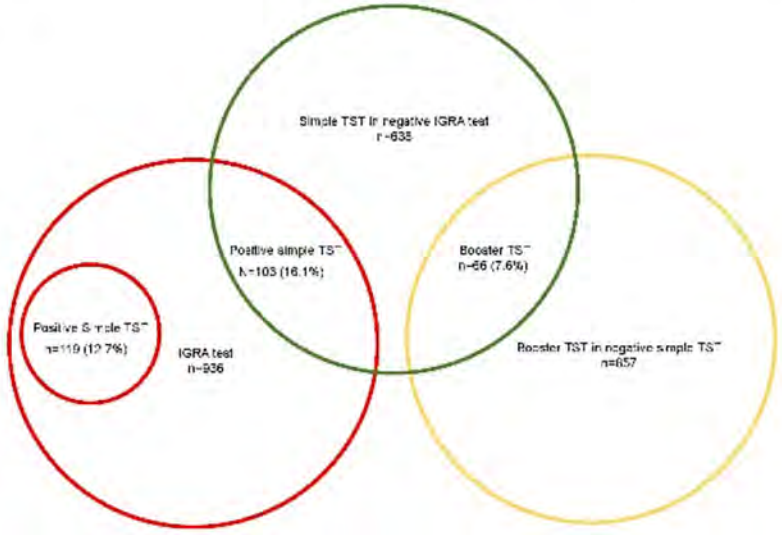


Figure 2. Increased sensitivity in detection of LTBI in patients with negative IGRA test with additional simple TST and booster TST.



Conclusion: LTBI is frequent between patients with rheumatic-IMID. Booster after negativesimple TST may be useful, since it can detect LTBI. Furthermore, IGRA and TST (+ booster)show a moderate fair grade of agreement. In addition, some patients who had a negative orindeterminate result on IGRA or TST could have a positive result in the other examination.This highlights the importance of performing both tests in all patients. Accordingly,performing both tests in patients with rheumatic-IMID before BT may be highlyrecommended.

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Abstract Number: 1943

IgG4-related Disease: 2010-2022 Case Review and Comparative Evaluation of Diagnostic Criteria

Pablo Martínez Calabuig[1], Jorge Juan Fragio[1], Roxana Gonzalez Mazarío[2], Amalia Rueda Cid[3], Mireia Lucía Sanmartín Martínez[1], Laura Salvador Maicas[1], Laura Abenza Barberá[1], María Cristina Sabater Abad[1], Antonio Sierra Rivera[1], Inmaculada Castelló Miralles[1], Juan José Lerma Garrido[1], Clara Molina Almela[3], Isabel Balaguer Trull[1] and Cristina Campos Fernández[1], [1]Hospital General Universitario Valencia, Valencia, Spain, [2]Hospital de Sagunto, Valencia, Spain, [3]Hospital General de Valencia, Valencia, Spain

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: IgG4 immunoglobulin-related disease (IgG4-RD) is a rare, systemic immune-mediated fibro-inflammatory process with an unclear etiology and pathophysiology with the capacity of affecting multiple organs. It exhibits common pathophysiological, serological, and clinical characteristics.

Objectives: To describe clinical presentation, evolution, and treatment heterogeneity among a series of IgG4-RD cases and to compare the accuracy of the last two most recent IgG4-RD classification and diagnostic criteria.

Methods: A single-center retrospective cross-sectional study was conducted, encompassing patients with a suspected diagnosis of IgG4-RD from various hospital departments (Rheumatology, Digestive Medicine, Internal Medicine and Pneumology). The study period lasted from January 2010 to August 2022. Exclusion criteria were applied to patients who were ultimately diagnosed with other pathologies, and for those patients who remained with a suspected diagnosis of IgG4-RD, the Umehara-Okazaki 2011 and ACR/EULAR 2019 criteria were subsequently employed.

Results: A total of 182 patients with elevated IgG4 and/or a suspected diagnosis of IgG4-RD were initially collected. After applying the exclusion criteria, 22 potential cases of IgG4-RD were described (Table 1). The Umehara and Okazaki 2011 diagnostic criteria were applied, resulting in the classification of 13 patients (mean age :60 years; 57% women); with 5 being classified as definitive disease, 3 as probable disease, and 5 as possible disease. One death was recorded in this group, which was related to heart failure. Furthermore, the ACR/EULAR 2019 classification criteria were applied to the same patient cohort (Table 1), resulting in the diagnosis of 7 patients (mean age:57 years; 71% women) with a mean follow-up of 5.3 years. In this group, 85.71% of patients had elevated IgG4 levels (mean: 176.3 mg/dL). Retroperitoneal fibrosis and aortitis were the most prevalent form of presentation for both groups (2011 and 2019 criteria) accounting for 38.5% and 28.6% respectively. Initially, 85.71% of the patients finally diagnosed with IgG4-RD received corticosteroids followed by other immunosuppressants such as Azathioprine, Methotrexate, Rituximab, surgical treatment, or maintenance doses of corticosteroids.

Conclusion: IgG4-RD is a recently recognized entity that exhibits significant heterogeneity in clinical, analytical, and histopathological presentation. Differences arise when utilizing different diagnostic criteria.

The most recent and stringent ACR/EULAR 2019 classification criteria allow for a more accurate classification of patients by emphasizing histopathology, different forms of presentation, and analytical data. Therefore, on many occasions, a multidisciplinary approach is often necessary.

Table 1. High diagnostic IgG4-RD group, Umehara and Okazaki 2011 and ACR/EULAR 2019 IgG4-RD criteria.

	High diagnostic IgG4-RD cases n=22	Umehara-Okazaki criteria 2011 n=13	ACR/EULAR criteria 2019 n=7
Age, median (IQR), years	62 (34-87)	60 (34-82)	57 (34-79)
Sex, female (%)	54,54	61,54	71,42
Follow-up, median (IQR), years	5,18 (1-28)	4,4 (1-9)	5,3 (1-9)
Death, n (%)	9,09	7,69	0
IgG4 level, median (IQR), mg/dL	152 (32,6- >194)	163,71 (56,6 ->194)	176,3 (109- >194)
Elevated IgG4, n (%)	63,63	84,62	85,71
Normal IgG4, n (%)	13,63	7,69	0
Not evaluated IgG4, n (%)	22,72	7,69	14,29
CRP, median (IQR), mg/dL	3,33 (0-10,7)	3 (0,1 -10,7)	6 (0,39 -7,8)
ESR, median (IQR), mm/h	32,89 (7-120)	42 (10 -120)	48,4 (16-120)
Available biopsy at IgG4 involvement site (%)	40,91	69,23	100
Clinical phenotypes			
Pancreatohepatobiliary, n (%)	18,18	15,38	14,28
Retroperitoneum and aorta, n (%)	40,91	38,46	28,57
Head and neck limited, n (%)	4,55	7,69	0
Mickulicz and systemic, n (%)	4,55	7,69	14,28
Undefined phenotype, n (%)	31,82	30,77	42,86
Initial corticotherapy, n (%)	90,91	84,61	85,71

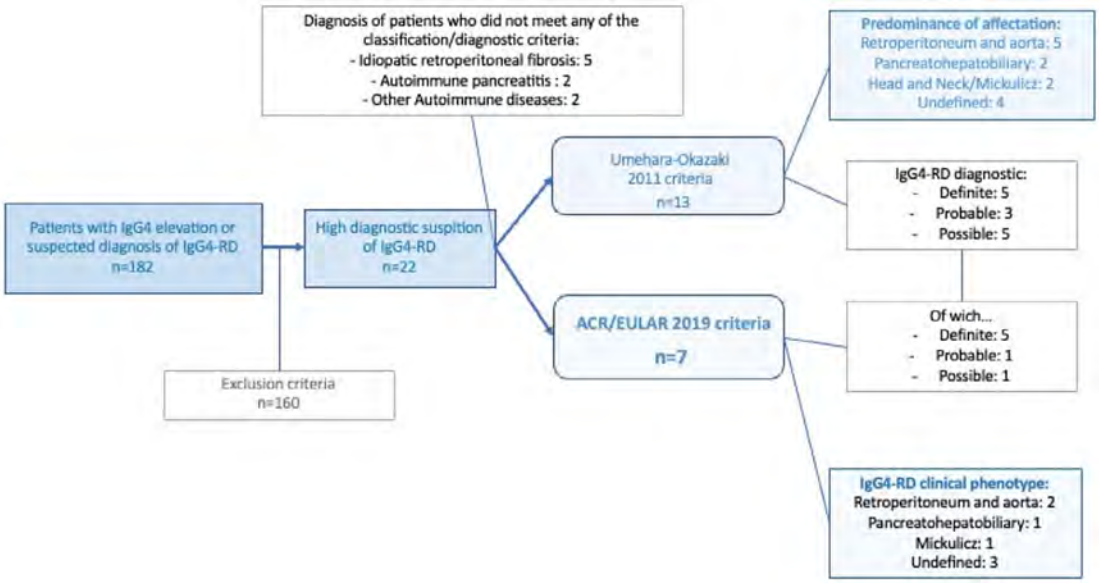

Image 1. Diagnostic sequence used with IgG4-RD patients.

Disclosure: P. Martínez Calabuig: None; **J. Fragio**: None; **R. Gonzalez Mazarío**: None; **A. Rueda Cid**: None; **M. Sanmartín Martínez**: None; **L. Salvador Maicas**: None; **L. Abenza Barberá**: None; **M. Sabater Abad**: None; **A. Sierra Rivera**: None; **I. Castelló Miralles**: None; **J. Lerma Garrido**: None; **C. Molina Almela**: None; **I. Balaguer Trull**: None; **C. Campos Fernández**: None.

Abstract Number: 1944

Characterization of Interstitial Pneumonia with Autoimmune Features (IPAF) in a National Referral Centre

Arturo Llobell[1], Belén Atienza-Mateo[2], David Iturbe-Fernández[3], Victor Mora-Cuesta[3], Marcos Lopez-Hoyos[4], Jose Cifrian[5] and Ricardo Blanco[6], [1]Parc Tauli University Hospital, Barcelona, Spain, [2]Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain, [3]Immunopathology Group, Marqués de Valdecilla University Hospital-IDIVAL; Department of Pneumology, Marqués de Valdecilla University Hospital, Santander, Spain, [4]Marques de Valdecilla University Hospital-IDIVAL, Santander, Spain, [5]Immunopathology Group, Marqués de Valdecilla University Hospital-IDIVAL; Department of Pneumology, Marqués de Valdecilla University Hospital; School of Medicine, Cantabria University, Santander, Spain, [6]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1913–1944) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) comprises a wide range of disorders categorized by clinical, radiographic and pathologic findings that is closely associated with autoimmune connective tissue diseases (CTD), requiring an investigation into a potential unknown CTD when diagnosing ILD. A significant number of patients can exhibit nonspecific signs of autoimmunity, either clinical and/or serologic, without meeting the criteria for a distinct CTD, which has led to the classification of this disease as Interstitial Pneumonia with Autoimmune Features (IPAF). In our study, we aim to characterize a cohort of patients with ILD who satisfy the IPAF criteria.

Table 1. Demographic, clinical, serologic and morphologic features of 34 patients with IPAF.

Characteristics	ILD patients with IPAF criteria
Age at ILD diagnosis (years), mean ± SD	58 ±11,84
Sex (men/women), n (%)	22/12 (65/25)
Smoking history, n (%)	27 (79)
PFTs at ILD diagnosis	
FVC (% predicted), mean ± SD	77.46 ± 23.1
DLCO (% predicted), mean ± SD	40.87 ± 15.8
Clinical domain, n (%)	
Raynaud's phenomenon	10 (29)
Inflammatory arthritis	8 (24)
Digital edema	2 (6)
Distal digital fissuring/ ulceration	1 (3)
Palmar telangiectasia	0 (0)
Gottron sign	0 (0)
Serologic domain, n (%)	
ANA >1:320 speckled, homogeneous or combined pattern	17 (50)
Rheumatoid factor	6 (18)
Anti-CCP Abs	3 (9)
Anti-B2 glicoprotein Abs	3 (9)
Anti-DNA Abs	2 (6)
Anti-Ssa Abs	2 (6)
Anti-Ku Abs	2 (6)
Anti-Ro52 Abs	1 (3)
Morphologic domain, n (%)	
HRCT pattern of UIP	11 (32)
HRCT pattern of probable UIP	7 (21)
HRCT pattern of NSIP	8 (24)
Other HRCT patterns	6 (18)
Suggestive histological patterns	17 (50)

DLCO: diffusing capacity of the lung for carbon monoxide; FVC: forced vital capacity; ILD: interstitial lung disease; PFTs: pulmonary function tests; SD: standard deviation; VA: alveolar volume; Abs: Antibodies; HRCT: high-resolution computed tomography; UIP: usual interstitial pneumonia; NSIP: non-specific interstitial pneumonia.

Methods: We collected data of patients assessed in a multidisciplinary clinic of Pneumology and Rheumatology at the Marqués de Valdecilla University Hospital (Santander, Spain). Included patients had a confirmed diagnosis of ILD, determined either through a chest high-resolution computed tomography (HRCT) or lung biopsy. Medical records were examined to assess clinical and/or serologic IPAF criteria, as well as HRCT and lung biopsy reports. Exclusion from the study took place if patients met classification criteria for a distinct CTD or if there was incomplete data to asses their case.

Results: From a cohort of 689 patients with ILD, we included a total of 34 individuals who fulfilled the criteria for IPAF. Among them, mean age at diagnosis was 58 ±11,84. 22 (65%) were male and 12 (35%) female. 27 (79%) had smoking history. 15 out of the 34 patients (44%) met the clinical criteria for IPAF, being Raynaud's phenomenon the most frequent (n=10), followed by inflammatory arthritis (n=8), digital edema (n=2) and digital ulceration (n=1). Serologic criteria for IPAF were fulfilled

by 28 out of 34 patients (84%). The most prevalent serologic criterion was the presence of an ANA higher than 1:320 (patterns: speckled, homogeneous or combined. n=17) followed by positive rheumatoid factor (n=6), anti-CCP (n=3), anti-ß2 glicoprotein (n=3), anti-DNA (n=2), anti-Ssa (n=2), anti-Ku (n=2) and anti-Ro52 (n=1). As for radiologic and morphologic criteria, 30 patients (88%) met the requirements for IPAF, being usual interstitial pneumonia (UIP) (n=11) the most frequently observed, followed by probable UIP pattern (n=7) and non-specific interstitial pneumonia (NSIP) (n=8). **Table 1** shows the demographic, clinical, serologic and morphologic features of our patients.

Conclusion: This is a single-center, retrospective study focused on patients who fulfilled IPAF criteria. Among this cohort, a majority of men was reported (65%), and a high proportion of patients presented smoking history (79%). Regarding clinical, serologic or morphologic features, even with less than half of the patients (44%) showing clinical features of CTD, serologic (84%) and radiologic-morphologic (88%) criteria were met by a majority of patients. Given the benefits of early immunosuppressive treatment in this disease, a thorough identification of findings in either clinical, serologic and/or morphologic domains must be prioritized when approaching patients when suspecting a IPAF diagnosis.

Disclosure: A. Llobell: None; **B. Atienza-Mateo**: None; **D. Iturbe-Fernández**: None; **V. Mora-Cuesta**: None; **M. Lopez-Hoyos**: None; **J. Cifrian**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6.

Abstract Number: 1945

Case Series of 6 Patients Exhibiting Myositis as a Rheumatologic Adverse Events Related to Cancer Immunotherapy in Two Spanish Hospitals

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Myositis is a rare inflammatory complication associated with immune related adverse events (irAE) of immune checkpoints inhibition (ICI) immunotherapy[1]. It is characterized by musculoskeletal inflammation, resulting in significant muscle weakness and pain. Diagnosis is based on clinical evaluations, blood tests, and imaging studies. Management of myositis may involve the suspension or adjustment of immunotherapy, as well as the administration of anti-inflammatory or immunosuppressive medications[2]. Although this complication can be severe, immunotherapy remains a valuable tool in cancer treatment for these patients.

Methods: A retrospective, descriptive study of patients treated with ICIs that developed myositis as a result of said treatment, at Parc Taulí and Marqués de Valdecilla University Hospitals, between 2016 and 2022. Medical records were reviewed by a rheumatologist to identify demographic and clinic relevant data.

Table 1: Patients clinical characteristics, presentation, treatments and outcomes.

Patient information	Patient Case				
	1	2	3	4	5
Age at ICI treatment	48	83	63	72	79
Gender	M	F	M	M	F
Tumor	Melanoma	Melanoma	Renal	Colorrectal	Urothelial
Treatment	Pembrolizumab	Pembrolizumab	Nivolumab	Durvalumab	Atezolizumab
Mechanism	PD1	PD1	PD1	PDL1	PDL1
Line of treatment	3	1	2	1	2
ICI on monotherapy?	Yes	Yes	Yes	No	Yes
Time before irAE onset (weeks)	4	4	4	4	4
Rheumatological Manifestations	Myositis	Myositis	Myositis	Myositis	Myositis
Other manifestations	Asthenia	Myasthenia	Hepatitis	Myasthenia, Myocarditis, Toxicodermia, Thyroiditis, Hepatitis, Pneumonitis	Asthenia, Myocarditis, meningo-encephalitis
Treatments					
GC	x	x	x	x	x
IVIG		x	x	x	x
Rituximab	x				
Mycophenolate				x	x
Discontinuation of ICI		x	x	x	x
Due to irAE		x	x	x	
Death		x	x		x
Related to irAE		x			

Results: From a cohort of 734 patients treated with ICIs, 54 presented rheumatologic irAEs, of which 5 developed myositis, (3 male/2 female). 3 were treated with anti-PD1, 2 with anti-PDL1. Underlying cancer types included melanoma (n=2), colorectal (n=1), renal (n=1) and urothelial (n=1). Patients presented concomitant irAEs, such as myasthenia (2), hepatitis (2), pneumonitis (1), meningoencephalitis (1) and myocarditis (1). All patients required treatment with high doses of glucocorticoids and the association of either intravenous immunoglobulins (IGIV) (n=4) and/or biologic (n=1) or synthetic (n=2) immunosuppressant (IS) drugs. In 4 out of 5 cases, this irAE was the main reason for ICI treatment discontinuation, and only 1 presented permanent response to treatment. **Table 1** shows the patients' clinical characteristics, presentation, treatments and outcomes. Serologically, only 1 patient presented elevated CRP, but 4 out of 5 presented positivity for autoantibodies, which included anti-Ro52 anti-PM Scl, ANA Nucleolar pattern, anti-GAD and anti-SRP.

Conclusion: Our study highlights the significant burden of irAE myositis in patients undergoing ICI therapy. All 5 patients in our study required intensive treatment with corticosteroids, 4/5 received intravenous immunoglobulin (IVIG), and 4/5 tested positive for autoantibodies and presented other irAEs. There was only complete response to the treatment of the irAE on 1 patient, with the remaining 5 requiring maintenance treatment and experiencing relapses or little improvement. 3 patients died, at least in one of them by irAE related complications. These findings emphasize the need for increased vigilance in monitoring and early intervention to manage irAEs such as myositis effectively. Further research is needed to understand the underlying mechanisms and improve detection and treatment strategies for this complication of immunotherapy.

Bibliography:

1.- Postow MA et al. Immune-Related Adverse Events Associated with Immune Checkpoint Blockade. NEJM. 2018 Jan 11;378(2):158-168.
2.- Boutros A et al. Neuromuscular and cardiac adverse events associated with immune checkpoint inhibitors: pooled analysis of individual cases from multiple institutions and literature. ESMO Open. 2023 Feb;8(1):100791.

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Abstract Number: 1946

Zetomipzomib Demonstrates Favorable Long-term Safety and Tolerability Profile Without Signs of Immunosuppression: Results from the PRESIDIO Study and Its Open-label Extension Study in Patients with Dermatomyositis and Polymyositis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Polymyositis (PM) and dermatomyositis (DM) are chronic autoimmune diseases characterized by muscle inflammation and weakness. In a collagen-induced myositis mouse model, immunoproteasome inhibition has shown to significantly revert the decreased grip strength and reduce the histopathological score of inflamed striated muscles. Zetomipzomib (KZR-616) is a first-in-class selective inhibitor of the immunoproteasome. PRESIDIO (NCT04033926) was a Phase 2 randomized, double-blind, placebo-controlled crossover study evaluating the safety, tolerability, efficacy and PK/PD of zetomipzomib 45 mg subcutaneously (SC) weekly (QW) treatment in patients (pts) with active PM and DM with an open-label extension (OLE) to evaluate the long-term efficacy and safety up to 96 weeks (NCT04628936). Results from PRESIDIO and its OLE study are reported here.

Methods: Pts were randomized to initially receive zetomipzomib 45 mg (first two doses: 30 mg) or placebo SC QW; pts received zetomipzomib or placebo treatment over 16 weeks, followed by crossover to the other arm for an additional 16 weeks (total study duration of 32 weeks). Study entry criteria included adults with probable or definite PM or DM based on the 2017 EULAR/ACR Classification Criteria with confirmed active disease (MMT-8 score of 80-136 and two other abnormal core set measures). The primary endpoint was the mean change in the Total Improvement Score (TIS). Pts completing 32 weeks of the double-blind treatment period could enroll in the OLE study up to 96 weeks.

Table 1: Zetomipzomib Treatment Demonstrated a Favorable Safety and Tolerability Profile in the PRESIDIO Study and Its OLE Study

Patients Experiencing Adverse Events, n (%)	Zetomipzomib N=25	Placebo N=22*	Zetomipzomib OLE N=18
Patients with any TEAE	22 (88.0)	15 (68.2)	16 (88.9)
Grade 1	21 (84.0)	14 (63.6)	15 (83.3)
Grade 2	8 (32.0)	8 (36.4)	10 (55.6)
Grade 3	2 (8.0)	2 (9.1)	2 (11.1)
Grade 4	0 (0)	0 (0)	0 (0)
Most common TEAE: Injection-site reaction	18 (72.0)	3 (13.6)	14 (77.8)
TEAEs leading to study discontinuation	1 (4.0)	0 (0)	3 (16.7)
Serious TEAE (all unrelated)	2 (8.0)	1 (4.5)	1 (5.6)
Infections TEAEs	7 (28.0)	6 (27.3)	7 (38.9)
Grade 1	5 (20.0)	5 (22.7)	5 (27.8)
Grade 2	2 (8.0)	3 (13.6)	3 (16.7)
Grade 3	0 (0)	1 (4.5)	0 (0)
Grade 4	0 (0)	0 (0)	0 (0)
Opportunistic Infections	0	0	0
Death	0	0	0

*Three patients withdrew prior to receiving placebo

Results: 25 pts with active DM (n=13) and PM (n=12) enrolled and 20 pts completed through end-of-treatment; 18 opted into the OLE study (4 pts received < 24 weeks of zetomipzomib dosing, 4 pts received 24-48 weeks of dosing, and 10 pts received ≥48 weeks of zetomipzomib dosing [1 pt had 96 weeks of treatment]). Overall, pts saw clinically meaningful improvements in TIS, but zetomipzomib demonstrated no significant differentiation from placebo. At Week 16, the zetomipzomib group achieved a mean TIS of 25.5 versus 25.0 in the placebo group. Following cross-over at Week 32, the pts receiving zetomipzomib beginning at Week 16 achieved a mean TIS of 34.2 versus 34.1 in those receiving placebo beginning at Week 16. Zetomipzomib treated patients also showed improvements in other efficacy endpoints. In the OLE, mean TIS generally continued to improve with reduced symptoms and improvement in strength. Treatment-emergent adverse events (TEAE) were generally mild-to-moderate (Table 1). The most common TEAEs were injection site reactions (ISRs), which were generally transient and manageable. ISRs occurred more frequently with zetomipzomib than with placebo. There was no evidence of immunosuppression observed, as measured by preserved cell counts and lack of ≥ Grade 3 infection or opportunistic infections. There were no off-target or new adverse events observed with >1-year weekly administration in the OLE.

Conclusion: Zetomipzomib demonstrated a favorable safety and tolerability profile without signs of direct immunosuppression upon prolonged exposure. Zetomipzomib did not show differentiation from placebo, but individual patients with DM or PM experienced a clinically meaningful improvement in TIS.

Disclosure: R. Aggarwal: Actigraph, 2, Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella Bioscience, 2, Corbus, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Mallinckrodt, 5, Merck, 2, Octapharma, 2, Pfizer, 2, 5, Q32, 5, Roivant, 2, Sanofi, 2, Teva, 2; **N. Goyal**: None; **D. Lam**: None; **A. Ng**: None; **R. Leff**: Kezar Life Sciences, 2, 8, 11, Sorrento Therapeutics, 7; **K. Ray**: Kezar Life Sciences, 3; **E. Park**: Kezar Life Sciences, 3, 11; **N. Henig**: Kezar Life Sciences, 3, 11.

Abstract Number: 1947

National Incidence, Prevalence & Mortality in Idiopathic Inflammatory Myopathies & Associated Interstitial Lung Disease in England

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

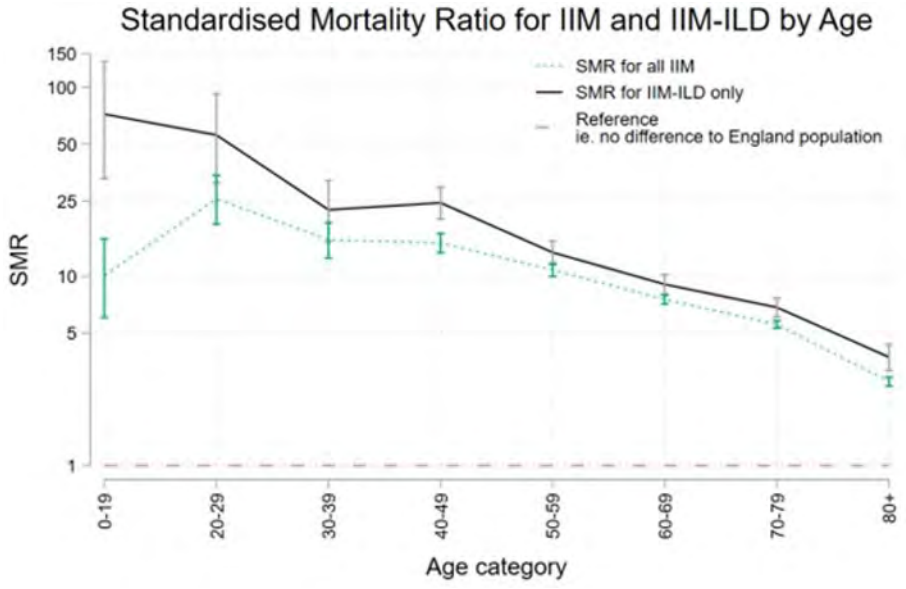
Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Ethnicity, sex, age & socioeconomic deprivation can all lead to health inequity. Impact of these factors in epidemiology of Idiopathic Inflammatory Myopathies (IIM) has not been widely researched.In collaboration with National Congenital Anomaly & Rare Disease Registration Service (NCARDRS), we described national incidence, prevalence & mortality in IIM and associated Interstitial Lung Disease (IIM-ILD) according to demographics.

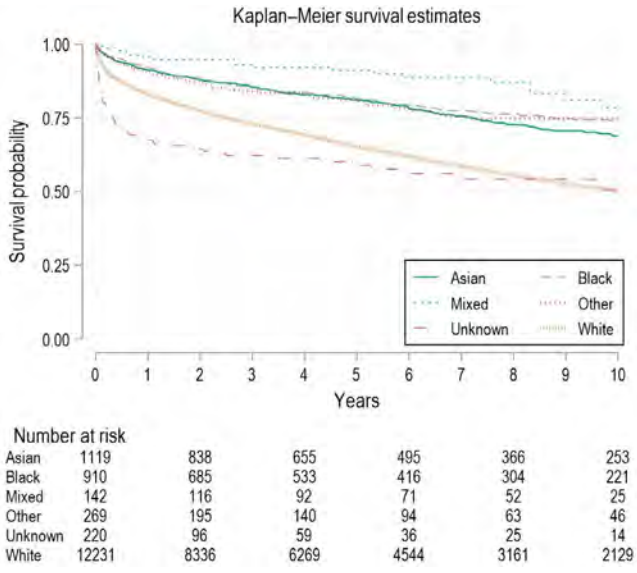
Methods: Hospital Episode Statistics (HES) collected at every NHS hospital admission in England, were used to create a national cohort of patients with IIM & IIM-ILD associated ICD-10 codes between 2006-2022. Cases were identified according to pre-validated methods (Hannah, 2022). Age, sex, ethnicity, Index of Multiple Deprivation (IMD) and death certification were collated. Denominator populations were extracted from Office of National Statistics publications. Incidence rates were calculated by multivariate Poisson regression, standardized mortality ratio (SMR) by indirect standardization, and survival analysis by multivariate Cox models. Incidence Rate Ratios (IRR) were mutually adjusted for age, sex & IMD (Ethnicity IRR was not adjusted for IMD due to lack of suitable denominator data). Cox models were adjusted for age, sex, ethnicity, IMD and ILD status.



SMR for IIM and subgroup of IIM-ILD compared to the population of England demonstrating increased SMR across all age categories

	Denominator population	Crude incident rates per 100,000 (95% CI)	Adjusted incidence rate ratio (95% CI)*	Mortality Rate per 1000 person years (95% CI)	Adjusted Hazard Ratio (95% CI) †
Sex					
Male	425,860,694	1.44 (1.40, 1.48)	Ref	85.02 (81.79, 88.38)	Ref
Female	438,435,489	2.00 (1.96, 2.04)	1.30 (1.25, 1.34)	66.26 (64.00, 68.61)	0.78 (0.74, 0.82)
Age in years					
<20	206,319,439	0.35 (0.33, 0.38)	0.07 (0.06, 0.07)	3.58 (2.29, 5.62)	0.03 (0.02, 0.04)
20-30	115,232,876	0.53 (0.49, 0.57)	0.10 (0.09, 0.11)	10.63 (7.99, 14.15)	0.08 (0.06, 0.10)
30-40	116,132,979	0.89 (0.83, 0.94)	0.17 (0.16, 0.18)	12.04 (9.75, 14.85)	0.08 (0.07, 0.10)
40-50	119,640,385	1.35 (1.29, 1.42)	0.26 (0.25, 0.28)	26.16 (23.30, 29.37)	0.18 (0.16, 0.21)
50-60	109,909,359	2.26 (2.17, 2.35)	0.44 (0.41, 0.46)	43.47 (40.23, 46.97)	0.30 (0.27, 0.33)
60-70	91,107,975	3.48 (3.36, 3.60)	0.67 (0.64, 0.70)	74.87 (70.90, 79.07)	0.52 (0.48, 0.56)
70-80	64,920,382	5.20 (5.03, 5.38)	Ref	146.48 (140.16, 153.09)	Ref
80-90	33,941,835	4.96 (4.73, 5.20)	0.94 (0.88, 0.99)	272.28 (257.51, 287.91)	1.77 (1.65, 1.91)
90+	7,090,953	2.74 (2.35, 3.12)	0.50 (0.44, 0.58)	518.54 (446.17, 602.65)	3.04 (2.60, 3.56)
Socioeconomic Status					
1 (most deprived)	173,533,908	1.56 (1.50, 1.62)	Ref	70.30 (66.10, 74.77)	Ref
2	175,849,262	1.69 (1.63, 1.75)	1.00 (0.95, 1.05)	69.51 (65.51, 73.76)	0.83 (0.76, 0.90)
3	174,080,644	1.72 (1.66, 1.79)	0.92 (0.87, 0.97)	79.77 (75.45, 84.34)	0.80 (0.74, 0.87)
4	171,481,922	1.78 (1.72, 1.85)	0.91 (0.86, 0.96)	76.65 (72.45, 81.09)	0.72 (0.66, 0.78)
5 (least deprived)	169,350,447	1.86 (1.80, 1.93)	0.93 (0.89, 0.98)	71.19 (67.27, 75.34)	0.65 (0.60, 0.71)
Ethnicity					
White	737,397,814	1.66 (1.63-1.69)	Ref	80.92 (78.73, 83.18)	Ref
Asian or Asian British	70,178,717	1.59 (1.50, 1.69)	1.56 (1.47-1.66)	41.99 (37.36, 47.20)	0.80 (0.71, 0.91)
Black or Black British	31,393,706	2.90 (2.71, 3.09)	2.77 (2.59-2.96)	36.37 (31.70, 41.74)	0.78 (0.67, 0.90)
Other	9,324,447	2.88 (2.54, 3.23)	2.97 (2.63-3.35)	41.87 (32.37, 54.16)	0.79 (0.61, 1.02)
Mixed	21,607,029	0.66 (0.55-0.77)	0.96 (0.82-1.14)	24.92 (16.41, 37.84)	0.81 (0.53, 1.23)
Unknown	n/a	n/a	n/a	131.34 (105.92, 162.86)	1.94 (1.56, 2.41)

Incidence Rate Ratios and mortality Hazard Ratio according to demographics. *Incidence rate ratios are adjusted for age, sex and socioeconomic status †Adjusted hazard ratios for age, sex, socioeconomic status, ethnicity and presence of ILD are mutually adjusted.



Kaplan-Meier survival curve showing increased mortality in Unknown and White ethnicity categories

Results: 14,891 incident IIM cases were identified giving an incidence rate of 1.72/100,000 person-years. Point prevalence was 17.9/100,000 in 2022. Mean age was 59.7 years with incidence peaking at 70-80 years. Multivariate models (Table) showed IIM incidence was higher in females IRR 1.30 (95%CI 1.25, 1.34), but mortality was lower (hazard ratio (HR) 0.78 (95%CI 0.74, 0.82)). Incidence was higher in Asian and Black ethnicities than White (IRR 1.56 and 2.77 respectively). Mortality was higher in White ethnicity (Asian HR 0.80 and Black HR 0.78). The most deprived population quintile had similar incidence IRR 1.06 (95%CI 1.02, 1.11), but higher mortality HR 1.34 (95%CI 1.25, 1.44) than less deprived populations. 17.2% of IIM cases had ILD. IIM-ILD incidence did not vary largely by socioeconomic deprivation, but was substantially higher in Black, Other and Asian populations compared to White (IRR 5.11, 4.07, 2.48). Mortality of IIM-ILD was also lower in Asian HR 0.76 (95%CI 0.61, 0.95) and Black HR 0.73 (95%CI 0.57, 0.93) patients. SMR was 5.13 for IIM and 7.92 for IIM-ILD. Crude mortality increases with age, but standardized mortality is highest in younger patients with ILD. Death certification was available in 7,159 cases. IIM was recognized as a contributory factor in 39%, and ILD in 10.6%. Malignancy was the most reported 'underlying cause of death' (24.7%), then cardiovascular disease (19.9%) and respiratory disease (15.8%). Asian and Black ethnicities were less likely to have malignancy mentioned on death certificates (IRR 0.48 and 0.61 respectively).

Conclusion: We have defined national incidence, prevalence and SMR estimates for IIM and IIM-ILD. Incidence is higher in females, Black, Asian and Other ethnicities. Mortality is higher in White ethnicities, increased deprivation and males. Increased mortality in White ethnicities may partially relate to increased malignancy-associated disease.

Disclosure: J. Hannah: None; **F. Pearce**: Vifor Pharma, 5; **M. Odingo**: None; **M. Rutter**: None; **J. Aston**: None; **J. Lai**: None; **M. Grainge**: None; **S. Mcphail**: None; **P. Lanyon**: Pfizer, 5; **M. Bythell**: None; **J. Galloway**: AbbVie, 2, 5, 6, AstraZeneca, 5, Biogen, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **P. Gordon**: Celltrion, 12, Support to attend EULAR conference 2023, Galapagos, 1.

Abstract Number: 1948

The Influence of Specific Myositis Antibodies on the Development of Interstitial Lung Disease

Ting-Yuan Lan[1], Tai-Ju Lee[1], Kuan-Yen Lin[2], Jui-Hung Kao[3], Chiao-Feng Cheng[4], Cheng-Hsun Lu[4], Chieh-Yu Shen[4], Ko-Jen Li[4] and Song-Chou Hsieh[4], [1]National Taiwan University Hospital Hsinchu Branch, Hsinchu City, Taiwan, [2]National Taiwan University Hsinchu branch, Hsinchu, Taiwan, [3]National Taiwan University Hospital Yunlin branch, Yunlin, Taiwan, [4]National Taiwan University Hospital, Taipei, Taiwan

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
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Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial Lung Disease (ILD), prevalent in Idiopathic Inflammatory Myositis (IIM) patients, significantly impacts prognosis. Certain myositis-specific antibodies, including anti-MDA5 and anti-aminoacyl-tRNA synthetases (ARS), are linked to increased ILD incidence, while other myositis antibodies were rarely discussed. Recent evidence suggests survival rates among Interstitial Pneumonitis with Autoimmune Feature (IPAF) patients harboring myositis specific antibodies (MSA) parallel those with IIM-ILD [1]. Our study aims to investigate the pulmonary involvement in IIM and IPAF patients, emphasizing the role of diverse myositis antibodies, within a single center cohort.

Methods: From Jan. 2010 to Dec. 2022, patients diagnosed with IIM who underwent myositis antibody testing were identified in a Taiwan medical center. Additionally, 49 patients diagnosed with IPAF per the 2015 ERS statement with positive myositis antibody result were also enrolled for analysis.[2] The diagnosis of ILD was confirmed by a HRCT finding. The myositis antibodies were determined through line-blot multiplex assay (Autoimmune Inflammatory Myopathies 16 Ag, Euroimmun, Lübeck, Germany), encompassing 16 autoantigens.

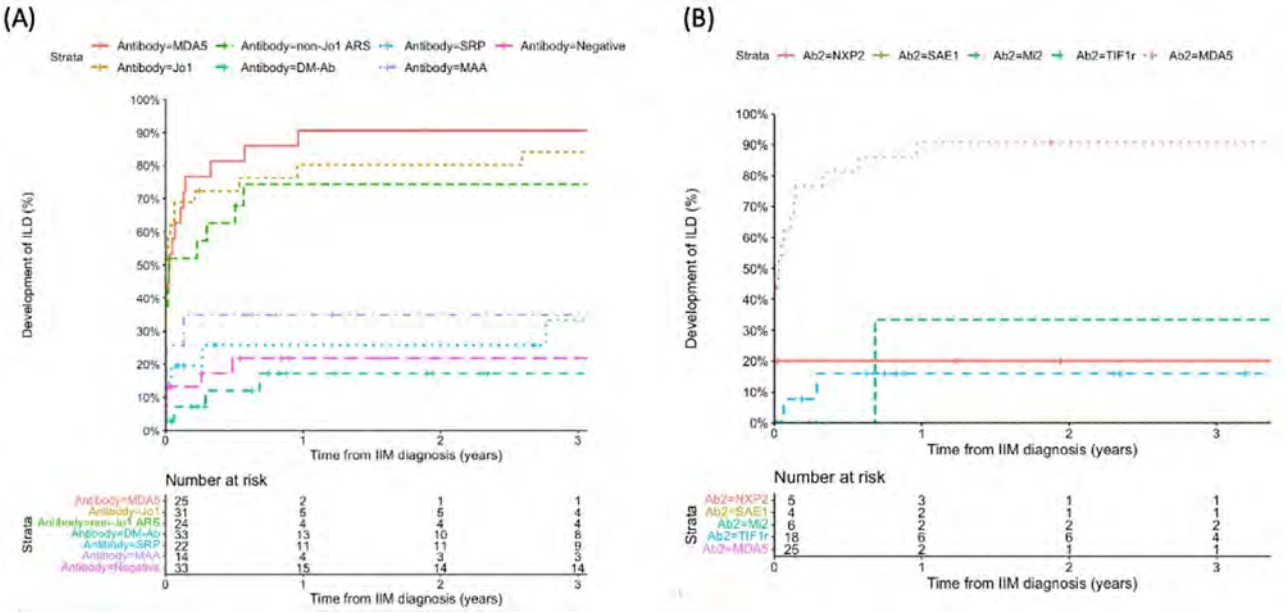
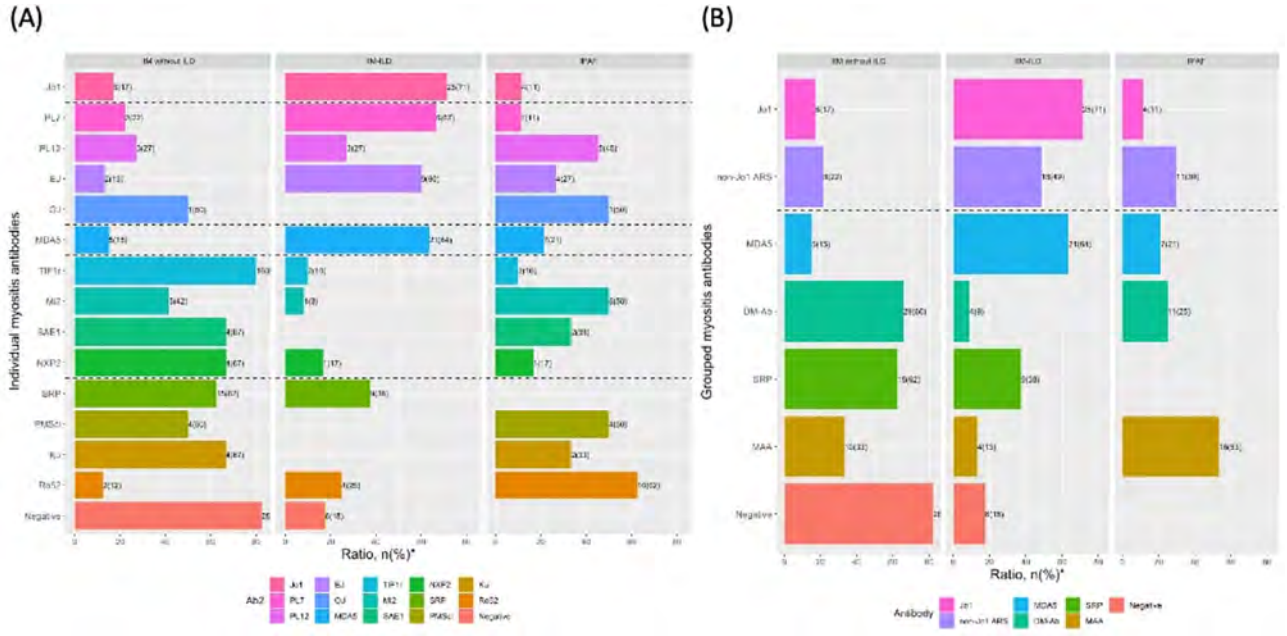
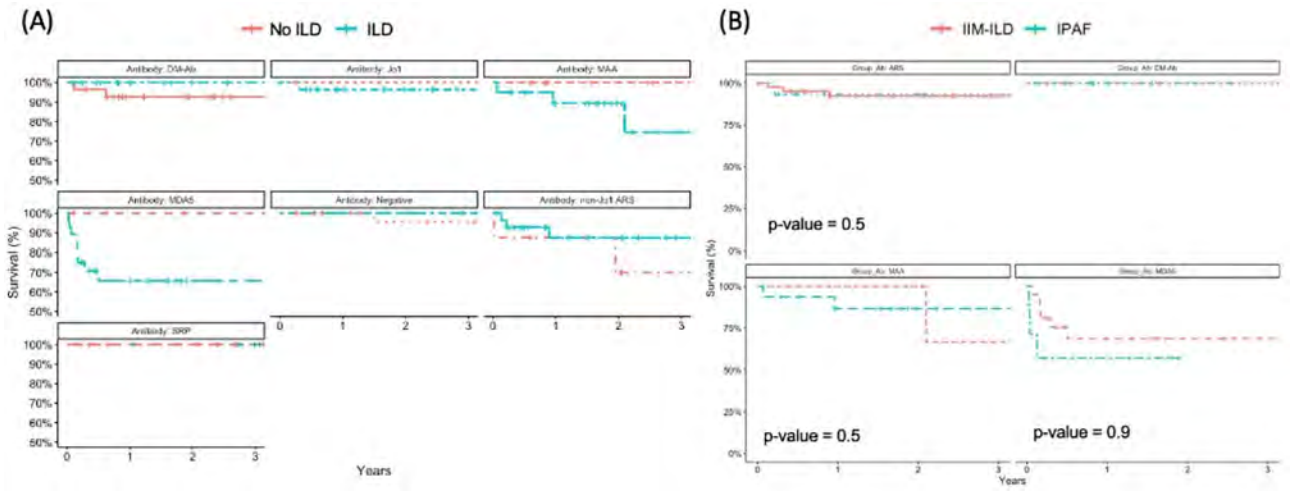


Fig.1: Cumulative incidence of ILD development stratified according to different myositis antibodies (A) and dermatomyoisits-specific antibodies (B). Anti-ARS=aminoacyl tRNA synthetase antibodies (including anti-Jo1, EJ, OJ, PL-7, PL-12), DM-Ab = dermatomyositis specific antibodies (including anti-TIF1r, NXP2, SAE, Mi2, MDA5).



Distribution of myositis antibodies among IIM without ILD, IIM-ILD, and IPAF patient groups, stratified according to individual antibodies (A) and grouped antibodies (B). Numbers beside each bar indicate patient count and respective percentage. Anti-ARS=aminoacyl tRNA synthetase antibodies (including anti-Jo1, EJ, OJ, PL-7, PL-12), DM-Ab = dermatomyositis specific antibodies (including anti-TIF1r, NXP2, SAE, Mi2, MDA5).



Kaplan–Meier survival curve for IIM and IPAF subgroups. (A) The survival impact of ILD stratified by different myositis antibodies. (B) The survival curve of patients with IIM-ILD and IPAF stratified by selected myositis antibodies.

Results: 118 IIM patients (mean age 52, 75% female) and 49 IPAF patients (mean age 67, 49% female) were enrolled. The anti-MDA5 and ARS were significantly associated with ILD development, exhibiting the 3-year incidence exceeding 70%, with most cases presenting within the first year post-diagnosis. Approximately 40% patients with anti-SRP ultimately developed ILD (Figure 1A). In patients with DM-specific antibodies (TIF1r, Mi2, SAE1, NXP2, MDA5, as defined by ENMC 2020 consensus) except for anti-MDA5, most remained ILD-free 3 years post-diagnosis (Figure 1B). A non-negligible fraction of patients with anti-MDA5, anti-ARS, and dermatomyositis-specific antibodies presented with IPAF instead of IIM or ASS (Figure 2). However, the correlation between ILD and poor prognosis only exist for patients with anti-MDA5 and MAA (Figure 3A). Furthermore, the 3-year survival rate for IIM-ILD and IPAF patients with anti-MDA5 (68% vs 57%, p=0.9) , anti-ARS (92% vs 93%, p=0.5) and DM-specific antibodies (100% vs 100%) were similar (Figure 3B).

Conclusion: Anti-MDA5 and ARS antibodies demonstrated a strong correlation with ILD development, and prognosis was consistent among IIM-ILD and IPAF patients. Other dermatomyositis-specific antibodies and anti-SRP were also associated with ILD development, albeit to a lesser extent, and the onset of ILD did not correlate with a poorer prognosis.

Disclosure: T. Lan: None; **T. Lee**: None; **K. Lin**: None; **J. Kao**: None; **C. Cheng**: None; **C. Lu**: None; **C. Shen**: None; **K. Li**: None; **S. Hsieh**: None.

Abstract Number: 1949

Relapse of Rapidly Progressive Interstitial Lung Disease in Patients with Anti-Melanoma Differentiation-Associated Gene 5 Autoantibody-Positive Dermatomyositis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
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Background/Purpose: Autoantibodies to Melanoma Differentiation-Associated Gene 5 (MDA5) are found specifically in patients with dermatomyositis (DM). Their presence is closely associated with rapidly progressive interstitial lung disease (RP-ILD) and poor prognosis. Although RP-ILD is a life-threatening condition, relapse of RP-ILD has rarely been reported after the success of the initial treatment. Nonetheless, some patients do relapse, but the clinical features and changes in laboratory biomarkers at the time of relapse of RP-ILD in patients with anti-MDA5-positive DM remain unclear. The aim of this study was to establish the clinical features of anti-MDA5-positive RP-ILD in patients with exacerbations after remission had been achieved.

Methods: Forty-one patients with classic DM or Clinically Amyopathic (CA) DM and ILD who were seen at Tokai University from 2011 to 2021 were retrospectively evaluated for their clinical and immunological characteristics including the occurrence of relapse during the clinical course after remission induction. Anti-MDA5 antibody was assayed by protein immunoprecipitation and enzyme-linked immunosorbent assays. Comparisons between relapse and non-relapse groups were made using the chi-square test.

Results: Forty-four patients with DM or CADM were found to have anti-MDA5 antibody. Three were excluded from the analysis because of insufficient clinical/immunological information. Of 41 patients (male/female: 7/34, mean age ± SD: 55.2 ± 11.9), 13 (32%) died despite initial intensive immunosuppressive treatment at an early phase of disease. Twenty-three patients achieved remission with the initial therapy and did not relapse during follow-up (56%). The remaining 5 patients (12%) in remission on initial treatment later relapsed. Of these 5 patients (male/female: 2/3, a mean age ± SD: 49.8 ± 11.2), one had classic DM and 4 had CADM. At the time of relapse, two patients complained of respiratory symptoms and all had worsening abnormal shadow on high resolution computed tomography (HRCT). Serum CRP, KL-6 and ferritin levels tended to be increased at the time of relapse. In 3 of the 5 (60%), the anti-MDA5 antibody titer was again above the cut-off level at relapse. The number of relapsing patients with anti-MDA5 antibody titer increasing again above the cut-off level was higher than in those who did not relapse (60% vs. 0%, P=0.003).

Conclusion: These results indicate that relapse may occur even after complete remission of RP-ILD has been achieved. Increased anti-MDA5 antibody titers, as well as respiratory symptoms and HRCT findings, are potential indicators of RP-ILD relapse in patients with DM.

Disclosure: N. Sasaki: None; **T. Ohisa**: None; **A. Ishii**: None; **M. Sugiyama**: None; **Y. Ota**: None; **C. Yamada**: None; **S. Sato**: MEDICAL & BIOLOGICAL LABORATORIES CO., LTD., 9.

Abstract Number: 1950

Thromboembolic Risk Associated with Intravenous Immune Globulin Use in Patients with Idiopathic Inflammatory Myopathy: A Large Database Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

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Background/Purpose: Intravenous immune globulin (IVIG) recently received regulatory approval for the treatment of dermatomyositis, one of the idiopathic inflammatory myopathies (IIM). The pivotal randomized trial informing approval observed 6 thrombotic adverse events among patients exposed to IVIG, which included both venous thromboembolism (VTE) and arterial thromboembolism (ATE). The objective of this study is to determine the real-world incidence of ATE and VTE among adults who received IVIG for IIM or other indications.

Methods: Patients from TriNetX, a large federated health records database, were included if they received ≥1 IVIG administrations. ATE and VTE were identified using ICD-9-CM/ICD-10-CM codes and patients were characterized as IIM if they received two codes separated by 30 days within 3 years of the first IVIG administration. Patients could contribute multiple IVIg exposure intervals, which could be 1 to 7 days long, depending on how many consecutive IVIg administrations a patient received. Risk periods were defined for each patient for each IVIG interval as follows: ATE (IVIg interval day 1 to 2 days after the last day of the IVIG interval), VTE (IVIg interval day 1 to 13 days after the last day of the IVIg interval), and control (14 days

Table 1: Characteristics of included patients, n = 38,230

Characteristic	Overall	IVIG	Myositis
Total Number of Patients	38,230	36,553	1,677
Total IVIG Administrations, mean (SD)	256,868	233,079	23,789
IVIG Administrations per Patient, mean (SD)	6.7 (14.3)	6.4 (13.3)	14.2 (26.5)
Age at Diagnosis, mean (SD)	55.7 (16.7)	55.7 (16.8)	54.6 (14.7)
Gender	-	-	-
Female	21,113 (55.2%)	19,915 (54.5%)	1,198 (71.4%)
Male	17,117 (44.8%)	16,638 (45.5%)	479 (28.6%)
Race/Ethnicity	-	-	-
White	24,132 (63.1%)	23,094 (63.2%)	1,038 (61.9%)
Black or African American	4,599 (12.0%)	4,311 (11.8%)	288 (17.2%)
Hispanic or Latino	2,551 (6.7%)	2,403 (6.6%)	148 (8.8%)
Asian	592 (1.5%)	564 (1.5%)	28 (1.7%)
Other / NA	6,356 (16.6%)	6,181 (16.9%)	175 (10.4%)
Admissions during Prior Year, mean (SD)	1.3 (4.7)	1.3 (4.8)	1.0 (2.5)
Encounters during Prior Year, mean (SD)	24.9 (42.0)	24.6 (42.1)	30.5 (40.5)
Comorbidities at Diagnosis	-	-	-
Charlson Comorbidity Index	1.7 (2.2)	1.7 (2.2)	1.4 (2.1)
Hypertension	15,494 (40.5%)	14,837 (40.6%)	657 (39.2%)
Hyperlipidemia	10,434 (27.3%)	9,972 (27.3%)	462 (27.5%)
Chronic Obstructive Pulmonary Disease	7,500 (19.6%)	7,152 (19.6%)	348 (20.8%)
Diabetes	7,455 (19.5%)	7,082 (19.4%)	373 (22.2%)
Renal Disease	7,021 (18.4%)	6,901 (18.9%)	120 (7.2%)
Obesity	3,989 (10.4%)	3,769 (10.3%)	220 (13.1%)
Liver Disease	3,871 (10.1%)	3,644 (10.0%)	227 (13.5%)
Coagulation Disorders	3,760 (9.8%)	3,643 (10.0%)	117 (7.0%)
Congestive Heart Failure	3,321 (8.7%)	3,197 (8.7%)	124 (7.4%)
Smoking	1,412 (3.7%)	1,348 (3.7%)	64 (3.8%)

Table 2: Incidence and incident rate ratios for venous and arterial thromboembolism in the overall cohort and within the subset of patients with myositis

Group	Outcome	Exposure Period	Events	Follow-up Time	Unadjusted Incident Rate Ratio IRR (95% CI)
Overall Cohort (n = 38,230)	Venous Thromboembolism	Control	153	5,233 Years	1.25 (1.01-1.55)
		IVIG-Exposure	190	5,204 Years	
	Arterial Thromboembolism	Control	96	5,233 Years	7.59 (5.51-10.4)
		IVIG-Exposure	62	445 Years	
Myositis Cohort (n = 1,677)	Venous Thromboembolism	Control	12	387 Years	0.73 (0.30-1.63)
		IVIG-Exposure	10	459 Years	
	Arterial Thromboembolism	Control	7	387 Years	1.24 (0.26-5.96)
		IVIG-Exposure	2	89 Years	

after the last day of the IVIg interval to 31 days after IVIg interval day 1). Unadjusted incident rate ratios (IRR) were calculated and adjusted analyses were performed using stratified and weighted Poisson regressions.

Results: This project included 38,230 patients who received a total of 256,868 IVIg administrations. A subset of 1,677 patients (4.4%) were categorized as IIM. The majority of IIM patients were female (71.4%) and white (61.9%). After excluding exposure time outside of the defined risk windows and censoring patients after their first event, there were 345 VTE and 158 ATE in the overall cohort. In the overall cohort, during the exposure and control periods the unadjusted incidence rates of VTE were 36.5 cases and 29.6 cases per 1,000 person-years, respectively (unadjusted IRR 1.23, 95% confidence interval (CI) 1.00-1.52) and the unadjusted incident rates of ATE were 139.0 cases and 18.3 cases per 1,000 person-years (unadjusted IRR 7.59, CI 5.51-10.40). Adjusted RR were 2.30 (95% CI 0.96-5.90) for VTE and 0.80 (95% CI 0.33-2.14) for ATE. Among patients with IIM, there were 22 VTE and 9 ATE. During exposure and control periods the unadjusted incidence rates of VTE were 21.8 cases and 31.0 cases per 1,000 person-years, respectively (unadjusted IRR 0.70, 95% CI 0.30-1.63) and the unadjusted incident rates of ATE were 22.4 cases and 18.1 cases per 1,000 person-years, respectively (IRR 1.24, CI 0.26-5.96). Adjusted rates could not be calculated for the subset with myositis given a low number of events.

Conclusion: In this study, the risk of ATE and VTE among patients exposed to IVIG was low. In unadjusted analysis, the rate of ATE and VTE was elevated after IVIG administration, but this did not persist in adjusted analyses. No increased risk was observed among patients with IIM in unadjusted analysis. Ongoing surveillance studies using randomized designs should be conducted to corroborate these findings.

Disclosure: R. Mehta: None; **M. Putman**: AbbVie/Abbott, 12, Trial participation, AstraZeneca, 12, Trial participation, Novartis, 2; **D. Saygin**: None.

Abstract Number: 1951

Valid and Reliable Physical Function Tests in Idiopathic Inflammatory Myositis

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SESSION INFORMATION
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Background/Purpose: Idiopathic inflammatory myopathies (IIM) can cause significant impairment in physical function. Sit to Stand (STS) and Timed Up and Go (TUG) are quick and operator-independent measures of physical function. We evaluated the psychometric properties (reliability, validity, and responsiveness) of these compared to established core set measures (CSMs) of disease activity and outcome. We also assessed the feasibility of patients self-performing these tests at home remotely.

Methods: Data from a 6-month prospective observational study on IIM: Myositis Patient Centered Tele-Research Study (My PACER) was analyzed. There were 2 cohorts, a Tele-Research Cohort (TRC; remote enrollment from anywhere in US) and a Center Based Cohort (CBC; in person enrollment from myositis centers). Patient reported assessments and functional assessments (STS and TUG) were collected monthly over 6-months. STS is the number of times a patient can stand from a seated position and sit back down in 30 seconds. TUG is the time needed to rise from a chair, walk 3 meters, return to the chair and sit down. For the CBC, patients were trained in person by the coordinator, whereas for TRC training was provided by pre-recorded video instructions and patients self-performed the tests remotely. These tests were done twice at each visit, with the average of the two used in analysis. In addition, myositis core set measures (CSMs) were assessed by myositis experts at baseline and 6 month follow up (done in person for CBC patients and remotely through telemedicine visits and medical records for TRC patients). We examined test-retest reliability using Spearman correlation. To assess validity, we compared STS and TUG against all CSMs and other disease activity measures at baseline. We assessed responsiveness by assessing differences of median changes in STS and TUG in different categories of improvement according to various outcome measures and compared them using the Mann Whitney Test.

Results: 120 patients (75% female,80.8% Caucasian, mean age of55.5+/- 13.43 years,39.2 % PM, 51.7% DM, 9.1% Necrotizing Myopathy [NM]) participated in the study. There was strong test-retest reliability between baseline and month 1 for STS (r=0.8) and TUG (r=0.87); p< 0.01.Reliability was high regardless of method of recruitment and training for STS, however, TUG showed higher reliability in patients recruited and trained remotely (TRC) as compared to locally (CBC). Reliability was maintained across clinical disease subtypes (DM, PM and NM). At baseline STS and TUG showed very strong correlation with each other (r=-0.75) as well as with all CSMs except Extra-Muscular Global and CK. Strong correlations were seen with Muscle Disease Activity and a validated PRO of physical function (PROMIS-PF 20).At 6 months, STS and TUG were significantly better among patients who improved according to 2016 EULAR/ACR myositis response criteria (Total Improvement Score) compared to those who didn't.

Conclusion: STS and TUG showed good reliability including when self-performed by patients remotely using video instructions, with excellent construct validity and responsiveness. STS and TUG are feasible functional assessment in myositis that can be performed in clinic or remotely.

Table 1. Demographic characteristics of participants

	Total (n=120)	Center Based Cohort (n=38)	Tele Research Cohort (n=82)
Age (in years) at Enrollment (Mean+/- SD)	55.5+/- 13.4	56.9+/-12.4	54.9+/-12.8
Gender			
Female	90 (75%)	28 (73.7%)	62 (75.6%)
Male	30 (25%)	10 (26.3%)	20 (24.4%)
Race			
White	97 (80.8%)	19 (67.9%)	68 (82.9%)
Non-White	15 (12.5%)	7 (25%)	8 (9.8%)
Data Not Available	8 (6.7%)	2 (7.1%)	6 (7.3%)
Sit To Stand (STS) Data			
Any STS Data	115 (95.8%)	36 (94.7%)	79 (96.3%)
No STS Data	5 (4.2%)	2 (5.3%)	3 (3.7%)
Timed Up and Go (TUG) Data			
Any TUG Data	115 (95.8%)	36 (94.7%)	79 (96.3%)
No TUG Data	5 (4.2%)	2 (5.3%)	3 (3.7%)
Myositis Disease Subtype			
Dermatomyositis	62 (51.7%)	20 (52.6%)	42 (51.2%)
Polymyositis	47 (39.2%)	14 (36.9%)	33 (40.2%)
Necrotizing Myopathy	11 (9.1%)	4 (10.5%)	7 (8.6%)

Table 2. Spearman Correlation of Sit to Stand (STS) and Timed Up and Go (TUG) with myositis Core Set Measures (CSMs) and other measures at baseline

	Sit to Stand (STS)		Timed Up and Go (TUG)	
	Correlation Coefficient(r)	P value	Correlation Coefficient (r)	P value
Core Set Measures				
Manual Muscle Testing	0.48	<0.01	-0.46	<0.01
Physician Global Disease Activity	-0.37	<0.01	0.28	<0.01
Patient Global Disease Activity	-0.47	<0.01	0.51	<0.01
Extra-Muscular Global Disease Activity	-0.15	0.12	0.11	0.27
Health Assessment Questionnaire – disability index (HAQ-DI)	-0.7	<0.01	0.67	<0.01
Muscle Enzyme (CK)	-0.06	0.55	-0.06	0.56
Other Measures				
Muscle Disease Activity (from Myositis Disease Activity Assessment Tool - MDAAT)	-0.45	<0.01	0.41	<0.01
PROMIS Physical Function-20	0.7	<0.01	-0.68	<0.01

Table 3. Change in Sit to Stand (STS) and Timed Up and Go (TUG) based on response as per 2017 ACR/EULAR Myositis Response Criteria and Patient Assessment of Change

	No Improvement (Median, IQR)	Improvement (Median, IQR)	Difference of Medians	P value
2016 ACR/EULAR Myositis Response Criteria (Total Improvement Score >=20 is Improvement)				
STS	1 (0, 2.9)	2.5 (0.75,5)	1.5	0.04
TUG	0.4 (-3.1,1.29)	1.85 (0.25,4)	1.45	0.002
Patient Assessment of Change				
STS	0.5 (-0.5, 2.5)	3 (0.625, 5.875)	2.5	0.001
TUG	0.5 (-1.5, 1.5)	1 (-0.875, 2.06)	0.5	0.22

Disclosure: T. Chandra: None; **R. Lomanto Silva**: None; **s. keret**: None; **A. Sharma**: None; **S. Moghadam-Kia**: None; **D. Ascherman**: None; **C. V. Oddis**: Boehringer-Ingelheim, 5, Cabaletta, 5, EMD Serono, 5, Novartis, 5, Pfizer, 1; **R. Aggarwal**: Actigraph, 2, Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella Bioscience, 2, Corbus, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Mallinckrodt, 5, Merck, 2, Octapharma, 2, Pfizer, 2, 5, Q32, 5, Roivant, 2, Sanofi, 2, Teva, 2.

Abstract Number: 1952

Anti-MDA5 Associated Dermatomyositis: Clinical Features and Outcomes in a Predominantly African-American Case Series

David Wang[1], Arezou Khosroshahi[2] and Prateek Gandiga[2], [1]Emory University School of Medicine, Atlanta, GA, [2]Emory University, Atlanta, GA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Individuals with autoantibodies against melanoma differentiation-associated protein 5 (MDA-5) are reported to have a significant risk of developing rapidly progressive and fatal interstitial lung disease (ILD) in clinically amyopathic dermatomyositis patients (CADM). Previous cohort studies of dermatomyositis patients who have been evaluated for the presence of anti-MDA5 antibodies and associated clinical features and outcomes have been largely performed in the Asian, generally Japanese population, or Caucasian patients in North American studies. Few studies have examined MDA5 manifestations in non-Asian subjects. Available reports suggest rates of CADM and ILD may be lower in Caucasian predominant MDA5 cohorts compared to Japanese or Chinese groups. Additionally, association between rapidly progressive interstitial lung disease (RP-ILD) and MDA5 was variable in these North American studies. The goal of this study is to describe the clinical findings and outcomes of a pre-dominantly black cohort in anti-MDA5 associated ILD and the rapidly progressive variant.

Methods: This retrospective case series identified 17 patients with CADM who had anti-MDA5 autoantibodies. Clinical characteristics, high-resolution computed tomography data, lab test results, presence of additional myositis autoantibodies (MAAs), and response to therapy and treatment outcomes were compared between 2 subgroups: black and non-black patients.

Results: Among 17 patients with CADM and anti-MDA 5 autoantibodies, 15 (88%) developed ILD with 6 patients (40%) having the rapidly progressive variant. All 6 patients with RP-ILD presented in the black sub-group. Out of the pre-dominantly black cohort (11 of 17 patients), 6 (55%) patients had at least one additional MAA. Within the black cohort, 5 patients were positive for ANA, 1 for anti-CCP, 3 for anti-SSA, 5 for anti-Ro52, and 1 for anti-synthetase antibodies. Black patients exhibited a higher prevalence of MAAs when compared to the non-black cohort. Average ferritin levels in black (951±2043) and non-black (976±805) patients were both elevated. Average values of CPK, aldolase, ferritin, FVC, and TLC did not differ significantly between black and non-black patients, but the majority of patients with anti-MDA5 antibody alone (4 of 5) developed ILD but not RP-ILD. Three out of four patients who died developed RP-ILD and all four had additional MAAs.

Conclusion: Black patients with anti-MDA5 positive DM exhibited many of the key phenotypic findings in other MDA5 positive DM populations. However, in our cohort, there was a notably increased incidence of RP-ILD and mortality among Black patients compared to non-Black patients. These potential phenotypic variations should be explored further as they can have implications for appropriate evaluation and treatment. Anti-MDA5 positive patients with CADM who are black have a higher prevalence of co-existent MAAs portending a poorer prognosis and a potentially greater predilection of developing RP-ILD than their non-black counterparts. Patients with anti-MDA5 antibodies alone generally have milder forms of ILD whereas coexistent MAAs serve as a possible marker for less favorable prognoses in anti-MDA5 positive patients.

	Total Cohort (n=17)	Black (n=11)	Non-Black (n=6)
Age at symptom onset, years	42	41	43
Avg disease duration, months	27.9	20.5	41.5
Female gender, n	12	9	3
Current smoker, n	3	2	1
Clinical Features, n			
RP-ILD	6	6	0
ILD	15	9	6
Hand swelling	10	6	4
Arthritis/arthralgias	9	6	3
Amyopathic	17	11	6
Clinically amyopathic	16	11	5
Skin ulceration	8	6	2
Palmar papules	5	4	1
Mechanics hand	6	6	0
Panniculitis	0	0	0
Calcinosis cutis	0	0	0
Alopecia	3	2	1
Heliotrope rash	11	7	4
Gottron's papules	12	7	5
Periungual telangectasias	8	6	2
Pruritis	4	3	1
Oral ulcers	2	2	0
Weight loss	10	6	4
Disease Course, months			
Disease onset to immunosuppression	2.1	1.7	2.8
Disease onset to high-dose CS	4.1	2.8	6.0
Disease onset to pulse steroids	6.6	5.5	10.5
Disease onset to death	10.5	10.5	no death
Immunosuppression to death	8.5	8.5	no death

Comparison of Clinical Manifestations between Black and non-Black patients

	Total Cohort (n=17)	Black (n=11)	Non-Black (n=6)
Lab Tests:			
Avg CPK ± SD	97 ± 139	104 ± 174	85 ± 84
Avg initial ferritin	562	382	833
Avg ferritin ± SD	961 ± 1626	951 ± 2043	976 ± 805
Range CPK	10-856	10-856	17-405
Range ferritin	20-6453	20-6453	204-2662
Range AST	15-329	20-329	15-162
Range ALT	11-332	11-332	13-180
Avg aldolase	7.5	7.8	7.1
LDH	22-735	335-735	22-475
Antibodies, n			
≧1 myositis-associated antibodies (MAA) besides MDA5 ab	10	6	4
ANA (≧1:160)	7	5	2
Anti-CCP Ab (unit/mL ≧7)	1	1	0
Anti-SSA	4	3	1
Anti Ro-52 (AU/mL ≧40)	7	5	2
Anti-synthetase	3	1	2
HRCT Abnormalities, n			
Ground glass opacities (GGO)	14	8	6
Consolidation	10	5	5
Reticulations	9	7	2
Bibasilar/lower lobe GGO	10	6	4
Honeycombing	0	0	0
Pneumomediastinum	3	1	2
Bronchiectasis	8	3	5

Serological Profile, HRCT characteristics

Disclosure: D. Wang: None; **A. Khosroshahi**: Horizon Therapeutics, 1, 2; **P. Gandiga**: None.

Abstract Number: 1953

Mortality Trends in Polymyositis and Dermatomyositis in Mexico: A General Population-based Study from 2000 to 2019

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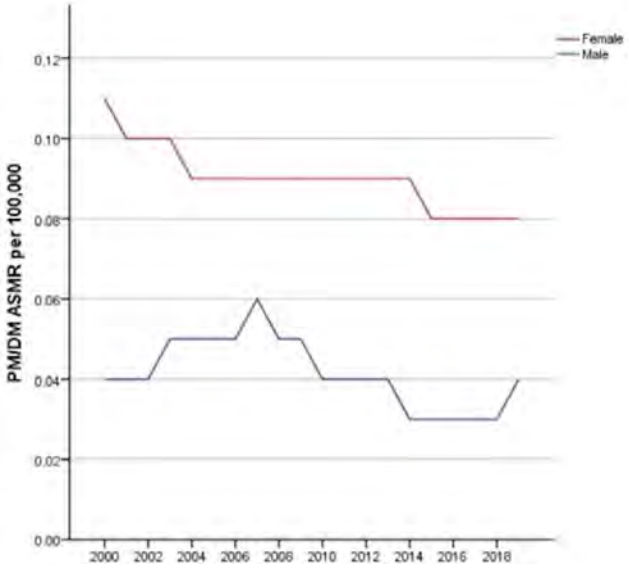
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with polymyositis and dermatomyositis (PM/DM) present multiple complications that may lead to increased mortality rates and data on PM/DM mortality in Mexico is lacking.

The objective of this study was to assess mortality trends in PM/DM idiopathic inflammatory myopathies (IMM) in Mexico between 2000 and 2019, overall and by sex, age group, and geographic regions.

Methods: Data were acquired from the General Board of Health Information Open Access databases, and we identified deaths for PM/DM (ICD codes, 10th edition), which were recorded from 2000 to 2019 from all public hospitals nationwide. Age-standardized mortality rates (ASMR) per 100,000 persons were calculated for PM/DM and non-PM/DM overall, by sexes, and by geographic region. Annual percentage change (APC) and average annual percentage change (AAPC) in ASMR were calculated using Joinpoint regression software.



Temporal trends in age-standardized mortality in PM/DM subjects by sex.

Results: We found 1,456 deaths from PM/DM and 11,343,652 non-PM/DM in Mexico from 2000 and 2019. The ASMR (per 100,000 inhabitants) was 0.07 over the period. The gender distribution of PM/DM deaths was 69.8% in women and 30.2% in men. Compared to non-PM/DM, PM/DM individuals had a higher proportion in the younger population (younger than 45 years) (40.2% vs. 22.3%). Overall, a significantly downtrend in the ASMR was identified from 2007 to 2017 in subjects with PM/DM (APC -3.2%; 95% CI, -5.3 to -1.0; p = 0.008), while mortality trends were stable for non-PM/DM individuals. Similar trends were identified by sex in PM/DM patients (Fig 1). The Joinpoint analysis did not identify variation in temporal trends in mortality rates by geographic region; however, an increment in the proportion of deaths in the ratio of PM/DM to non-PM/DM ASMR from 2000 to 2019 was detected in the Northern and Southern regions (+17.6% and +84.9%, respectively).

Conclusion: Over a 20-year period, we observed that deaths due to PM/DM occurred predominantly in females. A notable decrease in overall mortality rates was identified between 2007 and 2017. Differences by sex, age, and geographic region were also detected.

Disclosure: C. MENDOZA PINTO: None; **P. Munguía-Realpozo**: None; **I. Etchegaray-Morales**: None; **M. García-Carrasco**: None; **P. Cortés-Hernández**: None; **R. Arreguín-Reyes**: None; **J. Ayón-Aguilar**: None; **G. Rodríguez-Castillo**: None.

Abstract Number: 1954

Evaluation of Cancer Screening Methods in Patients Diagnosed with Inflammatory Muscle Disease at Kansas University Medical Center

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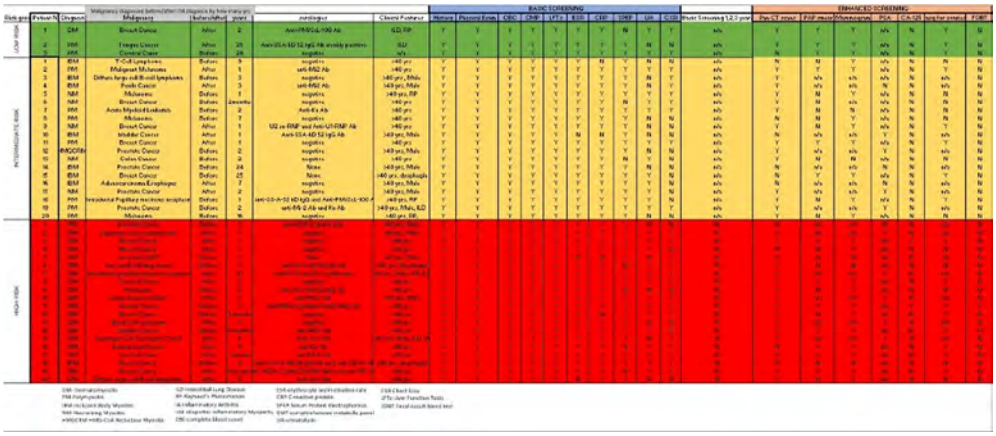
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

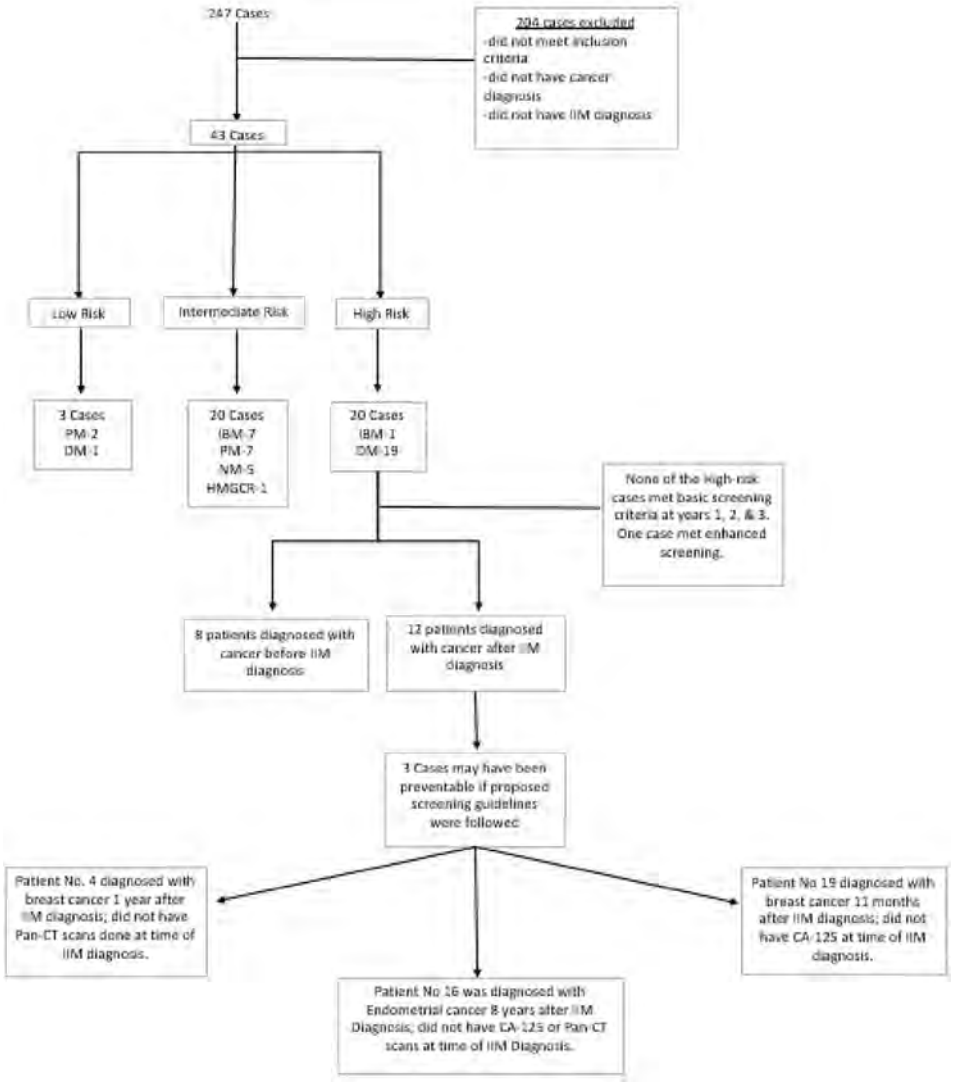
Background/Purpose: Idiopathic inflammatory myopathies (IIM) are characterized by muscle weakness and inflammation. There is an increased risk of developing cancer in patients (pts) with IIM compared to the general population. While most cancers are detected within the 1st year of IIM diagnosis, ongoing monitoring is recommended for 3-5 years post-diagnosis.

In November 2021, a systematic review and meta-analysis was conducted to inform cancer screening guidelines in IIM. The review aimed to evaluate the cancer screening investigations and develop evidence-based guidelines. These guidelines were subsequently developed in collaboration with experts from around the world, utilizing a Delphi process involving 75 participants from 22 countries. The manuscript detailing the proposed guidelines is forthcoming. The purpose of this study was to evaluate the effectiveness/appropriateness of the screening methods employed at our institution and compare them with the proposed guidelines.

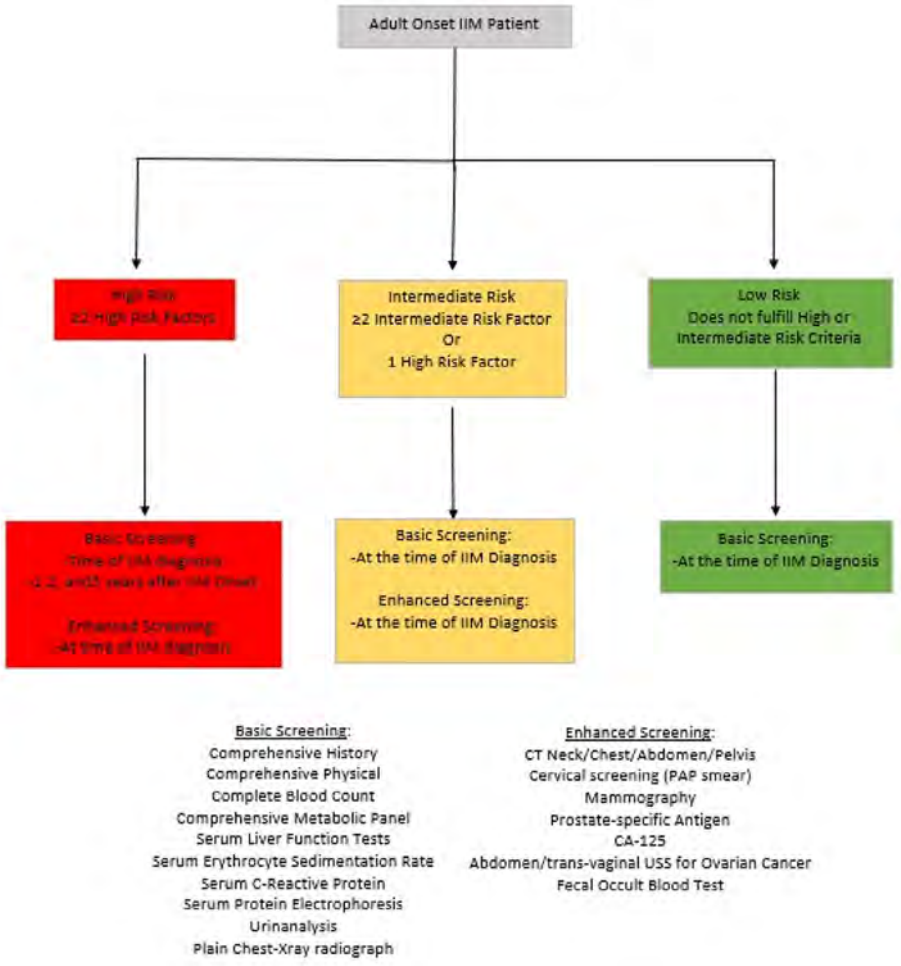
Methods: A retrospective chart review at our tertiary medical center using EMR-EPIC, Research Electronic Data Capture software, and Heron Research database, to identify pts being treated for IIM and diagnosed with malignancy between 1/2012 to 1/2022. We implemented risk stratification methods based on the proposed guidelines for malignancy screening in patients with IIM.



Data from analyzed cases organized into low, intermediate, and high risk categories. Special focus on type of IIM, malignancy, serologies, basic and enhanced screening.



Flow chart break down of cases analyzed. Special focus on 12 high-risk cases diagnosed with cancer after initial IIM diagnosis.



Flow chart explanation of how to categorize patients into low, intermediate, and high risk categories as well as what is included in basic and enhanced screening.

Results: Among the 20 high-risk cases identified, 12 pts were diagnosed with cancer after their IIM diagnosis, none met the basic screening recommendations for the first 3 years following IIM diagnosis. One patient met the criteria for enhanced screening. Among the 20 intermediate-risk cases, 7 were diagnosed with cancer after IIM diagnosis. 15 of 20 intermediate-risk cases did not undergo complete basic screening, and none met the criteria for enhanced screening. Among the 3 low-risk pts, 1 met the basic screening requirements. The most missed component of enhanced screening was fecal occult blood test, while the most frequently overlooked element of basic screening was chest x-ray. 3 high-risk pts may have had their cancers detected earlier if screening guidelines were followed.

9 of 15 female pts with gynecological and breast cancers were classified as high-risk. Among the 26 female intermediate/high-risk cases, 16 did not undergo PAP smears, 5 did not have mammograms, and 13 did not undergo abdominal/trans-vaginal ultrasounds. Additionally, there were 5 gastrointestinal malignancies, and 10 of 40 intermediate/high-risk pts did not have pan-CT scans.

Conclusion: We conclude the proposed guidelines, particularly for high-risk cases, play a vital role in detecting malignancies occurring after IIM diagnosis. Most high-risk cases were diagnosed with cancer within 1-5 years of initial IIM diagnosis. A significant proportion of malignancies observed were female-specific cancers (breast/gynecologic), many that occurred within 1-3 years of IIM diagnosis. This suggests the importance of enhanced screening up to 3-5 years beyond the initial diagnosis

of IIM in high-risk pts. It is evident that our institution did not fully adhere to the proposed guidelines; however, these results could form a quality improvement project aimed at enhancing cancer screening for pts with IIM.

Disclosure: P. Giri: None; **A. Bath**: None; **P. Bhadbhade**: None.

Abstract Number: 1955

Responsiveness and Minimal Important Difference of PROMIS Pain Interference, Fatigue, and Physical Function Forms in Adults with Idiopathic Inflammatory Myopathies

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

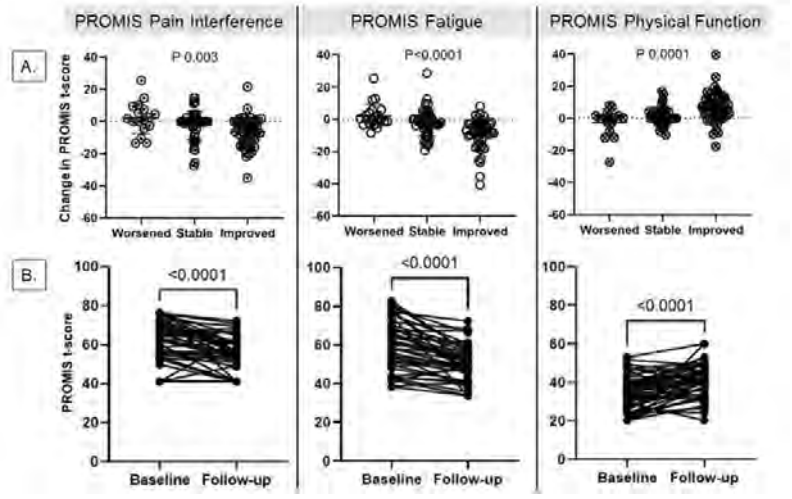
Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Patient reported outcome measures (PROMs) are critical in assessing clinical outcomes. There is a paucity of PROMs for use in patients with adult idiopathic inflammatory myopathies (IIM). The Outcome Measures in Rheumatology (OMERACT) Myositis Working Group was established to develop validated PROMs for adult IIM. Our previous

Figure 1. PROMIS instruments across the anchor categories (A) and over time change in the PROMIS scores of patients who reported anchor-specific improvement only (B).



work has included identifying the domains of interest as pain interference, fatigue, and physical function and demonstrating the content validity, test-retest reliability, and construct validity of the PROMIS pain interference (6a), fatigue (7a), and physical function (8b) instruments. In this study, our goal was to assess the responsiveness and minimal important difference of these instruments in a prospective longitudinal cohort of adults with IIM.

Methods: Adults with IIM who were seen in the outpatient clinics in United States of America (USA), Netherlands, South Korea, Sweden, and Australia, were enrolled in this prospective observational study with two study visits. Relevant myositis core set measures (manual muscle testing [MMT8, 0-80], physician and patient global disease activity [0-10]), and the PROMIS instruments for pain interference (6a), fatigue (7a), and physical function (8b) were collected at the baseline and follow-up visits. Domain-specific anchor questions for symptoms of pain, fatigue, and physical function were asked at the follow-up visit (a lot better, a little better, stable, a little worse, a lot worse). Responsiveness of the PROMIS instruments was assessed using i) ANOVA to compare the scores across the anchor categories (worsened, stable, improved), ii) paired t

Table 1. Baseline characteristics of the study participants.

		n (%) or median [IQR]
Number of participants		114
USA		32.5%
Netherlands		23.7%
South Korea		21.9%
Sweden		18.4%
Australia		3.5%
Age		60.0 [50.0 - 70.0]
Sex (F%)		67 (58.8%)
Interval between visits (days)		150.5 [99.0 – 199.3]
Myositis outcome measures		
Manual muscle testing (0-80)		74 [63 - 80]
Physician Global (0-10)		4 [2 - 6]
Patient Global (0-10)		4.6 [2 - 6.9]
PROMIS instruments		
PROMIS pain interference		55.7 [41.1 - 66.3]
PROMIS fatigue		57.9 [49.6 - 66.4]
PROMIS physical function		37.9 [31.8 - 45.1]
Anchor distribution at the follow-up		
Pain	A lot better	19.4%
	A little better	23.2%
	Stayed the same	41.7%
	A little worse	10.2%
	A lot worse	5.6%
Fatigue	A lot better	13.2%
	A little better	26.3%
	Stayed the same	41.2%
	A little worse	13.2%
	A lot worse	6.1%
Physical Function	A lot better	17.6%
	A little better	29.6%
	Stayed the same	37.9%
	A little worse	12.0%
	A lot worse	2.8%

IQR: Interquartile range, USA: United States of America, F: Female

Table 2. Effect size and standardized response mean of the PROMIS instruments across the anchor categories.

Anchor categories*	T-score		Change in T-score	SD	Effect size	Standardized response mean	n
PROMIS Pain Interference							
Worsened	Baseline Follow-up	61.4 63.6	2.3	9.9	0.23	0.23	17
Stable	Baseline Follow-up	49.4 47.2	-2.2	8.9	-0.24	-0.24	45
Improved	Baseline Follow-up	61.7 55.1	-6.6	9.3	-0.64†	-0.70†	46
PROMIS Fatigue							
Worsened	Baseline Follow-up	60.3 62.4	2.0	7.3	0.17	0.28	22
Stable	Baseline Follow-up	55.1 53.0	-2.1	8.3	-0.21	-0.25	47
Improved	Baseline Follow-up	59.7 50.5	-9.2	9.8	-0.83†	-0.93†	45
PROMIS Physical Function							
Worsened	Baseline Follow-up	39.1 36.5	-2.6	8.7	-0.27	-0.29	16
Stable	Baseline Follow-up	42.0 43.2	1.2	5.4	0.12	0.23	41
Improved	Baseline Follow-up	34.6 41.1	6.5	9.4	0.75†	0.70†	51

SD: Standard deviation

**Five anchor categories were lumped under 3 categories (worsened, stable, improved) due to small sample size in each subgroup.*

†*Large effect size and standardized response mean (interpreted as small <0.2, medium 0.2-0.5, large >0.5)*

test, effect size and standardized response mean for within-person score change, and iii) Pearson correlation with myositis outcome measures. Effect size was interpreted as small for < 0.2, medium for 0.2-0.5, and large for >0.5. Minimal important difference was calculated using the anchor-based method.

Results: 114 patients with IIM (median age of 60 [50-70], 60% female) completed two study visits at five international sites (USA [32.5%], Netherlands [23.7%], Korea [21.9%], Sweden [18.4%], Australia [3.5%])(Table 1). Changes in PROMIS pain interference, fatigue, and physical function were significantly different among anchor categories (Figure 1). Patients who reported improvement in domain-specific anchor questions had a significant improvement in their PROMIS scores with at least medium effect size (>0.5), while patients who reported worsening and stability in anchor questions did not show a significant change with weak effect size (< 0.2) (Table 2). PROMIS instruments had weak to moderate correlations with MMT, patient and physician global. Using the anchor-based method, the minimal important difference was 2.7 t-score for PROMIS pain interference, 4 for fatigue, and 3.3 for physical function.

Conclusion: This study provides evidence towards the responsiveness of the PROMIS instruments in a large international prospective cohort of adults with IIM supporting their use as PROMs in adult myositis. Further work is planned to examine responsiveness in a larger cohort of those who worsen and in clinical trials.

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1, Roche, 11, Xencor, 6; **M. Regardt**: None; **c. Sarver**: None; **M. de Visser**: Argenx, 1, 2, Novartis, 2; **I. maxwell**: None; **D. Beaton**: None; **J. Kim**: None; **M. Needham**: Abcuro, 6, Biogen, 6, Sanofi-Aventis, 6, Teva, 6; **H. Alexanderson**: None; **L. Christopher-Stine**: None; **C. Mecoli**: None.

Abstract Number: 1956

Rituximab Treatment in Adult Patients with Idiopathic Inflammatory Myositis (IIM): A Systematic Review and Meta-analysis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune myositis involves a spectrum of rare autoimmune disorders characterized by inflammation and damage to skeletal muscles. The management of these challenging conditions often requires immunosuppressive therapies. Rituximab (RTX), a monoclonal antibody targeting CD20-positive B cells, has emerged as a promising therapeutic option for patients with autoimmune myositis who are refractory to or intolerant of conventional treatments.This meta-analysis aims to evaluate the efficacy and safety of RTX treatment in patients with autoimmune myositis, encompassing polymyositis (PM), dermatomyositis (DM), juvenile dermatomyositis (JDM), antisynthetase syndrome (ASS), and immune-mediated necrotizing myositis (IMNM).

Methods: A comprehensive literature search was conducted using electronic databases:*PubMed and Embase*to identify relevant studies published up to September 2022. Studies reporting on the efficacy and safety outcomes of RTX treatment in patients with autoimmune myositis were included, case reports or series with less than 3 subjects were excluded. Data were extracted, and a random-effects model was used to calculate pooled estimates for clinical response rates, subgroup analysis, and adverse events. This study was registered withPROSPERO 2022 CRD42022353740

Results: A total of 17 studies, 1 RCT and 16 uncontrolled studies, involving 362 patients with autoimmune myositis were included in the meta-analysis. The pooled analysis demonstrated a notable overall clinical response rate of 70% (95% confidence interval [CI]: 57-82% I2=71.8%, p= < 0.001), Pooled complete remission rate after treatment with RTX was 13% (95% CI:3-25%, I2=79.5%, p=< 0.001), and partial remission rate was 48% (95% CI: 30–66%, I2=86.0%, p=< 0.001). Subgroup analyses showed high response rates in all typed of myositis PM 69% (95% CI: 42-91% I2=52.0%, p=0.04) DM 67% (95% CI: 45-86% I2=52.0%, p=0.04), ASS 70% (95% CI: 34-97% I2=79.4%, p=< 0.001), JDM 60% (95% CI: 21-94%) and NIIM (just one study) 86% (95% CI: 42-100%). Regarding RTX induction dose, subgroup analysis showed similar overall response with 1 g IV at days 0 and 14 days 68% (95% CI:47-86, I2=75.3% P=< 0.001) and 375 mg/m2 weekly for 4 weeks was 71% (95% CI:48–90, I2=24.6% P=0.80). Regarding safety, 120 adverse events were reported. The most reported adverse events from the 362 patients were infusion reactions in 67 (18.5%) and infections in 45 patients (12.4%).

Conclusion: The highly variable response and remission rates seen in this review warrant further controlled trials on RTX for autoimmune myositis. RTX demonstrates a favorable clinical response rate and muscle strength improvement. Potential adverse events, particularly infusion reactions and infections, should be considered. Further research is needed to optimize treatment protocols and assess long-term outcomes.

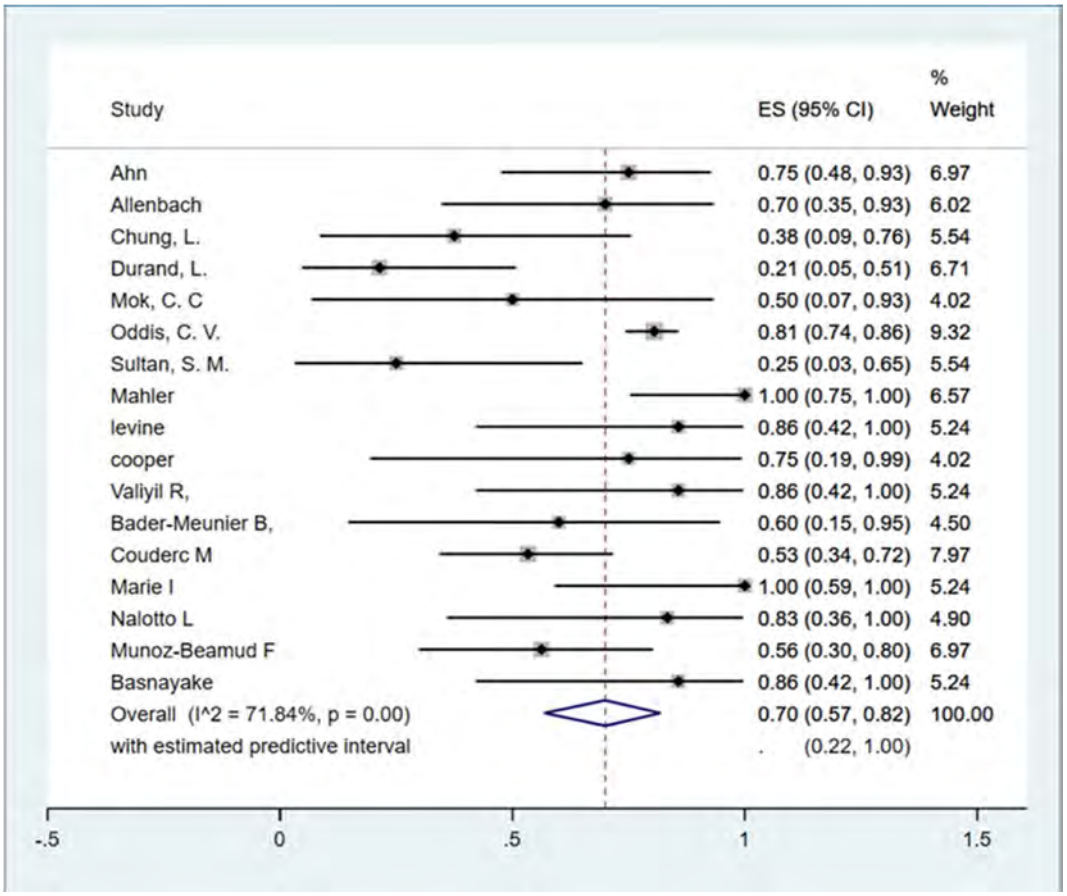

Figure 1 Meta-Analysis results for Overall response for RTX treatment in patient with IIM showing effect size estimate.

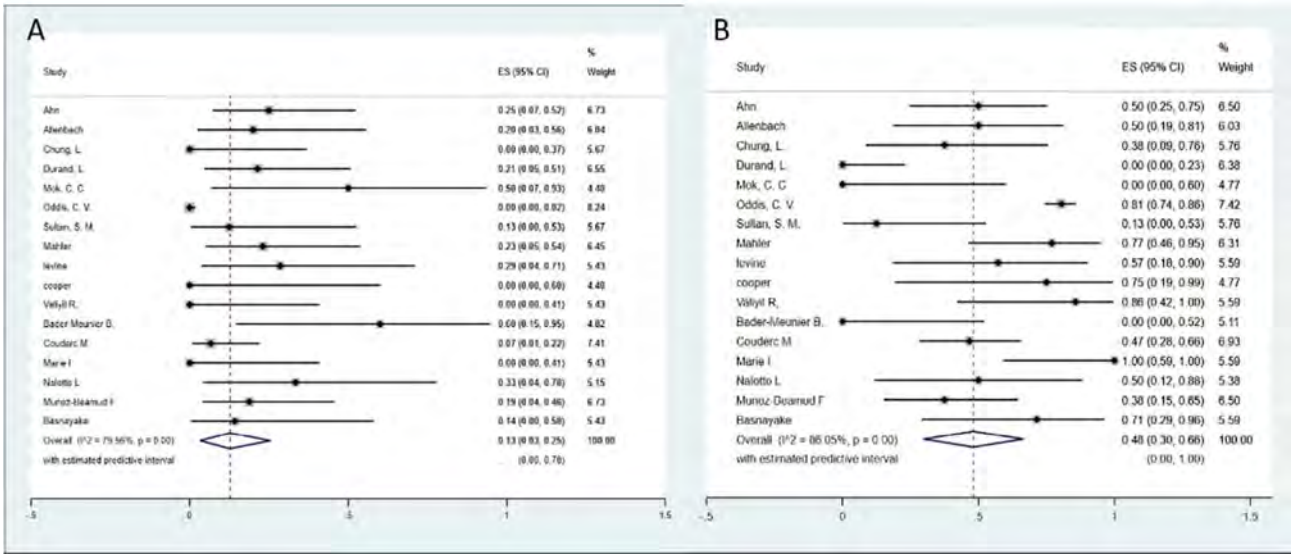

Figure 2. Meta-Analysis results for complete response (A) and partial response (B) for RTX treatment in patient with IIM showing effect size estimates.

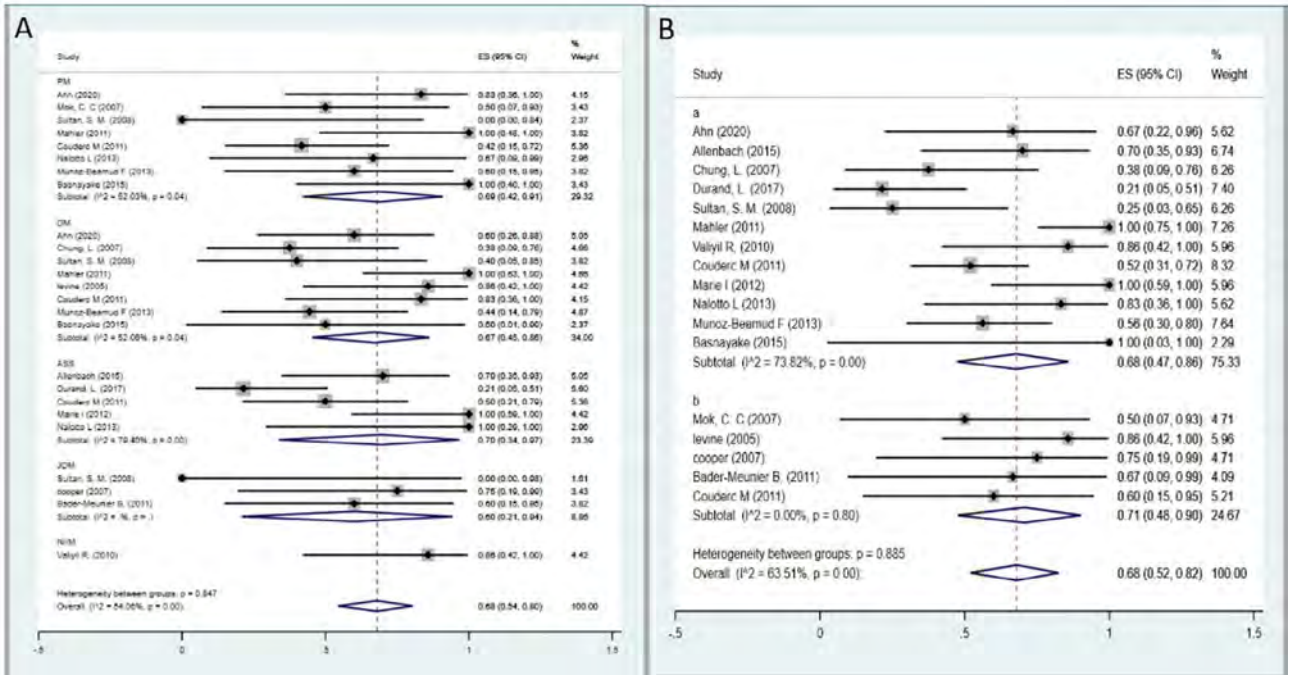

Figure 3 Forest plots of subgroup analysis results. RTX overall response in different IIM subtypes (A) and RTX overall response according to induction dose a=1gr Q 2weeks and b= 375 mg/m2 weekly for 4 weeks (B)

Disclosure: L. Otalora Rojas: None; **K. Ramsubeik**: None; **L. Sanchez-Ramos**: None; **S. Motilal**: None; **J. Singh**: Other, 2, 6, 11, 11, 12, Adaptimmune Therapeutics, GeoVax Labs, Pieris Pharmaceuticals, Enzolytics Inc., Seres Therapeutics, Tonix, Charlotte's Web, 12, Atai life sciences, kintara therapeutics, Intelligent Biosolutions, Acumen pharmaceutical, TPT Global Tech, Vaxart pharmaceuticals, Atyu biopharma, 12, speaker's bureau of Simply Speaking, other, 12, received institutional research support from Zimmer Biomet Holdings. JAS received food and beverage payments from Intuitive Surgical Inc./Philips Elec, Other, 12, Schipher, Crealta/Horizon, Medisys, Fidia, PK Med, Two labs Inc., Adept Field Solutions, Clinical Care options, Clearview healthcare partners, Putnam; **G. S Kaeley**: Abbvie, 5, Gilead, 5, Janssen, 5.

Abstract Number: 1957

Non-Linear Mendelian Randomization Analyses Support a Role for Low Vitamin D Status in Sarcopenia Risk

Tingting Sha[1], Yilun Wang[2], Yuqing Zhang[3], Nancy Lane[4], Changjun Li[5], Jie Wei[6], Chao Zeng[2] and Guanghua Lei[2], [1]Hunan Key Laboratory of Joint Degeneration and Injury, Changsha, China, [2]Department of Orthopaedics, Xiangya Hospital, Central South University, Changsha, China, [3]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, MA, [4]University of California, Hillsborough, CA, [5]National Clinical Research Center for Geriatric Disorders, Xiangya Hospital, Central South University, Changsha, China, [6]Health Management Center, Xiangya Hospital Central South University, Changsha, China

SESSION INFORMATION

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Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Vitamin D deficiency is commonly associated with sarcopenia; however, the latest International Clinical Practice Guidelines for Sarcopenia do not recommend vitamin D supplementation for sarcopenia owing to a lack of an apparent therapeutic effect on the indices of sarcopenia among participants with replete vitamin D concentration (i.e., 25[OH]D >50 nmol/L) from randomized controlled trials. While there is consensus in all vitamin D guidelines that serum levels of 25(OH)D < 25 nmol/L should be corrected, approximately 30% of the world population's 25(OH)D levels range from 25 to 50 nmol/L, and it remains unclear whether such suboptimal levels of 25(OH)D can maintain optimal health, including the risk of sarcopenia.

Methods: Among 295,489 participants of unrelated European ancestry from the UK Biobank, we examined the causal association between genetic variants for serum 25(OH)D concentration and the sarcopenia risk. The primary outcome was sarcopenia, defined by the European Working Group on Sarcopenia in Older People. The secondary outcomes

Table 1. Phenotypic associations between serum 25(OH)D level of each category and the risk of sarcopenia indices

	Serum 25(OH)D (nmol/L)			
	<25.0	25-49.9	50.0-74.9	≥75.0
Sarcopenia				
Event, n.	84	125	107	50
Crude OR (95%CI)	2.09 (1.57 to 2.78)	0.96 (0.74 to 1.25)	Ref	1.36 (0.98 to 1.91)
Adjusted OR (95%CI)	1.52 (1.09 to 2.13)	1.04 (0.79 to 1.37)	Ref	1.06 (0.75 to 1.51)
Grip strength				
mean (SD)	33.4 (11.3)	33.8 (11.3)	33.7 (11.3)	33.60 (11.1)
Crude β (95%CI)	-0.22 (-0.37 to -0.07)	0.17 (0.06 to 0.27)	Ref	-0.05 (-0.21 to 0.10)
Adjusted β (95%CI)	-0.51 (-0.61 to -0.41)	-0.06 (-0.13 to 0.01)	Ref	-0.06 (-0.16 to 0.04)
Appendicular lean mass index				
Mean (SD)	0.8 (0.2)	0.8 (0.2)	0.8 (0.2)	0.9 (0.2)
Crude β (95%CI)	-0.018 (-0.019 to -0.015)	-0.008 (-0.010 to -0.007)	Ref	0.009 (0.007 to 0.012)
Adjusted β (95%CI)	-0.012 (-0.013 to -0.011)	-0.004 (-0.005 to -0.003)	Ref	0.001 (-0.001 to 0.002)
Slow gait speed				
Event, n.	3,270	6,757	3,733	1,176
Crude OR (95%CI)	2.50 (2.38 to 2.63)	1.53 (1.47 to 1.59)	Ref	0.92 (0.86 to 0.98)
Adjusted OR (95%CI)	1.32 (1.24 to 1.40)	1.14 (1.09 to 1.20)	Ref	1.08 (0.99 to 1.16)

n, number; SD, standard deviation; OR, odds ratio; CI: confidence interval.

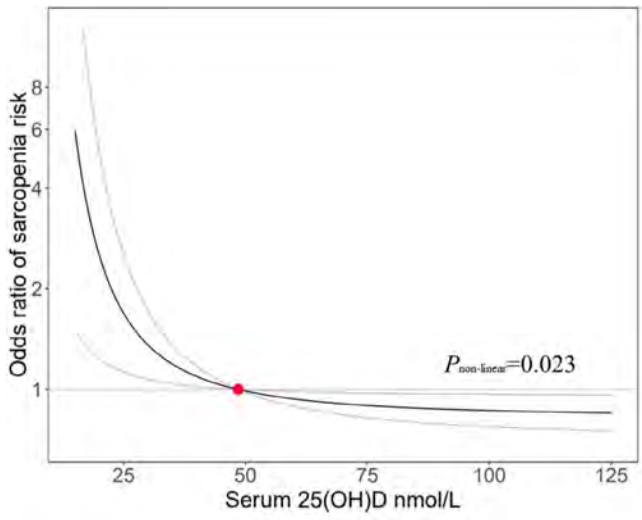


Figure 1 Genetic association of serum 25(OH)D with risk of sarcopenia using 35 SNPs to the instrument. The red dot represents the reference point of serum 25(OH)D of 50 nmol/L. The gray lines represent the 95% confidence intervals. The adjustment includes age, sex, assessment center, birth location, top 20 genetic principal components, genotyping array in both stages, and nuisance factors, which could affect serum 25(OH)D measurements, including the month in which the blood sample was taken, fasting time before the blood sample was taken, and sample aliquots for measurement.

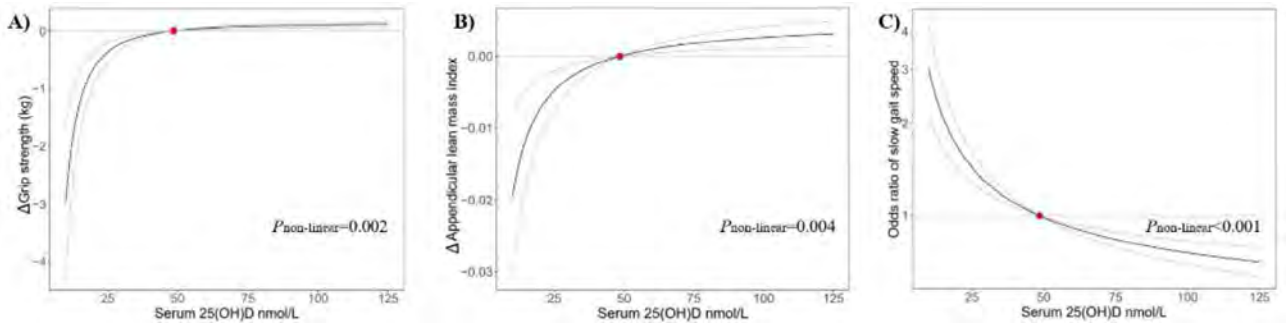


Figure 2 Genetic association of serum 25(OH)D with indices of sarcopenia using 35 SNPs to the instrument. (A) grip strength, (B) appendicular lean mass index, and (C) slow gait speed. The red dot represents the reference point of serum 25(OH)D of 50 nmol/L. The gray lines represent the 95% confidence intervals. The adjustment includes age, sex, assessment center, birth location, top 20 genetic principal components, genotyping array in both stages, and nuisance factors, which could affect serum 25(OH)D measurements, including the month in which the blood sample was taken, fasting time before the blood sample was taken, and sample aliquots for measurement.

consisted of three sarcopenia indices, i.e., grip strength, appendicular lean mass index, and gait speed. We calculated a weighted genetic score using 35 single nucleotide polymorphisms as instrumental variables for serum 25(OH)D concentration and performed non-linear Mendelian randomization to estimate the effect of serum 25(OH)D on sarcopenia risk and its indices.

Results: In the phenotypic association analyses, compared with serum 25(OH)D 50-74.9 nmol/L category, serum 25(OH)D levels below 50 nmol/L adjusted for multivariable factors were inversely associated with each of the sarcopenia indices (Table 1). There was an L-shaped ($P_{non\text{-}linear}$=0.023) association between genetically predicted serum 25(OH)D concentration and risk of sarcopenia (**Fig. 1**). The risk of sarcopenia decreased rapidly as serum 25(OH)D concentration increased until 50 nmol/L and then leveled off. The odds ratio of sarcopenia for serum 25(OH)D level of 25 nmol/L vs. 50 nmol/L was 1.69 (95% CI: 1.13 to 2.53). Similar patterns were also observed when the association between serum 25(OH)D concentration and risks of each of the sarcopenia indices were evaluated (**Fig. 2**).

Conclusion: Our study supports a causal relationship between suboptimal vitamin D levels and sarcopenia risk. These findings suggest that vitamin D supplementation needs to be considered for individuals with suboptimal vitamin D levels to reduce the burden of sarcopenia.

Disclosure: T. Sha: None; **Y. Wang**: None; **Y. Zhang**: None; **N. Lane**: None; **C. Li**: None; **J. Wei**: None; **C. Zeng**: None; **G. Lei**: None.

Abstract Number: 1958

Validity, Responsiveness and Minimal Clinically Important Difference of EQ-5D-5L in Inflammatory Myositis: A Longitudinal Study

Chengappa Kavadichanda[1], Parthibane S[1], Mamatha Gorijavolu[1], Sai Kumar Dunga[1], Amrita Nayak[1], Sitanshu Sekhar[1] and Rohit Aggarwal[2], [1]Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India, [2]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Idiopathic inflammatory myositis (IIM) significantly impacts health-related quality of life (HRQoL). EQ5D-5L is a widely used and validated tool to measure HRQoL. The health utility scores (HUS) derived from EQ5D-5L are used to calculate QALY and to analyze cost effectivity. To the best of our knowledge, there are no studies that have validated EQ5D-5L in IIM. To test the validity of EQ-5D HUS in assessing HRQoL in IIM. To assess the responsiveness to change and to calculate minimal clinically important differences (MCID) of EQ-5D HUS

Table 1: Mean change in the myositis core set measures and EQ5D-5L health utility scores across all patients using HAQ-DI and TIS as anchor

	Whole cohort			ΔHAQ-DI as anchor			TIS as anchor		
Difference between baseline and 6 months	*Mean change*	*SD*	*P-value*	*ΔHAQ-DI ≥ 0.22 N=32*	*ΔHAQ-DI < 0.22 N=26*	*P value*	*Any improvement N=41*	*No improvement N=17*	*P value*
				Mean change ± SD	*Mean change ± SD*		*Mean change ± SD*	*Mean change ± SD*	
MMT-8 (0-80)	13.41	12.64	<0.001	21.72 ±11.07	3.19 ± 3.92	<0.001	18.22 ±11.97	1.82 ±3.05	<0.001
HAQ-DI (0-3)	0.82	0.89	<0.001	-1.47 ± 0.6	-0.01 ±0.03	<0.001	-1.15 ±0.85	-0.01 ±0.02	<0.001
Physician global (0-10)	2.91	3.2	<0.001	-5.27 ± 2.02	-0.07 ± 1.74	<0.001	-4.32 ± 3.73	0.47 ±0.72	<0.001
Patient global (0-10)	5.02	3.28	<0.001	-7.1 ±1.99	-1.86±2.1	<0.001	-6.58 ± 2.43	-1.07 ± 0.96	<0.001
Extra-muscular disease (0-10)	2.28	2.48	<0.001	-3.8 ±2.01	-0.35±1.41	<0.001	-3.22 ± 3.38	0	<0.001
EQ5D-5L Health utility score (-1,+1)	0.625	0.59	<0.001	1.2 ±0.56	0.15 (0.18)	<0.001	0.99±0.64	0.11 ±0.15	<0.001

EQ5D-5L Euroqual 5 dimension 5 levels, HAQ-DI Health assessment questionnaire disability index, MMT Manual muscle testing

Table 2: Effect size represented by Cohens D across various comparisons for EQ-5D Health utility score (EQ-5D HUS) as well as myositis core set measures

Parameter	ES between active and inactive disease	ES of change in scores over 6 months in the entire cohort	ES of change in scores over with Δ HAQDI ≥0.22 as anchor	ES of change in scores with TIS as anchor
HAQ-DI	1.432	0.92	2.23	2.12
MMT-8	1.70	1.063	2.31	1.93
Patient Global	1.45	1.51	2.56	2.98
Physician global	1.03	0.93	2.73	2.76
Extra muscular global disease	0.74	0.88	1.56	1.23
EQ5D-Health utility score	1.28	1.05	2.82	2.18

Table 3: Estimation of Minimal clinically important difference (MCID) using various methods

	Anchor based			
	Estimated value for MCID	*AUC, Sensitivity and specificity*	*Spearman's Rho*	*95%CI*
Change in HAQ-DI ≥ 0.22	0.303	0.96, 96.9%, 88.5%	0.79 (<0.001)	0.90-1.0
	Distribution based method			
0.5*SD (MCID= 0.5 SD of the ΔSD score)	0.34	NA	NA	NA

Methods: This was a single centre prospective study involving patients with IIM. Patients were evaluated at 0 and 6 months with all 6 myositis core set measures and EQ5D-5L. The EQ5D-5L health states for Indian population were used to calculate HUS. Individuals with MMT8 of < 74/80 and / or those who had extra muscular disease activity of > 2/10 were considered active and the rest as inactive disease. Muscle weakness was classified as severe (MMT-8 < 54/80), mild-moderate (MMT-8 54 to 73/80) and inactive (MMT-8 ≥74). Construct validity of EQ5D-HUS (ability to differentiate different health states) was tested by comparing scores and Cohens'D effect size (ES) across disease severity. Responsiveness to change was estimated with ES for the change in scores between those with improvement and no improvement in HAQ-DI and total improvement scores (TIS). MCID was calculated using distribution-based method (0.5*SD of change) and anchor based method (ROC curve) using a change of ≥0.22 of HAQ-DI between 0 and 6 months as the anchor.

Results: Fifty-eight IIM patients with mean (SD) age of 37.6 (9.8), 76% (N=44) females were included in the study. Disease subset included 34 (58.6%) DM, 18 (31%) anti-synthetase syndrome, 3 (5.2%) immune mediated necrotizing myopathy and 3 (5.2%) PM.

Median MMT-8 (0-80) at baseline was 61.35 ±15.49 with a median (IQR) of extra-muscular disease activity (0-10) of 3 (0,5). The median (range) EQ5D-5L health utility score was 0.415 (-0.69, 0.87). Sixteen patients had severe myositis with EQ-5D HUS of -0.68, 34 mild to moderate had EQ-5DHUS of 0.42 and 8 had inactive disease EQ-5DHUS- 0.81 at baseline (p< 0.01). The changes in MMT-8, HAQ-DI, physician and patient global assessment, extra muscular diseases activity and EQ5-D HUS between 0 and 6 months in the cohort is represented in table 1.

The EQ-5D HUS increased by 0.625 (p < 0.001) in 6 months and was able to differentiate between patients with improvement based on HAQ-DI and 2016 ACR/EULAR Myositis response criteria (TIS ≥20) (Table 1). The ES of change in MMT-8, HAQ-DI, Physician and patient global assessment, extra muscular diseases activity and EQ5-D HUS between those with improvement as per HAQ-DI ≥0.22 and TIS ≥ 20 is in table 2.

Upon calculating the MCID to detect a minimal change in HAQ DI of 0.22, the best model with a sensitivity of 96.9 and specificity of 88.5 was at an EQ-5D HUS of 0.303. The distribution-based MCID calculation using the 0.5 SD method resulted in a value of 0.34 for EQ-5D HUS (Table 3).

Conclusion: Health utility scores derived from EQ5D-5L is a valid instrument for measuring the HRQoL in IIM. An MCID of 0.3- 0.34 had the highest sensitivity and specificity to detect change in clinical state among patients with IIM.

Disclosure: C. Kavadichanda: None; **P. S**: None; **M. Gorijavolu**: None; **S. Dunga**: None; **A. Nayak**: None; **S. Sekhar**: None; **R. Aggarwal**: Actigraph, 2, Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella Bioscience, 2, Corbus, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Mallinckrodt, 5, Merck, 2, Octapharma, 2, Pfizer, 2, 5, Q32, 5, Roivant, 2, Sanofi, 2, Teva, 2.

Abstract Number: 1959

Quantitative Scoring of High Resolution Chest Computed Tomography (HRCT) Images in Myositis and Antisynthetase Syndrome Related Interstitial Lung Disease in Comparison to Scleroderma Related Interstitial Lung Disease

Sangmee Bae[1], Fereidoun Abtin[2], Grace Kim[3], Siamak Moghadam-Kia[4], Chester V. Oddis[5], Lila Pourzand[2], Didem Saygin[5], Daniel Sullivan[6], Koichi Yamaguchi[7], Donald Tashkin[3], Christina Charles-Schoeman[8], Jonathan Goldin[3] and Rohit Aggarwal[5], [1]UCLA Rheumatology, Los Angeles, CA, [2]UCLA Radiological Sciences, Los Angeles, CA, [3]University of California Los Angeles, Los Angeles, CA, [4]University of Pittsburgh Medical Center, Pittsburgh, PA, [5]University of Pittsburgh, Pittsburgh, PA, [6]UCLA Pulmonology, Pittsburgh, PA, [7]University of Pittsburgh Medical Center Rheumatology, Pittsburgh, PA, [8]UCLA Medical Center, Santa Monica, CA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

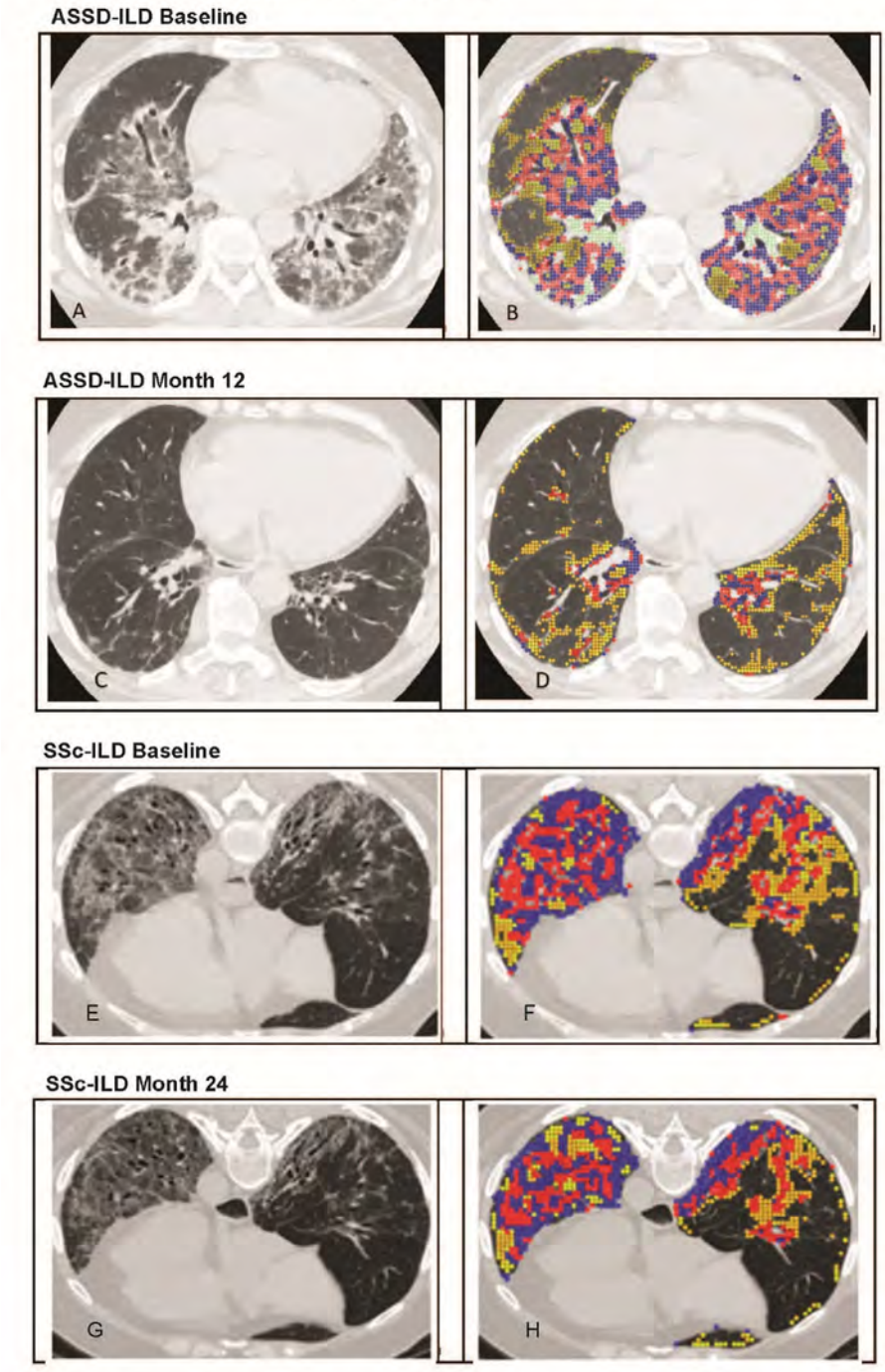
Background/Purpose: High resolution computed tomography (HRCT) of the chest has become an important modality in the evaluation of interstitial lung disease (ILD). A quantitative CT scoring method using a computer aided diagnostic system to measure the nature and extent of parenchymal diseases has been used to measure treatment response in the

Table 1. Baseline Characteristics of the Cohorts

	ASSD-ILD (N=17)	Myositis ILD (n=46)	SSc-ILD (N=137)
Age	53±9	52 ±13	52±10
Female	9(45%)	27(59%)	105(74%)
Disease Duration, years	2.5[1-4]	1[0.3-3]	2.6 ±1.8
Baseline PFT			
FVC % predicted	62±11	69 ±21	67±9
DLCO Hg % predicted	50± 13	62± 20	54±13
HAQ-DI (0-3)	0.5±0.4	0.8 ±0.7	0.7±0.7
HRCT scores, Whole lung			
QGG	20.0±7.3	16.7±8.8*	20.8± 9.4
QLF	19.0± 9.3*	9.2 ±7.6*	8.6±6.9
QHC	0.4 ±0.7*	0.2± 0.6*	0.1± 0.5
QILD	39.9 ±13.8*	26.2 ±14.1*	29.5±14.0
Zone of maximum involvement			
RUZ	2(12)	2(3)	2(1)
RMZ	0	3(4)	0
RLZ	4(24)	17(23)	56(41)
LUZ	5(29)	0	0
LMZ	0	13(18)	7(5)
LLZ	6(35)	37(51)	72(53)
HRCT scores, Zone of maximum involvement			
QGG	17.7±11.4*	19.1±12.9*	30.6 ±13.8
QLF	57.8±17.5*	17.8 ±19.6*	32.3 ±23.7
QHC	0.3±0.7	0.3± 0.9	0.2 ±1.7
QILD	77.8±10.4*	37.3±26.3*	63.1± 20.6

Values are in Mean±SD, Median[IQR] for skewed data, N(%) Zone of maximum involvement was defined as the lobe with the highest QLF score. Zones are defined as area-equivalent regions of the lung across the upper, middle and lower regions of each lung. Note, difference in disease duration. ASS was within 3 months or recent worsening, ssc was mean 2.6 years (0.3-7.1 years) Max lobe based on lobe with highest QILD2 *p<0.05 compared to SSc-ILD group

Figure 1. Representative subjects with favorable treatment response by HRCT in ASSD-ILD and SSc-ILD with quantitative map overlay



Representative subjects with favorable treatment response by high-resolution computed tomography (HRCT) in ASSD-ILD (A-D) and SSc-ILD (E-H). In the quantitative map overlay (right panel), the sum of the blue and red areas represents the extent of quantitative lung fibrosis (QLF), and the yellow area represents the extent of quantitative ground glass(QGG). The sum of all the colors represents quantitation of total ILD (QILD). (A,B) In ASSD-ILD, there is mixed ground glass and consolidative infiltrates in lower lobes with thick walled reticulations and mild bronchiectasis with some volume loss. The pattern of fibrosis is inconsistent with UIP and favors but not classic for organizing pneumonia. Follow up image (C,D) demonstrates significant decrease in the lung infiltrates with residual reticular lines and limited loss of volume. The quantitative overlay shows significant decrease in QLF and QGG. (E,F) In SSc-ILD, HRCT at baseline demonstrates lower lobe course ground glass opacity with reticulations and traction bronchiectasis/bronchiolectasis and relative subpleural sparing best seen on the left side. (G) After 24 months, there is subtle decrease in density of ground glass and extent and thickness of reticulations but persistent bronchiectasis/bronchiolectasis. (H) Quantitative map overlay at 24 months demonstrates decrease in QLF shaded as red and blue.

Table 2. Mean changes for study outcomes from baseline

	N	ASSD-ILD	N	SSc-ILD	P value
FVC ml change (%)	18	-0.01[-0.08,0.06]	110	0.02[0.003,0.04]	0.33
FVC %predicted change	18	0.17[-4.25,4.59]	110	0.02[0.01, 0.03]	0.37
DLCO ml change (%)	17	0.04[-0.08,0.15]	111	-0.04[-0.08,-0.01]	0.17
DLCO % predicted change	17	0.02[-0.04,0.09]	111	-0.01[-0.04,0.01]	0.24
HRCT scores, Whole lung					
QGG	12	-2.2[-5.9,1.5]	97	-2.6[-3.8,-1.3]	0.59
QLF	12	**-4.7[-12.3,2.9]***	97	-0.003[-0.9,0.8]	**0.04**
QILD	12	-6.8[-16.9,3.5]	97	-2.5[-4.3,-0.7]	0.59
HRCT scores, zone of maximum involvement					
QGG	12	-0.2[-7.1,6.7]	97	-4.4[-6.2,-2.6]	0.98
QLF	12	**-19.9[-40.6,0.8]***	97	-0.4[-2.9,2.1]	**0.01**
QILD	12	-20.3[-39.7,-1.0]	97	-4.7[-7.3,-2.1]	0.16

Values reported as mean change[95%CI]. Change in FVC in ml indicates (FVC in ml at 12 months – FVC in ml at baseline)/(FVC in ml at baseline) Change in DLCO in ml indicates (DLCO in ml at 12 months – DLCO in ml at baseline)/(DLCO in ml at baseline) % predicted change were absolute differences between baseline and 12 months Follow up time between quantitative CT scores were 12 months for ASSD-ILD trial and 24 months for SSc-ILD trial.

scleroderma lung study II (SLSII). The current study aims to describe quantitative CT scores in myositis and antisynthetase syndrome related ILD in comparison to scleroderma ILD (SSc-ILD).

Methods: Quantitative CT scores were performed on HRCT scans obtained from the Abatacept for the Treatment of Myositis-Associated ILD (Attack My-ILD) clinical trial which was a 12-month study including 20 adult patients with antisynthetase syndrome and active ILD (ASSD-ILD). We compared baseline scores with a subgroup of an observational cohort of myositis patients with ILD (Myositis-ILD), and the SLS II cohort which included patients with limited or diffuse scleroderma and active ILD (SSc-ILD). Quantitative CT scores were compared between the 3 ILD cohorts at baseline, and scores over time were compared between the two clinical trial cohorts (ASSD-ILD and SSc-ILD). Images were also assessed visually by thoracic radiologists.

Results: Baseline characteristics are described in Table 1. The ASSD-ILD group had lowest forced vital capacity(FVC) and diffusing capacity (DLCO) and highest quantitative scores for ground glass (QGG), fibrosis (QLF) , honeycombing (QHC) and total sum of disease (QILD) among the 3 cohorts. Zone of maximum involvement was shared throughout upper, middle and lower zones in ASSD- and Myositis-ILD, unlike SSc-ILD where 94% had maximum disease in the lower zones of the lung. Visual review of the ASSD-ILD and Myositis-ILD images revealed a pattern distinct from SSc-ILD (Figure 1). In ASSD- and Myositis-ILD, there are areas of confluent fibrosis that mimic organizing pneumonia with fibrosis and volume loss. Also, the disease extends to the periphery of the lung, unlike SSc-ILD which tends to spare the periphery. Both diseases demonstrate ground glass opacity and reticulations with bronchiectasis. In comparing subjects that showed favorable treatment response from the two clinical trials, the ASSD-ILD patient showed marked improvement in CT images (Figure 1-A to C) which was also reflected in changes in their quantitative scores (Figure 1-B to D), whereas in the SSc-ILD subject the improvement was more subtle (Figure 1 E,F to G,H). Mean changes in lung physiology and quantitative CT scores over the trial period demonstrated that QLF scores in the ASSD-ILD cohort showed greater improvement compared to the SSc-ILD cohort despite its shorter follow up time and the lack of differences in changes in FVC or DLCO between the groups (Table 2).

Conclusion: HRCT images from ASSD-ILD and Myositis-ILD demonstrate a pattern that is distinct from SSc-ILD. ASSD-ILD shows more marked improvement in HRCT images with treatment than SSc-ILD which is reflected as a significantly greater decrease in quantitative CT scores over time compared to SSc-ILD. Further studies are needed to better characterize and quantify HRCT images in myositis and antisynthetase syndrome related ILD.

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Boehringer Ingleheim, 2, 5, CSL Behring, 5, Galapagos, 2, Pfizer, 2, 5, Priovant, 2, 5, Recludix, 2; **J. Goldin**: MedQIA, 12, Founder; **R. Aggarwal**: Actigraph, 2, Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella Bioscience, 2, Corbus, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Mallinckrodt, 5, Merck, 2, Octapharma, 2, Pfizer, 2, 5, Q32, 5, Roivant, 2, Sanofi, 2, Teva, 2.

Abstract Number: 1960

From Clinical Amyopathy to Severe Oropharyngeal Dysphagia in Pure Dermatomyositis: A Greater Extent of Muscle Weakness Is Associated with a Higher Cancer Prevalence

Hao Cheng Shen[1], Victoria Ivensky[2], Yves Troyanov[3], Josiane Bourre-Tessier[1], Farah Zarka[2], Sabrina Hoa[4], Jessica Nehme[2], Jean-Paul Makhzoum[5], Anne-Marie Mansour[2], Rosalie-Selene Meunier[2], Alexandra Mereniuk[2], Darosa Lim[6], Jean-Pierre Raynauld[1], Eric Rich[1], Jean-Richard Goulet[1], Marianne Landry[7], Maude Bouchard-Marmen[8], Valerie Leclair[9], Hugues Allard-Chamard[10], Marie Hudson[11], Erin O'Ferrall[12], Rami Massie[12], Jason Karamchandani[13], Benjamin Ellezam[14], Ira N. Targoff[15], Minoru Satoh[16], Marvin Fritzler[17], Jean-Luc Senecal[1], Alain Meyer[18] and Oceane Landon-Cardinal[1], [1]Centre hospitalier de l'Université de Montréal (CHUM), Université de Montréal, Montréal, QC, Canada, [2]Hôpital du Sacré-Coeur de Montréal, Université de Montréal, Montreal, QC, Canada, [3]Hôpital du Sacré-Coeur de Montréal, Centre hospitalier de l'Université de Montreal (CHUM), Université de Montréal, Montreal, QC, Canada, [4]University of Montreal, Brossard, QC, Canada, [5]Vasculitis Clinic, Canadian Network for Research on Vasculitides, Hopital du Sacre-Coeur de Montreal, Montreal, QC, Canada, [6]University of Pennsylvania, Philadelphia, PA, [7]Hôpital de LaSalle, Montreal, QC, Canada, [8]CHU de Québec, Université Laval, Quebec City, QC, Canada, [9]Jewish General Hospital, McGill University, Montreal, QC, Canada, [10]Université de Sherbrooke, Sherbrooke, QC, Canada, [11]McGill University, Montréal, QC, Canada, [12]Montreal Neurological Institute, McGill University, Montreal, QC, Canada, [13]McGill University Health Center (MUHC), McGill University, Montreal, QC, Canada, [14]CHU Sainte-Justine, Université de Montréal, Montreal, QC, Canada, [15]Veteran's Affairs Medical Center, University of Oklahoma Health Sciences Center, Oklahoma Medical Research Foundation, Oklahoma City, OK, [16]University of Occupational and Environmental Health, Kitakyushu, Japan, [17]University of Calgary, Calgary, AB, Canada, [18]Hôpitaux Universitaires de Strasbourg, Strasbourg, France

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

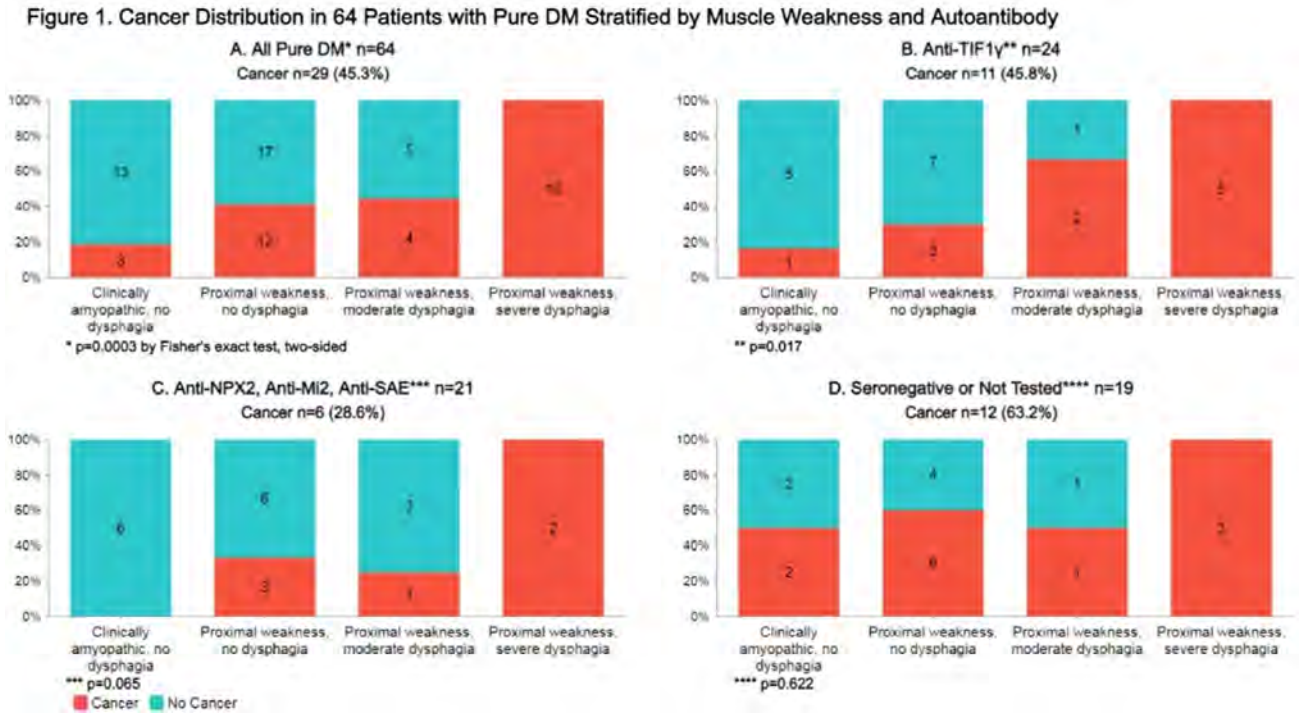
Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The risk of cancer is increased in patients with pure dermatomyositis (DM), i.e. patients with a DM rash and without an anti-MDA-5 syndrome, a suspected or confirmed anti-synthetase syndrome or scleromyositis. The aim of this study was to describe the relationship between the extent of muscle involvement and the prevalence of cancer in serologically-defined subsets of pure DM.

Methods: Patients with pure DM were selected from a retrospective cohort of incident autoimmune myositis (AIM) seen in two rheumatology academic centers between 2000 and 2021. All patients were classified by expert opinion into one of three serologically distinct groups: group 1 (anti-TIF1γ autoantibodies), group 2 (non-anti-TIF1γ autoantibodies) and group 3 (seronegative/not tested). The degree of muscle involvement was stratified in four mutually exclusive categories: clinically amyopathic (CADM), proximal muscle weakness alone, proximal muscle weakness with moderate dysphagia (no aspiration) on video fluoroscopy swallow study (VFSS) and proximal muscle weakness with severe dysphagia (by VFSS or clinical aspiration). A diagnosis of cancer within (±) three years of AIM was recorded.

Results: Of 250 patients with AIM, 64 had pure DM. Anti-TIF1γ autoantibodies were positive in 24 (37.5%) patients, anti-Mi-2 in 9 (14.1%), anti-NXP2 in 7 (10.9%) and anti-SAE in 5 (7.8%), while 9 (14.1%) patients were seronegative and 10 (15.6%) untested. Cancer occurred in 29 of 64 (45.3%) patients: 11 of 24 (45.8%) in group 1, 6 of 21 (28.6%) in group



2, and 12 of 19 (63.2%) in group 3 (Figure 1). When stratified by extent of muscle weakness, cancer was seen in 18.8% (n=3/16) of CADM, 41.4% (n=12/29) of patients with proximal muscle weakness alone, 44.4% (n=4/9) of those with moderate dysphagia and 100% (n=10/10) of patients with severe dysphagia (p=0.0003 by Fisher's Exact Test) (Figure 1, panel A). A statistically significant gradual increase in cancer frequency with incremental extent of muscle weakness was also seen in group 1 (p=0.017) (Figure 1, panel B). All 3 patients with CADM and cancer survived, whereas all 10 patients with severe dysphagia and cancer died from their cancer.

Conclusion: In pure DM, cancer prevalence within 3 years of AIM diagnosis significantly increases with increasing extent of muscle weakness. Severe oropharyngeal dysphagia combined with proximal weakness is associated with the highest prevalence of cancer and poorest prognosis. Assessing the extent of muscle involvement in pure DM may improve cancer risk stratification.

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Abstract Number: 1961

Anti-PM/Scl Autoantibodies in Juvenile Myositis Are Associated with a Distinct Phenotype Resembling Anti-synthetase Syndrome

Matthew Sherman[1], Payam Noroozi Farhad[2], Edward Trieu[3], Katherine Pak[4], Iago Pinal-Fernandez[4], Kakali Sarkar[2], Megan Neely[5], Ira Targoff[6], Frederick Miller[7], Andrew Mammen[8] and Lisa Rider[9], [1]NIAMS/NIH, Washington, DC, [2]Environmental Autoimmunity Group, National Institute of Environmental Health Sciences, National Institutes of Health, Bethesda, MD, [3]Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, [4]National Institutes of Health, Bethesda, MD, [5]Department of Biostatistics and Bioinformatics, Duke University, Durham, NC, [6]Veterans Affairs Medical Center, University of Oklahoma Health Sciences Center, and Oklahoma Medical Research Foundation, Oklahoma City, OK, [7]NIH, NIEHS, Chapel Hill, NC, [8]NIH, Bethesda, MD, [9]NIEHS, NIH, Bethesda, MD

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-PM/Scl autoantibodies (Abs) are an uncommon myositis-associated autoantibody (MAA) in juvenile myositis. The clinical features and outcomes associated with anti-PM/Scl Abs in juvenile myositis are largely uncharacterized.

Characteristic	Anti-PM/Scl positive, N = 19	Anti-PM/Scl negative, N = 532	p-value
Demographics			
Female	79% (15 / 19)	70% (372 / 532)	0.4
Caucasian	79% (15 / 19)	69% (366 / 532)	0.3
Black	0% (0 / 19)	13% (70 / 532)	0.2
Hispanic	0% (0 / 19)	6.2% (33 / 532)	0.6
Asian	5.3% (1 / 19)	2.3% (12 / 532)	0.4
Other	16% (3 / 19)	9.6% (51 / 532)	0.4
Age at diagnosis (years)	11.8 (8.3, 14.2)	7.5 (5.1, 11.7)	**0.003**
Duration from diagnosis to enrollment (years)	0.3 (0.2, 3.6)	1.6 (0.5, 3.6)	0.10
Clinical Subgroups			
JDM	53% (10 / 19)	84% (447 / 532)	**0.002**
JPM	11% (2 / 19)	6.6% (35 / 532)	0.4
JCTM	37% (7 / 19)	9.4% (50 / 532)	**0.002**
Juvenile myositis with SSc	21% (4 / 19)	0.6% (3 / 529)	**<0.001**
Autoantibodies			
Any MSA positive	16% (3 / 19)	80% (423 / 532)	**<0.001**
Anti-TIF1	5.3% (1 / 19)	33% (177 / 531)	**0.010**
Anti-NXP2	0% (0 / 19)	29% (154 / 531)	**0.006**
Anti-MDA5	11% (2 / 19)	8.0% (42 / 522)	0.7
Anti-Mi2	0% (0 / 19)	2.1% (11 / 532)	>0.9
Anti-Synthetase	0% (0 / 19)	4.5% (24 / 532)	>0.9
Anti-SRP	0% (0 / 19)	1.7% (9 / 532)	>0.9
Anti-HMGCR	0% (0 / 16)	1.2% (5 / 415)	>0.9
Anti-Ro60	0% (0 / 19)	9.6% (51 / 532)	0.2
Anti-Ro52	18% (3 / 17)	15% (75 / 485)	0.7
Anti-U1-RNP	0% (0 / 19)	5.1% (27 / 532)	0.6
Anti-NT5C1A	21% (3 / 14)	28% (98 / 356)	0.8
ANA titer	1,280 (1,040, 2,176)	320 (160, 870)	**0.006**
ANA with nucleolar pattern	92% (11 / 12)	3.4% (8 / 234)	**<0.001**

TABLE 1: Demographics and clinicoserologic subgroups of juvenile myositis patients with and without anti-PM/Scl autoantibodies. Abbreviations: ANA, antinuclear antibody; JCTM, juvenile connective tissue myositis; JDM, juvenile dermatomyositis; JPM, juvenile polymyositis; MSA, myositis-specific autoantibody; SSc, systemic sclerosis.

Methods: Patients with juvenile myositis enrolled in NIH myositis natural history studies were screened for anti-PM/Scl and other myositis Abs. Demographics, clinical manifestations, medications, and outcomes of those with and without anti-PM/Scl Abs were compared using Chi-squared, Fisher's exact test, or Wilcoxon rank-sum test. Multivariable logistic regression with adjustment for year of diagnosis and myositis autoantibodies was performed for statistically significant variables from the univariable analyses. A two-sided $p< 0.05$ was considered significant.

Results: Nineteen of 551 patients (3.4%) had anti-PM/Scl Abs by immunoprecipitation (**Table 1**). Among those with sera available for immunoblotting, 5 were positive for anti-PM/Scl-100, 1 was positive for anti-PM/Scl-75, 4 were positive for both antigens, and 3 were blot negative, likely reacting only to native protein. Patients with anti-PM/Scl Abs were older at diagnosis (11.8 vs 7.5 years, p=0.003) and more likely to have juvenile connective tissue disease myositis (37% vs 9.4%, p=0.002), frequently overlapping with systemic sclerosis (SSc) (21% vs 0.6%, $p< 0.001$). MSAs were less commonly associated with anti-PM/Scl Abs (16% vs 80%, $p< 0.001$). There was no difference in the frequency of anti-Ro52 Abs among patients with or without anti-PM/Scl Abs. ANA titer was higher (1:1280 vs 1:320, p=0.006) and a nucleolar pattern (92% vs 3.4%, $p< 0.001$) was more common among those with anti-PM/Scl Abs. Patients with anti-PM/Scl Abs had higher odds of certain clinical features (**Table 2**), including sclerodactyly (OR 22.4; 95% CI 6.74-71.5), mechanic's hands (OR 11.6; 95% CI 4.18-31.1), Raynaud's phenomenon (OR 8.11; 95% CI 3.14-21.3), and ILD (OR 7.54; 95% CI 2.19-23.9) and lower odds of malar rash (OR 0.29; 95% CI 0.11-0.73). There was also a lower odds of treatment with IV methylprednisolone (OR 0.32; 95% CI 0.10-0.91) for those with anti-PM/Scl Abs.

Characteristic	Anti-PM/Scl positive, N = 19	Anti-PM/Scl negative, N = 532	p-value	OR	95% CI
Clinical features					
Distal weakness	37% (7 / 19)	49% (255 / 521)	0.3		
Myalgia	32% (6 / 19)	66% (344 / 522)	**0.002**	0.26	0.09, 0.69
Falling	53% (10 / 19)	44% (230 / 526)	0.4		
Arthritis	68% (13 / 19)	52% (275 / 531)	0.2		
Arthralgia	68% (13 / 19)	65% (345 / 528)	0.8		
Heliotrope rash	74% (14 / 19)	79% (418 / 530)	0.6		
Gottron's papules	84% (16 / 19)	85% (449 / 530)	>0.9		
Mechanic's hands	42% (8 / 19)	5.7% (30 / 526)	**<0.001**	11.6	4.18, 31.1
Raynaud's phenomenon	53% (10 / 19)	12% (62 / 530)	**<0.001**	8.11	3.14, 21.3
V-sign rash	11% (2 / 19)	30% (161 / 530)	0.063		
Shawl sign rash	21% (4 / 19)	20% (108 / 528)	>0.9		
Malar rash	42% (8 / 19)	73% (386 / 531)	**0.004**	0.29	0.11, 0.73
Periungual capillary dilatation	74% (14 / 19)	79% (410 / 518)	0.6		
Sclerodactyly	32% (6 / 19)	2.4% (13 / 532)	**<0.001**	22.4	6.74, 71.5
Digital infarcts	21% (4 / 19)	5.8% (31 / 532)	**0.027**		
Calcinosis	26% (5 / 19)	32% (170 / 531)	0.6		
Dysphagia	53% (10 / 19)	41% (220 / 531)	0.3		
Interstitial lung disease	42% (8 / 19)	9.3% (49 / 527)	**<0.001**	7.54	2.19, 23.9
Dyspnea on exertion	58% (11 / 19)	29% (155 / 527)	**0.008**	2.99	1.08, 8.35
Weight loss	63% (12 / 19)	41% (218 / 528)	0.058		
Medications received					
Methylprednisolone (IV)	35% (6 / 17)	63% (307 / 491)	**0.023**	0.32	0.10, 0.91
Methotrexate	53% (9 / 17)	74% (365 / 491)	0.087		
Other DMARD	24% (4 / 17)	29% (142 / 491)	0.6		
IVIG	35% (6 / 17)	43% (213 / 491)	0.5		
Number of major medications, total	2.0 (1.0, 4.0)	3.0 (2.0, 5.0)	0.088		
Unknown	2	41			
Number of major medications, in combination	2.0 (1.0, 3.0)	2.0 (2.0, 4.0)	0.11		
Unknown	2	41			
Outcomes					
Monocyclic	23% (3 / 13)	21% (84 / 408)	0.7		
Chronic continuous	38% (5 / 13)	56% (229 / 408)	0.2		
Hospitalized	47% (9 / 19)	61% (311 / 512)	0.2		
Wheelchair use	16% (3 / 19)	21% (110 / 517)	0.8		
Complete clinical response	18% (3 / 17)	27% (133 / 488)	0.6		
Remission	5.9% (1 / 17)	22% (108 / 490)	0.14		
Mortality	11% (2 / 19)	5.3% (28 / 532)	0.3		

TABLE 2: Clinical features, medications received, and outcomes of juvenile myositis patients with and without anti-PM/Scl autoantibodies. Abbreviations: DMARD, disease-modifying antirheumatic drug; IV, intravenous; IVIG, intravenous immunoglobulin; MTX, methotrexate.

Characteristic	Anti-PM/Scl positive, N = 19	Anti-Synthetase positive, N = 24	p-value
Demographics			
Female	79% (15 / 19)	83% (20 / 24)	>0.9
Caucasian	79% (15 / 19)	62% (15 / 24)	0.2
Black	0% (0 / 19)	25% (6 / 24)	**0.027**
Clinical Subgroups			
JDM	53% (10 / 19)	54% (13 / 24)	>0.9
JPM	11% (2 / 19)	17% (4 / 24)	0.7
JCTM	37% (7 / 19)	29% (7 / 24)	0.6
Juvenile myositis with SSc	21% (4 / 19)	0% (0 / 24)	**0.031**
Autoantibodies			
Anti-Ro52	18% (3 / 17)	64% (14 / 22)	**0.004**
ANA with nucleolar pattern	92% (11 / 12)	6.2% (1 / 16)	**<0.001**
Clinical Features			
Myalgia	32% (6 / 19)	78% (18 / 23)	**0.002**
Arthritis	68% (13 / 19)	79% (19 / 24)	0.5
Mechanic's hands	42% (8 / 19)	38% (9 / 24)	0.8
Raynaud's phenomenon	53% (10 / 19)	38% (9 / 24)	0.3
Malar rash	42% (8 / 19)	46% (11 / 24)	0.8
Sclerodactyly	32% (6 / 19)	21% (5 / 24)	0.5
Digital infarcts	21% (4 / 19)	12% (3 / 24)	0.7
Dyspnea on exertion	58% (11 / 19)	62% (15 / 24)	0.8
Interstitial lung disease	42% (8 / 19)	62% (15 / 24)	0.2
Medications Received			
Methylprednisolone (IV)	35% (6 / 17)	73% (16 / 22)	**0.019**
Cyclophosphamide	0% (0 / 17)	18% (4 / 22)	0.12
IVIG	35% (6 / 17)	32% (7 / 22)	0.8
Number of major medications, in combination	2 (1, 3)	3 (2, 3)	0.11
Unknown	2	2	
Outcomes			
Chronic continuous illness course	38% (5 / 13)	71% (12 / 17)	0.078
Prednisone discontinued	41% (7 / 17)	36% (8 / 22)	0.8
Complete clinical response	18% (3 / 17)	23% (5 / 22)	>0.9
Remission	5.9% (1 / 17)	4.5% (1 / 22)	>0.9
Mortality	11% (2 / 19)	21% (5 / 24)	0.4

TABLE 3: Comparison of demographics, clinical subgroups, myositis-associated autoantibodies, clinical features, medications received, and outcomes between juvenile myositis patients with anti-PM/Scl and anti-synthetase autoantibodies. Abbreviations: ANA, antinuclear antibody; DMARD, disease-modifying antirheumatic drug; IV, intravenous; IVIG, intravenous immunoglobulin; JCTM, juvenile connective tissue myositis; JDM, juvenile dermatomyositis; JPM, juvenile polymyositis; SSc, systemic sclerosis.

Given the similarity in clinical features to anti-synthetase syndrome, patients with anti-PM/Scl were compared to those with anti-aminoacyl tRNA synthetase (ARS) Abs (**Table 3**). Anti-ARS Abs were present in 24 (4.3%) patients, similar in frequency to anti-PM/Scl Abs. Among patients with anti-PM/Scl Abs, none was Black (0% vs 25%, p=0.027) and overlap with SSc was more common (21% vs 0%, p=0.031). Those with anti-PM/Scl Abs less often had co-occurring anti-Ro52 Abs (18% vs 64%, p=0.004) and myalgia (32% vs 78%, p=0.002). The presence of ANA with nucleolar pattern (92% vs 6.2%, p< 0.001) was more frequent in anti-PM/Scl Ab-positive patients.

Conclusion: Anti-PM/Scl Abs, unlike other MAAs, were associated with a well-defined phenotype resembling anti-synthetase syndrome. Patients with anti-PM/Scl Abs, compared to those with anti-ARS Abs, were not Black, had an ANA with nucleolar pattern, and less frequently were positive for anti-Ro52 Abs.

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Abstract Number: 1962

Toll-Like Receptor 7/8 Activation of Immune and Non-Immune Cells in Muscle by RNA-Containing Immune Complexes Can Contribute to Inflammation and the Pathogenesis of Myositis

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SESSION INFORMATION
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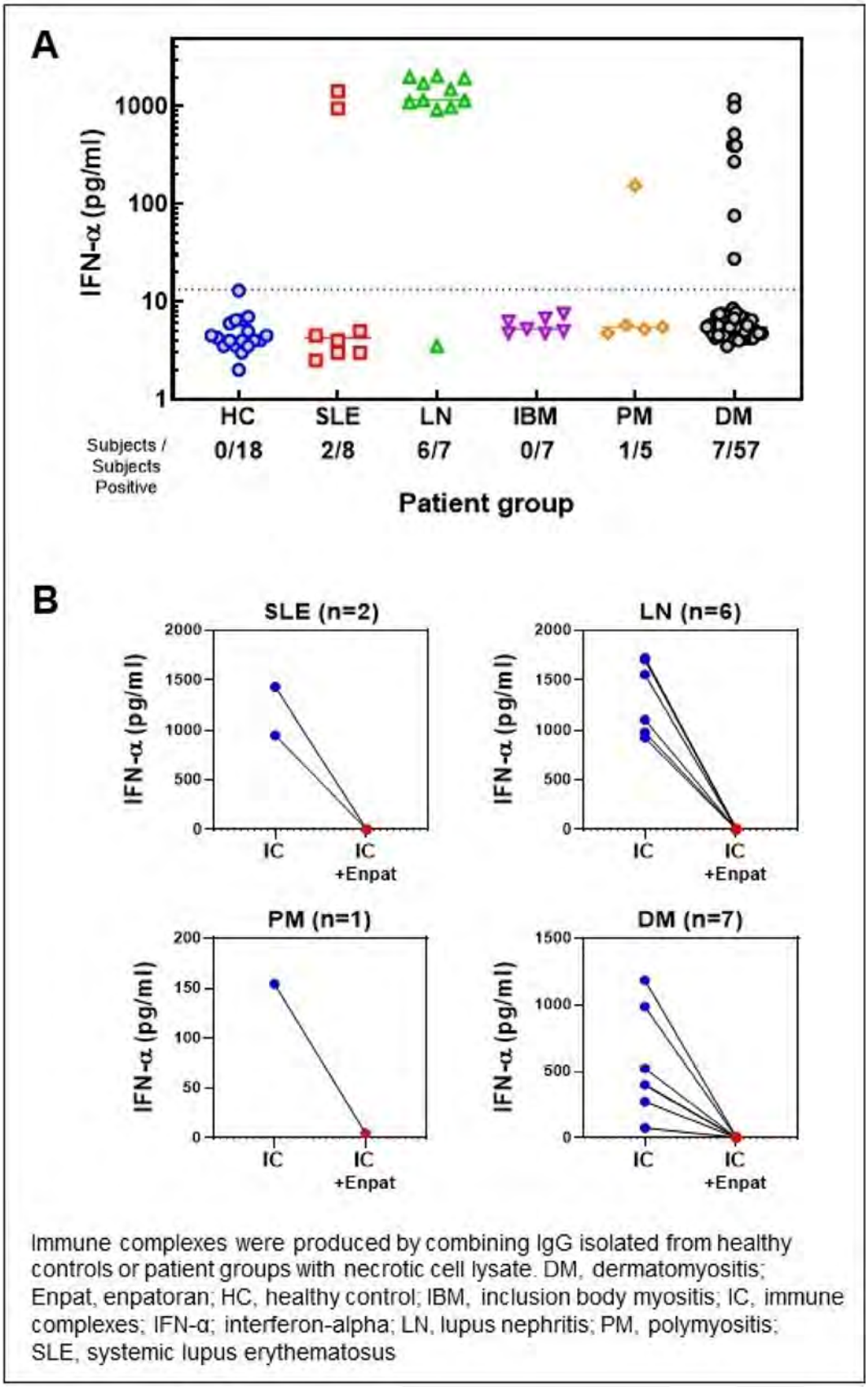
Background/Purpose: Tissue inflammation is a major disease driver in idiopathic inflammatory myopathies (IIM), leading to muscle weakness and, in the case of dermatomyositis (DM), a subtype of IIM, cutaneous manifestations. In some IIM subtypes, particularly DM, inflammation in the affected tissue is considered a major disease driver. The upstream pathways causing inflammation in IIM are poorly characterized; better understanding could lead to development of more effective treatments. Activation of endosomal toll-like receptors (TLR) is one possible driver of inflammation in IIM as hallmarks of TLR activation are observed in some patients, including high Type I interferon (IFN) and the presence of RNA-containing immune complexes. We studied the potential contribution of TLR7 and TLR8 in IIM pathogenesis.

Methods: Immune complexes from 69 patients with IIM as well as 15 lupus patients and 18 healthy controls were tested for their ability to activate healthy donor peripheral blood mononuclear cells (PBMCs) and the impact of the TLR7/8 inhibitor enpatoran on PBMC activation was evaluated in a subset of participants. Human myoblasts and satellite cells were treated with supernatants from TLR7/8-activated PBMCs and gene expression was evaluated by NanoString. Mice were dosed intramuscularly with the TLR7/8 agonist R848 and single cell RNA sequencing was run on the muscle to ascertain the cell types responding to TLR7/8 and the downstream effects.

Results: Immune complexes from patients with IIM and lupus stimulated the production of IFN-α from PBMCs and triggered significant gene expression changes, including induction of a Type I IFN-gene signature. IFN production was completely blocked by enpatoran **(Fig 1)**. DM patients, specifically those with autoantibodies targeting Jo-1, had the highest prevalence of activating immune complexes. Histidyl-transfer RNA, which is associated with the Jo-1 autoantibody, activated PBMCs in a TLR7/8-dependent manner. Myoblasts and satellite cells were activated by supernatants from TLR7/8 agonist-treated PBMCs, as determined by gene expression changes including increased expression of cytokines/chemokines and decreased expression of some muscle cell markers **(Fig 2)**. *In vivo*, monocytes/macrophages and endothelial cells in muscle were activated by R848. Both cell types produced inflammatory cytokines downstream of NF-κB and endothelial cells increased expression of adhesion molecules. There was also the appearance of an IFN-gene signature in multiple cell types.

Conclusion: TLR7/8 activation can lead to inflammation in muscle with deleterious effects. RNA in immune complexes from patients with IIM, particularly Jo-1-positive DM patients, may activate TLR7/8. These data suggest that enpatoran may reduce inflammation in myositis that is triggered by TLR7/8 activation.



Immune complexes were produced by combining IgG isolated from healthy controls or patient groups with necrotic cell lysate. DM, dermatomyositis; Enpat, enpatoran; HC, healthy control; IBM, inclusion body myositis; IC, immune complexes; IFN-α; interferon-alpha; LN, lupus nephritis; PM, polymyositis; SLE, systemic lupus erythematosus

Figure 1. Patient-derived immune complexes can induce IFN-α (A) downstream of TLR7/8 (B)

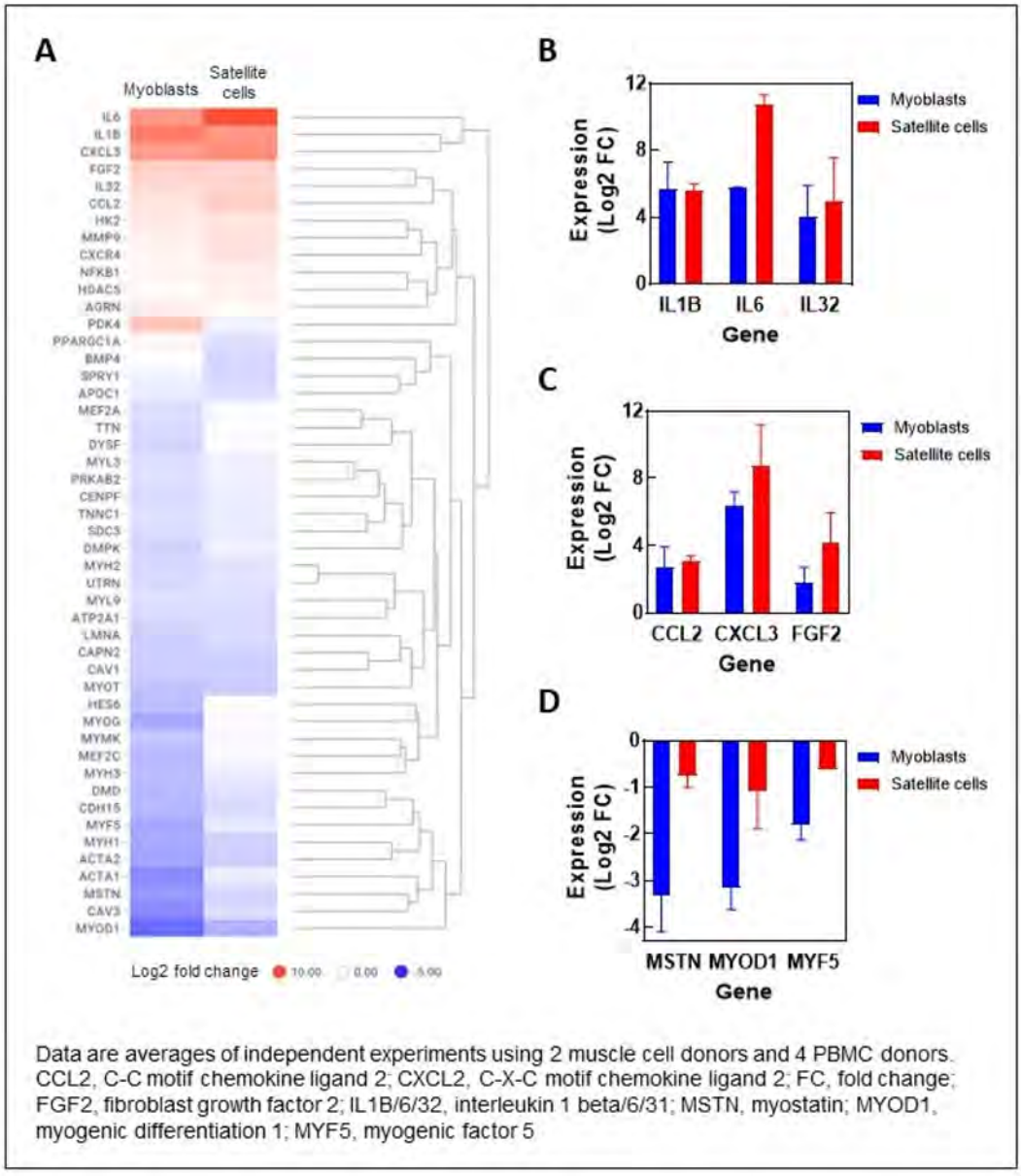


Figure 2. Myoblasts and satellite cells stimulated with supernatants from R848-activated PBMCs increase expression of muscle cell activating factors and cytokines (A, heatmap shows fold change vs control muscle cells; B, expression of selected genes shown)

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Abstract Number: 1963

Effect of JAK-STAT Inhibition by Baricitinib and Tofacitinib on Disease Phenotype in a Mouse Model of Myositis

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SESSION INFORMATION
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Background/Purpose: Dysregulation of the interferon (IFN) pathway plays a major role in the pathophysiology of autoimmune myositis. Upregulation of type 1 IFN stimulated genes (an IFN 'signature') is present in myositis patients and this signature is related to disease severity. The JAK family of tyrosine kinases, which mediate interferon signaling through the signal transducer and activators of transcription (STAT), have thus become therapeutic targets for treating myositis as well as other autoimmune diseases. Therefore, we investigated the effects of two JAK-STAT inhibitors, baricitinib and tofacitinib, on development of the disease process in the major histocompatibility complex (MHC) class I transgenic mouse model, which exhibits features very similar to human myositis, including an upregulation of type 1 IFN stimulated genes.

Methods: Myositis was induced in 21-day old female mice by removal of doxycycline. Mice were randomized into 4 groups (n=12/group); myositis no treatment, myositis + baricitinib, myositis + tofacitinib, and control. Baricitinib and tofacitinib were administered daily as a cherry syrup oral suspension at 10 mg/kg and 20 mg/kg body weight respectively for six weeks. Treatment groups were evaluated based on survival time, body weight, muscle strength and function (GSM, *in vitro* torque and treadmill exhaustion), histologic disease severity and expression levels of the type 1 IFN stimulated genes (ISG) Mx1, IFIT1, IRF7, and ISG15. Data were collected in a blinded fashion.

Results: Myositis mice had significantly reduced weight gain, muscle function and strength, and inflammation in the quadricep muscle compared to controls. Tofacitinib treatment resulted in significant improvement in survival of myositis mice, with 55% surviving to the end of the study compared to 27% for the myositis and baricitinib treatment groups. Expression levels of the type 1 interferon genes Mx1, IFIT1, IRF7, and ISG15, which were significantly elevated in myositis mice, were noticeably decreased in skeletal muscle of both baricitinib and tofacitinib treated mice. However, significant reductions in IFIT1 ($p = 0.03$) and IRF7 ($p = 0.04$) expression were observed only in the tofacitinib treated group. Neither tofacitinib nor baricitinib treatment resulted in significant functional improvement.

Conclusion: Overall, we observed that treatment with tofacitinib significantly improved survival and lowered the IFN signature, but this did not translate to functional improvement. Furthermore, baricitinib did not significantly improve any of the measures tested.While both tofacitinib and baricitinib interfere with the JAK1 pathway, tofacitinib additionally interferes with the JAK3 pathway which is involved in signal transduction of the γc family of cytokines. This difference could explain the increased efficacy of tofacitinib in this study.

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Abstract Number: 1964

Penn State Registry of Inflammatory Myopathies (PRIMO) Provides Insights into Disease Features and Co-Morbidity Screening Utilization

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Background/Purpose: Dermatomyositis (DM) is a relatively rare condition with significant morbidity and mortality across the lifespan.Recent advances in diagnostics and therapeutics have significant potential to improve outcomes.We set up the Penn State Registry of Inflammatory Myopathies (PRIMO) and sought to understand the current status of DM patients seen in the relatively rural population of south-central Pennsylvania.Objectives are to determine whether our patients have had access to optimal care and to explore approaches to improving outcomes.

Methods: Records for patients seen at Hershey Medical Center with diagnosis code M33 (including all subcodes) in a 10 year period starting 1/1/2010 were extracted from the EMR.Each record was reviewed (by JC) to confirm the 2017 EULAR/ACR classification criteria for idiopathic inflammatory myopathies. Features of108 patients with DM or juvenile DM were reviewed in detail (by JC and KR) using data extraction forms and compiled in a REDCap database.Descriptive statistics were used to summarize results.

Results: Most patients (87%) had adult DM; the overall average age was 52 years (range 7 to 88 years).Other demographic features are shown (Table 1).Encounters for the first myositis-related symptoms occurred most commonly in family medicine (44%), dermatology (16.7%) and pediatrics (13.1%); only 6% had an initial myositis-related encounter in rheumatology.Common presenting symptoms were rash (94.2%) and muscle weakness (81.7%).Autoimmune comorbidities included celiac disease (14.3%) and thyroid conditions (28.4%).Familial conditions included RA (35.7%), SLE (21.4%) and Sjogren's (14.3%); no patient reported a family history of DM or polymyositis.Lab testing at presentation showed elevated muscle enzymes (CK, LDH or transaminases) in 72% and ANA positivity in 66%; 2/3 had speckled pattern.Of myositis-specific autoantibodies (MSA) measured, the most prevalent was Tif-1 gamma, positive in 15.4% of those tested (Table 2).When performed, tissue biopsies were highly diagnostic (skin:43/49 patients tested, 88% positive; muscle 38/42, 90%).Muscle MRI done in 33 individuals showed inflammation in 73% and atrophy in 9%.Prevalence of malignancy (9.6%) was relatively low; screening for malignancies was not recorded for all patients (Table 3).Other testing for comorbidities included echocardiograms, which were normal in 88% of 25 examined and HRCT which showed ILD changes in 38% of 21 tested. Less than half of individuals had PFTs completed.

Table 1: Demographic Features in 108 DM patients	
Age	52 (22) years*
Juvenile (< 18 yrs)	13%
Female	76.9%
Race: White/Black/other	78.7/6.5/14.8%
Ethnicity: Hispanic/NonHispanic/unknown	12.1/84.1/3.7%
Status: Deceased/Alive/Lost to followup	8.6/70.5/21.0%
Never smoker/Never used alcohol	77.1%/61.9%

*Mean (SD)

Table 2: Autoantibody Testing			
Autoantibody	Positive	Negative	Unknown/not done
Jo-1	6	89	9
PL-12	0	83	21
PL-7	1	83	20
EJ	1	82	21
OJ	0	82	22
SRP	2	76	26
HMGCR*	1	5	98
MDA5	6	27	71
NXP-2	5	34	65
Mi2	6	70	28
Tif-1 gamma	16	23	65
Ro/SSA	5	57	42
PM-SCl	1	48	55
Ku	1	66	37
RNP	4	55	45

*HMGR = anti-HMG Co-A Reductase

Table 3: Malignancy Screening Tests in 84 Adult DM Patients	
CT Thorax	75.0%*
CT Abdomen/Pelvis	76.2%
PET CT	11.9%
Colonoscopy	48.8%
Mammogram (females only)	51.2%
Pelvic ultrasound (females only)	29.8%

*Percent tested

Conclusion: DM outcomes may be improving in part due to improved screening for comorbidities as well as availability of new treatment options.The rate of malignancy in our patients was lower than expected, despite the high prevalence of malignancy-related autoantibodies (TIF-1g, NXP-2) among those patients with evaluation for MSA. Whether this is related to length of followup is being further investigated.Our study also demonstrates that screening for comorbidities had lower than expected utilization representing a potential practice gap.Future studies are needed to determine if this a local trend, or a population shortfall in DM management. Development of personalized medicine approaches should be prioritized.

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Abstract Number: 1965

Discordance Between Patient and Physician Perception of Disease Activity Among Patients with Idiopathic Inflammatory Myopathies: Results from the COVAD Study

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SESSION INFORMATION

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Background/Purpose: Disease activity assessment is key in the management of patients with idiopathic inflammatory myopathies (IIM). However, patients' perception of disease may differ from clinicians. We tried to understand what factors lead to discrepancy between patients' and physicians' perception of disease activity in IIMs from the COVID-19 Vaccination in Autoimmune Diseases (COVAD) study.

Methods: The COVAD-1 study collected global cross-sectional data from adults with autoimmune diseases and healthy controls by a team of 106 experts from 94 countries from April-December 2021, on demographics; disease characteristics, treatment and glucocorticoid (GC) dose; and validated patient reported outcomes (PROs), including PROMIS SF10 physical function, VAS-pain and VAS-fatigue. Patient-perceived active disease was self-reported. Physician-reported active disease was defined as presence of joint swelling, active rash or worsened muscle weakness and/or GC dose ≥10mg prednisolone equivalents. Discordant and concordant pairs of patient-physician reported disease activity were compared, and predictors of discordance were analysed using multivariate regression models.

Table 1. Demographics and patient reported outcome measures among the disease subgroups. ASSD: anti-synthetase syndrome; DM: dermatomyositis; IBM: inclusion body myositis; NAM: Immune mediated necrotising myopathy; OM: overlap myositis; PF: physical function; PM: polymyositis; PROMIS, Patient-Reported Outcome Information System; VAS: visual analogue scale (0-10).

	DM n=377	PM n=152	ASSD n=149	OM n=152	NAM n=62	IBM n=325
Age in years	54.4±13.7	57.7±14.6	55±12	52.4±12.8	61±13.1	71±9.5
Female (%)	282 (74.8)	93 (61.6)	83 (55.7)	112 (73.7)	49 (79)	240 (74.5)
Race/Ethnicity						
Caucasian	302 (80.1)	137 (90.1)	125 (83.9)	140 (92.1)	59 (95.2)	231 (71.1)
African American	13 (3.4)	6 (3.9)	4 (2.7)	3 (2)		13 (4)
Asian	34 (9)	1 (0.7)	10 (6.7)	2 (1.3)	1 (1.6)	44 (13.5)
Hispanic	14 (3.7)	3 (2)	2 (1.3)	5 (3.3)	2 (3.2)	21 (6.5)
Others	14 (3.7)	5 (3.3)	8 (5.4)	2 (1.3)		16 (4.9)
PROMIS PF10a	39.19±8.62	35.99±8.94	37.99±7.86	35.47±9.42	32.45±10.32	25.3±9.22
Pain VAS	2.7±2.6	3±2.6	3.3±2.8	4.3±2.9	2.9±2.7	2.3±2.4
Fatigue VAS	4.3±2.6	4.5±2.7	4.3±2.8	5.5±2.5	4.8±2.9	4.8±2.5
Physician perceived active disease	184 (48.8)	77 (50.7)	80 (53.7)	78 (51.3)	43 (69.4)	181 (55.7)
Patients perceived active disease	260 (69)	94 (61.8)	117 (78.5)	120 (78.9)	49 (79)	293 (90.2)
Concordance	245 (65)	95 (62.5)	94 (63.1)	84 (55.3)	38 (61.3)	189 (58.2)
Disease activity by physician only (EA)	28 (21.21)	20 (35.09)	9 (16.36)	13 (19.12)	9 (37.5)	12 (8.82)
Disease activity by patient only (PA)	104 (78.79)	37 (64.91)	46 (83.64)	55 (80.88)	15 (62.5)	124 (91.18)

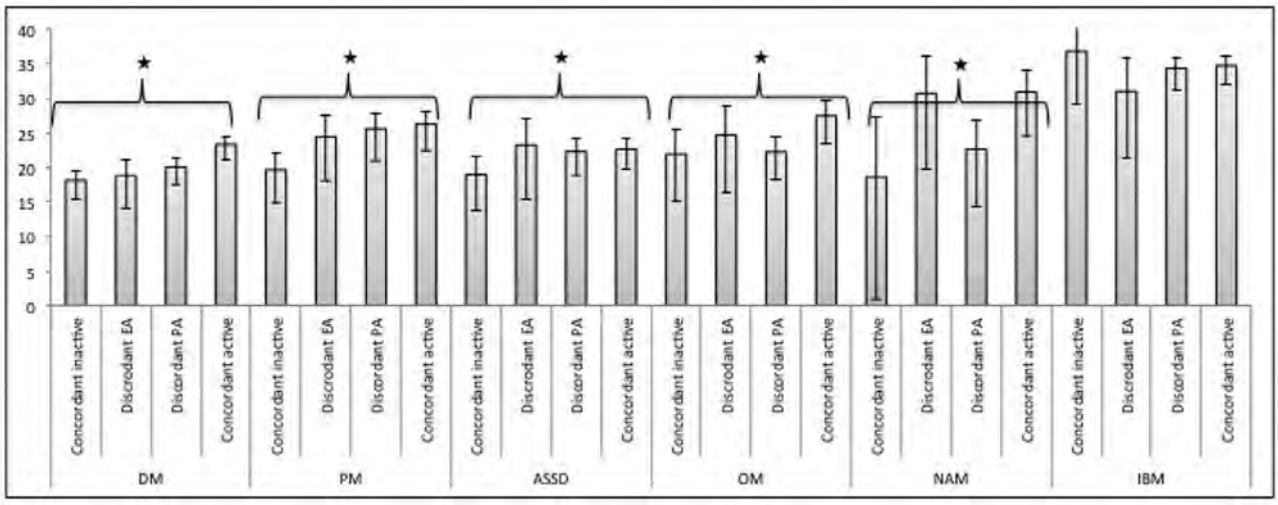

Figure 1. Distribution of the mean PROMIS PF10a scores according to the four perceived disease activity classes among the different disease subgroups. *= p value<0.001 by the Kruskal Wallis test. Abbreviations: ASSD: anti-synthetase syndrome; DM: dermatomyositis; EA: evaluator assessment as active disease; IBM: inclusion body myositis; NAM: Immune mediated necrotising myopathy; OM: overlap myositis; PA: patient assessment as active disease; PF: physical function; PM: polymyositis; PROMIS, Patient-Reported Outcome Information System.

Results: Among 16328 respondents, 1217 patients with IIM were included (median age 59 years (IQR 45-73), 70% females and 81.6% Caucasians, details in Table 1). Dermatomyositis (DM; 30.9%) was the most common subtype. Moderate concordance was seen between patient and physician disease activity. Discordance was identified in 38.8% (n=472)

Table 2. Multivariable regression analysis with the four groups of perceived disease activity as dependent variable. Only the parameter estimates of PROMISPF10a scores as the independent variables is shown in the table. The model was adjusted with the following covariates: age, gender, Fatigue VAS and pain VAS. a Other significant predictors: Pain for "Discordant PA": 1.27 (1.01-1.16), p=0.04; Fatigue for "Both active": 1.16 (1.002-1.33), p=0.048; b Other significant predictors: None; c Other significant predictors: None; d Other significant predictors: Age for "Discordant: PA": 0.94 (0.90-0.99), p=0.023 and for "Concordant: Both active": 0.94 (0.90-0.99), p=0.02; e Not fitted due to very low sample size in reference category; f Other significant predictors: None. Abbreviations: ASSD: anti-synthetase syndrome; CI: confidence interval; DM: dermatomyositis; EA: only physician's perceives disease as active and patient does not; IBM: inclusion body myositis; NAM: Immune mediated necrotising myopathy; N/D: Not done; OM: overlap myositis; OR: Odd's ratio; PA: only patient perceives disease as active and physician doses not; PF: physical function; PM: polymyositis; PROMIS, Patient-Reported Outcome Information System; VAS: visual analogue scale (0-10).

Disease subgroup	Disease activity groups	Estimate	OR (95% CI)	p-value
DM[a]	Discordant: EA	-0.04	0.96 (0.89-1.04)	0.31
	Discordant: PA	-0.07	0.94 (0.88-0.99)	0.02
	Concordant: both active	-0.14	0.87 (0.82-0.92)	<0.001
PM[b]	Discordant: EA	-0.08	0.92 (0.84-0.99)	0.036
	Discordant: PA	-0.12	0.88 (0.82-0.95)	0.001
	Concordant: both active	-0.13	0.87 (0.82-0.94)	<0.001
ASSD[c]	Discordant: EA	-0.14	0.87(0.749-1.011)	0.07
	Discordant: PA	-0.15	1.042 (0.836-1.298)	0.009
	Concordant: both active	-0.14	1.178 (0.953-1.457)	0.011
OM[d]	Discordant: EA	-0.06	0.94 (0.85-1.05)	0.26
	Discordant: PA	-0.03	0.97 (0.89-1.05)	0.48
	Concordant: both active	-0.12	0.88 (0.82-0.96)	0.005
NAM[e]	N/D			
IBM[f]	Discordant: EA	0.07	1.07 (0.98-1.17)	0.11
	Discordant: PA	0.02	1.03 (0.97-1.08)	0.37
	Concordant: both active	0.01	1.02 (0.96-1.08)	0.59

responses. Poorest concordance was observed in inclusion body myositis (IBM), overlap myositis (OM) and necrotising autoimmune myopathy (NAM) subgroups. Among patients with DM and OM, those with higher PROMIS physical function scores (i.e. better physical function) were more likely to be concordant (DM: OR=1.03, 95% CI: 1.01-1.05, p=0.012; OM: OR=1.04, 95% CI: 1.01-1.06, p=0.012) while older patients with DM were prone to discordance (OR =0.98, 95% CI: 0.97-0.99, p=0.03) PROMIS scores varied significantly among the four groups of perceived disease activity (active or inactive by patient and/or physician) and disease subgroups except IBM (Figure 1). Pain and Fatigue VAS scores also varied significantly among the four groups. Multivariable analysis, controlling for age, gender, fatigue and pain, showed respondents with higher PROMIS physical function scores were more likely to belong to one of the active disease perception groups, compared to concordant inactive groups, for all disease subgroups except IBM (Table 2). Addition of PROMIS increased area under the curve by 8-10% in model fitting. Simple cut-off scores based on PROMIS scores could be developed to distinguish active from inactive disease.

Conclusion: Our study provides invaluable insights into the factors determining patents' perception of self-reported disease activity, and the disease groups where these measures may be less reliable for remote monitoring and virtual trials. Patient-reported assessment might be discordant in IBM while likely to be fairly concordant in DM and younger individuals irrespective of pain and fatigue.

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Abstract Number: 1966

Investigating Esophageal Involvement in Anti-Synthetase Syndrome: How to Discover the Submerged?

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

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Background/Purpose: Anti-synthetase syndrome (ASS) is an idiopathic inflammatory myopathy, typically characterized from the triad interstitial lung disease (ILD), myositis and arthritis, together with anti-aminoacyl tRNA synthetase (ARS) antibodies (Ab) positivity. Recent data suggested esophageal involvement could commonly occurs, being related to a higher

risk of pulmonary complications, at first ab ingestis pneumonia, able to significantly worsen the respiratory function of ASS patients and related to a poor prognosis. Esophageal involvement can be assessed using both double-contrast conventional radiology (DCCR) and oro-pharyngeal-esophageal scintigraphy (OPES). Moreover, DCCR may show the presence of gastrointestinal (GI) pathologies, such as esophagitis, achalasia and hiatal hernia, with a prevalence in Italian population up to 33%, 0.03% and 10% respectively. The first aim of the study is to evaluate the prevalence of esophageal involvement in a monocentric cohort of patients with ASS; secondly, we aimed at comparing DCCR and OPES in highlighting swallowing dysfunctions or GI comorbidities.

Methods: We retrospectively analyzed medical records of consecutive patients with a diagnosis of ASS based on both physicians' clinical diagnosis and ARS Ab positivity, regularly followed at our Myositis Clinic from January 2018 to May 2023. Demographic and clinical data of patients, together with DCCR and OPES results were collected; moreover, patients were asked to fill in MD Anderson Dysphagia Inventory (MDADI) to evaluate their dysphagia. Intergroups comparisons were assessed by using Chi-square, t-test and ANOVA. P values < 0.05 were considered significant.

Results: We included 37 patients (21 female, 56.8%) with a mean age of 56.3±7.9 years; 12 (32.5%) reported dysphagia and, on 31 (83.7%) who filled in MDADI, 9 (29%) showed scores corresponding to a swallowing disability, significantly associated to subjective dysphagia ($p< 0.001$). Twenty patients (54.1%) performed OPES; up to 5/20 (25%) showed an increased esophageal (E) transit time (TT), oropharyngeal (OP) retention index (RI) was increased in up to 17/20 patients (85%) and E RI was increased in up to 12/20 patients (60%). DCCR was performed in 14 patients (37.8%); hypotone and hypokinesis were found in 7/14 (50%); besides, DCCR highlighted the presence of achalasia, esophagitis and hiatal hernia respectively in 7 (50%), 10 and 10 (71.4%) patients.

Conclusion: Less than one third of ASS patients perceive to have dysphagia; however, up to 85% of those who underwent OPES and up to 50% of those who performed DCCR showed a significant swallowing dysfunction. Moreover, DCCR showed a significantly higher prevalence of GI comorbidities in ASS patients than in the general population. This is the first study at our knowledge analyzing the prevalence of esophageal involvement in ASS, through 2 different methods and in comparison with patients' perception of dysphagia. Further studies are needed to confirm our data, but they already could suggest to investigate GI involvement and GI comorbidities in ASS, even in asymptomatic patients, with the aim of optimizing their quality of care, also reducing the risk of respiratory complications related to dysphagia.

Disclosure: F. Fattorini: None; **C. Cardelli**: None; **S. Barsotti**: None; **M. Diomedi**: None; **E. Laurino**: None; **M. Grosso**: None; **L. Carli**: None; **M. Mosca**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, GlaxoSmithKlein(GSK), 2, Otsuka, 2, UCB, 2.

Abstract Number: 1967

Infectious Myopathies in an Urban Inflammatory Idiopathic Myopathy Cohort: Frequency and Impact on Disease Course and Treatment

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Background/Purpose: Over the last few decades, it has been established that multiple infections can mimic idiopathic inflammatory myopathies (IIM). HIV, HTLV-1, and Lyme disease are all associated with chronic, progressive myopathies indistinguishable from IIM. While the similarities between IIM and these infectious myopathies have been reported, differences in disease course or treatment outcomes in this population with co-existing IIM and infectious myopathies has not been evaluated. Our aim was to compare the spectrum of organ involvement and treatment response in IIM patients with infections at risk for comorbid infectious myopathies in comparison to IIM patients without infections which may contribute to myositis.

Methods: A registry was created of Montefiore Medical Center patients that met 2017 EULAR/ACR classification criteria for IIM that included patient demographics, IIM subtype, clinical manifestations by organ system, comorbidities, and treatment history. Medication failure was defined by rheumatologist, discontinuation due to adverse effects, or medication change within 3 months. Medication control was defined by documented clinical improvement. Lyme and HTLV-1 statuses were based on confirmatory western blot testing and HIV status was confirmed by viral load. If these variables were positive, diagnosis date was also recorded. Statistical analysis was carried out with paired t-tests and signed rank tests. All p values < 0.05 were considered significant.

Results: Of our cohort of 153 IIM patients, 2 patients were found to have HIV, 9 were HTLV-1 positive, and one met criteria for active Lyme disease. Given the small number of patients with possible infectious myopathies, these were analyzed together in one group. Comparison of the IIM patients with infections and IIM patients without infectious comorbidities, we found a similar distribution of age, sex, Latinx ethnicity, and race between the two groups as shown in Table 1. When comparing IIM subtypes between the two groups, we found dermatomyositis was found more frequently in the non-infectious cohort ($p = 0.01$) and inclusion body myositis (IBM) was found more frequently in the infectious cohort ($p = 0.03$) (Table 1). There were no differences in cutaneous, gastrointestinal, or pulmonary manifestations between the two groups (Table 2). The rates of neoplasm and venous thrombosis complications were also comparable. There was no difference in steroid

Table 1: Comparison of IIM patient demographics based on presence of infectious disease.

Demographics	IIM Patient Group		P-value
	Infection (+) (n = 12)	Infection (-) (n = 141)	
Age at IIM, mean (SD)	47.89 (12.53)	52.07 (14.14)	0.34
Sex, n (%)			0.18
Female	7 (58.3)	107 (75.9)	
Male	5 (41.7)	34 (24.1)	
Latinx, n (%)			0.74
Yes	4 (33.3)	58 (41.1)	
No	8 (66.7)	77 (54.6)	
Unknown	0 (0)	6 (4.3)	
Race, n (%)			0.64
American Indian	0 (0)	2 (1.4)	
Asian	0 (0)	6 (4.3)	
Black	8 (66.7)	62 (44.0)	
White	2 (16.7)	44 (31.2)	
Unknown	2 (16.7)	27 (19.2)	
IIM Subtype, n (%)			
Polymyositis	4 (33.3)	41 (29.1)	0.75
Dermatomyositis	2 (16.7)	79 (56.0)	**0.01**
Amyopathic Dermatomyositis	2 (16.7)	9 (6.4)	0.21
Mixed Connective Tissue Disease	0 (0)	15 (10.6)	0.61
Immune-Mediated Necrotizing Myopathy	0 (0)	20 (14.2)	0.37
Inclusion Body Myositis	4 (33.3)	13 (9.2)	**0.03**

Table 2: Comparison of clinical Characteristics between IIM patients with and without infections associated with myositis.

Clinical Characteristics	IIM Patient Group		P-value
	Infection (+) (n = 12)	Infection (-) (n = 141)	
Heliotrope rash, n (%)			0.21
No	10 (83.3)	86 (61.0)	
Yes	2 (16.7)	55 (39.0)	
Grotton's papules or sign, n (%)			0.37
No	9 (75.0)	84 (59.6)	
Yes	3 (25.0)	57 (40.4)	
Dysphagia, n (%)			0.70
No	7 (58.3)	74 (52.5)	
Yes	5 (41.7)	67 (47.5)	
Interstitial lung disease, n (%)			0.76
No	8 (66.7)	83 (58.9)	
Yes	4 (33.3)	58 (41.1)	
Neoplasm, n (%)			1.00
No	10 (83.3)	119 (84.4)	
Yes	2 (16.7)	22 (15.6)	
Venous thromboembolism, n (%)			1.00
No	12 (100.0)	124 (87.9)	
Yes	0 (0)	17 (12.1)	

use or treatment outcomes for conventional disease-modifying agents or biologics between the two groups. In IIM patients with an infection, the infection had a median time of diagnosis 2 months prior to the IIM diagnosis.

Conclusion: While the type of IIM may be associated with infection, particularly IBM as has been reported in other literature, the presence of a infectious myopathy in IIM patients does not lead to a difference in organ involvement or treatment outcomes. The initial presentation of IIM is a crucial time for patients to be diagnosed with a concomitant infection. Further studies are needed to elucidate the link between IBM and specific infectious processes.

Disclosure: A. Valle: None; **T. Meisel**: None; **X. Xie**: None; **S. Mahmood**: Qiagen, 6.

Abstract Number: 1968

Pregnancy Outcomes in Idiopathic Inflammatory Myopathies: A Comparison to the General American Population

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Background/Purpose: Idiopathic inflammatory myopathies (IIM) are rare autoimmune conditions which cause multi-organ inflammation, particularly in the skin, lungs, and muscles. It is known that many autoimmune conditions affect a women's ability to become pregnant and may lead to adverse pregnancy outcomes. Studying pregnancy within IIM has been difficult due to limited cases, yet there is increasing evidence that women with IIM have increased risk of pregnancy adverse outcomes, including pre-eclampsia and low birth weight. However, few studies have evaluated the spectrum of pregnancy outcomes in IIM or compared how these outcomes compare to the general population. Our aim was to evaluate the rate of term

Table 1. Comparison of demographics and pregnancy outcomes of women with a history of IIM and a sample of women in the general American population.

Variables	National Survey (n = 6141)	IIM Patients (n = 86)
Race and Ethnicity, n (%)		
Hispanic	1230 (20.03)	34 (39.5)
White, Non-Hispanic	3648 (59.40)	9 (10.5)
Black, Non-Hispanic	902 (14.68)	39 (45.3)
Other	361 (5.88)	2 (2.3)
Unknown	0 (0)	2 (2.3)
Pregnancy Outcomes, Mean (SD)		
Living Children	1.20 (0.039)	2.13 (1.58)
Elective Abortion	0.152 (0.0.014)	0.140 (0.381)
Spontaneous Abortion	0.306 (0.017)	0.198 (0.429)
Ectopic Abortion	0.018 (0.003)	0.0349 (0.185)

pregnancies, preterm pregnancies, abortions, and living children in women with a history of IIM and to compare these with a sample of American women.

Methods: The Montefiore Medical Center Myositis registry was created from patients that met 2017 EULAR/ACR classification criteria for IIM. Demographics, including age, race, ethnicity were documented. IIM subtype and date of diagnosis were also recorded. Patients who did not identify as female and lacked an obstetrics history recorded by a physician were excluded. Pregnancy outcomes, including number of term and preterm pregnancies, abortions, and living children were recorded. A preterm birth was defined as < 37 while term birth was considered >37 weeks. Abortions were further classified into elective, spontaneous, therapeutic, ectopic, or reason unknown. These same pregnancy outcomes were extracted from Section B of the CDC's 2017-2019 National Survey of Family Group for comparison.

Results: Of 153 patients with IIM, 86 of them were female patients with an obstetrics history. The mean age of IIM diagnosis was 51.7 years old, and majority of women were of Latinx ethnicity (Table 1). There were a total number of 224 pregnancies; 185 were live births with 6 (3%) preterm births.The average number of live births was 2.13 per patient. There were 39 abortions, of which 17 (44%) were spontaneous, 12 (31%) were elective, 6 (15%) were therapeutic, 3 (8%) were ectopic and one was unknown. In comparison, the majority of women participated in the national survey were white and younger, with a mean of 32 years of age. The mean number of children was 1.2 per woman. The mean number of elective abortions were similar between the two groups (0.14 vs 0.152) and the mean number of spontaneous abortions was lower in women with a history of IIM in comparison to the general population (0.198 vs 0.306) (Table 1).

Conclusion: Female patients with a history of IIM did not confer higher frequencies of poor pregnancy outcomes, including spontaneous or elective abortions. Rate of preterm pregnancies were similar, if not lower, to national averages. Differences between our patient demographics and birth rates in comparison to the national sample may be due to cultural and socioeconomic factors. Lastly, our cohort was limited by its inability to differentiate pregnancy prior to or during active IIM disease.

Disclosure: A. Valle: None; **M. Fazzari**: None; **S. Mahmood**: Qiagen, 6.

Abstract Number: 1969

Multimorbidity and PROMIS Health Outcomes in Patients with Idiopathic Inflammatory Myopathies: Analysis from the COVAD Study

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SESSION INFORMATION

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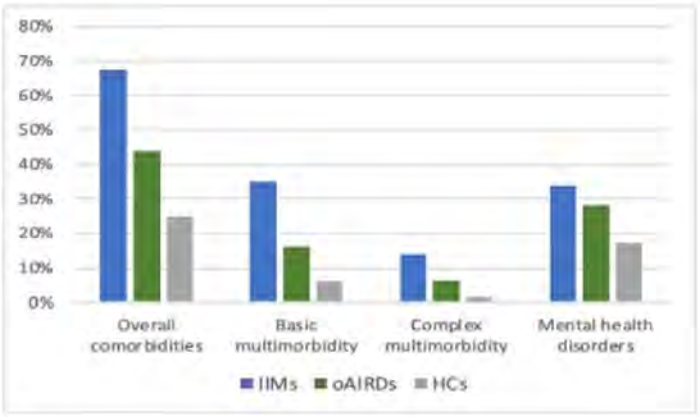
Background/Purpose: Comorbidities have a profound impact on the quality of life (QoL), though global data on the burden of comorbidities and its impact on health outcomes and QoL in vulnerable groups such as Idiopathic inflammatory myopathies (IIMs) is scarce.

Methods: We studied the prevalence, distribution and clustering of comorbidities and multimorbidity among patients with IIM, AIRDs and healthy controls (HCs) and its impact on health outcomes, utilizing data from the COVAD 2 study, a global patient-reported e-survey consisting of 167 collaborators from 110 countries. Basic multimorbidity (BM) /Complex multimorbidity (CM) were defined as the co-occurrence of ≥2 non-rheumatic comorbidities & ≥3 non-rheumatic chronic conditions affecting ≥3 different organ systems1 respectively. Human Development Index (HDI) of their country was taken as a surrogate marker for socioeconomic status (SES). PROMIS global physical health (PGP), mental health (PGM), fatigue 4a (F4a) and physical function short form (SF10) were analysed using descriptive statistics and linear regression models. Hierarchical Clustering on Principal Components was performed to outline the grouping.

Results: Among 10740 respondents, 1558 IIMs (15.9%), 4591 other AIRDs (46.8%) and 3652 HCs (37.3%) were analysed. IIMs comprised mainly of DM (30.2%) and IBM (24.1%) whilst AIRDs comprised 2450 inflammatory arthritis (53.4%), 2050 CTDs (44.6%) and 235 systemic vasculitis (5.1%).



A

B

	PROMIS Global Physical Health		PROMIS Global mental health		PROMIS Physical function (SF10a score)		Fatigue 4a	
	B	p-value	B	p-value	B	p-value	B	p-value
Age	0.35	0.03	0.51	0.004	-3.86	<0.001	-0.96	<0.001
Disease activity	-1.51	<0.001	-1.34	<0.001	-7.03	<0.001	1.45	<0.001
Gender (F/M)	0.08	0.67	-0.12	0.59	2.85	<0.001	0.33	0.21
Basic multimorbidity	-1.12	<0.001	-0.75	0.001	-2.95	<0.001	1.11	<0.001
Complex multimorbidity	0.27	0.39	0.40	0.26	-0.01	1.00	-0.24	0.58
Mental health disorders	-1.47	<0.001	-2.22	<0.001	-2.36	0.001	2.17	<0.001
HDI classification	-0.56	0.09	-0.11	0.76	-0.04	0.97	0.95	0.04

FIGURE 1: A: "Comorbidities in the COVAD cohort": highlighting thier increased incidence in IIMs as compared to other AIRDs or HCs. B: Linear regression analysis (PGP, PGM, SF10a and F4a scores in BM, CM and MHDs)

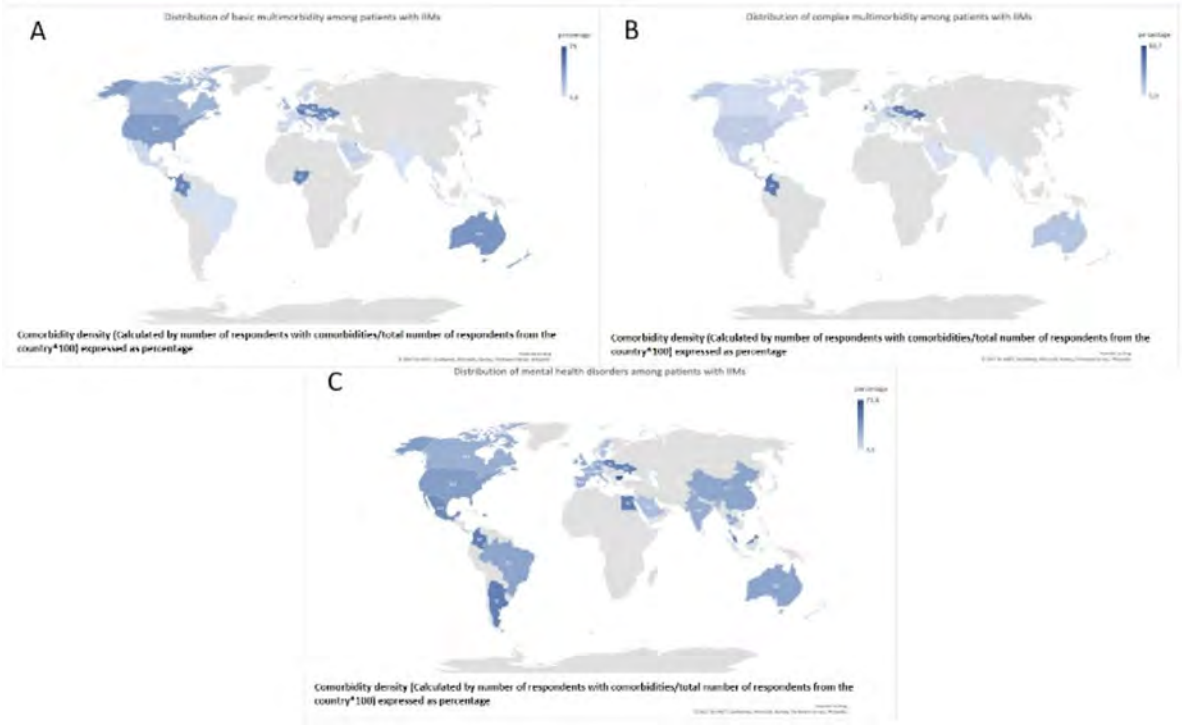
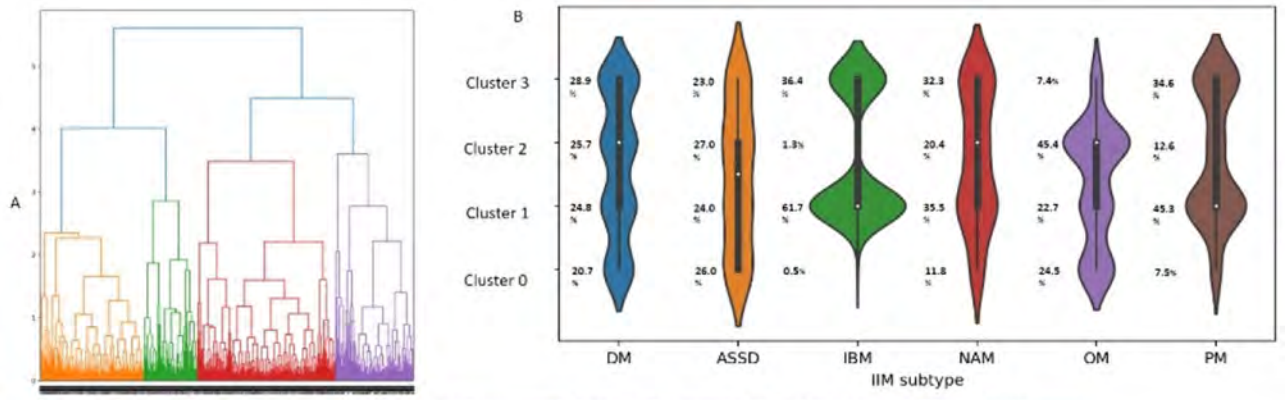


FIGURE 2: A, B, C Distribution of basic multi-morbidity, complex multi-morbidity, and mental health disorders among patients with IIMs



C

	Cluster 0 (n. 219)	Cluster 1 (n.564)	Cluster 2 (n. 318)	Cluster 3 (n.422)
Female, n. (%)	189 (86.3)[a]	358 (63.5)[b]	288 (90.6)[a]	258 (61.1)[b]
Age, mean ±SD	44 ±13[a]	66 ±10[b]	45 ±12[a]	66 ±9[b]
BM, n. (%)	10 (4.6)[a]	330 (58.5)[b]	44 (13.8)[c]	156 (37)[d]
CM, n. (%)	4 (1.8)[a]	153 (27.1)[b]	27 (8.5)[c]	31 (7.3)[c]
MHDs, n. (%)	39 (17.8)[a]	241 (42.7)[b]	176 (55.3)[c]	61 (14.5)[d]
PROMIS Global Physical health, mean	15.8 ±2.1[a]	10.2 ±1.9[b]	10.5 ±2.3[b]	14.5 ±1.7[c]
PROMIS Global Mental Health, mean	15.4 ±2.7[a]	11.2 ±2.7[b]	10.8 ±3.0[b]	15.2 ±2.4[a]
PROMIS Physical function SF10a, mean	45.8 ±4.5[a]	25.6 ±8.5[b]	34.3 ±8.6[c]	36.4 ±9.5[c]
PROMIS Fatigue 4a score, mean	7.2 ±2.4[a]	13.7 ±3.2[b]	13.8 ±3.3[b]	8.0 ±2.3[a]

FIGURE 3 A, B, C: Clusters in IIM C: Each superscript letter indicates a subset of the 4 groups analyzed for which the means or proportions showed no difference at a significance level of .05.

Individuals with IIMs exhibited high burden of any comorbidity (OR: 1.62 vs AIRDs and 2.95 vs HCs,$p < 0.01$), BM (OR 1.66 vs AIRDs and 3.52 vs HCs,$p < 0.01$), CM (OR: 1.69 vs AIRDs and 6.23 vs HCs,$p < 0.01$), and mental health disorders (MHDs) (OR 1.33 vs AIRDs and 2.63 vs HCs,$p < 0.01$)(FIG 1A, global distribution depicted as FIG 2)

IIM patients with comorbidities (and MHDs) had worse physical function (low PGP, PGM, SF10 and higher F4a scores, all *$p < 0.001$). Worse physical function (PGP, SF10a, F4a) and mental health (PGM) was predicted by age, active disease, BM, and MHDs. Worse SF10a and F4a scores were also associated with female gender and country HDI respectively. (FIG 1B)

4 distinct clusters were identified among IIMs: Cluster 0: lower comorbidity burden and good health status Cluster 1: older patients with higher comorbidity burden and poorer health status Cluster 2: patients with higher prevalence of MHDs, lower PGP, PGM and higher F4a scores Cluster 3: older patients with average comorbidity burden and good health status.

DM, Anti-synthetase syndrome and necrotizing autoimmune myopathy were similarly represented in all clusters, while IBM and PM were more pre-dominant in clusters 1 (61.7% and 45.3%) and 3(36.4 and 34.6), while overlap myositis was more represented in clusters 2 (45.4%). (FIG 3)

Conclusion: Patients with IIMs have a higher burden of comorbidities with identifiable syndemic clusters that adversely impact physical and mental health, calling for optimized approaches for holistic patient management.

References:

1. Harrison C, Britt H, Miller G, Henderson J. Examining different measures of multimorbidity, using a large prospective cross-sectional study in Australian general practice. BMJ Open. 2014 Jul 1;4(7):e004694.

Disclosure: M. Fornaro: None; **V. Venerito**: None; **F. Iannone**: Abbvie, 2, 5, BMS, 2, 5, Janssen, 2, 5, Lilly, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5; **N. R**: None; **E. Nikiphorou**: AbbVie/Abbott, 6, Celltrion, 6, Eli Lilly, 6, fresenius, 6, Galapagos, 6, Gilead, 1, 6, Pfizer, 6, Sanofi, 6; **M. Joshi**: None; **A. Tan**: Abbvie, 1, 6, Gilead, 6, Janssen, 6, Lilly, 6, Novartis, 6, Pfizer, 6, UCB, 6; **S. Saha**: None; **S. Shinjo**: None; **V. Agarwal**: None; **N. Ziade**: Abbvie, 6, Boehringer-Ingelheim, 6, Eli Lilly, 6, Janssen, 6, Newbridge, 6, Novartis, 6, Pfizer, 6, Pierre Fabre, 6, Roche, 6, sanofi, 6; **T. Velikova**: AstraZeneca, 6, Pfizer, 6; **E. Kadam**: None; **M. Milchert**: None; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia Pharmaceuticals, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Elli Lilly and Company, 5, 6, F. Hoffmann-La Roche AG, 5, 6, Gilead Sciences, 5, 6, GSK, 5, 6, Janssen Pharmaceuticals, 5, 6, Novartis, 5, 6, Otsuka Pharmaceutical, 5, 6; **A. Gracia-Ramos**: None; **L. Cavagna**: None; **M. Kuwana**: AbbVie/Abbott, 6, Asahi-Kasei, 5, 6, Astellas, 6, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, 6, Chugai, 2, 5, 6, Corbus, 2, Eisai, 6, GlaxoSmithKlein(GSK), 2, Horizon, 2, Janssen, 6, Kissei, 2, MBL, 2, 5, Mitsubishi Tanabe, 2, 5, 6, Mochida, 2, 6, Nippon Shinyaku, 6, Ono, 5, 6; **J. Knitza**: None; **A. Makol**: Boehringer-Ingelheim, 1, Sanofi-Genzyme, 1; **D. Dzifa**: Roche, 6; **C. TORO GUTIERREZ**: AbbVie/Abbott, 6, Boehringer-Ingelheim, 6, Janssen, 6; **C. CABALLERO**: None; **O. Distler**: 4P-Pharma, 2, 5, 6, AbbVie, 2, 5, 6, Acceleron, 2, 5, 6, Alcimed, 2, 5, 6, Altavant Sciences, 2, 5, 6, Amgen, 2, 5, 6, AnaMar, 2, 5, 6, Arxx, 2, 5, 6, AstraZeneca, 2, 5, 6, Bayer, 2, 5, 6, Blade Therapeutics, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Citus AG, 12, Co-Founder, Corbus Pharmaceuticals, 2, 5, 6, CSL Behring, 2, 5, 6, Galapagos, 2, 5, 6, Galderma, 2, 5, 6, Glenmark, 2, 5, 6, Gossamer, 2, 5, 6, Horizon Therapeutics, 2, 5, 6, Janssen, 2, 5, 6, Kymera, 2, 5, 6, Lupin, 2, 5, 6, Medscape, 2, 5, 6, Miltenyi Biotec, 2, 5, 6, Mitsubishi Tanabe, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Patent issued ‘‘mir-29 for the treatment of systemic sclerosis’’ (US8247389, EP2331143), 10, Prometheus Biosciences, 2, 5, 6, Redx Pharma, 2, 5, 6, Roivant, 2, 5, 6, Topadur, 2, 5, 6; **J. Day**: CSL limited, 5; **H. Chinoy**: AstraZeneca, 1, Biogen, 2, Eli Lilly, 5, GlaxoSmithKlein(GSK), 6, Novartis, 2, Orphazyme, 2, Pfizer, 1, UCB, 6; **V. Agarwal**: None; **R. Aggarwal**: Actigraph, 2, Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella Bioscience, 2, Corbus, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Mallinckrodt, 5, Merck, 2, Octapharma, 2, Pfizer, 2, 5, Q32, 5, Roivant, 2, Sanofi, 2, Teva, 2; **L. Gupta**: None; **C. Study Group**: None.

Abstract Number: 1970

Impaired Health-Related Quality of Life in Patients with Idiopathic Inflammatory Myopathies: A Cross-Sectional Analysis from the COVAD Dataset

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The significance of Health-related quality of life (HRQoL) in patients with autoimmune diseases is well acknowledged. Unfortunately, there is dearth of data on the HRQoL in patients with idiopathic inflammatory myopathies (IIMs)and factors adversely impacting it.

Methods: HRQoL was measured in patients classifiable as IIMs and compared with non-IIM autoimmune inflammatory rheumatic diseases (AIRDs), non-rheumatic autoimmune inflammatory diseases (NRAIDs), and healthy controls, using Patient-Reported Outcome Measurement Information System (PROMIS) instrument data obtained through the 2nd COVID-19 vaccination in autoimmune disease (COVAD-2), a global patient reported e-survey that was extensively validated and pilot tested by a team of experts (160 collaborators, 100 countries).

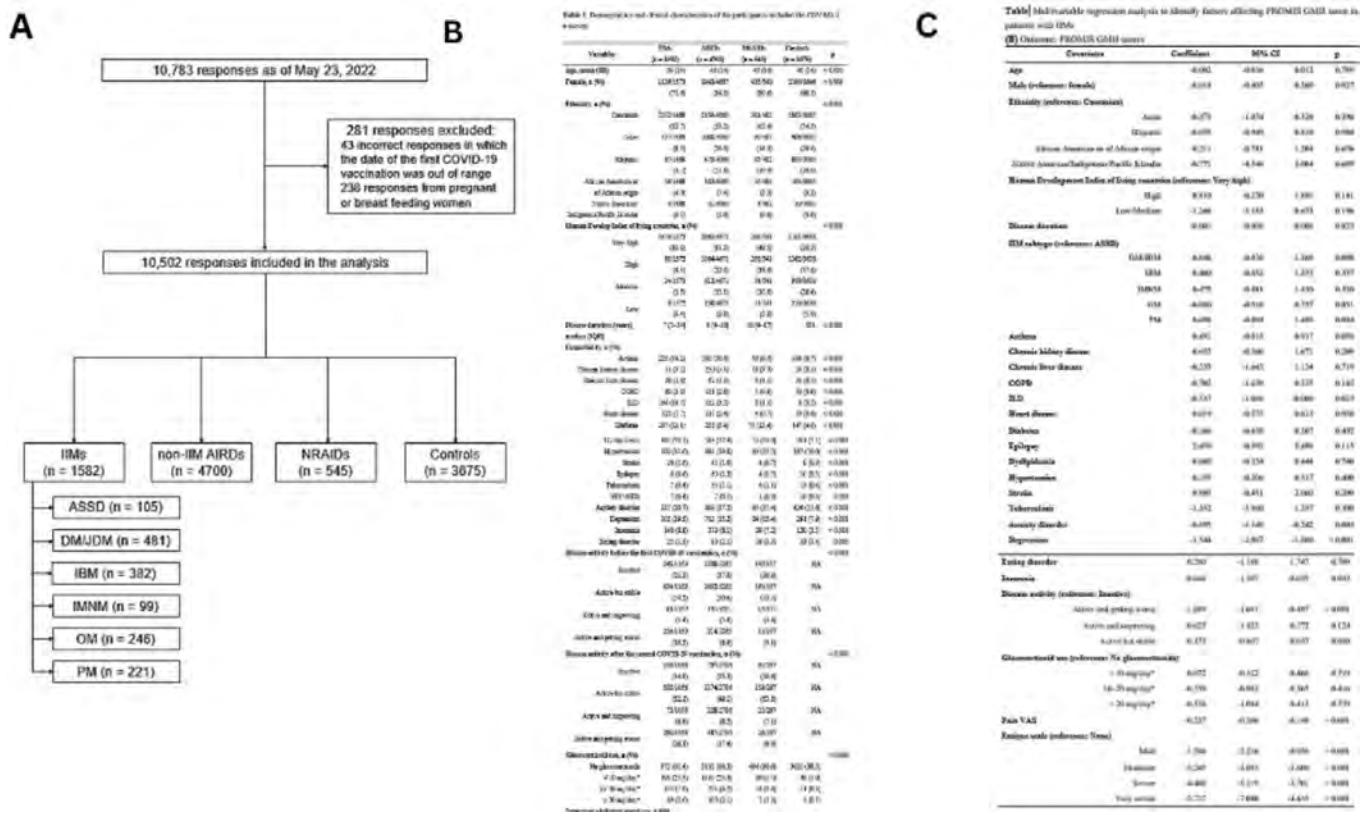

Figure 1 (A) A flow diagram of participant selection (B) Demographics and clinical characteristics of the participants included the COVAD-2 e-survey (C) Multivariable regression analysis to identify factors affecting PROMIS GMH score in patients with IIMs

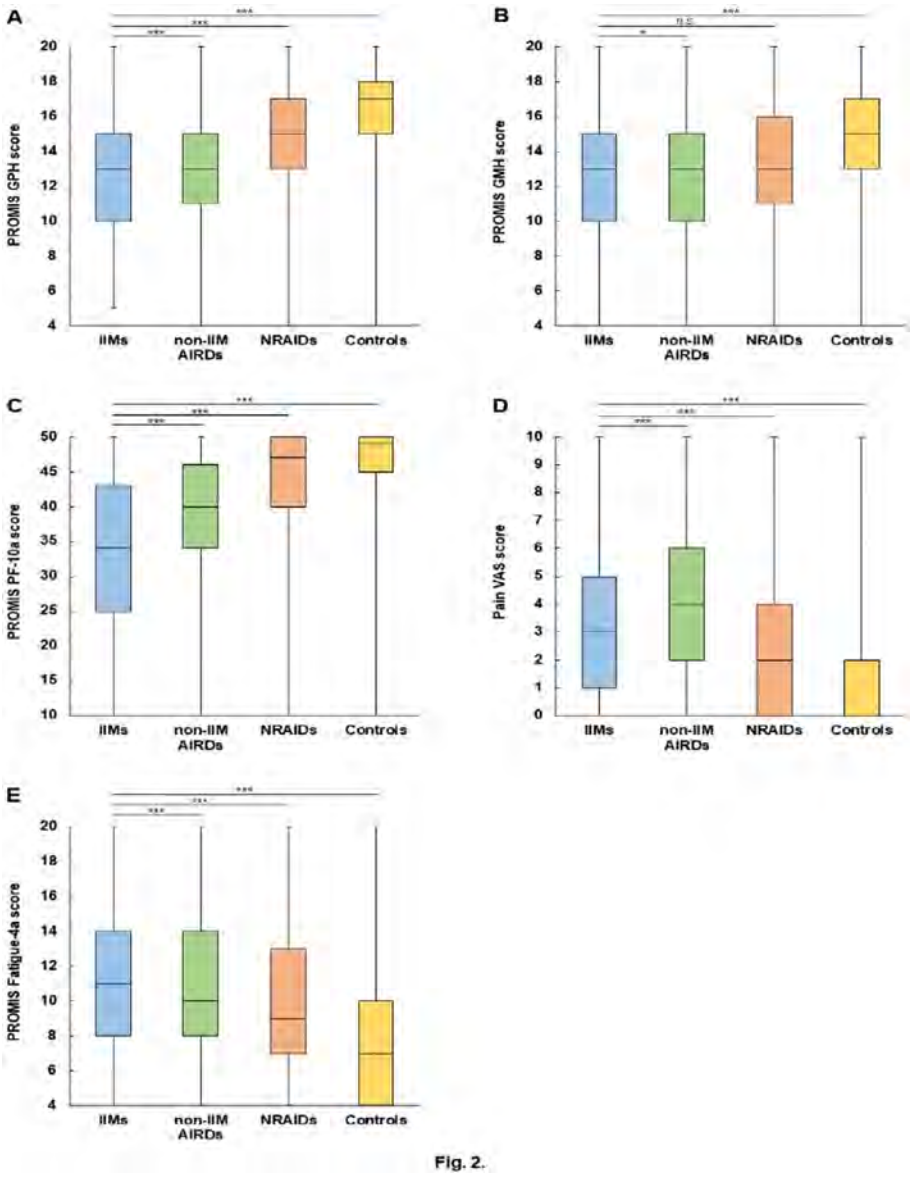

Fig. 2.

Figure 2: HRQoL in IIM patients, in comparison with non-IIM AIRDs, NRAIDs and Controls (A): PROMIS GPH scores (B): PROMIS GMH scores (C): PROMIS PH-10a score (D): Pain VAS score (E): PROMIS Fatigue-4a score

Demographics, diagnoses, comorbidities, disease activity, treatments, and PROMIS instrument data were extracted from the COVAD-2 database. (Fig. 1D) Primary outcomes were PROMIS Global Physical Health (GPH) and Mental Health (GMH). Secondary outcomes were PROMIS Physical Function 10a (PF-10a), Fatigue-4a scores, and Pain Visual Analog Scores (VAS).

Independent factors affecting GPH and GMH scores in IIMs, also in the whole population were identified using multivariable regression analysis (Fig. 2) Each PROM was stratified by IIM subgroups. (Fig. 3)

Results: Complete responses from 1582 IIMs, 4700 non-IIM AIRDs, 545 NRAIDs, and 3675 controls as of May 22 were analysed. (Fig. 1A)

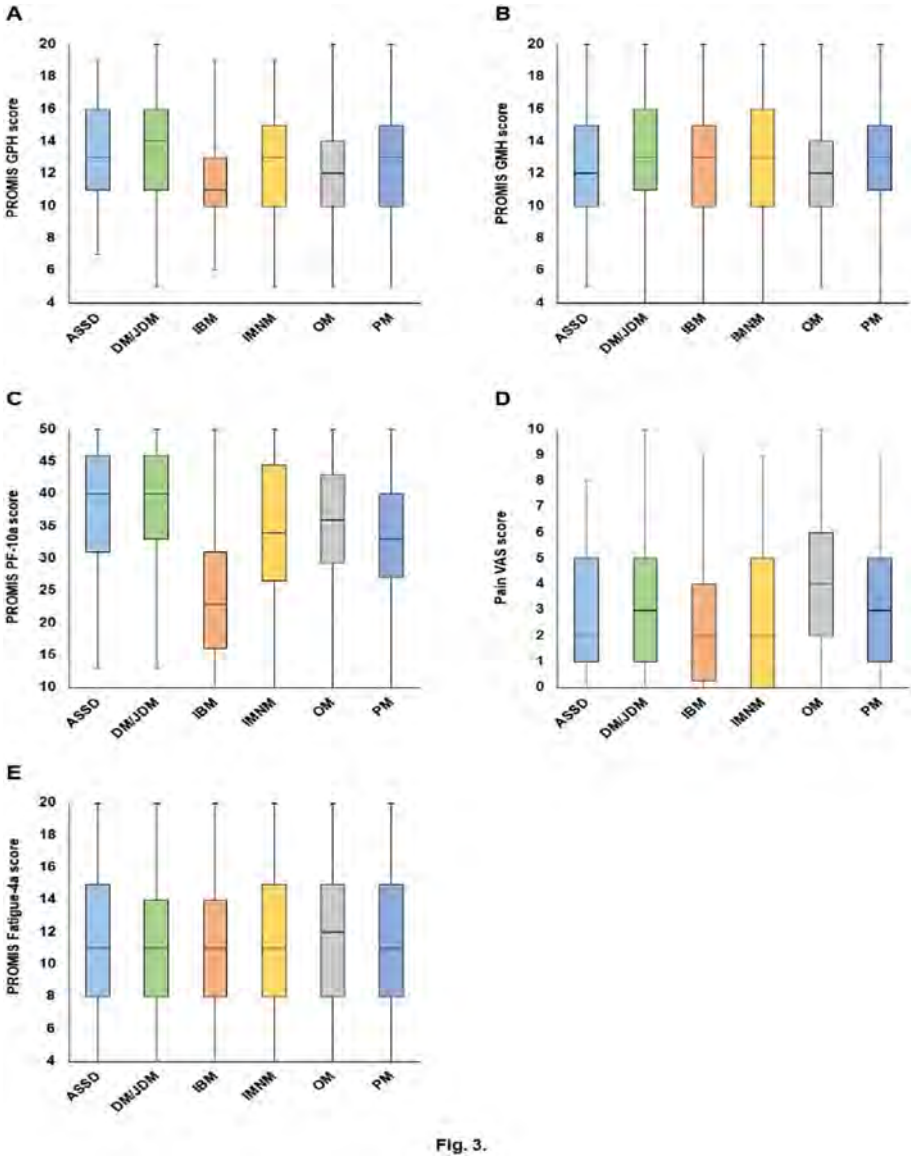

Figure 3: HRQoL in patients with IIMs subtypes (A): PROMIS GPH scores (B): PROMIS GMH scores (C): PROMIS PH-10a score (D): Pain VAS score (E): PROMIS Fatigue-4a score

Notably GPH scores were the lowest in IIMs (Fig. 2A). GMH scores in IIMs were also substantially lower than in controls (Fig. 2B) PROMIS PF-10a scores were the lowest in IIMs. (Fig. 2C) pain VAS scores were the highest in patients with non-IIM AIRDs (Fig. 2D) PROMIS Fatigue-4a scores were the highest in IIMs (Fig. 2E) indicating increased fatigue in patients with IIMs.

Among IIM subsets, PROMIS GPH and PF-10a scores were the lowest in patients with IBM. (Fig. 3A & 3C) PROMIS GMH scores were lower in patients with ASSD or OM compared to other subtypes (Fig. 3B). Pain VAS (Fig. 3D) andPROMIS Fatigue-4a scores were the highest in patients with OM (Fig. 3E).

Older age, IBM, hypertension, diabetes, active disease, glucocorticoid use, and higher fatigue scores were the factors for lower GPH scores in IIMs (Fig. 1B), whereas interstitial lung disease, mental disorders, active disease, higher pain VAS, and fatigue scores were independently associated with lower GMH scores in IIMs (Fig. 1C).

Multivariable regression analysis in the overall population identified older age, women, longer disease duration, diagnosis of autoimmune inflammatory diseases including IIMs, and comorbidities as independent factors for lower PROMIS GPH scores. (Fig. 1E) On the contrary, younger age, women, Asian ethnicity, diagnosis of autoimmune inflammatory diseases including IIMs, and comorbidities were independently associated with lower PROMIS GMH scores (Fig. 1F)

Conclusion: Both physical and mental health are significantly impaired in patients with IIMs particularly the elderly, IBM and those with specific comorbidities, calling for greater attention and optimized multidisciplinary care to enhance patient-reported experience and global well-being in this population.

Disclosure: A. Yoshida: None; **Y. Li**: None; **V. Maroufy**: None; **M. Kuwana**: AbbVie/Abbott, 6, Asahi-Kasei, 5, 6, Astellas, 6, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, 6, Chugai, 2, 5, 6, Corbus, 2, Eisai, 6, GlaxoSmithKlein(GSK), 2, Horizon, 2, Janssen, 6, Kissei, 2, MBL, 2, 5, Mitsubishi Tanabe, 2, 5, 6, Mochida, 2, 6, Nippon Shinyaku, 6, Ono, 5, 6; **N. R**: None; **A. Makol**: Boehringer-Ingelheim, 1, Sanofi-Genzyme, 1; **P. Sen**: None; **J. Lilleker**: None; **V. Agarwal**: None; **S. Kardes**: None; **J. Day**: CSL limited, 5; **M. Milchert**: None; **M. Joshi**: None; **T. Gheita**: None; **B. Salim**: None; **T. Velikova**: AstraZeneca, 6, Pfizer, 6; **A. Gracia-Ramos**: None; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia Pharmaceuticals, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Elli Lilly and Company, 5, 6, F. Hoffmann-La Roche AG, 5, 6, Gilead Sciences, 5, 6, GSK, 5, 6, Janssen Pharmaceuticals, 5, 6, Novartis, 5, 6, Otsuka Pharmaceutical, 5, 6; **E. Nikiphorou**: AbbVie/Abbott, 6, Celltrion, 6, Eli Lilly, 6, fresenius, 6, Galapagos, 6, Gilead, 1, 6, Pfizer, 6, Sanofi, 6; **A. Tan**: Abbvie, 1, 6, Gilead, 6, Janssen, 6, Lilly, 6, Novartis, 6, Pfizer, 6, UCB, 6; **A. Nune**: None; **L. Cavagna**: None; **M. Saavedra Salinas**: None; **S. Shinjo**: None; **N. Ziade**: Abbvie, 6, Boehringer-Ingelheim, 6, Eli Lilly, 6, Janssen, 6, Newbridge, 6, Novartis, 6, Pfizer, 6, Pierre Fabre, 6, Roche, 6, sanofi, 6; **J. Knitza**: None; **O. Distler**: 4P-Pharma, 2, 5, 6, AbbVie, 2, 5, 6, Acceleron, 2, 5, 6, Alcimed, 2, 5, 6, Altavant Sciences, 2, 5, 6, Amgen, 2, 5, 6, AnaMar, 2, 5, 6, Arxx, 2, 5, 6, AstraZeneca, 2, 5, 6, Bayer, 2, 5, 6, Blade Therapeutics, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Citus AG, 12, Co-Founder, Corbus Pharmaceuticals, 2, 5, 6, CSL Behring, 2, 5, 6, Galapagos, 2, 5, 6, Galderma, 2, 5, 6, Glenmark, 2, 5, 6, Gossamer, 2, 5, 6, Horizon Therapeutics, 2, 5, 6, Janssen, 2, 5, 6, Kymera, 2, 5, 6, Lupin, 2, 5, 6, Medscape, 2, 5, 6, Miltenyi Biotec, 2, 5, 6, Mitsubishi Tanabe, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143), 10, Prometheus Biosciences, 2, 5, 6, Redx Pharma, 2, 5, 6, Roivant, 2, 5, 6, Topadur, 2, 5, 6; **H. Chinoy**: AstraZeneca, 1, Biogen, 2, Eli Lilly, 5, GlaxoSmithKlein(GSK), 6, Novartis, 2, Orphazyme, 2, Pfizer, 1, UCB, 6; **V. Agarwal**: None; **R. Aggarwal**: Actigraph, 2, Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella Bioscience, 2, Corbus, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Mallinckrodt, 5, Merck, 2, Octapharma, 2, Pfizer, 2, 5, Q32, 5, Roivant, 2, Sanofi, 2, Teva, 2; **L. Gupta**: None; **C. Study Group**: None.

Abstract Number: 1971

Muscle Pathology in Patients with Primary Biliary Cholangitis

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SESSION INFORMATION

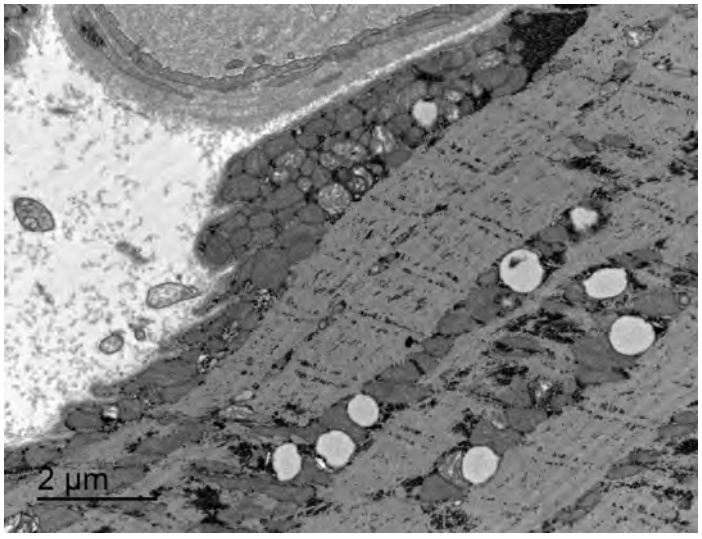
Session Date: Tuesday, November 14, 2023

Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

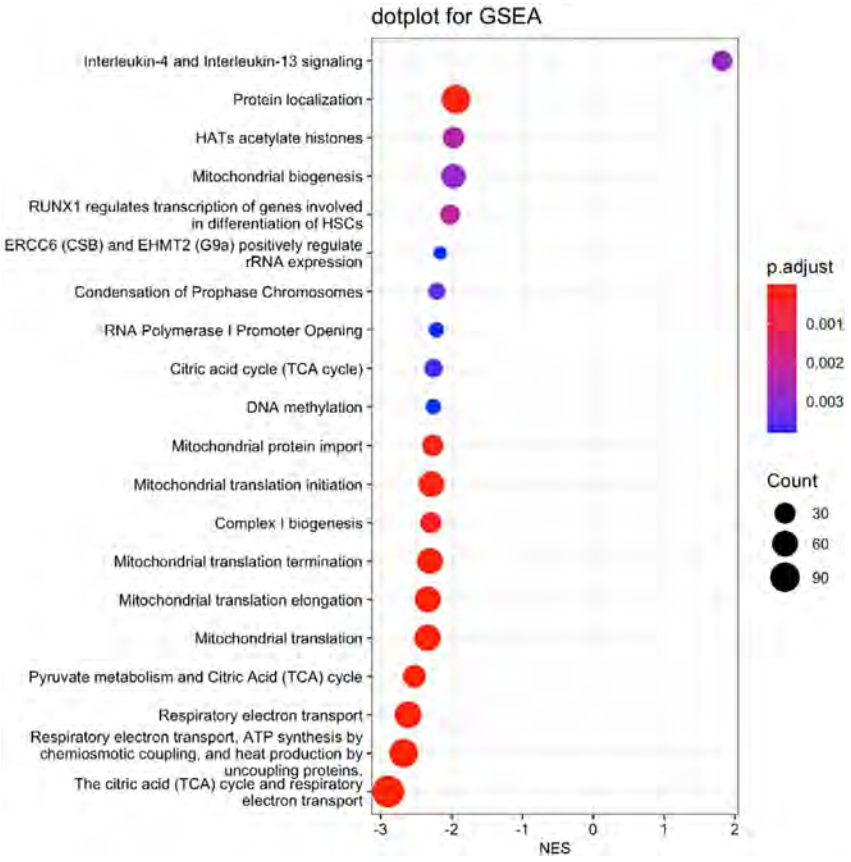
Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Primary biliary cholangitis (PBC) is a chronic autoimmune liver disease that primarily affects middle-aged women. It is characterized by elevated serum alkaline phosphatase levels, the presence of antimitochondrial antibodies (AMAs), and cholangiopathy on liver pathology. Fatigue is a common symptom experienced by up to 80% of patients at



ME. Mitochondrial accumulation at subsarcolemmal region



Dotplot for GSEA (PBC cases)

the time of diagnosis and during follow-up. Unfortunately, current treatments have not been effective in alleviating fatigue. The objective of this study is to evaluate fatigue and investigate any potential muscle involvement in PBC patients.

Methods: We conducted a single-center, cross-sectional study involving 50 patients who suffered from both PBC and fatigue. Muscle biopsies were performed to whom presented muscle weakness. Histopathological analysis was made and also RNA sequencing was performed on muscle biopsies (n=10) as well as 33 normal muscle biopsies. Muscle biopsies were stained for human immunoglobulin and PDC-E2.

Results: Abnormal accumulation of mitochondria in the subsarcolemal region was observed in both optical and electron microscopy. A significant set of immunoglobulin genes was specifically found to be overexpressed in CBP, while over 50 genes related to mitochondrial function were predominantly underexpressed. In muscle biopsies positive for AMA-M2, immunoglobulins were localized in the cytoplasm and colocalized with PDC-E2.

Conclusion: Based on these findings, we can conclude that there is muscular involvement in PBC, and we hypothesise it is likely mediated by AMA-M2 antibodies.

Disclosure: J. Milisenda: None; **I. Pinal-Fernandez**: None; **K. Pak**: None; **M. Casal-Dominguez**: None; **Y. Duque-Jaimez**: None; **G. Garrabou**: None; **S. Muñoz-Braceras**: None; **M. Guitart-Manpel**: None; **J. Torres-Ruiz**: None; **E. Tobias**: None; **M. Cano**: None; **I. Aldecoa**: None; **J. Grau**: None; **A. Mammen**: None.

Abstract Number: 1972

Evaluation of Myositis Autoantibodies as Predictors of Response to IVIG: Post-hoc Analysis of a Large Randomized, Double-Blind, Placebo-Controlled Phase III Trial

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1945–1972) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Dermatomyositis (DM) is an immune-mediated inflammatory myopathy (IIM). Two subsets ofautoantibodies have been identified in patients with IIM: Myositis-specific antibodies (MSA) and myositis-associated antibodies (MAA). Whereas MSA are highly specific for IIMs and represent unique clinical phenotypes and prognosis, MAA are also found in other autoimmune diseases. The ProDERM study recently demonstrated the efficacy and safety of IVIG in DM patients (1) but the potential effect of autoantibodies on treatment response has not yet been determined. This post-hoc analysis of the randomized, placebo-controlled ProDERM study investigated autoantibody status at baseline and its relationship to treatment response to IVIG.

Methods: DM patients received 2 g/kg IVIg treatment (n=47) or placebo (n=48) every 4 weeks for 16 weeks. From week 16 onwards eligible patients (N=91) received IVIG for a further 24 weeks. The primary endpoint was a Total Improvement Score (TIS) of at least 20 (= at least minimal improvement) at week 16 and no confirmed deterioration up to week 16. Serum

samples were taken at baseline and analysed for MSA (Jo-1, PL-7, PL-12, OJ, EJ, SRP, Mi-2, TIF-1, MDA5, NXP2, MJ, SUMO) and MAA (PM-SCL, Ku, U1RNP, U2RNP, U3RNP, Ro/SSA) by RNA and protein immunoprecipitations performed by the Oklahoma Medical Research Foundation. Patients were stratified according to their antibody (Ab) status as MSA-positive (including those also MAA+), MAA-positive only, or no Ab detected (Ab -ve) at baseline. Proportion of patients with minimal (TIS≥20), or moderate/major (≥ 40) response were evaluated for all patients (IVIG & placebo group) as well as separately at week 16 and 40.

Results: At baseline, a total of 49 (52%) patients were MSA-positive, 13 (14%) were MAA-positive, and in 33(35%) no Ab were detected. Demographics of patients in each group are shown in Table 1. Ten MSA+ patients were also MAA+. Figure 1 shows numbers of patients with each specific Ab. In the MSA+group (both IVIG & placebo arms), 71% (35/49) of patients had minimal response at week 16, compared to 55% (18/33) in the Ab -ve group (p= 0.12) and 38% (5/13) in the MAA+ group (p = 0.03). Of the 24 MSA+ patients randomized to IVIG 83% showed TIS response at week 16 compared to 60% of MSA+ patients receiving placebo (p= 0.07). In the AB -ve group significantly more patients responded in the IVIG

Table 1 Patient demographics and baseline characteristics

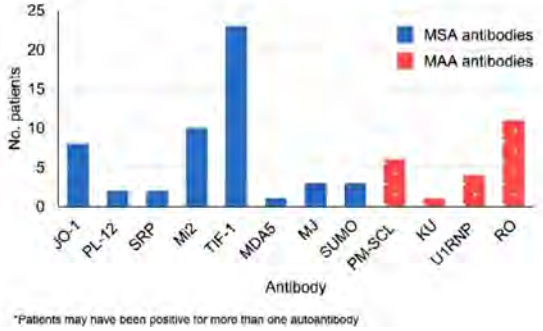
	MSA-positive* (N=49)	MAA-positive** (N=13)	No antibody detected (N=33)
Mean (range) age, years	51 (22–79)	54 (33–70)	54 (28–77)
Mean (range) time since diagnosis, years	3.66 (0.16–15.6)	5.04 (0.39–18.4)	5.8 (0.09–48.7)
Sex, n (% female)	39 (79.6)	11 (84.6)	12 (63.6)
Race, n (% White)	42 (85.7)	13 (100.0)	32 (97.0)
Mean BMI, kg/m^2	29.8	27.0	26.5
Disease severity, n (%)			
Mild	10 (20.4)	4 (30.8)	12 (36.4)
Moderate	31 (63.3)	8 (61.5)	17 (51.5)
Severe	8 (16.3)	1 (7.7)	4 (12.1)
CDASI score			
≤14	19 (38.8)	5 (38.5)	20 (60.6)
>14	30 (61.2)	8 (61.5)	13 (39.4)
Randomised treatment			
IVIg	24	4	19
Placebo	25	9	14

BMI, body mass index; CDASI, Cutaneous Disease Area and Severity Index; IVIg, intravenous immunoglobulin; MAA, myositis-associated antibodies; MSA, myositis-specific antibodies.

*10 patients positive for MSA were also positive for MAA.

**MAA-positive group contains only patients with MAA (no MSA).

Figure 1. Numbers of dermatomyositis patients with myositis-specific antibodies (MSA) and myositis-associated antibodies (MAA) in the ProDERM trial*



*Patients may have been positive for more than one autoantibody

arm than in the placebo arm (p= 0.001). For all patients no significant difference between the 3 Ab groups was seen in percentage of patients with 'moderate/major improvement' at either Week 16 or Week 40. A subanalysis of individual Ab showed no significant difference in response rates of Ab+ vs. Ab -ve patients at week 16 or 40 for anti-synthetase Ab (N=10, Jo-1, PL-12) nor for anti-Mi2 Ab (N=10). However, significantly more anti-TIF-1 + patients (N=21) had minimal response compared to anti-TIF-1 -ve patients at week 16 and 40 (p=0.02 and p=0.03 respectively).

Conclusion: MSA positive patients showed a trend of higher frequency of minimal improvement but not of moderate to major improvement when compared to MAA+ or Ab negative patients. However, the response to IVIG was similar to placebo across the 3 antibody groups, suggesting that IVIG is effective irrespective of myositis autoantibody status.

Disclosure: C. Charles-Schoeman: AbbVie, 2, 5, Alexion, 5, BMS, 2, 5, Boehringer Ingleheim, 2, 5, CSL Behring, 5, Galapagos, 2, Pfizer, 2, 5, Priovant, 2, 5, Recludix, 2; **J. Schessl**: Octapharma, 2; **R. Aggarwal**: Actigraph, 2, Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella Bioscience, 2, Corbus, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Mallinckrodt, 5, Merck, 2, Octapharma, 2, Pfizer, 2, 5, Q32, 5, Roivant, 2, Sanofi, 2, Teva, 2; **a. ProDERM investigators**: None.

Abstract Number: 1973

Work-related Impact in Young Patients with Chronic Back Pain Awaiting a Magnetic Resonance Imaging

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1973–1976) Orthopedics, Low Back Pain, & Rehabilitation Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic back pain (CBP) is one of the major causes for medical consultation among young people. Given the limited sources, it is relevant knowing the characteristics associated with a higher burden in order to prioritize the performance of imaging exams. We aimed to identify factors associated with sick leave in a cohort of young patients with CBP awaiting an MRI of the spine.

Methods: The project "Strategy for a Hospital Early Referral in Patients with Axial Spondyloarthritis" (SHERPAS) is a prospective ongoing study recruiting young patients (18 to 40 years) with CBP that are requested an MRI of the spine by other specialists different than rheumatologists in a tertiary hospital. The study period started in September 2021, and the dataset for this interim analysis was locked in October 2022. Patients completed a questionnaire concerning work status, including sick leave due to CBP (at-visit or prior to this). Besides, socio-demographic and clinical characteristics were collected. Patient-reported outcomes (PROs) for fatigue, Patient Global Assessment (PGA), physical function (Bath Ankylosing Spondylitis Functional Index -BASFI), and overall health (Assessment of Spondyloarthritis international Society Health Index -ASAS HI) were also evaluated. A logistic regression analysis was performed to evaluate the association of patients' characteristics with sick leave.

Table. Characteristics of employed patients by work status

		Total employed n=123	No sick leave n=58	Ever sick leave n=65	p-value
Demographics	Age	33.8 (4.8)	33.6 (5)	34.1 (4.8)	0.6
	Symptoms (months)	57.0 (54.0)	54.8 (54.1)	59.0 (54.3)	0.7
	BMI	25.4 (4)	25.4 (4.2)	25.4 (3.7)	0.9
	Female	65 (52.8)	33 (56.9)	32 (49.2)	0.5
	Education				
	Primary/secondary	66 (52.8)	27 (46.5)	38 (58.4)	0.2
	University	56 (45.5)	30 (51.7)	26 (40.0)	
	Type of work				
	Sendentary/ not active	33 (26.8)	19 (32.8)	14 (21.5)	0.5
	Physically active	76 (61.8)	38 (65.5)	38 (58.5)	
Characteristics of back pain	Buttock pain	42 (34.2)	17 (29.3)	25 (38.4)	0.4
	Night pain	58 (47.1)	21 (36.2)	37 (56.9)	0.02
	Inflammatory pain	29 (23.6)	14 (24.1)	15 (23.1)	1
	Flares of back pain	87 (70.7)	42 (72.4)	45 (69.2)	0.8
	Sudden onset	72 (58.5)	29 (50.0)	43 (66.1)	0.1
	Morning stiffness	76 (61.8)	32 (55.1)	44 (67.7)	0.2
PROs	Fatigue (0-10)	4.9 (3)	4 (3.1)	5.7 (2.7)	0.002
	PGA (0-10)	4.7 (2.9)	3.7 (2.9)	5.7 (2.6)	<0.001
	Physical function (BASFI)	3.2 (2.6)	2.4 (2.3)	4 (2.6)	<0.001
	Overall health (ASAS-HI)	6.7 (3.8)	5.6 (3.6)	7.8 (3.8)	0.002
Treatments	NSAIDs	109 (88.6)	52 (89.6)	57 (87.7)	0.2
	Muscular relaxants	88 (71.5)	33 (56.9)	55 (84.6)	<0.001
	Opioids	45 (36.6)	11 (18.9)	34 (52.3)	<0.001
	Antidepresants	19 (15.5)	4 (6.9)	15 (23.1)	0.01

Results: Of 152 recruited patients, 123 (80.9%) were actively employed, 22 (14.5%) were unemployed and 7 (4.6%) were students. Among the employed patients (52.8% female; mean age 33.8(4.8) years; 57.0 (54.0) months CBP duration), 65 (52.8%) patients had been on sick leave at some point (50 prior to visit and 15 at the study visit). Baseline characteristics are shown in **Table**. Night pain was more frequent in patients on sick leave (56.9 % vs 36.2%, p=0.02), and PROs on fatigue, PGA, physical function and overall health and functioning showed worse results in these patients, as compared to patients who had never been in sick leave. Additionally, patients with on sick leave had more frequently pharmacological treatment. After multivariable analysis, being male (OR 2.3, 95%CI 1.0-5.6), having night pain (OR=2.4, 95%CI 1.0-5.8) and reporting higher PGA (OR=1.1, 95%CI 1.0-1.4) were associated independently with being on sick leave.

Conclusion: One out of two young patients with CBP awaiting an MRI of the spine are on sick leave at some point. These patients have poorer quality of life and use more pharmacological treatment than active patients with CBP. Male sex and night pain are associated with being on sick leave due to CBP and therefore could be used to prioritize the use of spinal MRI aiming to optimize health resources.

Disclosure: D. Benavent: Abbvie, 5, Galapagos, 6, Janssen, 6, Novartis, 5, Roche, 6; **M. Tapia**: None; **D. Bernabeu**: None; **V. muley**: None; **C. Plasencia-Rodríguez**: Abbvie, 5, 6, Eli Lilly, 6, Novartis, 5, Pfizer, 5, 6, Roche, 6; **A. Balsa**: AbbVie/Abbott, 1, 2, 5, 6, Bristol-Myers Squibb(BMS), 1, 5, Eli Lilly, 1, 5, 6, Merck/MSD, 1, 5, Novartis, 5, Pfizer, 1, 5, 6, UCB, 1, 5, 6; **V. Navarro-Compán**: AbbVie, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, Janssen, 6, MoonLake, 2, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6.

Abstract Number: 1974

Comparison of Gait Spatiotemporal Measures Between Patients with Insertional Achilles Tendinopathy or Midportion Achilles Tendinopathy

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1973–1976) Orthopedics, Low Back Pain, & Rehabilitation Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Insertional and midportion Achilles tendinopathy (AT) are painful injuries affecting both active and sedentary populations. Patients with AT present with pain with loading, often reporting pain with walking. Compared to midportion AT, insertional AT is more frequently associated with pain in positions of dorsiflexion, experienced during walking, due to compression of the distal tendon on the calcaneus. It is unknown however, if differences exist in gait spatiotemporal measures between AT subtypes and further, if these measures relate to pain. Therefore, the purpose of this analysis is to compare spatiotemporal measures of gait between patients with midportion AT and patients with insertional AT. We also aimed to assess the relationship between pain and spatiotemporal measures within each subtype.

Methods: Patients with insertional AT and midportion AT ambulated at their self-selected pace for 10m. Gait speed and percent of time spent in swing, stance, load response, flat foot, and pre-swing on the most symptomatic limb were measured with inertial measurement units (MuscleLab). Patient Reported Outcomes Measurement Information System (PROMIS) pain interference was used to assess pain. Independent t-tests were used to assess for differences in outcome variables between AT subtypes. Pearson correlations were used to assess for relationship between PROMIS pain interference and gait measures in patients with insertional AT and patients with midportion AT.

Results: 42 patients with insertional AT (24 F; 51.8±9 years; 32.4±7 kg/m^2) and 178 patients with midportion AT (100 F; 47.1±13 years; 28.7±6 kg/m^2) were included. No significant differences were observed between AT subtypes in any gait spatiotemporal measures or PROMIS pain interference ($p > 0.05$). In patients with midportion AT, there was a significant negative relationship between PROMIS pain interference and gait speed ($r=-0.153$, $p=0.048$) but no significant relationship with all other gait measures (p's >0.05). In patients with insertional AT, there was a significant negative relationship between PROMIS pain interference and gait speed ($r=-0.387$, $p=0.012$) and a significant negative relationship between PROMIS pain interference and percent time in load response phase ($r=-0.489$, $p< 0.001$). There were no other significant relationships with remaining analysis in patients with insertional AT.

Conclusion: No differences were observed between gait parameters or pain interference between AT subtypes. In patients with midportion AT, increased pain interference was weakly correlated with slower gait speed. The same pattern was observed in patients with insertional AT, however, the relationship was moderate between increased pain interference and reduced gait speed. Further, in patients with insertional AT, increased pain interference was moderately related to percent of time in the load response phase. Therefore, gait in patients with insertional AT may be more associated with pain than in midportion AT.

Disclosure: H. Smitheman: None; **K. Seymore**: None; **A. Smith**: None; **M. Potter**: None; **N. Alghamdi**: None; **K. Silbernagel**: None.

Abstract Number: 1975

Do You Believe in Exercise for Osteoarthritis? Exploring Differences in Participant Characteristics with Treatment Beliefs in Exercise for Knee Osteoarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1973–1976) Orthopedics, Low Back Pain, & Rehabilitation Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Knee osteoarthritis (OA) is a leading cause of disability and functional limitation in older adults. Treatments for knee OA focus on symptom management, with physical activity, e.g., exercise, receiving high recommendations. However, misconceptions about exercise are common, affecting an individual's beliefs about the benefits of exercise. Currently, little is known about the characteristics of those who have high positive and high negative beliefs about exercise. This study aims to explore how demographic factors, baseline physical activity (steps/day), and knee related outcomes differ between those with positive and negative treatment beliefs related to exercise in adults with knee OA.

Methods: We conducted a secondary analysis of baseline data from a clinical trial examining a telehealth physical therapy intervention for adults with knee OA. Included were adults within the United States who met the National Institute of Health and Clinical Excellence criteria for knee OA (> 45 years, activity related knee pain, and < 30 min of morning stiffness) and did not regularly exercise. Positive and Negative treatment beliefs were measured using the Treatment Beliefs in Knee and Hip OA (TOA) Physical Exercise (PE) questionnaire which include positive and negative subscales. High positive beliefs were defined as scores greater than 14 on the positive subscale while high negative scores were defined as scores greater than 8 on the negative subscale. These represent more than neutral agreement to positive/negative beliefs. We reported subject characteristics stratified by High Positive and High Negative Beliefs, which included age, sex, BMI, race, Visual Analog Scale (VAS) pain, steps/day, Knee Osteoarthritis Outcome Survey Activities of Daily living subscale score (KOOS ADL), and Western Ontario and McMaster Universities Osteoarthritis Index Function subscale score (WOMAC Function).

Results: 126 participants (mean age = 59.9 years old, 82% female, mean BMI = 36.2 kg/m^2) were included in the analysis (Table 1). Of those included, 73% (92/126) of the sample had high positive treatment beliefs and 26% (33/126) had high negative treatment beliefs. The high positive belief sample had a smaller proportion of females (77.1% vs 94.1%) than the low positive belief sample. Participants with high negative beliefs tended to be younger (56.4 years vs 61.2 years), had a higher

Table 1: Baseline Characteristics of Overall Sample

	Total Sample (n = 126)
Age (mean ± SD, in years)	59.9 ± 8.8
Sex (n, % female)	103, 81.8%
BMI (mean ± SD, kg/m^2)	36.2 ± 9.1
Race (n, % not white)	21, 16.7%
Steps/day (mean ± SD)	3686.3 ± 1856.5
VAS pain	66.0 ± 17.8
KOOS ADL (mean ± SD)	63.3 ± 16.5
WOMAC Function (mean ± SD)	25.0 ± 11.2

Table 2: Baseline Characteristics by Positive and Negative TOA PE Subscale Scores

	High Positive (n=92)	Low Positive (n = 34)	High Negative (n = 33)	Low Negative (n = 93)
Age (mean ± SD, in years)	60.9 ± 9.0	57.4 ± 7.8	56.4 ± 8.0	61.2 ± 8.8
Sex (n, % female)	71, 77.1%	32, 94.1%	27, 81.8%	76, 81.7%
BMI (mean ± SD, kg/m^2)	35.7 ± 9.1	37.8 ± 9.0	39.1 ± 9.8	35.2 ± 8.6
Race (n, % not white)	14, 15.2%	7, 20.6%	3, 9.1%	18, 19.4%
Steps/day (mean ± SD)	3765.0 ± 1938.4	3506.7 ± 1669.5	4028.4 ± 1858.5	3567.9 ± 1852.9
VAS pain	64.4 ± 17.9	70.1 ± 17.1	72.6 ± 16.1	63.6 ±17.9
KOOS ADL (mean ± SD)	64.6 ± 15.3	59.8 ±19.0	58.4 ± 19.0	65.0 ± 15.2
WOMAC Function (mean ± SD)	24.1 ± 10.4	27.4 ± 12.9	28.3 ± 12.9	23.8 ± 10.3

BMI (39.1 kg/m^2 vs 35.2 kg/m^2), had higher pain (72.6 vs 63.6), had higher daily step count (4028.4 steps/day vs 3567.9 steps/day), and worse WOMAC physical function scores (28.3 vs 23.8) than those with low negative beliefs. (Table 2).

Conclusion: While the demographic makeup of individuals with high versus low positive treatment beliefs were relatively similar outside of sex, there may be some differences for high versus low negative treatment beliefs. A limitation to this study is that these differences were not formally tested due to relatively small sample size. This exploratory examination of group characteristics suggests that differences in treatment beliefs may be related to some patient characteristics, pain, and functional outcomes, however further research is needed to formally study these potential differences.

Disclosure: S. Liles: None; **J. Jakiela**: None; **T. Bye**: None; **J. Copson**: None; **D. White**: Viatris, 6.

Abstract Number: 1976

Distribution and Validity of Proposed Disability Categories from the Short-Valued Life Activities Questionnaire

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1973–1976) Orthopedics, Low Back Pain, & Rehabilitation Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rehabilitation (i.e., physical therapy and occupational therapy) is indicated to improve function and participation in life activities. Rehabilitation utilization is low among adults with rheumatoid arthritis (RA) despite high rates of functional limitation. A screening tool implemented at routine rheumatology visits may facilitate appropriate referral and utilization. The Short-Valued Life Activities (SVLA) questionnaire is a validated patient-reported outcome measure that uniquely assesses accommodation use with each activity (e.g., extra time, tools, assistance). This is important because individuals who report no difficulty with a task, but use an accommodation, are at increased risk for future disability, which may be amenable to rehabilitation. We propose categorizing disability status using responses on the SVLA, as these categories could guide meaningful referral. As a first step, the purpose of this study was to determine the distribution and construct validity of the proposed disability categories among adults with RA.

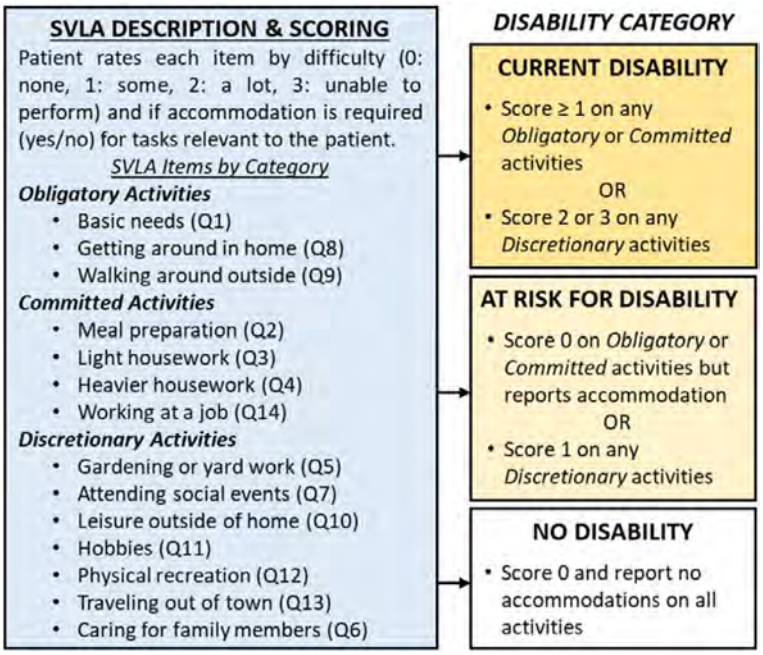

Figure 1. Proposed Disability Cat based on the SVLA

Table 1. Distribution of disability, functional limitation, and disease activity and associated correlations

	Proportion of the sample % (n)	Correlation with disability categories from the SVLA
Disability (Proposed categories from SVLA)		
No Disability	9% (27)	*n/a*
At-risk for Disability	10% (30)	
Current Disability	81% (236)	
Functional limitation (categories from PROMIS)		
No limitation (t-score > 50)	17% (51)	Rho = 0.57
Minimal limitation (50 ≥ t-score > 40)	37% (110)	p < 0.001
Moderate limitation (40 ≥ t-score > 30)	33% (97)	
Severe limitation (t-score ≤ 30)	12% (36)	
Disease activity (categories from RAPID3)		
Remission (score ≤ 3)	20% (58)	Rho = 0.56
Low severity (3 < score ≤ 6)	18% (52)	p < 0.001
Moderate severity (6 < score ≤ 12)	26% (75)	
High severity (score > 12)	36% (105)	

Methods: We conducted a cross-sectional survey study. We recruited adults with RA with at least two visits to UNC Health rheumatology clinics for RA, with at least one visit in 2020 or 2021. The survey was available electronically or verbally and included items regarding demographics, clinical information, and patient-reported outcomes. Our primary outcome was disability category (no disability, at-risk for disability, current disability) determined using responses regarding difficulty and accommodation use during 14 valued life activities in the SVLA (Figure 1). Functional limitations were assessed with the PROMIS PF10a, and categorized as no limitations, minimal limitations, moderate limitations, and severe limitations based on established t-score cutoffs. Disease activity severity was assessed with the RAPID3 and categorized as remission, low severity, moderate disease severity, and high severity based on established cutoffs. We used descriptive statistics to describe the distribution of disability categories. To assess construct validity, we calculated the correlation of the SVLA disability categories with the categories of physical function (PROMIS categories) and disease activity (RAPID3 categories) using Spearman rank test. Correlations were interpreted as moderate if $0.40 \leq \text{rho} < 0.60$ and strong if $\text{rho} \geq 0.60$.

Results: Of 1506 potential participants, 294 adults with RA completed the survey (age 56 ± 14 years, disease duration 10 ± 11 years, 82% women). The distribution of the sample in each disability category, functional limitation category, and disease activity category are detailed in Table 1. The disability categories were moderately correlated with functional limitation and disease activity categories (rho = 0.56-0.57; Table 1).

Conclusion: The proposed disability categories had good construct validity with established measures of functional limitation and disease activity in adults with RA. However, over 90% of the sample were categorized as at-risk or current disability with the proposed methods. Further research is needed to develop feasible methods to identify patients for whom rehabilitation referral should be prioritized.

Disclosure: L. Thoma: None; **K. Allen**: None; **B. Jonas**: None; **P. Katz**: None.

Abstract Number: 1977

Combined Datasets for CNTX-4975 Osteoarthritis Knee Pain (OAKP) Phase 3 Trials (OAKP 301 and 304) to Assess Overall Efficacy and Safety of an Intra-articular Injection (IAI) of CNTX-4975-05 (CNTX) in Subjects with Chronic, Moderate-to-severe Osteoarthritis Knee Pain (MSOAKP)

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Session Date: Tuesday, November 14, 2023
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Background/Purpose: 30+ million US adults have OAKP, (13% women / 10% men). After years of using NSAIDs, analgesics, surgery and IAI, many patients remain with OAKP. CNTX is a 1 mg dose of capsaicin for IAI to reduce OAKP.

Methods: The phase 3 trials powering was based on the phase 2 trial showing a standard effect size (SES) of 0.55. Although each phase 3 trial (OAKP 301 and 304) was powered at >95% on the primary outcome measure, to allow for sufficient power for the key secondary outcome measures. The phase 3 trials were likely underpowered. The two nearly identical phase 3 trials did not meet the primary endpoint but nevertheless showed numerical superiority of CNTX over placebo. Given that the trials were nearly identical (except for a second injection in the OA-304), the results were combined for an integrated analysis. The analysis assessed the primary time point at Week 12 with the numeric pain rating scale (Primary OA-301) between (NPRS [0 – 10; 0 = no pain, 10 worst pain possible]) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) A (Primary OA-304) (pain subscale; [0-50] -lower values have greater pain), WOMAC B (Knee stiffness [0-20]), WOMAC C (Function; [0-170]) and Patient Global Assessment of Change (PGIC;[0-7]).

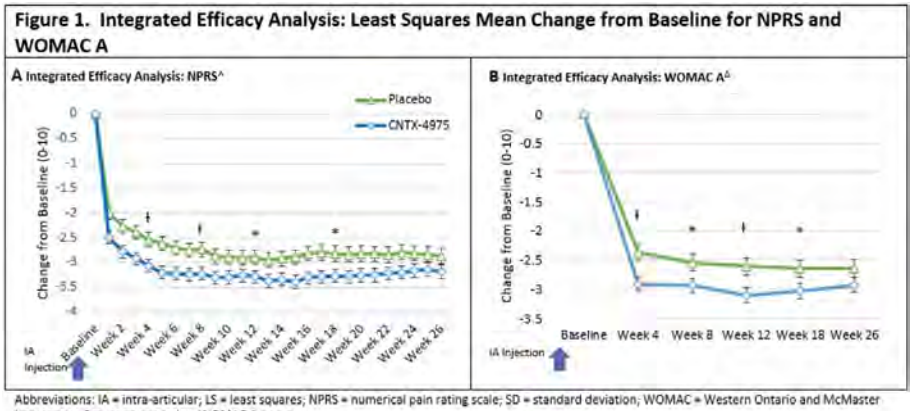
Results: Between the two trials, 650 subjects received 1 dose of study drug (276 placebo, 373 CNTX). The analysis of the primary and key secondary endpoints was conducted. With the combined data sets, CNTX-separated from placebo at all time points for 6 months after a single injection. (Figure 1). The Week 12 primary endpoint reached statistical significance across all endpoints (NPRS P=0.030, WOMAC A P = 0.005, WOMAC B P=0.004, WOMAC C P=0.006 and PGIC P=0.004), as shown in Table 1 and Figure 1.Significant differences between placebo and CNTX were also evident at multiple other timepoints through Week 26.

Table 1. Integrated Analysis of CNTX-301 and CNTX-304 First 6 Months After Single IAI (Difference Between Placebo and CNTX Displayed)*

Outcome Measures: Integrated Analysis										
	Primary Outcome Measures				Secondary Outcome Measures					
	NPRS		WOMAC A**		WOMAC B**		WOMAC C**		PGIC	
Week	Difference in LS Means	p-value	Difference in LS Means	p-value	Difference in LS Means	p-value	Difference in LS Means	p-value	Odds Ratio**	p-value
Week 4	-0.54	0.002	-0.53	0.002	-0.30	0.017	-0.52	0.003	1.81	<0.0001
Week 8	-0.49	0.007	-0.40	0.025	-0.17	0.165	-0.38	0.032	1.38	0.081
Week 12	**-0.39**	**0.030**	**-0.49**	**0.005**	**-0.37**	**0.004**	**-0.48**	**0.006**	**1.59**	**0.004**
Week 18	-0.45	0.014	-0.38	0.032	-0.35	0.007	-0.48	0.007	1.96	<0.0001
Week 26	-0.32	0.101	-0.28	0.126	-0.22	0.095	-0.29	0.108	1.70	0.001

* Post hoc integrated analysis of the pivotal Ph3 trials yielded clinically and statistically significant primary endpoint outcomes
** Scale normalized to 0-10 scale

Figure 1. Integrated Efficacy Analysis: Least Squares Mean Change from Baseline for NPRS and WOMAC A



Abbreviations: IA = intra-articular; LS = least squares; NPRS = numerical pain rating scale; SD = standard deviation; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; WOMAC A (pain)
Error bars represent standard error
Baseline NPRS Scores (mean [SD]): Placebo = 7.01 (1.09); CNTX-4975 = 7.04 (1.04)
Baseline Normalized WOMAC A scores (mean [SD]): Placebo = 6.21 (1.54); CNTX-4975 = 6.35 (1.48)
^ Due to visual spacing limits, only p values for weeks 4, 8, 12, 18, and 26 are represented
Δ Scale normalized to a 0-10 scale
* p value <0.05
† p value <0.01

Overall safety was acceptable with CNTX. Knee radiographs from Baseline to Week 52 showed no difference in KOA progression between placebo and CNTX in both trials, with no rapidly progressive osteoarthritis.

Conclusion: The separate Phase 3 trials did not meet their primary endpoints, suggesting that each trial by itself was underpowered. Combining the two trials demonstrated statistical separation and clinically meaningful benefit, and safety was acceptable. The safety database satisfies the International Conference on Harmonization (ICH) guideline for safety assessments.

Disclosure: J. Connolly: Centrexion Therapeutics Corporation, 3; **J. Campbell**: None; **R. Stevens**: Centrexion Therapeutics Corporation, 3; **C. Newman**: Centrexion Therapeutics Corp, 3.

Abstract Number: 1978

Infrapatellar Fat Pad Size and Subcutaneous Fat in Knee Osteoarthritis Radiographic Progression: Data from the Osteoarthritis Initiative

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SESSION INFORMATION
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Session Type: Poster Session C
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Background/Purpose: Adipose tissue is associated with knee osteoarthritis (KOA) progression. This study aimed to determine the association of infrapatellar fat pad (IPFP) size and subcutaneous adipose tissue around the distal thigh (SCAT*thigh*) on KOA progression.

Methods: This case-control study used data from the Osteoarthritis Initiative (OAI) that included 315 cases (defined as right knees with an increase of ≥1 Kellgren-Lawrence score (KL) from baseline to 48 months) and controls that were matched by age, sex, race, and baseline KL. Cross sectional area (CSA) of IPFP and SCAT*thigh* were measured using MRI images at baseline and 24 months. Multivariable conditional logistic regression models were used to estimate associations between IPFP and SCAT*thigh* with KOA progression. Mediation analysis was used to assess whether IPFP CSA or SCAT*thigh* mediates the relationships between KOA progression and obesity measures (body mass index [BMI] or abdominal circumference).

Results: IPFP CSA and SCAT*thigh* measurements were significantly increased in cases compared to controls at 24 months, but not at baseline, and were not associated with a significant increase in obesity measures. Adjusted ORs (95% CI) for KOA radiographic progression 9.299 (5.357 – 16.141) for ΔIPFP CSA, 1.646 (1.288-2.103) for ΔSCAT*thigh*, 1.286 (1.073-1.542) for baseline BMI, and 1.297 (1.091-1.541) for baseline abdominal circumference.ΔIPFP CSA significantly mediated the association between ΔSCAT*thigh* and KOA progression (39.5%), but not between obesity markers and KOA progression.

Conclusion: KOA radiographic progression was associated with IPFP size and SCAT*thigh* changes at 24 months, unrelated to an increase of BMI or abdominal circumference, suggesting that other factors trigger the worsening of local adipose tissue.

Baseline values	Case (n=315, mean±SD)	Control (n=315, mean±SD)	*P*
BMI (kg/m^2)	29.09±4.69	28.1±4.83	0.014
IPFP CSA (cm^2)	6.51±1.17	6.54±1.17	0.787
SCAT*thigh* (cm^2)	5.68±2.09	5.50±1.86	0.251
Abdominal circumference (cm)	103.90±12.82	100.95±12.62	0.004
Hoffa synovitis	0.78±0.72	0.44±0.54	<0.001
Effusion synovitis	0.71±0.67	0.41±0.51	<0.001

BMI: body mass index, IPFP CSA: cross sectional area of infrapatellar fat pad, SCAT*thigh*: subcutaneous fat assessment around distal thigh. Hoffa synovitis and effusion synovitis were scored based on MOAKS

Baseline values of obesity and imaging markers

Values at 24 months	Case (n=284, mean±SD)	Control (n=284, mean±SD)	*P*
BMI (kg/m^2)	29.33±5.07	28.20±4.90	0.006
IPFP CSA (cm^2)	6.96±1.20	6.23±1.11	<0.001
SCAT*thigh* (cm^2)	6.54±2.05	5.87±1.88	<0.001
Abdominal circumference (cm)	105.16±13.43	102.11±12.26	0.004
Hoffa synovitis	1.25±0.71	0.32±0.47	<0.001
Effusion synovitis	1.39±0.74	0.37±0.49	<0.001
Change over 24 months	**Case (n=284, mean±SD)**	**Control (n=284, mean±SD)**	***P***
Δ BMI (kg/m^2)	0.22±1.76	0.14±1.95	0.633
Δ IPFP CSA (cm^2)	0.47±0.54	-0.27±0.43	<0.001
Δ SCAT*thigh* (cm^2)	0.84±1.36	0.38±1.19	<0.001
Δ Abdominal circumference (cm)	1.40±9.32	1.33±9.67	0.934
Δ Hoffa synovitis	0.45±0.84	-0.13±0.5	<0.001
Δ Effusion synovitis	0.67±0.77	-0.06±0.52	<0.001

BMI: body mass index, IPFP CSA: cross sectional area of infrapatellar fat pad, SCAT*thigh*: subcutaneous fat assessment around distal thigh, Hoffa synovitis and effusion synovitis were scored based on MOAKS

Changes over 24 months in obeisty and imaging markers

Disclosure: K. Lee: None; **M. Banuls-Mirete**: None; **A. Lombardi**: None; **A. Posis**: None; **E. Chang**: None; **N. Lane**: None; **M. Guma**: None.

Abstract Number: 1979

Weight Loss Induced by Anti-obesity Medications and All-cause Mortality Among Patients with Knee or Hip Osteoarthritis

Jie Wei[1], david Hunter[2], Nancy Lane[3], Jing Wu[4], Chao Zeng[5], Guanghua Lei[5] and Yuqing Zhang[6], [1]Health Management Center, Xiangya Hospital Central South University, Changsha, China, [2]Sydney Musculoskeletal Health, University of Sydney, St. Leonards, Australia, [3]University of California, Hillsborough, CA, [4]Key Laboratory of Aging-related Bone and Joint Diseases Prevention and Treatment, Ministry of Education, Xiangya Hospital, Central South University, Changsha, China, [5]Department of Orthopaedics, Xiangya Hospital, Central South University, Changsha, China, [6]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, MA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1977–1995) Osteoarthritis – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The current international guidelines recommend weight loss for pain relief and functional improvement in overweight or obese patients with knee or hip osteoarthritis; however, there is a paucity of data on the relation of weight loss to all-cause mortality among patients with osteoarthritis. We aimed to examine the relation of the rate of weight loss induced by anti-obesity medications over 1-year to all-cause mortality among overweight/obese patients with knee or hip osteoarthritis.

Methods: Using IQVIA Medical Research Database in the United Kingdom, we identified overweight/obese people aged 40 years or older with knee or hip osteoarthritis. We emulated analyses of a hypothetical target trial using a "cloning, censoring, and weighting" approach to assess the effect of slow-to-moderate (2-10%) or fast (≥10%) weight loss induced by the initiation of anti-obesity medications (i.e., orlistat, sibutramine, and rimonabant) within 1-year on all-cause mortality and several secondary outcomes (i.e., incident hypertension, type 2 diabetes, venous thromboembolism, cardiovascular disease, and any cancer) over 5-year follow-up, respectively (Figure 1).

Results: Among 6,524 participants initiating anti-obesity medications, the 5-year all-cause mortality was 5.3%, 4.0%, and 5.4% for "weight gain/stable", "slow-to-moderate weight loss" and "fast weight loss" arms, respectively. Compared with the "weight gain/stable" arm, hazard ratios (HRs) of all-cause mortality were 0.72 (95% confidence interval [CI]: 0.56-0.92) for the "slow-to-moderate weight loss" arm and 0.99 (95%CI: 0.67-1.44) for the "fast weight loss" arm, respectively. In addition, we found dose-response protective effects of weight loss on incident hypertension, type 2 diabetes, and venous thromboembolism. However, a slightly higher risk of cardiovascular disease, albeit non-statistically significant, was observed in the "fast rate of weight loss" arm compared with the "weight gain/stable" arm (HR=1.20, 95%CI: 0.81-1.78). No apparent difference in the risk of cancer was observed between the "fast rate of weight loss" arm and the "weight gain/stable" arm (HR=1.04, 95%CI: 0.74-1.45) (Table 1).

Conclusion: In this population-based study, a slow-to-moderate, but not fast, rate of weight loss induced by anti-obesity medications within 1-year is associated with a lower risk of all-cause mortality in overweight/obese people with knee or hip osteoarthritis. Our findings that gradual weight loss by anti-obesity medications lower all-cause mortality, if confirmed by future studies, could guide policy-making, and improve the well-being of overweight/obese patients with knee or hip OA.

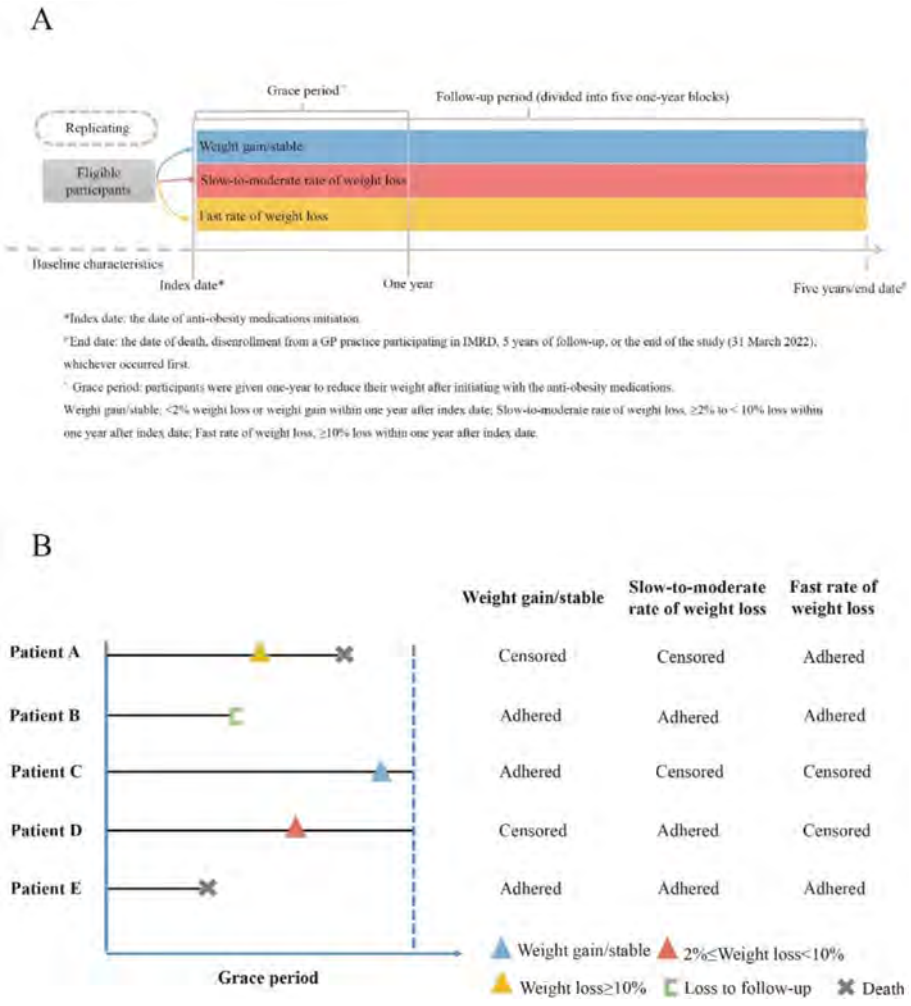

Figure 1. Study design of a hypothetical randomized controlled trial (“target trial”) on which we modeled our observational data analysis (A); Cloning and censoring in five hypothetical patients (B). Patient A lost ≥ 10% weight within one year after anti-obesity medications initiation. At time zero, 3 copies of the patient are made and they are randomly allocated to three groups. Patient A lost ≥ 10% weight within one year after anti-obesity medications initiation. The copy assigned to the “fast rate of weight loss” group is adhered with his/her assignment and will not be censored. However, the other two copies assigned to the “weight gain/stable” group and “slow-to-moderate rate of weight loss” group are violated with their assignment, and thus be censored at the time.

Table 1. Relations of weight reduction induced by anti-obesity medications within 1-year to all-cause mortality, incident hypertension, T2DM, VTE, CVD and cancer in overweight or obese knee or hip OA patients

	Weight gain/stable#	Slow-to-moderate rate of weight loss#	Fast rate of weight loss#
All-cause mortality			
Number	6,524	6,524	6,524
Weighted death (n)	286	237	271
Weighted risk over five years (%)	5.3	4.0	5.4
Weighted risk difference (%, 95% CI)	0.0 (reference)	-1.3 (-2.1 to -0.5)	0.1 (-2.0 to 1.3)
Weighted HR (95% CI)	1.00 (reference)	0.72 (0.56 to 0.92)	0.99 (0.67 to 1.44)
Hypertension			
Number	2,992	2,992	2,992
Weighted hypertension (n)	673	529	412
Weighted risk over five years (%)	24.6	19.7	19.4
Weighted risk difference (%, 95% CI)	0.0 (reference)	-5.0 (-7.1 to -2.2)	-5.2 (-8.2 to -0.3)
Weighted HR (95% CI)	1.00 (reference)	0.76 (0.66 to 0.87)	0.74 (0.60 to 0.91)
T2DM			
Number	5,109	5,109	5,109
Weighted T2DM (n)	678	560	301
Weighted risk over five years (%)	15.5	12.9	7.8
Weighted risk difference (%, 95% CI)	0.0 (reference)	-2.6 (-4.1 to -1.1)	-7.7 (-9.2 to -5.7)
Weighted HR (95% CI)	1.00 (reference)	0.78 (0.67 to 0.90)	0.48 (0.38 to 0.62)
VTE*			
Number	6,426	6,426	6,426
Weighted VTE (n)	159	110	70
Weighted risk over five years (%)	2.9	1.9	1.5
Weighted risk difference (%, 95% CI)	0.0 (reference)	-1.0 (-1.4 to -0.2)	-1.4 (-2.2 to -0.9)
Weighted HR (95% CI)	1.00 (reference)	0.68 (0.50 to 0.92)	0.46 (0.27 to 0.79)
CVD**			
Number	6,116	6,116	6,116
Weighted CVD (n)	207	189	216
Weighted risk over five years (%)	4.1	3.4	5.2
Weighted risk difference (%, 95% CI)	0.0 (reference)	-0.6 (-1.3 to 0.2)	1.2 (-0.3 to 2.4)
Weighted HR (95% CI)	1.00 (reference)	0.88 (0.68 to 1.15)	1.20 (0.81 to 1.78)
Cancer***			
Number	6,524	6,524	6,524
Weighted cancer (n)	332	300	319
Weighted risk over five years (%)	5.9	5.4	6.7
Weighted risk difference (%, 95% CI)	0.0 (reference)	-0.5 (-1.6 to 0.0)	0.8 (-1.3 to 1.4)
Weighted HR (95% CI)	1.00 (reference)	0.84 (0.68 to 1.05)	1.04 (0.74 to 1.45)

OA, osteoarthritis; HR, hazard ratio; n, number; 95% CI, 95% confidence interval; T2DM, type 2 diabetes; VTE, venous thromboembolism; CVD, cardiovascular disease.
*The VTE was defined as the combined endpoint of pulmonary embolism and deep vein thrombosis.
**The CVD was defined as the combined endpoint of myocardial infarction and stroke.
***The cancer was defined as the combined endpoint of lung, breast, colorectal, prostate, head and neck, and other cancers.
#Weight gain/stable: weight loss < 2% or weight gain; Slow-to-moderate rate of weight loss: 2% ≤ weight loss < 10%; Fast rate of weight loss: weight loss ≥ 10%.

Disclosure: J. Wei: None; **d. Hunter**: None; **N. Lane**: None; **J. Wu**: None; **C. Zeng**: None; **G. Lei**: None; **Y. Zhang**: None.

Abstract Number: 1980

Movement Evoked Pain as an Outcome Measure in Patients with Knee Osteoarthritis

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SESSION INFORMATION
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Background/Purpose: Pain, being one of the most crucial symptoms associated with knee OA, serves as a significant outcome measure for the increasing number of studies focusing on pain management strategies. Many people with OA have no or minimal pain at rest. Therefore, identifying procedures to evoke the pain associated with OA would be of value in evaluating both neurosensory pathways important for pain perception as well as possible acute interventions focused on relieving

pain. We believe there is potential clinical value in differentiating and measuring pain during physical activity as a separate construct from pain at rest. In this study, we aimed to evaluate a novel method for inducing knee pain using a stair-stepper machine.

Methods: This study was part of a randomized, double-blind, cross-over trial to evaluate the efficacy of a topical treatment for patients with knee OA (NCT01654302). In this trial, 40 patients were assessed in 2 visits at least one week apart. In each visit, two exercise sessions were conducted, one before treatment and one after treatment. In this abstract, we focus on the findings of the first exercise session. After providing consent, patients reported their baseline pain level using a Numerical Rating Scale (NRS) from 0 to 10, with 0 meaning no pain and 10 meaning worst imaginable pain. Patients were instructed to use a commercially available stair-stepper machine (STAMINA, Springfield, MO) for a maximum of 2 minutes or until they reached maximum bearable pain. After completion of the exercise, participants assessed their knee pain intensity at 1, 5, and 60 minutes after stopping. The primary outcome measure was a change in pain intensity after exercise. To evaluate if exercise caused a significant increase in pain, we conducted a repeated measures ANOVA model to compare the NRS levels before exercise with those at 1 minute, 5 minutes, and 60 minutes after stopping exercise for two visits. Subsequently, we performed pairwise comparisons using Tukey's Honestly Significant Difference (HSD) test to further examine specific differences between the time points.

Results: Participants included 24 females and 16 males with an average age of 58 ± 7.7 years; The average pain level is presented in Table 1 and Figure 1. The analysis revealed a significant effect ($F(3,df) = 31.52$, $p < 0.001$) for visit 1 and ($F(3,df) = 3.95$, $p < 0.01$) for visit 2, indicating differences among time points for both visits. Further analysis of multiple comparisons for visit 1 showed a statistically significant increase in NRS after 1, 5, and 60 minutes compared to the baseline. However, for visit 2, the only significant difference was observed for 1 minute compared to 60 minutes. This finding could potentially be attributed to the patients' prior experience with the exercise method.

Table 1. Pain NRS scores for visit 1 and visit 2

	Visit 1		Visit 2	
Time	Mean	SD	Mean	SD
Before exercise	6.10	±1.32	6.13	±2.07
1 minute after stopping exercise	7.80	±1.34	6.82	±1.64
5 minutes after stopping exercise	7.13	±1.40	6.11	±2.11
60 minutes hour after stopping exercise	6.63	±1.43	5.89	±2.05

Conclusion: The ability to reliably and reproducibly generate movement-evoked pain in patients with knee OA holds promise for assessing acute treatment interventions as well as evaluating neurosensory pathways, e.g., brain MRI which can help define the basis for pain perception in OA. Further studies with larger sample sizes are warranted to validate this approach and assess its sensitivity to treatment-induced pain changes.

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Abstract Number: 1981

The Association Between X-ray Progression and Clinical Outcomes in Patients with Hand Osteoarthritis with 5-year Follow-up

Olga Sleglova[1], Jiri Baloun[2], Jindriska Gatterova[1], Xiao Svec[1], Olga Ruzickova[1], Karel Pavelka[3] and Ladislav Senolt[4], [1]Rheumatology Institute, Prague, Czech Republic, [2]Institute of Rheumatology, Prague, Czech Republic, [3]Institut of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Praha, Czech Republic, [4]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Praha, Czech Republic

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1977–1995) Osteoarthritis – Clinical Poster III
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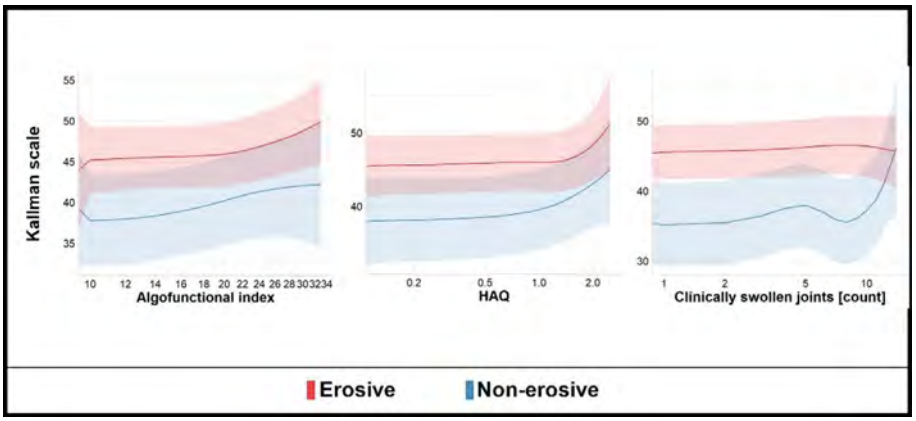
Background/Purpose: Hand osteoarthritis (HOA) is a heterogeneous disorder with two main subtypes, non-erosive and erosive. The progression of HOA is assessed by various radiographic scoring methods, including the Kallmann scale, and the understanding of the association between radiographic changes and clinical symptoms might help improve the monitoring of disease progression.This study aimed to investigate the association of the Kallman scale with clinical assessment parameters and the erosive subtype in a Czech population of HOA patients over 5 years.

Methods: Consecutive patients with symptomatic HOA fulfilling the American College of Rheumatology (ACR) criteria were included in this study. All patients were evaluated at baseline and follow-up examinations over 2 and 5 years. Clinical examinations were performed by qualified rheumatologists. The number of clinically tender and swollen joints was recorded. Pain,



Associations of the Kallman scale with the Algofunctional index, HAQ, and the number of clinically swollen joints in patients with erosive and non-erosive HOA.

stiffness, and function were assessed. Hand disability was evaluated based on the Algofunctional index. The visual analog scale (VAS-pain) and the health assessment questionnaire (HAQ) was used for the assessment of pain and function/disability. Postero-anterior plain radiographs of both hands were examined, and radiographs were scored by two trained readers (rheumatologists) according to the Kallman scale.

Results: Of 154 patients enrolled in this study, 129 subjects (89.3% females; mean age at baseline = 64.6±8.0 years) met the ACR classification criteria for HOA and were followed up over 5 years at the outpatient department of the Institute of Rheumatology in Prague. Out of these patients, 57 were diagnosed with the non-erosive form (87.7% females; mean age at baseline = 63.8±7.7 years) and 72 with the erosive form (90.3% females; mean age at baseline = 65.7±8.1 years), where erosive HOA was defined by at least one interphalangeal joint with radiographic signs of erosion. Firstly, we analyzed each examination separately and found that the Kallman scale was both significantly increased in patients with the erosive subtype (2.95 – 3.12-fold, $p< 0.001$ for all) and associated with age in all examinations ($\beta = 1.27 – 1.57$; $p< 0.001$ for all). Next, we used generalized additive modeling (GAM) to analyze data collected over five years and discovered the association of the scale with HOA subtypes and age ($p < 0.01$ for both). GAM also revealed associations of the Kallman scale with HAQ (edf=2.5, p=0.016) in all patients and patients with non-erosive HOA (edf=1.7, p=0.027). Similarly, the scale was associated with the number of clinically swollen joints in all HOA patients (edf = 1, p = 0.041) and patients with non-erosive HOA (edf=4, p=0.046). Eventually, the Algofunctionalindex (edf=1.9, p=0.02) was only associated with the scale in all HOA patients. Other parameters (e.g., AUSCANs) were insignificant.

Conclusion: Our 5-year longitudinal study revealed the associations of structural progressions with both subtypes and age at each time point. In contrast, functional impairments were only associated with progression in the non-erosive subset and all HOA patients. Further studies in a larger cohort of patients are needed to validate these data.

Acknowledgments: This work was supported by MHCR 023728 and AZV No. 18-00542.

Disclosure: O. Sleglova: None; **J. Baloun**: None; **J. Gatterova**: None; **X. Svec**: None; **O. Ruzickova**: None; **K. Pavelka**: Abbvie, 2, 6, Amgen, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Egis, 2, 6, MSD, 2, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 6; **L. Senolt**: None.

Abstract Number: 1982

Effect of Denosumab on Knee Pain and Bone Marrow Lesions in Symptomatic Knee Osteoarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1977–1995) Osteoarthritis – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: There are currently no licensed therapies which reduce progression of knee OA. Current therapies focus on reducing pain, have limited effect, and some have significant adverse effects. Bone marrow lesions (BMLs) - ill-defined areas of high signal intensity in subchondral bone MRIs - are present in ~80% of patients with symptomatic knee OA and are associated with knee pain and structural progression. Denosumab is a potent antiresorptive monoclonal

antibody targeted at RANK Ligand (RANKL). We hypothesised that in patients with symptomatic knee OA, and evidence of a BML on MRI, treatment with a subcutaneous injection of denosumab would reduce BML size, thus reducing knee symptoms.

Methods: The DISKO Trial (ISRCTN96920058) was a single centre, double-blind randomised placebo-controlled trial. Adults with symptomatic knee OA were randomly allocated 1:1 to a single injection of subcutaneous Denosumab (60mg), or matched placebo. All subjects received calcium and vitamin D supplements. Eligibility criteria: age ≥40 years; x-ray changes of tibio- or patella-femoral OA based on knee x-rays within previous 24 months; knee pain in past week ≥3 on a 0-10 numerical rating scale (NRS). Knee must have evidence of BMLs on screening knee MRI (Phillips 3T), plus Kellgren and Lawrence grade 2 or 3 disease in the painful knee and 25-OH vitamin D level > 50nmol/l. Symptoms were assessed at 3 and 6 months, repeat MRI at 6 months. Primary outcome: BML area at 6 months (mm^2), from sagittal PDFS pulse sequence. Secondary outcomes: imaging parameters (BML volume), severity of knee pain (10-point NRS), other knee symptoms, and quality of life (KOOS; SF-12v2; EQ-5D-5L questionnaires).

Results: 145 men and women were assessed for eligibility. Of these, 87 were excluded, 58 taking part in the trial (30 randomised to denosumab, 28 to placebo). Mean age of randomised subjects was 64.2 years, mean BMI 29.3 Kg/m^2; mean baseline pain in the past week (0-10 NRS) was 6.0 (SD 1.7); median BML area was 787.5mm^2 (IQR 370.0mm^2 to 1150.0mm^2). A complete case mixed-effects model (N=46) adjusting for baseline found little difference in BML area between groups at 6 months (marginal mean difference = 52.0mm^2; 95% CI -151.9 to 255.9; p = 0.62). Six months between-groups differences in BML volume (marginal mean difference = 278.0mm^3; 95% CI -1877.4 to 2433.4; p = 0.80) and synovitis-effusion volume (-582.9mm^3; 95% CI -3011.3 to 1845.6; p = 0.64) were also small. At 6 months, the denosumab group had slightly greater pain in the past week NRS (0-10) (marginal mean difference = -0.25 points; 95% CI -1.6 to 1.1; p = 0.75) and the KOOS pain (100-0) (marginal mean difference = 5.0 points; CI -5.4 to 15.3; p = 0.35) compared to placebo. There were no significant between-group differences in non-pain KOOS subscales or EQ-5D-5L subscales at 3 or 6 months. Sensitivity analyses using additional covariates and multiple imputation were concordant. There were 57 adverse effects (30 Denosumab; 27 placebo), 40 mild, and 1 serious adverse event, unrelated to the intervention.

Conclusion: We found no signal to suggest a beneficial effect of denosumab on symptoms or structure. These findings do not support use of subcutaneous Denosumab for symptomatic knee OA.

Disclosure: T. O'Neill: None; **M. Parkes**: None; **M. Bowes**: None; **R. Hodgson**: None; **D. Felson**: None.

Abstract Number: 1983

WITHDRAWN

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: (1977–1995) Osteoarthritis – Clinical Poster III
Session Type: Poster Session C
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Background/Purpose: Hand Osteoarthritis (OA) is common and causes pain and disability. Heat is anecdotally known to moderate symptoms and is conditionally recommended as a treatment for Hand OA by the American College of Rheumatology.

The purpose was to assess change in function after 6 weeks treatment with electrically heated mittens compared to sham mittens (electrical heating disabled) in participants with hand OA.

Methods: We performed a randomized superiority trial evaluating the potential benefit of heated mittens vs sham mittens during a 6-week trial period. We included participants diagnosed with hand OA according to the American College of Rheumatology classification criteria who had an AUSCAN (Australian/Canadian Osteoarthritis Hand Index) function of ≥ 40 on a 0-100 scale (higher scores indicate worse function). Participants were recruited from October 2020 to January 2023 and participated during the winter season (October to April 2020/21, 2021/22, 2022/23) in Denmark. Participants were randomly allocated (1:1) to heated mittens or sham mittens. The mittens appeared identically, including LED-lights that led when the heat function was activated. In the sham mittens, the heating was disabled. Participants were instructed to wear the mittens at least 15 minutes per day for 6 weeks. The primary outcome was change in AUSCAN function at week 6. Key secondary outcomes included AUSCAN pain, visual analog scale (VAS) global assessment of hand related problems, and grip strength. All analyses were based on the Intention-to-treat population, with continuous data modelled using repeated measures, mixed effects models adjusted for baseline variables.

Results: Two hundred participants were randomized to heated mittens (n = 100) or sham mittens (n = 100); 91 (Heat) and 95 (Sham) participants, completed the trial. The mean age was 71 years, 87 % were women, and median disease duration was 10 years (see Table 1). The mean (SE) change from baseline to week 6 in the AUSCAN function was -6.3 points (1.2) in the Heat group, and -3.3 points (1.2) in the Sham group, corresponding to a group difference of -3.0 points (95%CI, -6.3 to 0.4; $P = 0.085$; see Figure 1 and Table 2). Key secondary outcomes showed a statistically significant difference in AUSCAN pain of -5.9 points (95%CI, -9.5 to -2.2; $P = 0.002$), while no significant differences were found for VAS global assessment of hand related problems (0-100 VAS score) or grip strength.

Conclusion: Heated mittens were not superior to sham-heated mittens after 6 weeks regarding AUSCAN function but improvement in hand pain was observed.

Abstract Number: 1984

Therapeutic Effects of Pentosan Polysulfate Sodium on Clinical and Disease Modifying Outcomes in Subjects with Knee Osteoarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1977–1995) Osteoarthritis – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is an inflammatory joint disease, causing chronic pain, disability, and reduced quality of life. Affected joints may include the knee, hip, and hands. This study evaluated clinical and disease modifying biomarker and structural changes in subjects with knee OA pain treated with injectable pentosan polysulfate sodium (iPPS) or placebo.

Methods: In this phase 2, double-blind study, subjects were randomized to iPPS 2.0 mg/kg ideal body weight (IBW) twice weekly, 2.0 mg/kg IBW PPS once weekly + placebo once weekly, or placebo twice weekly for 6 weeks, followed by a 46-week follow-up. Subjects were evaluated at baseline, days 56 and 168 for clinical outcomes using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and synovial fluid (SF), serum and urine samples were obtained for biomarker assays. Magnetic resonance imaging (MRI) was performed at Day 168 to assess joint structure changes.

Safety was evaluated by assessing adverse events (AEs).

All comparisons were exploratory at 5% significance. The percentage change from baseline to Day 56 and Day 168 were compared between treatment groups using a mixed model for repeated measures (MMRM) analysis. Biomarkers were quantitated using verified ELISA kits. Whole-Organ MRI Scoring (WORMS) was used to assess changes in the joint structures.

Results: 61 subjects were randomized (17, 15 and 21 to twice weekly iPPS, once weekly iPPS and placebo respectively. Median age was 60 years; 57% were male; median BMI was 28.8 and KL 3-4 was 78% overall. Baseline clinical values were similar among groups. At Day 56, significant improvements in WOMAC pain (p=0.05), function (p=0.017) and overall (p=0.022) scores were observed in subjects treated with iPPS twice weekly vs placebo and all improvements continued through Day 168. Once weekly iPPS showed improvement but differences from placebo did not reach statistical significance. At Day 56 favorable changes were observed in 6 SF biomarkers (IL-6, TNF-α, βNGF, COMP, ARGS [p=0.036], TIMP-1) in iPPS-treated subjects vs placebo. At Day 168, SF biomarkers ARGS and COMP, serum biomarker ARGS (p=0.024), COMP and C2C (p=0.024), and urine biomarker CTX II demonstrated favorable changes in iPPS-treated subjects vs placebo.

MRI results showed improvements in structural disease features, most apparent in the once-weekly iPPS treated subjects: a 21% improvement in cartilage loss score in the medial femur vs 4% worsening in placebo (p=0.065), and a 17% decrease of bone marrow edema lesions in the lateral tibiofemoral compartment with an increase of 56% in the placebo (p=0.028).

Related AEs occurred in 55.0%, 73.7% and 36.4% of subjects in the iPPS once weekly, iPPS twice weekly, and placebo-treated subjects, respectively. There were no serious AEs or AEs of special interest. The majority of AEs were mild to moderate in severity. The most common related AEs were headache and injection site reactions.

Conclusion: These findings show promising effects of iPPS for pain relief and improved function while changes in biomarkers and MRI assessments show potential DMOAD effects of iPPS in patients with knee OA. Paradigm is conducting larger global studies to confirm the observed clinical and DMOAD effects of iPPS.

Disclosure: M. Ahuja: ChitogenX, 11, Paradigm Biopharmaceuticals, 3, 11; **D. Skerrett**: Paradigm Biopharmaceuticals, 3, 4, 11, 11; **C. Gravance**: Paradigm Biopharmaceuticals, 3; **D. Navuru**: Paradigm Biopharmaceuticals, 3; **R. Krishnan**: Paradigm Biopharmaceuticals, 3, 11; **C. Inderjeeth**: Paradigm Biopharmaceuticals, 5; **P. Bloom**: Paradigm Biopharmaceuticals, 5, 11; **S. Thomas**: AstraZenica, 2, Eli Lilly, 2, GlaxoSmithKline, 2, Horizon, 2, IBSA Group, 2, Merck, 2, Moebius Medical, 2, Orion, 2, Paradigm Biopharmaceuticals, 5, Pfizer, 1, 2, Regeneron, 2, Xalud Therapeutics, 2.

Abstract Number: 1985

Preliminary Results for the Total Knee Replacement Coaching Program for Patients Preparing to Undergo Total Knee Arthroplasty, a Pilot Randomized Trial

Noelia Hernandez[1], Yuliana Dominguez Paez[2], Assem Jabri[2], Mackenzie Brown[2], Geyanne Lui[3], Wai-Kwong Hui[4], Michael Parks[4], Alejandro Gonzalez Della Valle[4], Fred Cushner[4], Peter Sculco[4], Thomas Sculco[4], Mathias Bostrom[4], Alejandro Leali[4], Jason Blevins[4], Jose Rodriguez[4], Gwo-Chin Lee[4], Lisa Mandl[5], Susan Goodman[4], Samprit Banerjee[2], Monika Safford[6] and Iris Navarro-Millán[7], [1]Weill Cornell Medicine, The Bronx, NY, [2]Weill Cornell Medicine, New York, NY, [3]New York Institute of Technology, New York, NY, [4]Hospital for Special Surgery, New York, NY, [5]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [6]WCM Department of Medicine, New York, NY, [7]Weill Cornell Medicine, Hospital for Special Surgery, New York, NY

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1977–1995) Osteoarthritis – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Up to 30% of patients with primary knee osteoarthritis (KOA) who have undergone Total Knee Replacement (TKR) continue to experience knee pain after surgery.High levels of anxiety and/or depression before TKR have been identified as predictors of post-TKR painand are barriers to engaging in post-TKR rehabilitation. The Moving Well is a pre- and post-TKR intervention thatcombinesprinciples of cognitive behavioral therapy (CBT) and home exercisesalongside a peer coach with the goal of reducing anxiety, depression, and knee pain post-TKR.A peer coach is a person with KOA who had undergone TKR and is guiding another person with KOA in the Moving Well interventionto prepare and recover from TKR. The goal of this abstract is to present the preliminary results of this pilot study regardingthe effectiveness and feasibility of Moving Well.

Methods: We included patients with KOA scheduled for TKR 8 weeks in advance between 50-89 years, had access to a computer, internet, and spoke English. Exclusion criteria were prior joint replacement surgery,unable to exercise, or any-rheumatic diseases. Participants were randomized to either Moving Well intervention or Staying Well attention control arm. Each group received weekly 1-hour phone sessions, 7 sessions pre-TKR and 5 sessions post-TKR. The Staying Well arm covered topics on nutrition and preventive medicine anddid not receive information on TKR, exercise, or CBT principles. We used one sided t-test to determine differences in mean Generalized Anxiety Disorder (GAD)-7, Patient Health Questionnaire (PHQ)-8 scores and mean changes in Knee Injury Osteoarthritis Outcome Score (KOOS)scoresbetween arms and between baseline (8 weeks pre-TKR) and 6 weeks after TKR.

Results: Thereare 38 participants enrolled out of a target of 74 individuals for this pilot, with 22 in the Moving Well arm and 16 in the Staying Well arm. The meanage of participants is 68 years, and the population is mostly white and highly educated (Table 1). While there was no significant differencein depression (PHQ-8) or anxiety (GAD-7)scoresbetween arms (Figure 1), participants in the Moving Well program experienceda large improvement in KOOS scores 6-weeks post-TKR (Figure 2). None of the values were significant given the small sample. No participant from Moving Well dropped out while 3 dropped out from Staying Well, which suggests that the intervention is feasible and engaging for completion.

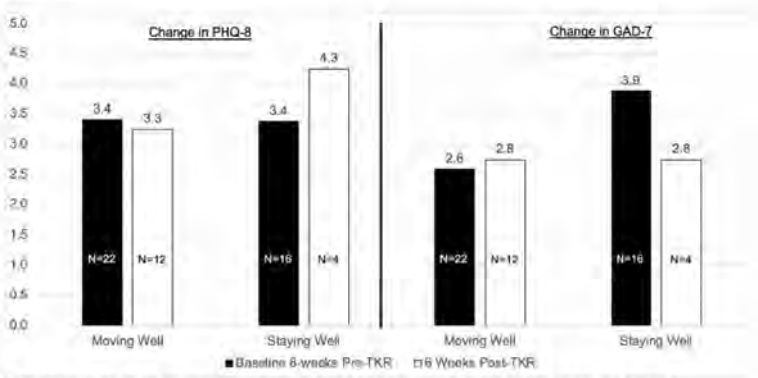
Conclusion: There were no significant changes in depression or anxiety levels between Moving Well and control groups. However, the Moving Well group demonstrated a noteworthy improvement in KOOS scorespost-TKR. These findings emphasize the potential benefits of a holistic approach in managing the challenges faced by KOA patients undergoing TKR, highlighting the importance of incorporating psychological support and exercise programs into pre- and post-

Table 1 – Demographic information of participants of the Total Knee Replacement Coaching Program 8 weeks before TKR (Baseline)

	Total (N=38)	Moving Well (N=22)	Staying Well (N=16)
Age, Mean (SD)	68.4 (6.8)	68.1 (7.2)	68.7 (6.5)
Sex, N			
Female	29	18	11
Male	9	4	5
Race*, N			
White	29	15	14
Hispanic/Latino	1	1	0
Black or African American	6	5	1
Asian/Pacific Islander	0	0	0
Native American or Alaskan Native	1	1	0
Other	1	0	1
Prefer not to say	0	0	0
Educational Level, N			
High School	1	1	0
Some college	0	0	0
Associate's degree	5	2	3
Bachelor's degree	15	10	5
Advanced degree (Doctorate or Master's degree)	14	8	7
Other	3	1	2
Insurance*, N			
Medicare	18	11	7
Medicaid	0	0	0
Medicare AND Medicaid	0	0	0
Private	20	11	9
Uninsured	0	0	0
Household Income, N			
Less than $24,000	0	0	0
$25,000-$50,000	3	1	2
$51,000-$100,000	10	8	2
Greater than $100,000	19	8	11
Work Status, N			
Unemployed	0	0	0
Disabled	1	0	1
Working, part time	4	4	0
Working, full time	14	8	6
Retired	18	9	9
Marital Status, N			
Single	7	5	2
Married	23	14	9
Widowed	3	0	3
Divorced	3	1	2
Partnership	0	0	0
Other	1	1	0
Knee Injury and Osteoarthritis Outcome Score (KOOS), Mean (SD)			
KOOS Pain	50.0 (19.9)	49.50(18.1)	50.8 (22.7)
KOOS Activities of Daily Living	55.1 (21.1)	54.8 (18.6)	55.7 (24.7)
KOOS Quality of Life	25.8 (17.6)	26.3 (17.3)	25.1 (18.9)
KOOS Average	39.9 (16.1)	39.3 (13.6)	40.8 (19.8)
*Participants had the option to select more than one answer.			

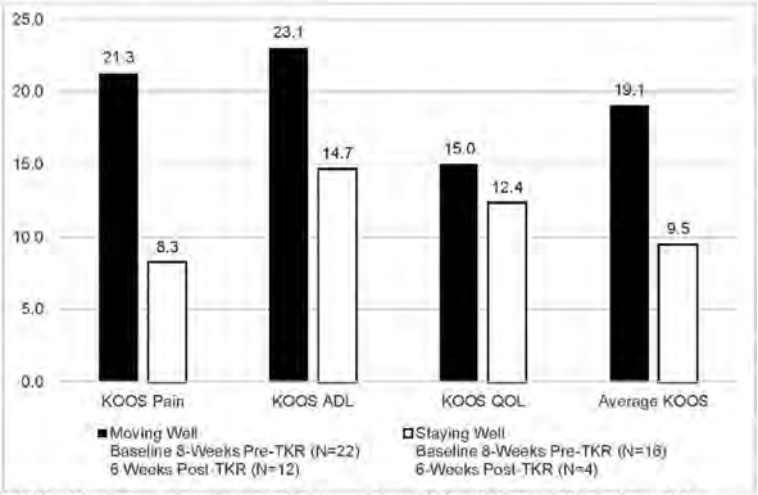
operative rehabilitation protocols. Ongoing efforts are focused recruiting the 74 patients that are part of this intervention and determiningthelong-term effects (1-year post-TKR data) of the Moving Well intervention in reducing post-TKR pain.

Figure 1 – Mean Scores of PHQ-8 and GAD-7 at Baseline (8 weeks pre-TKR) and 6 weeks post-TKR*



The Patient Health Questionnaire-8 (PHQ-8) is an 8-question questionnaire used to assess depression. The Generalized Anxiety Disorder-7 (GAD-7) is a 7-question questionnaire used to assess anxiety. A low is score in either instrument signifies low levels of anxiety or depression.
*No significant differences between the groups.

Figure 2 – Mean Changes in Knee Injury and Osteoarthritis Outcome Score (KOOS) Pain, Function in Daily Living (ADL), Quality of Life (QOL), and Overall, Between Baseline (8 weeks pre-TKR) and 6 weeks post-TKR.



KOOS = Knee injury and Osteoarthritis Outcome Score; ADL = Activities of Daily Living; QOL = Quality of life.
High KOOS scores represent low pain levels, high function level, and high quality of life.
*No significant differences between the groups.

Disclosure: N. Hernandez: None; **Y. Dominguez Paez**: None; **A. Jabri**: None; **M. Brown**: None; **G. Lui**: None; **W. Hui**: None; **M. Parks**: None; **A. Gonzalez Della Valle**: None; **F. Cushner**: None; **P. Sculco**: DePuy Synthes, 2, EOS Imaging, 2, Intellijoint Surgical, 2, 5, Lima Corporate, 2, Zimmer Biomet, 2, 5; **T. Sculco**: None; **M. Bostrom**: None; **A. Leali**: None; **J. Blevins**: None; **J. Rodriguez**: None; **G. Lee**: None; **L. Mandl**: Annals of Internal Medicine, 12, Associate Editor, Regeneron Pharmaceuticals, 5, Up-to-Date, 9; **S. Goodman**: NIH, 5, Novartis, 5; **S. Banerjee**: None; **M. Safford**: None; **I. Navarro-Millán**: None.

Abstract Number: 1986

Deep Immunophenotyping of Osteoarthritis Patients Demonstrates Baseline Alterations in Monocyte Populations in OA, Dendritic Cell Subpopulations Among Radiographic Progressors, and Th17 Cells Among Pain Progressors

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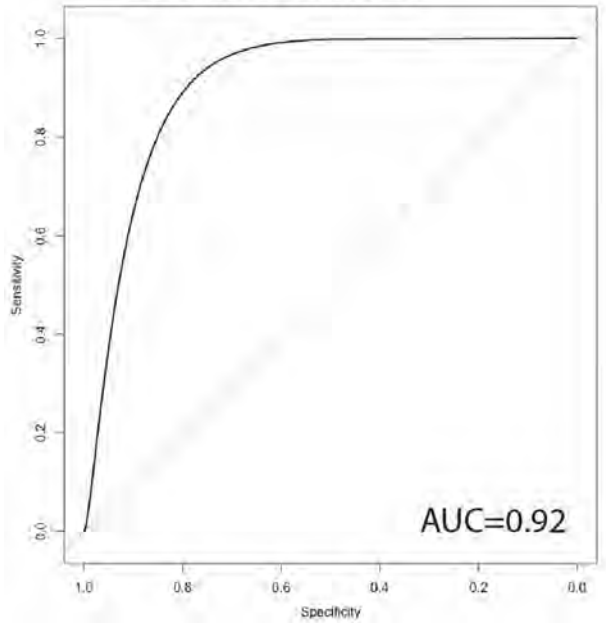
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1977–1995) Osteoarthritis – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies have suggested low-level chronic inflammation plays a key role in knee osteoarthritis (OA) development and progression. In the present study, we set out to investigate, via mass cytometry, differences in circulating blood immunophenotypes in moderate-stage OA patients compared to controls, and to investigate differences in baseline immunophenotypes in OA patients who later experienced radiographic or pain progression within the subsequent 2 years.

Methods: Early OA patient samples were obtained from the Oklahoma SOONER OA cohort, defined as baseline K/L grade 0-3 and knee pain on most days for the past 6 months. Fixed-flexion radiographs and WOMAC information from visits every 6 months was analyzed. Radiographic progressors were defined as having mean medial TF joint space narrowing of ≥0.7mm within 24 months. Pain progressors were defined as having a WOMAC pain subscale worsening of at least

Figure 1: Receiver operator characteristic (ROC) curve for OA vs. control classification model



10 points on a 0-100 normalized scale within 24 months. Matched controls were obtained from the Oklahoma Immune Cohort. The final analysis included 13 OA patients and 13 controls. Among OA patients, 4/13 were radiographic progressors and 5/13 were pain progressors. Baseline blood samples were stained with Maxpar Direct immune profiling assay kit (Fluidigm), then subjected to mass cytometry analysis. Quantitative analysis of 37 immune cell populations was then performed and group differences defined with a student T-test. Generalized logistic models were then developed to classify patients into the above groups.

Results: Comparing all OA patients to controls, there were increases in MAIT/NK T cells (OA: 3.3±0.6 vs. healthy: 1.5±0.2, mean % of parent cell population±SEM, P=0.02) (Table 1) and eosinophils (4.2±0.7 vs. 1.6±0.5, P=0.01), as well as decreases in classical- (91.6±0.7 vs. 94.3±0.7, P=0.03) and transitional-monocytes (6.8±0.5 vs. 4.8±0.6, P=0.03) noted. Radiographic progressors were characterized by baseline decreases plasmacytoid- (35.8±2.5 vs. 32.6±3.2, P=0.03) and increases in myeloid-dendritic cells (64.2±2.5 vs. 67.5±3.2, P=0.03). Pain progressors were found to have increases in Th17 T-cells (13.0±2 vs. 7.4±0.6, P=0.02). A machine learning logistic model was then trained to differentiate OA patients from healthy controls and underwent 3-fold cross-validation with internal tuning. The model demonstrated 84% accuracy with a receiver operator characteristic area under the curve (ROC-AUC) of 0.92 (Figure 1).

Conclusion: Our study is the first to perform deep immunophenotyping of peripheral blood on a small group of OA patients and well-matched controls. The results suggest that significant alterations in certain immune cell subpopulations are present among OA patients and at baseline prior to future radiographic or pain progression, and provide additional support for the hypothesis that OA represents a systemic disease characterized by low-level immune dysregulation. Future research should confirm our findings and investigate the pathophysiological consequences of these variations.

Disclosure: G. Dyson: None; **M. Barrett**: None; **M. Jeffries**: None.

Abstract Number: 1987

Clinical and Imaging Characteristics of Individuals Who Underwent Knee Replacement During Years 3 to 5 in the FORWARD Study: A Post Hoc Analysis

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SESSION INFORMATION
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Background/Purpose: Sprifermin is an investigational intra-articular (IA) recombinant human truncated fibroblast growth factor-18 (rhFGF-18) therapy evaluated to date in three knee osteoarthritis (KOA) trials (NCT00911469 [first-in-human {FIH} study]; NCT01033994; NCT01919164 [Phase 2 'FORWARD' study]) as a potential disease modifying OA drug. One of the treatment goals related to slowing OA structural progression is to significantly delay/prevent joint failure. In the FIH study, which enrolled a population planned to undergo knee replacement (KR), and in FORWARD, which enrolled those not planning to undergo KR for at least 2 years, a numeric reduction in KR incidence was seen within the study follow-up

period of 6 months or years (Y) 3 to 5, respectively, for the highest doses of sprifermin. This post hoc analysis explores clinical and structural data on FORWARD study participants (pts) who underwent KR in Y3-5.

Methods: Pts with KOA were randomized 1:1:1:1:1 in FORWARD to receive cycles (one IA injection weekly x 3 weeks) of placebo (PBO) or sprifermin at 30 or 100 μg IA every 6 or 12 months (Q6M, Q12M) through month 18, and were followed through to Y2 (treatment period) and Y5 (post-treatment period). Baseline (BL) and week 104 (W104) clinical and imaging data were analyzed post hoc for the population with a BL and ≥1 post-BL MRI (modified intent-to-treat [mITT]) who completed the treatment period by KR receipt in Y3-5. The Q6M and Q12M data for the sprifermin 30 μg and 100 μg arms were combined for analysis and reported descriptively. No imputation for missing data and no statistical tests were performed.

Table 1. Baseline Characteristics and Week 104 Change from Baseline in Symptomatic and Structural Aspects – mITT

Baseline Characteristic (unless otherwise stated)		Placebo (n=96)		Sprifermin 30 μg combined (n=198)		Sprifermin 100 μg combined (n=200)		Total (N=494)	
		No KR n=92	KR n=4	No KR n=189	KR n=9	No KR n=198	KR n=2	No KR n=479	KR n=15
Mean age, years (SD)		63.8 (8.6)	61.5 (10.0)	64.2 (8.7)	63.8 (6.3)	64.9 (8.0)	55.5 (0.7)	64.4 (8.4)	62.1 (7.2)
Female, n (%)		64 (69.6)	2 (50.0)	131 (69.3)	8 (88.9)	137 (69.2)	1 (50.0)	332 (69.3)	11 (73.3)
Asian race, n (%)		20 (21.7)	1 (25.0)	40 (21.2)	3 (33.3)	42 (21.2)	0	102 (21.3)	4 (26.7)
White race, n (%)		72 (78.3)	3 (75.0)	149 (78.8)	6 (66.7)	156 (78.8)	2 (100)	377 (78.7)	11 (73.3)
Hispanic/Latino, n (%)		1 (1.1)	0	1 (0.5)	0	0	0	2 (0.4)	0
Mean BMI (kg/m^2) (SD)		29.4 (5.8)	32.8 (6.6)	29.0 (5.2)	31.2 (8.4)	29.1 (5.2)	32.6 (NA)	29.1 (5.3)	31.8 (7.3)
≥30, n (%)		37 (41.1)	2 (50.0)	74 (40.4)	5 (55.6)	73 (37.8)	1 (NA)	184 (39.5)	8 (57.1)
KL Grade 3, n (%)		28 (30.4)	3 (75.0)	56 (29.6)	7 (77.8)	61 (30.8)	0	145 (30.3)	10 (66.7)
Mean medial mJSW, mm (SD)		3.8 (1.2)	3.3 (1.3)	3.7 (1.0)	3.6 (1.5)	3.8 (1.1)	4.9 (0.7)	3.7 (1.1)	3.7 (1.4)
WOMAC Pain (0-100) (SD)	Baseline	46.3 (14.3) n=91	51.5 (17.0) n=4	45.9 (15.4) n=186	49.6 (11.8) n=9	46.9 (15.9) n=197	48.0 (NA) n=1	46.4 (15.3) n=474	50.0 (12.4) n=14
	Δ at W104	-26.4 (19.0) n=78	-3.5 (42.1) n=4	-23.3 (20.1) n=173	-5.6 (32.8) n=9	-24.1 (19.0) n=188	-28.0 (NA) n=1	-24.2 (19.4) n=439	-6.6 (33.3) n=14
WOMAC Function (0-100) (SD)	Baseline	45.5 (17.0) n=91	51.3 (20.0) n=4	44.6 (17.5) n=186	52.4 (15.4) n=9	44.0 (18.8) n=197	50.6 (NA) n=1	44.5 (17.9) n=474	52.0 (15.4) n=14
	Δ at W104	-21.7 (20.0) n=78	-4.0 (28.0) n=4	-20.8 (20.4) n=173	-5.7 (29.5) n=9	-18.6 (20.6) n=188	-10.0 (NA) n=1	-20.0 (20.4) n=439	-5.5 (26.8) n=14
TFTC Cartilage thickness, mm (SD)	Baseline	1.81 (0.27) n=91	1.70 (0.36) n=4	1.81 (0.25) n=187	1.76 (0.33) n=9	1.81 (0.27) n=196	2.11 (0.20) n=2	1.81 (0.26) n=474	1.79 (0.33) n=15
	Δ at W104	-0.01 (0.05) n=79	-0.16 (0.21) n=4	-0.01 (0.06) n=169	-0.06 (0.13) n=9	0.03 (0.07) n=178	-0.09 (0.21) n=2	0.01 (0.07) n=426	-0.09 (0.16) n=15

Δ=change; BMI=body mass index; KL=Kellgren Lawrence; KR=knee replacement; mITT=modified intent-to-treat; N=total sample size; n=sample evaluated; NA=not applicable; SD=standard deviation; TFTC=total femorotibial compartment; W104=Week 104; WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index.

Table 2. %Denuded Area of Subchondral Bone (dAB) and Week 104 Change from Baseline in %dAB – mITT

Absolute %dAB		Placebo (n=84)		Sprifermin 30 μg combined (n=185)		Sprifermin 100 μg combined (n=186)		Total (N=455)	
		No KR n=80	KR n=4	No KR n=176	KR n=9	No KR n=184	KR n=2	No KR n=440	KR n=15
Any FTJ dAB, n (%)	Baseline	44 (55.0)	4 (100.0)	96 (54.5)	8 (88.9)	102 (55.4)	1 (50.0)	242 (55.0)	13 (86.7)
cMF (SD)	Baseline	2.75 (5.65)	9.53 (7.15)	2.80 (7.29)	4.82 (3.63)	4.14 (9.47)	0.00 (0.00)	3.35 (8.05)	5.44 (5.30)
	Δ at W104	0.29 (2.83)	19.68 (39.83)	0.53 (2.65)	5.80 (18.33)	0.70 (3.87)	8.99 (12.71)	0.56 (3.24)	9.93 (24.12)
MFTC (SD)	Baseline	1.49 (3.21)	4.30 (1.06)	1.47 (4.24)	2.02 (1.71)	2.17 (5.79)	0.00 (0.00)	1.77 (4.81)	2.36 (1.96)
	Δ at W104	0.24 (2.70)	18.53 (33.97)	0.45 (2.19)	3.21 (9.45)	0.47 (2.46)	4.95 (7.00)	0.42 (2.40)	7.53 (18.69)
cLF (SD)	Baseline	2.09 (4.68)	4.46 (5.19)	2.49 (5.43)	4.76 (5.99)	2.26 (4.49)	2.33 (3.30)	2.32 (4.91)	4.36 (5.27)
	Δ at W104	0.26 (0.91)	2.15 (3.43)	0.19 (1.45)	0.84 (2.44)	0.09 (0.98)	-0.35 (0.50)	0.16 (1.18)	1.03 (2.57)
LFTC (SD)	Baseline	2.06 (5.63)	2.54 (3.09)	2.11 (4.03)	4.92 (7.00)	2.01 (4.13)	0.85 (1.21)	2.06 (4.39)	3.74 (5.72)
	Δ at W104	0.17 (0.49)	0.96 (1.22)	0.15 (1.03)	1.64 (4.17)	0.13 (0.71)	-0.13 (0.19)	0.15 (0.82)	1.22 (3.26)

Δ=change; cLF=central lateral femur; cMF=central medial femur; FTJ=femorotibial joint; KR=knee replacement; LFTC=lateral femorotibial compartment; MFTC=medial femorotibial compartment; mITT=modified intent-to-treat; N=total sample size; n=sample evaluated; SD=standard deviation; W104=Week 104.

Results: In the PBO and sprifermin 30 μg Q12M, 30 μg Q6M, 100 μg Q12M, and 100 μg Q6M arms, the overall incidence of KR during Y3-5 was 5%, 4%, 5%, 2%, and 0% (n=4/87, 4/99, 5/92, 2/98, and 0/96), respectively. Study pts who received KR were younger than those without (Table 1). Most KRs (67%) occurred in Kellgren-Lawrence grade 3 knees at BL. The total KR population at BL had slightly greater pain, slightly more functional impairment, thinner total femorotibial compartment (TFTC) cartilage, and more denuded cartilage area of subchondral bone (dAB) than the non-KR population (Tables 1 and 2). At W104, the total KR population had numerically less improvement in pain and function, more cartilage thickness loss, and more medial femorotibial compartment (MFTC) dAB than the non-KR population (Tables 1 and 2), more so in the weight-bearing central medial femur [cMF] than in the medial tibia. These changes appeared more pronounced in the PBO group than the sprifermin 30 μg and 100 μg combined groups. Changes in dAB at W104 in the lateral femorotibial compartment (LFTC) were less marked than those in the MFTC.

Conclusion: Pts treated with IA sprifermin 100 μg had a lower incidence of KR than those receiving PBO or sprifermin 30 μg, with the incidence of KR being similar in the latter groups. Although the overall incidence of KR was low, differences in clinical and structural features (especially in the medial compartment) of KOA were apparent at BL and W104, with less symptomatic improvement and more structural worsening at W104, in those who received KR compared to those who did not. These findings need to be confirmed in a prospective study.

Disclosure: P. Conaghan: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, Genascense, 2, GlaxoSmithKlein(GSK), 2, Grunenthal, 2, Janssen, 2, Levicept, 2, Merck/MSD, 2, Moebius Medical, 2, Novartis, 2, 6, Stryker, 2, Takeda, 2, TrialSpark, 2; **F. Eckstein**: 4P Moving, 2, Kolon Tissue Gene, 2, Merck, 2, Novartis, 2, TrialSpark, 2; **W. Wirth**: Chondrometrics GmbH, 3, 11, TrialSpark, 2; **M. Hochberg**: TrialSpark, 2; **A. Guermazi**: BICL, LLC, 11, ICM, Coval, TrialSpark, TissueGene, Medipost, 2, Novartis, 2, Pfizer, 2; **L. Zhao**: TrialSpark, 3, 11; **N. Goel**: TrialSpark, 3, 11.

Abstract Number: 1988

Extended-Release versus Immediate-Release Triamcinolone Acetonide for Osteoarthritis of the Knee with Comorbid Diabetes Type 2 Diabetes Mellitus: A Post Hoc Analysis

Andrew Spitzer[1], Helena Rodbard[2], Sheikh Usman Iqbal[3], Masato Nakazawa[3], Mary DiGiorgi[3] and Roy Winston[3], [1]Cedars-Sinai Medical Center, Los Angeles, CA, [2]Endocrine and Metabolic Consultants, Rockville, MD, [3]Pacira BioSciences, Inc., Tampa, FL

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1977–1995) Osteoarthritis – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Intraarticular (IA) corticosteroids are generally considered safe and effective to treat osteoarthritis of the knee (OAK) but may cause hyperglycemia that may last for weeks and can be particularly severe for up to 72 hours after injection; this hyperglycemia can have adverse implications for patients who have comorbid type 2 diabetes mellitus (T2D). A phase 2 study of 33 patients with OAK and T2D (NCT02762370) found that there were minimal blood glucose disruptions when patients were administered extended-release triamcinolone acetonide (TA-ER) compared with immediate-release triamcinolone acetonide (TA-IR). The purpose of this post hoc analysis is to characterize the clinical meaningfulness and relevance of the results of the phase 2 study.

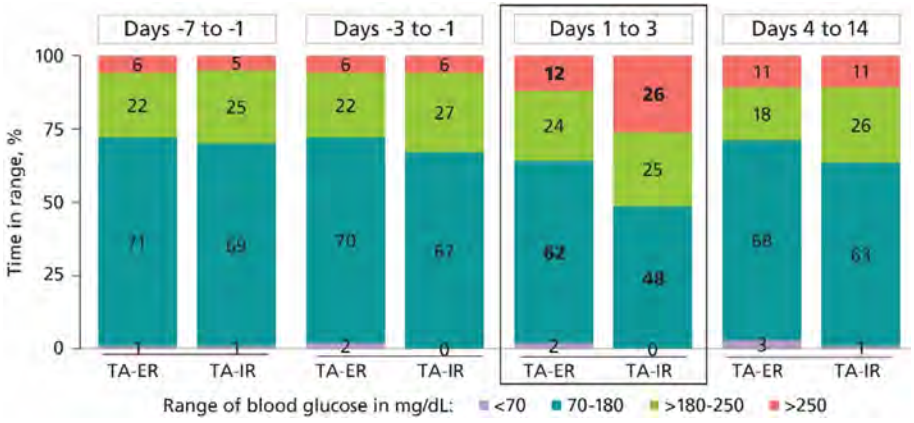

Figure 1: Percentage of time in specific blood glucose ranges. Black box indicates the critical 72-hour window. TA-ER, triamcinolone acetonide extended-release; TA-IR, triamcinolone acetonide immediate-release.

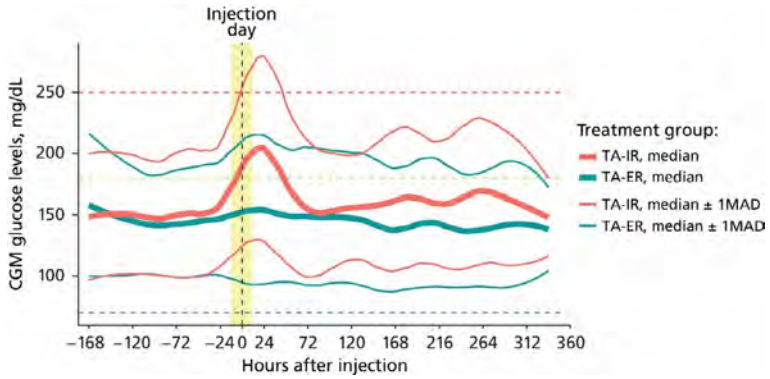

Figure 2. CGM levels over time. Median glucose levels (thick lines), median glucose levels ± 1MAD (think lines), injection day (yellow shading), and target range limits (horizontal dashed lines) are indicated. The red dashed line indicates the severe hyperglycemia threshold, while the green and blue dashed lines indicate the >180- and ≥70-mg/dL thresholds, respectively. CGM, continuous glucose monitoring; 1MAD, 1 mean absolute deviation; TA-ER, triamcinolone acetonide extended-release; TA-IR, triamcinolone acetonide immediate-release.

Methods: Patients who had T2D for ≥1 year, symptomatic OAK for ≥6 months (as defined by the American College of Rheumatology criteria for the Classification of OA of the Knee), and glycated hemoglobin ≥6.5% and < 9.0% were considered eligible and randomized to IA TA-ER or TA-IR. Before IA injection and throughout the subsequent 14 days, continuous glucose monitoring (CGM) provided an ambulatory glucose profile that summarized blood glucose levels (BGLs). Percentage of time in target range (70-180 mg/dL) and percentage of time above range (TAR; including >250 mg/dL) as defined by internationally recognized thresholds, changes from baseline in daily average BGL, and glycemic variability were compared between groups. Kaplan-Meier analysis was used to determine the time to reach 250 mg/dL and maximum BGL.

Results: Across days 1-3, IA TA-ER versus TA-IR resulted in an increased percentage of time in the target range (62% vs 48%; *P*=0.123) and a significant 2-fold lower percentage of TAR >250 mg/dL (12% vs 26%; *P*=0.047) (Figure 1). IA TA-ER had a smaller percentage of patients with maximum CGM BGL >250 mg/dL versus TA-IR (50% vs 93%). The ambulatory glucose profile analyses demonstrated more controlled BGLs and lower glucose spikes for patients receiving IA TA-ER compared with TA-IR (Figure 2). IA TA-ER had significantly higher time to maximum BGL versus TA-IR (34 vs 13 hours; *P*=0.007) and median time to 250 mg/dL (44 vs 6 hours; *P*=0.003).

Conclusion: This post hoc analysis suggests that IA TA-ER provides a clinically meaningful reduction in hyperglycemia versus TA-IR in patients with OAK and T2D. Glucose management is expected to improve with TA-ER compared with TA-IR because of the increased percentage of time in the target range. Lower and more controlled glucose spikes may lead to

fewer short-term hyperglycemia-related adverse events for patients receiving TA-ER versus TA-IR. Overall, TA-IR may reduce adverse events and healthcare utilization while improving long-term glucose control and patient well-being, particularly with repeat injections.

Disclosure: A. Spitzer: BrainLab Inc., 2, DePuy/Synthes, Inc., 2, 5, Pacira BioSciences, 2, 5; **H. Rodbard**: Bayer, 2, 6, Boehringer Ingelheim, 2, 6, Eli Lilly, 2, 6, Novo Nordisk, 2, 6, Sanofi, 2, 6; **S. Iqbal**: Pacira BioSciences, Inc., 2, 5; **M. Nakazawa**: Pacira BioSciences, Inc., 3; **M. DiGiorgi**: Pacira BioSciences, Inc., 3, 11; **R. Winston**: Pacira BioSciences, Inc., 3, 11.

Abstract Number: 1989

Shared Variation Among Cartilage Thickness Change Maps and Baseline Clinical Features at the Initiation of Structural Knee Osteoarthritis

Thomas Keefe[1], Marc Niethammer[1], Boqi Chen[1], Zhengyang Shen[1], Daniel Nissman[1], Mary Catherine Minnig[2], Yvonne Golightly[3], J.S. Marron[1] and **Amanda Nelson**[1], [1]University of North Carolina at Chapel Hill, Chapel Hill, NC, [2]University of North Carolina at Chapel Hill, Durham, NC, [3]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1977–1995) Osteoarthritis – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: To identify features of cartilage thickness change and baseline clinical indicators associated with the transition from normal to mildly reduced joint space as an early indicator of structural knee osteoarthritis (KOA).

Methods: We identified knees with radiographic medial joint space narrowing (JSN) grade 0 that transitioned to JSN grade ≥1 between any two timepoints during 96 months of follow-up in the Osteoarthritis Initiative (OAI, n=349) and selected cartilage maps (using a 3D U-Net as described in 10.1016/j.ocarto.2023.100334) from the last visit with JSN=0 and the first visit with JSN≥1. Difference maps reflecting the change in cartilage thickness at this transition for the femur and for the tibia were generated and used as data blocks. Angle-based Joint and Individual Variation Explained (AJIVE) was applied to identify the modes of variation expressed in 3 data blocks: (i) femoral cartilage change maps (ii) tibial cartilage change maps, and (iii) baseline clinical and demographic features. We examined how these blocks (different data types) varied together (shared, or "joint" variation), that may reflect features of early OA (at the transition from JSN=0 to JSN≥1). The modes of variation are visualized using loadings plots, which show the contribution of each cartilage pixel and of each OAI variable to the mode of variation (**Figure**).

Results: This analysis includes n=198 knees (from individuals with a mean age of 63 years, mean BMI of 30 kg/m^2, about ¼ with pain, after excluding outliers and those with missing data), each with (i) 57,117-pixel femoral cartilage change map, (ii) 56,204-pixel tibial cartilage change map, and (iii) 86 clinical measurements. The top three directions of shared/joint variation between the three data blocks are discussed below. **Shared direction 1** (Column 1 in **Figure**) reflects overall cartilage thinning between the transition time points (JSN=0 to JSN≥1). This pattern of overall cartilage loss is associated with poorer physical health, greater stiffness and disability, more depression, and higher BMI. **Shared direction 2** demonstrates an association with medial-predominant thinning in those with more stiffness (indicated by both WOMAC and force speeds), higher BMI, poorer physical function and mental health, greater baseline symptoms and disability, alignment, and taking

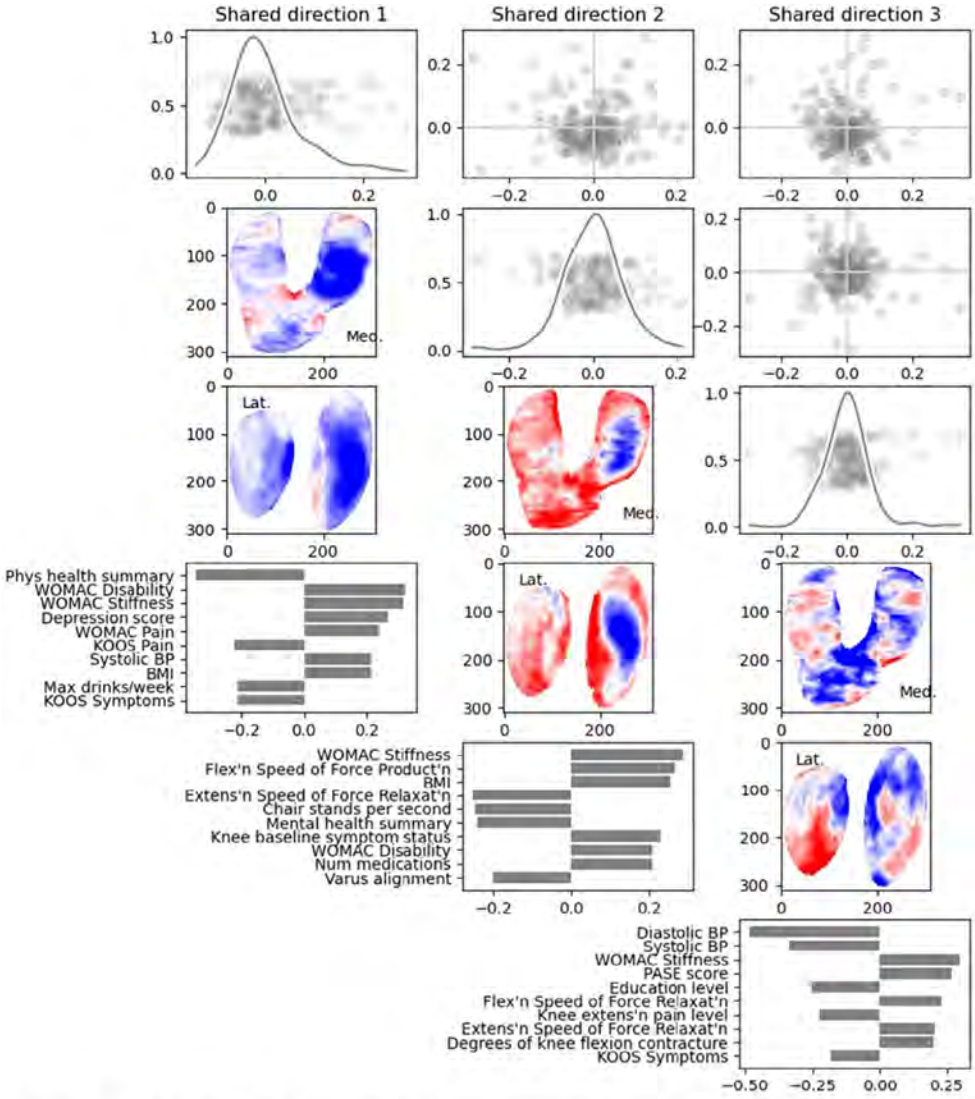

Figure. First 3 directions (columns 1-3) representing joint variation in femoral cartilage thickness change, tibial cartilage thickness change, and baseline clinical features based on AJIVE analysis using OAI baseline data. Blue=thinner and red=thicker cartilage.

more medications. **Shared direction 3** shows thinning over the femur with anterior/posterior differential loss in the tibia that is associated with lower blood pressure, education level, and extension pain but higher stiffness, physical activity, and flexion contracture.

Conclusion: These results utilize the OAI data in a novel analysis which provides directions of shared variations. There was a strong association with self-reported (via WOMAC) and functional (via force measures) stiffness in knees that subsequently transitioned from JSN=0 to JSN≥1, suggesting that stiffness (which is often overlooked or even removed from analyses) may be an important feature in early structural KOA.

Disclosure: T. Keefe: None; **M. Niethammer**: None; **B. Chen**: None; **Z. Shen**: None; **D. Nissman**: None; **M. Minnig**: None; **Y. Golightly**: None; **J. Marron**: None; **A. Nelson**: None.

Abstract Number: 1990

Effects of Exercise on Movement-Evoked Pain in People with Knee Osteoarthritis

Ehyun Kim[1], Tuhina Neogi[2], Benjamin Senderling[1], Mary Gheller[1], Lee Marinko[1], Michael LaValley[3], Lukas Adamowicz[4], Pirinka Georgiev[4], Charmaine Demanuele[4], Paul Wacnik[4] and Deepak Kumar[1], [1]Boston University, Boston, MA, [2]Boston University School of Medicine, Boston, MA, [3]Boston University School of Public Health, Arlington, MA, [4]Pfizer Inc., Cambridge, MA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1977–1995) Osteoarthritis – Clinical Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Movement-evoked pain (MEP), i.e., pain that appears with or is made worse by movement, is a common complaint in people with knee osteoarthritis (OA). MEP is more intense and bothersome than spontaneous pain and is related to greater disability. However, little is known about whether exercise, the first-line recommendation for managing chronic pain due to knee OA, can reduce MEP and factors that may predict treatment response. The objectives of this study were: (1) to investigate the effect of a 12-week exercise-based physical therapy intervention on MEP in people with knee OA and (2) to examine whether baseline psychological factors and nociceptive dysfunction predict change in MEP.

Characteristics, mean ± SD	Total cohort n = 60	Responder n = 36	Non-responder n = 21
Age (years)	66.3 ± 7.4	65.9 ± 6.5	66.1 ± 8.9
Body mass index (kg/m²)	29.0 ± 4.8	28.9 ± 5.3	29.0 ± 4.4
Female, n (%)	45 (75%)	29 (80.6%)	14 (66.7%)
Modified CCI	0.4 ± 0.8	0.6 ± 0.8	0.3 ± 0.7
*KOOS pain score (range 0-100)	64.6 ± 11.8	64.8 ± 11.6	65.6 ± 12.5
Exposure Variables			
†CSI (range 0-100)	21.7 ± 12.3	21.9 ± 13.4	21.7 ± 10.9
‡CES-D (range 0-60)	6.6 ± 5.9	6.5 ± 5.1	6.7 ± 7.2
‡PCS-short form (range 0-12)	2.9 ± 2.1	2.7 ± 2.0	3.2 ± 2.3
QST Measures			
PPT (kgf)	4.2 ± 2.5	4.6 ± 2.5	3.7 ± 2.4
Presence of central sensitization based on mechanical TS, n (%)	30 (50%)	18 (50%)	12 (57.1%)
Had an adequate CPM, n (%)	27/47 (61.7%)	16/28 (57.1%)	11/17 (64.7%)
Outcomes (0-10)			
PainNA	5.2 ± 2.0	5.1 ± 2.1	5.2 ± 1.8
Functional MEP	1.0 ± 0.7	1.0 ± 0.7	1.0 ± 0.8
Exercise MEP	1.5 ± 1.2	1.3 ± 0.9	1.8 ± 1.7
Δ in MEP from week 12 - baseline			
PainNA	-2.4 ± 2.0	-2.6 ± 2.5	-2.4 ± 1.9
Functional MEP	-0.5 ± 0.6	-0.8 ± 0.5	-0.1 ± 0.5
Exercise MEP	-0.7 ± 1.0	-0.7 ± 1.0	-0.8 ± 1.0

Abbreviations. CCI, Charlson Comorbidity Index; CES-D, Center for Epidemiological Studies-Depression; CSI, Central Sensitization Inventory; KOOS, Knee Injury and Osteoarthritis Outcome Score; MEP, movement-evoked pain; PCS, Pain Catastrophizing Scale; QST, quantitative sensory testing; SD, standard deviation; TS, temporal summation.

*Lower scores indicate greater pain.
†Higher scores indicate higher probability of central sensitization.
‡Higher scores indicate greater symptomology.

Table 1. Cohort characteristics

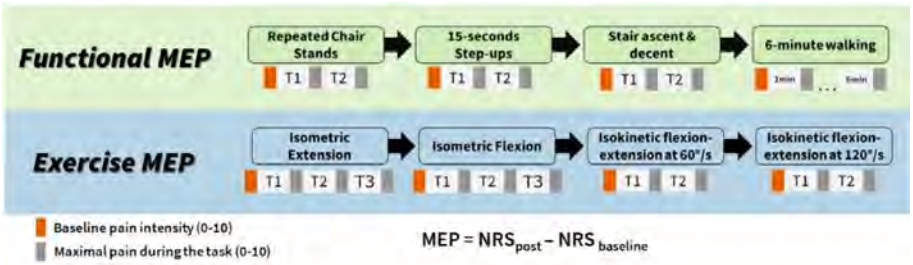

Figure 1. Assessment of functional MEP and exercise MEP. Functional MEP was assessed as the average increase in knee pain (0-10 scale) during a series of functional tasks, including repeated chair stands (x2), 15-seconds step-ups (x2), stair ascent and descent (x2), and 6-minute walk. Exercise MEP was assessed as the average increase in knee pain (0-10 scale) during a series of knee exercises including isometric extension (x3), isometric flexion (x3), and isokinetic flexion-extension at 60°/s (x2) and 120°/s (x2).

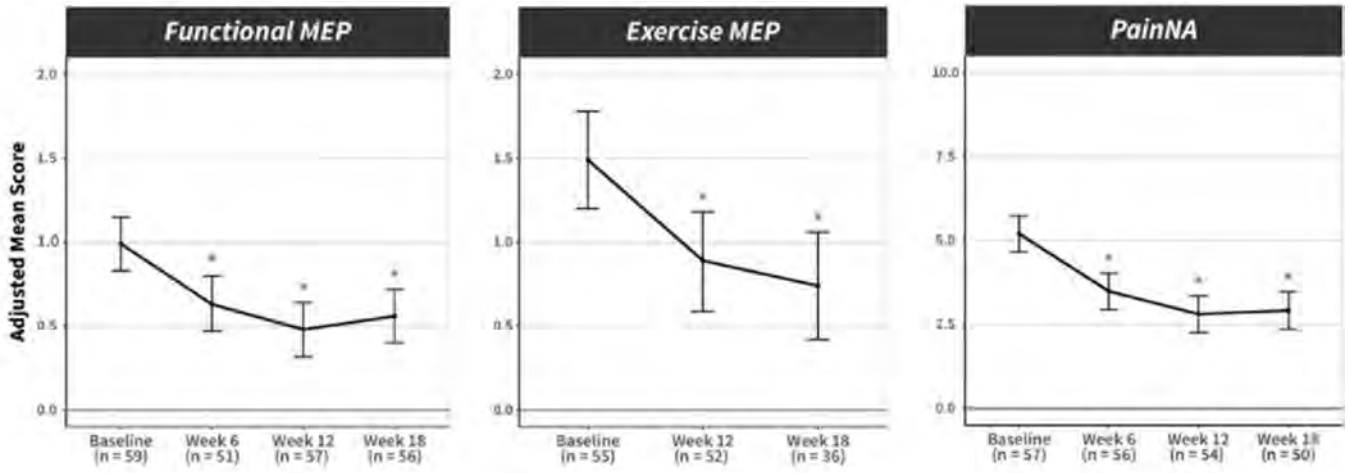

Figure 2. Adjusted means and 95% confidence intervals for measures of MEP at each study visit.
* denotes a significant change compared to baseline.

Methods: For this study, we used data from a single-arm clinical trial (#NCT04243096) of a 12-week exercise intervention in people with symptomatic knee OA (n = 60, **Table 1**) with age ≥ 50 and BMI ≤ 40 kg/m^2. Participants received 18 sessions (8 via telehealth) of an exercise intervention with a physical therapist over 12 weeks. Our primary outcome was MEP during functional activities (functional MEP), and secondary outcomes included exercise MEP and knee pain during nominated activity (PainNA, 0-10 scale) (**Figure 1**). These outcomes were assessed at baseline, and weeks 6, 12, and 18. At baseline, nociceptive functioning was assessed using quantitative sensory testing that included pressure pain threshold (PPT), mechanical temporal summation (TS), and conditioned pain modulation (CPM). At baseline, participants also completed Center for Epidemiologic Studies Depression Scale (CES-D), Central Sensitization Inventory (CSI), and pain catastrophizing scale (PCS; 3-items). Responders were individuals with ≥ 50% improvement in functional MEP from baseline to week 12. The effect of an exercise intervention on MEP from baseline to follow-up was evaluated with mixed model repeated measures (MMRM) adjusting for age, sex, BMI, and presence of comorbidities. Log-binomial regression was used to determine whether any baseline measures predicted treatment response based on functional MEP while adjusting for sex and BMI.

Results: We observed a significant improvement in all MEP outcomes with exercise at week 6 and week 12 with the improvements being sustained at week 18 (**Figure 2**). In our cohort, 63.2% of participants met our definition of responders based on functional MEP. None of the baseline measures were predictive of treatment response based on functional MEP.

Conclusion: Participants with symptomatic knee OA undergoing a 12-week exercise intervention demonstrated reductions in MEP, supporting the use of exercise as a core treatment for this population. Given the lack of a control group, it is possible that regression to the mean or other factors may have contributed to observed improvements in MEP. While minimal important change for functional MEP and exercise MEP is not known, the improvements in PainNA at week 12 were clinically meaningful. The lack of associations between baseline psychological factors as well as measures of nociceptive function suggests that exercise may be an effective intervention for MEP, irrespective of alterations in these measures in people with knee OA.

Disclosure: E. Kim: None; **T. Neogi**: None; **B. Senderling**: None; **M. Gheller**: None; **L. Marinko**: None; **M. LaValley**: None; **L. Adamowicz**: Pfizer, 3; **P. Georgiev**: Pfizer, 3, 11; **C. Demanuele**: Pfizer, 3, 11; **P. Wacnik**: Pfizer, 11; **D. Kumar**: Eli Lilly, 5, Pfizer, 5.

Abstract Number: 1991

Therapeutic Efficacy of Intra Articular Injection of Human Bone Marrow Derived Mesenchymal Stem Cells in Knee Osteoarthritis; Randomized, Double-blind, Placebo-controlled Clinical Trial

Ji Won Yang, Bong-Woo Lee, Jennifer Lee and Ji Hyeon Ju, Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1977–1995) Osteoarthritis – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is severe and intractable musculoskeletal disease that eventually leads to joint failure and pain due to inflammation and joint injury. Mesenchymal stem cells (MSCs) are expected to repair damaged tissues due to their multipotency for differentiation and immunomodulatory properties. MSCs have been the promising treatment source for osteoarthritis. However, few studies reported about outcomes of an intra-articular (IA) injection of allogenic bone marrow derived MSCs (BM-MSCs). This study aimed to assess the efficacy and safety of a single IA injection of BM-MSCs for patients with knee OA.

Methods: We performed a randomized, double-blind, placebo-controlled study. Twenty-four knee OA patients were randomized to receive single IA injection of MSCs ($1x10^8$ cells/ 2 mL) or normal saline (2 mL). The change of patient reported outcome measures (PROMs) including the visual analogue scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Knee Injury and Osteoarthritis Outcome Score (KOOS) after IA injection were assessed at serial 3, 6, 9, and 12 months from baseline. Furthermore, we performed imaging studies using magnetic resonance (MR) with T2 mapping sequences to analyze knee cartilage in all patients at baseline, 3 months, and 12 months.

Results: A total of twenty-three patients entered the final analysis, with eleven in MSCs treatment group and twelve in control group. Within group improvement of pain, measured by KOOS and WOMAC, when compared with baseline was statistically significant throughout all time points only in treatment group. Comparison between group differences revealed that treatment group had significantly more improvement of KOOS pain (23.9±18.3 vs 7.2±15.9, p=0.03) and WOMAC pain (-5.0±3.6 vs -0.1±5.5, p=0.02) at 9 months compared with control group. However, the superiority was not sustained until 12 months. In comparison of percentage change from baseline, total KOOS in treatment group had improved significantly compared with control group at 3 and 9 months. The analysis of knee cartilage using MR T2 mapping revealed that the treatment group exhibited a less sharply increase in mean T2 value compared to the control group. Specifically, the mean difference of T2 values between baseline and 12 months was found to be significantly different between treatment group and control group (2.7 ± 13.2 and 5.1 ± 12.8, respectively. p=0.009). Nine patients of treatment group experienced the acute knee pain and swelling relieved by medical treatment, but there were no serious adverse events in all patients.

Conclusion: An intra-articular injection of allogenic BM-MSCs provided satisfactory pain relief for patients with knee OA compared to control group at 9 months' follow-up. Also, comparison of T2 values from MR T2 mapping for cartilage between two groups showed that IA BM-MSCs could have a preventive effect of OA progression. Further studies with larger sample size, repetitive injections, and long-term MR follow-up are required.

Table 1. Difference between values in pain index of patient-reported outcome from the baseline to each follow-up visit.

Variables	Placebo (N=12)	MSCs-group (N=11)	p-value#
VAS pain score			
Month 3- Baseline	-14.1 (18.6) *	-17.9 (20.1) *	0.64
Month 6- Baseline	-19.8 (18.0) **	-20.5 (17.2) **	0.92
Month 9- Baseline	-12.8 (16.2) *	-19.8 (23.5) *	0.41
Month 12- Baseline	-14.7 (18.3) *	-21.2 (23.9) *	0.47
KOOS Pain			
Month 3- Baseline	11.6 (19.9)	27.1 (17.3) **	0.06
Month 6- Baseline	13.2 (23.5)	29.5 (19.4) **	0.09
Month 9- Baseline	7.2 (15.9)	23.9 (18.3) **	0.03
Month 12- Baseline	12.0 (22.1)	23.2 (24.9) *	0.27
WOMAC Pain			
Month 3- Baseline	-1.6 (4.6)	-5.0 (4.2) **	0.08
Month 6- Baseline	-2.3 (4.6)	-4.9 (4.5) **	0.17
Month 9- Baseline	-0.1 (5.5)	-5.0 (3.6) **	0.02
Month 12- Baseline	-0.6 (5.5)	-4.3 (5.2) *	0.11

Value: Mean (SD)

* There was statistically significant within-group difference (p<0.05)

** There was statistically significant within-group difference (p<0.01)

Comparison in difference of values between placebo and MSCs-group

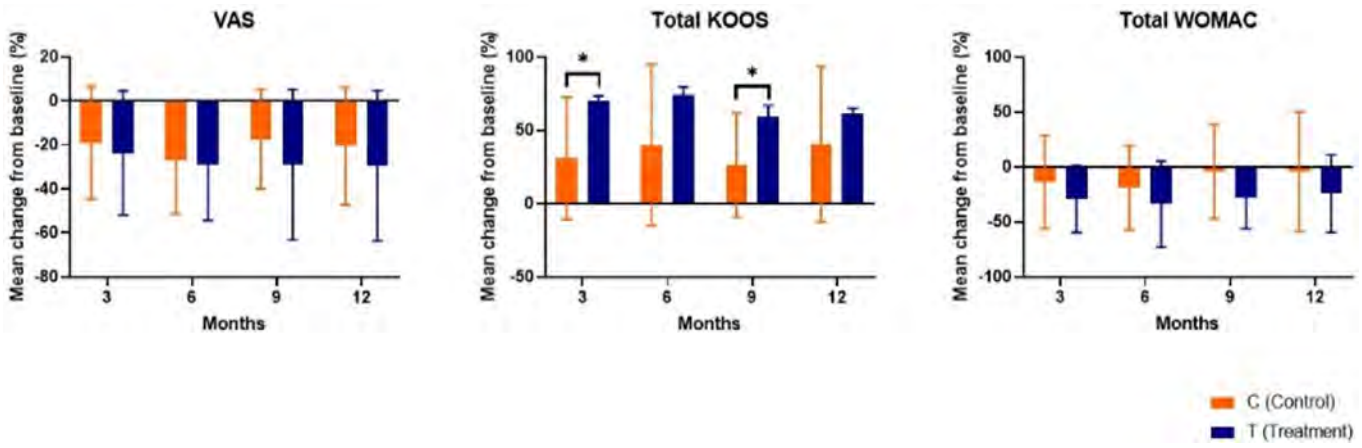

Figure 1. Percentage change in index of patient-reported outcome from the baseline to each follow-up visit.

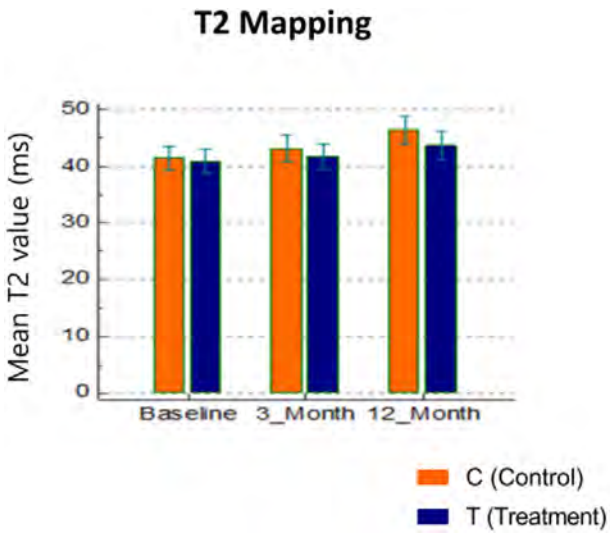

Figure 2. Comparison of T2 values in MR T2 mapping of cartilage at baseline, 3 months, and 12 months after IA injection.

Disclosure: J. Yang: None; **B. Lee**: None; **J. Lee**: None; **J. Ju**: None.

Abstract Number: 1992

Association Between Knee Osteoarthritis Pain and Concomitant Drug Use: A Post-hoc Analysis of Two Phase 3 Clinical Trials

Claire Miller[1], Matthew Baker[2], Peter Alexandersen[3], Alejandro Mondragón[1], Ida Sofie Adrian[1], Morten Karsdal[4], Jeppe Andersen[5] and Asger Bihlet[1], [1]NBCD, Soeborg, Denmark, [2]Stanford University, Menlo Park, CA, [3]Sanos Clinics, Gandrup, Denmark, [4]Nordic Bioscience, Herlev, Denmark, [5]Sanos Group, Soeborg, Denmark

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1977–1995) Osteoarthritis – Clinical Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with knee osteoarthritis are often overweight and suffer from comorbidities, which are frequently treated pharmacologically. Our understanding of the potential disease-modifying and/or symptom-modifying effects of commonly used pharmacological treatments is scarce, but recent studies have indicated beneficial effects of metformin, antihistamines, and vitamin D. The objective of this analysis was to investigate the effects of commonly used medications on changes in structural outcomes and WOMAC pain over a two-year period.

Table: Concomitant use and associations with change in WOMAC pain/JSW over 2 year (adjusted for baseline variables)

	Treatment duration group, days	Mean ΔWOMAC pain (0-500 mm), mm (SE), *n*				Mean ΔJSW, mm (SE), *n*			
		Target	p-value	Non-Target	p-value	Target	p-value	Non-Target	p-value
N02B, Other analgesics and antipyretics	0	-119 (4.4), *1178*	0.33	-66 (5.7), *178*	**0.03**	-0.37 (0.03), *521*	0.42	-0.25 (0.03), *514*	0.09
	1-49	-122 (8.6), *172*		-74 (10.8), *172*		-0.30 (0.06), *125*		-0.15 (0.06), *123*	
	50-299	-125 (12.0), *76*		-26 (15.8), *76*		-0.33 (0.08), *65*		-0.39 (0.08), *62*	
	≥300	-111 (3.6), *780*		-53 (4.4), *780*		-0.30 (0.03), *774*		-0.24 (0.02), *752*	
M01A, NSAIDs	0	-125 (4.3), *1187*	**0.02**	-67 (5.8), *1187*	0.18	-0.29 (0.03), *546*	0.14	-0.23 (0.03), *538*	0.76
	1-49	-112 (7.3), *218*		-55 (8.4), *218*		-0.31 (0.05), *165*		-0.23 (0.05), *162*	
	50-299	-98 (4.3), *107*		-42 (12.4), *107*		-0.28 (0.07), *96*		-0.28 (0.06), *93*	
	≥300	-111 (3.8), *694*		-54 (4.7), *694*		-0.37 (0.03), *678*		-0.26 (0.03), *658*	
C10A, Lipid modifying agents, plain	0	-115 (3.1), *1733*	0.87	-57 (3.9), *1733*	0.10	-0.33 (0.02), *1030*	0.32	-0.25 (0.02), *1009*	0.56
	1-49	-129 (23.2), *18*		-36 (29.6), *18*		-0.04 (0.17), *15*		-0.10 (0.16), *14*	
	50-299	-125 (17.2), *43*		-118 (25.1), *43*		-0.42 (0.12), *33*		-0.13 (0.11), *33*	
	≥300	-114 (4.9), *412*		-58 (6.2), *412*		-0.32 (0.03), *407*		-0.24 (0.03), *395*	
J01C, Beta-lactam antibacterials, Penicillins	0	-116 (2.9), *1777*	0.63	-59 (3.7), *1777*	0.52	-0.33 (0.02), *1160*	**0.04**	-0.25 (0.02), *1130*	0.26
	1-49	-111 (5.47), *416*		-54 (7.0), *416*		-0.28 (0.04), *314*		-0.20 (0.04), *310*	
	50-299	-137 (34.9), *10*		-23 (38.5), *10*		-0.70 (0.24), *8*		-0.27 (0.22), *8*	
	≥300	-159 (56.9), *3*		-149 (94.1), *3*		-1.13 (0.39), *3*		-0.77 (0.36), *3*	
B01A, Antithrombotic agents	0	-115 (2.9), *1877*	0.33	-58 (3.7), *1877*	0.58	-0.34 (0.03), *1187*	0.58	-0.25 (0.02), *1169*	0.86
	1-49	-145 (16.7), *53*		-47 (19.6), *53*		-0.31 (0.12), *32*		-0.27 (0.13), *24*	
	50-299	-117 (17.7), *38*		-86 (22.2), *38*		-0.30 (0.12), *31*		-0.16 (0.11), *31*	
	≥300	-112 (6.6), *238*		-57 (8.3), *238*		-0.27 (0.04), *235*		-0.23 (0.04), *227*	
C09A, ACE inhibitors	0	-111 (2.9), *1893*	**0.001**	-55 (3.7), *1893*	0.16	-0.31 (0.02), *1187*	0.46	-0.24 (0.02), *1163*	0.92
	1-49	-170 (29.7), *13*		-108 (47.2), *13*		-0.33 (0.25), *7*		-0.13 (0.25), *6*	
	50-299	-104 (14.7), *50*		-42 (17.8), *50*		-0.38 (0.10), *45*		-0.20 (0.10), *41*	
	≥300	-136 (6.4), *250*		-71 (8.1), *250*		-0.39 (0.04), *246*		-0.26 (0.04), *241*	
C03A, Low-ceiling diuretics, Thiazides	0	-114 (2.9), *1909*	0.89	-57 (3.6), *1909*	0.70	-0.30 (0.02), *1203*	**0.004**	-0.23 (0.02), *1185*	0.21
	1-49	-98 (69.7), *6*		-29 (66.5), *6*		-0.08 (0.47), *2*		0.13 (0.43), *2*	
	50-299	-115 (24.7), *22*		-90 (35.7), *22*		-0.22 (0.17), *16*		-0.11 (0.15), *16*	
	≥300	-120 (6.2), *269*		-62 (7.9), *269*		-0.47 (0.04), *264*		-0.31 (0.04), *248*	
C07A, Beta-blocking agents	0	-115 (2.8), *1924*	0.14	-56 (3.6), *1924*	0.54	-0.33 (0.02), *1215*	0.84	-0.25 (0.02), *1182*	0.10
	1-49	-169 (25.5), *15*		-84 (31.5), *15*		-0.18 (0.18), *14*		0.00 (0.16), *14*	
	50-299	-133 (20.5), *26*		-86 (26.1), *26*		-0.34 (0.14), *23*		0.01 (0.13), *23*	
	≥300	-113 (6.6), *241*		-61 (8.4), *241*		-0.31 (0.05), *233*		-0.24 (0.04), *232*	
C08C, Selective calcium channel blockers	0	-115 (2.8), *1936*	0.42	-57 (3.6), *1936*	0.41	-0.31 (0.02), *1238*	0.23	-0.24 (0.02), *1212*	0.60
	1-49	-153 (26.4), *19*		-100 (33.2), *19*		-0.30 (0.19), *12*		-0.01 (0.18), *12*	
	50-299	-125 (16.4), *44*		-81 (22.1), *44*		-0.31 (0.11), *36*		-0.24 (0.11), *32*	
	≥300	-111 (7.1), *207*		-60 (9.1), *207*		-0.42 (0.05), *199*		-0.26 (0.04), *195*	
N02A, Opioids	0	-117 (2.8), *1943*	0.39	-59 (3.4), *1943*	0.28	-0.33 (0.02), *1268*	0.82	-0.25 (0.02), *1255*	0.26
	1-49	-106 (9.6), *139*		-49 (11.7), *139*		-0.28 (0.07), *103*		-0.20 (0.06), *94*	
	50-299	-125 (18.7), *34*		-93 (23.0), *34*		-0.26 (0.13), *26*		-0.46 (0.14), *20*	
	≥300	-102 (10.6), *90*		-45 (14.2), *90*		-0.32 (0.07), *88*		-0.17 (0.07), *82*	
R06A, Antihistamines for systemic use	0	-116 (2.7), *2028*	0.70	-57 (3.5), *2028*	0.12	-0.34 (0.02), *1327*	**0.03**	-0.24 (0.02), *1294*	0.41
	1-49	-116 (12.2), *80*		-74 (16.8), *80*		-0.29 (0.08), *64*		-0.29 (0.08), *64*	
	50-299	-90 (21.5), *25*		-2 (28.3), *25*		0.00 (0.15), *21*		-0.38 (0.14), *20*	
	≥300	-118 (11.6), *73*		-72 (13.4), *73*		-0.19 (0.08), *73*		-0.15 (0.07), *73*	
A11C, Vitamin D and/or A	0	-117 (2.7), *2085*	0.26	-59 (3.4), *2085*	0.62	-0.34 (0.02), *1371*	**0.002**	-0.25 (0.02), *1338*	0.33
	1-49	-107 (26.3), *18*		-71 (33.5), *18*		0.22 (0.18), *14*		0.06 (0.16), *14*	
	50-299	-87 (18.0), *32*		-31 (22.2), *32*		-0.21 (0.12), *30*		-0.25 (0.11), *29*	
	≥300	-103 (11.8), *71*		-54 (14.9), *71*		-0.17 (0.08), *70*		-0.24 (0.07), *70*	
A10BA, Metformin	0	-114 (2.6), *2122*	**0.02**	-58 (3.4), *2122*	0.72	-0.33 (0.02), *1406*	0.82	-0.25 (0.02), *1375*	0.11
	1-49	-72 (40.2), *6*		-41 (54.4), *6*		-0.38 (0.34), *4*		0.34 (0.36), *3*	
	50-299	-86 (25.4), *15*		-27 (28.5), *15*		-0.18 (0.17), *15*		0.05 (0.16), *14*	
	≥300	-149 (12.8), *63*		-59 (18.3), *63*		-0.37 (0.09), *60*		-0.27 (0.08), *59*	

Methods: This is a post-hoc analysis of two large phase III trials investigating oral salmon calcitonin in knee OA (NCT00486434 and NCT00704847). The main inclusion criteria included American College of Rheumatology (ACR) criteria for diagnosis of knee OA and at least 150 out of 500 mm Western Ontario and McMaster Universities Osteoarthritis (WOMAC) knee pain at baseline. Eligible participants for the current study had knee x-rays with joint space width (JSW) and WOMAC pain questionnaires completed at baseline and two-year follow-up. Reported use of concomitant medication was grouped according to 3rd level ATC codes, and the duration of use was divided into the following categories: 1) no use, 2) 1-49 days, 3) 50-299 days, or 4) more than 300 days. The effects of the 13 most used medications on change in WOMAC pain and change in JSW from baseline to two years was evaluated using ANCOVA analysis, adjusting for baseline variables of age, sex, body mass index (BMI), and WOMAC pain/JSW.

Results: A total of 2,206 participants were randomized in the trials. A reduction in target knee pain was associated with the use of metformin, with changes in the WOMAC pain score of -114, -72, -86, and -149 respectively for groups 1-4 (p=0.02), as well as ACE inhibitors, with changes in the WOMAC pain score of -111, -170, -104, and -136 respectively for groups 1-4 (p=0.001) (**Table**). Non-steroidal anti-inflammatory drug (NSAID) use was associated with a reduced improvement in pain over time (p=0.02). As previously reported, associations between the use of vitamin D, antihistamines, and thiazides with delayed structural progression were significant (p=0.002, p=0.03, and p=0.005, respectively). These findings, however, did not translate into a significant association with change in pain. Finally, paracetamol use was associated with a significant reduction in pain in the non-target knee (p=0.03).

Conclusion: Based on this exploratory analysis, commonly used medications in the OA knee population, such as metformin, NSAIDs, antihistamines, ACE inhibitors, vitamin D, and thiazides, may significantly impact structural and symptomatic changes over time. Further research is needed to substantiate the observed findings and to evaluate the underlying pathways that may mediate these associations.

Disclosure: C. Miller: NBCD, 3; **M. Baker**: Mobility Bio, 8, Nēsos, 2; **P. Alexandersen**: NBCD, 3; **A. Mondragón**: NBCD, 3; **I. Adrian**: NBCD, 3; **M. Karsdal**: Nordic Bioscience, 3, 4, 8; **J. Andersen**: NBCD, 8; **A. Bihlet**: NBCD, 8, Nordic Biosciences, 3, 11.

Abstract Number: 1993

Impact of Metabolic Syndrome on Ultrasonographic Findings and Quality of Life in Patients with Early Osteoarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1977–1995) Osteoarthritis – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is a common disorder with increased incidence with age. Metabolic syndrome (MS) is frequently associated with OA, although other factors are considered the primary cause of the development of OA, such as: genetic, inflammatory, neuroendocrine, and mechanical stress. Conventional radiography (CR) is used to diagnose the changes of knee OA (KOA) (joint space, osteophytes, sclerosis); however early changes are difficult to assess, and few articles report these abnormalities. Previous research demonstrated a higher sensibility in ultrasonography (US) in detecting

early abnormalities compared to CR in early knee OA (eKOA). The objective of this study is to estimate the impact of metabolic syndrome in relation to prevalence of US findings and quality of life in patients with eKOA.

Methods: We included patients with eKOA diagnosis from out-patients clinical of rheumatology department, eKOA was describe as grade I and II by Kellgren and Lawrence scale. We evaluated for presence of metabolic syndrome based of ATP-III. Using a structured clinical questionnaire, we recorded epidemiologic data. Quality of life and joint functionality was evaluated with Lequesne index, EQ-5D and WOMAC. Patients were divided in two groups: eKOA with and without MS. An US was performed in each patient, structural changes in eKOA we evaluated was based in the OMERACT definitions. The structures evaluated include medial superior and lateral recess, anserine and infrapatellar bursitis, medial and lateral meniscus extrusion were scanned in each knee.

Statistical Analysis. Descriptive analysis of variables was done. In order to compare two variables, we used bivariate analysis, using t-student, Wilcoxon test, chi2

Results: We include 154 patients, female 132 patients (85.7%) vs. 22 men (14.3%). 51 (33%) patients with MS vs. 108 (67 %) without MS; of MS patients there were 9 (41%) men vs. 42 (59%) women (p=0.402). Median age of females was 47.03 ± 6.85 vs. 46 ± 7.43 in males (p=0.519). The patient with MS realized less physical activity compared with

Ultrasound findings	With MS (n=51)	Without MS (n=103)	P value
Injured knee			0.08
Right	33 (64)	49 (48.51)	
Left	18 (35.29)	48 (47.57)	
Dilateral	0 (0)	4 (3.96)	
Medial Superior Recess			
Synovitis			
Right	23 (45.10)	34 (36.56)	0.031
Left	23 (45.10)	42 (45.16)	0.999
Doppler			
Right	0 (0)	1 (1.08)	0.457
Left	0 (0)	0 (0)	-
Presence of infrapatellar bursa			
Right	5 (9.80)	5 (5.38)	0.318
Left	4 (7.84)	7 (7.53)	0.946
Presence of anserine bursa			
Right	1 (1.96)	0 (0)	0.175
Left	0 (0)	1 (1.08)	0.457
Lateral Recess			
Synovitis			
Right	35 (68.63)	63 (67.74)	0.913
Left	36 (70.59)	57 (61.29)	0.265
Doppler			
Right	2 (3.92)	0 (0)	0.05
Left	1 (1.96)	1 (1.09)	0.670
Medial meniscus extrusion n (mm)			
Right	8 (3.25 ± 1.58)	12 (2.5±0.90)	0.192
Left	6 (3.2 ± 0.82)	7 (2.77±1.7)	0.523
Lateral meniscus extrusion n (mm)			
Right	14 (3.06±1.29)	24(3.61±0.99)	0.152
Left	20 (2.94±2.35)	30 (3.41±1.20)	0.202
Osteophytes			
Medial femoral right knee			0.88
No osteophytes	35 (68.6)	62 (67.39)	
Grade I	9 (17.65)	19 (20.65)	
Grade II	6 (11.76)	8 (8.70)	
Grade III	1 (1.96)	3 (3.26)	
Lateral femoral right knee			0.514
No osteophytes	29 (56.86)	43 (46.74)	
Grade I	14 (27.45)	29 (31.52)	
Grade II	5 (9.80)	16 (17.39)	
Grade III	3 (5.88)	4 (4.35)	
Medial femoral left knee			
No osteophytes	23 (45.10)	56 (60.87)	0.016
Grade I	21 (41.18)	16 (17.39)	
Grade II	6 (11.76)	19 (20.65)	
Grade III	1 (1.96)	1 (1.09)	
Lateral femoral left knee			
No osteophytes	21 (41.18)	49 (53.26)	0.259
Grade I	20 (39.22)	26 (28.26)	
Grade II	9 (17.65)	17 (18.48)	
Grade III	1 (1.96)	0 (0)	

Ultrasound findings on metabolic syndrome and OA patients

patients without MS. 78.2 % without MS vs. 21.8% (p=0.02). The patient with MS reported some comorbidities: Diabetes Mellitus 38.46%, hypertension 42.1%, hypothyroidism 7.69% and others 13.73% vs patients without MS: Diabetes Mellitus 10.71%, hypertension 17.86 %, dyslipidemia 7.14, venous insufficiency 46.43%, other 17.86 (p=0.003). We found statistical significance in the metabolic syndrome group finding synovitis in medial superior recess of the right knee (p =0.031) and Doppler activity in lateral recess of right knee (p=0.05), without significance in the presence of osteophytes. Quality of life and functionality we did not find statistical significance. (Table 1)

Conclusion: Patients with eKOA have a good QofL. The ultrasound could have an important role in eKOA to find risk factors of progression and phenotypes. There are increased prevalence of risk factors in MS patients.

Disclosure: M. Gonzalez-Hernandez: None; **R. Espinosa-Morales**: None; **C. Pineda**: None; **A. Peña**: None; **A. Bernal**: None; **A. Alabarda**: None.

Abstract Number: 1994

How Is Paracetamol Prescribed in Low Back Pain and Osteoarthritis in France? Paracetamol Prescription Patterns in the Real-World General Practice

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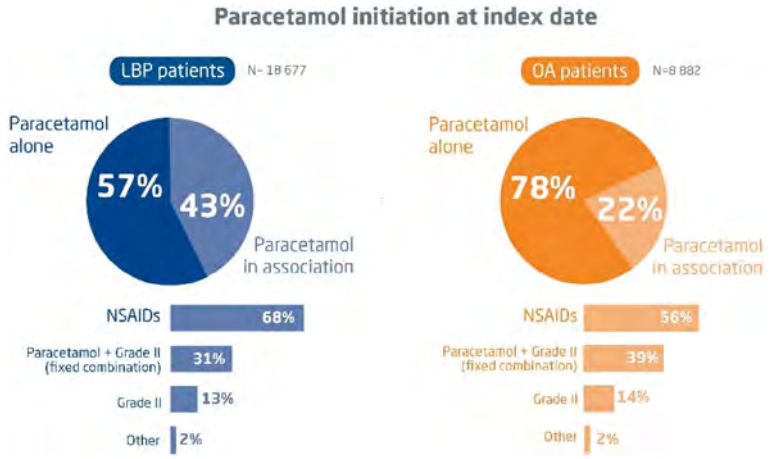
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1977–1995) Osteoarthritis – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Lower back pain (LBP) and osteoarthritis (OA) are the most frequent musculoskeletal disorders in the general population significantly impacting patients' quality of life. An adequate pain management is key. General practitioners (GPs) are the front-line decision-makers in the French primary care system. In France, paracetamol remains a first-line analgesic in LBP and OA, according to the national guidelines. Few data on the real-world paracetamol prescriptions in LBP and OA are available.

Methods: This observational retrospective cohort study using the IQVIA electronic medical records database aimed to identify the paracetamol prescription patterns in patients with LBP and OA in real-world GP practice. Prescription data of approximately 1,200 GPs and27,559 patients were analyzed. Patients aged more than 18 years old with a registered diagnosis of LBP and OA and a paracetamol prescription during a GP consultation over a 10-month period were included in the analyses.

Results: A total of 18,677 LBP and 8,882 OA patients were included. In more than 90% of these patients, the paracetamol prescriptions were not preceded by any other analgesic for the same diagnosis within the previous month. Paracetamol was mainly prescribed alone (57% LBP, 78% OA). The most frequent associations were NSAIDs and grade II analgesics. Fewer NSAID prescriptions were observed in older patients and in patients with hypertension, heart failure and renal insufficiency in both LBP and OA. Treatment discontinuation at Month 1 was the most frequent event (67% LBP and 52% OA). In case of treatment restart, paracetamol was prescribed again in 57% LBP and 81% OA patients. At Month 3, 78% LBP and 71% OA patients discontinued treatment.



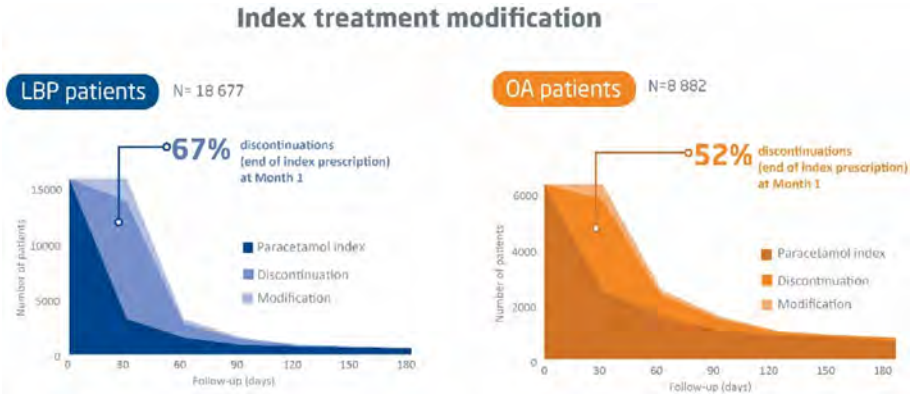
Paracetamol initiation at index date in patients with common low back pain and osteoarthritis

Conclusion: Paracetamol remains a pivotal analgesic prescribed first line in both LBP and OA from the time of initiation and during follow-up. It is the treatment of a given acute painful episode, with high proportion of treatment discontinuations after a short treatment duration. It is the analgesic of choice for recurrent pain and a satisfactory option for physicians in managing older patients and patients with comorbidities and risk factors.

	n	Age (years)#,*			Hypertension#,*		Heart failure*		Renal insufficiency		Hepatic insufficiency#,*	
Patients LBP	**15 791**	**≤ 30**	**31-49**	**> 49**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**
Paracetamol alone	9 012	54,0	47,5	61,1	64,3	52,4	72,1	57,0	75,5	56,8	59,3	57,0
Paracetamol in associations	6 779	46,0	52,5	38,9	35,7	47,6	27,9	43,0	24,5	43,2	40,7	43,0
Patients OA	**6 518**	**≤ 75**	**> 75**		**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**
Paracetamol alone	5 057	66,6	76,6		79,4	74,0	79,8	77,5	89,2	77,3	78,8	77,6
Paracetamol in association	1 461	33,4	23,4		20,6	26,0	20,2	22,5	10,8	22,7	21,2	22,4

Data % in the columns. #: p-value <0,05 (test Chi-2) for the LBP patients; *: p-value <0,05 (test Chi-2) for the OA patients
Table 1. % of paracetamol prescribed alone or in association based on patients' age and comorbidities

Proportion of patients receiving paracetamol alone or in association based on age and comorbidities



Index treatment modification in patients with common low back pain and osteoarthritis

References: 1. Blyth FM et al ., Am J Public Health. 2019 Jan;109(1):35–40. 2. Sprangers MA et al., J Clin Epidemiol. 2000 Sep;53(9):895–907. 3. Thakral M et al., J Gerontol A Biol Sci Med Sci. 2019 Apr 23;74(5):733–41. 4. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. The Lancet. 2019 Apr 27;393(10182):1745–59. 5. Goode AP et al., Curr Rheumatol Rep. 2013 Jan 11;15(2):305. 6.Gourmelen J et al, Ann Readapt Med Phys 2007;50:640-4. 7. Haute Autorite de Santé (HAS). Prise en charge du patient présentant une lombalgie commune. Published March 27, 2019. Accessed August 4, 2022. https://www.has-sante.fr/jcms/c_2961499/fr/prise-en-charge-du-patient-presentant-une-lombalgie-commune. 8. Haute Autorite de Santé (HAS) MG. Arthrose : le paracétamol en 1re intention lors des crises douloureuses. Published June 4, 2019. Accessed August 4, 2022. https://www.has-sante.fr/jcms/pprd_2974704/fr/arthrose-le-paracetamol-en-1re-intention-lors-des-crises-douloureuses

Disclosure: J. Cittée: GlaxoSmithKlein(GSK), 1, UPSA SAS, 1; **P. Lemire**: IQVIA, 3; **A. Annenkova**: UPSA SAS, 3; **J. Milon**: UPSA SAS, 3; **S. Perrot**: Grunenthal, 1, Menarini, 1, Pfizer, 1, Sanofi, 1, UPSA SAS, 1.

Abstract Number: 1995

Cross-cultural Adaptation, Reduction, and Validation of the Turkish Versions of the Flare-OA Questionnaire for Hip and Knee Osteoarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1977–1995) Osteoarthritis – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The Flare-OA is a recently developed self-reported questionnaire to assess the occurrence and severity of flares in knee and hip osteoarthritis (OA). It evaluates five aspects (pain, swelling, stiffness, consequences of symptoms, and psychological) of flare. This study aimed to translate and cross-culturally adapt the Flare-OA and its short forms using classical psychometric analysis methods in a Turkish population.

Methods: The French/English version of the questionnaire was cross-culturally adapted and translated into Turkish following an established forward–backward translation procedure. The Turkish version was checked by an expert committee for translation understandability, interpretation, and cultural relevance with ten patients (Face validity). Patients who were≥45 -years of age with clinical and radiological OA of the knee or hip, according to ACR criteria were included. The Flare OA scale consists of 33 items and has been reduced to 19 items by factor analysis and content approach. Further work with the Rasch analysis allowed to refine and shorten the questionnaire to a 16-item version with a satisfactory interval scale. The reliability of Flare-OA was assessed by internal consistency (Cronbach's alpha coefficient) and test-retest reliability at 15 days in patients without change. The sensitivity to change was assessed by standardized response mean (SRM) in those reporting change over the period. The convergent validity was assessed by the correlation of the Flare-OA with the Hip Disability and Osteoarthritis Outcome score (HOOS), Knee Injury and Osteoarthritis Outcome Score (KOOS), and the Mini Osteoarthritis Knee and Hip Quality of Life Questionnaire (Mini-OAKHQOL).

Results: A total of 185 (71.9% females) patients with a mean age of 63.2 (SD:9.1) years participated. One hundred-sixty (86.5%) of the patients had knee OA, 25(13.5%) had hip OA, and 70 (37.8%) had experienced worsening of the knee or hip OA during the last four weeks. The confirmatory factor analysis found the model with 19 items acceptable (RMSEA=0.08; SRMR=0.05; and CFI=0.95). Cronbach's alpha coefficient was 0.987 (95% CI:0.984-0.990) for 33-item,

Table. Pearson's correlation coefficients of the Flare-OA questionnaire with the other parameters for construct validity

Parameters	r	p	r	p	r	p
	33-item		19-item		16-item	
HOOS (0-100) (n=25)	0.69	0.565	0.68	0.603	0.67	0.646
KOOS (0-100) (n=160)						
The activity of daily living	-0.83	<.001	-0.83	<.001	-0.83	<.001
Other symptoms	-0.79	0.006	-0.78	0.01	-0.78	0.01
Pain KOOS	-0.83	<.001	-0.83	<.001	-0.83	<.001
Quality of life	-0.78	<.001	-0.78	<.001	-0.78	<.001
Sport and recreation	-0.69	<.001	-0.69	<.001	-0.70	<.001
Mini-OAKHQOL (0-100) (n=185)						
Mental health	-0.82	<.001	-0.81	<.001	-0.81	<.001
Pain OAKHQOL	-0.86	<.001	-0.87	<.001	-0.87	<.001
Physical activities	-0.84	<.001	-0.84	<.001	-0.85	<.001
Social functioning	-0.07	1	-0.07	1	-0.07	1
Social support	0.05	1	0.05	1	0.05	1

0.978 (95% CI:0.973-0.982) for 19-item, and 0.972 (95% CI:0.966-0.978) for 16-item. The intraclass correlation coefficient was 0.913 (95% CI:0.868-0.943), 0.915 (95% CI:0.870-0.944), and 0.912 (95% CI:0.866-0.943) in 79 patients for the test–retest reliability of the 33, 19, and 16 items, respectively. Sensitivity to change (n=89) was good in 9 patients with flare improvement [SRM 1.2 (95% CI:0.6–1.7), 1 (95% CI:0.5–1.4, and 1 (95% CI:0.5–1.5); 33, 19, and 16 items, respectively] over the period. The discriminant validity was evidenced by a significant score difference [36.2 (95% CI:29.9-42.6), 36.6 (95% CI:30.2-43.0), and 36.7 (95% CI:30.3-43.0)]for 33, 19, and 16 items, respectively between patients with and without flare. Pearson's correlation coefficients of the questionnaire with the other parameters for construct validity are represented in Table.

Conclusion: This study demonstrated that all the 33, 19, and 16-items Turkish versions of the Flare OA questionnaire are reliable and valid tools for assessing flaring in patients with knee and hip OA.

Disclosure: M. Duruöz: None; **H. Gezer**: None; **J. Epstein**: None; **M. Soudant**: None; **F. Guillemin**: None.

Abstract Number: 1996

Variation in Dual-energy X-ray Absorptiometry Reporting: A National Survey of Veterans Health Administration Clinics

Karla Miller[1], Melissa Steffen[2], Kimberly McCoy[2], Michelle Mengeling[2], Heather Davila[2], Shylo Wardyn[2] and Samantha Solimeo[2], [1]University of Utah School of Medicine, Salt Lake City, UT, [2]Department of Veterans Affairs, Iowa City VA HCS, Iowa City, IA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1996–2018) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Dual-energy x-ray absorptiometry (DXA) is an important tool to identify Veterans with osteoporosis, assess fracture risk, and monitor treatment response. Variability in DXA acquisition, analysis, interpretation, and reporting is common despite existing best practice guidelines, and can adversely impact the information communicated to the ordering provider. The purpose of this quality improvement study was to evaluate the processes for national VA DXA reporting. This project was part of a larger evaluation to understand access to and quality of DXA services in the VA.

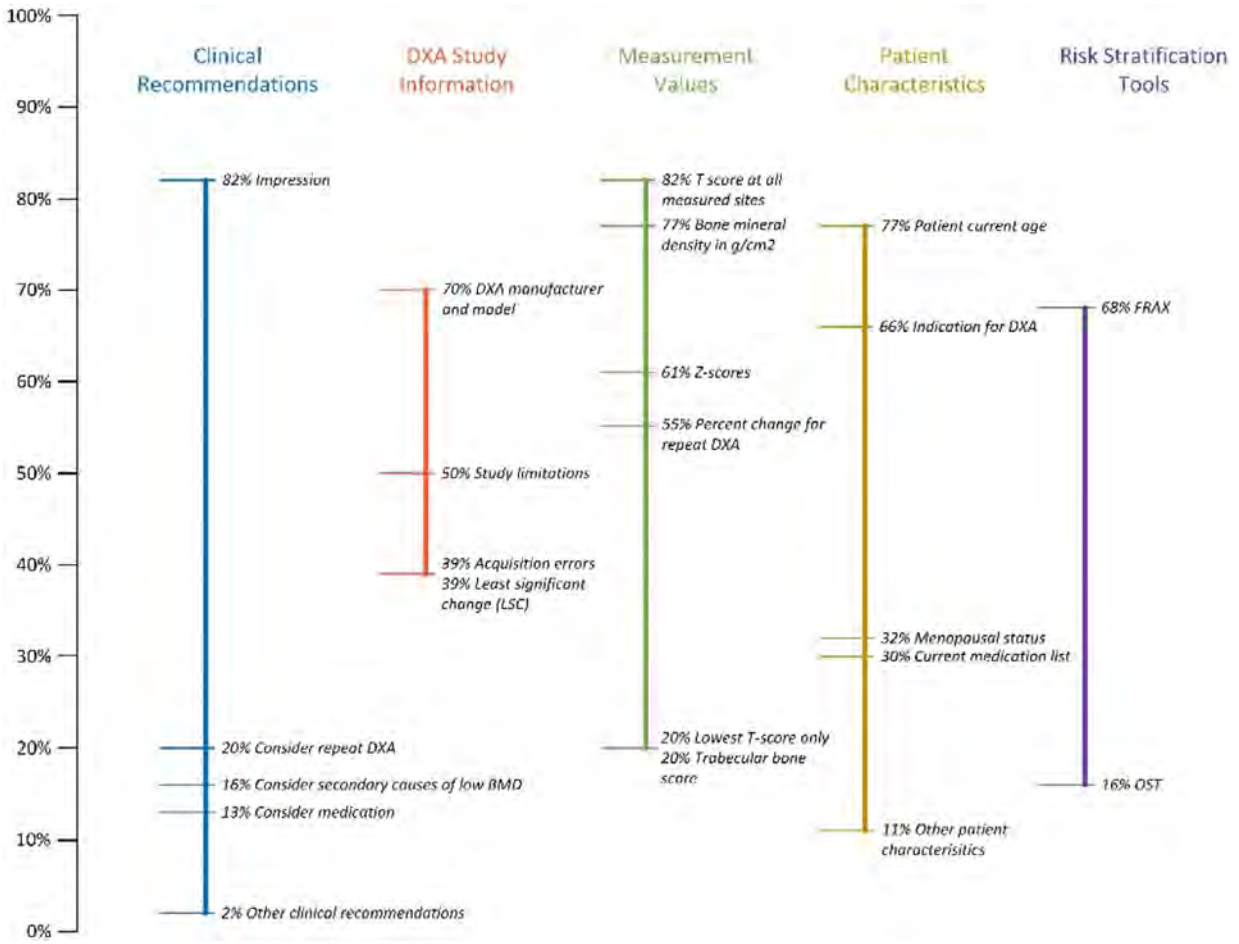
Methods: A work group of radiologists, nuclear medicine physicians, social scientists, endocrinologists, and rheumatologists were convened to develop a national bone densitometry survey. Through an iterative process, the group drafted domains, then identified topics and developed questions for each domain. The DXA reporting domain evaluated information typically included on DXA reports received by the ordering VA provider and time spent creating the reports. This study was reviewed by the Iowa City VA Research and Development Office. Survey invitations were emailed to personnel involved in DXA acquisition and interpretation at 178 facilities. Staff were given 60 days to complete the survey.

Results: Fifty-six of 178 sites (31%) completed information on data elements included in a standard DXA report. Most reports provided information on age (n=43,77%), DXA manufacturer and model (n=39,70%), and indication for DXA (n=37, 66%), while few routinely reported study limitations (n=28,50%), acquisition errors (n=22,39%), menopausal status (n=18,32%), and relevant medications (n=17,30%).DXA report elements used in clinical decision-making varied with most sites reporting T-scores at all measured sites (n=46,82%), impression (n=46,82%), bone mineral density (BMD) in g/cm2 (n=43,77%), and FRAX® (n=38,68%).Some sites reported Z-scores (n=34,61%), percent change in BMD on repeat DXA (n=31,55%), and least significant change (n=22,39%), while few reported trabecular bone score (n=11,20%), lowest T-score only (n=11,20%), and Osteoporosis Self-assessment Tool scores (n=9,16%).Few sites provided guiding recommendations beyond the DXA impression such as considering medications to reduce bone loss (n=7,13%), evaluation for

	Frequency	(%)
Clinical recommendations		
Impression	46	(82)
Consider secondary causes of low BMD	9	(16)
Consider medication	7	(13)
Consider repeat DXA	11	(20)
*Other clinical recommendations**	1	(2)
DXA study information		
DXA manufacturer and model	39	(70)
Least significant change (LSC)	22	(39)
Study limitations	28	(50)
Acquisition errors	22	(39)
Measurement values		
Bone mineral density in g/cm2	43	(77)
T-score at all measured sites	46	(82)
Lowest T-score only	11	(20)
Z-scores	34	(61)
Trabecular bone score	11	(20)
Percent change for repeat DXA	31	(55)
Patient characteristics		
Patient current age	43	(77)
Indication for DXA	37	(66)
Current medication list	17	(30)
Menopausal status, where applicable	18	(32)
Other patient characteristics†	6	(11)
Risk stratification tools		
OST	9	(16)
FRAX	38	(68)

** Other clinical recommendations include osteopenia and 10-year fracture risk*
† Other patient characteristics include patient date of birth, height, weight, patient sex, patient ID, treatment medications, date of exam, and pertinent current and past medical history

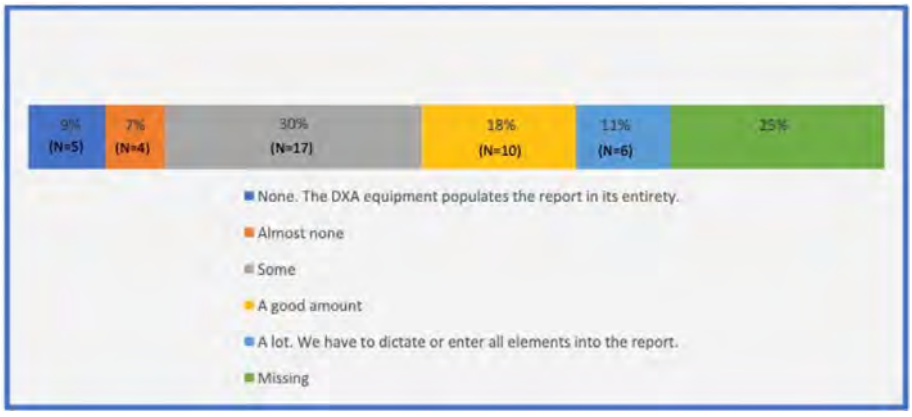
Information Routinely Included on DXA Reports (n=56)



Information Routinely Included on DXA Reports

secondary causes of osteoporosis (n=9,16%), or when to repeat DXA (n=11,20%).Nearly a third of sites (n=16,29%) indicated that DXA reports requires a "good amount" or "a lot" of time to prepare.

Conclusion: There is significant variability in the degree to which DXA facilities follow best practice standards for DXA reports, even in an integrated healthcare system. Most VA DXA reports include basic information for clinical decision-making, but many do not routinely provide elements important to interpretation of the report and clinical care guidance.



Perceived Effort Associated with Preparing a DXA Report

Many DXA sites report substantial effort is needed by diagnosticians to prepare DXA reports. This study uses self-reported data and is limited by number of respondents. Our results will be used to facilitate improvement in DXA reporting quality across radiology and specialty care services in the VA.

Disclosure: K. Miller: None; **M. Steffen**: None; **K. McCoy**: None; **M. Mengeling**: None; **H. Davila**: None; **S. Wardyn**: None; **S. Solimeo**: None.

Abstract Number: 1997

A Randomized, Double-blind, Phase III Study to Compare SB16 (Proposed Denosumab Biosimilar) to Reference Denosumab in Patients with Postmenopausal Osteoporosis

Richard Eastell[1], **Bente Langdahl**[2], Yoon-Sok Chung[3], Rafal Plebanski[4], Edward Czerwinski[5], Eva Dokoupilova[6], Jerzy Supronik[7], Jan Rosa[8], Anna Rowińska-Osuch[9], Ki-Hyun Baek[10], Audrone Urboniene[11], Sohui Ahn[12], Younghee Rho[12] and Jisuk Ban[12], [1]University of Sheffield, Sheffield, United Kingdom, [2]Aarhus University Hospital, Aarhus, Denmark, [3]Ajou University Hospital, Suwon, South Korea, [4]Klinika Zdrowej Kosci, Łódź, Poland, [5]Futuremeds, Krakowskie Centrum Medyczne sp z oo, Krakow, Poland, [6]Masaryk University, Faculty of Pharmacy, Department of Pharmaceutical Technology; MEDICAL PLUS sro, Brno, Czech Republic, [7]OsteoMedic sc A Racewicz J Supronik, Bialystok, Poland, [8]Affidea Praha, s.r.o.; Faculty of Medicine in Hradec Kralove, Charles University, Prague; Hradec Kralove, Czech Republic, [9]ETG Warszawa, Warszawa, Poland, [10]Yeouido ST. Mary's Hospital, Seoul, South Korea, [11]JSC Saules seimos medicinos centras, Kaunas, Lithuania, [12]Samsung Bioepis, Incheon, South Korea

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: (1996–2018) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: SB16 is a human monoclonal antibody to the receptor activator of nuclear factor κB ligand that has been developed as a proposed biosimilar to reference denosumab (brand name: Prolia, DEN hereafter). This Phase III study was a randomized double-blind study to compare efficacy, safety, pharmacokinetics (PK), pharmacodynamics (PD) and immunogenicity of SB16 with DEN in postmenopausal osteoporosis (PMO) patients (NCT04664959). Results up to Month 12 are presented here.

Methods: PMO patients were randomized in a 1:1 ratio to receive either 60 mg of SB16 or DEN subcutaneously at Month 0, Month 6, and Month 12. At Month 12, patients in DEN were re-randomized in a 1:1 ratio to switch to SB16 or maintain DEN. The primary endpoint was percent (%) change from baseline in lumbar spine bone mineral density (BMD) at Month 12. Equivalence between SB16 and DEN was declared if the 95% confidence interval (CI) of Least Squares Means (LSMeans) difference of % change in lumbar spine BMD at Month 12 was within the pre-defined equivalence margin. Other secondary efficacy, PD (serum C-telopeptide of type I collagen [CTX] and procollagen type I N-terminal propeptide [P1NP]), PK and safety endpoints were also measured.

Results: Among 457 patients, 225 patients were randomized to SB16 and 232 patients to DEN. Baseline characteristics were comparable between SB16 and DEN. The mean % change from baseline in lumbar spine BMD at Month 12 was5.6% and 5.3% in SB16 and DEN, respectively (Figure 1), and the difference in LSMeans % was 0.39, 95%CI [–0.36, 1.13] for the per-protocol set, and 0.33, 90%CI [–0.25, 0.91] for the full analysis set, both within the pre-defined equivalence margin. The mean % change from baseline in total hip BMD at Month 12 was 3.5% and 3.2% in SB16 and DEN, respectively. The mean % change from baseline in femoral neck BMD at Month 12 was 2.8% and 2.3% in SB16

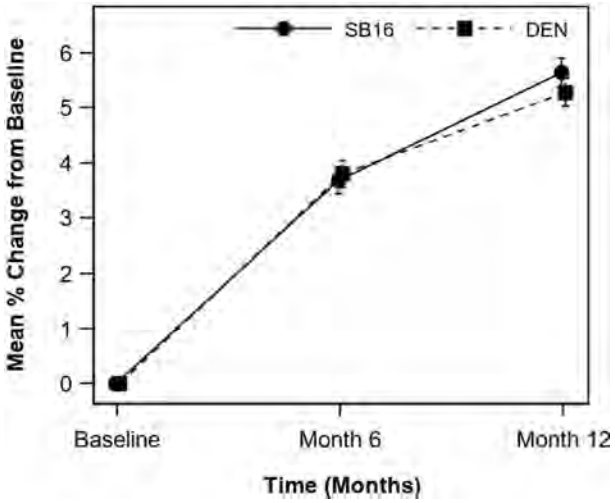


Figure 1. Mean Percent (%) Change from Baseline in Lumbar Spine BMD up to Month 12 (Full Analysis Set)

and DEN, respectively. The incidence and distribution of adverse events were comparable between SB16 and DEN up to Month 12. Serum CTX, P1NP and denosumab concentrations were comparable between SB16 and DEN up to Month 12. The median % change from baseline in serum CTX concentration over time was a decrease of at least 50% at all time points. Only 3 subjects (1 in SB16 and 2 in DEN) had non-neutralizing anti-drug antibodies.

Conclusion: This study demonstrated biosimilarity of SB16 to DEN through equivalent efficacy and comparable PD, PK, immunogenicity and safety up to Month 12.

Disclosure: R. Eastell: Alexion, 5, 6, Amgen, 6, Biocon, 2, CL Bio, 2, 5, Immunodiagnostic Systems, 2, 5, Pharmacosmos, 6, Samsung Bioepis, 2, Sandoz, 2, Takeda, 2, UCB, 6; **B. Langdahl**: Amgen, 6, Astellas, 6, AstraZeneca, 6, Gedeon-Richter, 6, Novo Nordic Foundation, 5, Samsung Bioepis, 2, 5, 6, UCB, 1, 6; **Y. Chung**: Samsung Bioepis, 2, 5; **R. Plebanski**: Samsung Bioepis, 5; **E. Czerwinski**: Samsung Bioepis, 5; **E. Dokoupilova**: AbbVie/Abbott, 5, Eli Lilly, 5, Galapagos NV, 5, Gilead, 5, GlaxoSmithKlein(GSK), 5, Hexal, 5, Janssen, 5, Novartis, 5, Pfizer, 5, Samsung Bioepis, 5, Sanofi, 5, UCB, 5; **J. Supronik**: Samsung Bioepis, 5; **J. Rosa**: Samsung Bioepis, 5; **A. Rowińska-Osuch**: Samsung Bioepis, 5; **K. Baek**: Samsung Bioepis, 5; **A. Urboniene**: Samsung Bioepis, 5; **S. Ahn**: Samsung Bioepis, 3; **Y. Rho**: Samsung Bioepis, 3; **J. Ban**: Samsung Bioepis, 3.

Abstract Number: 1998

How to Tailor Osteoporosis Therapies in Patients with Advanced Liver Disease? Variations of Renal Function by Creatinine and Cystatin C

Cristina Rodríguez-Alvear[1], Mª Carmen López-González[2], Elisabet Perea-Martínez[3], Antonio Avilés-Hernández[3], Eduardo Garín Cascales[3], Nuria Buendía Sánchez[3], Irene Calabuig-Sais[1], Pilar Bernabeu-Gonzálvez[3], Agustín Martínez-Sanchís[1], Joaquim Esteve-Vives[3], PALOMA VELA[4], Cayetano Miralles Maciá[3], Vega Jovani[5] and Mariano Andrés[1], [1]Dr Balmis Alicante General University Hospital-ISABIAL, Alicante, Spain, [2]General University Hospital Dr. Balmis, Alacante, Spain, [3]General University Hospital Dr. Balmis, Alicante, Spain, [4]Rheumatology, Hospital General Universitario Alicante, Alicante, Spain, [5]Department of Rheumatology, Hospital General Universitario Dr. Balmis, Alicante, Spain

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: (1996–2018) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rapid bone loss and increased fractures have been described after liver transplantation. Bisphosphonates are restricted in patients with significant kidney disease, as the drugs are excreted by the urine. Evaluating renal function in patients with advanced liver cirrhosis can be challenging and underestimated by standard methods, and this issue may impact the choice of the anti-osteoporosis (OP) agent.

This study analyses variations in renal function across different glomerular filtration rate (GFR) equations in patients with advanced liver disease included in a pre-transplantation assessment to tailor the use of anti-OP agents.

Methods: A descriptive cross-sectional study of patients from a tertiary center selected for a assessment before liver transplantation from February 2019 to December 2022. Sex, age, ethnicity, and serum creatinine and cystatin C (a more sensitive marker than creatinine for estimating GFR in patients with cirrhosis) levels are collected. The indication for anti-OP treatment is established in the presence of T< -1.0 by densitometry (DXA), vertebral radiographic wedging, or a history of a fragility fracture. GFR adjusted by creatinine, cystatin C, and creatinine-cystatin C was calculated using the online calculation tool MediCalc. Results are later categorized as below or above 30ml/min^2 (usual cut-off to contraindicate the use of bisphosphonates), finally comparing the rate of patients with GFR < 30 ml/min across three methods. A descriptive study is presented. Comparisons of variables are performed by Fisher's exact test, and P-values of < 0.05 are considered statistically significant.

Results: A total of 162 patients (75.9% men) were included, all Caucasian, with a mean age of 60 years (SD 7.6) and a mean BMI of 27.9 (SD 4.9). Seventy-six percent (n=120) were candidates for anti-OP therapy, and 68.5% (n=111) ultimately received it (88% bisphosphonates, 11% denosumab, and 1% teriparatide). Three percent (n=5) presented a fragility fracture, and 9.5% (n=17) showed a radiographic vertebral fracture. Fifty-one percent (n=80) had osteopenia, and 22.9% (n=36) had osteoporosis at DXA scans. Regarding renal function, mean serum creatinine and cystatin C levels were 0.99 mg/dl (SD 1) and 1.7 mg/L (SD 1), respectively. The mean estimated GFR levels using creatinine, cystatin C and creatinine-cystatin were 87 ml/min (SD 24.8), 49.3 (SD 23.4), and 63.9 (SD 23.3), respectively. The percentage of patients with GFR < 30ml/min was 1.9% if measured by creatinine, 20.5% by cystatin, and 5.6% by creatinine-cystatin (figure 1). Differences between rates were statistically significant. In this sense, anti-OP therapy was tailored accordingly in 12 patients (10.9%) with treatment indication, using denosumab instead of bisphosphonates.

Conclusion: In a setting of advanced liver disease eligible for transplantation, renal function estimates significantly varied depending on the GFR equation used, thus largely modifying the rates of patients with a contraindication for using bisphosphonates, despite the high fracture risk. Further studies are necessary to establish the best method to assess renal function in advanced liver disease patients to tailor anti-OP strategies.

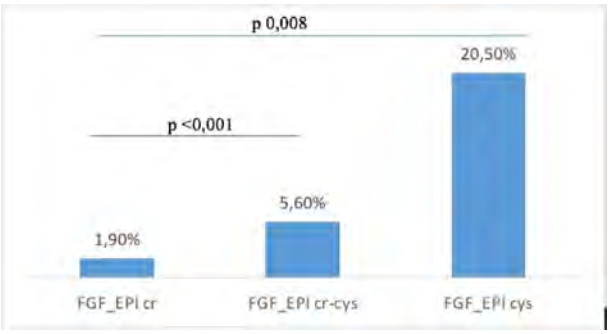


Figure 1. Patients with GFR <30 ml/min by different equations

Disclosure: C. Rodríguez-Alvear: None; **M. López-González**: None; **E. Perea-Martínez**: None; **A. Avilés-Hernández**: None; **E. Garín Cascales**: None; **N. Buendía Sánchez**: None; **I. Calabuig-Sais**: None; **P. Bernabeu-Gonzálvez**: None; **A. Martínez-Sanchís**: None; **J. Esteve-Vives**: None; **P. VELA**: AbbVie/Abbott, 5, AstraZeneca, 5, Eli Lilly, 5, 6, GlaxoSmithKlein(GSK), 6, Novartis, 5, Pfizer, 5; **C. Miralles Maciá**: None; **V. Jovani**: None; **M. Andrés**: None.

Abstract Number: 1999

One-year Incidence of Clinical Fragility Fractures After Implementing an Osteoporosis Care Protocol in Patients Eligible for Liver Transplantation

Cristina Rodríguez-Alvear[1], Mª Carmen López-González[2], Elisabet Perea-Martínez[3], Antonio Avilés-Hernández[3], Irene Calabuig-Sais[1], Maria-Luisa Peral-Garrido[4], Pilar Bernabeu-Gonzálvez[3], Agustín Martínez-Sanchís[1], Joaquim Esteve-Vives[3], PALOMA VELA[5], Cayetano Miralles Maciá[3], Vega Jovani[6] and Mariano Andrés[1], [1]Dr Balmis Alicante General University Hospital-ISABIAL, Alicante, Spain, [2]General University Hospital Dr. Balmis, Alacante, Spain, [3]General University Hospital Dr. Balmis, Alicante, Spain, [4]Vinalopó University Hospital, Novelda, Spain, [5]Rheumatology, Hospital General Universitario Alicante, Alicante, Spain, [6]Department of Rheumatology, Hospital General Universitario Dr. Balmis, Alicante, Spain

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: (1996–2018) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: In solid organ transplantation, liver transplants are among those most frequently associated with the development of low bone mass, which occurs in up to 85% of patients. The estimated incidence of fractures in the post-transplant period, especially in the first six months, ranges from 17% to 65%. However, this can drop to as low as 3.5% after establishing a fracture prevention protocol. In 2019, our center developed an action plan for preventing osteoporotic fractures in the post-transplant period. In a previous report, we observed that 77.3% of liver transplant recipients were candidates to start anti-osteoporosis treatment at the baseline evaluation.

The aim is to estimate the incidence of clinical fragility fractures in patients included in the pre-liver transplant study one year after the baseline evaluation of their bone health.

Methods: In this prospective cohort study, the incidence of clinical fragility fractures was analyzed one year after a multidisciplinary pre-liver transplant assessment in a tertiary academic center in Spain. The study included patients who underwent an initial study from February 2019 to December 2021, underwent liver transplantation and had complete follow-up at one

Table 1. Characteristics of patients with clinical fragility fractures in the year following liver transplant

		Patient			
Characteristics		**1**	**2**	**3**	**4**
Type of fracture		L2 vertebra	L1 vertebra	Hip	Distal radius
Time (months) between transplant and fracture		7	6	9	11
Sex		Male	Male	Male	Male
Age (years) at baseline		63	66	62	61
Bone densitometry at baseline	*Femoral neck*	−2.6	−0.8	−1.3	−1.2
	Total hip	−2.7	−1.2	−0.8	−0.9
	Lumbar spine	−4.5	−1.8	0.3	−2.8
Previous fracture		—	—	—	T12, L2
Treatment received		Zoledronate	—	Zoledronate	Zoledronate

year. The indication for anti-osteoporotic treatment at baseline was defined as bone densitometry with a T SCORE value of less than –1, vertebral wedging assessed by X-ray, or fragility fracture. During the annual follow-up visits, patients were examined for clinical fragility fracture. This descriptive study shows the cumulative incidence at one year and its 95% confidence interval (CI).

Results: Of the 162 patients who underwent the initial evaluation, 79 (48.8%) received a liver transplant and had a full follow-up at one year. Three-quarters of the sample were men, with a mean age of 60 years (standard deviation [SD] 7.5) and a mean body mass index (BMI) of 28.24 kg/m^2 (SD 4.35). Most (73.4%) were smokers, and 67% were moderate or heavy drinkers. At baseline, 2.5% (n=2) presented a fragility fracture, and 7.6% (n=6) a vertebral fracture as assessed by X-ray. Half (50.6%, n=40) presented osteopenia, and 21.5% (n=17) osteoporosis. Anti-osteoporosis therapy was indicated in 74.7% (n=59) and administered in 69.7% (n=55), consisting of bisphosphonates (92.7%) or denosumab (7.3%). Of the total liver transplant recipients with follow-up at one year, 4 experienced a clinical fracture (cumulative incidence 5%, 95% CI 1.9-12.3%; Table 1).

Conclusion: After establishing a protocol for preventing fractures in patients who are candidates for liver transplantation, the rate of post-transplant fractures was lower than in the historical series and comparable to another series with pre-transplant care.

Disclosure: C. Rodríguez-Alvear: None; **M. López-González**: None; **E. Perea-Martínez**: None; **A. Avilés-Hernández**: None; **I. Calabuig-Sais**: None; **M. Peral-Garrido**: None; **P. Bernabeu-Gonzálvez**: None; **A. Martínez-Sanchís**: None; **J. Esteve-Vives**: None; **P. VELA**: AbbVie/Abbott, 5, AstraZeneca, 5, Eli Lilly, 5, 6, GlaxoSmithKlein(GSK), 6, Novartis, 5, Pfizer, 5; **C. Miralles Maciá**: None; **V. Jovani**: None; **M. Andrés**: None.

Abstract Number: 2000

Efficacy of Romosozumab for Glucocorticoid-induced Osteoporosis in Patients with Rheumatic Diseases; A Prospective Study

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SESSION INFORMATION
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Session Title: (1996–2018) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Glucocorticoids are widely used to treat a variety of diseases, including rheumatic diseases. Although glucocorticoids improve the outcome for these diseases, various side effects of long-term treatment, such as osteoporosis, have become an important problem. Although the effects of glucocorticoids on bone metabolism remain unclear, Wnt signaling is now known to be involved in bone formation and resorption. We previously found that glucocorticoid therapy caused increase serum sclerostin, which inhibits Wnt signaling, and decrease Wnt3a, suggesting that suppression of Wnt/β-catenin signaling pathway might contribute glucocorticoid-induced osteoporosis (GIO). Therefore, inhibition of sclerostin could be a treatment for GIO. Romosozumab (ROMO) is a monoclonal antibody against sclerostin. Efficacy of ROMO in patients with postmenopausal osteoporosis and men with osteoporosis has been demonstrated in clinical trials. However, the effectiveness of ROMO in GIO is not clear. The purpose of this study was to evaluate the efficacy of ROMO compared to existing therapy by measuring bone mineral density (BMD) in patients recently initiated on glucocorticoid therapy.

Methods: This is a randomized, prospective, interventional study. Patients with rheumatic diseases who had not previously received osteoporosis treatment and were newly treated with prednisolone (PSL) 15 mg/day or more were randomly assigned to receive either ROMO, denosumab (DMAb), or bisphosphonate (BP). They were stratified at randomization according to age, sex, dose of PSL and T-scores of the lumbar spine or femoral neck. We measured BMD of the lumbar spine (L2-L4) and femoral neck at 0, 6, 12 months and serum bone turnover markers at 0, 3, 6, 9 and 12 months after initiation of glucocorticoid therapy.

Results: Ten patients were assigned to the ROMO group, 14 to the DMAb group, and 14 to the BP group. Base line data were shown in Table 1. The mean percent change of lumbar spine BMD from baseline at 12 months was greatest for the ROMO group among the three groups (ROMO; 5.7 ± 9.8%, DMAb; 5.2 ± 6.0%, BP; 0.5 ± 5.1%) (Figure 1). The mean change of femoral neck BMD at 12 months was greatest for the DMAb group (ROMO; -2.2 ± 6.0%, DMAb; 2.1 ± 3.7%, BP; -2.9 ± 5.8%). Serum bone alkaline phosphatase (BAP) level, a marker of bone formation, slightly increased in the ROMO group, but decreased in the DMAb group (Figure 2). Serum N-terminal propeptide of type I procollagen (P1NP) and osteocalcin (OC), other bone formation markers, decreased in all three groups, but the change was smaller in the ROMO group. Serum bone resorption markers, N-telopeptide crosslinked of type I collagen (NTX) and tartrate-resistant acid phosphatase isoform 5b (TRACP-5b) decreased in all groups. Urine pentosidine, bone matrix-related marker, decreased in all groups.

Conclusion: Even under treatment with PSL, patients treated with ROMO had increased lumbar spine BMD, but not femoral neck BMD, compared to patients receiving existing osteoporosis treatment with DMAb or BP. This is the first study to analyze the effect of ROMO on GIO, but further validation in a large number of cases is needed.

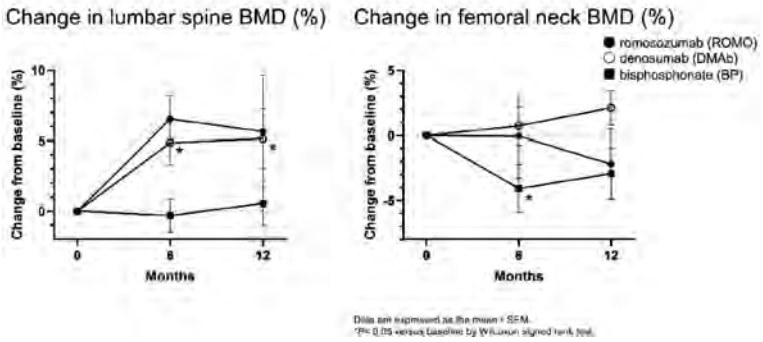
Table 1. Demographics and clinical data at baseline of the study population

	ROMO group (n=10)	DMAb group (n=14)	BP group (n=14)
Age (years)	77.0 ± 6.9	71.0 ± 9.2	72.0 ± 11.0
Male/female	2/8	6/8	4/10
Postmenopausal women (%)	8 (100)	8 (100)	10 (100)
Body mass index (kg/m^2)	20.4 ± 2.4	20.9 ± 2.5	22.1 ± 3.2
Mean daily prednisolone dose (mg)	21.5 ± 14.3	31.8 ± 17.7	31.4 ± 17.6
Bone mineral density (g/cm^2)			
Lumbar spine	0.88 ± 0.22 0.82 [0.72 - 0.99]	0.92 ± 0.24 0.84 [0.69 - 1.2]	0.96 ± 0.17 0.95 [0.83 - 1.1]
Femoral neck	0.64 ± 0.18 0.63 [0.47 - 0.75]	0.69 ± 0.15 0.67 [0.56 - 0.81]	0.66 ± 0.10 0.64 [0.61 - 0.72]
Diagnosis, No. (%)			
Polymyalgia rheumatica	8 (80.0)	6 (42.9)	6 (42.9)
RS3PE syndrome	0 (0)	2 (14.3)	1 (7.1)
Vasculitis syndrome	1 (10.0)	3 (21.4)	3 (21.4)
Polymyositis/Dermatomyositis	0 (0)	2 (14.3)	3 (21.4)
IgG4 related disease	0 (0)	1 (7.1)	1 (7.1)
Systemic lupus erythematosus	1 (10.0)	0 (0)	0 (0)
Serum markers			
eGFR (mL/min/1.73m^2)	76.6 ± 18.2 75.6 [62.0 - 89.5]	83.0 ± 21.1 82.7 [67.2 - 96.6]	78.6 ± 27.5 81.5 [61.4 - 96.2]
25-hydoroxyvitamin D (ng/mL)	14.2 ± 8.5 11.2 [8.1 - 18.4]	15.1 ± 5.7 12.6 [11.4 - 20.6]	17.0 ± 5.4 16.0 [12.0 - 22.3]
P1NP (μg/L)	33.6 ± 14.2 33.3 [23.0 - 48.1]	39.8 ± 14.2 42.3 [29.3 - 51.3]	44.2 ± 20.3 42.9 [28.7 - 50.5]
BAP (μg/L)	8.9 ± 1.5 9.2 [7.2 - 10.4]	8.3 ± 3.4 8.2 [6.1 - 9.6]	10.1 ± 4.0 9.7 [6.3 - 12.3]
NTX (nmolBCE/L)	22.2 ± 9.5 19.2 [15.5 - 32.6]	20.4 ± 6.7 19.3 [14.8 - 25.1]	20.4 ± 7.2 19.7 [13.9 - 24.0]
TRACP-5b (mU/dL)	246.0 ± 111.2 212.0 [182.3 - 349.3]	296.1 ± 139.5 284.5 [210.0 - 325.0]	239.2 ± 101.6 217.0 [168.8 - 315.5]
OC (ng/mL)	9.2 ± 3.8 9.1 [6.3 - 11.9]	12.7 ± 5.4 12.1 [8.6 - 17.1]	12.6 ± 6.1 11.1 [8.5 - 15.0]
ucOC (ng/mL)	1.7 ± 1.3 1.5 [0.5 - 3.1]	2.7 ± 2.1 1.8 [0.9 - 4.2]	3.1 ± 2.2 2.4 [1.4 - 5.1]
Urine pentosidine (pmol/mg Cr)	28.4 ± 11.3 24.5 [22.0 - 30.1]	24.6 ± 13.8 18.9 [14.7 - 33.2]	23.7 ± 10.4 21.7 [15.1 - 35.9]

BAP, bone alkaline phosphatase; BP, bisphosphonate; DMAb, denosumab; eGFR, estimated glomerular filtration rate; NTX, N-telopeptide cross-linked type I collagen; OC, osteocalcin; P1NP, N-terminal peptide of type I procollagen; ROMO, romosozumab; RS3PE, remitting seronegative symmetrical synovitis with pitting edema; TRACP-5b, tartrate-resistant acid phosphatase isoform 5b; ucOC, undercarboxylated osteocalcin. Data are expressed as the mean ± SD and median [25th to 75th percentile range].

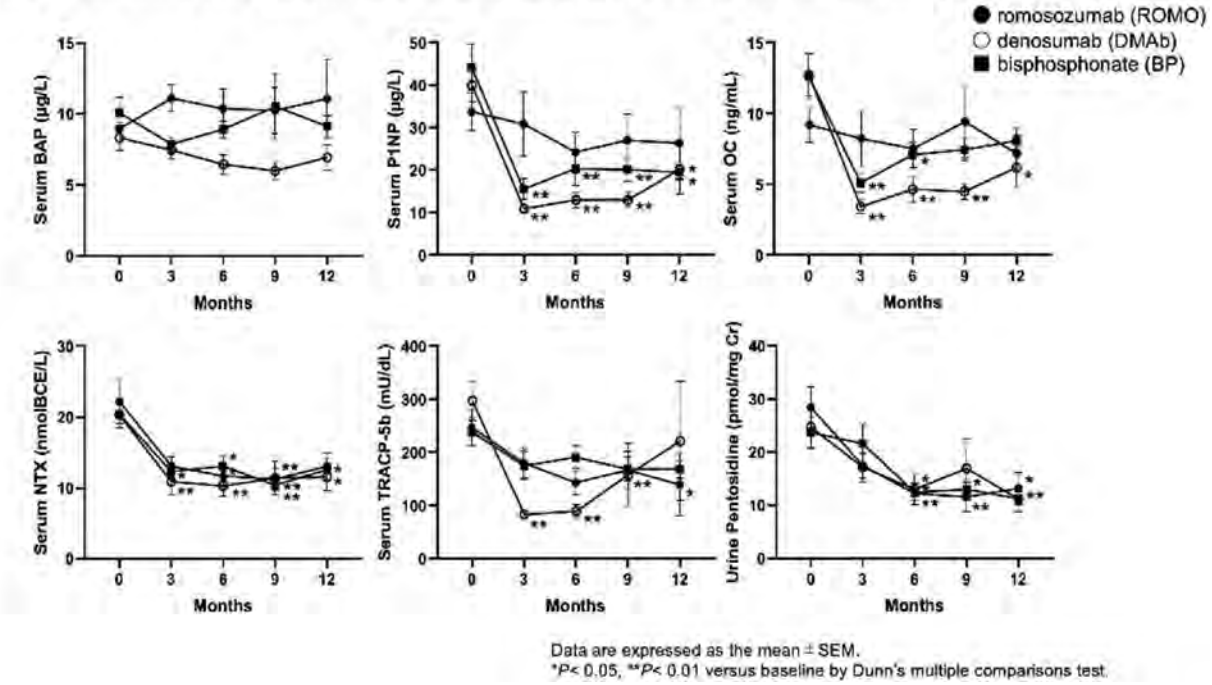
Demographics and clinical data at baseline of the study population

Figure 1. Percent change of BMD in lumbar spine and femoral neck



Percent change of BMD in lumbar spine and femoral neck

Figure 2. Serum levels of BAP, P1NP, OC, NTX and TRACP-5b, and urine pentosidine



Serum levels of BAP, P1NP, OC, NTX and TRACP-5b, and urine pentosidine

Disclosure: M. Kawazoe: Asahi Kasei Pharma Corp, 6, AstraZeneca, 6, Ayumi Pharmaceutical Corporation, 6, GlaxoSmithKlein(GSK), 6; **K. Kaneko**: AbbVie/Abbott, 6, AstraZeneca, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, Gilead, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, Novartis, 6, Pfizer, 6, UCB, 6; **S. Masuoka**: None; **S. yamada**: None; **Z. Yamada**: Janssen, 6; **S. Muraoka**: None; **K. Furukawa**: None; **H. Sato**: None; **E. Watanabe**: GlaxoSmithKlein(GSK), 5; **K. Koshiba**: None; **I. Irita**: None; **M. Kanaji**: None; **T. Nanki**: AbbVie GK, 5, 6, Asahikasei Pharma Corp., 5, 6, Astellas Pharma Inc., 6, AstraZeneca K.K., 6, Ayumi Pharmaceutical Co., 5, 6, Bristol-Myers Squibb K.K., 5, Chugai Pharmaceutical Co., 2, 5, 6, Eisai Co.,Ltd., 5, 6, Eli Lilly Japan K.K., 5, 6, GlaxoSmithKline plc., 6, Janssen Pharmaceutical K.K., 6, Mitsubishi-Tanabe Pharma Co., 5, 6, Mochida Pharmaceutical Co., Ltd., 5, 6, Nippon Boehringer Ingelheim Co., Ltd., 5, 6, Nippon Kayaku Co., Ltd., 5, Ono Pharmaceutical Co., Ltd., 5, 6, Pfizer Japan Inc., 6, Shionogi & Co., Ltd., 5, Taisho Pharmaceutical Co.,Ltd., 5, Takeda Pharmaceutical Co., Ltd., 6, Teijin Pharma Ltd., 5, UCB Japan Co. Ltd., 1, 6.

Abstract Number: 2001

Burden of Metabolic Bone Disease in Patients with IgG4-Related Disease with and Without Autoimmune Pancreatitis

Guy Katz[1], Aubree McMahon[1], Grace McMahon[1], Isha Jha[1], Marcy Bolster[2], Ana Fernandes[1], Zachary Wallace[3], Cory Perugino[1], John Stone[4] and Yasmin Hernandez-Barco[1], [1]Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital, Concord, MA, [3]Massachusetts General Hospital, Newton, MA, [4]Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Concord, MA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Metabolic bone disease (MBD), including osteopenia and osteoporosis, is common in patients with inflammatory disorders, due to disease factors and glucocorticoid (GC) use, and in those with chronic pancreatitis, due to exocrine pancreatic insufficiency (EPI). IgG4-related disease (IgG4-RD) is a systemic immune-mediated disease that commonly causes autoimmune pancreatitis (AIP) and resultant EPI. We aimed to evaluate the screening frequency and prevalence of MBD in a large single-center cohort of patients with IgG4-RD, comparing those with and without AIP.

Methods: We retrospectively assessed for the presence of MBD and associated risk factors and treatments in all patients who met ACR/EULAR Classification Criteria for IgG4-RD in our cohort using two parallel study designs. First, we conducted a chart review and extracted details on risk factors, screening frequencies, prevalence, and treatment of MBD. We limited the chart review to patients who have close follow-up in our system, defined as 1) primary care provider (PCP) in the system with ≥ 1 visit with the PCP in the previous year; or 2) ≥ 2 years of follow-up, ≥ 3 total visits in our system in the last year, and ≥ 1 visit with a non-rheumatology provider in our system in the last year. Second, we sent surveys to all living subjects in our cohort with up-to-date contact information and collected patient-reported data on MBD prevalence, risk factors, screening, and treatment. Unpaired T tests and Chi-square tests were used to compare continuous and categorical variables, respectively, between patients with and without AIP.

Results: 70 subjects (n=17 with AIP and n=53 without) met inclusion criteria for the chart review. Demographics and data on MBD, extracted from chart review, are summarized in **Table 1**. Subjects with AIP had a significantly lower mean BMI than those without. Otherwise, risk factors and MBD characteristics were similar between the two groups. Mean age was 66 years. Dual-energy X-ray absorptiometry (DXA) scans were performed in 24 (34%), and 21 subjects (30%) met World Health Organization criteria for osteoporosis or osteopenia.

Of 278 patient surveys distributed, 117 (42%) were completed (49 with AIP and 68 without). In the patient-reported data, weight was significantly lower in subjects with AIP, but other demographics and MBD risk factors were similar (**Table 2**). 73 subjects (62%) reported ≥ 3 months of cumulative GC exposure, yet only 44 (38%) had a DXA recorded. Moreover, 20 subjects (17%) reported receiving a diagnosis of MBD requiring pharmacologic intervention, yet 10 (9%) reported taking medication for MBD.

Conclusion: MBD and associated risk factors are common in patients with IgG4-RD. Although our study was underpowered to detect between-group differences, patients with AIP had lower weight and BMI than those without, emphasizing that this population may be at higher risk for MBD due to EPI. Despite high rates of MBD risk factors, DXA screening frequency

	All Subjects	IgG4-RD with AIP	IgG4-RD without AIP	P-Value
N	70	17	53	N/A
Age, years, mean (SD)	65.9 (13.4)	69.6 (12.4)	64.7 (13.6)	0.19
Female sex, n (%)	30 (43)	5 (29)	25 (47)	0.33
BMI, mean (SD)	27.3 (4.9)	25.3 (4.2)	28.0 (5.0)	**0.045**
Smoking status				
Never	34 (40)	9 (53)	25 (47)	0.77
Former	27 (39)	8 (47)	19 (36)	0.52
Current	9 (13)	0 (0)	9 (17)	0.09
Weekly alcohol use, n (%)	27 (39)	7 (41)	20 (38)	0.84
Ever on PPIs, n (%)	36 (51)	11 (65)	25 (47)	0.38
Calcium and vitamin D supplementation, n (%)				
Calcium and vitamin D	11 (16)	5 (29)	6 (11)	0.10
Calcium only	1 (1)	0 (0)	1 (2)	0.57
Vitamin D only	31 (44)	8 (47)	23 (43)	0.84
Neither	23 (33)	4 (24)	19 (36)	0.44
Unknown	4 (6)	0 (0)	4 (8)	0.26
25(OH) Vitamin D levels available, n (%)	43 (61)	12 (71)	31 (58)	0.58
25(OH) Vitamin D <30 ng/mL, n (%)	27 (39)	6 (35)	21 (40)	0.80
Prior or current immunosuppression, n (%)	58 (83)	16 (94)	42 (79)	0.56
Lifetime rituximab doses, n (%)				
0	14 (20)	1 (6)	13 (25)	0.13
1-2	18 (26)	4 (24)	14 (26)	0.84
3-4	19 (27)	6 (35)	13 (25)	0.46
5 or more	19 (27)	6 (35)	13 (25)	0.46
Fragility fracture, n (%)	6 (9)	1 (6)	5 (9)	0.66
DXA results available, n (%)	24 (34)	6 (35)	18 (34)	0.93
DXA scan results, mean (SD)				
Femoral neck T-score	-1.40 (1.26)	-1.52 (0.88)	-1.37 (1.39)	0.81
Femoral neck Z-score	0.27 (1.23)	-0.18 (0.76)	0.43 (1.34)	0.36
Total hip T-score	-0.72 (1.20)	-0.90 (0.79)	-0.65 (1.34)	0.70
Total hip Z-score	0.46 (1.30)	-0.08 (0.85)	0.68 (1.42)	0.29
L-spine T-score	-0.53 (1.49)	-0.75 (1.83)	-0.45 (1.40)	0.68
L-spine Z-score	0.83 (1.80)	-0.18 (1.91)	1.22 (1.67)	0.14
Pharmacologic treatment for MBD, n (%)	8 (11)	4 (24)	4 (8)	0.09
Investigator-determined diagnosis n (%)				
Osteoporosis	12 (17)	3 (18)	9 (17)	0.95
Osteopenia	9 (13)	2 (12)	7 (13)	0.89
Low FRAX	1/9 (11)	1/2 (50)	0/7 (0)	0.06
High FRAX	3/9 (33)	1/2 (50)	2/7 (29)	0.64
FRAX unknown	5/9 (56)	0/2 (0)	5/7 (71)	0.23
Low bone mass for age	0 (0)	0 (0)	0 (0)	N/A
None	49 (70)	12 (71)	37 (70)	0.97

Risk factors and characteristics of metabolic bone disease by chart review. BMI: body mass index, PPIs: proton pump inhibitors, AIP: autoimmune pancreatitis, DXA: dual-energy X-ray absorptiometry, MBD: metabolic bone disease.

was low, and patient-reported prescriptions and adherence to pharmacologic treatment were low. These results highlight the need for clinicians to consider MBD when managing patients with IgG4-RD. Further studies are warranted to better define and address the burden of MBD in this population.

	All Subjects	IgG4-RD with AIP	IgG4-RD without AIP	P-Value
N	117	49	68	N/A
Height, inches, mean (SD)	67.6 (3.6)	68.0 (3.2)	67.3 (3.8)	0.28
Weight, pounds, mean (SD)	180.3 (44.3)	170.4 (28.9)	187.4 (51.7)	**0.043**
Female sex, n (%)	35/115 (30)	10/49 (20)	25/66 (38)	0.09
Age, years, mean (SD)	64.7 (13.6)	65.3 (14.4)	64.2 (13.1)	0.67
Postmenopausal, n (%)	17/34 (50)	7/9 (78)	20/25 (80)	0.95
Years since last menstrual period, mean (SD)	17.0 (11.9)	18.0 (7.5)	16.8 (13.2)	0.84
Height loss ≥2 inches, n (%)	10/115 (9)	4/48 (8)	6/67 (9)	0.91
Fracture as an adult, n (%)	35/117 (30)	13/49 (27)	22/68 (32)	0.57
Vertebral	3/117 (3)	1/49 (2)	2/68 (3)	0.76
Hip or pelvic	5/117 (4)	1/49 (2)	4/68 (6)	0.32
Wrist	4/117 (3)	1/49 (2)	3/68 (4)	0.49
Other	21/117 (18)	8/49 (16)	13/68 (19)	0.73
One or more falls in the past year, n (%)	21/116 (18)	6/49 (12)	15/67 (22)	0.20
Parental history of hip or pelvic fracture, n (%)	18/114 (16)	10/49 (20)	8/65 (12)	0.28
Cumulative use of GC ≥3 months, n (%)				
Yes	73/117 (62)	30/49 (61)	43/68 (63)	0.89
No	34/117 (29)	16/49 (33)	18/68 (26)	0.54
Unsure	10/117 (9)	3/49 (6)	7/68 (10)	0.45
Treatment with immunosuppressive agents, n (%)	98/117 (84)	44/49 (90)	54/68 (79)	0.54
Daily intake of calcium ≥600mg, n (%)	57/116 (49)	25/49 (51)	32/68 (47)	0.76
Dose of calcium supplement, if taken, mean (SD)	415 (268)	326 (249)	526 (263)	0.12
Vitamin D supplementation, n (%)	73/114 (64)	34/49 (69)	39/68 (57)	0.42
Dose of Vitamin D, IU, if taken, mean (SD)	3156 (6848)	2369 (2286)	3887 (9277)	0.42
Proton pump inhibitors ≥12 weeks, n (%)				
Yes	39/117 (33)	22/49 (45)	17/68 (25)	0.07
No	73/117 (62)	26/49 (53)	47/68 (69)	0.28
Unsure	5/117 (4)	1/49 (2)	4/68 (6)	0.32
Currently taking proton pump inhibitors, n (%)	21/117 (18)	11/49 (22)	10/68 (15)	0.33

Patient-reported demographics and metabolic bone disease risk factors in patients with IgG4-related disease with and without autoimmune pancreatitis. AIP: autoimmune pancreatitis, GC: glucocorticoids, IU: international units.

	All Subjects	IgG4-RD with AIP	IgG4-RD without AIP	P-Value
N	117	49	68	N/A
Patient-reported diagnosis of osteoporosis or osteopenia requiring pharmacologic treatment, n (%)	20/116 (17)	9/49 (18)	11/67 (16)	0.80
Years since diagnosis of osteoporosis or osteopenia, mean (SD)	8.4 (9.6)	7.0 (7.4)	9.4 (11.2)	0.61
Treatment for MBD, n (%)	10/117 (9)	6 (12)	4/68 (6)	0.25
PO bisphosphonate	9/117 (8)	5 (10)	4 (6)	0.41
IV bisphosphonate	5/117 (4)	4 (8)	1 (1)	0.08
Denosumab	0/117 (0)	0 (0)	0 (0)	
PTH analogs	0/117 (0)	0 (0)	0 (0)	
Romosozumab	1/117 (1)	1 (2)	0 (0)	0.24
Raloxifene	0/117 (0)	0 (0)	0 (0)	
DXA, n (%)				
Performed	44/117 (38)	17 (35)	27 (40)	0.66
Not performed	60/117 (51)	24 (49)	36 (53)	0.77
Recommended, but patient declined	0/117 (0)	0 (0)	0 (0)	
Unsure	13/117 (11)	8 (16)	5 (5)	0.15

Patient-reported prevalence and treatment of metabolic bone disease in patients with IgG4-RD with and without autoimmune pancreatitis. AIP: autoimmune pancreatitis, MBD: metabolic bone disease, DXA: dual-energy X-ray absorptiometry.

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2, Bristol Myers Squibb, 2, 5, Celgene, 2, Chemocentryx, 2, Chugai, 2, GSK, 2, Horizon Therapeutics, 1, 2, 5, InflaRx, 2, IQVIA, 1, 2, Kyverna, 2, Mirabio, 2, NIH, 5, Novartis, 2, PPD, 2, Prometheus, 2, Q32, 2, Regeneron, 2, Roche-Genentech, 2, Roivant, 2, Sanofi, 2, 5, Spruce Biosciences, 2, Star Therapeutics, 2, Steritas, 12, Chair, Scientific Advisory Board (no fiduciary responsibilities), ZenasBio, 2; **Y. Hernandez-Barco**: Nestle Health Science, 1.

Abstract Number: 2002

Cost-Effectiveness Analysis of Sequential Treatment with Abaloparatide Followed by Alendronate in US Women and Men with Multiple Previous Fractures

Mickael Hiligsmann[1], **Stuart Silverman**[2], Andrea J Singer[3], Yamei Wang[4], Leny Pearman[4], John Caminis[4] and Jean-Yves Reginster[5], [1]Maastricht University, Maastricht, Netherlands, [2]Cedars-Sinai Medical Center and UCLA School of Medicine, Los Angeles, CA, [3]MedStar Georgetown University Hospital, Washington, DC, [4]Radius Health, Inc., Boston, MA, [5]University of Liège, Liège, Belgium

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with multiple previous fractures are at very high risk of subsequent fractures. Common treatment strategies for these patients include generic alendronate (ALN) monotherapy or sequential therapy with an anabolic agent first (such as abaloparatide [ABL] or teriparatide [TPTD]) followed by generic ALN. Due to mounting pressure on healthcare systems, cost-effectiveness analyses are increasingly important to support decision makers in efficient healthcare resource allocation. This study was designed to evaluate the cost-effectiveness of sequential treatment with ABL followed by ALN compared to relevant alternative strategies in women and men with two previous fractures in the United States (US).

Methods: A lifetime microsimulation model estimated the US healthcare costs (in 2022 dollars) and quality-adjusted life years (QALYs) associated with sequential ABL/ALN and three relevant comparators: (1) a similar sequence beginning with unbranded TPTD; (2) generic ALN monotherapy; and (3) no treatment, which must be included as a comparator as many patients at very high fracture risk do not receive an osteoporosis medication. The analyses were conducted in men and women aged 50 to 90 years with two previous fractures and densitometric osteoporosis (bone mineral density T-score ≤–2.5). Sequential ABL/ALN is considered dominant if it is associated with more QALYs for lower costs than the comparator strategy, and is cost-effective if the cost per QALY gained falls below the US cost-effectiveness threshold of $150,000 per QALY gained. Various scenarios and sensitivity analyses were conducted to investigate uncertainty, including analyses on gender, age (50-90 years), and site of previous fractures.

Results: In both US women and men aged 50-90 years, sequential ABL/ALN was dominant compared to sequential unbranded TPTD/ALN. The costs per QALY gained of sequential ABL/ALN compared to no treatment were below the cost-effectiveness threshold in men aged ≥50 years with two previous fractures, in women aged ≥55 years with two previous fractures, and those aged ≥50 years with history of hip or vertebral fracture. When compared to ALN monotherapy, the costs per QALY gained of sequential ABL/ALN were estimated at $82,288 and $111,584 in men and women aged 70 years with two previous fractures, respectively. These numbers decreased to $35,283 and $66,707 with history of hip fracture. Sequential ABL/ALN was further cost-effective in men ≥50 years with two previous fractures, in women ≥55 years with two previous fractures including a hip or vertebral fracture, and in women ≥65 years for other types of fractures.

Conclusion: Sequential ABL/ALN is dominant in all analyses completed compared to unbranded TPTD/ALN and is cost-effective compared to generic ALN monotherapy in men aged ≥50 years, in women aged ≥55 years with history of hip or vertebral fracture, and in women aged ≥65 years with other fracture types.

Disclosure: M. Hiligsmann: Amgen, 5, IBSA, 6, Mylan Pharmaceuticals, 6, Radius Health, Inc., 5, UCB, 2; **S. Silverman**: Amgen, 2, 5, Radius Health, Inc, 2, 5; **A. Singer**: Agnovos, 2, Amgen, 2, 6, Radius Health, Inc, 2, 6, Radius Health, Inc., 5, UCB, 2, 5; **Y. Wang**: Radius Health, Inc, 3; **L. Pearman**: Radius Health, Inc, 3; **J. Caminis**: Radius Health, Inc, 12, Former Employee; **J. Reginster**: CNIEL, 5, 6, Dairy Research Council, 6, IBSA-Genevrier, 2, 5, 6, Mylan, 5, 6, Pierre Fabre, 1, Radius Health, Inc, 2, 5, 5, Teva, 2, 6.

Abstract Number: 2003

Effects of Abaloparatide on Cortical and Trabecular Compartments by 3D-DXA in Men with Osteoporosis

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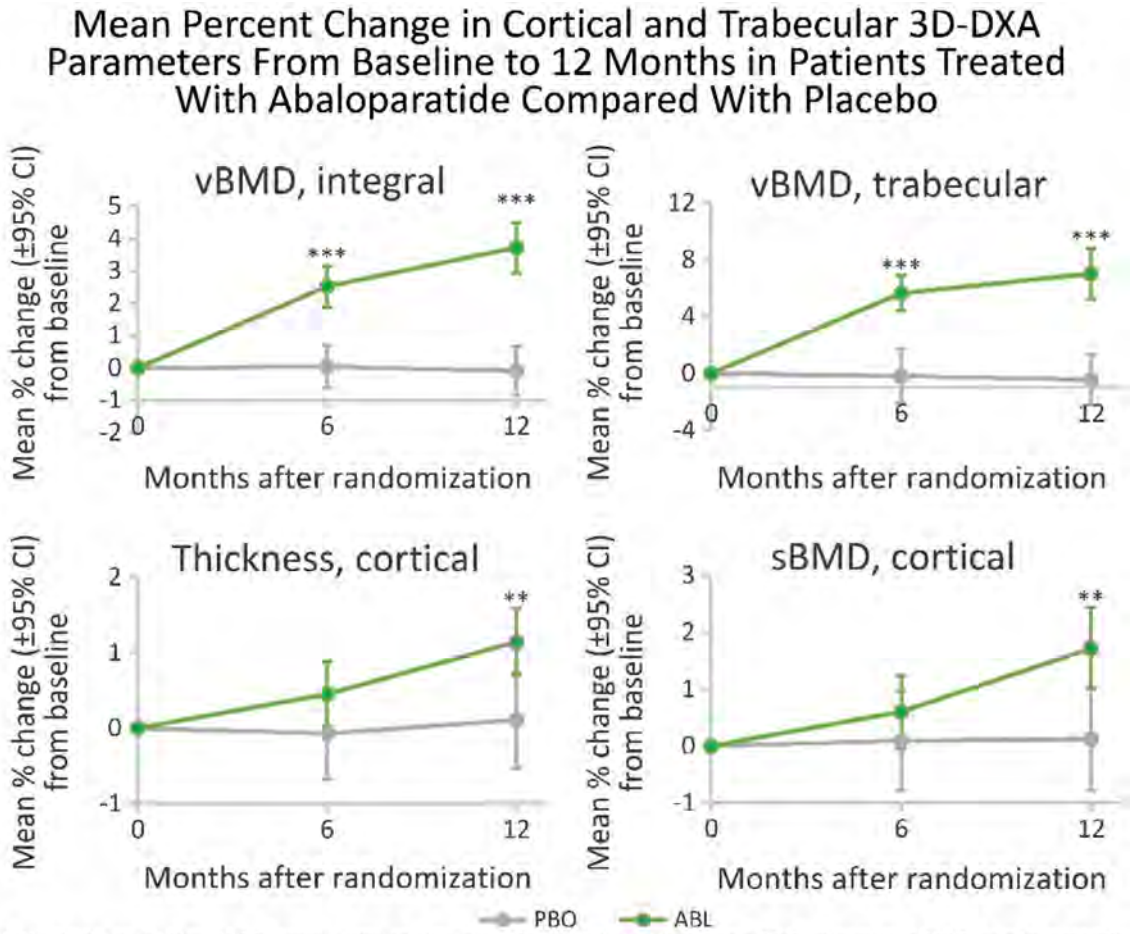
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Abaloparatide (ABL) increases BMD in men with osteoporosis. In the Abaloparatide for the Treatment of Men with Osteoporosis (ATOM) trial, DXA-measured BMD change with ABL 80 μg/day was greater than placebo (PBO) at the lumbar spine, total hip, and femoral neck. The purpose of this study was to evaluate the effects of ABL on cortical and trabecular compartments of the proximal femur in men with osteoporosis using 3D-DXA modeling.

Methods: Blinded hip DXA images from all randomized men in the ATOM trial (n=149 ABL; n=79 PBO) were retrospectively analyzed by 3D-DXA (3D-Shaper software v2.12.0, 3D-Shaper Medical) to evaluate changes from baseline at months 6 and 12 at the total hip. The ATOM trial included men with T-scores ≤–2.5 at the lumbar spine or hip. Men with T-scores ≤–1.5 with a history of radiologic vertebral fracture or low trauma nonvertebral fracture in the past 5 years or ≤–2.0 if >65 years of age were also eligible. Comparisons from baseline were made using paired *t* tests. Between-group comparisons were made for percent change from baseline data based on a mixed-effect repeated-measure model with treatment, visit, treatment-by-visit interaction and DXA scanner as fixed effects. Other covariates include BMI, age, and value at baseline.

Results: At 12 months, significant within group increases from baseline ($P < 0.0001$) in integral volumetric BMD (vBMD) (3.7%), trabecular vBMD (7.0%), cortical thickness (1.1%), and cortical surface BMD (sBMD; 1.7%) were observed with ABL. Mean percent change from baseline was greater for ABL compared to PBO ($P < 0.01$) for all 4 variables (integral vBMD, trabecular vBMD, cortical thickness, cortical sBMD) at 12 months (**Figure**).Greater increases ($P < 0.0001$) were also observed at 6 months between ABL and placebo for integral vBMD (2.5% vs 0.04%) and trabecular vBMD (5.7% vs –0.2%).

Conclusion: In men with osteoporosis in ATOM, 6 months of ABL improved trabecular 3D-DXA parameters at the total hip; 12 months of treatment improved cortical and trabecular 3D-DXA parameters at the total hip. These results are broadly consistent with those in postmenopausal women in the ACTIVE study.



ABL, abaloparatide; BMD, bone mineral density; CI, confidence interval; PBO, placebo; sBMD, surface BMD; vBMD, volumetric BMD.
** $P<0.01$; *** $P<0.0001$

Disclosure: R. Dhaliwal: Alexion, 1, 5, Amgen, 1, Ascendis, 1, Radius Health, Inc, 1, 5, Shire, 5, Takeda, 5, Ultragenyx, 1; **J. Boxberger**: Radius Health, Inc, 3; **Y. Wang**: Radius Health, Inc, 3; **B. Mitlak**: Radius Health, Inc, 3; **L. Humbert**: 3D-Shaper Medical, 3, 11; **N. Binkley**: Amgen, 2, 5, Radius Health, Inc, 2, 5.

Abstract Number: 2004

Bone Health Following Bariatric Surgery: A Single Center Quality Improvement Study

Andrew Benck, Haley Zimmerman, Amy Trang, Najia Shakoor and Sonali Khandelwal, Rush University, Chicago, IL

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoporosis related fractures cause significant morbidity and mortality. Bariatric weight loss surgery is an independent risk factor for osteoporosis. Post-surgery dual energy X-Ray absorptiometry (DEXA) scans as well as close monitoring for calcium and vitamin D are suggested by current Bariatric surgery guidelines. This retrospective study

Table 1

Mean Age + STD	39.41+/- 6 years
Gender	
Male	50 (14.40%)
Female	298 (85.60%)
Race	
African American	185 (53.2%)
White	82 (23.6%)
Asian	4 (1.1%)
Hispanic	69 (19.8%)
Other	8 (2.3%)
Surgery Type	
Roux-En-Y Gastric Bypass	132 (37.9%)
Sleeve Gastrectomy	216 (62.1%)
Laparoscopic adjustable gastric band	0 (0%)
Biliopancreatic diversion with duodenal switch	0 (0%)
BMI	
BMI mean (Pre-Surgery)	46.7 Kg/m^2 +/-7.0
BMI Mean (Post-Surgery)	37.03 K Kg/m^2 +/-7.3
Vitamin and Calcium Levels Pre and Post-Surgery	
Mean Vit D Pre-surgery	20.16 ng/dl +/-11.6
Mean Vitamin D level Post-surgery	30.96 mg/dl +/- 16.51
Mean Calcium level Pre-surgery	9.48 ng/mL +/- 0.44
Mean Calcium Level Post-surgery	9.22 ng/mL +/- 0.48

of bariatric surgery patients was conducted to determine if current guidelines for osteoporosis screening are being adhered to. In addition, educational seminars were provided to increase bone health education to bariatric surgery providers and patients.

Methods: This was a single-center, retrospective study of patients who had bariatric surgery from 2018 through 2020. Qualifying surgeries were Roux-en-Y gastric bypass, sleeve gastrectomy, Lap band and biliopancreatic diversion with duodenal switch. Patients aged 18-49 were included. Excluded were patients with any history of steroid use, autoimmune disease, primary hyperparathyroidism and malabsorption disorders or those already being treated for bone loss. Demographics, type of surgery, pre and post-surgical vitamin D calcium levels and BMI were collected. Descriptive statistics and paired samples t-tests were used for comparisons. Two educational interventions were completed after the results of the retrospective data. One included an educational lecture on bone health guidelines for this population delivered to bariatric surgeons. Another lecture was directed towards patients who were planning or had completed surgery. Pre and post educational surveys were delivered.

Results: 348 charts were reviewed. Demographic data and results are in Table 1. Calcium levels statistically decreased post-surgically while vitamin D levels increased . The decrease in calcium was most pronounced with Roux-en-Y gastric bypass as compared to sleeve gastrectomy 9.13 ng/ml vs. 9.27 ng/ml ($P< 0.01$). Only one patient in the study period had a post-surgical DEXA scan which revealed low bone mineral density for chronological age (Z score -2.7). Surveys following educational intervention revealed very positive results using Likert scale (Image1 and 2) but did not increase DEXA scans in the study period.

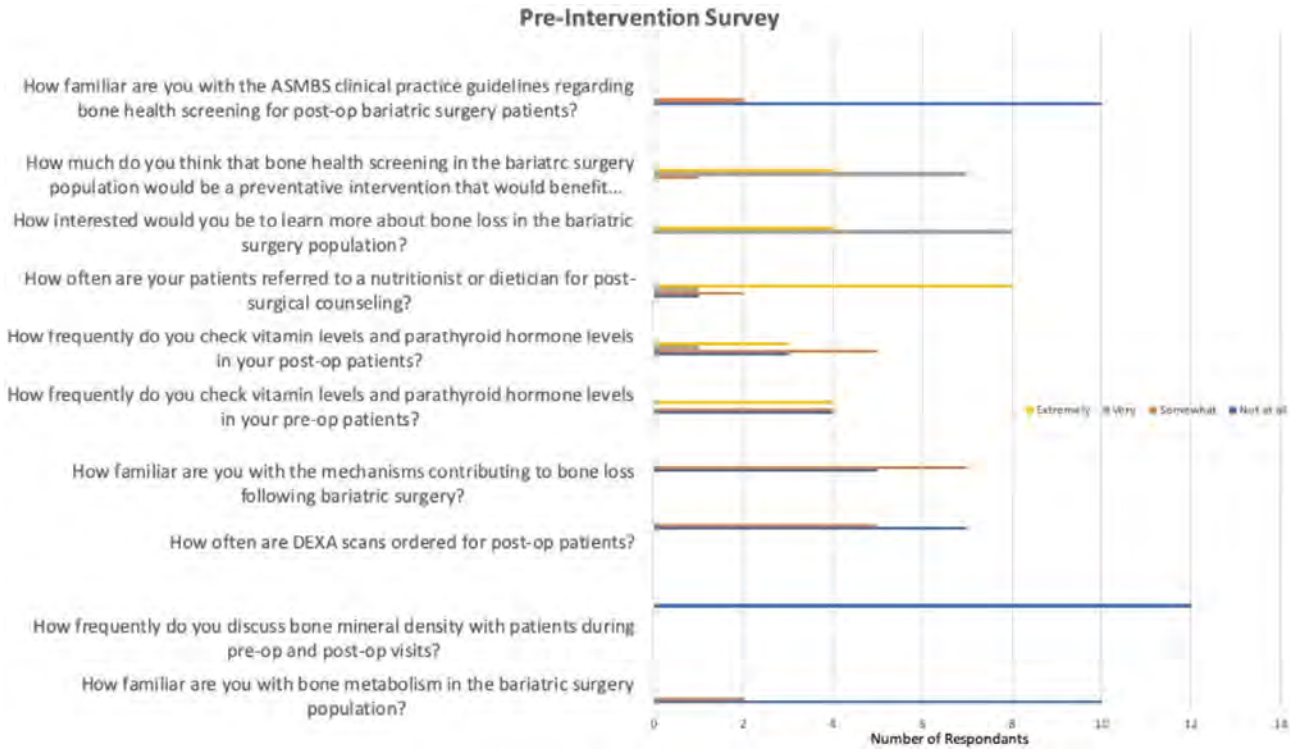


Image 1- Pre-education Survey Results

Conclusion: Screening with DEXA scans after bariatric surgery is not being done based on this brief retrospective study. This may be due to poor follow-up after surgery or the short study period following the interventions. Continued educational interventions may be successful if expanded to target primary care providers in addition to bariatric surgeons given the poor rate of patient follow-up. Our educational interventions were positively surveyed. Moreover this study found, post-surgically,

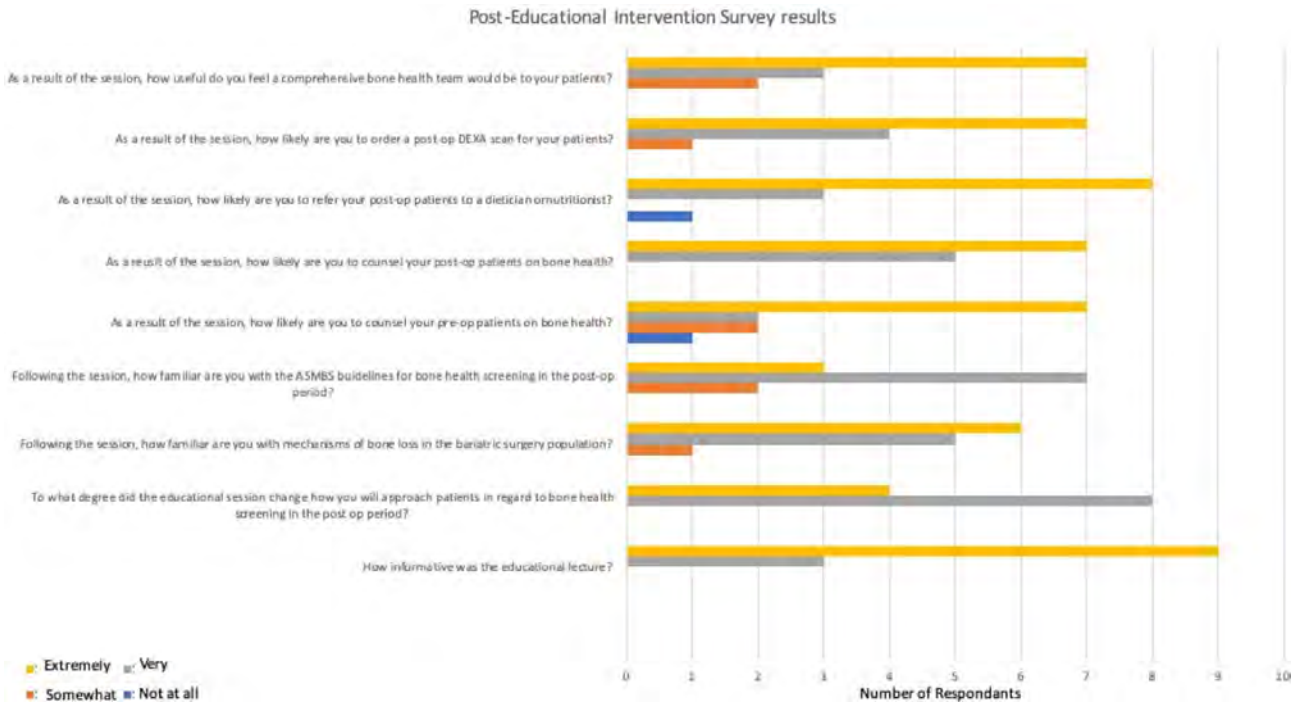


Image 2- Post-education Survey Results

calcium levels decreased and vitamin D level increased. In addition, calcium levels decreased more with Roux-en-Y gastric bypass. The inverse relationship of Vitamin D with weight loss has been reported elsewhere presumed to be related to redistribution of adipose stored vitamin D. These findings raise another potential area for modification of practice. Perhaps in addition to guided Vitamin D management and supplementation more dedicated calcium supplementation management should also be considered for these patients.

Disclosure: A. Benck: None; **H. Zimmerman**: None; **A. Trang**: None; **N. Shakoor**: None; **S. Khandelwal**: None.

Abstract Number: 2005

Secondary Prevention of Osteoporosis in Hip Fracture Care for Elderly Patients. Clinical and Functional Profile of Users

Belén Miguel Ibáñez, Alfonso González Ramírez, Olga Martínez González, Ana Isabel Turrión Nieves, Marta Ibáñez Martínez, Carolina Cristina Chacón Vélez, Laura Blanco Ramis, Manuel Cipriano Martín Martínez, Cristina Hidalgo Calleja, Carlos Alberto Montilla Morales, Susana Gómez Castro, Juan Francisco Blanco Blanco and Carmen Pablos Hernández, University Healthcare Complex of Salamanca, Salamanca, Spain

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoporosis is a first-rate problem in an increasingly ageing population. Falls among the elderly are a severe geriatric syndrome with relevant secondary effects. Fractures associated with both entities among the elderly are a cause of high costs and high morbidity and mortality rates. An adequate treatment of osteoporosis and fall prevention are essential factors to safeguard their well-being. The objective of this study is to analyze the clinical characteristics and circumstances of hip fractures, as well as previous fractures and anti-osteoporotic treatments in 239 elderly patients who were admitted with hip fractures in the year 2022 in the Department of Geriatric Care and Traumatology.

Methods: A descriptive, retrospective, observational and longitudinal study was conducted by analyzing the geriatric indexes, and demographic and clinical characteristics of 239 patients aged 66-99 years old who presented with low-impact hip fracture in 2022. The data analysis was carried out with SPSS.

Results: The average age of the patients was 86.79 years, with a range of 66-99 years and a predominance of women (180). During admission, a comprehensive geriatric evaluation of the situation prior to the fracture was completed. At a functional level (Table 1), the Barthel Index revealed that 182 patients had slight dependency in their daily life activities. Regarding their instrumental activities, 55 patients showed a score ≥5 out of 8. After their hip fracture, 229 patients received physical therapy in hospital and 108 patients required social interventions for their subsequent recovery. All the hip fractures were the consequence of low-impact trauma. 168 patients had suffered falls over the last year. However, according to the Downton scale, all of them (239) presented at least one risk factor for falls. These factors are detailed in Table 2. Prior to their hip fracture, 110 patients had suffered a previous low-impact fracture. The most common location was the lower limbs (46). Table 2 shows the different types of fractures. More than one previous fracture was found in 14 cases. None of the patients with previous fractures were being monitored by the Rheumatology Department. Only 22 out of the 110 patients with previous fractures were receiving or had received antiresorptive or bone-forming therapy with bisphosphonates (16), denosumab (3), denosumab after bisphosphonates (2) or teriparatide after bisphosphonates (1). All the patients received anti-

TABLE 1: DEMOGRAPHY, BASAL CONDITION AND COMORBIDITIES PRIOR TO HIP FRACTURE		
DEMOGRAPHY	Gender (female/male)	180(75.31%)/59 (24.69%)
	Age range Average age:86.79	66-79: 32/13.39% 80-89: 119/49.79% 90-99:88/36.82%
PREVIOUS BASAL CONDITION **Geriatric indexes**	Barthel	N/A: 5/2.09% Complete, <20 points: 10/4.18% Severe, 20-35 points: 18/7.53% Moderate, 40-55 points: 24/10.04% Mild, ≥60 points:182/76.15%
	Lawton Brody	N/A: 5/2.09% 0-1: 116/48.54% 2-4: 63/26.36% ≥5: 55/23.01%
	Katz	N/A:4/1.67% A-B: 107/44.77% C-D-E:83/34.73% F-G: 45/18.83%
PREVIOUS CLINICAL SITUATION	Renal glomerular filtration < 30 ml/min/m^2: 69/28.87% Digestive malabsorption: 35/14.64% Radiation history: 7/2.93%	

Table 2: FRACTURES, FALLS, OSTEOPOROSIS AND TREATMENTS		
HIP FRACTURE: 239/100%		
TYPES	CONDITIONS	TREATMENT UPON DISCHARGE: 239/100%
Intracapsular: 118/49.37% Extracapsular: 111/46.44% Periprosthetic: 10/4.18%	Low-impact trauma: 239/100% In-hospital physical therapy: 229/95.81% Social intervention: 108/45.19%	Denosumab: 165/69.04% Bisphosphonates: 66/27.61% Teriparatide: 8/3.35%
PREVIOUS FALLS: 168/70.29%		
RISK FACTORS:239/100%	Multidrug therapy: 191/79.92% Sensory disorders: 177/74.06% Gait disorders: 204/85.36%	
PREVIOUS FRACTURES: 110/46.03%		
TYPE		ANTIRESORPTIVE OR BONE-FORMING TREATMENT: 22/20%
Upper limb: 39 Lower limb: 46 Vertebral fractures: 25 **≥2 previous fractures: 14**		Bisphosphonates: 16/72.73% Denosumab: 3/13.64% Denosumab after bisphosphonates: 2/9.09% Teriparatide after bisphosphonates: 1/4.54%

osteoporotic treatment as secondary prevention upon discharge, together with denosumab (165), bisphosphonates (66) or teriparatide (8), after ruling out the scenarios included in Table 1 which could advise against their use.

Conclusion: Osteoporosis is an underdiagnosed and undertreated condition. Previous fractures often go untreated, which leads to new fractures that compromise the patients' independence and quality of life. Hip fractures show the highest rates of morbidity and mortality. Falls play a major role in fractures among the elderly population. Their primary prevention and an adequate osteoporotic treatment must be a priority in elderly care.

Disclosure: B. Miguel Ibáñez: None; **A. González Ramírez**: None; **O. Martínez González**: None; **A. Turrión Nieves**: None; **M. Ibáñez Martínez**: None; **C. Chacón Vélez**: None; **L. Blanco Ramis**: None; **M. Martín Martínez**: None; **C. Hidalgo Calleja**: None; **C. Montilla Morales**: None; **S. Gómez Castro**: None; **J. Blanco Blanco**: None; **C. Pablos Hernández**: None.

Abstract Number: 2006

Improvement of Care: Osteoporosis Screening in a Resident-led Primary Care Clinic

Massiel Jimenez Artiles[1], Roshan Subedi[2], Qi Wang[3], Bishara Jahshan[4], Khalid Gadir[4] and Waleed Quwatli[5], [1]Unity Hospital, Rochester Regional Health, Greece, NY, [2]Rochester Regional Health/Unity Hospital, Greece, NY, [3]Rochester Regional Health/Unity Hospital, Rochester, NY, [4]Unity Hospital, Rochester Regional Health, Rochester, NY, [5]Unity Hospital/ Rochester Regional Health, Rochester, NM

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster

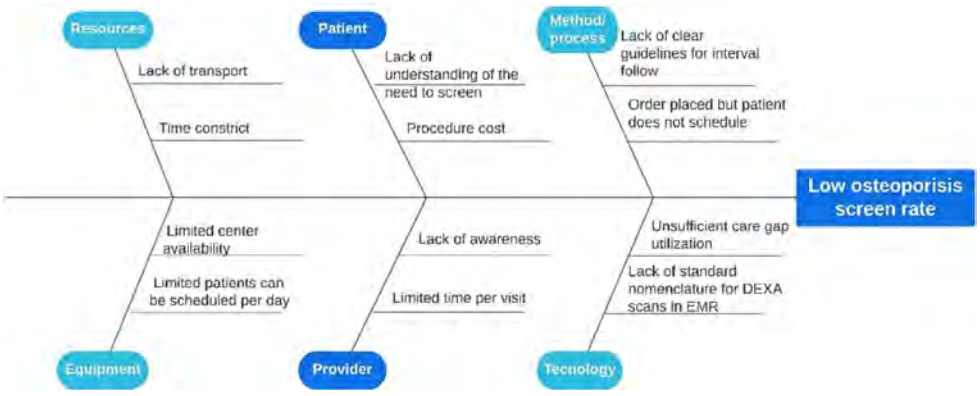
Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

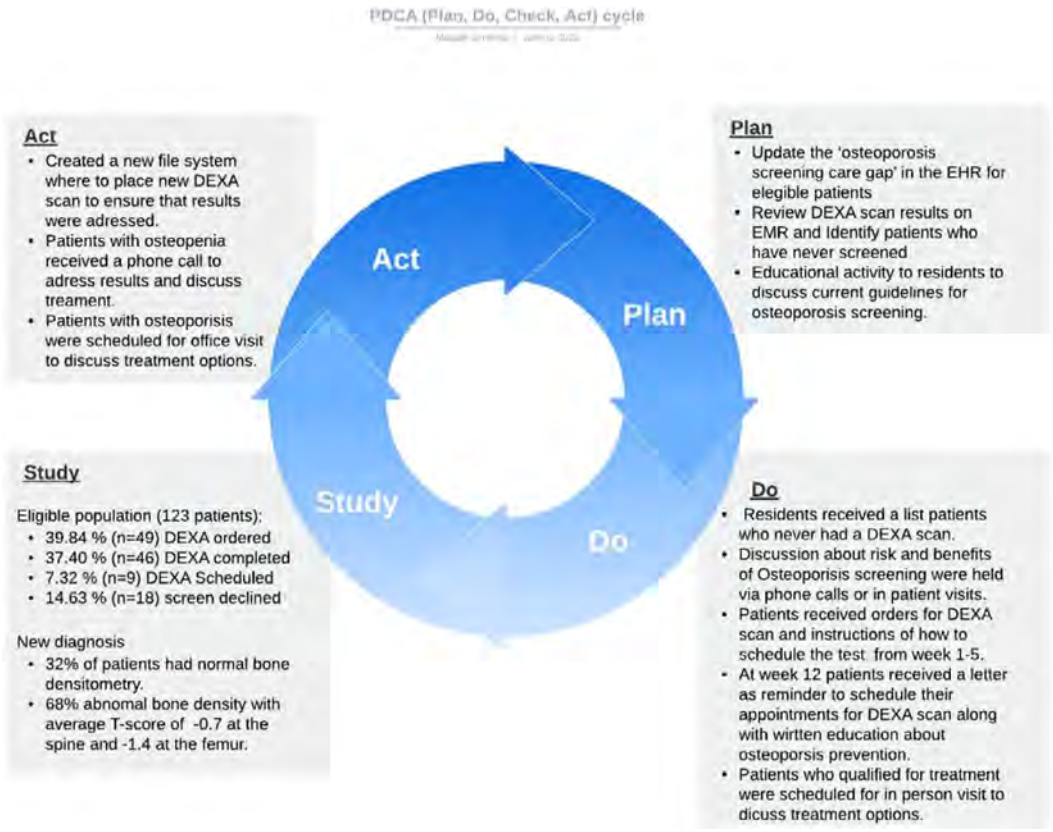
Background/Purpose: Osteoporotic fractures, especially hip fractures, are associated with significant morbidity, including limitations in ambulation, disability, and decreased quality of life. The aim of this quality improvement project was to increase the percentage of woman aged 65 or older screened for Osteoporosis in a resident-led primary care clinic and subsequently identify a population that would benefit from treatment to reduce the risk of fragility fracture.

Methods: Per the U.S. Preventive Services Task Force (USPSTF) osteoporosis screening guidelines, all female patients aged 65 or above followed by the resident primary care clinic who had not yet received osteoporosis screening by December 31st, 2022, were included. A list of eligible patients was generated through the Electronic Health Record (EHR) using patient's age, sex, and primary care physician location. A team of residents and faculty along with the associate director of quality identified possible barriers that limited the osteoporosis screening in a fishbone diagram (figure 1). A package of interventions, based on a Pareto analysis of factors in the fishbone, were prepared, completed, and analyzed through a Plan-Do-Study-Act cycle (figure 2).

Results: For the eligible group of patients (n=123), the risks and benefits of screening for osteoporosis with DEXA scan were discussed via phone call or during in person office visits. At week 12, the patients who were unable to be reached despite multiple attempts received a letter from the office with educational material about fragility fractures and benefits of undergoing osteoporosis screening. In 4 months, 37.40 % (n=46) of identified patients had their DEXA scan completed and 7.32 % (n=9) were scheduled for the upcoming weeks. 39.84% (n=49) of patients had a DEXA scan ordered without a documented scheduled date. 14.63% (n=18) of patient declined DEXA scan. The most common reason for declining screening was reluctance to start treatment. Out of the 46 patients who completed the initial screening, 68% were diagnosed with abnormal bone mass, of



Identified barriers that limit the osteoporosis screening



Plan-Do-Study-Act cycle

which 32% met osteoporosis criteria. At the 4-month mark, the overall rate of screening for all females aged 65 or older in our clinic increased from 75 to 85% and is expected to continue to improve in the upcoming months.

Conclusion: The use of osteoporosis screening reminder in the EHR along with continued provider and patient education resulted in a 10% increase over 4 months in the osteoporosis screening rate in a resident clinic.

Disclosure: M. Jimenez Artiles: None; **R. Subedi**: None; **Q. Wang**: None; **B. Jahshan**: None; **K. Gadir**: None; **W. Quwatli**: None.

Abstract Number: 2007

Effects of IL-17 Blockade on Skeletal Microarchitecture in Patients with Axial Spondyloarthritis: An HR-pQCT Study

Insa Mannstadt, Donald McMahon, Douglas Mintz, Weija Yuan, Linda Russell, Susan Goodman, Emily Stein and Dalit Ashany, Hospital for Special Surgery, New York, NY

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthritis (AxSpA), a chronic inflammatory rheumatic disease causes abnormal bone growth at the spine and paradoxically has been linked to osteoporosis and fragility fractures. While tumor necrosis factor alpha inhibitors have been shown to improve skeletal health in patients with AxSpA, the effect of newer medications that block interleukin-17 (IL17) on bone metabolism remains unclear. This prospective study investigated the impact of IL17 blockade on bone density (BMD) and microarchitecture in AxSpA. We hypothesized that treatment initiation would be associated with improved BMD and microarchitecture.

Methods: Skeletal assessments included areal BMD (aBMD) and trabecular bone score (TBS) by DXA, volumetric BMD (vBMD) and microarchitecture by high-resolution peripheral quantitative computed tomography (HRpQCT2) at baseline and 12-months. DXA and HRpQCT measurements from patients were compared to those of age-matched individuals in reference cohorts. Changes in imaging parameters were compared using Wilcoxon and paired t-tests, and predictors of change in HRpQCT were analyzed using multivariate linear regression.

Results: Of the 22 AxSpA participants, 55% were female (33% postmenopausal), mean age 40 years, and mean BMI 30 kg/m^2. 55% were HLA-B27 positive, mean symptom duration was 10 years, and C-reactive protein (CRP) was elevated in 32% of participants, respectively. At baseline, mean DXA and HRpQCT Z-scores were within 1 standard deviation of sex and age matched controls. At 12-months, >80% of participants reported 100% medication adherence. Standardized assessments of disease activity improved, with a decrease in Bath Ankylosing Spondylitis Disease Activity (BASDAI -33%, $p< 0.01$) and Metrology Index (BASMI -22%, $p=0.01$). In contrast, there was no significant improvement in aBMD, TBS, or microarchitecture by HRpQCT. In fact, decreases were observed in radial total vBMD (-2%, $p=0.04$) and trabecular vBMD (-2%, $p=0.04$). Radial trabecular separation tended to increase (4%, $p=0.06$). Elevated CRP tended to be associated with decrease in total vBMD (tibia $R^2=0.2$, $p=0.06$; radius $R^2=0.3$, $p=0.09$).

Conclusion: In summary, participants with AxSpA who began IL17 blockade had significant improvements in clinical symptoms, but no change or small declines in BMD and microarchitecture. Our uncontrolled study lacks data regarding whether treatment attenuated skeletal declines. Larger controlled studies are needed to investigate the long-term skeletal effects of IL-17 blockade.

Disclosure: I. Mannstadt: None; **D. McMahon**: None; **D. Mintz**: None; **W. Yuan**: Novartis, 1; **L. Russell**: None; **S. Goodman**: NIH, 5, Novartis, 5; **E. Stein**: Radius Pharmaceuticals, 8, 12, Research support; **D. Ashany**: None.

Abstract Number: 2008

Comparative Effectiveness of Denosumab versus Alendronate Among Postmenopausal Women with Osteoporosis in the U.S. Medicare Program

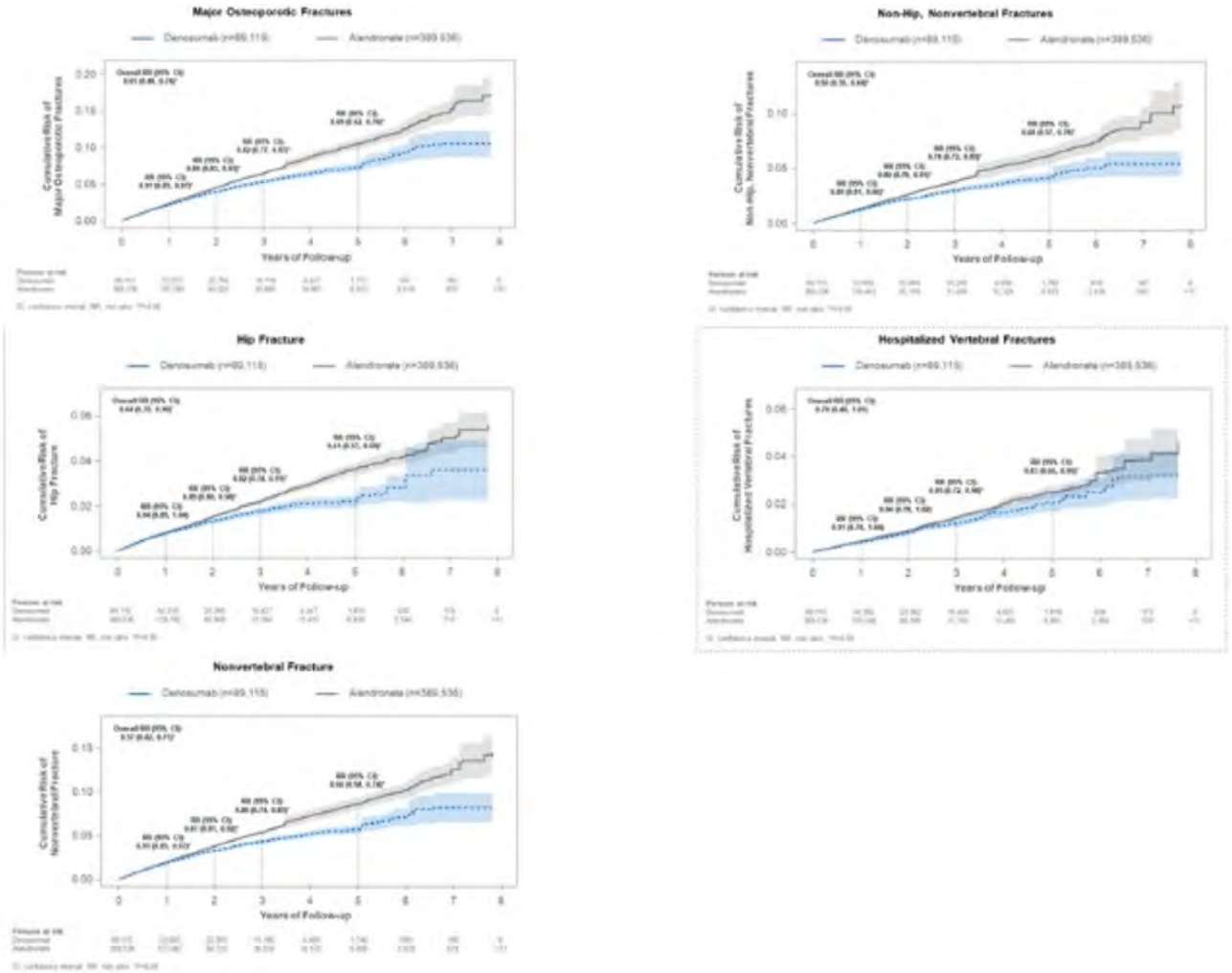
Jeffrey Curtis[1], Tarun Arora[2], Ye Liu[1], Tzu-Chieh Lin[3], Leslie Spangler[3], Vanessa C. Brunetti[3], Robert K. Stad[3], Michele McDermott[3], Brian D. Bradbury[3] and Min Kim[3], [1]University of Alabama at Birmingham, Birmingham, AL, [2]Foundation for Advancing Science, Technology, Education, and Research, Birmingham, AL, [3]Amgen, Inc., Thousand Oaks, CA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Although clinical trials have shown that denosumab (Dmab) significantly increases bone mineral density at key skeletal sites more than oral bisphosphonates, evidence is lacking from head-to-head randomized trials evaluating fracture outcomes. This retrospective observational study evaluated the comparative effectiveness of Dmab versus alendronate (Aln) in reducing fracture risk among postmenopausal women with osteoporosis (PMO) in the U.S.

Methods: Female Medicare fee-for-service beneficiaries ≥ 66 years of age who newly initiated Dmab (n=89,115) or Aln (n=389,536) between January 1, 2012 to December 31, 2018 with no prior history of osteoporosis treatment, were followed from treatment initiation until the first instance of a specific fracture outcome, treatment discontinuation (defined as the end of treatment supply + 60-day allowable gap) or switch, Medicare disenrollment, death, or end of available data (December 31, 2019). A doubly robust inverse-probability of treatment (weights estimated from multivariate logistic regression models) and censoring (weights estimated from multivariate Cox Proportional Hazards regression models) weighted function was used to estimate the relative risk (RR) associated with the use of Dmab compared with Aln for hip, nonvertebral (NV; includes hip, humerus, pelvis, radius/ulna, other femur), non-hip, nonvertebral (NHNV), hospitalized vertebral (HV), and major osteoporotic (MOP; nonvertebral and hospitalized vertebral) fractures.

Results: Overall, Dmab reduced the risk of MOP by 39% (RR=0.61; 95% CI: 0.48-0.74), hip by 36% (0.64; 0.39-0.90), NV by 43% (0.57; 0.42-0.71), NHNV by 50% (0.50; 0.35-0.64), and HV fractures by 30% (0.70; 0.40-1.01) compared with Aln. Dmab reduced the risk of MOP fractures by 9% (0.91; 0.85-0.97) at year 1, 12% (0.88; 0.83-0.93) at year 2, 18% (0.82;



0.77-0.87) at year 3, and 31% (0.69; 0.62-0.76) at year 5.An increase in the magnitude of fracture risk reduction with increasing duration of exposure was also observed for other NV outcomes(Figure).

Conclusion: In a cohort of almost a half million, treatment-naive PMO, we observed robust and significant reductions in the risk of MOP, hip, NV, NHNV, and HV fractures for patients on Dmab compared to Aln. Patients who remained on Dmab for longer periods of time experienced greater reductions in fracture risk.

Disclosure: J. Curtis: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, 5, CorEvitas, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **T. Arora**: Amgen, 5; **Y. Liu**: None; **T. Lin**: Amgen, 3, 3, 3, 11, 11, 11; **L. Spangler**: Amgen, 3, 11; **V. Brunetti**: Amgen, 3, 11; **R. Stad**: Amgen, 3, 11; **M. McDermott**: Amgen, 3, 11; **B. Bradbury**: Amgen, 3, 11; **M. Kim**: Amgen, 3, 11.

Abstract Number: 2009

Screening and Treatment of Low Bone Mineral Density in Allogeneic Hematopoietic Cell Transplant Patients

Perry Fuchs, Christina Ferraro, Chao Zhang, Chad Deal, Betty Hamilton and Sarah Keller, Cleveland Clinic Foundation, Cleveland, OH

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

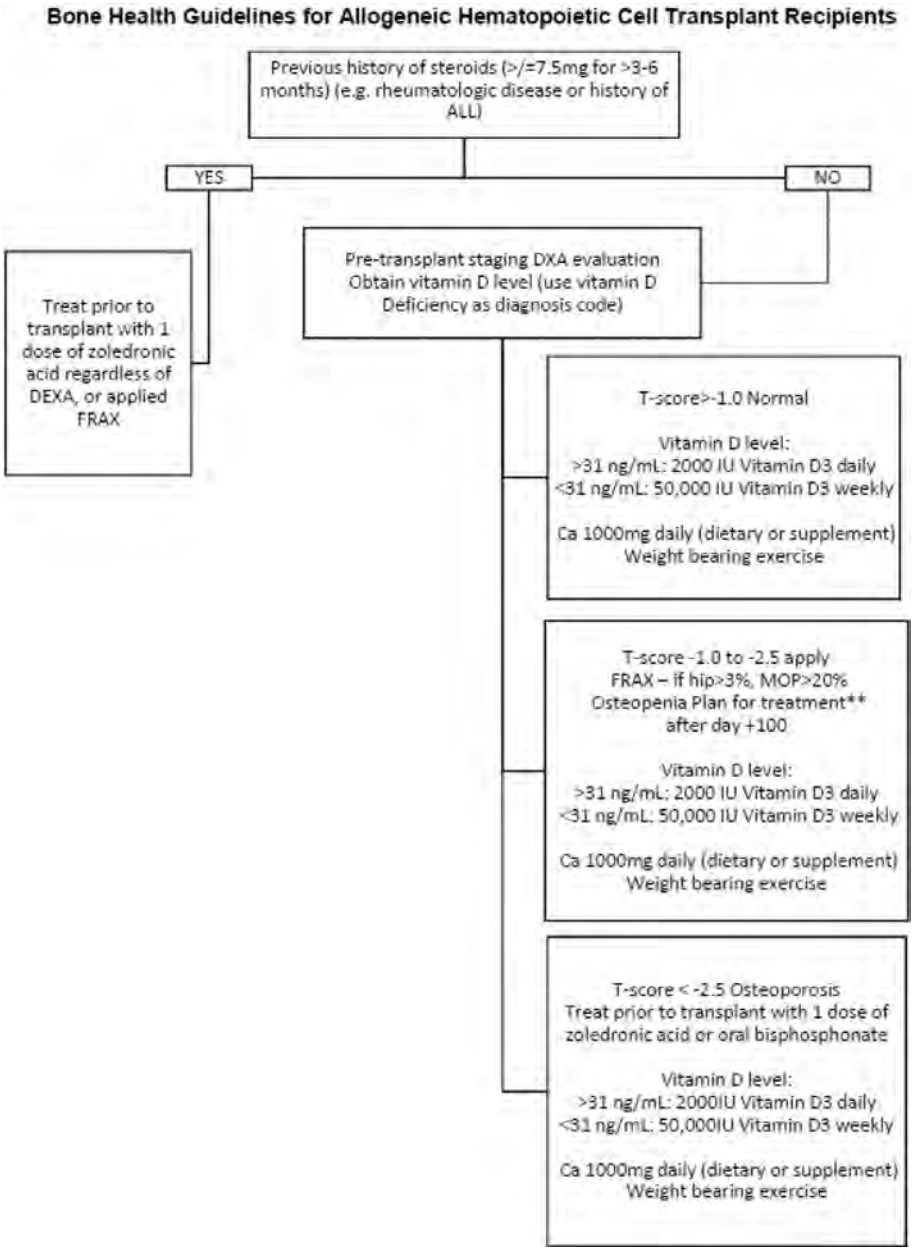
Background/Purpose: Bone mineral density (BMD) loss and fracture are important causes of increased morbidity following allogeneic hematopoietic stem cell transplant (allo-HCT).Recent societal recommendations support screeningDual X-ray Absorptiometry (DXA) both before and within 1 year after allo-HCT. Our institutionimplemented a new management algorithm that emphasized pre-transplant screening for allo-HCT patients and contained guidance on use of bone strengthening agentstoimproveBMDrelated outcomes in this population. This study evaluatedthe rate of screening and treatment of low BMD and fracture in allo-HCT patients and determined the effect that the quality improvement intervention had on these measures.

Methods: This was a retrospective chart review ofallo-HCT recipients at the Cleveland Clinic Foundationfrom April 2016 toMarch 2022. 244 patients with at least 1-year of follow up from allo-HCT were identified for analysis.The BMD management algorithm was implemented in 10/2019, and we compared rates of DXA screen (pre- and post-HCT), treatment, and fragility fractures between allo-HCT recipients before and after this time point.We also analyzed available T-scores at the spine, femoral neck, and total hip and FRAX risk scores before and after allo-HCT. Treatment was guided by National Osteoporosis Foundation (NOF) recommendations (T-score of –2.5 or less, or T-score of –1 to –2.4 and a 10-year probability of hip fracture >/= 3% or any major fracture >/= 20% as calculated by FRAX).

Results: After intervention, thepre-transplant DXA screening increased from 0% to 95%, though post-transplant DXA screening (≤13 months from HCT) decreased from 67% to 36% ($p < 0.001$). Rate of treatment indecreased from 67.23% to 35.58% ($p < 0.001$).Rate of treatment in patients meeting NOF criteria was similar pre- and post-intervention (62% vs 62%). Subgroup analysis showed treatment of osteoporosisalso remained similar between groups (75% vs 72%),however

the rate of treatment of osteopenia with a high FRAX score was improved in the post-intervention group (0% vs 38%, p = 0.204). The fracture rate was significantly lower in the post-intervention group (7.7% vs 19.3%, p = 0.004).

Conclusion: Implementation of analgorithm for screening and treatment of low BMD in allo-HCT recipientswith a focus on pre-transplant DXA screening resulted in an expected increase in pre-transplant screening, but anunexpected decreased rate of follow-up DXA within the 13 months post-transplant. This intervention alsoledto an increased rate of treatment of patients with osteopenia and elevated FRAX. The intervention led to a significantly decreased rate of fractures, which may be related to the increased awareness of low BMD and potentially due to the timing of treatment initiation, which was not directly assessed in this analysis.Allo-HCT patients are a complex population of patients that are prone to low BMD and focusing on the detection and management of this important cause of morbidity is correlated with improved outcomes.



Guidance Algorithm for Management of Low BMD in Allogeneic Hematopoietic Stem Cell Transplant Patients

Table 1. Results with p-values of screening, treatment, and fracture pre- and post-intervention

Outcome Measure	Pre-Intervention	Post-Intervention	P-Value
Pre-Transplant Screening DXA	0 (0%)	101 (95.28%)	<0.001
Screening DXA within 13 months Post-Transplant	80 (67.23%)	37 (35.58%)	<0.001
Treatment of T-score </= -2.5, OR T-score between -1 and -2.4 with FRAX Hip > 3% OR FRAX MOP > 20%	18 (62.07%)	16 (61.54%)	1
Treatment of T </= -2.5	18 (75%)	13 (72.22%)	1
Treatment of T-score between -1 and -2.4 with FRAX Hip > 3% OR FRAX MOP > 20%	0 (0%)	3 (37.5%)	0.204
Fragility Fracture Post-Transplant	23 (19.33%)	8 (7.69%)	0.004

Disclosure: P. Fuchs: None; **C. Ferraro**: None; **C. Zhang**: None; **C. Deal**: None; **B. Hamilton**: Angiocrine, 1, Equilium, 1, incyte, 1, Kadmon, 1, Malinkrodt, 6, Nkarta, 1; **S. Keller**: None.

Abstract Number: 2010

B-FROST: Chronic OBstructive Pulmonary Disease and Vertebral FRacture of OSTeoporotic Origin: Results of a Real-life Cohort

Amine Mouamnia, Armentieres Hospital Center, Armentieres, France

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic obstructive pulmonary disease (COPD) is a chronic disease of the airways. It is mainly caused by smoking. Active smoking is a risk factor for osteoporosis. The occurrence of thoracic vertebral fractures can lead to additional deformities and ventilatory disorders. Moreover, little is known about the consequences of VF in COPD.

The objective is to determine the occurrence of vertebral fractures in a real-life COPD population hospitalized for exacerbation, and the risk factors involved.

Methods: The clinical characteristics of patients hospitalized in the pulmonology department from January 1 to December 31, 2022 were assessed. The diagnosis of vertebral fracture (VF) was assessed on standard chest X-rays.

Results: Of the 136 files analyzed, 106 patients were included. The main characteristics are shown in Table 1. The diagnosis of VF was largely underestimated (only 3.77% of VFs were described on standard chest X-rays). The prevalence of VF was 21.7%. The incidence rate was 23 cases per 106 patient-years. Lower BMI appears to be associated with the occurrence of

Table 1. Characteristics of patients

	FV	Non-FV	Significance
	Mean ± SD Median [IQR] Or Number (%)	Mean ± SD Median [IQR] Or Number (%)	
Population	23/106 (21.7)	83/106 (78.3)	
Age (years)	73.8 ± 11.5 76 [67-81]	70.4 ± 11.9 71 [63-80]	ns
Sex (F)	N=10 (43.5%)	N=39 (47.0%)	ns
BMI (kg/m2)	26.7 ± 8.6 25 [22-31]	31.2 ± 10.4 29 [23.7-37]	p<0.05
Smoking (pack-year)	33.3 ± 14.2 30 [27.5-42.5]	45.7 ± 25.3 40 [30-60]	ns
Alcohol	N=1 (4.3%)	N=16 (19.3%)	p<0.05
Inhaled steroids	N=14 (60.9%)	N=41 (49.4%)	ns
FEV1 (% of predicted)	48.0 ± 13.2 47.5 [40.5-55]	47.6 ± 20.0 45 [34-60]	ns
GOLD status	3.8 ± 0.6 4 [4-4]	3.5 ± 1.0 4 [3-4]	ns
Length of hospital stay (days)	12.0 ± 7.2 11 [7.5-14.5]	10.6 ± 9.6 8 [5.5-13.5]	ns
Number of exacerbation per year	1.4 ± 0.7 1 [1-2]	1.3 ± 0.6 1 [1-1]	ns
Intensive care admission	N=4 (17.4%)	N=15 (18.0%)	ns
Death of hospitalized patients	N=1 (4.3%)	N=6 (7.2%)	ns

SD: Standard Deviation; IQR: Interquartile Range; F: Female; BMI: Body Mass Index; kg/m2: kilogram per square meter; FEV1: Forced Expiratory Volume In 1 Second; GOLD: Global Initiative for Chronic Obstructive Lung Disease.

VF p< 0.05. Patients with VF were hospitalized longer on average and had more exacerbations during the year, but this was not significant. There was no difference in mortality between the 2 groups.

Conclusion: VF are common in COPD patients, yet they remain under-diagnosed and may contribute to increased morbidity and mortality in this population over the long terme.

Disclosure: A. Mouamnia: None.

Abstract Number: 2011

Predicting Fractures in Patients with Isolated Lumbar Spine Osteoporosis Compared to Those with Isolated Hip Osteoporosis

Nicholas Rossi[1], Aamir Saeed[2], Aqib Khan[3], Hamzah Amin[2], Ummaz Nadeem[2], Zain Sultan[3] and Marwan Bukhari[2], [1]University Hospitals of Morecambe Bay Foundation Trust, Worksop, United Kingdom, [2]Lancaster University, Lancaster, United Kingdom, [3]University Hospitals of Morecambe Bay Foundation Trust, Lancaster, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoporosis (OP) presents with fragility fractures, which can cause significant disability and cost to health services globally. There has been extensive research looking at risk factors for osteoporosis and fractures but less into how these factors are predicted at different bony sites. We aimed to compare risk fractures for fractures in patients with isolated L1-L4 vertebrae OP compared to isolated hip OP in a large dataset.

Methods: Data were obtained from patients referred for DEXA scan in the North-West of England between 2004 and 2011. Upon attendance, demographic details, full medical history including risk factors for fracture presence of fracture were recorded. These data was retrospectively analysed using STATA(tm) , with chi squared test used for categorical data and independent sample t-test for continuous data. We then fitted logistical models reporting odds of fracture using risk factors included in the FRAX(tm) tool (age, height, weight, family history, smoking, alcohol excess, rheumatoid arthritis and steroid use) to look for predictors of fracture.

Results: The total cohort comprise 31546 patients (82% female). 2530 patients had isolated vertebral osteoporosis and 1363 had isolated hip OP. Results are shown in table 1 below. Age was significantly associated with fractures at both sites with greater fracture risk at the hips compared to the spine. Height was protective for fractures and osteoporosis at both sites. Interestingly, whilst height was less associated with fracture in patients with hip OP, it gave greater protection against fractures at the spine. Weight was more protective for fractures at the hips compared to the spine but whilst it was protective for OP at both sites, there was no significant difference between them. Smoking increased risk of OP but with no significant difference between the two sites and had no effect on fracture risk. Use of steroids was surprisingly protective of fractures at both sites, without a significant difference between them. Excess alcohol was protective against fracture in both sites with no significant difference between them and was associated with an increased risk of fractures in the spine but not in the hip. Rheumatoid arthritis (RA) increased risk of osteoporosis in the hip but not in the spine. RA also inferred greater risk of fractures at the hips but unfortunately didn't reach statistical significance in the spine.

Table 1 - Risk factors affecting neck of femurs and spinal vertebrae

Risk Factor	NOF fracture		Spine fracture	
	Odds Ratio	95% Confidence Intervals	Odds Ratio	95% Confidence Intervals
Age	1.05	1.045 - 1.056	1.045	1.041 - 1.049
Height	0.994	0.987 - 0.999	0.978	0.974 - 0.983
Weight	0.983	0.979 - 0.987	0.995	0.992 - 0.997
Current Smoker	0.911	0.772 - 1.075	1.021	0.906 - 1.151
Steroid Therapy	0.683	0.595 - 0.783	0.709	0.641 - 0.785
Excess Alcohol	0.9	0.703 - 1.153	1.384	1.203 - 1.591
Rheumatoid Arthritis	1.09	0.882 - 1.346	0.784	0.655 - 0.938

Conclusion: Our study shows that established risk factors for fractures may affect different bony sites in distinct ways. The FRAX(tm) risk factors underperform in both cohorts This suggests that isolated spinal or hip OP may be a distinct disease and might need be assessed and treated differently. Our strengths include the large numbers included, but weaknesses exist in referral bas and lack of knowledge of length of exposure to risks. Further research is needed to assess how risk factors affect different bony sites, including the forearms and ribs, as well as the pathophysiology behind the differences observed.

Disclosure: N. Rossi: None; **A. Saeed**: None; **A. Khan**: None; **H. Amin**: None; **U. Nadeem**: None; **Z. Sultan**: None; **M. Bukhari**: AbbVie/Abbott, 2, Amgen, 1, Gilead, 1, Janssen, 1, UCB, 1.

Abstract Number: 2012

Incidence of Hyperparathyroidism in Patients with Osteoporosis Treated with Zoledronic Acid or Denosumab

Carmen Riesco Barcena[1], Jose Ivorra Cortes[2], Elena Grau Garcia[2], Samuel Leal Rodriguez[2], Luis Gonzalez Puig[2], Anderson Victor Huaylla Quispe[2], Pablo Francisco Muñoz Martínez[3], Alba Maria Torrat Noves[2], Daniel Ramos Castro[2], Laura Mas Sanchez[4], Ines Canovas Olmos[2], Hikmat Charia[2], Isabel Martinez Cordellat[2], Carmen Najera Herranz[2], Rosa Negueroles Albuixech[2], Jose Eloy Oller Rodriguez[2], Marta De la Rubia Navarro[4], Ernesto Tovar Sugrañes[2], Elvira Vicens Bernabeu[2], Iago Alcantara Alvarez[2], Belen Villanueva Mañez[2] and Jose Andres Roman Ivorra[5], [1]Hospital Universitario y Politécnico La Fe, Valencia, Spain, [2]Rheumatology Department. HUP La Fe, Valencia, Spain, [3]Rheumatology Department. HUP La Fe, Sagunto, Spain, [4]Rheumatology Department. HUP La Fe, Valéncia, Spain, [5]Hospital Universitari i Politècnic la Fe, Valencia, Spain

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Denosumab and Zoledronic acid are antiresorptive drugs commonly used in the treatment of osteoporosis (OP). Zoledronic acid is a third-generation bisphosphonate that inhibits osteoclastic bone resorption through the mevalonate pathway. Denosumab is a humanized monoclonal antibody that binds to RANK-L preventing osteoclastic activation. Both can cause hypocalcemia and parathormone (PTH) elevations have been described during their use. Its prevalence, the mechanism by which it occurs, and the clinical repercussions are unknown.

The aim of our study was to analyze the prevalence of PTH elevation above the reference value in patients receiving zoledronic acid or denosumab and its relationship with other clinical-analytical parameters.

Methods: Retrospective observational study in patients with OP who have received treatment with denosumab or zoledronic at least two years. Patients were successively recruited from our service's osteoporosis database.

Patients diagnosed with primary hyperparathyroidism or with glomerular filtration rate < 30ml/min at the baseline visit were excluded from the study. Clinical and demographic data were obtained from the electronic health record. Statistical analysis was performed using R software.

Results: 91 patients with a mean age (Standard Deviation-SD) of 68 (11.3) years at the start of treatment were included.

49 (81.6% women) patients started treatment with zoledronic and 42 (61.9% women) with Denosumab.

		ZOLEDRONIC ACID N= 49			DENOSUMAB N=42		
		Baseline visit	Visit year 1	Visit year 2	Baseline visit	Visit year 1	Visit year 2
		Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Glomerular filtration rate (mL/min/1.73m²)		88.57 (17.2)	83.46 (18.37)	82.41 (17.12)	77.48 (16.52)	76.71 (19.21)	77.34 (16.47)
Calcium corrected for albumin (mg/dL)		9.24 (0.33)	9.12 (0.52)	9.2 (0.41)	9.2 (0.29)	9.1 (0.47)	8.96 (0.79)
P1NP (ng/mL)		68.74 (50.63)	31.12 (17.6)	30.66 (13.66)	49.05 (26.97)	23.76 (18.62)	23.27 (19.9)
BCTX (ng/mL)		0.49 (0.4)	0.16 (0.19)	0.13 (0.09)	0.49 (0.34)	0.11 (0.2)	0.11 (0.15)
		N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
25-OH-Vitamin D							
	Deficiency (<10ng/mL)	8 (16.33%)	1 (2.13%)	2 (4.26%)	5 (11.9%)	5 (12.5%)	2 (4.76%)
	Insuficiency (10-29 ng/mL)	13 (26.53%)	7 (14.89%)	7 (14.89%)	15 (35.71%)	6 (15%)	12 (28.57%)
	Normal (≥30ng/mL)	28 (57.14%)	39 (82.98%)	38 (80.85%)	22 (52.38%)	29 (72.5%)	28 (66.67%)
Higher PTH (≥65pg/mL)		0 (0%)	6 (12.77%)	6 (14.29%)	0 (0%)	11 (26.83%)	13 (32.5%)

Table 1. Analytical parameters of greatest interest throughout the follow-up of the patients.

(PINP-Procollagen type I N-terminal propeptide; CTX-C- Type I Collagen Cross-linked C-Telopeptide)

Variables	Estimate	Lower 95%	Upper 95%	p.value
Age of onset	0.002	0.949	1.058	0.945
Glomerular filtration rate	-2.742	0.006	0.588	0.017
Calcium corrected for albumin	-24.736	0	0	<0.001
25-OH-Vitamin D	-0.484	0.198	1.818	0.384
Gender Women	0.592	0.636	5.791	0.287

Table 2. Logistic regression model between elevated PTH and other clinical-analytical variables.

Table 1 shows the analytical parameters throughout the follow-up.

18.4% of the patients treated with zoledronic had elevated PTH levels on some occasion compared to 35.7% of the patients treated with Denosumab (p=0.055).

Patients with persistently elevated PTH during the two visits were 3 (6%) with zoledronic and 9 (21.4%) with Denosumab (p< 0.02).

Using a logistic regression model, we analyzed the possible relationship between the elevated value of PTH (≥65pg/mL) and other clinical-analytical variables (Table 2).

Variables	Estimate	Lower 95%	Upper 95%	p.value
Antiresorptive at time of baseline visit	-0.214	-0.505	0.076	0.147
Age of onset	0.006	-0.01	0.022	0.479
Glomerular filtration rate	0.392	-0.291	1.075	0.257
Calcium corrected for albumin	-0.88	-2.674	0.914	0.332
25-OH-Vitamina D	0.11	-0.219	0.44	0.508
Normal PTH (<65pg/mL)	-0.457	-0.802	-0.113	0.01
Women gender	-0.33	-0.599	-0.061	0.017

Table 3. Linear regression model between Delta T-Score at lumbar region with other clinical-analytical variables

We found an inverse statistically significant association between corrected calcium and glomerular filtration rate compared to elevated PTH.

We calculated the progression of the T. Score between the baseline visit and the second visit in the lumbar spine, femoral neck, and total hip. We call this parameter "delta T Score".

Using a linear regression model, we analyzed the lumbar Delta T-Score against the variables listed in table 3.

Normal PTH values and female gender are associated in a statistically significant way with a worse evolution of bone mineral density at the lumbar region.

We did not find these associations in femoral neck or total hip.

Conclusion: We found a high prevalence of hyperparathyroidism in our patients, higher in those treated with Denosumab.

The elevation of PTH seems to be associated, inversely, with serum levels of ionic calcium and glomerular filtration rate. Elevated PTH levels are associated with a better evolution of bone mineral density. In this context, we believe that the elevation of PTH could act as a marker of treatment effectiveness. Other studies would be necessary to corroborate these findings.

Disclosure: C. Riesco Barcena: None; **J. Ivorra Cortes**: None; **E. Grau Garcia**: None; **S. Leal Rodriguez**: None; **L. Gonzalez Puig**: None; **A. Huaylla Quispe**: None; **P. Muñoz Martínez**: None; **A. Torrat Noves**: None; **D. Ramos Castro**: None; **L. Mas Sanchez**: None; **I. Canovas Olmos**: None; **H. Charia**: None; **I. Martinez Cordellat**: None; **C. Najera Herranz**: None; **R. Negueroles Albuixech**: None; **J. Oller Rodriguez**: None; **M. De la Rubia Navarro**: None; **E. Tovar Sugrañes**: None; **E. Vicens Bernabeu**: None; **I. Alcantara Alvarez**: None; **B. Villanueva Mañez**: None; **J. Roman Ivorra**: None.

Abstract Number: 2013

Clinical Characteristics and Risk Factors Associated with Fragility Fractures in Patients with Primary and Idiopathic Mast Cell Activation Syndromes

Ana Isabel Ramos Lisbona[1], Karen Carpio Astudillo[1], Filip Skrabski[1], Alicia Prieto García[1], Isabel Castrejon[1], Javier Rivera[2], José María Álvaro-Gracia[1] and Teresa González[1], [1]Hospital General Universitario Gregorio Marañón, Madrid, Spain, [2]Hospital General Universitario Gregorio Marañon, Madrid, Spain

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Mast Cell Activation Syndromes (MCAS) are a group of disorders presenting with episodic multisystem symptoms, predominantly anaphylaxis, as the result of mast cell mediator release. Primary MCAS, that are those with a clonal origin such as systemic mastocytosis (SM), present a high prevalence of fragility fractures (FF), which varied from 5 to 37% of patients [1]. On the contrary, the idiopathic (non-clonal) forms of MCAS, do not appear to be associated with this risk [2]. The main objective of our study is to describe the presence of osteoporosis (OP), FF and the principal risk factors associated with FF in patients with MCAS.

Table 1. Characteristics of patients with Primary and Idiopathic MCAS.

	Primary MCAS (N=36)	Idiopathic MCAS (N=12)	p
Male, n (%)	14 (38.9)	4 (33.33)	1.00
Mean age of onset of symptoms (SD)	37.7 (17.8)	44.5 (13.1)	0.24
Mean age of diagnosis (SD)	45.4 (18.3)	51.7 (12.4)	0.27
Mean BMI (SD)	21.65 (4.25)	26.2 (5.3)	0.004
BMI <19 kg/m^2, n (%)	7 (19.44)	0 (0)	0.17
Skin symptoms, n (%)	21 (58.33)	12 (100)	0.007
Anaphylaxis, n (%)	17 (47.2)	12 (100)	0.001
Digestive symptoms, n (%)	16 (44.4)	9 (75)	0.98
Mean basal tryptase (SD)	22.60 (18.02)	5.83 (3.46)	0.003
General risk factors for OP, n (%)	19 (52.8)	3 (25)	0.18
Osteoporosis, n (%)	14 (38.9)	2 (16.67)	0.16
Fragility fractures, n (%)	9 (25)	1 (8.33)	0.22
Mean T-score in the femoral neck (SD)	-1.07 (1.18)	-0.47 (1.09)	0.12
Mean T-score in the lumbar spine (SD)	-1.39 (1.41)	-0.66 (1.43)	0.14
Mean FRAX score for overall fracture (SD)	4.06 (2.85)	4.81 (5.12)	0.56
Mean FRAX score for hip fracture (SD)	1.19 (1.63)	1.10 (2.22)	0.89

SD: standard deviation

Methods: The study population included all the patients with primary MCAS and idiopathic MCAS evaluated by the Rheumatology and Allergology departments at Hospital General Universitario Gregorio Marañón (Madrid, Spain), a tertiary-level hospital, until January 2023. The diagnosis was made according to the diagnostic and classification criteria updated in the consensus of 2021 [3]. Demographic, clinical, and analytical characteristics were collected. Bone involvement was defined as densitometric OP (T score ≤ -2.5) and/or the presence of FF on thoracic and lumbar spine X-rays. Fracture Risk Assessment Tool (FRAX) was used for estimating the risk of osteoporotic fracture with a 10-year probability. The differences between groups were tested using t-student test for continuous variables and chi-square test for categorical variables. A value of $p < 0.05$ was considered statistically significant.

Results: A total of 48 patients were included: 36 with primary MCAS (33 with mastocytosis, 5 cutaneous and 28 non-advanced systemic forms, and 3 clonal MCAS) and 12 patients with idiopathic MCAS. In the primary MCAS group, 25% of patients developed at least one FF, of which 44.4% were men with a mean age of 42 years (p=0.02); these patients also have a lower bone mineral density at the femoral neck (T-score -1.07; p=0.04) and a higher FRAX score compared to those who did not present fractures. In the group of patients with idiopathic MCAS, only one presented FF. Table 1 shows a comparison between the primary and idiopathic MCAS patients. Patients with primary MCAS have a higher prevalence OP and FF, higher tryptase levels (p=0.003) and a lower body mass index (BMI) (p=0.004). However, the risk of fracture calculated by FRAX, both for major and hip fractures, is increased in both groups.

Conclusion: The prevalence of OP and FF is higher in patients with primary MCAS compared to patients with idiopathic MCAS. A higher BMI and lower tryptase levels could explain the lower risk in the idiopathic MCAS group, although due to the small sample size the results must be handled with caution.

Disclosure: A. Ramos Lisbona: None; **K. Carpio Astudillo**: None; **F. Skrabski**: None; **A. Prieto García**: None; **I. Castrejon**: None; **J. Rivera**: None; **J. Álvaro-Gracia**: None; **T. González**: None.

Abstract Number: 2014

The Role of Orosomucoid 2 in the Regulation of Bone Remodeling by Inhibiting Osteoclastogenesis and Promoting Osteogenesis

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SESSION INFORMATION

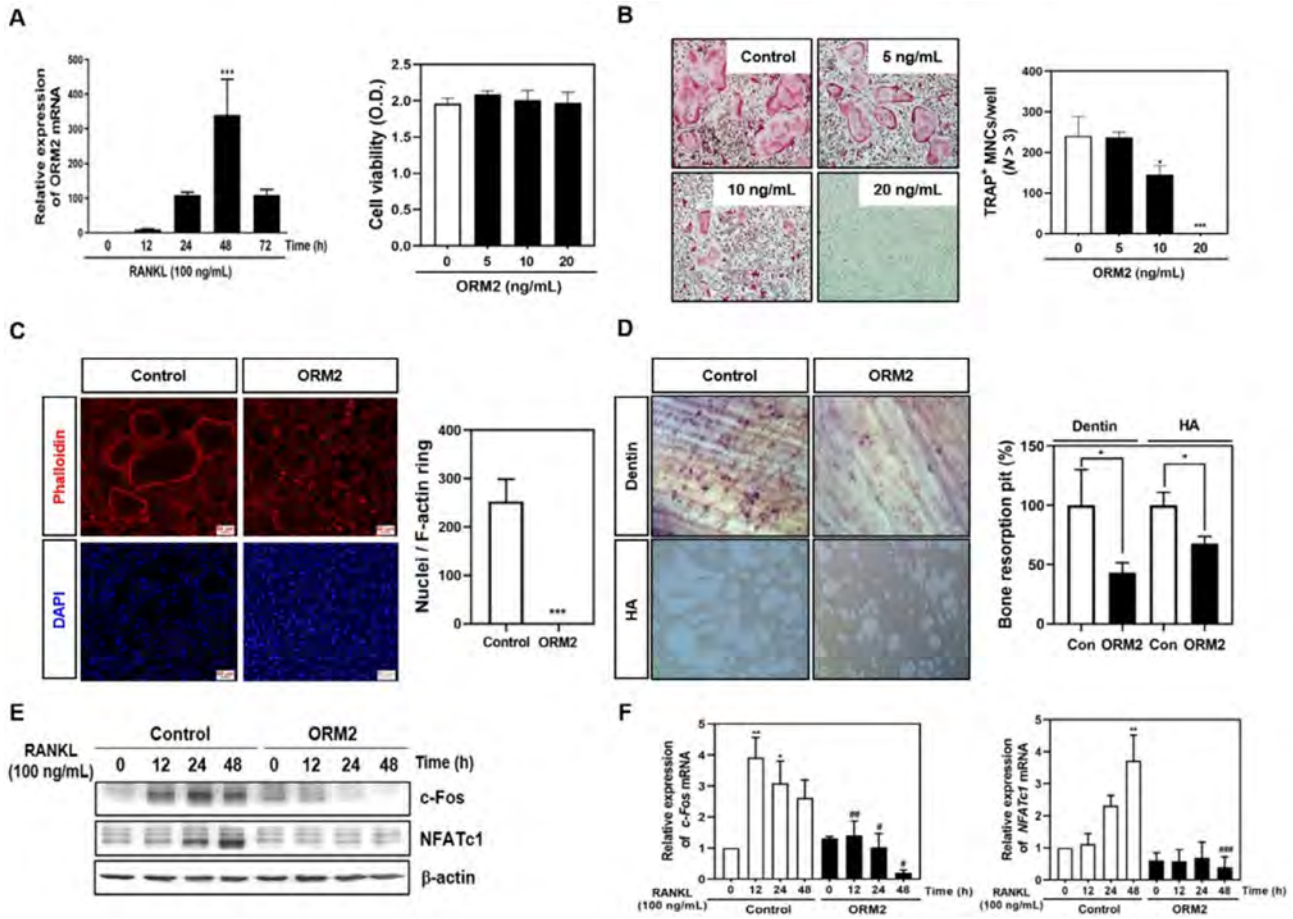
Session Date: Tuesday, November 14, 2023

Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster

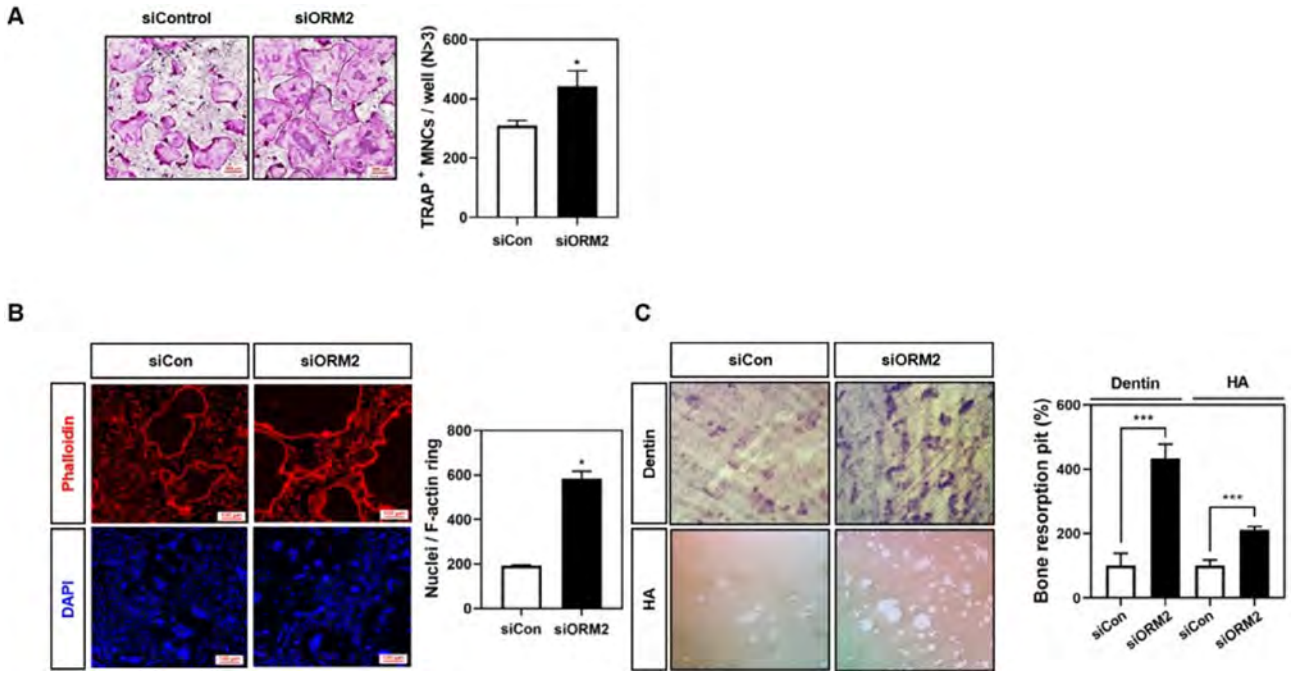
Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

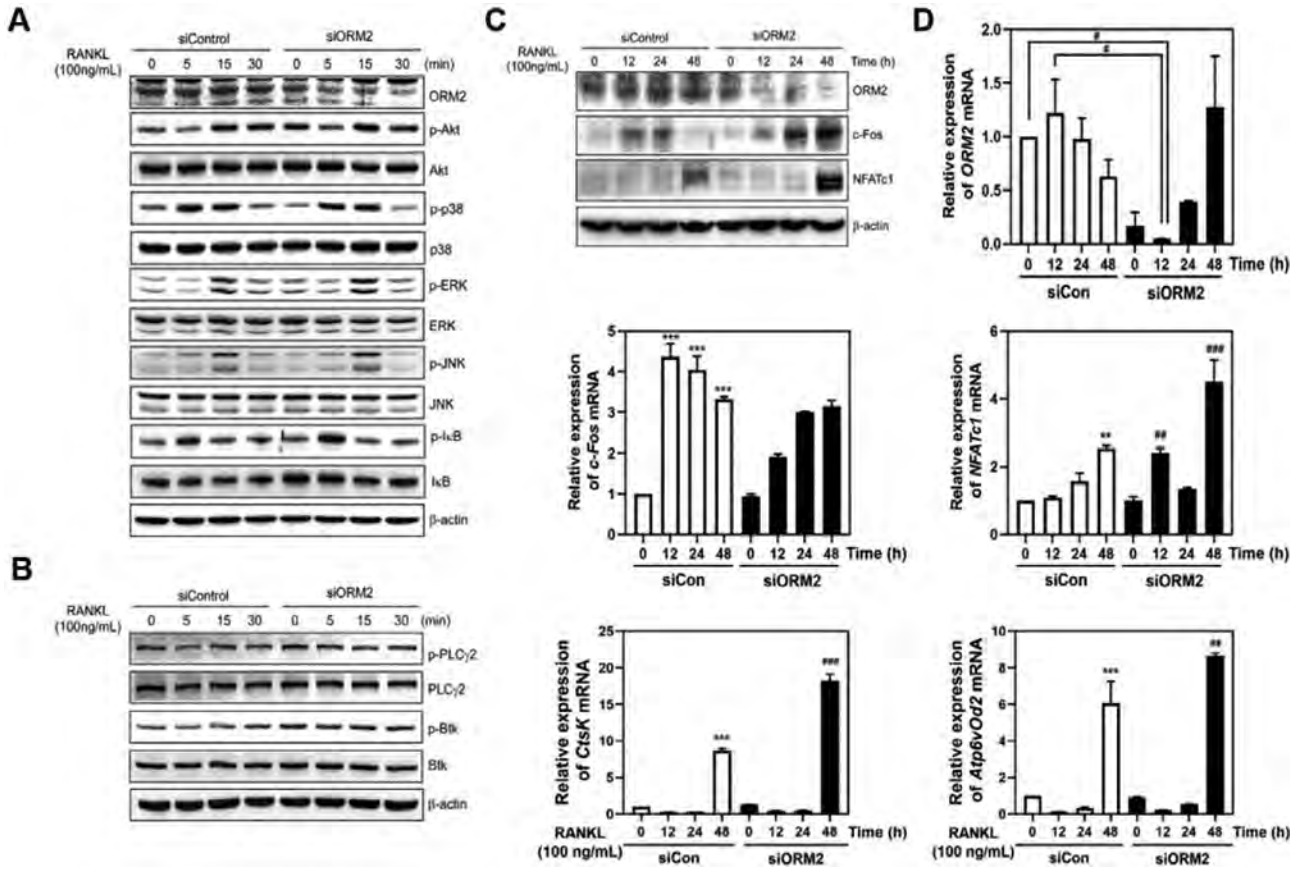
Background/Purpose: Orosomucoid (ORM) is one of the acute phase reactant protein family and is expressed in hepatocytes and secreted into plasma under stress conditions such as tissue injury, infection, and inflammation. Three types of ORM are known to date (ORM1, 2 and 3), and ORM2 is mainly expressed in bone marrow cells. ORM2 has only some studies on hepatic metabolism, inflammation and immune regulation, and no studies on bone metabolism have been reported. The aim of this study is to reveal the role of ORM2 in the differentiation and function of osteoclasts and osteoblasts



ORM2 expression was increased during RANKL-induced osteoclast differentiation and the administration of recombinant ORM2 protein restrained the formation of osteoclast and bone resorption function.



The knock down of ORM2 improved osteoclast differentiation and bone resorbing function.



The knock down of ORM2 leaded to osteoclast differentiation by increasing RANKL-mediated MAPKs (ERK, JNK), NF-KB, Akt and Btk-PLCr2 calcium signaling.

Methods: To determine the effect of ORM2 on RANKL-induced osteoclast differentiation and function, we performed TRAP staining, F-actin stating, and bone resorbing assay using ORM2 recombinant protein or ORM2 siRNA. Also, the effect of ORM2 on osteogenesis was confirmed by ALP and ARS assay. The intracellular mechanisms responsible for the dual regulation of osteoclastogenesis and osteogenesis of ORM2 were revealed by western blotting and quantitative real-time RT-PCR.

Results: We found that ORM2 is a potential target for osteoporosis therapeutics, as treatment with this agent enhances osteoblast differentiation and bone growth and suppresses osteoclast differentiation and bone resorption by performing gain- and loss-of-function studies. During ORM2-mediated regulation of osteoclastogenesis, phosphorylation of early signal transducers such as p38, JNK, Akt, IB, PLC 2, and Btk was affected, which in turn altered the mRNA and protein levels of c-Fos and NFATc1. ORM2 also increased ALP, Alizarin Red-mineralization activity, and the expression of osteoblastogenic gene markers, such as Runx2, osteocalcin (OCN), and ALP in mouse calvarial primary osteoblasts, and activated the p38-Runx2 pathway, which enhanced osteoblast differentiation.

Conclusion: we suggest that ORM2 may be a promising candidate for gene therapy for bone metabolic diseases, and further serve as a potentially important biomarker in the field of bone disease diagnosis.

Disclosure: C. CHUNG: None; **M. Lee**: None; **C. Lee**: None.

Abstract Number: 2015

Synergistic Effect Between Denosumab and Immune Checkpoint Inhibitors : A Retrospective Study of 268 Patients with Bone Metastases

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Bone is the third site of metastasis. Bone metastases are associated with poorer survival of patients and impaired quality of life with the occurrence of skeletal related events. Denosumab (D-MAB), a recombinant fully monoclonal human IgG2 antibody directed against the receptor activator of nuclear factor kappa-B ligand (RANKL) is used for the prevention of skeletal related events (SRE) in advanced solid tumors with bone metastases. RANK/RANKL axis seems also essential in numerous immunological processes. Moreover, oncology had evolved last years with increasing use of Immune Checkpoint Inhibitors (ICI) that suppress tumor-induced immune system inhibition mechanisms. We hypothetized that there could be a synergistic anti-tumor effect between immunotherapy and denosumab according to case-reports, small cohorts and *in vivo* studies.

Methods: We used a retrospective database in oncology named IMMUCARE and developed in Hospices Civils de Lyon at Centre Hospitalier Lyon Sud. All patients treated with ICI from 2014 are included in this database. We analysed only patients with bone metastases and collected data in their medical file.

We analyzed overall survival (OS), progression-free survival (PFS) and switch of treatment line in different populations according to whether or not use of Denosumab. We designed three different groups, without Denosumab, ICI then Denosumab and Denosumab then ICI. We performed survival curves and Cox model for multivariate analysis.

Results: 268 patients presented with bone metastases in the whole cohort. We did not found significant difference for overall survive (OS) and progression free survival (PFS) in favor of combination of Denosumab and ICI but we have a visual impression of superiority on the survival curves in the ICI then D-MAB group. This visual impression of a beneficial effect starting around the 6th month. We identified significant difference for changing of treatment line in the ICI then D-MAB group (p = 0.022) in the conservative population, and at the limit in the corrected population (p = 0.057).

Table 1 - Population characteristics - True = with Denosumab

Table 1
Population characteristics. True = with Denosumab

Characteristic	FALSE, N = 154[1]	TRUE, N = 114[1]	p-value[2]
year_ici			0.005
2018	69 (45%)	32 (28%)	
2017	49 (32%)	36 (32%)	
2016	26 (17%)	28 (25%)	
2015	9 (5.8%)	18 (16%)	
2014	1 (0.6%)	0 (0%)	
age	65.7 (10.5)/ 65.5 (13.2)	65.1 (9.5)/ 65.8 (11.9)	0.83
Sexe			0.52
homme	108 (70%)	84 (74%)	
femme	46 (30%)	30 (26%)	
ECOG_PT	1.3 (0.7)/ 1.0 (1.0)	1.2 (0.7)/ 1.0 (1.0)	0.38
Unknown	9	4	
Poids_PT	68.2 (18.5)/ 65.5 (21.2)	68.2 (14.2)/ 67.0 (18.5)	0.61
Unknown	2	0	
Taille	168.1 (14.7)/ 170.0 (11.2)	167.0 (18.0)/ 170.0 (10.0)	0.95
Unknown	2	1	
BMI_PT	29.2 (62.6)/ 22.9 (6.6)	27.8 (27.6)/ 23.4 (5.6)	0.47
Unknown	2	1	
Tabac			0.59
actif	64 (42%)	50 (44%)	
sevré	60 (39%)	47 (42%)	
non	29 (19%)	16 (14%)	
Unknown	1	1	
type_immuno			>0.99
antiPD1	153 (99%)	113 (99%)	
antiPD1_antiPD1	1 (0.6%)	1 (0.9%)	

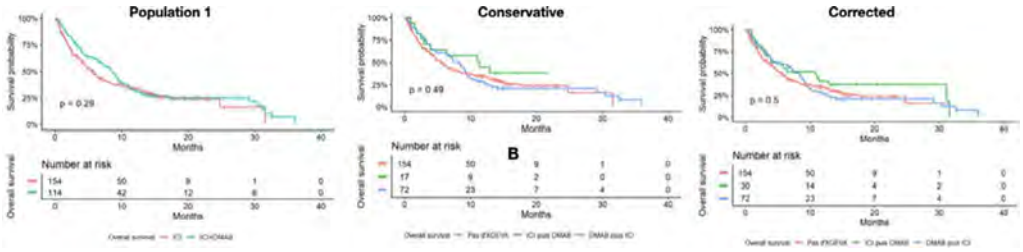

Figure 1 - Survival curves for overall survival (OS)

Conclusion: This retrospective study found no statistical benefit of association of D-MAB with ICI in the whole population but a sequence using ICI and then D-MAB seems to be beneficial to patients. It would be interesting to conduct dedicated studies in bigger cohort to confirm these latter statement.

Disclosure: E. Massy: None; **E. Mabrut**: None; **S. Mainbourg**: None; **C. Confavreux**: None.

Abstract Number: 2016

Generation of a Human 3D *in Vitro* Bone Model That Mimics Glucocorticoid-induced Osteoporosis

Moritz Pfeiffenberger[1], Johannes Plank[1], Alexandra Damerau[1], Timo Gaber[1] and **Frank Buttgereit**[2], [1]Charité Universitatsmedizine - Berlin, Berlin, Germany, [2]Charité Universitätsmedizin, Dept. Rheumatology, Berlin, Germany

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoporosis is a bone disease characterized by low bone mass and changes in bone architecture, leading to pain and reduced mobility in patients. Glucocorticoid-induced osteoporosis (GIOP) is the best known form of secondary osteoporosis. Glucocorticoids (GC) are commonly used to treat inflammation, such as in rheumatic diseases. However, GC use can have a negative effect on the skeletal system and lead to osteoporosis.

(i) Establishing and characterizing a human *in vitro* bone model consisting of osteoblasts and osteoclasts embedded in β-TCP ("healthy" bone model), (ii) treatment with dexamethasone to induce GIOP ("osteoporotic" bone model) and (iii) using this model as a testing platform for the treatment of osteoporosis.

Methods: Our model includes osteoblasts and osteoclasts, which are mainly responsible for bone remodeling. We defined an osteoclast differentiation protocol using low-attachment plates and cultured the cells for 21 days in ∝MEM medium, 5% FCS, 5% human AB serum, 2 mmol L-glutamine, 25 ng/ml M-CSF, and 50 ng/ml RANKL. To provide the basic scaffold for the structure of the "healthy" bone model, mesenchymal stromal cells (MSCs) were seeded on β-tricalcium phosphate (β-TCP). This bone model, consisting of differentiated osteogenic cells, was fully characterized in our previous work [1].

Results: The multinuclearity, typical ß-actin ring formation, cellular activity by TRAP staining and functionality in resorption assays proved functional osteoclasts. Our protocol allowed us to passage these cells without cell loss or loss of function. To establish the previously "healthy" (i.e., untreated) bone model, we seeded osteoclasts onto a pre-seeded β-TCP

construct and cultured the co-culture for 7 days. We then analyzed the supernatant and detected marked secretion of RANKL, MMP-9, and free phosphate. This indicates the functionality of both osteoclasts and osteoblasts in our 3D model. Subsequently, the healthy model will be transferred to the osteoporosis-simulating model where treatment with dexamethasone will be applied. Once established, we plan to use the model we have developed for in vitro preclinical trials to test marketed drugs.

Conclusion: Ultimately, we will obtain an *in vitro* 3D co-culture of osteoblasts/osteoclasts simulating human native bone, which will be treated with dexamethasone to mimic key aspects of GIOP *in vitro*.

Disclosure: M. Pfeiffenberger: None; **J. Plank**: None; **A. Damerau**: None; **T. Gaber**: None; **F. Buttgereit**: AbbVie/Abbott, 6, Horizon Therapeutics, 5, Pfizer, 5, 6, Roche, 6.

Abstract Number: 2017

Lupus Nephritis Is Strongly Associated with Low Bone Mineral Density and Osteoporosis in Patients with Systemic Lupus Erythematosus

Edgar Wiebe[1], Elisa Schilling[2], Dörte Huscher[3], Andriko Palmowski[4], Zhivana Boyadzhieva[5], Sandra Hermann[1], Burkhard Muche[1], Tobias Alexander[6], Falk Hiepe[5] and Frank Buttgereit[1], [1]Charité Universitätsmedizin, Dept. Rheumatology, Berlin, Germany, [2]Charité Universitätsmedizin Berlin, Dept. Rheumatology, Berlin, Germany, [3]Institute of Biometry and Clinical Epidemiology and Berlin Institute of Health, Charité Universitätsmedizin Berlin, Berlin, Germany, [4]Charité - Universitätsmedizin Berlin, Berlin, Germany, [5]Charité Universitatsmedizine - Berlin, Berlin, Germany, [6]Charité Universiätsmedizin Berlin, Dept. Rheumatology, Berlin, Germany

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
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Background/Purpose: Patients with systemic lupus erythematosus (SLE) are at increased risk for osteoporosis and fragility fractures. This risk is mediated by a variety of factors such as chronic inflammation, treatment with glucocorticoids (GC), vitamin D deficiency, and others. The role of disease-specific factors of SLE has not been fully elucidated.

We aimed to identify factors associated with bone mineral density and osteoporosis including fragility fractures to better understand the interplay between disease-specific factors and general risk factors that drive bone loss in this patient population.

Methods: Rh-GIOP is a prospective observational cohort study investigating bone health in consecutive patients ≥18 years with inflammatory rheumatic diseases and current or prior GC treatment. This cross-sectional analysis assessed the baseline visits of all patients with SLE fulfilling the EULAR/ACR 2019 SLE classification criteria. Multivariable linear regressions models were fitted to identify factors associated with bone mineral density (BMD). As a second outcome, we investigated factors associated with clinical osteoporosis (OP, defined by either a T-Score of ≤ -2,5, anti-osteoporotic treatment and/or fragility fractures) by multivariable logistic regression analysis.

Results: Baseline data from 110 patients with SLE were analyzed. The mean age was 48.1±14.5 years, mean disease duration 16.3±9.9 years, and 41% of the cohort was identified as having OP. Lupus nephritis was present in 35% of the SLE patients, of whom 55% had active nephritic disease at baseline osteoporosis screening visit. Class IV and V accounted for

most nephritis cases (61%). In multivariable linear regression analysis, lupus nephritis class IV and V (reg. coefficient (95%CI): -0.745 (-1.395;-0.095)), the presence of U1-RNP antibodies (-0.750 (-1.314;-0,187)) as well as C-reactive protein (CRP, -0.015 (-0.026;-0.003)) and longer disease duration (-0.037 (-0.056;-0.018)) were significantly associated with low BMD. Conversely, clinical remission (defined as SLEDAI-2K=0 and GC dosage ≤5 mg prednisone equivalent per day) was positively associated with BMD (0.447 (0.037;0.857)), as were Siglec-1 levels on monocytes as surrogate for Type-I interferon activity (0.558 (0.150;0.967)), BMI (0.045 (0.014;0.076)), and health assessment questionnaire (HAQ, 0.307 (0.078;0.536)). In multivariable logistic regression analysis, active lupus nephritis (OR (95%CI): 7.42 (1.256;43.868)) was strongly associated with OP in patients with SLE. Additionally, age (1.06 (1.020;1.100)), HAQ (0.29 (0.120;0.682)) and complement factor 3 (1.27 (1.002;1.601)) were found to be significantly related to the presence of OP. Neither current GC use, cumulative GC dose nor GC duration were significantly associated with BMD or clinical OP.

Conclusion: In patients with SLE, indicators of disease severity, expressed by (active) lupus nephritis, high CRP, U1-RNP antibodies, and long disease duration, are related to poor bone health in addition to commonly known risk factors such as low BMI and higher age. The knowledge of these disease-specific factors helps to identify patients with SLE at particular high risk for OP and fragility fractures.

Disclosure: E. Wiebe: EW reports consultancy fees, honoraria and travel expenses from Medac and Novartis., 2, 6, 12, Travel Expenses; **E. Schilling**: None; **D. Huscher**: None; **A. Palmowski**: None; **Z. Boyadzhieva**: None; **S. Hermann**: None; **B. Muche**: BM received consulting and speaker honoraria and/or congress support from UCB Pharma Germany, Amgen Germany, Stadapharm., 6, 12, congress support; **T. Alexander**: None; **F. Hiepe**: None; **F. Buttgereit**: AbbVie/Abbott, 6, Horizon Therapeutics, 5, Pfizer, 5, 6, Roche, 6.

Abstract Number: 2018

Development of an Osteoporosis Treatment Gap Dashboard

Rulan Lyu[1], Patrick O'Brien[1], Tracey Wilkie[1], Yun Chang[1] and **Jonathan Cheah**[2], [1]UMass Memorial Health, Worcester, MA, [2]UMass Chan Medical School, Shrewsbury, MA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session C
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Background/Purpose: Osteoporosis and the clinical event of fragility fracture is an ever-increasing public health burden. A significant osteoporosis treatment gap remains, whereby individuals with a fragility fracture are never prescribed therapies for fracture risk reduction. In addition, recent specialty guidelines for the treatment of osteoporosis have started to risk stratify individuals for the purposes of sequential treatment strategies over time. The aim of this work is to utilize multiple sources of data within the electronic medical record (EMR) to identify individuals eligible, but who have not yet received therapies for fracture risk reduction who can then be targeted for intervention.

Methods: Within a single academic health system and focusing on the criteria distinguishing between high- and very high-risk patients as described by specialty guidelines relating to osteoporosis treatment, candidate items were identified to be incorporated into the dashboard. These included 1: demographic data such as race/ethnicity and primary insurance coverage, 2: ICD10 codes on problem lists relating to osteoporosis and fracture, 3: abstraction of T-scores from dual energy x-ray absorptiometry scans, 4: abstraction of vertebral compression fractures from CT and MRI reports and 5: information on

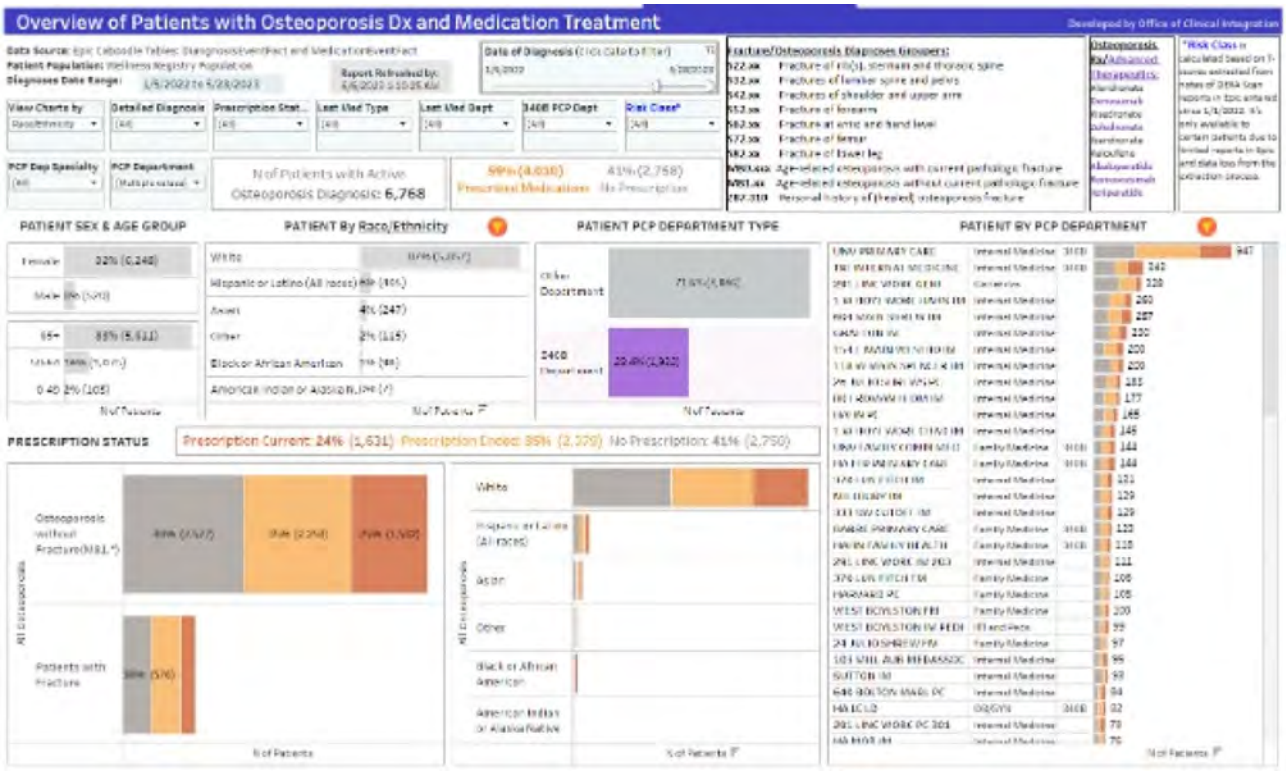

Figure 1: high level overview of osteoporosis treatment gap dashboard

prescriptions for FDA-approved medications for fracture risk reduction. The Epic Caboodle database was utilized to obtain most of the data, however, data relating to T-scores and vertebral compression fractures were abstracted separately. Once these individual pieces of data were identified, a treatment dashboard was created to present this data in an actionable format.

Results: An osteoporosis treatment gap dashboard was created (Figure 1) to identify individuals who meet diagnosis for osteoporosis by: ICD 10 code, T-score, vertebral compression fracture noted on CT or MRI reports and to stratify individuals by risk level (presence of fracture, very low t-score), as well as a number of other factors such as age, race/ethnicity, primary care provider and primary insurance coverage. Information on whether an individual has received a therapy for fracture risk reduction is also included. Specific lists of individuals can be generated accordingly, for example by primary care practice, or risk level of future fracture, to allow for locally guided interventions to address the osteoporosis treatment gap.

Conclusion: An osteoporosis treatment gap dashboard has been created which is able to identify and risk stratify individuals who per specialty guidelines would qualify for therapies for fracture risk reduction. Additional work is underway to utilize this dashboard with the aim to reduce the osteoporosis treatment gap.

Disclosure: R. Lyu: None; **P. O'Brien**: None; **T. Wilkie**: None; **Y. Chang**: None; **J. Cheah**: AbbVie/Abbott, 1.

Abstract Number: 2019

2023 EULAR Recommendations for the Management of Fatigue in People with Inflammatory Rheumatic and Musculoskeletal Diseases

Emma Dures[1], **Bayram Farisogullari**[2], Eduardo Santos[3], Anna Molto[4], Caroline Feldthusen[5], Claire Harris[6], Corinna Elling-Audersch[7], Deirdre Conolly[8], Elena Elefante[9], Fernando Estévez-López[10], Ilaria Bini[11], Jette Primdahl[12], Kirsten Hoeper[13], Marie Urban[14], Mart van de Laar[15], Marta Redondo[16], Peter Böhm[17], Raj Amarnani[18], Rhys Hayward[6], Rinie Geenen[19], Simona Rednic[20], Susanne Pettersson[21], Tanja Thomsen[22], Till Uhlig[23], Valentin Ritschl[24] and Pedro Machado[25], [1]Academic Rheumatology, Bristol Royal Infirmary; and Faculty of Health and Applied Sciences, University of the West of England, Bristol, United Kingdom, [2]Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey, [3]Health Sciences Research Unit: Nursing (UICISA: E), Nursing School of Coimbra (ESEnfC), Coimbra, Portugal, [4]HOPITAL COCHIN AP-HP, Service de Rhumatologie, Paris, France, [5]Institute of Neuroscience and Physiology, University of Gothenburg, Department of Health and Rehabilitation, Unit of Physiotherapy, Sahlgrenska Academy, Gothenburg, Sweden, [6]Northwick Park Hospital, London North West University Healthcare NHS Trust, Department of Rheumatology, London, United Kingdom, [7]Deutsche Rheuma-Liga Bundesverband e.V., Patient Research Partner, Bonn, Germany, [8]School of Medicine, Trinity College Dublin, Discipline of Occupational Therapy, Dublin, Ireland, [9]Rheumatology Unit, Department of clinical and experimental medicine, University of Pisa, Pisa, Italy, [10]Harvard T.H. Chan School of Public Health, Department of Social and Behavioral Sciences, Boston, MA, [11]Anmar, Young, Rome, Italy, Rome, Italy, [12]University Hospital of Southern Denmark, Danish Hospital for Rheumatic Diseases, Sønderborg, Denmark, [13]Hannover Medical School, Department of Rheumatology and Immunology, Hannover, Germany, [14]University Hospitals Bristol, Research Design Service, Bristol, United Kingdom, [15]University of Twente, Department of Psychology, Health and Technology, Enschede, Netherlands, [16]Camilo José Cela University, Faculty of Heath Sciences, Madrid, Spain, [17]German League against rheumatism, Forschungspartner, Bonn, Germany, [18]Barts Health NHS Trust, Barts Health Rheumatology Service, London, United Kingdom, [19]Utrecht University, Vorstenbosch, Netherlands, [20]Prof Dr Simona Rednic, Cluj, Romania, [21]Karolinska Institute, Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden, [22]University of Copenhagen, Copenhagen Centre for Arthritis Research, Centre for Rheumatology and Spine Diseases VRR, Rigshospitalet, Copenhagen, Denmark, [23]Center for Treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway, [24]Medical University of Vienna, Vienna, Austria, [25]Centre for Rheumatology & Department of Neuromuscular Diseases, University College London, London, UK. Department of Rheumatology, Northwick Park Hospital, London North West University Healthcare NHS trust, London, UK., London, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Patient Outcomes, Preferences, & Attitudes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Fatigue is prevalent in people with inflammatory rheumatic and musculoskeletal diseases (I-RMDs) and recognized as one of the most challenging symptoms to manage (1). The existence of multiple factors that are correlated with fatigue, the lack of clarity around causal pathways and the evidence about what helps has led to a multifaceted approach to symptom management. However, there are no recommendations for fatigue management in people with I-RMDs. This lack of guidance is difficult for those living with fatigue and for healthcare professionals delivering clinical care.

Methods: A multi-disciplinary taskforce comprising 26 members from 14 European countries was convened and two systematic reviews (SRs) were conducted. The taskforce developed the recommendations based on the SR evidence and taskforce members' personal and professional experience of fatigue in I-RMDs.

Results: Four overarching principles and four recommendations were developed, which include health professionals' awareness that fatigue should be monitored and assessed, and people with I-RMDs should be offered management options. Shared decisions about fatigue management should consider the individual's needs and preferences, as well as their clinical disease activity, comorbidities and other psychosocial and contextual factors (**Table**).

Table: EULAR overarching principles and recommendations for the management of fatigue in people with inflammatory rheumatic and musculoskeletal diseases (I-RMDs)

Overarching principles			LoA Mean (SD)	LoA % with score ≥8
1. Health professionals should be aware that fatigue encompasses multiple and mutually interacting biological, psychological and social factors.			9.9 (0.3)	100
2. In people with I-RMDs, fatigue should be monitored, and management options should be offered as part of their clinical care.			9.6 (1.0)	96
3. Management of fatigue should be a shared decision between the person with an I-RMD and health and well-being professionals.			9.7 (0.7)	100
4. Management of fatigue should be based on the needs and preferences of people with I-RMDs, as well as their clinical disease activity, comorbidities and other individual psychosocial and/or contextual factors.			9.9 (0.3)	100
Recommendations	**LoE**	**GoR**	**Mean (SD)**	**% with score ≥8**
1. Health professionals should incorporate regular assessment of fatigue severity, impact and coping strategies into clinical consultations.	5	D	9.5 (1.3)	91
2. As part of their clinical care, people with I-RMDs and fatigue should be offered access to tailored physical activity interventions and encouraged to engage in long-term physical activity.	1a	A	9.6 (1.0)	96
3. As part of their clinical care, people with I-RMDs and fatigue should be offered access to structured and tailored psychoeducational interventions.	1a	A	9.5 (1.2)	96
4. The presence or worsening of fatigue should trigger evaluation of inflammatory disease activity status and consideration of immunomodulatory treatment initiation or change, if clinically indicated.	1a	A	9.4 (1.2)	82

EULAR, European Alliance of Associations of Rheumatology; LoA, Level of Agreement; LoE, Level of Evidence (1 to 5; 1=high quality RCT, and 5=expert opinion), GoR, Grade of Recommendation (A to D; A=consistent level 1 studies, and D=level 5 evidence); SD, standard deviation

Conclusion: These 2023 EULAR recommendations provide consensus and up-to-date guidance on the management of fatigue in people with I-RMDs.

Disclosure: E. Dures: None; **B. Farisogullari**: None; **E. Santos**: None; **A. Molto**: None; **C. Feldthusen**: None; **C. Harris**: None; **C. Elling-Audersch**: None; **D. Conolly**: None; **E. Elefante**: None; **F. Estévez-López**: None; **I. Bini**: None; **J. Primdahl**: None; **K. Hoeper**: None; **M. Urban**: None; **M. van de Laar**: Eli Lilly, 5, 6; **M. Redondo**: None; **P. Böhm**: None; **R. Amarnani**: None; **R. Hayward**: AbbVie/Abbott, 6; **R. Geenen**: None; **S. Rednic**: None; **S. Pettersson**: None; **T. Thomsen**: None; **T. Uhlig**: Galapagos, 2, 6, Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **V. Ritschl**: None; **P. Machado**: AbbVie/Abbott, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Orphazyme, 2, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 6.

Abstract Number: 2020

Exploring Experiences and Perspectives of Canadian Patients with Lupus Nephritis Through Photovoice

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Patient Outcomes, Preferences, & Attitudes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: LN is a major cause of morbidity and mortality and develops in up to 60% of adult SLE patients. The experiences of patients with SLE have been explored quantitatively and qualitatively. However, we know little of the lived experiences of patients with LN. This research used a social constructionist perspective to explore patient experiences and perspectives of LN.

Methods: Patients aged≥18 years with biopsy-proven pure or mixed ISN/RPS Class III, IV, or V LN and fulfilling the ACR 1997 or SLICC 2012 Classification Criteria for SLE were purposefully recruited from a Canadian lupus cohort to participate in an innovative photovoice exercise. Over a 2-week period, participants took photos of what LN means to them, how LN impacts their daily life, and factors that impact how they manage their LN. Photos (3–5 participants) were shared and discussed in two virtual focus groups. Discussions were transcribed verbatim for subsequent thematic analysis using NVivo Software.

Table 1. Patient Characteristics

Characteristic	Total sample (N=13)
Age, mean (SD), years	41.7 (14.0)
Age at LN diagnosis, mean (SD), years	26.2 (10.1)
Age at SLE diagnosis, mean (SD), years	23.9 (10.4)
Female, %	92.3
Race & ethnicity, %	
Asian	30.8
White	61.5
Medications (ever), %	
Hydroxychloroquine	100.0
Immunosuppressants/biologics	100.0
Azathioprine	46.2
Belimumab	23.1
Cyclophosphamide	30.8
Mycophenolate mofetil/mycophenolic acid	84.6
Rituximab	23.1
Tacrolimus	23.1
LN classification, %	
Class III	33.3
Class IV	33.3
Class V	16.7
Mixed	16.7
Dialysis (ever), %	23.1
Renal transplant, %	15.4
Biopsy-proven LN within the past year and currently receiving immunosuppressants/biologic therapy, %	15.4
Biopsy-proven LN 1–5 years prior and currently receiving immunosuppressants/biologic therapy, %	23.1
Biopsy-proven LN >5 years prior and currently receiving immunosuppressants/biologic therapy, %	46.2
Biopsy-proven LN >5 years prior and no longer receiving immunosuppressants/biologic therapy, %	15.4
Women who have been pregnant or are currently pregnant and received immunosuppressants/biologic therapy during pregnancy, %	7.7

SD, standard deviation

Table 2. Results Overview

Photo Example	Primary Theme Presented in Photo	# of Photos	# of Participants	Secondary Themes Discussed	Illustrative Quote
	Wellbeing-making	n=14	n=6	-Contributing behaviours to wellbeing (e.g., rest, physical activity, listening to music, hydration, walking, diet, dogs) -Reminders of LN challenges (e.g., need for caution, symptoms, altered life trajectories)	*The mountains are also a sacred place for me, where I go to recharge and take in the fresh air and have a bath in nature... And so I believe in that, and I do find that it makes a huge difference for me. (Participant 12)*
	Participant themselves	n=13	n=6	-LN symptoms Medication side effects -Physical environment challenges -Individual management behaviours	*Sometimes they'll have a rounded doorknob, and I'm unable to enter, and they don't have the button or anything like that. Because my hands are so stiff, and I'm unable to move them, I can't open the door. One time I locked myself in a bathroom because it was a rounded doorknob. (Participant 5)*
	Healthcare experiences	n=10	n=7	-Medication challenges (e.g., number of medications required, side effects, frequency of appointments, time required, missed work, geographical distance) -Individual management behaviours	*It's a struggle sometimes, because to remember when to take them, and taking everything on time, and making sure you're taking them every day is a lot of work. As you can see there's a lot of medications that you have to take, and each of them all have different side effects. So it's hard managing some of those side effects on a daily basis. (Participant 7)*
	Home	n=5	n=4	-Reminders of LN challenges (e.g., balance of physical activity with need to be cautious) Emotional burden Reminders of responsibilities (to themselves, to family)	*This represents how it feels when you are trapped. I have called it an ice igloo, and looking out I promise myself that as soon as I'm able, I plan on taking off, but it's kind of a relief that right now I don't have to, because I feel terrible. I don't feel well, and so I have an excuse for not moving...now I live with a fairly constant fear of failure. Fear that I'm not going to be able to take off and do what I once did. (Participant 3)*
	Community	n=2	n=2	Transportation challenges LN symptoms (e.g., brain fog)	*On the train, sometimes I experience a lot of brain fog, and it's kind of holding me back right now because I want to go to school... sometimes I'll be coming home from work, and I'll be like, Wait! Where am I going? I feel confused and just lost for a few seconds. (Participant 5)*
	Friends	n=2	n=2	-Value of friendship -Reminder of physical symptoms - Individual management behaviours	*Sometimes you have to go out in the sun, to make fun with your friends. But it's a struggle to go under the sun, and after this... at the end of the day I was feverish, and having symptoms. (Participant 6)*
	Work	n=2	n=2	-Employment impacts (e.g., need for flexibility/ accommodations) Employment challenges (e.g., if flexibility/ accommodations not possible)	*Attempting to work from home just because it was a bad day, and I couldn't get out of bed. (Participant 1)*
	Other challenges	n=6	n=4	-Challenges associated with invisible illness -Financial challenges (e.g., insurance coverage for medication) -Challenges of family planning	*We were always told it was going to be harder to get pregnant. There's a lot more doctors, and medication, and appointments involved, and there's obviously a high risk of miscarriage. This is from when we had our first miscarriage, we've since had another one. Just the hardships that come with that... I've got kidney disease and it's just one of those additional complexities that you never think of. You don't realize how it's going to impact your life until it does. There's nothing you can really do about it, there's not a lot of information either. (Participant 8)*

Results: Thirteen patients withLN participated; 92.3% were female, mean (SD) age was 41.7 (14.0) years (**Table 1**). Of the 54 photos, images depicting activities/settings that contribute to wellbeing (n=14), the participants themselves (n=13), healthcare experiences (n=10), home (n=5), work (n=2), community (n=2), friends (n=2), and other challenges (n=6) were shared (**Table 2**). All participants described the physical (e.g., fatigue, joint pain, rash) and psychosocial (e.g., fear, stress, social exclusion, feeling trapped, grief, and loss) impacts of living with LN. Although twelve discussed activities that contribute to well-being (e.g., listening to music, biking, walking dogs, spending time with family/friends, spending time in nature), participants were consistently reminded of their LN during/following these activities due to physical symptoms (*There'd be days where my hands would cramp up and my knees would be stiff, but I just push through… because I love that experience of looking around at my surroundings, and the leaves falling (P5)*), the need for caution while participating (*I only rode [the bike] once, because I am always hearing my doctors very sage advice in my ear. Be careful, don't overdo it (P3)*), and altered life trajectories (*My husband and I had envisioned we'd be playing with grandchildren… but I was never able to carry… [The dogs] are affectionate, loyal, and they need us… so they are sort of the light (P3); You're always at a crossroad, you're always having to make a decision… you have to turn left or right, you can't keep going straight (P8)*). Eleven participants discussed the need for, and burden of, medications to manage their LN; side effects (n=10) and medication-related financial challenges (n=5) were highlighted.

Conclusion: Respondents reported a substantial psychosocial burden associated with their LN diagnosis. While activities that contribute to well-being were emphasized, the physical, emotional, and lifestyle impacts of LN and the associated medication journey serve as frequent reminders of the disease burden, both now and into the future. The need for flexibility (i.e., from friends, employers, and themselves) is an essential component of navigating altered life trajectories.

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Disclosure: F. Cardwell: None; **S. Elliott**: None; **M. Barber**: AbbVie/Abbott, 2, AstraZeneca, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Sanofi-Genzyme, 2; **K. Cheema**: Alexion, 1, 6, Novartis, 1, Otsuka, 6; **S. George**: GlaxoSmithKlein(GSK), 3; **A. Boucher**: GlaxoSmithKlein(GSK), 3; **A. Clarke**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(-GSK), 2, 5, Otsuka, 2, Roche, 2.

Abstract Number: 2021

Beliefs, Attitudes, and Preferences of Patients with Rheumatoid Arthritis (RA) and Concomitant Cancer with Respect to RA Therapy

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Treatment of rheumatoid arthritis (RA) in patients with cancer could potentially result in poor cancer outcomes because of immunosuppression. Adequate data for shared decision-making in patients with RA and cancer is scarce, as there are uncertainties about the risk of various RA therapies on cancer progression and recurrences. The aim of this study was to identify the beliefs, preferences, and informational needs of patients with RA and cancer with respect to the harms, benefits, and risk uncertainties of RA therapy.

Methods: We conducted individual interviews of 20 patients with RA and cancer recruited consecutively at outpatient clinics in a cancer center. We used a semi-structured guide for the interviews. We explored the following themes: i) past experiences in medical encounters, ii) beliefs and attitudes about harms and benefits of RA, and iii) decision making process about RA treatment. We conducted a thematic analysis to interpret data.

Results: Fifteen (75%) patients were female, mean age was 59.4 years (SD 10.2). Median RA duration was 11 years. Four (20%) patients had breast cancer, four (20%) had melanoma, two (10%) had lymphoma, and each of the other 10 had another different cancer. (1) Past experiences. Patients reported discussing concerns with their physicians about RA symptoms, the impact of RA treatment on RA, adverse events, interactions between RA and oncologic therapies, and discontinuation of RA treatment after cancer diagnosis. Most patients felt their concerns were addressed after the discussion with their providers. (2) Beliefs and attitudes. Few patients were concerned about the risk of cancer development or recurrence with RA treatment, and some mentioned lymphoma risk with biologics. Patients were concerned about the impact of cancer treatment on RA, RA flare-ups, and suppression of their immune system. (3) Decision making process. Most patients felt decisions were shared with their providers including discontinuing, changing, or adding new drugs. Most common decision facilitators included discussions with their physicians and their own previous experiences. Most patients would consider taking a drug to improve RA even if the effect on cancer were unknown. Informational needs included the following areas: (i) adverse events and efficacy of drugs, (ii) drug interactions, (iii) impact of RA drugs on cancer, and (iv) costs. With respect to delivery of information, many patients, but not all, found other patients' testimonials helpful. Preferred types and formats for information included pictures, graphs, and numerical information (e.g. probabilities) on benefits and harms. Various modes of delivery were identified such as mailings, emails, websites, electronic medical records, videos, and through discussion with providers.

Conclusion: We identified important aspects related to the preferences, concerns, and informational needs in the treatment decision making process of patients with RA and cancer. Discussions with physicians were the most important factor to make decisions about RA treatment, but patients also identified other potential sources of information that could aid in this process.

Disclosure: J. Ruiz: None; **S. Madramootoo**: None; **M. Lopez-Olivo**: None; **N. Singh**: None; **M. Suarez-Almazor**: Celgene, 1, Eli Lilly, 2, Pfizer, 2, Syneos Health, 1.

Abstract Number: 2022

Development of an mHealth App for Lupus: Insights from a Human-Centered Design Approach

Anna Deck[1], Kiran Singh[2], Lucas Dantas[3], Amy LeClair[2], Lisa Mandl[4], Timothy McAlindon[5], Faye Chiu[6], Monique Gore-Massy[7] and Shanthini Kasturi[2], [1]Tufts University School of Medicine, Boston, MA, [2]Tufts Medical Center, Boston, MA, [3]Ambulomics, Boston, MA, [4]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [5]Tufts Medical Center, Arlington, MA, [6]N/A, New York, NY, [7]Covid-19 GRA, West Orange, NJ

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Patient Outcomes, Preferences, & Attitudes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Mobile health (mHealth) technology offers promising tools to facilitate the self-management of chronic diseases, including systemic lupus erythematosus (SLE). However, currently available mHealth applications (apps) for SLE are of limited quality and functionality, having largely been developed without the direct input of individuals living with

SLE. Human-centered design is a method of problem-solving that strives to put real people at the center of the development process and involves three steps: inspiration, ideation, and implementation. Here we describe the application of human-centered design methodology to elicit patient preferences and guide the development of an mHealth app for the management of fatigue in SLE.

Methods: Patient perspectives and preferences for an mHealth app addressing fatigue in SLE were explored in the inspiration phase through literature review, focus groups, and targeted conversations with patients. Key features for the app were identified and an initial prototype was developed in the ideation phase. Individuals with SLE reviewed the prototype in in-depth interviews and surveys. Participants were purposefully sampled around age, sex, race, ethnicity, and disease duration. They provided open-ended feedback on app functionalities and format, and rated features using a 5-point Likert scale. Interviews were conducted online using cloud-based video conferencing (Zoom) and were recorded, transcribed, and analyzed using a rapid analysis protocol and feedback capture grid. The prototype was iteratively refined in multiple cycles of feedback.

Table 1. Interview participant characteristics (n=10)

Characteristic	Value
Age Mean (SD) years	41.5 (8.6)
SLE disease duration Mean (SD) years	14.2 (7.8)
Sex	
Female	8 (80%)
Male	2 (20%)
Race	
White	4 (40%)
Black or African-American	3 (30%)
Asian	1 (10%)
More than one race	2 (20%)
Ethnicity	
Hispanic	4 (40%)
Non-Hispanic	6 (60%)
Insurance Type	
Medicaid	1 (10%)
Medicare	2 (20%)
Third party/private	6 (60%)
None	1 (10%)
Education	
High school graduate	2 (20%)
Associate degree	1 (10%)
Bachelor's degree	4 (40%)
Graduate degree	3 (30%)
Employment	
Part Time	1 (10%)
Full Time	4 (40%)
Self-Employed	2 (20%)
On Disability	3 (30%)

Table 2. Prototype Ratings [mean (standard deviation), where 1= Love it and 5= Hate it]

	Prototype 1 (n=10)	Prototype 2 (n= 7)
Features		
Education	1.6 (0.7)	Not rated
Self-Assessment Quizzes	2.1 (1.2)	Not rated
Goal setting and logs	1.6 (1.0)	Not rated
Trackers (steps/sleep/mood)	1.7 (1.0)	Not rated
Reminders	1.4 (0.7)	Not rated
Community/Social connection	1.4 (0.5)	Not rated
Format		
Color scheme	2.1 (0.8)	2.1 (1.1)
Layout	2.0 (0.9)	1.1 (0.4)
Text	2.0 (1.0)	1.9 (0.9)
Graphics/Images	1.9 (0.9)	1.9 (0.9)
Likeliness to use app	1.7 (0.9)	1.7 (0.8)

Results: Twelve patients from two academic medical centers participated in two initial focus groups and brainstormed features and functionalities for the app. Research team members, including two patient stakeholders, developed an initial app prototype based on ideas generated in the inspiration phase. Ten individuals with SLE (Table 1) provided feedback on the initial prototype and subsequent iterations in two rounds of surveys and interviews. Overall, participants rated the features and format of the prototypes highly (Table 2) and over 80% reported they were likely or highly likely to use the proposed app. Several themes around preferences for the app emerged from the interviews (Figure 1), including the importance of 1) community/social connection; 2) accessibility and inclusion, and 3) options for customization and integration of the app with existing digital health tools and health care. Participants highlighted the potential of the app to facilitate self-management and improve quality of life, but noted sustained engagement as a possible challenge.

Conclusion: A patient-engaged, human-centered design approach provided valuable insights into patient preferences and priorities for an mHealth app for the management of fatigue in SLE. Feedback from the inspiration and ideation phases will inform iterative prototype refinement and guide app pilot testing (implementation).

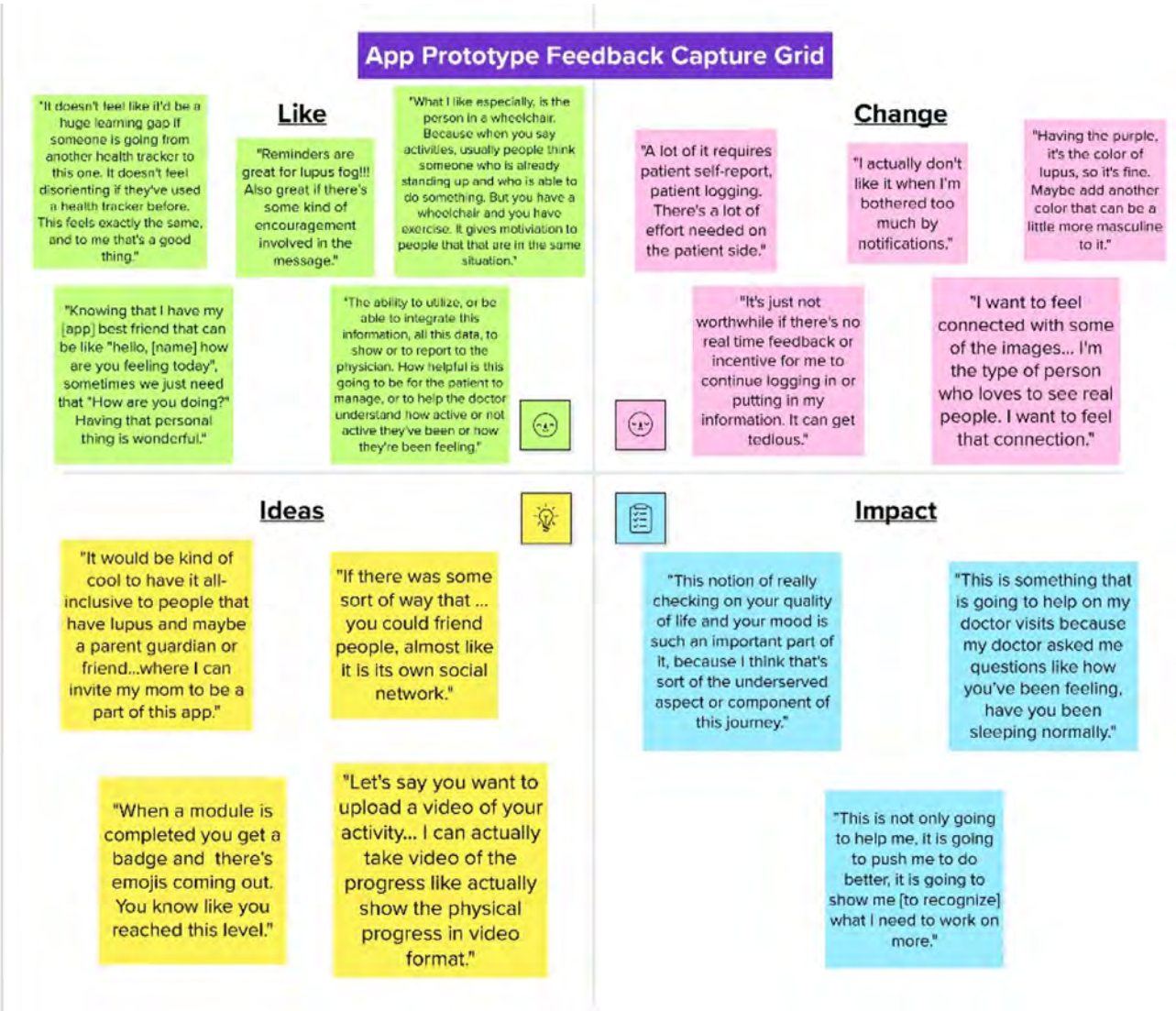


Figure 1. Feedback Capture Grid

Disclosure: A. Deck: None; **K. Singh**: None; **L. Dantas**: None; **A. LeClair**: None; **L. Mandl**: Annals of Internal Medicine, 12, Associate Editor, Regeneron Pharmaceuticals, 5, Up-to-Date, 9; **T. McAlindon**: None; **F. Chiu**: None; **M. Gore-Massy**: Aurinia Pharmaceuticals, 1, 2, 7, Bristol-Myers Squibb(BMS), 2, 6, 7, Janssen, 1, 2, 7, Lupus foundation of America, 1; **S. Kasturi**: GlaxoSmithKlein(GSK), 1.

Abstract Number: 2023

Transition Readiness over Time in a Rheumatology Transition Clinic

SESSION INFORMATION

Session Date: **Tuesday, November 14, 2023**
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In 2018 we designed a Rheumatology Transition clinic to care for adolescent patients with autoimmune disease. We incorporate Health Care Transition curriculum (HCT) into our clinic to improve Transfer outcomes as patients move from a pediatric to adult healthcare model. As part of this HCT, we ask our participants to complete a Transition Readiness Assessment (TRA) that mirrors the same assessment available from the GotTransition website. This assessment quantifies a patient's preparedness to become independent in managing their own health care. This abstract presents

Table 1: Patient demographics

Variable	Summary (N=129)
Age at diagnosis: Mean (SD)	13.2 (4.3)
Median (IQR)	15.0 (11.0, 16.0)
Range	(1.4, 19.0)
Age at enrollment: Mean (SD)	18.8 (1.8)
Median (IQR)	19.0 (18.0, 20.0)
Range	(14.0, 25.0)
Sex: Female	97 (75.2%)
Male	32 (24.8%)
Gender Identity: Cis-female	46 (70.8%)
Cis-male	12 (18.5%)
Non-binary	3 (4.6%)
other	4 (6.2%)
Race: American Indian or Alaskan Native	1 (0.8%)
American Indian or Alaskan Native/Black or African American/White	1 (0.8%)
Asian	4 (3.1%)
Asian/Native Hawaiian or Other Pacific Islander	1 (0.8%)
Black or African American	4 (3.1%)
Black or African American/White	1 (0.8%)
Hawaiian or Other Pacific Islander	2 (1.6%)
Not Reported	3 (2.3%)
Other	4 (3.1%)
Unknown	3 (2.3%)
White	105 (81.4%)
Ethnicity: Hispanic or Latino	21 (16.3%)
NOT Hispanic or Latino	101 (78.3%)
Not Reported	3 (2.3%)
Unknown	4 (3.1%)
Time between surveys: Mean (SD)	358.9 (238.2)
Median (IQR)	290.5 (187.8, 401.5)
Range	(91.0, 906.0)

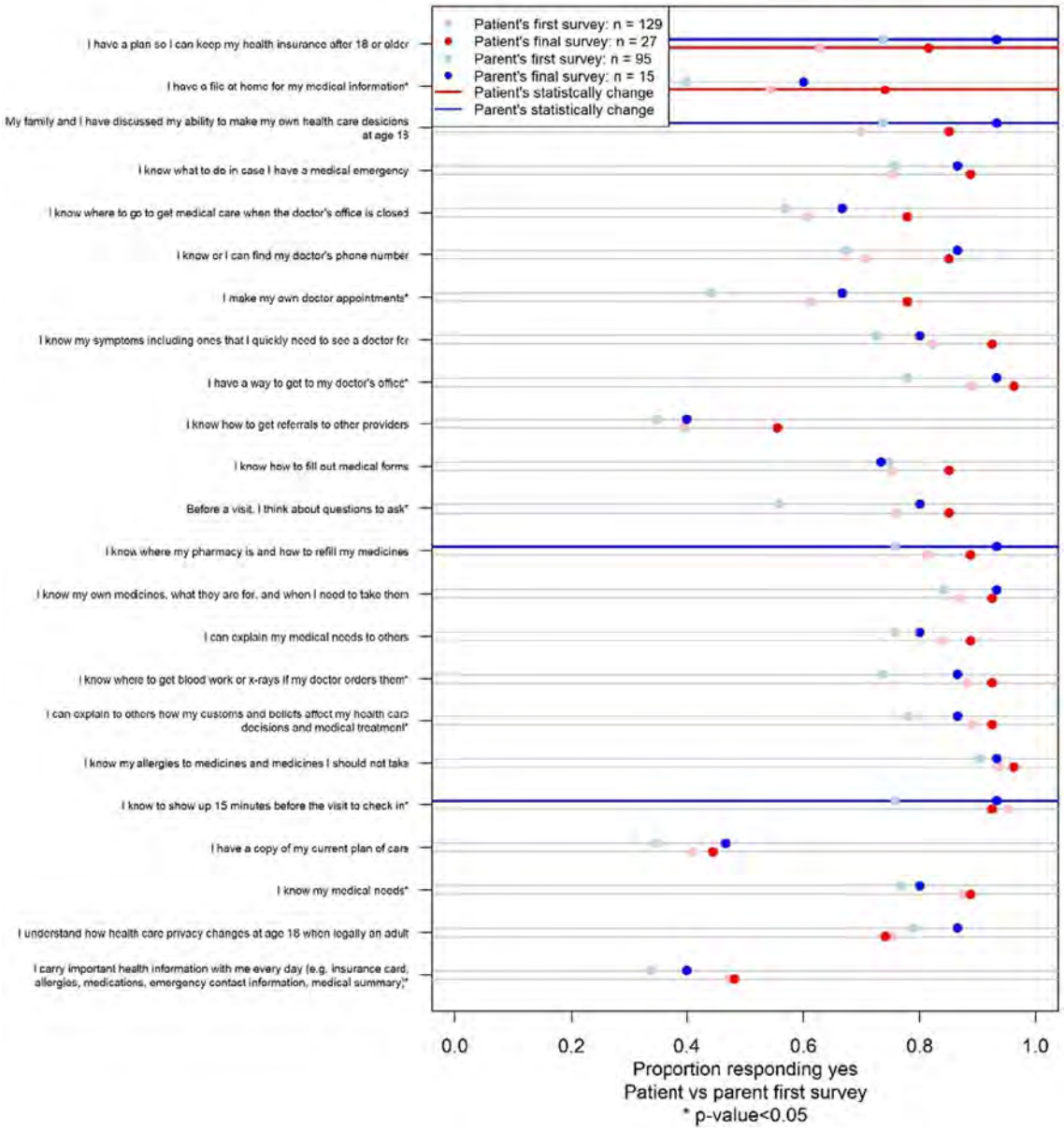
Missing values: Age at diagnosis = 3, Age at enrollment = 3, Gender Identity = 64, Time between surveys = 105.

preliminary data from the TRA, contrasting responses over time in individual patients and parents, and the responses from the patients versus their parents or legal guardians.

Methods: Participants are asked to complete the TRA. The TRA is requested at two time points. First, when patients are first evaluated. Second, just before their first clinical visit with an adult Rheumatologist in an adult Rheumatology clinic.

Responses from the patients at the two time points were evaluated and compared using appropriate statistical analyses. To assess the significance of changes in responses over time, a t-test was conducted to compare the patients' first and second answers. The mean (SD) was calculated to summarize the age at diagnosis, age at enrollment, and the number of days from the first survey to the second survey. Additionally, the median (interquartile range, IQR) and range were used to summarize the distribution of these variables. Categorical variables such as sex, gender identity, race, and ethnicity were summarized using N (%) to indicate the number and percentage of patients within each category.

Figure 1: TRA responses over time



Results: As of May 2023, we had 129 patient and 95 parent participants in the first TRA; and 27 patient and 15 parent participants in the second TRA (Table 1: Patient demographics). In all but two variables, patients and parents report improvement in Transition readiness. Patients report better Transition readiness, than do parents, when they are first enrolled into the registry. Where there is a statistically significant disparity between patients and parents in their assessment, it is patients who report better Transition readiness at registry enrollment. However, where there is a statistically significant disparity in their assessment over time, it is parents who are more likely to report a longitudinal improvement in their child's Transition readiness over time (Figure 1: TRA responses over time).

Conclusion: These findings alone do not prove a causative effect between the HCT curriculum in our Transition clinic and improved Transition readiness over time. However, this improvement in Transition readiness over time is encouraging. Potential confounders might include an independent progression in maturity and independence with age that might also improve Transition readiness. In our future research, we will work to understand patient-specific variables that influence improved Transition readiness, and if there is a correlation with Transition readiness and Transfer and medical outcomes.

Abstract Number: 2024

Patient-Reported Outcomes in Patients with Lupus Nephritis: A Post Hoc Analysis of Control Arm Data from Two Completed Phase III Randomized Clinical Trials

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis (LN) is a severe and common (50%) organ-threatening manifestation of systemic lupus erythematosus and is associated with a high risk of progression to chronic kidney disease and kidney failure.[1] LN treatment goals include normalization of kidney function, low disease activity and, increasingly, improvements in health-related quality of life (HRQOL). Assessment of content validity for the Short Form-36 (SF-36) and FACIT-Fatigue scales have identified fatigue, pain, vitality and physical well-being as particularly impactful in patients with LN compared with healthy controls.[2,3] Limited data exist on the relationship between renal function and HRQOL in patients with LN.

Methods: We conducted a post hoc descriptive analysis of data collected from the control arms of 2 global Phase III LN RCTs: LUNAR (NCT00282347)[4] and BELONG (NCT00626197).[5] We excluded active-arm patients to focus on patients receiving standard of care (SOC) therapy. These studies included adult ANA+ patients with biopsy-confirmed class III/IV LN and proteinuria. We described patients according to baseline factors and characterized HRQOL scores over study week. The LUNAR trial included the Expanded Health Survey (EHS) (Weeks 0, 12, 24 and 52), and BELONG included the SF-36, FACIT-Fatigue and modified Brief Pain Inventory (Weeks 0, 12, 24, 36 and 48). The SF-36 and EHS include information on general health, social/physical functioning, role limitations due to physical/emotional problems, vitality, emotional well-being and pain. We analyzed these tools based on recoding responses to a range of 0 to 100, with higher values representing better HRQOL. We assessed the relationship between (1) baseline proteinuria (urine protein creatinine ratio [UPCR]) and (2) complete renal response (CRR) and mean change in fatigue and general health scores using stratified analyses and Mann-Whitney test for differences.

Results: Table 1 describes baseline study-specific patient characteristics. The lowest baseline scores were identified for general health and vitality in the SF-36 and for fatigue, tiredness and energy in the FACIT-Fatigue. **Figure 1** provides SF-36 scores for general health, pain, vitality, physical functioning and fatigue by study week. HRQOL trajectories suggest consistent patterns across trials with improvements in domains such as fatigue and pain. Patients with baseline UPCR ≥3 had greater change in fatigue score at Week 52/48 than those with UPCR < 3 (**Figure 2**). We did not identify significant changes in fatigue score by CRR status, nor change in general health score at Week 52/48 according to baseline UPCR or CRR.

Table 1. Description of Study Population at Baseline: Control Arm Data From the LUNAR and BELONG LN Trials

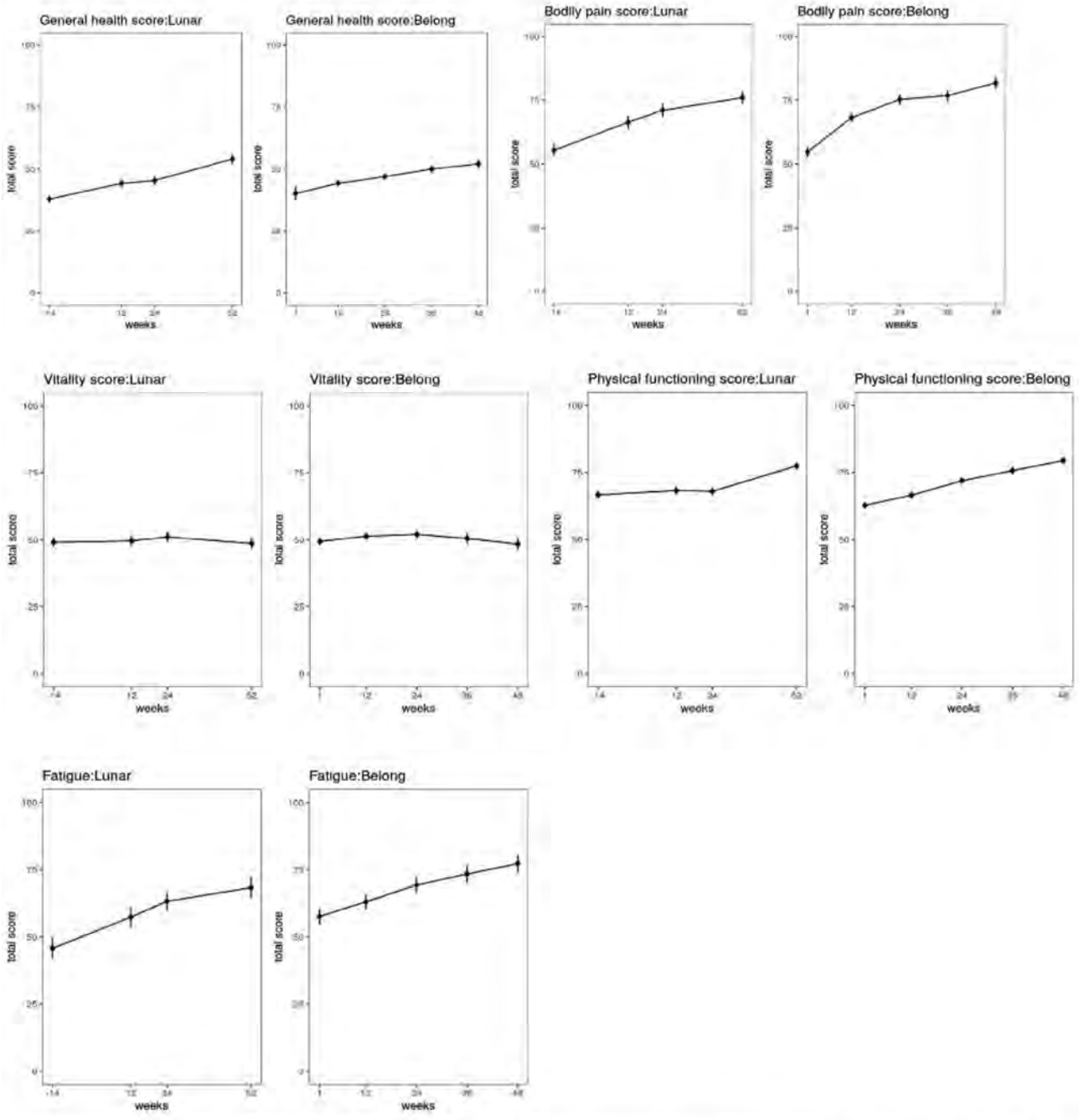
	LUNAR (N=72)*	BELONG (N=126)†
Study period	Jan 2006 – Nov 2009	Feb 2008 – Sept 2010
SOC used in control arm	MMF	MMF or CYC/AZA
Follow-up time, median (Q1, Q3), months	18.5 (17.0, 24.3)	14 (10.8, 18.0)
Age, mean (SD), years	29.4 (9.3)	31.4 (9.9)
Female sex, n (%)	67 (93.1)	107 (84.9)
Race and ethnicity, n (%)		
American Indian or Alaskan Native	0 (0)	17 (13.5)
White	26 (36.1)	58 (46.0)
Black or African American	19 (26.4)	5 (4.0)
Asian	3 (4.2)	35 (27.8)
Other	23 (31.9)	11 (8.7)
Multiple	1 (1.4)	0 (0)
Region, n (%)		
Latin America	20 (27.8)	47 (37.3)
United States	52 (72.2)	15 (11.9)
Europe	0 (0)	31 (24.6)
Asia	0 (0)	31 (24.6)
Africa	0 (0)	1 (0.8)
LN Class		
III ± V	24 (33.3)	30 (23.8)
IV ± V	48 (66.6)	96 (76.2)
Serum creatinine, mean (SD), mg/dL	1 (0.5)	0.89 (0.4)
UPCR, mean (SD), mg/mg	4.4 (3.1)	6.3 (27.2)
eGFR, mean (SD), mL/min/1.73m²	93.7 (36.6)	98.2 (29.5)
C3, mean (SD), mg/dL	74.1 (27.9)	64.7 (25.6)
C4, mean (SD), mg/dL	13.8 (9.4)	14.9 (8.5)

AZA, azathioprine; CYC, cyclophosphamide; eGFR, estimated glomerular filtration rate; LN, lupus nephritis; MMF, mycophenolate mofetil; SOC, standard of care.

*The LUNAR trial was a Phase III, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of rituximab in combination with MMF compared with placebo in combination with MMF in patients diagnosed with International Society of Nephrology/Renal Pathology Society (ISN/RPS) 2003 Class III or IV LN.

†The BELONG trial was a Phase III, randomized, double-blind, placebo-controlled, multicenter, parallel-group study designed to evaluate the efficacy and safety of ocrelizumab added to SOC (corticosteroid plus 1 of 2 immunosuppressant regimens) compared with placebo added to SOC in patients with WHO or ISN Class III or IV LN. The BELONG trial terminated early (October 19, 2009) due to an imbalance in infections in the active arm of the trial. Thus, the maximal follow-up for this post hoc analysis was 48 weeks.

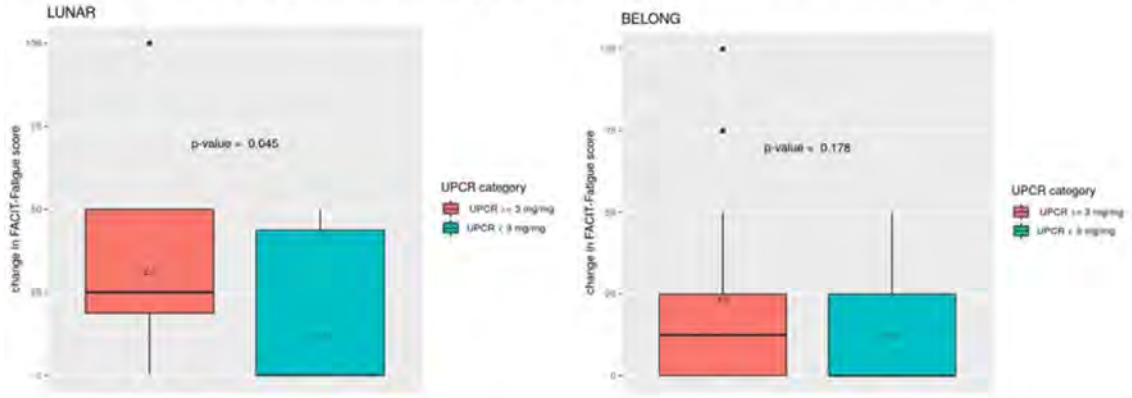
Figure 1. SF-36 Scores* According to Study Week in Control Arm Patients From the LUNAR and BELONG Trials for General Health, Pain, Vitality, Physical Well-Being and Fatigue†



*Patient responses were recoded on a range of 0 to 100, with higher values representing better HRQOL, consistent with Rand Corporation SF-36 scoring instructions. Standard errors were calculated for each score.
†The time frame for each domain was as follows: general health = now; pain, physical well-being and vitality = prior 4 weeks; fatigue = prior 4 weeks in the LUNAR trial and prior 7 days in the BELONG trial.

Conclusion: Initial post hoc analysis of patients in the control arms of the LUNAR and BELONG trials suggest greater improvements in fatigue among patients with baseline UPCR ≥3. Additional multivariate analyses will provide enhanced understanding of the relationship between renal function and HRQOL over time.

Figure 1. Mean Change in Fatigue Scores According to Baseline Proteinuria in the LUNAR and BELONG Trials



Fatigue†	LUNAR			BELONG		
	Baseline proteinuria (UPCR)*			Baseline proteinuria (UPCR)*		
	≥3 mg/mg (n=37)	<3 mg/mg (n=23)	Overall (N=72)	≥3 mg/mg (n=59)	<3 mg/mg (n=64)	Overall (N=126)
Baseline						
Mean (SD)	45.8 (30.8)	53.3 (30.4)	45.7 (31.3)	52.3 (30.4)	62.3 (27.6)	57.6 (29.1)
Median (Q1, Q3)	50.0 (25.0, 75.0)	50.0 (25.0, 75.0)	50.0 (25.0, 75.0)	50.0 (25.0, 75.0)	75.0 (50.0, 75.0)	50.0 (37.5, 75.0)
Min to max	0 to 100	0 to 100	0 to 100	0 to 100	0 to 100	0 to 100
Missing, n (%)‡	1 (2.7)	0 (0)	2 (2.8)	5 (8.5)	5 (7.8)	11 (8.7)
Week 52/48§						
Mean (SD)	70.0 (27.0)	61.8 (28.1)	69.0 (27.0)	78.0 (24.3)	77.2 (22.5)	77.6 (23.2)
Median (Q1, Q3)	75.0 (50.0, 100.0)	50.0 (50.0, 75.0)	75.0 (50.0, 100)	75.0 (75.0, 100.0)	75.0 (75.0, 100.0)	75.0 (75.0, 100)
Min to max	0 to 100	25 to 100	0 to 100	25 to 100	25 to 100	25 to 100
Missing, n (%)‡	12 (32.4)	6 (26.1)	22 (30.6)	34 (57.6)	41 (64.1)	78 (61.9)
Change in score at Week 52/48§						
Mean (SD)	27.0 (28.8)	7.35 (31.6)	23.5 (31.7)	19.0 (28.2)	7.61 (23.2)	13.5 (26.3)
Median (Q1, Q3)	25.0 (0, 50.0)	0 (0, 25.0)	25.0 (0, 50.0)	0 (0, 25.0)	0 (0, 25.0)	0 (0, 25.0)
Min to max	−50 to 100	−50 to 50	−50 to 100	−25 to 100	−25 to 50	−25 to 100
Missing, n (%)‡	12 (32.4)	6 (26.1)	22 (30.6)	34 (57.6)	41 (64.1)	78 (61.9)

UPCR, urine protein creatinine ratio.
*UPCR >1 was an inclusion criteria for entry into both the LUNAR and BELONG trials.
†The look back time frame for fatigue differed between the LUNAR and BELONG trials where the LUNAR trial referred to the prior 4 weeks and the BELONG trial referred to the prior 7 days.
‡Missing or discontinued.
§Week 52 for the LUNAR trial and Week 48 for the BELONG trial.

References:

1. Parikh SV, et al. *Am J Kidney Dis*. 2020;76:265-281.
2. Williams-Hall R, et al. *Lupus Sci Med*. 2022;9:e000712.
3. Kharawala S, et al. *Lupus*. 2022;31:1029-1044.
4. Rovin BH, et al. *Arthritis Rheum*. 2012;64:1215-1226.
5. Mysler EF, et al. *Arthritis Rheum*. 2013;65:2368-2379.

Disclosure: C. Tchakoute: F. Hoffmann-La Roche Ltd, 11, Genentech, Inc., 3; **H. Mao**: F. Hoffmann-La Roche Ltd, 11, Hoffmann-La Roche Ltd, 3; **G. Wallenstein**: F. Hoffmann-La Roche Ltd, 11, Genentech, Inc., 3; **J. Ross Terres**: F. Hoffmann-La Roche Ltd, 11, Genentech, Inc., 3; **S. Yoshida**: F. Hoffmann-La Roche Ltd, 11, Genentech, Inc., 3; **L. Lindsay**: F. Hoffmann-La Roche Ltd, 11, Genentech, Inc., 3.

Abstract Number: 2025

Osteoporosis Treatment Attributes and Levels for an Online Decision-Making Tool for Patients: Findings from Adaptive Choice-Based Conjoint Analysis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoporosis (OP) treatment options have different attributes based on mode of administration, frequency of administration, risks of minor and serious side effects, and effectiveness, among others. People living with OP (pts) prioritize different aspects of OP treatment based on their own preferences and on physician recommendations. The study's objective was to assess individual preferences among pts to inform an online decision-making tool for OP treatment.

Methods: An adaptive choice-based conjoint (ACBC) analysis survey was developed to quantify the relative importance of 6 OP medication attributes. Pts from Cedars-Sinai academic medical center were invited to complete the online conjoint exercises. The conjoint software determined each pt's preferences by calculating importance scores for each medication attribute (higher=more important). Results of the conjoint exercise were used to develop an online treatment decision-making tool for OP. We then tested the tool and the website it lives on with OP pts to improve functionality. User testing

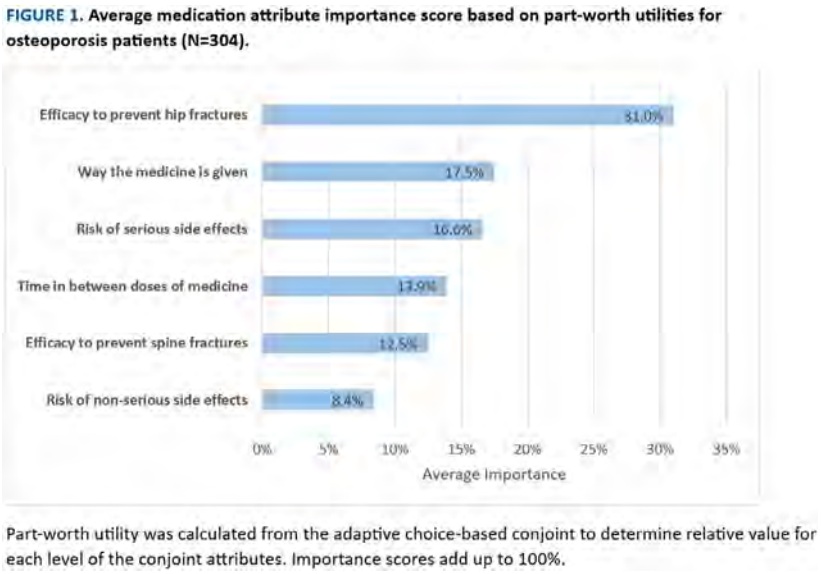

FIGURE 1. Average medication attribute importance score based on part-worth utilities for osteoporosis patients (N=304). Part-worth utility was calculated from the adaptive choice-based conjoint to determine relative value for each level of the conjoint attributes. Importance scores add up to 100%.

TABLE 1. Final attributes and levels included in the online decision tool.

Scenario attribute	Attribute levels
Way the medicine is given	• By mouth, self-administered, daily • By mouth, self-administered, weekly • By mouth, self-administered, monthly • Injection, self-administered, daily • Injection, provider-administered, monthly • Injection, provider-administered, every 6 months • Intravenous, provider-administered, yearly
Effectiveness to prevent spine fractures	• 50% • 80%
Effectiveness to prevent hip fractures	• 0% • 25% • 50%
Effectiveness to improve bone mineral density	• 4% at the hip and 9% at the spine • 9% at the hip and 18% at the spine
Risk of non-serious side effects	• No increased risk compared to not taking the medicine • 2% increased risk compared to not taking the medicine • 4% increased risk compared to not taking the medicine
Risk of serious side effects	• No increased risk compared to not taking the medicine • 1 out of 100,000 people (0.001%) • 10 out of 100,000 people (0.01%)

TABLE 1. Final attributes and levels included in the online decision tool.

involved recruiting a sample group of OP pts from the ArthritisPower research registry to review the website and use the tool while researchers remotely observed their behavior and collected feedback.

Results: A total of 304 pts completed the ACBC survey. Based on importance score, the most important attributes in the decision-making process were efficacy at preventing hip fractures (31.0%), way the medicine is given (17.5%), and risk of serious side effect (16.6%) (Figure 1). Attributes and levels for the final decision-making tool were based on results of the ACBC survey and informed by currently available treatment options, iterative feedback from providers and drug manufacturers, and user testing with 5 OP pts. Effectiveness to improve bone mineral density (BMD) was added as an attribute to reflect currently available OP treatments that demonstrate improvement in BMD but lack clinical data demonstrating effectiveness to prevent fractures. User testers encountered challenges with understanding how certain questions worked. While the question types could not be changed, as they are fundamental to the conjoint analysis exercise, the functionality of some of the questions were improved and additional directions were added at the start of the tool.The decision-making tool with final list of attributes and levels is being developed and disseminated by a patient advocacy organization (Table 1).

Conclusion: Pts with OP may benefit from identifying personal preferences using an online treatment decision-making tool developed with input from pts, providers, and researchers. A publicly available tool such as this may facilitate productive patient-provider conversations and foster shared decision-making for OP therapies in fracture liaison services and other clinical settings.

Disclosure: J. Curtis: AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, CorEvitas, 2, 5, Eli Lilly and Company, 2, 5, Janssen, 2, 5, Myriad, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **K. Gavigan**: Global Healthy Living Foundation, 3; **W. Nowell**: AbbVie/Abbott, 2, 5, Amgen, 5, Janssen, 2, 5, Scipher Medicine, 5; **D. Curtis**: Global Healthy Living Foundation, 3; **D. Ali**: Global Healthy Living Foundation, 3; **X. Liu**: None; **K. Makaroff**: None; **C. Almario**: None; **C. Khalil**: None; **S. Choi**: None; **B. Spiegel**: Alnylum, 5, Amgen, 5, Ardelyx, 1, Ferring, 1, Ironwood, 1, 5, Takeda, 1, 5.

Abstract Number: 2026

Developing a Guided Joint Self-Exam for Rheumatoid Arthritis Patients to Use in Telehealth-Delivered Care

Kelly Gavigan[1], David Curtis[2], Jeffrey Curtis[3], W. Benjamin Nowell[4], Danielle Ali[5], Neelkamal Soares[6], John Cush[7], Rebecca Grainger[8], Manas Jinka[9], Sandeep Sodhi[10], Natalie Fortune[9] and Swamy Venuturupalli[9], [1]Global Healthy Living Foundation, Upper Nyack, NY, [2]Global Healthy Living Foundation, San Francisco, CA, [3]University of Alabama at Birmingham, Birmingham, AL, [4]Global Healthy Living Foundation, Nyack, NY, [5]Global Healthy Living Foundation, Upper Nayack, NY, [6]Western Mich Univ Homer Stryker MD Sch of Medicine, Kalamazoo, MI, [7]University of Texas Southwestern Medical School, Dallas, TX, [8]University of Otago, Wellington, New Zealand, [9]Attune Health, Beverly Hills, CA, [10]Illumination Health, Hoover, AL

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Patient Outcomes, Preferences, & Attitudes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Telehealth services and, increasingly, remote therapeutic monitoring, can be used to enable the continuum of clinical care in out-of-office settings. This remotely provided care can increase personalization of healthcare by using patient-relevant data, but lack of opportunity for in-person examination may remain a barrier. Our objective was to develop and pilot a smartphone application (app)-based program to teach patients to perform guided self-examination to measure the disease activity of their rheumatoid arthritis (RA), to facilitate remote care.

Methods: An in-app tool to instruct patients with RA to conduct a self-guided 28 tender and swollen joint count (28-TJC, 28-SJC) was developed for the ArthritisPower research registry app based on previously developed videos[1]. An instructional script of on-screen messaging and animations was iteratively refined by the study team of physicians, researchers, patients, and patient advocates. A storyboard of the final script was user tested with ArthritisPower members living with RA. The tool was then piloted in the ArthritisPower app by RA patients in a community rheumatology practice to gain feedback on the user interface and user experience. Participation in the pilot consisted of registering for ArthritisPower, completing six physical and social health patient reported outcomes (PROs) (PROMIS measures for Pain Interference, Physical Function, Fatigue, and Satisfaction with Participation in Discretionary Activities; RADAI-5; and OMERACT RA Flare), and completing the guided, self-conducted 28-TJC, 28-SJC. The in-app assessment was compared to in-person assessment by a rheumatologist within 6 days of a scheduled office visit.

Results: Five RA patients participated in the pilot testing. The mean (SD) time to completion for the PROs and joint self-assessment tool was 18.3 (3.5) minutes, with the PROs taking 5.4 (0.9) minutes on average and the joint self-assessment taking 12.9 (3.5) minutes on average to complete. Based on this pilot, edits were made to the tool. These included simplifying the language in the registration process, clarifying what was required to successfully complete participation and the expected time commitment, clarifying concepts of tender and swollen joints, adding inspirational progress messaging, and refining the instructional tool. Example screens from the in-app module can be found in Figure 1.

Conclusion: Piloting in real-world settings highlighted areas for change that are hoped to increase successful participation, such as simplifying language, clarifying requirements, and adding motivational messaging. The refined tool is currently being deployed in a larger study to evaluate the accuracy and utility of patient-conducted TJC and SJC for guiding RA management decisions. [1]Grainger, et al. ACR Open Rheum. 2020;2(12):705-709.

FIGURE 1. Example Screens from the In-App Joint Count Tool

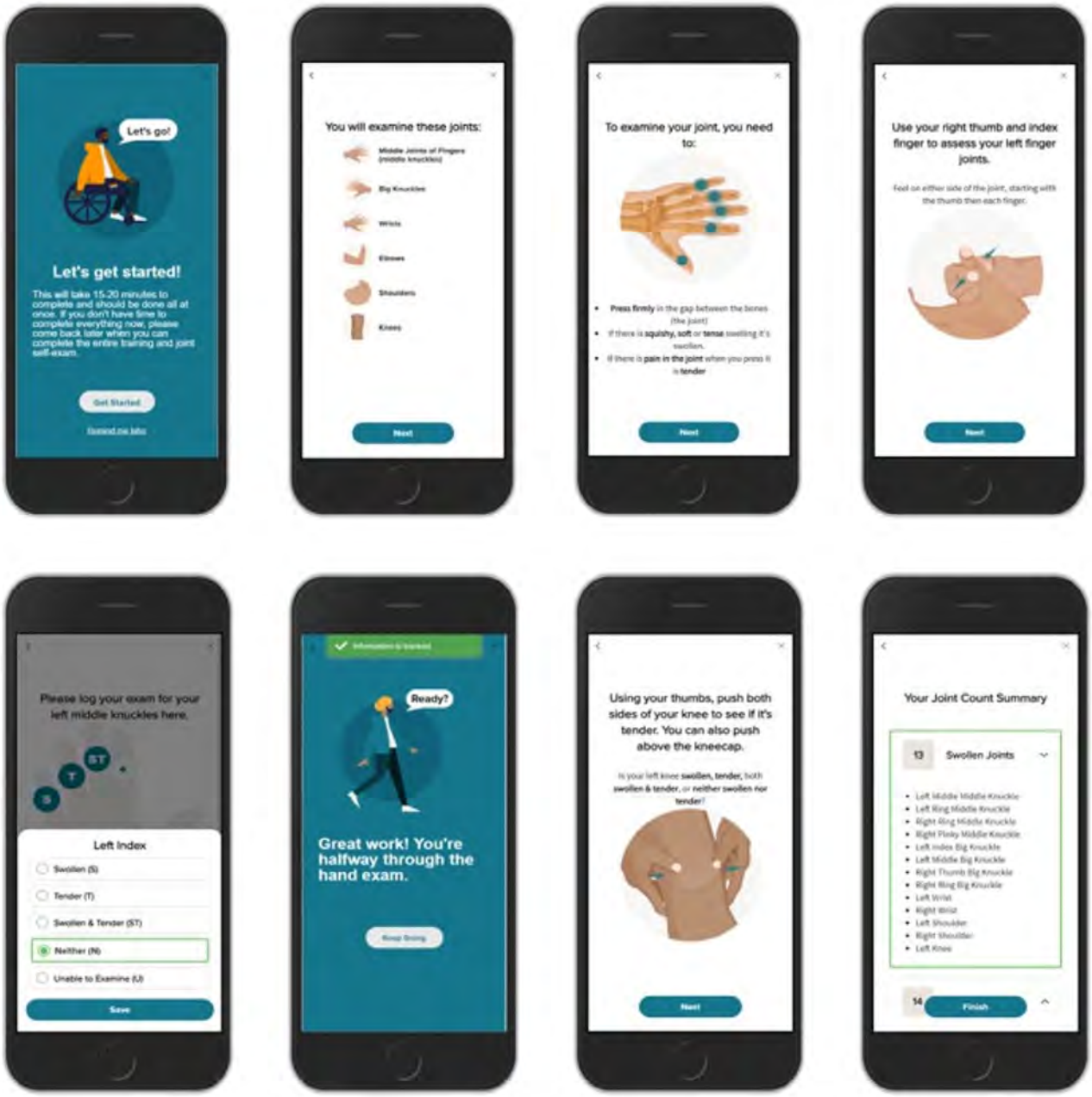

FIGURE 1. Example Screens from the In-App Joint Count Tool

Disclosure: K. Gavigan: Global Healthy Living Foundation, 3; **D. Curtis**: Global Healthy Living Foundation, 3; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, CorEvitas, 2, 5, Eli Lilly and Company, 2, 5, Janssen, 2, 5, Myriad, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **W. Nowell**: AbbVie/Abbott, 2, 5, Amgen, 5, Janssen, 2, 5, Scipher Medicine, 5; **D. Ali**: Global Healthy Living Foundation, 3; **N. Soares**: None; **J. Cush**: None; **R. Grainger**: AbbVie, 2, 6, Cornerstones, 6, Janssen, 6, Novartis, 2, Pfizer, 6; **M. Jinka**: None; **S. Sodhi**: None; **N. Fortune**: None; **S. Venuturupalli**: None.

Abstract Number: 2027

Developing and Implementing a Pilot Educational Intervention to Improve Readiness for Self-Management Among Patients with Rheumatic Diseases in Uganda

Trina Pal[1], Auther Jjunju[2], joshua bilsborrow[3], Lillian Tugume[4], Rachel Galvao[3], Evelyn Hsieh[5] and Mark Kaddumukasa[4], [1]Section of Rheumatology, Yale School of Medicine, West Hartford, CT, [2]The Arthritis Association of Uganda, Kampala, Uganda, [3]Section of Rheumatology, Yale School of Medicine, New Haven, CT, [4]Department of Medicine, School of Medicine, College of Health Sciences, Makerere University, Kampala, Uganda, [5]Yale University, Department of Medicine, Section of Rheumatology; Yale School of Public Health; Section of Rheumatology, VA Connecticut Healthcare System, Westport, CT

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Self-management is an effective strategy for improving health outcomes among patients with chronic conditions such as rheumatic diseases. Patient education about self-management among patients with rheumatic disease in Uganda is limited. In collaboration with The Arthritis Association of Uganda (TAAU), a fully registered, patient-led NGO, this pilot study aimed to evaluate the feasibility of developing and implementing a virtual patient education series and collecting information regarding self-management.

Methods: Four virtual sessions were developed together with direct input from the Ugandan rheumatology patient perspective. Adults ≥18 years of age receiving care at the Mulago Hospital Rheumatology Clinic were invited to participate. Patients were asked to complete a survey at enrollment regarding demographic and clinical characteristics and self-management readiness via the validated 13-item Patient Activation Measure (PAM) tool (see table), and an Exit Survey to re-assess the PAM. Feasibility and acceptability metrics were collected including the ability of the study team to develop and deliver all sessions as planned, attendees per session, attendees who returned for subsequent sessions, attendees who completed each of the surveys, barriers that were faced, and patient satisfaction.

Results: The four topics selected and developed, based upon the experience and input of TAAU, encompassed: Introduction to Arthritis, Exercise & Nutrition, Women's Health & Rheumatic Disease, and Understanding My Disease & Rheumatology Medications. Sessions were delivered over Zoom from 1/2023 - 5/2023, approximately every other week prior to the start of the morning clinic. Each topic was presented twice to maximize patient participation. Local team members simultaneously interpreted content into Luganda. An average of 21 participants (range 17-24) attended each session (mean age 48 ±14 years, 72% women). Reported diagnoses included rheumatoid arthritis, osteoarthritis, systemic lupus erythematosus, crystalline arthritis, psoriatic arthritis, and "not sure". A total of 33 Enrollment Surveys and 41 Exit Surveys were collected. Mean raw PAM scores were 36.9±3.8 at enrollment and 41.5±2.2 at exit. Challenges encountered and discussed included language barriers, adapting medical terminology to health literacy levels, and administrative/logistical hurdles (internet connection reliability, preparing and managing hard copies of the surveys, accessing the meeting space, inclement weather, accommodating interest in remote participation). Patients reported sessions were useful, appropriate and engaging, and expressed a strong interest in additional future sessions.

Conclusion: In this pilot study, we demonstrated the feasibility of developing and implementing an educational series focused on self-management for patients with rheumatic diseases and collecting associated measures. Our findings will directly inform the design and delivery of future expanded interventions on this topic. Next steps will include formal cultural

Table 1: 13-Item Patient Activation Measure

	When you think about your rheumatic condition and your rheumatology care, how much do you agree or disagree with the following statements? *(Check the box that applies)*	Strongly Disagree	Disagree	Agree	Strongly Agree	Not Applicable
1	When all is said and done, I am the person who is responsible for managing my rheumatic condition					
2	Taking an active role in my own health care is the most important factor in determining my musculoskeletal health and ability to function					
3	I am confident that I can take actions that will help prevent or minimize some symptoms or problems associated with my rheumatic condition					
4	I know what each of my prescribed rheumatology medications do					
5	I am confident that I can tell when I need to go get rheumatology care and when I can handle a musculoskeletal health problem myself					
6	I am confident I can tell my rheumatology care provider concerns I have even when he or she does not ask					
7	I am confident that I can follow through on rheumatology treatments I need to do at home					
8	I understand the nature and causes of my rheumatic condition(s)					
9	I know the different treatment options available for my health condition					
10	I have been able to maintain the lifestyle changes that I have made for my musculoskeletal health					
11	I know how to prevent further problems with my health condition					
12	I am confident I can figure out solutions when new situations or problems arise with my rheumatic condition					
13	I am confident that I can maintain lifestyle changes, like diet and exercise, even during times of stress					

adaptation and validation of the 13-item PAM, incorporation of remote participation, and direct assessment of knowledge gaps, and self-management practices.

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Abstract Number: 2028

Endorsement of Core Domain Definitions to Measure the Impact of Glucocorticoids in Patients with Rheumatic Diseases: A Report from the OMERACT Working Group on Glucocorticoid Impact

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SESSION INFORMATION

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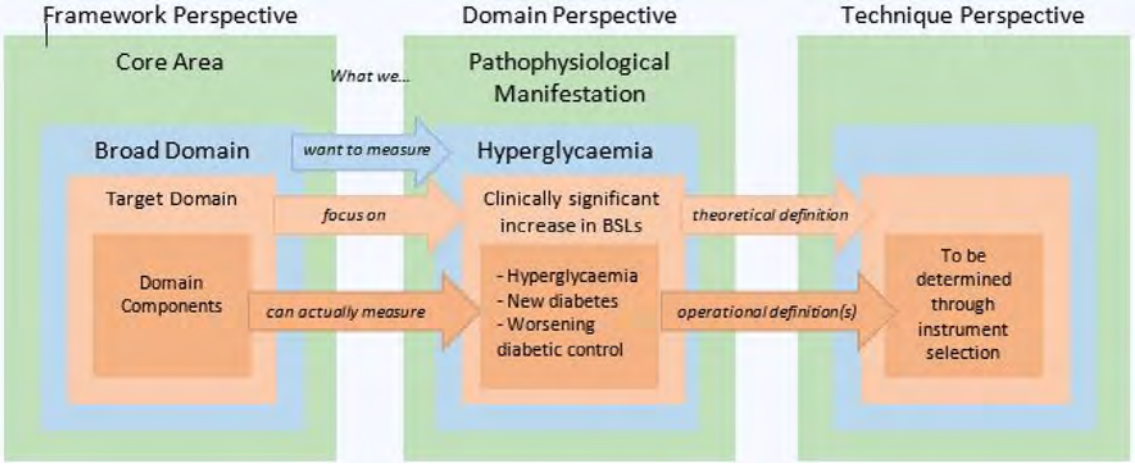
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Healthcare research has historically been medically oriented, less focused on the patients' perspective that research shows can improve the quality of care. OMERACT advocates for the development of core outcome sets to improve outcome measures in rheumatology by incorporating the patient perspective, which is often neglected in research. The OMERACT Glucocorticoid (GC) Impact Working Group has been working to develop a core domain set to measure the impact of GCs. Based on qualitative research and multiple rounds of Delphi-type exercises, the group identified mandatory domains for inclusion in all clinical trials where the effects of GCs are measured. These include infections, bone fragility, mood disorders, hypertension, diabetes, weight, fatigue, and mortality.

A fundamental aim of the GC Impact Working Group is to develop a core outcome set of measurement tools or instruments to represent and assess relevant outcomes, through application of the well-established OMERACT methodology. Before progressing to instrument selection, the Working Group sought to establish precise definitions of all mandatory domains within the core domain set to facilitate measurement.



The layered definition approach that provides a detailed definition of the domain and the elements of that domain that should be found in a suitable instrument using that technique. BSL – Blood Sugar Level, Example of mandatory domain

Methods: OMERACT methodology was applied with the use of evidence and consensus-based decision making of all stakeholder groups (patient research partners, health care professionals, clinician researchers, industry members and methodologists) to develop detailed definitions for the broad domain, target domain, and domain components, considering sources of variability that could impact the outcome measure assessed by a given instrument (fig 1). The working group synthesized prior qualitative studies, quantitative work, and results from Delphi rounds, to develop a rich definition of 'what' is to be measured.

Results: Over a 2-year period, from 2021–2023, the OMERACT Working Group on GC Impact conducted virtual meetings to establish domain definitions. The core area identified for all domains was pathophysiological, except weight, which was divided into both pathophysiological and life impact manifestations, and fatigue which has only life impact manifestations. Sources of variability were recognized, including cultural factors, age, gender, education level, socioeconomic status, personal experiences, emotional state, and language barriers. To minimize the impact of potential variability, instrument selection will require rigorous validation procedures. The domain definitions endorsed, through this consensus-based decision-making process, will form the foundation for instrument selection and the initial step of domain / concept match and content validity in the OMERACT pillar of 'truth' before moving on to feasibility, and discrimination

Conclusion: The OMERACT GC Impact Working Group have endorsed detailed domain definitions for core domains. The next step of the working group is to select instruments and develop the core outcome set for inclusion in all clinical trials where the effects of GCs are measured.

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Abstract Number: 2029

Health-Related Quality of Life in Idiopathic Inflammatory Myopathies: How to Act for Improving the Disease Burden of Patients?

Chiara Cardelli[1], Simone Barsotti[2], Elenia Laurino[1], Michele Diomedi[1], Federico Fattorini[1], Dina Zucchi[3], Alessandra Tripoli[1], Linda Carli[1] and Marta Mosca[1], [1]Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy, [2]Internal Medicine, Ospedale di Livorno, Pisa, Italy, [3]Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Italy; Department of Medical Biotechnologies, University of Siena, Pisa, Italy

SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Idiopathic Inflammatory Myopathies (IIM) are rare, multisystemic and complex diseases that strongly impact the Quality of Life (QoL) of those affected. Patient Reported Outcomes (PROs) are validated tools that assess the overall health status of patients, particularly with regard to emotional and functional domains. The aim of the study was to evaluate the impact of disease clinical features and comorbidities on Health-Related (HR) QoL in a monocentric cohort of IIM patients.

Methods: Consecutive adult patients with a diagnosis of IIM (2017 EULAR/ACR criteria) followed at our Myositis Clinic were enrolled in this cross-sectional study. Demographic and clinical data were collected at enrolment. HRQoL was evaluated by administration of generic PROs: Patient Global Assessment (PGA), Health Assessment Questionnaire (HAQ), Short-Form 36 Items Health Survey (SF36), Functional Assessment of Chronic Illness Therapy Fatigue Subscale (FACIT-F), Hospital Anxiety and Depression Scale (HADS). Intergroup comparisons were assessed using t-test and Mann-Whitney tests, as appropriate. Multivariate analysis was performed by a linear regression model.

Results: We enrolled 85 patients (67.1% female; mean age 65.7±12.5 years; mean disease duration 7.9±6.5 years) with the following diagnosis: 44 dermatomyositis (51.8%), 36 polymyositis (42.3%), 5 inclusion body myositis (5.9%). Among clinical features, dysphagia and sicca symptoms were found to have the greatest impact on HRQoL: in fact, dysphagia was associated with worse outcomes in all PROs (PGA $p< 0.001$, HAQ $p< 0.001$, SF36 $p\leq0.031$, FACIT-F $p< 0.001$, HADS $p=0.023$ for anxiety and $p=0.002$ for depression), while sicca symptoms were found to be associated with worse scores in three of four SF36 domains of both mental and physical health ($p\leq0.044$ and $p\leq0.027$, respectively) and in a greater fatigue assessed by FACIT-F ($p=0.006$). As expected, HRQoL was significantly impaired by the coexistence of fibromyalgia (FM), which indeed determined worse scores of HAQ ($p=0.031$) and all SF36 domains ($p\leq0.021$), higher fatigue levels ($p=0.006$) and higher levels of anxiety and depression evaluated by HADS ($p=0.025$ and $p=0.05$, respectively); also osteoporosis (OP) was found to significantly impact on PGA ($p=0.027$) and physical functioning and general health evaluated by SF-36 ($p=0.044$ and $p=0.029$, respectively). At multivariate analysis, among clinical variables, only dysphagia maintained a significant impact on almost all PROs ($p\leq0.018$, except for pain and physical role domains of SF36); among comorbidities, FM had a significant impact on all PROs ($p\leq0.05$), whereas OP had an impact only on the SF36 domains ($p\leq0.03$).

Conclusion: Our data could help rheumatologists to focus their attention on specific clinical domains of IIMs in the perspective of preserving patients' QoL. In particular, dysphagia and FM were found to be the main determinants of HRQoL in IIM patients, thus suggesting their better control and optimized management could significantly improve patients' physical and psychological functioning. Moreover, OP prevention might further reduce the disease burden in this group of patients, thus ameliorating their quality of care.

Disclosure: C. Cardelli: None; **S. Barsotti**: None; **E. Laurino**: None; **M. Diomedi**: None; **F. Fattorini**: None; **D. Zucchi**: None; **A. Tripoli**: None; **L. Carli**: None; **M. Mosca**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, GlaxoSmithKlein(GSK), 2, Otsuka, 2, UCB, 2.

Abstract Number: 2030

Positive Psychosocial Factors May Protect Against Perceived Stress in a Multiethnic Cohort of People with SLE with and Without Trauma History

Kimberly DeQuattro[1], Laura Trupin[2], Sarah Patterson[3], Stephanie Rush[2], Caroline Gordon[4], Kurt Greenlund[5], Kamil Barbour[5], Cristina Lanata[6], Lindsey Criswell[7], Maria Dall'Era[2], Jinoos Yazdany[2] and Patti Katz[8], [1]University of Pennsylvania, Media, PA, [2]University of California San Francisco, San Francisco, CA, [3]University of California San Francisco, Pacifica, CA, [4]Institute of Inflammation and Ageing, University of Birmingham, Birmingham, United Kingdom, [5]Centers for Disease Control and Prevention, Atlanta, GA, [6]National Human Genome Research Institute, Washington, DC, [7]NIH/NHGRI, Bethesda, MD, [8]University of California San Francisco, San Rafael, CA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Patient Outcomes, Preferences, & Attitudes Poster III

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Session Time: 9:00AM–11:00AM

Background/Purpose: Trauma exposures are associated with SLE onset and disease activity; perceived stress is also associated with greater SLE disease activity and worse patient-reported outcomes. However, perceptions of stress vary in response to life events and may be influenced positively and negatively by psychosocial factors. In an SLE cohort, we examined the association of stressful events with perceived stress, whether psychosocial factors affected perceived stress, and whether these relationships varied by prior trauma exposures.

Methods: Data were from a sample of adults with SLE from the California Lupus Epidemiology Study (n = 242). We first examined correlations of stressful events that occurred in the past year (Life Events Inventory: queries potentially stressful health, living situation, family, financial, and legal events) and psychosocial factors (3 positive: resilience, self-efficacy, emotional support; 1 negative: social isolation) with perceived stress (Perceived Stress Scale). Because of high correlations among positive psychosocial variables, we used principal components analyses to create a positive psychosocial factor score. We then used multivariable linear regression to examine independent associations of stressful events and psychosocial variables with perceived stress, controlling for age, sex, disease duration, and educational attainment for the total sample and stratified by lifetime trauma history (Brief Trauma Questionnaire, BTQ; any traumatic event vs none). Analyses stratified by history of adverse childhood experiences (ACEs; 0-1 events vs ≥2 events) among the subset for whom ACEs data were available (n = 180) were performed.

Results: Sample characteristics are shown in **Table 1**. Individuals who had experienced trauma (71%, BTQ) had significantly higher perceived stress scores, more stressful events, lower emotional support scores, and higher social isolation scores (**Table 2**). Overall, a greater number of stressful events over the previous year and social isolation were correlated with greater perceived stress, and positive psychosocial factors (resilience, self-efficacy, and emotional support) were

Table 1. Characteristics of study participants with SLE, by trauma history*

Characteristics	Overall (N = 242)	No Trauma History (N = 71)	Trauma History (N = 171)	*p*-value
Sociodemographic Factors	% (N) unless specified			
Age, mean ± SD	49.4 ±13.4	46.2 ±13.7	50.7 ±13.1	0.02
Female	90.1 (281)	88.7 (63)	90.6 (155)	0.64
Race				0.125
White	33.9 (82)	25.4 (18)	37.4 (64)	
Hispanic	24.0 (58)	29.6 (21)	21.6 (37)	
African American	9.1 (22)	8.5 (6)	9.4 (16)	
Asian	30.6 (74)	36.6 (26)	28.1 (48)	
Unspecified/other	2.5 (6)	0	3.5 (6)	
High school education or less	15.3 (37)	19.7 (14)	13.5 (23)	0.22
Income below poverty**	11.9 (27)	13.4 (9)	11.3 (18)	0.64
SLE Specific Characteristics				
SLE disease duration, years, mean ± SD	22.2 ±10.7	20.2 ± 10.9	23.0 ± 10.5	0.07
Pediatric onset disease (diagnosis < age 18)	18.6 (45)	22.5 (16)	17.0 (29)	0.31
Self-report disease damage by BILD, score >2	47.5 (115)	38.0 (27)	51.5 (88)	0.06

Abbreviation: BILD: Brief Index of Lupus Damage
*Trauma defined as any perceived danger or threat to life according to Brief Trauma Questionnaire
**Poverty income defined as ≤125% of the federal poverty level based on household size
Tabled values are % (n) unless otherwise noted.
P-values calculated using chi-squared tests for categorical measures and t-tests for continuous measures.

Table 2. Association of Perceived Stress Scale with Life Events Inventory, measures of positive (resilience, self-efficacy, emotional support) and negative (social isolation) factors, by trauma history

	Overall (N = 242)	No Trauma History (N = 71)	Trauma History (N = 171)	p†
Mean ± SD				
Perceived Stress Scale	4.7 ±3.2	3.5 ± 2.9	5.2 ± 3.2	0.0001
Life Events Inventory	4.4 ±3.0	3.5 ± 2.6	4.9 ±3.1	0.001
Brief Resilient Coping Scale	8.4 ±1.9 (0–12)	8.1 ±2.0 (0–12)	8.5 ±1.9 (4–12)	0.17
PROMIS Self Efficacy*	49.8 ±9.3	51.1 ± 9.9	49.2 ± 9.0	0.13
PROMIS Emotional Support*	66.6 ±8.5	68.9 ± 7.8	65.7 ± 8.6	0.008
PROMIS Social Isolation*	34.7 ± 6.6	31.9 ± 6.0	35.9 ± 6.5	<0.0001
Correlations with Perceived Stress Scale, r (*p*-value)				
Life Events Inventory	0.19 (0.003)	-0.07 (0.55)	0.22 (0.006)	
Brief Resilient Coping Scale	-0.22 (0.001)	-0.26 (0.27)	-0.24 (0.001)	
PROMIS Self Efficacy*	-0.51 (<0.0001)	-0.60 (<0.0001)	-0.47 (<0.0001)	
PROMIS Emotional Support*	-0.49 (<0.0001)	-0.56 (<0.0001)	-0.43 (<0.0001)	
PROMIS Social Isolation*	0.65 (<0.0001)	0.65 (<0.0001)	0.62 (<0.0001)	

Brief Resilience Coping Scale range from 0 (low resilience) to 12 (high resilience).
r – Pearson correlation coefficient
*Patient Reported Outcomes Measurement Information System (PROMIS) scales, reported as T-scores
†*p*-values from t-tests comparing scores of individuals with and without trauma history.

associated with lower perceived stress (**Table 2**). In analyses stratified by BTQ trauma and ACEs (38%), associations of positive and negative psychosocial factors with perceived stress were similar between groups. However, the number of recent stressful life events was significantly associated with perceived stress only for people with BTQ trauma or ACEs (**Table 3**).

Table 3. Association of perceived stress and stressful events (Life Events Inventory), measures of positive psychosocial and negative (social isolation) factors, by trauma history (Brief Trauma Questionnaire and adverse childhood experiences), in models with adjustment

	Full sample (N = 242)		No Trauma History, BTQ (N = 71)		Trauma History, BTQ (N = 171)	
	Beta (95% CI)	*P*	Beta (95% CI)	*P*	Beta (95% CI)	*P*
Life Events Inventory	0.15 (0.05, 0.25)	0.004	-0.03 (-0.22, 0.17)	0.77	0.18 (0.06, 0.30)	0.003
Positive psychosocial factor score*	-0.70 (-0.97, -0.43)	<.0001	-0.75 (-1.22, 0.28)	0.002	-0.64 (-0.98, -0.30)	0.0003
PROMIS Social Isolation	0.24 (0.18, 0.29)	<.0001	0.23 (0.13, 0.32)	<.001	0.22 (0.15, 0.29)	<.0001
Model R^2	0.51		0.58		0.49	
	Full sample (N = 180)		No Childhood Trauma (ACEs) (N = 111)		Childhood Trauma History (ACEs) (N = 69)	
Life Events Inventory	0.19 (0.06, 0.32)	0.003	0.06 (-0.12, 0.25)	0.49	0.32 (0.12, 0.52)	0.002
Positive psychosocial factor score*	-0.60 (-0.93, -0.28)	0.0003	-0.57 (-0.97, -0.18)	0.004	-0.81 (-1.46, -0.17)	0.015
PROMIS Social Isolation	0.23 (0.16, 0.29)	<.0001	0.25 (0.17, 0.33)	<.0001	0.18 (0.07, 0.30)	0.003
Model R^2	0.46		0.46		0.50	

Abbreviations: BTQ: Brief Trauma Questionnaire; PROMIS: Patient Reported Outcomes Measurement Information System; ACEs: adverse childhood experiences
*First eigenvalue from principal component analysis of resilience, emotional support, and self-efficacy scores
Models include Life Events Inventory, positive psychosocial factor score, PROMIS Social Isolation T-score, and age, sex, disease duration, and education ≤high school, Brief Index of Lupus Damage ≥2.

Conclusion: Perceived stress was higher in individuals with SLE with BTQ trauma and/or ACEs. Individuals with trauma history may be more vulnerable to current interpersonal, economic, or other stressful experiences that lead to higher perceived stress levels. Given demonstrated associations between perceived stress and poor health outcomes in SLE, modifiable positive psychosocial resources such as self-efficacy and emotional support may be important in managing perceptions of stress. Increased access to interventions that strengthen positive psychosocial factors and lessen negative ones to lower perceived stress is a next step towards improving outcomes in SLE.

Disclosure: K. DeQuattro: None; **L. Trupin**: None; **S. Patterson**: None; **S. Rush**: None; **C. Gordon**: AbbVie, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, Sanofi, 2, UCB Pharma, 2; **K. Greenlund**: None; **K. Barbour**: None; **C. Lanata**: None; **L. Criswell**: None; **M. Dall'Era**: Annexon Biosciences, 2, 5, AstraZeneca, 2, Aurinia, 2, Biogen, 2, GlaxoSmithKlein, 2, 5, Pfizer, 2; **J. Yazdany**: Astra Zeneca, 2, 5, Aurinia, 5, Gilead, 5, Pfizer, 2; **P. Katz**: None.

Abstract Number: 2031

Involving Patients Research Partners in Research in Rheumatology: Where Do We Stand? A Scoping Review of Recent Randomized Controlled Trials and Translational Science Studies

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients bring valuable insights to research; the inclusion of patient research partners (PRPs) in research projects is increasingly recognised and recommended in medical research, also by the Food and Drug Administration. The level of involvement of PRPs in translational rheumatology research projects remains unknown, while in randomized clinical trials (RCTs) published between 2016 and 2020, it has been reported to be as low as 2%[1]. The objective of this study was to assess the involvement of PRPs in recent translational studies and RCTs in rheumatology.

Methods: In this scoping review, we analyzed the 80 most recent articles (40 for translational studies and 40 for RCTs) in each of the target diseases (rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus and lower-extremity osteoarthritis), published up until March 1st, 2023, in rheumatology and general scientific journals with an impact factor of >5. The extent of PRP involvement was assessed, as reported in the Methods, affiliations of authors and acknowledgments sections. General data on the studies was also collected. The analysis was descriptive.

Results: Overall, 221 studies were screened; most were excluded due to wrong study design or wrong disease. Among the 40 translational studies (10 for each disease studied), half were published in rheumatological journals. Fifty percent of the studies were conducted in Asia, 30% in Europe and 20% in North America. None of the included translational studies reported PRP involvement (Figure 1). Of 40 clinical trials (10 for each disease studied), 78% were published in rheumatology journals. Fifty-two percent of the studies were conducted in North America, 25% in Europe and 23% in Asia. Among the 40 RCTs, 8 studies (20%) reported PRP involvement (Figure 1). These trials were from Europe (6/8, 75%), and North

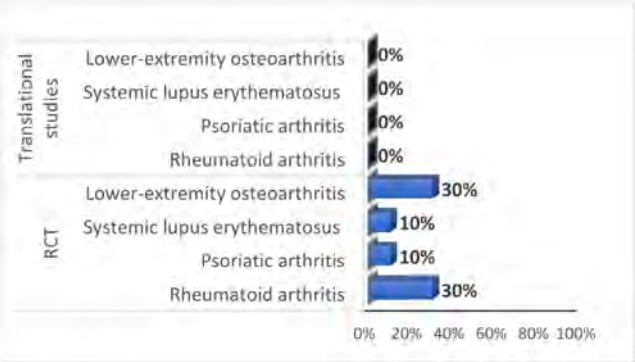

Figure 1: Involvement of patient research partners in recent translational studies and RCTs

America (2/8, 25%). Most of them (6/8, 75%) were non-industry funded. The type of PRP involvement was reported in 4/8 studies (50%); four studies reported PRP participation in the study design and two studies reported involvement in the interpretation of the results. All the trials reporting the number of PRPs (6/8, 75%), involved at least two PRPs.

Conclusion: Despite a world-wide movement advocating for increased patient involvement in research, the involvement of PRPs in translational research and RCTs in rheumatology remains low. While there has been an improvement in PRP involvement in RCTs compared to previous literature reviews (20% vs. 2%)[1], PRPs are still absent in translational research projects. This under-representation of PRP involvement in research highlights a persistent gap between recommendations and practice.

References:

1. Wang H, et al. Patient research partner involvement in rheumatology clinical trials: analysis of journal articles 2016–2020. Ann Rheum Dis 2021;80:1095-1096

Disclosure: D. Benavent: Abbvie, 5, Galapagos, 6, Janssen, 6, Novartis, 5, Roche, 6; **M. Elhai**: AstraZeneca, 12, Travel to Congress support, Janssen, 12, Congress support; **K. Aouad**: None; **P. Studenic**: None; **M. de Wit**: Celgene, 2, Eli Lilly, 2, Janssen, 2, Pfizer, 2, UCB Pharma, 2; **L. Gossec**: AbbVie, 2, 12, Personal fees, Amgen, 2, Biogen, 5, BMS, 12, Personal fees, Celltrion, 12, Personal fees, Eli Lilly, 5, 12, Personal fees, Galapagos, 12, Personal fees, Janssen, 12, Personal fees, MSD, 12, Personal fees, Novartis, 5, 12, Personal fees, Pfizer, 12, Personal fees, Sandoz, 5, 12, Personal fees, UCB Pharma, 5, 12, Personal fees.

Abstract Number: 2032

Goal Concordance in Rheumatoid Arthritis Patients with Depression – What Do Patients Prioritize?

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Depression prevalence in patients with rheumatoid arthritis (RA) is higher than the general population (~40% and 4.1%, respectively). Patients with depressive symptoms show reduced biologic therapy response. Patient-clinician goal concordance has been linked to improved outcomes in other chronic conditions including diabetes but has not been explored in RA patients with depression. Our objective was to (a) describe treatment goals for RA patients with and without depression and (b) assess whether RA patient-clinician goal concordance varies by depression status.

Methods: RA patients seen in the prior 12 months at one of two rheumatology clinics (Veterans Affairs- and university-based) were enrolled in a cross-sectional survey study. Patients and their rheumatology clinician independently ranked their top three (of eight) RA treatment goals. PHQ8 score ≥10 defined depression. Descriptive statistics were used to characterize treatment goals for both groups. Fisher's exact test was used to determine statistical significance with a Bonferroni correction to account for multiple comparisons (p= 0.006). Goal concordance, defined as a patient's top goal ranked in their clinician's top three goals, was compared between groups.

Results: 148 dyads were included in the analysis (148 patients, 14 clinicians). Patients were 51% female and 28% non-white, with mean disease duration of 12 years (SD= 9). 32 patients (22%) met depression criteria. Overall, "less pain" was identified as a treatment goal most often, regardless of depression status (81% depressed, 91% non-depressed, p= 0.21). Similarly, "fewer problems doing my daily activities" was the second-most selected treatment priority for patients with and without depression (56% and 69%, respectively, p= 0.21). However, patients with depression identified "feel less tired" as their third-most selected goal (47% depressed, 33% non-depressed, p=0.15), while those without depression identified "avoid side effects from medication" third-most frequently (41% non-depressed, 28% depressed, p=0.22). Patients with depression also identified "improve sleep" as a goal more often than patients without depression (41% depressed, 16% non-depressed, p= 0.006). Goal concordance did not differ significantly between patients with and without depression (91% and 78% meeting concordance definition, respectively, p= 0.1).

Conclusion: RA patients, regardless of concomitant depressed mood, most often prioritized "less pain," followed by "fewer problems doing my daily activities." However, differences emerged in the third-most valued goal such that patients with depression ranked "feel less tired" and patients without depression ranked "avoid side effects from medication" more often. Goal concordance did not differ significantly between groups, which may be explained by the high value placed on pain in goal ranking and our patient-centered definition of concordance. Pain is a common symptom in RA and routinely elicited at clinic visits, prompting discussions between patients and clinicians. Research to explore ways to improve goal elicitation beyond pain among all RA patients and their clinicians is warranted.

Disclosure: A. Schue: None; **R. Matsumoto**: None; **J. Barton**: None.

Abstract Number: 2033

Sex Differences in Patient-Reported Outcomes in Patients with Rheumatoid Arthritis After Starting a New Disease-Modifying Antirheumatic Medication

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patient-Reported Outcome Measurement Information System (PROMIS®) measures are valued in the assessment of health outcomes for patients with rheumatoid arthritis (RA). However, little is known about sex differences in change in key PROMIS domains following initiation of DMARD therapy. We aimed to examine sex differences in PROs among patients with RA after starting a new DMARD.

Methods: In this retrospective study, patients with RA seen at a single institution between 1/2020 and 10/2021 were included. RA patients were identified by presence of 2 diagnostic codes (ICD-10: M05.x/M06.x, excluding M06.1) and prescription of a DMARD. PROMIS computer adaptive tests for Physical Function, Pain Interference, Fatigue, Depression, and Ability to Participate in Social Roles and Activities were routinely collected at each clinical visit. Patients with available PROMIS measures at the start of a new conventional synthetic (cs), biologic (b), or targeted synthetic (ts) DMARD and at least one subsequent visit were included in the analysis. Minimum clinically important differences (MCID) and meaningful differences were defined for each PROMIS measure (ref: Bartlett et al, AC&R 2022). Generalized binomial models with logit link were used to examine sex differences in improvement or worsening of PROMIS measures over time, adjusting for age, DMARD type and duration.

Results: A total of 179 patients with RA (76% female; 93% white; mean age 56.2 years) who started 202 new DMARDs (85 csDMARDs, 88 bDMARDs and 29 tsDMARDs) were studied. Median follow-up was 5.8 (interquartile range: 3.7-9.4) months per DMARD. Mean (±SD) PROMIS measures at DMARD initiation were 38.7 (±7.0) for physical function, 44.7 (±7.8) for social participation, 62.7 (±5.8) for Pain interference, 58.6 (±9.2) for fatigue and 5.20 (±8.7) for depression. Women were 3 times more likely to have worsening of their depression score by at least 2 points after starting a new DMARD (36% of women worsened vs 18% of men; odds ratio: 3.07; 95% CI: 1.29-7.30; Table). This association persisted after adjusting for change in physical function (OR: 2.86; 95% CI: 1.16-7.01). This association also persisted (but did not reach statistical significance) in the subset of patients who experienced a meaningful improvement in physical function (OR: 4.16; 95% CI: 0.71-24.44). No statistically significant sex differences were noted in pain interference (p=0.69) or ability to participate (p=0.23). Women were somewhat more likely to experience worsening physical function (OR: 2.24; 95% CI: 0.92-5.48; p=0.08) and were somewhat less likely to experience worsening fatigue (OR: 0.56; 95% CI: 0.26-1.21; p=0.14) compared to men, but these associations did not reach statistical significance.

Conclusion: We observed that women with RA initiating a new DMARD were more likely to experience worsening depression as compared to men, even when they experienced treatment-associated improvement in physical function. The findings point to important sex differences in PRO responses to DMARD therapy and highlight the value of PROMIS measures in understanding sex differences in RA health outcomes.

Table. PROMIS measures at DMARD initiation and subsequent changes in women and men with RA.

	Women				Men			
PROMIS measure	At DMARD initiation Mean (±SD)	Improved by ≥2 points	No meaningful change	Worsened by ≥2 points	At DMARD initiation Mean (±SD)	Improved by ≥2 points	No meaningful change	Worsened by ≥2 points
Physical Function	38 (±7)	37%	69%	32%	40 (±6)	36%	45%	18%
Ability to Participate	45 (±8)	44%	25%	32%	45 (±7)	41%	23%	36%
Pain Interference	63 (±6)	49%	23%	28%	63 (±5)	53%	26%	21%
Fatigue	60 (±9)	45%	21%	34%	55 (±9)	29%	18%	53%
Depression	52 (±9)	39%	24%	36%	51 (±8)	36%	47%	18%

Disclosure: J. Davis: Girihlet, 9, Pfizer, 5, Remission Medical, 9; **S. Achenbach**: None; **C. Arment**: None; **D. Bekele**: None; **V. Kronzer**: None; **T. Mason**: None; **E. Myasoedova**: None; **L. Peterson**: None; **K. Wright**: None; **C. Crowson**: None.

Abstract Number: 2034

Assessment of the Immediate and Short-term Impact of an Information Course on Patients' Knowledge About Rheumatoid Arthritis: Evaluation Using a Self-prepared and Validated Assessment Questionnaire

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Patient Outcomes, Preferences, & Attitudes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Long-term outcomes in rheumatic diseases can be improved by improving patients' knowledge, beliefs and perception about their disease which can help them in coping with the disease better. However, there is a lack of tools/instruments in rheumatoid arthritis (RA) to 1. objectively assess patients' knowledge in various domains & 2. To assess the impact of a patient education program. The aim of the study is to develop, validate and assess the performance of a self-prepared questionnaire for assessing patients' knowledge about their disease and to use this tool to assess the impact of an information course in improving the above-mentioned elements among patient.

Table – 1 Question-wise assessment of responses before and after the information course and the statistical significance of the change

S. No.	Question	Pre-Test Performance (n=274)			Post-Test Performance (n=141)			Statistical Significance ($p<0.05$)* Y/N
		Correct (%)	Incorrect (%)	I don't know (%)	Correct (%)	Incorrect (%)	I don't know (%)	
1.	Name of disease	48.54	2.76	48.7	92.2	1.4	6.4	Y
2.	Etiology of disease	21.53	20.27	58.2	63.83	18.47	17.7	Y
3.	Hereditary nature	28.47	33.83	37.7	84.4	8.5	7.1	Y
4.	Dietary restrictions in RA	28.83	48.07	23.1	88.65	6.35	5.0	Y
5.	Extra-articular manifestations	20.44	53.56	26	62.41	28.39	9.2	Y
6.	Complications of long-standing disease	63.14	4.66	32.2	86.52	2.18	11.3	Y
7.	Possibility of cure	38.69	21.01	40.3	89.36	3.54	7.1	Y
8.	Blood tests (CBC, LFT, RFT)	27.74	52.16	20.1	73.05	22.65	4.3	Y
9.	Repeat Rf and Anti-CCP	10.58	37.42	52	68.79	17.01	14.2	Y
10.	Repeat ESR and CRP	20.07	33.73	46.2	36.17	51.03	12.8	N
11.	Identification of steroids	7.66	26.64	65.7	43.97	37.63	18.4	Y
12.	Identification of NSAIDs	24.82	14.98	60.2	56.74	19.86	23.4	Y
13.	Identification of DMARDs	25.91	23.59	50.5	67.38	14.92	17.7	Y
14.	Safe drugs in pregnancy	5.11	6.59	88.3	50.35	20.55	29.1	Y
15.	NSAIDs adverse effects	56.20	7.5	36.3	73.05	10.65	16.3	Y
16.	Duration of treatment in RA	48.54	4.56	46.9	87.23	4.27	8.5	Y
17.	Use of alternative medicine	20.44	23.56	56	76.6	9.2	14.2	Y
18.	Steroid adverse effects	9.12	24.18	66.7	41.13	36.17	22.7	Y
19.	Onset of DMARDs action	30.29	41.11	28.6	70.92	17.78	11.3	Y
20.	Role of exercise in RA	11.31	35.19	53.5	62.25	19.35	18.4	Y
21.	Role of exercise in RA	28.47	14.03	57.5	68.09	16.31	15.6	Y
22.	Exercise from swollen/painful joints	32.48	18.02	49.5	77.3	9.2	13.5	Y
23.	Prevention of joint damage	16.06	23.54	60.4	61.7	24.1	14.2	Y
24.	Energy conservation in RA	10.5	27.6	61.9	47.52	38.28	14.2	Y

*change with respect to the correct responses before and after the information course (Assessed by McNemar test)

Methods: A self-prepared questionnaire (Hindi/English) containing 24 multiple choice or true-false type questions with single correct answer assessing patients' knowledge about RA in 3 domains (a. etiology, disease process, signs & symptoms b. drug therapy & monitoring c. joint protection, exercise, coping) was prepared. All questions had an item-level content validity index (I-CVI) of at least 0.9. The scale-level content validity index based on the universal agreement method (S-CVI/UA) was 0.8 for the whole questionnaire as assessed by 6 experts. All questions had an option of 'I don't know' which would prevent patients from guessing the answer from the available options. Each question was given a score of 1 if answered correctly. The questionnaire was applied 3 times: at baseline, immediately after an information course to see the immediate impact and after 4 months to see the retention of the information. Information on demographic features and socio-economic status was also collected. Frequency data were compared using McNemar test for paired nominal data & kappa statistics for ordinal data. Student's paired t-test was used for comparison of mean scores to see the impact.

Results: At baseline, the questionnaire was applied to 274 patients with RA (F:M=248:26; mean age 44±11.9 years) and the median(range) score was poor 5(0-21) (Table–1). Among them, 141 patients attended the information course. The option 'I don't know' was exercised 3186 times (48.24%) before the information course which reduced to 469 (13.86%) times after the course. After the information course, all the questions recorded a higher number of correct responses as compared to before the course. Twenty-one questions had significantly higher correct response rate (Table–1). Median score for increased from 5(0-21) to 17(0-24) ($p< 0.001$) which was irrespective of the socio-economic classes and education status of the patients (Figure-1). Upon re-administering the questionnaire after 4 months, the median score 13(0-24) of the questionnaire (n=78) remained significantly higher ($p< 0.001$) as compared to baseline score (Figure 1) with 21 out of 24 questions achieving statistical significance (Table–2).

Conclusion: Indian patients with RA have a poor knowledge base about their disease which one may strive to improve by implementing short information courses. The information course was found to be effective across the socio-economic classes and educational status. The provided information was retained at 4th month of follow up months without any reinforcement course.

Table – 2 Question-wise assessment of responses before the information course and after 4 months with the statistical significance of the change

S. No.	Question	Pre-Test Performance (n=274)			4 months responses (n=78)			Statistical Significance ($p<0.05$)* Y/N
		Correct (%)	Incorrect (%)	I don't know (%)	Correct (%)	Incorrect (%)	I don't know (%)	
1.	Name of disease	48.54	2.76	48.7	91	0.03	9	Y
2.	Etiology of disease	21.53	20.27	58.2	60.26	10.24	29.5	Y
3.	Hereditary nature	28.47	33.83	37.7	60.26	14.14	25.6	Y
4.	Dietary restrictions in RA	28.83	48.07	23.1	61.54	29.46	9	Y
5.	Extra-articular manifestations	20.44	53.56	26	42.31	52.59	5.1	Y
6.	Complications of long-standing disease	63.14	4.66	32.2	88.46	1.24	10.3	Y
7.	Possibility of cure	38.69	21.01	40.3	76.92	11.58	11.5	Y
8.	Blood tests (CBC, LFT, RFT)	27.74	52.16	20.1	61.54	35.86	2.6	Y
9.	Repeat Rf and Anti-CCP	10.58	37.42	52	39.74	44.86	15.4	Y
10.	Repeat ESR and CRP	20.07	33.73	46.2	39.74	48.76	11.5	N
11.	Identification of steroids	7.66	26.64	65.7	20.51	43.59	35.9	Y
12.	Identification of NSAIDs	24.82	14.98	60.2	41.03	21.77	37.2	Y
13.	Identification of DMARDs	25.91	23.59	50.5	55.13	15.37	29.5	Y
14.	Safe drugs in pregnancy	5.11	6.59	88.3	15.38	23.12	61.5	N
15.	NSAIDs adverse effects	56.20	7.5	36.3	79.49	6.41	14.1	Y
16.	Duration of treatment in RA	48.54	4.56	46.9	80.77	5.13	14.1	Y
17.	Use of alternative medicine	20.44	23.56	56	65.38	14.12	20.5	Y
18.	Steroid adverse effects	9.12	24.18	66.7	17.95	41.05	41	N
19.	Onset of DMARDs action	30.29	41.11	28.6	50.00	44.90	5.1	Y
20.	Role of exercise in RA	11.31	35.19	53.5	34.62	42.28	23.1	Y
21.	Role of exercise in RA	28.47	14.03	57.5	64.10	16.70	19.2	Y
22.	Exercise from swollen/painful joints	32.48	18.02	49.5	71.79	12.81	15.4	Y
23.	Prevention of joint damage	16.06	23.54	60.4	57.69	23.11	19.2	Y
24.	Energy conservation in RA	10.5	27.6	61.9	39.74	35.86	24.4	Y

*change with respect to the correct responses at 4 months compared to the correct responses before the information course

(Assessed by McNemar test)

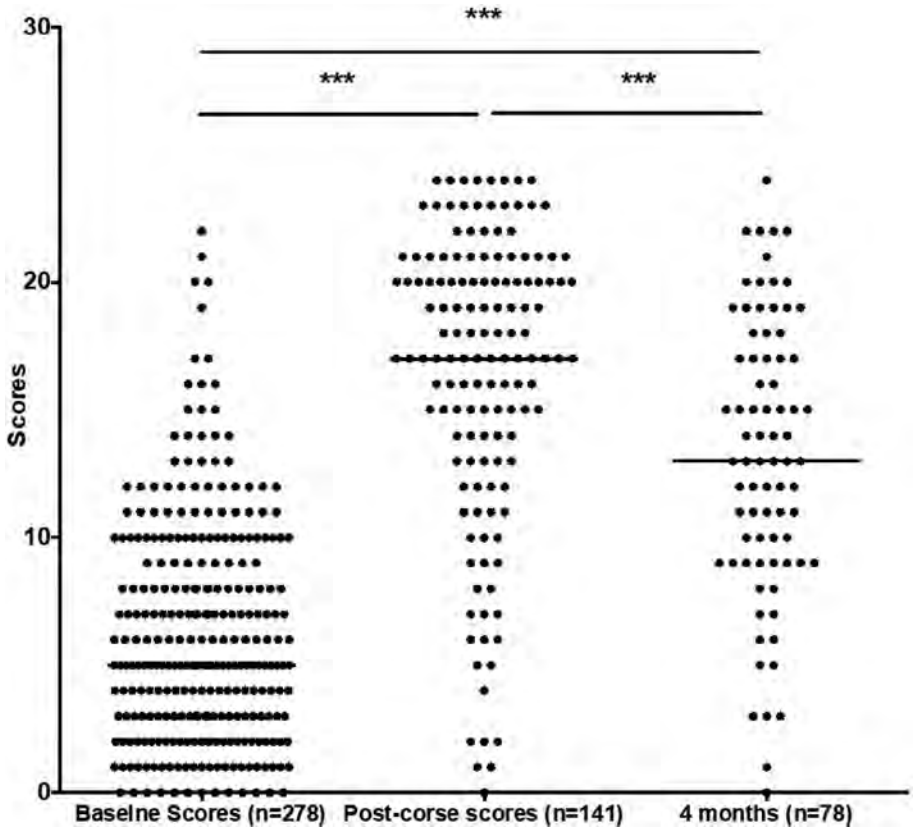

Figure 1. Median scores before, after and at 4 months of information course

Disclosure: R. Gupta: None; **R. Goswami**: None; **M. Yadav**: None; **S. Saini**: None; **A. Mohan**: None; **V. Perumal**: None.

Abstract Number: 2035

Intimate Partner Violence Is Associated with a Poorer Health-Related Quality of Life (HR-QoL) in Women with Systemic Lupus Erythematous

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Patient Outcomes, Preferences, & Attitudes Poster III

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Background/Purpose: Systemic lupus erythematosus (SLE) is an inflammatory, multisystemic, chronic disease more prevalent in women and can significantly impact health-related quality of life (HRQoL).[1] Sociodemographic factors have been associated with reduced HRQoL in patients with SLE such as experiencing violence particularly intimate partner violence

(IPV). IPV includes physical violence, sexual violence, and psychological aggression by a romantic or sexual partner.[2] Women with SLE are at risk for IPV and should be evaluated to recognize this problem. The aim of this study was to evaluate the impact of IPV in HRQoL in women with SLE.

Methods: We performed a cross-sectional study from September 2022 to April 2023 in an outpatient rheumatology clinic at Hospital Universitario "Dr. José Eleuterio González" in Northeast Mexico. We included female patients who were ≥ 18 years, met EULAR/ACR 2019 SLE classification criteria for at least 24 weeks, had ≥ 2 in the last 12 months, and had one of the following statuses: romantic relationship, divorced/separated or widowed and single/never married.[2]

At first, we performed consultations and assessments of the following: disease activity measured by Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), response to treatment measured by Physician Global Assessment (PhGA), and cumulative damage measured by Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index (SDI). After consultation, patients were invited to participate, those who accepted were located in a private room to hand a written consent. Patients answered the following questionnaires: IPV,

Table 1. Baseline demographic characteristics

	n = 24
Age in years, mean ± SD	34.33 ± 10.26
Marital status, n (%)	
o Single	8 (33.33)
o Married	5 (20.83)
o Never married	9 (37.50)
o Widow	2 (8.33)
Number of romantic partners, mean ± SD	2.1 ± 1.04
Current romantic partner, n (%)	
o Yes	15 (62.50)
o No	9 (37.50)
Educational level, n (%)	
o Elementary school	3 (12.50)
o Junior High School	8 (33.33)
o Senior high school	11 (45.83)
o College	2 (8.33)
Employment status, n (%)	
o Paid employment	9 (37.50)
o Not employed	15 (62.50)
Monthly income in dollars	
o Less than 290	3 (33.33)
o 290 – 600	4 (44.44)
o 600 – 1, 150	2 (22.22)
o More than 1, 1150	0
Housework, n (%)	
o Yes	22 (91.66)
o No	2 (8.33)
Health insurance, n (%)	
o Yes	22 (91.66)
o No	2 (8.33)
SLEDAI-2K, mean ± SD	4.8 ± 1.7
LupusQoL, mean ± SD	
Physical domain	84.93 +-13.34
Emotional domain	80.81 + -18.06
Body image domain	81.08 +-21.05
Burden to others	73.02 +- 29.38
Sexual domain	74.41 +- 28.79
Total	78.85 +- 16.23

SD, standard deviation; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; LupusQoL, Lupus Quality of Life

chronic pain syndromes, and quality of life. Participants were required to answer the Spanish version of the following questionnaires: Hurt, Insulted, Threatened with harm, and Screamed at (HITS), Index of Spouse Abuse Physical Scale (ISA-P) and Lupus Quality of Life (LupusQoL).

Results: From October 2022 to April 2023, 24 patients were included. The baseline demographic characteristics are listed in Table 1. Six patients had experienced IPV. IPV, HITS and ISA-P results are seen in table 2 and 3.

Conclusion: Data about IPV in women with SLE in our country are missing. IPV prevalence in our study was 33.33% higher than reported by Sardinha L. et al 2018 which evaluated violence in women without autoimmune diseases at 16%. The analysis performed between patients who were victims of IPV and quality of life showed a statistical trend in patients having experienced IPV in the last year in the emotional domain of Lupus QoL, but this was not observed in women who experienced IPV in their lifetime. With these results, we concluded that IPV in women with SLE has an impact in the emotional domain on the quality of life of Lupus (HR-QoL).

1.- Coll CVN, et al. Intimate partner violence in 46 low-income and middle-income countries: an appraisal of the most vulnerable groups of women using national health surveys. BMJ Global Health 2020;5: e002208.

2.- Sardinha L, Maheu-Giroux M, Stöckl H, Meyer S, García-Moreno C. Global, regional, and national prevalence estimates of physical or sexual, or both, intimate partner violence against women in 2018. Lancet 2022; 399: 803–13.

Table 2. HITS and ISA-P characteristics in patients with intimate partner violence

HITS questionnaire	
Last year IPV HITS punctuation, mean ± SD	5.45 ± 2.78
Psychometric interpretation - Last year IPV HITS, n (%)	
o Having experienced intimate partner violence	6 (25)
o No experience of intimate partner violence	18 (75)
Lifetime IPV HITS punctuation, mean ± SD	5.8 ± 3.33
Psychometric interpretation: Lifetime IPV HITS punctuation, n (%)	6 (25)
o Having experience with intimate partner violence	18 (75)
o No experience of intimate partner violence	
ISA-P	
Last year psychological domain punctuation, mean ± SD	9.38 ± 14.35
Psychometric interpretation last year psychological domain punctuation, n (%)	
o Having experience with intimate partner violence	6 (25)
o No experience of intimate partner violence	18 (75)
Lifetime Psychological domain punctuation, mean ± SD	2.12 +-3.60
Psychometric interpretation Lifetime Psychological domain punctuation, n (%)	
o Having experience with intimate partner violence	3 (12.5)
o No experience of intimate partner violence	21 (87.5)
Last year Physical domain punctuation, mean ± SD	11.69 ± 15.55
Psychometric interpretation last year Physical domain punctuation, n (%)	
o Having experience with intimate partner violence	8 (33.33)
o No experience of intimate partner violence	16(66.66)
Lifetime Physical domain punctuation, mean ± SD	4.52 ± 9.61
Psychometric interpretation Lifetime Physical domain punctuation, n (%)	
o Having experience with intimate partner violence	6 (25)
o No experience of intimate partner violence	18 (75)

Table 3. LupusQoL of patients with and without intimate partner violence

	Having experienced intimate partner violence n = 6	Not having experienced intimate partner violence n = 18	p=value
Last year intimate partner violence	76.5 (62.25 – 87.75)	93 (81.5 – 98)	0.056†
Physical domain, median (IQR)	67 (59 – 76)	92 (70 – 100)	0.027†
Emocional domain, median (IQR)	78 (57 - 85)	92 (70 – 100)	0.177†
Imagen Corporal, median (IQR)	66.50 (44.75 – 86)	90 (49.75 – 100)	0.104†
Burden to others, median (IQR)	80 (52.5 – 85)	85 (69.75 – 100)	0.494†
Sexual domain, median (IQR)	70.44 (14.90)	81.65 (16.06)	0.147*
Lifetime intimate partner violence			
Physical domain, median (IQR)	85 (70.25 – 94.5)	90.5 (71.75 - 98)	0.653†
Emotional domain, median (IQR)	83 (64 – 96.5)	84.5 (64 - 98)	0.881†
Corporal image, median (IQR)	86 (77 - 100)	88 (51.25 - 100)	0.610†
Burden to others, median (IQR)	83 (56.5 – 96.5)	87 (30.25 - 100)	0.976†
Sexual, median (IQR)	85 (80 - 97.5)	80 (37.5 – 98.25)	0.264†
LupusQol, mean (DS)	83.42 (11.14)	76.57 (18.15)	0.267*

Disclosure: E. Campos-Tinajero: None; **G. Serna-Peña**: None; **J. Esquivel-Valerio**: None; **R. Castillo-de la Garza**: None; **G. García Arellano**: None; **P. Gamez-Siller**: None; **E. Aguilar-Rivera**: None; **P. Gonzalez-Garcia**: None; **D. Galarza-Delgado**: None.

Abstract Number: 2036

Switch or Stay the Same? Preferences of People with Autoimmune Disease on Rituximab for Different Types of COVID-19 Vaccine Boosters

Todd Wilson[1], **Paul R. Fortin**[2], Ines Colmegna[3], Sonia Theriault[4], Nathalie Amiable[5], Alexandra Godbout[5] and Glen Hazlewood[1], [1]University of Calgary, Calgary, AB, Canada, [2]Centre ARThrite - CHU de Québec - Université Laval, Quebec City, QC, Canada, [3]The Research Institute of the McGill University Health Centre, Montréal, QC, Canada, [4]The Research Institute of the McGill University Health Centre, Montreal, QC, Canada, [5]Centre ARThrite - CHU de Quebec - Universite Laval, Quebec City, QC, Canada

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Patient Outcomes, Preferences, & Attitudes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: COVID-19 vaccines are now being offered as regular boosters every 6-12 months for people with autoimmune rheumatic diseases, particularly for people on rituximab, where serological responses to vaccination are poor. We were interested in understanding the preferences of patients taking rituximab for a booster with the same messenger RNA (mRNA) vaccine, versus a switch to a protein subunit vaccine.

Methods: We conducted a discrete-choice experiment (DCE) within a clinical trial comparing vaccine types for 4th (Trajectory A) and 5th (Trajectory B) doses in people with autoimmune rheumatic diseases, all of whom had received prior mRNA vaccines. In this open label, non-randomized, comparative trial, people could choose between an mRNA or protein subunit vaccine. In the DCE, people were asked to choose between two different vaccine types or "no vaccine" in a series of ten hypothetical questions, where the vaccine choices varied in terms of their effectiveness, likelihood of a flare, and type of vaccine (same (mRNA) versus switch to a protein subunit vaccine). The DCE was administered by computer in French and English at the two trial sites in Quebec, Canada. We used a hierarchal Bayes model with continuous levels to estimate average and individual part-worth utilities and attribute importance across the range of levels presented for the three attributes. We compared the preferences of people who chose the different vaccine types through a Wilcoxon rank-sum test on the median individual part-utility values.

Results: Among 78 people who agreed to participate, 69 (88%) completed the survey.Participants had an average age of 58 years, 78% were female, and 58% had above high school education. The type of autoimmune disease was rheumatoid arthritis (43%), ANCA associated vasculitis (32%), systemic lupus erythematosus (9%) and other (16%), with a median disease duration of 9 years. 65% of respondents had a prior COVID-19 infection at study entry. Of the 69 participants, 36 (52%) people chose an mRNA vaccine and 33 (48%) people chose a protein subunit vaccine. On average, people preferred to stay with the same vaccine type, rather than switch to a protein subunit vaccine. However, people would accept a protein subunit vaccine if it was associated with an 18% absolute increase in effectiveness, or a 6% absolute reduction in the risk of flare. People who chose the protein subunit vaccine placed a higher importance on vaccine effectiveness ($p < 0.001$) and lower importance on vaccine type ($p < 0.001$).

Conclusion: People with autoimmune diseases on rituximab who had received prior mRNA COVID-19 vaccines preferred to stay with mRNA vaccines for subsequent doses unless the new protein subunit vaccine was substantially more effective (~20%) or safe, although variability in preferences was found. This supports current approaches of booster immunizations with the same vaccine, and provides an estimate of what would be considered a worthwhile increase in effectiveness for high-risk patients to choose a different vaccine type.

Disclosure: T. Wilson: None; **P. Fortin**: AbbVie, 1, AstraZeneca, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Roche-Genentech, 1; **I. Colmegna**: None; **S. Theriault**: None; **N. Amiable**: None; **A. Godbout**: None; **G. Hazlewood**: None.

Abstract Number: 2037

Assessing Risk of Depression in Common Rheumatologic Disorders Using Diagnostic Codes, Survey Scores, and Propensity Score Matching Methodology

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Many studies have shown that rheumatologic conditions are associated with a higher risk of depression. The two most common methods to detect depression in these studies used DSM/ICD criteria; alternatively, self-report screening questionnaires, such as the Patient Health Questionnaire (PHQ). However, using one or the other

method to detect depression might lead to decreased sensitivity to detect depression, and the statistical analysis can be fraught with difficulty since numerous confounding variables affect depression. In this study, we aim to implement both methods to detect depression in patients with Systemic sclerosis (SSc), Dermatomyositis (DM), and Fibromyalgia(FM) using propensity-score matching in a national cohort database.

Methods: ICD 9/10 codes were used to identify SSc, DM, and FM, of which a propensity score matching (PSM) analysis was used to evaluate the effect of disease on the risk of developing depression in a cohort of 240,353 Americans enrolled in the "All of Us database." ICD 9/10 codes were used, and it can be inferred that the ACR classification criteria for the diseases were met. Covariates for matching included age, gender, race, ethnicity, income level, education level, marital status, cigarette exposure, alcohol exposure, drug exposure, and comorbidities. The control groups were matched with a ratio of 1 to each patient group based on propensity scores. The PSM reduces any confounding factors between the case and control cohorts. A logistic regression analysis determined the association between each disorder and depression. Global Mental Health Scores (GMHS) were compared between control and disease groups using a t-test or Mann-Whitney U test. GMHS is a patient-reported perspective of their mental health, with a score range of 0-20, with the maximum score representing optimum health status.

Results: Out of 240,353 individuals, 638 patients with SSc, 358 patients with DM, and 21,263 FM patients were identified. Control groups for each disease were statistically not different ($p \geq 0.05$) from the case groups for age, gender, race, ethnicity, income level, education level, marital status, cigarette exposure, alcohol exposure, drug exposure, and Charlson comorbidity scores. Only FM was associated with increased risk of depression (OR 2.32 [95% CI: 2.23-2.41], $p < 0.001$), which was in line with the lower average GMHS of FM patients (13.1) compared to control (13.8) ($p < 0.001$). SSc (OR 0.94, 95% CI: 0.75-1.17, p=0.571) and DM (OR 1.07, 95% CI: 0.80-1.44, p=0.649) were not associated with an increased risk of depression. The average GMHS of SSc (13.6) and DM (13.4) patients were statistically not different from their respective control groups.

Conclusion: When used concurrently, diagnostic codes for depression and self-reported screening questionnaires were congruent in assessing the association of depression with common rheumatologic disorders. In addition, the use of propensity score matching helped eliminate confounding variables.

Disclosure: C. ANIM-KORANTENG: None; **Y. EUN**: None; **O. Akpoigbe**: None; **A. SAMMUT**: None.

Abstract Number: 2038

Impact of COVID-19 Pandemic on Preventative Health Screenings in Rheumatology Outpatients

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III
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Session Time: 9:00AM–11:00AM

Background/Purpose: The COVID-19 pandemic created significant barriers to accessing recommended preventative health screening. Patients already managing a chronic disease, particularly those using immunosuppressive medications, may have been disproportionately impacted due to heightened concerns about nosocomial COVID-19 infection risks. The goal of this study was to identify delays in preventative health screening among rheumatology outpatients and assess risk factors associated with delays.

Methods: Between 03/09/2022 and 06/15/2022, 9918 adults enrolled in a single center COVID-19 Rheumatology Registry in New York City were asked whether they skipped or delayed pap smears, mammograms and/or colonoscopy screenings due to the COVID-19 pandemic. Participants living in NY, NJ, or CT were also assigned a census tract-based Social Vulnerability Index (SVI). ICD-10 algorithms identified systemic rheumatic diseases (SRDs). We compared differences between those who did or did not delay screenings using Chi-square, Fisher's exact, or Wilcoxon rank-sum tests as appropriate. We used multivariable models to assess risk factors associated with delay of each screening test in both the whole cohort and separately in the subgroup with SVI scores.

Table 1: Baseline Characteristics of COVID-19 Registry Participants Recommended to have Mammograms, Pap Smears, or Colonoscopies

Table 1: Baseline Characteristics of COVID-19 Registry Participants Recommended to have Mammograms, Pap Smears, or Colonoscopies

	Mammograms (n=1426)			Pap Smears (n=1093)			Colonoscopies (n=1551)		
	Delayed (n=350)	No Delay (n=1076)	P-value	Delayed (n=286)	No Delay (n=807)	P-value	Delayed (n=306)	No Delay (n=1245)	P-value
Age (years), median (IQR)	65 (56, 72)	68 (60, 74)	**<0.001**	61 (51, 68)	63 (54, 71)	**0.002**	67 (61, 73)	69 (62, 75)	**0.006**
Sex, N (%)									**<0.001**
Female	350 (24.5)	1076 (75.5)	—	286 (26.2)	807 (73.8)	—	255 (22)	897 (78)	
Male	—	—		—	—		51 (13)	348 (87)	
Race, N (%)			**0.017**			**0.011**			0.6
American Indian/Alaska Native/Native Hawaiian or Pacific Islander	1 (33)	2 (67)		1 (50)	1 (50)		1 (50)	1 (50)	
Asian	16 (47)	18 (53)		14 (52)	13 (48)		6 (26)	17 (74)	
Black or African American	10 (20)	39 (80)		12 (32)	26 (68)		9 (23)	31 (78)	
Other	17 (33)	35 (67)		15 (33)	30 (67)		9 (20)	37 (80)	
White	306 (24)	977 (76)		242 (25)	734 (75)		281 (20)	1,155 (80)	
Ethnicity, N (%)			**0.02**			**0.042**			0.8
Hispanic/Latinx	25 (36)	44 (64)		22 (37)	37 (63)		12 (21)	46 (79)	
Not Hispanic/Latinx	323 (24)	1,029 (76)		261 (25)	768 (75)		292 (20)	1,197 (80)	
Education, N (%)			0.073			0.4			0.3
Elementary School through Some College	123 (25)	367 (75)		97 (24)	301 (76)		113 (22)	404 (78)	
College graduate	40 (19)	176 (81)		37 (24)	116 (76)		42 (19)	185 (81)	
Masters, professional, doctorate	187 (26)	530 (74)		152 (28)	389 (72)		151 (19)	654 (81)	
CDC Comorbidities[‡], N (%)			0.3			0.8			0.8
0	206 (24)	652 (76)		177 (26)	514 (74)		182 (20)	717 (80)	
1	87 (23)	285 (77)		75 (28)	195 (72)		74 (19)	314 (81)	
2 or more	57 (29)	139 (71)		34 (26)	98 (74)		50 (19)	214 (81)	
Insurance, N (%)			0.051			**0.015**			0.13
Commercial Only	173 (27)	479 (73)		181 (28)	475 (72)		140 (21)	527 (79)	
Medicaid (alone or in combination)	12 (40)	18 (60)		12 (50)	12 (50)		7 (30)	16 (70)	
Medicare (excluding Medicaid)	156 (22)	546 (78)		86 (23)	293 (77)		153 (19)	655 (81)	
Self-pay or uninsured	8 (20)	32 (80)		7 (21)	26 (79)		5 (10)	44 (90)	
Immunomodulatory or Immunosuppressive Medication Use at Registry Enrollment, N (%)									
Any Immunomodulatory or immunosuppressive medications[*]	216 (28)	559 (72)	**0.008**	193 (30)	446 (70)	**<0.001**	178 (22)	640 (78)	**0.025**
Antimalarials[*]	78 (27)	208 (73)	0.3	78 (30)	178 (70)	0.1	53 (20)	207 (80)	0.7
Biologics, DMARDs, small molecules[**]	127 (26)	361 (74)	0.6	126 (31)	286 (69)	**0.017**	117 (22)	412 (78)	0.077
Steroids[***]	100 (29)	244 (71)	0.052	88 (32)	190 (68)	**0.024**	85 (23)	292 (77)	0.1
Systemic Rheumatic Diseases (SRD), N (%)									
Any SRD[‡]	192 (25)	575 (75)	0.6	174 (28)	457 (72)	0.2	170 (22)	614 (78)	0.051
Inflammatory Arthritis	90 (24)	290 (76)	0.6	89 (30)	207 (70)	0.078	81 (21)	304 (79)	0.4
Spondyloarthritis	37 (27)	100 (73)	0.5	31 (25)	94 (75)	0.7	38 (21)	144 (79)	0.7
Vasculitis/Scleroderma/Myositis	19 (26)	55 (74)	0.8	13 (24)	41 (76)	0.7	20 (27)	53 (73)	0.088
SLE/Sjogren's/MCTD/UCTD	67 (27)	184 (73)	0.4	64 (29)	158 (71)	0.3	55 (27)	152 (73)	**0.007**

[†] include any of the following identified by the Centers for Disease Control and Prevention in 2/2023 as being most relevant for COVID-19 risk: Asthma or lung disease, Cancer, Chronic Kidney Disease, Diabetes, Congestive Heart Failure or Myocardial Infarction, Ever-smoking, Stroke

[‡]Patients could select ≥1 medication option

*Chloroquine or hydroxychloroquine

** Abatacept, belimumab, IL-1i, IL-6i, IL-17i, IL-12/23i, TNFi, rituximab, azathioprine, cyclosporine, cyclophosphamide, leflunomide, methotrexate, mycophenolate, sulfasalazine, tacrolimus, apremilast, JAKi

***Methylprednisolone, prednisone

[‡]Patients were able to meet ≥1 ICD code algorithm for individual systemic rheumatic diseases

All p-values <.05 bolded

Number of patients per category may not always equal to column total (N) due to missing data

Table 2: Census-Tract Level Characteristics of COVID-19 Registry Participants Residing in NY, NJ, and CT Recommended to have Mammograms, Pap Smears, or Colonoscopies

Table 2: Census-Tract Level Characteristics of COVID-19 Registry Participants Residing in NY, NJ, and CT Recommended to have Mammograms, Pap Smears, or Colonoscopies

Mammograms	**Total (n=1338)**	**Delay (n=325)**	**No Delay (n=1013)**	**p-value**
Overall SVI[¥]				**0.046**
Highly Vulnerable*	84	28 (33%)	56 (67%)	
Not Highly Vulnerable	1254	297 (24%)	957 (76%)	
Socioeconomic Status SVI[£]				**0.014**
Highly Vulnerable*	85	30 (35%)	55 (65%)	
Not Highly Vulnerable	1253	295 (24%)	958 (76%)	
Pap Smears	**Total (n=1035)**	**Delay (n=272)**	**No Delay (n=763)**	**p-value**
Overall SVI[¥]				0.058
Highly Vulnerable*	86	30 (35%)	56 (65%)	
Not Highly Vulnerable	949	242 (26%)	707 (74%)	
Socioeconomic Status SVI[£]				0.058
Highly Vulnerable*	86	30 (35%)	56 (65%)	
Not Highly Vulnerable	949	242 (26%)	707 (74%)	
Colonoscopies	**Total (n=1435)**	**Delay (n=286)**	**No Delay (n=1149)**	**p-value**
Overall SVI[¥]				0.6
Highly Vulnerable*	78	16 (21%)	62 (79%)	
Not Highly Vulnerable	1357	270 (20%)	1087 (80%)	
Socioeconomic Status SVI[£]				0.9
Highly Vulnerable*	84	15 (18%)	69 (82%)	
Not Highly Vulnerable	1351	271 (20%)	1080 (80%)	

[¥]Neighborhood CDC Social Vulnerability Index (SVI)
[£] Neighborhood CDC Social Vulnerability Index (SVI) related to socioeconomic status subtheme
*Highly Vulnerable defined as falling in the worst quartile of the CDC social vulnerability index

Results: 2735/9918 (27.6%) participants responded. Mean age was 65.4 years (SD=12.7), 90.6% White, 4.6% Hispanic/LatinX. 2000 were recommended to have regular preventive health screens. Delays were reported in 286/1093 pap smears (26.2%); 350/1426 mammograms (24.5%); and 306/1551 colonoscopies (19.7%). More Hispanic/LatinX vs. non-Hispanic/LatinX participants delayed pap smears (37% vs. 25%, p=.04) and mammograms (36% vs. 24%, p=.02). Fewer White participants delayed pap smears (25% of White participants delayed, 32% Black, 52% Asian, 33% Other; p=.01). Mammogram delays also differed by race (24% of White participants delayed, 20% Black, 47% Asian, and 33% Other; p=.02). More females than males delayed colonoscopies (22% vs. 13%, $p < .001$). Younger age was associated with delaying all three screens (all $p< 0.05$). Participants living in census tracts with the worst socioeconomic vulnerability had higher proportions of delayed mammograms (35% vs. 24%, p=.01). Participants using any immunomodulatory/immunosuppressive medication at registry enrollment were more likely to report delaying all three screens (p=.03). Having an SRD was not associated with delays. In multivariable models, adjusting for all other covariates, those on immunomodulatory/immunosuppressive medications were more likely to delay pap smears (OR 1.55, 95% CI: 1.14, 2.12) and colonoscopies (OR 1.33, 95% CI: 1.01, 1.77), but not mammograms (OR 1.22, 95% CI: 0.93-1.59). Males were less likely to delay colonoscopies (OR 0.55, 95% CI: 0.39, 0.78). For every one-year increase in age, the odds of delaying a mammogram decrease by 1.7% (OR 0.98, 95% CI: 0.97, 0.996).

Conclusion: Immunomodulatory/immunosuppressive medications but not SRD diagnosis was associated with preventive screening delays. These data can help identify rheumatology patients at risk for preventative screening delays. The impact of race, ethnicity, and SES on delaying health screening should be explored in more diverse populations.

Table 3: Multivariable Logistic Regressions: Odds of Delaying Preventative Health Screenings Due to the COVID-19 Pandemic

Table 3: Multivariable Logistic Regressions: Odds of Delaying Preventative Health Screenings Due to the COVID-19 Pandemic*

	Model 1: Mammogram Delay (n=1282) OR (95% CI)	Model 2: Pap Smear Delay (n=992) OR (95% CI)	Model 3: Colonoscopy Delay (n=1372) OR (95% CI)
Age, years	**0.98 (0.97, 0.996)**	1.00 (0.98, 1.01)	**0.99 (0.97, 1.00)**
Sex			
Female	NA	NA	Ref.
Male	NA	NA	**0.56 (0.39, 0.78)**
Neighborhood Social Vulnerability related to socioeconomic status			
Q1 (lowest vulnerability)	Ref.	Ref.	Ref.
Q2	1.06 (0.79, 1.42)	1.16 (0.83, 1.61)	1.31 (0.97, 1.76)
Q3	1.06 (0.70, 1.58)	1.20 (0.77, 1.86)	0.94 (0.60, 1.42)
Q4 (highest vulnerability)	1.50 (0.88, 2.50)	1.31 (0.76, 2.21)	0.95 (0.48, 1.79)
Race			
White	Ref.	Ref.	Ref.
Non-White¥	1.23 (0.79, 1.89)	1.46 (0.91, 2.30)	1.18 (0.68, 1.96)
Ethnicity			
Hispanic or Latino	Ref.	Ref.	Ref.
Not Hispanic or Latino	0.72 (0.40, 1.35)	0.90 (0.48, 1.73)	1.47 (0.68. 3.56)
Education			
Elementary through some college	Ref.	Ref.	Ref.
College Graduate	1.35 (0.88, 2.10)	0.84 (0.53, 1.35)	1.07 (0.70, 1.65)
Masters, Professional, Doctorate	**1.53 (1.02, 2.35)**	1.08 (0.70, 1.71)	0.94 (0.63, 1.43)
CDC comorbidities			
<2	Ref.	Ref.	Ref.
>=2	1.40 (0.98, 1.99)	0.99 (0.62, 1.53)	0.90 (0.61, 1.29)
Any immunomodulatory or immunosuppressive medication use	1.22 (0.93, 1.59)	**1.55 (1.14, 2.12)**	**1.33 (1.01, 1.77)**

* All models controlled for age, sex, SVI, SES, race, ethnicity, education, CDC comorbidities, Immunomodulatory/Immunosuppressive medication use at registry enrollment

¥ American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, and Other

Bold=p< 0.05

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Abstract Number: 2039

Clinical, Immunologic, and Genetic Characteristics in Patients with Syndrome of Undifferentiated Recurrent Fevers (SURF)

Marci Macaraeg, Michael Matt, Elizabeth Handorf, Elizabeth Baker and Grant Schulert, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

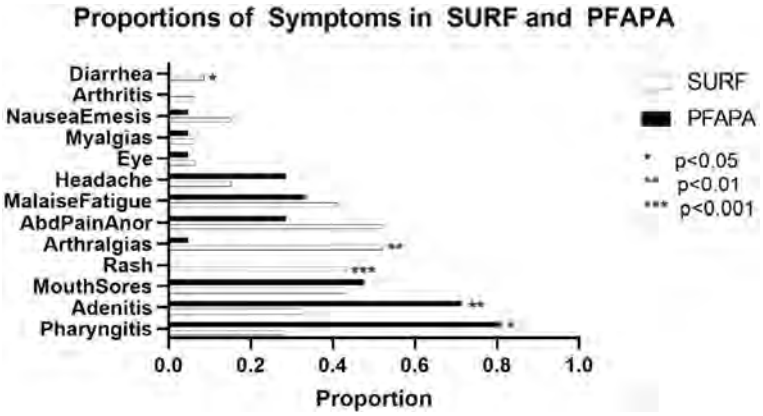
SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Pediatric Rheumatology – Clinical Poster III: Potpourri

Session Type: Poster Session C

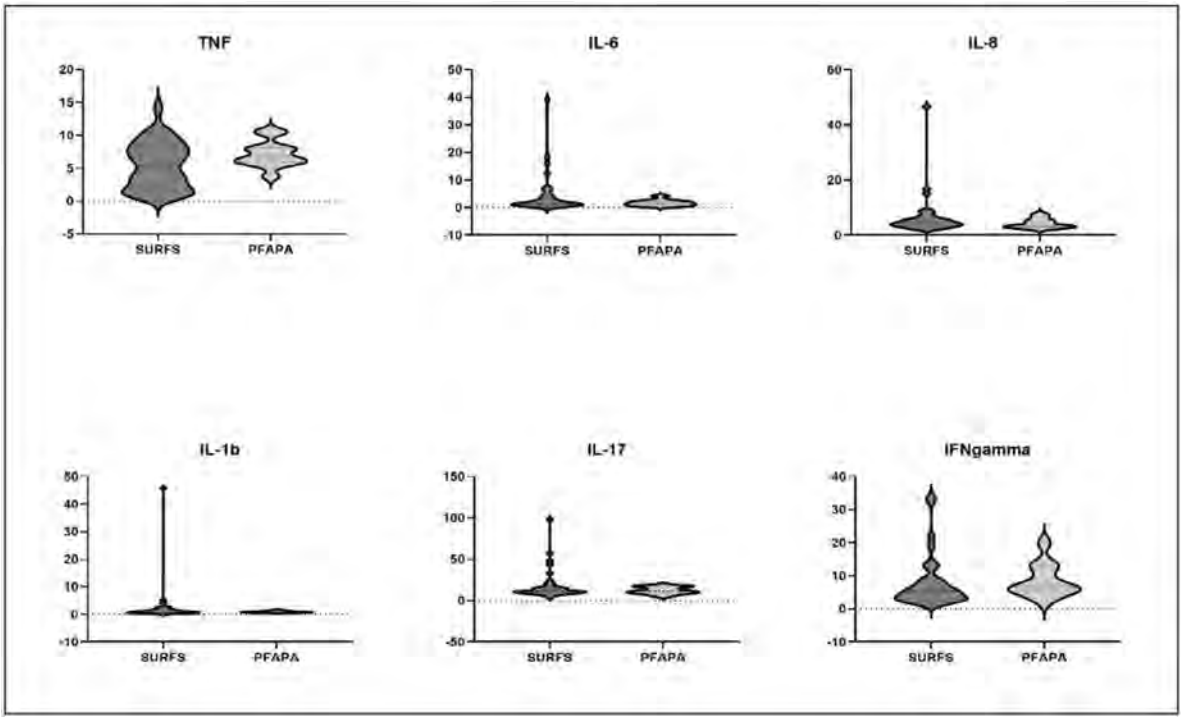
Session Time: 9:00AM–11:00AM



Proportion of symptoms in patients with SURF versus PFAPA. Symptoms that were significantly different between the two groups are noted with an asterisk.

Background/Purpose: Unexplained recurrent fevers are a common presentation to pediatric rheumatology and a significant burden to affected families due to missed daycare or school days for the child and missed work days for the parent. Syndrome of Undifferentiated Recurrent Fevers (SURF) represents a group of disorders characterized by self-limited recurrent fevers and systemic autoinflammation without confirmed molecular diagnosis of a Hereditary Recurrent Fever syndrome (HRF) as well as not fulfilling criteria for Periodic Fever, Adenitis, Pharyngitis, Aphthous stomatitis syndrome (PFAPA). This study aims to differentiate the clinical and chemical findings between SURF and PFAPA; to characterize the clinical, chemical, and genetic findings; and to describe treatment responses of SURF patients.

Methods: We enrolled 47 patients followed at the Cincinnati Children's Hospital (CCHMC) Autoinflammatory Treatment and Research Center who met criteria for SURF based on history of recurrent fevers, genetic testing negative for HRF, and did not meet EULAR/PRINTO classification criteria for PFAPA. Baseline data was collected at enrollment, including their



Violin plot of pro-inflammatory cytokines where SURF patients were found to have very elevated, outlier measurements.

	On Demand Steroids *n (%)*	T&A *n (%)*	Colchicine *n (%)*	Cimetidine *n (%)*	Anti-IL1 *n (%)*
Complete response	11 (64.7)	7 (58.3)	8 (42.1)	1 (25)	8 (47)
Incomplete response	4 (23.5)	3 (25)	5 (26.3)	1 (25)	4 (23.5)
No response	1 (5.9)	2 (1.7)	5 (26.3)	1 (25)	4 (23.5)
Did not tolerate medication			1 (5.3)	1 (25)	1 (5.9)
Dual Anti-IL1 therapy					3 (17.6)
Total Attempted on Treatment	17	12	19	4	17

Treatment response table showing total number of patients who were trialed on a therapy, as well as the number and percentage of patients who who had a complete, incomplete, or no response.

symptoms during episodes, family history, genetic testing, and inflammatory markers/cytokines. Cytokines were run using a cytokine multiplex assay. In some patients, exome sequencing was performed with focused analysis of 394 genes implicated in known inflammatory disorders as well as primary immunodeficiency syndromes. Clinical symptoms between SURF and PFAPA were compared using Welch's T-Test and two-tailed Fisher's exact test. Cytokines for SURF and PFAPA were compared using Mann-Whitney U Test and hierarchical clustering.

Results: Rash and arthralgias were each more likely to occur in SURF, while pharyngitis was more in PFAPA. Symptoms in SURF and PFAPA patients are shown in Figure 1. Our analysis showed similar cytokine levels between PFAPA and SURF, however SURF patients had more outliers including IL-1beta, IL-6, IL-8, and IL-17A (Figure 2). Hierarchical clustering showed a distinct subgroup of SURF patients with elevated IFNg, IL17a, IL12p70, and IL23. Treatment response for SURF patients ranged from self-resolution to the use of biologics and are further detailed in Table 1. Genetic variants of unknown clinical significance (VUCS) were frequently found in patients with SURF. Several patients had mutations in genes that are implicated in B cell development, immunodeficiencies, granulocyte/monocyte development, and inflammatory bowel disease risk.

Conclusion: SURF is a group of patients with recurrent fevers but without a known monogenic cause. Our preliminary findings suggest SURF has distinct clinical features from PFAPA, with a subgroup that is chemically different. They also suggest SURF is heterogeneous in clinical, chemical, and genetic findings, and in treatment responses. We find frequent VUCS in pathways which may have relevance to disease pathogenesis, and possible associations to SURF endotypes. Further research is necessary to understand these SURF endotypes, what drives the disorder, and how physicians can better predict which treatment will be most successful for each patient.

Disclosure: M. Macaraeg: None; **M. Matt**: None; **E. Handorf**: None; **E. Baker**: None; **G. Schulert**: IpiNovyx, 5, SOBI, 2.

Abstract Number: 2040

Distinguishing Multisystem Inflammatory Syndrome in Children from Typhus Using Artificial Intelligence: MISC vs. Endemic Typhus (AI-MET)

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SESSION INFORMATION

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Background/Purpose: Multisystem inflammatory syndrome in children (MIS-C) following SARS-CoV2infection is a recognized mimic of other inflammatory disorders, including Kawasaki Disease and macrophage activation syndrome. However, MIS-C can also mimic acute infections, such as endemic typhus, presenting a diagnostic challenge with discordant treatments. We aimed to use artificial intelligence (AI) to develop a clinical decision support system that rapidly and accurately distinguishes **M**IS-C versus **E**ndemic **T**yphus (MET).

Methods: With local IRB approval, 49 demographic, clinical, and laboratory features (21 categorical and 28 continuous) available within 6 hours of presentation were retrospectively extracted from the electronic medical records of 133 MIS-C and 87 typhus patients admitted to a single quaternary pediatric system between January 1, 2020 and December 31, 2021. Laboratory values were considered high, low or normal based on institutional norms. Using the attention module of a deep learning model and prioritizing accuracy, during training and testing we iteratively narrowed down to the 30 features necessary to maintain complete accuracy in classification. The AI-MET clinical decision support system was built to use these 30 clinical features, combined with the importance assigned to them by the attention module, to assist providers in distinguishing between MIS-C and typhus manually (i.e., without software) as often as possible.

Results: AI-MET is a two-phase clinical decision support system. In phase 1 of AI-MET, a provider uses 17 features to manually calculate a score (MET-17) to arrive at a diagnostic classification (Table I). If the MET-17 score does not surpass a predetermined confidence level, 13 additional features are added and the MET-30 score is calculated using a recurrent neural network. While 24 of the 30 features (80%) were statistically different between patients with MIS-C and typhus, values for

Table I. MET-17 Features and Scoring

Features with Thresholds	Threshold	Points if ≥	Points if <
Age (years)	11	(−)4	(-)4
Fever Before Presentation (days)	7	(−)8	(-)8
Tmax (°F)	103	(-)6	(−)6
Highest Heart Rate (bpm)	124	(-)4	(−)4
NLR (ANC/ALC)	3.67	(-)4	(−)4
Features with Multiple Inputs	**Points if Low**	**Points if WNL**	**Points if High**
AST (U/L)	(-)3	(-)11	(−)11
ALT (U/L)	(-)8	(-)8	(−)8
Sodium (mmol/L)	(-)2	(−)2	(-)2
Troponin I (ng/mL)	(−)9	(−)9	(-)9
BNP (pg/mL)	(−)10	(−)10	(-)10
Fibrinogen (mg/dL)	(−)4	(−)16	(-)16
Categorical Features		**Points if Yes**	**Points if No**
Epidemiologic Link to COVID-19		(-)5	(−)5
Antecedent Illness		(-)2	(−)2
Conjunctivitis		(-)4	(−)4
Rash		(−)3	(-)3
The patient is classified as typhus if the total score is ≥62. The patient is classified as MIS-C if the total score is ≤ (-)35. If the total score falls between (-)35 and 62, proceed to MET-30.			

Abbreviations: ALC, absolute lymphocyte count; ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; BNP, B-type natriuretic peptide; bpm, beats per minute; °F, degree Fahrenheit; NLR, neutrophil to lymphocyte ratio, Tmax, maximum temperature; WNL, within normal limits

each feature alone were so overlapping between the two patient groups that the features were irrelevant distinguishers as individual parameters. However, AI-MET successfully classified all 220 typhus and MIS-C patients with 100% accuracy. Approximately half of the patients were classified manually with sufficient confidence during phase I using MET-17 that MET-30 (i.e., software) was not needed. A validation cohort of 111 additional MIS-C patients with all 30 AI-MET features available was also classified as MIS-C with 99% accuracy (110/111).

Conclusion: There is significant diagnostic overlap between MIS-C and endemic typhus. Artificial intelligence can successfully distinguish these diagnoses using features typically available within the first 6 hours of patient presentation. As a clinical decision support system, AI-MET will be a valuable tool for front-line providers facing the difficulty of timely diagnosis of a febrile child in endemic areas.

Disclosure: A. Chun: None; **A. Bautista-Castillo**: None; **I. Osuna**: None; **K. Nasto**: None; **F. Munoz**: Gilead, 5, Pfizer, 5, 12, DSMB; **G. Schutze**: None; **S. Devaraj**: None; **E. Muscal**: Sobi, 1, 11; **M. De Guzman**: None; **K. Sexson Tejtel**: None; **I. Kakadiaris**: None; **T. Vogel**: Moderna, 2, Novartis, 2, Pfizer, 2, SOBI, 2.

Abstract Number: 2041

An Analysis of Recurrent Parotitis Patients Referred to Rheumatology Clinic

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Background/Purpose: Juvenile recurrent parotitis (JRP) is characterized by non-obstructive, non-suppurative inflammation of the parotid glands of unknown etiology. The onset of symptoms occurs typically between ages 3-6 and there is a tendency for spontaneous resolution after puberty. Patients are primarily managed by Otolaryngology and approximately 2/3 of patients respond to sialadenoscopy after failing conservative measures, however additional medical therapies are sometimes required. The purpose of this study was to analyze the subset of patients who are referred to rheumatology and to describe the immunosuppressive treatment utilized.

Methods: With approval from our Institutional Review Board, patients were identified via our electronic medical records (EMR) using the ICD-9 and ICD-10 codes for "recurrent parotitis" and "parotitis" between 2013 and 2023 who were seen by rheumatology. Patients 21 years and younger, with at least 3 episodes of parotitis per year or 2 within 6 months, were included. Demographic and clinical information was obtained. Treatment response was determined as complete remission (no episodes in 12 months) or partial response (less than 3 episodes per year or less than 2 episodes per 6 months). Data were evaluated using standard descriptive statistics.

Results: A total of 26 patients met inclusion criteria. Average age was 7 (range 3-21), majority were female (73%), white (77%), and non-Hispanic (62%). Average total episodes of parotitis were 7 (range 2-42), with 4 episodes per year on average. Bilateral parotitis was noted in 81%. Average duration of symptoms prior to referral to rheumatology was 20 months (range 2-84). The more common referral reasons included recurrence (35%) and concern for autoimmune etiology based

Table 1: Comparison of Patients with Idiopathic JRP and Patients with Rheumatologic Diagnoses		
	Idiopathic JRP N=19 Average (Range)	Patients with Diagnosis N=5 Sjogrens 2, Sarcoidosis 2, Granulomatous disease NOS 1 Average (Range)
Age	7.16 (3 to 21)	8.2 (3 to 14)
Sex	Female (63%) Male (37%)	Female (100%)
Time to rheumatology referral in months	24 (2 to 84)	9.6 (3 to 22)
ANA test	Positive (21%) Negative (68%) Not checked (11%)	Positive (60%) Negative (20%) Not checked (20%)
SSA Antibody	Positive 0 Negative (95%) Not Done (5%)	Positive (40%) Negative (60%)
SSB Antibody	Positive 0 Negative (95%) Not Done (5%)	Positive (40%) Negative (60%)
Rheumatoid Factor	Positive 0 Negative 84% Not Checked 16%	Positive 20% Negative 40% Not Checked 40%
Accompanying Symptoms at Presentation	Facial pain (89%) Fever (42%) Arthralgia (21%) Dry eyes (21%) Dry mouth (16%) Caries (21%) Arthritis (5%)	Facial Pain (60%) Fever (40%) Arthralgia (40%) Dry eyes (40%) Dry mouth (5%) Caries (40%) Arthritis (0)
Salivary Gland Biopsy	N=8 -Lymphoplasmacytic infiltrate/sialadenitis: 50% -Granulomatous Inflammation: 12.5% -Nonspecific inflammation: 12.5% -Inadequate sample: 25%	N=3 -Non necrotizing granulomatous inflammation (67%) -Granulomatous parotiditis (33%)
Treatment	NSAIDS (37%) Antibiotics (26%) Oral steroids (26%) IV steroids (5%) MTX (16%) HCQ (11%)	NSAIDS (60%) Antibiotics (40%) Oral steroids (60%) IV steroids (0) MTX (40%) HCQ (40%) Other: Colchicine (20%), Humira (20%)
Patients achieving remission	N=12 Complete response: 36% Partial response: 9% No response: 27% Not enough information: 27%	N=5 Complete response: 40% Partial response: 40% No response: 20%

Table 2: Rheumatologic Therapy for patients with idiopathic JRP				
Patient	Age	Rheumatologic Treatment	Outcome	Notes
Patient 1	4	Oral corticosteroids	No response	Did improve per rheumatology provider but did not meet partial or complete remission criteria
Patient 2	5	Oral corticosteroids	Not enough information	First episode of parotitis did improve but did not meet partial or complete remission criteria.
Patient 3	5	Oral corticosteroids	No response	
Patient 4	5	Hydroxychloroquine	Not enough information	Started on medication early this year without documented relapses but has not had a follow up visit.
Patient 5	10	Oral corticosteroids, hydroxychloroquine, methotrexate	Complete response	
Patient 6	16	Oral/IV corticosteroids methotrexate	No response	Radiologic improvement of parotitis but still with frequent pain episodes.
Patient 7	6	Methotrexate	Complete response	

on laboratory evaluation or biopsy (27%). Five (18.6%) patients had a rheumatologic diagnosis: 2 with Sjogren's syndrome, 2 with sarcoidosis and 1 with unspecified granulomatous parotitis. Among patients referred, ANA was checked in 23 of 26 patients of which 57% were positive. Fifty percent of patients in the group underwent biopsy. Ten out of 26 patients underwent sialadenoscopy with steroid injection, 6 with Kenalog (60%), 3 with ciprofloxacin/dexamethasone (30%), and one with both (10%). Patients were followed for a mean of 25.7 months (range 0.5 -97).Of those without rheumatologic or infectious diagnosis, 7 (37%) patients received immunomodulatory treatment of which 2 achieved complete remission (29%). Treatment included corticosteroids, NSAID, methotrexate, and hydroxychloroquine (Table 2). Among the 12 patients without therapy, 2 (17%) had complete remission.

Conclusion: Patients with JRP were referred to rheumatology clinic due to suspicion for autoimmune conditions or refractory course. In this cohort only a small number of patients had a rheumatologic diagnosis and few idiopathic JRP received immunomodulatory therapy. A subset of children with recurrent parotitis may benefit from rheumatologic consultation and possible treatment with anti-inflammatory and immunomodulatory therapy. Limitation of this study include its retrospective nature, small number of patients and short follow up periods.

Disclosure: Y. Pina: None; **E. Lambert**: None; **M. Pereira**: None; **M. De Guzman**: None.

Abstract Number: 2042

Intraocular Cytokine Profiling of Autoimmune Uveitis

Maryrose Hahn[1], Madison Mangin[2], Marc Todd[1], Pui Lee[1], Mindy Lo[1], Bharti Gangwani[3], Ankoor Shah[3], Amanda Colombo[4], Jessica Scott[4], Stephen Anesi[4], C. Stephen Foster[4], Peter Chang[4], Peter Nigrovic[2] and Margaret Chang[2], [1]Division of Immunology, Boston Children's Hospital, Boston, MA, [2]Boston Children's Hospital, Boston, MA, [3]Department of Ophthalmology, Boston Children's Hospital, Boston, MA, [4]Massachusetts Eye Research and Surgery Institution, Waltham, MA

SESSION INFORMATION
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Background/Purpose: Autoimmune uveitis is an inflammatory disorder of the eye that is associated with significant morbidity, including vision-threatening complications and chronic reliance on immunosuppressive therapies. Each uveitis subtype is categorized by the affected region of the eye and is associated with different autoimmune disorders with distinct immunopathology (i.e. juvenile arthritis, sarcoidosis and Behcet's disease). However, it is unclear how these differences translate into differences in intraocular pathology. Here, we sought to evaluate the intraocular cytokine profile within each uveitis subtype.

Methods: We obtained intraocular fluid samples from patients at Boston Children's Hospital and Massachusetts Eye Research & Surgery Institution with uveitis or non-inflammatory controls undergoing eye surgery. We also collected clinical information such as slit-lamp examinations and medications at the time of surgery. Cytokine content in the aqueous humor was assessed through the Olink proteomics platform, which utilizes proximity extension assay technology to detect 45 cytokines through a multiplex immunoassay. To identify differences in the presence of specific cytokines, we used generalized linear models (LIMMA) on $\log_2$ transformed data. Each uveitis subtype was compared to the controls using Bayesian post-hoc testing. Thresholds for differential cytokine levels were adjusted $p< 0.05$ and fold change >1.

Results: We collected aqueous humor samples from control patients (n=10) and patients with anterior uveitis (n=13), intermediate uveitis (n=2), posterior uveitis (n=4), and panuveitis (n=7). At the time of sample collection, all patients had near-quiet disease activity on slit-lamp examination with anterior chamber cells grades between 0 and 0.5+ by SUN criteria. As expected, non-inflammatory control patients displayed low cytokine levels in their aqueous humor. Anterior uveitis and panuveitis had elevated cytokine expression, while intermediate uveitis and posterior uveitis showed cytokine levels comparable to controls, reflecting the anatomical regions affected by each uveitis subtype. Patients with anterior uveitis segregated into two groups, those with increased inflammatory cytokines (n=6) and those without (n=7). However, there were no significant differences in examination findings or medication usage between these two groups. Among the inflamed anterior uveitis samples, there was significant upregulation of TNF, IL-17, IL-10, IL-6, CXCL9 and IL-15, as well as several chemokines and matrix metalloproteinases compared to controls. Panuveitis also displayed a similar pattern of cytokine upregulation with no significant differences in expression between inflamed anterior uveitis and panuveitis.

Conclusion: While ophthalmic examinations indicated near-quiet clinical disease activity at the time of surgery, panuveitis patients and a subset of anterior uveitis patients displayed persistent inflammation within their intraocular fluid. Further, the similarities in the intraocular cytokine profile between anterior uveitis and panuveitis suggest convergence in inflammatory pathways.

Disclosure: M. Hahn: None; **M. Mangin**: None; **M. Todd**: None; **P. Lee**: None; **M. Lo**: None; **B. Gangwani**: None; **A. Shah**: None; **A. Colombo**: None; **J. Scott**: None; **S. Anesi**: None; **C. Foster**: None; **P. Chang**: None; **P. Nigrovic**: None; **M. Chang**: None.

Abstract Number: 2043

Phenotype of Musculoskeletal Manifestations in a Canadian Inception Cohort of Pediatric Patients with Inflammatory Bowel Disease

Emily Dzongowski[1], Michael Miller[1], Melanie Schmidt[1], Nidhi Rashmikant Suthar[1], Thomas D Walters[2], Anne Griffiths[2], Wael El-Matary[3], Eric Benchimol[2], Jennifer deBruyn[4], **Roberta A Berard**[1] and Eileen Crowley[1], [1]Children's Hospital - London Health Sciences Centre, London, ON, Canada, [2]The Hospital for Sick Children, Toronto, ON, Canada, [3]University of Manitoba, Winnipeg, MB, Canada, [4]Alberta Children's Hospital, Calgary, AB, Canada

SESSION INFORMATION

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Background/Purpose: Musculoskeletal (MSK) manifestations, including arthritis and arthralgia, are among the most common extraintestinal manifestations (EIMs) of inflammatory bowel disease (IBD), reported in 20-30% of adult patients. While patterns of MSK EIMs have been well-characterized in the adult population, there remains a paucity of data in pediatrics. The purpose of this study was to determine the frequency of MSK EIMs in a contemporary cohort of Canadian pIBD patients and describe the phenotype of MSK EIMs in this population.

Methods: This was a prospective longitudinal cohort study using data from the inception cohort of CIDsCaNN (Canadian Children IBD Network). This is a national network involving 12 academic pediatric centers in Canada. The inception cohort is comprised of patients aged 2 to 17 enrolled at diagnosis and followed prospectively. The study included data from creation of the inception cohort (01-04-2014) to the end of the previous calendar year (31-12-2021). Frequency of MSK EIMs was calculated for the entire inception cohort, as well as for subgroups based on age (< 5, 5 to 12, and 12 to 17), sex, and IBD type. For patients with MSK EIMs, phenotype was described by analyzing case report forms for specific EIM features as reported by treating physician. Variables were compared with Pearson Chi-square or Fisher's exact test, where cell counts were < 5. Statistical significance was defined as two-tailed p-value < 0.05. For patients without MSK EIM at time of IBD diagnosis, a Cox regression survival analysis was used to examine differences in age, sex, and ethnicity in terms of time to MSK EIM development, with right censoring for patients who never reported MSK EIMs over the course of follow up.

Results: A total of 1330 pIBD patients were included. 81 patients (6.1%) were reported to have MSK EIMs at IBD diagnosis or any point during follow up. There was no significant difference in overall MSK EIM frequency between sex or age groups. MSK EIMs were present in 63 CD (7.6%), 10 UC (2.6%), and 8 IBD-U (6.4%) patients. Patients with CD were more likely to have MSK EIMs than those with UC or IBD-U (7.6% vs 3.6%, p=0.002). 47 patients (58.0%) had MSK EIMs at or prior to IBD diagnosis while 34 patients developed MSK EIMs >4 weeks after IBD diagnosis. There was no difference in time to MSK EIM development by age or ethnicity. Females were more likely to develop MSK EIMs after IBD diagnosis than males, with odds of MSK EIM development increasing by factor of 4.68 for each year after IBD diagnosis (p=0.047). Of MSK EIM patients, 59 (74.7%) were evaluated by a rheumatologist. Peripheral MSK disease (arthritis, enthesitis, and dactylitis) was reported in 51 patients (63%). Data regarding axial disease (sacroiliitis and ankylosing spondylitis) were only available in 37 patients, 19 of whom reported axial distribution. Peripheral and axial MSK symptoms followed the course of bowel disease in 40.3% and 28.1% of patients respectively, which were not significantly different.

Conclusion: MSK EIMs affect 6.1% of a contemporary cohort of Canadian pIBD patients. This is less than reported in literature, which may be related to physician-reported nature of our data. Their phenotype is variable, with peripheral disease more frequent than axial disease across IBD types.

Disclosure: E. Dzongowski: None; **M. Miller**: None; **M. Schmidt**: None; **N. Rashmikant Suthar**: None; **T. Walters**: AbbVie/Abbott, 1, 5, 6, Janssen, 1, 6, Merck/MSD, 1, Pfizer, 1, 6; **A. Griffiths**: AbbVie/Abbott, 2, 5, 6, 12, Participation in Data Safety Monitoring Board/Advisory Board, Amgen, 2, 12, Participation in Data Safety Monitoring Board/Advisory Board, Bristol Myers Squibb, 2, Janssen, 2, 6, Lilly, 2, Merck, 2, Other, 9, 12, Royalties from use of PUCAI score or TUMMY-UC score in industry-sponsored trials, Takeda, 2, 6, Viatris, 2; **W. El-Matary**: None; **E. Benchimol**: None; **J. deBruyn**: Pfizer, 1; **R. Berard**: None; **E. Crowley**: AbbVie/Abbott, 5, 6, Pfizer, 2, 5.

Abstract Number: 2044

Monogenic Interferon Mediated Diseases: Novel Phenotype and Genotype Characteristics from Saudi Population

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Background/Purpose: IFN-mediated diseases are mendelian innate immunodysregulatory disorders that present early in life with fevers, sterile organ inflammation, and a high type-I IFN-response gene signature in peripheral blood cells. To date, monumental discoveries of novel genetic variants with various phenotypic features have been recognized. We sought to describe novel genotype and phenotype findings in Saudi children with a final diagnosis of autoinflammatory interferonopathy and compare our data to previous studies.

Methods: This is a descriptive retrospective cohort study of pediatric patients with final genetically confirmed type I interferonopathies. Medical records were reviewed for demographic, family history, clinical and genetic data.

Results: Total of 17 patients (11 female) were included in the study. Eight patients (47%) presented within the first six months. Median age of disease onset was nine months (IQR: 3-36), and the median age of diagnosis was four years (IQR: 2-9). The rates of consanguinity and family history of affected members were high (88% and 47%, respectively). Whole exome sequencing was performed in 13 patients, two had a Leukoencephalopathy genetic panel and two target gene tests. six patients with Aicardi-Goutières syndrome (RNASEH2A, RNASEH2C, IFIH1), two patients with STING-associated vasculopathy with onset in infancy (TMEM173), 1 patient with chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (PSMB8), one patient with DNASE2. seven patients had rare interferonopathy conditions (3=ISG15, 2=ZNFX1, 1=SOCS1, 1=STAT1). Of 17 patients, 11 (64%) had novel genetic variants. The most frequent features were fever (76%), neurology (70%), mucocutaneous (59%), gastrointestinal (53%), and pulmonary (47%). Hypogammaglobinemia and recurrent infections were seen in (47%) and (23%) respectively. Thirteen patients (76%) had elevated inflammatory markers. More than half patients treated aggressively; corticosteroids (59%), Jak inhibitor (35%), IVIG (29%), and various immunosuppressive agents in (23%) patients. Most of the patients had partial response to treatment. The majority had features of disease damage: growth failure (70%) followed by developmental delay (159%) and zero death.

Conclusion: This Saudi monogenic interferonopathies cohort represents the largest single center study from the Arab population. Our findings support the previous reports; early-onset fever, neurology and respiratory features should raise the suspicion of interferonopathies. However, there is eminent evidence of novel phenotypic variability. Our data expands the spectrum of clinical finding in relation to novel genetic variants.

Disclosure: A. Alsaleem: None; **S. Al-Mayouf**: None; **S. Alansari**: None.

Abstract Number: 2045

Treatment Response in a Cohort of Pediatric Patients with Autosomal Dominant Neovascular Inflammatory Vitreoretinopathy (ADNIV)

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SESSION INFORMATION

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Background/Purpose: Pediatric uveitis often requires systemic immunomodulatory therapy (IMT) to prevent sight-threatening complications. Autosomal dominant neovascular inflammatory vitreoretinopathy (ADNIV) is a rare autoimmune condition caused by variants in CAPN5, diagnosed in adulthood, and characterized by intermediate uveitis, retinal degeneration and neovascularization. It is asymptomatic in early stages but inevitably leads to permanent blindness despite treatment. Proteomic studies report elevated IL6 and VEGF in the vitreous, suggesting a role for targeted therapy to alter disease trajectory. Our aim is to present the visual outcomes of a pediatric ADNIV cohort after systemic IMT.

Methods: Cohort study of patients ≤18 years old with a genetic diagnosis of ADNIV, (+) CAPN5 variants (p.Leu244Pro), ultra-widefield fluorescein angiography (UWFA) and optical coherence tomography (OCT) imaging, and a minimum follow-up of 6 months (m) of systemic IMT. Treatment response was defined as a decrease in 1) vitreous cells on clinical examination, 2) retinal vascular leakage on UWFA, and/or 3) macular edema on OCT.

Results: 8 children (16 eyes) met inclusion criteria (Table 1). Five were female, median age at diagnosis was 14 (range [R] 9-16) years and 4 were asymptomatic. Median follow-up was 18 m (R 6-20). On initial exam, visual acuity in the worse eye was 20/100 or better, 0 had anterior uveitis, while 7 patients had vitreous cells, 8 vascular leakage (UWFA), 2 neovascularization (UWFA), 3 macular oedema (OCT) and 1 cataract. Five patients were initially treated with oral (n=5) or local/injected corticosteroids (n=4), and anti-VEGF therapy (n=2). Due to persistent inflammation, systemic IMT was started in 7/8 patients

Table 1

Table 1. Characteristics of children with uveitis associated with Autosomal Dominant Neovascular Inflammatory Vitreoretinopathy (ADNIV) at diagnosis.

	n = 8 patients, 16 eyes n (%) unless otherwise stated
Caucasian	8 (100)
Hispanic or Latino	0 (0)
Female	5 (62.5)
Age at ADNIV diagnosis, years, median (range)	14 (9-16)
Duration of ADNIV, mos, median, (range)	18 (6-20)
Asymptomatic at diagnosis	3 (37.5)
Labs, in those who had them performed	
Earliest ESR, elevated n=8	0 (100)
Earliest Vitamin D, decreased, n = 7	3 (37.5)
ANA positive, n = 8	0
ACE positive, n = 6	0
Lysozyme positive, n = 3	0
Initial ocular examination and imaging per patient (P) and eyes (E)	
Bilateral ocular involvement	8 (100)
Visual acuity range, worse eye, median (range) in LogMar	0.1 (0-0.7)
Patients with impaired visual acuity	1 (12.5)
Anterior chamber cells present	0 (0)
Vitreous cells present	7 P (87.5), 13 E (81.2)
Macular edema on OCT	3 P (37.5), 6 E (37.5)
Retinal leakage on UWFA	8 P (100), 16 E (100)
Neovascularization on clinical exam/UWFA	2 P (25), 4 E (25)
Cataract	2 P (25), 4E (25)
Vitreous Hemorrhage	1 P (12.5), 1 E (6.2)

Abbreviations: ADNIV- Autosomal Dominant Neovascular Inflammatory Vitreoretinopathy; OCT- Optical coherence tomography; UWFA- Ultra-widefield angiography, E= eyes, P=patients, ESR: Erythro-sedimentation rate, CRP: C reactive protein, ANA: antinuclear antibody, ACE: angiotensin converting enzyme, mos: months

Table 2

Table 2: Local and systemic treatment administered to children with ADNIV	
Treatment administered	n (%) n = 7 patients
Patients on treatment	7
Anti-VEGF	2 (28.5)
Glucocorticoids	6 (85.7)
Oral	6 (85.7)
Injection	6 (85.7)
Time from ADNIV diagnosis to steroid, mos, median (IQR)	0 (0-0.9)
Intraocular Methotrexate injection	3 (42.8)
Methotrexate (25 mg/weekly SQ)	7 (100)
Time from ADNIV diagnosis to MTX, mos, median (R)	1.5 (0.5-2)
Duration on methotrexate, mos, median (range)	11 (6-14)
Infliximab/inflectra (10mg/kg/every 4 weeks IV)	7 (100)
Time from ADNIV diagnosis to start infliximab, mos, median (IQR)	3.1 (2.5-3.2)
Duration on infliximab/inflectra, mos, median (R)	7 (3.5-10)
Number of patients who responded to infliximab OR Patients who responded to infliximab, n (if you choose this second option make sure to update all meds rows)	0/7
Number of patients who stopped infliximab for inefficacy	7 (100)
Tocilizumab (10-12 mg/kg/every 2 weeks IV)	5 (71.4)
Time from ADNIV diagnosis to start tocilizumab, mos, median (R)	9 (8-12)
Duration on tocilizumab, mos, median (R)	8 (5-9)
Number of patients with ocular improvement on tocilizumab	0/5
Number of patients who stopped tocilizumab	2/5 (40)
Adalimumab (40 mg/every other weeks SQ)	1 (12.5)
Time from ADNIV diagnosis to start adalimumab, mos	13
Duration on adalimumab, mos	6
Number of patients who responded to adalimumab	0/1 (0)
Number of patients who stopped adalimumab for inefficacy	1 (12.5)
List of abbreviation: ADNIV- Autosomal Dominant Neovascular Inflammatory Vitreoretinopathy; VEGF- Vascular endothelial growth factor, E= eyes, P=patients, Anti-VEGF: anti Vascular endothelial growth factor, mos: months, MTX: methotrexate, IFX: infliximab, TCZ: tocilizumab, IQR interquartile range	

(Table 2). Methotrexate (MTX) (20 mg/weekly SQ) was the first treatment in 7 patients with the addition of infliximab (IFX) (10 mg/kg/dose every 4 weeks) after a median time from diagnosis of 3 m (R2.5-3.1) and continued for a median time of 7 m (R3.5-10). However, treatment was ineffective in all patients, and 5/7 switched to tocilizumab (TCZ) (10 mg/kg/every 2-3 weeks IV) after a median time from diagnosis of 9 m (R1-12) and 1/7 to adalimumab (ADA) (40 mg/every 2 weeks SQ) after 13 m from diagnosis. TCZ was continued for a median time of 8 m (5-9), but none of the patients showed an ocular

Table 3

Table 3: Ocular outcomes at diagnosis and at the last available follow-up after treatment by patient (P) and eyes (E)		
Ocular outcomes	**Onset, n (%)**	**Last Follow-up, n (%)**
Visual acuity worse eye, LogMar median (range)	0.1 (0-0.7)	0.2 (0.1-1.2)
N° of patients with VA >0.3	1 (12.5)	3 (37.5)
AC cells present	0 (0)	0 (0)
Vitreous cells present	7 P (87.5) 13 E (81.2)	5 P (62.5) 10E (62.5)
Macular edema on OCT	3 P (37.5) 6E (37.5)	1P (12.5) 1 E (6.2)
Retinal leakage on UWFA	8 P (100) 16E (100)	8 P (100) 16 E (100)
Neovascularization on clinical exam/UWFA	2 P (25) 4 E (25)	2 P (25) 4 E (25)
History of Vitreous Hemorrhage	1P (12.5) 1 E (6.2)	2 P (25) 3 E (18.7)
Cataract	2 P (25) 4E (25)	5P (62.5) 9 E (56.2)
Ocular Hypertension (>21 mmHg)	0	4 P (50) 7 E (43.7)
Retinal pigmentation changes	3 P (37.5) 5 (31.2)	3 P (37.5) 5 (31.2)
Abbreviations: ADNIV- Autosomal Dominant Neovascular Inflammatory Vitreoretinopathy; OCT- Optical coherence tomography; UWFA- Ultra-widefield angiography; VEGF- Vascular endothelial growth factor, E= eyes, P=patients, VA visual acuity		

response. Only 1/5 was able to increase the interval of administration of intraocular corticosteroids. Four/five patients discontinued TCZ for inefficacy. The single patient discontinued ADA due to inefficacy. Outcomes at the last available follow-up are reported in Table 3. Of 6 patients, 2 switched to tofacitinib and 5 received steroid implants.

Conclusion: We report the visual outcomes of the largest series of children with ADNIV treated with systemic IMT. Early testing for CAPN5 gene in at risk children, and regular screening for uveitis and vasculitis will lead to prompt intervention. MTX, IFX and TCZ were ineffective. However, we observed that TCZ was able to decrease the need of intraocular corticosteroids in one patient. Further studies are needed to determine optimal treatment in terms of molecules chosen but also of route of administration in these children.

Disclosure: I. Maccora: None; **A. Sood**: Alimera Sciences, 2, Carl Zeiss Meditec, Inc., 2, EyePoint Pharmaceuticals, 2; **G. Schulert**: IpiNovyx, 5, SOBI, 2; **A. Duell**: None; **P. Land**: None; **C. Sapp**: None; **J. Huggins**: None; **T. Nguyen**: None; **M. Quilan-Waters**: None; **S. Sharma**: AbbVie/Abbott, 2, Alimera, 2, Allergan, 2, Apellis, 2, Bausch and Lomb, 2, Clearside, 2, Eyepoint, 2, Genentech, 2, 5, Gilead, 5, Regeneron, 2, RegenxBio, 2, Roche, 2, 5; **S. Srivastava**: AbbVie/Abbott, 2, Allergan, 5, Bausch and Lomb, 2, Eyepoint, 2, 5, Eyevensys, 2, 5, Novartis, 2, Regeneron, 2, 5, Santen, 5, Zeiss, 2; **S. Angeles-Han**: None.

Abstract Number: 2046

Implementation of an Automated Transition Readiness Assessment in a Pediatric Rheumatology Clinic

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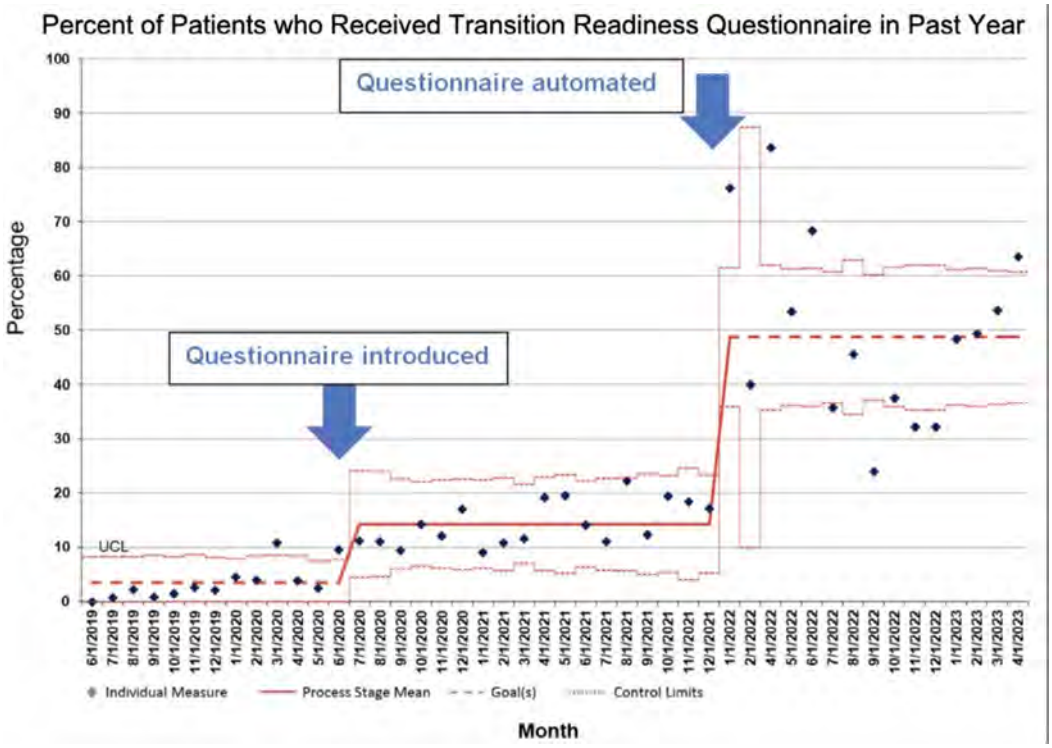
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Pediatric Rheumatology – Clinical Poster III: Potpourri
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Many pediatric patients are inadequately prepared for the transition from pediatric to adult subspecialty healthcare, and patients who fail to transition successfully are more vulnerable to poor health outcomes.Frequently, pediatric rheumatology clinics do not provide formal training or resources to develop skills related to this transition. Interventions to improve the transition process include implementing a transition policy andperiodically assessing patient and parent or caregiver readiness to transition.

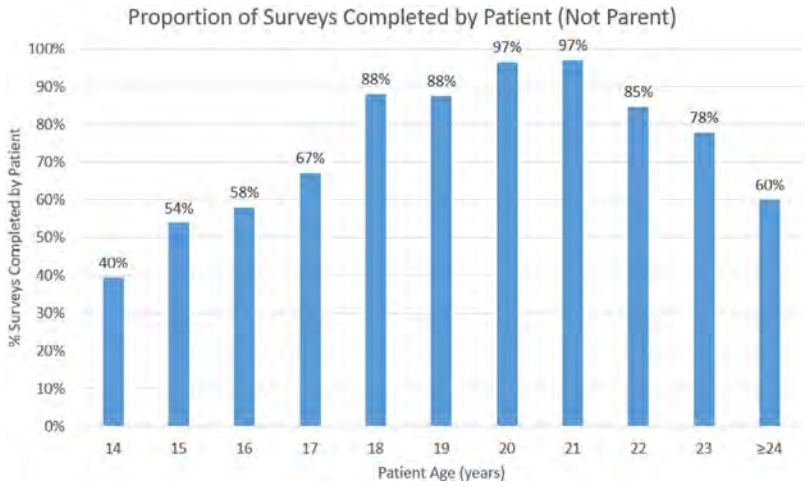
Methods: A multidisciplinary transition team formed to improve processes related to transition to adult care by using quality improvement (QI) methodology. Beginning in July 2020, a modified Transition Readiness Assessment Questionnaire (TRAQ) was delivered through the electronic health record (EHR) for patients aged ≥ 14 years with ≥2 visits in the prior 3 years. Beginning in December 2021, questionnaires were automatically assigned annually during routine care. Questionnaires asked about patients' interest in and perceived readiness for moving to an adult rheumatology setting by age 21, as well as need for education on skills required to navigate the medical system and advocate for one's own needs. Questionnaires could be completed by either the patient or a parent or caregiver. Data was extracted via EHR reporting tools. QI methodology and descriptive statistics were used.



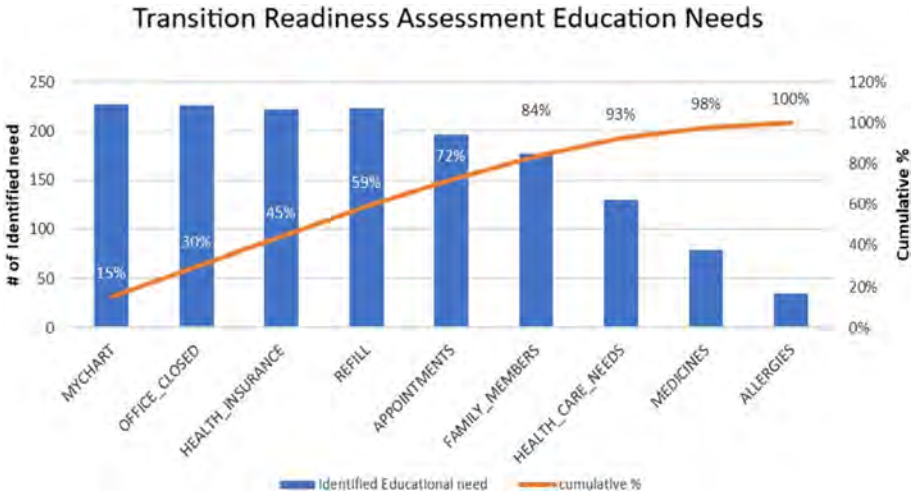
Integrating automated questionnaires within the EHR significantly increased the proportion of patients aged ≥ 14 years who received a questionnaire (p<0.001)

Results: Integrating automated questionnaires within the EHR significantly increased the proportion of patients aged ≥ 14 years who received a questionnaire from less than 20% to nearly 50% of patients (p< 0.001). This increase was sustained over the 16 months following the introduction of automated questionnaires (Figure 1).

From January 2022 to April 2023, 1091 questionnaires were administered. Of these, 862 (79%) were fully completed and 918 (84%) had at least one question answered by 868 unique patients. The median age was 16 years [interquartile range 15, 18]. Fewer than half of 14-year-old patients completed the questionnaire themselves; the patient completion rate increased up to age 20-21, then decreased (Figure 2).



The patient completion rate increased up to age 20-21, then decreased.



The most frequently identified educational needs related to EHR messaging, obtaining care if the office is closed, health insurance, refilling medications, making appointments, and awareness of family history.

The most frequently identified educational needs related to EHR messaging, obtaining care if the office is closed, health insurance, refilling medications, making appointments, and awareness of family history. Together, these six factors accounted for over 80% of the identified needs (Figure 3).

Unsurprisingly, older patients reported less need for education on each skill assessed. Patients aged 14-17 were about twice as likely to report they could not complete each skill independently.

Conclusion: Integrating a transition readiness assessment in the EHR is feasible and can identify population-wide knowledge gaps as well as facilitate targeted individual education. In our population, the most perceived educational needs include EHR messaging, emergency care, health insurance, and refilling medications. Older patients are generally more likely to report competence at each skill assessed. This process can be implemented at other sites to help streamline transition readiness assessment and increase response rates.

Disclosure: E. Murray: None; **M. Argraves**: Lupus Foundation of America, 6; **A. Taxter**: None; **K. Wise**: Amgen, 3, Novartis, 2; **P. Jensen**: None; **A. Goldstein-Leever**: None; **B. Thomas**: None; **A. Scott**: None; **J. Hughes**: None; **J. Gallup**: None; **D. Sumano Vicente**: None; **S. Ardoin**: None; **V. Sivaraman**: Merck/MSD, 11.

Abstract Number: 2047

Safety of Baricitinib for COVID-19 Related Hyperinflammation in Pediatric Patients: A Large Tertiary Care Center Experience

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Pediatric Rheumatology – Clinical Poster III: Potpourri
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: A small proportion of children with acute COVID-19 experienced life-threatening hyperinflammation. It has been proposed that an innate immune recognition of viral RNA triggers excessive cytokine and interferon production. Adult studies have shown baricitinib usage (as part of an emergency use authorization) to be associated with stabilization of severe disease and reduced mortality. There is a paucity of pediatric data regarding COVID-19-associated JAK inhibition. We collected data on inflammation, disease progression, and safety of baricitinib in children hospitalized with COVID-19.

Methods: Retrospective medical record review was conducted of children admitted with COVID-19. Demographics, laboratory, and clinical features were collected from all children treated with baritcitinib for COVID-19 pneumonia and secondary hyperinflammation throughout all major surges of the pandemic under the auspices of an IRB approval.

Results: The demographics and clinical features of 10 patients treated with a JAK inhibitor are shown in Table 1. Nine (90%) were Hispanic, and 7 (70%) were male. All patients were obese (BMI >95th percentile) but were otherwise healthy. All children treated with baricitinib were infected during Delta strain predominance. All had fever and respiratory distress as presenting symptoms, and 60% had GI symptoms. Median onset of symptoms was 7 days prior to admission (IQR 7-11 d). No patients met criteria for MIS-C. Baricitnib was initiated on median hospital day 2 (IQR 1.5-2 d) and administered for a median of 10 days (IQR 6-14 d). All patients were on dexamethasone and remdesivir and had improvements in their inflammatory markers during their course. Two children required escalation to ECMO after initiation of baricitinib. One of these

Table 1. Patient characteristics, N=10

Median age (years)	15.5 (IQR 14-19)
Sex	
Male	70%
Female	30%
Race/ethnicity	
Hispanic	90%
White	10%
Median BMI (kg/m^2)	37.7 (IQR 30.2-46.5)
Comorbid conditions	
Obesity	100%
Autism Spectrum Disorder	10%
Asthma	10%
Obstructive sleep apnea	10%
History of seizures	10%

children passed away. Of the surviving patients, median time to clinical recovery, assessed by a score of 1 on NIAID-OS, was 10 days (IQR 8-16 d). Median ICU stay was 9.5 days (IQR 5.8-18.5 d), and length of hospital stay was 11 days (IQR 11-23.5 d). Baricitinib was stopped in only one patient due to clinical concern of pulmonary embolism (unable to be imaged). Three patients developed secondary infections followingbaricitinib initiation (MSSA and culture-negative pneumonia in two). One critically ill patient developed numerous infections during the hospital stay (UTIs [*E.coli* and *Klebsiella*], MSSA pneumonia/ bacteremia, *Proteus mirabilis* and *E. faecalis* wound infections). Baricitinib was safely continued with mild-moderate increased transaminases in 7 patients (Table 3). One patient developed neutropenia, and two lymphopenia. Hematologic events were transient and did not require cessation of baricitinib.

Conclusion: Children with Delta-variant associated hyperinflammation tolerated adjunctive treatment with baricitinib with a lower-than-expected adverse event and cessation rate. Additional data from other centers may be necessary to understand the role of JAK inhibition in enhancing the survival of children with severe COVID pneumonias and inflammation.

Table 2. Clinical course, N=10

Presenting symptoms on admission	
Fever	100%
Respiratory symptoms	100%
GI symptoms	60%
Rash	10%
Median symptom onset prior to admission (days)	7 (IQR 7-11)
Initial respiratory support on admission	
HFNC	40%
BiPAP	20%
Mechanical Ventilation	20%
ECMO	0%
% requiring respiratory support throughout course:	100%
HFNC	100%
BiPAP	80%
Mechanical ventilation	40%
ECMO	20%
% requiring escalation of support after initiation of baricitinib	20%
Median time to clinical recovery (days) (assessed by score of 1 on NIAID-OS)	10 (IQR 8-16 days)
Median PICU length of stay	9.5 (IQR 5.8-18.5 days)
Median hospital length of stay	11 (IQR 11-23.5 days)
Death	10%

Table 3. Laboratory values

Inflammatory markers	*Median value (IQR)*	*Safety data*	*Median value (IQR)*
Initial CRP (mg/dL)	16.4 (8.4-24.0)	AST at admission (IU/L)	82.5 (75.8-138.8)
Time for CRP to reach half of its max (days)	2.5 (1.0-3.3)	Peak AST level (IU/L)	89.5 (82.3-150)
Hospital day CRP normalized	9.5 (7.8-14.3) *(n/a in 40%)*	ALT at admission (IU/L)	56.0 (46.3-76.0)
CRP at discharge (mg/dL)	1.2 (0.7-2.6)	Peak ALT level (IU/L)	105.5 (60.5-224)
D-dimer at admission (µg/mL)	1.8 (0.8-2.8)	Initial ANC (IU/L)	6.36 (4.21-9.88)
Time for d-dimer to reach half of its max (days)	5.0 (2.0-9.0)	ANC nadir (cells/µL)	2.71 (1.99-4.59)
D-dimer at discharge (µg/mL)	1.8 (0.4-2.3)	Initial ALC (IU/L)	0.81 (0.60-0.93)
Ferritin at admission (ng/mL)	816 (681-941)	ALC nadir (cells/µL)	0.71 (0.60-0.83)
Time for ferritin to reach half of its max (days)	5.0 (3.0-7.0)	Initial Cr (mg/dL)	0.70 (0.58-0.73)
Ferritin at discharge (ng/mL)	252 (163-345)	Cr peak (mg/dL)	0.70 (0.61-0.75)

Disclosure: M. Rae: None; **J. Nguyen**: None; **M. DeGuzman**: None; **C. Foster**: None; **F. Munoz**: Gilead, 5, Pfizer, 5, 12, DSMB; **E. Muscal**: Sobi, 1, 11.

Abstract Number: 2048

Development and Usability Testing of Web-based Standardized Scoring Tool for Magnetic Resonance Images from Children with Chronic Nonbacterial Osteomyelitis (CNO)

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Pediatric Rheumatology – Clinical Poster III: Potpourri

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The ChRonic nonbacterial Osteomyelitis Magnetic Resonance Imaging Scoring (CROMRIS) tool was developed but it was not digitized yet. Our objectives are: 1) to adapt the CROMRIS tool to a web-based platform and 2) assess the usability of this system among radiologists.

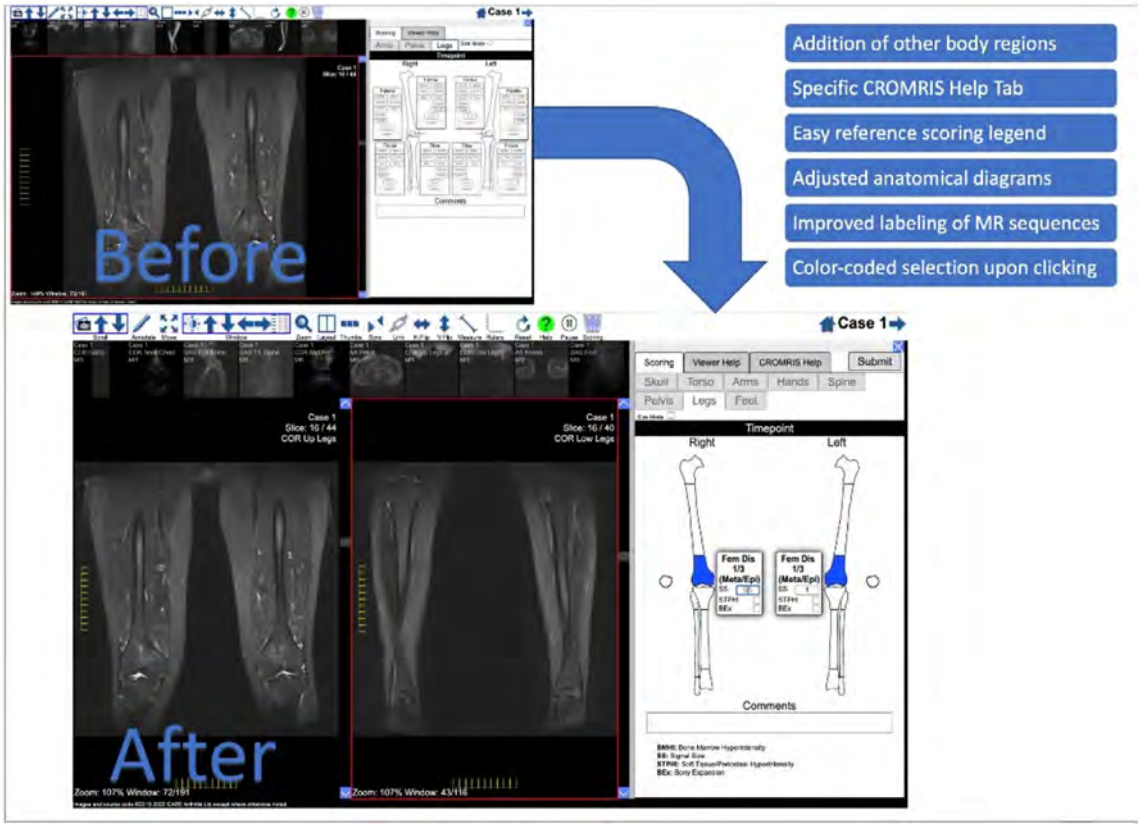

Figure 1. Screenshot of Web-based CROMRIS Portal on Tab for Long Bones of Lower Extremity Before and After Feedback Sessions/Usability Testing

Methods: A prototype web-based CROMRIS tool was developed by CARRA's CNO Workgroup and CARE-Arthritis in 2019. Since then, monthly meetings between software developers, rheumatologists, radiologists and an illustrator led to a beta version that included the whole skeleton. A group of radiologists (n=7) provided feedback on the beta version in a demo

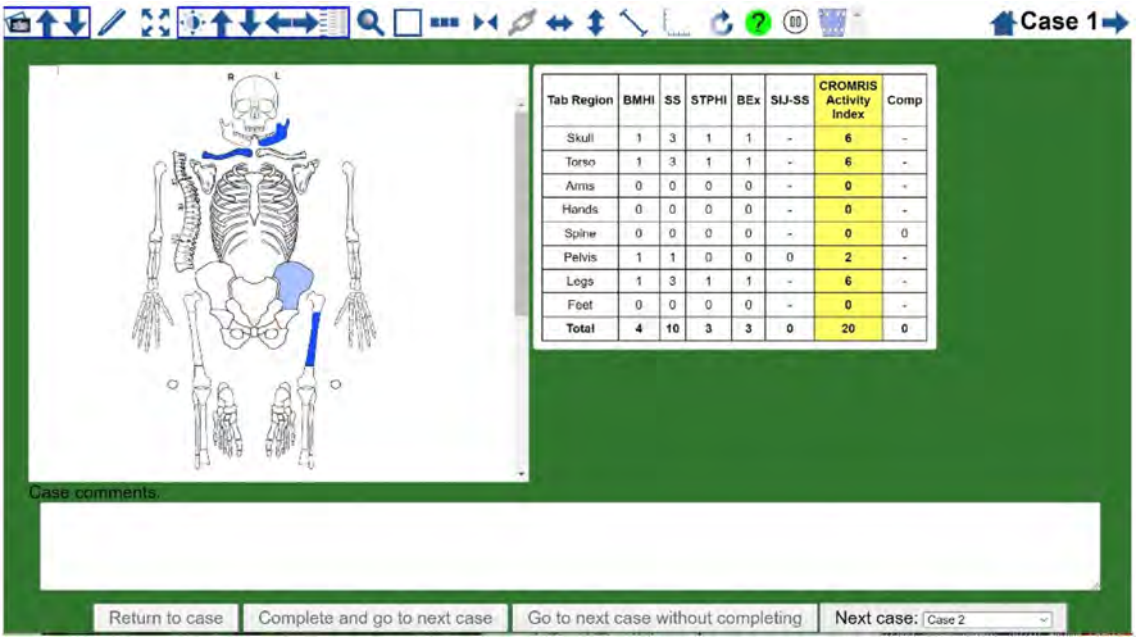

Figure 2. Screenshot of Summary Page for Final Web-based CROMRIS Portal

Table 1. Scoring of Active CNO Lesions in General Bone Units in the Web-Based CROMRIS

CNO Lesion Characteristic		SCORE
Bone marrow hyperintensity (BMHI)	Absent	0
	Present	1
Signal Size (SS)	< 25%	1
	25–50%	2
	> 50%	3
Soft tissue hyperintensity/periosteal reaction (ST/PHI)	Absent	0
	Present	1
Bony expansion (BEx)	Absent	0
	Present	1

1.The characteristics included and score assigned to each variable for active CNO lesions within bone units as described in the Atlas for the web-based CROMRIS portal in general. Adding up all parameters for a maximum score of six for each bone unit, except sacroiliac joints, which is scored separately. Bone units are defined in the Atlas.
2.The sum of individual bone unit scores is the CROMRIS Activity Index.

session on 4/11/22 via semi-structured surveys (#IRB2021-00033). Usability was assessed by surveys using the System Usability Scale (SUS), a Likert scale in which respondents indicate their level of agreement or disagreement on a scale of 1 to 5 for 10 statements on ease of use, effectiveness, and satisfaction in content of use. Feedback was reported with descriptive content analysis, continuous variables as means and categorical variables as percentages.

Results: A clickable-schematic-based CROMRIS was developed to include all body regions [Figure 1]. Notable features are the ability to immediately highlight a schematic region upon selection to directly input scores. Suggested changes included labeling of individual spine and rib segments, insertion of scoring legend on each tab for reference and creation of a summary page with a composite diagram where one can visualize the location and size of lesions by color as well as a numerical CROMRIS activity index [Figure 2]. The general scoring on the portal is indicated by clicking on a bone unit to indicate the presence of bone marrow hyperintensity consistent with an active CNO lesion, which is qualified by other lesion parameters [Table 1]. A video tutorial and MRI Atlas is on the platform for training (https://www.carearthritis.com/mriportal/crmo/index/). Visual factors and anatomical diagrams were among the features "liked best" by the survey respondents. Mean SUS scores increased from 64.5 (below average) to 75 (above average). All respondents agreed that the final version of the web-based CROMRIS was "easy to learn" and found that the "various functions of the web-based CROMRIS were well integrated, and "would like to use the web-based CROMRIS in future clinical trials."

Conclusion: The web-based CROMRIS portal shows good usability amongst radiologists. Studies of interrater reliability among experienced pediatric radiologists are underway. Once validated, this tool can be used as a semi-quantitative MRI scoring tool to allow for standardization of reporting output of radiological interpretations of MRI in CNO. The authors wish to acknowledge CARRA and the ongoing Arthritis Foundation financial support of CARRA.

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Abstract Number: 2049

Vaccination Coverage and Caregiver Perspectives for Children with Rheumatic Diseases Compared to Healthy Controls

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Pediatric Rheumatology – Clinical Poster III: Potpourri
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Background/Purpose: Children with rheumatic diseases (RD) have an increased incidence of infections and their complications, both from underlying disease activity and immunosuppressive treatments. Vaccines have been well-established as effective intervention in combating these. Studies assessing vaccination barriers remain limited.

To assess the vaccination status of children with RD and identify immunization facilitators and barriers of families compared to healthy controls (HC)

Methods: A cross-sectional study of children with RD and HC (fracture clinic) at a single tertiary care center was performed. Demographics, diagnosis, and current treatments were obtained from health records. Children with RD were considered immunosuppressed, if they were currently received corticosteroids, nonbiologic or biologic disease-modifying agent. A unique provincial electronic database that records accurate vaccine history was used to obtain actual patient vaccination history. Perceived immunization barriers, concerns, factors promoting vaccination, and satisfaction with information received were captured from a caregiver questionnaire. Descriptive statistical methods were used to analyze the data.

Results: A total of 144 children with RD (76% considered immunosuppressed) and 111 HC were recruited into the study. Vaccination database: Both, children with RD and HC received most of the provincial recommended vaccines at rates of 85% or above, except for Influenza. Influenza vaccine had the lowest adherence rate at 34% RD vs 21% HC: 25% vs 43% in the 1 – 4 years old group, 32% vs 24% in the 5 – 11 years old group, and 38% vs 10% in the 12+ years old group. Caregiver questionnaire: In 31% of children with RD at least one vaccination was withheld, most commonly for active disease (27%), recommendation against receiving vaccinations by health care provider (25%), concerns about side effects post vaccination (18%) and/or disease flare (14%). In 27% of HC at least one vaccination was withheld, most commonly for concerns about side effects post vaccination (13%). Several sources of information were utilized. Both groups listed the primary vaccination information source as the family doctor (66% in RD vs 69% in HC). At least 85% of survey respondents in each group felt satisfied by the amount of information received. The following information gaps were identified: 1) risks and contraindications of vaccinations in general and in children with rheumatic diseases, 2) age-appropriate vaccination schedules and modalities, 3) best practice of vaccination documentation. Vaccination reminders were identified as useful, with several comments indicating that e-mail alerts, reminders, and a method to track this information would be useful.

Conclusion: Most children with RD and HC equally received the recommended vaccines. Immunization gaps were identified for Influenza in both groups and presents an area of improvement. Knowledge regarding contraindications to vaccination is well understood. Concerns about perceived safety limit vaccination completeness in both groups.

Disclosure: S. Vazhappilly: None; **R. Githumbi**: None; **N. Johnson**: None; **O. Vanderkooi**: None; **H. Schmeling**: Bristol-Myers Squibb(BMS), 5, Janssen, 5, Pfizer, 5, Sanofi, 5, 12, Sanofi provided Hep A vaccine supplies for a Hep A vaccine study, UCB, 5.

Abstract Number: 2050

Variability in Vaccination Practices in Children with Rheumatic Diseases: Results of a Rheumatology Provider Childhood Arthritis and Rheumatology Research Alliance (CARRA)-wide Survey

Randal De Souza[1], Merav Heshin Bekenstein[2], Beth Rutstein[3], Maria Schletzbaum[4], Nora Singer[5], Melanie Kohlheim[6], vincent del gaizo[7], Kelly Wise[8], Melica Nikahd[9], Guy Brock[10], Rebecca Sadun[11], Monica Ardura[1], Vidya Sivaraman[1] and For The CARRA Registry Investgators[7], [1]Nationwide Children's Hospital, Columbus, OH, [2]Dana Children's Hospital of Tel Aviv Medical Center, Tel Aviv, Israel, [3]Division of Rheumatology at Children's Hospital of Philadelphia, Philadelphia, PA, [4]St. Louis Children's Hospital / Washington University in St. Louis, Middleton, WI, [5]The MetroHealth System at Case Western Reserve University School of Medicine, Cleveland, OH, [6]Self, Granville, OH, [7]CARRA, Inc, Washington, DC, [8]Nationwide Children's Hospital, Hilliard, OH, [9]Ohio State University, Columbus, OH, [10]Dept. of Biomedical Informatics, Columbus, OH, [11]Duke University, Durham, NC

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Pediatric Rheumatology – Clinical Poster III: Potpourri

Session Type: Poster Session C

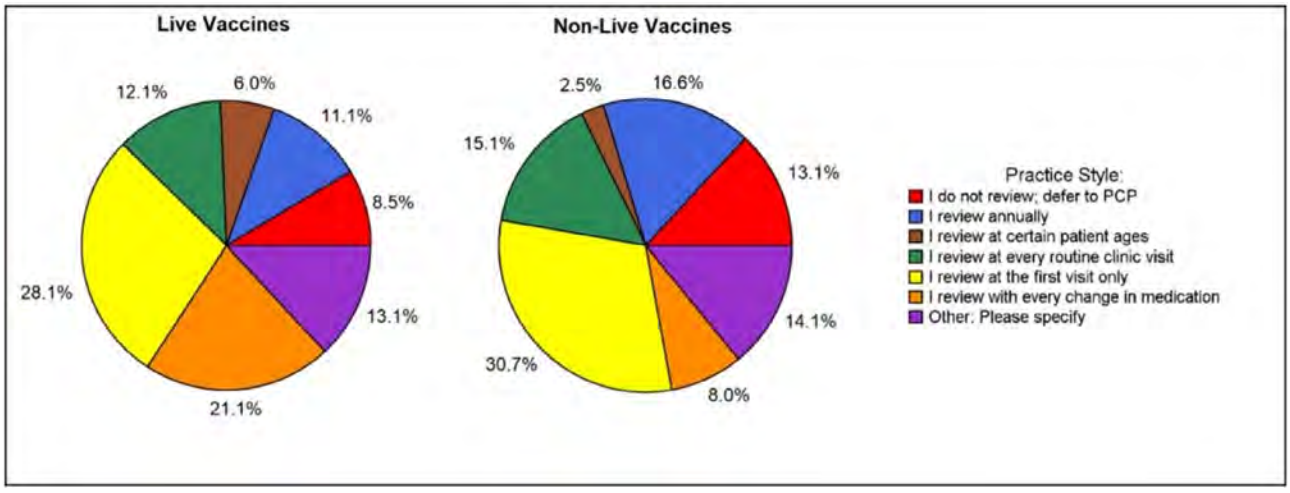
Session Time: 9:00AM–11:00AM

Background/Purpose: Immunocompromised children (ICC), including children with rheumatic diseases receiving immunosuppressive therapies (IST) are at increased risk of morbidity from vaccine-preventable infections. The 2022 American College of Rheumatology (ACR) Vaccination Guidelines emphasize the need to vaccinate ICC and minimize missed opportunities for immunizations. Children with rheumatic diseases receiving IST are eligible to receive inactivated vaccines, however vaccination rates remain unacceptably low in these children. The CARRA Vaccination Workgroup (WG) surveyed North American pediatric rheumatologists about their vaccination practices when caring for children receiving IST.

Methods: The CARRA Vaccination WG developed and electronically distributed a REDCap survey to CARRA member healthcare professionals from March-May 2022.

Results: The survey was completed by 219 pediatric rheumatology providers with a response rate of 60% (74% attendings, 21% fellows). More than 90% of rheumatology providers reviewed their patients' vaccinations, with most reviewing live (28%) and non-live vaccines (31%) at the first visit only (Figure 1). Several providers used comments to clarify their vaccine review practices, most commonly reporting reviewing influenza and COVID vaccines alone, or in combination with other vaccines. Thirty-nine percent of providers reviewed conjugate (PCV-13) and polysaccharide (PPSV 23) pneumococcal vaccine status, especially in patients with childhood-onset SLE (c-SLE). Twenty-six percent reviewed vaccination status based on initiation or type of IST, and age, whereas half of respondents reported used a disease-specific review approach, focused primarily on c-SLE (89%), followed by systemic vasculitis (42%), juvenile dermatomyositis (39%) and juvenile idiopathic arthritis (28%). Forty-two percent of providers reported medication-specific review, including prior to Rituximab initiation (57%), initiation of any IST (20%), IVIG (10%), or cyclophosphamide (7%). There was also variability in communication about vaccines between rheumatology provider and primary care pediatricians (PCPs), with 41% of rheumatologists indicating they did not contact the PCP, 22% contacting the PCP regarding live vaccines only, 30% for live and non-live vaccines, 19% for pneumococcal vaccines, and 18% for 'Other', of which more than half of those who wrote narrative comments stated vaccine recommendations were included in the clinic note to the PCP.

Conclusion: This survey demonstrated significant variability in rheumatology provider approaches to vaccinations in ICC. While 90% of rheumatology providers reviewed vaccinations, less than half reviewed seasonal vaccines or pneumococcal vaccines, and those who did, mainly reviewed vaccinations in the setting of specific diseases, specific medications, or



Provider Practices for Review of Patient Vaccinations

new patient visits. Our results highlight opportunities for improvement in the care of ICC by increasing awareness of the need for vaccination against vaccine-preventable infections. This study underscores the need for standardized vaccination practices in ICC and improved communication between providers to maximize immunization opportunities for ICC.

Disclosure: R. De Souza: None; **M. Heshin Bekenstein**: None; **B. Rutstein**: None; **M. Schletzbaum**: None; **N. Singer**: Merck, 5, 12, Travel grant; **M. Kohlheim**: None; **v. del gaizo**: None; **K. Wise**: Amgen, 3, Novartis, 2; **M. Nikahd**: None; **G. Brock**: None; **R. Sadun**: None; **M. Ardura**: Karius, 2, Merck, 5, Miravista, 5; **V. Sivaraman**: Merck/MSD, 11; **F. The CARRA Registry Investgators**: None.

Abstract Number: 2051

Screening Multisystem Inflammatory Syndrome in Children: Accuracy of SickKids Screening Pathway Compared to ACR Algorithm

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
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Session Time: 9:00AM–11:00AM

Background/Purpose: Multisystem Inflammatory Syndrome in Children (MIS-C), also known as Pediatric Inflammatory Multisystem Syndrome temporally associated with COVID-19 (PIMS), is one of the most serious complications associated with COVID-19.The clinical features of MIS-C are not unique and are commonly seen in childhood febrile conditions. Thus, there is a need to identify those febrile children with MIS-C to enable early diagnosis and treatment. In response to the health care emergency, a multidisciplinary team from The Hospital for Sick Children (SickKids) of Toronto developed a preliminary screening pathway for the evaluation of possible MIS-C. The primary objective is to determine if the SickKids screening

pathway is sensitive and specific to identify patients with MIS-C from other febrile children with suspected but not confirmed diagnosis of MIS-C. The secondary objective of this study is to determine how the ACR MIS-C algorithm performs compared to the SickKids screening pathway in differentiating children with MIS-C from the febrile controls.

Methods: Retrospective case-controlled, cross-sectional study including children who have been assessed at SickKids with suspected or confirmed MIS-C from March 2020 to March 2022. The MIS-C group included all children meeting the most permissive case definition as per international MIS-C and PIMS definitionsand adjudicated by our multi-disciplinary MIS-C working group; the febrile control group consisted of all patients with a history of three or more days of fever who were suspected of MIS-C and qualified for the SickKids MIS-C screening pathway, but did not fulfill criteria for MIS-C after adjudication by our multi-disciplinary group. SickKids and ACR pathways were retrospectively applied to both groups.The diagnosis result obtained using the pathways was compared with the final clinical diagnosis made using the WHO definition criteria, used as the gold standard. From the contingency table, sensitivity and specificity have been calculated along with a 95% confidence interval.

Results: 402 children (241 with MIS-C and 161 febrile controls) were included in the study. The median age was 4.18 years (IQR: 1.9 to 9.0) and 237 (60%) were male. For the SickKids screening pathway, the sensitivity was 62% (95%CI, 54.2% to 70.4%), and specificity was 91% (95%CI, 86.9% to 94.2%). The positive predictive value (PPV) was 79% and the negative predictive value (NPV) was 81%. Overall, the balanced accuracy was equal to 76%. The ACR screening pathway had 74% sensitivity (95%CI, 67.3% to 81.4%), and 99% specificity (95%CI, 98.1% to 100%), with PPV of 98% and NPV of 87%. The balanced accuracy was 87%.

Conclusion: The SickKids MIS-C screening pathway has a high specificity, but a low sensitivity and accuracy in capturing children with MIS-C at the onset of the disease. Overall, the ACR algorithm performs better at differentiating children with MIS-C from febrile controls.

Disclosure: G. Mastrangelo: None; **P. Tsoukas**: None; **T. Mizzi**: None; **B. Gamulka**: None; **A. Xu**: None; **A. Cheng**: None; **R. Yeung**: Pfizer, 6.

Abstract Number: 2052

Risk Factors for Hospitalization for SARS-CoV-2 in Pediatric Patients with Rheumatic Diseases: A Systematic Review and Meta-analysis

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SESSION INFORMATION
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Background/Purpose: Among adults who develop SARS-CoV-2 infection, those with rheumatic diseases (RDs) have similar hospitalization rates compared to those without RDs. Similar comparisons are lacking in children, due to the overall rarity of hospitalization due to SARS-CoV-2 in this population. We aimed to examine hospitalization risk for SARS-CoV-2 in pediatric patients with rheumatic diseases and its associated risk factors.

Author	Year	Country	Type	Study design	Calendar period	Total number	Rheumatic diseases included	Newcastle-Ottawa scale
Kearsley-Fleet	2022	25 countries EULAR, CARRA	Article	Cohort	Mar 2020- Jul 2021	607 RD	JIA, SLE/CTD, vasculitis, AID	8
Haslak	2022	Turkey	Article	Cohort	Mar 11 2020-Dec 11 2021	152 RD, 506 healthy	JIA, SLE/CTD, vasculitis, AID	8
Sozeri	2022	Turkey	Article	Cohort	Apr 2020-2021	113 RD	JIA, SLE/CTD, AID, vasculitis	8
Villacis-Nunez	2021	USA	Article	Cohort	May 2020-Jan 2021	55 RD	JIA, SLE/CTD, idiopathic uveitis, sarcoidosis, RA, vasculitis	8
Clemente	2021	Spain	Article	Cohort	Mar 2020-Mar 2021	77 RD	JIA, SLE/CTD vasculitis, AID	7
Garazzino	2021	Italy	Article	Cohort	Mar- Sep 2020	8 RD, 751 no RD	Unknown	8
Uka	2022	Switzerland	Article	Cohort	Mar- Oct 2020	7 RD, 671 no RD	JIA, vasculitis, AID	8

AID, autoinflammatory disease; CARRA, Childhood Arthritis and Rheumatology Research Alliance; CTD, connective tissue disease; EULAR, European Alliance of Associations for Rheumatology; JIA, juvenile idiopathic arthritis; RA, rheumatoid arthritis; RD, rheumatic disease; SLE, systemic lupus erythematosus.

Methods: We conducted a systemic literature search in MEDLINE, EMBASE, Web of Science, and China National Knowledge Infrastructure from December 1, 2019 through April 20, 2023. We included observational studies of pediatric rheumatic disease populations with sufficient data to calculate at least one odds ratio (ORs) for the primary outcome of COVID-19-related hospitalization(Fig 1). We assessed risk of bias using the Newcastle-Ottawa Scale for cohort studies.

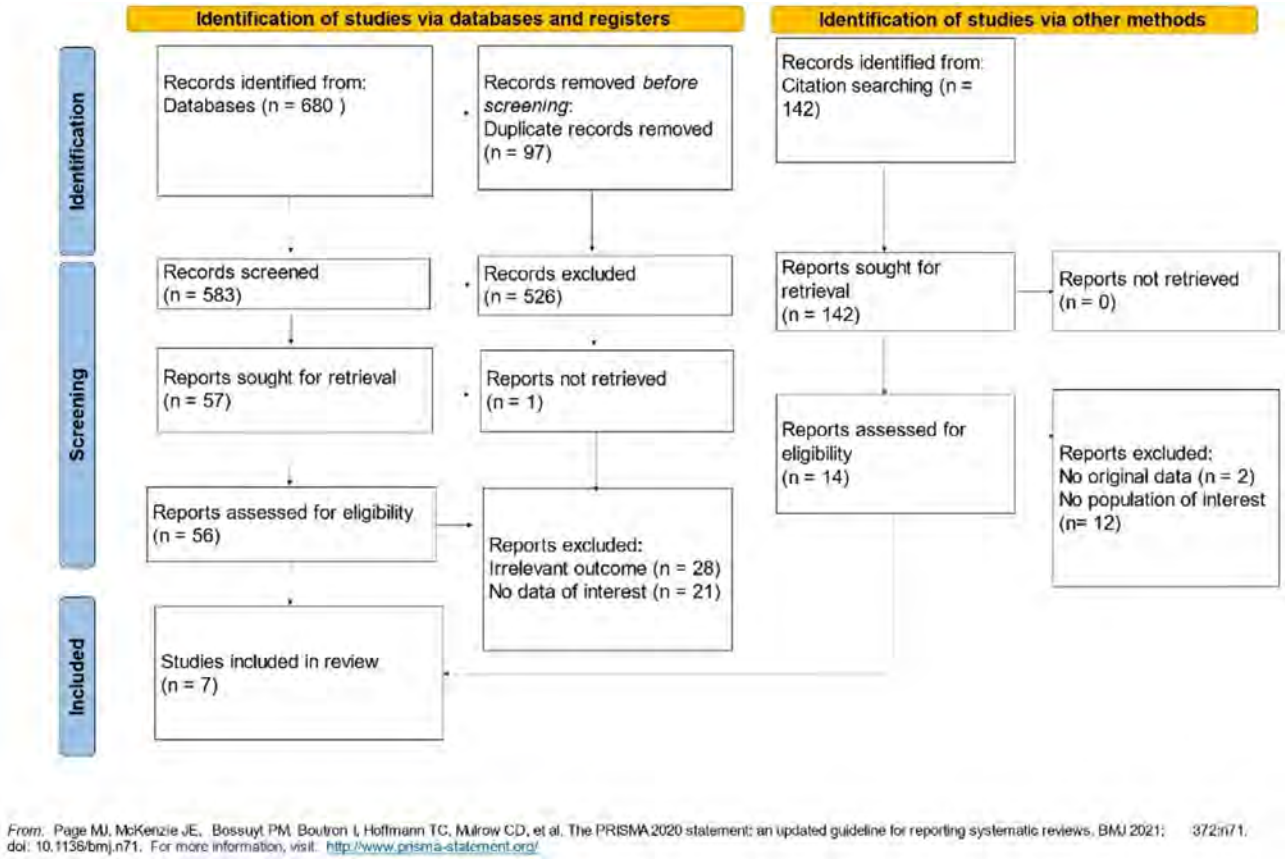

Figure 1. PRISMA Flow chart of the methods used for identification of studies.

Study heterogeneity was assessed by Q statistics and I^2 statistic. ORs with 95% confidence intervals (95% CIs) were calculated using fixed-effect models based on the Mantel-Haenszel method if $I^2 < 50\%$.

Results: Sevencohort studies capturing 1,019 pediatric RD patients with confirmed SARS-CoV-2 were included (Table 1, Fig 1). Odds of hospitalization was increased in children with RD compared to healthy children ((OR 2.31; [95% CI, 1.17-4.58]), Fig. 2A). The diagnoses of systemic lupus erythematosus/connective tissue disease (SLE/CTD) ((OR 2.83; [95% CI 1.25, 6.40), Fig. 2B) and systemic juvenile idiopathic arthritis (JIA) ((OR 2.54, [95% CI, 1.01-6.40]), Fig. 2D) were associated with increased odds of hospitalization, while total JIA was associated with reduced odds ((OR 0.42, [95% CI, 0.26-0.67]), Fig. 2C). Use of rituximab ((OR 4.62, [95% CI, 1.87-11.4], Fig. 2E)), glucocorticoids ((OR 3.75; 95% CI [2.17-6.48]), Fig. 2F) or IL-1 inhibitors ((OR 2.28, [95% CI, 1.09-4.78], Fig. 2G) was associated with increased odds of hospitalization; use of TNF inhibitors was associated with reduced odds ((OR 0.35, [95% CI, 0.19-0.65], Fig. 2H). Use of tocilizumab (OR 0.99, [95% CI, 0.34-2.87]), tofacitinib (OR 3.01, [95% CI, 0.69-13.12]) and traditional DMARDs (OR 0.71, [95% CI, 0.43-1.17] were not associated with a change in odds of hospitalization. A limitation of the study was the predominantly Caucasian population, with no data for patients from China, India, Korea or Japan.

Conclusion: Pediatric patients with RDs have higher oddsof SARS-CoV-2 related hospitalization than healthy children, especially those with SLE/CTD and those using Rituximab, glucocorticoids and IL-1 inhibitor.In contrast, JIA and anti-TNF inhibitor use was associated with a reduced odds of hospitalization.

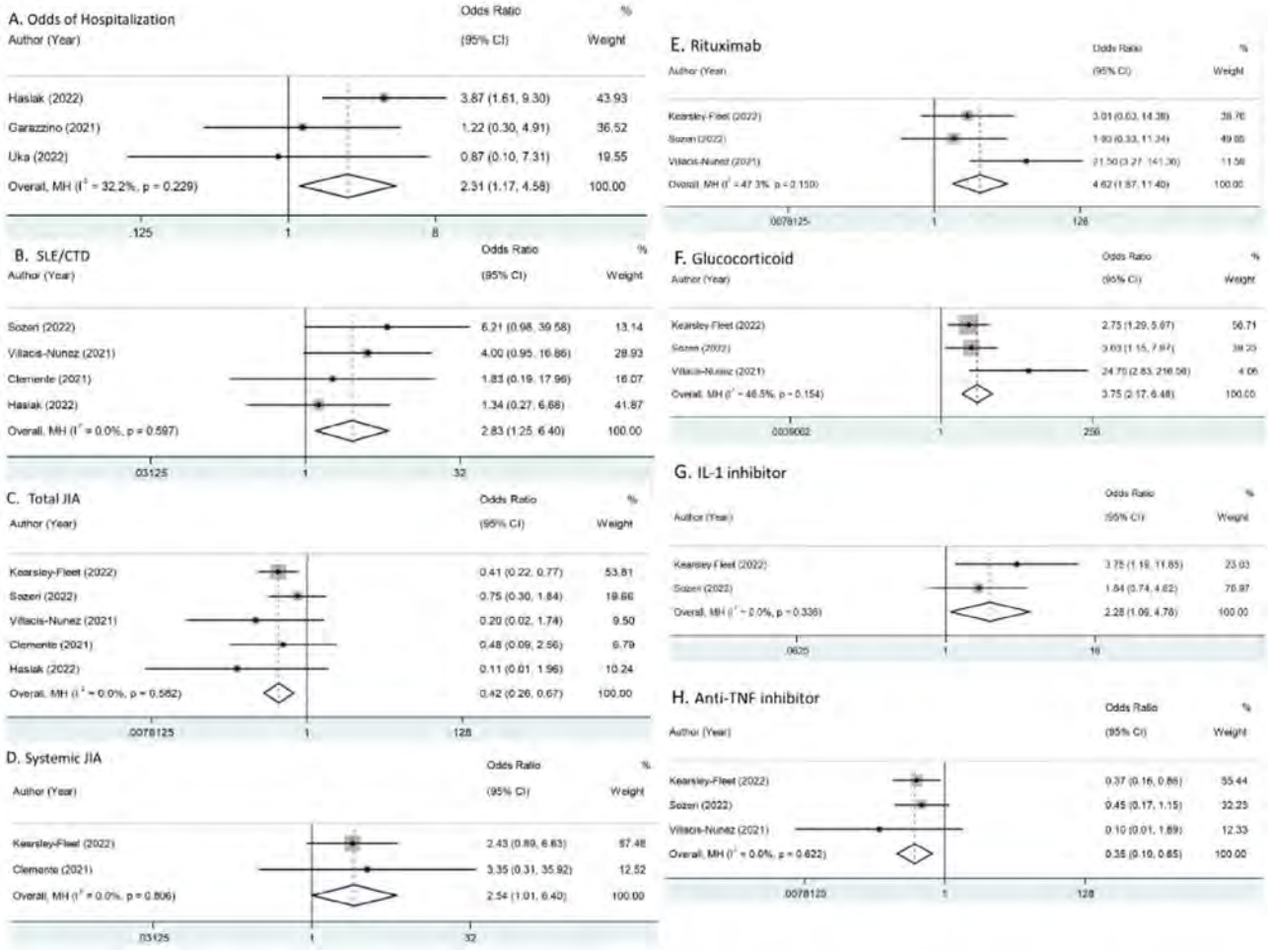

Figure 2. Forest plots demonstrating odds ratio of hospitalization in children with rheumatic diseases and associated risk factors of hospitalization: A. odds of hospitalization, B. SLE/CTD, C. total JIA, D. systemic JIA, E. Rituximab, F. Glucocorticoid, G. IL-1 inhibitor, H. anti-TNF inhibitor

Disclosure: Q. Zhao: None; **B. Wallace**: None; **L. Jung**: None; **T. Ronis**: None.

Abstract Number: 2053

Predictive Factors Associated with Treatment Response in Chronic Nonbacterial Osteomyelitis

Katherine Nowicki[1], Nathan Rogers[2], Carson Keeter[2], Nathan Donaldson[2], Jennifer Soep[2] and Yongdong (Dan) Zhao[3], [1]University of Colorado, Lakewood, CO, [2]University of Colorado, Aurora, CO, [3]University of Washington, Redmond, WA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Pediatric Rheumatology – Clinical Poster III: Potpourri

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Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic nonbacterial osteomyelitis (CNO) is characterized by sterile inflammatory bone lesions and most commonly affects skeletally immature children. Non-steroidal anti-inflammatory drugs (NSAIDs) are the first-line treatment, but in some cases second-line treatments including methotrexate, TNF-alpha inhibitors, and bisphosphonates are required. It remains unclear which patients are most likely to respond to NSAIDs or require a second-line treatment based on their initial presentation. In this study, we sought to describe our CNO cohort and to determine which pre-treatment clinical variables are associated with response to NSAID monotherapy versus requiring a second-line medication.

Methods: A retrospective chart review of patients with a diagnosis of CNO made before 18 years of age who attended the CNO clinic at Children's Hospital Colorado between 1/1/05 and 1/31/22 was performed. The standardized treatment approach involved 6 months of NSAIDs, followed by a trial of discontinuation in responders. Patients who failed the discontinuation trial were given a longer NSAID course. Patients with spinal involvement, patients with comorbidities such as psoriasis or inflammatory bowel disease, and NSAID-non-responderswere treated with second-line therapies. Clinical characteristics were recorded,including which of 6 regions (head and face, neck and back, upper torso,upper extremities, lower torso, lower extremities) were affected by CNO. Patients were divided into three groups: NSAID-short (NSAID monotherapy for 3 to < 7 months), NSAID-long (NSAID monotherapy for ≥7 months), or second-line treatment. A multiple linear regression model was constructed to determine the relationship between total NSAID monotherapy days and relevant predictors. Multiple logistic regression was used to determine the odds of needing second-line treatment when considering those same predictors. Both models contained combinations of variables which minimized the Akaike Information Criteria (AIC), resulting in models with low multicollinearity and high predictive power.

Results: 164 patients fulfilled inclusion criteria and 70 patients were excluded. Cohort characteristics overall and for each of the 3 treatment groups are presented in Table 1. Comparison between the NSAID-short and NSAID-long groups showed that patients with unifocal disease at diagnosis required 47% less days of NSAID treatment than those with multifocal disease at diagnosis (Table 2). Comparison of the NSAID monotherapy groups to the second-line treatment group showed that patients with 2 or more regions affected by CNO were 1.94 times more likely to require a second-line treatment ($p < 0.05$) and that patients with symmetric bone lesions were 6.86 times more likely to require a second-line treatment ($p< 0.0001$) (Table 3).

Conclusion: Our cohort is similar to other reported CNO cohorts in terms of clinical characteristics. Patients with unifocal CNO involvement at diagnosis are more likely to require shorter NSAID treatment courses. Patients with 2 or more regions affected by CNO and those with symmetric bone lesions are more likely to require a second-line treatment. These findings may inform treatment choices for patients with CNO.

Table 1. Cohort Characteristics

Table 1. Cohort characteristics					
	NSAID-short (N=32)	NSAID-long (N=62)	Second-line (N=70)	P value	Overall (N=164)
Mean age at symptom onset, years (± SD)	8.46 (± 4.41)	8.94 (±3.05)	8.99 (±3.36)	0.757	8.87 (±3.46)
Mean interval from symptom onset to treatment onset, days (± SD)	124 (±210)	269 (±333)	293 (±388)	**0.0588**	251 (±343)
Mean interval from symptom onset to diagnosis, days (± SD)	119 (±211)	270 (±327)	324 (±403)	**0.0226**	263 (±351)
Mean follow-up, years (± SD)	1.21 (±1.51)	2.70 (±2.07)	3.83 (±2.34)	**<0.001**	2.89 (±2.30)
Female sex, n (%)	17 (53%)	37 (60%)	42 (60%)	0.775	96 (59%)
Race and ethnicity, n (%)					
Asian	1 (3%)	0 (0%)	1 (1%)	0.714	2 (1%)
Black	1 (3%)	1 (2%)	1 (1%)		3 (2%)
Multiracial	0 (0%)	2 (3%)	3 (4%)		5 (3%)
Native American	0 (0%)	0 (0%)	1 (3%)		1 (1%)
White	29 (91%)	56 (90%)	59 (84%)		144 (88%)
Other	0 (0%)	1 (2%)	4 (6%)		5 (3%)
Unknown	0 (0%)	1 (2%)	0 (0%)		1 (1%)
Missing	1 (3%)	1 (2%)	1 (1%)		3 (2%)
Ethnicity, n (%)					
Hispanic	0 (0%)	6 (10%)	11 (16%)	0.0835	17 (10%)
Non-Hispanic	31 (97%)	54 (87%)	58 (83%)		143 (87%)
Unknown	0 (0%)	1 (2%)	0 (0%)		1 (1%)
Missing	1 (3 %)	1 (2%)	1 (1%)		3 (2 %)
Family history, n (%)					
Inflammatory arthritis	0 (0%)	3 (5%)	5 (7%)	0.274	8 (5%)
Inflammatory Bowel Disease	0 (0%)	0 (0%)	2 (3%)	0.361	2 (1%)
Psoriasis	0 (0%)	1 (2%)	1 (1%)	1	2 (1%)
Mean ESR at presentation, mm/hr (± SD)	19.7 (±18.5)	19.6 (±19.6)	27.6 (±25.3)	0.093	22.8 (±20.5)
Missing ESR, n (%)	3 (9.4%)	13 (21%)	17 (24%)		33 (20%)
Mean CRP at presentation, mg/dL (± SD)	1.57 (±2.96)	0.950 (±2.14)	2.69 (±4.88)	0.0601	1.83 (±3.75)
Missing CRP, n (%)	3 (9.4%)	16 (25.8%)	15 (21.4%)		34 (20.7%)
Biopsy performed, n (%)	22 (69%)	46 (74%)	66 (94%)	**0.0025**	134 (82%)
CNO lesion apparent on plain radiographs at presentation, n (%)	19 (59%)	36 (58%)	31 (44%)	0.229	86 (52%)
Missing, n (%)	1 (3 %)	0 (0%)	2 (3%)		3 (2%)
Unifocal disease at diagnosis, n (%)	23 (72%)	29 (47%)	29 (41%)	**0.015**	81 (49%)
Total number of whole-body MRIs, n (%)					
0	28 (88%)	51 (82%)	29 (41%)	**<0.001**	106 (66%)
1	4 (12%)	8 (13%)	16 (23%)		28 (17%)
2	0 (0%)	3 (5%)	8 (11%)		11 (7%
≥3	0 (0%)	0 (0%)	17 (24%)		17 (10%)
Patients with affected regions, n (%)					
Head & face	0 (0%)	0 (0%)	3 (4%)	0.233	3 (2%)
Neck and back	2 (6%)	9 (15%)	18 (26%)	**0.046**	29 (18%)
Upper torso	3 (9%)	8 (13%)	9 (13%)	0.902	20 (12%)
Upper extremity	4 (12%)	11 (18%)	22 (31%)	**0.046**	37 (23%)
Lower torso	7 (22%)	19 (31%)	33 (47%)	**0.029**	59 (36%)
Lower extremity	23 (72%)	34 (55%)	59 (84%)	**<0.001**	116 (71%)
Mean number out of 6 regions affected (± SD)	1.22 (± 0.608)	1.31 (± 0.561)	2.06 (± 1.03)	**<0.001**	1.61 (± 0.890)
Symmetric involvement in the same bone, n (%)	5 (16%)	14 (23%)	51 (73%)	**<0.001**	70 (43%)
Mean days on NSAID monotherapy, days (± SD)	175 (± 26.5)	725 (±512)	441 (±536)	**<0.001**	497 (±511)
Number of NSAIDs Trialed, n (%)					
0	0 (0%)	0 (0%)	2 (3%)	**<0.001**	2 (1%)
1	30 (94%)	28 (45%)	17 (24%)		75 (46%)
2	2 (6%)	32 (52%)	45 (64%)		79 (48%)
3 or more	0 (0%)	3 (3%)	6 (9%)		8 (5%)
Patients in each disease activity state at study end date, n (%)					
Active disease	0 (0%)	7 (11%)	14 (20%)	**0.024**	21 (13%)
Inactive disease on treatment	2 (6%)	11 (18%)	20 (29%)	**0.0285**	33 (20%)
Remission	30 (94%)	44 (71%)	36 (51%)	**<0.001**	110 (67%)

Table 2. Linear regression modeling with IC-based variable selection comparing the NSAID-short and NSAID-long groups

Study Variable	Coefficient	P-value
Onset to treatment interval	0.000	0.162
Number of regions affected	-0.225	0.141
Unifocal disease suspected at diagnosis	-0.386	**0.029**

Table 2. Linear regression modeling with IC-based variable selection comparing the NSAID-short and NSAID-long groups

Table 3. Logistic regression modeling of the odds of requiring second-line treatment with IC-based variable selection

Study Variable	OR	P-value
Days from symptom onset to treatment	1.000	0.116
Family history present	3.770	0.113
Number of regions affected	1.941	**0.012**
Presence of symmetric bone lesions	6.862	**<0.001**

Table 3. Logistic regression modeling of the odds of requiring second-line treatment with IC-based variable selection

Disclosure: K. Nowicki: None; **N. Rogers**: None; **C. Keeter**: None; **N. Donaldson**: None; **J. Soep**: None; **Y. Zhao**: Bristol-Myers Squibb(BMS), 5.

Abstract Number: 2054

Superiority of Adalimumab in Treating Childhood Chronic Idiopathic Uveitis: Evidence from a Multicentre Experience

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SESSION INFORMATION

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Session Type: Poster Session C

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Background/Purpose: Childhood Chronic Idiopathic Uveitis (cCIU) is a severe ocular condition that accounts for the 40% of all uveitis in children. Its timely and proper treatment is critical to prevent severe complications. Our purpose isto report the treatment response of a large cohort of cCIU.

Methods: This is a retrospective multicentre international observation study conducted at Meyer Children's Hospital IRCCS and Bristol Royal Hospital for children. The medical records of children were reviewed if they have a diagnosis of cCIU prior to 16 years old, and received a systemic treatment other than corticosteroids. We collected demographic, clinical and laboratory data. The main outcome was the achievement of response and remission on treatment according to SUN criteria.

Results: 146 cCIU (76 male, 42 ANA positive) with a median age at onset of 112months (range 20-199), 122 had a bilateral involvement (83.6%), 78 had anterior uveitis (53.4%), 17 anterior+intermediate (11.6%), 32 intermediate (21.9%) and 19 panuveitis (13%) were screened for inclusion criteria (see table 1). 115 patients received at least one systemic therapy other than corticosteroids (78.8%), 68 two different lines (46.6%), 20 three-line treatment (13.7%), and 3 four-line treatment (2.1). The median time for the first drug administered was 6 months (range 0-73). As first line-treatment 93 children received

Table 1

Table 1: demographic, laboratory and clinical characteristics of the population with cCIU

Variable in study	Entire cohort N=146	Anterior N=78	Ant+intermediate N=17	Intermediate N=32	Panuveitis N=19	p
Female	70	40	7	14	9	ns
Age at onset months	111.5 (20-199)	99 (20-188)	110 (62-199)	122.5 (70-153)	117 (65-183)	Ns
Duration of FU	40.5 (4-149)	36 (4-138)	44 (4-122)	56 (7-149)	36 (4-103)	ns
Ethnicity						
Caucasian	129	60	14	31	16	
African	6	1	2	1	2	ns
Asian	5	5	0	0	0	
Mixed	1	0	0	0	1	
Arab	3	3	0	0	0	
Presence of comorbidities	48	28	3	8	9	ns
ANA positivity, performed in 121	42	**31***	1	5	5	χ2 11.8, p 0.008
ANCA	8	6	0	0	2	
ESR at onset (mm/h)	10 (1-46)	14 (2-42)	12 (2-40)	**2 (1-17)***	27 (2-46)	<0.001
CRP at onset (mg/dl)	0.29 (0.02-5.63)	1 (0-1)	0.26 (0.07-5.6)	0.29 (0.06-1.83)	0.15 (0.06-1.11)	ns
HLA B27, performed in 78	13	10	1	0	2	ns
HLA B51 performed in 55	12	3	2	**6***	1	χ2 12.7, p 0.005
Bilateral Uveitis	122	63	16	27	16	ns
VA at onset WE, LogMar	0 (0-2.3)	**0.047 (-0.2-2.3)***	0.2 (0-1.9)	0.4 (0-2.3)	0.35 (0-2.7)	0.046
VA WE stratified onset						
<0.4	67	36	11	12	8	ns
0.4-1	25	7	4	9	5	
>1	14	5	2	4	3	
Presence of complications	97	54	11	18	14	ns
N of complications onset	2 (0-7)	2 (0-7)	2 (0-5)	**1 (0-4)***	2.5 (0-6)	0.009
N of Systemic therapy	1 (0-4)	1 (0-4)	1 (0-4)	1 (0-3)	1 (0-3)	ns
Remission at LFU	88	47	9	20	12	ns
VA LFU WE, LogMar	0 (0-2.7)	0 (-0.2-2.7)	0 (-0.1-0.475)	0 (-0.2-0.85)	0 (-0.1-2)	ns
VA WE, LFU						
<0.4	115	63	13	25	14	ns
0.4-1	19	7	3	6	3	
>1	6	4	0	0	2	
Presence of complications LFU	70	35	**4***	18	13	χ2 7.6, p 0.05
N of complications LFU	1 (0-6)	1 (0-6)	**0 (0-2)***	1 (0-4)	2 (0-6)	0.005

List of abbreviations: N number, LFU last follow-up, VA visual acuity, WE worst eye,

Table 2

Table 2: Treatment performed in cohort of Childhood CNIU

Treatment	First Course of Systemic treatment					Second course of systemic treatment				
	Overall (115)	Mtx (93)	MM (1)	ADA (21)*	P value	Overall (66)	Mtx (6)	ADA (15)	MM (15)	P value
Concomitant therapy	*4 MTX					41 MTX and 2 MM (Group ADA)				
Time of administration median (IQR)	6 (0-73)	5 (2-73)	4	7 (1-39)	NS	15 (8.25-76)	41.5 (27-55)	12 (7-17)	16 (4-76)	0.006
Duration of therapy	22 (3-105)	23 (3-105)	5	19 (6-36)	NS	24 (1-114)	21.5 (3-32)	23 (1-97)	33.5 (1-114)	NS
Achievement of response	74/113	55/91	0/1	19/21	χ^2 8.7 p 0.013	61/64	6/6	43/44	12/14	NS
Achievement of remission on therapy N (%)	61/108	42/87	-	19/21	χ^2 12.25 p <0.001	52/57	5/6	38/39	9/12	χ^2 6.29 p 0.04
Relapse on therapy	16/65	12/44	-	4/21	Ns	20/52	1/6	15/37	4/9	NS
Time for achievement remission	6 (5-15)	6 (4-15)		6 (3-11)	NS	6 (3-36)	5 (4-9)	6 (4-36)	9 (3-15)	Ns
N of pts who stop drug for persistent remission	25/107	22/66	-	4/19	NS	26/56	3/6	19/38	4/12	NS
Relapse out of therapy N (%)	12/26	12/22	-	1/4	NS	17/27	0/3	15/20	2/4	χ^2 6.6 p 0.03
Time free from relapse out of therapy	4.5 (1-78)	4.5 (1-45)		40 (2-78)	0.036	6 (2-68)	4 (2-68)	6 (2-36)	6.5 (3-42)	ns

List of abbreviations: *ADA: adalimumab, MM: mycophenolate mofetil, MTX methotrexate, IFN: infliximab, N number, IQR interquartile range, NS non significant.*

methotrexate (63.7%), 21 adalimumab (14.4%) (of whom 4 with concomitant methotrexate), and 1 mycophenolate mofetil (MMF) (0.7%). As second line treatment 6 received methotrexate, 45 adalimumab, 15 MMF, 1 azathioprine, and 1 tacrolimus. Among the first-line therapies, we observed that patients treated with adalimumab achieved more frequently ocular response (19/21 vs 55/91 χ^2 8.72 p 0.01) and ocular remission (19/21 vs 42/45 χ^2 12.2 p < 0.001), with no difference in frequency of relapse on therapy and time to first relapse on the therapy (see table 2). Additionally, cCIU with worse visual acuity (>0.4 LogMAR) were less likely to achieve disease remission with methotrexate as first-line treatment (χ^2 6.7p 0.035). Among the second-line therapy, adalimumab achieved more frequently ocular remission (38/1 (ADA) vs 5/1 (MTX) vs 9/12 (MMF), χ^2 6.29 p 0.043) (table 2).

Conclusion: Adalimumab showed better chance to achieve ocular remission, as first and second line treatment, as well as in patients with worst outcome: ANA positivity, worse visual acuity, intermediate uveitis. **Acknowledgements:** All the patients that received adalimumab as first line treatment were followed at Meyer Children's Hospital IRCCS, and the off label prescription authorization was obtained.

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Abstract Number: 2055

A Randomized Controlled Trial of Two Hepatitis a Vaccine Doses Among Adolescents with Juvenile Idiopathic Arthritis and Crohn's Disease on Immunosuppressive Therapy: A Pilot Study

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Pediatric Rheumatology – Clinical Poster III: Potpourri
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Background/Purpose: Juvenile idiopathic arthritis (JIA) and Crohn's disease (CD) are now controlled using immunosuppressive medications. However, disease control comes at the risk of increased infection. It remains unclear if immunosuppressed pediatric patients mount a blunted and/or rapidly waning immune response to the Hepatitis A virus (HAV) vaccine. We conducted a randomized controlled pilot trial to compare vaccine immunogenicity to either pediatric or adult doses of HAV seronegative adolescents, aged 12-15 years, receiving immunosuppressive medications for JIA or CD.

Methods: Participants were recruited from the outpatient Rheumatology and Gastroenterology clinics at a single center. Demographics, diagnosis, and current treatments were obtained from health records**.**19 participants, confirmed to be HAV seronegative, were randomized such that 10 were assigned to receive HAV Pediatric 80 antigen units and 9 HAV 160 antigen units. Serum samples were analyzed using the Elecsys anti-HAV assay.All serum samples were tested at 4-time points; pre-vaccine dose 1 (t1), ∼ 28 days post-vaccine dose 1 (t2), pre-vaccine dose 2 (t3) and ∼ 28 days post-

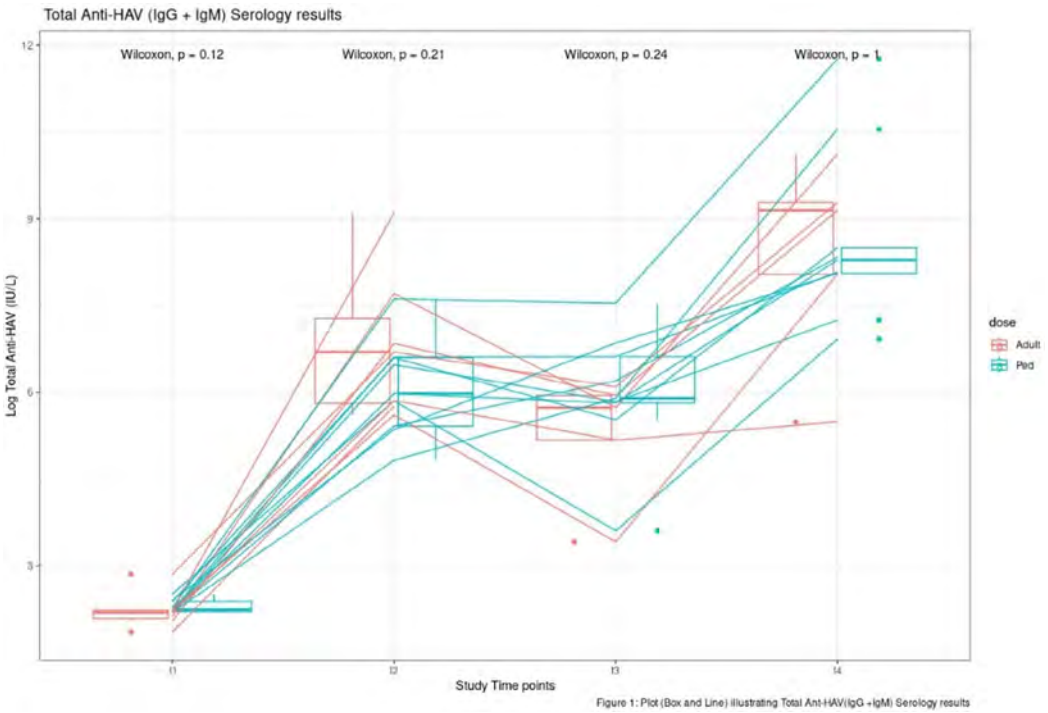

Figure 1: Plot (Box and Line) illustrating Total Ant-HAV(IgG +IgM) Serology results

vaccine dose 2 (t4).Participants were considered seropositive if they achieved a threshold of ≥ 20 IU/L anti-HAV. Descriptive statistics and a Wilcoxon rank test was used to analyze the data.

Results: 16/19 participants completed the 2-dose regimen (each dose 6 months apart). 10/6 were female/male; aged 13.32 ± 1.29 years (mean ± SD); diagnosed with CD (3/16) or JIA (13/16). Seven patients were treated with DMARDs and 2 with TNF-alpha Inhibitor monotherapy. Three patients were treated concomitantly with Methotrexate/Sulfasalazine and 4 with methotrexate/TNF-alpha Inhibitors. All participants (16/16) mounted a seropositive response ∼ 28 days after vaccine dose 1 (t2) that was maintained at t3 and t4. Figure 1 illustrates individual (lines) median, and interquartile ln transformed values (box plot) for both dose assignments over the study time points. Serological response between participant's assigned to pediatric vs adult doses were not statistically significant ($p < 0.05$) at all time points; however, participants receiving the adult vaccine appeared to have a higher median serology value 28 days post-vaccine dose 2. Adverse events were reported by 2/16 participants after the first dose. All adverse events resolved without sequelae. No serious adverse events were reported.

Conclusion: This is the first randomized controlled trial that compares the immunogenicity of pediatric vs. adult doses of HAV vaccine in immunosuppressed pediatric patients. We found no statistical difference in the serological response to Pediatric or Adult vaccine formulations. However, our results support evidence of the immunogenicity of HAV vaccine in immunosuppressed CD and JIA patients. Uniquely, this trial provides a preliminary pragmatic approach that will inform future studies and vaccination guidelines on the comparative benefits of both formulations. Future studies with longer follow up time frame, larger sample sizes and healthy controls will need to be conducted.

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Abstract Number: 2056

Pediatric Acute-onset Neuropsychiatric Syndrome: Markers of Inflammation/autoimmunity at Clinical Presentation and Eventual Development of Arthritis and Other Autoimmune Diseases

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
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Background/Purpose: Certain psychiatric conditions are associated with systemic inflammatory processes. We aimed to evaluate whether a pediatric condition characterized by a sudden onset of severe neuropsychiatric symptoms, pediatric acute-onset neuropsychiatric syndrome (PANS), is related to inflammatory disease.

Methods: This retrospective, observational analysis is based on longitudinal clinical data from patients with PANS from the Stanford Immune Behavioral Health (IBH) Clinicfrom 2012-2021.We reviewed patient medical records since birth to evaluate immune activation markers during psychiatric flare episodes, arthritis andautoimmune disease diagnoses. We describe

laboratory, physical exam, and musculoskeletal ultrasoundresults and estimate the cumulative risk of developing arthritis and autoimmunediseases using product limit (Kaplan-Meier) survival probability.

Results: We analyzed data from 193 children who had a sudden onset of severe neuropsychiatric symptoms at approximately 7.5 ± 3.5 years of age.These patients had been followed in the IBH Clinic for an average of47.9 ± 25.5 months (mean age: 13.9 ± 4.7 yearsat data collection). Among those tested for immune activation markers, 55% had results indicative of autoimmunity, 12% of immune dysregulation, and 45% of vasculopathy (Table 1). By 14 years of age, the estimated cumulative incidence of juvenile-onset arthritis was 28% (95% CI: 21%, 36%) and of autoimmune disease was 8% (95% CI: 4%, 12%).We report novel findings among children with arthritis, including capsular thickening (55%), DIP tenderness (82%), and spinous process tenderness (80%) (Table 2).

Table 1. Non-specific laboratory markers and physical signs of immune activation measured at the first flare captured in clinic among Stanford University Immune Behavioral Health Clinic patients with sudden-onset, severe neuropsychiatric symptoms, N=193

Autoimmune markers (non-specific)	
Antinuclear antibody (ANA), *titer ≥ 1:80*	23/109 (21.1%)
Anti-histone antibody, *high*	16/82 (19.5%)
Anti-thyroid antibodies, *high*[b]	16/114 (14.0%)
C1q binding assay, *high*	27/136 (19.9%)
Complement 3, *low*	12/137 (8.8%)
Complement 4, *low*	44/140 (31.4%)
Among those tested for at least one marker (n=179) --	
At least one positive result	*98/179 (54.7%)*
At least two positive results	*30/179 (16.8%)*
Among those tested for all 6 markers above (n=39) --	
At least one positive result	*27/39 (69.2%)*
At least two positive results	*14/39 (35.9%)*
Immune dysregulation/inflammation markers (non-specific)	
Leukopenia, *white blood cell<4,000/mm³*	8/183 (4.4%)
Thrombocytosis, *platelet >400,000/mm³*	8/183 (4.4%)
C-reactive protein (CRP), *high*	3/118 (2.5%)
erythrocyte sedimentation rate (ESR), *high*	6/96 (6.3%)
Among those tested for at least one marker (n=184) --	
At least one positive result	*22/184 (11.5%)*
At least two positive results	*2/184 (1.1%)*
Among those tested for all 4 markers above (n=78) --	
At least one positive result	*16/78 (20.5%)*
At least two positive results	*2/78 (2.6%)*
Vasculopathy/vascular inflammation markers (non-specific)	
von Willebrand factor antigen, *high*	14/129 (10.9%)
D-dimer, *high*	9/122 (7.4%)
Onychodermal band, *abnormally prominent*	39/193 (20.2%)
Livedo reticularis, *present*	46/193 (23.8%)
Periungual redness, *present*	21/193 (10.9%)
Palatal petechiae, *present*	6/193 (3.1%)
Among those tested for at least one marker (n=172) --	
At least one positive result	*69/172 (40.1%)*
At least two positive results	*43/172 (25.0%)*
Among those tested for all 6 markers above (n=27) --	
At least one positive result	*26/27 (96.3%)*
At least two positive results	*22/27 (81.5%)*

[a] Due to the severe psychiatric symptoms and young age of the study sample, we were not able to complete the standard workup below in all patients; denominators are reported for each marker

[b] Thyroglobulin antibodies and/or thyroperoxidase antibodies

Table 2. Juvenile-onset arthritis, musculoskeletal characteristics, and other autoimmune/autoinflammatory diseases in Stanford University Immune Behavioral Health Clinic patients with sudden-onset, severe neuropsychiatric symptoms, N=193

Juvenile-onset arthritis			
Any juvenile-onset arthritis		**55 (28.5%)**	
Age at diagnosis (years), mean ± SD		12.7 ± 3.7	
Subtype based on ILAR Criteria [c]	Enthesitis-Related Arthritis (ERA)	37 (19.2%)	
	Psoriatic Arthritis (PsA)	10 (5.2%)	
	Oligoarticular Arthritis-Persistent	3 (1.6%)	
	Oligoarticular Arthritis-Extended	0	
	RF positive polyarthritis	0	
	RF negative polyarthritis	0	
	Undifferentiated Arthritis	0	
Subtype based on ASAS Criteria [b]	Spondyloarthritis	27 (14.0%)	
	Peripheral		26/27
	Axial		7/27
Musculoskeletal characteristics, stratified by arthritis status			
		Met arthritis criteria (n=55)	**Did not meet arthritis criteria (n=138)**
Inflammatory Back Pain (IBP)			
	Meets Calin criteria for IBP	35 (63.6%)	17 (12.3%)
Physical Exam (N=193)			
	Most common sites of tenderness		
	Distal Interphalangeal Joints (DIP)	45 (81.8%)	39 (28.3%)
	Spinous process tenderness	44 (80.0%)	34 (24.6%)
	Sacroiliac (SI) joint tenderness	38 (69.1%)	30 (21.7%)
	Achilles tendon insertion (i.e., heel enthesitis)	31 (56.4%)	19 (13.8%)
	Other characteristics		
	Nail pitting	9 (16.4%)	13 (9.4%)
		Met arthritis criteria (n=40)	**Did not meet arthritis criteria (n=27)**
Joint ultrasounds (N=67)			
	normal	3 (7.5%)	16 (59.3%)
	abnormal	37 (92.5%)	11 (40.7%)
	Joint effusion	31	8*
	Capsular thickening (capsulitis)	22	0
	Synovial thickening/proliferation (synovitis)	22	4*
	Bone erosion	1	0
	Ganglion cyst	1	0
	Tendinous thickening/Tenosynovitis	1	0
	Bone edema	0	0
	Joint narrowing	0	0
	Joint widening	0	0
	Subchondral sclerosis	0	0
	Bursitis	0	0
	other	8	2*
Autoimmune/inflammatory diseases (beyond arthritis and PANS)			
Any autoimmune disease		**21 (10.9%)**	
	Age at diagnosis (years), mean ± SD		12.4 ± 6.4
	Has more than one comorbid autoimmune disease		5/21 (23.8%)
Thyroiditis		8 (4.1%)	
Psoriasis		5 (2.6%)	
Inflammatory bowel disease (IBD) [d]		5 (2.6%)	
Celiac disease		4 (2.1%)	
Behcet's disease		2 (1.0%)	
Systemic lupus erythematosus (SLE)		1 (1.0%)	
Diabetes mellitus (DM) type I		1 (1.0%)	

Conclusion: Patients with PANS show signs of immune activation during psychiatric flare episodes and have a heightened risk of arthritis and other autoimmune diseases compared to the general pediatric population. These findings suggestPANS may be a systemic inflammatory condition rather than an isolated psychiatric or neuroinflammatory disorder.

Disclosure: M. Ma: None; **E. Masteron**: None; **J. Frankovich**: None.

Abstract Number: 2057

Medical Trauma and Its Association with Pain and Disability Risk in Children with Inflammatory Arthritis

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SESSION INFORMATION
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Session Title: Pediatric Rheumatology – Clinical Poster III: Potpourri
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: This study aims to determine the prevalence of medical trauma and its impacts on outcomes in a sample of children with inflammatory arthritis. We hypothesize that medical trauma is an underrecognized entity in this population, and that it is associated with worse pain outcomes and disability risk.

Methods: Children aged 8-18 years with juvenile idiopathic arthritis (JIA) or juvenile lupus erythematosus (jSLE) with a history of inflammatory arthritis were recruited from a single center pediatric rheumatology clinic. Participants completed a questionnaire assessing for medical trauma related to their arthritis with an adapted Child PTSD Symptom Scale for DSM-V (CPSS-V). Further questionnaires assessed for self-efficacy to function despite pain (Child Self-Efficacy Scale), pain scores (Verbal Rating Scale, 0-10), juvenile fibromyalgia (JFM) (Pain and Symptom Assessment Tool), anxiety sensitivity (Childhood Anxiety Sensitivity Index), and other adverse childhood experiences (ACEs). Demographic and disease activity data were collected. Differences between those with and without probable medical PTSD (CPSS-V score >31 vs ≤ 31) were assessed using rank sum and exact tests. Linear regression examined continuous associations with CPSS-V.

Results: Fifty children and adolescents with JIA (n=42) or jSLE (n=8) completed the study. Twenty (40%) children had CPSS-V scores of moderate or greater severity and 7 (14%) scored in the probable medical PTSD range. Those with juvenile spondyloarthropathy and rheumatoid factor positive polyarticular JIA had the highest trauma scores, but there was no overall difference in trauma scores between JIA and jSLE. CPSS-V scores in the probable medical PTSD range were significantly associated with older age, higher pain and anxiety sensitivity scores, more ACEs and depression history, and higher JIA disease activity scores (cJADAS-10) but not jSLE activity scores (SLEDAI-2K). There was a trend towards poorer self-efficacy scores and meeting JFM criteria in the probable medical PTSD group. Poorer self-efficacy scores were significantly associated with higher CPSS-V scores when assessed as a continuous variable. Nine (18%) participants met criteria for JFM and had higher average trauma scores compared to those who did not. Trauma scores were not associated with history of hospitalization or injected medication use.

Conclusion: Medical trauma symptoms were reported by many participants in this cohort of children with inflammatory arthritis. Those who have experienced more trauma from their rheumatologic disease may be at risk for worse pain outcomes and increased disability, specifically poor self-efficacy and high anxiety sensitivity. Further studies are necessary to

Table 1. Demographic and disease history data for children and adolescents with inflammatory arthritis, stratified by CPSS-V scores above or below the probable medical PTSD range (> 31). cJADAS-10 = Clinical Juvenile Arthritis Disease Activity Scores, 10 joints; CPSS-V = Child PTSD Symptom Scale for DSM-V; IV = intravenous; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000; subQ = subcutaneous.

	Overall (n=50)	CPSS-V ≤ 31 (n=43)	CPSS-V > 31 (n=7)	P value
Age, years	15	15	17	0.027
Female (%)	33 (66)	27 (63)	6 (86)	0.485
Rheumatologic diagnosis (%)				1.000
JIA, all subtypes	42 (84)	36 (84)	6 (86)	
jSLE	8 (16)	7 (16)	1 (14)	
Race (%)				0.611
White	29 (58)	23 (54)	6 (86)	
Non-white	11 (22)	11 (26)	0	
>1 Race	4 (8)	3 (7)	1 (14)	
Hispanic or Latino	18 (36)	15 (35)	3 (43)	0.403
Annual household income (%)				0.793
<$25,000 to 49,999	4 (8)	3 (7)	1 (14)	
$50,000 to >100,000	37 (74)	32 (74)	5 (71)	
History of (%)				
Depression	15 (30)	10 (23)	5 (71)	0.020
Anxiety	21 (42)	16 (37)	5 (71)	0.115
Ever hospitalized (%)	15 (30)	14 (33)	1 (14)	0.659
Ever IV or subQ medications (%)	35 (68)	30 (70)	4 (57)	0.666
cJADAS-10 score, median	8.0	7.5	11.5	0.032
SLEDAI-2K score, median	8.5	7.0	10	0.825

Table 2. Questionnaire score data for children and adolescents with inflammatory arthritis, stratified by CPSS-V scores above or below the probable medical PTSD range (> 31). Data represent median scores, unless otherwise stated. ACEs = Adverse Childhood Experiences questionnaire; CASI = Childhood Anxiety Sensitivity Index; CPSS-V = Child PTSD Symptom Scale for DSM-V; CSES = Child Self-Efficacy Scale; PSAT = Pain and Symptom Assessment Tool.

	All Participants, n=50	CPSS ≤ 31, n=43	CPSS-V > 31, n=7	P value
CPSS-V	14.00	12.00	46.00	2.70E-05
ACEs	1.76	1.00	3.00	0.005
CSES	18.21	18.00	20.00	0.149
PSAT met juvenile fibromyalgia criteria, n (%)	9 (18%)	6 (14%)	3 (43%)	0.100
CASI	29.50	29.00	39.00	0.008
Pain Score	4.00	3.00	4.00	0.043

determine the true prevalence of medical trauma in this population, its impact on pain and disability, potential interventions, and the importance of trauma-informed care.

Disclosure: L. Medrano: None; **B. Bursch**: None; **J. Weiss**: None; **A. Hoftman**: None; **J. Li**: None; **N. Jackson**: None; **D. McCurdy**: None.

Abstract Number: 2058

IL-1 Blocking Treatment Slows the Progression of Sensorineural Hearing Loss in Patients with NOMID

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SESSION INFORMATION

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Background/Purpose: NOMID is a severe form of cryopyrin-associated periodic syndrome characterized by systemic inflammation and CNS manifestations, including sensorineural hearing loss. IL-1 blocking agents, Anakinra and canakinumab, are standard treatment, we assessed the long-term impact of IL-1 blocking treatment on progression of hearing loss.

Methods: Pts (n=39) enrolled in NCT02974595 protocol underwent hearing tests at baseline and on treatment (n=447) Table 1. Bone conduction at four frequency (4F-PTA) (average hearing at 500, 1000, 2000, 4000 Hz) and bone conduction at 4000 Hz only (surrogate for high frequency (HF) hearing) were longitudinally evaluated. 4F-PTA >25 dB, or HF >25 dB at baseline were defined as baseline 4F-PTA or HF hearing loss respectively.

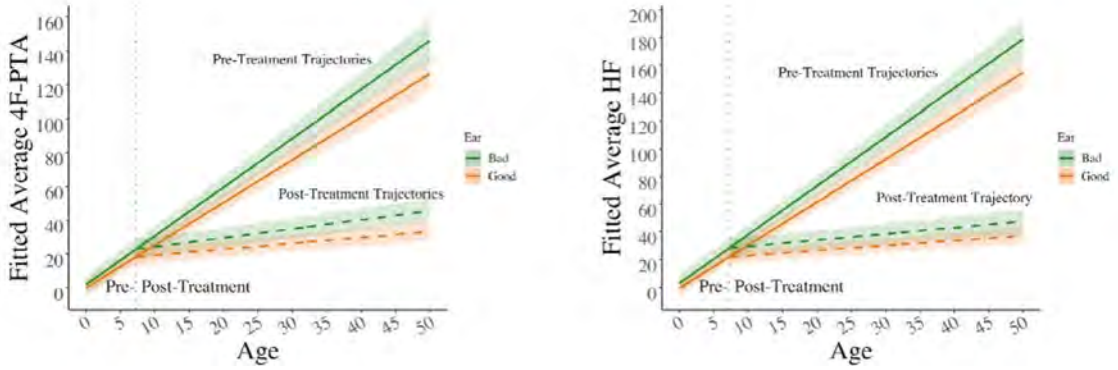
Progressive 4F-PTA hearing loss was defined as 20dB increase in one frequency or 10dB increase in two consecutive frequencies and progressive HF hearing loss as change from baseline by 10dB. Pts' ears were analyzed separately as 'good' and 'bad,' where hearing levels differed. Pts with a hearing level of >80 dB were excluded from trajectory analysis. Incidences of upper respiratory infections were extracted from records and brain MRI scored for cochlear enhancement. 36 or 39 pts. had a lumbar puncture at their last visit; 65 biomarkers were measured in CSF and compared with three healthy controls.

Linear mixed models were applied to trajectories of hearing loss before and after treatment. Multivariate and univariate logistic regression assessed the impact of baseline hearing loss and infections on progression and of CSF inflammatory cytokines on MRI cochlear enhancement and hearing loss.

Table 1: Characteristics of the NOMID cohort who underwent serial hearing assessment

Demographics		NOMID N=39
Current Age	Years Median (range) years	20 (8-43)
	Gender Female (%)	23 (59%)
	Ethnicity White (%)	26 (66%)
Genetic diagnosis	*NLRP3* mutations # (somatic, germline)	7 Somatic 32 Germline
Age at treatment initiation	Years Median (range)	7 (1, 28)
Duration of treatment	Years Median (range)	15 (7-18)
Treatment regimen	Anakinra (Canakinumab)	34 (5)

Figure 1: The trajectory of hearing loss, in both 4F-PTA and HF, significantly differed between treated and untreated patients (p<0.00001), indicating that IL-1 blockade slows down progression of the hearing loss.



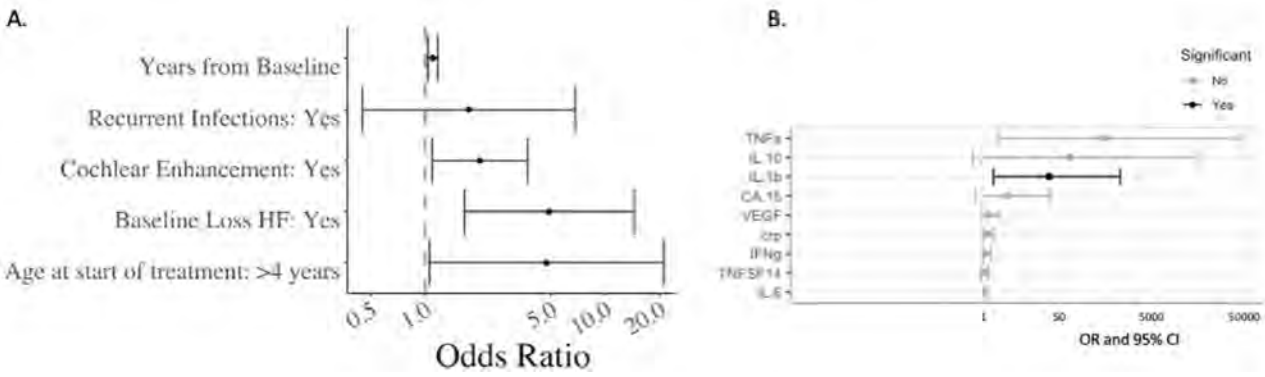
Results: The trajectory of hearing loss significantly differed between treated and untreated patients, indicating that IL-1 blockade slows down progression (p< 0.00001) (Figure 1). Yearly 4F-PTA increase on treatment was 0.35 dB in the good ear and 0.5 dB in the bad ear, compared to a 2.5 dB increase in the good ear and 2.9 dB in the bad ear prior to treatment. Yearly HF hearing loss worsened by 0.36 dB in the good ear (0.5 dB bad ear), compared to 3.11 dB in the good ear and 3.5 dB in the bad ear prior to treatment (Figure 1). Cochlear enhancement, age at start of treatment and baseline hearing loss significantly contributed to hearing loss progression; recurrent infections did not reach significance. The univariate logistic regression identified elevated cytokines associated with cochlear enhancement in the corresponding MRI. In 36 pts' CSF, IL-1b, and markers of endothelial, neutrophil and macrophage activation, E-Selectin, NGAL, and CD163, were significantly associated with cochlear enhancement.

Conclusion: Hearing loss continues to progress more than expected for age despite treatment. IL-1 blocking treatment (84 % on anakinra) in NOMID patients however significantly retards progression of hearing loss. Baseline hearing loss, older age at the start of treatment, and cochlear enhancement on brain MRI were associated with faster progression of hearing loss in treated NOMID patients. Cochlear enhancement was significantly associated with CSF levels of IL-1b and markers of neutrophil and macrophage activation, suggestive of subclinical inflammation as driver of onging hearing loss.

Figure 2:

A. Multivariate regression analysis revealed that aging, cochlear enhancement in MRI, presence of hearing loss at baseline, and late treatment initiation are associated with hearing loss progression.

B. Univariate regression of revealed that cochlear enhancement was associated with abnormal biomarkers in the CSF (E-Selectin, CD163, NGAL and IL-1β)



Disclosure: S. Alehashemi: None; **A. Ortega-Villa**: None; **M. Garg**: None; **K. Myint-Hpu**: None; **K. Johnson**: None; **F. BHUYAN**: None; **K. King**: None; **C. Zalewski**: None; **D. Fink**: None; **D. Kuhns**: None; **J. Butman**: None; **C. Brewer**: None; **H. Kim**: None; **D. Follmann**: None; **R. Goldbach-Mansky**: None.

Abstract Number: 2059

Management of Iatrogenic, Recombinant Interleukin-1 Receptor Antagonist-type Amyloidosis on NOMID in Patients on Anakinra

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Pediatric Rheumatology – Clinical Poster III: Potpourri

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with Neonatal-Onset Multisystem Inflammatory Disease (NOMID) often require long-term high-dose treatment with anakinra at 5-8 mg/kg daily subcutaneous injections to control CNS inflammation that includes aseptic meningitis, hydrocephalus, and sensorineural hearing loss. We recently described anakinra-associated amyloidomas that present with "fixed subcutaneous lumps" at the site of anakinra injections in patients with NOMID after 13 and 16 years of treatment [1] and screened our cohort for development of iatrogenic (Interleukin-1 receptor antagonist protein)-type amyloid (anakinra) (AIL1RAP).

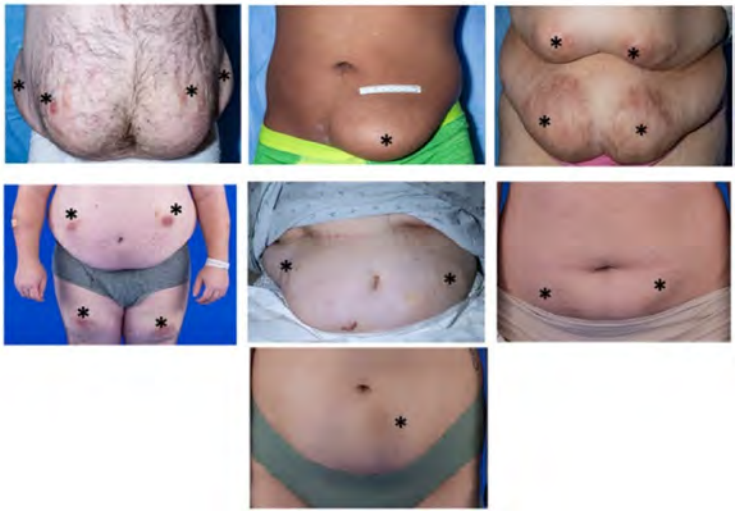
Methods: Telephone screening of 41 NOMID pts enrolled in NCT02974595 identified 10 pts with fixed subcutaneous lumps at the anakinra injection site. Of those six patients underwent skin biopsies, clinical assessment of treatment response, and serum IL-1 receptor antagonist measurements by ELISA, which measures endogenous and recombinant IL-1 receptor antagonist (anakinra). Liquid chromatography-tandem mass spectrometry (LC-MS/MS) was performed to chemically characterize microdissected amyloid deposits in skin biopsies.

Results: All seven patients biopsied had amyloid deposits at the deep dermis that by mass spectrometry was identified as recombinant of anakinra-type amyloid (AIL1RAP)[2] (Figure 1). All patients had been on a median 19 yrs. of treatment and received a median dose of 320 mg (3 syringes) daily. Table 1. All were in clinical remission with normal CRPs. One patient

Table 1: Characteristics of the NOMID cohort who developed recombinant IL-1 receptor antagonist-type amyloidosis

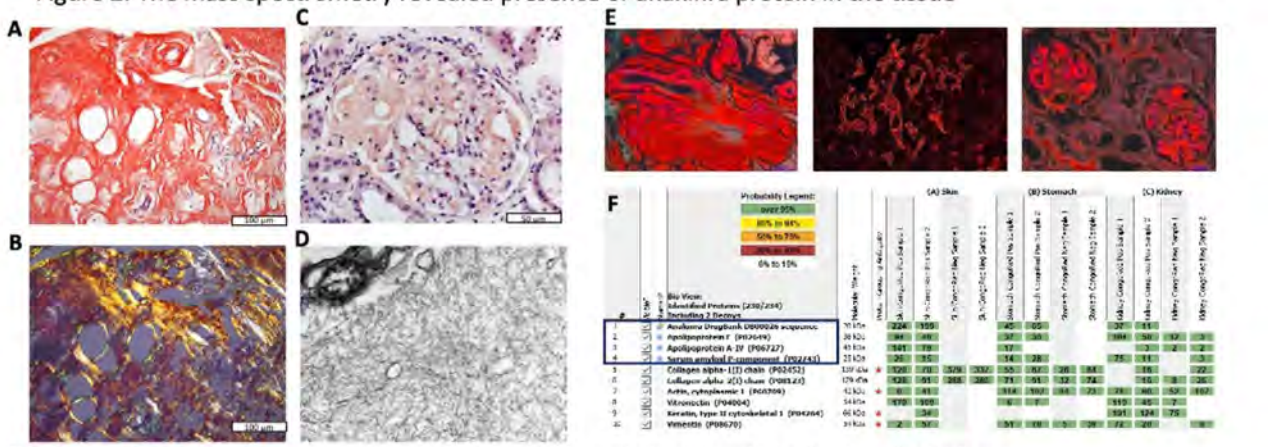
	NOMID N=7
Age median (range, yrs.)	31 (18-47)
Gender, female (%)	4 (60%)
BMI median (range)	31.5 (26-36)
Anakinra dose median (range)	320 (300-600 mg/day) 3 (3-6 mg/kg)
Years on treatment median (range, yrs)	19 (15-19)

Figure 1: Subcutaneous nodules at the site of anakinra injections



with nephrotic range proteinuria and early satiety had kidney and gastric biopsies that showed AIL1RAP deposits in glomeruli, the tubular basement membrane, and in-between glands in the gastric mucosa. The six other patients had no clinical evidence of disseminated amyloidosis. Serum IL-1ra levels (n=6) ranged from 7500 to 18,000 ng/mL, compared levels between 100-400 pg/mL in healthy controls (n=11). Patients with the focal form of the AIL1RAP amyloidosis were switched to the combination of canakinumab injections every 4 wks and anakinra injections between 50-200 mg daily, that were required to achieve control of headache and CNS inflammation. The patient with systemic Amyloidosis only received canakinumab but developed headaches. The CSF evaluation showed a rise in the IL-6 (from 2 pg/mL on anakinra alone before the switch) to 403 pg/mL (nl< 7.5 pg/mL) on canakinumab monotherapy (300mg/month).

Figure 2: The mass spectrometry revealed presence of anakinra protein in the tissue



A) Skin biopsy with extensive subcutaneous Congo red-positive amyloid deposits in an interstitial and perivascular distribution.
B) Apple-green birefringence of the Congo red-stained cutaneous amyloid under polarized light.
C) Kidney biopsy with Congophilic deposits in the mesangium and a capillary wall. D) High magnification transmission electron microscopy (TEM) image of amyloid deposits that revealed randomly oriented fibrils(X50,000).
E) Microdissection of the amyloid deposits F) liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis of CongoRed postive and Congo red-negative areas in the skin, stomach, and kidney biopsies. Proteins in the blue box indicate the amyloidogenic anakinra (dual yellow/blue star) and the three universal amyloid signature proteins (blue stars). Numbers in green boxes indicate the total number of MS/MS spectra matched to the protein in the corresponding biopsy and are a semi-quantitative measure of abundance. High spectral counts of the amyloid signature proteins (Apolipoprotein E, Apolipoprotein A-IV, and serum amyloid P-component) and the amyloidogenic IL1RA protein (anakinra) are present in CongoRed positive areas and absent in CongoRed negative areas.

Conclusion: AIL1RAP skin amyloidosis developed in 7 NOMID patients (20 % of screened patients) on high-dose long-term, anakinra treatment; one patient developed systemic AIL1RAP amyloidosis. Combination of canakinumab with lower anakinra doses, controlled CNS inflammation however "safe" serum levels that prevent the development and dissemination iatrogenic AIL1RAP amyloidosis have not been established. Screening all patients, early diagnosis of AIL1RAP-type amyloid and treatment adjustments are critical in assuring adequate treatment and in reducing the risk of developing systemic AIL1-RAP amyloidosis.

Disclosure: S. Alehashemi: None; **A. Metpally**: None; **S. Dasari**: None; **K. Uss**: None; **L. Hathaway**: None; **D. Kuhns**: None; **D. Fink**: None; **C. Lee**: None; **L. Castelo-Soccio**: None; **E. Cowen**: None; **S. Nasr**: None; **E. McPhail**: None; **R. Goldbach-Mansky**: None.

Abstract Number: 2060

Creation of a Standardized and Collaborative Transfer Process from Pediatric to Adult Rheumatology

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Pediatric Rheumatology – Clinical Poster III: Potpourri
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The transfer of care from pediatric to adult rheumatology (AR) is a complex process dependent on communication between medical teams within and across institutions, resource allocation, and patient factors. We outline a successful workflow for the transfer of care that optimizes clinical informatics and includes the creation of a formal collaboration between pediatric rheumatology (PR) and AR.

Methods: In January 2020 a transition-focused partnership was formed between PR and AR physicians, advanced practice providers, nurses, and pharmacists within the University of Colorado (CU)health system. Upon initiation of the transfer process in PR, a standardized electronic medical record checklist is used to guide the transfer workflow and leverage smart data elements to optimize patient tracking. A pediatric transition committee monitors each patient's transfer progress, ensuring checklist items are complete and initiating direct communication with AR. A cross-institutional transfer log is maintained using a HIPAA-compliant platform. Patients transferring to CU AR are reviewed quarterly at interdisciplinary transfer rounds attended by PR and AR members. Each patient is reviewed to identify barriers for those who have not been scheduled in AR. The records of all patients are periodically reviewed to identify correlates of success as well as risks and system barriers for transfer delays and failures.

Results: The creation of customized templates and data collection tools in the electronic medical record, a cross-institutional patient tracking system, and a collaborative PR-AR transition committee with quarterly transfer rounds have all been sustainable successes. Since the initiation of transfer rounds in January 2022, 54% of patients initially identified as lost to transfer were recaptured, with subsequent successful scheduling in AR. Of the forty-three patients reviewed to date by this committee, only four remain lost to follow-up.

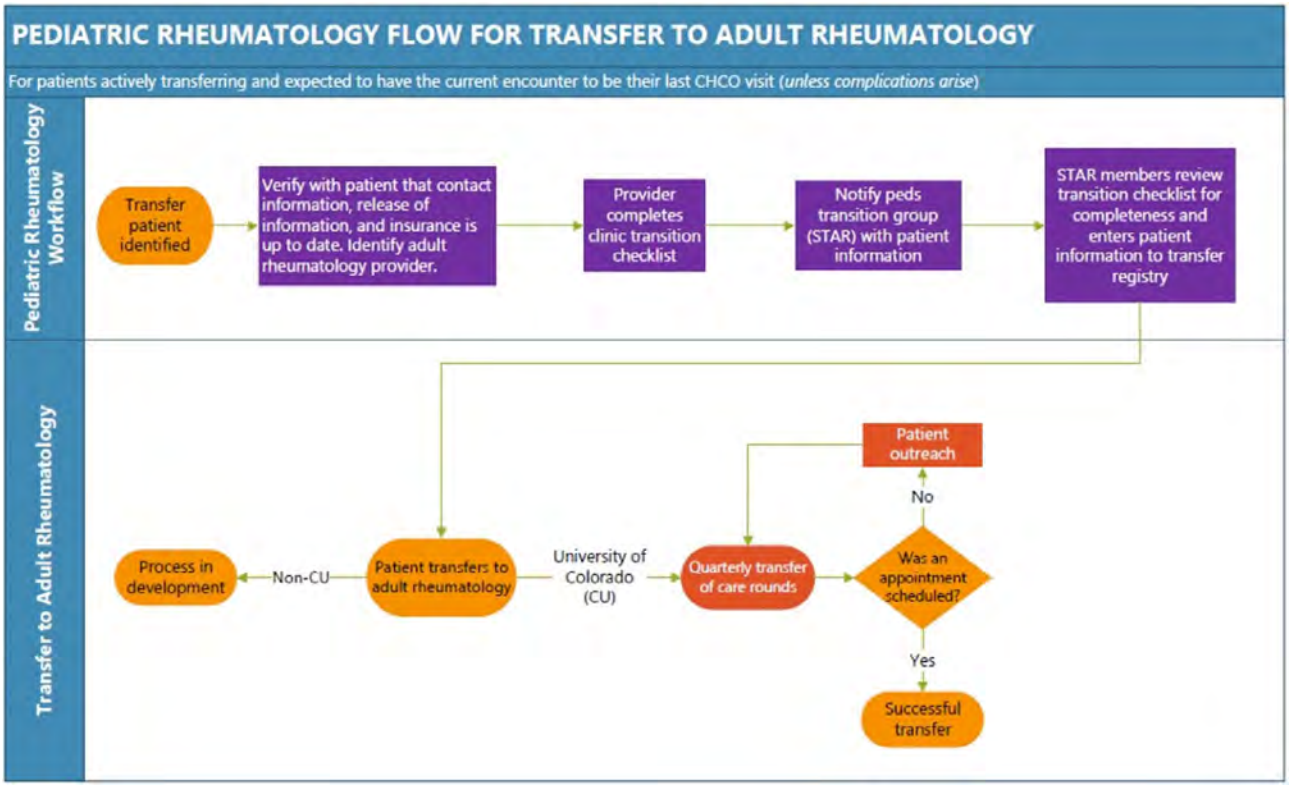

Figure 1: Transfer of Care Process

Conclusion: Pediatric and adult rheumatology team members successfully formed an interdisciplinary partnership with a standardized process for identifying and tracking patients who transfer from pediatric to adult care within one health system. Standardized electronic medical record workflows and the use of a PR-AR transfer log help centralize information and facilitate review during transfer rounds, allowing for the identification of system and patient-level barriers. Transfer rounds minimize loss of patient follow-up and facilitate opportunities for iterative changes to the rheumatology transfer process. The establishment of a pediatric and adult subspecialty committee is a sustainable intervention that could be carried out with extramural adult practices and holds promise for improving transfer of care outcomes.

Disclosure: A. Haussmann: None; **L. Taylor-Maloney**: None; **I. Pan**: None; **K. Nowicki**: None; **J. Zell**: None; **K. Moore**: None.

Abstract Number: 2061

Evaluation of a Tool to Enhance Training of the Physical Examination of the Temporomandibular Joint (TM Joint) in Juvenile Idiopathic Arthritis (JIA)

Tova Ronis[1], Nancy Pan[2], Rebecca Sadun[3], Melissa Lerman[4], Cory Resnick[5], James Bost[6], Peter Stoustrup[7], Marinka Twilt[8] and for the CARRA TMJ Arthritis Workgroup[9], [1]Children's National Hospital, Chevy Chase, MD, [2]Hospital for Special Surgery, New York, NY, [3]Duke University, Durham, NC, [4]Children's Hospital of Philadelphia, Philadelphia, PA, [5]Harvard Medical School, Boston, MA, [6]Children's Health Center, Children's National Medical Center, Washington, DC, [7]Aarhus University, Aarhus, Denmark, [8]Alberta Children's Hospital, Calgary, AB, Canada, [9]Childhood Arthritis and Rheumatology Research Alliance, Washington, DC

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Arthritis of the TM joint is a frequent finding in patients with JIA, potentially leading to dentofacial deformities, pain, and lower quality of life.[1] Orofacial examination enables early detection of TM joint involvement.[2] The TM Joint Juvenile Arthritis Work Group published a standardized physical exam (article) to assess for JIA-induced orofacial manifestations.[2] Training programs do not routinely teach a standardized TM joint exam. The aim of the study was to demonstrate the effectiveness of a novel e-learning module in teaching the physical exam of the TM joint in JIA.

Methods: A 20-minute e-learning module consisting of instructive videos and interactive questions was created. Pediatric rheumatology fellows participated in a study to assess the module. Block randomization was performed, and fellows were stratified by post-graduate year. One group received the article while the second group received both the article and access to the e-learning module. All participants completed a written pre-test before the learning intervention andthen underwent both: an in-person objective structured clinical examination (OSCE)during the Childhood Arthritis and Rheumatology Research Alliance Scientific Meeting inMarch 2023; and a written post-test. The maximum OSCE score was 18. Crosstab tables and Chi-squared tests were used to assess categorical variables across groups. For continuous measures when comparing the two groups, Wilcoxon Rank Sum tests were used due to the small sample size.

Results: Twenty-two pediatric rheumatology fellows enrolled, with 11 in each group. Both reported an equal amount of time spent preparing for the OSCE (mean 34.8 mins). *Written test:* The two groups performed equally. There was a trend toward significance in defining maximal incisal opening (MIO) on the written test in the module group. Both groups had a trend towards improvement in recognition of patient profiles and facial asymmetry. *OSCE:* The mean OSCE score was 11.1 (SD 3.3) in the article group and 13.5 (SD 1.9) in the module group, with a trend towards significance (p=0.059). Significant differences were seen on the OSCE in learning domains related to measuring MIO, calculating maximal unassisted mouth opening (MUMO), and assessment of facial symmetry. There were no differences in other domains (see Table 1). Confidence in TM joint exam skills was increased in all fellows after the intervention with no difference between groups (Figure 1). Enjoyment scores in the module group were higher than in the article group (mean 7.7/10 vs 5.9/10, p=0.017) (Figure 2).

Table 1. OSCE scores by learning group. OSCE: objective structured clinical examination, MUMO: maximal unassisted mouth opening.

	Module Mean (SD)	Article Mean (SD)	P value (Wilcoxon Rank Sum Test)
OSCE total score	13.54 (1.91)	11.09 (3.27)	0.059
History taking	3.09 (0.94)	2.82 (1.08)	0.581
Palpation	2 (0.63)	2.27 (0.90)	0.214
Mandibular deviation	2.54 (1.13)	2.09 (1.37)	0.418
Measurements	4.09 (1.38)	2.36 (1.21)	0.005
MUMO calculation	1.45 (0.93)	0.36 (0.81)	0.012
Symmetry	1 (0)	0.63 (0.50)	0.030
Profile	0.81 (0.40)	0.91 (0.30)	0.543

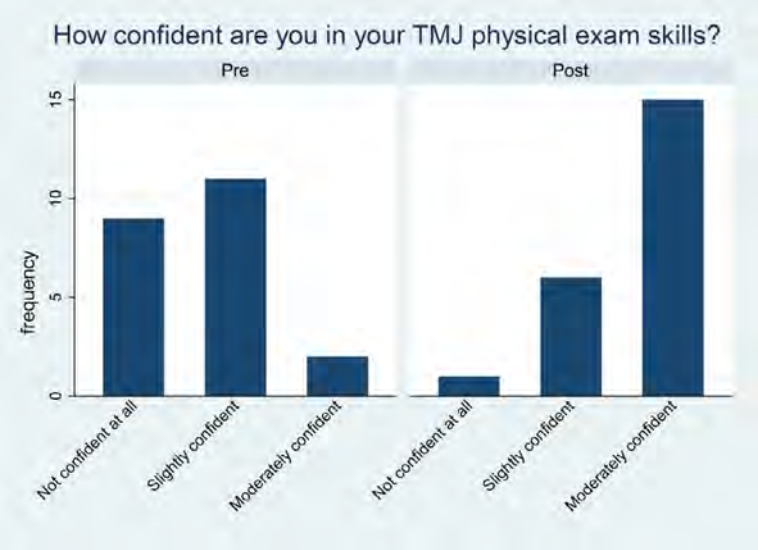

Figure 1. Self-reported confidence in TM Joint physical exam skills before and after the learning intervention for all participants. No difference was noted between groups.

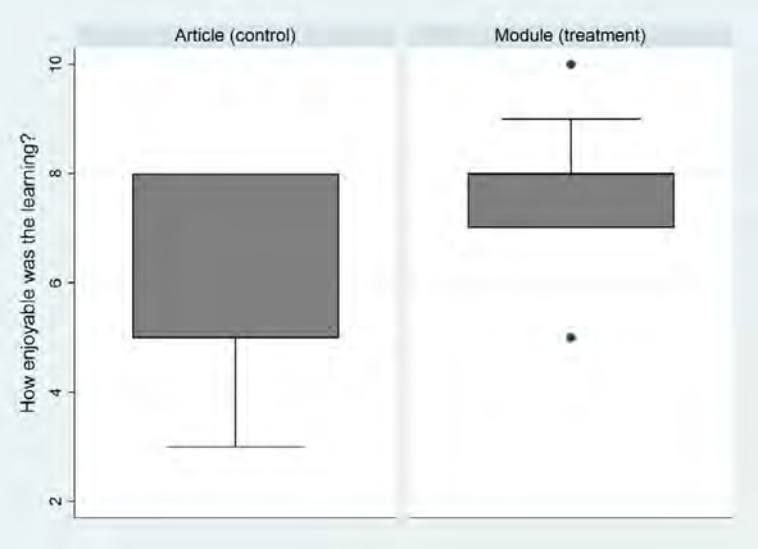

Figure 2. Participant response to "How enjoyable was the learning?"

Conclusion: This study demonstrated effectiveness of a novel e-learning module in teaching the physical exam of the TM joint in JIA. Learners who viewed the module were more adept at obtaining quantitative TM joint measurements than those who read the article. Both groups showed improvement in overall skill and confidence level, although the module group enjoyed the learning experience more.

References:

1.Stoll ML et al. TM joint arthritis in JIA, now what? *Pediatr Rheumatol*. 2018;16(1):32.
2.Stoustrup P et al. Standardizing the clinical orofacial examination in JIA: An interdisciplinary, consensus-based, short screening protocol. *J Rheumatol*. 2020:47(9):1397

Disclosure: T. Ronis: None; **N. Pan**: None; **R. Sadun**: None; **M. Lerman**: None; **C. Resnick**: AbbVie/Abbott, 2; **J. Bost**: None; **P. Stoustrup**: None; **M. Twilt**: None; **f. the CARRA TMJ Arthritis Workgroup**: None.

Abstract Number: 2062

A Mental Health Workshop for Pediatric Rheumatology Fellows

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Many children with a rheumatic disease have concurrent mental and behavioral health challenges, but only ~40% of these symptoms are brought to medical attention. Per an American Board of Pediatrics (ABP) survey, more than 75% of pediatric rheumatology fellows believe it is important for them to address the mental health needs of their patients, but fewer than 25% feel confident in their skills to do so. Importantly, a Childhood Arthritis and Rheumatology Research Alliance (CARRA) survey demonstrated that both rheumatology patients and their parents feel most comfortable discussing their mental health concerns with their pediatric rheumatologist.

Methods: Using the ABP Roadmap Project curriculum as a framework, a 2-hour virtual mental health workshop specifically tailored to the needs of pediatric rheumatology fellows was developed and delivered as a collaboration between a child and adolescent psychiatrist and a pediatric rheumatologist. Through the workshop, participants were instructed in a strategic approach to mental health conversations, taught to utilize validated mental health screening tools, and provided guidelines on the identification of high-risk patients who need urgent mental health services. Participant confidence in addressing 11 mental healthcare domains was assessed using a retrospective pre/post survey with a 4-point Likert scale (very low to very high confidence). Descriptive statistics and a paired t-test were used in data analysis.

Results: Twenty-six of the 37 (70%) participatingpediatric rheumatology fellows completed the workshop survey, with roughly equal distribution across the three years of fellowship training (Table 1). The retrospective pre/post survey revealed a significant increase in participants' confidence across all 11 mental health domains (Table 2). No difference was detected by postgraduate year. Pre-workshop, participants reported the least confidence in safety planning for high-risk patients (mean = 2.03), with level of confidence rising by more than 1 point post-workshop (mean = 3.13). Pre-workshop, participants reported the highest confidence in recognizing the signs and symptoms of depression and anxiety (mean = 2.93), with confidence rising to 3.37 post-workshop. Confidence scores across the 11 domains increased from 2.34 (2=low confidence) to 3.29 (3=high confidence). No participants rated their comfort level as very low for any of the 11 domains following

Table 1. Pre- and post-workshop confidence (averaged over all 11 domains) stratified by fellowship year, juxtaposed with averaged pre- and post-workshop confidence of the four participating pediatric rheumatology faculty. Confidence level measured on a 4-point Likert scale (1 = "very low" confidence, 2 = "low" confidence, 3 = "high" confidence, 4 = "very high" confidence).

	Respondent Number (%)	Pre-Workshop Mean	Post-Workshop Mean	Mean Confidence Gain
Fellows				
First year	10 (33%)	2.34	3.29	0.95
Second year	8 (27%)	2.33	3.19	0.86
Third year	8 (27%)	2.42	3.45	1.03
Faculty				
Total	4 (13%)	2.20	3.16	0.95

Table 2. Pre- and post-workshop confidence for each of the 11 domains. Confidence level measured on a 4-point Likert scale (1 = "very low" confidence, 2 = "low" confidence, 3 = "high confidence, 4 = "very high" confidence).

Domain	Pre-Workshop Mean	Post-Workshop Mean	P-value
Initiate a conversation with patients and their caregivers about mental health concerns	2.70	3.53	< 0.0001
Recognize the signs and symptoms of depression and anxiety	2.93	3.37	0.0002
Talking with caregivers about things in their lives that cause them stress related to their child's health or care	2.40	3.20	< 0.0001
Providing individual resources and guidance to improve the mental health and quality of life for patients	2.07	3.23	< 0.0001
Providing individual resources and guidance to improve the mental health and quality of life for caregivers and families	2.07	3.17	< 0.0001
Interpreting a PHQ-9	2.70	3.50	< 0.0001
Interpreting a GAD-7	2.40	3.23	< 0.0001
Discussing suicidal ideation with a patient	2.20	3.40	< 0.0001
Stratifying a patient's risk of suicide	2.17	3.27	< 0.0001
Providing safety planning to reduce the likelihood of death by suicide	2.03	3.13	< 0.0001
Explaining the risks and benefits of an SSRI to a patient and caregivers	2.07	3.17	< 0.0001
Overall	**2.34**	**3.29**	**< 0.0001**

the workshop. When asked what changes they will implement following the workshop, 60% stated they will routinely screen patients, 30% will discuss mental and emotional health with all patients, and 30% plan to explore mental health resources in their state. On a 10-point Likert scale, with 10 being extremely relevant or extremely helpful, participants rated the workshop at a relevance of 9.67 and a helpfulness of 9.33.

Conclusion: A virtual training workshop improved pediatric rheumatology fellows' confidence in addressing the mental and emotional healthcare needs of their patients. Additional training could further foster a robust and standardized approach to assessing and addressing the mental health needs of pediatric patients with rheumatic disease.

Disclosure: C. Pinotti: None; **A. Manning**: None; **S. Edison**: None; **R. Sadun**: None.

Abstract Number: 2063

Training to Increase Minority Enrollment in Lupus Clinical Trials with CommunitY Engagement (TIMELY): Assessing Behavioral Predictors of Clinical Trial Referrals Among Healthcare Providers

Saira Sheikh[1], Tessa Englund[1], Andrew Simkus[2], Nicole Wanty[3], Annie McNeill[4], Kristen Holtz[4], Tenesha Hood[5], Starla Blanks[6], Maria Allen[7] and Allen Anandarajah[7], [1]University of North Carolina at Chapel Hill, Chapel Hill, NC, [2]KDH Research & Communication, Asheville, NC, [3]KDH Research & Communication, Marietta, GA, [4]KDH Research & Communication, Atlanta, GA, [5]ACR, Atlanta, GA, [6]American College of Rheumatology, Atlanta, GA, [7]University of Rochester Medical Center, Rochester, NY

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The aim of this study is to assess outcomes among healthcare providers in the American College of Rheumatology's (ACR) Training to Increase Minority Enrollment in Lupus Clinical Trials with CommunitY Engagement (TIMELY) program. The TIMELY program was designed to improve engagement of healthcare providers and therefore promote referrals of underrepresented patients with lupus to clinical trials (LCTs). Enrolled providers participated in two components of the TIMELY program: 1) The ACR's Materials to Increase Minority Involvement in Clinical Trials (MIMICT) continuing medical education (CME) course; and 2) Roundtable meetings where providers learned about and discussed barriers, strategies, and opportunities to advance participation of underrepresented patients in LCTs.

Methods: This roundtable study used an online survey to evaluate pre-post changes in theory-based behavioral predictors of clinical trial referrals, including attitudes, self-efficacy, and intentions to refer underrepresented patients to LCTs. Research teams at two participating sites, the University of North Carolina at Chapel Hill (UNC) and University of Rochester Medical Center (URMC), began enrollment in June 2022 and implemented the TIMELY roundtables between September 2022 and April 2023. Community members, community health workers, and advisory committee members provided extensive support and guidance to facilitate TIMELY roundtable implementation. In conjunction with the ACR, sites recruited participants and hosted roundtables in-person and online with regional providers who care for patients with lupus. Providers completed a baseline survey prior to roundtable participation, and post-roundtable, and 3-month follow-up surveys. We conducted paired t-tests between baseline and follow-up to assess differences in composite scores and individual measures for each outcome.

Results: As of April 2023, the sample included 35 providers. From baseline to follow-up, composite scores for self-efficacy increased from 6.62 to 7.42 ($p< 0.01$) and composite scores for intentions increased from 7.14 to 8.21 ($p=0.001$).

Conclusion: These promising findings highlight the potential of the TIMELY program to improve theory-based behavioral predictors of provider referrals of underrepresented patients to LCTs.

Disclosure: S. Sheikh: AstraZeneca, 2, Aurinia Pharmaceuticals Inc., 2, Biogen, 2, GSK, 1, 1, 2, Lilly USA, 2, Pfizer, 5; **T. Englund**: None; **A. Simkus**: None; **N. Wanty**: None; **A. McNeill**: None; **K. Holtz**: None; **T. Hood**: None; **S. Blanks**: None; **M. Allen**: None; **A. Anandarajah**: None.

Abstract Number: 2064

Perceptions of Rheumatology Fellows on Mentorship Quality After Implementation of a Formalized Mentorship Program

Sarah Capponi[1] and Rachel Hilburg[2], [1]Hospital of the University of Pennsylvania, New Hope, PA, [2]Hospital of the University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite the importance of mentorship, there are few formalized mentorship organizations in fellowship training programs. Rheumatology is a field with increasing popularity[1], and mentorship is suggested as one of many reasons for this trend[2], yet no formalized mentorship programs in adult Rheumatology fellowships have been described at the time of this writing. In the 2022-2023 academic year, the Hospital of the University of Pennsylvania (Penn) Rheumatology fellowship program implemented a formalized mentorship program for trainees. Trainees identified a faculty member to serve as their mentor and pairs met quarterly to discuss educational, personal, and career goals. It was hypothesized that this program would improve trainee satisfaction overall compared with fellows who had completed fellowship without formal mentorship.

Methods: Data from previously graduatedPenn Rheumatology Fellows and currentPenn Rheumatology Fellows was collected via anonymous survey.

Results: 32 fellows with graduation years from 2016 – 2024 were surveyed and 26 responded, with an 81% overall response rate of current and former Penn Rheumatology fellows.

In the group of former fellows, 28% did not identify a faculty mentor and 72% did. Cited barriers to having a mentor included lack of time, lack of faculty interest, and the absence of the establishment of a formal mentoring relationship with faculty. In the current fellow cohort, 100% identified mentors.

Fellows who graduated prior to the mentorship program reported 11.8% more satisfaction with perceived effectiveness of their mentor's ability to advance their clinical skills (p-value 0.01).

Fellows who experienced the formalized mentorship program were 12.1% more satisfied with their assigned mentor's ability to help them network and increase opportunities for professional development; they also were 12.1% more satisfied with their mentor's sponsorship and advocacy during training (p-value 0.03).

There were no differences between the two cohorts of fellows with respect to their mentor's impact on their post fellowship career planning, perceived research productivity, and guidance through handing sensitive or challenging issues that arose during fellowship.

Overall, perceptions of the fellowship program independent of mentorship were largely positive, without statistically significant differences between the two cohorts of fellows.

Conclusion: Implementation of formalized mentorship programs in fellowship leads to improved trainee perceptions of faculty investment in their careers through sponsorship and networking; however, this small, single program survey did not show the establishment of a formalized mentor-mentee relationship improved trainee perceptions of improved clinical skills, research productivity, or ability to handle challenging interactions during fellowship.

[1] Tran, Mathias, and Panush, "Has Rheumatology Become a More Attractive Career Choice?"

[2] Kolasinski et al., "Subspecialty Choice."

Disclosure: S. Capponi: None; **R. Hilburg**: None.

Abstract Number: 2065

Exploring the Power of Ultrasound in Rheumatology: Insights from Young Rheumatologists in Mexico

Mario R. Garcia-Pompermayer[1], Sarah G. Ayton[2], Karina Silva Luna[3] and Mario Alberto Garza Elizondo[3], [1]Hospital San Jose, TecSalud, Tecnologico de Monterrey, Monterrey, Mexico, [2]Mailman School of Public Health, Columbia University, New York, NY, [3]Hospital Zambrano-Hellion, TecSalud, Tecnologico de Monterrey, Monterrey, Mexico

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
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Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Musculoskeletal ultrasound (MSUS) is a valuable tool in Rheumatology as it is non-invasive, cost-effective, and useful in regular clinical practice. However, its adoption has been slow and MSUS education in Mexico is limited. Our objective is to assess MSUS knowledge, attitudes, and practices in young Rheumatologists in Mexico and identify potential barriers and facilitators to its clinical use.

Methods: An online survey was distributed to ReumaJoven, a network of young Rheumatologists in Mexico. The survey captured demographics, and general, institutional, and personal MSUS information. The need for MSUS in Rheumatology in Mexico was assessed for association with knowledge, attitudes, and practices. Multivariable analysis using elastic net and bootstrapping identified drivers of respondent attitudes.

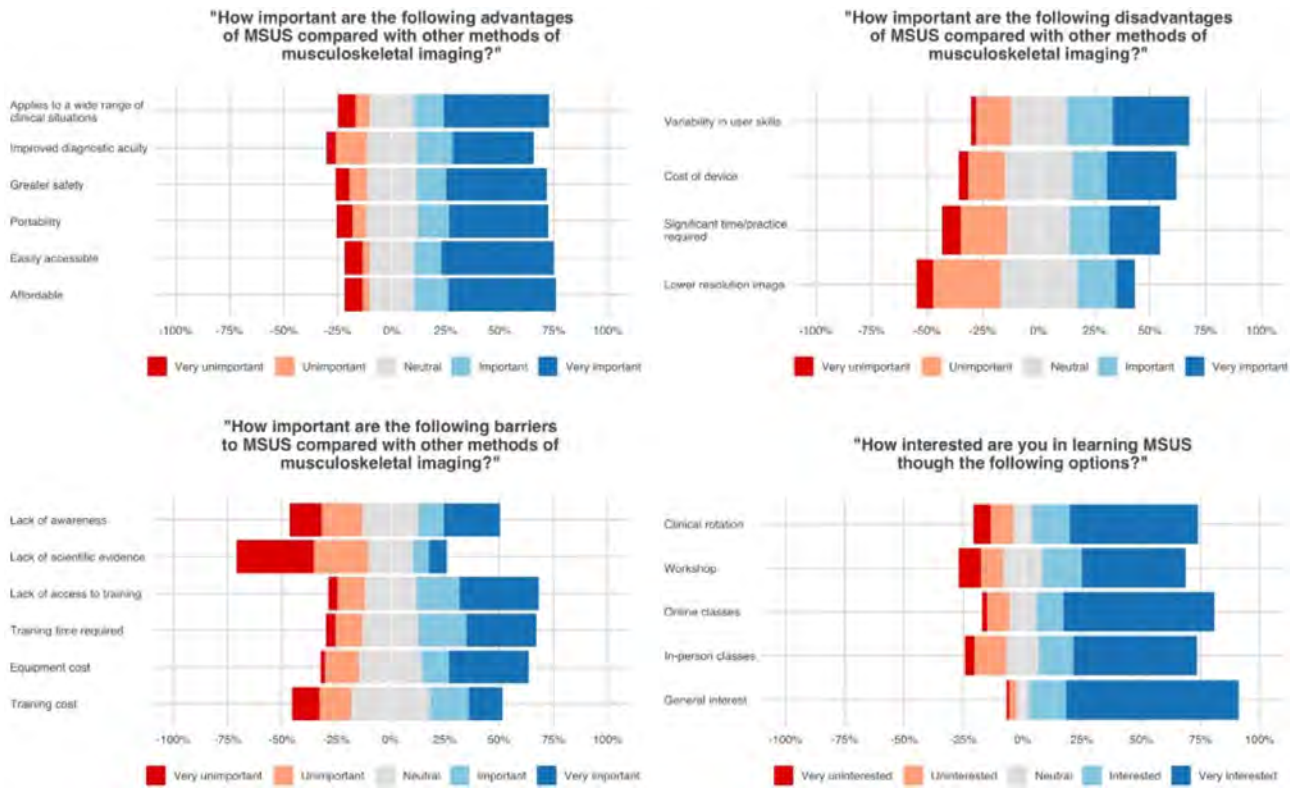

Figure 1. Responses to questions about the advantages, disadvantages, interest in learning, and barriers to implementing (clockwise from top left) MSUS among young Rheumatologists in Mexico.

Results: Rheumatologists (n=91) completed the survey (women: n=52, 54.17%, age: median=35.08, IQR: 32.79-37.73 years). Most worked in public hospitals (n=65, 67.71%) and private practices (n=80, 83.33%), including residents (n=5, 5.21%), professors (n=37, 38.54%), and non-academic clinicians (n=54, 56.25%). The most prominent barriers to MSUS were lack of access to training (important or very important: n=54, 56.25%) and training time required (n=52, 54.17%). Lack of scientific evidence was not an important barrier to MSUS use (unimportant or very unimportant: n=58, 60.42%). Most (n=78, 81.25%) reported MSUS is necessary in clinical Rheumatology practice in Mexico. This positive MSUS attitude was significantly associated with learning about MSUS from conferences (p=0.029) and colleagues (p=0.005), formal (p=0.043) and in-person training (p=0.020), use in the respondent's practice (p=0.027), and MSUS use by Radiologists in the respondent's institute (p< 0.001). Most were interested in learning MSUS (n=85, 88.54%), which was significantly increased in those reporting positive MSUS attitudes (n=74, 94.49%, p< 0.001). Elastic net identified drivers of positive MSUS attitudes, including learning about MSUS from conferences, colleagues, and in residency; use of MSUS in the respondent's practice, the respondent performing MSUS, using MSUS for diagnosis or monitoring of Synovitis/Inflammatory joint disease; and use of MSUS by Radiologists in the respondent's institute. Use of MSUS for diagnosis or monitoring of Synovitis/Inflammatory joint disease (OR=1.43, 95%CI: 1.00-2.05) and use of MSUS by Radiologists in the respondent's institute (OR=1.70, 95%CI: 1.20-2.90) were statistically significantly associated with positive MSUS attitudes in the final multivariable analysis.

Conclusion: This study assessed knowledge, attitudes, and practices of MSUS among young Rheumatologists in Mexico and identified barriers and facilitators to its implementation. Most recognized the necessity of MSUS in clinical practice, particularly those with prior training, who used MSUS in their practice, and had access to MSUS expertise. Improving MSUS

Table 1. Characteristics of MSUS knowledge, practices, and attitudes among 96 young Rheumatologists in Mexico.

	Characteristic	Overall	Need for MSUS in Rheumatology Practice in Mexico			Multivariable Analysis (Elastic Net)	
			Necessary (N = 78)	Not Necessary (N = 18)	P-value		
		N (%)	N (%)	N (%)		OR	(95% CI)
	Total	96 (100%)	78 (81.25%)	18 (18.75%)			
Knowledge	**First Learned about MSUS**						
	Academic Articles	55 (57.29%)	46 (58.97%)	9 (50.00%)	0.500	-	
	Conferences/ Congresses	59 (61.46%)	52 (66.67%)	7 (38.89%)	0.029	1.01	(0.61 - 1.02)
	Colleagues	50 (52.08%)	46 (58.97%)	4 (22.22%)	0.005	1.50	(0.98 - 2.26)
	Medical School	22 (22.92%)	19 (24.36%)	3 (16.67%)	0.800	-	
	Residency	69 (71.88%)	59 (75.64%)	10 (55.56%)	0.088	1.02	(0.54 - 1.05)
	MSUS Specialty	1 (1.04%)	1 (1.28%)	0 (0.00%)	>0.900	-	
	Any Prior MSUS Training	55 (57.29%)	46 (58.97%)	9 (50.00%)	0.500	-	
	Hours of Formal MSUS Training				0.043	-	
	<15 hours	14 (31.82%)	11 (28.21%)	3 (60.00%)			
	15-30 hours	7 (15.91%)	5 (12.82%)	2 (40.00%)			
	45-60 hours	1 (2.27%)	1 (2.56%)	0 (0.00%)			
	>60 hours	22 (50.00%)	22 (56.41%)	0 (0.00%)			
	Form of MSUS Training						
	In-Person Classes	28 (29.17%)	24 (30.77%)	4 (22.22%)	0.500	-	
	In-Person Class Duration				0.020	-	
	<1 week	10 (27.03%)	7 (21.88%)	3 (60.00%)			
	1-2 weeks	4 (10.81%)	2 (6.25%)	2 (40.00%)			
	3-4 weeks	3 (8.11%)	3 (9.38%)	0 (0.00%)			
	1-6 months	7 (18.92%)	7 (21.88%)	0 (0.00%)			
	>6 months	13 (35.14%)	13 (40.62%)	0 (0.00%)			
Practices	**MSUS Use in Respondent's Practice**						
	Used in Clinical Practice	74 (77.08%)	64 (82.05%)	10 (55.56%)	0.027	1.07	(0.52 - 1.14)
	Performs MSUS in Clinical Practice	20 (20.83%)	20 (25.64%)	0 (0.00%)	0.020	1.19	(0.94 - 1.41)
	Application of MSUS Use in Respondent's Practice						
	Diagnosis	52 (54.17%)	48 (61.54%)	4 (22.22%)	0.003	1.18	(0.80 - 1.39)
	Tendon/Muscular/Ligament Pathology	46 (47.92%)	42 (53.85%)	4 (22.22%)	0.015	-	
	Synovitis/Inflammatory joint disease	50 (52.08%)	47 (60.26%)	3 (16.67%)	<0.001	1.43	(1.00 - 2.05)
	Sjogren's syndrome	8 (8.33%)	8 (10.26%)	0 (0.00%)	0.300	-	
	Vasculitis	6 (6.25%)	6 (7.69%)	0 (0.00%)	0.600	-	
	Guided Infiltration/Aspiration Procedures	32 (33.33%)	30 (38.46%)	2 (11.11%)	0.027	-	
	Specialists Using MSUS in Respondent's Institute						
	Rheumatologists	30 (31.25%)	25 (32.05%)	5 (27.78%)	0.700	-	
	Radiologists	45 (46.88%)	43 (55.13%)	2 (11.11%)	<0.001	1.70	(1.20 - 2.90)
	Orthopedists	7 (7.29%)	7 (8.97%)	0 (0.00%)	0.300	-	
	Physiotherapists	4 (4.17%)	4 (5.13%)	0 (0.00%)	>0.900	-	
	Rehabilitation	1 (1.04%)	0 (0.00%)	1 (5.56%)	0.200	-	

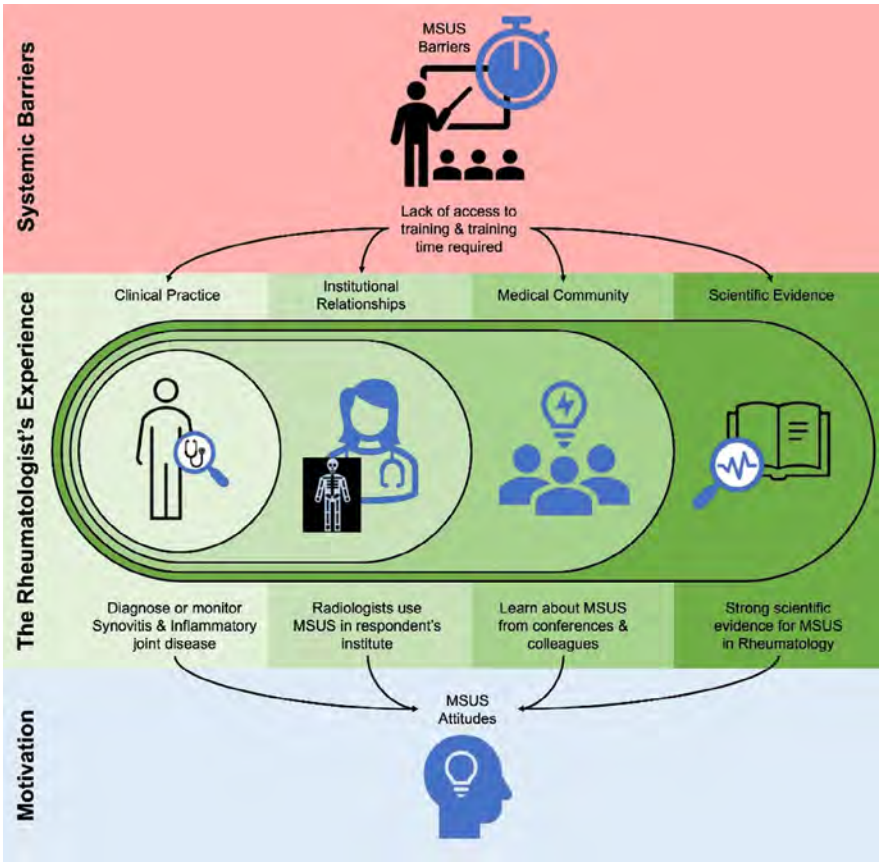

Figure 2. Overview of facilitators and barriers to implementing MSUS in clinical practice. Systemic barriers to MSUS implementation impact the Rheumatologist's experience of their clinical practice, institutional resources, knowledge shared in the medical community, and the available scientific evidence. Notably, use of MSUS for diagnosis and monitoring synovitis and inflammatory joint disease in clinical practice, having Radiologists who use MSUS in their institute, learning about MSUS from the medical community, and the strong scientific evidence surrounding MSUS all drive positive attitudes and impact motivation to implement MSUS.

education and training opportunities, and promoting collaboration between Rheumatologists and Radiologists may overcome barriers to adoption of MSUS in Mexico, ultimately improving patient care.

Disclosure: M. Garcia-Pompermayer: None; **S. Ayton**: None; **K. Silva Luna**: None; **M. Garza Elizondo**: None.

Abstract Number: 2066

Ultrasound Guided Synovial Biopsy Course: Achievement of Learner Self Efficacy

Diane Horowitz[1], Darren Tabechian[2], Ami Ben-Artzi[3], Karina Torralba[4] and Arthur Mandelin[5], [1]Northwell Health, Great Neck, NY, [2]University of Rochester Medical Center, Rochester, NY, [3]Ami Ben Artzi, MD, San Diego, CA, [4]Loma Linda University, Loma Linda, CA, [5]Northwestern University Feinberg School of Medicine, Chicago, IL

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Professional Education Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Ultrasound guided synovial biopsy (UGSB) is a minimally invasive, safe and effective tool to obtain synovium for clinical and research purposes. Described in Europe in 1997, UGSB was introduced to US rheumatologists in 2015 via the NIH-AMP program. Logistical barriers, learner confidence and the lack of a critical mass of trained rheumatologists to assist new learners have impeded the adaptation of UGSB in the USA. UGSBy, a collaborative group of four USA-based rheumatologists who completed the 2015 NIH-AMP program, was formed to develop a network of rheumatologists skilled in UGSB. In 2022, UGSBy partnered with the Ultrasound School of North American Rheumatologists (USSONAR) and conducted 3 courses in the USA to expand the workforce of USGB trained rheumatologists. An emphasis on patient safety was an integral feature of these courses. This study was conducted to determine the effectiveness of these courses in allowing learners to integrate knowledge with acquisition of skills in UGSB.

Methods: Three courses were conducted (1:15 students, 2:16 students, 3:14 students). Each course consisted of didactic and hands-on cadaver training. Instructor to learner ratio was 1:4. Musculoskeletal ultrasound competence was a course prerequisite which was defined as prior certification and/or documented course completion in basic-advanced musculoskeletal ultrasound. Serial surveys were deployed at the course completion (T0) and every 3 months after (T3, T6…). Learner confidence was assessed with the L-SES, a validated learning self-efficacy scale (L-SES) for Clinical Skills, consisting of 12 five-point Likert scale (strongly disagree-strongly agree) based questions to measure three domains: cognitive (Cog), affective (Aff) and psychomotor (Psy). The L-SES has been shown to directly correlate with academic achievement and effective learning strategy use.

Results: Learners from the first course reported positive mean L-SES in the cognitive domain (Cog=3.85, Aff=2.9, Psy=2.9, n=5) at T6. Learners from the second course demonstrated a positive mean LES in all three domains at T0 (Cog=4.4, Aff=3.7, Psy=3.84, n=16); at T3 the cognitive and psychomotor domains had a positive L-SES (Cog=3.9, Aff=2.9, Psy=3.25, n=4). A learner from the first course performed a first biopsy 5 months after the course.

Conclusion: Integration of knowledge with skill acquisition in UGSB is important in determining the quality of education received in these courses. Learners in these courses report a positive L-SES. Further analysis with serial data will explore (1) serial changes in L-SES, (2) the relationship between adaptation UGSB and L-SES, and (3) impact of the presence of a colleague in the same practice situation who is skilled in UGSB and time to adaptation of UGSB after training.

Disclosure: D. Horowitz: SetPoint Medical, 5; **D. Tabechian**: amgen, 12, share holder; **A. Ben-Artzi**: None; **K. Torralba**: None; **A. Mandelin**: None.

Abstract Number: 2067

A New Tool Assessing Trainees' Interventional Musculoskeletal Ultrasound Skills

Stine Maya Dreier Carstensen[1], Lene Terslev[2], Søren Just[3], Mikkel Østergaard[4], Mogens Pfeiffer-Jensen[1] and Lars Konge[5], [1]Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Centre for Head and Orthopaedics, Copenhagen University Hospital – Rigshospitalet Glostrup, Copenhagen, Denmark, [2]Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup, Denmark, [3]Section of Rheumatology, Department of Medicine, Odense University Hospital – Svendborg Hospital, Odense, Denmark, [4]Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Centre for Head and Orthopaedics, Rigshospitalet; University of Copenhagen, Copenhagen, Denmark, [5]Copenhagen Academy for Medical Education and Simulation The Capital Region of Denmark, Copenhagen, Denmark

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Interventional musculoskeletal ultrasound (MSUS) procedures, such as ultrasound-guided arthrocentesis and joint injections, are routinely used in rheumatology practice. However, the efficacy and safety of these procedures rely on the competence of the individual physician, and intensive training is essential before independent practice. Assessment tools play a pivotal role in providing structured feedback to the trainees and ensuring end-of-training competence. An international expert panel of radiologists developed the Interventional Ultrasound Skills Evaluation (IUSE) tool to evaluate operator competence in invasive ultrasound procedures relevant for abdominal and thoracal interventions. It is unsuitable for assessing MSUS procedures and therefore, we aimed to develop and establish valid evidence for a modified version of the IUSE assessment tool designed for evaluating trainees in interventional MSUS procedures relevant in rheumatology.

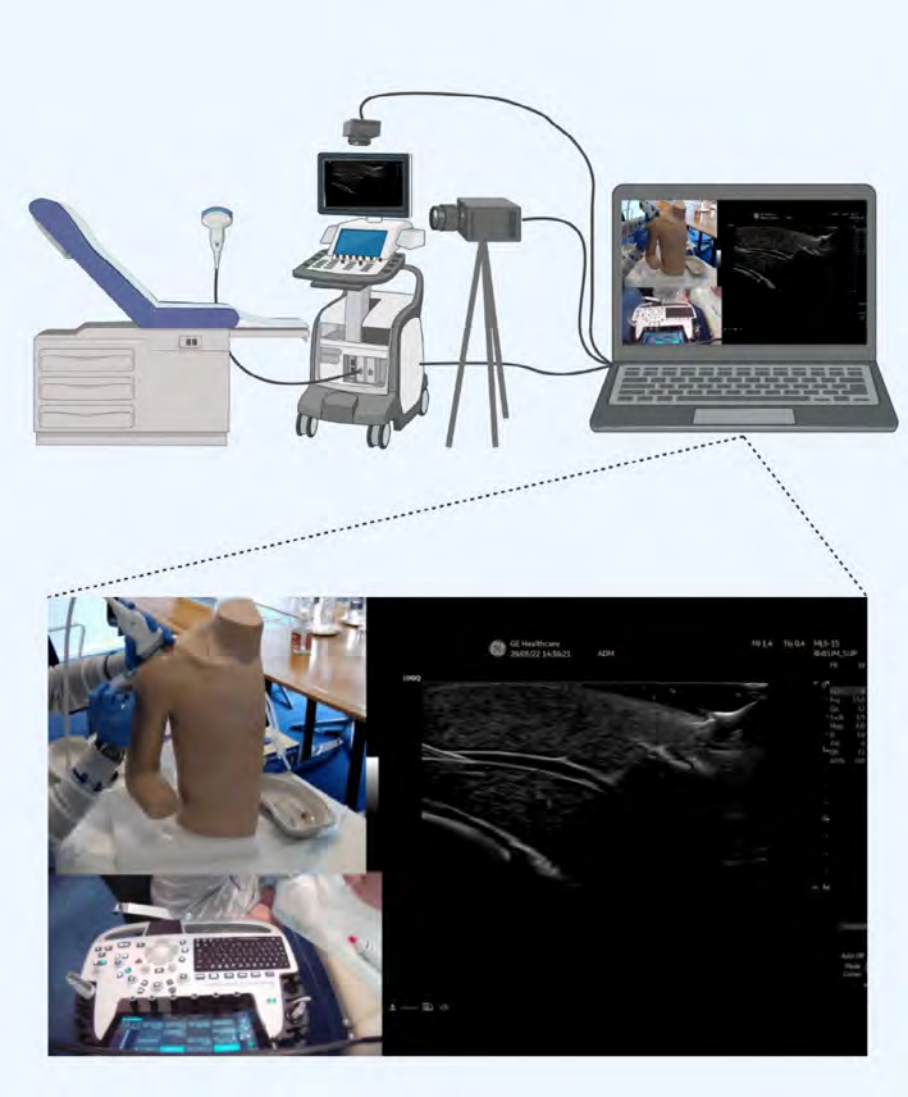

Figure 1: The setup included three different video inputs: the ultrasound image, how the participant handled the machine and adjusted the buttons, and how the participant performed the procedure on the fantom. The videos were subsequently uploaded to an online rating platform.

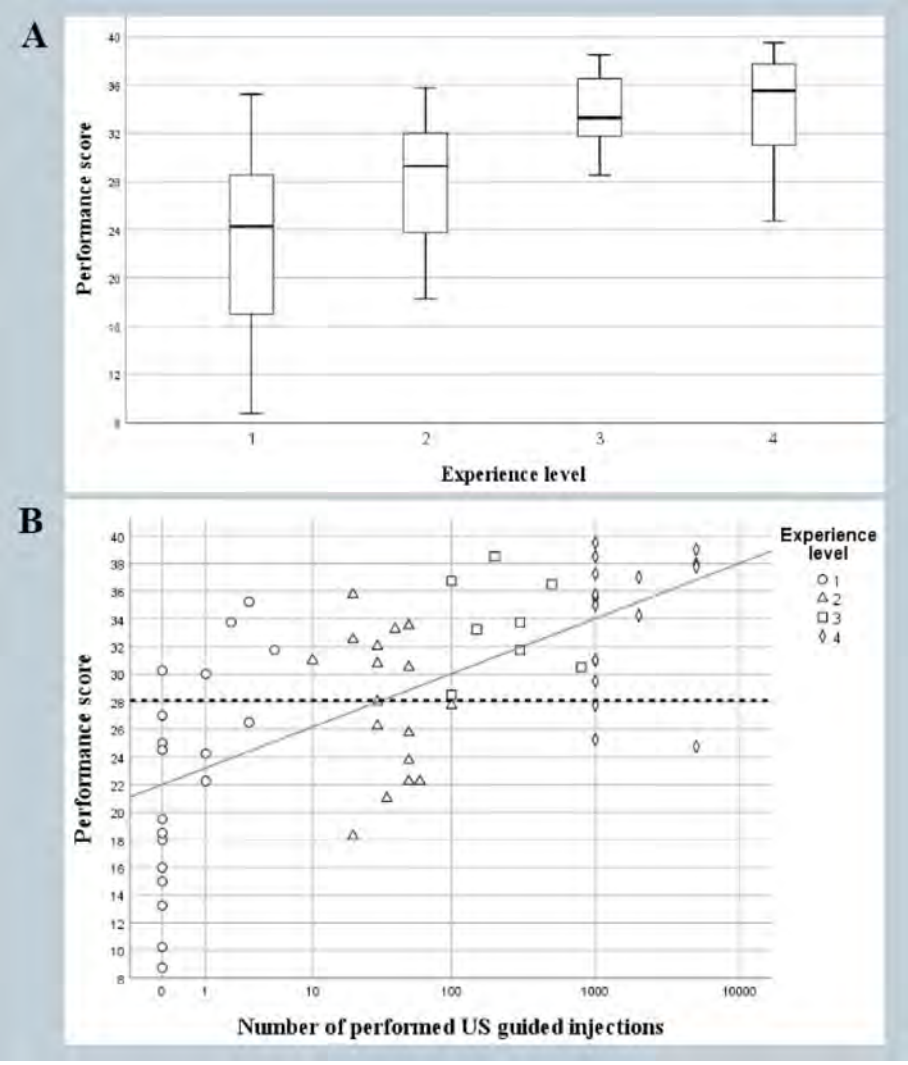

Figure 2: Experience and Performance. A) Boxplot illustration of the mean AIMUS performance score in the four different groups (1:novices, 2: intermediates, 3:experienced, and 4:experts). B) Number of previously performed interventional MSUS procedures correlated to the AIMUS performance score, divided into the same four experience levels.

Methods: An expert panel of rheumatologists modified the IUSE tool to reflect the essential steps in interventional MSUS procedures. The modified tool was named the Assessment of Interventional Musculoskeletal Ultrasound Skills (AIMUS) and included 8 items: indications, contraindications, preparation, US equipment, procedural instruments, route, hand-eye coordination and, procedure and outcome. To gather validity evidence for the AIMUS tool, physicians with different levels of interventional MSUS experience were enrolled in the study and instructed to perform two interventional MSUS procedures on simulated patient cases, i.e., subdeltoid bursitis and biceps tenosynovitis. The procedures included both ultrasound-guided aspiration and injection techniques and were performed on a shoulder rubber fantom with ultrasound capabilities, Figure 1. All examinations were video recorded (n=130), anonymized, and subsequently assessed in random order by two blinded raters using the AIMUS tool.

Results: Sixty-five physicians from 21 different countries attending the EULAR 2022 conference were included and categorized into four groups based on their experience with interventional MSUS, determined by the number of procedures performed: 19 novices (0-10), 18 intermediate (10-100), 9 experienced (100-1000), and 17 experts (>1000). Two participants were excluded from the analysis due to a lack of data on their experience. The internal consistency of the AIMUS tool was excellent, with a Cronbach alpha of 0.9. The inter-case reliability was good with a Pearson's correlation coefficient

(PCC) of 0.7 and the inter-rater reliability was moderate to good (PCC 0.6). The ability to discriminate between different levels of experience was highly significant ($p < 0.001$), with a linear correlation between the performance scores and the participant experience levels, Figure 2.

Conclusion: We have developed and established solid validity evidence for the AIMUS tool for evaluating trainees' interventional MSUS skills. The AIMUS tool can be used in daily clinical practice and implemented in training curricula for establishing competency-based training for interventional MSUS procedures in the future.

Disclosure: S. Carstensen: None; **L. Terslev**: Eli Lilly, 1, Janssen, 1, 6, Novartis, 6, UCB, 1; **S. Just**: None; **M. Østergaard**: AbbVie, 2, 5, 6, Amgen, 5, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Hospira, 2, 6, Janssen, 2, 6, MEDAC, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Novo Nordisk, 2, 6, Orion, 2, 6, Pfizer, 2, 6, Regeneron, 2, 6, Roche, 2, 6, Sandoz, 2, 6, Sanofi, 2, 6, UCB, 2, 6; **M. Pfeiffer-Jensen**: None; **L. Konge**: None.

Abstract Number: 2068

Integration of Basic Science into Virtual Patient Cases to Enhance Clinical Reasoning Skills

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Digital education, also known as e-learning, comprises several different learning modalities e.g. virtual patient (VP) simulations. VPs have been proposed to be an effective way of exposing health profession students to greater quantities of patient cases, also ensuring that students encounter diagnoses and presentations that serve the needs of their learning outcomes, regardless of the patients they happen to encounter during clinical rotations.

Our aim was to explore medical students' perceptions and emotions towards integration of basic science aspects in VP cases within rheumatology, and evaluate their self-perceived acquirement of clinical reasoning (CR) skills. A secondary aim was to collect information that would be utilised for the development of a model, with concepts and strategies for how to integrate basic science concepts into case-based CR training platforms.

Methods: We performed an interventional, explorative phenomenological study, with medical students recruited from a one-week long clinical placement in rheumatology. The integration was implemented in five VP scenarios. During the last day of the week, the VP cases were discussed during a seminar, together with discussion of the basic science integration. The VP cases had been created with Virtual interactive case simulator (VIC). Students' perceptions and emotions of basic science as well as CR skills were explored through thematic content analysis of transcribed interviews. Transcriptions were coded and analysed using Malterud's systematic text condensation. Transcriptions were read by the entire research team. Next, condensations and themes were presented to the research team to discuss internal validity of the material. Quotes and condensations were then translated to English. Finally, all transcriptions were re-read one last time to ensure that the themes and general concepts still corresponded to the material.

Results: A total of 14 students were tasked to complete five basic science-enhanced VP cases. After data analysis, we identified five themes, illustrating students' perceptions of basic science integration into VP cases and its possible impact on the self-perception of their CR ability: (i) appreciation of basic science knowledge and the role in future work; (ii) ambiguity towards basic science in practice as an obstacle for integration; (iii) the effect of basic science integration on self-perception of CR; (iv) an attractive design of basic science integration; (v) low knowledge of the concept of CR.

Overall, student's perceptions towards basic science were positive but their motivation for performing the integrative activity themselves was low. Students reported enhanced CR ability after having performed the activity. They also reported a value of continuous integration of basic science during rotations in the hospital environment. However, this was hindered by a fear of asking senior colleagues questions related to basic science, as they perceived that they "should have known this themselves".

Conclusion: Our results suggest that student's are positive to basic science integration within educational activities at the medical programme, accompanied by the fact that it might improve their CR abilities.

Disclosure: K. Rombo: None; **A. Borg**: None; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia Pharmaceuticals, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Elli Lilly and Company, 5, 6, F. Hoffmann-La Roche AG, 5, 6, Gilead Sciences, 5, 6, GSK, 5, 6, Janssen Pharmaceuticals, 5, 6, Novartis, 5, 6, Otsuka Pharmaceutical, 5, 6.

Abstract Number: 2069

Navigating the Residency-to-Fellowship Transition in Rheumatology

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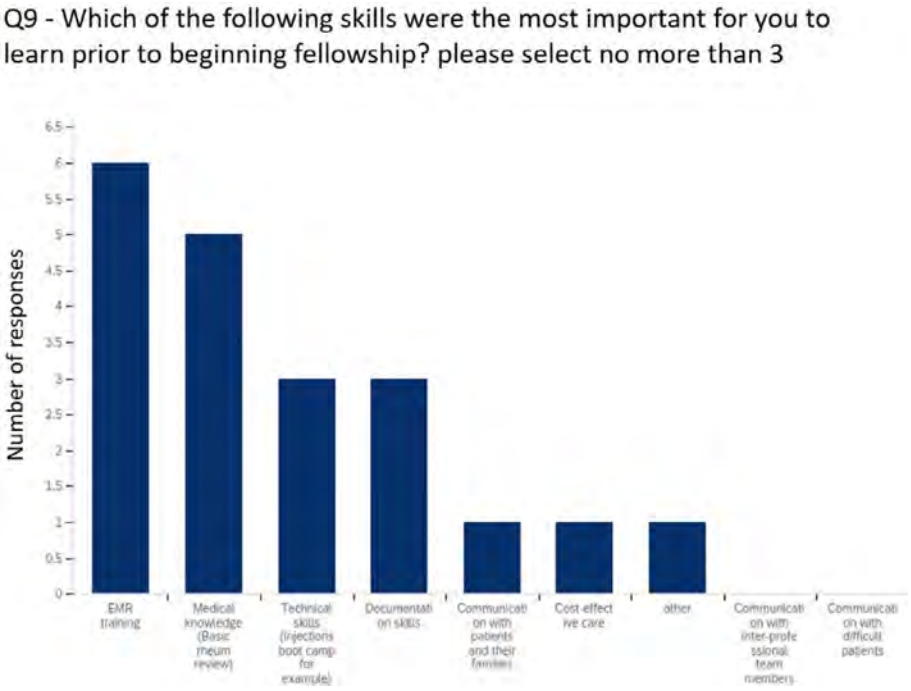
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Transitioning from residency to fellowship is a significant milestone in a medical professional's career. Physicians acquire foundational knowledge and skills during residency, while fellowship allows physicians to gain advanced expertise and specialized training in a specific area of medicine. This transition can be exciting and challenging, as fellows must adapt to a new learning environment, work with different colleagues, and take on greater responsibility in patient care. Nonetheless, with the right mindset, resources, and support, the transition from residency to fellowship can be a rewarding and fulfilling experience that prepares physicians for a successful medical career. This project assesses the transition process from internal medicine residence to rheumatology fellowship.

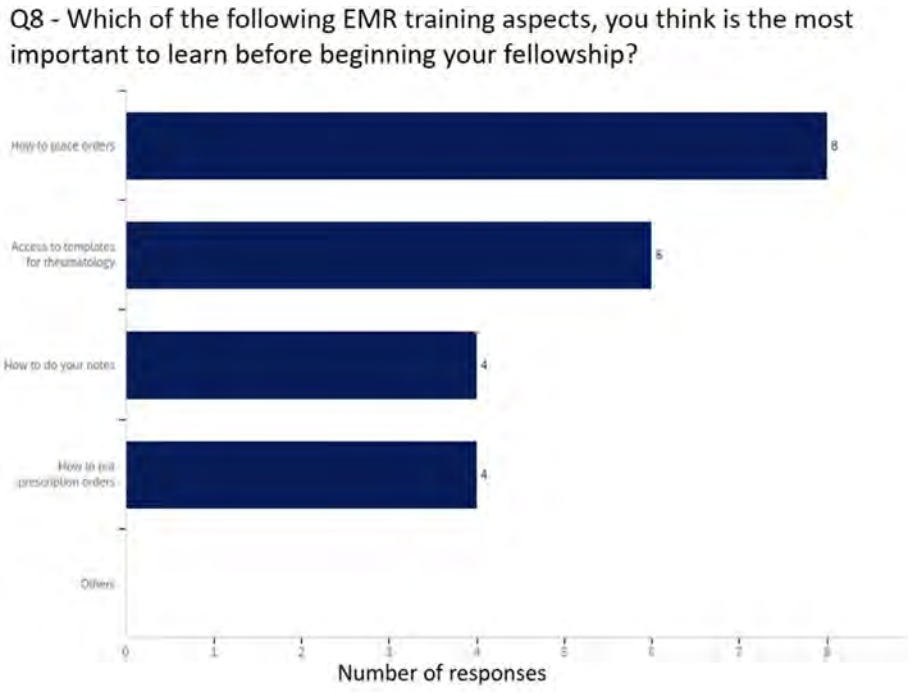
Methods: A cross-sectional survey of rheumatology fellows in Florida in April 2022 was conducted. We used a voluntary, brief, anonymous Qualtrics questionnaire to assess the transition from internal medicine residence to Rheumatology Fellowship. The survey was sent to 28 fellows. The survey assessed their perception of the transition process, including the level of preparedness, challenges encountered during the transition, and satisfaction with the support provided during the transition process, including mentorship, orientation, and institutional resources.

Results: A total of 12 fellows completed the survey, with a response rate of 43%. Age range was: 33.33%: 25-30 years, 50%: 30-35 years, and 16.67% >35 years, 91.67% were female, 33.33% were PYG 4, 50% PGY 5, and 16.67% PGY6. The majority of respondents reported feeling adequately prepared for fellowship. 41.67% (n=5) responded that the transition

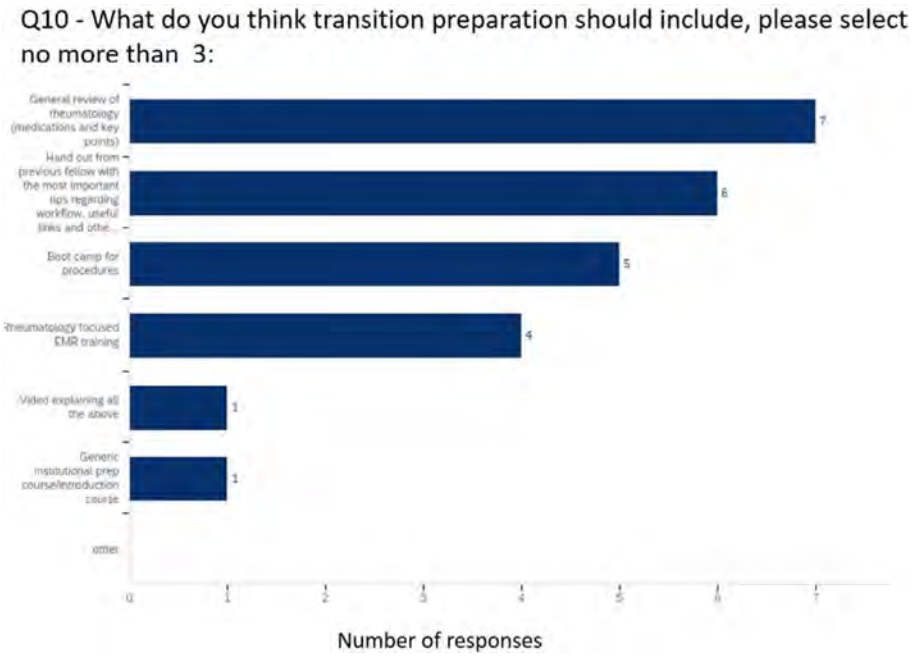
process from residence to fellowship was good, 25% excellent, 8.3% average, and 24% poor. 50% of responders did not participate in a generic institutional preparation course or specialty fellow preparation course. Most of the fellowship introductions lasted less than one week (72.73%). Fellows considered that the most important skill to learn before beginning the fellowship was EMR training (30%), followed by medical knowledge (basic rheumatology review) (25%), injections, and documentation skills. Regarding specific questions about EMR training, the most voted option was how to place orders



Report of the most important skills prior to beginning fellowship.



Report of most important EMR training aspects to learn before beginning fellowship.



(36.36%) and access to templates in rheumatology (27.27%). Most residents (29.17%) responded that transition preparation should include a general review of rheumatology, handouts from previous fellows (25%), boot camp for procedures (20.8,3%) and rheumatology-focused EMR training 16.67%.

Conclusion: Although most respondents reported being satisfied with the support provided during the transition, there are some areas of improvement during the transition process, especially in EMR training. These findings highlight the need for ongoing evaluation and improvement of the transition process from residency to fellowship. Targeted interventions, such as EMR training, general rheumatology and procedures boot camps, and handouts from previous fellows with important tips may help improve the transition experience's quality and better prepare residents for success in their fellowship programs.

Disclosure: L. Otalora Rojas: None; **G. S Kaeley**: Abbvie, 5, Gilead, 5, Janssen, 5.

Abstract Number: 2070

Augmenting Medical Education: An Evaluation of GPT-4 and ChatGPT in Answering Rheumatology Questions from the Spanish Medical Licensing Examination

Alfredo Madrid García[1], zulema Rosales[2], Dalifer Freites[2], Inés Pérez Sancristóbal[3], Benjamin Fernandez[3] and Luis Rodríguez Rodríguez[3], [1]Fundación Investigación Biomédica Hospital Clínico San Carlos, Madrid, Spain, [2]Hospital Clínico San Carlos, Madrid, Spain, [3]Hospital Clinico San Carlos, Madrid, Spain

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

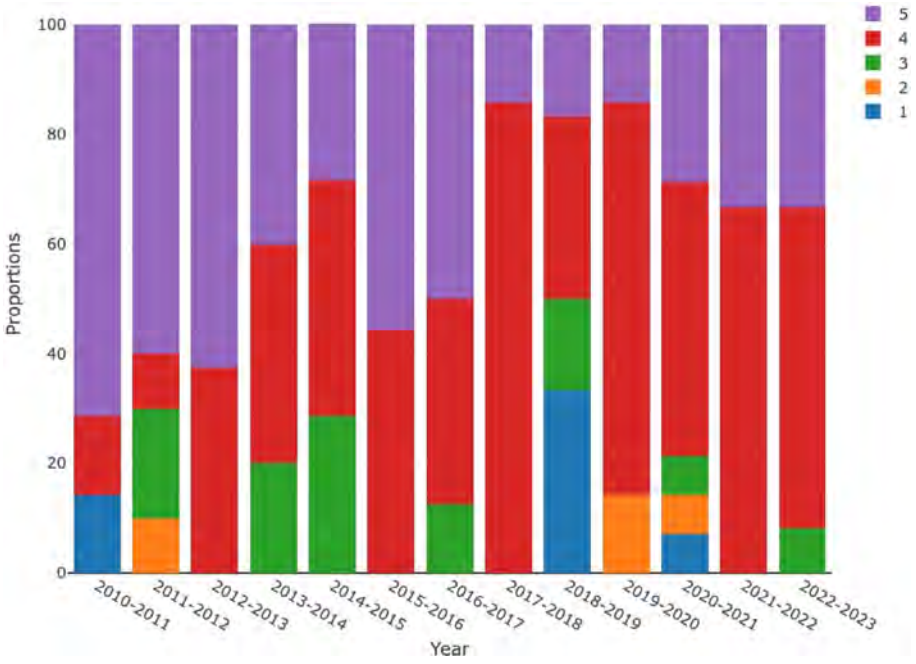
Background/Purpose: The emergence of Large Language Models (LLM) with remarkable performance such as GPT-4 and ChatGPT, has led to an unprecedented uptake in the population. One of the most promising and studied applications for these models concerns education. Their ability to understand and generate human-like text creates a multitude of opportunities for enhancing educational practices and outcomes. The objectives of this study were to assess the success rate of GPT-4/ChatGPT in answering rheumatology questions from the access exam to specialized medical training in Spain (MIR), and to evaluate the medical reasoning followed by ChatGPT/GPT-4.

Methods: Rheumatology questions from the MIR exam published from 2010 onwards were selected and used as prompts. Questions present clinical cases or factual queries, followed by four to five responses with a single correct answer. Questions containing images were excluded.

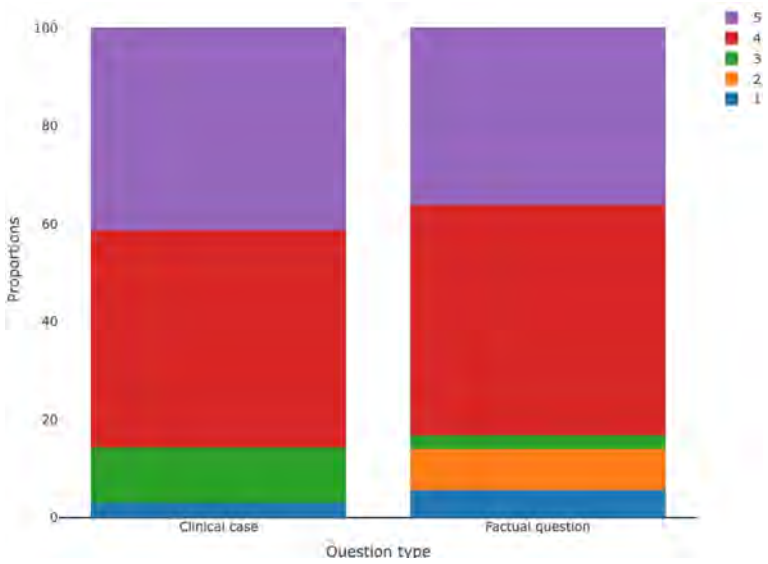
Official responses were compared with those provided by GPT-4/ChatGPT to estimate the chatbots accuracy. Differences between LLM were evaluated using McNemar's test.

A rheumatologist with teaching experience in preparing students for the MIR exam assessed the correctness of the medical reasoning of the LLM given for each of the questions, using a 5-point Likert scale, where 5 indicates that the reasoning was entirely correct. The influence in the medical reasoning score of the chatbot model used was analyzed using McNemar's test. The influence of the year of the exam question, type of question (clinical case vs. factual), patient's gender in the clinical case questions, and pathology addressed were assessed using logistic regression models, after dichotomizing the Likert scale into two groups: low score (i.e.,1,2,3) vs high score (i.e., 4, 5).

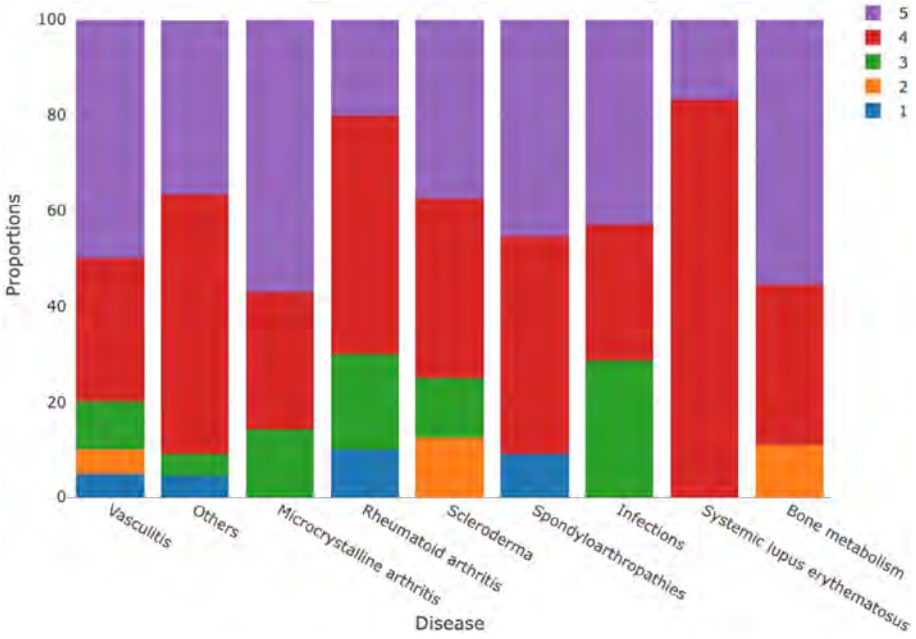
Results: After applying the inclusion criteria, 106 questions remained, including 36 (34%) factual queries and 70 (66%) clinical case questions. 99 (93.4%) and 69 (65.1%) questions were correctly answered by GPT-4 and ChatGPT, respectively. Most of the questions that GPT-4 failed were factual queries (5/7, 71.4%). We observed a significantly higher proportion of correct answers provided by GPT-4 ($p=1.2x10^{-7}$). Moreover, the clinical reasoning score of this LLM was also higher ($p=4.7x10^{-5}$). Regarding the other variables, there were no statistically significant differences in the clinical reasoning score for GPT-4/ChatGPT across the various categories studied. Figures 1, 2 and 3 show the scores given to each question, considering the year, question type and disease.



GPT-4 medical reasoning score of the questions according to the year



GPT-4 medical reasoning score of the questions according to its type



GPT-4 medical reasoning score of the questions according to the disease

Conclusion: GPT-4 showed a significantly higher accuracy and clinical reasoning score than ChatGPT.

No significant differences in the clinical reasoning correctness were observed regarding the type of question or the condition evaluated.

GPT-4 could become a valuable asset in medical education, although its precise role still has to be defined.

Disclosure: A. Madrid García: None; **z. Rosales**: None; **D. Freites**: None; **I. Pérez Sancristóbal**: None; **B. Fernandez**: None; **L. Rodríguez Rodríguez**: None.

Abstract Number: 2071

A Consensus Based Shoulder Examination for Rheumatology Training

Huseyin Berk Degirmenci[1], Robert Kalish[2], Ratnesh Chopra[3], Kat Gilek-Seibert[4], Fotios Koumpouras[5], Vasileios Kyttaris[6], Santhanam Lakshminarayanan[7], Bonita Libman[8], Stephanie Mathew[9], Kenneth O'Rourke[10], Anthony Reginato[11] and Eugene Kissin[12], [1]St. Elizabeth's Medical Center, Boston, MA, [2]Tufts University School of Medicine, Boston, MA, [3]UMass Chan Medical School, Shrewsbury, MA, [4]Roger Williams Medical Center, Sharon, MA, [5]Yale School of Medicine, New Haven, CT, [6]BIDMC, Boston, MA, [7]University of Connecticut School of Medicine, Farmington, CT, [8]The University of Vermont Medical Center, Burlington, VT, [9]Dartmouth-Hitchcock Medical Center, Hanover, NH, [10]Maine Medical Center, Falmouth, ME, [11]The Warren Alpert Medical School of Brown University, Providence, RI, [12]Boston University, Newton, MA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Professional Education Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Physical examination of a patient with nonspecific shoulder pain is a non-standardized teaching objective among rheumatology fellowship programs. We used the Delphi methodology to identify both variability in shoulder examination performed by rheumatology fellows and areas of consensus among rheumatology fellowship program directors (PDs) in New England.

Methods: Past or present rheumatology PDs currently working in New England were recruited. Participants taught a 5-minute shoulder examination to one of their trainees and recorded the resulting video of the shoulder examination by the trainee. We compiled a comprehensive list of all the performed maneuvers from these videos. Participants received an anonymized electronic survey instructing them to rank each maneuver into one of the three categories: *(Tier 1) Teach all fellows & should be performed routinely; (Tier 2) Teach all fellows BUT should be performed only in specific scenarios; (Tier 3) Teach only to selected fellows & should be performed only in specific scenarios*. When a significant variation in technique between trainees was observed, we surveyed PDs for the best technique (independently of the results of tier consensus). We encouraged participants to include comments explaining reasoning, and/or literature support for their choices. Participants received a compilation of anonymized comments and results of the 1st survey round. Items not meeting ≥70% consensus threshold were included in the 2nd survey. This process was repeated for a 3rd survey. A separate survey collected PD demographics.

Table 1. Demographics of the program directors

Table 1. Demographics of the program directors	Mean ± Standard Deviation (SD)	(Range)
# of years working as clinical rheumatologist	21 ± 7.7	(9-31)
# of years serving (or had served) as fellowship program director	9 ± 5.6	(3-22)
# of fellows accepted to their rheumatology fellowship program	2 ± 0.6	(1-3)
Estimated % of MSK exam knowledge fellows learn(ed) from the participant compared to total MSK exam knowledge of the fellows	39 ± 16.2	(10-70)
Estimated % of time spent for direct patient care compared to total work hours	60 ± 12.2	(33-75)
Estimated % of patient encounters for shoulder pain compared to all patient counters	14 ± 6.1	(7-25)
Estimated % of use of the US of the shoulder for shoulder pain encounters	15 ± 29.2	(0-82)
Self-rating of the MSK examination skills from 0-100 (0 being no skills, 100 being best possible skills)	75 ± 10.6	(50-95)

Table 2. Tier consensus items for shoulder examination maneuvers

Table 2. Tier consensus items for shoulder examination maneuvers	Items met consensus threshold for Tier 1	Items met consensus threshold for Tier 2	Items did not meet consensus threshold
INSPECTION	Adequate exposure (2 shoulders without overlaying clothes)*, Observation from front*, Observation from behind*	N/A	N/A
PALPATION	SC joint*, AC joint*, Subacromial space*, Biceps (long)**, Acromion**, Glenohumeral space**, Clavicle***	Coracoid process** Spinous process of the C-spine** Scapular spine***	Deltoid muscle (Tier 1: 7/11; Tier 2: 3/11; Tier 3: 1/11) Trapezius muscle (Tier 1: 6/11; Tier 2: 5/11; Tier 3: 0/11) Elbow lateral epicondyle (Tier 1: 1/11; Tier 2: 6/11; Tier 3: 4/11)
ACTIVE ROM	Abduction*, Internal rotation*, External rotation*, Forward flexion*	Neck lateral rotation** Neck lateral flexion** Neck forward flexion** Neck retroflexion/extension** Elbow pronation/supination***	Retroflexion/Extension (Tier 1: 7/11; Tier 2: 4/11; Tier 3: 0/11)
PASSIVE ROM	Abduction*, Internal rotation*, External rotation*, Forward flexion*	N/A	Retroflexion/Extension (Tier 1: 6/11; Tier 2: 4/11; Tier 3: 1/11) Elbow flexion/extension (Tier 1: 2/11; Tier 2: 6/11; Tier 3: 3/11)
RESISTIVE MANEUVERS	Resistive internal rotation* Resistive external rotation* Empty Can (Jobe's) test* Painful arc test* Cross arm adduction test* Resistive abduction** Speed's test**	Belly press test* Scapular winging test* Shoulder apprehension test* Wright's (hyperabduction) test* Drop arm test** Yergason's test** Spurling's test***	Lift off test (Tier 1: 4/11; Tier 2: 7/11; Tier 3: 0/11) Hawkins Kennedy test (Tier 1: 5/11; Tier 2: 6/11; Tier 3: 0/11) Neer's test (Tier 1: 5/11; Tier 2: 6/11; Tier 3: 0/11) Resistive neck forward flexion (Tier 1: 1/11; Tier 2: 3/11; Tier 3: 7/11) Hornblower's Test (Tier 1: 1/11; Tier 2: 3/11; Tier 3: 7/11) Resistive elbow flexion test (Tier 1: 3/11; Tier 2: 4/11; Tier 3: 4/11)
Legend for Table 2: ***Consensus threshold definition: ≥70% (or ≥8/11 answers)*** ***Tier 1: Teach all fellows & should be performed routinely; Tier 2: Teach all fellows BUT should be performed only in specific scenarios; Tier 3: Teach only to selected fellows & should be performed only in specific scenarios*** *Red superscript asterisks added next to the items that met consensus threshold to represent survey rounds during which they met the consensus as following:* **: met consensus during the 1st round; **: met consensus during the 2nd round; ***: met consensus during the 3rd round*			

Table 3. The preferred method for different examination techniques

Table 3. The preferred method for different examination techniques	Technique 1.	Technique 2.	Technique 3. (if available)
PALPATION			
Biceps (long) palpation	with static humeral head (4/11)	with dynamic humeral head (7/11)	N/A
Glenohumeral space palpation*	anterior/posterior palpation (9/11)	anterior palpation only (2/11)	N/A
Scapular spine palpation**	scapular spine only (8/11)	scapular spine and scapular region (3/11)	N/A
ACTIVE ROM			
External rotation during active ROM***	with elbow at side (8/11)	with shoulder abducted at 90' degrees (2/11)	by asking the patient to "reach behind the head" (1/11)
PASSIVE ROM			
Abduction during passive ROM	abduction to 90' degrees (7/11)	abduction to 180' degrees (4/11)	N/A
Forward flexion during passive ROM*	forward flexion to 30' degrees (3/11)	forward flexion to 180' degrees (8/11)	N/A
Internal rotation during passive ROM	with elbow at side (0/11)	with shoulder abducted at 45-60' degrees (5/11)	with shoulder abducted at 90' degrees (6/11)
External rotation during passive ROM	with elbow at side (4/11)	with shoulder abducted at 45-60' degrees (2/11)	with shoulder abducted at 90' degrees (5/11)
RESISTIVE MANEUVERS			
Empty Can (Jobe's) test*	with shoulder forward extension to 30' degrees (8/11)	with shoulder forward extension to 60' degrees (3/11)	N/A
Hawkins Kennedy test	both active and passive motion with shoulder forward flexion (3/11)	just passive motion with shoulder abduction (1/11)	just passive motion with shoulder forward flexion (7/11)
Neer's test**	passive motion without arm pronation (1/11)	passive motion with arm pronation (10/11)	active motion without arm pronation (0/11)
Speed's test*	with simultaneous biceps palpation (3/11)	without simultaneous biceps palpation (8/11)	N/A
Cross arm adduction test**	with passive motion (9/11)	with active motion (2/11)	N/A
Legend for Table 3: ***Consensus threshold definition: ≥70% (or ≥8/11 answers)*** *Red superscript asterisks added next to the items that met consensus threshold to represent survey rounds during which they met the consensus as following:* **: met consensus during the 1st round; **: met consensus during the 2nd round; ***: met consensus during the 3rd round*			

Results: 11 of 13 recruited PDs agreed to participate and 100% of participants completed all rounds of the study. Participants were PDs for nine years (range 3-22), 45% are/were the main teachers for the MSK examination in their fellowship programs, andrated themselves 75 (range 50-95) on a 100-point scale for prowess in physical examination (Table 1). The study addressed 65 items: 52 questions for tier designation of the exam maneuvers and 13 questions for different examination techniques. Participants achieved consensus for 40/52 tier designation items (Table 2) and for 8/13 technique items (Table 3). Consensus for tier designation items increased from 44% in round 1, to 69% in round 2, and 77% by round 3. For technique-related items, consensus increased from 31% to 54% to 61% (Tables 2 and 3).

Conclusion: This is the first study focused on shoulder examination specific to rheumatology training and practice, which may be distinct from that required for orthopedics, physiatry, or primary care. By collecting anonymized video recordings from each participant, we cataloged the range of shoulder physical exam maneuvers and techniques performed in almost all teaching programs in New England. The Delphi methodology allowed consensus building among PDs for which shoulder examination techniques to teach, which to perform routinely vs. selectively, and how to perform them. These results, in the context of "nonspecific" shoulder pain, should be generalizable and can provide guidance for all US rheumatology fellowship training programs given the similarity in the scope of practice and education.

Disclosure: H. Degirmenci: None; **R. Kalish**: None; **R. Chopra**: None; **K. Gilek-Seibert**: AbbVie/Abbott, 6; **F. Koumpouras**: AstraZeneca, 6, Bristol-Myers Squibb(BMS), 5, Cabaletta Bio, 1, GlaxoSmithKlein(GSK), 6, LRA, 5, Novartis, 1; **V. Kyttaris**: AbbVie/Abbott, 5, AstraZeneca, 2, Aurinia, 1, EMD Serono, 5, Exagen, 2, 5, Fresenius Kabi, 1, Horizon Pharmaceuticals, 1, Novartis, 5, Scipher, 1, Takeda, 5, Vertex, 2; **S. Lakshminarayanan**: None; **B. Libman**: AbbVie/Abbott, 12, Principal Investigator; **S. Mathew**: None; **K. O'Rourke**: None; **A. Reginato**: None; **E. Kissin**: None.

Abstract Number: 2072

Utility of a Novel Pediatric Rheumatology Interactive Teleconference Series: Rheum2Play

Sarah Molina[1], **Tresa Ambooken**[2], Christina Gulla[3], Miriah Gillispie-Taylor[4] and Ginger Janow[5], [1]Baylor College of Medicine - Pediatrics Residency Program, Houston, TX, [2]Hackensack Meridian Health, Hackensack, NJ, [3]HUMC pediatrics residency, Hackensack, NJ, [4]Baylor College of Medicine, Texas Children's Hospital, Houston, TX, [5]Joseph M. Sanzari Children's Hospital at Hackensack Meridian Health, Glen Rock, NJ

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Within pediatric subspecialities, pediatric rheumatology remains one of the newest and smallest, with a paucity of resources available for new trainees and those interested in learning more. It is estimated that 1 in every 250 children has juvenile arthritis, but there are only approximately 400 practicing pediatric rheumatologists nationwide. Most pediatric rheumatologists are concentrated in larger cities, leaving a significant part of the country underserved, meaning pediatric trainees often also lack exposure to pediatric rheumatology. Estimates suggest that approximately 33% of medical schools and 40% of pediatric residency programs lack access to a pediatric rheumatologist, significantly impacting training. Lack of exposure of pediatric rheumatology by learnders early in training and lack of access to pediatric rheumatology clinical experience during any part of training are likely contributing factors to delays in presentation to care of affected patients. To help bridge this gap, social media, particularly the podcast platform, has been increasingly utilized and may be a large part of the future of medical education.

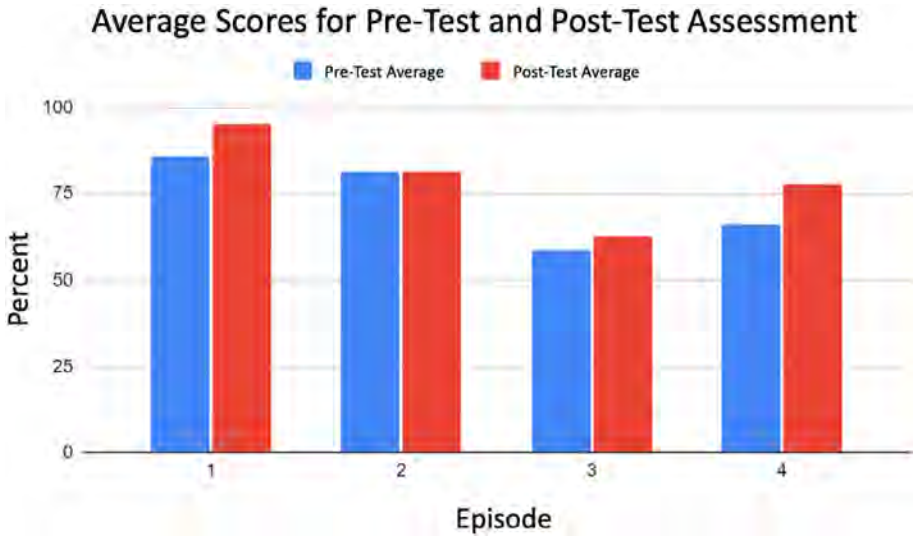


Figure 1. Pre and post-test assessment scores for four live conference sessions. Assessments included questions regarding knowledge and confidence. Scores did show improvement for three of the four sessions when combining both knowledge and confidence assessments.

Methods: Four live, interactive educational teleconferences were held for an audience of pediatric residents and pediatric rheumatology fellows. Each session focused on a different subtype of juvenile idiopathic arthritis arthritis (JIA). Recruitment was via email to pediatric residency program directors and pediatric rheumatology fellowship directors. Pre- and post-tests were developed based on learning objectives to assess specific knowledge and confidence regarding ability to recognize and workup JIA. Test scores for which there were paired pre- and post-test data were included in the analysis. Per session, average pre and post test scores were calculated and compared to assess uptake of knowledge and increase in confidence potentially attributable to the session. Given the small number of participants statistical significance could not be assessed.

Results: Number of participants per session ranged from 3-8. Average assessment averages increased in 4 of the 5 sessions (Figure 1) and average confidence increased after all sessions (Figure 2).

Conclusion: Our results suggest that a live teleconference is likely effective at increasing medical knowledge and confidence in recognition and workup of JIA. Recruitment provided some challenges and we intend to improve dissemination by converting sessions into podcasts. While knowledge scores did not show dramatic improvement. Sessions are unscripted

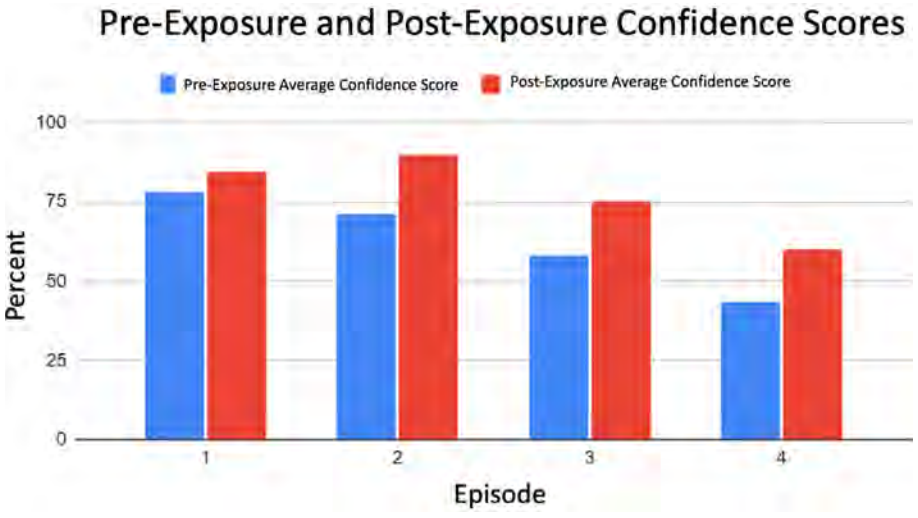


Figure 2. In all assessments, post-exposure assessment of confidence scores were higher than pre-exposure assessment scores for all episodes.

and conversational, which may prove more difficult to include the specific content in the pre-and post-tests. There was a more impressive increase in confidence scores, suggesting that the learners found the sessions useful in future diagnosis and management of conditions discussed, making this a valuable learning experience. To overcome these challenges, we plan to convert these teleconference sessions to podcasts with an associated web-based platform, and develop pre-and post-tests that are congruent with our podcast content. Overall, the tools developed provide useful and portable educational resources for a wide audience of pediatric health practitioners.

Disclosure: S. Molina: None; **T. Ambooken**: None; **C. Gulla**: None; **M. Gillispie-Taylor**: None; **G. Janow**: None.

Abstract Number: 2073

Outcomes of the First Year of a Rheumatology Curriculum at Two Internal Medicine Residency Programs

Laura Arneson[1], Biana Modilevsky[2] and Anisha Dua[1], [1]Northwestern University, Chicago, IL, [2]University of Arizona - Tucson / Banner University Medical Center, Tucson, AZ

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Enhancing rheumatology education in Internal Medicine (IM) residency may encourage residents to pursue rheumatology careers, and promote familiarity with rheumatology among those entering other fields. A needs assessment of rheumatology training in IM residency was conducted at an academic program (A) and community program (B) in the same city in 2021. At baseline, all third-year residents at B rotated in a rheumatology clinic for one month; A had no required rheumatology rotation. Neither program had structured rheumatology didactics. Surveys of residents and analysis of In-Training Exam (ITE) scores guided development of a rheumatology curriculum. An assessment of curriculum outcomes after the first year is presented.

Methods: A baseline survey was sent to all IM residents at A and B in Spring 2021, with questions on amount of rheumatology training in residency, interest in learning about rheumatology, interest and confidence in specific topics, and preferred curriculum formats. Results informed the curriculum, implemented starting August 2021. Noon conferences about rheumatology labs and systemic lupus erythematosus (SLE) were delivered at A and B, including pre- and post-quizzes and reference handouts. At A, conferences were also delivered on spondyloarthropathies and vasculitis, and each intern was scheduled for one half-day in rheumatology clinic. The survey was repeated in Spring 2022. ITE scores before and after curriculum implementation were compared (Fall 2020 and 2022).

Results: Baseline surveys were completed by 46% of residents (n=53) at A and 87% (n=20) at B. Post-surveys were by completed by 19% of residents (n=22) at A and 100% (n=23) at B. From 2021 to 2022, ratings of amount of rheumatology training in residency, interest in learning about rheumatology, and confidence in topics covered in conferences increased non-significantly (Figure 1). Preference for in-person curriculum formats increased at A and remained high at B (Figure 2). During the conference on labs, average quiz score increased at A: 40% (n=17, SD 26%) to 74% (n=20, SD 20%), and at B: 27% (n=6, SD 10%) to 77% (n=5, SD 15%). For the conference on SLE, average quiz score increased at A: 42% (n=8, SD 15%) to 90% (n=6, SD 17%), and at B: 52% (n=11, SD 10%) to 93% (n=14, SD 13%). From 2020 to 2022, scores on

the rheumatology portion of the ITE increased from 65th to 89th national percentile at A, and decreased from 5th to 4thpercentile at B. Ranking ITE performance in the 11 IM subspecialties by percentile, A's rheumatology scoreincreased from 10th to 3rd (tied) subspecialty, while B's decreased from 6th (tied) to 10th (tied).

Conclusion: Implementation of a rheumatology curriculum resulted in several advances after one year; outcomes varied between two programs. Residents demonstrated knowledge gains during conference sessions at both A and B. Rheumatology ITE score percentile improved only at A, which received additional didactics. Resident-reported metrics of their rheumatology training improved slightly at both. Preferred curriculum formats shifted from virtual to in-person from 2021 to 2022. Incomplete resident participation at A was a limitation. Next steps include adding additional conferences and reference materials.

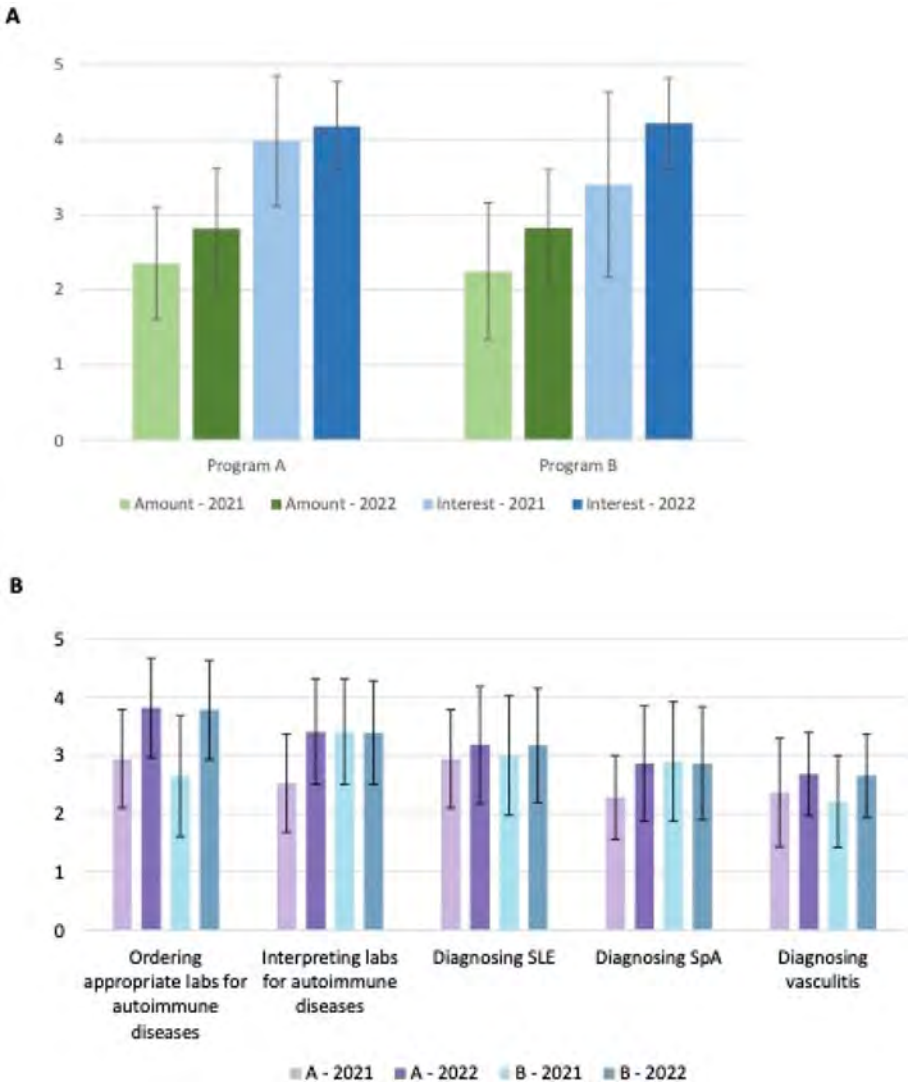


Figure 1. Resident survey responses from internal medicine programs A and B, before and after implementation of a rheumatology curriculum. Pre-surveys (lighter bars) were conducted in Spring 2021 at A (n=53, response rate 46%) and B (n=20, response rate 87%). Post-surveys (darker bars) were conducted in Spring 2022 at A (n=22, response rate 19%) and B (n=23, response rate 100%). Error bars represent standard deviations. Panel A: Rating of the amount of rheumatology training received in residency on a 5-point Likert scale (1 = very inadequate, 5 = more than adequate) is shown in green; rating of interest in learning about rheumatology on a 5-point Likert scale (1 = not at all interested, 5 = very interested) is shown in blue. Panel B: Rating of confidence in rheumatology topics on a 5-point Likert scale (1 = not at all confident, 5 = very confident) is shown in purple for A and blue for B. SLE = systemic lupus erythematosus; SpA = spondyloarthropathies.

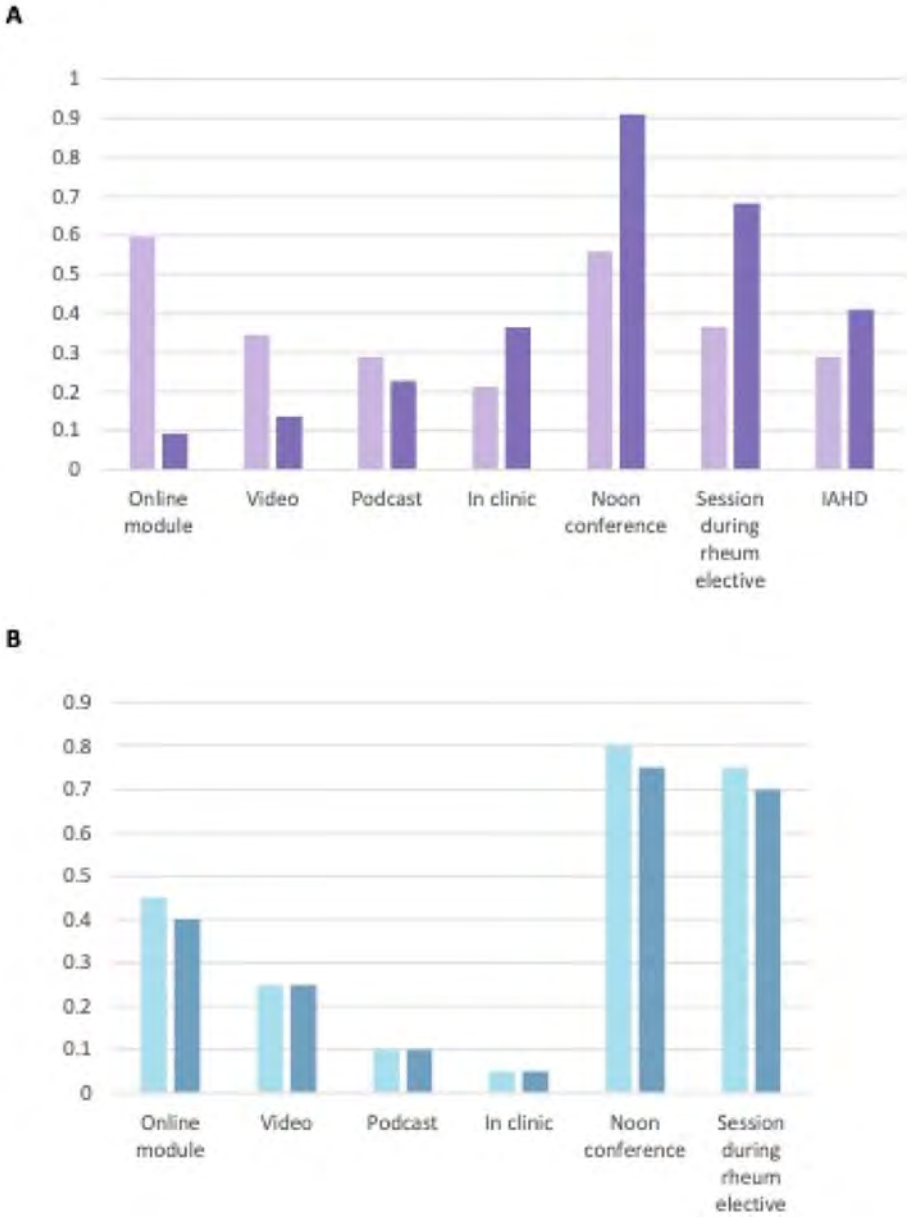


Figure 2. Resident preferences for format of a rheumatology curriculum in 2021 compared to 2022, at program A (panel A) and program B (panel B). Pre-surveys (lighter bars) were conducted in Spring 2021 at A (n=53, response rate 46%) and B (n=20, response rate 87%). Post-surveys (darker bars) were conducted in Spring 2022 at A (n=22, response rate 19%) and B (n=23, response rate 100%). Residents were asked to select 1-3 preferred formats; percent of residents selecting each format is shown. Rheum = rheumatology; IAHD = intern academic half-day, a format available only at A.

Disclosure: L. Arneson: None; **B. Modilevsky**: None; **A. Dua**: AbbVie/Abbott, 2, Amgen, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2, sanofi, 2.

Abstract Number: 2074

Creation and Dissemination of a Near-Peer Rheumatology Fellowship Bootcamp

Sarah Donohue, Tiffany Lin and Justin Levinson, University of Wisconsin, Madison, WI

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Transitions in medical education, such as the matriculation from residency to fellowship, can be a challenging experience with increased knowledge expectations in new clinical settings. Despite the growing number of transition courses, or "bootcamps," there remains a paucity of medical education research, a leaning towards virtual programs, and no published orientation curricula for subspecialized training in rheumatology. We compared the effect of a near-peer rheumatology fellowship bootcamp on new fellows' self-assessments before, after, and 6 months following our intervention along with fellows' clinical knowledge exam scores and performance evaluations by faculty.

Methods: We designed a 3-day intensive, interactive, multi-modality curriculum that included near-peer senior fellow led introductory sessions, workspace tour, and workflow workshops. In addition, incoming fellows were exposed to hands-on SIM center physical exam teaching skills, MSK ultrasound introduction, injection teaching, and disease specific didactic sessions. The 2 junior rheumatology fellows were then assessed with a pre-, post-, and 6-month follow-up 46 question survey. Rheumatology faculty completed a 20-question survey comparing consecutive year fellows who did not complete a bootcamp to those who did. 10 clinical knowledge questions on basic concepts in rheumatology were administered to the fellows with each survey.

Table 1. Fellow Self-Assessment Survey Results & Clinical Knowledge Exam Scores

Learning Objective (# of questions)	Pre – Bootcamp Survey Results (SD)	Post – Bootcamp Survey Results (SD)	6 Month Follow-up Survey (SD)	F-statistic value	P-value
Level of clinical knowledge (n=7)	2.0 (0.65)	3.0 (0.58)	3.5 (0.41)	13.21	<0.001
Developing Work-Up Plan (n=10)	1.9 (0.46)	2.6 (0.39)	3.1 (0.70)	12.77	<0.001
Developing Treatment Plans (n=10)	1.95 (0.37)	2.7 (0.26)	3.3 (0.75)	16.13	<0.001
Arthrocentesis Capability (n=3)	1.33 (0.58)	1.83 (0.29)	3.17 (0.29)	16.15	0.004
MSK Ultrasound (n=1)	1.00	1.50	3.50	-	-
Work-Flow/Administrative Tasks (n=9)	1.75 (1.7)	2.81 (0.88)	3.81 (0.46)	7.39	0.003
Clinical Knowledge Question Scores (n=10)	85%	90.00%	100%	-	-

Key: Likert scale of survey. 1= Not at all/Poor, 2=A little/Fair, 3=Somewhat/Good, 4= Very, 5=Extremely/Excellent.

Results: With 46 survey questions grouped into learning objectives, we compared self-assessed comfort in: Level of clinical knowledge (n=7), Developing work-up plans (n=10), Developing treatment plans (n=10), Arthrocentesis capability (n=3), MSK ultrasound (n=1), and Workflow/administrative tasks (n=9; Table 1). We found that the bootcamp increased fellow level of confidence in all proposed learning objectives, and improvement continued at the 6-month follow-up retention of knowledge survey. The pre-bootcamp clinical knowledge mean exam score was 85%, improved to 90% on the post-bootcamp exam, and ultimately 100% correct at the 6 month follow up. Post intervention, the faculty survey discovered that our junior fellows were better equipped to develop a work-up plan ($p< 0.00001$) and treatment plan ($p< 0.00001$; Table 2). Faculty assessed the success in introducing high yield concepts between "good" and "very" with a score of 3.4 on a 5-point Likert scale. A secondary objective of comparing the creation of working relationships between faculty and new fellows was graded as 3.7.

Conclusion: This innovative University of Wisconsin rheumatology fellowship bootcamp represents the first published iteration for a near-peer led rheumatology curriculum. Distinctively, this curriculum included simulation center actors, a hands-on course on arthrocentesis and dedicated senior fellow led clinical setting workshops and tour. The fellow-led teaching model further consolidates the knowledge in senior fellows. Future directions include expansion of the bootcamp to prospectively collect baseline data and increase the sample size.

Table 2. Faculty Survey Results

Learning Objective (# of questions)	Pre – Bootcamp Faculty Survey (SD)	Post – Bootcamp Faculty Survey (SD)	T- value	P-value
Level of clinical knowledge (n=7)	2.19 (0.29)	2.32 (0.15)	1.96	0.098
Developing Work-Up Plan (n=10)	1.98 (0.25)	2.62 (0.21)	12.30	< 0.00001
Developing Treatment Plans (n=10)	2.01 (0.29)	2.63 (0.25)	9.59	< 0.00001
Work-Flow/Administrative Tasks (n=7)	-	3.23	-	-
Overall Success of the Bootcamp Objectives (n=3)	-	3.50	-	-

Key: Likert scale of survey. 1= Not at all/Poor, 2=A little/Fair, 3=Somewhat/Good, 4= Very, 5=Extremely/Excellent.

Disclosure: S. Donohue: None; **T. Lin**: None; **J. Levinson**: None.

Abstract Number: 2075

The Impact of Rheumatology Fellow Initiated Curriculum Design on Resident Education

Karen Kruzer[1], Vincent Vertalino[1], Nilson Tapia[1], Andrew Long[1], Amy Blatt[2], Ummara Shah[1] and Bethany Marston[1], [1]Department of Rheumatology, University of Rochester Medical Center, Rochester, NY, [2]Department of Medicine, University of Rochester Medical Center, Rochester, NY

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Professional Education Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatology fellows have a critical role as medical educators for residents and offer unique perspectives on patient care. Fellow scholarly activity is an ACGME requirement in the practice of rheumatology. The purpose of this medical education initiative was for rheumatology fellows to create a longitudinal educational curriculum for internal medicine (IM) residents, and to assess efficacy through both objective knowledge questions and subjective feedback questions.

Methods: The rheumatology fellows at the University of Rochester Medical Center (URMC) developed a needs-assessment of rheumatology core topics from the American Board of Internal Medicine Certification Examination Blueprint. Topics were selected based on IM resident feedback from a needs-assessment. Each fellow created an interactive discussion-based didactic education session for a total of four sixty-minute sessions throughout the 2022-2023 academic year. Self-assessment surveys were completed by residents before and immediately after participation in fellow-led didactics, and percent improvement between pre and post assessments was calculated. The objective knowledge assessments included questions addressing diagnosis, laboratory findings, imaging, and treatments for each topic. A subjective questionnaire soliciting resident feedback assessed effectiveness for resident academic training, applicability to inpatient rotations and residency clinics, and impact on clinical management.

Results: Curriculum topics were selected based on needs-assessment responses from IM residents (N=26), where each resident selected one topic. The most requested topics included dermatologic manifestations of rheumatologic disease (38.5%), vasculitis (30.8%), seronegative spondyloarthropathies (11.5%), and crystal arthropathy (7.7%). After implementing the longitudinal education series, there was a 35% improvement in rheumatology-dermatology knowledge questions,

Table 1. Results of needs-based assessment.

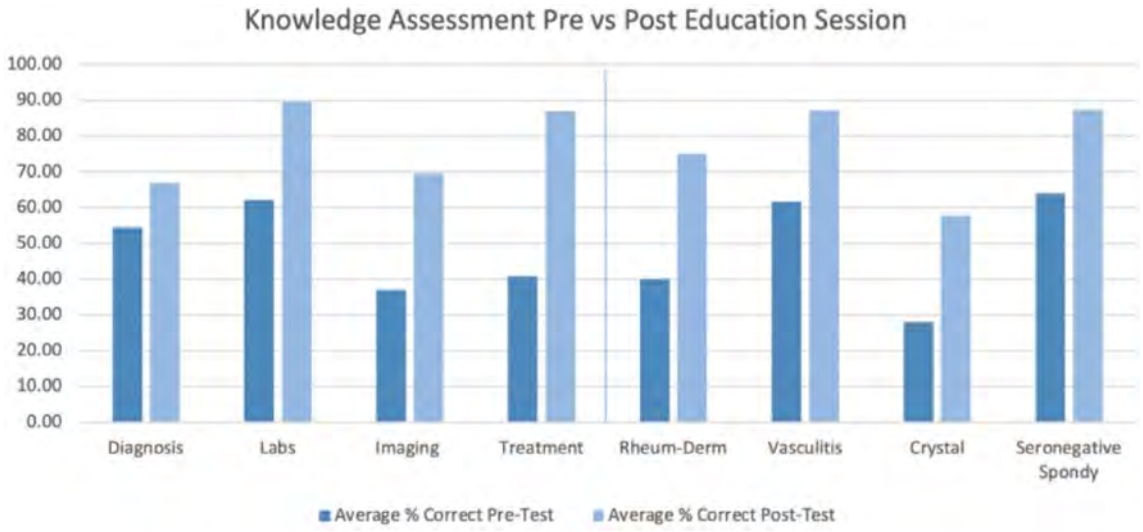
Topic	Total Responses (n=26)	Percent (%)
Crystal arthritis and septic arthritis	2	7.7
Dermatologic manifestations of rheumatologic conditions	10	38.5
Inflammatory myopathy	0	0
Lupus	1	3.8
Osteoarthritis, metabolic bone disease, osteoporosis	1	3.8
Rheumatoid Arthritis	0	0
Scleroderma	1	3.8
Seronegative Spondyloarthropathies	3	11.5
Vasculitis	8	30.8

Table 2. Results of knowledge assessment pre and post education session. Table depicts the total number of responses and percent correct responses for diagnosis, labs, imaging, and treatment specific questions.

		Diagnosis	Labs	Imaging	Treatment	Overall % Improvement
Dermatology-Rheumatology						
	Pre-Test	5 (38.5%)	7 (53.9%)	5 (38.5%)	3 (23.1%)	
	Post-Test	9 (56.3%)	11 (68.8%)	11 (68.8%)	15 (93.8%)	35
Vasculitis						
	Pre-Test	6 (50%)	9 (75%)	8 (66.7%)	7 (58.33)	
	Post-Test	6 (66.7%)	9 (90%)	9 (90%)	10 (100%)	25.7
Crystal Arthritis						
	Pre-Test	3 (30%)	2 (20%)	1 (10%)	2 (20%)	
	Post-Test	4 (44.4%)	9 (100%)	4 (44.4%)	6 (66.7%)	32
Seronegative Spondyloarthropathy						
	Pre-Test	8 (100%)	8 (100%)	3 (32.5%)	5 (62.5)	
	Post-Test	8 (100%)	8 (100%)	6 (75%)	7 (87.5%)	23.5
Improvement (%)		12.2	27.5	32.7	46	29.1

25.7% improvement in vasculitis questions, 32% improvement in crystal arthropathy questions, and 23.5% improvement in seronegative spondyloarthropathy questions. The majority of residents found the education session helpful for their academic training (96%), helpful for inpatient medicine rotations and clinic (84.4%), and felt it would change their clinical management (88.8%).

Conclusion: This innovative rheumatology fellow initiated curriculum design project was an effective way to educate resident learners on rheumatology topics, as well as for rheumatology fellows to build medical education skills. By creating a unique culture of collaboration among fellows and residents there is potential for broad positive effects and improvement in patient care. There were improvements in each disease category, which were not proportional to the percentage of students who requested these topics during the needs-assessment. This study was limited by sample size, as many residents were unable to attend the full education session. We plan to continue this education series in future years by including additional rheumatology topics, and expanding to incorporate additional IM subspecialty fellowship programs in the education sessions.



Graph 1. Results of knowledge assessment before and after the education sessions.

Disclosure: K. Kruzer: None; **V. Vertalino**: None; **N. Tapia**: None; **A. Long**: None; **A. Blatt**: None; **U. Shah**: None; **B. Marston**: None.

Abstract Number: 2076

Piloting a Rheumatology and Sports Medicine Case-Based Collaborative Learning Curriculum for Medical Students

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Case-based collaborative learning (CBCL) is an interactive teaching method that integrates cases with key concepts. CBCL is recognized as a means for knowledge improvement for learners and consequently has become increasingly utilized in medical education. Herein, our group created a CBCL curriculum with rheumatology and sports medicine content.

Methods: All medical students on a 10-week Internal Medicine (IM) Core Clerkship were enrolled in this study measuring the efficacy of this curriculum. The 1.5-hour rheumatology and sports medicine CBCL curriculum was performed in-person once per clerkship cycle. The CBCL is led by an internal medicine resident rotating on a dedicated teaching rotation.The CBCL consists of several topics, including crystalline arthropathies, osteoarthritis, inflammatory arthritis, and sports medicine. To assess knowledge improvement, we developed a pre/post multiple-choice question knowledge assessment and analyzed score differentials. To elaborate, students completed an 8-question pretest knowledge assessment two days prior to the CBCL curriculum. Answers to the pretest questions were not provided to the students at the completion of the pretest. The questions/answers to the pretest were not explicitly discussed during the CBCL presentation. Students then completed the same 8 question quiz after the CBCL curriculum. The posttest was made available 1 day after the CBCL curriculum ended and was required to be completed within 4 days of the session. All students completed both the pre/post assessment.

Results: Institutional Review Board approval was obtained, and data was collected from January 2022-December 2022. Statistical differences were analyzed using paired t-testing and analysis of variance (ANOVA).136students completed both CBCL quizzes. The mean scores of the pre- and post-quizzes were 61.4% (SD +/- 23.0%) and 70.6% (SD +/- 19.4%), respectively. The score improvement for the overall cohort was 9.2% ($p< 0.001$). All medical student blocks had a statistically significant improvement in quiz scores except for block 3 ($p=0.354$). ANOVA testing demonstrated consistency across the four blocks regarding mean pretest ($p=0.284$), posttest ($p=0.687$) and score improvement ($p=0.565$) with no significant differences between blocks.

Conclusion: CBCL was an effective alternative to lecture-based teaching, and consequently, this curriculum was integrated into the IM Clerkship Curriculum. A limitation of this project was the inability to determine long-term retention of concepts acquired during the CBCL. Future directions of this project may include diversification of pre- and post-tests and obtaining student-centered feedback on the curriculum.

Disclosure: M. Dimachkie: None; **B. Bettendorf**: None; **M. Sanders**: None.

Abstract Number: 2077

A Curriculum of Online Education Significantly Improved Rheumatologists' Knowledge, Competence and Confidence in Managing Patients with Spondyloarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) are challenging conditions for rheumatologists to manage. There is an increasing focus on virtual training modalities post-pandemic. We assessed whether a curriculum of online educational activities could improve rheumatologists' knowledge, competence and confidence in managing patients with spondyloarthritis.

Methods: A curriculum of virtual activities was developed on the evolving therapeutic landscape in the treatment of psoriasis (PSO) and spondyloarthritis (SpA). Data presented here are from the initial 4 activities on SpA, including 2 on line panel discussions and enduring versions of symposia from EADV 2022 and ACR 2022. Data were collected between 2022 and 2023 with n numbers for each activity ranging from 108 to 549 completing pre- and post-activity questions. Educational effect was assessed with a repeated-pairs pre-/post-assessment; 3 multiple-choice, knowledge or competence questions and 1 self-efficacy, 5-point Likert scale confidence question were analyzed. Data were subsequently combined and analyzed by 5 themes to provide a summative overview of the effect of the education across the combined activities. A McNemar's test was conducted to assess statistical significance of changes from pre- to post-assessment.

Results:

- 12,256 MD learners across the globe participated in the activities including 3,877 rheumatologists, 3,180 dermatologists and 4,104 primary care physicians
- Rheumatologists demonstrated a statistically significant improvement in knowledge or competence across 4 of the 5 learning themes (clinical data informing disease management, individualizing treatment to limit disease progression, monitoring disease activity and treatment goals for PsA and axSpA; all $P < 0.01$)
- Overall, 79% of rheumatologists gained competence and 26% gained knowledge
- Overall, 33% of rheumatologists reported increased confidence e.g. in setting appropriate treatment goals or implementing a treat-to-target strategy: for confidence questions aligned with each individual activity, the percentage of rheumatologists who gained confidence ranged from 19% to 59%

Conclusion: These results highlight the benefits of an on-line curriculum of education in challenging rheumatologists to better manage patients with PsA and axSpA. As the treatment landscape for these diseases continues to evolve, rheumatologists will likely benefit from further innovative educational modalities on key clinical data for emerging medicines and strategies for their deployment in clinical practice.

Disclosure: E. Bell: None; **M. Calle**: None; **I. McInnes**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Bristol Myers Squibb, 2, 5, Cabaletta, 2, 11, Causeway Therapeutics, 2, 11, Celgene, 2, 5, Compugen, 2, 11, Dextera, 11, Eli Lilly, 2, EveloBio, 1, 2, 4, 11, Gilead, 2, Janssen, 2, 5, Moonlake, 2, NHS GGC, 4, Novartis, 2, 5, Pfizer, 2, Sanofi, 2, UCB, 2, 5, Versus Arthritis, 12, Trustee Status.

Abstract Number: 2078

Interim Evaluation of a 6 Year Remote Online Adaptive Learning Platform Module for Rheumatology Fellows: Applied Rheumatology on the Go

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
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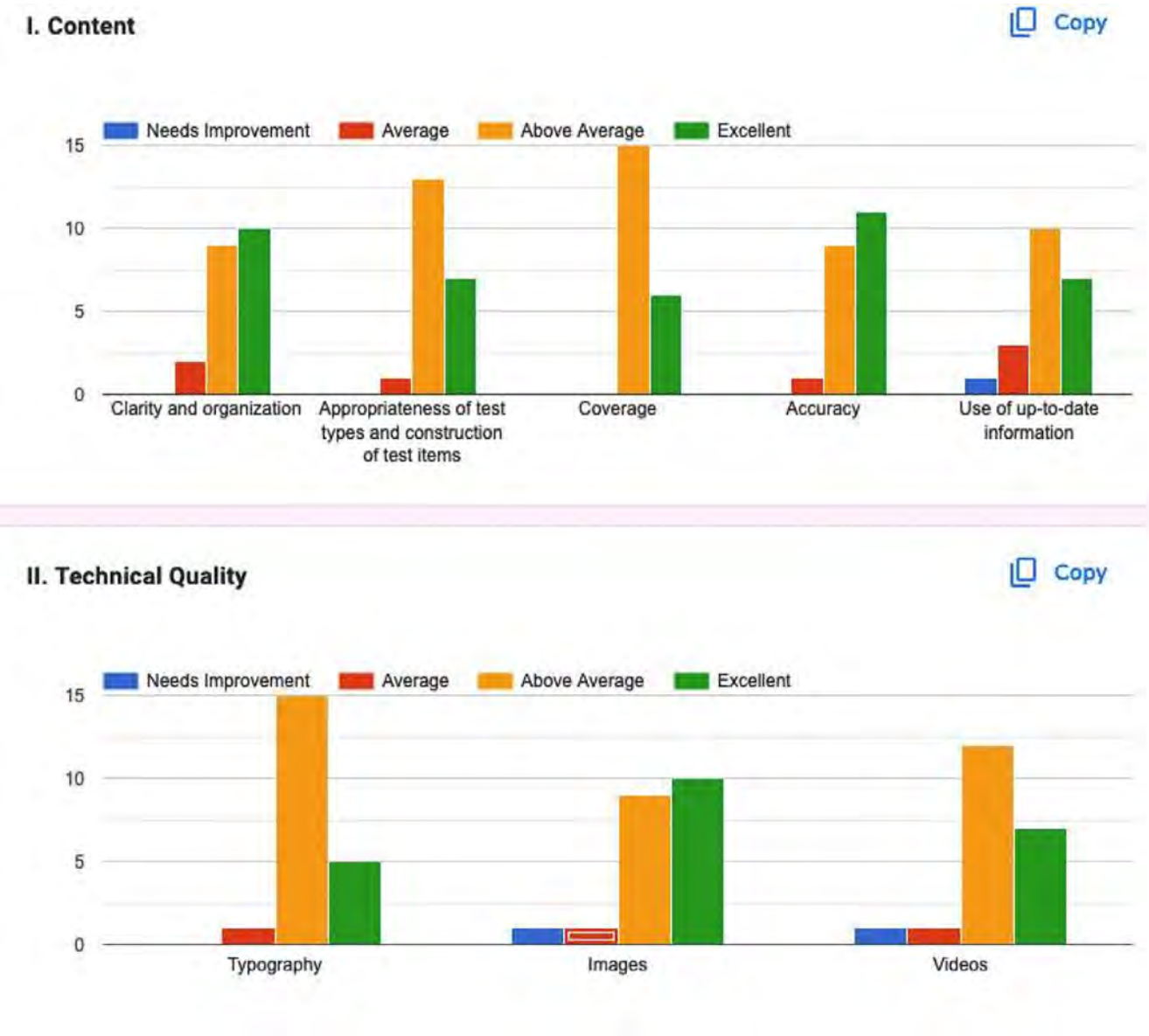
Session Time: 9:00AM–11:00AM

Background/Purpose: The ARGO Project (applied rheumatology on the go) is an online learning tool in Rheumatology. It uses Cerego, an adaptive learning technology online/mobile platform. Started in 2017, by integrating distance learning (or e-learning), busy trainees or early career Rheumatologists can review or update themselves in Basic and Applied Rheumatology. The 20 modules of various rheumatology question materials are presented to the learner depending on their individual learning patterns. Items that the learner seems to have more difficulty with will be shown more frequently compared to items they find easy. There are notes, and external resources for the learner to facilitate asynchronous learning. Users and instructors can track progress and determine the difficulty of questions.

Methods: The platform is catered towards helping recently graduated fellows into reviewing prior to their board exams. Enrollment is voluntary through interest and word of mouth from past fellows. This year, instructor editors were invited to help update the content of the project.

Usability surveys on the use of the platform were sent to the society communications group. Descriptive analysis was used to analyze the results. Free text answers were categorized into themes.

Results: At the time of this interim analysis only 21 of the prior 70 past and current fellows agreed to evaluate the platform. 33% of the respondents were from the first batch of 2017, followed by 2019. 66% of the fellows did not know how to use the Spaced Repetition concept. For those who used the platform for more than 1 yr (those who did not pass the board exam the first time), only 2 out of 9 respondents used it less for the second year. When asked about the content of the modules, the majority of the respondents answered it was above average. It is expected to see some feedback about the need to upgrade the information since the module was originally started in 2017. With regards to technical quality, a few respondents recommended adding more images and videos. This is important feedback given the increase in use of musculoskeletal ultrasound in our curriculum over the last few years. Nevertheless it is reassuring to see that navigation was still easy for the users. When asked which part of the project they favored the most, the majority selected the flashcards and mnemonic notes. All respondents felt they would recommend the platform as a learning tool. For the free text comments, there appeared to be some common suggestions themes such as



Usability survey of the ARGO project: Content and Technological Quality

automation: notification messages or emails when not logging in at appropriate intervals. Another common suggestion theme was to use the platform in tandem with the examination blueprint topics.

Conclusion: The survey will continue until the next interval progress report as part of the ILAR grant requirements. It is reassuring to see that a 6 year old module retains most of it's usability for medical education. Additional images and videos may be needed for improved user experience. For the next phase of the project, a separate feedback form will be sent to the instructor-editor groups invited to update the content of the modules.

Usability survey of the ARGO project: Navigation and favorite feature

Disclosure: L. Traboco: None; **K. Chua**: None; **S. Reyes**: None; **S. Navarra**: Astellas, 6, AstraZeneca, 6, Biogen, 2, Boehringer-Ingelheim, 2, GSK, 6, Novartis, 6, Pfizer, 6.

Abstract Number: 2079

Comparative Analysis of Teledidactic and On-Campus Training in Musculoskeletal Ultrasound – the TELMUS Study

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Musculoskeletal ultrasound (MSUS) plays a vital role as a diagnostic imaging modality in rheumatology, while also serving as an effective teaching tool to enhance medical students' comprehension of functional anatomy. Amidst the COVID-19 pandemic, the utilization of portable ultrasound equipment and telemedicine teaching methods ensured the continuity of practical skill instruction, with the potential to further broaden teaching prospects in medical schools going forward.

Methods: In this study we assessed and compared the learning success of medical students in MSUS, achieved through a conventional and a teledidactic course. During the theoretical teaching sessions, an ultrasound-certified course instructor (DEGUM/EFSUM level III-highest level) introduced the most important standard sections in a video-based approach using the validated course concept of the MUDE study [1] . Following that, both groups received practice time and individualized feedback during hands-on sessions. Throughout the course, all students were equipped with an 8th generation Apple iPad and a ButterflyIQ+® portable ultrasound system. To assess student learning objectively, an Objective Clinical Structured Examination (OSCE) was conducted before the course commenced and upon its completion.

Results: A total of thirty medical students in clinical semesters were randomly assigned to either a conventional on-campus cohort or a teledidactic teaching cohort, receiving virtual teaching exclusively. Prior to the course, students achieved an average score of 20.68% (SD ± 6.67) in the OSCE, whereas the average score following the course completion was 96.83% (SD ± 6.71). There were no statistically significant differences in OSCE scores between the two teaching cohorts (p=0.479), indicating that neither course was inferior to the other.

Conclusion: The teledidactic teaching concept utilizing portable ultrasound devices resulted in a significant increase in MSUS knowledge among medical students, demonstrating a comparable learning outcome to the conventional course. This worldwide pilot study extends MSUS training opportunities for medical students through innovative teaching methods, contributing to the development of future rheumatologists by emphasizing ultrasound as a crucial imaging tool in rheumatology.

[1] Grobelski J, Recker F, Wilsmann- Theis D, et al. Establishment and validation of a didactic musculoskeletal ultrasound course for dermatologists using an innovative handheld ultrasound system – the MUDE study (Musculoskeletal Ultrasound in Dermatology). J Deutsche Derma Gesell 2021; 19: 1753–1759. doi:10.1111/ddg.14614

Disclosure: R. Neubauer: None; **F. Recker**: None; **C. Bauer**: None; **S. Petzinna**: None; **P. Karakostas**: None; **C. Behning**: None; **V. Schäfer**: None.

Abstract Number: 2080

Implementation of a Clinically-Focused Online Journal Club in Rheumatology: Experience from TheMednet

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Journal clubs are an essential part of lifelong learning for physicians. After fellowship, access to journal club discussions may be limited. TheMednet is a physician-only online platform that allows for dissemination of expert knowledge in a searchable, private, and moderated question and answer (Q&A) format. A clinically focused online journal

Trial	Questions	Total Views	Total Users Reached	Total Institutions
ADVOCATE	How long do you recommend using avacopan as maintenance therapy in AAV? How should the results of the ADVOCATE trial be applied in AAV patients who receive rituximab induction and maintenance therapy? Are there particular subsets of AAV patients in which avacopan is more effective? Should the use of avacopan be limited to those patients at increased risk of steroid toxicity given the anticipated high cost of this medication?	727	240	117
SEAM-RA	What was the rationale for abrupt discontinuation of etanercept rather than gradual tapering in the SEAM-RA trial? Were the patients enrolled in the SEAM-RA trial prior methotrexate monotherapy non-responders? Are the results of the SEAM-RA trial generalizable to other TNF inhibitors given the differences in immunogenicity? Was the methotrexate dose reduced over time in the combination therapy or methotrexate monotherapy groups in the SEAM-RA trial?	721	236	127
ORAL	How do you approach CV risk assessment in RA patients when RA itself is associated with some degree of increased CV risk at baseline? What role do you see for JAK inhibitors in RA treatment strategies given the data we now have regarding CV and cancer outcomes? Would you recommend that a patient with stable coronary artery disease and well-controlled RA on a JAK inhibitor continue on their current therapy? How do you counsel patients regarding the cardiovascular and cancer risks associated with tofacitinib? Do you still plan to offer tofacitinib to RA patients over 65 if they have one or more additional C	1777	450	115
DISCOVER 2	Where in the sequence of biologics would you consider guselkumab for patients with active psoriatic arthritis despite standard DMARD therapy? How do you interpret treatment response in the DISCOVER-2 Trial when patients were allowed to remain on up to 10mg of prednisone equivalent for disease control while on guselkumab? How long would you recommend that a patient continues guselkumab prior to deciding that the therapy is not effective?	1050	287	168
Racial Disparities in Pediatric Lupus Nephritis	Are there any major differences in clinical manifestations or autoantibody profiles in children with SLE based on ethnicity? What are some explanations for the persistent renal outcome disparity gaps affecting certain minority groups of patients with pediatric SLE despite improvement in overall renal outcomes? How can ethnic representation in clinical research studies in childhood and adult SLE be improved?	465	179	87

club was designed and hosted on theMednet to engage rheumatologists and rheumatology fellows. Here we describe our experience in establishing a rheumatology journal club on theMednet.

Methods: TheMednet launched in Rheumatology in July 2020 and the first online journal club was implemented in March 2021. A physician editorial team reviewed major rheumatology publications and identified journal articles with significant clinical impact. An academic partnership with the journals allowed for sharing of the article with theMednet community. The article was distributed via email to registered rheumatologists with a call for questions. Study authors and content experts were recruited by the editorial team to answer questions submitted by the rheumatology community. The Q&A was distributed over 3-4 weeks in email newsletters.

Results: Five journal clubs were conducted between March 2021 and January 2023. Journal club articles and questions are listed in Table 1. The articles were downloaded 936 times. On average, 278 users at 122 unique institutions, including academic and community were reached during each journal club. A total of 19 questions were included among the five programs and comprised 36 individual answers from 6 authors and 3 non-author content experts. Q&A were viewed 4,740 times. In all five journal clubs, at least one author of the chosen manuscript participated in the online discussion and in three of the five journal clubs, non-author content experts participated. Eleven polls created by the editorial team resulted in 430 individual poll voters participating and a total of 447 votes. The most engaging journal club was ORAL Surveillance with 1,777 question views and least engaging was Racial Disparities in Pediatric Lupus Nephritis with 465 question views. As of May 2023, theMednet rheumatology community included 1,760 practicing rheumatologists across the United States.

Conclusion: TheMednet Journal Club feature is an effective way to connect academic and community rheumatologists around high impact publications in the field of rheumatology. Journal club engages physician users to submit Q&A and participate in interactive polls. Physicians are able to share insights on clinical practice and to exchange viewpoints on translation of data into clinical practice.

Disclosure: N. Couette: themednet.org, 7; **M. Briones**: theMednet.org, 3, 11; **N. Housri**: themednet.org, 3, 8.

Abstract Number: 2081

Harnessing the Power of Social Media for Good: Using Instagram as a Formative Assessment Tool

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
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Session Time: 9:00AM–11:00AM

Background/Purpose: Childhood rheumatologic and musculoskeletal diseases (RMDs) have an estimated prevalence of 1:300,000 in the general population and are associated with morbidity and mortality in children. Approximately 30% of acute pediatric visits are for musculoskeletal (MSK) complaints, often the initial presenting symptom of RMDs, while only 2% of pediatric board examinations cover rheumatologic topics. Additionally, there is a variable amount of graduate medical education (GME) pediatric rheumatology training due to a paucity of pediatric rheumatologists nationwide, with 33% of medical schools and 40% of pediatric residency programs having no affiliated pediatric rheumatologist. This discrepancy highlights

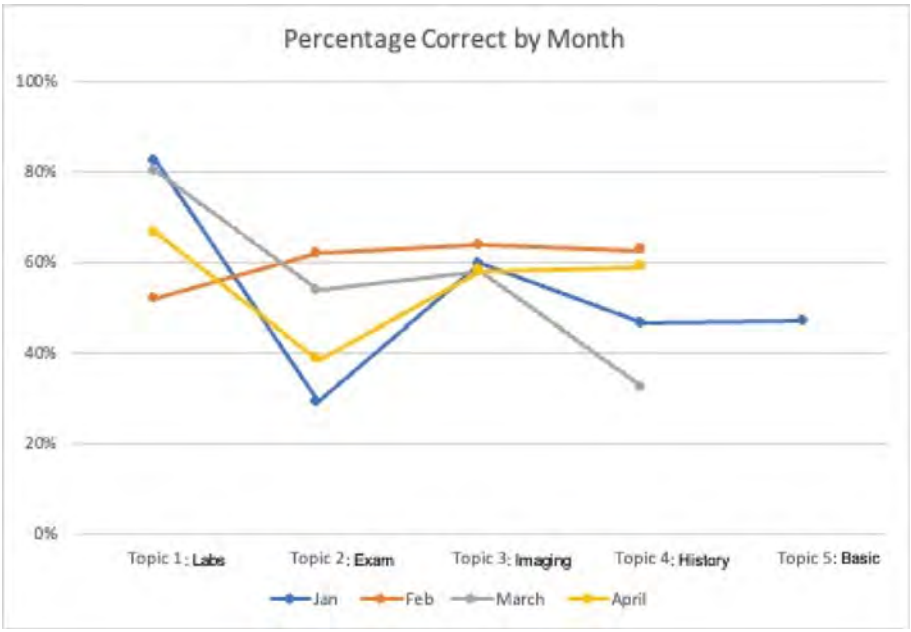

Figure 1. Percent of correct answers separated by month. Questions released during the first week of the month always cover laboratory studies in RMD, week two covers physical exam findings, week 3 covers imaging, week 4 covers history and clinical criteria, and when there is a 5th week, it is dedicated to basic science. Users most consistently correctly responded to questions covering imaging in RMD, ~60% of respondents answered correctly. Of all items, 12% were noted to be "easy," 6% were "difficult," and the remaining 82% were in the "average" difficulty index.

the need to improve the education of pediatric providers to evaluate and appropriately triage presentations concerning for RMDs.

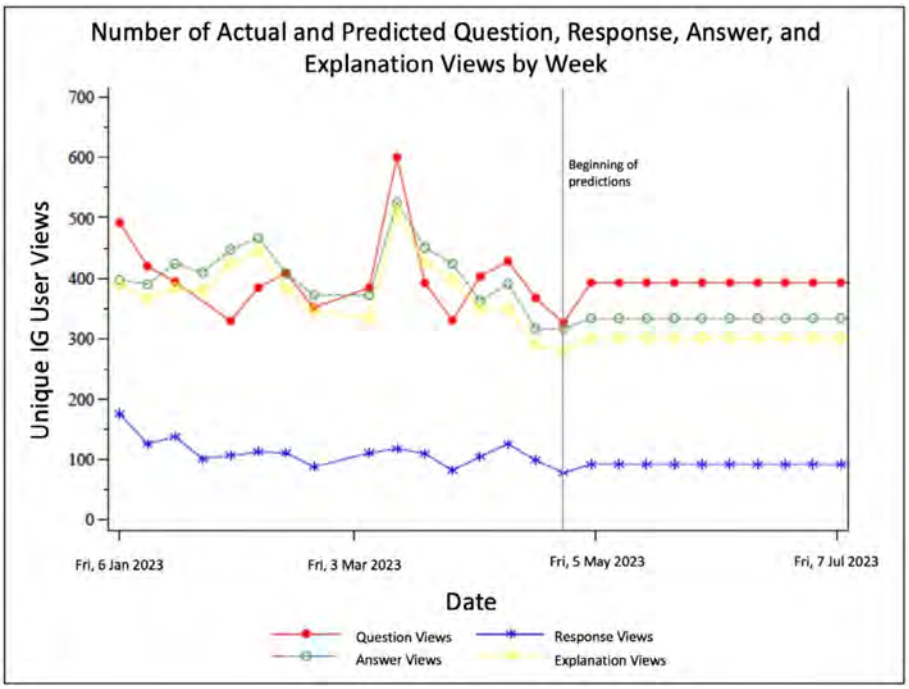

Figure 2. Number of actual and predicted unique users engaging with IG content by week. For the first 17 weeks, there were 395 question views, 110 responses, 403 answer views, and 376 explanation views. The total number of question views was not recorded for week 4, so this week was not used to forecast. Of note, there was also a notable jump in views on week 11, which coincided with resident match day. Predictions were made for the next three months using the SAS ESM procedure, which generates forecasts using exponential models with optimized smoothing weights for time series models.

Within GME, learner engagement, motivation, and enjoyment pose a significant challenge. Previous studies have shown gamification to be an effective strategy in addressing these issues by promoting risk-free decision-making, providing quick feedback, and demonstrating improvement in student knowledge and achievement. In this vein, we developed a gamified rheumatology review intervention using, Instagram (IG), a social media platform to determine effects on learner engagement and information retention.

Methods: Board-style questions covering RMDs were written to target GME learners. A Question of the Week (QOTW) is posted weekly to the Baylor College of Medicine (BCM) Pediatric Residency business IG page (with approximately 1600 followers) for 24 hours. The correct response is revealed immediately, and the following day an explanation is posted for 24 hours. Available data from IG was collected, including number of viewers per question and response, and response breakdown. The following week, the usernames associated with the first five correct answers are posted, incorporating gamification and friendly competition. Additionally, surveys collected information on enjoyment of QOTW, perceived knowledge acquisition, and preferred question difficulty.

Results: Engagement with QOTW has been tracked for 4 months and was higher than expected. Figure 1 depicts the percent correct broken down by month and weekly topic, showing the highest average of correct answers regarding imaging. Figure 2 illustrates user engagement derived from unique username. Additional IG surveys showed 94% of users enjoyed QOTW, 100% learned from it, and 56% of respondents would prefer more challenging questions.

Conclusion: This data indicates that the QOTW educational intervention utilizing IG as a delivery method unites gamification and formative assessment in the social media space. Given the frequent interaction with social media by young learners, we are successfully able to utilize this platform to reach and engage many more learners than traditional teaching methods. Ultimately, we believe this method is an effective way to educate our target audience - pediatricians, residents, and medical students - which will improve recognition, work up, and timely, appropriate referral for those patients with concerns for RMDs.

Disclosure: A. Thompson: None; **J. Nguyen**: None; **A. Braddock**: None; **S. Kumar**: None; **M. Gillispie-Taylor**: None.

Abstract Number: 2082

Delivery of Rheumatology Education to Internal Medicine Residents in Rwanda: Evaluation of a New Virtual Rheumatology Course Supplemented by On-site Clinical Teaching

Carol Hitchon[1], Becky Abdissa Adugna[2], Richard Akintayo[3], Paul Caldron[4], Ines Colmegna[5], Ida Dey[6], Paul McGill[7], Andres Ponce[8], Rosie Scuccimarri[9], Mohammed Tikly[10], Girish Mody[11] and Michele Meltzer[12], [1]University of Manitoba, Winnipeg, MB, Canada, [2]Addis Ababa University, Addis Ababa, Ethiopia, [3]Dumfries and Galloway Royal Infirmary, Edinburgh, United Kingdom, [4]Arizona Arthritis & Rheumatology Associates, P.C. - Emeritus (no longer in patient care role), Depoe Bay, OR, [5]The Research Institute of the McGill University Health Centre, Montréal, QC, Canada, [6]University of Ghana Medical School, Accra, Ghana, [7]Department of Rheumatology Stobhill Hospital, Glasgow, United Kingdom, [8]Jefferson, Philadelphia, PA, [9]McGill University/Montreal Children's Hospital, Montréal, QC, Canada, [10]Wits University, Johannesburg, South Africa, [11]University of KwaZulu-Natal, Durban, South Africa, [12]Thomas Jefferson University/ Rheumatology for All,Inc., Philadelphia, PA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Professional Education Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: There exists a critical lack of rheumatology resources in many parts of the world including sub-Saharan African countries. As a result, in these countries, rheumatology education is limited and often provided by specialists with variable rheumatology expertise. As an initial step to improving rheumatology capacity in Africa, our organization "Rheumatology For All" (RFA) has developed a rheumatology program for Internal Medicine (IM) Residents that can be delivered in person or virtually. Here we describe the evolution, implementation and acceptance of the virtual educational program in Rwanda.

Methods: We delivered a virtual rheumatology curriculum course for second year IM residents (approximately 30/year) in the University of Rwanda, Rwanda in 2021,2022 and 2023.Weekly lectures and tutorials were delivered (in English) over 16 weeks by rheumatology faculty from Ghana, Ethiopia, South Africa, United Kingdom, United States and Canada. In 2021, prerecorded lectures were uploaded to a central course website for students to review in preparation for weekly interactive online tutorials. In 2022 and 2023, there were no prerecorded lectures only the interactive lectures and tutorials. Additional teaching material including customized videos demonstrating musculoskeletal exam techniques and reading material was uploaded to a central website. In 2023, the virtual lecture series was followed by a week-long program delivered in Kigali by 4 faculty (CH, IC, MM, RS) consisting of supplementary lectures, case-based tutorials and clinical skill teaching. We evaluated virtual course experiences from 29 responding students (13 in 2021; 12 in 2022; 4 in 2023) and evaluated on-site teaching experiences from 10 students.

Results: Feedback from 2021 was incorporated into the 2022 and 2023 courses when feasible. Only 8/29 (27%) were able to attend all virtual lectures. All students found lectures and tutorials beneficial, especially physical exam videos. Half (52%) wanted more interaction with faculty (2021 vs 2022 p=NS).Some students reported difficulty accessing online content, though this improved in 2022 after switching to a university-based platform. Case-based discussions were considered important and culturally relevant images were appreciated. Students requested more clinical cases, including student-led case presentations even if this extended course/tutorial duration. While appreciative of the online course, many students requested on-site training to allow more face-to face discussion, bedside teaching, and hands-on demonstration of rheumatology skills. Student comment: "*… we hope this will continue for the coming years and probably not only virtually but also [face-to-face] … It would be good if we share cases … (though we don't have all investigations) …*" At the end of the courses, students' confidence level with rheumatology cases was good with a median rating of 7/10 (range 5-9) for the virtual course and 7.5 (range 5-8) for the in-person course.

Conclusion: The RFA virtual rheumatology course is a feasible means to provide rheumatology education to African medical students but does not replace the need for in person teaching. This program will continue to evolve in response to regional needs.

Disclosure: C. Hitchon: Astra Zeneca, 1, Pfizer, 5; **B. Adugna**: None; **R. Akintayo**: None; **P. Caldron**: None; **I. Colmegna**: None; **I. Dey**: Roche, 6; **P. McGill**: None; **A. Ponce**: None; **R. Scuccimarri**: None; **M. Tikly**: None; **G. Mody**: None; **M. Meltzer**: None.

Abstract Number: 2083

Compiled Verbal Feedback as a Novel Mechanism for Faculty Feedback from Rheumatology Fellows-in-Training

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Feedback from fellows-in-training (FITs) is important for faculty professional development and to enrich clinical teaching in rheumatology fellowship training programs. Most fellowship training programs use online evaluations completed annually by FITs to provide feedback on clinical teaching by faculty. The quality of feedback provided through this mechanism may be limited by time burden on trainees and concerns for confidentiality. We sought to evaluate the effectiveness of online evaluations vs. a novel feedback mechanism of compiled verbal feedback.

Methods: We developed a novel feedback system in which FITs provided verbal feedback on all faculty to a facilitator who then compiled the feedback and shared it in a de-identified manner with individual faculty members. Based on the FITs' preferences, this was done with all FITs together as a group and facilitated by the fellowship training program director. FITs also completed standard annual anonymous online evaluations for all faculty with whom they worked. All FITs and faculty in our institution's Rheumatology Division were invited to participate voluntarily in the study; study investigators (one FIT, two faculty) were excluded. Participating FITs and faculty completed surveys assessing the perceived effectiveness of feedback and confidentiality of both forms of evaluation. Surveys used Likert scales (1="Strongly Disagree"; 5="Strongly Agree"). Responses were converted into two categorical variables: "Favorable," representing responses 4-5 or 1-2 depending on question phrasing; and "Neutral/Unfavorable," representing all other answer choices. Comparisons of paired responses between the two feedback mechanisms were performed using McNemar tests.

Results: Thirteen of 15 eligible faculty and 4/4 eligible FITs completed both surveys. Faculty responses in both surveys are summarized in **Table 1**. Favorable responses were numerically higher in all questions for the compiled verbal feedback system and statistically significantly higher in questions on the feedback's effectiveness in explaining strengths, specificity, actionability, and consistency with faculty self-assessment of strengths. FIT responses are summarized in **Table 2**. FITs responses were largely neutral/unfavorable in most questions regarding online evaluations; no FITs responded favorably to the two questions on confidentiality of online evaluations. In contrast, all FITs responded favorably to every question in the survey on compiled verbal feedback with one exception: concerns about confidentiality. Although only one FIT responded favorably to this question, all FITs responded favorably regarding concerns about future interactions with evaluated faculty.

Table 1. Faculty responses regarding online evaluation and compiled verbal feedback formats. All values reported as N (%).

	Online Evaluations		Compiled Verbal Feedback		P-Value
	Favorable	Unfavorable/Neutral	Favorable	Unfavorable/Neutral	
Quality of Feedback					
Explains strengths	7 (54)	6 (46)	13 (100)	0 (0)	**0.041**
Explains areas for improvement	4 (31)	9 (69)	9 (69)	4 (31)	0.131
Improves teaching skills	2 (15)	11 (85)	7 (54)	6 (46)	0.131
Specific	0 (0)	13 (100)	7 (54)	6 (46)	**0.023**
Actionable	2 (15)	11 (85)	8 (62)	5 (38)	**0.041**
Prompts reflection	6 (46)	7 (54)	10 (77)	3 (23)	0.221
Consistency with self-assessment					
Strengths	5 (38)	8 (62)	12 (92)	1 (8)	**0.023**
Areas for improvement	3 (23)	10 (77)	7 (54)	6 (46)	0.289
Confidentiality					
Unable to identify evaluator	8 (62)	5 (38)	11 (85)	2 (15)	0.450

Table 2. FIT responses regarding online evaluation and compiled verbal feedback systems. All values reported as N (%).

	Online Evaluations		Compiled Verbal Feedback		P-value
	Favorable	Unfavorable/Neutral	Favorable	Unfavorable/Neutral	
Quality of feedback					
Specific	3 (75)	1 (1)	4 (100)	0 (0)	1
Provides positive feedback	4 (100)	0 (0)	4 (100)	0 (0)	N/A
Provides feedback on areas for improvement	2 (50)	2 (50)	4 (100)	0 (0)	0.480
Reflective and meaningful	1 (25)	3 (75)	4 (100)	0 (0)	0.248
Improves faculty teaching	1 (25)	3 (75)	4 (100)	0 (0)	0.248
Confidentiality					
Concerns about confidentiality	0 (0)	4 (100)	1 (25)	3 (75)	1.000
Concerns about future faculty interactions	0 (0)	4 (100)	4 (100)	0 (0)	0.134

Conclusion: Compiled verbal feedback by FITs produced more actionable and effective feedback with no concerns for future interactions with faculty when compared with standard online evaluations, as perceived by both FITs and faculty. Other fellowship training programs may consider incorporating compiled verbal feedback to enrich the quality of feedback provided to faculty on clinical teaching. Further study of this method across different program sizes and institutions is warranted.

Disclosure: G. Katz: None; **E. Miloslavsky**: None; **A. Fernandes**: None; **M. Bolster**: American Board of Internal Medicine, 6, American College of Rheumatology, 4, Corbus, 5, Cumberland, 5, Elsevier, 2, Mitsubishi, 5, Novartis, 1, Rheumatology Research Foundation, 5, The Merck Manual, 6.

Abstract Number: 2084

Enhancing Internal Medicine Curriculum: Key Rheumatology Themes in Inpatient Setting

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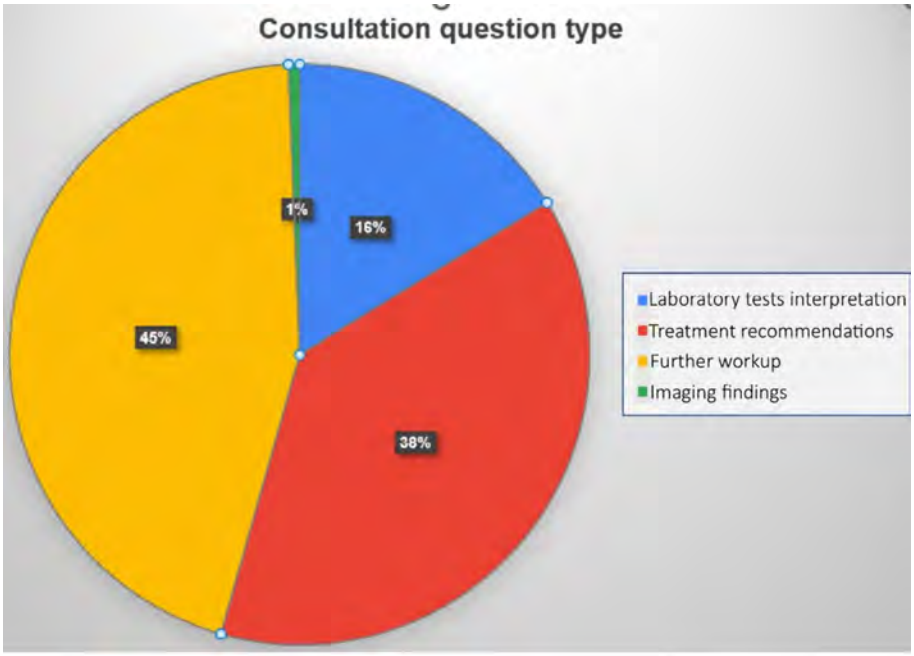
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite rheumatology being a critical component of internal medicine (IM) residency training, internists are often inadequately trained to identify and manage rheumatologic disorders. In order to evaluate teaching gaps in the core inpatient curriculum, we surveyed inpatient rheumatology consults placed by IM residents over 6 months period. To help inform curriculum revisions, we compared the extracted data to the current curriculum objectives and identified areas of improvement for the inpatient setting.



Methods: Using Epic SlicerDicer we performed a qualitative analysis of inpatient consult encounters from June 2022-January 2023. Extracted data was exported into an excel sheet for analysis. Each consult question was attributed to one theme category: 1) laboratory test interpretation;2) imaging findings;3) workup for complex presentations; 4) management of rheumatic disease. Rheumatologic diagnosis was extracted in the sheet if mentioned in the consult question. Of note, some consult questions contained more than one diagnosis and theme.

Results: 160 consultations were assessed. The purpose of the consultations was recommendation regarding further workup in 72 (45%), treatment recommendation in 61 (38%), laboratory tests interpretation 26 (16%), imaging findings in one (1%). A broad range of rheumatic diseases was covered in the consult questions. Most common was arthralgia/ RA33%, gout 19%, SLE 15%, ILD 10%, vasculitis 5%, myopathy 5%, scleroderma 4%, GCA 4%, APLS 3%, rashes 2% and 1.6% for Sjogren's syndrome, dermatomyositis, MCTD, SJS/TEN, IgG4-RD.The most concise questions were about gout or lupus flare. When our rheumatology curriculum was examined, we found that 40% of consultation topics were not included.

Conclusion: Our analysis of consult questions revealed gaps in internists' training related to rheumatologic disorders. Most common consults were regarding gout and unspecified joint pain which can be commonly managed by the IM team. The variety of rheumatic diseases covered in the consult questions underscores the importance of comprehensive training in this field. By addressing these gaps and expanding the trainees' knowledge base, we can improve the overall academic and clinical training in rheumatology for internal medicine residents.

Disclosure: J. Ferraz Neto: None; **D. Ismail**: None; **S. Esagian**: None; **M. Vukelic**: None.

Abstract Number: 2085

A Survey on Giant Cell Arteritis-Related Knowledge Among Internal Medicine Residents

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Giant Cell Arteritis (GCA) poses challenges in clinical practice, necessitating a deep understanding. Internal medicine residents play a crucial role in patient care and management. This study evaluates their comprehension of GCA diagnosis and management, aiming to identify knowledge gaps and develop tailored educational programs. GCA, a medical emergency with risks of blindness and cerebrovascular complications, relies on diagnostic tools such as imaging and biopsies alongside clinical judgment. Glucocorticoids form the foundation of treatment, while future strategy involve targeted biologics. Enhancing training and addressing knowledge gaps empower residents to effectively identify and manage GCA, ensuring optimal patient outcomes.

Methods: An 18-item questionnaire was developed following the latest guidelines from the ACR and EULAR. A cross-sectional survey was conducted among residents from three different programs located in New York, Colorado, and Florida. The questionnaire encompassed 11 questions related to the presentation, diagnosis, and management of GCA. The

remaining questions were focused on assessing the residents' comfort level in diagnosing and managing GCA patients, as well as evaluating their educational training in this area.

Results: Out of 107 participants, 48 (approximately 44%) completed the survey, yielding significant insights. The response rates varied across different levels of training, with 27% of PGY1, 33.33% of PGY2, and 37% of PGY3 participants providing their feedback. While 40% of respondents expressed satisfaction with their instruction, around 41% admitted to not attending teaching sessions, and 47% had no experience in caring for GCA patients. Surprisingly, although 56% felt confident in diagnosing GCA, only 31% were comfortable managing such patients. Furthermore, only 37% demonstrated familiarity with FDA-approved GCA medications. While 90% correctly identified prednisone as the initial drug of choice, only 50% knew the recommended dosage. Awareness of alternative diagnostic methods and appropriate ocular symptom management was limited among the participants. However, 89% acknowledged the importance of annual DEXA scans for monitoring bone health. These findings highlight the specific areas that require further education and training in the field of GCA.

Conclusion: The findings of this study reveal significant limitations in the understanding of GCA recognition and treatment among internal medicine residents. Although some residents expressed confidence in diagnosing GCA, there was a notable lack of familiarity with FDA-approved medications and discomfort in managing patients. Challenges were identified in comprehending initial dosages, utilizing alternative diagnostic techniques, and addressing ocular symptoms. These findings emphasize the critical need for targeted educational initiatives aimed at bridging these gaps and improving GCA care and management. By enhancing residents' understanding, we can strive for better patient outcomes and advance the management of GCA.

Disclosure: H. Maharjan: None; **M. Abdullah**: None; **S. Afridi**: None; **A. Osman**: None; **A. Sammar**: None; **A. Raja**: None.

Abstract Number: 2086

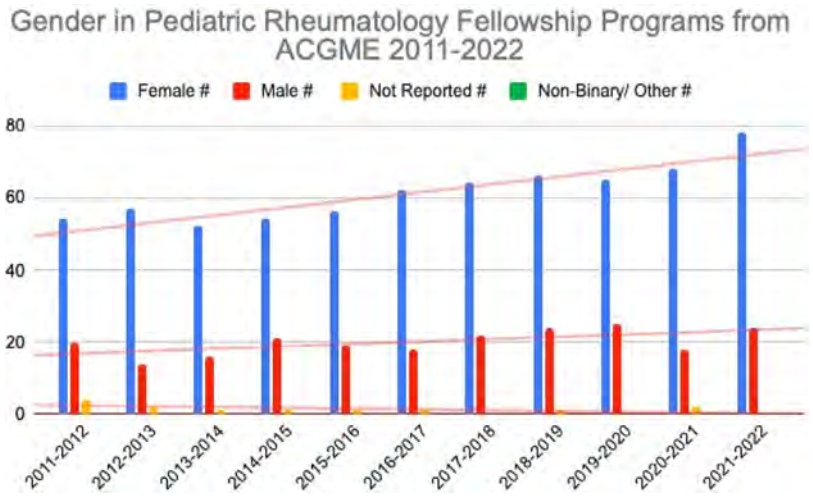
From Fellow to Fellowship Director: Gender Equity in Pediatric Rheumatology Pipeline

Bessie Roca loor[1], Maya Pandit[2], **Tracey Wright**[3] and Mill Etienne[4], [1]New York Medical College, Yonkers, NY, [2]Columbia University, New York, NY, [3]UT Southwestern, Dallas, TX, [4]New York Medical College, Valhalla, NY

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: As the demand for pediatric rheumatologists rise across the United States with a projected demand of almost 100% more pediatric rheumatologists needed by 2030 (1), it is essential to create a more balanced healthcare workforce, in hopes of achieving gender equity. We investigated the proportions of male-to-female fellows in pediatric rheumatology from 2011 to 2022 and compared this data to the gender diversity of the current pediatric rheumatology fellowship directors across the country.

Methods: This is a retrospective analysis of data extracted from the Accreditation Council of Graduate Medical Education (ACGME) Data Resource Books from 2011 to 2022. The data collection and trend analysis were conducted on Microsoft Excel. Gender was categorized as male, female and unreported. However, in the last two academic years, non-binary was added as a gender category. Additionally, to identify each pediatric rheumatology fellowship program director, the American Medical Association's Fellowship and Residency Electronic Interactive Database Access System (FREIDA) was utilized. The



pronouns each director used were extrapolated from their publicly available biographies to classify their gender. This data was publicly available therefore, IRB approval was not required.

Results: From 2011 to 2022, the reported data indicate female representation in pediatric rheumatology fellowship programs increased from 69% to 76.50% while the proportion of male fellows decreased from 26% to 23.5%. The representation of female fellows is approximately 40 to 50% higher than their male counterparts for each academic year in the period reported. Moreover, of the 38 pediatric rheumatology fellowship programs, 78.9% of the program directors were female.

Conclusion: More than three-fourths of pediatric rheumatology fellows as well as fellowship program directors are women. These findings are consistent with the 2015 American College of Rheumatology Workforce Study's overall prediction that women will constitute the majority of the rheumatology workforce by 2025. These results are also consistent with trends within the field of pediatrics with more females in training and pediatric practice (2). Pediatric rheumatology leadership mirrors the pediatric rheumatology pipeline, which is not consistent seen in fields that are predominantly women. Pediatric rheumatology's leadership pipeline can serve as a model for other fields that are predominantly women. To achieve gender equity in this subspeciality, future studies must examine the underlying causes of this gender shift and explore strategies to ensure broad exposure and recruitment of males into pediatric rheumatology.

Disclosure: B. Roca loor: None; **M. Pandit**: None; **T. Wright**: None; **M. Etienne**: None.

Abstract Number: 2087

Racial and Ethnic Diversity in Pediatric Fellowships: Fortifying the Pipeline

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SESSION INFORMATION

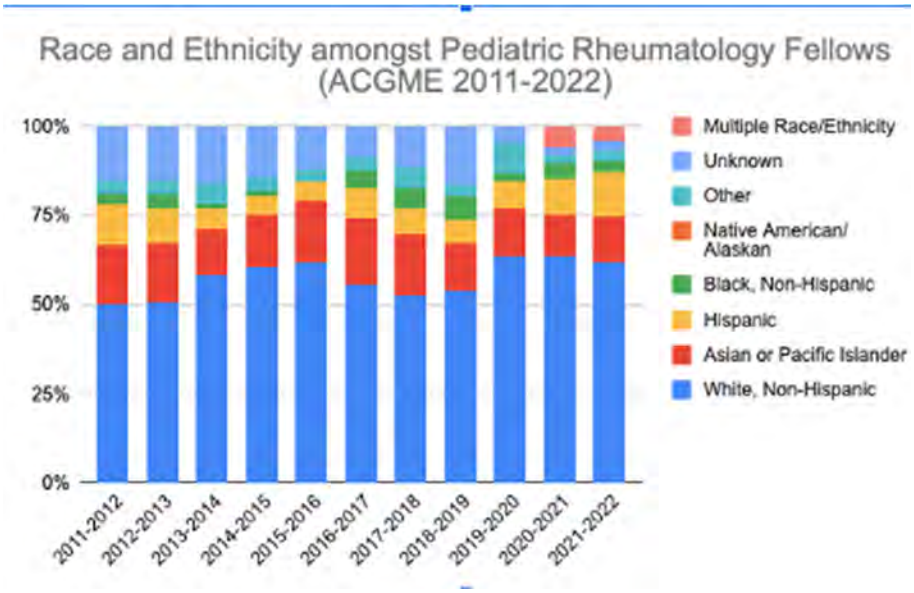
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The 2015 American College of Rheumatology Workforce study estimated the pediatric rheumatology full-time equivalent workforce to be 300 providers while the estimated excess demand was 95 providers (33%), with an estimated demand increase to almost 100% by 2030 (1). Nine states do not have a pediatric rheumatologist and the shortage is especially severe in Black, Hispanic, and Native American communities. This further emphasizes the need for physicians from demographics underrepresented in medicine (URiM), who are more likely to work in underserved communities, to care for children with rheumatic disease, while contributing to diverse perspectives in medical practice. This study explores trends of racial and ethnic diversity among US pediatric rheumatology fellows and consider consequences of these results on healthcare access, quality, and outcomes.

Methods: This is a quantitative analysis of the Accreditation Council for Graduate Medical Education (ACGME) Data Resource Book from 2011 to 2022. Demographics, including race and ethnicity of pediatric rheumatology fellows, were extracted, and analyzed in Microsoft Excel. A Chi-square analysis was utilized, and expected values were calculated using the 2020 census data (2011 to 2019) and the 2020 US census data for 2020 onwards. The primary outcome was trend in URiM representation (as defined by Licensing Committee on Medical Education) in pediatric rheumatology fellowship programs. The data was publicly available therefore IRB approval was not required.

Results: There were 910 pediatric rheumatology fellows between 2011-2022. Chi-square analysis demonstrated significant underrepresentation of Black, Hispanic, and Native Americans ($p < 0.0001$) in US pediatric rheumatology fellowship training programs. As seen in Figure 1, there were 3.4% Black (31/910), 8.4% Hispanic (76/910), and 0% Native Americans (0/910) fellows. The number of the fellows with these respective race and ethnicities was consistent throughout the 11 years analyzed. This data indicates that the percentage of URiM fellows in pediatric rheumatology fellowship programs is falling behind compared to the demographic shift in the US.

Conclusion: This data underscores the need to attract URiM physicians to pediatric rheumatology to practice in underserved communities and help address health equity gaps. The ACGME has prioritized the expansion and support of a diverse physician workforce, representative of the population it serves. Medical institutions throughout the US should be intentional in recruiting, cultivating, and retaining URiM fellows to create a culturally informed and inclusive clinical environment that will better serve our growingly diverse population. This call to action will improve health outcomes in underserved groups by training more physicians who are aware of these disparities and fostering patients' trust in the healthcare system.



References: 1. Correll CK, Ditmyer MM, et al. 2015 American College of Rheumatology Workforce Study and Demand Projections of Pediatric Rheumatology Workforce, 2015-2030. Arthritis Care Res (Hoboken). 2022 Mar;74(3):340-348.

Disclosure: B. Roca Loor: None; **M. Pandit**: None; **T. Wright**: None; **M. Etienne**: None.

Abstract Number: 2088

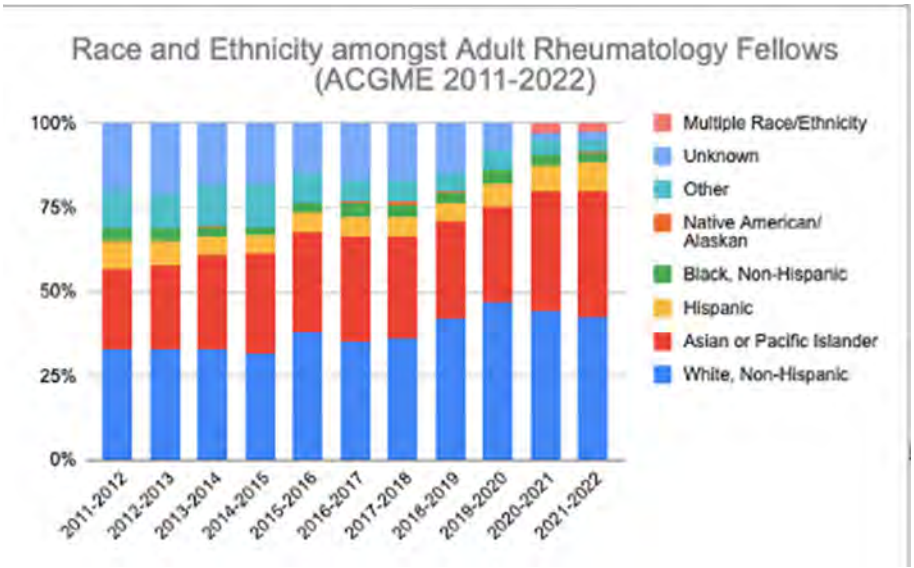
Room for Racial and Ethnic Diversity in Adult Rheumatology Fellowship Pipeline

Bessie Roca Loor[1], Maya Pandit[2], **Tracey Wright**[3] and Mill Etienne[4], [1]New York Medical College, Yonkers, NY, [2]Columbia University, New York, NY, [3]UT Southwestern, Dallas, TX, [4]New York Medical College, Valhalla, NY

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Professional Education Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The 2015 American College of Rheumatology Workforce study showed 8 of 1011 adult rheumatologists identified as Black, 85 Hispanic and 3 American Indian or Alaska Native (1). Recent studies show persistent disparities in disease activity and clinical outcomes for minoritized patients versus their White counterparts, including in minoritized patients with Systemic Lupus Erythematosus (2). Diversifying the physician workforce is a necessary strategy to address equity in patient care as URiM (Underrepresented in Medicine) physicians are more likely to work in underserved communities, while also providing diverse perspectives. We investigated the trends of URiM representation, as defined by the Licensing Committee on Medical Education (LCME), among adult rheumatology fellows.

Methods: This is a quantitative analysis of the Accreditation Council for Graduate Medical Education (ACGME) Data Resource Book from 2011 to 2022. This data was publicly available therefore no IRB approval was required. Demographic data including race, ethnicity, and gender of US adult rheumatology fellows were extracted and analyzed in Microsoft Excel.



Additionally, a multiracial category was introduced as an option in 2020. Chi-Square test was utilized and expected values were calculated using the 2010 census data (2011) to (2019) and the 2020 US census data for 2020 onwards.

Results: There were 5151 adult rheumatology fellows between 2011-2022. Chi-square analysis demonstrated significant underrepresentation of Black, Hispanic and Native Americans ($p < 0.0001$) in US adult rheumatology fellowship programs. As seen in figure 1, Three percent of fellows were Black (171/5151), 7% were Hispanic (337/5151), and 0.2% were Native American (11/5151). Although, trend analysis demonstrated a gradual increase in percentage of Hispanic and Black fellows over time, the proportion of URiM adult rheumatology fellows still lags behind the proportion of minority racial/ethnic groups in the US population.

Conclusion: Despite recent increased attention to the importance of diversity in healthcare, the pipeline of adult rheumatology fellows has not shown a significant increase in URiM representation. Actionable and attainable strategies for diversification amongst US adult rheumatology fellows are urgently needed for the workforce to better reflect the rheumatic disease patient population where a greater disease burden is prevalent in minoritized groups. Engaging URiM students in grade school, college and those entering medical school is essential to ensure early and sustained exposure to rheumatology via career awareness, mentorship, and access to research opportunities.

References:

1. Battafarano DF, Ditmyer M, et al. 2015 American College of Rheumatology Workforce Study: Supply and Demand Projections of Adult Rheumatology Workforce, 2015-2030. Arthritis Care Res (Hoboken). 2018 Apr;70(4):617-626.

2. Feldman C.H., Hiraki L.T., Liu J., et. al.: Epidemiology and sociodemographics of systemic lupus erythematosus and lupus nephritis among US adults with Medicaid coverage, 2000-2004. Arthritis Rheum 2013; 65: pp. 753-763.

Disclosure: B. Roca Loor: None; **M. Pandit**: None; **T. Wright**: None; **M. Etienne**: None.

Abstract Number: 2089

Social Listening Analysis of IgG4-Related Disease Social Media Discussions

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Patient Education/Community Service – Interprofessional Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Immunogobulin G4-Related Disease (IgG4-RD) is a rare chronic immune-mediated fibroinflammatory disorder that often manifests with tumor-like masses and/or enlargement of multiple organs. In order to guide future communications for people living with IgG4-RD, our objective was to examine the emotions expressed in social media discussions regarding IgG4-RD.

Table 1: Text Analysis Results of Aggregated YouTube Comments (N=314 words)

Table 1: Text Analysis of Aggregated YouTube Video Comments, n (%) (N=314 words)

Sentiment		
Positive*	165 (52.5%)	
Negative**	149 (47.5%)	
Emotion		**Associated Words**
Trust	116 (36.9%)	Advice, aspiring, intelligent
Sadness	84 (26.8%)	Pain, suffering
Anticipation	79 (25.2%)	Finally, hopeful
Fear	79 (25.2%)	Infection, diagnosis
Joy	64 (20.4%)	Hope, advance, progress
Anger	56 (17.8%)	Dying, anxiety, cancer
Disgust	50 (15.9%)	Suffering, insane
Surprise	37 (11.8%)	Chance, hope

*Positive: Trust, Joy, Surprise, Anticipation

**Negative: Sadness, Fear, Anger, Disgust

Methods: Data from YouTube and Reddit conversations from January 2017 to March 2023 were accessed using R packages*tuber*, for YouTube, and *RedditExtractoR*, for Reddit. The top viewed YouTube videos and their comments were searched using the terms "IgG4-RD" or "IgG4-Related Disease". Resulting words from the video comments were used for sentiment analysis. Because IgG4-RD does not have its own subreddit,the subreddit r/Autoimmune was used for the Reddit analysis. We applied the same search terms to the top eight most commented subreddit threads for the analysis because these were the only IgG4-RD-related posts with comments. Data were separated into two groups: posts and comments on posts. Text was analyzed by classifying words within the *Emotional Dynamic Classification System* (EmoLex). Each word was assigned a positive or negative sentiment; each sentiment has four exclusive possible emotions associated with them. Depending on the sentiment, the word was assigned one to four negative or positive emotions. Only words with strong associations according to the EmoLex's Association Score were included.

Results: Comments from seven YouTube videos, all created by or featuring physicians, were included in the analysis, with a total of 314 words analyzed. Fifty-three (165/314) words from comments had a positive sentiment (Table 1). Trust (37%) was the emotion most frequently associated with the text, followed by sadness (27%), anticipation (25%), fear (25%) and joy (20%). Advice and intelligence were words used evoking trust in the comments. Pain and hopeful evoked the emotions sadness and anticipation in the comments, respectively (Table 1). For Reddit, eight posts and their comments were included in the analysis. Posts had a total of 753 words and comments had 585 words. Posters to the subreddit were either recently

Table 2a: Text Analysis Results of Aggregated Reddit Posts (N=753 words)

Table 2a: Text Analysis of Aggregated Reddit Posts, n (%) (N=753 words)

Sentiment		
Negative**	532 (70.7%)	
Positive*	221 (29.3%)	
Emotion		**Associated Words**
Sadness	319 (42.4%)	Discomfort, irritation
Fear	252 (33.5%)	Alarming, anxiety, worsening
Trust	162 (21.5%)	Experienced, strength
Disgust	154 (20.5%)	Constipation, bleeding
Anticipation	144 (19.1%)	Progression
Anger	140 (18.6%)	Broken, depressed, hurt
Surprise	91 (12.1%)	Safe, shot
Joy	90 (12.0%)	Kind

*Positive: Trust, Joy, Surprise, Anticipation

**Negative: Sadness, Fear, Anger, Disgust

Table 2b: Text Analysis Results of Aggregated Reddit Comments (N=585 words)

Table 2b: Text Analysis of Aggregated Reddit Comments, n (%) (N=585 words)

Sentiment		
Positive*	301 (51.5%)	
Negative**	284 (48.5%)	
Emotion		**Associated Words**
Trust	246 (42.1%)	Specialist, objective, understanding
Anticipation	182 (31.1%)	Hope, finally
Sadness	162 (27.7%)	Impossible, worried,
Fear	158 (27.0%)	Biopsy, diagnosis
Anger	101 (17.3%)	Anxiety, bias
Joy	94 (16.1%)	Completion, approval
Disgust	88 (15.0%)	Abnormal, coldness, bloated
Surprise	68 (11.6%)	Finally

*Positive: Trust, Joy, Surprise, Anticipation

**Negative: Sadness, Fear, Anger, Disgust

diagnosed with IgG4-RD or seeking information on getting a diagnosis. Seventy-one percent (532/753) of words in these posts expressed negative sentiment (Table 2a). The top negative emotions for posts were sadness (42%), fear (34%), and disgust (21%) based on words like discomfort and anxiety (Table 2a). Trust was the only positive emotion associated with more than a fifth of the words (22%). Aggregated comment emotions were similar to those of YouTube comments, with trust as the most frequently associated emotion (42%), followed by anticipation (31%), sadness (28%), and fear (27%) (Table 2b).

Conclusion: Social media discussions of IgG4-RD provide insight into the patient experience. People living with IgG4-RD may benefit from patient-centered educational and supportive resources that focus on trust of health care providers and address negative emotions associated with the disease journey.

Disclosure: E. Rivera: Global Healthy Living Foundation, 3; **K. Gavigan**: Global Healthy Living Foundation, 3; **D. Hernandez**: Global Healthy Living Foundation, 3; **M. Picone**: TREND Community, 3, 12, Shareholder; **A. Cordova**: None; **L. Dougherty**: None; **K. Davidson**: Horizon Therapeutics, 3, 12, Stockholder; **B. LaMoreaux**: Horizon Therapeutics, 3, 12, Stockholder; **A. Amatucci**: Horizon Therapeutics, 3, 11; **W. Nowell**: AbbVie/Abbott, 2, 5, Amgen, 5, Janssen, 2, 5, Scipher Medicine, 5.

Abstract Number: 2090

Adaptation of the Making it Work^{TM} for People with Systemic Sclerosis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Patient Education/Community Service – Interprofessional Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) limits participation in paid employment, threatening well-being. Few resources exist to help people with SSc remain in the work force despite the high prevalence of work disability[1]. The programs that do exist were developed for other rheumatic conditions such as arthritis.[2] The objective is to engage workers with

SSc to adapt the Making it Work™ (MiW) program, an evidence-based program developed to prevent work loss and maintain productivity for Canadians with arthritis.

Methods: Participants were adults ≥18 years of age who were currently employed in the United States (U.S.), English-speaking, and self-reported SSc diagnosis affecting work. Participants were recruited through the National Scleroderma Foundation and word of mouth. This session provides results from the first steps of the ADAPT-ITT model of implementation science.[3] Fourteen people with SSc engaged in 3 focus groups to help the researchers understand the unique needs of workers with SSc in the U.S. Nine people with SSc reviewed at least one online module from the MiW program with researchers, and described their perceptions using the think-aloud technique. Participants completed a survey rating the relevance of the content to SSc. Interviews were recorded and transcribed.

Results: Focus group participants generated a list of over 50 unique workplace challenges. While some challenges overlapped with those identified in the original MiW program, notable differences included an emphasis on hand function, sensitivity to temperature, and the systemic nature of SSc affecting all body systems. Think-aloud interview participants confirmed that the adapted MiW program should include accommodations and strategies for pulmonary, cardiac, and systemic affects for people with SSc. Also echoing focus groups, interview participants emphasized that oftentimes, people with SSc "don't even know any of [the MiW resources] exists" and therefore cannot ask for them. While many had already worked through their own employment issues, they stated that had it been available, the MiW program would have efficiently guided their work plans. Participants reacted positively to plans to add a fillable workbook to increase interaction and implementation of the content, promote goal setting and follow through, and act as a resource during discussions with their employers and healthcare professionals.

Conclusion: Workers with SSc have unique needs that remain unaddressed in existing programs tailored to other rheumatic conditions. Our next step is to continue working with patients and other topic experts to make the necessary adaptations to the MiW program for SSc and pilot test its effectiveness.

1.Lee JJ et al. Employment outcomes in systemic sclerosis. Best Pract Res Clin Rheumatol. 2021;35:101667. 2. Luquini A, et al. Effectiveness of the Making It Work™ Program at Improving Presenteeism and Work Cessation in Workers with Inflammatory Arthritis–Results of a Randomized Controlled Trial. Arthritis Rheum. 2020;72(S10):2960-62.

3.Wingood GM, DiClemente RJ. The ADAPT-ITT model: a novel method of adapting evidence-based HIV Interventions. J Acquir Immune Defic Syndr. 2008:1;47:S40-6.

Disclosure: J. Poole: None; **K. Carandang**: None; **M. Thelander Hill**: None; **A. Koch**: None; **P. Rogers**: None; **D. Lacaille**: None.

Abstract Number: 2091

Reach and Representativeness of Participants in an Evidence-Based, Community-Delivered Physical Activity Intervention in Adults with Arthritis

Dina Jones[1] and Jennifer Hootman[2], [1]West Virginia University, Morgantown, WV, [2]Centers for Disease Control and Prevention, Atlanta, GA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Patient Education/Community Service – Interprofessional Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: It is imperative that adults with arthritis and other chronic conditions are active enough to maintain health. Enhance®Fitness (EF) is an evidence-based physical activity intervention for older adults. Although EF has been nationally disseminated, its impact specifically in adults with arthritis, across the adult age spectrum, has not been evaluated. We conducted a community-based, non-randomized, wait-list controlled effectiveness trial of 12 weeks of EF in 4 urban and 5 rural West Virginia (WV) counties. This study determined if EF reached those in need, and how representative participants were of other adults with arthritis. We expected to reach at least 82% of eligible respondents.

Methods: Eligible participants were sedentary/low-active adults, aged 18 years or older, with self-reported physician-diagnosed arthritis. We documented the number of people who were screened for eligibility, deemed eligible, and enrolled. Reach was the number of enrolled participants divided by the number of eligible participants, multiplied by 100. Baseline data on sociodemographics, chronic conditions, obesity, arthritis-attributable activity and work limitations, disability (1. activities limited by physical, mental, or emotional problems; 2. needed special equipment), and falls in the past 3 months were used to determine representativeness. Descriptive statistics were calculated and compared with WV and US general population data, and data from other EF studies.

Results: We screened 672 people of which 437 (65%) were eligible. Of 437 eligible participants, 323 (74%) enrolled and 114 (26%) declined. Reach was 74% (323 enrolled of 437 eligible). Non-enrollees were significantly younger than enrollees ($p < 0.01$) and more likely to be from rural versus urban areas ($p < 0.01$). Participants had a mean ± SD age of 68.3 ± 10.6 years (range 27-95) and were primarily white (94.6%), non-Hispanic (99%), and women (86.1%). Participants had high rates of diabetes (24.2%), hypertension (63.1%), obesity (56.2%), arthritis-attributable activity (75.7%) and work (50.0%) limitations, disability (1. activities limited 38.2%, 2. needed special equipment 19.7%), and recent falls (21.4%). Participants were representative of WV and US adults with arthritis on age. Participants were mostly non-Hispanic whites and representative of WV but not of the US or other EF studies. Participants had higher rates of diabetes, obesity, and arthritis-attributable activity limitations than other WV or US populations with arthritis. Compared with other EF studies, participants had a higher prevalence of diabetes, hypertension, disability, and falls.

Conclusion: Although the study reach was good, it was lower than expected. Perhaps, offering evening and weekend classes could have improved reach into the younger adult population. Overall, participants were less diverse, with a higher prevalence of chronic conditions, arthritis-attributable activity limitations, disability, and falls than other arthritis populations and EF study participants. Thus, this study reached adults with arthritis in need of a physical activity intervention in the state with the highest US prevalence of arthritis.

Disclosure: D. Jones: None; **J. Hootman**: None.

Abstract Number: 2092

Feasibility and Efficacy of Culturally Appropriate Spanish Language-First Patient Education for Rheumatoid Arthritis

Daniel Hernandez[1], Julio Bravo[2], Juan Maya Villamizar[3], Oscar Soto[4], Angel Tapia[5], Guillermo Valenzuela[6], W. Benjamin Nowell[7] and Shilpa Venkatachalam[8], [1]Global Healthy Living Foundation, St. Johns, FL, [2]Novant, Winston-Salem, NC, [3]Rheumatology Center of Palm Beach, PLLC, Boca Raton, FL, [4]Mindful Rheumatix and Medical Research Group, San

Juan, PR, [5]Global Healthy Living Foundation, Upper Nyack, NY, [6]Integral Rheumatology & Immunology Specialists, Plantation, FL, [7]Global Healthy Living Foundation, Nyack, NY, [8]Global Healthy Living Foundation, New York, NY

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Patient Education/Community Service – Interprofessional Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Spanish-speaking patients with rheumatic arthritis (RA) need RA education that is medically accurate, conversational, and engaging. Our study examined the feasibility and efficacy of creating and disseminating such education online.

Methods: Members of our research team who are fluent in Spanish collaborated with Hispanic/Latin(a/o/x) rheumatologists and RA patients to create culturally appropriate, medically accurate, Spanish-language, patient education on RA. Educational topics, identified as needs by Hispanic/Latin(a/o/x) RA patients, included RA causes, disease-modifying antirheumatic drugs (DMARDs), remission, treating to target, and lifestyle modification. Each topic was created as a distinct module that included a pre-education question to answer before viewing the module. The same question was repeated at the end of the module and had to be answered before progressing to the next. After posting modules to the CreakyJoints Español website (Fig 1), the education was promoted through national bilingual radio and television and in Spanish on social media sites (e.g., YouTube patient story videos, TikTok music videos, Instagram campaigns, and WhatsApp direct messaging). All responses were collected with SurveyMonkey with internet protocol (IP) addresses and timestamps. We calculated the number and percentage of correct and incorrect answers and the number and proportion of people who answered both

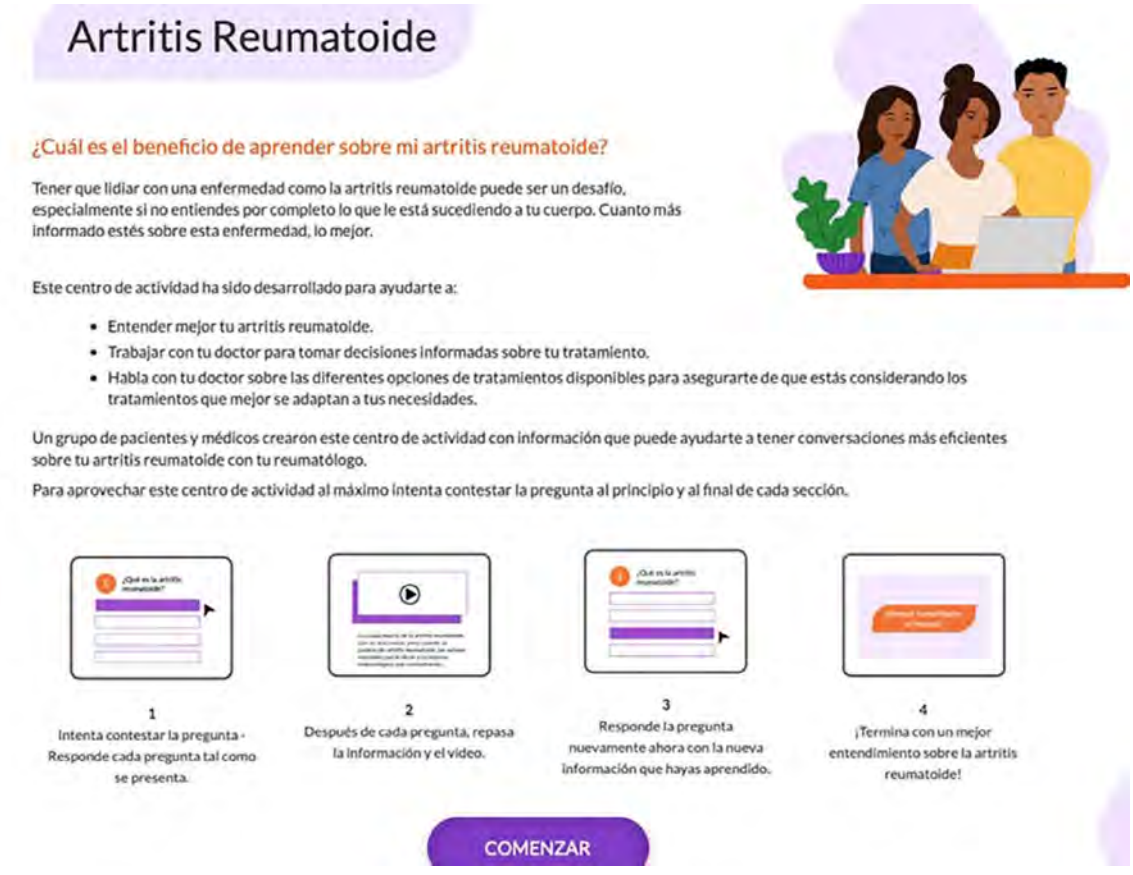


Figure 1. A screenshot of the landing page where the educational modules were hosted.

Table 1. Participants Pre- and Post-Education Test Results by Module

	Module 1	Module 2	Module 3	Module 4	Module 5
Answered pre-test question (n,% of intention to educate cohort)	1048 (100%)	653 (62%)	517 (49%)	412 (39%)	346 (33%)
Answered post education question (n, % of intention to educate cohort)	737 (70%)	527 (50%)	444 (42%)	344 (33%)	306 (29%)
Mean time on module (min, SD)	3.73 (18.54)	3.36 (6.02)	3.32 (6.32)	2.38 (3.22)	2.54 (3.24)
Correct pre-test answers, (% of n who answered pre-test question)	535 (51%)	310 (47%)	252 (49%)	247 (60%)	185 (53%)
Correct post-test answers, (% of n who answered post-test question)	538 (73%)	347 (66%)	342 (77%)	271 (79%)	250 (82%)

Table 2. Changes in Answers After Viewing Educational Content

	Module 1	Module 2	Module 3	Module 4	Module 5
			n (%)		
Pre-test and post-test incorrect	99 (13%)	113 (21%)	78 (18%)	23 (7%)	40 (13%)
Pre-test and post-test correct	432 (59%)	233 (44%)	229 (52%)	254 (73%)	177 (58%)
Pre-test incorrect, post-test correct	106 (14%)	112 (21%)	112 (25%)	47 (14%)	77 (25%)
Pre-test correct, post-test incorrect	100 (14%)	69 (13%)	25 (6%)	20 (6%)	12 (4%)
P-value for observed changes	.46	.08	<.001	.12	<.001

pre- and post-education questions correctly or incorrectly or changed their answer from incorrect to correct and vice-versa. Changes in knowledge for those who completed each module and for those who completed all five modules were evaluated with the two-tailed Student's paired t-test.

Results: Over six months, 1,048 users started the first module, and 70% completed it. Of those who completed the first module, 306 (33%) completed all five modules (Table 1). Responders spent a mean 3.59 minutes (SD, 11.25 minutes) on each module. Correct answers increased from pre- to post-education for all modules, as did the proportion of correct answers for all modules. Knowledge improvements (Table 2) were statistically significant for two modules at a 95% confidence interval (CI) ($P< .001$) and for one at a 90% CI ($P< .08$). One module without significant knowledge gains had similar numbers of answers changed from correct to incorrect and vice versa. The other without significant knowledge gains had a high proportion (74%) of correct answers on the pre-test. For the 306 people who completed all five modules (29%), the sum of post-education vs the sum of pre-education scores showed a statistically significant 12.5% improvement in knowledge ($P=.001$) with a medium effect size (Cohen's d=.52).

Conclusion: Over 1,000 people accessed culturally appropriate, online, Spanish-language patient education. Among those who viewed all modules, knowledge increased. Three of five modules led to significant knowledge gains. For modules without significant gains, it appears one was ineffective, and another used a pre-test question that could not measure knowledge increases. Together, these data suggest it is feasible to deliver medically accurate, Spanish, RA patient education online to effectively improve health literacy.

Disclosure: D. Hernandez: Global Healthy Living Foundation, 3; **J. Bravo**: None; **J. Maya Villamizar**: None; **O. Soto**: None; **A. Tapia**: None; **G. Valenzuela**: AbbVie, 2, Bristol-Myers Squibb, 12, Investigator, Celgene, 2, Eli Lilly, 2, Genentech, 2, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, Merck, 2, MLKCDT, 12, Investigator, Novartis, 2, Pfizer, 2, Regeneron, 2, Sanofi, 2, UCB, 2; **W. Nowell**: AbbVie/Abbott, 2, 5, Amgen, 5, Janssen, 2, 5, Scipher Medicine, 5; **S. Venkatachalam**: Global Healthy Living Foundation, 3.

Abstract Number: 2093

Meeting the Educational and Language Needs of the Lupus Community: A Snapshot of 2022 Lupus Inquiries

Leticia Ocana[1], Ashley Holden[1], Joy Buie[2] and Melicent Miller[1], [1]Lupus Foundation of America, Washington, DC, [2]Lupus Foundation of America, York, SC

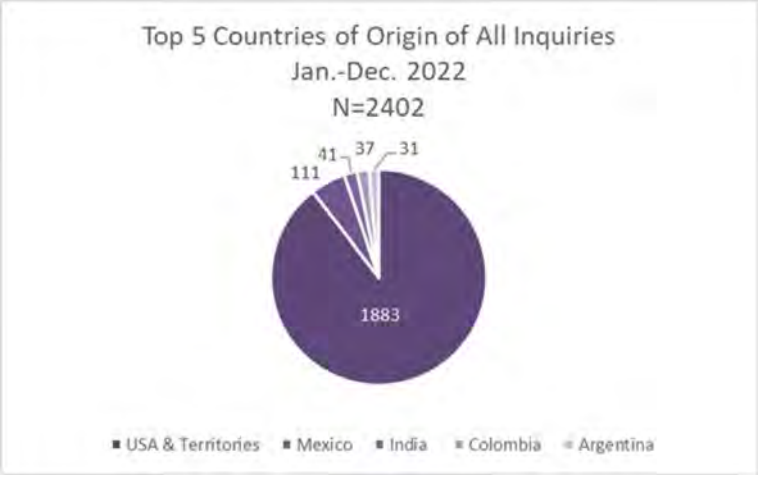
SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Patient Education/Community Service – Interprofessional Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Each year, the Lupus Foundation of America's (LFA) Health Education Specialists (HES) respond to thousands of national and international inquiries from people affected by lupus providing free and tailored non-medical support, disease education, and helpful resources. The vast majority of inquiries are submitted in English and Spanish languages. A team of four HES including two bilingual-bicultural HES respond to the inquiries by email, phone or mail. A review of the inquiry database was conducted to analyze the topics by language and country origin.

Methods: Demographic and inquiry information are collected using Salesforce, a cloud-based Customer Relationship Management (CRM) platform. HES tag each inquiry with topic(s) as applicable. Reports are generated from the database. Topics from the US inquiries by language and the non-US Spanish inquiries were compared.

Results: In 2022, the Lupus Foundation of America responded to a total of 2,402 inquiries from the US and 67 other countries. Eighty percent (n=1,907) of the inquiries were in English and 20% (n=495) were in Spanish. Data demonstrates that the majority of inquiries originated in the US and US Territories (78%), followed by Mexico (5%), India (2%), Colombia (2%) and Argentina (2%) (Graph 1). Graph 2 shows that while 37% of the Spanish-language inquiries originated from the US (n=181), a significant number also come from Mexico (n=98), Colombia (n=37), Argentina (n=29), and Peru (n=27), among other countries. Analysis of the topics show that there is little variation among the English- and Spanish- language inquiries and whether they are US or non-US inquiries. Chart 3 shows the ranking of the top five topics of inquiries by language and country of origin. Data shows that regardless of the language or origination of the inquiry, the top two topics are 1. resources and 2. living and coping. Topics for English-language inquiries from the US include diagnosis, support groups and physician



Top 5 Countries of Origin of All Inquiries

	English-language inquiries form US & Territories	Spanish-language inquiries from US & Territories	Spanish-language inquiries from outside the US
RANK			
#1	Resources (406)	Resources (50)	Living and Coping (99)
#2	Living and Coping (254)	Living and Coping (40)	Resources (93)
#3	Diagnosis (207)	Support groups (25)	Treatment (50)
#4	Support Groups (221)	Treatment (20)	Diagnosis (35)
#5	Physician Referral (198)	Diagnosis (14) & Physician Referral (14) (tied)	Understanding Lupus (29)

Top 5 Countries of Origin of Spanish-Language Inquiries

	English-language inquiries form US & Territories	Spanish-language inquiries from US & Territories	Spanish-language inquiries from outside the US
RANK			
#1	Resources (406)	Resources (50)	Living and Coping (99)
#2	Living and Coping (254)	Living and Coping (40)	Resources (93)
#3	Diagnosis (207)	Support groups (25)	Treatment (50)
#4	Support Groups (221)	Treatment (20)	Diagnosis (35)
#5	Physician Referral (198)	Diagnosis (14) & Physician Referral (14) (tied)	Understanding Lupus (29)

Top 5 Topics of Inquiries

referrals. Spanish-language inquiries (US and non-US) include support groups, treatment, diagnosis, physician referral and understanding lupus. There is a need for not only more lupus information but financial resources as evidenced by resources being a top topic across all languages.

Conclusion: The LFA HES fill an important knowledge gap by providing lupus non-medical support and resources in both English and Spanish to people in the US and around the world. English and Spanish language inquiries from within and outside the US show that the top topics discussed in the inquiries are similar and differ only in ranking, highlighting the similarities in the needs of people affected by lupus. These findings further support the organization's goals of increasing language capabilities that meet the universal needs of people affected by lupus.

Disclosure: L. Ocana: None; **A. Holden**: None; **J. Buie**: None; **M. Miller**: None.

Abstract Number: 2094

Increasing Collaboration, Education, and Awareness of Scleroderma Through an Interprofessional Education Program: Emphasizing the Importance of a Multidisciplinary Team and the Patient as the Primary Educator

Corey Fellon[1], Hannah Bowen[2] and Lee Shapiro[3], [1]Albany Medical College, Albany, NY, [2]Steffens Scleroderma Foundation, Batavia, NY, [3]Albany Medical College, Stillwater, NY

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Patient Education/Community Service – Interprofessional Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Scleroderma is a condition that can affect almost every organ system and thus requires an interprofessional team to optimally manage symptoms and improve patient quality of life. The Steffens Scleroderma Foundation and participating colleges developed an Interprofessional Education (IPE) Program to promote awareness of this disease among health professional students and emphasize the importance of interprofessional collaboration. Held annually since 2018, the program's unique feature is its utilization of the patient as the educator.

Methods: Each year, the program connects 25 or more individuals with scleroderma with students of 9 distinct health-related disciplines including medicine, pharmacy, physical therapy, occupational therapy, nutrition, dentistry, nursing, psychology, and public health. These students are assigned to small groups to interview a patient with scleroderma, asking about the individual's experience with the disease and critical aspects of care. After an interlude in which student questions are answered by a panel of experts from various disciplines, each group of students is assigned a new patient with a unique perspective of their disease. Afterwards, all attendees are asked to complete an anonymous survey regarding the event.

Results: The IPE program demonstrated an over five-fold increase in awareness of scleroderma in participating students, from 16.5% aware/very aware pre-event to 93.67% post-event. After the event, 55.7% of students felt confident/very confident they could recognize the condition in a clinical setting and 62.5% commented in an open response that the most important knowledge they gained regarded the diagnosis, symptoms, and treatment of scleroderma. Importantly, 95% of students said the patient educator was their favorite aspect of the IPE program, and 92.21% believed having the patient as the educator was important/very important for a condition such as scleroderma. In terms of multidisciplinary teams, 94.67% of students felt a collaborative team approach for the care of a multifaceted disease like scleroderma was very important/important.

The patient survey results reaffirmed the students: 89.47% of patients believed the IPE program was effective/very effective at increasing scleroderma awareness in students, and 84.21% were confident/very confident in the students' abilities to be successful in a collaborative healthcare team. The patients also emphasized the importance of an interprofessional team

management approach in a multi-system disease, with 94.74% saying it was very important and the remaining 5.26% saying it was important.

Conclusion: The IPE program provides an opportunity to connect graduate students from several disciplines and promote interprofessional collaboration for scleroderma. It highlights the importance of awareness and education for early diagnosis and uniquely places the patient at the center of the education model. Our goal is to replicate this IPE program on a National level at other scleroderma centers and universities. Expanding this pilot model nationally can promote the collaboration necessary among future healthcare professionals to assure the best quality of care for those living with scleroderma.

Disclosure: C. Fellon: None; **H. Bowen**: None; **L. Shapiro**: None.

Abstract Number: 2095

Integrated Analysis of Gene Expression and Methylation Identifies Biomarkers Associated with Mode of Action of Upadacitinib Treatment in Rheumatoid Arthritis

Preeti Lal[1], Yilin Xu[1], Thierry Sornasse[1], Rhiya Sharma[1], Laleh Jafarpour[1], Heidi Camp[1] and **Iain McInnes**[2], [1]AbbVie, Inc., North Chicago, IL, [2]University of Glasgow, Glasgow, United Kingdom

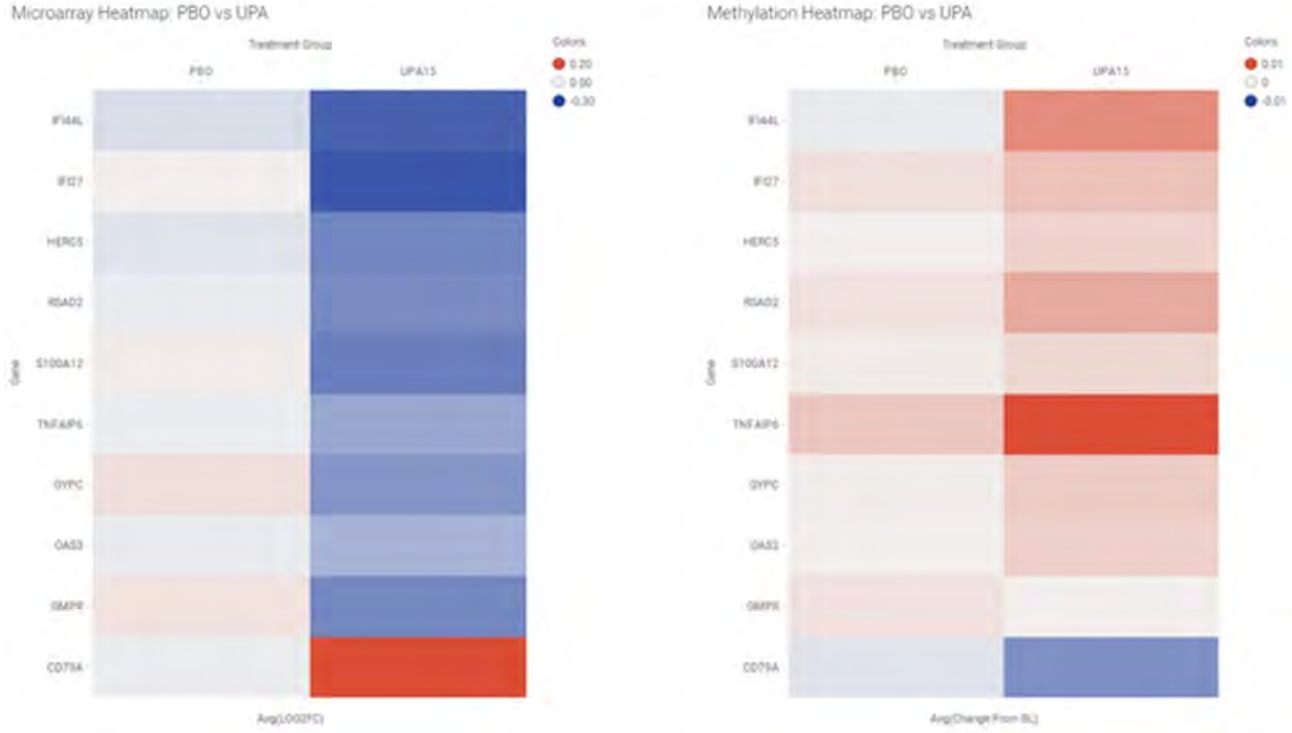
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Upadacitinib (UPA), an oral Janus kinase (JAK) inhibitor, significantly improves the signs and symptoms of RA patients[1-3]. The present study aims to elucidate the mechanism of action of UPA by integrating changes in a genome-wide analysis of methylome data and the blood transcriptome over time from patients enrolled in three phase-3 studies of UPA.

Methods: Longitudinal (baseline [BL], week [W] 2 and W12]) peripheral whole blood samples were randomly selected for analysis (SELECT-NEXT [1]; placebo [PBO], n = 62; UPA 15 mg once daily [QD], n = 61), SELECT-BEYOND [2] (PBO, n = 53; UPA 15 mg QD, n = 55) and SELECT-COMPARE [3] (PBO, n = 181; UPA 15 mg QD, n = 101). This analysis assessed the impact of UPA treatment on all subjects regardless of change in the disease activity. The biospecimen were used to analyze gene expression with a transcriptome-wide gene-level expression profiling tool and methylation profiling with a genome-wide methylation screening tool array. Transcriptome data from the 3 studies were combined following single channel array normalization. Linear models for microarray and RNA-Seq data model (LIMMA package) were used to evaluate transcriptome and methylation changes at W2 and W12 compared to BL. The threshold of significance was defined by false discovery rate < 0.05 and $\log_2$ fold-change above the levels observed in the PBO samples. Canonical and Upstream Regulators Pathway analyses were performed with ingenuity pathway analysis (IPA).

Results: The transcripts for 294 genes were differentially expressed (DE) at W2, of which 114 remained DE at W12. An additional 98 genes were DE at W12 vs baseline. Pathway analysis of DE genes shows early modulation of key pathways like IFN, IL10 and S100 signaling. Furthermore, pathway analysis predicted that UPA downregulates pathways related to IL1B, TNF, types 1 and 2 IFN, IL17A, and IL6 biology. The methylation data covered 282 genes out of the 294 identified above. Of the

Figure 1. Top 10 differentially expressed genes and their corresponding methylation pattern.



282, 34% (n=97) of the genes were significantly differentially methylated and consistent with the RNA expression data. Pathway analysis based on these 97 genes predicted the upstream downregulation of inflammatory regulators such as TNF, IFNα, TGF-β, IL1B, and IL17.

Conclusion: The present study reveals the effect of treatment with UPA on the transcription machinery of leukocytes from RA patients at the RNA and DNA methylation levels. While UPA may directly affect the methylation state and expression of target genes, we cannot exclude that some of the observed changes reflect a change in blood cell composition. This integrated analysis confirms that UPA normalizes key pathological pathways associated with RA, expanding our understanding of its mode of action in RA and creates a framework for multi-omic biomarker discovery for response to JAK inhibitors.

1. Burmester GR, et al. (2018) *Lancet* 391:2503–12.
2. Genovese MC, et al. (2018) *Lancet* 391:2513–24.
3. Fleischmann R, et al. (2019) *Arthritis Rheumatol* 71:1788–800

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Abstract Number: 2096

Association of Left Ventricular Mass with Interleukin-17 in Rheumatoid Arthritis Patients Without Clinical Heart Failure

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Elevated left ventricular (LV) mass (LVM) is an important precursor to clinical heart failure (HF) in the general population. In fact, rheumatoid arthritis (RA) patients without HF demonstrate higher LVM than non-RA patients without HF. However, few studies have established direct associations between LVM and inflammatory cytokines in RA patients without clinical HF. Interleukin-17 (IL-17) is an important contributor to LV structural abnormalities in RA, given its dual pathologic roles in myocardial fibrosis and articular cartilage breakdown. Here we present previously unreported associations between IL-17, obtained from a large inflammatory cytokine panel, and LVM in a RA cohort without clinical HF.

Table 1. Univariable and Multivariable Regression Table for LVMI (2.7)

3D LVMI$^{2.7}$	Univariable (n=154)		Multivariable (n=91)	
Demographics (baseline)	**B**	**P**	**B**	**P**
Age, per year	**0.057**	**0.089**	-0.0197	0.67
Male versus female	-0.72	0.52	...	...
Race (white vs non-white)	***2.75***	***0.001***	***2.04***	***0.032***
BMI, per kg/m^2	***0.24***	***<0.01***	***0.18***	***0.023***
RA Factors (baseline)	B	P	B	P
Clinical Disease Activity Index (CDAI) (square root)	***0.53***	***0.040***	0.15	0.61
Cyclic Citrullinated Peptide (CCP)>250	***2.32***	***0.007***	0.98	0.25
Prednisone use	0.57	0.53	...	...
Methotrexate use	-0.14	0.87	...	...
Tumor Necrosis Factor (TNF) inhibitor use	0.98	0.28	***2.66***	***0.0053***
Interleukin-6 binary (>5.4 pg/ml)	1.41	0.16	...	...
C-Reactive Protein (CRP) (Log), per ug/ml	***0.75***	***0.010***	...	...
IL-17 binary (>2.6 pg/ml)	**2.04**	**0.086**	***2.66***	***0.036***
CV Risk Factors (baseline)	B	P		
Current smoker, yes versus no	1.60	0.23	0.93	0.56
Ever smoker, yes versus no	-0.69	0.41	...	...
Systolic Blood Pressure (SBP) (baseline), mm/Hg	***0.052***	***0.038***	***0.064***	***0.022***
Statin use, yes versus no	-0.68	0.56	...	...
Aspirin use, yes versus no	0.73	0.58	...	...
Brain Natriuretic Peptide (BNP) (log), per pg/mL	**-1.48**	**0.073**	...	...
Troponin-I (log), per pg/mL	***1.11***	***0.003***	0.12	0.81
PET/CT Cardiac Measures (baseline)	B	P		
Log mean Myocardial SUV, per unit	0.86	0.26	***2.06***	***0.013***
Log max Myocardial SUV, per unit	0.79	0.23	...	...
CAC score>100	-0.065	0.95	...	...
CAC score>300	0.40	0.77		
MFR	***-2.13***	***0.001***	***-2.21***	***0.001***
Prob>F	...		***<0.00001***	
R-Squared	...		0.45	
Adjusted R-Squared	...		0.37	

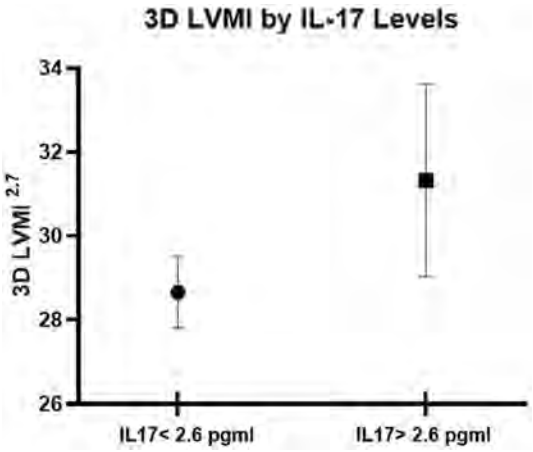

Figure 1. 3D LVMI by IL-17 levels, adjusted for RA and CV covariates

Methods: RA patients (n=158) without clinical HF underwent RA and cardiovascular (CV) clinical assessment, including myocardial inflammation and myocardial flow reserve (MFR) measured on 18F-Fluorodeoxyglucosecardiac positron emission tomography–computed tomography (FDG-PET/CT), as well as transthoracic echocardiography (TTE) at baseline. A subset (n=60) returned for follow-up TTE 3-6 years later. Real-time 3-dimensional (3D) TTE was utilized to calculate LVM (indexed to height ($m^{2.7}$); LVMI). Baseline plasma from all RA patients was assayed using the Rule Based Medicine (RBM)/ Inflammation MAP v 1.1, a 54-marker Discovery Panel, assaying a broad group of inflammatory proteins. Multivariable (MV) regression models with LVMI as the outcome were constructed, adjusting for biologically plausible confounders identified from univariable regressions.

Results: The baseline cohort was predominantly middle aged, female, with moderate RA disease activity, and multiple CV risk factors. LVMI did not change significantly from baseline to follow-up. Up to 14% of the baseline cohort had IL-17 levels >2.6 pg/ml (lower limit of quantitation). In a MV model adjusted for demographics including BMI, RA disease activity, seropositivity, TNF inhibitor use, blood pressure, smoking, troponin levels, myocardial inflammation and MFR, baseline IL-17 levels >2.6 were associated with a higher baseline LVMI (*Table 1*; MV model). *Figure 1* demonstrates adjusted LVMI stratified by IL-17 levels (based on aforementioned MV regression model). IL-17 levels were not significantly associated in univariable and MV models with myocardial measures such as MFR and myocardial inflammation (mean standardized uptake value; SUV), as well as baseline and follow-up diastolic dysfunction, and baseline/annual rate of change in ejection fraction (-*Tables not shown*).

Conclusion: In an RA cohort without clinical HF, higher IL-17 levels were associated with higher LVMI, while adjusting for important RA and CV covariates. Whether anti IL-17 therapy could ameliorate these LV mass abnormalities, needs to be explored in future clinical studies.

Disclosure: E. Park: Pfizer, 5; **K. Ito**: None; **C. Depender**: None; **J. Giles**: AbbVie, 2, Eli Lilly, 2, Gilead, 2, Novartis, 2, Pfizer, 2; **J. Bathon**: None.

Abstract Number: 2097

Comparing the World Health Organization and the American College of Cardiology/American Heart Association Algorithms for Detection of Carotid Plaque

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular disease is the major cause of death in rheumatoid arthritis (RA) patients. Cardiovascular risk algorithms are employed to assess the likelihood of experiencing a major cardiovascular event within 10 years based on the presence of conventional cardiovascular risk factors, however, no algorithm existed for the Hispanic population until the World Health Organization (WHO) published the cardiovascular disease risk charts for 21 regions, including Mexico. This study aimed to compare the effectiveness of the 2019 WHO algorithm and the 2013 ACC/AHA algorithm in detecting the presence of carotid plaque (CP) in patients with RA.

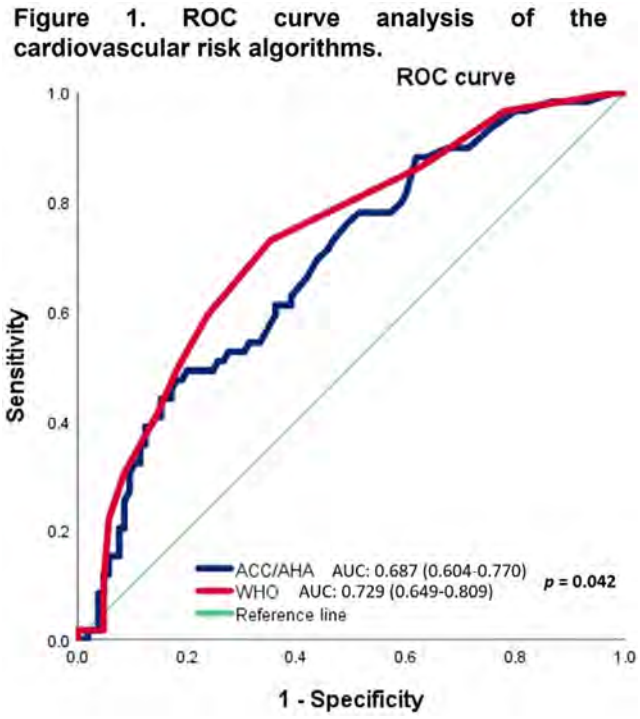
Methods: This was a cross-sectional study. We recruited a total of 164 patients with RA diagnosis, according to the 2010 ACR/EULAR classification criteria, aged 40-75 years. Patients with a previous cardiovascular event were excluded. Cardiovascular risk was evaluated with the 2019 WHO algorithm for the Mexican population and the 2013 ACC/AHA cardiovascular algorithm. The results were multiplicated by 1.5, according to current guidelines. A carotid ultrasound was performed to all study subjects by a certified radiologist blinded to clinical information. Distribution was evaluated with the Kolmogorov-Smirnov test. Correlations were performed with the Spearman-rho coefficient (rho). A ROC-curve analysis was performed for both algorithms. The areas under the curve (AUC) of the algorithms were compared using the method of DeLong. A p-value < 0.05 was considered statistically significant.

Table 1. Demographic characteristics of RA patients.

Characteristics	RA patients (n=164)
Age, years, mean ± SD	55.82 ± 8.94
Women, n (%)	157 (95.73)
T2DM, n (%)	27 (16.46)
Hypertension, n (%)	53 (32.32)
Dyslipidemia, n (%)	58 (35.36)
Obesity, n (%)	56 (34.15)
Active smoking, n (%)	15 (9.15)
WHO algorithm, median (IQR)	4.5 (3.0-9.0)
ACC/AHA algorithm, median (IQR)	3.75 (1.80-9.26)
Carotid plaque, n (%)	59 (36.0)

RA, rheumatoid arthritis; T2DM, type 2 diabetes mellitus; WHO, world health organization; ACC/AHA, American College of Cardiology/American Heart Association.

RA, rheumatoid arthritis; T2DM, type 2 diabetes mellitus; WHO, world health organization; ACC/AHA, American College of Cardiology/American Heart Association.



Results: The presence of CP was detected in 59 (36.0%) patients. Demographic characteristics are shown in Table 1. There was a large positive correlation between the WHO and the ACC/AHA algorithms (rho = 0.880, $p = < 0.001$). Both algorithms showed significant discrimination for the presence of CP in RA patients, the WHO algorithm had an AUC 0.729 (95% CI 0.649-0.809, $p = < 0.001$) and the ACC/AHA algorithm had an AUC 0.687 (95% CI 0.604-0.770, $p = < 0.001$). However, there was a difference when comparing the AUC for both algorithms, with the WHO algorithm demonstrating a higher AUC value ($p = 0.042$) (Figure 1).

Conclusion: Our findings indicate that both algorithms exhibited significant discrimination for the presence of CP. However, in the Hispanic RA population, the 2019 WHO algorithm displayed superior capacity for detecting CP compared to the 2013 ACC/AHA algorithm. The WHO algorithm is more suitable for the Hispanic RA population due to its tailored design specifically for their demographic characteristics. Consequently, it outperforms the ACC/AHA algorithm in accurately detecting and assessing cardiovascular risk factors in this population.

Disclosure: N. Guajardo-Jauregui: None; **I. Colunga**: None; **J. Azpiri-López**: None; **D. Galarza-Delgado**: None; **R. Arvizu-Rivera**: None; **J. Cardenas-De la Garza**: None.

Abstract Number: 2098

Contribution of Rare Deleterious Exonic Variants in Telomere Related Genes to Interstitial Lung Disease Risk in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: RA-associated interstitial lung disease (ILD) and idiopathic pulmonary fibrosis (IPF) share genetic risk factors such as *MUC5B* rs35705950. The exact role of telomere related genes (TRG) in the RA-ILD genetic background is unclear. A previous work found an excess of TRG rare deleterious variants in RA-ILD compared to healthy controls but did not allow to conclude without a control population of patients with RA without ILD. Our aim was to test for association TRG rare deleterious exonic variants with ILD in patients with RA.

Methods: This genetic case-control association study was composed of a derivation (France) and a replication (US) population. Cases with RA-ILD and controls with RA without ILD (RA-noILD) that had whole exome sequencing (WES) data were included. ILD status and pattern (usual interstitial pattern, UIP or non-UIP) was determined by review of clinically-indicated high-resolution computed tomography (HRCT) chest imaging. Rare deleterious exonic variants from 14 candidate TRG previously associated with pulmonary fibrosis (*TERT, TERC, PARN, RTEL1, CTC1, TINF2, ACD, POT1, NAF1, ZCCHC8, NHP2, NOP10, WRAP53,* and *DKC1*) were selected using 1) a reported frequency in gnomAD database < 0.1%, 2) a deleterious impact predicted by SIFT, POLYPHEN-2, and 3) a CADD score > 15. Proportions of variants carriers in RA-ILD and RA-noILD were compared using a classical burden test adjusted for sex, age at RA, RA duration, *MUC5B* rs3570590 genotype and a principal component analysis using ancestry informative markers. Results were combined in a meta-analysis.

Table 1. Characteristics of the included patients ACPA: anti-citrullinated peptides antibodies; HRCT: high resolution computed tomography; ILD: interstitial lung disease; MAF: minor allele frequency; RF: rheumatoid factor; UIP: usual interstitial pneumonia.

	French derivation set		US replication set	
	RA-ILD cases (n=157)	RA-noILD controls (n=231)	RA-ILD cases (n=85)	RA-noILD controls (n=305)
Female sex	85/157 (54.1)	188/231 (81.4)	61/85 (71.8)	229/305 (75.1)
Mean age at ILD onset or last normal HRCT, years (SD)	63.2 ± 11.0	58.3 ± 13.5	65.7 ± 17.6	60.2 ± 19.2
Ever smokers	92/153 (60.1)	170/296 (57.4)	54/79 (68.4)	88 (57.5)
Mean age at RA onset, years (SD)	54.1 ± 13.0	44.2 ± 12.8	53.1 ± 12.7	50.6 ± 15.0
Mean RA duration at ILD or las normal HRCT, years (SD)	9.3 ± 10.7	14.1 ± 7.3	12.6 ± 14.8	9.6 ± 11.5
RF positivity	118/144 (81.9)	171/217 (78.8)	58/81 (71.6)	155/294 (52.7)
ACPA positivity	120/147 (81.6)	154/226 (68.1)	48/73 (65.8)	138/268 (51.5)
Seropositivity	136/148 (91.9)	197/226 (87.2)	64/81 (79.0)	179/281 (63.7)
MUC5B rs35705950, MAF	0.30	0.13	0.22	0.09
UIP pattern	76/157 (48.4)	-	29/85 (34.1)	-

Table 2. Classical burden test comparing the frequency of TRG rare deleterious variants in patients with RA-ILD (cases) and patients with RA-noILD (controls). ILD: interstitial lung disease, OR [95% IC]: Odd ratios with 95% confidence interval; TRGs: telomere related genes; UIP: usual interstitial pneumonia.

	Number of TRG rare variants carriers (%) in cases	Number of TRG rare variants carriers (%) in comparators	OR [95% CI]	P-value
FRANCE				
RA-ILD *vs* RA-noILD	13/157 (8.2%)	8/231 (3.5%)	2.83 [0.96 – 8.58]	0.06
RA-UIP *vs* RA-noILD	8/76 (10.5%)	8/231 (3.5%)	4.66 [1.27 – 16.86]	0.02
nonUIP RA-ILD *vs* RA-noILD	5/81 (6.2%)	8/231 (3.5%)	2.14 [0.48 – 8.26]	0.29
RA-UIP *vs* nonUIP RA-ILD	8/76 (10.5%)	5/81 (6.2%)	2.05 [0.59 – 7.76]	0.27
US				
RA-ILD *vs* RA-noILD	9/85 (10.5%)	19/305 (6.2%)	1.83 [0.72 – 4.33]	0.18
RA-UIP *vs* RA-noILD	4/29 (13.8%)	19/305 (6.2%)	2.26 [0.48 – 8.53]	0.26
nonUIP RA-ILD *vs* RA-noILD	5/56 (8.9%)	19/305 (6.2%)	1.60 [0.50 – 4.34]	0.38
RA-UIP *vs* nonUIP RA-ILD	4/29 (13.8%)	5/56 (8.9%)	1.01 [0.17 – 5.61]	0.99
META-ANALYSIS				
RA-ILD *vs* RA-noILD	23/242 (9.5%)	27/536 (5.0%)	2.16 [1.09 – 4.26]	0.03
RA-UIP *vs* RA-noILD	12/105 (11.4%)	27/536 (5.0%)	3.28 [1.30 – 8.27]	0.01
nonUIP RA-ILD *vs* RA-noILD	11/137 (8.0%)	27/536 (5.0%)	1.77 [0.79 – 3.96]	0.16
RA-UIP *vs* nonUIP RA-ILD	12/105 (11.4%)	11/137 (8.0%)	1.57 [0.55 – 4.50]	0.40

Results: The French derivation dataset included 388 patients, 157 cases (40.5%), mean age at ILD or last normal HRTC 60.1 years, 273 female (70.4%); **Table 1**. 22 rare deleterious variants were identified in 13/157 cases (8.3%) and 8/231 controls (3.5%). The burden test suggested an excess of TRG rare variants in RA-ILD (OR 2.83, 95% CI 0.96-8.58; p=0.06); (**-Table 2, Figure 1)**. A significant association was observed for usual interstitial pneumonia (UIP) HRCT pattern (OR 4.66, 95% CI 1.27-16.86; p=0.02) whereas no association was detected for patients with RA-ILD and a non-UIP HRCT patterns (OR 2.14, 95% CI 0.48-8.26; p=0.29). The US replication dataset included 390 patients, 85 cases (21.8%), mean age at ILD or last normal HRCT was 61.4 years and 74.4% were female. Similar trend for an excess of TRG rare variants was observed with 28 variants identified in 9/85 cases and 19/305 controls (10.5% vs 6.2%, OR 1.83, 95% CI 0.72-4.33; p=0.18); (**-Table 2**, **Figure 1)**. Like in the derivation population, the excess of rare variants was more pronounced for RA-UIP: 13.8% vs 6.2% (OR 2.26, 95% CI 0.48-8.53; p=0.26) The meta-analysis provide evidence for a significant contribution of TRGs rare

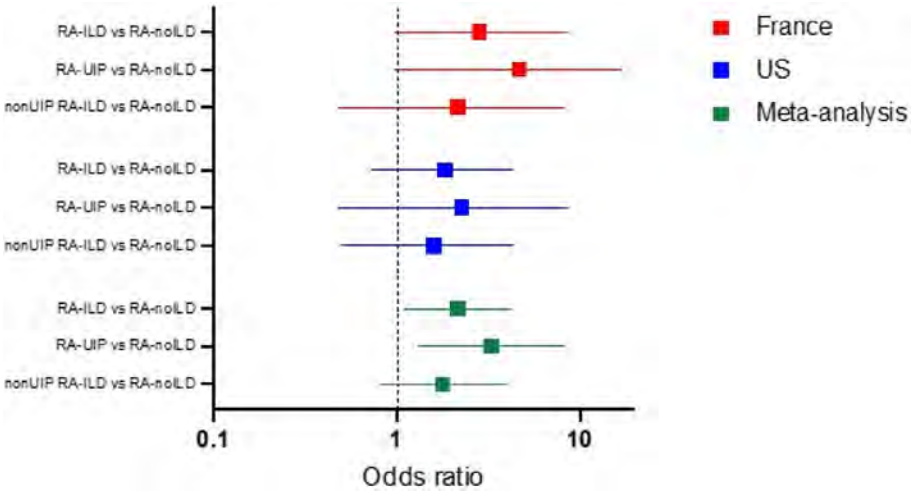

Figure 1. Results from the Burden test assessing TRG rare deleterious variants contribution in RA-ILD. Forest plot of odds ratios (OR) and 95% confidence intervals (CI). The boxes indicate OR, and the horizontal lines indicate 95% CI for the burden test comparing frequency of telomere related genes (TRG) rare deleterious exonic variants carriers in cases vs controls.

variants to RA-ILD (OR 2.16, 95% CI 1.09-4.26; p=0.03), more specifically for the UIP pattern (OR 3.28, 95% CI 1.30-8.27; p=0.01). No significant association was found for non-UIP patterns in the meta-analysis (OR 1.77, 95% CI 0.79-3.96; p=0.16).

Conclusion: TRG rare deleterious exonic variants contribute to the risk of ILD in patients with RA, more specifically in RA-UIP. These results confirmed the shared genetic architecture between RA-ILD and IPF.

Disclosure: P. Juge: None; **L. Kawano-Dourado**: None; **S. Gazal**: None; **G. McDermott**: None; **K. Hayashi**: None; **J. Cui**: None; **M. Debray**: None; **L. Stervinou-Wemeau**: None; **S. Marchand-Adam**: None; **C. Richez**: AbbVie/Abbott, 2, 6, Amgen, 6, AstraZeneca, 2, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, 12, receipt of drugs, GlaxoSmithKlein(GSK), 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **H. Nunes**: None; **J. Avouac**: AbbVie, 6, AstraZeneca, 6, Biogen, 6, BMS, 5, 6, Fresenius Kabi, 5, 6, Galapagos, 5, 6, Janssen, 6, Lilly, 6, Medac, 6, MSD, 6, Nordic Pharma, 6, Novartis, 6, Novartis (Dreamer), 5, Pfizer, 6, Pfizer (Passerelle), 5, Roche-Chugai, 6, Sandoz, 6, Sanofi, 6; **R. Flipo**: AbbVie, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, Medac, 2, MSD, 2, Nordic Pharma, 2, Novartis, 2, Pfizer, 2, Roche-Chugaï, 2, Sandoz, 2, Sanofi, 2; **V. Cottin**: Boehringer Ingelheim, 2, 5, 6, 12, Support for attending meetings, Celgene/BMS, 1, 2, CSL Behring, 2, Ferrer, 2, 6, 12, Support for attending meetings, FibroGen, 1, Galapagos, 1, 2, Galecto, 1, GlaxoSmithKline, 2, Pliant, 2, Pure Tech, 2, Redx, 2, Roche, 1, 2, 6, 12, Support for attending meetings, Sanofi, 2, Shionogi, 2; **M. Soubrier**: None; **N. Saidenberg Kermanac'h**: None; **C. Kannengiesser**: None; **R. Borie**: None; **B. Crestani**: None; **T. Doyle**: None; **S. Raychaudhuri**: AbbVie, 6, Janssen, 1, Mestag, Inc, 2, 8, Pfizer, 1, Sanofi, 1, Sonoma, 1, 8; **E. Karlson**: None; **J. Sparks**: AbbVie, 2, Amgen, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, 5, Gilead, 2, Inova Diagnostics, 2, Janssen, 2, Optum, 2, Pfizer, 2, ReCor, 2; **P. Dieudé**: AbbVie, 2, 6, Boehringer Ingelheim, 1, 2, 6, Bristol-Myers Squibb, 1, 2, 5, 6, Chugai, 5, Galapagos, 5, 6, Janssen, 2, 6, Novartis, 2, Pfizer, 1, 2, 5, 6.

Abstract Number: 2099

Lesser Impact of Lower-Small Joint Involvement on Pain Than Upper-Small Joint in Rheumatoid Arthritis: Analysis Based on a Large Rheumatoid Arthritis Database in Japan

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies have highlighted the influence of pain, functional impairment, and affected joint distribution on the discordance in the global assessment of disease activity between patients with rheumatoid arthritis (RA) and their physicians. This study aimed to analyze the effect of affected joint distribution on pain in patients with RA, based on a nationwide RA database in Japan (*NinJa*).

Methods: The affected joints were divided into four regions: upper-large (shoulder, sternoclavicular, elbow, and wrist), upper-small (proximal interphalangeal and metacarpophalangeal), lower-large (hip, knee, ankle, and tarsometatarsal), and lower-small (metatarsophalangeal) joints. The modified joint index (JI) was calculated using the following formula: number

of tender joint counts (instead of the sum of tender and swollen joint counts in the original JI [Rheumatol Int 32:2569, 2012]) divided by the number of evaluable joints within each region. Multiple regression analysis was performed using the pain visual analog scale (VAS) as an objective variable and modified Health Assessment Questionnaire (mHAQ), CRP, and affected joint variables, including JIs and tender joint counts, as explanatory variables.

Results: Multiple regression analysis involving 13,653 RA patients revealed that mHAQ, upper-large joints, lower-large joints, CRP, and upper-small joints significantly contributed to pain VAS in the order of standardized partial regression coefficients (SPRCs), although the contribution of lower-small joints was insignificant (Figure 1). Further analysis using tender joint counts showed the impact of each affected joint on pain VAS in the following order of SPRCs: wrists, knees, ankles, shoulders, proximal interphalangeal (PIP) joints, elbows, metacarpophalangeal (MCP) joints, distal interphalangeal (DIP) joints, and hips (Figure 2). Notably, the effects of metatarsophalangeal (MTP) and toe interphalangeal (IP) joints, which were excluded from the disease activity score-28 (DAS28), were not statistically significant.

Conclusion: The effect of lower-small joint involvement on pain in RA is smaller than that of upper-small joint involvement. Thus, patients with RA are relatively less aware of MTP and toe IP joint pain as compared to PIP and MCP joints, and may not complain to their physicians, which could lead to forefoot joint deformities. Therefore, it is necessary to consider lower-small joint involvement, which is not included in DAS28 evaluation, and pay attention to its potential impact on management in RA patients.

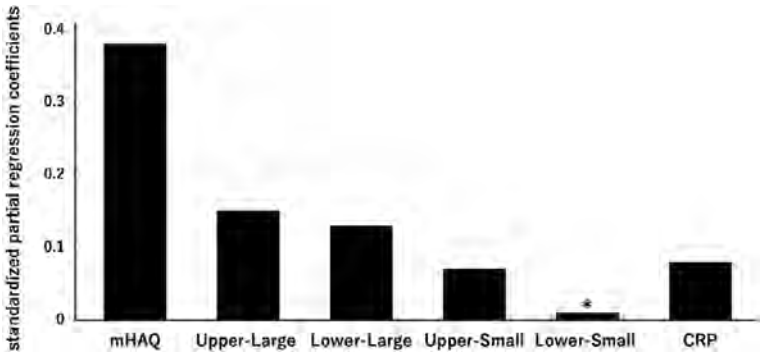


Figure 1 Impact of affected joint distribution on pain visual analog scale in patients with rheumatoid arthritis. *Lower-small joint involvement is not statistically significant. mHAQ: modified Health Assessment Questionnaire; CRP: C-reactive protein.

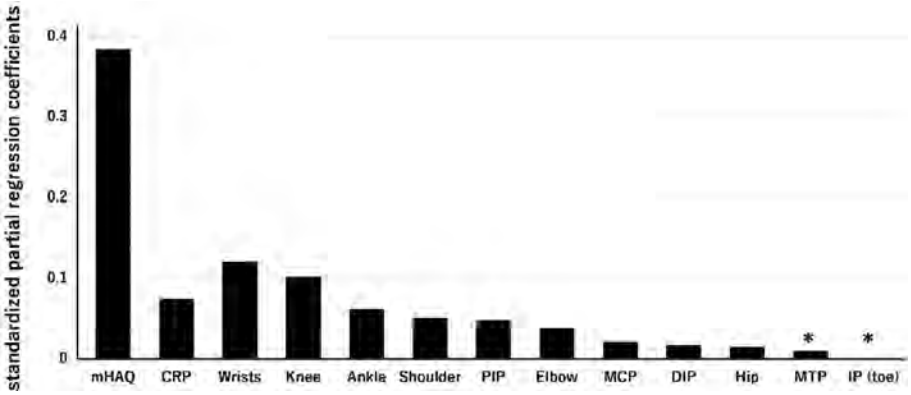


Figure 2 Impact of affected joint on pain visual analog scale in patients with rheumatoid arthritis. *Lower-small joint involvement is not statistically significant. mHAQ: modified Health Assessment Questionnaire; CRP: C-reactive protein.

Disclosure: T. Sawada: AbbVie/Abbott, 5, 6, Asahikasei, 5, 6, AstraZeneca, 6, Chugai, 5, 6, Eisai, 6, Eli-Lily, 6, Jansen, 6, Mitsubishi-Tanabe, 6, Ono Pharmaceutical, 6, Pfizer, 6, Taisho, 6, UCB, 6, Viatris, 6; **S. Nishiyama**: AbbVie/Abbott, 6, Asahi Kasei Pharma Corporation, 1, AstraZeneca, 6, AYUMI Pharmaceutical Corporation, 12, Financial support for the OKAYAMA medical conference., Chugai Pharma Manufacturing Co., Ltd., 6, Eisai Co., Ltd., 6, GlaxoSmithKlein(-GSK), 1, 6, Kissei PharmaceuticalCo., Ltd., 6, Santen Pharmaceutical Co., Ltd., 6, Taisho Pharmaceutical Co., Ltd., 6; **S. Igari**: None; **T. Matsui**: Abbie, 6, Asahikasei Pharma Corp., 5, 6, Astellas, 6, Chugai Pharmaceutical Co, Ltd., 5, 6, Eisai Co., Ltd., 6, Eli Lilly Japan, 6, Ono Pharmaceutical Co., Ltd., 6, Pfizer Japan Inc., 6; **S. Tohma**: AbbVie/Abbott, 5, AsahiKASEI Co., Ltd., 6, Chudai Pharmaceutical Co., Ltd., 5, Mitsubishi Tanabe Pharma Corporation, 5, Pfizer Japan Inc., 6.

Abstract Number: 2100

Paradoxical Antagonistic Association of Visceral and Subcutaneous Adipose Tissue with Circulating C-Reactive Protein in Rheumatoid Arthritis

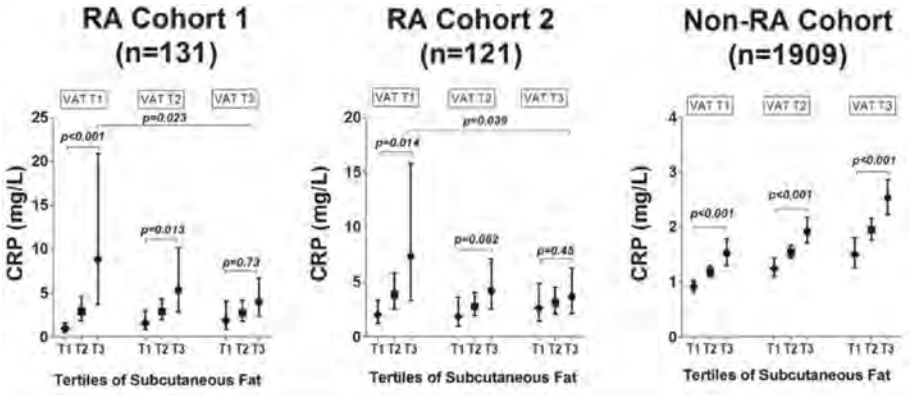
Jon Giles and Joan Bathon, Columbia University, New York, NY

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: C-reactive protein (CRP) is used as an indicator of disease activity in people with RA.However, adipose tissue also expresses inflammatory cytokines that induce hepatic CRP production.Both visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) express inflammatory cytokines, with effects on CRP that are additive.However, whether this is also true for RA has not been explored.

Methods: RA patients were from two independent cohorts exploring subclinical cardiovascular disease.Non-RA controls were from a large multi-center cohort study, also studying subclinical cardiovascular disease.Known cardiovascular disease was an exclusion criterion for all 3 cohorts.In all 3 cohorts, participants underwent abdominal CT scanning with quantification



Adjusted means and 95% CIs are depicted. T1, T2, T3=tertile groups. RA Cohort 1 adjusted for sex, smoking, HDL-C, RA duration, rheumatoid factor, swollen joint count, tender joint count, methotrexate use, and TNF inhibitor use. p-value for interaction=0.004. RA Cohort 2 adjusted for sex, smoking, RA duration, swollen joint count, tender joint count, and TNF inhibitor use. p-value for interaction=0.054. Non-RA cohort adjusted for age, sex, race/ethnicity, smoking, hypertension, diabetes, LDL-C, HDL-C, triglycerides.

of the areas of VAT and SAT at the L4/L5 disc interspace.VAT and SAT were interpreted by the same reader for both RA cohort 1 and the non-RA cohort.Readers were unaware of patient characteristics.For each cohort, stored serum samples were assayed for CRP via a central lab in single batches.Generalized linear models were constructed to explore the interaction of VAT and SAT with CRP.

Results: There were 131 RA patients in RA cohort 1 and 121 RA patients in RA cohort 2 (total n=252).The mean age of the combined RA cohorts was 57 years.The RA patients were mostly women (71%) of non-Hispanic White race (63%) with a median RA duration of 8.1years, 80% seropositive for RF or anti-CCP and a median DAS28 of 3.7.Non-biologics, biologics, and prednisone were used in 81%, 39, and 35%, respectively.In the non-RA cohort, higher SAT was associated with significantly higher CRP levels within each tertile of VAT, with progressively higher CRP with both higher SAT and VAT (Fig).In contrast, in both RA cohorts, there was a strong and significant association of higher SAT with CRP among those in the lowest tertile of VAT.However, the association of SAT with CRP among those in the highest tertile of VAT was weaker and not statistically significant in both RA cohorts (Fig).For those in the highest tertile of SAT, CRP was significantly lower among those in the highest vs lowest tertile of VAT, despite those in the highest tertile of VAT having a higher BMI (35.6 vs 32.6 kg/m2 for the combined RA cohorts) and similar DAS28, swollen, and tender joints counts.Use of biologic and non-biologic DMARDs and prednisone was not different between the groups. Adjusting for demographics and BMI did not reduce the significance of the antagonistic interaction.

Conclusion: We observed a similar paradoxical association of VAT and SAT on circulating CRP level in two independent cohorts of RA patients.These findings have implications on how elevated CRP levels are interpreted in RA patients and warrant additional study into the mechanism of how higher VAT may suppresses SAT-associated inflammation in RA.

Disclosure: J. Giles: AbbVie, 2, Eli Lilly, 2, Gilead, 2, Novartis, 2, Pfizer, 2; **J. Bathon**: None.

Abstract Number: 2101

Diagnosis of Mental Disorder Complicated by Rheumatoid Arthritis: A Study of the Validity of a Psychiatrist's Diagnosis and Questionnaire Method

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: It has been reported that about 15% of patients with rheumatoid arthritis (RA) have depression, and most of these studies have used questionnaire methods. For example, the Patient Health Questionnaire-9 (PHQ-9) and Center for Epidemiologic Studies Depression Scale (CES-D) questionnaires were used; a score of 10 or more on the PHQ-9 and 16 or more on the CES-D was considered a cutoff. Most of the studies have used questionnaires for depression. Because the depression questionnaire includes questions about physical symptoms, it is necessary to interpret the results carefully when there is an underlying disease. In addition, there are no studies on other mental disorders. In this study, we examined the validity of the questionnaire method for diagnosing RA complicated by psychiatric disorders and searching for optimal cutoff values in patients with rheumatoid arthritis.

Methods: One hundred twenty-three outpatients with RA who agreed to participate in this study were included. Age, gender, type of Disease-modifying anti-rheumatic drugs, prednisolone use, presence of diabetes, hypertension, dyslipidemia, and CRP were investigated. The PHQ-9 and CES-D questionnaires were used. The psychiatrist was blinded to the questionnaire results and conducted a structured interview in a separate room. The psychiatrist's diagnosis was defined as the Gold Standard and was compared with the PHQ-9 and CES-D.

Results: Twenty-three patients were excluded. Seven patients disagreed and withdrew their consent, and 16 could not adjust their schedules. The psychiatrist's diagnosis was abnormal in 15 patients. This included one patient with major depression, two patients with moderate depression, five patients with minor depression, two patients with adjustment disorder, two patients with neurosis, one with anxiety, one with insomnia, and one with mental retardation. The Receiver Operating Characteristic curve produced the following cutoff values. A score of 3 or more on the PHQ-9 and 17 or more on the CES-D was considered a cutoff. The PHQ-9 had a specificity of 62.4%, a sensitivity of 93.3%, and the area under the curve (AUC) was 0.792 (95%CI 0.674-0.91). The CES-D had a specificity of 89.4%, a sensitivity of 73.3%, and an AUC was 0.881 (95%CI 0.808-0.955).

Conclusion: The PHQ-9 and CES-D may be helpful in screening for psychiatric disorders, including those associated with RA. However, a different cutoff value should be used than the standard cutoff value.

Disclosure: Y. Miwa: None; **Y. Miwa-mitamura**: None; **H. Tomioka**: None; **M. Hosaka**: None.

Abstract Number: 2102

Is This Prosthetic Joint Infected or Flaring?

Susan Goodman, Insa Mannstadt, Kathleen Tam, Alejandro Kochen, Lorien Shakib, Peter Sculco, Mark Figgie, Alberto Carli, Andy Miller, Linda Russell, Allina Nocon and Laura Donlin, Hospital for Special Surgery, New York, NY

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Diagnosis of a periprosthetic joint infection (PJI) in a patient with inflammatory arthritis (IA) is challenging, as features of IA flares can mimic an infection. We aimed to identify the optimal tests to diagnose a PJI accurately and efficiently in patients with IA.

Methods: We included participants in three patient groups: 1) IA patients with a flaring native joint, 2) IA patients with a prosthetic joint undergoing aseptic revision, and 3) patients with PJI regardless of IA. Demographic characteristics were compared across the three groups. Blood and synovial fluid markers were compared across groups to assess the sensitivity and specificity in diagnosing PJI versus IA flares.

Results: This study included 52 participants, mostly female (60%), and 40% had rheumatoid arthritis. Among the three groups, the confirmed PJI patients were older (p=0.03), while no significant statistical differences were observed in the remaining demographic variables. Synovial fluid and blood markers were significantly different between groups. PJI cases had the highest average C-Reactive Protein (CRP) and there was a significant difference between the groups (PJI: 82 mg/dl, IA flares: 29 mg/dl, aseptic revisions:10 mg/dl, $p< 0.05$) (Table 2). Similarly, the percent of synovial fluid polymorphonuclear neutrophils (PMNs) was highest in PJI cases and significantly differed between groups (PJI: 88.9%, IA flares: 54%, aseptic

revisions: 17%, p< 0.01). Among PJI cases, alpha-defensin was positive in 93%. However, positive alpha-defensin was also observed in 20% of flares and 6% of aseptic revisions, with a significant difference (p< 0.01). There was no significant difference in procalcitonin and IL-6 levels across groups. Synovial white blood cells (WBC) exceeding 3,000 cells/μL, positive alpha-defensin, CRP levels exceeding 3 mg/dl, and PMNs exceeding 80% were highly sensitivity but less specific in diagnosing PJI (Table 3). Synovial WBC counts exceeding 3,000 cells/μL, alpha-defensin positivity, CRP level exceeding 3 mg/dl, and PMNs exceeding 80% were highly sensitive yet less specific for PJI diagnosis. For example, while synovial WBC counts exceeding 3,000 cells/μL and positive alpha-defensin had 100% sensitivity for identifying PJI, their specificity was poor with 50% of IA native joint flares and 79% of aseptic revisions scoring positive for an infection, respectively. The relatively poor specificity of synovial WBC and alpha-defensin indicate that that there is a higher likelihood of these tests incorrectly detecting PJI in cases where it is not present. Positive tests for alpha-defensin or synovial fluid PMNs exceeding 80% increased the likelihood of diagnosing PJI by 5 and 6 times, respectively. However, in cases without PJI, a negative result for PMNs exceeding 80% only marginally increased the likelihood of accurately ruling out diagnosis by 1 time. IL-6, procalcitonin, and D-Dimer demonstrated high sensitivity and specificity, while ESR and CRP had 80% sensitivity but had significantly lower specificity.

Table 1: Demographic and clinical characteristics of study patients*

	Overall (n=52)	PJI revision (n=15)	IA prosthetic joint revision (n=17)	IA native joint flare (n=20)	p-value**
Age, mean ± SD years	53.4 (18.4)	65.3 (16.8)	57.1 (15.0)	49.0 (17.4)	0.03
Sex, female	31 (59.6%)	10 (66.7%)	11 (64.7%)	10 (50%)	0.63
Medical history					
BMI, mean ± SD	27.7 (5.8)	28.8 (6.2)	30.0 (6.6)	25.8 (4.5)	0.19
Hypertension	20 (38.5%)	4 (26.7%)	10 (58.8%)	6 (30%)	0.14
Heart failure	4 (7.7%)	1 (6.7%)	1 (5.9%)	2 (10%)	1.0
Lung disease	4 (7.7%)	1 (6.7%)	1 (5.9%)	2 (10%)	1.0
Diabetes mellitus Type 1	2 (3.9%)	1 (6.7%)	0 (0%)	1 (5%)	0.74
Chronic Obstructive Pulmonary Disease	2 (3.9%)	1 (6.7%)	0 (0%)	1 (5%)	0.74
Kidney disease	2 (3.9%)	0 (0%)	0 (0%)	2 (10%)	0.32
Inflammatory bowel disease	1 (1.9%)	0 (0%)	0 (0%)	1 (5%)	1.0
Inflammatory arthritis type					
Rheumatoid Arthritis	21 (40.4%)	3 (20%)	8 (47.1%)	10 (50%)	0.15
Psoriatic Arthritis	10 (19.2%)	0 (0%)	5 (29.4%)	5 (25%)	0.05
Ankylosing Spondylitis	4 (7.7%)	0 (0%)	1 (5.9%)	3 (15%)	0.37
Systemic Lupus Erythematosus	4 (7.7%)	1 (6.7%)	3 (17.7%)	0 (0%)	0.13
Gouty arthritis	1 (1.9%)	0 (0%)	0 (0%)	1 (5%)	1.0
Polymyalgia rheumatica	1 (1.9%	0 (0%)	0 (0%)	1 (5%)	1.0
Non-inflammatory arthritis	11 (21.2%)	11 (73.3%)	0 (0%)	0 (0%)	<0.01
Medications					
Nonsteroidal anti-inflammatory drugs	29 (55.8%)	8 (53.3%)	7 (41.2%)	14 (70%)	0.22
Disease modifying antirheumatic drugs	11 (21.2%)	3 (20%)	4 (23.5%)	4 (20%)	1.0
Glucocorticoids	10 (19.6%)	2 (13.3%)	4 (23.5%)	4 (21.1%)	0.83
Biologics	7 (13.5%)	0 (0%)	4 (23.5%)	3 (15%)	0.15
Methotrexate	2 (3.8%)	0 (0%)	2 (11.8%)	0 (0%)	0.18

*Except where indicated otherwise values are the number (%) of participants.
**p-value represents the statistical significance of the differences observed in values across the three groups

Table 2: Synovial fluid and blood markers

	PJI revision (n=15)	IA prosthetic joint revision (n=17)	IA native joint flare (n=20)	p-value*
Hemoglobin g/dL	11.1 (2.1)	12.4 (1.5)	13.3 (1.5)	<0.01
Erythrocyte Sedimentation Rate (ESR) mm/hr	72.4 (44.9)	23.6 (14.7)	41.7 (36.4)	<0.01
C-Reactive Protein (CRP) mg/dL	82.4 (138.4)	9.5 (7.7)	29.3 (39.3)	<0.05
Procalcitonin ng/mL	0.2 (0.3)	0.1 (0)	1.3 (5.5)	>0.10
Interleukin-6 (IL-6) pg/mL	8.1 (12.6)	2.1 (0.3)	10.2 (18.5)	>0.10
Synovial fluid polymorphonuclear neutrophils (PMNs) %	88.9 (8.6)	17.3 (17.6)	54.8 (29.4)	<0.01
Synovial fluid lymphocytes %	8.6 (10.7)	44.8 (7.9)	33.2 (28.5)	<0.01
Synovial fluid culture positive	15 (100%)	0 (0%)	0 (0%)	<0.0001
SARS-CoV-2 Antibody IgG				<0.01
Not performed	2 (13%)	7 (41%)	4 (20%)	
Negative	2 (13%)	9 (53%)	5 (25%)	
Positive	11 (73%)	1 (6%)	11 (55%)	
Alpha-Defensin				<0.01
Not performed	1 (7%)	8 (47%)	6 (30%)	
Negative	0 (0%)	8 (47%)	10 (50%)	
Positive	14 (93%)	1 (6%)	4 (20%)	

**p-value represents the statistical significance of the differences observed in values across the three groups.*

Table 3: Sensitivity, specificity, positive likelihood ratio, and negative likelihood ratios of blood and synovial markers for diagnosing prosthetic joint infection*

	Sensitivity (Sn)	Specificity (Sp)	Positive likelihood Ratio	Negative likelihood Ratio
Synovial fluid markers				
Synovial White Blood Cells (>200/uL)	1.000	0.161	1.19	0.00
Synovial White Blood Cells (>3000/uL)	1.000	0.484	1.94	0.00
C-Reactive protein (CRP) (>3.0 mg/L)	0.929	0.565	2.14	0.13
C-Reactive protein (CRP) (>6.9 mg/L)	0.714	0.739	2.74	0.39
Alpha-Defensin positive	1.000	0.792	4.80	0.00
Percentage of polymorphonuclear neutrophils (PMN) (>80.0%)	0.917	0.846	5.96	0.10
Elevated blood markers				
Erythrocyte sedimentation rate (>20 mm/hr)	0.800	0.324	1.18	0.62
Erythrocyte sedimentation rate (>30 mm/hr)	0.800	0.471	1.51	0.42
C-Reactive protein (>10.0 mg/L)	0.800	0.583	1.92	0.34
Interleukin-6 (>2.0 pg/mL)	0.600	0.694	1.96	0.58
D-Dimer (>229 ng/mL)	0.800	0.697	2.64	0.29
Procalcitonin (>.07 ng/mL)	0.133	0.889	1.20	0.98
White Blood Cells (>11.7/nl)	0.067	0.914	0.78	1.02
D-Dimer (>860 ng/mL)	0.333	0.939	5.50	0.71

**The European Bone and Joint Infection Society (EBJIS) 2021 definition served as the gold standard; CRP, serum C-reactive Protein, WBC, synovial white blood cell count; PMN, percentage of polymorphonuclear neutrophils in synovial white blood cell count; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.*

Conclusion: Diagnosing PJI in patients with inflammatory arthritis remains challenging. Current efforts are examining whether next-generation sequencing may prove more effective than common clinical tests.

Disclosure: S. Goodman: NIH, 5, Novartis, 5; **I. Mannstadt**: None; **K. Tam**: None; **A. Kochen**: None; **L. Shakib**: None; **P. Sculco**: DePuy Synthes, 2, EOS Imaging, 2, Intellijoint Surgical, 2, 5, Lima Corporate, 2, Zimmer Biomet, 2, 5; **M. Figgie**: hs2, 8, joint effort aso, 8, lima, 2, 9, wishbone medical, 2, 4, 8, 9, 10; **A. Carli**: None; **A. Miller**: None; **L. Russell**: None; **A. Nocon**: None; **L. Donlin**: Bristol-Myers Squibb(BMS), 2, Stryker, 2.

Abstract Number: 2103

Inflammation and Immunomodulatory Therapies Influence the Relationship Between ATP-binding Cassette Transporter A1 (ABCA1)-mediated Cholesterol Efflux and Coronary Atherosclerosis in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: High-density lipoprotein (HDL) eliminates cholesterol from atherosclerotic lesions, a function known as cholesterol efflux capacity (CEC). ATP-binding-cassette A1 (ABCA1) membrane transporter initiates cholesterol transfer from plaque macrophages to pre-b HDL particles. Methotrexate and biologic disease modifying drugs (bDMARDs) are atheroprotective whereas corticosteroids are proatherogenic. We here evaluated the influence of inflammation and these treatments on ABCA1-CEC and its relationship with coronary atherosclerosis burden, progression and cardiovascular risk in patients with rheumatoid arthritis (RA).

Methods: Coronary atherosclerosis (noncalcified, partially or fully calcified plaque) was evaluated with computed tomography angiography in 140 patients without cardiovascular disease and reassessed in 99 after 6.9±0.4 years. Incident cardiovascular events were recorded. ABCA1-CEC was measured in J774 macrophages. Multivariable negative binomial and

Figure 1 Impact of inflammation and disease-specific therapies on the relationship between ABCA1-CEC and baseline plaque burden in RA

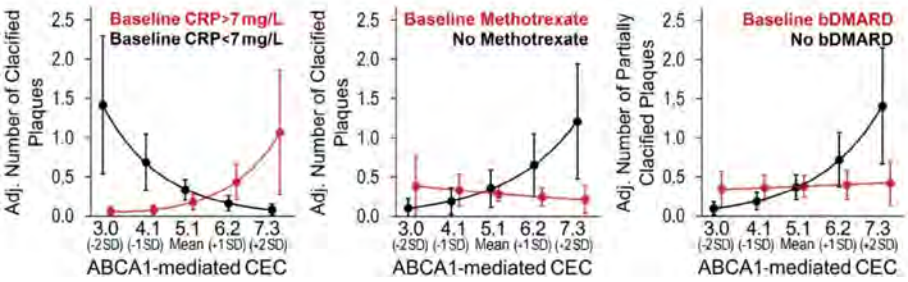
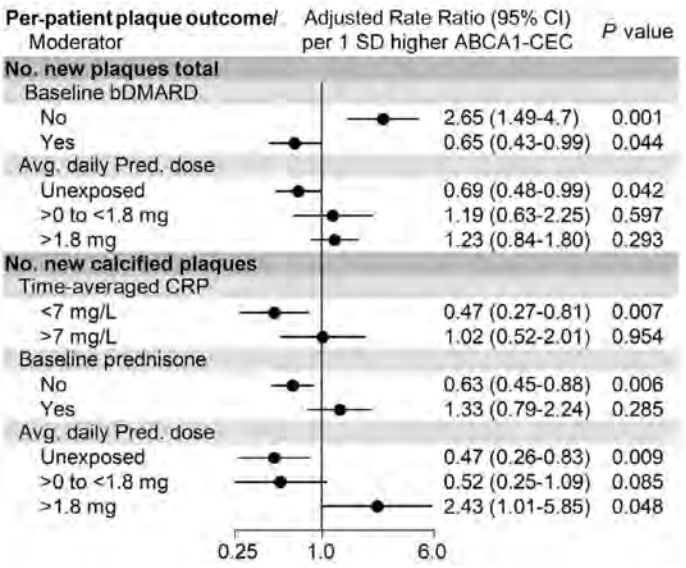


Figure 2 Impact of inflammation and disease-specific therapies on the relationship between ABCA1-CEC and baseline plaque burden in RA



robust logistic regression evaluated associations of ABCA1-CEC with baseline plaque numbers and their progression at follow-up respectively. The moderating role of baseline inflammation, prednisone, methotrexate and bDMARD use on the relationship between ABCA1-CEC and cardiovascular risk was examined in multivariable Cox models including the respective moderators and their interaction term with ABCA1-CEC.

Results: ABCA1-CEC had no main effect on baseline atherosclerosis; prednisone use did not influence this relationship. Higher ABCA1-CEC (per standard deviation increment) associated with (i) more calcified plaques at baseline only in patients with CRP > 7mg/L (median) (p for interaction = 0.001), more calcified plaques only in methotrexate nonusers (p for interaction = 0.037), and more partially-calcified plaques only in bDMARD nonusers (p for interaction = 0.029, Figure 1); (ii) fewer new calcified plaques in patients with time-averaged CRP < 7mg/L (median) (p for interaction = 0.028, Figure 2); (iii) fewer new calcified plaques in baseline prednisone nonusers but not users (p for interaction = 0.021); (iv) fewer new total plaques in prednisone unexposed but not those exposed to prednisone during follow-up (p for interaction = 0.034), and fewer new calcified plaques in prednisone unexposed and more in those with high time-weighted average dose (p for interaction = 0.004); (v) more new plaques in baseline bDMARD nonusers and fewer in bDMARD users (p for interaction≤0.001); (vi) greater cardiovascular risk in baseline prednisone users but not nonusers (p for interaction = 0.027).

Conclusion: ABCA1-CEC attenuated coronary atherosclerosis burden and progression in patients with low baseline and cumulative inflammation and baseline methotrexate and bDMARD use. In contrast, ABCA1-CEC associated with plaque increase in corticosteroid users, methotrexate and bDMARD nonusers. While in well-treated, controlled disease ABCA1-CEC is atheroprotective, in uncontrolled RA its action may be masked or fails to counteract the proatherogenic state promoted by inflammation.

Disclosure: G. Karpouzas: Janssen, 1, Pfizer, 5, Scipher, 1; **B. Papotti**: None; **S. Ormseth**: None; **M. Palumbo**: None; **E. Hernandez**: None; **M. Adorni**: None; **F. Zimetti**: None; **M. Budoff**: None; **N. Ronda**: None.

Abstract Number: 2104

Relationship Between Frailty and Large Joint Symptoms in Rheumatoid Arthritis Patients

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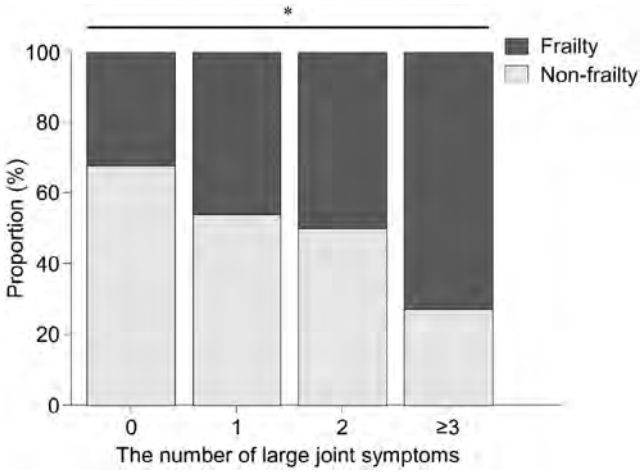
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a causative factor in frailty. Large joint symptoms in RA patients may be more strongly associated with physical disability than small joint symptoms. The aim of this study was to investigate the relationship between large joint symptoms and frailty in RA patients.

Methods: The T-FLAG (Tsurumai - Frailty and Locomotive syndrome of rheumatoid Arthritis for Globalization) Study included 630 RA patients who consecutively visited our hospitals between June and August 2021, of which 591 had background information available, including Clinical Disease Activity Index (CDAI) and the Kihon Checklist (KCL). Frailty was defined as a KCL score of 8 points or more. Large joint symptoms were defined as tenderness or swelling in any of the following joints: shoulders, elbows, hips, knees, and feet. The cut-off value for the number of large joint symptoms (tender joint count + swollen joint count) associated with frailty was calculated using Receiver Operating Characteristic (ROC) analysis. Furthermore, the odds ratios of large joint symptoms associated with frailty (by site) were determined by a multivariable logistic regression analysis, which was adjusted for age, sex, disease duration, and CDAI.

Results: Out of the 591 patients analyzed, 71.7% were female, with an age of 67.4 ± 13.9 years (mean ± standard deviation), disease duration of 11.8 ± 9.8 years, CDAI of 6.5 ± 7.5, KCL score of 7.2 ± 4.8 points. The proportions of patients with large joint symptoms (shoulders, elbows, hips, knees, and feet) were 13.2%, 10.5%, 7.5%, 20.0%, and 14.2%, respectively. The specificity of large joint symptoms for frailty (proportions of patients without large joint symptoms among those without frailty) was 92.2%, 93.9%, 95.9%, 88.1%, and 92.2%, respectively. The proportion of frailty significantly increased as the



The proportions of frailty by the number of large joint symptoms (tender joint count + swollen joint count of large joints). The Kihon Checklist <8 points, non-frailty; ≥8 points, Frailty. (*) P<0.001 by Cochran Armitage trend test.

number of large joint symptoms increased (p< 0.001, Cochran Armitage trend test). The cut-off value for the number of large joint symptoms associated with frailty was 1 site (specificity 74.4%; sensitivity 51.0%; Area under curve 0.647). Knee joint (odds ratio 1.72, 95% confidence interval 1.02-2.91) and ankle joint (odds ratio 1.81, 95% confidence interval 1.02-3.20) symptoms were significantly associated with frailty.

Conclusion: This study suggests that even one site of large joint symptom in RA patients indicates a high possibility of frailty. Among large joint symptoms, lower extremity disability (specifically, knee and ankle joints) was found to have a significant effect on frailty. Therefore, it may be prudent to adopt a more aggressive intervention of RA treatment for RA patients with large joint symptoms (e.g., elderly-onset RA) to prevent frailty. Additionally, if RA patients have large joint destruction and frailty, total joint replacement surgery may be an effective means of improving frailty. Focusing on large joint symptoms is crucial for the prevention of frailty.

Disclosure: Y. Sobue: None; **M. Suzuki**: None; **y. Ohashi**: None; **S. Asai**: None; **S. Imagama**: None.

Abstract Number: 2105

Cohort-wide Immuno-phenotype Deconvolute Immunological and Clinical Heterogeneity Across Autoimmune Rheumatic Diseases

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune rheumatic diseases (AIRDs) are systemic but heterogeneous diseases characterized by orchestration of disrupted self-tolerance of immune systems. We face a challenge in characterizing clinical immune features and selecting best treatment strategy of the AIRD patients. Deconvolution of immunological and clinical heterogeneity within and across AIRDs is an essential step towards implementation of personalized medicine. Immuno-phenotypes, immune-related cell types in peripheral blood mononuclear cells quantified by flow-cytometry analysis, can less invasively describe immune profiles of individuals and is considered as a promising technique.

Methods: We conducted large-scale and cohort-wide immuno-phenotyping of 46 peripheral immune cells using the Human Immunology Protocol of comprehensive 8-color flow cytometric analysis. The dataset consisted of >1,000 Japanese patients of 11 AIRDs and controls with deep clinical information registered at the FLOW study, including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE),systemic sclerosis (SSc), ANCA related vasculitis (AAV), idiopathic inflammatory myopathy (IIM), psoriasis, IgG4 related disease (IgG4RD), mixed connective tissue disease (MCTD), ankylosing spondylitis (AS), Sjogren's syndrome (SjS), and giant cell aortitis (GCA). In depth and longitudinal clinical analysis was

conducted for the identified RA patient clusters registered at the FIRST registry. Inborn human genetics represented by genome-wide polygenic risk score (PRS) were estimated for the RA patients.

Results: Multimodal clustering of immuno-phenotypes deciphered underlying disease-cell type network, providing immune cell type specificity shared or distinct across AIRDs (**Figure 1**), such as close immunological network of MCTD with SLE rather than with SSc. Individual patient-level clustering deconvoluted the AIRD patients into several clusters with different immunological features (**Figure 2**). Of these, RA- or SLE-like clusters were exclusively dominant, showing immunological polarization between RA and SLE across AIRDs (the patient clusters 4-6 and 1-3 for RA and SLE, respectively). In depth and longitudinal clinical analysis of RA revealed that such patient clusters differentially defined clinical heterogeneity in disease activity and treatment responses, which were supported by immune cell-type specificity (e.g., decreased regulatory T cells associated with treatment resistance in the RA patients with SLE-like immuno-phenotypes). PRS based on RA case-control genome-wide association study (GWAS) and within-case stratified RA GWAS were associated with patient characteristics, disease activity, and immuno-phenotypes of the RA patients, such as dendritic cells for RA-interstitial lung disease (**Figure 3**).

Conclusion: Our study demonstrated a value of cohort-wide and cross-disease immuno-phenotyping to elucidate clinically heterogenous patient subtypes existing within the single disease in an immune cell type-specific manner.

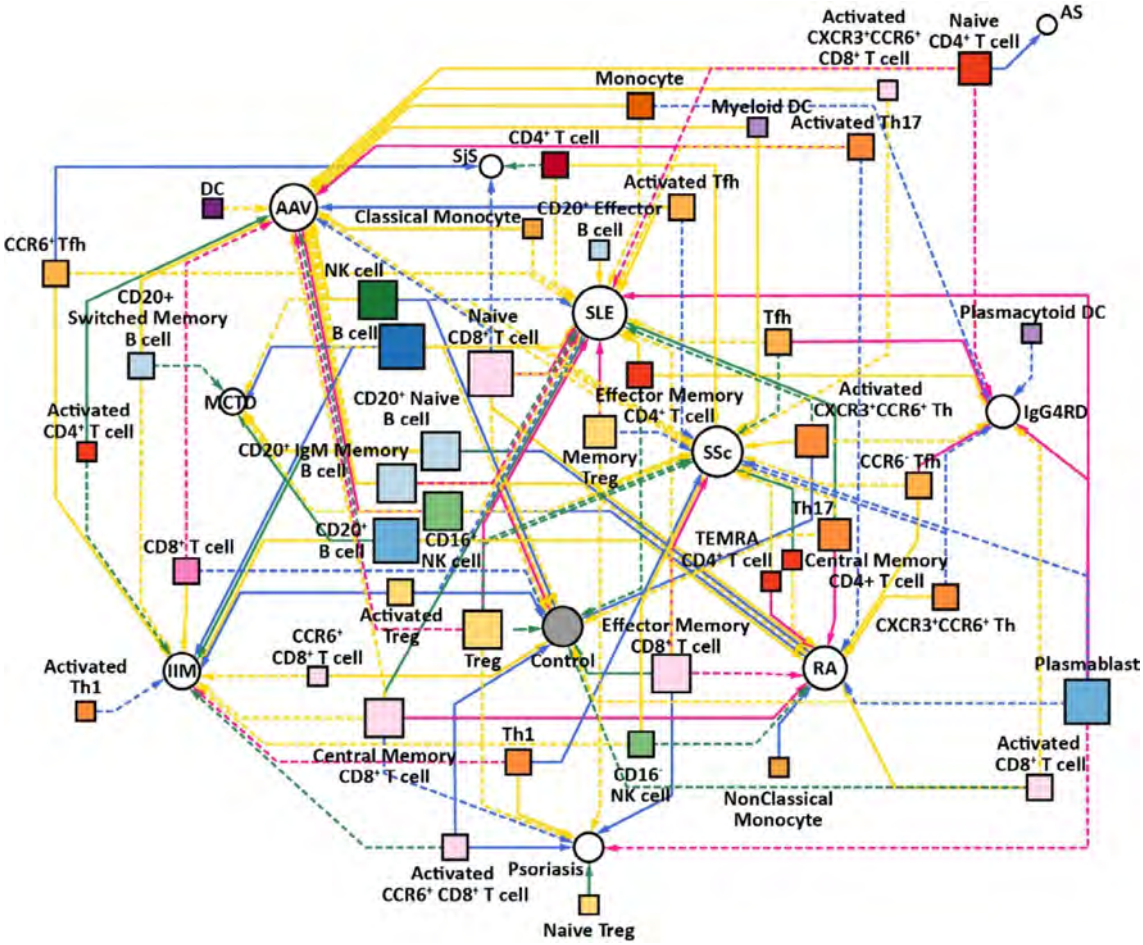

Figure 1 Immune-phenotype network across AIRDs and immune cell types. AIRD-immune cell type associations based on backward-forward stepwise logistic regression adjusted by sex were visualized as a network plot.

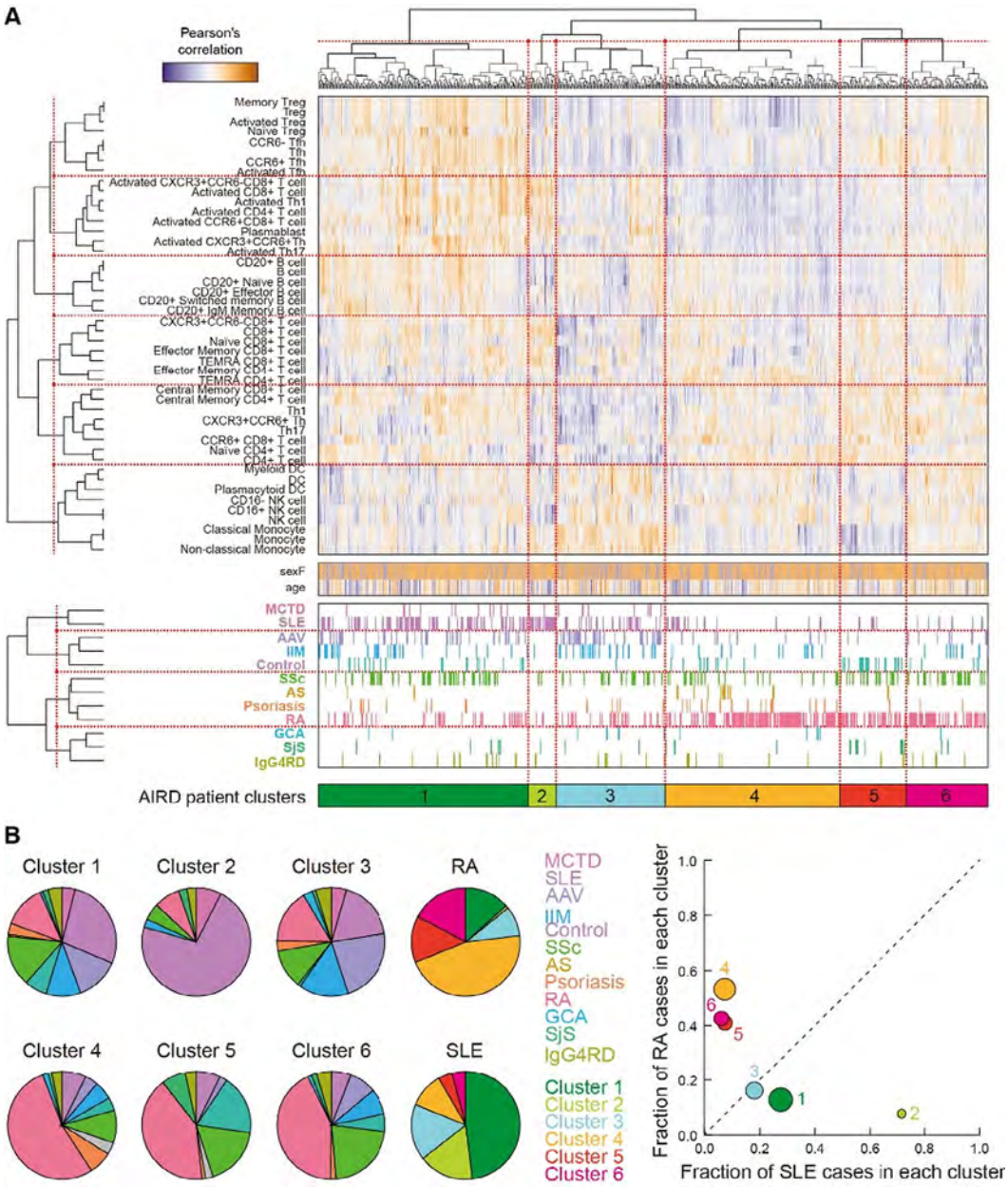

Figure 2. Patient-level clustering of the 11 AIRDs based on the cohort-wide immuno-phenotypes. (A) Unsupervised clustering of individual AIRD patients according to the immuno-phenotypes of the 46 peripheral immune cells. (B) Pie charts showing proportions of the AIRDs within each cluster, and those of the clusters within RA and SLE (left). A co-plot of the fractions of the RA and SLE patients within each cluster (right).

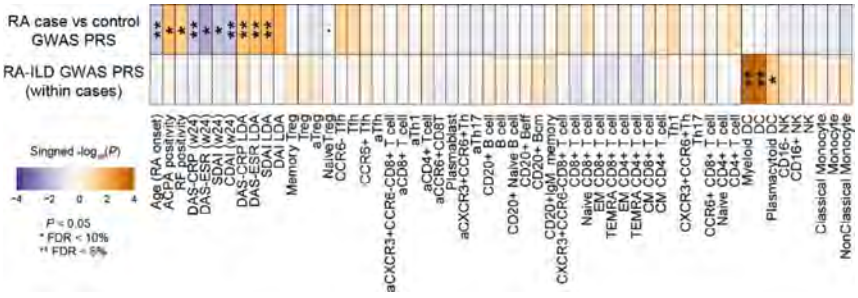

Figure 3. Associations of PRS with clinical and immunological information Associations of the PRS based on RA case-control GWAS and within RA case GWAS for RA-ILD with clinical information and immune-phenotypes of the cell types are indicated.

Disclosure: H. Tanaka: None; **Y. Okada**: None; **S. Nakayamada**: None; **Y. Miyazaki**: None; **K. Sonehara**: None; **S. Namba**: None; **S. Honda**: None; **Y. Shirai**: None; **K. Yamamoto**: None; **K. Ikari**: AbbVie/Abbott, 6, Asahi Kasei, 6, Astellas Pharma, 6, Ayumi Parmaceutical, 6, Bristol-Myers Squibb(BMS), 6, Chugai Parmaceutical, 6, Eisai, 6, Eli Lilly, 6, Janssen, 6, Kaken Pharmaceutical, 6, Mitsubishi Tanabe Pharma, 6, Pfizer, 6, Takeda Pharmaceutical, 6, Teijin Pharma, 6, UCB, 6; **M. Harigai**: Astellas Pharma, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, 12, Post marketing surveillence, Novartis, 5; **K. SONOMOTO**: AbbVie/Abbott, 6, Eli Lilly, 6, UCB, 5; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer-Ingelheim, 6, Chugai, 5, 6, Eisai, 5, 6, Eli Lilly, 6, Gilead, 6, GSK, 6, Mitsubishi-Tanabe, 5, Pfizer, 6, Taiho, 6, Taisho, 5, 6.

Abstract Number: 2106

Evaluation of the Construct of Constitutional Stiffness (CS) in Anti-CCP-Antibody-Positive Rheumatoid Arthritis (ACPA+RA) and Controls

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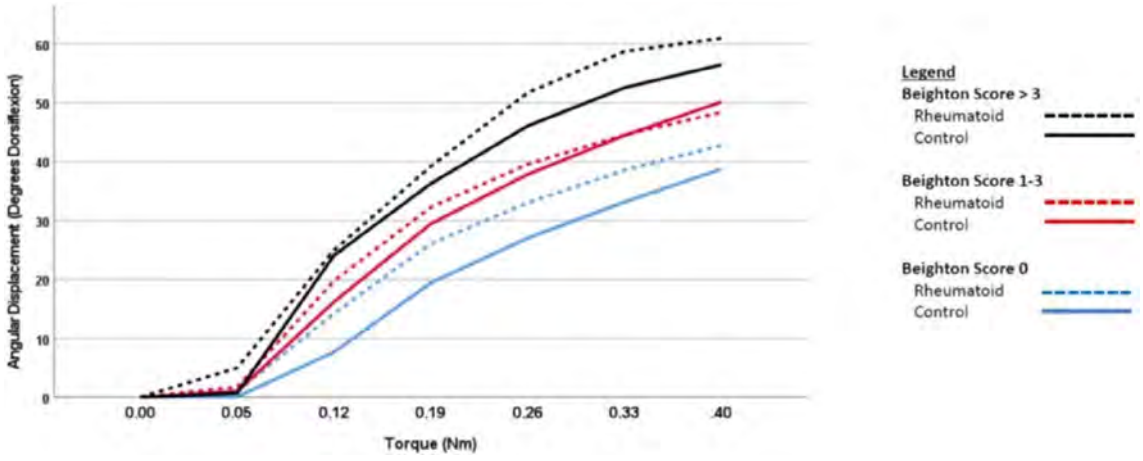
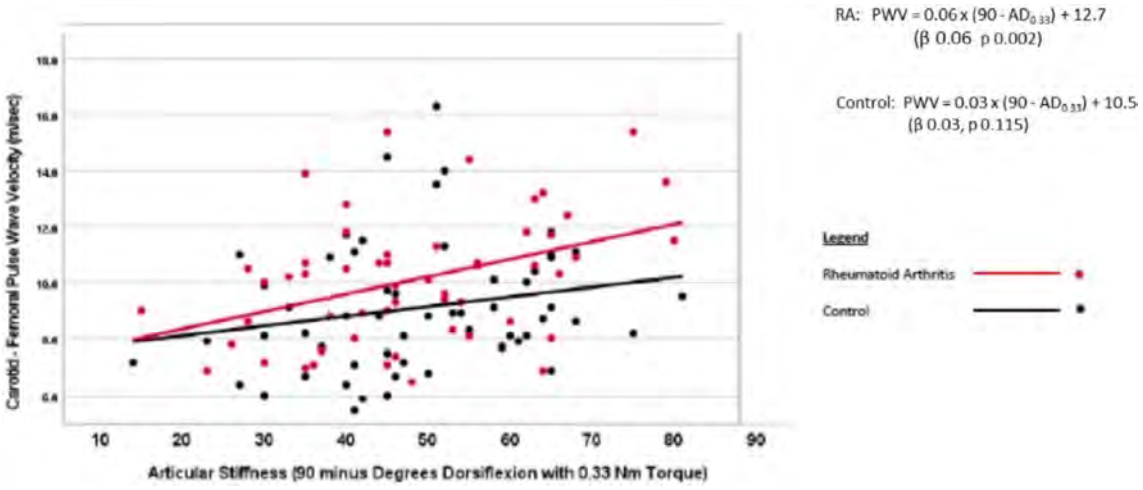
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The risk of developing ACPA+RA, predictors of severity and causes of excess cardiovascular disease (CVD) are incompletely understood. We have observed that RA patients with concurrent benign joint hypermobility have less severe arthritis and lower arterial stiffness. We hypothesise that biomechanical characteristics are similar in different connective tissues within individuals and that Constitutional Stiffness (CS) is a common determinant of RA severity and risk of CVD.

The aimof this study was to evaluate the validity of biomechanical assessments of a single joint (right 5th metacarpophalageal joint R-MCPJ5) as a measure of total body articular stiffness and to compare these assessments with measurements of skin and arterial stiffness in RA and Control.



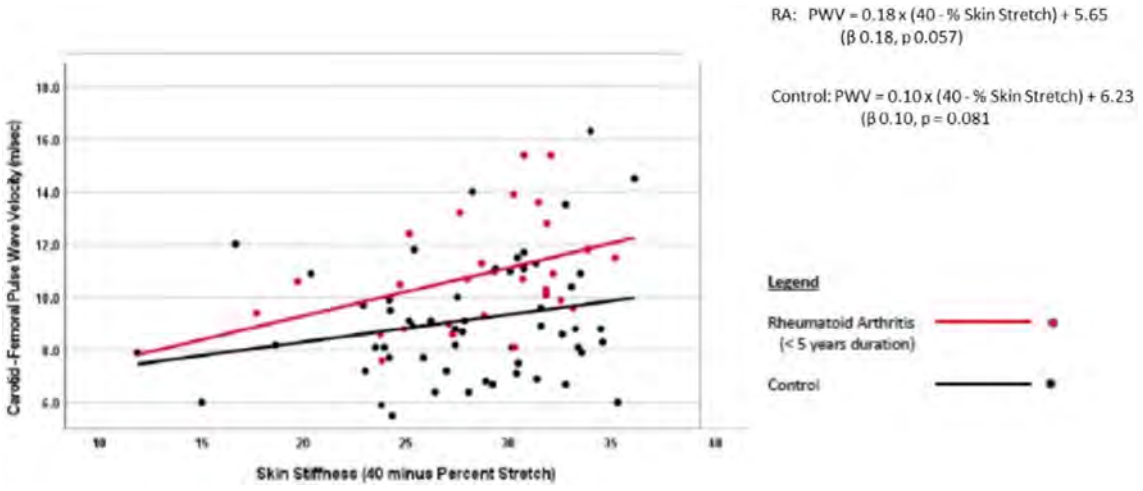
Right 5th MCPJ Stress-Strain responses for Rheumatoid Arthritis (dashed lines) and Control (solid lines) subjects. For both groups there is correlation between Right 5th MCPJ Stiffness (Strain responses measured as dorsal angular displacement) and Overall Total Body Articular Stiffness (Beighton Score).



Arterial Stiffness (Carotid-Femoral Pulse Wave Velocity) versus Articular Stiffness in RA (red) and Control (black) Groups. Scatterplots with univariate linear regression lines of best fit. Note that Articular stiffness has been expressed as (90 minus Angular Displacement degrees dorsiflexion) so that greater values indicate greater stiffness.

Methods: Fifty-eight ACPA+RA and 57 controls (47 Healthy Volunteers and 10 Benign Joint Hypermobility) were recruited. R-MCPJ5 stiffness was measured as angular displacement (AD) degrees passive extension in response to a range of torque moments. Stress-strain responses were evaluated. Responses to 0.33Nm torque ($AD_{0.33}$) were examined in detail. Beighton Scores (BS) used clinically to assess hypermobility were categorised as Low (BS 0), moderate (BS 1-3) and High (BS >3). Skin Stretch (SKST) was measured as percentage increase in distance between 2 dots dorsal right hand upon manual traction (Vernier calipers 0.1 mm resolution). Scores were dichotomised as High Stiffness ≤ 9.7% or Low Stiffness > 9.7%. Arterial stiffness was measured as Carotid-Femoral Pulse Wave Velocity (PWV metres/sec). Scores were dichotomised as High Stiffness ≥ 9.3 m/sec or Low Stiffness < 9.3 m/sec.

Results: Reproducibility (ICC/Kappa): $AD_{0.33}$ 0.94, BS 0.67, SKST 0.27 and PWV 0.99. Stress-Strain responses curves found that R-MCPJ5 assessments correlate with BS. BS correlated with $AD_{0.33}$ in ACPA+RA (BS_0:37, $BS_{1\text{-}3}$:45, $BS_{>3}$:54, p0.000) and Control (BS_0:33, $BS_{1\text{-}3}$:45, $BS_{1\text{-}3}$:53, p0.000). High PWV (>9.3 m/sec) was associated with lower $AD_{0.33}$ in ACPA+RA (38 vs 47, p0.011) and Controls (38 vs 43, p0.206). Linear regression found negative correlation with $AD_{0.33}$ in



Arterial Stiffness (Carotid-Femoral Pulse Wave Velocity) versus Skin Stiffness in RA <5 years duration (red) and Controls (black). Scatterplots with univariate linear regression lines of best fit. Note that skin stretch is expressed as 40 - Percent stretch so that higher values represent greater stiffness.

ACPA+RA (β -0.06, p 0.002) and Controls (β -0.03, p 0.115). PWV correlated negatively with BS in ACPA+RA (BS_0:10.5, BS_{1-3}:9.4, $BS_{>3}$:9.4, p0.207) and Controls (BS_0:9.4, BS_{1-3}:9.8, $BS_{>3}$:7.1, p0.004). SKST correlated with lower $AD_{0.33}$ significantly in RA ≤5 years duration (31 vs 44, p0.027) with similar trends for BS in ACPA+RA (BS_0:11%, BS_{1-3}:12% $BS_{>3}$:13%, p0.746) and in Controls for $AD_{0.33}$ (39 vs 43, p0.2638) and BS (BS_0:10%, BS_{1-3}:12%, $BS_{>3}$:15%, p0.008). Skin stiffness correlated with PWV in Control (OR 1.91, p0.242) and ACPA+RA (Odds Ratio 2.2, p0.157). In RA ≤5 years duration no subjects with High PWV had Low skin stiffness (OR infinite, p0.000). Linear regression PWV correlated negatively with SKST in ACPA+RA of less than 5 years duration (β -0.18, p 0.057) and Controls (β -0.10, p 0.081).

Conclusion: R-MCPJ5 assessments are representative of total body articular biomechanical properties. There is correlation between articular, arterial and skin biomechanical characteristics supporting the construct of CS. CS is a plausible common determinant of articular and arterial disease.

Disclosure: S. Oakley: AbbVie/Abbott, 5, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Novartis, 6, UCB, 6; **S. Stott**: None; **K. Gill**: None; **C. Virgil**: None; **L. Weston**: None; **T. de Malmanche**: None.

Abstract Number: 2107

Social Determinants of Health and Clinical Outcomes in Rheumatoid Arthritis: A Single Center Study

Nicholas Wiemer[1], Yue Yin[2] and Tarun Sharma[1], [1]Allegheny Health Network, Pittsburgh, PA, [2]Allegheny Health Network Singer Research Institute, Pittsburgh, PA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic and potentially debilitating disease.Social determinants, including smoking and depression, have been shown to be linked to worse clinical outcomes in RA.In this study, we aim to determine the prevalence of eleven social determinants of health (SDOH) in the RA cohort at our health system.

Table 1: Comparison of SDoH Between CDAI Groups

Variable	CDAI < 10 (n=32)	CDAI ≥ 10 (n=18)
Smoking	10 (31.25%)	10 (55.56%)
Alcohol use	11 (34.38%)	6 (33.33%)
Food insecurity	19 (59.38%)	8 (44.44%)
Housing stability	0	2 (11.11%)
Safety environment	1 (3.13%)	1 (5.56%)
Financial strain	1 (3.13)	1 (5.56%)
Transportation	0	2 (11.11%)
Depression	2 (6.25%)	3 (16.67%)
PHQ9	0.88	18
Stress	15 (46.88%)	7 (38.89%)
Health literacy	1 (3.13%)	2 (11.11%)
Social connection	15 (46.88%)	9 (50%)

SDoH: social determinants of health, CDAI: clinical disease activity index, PHQ: patient health questionnaire

Table 2: Logistic Regression for Univariate and Multivariate Analyses				
Variable	Univariate		Multivariable	
	OR[95% CI]	P value	OR[95% CI]	P value
Smoking	2.32[1.08, 5.02]	.0321	2.25[1.03, 4.89]	.0413
Alcohol use	1.09[0.54, 2.18]	.8135	-	-
Food insecurity	0.78[0.43, 1.41]	.4109	-	-
Housing stability	3.39[0.28, 41.23]	.3384	-	-
Safety environment	1.31[0.30, 5.65]	.7179	-	-
Financial strain	1.30[0.31, 5.50]	.7180	-	-
Transportation	2.92[0.43, 19.70]	.2712	-	-
Depression	3.00[0.45, 19.92]	.2556	-	-
PHQ9	1.11[0.97, 1.28]	.1324	1.06[0.90, 1.24]	.5072
Health literacy	1.79[0.43, 7.53]	.4271	-	-
Social connection	1.29[0.64, 2.62]	.4742	-	-

PHQ: patient health questionnaire

Methods: A retrospective review of patients seen as part of the RA Care Pathway, a well-defined cohort of adult patients with RA at AHN Rheumatology, was performed.Demographics, serologies, medications, and SDOH metrics were captured and validated via chart review. Patients were included if they had a RA Clinical Disease Activity Index (CDAI) and at least 3 social determinants completed within 6 months of each other. Patients were then examined in two groups, CDAI ≥10 (moderate-severe RA) and CDAI < 10 (remission and low disease activity) to assess any differential impact of SDOH.

Results: A total of 137 patients were reviewed, of which 50 met inclusion criteria. Average age was 65.5 years, 74% were female, and 66% were Caucasian. Mean CDAI was 9.64 with 36% patients in the moderate-severe CDAI group. Several SDOH metrics were unfavorably distributed in the CDAI ≥10 compared to < 10 group, including smoking (55.56% vs 31.25%), housing instability (11.11% vs 0%), depression (16.67% vs 6.25% with mean PHQ9 scores 18 vs 0.88, respectively), and low health literacy (11.11% vs 46.88%).Smoking patients were more likely to have high disease activity (OR 2.25, 95% CI [1.03, 4.89], p=0.04).

Conclusion: Our data reveals that RA patients with moderate-high disease activity are more likely to have high risk social determinants of health including high likelihood of smoking, housing instability, and depression. A team-based care approach has been implemented at AHN Rheumatology. Our next steps are to better capture SDOH and determine the impact of SDOH interventions on clinical outcomes in RA.

Disclosure: N. Wiemer: None; **Y. Yin**: None; **T. Sharma**: None.

Abstract Number: 2108

Specific Symptom Clusters at Diagnosis Signal a Poorer Early RA Prognosis: Data from the Canadian Early Arthritis Cohort (CATCH)

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

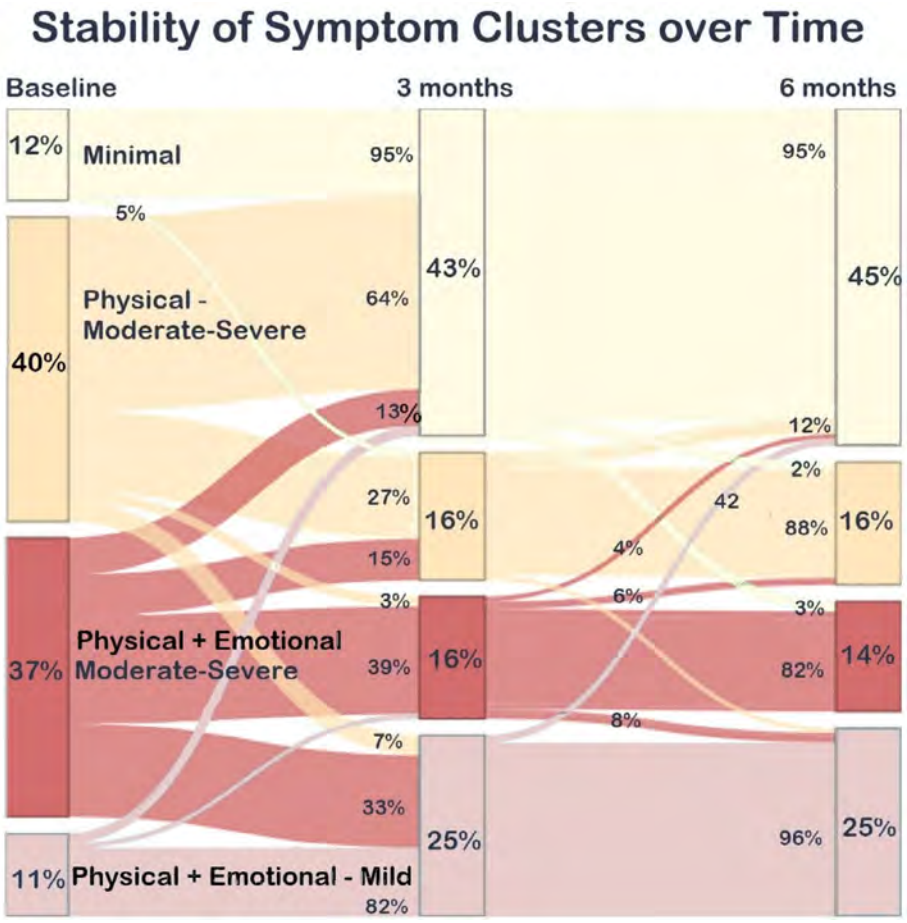
Background/Purpose: Symptom clusters are stable groups of 2+ symptoms that are related to each other and frequently co-occur. Identifying symptom clusters in early RA may point to underlying mechanisms and RA subtypes, help predict disease trajectories and personalize symptom management to improve outcomes. We used scores from PROMIS-29 to identify symptom clusters at diagnosis in MTX-naïve patients starting MTX therapy. We evaluated the stability of these clusters and likelihood of transitioning between clusters over the first 6 months of treatment.

Methods: Data were from new onset RA patients (sx < 1 year) enrolled in the Canadian Early Arthritis Cohort (CATCH) who started MTX and had clinical and PROM measures available at 0, 3, and 6-months. Based on empirical and qualitative data, we used latent class analyses to identify symptom clusters from PROMIS-29 physical (pain, fatigue, sleep) and emotional (depression, anxiety) scales (levels: minimal, mild, moderate, severe). Models were compared using AIC, BIC, G-square and log-likelihoods. We estimated transitioning between clusters at 3- and 6-months using latent transition analyses.

Results: Of 310 adults with new RA, followed for 6 months and starting MTX, 67% were women and 78%White. Participants had a mean age of 56 yrs, CDAI 29.3, and RA symptom durationof 5 months. Optimal clusters included pain, fatigue, anxiety and depression and three intensity levels. We identified 4 discrete symptom clusters at diagnosis:**MINIMAL** (12%); **Moderate-Severe Physical** (**M-S P**: 40%); **Mild Physical + Emotional** (**MILD P+E:** 11%); **Moderate-Severe Physical + Emotional** (**M-S P+E** 37%). Clusters had similar sociodemographics except the **MINIMAL**class were slightly older and fewer were women; **M-S P+E** had a greater likelihood of depression history (Table). SJC and TJC were similar among classes; worse symptoms were associated with higher CDAI. Classes with emotional sx had significantly worse mood and sleep, and the **M-S P** class were more likely to report a history of depression. More patients with moderate-severe symptoms were on parenteral steroids. Most transitions occurred over the first 3 months. The best prognosis was for the

RA patient characteristics by symptom clusters identified at diagnosis.

	Physical		Physical and Emotional		
Baseline Values (mean SD, N %)	**Minimal** N=38 (12%)	**Moderate-Severe** N=124 (40%)	**Mild** N=34 (11%)	**Moderate-Severe** N=114 (37%)	**SIG**
Age	**61 (14)**	**59 (13)**	**58 (14)**	**52 (14)**	**0.0003**
Women	**22 (58%)**	**74 (60%)**	**25 (74%)**	**88 (77%)**	**0.0148**
White race	29 (76%)	103 (83%)	24 (71%)	87 (76%)	0.4735
Education >high school	22 (58%)	79 (64%)	25 (74%)	64 (56%)	0.1317
Current smoker	2 (5%)	16 (13%)	4 (12%)	23 (20%)	0.1446
Obese BMI (≥ 30)	9 (24%)	36 (31%)	8 (28%)	37 (36%)	0.5616
RDC Index	1.0 (1.0)	1.3 (1.4)	0.9 (1.1)	1.4 (1.3)	0.2733
Symptom duration	4.9 (2.5)	5.1 (2.7)	4.9 (2.6)	4.6 (2.6)	0.5861
History of depression	**2 (5%)**	**6 (5%)**	**7 (21%)**	**25 (22%)**	**0.0002**
Patient Global (0-10)	**2.6 (2.4)**	**4.8 (2.3)**	**3.9 (2.2)**	**6.9 (2.0)**	**<0.0001**
PROMIS-29					
Anxiety ≥ 55	**1 (3%)**	**15 (12%)**	**28 (82%)**	**108 (95%)**	**<0.0001**
Depression ≥ 55	**0 (0%)**	**14 (11%)**	**22 (65%)**	**100 (88%)**	**<0.0001**
Fatigue ≥ 55	**3 (8%)**	**49 (40%)**	**12 (35%)**	**106 (93%)**	**<0.0001**
Pain Interference ≥ 55	**0 (0%)**	**124 (100%)**	**25 (74%)**	**113 (99%)**	**<0.0001**
Physical Function ≤ 45	**9 (24%)**	**107 (86%)**	**25 (74%)**	**111 (97%)**	**<0.0001**
Participation ≤ 45	**5 (13%)**	**81 (65%)**	**17 (50%)**	**108 (95%)**	**<0.0001**
Sleep ≥ 55	**2 (5%)**	**46 (37%)**	**17 (50%)**	**88 (77%)**	**<0.0001**
Stiffness (0-10)	**3.2 (2.4)**	**6.3 (2.4)**	**4.3 (2.3)**	**7.7 (1.8)**	**<0.0001**
Oral steroids	16 (42%)	40 (32%)	14 (41%)	29 (25%)	0.1470
Parenteral steroids	**8 (21%)**	**44 (35%)**	**7 (21%)**	**62 (54%)**	**<0.0001**
TJC-28, median (IQR)	8 (6,12)	9 (5,13)	7 (5,12)	9 (5,13)	0.4626
SJC-28, median (IQR)	7 (5,12)	8 (4,12)	6 (3,11)	7 (4,12)	0.4396
CDAI, mean (SD)	**25.5 (11.4)**	**29.2 (12.7)**	**24.8 (12.6)**	**32.0 (14.0)**	**0.0103**



MINIMAL class; 95% were classified similarly at 3 and 6 months. Among those with **MILD P+E ,** almost all were classified similarly at 3 (82%) and 6 (96%) months. Participants with **M-S P** at diagnosis were also likely to transition to **MINIMAL** (64%) or **MILD P+E** (7%). The worse prognosis was among those with **M-S P+E**; at 3 months, a minority transitioned to **MINIMAL** (13%) or **MILD P+E** (33%) classes. Patients with either mild or moderate-severe emotional symptoms were the least likely to transition to milder symptom classes.

Conclusion: We identified 4 ERA patient subsets with varying physical (pain, fatigue) and emotional (depression, anxiety) symptoms and evaluated transitions over 6-months of initial MTX treatment. At baseline, most participants had moderate-severe Physical +/- Emotional symptoms. Patient subsets with emotional symptoms at RA-diagnosis were less likely to transition to better controlled symptom classes. Our results suggest that co-occurring emotional symptoms at diagnosis may reflect important subsets and signal a more guarded RA prognosis over the first 6 months.

Disclosure: S. Bartlett: Janssen, 6, Merck/MSD, 2, 6, Novartis, 2, Organon, 1, 6, PROMIS Health Organization, 4, Sandoz, 2, 6; **C. Bingham**: None; **O. Schieir**: None; **M. Valois**: None; **J. Pope**: AbbVie, 1, 2; **L. Bessette**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol Myers Squibb, 2, 5, 6, Eli Lilly, 2, 5, 6, Fresenius Kabi, 2, 6, Gilead, 2, 5, 6, JAMP Pharma, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Organon, 2, 6, Pfizer, 2, 5, 6, Sandoz, 2, 6, Sanofi, 2, 5, 6, Teva, 2, 6, UCB, 2, 5, 6, UCBA, 5; **G. Boire**: Eli Lilly, 1, Janssen, 6, Organon, 1, Orimed Pharma, 1, 6, Otsuka, 1, Pfizer, 1, 5, Sandoz, 1, Teva, 1, Viatris, 1, 6; **C. Hitchon**: Astra Zeneca, 1, Pfizer, 5; **E. Keystone**: AbbVie/Abbott, 2, 6, Amgen, 2, 6, celltrion, 2, 6, Eli Lilly, 2, 6, Fresenius Kabi, 2, 6, Pfizer, 2, 6, Samsung Bioepsis, 2, sandoz, 2, 6; **C. Thorne**: Abbvie, 1, Biogen, 2, Nordic Pharma, 1, Pfizer, 1, 5, Roche, 1, Sandoz, 1, 2; **D. Tin**: None; **G. Hazlewood**: None; **V. Bykerk**: Abbvie, 2, BMS, 2, Pfizer, 2.

Abstract Number: 2109

Real-world Positivity of 14-3-3η Protein in Rheumatoid Arthritis

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SESSION INFORMATION
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Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
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Background/Purpose: 14-3-3η protein may be elevated in the blood of inflammatory arthritis patients. It is a commercially available novel biomarker used to aid in the diagnosis of rheumatoid arthritis (RA), in addition to rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP), especially in seronegative patients. 14-3-3η is not routinely checked in all patients with arthritis. We aim to see the positivity rate of the 14-3-3η in real-world patients with rheumatoid arthritis compared to other arthritis.

Methods: A retrospective study was conducted via review of electronic medical records after approval by the institutional review board. All patients with a result for the lab test of 14-3-3η in the last five years (March 2018 – February 2023) were included. The data, including demographics, arthritis diagnosis, and relevant lab components, were compared.

Results: Three hundred and twenty-eight patients were tested for 14-3-3η, with 26 (8%) positive results. The mean age was 55 ± 15 years, with 72% female and 84% white. The characteristics of the patients with positive and negative 14-3-3η results are summarized in Table 1. Eighty patients (24%) with positive results were diagnosed with RA, with 39 patients being seropositive. The positivity rate of 14-3-3η was significantly higher in RA patients than other arthritis (14% vs. 6%, p=0.048). Other diagnoses with positive values included undifferentiated arthritis (n=14) and reactive arthritis (n=1). No patients with

Table 1: Distribution of the positive and negative 14-3-3η result

Characteristics	Mean positive 14-3-3η ± SD (ng/ml)	14-3-3η result (positive vs negative)		
		Positive N (%)	Negative N (%)	p-value
Mean age (years)	-	56.3	54.7	0.555
Sex				0.896
Female	3.6 ± 6.3	18 (8)	219 (92)	
Male	2.9 ± 3.7	8 (9)	83 (91)	
Arthritis type				**0.048**
Rheumatoid arthritis (RA)	6.2 ± 7.6	11 (14)	69 (86)	
Other*	1.3 ± 2.1	15 (6)	233 (94)	
Rheumatoid arthritis type				0.343
Seropositive	8.1 ± 8.8	7 (18)	32 (82)	
Seronegative	1.3 ± 1.5	4 (10)	37 (90)	
Rheumatoid factor in RA				0.330
Positive	6.2 ± 7.8	6 (17)	29 (83)	
Negative	4.8 ± 2.4	4 (9)	39 (91)	
Anti-cyclic citrullinated peptide in RA				0.399
Positive	6.8 ± 11.4	3 (20)	12 (80)	
Negative	2.7 ± 4.7	7 (11)	55 (89)	

*Other: Undifferentiated arthritis (including reactive arthritis, osteoarthritis, non-RA and non-psoriatic inflammatory arthritis) (n=195), psoriatic arthritis (n=30), ankylosing spondylitis (n=3)

psoriatic arthritis had positive values. The mean value for 14-3-3η in RA patients was 6.2 ± 7.6 compared to 1.3 ± 2.1 in non-RA patients (p=0.06; reference range 0.2 ng/ml - >20 ng/ml). In the patients with RA, RF was positive in 44%, anti-CCP positive in 19%, and both were positive in 14%, and antinuclear antibody was positive in 25%. The positivity rate of 14-3-3η was numerically higher in seropositive RA compared to those with seronegative RA (18% vs. 10%, p=0.343). The mean value for 14-3-3η in seropositive RA was 8.1 ± 8.8 compared to 1.3 ± 1.5 in seronegative (p=0.09). Logistic regression showed no association between 14-3-3η positivity with age, sex, erythrocyte sedimentation rate, C-reactive protein, RF, or anti-CCP in patients with RA.

Conclusion: 14-3-3η protein is positive more often in patients with RA than in other causes of arthritis but is not exclusive to RA. Although 14-3-3η has been thought to increase the sensitivity of diagnosis of seronegative patients, the positivity rate was only 10% in our study. Further studies are needed to better understand its importance in seronegative patients.

Disclosure: R. Subedi: None; **M. Jimenez Artiles**: None; **A. Al Najada**: None; **A. Misbah**: None; **Q. Wang**: None; **A. Kusnik**: None; **Z. Tang**: None; **S. Zabiullah**: None; **A. Ocon**: None.

Abstract Number: 2110

Rheumatoid Arthritis and Changes in Pulmonary Function Measures on Spirometry in a Prospective Longitudinal Cohort of Smokers

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SESSION INFORMATION
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Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
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Background/Purpose: Rheumatoid arthritis (RA) has known extra-articular manifestations that can result in restrictive and obstructive patterns on pulmonary function measures, especially in smokers. However, investigations comparing RA and non-RA for pulmonary function change have not been performed. In this study, we compared longitudinal spirometry measures between smokers with and without RA.

Methods: We analyzed longitudinal data from COPDGene, a multicenter prospective cohort of smokers with at least 10 pack-years. We investigated longitudinal pulmonary function measures in people with RA compared to non-RA comparators and healthy non-smokers. Spirometry was conducted at baseline (2007-2011) and at a second visit 5 years later. RA cases were identified by self-reported RA and DMARD use (PPV 88%); non-RA comparators reported no RA and no DMARD use. The outcomes were the annual change in postbronchodilator percent predicted forced expiratory volume in one second (%FEV_1), percent predicted forced vital capacity (%FVC), and FEV_1/FVC ratio. We compared these outcomes between RA cases and non-RA comparators using linear regression, adjusted for age, sex, BMI, smoking status (current/past), pack-years, baseline spirometry results, and inhaled/systemic medication use for obstructive lung diseases. An

Table 1. Baseline characteristics of RA cases, non-RA comparators and healthy non-smokers (n=5220)

Table 1. Baseline characteristics of RA cases, non-RA comparators and healthy non-smokers (n=5220)

	RA smoker cases (n=45)	Non-RA smoker comparators (n=5175)
Demographic		
Age at enrollment (years, mean, SD)	63.4 (8.0)	59.7 (8.7)
Female (n, %)	30 (67%)	2549 (49%)
White Race (n, %)	33 (73%)	3665 (71%)
Black Race (n, %)	12 (27%)	1510 (29%)
Lifestyle		
Current smoker (n, %)	16 (36%)	2497 (48%)
Former smoker (n, %)	29 (64%)	2678 (52%)
Pack-years (mean, SD)	42.4 (18.6)	42.1 (23.3)
BMI (kg/m^2, mean, SD)	30.8 (8.6)	29.0 (6.0)
Pulmonary features		
Spirometry pattern (n, %)		
Restrictive: %FVC <80% & FEV_1/FVC ≥70%	8 (18%)	662 (13%)
Obstructive: FEV_1/FVC <70%	14 (31%)	2083 (40%)
Normal: none of the above	23 (51%)	2430 (47%)
Inhaled/systemic medication use for obstructive lung disease (n, %)	24 (53%)	1706 (33%)

additional analysis used inverse probability of censoring weighting (IPCW) to account for possible differential censoring, defined by drop-out or death before the follow-up visit was due. We also stratified the analysis by the presence of obstructive pattern (FEV_1/FVC< 0.7) at baseline.

Results: We analyzed 45 RA smoker cases and 5175 non-RA smoker comparators with available follow-up spirometry data (**Table 1**). The mean %FEV_1 at baseline was 77% in RA cases and 80% in non-RA comparators. The mean change in %FEV_1 from baseline to the 5-year follow-up was +1.8% in RA cases and -2.3% in non-RA comparators. Proportions of each group with improved, stable, and declined %FEV_1 are shown in **Figure 1**. In the multivariable linear regression models, both %FEV_1 and FEV_1/FVC showed significantly less decline in RA cases compared to non-RA comparators (%FEV_1: β 0.68, p=0.026; FEV_1/FVC: β 0.52, p=0.002; **Table 2**). This result was more prominent in participants with obstructive pattern at baseline (RA vs. non-RA: %FEV_1: β 1.17, p=0.0025; FEV_1/FVC: β 1.73, p< 0.001). There was no significant difference in the annual change in %FVC between the two groups. Results were similar after accounting for possible differential loss to follow-up or death.

Figure 1. Proportions of each group with improved, stable, and declined %FEV_1 among RA smoker cases (n=45) and non-RA smoker comparators (n=5175).

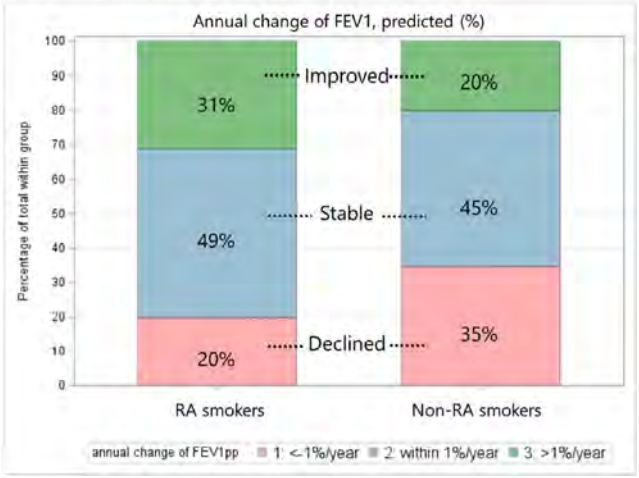

Figure 1. Proportions of each group with improved, stable, and declined %FEV1 among RA smoker cases (n=45) and non-RA smoker comparators (n=5175).

Table 2. Results from the linear regression of annual change of measures in pulmonary function test (PFT), comparing RA smoker cases vs. non-RA smoker comparators.

Table 2. Results from the linear regression of annual change of measures in pulmonary function test (PFT), comparing RA smoker cases vs. non-RA smoker comparators.

Outcome	Unadjusted model		Multivariable model		Multivariable model with IPCW	
Spirometric measure (annual change)	β (SE) (RA vs. non-RA smokers)	P-value	β (SE) (RA vs. non-RA smokers)	P-value	β (SE) (RA vs. non-RA smokers)	P-value
All participants, RA cases: n=45, non-RA comparators: n=5175						
%FEV	**0.76 (0.29)**	**0.009**	**0.68 (0.28)**	**0.026**	**0.60 (0.29)**	**0.038**
$FEV_1/FVC_{(*100)}$	**0.47 (0.17)**	**0.007**	**0.52 (0.17)**	**0.002**	**0.45 (0.17)**	**0.009**
%FVC	0.33 (0.33)	0.311	0.21 (0.33)	0.517	0.08 (0.32)	0.813
Obstructive pattern ($FEV_1/FVC<70\%$) at baseline: RA cases: n=14, non-RA comparators: n=2083						
%FEV	**1.37 (0.54)**	**0.012**	**1.17 (0.52)**	**0.025**	**1.05 (0.53)**	**0.048**
$FEV_1/FVC_{(*100)}$	**1.81 (0.38)**	**<0.001**	**1.73 (0.37)**	**<0.001**	**1.62 (0.37)**	**<0.001**
No obstructive pattern ($FEV_1/FVC\geq70\%$) at baseline: RA cases: n=31, non-RA comparators: n=3093						
%FEV	0.38 (0.35)	0.274	0.21 (0.33)	0.529	0.17 (0.34)	0.611
$FEV_1/FVC_{(*100)}$	-0.12 (0.17)	0.497	-0.07 (0.17)	0.666	-0.06 (0.18)	0.712

Annual change of spirometric measure = (PFT at baseline – PFT at 2nd visit)/(years from baseline to 2nd visit)
Adjusted for age, sex, smoking status (current/past), pack-years, body mass index, spirometric measure (%FEV_1, FEV_1/FVC, or %FVC) at baseline, and medication use for obstructive lung diseases
Inverse probability of censoring weighting (IPCW) was calculated using baseline characteristics (RA/non-RA status, age, sex, race, smoking status, pack-years, body weight, body mass index, limit of walking, cancer, cardiovascular disease, diabetes, hypertension, hyperlipidemia, and spirometric measure at baseline).

Conclusion: In this first comparative study among smokers to examine longitudinal pulmonary function in RA, RA cases were less likely to have %FEV_1 and FEV_1/FVC declines than non-RA comparators. Results were strongest among RA cases with baseline obstructive defect and not explained by differences in smoking, suggesting that RA with obstruction may be a unique phenotype. Further studies are needed to replicate with larger sample size and to examine mechanisms and potential for reversibility related to systemic inflammation, autoimmunity, and RA treatment.

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Abstract Number: 2111

Self-reported Methotrexate Adherence Underestimates Biochemical Adherence: Results from the Methotrexate Use Improvement in Rheumatoid Arthritis Using Biomarker Feedback Trial

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SESSION INFORMATION

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Background/Purpose: Methotrexate (MTX) adherence is suboptimal and is associated with disease flare, DAS-28 response, radiographic damage and healthcare costs. Adherence can be measured using self-reported questionnaires such as the validated Medication Adherence Report Scale (MARS-5). Often the prescriber is blinded to patient non-adherence and self-reported adherence may be an underestimate. Our group has previously developed a sensitive biochemical assay for the detection of MTX adherence, The Methotrexate use Improvement in Rheumatoid Arthritis using Biomarker Feedback (MIRA) is a feasibility trial designed to assess the feasibility of a randomised controlled trial of MTX biochemical adherence biofeedback. Here we investigate the agreement between self-reported and biochemical adherence.

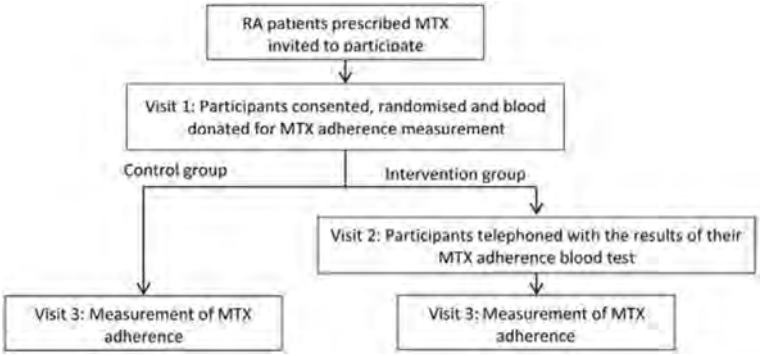

Figure 1. Trial Flow Chart

Table 1. Baseline clinico-demographics.

	Control cohort (n=23)	*Intervention cohort (n=26)*
Female gender (n; %)	17 (74)	19 (73)
Age, yrs (mean; STD)	68 (11)	69 (11)
White ethnicity (n; %)	23 (100)	25 (96)
Married (n; %)	16 (70)	14 (54)
Retired (n; %)	15 (65)	17 (65)
Concomitant biologic DMARD (n; %)	4 (17)	7 (27)
Symptom duration, yrs (mean; STD)	13 (14)	14 (18)
Baseline DAS(CRP)-28 (mean; STD)	3.07 (0.97)	3.30 (1.09)
Baseline biochemical non-adherence	4 (17)	4 (15)

Table 2. Biochemical and self-reported adherence at baseline and follow-up

Biochemical Adherence n(%)	Self-reported MARS-5 Adherence		
Baseline	Non-adherent	Adherent	Missing
Adherent	3 (6)	35 (71)	3 (6)
Non-adherent	5 (10)	3 (6)	0 (0)
Follow-up	Non-adherent	Adherent	Missing
Adherent	6 (12)	32 (65)	2 (4)
Non-adherent	3 (6)	5 (10)	1 (2)

Methods: MIRA is a prospective multi-centre randomised controlled trial investigating the feasibility of a fully powered randomised controlled trial to examine if a biochemical adherence guided intervention is superior to standard clinical care in RA patients. All analyses are exploratory in nature. RA patients prescribed oral MTX for ≥ two years were randomised 1:1 to receive biochemical adherence biofeedback or control (figure 1). Clinico-demographics, biochemical MTX adherence, MARS-5 and DAS-28 were measured at baseline and three months. Self-reported MARS-5 adherence was dichotomised and agreement with biochemical adherence analysed using Cohen's Kappa.

Results: 57 participants were recruited, withdrawal rate was 14% and reasons given were intercurrent illness, lost contact, withdrawn consent and one patient died during follow-up leaving full outcome data available for 49 participants. Baseline clinico-demographics were similar in control and intervention cohorts (Table 1).

Biochemical adherence worsened in the control cohort and improved in the intervention cohort (83 to 70%, 85 to 92% respectively) whilst change in DAS(CRP)-28 worsened in the control cohort and improved in the intervention cohort (-0.04 STD 1.26 and 0.38 STD 0.78 respectively). Self-reported and biochemical adherence demonstrated fair agreement (κ=0.24) at baseline but poor (κ=0.09) at follow-up (Table 2).

Conclusion: The MIRA trial has shown early evidence of biofeedback improving MTX biochemical adherence and DAS-28 compared to control. Poor agreement between self-reported and biochemical adherence suggests biochemical adherence may be a more clinically useful measure of adherence.

Disclosure: J. Bluett: Fresenius Kabi, 12, Travel/conference fees, Pfizer, 5; **K. Hyrich**: Abbvie, 6, Bristol-Myers Squibb(BMS), 5, Pfizer, 5; **B. Keevil**: None; **P. Doran**: None; **A. Barton**: Bristol-Myers Squibb(BMS), 5, Pfizer, 5.

Abstract Number: 2112

Physical Activity in a Cohort of Patients with Rheumatoid Arthritis

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SESSION INFORMATION

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Session Type: Poster Session C
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Background/Purpose: Physical activity has numerous benefits for Rheumatoid Arthritis (RA) patients such as reducing symptoms like fatigue and pain and improving physical function. The International *Physical Activity Questionnaire - Short Form* (IPAQ-SF) is a widely used self-administered questionnaire consisting of seven items that measures physical activity levels in minutes and metabolic equivalents (METs) over the previous week. The aim of this study was to evaluate physical activity levels in RA patients and explore potential associations with patient characteristics, disease activity, functional capacity, quality of life, anxiety, depression, and treatment.

Methods: Multicenter, analytical, observational, cross-sectional study. Patients ≥ 18 years old with a diagnosis of RA (ACR-EULAR 2010) were included. Sociodemographic data, habits, comorbidities, body mass index (BMI), RA characteristics, Clinimetrics measures and treatment were collected. In addition, participant's physical activity levels were assessed using the IPAQ-SF. **Statistical analysis:**Descriptive statistics. The results of IPAQ-SF were compared according to patient characteristics, disease activity, functional capacity, quality of life, anxiety, depressionand treatment by means of an appropriate test: Student T-test, Wilcoxon, Pearson, ANOVA, or Spearman. Significance level was set at 0.05.

Results: A total of 101 patients from five centers were included. Patient characteristics are shown in **Table 1**. Results of clinical measurements can be observed in **Table 2** and RA treatment in the **Figure**.A total of 31% practiced sports, with a mean of 24 months (SD 8.5). The IPAQ-SF reported a median total physical activity of 1386 METs (IQR 594-3066), with an average frequency of 7 days (IQR 3-7) and 119 minutes (SD 94.9) per week: 42% had low activity, 31% moderate, and 28% high. Median sitting time was 4.4 hours per day (IQR 2-7). Total METs median was associated with higher education (p=0.008) and sports practice (p< 0.0001). Correlation was negative with BMI (p=0.01), functional class (FC, p=0.002), P-VAS (p=0.008), PtGA-VAS (p=0.01), fatigue VAS (p=0.02), DAS28 (p=0.009) and HAQ-A (p< 0.0001). Mean total MET was higher in patients who didn't required assistance in daily activities (p=0.0005). In addition, weekly physical activity minutes showed a negative

Table 1. Patient characteristics (N=101)

Table 1. Patient characteristics (N=101)	
Age in years, mean (SD)	54 (11)
Women, n (%)	87 (86)
Years of study, mean (SD)	11 (3)
BMI, mean (SD)	27 (4)
Comorbidities, n (%)	68 (67)
Arterial hypertension, n (%)	31 (31)
Dyslipidemia, n (%)	20 (20)
Disease duration in months, median (IQR)	72 (36-172)
Erosive disease, n (%)	66 (65)
RF, n (%)	85 (84,16)
ACPA, n (%)	92 (91,09)
Functional class, n (%)	
- I	35 (34,65)
- II	34 (33,66)
- III	29 (28,71)
- IV	3 (2,97)

SD= Standard deviation; BMI= Body mass index; IQR= Interquartile range, ACPA= Anti-citrullinated peptides/protein antibodies, RF= Rheumatoid factor.

Table 2. Results of clinical measurements (N=101)

Table 2. Results of clinical measurements (N=101)

Clinical measures	Median (IQR)
P-VAS	30 (10-50)
PtGA-VAS	20 (10-60)
PGA-VAS	20 (10-40)
F-VAS	10 (0-40)
DAS28	3.1 (2.22-4.32)
SDAI	11.08 (3.03-18)
CDAI	9 (2-14)
HAQ-A	0.88 (0.38-1.75)
QOL-RA	6.83 (5.5-8.75)
PHQ9	3 (1-9)
GAD7	4 (1-9)

*IQR= Interquartile range; **P-VAS** = Pain visual analog pain scale; **PtGA-VAS=** Patient global assessment visual analogue scale; **PGA-VAS=** Physician global assessment visual analogue scale; **F-VAS=** Fatigue visual analog scale; **DAS-28** = Disease Activity Score 28; **SDAI** = Simple Disease Activity Index; **CDAI** = Clinical Disease Activity Index; **HAQ-A** = Health Assessment Questionnaire Argentine version; **QOL- RA II** = Quality Of Life Rheumatoid Arthritis II; **GAD-7** = General Anxiety Disorder 7; **PHQ-9** = Patient Health Questionnaire 9.*

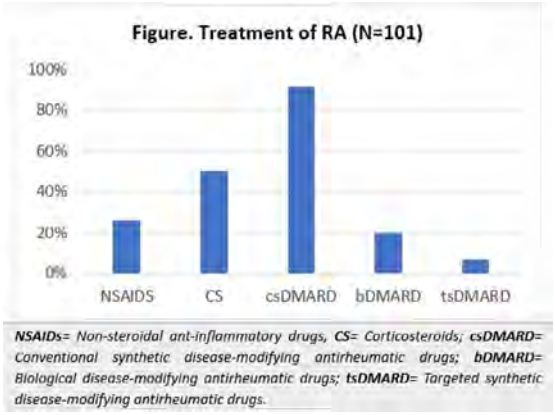

Figure. Treatment of RA (N=101)

association with PtGA-VAS (p=0.02). A higher minute mean was observed in those who practiced sports (p=0.0001), had no comorbidities (p=0.04) and didn't need assistance (p=0.01). Physical activity day mean was higher in non-smokers (p=0.02), sports players (p=0.002), those with no erosive disease (p=0.002) and those with no need for assistance (p=0.001). High physical activity was linked to no comorbidities (p=0.02), sport practice (p< 0.001) and no assistance need (p=0.004). Patients without corticosteroids (p=0.012) and no erosive disease (p=0.012) showed more moderate/high physical activity.

Conclusion: Fifty-eight percent of the patients had moderate/high physical activity, positively associated with sports, lower RA activity and better function. Fewer comorbidities and glucocorticoid treatment were observed in this RA cohort.

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Abstract Number: 2113

Impact of Sociodemographic Factors on Efficacy and Safety of Tofacitinib in Patients with Rheumatoid Arthritis: A Post Hoc Analysis of Phase 2/3/3b/4 Studies

Grace Wright[1], Eduardo Mysler[2], Kevin Roberts[3], Lindsay Sweet[4] and Ahmed Shelbaya[5], [1]Grace C Wright MD PC, New York, NY, [2]Organizacion Medica de Investigacion, Buenos Aires, Argentina, [3]Pfizer Inc., Cambridge, MA, [4]Pfizer Inc., Collegeville, PA, [5]Pfizer Inc., New York, NY

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Sociodemographic factors can impact treatment response and safety outcomes in patients (pts) with RA. Here, we explore the impact of sociodemographic index (SDI) on the efficacy and safety of tofacitinib and adalimumab in pts with RA.

Table 1. Demographics and BL disease characteristics for all pts,[a] stratified by SDI tertiles[b]

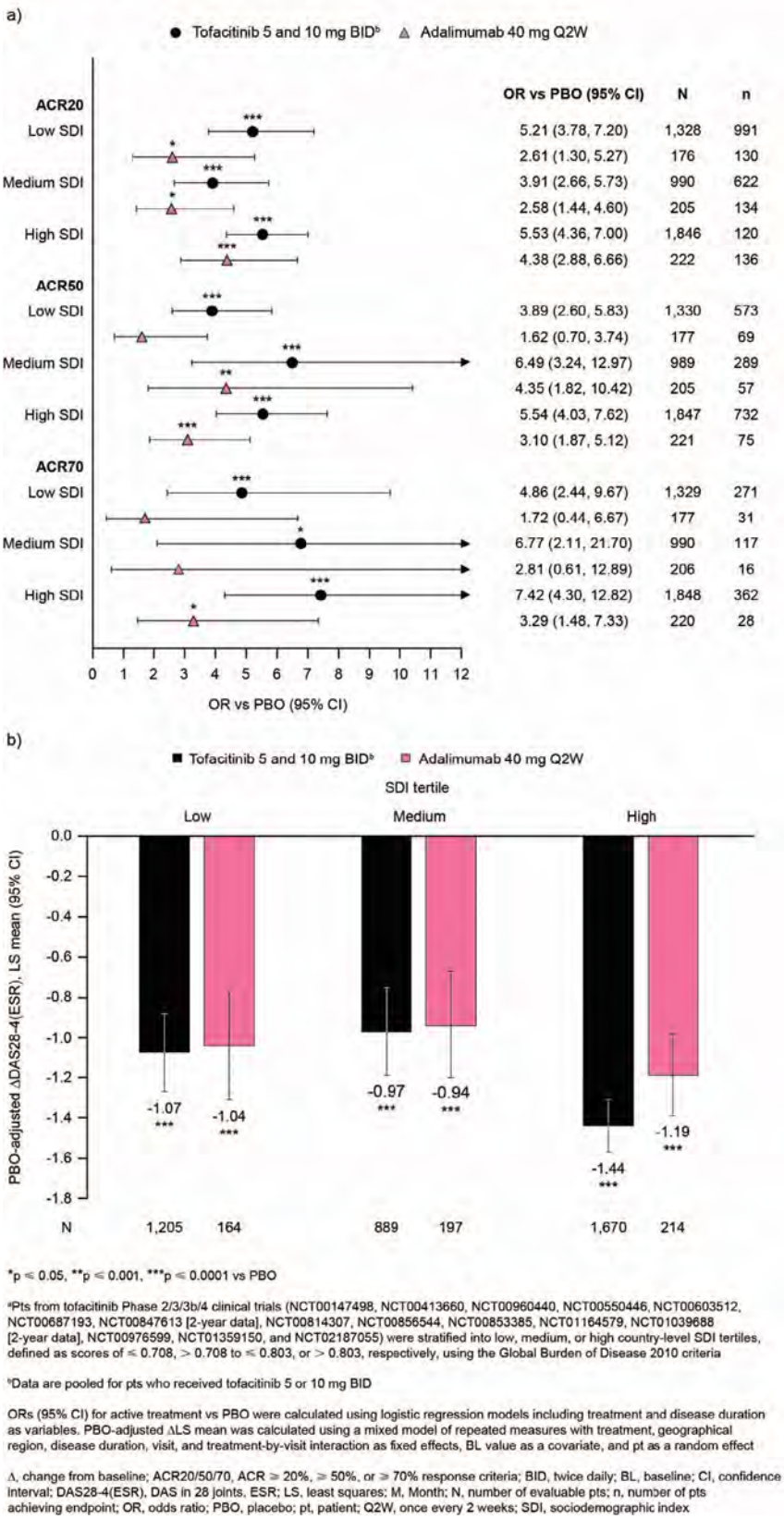
	Low SDI (N=1,969)	Medium SDI (N=1,538)	High SDI (N=3,071)
Age (years), mean (SD)	47.5 (12.0)	52.9 (12.1)	53.8 (11.6)
Age group (years), n (%)			
18 to 45	813 (41.3)	368 (23.9)	696 (22.7)
46 to < 50	244 (12.4)	168 (10.9)	287 (9.3)
50 to < 65	773 (39.3)	747 (48.6)	1,558 (50.7)
≥ 65	139 (7.1)	255 (16.6)	530 (17.3)
Female, n (%)	1,756 (89.2)	1,244 (80.9)	2,439 (79.4)
Geographical region, n (%)			
North America (US and Canada)	0	0	1,511 (49.2)
European Economic Area	0	1,033 (67.2)	729 (23.7)
Latin America	1,194 (60.6)	3 (< 1.0)	0
East/South Asia	666 (33.8)	0	689 (22.4)
Rest of World	109 (5.5)	502 (32.6)	142 (4.6)
Race, n (%)			
White	660 (33.5)	1,525 (99.2)	2,107 (68.6)
Asian	673 (34.2)	1 (< 1.0)	707 (23.0)
Black	67 (3.4)	1 (< 1.0)	149 (4.9)
Other	569 (28.9)	11 (< 1.0)	108 (3.5)
Smoking, n (%)			
Never smoked	1,524 (77.4)	1,084 (70.5)	1,652 (53.8)
Current smoker	194 (9.9)	260 (16.9)	641 (20.9)
Past smoker	196 (10.0)	168 (10.9)	729 (23.7)
Unknown	55 (2.8)	26 (1.7)	49 (1.6)
RA disease duration, mean (SD)	6.8 (7.0)	7.7 (7.7)	8.5 (8.5)
Prior bDMARD treatment (yes), n (%)			
TNFi	83 (4.2)	101 (6.6)	843 (27.5)
Other bDMARD (non-TNFi)	52 (2.6)	46 (3.0)	217 (7.1)
Concomitant corticosteroids at BL (yes), n (%)	1,243 (63.1)	755 (49.1)	1,678 (54.6)
Diabetes at BL (yes), n (%)	140 (7.1)	94 (6.1)	299 (9.7)
Hypertension at BL (yes), n (%)	501 (25.4)	606 (39.4)	1,165 (37.9)

[a]Includes pts enrolled in tofacitinib Phase 2/3/3b/4 clinical trials (NCT00147498, NCT00413660, NCT00960440, NCT00550446, NCT00603512, NCT00687193, NCT00847613 [2-year data], NCT00814307, NCT00856544, NCT00853385, NCT01164579, NCT01039688 [2-year data], NCT00976599, NCT01359150, and NCT02187055), receiving tofacitinib 5 mg BID, tofacitinib 10 mg BID, placebo, adalimumab, or methotrexate

[b]Pts were stratified into low, medium, or high country-level SDI tertiles, defined as scores of ≤ 0.708, > 0.708 to ≤ 0.803, or > 0.803, respectively, using the Global Burden of Disease 2010 criteria

bDMARD, biologic DMARD; BID, twice daily; BL, baseline; N, number of evaluable pts; n, number of pts with characteristic; pt, patient; SD, standard deviation; SDI, sociodemographic index; TNFi, TNF inhibitor; US, United States

Fig 1. a) ORs (95% CI) for ACR20/50/70 responses and b) ΔDAS28-4(ESR), at M3, stratified by treatment group and SDI tertile[a]



*p ⩽ 0.05, **p ⩽ 0.001, ***p ⩽ 0.0001 vs PBO

[a]Pts from tofacitinib Phase 2/3/3b/4 clinical trials (NCT00147498, NCT00413660, NCT00960440, NCT00550446, NCT00603512, NCT00687193, NCT00847613 [2-year data], NCT00814307, NCT00856544, NCT00853385, NCT01164579, NCT01039688 [2-year data], NCT00976599, NCT01359150, and NCT02187055) were stratified into low, medium, or high country-level SDI tertiles, defined as scores of ⩽ 0.708, > 0.708 to ⩽ 0.803, or > 0.803, respectively, using the Global Burden of Disease 2010 criteria

[b]Data are pooled for pts who received tofacitinib 5 or 10 mg BID

ORs (95% CI) for active treatment vs PBO were calculated using logistic regression models including treatment and disease duration as variables. PBO-adjusted ΔLS mean was calculated using a mixed model of repeated measures with treatment, geographical region, disease duration, visit, and treatment-by-visit interaction as fixed effects, BL value as a covariate, and pt as a random effect

Δ, change from baseline; ACR20/50/70, ACR ⩾ 20%, ⩾ 50%, or ⩾ 70% response criteria; BID, twice daily; BL, baseline; CI, confidence interval; DAS28-4(ESR), DAS in 28 joints, ESR; LS, least squares; M, Month; N, number of evaluable pts; n, number of pts achieving endpoint; OR, odds ratio; PBO, placebo; pt, patient; Q2W, once every 2 weeks; SDI, sociodemographic index

Methods: This post hoc analysis used pooled data from Phase 2/3/3b/4 studies of pts with RA receiving tofacitinib 5 or 10 mg twice daily (BID), adalimumab 40 mg every 2 weeks, or placebo (PBO). At a country level, pts were stratified into low, medium, or high SDI tertiles, defined as scores of ≤ 0.708, > 0.708 to ≤ 0.803, or > 0.803, respectively, using the Global Burden of Disease 2010 criteria. Efficacy outcomes assessed at Month (M)3 included ACR20/50/70 responses (odds ratios for active treatment vs PBO calculated via logistic regression models, by SDI tertile) and change from baseline (Δ) for DAS in 28 joints, ESR (DAS28-4[ESR]; PBO-adjusted, assessed for active treatments via a mixed model of repeated measures, by SDI tertile). Incidence rates (IRs; pts with first events/100 pt-years) for safety outcomes to M24 were calculated for each treatment group, by SDI tertile.

Results: Of pts included (low SDI, N=1,969; medium SDI, N=1,538; high SDI, N=3,071), there was a higher percentage aged > 50 years, located in North America, of ever smokers and prior biologic DMARD users, and RA duration was longer, in the high vs low/medium SDI tertiles (Table 1). Across SDI tertiles, efficacy at M3 was generally greater with tofacitinib and adalimumab vs PBO (Fig 1). Odds ratios vs PBO showed that ACR20/50/70 responses at M3 for tofacitinib and adalimumab were generally numerically greatest in the high SDI tertile, but 95% confidence intervals (CIs) overlapped between tertiles (Fig 1a). PBO-adjusted ΔDAS28-4(ESR) at M3 was numerically greater in the high vs medium/low SDI tertile with tofacitinib and adalimumab (Fig 1b). In the PBO group at M3, fewer pts in the high vs low SDI tertile achieved ACR20/50/70 (ACR20: 25.3% [113/447] vs 35.1% [71/202]); similarly, mean ΔDAS28-4(ESR) was smaller in pts with high vs low SDI (-0.58 [N=406] vs -1.17 [N=173]). Across treatments,IRs for safety outcomes were generally numerically greatest in the high SDI tertile, but 95% CIs overlapped between tertiles (Table 2).

Conclusion: Pts with RA responded better to active treatment vs PBO at M3, regardless of SDI. Across efficacy outcomes, PBO-adjusted treatment responses were generally numerically greatest in the high SDI tertile; PBO responses were lowest in this tertile. IRs of adverse events were generally numerically highest in the high SDI tertile, in all treatment groups. 95% CIs overlapped for numerical differences between tertiles. Results were confounded by differences in baseline smoking status, prior biologic DMARD use, concomitant medications, and RA duration between SDI tertiles. Data represent SDI at country level, which does not account for within-country variation.

Table 2. IRs (95% CI) for safety outcomes up to M24, stratified by treatment group and SDI category[a]

	IR (95% CI)								
	Tofacitinib 5 and 10 mg BID[b]			Adalimumab 40 mg Q2W			PBO		
	Low SDI (N=1,444)	Medium SDI (N=1,068)	High SDI (N=2,121)	Low SDI (N=191)	Medium SDI (N=214)	High SDI (N=238)	Low SDI (N=253)	Medium SDI (N=184)	High SDI (N=642)
TEAEs	159.81 (150.23, 169.83)	114.39 (106.04, 123.22)	225.36 (214.37, 236.77)	126.38 (105.12, 150.68)	125.10 (104.75, 148.26)	187.65 (160.65, 217.88)	306.16 (258.20, 360.45)	200.59 (158.81, 249.99)	327.17 (293.26, 363.92)
SAEs	6.94 (5.66, 8.43)	7.12 (5.64, 8.88)	12.28 (10.72, 13.99)	5.93 (2.84, 10.91)	6.45 (3.33, 11.27)	11.07 (6.86, 16.93)	6.21 (2.02, 14.49)	10.99 (4.03, 23.91)	15.00 (9.61, 22.32)
Discontinuations due to AEs	7.31 (6.00, 8.82)	5.35 (4.10, 6.88)	11.39 (9.92, 13.02)	10.04 (5.85, 16.07)	11.32 (7.00, 17.30)	12.53 (8.03, 18.65)	7.46 (2.74, 16.23)	7.30 (1.99, 18.70)	17.47 (11.61, 25.25)
AESI									
All infections[c]	52.15 (47.94, 56.62)	42.50 (38.28, 47.06)	71.35 (66.77, 76.17)	44.73 (34.37, 57.23)	35.41 (26.70, 46.13)	63.59 (51.32, 77.90)	88.94 (68.03, 114.24)	57.64 (38.60, 82.77)	86.15 (71.60, 102.79)
Serious infections	3.01 (2.19, 4.02)	1.57 (0.93, 2.49)	2.88 (2.17, 3.75)	1.76 (0.36, 5.13)	1.06 (0.13, 3.84)	2.06 (0.56, 5.26)	1.23 (0.03, 6.85)	0.00 (0.00, 6.69)	3.08 (1.00, 7.18)
HZ (non-serious/serious)	2.70 (1.93, 3.68)	2.22 (1.44, 3.28)	4.67 (3.74, 5.76)	1.76 (0.36, 5.14)	2.68 (0.87, 6.25)	1.55 (0.32, 4.54)	4.98 (1.36, 12.75)	0.00 (0.00, 6.69)	1.23 (0.15, 4.44)
Malignancies excl. NMSC	0.13 (0.02, 0.48)	0.26 (0.05, 0.77)	0.89 (0.52, 1.42)	0.00 (0.00, 2.16)	0.00 (0.00, 1.96)	0.51 (0.01, 2.86)	0.00 (0.00, 4.54)	0.00 (0.00, 6.69)	0.00 (0.00, 2.26)
NMSC	0.13 (0.02, 0.48)	0.17 (0.02, 0.63)	0.84 (0.48, 1.36)	0.00 (0.00, 2.16)	0.53 (0.01, 2.97)	1.01 (0.13, 3.74)	0.00 (0.00, 4.54)	0.00 (0.00, 6.69)	1.23 (0.15, 4.44)
Deaths	0.27 (0.07, 0.68)	0.09 (0.00, 0.49)	0.36 (0.15, 0.75)	0.00 (0.00, 2.16)	0.00 (0.00, 1.96)	0.51 (0.01, 2.86)	1.23 (0.03, 6.85)	0.00 (0.00, 6.69)	0.00 (0.00, 2.26)

[a]Pts from tofacitinib Phase 2/3/3b/4 clinical trials (NCT00147498, NCT00413660, NCT00960440, NCT00550446, NCT00603512, NCT00687193, NCT00847613 [2-year data], NCT00814307, NCT00856544, NCT00853385, NCT01164579, NCT01039688 [2-year data], NCT00976599, NCT01359150, and NCT02187055) were stratified into low, medium, or high country-level SDI tertiles, defined as scores of < 0.708, > 0.708 to < 0.803, or > 0.803, respectively, using the Global Burden of Disease 2010 criteria

[b]Data are pooled for pts who received tofacitinib 5 or 10 mg BID

[c]Infections included: non-serious/serious infections, opportunistic infections excl. tuberculosis, tuberculosis, and HZ (non-serious/serious)

IRs were censored at the day of the first event or up to last dose − 28 days

AE, adverse event; AESI, adverse events of special interest; BID, twice daily; CI, confidence interval; excl., excluding; HZ, herpes zoster; IR, incidence rate; M, Month; N, number of evaluable pts; NMSC, non-melanoma skin cancer; PBO, placebo; pt, patient; Q2W, once every 2 weeks; SAE, serious adverse event; SDI, sociodemographic index; TEAE, treatment-emergent adverse event

Study sponsored by Pfizer. C Kinch, Pfizer, was involved in the conception/development of these analyses. G Schroeder, Syneos Health (paid contractors of Pfizer), was involved in data collection/analysis/interpretation. Medical writing support provided by L Hogarth, CMC Connect; funded by Pfizer.

Disclosure: G. Wright: AbbVie, 2, 6, Amgen, 2, 6, Association of Women in Rheumatology, 4, AstraZeneca, 2, 6, Bristol Myers Squibb, 5, Eli Lilly, 2, 6, Gilead Sciences, 5, GSK, 2, 6, Janssen, 2, 5, 6, Novartis, 2, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 6; **E. Mysler**: AbbVie, 1, 2, 6, Amgen, 6, AstraZeneca, 1, 5, 6, Bristol Myers Squibb, 5, GSK, 2, 5, Janssen, 1, 5, 6, Lilly, 5, 6, Novartis, 5, Pfizer, 1, 2, 6, Roche, 5, Sandoz, 6; **K. Roberts**: Pfizer Inc, 3, 11; **L. Sweet**: Pfizer Inc, 3, 11; **A. Shelbaya**: Pfizer Inc, 3, 11.

Abstract Number: 2114

The Relationship Between Disease Activity of Rheumatoid Arthritis and Kidney Function

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic kidney disease (CKD) is a common comorbidity of rheumatoid arthritis (RA) affecting 10-20% of patients. However, the influence of the longitudinal RA disease activity on the long-term prognosis of kidney function has not been thoroughly evaluated.

Methods: We conducted a longitudinal study using the prospective CorEvitas RA registry and included patients with eGFR ≧60 mL/min/1.73 m^2 at baseline for whom kidney function was recorded at least twice from 2001 to 2022. The primary outcome was eGFR change from the baseline visit; secondary outcome was development of CKD G3b or worse (eGFR < 45 mL/min/1.73 m^2 for more than 3 months). The category of time-averaged Clinical Disease Activity Index (CDAI) until each visit was an exposure of interest. We used all visit data in primary analyses, and data only from patient visits where time-averaged CDAI was stable in one category from the baseline were used in secondary analyses. Multivariable mixed-effect random intercept and slope model with the interaction term of time and time-averaged CDAI was used to evaluate the association between CDAI categories and changes in the slope of eGFR. We adjusted for baseline variables including age, sex, race, eGFR, RF/CCP, and secondary Sjogren's syndrome. Body mass index, smoking status, modified Health Assessment Questionnaire, C-reactive protein, comorbidities, and the use of medications (non-steroidal anti-inflammatory drugs, glucocorticoids, and each of disease-modifying antirheumatic drugs) were included as time-varying covariates. Kaplan-Meier curves and multivariable Cox proportional hazard models were used to evaluate the hazard ratio (HR) of time-averaged CDAI categories for the development of CKD G3b or worse renal function. We adjusted for baseline covariates in the survival analyses.

Results: We included 31,129 patients with 234,973 visits in the analyses. The mean (standard deviation) age was 57.3 (12.9) years, and 23,758 (76.3%) were female with a median follow-up of 3.5 years. The mean baseline eGFR was 90.2 ml/min/1.73 m^2 (Table 1). The mixed-effect model showed that the annual eGFR decline was -0.855 mL/min/1.73 m^2 in

Table 1. Baseline characteristics of patients with rheumatoid arthritis by the disease activity

	Remission N=6,647	Low disease activity N=10,028	Moderate disease activity N=8,548	High disease activity N=5,906
Age, years	57.0 (13.3)	57.9 (12.8)	57.3 (12.8)	56.7 (12.5)
Female	72.6%	75.6%	78.2%	78.9%
Race White	83.5%	83.5%	82.5%	78.6%
Hispanic	6.5%	6.6%	7.1%	9.9%
Black	5.5%	5.7%	6.5%	6.6%
Asian	2.2%	1.9%	1.4%	1.8%
Others	2.4%	2.4%	2.5%	3.1%
Body mass index	28.4 (6.3)	29.4 (7.0)	30.3 (7.5)	30.4 (7.5)
Smoke Current	9.0%	11.8%	13.7%	15.3%
Previous	26.4%	26.7%	26.9%	26.3%
None	64.6%	61.5%	59.4%	58.4%
The number of visits	6.0 (3.0-10.0)	6.0 (3.0-10.0)	5.0 (3.0-9.0)	5.0 (3.0-9.0)
Interval between visits, year	0.7 (0.5-1.0)	0.7 (0.5-1.0)	0.7 (0.5-0.9)	0.7 (0.5-0.9)
Total follow up, year	3.8 (1.9-7.2)	3.6 (1.7-7.0)	3.3 (1.5-6.6)	3.0 (1.3-6.2)
eGFR	89.1 (15.4)	89.3 (15.4)	90.7 (15.7)	92.4 (16.0)
Seropositive	82.8%	81.8%	80.3%	79.6%
Positive rheumatoid factor	66.4%	66.1%	65.3%	66.0%
Positive anticyclic citrullinated peptide antibody	64.7%	61.9%	60.5%	59.3%
Duration of rheumatoid arthritis	6.0 (2.0-12.0)	6.0 (2.0-13.0)	5.0 (1.0-13.0)	5.0 (1.0-12.0)
CDAI (Clinical disease activity index)	1.2 (0.8)	6.2 (2.1)	15.3 (3.4)	33.9 (10.3)
mHAQ (modified Health Assessment Questionnaire)	0.00 (0.00-0.12)	0.12 (0.00-0.50)	0.38 (0.12-0.75)	0.62 (0.25-1.00)
C-reactive protein, mg/L	3.0 (1.0-6.0)	4.0 (1.4-8.2)	5.0 (2.0-11.0)	6.3 (2.2-16.6)
Secondary Sjogren's Syndrome	6.9%	11.9%	15.0%	17.6%
Comorbidities				
Hypertension	21.3%	26.8%	27.8%	29.9%
Diabetes	5.2%	6.5%	8.1%	8.9%
Dyslipidemia	15.2%	16.5%	16.4%	16.1%
Medications				
Non-steroidal anti-inflammatory drugs	51.7%	57.5%	60.8%	59.5%
Glucocorticoid	16.1%	25.1%	33.4%	39.1%
Methotrexate	67.9%	68.4%	68.6%	69.0%
Other Conventional synthetic DMARDs	30.6%	34.0%	35.9%	34.5%
Biological DMARDs	47.0%	46.5%	48.2%	51.1%
JAK inhibitors	1.6%	2.2%	2.9%	2.9%

Note:
DMARDS: disease-modifying antirheumatic drugs.
Categorical variables were presented as percentages. Continuous variables are presented as mean (standard deviation) or median (interquartile range) based on their distribution.

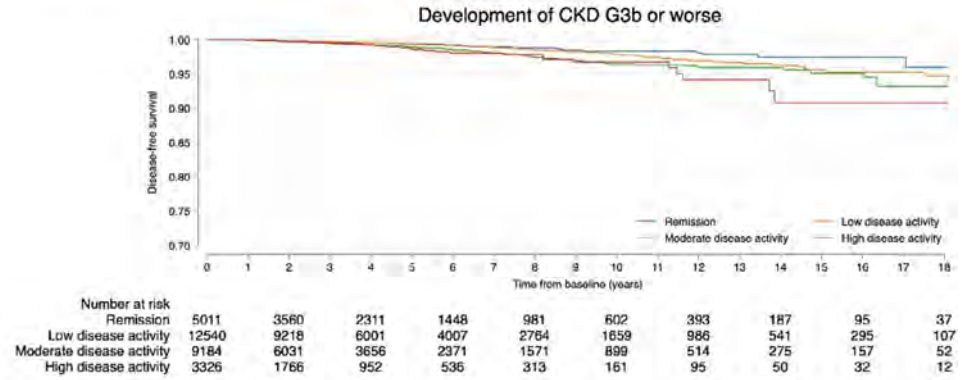
RA remission. Patients with low, moderate, and high disease activity had additional -0.070, -0.150, and -0.168 ml/min/1.73 m^2 declines annually vs. patients in remission. Secondary analyses revealed larger differences in the eGFR slopes between time-averaged CDAI categories (Table 2). Kaplan-Meier curve showed RA patients with higher disease activity developed more CKD G3b (Figure 1). Adjusted HRs (95%CI) were 1.12 (0.77-1.63) in low, 1.47 (1.00-2.20) in moderate, and 1.84 (1.11-3.05) in high disease activity patients for CKDG3b.

Table 2. Disease activity of rheumatoid arthritis and annual eGFR slope changes

	Primary analyses				Secondary analyses			
	Coefficient	95%CI		p value	Coefficient	95%CI		p value
Annual eGFR change (mL/min/1.73 m2)	-0.855	-0.912	-0.799	< 0.001	-0.819	-0.926	-0.711	< 0.001
Differences in the eGFR slope (mL/min/1.73 m2)								
Remission	Ref				Ref			
Low Disease Activity	-0.070	-0.130	-0.010	0.021	-0.108	-0.247	0.031	0.128
Moderate Disease Activity	-0.150	-0.221	-0.079	< 0.001	-0.403	-0.562	-0.243	< 0.001
High Disease Activity	-0.168	-0.270	-0.066	0.001	-0.456	-0.645	-0.267	< 0.001

Note:
CI: confidence intervals, eGFR: estimated Glomerular Filtration Rate.
We used all visit data in primary analyses. In secondary analyses, data only from patient visits where ta-CDAI was stable in one category from baseline were used.
We adjusted for age, sex, race, eGFR, RF/ACPA, and secondary Sjogren's syndrome at baseline. Body mass index, smoking status, modified Health Assessment Questionnaire, C-reactive protein, comorbidities, and the use of medications were included as time-varying covariates.

Figure 1. Development of CKDG3b or worse by disease activity of rheumatoid arthritis



Number at risk										
Remission	5011	3560	2311	1448	981	602	393	187	95	37
Low disease activity	12540	9218	6001	4007	2764	1659	986	541	295	107
Moderate disease activity	9184	6031	3656	2371	1571	899	514	275	157	52
High disease activity	3326	1766	952	536	313	161	95	50	32	12

Note:
CKD: chronic kidney disease. CKD G3b was defined as eGFR < 45 mL/min/1.73 m^2 for more than 3 months.
We adjusted for baseline variables including age, sex, race, body mass index, smoking status, eGFR, comorbidities, secondary Sjogren's syndrome, RF/ACPA, modified Health Assessment Questionnaire, C-reactive protein, and medications

Conclusion: After adjusting for potential confounders, RA patients with higher disease activity had a larger decline in eGFR and developed clinically significant CKD more frequently. This study suggests that controlling the disease activity of RA may potentially improve renal prognosis.

Disclosure: S. Fukui: None; **W. Winkelmayer**: Akebia, 2, Ardelyx, 2, AstraZeneca, 1, Bayer, 1, 2, Boehringer-Ingelheim, 1, GlaxoSmithKlein(GSK), 1, 6, Merck/MSD, 1, 2, Pharmacosmos, 6, Unicycive, 2, Zydus, 1, 2; **S. Tedeschi**: Novartis, 2; **J. Marrugo**: None; **H. Guan**: None; **L. Harrold**: AbbVie, 2, Bristol-Myers Squibb(BMS), 2, 6, Pfizer, 2; **H. Litman**: CorEvitas, 3, 12, Shareholder; **T. Shinozaki**: None; **D. Solomon**: CorEvitas, 5, Janssen, 5, Moderna, 5, Novartis, 5.

Abstract Number: 2115

Genetic Risk Load as a Predictor of Radiographic Damage and Mortality in Female Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune disease characterized by an unpredictable prognosis and increased mortality risk. Although the role of genetics in RA mortality remains undefined, this study aimed to investigate the clinical and genetic contributions to radiographic damage and mortality in female RA patients.

Methods: The Korean patients with RA were recruited from a prospective BAE RA cohort at Hanyang University Hospital for Rheumatic Diseases since 2001. Baseline demographics, clinical features, autoantibodies profiles, and radiologic damage were collected. All patients were genotyped using four-digit HLA–DRB1 typing and genome-wide association study (GWAS). Weighted genetic risk score (wGRS) was calculated from 100 well-validated non-HLA SNPs and HLA–DRB1 haplotypes in amino acid positions 11, 13, 71, and 74. Individual wGRS was tested for associations with clinical features, and radiologic damage by using multivariable regression. Cox proportional hazards models were used to examine the associations with wGRS and mortality.

Results: A total of 1,788 female patients were genotyped and included in the analysis. Mortality data were obtained from registered death records provided by Statistics Korea for the period between 2001 and 2018, with 175 deaths reported during this observation period. Multivariable linear regression analysis was employed to assess the independent effects of genetic risk load on radiographic damage and mortality, irrespective of age and disease duration. The analysis revealed a significant association between ever-smokers and high wGRS with increased radiographic damage. Moreover, patients with erosive RA exhibited a higher incidence risk of all-cause mortality, even after adjusting for age, smoking status, and disease duration.

Conclusion: The findings of this study demonstrate that genetic risk load, which implicates pathogenesis, could serve as a predictor of a poor clinical course in female patients with RA. These results emphasize the importance of considering genetic factors in assessing the prognosis and mortality risk in RA patients.

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Abstract Number: 2116

Risk of Tuberculosis in Patients with Rheumatoid Arthritis: A Nationwide Population-based Cohort Study

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) are known to have an increased risk of tuberculosis, particularly in association with the use of biologic disease-modifying anti-rheumatic drugs (bDMARD) including tumor necrosis factor-α (TNF-α) inhibitors. Korea is a country with a intermediate risk of tuberculosis, and large-scale studies on the risk of tuberculosis in patients with RA in Korea are still lacking. Our study aimed to identify the risk of tuberculosis in patients with RA compared to the general population in a large population-based cohort, and to identify factors associated with the risk of tuberculosis in patients with RA.

Methods: Among patients diagnosed with RA between 2010 and 2017, patients who had undergone a national health examination within two years prior to RA diagnosis were included in the study (n = 59,577). Control group included age- and sex-matched non-RA controls who received a health check-up at the same time as RA patients (n = 297,885). The primary outcome of the study was incident tuberculosis, which was defined by an ICD-10 code and enrollment in the rare intractable disease program. Kaplan-Meier curves and Cox proportional hazards regression analysis were used for the analysis

Results: During a mean follow-up period of 4.5 ± 2.2 years, 979 subjects in the control group and 619 patients in the RA group developed tuberculosis. Patients with RA had a 3-fold higher risk of tuberculosis than age- and sex-matched non-RA controls (adjusted hazard ratio [aHR] 3.02, 95% confidence interval [CI] 2.73–3.35). The association between RA and tuberculosis was more prominent in young adults aged 20-39 years. Using the control group as the reference, the aHR of tuberculosis in bDMARD-naïve patients with RA was 2.87 (95% CI 2.58–3.19), and the aHR of tuberculosis in bDMARD-exposed patients with RA was 4.97 (95% CI 3.92–6.29). In patients with RA, male sex, advanced age, underweight, diabetes, hypertension, airway disease, and bDMARD exposure were associated with an increased risk of tuberculosis.

Conclusion: In a nationwide population-based cohort in Korea with a intermediate risk of tuberculosis, patients with RA had a three-fold higher risk of tuberculosis than age- and sex-matched controls, and even bDMARD-naïve patients had a higher risk of tuberculosis than the general population. Even in patients who do not use bDMARDs, if suspicious symptoms occur, the possibility of tuberculosis should be considered.

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Abstract Number: 2117

Frailty Is Associated with Mortality in Veterans with Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Frailty is established as an important predictor of mortality in the general population.1Rheumatoid arthritis (RA) is associated with higher rates of frailty than the general population,[2] yet how frailty impacts important outcomes in RA, such as mortality, is less well understood. We sought to evaluate the relationship between frailty and mortality in a cohort of Veterans with RA.

Methods: Data were obtained from the Veterans Affairs Rheumatoid Arthritis (VARA) Registry from 1/2003 through 12/2021. The VA Frailty Index(VA-FI) is a validated deficit accumulation index based on 31 health deficits mapped from >6000 diagnostic codes found in administrative claims and electronic health records of Veterans. The VA-FI was calculated

for each participant at baseline using diagnostic codes with a 3-year look-back period. The VA-FI scores were categorized as robust, pre-frail and frail based on established cutoffs. Death data were obtained from the VA Corporate Data Warehouse vital statistics records. Cox proportional hazard regression models were used to evaluate the relationship between baseline frailty and mortality controlling for baseline age, sex, race, body mass index, anti-cyclic citrullinated peptide (CCP) status, RA disease duration, smoking status, rheumatic disease comorbidity index, use of prednisone, conventional synthetic disease modifying anti-rheumatic drugs (DMARDs) and biologic DMARDs.

Results: 3,007 Veterans were studied with a mean age of 64.4±11.1 years and 85% were male (Table 1). Over 16,515 person-years of follow-up, 43% (N=1,293) Veterans died. Those who died were older (68.9 vs. 61.0 years), more likely to be male (95% vs. 82%) and had higher rates of high disease activity (21% vs 12%, respectively). Those who died also had

Table 1: Participant Demographics and Baseline Disease Characteristics.

	Survived	Died	Total
	N=1,714 (57%)	N=1,293 (43%)	N=3,007
Frailty			
Robust	609 (36%)	274 (21%)	883 (29%)
Pre-frail	588 (34%)	522 (40%)	1,110 (37%)
Frail	517 (30%)	497 (38%)	1,014 (34%)
Age	61.0 (11.0)	68.9 (9.4)	64.4 (11.1)
Sex			
Male	1,400 (82%)	1,228 (95%)	2,628 (87%)
Female	299 (17%)	61 (5%)	360 (12%)
Race			
Black	317 (19%)	185 (14%)	502 (17%)
White	1,235 (72%)	1,049 (81%)	2,284 (76%)
Other	162 (10%)	59 (5%)	221 (7%)
Smoking Status			
Never Smoker	425 (25%)	210 (16%)	635 (21%)
Current/Former Smoker	1,223 (71%)	1,077 (83%)	2,300 (77%)
Baseline BMI			
<18.5	7 (<1%)	12 (1%)	19 (1%)
18.5 – 24.9	263 (15%)	389 (30%)	652 (22%)
25.0 – 29.9	559 (33%)	459 (36%)	1,018 (34%)
30.0 – 34.9	370 (22%)	241 (19%)	611 (20%)
35.0 – 39.9	143 (8%)	85 (7%)	228 (8%)
≥40.0	371 (22%)	101 (8%)	472 (16%)
RDCI at baseline	3.2 (2.0)	3.7 (1.8)	3.4 (2.0)
CCP antibody status*			
CCP negative	299 (24%)	254 (21%)	553 (23%)
CCP positive	953 (76%)	951 (79%)	1,904 (77%)
Missing	462 (27%)	88 (7%)	550 (18%)
DAS28ESR			
Remission	400 (23%)	198 (15%)	598 (20%)
Low	210 (12%)	150 (12%)	360 (12%)
Moderate	521 (30%)	411 (32%)	932 (31%)
High	213 (12%)	270 (21%)	483 (16%)
Missing	370 (22%)	264 (20%)	634 (21%)
Baseline disease duration (years)	9.7 (10.1)	12.9 (12.2)	11.1 (11.2)
csDMARD use at baseline	1,299 (76%)	1,002 (78%)	2,301 (77%)
Prednisone use at baseline	489 (29%)	513 (40%)	1,002 (33%)
Biologic DMARD at baseline	540 (32%)	327 (25%)	867 (29%)

-Data are presented as mean (SD) for continuous measures, and n (%) for categorical measures.
-BMI: body mass index, RDCI: rheumatic disease comorbidity index, RF: rheumatoid factor, CCP: cyclic citrullinated peptide, DAS28ESR: disease activity score 28 with erythrocyte sedimentation rate, csDMARD: conventional synthetic disease modifying anti-rheumatic drug.
-Variables with <5% missing data were not included in this table.
*CCP antibody status variable is missing N = 550 (18%). Data above for CCP antibody status are % of non-missing.

Table 2: Unadjusted and adjusted Cox proportional hazard models showing the risk of mortality by baseline frailty status.			
	Hazard Ratio (HR)	[95% confidence interval]	p-value
Unadjusted*			
Robust	Ref	--	--
Pre-Frail	1.69	1.46 – 1.95	<0.0001
Frail	1.89	1.63 – 2.20	<0.0001
Adjusted**			
Robust	Ref	--	--
Pre-Frail	1.43	1.22 – 1.69	<0.0001
Frail	1.90	1.56 – 2.30	<0.0001
*Unadjusted model: Number of subjects = 3,008 subjects. Number of deaths = 1,291. **Adjusted model: Number of subjects = 2,373 subjects. Number of deaths = 1,187. Model adjusted for age, sex, race, body mass index, anti-CCP status, disease duration, smoking status, rheumatic disease comorbidity index, prednisone use, csDMARD use and bDMARD use.			

higher prevalence of baseline pre-frailty and frailty compared to those who did not die (40% vs. 34% and 38 vs. 30%, respectively). In multivariable models, pre-frailty and frailty were independently associated with a higher risk of death(HR 1.43 [95%CI 1.22-1.69] and 1.90 [95%CI 1.56-2.30], respectively) (Table 2).

Conclusion: Higher baseline frailty is independently associated with an increased risk of death in Veterans with RA. The VA-FI may serve as a tool to aid in early recognition of frailty in people with RA. Further research is necessary regarding the applicability of these findings in informing prognostication and RA disease interventions in vulnerable adults.

References

Orkaby et al. The Burden of Frailty Among U.S. Veterans and Its Association With Mortality, 2002-2012. J Gerontol A Biol Sci Med Sci 2019, 74 (8), 1257–1264.
Gao et al. Frailty in Rheumatoid Arthritis: A Systematic Review and Meta-Analysis. Joint Bone Spine 2022, 89 (4), 105343.

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Abstract Number: 2118

New Onset Disability in Rheumatoid Arthritis Is an Underrecognized Cardiovascular Risk Factor: A Retrospective Cohort Study Using the CorEvitas Registry

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
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Background/Purpose: Cardiovascular disease (CVD) is the most common cause of death among patients with RA. Prior research found a higher rate of CVD events associated with disability among patients with RA. There is insufficient data however on disease activity and duration in this population, and the impact of new-onset disability is unknown. We need to understand these factors to develop sufficient preventive measures for patients with RA and disability. We hypothesize that

Table 1. Baseline characteristics of patients with rheumatoid arthritis younger than age 65, overall and by disability status*.

Table 1. Baseline characteristics of patients with rheumatoid arthritis younger than age 65, overall and by disability status*.

Characteristic	Overall	New-Onset Disability	Consistently Working	p-value
	N = 8370	N = 1674	N = 6696	
Demographics				
Age (years), mean (SD)	52.97 (7.4)	53.67 (7.33)	52.8 (7.41)	< 0.001
Female, %	80.70	80.70	80.70	1.000
White, %	83.15	82.22	83.38	0.412
Black, %	6.39	7.05	6.23	
Other, %	10.46	10.73	10.39	
College educated, %	62.38	55.38	64.12	< 0.001
Married, %	71.24	71.58	71.15	0.730
Sedentary, %	33.49	39.03	32.12	< 0.001
Current smoker, %	17.08	23.42	15.49	< 0.001
Any current alcohol use, %	52.09	40.26	55.08	< 0.001
Health Insurance, %				
Medicaid	3.44	9.36	1.85	< 0.001
Private	92.11	83.52	94.40	< 0.001
None	3.40	5.76	2.76	< 0.001
RA related variables				
RA disease duration (years), mean (SD)	7.63 (8.18)	10.59 (8.79)	6.89 (7.85)	< 0.001
Patient pain/0.5, mean (SD)	1.74 (1.4)	2.37 (1.46)	1.59 (1.34)	< 0.001
Patient global assessment/20, mean (SD)	1.59 (1.34)	2.24 (1.43)	1.43 (1.26)	< 0.001
mHAQ, mean (SD)	0.37 (0.46)	0.67 (0.56)	0.3 (0.39)	< 0.001
CDAI > 10, %	48.09	55.66	46.18	< 0.001
TJC-SJC > 8, %	6.72	11.05	5.63	< 0.001
Patient Fatigue Score (0-100), mean (SD)	41.75 (30.8)	51.43 (30.68)	38.68 (30.21)	< 0.001
Comorbidities				
Depression, %	16.51	46.00	9.14	< 0.001
Fibromyalgia, %	6.17	6.35	6.11	0.769
Diabetes, %	5.96	7.41	5.60	0.005
Hypertension, %	24.48	28.61	23.45	< 0.001
Hyperlipidemia, %	10.80	7.00	12.01	< 0.001
Obesity (BMI ≥ 30), %	43.80	48.98	42.49	< 0.001
Medications				
Prednisone dose > 5mg, %	10.73	12.07	10.39	0.048
Aspirin, %	10.56	12.66	10.04	0.002
Opioid use, %	19.60	34.45	16.04	< 0.001
Statin, %	13.03	15.83	12.34	< 0.001

*Disabled and working groups were coarse-matched by age in 10-year intervals and matched by sex 4:1.

among patients with RA younger than 65 years of age, new-onset disability is associated with a higher risk for CVD, and the primary contributing factors include traditional risk factors, disease characteristics, and medications.

Methods: This retrospective cohort study using the CorEvitas RA registry included patients age < 65 years who were working as of registry enrollment and had no history of CVD (MI, CAD, CVA, TIA, or PAD). The exposure was new-onset disability defined as a change from working to disabled while < 65 years or to retired while < 60 years. The comparator group was patients consistently working who were age- and sex-matched in a 4:1 ratio to the newly disabled. Demographics, comorbidities, RA-specific variables, and medications at baseline (time of onset of disability or enrollment for matched controls) were analyzed using descriptive statistics. Incidence rates of CVD for each group were calculated using Poisson regression. We built sequential Cox proportional hazards models with age as the time axis to identify the factors that best explained the excess CVD risk associated with disability among patients with RA. We selected covariates based on the association with CV risk or new-onset disability in the univariate analysis.One set of models used all factors at baseline; a second set allowed for time-varying covariates.

Results: 8370 patients were included (1674 in the disabled group and 6696 in the working group) with an overall mean age of 53 years and 80.7% female (Table 1). Mean follow-up was 10 years. Almost half (46%) of the disabled group reported depression compared to 9.14% in the working group ($p < 0.001$). The age and sex-adjusted incidence rate of CV events was 5.40 (95% CI 3.88, 7.52) events per 1000 person-years in the disabled group and 2.17 (95% CI 1.68, 2.80) in the non-disabled group ($p < 0.001$). The hazard ratio (HR) for CVD associated with disability was 2.32 (95% CI 1.52, 3.53) in the age- and sex-adjusted model, 1.78 (95% CI 1.09, 2.91) in the fixed covariate model, and 1.86 (95% CI 1.12, 3.08) in the time-varying model (Table 2). No model fully explained the excess risk for CVD in the disabled population as a significant association persisted despite multivariate adjustment.

Table 2. Hazard ratio (HR) for cardiovascular disease event among RA patients with and without disability. Univariate and multivariable-adjusted Cox proportional hazards models with fixed and time-varying covariates shown.

Table 2. Hazard ratio (HR) for cardiovascular disease event among RA patients with and without disability. Univariate and multivariable-adjusted Cox proportional hazards models with fixed and time-varying covariates shown.

	Univariate Model		**Adjusted Models**			
	Univariate		Baseline (Fixed) Covariates		Time Varying Covariates[a]	
Variable	Hazard Ratio (95% CI)	P-Value	Hazard Ratio (95% CI)	P-Value	Hazard Ratio (95% CI)	P-Value
Disabled	**2.32 (1.52, 3.53)**	**<0.001**	**1.78 (1.09, 2.91)**	**0.022**	**1.86 (1.12, 3.08)**	**0.016**
CVD risk factors present* vs. no CVD risk factors	2.14 (1.42, 3.23)	<0.001	1.85 (1.19, 2.89)	0.006	1.45 (0.91, 2.31)	0.114
mHAQ (continuous, divide scale by 0.2)	1.17 (1.09, 1.26)	<0.001	1.08 (0.99, 1.18)	0.089	1.10 (1.00, 1.21)	0.062
Smoker (Previous or Current) vs. never smoker	1.92 (1.28, 2.89)	0.002	1.76 (1.13, 2.76)	0.013	1.64 (1.02, 2.63)	0.039
Opioid vs. no opioid use	1.88 (1.20, 2.96)	0.006	1.37 (0.84, 2.24)	0.205	1.15 (0.67, 1.95)	0.617
Prednisone > 5mg vs. prednisone <= 5mg (including none)	1.84 (1.11, 3.05)	0.017	2.08 (1.24, 3.49)	0.006	1.57 (0.78, 3.18)	0.210
Education (college vs. no college education)	0.61 (0.40, 0.93)	0.020	0.68 (0.44, 1.05)	0.083	0.62 (0.39, 0.99)	0.045

CVD = cardiovascular disease
mHAQ = modified Health Assessment Questionnaire.
Notes: All models adjusted by age and sex as the disabled and working groups were matched by age and sex.
*CVD risk factor present means the presence of at least one of the following: hypertension, diabetes, hyperlipidemia.
[a]Time varying covariates included CVD risk factors, mHAQ, Smoking status, Opioid use, and Prednisone dose> 5mg.

Conclusion: Patients younger than 65 with RA who experience new-onset disability are at significantly higher risk for CVD compared to age- and sex-matched non-disabled patients with RA. This excess risk is partially explained by traditional risk factors, reduced physical function, and medications, but much of the risk remains unexplained. This is likely due to unmeasured variables, such as social determinants of health and related health behaviors. We thus need to examine how a holistic approach in patient care may mitigate this excess CVD risk in RA patients with disability.

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Abstract Number: 2119

Serum Alarmin Concentrations and Risk of Incident Major Adverse Cardiovascular Events and Heart Failure in a Multicenter, Prospective Rheumatoid Arthritis Cohort

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SESSION INFORMATION

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Background/Purpose: Alarmins are endogenous cytokines released following cellular damage and physiologic stress to promote homeostasis through tissue inflammation, remodeling, and fibrosis. Alarmins may facilitate maladaptive responses that play a role in the development of chronic inflammatory diseases, including RA (*Ebina-Shibuya R, Nat Rev Immunol*

Table 1. Association of serum alarmins with prevalent cardiovascular disease

Table 1. Association of serum alarmins with prevalent cardiovascular disease (N=2,528)

	Overall CVD (N=505)	MACE (N=385)	HF (n=202)	CAD (N=273)	Stroke (N=139)
IL-33, per 1 SD	**1.29 (1.04-1.60)**	**1.32 (1.04-1.68)**	0.96 (0.70-1.32)	1.31 (0.99-1.73)	1.16 (0.81-1.64)
TSLP, per 1 SD	1.05 (0.87-1.27)	1.12 (0.91-1.37)	0.89 (0.67-1.19)	1.16 (0.91-1.46)	0.82 (0.60-1.14)
IL-25 tertile					
Undetectable	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
T1	0.85 (0.56-1.30)	0.92 (0.58-1.47)	1.06 (0.57-1.98)	0.76 (0.45-1.31)	1.69 (0.77-3.70)
T2	0.97 (0.64-1.47)	1.08 (0.68-1.71)	1.17 (0.63-2.16)	1.05 (0.63-1.76)	1.92 (0.88-4.19)
T3	0.92 (0.61-1.38)	1.03 (0.65-1.62)	0.81 (0.43-1.52)	0.90 (0.54-1.52)	1.57 (0.72-3.42)

Values are adjusted odds ratios (95% confidence interval) estimated in Cox regression models adjusted for age, sex, race/ethnicity, body mass index, smoking status, RA disease activity, hypertension, diabetes, lung disease, and LDL cholesterol.

Bold indicates p value <0.05

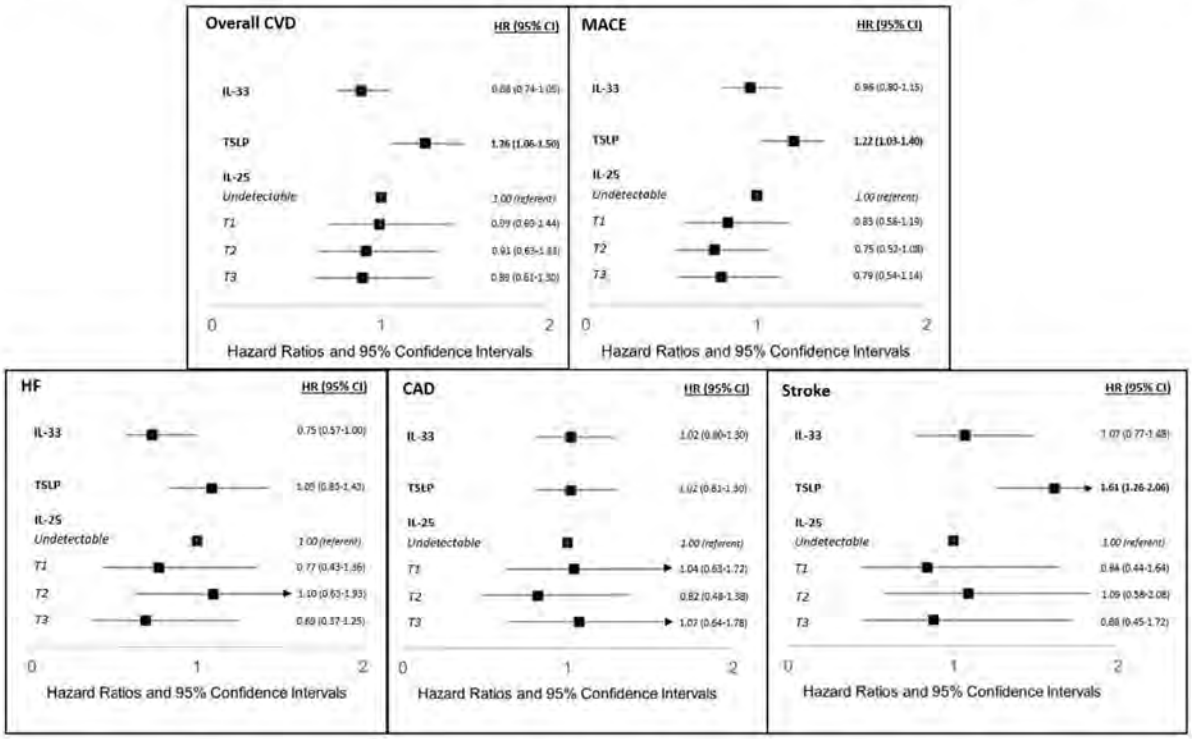
Abbreviations: CAD, coronary artery disease; CVD, cardiovascular disease; HF, heart failure; MACE, major adverse cardiovascular event; Ref, referent; TSLP, thymic stromal lymphopoietin.

2023). Whereas studies have implicated alarmins in cardiovascular disease (CVD) pathogenesis, it is unknown whether they may serve as a marker of CVD risk in RA. We examined associations of serum alarmin concentrations with CVD in a prospective RA cohort.

Methods: In a multicenter, prospective cohort of US Veterans with RA, we identified MACE (myocardial infarction, coronary revascularization, stroke, or CVD-related death) and heart failure (HF) hospitalizations before and after registry enrollment using validated administrative algorithms in linked VA, Medicare, and National Death Index data. From banked serum at registry enrollment, we measured the alarmins IL-25, IL-33, and thymic stromal lymphopoietin (TSLP) using U-PLEX immunoassay (Meso Scale Discovery). Given their distributions, IL-33 and TSLP concentrations were log-transformed and standardized (per 1 SD).Detectable IL-25 was categorized into tertiles (undetectable values as referent). Cross-sectional associations of alarmin concentrations with prevalent CVD were examined in multivariable logistic regression models. We then followed participants without prevalent CVD from registry enrollment to incident MACE, HF hospitalization, death, or end of study (12/2020). Associations of circulating alarmin concentrations with incident CVD events were tested in multivariable Cox regression models, adjusting for age, sex, race/ethnicity, smoking status, body mass index, DAS28, hypertension, diabetes, lung disease, LDL cholesterol, statin use, NSAID use, and aspirin use.

Results: Among 2,528 patients (mean age 64 years, 88% male, mean DAS28 3.6), 505 (20.0%) patients had prevalent MACE or HF. We observed CVD outcomes in 414 (20.5%) of the remaining 2,023 patients over a mean follow up of 7.3 years. After multivariable adjustment, IL-33, but not TSLP or IL-25, concentrations were associated with an increased odds of prevalent CVD (**Table 1**; aOR 1.29 [1.04-1.60] per 1 SD increase) and MACE (aOR 1.32 [1.04-1.68]). For incident

Figure 1. Multivariable associations of serum alarmin concentrations with incident cardiovascular disease events in patients with rheumatoid arthritis



Adjusted hazard ratios (95% confidence intervals) for analytes estimated in separate Cox regression models adjusted for age, sex, race/ethnicity, BMI, smoking status, RA disease activity, hypertension, diabetes, lung disease, LDL cholesterol, statin use, NSAID use, and aspirin use. Bold indicates p<0.05.

Abbreviations: CAD, coronary artery disease; CVD, cardiovascular disease; HF, heart failure; MACE, major adverse cardiovascular event; T1/2/3, tertile 1/2/3; TSLP, thymic stromal lymphopoietin

Figure 1. Association of serum alarmins with incident cardiovascular disease

disease, TSLP concentrations were most strongly associated with CVD risk (**Figure 1**; aHR 1.26, [1.06-1.50]), which was driven by its association with stroke (aHR 1.61 [1.26-2.06]) and MACE (aHR 1.22 [1.03-1.20]). A trend toward an inverse association between IL-33 and HF was observed, otherwise no associations were seen between IL-33 or IL-25 with incident CVD in fully adjusted models.

Conclusion: In this large, multicenter, prospective RA cohort, serum IL-33 concentration was independently associated with prevalent CVD, whereas TSLP concentration was associated with incident CVD, particularly stroke and MACE. These findings suggest that alterations in endogenous alarmins occurring in RA may contribute to RA-associated CVD risk. Further study is warranted to determine whether serum alarmins can improve CVD risk stratification in RA.

Disclosure: T. Johnson: None; **Y. Yang**: None; **P. Roul**: None; **M. Duryee**: None; **C. Hunter**: None; **J. Baker**: CorEvitas, 2, Cumberland Pharma, 2, Horizon Pharmaceuticals, 5; **B. Sauer**: None; **G. Cannon**: None; **A. Joseph**: None; **K. Wysham**: None; **A. Lenert**: None; **G. Thiele**: None; **J. Poole**: AstraZeneca, 12, I have received no monies. I received anti-IL-33 monoclonal antibody from AstraZeneca for animal research sutdies.; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **B. England**: Boehringer-Ingelheim, 2, 5.

Abstract Number: 2120

Independent and Combined Impact of Interstitial Lung Disease and Airway Disease on Rheumatoid Arthritis Disease Activity and Infections

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SESSION INFORMATION

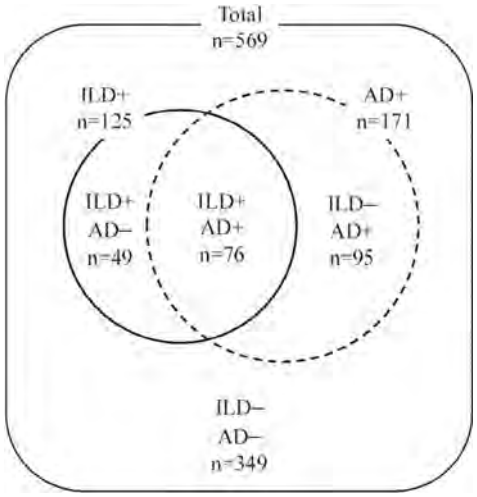
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: How interstitial lung disease (ILD) and airway disease (AD) independently affect the clinical course of rheumatoid arthritis (RA) is unclear since previous studies conflated ILD and AD. We aimed to clarify the effects of ILD, AD, and their combination on RA disease activity and infections.

Methods: RA patients at our facilities during 2011 and 2021 that had chest computed tomography (CT) scans were investigated retrospectively. Baseline was defined as 'time of first CT scan', and final observation as 'last visit'. Two experienced radiologists evaluated CT findings. We excluded patients with incomplete evaluation of ILD/AD in CT scans. The study primary outcome was development of infection requiring hospitalization, while the secondary was RA disease activity at final observation. We compared patients with and without ILD, and with and without AD. To identify factors associated with RA disease activity or infections, multivariate analyses were performed.

Results: We enrolled 569 patients (75.7% female, mean: age 60.9 yrs, observation period 73.9 mo.), including 125 (22.0%) with ILD, 171 (30.1%) AD, and 76 (13.4%) both (Figure 1).

At baseline, ILD+ and AD+ patients were older significantly than ILD– and AD– patients. ILD+ patients received significantly less methotrexate (MTX) than ILD– patients, while treatments for AD+ and AD– patients were comparable. RA disease activity was similar among groups.

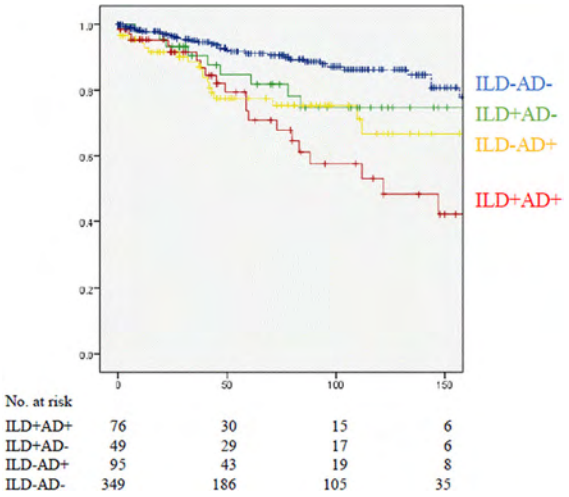


Schematic representation of the cohort

At final observation, ILD+ and AD+ patients had significantly higher Disease Activity Score 28 based on C-reactive protein (DAS28-CRP) (mean 2.4 vs. 2.1 and 2.3 vs. 2.1) and Simplified Disease Activity Index (SDAI) (mean 7.6 vs. 5.8 and 7.4 vs. 5.6) than ILD– and AD– patients. ILD+ patients received significantly less MTX but more glucocorticoids than ILD– patients. ILD+AD+ patients had higher RA activity than the other groups.

Analysis of covariance revealed significant association between DAS28-CRP and ILD [F(1,155) = 7.248], but not AD or their interaction. Similar results were found for SDAI. Kaplan-Meier analysis with log-rank tests revealed significantly lower infection-free rate in ILD+ and AD+ than ILD– and AD– patients. In ILD+ patients, the rate decreased prominently after 50 months. The infection-free rate was lower in ILD+AD+ patients than the other groups (Figure 2).

Cox regression analysis revealed significant association between infections and AD (hazard ratio [HR] 1.970, 95% confidence interval [CI] 1.065-3.646), but not ILD or their interaction. Cox regression analysis with time-dependent covariates, categorizing ILD into >50 and ≤50 months, showed significant association between infections and ILD >50 months (HR 3.702, 95% CI 1.637-8.372) and AD (HR 1.744, 95% CI 1.054-2.885), but not ILD ≤50 months.



Cumulative rate of total infectious events

Conclusion: Disease activity of RA was independently associated with ILD but not AD, suggesting an impact of reduced MTX in ILD. Risks of developing infections included ILD after 50 months and AD, both independently. The ILD+AD+ group showed higher RA activity and a greater susceptibility to infection than the other groups. Careful detection of ILD and AD, along with implementation of safe and effective alternative treatments, is necessary.

Disclosure: M. Yoshida: None; **t. Zoshima**: None; **I. Mizushima**: None; **M. Kawano**: None.

Abstract Number: 2121

Clinical Significance of Negative Seroconversion of Anti-CCP and Anti-Mutated Citrullinated Vimentin Antibodies in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
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Background/Purpose: Anti-cyclic citrullinated peptide antibody (anti-CCP Ab) positivity is closely associated with bone destruction in rheumatoid arthritis (RA) patients, but the correlation between the Ab titer and disease activity is poor. On the other hand, anti-mutated citrullinated vimentin (MCV) Ab, a subset of anti-citrullinated protein/peptide Abs (ACPA), have been suggested to be pathogenic in animal model (Harre U, et al, J Clin Invest, 2012) and an association between negative conversion of this Ab and radiographic remission has been reported in RA patients (Kastbom A, et al. Ann Rheum Dis, 2016). In this study, we aimed to determine the association of negative seroconversion of anti-CCP and MCV Abs with clinical and functional remission of RA.

Methods: Four-hundred and thirty-nine RA patients (female 74.9%, mean age 62.1 years old, and disease duration 8.1 years) who are followed up in our hospital and had anti-CCP and MCV Abs measured sequentially for more than 2 years were enrolled. Both Ab titers were measured using ELISA and the association of negative conversions of these Abs with clinical disease activity was investigated.

Results: 1) There were 12 cases (2.8%) with anti-CCP Ab (cut off 4.5 U/mL) and 57 cases (13.0%) with anti-MCV Abs (cut off 20 IU/mL) those had negative conversion at least once during the course. Whereas negative conversion of anti-CCP Abs was not observed in patients with titers >36.2 U/mL (approximately 8 times of the upper limit of normal) at the first determination, anti-MCV Abs with high titers >35 times of the upper limit of normal decreased to negative. There were cases in which high anti-MCV Ab titer (=719.6 IU/mL) turned to negative in 1 year. In the anti-MCV Ab negative conversion cases, 24.6% of cases with high anti-CCP Ab titers (≧100 U/mL) were also included. 2) In anti-MCV Ab negative conversion cases, disease activity score-ESR (DAS28-ESR) (3.21 vs. 2.44, P< 0.001), simplified disease activity index (7.89 vs.4.29, P< 0.001), and health assessment questionnaire score (0.62 vs.0.49, P< 0.001) were significantly decreased after negative conversion. However, similar changes were not observed in anti-CCP Ab negative conversion cases. 3) Clinical remission using DAS28-ESR was more frequently achieved after negative conversion of anti-MCV Ab than of anti-CCP Ab (67.9 vs. 33.3%, P=0.046). In cases with low disease activity or higher, clinical remission rate was also significantly higher in anti-MCV Ab negative conversion than in anti-CCP Ab negative conversion cases (58.9 vs. 14.3%, P=0.045).

Conclusion: Unlike anti-CCP Ab, negative conversion of anti-MCV Ab was associated with clinical remission. "Immunological remission" with anti-MCV Abs may have clinical implications in RA patients.

Disclosure: T. Fujii: AbbVie/Abbott, 5, 6, Asahi-Kasei, 5, 6, Astellas, 5, 6, Boehringer-Ingelheim, 5, 6, Chugai, 5, 6, Eisai, 5, 6, Eli Lilly, 5, 6, GlaxoSmithKlein(GSK), 5, 6, Janssen, 5, 6, Mitsubishi Tanabe, 5, 6, Ono, 5, 6, Pfizer, 5, 6, UCB, 5, 6; **K. Tanaka**: None; **R. Matsumiya**: None; **K. Tabata**: None; **S. Iwata**: None.

Abstract Number: 2122

Coronary Calcium and Carotid Artery Stiffness as Predictors of Cardiovascular Events and Mortality in Patients with Rheumatoid Arthritis: A 10-year Prospective Follow-up Study

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The risk of mortality is increased in patients with RA compared to the general population. Different non-invasive surrogate markers of atherosclerosis have been implemented to identify RA patients who are at high risk of cardiovascular (CV) disease.

In the present study, we aimed to establish the predictive capacity of the following surrogate markers: Coronary calcium (CAC) and carotid pulse wave velocity (PWV) to predict CV events and all-cause mortality in a cohort of RA patients prospectively followed.

Methods: We conducted a prospective longitudinal study that included 126 patients with RA. The patients were recruited in 2011 and followed-up for 10 years. All patients had undergone baseline CAC score, and carotid PWV by US. Multivariate Cox regression analysis was performed to identify the predictive ability of these surrogate markers for CV events and all-cause mortality.

Results: A total of 126 patients were included, 92 women (73%), with a mean age of 59±10 years. The main baseline characteristics, CV risk factors, disease activity data and treatments are detailed in **Table 1**, as well as the baseline parameters that showed statistically significant association with mortality and CV events. After a follow-up of 14,479 person-months, there were 15 deaths and 24 cardiovascular events in 18 patients. The main causes of mortality were infections (n=7, 46.7%) and neoplasms (n=5, 33.3%). In univariate analysis, CAC values above 400 Agatston units were associated with a statistically significant increased risk of overall mortality (HR 5.13 (1.03-25.41 95% CI), p=0.045) **(Table 2).** However, in multivariate analysis adjusted for classical CV risk factors, the results obtained were not statistically significant. Increasing CAC value as a continuous variable was significantly associated with an increased risk of cardiovascular event in both univariate

Table 1. Baseline characteristics of a cohort of 126 arthritis patients without previous cardiovascular events.

		Death			CV events		
		HR	IC (95%)	P	HR	IC (95%)	p
Age, years, (mean±sd)	59±10	**1.12**	**1.04-1.21**	**0.003**	**1.09**	**1.02-1.15**	**0.010**
Male/female, n (%)	92 (73)	1.33	0.45-3.89	0.61	1.02	0.37-2.87	0.96
Past or Current smoker, n (%)	64 (51)	1.50	0.53-4.20	0.45	0.96	0.38-2.42	0.93
Obesity, n (%)	42 (33)	0.70	0.22-2.20	0.54	0.74	0.26-2.07	0.57
Hypertension, n (%)	53 (42)	1.59	0.58-4.38	0.37	1.14	0.45-2.90	0.78
Diabetes Mellitus, n (%)	9 (7)	0.89	0.11-670	0.90	2.90	0.85-10.05	0.092
Dyslipidemia, n (%)	64 (51)	0.63	0.22-1.76	0.37	0.97	0.39-2.45	0.95
Hytriglyceridemia	20 (16)	1.00	0.99-1.00	0.65	1.00	0.99-1.00	0.84
BMI, kg/m2 (mean±sd)	29 ± 10	1.00	0.93-1.05	0.77	0.99	0.93-1.03	0.61
Abdominal circumference, cm (mean±sd)	88 ± 30	1.02	0.97-1.10	0.47	1.00	0.98-1.02	0.99
Cholesterol, mg/dl (mean±sd)							
Total Cholesterol	214 ±43	1.00	0.99-1.01	0.78	1.00	0.98-1.01	0.39
High-density lipoprotein (HDL)	64 ± 19	1.00	0.97-1.02	0.62	1.00	0.98-1.03	0.91
Low-density lipoprotein (LDL)	129 ± 36	1.00	0.99-1.01	0.58	0.99	0.98-1.00	0.22
Triglyceridemia	108 ±60	1.00	0.99-1.01	0.65	1.55	0.51-4.71	0.44
Disease duration, years (median, [IQR])	8.6 (4.5-14.5)	1.01	0.96-1.08	0.58	1.01	0.96-1.07	0.57
CRP, mg/l (median, [IQR])	2.2 (0.8-6.6)	1.01	0.98-1.04	0.47	0.99	0.95-1.04	0.64
ESR, mm/ 1º hour (median, [IQR])	12 (6-20)	1.01	0.99-1.04	0.56	0.99	0.95-1.03	0.43
Rheumatoid factor/ ACPA, n (%)	79 (63)/80 (63)	2.50	0.70-8.83	0.16	2.20	0.72-6.70	0.16
DAS28-ESR (mean±sd)	3.15 ± 1.36	0.88	0.60-1.29	0.50	1.18	0.86-1.64	0.31
DAS28-PCR (mean±sd)	2.98 ± 1.19	0.78	0.49-1.23	0.28	1.30	0.91-1.87	0.15
Score EULAR 2016 (mean±sd)	1.5 (0.0-3.0)	**1.16**	**1.07-1.25**	**0.000**	1.02	0.91-1.16	0.70
Score 2 (mean±sd)	4.7 (2.8-7.1)	1.00	0.99-1.01	0.56	1.00	0.98-1.01	0.58
Qrisk3 (mean±sd)	12.7 (6.6-21.1)	**1.06**	**1.02-1.10**	**0.005**	**1.04**	**1.01-1.08**	**0.013**
NSAIDs, n (%)	52 (41)	0.94	0.34-2.65	0.91	1.17	0.46-2.96	0.74
Prednisone, n (%)	59 (47)	0.55	0.19-1.62	0.28	1.45	0.57-3.66	0.44
Prednisone dose, mg/day (median, [IQR])	0 [0-5]	0.89	0.71-1.10	0.28	1.10	0.94-1.29	0.24
c-DMARDS, n (%)							
Metotrexate	90 (71)	1.10	0.35-3.47	0.87	0.83	0.31-2.20	0.71
Leflunomide	13 (10)	0.61	0.08-4.60	0.63	1.73	0.50-6.00	0.38
Hydroxychloroquine	22 (17)	0.70	0.60-3.13	0.65	1.93	0.69-5.41	0.21
Salazopyrin	0 (0)						
b-DMARDS, n (%)							
TNFi	22(17)	0.34	0.04-2.60	0.30	1.48	0.49-4.49	0.49
Tocilizumab	21 (17)	0.35	0.05-2.63	0.31	1.06	0.31-3.67	0.93
Rituximab	5 (4)	1.84	0-24-14-00	0.56	4.22	0.97-18.40	0.055
Abatacept	2 (2)	1.23e-14	-	1.00	3.39	0.45-25.40	0.24
JAK inhibitors, n (%)	4 (3)	2.19	0.29-16.60	0.45	5.97e-16	-	0.00

(HR 1.002 (1.0008-1.003 95% CI), p=0.001) and multivariate (HR 1.002 (1.0004- 1.003), p=0.011) analyses. The increase in carotid arterial stiffness value measured by PWV was statistically significantly related to overall mortality in the univariate analysis. The same was observed when categorizing this variable, as values higher than 10 m/s in the univariate analysis were statistically associated with overall mortality. However, this relationship did not maintain in the multivariate analysis, nor could it be demonstrated for CV events.

Table 2. Cox regression analysis hazard ratios for death of any cause and cardiovascular events of non-invasive surrogate markers of atherosclerosis.

	Death of any cause					Cardiovascular event				
	Hazard ratio, (95% confidence interval), p									
CAC										
CAC, Agatson units	1.00	0.99-1.00	0.25			**1.002**	**1.0008-1.003**	**0.001**	**1.002 (1.0004-1.003)**	**0.011**
log CAC, Agatson units	1.10	0.78-1.55	0.59			**1.81**	**1.20-2.75**	**0.005**	**1.91 (1.15-3.17)**	**0.012**
CAC Categ										
0	ref.			ref.		ref.			ref.	
1-100	2.47	0.64-0.58	0.19	0.78 (0.16-3.75)	0.76	1.31	0.40-4.28	0.66	0.77 (0.21-2.84)	0.69
101-400	2.21	0.37-13.22	0.39	0.83 (0.12-5.66)	0.85	1.34	0.26-6.93	0.72	0.72 (0.13-4.13)	0.71
>400	**5.13**	**1.03-25.41**	**0.045**	1.55 (0.23-10.45)	0.65	**5.71**	**1.64-19.82**	**0.006**	2.23 (0.45-11.03)	0.32
CAROTID STIFFNESS										
PWV, m/s	**1.29**	**1.06-1.52**	**0.004**	1.18 (0.96-1.44)	0.12	1.14	0.99-1.31	0.078	1.04 (0.85-1.26)	0.73
PWV > 10 m/s	**3.19**	**1.11-9.20**	**0.032**	2.29 (0.69-7.63)	0.18	1.90	0.67-5.40	0.23		

Conclusion: CAC measurement in RA patients is predictive of CV events. In our cohort of 126 RA patients, increased PWV values did not correlate with overall mortality or CVD after 10 years of follow-up.

Disclosure: C. Corrales Selaya: None; **N. Vegas Revenga**: None; **J. Parra**: None; **V. Portilla**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6; **M. Gonzalez-Gay**: AbbVie/Abbott, 5, 6, Amgen, 5, 6, Pfizer, 5, 6; **I. Ferraz Amaro**: AbbVie/Abbott, 5, 6, Amgen, 5, 6, Bristol-Myers Squibb(BMS), 6; **A. Corrales**: None.

Abstract Number: 2123

Dose Trabecular Bone Score (TBS) Add Predictive Value to Fracture Risk Assessment (FRAX) in Rheumatoid Arthritis?

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

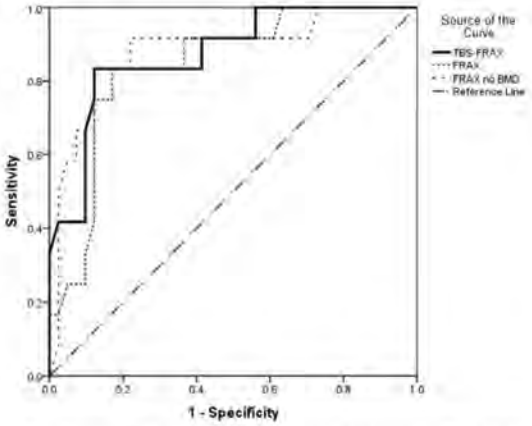
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Trabecular bone score (TBS) of lumbar spine is a dual X-ray densitometry (DXA)-based tool to evaluate bone microarchitecture, providing information on bone quality in metabolic bone diseases. The aim of this study is to assess whether TBS provides additional benefit to Fracture Risk Assessment (FRAX) tool to predict fractures in rheumatoid arthritis (RA) patients.

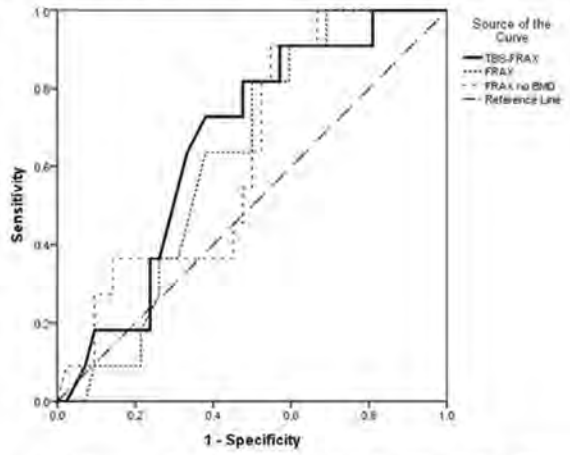
Image 1. ROC curve analysis for prevalent vertebral fracture by different FRAX models



Model	The area under the curve	Standard error	95% confidence interval	p-value
TBS-FRAX	0.874	0.057	0.760-0.988	<0.001
FRAX	0.842	0.061	0.720-0.965	<0.001
FRAX-no BMD	0.881	0.062	0.757-1.000	<0.001

Comparison between ROC curves: TBS-FRAX vs. FRAX, p=0.42; TBS-FRAX vs. FRAX-no BMD, p=0.86; FRAX vs. FRAX-no BMD, p=0.24. Abbreviations: Receiver operating characteristic (ROC); Fracture Risk Assessment (FRAX); Trabecular bone score (TBS); bone mineral density (BMD).

Image 2. ROC curve for new fractures within three years by different FRAX models



Model	Area under the curve	Standard error	95% confidence interval	p-value
TBS-FRAX	0.662	0.082	0.498-0.826	0.052
FRAX	0.626	0.078	0.470-0.781	0.114
FRAX-no BMD	0.633	0.085	0.462-0.804	0.127

Comparison between ROC curves: TBS-FRAX vs. FRAX, p=0.26; TBS-FRAX vs. FRAX-no BMD, p=0.64; FRAX vs. FRAX-no BMD, p=0.88. Abbreviations: Receiver operating characteristic (ROC); Fracture Risk Assessment (FRAX); Trabecular bone score (TBS); bone mineral density (BMD).

Methods: This is a retrospective study enrolling RA patients who fulfilled ACR/EULAR 2010 criteria from September 2014 to April 2021. We recruited participants aged between 40-90 and excluded those with malignancy. At enrollment, we measured bone mineral density (BMD) by Dual X-ray densitometry (DXA) at hip and lumbar spine, and assessed TBS at the lumbar spine. The 10-year risk of major osteoporotic fractures and TBS-adjusted risks were calculated on the FRAX website (https://frax.shef.ac.uk/tbs/index.aspx), and the FRAX scores were adjusted by glucocorticoid dose. In current studies, three FRAX models were evaluated, including conventional FRAX score, FRAX adjusted by TBS (TBS-FRAX) and FRAX without input of BMD (FRAX-noBMD). All patients were followed for at least three years to monitor fractures. We defined prevalent vertebral fracture by the morphometric change of vertebral bodies on the X-rays at baselines, according to Genant's semiquantitative assessment. New fracture was defined by any clinical fragility fractures by medical records or vertebral body morphometrical changes after comparing baseline and final X-ray images by independent radiologists. Receiver operating characteristic (ROC) curves were illustrated to compare prediction models.

Results: Fifty-three RA participants were enrolled in current study, with a mean age of 55.8± 9.6 years and female predominant (83.0%). Among them, 14 (26.4%) had prevalent vertebral fractures at baseline, while 11 (20.8%) developed new fractures during follow-up. For prevalent vertebral fracture, the area under ROC curves (AUCs) of TBS-FRAX, FRAX, FRAX-noBMD were 0.874, 0.842, and 0.881(all p-value < 0.001), respectively, and there was no statistical significance between different models (Image 1). Regarding new fracture, the AUCs were 0.662, 0.626, and 0.633, and the p-values were 0.052, 0.114, and 0.127, respectively. Also, no statistical significance was displayed between models (Image 2).

Conclusion: FRAX alone demonstrates good prediction ability for prevalent vertebral fractures, so TBS-adjusted FRAX does not add much value to the outcome. The performance of test models is not optimal for new fractures, and adding TBS might improve prediction ability with a borderline of statistical significance.

Disclosure: J. Chen: None; **T. Cheng**: None; **H. Kang**: None.

Abstract Number: 2124

Expansion of Atypical B Cells Accompanies Rheumatoid Arthritis-like Immune Dysregulation in ACPA+ At-risk Individuals

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Seropositive RA is preceded by an at-risk stage characterized by elevated circulating autoantibodies (AAb), including ACPA, in otherwise healthy individuals without clinically-apparent inflammatory arthritis. Rising autoantibody levels prior to clinical diagnosis suggest changing immune activity but what additional immune dysregulation may be occurring in this period is incompletely understood. The purpose of this study was to profile the immune state that accompanies elevated AAb to identify novel immune features present in individuals at-risk (ARI) to develop clinical RA.

Methods: We profiled 1463 plasma proteins, 69 peripheral blood mononuclear cell (PBMC) phenotypes, and 1,973,362 PBMCs by single-cell RNA sequencing (scRNA-seq) for a cross-sectional analysis of ARI with high levels of ACPA (anti-CCP3 IgG > 40 units) compared to healthy control individuals (HCI) (Table 1). Linear regression models were used to identify differentially expressed proteins (ARI/HCI), and to identify lineage-defining gene programs in scRNA-seq. PBMC phenotypes were selected and analyzed based on their identification in the clinical RA literature to evaluate features of clinical disease present in ARI. Wilcoxon rank sum was used to evaluate the association of B cells to AAb levels. Finally, NicheNet was used to identify putative relationships between plasma proteins and gene expression in the target cells.

Results: 314 proteins exhibited significant differential expression between ARI and HCI, including CCN1, CXCL6, CCL18, OSM, CCL5, and SERPINE1, all of which were not previously reported in ARI, as well as proteins related to B cell biology, including CXCL13, SEMA4D, LIGHT, and BAFF (Fig 1A). In addition, we found evidence for features of classifiable RA, including increased IL-1B, IL-6, TNF, CCL3, and CXCL8 plasma proteins and elevated PBMC phenotypes. Among PBMC, atypical (IgD- CD27-) B cells and Tph-like (CXCR5- PD1+) CD4T cells (Fig 1B) were significantly increased. Transcriptomic

Table 1. Characteristics of participants in this study

Variable	At-risk individuals	Controls	P value
Age at sample collection, median	62	57	0.01
Sex at birth, %	36 (78%)	41 (79%)	1.000
Race, %			
African-American	8.70	0.00	0.05
Asian	2.17	7.69	0.37
Caucasian	82.61	88.46	0.57
Other	6.52	3.85	0.66
Ethnicity, Hispanic or Latino, %	4.35	3.85	1.00
Ever smoked tobacco, n (%)	17 (37%)	8 (15%)	0.036
Autoantibodies, units (%)			
Serum CCP3+, median (IQR)	60 (42.5, 183)	0 (0,2)	< 1e-6
Serum RFIgM+, median (IQR)	0.57 (0.25, 22.23)	0 (0,4.3)	2.5e-4

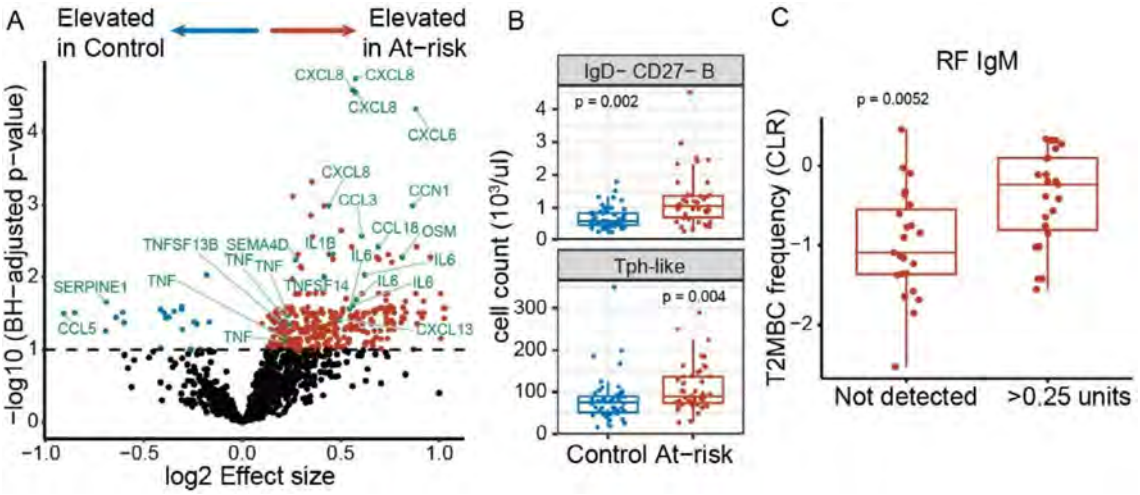

Figure 1. (A) Volcano plot of differential plasma protein expression between at-risk (red) and control (blue) individuals. Effect sizes and P values were determined using a linear regression model. Replicate annotations of the same protein result from repeated plate assays as part of Olink's standard protocol. (B) PBMCs from at-risk (red) and control (blue) individuals were compared for IgD- CD27- B cells (top) and CXCR5- PD1+ CD4 T cells (Tph-like; bottom) and were tested using Wilcoxon Rank Sum with Benjamini/Yekutieli correction. Each dot represents a participant. (C) At-risk individuals were categorized by RF-IgM levels as Not detected (≤ 0.25 units) or > 0.25 units and the frequency of type 2-polarized memory B cells (T2MBC) in PMBCs was tested using Wilcoxon Rank Sum.

analysis (scRNA-seq) of atypical B cells, enriched in ARI, demonstrated a gene program indicative of type 2-polarized memory B cells (T2MBC), including IL4R, IL13RA1, FCER2, IGHG4, IGHE, and MEF2C (Fig 2). T2MBC abundance was correlated to RF-IgM levels (Fig 1C). NicheNet analysis identified differentially-regulated proteins CCL3 (Pearson correlation coefficient (r) = 0.093), TNFSF13B (BAFF) (r = 0.077), TNFSF14 (LIGHT) (r = 0.048), and TNF (r = 0.047), as potential regulators of the T2MBC gene program.

Conclusion: We find that otherwise healthy at-risk individuals have immune dysregulation characterized by plasma protein and PBMC phenotype changes, including some that are similar to published findings in clinical RA. In particular, the number of T2MBC B cells were elevated in ARI and we recognized a relationship to RF-IgM AAb levels. Based on NicheNet analysis,

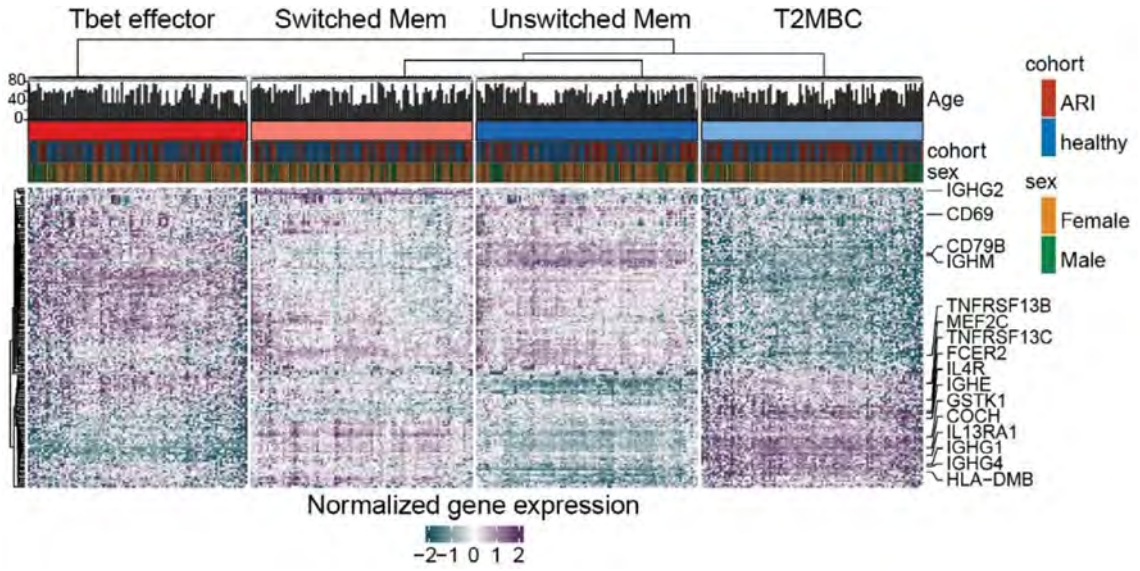

Figure 2. Gene expression heatmap indicating the DEGs (AUC > 0.55 or AUC < 0.45 and absolute log2 fold change > 0.1) between T2MBC and switch/unswitched memory B cells. Tbet effector are shown for comparison. Scaled normalized transcripts of pseudobulk samples are displayed.

we hypothesize that circulating plasma proteins in ARI reflect the maintenance or generation of T2MBC. These data deepen our understanding of this critical at-risk state and further emphasize the tight link between the dysregulation within the B cell compartment and autoimmune disease, which could be exploited for preventative therapeutic intervention.

Disclosure: A. Savage: Adaptive Biotechnologies, 3, 11, Eli Lilly, 2, 5; **Z. He**: Eli Lilly, 2, 5; **M. Glass**: Eli Lilly, 2, 5; **J. Reading**: None; **L. Moss**: None; **M. Feser**: None; **V. Tsaltskan**: None; **K. Nguyen**: None; **K. Demoruelle**: Boehringer-Ingelheim, 5, Gilead, 5, Pfizer, 5; **k. Kuhn**: pfizer, 5, ucb, 2; **D. Boyle**: None; **C. Speake**: None; **X. Li**: Eli Lilly, 5; **P. Skene**: Eli Lilly, 2, 5; **T. Torgerson**: Eli Lilly, 2, 5, Pharming Healthcare, 2, Takeda, 2; **T. Bumol**: Omeros Corporation, 4; **V. Holers**: None; **J. Buckner**: Bristol-Myers Squibb(BMS), 2, gentibio, 1, 10, 11, hotspot therapeutics, 2, Janssen, 2; **G. Firestein**: Eli Lilly, 5; **k. Deane**: Bristol-Myers Squibb(BMS), 1, Gilead, 5, Janssen, 5, Werfen, 1, 12, Biomarker kits; **M. Gillespie**: Eli Lilly, 2, 5, Novo Nordisk, 3, 12, Stock.

Abstract Number: 2125

Comparing the ITIS Diet and the Mediterranean Diet in Rheumatoid Arthritis: Preliminary Findings on Clinical and Microbiome Outcomes

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SESSION INFORMATION

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Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic condition characterized by persistent joint inflammation, functional impairment, and disability. Adhering to a Western diet has been associated with an overproduction of pro-inflammatory mediators and a reduced release of anti-inflammatory mediators. The gut microbiota plays a crucial role in determining the metabolic response to specific nutrients and can influence the levels of circulating pro- and anti-inflammatory mediators. The objective of this study is to compare the response of RA patients following either the anti-inflammatory ITIS diet or the Mediterranean diet (MD), assessing their respective improvements in various outcomes and examining the microbiome variations associated with each dietary approach.

Methods: We evaluated the effect of either ITIS diet or the MD for a period of 3 months in an evaluator blinded randomized clinical trial. In an ongoing trial, RA patients with active disease are being recruited. Physical examination is performed at each visit, along with the collection of clinical data, data on dietary adherence, and fecal samples for microbiome analysis. 16S rRNA gene amplicon profiling of the stools was performed. A generalized linear model was employed to assess the relationship between time and diet. Microbiome analysis was conducted using RStudio to describe variations in the abundance of microbial taxa associated with different diet groups and responses, defined as patients with a 50% pain improvement.

Results: A total of 44 patients (95.45% women, age average: 52.82, standard deviation (SD): 9.42), clinical disease activity index (CDAI) average 34.55 (17.44)) diagnosed with RA were recruited for this study. The study findings revealed significant improvements in health indicators among patients following the ITIS diet and MD. Specifically, patients on the ITIS diet

Table 1. Table with changes of outcomes through visits in each diet, ITIS and Mediterranean diet. Significant p-values are seen in bold font. Outcomes showed here are pain measured with visual analog scale (VAS), fatigue measured with VAS, clinical disease activity index (CDAI), VAS from overall health from physician's evaluation and VAS overall health from patient

	ITIS					Mediterranean Diet				
Outcome	**Baseline**	**Day15**	**2m**	**3m**	**p-value**	**Baseline**	**Day15**	**2m**	**3m**	**p-value**
Pain	4.90±2.58	3.65±2.18	3.85±2.40	3.03±2.05	**0.03**	5.21±2.31	4.66±2.71	3.56±2.59	3.86±2.86	0.06
Fatigue	5.47±2.52	4.54±2.60	3.43±2.69	3.88±2.74	**0.02**	4.47±2.27	4.59±2.9	3.53±3.05	3.90±2.86	0.32
CDAI	33.38±18.18	30.07±18.48	24.90±17.31	22.07±15.51	**0.02**	34.55±17.44	29.92±18.87	22.12±16.38	21.38±15.88	**0.01**
VAS_MD	4.88±1.71	4.45±1.66	3.77±2.24	3.20±2.10	**0.004**	5.13±1.37	4.37±2.04	3.43±2.12	3.39±2.43	**0.004**
VAS_PT	4.29±2.46	3.25±2.17	2.97±2.43	2.86±2.37	0.06	4.44±2.71	4.47±2.68	3.38±2.48	4.01±2.77	0.33

experienced significant reductions in pain (p=0.03), fatigue (p=0.02),CDAI (p=0.02) and visual analog scale (VAS) from physician (p=0.004) at 3 months. Patients following MD had a significant decrease of CDAI (p=0.01) and VAS from physician (p=0.004) at 3 months (**Table 1**). Remission was achieved by 11.11% of patients on the ITIS diet, while no patients following the MD reached remission. In microbiome analysis, the differential abundance between responders (R) and non-responders

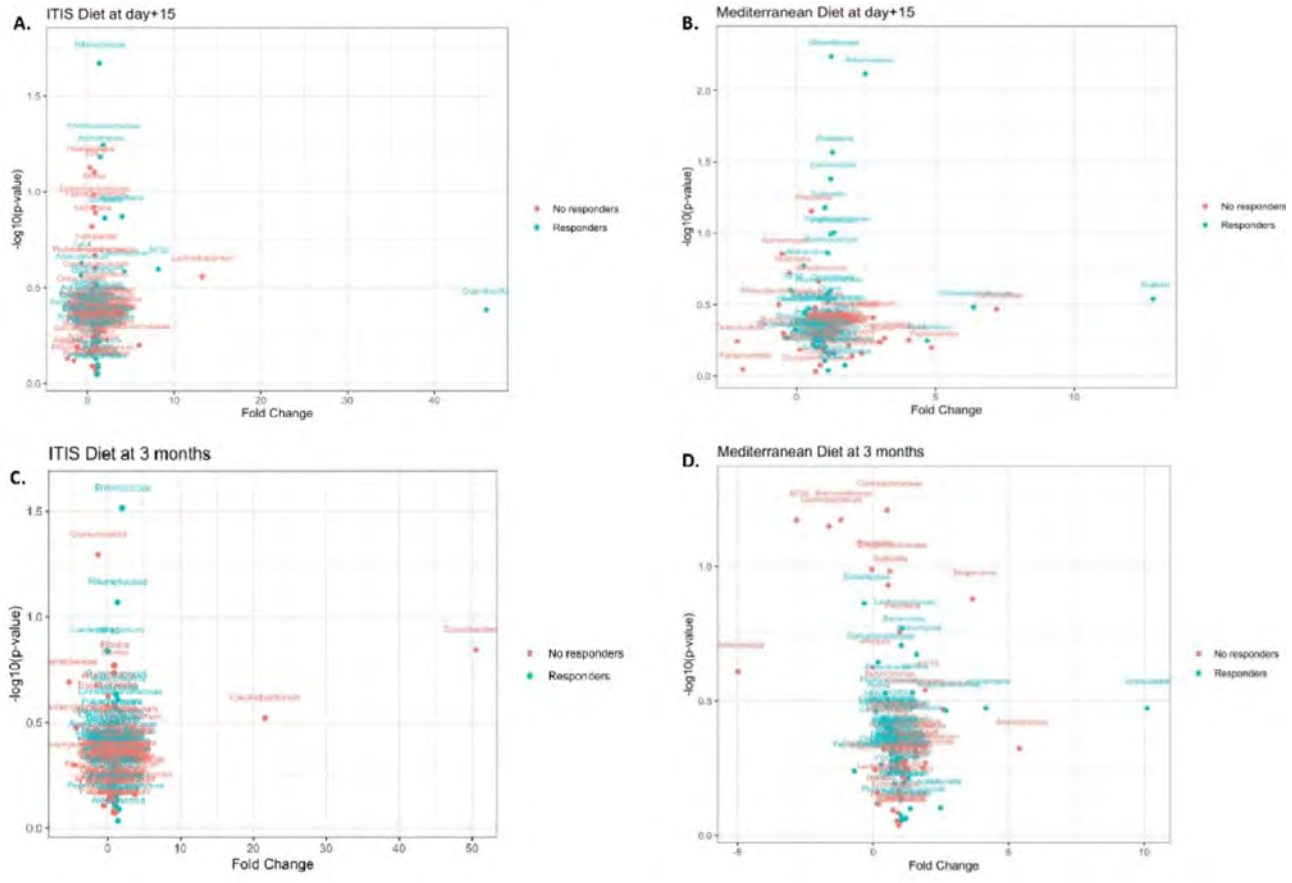

Figure 2. Volcano plots representing the distribution of the relative abundance of the microbiome at baseline. A) Distribution of the response at day +15 of ITIS diet patients. Blue color means that responders have higher relative abundance compared to non-responders. Red color means that non-responders have higher relative abundance compared to responders. B) Distribution of the response at day +15 of Mediterranean diet patients. C) Distribution of the response at the end of the trial of ITIS patients. D) Distribution of the response at the end of the trial of Mediterranean diet patients.

(NR) for each diet was calculated. **Figure 1** shows the volcano plots representing the distribution of the relative abundance of the microbiome at baseline within R and NR of each diet after 15 days and 3 months of diet intervention.

Conclusion: Preliminary results of our randomized clinical trial show improvements in clinical outcomes for both the ITIS diet and the MD. We also observed baseline differences in the microbiome between R and NR. More patients are being recruited to further investigate the differences in clinical and microbiome outcomes between the two diets.

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Abstract Number: 2126

Performance of the Rheumatoid Arthritis Impact of Disease (RAID) Score in Relation to Flares in Disease Activity

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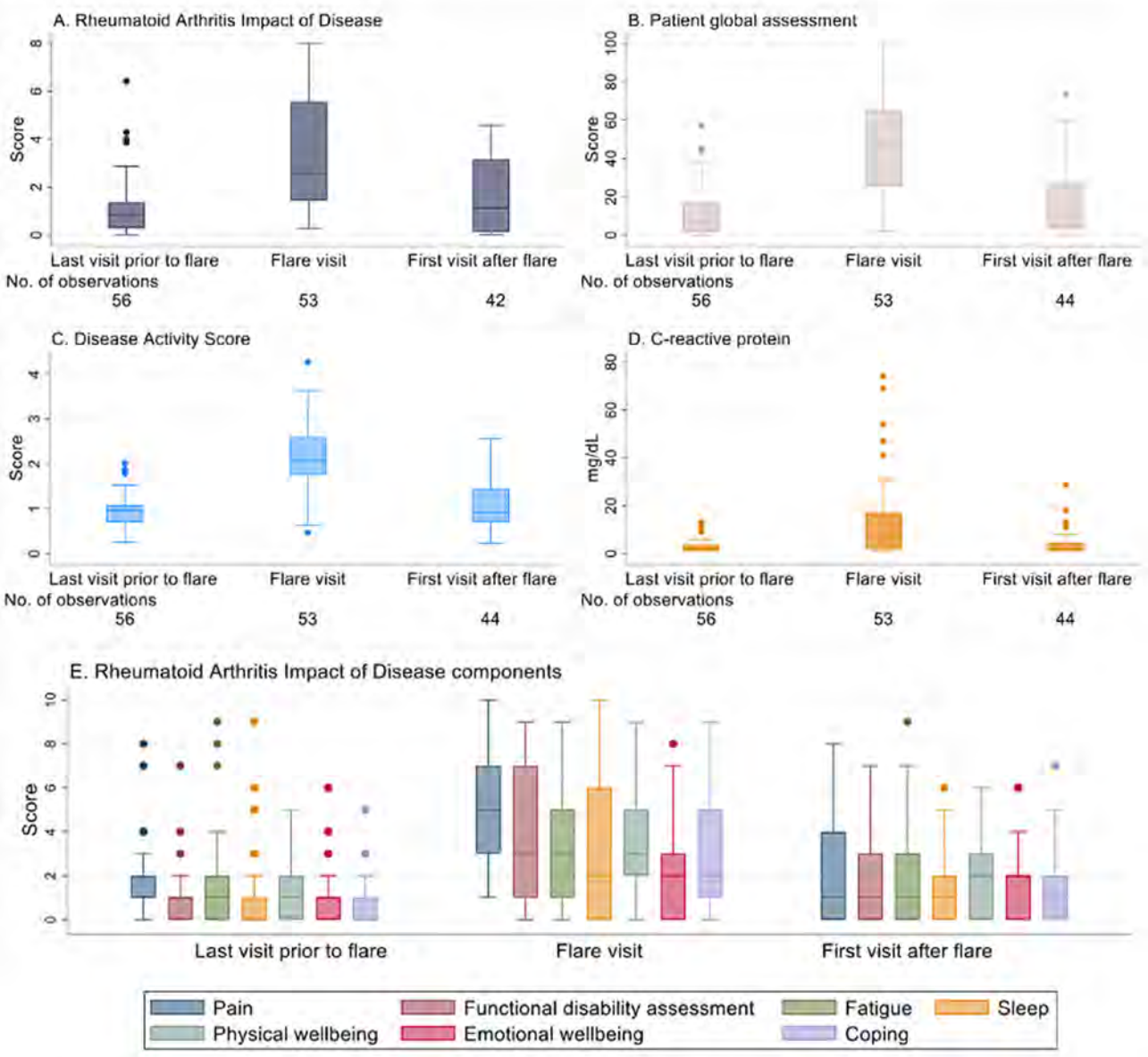
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The Rheumatoid Arthritis Impact of Disease (RAID) is a patient-reported outcome measure (PROM) originating from a EULAR initiative. It might support patient-centred care and shared decision-making between patient and health care provider. RAID could be a useful tool in regular clinical settings and remote monitoring, and its association with disease activity is thus of interest. RAIDs performance with regard to flare is not known, and our aim was to explore its responsiveness and discriminative abilities with regard to flares in disease activity.

Methods: We used pooled data from the first 12 months of the two ARCTIC REWIND trials assessing tapering of TNFi and csDMARDs (ClinicalTrials.gov: NCT01881308) (Lillegraven et al, JAMA, 2021). Eligible participants had RA according to the ACR/EULAR 2010 criteria, were in sustained remission for ≥12 months on stable DMARDs with Disease Activity Score (DAS) remission combined with no swollen joints at inclusion. Patients were randomized to continued stable treatment or tapered treatment. Study visits were conducted every four months, if a flare was suspected between visits the patient was seen within a week. Flare was defined as a combination of DAS >1.6, a ≥0.6 units increase and minimum 2 swollen joints, or a flare could be recorded in consensus between patient and rheumatologist. We evaluated the median RAID (total score and components) at the last visit before flare, at the flare visit and first visit after flare in relation to the suggested ≤2 RAID threshold for patient acceptable symptom state (PASS), and assessed the changes between those visits using Wilcoxon signed-rank test. The discriminative accuracies of RAID (total score and components) with respect to flares were assessed using area under the ROC curve (AUC) analyses based on logistic regression models. For comparison, similar analyses were performed for patient global assessment (PGA), DAS and C-reactive protein (CRP).

Results: Of the 248 patients included, 159 (64%) were female. Mean (SD) age and disease duration were 56.1 (11.8) and 6.3 (5.7) years. For patients who experienced a flare the median (IQR) RAID score was 0.9 (0.3, 1.4) at last visit prior to flare with 86% of scores below the PASS threshold (**Figure**). At the flare visit median RAID was 2.6 (1.4, 5.6) with 70% of scores above the PASS. Similar changes were observed in DAS, PGA and CRP (**Figure, Table**). All seven RAID domains increased significantly at the flare visit (p-values < 0.001), with the largest increase in pain. AUC (95% CI) values were0.88 (0.83, 0.93) for RAID, 0.92 (0.87, 0.97) for PGA, 0.94 (0.90, 0.98) for DAS and 0.76 (0.69, 0.84) for CRP. The RAID components with highest and lowest discriminative accuracies were pain (0.91 (0.86 to 0.95)) and sleep (0.69 (0.59 to 0.79)).

*Figure. Outcome measures at last visit before flare, at flare visit and first visit after flare. A: Rheumatoid Arthritis Impact of Disease[1] B: Patient global assessment VAS[2] C: Disease Activity Score[3] D: C-reactive Protein[4] E: Rheumatoid Arthritis Impact of Disease components**



*[1]RAID (NRS 0-10). [2]Patient global assessment (PGA) of the disease activity from 0-100 mm on a visual analogue scale. [3]Disease Activity Score (0-10) includes a swollen joint count of 44 joints, assessment of tender joints by Ritchie Articular Index, erythrocyte sedimentation rate (ESR) and PGA. [4]C-reactive protein (mg/dL). *Higher values indicate poorer outcome.*
Boxes indicate first and third quartiles, the band inside the box mark the second quartile (the median), while the whiskers indicate the highest and lowest values within 1.5 × the interquartile range (IQR). Dots represent individual patients (outliers).

Table. Mean (SD) changes in RAID score and single domains, PGA, DAS and CRP from the last visit before flare to flare visit and from flare visit to first visit after flare. Wilcoxon signed-rank test of significance in change between visits with proportion of increased scores at the flare visit and reduced scores at first visit after flare (z and p-values)

	Mean (SD) change at flare visit	Wilcoxon signed-rank test, Z and p-value	Proportion of increased scores at flare visit, n/N (%)	Mean (SD) change at first visit after flare	Wilcoxon signed-rank test, Z and p-value	Proportion of reduced scores at first visit after flare, n/N (%)
RAID						
Total score	2.2 (2.0)	6.0 <0.0001	47/53 (89)	1.9 (2.1)	-4.4 <0.0001	34/42 (81)
Pain	3.1 (2.6)	6.0 <0.0001	48/53 (91)	2.9 (2.9)	-4.9 <0.0001	34/42 (81)
Functional disability assessment	2.8 (2.6)	5.9 <0.0001	41/53 (77)	2.4 (2.7)	-4.5 <0.0001	30/42 (71)
Fatigue	2.0 (2.5)	4.9 <0.0001	34/53 (64)	1.4 (2.5)	-2.9 <0.003	23/42 (55)
Sleep	2.1 (3.1)	4.0 <0.0001	30/53 (59)	1.9 (3.1)	-3.3 0.0007	22/42 (52)
Physical well-being	2.5 (2.4)	5.9 <0.0001	45/53 (85)	2.0 (2.7)	-4.1 <0.0001	28/42 (67)
Emotional well-being	1.3 (2.2)	4.0 <0.0001	32/53 (60)	0.9 (1.8)	-2.7 0.006	21/41 (51)
Coping	2.1 (2.4)	5.4 <0.0001	37/53 (70)	1.5 (2.8)	-3.4 0.0004	29/42 (69)
PGA	34.9 (26.0)	6.1 <0.0001	51/53 (96)	31.1 (32.1)	-4.7 <0.0001	35/44 (80)
DAS	1.2 (0.7)	6.3 <0.0001	51/53 (96)	1.0 (0.9)	-5.2 <0.0001	40/44 (91)
C-reactive protein	9.4 (16.0)	4.8 <0.0001	33/53 (62)	9.9 (17.0)	-4.0 <0.0001	27/44 (61)

RAID, Rheumatoid Arthritis Impact of Disease, Numeric Rating Scale (0-10). PGA, patient global assessment, of the disease activity from 0-100 mm on a visual analogue scale. DAS, Disease Activity Score (0-10) includes a swollen joint count of 44 joints, assessment of tender joints by Ritchie Articular Index, erythrocyte sedimentation rate (ESR) and PGA.

Conclusion: Disease activity flares were associated with a significant increase in median RAID, supporting RAIDs ability to respond to flare. RAID and PGA discriminated well between flare and non-flare, hence both PROMs might contribute to identification of flare in a regular clinical setting as well as in remote monitoring of disease activity.

Disclosure: K. Holten: None; **N. Sundlisæter**: None; **J. Sexton**: None; **L. Nordberg**: None; **T. Uhlig**: Galapagos, 2, 6, Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **T. Kvien**: AbbVie/Abbott, 1, 2, 6, Bristol-Myers Squibb(BMS), 5, Galapagos, 2, 5, Gilead, 2, grunenthal, 6, Janssen, 2, 6, Novartis, 5, Pfizer, 2, 5, sandoz, 2, 6, UCB, 2, 5, 6; **E. Haavardsholm**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Eli Lilly, 2, Gilead, 2, Pfizer, 6, UCB, 6; **S. Lillegraven**: Boehringer-Ingelheim, 5; **A. Aga**: AbbVie, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6.

Abstract Number: 2127

Associations Between Rheumatoid Arthritis, Frailty Status and Mortality in Older Adults with Bladder Cancer

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is associated with an increased risk of developing certain cancers, including bladder cancer (*Beydon et al*. 2023[1]). However, few studies have examined the outcomes following a bladder cancer diagnosis in patients with RA. RA is also associated with an increased risk of frailty. Bladder cancer is the second most common urologic cancer with a mean age of diagnosis of 73 years and a high burden of frailty and comorbidity. Importantly, among patients with bladder cancer, frailty is associated with an increased risk of mortality. We sought to evaluate associations between RA and all-cause and cancer-specific mortality in older adults with bladder cancer, adjusted for frailty.

Methods: In this retrospective cohort study, using the Surveillance Epidemiology and End Results cancer registry and linked Medicare claims data (SEER-Medicare), we included patients ^{3}65 years old with incident bladder cancer diagnosed between 2004 and 2017. Patients with a pre-existing diagnosis of RA were identified based on the presence of ^{3}2 ICD-10 codes ≥ 30 days and < 365 days apart. A validated claims-based Frailty Index (*Kim et al*. 2017[2]) and National Cancer Institute (NCI) Comorbidity Index were derived from claims in the 12 months prior to bladder cancer diagnosis. Patients with a frailty score > 0.2 were categorized as frail. Separate Cox proportional hazards regression models evaluated the association between RA and frailty and 1) overall mortality and 2) bladder cancer-specific mortality, after adjusting for demographics, socioeconomic status, comorbidities, cancer stage, and receipt of guideline-directed bladder cancer treatment per stage. We evaluated the interaction between RA and frailty and performed stratified analyses by frailty status.

Table 1: Demographic and clinical characteristics of patients with bladder cancer with rheumatoid arthritis

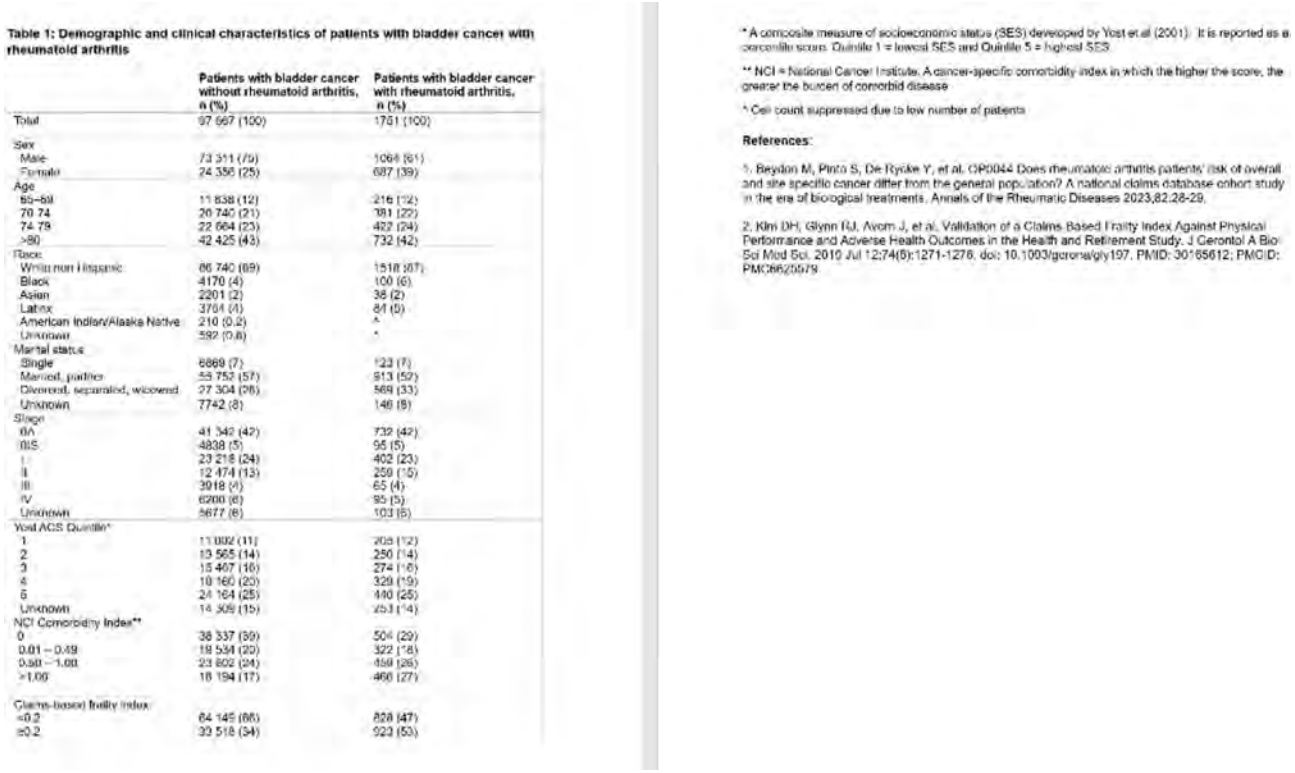

Table 1: Demographic and clinical characteristics of patients with bladder cancer with rheumatoid arthritis

	Patients with bladder cancer without rheumatoid arthritis, n (%)	Patients with bladder cancer with rheumatoid arthritis, n (%)
Total	97 667 (100)	1751 (100)
Sex		
Male	73 311 (75)	1064 (61)
Female	24 356 (25)	687 (39)
Age		
65–69	11 838 (12)	216 (12)
70 74	20 740 (21)	381 (22)
74 79	22 664 (23)	422 (24)
>80	42 425 (43)	732 (42)
Race		
White non Hispanic	86 740 (89)	1518 (87)
Black	4170 (4)	100 (6)
Asian	2201 (2)	38 (2)
Latinx	3764 (4)	81 (5)
American Indian/Alaska Native	210 (0.2)	^
Unknown	582 (0.6)	^
Marital status		
Single	6869 (7)	123 (7)
Married, partner	55 752 (57)	913 (52)
Divorced, separated, widowed	27 304 (28)	569 (33)
Unknown	7742 (8)	146 (8)
Stage		
0A	41 342 (42)	732 (42)
0IS	4838 (5)	95 (5)
I	23 218 (24)	402 (23)
II	12 474 (13)	259 (15)
III	3918 (4)	65 (4)
IV	6200 (6)	95 (5)
Unknown	5677 (6)	103 (6)
Yost ACS Quintile*		
1	11 002 (11)	208 (12)
2	13 565 (14)	250 (14)
3	15 467 (16)	274 (16)
4	19 160 (20)	329 (19)
5	24 164 (25)	440 (25)
Unknown	14 309 (15)	253 (14)
NCI Comorbidity Index**		
0	38 337 (39)	504 (29)
0.01 – 0.49	19 534 (20)	322 (18)
0.50 – 1.00	23 802 (24)	459 (26)
>1.00	16 194 (17)	466 (27)
Claims-based frailty index		
≤0.2	64 145 (66)	828 (47)
≥0.2	33 518 (34)	923 (53)

* A composite measure of socioeconomic status (SES) developed by Yost et al (2001). It is reported as a percentile score. Quintile 1 = lowest SES and Quintile 5 = highest SES

** NCI = National Cancer Institute. A cancer-specific comorbidity index in which the higher the score, the greater the burden of comorbid disease

^ Cell count suppressed due to low number of patients

References:

1. Beydon M, Pinto S, De Rycke Y, et al. OP0044 Does rheumatoid arthritis patients' risk of overall and site specific cancer differ from the general population? A national claims database cohort study in the era of biological treatments. Annals of the Rheumatic Diseases 2023;82:28-29.

2. Kim DH, Glynn RJ, Avorn J, et al. Validation of a Claims-Based Frailty Index Against Physical Performance and Adverse Health Outcomes in the Health and Retirement Study. J Gerontol A Biol Sci Med Sci. 2019 Jul 12;74(8):1271-1276. doi: 10.1093/gerona/gly197. PMID: 30165612; PMCID: PMC6625579

Table 2: Cox regression model for mortality among older adults with bladder cancer stratified by frailty status.

Table 2: Cox regression model for mortality among older adults with bladder cancer stratified by frailty status.

	Hazards Ratio* *Rheumatoid arthritis vs. no rheumatoid arthritis*	95% Confidence Interval
Overall mortality	1.11**	1.04 – 1.16
Stratified for frailty score <0.2	1.18	1.08 – 1.29
Stratified for frailty score ≥0.2	0.97	0.90 – 1.04
Bladder cancer-specific mortality	1.07	0.98 – 1.18
Stratified for frailty score <0.2	1.23	1.07 – 1.41
Stratified for frailty score ≥0.2	0.93	0.82 – 1.05

** Model is adjusted for sex, age, race, marital status, cancer stage, Yost ACS Quintile, NCI Comorbidity Index, and bladder cancer treatment*

***Interaction term of RA*frailty for overall mortality is p = 0.0006*

Results: We identified 99,418 patients with bladder cancer of whom 1751 (1.8%) had pre-existing RA (Table 1). Among patients with RA, 923 (52.7%) were frail while 33,518 (34.3%) of patients without RA were frail (p< 0.0001). Median follow-up for survivors overall was 5.3 years (interquartile range, IQR, 2.8-8.8) during which time 61,499 patients died. The 5-year overall survival was 73.0% versus 71.9% for patients with and without RA respectively (p< 0.0001) and was 73.0% versus 68.6% for patients with and without frailty (p=0.0001). Among non-frail patients, RA was associated with an increased risk of cancer-specific (aHR 1.22, 95% CI 1.07 – 1.41) and overall mortality (aHR 1.18, 95% CI 1.08-1.29) (Table 2). However, among frail patients, RA was not associated with an increased risk of cancer-specific (aHR 0.92, 95% CI 0.82 – 1.05) or overall mortality (aHR 0.97, 95% CI 0.90-1.04).

Conclusion: RA was associated with a higher risk of bladder cancer-specific and overall mortality in non-frail pts with bladder cancer. Limitations of our study include retrospective nature, potential selection bias, and unmeasured confounding. Our hypothesis-generating results support further evaluation of the association between RA, frailty, and survival in older adults with bladder cancer.

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Abstract Number: 2128

Higher Vitamin D Levels Before Methotrexate Start Are Associated with Lower Subsequent Mortality in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Vitamin D is an immune-modulating hormone. Low Vitamin D levels have been associated with development of autoimmune disease and higher disease activity in early Rheumatoid Arthritis (RA). Furthermore, Vitamin D supplementation may reduce incidence of autoimmune disease. Finally, low Vitamin D levels have been associated with subsequent mortality in non-autoimmune disease populations. Here in the setting of RA we investigated the relationship between serum 25-hydroxyvitamin D (25(OH)D) levels before starting methotrexate (MTX) therapy and subsequent all-cause mortality in national and local Cleveland Veterans Affairs (VA) cohorts.

Methods: This is a retrospective cohort study of patients with an ICD-9/10 diagnosis of RA seen in Rheumatology clinic visits. The data collected was time oriented around initial prescribing of MTX, a MTX medication possession ratio > 75%, and a clinical 25(OH)D level before starting MTX in the national (n=15,109) and local Cleveland (n=197) VA cohorts. Chart adjudication to verify RA diagnosis and Vitamin D supplementation was performed for the Cleveland cohort (n=197). We examined survival in groups of RA patients with adequate serum 25(OH)D (> 20 ng/mL) and deficient 25(OH)D (< 20 ng/mL) levels using Cox Proportional-Hazards Model. The model was adjusted for traditional cardiovascular risk factors, including age, sex, race and ethnicity, smoking status, body mass index (BMI), statin use, and the Charlson comorbidity index. We used a signed rank test to evaluate changes among patients with 25(OH)D levels measured before and after supplementation.

Results: Patients with 25(OH)D levels > 20 ng/mL before starting MTX had a 28% reduced risk of mortality when compared to patients with 25(OH)D levels < 20 ng/mL (HR 0.72; CI 0.64, 0.80; $p < 0.001$) in the national VA cohort. Age, gender, smoking status, Charlson comorbidity index, and BMI were also independently associated with mortality. We observed higher 25(OH)D levels after Vitamin D supplementation compared to before ($p=0.008$) in the Cleveland chart-reviewed cohort in which supplementation status was obtained.

Conclusion: RA patients with adequate Vitamin D levels (> 20 ng/mL) have lower subsequent mortality when compared to those with Vitamin D deficiency (< 20 ng/mL) in a large national RA cohort receiving standard of care MTX. The relationship between Vitamin D level and mortality held after adjusting for Charlson comorbidity score and traditional cardiovascular disease risk factors. The data from Cleveland demonstrate the feasibility of normalizing serum Vitamin D levels with Vitamin D supplementation in this patient population. The extent to which correction of serum Vitamin D levels in patients who were initially found to be Vitamin D deficient impacts upon all-cause mortality in RA is yet to be determined.

Disclosure: S. Malakooti: None; **H. Siddiqui**: None; **B. Wilson**: None; **T. Bej**: None; **M. O'Mara**: None; **N. Singer**: Merck, 5, 12, Travel grant; **G. McComsey**: None; **L. Kostadinova**: None; **M. Mattar**: None; **D. Zidar**: None; **D. Anthony**: None.

Abstract Number: 2129

SCORE and SCORE2 Comparison in Cardiovascular Risk Estimation in Rheumatoid Arthritis Patients: A Cross-sectional Study Including Carotid Ultrasound

Cristina Campos Fernández[1], Pablo Martínez Calabuig[2], Jorge Juan Fragío Gil[1], Roxana González Mazarío[1] and Jose Andres Roman Ivorra[3], [1]Escuela de Doctorado, Universidad Católica de Valencia San Vicente Mártir, Valencia, Spain, [2]Hospital General Universitario Valencia, Valencia, Spain, [3]Hospital Universitari i Politècnic la Fe, Valencia, Spain

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by joint inflammation and cartilage destruction. RA has been recognized as a systemic disease associated with an increased risk of cardiovascular disease. Current CV risk screening and management strategies underestimate the actual CV risk in RA.Thus, an adequate CV risk stratification has special relevance in RA to identify patients at risk of CV disease.

To evaluate the cardiovascular risk profile in patients with RA by assessing both traditional CVD risk factors, carotid ultrasound finding and risk estimation using SCORE and SCORE2.

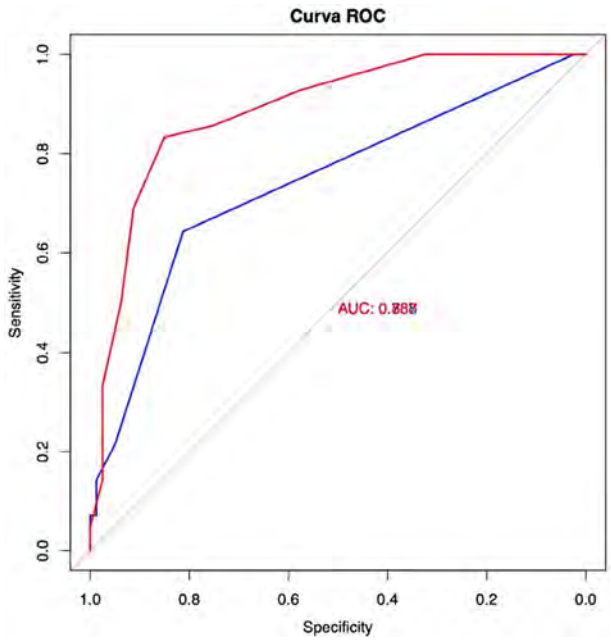
Methods: A cross-sectional study was performed including adult moderate to severe RA patients who had initiated treatment with JAK inhibitors or anti TNF. Traditional risk factors were evaluated. The Systematic Coronary Risk Evaluation (SCORE) and its updated version, SCORE2, were employed to estimate the global cardiovascular risk in this population. Furthermore, carotid ultrasound examinations were conducted to investigate subclinical atherosclerosis in RA patients. Measurements of carotid intima-media thickness (IMT) were obtained as a surrogate marker of early vascular damage. Additionally, the presence of atherosclerotic plaques, a hallmark of advanced vascular disease, was documented. This study was performed from September-2022 to April-2023 and was approved by the Ethics Committee. Statistical analysis was performed using R.

Results: A total of 123 patients were included in the study. Demographical and clinical variables are shown in table 1. Among the RA patients, a high prevalence of CVD risk factors was observed. The mean values of SCORE and SCORE2 indicated a moderate to high estimated 10-year risk of fatal CVD events in this population (mean SCORE: 2.77%, mean SCORE2: 4.07%). Carotid ultrasound measurements revealed an increased mean IMT in RA patients (mean right carotid cIMT: 0.64 [0.12]; mean left carotid cIMT 0.69 [0.11]). Furthermore, a substantial proportion of patients (34.1%) displayed the presence of atherosclerotic plaques. The concordance correlation coefficient between SCORE and SCORE2 demonstrated a significant moderate positive relationship (estimate 0.32 [0.19-0.43] IC 95%). ROC curves were calculated for SCORE and SCORE2 regarding their predictive capacity for plaques, showing a significant difference between them ($p< 0.001$) indicating a superior predictive capacity of SCORE2. A linear regression model, adjusted for confounding factors, was used to assess the relationship between SCORE and SCORE2 with IMT. Both SCORE (estimate 1.41 $p=0.02$, $R2=0.045$) and SCORE2 (estimate 1.55 $p< 0.01$, $R2=0.015$) were positively associated with IMT.

Table 1

Table 1: Demographic, clinical characteristics and Ultrasound Results

Characteristic	All RA patients n=123
Age - years	56.01 (10.84)
Female sex – number (%)	104 (84.5%)
BMI – value (ds)	27.6 (4.5)
Smoking habit (%)	
Never Smoked	87 (70.7%)
Ex-smoker	4 (3.3%)
Active smoker	32 (26%)
Race – number (%)	
Caucasian	119 (96.7%)
Comorbidities – number (%)	
High blood pressure	62 (50.4)
Dyslipemia	80 (65)
Diabetes Mellitus	21 (17.1)
Ultrasound findings	
Right carotid cIMT	0.64 (0.12)
Left carotid cIMT	0.69 (0.11)
Plaques	42 (34.1%)
Bilateral	16 (13%)
Right carotid	12 (9.8%)
Left carotid	14 (11.4%)



ROC

Conclusion: The relationship between SCORE and SCORE2 was found to be satisfactory, indicating their adequacy for prediction plaque development. However, the predictive capacity of both scores may be further enhanced by incorporating multiplication factors. Additionally, both SCORE and SCORE2 were positively associated with IMT, but SCORE2 demonstrated a greater predictive capacity in this regard. Furthermore, the SCORE2 explained a higher proportion of the IMT variation compared with SCORE.

Disclosure: C. Campos Fernández: None; **P. Martínez Calabuig**: None; **J. Fragío Gil**: None; **R. González Mazarío**: None; **J. Roman Ivorra**: None.

Abstract Number: 2130

Prevalence and Risk Factors of *Pneumocystis Jirovecii* Colonization in Patients with Rheumatoid Arthritis Treated with Tumor Necrosis Factor Inhibitors and Tocilizumab

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) are susceptible to *Pneumocystis jirovecii* colonization and prone to develop life-threatening *Pneumocystis* pneumonia (PCP). An increased risk of *P. jirovecii* colonization and PCP was found in RA patients treated with tumor necrosis factor (TNF) inhibitors. However, the impact of other biologics on *P. jirovecii* colonization remains unrecognized. This study aims to investigate the prevalence and risk factors of *P. jirovecii* colonization in patients with rheumatoid arthritis treated with TNF inhibitors and tocilizumab.

Methods: We enrolled the patients with RA, who were treated with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), TNF inhibitors, and tocilizumab between March 2022 to February 2023. The patients with acute respiratory symptoms were excluded. *P. jirovecii* polymerase chain reaction (PCR) assays of induced sputum, nasal swab, and oral wash were performed. Factors associated with *P. jirovecii* colonization were evaluated.

Results: A total of 94 patients with RA were included, and none of these patients received chemoprophylaxis for PCP. *P. jirovecii* colonization was found in 8 (8.5%) patients, and positive *P. jirovecii* PCR was detected in 3 (3.2%) specimens of induced sputum, 4 (4.2%) in nasal swabs, and 2 (2.1%) in oral washes. One patient exhibited positive *P*. jirovecii PCR in both induced sputum and oral wash samples. The mean (standard deviation, SD) age was 63.1 (11.6) years, and 73 (77.7%) patients were female. There were 39 (41.5%) patients treated with TNF inhibitors, 25 (26.6%) with tocilizumab, and 30 (31.9%) with csDMARDs only. In the TNF inhibitors group, 21 (53.8%) patients were treated with etanercept, 11 (28.2%) with adalimumab, 6 (15.4%) with golimumab, and 1 (2.6%) with certolizumab. One (2.6%) patient in the TNF inhibitors group had *P. jirovecii* colonization, 5 (20.0%) patients in the tocilizumab group, and 2 (6.7%) patients in the csDMARDs group. The chi-square test revealed a significant difference among TNF inhibitors, tocilizumab, and csDMARDs groups (chi-square = 6.141; *P*= 0.046). Patients with *P. jirovecii* colonization had a higher rate of tocilizumab use (62.5%

Table 1 Baseline demographics of patients

Table 1 Baseline demographics of patients

Characteristics	Total (n=94)	Patients with *P. jirovecii* colonization (n=8)	Patients without *P. jirovecii* colonization (n=86)	*P* value
Age, years, mean (SD)	63.1 (11.6)	62.1 (11.4)	63.2 (14.1)	0.611
Female, n (%)	73 (77.7)	8 (100)	65 (75.6)	0.192
Disease duration, years, mean (SD)	8.1 (5.6)	9.6 (8.2)	8.0 (5.4)	0.655
Rheumatoid factor, n (%)	76 (80.9)	6 (75.0)	70 (81.4)	0.646
Anti-cyclic citrullinated peptide antibody, n (%)	61 (64.9)	6 (75.0)	55 (64.0)	0.708
Ever smoking, n (%)	8 (8.5)	0 (0)	8 (9.3)	>0.900
Pulmonary disease, n (%)	10 (10.6)	0 (0)	10 (11.6)	0.593
Chronic hepatitis B, n (%)	7 (7.4)	1 (12.5)	6 (7.0)	0.475
Chronic hepatitis C, n (%)	12 (12.8)	2 (25.0)	10 (11.6)	0.270
Chronic kidney disease, n (%)	10 (10.6)	0 (0)	10 (11.6)	0.593
Prednisolone, n (%)	46 (48.9)	6 (75.0)	40 (46.5)	0.154
Daily prednisolone dose, mg, mean (SD)	5.6 (3.1)	4.0 (1.7)	5.9 (3.2)	0.160
csDMARDs				
Methotrexate, n (%)	52 (55.3)	5 (62.5)	47 (54.7)	0.728
Hydroxychloroquine, n (%)	65 (69.1)	5 (62.5)	60 (69.8)	0.699
Sulfasalazine, n (%)	50 (53.2)	6 (75.0)	44 (51.2)	0.276
Leflunomide, n (%)	15 (16.0)	1 (12.5)	14 (16.3)	>0.900
Cyclosporin, n (%)	2 (2.1)	0 (0)	2 (2.3)	>0.900
Azathioprine, n (%)	1 (1.1)	0 (0)	1 (1.2)	>0.900
bDMARDs				
Tumor necrosis factor inhibitors, n (%)	39 (41.5)	1 (12.5)	38 (44.2)	0.134
Tocilizumab, n (%)	25 (26.6)	5 (62.5)	20 (23.3)	0.029
csDMARDs only, n (%)	30 (31.9)	2 (25.0)	28 (32.6)	>0.900
Duration of bDMARD therapy, years, mean (SD)	5.4 (3.4)	5.9 (2.5)	5.4 (3.5)	0.762
Lymphocyte count, cell/mm^3, mean (SD)	1648 (640)	1252 (374)	1685 (649)	0.053
CRP, mg/dL, mean (SD)	0.27 (0.63)	0.34 (0.80)	0.26 (0.61)	0.163
ESR, mm/hr, mean (SD)	11.5 (12.7)	8.5 (13.6)	11.8 (12.8)	0.065

Data are presented as number (percentage) unless otherwise specified.

bDMARDs = biologic disease-modifying antirheumatic drugs; CRP = C-reactive protein; csDMARDs = conventional synthetic disease-modifying antirheumatic drugs; ESR = erythrocyte sedimentation rate; SD = standard deviation

Table 2 Logistic regression analysis for factors associated with *Pneumocystis jirovecii* colonization

Table 2 Logistic regression analysis for factors associated with *Pneumocystis jirovecii* colonization

	Univariable analysis			Multivariable analysis		
Characteristics	OR	95% CI	*P* value	OR	95% CI	*P* value
Age ≥ 65 years	0.366	(0.070 - 1.915)	0.234			
Disease duration > 3 years	0.851	(0.159 - 4.562)	0.850			
Rheumatoid factor	0.686	(0.127 - 3.716)	0.662			
Anti-CCP antibody	1.691	(0.322 - 8.891)	0.535			
Prednisolone	3.450	(0.659 - 18.06)	0.143	8.255	(1.238 - 55.059)	0.029
Methotrexate	1.383	(0.311 - 6.155)	0.670			
Hydroxychloroquine	0.722	(0.161 - 3.248)	0.671			
Sulfasalazine	2.864	(0.547 - 14.99)	0.213			
Leflunomide	0.735	(0.084 - 6.448)	0.781			
Tumor necrosis factor inhibitors	0.180	(0.021 - 1.531)	0.116			
Tocilizumab	5.500	(1.207 - 25.05)	0.028	11.658	(2.037 - 66.718)	0.006
csDMARDs only	0.690	(0.131 - 3.641)	0.662			
Lymphopenia (< 1000 cells/mm^3)	3.369	(0.716 - 15.85)	0.124			
CRP > 0.5 mg/dL	0.974	(0.109 - 8.692)	>0.900			
ESR > 15 mm/hr	0.416	(0.048 - 3.570)	0.424			

Anti-CCP antibody = anti-cyclic citrullinated peptide antibody; CI = confidence interval; CRP = C-reactive protein; csDMARDs = conventional synthetic disease-modifying antirheumatic drugs; ESR = erythrocyte sedimentation rate; OR = odds ratio

Table 3 Characteristics of 8 patients with *Pneumocystis jirovecii* colonization

Table 3 Characteristics of 8 patients with *Pneumocystis jirovecii* colonization

Patient number	1	2	3	4	5	6	7	8
Age, years	84	81	64	59	43	54	60	52
Sex	Female	Female	Female	Female	Female	Female	Female	Female
Site of positive *P. jirovecii* PCR	Induced sputum	Induced sputum	Nasal swab	Oral wash	Nasal swab	Induced sputum, Oral wash	Nasal swab	Nasal swab
RA Treatment	MTX + SSZ + TCZ	HCQ + SSZ + TCZ	MTX + HCQ + TCZ	HCQ + SSZ + TCZ	LEF + SSZ + TCZ	MTX + SSZ + ETN	MTX + HCQ	MTX + HCQ + SSZ
Disease duration, years	10.7	8.3	26.9	10.9	7.5	11.3	0.4	0.8
Duration of bDMARD therapy, years	4.7	4.2	5.8	5.3	4.6	10.9	NA	NA
Use of prednisolone	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Daily prednisolone dose, mg	NA	NA	2.5	5	5	1.25	5	5
Rheumatoid factor	-	+	+	+	+	+	+	-
Anti-CCP antibody	-	-	+	+	+	+	+	+
Lymphocyte count, cells/mm^3	942	1469	1520	1860	1400	1169	776	880
CRP, mg/dL	0.04	0.02	0.02	0.02	0.02	0.22	2.31	0.07
ESR, mm/hr	7	3	1	2	1	11	41	2

Anti-CCP antibody = anti-cyclic citrullinated peptide antibody; bDMARD = biologic disease-modifying antirheumatic drug; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; ETN = etanercept; HCQ = hydroxychloroquine; LEF = leflunomide; MTX = methotrexate; NA = not applicable; RA = rheumatoid arthritis; SSZ = sulfasalazine; TCZ = tocilizumab

vs. 23.3%, *P*= 0.029), a numerically higher rate of prednisolone use (75.0% vs. 23.3%, *P*= 0.154), and a numerically lower lymphocyte count (1252 vs. 1685 cell/mm^3; *P*= 0.053) than patients without *P. jirovecii* colonization (Table 1). In the backward multivariable logistic regression analysis, tocilizumab (OR 11.658; 95% CI 2.037-66.718; *P*= 0.006) and prednisolone (OR 8.255; 95% CI 1.238-55.059; *P*= 0.029) were independent risk factors of *P. jirovecii* colonization (Table 2). The detailed characteristics of the 8 patients with *P. jirovecii* colonization were outlined in Table 3, and no PCP was observed during the study period.

Conclusion: We demonstrated the prevalence of *P. jirovecii* colonization in RA by the combined sampling of the induced sputum, nasal swab, and oral wash. Tocilizumab and prednisolone might be associated witha higher risk of*P. jirovecii* colonization in patients with RA.

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Abstract Number: 2131

Time-course Analysis from the First Wave to Early 2023 in Critically Ill Patients with Novel Coronavirus Infection in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

	All patients	3/1/2020~11/30/2021	12/1/2021~2/28/2023
N(%)	316(100)	25(7.9)	291(92.1)
Patient characteristics			
Age(y)	57.8+/-12.8	55.3+/-15.2	58.1+/-12.6
Sex, n(%)			
Female	267(84.5)	23(92.0)	244(83.8)
Male	49(15.5)	2(8.0)	47(16.2)
RA duration(y)	10.9+/-7.2	12.3+/-7.6	10.8+/-7.2
CDAI at C19 infect.	3.4+/-2.8	3.9+/-3.0	3.4+/-2.8
MTX use(%)	223(70.6)	18(72.0)	205(70.4)
GC use(%)	26(8.2)	6(24.0)	20(6.9)
b/tsDMARDs use(%)	74(23.4)	4(16.0)	69(23.7)
TNFi(%)	22(7.0)	2(8.0)	20(6.9)
IL-6i(%)	24(7.6)	0(0)	24(8.2)
ABT(%)	6(1.9)	1(4.0)	5(1.7)
JAKi(%)	19(6.0)	1(4.0)	18(6.2)

Patient characteristic of COVID-19 in RA

Background/Purpose: We analyzed trends in the incidence and severity of novel coronavirus disease (COVID-19) from the first wave to early 2023 in patients with rheumatoid arthritis (RA).

Methods: Cases who were diagnosed according to ACR/EULAR 2010 classification criteria were recruited to SHin-yokohama Arthritis REgister (SHARE) between 2020 and 2023. We conducted a retrospective cohort study investigating COVID-19 outcomes in clinic-confirmed rheumatoid arthritis patients from March 1, 2020 to February 28, 2023. We aggregated the total number of COVID-19 cases and the number of critically ill cases (hospitalized or died) and calculated the number of severe cases of COVID-19 by calendar period. compared the proportions. We estimated the clinical features of severe COVID-19 in each period. Rheumatic Disease Comorbidity Index (RDCI) were analyzed to detect the clinical features of severe COVID-19 in RA patients.

Results: 2,481 RA patients were enrolled. 316 cases were diagnosed as COVID-19 (12.8%, average age 57.8-+/-12.8 years, female 84.5%). There were 7 cases of severe COVID-19 (2.2%). The proportion of serious outcomes due to COVID-19 decreased over calendar time ($p < 0.0001$). 16% of cases were severe in the early stage of COVID-19

3/2020~11/2021, N=25	Hospitalized	Non-hospitalized	*p* value
	4(16.0)	21(84.0)	
Age(y)	74.5+/-7.6	55.3+/-15.2	0.0054
Sex, female(%)	4(100)	19(90.5)	ns
RA duration(y)	14.4+/-2.1	11.9+/-8.2	ns
CDAI at C19 infect.	4.3+/-2.7	3.9+/-3.1	ns
MTX use(%)	2(50.0)	16(76.2)	0.0441
GC use(%)	3(75.0), 6.0mg/day	3(14.3), 4.7mg/day	ns
b/tsDMARDs use(%)	0(0)	4(19.0)	ns
Never smoked(%)	4(100)	18(85.7)	ns
Vaccination(%)			ns
Deceased	1(25.0)	0(0)	0.0483
Comorbidities			
RDCI (score, 0-9)	1.5+/-1.3	0.4+/-0.7	0.0388
RA-ILD	0(0)	2(9.5)	ns
MACE	0(0)	0(0)	ns
Hypertension	3(75.0)	1(4.8)	0.0021
Diabetes	2(50.0)	1(4.8)	0.0291

RDCI,Rheumatic disease comorbidities score

The clinical features of severe COVID-19 in the early stage (March 1, 2020-November 30, 2021)

12/2021~2/2023, N=291	Hospitalized	Non-hospitalized	*p* value
	3(1.0)	288(99.0)	
Age(y)	76.0+/-11.5	57.9+/-12.5	0.0292
Sex, female(%)	1(33.0)	244(84.7)	0.0152
RA duration(y)	5.0+/-4.0	10.8+/-7.2	ns
CDAI at C19 infect.	3.7+/-2.5	3.4+/-2.8	ns
MTX use(%)	1(33.0)	204(70.8)	ns
GC use(%)	1(33.0), 4.0mg/day	19(6.6), 3.1mg/day	ns
b/tsDMARDs use(%)	1(33.0)	68(23.6)	ns
Never smoked(%)	1(33.0)	198(68.8)	ns
Vaccination(%)	3(100)	266(92.4)	ns
Deceased	2(67.6)	0(0)	<0.0001
Comorbidities			
RDCI (score, 0–9)	4.0+/-2.6	0.4+/-0.8	0.0002
RA-ILD	2(67.6)	6(2.1)	<0.0001
MACE	0(0)	3(1.0)	ns
Hypertension	3(100)	39(13.5)	0.0006
Diabetes	0(0)	13(4.5)	ns

RDCI:Rheumatic disease comorbidities score

The clinical features of severe COVID-19 in the after omicron stage (December 1, 2021-February 28, 2023)

(March 1, 2020-November 30, 2021), compared with after omicron stages (December 1, 2021-February 28, 2023) was 1.0%.

In the early stage of COVID-19, elderly age (p=0.0054), hypertension (p=0.0021), diabetes (p=0.0291) and RDCI (1.5+/-1.3 vs. 0.4+/-0.7, p=0.0388) were associated with critical ill cases. After omicron stages of COVID-19, elderly age (p=0.0292), hypertension (p=0.0006), RA-ILD (p< 0.0001) and RDCI (4.0+/-2.6 vs. 0.4+/-0.8, p=0.0002) were associated with critical ill cases.

Conclusion: CONCLUSIONS Although the proportion of severe COVID-19 RA cases has decreased in after omicron stages compared to early stages of COVID-19, the clinical features of severe COVID-19 were very similar between two groups.

Disclosure: M. YAMASAKI: None.

Abstract Number: 2132

Systematic Screening for Multimorbidities Leads to an Increased Use of Comorbidity-preventing Medications and Lower Hospitalization Rates

Claire Daien[1], Vera Georgescu[2], Guillaume Decarriere[3], Gael Mouterde[3], Cedric Lukas[4], Gregoire Mercier[2] and JACQUES MOREL[5], [1]University Hospital, Montpellier, France, [2]Department of Medical Information, Montpellier, France, [3]Rheumatology, Montpellier, France, [4]CHU Montpellier, Montpellier, France, [5]Protocole thérapeutique immuno-rhumatologie, Montpellier, France

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systematic screening for multimorbidities has been carried out since 2014 at Montpellier University Hospital in patients with chronic inflammatory rheumatism (IRD). The aim of this work was to evaluate the impact of this screening on patient management and hospitalization rates during a 3-year follow-up.

Methods: IRD patients benefiting from the screening program (index date) were identified in the French national health database SNDS and matched to 3 controls on age, sex, IRD and disease duration. The primary endpoint was a composite score assessing the dispensing of comorbidity-preventing drugs (vaccines, anti-platelet treatments, lipid-lowering drugs, anti-osteoporotic drugs) in the year following the index date. Secondary endpoints were cardiologist/pneumologist consultation, all-cause hospitalization rate, hospitalization for fractures, cardiovascular events or infections. Odds ratios (IC95%) were calculated, with multivariate logistic regression adjusted for medical history (hypertension, diabetes, heart failure, CV disease, lung disease, osteoporotic fractures) and medications related to IRD or included in the primary endpoint in the previous year.

Results: 441 patients who had participated in the screening program (exposed) were identified in the national database and matched with 1323 unscreened patients (controls). Of these, 73.9% suffered from rheumatoid arthritis, 18.1% from ankylosing spondylitis and 7.9% from psoriatic arthritis. Exposed patients had significantly less diabetes than controls (4.5 vs. 7.6%) and received significantly less glucocorticoids (36.5 vs. 42.1%), more csDMARDs (56.9 vs. 42.8%) and more bDMARDs (57.4 vs. 32.6%) than controls. The use of drugs evaluated in the primary criteria was more frequent in the year prior to inclusion in the exposed group than in controls (58.4 vs. 45.3%). Exposed patients met the primary endpoint almost twice as often as controls (OR=1.9 [1.5-2.4]). The initiation of preventive medication for comorbidity remained significantly more frequent after adjustment for medical history and previous medication (OR=1.5 [1.1-2.1]). After adjustment for baseline comorbidities, exposed patients consulted significantly more cardiologists or pulmonologists in the year following screening than controls (OR=1.6 [1.2-2.1]). Controls had a three-fold higher risk of all-cause hospitalization (3.1 [2.1-4.6]) at one-year follow-up, which remained significant after adjustment (2.4 [1.5-4.0]). Controls had a significantly higher risk of hospitalization for cardiovascular events (2.1 vs. 0.3%), infections (6.8 vs. 3.6%) and emergency room admissions (20.3 vs. 10.6%) than controls at 2-year follow-up.

Conclusion: The recommendations given during the comorbidity screening program were applied, with an increase in the use of preventive medication for comorbidities and more consultations with specialists. After adjusting for comorbidities and medications at baseline, we observed a decrease in the risk of hospitalization rates, which may reflect the positive impact of carrying out systematic screening for multi-morbidities in IRD patients.

Disclosure: C. Daien: None; **V. Georgescu**: None; **G. Decarriere**: None; **G. Mouterde**: None; **C. Lukas**: Abbvie, 2, 6, Amgen, 2, 6, Biogen, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche Chugai, 2, 6, UCB, 2, 6; **G. Mercier**: None; **J. MOREL**: None.

Abstract Number: 2133

Cardiovascular Risk Factors Are Associated with Discontinuation of Advanced Therapies Due to Treatment Failure in Rheumatoid Arthritis: Results from the OBRI

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

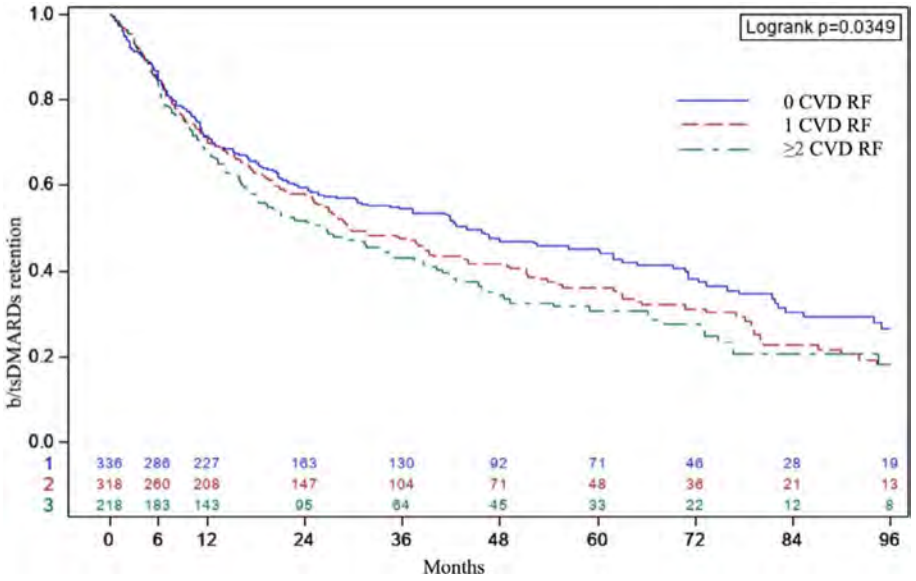

Figure. Kaplan Meier survival analysis of b/tsDMARDs, stratified by the number of cardiovascular risk factors

Background/Purpose: Cardiovascular (CVD) comorbidity can impact overall RA care. We demonstrated that CVD risk factors were associated with higher disease activity and disability. Here, we investigated whether CVD risk factors reduce treatment response by influencing retention of a first biologic disease-modifying antirheumatic drug (bDMARD) or targeted synthetic DMARD (tsDMARDs).

Methods: Participants enrolled in the Ontario Best Practices Initiative (OBRI) RA registry were included if they initiated their first bDMARD or tsDMARD. They were grouped by the number of baseline CVD risk factors (0, 1 or ≥2) including hypertension, dyslipidemia, diabetes, obesity and current smoking. The primary outcome was time-to-discontinuation of therapy for any reason. Secondary outcomes included discontinuation for primary failure, secondary failure or due to adverse events. Multivariable Cox proportional hazards model, adjusted for clinically important confounders, estimated the association between CVD risk factors and drug retention.

Results: A total of 872 patients were included, of which 62% had at least one CVD risk factor. The baseline characteristics are described in Table 1. Fifty-eight percent (N=508) of the study population discontinued their initial b/tsDMARD after a median of 13 (interquartile range [IQR], 6 to 29) months. The most common causes for treatment discontinuation were primary failure (N=72), secondary failure (N=126), and adverse events (N=133). Patients with no CVD risk factors experienced

Table. Multivariate analysis of reasons for discontinuation of the initial bDMARD or tsDMARD based on CVD risk factor status.

Reason for discontinuation	One CVD risk factor		Two or more CVD risk factor	
	SHR (95% CI)	p-value[a]	SHR (95% CI)	p-value[a]
Primary failure	1.71 (0.90, 3.25)	0.10	1.21 (0.60, 2.44)	0.60
Secondary failure	1.34 (0.80, 2.22)	0.26	1.79 (1.04, 3.08)	0.03
All treatment failure (primary and secondary)	1.53 (1.03, 2.28)	0.03	1.54 (1.01, 2.35)	0.04
Adverse events	1.15 (0.74, 1.77)	0.54	1.16 (0.71, 1.89)	0.56
All treatment failure and adverse events	1.36 (1.02, 1.83)	0.04	1.39 (1.01, 1.92)	0.04

Abbreviations: CVD, cardiovascular disease; SHR, Subdistribution hazard ratio; CI, confidence interval

[a]Adjusted hazard ratios by age (categorized into two groups as <65 and ≥65), gender, CDAI score, disease duration, HAQ disability index score, number of non-CVD comorbidities, concurrent conventional DMARD use or oral glucocorticoid use

longer drug survival, with a median (IQR) duration of 44 months (30 to 62). In contrast, patients with 1 or ≥2 CVD risk factors had significantly shorter drug survival, averaging 29 (IQR 25 to 39) and 26 (IQR 18-34), respectively (p= 0.03). Compared to patients with no CVD risk factors, only patients with ≥2 CVD risk factors had a significant increase in all-cause discontinuation: HR 1.32 (95% CI 1.07, 1.65, p= 0.01). In multivariate-adjusted analysis, no significant association was found between all-cause discontinuation and CVD risk factor status. However, there was a significant association between the presence of >1 CVD risk factor and drug discontinuation, notably for secondary failure (Table 2).

Conclusion: The presence of multiple CVD risk factors increases the risk of treatment failure, primarily secondary failure, among biologic naïve patients starting their first advanced therapy. Future research is needed to explore the effect of interventions aiming at reducing these modifiable risk factors on the response to targeted therapies.

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Abstract Number: 2134

Autoantibodies to Joint-related Proteins Predict Remission with High Specificity in New Onset RA

Monica Leu Agelii[1], Outi Sareila[2], Erik Lönnblom[2], Kristina Forslind[3], Maria Andersson[3], Alf Kastbom[4], Christopher Sjöwall[5], Lennart Jacobsson[6], Jan Kihlberg[7], Rikard Holmdahl[2], Ingiäld Hafström[2] and **Inger Gjertsson**[8], [1]Gothenburg University, Goteborg, Sweden, [2]Karolinska Institutet, Stockholm, Sweden, [3]FoU Spenshult, Halmstad, Sweden, [4]Linköping University, Linköping, Sweden, [5]Department of Biomedical and Clinical Sciences, Division of Inflammation and Infection/Rheumatology, Linköping University, Linköping, Sweden, [6]University of Gothenburg, Malmö, Sweden, [7]Uppsala University, Uppsala, Sweden, [8]Department of Rheumatology and Inflammation research, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

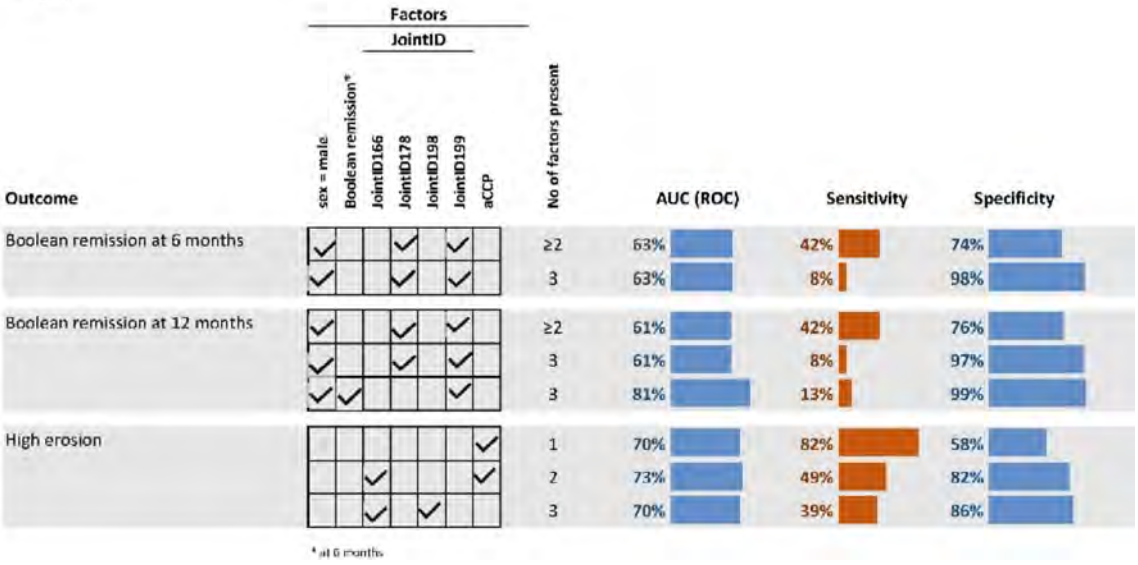
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: One of the major challenges in the management of rheumatoid arthritis (RA) is to determine individual treatment and predict the prognosis. On a group level, high disease activity and antibodies specific for citrulline (ACPA) and immunoglobulins (RF) are factors associated with poor prognosis. New alternative biomarkers, which could provide more specific information, are antibodies to disease-related targets in the joints.

The purpose of this study is to identify circulating autoantibodies to joint-related proteins (hereafter named JointIDs) that predict disease outcome in patients with new onset RA

Methods: Sera at diagnosis from BARFOT and TIRA-2 cohorts (n=1986) with new onset RA patients were screened with a bead-based multiplex flow immunoassay to detect IgG autoantibodies against 47 peptides derived from joint proteins (JointIDs). Disease outcomes included Boolean remission at 6 and 12 months, swollen joint count (SJC) and radiological progression at 12 months (>8% affected feet joints and >3% affected hand joints) in patients who were without joint damage at inclusion. Multivariate logistic regression and zero-inflated negative binomial models adjusted for clinical factors (age, gender, ACPA, RF, changes in medication at 3 and 6 months) were used to identify JointIDs with the strongest potential to predict prognosis

Table 1



Results: Six JointIDs were identified as predictors for these disease outcomes in multivariate analyses. Presence of JointID178 predicted an average decrease in SJC at 6 months with 41% and with 33% at 12 months. Presence of at least 2 of the following factors: JointID178 positive and JointID199 negative at inclusion in combination with male sex identified approx. 40% of the patients in Boolean remission at 6 months with approx. 75% specificity (Table 1). A similar test performance was obtained even for Disease Activity Score 28 remission. The sensitivity and specificity for being in Boolean remission at 12 months if the patients were male, negative for JointID199 and in Boolean remission at 6 months was 13% (CI 9%;16%) and 99% (CI 99%;100%), respectively. RF and ACPA did not predict remission but were the strongest predictors of joint destruction at 12 months although with low specificity (58%). Addition of JointID166 significantly increased the specificity at the expense of sensitivity.

Conclusion: Autoantibodies to joint-related proteins at RA diagnosis can predict remission with a high specificity at 6 and 12 months. This knowledge is of clinical importance as patients positive or negative for these JointIDs in combination with clinical factors may potentially guide future treatment choices.

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Abstract Number: 2135

Synovial Fluid High-density Lipoprotein (HDL)-miR-1246 Is Enriched in Patients with Inflammatory Arthritis Compared to Osteoarthritis and Increases Synovial Fibroblast IL-6 Expression

Olivia Posey[1], Qiong Wu[1], Anastasiia Phothisane[1], Christine Pham[2], Deborah Parks[2], Antonina Akk[3], Danielle Michell[1], Kasey Vickers[1] and Michelle Ormseth[1], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Washington University, St. Louis, MO, [3]Washington University in St. Louis, St. Louis, MO

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: High-density lipoprotein (HDL), known for its anti-atherogenic reverse cholesterol transport function, also transports miRNAs between cells, altering cellular function. We found that compared to control subjects, patients with rheumatoid arthritis (RA) - a type of inflammatory arthritis (IA) – have increased plasma HDL-bound miR-1246, which increased macrophage IL-6 expression. Previous reports indicate that HDL is enriched in the synovial fluid of patients with RA versus osteoarthritis (OA). We hypothesize that in IA the higher concentration of synovial HDL promotes joint inflammation by delivering a higher cargo load of miR-1246 to synovial fibroblasts and enhancing the release of inflammatory cytokines. The purpose of this study is to determine if HDL and HDL-miR-1246 is enriched in IA versus OA synovial fluid and increases synovial fibroblast proinflammatory cytokine expression.

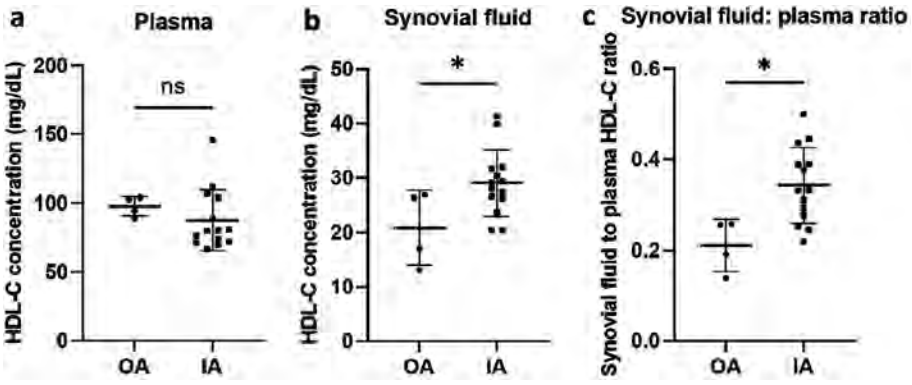

Figure 1. NMR-based HDL-C concentration (mg/dL) in plasma (a), synovial fluid (b), and ratio of synovial fluid to plasma (c) in patients with osteoarthritis (OA) versus inflammatory arthritis (IA). Plasma HDL is similar compared IA and OA (P=0.19) (a). Synovial fluid HDL is significantly enriched 1.4-fold in IA versus OA (b). The ratio of synovial fluid to plasma HDL-C was 1.6-fold enriched in IA versus OA (c). HDL-C = high-density lipoprotein – cholesterol. IA = inflammatory arthritis. OA = osteoarthritis. ns= not significant. *P<0.05. Bars = mean, whiskers = standard deviation. Mann-Whitney U test.

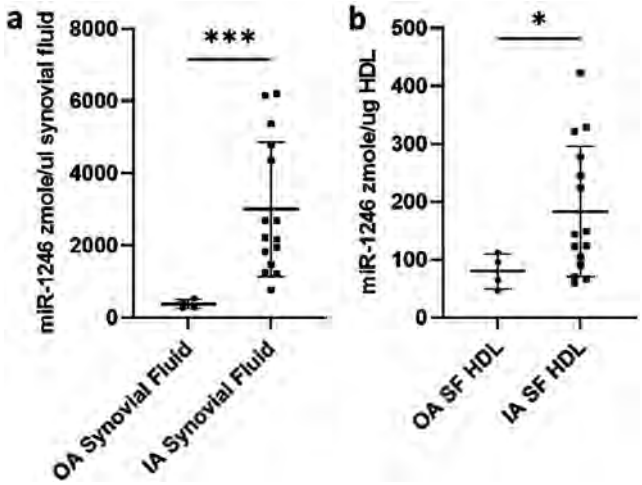

Figure 2. Concentration of miR-1246 in synovial fluid (a) and purified synovial fluid HDL (b) from patients with osteoarthritis (OA) versus inflammatory arthritis (IA). miR-1246 in synovial fluid is 7.9-fold enriched in IA versus OA (a). miR-1246 in purified synovial fluid HDL is 2.3-fold enriched in IA versus OA (b). SF= synovial fluid. *P<0.05, ***P< 0.001. Bars=mean, whiskers= standard deviation. Mann-Whitney U test.

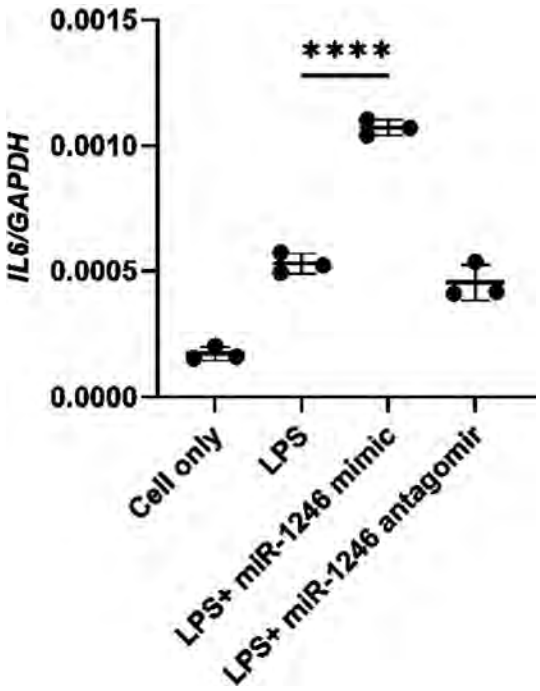

Figure 3. Synovial fibroblasts treated with LPS then miR-1246 expressed 2.0-fold more IL-6 versus LPS alone. Treatment with LPS then an antagomir to block endogenous miR-1246 production did not significantly alter IL-6 expression. IL-6 = interleukin 6. GAPDH = glyceraldehyde-3-phosphate dehydrogenase. LPS = lipopolysaccharide. ****P < 0.0001. Bars = mean, whiskers = standard deviation. T-test.

Methods: Synovial fluid and plasma were collected consecutively from 15 IA (10 RA and 5 with immune-checkpoint inhibitor-induced IA) and 4 OA patients who underwent arthrocentesis for routine care. Nuclear magnetic resonance was used to measure the synovial fluid and plasma lipoproteins. Synovial fluid HDL was isolated by fast protein liquid chromatography. Synovial fluid miR-1246 and synovial fluid HDL-miR-1246 were measured by qPCR and normalized to a spike-in miRNA and DNA mimic standard to determine miRNA concentration. RA synovial fibroblasts were activated with LPS for 24-hours then washed and treated with a miR-1246 mimic or antagomir for 24-hours. Cellular *IL-6* expression was measured by qPCR.

Results: HDL-cholesterol (HDL-C) concentration was similar in IA versus OA plasma (P=0.19). However, synovial fluid HDL was enriched 1.4-fold in IA (29 mg/dl ± 6.1 mg/dl) versus OA (21mg/dl ± 6.9mg/dl) (P=0.04). Similarly, the ratio of synovial fluid to plasma HDL-C was 1.6-fold enriched in IA versus OA patients (P=0.02) (Figure 1). Synovial fluid miR-1246 concentrations were increased 7.9-fold in IA (3000 zmol/uL ± 1860 zmol/uL) versus OA patients (379 zmol/uL ± 126 zmol/uL, P=0.0005). Synovial fluid HDL miR-1246 concentrations were also increased 2.3-fold in IA (183 zmol/ug HDL ± 113 zmol/ug HDL) versus OA patients (80 zmol/ug HDL ± 30 zmol/ug HDL, P=0.049) (Figure 2). Treatment of activated synovial fibroblasts with miR-1246 increased *IL-6* expression 2.0-fold (P< 0.0001, Figure 3).

Conclusion: HDL is concentrated in synovial fluid and enriched in miR-1246 in patients with IA versus OA. miR-1246 is proinflammatory to synovial fibroblasts. These data suggest that the HDL may enhance IA synovial inflammation by transport of proinflammatory miRNAs. Future studies will be dedicated to examining HDL-mediated transfer of miR-1246 to synovial fibroblasts and its effect *in vivo*.

Disclosure: O. Posey: None; **Q. Wu**: None; **A. Phothisane**: None; **C. Pham**: Insmed, 1, 9; **D. Parks**: None; **A. Akk**: None; **D. Michell**: None; **K. Vickers**: None; **M. Ormseth**: None.

Abstract Number: 2136

Arthritogenic Cells Found in the Peripheral Blood of Rheumatoid Arthritis Patients Transfer the Disease to NSG-DR4 Mice

Janine Rupp[1], Johannes Fessler[2], Silvia Hayer[3], Barbara Dreo[4], Angelika Lackner[2], Patrizia Fasching[2], Wolfgang Helmberg[2], Peter Schlenke[2], Jens Thiel[5], Guenter Steiner[6], Cornelia M. Weyand[7] and Martin Stradner[2], [1]Medical University Graz, Rochester, MN, [2]Medical University of Graz, Graz, Austria, [3]Medical University of VIenna, Vienna, Austria, [4]Division of Rheumatology and Immunology, Medical University of Graz, Graz, Austria, [5]University Hospital Freiburg, Freiburg, Germany, [6]Division of Rheumatology, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria, [7]Mayo Clinic School of Medicine and Stanford University, Rochester, MN

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: T cells play an important role in the genesis of rheumatoid arthritis (RA). HLA class II genes, such as HLA-DRB1*0401 (HLA-DR4), confer the strongest genetic risk and suggest involvement of $CD4^+$ T cells. However, the exact pathogenesis of RA is still elusive. Existing mouse models mimic specific aspects of the disease but do not fully recapitulate the human immune system. Thereby current research is limited and would profit from a humanized mouse model. We aimed to identify arthritogenic cells by transferring HLA-$DR4^+$ peripheral blood mononuclear cells (PBMC) of RA patients into NSG-DR4 mice. Thereby generating a novel mouse model with inflammatory joint disease, only triggered by the transfer of human immune cells.

Methods: Humanized NSG-DR4 mice (NSG-AB^0 Tg(HLA-DR4)) were generated by injecting PBMC of HLA-DR4 positive patients or controls. Engraftment within peripheral blood, bone marrow, skin, liver, and spleen was assessed comprehensively using multicolor flow cytometry. Development of RA was monitored by examination of the joints, followed by micro computed tomography analysis and histology. Joints were analyzed regarding pannus formation, bone erosions, cartilage damage, and human cell infiltration.

Results: Here, we show that $DR4^+$ T cells of the peripheral blood of RA patients are capable of inducing an RA-like disease in NSG-DR4 mice. These mice recapitulate different hallmarks of the disease including immune cell infiltration, pannus formation, increased osteoclastogenesis, cartilage damage, and bone erosions. Compared to healthy controls, cells of RA patients are more likely to develop inflammatory joint disease in these mice (RA donor 70% vs. healthy control 20%, p=0.00196). T-helper 1 (Th1) cells, dominated the human immune cell composition in humice, while regulatory T cells (Tregs) were diminished compared to donor PBMC composition. Transfer of *in vitro* Th1 polarized T cells increased arthritis incidence.

Conclusion: Arthritogenic cells found in the peripheral blood of RA patients are capable of inducing an RA-like disease in NSG-DR4 mice. This novel mouse model will allow to identify these cells on a patient-personalized level.

Disclosure: J. Rupp: None; **J. Fessler**: None; **S. Hayer**: None; **B. Dreo**: None; **A. Lackner**: None; **P. Fasching**: None; **W. Helmberg**: None; **P. Schlenke**: None; **J. Thiel**: None; **G. Steiner**: None; **C. Weyand**: None; **M. Stradner**: None.

Abstract Number: 2137

Line of Therapy of Biologics and JAK Inhibitors in RA, PsA and AxSpA: Implications for Design and Uptake of New Drugs and Diagnostics

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondyloarthritis (AxSpA) have an increasing array of treatment options available, and new blood-based diagnostic tests to predict future treatment response are commercially available or are in development. Moreover, certain medications are restricted to patients who are already biologic experienced. We examined the point prevalence of the line of therapy (LoT) by type of arthritis to assess the size of the eligible patient population.

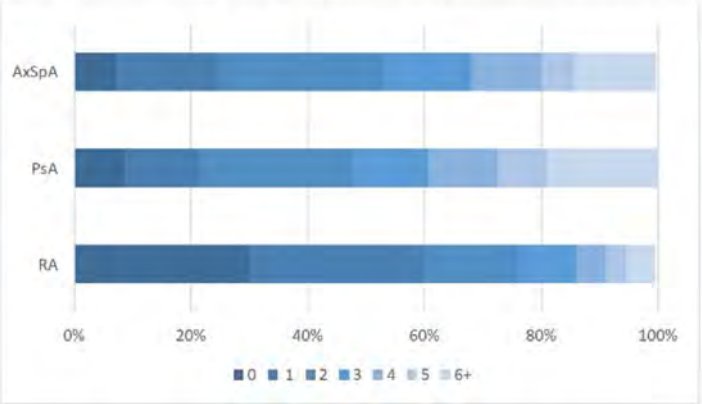
Methods: We queried the data warehouse of the Excellence Network in Rheumatology (ENRGY), a national practice-based research network (PBRN), to identify patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondyloarthritis (AxSpA). Data from the electronic health record (EHR) was linked to a custom in-office tablet app that captures patients' lifetime treatment history, disease duration and other disease features. We used both linked data sources to identify current users of conventional, biologic, or targeted synthetic DMARDS (cs/b/tsDMARDs) and classify them as to their prior treatment history over their lifetime. Results were reported by disease and by medication class

Table: Characteristics of RA, PsA and AxSpA patients eligible for analysis requiring EHR data linked to in-office tablet data

	RA	PsA	AxSpA
N	6,740	1,901	471
Age	64 (55, 72)	60 (50, 69)	54 (44, 64)
Female	5,294 (79%)	1,155 (61%)	234 (50%)
Disease duration, years	6 (4, 11)	5 (3, 11)	5 (3, 11)
Current therapy, %			
MTX, with or without other csDMARDs	1,806 (27%)	251 (13%)	24 (5.1%)
csDMARD(s) without MTX	1,368 (20%)	94 (4.9%)	38 (8.1%)
Apremilast (without biologics/JAKi)	0 (0%)	196 (10%)	1 (0.2%)
TNFi	1,967 (29%)	722 (38%)	312 (66%)
IL-6Ri	238 (3.5%)	0 (0%)	0 (0%)
Abatacept	394 (5.8%)	28 (1.5%)	1 (0.2%)
Rituximab	223 (3.3%)	0 (0%)	0 (0%)
JAKi	744 (11%)	80 (4.2%)	15 (3.2%)
IL-12/23	0 (0%)	46 (2.4%)	2 (0.4%)
IL-17	0 (0%)	338 (18%)	74 (16%)
IL-23	0 (0%)	146 (7.7%)	4 (0.8%)
Glucocorticoids, %	4,040 (60%)	947 (50%)	235 (50%)
Opioids, %	993 (15%)	239 (13%)	72 (15%)
Area deprivation index >=80% (i.e. deprived), %	831 (12%)	161 (8.5%)	55 (12%)

Data shown as median (IQR) or n(%)

Figure 1: Number of Prior Biologics or JAKi in AxSpA, PsA, and RA patients (n=9,112)



Results: As of Q4 2022, we identified 6,740 RA, 1,901 PsA, and 471 AxSpA patients who had linked EHR and self-reported lifetime treatment history data available who were current users of any cs/b/tsDMARDs (Table). The point prevalence of the number of prior biologics and JAKi is shown in the Figure. The proportion of patients who were biologic and JAKi naïve was 30% in RA, 9% in PsA, and 7% in AxSpA (Figure, left-most dark blue panel). The proportion of patients who were biologic naïve or treatment experienced with only 1 current or past biologic or JAKi was 25% in AxSpA, 22% in PsA, and 60% in RA.

Conclusion: Stakeholders interested in developing or marketing new therapies and diagnostic tests that target RA, PsA or AxSpA patients who are biologic naïve or minimally treatment experienced will be advantaged by these estimates as they estimate the potential opportunity and size of the eligible patient population. These proportions are being extrapolated to the U.S. to provide an estimate of the number of patients who might be eligible to receive various treatments or diagnostics that might be positioned or marketed according to line of therapy

Disclosure: J. Curtis: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Janssen, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5; **F. Xie**: None; **Y. Su**: None; **P. Stewart**: None; **A. Mudano**: None.

Abstract Number: 2138

Frailty Is a Predictor of Incident Osteoporotic Fractures in Veterans with Rheumatoid Arthritis

K Wysham[1], Hannah Brubeck[2], Aaron Baraff[3], Punyasha Roul[4], Namrata Singh[5], James Andrews[6], Grant Cannon[7], Gary Kunkel[8], Ted R Mikuls[9], Bryant England[4], Dolores Shoback[10], Patti Katz[11], Jose Garcia[12], Ariela Orkaby[13] and Joshua Baker[14], [1]VA Puget Sound/University of Washington, Seattle, WA, [2]VA Puget Sound Health Care System, Seattle, WA, [3]VA Puget Sound Seattle, Seattle, WA, [4]University of Nebraska Medical Center, Omaha, NE, [5]University of Washington, Bellevue, WA, [6]University of Washington, Seattle, WA, [7]University of Utah and Salt Lake City VA, Salt Lake City, UT, [8]University of Utah, Salt Lake City, UT, [9]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE, [10]San Francisco VA Medical Center, San Francisco, CA, [11]University of California San Francisco, San Rafael, CA, [12]VA Puget Sound Healthcare System, Seattle, WA, [13]Veterans Affairs Boston Healthcare System & Brigham and Women's Hospital, Harvard Medical School, Boston, MA; VA Geriatric Research Education and Clinical Center, Boston, MA, [14]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Table 1. Baseline demographics and clinical characteristics.			
	No Fracture N=2673 (92%)	Fracture N=240 (8%)	Total N=2913
Age	64.3 ± 11.1	64.5 ± 9.9	64.3 ± 11.0
Female Sex	305 (11%)	45 (19%)	350 (12%)
Black Race	448 (17%)	25 (10%)	473 (16%)
BMI			
<18.5	24 (1%)	2 (1%)	26 (1%)
18.5-24.9	643 (24%)	64 (27%)	707 (24%)
25.0-29.9	979 (37%)	94 (39%)	1073 (37%)
30.0-34.9	624 (23%)	46 (19%)	670 (23%)
35.0-39.9	226 (9%)	21 (9%)	247 (9%)
≥40	105 (4%)	12 (5%)	117 (4%)
Anti-CCP Positivity*			
Positive	1730 (78%)	175 (76%)	1905 (78%)
Negative	497 (22%)	56 (24%)	553 (22%)
Smoking			
Never	558 (21%)	58 (24%)	616 (21%)
Former	1406 (53%)	114 (48%)	1520 (52%)
Current	645 (24%)	66 (28%)	711 (24%)
Prior Fracture	747 (28%)	83 (35%)	830 (29%)
DAS28ESR (mean)	3.8 ± 1.6	4.0 ± 1.5	3.8 ± 1.6
Prednisone use	892 (33%)	92 (38%)	984 (34%)
csDMARD use	2056 (77%)	183 (76%)	2239 (77%)
bDMARD use	763 (29%)	65 (27%)	828 (28%)
Frailty Category			
Robust	824 (31%)	59 (25%)	883 (30%)
Pre-Frail	1025 (38%)	86 (36%)	1111 (38%)
Mild Frailty	461 (17%)	59 (25%)	520 (18%)
Moderate Frailty	177 (7%)	25 (10%)	202 (7%)
Severe Frailty	64 (2%)	11 (5%)	75 (3%)

-BMI: body mass index, CCP: cyclic citrullinated peptide, DAS28ESR: disease activity score 28 with ESR, csDMARD: conventional synthetic disease modifying antirheumatic drug, bDMARD: biologic disease modifying antirheumatic drug.
* Anti-CCP percentage based on total of those without missing data. Missing N=455 (16%).

Background/Purpose: Frailty occurs prematurely in RA. Levels of frailty are higher in Veteran populations than civilians[1]. Frailty has been shown to predict osteoporotic fractures in a single Canadian RA cohort, however the frailty instrument lacked external validation[2]. The aim of this study was to evaluate whether frailty predicted incident osteoporotic fractures in Veterans with RA using an externally validated frailty index.

Methods: We used data from the national Veterans Affairs Rheumatoid Arthritis (VARA) Registry 1/2003-12/31/2021. Baseline frailty was calculated using the VA Frailty Index (VAFI)[1]. The VAFI is based on diagnostic and CPT codes which are categorized into 31 deficits including morbidity, function, mood, cognition and geriatric syndromes. Osteoporotic fractures were identified by searching fracture-related diagnostic and procedure codes and subsequently validated by chart review. High-trauma, periprosthetic and pathologic fractures related to cancer were excluded. Missing data at baseline were imputed using multiple imputation with chained equations with 10 iterations and for further time points using the last observation carried forward. Age-adjusted fracture incidence rates were calculated. Multivariable Cox regression evaluating the relationship between baseline frailty and incident osteoporotic fracture was performed adjusting for baseline age, sex, race, smoking status, anti-cyclic citrullinated peptide (CCP) positivity and prior osteoporotic fracture; and time-varying body mass index (BMI), DAS28ESR, prednisone use, conventional synthetic disease modifying antirheumatic drug (DMARD) use, and biologic DMARD use. Participants were followed from enrollment and censored at osteoporotic fracture, death or end of study period.

Results: 2,930 Veterans were included, mean age 64±11 years. Compared to those without incident osteoporotic fracture, those with fracture were more frequently female (19% vs 11%), less frequently Black (10% vs 17%) and had more pre-enrollment fractures (35% vs 28%) (Table 1). Age, anti-cyclic citrullinated peptide (CCP) positivity, BMI, disease activity and medication use at baseline were similar between those who did and did not fracture. There were higher rates of baseline

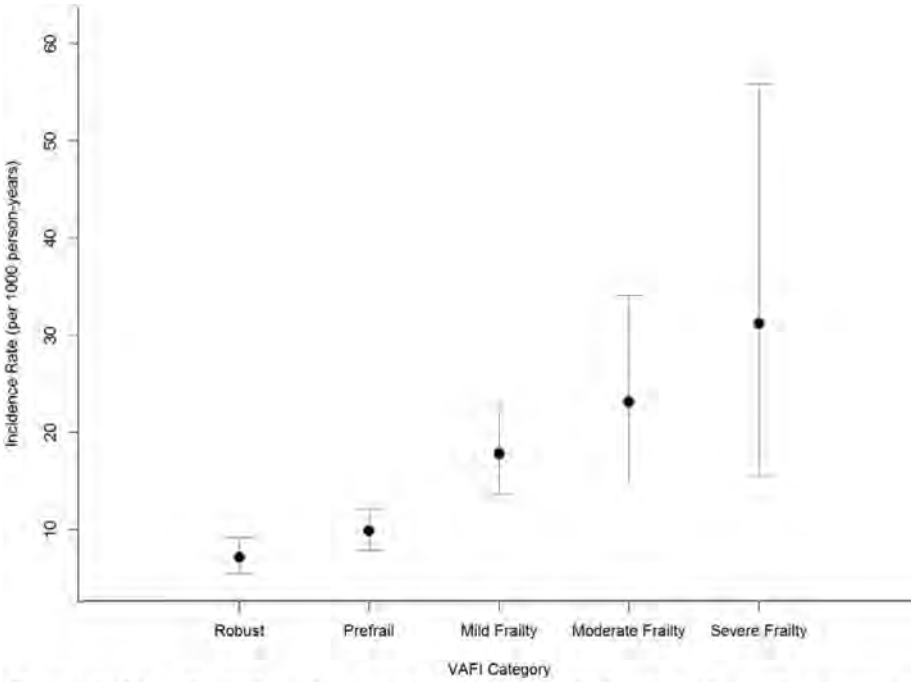


Figure 1. Age-adjusted incidence rates of osteoporotic fractures by frailty category.

Table 2. Unadjusted and adjusted cox models evaluating relationship between frailty and incident osteoporotic fracture.

Frailty Category	HR	95% CI	p-value	aHR*	95% CI	p-value
Robust	ref	--	--	ref	--	--
Pre-Frail	1.54	1.10-2.16	0.0134	1.38	0.97-1.95	0.0748
Mild Frailty	2.85	1.96-4.13	<0.0001	2.16	1.45-3.22	0.0002
Moderate Frailty	3.88	2.41-6.25	<0.0001	3.04	1.83-5.03	<0.0001
Severe Frailty	5.32	2.77-10.21	<0.0001	4.54	2.28-9.03	<0.0001

*Model was adjusted for baseline age, sex, race, smoking status, anti-cyclic citrullinated peptide (CCP) positivity and prior osteoporotic fracture; and time-varying body mass index (BMI), DAS28ESR, prednisone use, conventional synthetic disease modifying antirheumatic drug (DMARD) use and biologic (DMARD) use.

frailty in the fracture group (25% vs 17% mild frailty, 10% vs 7% moderate frailty, and 5% vs 2% severe frailty). Over the 21,800 person-years of observation, 240 incident osteoporotic fractures occurred (79 extremity, 58 rib, 47 spine, 43 hip and 13 pelvis). Age-adjusted incidence rates of osteoporotic fractures increased by frailty category (Figure 1). In the multivariable Cox model, mild, moderate and severe frailty each had significantly increased risk of incident osteoporotic fracture compared to those who were robust (Table 2; aHR 2.16 [95% CI 1.45-3.22], 3.04 [95%CI 1.83-5.03] and 4.54 [95%CI 2.28-9.03]; all $p < 0.001$, respectively).

Conclusion: Baseline frailty is associated with incident osteoporotic fractures in Veterans with RA. Frailty measurement in RA using the VAFI, a validated, automated tool, may prove to be useful in identifying Veterans at high risk for osteoporosis and fractures. [1]Orkaby AR et al. *J Gerontol A Biol Sci Med Sci*. 2019 [2] Li G et al. Bone. 2019

Disclosure: K. Wysham: None; **H. Brubeck**: None; **A. Baraff**: None; **P. Roul**: None; **N. Singh**: None; **J. Andrews**: None; **G. Cannon**: None; **G. Kunkel**: None; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **B. England**: Boehringer-Ingelheim, 2, 5; **D. Shoback**: None; **P. Katz**: None; **J. Garcia**: None; **A. Orkaby**: Anthos therapeutics, 2; **J. Baker**: Bristol-Myers Squibb(BMS), 2, Burns-White, LLC, 2, CorEvitas, LLC, 2, Pfizer, 2.

Abstract Number: 2139

Associations of Adipocytokines with Cancer Incidence in a Prospective Rheumatoid Arthritis Cohort

Namrata Singh[1], Aaron Baraff[2], K Wysham[3], Punyasha Roul[4], Grant Cannon[5], Brian Sauer[6], Geoffrey Thiele[4], Bryant England[4], Ted R Mikuls[7] and Joshua Baker[8], [1]University of Washington, Bellevue, WA, [2]VA Puget Sound Seattle, Seattle, WA, [3]VA Puget Sound/University of Washington, Seattle, WA, [4]University of Nebraska Medical Center, Omaha, NE, [5]University of Utah and Salt Lake City VA, Salt Lake City, UT, [6]Salt Lake City VA/University of Utah, Salt Lake City, UT, [7]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE, [8]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: A prior study suggested a higher risk of cancer mortality in patients with rheumatoid arthritis (RA) with higher levels of circulating leptin, an adipocytokine [1]. Leptin and leptin receptor signaling pathway have been implicated in various key processes in cancer progression, such as cell proliferation, metastasis, and angiogenesis [2]. We examined the associations between circulating adipocytokines with incident cancer in Veterans with RA.

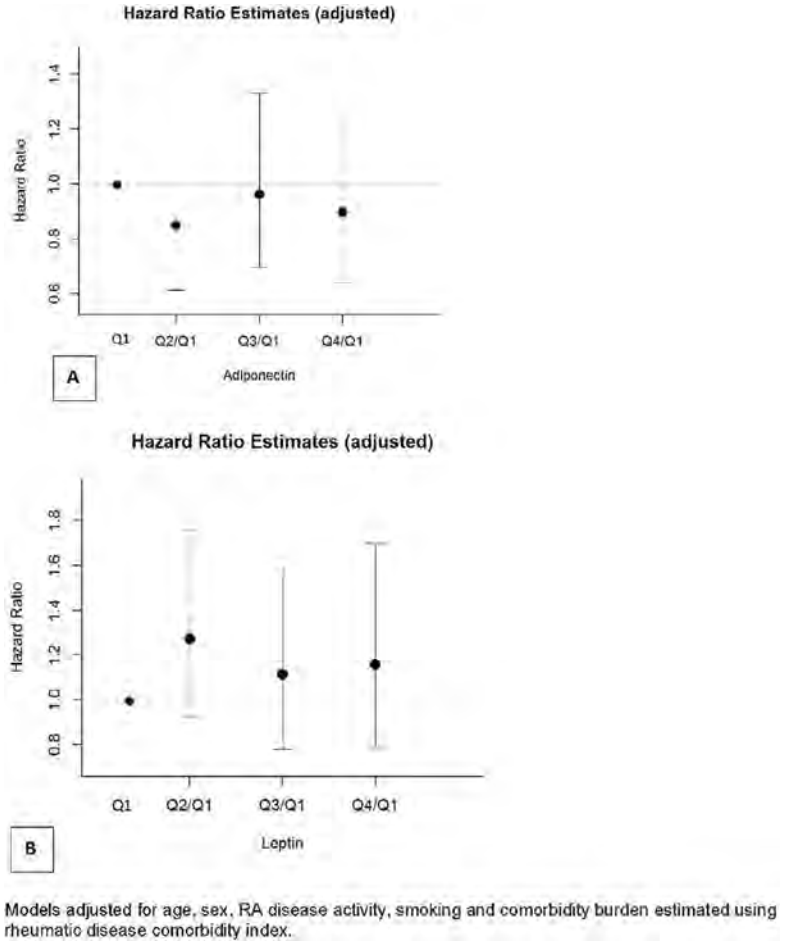


Figure 1. Multivariable model of adipocytokine quartiles and incident overall cancer with reference to quartile 1.

Methods: Veterans enrolled in Veterans Affairs RA (VARA) registry, a multicenter prospective RA cohort, without a prior history of cancer were eligible for this study. Adipocytokines (adiponectin and leptin) were measured as part of a multi-analyte panel on banked serum at VARA enrollment. Records were linked to VA central cancer registry to identify incident cancers. Participants were followed from enrollment to the first of incident cancer, death, or end of study period (2/1/23). Associations between adipocytokine levels (divided into quartiles) and incident overall cancers were assessed in Cox regression models accounting for covariates (measured at baseline) including age, sex, RA disease activity, smoking status, and comorbidity burden estimated using rheumatic disease comorbidity index (RDCI). In a sub-analysis, we also assessed associations between adipocytokine levels and incident lung cancer, the most frequent malignancy in this cohort.

Results: 2391 Veterans met eligibility criteria of whom 87.7% were male. Higher adiponectin levels were associated with older age, lower BMI, former smoking status. Higher leptin levels were associated with higher BMI and higher comorbidity scores. Over a median (interquartile range) 6.2 (6.9) years of follow-up, there were 322 incident cancers. The most common cancers observed were: lung (n= 75), prostate (n= 61), gastrointestinal cancers (n=42), and hematological (n=40). In multivariable Cox Proportional hazard models, we did not observe a significant association between levels of adiponectin

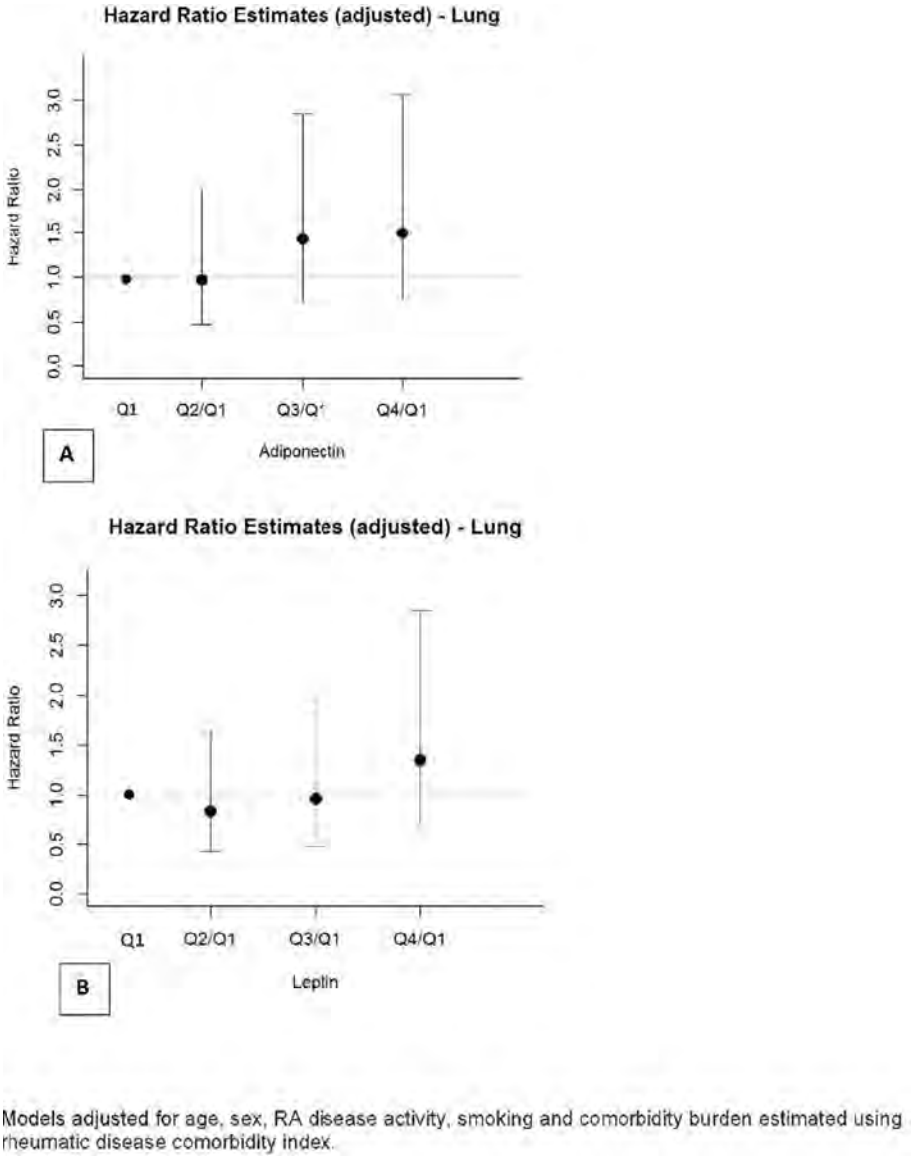


Figure 2. Multivariable model of adipocytokine quartiles and incident lung cancer with reference to quartile 1.

(HR 0.90, 95% confidence interval, CI, 0.64-1.26 for quartile 4 versus quartile 1) (**Figure 1, panel A**) or leptin (HR for quartile 4 versus first quartile 1.16, 95% CI 0.79-1.70) with incident cancer (**Figure 1, panel B**). Those with the highest adiponectin or leptin levels tended to have higher incidence of lung cancer although the associations were not statistically significant (**Figure 2**).

Conclusion: In this study, we did not observe an association between levels of adipocytokines and incident overall cancer risk and specifically lung cancer risk in Veterans with RA. Further studies will explore the association between adipocytokines and incidence of specific cancers, especially obesity-related cancers.

References: 1. Baker JF, England BR, George MD, et al. Elevations in adipocytokines and mortality in rheumatoid arthritis. *Rheumatology (Oxford)*. 2022;61(12):4924-4934. 2. Lin TC, Hsiao M. Leptin and Cancer: Updated Functional Roles in Carcinogenesis, Therapeutic Niches, and Developments. *Int J Mol Sci*. 2021;22(6).

Disclosure: N. Singh: None; **A. Baraff**: None; **K. Wysham**: None; **P. Roul**: None; **G. Cannon**: None; **B. Sauer**: None; **G. Thiele**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **J. Baker**: CorEvitas, 2, Cumberland Pharma, 2, Horizon Pharmaceuticals, 5.

Abstract Number: 2140

Serum Alarmins and the Risk of Interstitial Lung Disease in Patients with Rheumatoid Arthritis

Ted R Mikuls[1], Bryant England[2], Harlan Sayles[2], Tate Johnson[2], Michael Duryee[2], Carlos Hunter[2], Joshua Baker[3], Gail Kerr[4], Gary Kunkel[5], Grant Cannon[6], Brian Sauer[7], K Wysham[8], Amy Joseph[9], Beth Wallace[10], Geoffrey Thiele[2] and Jill Poole[2], [1]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE, [2]University of Nebraska Medical Center, Omaha, NE, [3]University of Pennsylvania, Philadelphia, PA, [4]Washington DC VAMC/ Georgetown and Howard Universities, Washington, DC, [5]University of Utah, Salt Lake City, UT, [6]University of Utah and Salt Lake City VA, Salt Lake City, UT, [7]Salt Lake City VA/University of Utah, Salt Lake City, UT, [8]VA Puget Sound/University of Washington, Seattle, WA, [9]Washington University / St. Louis VA, St. Louis, MO, [10]Ann Arbor VA, Ann Arbor, MI

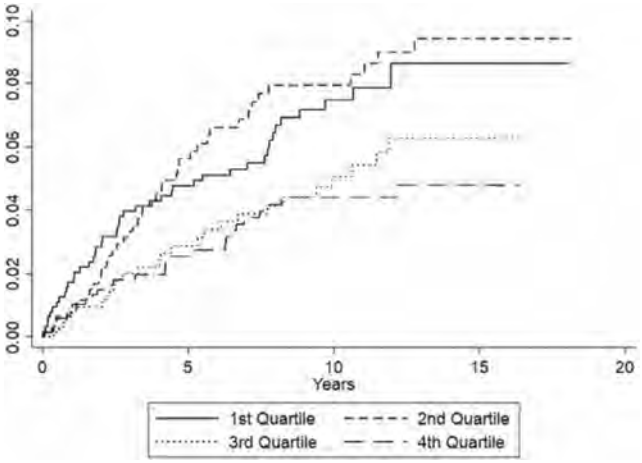
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Alarmins are proteins found in the nuclei of epithelial, endothelial, and immune cells that are released following cell damage and act as stress signals. Facilitating tissue homeostasis and repair, alarmins have also been implicated in the pathogenesis of both rheumatoid arthritis (RA) and tissue fibrosis in other conditions including idiopathic pulmonary fibrosis (Lee JU et al. BMC Pulm Med 2017). The objective of the current study was to quantify associations of serum alarmins with risk of rheumatoid arthritis-associated interstitial lung disease (RA-ILD).

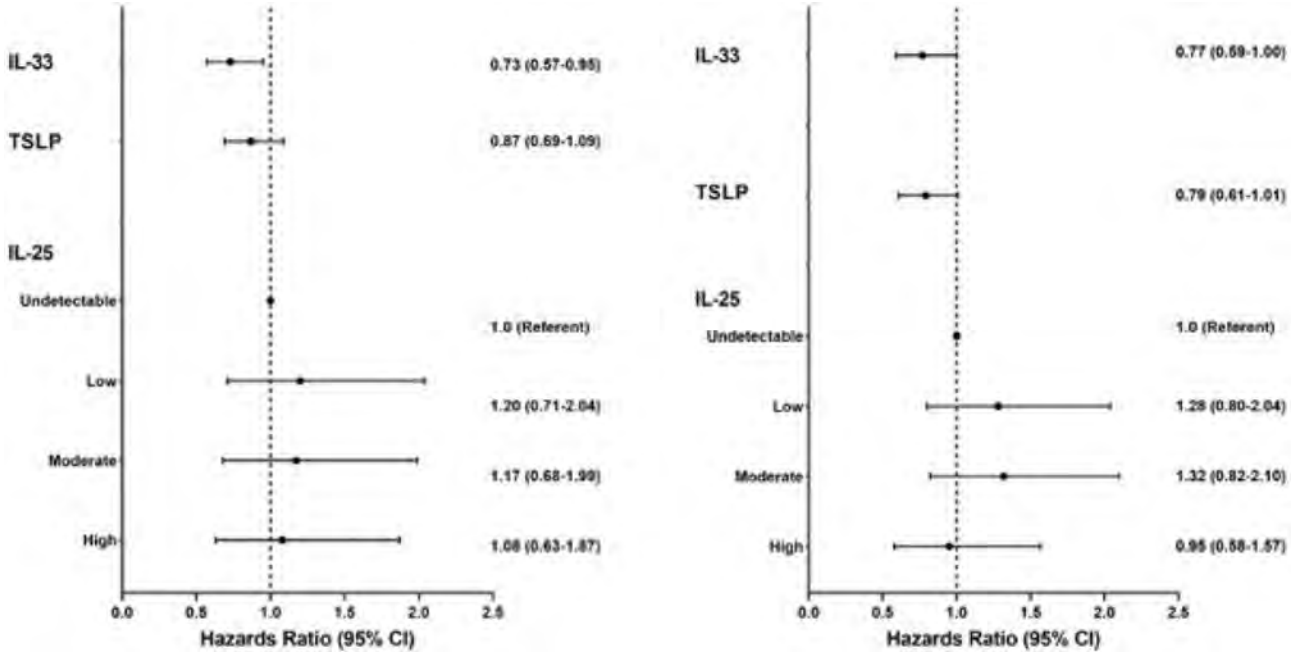
Methods: Three alarmins (IL-33, thymic stromal lymphopoietin [TSLP], and IL-25) were measured using serum collected at enrollment from the multicenter prospective Veterans Affairs RA registry. RA-ILD was classified using systematic medical record review and based on a provider diagnosis of ILD, plus either consistent findings from chest CT or histopathological abnormalities. Given their distributions, IL-33 and TSLP concentrations were log-transformed and standardized (per 1 SD), while detectable IL-25 was categorized into tertiles (undetectable as referent). Cross-sectional associations of alarmin values with RA-ILD at enrollment (prevalent RA-ILD) were examined using separate logistic regression models. Associations

of alarmins with incident RA-ILD were examined using Cox proportional hazards regression. Covariates in multivariate models included age, sex, race, smoking status, RA disease activity score, and anti-CCP antibody positivity. For analytes associated with incident RA-ILD, the cumulative incidence of ILD was summarized graphically by alarmin quartile.

Results: Of 2,835 study participants (88% male, mean age 65 ± 11 years, 77% White, 76% current or former smoker), 115 participants (4.1%) had prevalent RA-ILD at baseline. An additional 146 (5.1%) developed incident ILD over a median follow-up of 3.0 years (IQR 1.2-6.3 years). There were no associations between serum alarmins and prevalent ILD in unadjusted or adjusted logistic regression models (not shown). Likewise, no significant associations of TSLP or IL-25 with incident ILD were observed. The cumulative incidence of RA-ILD development by IL-33 quartile among those without ILD at enrollment is shown in **Figure 1.** After 10 years of follow-up, approximately 8% of uncensored patients with RA in the lower



Cumulative incidence of developing incident RA-ILD based on baseline IL-33 quartile.



Univariate (left) and multivariable (right) associations of alarmin concentrations with the development of incident RA-ILD. Models for each analyte examined separately; multivariable models adjusted for age, sex, race, smoking status, DAS28, and anti-CCP status; univariate p-values for IL-33 = 0.018; TSLP = 0.222; IL-25 (trend test) = 0.930; multivariable p-values for IL-33 = 0.047; TSLP = 0.056; IL-25 (trend test) = 0.912; IL-33 and TLSP log-transformed, HR reported per log-fold increase.

two IL-33 quartiles had developed ILD compared to approximately 4% in the upper two quartiles. There was a significant inverse association between IL-33 concentration and risk of developing incident RA-ILD in unadjusted (HR 0.73 per log-fold increase; 95% CI 0.57-0.95; p=0.018) and adjusted (HR 0.77; 95% CI 0.59-1.00, p=0.047) models (**Figure 2**).

Conclusion: In contrast to our a priori hypothesis, we observed a significant inverse association between serum IL-33 concentration and the risk of developing incident RA-ILD. These results suggest that by promoting tissue homeostasis and repair, circulating IL-33 could play a protective role in the 'pre-clinical' stages of RA-ILD and its measurement could improve risk stratification efforts in addition to informing future strategies of treatment and prevention.

Disclosure: T. Mikuls: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **B. England**: Boehringer-Ingelheim, 2, 5; **H. Sayles**: None; **T. Johnson**: None; **M. Duryee**: None; **C. Hunter**: None; **J. Baker**: CorEvitas, 2, Cumberland Pharma, 2, Horizon Pharmaceuticals, 5; **G. Kerr**: AstraZeneca, 2, Aurinia, 6, Horizon, 2, Janssen, 2, Pfizer, 1, Sanofi, 2; **G. Kunkel**: None; **G. Cannon**: None; **B. Sauer**: None; **K. Wysham**: None; **A. Joseph**: None; **B. Wallace**: None; **G. Thiele**: None; **J. Poole**: AstraZeneca, 12, I have received no monies. I received anti-IL-33 monoclonal antibody from AstraZeneca for animal research sutdies.

Abstract Number: 2141

Glucocorticoid Treatment in Early Rheumatoid Arthritis Is Associated with Increased Proprotein Convertase Subtilisin/kexin Type 9 (PCSK9) Levels: A Post-hoc Analysis of a Randomized Controlled Trial (NORD-STAR)

Kristina Lend[1], Jos W.R. Twisk[2], Nupur Kumar[3], John Lampa[4], Anna Rudin[5], Merete Hetland[6], Till Uhlig[7], Dan Nordstrom[8], Mikkel Østergaard[9], Marte Schrumpf Heiberg[10], Espen A Haavardsholm[10], Bjorn Gudbjornsson[11], Tuulikki Sokka-Isler[12], Gerdur Maria Grondal[13], Kim Hørslev-Petersen[14], Michael Nurmohamed[2], Ronald van Vollenhoven[2] and Johan Frostegård[3], [1]Amsterdam UMC, Karolinska Institute, Stockholm, Sweden, [2]Amsterdam University Medical Centers, Amsterdam, Netherlands, [3]Karolinska Institutet, Stockholm, Sweden, [4]Stockholm County, Hässelby, Sweden, [5]Department of Rheumatology and Inflammation Research, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, [6]Copenhagen Center for Arthritis Research, Rigshospitalet, Copenhagen, Denmark, [7]Center for Treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway, [8]Helsinki University Hospital, Helsinki, Finland, [9]Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Centre for Head and Orthopaedics, Rigshospitalet; University of Copenhagen, Copenhagen, Denmark, [10]Diakonhjemmet Hospital, Oslo, Norway, [11]Centre for Rheumatology Research, University Hospital, Reykjavik, Iceland, [12]Jyvaskyla Central Hospital, Jyväskylä, Finland, [13]Department for Rheumatology, Landspitali University Hospital, Reykjavik, Iceland, [14]University of Southern Denmark, Odense, Denmark

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Treatments Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is associated with an elevated risk for developing atherosclerotic cardiovascular disease (CVD). Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a key regulator of low-density lipoprotein (LDL) metabolism as it gives an increased breakdown of LDL-receptors on the liver resulting in enhanced LDL-cholesterol levels. We aimed to investigate i) the influence of glucocorticoids and biologic treatments on PCSK9 levels and ii) whether the presence of autoantibodies associates with the changes in the PCSK9 levels in DMARD-naïve early RA patients after treatment.

Table 1. Baseline characteristics and the medication of interest at baseline and at 24 weeks of patients with early rheumatoid arthritis.

	Group 1: glucocorticoids plus methotrexate (n=75)	Group 2: certolizumab-pegol plus methotrexate (n=84)	Group 3: abatacept plus methotrexate (n=89)	Group 4: tocilizumab plus methotrexate (n=82)	Total (n=330)
Baseline characteristics					
Female	49/75 (65%)	57/84 (68%)	60/89 (67%)	56/82 (68%)	222/330 (67%)
Age (years)	57.5 (14.7)	54.3 (16.2)	55.5 (15.2)	54.0 (12.8)	55.3 (14.8)
Body-mass index, kg/m^2	26.4 (5.0)	25.2 (4.4)	26.1 (4.4)	26.4 (5.0)	26.0 (4.7)
Anti-citrullinated peptide antibody positive	62/75 (83%)	66/84 (79%)	73/89 (82%)	71/82 (87%)	272/330 (82%)
Rheumatoid factor positive	55/75 (73%)	66/84 (79%)	71/89 (80%)	67/82 (82%)	259/330 (79%)
Antinuclear antibody positive	24/69 (35%)	30/78 (39%)	34/87 (39%)	21/80 (26%)	109/314 (35%)
Medication of interest					
Statin use at baseline	8/75 (11%)	6/84 (7%)	9/89 (10%)	5/82 (6%)	28/330 (9%)
Statin use at 24 weeks	11/75 (15%)	6/84 (7%)	8/89 (9%)	7/82 (9%)	32/330 (10%)
Oral glucocorticoids dose at 24 weeks (mg)	4.9 (1.3)	0.1 (0.8)	0.2 (1.0)	0.4 (1.5)	1.3 (2.3)
Cumulative glucocorticoids dose (mg)	1500.3 (170.4)	29.8 (136.4)	42.7 (207.5)	96.4 (298.0)	384.0 (642.5)

Data are n/N (%) or mean (SD). PCSK9= Proprotein convertase subtilisin/kexin type 9.

Methods: In this post-hoc analysis of the phase 4 NORD-STAR randomized controlled trial, PCSK9 levels were assessed in 330 Swedish patients who were randomised (1:1:1:1) to receive methotrexate (MTX) in combination with glucocorticoids (GC), certolizumab-pegol (CZP), abatacept (ABA), or tocilizumab (TCZ). PCSK9 levels were determined by commercial ELISA kit (R&D Systems, UK) at baseline and 24 weeks after the initiation of randomised RA treatment. The assay range of ELISA was 125.0–8000 pg/mL. Linear regression models were used to analyse the difference between the treatment groups on PCSK9 levels at 24 weeks. Analyses were adjusted for the baseline level of PCSK9, sex, age, BMI, DAS28-CRP, anti-citrullinated protein antibody (ACPA) status, rheumatoid factor (RF) status, and statin use at 24 weeks. In a second analysis, the interaction between the treatment groups and RF, ACPA and antinuclear antibody (ANA) were added to the model.

Results: Baseline characteristics and the medications of interest are shown in Table 1. The mean PCSK9 levels at baseline were similar across treatment groups. At 24 weeks, highest PCSK9 levels were observed in the MTX+GC treatment group (see table 2). The mean PCSK9 levels at 24 weeks were as follows: MTX+GC (1934 pg/mL [SD 888]); CZP+MTX (1679 [759]); ABA+MTX (1693 [634]); and TCZ+MTX (1784 [761]). Because the effect of the three biological treatment groups on PCSK9 levels at week 24 were more or less the same, for the analyses with the interactions with RF, ACPA and ANA, we

Table 2. Mean levels of PCSK9 at baseline and 24 weeks after the initiation of randomised RA treatment.

PCSK9 (pg/mL)	Baseline	At 24 weeks
Glucocorticoids plus methotrexate	1656 (895)	1934 (888)
Certolizumab-pegol plus methotrexate	1655 (865)	1679 (759)
Abatacept plus methotrexate	1669 (689)	1693 (634)
Tocilizumab plus methotrexate	1772 (965)	1784 (761)

Data are mean (SD). PCSK9=Proprotein convertase subtilisin/kexin type 9.

Table 3. Results of interaction analysis estimating the influence of autoantibody status on PCSK9 levels between glucocorticoid treatment and pooled biologic treatment at 24 weeks.

	Glucocorticoid treatment plus methotrexate (n=75)	Biologic treatment plus methotrexate (n=255)	P interaction
PCSK9 (pg/mL) levels at 24 weeks	**Ref**	-194.9 (-374.1 to -15.8); **p=0.03**	-
Interaction analyses			
Rheumatoid factor status			
positive	**Ref**	-311.8 (-517.5 to -106.1); **p=0.003**	**0.03**
negative	**Ref**	154.7 (-201.2 to 510.6); p=0.39	
Anti-citrullinated peptide antibody status			
positive	**Ref**	-278.2 (-474.0 to -82.4); **p=0.005**	**0.04**
negative	**Ref**	207.7 (-222.5 to 637.8); p=0.34	
Antinuclear antibody status			
positive	**Ref**	-440.2 (-763.8 to -116.5); **p=0.008**	**0.09**
negative	**Ref**	-98.5 (-328.9 to 131.9); p=0.40	

PCSK9=Proprotein convertase subtilisin/kexin type 9. Biologic treatment refers to a treatment with either certolizumab-pegol, abatacept, or tocilizumab. Analyses were adjusted for the baseline PCSK9 level, sex, age, BMI, DAS28-CRP, ACPA status, RF status, and statin use at 24 weeks.

combined the three biological treatment groups into one group in order to increase power. At 24 weeks, PCSK9 levels were significantly lower in the pooled biologic treatment group compared with the GC+MTX treatment group(β coefficient -194.9; 95% CI -374.1 to -15.8). Interaction analyses demonstrated that the differences between MTX+GC and biological treatments was most pronounced for RF, ACPA and ANA positive patients (See table 3).

Conclusion: Glucocorticoid treatment was associated with increased PCSK9 levels at 24 weeks. These increases were observed primarily in RF, ACPA, ANA positive patients. Our data provide a potential mechanistic link between glucocorticoid treatment and cardiovascular disease.

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Abstract Number: 2142

Adherence Patterns in Rheumatoid Arthritis Patients Receiving a Janus Kinase (JAK) Inhibitor or a Tumor Necrosis Factor α Inhibitor (TNFi) After the Addition of a Black Box Warning to JAK Inhibitors

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In 2021, the FDA concluded that there is an increased risk of serious heart-related events with the Janus Kinase (JAK) inhibitor tofacitinib, which is currently indicated for rheumatoid arthritis (RA), psoriatic arthritis (PsA), ulcerative colitis (UC), ankylosing spondylitis (AS) and polyarticular course juvenile idiopathic arthritis (pcJIA). Accordingly, a black box warning was applied to the JAK class for drugs that are indicated for the treatment of arthritis and other inflammatory conditions. Tumor necrosis factor α inhibitors (TNFi) do not carry a black box warning for these adverse events. It is unknown if prescribing patterns or patient behavior was impacted in response to the new black box warning.

Methods: This is a retrospective cohort study of RA patients receiving a JAK inhibitor or TNFi. Patients were included if they received at least 3 fills for a JAK inhibitor or TNFi between 4/1/2021 and 8/31/2022 and maintained coverage until 8/31/2022. Three periods were assessed: pre-black box warning (4/1/2021 – 8/31/2021), washout (9/1/2021-12/1/2021), and post-black box warning period (12/2/2021-8/31/2022). Propensity score matching was conducted utilizing the patient's demographic profile, including age, gender, socioeconomic status (SES), location, and comorbid conditions. Adherence was measured using proportion of days covered (PDC) and was evaluated overall and during each period. Discontinuation was determined if the last fill occurred greater than 30 days from the end of the study. Discontinuation rates were calculated for each period; p-values < 0.05 were significant.

Results: A total of 815 patients were included in the unmatched analysis, with 215 (26.4%) receiving JAK inhibitors. Differences in age and gender were found between JAK inhibitor and TNFi patients (mean age (SD): 54.8 [8.9] vs 52.4 [11.4] years in JAK inhibitor vs TNFi, $p = 0.002$; 36 (16.7%) vs 149 (24.8%) males in JAK inhibitor vs TNFi, $p=0.02$). No differences in SES or comorbidity were found. Patients prescribed JAK inhibitors had higher median PDC (5.6%; $p=0.022$) during the study compared to TNFi patients and higher median PDC (7.1%; $p = 0.014$) during the post-black box warning period. No difference in discontinuation rates were found overall and stratified by study period. After matching, 408 patients were evaluated with 50% receiving JAK inhibitors; no differences in underlying demographics or comorbidities were found. Adherence metrics were similar between matched cohorts. There were no significant differences in median PDC (1.8%; $p=0.235$) or discontinuation rates (28.9% vs 27.9%), in JAK inhibitor and TNFi groups, respectively, $p = 0.529$.

Conclusion: Adherence and persistence to JAK inhibitors were not significantly impacted by the addition of the black box warning.

Disclosure: W. Rutter: CVS Health, 3, 11; **K. Patel**: CVS Health, 3, 11; **S. Delgado**: CVS Health, 3, 11; **G. Cozzi**: CVS Health, 3, 11; **E. Avalos-Reyes**: AstraZeneca, 11, CVS Health, 3, 11, GlaxoSmithKlein(GSK), 11, Haleon, 11, Johnson & Johnson, 11, Moderna, 11, Novavax, 11, Pfizer, 11, Viatris, 11; **W. Cavers**: Amedisys Inc, 11, Baxter, 11, Conmed

Corp, 11, CVS Health, 3, 11; **C. Liu**: CVS Health, 3, 11; **R. Grover**: CVS Health, 3, 11; **L. Feczko**: Baxter, 11, CVS Health, 3, 11; **K. Johnson**: CVS Health, 3, 4, 11, HC Technology Patent, 10.

Abstract Number: 2143

Efficacy of Filgotinib in Patients with Rheumatoid Arthritis: Week 156 Results from a Long-term Extension Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Treatments Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: In the treatment of RA, JAK inhibitors are a valuable option to meet remission or low disease activity (LDA) treatment targets following an inadequate response (IR) or intolerance to ≥ 1 conventional synthetic disease-modifying antirheumatic drug (DMARD). Filgotinib (FIL) is a JAK1 preferential inhibitor available in two doses for the treatment of moderate to severe RA. The objective of this analysis was to evaluate long-term efficacy of two doses of FIL in clinically relevant pt populations. Response rates for Boolean remission 2.0 were reported as an exploratory objective.

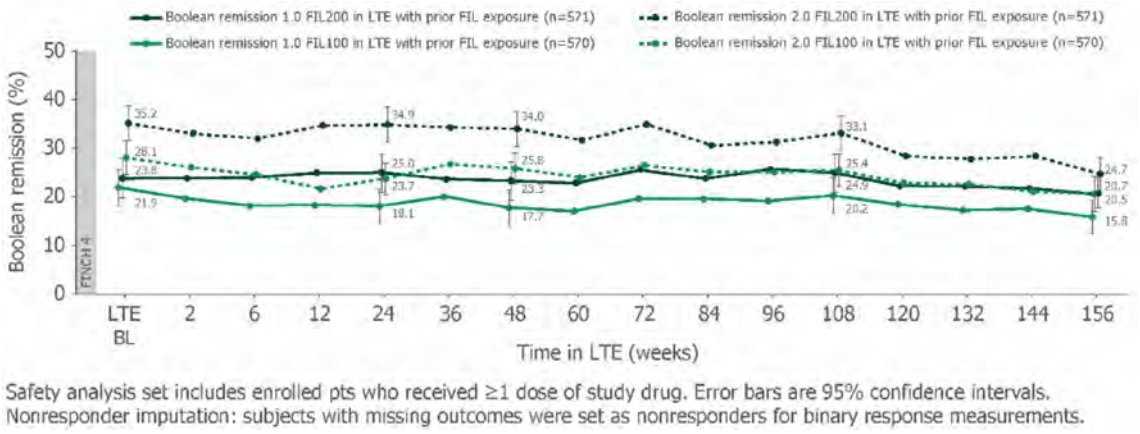

Figure. Boolean remission 1.0 and 2.0 for MTX-IR pts in FINCH 4 LTE through W156 (safety analysis set, nonresponder imputation)

Table. Efficacy in MTX-IR and bDMARD-IR pts through W156 in FINCH 4 (safety analysis set; nonresponder imputation)

		n*	DAS28-CRP <2.6 n (%)	CDAI ≤2.8 n (%)	SDAI ≤3.3 n (%)	Pain mean change (SD)	HAQ-DI mean change (SD)
MTX-IR							
LTE BL	**FIL200/FIL200**	571	344 (60.2)	190 (33.3)	195 (34.2)	−43 (26.5)	−0.95 (0.648)
	FIL100/FIL100	570	301 (52.8)	159 (27.9)	156 (27.2)	−41 (26.1)	−0.81 (0.641)
	ADA/FIL200	128	77 (60.2)	32 (25.0)	40 (31.3)	−43 (24.4)	−0.82 (0.630)
	ADA/FIL100	130	70 (53.8)	39 (30.0)	38 (29.2)	−38 (27.4)	−0.86 (0.642)
LTE W156	**FIL200/FIL200**	571	253 (44.3)	153 (26.8)	151 (26.4)	−42 (27.0)	−0.94 (0.666)
	FIL100/FIL100	570	216 (37.9)	125 (21.9)	121 (21.2)	−38 (27.6)	−0.77 (0.645)
	ADA/FIL200	128	50 (39.1)	29 (22.7)	28 (21.9)	−40 (25.6)	−0.81 (0.642)
	ADA/FIL100	130	38 (29.2)	24 (18.5)	25 (19.2)	−33 (26.3)	−0.78 (0.639)
bDMARD-IR							
LTE BL	**FIL200/FIL200**	132	46 (34.8)	29 (22.0)	25 (18.9)	−34 (28.4)	−0.68 (0.627)
	FIL100/FIL100	124	37 (29.8)	23 (18.5)	25 (20.2)	−31 (31.2)	−0.54 (0.663)
	PBO/FIL200	59	8 (13.6)	3 (5.1)	3 (5.1)	−17 (29.4)	−0.26 (0.583)
	PBO/FIL100	55	10 (18.2)	6 (10.9)	4 (7.3)	−21 (28.6)	−0.38 (0.604)
LTE W156	**FIL200/FIL200**	132	42 (31.8)	32 (24.2)	29 (22.0)	−39 (30.4)	−0.76 (0.741)
	FIL100/FIL100	124	31 (25.0)	17 (13.7)	14 (11.3)	−35 (28.3)	−0.70 (0.713)
	PBO/FIL200	59	15 (25.4)	9 (15.3)	8 (13.6)	−27 (30.1)	−0.67 (0.866)
	PBO/FIL100	55	12 (21.8)	7 (12.7)	8 (14.5)	−27 (25.9)	−0.58 (0.734)

*Pain and HAQ-DI: MTX-IR LTE BL FIL200/200 (n=569); LTE W156 FIL200/200 (n=414), FIL100/100 (n=405), ADA/FIL200 (n=87), ADA/FIL100 (n=83). bDMARD-IR LTE BL FIL100/100 (n=123); LTE W156 FIL200/200 (n=80), FIL100/100 (n=74), PBO/FIL200 (n=38), PBO/FIL100 (n=38).
ADA, adalimumab; PBO, placebo; SD, standard deviation.

Methods: In this interim analysis, efficacy (nonresponder imputation) of FIL 200 mg (FIL200) and 100 mg (FIL100) was assessed from long-term extension (LTE) baseline (BL) to Week (W) 156 in patients (pts) with an IR to methotrexate (MTX-IR) and biologics (bDMARD-IR), enrolled from FINCH 1 (NCT02889796) and 2 (NCT02873936) parent studies, respectively, receiving ≥ 1 FIL dose in FINCH 4 (NCT03025308).

Results: Study design, BL characteristics and W48 outcomes for MTX-IR[1] and bDMARD-IR[2] pts were reported previously. For MTX-IR and bDMARD-IR pts who received FIL200 or FIL100 in the parent study, W156 remission rates using Boolean 1.0 criteria were 20.5% and 15.8%, and 18.2% and 8.9%, respectively. Adopting the Boolean 2.0 criteria slightly increased remission rates for FIL200 and FIL100 at W156: +4.2% and +4.9% for MTX-IR pts, and +1.5% and +2.4% for bDMARD-IR pts, respectively. For pts rerandomized to FIL on entering the LTE, Boolean 2.0 criteria also increased remission rates vs Boolean 1.0. Both MTX-IR (**Figure**) and bDMARD-IR pts maintained long-term Boolean remission through W156 with FIL200 and FIL100, irrespective of prior FIL. Results for Disease Activity Score in 28 joints using C-reactive protein (DAS28-CRP) < 2.6, Clinical Disease Activity Index (CDAI) ≤ 2.8 and Simplified Disease Activity Index (SDAI) ≤ 3.3, and mean change from parent study BL in Health Assessment Questionnaire–Disability Index (HAQ-DI) and pain are shown (**Table**). Similar trends in efficacy were seen for LDA and ACR response criteria.

Conclusion: In FINCH 4, both FIL200 and FIL100 showed sustained efficacy up to W156 in clinically relevant pt populations. Boolean 2.0 criteria classified more pts in remission, in line with the range reported in the validation study.[3]

References:

1. Combe B, et al. Arthritis Rheumatol 2021;73(Suppl 9):POS1697
2. Buch M, et al. Arthritis Rheumatol 2021;73(Suppl 9):POS1696
3. Studenic P, et al. Arthritis Rheumatol 2023;82:74–80

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Pfizer, 2, 12, Paid to host institution; **D. Aletaha**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Janssen, 2, 6, Lilly, 2, 5, 6, Merck, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6, Sandoz, 2, 6, Sanofi, 5, Sobi, 5; **R. Caporali**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celltrion, 2, 6, Fresenius Kabi, 2, Galapagos, 2, 6, Janssen, 2, 6, Lilly, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, Sandoz, 2, 6, UCB, 2, 6; **B. Combe**: AbbVie, 2, 6, BMS, 6, Celltrion, 2, Eli Lilly, 1, 2, 6, Galapagos, 2, 6, Gilead, 2, Janssen, 2, 6, MSD, 6, Nordic Pharma, 5, Novartis, 1, Pfizer, 6, Roche-Chugai, 2, 6; **H. Schulze-Koops**: AbbVie, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Pfizer, 2, 6; **J. Gottenberg**: AbbVie, 2, BMS, 2, 5, Galapagos, 2, Gilead, 2, Lilly, 2, MSD, 2, Novartis, 2, Pfizer, 2, 5; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer-Ingelheim, 6, Chugai, 5, 6, Eisai, 5, 6, Eli Lilly, 6, Gilead, 6, GSK, 6, Mitsubishi-Tanabe, 5, Pfizer, 6, Taiho, 6, Taisho, 5, 6; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6; **T. Takeuchi**: AbbVie, 2, 5, 6, AYUMI, 5, Bristol-Myers Squibb, 6, Chugai, 2, 5, 6, Daiichi Sankyo, 5, Eisai, 5, 6, Eli Lilly Japan, 2, 6, Gilead, 2, 6, Janssen, 6, Mitsubishi-Tanabe, 2, 5, 6, ONO, 5, Pfizer Japan, 6, Taiho, 2; **E. Ekoka Omoruyi**: Galapagos, 2, Janssen, 2, UCB, 11; **K. Van Beneden**: Galapagos, 3, 11; **V. Rajendran**: Galapagos, 3, 11; **C. Watson**: Galapagos, 3, 11; **F. De Leonardis**: Galapagos, 3; **P. Emery**: Boehringer Ingelheim, 2, Eli Lilly, 2, Novartis, 2.

Abstract Number: 2144

Pharmacodynamic Effects of Nipocalimab in Patients with Moderate to Severe Active Rheumatoid Arthritis (RA): Results from the Multicenter, Randomized, Double-blinded, Placebo-controlled Phase 2A IRIS-RA Study

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Nipocalimab is a fully human, immunoglobulin G (IgG) 1 monoclonal antibody that blocks the neonatal crystallizable fragment receptor (FcRn), thereby lowering IgG levels. RA is a chronic inflammatory autoimmune disease with a multitude of pathogenic mechanisms. Anti-citrullinated protein autoantibody (ACPA) is one of the hallmark autoantibodies that may contribute to the pathogenesis and active inflammation in RA. In a phase 2a proof-of-concept study (IRIS-RA; NCT04991753), nipocalimab demonstrated numerically greater improvements in clinical endpoints (reported separately). Here, we report the initial pharmacodynamics of nipocalimab and associated disease biomarkers in the IRIS-RA study.

Methods: IRIS-RA was a phase 2a, multicenter, randomized, double-blind, placebo-controlled study. Eligible adult patients had active, seropositive RA with prior inadequate response or intolerance to≥1 tumor necrosis factor inhibitors. Nipocalimab or placebo was given intravenous every 2 weeks from Weeks 0-10. Blood samples were collected from consenting patients for the measurement of serum immunoglobulin levels, including total IgG and IgG subclasses. Levels of serum ACPA IgG were measured by an anti-cyclic citrullinated peptide 2 (CCP2) assay. Circulating immune complexes (CICs), complement activation markers, and serum inflammatory markers, including cytokines and C-reactive protein (CRP), were also measured. Associations between changes in biomarker levels and clinical responses at Week 12 were assessed.

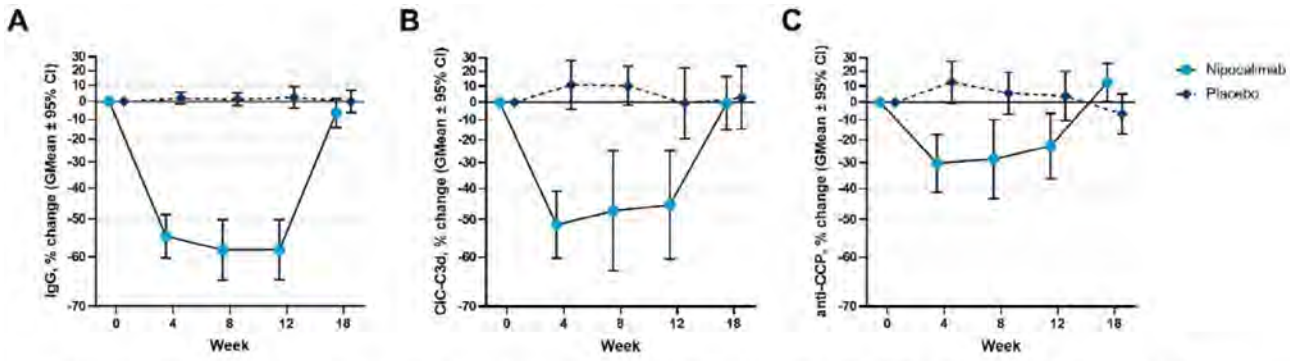

Figure 1. Changes in pharmacodynamic biomarkers: (A) total IgG, (B) CIC, and (C) ACPA IgG (anti-CCP). Values after treatment failure reported as missing; for change in anti-CCP analyses, patients with baseline anti-CCP below lower limit of quantitation excluded. GMean and 95% CI based on ratio of value at visit over baseline value, with y-axes transformed to corresponding % change value (= 100% × [ratio – 1]).

ACPA, anti-citrullinated protein autoantibodies; CI, confidence interval; GMean, geometric mean; IgG, immunoglobulin G; anti-CCP, anti-cyclic citrullinated peptide antibody; CIC, circulating immune complex.

Results: A total of 53 patients (nipocalimab, n=33; placebo, n=20) were enrolled in the study. Baseline biomarker levels were generally comparable between groups. Serum total IgG levels were reduced by nipocalimab from Weeks 4 through 12 and returned to baseline levels at Week 18. At Week 12, there was a 58% reduction (geometric mean) in the total IgG level observed in the nipocalimab group compared to a 2.4% increase in the placebo group (**Figure 1**). Decreases from baseline in all IgG subclasses were consistent with those observed for total IgG levels. Significant reductions of total CIC and ACPA IgG levels were also observed in the nipocalimab group versus the placebo group (**Figure 1**), with a trajectory similar to total IgG reduction. Relative to the baseline, no changes in complement activation markers or serum inflammatory markers were observed in either group. In nipocalimab group, those who achieved remission in the Disease Activity Score 28-CRP at Week 12 had numerically greater reduction in ACPA compared to non-responders.

Conclusion: Nipocalimab significantly and reversibly reduced IgG, ACPA, and CICs, consistent with the expected mechanism of action, but did not impact complement activation markers or serum inflammatory markers. Reduction in ACPA by nipocalimab was associated with clinical remission. These findings support the observed clinical response and suggest that combination of nipocalimab and a therapy with an orthogonal mechanism may provide clinical benefits for patients with refractory RA.

Disclosure: R. Panchakshari: Janssen, 3, Johnson & Johnson, 11; **M. Loza**: Janssen, 3, Johnson & Johnson, 11; **T. Huizinga**: None; **G. Schett**: None; **K. Ma**: Janssen, 3, Johnson & Johnson, 11; **J. Leu**: Janssen, 3, Johnson & Johnson, 11; **S. Liva**: Janssen, 3, Johnson & Johnson, 11; **F. Ibrahim**: Janssen, 3, Johnson & Johnson, 11; **B. Zhou**: Janssen, 3, Johnson & Johnson, 11; **Q. Wang**: Janssen, 3, Johnson & Johnson, 11; **R. Cella**: Janssen, 3, Johnson & Johnson, 11; **C. Karyekar**: Janssen, 3, Johnson & Johnson, 11; **K. Fei**: Janssen, 3, Johnson & Johnson, 11; **C. Cuff**: Janssen, 3, Johnson & Johnson, 11; **S. Gao**: Janssen, 3, Johnson & Johnson, 11.

Abstract Number: 2145

Patterns of Use, Effectiveness, Persistence and Cardiovascular Risk in Patients with Rheumatic Diseases Treated with Upadacitinib in a Real-world Setting. UPAREAL Study

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Based mainly on results from a randomized clinical trial (RCT) in rheumatoid arthritis (RA) patients (ORAL Surveillance), major regulatory agencies have concluded that JAK inhibitors, including Upadacitinib (UPA), a selective and reversible JAK1 inhibitor, may be associated with an increased risk of serious cardiovascular events and cancer compared with tumor necrosis factor inhibitors (TNFi). In this context, evidence on safety, effectiveness and risk minimization measures in patients treated with UPA in routine clinical practice are of particular interest.

Methods: Observational, retrospective, and multicenter study including patients diagnosed with RA, and spondylarthritis (SpA) (psoriatic arthritis, and axial-SpA), who received UPA for at least 3 months between January 1, 2021, and March 31, 2023. For a comparison of baseline cardiovascular risk (CVR), RA and SpA patients who initiated TNFi treatment during this same period were also analyzed. Baseline demographic and disease characteristics, changes over time in DAS28 or BASDAI, baseline CVR by Systemic Coronary Risk Estimation (SCORE)2 or SCORE2_OP (patients >70 years), concomitant medications, line and persistence of UPA treatment, and adverse events data were collected. Cox regression and Kaplan-Meier curves were used to analyze the UPA persistence, and a general mixed linear model to study the variation of disease activity over time. Chi-squared, t-Student, and U-Mann-Whitney tests were used to compare groups.

Results: A total of 104 patients treated with UPA, 80 RA (77%) and 24 (23%) SpA, were included. The mean follow-up time was 12.8±6.7 (SD) months. Table 1 shows baseline demographic and disease characteristics, disease activity, and CVR factors, including baseline SCORE2 of patients treated with UPA and TNFi. UPA showed significant effectiveness in controlling RA disease activity by DAS28 during follow-up ($p< 0.001$). UPA persistence in both RA and SpA patients is shown in Figure 1, with a tendency to a better persistence in SpA (log rank: 2.9, $p=0.08$). According to the COX regression analysis, the only factor associated with lower UPA persistence was its use in 2nd or higher line (HR 7.1 $_{95\%}$CI 0.98-52.08, $p= 0.052$). The main reason for discontinuation of UPA was adverse events (n=11, 44%), followed by ineffectiveness (n=8, 32%) and loss to follow-up (n=6, 24%). To examine changes over time in CVR minimization in UPA-treated patients, 109 patients who initiated TNFi during the same period with similar demographic characteristics and clinical activity (Table 1) were analyzed as a comparator. SCORE2, both as a percentage ($p=0.47$) and categorized ($p=0.21$), were similar between patients treated with UPA or TNFi (Table 1). However, when SCORE2 was categorized and analyzed by trimester, a significant reduction ($p=0.03$) was observed in moderate-high risk patients who initiated UPA versus TNFi since April 2022 (Table 2).

Table 1. Basal demographics, disease characteristics, treatments and cardiovascular risk of patients included.

	Upadacitinib			TNFi			
	AR (N = 80)	SpA (N = 24)	Total (N = 104)	AR (N = 52)	SpA (N = 57)	Total (N = 109)	P value*
Age (years), mean±SD	53.2 ± 10.5	48.6 ± 8.2	52.2 ± 10.2	54.4 ± 11.2	45.5 ± 11.4	49.8 ± 11.1	0.131
Female, n (%)	69 (86)	12 (50)	81 (78)	41 (79)	32 (56)	73 (67)	0.092
Disease duration (years), median (IQR)	13.3 (7.2;19.2)	8.9 (3.9;16.7)	12.5(6.6;18.7)	5.0 (2.2; 10.6)	3.0 (1.1; 7.3)	3.7 (1.7; 9.1)	<0.001
Joint involvement, n (%)							
Axial radiographic		12 (50)			24 (42)		
Axial non-radiographic		6 (25)			5 (9)		
Peripheral		5 (21)			22 (39)		
Mixed		1 (4)			6 (11)		
Disease activity indexes, mean±SD							
DAS-ESR	4.34 ± 1.28			3.72 ± 1.82			0.057
DAS-CRP	4.14 ± 1.09			3.65 ± 1.57			0.066
ASDAS-CRP		3.40 ± 0.97			4.64 ± 1.35		0.154
BASDAI	-	5.17 ± 2.01		-	6.01 ± 2.03		0.184
BASFI	-	6.03 ± 2.67		-	5.41 ± 2.57		0.599
Biologic activity, median (IQR)							
ESR mm/h	16 (6; 31)	8 (3.5; 18)	14 (6; 28)	14 (6; 24)	8 (5; 17)	9 (5; 20)	0.061
CRP mg/L	5.4 (1.5; 12.1)	6.6 (3.2; 15.8)	5.8 (2; 12.7)	4.5 (1.1; 12.8)	3.0 (0.4; 6.5)	3.6 (0.8; 9.3)	0.014
Monotherapy, n (%)	31 (40)	14 (58)	45 (45)	20 (38)	35 (62)	55 (50)	0.728
Glucocorticoids	50 (65)	10 (42)	60 (59)	16 (31)	5 (9)	21 (19)	<0.001
Line of UPA, n (%)							
1	16 (20)	3 (13)	19 (18)	52 (100)	57 (100)		
2	14 (18)	2 (8)	16 (16)				
≥ 3	49 (62)	19 (79)	68 (66)				
CRF							
BMI, mean (SD)	26.7 ± 4.7	27.5 ± 5.1	26.9 ± 4.8	28.2 ± 6.1	27.1 ± 5.8	27.6 ± 6.0	0.327
≥30, n (%)	15 (21)	6 (29)	21 (22)	19 (36)	13 (23)	32 (29)	0.267
Total cholesterol	188.8 ± 32.7	181.1 ± 44.1	187.0 ± 35.7	187.6 ± 29.8	194.5 ± 37.4	191.2 ± 34.0	0.381
HDL cholesterol	57.8 ± 15.5	57.0 ± 19.1	57.6 ± 16.4	58.5 ± 15.0	55.9 ± 14.7	57.1 ± 14.8	0.823
Systolic pressure	130.6 ± 19.9	134.6 ± 17.9	131.9 ± 19.2	132.7 ± 19.9	126.3 ± 17.6	129.4 ± 18.9	0.416
Tobacco, n (%)							0.593
Current, n (%)	12 (15)	7 (29)	19 (18)	8 (15)	14 (25)	22 (20)	
Former, n (%)	16 (20)	3 (13)	19 (18)	13 (25)	12 (21)	25 (23)	
Arterial hypertension, %	24 (30)	9 (38)	33 (32)	24 (46)	13 (23)	37 (34)	0.772
Diabetes Mellitus II, n (%)	8 (10)	3 (13)	11 (11)	7 (14)	5 (9)	12 (11)	0.958
SCORE2, mean±SD	3.28 ± 2.76	3.00 ± 2.23	3.22 ± 2.64	4.06 ± 3.03	2.99 ± 3.09	3.50 ± 3.09	0.471
median (P_{25}; P_{75})	2.33 (1.33; 4.60)	2.43 (1.66; 3.53)	2.34 (1.37; 4.41)	3.52 (1.73; 5.71)	1.79 (0.70; 4.64)	2.61 (0.84; 5.23)	0.957
By age groups							
< 50 years	1.06 (0.62; 1.46)	1.97 (1.27; 2.51)	1.27 (0.75; 1.98)	0.71 (0.43; 2.56)	0.84 (0.45; 1.79)	0.83 (0.45; 1.88)	0.197
[50, 70) years	3.39 (2.23; 5.02)	4.92 (2.62; 6.88)	3.41 (2.27; 5.03)	4.91 (2.94; 6.63)	5.07 (2.95; 7.92)	4.91 (2.95; 6.87)	**0.008**
≥ 70 years	12.33 (9.97; 12.86)	-	12.33 (9.97; 12.86)	5.72 (5.43; 8.13)	-	5.72 (5.43; 8.13)	0.200
Categorized CRF by SCORE2							0.212
Low	63 (79)	17 (71)	80 (77)	33 (64)	41 (72)	74 (68)	
Medium	16 (20)	7 (29)	23 (22)	17 (33)	14 (25)	31 (28)	
High	1 (1)	-	1 (1)	2 (4)	2 (3)	4 (4)	

*p-value between Total columns

Anti-CCP: Anti-cyclic citrullinated peptide; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BMI: Body Mass Index; RP: C-reactive protein; CRF: Cardiovascular Risk Factors; DAS: Disease Activity Score; ESR: Erythrocyte Sedimentation Rate; IQR: Interquartile Range; SCORE: Systemic Coronary Risk Estimation; SD: standard deviation; UPA: Upadacitinib.

Conclusion: UPA shows sustained effectiveness in patients with RA and especially in those with SpA, with a safety profile equivalent to that shown in RCTs. The recommendations of the regulatory authorities to minimize CVR in patients treated with JAKi seem to have been adopted and even anticipated in daily clinical practice.

Table 2. Contingency table of patients initiating UPA or TNFi with moderate-high cardiovascular risk by SCORE2 before and after April 2022.

Time		Upadacitinib	TNFi	Total
Before April 2022	N of patients	18	16	34
	%	75.0%	45.7%	57.6%
After April 2022	N of patients	6	19	25
	%	25.0%	54.3%	42.4%
Total	N of patients	24	35	59
	%	100.0%	100.0%	100.0%

P=0.033

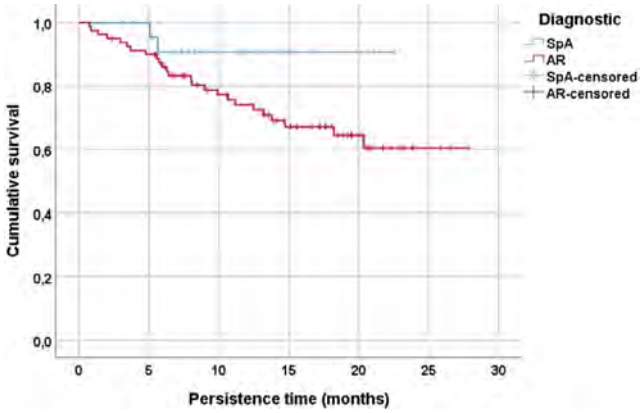

Figure 1. Kaplan-Meier curves of UPA persistence in RA and SpA patients

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After JAK Inhibitor Failure, "Switching" or "Cycling"?

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SESSION INFORMATION
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Background/Purpose: The appearance of JAK inhibitors (JAKi) in the last few years has proved a great clinical application in rheumatic pathology and it has become an innovative and widely-used therapeutic line. In fact, JAKi has been recently included in the management algorithms of psoriatic arthritis, axial spondyloarthritis or rheumatoid arthritis. Nevertheless, the evidence of therapeutic alternatives in real life after the failure of a JAK inhibitor is limited: another JAKi or the change in therapeutic target.

The purpose of the study is to analyze the treatment alternatives after JAKi failure in real life conditions and in multiple diseases.

Methods: Retrospective longitudinal observational study of patients that started JAKi treatment and was discontinued from 2013 to 2022. Demographic and clinical variables were collected from the electronic medical record. "Switching" and "cycling" were analyzed depending on the prescribed medicine after the JAKi, classifying them in the following targets: anti-TNF, anti-IL6, anti-CTLA4, anti-IL12/23, anti-IL17, anti-IL23, another JAKi or other situations like anti-CD20. We studied the retention rate at 9 months after the start of the new treatment.

Results: In our series, the most prescribed JAKi was Tofactinib (n=119), followed by Baricitinib (n=76), Upadacitinib (n=66) and Filgotinib (n=4). The most recurrent indications for JAKi treatment were rheumatoid arthritis (n=71) and psoriatic arthritis (n=12).

Out of 265 JAKi prescriptions, 95 failures to JAKi treatment were included in this study. The JAKi with higher failure rate was tofacitinib (n=61) followed by baricitinib (n=22) and upadacitinib (n=12). We do not have data from filgotinib due to its recent incorporation to the Spanish national market. The main cause of end of treatment was adverse reaction (34.74%), followed by secondary failure (28.42%).

After all the JAKi failures, "switching" to other families like anti-TNF or anti-IL6 was the main therapeutical choice (n=57), followed by "cycling" to another JAKi (n=25). 8 patients did not start a new treatment after JAKI failure.

The retention rate at 9 moths after the treatment showed that the 83,33% of the "cycling" to another JAKi and the 73,5% of the "switching" to another therapeutic target maintained the treatment (see image). The retention rate was not studied in 17 patients because the treatment period was less than 9 months.

Table 1. Total of "switching" and "cycling"

Total of "switching" and "cycling" n=82	JAKi "cycling" n=25	Anti-TNF n=16	Anti-IL6 n=15	Anti-CTLA4 n=7	Anti-IL12/23 n=1	Anti-IL17 n=2	Anti-IL23 n=3	Others n=13	Lost follow-up n=5
Age when JAKi starts-years (sd)	51.56 (12.21)	52.81 (16.19)	55.07 (10.31)	62.57 (12.93)	69 (NA)	50.5 (7.78)	56.33 (4.16)	47.69 (16.6)	63.6 (16.46)
Female – n (%)	24 (96)	11 (68.75)	12 (80)	6 (85.71)	1 (100)	1 (50)	1 (33.33)	9 (69.23)	5 (100)
Diagnosis - n (%) Rheumatoid Arthritis Axial Spondyloarthritis Psoriatic arthritis Juvenile Idiopathic Arthritis Others	21 (84) 0 (0) 2 (8) 1 (4) 1 (4)	12 (75) 2 (12.5) 1(6.25) 1(6.25) 0 (0)	14 (93.33) 0 (0) 0(0) 1(6.67) 0 (0)	6 (86) 0 (0) 1 (14) 0 (0) 0 (0)	0 (0) 0 (0) 1(100) 0 (0) 0 (0)	0 (0) 0 (0) 2(100) 0 (0) 0 (0)	0 (0) 0 (0) 3(100) 0 (0) 0 (0)	8(62) 0 (0) 2(15) 3 (23) 0 (0)	3 (60) 2 (40) 0(0) 0 (0) 0 (0)
Previous bDMARD - n (%) Failure to 1 Failure to 2 Failure to 3	3 (12.5) 4 (16) 9 (37.5)	4 (30.8) 1 (7.7) 5 (33.33)	5 (36) 5 (38) 3 (21)	2(33) 2(33) 1 (17)	1 (100) 0 (0) 0 (0)	0 (0) 0 (0) 2 (100)	0 (0) 1 (33) 2 (67)	1 (7.7) 0 (0) 10 (77)	1 (20) 0 (0) 2 (40)
Original JAKi - n (%) Tofacitinib Baricitinib Upadacitinib	17 (68) 7 (28) 1 (4)	12 (75) 1 (6.25) 3 (18.75)	8 (53) 7 (47) 0 (0)	6 (85.71) 0 (0) 1 (14.29)	1 (100) 0 (0) 0 (0)	2 (100) 0 (0) 0 (0)	1 (33.33) 0 (0) 2 (66.67)	6 (46.15) 6 (46.15) 1 (7.69)	2 (40) 1 (20) 2 (40)
Cause of failure - n (%) Primary Secondary Side effects Others	3(12) 14 (56) 6 (24) 2 (8)	7 (43.75) 2 (11.76) 5 (32.73) 2 (11.76)	4 (26.67) 3 (20) 6 (40) 2 (13.33)	1 (14.29) 1 (14.29) 4 (57.13) 1 (14.29)	0 (0) 0 (0) 1 (100) 0 (0)	0 (0) 1 (50) 1 (50) 0 (0)	1 (33.33) 1 (33.33) 1 (33.33) 0 (0)	3 (23.07) 5 (38.46) 4 (30.77) 1 (7.7)	0 (0) 0 (0) 3 (60) 2 (40)

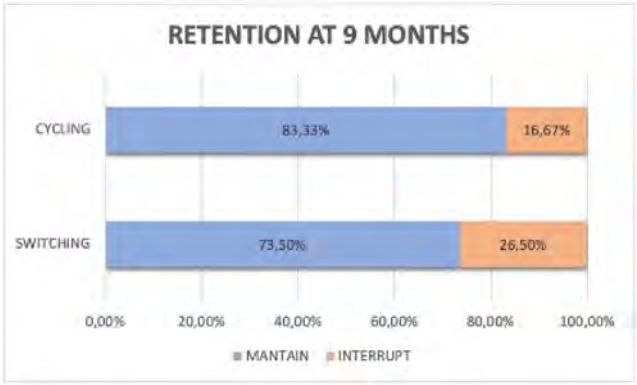

Image 1. Retention rate at 9 months

Conclusion: After a JAKi failure, "switching" is the most recurrent alternative in our series, used most frequently in patients with side events or primary failure. "Cycling" was the most common alternative used with patients who stopped receiving treatment due to secondary failure and in patients with a major proportion of failure to bDMARD.

The retention rate after 9 months was 83,33% for "cycling" and 73,50% for "switching" groups.

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Abstract Number: 2147

Safety and Effectiveness in Cycling Between Non-Selective and Selective JAKi in a Multi-Center Registry of Rheumatoid Arthritis in the Middle East

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Background/Purpose: Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease. Strategies for addressing treatment failure with TNF inhibitors according to the recent EULAR recommendations include switching to an alternate TNF inhibitor (known as "switching" or "cycling") or moving to a different class of targeted agents with an alternative mechanism of action ("swapping"). Although efficacy data on switching from one TNFi after failure to another TNFi are available,

Table 1. Patient characteristics of total cohort, patients exposed to selective JAKi and patients with switches from non-selective JAKi to selective JAKi.

	Total Cohort	Exposure to Selective JAKi (Upa)	Switch Among JAKis (Tofa and/or Bari to Upa)
n	186	55	27
Age at time of diagnosis (Mean±SD)	40±16	48±9.2	47.5±11.6
Females (%)	88	82	89
BMI (kg/m²)	31±7	31±7	31±6
Duration of RA diagnosis (years)	10±7	9±6	10±6
RF positive (%)	64	47	52
ACPA positive (%)	59	45	52
Erosions on X-ray (%)	42	35	42
csDMARDs use (%)	100	100	100
bDMARDs use (%)	56	36	30
Prednisolone use (%)	59	52	62
Positive TB QuantiFERON (%)	12	13	15
Herpes zoster (%)	5	6	8
tsDMARDs use (n, %)	186, 100	55, 100	27, 100
Tofa (%)	68	38	78
Bari (%)	25	8	37
Upa (%)	30	100	100
JAKi drug exposure (months)	56.7	51.2	51

Table 2. Adverse effects in the total cohort, patient exposed to non-selective and selective JAKi and patients with switches from non-selective and selective.

Adverse Effects	Total Cohort (n, %)	Exposure to Selective JAKi (Upa) (n, %)	Switch Among JAKis (Tofa and/or Bari to Upa) (n, %)
Primary failure	53, 54	27, 69	25, 76
Secondary failure	47, 47	12, 31	8, 24
Infections	**7, 7**	**3, 8**	**2, 6**
VZV reactivation	3, 3	2, 5	1, 3
HSV reactivation	1, 1	0, 0	0, 0
Pneumonia	1, 1	0, 0	0, 0
TB reactivation	1, 1	0, 0	0, 0
Recurrent infections	1, 1	1, 3	1, 3
Respiratory	**4, 4**	**0, 0**	**0, 0**
ILD	2, 2	0, 0	0, 0
SOB	2, 2	0, 0	0, 0
Cardiovascular	**2, 2**	**1, 3**	**0, 0**
MACE	0, 0	0, 0	0, 0
DVT	1, 1	1, 3	0, 0
Palpitations	1,1	0, 0	0, 0
Malignancy	**1,1**	**1, 3**	**0, 0**
Patient factors	**22, 22**	**4, 10**	**3, 9**
Patient preference	3, 3	0, 0	0, 0
Non compliance	18, 18	4, 10	3, 9
Pregnancy	1, 1	0, 0	0, 0
Side Effects	**10, 10**	**2, 5**	**2, 6**
Dizziness	1, 1	0, 0	0, 0
GI upset	5, 5	0, 0	0, 0
Transaminitis	1, 1	1, 3	1, 3
Skin rash	1, 1	0, 0	0, 0
Facial acne	1, 1	1, 3	1, 3
Facial swelling	1,1	0, 0	0, 0
Unknown reason	**1,1**	**1, 3**	**0, 0**

Table 3. CDAI, DAS-ESR and CRP at baseline and after 6 months from switching to Upa.

	Baseline prior switching from Tofa or Bari to Upa (Mean±SD)	6 months after switching from Tofa or Bari to Upa (Mean±SD)	p value
CDAI	29.4±9.7	6.7±5.3	<0.0001
DAS28-ESR	5.5±1.1	2.9±0.6	<0.0001
DAS28-CRP	4.6±0.9	2.5±1.0	<0.0001

information on switching from one JAK inhibitor (JAKi) to another JAKi is lacking and it is unclear whether cycling or swapping is preferable between JAKis. We evaluated the overall safety of JAKis in the Middle Eastern population, as well as the clinical efficacy of cycling from Tofacitinib (Tofa) or Baricitinib (Bari) to Upadacitinib (Upa).

Methods: Between May 2015 and May 2023, 186 patients with RA received Tofa, Bari, or Upa in any order in clinical practice at 3 centers (UAE, Saudi Arabia and Jordan). The drug retention rate, the drug's safety, and the reason for switching due to ineffectiveness or an adverse event were all obtained. We compared the efficacy of switching from a non-selective JAKi to a more selective JAKi in terms of CDAI, DAS28 ESR and CRP evolution over the course of 6 months after starting the second treatment. Unpaired t test was used for comparison of disease activity. The level of significance was $p < 0.05$.

Results: 186 patients were exposed to Tofa, Bari and Upa (67%, 25% and 30% respectively). The mean age at the time of RA diagnosis was 40±16 (Mean±SD) years, with a BMI of 31±7 kg/m^2, and a disease duration of 10±7 years. At baseline, the most common comorbidities were hypertension, dyslipidemia, and diabetes (30%, 33% and 26% respectively). Prior to starting any JAKi, there was a history of cardiovascular disease (10%) and cancer (6%). 3% had a previous history of varicella zoster (VZV) infection. All patients had previously received csDMARD, however 56% received bDMARD and 59% received oral prednisolone. Mean drug retention for Tofa (27.7±21.9), Bari (17.3±14.4) and Upa (11.7±6.6) months. Of the 186 patients, 55 patients (30%) were exposed to Upa. 6% had a previous history of VZV infection. Over the course of the 51.2 months of JAKi drug exposure, two patients developed VZV reactivation, one patient developed a DVT with no MACE. 27 patients out of the 55 exposed to Upa had prior use of Tofa or Bari. There were 31 instances of cycling among JAKis: 3 (Tofa to Bari), 18 (Tofa to Upa) and 9 (Bari to Upa). Over the course of the 51 months of JAKi drug exposure, 1 patient developed VZV reactivation (Tofa to Upa) with no reported DVT or MACE. Over a 6-month period, the switch to Upa was well tolerated and patients maintained a low disease activity response. Prior to switching from Tofa or Bari to Upa, the baseline CDAI, DAS-ESR, and CRP were (29.4±9.7, 5.5±1.1 and 4.6±0.9 respectively) and after 6 months were (6.7±5.3, 2.9±0.6 and 2.5±1.0 respectively; p value < 0.0001).

Conclusion: Our findings show that switching from non-selective JAKi to selective JAKi is feasible and safe, and that it may improve disease activity outcomes in patients who have failed to achieve low disease activity or remission with a previous JAKi.

Disclosure: R. Namas: None; **J. Alameri**: None; **S. Al Qassimi**: None; **H. Yu**: None; **M. Elarabi**: None; **H. Shatnawi**: None; **L. Memisoglu**: None; **A. Al Marzooqi**: None; **A. Mubashir**: None; **E. Mysler**: AbbVie, 2, 5, Amgen, 2, 5, Astra Zeneca, 2, 5, BMS, 2, 5, GSK, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 2, 5, Sanofi, 2, 5.

Abstract Number: 2148

Do High RF Titers Impact Response to TNF Inhibitors? Comparison of Certolizumab Pegol and Adalimumab in Patients with RA and High Titers of RF: A Post Hoc Analysis of a Phase 4 Trial

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Treatments Poster III

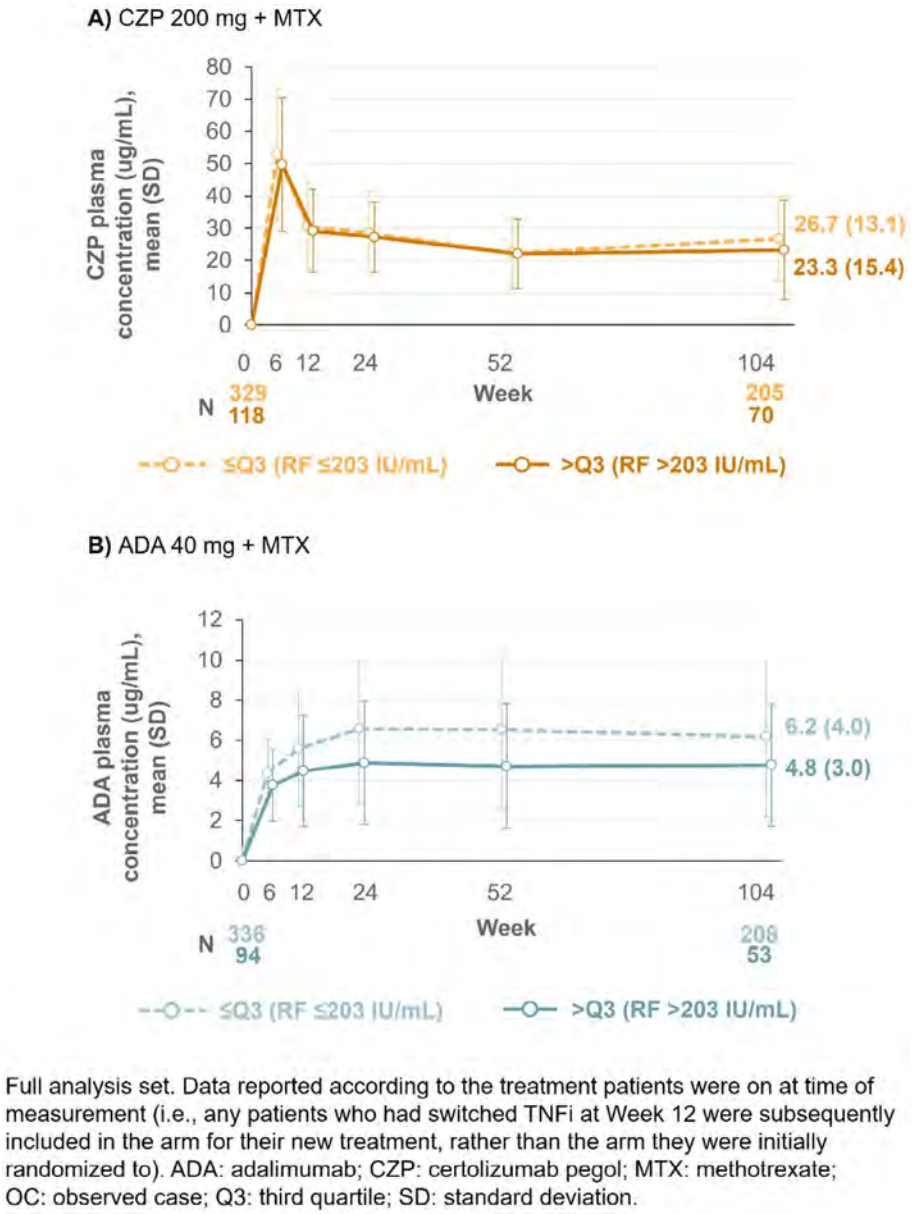
Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: In patients with RA, high RF titers are considered a poor prognostic factor and are associated with higher disease activity, risk of radiographic progression, and decreased response to TNF inhibitors (TNFis).[1–3] Recent data suggest that patients with RA and high RF titer may achieve and maintain greater clinical improvement with TNFis without a crystallizable fragment (Fc) compared to TNFis with an Fc.[4] In this post hoc analysis of the EXXELERATE trial, we assessed efficacy outcomes of certolizumab pegol (CZP), a PEGylated Fc-free TNFi, versus adalimumab (ADA; Fc-containing TNFi) in patients with RA and high RF titers.

Methods: The phase 4 EXXELERATE trial (NCT01500278) compared the efficacy and safety of CZP to ADA in a head-to-head comparison; full study design and primary outcomes have been reported previously.[5] Patients were randomized 1:1 to CZP 200 mg every 2 weeks (Q2W) plus methotrexate (MTX), or ADA 40 mg Q2W plus MTX. At Week (Wk) 12, patients were classified as responders or non-responders; non-responders were switched to the other TNFi with possible follow-up to Wk 104. Both Wk 12 responders and non-responders were included in this analysis. Here, we report drug plasma concentrations, mean disease activity score (DAS)28-CRP score, and proportion of patients achieving low disease activity (LDA; threshold: DAS28-CRP ≤2.7) to Wk 104. Results are stratified by RF titer quartile (≤Q3: ≤203 IU/mL; >Q3: >203 IU/mL; measured by Roche Tina-quant®) and reported as observed data.

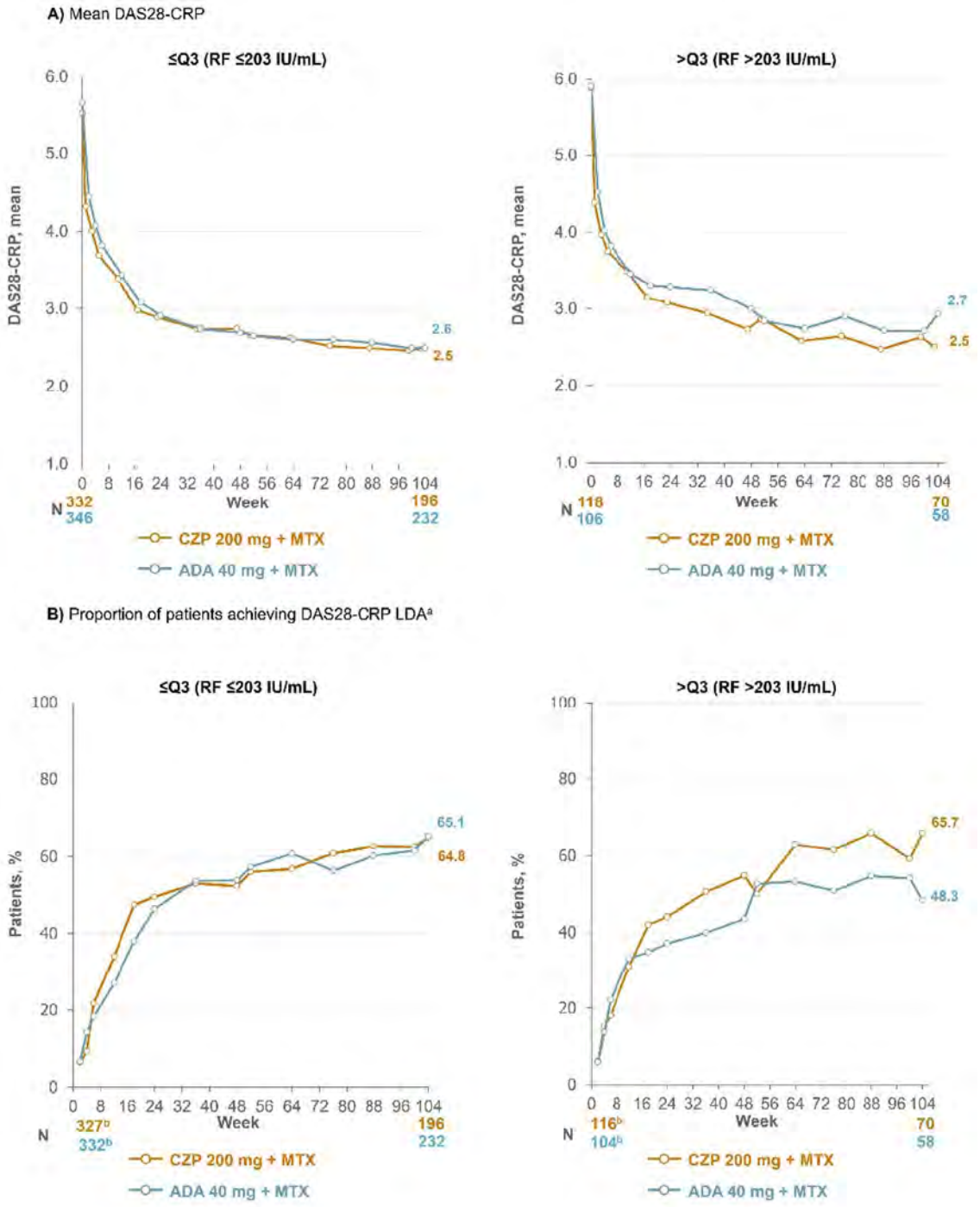
Results: Baseline (BL) data by RF quartile were available for 453 CZP-randomized patients (≤Q3: n=334; >Q3: n=119) and 454 ADA-randomized patients (≤Q3: n=347; >Q3 n=107). BL characteristics were similar between CZP- and ADA-randomized patients across the RF titer quartiles. At Wk 12, 66 CZP-treated patients switched to ADA and 59 ADA-treated patients switched to CZP. At Wk 104, mean ADA plasma concentrations were 22.9% lower in patients with RF >203 IU/mL vs those with RF ≤203 IU/mL; in CZP-treated patients, this difference was smaller (13.0%; **Figure 1**). For patients in RF ≤Q3, mean DAS28-CRP scores were similar between CZP- and ADA-treated patients through Wks 0–104 (mean [SD] DAS28 at Wk 104: 2.48 [1.18] CZP vs 2.49 [1.14] ADA). However, for patients in RF >Q3, mean DAS28-CRP scores were nominally lower in CZP- vs ADA-treated patients (Wk 104: 2.50 [1.18] CZP vs 2.93 [1.22] ADA; **Figure 2**). A similar pattern was observed for the proportion of patients achieving LDA at Wk 104 (≤Q3: 64.8% CZP vs 65.1% ADA; >Q3: 65.7% CZP vs 48.3% ADA).



Full analysis set. Data reported according to the treatment patients were on at time of measurement (i.e., any patients who had switched TNFi at Week 12 were subsequently included in the arm for their new treatment, rather than the arm they were initially randomized to). ADA: adalimumab; CZP: certolizumab pegol; MTX: methotrexate; OC: observed case; Q3: third quartile; SD: standard deviation.

Figure 1. Mean drug plasma concentrations of (A) CZP and (B) ADA to Week 104, stratified by RF titer quartiles [OC]

Conclusion: CZP-treated patients with RA and high titer RF had similar drug concentrations and clinical responses to patients with RA and low titer RF, a pattern not observed in ADA-treated patients. These data, together with previous reports where CZP showed consistent efficacy irrespective of BL RF titer,[6,7] suggest CZP may be a suitable therapy for patients with RA and high RF titer. **References:1.** Vastesaeger N. Rheumatology 2009;48:1114–21. **2.** Cuchacovich M. Clin Rheumatol 2014;33:1707–14. **3.** Takeuchi T. Arthritis Res Ther 2017;19:194. **4.** Nakayama Y. Rheumatol Int 2022;42:1227–34. **5.** Smolen J. Lancet 2016;388:2763–74. **6.** Martínez-Feito A. Ann Rheum Dis 2022;81:594–5. **7.** Tanaka Y. Int J Rheum Dis 2023;00:1–12.



Full analysis set. Data reported according to the treatment patients were on at time of measurement (i.e., any patients who had switched TNFi at Week 12 were subsequently included in the arm for their new treatment, rather than the arm they were initially randomized to). [a] Defined as DAS28 ≤2.7. [b] N at Week 2. ADA: adalimumab; CZP: certolizumab pegol; DAS28: Disease Activity Score-28 joint count; LDA: low disease activity; MTX: methotrexate; OC: observed case; Q3: third quartile.

Figure 2. Response to CZP and ADA to Week 104 measured by (A) DAS28-CRP and (B) proportion of patients achieving DAS28-CRP LDA, stratified by RF titer quartiles [OC]

Disclosure: J. Smolen: AbbVie, 5, 6, Amgen, 6, Annals of the Rheumatic Diseases, 12, Editor, AstraZeneca, 5, 6, Astro, 6, Bristol-Myers Squibb, 6, Celgene, 6, Celltrion, 6, Chugai, 6, Eli Lilly, 5, EULAR Task Forces and T2T Task Forces, 12, Convenor, Gilead, 6, ILTOO, 6, Janssen, 6, Lilly, 6, Merck Sharp & Dohme, 6, Novartis, 5, Novartis-Sandoz, 6, Pfizer,

6, Rheumatology 7E/8E, 12, Co-editor, Roche, 5, 6, R-Pharma, 6, Samsung, 6, Sanofi, 6, UCB Pharma, 6; **P. Taylor**: AbbVie, 2, Biogen, 2, Eli Lilly, 2, Fresenius, 2, Galapagos, 2, 5, Gilead Sciences, 2, GSK, 2, Janssen, 2, Nordic Pharma, 2, Pfizer Inc, 2, Sanofi, 2, UCB, 2; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer-Ingelheim, 6, Chugai, 5, 6, Eisai, 5, 6, Eli Lilly, 6, Gilead, 6, GSK, 6, Mitsubishi-Tanabe, 5, Pfizer, 6, Taiho, 6, Taisho, 5, 6; **C. Cara**: UCB Pharma, 3, 11; **B. Lauwerys**: UCB Pharma, 3, 11; **R. Xavier**: AbbVie, 2, 6, AstraZeneca, 2, 6, Janssen, 2, 6, Organon, 2, 6, UCB Pharma, 2, 6; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, BMS, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Genentech, 2, 5, Janssen, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB Pharma, 2, 5; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **M. Weinblatt**: AbbVie, 2, 5, Aclaris, 2, Amgen, 2, Aqtual, 2, 5, BMS, 2, 5, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, GSK, 2, Horizon, 2, Janssen, 5, Johnson and Johnson, 2, Pfizer, 2, Prometheus, 2, Rani, 2, Revolo, 2, Sanofi, 2, Sci Rhom, 2, Scipher, 2, Set Point, 2, UCB Pharma, 2.

Abstract Number: 2149

Biologic IRL201805 Drives Differential Cell-contact and Metabolism Transcriptional Profiles in Monocytes from RA Patients Compared to Healthy Donors

Yuriko Yamamura[1], Kieran Woolcock[2], Valerie Corrigall[3], Lara Ravanetti[4], Jorge De Alba[4], Roly Foulkes[5], Paul Eggleton[6] and Carl Goodyear[2], [1]School of Infection & Immunity, University of Glasgow, Glasgow, United Kingdom, [2]University of Glasgow, Glasgow, United Kingdom, [3]Revolo Biotherapeutics, Tadworth, United Kingdom, [4]Revolo Biotherapeutics, London, United Kingdom, [5]Revolo Biotherapeutics, Slough, United Kingdom, [6]Revolo Biotherapeutics, Exeter, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: IRL201805 is a novel biologic derived from Binding Immunoglobulin Protein (BiP) that has been developed for the treatment of Rheumatoid arthritis (RA) (P Eggleton, et al, J Cell Mol Med, 2023;27:322-339). A phase I/IIa clinical trial with a single IRL201805 intravenous infusion has demonstrated improvement in Disease Activity Score 28 (DAS28) (B Kirkham, et al, Rheumatology, 2016;55:1993-2000). Moreover, IRL201805 directly interacts with

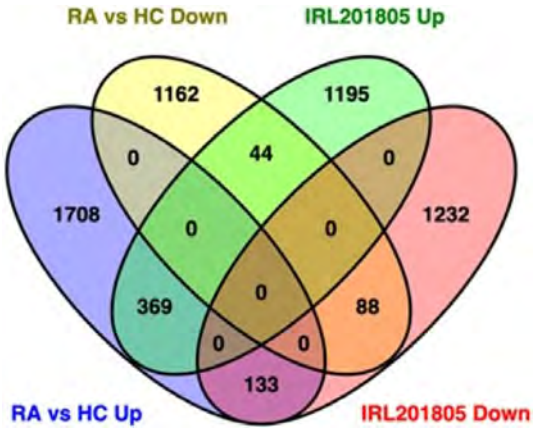


Fig 1. Venn Diagram of the transcriptional changes in RA monocytes vs HC monocytes (RA Up and RA Down) compared to the transcriptional changes in RA monocytes treated with IRL201805 (RA IRL201805 Up and RA IRL201805 Down). In RA monocytes, 44 of the downregulated genes are upregulated with IRL201805 treatment, while upregulated 133 genes were downregulated by IRL201805 treatment.

Monocytes, which play a key role in initiation of inflammation and bone erosion in RA. Thus, there is a need to identify the inflammatory pathways that drive the involvement of the myeloid compartment in RA and to how IRL201805 modulates these pathways. Herein, we performed a comprehensive RNA-seq analysis on monocytes from RA patients compared with healthy donors in the presence or absence of IRL201805 to investigate the impact on transcriptional profiles.

Methods: $CD14^{+}CD16^{-}$ monocytes were isolated from peripheral blood mononuclear cells (RA patients with active disease and healthy controls (HC)), and cultured overnight with macrophage-colony stimulating factor (M-CSF). RNAseq was performed on the monocytes collected with or without 24h IRL201805 stimulation.

Results: Evaluation of the transcription profiles changes in monocytes from active RA patients and age-gender matched HC in the presence or absence of IRL201805 revealed that untreated monocytes from RA patients had 2210 upregulated differentially expressed genes (DEGs) and 1294 downregulated DEGs when compared to HC cells (adjusted $p < 0.05$ & absolute log2fold > 0.58). Furthermore, exposure to IRL201805 resulted in the upregulation of 1608 transcripts and downregulated of 1453 in RA monocytes whilst only altering the expression of < 20 genes in cells derived from HC. In RA samples, the upregulated transcripts were associated with cell adhesion and chemotaxis whilst the downregulated transcripts were associated with metabolic processes. To further investigate the effect of IRL201805 upon monocytes, we compared the DEGs in IRL201805 treated RA monocytes (vs untreated RA macrophages) to the DEGs in circulating RA monocytes (vs HC monocytes). This revealed that 133 upregulated DEGs in RA were decreased and 44 downregulated DEGs in RA were increased with IRL201805 treatment. Notably, a larger proportion of DEGs in RA circulating monocytes were altered in the same direction with IRL201805 treatment.

Conclusion: Our data suggests that IRL201805 selectively target transcriptional changes in RA and not healthy monocytes. Notably, IRL201805 downregulates transcripts that are upregulated in RA whilst simultaneously upregulating transcripts that are downregulated in RA. Combined this suggests that IRL201805 has the capacity to 'reset' a number of cell-cell and metabolic linked inflammatory pathways in disease-state cells.

Disclosure: Y. Yamamura: Revolo Biotherapeutics, 5; **K. Woolcock**: None; **V. Corrigall**: Revolo Biotherapeutics, 2, 11; **L. Ravanetti**: Revolo Biotherapeutics, 3; **J. De Alba**: Revolo Biotherapeutics, 3; **R. Foulkes**: Revolo Biotherapeutics, 2; **P. Eggleton**: Revolo Biotherapeutics, 3; **C. Goodyear**: Abbvie, 6, AstraZeneca, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 5, Eli Lilly, 5, Galvani, 2, 5, GlaxoSmithKlein(GSK), 5, Istesso, 5, Janssen, 5, MedAnnex, 2, 5, Medincell, 2, MiroBio, 5, Revolo, 5, UCB, 5, 6.

Abstract Number: 2150

Novel Biologic IRL201805 Inhibits Osteoclastogenesis in Monocytic Cells from RA Patients

Yuriko Yamamura[1], Valerie Corrigall[2], Lara Ravanetti[3], Jorge De Alba[3], Roly Foulkes[4], Paul Eggleton[5] and Carl Goodyear[6], [1]School of Infection & Immunity, University of Glasgow, Glasgow, United Kingdom, [2]Revolo Biotherapeutics, Tadworth, United Kingdom, [3]Revolo Biotherapeutics, London, United Kingdom, [4]Revolo Biotherapeutics, Slough, United Kingdom, [5]Revolo Biotherapeutics, Exeter, United Kingdom, [6]University of Glasgow, Glasgow, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

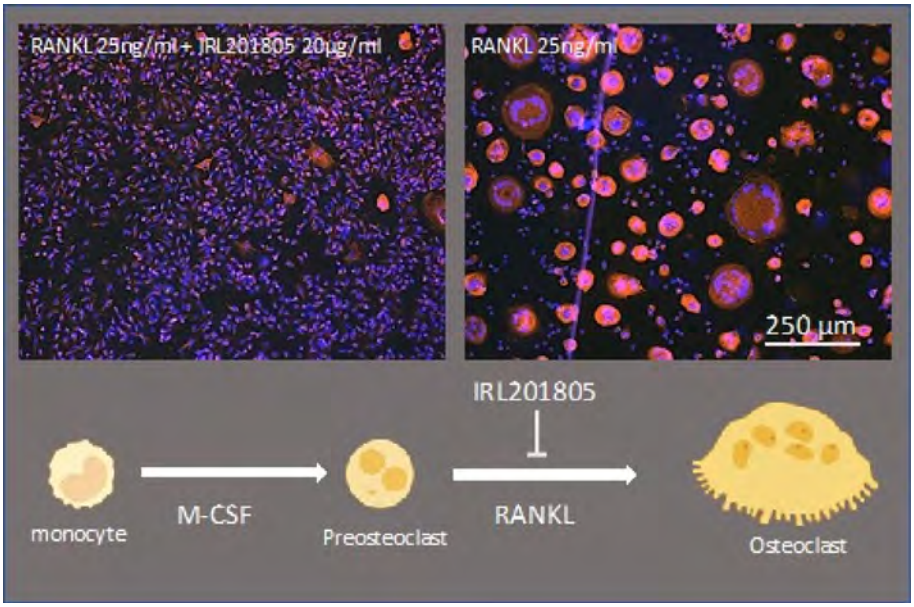


Figure 1. Osteoclast differentiation is inhibited by IRL201805 treatment, which involves down regulation of several osteoclast and metabolic genes.

Background/Purpose: In Rheumatoid arthritis (RA), osteoclasts derived from $CD14^+$ Monocytes are associated with a risk of progressive bone and joint destruction, which fundamentally impacts quality-of-life. Current RA treatments such as immunosuppressants, steroids, and biologics can in part ameliorate joint destruction and decrease the need for subsequent orthopaedic surgery. However, such treatments are far from perfect and knowledge of their mode-of-action in preventing osteoclast induced bone destruction is limited. IRL201805 is a novel biologic derived from Binding Immunoglobulin Protein (BiP) that has been developed for the treatment of RA (P Eggleton, et al, J Cell Mol Med, 2023;27:322-339). In a Phase I/IIa clinical trial, a single IRL201805 intravenous infusion was demonstrated to improve Disease Activity Score 28 (DAS28) (B Kirkham, et al, Rheumatology, 2016;55:1993-2000). Moreover, IRL201805 was also shown to inhibit osteoclast function (V M Corrigall, et al, Immunology, 2009;128: 218-226). In this study, we have further investigated the capacity and mode-of-action of IRL201805 on receptor activator of nuclear factor-kB ligand (RANKL)-induced osteoclastogenesis in the context of RA patient derived $CD14^+$ monocytes.

Methods: Pre- and mature osteoclasts were derived from $CD14^+CD16^-$ monocytes, isolated from peripheral blood mononuclear cells of RA patients and healthy individuals, in *in vitro* cultures supplemented with macrophage-colony stimulating factor (M-CSF) and RANKL. Changes in gene transcript levels in preosteoclasts was examined by RNAseq, 24h after drug treatment.

Results: IRL201805 reduced the numbers of osteoclasts generated from preosteoclasts derived from both RA patients (vehicle: 777±587 vs IRL201805: 102±12; n=5) and healthy controls (vehicle: 812±569 vs IRL201805: 148±179; n=5), as visualized by immunofluorescent TRAP staining(**Figure 1**). Notably, IRL201805 also inhibited actin ring formation. Transcriptional evaluation of pre-osteoclast exposure to IRL201805 revealed that several genes implicated in osteoclast differentiation were significantly downregulated (e.g. *TNFSF11A* ($p< 0.002$)) or upregulated (e.g. *NFKBIZ* ($p< 0.01$)). Moreover, several vacuolar ATPases (i.e. *ATP6V0E2* ($p< 0.001$) and *ATP6V1C1* ($p< 0.01$)), which play a role in acidification of osteoclasts and bone resorption, were strongly downregulated.

Conclusion: Our finding suggest that IRL201805 inhibits osteoclast differentiation via modulation of RANK/RANKL signaling. Notably, there is an impact on metabolic pathways such as V-ATPases, which are critical for bone resorption. This is particulary revelant, as antiresorptive drugs that inhibit V-ATPase activity in osteoclasts have become an area of development. Taken together, these findings underpin the need for further investigations in RA patients and upcoming clinical phase IIb RA trials.

Disclosure: Y. Yamamura: Revolo Biotherapeutics, 5; **V. Corrigall**: Revolo Biotherapeutics, 2, 11; **L. Ravanetti**: Revolo Biotherapeutics, 3; **J. De Alba**: Revolo Biotherapeutics, 3; **R. Foulkes**: Revolo Biotherapeutics, 2; **P. Eggleton**: Revolo Biotherapeutics, 3; **C. Goodyear**: Abbvie, 6, AstraZeneca, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 5, Eli Lilly, 5, Galvani, 2, 5, GlaxoSmithKlein(GSK), 5, Istesso, 5, Janssen, 5, MedAnnex, 2, 5, Medincell, 2, MiroBio, 5, Revolo, 5, UCB, 5, 6.

Abstract Number: 2151

Effects of Methotrexate on Blood Pressure in Rheumatoid Arthritis: A Randomized Controlled Trial

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Treatment with methotrexate (MTX) has been shown to be associated with lower cardiovascular risk and lower blood pressure (BP) compared with other disease modifying anti-rheumatic drugs (DMARDs) in cross-sectional and epidemiological studies in patients with rheumatoid arthritis (RA). However, the evidence in longitudinal, randomized trials is lacking. We sought to address this issue by performing a randomized trial comparing the effect of MTX on BP against a control group on sulfasalazine.

Methods: Adult treatment-naïve patients, recently diagnosed with RA according to the 2010 ACR/EULAR criteria, were randomized to clinically guided doses of subcutaneous MTX (Group 1, n=31, age 57±15 years, 65% females) or the DMARD sulfasalazine (SSZ, Group 2, n=31, age 54±17 years, 58% females). Clinic systolic (SBP, primary study endpoint), diastolic

Table 1. Baseline clinical and demographic characteristics of the MTX (group 1) and the SSZ (group 2) groups.

Variables	Group 1 (n = 31)	Group 2 (n = 31)	p value
Age	57 ± 15	54 ± 17	ns
Gender (% of female)	65	58	ns
BMI (Kg/m^2)	30 ± 6	31 ± 8	ns
DAS28 - CRP	4.73 ± 1.20	5.00 ± 0. 83	ns
DAS28 - ESR	5.29 ± 1.44	5.31 ± 1.22	ns

DAS28, disease activity score 28; BMI, body mass index; CRP, C-reactive protein, ESR, erythrocyte sedimentation rate; MTX, methotrexate; SSZ, sulfasalazine.

Table 2. Differences between MTX-group (Group 1) and SSZ group (Group 2) after 1 month and 6 months of treatment

	Differences (mean ± SD) between Group 1 and Group 2 after 1 month	*p* value	Differences (mean ± SD) between Group 1 and Group 2 after 6 months	*p* value
Clinical peripheral SBP (mmHg)	-2.6 ± 10.6	.09	-4.0 ± 10.8	.038*
Clinical peripheral DBP (mmHg)	-1.8 ± 6.7	.053	-0.7 ± 6.8	.053*
Clinical peripheral PP (mmHg)	-.8 ± 7.2	ns	-4.8 ± 11.3	ns
Clinical peripheral MAP (mmHg)	-2.1 ± 7.5	.049	-4.3 ± 17.9	.023*
AIx (%)	-1.1 ± 1.6	ns	-0.5 ± 1.6	ns

*Not corrected for ties

MTX, methotrexate; SSZ, sulfasalazine; SD, standard deviation; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure.

(DBP), and mean arterial pressure (MAP), and the augmentation index (AIx), (a marker of arterial wave reflection) were measured at baseline (before treatment), and after 1 and 6 months (ClinicalTrials.gov: NCT03254589).

Results: At baseline, the two groups were matched for age, gender, body mass index, and 28-joint disease activity score (p>0.05 for all comparisons). After 1 month of treatment, group 1 had a trend towards a significant reduction in SBP (mean difference -2.6±10.6 mmHg, p=0.09) and DBP (mean difference -1.8±6.7 mmHg, p = 0.053) and a significant reduction in MAP (mean difference -2.1±7.5 mmHg, p=0.049) compared to Group 2. After 6 months of treatment, group 1 had a significant reduction in SBP (mean difference -4.0±10.8 mmHg, p=0.038) and MAP (mean difference -4.3±17.9 mmHg, p=0.023) and a trend towards a significant reduction in DBP (mean difference -0.7±6.82 mmHg, p=0.053). There were no significant between-group differences in AIx over time.

Conclusion: The results of this study provide the first evidence that MTX treatment causes a significant reduction in SBP (primary endpoint) at 6 months in RA patients in intervention studies. The effects of MTX on BP are not mediated by changes in arterial wave reflections. Further research is warranted to identify the mechanisms involved in the MTX-induced BP lowering effects and whether such effects account for the protective effects of MTX against cardiovascular disease observed in RA.

Disclosure: S. Tommasi: None; **R. Woodman**: None; **M. Wiese**: None; **M. Shanahan**: None; **A. Mangoni**: None.

Abstract Number: 2152

Survival Benefits of Knee and Hip Arthroplasty in Patients with Rheumatoid Arthritis: A General Population-based Cohort Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Treatments Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is associated with increased risk of cardiovascular disease (CVD), venous thromboembolism (VTE), and mortality. Many patients with RA underwent knee and hip replacement surgeries, i.e., knee arthroplasty and hip arthroplasty. The primary role of knee arthroplasty and hip arthroplasty is to remove the structural abnormality, leading to significant improvements in pain and function. However, the aforementioned improvements may not translate into a lower risk of all-cause mortality, one of the most important indicators for the net risk-benefit effect of any clinical treatment regimen, among patients with RA. Considering physical inactivity and use of non-steroidal anti-inflammatory drugs (NSAIDs) are major risk factors for CVD, one would anticipate that there is a potential cardioprotective advantage coupled with knee arthroplasty and hip arthroplasty as they enhance the capacity for physical activity and reduced usage of analgesics (e.g., NSAIDs). Nevertheless, the impact of these surgeries on CVD risk among patients with RA also needs to be yet confirmed. We aimed to examine the relation of knee or hip arthroplasty to the risk of all-cause mortality, CVD and VTE among patients with RA.

Methods: We included patients with RA (ages≥20 years) from the IQVIA Medical Research Data primary care database in the United Kingdom. The primary outcome was all-cause mortality. The secondary outcomes included CVD and VTE. We conducted propensity score-matched cohort studies to compare the risks of each outcome between subjects with knee arthroplasty (n=2,387) and hip arthroplasty (n=1,681), and those without knee arthroplasty (n=2,387) or hip arthroplasty (n=1,681), respectively.

Results: Subjects with knee arthroplasty had 23% lower risk of mortality than those without knee arthroplasty (HR: 0.77, 95%CI: 0.65-0.90) (Figure 1A). Similarly, a lower, albeit non-statistically significant, mortality rate was observed among subjects with hip arthroplasty than those without arthroplasty (HR: 0.87, 95%CI: 0.73-1.04) (Figure 1B). Compared with those without arthroplasty, subjects with knee or hip arthroplasty had a lower, albeit non-statistically significant, risk of CVD. The corresponding HRs were 0.86 (95%CI: 0.73-1.01) and 0.84 (95%CI: 0.69-1.02), respectively (Figure 2). Both subjects with knee or hip arthroplasty showed a higher risk of VTE than their counterparts (HR for knee arthroplasty: 1.63 (95%CI: 1.23-2.17); HR for hip arthroplasty: 2.19 (95%CI: 1.54-3.11) (Figure 3). The associations of knee and hip arthroplasty with the risks of mortality, CVD and VTE were generally consistent across strata of age and sex.

Conclusion: Our population-based cohort study provides the first evidence that knee and hip arthroplasty were associated with lower risks of mortality and CVD but increased risk of VTE among patients with RA.

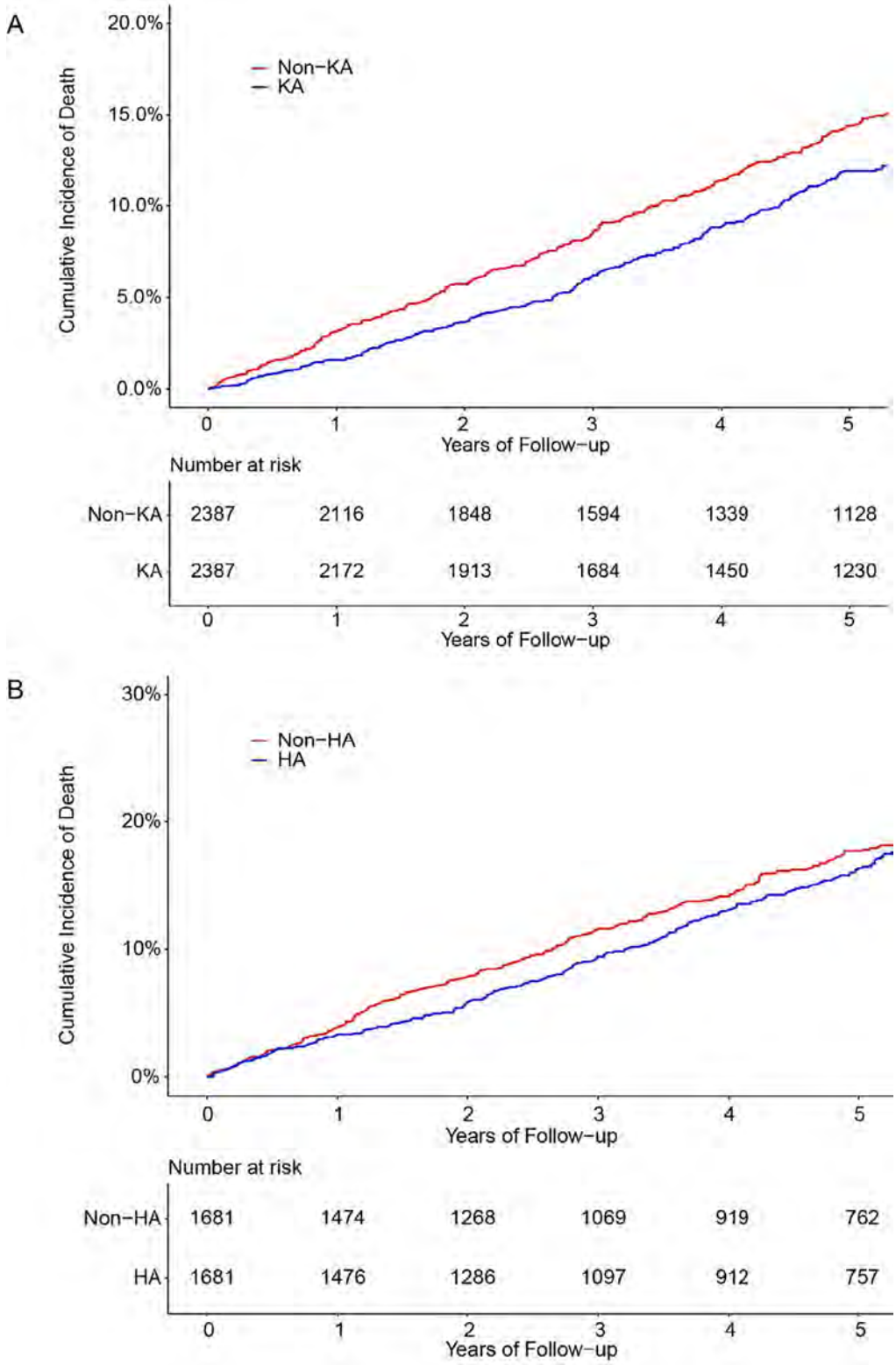

Figure 1. Cumulative incidence of death among subjects with knee or hip arthroplasty compared subjects without knee or hip arthroplasty. A, subjects with knee arthroplasty compared subjects without knee arthroplasty; B, subjects with hip arthroplasty compared subjects without hip arthroplasty. KA, knee arthroplasty; HA, hip arthroplasty.

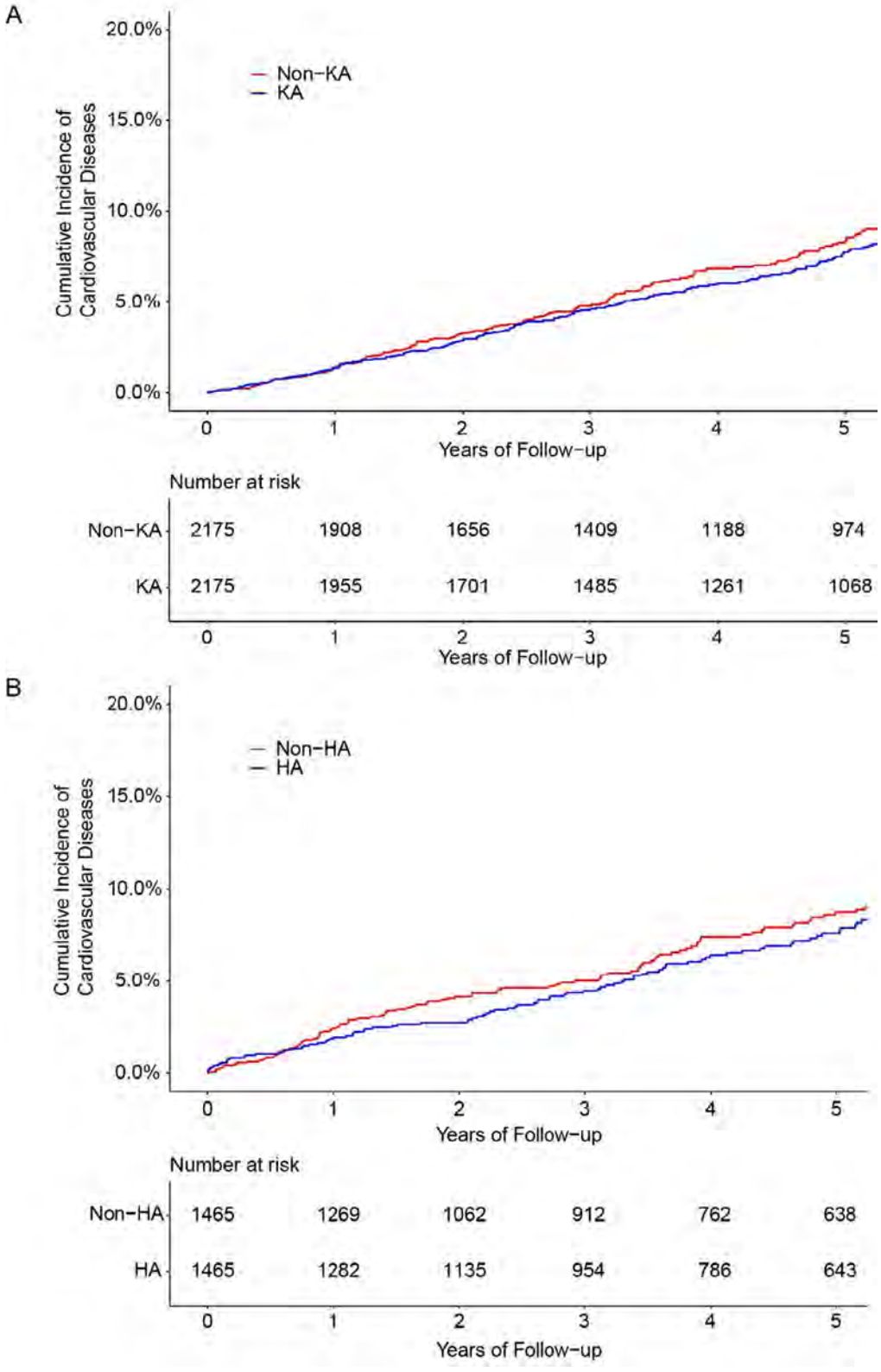

Figure 2. Cumulative incidence of cardiovascular disease among subjects with knee or hip arthroplasty compared subjects without knee or hip arthroplasty. A, subjects with knee arthroplasty compared subjects without knee arthroplasty; B, subjects with hip arthroplasty compared subjects without hip arthroplasty. KA, knee arthroplasty; HA, hip arthroplasty.

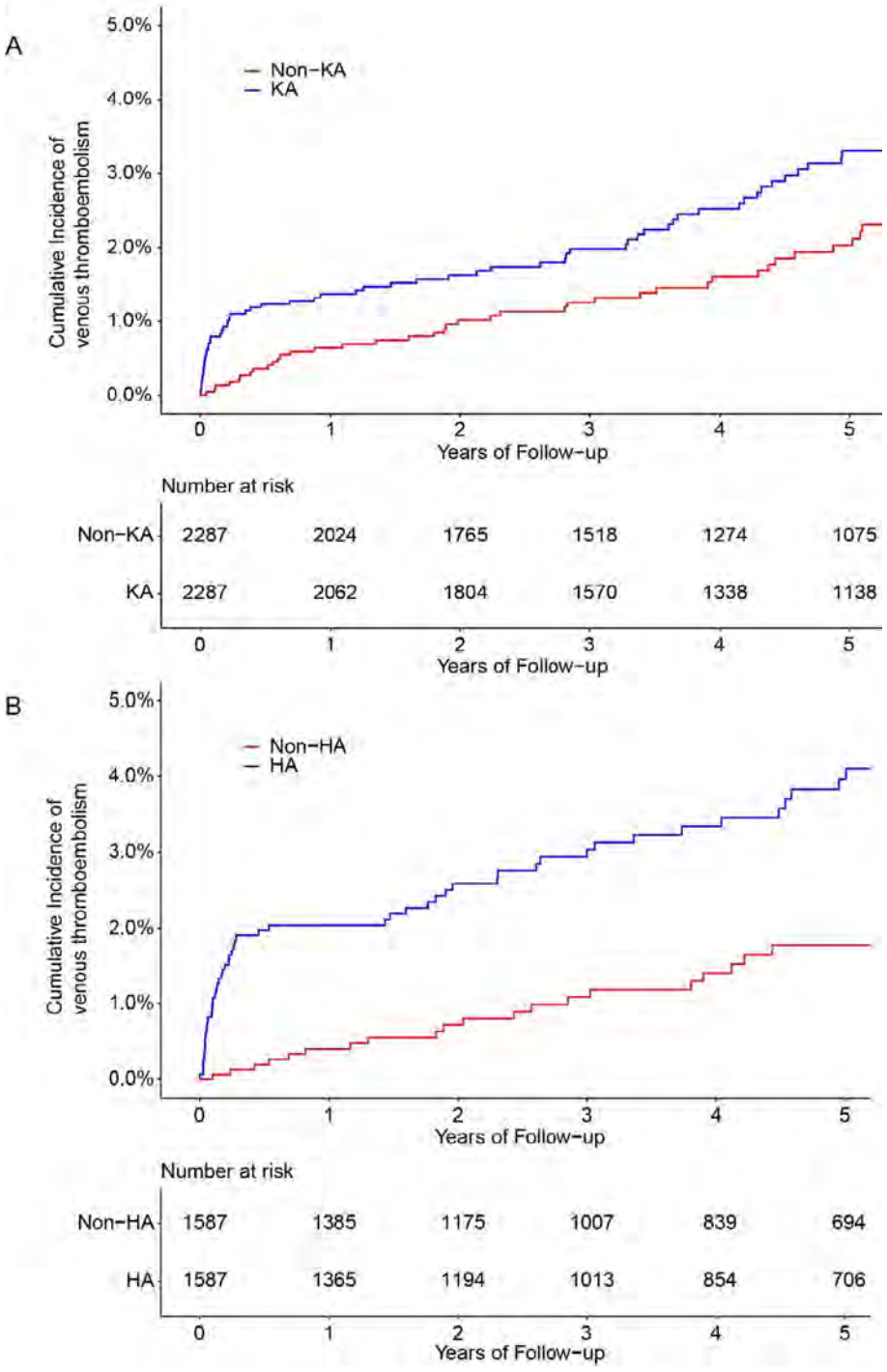

Figure 3. Cumulative incidence of venous thromboembolism among subjects with knee or hip arthroplasty compared subjects without knee or hip arthroplasty. A, subjects with knee arthroplasty compared subjects without knee arthroplasty; B, subjects with hip arthroplasty compared subjects without hip arthroplasty. KA, knee arthroplasty; HA, hip arthroplasty.

Disclosure: X. Deng: None; **Y. Zhang**: None; **Y. Wang**: None; **N. Lu**: None; **D. Xie**: None; **H. Lyu**: None; **J. Wei**: None; **C. Zeng**: None; **G. Lei**: None; **H. Li**: None.

Abstract Number: 2153

Effects of One-year Tofacitinib Therapy on Angiogenic Biomarkers in Rheumatoid Arthritis

György Kerekes[1], Monika Czókolyová[1], Attila Hamar[1], Anita Pusztai[1], Gábor Tajti[1], Mónika Katkó[1], Edit Végh[1], Zsófia Pethő[1], Nóra Bodnár[1], Ágnes Horváth[1], Boglárka Soós[1], Szilvia Szamosi[1], Zsolt Hascsi[1], Mariann Harangi[1], Katalin Hodosi[1], György Panyi[1], Tamas Seres[2], Gabriella Szücs[1] and **Zoltán Szekanecz**[1], [1]University of Debrecen, Faculty of Medicine, Debrecen, Hungary, [2]University of Colorado Anschutz Medical Campus, Aurora, CO

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular (CV) morbidity, mortality and perpetuated synovial angiogenesis have been associated with rheumatoid arthritis (RA). In our study we evaluated angiogenic factors in relation to vascular inflammation and function and clinical markers in RA patients undergoing one-year tofacitinib therapy.

Methods: Thirty RA patients treated with either 5 mg or 10 mg bid tofacitinib were included in a 12-month follow-up study. Eventually 26 patients completed the study and included in data analysis. Levels of various angiogenic cytokines (TNF-α, IL-6), growth factors (VEGF, bFGF, EGF, PlGF), cathepsin K (CathK), CXCL8, galectin-3 (Gal-3) and NT-proBNP were determined at baseline, 6 and 12 months after initiating tofacitinib treatment. In order to assess flow-mediated vasodilation (FMD), common carotid intima-media thickness (ccIMT) and carotid-femoral pulse-wave velocity (cfPWV) ultrasonography was performed. Synovial and aortic inflammation was also assessed by ^{13}F-FDG-PET-CT.

Results: One-year tofacitinib therapy significantly decreased IL-6, VEGF, bFGF, EGF, PlGF and CathK, while increased Gal-3 production ($p < 0.05$). Basic FGF, PlGF and NT-proBNP levels were higher, while PECAM-1 levels were lower in RF seropositive patients ($p < 0.05$). TNF-α, bFGF and PlGF correlated with post-treatment synovial inflammation, while aortic inflammation was rather dependent on IL-6 and PECAM-1 as determined by PET/CT ($p < 0.05$). In the correlation analyses, NT-proBNP, CXCL8 and Cath variable correlated with ccIMT ($p < 0.05$).

Conclusion: Decreasing production of bFGF, PlGF or IL-6 by one-year tofacitinib therapy potentially inhibits synovial and aortic inflammation, respectively. Although NT-proBNP, CXCL8 and CathK were associated with ccIMT, their role in RA-associated atherosclerosis needs to be further evaluated.

Disclosure: G. Kerekes: None; **M. Czókolyová**: None; **A. Hamar**: None; **A. Pusztai**: None; **G. Tajti**: None; **M. Katkó**: None; **E. Végh**: None; **Z. Pethő**: None; **N. Bodnár**: None; **Á. Horváth**: None; **B. Soós**: None; **S. Szamosi**: None; **Z. Hascsi**: None; **M. Harangi**: None; **K. Hodosi**: None; **G. Panyi**: None; **T. Seres**: None; **G. Szücs**: None; **Z. Szekanecz**: Pfizer, 1, 2, 5, 6.

Abstract Number: 2154

Two-Year Persistence of First-Line Biological or JAK Inhibitor Treatment in Patients with Long-Standing Rheumatoid Arthritis and Failure of Triple Therapy with Synthetic DMARDs

Sebastian Ibanez Vodnizza[1], María Paz Poblete[2], María Francisca Valenzuela[3], María Magdalena Canals[2], Dominga García[2] and Carla Jaque[3], [1]Clinica Alemana de Santiago / Facultad de Medicina Universidad del Desarrollo-CAS, Santiago, Chile, [2]Hospital Padre Hurtado / Facultad de Medicina Universidad del Desarrollo-CAS, Santiago, Chile, [3]Hospital Padre Hurtado, Santiago, Chile

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: RA – Treatments Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: In Chile, patients with rheumatoid arthritis (RA) can apply to receive state-funded biological or JAK inhibitor treatment if they have failed (defined as a DAS28-ESR persistently greater than 5.1) to the combination of three synthetic DMARDs (including methotrexate, leflunomide, sulfasalazine, and/or hydroxychloroquine) used for at least 6 months. Our objective was to evaluate the two-year persistence of the first biologic or JAK inhibitor used in this group of patients.

Methods: We conducted a retrospective evaluation of patients benefiting from state-funded biological or JAK inhibitor treatments at two healthcare centers. Demographic variables were recorded, including gender, age, comorbidities (Charlson Comorbidity Index), years since RA diagnosis, synthetic DMARDs used at the time of starting biological or JAK inhibitor treatment, use of corticosteroids and NSAIDs, the specific biological or JAK inhibitor used, persistence with the medication after two years, and, for those who discontinued treatment, the cause of discontinuation and duration of persistence. The relationship between persistence and different demographic and baseline variables was evaluated using logistic binary regression.

Table 1. Baseline use of synthetic DMARDs, corticosteroids, and NSAIDs.

Drug	Number of patients (% of total)
Methotrexate	41 (68.3)
Leflunomide	35 (58.3)
Sulfasalazine	24 (40)
Hydroxychloroquine	32 (53.3)
Corticosteroids	47 (78.3)
NSAIDs	41 (68.3)

Table 2. Two-year persistence of the first biologic or JAK inhibitor.

Biologic or JAK inhibitor	Two-year persistence	
	Yes	No
Abatacept	10	19
Etanercept	11	5
Adalimumab	1	8
Tocilizumab	1	1
Golimumab	2	0
Rituximab	1	0
Tofacitinib	1	0
Total	27	33

Results: We included 60 patients, of whom 52 were women (86.7%). The mean age was 58 years (standard deviation 12.5), and the Charlson Comorbidity Index was 3 or higher in 40% of patients. The median baseline DAS28-ESR was 5.8 (interquartile range 5.4-6.7), and the median years since diagnosis was 10.5 (IQR 5.7-16.5). Table 1 provides the distribution of synthetic DMARDs, corticosteroids, and NSAIDs used at the start of biologic or JAK inhibitor treatment. Table 2 presents the first-line biologic or JAK inhibitor used and its persistence. At the two-year mark, 27 patients (45%) persisted with the first-line biologic or JAK inhibitor. Among the 33 patients who discontinued treatment, the mean duration of persistence was 323 days (SD 176). The univariate analysis revealed significant associations between persistence and the use of baseline sulfasalazine (62.5% of users persisted at 2 years, compared to 33.3% of non-users), as well as with the specific first biologic or JAK inhibitor used (see Table 2). The primary cause of treatment discontinuation was loss of efficacy (60.6%), followed by adverse effects (24.2%).

Conclusion: The two-year persistence rate of the first biologic or JAK inhibitor in this group of patients with long-standing rheumatoid arthritis, high comorbidity index, and failure of synthetic DMARDs triple therapy was low, at only 45%. Loss of efficacy was the main reason for treatment discontinuation. A trend towards lower persistence with the use of adalimumab was observed, but this finding should be interpreted with caution as adalimumab was the only biologic that underwent exchanges between biosimilars and the original molecule. The association between greater persistence and the initial use of sulfasalazine should be explored in future studies. Notably, the utilization of JAK inhibitors as first-line advanced therapy was very low.

Disclosure: S. Ibanez Vodnizza: AbbVie/Abbott, 1, 6, Janssen, 1, 6, Novartis, 1, 6; **M. Poblete**: None; **M. Valenzuela**: None; **M. Canals**: None; **D. García**: None; **C. Jaque**: None.

Abstract Number: 2155

The Impact of Filgotinib on Disease Activity Outcomes with Concomitant Pain Control in the Phase 3 FINCH Studies

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

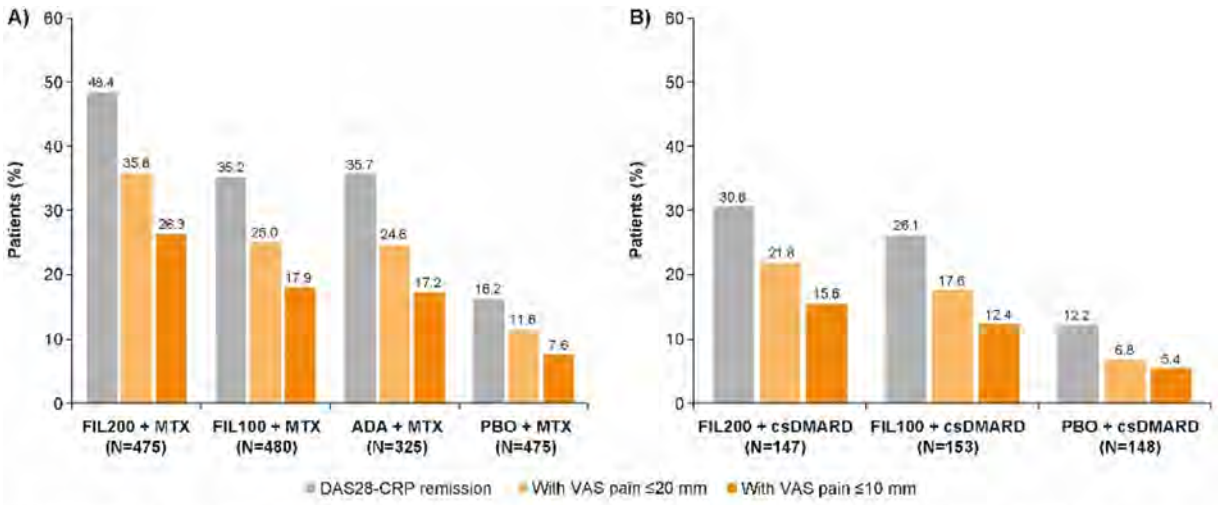
Background/Purpose: Patients (pts) with rheumatoid arthritis (RA) often experience substantial pain despite treatment, and consider pain control an important treatment outcome. This p*ost hoc* analysis of the FINCH studies assessed specific effects of filgotinib (FIL) on pain and its relationship with efficacy in pts with RA.

Table. Duration of threshold pain response achieved over observation period for pain VAS ≤10 mm and ≤20 mm; full analysis set excluding responders at baseline

	FINCH 1 (Week 52)			
	FIL200 + MTX (N=475)	FIL100 + MTX (N=480)	ADA + MTX (N=325)	PBO + MTX (N=475)*
Duration of VAS pain ≤10 mm	n=472	n=475	n=322	n=474
Number of weeks, mean (SD)	13.2 (17.36)	10.6 (15.32)	10.1 (15.04)	1.5 (3.77)
% of total duration, mean (SD)	26.3 (34.18)	21.6 (30.12)	20.4 (30.07)	6.2 (15.81)
Duration of VAS pain ≤20 mm	n=459	n=467	n=314	n=467
Number of weeks, mean (SD)	20.5 (19.98)	17.6 (18.27)	17.1 (18.01)	3.4 (5.82)
% of total duration, mean (SD)	40.7 (38.82)	35.6 (35.68)	34.4 (35.33)	14.4 (24.54)
	FINCH 2 (Week 24)			
	FIL200 + csDMARD (N=147)	FIL100 + csDMARD (N=153)	PBO + csDMARD (N=148)	
Duration of VAS pain ≤10 mm	n=146	n=150	n=146	
Number of weeks, mean (SD)	3.7 (6.07)	2.8 (5.68)	1.0 (3.23)	–
% of total duration, mean (SD)	16.0 (25.93)	11.6 (23.26)	4.6 (14.73)	–
Duration of VAS pain ≤20 mm	n=143	n=146	n=143	
Number of weeks, mean (SD)	7.3 (8.18)	5.6 (7.99)	2.3 (4.89)	–
% of total duration, mean (SD)	31.3 (34.64)	23.5 (33.31)	10.0 (21.29)	–

*Placebo-treated patients were re-randomized to FIL at Week 24.
ADA, adalimumab; csDMARD, conventional synthetic disease-modifying antirheumatic drug; FIL(100/200), filgotinib 100/200 mg; MTX, methotrexate; PBO, placebo; SD, standard deviation; VAS, visual analog scale.

Methods: FINCH 1–3 (NCT02889796, NCT02873936, NCT02886728) were Phase 3, randomized, double-blind trials of FIL 100 mg and 200 mg (FIL100/200). In FINCH 1, pts with an inadequate response (IR) to methotrexate (MTX) received FIL, adalimumab (ADA) or placebo (PBO) + MTX for 52 weeks. In FINCH 2, pts with an IR to bDMARDs received FIL or PBO + csDMARDs for 24 weeks. In FINCH 3, MTX-naïve pts received FIL ± MTX or MTX for 52 weeks. For each treatment group, pts reported pain on a 100-mm visual analog scale (VAS). VAS pain ≤ 20 mm indicated health status was not negatively affected by pain; ≤ 10 mm reflected limited to no pain.[1] Time to first VAS pain ≤ 10 mm was assessed. The duration of



ADA, adalimumab; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAS28-CRP, Disease Activity Score in 28 joints using C-reactive protein; FIL(100/200), filgotinib (100/200 mg); MTX, methotrexate; PBO, placebo; VAS, visual analog scale.

Figure 1. DAS28-CRP remission and improvement in VAS pain score (up to Week 24) in (A) FINCH 1 and (B) FINCH 2

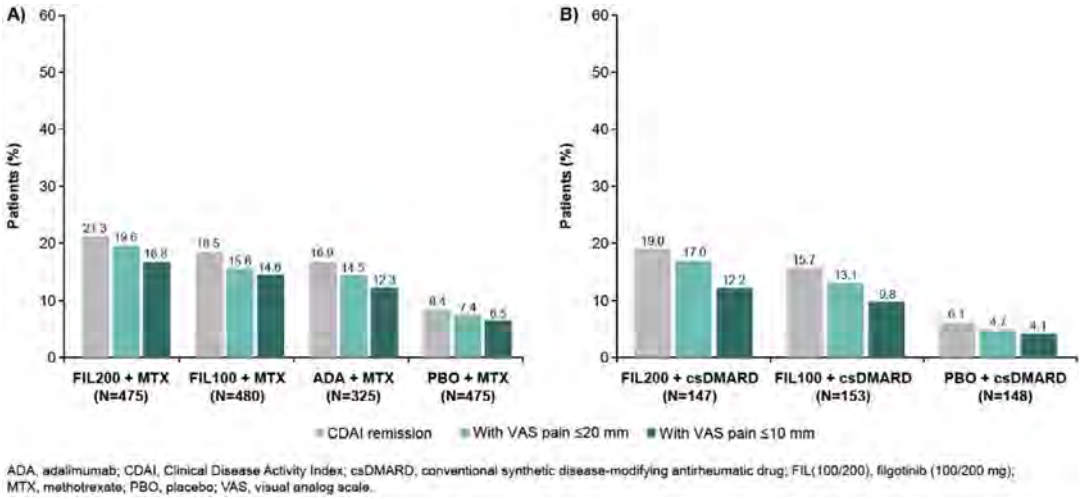


Figure 2. CDAI remission and improvement in VAS pain score (up to Week 24) in (A) FINCH 1 and (B) FINCH 2

the study period during which VAS pain was ≤ 20 mm or ≤ 10 mm and the proportion of pts who achieved remission (DAS28-CRP < 2.6 or CDAI ≤ 2.8) at Week 24 was evaluated. Of pts who achieved DAS28-CRP or CDAI remission, the proportion who also reported VAS pain ≤ 20 mm or ≤ 10 mm was determined.

Results: In FINCH 1, there was a higher probability of achieving VAS pain ≤ 10 mm with FIL200, vs ADA + MTX or PBO + MTX; responses were better or comparable with FIL100 vs other treatments. Similar findings were seen in FINCH 2 and 3. In FINCH 1, the time during which VAS pain score was ≤ 20 mm or ≤ 10 mm was greatest in the FIL200 group, and comparable between the FIL100 and ADA groups (**Table**). The duration of time under each pain threshold was greater in each FIL group vs PBO in FINCH 2 (**Table**) and in each FIL group vs MTX in FINCH 3. In FINCH 1, the proportion of pts achieving DAS28-CRP remission was greater with FIL200 + MTX (48.4%) and comparable for FIL100 + MTX (35.2%) vs ADA + MTX (35.7%; **Figure 1A**). The proportion of pts who achieved VAS pain ≤ 20 mm and ≤ 10 mm in addition to DAS28-CRP remission was 35.8% and 26.3%, respectively, in the FIL200 + MTX group, vs 24.6% and 17.2% in the ADA + MTX group (**-Figure 1A**). In FINCH 2, a greater proportion of pts in the FIL groups achieved DAS28-CRP remission and pain responses in addition to DAS28-CRP remission vs the PBO group (**Figure 1B**). Findings were similar when CDAI remission was assessed for FINCH 1 and 2 (**Figure 2A and B**). In FINCH 3, the proportion of pts to achieve remission and pain responses in addition to remission was greater in the FIL vs MTX groups; e.g. DAS28-CRP remission and VAS pain ≤ 10 mm was achieved by 23.3% of pts on FIL200, 33.2% on FIL200 + MTX, 27.5% on FIL100 + MTX and 14.9% on MTX.

Conclusion: Across the studies, duration of threshold pain responses achieved over the observation periods was greater with FIL vs comparators. In FINCH 1, FIL200 had a particularly favorable impact when pain response and remission were assessed together; results were comparable between FIL100 and ADA. Similar findings were seen with FIL vs PBO and MTX in FINCH 2 and 3, respectively. These findings suggest that JAK1 inhibition may offer potential added value with respect to patient-reported pain as well as treat-to-target goals.

Reference:

1. Taylor PC, et al. J Clin Med 2019;8:831

Disclosure: P. Taylor: AbbVie, 2, Biogen, 2, Eli Lilly, 2, Fresenius, 2, Galapagos, 2, 5, Gilead Sciences, 2, GSK, 2, Janssen, 2, Nordic Pharma, 2, Pfizer Inc, 2, Sanofi, 2, UCB, 2; **A. Kavanaugh**: Amgen, 2, BMS, 2, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2; **P. Nash**: AbbVie, 5, 6, Bristol Myers Squibb, 5, 6, Celgene, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, GSK, 5, 6,

Janssen, 5, 6, Novartis, 5, 6, Pfizer Inc, 5, 6; **J. Pope**: AbbVie, 1, 2; **G. Pongratz**: AbbVie, 2, 6, Boehringer Ingelheim, 2, 6, Galapagos, 2, Lilly, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 6; **B. Fautrel**: AbbVie, 2, BMS, 2, Chugai, 2, Fresenius Kabi, 2, Galapagos, 2, Lilly, 2, Medac, 2, Nordic Pharma, 2, Novartis, 2, Pfizer, 2, Sobi, 2, UCB, 2; **R. Alten**: AbbVie, 2, 6, Amgen, 2, 6, Biogen, 2, 6, BMS, 2, 6, Celltrion, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Lilly, 2, 6, Medac, 2, 6, MSD, 2, 6, Mylan, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sandoz, 2, 6, Sanofi-Genzyme, 2, 6, UCB, 2, 6, Viatris, 2, 6; **K. Hasegawa**: Gilead, 3, 11; **S. Rao**: Gilead, 3; **D. de Vries**: Galapagos, 3, 11; **P. Stiers**: Galapagos, 3, 11; **C. Watson**: Galapagos, 3, 11; **R. Westhovens**: Celltrion, 2, 6, Galapagos, 2, 6, Gilead, 2, 6.

Abstract Number: 2156

Efficacy of Olokizumab in Comorbid Depressive Disorder in Patients with Rheumatoid Arthritis: Preliminary Results of a Study

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Interleukin-6 (IL) plays an important role in the pathogenesis of comorbid rheumatoid arthritis (RA) depression, and IL-6 inhibitors used to treat RA patients may have antidepressant effects. The **objective** was to evaluate the efficacy of IL-6 inhibitor olokizumab (OKZ) in reducing the symptoms of depression in patients with moderate/high RA disease activity.

Methods: To date, 76 RA patients have been included, of which 65 (85.5%) are women, with an average age of 48.2 ±11.5 years; with predominantly high RA disease activity according to DAS28 (CRP) (89.2%), SDAI (83.8%) and CDAI (79.7%) indices and inefficacy of stable 12-week csDMARD therapy. In all patients, a psychiatrist diagnosed chronic or recurrent depression of varying severity (in accordance with ICD-10) during a semi-structured interview. At week 0, all patients were randomized by the method of sequential numbers in a ratio of 1:1:1 to one of the 3 study groups: group 1 – csDMARDs+OKZ 64 mg subcutaneously once every 4 weeks (n=27); group 2 – csDMARDs+OKZ 64 mg subcutaneously once every 4 weeks + psychopharmacotherapy (PPT) (n=39); group 3 – csDMARDs+PPT (n=10). The duration of the study is 24 weeks. The dynamics of depression severity were assessed by the Patient's Health Questionnaire – 9 (PHQ-9), Montgomery – Asberg Depression Rating Scale(MADRS); anxiety – Hamilton Anxiety Rating Scale (HAM-A); experimental psychological projective tests were also used.

Results: There were no differences between the three groups in the duration of RA, severity of pain, TJC, SJC, nor patient or physician global assessments, physical function limitations according to the HAQ DI and health related quality of life according to EQ-5D-3L. After 12 and 24 weeks of therapy, there was a significant decrease in the severity of depression and anxiety in all groups of patients. However, the difference between the final and initial values of all scales was statistically significantly greater ($p < 0.05$) in the groups of patients receiving PPT: csDMARDs+PPT (ΔPHQ-9 24–0=–15.5±3.53; ΔMADRS 24–0=–25.0±1.41; ΔHAM-A 24-0=–18.5±3.53) and csDMARDs+OKZ+PPT (ΔPHQ-9 24–0=–5.73±4.31; ΔMADRS 24–0=–22.3±4.44; ΔHAM-A 24-0=–12.5±4.22), compared with the csDMARDs+OKZ group (ΔPHQ-9 24–0=–

Table 1. Changes in the severity of depression according to MADRS and PHQ-9 and anxiety according to HAM-A over time Footnotes: csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; OKZ, olokizumab; PPT, psychopharmacological treatment; p, significance of inter-group differences; MADRS, Montgomery – Asberg Depression Rating Scale; HAM-A, Hamilton Anxiety Rating Scale; PHQ-9, Patient's Health Questionnaire; n/s, inter-group differences were not significant.

Score	Group 1: csDMARDs+OKZ (n=27)	Group 2: csDMARDs+OKZ+PPT (n=39)	Group 3: csDMARDs+PPT (n=10)	P
MADRS, M±σ				
At baseline	22.1±5.3	25.7±5.6	25.5±3.2	p_{1-2}=0.011
At week 12	15.6±7.1	8.8±4.9	6.7±4.6	p_{1-2} <0.001 p_{1-3}=0.005
At week 24	15.5±7.5	5.0±3.9	4.7±1.2	p_{1-2} <0.001 p_{1-3}=0.024
ΔMADRS (week 12–0)	−6.6±5.9	−18.7±6.4	−21.4±3.3	p_{1-2} <0.001 p_{1-3} <0.001
ΔMADRS (week 24–0)	−5.3±7.3	−22.3±4.4	−25.0±1.4	p_{1-2}<0.001 p_{1-3}=0.003
Significance of differences in MADRS score in the group (p)	p_{0-12} <0.001 p_{0-24}=0.001	p_{0-12}<0.001 p_{0-24}<0.001 p_{12-24} =0.003 pΔ12–24=0.042	p_{0-12}=0.001 p_{0-24}<0.001	
HAM-A, M±σ				
At baseline	16.6±4.5	18.2±3.2	18.2±3.6	n/s
At week 12	12.5±5.6	7.8±3.5	5.6±2.6	p_{1-2} <0.001 p_{1-3}=0.004
At week 24	12.2±5.8	6.0±2.7	4.5±0.7	p_{1-2} <0.001
ΔHAM-A (week 12–0)	−4.4±6.5	−10.8±3.6	−13.0±7.9	p_{1-2}<0.001 p_{1-3} =0.019
ΔHAM-A (week 24–0)	−5.8±7.7	−12.5±4.2	−18.5±3.5	p_{1-2} =0.007 p_{1-3}=0.045
Significance of differences in HAM-A score in the group (p)	p_{0-12}=0.008 p_{0-24}=0.006	p_{0-12}<0.001 p_{0-24}<0.001 p_{12-24} =0.046	p_{0-12}=0.006 p_{0-24}=0.012	
PHQ-9, M±σ				
At baseline	6.6±3.8	9.9±5.4	11.4±4.8	p_{1-2}=0.009 p_{1-3}=0.003
At week 12	4.1±2.8	4.6±3.2	6.0±3.1	n/s
At week 24	3.0±2.4	3.6±2.6	2.0±0.01	n/s
ΔPHQ-9 (week 12–0)	−2.9±4.5	−5.7±4.6	−5.8±5.6	p_{2-3}=0.043
ΔPHQ-9 (week 24–0)	−3.1±3.7	−5.7±4.3	−15.5±3.5	p_{2-3}=0.008 p_{1-3} <0.001
Significance of differences in PHQ-9 score in the group (p)	p_{0-12}=0.015 p_{0-24} <0.008	p_{0-12}<0.001 p_{0-24}<0.001	p_{0-12} =0.020 p_{0-24} =0.020	

3.08±3.67; ΔMADRS 24-0=–5.25±7.33; ΔHAM-A 24–0=–5.75±7.74) (Table 1). According to a semi-structured psychiatric interview and experimental psychological tests, the proportion of patients without depression after 24 weeks of therapy was significantly higher in the groups of patients receiving PPT: 100% in the group of csDMARDs+PPT and 83% - csDMARDs +OKZ+PPT, as opposed to 22% in the group of csDMARDs+OKZ. OKZ therapy contributed to the normalization of night sleep but did not lead to a decrease in the frequency and severity of cognitive impairments (CI).

Conclusion: OKZ has an antidepressant effect, leads to a decrease in the frequency of sleep disorders, but a complete regression of depression was also found in 22% of patients who received OKZ without PPT, mainly in patients with mild depression. The combination of OKZ and PPT was optimal for the complete regression of depression, anxiety and a decrease in the frequency and severity of CI.

Disclosure: V. Strand: Abbvie, 2, Alpine Immune Sciences, 2, Amgen, 2, Arena, 2, AstraZeneca, 2, Bayer, 2, Biosplice, 2, Bioventus, 2, Blackrock, 2, 2, BMS, 2, Boehringer Ingelheim, 2, Celltrion, 2, Chemocentryx, 2, EMD Serono, 2, Equillium, 2, Ermium, 2, Eupraxia Pharmaceuticals, 2, Flexion, 2, Galapagos, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon, 2, Ichnos, 2, Inmedix, 2, Janssen, 2, Kiniksa, 2, 2, Kypha, 2, Lilly, 2, Merck, 2, MiMedx, 2, Novartis, 2, Omeros, 2, Pfizer, 2, Regeneron, 2, Rheos, 2, R-Pharm, 2, Samsung, 2, Sandoz, 2, Sanofi, 2, Scipher, 2, Setpoint, 2, Sorrento, 2, Spherix, 2, Tonix, 2, UCB, 2, Urica, 2; **T. Lisitsyna**: None; **A. Abramkin**: None;

D. Veltishchev: None; **O. Seravina**: None; **O. Kovalevskaya**: None; **A. Borisova**: None; **S. Kuzkina**: R-Pharm, 3; **V. Ignatiev**: R-Pharm, 3; **E. NASONOV**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 6, Novartis, 6, Pfizer, 6, R-Pharm, 6.

Abstract Number: 2157

Exploratory Analysis of the Mechanisms of Action of the Potential Analgesic Effect of Tofacitinib and Adalimumab over Placebo in Patients with Rheumatoid Arthritis: Results of a Mediation Modeling Analysis

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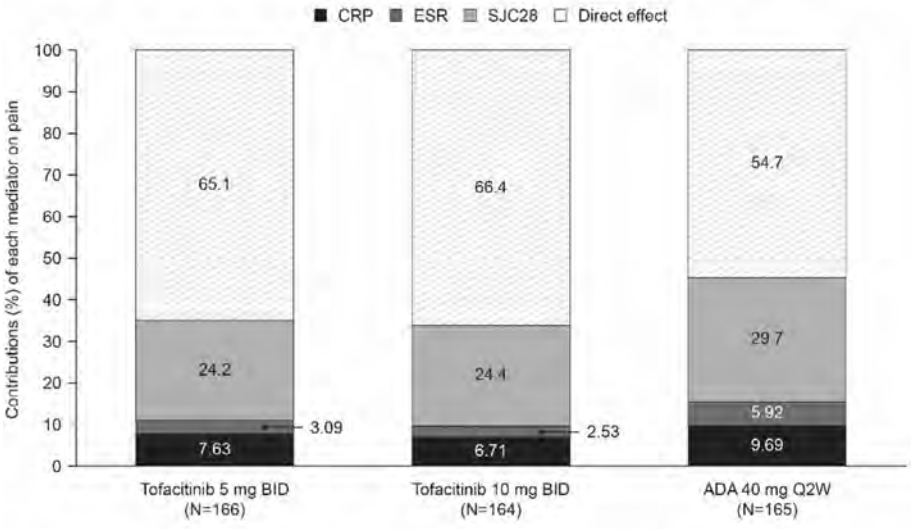
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Pain is the most common symptom reported by patients (pts) with rheumatic disorders, such as RA.[1] Improvement in pain with antirheumatic drugs is generally believed to be mediated by anti-inflammatory effects; however, a possible direct effect on pain of new antirheumatic drugs, such as Janus kinase inhibitors, is being debated.[2] Here, we used mediation modeling to explore the mechanisms of action of the effects of tofacitinib on pain in pts with RA.

Fig. Mediation effects: percentage contribution of indirect effects (via CRP, ESR, and SJC28) and direct effects on pain over PBO at M3 in pts receiving tofacitinib 5 mg BID, tofacitinib 10 mg BID, and ADA in ORAL Standard



Pain was assessed using Pt's Assessment of Arthritis Pain (Visual Analog Scale; 0–100 mm) scores at M3. Parameter estimates of the mediation model were linearly combined to calculate the direct and indirect effects. The software package PROC CALIS (SAS version 9.4) was used

ADA, adalimumab; BID, twice daily; M, Month; N, number of pts in each treatment group; PBO, placebo; pts, patients; Q2W, once every 2 weeks; SJC28, swollen joint count in 28 joints

Methods: This post hoc analysis used data at Month (M)3 from pts with active RA enrolled in the 12-month, Phase 3, randomized, placebo (PBO)-controlled ORAL Standard (NCT00853385) trial.[3] Pts received tofacitinib 5 or 10 mg twice daily (BID), adalimumab (ADA) 40 mg once every 2 weeks, or PBO (advancing to tofacitinib 5 or 10mg BID at M3), with stable doses of background methotrexate.[3] A mediation, or path, analysis was performed, with pain (Visual Analog Scale; 0–100mm) scores at M3 the dependent variable, treatment (tofacitinib 5 or 10 mg BID or ADA) the independent variable, and inflammation (measured by inflammatory markers CRP, ESR, and swollen joint count in 28 joints [SJC28]) a mediator. An indirect effect was defined as the treatment effect on pain over PBO mediated by CRP, ESR, and SJC28. A direct effect (over PBO) was defined as the treatment effect on pain not attributable to CRP, ESR, and SJC28. M3 data were used without imputations.

Results: Data for 580 pts were included: 166, 164, 165, and 85 pts received tofacitinib 5mg BID, tofacitinib 10 mg BID, ADA, and PBO, respectively. At M3, the percentage contribution of the indirect effect on pain (ie, attributable to CRP, ESR, or SJC28) over PBO was significant for all treatment arms (all $p < 0.001$) with the mediation effect being greater for SJC28 vs CRP and ESR (Fig). The percentage contribution of the indirect effect was numerically lower with tofacitinib 5 mg BID (34.9% [95% confidence intervals: 18.1, 51.7]) and 10 mg BID (33.6% [17.1, 50.1]) compared with ADA (45.3% [19.6, 70.9]) (Fig). The percentage contribution of the direct effect on pain over PBO (ie, not attributable to CRP, ESR, or SJC28) was numerically higher with tofacitinib 5 mg BID (65.1% [48.3, 81.9]) and 10 mg BID (66.4% [49.9,82.9]) compared with ADA (54.7% [29.1, 80.4]) (Fig), and significant for all treatment arms (allp < 0.000).

Conclusion: Inflammation, particularly measured by SJC28, was a significant mediator of the effect of tofacitinib 5 and 10 mg BID and ADA on pain. However, the majority of the treatment effects on pain were not attributable to inflammatory changes; this was particularly the case for tofacitinib 5 and 10 mg BID (> 65%). Therefore, more work is needed to assess whether additional mediators of pain can be found. Limitation: this analysis could only assess variables that were collected in the ORAL Standard study as mediators.

1. American College of Rheumatology Pain Management Task Force. Arthritis Care Res (Hoboken) 2010; 62: 590–9
2. Simon et al. Semin Arthritis Rheum 2021; 51: 278–84
3. Van Vollenhoven et al. N Engl J Med 2012; 367: 508–19

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Disclosure: M. Dougados: AbbVie, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Roche, 2, 5, UCB, 2, 5; **P. Taylor**: AbbVie, 2, Biogen, 2, Eli Lilly, 2, Fresenius, 2, Galapagos, 2, 5, Gilead Sciences, 2, GSK, 2, Janssen, 2, Nordic Pharma, 2, Pfizer Inc, 2, Sanofi, 2, UCB, 2; **D. Gruben**: Pfizer Inc, 3, 11; **M. Kessouri**: Pfizer Inc, 3, 11.

Abstract Number: 2158

Continued Nintedanib Treatment in Patients with Progressive Pulmonary Fibrosis Related to Autoimmune Disease: Data from INBUILD-ON

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SESSION INFORMATION
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Session Title: RA – Treatments Poster III
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Session Time: 9:00AM–11:00AM

Background/Purpose: In the INBUILD trial in patients with progressive pulmonary fibrosis, nintedanib reduced the rate of decline in forced vital capacity (FVC) compared with placebo, with a safety profile characterized predominantly by gastrointestinal events. The open-label extension of the INBUILD trial, INBUILD-ON, collected data on adverse events and FVC decline over longer-term treatment with nintedanib. We analyzed data from patients with progressive pulmonary fibrosis related to autoimmune disease in INBUILD-ON.

Methods: Patients in the INBUILD trial had diffuse fibrosing interstitial lung disease (ILD) (reticular abnormality with traction bronchiectasis, with or without honeycombing) of >10% extent on HRCT and met criteria for progression of ILD within the prior 24 months, despite management deemed appropriate in clinical practice. Patients who completed the INBUILD trial on treatment were eligible to enter INBUILD-ON. Patients who received nintedanib in INBUILD and continued to take it in INBUILD-ON comprised the "continued nintedanib" group. Patients who received placebo in INBUILD and initiated nintedanib in INBUILD-ON comprised the "initiated nintedanib" group. In descriptive analyses, we analyzed adverse events and changes in FVC in patients with autoimmune disease-related ILDs. Median exposure to nintedanib in INBUILD-ON in these patients was 21.8 months.

Results: Of the 434 patients treated in INBUILD-ON, 113 had autoimmune diseases (52 rheumatoid arthritis, 29 systemic sclerosis, 13 mixed connective tissue disease, 19 other diseases). Of these patients, 66.4% received ≥1 disease-modifying anti-rheumatic drug or high-dose glucocorticoid (>20 mg/day prednisone or equivalent) at baseline or during the trial. Diarrhea was the most frequently reported adverse event (Table). Serious adverse events were reported in 27 (51.9%) patients in the continued nintedanib group and 37 (60.7%) patients in the initiated nintedanib group. In the continued and initiated nintedanib groups, respectively, 10 (19.2%) and 31 (50.8%) patients had ≥1 dose reduction and 15 (28.8%) and 28 (45.9%) patients had ≥1 treatment interruption. Adverse events led to discontinuation of nintedanib in 17 (32.7%) patients in the

Table. Most frequent adverse events in patients with autoimmune disease-related progressive pulmonary fibrosis in INBUILD-ON.

	Continued nintedanib (n=52)	Initiated nintedanib (n=61)
Diarrhea	28 (53.8)	40 (65.6)
Dyspnea	5 (9.6)	10 (16.4)
Nausea	6 (11.5)	11 (18.0)
Weight decreased	8 (15.4)	9 (14.8)
Cough	6 (11.5)	11 (18.0)
Progression of ILD*	7 (13.5)	8 (13.1)
Vomiting	6 (11.5)	8 (13.1)
Alanine aminotransferase increased	2 (3.8)	12 (19.7)
Aspartate aminotransferase increase	2 (3.8)	12 (19.7)
Bronchitis	2 (3.8)	8 (13.1)
Gamma-glutamyltransferase increased	1 (1.9)	8 (13.1)

Data are n (%) of patients with ≥1 such adverse event with onset date between first nintedanib intake and last intake plus 28 days. Adverse events reported in >12% of patients in either group are shown. Adverse events were coded according to preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA). *Based on MedDRA preferred term "interstitial lung disease"

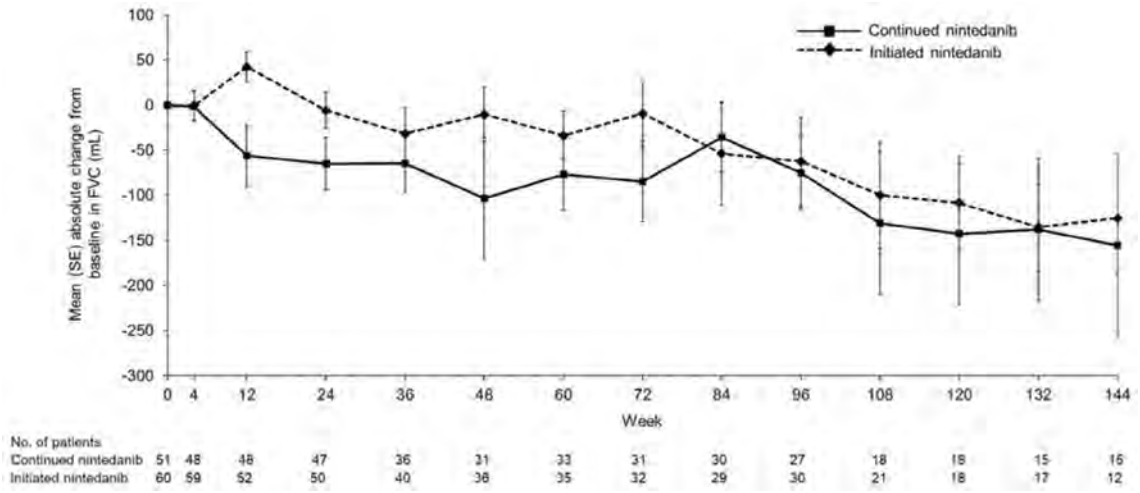

Figure. Changes in FVC (mL) over 144 weeks in patients with autoimmune disease-related progressive pulmonary fibrosis in INBUILD-ON.

continued nintedanib group and 28 (45.9%) patients in the initiated nintedanib group. Mean (SE) changes in FVC from baseline to week 144 of INBUILD-ON were –155.3 (101.8) mL in the continued nintedanib group and –125.2 (61.6) mL in the initiated nintedanib group (Figure).

Conclusion: The adverse event profile of nintedanib in patients with progressive pulmonary fibrosis due to autoimmune disease in INBUILD-ON was consistent with that observed in patients with autoimmune diseases in the INBUILD trial. Permanent discontinuations of nintedanib were less frequent in patients who continued nintedanib in INBUILD-ON than in those who initiated nintedanib in INBUILD-ON. These data should be interpreted with caution given the small number of patients who provided data, particularly at the later time-points.

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Abstract Number: 2159

Results of a 24-week Open-label, Non-interventional Study of the Efficacy and Safety of Olokizumab Therapy in Patients with Rheumatoid Arthritis After Switching from Anti-B-cell Therapy During the SARS-COV-2 Pandemic

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The COVID-19 pandemic has significantly changed the understanding of the safety profile of therapies for immunoinflammatory rheumatic diseases. This is primarily due to the negative impact of a number of DMARDs and biological DMARDs on the course and outcomes of a new coronavirus infection. A number of studies have shown that anti-B-cell therapy (rituximab) was associated with statistically significant increase in the risk of severe COVID-19 and an increase in mortality. At the same time, the analysis of real clinical practice data dictated the need to establish a number of restrictions on the use of certain classes of biological DMARDs and to search for alternative therapeutic approached to maintain control over disease activity.

We evaluate the efficacy and safety of olokizumab, solution for subcutaneous injection, 160mg/ml - 0.4ml for the treatment of patients with RA in real clinical practice after switchingfrom rituximab during the COVID-19 pandemic.

Methods: The study included 19 patients with a confirmed diagnosis of RAwho were previously on rituximab therapy at a dose of 1000 (500) mg twice with an interval of 2 weeks not less than 6 months,and received at least one course of therapy with this drug. As RA worsened, patients switched to olokizumab and continued to receive standard DMARDs. At weeks 0, 4, 8, 12, 16, 20 and 24 after the switch, the following parameters were assessed: the severity of pain(VAS scale), the number of tender and swollen joints (TJC28 and TSC28), the level of acute phase markers of inflammation, the disease activity

Table 1. Main Efficacy Results Dynamic. Footnotes: *p<0.05 compared to baseline; Me [Q1;Q3]. median [1st; 3nd quartile]

Me [Q1;Q3]	Baseline	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24
TJC28	10,0 [6,0; 13,0]	6,0* [4,0; 10,0]	3,0* [2,0; 9,0]	5,0* [3,0; 9,0]	3,0* [2,0; 8,0]	3,0* [3,0; 7,0]	4,0* [3,0; 8,0]
SJC28	7,0 [4,0; 10,0]	3,0* [2,0; 6,0]	2,0* [1,0; 4,0]	2,0* [1,0; 4,0]	2,0* [0,0; 3,0]	1,0* [0,0; 3,0]	2,0* [1,0; 3,0]
CRP (mg/l)	18,0 [10,0; 37,0]	0,6* [0,4; 1,0]	0,5* [0,4; 0,7]	0,5* [0,3; 0,7]	0,4* [0,3; 0,6]	0,5* [0,3; 1,0]	0,5* [0,4; 1,0]
ESR (mm/hr)	30,0 [18,0; 54,0]	5,0* [3,0; 10,0]	5,0* [3,0; 6,0]	5,0* [4,0; 10,0]	5,0* [4,0; 10,0]	6,0* [5,0; 10,0]	5,0* [4,0; 8,0]
DAS28-ESR	5,5 [4,9; 6,3]	3,6* [2,6; 4,8]	3,3* [2,6; 3,4]	3,1* [2,6; 3,9]	3,2* [2,7; 3,9]	2,8* [2,5; 4,3]	3,0* [2,7; 4,1]
DAS28-CRP	5,3 [4,5; 5,9]	3,5* [2,9; 4,3]	3,2* [2,6; 4,0]	3,3* [2,7; 3,9]	2,8* [2,7; 3,6]	2,8* [2,4; 3,6]	3,1* [2,7; 3,6]
CDAI	27,0 [19,0; 31,0]	17,0*[11,0;26,0]	12,0* [9,0; 20,0]	15,0* [9,0; 20,0]	10,0* [9,0; 17,0]	10,0* [8,0; 16,0]	12,0* [9,0; 18,0]
HAQ	1,63 [1,25; 1,88]	1,50* [1,00; 1,63]	1,50* [1,00; 1,50]	1,50* [1,00; 1,50]	1,25* [1,00; 1,50]	1,25* [1,00; 1,50]	1,13* [1,00; 1,50]

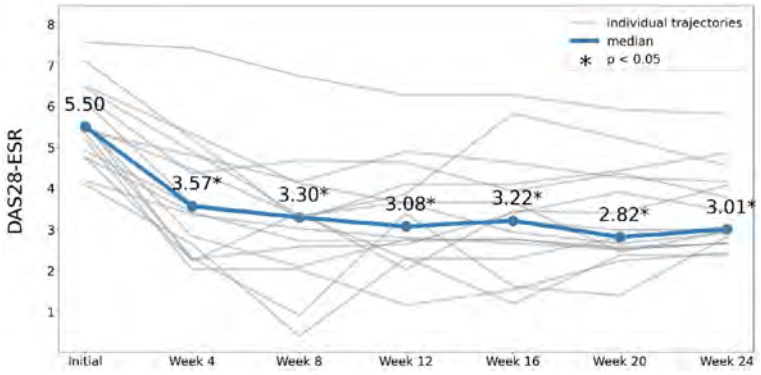

Figure 1. DAS28-ESR Dynamic

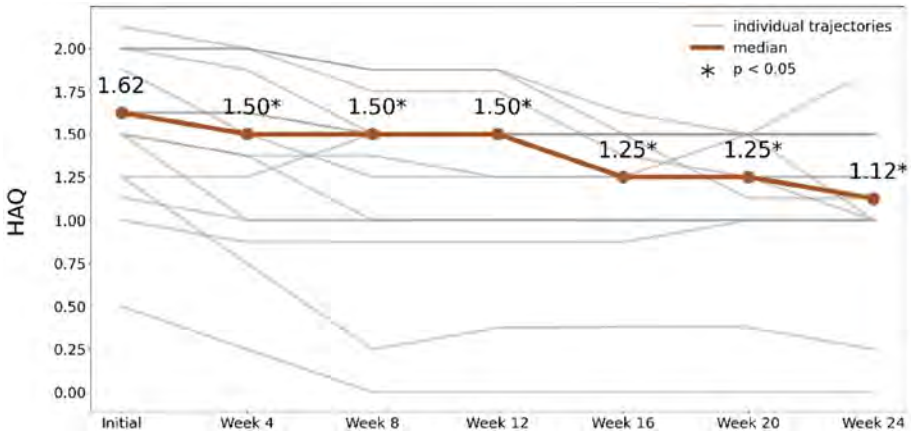

Figure 2. HAQ Dynamic

index (DAS28) calculated using ESR and CRP, and the CDAI (clinical disease activity index), functional state index HAQ, as well as the safety profile of therapy.

Results: Data analysis was performed using median values (Me). TJC28 and SJC28 decreased 4 weeks after the injection of olokizumab in comparison to baseline values (Table 1). Laboratory markers of inflammation analysis showed a decrease in CRP and ESR levels after 4 weeks of treatment with positive trend in place at weeks 8, 12, 16, 20 and 24. The level of CRP by the week 4 became within the normal range, regardless of the baseline values (Table 1). All activity indices improved from the week 4 in each evaluation period compared to baseline (Table 1, for DAS28-ESR see Figure 1). All patients showed a reduction in pain (VAS scale) improved starting from week 4. There was a significant improvement in the functional status of patients by study week 4 according to the HAQ index (Figure 2).

Conclusion: The study found that non-medical switching from rituximab to olokizumab was effective and safe during the COVID-19 pandemic.

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Abstract Number: 2160

Poly-Refractory Rheumatoid Arthritis: All B/tsDMARD Classes Exhausted - An Uncommon Disease Subset with Distinct Inflammatory and Non-inflammatory Phenotypes

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and Musculoskeletal Medicine, University of Leeds, and NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, [5]Leeds Biomedical Research Centre, University of Leeds, Leeds, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: We previously reported on difficult to treat Rheumatoid Arthritis (RA) in nearly 1600 patients treated with biologic (b) or target synthetic (ts) DMARDs including failure or were intolerant to all classes, i.e. what we termed poly-refractory RA (1).Here, we sought to characterise this further, by exploring whether there is an underlying inflammatory drive underpinning this response, by utilizing ultrasound.

Table 1. PIRRA and NIRRA subgroups within Poly-Refractory RA pool

	Poly refractory RA valid with US scan (N= 34)		
	NIRRA(N=11)	PIRRA (N=23)	Significance
Demographics			
Age, median (IQR)	59 (46-69)	64 (57-73)	No
Female, N (%)	6 (55%)	19 (83%)	No
BMI, median (IQR)	30 (26-33)	27 (23-31)	No
Osteoarthritis	9 (82%)	16 (70%)	No
Fibromyalgia	1 (9%)	0 (0%)	No
Depression	0 (0%)	1 (4%)	No
Chronic widespread pain	1 (9%)	2 (9%)	No
Osteoporosis, N (%)	4 (36%)	4 (17%)	No
Osteoporotic fractures, median	0 (0-0)	0 (0-0)	No
Joint replacements, median	1 (0-3)	0.5 (0-1)	No
Disease characteristics			
Age at onset	45 (31-51)	45 (34-49)	No
Disease duration in years, median (IQR)	18 (14-19)	18 (15-20)	No
Time since 1st bDMARDs, median (IQR)	11 (9-18)	13 (11-16)	No
Time from diagnosis to start 1st b/tsDMARDs (years), median (IQR)	2 (0-7)	2 (2-4)	No
TJC28, median (IQR)	15 (7-21)	11 (9-15)	No
SJC28, median (IQR)	1 (0-2)	7 (5-9)	**<0.001**
Main joint involvement, N (%)			
Small	8 (72%)	17 (74%)	No
Large	1 (9%)	0 (0%)	No
Both	2 (18%)	6 (26%)	No
VAS in mm, median (IQR)	60 (50-70)	70 (60-80)	0.095
DAS28, mean ±SD	4.75 (4.1-5.6)	5.42 (4.9-6.1)	**0.05**
Current use of steroids, N (%)	3 (27%)	17 (74%)	**0.023**
Current use of oral glucocorticoid therapy, N (%)	1 (9%)	14 (61%)	**0.008**
Patients with extra-articular manifestations, N (%)			
Vasculitis	1 (9%)	0 (0%)	No
Glomerulonephritis	0 (0%)	0 (0%)	CNC
Scleritis	0 (0%)	3 (13%)	No
Pericarditis	1 (9%)	0 (0%)	No
CRP, median (IQR)	5 (5-16)	15 (5-29)	0.067
CRP elevated >10, N (%)	3 (27%)	13 (57%)	No
Erosions by US	9 (82%)	18 (86%)	No
RF positive, N (%)	9 (82%)	17 (74%)	No
Anti-CCP positive, N (%)	11 (100%)	18 (78%)	No

Methods: We reviewed electronic medical records of all D2TRA and identified 40 patients with poly-refractory RA. In addition to clinical assessment, we performed musculoskeletal ultrasonography (US) of clinically swollen joints. Patients were divided into two groups according to the presence or absence of US synovitis, respectively Persistent Inflammatory Refractory RA (PIRRA) and Non-inflammatory Refractory RA (NIRRA). US synovitis was considered as the presence of both grey-scale and power Doppler grades of at least 1. Univariate analyses were performed to differentiate the two groups' characteristics.

Results: Only 40 out of 1591 patients with poly-refractory RA representing only 2.5% of cases. Of these, 34 (85%) had a recent US. 3/34 died and 3/34 were lost to follow-up from our clinic. 23/34 (67.6%) had US synovitis and therefore had PIRRA, while 11/34 (32.4%) with no US synovitis were classified as NIRRA, with baseline characteristics of both grops described in Table 1. When compared to NIRRA, PIRRA poly-refractory patients had significantly higher SJC (7 vs 1, $p < 0.001$) and, as expected, DAS-28-CRP scores (5.42 vs 4.75, $p = 0.05$), as well as higher need for corticosteroids to control their symptoms (61% vs 9%, $p = 0.008$). CRP levels were numerically but not significantly higher in the PIRRA group (median 15 vs 5mg/L, $p = 0.067$). The NIRRA group had a higher BMI, that may have impacted on CRP levels, and contained more fibromyalgia patients.

Conclusion: Poly-Refractory RA represented only 2.5% of RA cases under b/tsDMARDs and at least one-third of those patients had no signs of active inflammation on US. Patients that had exhausted all available b/tsDMARD options, the NIRRA group, with objective evidence of inflammation comprised only 1.5% of RA.

References:

1- David P et al. EULAR 2023. Supplementary

Disclosure: P. David: None; **A. Di Matteo**: None; **O. Hen**: None; **S. Dass**: None; **H. Marzo-Ortega**: AbbVie, 2, 6, Biogen, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 5, 6, MoonLake, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Takeda, 2, 6, UCB Pharma, 2, 5, 6; **P. Emery**: Boehringer Ingelheim, 2, Eli Lilly, 2, Novartis, 2; **B. Saleem**: None; **D. McGonagle**: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Janssen, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 2161

Pharmacokinetic and Safety Similarity of High- and Low-Concentration Formulations of Adalimumab Biosimilar ABP 501

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: ABP 501 has been developed as a biosimilar for Humira® (adalimumab), a fully human monoclonal antibody targeting tumor necrosis factor alpha (TNFα). ABP 501 is the first adalimumab biosimilar approved in the United States (AMJEVITA™) and European Union (AMGEVITA®) as a 50 mg/mL formulation for treating certain immune-mediated inflammatory diseases. An ABP 501 100 mg/mL formulation is being developed as a high-concentration formulation and requires half the injection volume to deliver the same subcutaneous (SC) dose. This study evaluates the similarity

Table 1. Summary of Statistical Assessment of PK Parameters

Treatment and Comparison	AUC_{inf} (hr*µg/mL) LS Geometric Mean [n]	C_{max} (µg/mL) LS Geometric Mean [n]
ABP 501-HCF	2177 [154]	3.75 [180]
ABP 501-LCF	2086 [153]	3.52 [184]
Ratio of LS Geometric Means (90% CI)		
ABP 501-HCF vs ABP 501-LCF	1.04 (0.9634, 1.1297)	1.06 (0.9960, 1.1380)

ANCOVA = analysis of covariance; AUC = area under the concentration-time curve; AUC_{inf} = AUC from time 0 extrapolated to infinity; CI = confidence interval; C_{max} = maximum observed concentration; HCF = high-concentration formulation; LCF = low-concentration formulation; LS = least squares; PK = pharmacokinetics.
Note: Primary analysis of mean geometric LS, ratio of geometric LS means, and 90% CI were estimated based on the ANCOVA model with a fixed effect for treatment and adjusting for baseline weight.

between single-dose pharmacokinetics (PK), safety, and immunogenicity of the low-concentration (ABP 501-LCF) and high-concentration (ABP 501-HCF) formulations of ABP 501 in healthy adult subjects.

Methods: In this randomized, single-blind, single-dose, 2-arm, parallel-group study in healthy adults, approximately 350 subjects were planned for dosing. Eligible subjects were randomized in a 1:1 ratio to receive a single 40 mg SC injection of either ABP 501-HCF (n = 175) or ABP 501-LCF (n = 175). The primary objective was to determine PK similarity of ABP 501-HCF with ABP 501-LCF, as assessed by area under the concentration time curve from time 0 extrapolated to infinity (AUC_{inf}) and maximum observed concentration (C_{max}). Pre-specified similarity criterion for the primary PK analysis was the standard 90% confidence interval (CI) for the ratio of least square (LS) geometric means (GM) to be within 0.80 to 1.25. Secondary endpoints included other PK parameters, safety, tolerability, and immunogenicity.

Results: A total of 370 of 372 randomized subjects received study drug (ABP 501-HCF, n = 183 of 185; ABP 501-LCF, n = 187 of 187). Demographic and baseline characteristics were comparable between the two treatment groups. Ratios of LS GM (90% CIs) between ABP 501-HCF and ABP 501-LCF for AUC_{inf} and C_{max} were 1.04 (0.9634, 1.1297) and 1.06 (0.9960, 1.138); the 90% CIs (for the ratio of LS GM between ABP 501-HCF and ABP 501-LCF for AUC_{inf} and C_{max}) were fully contained within the prespecified PK similarity margin (0.8 – 1.25) (Table 1). Both the high- and low-concentration formulations were well tolerated; the frequency, type, and severity of adverse events (AEs) were comparable between ABP 501-HCF and ABP 501-LCF and were consistent with the safety profile of adalimumab (Table 2). Headache was the most commonly reported AE in both treatment groups (ABP 501-HCF, n = 8; ABP 501-LCF, n = 9). Subjects in both groups tested positive for pre-existing binding anti-drug antibodies (ADAs) and neutralizing ADAs at baseline; 182 subjects in the

Table 2. Overall Summary of Adverse Events

	ABP 501-HCF (N = 183) n (%)	ABP 501-LCF (N = 187) n (%)
Any adverse event	49 (26.8)	51 (27.3)
Any grade ≥ 3 adverse event	0 (0.0)	0 (0.0)
Any fatal adverse event	0 (0.0)	0 (0.0)
Any serious adverse event	0 (0.0)	0 (0.0)
Any adverse event leading to discontinuation of study	1 (0.5)	1 (0.5)
Any adverse event of interest	12 (6.6)	11 (5.9)
Any COVID-19-related adverse event	5 (2.7)	3 (1.6)

HCF = high-concentration formulation; LCF = low-concentration formulation.
Note: Only treatment-emergent adverse events were summarized by actual treatment received. For each category, subjects were included only once, even if they experienced multiple adverse events in that category.

Table 3. Antidrug Antibody Results

Variable	ABP 501-HCF (N = 183) n (%)	ABP 501-LCF (N = 187) n (%)
Subjects with an on-study result[a]	**183**	**187**
Total antibody incidence, n (%)		
Binding antibody positive anytime	172 (94.0)	179 (95.7)
Neutralizing antibody positive anytime	32 (17.5)	29 (15.5)
Subjects with a result at baseline	**183**	**187**
Pre-existing antibody incidence, n (%)		
Binding antibody positive at or before baseline	7 (3.8)	8 (4.3)
Neutralizing antibody positive at or before baseline	1 (0.5)	0 (0.0)
Subjects with a post-baseline result through EOS	**182**	**185**
Treatment boosted antibody incidence, n (%)		
Binding antibody positive at baseline with a ≥ 4x increase in magnitude post-baseline	4 (2.2)	6 (3.2)
Developing antibody incidence, n (%)		
Binding antibody positive post-baseline with a negative or no result at baseline	165 (90.7)	171 (92.4)
Transient[b]	4 (2.2)	3 (1.6)
Neutralizing antibody positive post-baseline with a negative or no result at baseline	31 (17.0)	29 (15.7)
Transient[b]	1 (0.5)	0 (0.0)

EOS = end-of-study; HCF = high-concentration formulation; LCF = low-concentration formulation.
Note: Baseline was defined as the last non-missing assessment taken prior to the first dose of study investigational product. Percentages were calculated using the corresponding category count as the denominator.
[a] Subjects were considered on-study after signing informed consent.
[b] Negative result at the subject's last time point tested within the study period

ABP 501-HCF group and 185 in the ABP 501-LCF group had post-baseline results through end of study (Table 3). In the ABP 501-HCF group, 165 (90.7%) subjects developed binding ADAs and 31 (17%) developed neutralizing ADAs. In the ABP 501-LCF group, 171 (92.4%) subjects developed binding ADAs and 29 (15.7%) developed neutralizing ADAs.

Conclusion: Results of this study demonstrate PK similarity between ABP 501-HCF (100 mg/mL) and ABP 501-LCF (50 mg/mL) following a single SC injection in healthy adult subjects. Immunogenicity and safety of ABP 501-HCF and ABP 501-LCF were also found to be similar.

Disclosure: V. Chow: Amgen Inc., 3; **M. Zhou**: Amgen Inc., 3; **D. Mytych**: Amgen Inc., 3, 11; **A. Colbert**: Amgen Inc., 3; **M. Miller**: Amgen Inc., 3; **I. Wala**: Amgen Inc., 3; **W. Radziszewski**: Amgen Inc., 3, 11.

Abstract Number: 2162

Safety and Efficacy of Filgotinib: An Update from the DARWIN 3 Phase 2 Long-term Extension with a Maximum of 8.2 Years of Exposure

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: DARWIN 3 (NCT02065700) is a long-term extension (LTE) study assessing the safety and efficacy of filgotinib (FIL) in patients with rheumatoid arthritis (RA) and an inadequate response to methotrexate (MTX).[1] In the DARWIN 1 (NCT01888874) and DARWIN 2 (NCT01894516) parent studies, patients received FIL in combination with MTX or FIL monotherapy, respectively. This analysis aimed to provide an update on the safety and efficacy of FIL 200 mg (FIL200) in patients with RA, with or without MTX, with a maximum of 8.2 years of exposure.

Methods: Patients completing the DARWIN 1 (FIL + MTX) and DARWIN 2 (FIL monotherapy) Phase 2 studies could enter DARWIN 3, receiving FIL200. The proportion of patients experiencing treatment-emergent adverse events (TEAEs) were reported using the safety analysis set, comprising data from both the parent and LTE studies. Efficacy was assessed from LTE baseline using the American College of Rheumatology (ACR) 20/50/70 improvement criteria and Disease Activity Score in 28 joints using C-reactive protein (DAS28-CRP), up to 264 weeks. Low disease activity and remission were defined as DAS28-CRP $\leq$ 3.2 and $<$ 2.6, respectively.

Results: In total, 739 patients were enrolled in DARWIN 3. Mean (standard deviation; SD) FIL exposure was 4.89 (2.72) years in the FIL + MTX group and 4.78 (2.79) years in the FIL monotherapy group. In the FIL + MTX vs FIL monotherapy groups, TEAEs were reported for 90.9% and 92.1% of patients, respectively (**Table**). The most common TEAE was infection. In both treatment groups, 8 patients had a TEAE leading to death (1.6% and 3.3%, respectively). Exposure-adjusted incidence rates, censored at time of first event for major adverse cardiovascular event, venous thromboembolism, herpes zoster, infections, serious infections, nonmelanoma skin cancer (NMSC), malignancies excluding NMSC, gastrointestinal perforations and TEAEs leading to death, will be reported. Through 5 years, ACR20/50/70 responses were maintained in 86.3%/66.7%/50.7% of the FIL + MTX group and 90.8%/74.8%/51.4% of the FIL monotherapy group, respectively (observed data). DAS28-CRP low disease activity and remission rates (nonresponder imputation) at DARWIN 3 baseline were 46.1%/40.1% (FIL + MTX) and 29.6%/24.8% (FIL monotherapy) (**Figure**). At Week 264, the proportion of patients achieving low disease activity and remission were 34.0%/34.3% (FIL + MTX) and 27.0%/24.8% (FIL monotherapy).

Table. TEAEs of interest

	FIL + MTX N=497	FIL monotherapy N=242
Any TEAE	452 (90.9)	223 (92.1)
MACE	4 (0.8)	3 (1.2)
VTE	3 (0.6)	0
Herpes zoster	30 (6.0)	14 (5.8)
Infections	317 (63.8)	140 (57.9)
Serious infections	28 (5.6)	19 (7.9)
NMSC	6 (1.2)	2 (0.8)
Malignancies excluding NMSC	12 (2.4)	8 (3.3)
GI perforations	1 (0.2)	0
TEAEs leading to death	8 (1.6)	8 (3.3)

Data are n (%).
FIL, filgotinib; GI, gastrointestinal; MACE, major adverse cardiovascular event; MTX, methotrexate; NMSC, nonmelanoma skin cancer; TEAE, treatment-emergent adverse event; VTE, venous thromboembolism.

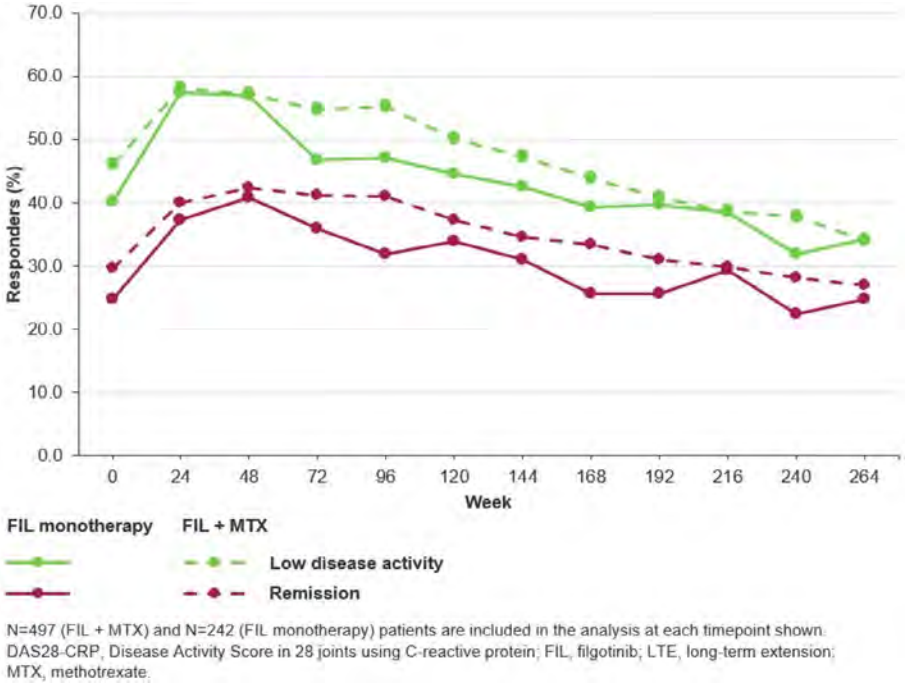

Figure. Proportion of patients achieving DAS28-CRP low disease activity and remission, from LTE baseline to Week 264 (nonresponder imputation analysis)

Conclusion: With a maximum of 8.2 years of exposure in patients with RA, the FIL safety profile is similar between the background MTX and monotherapy treatment arms. Both arms show sustained efficacy over time.

Reference:

1. Kavanaugh A, et al. J Rheumatol 2021;48:1230–8

Disclosure: R. Westhovens: Celltrion, 2, 6, Galapagos, 2, 6, Gilead, 2, 6; **R. Alten**: AbbVie, 2, 6, Amgen, 2, 6, Biogen, 2, 6, BMS, 2, 6, Celltrion, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Lilly, 2, 6, Medac, 2, 6, MSD, 2, 6, Mylan, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sandoz, 2, 6, Sanofi-Genzyme, 2, 6, UCB, 2, 6, Viatris, 2, 6; **L. Dagna**: AbbVie, 2, AstraZeneca, 2, Biogen, 2, BMS, 2, 5, Boehringer Ingelheim, 2, Celltrion, 5, Eli Lilly, 2, Galapagos, 2, GSK, 1, Janssen, 2, Kiniksa Pharmaceuticals, 2, 5, Novartis, 2, 6, Pfizer, 2, 5, Sobi, 2, 5, 6; **A. Kavanaugh**: Amgen, 2, BMS, 2, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2; **K. Withrop**: AbbVie, 2, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GSK, 2, Novartis, 2, Pfizer, 2, 5, Regeneron, 2, Roche, 2, Sanofi, 2, UCB, 2; **J. Barry**: Galapagos, 3, 11; **R. Besuyen**: Galapagos, 3, 11; **C. Corallo**: Galapagos, 3, 11; **D. de Vries**: Galapagos, 3, 11; **N. Martin**: Galapagos, 7; **C. Watson**: Galapagos, 3, 11; **M. Genovese**: Gilead, 3, 11; **A. Spindler**: None; **M. Stanislavchuk**: Amgen, 5, AstraZeneca, 5, Celgene, 5, Eli Lilly, 5, Galapagos, 5, Gilead, 5, Human Genome, 5, Janssen, 5, MSD, 5, Nichi-Iko Pharmaceutical, 5, Pfizer, 5, Roche, 5; **M. Greenwald**: AbbVie, 5, Aclairs, 5, Eli Lilly, 5, Galapagos, 5, Janssen, 5, Nimbus, 5; **P. Emery**: Boehringer Ingelheim, 2, Eli Lilly, 2, Novartis, 2.

Abstract Number: 2163

Omnipresent Poor Prognostic Factors in Early Rheumatoid Arthritis in the IMPROVED Trial; Is Earlier bDMARD Treatment Escalation for All Necessary?

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The EULAR recommendations for the treatment of RA state, by expert opinion, that if a treatment target is not achieved with the first csDMARD strategy, addition of a bDMARD or a tsDMARD should be considered if at least 1 poor prognostic factor (PPF) is present. PPF are defined as: moderate to high disease activity after csDMARDs, high acute phase reactant levels, high swollen joint counts presence of RF and/or ACPA (especially in high levels), combinations of aforementioned PPFs and presence of early erosions. We investigated the presence of PPF in early RA patients, aiming to compare the clinical response on either csDMARD combination or bDMARD therapy in relation to presence or absence of PPF, in the IMPROVED trial.

Methods: In the IMPROVED trial, 479 patients with rheumatoid arthritis (2010-criteria) started treatment with MTX and a 4-month tapered high dose of prednisone bridging scheme. Patients not in early remission (DAS ≥1.6) after 4 months of the initial treatment were randomized to either 4 months MTX + HCQ + SSZ + continued low dose prednisone (arm 1) or to 4 months MTX + adalimumab (arm 2). A maximum of 5 PPFs could be present in any patient. High acute phase reactants were defined as CRP ≥0.8 mg/dl or ESR levels >20 mm/hour in women and >15 mm/hour in men. For swollen joint counts (SJC), we defined a high SJC as >10 in our main analysis and performed a sensitivity analysis with a definition of high SJC when the SJC was >4.

Results: Almost all RA patients had at least one PPF as mentioned in the EULAR recommendations. Presence of each PPF is displayed in figure 1. High inflammatory parameters and presence of antibodies at baseline were the most frequent PPFs (present in 366 and 390 patients, respectively). Presence of PPFs was evenly distributed between the randomization arms (figure 1b). Only 5 patients (1%) had no PPFs in the main analysis and only 10 (2%) in the sensitivity analysis. Of these, 2/5 and 2/10 patients did not achieve early remission and were randomized to the two treatment arms. Due to these small numbers, no further comparison in treatment response was done. In total, 65 patients with PPFs were evenly randomized to each study arm. Mean (SD) DAS change in arm 1 was -0.47 (-0.79) and in arm 2 -0.57 (-0.74), p = 0.48. Changes in HAQ were similar, median (IQR) HAQ change was -0.13 (-0.13 ; 0.13) in arm 1 and -0.13 (-0.25 ; 0.25) in arm 2, p=0.13. In the 5 and 6 patients that showed progression of radiographic damage, median (IQR) progression was 1 (0.5 ; 2) in arm 1 and 0.5 (0.5 ; 1) in arm 2, p =0.48.

Conclusion: Empirically identified PPFs were present in up to 99% of patients with early RA. High prevalence of PPFs is probably due to a large overlap between these PPFs and the 2010 RA classification criteria. According to current EULAR recommendations, it is recommended to start a b/tsDMARD in patients with PPF after failing first therapy with MTX and GC bridging. After failure to achieve the treatment target on this first treatment, we found no significantly better response in these patients on bDMARDs compared to csDMARDs. No comparison could be made with non-PPF patients.

Figure 1a: presence of poor prognostic factors in all RA patients

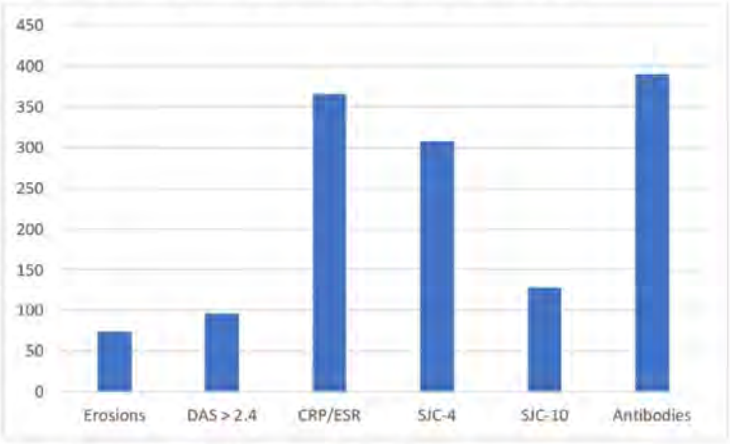
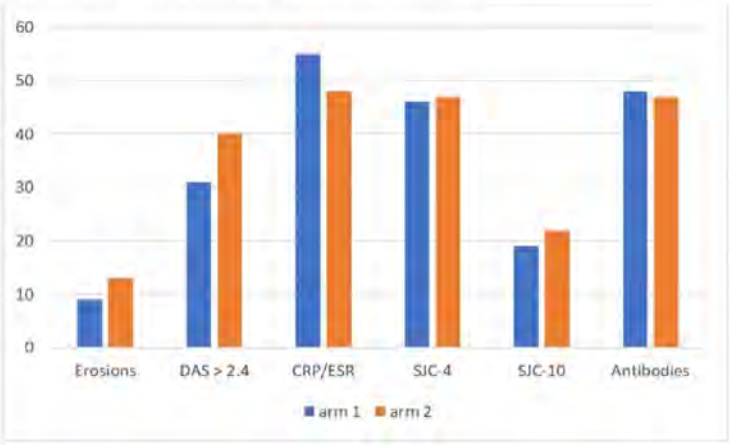


Figure 1b: presence of PPFs per randomization arm



Erosions: presence of baseline erosions, DAS > 2.4: moderate/high DAS after 4 months of treatment with MTX + prednisone bridging, CRP/ESR: high c-reactive protein or erythrocyte sedimentation rate at baseline, SJC-4: presence of >4 swollen joints at baseline, SJC-10: presence of >10 swollen joints at baseline, antibodies: presence of ACPA or RF at baseline. Patients can be present in multiple categories; numbers don't add up to 479 RA patients in figure 1a.

Disclosure: J. van der Pol: None; **S. Bergstra**: Pfizer, 5; **T. Huizinga**: None; **C. Allaart**: AbbVie/Abbott, 5.

Abstract Number: 2164

Real-world Persistence of Initial Targeted Therapy Strategy in Monotherapy versus Combination Therapy in Patients with Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Clinical practice guidelines, based on information from clinical trials, provide different recommendations for the use of combination therapies for the treatment of rheumatoid arthritis (RA), ankylosing spondylitis (AS), and psoriatic arthritis (PsA). Few studies have evaluated the persistence of different treatment strategies (combination *vs*. monotherapy) as a primary endpoint based on data from real-world settings. The aim of this study was to evaluate the persistence of the initial strategy with or without conventional synthetic (cs) disease-modifying antirheumatic drugs (DMARDs) (combination and monotherapy strategies, respectively) of targeted therapy in patients with RA, AS and PsA under real-life conditions. Factors associated with maintenance of the initial strategy were also analyzed.

Methods: Nested cohort study within BIOBADASER III, a prospective Spanish registry of patients with rheumatic diseases treated with targeted therapy, including biologic(b) and targeted synthetic(ts) DMARDs. Bivariate comparisons and multivariate Cox proportional hazards models were used for the analyses.

Results: A total of 2,521 patients were included in the study. Baseline demographics and disease characteristics, disease activity, type of targeted therapy, and concomitant medications are shown in Table 1. In the multivariate model, the initial strategy of combination therapy was associated with shorter persistence in patients with RA (hazard ratio [HR] 1.58;95% confidence interval [CI] 1.00 to 2.50; p=0.049), PsA (HR 2.48; 95%CI 1.65 to 3.72) and AS (HR 16.77; 95%CI 7.37 to 38.16; p < 0.001). 48; 95%CI 1.65 to 3.72; p < 0.001) and AS (HR 16.77; 95%CI 7.37 to 38.16; p < 0.001), regardless of age, sex, time of disease progression, baseline disease activity or type of b/tsDMARD. Figure 1 shows the analyses of persistence by disease using Kaplan-Meier curves. Overall, the combination strategy was associated with an increased incidence of adverse events (incidence rate ratio [IRR] 1.13; 95%CI 1.05-1.21).

Table 1. Baseline characteristics of the patients included in the analysis.

Table 1. Baseline characteristics of the patients included in the analysis

	Rheumatoid arthritis N=1192			Psoriatic arthritis N=697			Ankylosing spondylitis N=632			Total N=2521		
Variable (%)	**Mono N=245 (20.5)**	**Combo N=947 (79.5)**	**p value**	**Mono N=248 (35.6)**	**Combo N=449 (64.4)**	**p value**	**Mono N=485 (76.7)**	**Combo N=147 (23.3)**	**p value**	**Mono N=978 (38.8)**	**Combo N=1543 (61.2)**	**p value**
Age at b/tsDMARD initiation (years), mean±SD	58.31±2.6)	55.3±12.3	<0.001	51.3 (12.2)	49.9 (11.3)	0.122	45.6±12.9	48.0±14.3	0.053	50.2±13.7	53.1 ±12.6	<0.001
Sex (females), n (%)	204 (83.3)	712 (75.2)	0.008	130 (52.4)	236 (52.6)	0.971	146 (30.1)	49 (33.3)	0.458	480 (49.1)	997 (64.6)	<0.001
DAS28	4.7 (1.2)	4.8 (1.3)	0.375	4.9 (2.6)	4.9 (2.7)	0.945				4.2 (1.3)	4.6 (1.3)	<0.001
BASDAI				4.1 (1.2)	4.2 (1.2)	0.490	5.6 (2.1)	5.4 (2.3)	0.400	5.5 (2.2)	5.3 (2.4)	0.200
Disease duration (years), mean (SD)	7.6 (8.0)	7.1 (7.8)	0.432	5.7 (6.4)	4.9 (5.5)	0.074	7.2 (9?)	7.4 (9.2)	0.792	6.9 (8.6)	6.5 (7.4)	0.352
First b/tsDMARD, n (%)[a]												
TNFi	93 (13.0)	621 (87.0)		132 (27.6)	346 (72.4)		416 (75.2)	137 (24.8)		641 (36.7)	1104 (63.3)	
Anti-IL6	52 (42.3)	71 (57.7)								52 (42.3)	71 (57.7)	
Anti-B-cell (CD20)	13 (18.8)	56 (81.2)								13 (18.8)	56 (81.2)	
JAKi	56 (35.0)	104 (65.0)		4 (57.1)	3 (42.9)					60 (35.9)	107 (64.1)	
Anti-IL1	1 (50.0)	1 (50.0)	<0.001			<0.001			0.04	1 (50.0)	1 (50.0)	<0.001
Anti-IL17A				40 (46.5)	46 (53.5)		67 (88.2)	9 (11.8)		107 (66.1)	55 (34.0)	
Anti-IL12/23				17 (47.2)	19 (52.8)		2 (66.7)	1 (33.3)		20 (50.0)	20 (50.0)	
PDE4i				55 (61.1)	35 (38.9)					55 (61.1)	35 (38.9)	
Abatacept	29 (61.1)	94 (38.9)								29 (23.6)	94 (76.4)	
Glucocorticoids (yes), n (%)	147 (60.0)	612 (64.6)	0.845	63 (69.2)	149 (70.3)	0.855	22(4.5)	44 (29.9)	<0.001	232 (23.7)	805 (52.2)	<0.001

[a]Percentages were calculated by row.

bDMARD, biologic disease-modifying antirheumatic drug; IL, interleukin; JAKi, Janus kinase inhibitor; PDE4i, phosphodiesterase 4 inhibitor; SD, standard deviation; TNFi, tumor necrosis factor inhibitor

Figure 1. Persistence of biologic disease-modifying antirheumatic drug treatment strategy (Kaplan-Meier plots).

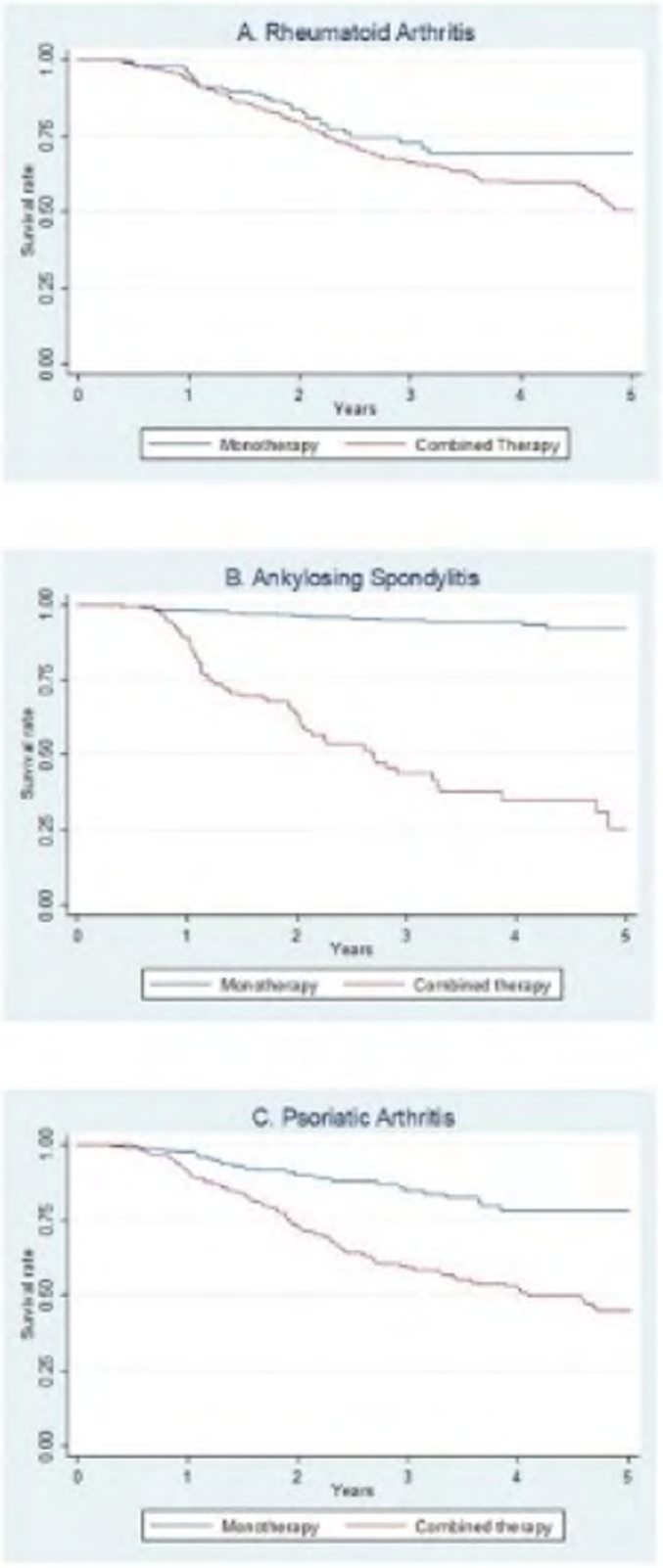

Figure 1. Persistence of biologic disease-modifying antirheumatic drug treatment strategy (Kaplan-Meier plots).

Conclusion: Analysis of a large database collected under real-world conditions shows that initiation of targeted therapy in monotherapy has a significantly better persistence and safety profile than in combination with csDMARD(s) in patients with PsA and AS. In patients with RA, the results also suggest that monotherapy should be considered as a therapeutic option as it offers a higher chance of persistence.

Disclosure: C. Sánchez-Piedra: None; **L. Expósito**: None; **P. VELA**: AbbVie/Abbott, 5, AstraZeneca, 5, Eli Lilly, 5, 6, GlaxoSmithKlein(GSK), 6, Novartis, 5, Pfizer, 5; **M. Moreno Ramos**: None; **C. Campos**: None; **C. Bohorquez**: None; **J. Calvo**: None; **Z. Plaza**: None; **M. Domínguez**: None; **J. Diaz-Gonzalez**: None.

Abstract Number: 2165

Efficacy of Abatacept in Rheumatoid Arthritis- associated Usual Interstitial Pneumonia. National Multicenter Study of 233 Patients During a Long-Term Follow Up

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a severe extra-articular manifestation of rheumatoid arthritis (RA). Usual interstitial pneumonia (UIP) is the most frequent, and severe ILD pattern in RA. Abatacept (ABA) has demonstrated effectiveness in RA-ILD during a 12-month period of treatment [*Rheumatology (Oxford)* 2020;59(12):3906-16, *Rheumatology (Oxford)* 2021;61(1):299-308]. However, little is known about the specific effect of ABA in the UIP pattern. Therefore, the aim of this study was to assess the effectiveness and safety of ABA in RA-ILD patients with radiological pattern of UIP during a long-term follow-up.

Methods: From a large observational multicenter study of 509 RA-ILD patients treated with ABA, we selected those with UIP. The following outcomes were assessed from baseline to final follow-up: **a)** pulmonary function tests (PFTs) -forced vital capacity (FVC) and diffusing capacity of the lungs for carbon monoxide (DLCO)-, **c)** chest high resolution computed tomography (HRCT), **d)**dyspnea (evaluated with the modified Medical Research Council scale), and **e)** arthritis activity (measured with DAS28-ESR).

Results: We included a total of 233 patients with UIP (118 women/115 men; mean age of 67.5±9.9 years). **Table 1** shows baseline demographic and clinical characteristics. The median ILD duration up to ABA initiation was relatively short, with a median [IQR] of 9.5 [2-36] months. Mean baseline values of FVC and DLCO were >80% and >60%, respectively. During a median of 22 [6-43] months of ABA therapy, 73.8% and 59.4% of patients showed an improvement/ stabilization of FVC

Table 1. Main general clinical features at baseline.

	RA-ILD patients with UIP (n=233)
Age, years mean±SD	68±10
Women, n (%)	118 (51)
Smoker ever, n (%)	123 (53)
ILD duration up to ABA, months, median [IQR]	9.5 [2-36]
RF // ACPA, n (%)	216 (93) // 205 (88)
DAS28-ESR, mean±SD	4.4±1.6
FVC (% of the predicted), mean±SD	85±22
DLCO (% of the predicted), mean±SD	64±20
ABA monotherapy, n (%)	102 (44)
ABA combined + MTX /other cDMARD, n (%)	131 (56)
Prednisone at baseline, mg/day, median [IQR]	5 [5-10]
Previous immunosuppressive therapy, n (%)	
MTX	167 (72)
Leflunomide	107 (46)
Sulfasalazine	27 (12)
Hydroxychloroquine	69 (30)
Anti-TNF drugs	90 (39)
Rituximab	28 (12)
Tocilizumab	19 (8)
JAK inhibitors	7 (3)

ABA, abatacept; ACPA, anti-citrullinated protein antibodies; cDMARD, conventional disease-modifying antirheumatic drug; DAS28, disease activity score on 28 joints; DLCO, diffusing capacity of the lung for carbon monoxide; ESR, erythrocyte sedimentation rate; FVC, forced vital capacity; ILD, interstitial lung disease; IQR, interquartile range; MTX, methotrexate; RA, rheumatoid arthritis; RF, rheumatoid factor; SD, standard deviation; TNF, tumor necrosis factor; UIP, usual interstitial pneumonia.

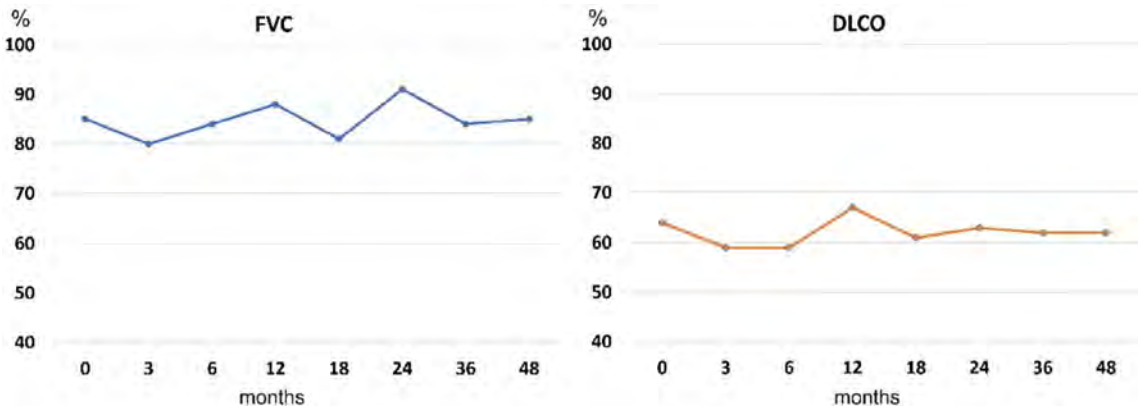

Figure 1. Evolution of pulmonary function tests (mean % of the predicted FVC and DLCO) in RA-ILD patients with UIP pattern at baseline and 48 months of follow-up.

and DLCO, respectively. **Figure 1** displays the evolution of PFTs along 48 months. Available chest HRCT images improved/stabilized in 67.1% of patients. Stabilization or improvement of dyspnea was found in 79.5% of patients. The majority of patients showed articular remission or low activity (mean DAS28-ESR of 4.4±1.6 at baseline and 2.6±1.3 at 48 months). ABA was withdrawn in 50 (21.5%) patients due to ILD worsening (n=20), articular inefficacy (n=15), serious infections (n=7), and other causes (n=8, development of malignancy in 3, neutrophilic dermatosis in 1, diagnosis of giant cell arteritis and change to tocilizumab in 1, patient's decision in 1, and 2 deceases).

Conclusion: ABA demonstrates a long-term efficacy and safety in patients with RA-associated UIP, the most severe pattern of ILD in RA patients.

Disclosure: B. Atienza-Mateo: None; **A. Serrano-Combarro**: None; **N. del Val del Amo**: None; **I. Casafont-Sole**: None; **R. Melero-Gonzalez**: None; **I. Serrano-García**: None; **S. Castañeda**: None; **J. Calvo**: None; **N. Mena Vazquez**: None; **N. Vegas Revenga**: None; **L. Domínguez-Casas**: None; **M. Osorio Sanjuan**: None; **C. Díez Morrondo**: None; **L. Perez-Albadalejo**: None; **R. Lopez-Sanchez**: None; **M. Mazano Canabal**: None; **A. Brandy-Garcia**: None; **P. Lopez-Viejo**: None; **G. Bonilla**: None; **O. Maiz-Alonso**: None; **C. carrasco-Cubero**: None; **M. Garijo Bufort**: None; **M. Moreno**: None; **A. Urruticoechea**: None; **S. Ordonez-Palau**: None; **C. Gonzalez-Montagut Gomez**: None; **a. Garcia-Valle**: None; **J. De Dios**: None; **F. Lozano**: None; **T. Vazquez-Rodriguez**: None; **P. Carreira**: None; **J. Blanco-Madrigal**: None; **S. ROJAS HERRERA**: None; **I. Brana Abascal**: None; **J. Loarce-Martos**: Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Galapagos, 6; **E. Giner-Serret**: None; **J. Sarmiento-Monroy**: None; **C. ventin-Rodriguez**: None; **M. Rodriguez-lopez**: None; **P. Andujar-Brazal**: None; **J. Fernandez-Melon**: None; **L. Lopez**: None; **c. Fernandez-Diaz**: None; **J. Loricera**: None; **I. Ferraz Amaro**: AbbVie/Abbott, 5, 6, Amgen, 5, 6, Bristol-Myers Squibb(BMS), 6; **D. Ferrer**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6; **O. Collaborative Group Members**: None.

Abstract Number: 2166

Long-Term Effects of Abatacept on Arthritis and Atherosclerosis in Older vs Younger Patients with Rheumatoid Arthritis: 3-year Results of a Prospective, Multicenter, Observational Study

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) are at an increased risk of cardiovascular disease secondary to atherosclerosis. Although it has been reported that TNF inhibitor improved carotid intima-media thickness (IMT) progression, the effect of abatacept (ABT) is unknown. We reported that 24-week ABT treatment was efficacious and safe in both older vs younger patients with RA who were refractory to csDMARDs. Presently, we report the long-term results of ABT on disease activity and safety for 3 years (156 weeks) in the same population while focusing on the effectiveness of ABT on atherosclerosis progression.

Methods: This was a prospective observational study. Patients were stratified by age and treatment into four groups: younger (20-64 years old) and older (≥65 years) patients taking ABT (AY and AO) and csDMARD (CY and CO). Patients could either initiate ABT (ABT group), and those in the csDMARD group could add a csDMARD to their prescribed regimen, or switch to a new csDMARD. Change from baseline in mean IMT of the common carotid artery, IMT max (bulbus, bifurcation,

Table 1. Changes in intima-media thickness, plaque score and pulse wave velocity at weeks 156.

Table 2. Factors affecting the extent of changes in plaque score using a linear mixed model.

Figure 1. Proportions of patients with rheumatoid arthritis who had the indicated EULAR responses at Weeks 52, 104 and 156.

internal and common carotid artery), plaque score, pulse wave velocity (PWV), and EULAR response in the ABT vs csDMARD groups in younger vs older patients were analyzed up to week 156.

Results: By age and treatment, 216 patients were evaluated (AY, n=52; AO, n=73; CY, n=41; CO, n=50). Change of mean IMT of the common carotid artery and max IMT in the ABT group tended to be small compared with the csDMARD group at week 156 (Table 1). Change of plaque score in the ABT group also tended to be small compared with the csDMARD group at week 156, which was statistically significant in the older patients (p=0.0302). Overall, there was no consistent trend in PWV. Furthermore, multivariate analysis, which also considered disease activity, showed that change in plaque score was significantly smaller in ABT group (AY+AO) compared with csDMARD group (CY+CO) (p=0.0303) (Table 2). In AY vs CY groups, the patient proportions with good or good/moderate EULAR response were higher in the ABT vs csDMARDs group at all time points (Figure 1). In AO vs CO groups, proportions of patients with good or good/moderate EULAR response were also higher in the ABT group. Decrease in DAS28-ESR, simple disease activity index, clinical disease activity index, or HAQ was significantly greater in the ABT vs csDMARDs group in both younger vs older patients. No significant differences in good or good/moderate EULAR response, DAS28-ESR, simple disease activity index, clinical disease activity index, or HAQ were observed between younger vs older patients in ABT-treated groups (AY vs AO). ABT retention rates were not significantly different between younger vs older patients. Adverse events tended to be more frequent in the ABT group, but no significant differences were found.

Conclusion: ABT may be effective in slowing atherosclerosis. ABT efficacy on disease activity was maintained for 3 years without differences in older vs younger patients. No new safety signals were detected.

Disclosure: Z. Yamada: Janssen, 6; **S. Muraoka**: None; **M. Kawazoe**: Asahi Kasei Pharma Corp, 6, AstraZeneca, 6, Ayumi Pharmaceutical Corporation, 6, GlaxoSmithKlein(GSK), 6; **W. Hirose**: Eli Lilly, 6, Pfizer, 6; **H. Kono**: AbbVie/Abbott, 6, Asahikasei Pharm, 5, 6, Asteras Pharm, 6, Ayumi Pharm, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Chugai Pharm, 5, 6, Gilead, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, Kissei, 2, 6, Pfizer, 6, Tanabe Mitsubishi, 6, UCB, 6; **S. Yasuda**: Abbvie, 5, 6, Asahi-Kasei, 5, 6, Astellas Pharma Inc., 6, AstraZeneca, 6, AYUMI Pharmaceutical Corporation, 5, 6, Bayer Yakuhin, Ltd, 6, Chugai, 1, 5, 6, CSL Behring K.K, 5, 6, Eisai, 2, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Human Life CORD Japan Inc., 5, Immunoforge Inc., 1, Janssen, 6, Japan Blood Products Organization, 5, Kyowa Kirin Co., Ltd., 6, NIPPON KAYAKU Co., Ltd., 5, Novartis, 6, Ono Pharmaceutical, 6, Otsuka Pharmaceutical Co., Ltd, 2, Pfizer, 6, Seed Planning, Inc., 1, Stratoimmune Co., Ltd, 1, SYSMEX CORPORATION, 6, TAISHO PHARMACEUTICAL Co., Ltd., 5, 6, Takeda Pharmaceutical Co., Ltd, 5, Tanabe-Mitsubishi, 5, 6, TEIJIN PHARMA LIMITED, 2, 5, UCB, 5, 6; **T. Sugihara**: AsahiKASEI Co., Ltd., 5, 6, Chugai Pharmaceutical Co., Ltd., 5, 6, Daiichi Sankyo., 5, 6, Eli Lilly, 6, Ono Pharmaceutical., 5, 6, Pfizer, 6, Taisho Pharmaceutical Co., Ltd., 6; **T. Nanki**: AbbVie GK, 5, 6, Asahikasei Pharma Corp., 5, 6, Astellas Pharma Inc., 6, AstraZeneca K.K., 6, Ayumi Pharmaceutical Co., 5, 6, Bristol-Myers Squibb K.K., 5, Chugai Pharmaceutical Co., 2, 5, 6, Eisai Co.,Ltd., 5, 6, Eli Lilly Japan K.K., 5, 6, GlaxoSmithKline plc., 6, Janssen Pharmaceutical K.K., 6, Mitsubishi-Tanabe Pharma Co., 5, 6, Mochida Pharmaceutical Co., Ltd., 5, 6, Nippon Boehringer Ingelheim Co., Ltd., 5, 6, Nippon Kayaku Co., Ltd., 5, Ono Pharmaceutical Co., Ltd., 5, 6, Pfizer Japan Inc., 6, Shionogi & Co., Ltd., 5, Taisho Pharmaceutical Co.,Ltd., 5, Takeda Pharmaceutical Co., Ltd., 6, Teijin Pharma Ltd., 5, UCB Japan Co. Ltd., 1, 6.

Abstract Number: 2167

24-week, Post-Marketing Surveillance Analysis of Upadacitinib in Japanese Patients with Rheumatoid Arthritis (Encore[1])

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SESSION INFORMATION

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Session Title: RA – Treatments Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Upadacitinib (UPA) was approved in 2020 in Japan for the treatment of "Rheumatoid arthritis (RA) patients with inadequate response to conventional therapy, including inhibition of structural damage progression". All-case post-marketing Surveillance (PMS) in Japan was started at the same time of the market launch and is currently collecting data up to 3-years (24-week data for solicited events). In Japanese label, UPA15 mg should be orally administered once daily for adult RA patients. UPA 7.5 mg may be acceptable for some patients according to their condition.

Table 1. Patient baseline characteristics

Variable		Patients included in safety analysis set, N=2,106	Patients included in efficacy analysis set, N=1,482
Sex	Male	416 (19.8)	298 (20.1)
	Female	1,690 (80.2)	1184 (79.9)
Age	Years, Mean (SD)	65.3 (13.7)	65.1 (13.6)
	<65	873 (41.5)	624 (42.1)
	≥65	1,233 (58.5)	858 (57.9)
Body weight	kg, Mean (SD)	55.74 (12.00), N=1,938	55.76 (11.68), N=1,390
	<50	618 (29.4)	437 (29.5)
	≥50 and <70	1,083 (51.4)	783 (52.8)
	≥70 and <90	210 (10.0)	152 (10.3)
	≥90	27 (1.3)	18 (1.2)
	Unknown/Unlisted	168 (8.0)	92 (6.2)
Disease duration	Years, Mean (SD)	11.99 (10.80), N=1,928	12.13 (10.99), N=1,396
	<2	325 (15.4)	251 (16.9)
	≥2 and <5	308 (14.6)	212 (14.3)
	≥5 and <10	352 (16.7)	245 (16.5)
	≥10	943 (44.8)	688 (46.4)
	Unknown/Unlisted	178 (8.5)	86 (5.8)
RA treatment history	Yes	2,091 (99.3)	1,471 (99.3)
	MTX	1,852 (87.9)	1,314 (88.7)
	MTX > 8mg/w continued for at least 3 months	1,299 (61.7)	920 (62.1)
	csDMARD (immunosuppressant excl. MTX)	572 (27.2)	426 (28.7)
	csDMARD (immunomodulator excl. MTX)	1,178 (55.9)	843 (56.9)
	JAK inhibitor	1,011 (48.0)	722 (48.7)
	bDMARDs (TNF inhibitor)	1,260 (59.8)	904 (61.0)
	bDMARDs (IL-6 inhibitor)	897 (42.6)	658 (44.4)
	bDMARDs (CTLA-4-Ig)	558 (26.5)	385 (26.0)
	Corticosteroid	1,374 (65.2)	979 (66.1)
	No	13 (0.6)	11 (0.7)
	Unknown/Unlisted	2 (0.1)	0 (0.0)

Numerical values refer to the number of patients (%) unless otherwise stated; SD: standard deviation; csDMARD: conventional synthetic disease-modifying antirheumatic drug; CTLA4-Ig: T-cell-selective co-stimulation modulator; IL-6: interleukin 6; JAK: Janus kinase; MTX: methotrexate; RA: rheumatoid arthritis; TNF: tumor necrosis factor

Table 2. Incidences of adverse events / drug reactions up to Week 24

Variable	Patients included in safety analysis set N=2,106 Number of patients (%)	Patients with MTX at least 8mg per week, for more than 3 months N = 1,299 Number of patients (%)	Patients without MTX at least 8mg per week, for more than 3 months N = 806 Number of patients (%)
Adverse events	464 (22.0)	268 (20.6)	196 (24.3)
Serious adverse events	99 (4.7)	47 (3.6)	52 (6.5)
Adverse drug reactions	329 (15.6)	184 (14.2)	145 (18.0)
Clinically significant adverse drug reactions	50 (2.4)	22 (1.7)	28 (3.5)

1 subject was unknown or undescribed for MTX dose and duration regarding guideline for the proper use of Upadacitinib in post-marketing surveillance.
"Adverse drug reactions" are defined as adverse events considered to be related to upadacitinib by the treating physician.

Japan College of Rheumatology guideline for the proper use of Upadacitinib in post-marketing surveillance, revised October 23, 2022, defines eligible patients as below. "Patients with an inadequate response to MTX > 8mg per week continued for at least 3 months are eligible. From a safety perspective, patients who cannot receive MTX e.g., patients with high risk of infection, renal dysfunction, or interstitial pneumonia, principally should not be eligible[1]."

Methods: This ongoing PMS includes all patients with RA prescribed with UPA since April 2020. An interim analysis of PMS was performed to evaluate the safety and the effectiveness (disease activity) of UPA for 24 weeks.

Results: As of August 15, 2022, 2878 patients were enrolled, with 2,106 and 1,482 patients included in the safety (mean age=65.3 years old; >65 years old=58.5%; female=80.2%; mean RA duration=12.0 years) and efficacy analysis set, respectively (Table 1). In the safety analysis set, 1,694 (80.4%) continued UPA treatment for 24 weeks. UPA doses at onset were 7.5mg/day in 540 (25.6%), 15mg/day in 1,549 (73.6%) of patients in the safety analysis set, respectively. At baseline, 44.4% and 41.0% of patients in the safety analysis set received methotrexate (MTX) and glucocorticoid, respectively, and 22.4% had mild or greater renal failure. Most common comorbidities were osteoporosis, hypertension, and gastroesophageal reflux disease. AEs and serious AEs (SAEs) occurred in 464 (22.0%) and 99 (4.7%) patients, respectively. In the 1,299 patients receiving MTX >8 mg/week for ≥3 months,[2] AEs occurred in 268 (20.6%) and SAEs in 47 (3.6%). In the 806 patients not receiving MTX > 8mg/week for ≥3 months, AEs occurred in 196 (24.3%) and SAEs in 52 (6.5%) (Table 2). Ten deaths were reported, with causes including lung tumor, subarachnoid hemorrhage, organizing pneumonia, bacterial pneumonia, pneumocystis jirovecii, COVID-19 and unknown. Serious infections were reported in 37 (1.8%) patients. Herpes zoster in 69 (3.3%), impaired liver function in 59 (2.8%), serious cytopenia in 3 (0.1%), renal impairment in

Table 3. Adverse event of special interest up to Week 24

	Number of patients (%)	Number of events	Dose at onset 15 mg/day n = 1,549	7.5 mg/day n = 540	Other n = 16
Adverse event of special interest	190 (9.0)				
Serious infection	37 (1.8)	42	33	9	0
Herpes zoster	69 (3.3)	75	53	20	2[a]
Malignancy	10 (0.5)	12	11	1	0
Cardiovascular event	8 (0.4)	8	5	3	0
Venous thromboembolism	1 (0.0)	2	2	0	0
Impaired liver function	59 (2.8)	62	45	17	0
Renal impairment	11 (0.5)	11	9	2	0
Interstitial pneumonia	5 (0.2)	5	5	0	0
Serious cytopenia	3 (0.1)	3	1	2	0
Gastrointestinal perforation	3 (0.1)	3	3	0	0
Hepatitis B reactivation	1 (0.0)	1	1	0	0
Event leading to death	10 (0.5)	10	9	1	0

"Solicited adverse events" in this study are as follows: events leading to death, serious infection, hepatitis B virus reactivation, interstitial pneumonia, malignancy, cardiovascular event, venous thromboembolism, gastrointestinal perforation, herpes zoster, Impaired liver function, renal impairment, rhabdomyolysis/myopathy, and serious cytopenia (neutropenia, lymphopenia, hemoglobin level decreased). Rhabdomyolysis or myopathy is not listed because these events did not occur. Numbers of 15 mg / day, 7.5 mg / day, and other indicate patient number of each group by starting dose, respectively.

[a]One patient who occurred while on doses other than 7.5 mg/day or 15 mg/day was included. One patient withdrew at the first onset of herpes zoster and 16 days after withdrawal, a second herpes zoster event was developed which was included.

11 (0.5%), malignancy in 10 (0.5%), cardiovascular event in 8 (0.4%), interstitial pneumonia in 5 (0.2%), and venous thromboembolism (VTE) in 1 (0.0%) were reported, respectively (Table 3). 6 of 10 patients with malignancies were diagnosed within 2 months of UPA initiation. 621 patients were assessed in DAS28-CRP, of which 488 (78.6%) achieved LDA or CR and 382 (61.5%) achieved CR.

Conclusion: The 24-week interim analysis of all-case PMS in Japan showed that more than half of the patients receiving UPA are over aged 65 years or older. Although the mean age is higher than that of patients in clinical studies, the safety profile was consistent with clinical trials, and no new safety signals were identified.[3,4] The safety and efficacy data from this real-world setting will continue to be collected to assess for RA patients treated with UPA in Japan.

References

1 Mod Rheumatol suppl 2023(33): S179, presented at the JCR2023, Apr 24–26, Japan.
2 JCR guideline for proper use of UPA in PMS
3 Burmester, et al. RMD Open 2023;9: e002735
4 Yamaoka, et al. Drug Saf. 2021 Jun;44(6):711-722.

Disclosure: T. Atsumi: AbbVie, 5, 6, Alexion, 5, 6, Astellas, 5, 6, Boehringer-Ingelheim, 2, Bristol-Myers Squibb, 6, Chugai, 5, 6, Daiichi Sankyo, 5, 6, Eisai, 5, 6, Eli Lilly, 5, 6, Gilead, 5, 6, GSK, 2, 5, Merck Sharp & Dohme, 2, 6, Mitsubishi Tanabe Pharma, 5, 6, Otsuka, 5, 6, Pfizer, 5, 6, Sanofi/Genzyme, 2, 6, Takeda, 5, 6, UCB, 5, 6; **N. Okamoto**: None; **N. Takahashi**: AbbVie/Abbott, 6, Asahi-Kasei, 6, Astellas, 6, Bristol-Myers Squibb(BMS), 6, Chugai, 6, Daiichi Sankyo, 6, Eisai, 6, Eli Lilly, 6, Janssen, 6, Mitsubishi Tanabe, 6, Novartis, 6, Pfizer, 6, Sanofi, 6, UCB, 6; **N. Tamura**: AbbVie/Abbott, 5, 6, Asahi-Kasei, 5, 6, Ayumi, 5, 6, Boehringer-Ingelheim, 5, 6, Chugai, 5, 6, Eisai, 5, 6, Janssen, 5, 6, Mitsubishi Tanabe, 5, 6, Novartis, 5, 6, Taisho, 5, 6; **A. Nakajima**: None; **A. Nakajima**: AbbVie/Abbott, 5, 6, Asahi-Kasei, 5, 6, AstraZeneca, 5, 6, Ayumi, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Chugai, 5, 6, Eisai, 5, 6, Eli Lilly, 5, 6, GlaxoSmithKlein(GSK), 5, 6, Janssen, 5, 6, Kissei, 5, 6, Mitsubishi Tanabe, 5, 6, Nippon Kayaku, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Taisho, 5, 6; **T. Fujii**: AbbVie/Abbott, 5, 6, Asahi-Kasei, 5, 6, Astellas, 5, 6, Boehringer-Ingelheim, 5, 6, Chugai, 5, 6, Eisai, 5, 6, Eli Lilly, 5, 6, GlaxoSmithKlein(GSK), 5, 6, Janssen, 5, 6, Mitsubishi Tanabe, 5, 6, Ono, 5, 6, Pfizer, 5, 6, UCB, 5, 6; **H. Matsuno**: None; **T. Kawaberi**: AbbVie/Abbott, 3, 11; **N. Sunaga**: AbbVie/Abbott, 3, 11; **Y. Tsujita**: AbbVie/Abbott, 3, 11; **S. Chonan**: AbbVie/Abbott, 3, 11; **M. Kuwana**: AbbVie/Abbott, 6, Asahi-Kasei, 5, 6, Astellas, 6, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, 6, Chugai, 2, 5, 6, Corbus, 2, Eisai, 6, GlaxoSmithKlein(GSK), 2, Horizon, 2, Janssen, 6, Kissei, 2, MBL, 2, 5, Mitsubishi Tanabe, 2, 5, 6, Mochida, 2, 6, Nippon Shinyaku, 6, Ono, 5, 6; **M. Takagi**: None.

Abstract Number: 2168

The Potential of Autologous Patient-derived Circulating Extracellular Vesicles to Improve Drug Delivery in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

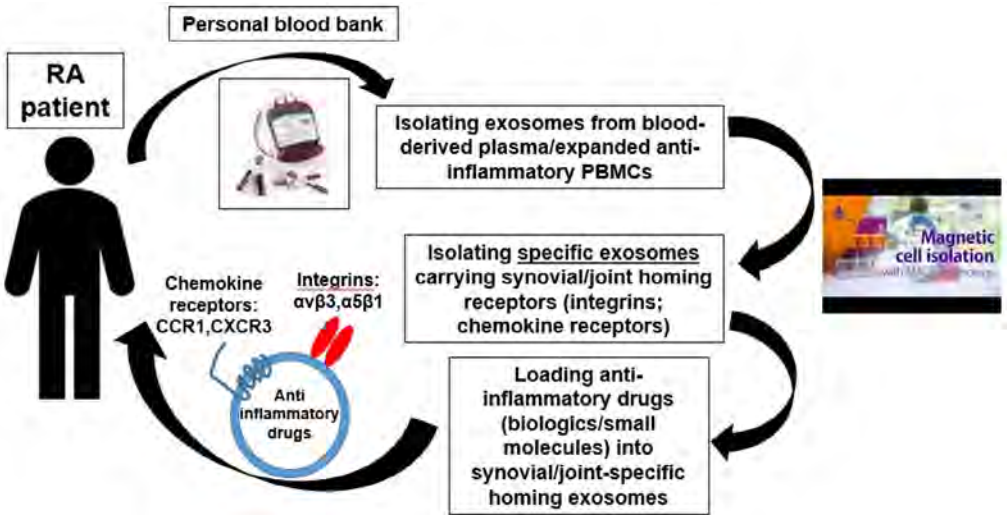

Figure 1: Our proposed strategy: Enrichment of autologous patient-derived 'joint-specific' homing exosomes for the treatment of RA patients.

Background/Purpose: The use of biological treatment in patients with rheumatoid arthritis (RA) can induce non-specific immune suppression, which might result in higher rates of infections. Therefore, there are still unmet needs to develop more specific and safe therapies in the management of RA patients. Accumulating evidence suggests that extracellular vesicles (EVs) may play a role in the modulation and maintenance of autoimmune processes. In the current study, we aimed to prove that isolation of circulating autologous 'tissue-specific' homing EVs from RA patients - may improve the delivery of current FDA-approved anti-inflammatory drugs, which will be encapsulated into these EVs. We assume that the drug-loaded EVs will find their way specifically to the inflamed tissue, following their administration to the same patient (Figure 1).

Methods: Plasma/serum-derived EVs had been isolated from arthritic mice (collagen-induced arthritis [CIA] model) and RA patients using: ultrafiltration, commercial exosome purification kit (NORGEN BIOTEK CORP) and size exclusion chromatography techniques. Characterization of these EVs have been conducted using nanoparticle tracking analysis, transition electron microscopy and western blot analysis. The expression of 'tissue-specific homing receptors' such as integrins, on plasma/serum-derived EVs isolated from arthritic mice (CIA model) or RA patients, had been examined, using WB analysis. EVs were labelled using DiR fluorescent dye and their potential *in-vivo* migration towards inflamed synovia, had been explored in collagen antibody-induced arthritis (CAIA) model, using In Vivo Imaging System (IVIS). Cellular uptake of RA patients-derived labelled EVs have been conducted using SW982, a human synovial cells.

Results: We found that autologous labeled EVs, derived from blood of arthritic mice with CAIA, can migrate towards inflamed synovia. Moreover, we show that these EVs strongly expresses glucose transporter 1 (mGLUT1) which in turn, improve their therapeutic potential to be loaded with anti-inflammatory drugs using glucose-coated gold nanoparticles (GNPs). Finally, we show that EVs derived from plasma of RA patients expresses the joint/synovia-specific homing receptor αVβ3 integrin and can be taken up by LPS/TNFα-induced activated human synovial cell line *in vitro*.

Conclusion: Overall, we show the potential of autologous circulating EVs of RA patients to serves as natural nano-carrier for current FDA-approved drugs. We believe that this strategy will increase the specificity and efficiency of current treatment, possibly reducing side effects and will improve the quality of life of RA patients and potentially other autoimmune disease patients.

Disclosure: G. Halpert: None; **O. Moskovitch**: None; **A. Anaki**: None; **T. Caller**: None; **O. Gendelman**: None; **A. watad**: None; **R. Mehrian-Shai**: None; **R. Popovtzer**: None; **B. Guilbord**: None; **O. Segal**: None; **H. AMITAL**: Janssen, 5.

Abstract Number: 2169

Cost-utility of a Progressive Spacing of Tocilizumab or Abatacept in Patients with Rheumatoid Arthritis in Sustained Remission: A Medico-economic Analysis of the Towards the Lowest Efficacious Dose Trial

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
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Background/Purpose: Biologic Disease Modifying Anti-Rheumatic Drugs (bDMARDs) progressive tapering is a real opportunity in people living with rheumatoid arthritis (RA) having achieved remission both from the patient (reduction in the disease and drug-related burden) and the Society (cost alleviation) perspectives. The ToLEDo (Towards the Lowest Efficacious Dose) trial aimed to assess a disease activity-driven progressive tapering strategy of tocilizumab (TCZ) or abatacept (ABA) compared to their maintenance at full dose in RA patients in sustained remission. Non-inferiority (NI) was not demonstrated in terms of disease activity nor relapses, major relapses, radiographic progression. The aim of this secondary analysis was to assess the cost-utility of the spacing strategy (S-arm) in the ToLEDo trial compared to full dose maintenance (M-arm).

Methods: ToLEDo is a multicenter 2-year NI randomized open-label controlled trial, which enrolled 228 patients (113 in the S-arm and 115 in the M-arm). A cost-utility analysis was conducted on the per protocol population. In each arm, health benefits were estimated every 6 months by Short Form Health Survey (SF-6D) and EuroQoL (EQ-5D)-derived utility measurements. Cost elicitation integrated health resource use including bDMARD costs (direct cost) as well as productivity loss

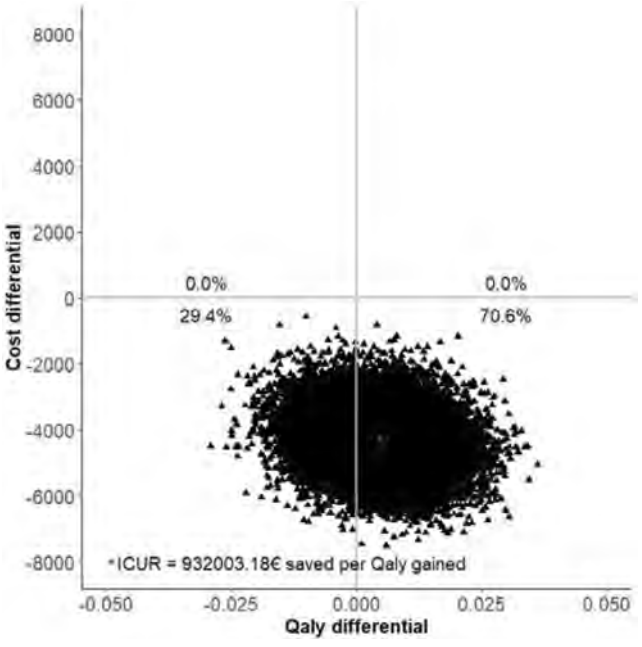

Figure 1: cost-utility plane (spacing versus maintenance), with utilities derived from PP SF-6D

Table 1: ICUR in ABA subgroup, TCZ subgroup, using EQ-5D-derived utilities, and stochastic sensitivity analysis

	ABA subgroup (PP SF-6D)	TCZ subgroup (PP SF-6D)	PP EQ-5D	Stochastic sensitivity analysis (PP SF-6D)
ICUR, €/QALY gained	-420,076.22 (95%CI -1,044,462 ; 1,461,037)	-1,008,225 (95%CI -2,436,237; 1,898,967)	-52,005 (95%CI -458,934; 369,967)	-481,029.28 (95%CI -1,300,747; 1,867,263)

(indirect cost).The incremental cost-utility ratios (ICUR) were calculated by dividing the difference of costs between S-arm and M-arm by the difference of utilities between the 2 arms. 95% confidence interval (95%CI) were calculated by bootstrap (20,000 iterations). The incremental net benefit (INB) was calculated for willingness to pay (WTP) values ranging from 0 to 150,000€. The analyses were replicated using SF-6D (primary analysis) or EQ-5D, and in ABA and TCZ subgroups. Acceptability analyses as well as stochastic sensitivity analyses (simulating costs and utilities using MCMC algorithms) were also performed.

Results: Overall, 178 patients were included (82 in S-arm, 96 in M-arm) in the per protocol analysis. At the end of the follow-up in the S-arm, 15.0% of patients discontinued their biologic, 48.7% spaced the injections, and 36.3% remained at the standard dose. The difference in terms of two-years utility gains between S-arm and M-arm was 0.004 (95%CI -0.012, 0.021) with SF-6D. The difference of total costs between S-arm and M-arm was -4,275 € (95%CI -5,955 to -2,542). The estimated ICUR of the spacing strategy over the maintenance at full dose was €932,003 saved per QALY (95% CI -7,534,788 to 6,720,372) with SF-6D. The INB was 4,734.6€ for a WTP of 100,000€. With a willingness to accept of 0 €/QALY lost, the probability to be cost-effective for the spacing strategy was 70.6% (***Figure 1***). The results were consistent when using EQ-5D-derived utilities, in ABA and TCZ subgroups, as well as in the stochastic sensitivity analyses (***Table 1***).

Conclusion: Although the ToLEDo trial did not demonstrate non-inferiority, the tested disease activity-driven tapering strategy was not associated with health loss in terms of utilities and incurred for substantial cost savings, making this strategy potentially dominant.

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Abstract Number: 2170

Systemic Glucocorticoids Are Associated with a Time and Dose-dependent Risk of Major Adverse Cardiovascular Event in Patients with Rheumatoid Arthritis: A Population-based Study

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
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Background/Purpose: Rheumatoid arthritis (RA) and systemic glucocorticoid (GC) use are associated with increased risk of cardiovascular disease. The latest RA management recommendations from the American College of Rheumatology (ACR, updated in 2021) and European Alliance of Associations for Rheumatology (EULAR, updated in 2022) are divergent in terms of GC use. Whether there exists a CV-safe dose or duration of GC in the treatment of RA is still debatable and of great clinical interest.

Methods: This was a population-based retrospective cohort study. RA patients without major MACE at baseline were recruited from a Hong Kong citywide database from 2006 to 2015, and followed till the end of 2018. The primary outcome was the first occurrence of a major adverse cardiovascular events (MACE). Cox regression analysis with time-varying covariates was used to evaluate the association of GC and MACE, adjusting for demographics, traditional CV risk factors, inflammatory markers and the usage of anti-rheumatic drugs.

Results: Among 12,233 RA patients with 105,826 patient-years of follow-up with a mean follow-up duration of 8.7 years, 860 (7.0%) developed MACE. The crude incidence rate was 8.13 per 1,000 person-years. The baseline characteristics of the subjects are summarized in Table 1. In the time-varying analyses after controlling for confounding factors, a daily prednisolone dose of ≥ 5mg significantly increased the risk of MACE (erythrocyte sedimentation rate [ESR] model: HR 2.02, 95%CI 1.72-2.37; C-reactive protein [CRP] model: HR 1.87, 95%CI 1.60-2.18), while a daily dose below 5mg was not associated with MACE risk, compared to no GC use. The adjusted hazard ratios (HRs) of all candidate covariates are summarized in the forest plots (Figure 1). The MACE-free Kaplan-Meier survival curves of the groups receiving different GC doses are shown in Figure 2. In patients receiving daily prednisolone ≥5mg, both intermediate- (up to 180 days) and long-term (longer than 180 days) use of prednisolone ≥5mg daily were significantly associated with increased risk of MACE, with an adjusted HR of 1.07 (p-value < 0.001) per month of GC use.

Conclusion: In this population-based real-world database, after controlling for multiple confounding factors, the use of GC was associated with up to two-fold increased risk of incident MACE on long term follow-up. No safe duration of use was found in patients receiving daily prednisolone ≥5mg.Very low dose prednisolone (< 5mg daily) did not appear to increase CV risk.

Disclosure: H. SO: None; **T. LAM**: None; **H. MENG**: None; **S. LAM**: None; **L. Tam**: AbbVie, 5, Amgen, 2, 5, Boehringer-Ingelheim, 2, 5, Eli Lilly, 2, GSK, 5, Janssen, 2, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 2.

Abstract Number: 2171

Common IL-6 Signaling Is Inhibited by IL-6 Inhibitors and JAK Inhibitors, but Which Is Better at Preventing Bone Destruction in RA?

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SESSION INFORMATION
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Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: To date, there are no head-to-head clinical trials directly comparing the effects between IL-6i and JAKi on bone destruction in RA. In recent years, a series of JAK inhibitors (JAKi) have been introduced, all of which have JAK1 inhibitory activity, and inhibition of IL-6 signaling plays an important role in their pharmacological actions. IL-6 inhibitors

(IL-6i)have also been commonly used for rheumatoid arthritis (RA), and several anti-receptor antibodies are in clinical application. Recent studies have revealed the molecular basis of the immune cell-fibroblast-bone triad interactions in RA bone destruction. Therefore, to examine changes in peripheral blood gene expression after IL-6i or JAKi treatment, which inhibit a common pathway, and to estimate their respective effects on the bone immune system.

Methods: Peripheral blood gene expression changes in 38 RA patients (Tocilizumab(TCZ)=13, Tofacitinib(TOF)=15, Baricitinib (BAR)=10) were analyzed before and 3 months after the initiation of treatment using next generation sequencing. Changes in gene expression of molecules involved in bone immunity were analyzed before and after each treatment.

Results: Comparison of L-6i and JAKi showed that JAKi treatment significantly suppressed RANKL expression in peripheral blood. At the same time, significant suppression of RANK, ETS1, and IL-34 gene expression was also observed with JAKi treatment. Comparison of TOF and BAR treatment showed significant suppression of IL-4 expression in TOF and significant suppression of MMP-2 and IL-12 expression in BAR.

Conclusion: JAKi suppressed RANKL expression significantly compared to IL-6i, suggesting that JAKi is more potent than IL-6i in suppressing bone destruction. Furthermore, assuming that the promoter regions of RANK in synovial osteoclasts and ETS1 in fibroblasts are similar to those in peripheral blood, the following prediction emerges. JAKi suppresses RANK and ETS1 expression more than IL-6i, suggesting that JAKi may be favorable for preventing bone destruction in terms of (1) suppressing osteoclast differentiation and (2) suppressing tissue-destructive fibroblasts. The effect on gene expression of molecules involved in bone immunity was found to vary among each JAK inhibitor.

Disclosure: Y. Koyama: AbbVie/Abbott, 5, 6, Asahikasei, 6, Ayumi, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 5, Mitsubishi Tanabe, 6, Novartis, 5; **Y. Sato**: None; **M. Tokunaga(Sakamoto)**: None; **Y. Nakai**: None.

Abstract Number: 2172

Subcutaneus vs Intravenous Abatacept in Rheumatoid Arthritis-Interstitial Lung Disease. National Multicenter Study of 509 Patients

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SESSION INFORMATION

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Session Title: RA – Treatments Poster III

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Background/Purpose: Interstitial lung disease (ILD) is a severe extra-articular manifestation of rheumatoid arthritis (RA). Abatacept (ABA) has demonstrated efficacy in RA-ILD**.** Clinical trials have shown equivalence in subcutaneous (SC) and intravenous (IV) administration of ABA for articular manifestations**.** However, it has not been studied in RA-ILD. Our objective was tocompare the effectiveness of ABA in RA-ILD patients according to the route of administration (IV-ABA vs SC-ABA).

Methods: National multicenter study of RA-ILD patients on treatment with ABA. They were divided into 2 groups according to the route of administration: a) IV, and b) SC. We analyzed from baseline the following outcomes in both groups: **a)** forced vital capacity (FVC), **b)** diffusing capacity of the lungs for carbon monoxide (DLCO), **c)** chest high resolution computed tomography (HRCT), **d)** dyspnea (assessed with the modified Medical Research Council scale), **e)** arthritis activity (assessed with DAS28-ESR or described in clinical records), and **f)** sparing corticosteroids effect.

Table 1. Main general features at baseline of RA-ILD patients with subcutaneous vs intravenous ABA.

	All ABA (n=509)	ABA IV (n=100)	ABA SC (n=360)	p
Age, years mean±SD	66 ± 10	66 ± 10	66 ± 10	0.97
Women, n (%)	286 (56)	61 (61)	201 (56)	0.47
Smoker ever, n (%)	286 (56)	52 (52)	199 (55)	0.48
ILD duration up to ABA, months, median [IQR]	9 (11-45)	10 (3-48)	10 (2-36)	0.52
RF, n (%)	442 (87)	85 (85)	317 (88)	0.65
ACPA, n (%)	425 (85)	83 (83)	310 (87)	0.79
DAS28-ESR	4.37 ± 1.59	4.33±1.55	4.47±1.52	0.46
ILD pattern, n (%)				
NIU	233 (47)	51 (51)	165 (46)	
NINE	145 (29)	20 (22)	111 (31)	0.26
Other	98 (25)	29 (29)	83 (23)	
FVC (% of the predicted), mean±SD	87 ± 22	87 ± 23	87 ± 21	0.92
DLCO (% of the predicted), mean±SD	66 ± 20	67 ± 20	66 ± 20	0.66
Prednisone at baseline, mg/day, median [IQR]	5 (5-10)	7.5 (5-10)	5 (5-10)	0.37

ABA: Abatacept; ACPA, anti-citrullinated protein antibodies; DLCO, diffusing capacity of the lung for carbon monoxide; DMARD, disease-modifying antirheumatic drug; FVC, forced vital capacity; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; JAKi, JAK inhibitor; RA, rheumatoid arthritis; RF, rheumatoid factor; UIP, usual interstitial pneumonia.

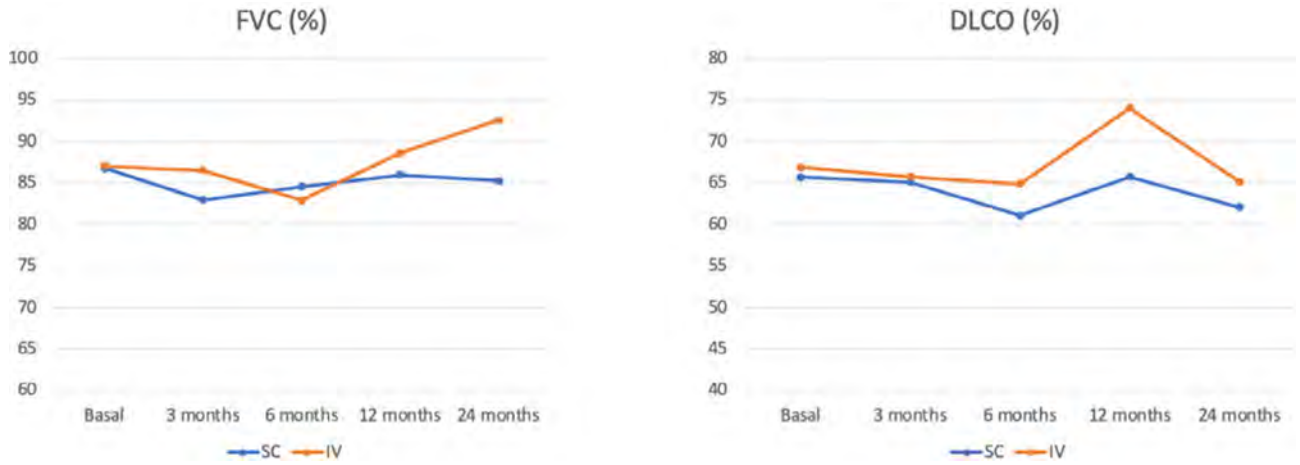

Figure 1. Evolution of pulmonary function tests (mean % of the predicted FVC and DLCO) in RA-ILD patients with SC-ABA vs IV-ABA therapy at baseline and 24 months.

Results: We studied a total of 509 [SC-ABA/IV-AB; 360/100 (available data)] patients. Baseline demographic and clinical characteristics are shown in **Table 1.**Patients were followed-up for a median [IQR] of 24 [7-48] months.FVC and DLCO remain stable during the first 24 months in both SC-ABA and IV-ABA **[Figure 1].** Dyspnea stabilized or improved in 84% of patients (89% of IV-ABA; 82% of SC-ABA). ABA was withdrawn in 106 patients: 81(34%) in SC-ABA group and 25 (40%) in IV-ABA group. ILD worsening and articular inefficacy were the most common reasons of ABA discontinuation.

Conclusion: In RA-ILD, ABA seems equally effective and safe regardless of the route of administration IV or SC.

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Abstract Number: 2173

Window of Opportunity in the Treatment of Rheumatoid Arthritis-Interstitial Lung Disease with Abatacept. National Multicenter Study of 509 Patients

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SESSION INFORMATION

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Background/Purpose: Interstitial lung disease (ILD) is a severe complication of rheumatoid arthritis (RA). Abatacept (ABA) has demonstrated efficacy in the treatment of RA-ILD, especially if it is initiated early during the ILD. Our objective was to compare the efficacy of ABA in RA-ILD patients according to ILD duration.

Methods: National multicenter study of 509RA-ILD patients treated with ABA. Patients with ABA initiation early in the disease (during the first 6 months since ILD diagnosis) were compared to those in whom ABA was started after 2 years of ILD diagnosis ("early" vs. "late" group, respectively). We analyzed in the 2 groups the following outcomes: **a)** forced vital capacity (FVC), **b)** diffusing capacity of the lungs for carbon monoxide (DLCO), **c)** chest high resolution computed tomography (HRCT), **d)**dyspnea (modified Medical Research Council scale), and **e)** arthritis activity (DAS28-ESR or clinical records).

Results: A total of 216 patients were included in the "early" group and 165 patients in the "late" group. Baseline demographic and clinical characteristics are shown in **Table 1**. Mean baseline values of FVC were significantly higher in the "early" group. The evolution of FVC and DLCO for 48 months is shown in **Figure 1.** Both parameters remained stable during 48 months of ABA therapy, with statistically significant differences found in case of FVC (although lower stable values of

Table 1. Main general features at baseline of RA-ILD patients with "early" vs. "late" initiation of ABA in ILD course.

	All RA-ILD patients (n=509)	"Early" RA-ILD (n=216)	"Late" RA-ILD (n=165)	"Early" vs "Late" p
Age years mean±SD	66 ± 10	66 ± 9	66 ± 10	0.79
Women n (%)	286 (56)	98 (45)	91 (55)	0.91
Smoker ever, n (%)	269 (52)	117 (54)	85 (52)	0.61
ILD duration up to ABA, months, median [IQR]	9 (11-45)	2 (1-4)	52 (36-90)	**<0.001**
RF n (%); ACPA n (%)	442 (87); 425 (85)	187 (87); 185 (86)	146 (88); 140 (86)	0.58; 0.96
DAS28-ESR	4.37 ± 1.59	4.14 ± 1.55	4.43 ± 1.64	0.13
ILD pattern n (%)				
NIU	233 (47)	100 (47)	71 (44)	0.73
NINE	145 (29)	63 (30)	49 (30)	
FVC (% of the predicted) mean±SD	87 ± 22	88 ± 23	81 ± 19	**0.003**
DLCO (% of the predicted) mean±SD	66 ± 20	65 ± 19	64 ± 21	0.66
ABA monotherapy n (%)	226 (45)	101 (47)	73 (45)	0.56
ABA combined n (%)	276 (55)	112 (53)	90 (55)	
Prednisone at baseline, mg/day, median [IQR]	5 (5-10)	7.5 (5-10)	5 (5-10)	0.32
Previous immunosuppressive therapy n (%)				
MTX	379 (75)	172 (80)	118 (72)	0.05
Leflunomide	233 (46)	93 (43)	77 (47)	0.48
Sulfasalazine	68 (13)	27 (13)	23 (14)	0.66
Hydroxychloroquine	161 (32)	70 (33)	52 (32)	0.83
Anti-TNF drugs (IFX; ADA; ETA)	42 (8); 69 (14); 73 (14)	14 (6); 37 (17); 31 (14)	13 (8); 18 (11); 25 (15)	0.59; 0.08; 0.83
Rituximab	61 (12)	21 (10)	23 (14)	0.20
Tocilizumab	56 (11)	26 (12)	18 (11)	0.73

*IFX: Infliximab; ADA: Adalimumab; ETA: Etanercept.

FVC in the "late" group). Available chest HRCT images improved/ stabilized in 76% and 54% of patients in the "early" and "late" group, respectively. Stabilization or improvement of dyspnea was found in most patients of both groups.

Conclusion: Our study suggests a window of opportunity for the treatment of RA-ILD patients with ABA. However, treatment with ABA at any time of the course in the ILD seems to prevent interstitial lung progression.

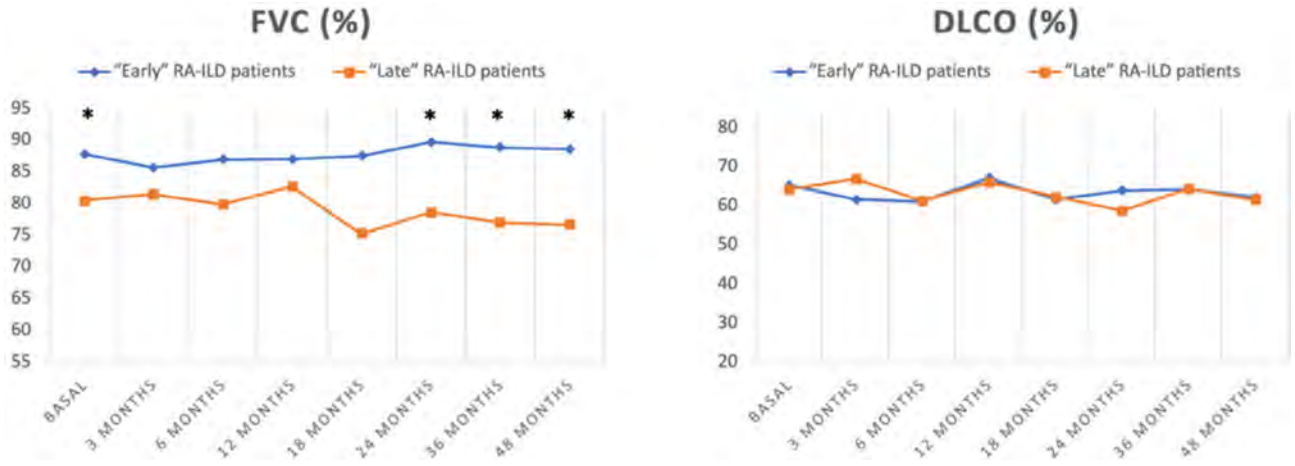

Figure 1. Evolution of pulmonary function tests in RA-ILD patients with "early" and "late" initiation of ABA in ILD course. FVC and DLCO are expressed as mean (95%CI) and compared between the 2 groups. (*) P value is statistically significant in FVC at baseline, 24, 36 and 48 months of follow up.

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Abstract Number: 2174

JAK Inhibitors in Rheumatoid Arthritis-Interstitial Lung Disease. National Multicenter Study of 73 Patients, 55 of Baricitinib

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Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a severe extra-articular manifestation of rheumatoid arthritis (RA). Abatacept and Rituximab are the recommended drugs**.** JAK inhibitors (JAKi) have demonstrated efficacy in RA. However, in clinical trials patients with active ILD were usually excluded. Moreover, a warning on ILD toxicity is included in SmPC (Summary of Product Characteristics) with tofacitinib (TOFA). Nonetheless, evidence on efficacy of JAKi in RA-ILD is growing. The objective of the study was to assess **a)** the effectiveness and **b)** the safety of JAKi in AR-ILD patients.

Methods: National multicenter study of 73 RA-ILD patients on treatment with JAKi. We analyzed from baseline the following outcomes: **a)** forced vital capacity (FVC), **b)** diffusing capacity of the lungs for carbon monoxide (DLCO), **c)** chest high resolution computed tomography (HRCT), **d)**dyspnea (modified Medical Research Council scale), **e)** arthritis activity (DAS28-ESR or clinical records), and **f)** sparing corticosteroids effect.

Results: We studied 73 patients (50 women/ 23 men; mean age 66 ± 10 years) from clinical practice on treatment with JAKi [Baricitinib (BARI)= 55 (74%), TOFA= 8 (11%), Upadacitinib (UPA)= 8 (11%), Filgotinib (FILGO)= 2 (3%)]. Baseline demographic and clinical characteristics are shown in **Table 1**. All patients had received disease-modifying antirheumatic drugs (DMARDs) before JAKi [Methotrexate (63; 86%), Leflunomide (46; 63%), Sulfasalazine (19; 26%), Hydroxychloroquine (16; 22%), Abatacept (47; 64%), Tocilizumab (26; 36%) and Rituximab (16; 22%)]. Since most patients were on BARI we focused on this group (n=55). Median [IQR] ILD duration up to BARI initiation was of 29 [15-64] months. Mean baseline values of FVC and DLCO (% predicted) were 88±27 and 69±20, respectively. Patients were followed-up for a mean of 36 ± 23 months. The evolution of FVC and DLCO remained stable during the first 12 months **(Figure 1).** At the end of the follow-up, available chest HRCT images improved/ stabilized in 76% of patients. Stabilization or improvement of dyspnea was found in 95% of patients. Most patients showed articular remission or low activity. BARI was withdrawn in 22 (42%) patients due to articular inefficacy (n=15), lung inefficacy (n=4), development of hypersensitivity pneumonitis (n=1), and appearance of brain cancer (n=1).

Table 1. Baseline characteristics of RA-ILD patients treated with JAKi.

	RA-ILD with JAKi (n=73)
Age, years mean±SD	66 ± 10
Women, n (%)	50 (69)
Smoker ever, n (%)	47 (64)
Time since ILD diagnosis, months, median [IQR]	35 [16-64]
RF // ACPA, n (%)	69 (95) // 69 (95)
FVC (% of the predicted), mean±SD	90 ±26
DLCO (% of the predicted), mean±SD	81 ± 16
UIP-like fibrotic pattern on HRCT, n (%)	36 (51)
Joint activity n (%)	40 (56)
Type of JAKi, n (%)	
Baricitinib (BARI)	55 (74)
Tofacitinib (TOFA)	8 (11)
Upadacitinib (UPA)	8 (11)
Filgotinib (FILGO)	2 (3)
Previous immunosuppressive therapy, n (%)	
Conventional / biologic DMARD	73 (100) / 62 (85)
Concomitant immunosuppresive therapy, n (%)	32 (44)
Concomitant antifibrotic therapy, n (%)	6 (8)

ACPA, anti-citrullinated protein antibodies; DLCO, diffusing capacity of the lung for carbon monoxide; DMARD, disease-modifying antirheumatic drug; FVC, forced vital capacity; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; JAKi, JAK inhibitor; RA, rheumatoid arthritis; RF, rheumatoid factor; UIP, usual interstitial pneumonia.

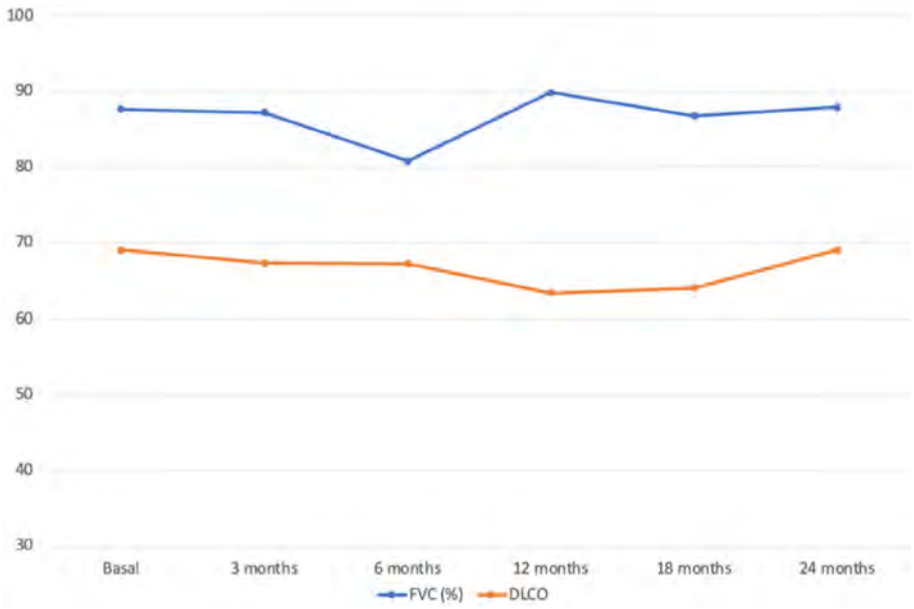

Figure 1. Evolution of pulmonary function tests (mean % of the predicted FVC and DLCO) in RA-ILD patients with BARI therapy at baseline and 24 months.

Conclusion: JAKi, especially BARI, may be useful and safe in controlling the course of both pulmonary and joint disease in RA-ILD patients, even in refractory cases.

Disclosure: A. Serrano-Combarro: None; **B. Atienza-Mateo**: None; **J. Valero-Jaimes**: None; **M. Pastor-Mena**: None; **R. Melero-Gonzalez**: None; **D. Castro-Corredor**: None; **M. Martin-Lopez**: None; **S. Castañeda**: None; **J. Loarce-Martos**: Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Galapagos, 6; **N. Mena Vazquez**: None; **C. carrasco-Cubero**: None; **C. Diez-Morrondo**: None; **a. Garcia-Valle**: None; **G. Bonilla**: None; **J. Blanco-Madrigal**: None; **N. del Val del Amo**: None; **N. Vegas Revenga**: None; **L. Perez-Albadalejo**: None; **R. Ortega Castro**: None; **D. Palma-Sanchez**: None; **A. fernandez-Ortiz**: None; **P. Lopez-Viejo**: None; **M. Lopez-Lasanta**: None; **M. Garijo Bufort**: None; **I. Casafont-Sole**: None; **O. Maiz-Alonso**: None; **J. Moreno-Morales**: None; **A. Urruticoechea**: None; **C. Perez-Garcia**: None; **J. Rosas**: None; **V. Ruiz-Esquide**: None; **D. Fernández-Lozano**: None; **I. Brana Abascal**: None; **E. Cervantes-Perez**: None; **J. Fernandez-Melon**: None; **C. Fernandez**: None; **B. Flores Robles**: None; **D. Ferrer**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6.

Abstract Number: 2175

Real-World Drug Persistence of GP2015, an Etanercept Biosimilar, in Patients with Rheumatoid Arthritis: Results from the Multi-Country COMPACT Study

Marc Schmalzing[1], Charlotte Both[2], Ines Brueckmann[2], Javier de Toro Santos[3], Tom Sheeran[4], Herbert Kellner[5] and Ayman Askari[6], [1]University Hospital, Rheumatology/Clinical Immunology, Department of Internal Medicine II, Würzburg, Germany, [2]Sandoz Hexal AG, Rheumatology, Holzkirchen, Germany, [3]University Hospital Coruña, Rheumatology, A Coruña, Spain, [4]University of Wolverhampton, New Cross Hospital, Wolverhampton, United Kingdom, [5]Hospital Neuwittelsbach, Center for Rheumatology and Gastroenterology, Munich, Germany, [6]Robert Jones and Agnes Hunt Orthopaedic Hospital NHS Foundation Trust, Rheumatology, Shropshire, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: COMPACT is a multi-country, non-interventional study that evaluated the drug persistence, effectiveness, safety and patient-reported outcomes in patients with rheumatoid arthritis (RA), axial spondyloarthritis and psoriatic arthritis treated with GP2015 (an etanercept biosimilar) in real-world conditions. Here, we report the drug persistence of GP2015 in patients with RA after 12 months.

Methods: RA patients aged ≥18 years on GP2015 treatment prior to study were enrolled. Patients were categorized based on prior treatment status: patients in clinical remission or low disease activity under treatment with reference etanercept (ETN) or other biosimilar ETN (initial ETN: [iETN]) and switched to GP2015 (Group A) or patients who received non-ETN targeted therapies and switched to GP2015 (Group B) or biologic-naïve patients who started GP2015 as the first biologic treatment after conventional therapy failure (Group C) or DMARD-naïve patients with recent diagnosis of RA considered suitable for treatment initiation with a biologic and started on treatment with GP2015 (Group D). Patients' drug persistence from GP2015 treatment start was assessed and is presented here. Median drug persistence was calculated using the median time estimate from Kaplan-Meier curve.

Results: Of 1466 patients enrolled, 844 (57.6%) patients had RA reported as the primary indication. Of the 844 patients with RA, 295 patients were switched from iETN (Group A), 88 were switched from other targeted therapies (Group B), 451 were biologic-naïve (Group C), and 10 were DMARD-naïve (Group D).[1] Drug persistence from start of GP2015 treatment in RA patients is presented in **Figure 1**. In the overall RA population, the discontinuation rate was 18.0% at Month 12 after initiation of GP2015 treatment. At Month 12, patients in Group A reported the lowest rate of discontinuation of 10.2%, while patients in Group B and C reported discontinuation rates of 23.9%, and 21.8%, respectively. Due to limited patient numbers in Group D (n=10) the drug persistence rate was difficult to interpret.

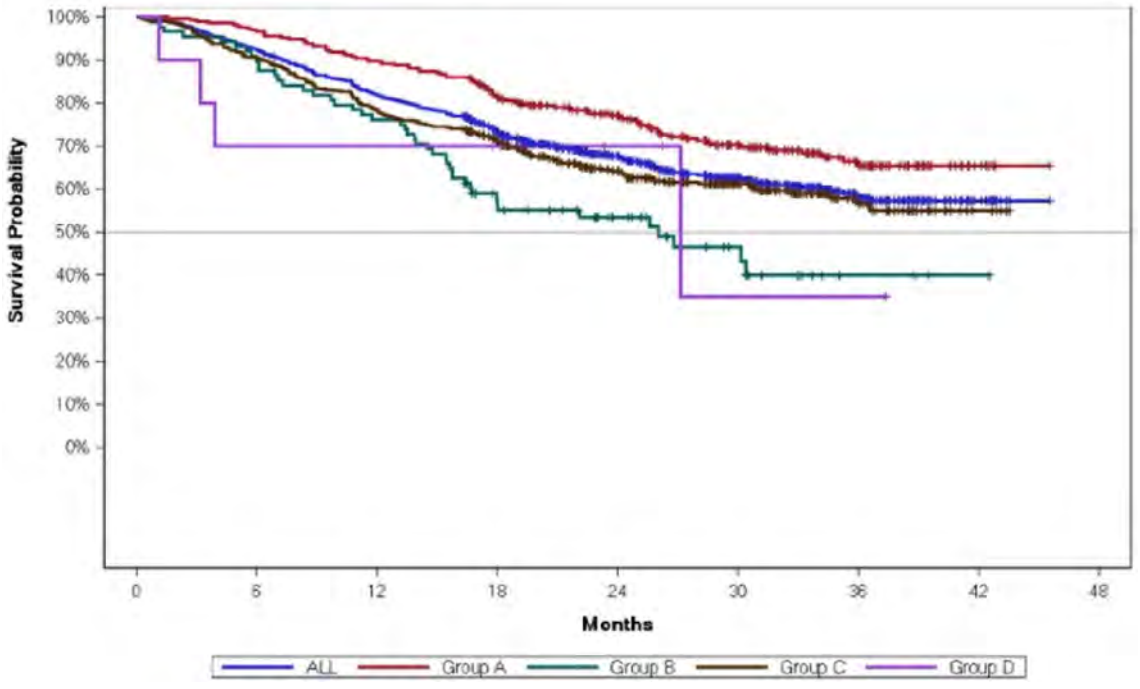

Figure 1. Drug persistence from GP2015 treatment start in patients with rheumatoid arthritis

Conclusion: The results of the study show high treatment persistence under GP2015 treatment in RA patients under real-world conditions. The results are in line with the reported persistence rates in the overall study population. Patients who were on previous iETN treatment and who had stable disease presented the highest drug survival rates after switch to GP2015.

Reference: 1. Schmalzing, et al. *Ann Rheum Dis*. 2022;81(Suppl 1):589–90.

Disclosure: M. Schmalzing: AbbVie, 2, 6, Boehringer Ingelheim, 2, 5, 6, Chugai/Roche, 2, EUSA-Pharma, 2, 6, Galapagos, 2, 5, 6, Hexal/Sandoz, 2, Janssen-Cilag, 2, 6, Lilly, 2, onkowissen.de, 2, UCB, 2, 5; **C. Both**: SANDOZ, 3; **I. Brueckmann**: SANDOZ, 3; **J. Santos**: AbbVie, 2, Fresenius Kabi, 2, Galapagos, 2, Janssen-Cilag, 2, Lilly, 2, MSD, 2, Novartis, 2, SANDOZ, 2, UCB, 2; **T. Sheeran**: BMS, 2, Novartis, 2, Pfizer, 2, Roche, 2; **H. Kellner**: None; **A. Askari**: None.

Abstract Number: 2176

Cellular and Proteomic Changes Following Administration of Peresolimab, in a Phase 2a Trial in Rheumatoid Arthritis

Robert J. Benschop[1], Jay Tuttle[1], Paul Emery[2], Christoph Preuss[1], Mark Daniels[1], Veavi Ching-Yun Chan[1], Pia Yachi[1] and Ajay Nirula[1], [1]Eli Lilly and Company, Indianapolis, IN, [2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, and NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: RA – Treatments Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Peresolimab is a humanized immunoglobulin G1 monoclonal antibody that stimulates human programmed cell death protein 1 (PD-1). Peresolimab demonstrated superiority to placebo in Disease Activity Score-28 with CRP (DAS28-CRP) improvements from baseline at Week 12 in a Phase 2a placebo-controlled, double-blind, randomized clinical trial (NCT04634253) in adult patients with moderate to severe Rheumatoid Arthritis (RA).[1] We report here, changes in exploratory biomarkers from this study.

Methods: Ninety-eight adult patients with moderate-to-severe RA (defined per American College of Rheumatology [ACR] criteria) were randomized 2:1:1 to peresolimab 700mg, 300mg, or placebo for 12 weeks. Whole blood, serum, and plasma were collected at baseline through Week 14 (end of the placebo control period). Cells were stained for CD3, CD4, CD8, CD19, CD16/56, and PD-1, processed and analyzed using standard flow cytometry methods. Serum samples were analyzed using the Olink Explore3072 panel which includes proteins that were detected in at least 25% of patients. Thirty age- and sex-matched healthy control samples were included for comparison. A gene set enrichment analysis approach was used to analyze proteomic results, and analyses were performed on comparing the combined peresolimab dose groups versus placebo.

Results: Peresolimab treatment reduced the number of peripheral CD4+ PD-1 high and PD-1 intermediate T cells by 53.6-57.7% and 33.8-38.5%, respectively, relative to baseline from weeks 2 through 12. No meaningful differences were observed for PD-1 low cells; Figure 1. There were no meaningful changes with major circulating cell types (ie, CD3+, CD4+, CD8+ T cells, B or NK cells) following treatment with peresolimab. Analysis of the proteomic data identified multiple pathways that showed differences between peresolimab-treated patients and placebo controls starting at week 8. This included treatment-induced down-modulation of cytokines and chemokines in interleukin signaling pathways, including

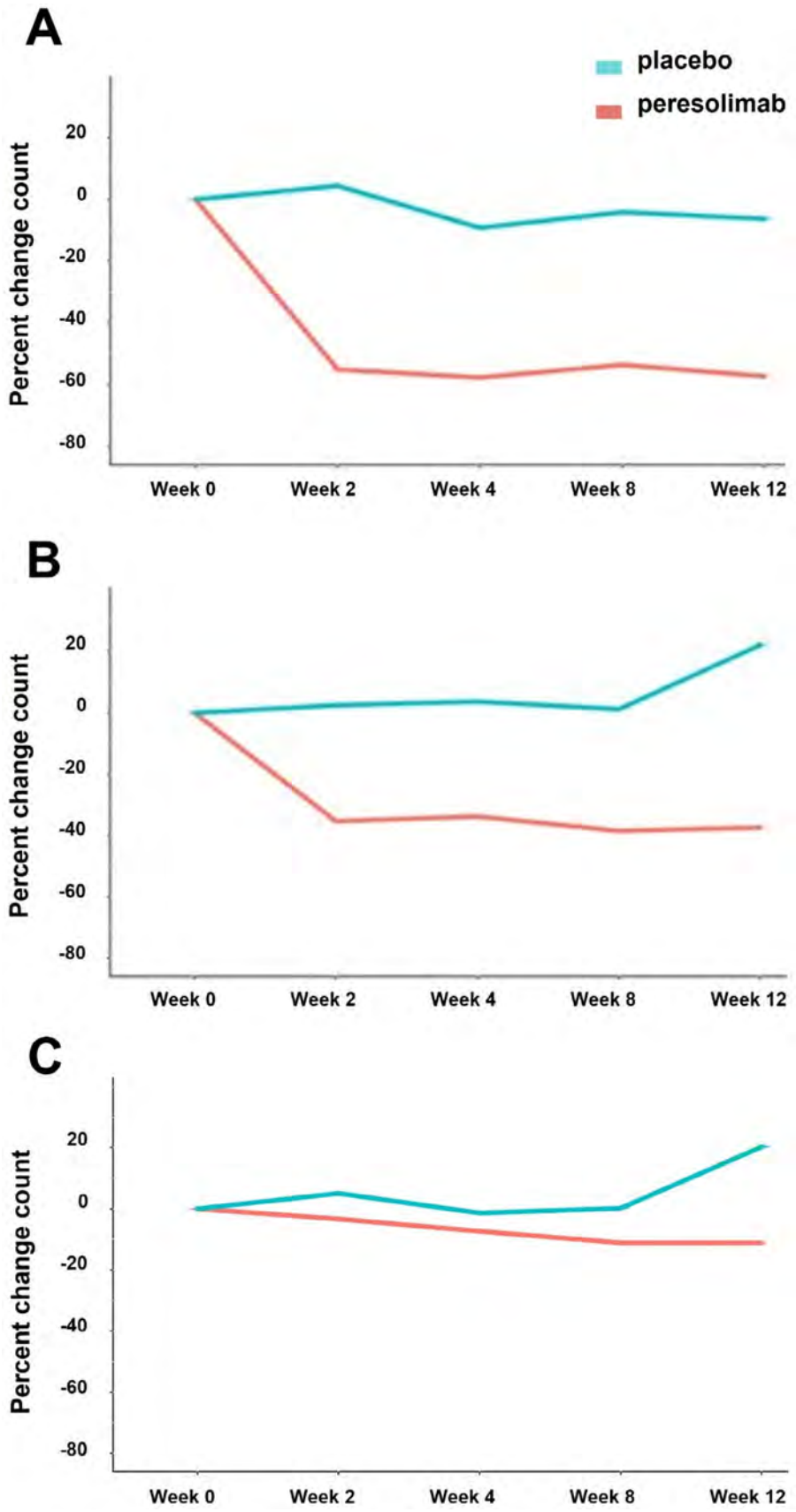

Figure 1. Peresolimab reduced peripheral CD4+ A) PD-1 high, B) PD-1 intermediate, and C) PD-1 low CD4+ T cells through 12 weeks of treatment in samples from patients with RA.

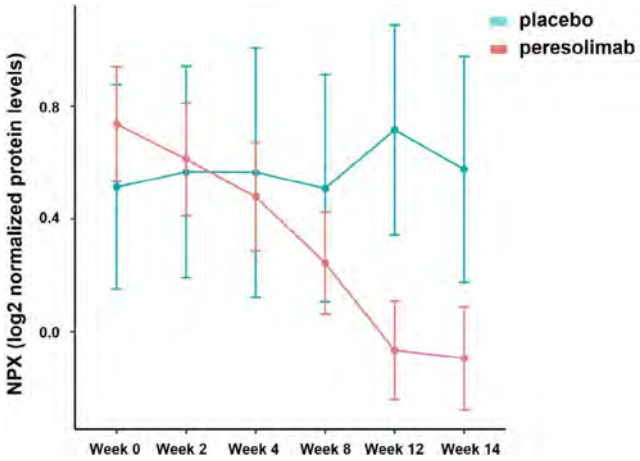

Figure 2. Peresolimab treatment decreases IL-6 protein levels (mean ± SEM) in serum samples from patients with moderate to severe RA through 14 weeks of treatment.

IL-6, Figure 2. Similar patterns of change were observed for several other immune-related pathways. Overall, pathway analysis suggests that protein levels of peresolimab-treated patients trend toward what was observed in age- and sex-matched healthy controls.

Conclusion: We report here changes in several exploratory biomarkers from patients enrolled in the Phase 2a study of peresolimab in RA patients. A rapid reduction was observed in circulating PD-1 high CD4+ T cells lasting through week 12, but no changes in any of the major lymphocyte subsets were detected with peresolimab treatment. Several molecular pathways that are altered in RA patients, trended towards patterns in healthy subjects with peresolimab treatment as early as week 8, which corresponds to the timing of DAS28-CRP improvements. These results provide insights into the timing and impact of PD-1 inhibition with peresolimab in the treatment of patients with moderate to severe RA.

1. N Engl J Med 2023; 388:1853-1862

Disclosure: R. J. Benschop: Eli Lilly and Company, 3, 11; **J. Tuttle**: Eli Lilly and Company, 3, 11; **P. Emery**: Boehringer Ingelheim, 2, Eli Lilly, 2, Novartis, 2; **C. Preuss**: Eli Lilly and Company, 3, 11; **M. Daniels**: Eli Lilly and Company, 3, 11; **V. Chan**: Eli Lilly and Company, 3, 11; **P. Yachi**: Eli Lilly and Company, 3, 11; **A. Nirula**: Eli Lilly and Company, 3, 11.

Abstract Number: 2177

Characterization of Crevicular Fluid Microbiota in Primary Sjögren's Syndrome

Gabriela Hernandez-Molina[1], Alberto Lopez-Reyes[2], Carlos Hernandez-Hernandez[3], Vanessa Ruiz[3], Amaya Llorente-Chavez[4], Vanessa Saavedra-González[4], Luis llorente[4] and Gabriela Martínez-Nava[2], [1]Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, [2]Laboratorio de Gerociencias, Instituto Nacional de Rehabilitación Luis Guillermo Ibarra Ibarra, Mexico City, Mexico, [3]Servicio Dental. Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, [4]Departamento de Inmunología y Reumatología, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: To describe the taxonomic composition of the microbiota in the crevicular fluid of patients with primary Sjögren's syndrome (PSS), and to assess their association with parotid gland enlargement, periodontal disease, oral quality of life, and anti-Ro/SSA and anti-La/SSB antibodies.

Methods: We included 48 PSS patients according to the ACR/EULAR criteria. We excluded patients with concomitant connective tissue disease, diabetes mellitus, active neoplasia, antibiotic use in the two weeks before the study, or with current active infection. A single rheumatologist registered the following variables: demographics, disease duration, oral/ocular sicca symptoms, parotid enlargement and serology. We evaluated the non-stimulated whole salivary flow (NSWSF). Patients rated the ESSPRI and the Xerostomia-related Quality of Life Scale (XeQoLS). Two experienced periodontists systematically examined six sites per tooth of each patient, to determine the presence of periodontal disease. Crevicular fluid was collected from 6 teeth with the greatest periodontal pocket depth using filter paper (sterile paper points). Samples were immediately frozen at -86 °C until processing. We also included 17 control subjects from the same hospital's Dentistry department matched by

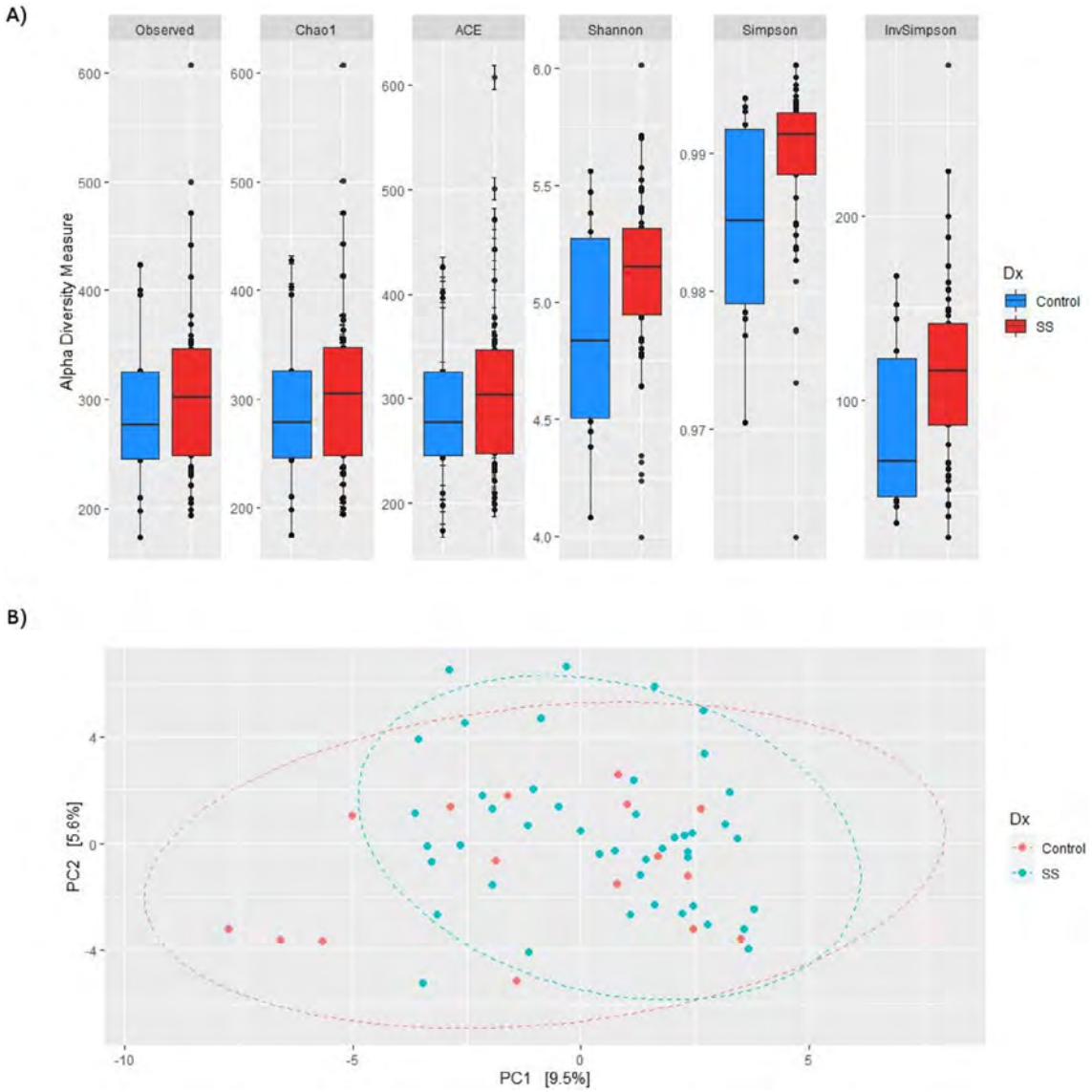

Figure 1 . Alfa diversity indexes stratified by the presence of (A) anti-Ro/SSA, (B) anti-La/SSB, and (C) parotid enlargement; and beta diversity compared between the presence of (D) anti-Ro/SSA , (E) anti-La/SSB, and (F) parotid enlargement.

gender and age (±5 years). Bacterial DNA was extracted from the crevicular fluid sample using a commercial kit. 16SrRNA V3-V4 region was sequenced using reversible adaptor technology. Sequences were pre-processed and analyzed with QIIME2 and phyloseq software programs. Functionality profiles were predicted using the Tax4Fun2 package.

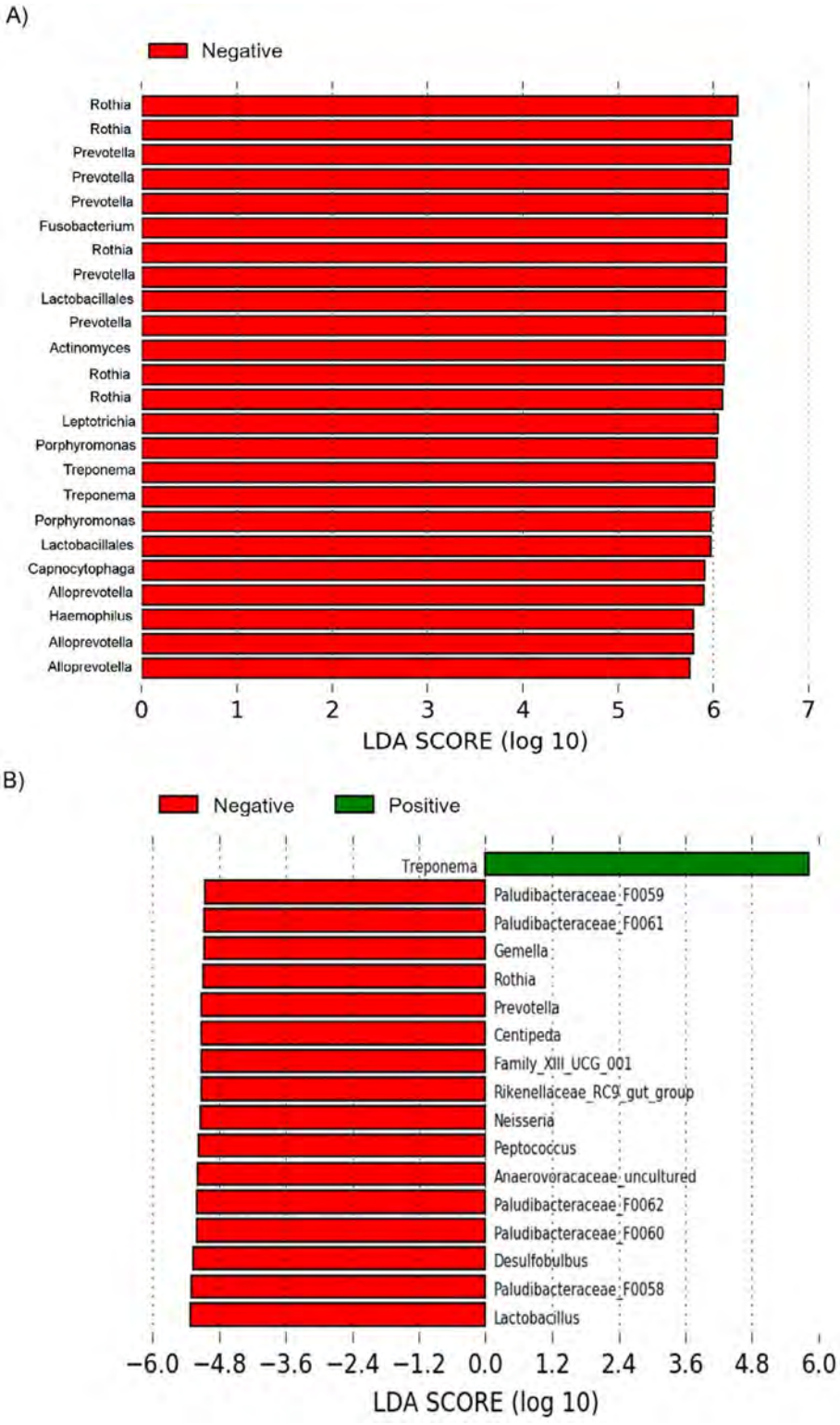

Figure 2 ASVs that best describe the crevicular fluid microbiota of SS patients and healthy controls (A) SS patients negative to anti-Ro/SSA or anti-La/SSB and (B) SS patients with and without parotid enlargement

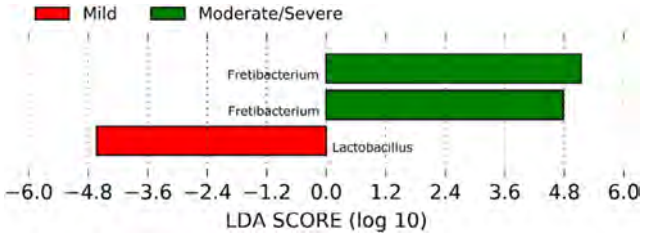

Figure 3 Bacteria genus ASVs whose relative abundance best describe the crevicular fluid microbiota of SS patients with mild and moderate or severe periodontal disease.

Results: Most patients were women, the mean age was 52.4 years and the median disease duration was 9.3 years. We found that the microbiota of PSS patients contained more bacteria of the genera *Prevotella, Streptococcus, Veillonella, Fusobacterium*, and *Leptotrichia* genera and fewer bacteria of the genus *Selenomonas* than that of healthy subjects. We also found significant differences in microbiota taxonomy between patients with anti-Ro or anti-La positive antibodies, parotid gland enlargement (Figure 1) , and periodontal disease severity (Figure 2) . We found no correlation between microbiota and NSWSF, and oral quality of life. The predicted functional profile showed that the microbiota of PSS patients contained more genes encoding for accessory secretory proteins than healthy controls.

Conclusion: The composition of the crevicular fluid microbiota of PSS patients and healthy subjects differed significantly. Differences were found among patients with parotid gland enlargement as well as anti-Ro and anti-La antibody positivity, suggesting that autoimmunity per se may play an important role in the composition of the oral microbiota in PSS.

Disclosure: G. Hernandez-Molina: None; **A. Lopez-Reyes**: None; **C. Hernandez-Hernandez**: None; **V. Ruiz**: None; **A. Llorente-Chavez**: None; **V. Saavedra-González**: None; **L. Ilorente**: None; **G. Martínez-Nava**: None.

Abstract Number: 2178

Increased Risk of Dementia in Patients with Primary Sjogren's Syndrome: A Nationwide Population-based Cohort Study

Kyung-Ann Lee[1], **Hyeji Jeon**[1], Hyun-Sook Kim[1] and Gi Hyeon Seo[2], [1]Soonchunhyang University Seoul Hospital, Seoul, South Korea, [2]Health Insurance Review and Assessment Service, Wonju, South Korea

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmunity and systemic inflammation may play a role in early-stage dementia. Few studies have investigated whether primary Sjogren's syndrome (pSS) increases the risk of dementia. As hydroxychloroquine (HCQ) has recently been shown to inactivate STAT3 in microglia, neurons, and astrocytes, we also evaluated the association of HCQ use with the development of dementia in patients with pSS.

Methods: This cohort study used data from the Health Insurance Review and Assessment Service, a representative national healthcare database in Korea. From the database, we established a cohort of patients with pSS without a history of dementia between January 2008 and December 2020. The control group consisted of sex- and age-matched individuals with neither a history of autoimmune disease nor dementia. We assessed the incidence of newly diagnosed dementia in patients

Table 2. Risk of Newly Diagnosed dementia in the pSS Group Compared with the Control Group

Variable	pSS	Control	P-value
Total no. of subjects	20,160	100,800	
Newly diagnosed dementia	980 (4.9%)	4243 (4.2%)	<0.001
Incidence rate, /100 person-yr	0.68 (0.64-0.72)	0.58(0.56-0.60)	
Crude HR	1.17 (1.09-1.25)	reference	<0.001
adjust HR(age group, sex, comorbidity)	1.20 (1.10-1.31)	reference	<0.001
adjust HR(age group, sex, comorbidity)		reference	
Use of HCQ	1.12 (1.00-1.24)		0.043
Non-use of HCQ	1.24 (1.13-1.36)		<0.001
adjust HR(age group, sex, comorbidity)			
Use of HCQ	0.38 (0.73-0.95)		
Non-use of HCQ	Reference		

pSS: primary Sjogren's syndrome, HR, hazard ratio, HCQ: hydroxychloroquine

with pSS and the matched cohort. A Cox proportional hazard analysis was performed to identify the association of pSS with the development of dementia.

Results: We identified 20,160 patients with pSS and 10,800 matched controls. The incidence of dementia was 0.68 (95% confidence interval [CI], 0.64-0.72) cases per 100 person-years in pSS, and it was 0.58 (95% CI: 0.56-0.60) in matched controls. In multivariate analysis adjusted for age, sex, and comorbidities, the adjusted hazard ratio (aHR) of developing dementia was 1.20 (95% CI 1.10–1.31) times greater in the pSS group than in the matched controls. When stratified by the use of HCQ, HCQ users had 1.12 (95% CI 1.00-1.24) times the risk, and HCQ non-users had 1.24 (1.13-1.36) times the risk of developing dementia compared to the matched controls. Indeed, multivariate analysis showed that the use of HCQ lowered the development of dementia in patients with pSS (aHR 0.83, 95% CI 0.73-0.95).

Conclusion: pSS is independently associated with the development of dementia. HCQ may have a preventive role in dementia for patients with pSS.

Disclosure: K. Lee: None; **H. Jeon**: None; **H. Kim**: None; **G. Seo**: None.

Abstract Number: 2179

Disease Burden of Patients with Primary Sjögren's Disease: Results from a Multinational Real-World Survey

Sara McCoy[1], Alan Baer[2], **Ann Xi**[3], Corey Moorhead[4], Giorgio Castellano[4], Anthony Amatucci[5], Ilias Alevizos[6] and Haridarshan Patel[7], [1]University of Wisconsin School of Medicine and Public Health, Middleton, WI, [2]Johns Hopkins University School of Medicine, Baltimore, MD, [3]Horizon Therapeutics, Indianapolis, IN, [4]Adelphi Real World, Bollington, United Kingdom, [5]Horizon Therapeutics, Cambridge, MA, [6]Horizon Therapeutics, Rockville, MD, [7]Horizon Therapeutics, Deerfield, IL

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren's disease (SjD) is a debilitating disease that has been shown to impact patients' quality of life (QoL). Though oral and ocular dryness are well-recognized causes of reduced QoL, there is limited evidence on impact of dental decay and vaginal dryness on QoL. Our study aims to describe the disease burden of patients with SjD, as measured by clinical testing and patient-reported outcome (PRO) measures in real-world clinical settings.

Table 1. Physician-reported symptoms in patients with Sjögren's disease at the time of data collection.

	Patients with Sjögren's disease and completed patient record forms from rheumatologists N=1879
Symptoms reported in >20% patients, n (%)	
Dry eyes	1711 (91.1)
Physical fatigue	1452 (77.3)
Xerostomia	1326 (70.6)
Diffuse pain	716 (38.1)
Mental fatigue	667 (35.5)
Muscle pain	662 (35.2)
Limb pain	621 (33.0)
Disturbed sleep	592 (31.5)
Vaginal dryness	503 (30.0) [N=1677 female patients]
Blurred vision or light sensitivity	558 (29.7)
Xeroderma	533 (28.4)
Glandular swelling	497 (26.5)
Anxiety	435 (23.2)
Dental decay	405 (21.6)

Table 2. Patient reported outcome (PRO) scores for all patients with Sjögren's disease (SjD), SjD patients with dental decay and SjD patients with vaginal dryness. Note that base size fluctuates due to data completeness for all variables. The EQ-5D-3L Utility score is measured on a scale of 0-1 where 1 indicates full health and 0 death. The EQ-VAS is measured on a 0-100 scale with 100 indicating full health. The FACIT-Fatigue is measured on a scale of 0-52 where lower scores indicate more severe fatigue. EQ-5D-3L Utility and EQ-VAS population norms are taken from Janssen, MF et al., 2019 (https://doi.org/10.1007/s10198-018-0955-5), and the FACIT-Fatigue population norm from Montan et al., 2018 (https://doi.org/10.1016/j.jval.2018.03.013). WPAI is measured using a series of questions asked to patients about how their disease affects their work and normal activities. Absenteeism refers to work time missed due to disease. Presenteeism refers to impairment whilst working due to disease. FACIT: Functional assessment of chronic illness therapy; SD: standard deviation; US: United States; VAS: visual analogue scale

	All patients with Sjögren's disease and complete form	Patients with dental decay	Patients with vaginal dryness	Patients with vaginal dryness			Population normative values
				Mild	Moderate	Severe	
EQ-5D-3L Utility Score *(US Tariff)*	**N=878**	**N=176**	**N=222**	**N=109**	**N=106**	**N=7**	
Mean [SD]	0.740 [0.24]	0.680 [0.25]	0.672 [0.27]	0.705 [0.27]	0.648 [0.27]	0.517 [0.24]	0.867
EQ-VAS score	**N=874**	**N=174**	**N=223**	**N=108**	**N=108**	**N=7**	
Mean [SD]	63.5 [19.02]	58.7 [19.01]	58.8 [18.51]	59.8 [19.03]	58.0 [18.30]	56.7 [14.45]	79.3
FACIT-Fatigue Score	**N=880**	**N=176**	**N=223**	**N=109**	**N=107**	**N=7**	
Mean [SD]	31.3 [10.91]	28.6 [10.43]	28.9 [9.54]	29.7 [9.52]	28.0 [9.56]	31.7 [9.29]	43.5
Work productivity and activity impairment (WPAI)							
% Overall work impairment, Mean [SD]	**(N=375)** 31.4 [21.93]	**(N=66)** 40.1 [23.31]	**(N=97)** 37.2 [21.95]	**(N=48)** 37.0 [22.78]	**(N=46)** 35.5 [20.49]	**(N=3)** 66.5 [10.88]	-
% Absenteeism, Mean [SD]	**(N=383)** 5.0 [15.55]	**(N=68)** 7.3 [19.38]	**(N=100)** 6.9 [17.50]	**(N=50)** 6.6 [18.10]	**(N=47)** 5.9 [16.20]	**(N=3)** 28.4 [19.28]	-
% Presenteeism, Mean [SD]	**(N=464)** 29.8 [21.07]	**(N=77)** 35.8 [21.42]	**(N=121)** 35.3 [19.58]	**(N=58)** 34.8 [19.85]	**(N=60)** 34.8 [19.53]	**(N=3)** 53.3 [5.77]	-
% Activity impairment due to Sjögren's disease, Mean [SD]	**(N=841)** 37.8 [21.65]	**(N=170)** 44.9 [21.24]	**(N=209)** 42.7 [19.25]	**(N=101)** 40.2 [18.92]	**(N=101)** 44.3 [19.56]	**(N=7)** 55.7 [12.72]	-

Methods: Data were drawn from the 2018 Adelphi Primary Sjögren's Disease Specific Programme™, a cross-sectional survey with retrospective data collection of rheumatologists and their consulting patients with SjD in France, Germany, Italy, Spain and the United States. Rheumatologists completed patient record forms for their next 6 primary SjD patients with systemic disease activity and reported on patient demographics, clinical characteristics, and patient assessments. Patients were invited to complete a form capturing PROs, including EQ-5D-3L, the Work Productivity and Activity Impairment Questionnaire (WPAI), and Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F). QoL, work productivity, and fatigue were evaluated and all data were analyzed descriptively.

Results: 316 rheumatologists provided data for 1,879 patients: mean [SD] age 53 [12] years, 89% female, 89% White. Patients had a mean [SD] of 13 [7] tests leading up to diagnosis and 7 [12] consultations in the past 12 months. Patients are most commonly co-managed by PCP/GPs (48%) and ophthalmologists (47%), with other health care professional types co-managing < 20% of patients. Rheumatologists recorded dry eyes, physical fatigue, and dry mouth as the most common symptoms in 91%, 77%, and 71% of patients respectively. Of note, 22% of patients reported dental decay and nearly 1 in 3 female patients experienced vaginal dryness (**Table 1**). EQ-5D-3L utility, EQ-5D-3L VAS, and FACIT-F scores were 0.741, 63.5 and 31.3 across all SjD patients respectively, compared to the population norms of 0.867, 79.3 and 43.5. Patients with SjD experiencing dental decay or vaginal dryness reported lower PRO scores than the overall SjD population (**Table 2**).

Conclusion: Analyses from this multinational survey revealed that patients with SjD are burdened with multiple diagnostic tests and physician consultations to manage their symptoms following diagnosis. There is a substantial impact of SjD on patients' general QoL, fatigue, and work productivity, which is worsened in patients with dental decay or vaginal dryness, which highlights the systemic nature of dryness and downstream consequences of oral dryness. These findings suggest an unmet need among patients with SjD, who may require additional management by dentists or sexual health professionals who currently have limited involvement in patient care.

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Abstract Number: 2180

Salivary and Plasma Mitochondrial Double-strand RNAs as a Diagnostic Biomarker for Sjögren Syndrome

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Since mitochondrial double-stranded RNAs (mt-dsRNAs), an endogenous activator of interferon signaling, are elevated in primary Sjögren's syndrome (pSS), we evaluated their association with the expression levels of interferon-inducible genes (IFIGs) and their diagnostic performance.

Table 1. Results of multivariate logistic regressions. UWS = unstimulated whole saliva; OR = odds ratio; CI = confidence interval; PBMC = peripheral blood mononuclear cell

Samples	Transcripts	coefficient β	OR [95% CI]	*p* value
UWS	ND1	2.159	8.665 [3.639-20.633]	1.07×10^{-6}
	ND6	−1.867	0.155 [0.052-0.459]	0.001
Plasma	ND1	−1.090	0.336 [0.189-0.599]	2.19×10^{-4}
	ND4	0.714	2.093 [1.507-2.906]	1.05×10^{-5}
PBMC	IFIT1	0.796	2.216 [1.172-4.192]	0.014
	IFIT3	0.828	2.289 [1.156-4.534]	0.018
	IFT44L	0.755	2.128 [1.014-4.464]	0.046
	OAS1	−1.250	0.286 [0.132-0.623]	0.002

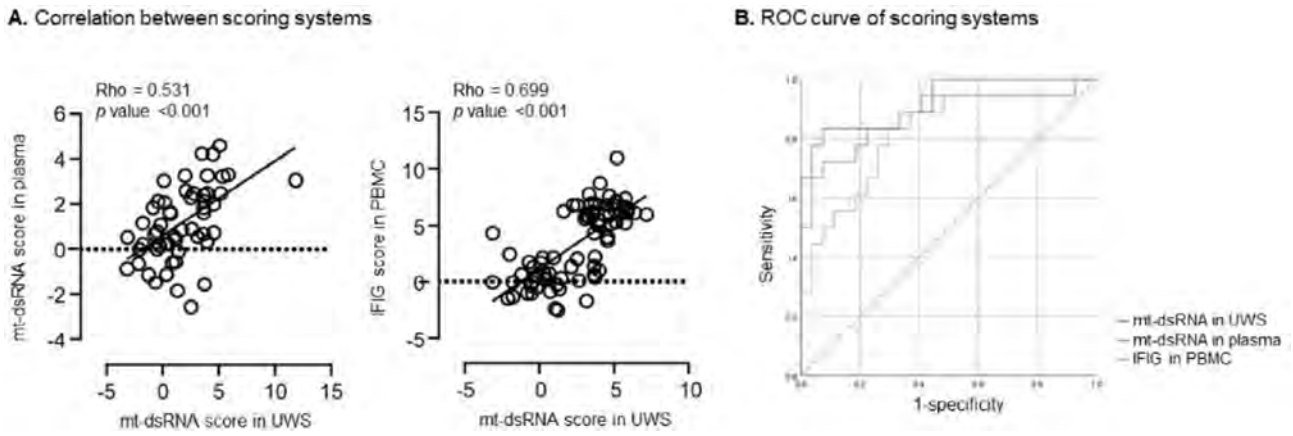

Figure 1. Correlation between mt-dsRNA scores and IFIG scores (A) and ROC curves of mt-dsRNA and IFIG scores for in primary Sjögren's syndrome. IFIG = interferon inducible genes; mt-dsRNA = mitochondrial double strand RNA; PBMC = peripheral blood mononuclear cell; SS = Sjögren's syndrome; UWS = unstimulated whole saliva

Methods: One hundred four pSS patients satisfying the 2016 ACR/EULAR criteria, 14 non-SS sicca patients, and 25 healthy controls were included. Seven mt-dsRNAs levels (CYTB, ND1, CO1, ND4, CO2, ND5, and ND6) in unstimulated whole saliva (UWS) and plasma samples and 8 IFIGs (IFIT1, IFIT3, IFI44, IFI44L, LY6E, OAS1, MX1, and ISG15) levels in peripheral blood mononuclear cells (PBMCs) were measured using RT-PCR. Z-score-based standardized mt-dsRNAs and IFIGs scoring systems were constructed using multivariate logistic regressions. The area under the ROC curve (AUC), sensitivity and specificity, andYouden's index were calculated.

Results: mt-dsRNAs ND1 and ND6 in UWS and ND1 and ND4 in plasma and IFIT1, IFIT3, IFI44L, and OAS1 in PMBCs remained to be significantly associated with pSS. The mt-dsRNA score was defined as (2.16′ND1)–(1.87′ND6) in UWS and (–1.09′ND1)+(0.74′ND6) in plasma. The IFIG score in PBMC was calculated using (0.80′IFIT1)+(0.83′IFIT3)+(0.76′IFI44L) –(1.25′OAS1). Despite that they were derived from different samples, all three scores were significantly correlated mutually. The AUC of UWS (0.924) and plasma (0.874) mt-dsRNA scores were larger than that of PMBC IFIG score (0.817). With the optimal cut-off of 1.71, the sensitivity and specificity of UWS mt-dsRNA score were 97.4% and 89.7%, respectively.

Table 2. Diagnostic performance of mt-dsRNA and IFIG scores in Sjögren's syndrome AUC = area under the curve; CI = confidence interval; IFIG = interferon inducible genes; mt-dsRNA = mitochondrial double strand RNA; PBMC = peripheral blood mononuclear cell; SS = Sjögren's syndrome; UWS = unstimulated whole saliva

	AUC [95% CI]	At the optimal cut-offs for each score		
		Sensitivity	Specificity	Youdens index
mt-dsRNA in UWS	0.924 [0.844-1.000]	97.4	89.7	0.810
mt-dsRNA in plasma	0.874 [0.758-0.991]	87.5	66.7	0.542
IFIG in PBMC	0.817 [0.686-0.948]	76.8	89.2	0.660

Conclusion: Increased transcript levels of some mt-dsRNA in UWS and plasma were significantly associated with pSS. A novel mt-dsRNA scoring system could be a potential diagnostic marker for pSS diagnosis.

Disclosure: S. CHOI: None; **J. Lee**: None; **Y. Choi**: None; **Y. Ha**: None; **E. Kang**: None; **Y. Lee**: None.

Abstract Number: 2181

Secretagogue Effect of PDE4 Inhibitor Apremilast on Human Salivary Gland Organoids Obtained from Primary Sjögren's Syndrome Patients

Valeria Manfrè[1], Salvatore Parisi[2], Isabella Caligiuri[2], Ombretta Repetto[3], Alen Zabotti[1], Enrico Pegolo[4], Cinzia Fabro[1], Salvatore De Vita[1], Vincenzo Canzonieri[2], Carla Di Loreto[4], Flavio Rizzolio[2] and Luca Quartuccio[1], [1]Division of Rheumatology, Department of Medicine, University of Udine, Udine, Italy, [2]Pathology Unit, Centro di Riferimento Oncologico di Aviano (CRO) IRCCS, Aviano, Italy, [3]Facility of Bio-Proteomics, Immunopathology and Cancer Biomarkers, Centro di Riferimento Oncologico di Aviano (CRO) IRCCS, Aviano, Italy, [4]Institute of Pathology, Azienda Sanitaria Universitaria Friuli Centrale c/o Università degli studi di Udine, Udine, Italy

SESSION INFORMATION

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Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: In primary Sjögren's syndrome (pSS), salivary epithelial cells show an active role in the initiation and reiteration of the immunomediated damage. Epithelial saliva production is regulated by autonomic stimuli, intracellular calcium and cAMP concentration. The latter controls the action of cystic fibrosis transmembrane conductance regulator (CFTR), whose malfunction is postulated in sicca syndrome and pSS pathogenesis. (1) Forskolin is an activator of CFTR used in organoid swelling test in human salivary-gland derived organoid culture systems. Interestingly, also PDE4 is involved in intracellular cAMP deregulation: PDE4 inhibition might thus stimulate salivary function in pSS. (2-3) To the best of our knowledge, no data on the application of human salivary gland organoids specifically for testing drugs effective on xerostomia in pSS are found in literature. The objectives of this study are: to culture vital salivary gland organoids obtained through labial or parotid biopsy of pSS patients; to evaluate the morphological structure and functional capacity of organoids in basal condition and after stimulation with forskolin and PDE4 inhibitor apremilast.

Methods: Salivary gland tissues were harvested from 5 pSS patients through labial or parotid biopsy. After tissue processation and vital organoids obtainment, swelling essay and cell proliferation tests were performed after forskolin and apremilast application, compared to DMSO-treated controls. Immunohistochemistry evaluation on original salivary gland tissue and corresponding organoids was performed, by testing: alpha-amylase and AQP5 for acinar differentiation; EMA for ductal differentiation; calponin for myoepithelial differentiation and CK5 for basal differentiation; CK14, cKit and CD34 as markers of progenitor/stem cells.

Results: After application of forskolin or apremilast, we observed organoid swelling after 30 minutes, compatible with positive functional status and enhancement of saliva production. DMSO-treated controls were instead unaffected. In 3 cases apremilast induced proliferation of the organoids (Fig.1). All the cases were positive for CK14, most of the cases for CK5. All the cases were positive for amylase; its secretion, and thus functional status of organoids, was confirmed by its high concentration in the culture medium. A focal ductal differentiation was found in some cases, highlighted by EMA positivity. The more differentiated EMA positive areas were negative for the staminal marker CK14, showing a sort of "complementary staining" (Fig.2).

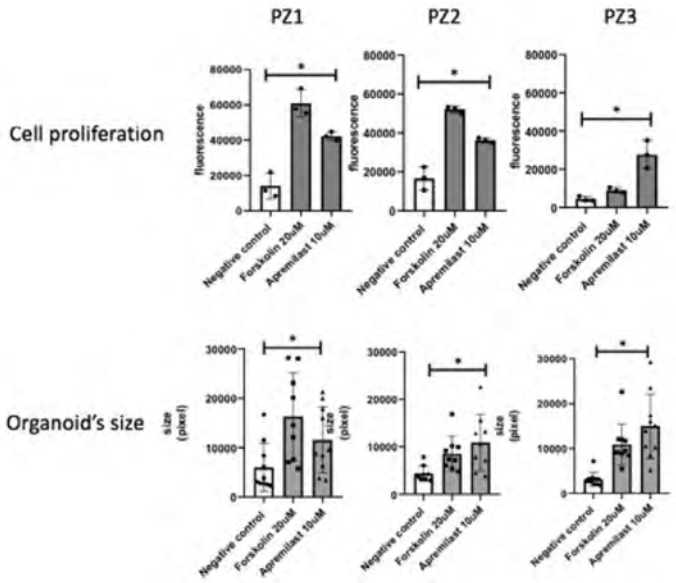

Figure 1. *The swelling of salivary organoids was induced by the activation of cystic fibrosis transmembrane conductance regulator (CFTR) using forskolin and Apremilast. It was observed organoid swelling after 30 minutes, whereas DMSO-treated control organoids were unaffected. Of note, Apremilast increased organoid growth rate compared to control group.*

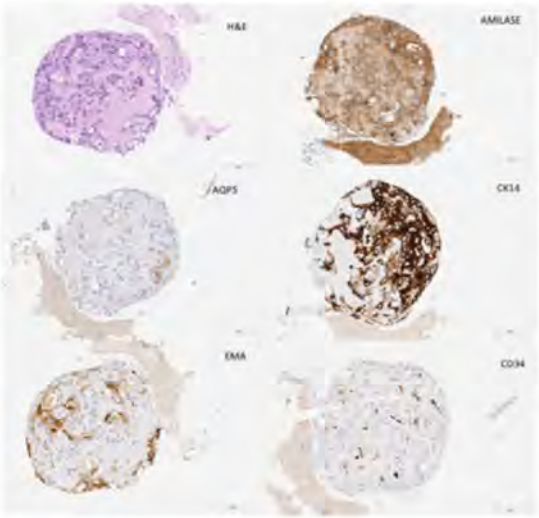

Figure 2. *Hematoxylin and eosin-stained section of a representative organoid (Hematoxylin and eosin stain, original magnification 20X) and pictures showing immunohistochemical expression of some markers on the same cells; in particular amylase, aquaporin5, CK14, EMA and CD34. Note that the EMA positive cells are negative for CK14 and vice versa, showing a sort of complementary positivity, related to a different level of differentiation.*

Conclusion: Our data confirm that, from pSS epithelium, differentiated cells that escape senescence and vital and functional organoids that recapitulate the development of original salivary glands can be obtained from different target tissues of pSS. The direct stimulating effect of PDE4 inhibitor apremilast on pSS human salivary gland organoids is reported, opening new perspectives on targeting oral dryness with drugs that combine secretagogue and immunomodulatory effects.

References:

(1) Zeng M et al. Gastroenterology, 2017
(2) Boyd A et al. Biochem J, 2021
(3) Yoshimoto S et al. Dis Model Mech, 2020

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Abstract Number: 2182

Mitochondrial Alterations in Primary Sjögren´s Syndrome

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Primary Sjögren's Syndrome (pSS) is a systemic autoimmune disorder characterized by lymphocytic infiltrations in exocrine glands. T-cells are considered major players in the pathogenesis of pSS. Previously, we reported naïve CD4+ T-cells exhibited signs of immune cell aging including shortened telomeres, increased senescence-associated -β-galactosidase activity, a reduction in IL-7R expression and reduced level of T-cell receptor excision circles. Homeostatic proliferation of naïve CD4+ T-cells was impared both ex vivo and after stimulation in vitro. Senescencence and impaired homeostasis of pSS naïve CD4+ T-cells lead to peripheral lymphopenia, a frequent finding in pSS patients. As mitochondrial fitness has been linked to cellular aging and AI conditions, we assessed mitochondrial parameters in T cells of pSS patients.

Methods: Peripheral blood mononuclear cells (PBMC) were isolated from venous blood of pSS patients fulfilling 2016 ACR/EULAR classification criteria and sex- and age-matched healthy control subjects (HC). Flow cytometric analysis was performed to identify and further characterise CD4+ T-cell subsets (Naïve, Central memory, Effector memory and Terminally differentiated effector memory) at single-cell level: staining with mitochondrion-selective fluorescent dyes MitoTracker® Green (MTG), MitoTracker® Deep Red (MTDR), MitoSox Red was performed to assess mitochondrial mass, membrane potential (MtMP) and superoxide production, respectively. Mitochondrial fitness was assessed by combined staining method with MTG and MTDR.Uptake of glucose analogue 2-NBDG was used to monitor glucose uptake ability of the CD4+ T-cell subsets.

Results: Staining with MTG and MTDR showed decreased mitochondrial mass and mitochondrial membrane potential in all CD4+ T-cell subsets of pSS patients. Despite having reduced mitochondrial mass and MtMP, we observed that pSS T-cells produced higher amount of mitochondrial superoxides compared to HC. Percentage of dysfunctional mitochondria (MTG

high, MTDR low) was significantly increased in pSS, probably due to accumulation of mitochondrial superoxides. On the other hand, glucose uptake was increased in all pSS CD4+ T-cells, which can indicate enhanced glycolysis.

Conclusion: We found that T-cells premature aging in pSS patients is linked with mitochondrial dysfunction associated with accumulation of mitochondrial superoxides and enhanced glucose uptake ex vivo. The underlying mechanisms of mitochondrial dysfunction of T-cells in primary Sjögren's Syndrome should be investigated in further studies.

Disclosure: P. Javorova: None; **J. Fessler**: None; **M. Zeiler**: None; **A. Lackner**: None; **J. Hermann**: None; **S. Zenz**: None; **J. Thiel**: None; **M. Stradner**: None.

Abstract Number: 2183

Evolution of Lymphoma Predictors in Primary Sjogren's Syndrome by Data Driven Analysis in Harmonized Patients

Andreas Goules[1], Loukas Chatzis[2], Vasileios pezoulas[3], Francesco Ferro[4], Valeria Manfrè[5], Dimitrios Fotiadis[3], Luca Quartuccio Quartuccio[6], Chiara Baldini[7], Salvatore De Vita[5] and Athanasios Tzioufas[1], [1]Dept. of Pathophysiology, School of Medicine, University of Athens, Athens, Greece, [2]Dept. of Pathophysiology, School of Medicine, University of Athens, Cholargos Athens, Greece, [3]Unit of Medical Technology and Intelligent Information Systems, Dept. of Materials Science and Engineering, University of Ioannina, Ioannina, Greece, [4]Clinical and Experimental Medicine Department, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy, [5]Clinic of Rheumatology, Dept. of Medical and Biological Sciences, Udine University, Udine, Italy, [6]Rheumatology Division, Department of Medicine, University of Udine, Udine, Italy, [7]University of Pisa, Pisa, Italy

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Lymphoma is the most serious complication of primary Sjogren's syndrome (pSS), occurring as a late sequel during disease course. So far, lymphoma predictors have been identified only at the time of pSS diagnosis in single center cohorts using classical logistic regression models. The current work aims to study the evolution of lymphoma predictors towards lymphoproliferation by employing data driven analysis on totally harmonized pSS patients.

Methods: Two curated and harmonized datasets with pSS patients from3 centers (Athens, Piza, Udine) were constructed to be analyzed for lymphoma predictors at two different time points before lymphoma diagnosis. Each dataset incorporated the same set of 30 clinically useful features covering the major aspects of the disease (Table 1, 2). The first dataset included 80 lymphoma patients and non-lymphoma controls (1:1 ratio), representing the time point of pSS diagnosis and the second dataset 68 lymphoma and non-lymphoma controls (1:1 ratio) representing the time point of 3-4 years before lymphoma diagnosis. All included patients fulfilled the 2016 ACR/EULAR criteria and non-lymphoma controls were matched according to age, gender, disease duration from pSS diagnosis to last follow up and treatment modalities. Systemic manifestations were defined as described in the ESSDAI domains and for those not included in the ESSDAI system, either by tissue biopsy or by applying international consensus criteria. A Fast-Correlation based feature selection (FCBF)/logistic regression (LR) model with lymphoma as an outcome, was applied on both datasets as described previously (1).

Results: Regarding the time point of pSS diagnosis, 5 prominent features in terms of magnitude of order were identified by the FCBF algorithm as potential predictors including rheumatoid Factor (RF), cryoglobulinemia, ACA pattern, ESSDAI≥5 and lacrimal gland enlargement of which only RF was finally proven an independent lymphoma predictor (Table 1). For the

Table 1. FCBF-based multivariable logistic regression analysis for lymphoma predictors at pSS diagnosis*

Prominent feature*	Regression coefficient	Odds ratio	p-value	CI upper	CI low
Rheumatoid Factors**	**1.2**	**3.332**	**<0.001**	**5.644**	**1.967**
Cryoglobulinemia	1.112	3.071	0.193	16.374	0.581
ACA pattern	1.441	4.237	0.084	21.565	0.842
ESSDAI≥5	0.693	2.022	0.072	4.048	1.01
Lacrimal Gland enlargement	0.885	2.438	0.524	37.321	0.163

* Features/Variables analysed by the FCBC algorithm: Gender, age at pSS diagnosis, disease duration from SS to lymphoma diagnosis, disease duration from SS onset to SS diagnosis, dry mouth, dry eyes, salivary gland swelling, lacrimal gland enlargement, Raynaud's phenomenon, arthritis, arthralgias, palpable purpura, lymphadenopathy, renal disease-glomerulopathy, renal disease-tubulointerstitial nephritis, pulmonary disease-small airways disease, interstitial lung disease, liver disease-autoimmune hepatitis, primary biliary cirrhosis, peripheral nervous system disease, central nervous system disease, autoimmune thyroiditis, ANA, anti-La antibodies, anti-Ro antibodies, rheumatoid factors, cryoglobulinemia, low C4, ACA, ESSDAI≥5

** < 0.05 (95% confidence interval)

FCBF-based multivariable logistic regression analysis for lymphoma predictors at pSS diagnosis

Table 2. FCBF-based multivariable logistic regression analysis for lymphoma predictors at 3-4 years before lymphoma diagnosis*

Prominent feature*	Regression coefficient	Odds ratio	p-value	CI upper	CI low
ESSDAI≥5**	**1.342**	**3.871,**	**0.002**	**8.852,**	**1.694,**
Rheumatoid Factors**	**1.294**	**3.683,**	**<0.01**	**6.467,**	**2.097**
ACA pattern	1.382	3.995	0.107	21.246	0.763

* Features/Variables analysed by the FCBC algorithm: Gender, age at pSS diagnosis, disease duration from SS to lymphoma diagnosis, disease duration from SS onset to SS diagnosis, dry mouth, dry eyes, salivary gland swelling, lacrimal gland enlargement, Raynaud's phenomenon, arthritis, arthralgias, palpable purpura, lymphadenopathy, renal disease-glomerulopathy, renal disease-tubulointerstitial nephritis, pulmonary disease-small airways disease, interstitial lung disease, liver disease-autoimmune hepatitis, primary biliary cirrhosis, peripheral nervous system disease, central nervous system disease, autoimmune thyroiditis, ANA, anti-La antibodies, anti-Ro antibodies, rheumatoid factors, cryoglobulinemia, low C4, ACA, ESSDAI≥5

** < 0.05 (95% confidence interval)

FCBF-based multivariable logistic regression analysis for lymphoma predictors at 3-4 years before lymphoma diagnosis

second time point of 3-4 years before lymphoma diagnosis, a similar set of prominent features was found by the FCBF algorithm with the exception of lacrimal gland enlargement and cryoglobulinemia while RF and ESSDAI≥5 were identified as independent lymphoma risk factors (Table 2). Both FCBF/LR models had good overall performance after 10-fold cross validation strategy (pSS diagnosis: accuracy=63%, sensitivity=63%, specificity=63%, AUC=76% and for the second time point of 3-4 years before lymphoma diagnosis: accuracy=65%, sensitivity=65%, specificity=71%, AUC=75%).

Conclusion: Rheumatoid factor is the earliest and more persistent pSS associated lymphoma predictor while high ESSDAI≥5 in combination with RF connote an advanced stage across the lymphomagenesis process, predicting the occurrence of lymphoma in approximately 4 years before.

Disclosure: A. Goules: None; **L. Chatzis**: None; **V. pezoulas**: None; **F. Ferro**: None; **V. Manfrè**: None; **D. Fotiadis**: None; **L. Quartuccio**: None; **C. Baldini**: GlaxoSmithKlein(GSK), 6, Horizon, 6, Sanofi, 6; **S. De Vita**: None; **A. Tzioufas**: None.

Abstract Number: 2184

Development of Salivary Gland Organoids to Study Sjögren Syndrome

Loïc Meudec[1], Negaar Goudarzi[2], Juliette Pascaud[3], Fanny Jaulin[2], Xavier Mariette[4] and Gaetane Nocturne[5], [1]CHU Kremlin-Bicêtre, Rheumatology, Le Kremlin-Bicêtre, France, [2]INSERM UMR 981, Institut Gustave Roussy, Villejuif, France, Villejuif, France, [3]Center for Immunology of Viral Infections and Autoimmune Diseases, INSERM UMR 1184, FHU CARE, Université Paris-Saclay, Le Kremlin-Bicêtre, France, [4]Université Paris-Saclay, Le Kremlin-Bicêtre, France, [5]APHP, Le Kremlin-Bicêtre, France

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren disease (Sjo) is an autoimmune disease characterized by the infiltration of exocrine glands by immune cells, especially salivary glands (SG). SG epithelial cells (SGEC) are involved in Sjo pathogenesis, mostly through their crosstalk with immune cells. The primary 2D culture of SGEC derived from Sjo patients has been very useful to better understand Sjo pathogenesis but does not recapitulate the complexity of the SG and lacks epithelial readout, highlighting the necessity to develop new relevant models. Our objective was to develop and characterize differentiated organoids of SGEC derived from minor salivary gland (MSG) of Sjo patients and controls.

Methods: We included Sjo patients fulfilling the ACR/EULAR 2016 criteria and controls with sicca syndrome. MSG were firstly dissociated enzymatically, then encapsulated in Matrigel© and cultured in Growth Expansion Medium (GEM) containing growth factors, until organoids formation. Organoids were passaged every 7-11 days for self-renewal and cultured in a Differentiation Medium (DM) inhibiting the NOTCH pathway, to develop mature organoids. Proliferation was assessed by cell counting and SGEC markers were investigated by RT-qPCR and immunofluorescence.

Results: Ten patients were included: 8 controls and 2 Sjo patients. Organoids with an average size of 100-200 μm were forming and differentiating in both patients and controls (**Figure 1A**). The mean culture duration was 2.7 ± 1.7 months and was continued for up to 6 months. The self-renewal capacity of organoids in expansion condition was comparable between the two groups, as evidenced by comparable growth curves for the 2 groups (**Figure 1B**) and the high expression of the Ki67 marker in the periphery of organoids, arguing an active cell proliferation (**Figure 1C**). We then differentiated the organoids. Mature organoids highly expressed the ductal markers CK7/CK18 and, to a lesser degree, the acinar markers AQP5 and α-amylase, in both Sjo patients and controls (**Figure 1D**). We confirmed these results in RNA expression, showing an enhanced expression of acinar and ductal markers with DM compared to GEM (**Figure 1E**). Last, we have performed one preliminary experiment in which we have been able to develop immune-organoids by adding PBMC in the organoids (**-Figure 1F**). Work is still in progress to assess the impact of immune cell infiltrate on organoid characteristics.

Conclusion: We established a culture system of SG organoids from MSG in Sjo patients and controls with long term expansion and maturation markers expression. Additional investigations are ongoing to assess the functionality of the organoids and to develop immune-organoids for assessing the impact of adding immune cells in the system. **Bibliography**
1. Pringle S, et al. Arthritis Rheumatol. 71(1):133-42.

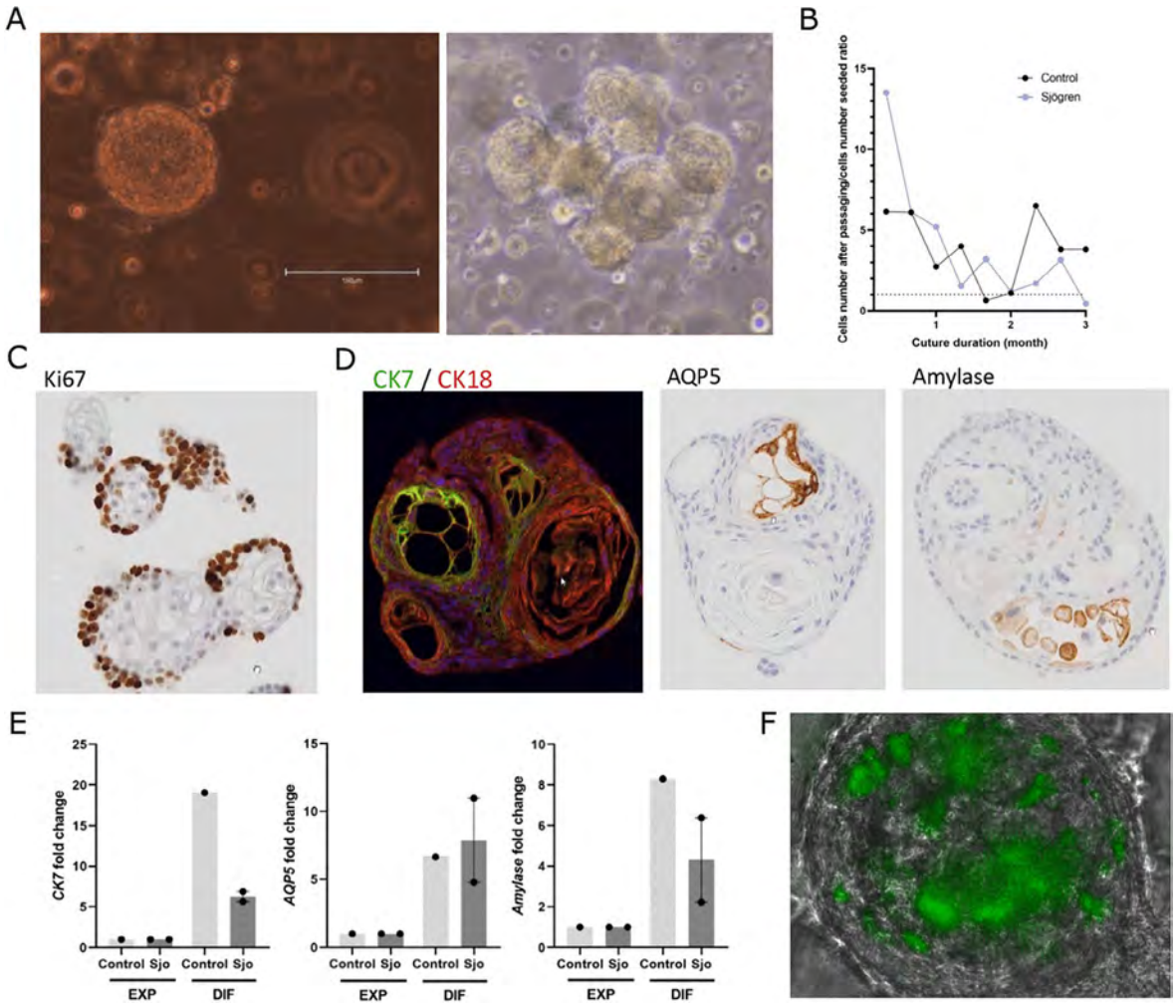

Figure 1: Characterization of SG organoids from Sjo patients and control (A) SG organoids in expansion and differentiation captured by photonic microscopy. (B) SGEC expansion by the ratio between cell count at seeding and at passaging. (C) Ki67 expression in organoids cultured in GEM. (D) CK7/CK18 (ductal), AQP5 and α-amylase (acinar) expression in organoids cultured in DM. (E) CK7, AQP5, and α-amylase RNA expression in SG organoids cultures in GEM and DM (n=3). (F) Infiltration of SG organoid by CFSE-labelled PBMC.

Disclosure: L. Meudec: None; **N. Goudarzi**: None; **J. Pascaud**: None; **F. Jaulin**: None; **X. Mariette**: AstraZeneca, 2, 6, BMS, 2, 6, Galapagos, 2, 6, GSK, 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **G. Nocturne**: None.

Abstract Number: 2185

35 Years Follow-up of Primary Sjögren's Disease: A Single Center Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Primary Sjögren's syndrome (pSS) is an autoimmune rheumatic disease characterized by lymphocytic infiltration of exocrine glands. Its clinical manifestations are heterogeneous. Currently, the evidence regarding the outcomes of the disease during a long term of follow-up is poor.

We studied a cohort of Sjogren's syndrome patients followed for up to over 35 years to analyze their outcomes during the course of the disease.

Methods: A cohort of 232 patients who were diagnosed with pSS and under care in a single center (University College London Hospital) between 1984 and December 2022 were retrospectively screened. The authors reviewed case notes, computer records, and primary healthcare databases on an audit basis. Demographic features and clinical features were assessed, as well as the outcome, death, and cause of death. Statistical analysis using frequencies, univariant analysis ($\chi 2$ and Fisher's tests), multivariant analysis, logistic regression, and bivariant analysis were performed.

Results: The mean age at diagnosis was 50.5 years (SD=14.78 years). The mean years of follow-up since diagnosis was 12.1 years (SD= 8.65); 48 patients (20.7%) were lost to follow-up at some point during the study period and 37 patients (20.1%) died during this period. Lymphoma developed in 20 patients. When compared with the rest of the patients, the incidence of glandular manifestations was significantly higher in the lymphoma group (11 [55%] vs 59 [37.8%]; p=0.005). In an independent multivariate regression analysis, parotid swelling at the time of diagnosis was found to be the most important predictive factor ($p< 0.001$). The majority of lymphomas developed < 15 years post-diagnosis. Death occurred in 37 patients (20%), with a mean age of 80.20 years old (SD=8.547). Infection was the commonest cause of death, followed by malignancy related.

Conclusion: In our very long-term follow-up of Sjogren's patients, the main complication associated with the disease was related to lymphoma development, which invariably occurred during the first years after diagnosis. In contrast, in our cohort among the patients who died, the majority were over 70 years old, confirming that the disease is clearly compatible with a long-life expectancy. Infection was the commonest cause of death.

Table 1: General characteristics of primary SS patients

Parameters	n (%); 232
Age at diagnosis (mean ± SD)	50.5 ± 14.78
Female/Male	220/12 (94.8)
Race	217/232
- Caucasian	143 (61.6)
- Asian	29 (12.5)
- Black	19 (8.2)
- Afro-Caribbean	6 (2.6)
- Mixed	4 (1.7)
- Other	16 (6.9)
Years of follow-up (mean ± SD)	12.1 ± 8.65
Clinical characteristics	
- Parotid swelling at diagnosis	59/205 (28.5)
- Lymphadenopathy at diagnosis	32/205 (15.6)
- Arthritis	63/231 (27.2)
- Raynaud's phenomenon	82/230 (34.7)
- Rash	71 (30.6)
- Ulcers	39/231 (16.8)
- Vasculitis	20/231 (8.6)
Outcome	
- Still on follow-up	147 (79,9)
- Deceased	37 (20.1)
- Lost to follow-up	48 (20.7)
Lymphoma development	20 (8.6)
- Hodgkin lymphoma	1
- Non-Hodgkin lymphoma	19
• MALT	12
• Others	7
Other tumors	30 (12.9)

Table 2 - Comparison of characteristics between dead and alive patients with primary SS diagnosis

	Primary SS with NHL	Primary SS without NHL	P value
Total, n, (%)	20	212	
Age at diagnosis (mean ± SD)	49.7 ± 13.58	50.62 ± 14.9	0.810
Female/Male	20/0	200/12	0.606
Caucasian vs non-Caucasian	12/8	131/66	0.392
Years of follow-up (mean ± SD)	10.88 ± 7.65	12.25 ± 8.73	0.543
Glandular involvement	11 (55)	59 (37.8)	**0.005**
Parotid swelling at diagnosis	10 (50)	49 (23.1)	**<0.001***
Lymphadenopathy at diagnosis	4 (20)	28 (13.2)	**0.013***
Raynaud's phenomenon	6 (30)	76 (35.8)	0.206*
Vasculitis	4 (20)	16 (7.5)	0.159*
Death	7 (35)	30 (14.2)	0.120*

Disclosure: L. Montano-Tapia: None; **R. Yildrim**: None; **A. Abrantes**: None; **D. Isenberg**: None.

Abstract Number: 2186

Neurological Complications in Sjögren's: Occurrence & Impact on Patient Quality of Life

Matt Makara, Janet Church and Katherine Hammitt, Sjögren's Foundation, Reston, VA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren's is a serious and systemic autoimmune disease that affects the entire body, including the nervous system. This study aimed to better understand the occurrence of neurological symptoms and comorbidities as well as their impact on quality of life (QoL) in Sjögren's patients.

Methods: An online survey was administered between October and November 2021 to U.S.-based Sjögren's patients aged ≥18 years. The survey was reviewed by the Western Clinical Group IRB and determined to be exempt under 45 CFR § 46.104(d)(2).

Results: Of the total respondents (n=3,622), 83% reported having been diagnosed with ≥1 nervous system-related condition. The most common diagnoses were anxiety/depression (50%), brain fog (47%), and neuropathy (45%). Notable differences in QoL were found between those reporting a comorbid neurological-related diagnosis and those who did not. Those with ≥1 neurological condition were more likely to experience a greater negative impact on their ability to exercise, participate in social activities, be independent, their overall mood, and when performing activities of daily living (OR Ranges: 1 neurological condition, 1.96-2.35; ≥5 conditions, 11.46-17.78). Additionally, respondents with neurological conditions were more likely to state that they did not feel they were living a fulfilling life (1, OR 1.67; ≥5, 6.88). An analysis of neurological symptoms found that more than half of the respondents reported experiencing the following during the prior 12 months: brain fog (80%), trouble sleeping (73%), anxiety (66%), forgetfulness (64%), neuropathy (64%), and headache (56%). When askedhowimpactful each of these symptoms was on their lives, the majority of respondents noted that they experienced a major-to-moderate impact(range: 58%-88%). When looking at neurological symptoms collectively,respondents, on average, stated they experienced nearly 6 neurological symptoms during the prior 12 months and 97.8% of respondents experienced ≥1. Furthermore, 92.0% of respondents stated they experienced ≥1 neurological symptom either daily or weekly and 89.5% of respondents noted experiencing ≥1 neurological symptom to a moderate or

severe degree during the past 12 months. When respondents were asked to identify a single symptom that has the greatest negative impact on their life, 5 of the top 10 symptoms were related to the nervous system. Respondents also expressed a critical need for new therapies to address a range of neurological-related issues, including sleep problems (77%), brain fog/forgetfulness (77%), and neuropathy (68%).

Conclusion: Neurologicalsymptoms and comorbid diagnoses frequently occur in Sjögren's patients and are associated with worsening QoL. Greater awareness and further study into these connections is needed to inform optimal approaches to recognition, diagnosis and care. Due to a lack of currently available or effective treatments, Sjögren's patients feel strongly that more and improved therapies are needed to address neurological disease manifestations.Because of its multifactorial nature, fatigue was not included in this analysis, though it remains one of the biggest issues for Sjögren's patients.

Disclosure: M. Makara: None; **J. Church**: Sjögren's Foundation, 3; **K. Hammitt**: Sjögren's Foundation, 3.

Abstract Number: 2187

Association Between Illness Perception, Anxiety and Depression State, Disease Activity and Glucocorticoid Therapy in Patients with Sjögren's Syndrome

Chiara Baldini[1], Elena Elefante[2], Inmaculada Conception Navarro Garcia[2], Francesco Ferro[3], Gaetano La Rocca[4], Giovanni Fulvio[1], Silvia Fonzetti[5], Michele Moretti[6] and Marta Mosca[2], [1]University of Pisa, Pisa, Italy, [2]Rheumatology Unit, Department of clinical and experimental medicine, University of Pisa, Pisa, Italy, [3]Clinical and Experimental Medicine Department, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy, [4]University of Pisa, Rheumatology Unit, Pisa, Italy, [5]AOUP, Pisa, Italy, [6]Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren's syndrome (SS) may affect several aspects of patients' daily lives, leading to impairment of quality of life and patient functioning. Aims of this study were: a) to investigate the relationship between disease activity, illness perception and psychopathological state in patients with SS; b) to specifically explore the impact of glucocorticoid (GC) therapy on patient-reported outcome measures (PROMs).

Methods: This is an observational cross-sectional study including consecutive SS patients (ACR/EULAR 2016) from November 2022 to May 2023. We collected demographic and clinical data including disease duration, ESSDAI, systemic manifestations and pharmacotherapy (GC therapy dose, antimalarial agents, psychotropic and DMARDs). We also assessed the following PROMs: ESSPRI, Visual analogue scale (VAS) for dry mouth, VAS for dry eyes, FACIT-Fatigue, Hospital Anxiety and Depression Scale (HADS). Patients were subdivided into two groups: no GC-treatment vs GC-treatment of ≥1 year. ANOVA, t-tests, Mann Whitney and $\chi 2$ tests were used to assess differences between the two groups. Spearman's correlation was used to measure the correlations between continuous variables. Logistic regression analysis was used to assess independent variables associated with GC therapy.

Results: We included 204 patients (197 F:7M), mean age (DS): 62.6(12.4) yrs; mean follow-up (DS): 9.9 (8-4) yrs. A fifth of the patients showed an ESSDAI≥5, 109/204 (53.4%) presented an ESSPRI≥5 and an ESSDAI< 5 and 55/204 (27%) had both an ESSPRI< 5 and an ESSDAI< 5. The ESSDAI did not correlate either with the ESSPRI nor with other PROMs.

However, Cryo positive patients and subjects with moderate-to-high activity in the glandular domain of the ESSDAI presented significantly higher scores in the VAS questionnaire for dry mouth (8.7 (2.3) vs (6.2 (2.9), p=0.02 and 8.0 (2.1) vs 6.2 (2.9), p=0.02, respectively). By contrast, the ESSPRI scores were significantly lower in patients with low-to-moderate disease activity in the biological domain of the ESSDAI (5.2 (2.8) vs 6.3 (2.4), p =0.01). ESSPRI, HADS, VAS for dry mouth, VAS for dry eyes, and FACIT-Fatigue were statistically significantly correlated with each other (p< 0.001, Table 2). At the inclusion, 40/204 patients (19.6%) were assuming low-dose GC (i.e., ≤7.5 mg of prednisone or equivalent per day). Table 1 summarizes the demographic, disease characteristics and PROMs of the study population comparing patients treated with GC versus no-GC treated patients. The former had a longer disease duration, higher scores in ESSDAI, ESSPRI and HADS depression questionnaire and lower FACIT-Fatigue scores. GC therapy was independently associated with the ESSDAI (OR 1.073 (1.005-1.145), p=0.035) and with the HADS depression questionnaire (OR 1.134 (1.038-1.204), p=0.005)(Fig 1).

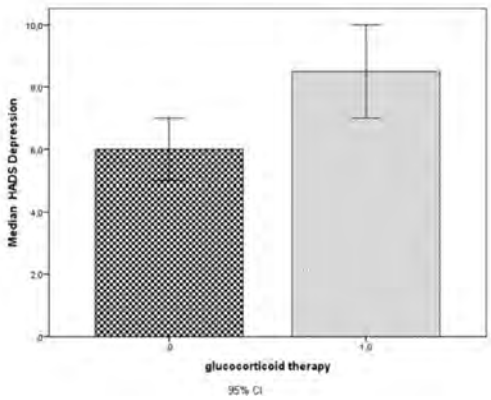
Table 1: Study population: demographics and characteristics

	ALL (204)	GC-Treated (40)	NO GC-Treated (164)	p-value
Gender (Female)	197 (96.6)	37 (92.5)	160 (97.6)	ns
Age	62.6(12.4)	64.4(11.4)	62.2(12.6)	ns
Disease duration	9.9(8.3)	13.4(10.6)	9.1 (7.5)	ns
Education level				
-Primary	28 (15)	10 (26.3)	18 (12.1)	ns
-Lower secondary	62(33.2)	10 (26.3)	52 (34.9)	
-Upper secondary	62(33.2)	13 (34.2)	49 (32.9)	
-Higher education	35 (18.7)	5 (13.2)	30 (20.1)	
Civil status				ns
-Single	22(11.5)	4 (10.3)	18 (11.8)	
-Married	138 (71.9)	29 (74.4)	109 (71.2)	
-Divorced/separated	10 (5.2)	1 (2.6)	9 (5.9)	
-Widowed	22(11.5)	5 (12.8)	17 (11.1)	
Anti-Ro/SSA	135 (66.2)	32 (80)	103 (62,8)	ns
Cryoglobulins	6 (3.1)	3 (7.9)	3 (1.9)	ns
Fibromyalgia	81 (39,7)	15 (37,5)	66 (40,2)	ns
ESSDAI	2.9 (5.0)	4.7 (5.9)	2.5 (4.7)	**0.02**
ESSPRI	5.9 (2.6)	6.7 (2.2)	5.7 (2.6)	**0.03**
VAS dry mouth	6.3 (2.9)	7.2 (2.7)	6.1 (2.9)	**0.02**
VAS dry eys	6.4 (2.9)	6.5 (2.9)	6.3 (2.9)	ns
FACIT-Fatigue	34.8 (10.3)	30.9 (9.7)	35.7 (10.3)	**0.008**
HADS_A	7.1 (3.5)	7.6 (3.5)	6.9 (3.6)	ns
HADS_D	7.0 (4.3)	9.1 (4.1)	6.5 (4.1)	**0.002**

Table 2: ESSDAI, ESSPRI and PROMs correlations

	ESSPRI	ESSDAI	FACIT-fatigue	HADS_A	HADS_D	VAS dry mouth	VAS dry eyes
ESSPRI	1						
ESSDAI	-0.039						
FACIT-Fatigue	-0.620**	-0.073					
HADS_A	0.369**	0.073	-0,550**				
HADS_D	0.461**	0.078	-0.710**	0.527**			
VAS dry mouth	0.634**	0.024	-0.459**	0.349**	0.442**		
VAS dry eyes	0.630**	-0.015	-0.349**	0.202**	0.277**	0.581**	1

Fig 1: Median HADS_ Depression in patients treated with GC versus no-GC treated patients.



Conclusion: We confirmed a limited correlation between disease activity and PROMs in real life. GC therapy, even at the low dosage, contributes to patients' perception of a poorer control of SS with a negative impact on self-reported depression scores.

Disclosure: C. Baldini: GlaxoSmithKlein(GSK), 6, Horizon, 6, Sanofi, 6; **E. Elefante**: None; **I. Navarro Garcia**: None; **F. Ferro**: None; **G. La Rocca**: None; **G. Fulvio**: None; **S. Fonzetti**: None; **M. Moretti**: None; **M. Mosca**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, GlaxoSmithKlein(GSK), 2, Otsuka, 2, UCB, 2.

Abstract Number: 2188

Lung Cysts in Primary SS: New Findings on an Allegedly Innocuous liagnosis

Regis Sewa Marques, Maria Fernanda Zacarin, Pamela Bellini, Raissa Dudienas D Pereira, Aloma Guinami Scabora, Zoraida Sachetto, Manoel Bertolo and ALISSON PUGLIESI, Universidade Estadual de Campinas, Campinas, Brazil

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Lung cysts are a frequent finding in patients with SS, with previous data indicating a prevalence of approximately 30% on chest CT scans. In SS, it is postulated that, among others, its genesis may be due to bronchiolar obstruction by the lymphoid tissue. Retrospective and small-sample data showed that the disease was not associated with radiological progression, suggesting an innocuous disease. However, prospective data are scarce.

Methods: Between 2015 and 2019, patients classified as having primary SS (pSS) according to the 2002 American-European Consensus or the 2016 ACR/EULAR classification criteria and respiratory asymptomatics were systematically evaluated using high-resolution chest CT. Cysts were defined as an air space delimited by a thin (< 2 mm) layer of thin layer.Other findings were classified according to the standard descriptive guidelines. Patients with findings of pulmonary cysts on examination were subsequently evaluated with a new CT scan within at least 1 year, using the same CT machine, and analyzed by the same thoracic radiologist. The cysts were characterized comparatively by their largest diameters and numerically. Patients who increased in size by at least 0.5 cm and the total number of cysts were considered to have radiological progression.

Table 1: Main radiological characteristics of prospectively evaluated patients with pulmonary cysts

Patient (year of birth and sex)	Smoking history	Size of the largest cyst in the first image	Size of the largest cyst in comparative image	Ground Glass Opacities on CT	Cyst progression in size and number
Patient 1 (1970, F)	no	1.2cm	1.2cm	no	no
Patient 2 (1962, F)	yes	0.6cm	0.6cm	no	no
Patient 3 (1957, F)	yes	2.5cm	3.3cm	yes	yes
Patient 4 (1985, F)	no	2.0cm	3.1cm	yes	yes
Patient 5 (1970, F)	no	6.8cm	7.3cm	no	yes
Patient 6 (1954, F)	no	1.7cm	2.3cm	yes	yes

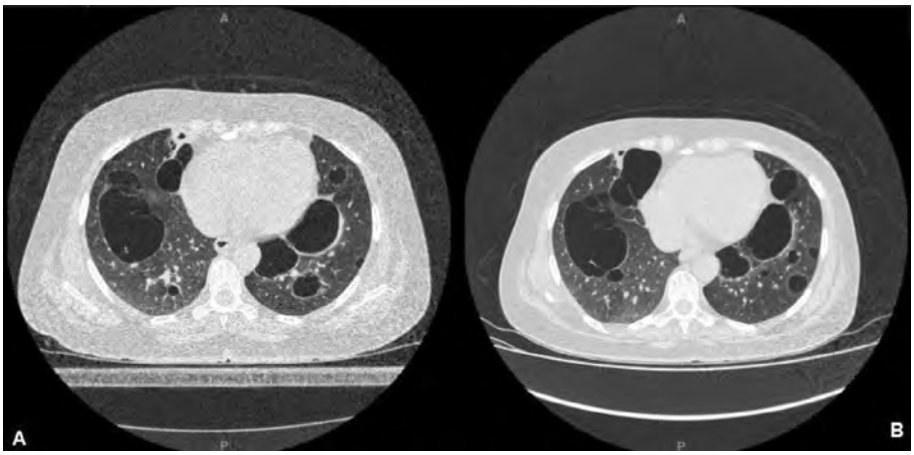


Figure 1 – Thoracic imaging of a 52-year-old woman with cystic lung disease. (A) CT scan done in 2015 showing multiple lung cysts. (B) Progression of cysts in number and size on CT scan taken in 2018

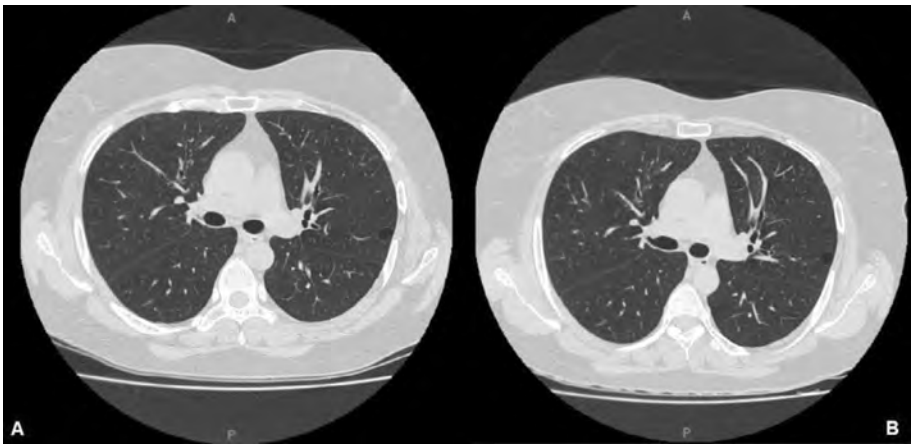


Figure 2 – Thoracic imaging of a 52-year-old woman with cystic lung disease. (A) CT scan done in 2018 with a lung cyst in left lung lobe. (B) New CT scan done in 2019 with no progression of the cyst.

Results: Thirty-five patients with pSS without respiratory symptoms were evaluated using high-resolution chest CT. Of these, 11 (31.4%) had at least one lung cyst, and in six, a prospective evaluation was performed (the remaining patients were not evaluated because of difficulties caused by the Covid-19 pandemic). Among them, four patients showed an increase in both the size and quantity of the cysts, especially those with cysts larger than 2 cm in diameter and with ground-glass opacities on CT. Two patients who had fewer than five cysts each, all smaller than 1.3 cm, had no radiological evolution. In figure 1, we summarize the main radiological characteristics of the evaluated patients, and in figures 2 and 3, we illustrate two patients with lung cysts but with different evolutions.

Conclusion: We found a high prevalence (31.4%) of lung cysts in asymptomatic respiratory patients with pSS who underwent chest CT scans, with most showing radiological progression. In our small sample, patients with cysts > 2 cm or those with ground-glass opacity showed radiological progression. Our findings do not support the hypothesis that lung cysts in patients with pSS do not progress, and point to the need for further larger studies to better evaluate this common lung manifestation of pSS.

Disclosure: R. Sewa Marques: None; **M. Zacarin**: None; **P. Bellini**: None; **R. Dudienas D Pereira**: None; **A. Guinami Scabora**: None; **Z. Sachetto**: None; **M. Bertolo**: None; **A. PUGLIESI**: None.

Abstract Number: 2189

Lymphopenia Fluctuation Patterns Determine the Trajectory of the Disease in Sjogren's Patients with Hematological Involvement

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjogren's disease (SjD) is characterized by a moderate prevalence of cytopenia, mainly neutropenia and lymphocytopenia with a typical fluctuating pattern. The associations between clinical manifestations and cumulative hematological involvement are well described. However, the prognostic value of white blood cell counts over time is still not fully understood. Our aim was to determine the prevalence of neutropenia and lymphopenia in patients with SjD, their variations over time and the corresponding clinical associations.

Methods: This is a multicentric study conducted at the University of Pisa and Lisbon Academic Medical Centre. Data of SjD patients (ACR/EULAR 2016 criteria) with hematological involvement were retrospectively collected. Patients were divided into groups accordingly to the presence of lymphopenia and neutropenia throughout their disease course: no cytopenia, cytopenia only present at baseline, cytopenia only present at the last follow up and persistent cytopenia. Demographic and cumulative clinical features, such as serological markers, organ involvement (assessed by ESSDAI), and salivary gland biopsy findings were analyzed. Univariate and multivariate logistic regression analysis was performed.

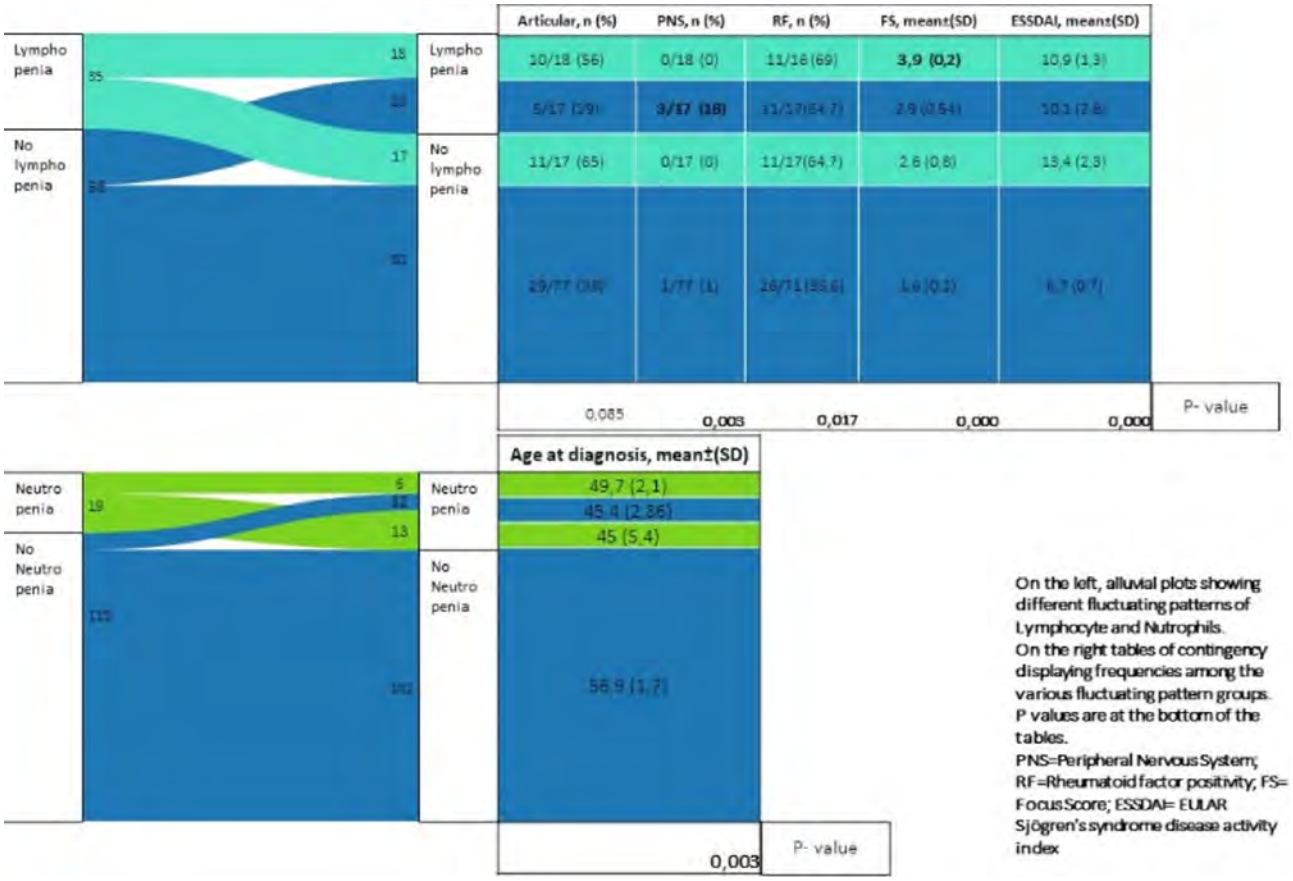
Results: We included 143 patients, 92.3 % were female and the mean follow up was 8,46±0,76 (Table 1). During the disease course, lymphopenia and neutropenia were present in 61/136 pts (44.9%) and32/133 (26.31%), respectively. Lymphopenia was associated with a longer disease duration, serological features (SSB positivity, RF positivity and cryoglobulinemia), higher focus score, higher disease activity as assessed by ESSDAI, more common involvement of the peripheral nervous system, articular and muscular systems, and a higher risk of lymphoma development. Neutropenia was associated with a younger age at diagnosis and lower C3 levels at baseline. A trend was observed for sex (0/35 vs 11/98, p=0.07), as male patients did not have neutropenia (Table 2). In multivariate analysis, lymphopenia was independently associated with focus score (OR 1,312 C.I. 1.02-1.68, p-value 0,034), whereas neutropenia remained associated with both age and C3 (OR 0.95, C.I 0.92-0.99, p-value 0,014; OR 0.95, C.I. 0,92-0.99, respectively). Patients presented different features depending on variations of blood cell levels: persistent lymphopenia tended to be associated with higher focus score, whereas the onset of lymphopenia during the disease course was associated with peripheral nervous involvement (p=0.003) Variations in neutropenia were not associated with any specific SjD clinical manifestations (Fig.1).

	All patients (143)	No-cytopenia§ (50)	Lymphopenia (48)	Neutropenia 25)	Lympho and Neutropenia (10)	P-value
Gender Female	132/143 (92.3)	43 (86)	44 (91.7)	25 (100%)	10 (100%)	ns
Age at dx	51 (15)	57(13)	51 (14)	50(15)	45 (17)	0.003
Focus score	2.2 (2.1)	1.8 (1.5)	3.2 (2.9)	1.5 (1.3)	1.7 (0.9)	0.026
ESSDAI	8.3 (7.6)	6.7(6.3)	12 (9.2)	6.3 (4.3)	7.4(6.7)	0.001
Follow-up	8.5 (7.6)	5.9 (5.2)	8.8 (8.5)	9.0 (6.6)	11.9 (11)	0.049
Anti-Ro/SSA	123/143 (86)	42/50 (84)	42/48 (87.5)	20/25 (80)	9/10(90)	ns
Anti-La/SSB	61/43 (42.7)	12/50 (24)	25/48(52)	11/25 (44)	4/10 (40)	0.04
Rheumatoid Factor	66/131 (50.4)	17/44 (38)	31/46(67.4)	8/22 (27)	5/9 (55%)	0.006
Low C3	36/133 (27.1)	10/46 (21.7)	16/47 (34)	5/23 (21.7)	4/9 (44.4)	ns
Low C4	21/132 (15.9)	5/46 (10.9)	12/47 (25.5)	2 /22(9.1)	1/9 (11.1)	ns
Cryo	5/83 (6)	0/36 (0)	5/27 (18.5)	0/9 80)	0/7 (0)	0.02

§ patients with hematological abnormalities different from lymphopenia and neutropenia

	All pts n=143	Never Lymphopenia N=75	Lymphopenia N=61	p-value	Never neutropenia n= 98	Neutropenia n=35	p-value
Age at diagnosis, mean±(SD)	50,57 (1,26)	53,1 (1,6)	48,3 (1,9)	0,06	53,4 (1,4)	45,3 (2,5)	**0,00**
Age last visit, mean±(SD)	59,12 (1,27)	60 (1,7)	58 (2)	0,45	60,7 (1,4)	55,1 (2,8)	0,06
Follow up, mean±(SD)	8,46 (0,76)	6,9 (0,7)	9,7 (1,1)	**0,03**	7,3 (0,7)	9,8 (1,4)	0,09
Gender, n (%)	11/143 (7,7)	7\75 (9)	4\61 (7)	0,75	11\98 (11)	0\35 (0)	0,07
Focus Score, mean±(SD)	2,23 (0,23)	1,7 (0,2)	3 (0,5)	**0,01**	2,4 (0,3)	1,6 (0,3)	0,20
ANA, n (%)	133/136 (97,8)	73\75 (97)	60\61 (98)	1,00	96\98 (98)	34\35 (97)	1,00
SSA, n (%)	121/143 (86)	62\75 (83)	54\61 (89)	0,47	84\98 (86)	29\35 (83)	0,78
SSB, n (%)	61/143 (42,7)	23\75 (31)	32\61 (52)	**0,01**	37\98 (38)	15\35 (43)	0,69
Rheumatoid Factor, n (%)	66/131 (50,4)	23\66 (35)	39\58 (67)	**0,00**	48\90 (53)	11\31 (35)	0,10
Low C3, n (%)	36/133 (27,1)	15\69 (22)	21\58 (36)	0,08	26\93 (28)	9\32 (28)	1,00
Low C4, n (%)	21/132 (15,9)	7\68 (10)	14\58 (24)	0,05	17\93 (18)	3\33 (10)	0,40
Cryoglobulinemia, n (%)	5/83 (6)	0\45 (0)	5\35 (14)	**0,01**	5\63 (8)	0\16 (0)	0,56
ESSDAI, mean±(SD)	8,27 (7,57)	6,6 (0,7)	10,8 (1,2)	**0,00**	9,4 (0,8)	6,6 (0,9)	0,07
Constitutional domain, n (%)	23/139 (16,6)	11\72 (15)	11\60 (18)	0,65	18\96 (19)	4\33 (12)	0,59
Lymphadenopaty domain, n (%)	32/139 (23)	15\72 (21)	16\60 (27)	0,54	26\96 (27)	5\33 (15)	0,24
Glandular domain, n (%)	25/139 (18)	9\72 (13)	14\60 (23)	0,11	17\96 (18)	0\33 (18)	1,00
Articular domain, n (%)	57/139(41)	25\72 (35)	32\60 (53)	**0,04**	43\96 (45)	12\33 (36)	0,42
Cutaneous domain, n (%)	20/139 (14,4)	7\72 (10)	12\60 (20)	0,13	16\96 (17)	3\33 (9)	0,40
Pulmonary domain, n (%)	14/139 (10,1)	8\72 (11)	6\60 (10)	1,00	13\96 (14)	1\33 (3)	0,11
Renal domain, n (%)	5/139 (3,6)	1\72 (1)	4\60 (7)	0,18	5\96 (5)	0\33 (0)	0,33
Muscular domain, n (%)	3/139 (2,1)	1\72 (1)	2\60 (3)	0,59	3\96 (3)	0\33 (0)	0,57
PNS domain, n (%)	4/139 (2,9)	0\72 (0)	4\60 (7)	**0,04**	3\96 (3)	1\33 (3)	1,00
CNS domain, n (%)	1/139 (0,7)	1\72 (1)	0\60 (0)	1,00	1\96 (1)	0\33 (0)	1,00
Biological domain, n (%)	81/139 (58,3)	38\72 (53)	41\60 (68)	0,08	57\96 (59)	21\33 (64)	0,84
Hematological Neoplasia, n (%)	7/132 (5,3)	1\72 (1)	6\60 (10)	**0,05**	7\96 (7)	0\33 (0)	0,19
LAB TEST AT BASELINE							
Hemoglobin, mean±(SD)	12,52 (0,12)	12,6 (0,2)	12,5 (0,2)	0,77	12,5 (0,2)	12,6 (0,2)	0,65
Platelets, mean±(SD)	231314,81 (8353)	242467,7 (12930,1)	216282,6 (8682,2)	0,12	238797,6 (10046,7)	205125 (12155,3)	0,09
Monocytes, mean±(SD)	414,91 (29,20)	505,7 (42,9)	289,4 (23,7)	**0,00**	428,4 (34,6)	367,8 (50,9)	0,35
VES, mean±(SD)	38,01 (3)	38,2 (4)	37,8 (4,6)	0,96	39,8 (3,6)	31,1 (5,6)	0,23
IgG levels, mean±(SD)	1602,16 (71)	1576,4 (87,9)	1634,9 (118,6)	0,69	1583,5 (76,7)	1700,1 (196,7)	0,55
IgM levels, mean±(SD)	123,03 (13)	99,3 (9,8)	151 (27,5)	0,06	125,7 (16,6)	110,9 (18,9)	0,69
IgA levels, mean±(SD)	261,13 (19)	272,9 (26,3)	247,3 (27,7)	0,51	265,3 (19,5)	242,2 (59,3)	0,64
Free light chain K, mean±(SD)	659 (84,44)	676,2 (145,7)	646,1 (105,2)	0,87	701,7 (100)	479,5 (98,1)	0,11
Free light chain L, mean±(SD)	336,43 (46)	329,9 (76,2)	341,3 (59,8)	0,91	367,9 (53,5)	202,5 (43)	0,16
Ratio K/L, mean±(SD)	2,08 (0,09)	2,1 (0,2)	1,9 (0,1)	0,38	1,9 (0,1)	2,4 (0,2)	**0,05**
B2 microglobulinemia, mean±(SD)	2437 (111)	2448,8 (188,3)	2431,9 (142,8)	0,95	2504,4 (135,2)	2236,7 (179,4)	0,31
LDH, mean±(SD)	222,84 (9,7)	210,6 (10,6)	237 (16,9)	0,18	221,6 (10,5)	230 (26,9)	0,76
C-Reactive Protein, mean±(SD)	0,61 (0,16)	0,7 (0,2)	0,5 (0,2)	0,55	0,7 (0,2)	0,5 (0,3)	0,62
C3 levels, mean±(SD)	102,7 (2,5)	103,5 (4,2)	101,9 (2,8)	0,75	105,3 (2,8)	90,3 (6)	**0,03**
C4 levels, mean±(SD)	18,3 (0,8)	18,8 (1)	17,8 (1,3)	0,55	18,4 (0,9)	18,2 (1,5)	0,95

Table1
In the upper part of the tabel cumulative manifestations of Sjogren's Syndrome, in the lower part laboratory test collected at baseline. PNS= peripheral nervous system; CNS=central nervous system;ESSDAI= EULAR Sjögren's syndrome disease activity index



Conclusion: Our study highlights the associations of lymphopenia with key histological, serological and clinical features of SjD. Interestingly, lymphocytopenia may show different pattern of variations, ultimately associated with higher disease activity and tissue infiltration. This is consistent with the hypothesis of glandular tissue homing of circulating lymphocytes in the pathogenesis of SjD and should be further explored.

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Abstract Number: 2190

Saliclick: A Novel Technology for Minimal Invasive Salivary Gland Biopsy in Suspected Sjögren's Syndrome

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Labial minor salivary gland (MSG) biopsy is a major element in the diagnosis of Sjögren´s Syndrome and the exclusion of other pathologies, respectively. Transient local paraesthesia as a complication of MSG biopsy has been described in up to 11%. We recently developed a device in the form of a lip clamp exerting transcutaneous pressure on the salivary glands thus allowing a more superficial incision and less invasive procedure. In this study we report four years experience of MSG using this device in our rheumatology department.

Methods: Retrospective study of 114 MSG biopsies performed with the use of Saliclick (Curmed, Switzerland). For each MSG biopsy we recorded complications, salivary gland surface, intervention time, need of assistance and focus score.

Results: In 106 (95%) out of114 MSG biopsies, representative salivary gland material was obtained. No numbness was recorded. No stitches were needed. In 6 (5.2%) patients, moderate haemorrhage occurred which was controllable by intraoral pressure using a swab. 4 (3.5%) patients suffered from a vaso-vagal reaction. The mean (SD) duration of the intervention was 10.4 (3.5) min. 85% of the interventions could be performed by a rheumatologist without the technical assistance of another person. The mean glandular surface area was 5.9 mm2. A focal lymphocytic sialadenitis was reported in 21 patients (20%), with a focus score >1 for 62% of them.

Conclusion: MSG biopsy using Saliclick is a safe and rapid procedure for the diagnosis in Sjögren's Syndrome without observed numbness occurring in this study. The lack of technical assistance safed resources and the procedure was integrated more quickly into the clinical workflow.

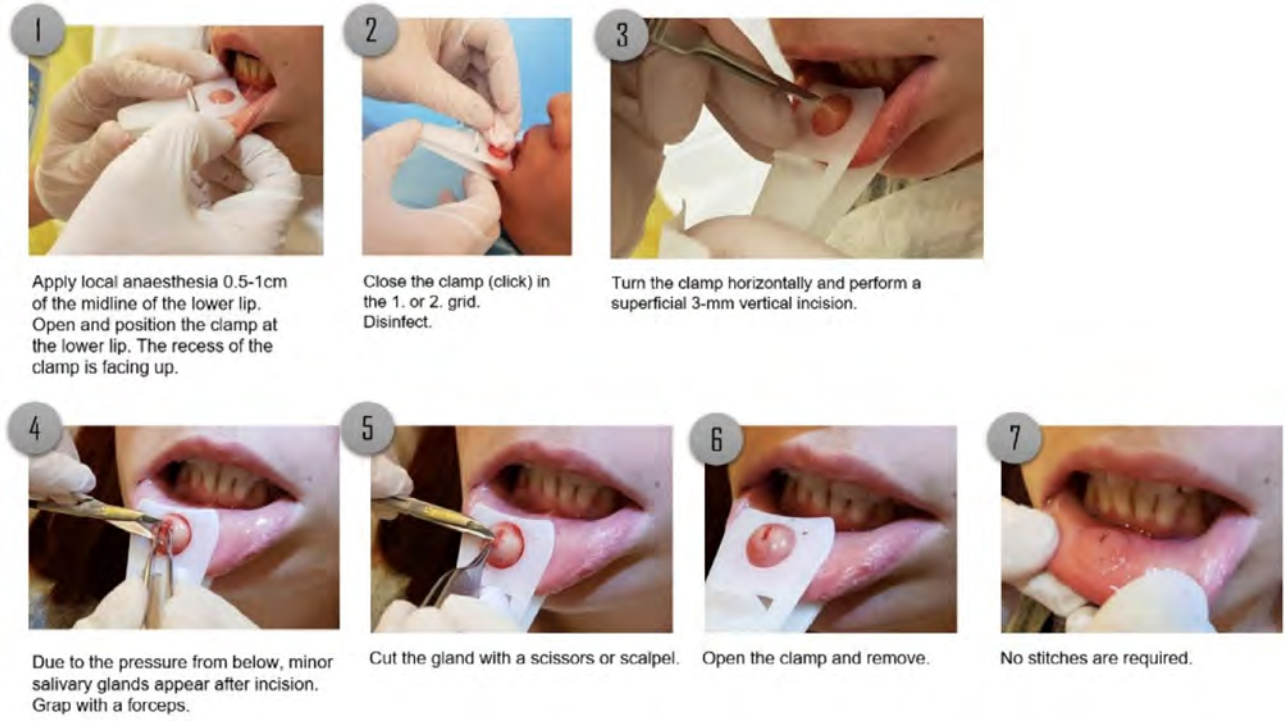


Figure 1. Step-by-step description of the lLabial minor salivary gland biopsy using the novel device 'Saliclick'.

Disclosure: T. Hügle: Atreon SA, 8, Curmed, 9, Eli Lilly, 6, Fresenius Kabi, 2, 5, Galapagos, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, Merck/MSD, 6, Pfizer, 6; **D. Dan**: None; **A. Dumusc**: None.

Abstract Number: 2191

Efficacy of anti-CD38 Treatment with Daratumumab in Two Cases of Refractory and Severe Sjogren Disease

Gaetane Nocturne[1], Mathilde di Filippo[2], Oriane Marmontel[2], Pascale Chretien[1], Roman Krzysiek[1], François Lifermann[3], Nawal Rahal[1], Rakiba Belkhir[4], Philippe Moulin[2] and Xavier Mariette[5], [1]APHP, Le Kremlin-Bicêtre, France, [2]Hospices Civils de Lyon, Lyon, France, [3]Department of Internal Medicine, Centre Hospitalier de Dax, Dax, France, [4]Rheumatology Department, Université Paris-Saclay, INSERM U1184, Hôpital Bicêtre, APHP, FHU CARE, Le Kremlin-Bicêtre, France, [5]Université Paris-Saclay, Le Kremlin-Bicêtre, France

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren's disease (Sjo) is a systemic autoimmune disease. In 80% of the patients, Sjo is responsible for dryness, fatigue, and joint pain. In 10% of the patients, severe and potentially life-threatening systemic disease occur. B cell-targeted therapies have shown efficacy in some of these systemic manifestations, but some patients remain refractory to anti-CD20 therapy. Plasmablasts and plasma cells have been identified as key drivers of disease activity in Sjo, suggesting them as a potential therapeutic target. Daratumumab, a monoclonal antibody targeting CD38 and approved for multiple myeloma, depletes plasmablasts and plasma cells. Here, we present the two first cases of patients with severe Sjo complications refractory to rituximab (RTX) successfully treated with daratumumab.

Methods: Patient 1 is, an 18-year-old woman with a diagnosis of Sjo at age of 13 years old. She had positive anti-SSA and SSB antibodies, positive rheumatoid factor, hypergammaglobulinemia at 18 g/l and severe hypertriglyceridemia at 52 g/l due to an autoimmune hyperchylomicronemia with positive anti GPIHBP1 complicating Sjo. RTX treatment had no effect on triglyceride levels, leading to the decision to treat the patient with daratumumab at a dose of 16 mg per kilogram of body weight once a week for 4 weeks. Patient 2, a 68-year-old woman with Sjo, presented with positive anti-SSA and SSB antibodies, type II cryoglobulinemia-associated vaculitis, polyneuropathy, and glomerulonephritis. Despite multiple lines of treatment-included cyclophosphamide and the association rituximab/belimumab, vasculitis relapsed. Daratumumab treatment was initiated following the protocol used for Patient 1.

Results: The follow-up after daratumumab was 8 months for the 2 patients. After daratumumab treatment, Patient 1 showed normalized triglyceride levels (0.67 g/L), decreased gammaglobulin levels from 18 g/l to 9 g/l, and a dramatic decrease in anti-GPIHBP1 antibodies from 6121 U/ml to 234 U/ml(Figure 1). Patient 2 experienced no more purpura flare, negative proteinuria, normalization of complement level, negativation of cryoglobulinemia, and a very important decrease in rheumatoid factor titer from 339 to 48 UI/ml (Figure 2). For the 2 patients, no severe adverse events occurred during follow-up, and no hospitalization was required for the management of Sjo, infections or comorbidities.

Conclusion: Daratumumab may be an effective therapeutic strategy in severe and refractory Sjo patients, particularly when systemic manifestations are driven by pathogenic autoantibodies. Further studies are needed to assess the long-term efficacy and impact of daratumumab on autoreactive B cell repertoire and the room of daratumumab in the therapeutic arsenal of the disease.

Figure 1

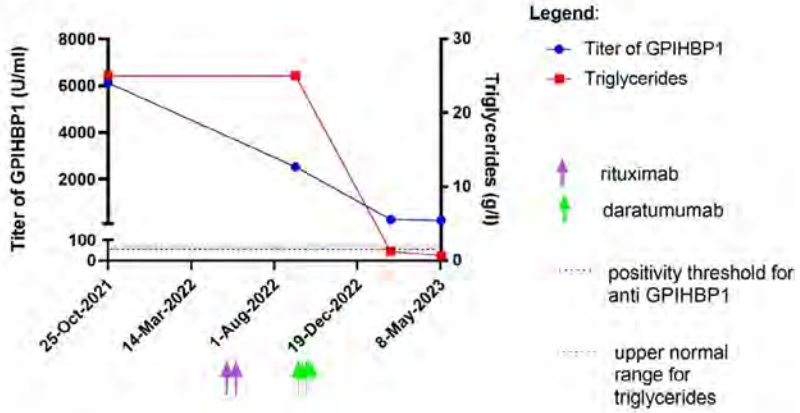
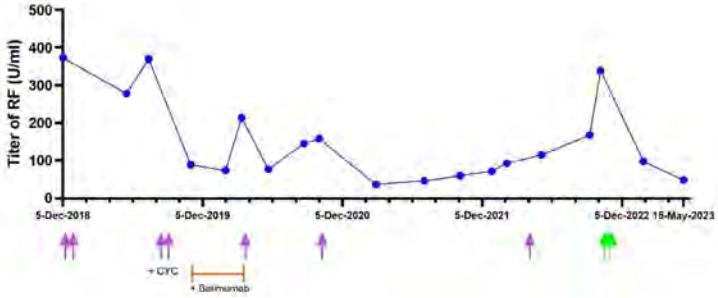


Figure 2



Disclosure: G. Nocturne: None; **M. di Filippo**: None; **O. Marmontel**: None; **P. Chretien**: None; **R. Krzysiek**: None; **F. Lifermann**: None; **N. Rahal**: None; **R. Belkhir**: None; **P. Moulin**: None; **X. Mariette**: AstraZeneca, 2, 6, BMS, 2, 6, Galapagos, 2, 6, GSK, 2, 6, Novartis, 2, 6, Pfizer, 2, 6.

Abstract Number: 2192

New Inducible Mouse Model of Sjögren's Syndrome Represents a Valuable Tool to Assess the Impact of Gene Knockout on the Disease's Physiopathology

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Primary Sjögren's syndrome (pSS) is a chronic rheumatic disease characterized by lymphocytic infiltration of exocrine glands, resulting in sicca syndrome with extra-glandular autoimmune features. The etiopathogeny is unknown, involving environmental and hormonal factors on a predisposing genetic background. For fundamental research, several inbred

mice strains predisposed to SS exist but backcrossing them with transgenic mice from another genetic background is tedious and time consuming. The aim of this work is to describe an inducible model of pSS that is easy to implement and compatible with CreLox transgenic mice on a C57Bl/6 background, using NFAT5 conditional knockout (KO) mice as a proof of concept.

Methods: Female C57Bl/6 UbC-Cre-NFAT5flx/flx or UbC-Cre+NFAT5flx/flx mice were injected subcutaneously at weeks 12 and 15 with either 25mg/kg 5,6-dimethylxanthenone-4-acetic acid (DMXAA) or vehicule, then at week 17 with two consecutive intraperitoneal injections (at 24h interval) of either 100µl of corn oil or 20mg/ml tamoxifen (TAM). Saliva and lacrymal flow were measured under pilocarpine stimulation at week 18. Mice were sacrified at week 19. Orbit content, submandibular and lacrymal glands were evaluated by histology. Anti-Ro/SSA, anti-Ro/SSB and rheumatoid factor (RF) antibodies were detected by ELISA. FACS analysis of lymphocytic populations was performed on submandibular glands. RNA-sequencing was performed to generate a comprehensive global gene expression profile of submandibular glands from DMXAA-treated groups compared to controls.

Results: Compared to controls, DMXAA/oil- and DMXAA/TAM-treated Cre- mice display a significant decrease in salivary flow (p=0.0009) and Schirmer's test (p=0.03). Histologically, treated groups show low-grade focal sialadenitis within the submandibular glands, increased corneal epithelium thickness but no reproducible dacryoadenitis within the external lacrimal glands. FACS analysis on submandibular glands confirms the presence of predominantly CD8+ and CD4+ T-cells infiltrate. Treated groups also show higher serum reactivity for Ro/SSA (p=0.011), anti-Ro/SSA and RF positivity (both 0% vs 12.5% vs 31.2%, p=0.0232). Only 1 out of 21 mice in the DMXAA/TAM-treated Cre- group showed double anti-Ro/SSA and anti-La/SSB positivity. Comparative analysis of the transcriptomes revealed distinct gene expression patterns in DMXAA-treated groups compared to control mice. Notably, there was in both DMXAA-treated group a significant enrichment of interferon (IFN)-related genes. Compared to DMXAA/TAM-treated Cre- mice, induction of NFAT5 KO in DMXAA/TAM-treated Cre+ mice results in reduced focus-score (p=0.0238), anti-Ro/SSA reactivity (p=0.0127), but does not restore salivary (p=0.77) or lacrimal flow (p=0.9355).

Conclusion: DMXAA-based inducible mouse model of pSS – demonstrating key phenotypic features of human pSS – is an attractive alternative to spontaneous inbred models, allowing the use of any C57Bl/6 mice in pSS experiments.In this study, induction of NFAT5 KO at week 17 reduced focal sialadenitis and anti-Ro/SSA levels but did not rescue salivary and lacrimal flow at week 19.

Disclosure: D. Parisis: None; **N. Bolaky**: None; **A. Benchehida**: None; **C. Küper**: None; **j. Perret**: None; **M. Soyfoo**: None; **C. Delporte**: None.

Abstract Number: 2193

Anti-citrullinated Protein Antibodies in Sjögren's Syndrome Define a Subset of Patients with Lower B Cell Activation Markers and Higher Risk of Lung Involvement

Augusto Silva[1], Filipa Costa[2], Mariana Silva[2], Giovanni Fulvio[3], Matilde Bandeira[2], Manuel Silvério-António[4], Nikita Khmelinskii[2], Chiara Baldini[3] and Vasco Romão[2], [1]Santa Maria Hospital, Maceira, Portugal, [2]Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal, [3]University of Pisa, Pisa, Italy, [4]Hospital Santa Maria, Lisboa, Portugal

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Table 1 - Clinical features of patients with Sjögren's syndrome

Parameter (0)	ACPA positive, N = 57	ACPA negative, N = 119	P value
Female	54 (94.7%)	114 (95.8%)	0.752
Age at diagnosis (years)	52.7±13.4 (19-78)	50.6±14.6 (17-80)	0.928
Smoking status			0.814
- Never smoker	25 (73.5%)	65 (67.7%)	
- Active Smoker	3 (8.8%)	11 (11.5%)	
- Former smoker	6 (17.7%)	20 (20.8%)	
SS duration (years)	8.9±8.1 (0-39)	10.7±8.5 (1-47)	0.069
Disease assessment at diagnosis			
- ESSDAI	4.0±4.0	3.8±6.1	0.107
- ESSPRI	5.8±2.3	6.0±2.3	0.523
- ESS	5.7±2.6	5.9±2.6	0.891
- PROFAD-SSI	24.7±16.1	27.1±9.2	0.426
Disease assessment at last visit			
- ESSDAI	4.5±7.8	2.0±3.0	0.194
- ESSPRI	4.3±1.8	5.9±1.9	0.373
- ESS	4.3±2.9	5.5±1.9	0.189
Salivary and lacrimal gland assessment			
- Xerostomia	46/54 (85.2%)	40/44 (90.9%)	0.297
- Unstimulated salivary flow (ml/15min)	4.7±5.6	4.1±5.2	0.309
- Clinical oral dryness score	3.7±1.5	3.6±1.8	0.325
- Focus score	2.2±2.7	1.6±1.7	0.983
- Salivary gland swelling	8/36 (22.2%)	23/107 (21.5%)	0.371
- Xerophthalmia	43/46 (93.5%)	41/45 (91.1%)	0.488
- Schimer's test	3.5±2.2	3.2±2.7	0.487
- van Bijsterveld ocular score	2.4±2.4	1.8±1.8	0.108
- Tear break-up time	7.7±4.6	7.7±4.4	0.776
Autoantibodies, n (%)			
- ANA	48 (84.2%)	106 (89.1%)	0.147
- Anti-Ro52	30 (52.6%)	84 (70.6%)	**<0.001**
- Anti-Ro60	29 (50.9%)	75 (63.0%)	**0.009**
- Anti-SSB	17 (29.8%)	69 (58.0%)	**<0.001**
- Rheumatoid Factor	41 (71.9%)	97 (81.5%)	0.107
Biological markers of disease activity			
- ESR elevation	14/50 (28%)	24/77 (31.2%)	0.430
- CRP elevation	15/53 (28.3%)	17/73 (23.3%)	0.332
- C3 consumption	8/57 (14.0%)	10/28 (35.7%)	**0.024**
- C4 consumption	8/56 (14.3%)	6/28 (21.4%)	0.297
- Hypergammaglobulinemia	17/55 (30.9%)	17/31 (54.8%)	**0.026**
- Hypogammaglobulinemia	1/57 (1.8%)	0/119 (0%)	0.324
- IgG elevation	11/52 (21.2%)	46/62 (74.2%)	**<0.001**
- Cryoglobulinemia	2/51 (3.9%)	6/97 (6.2%)	0.414
- MGUS	1/57 (1.8%)	4/119 (3.4%)	**0.048**
Joint involvement, n (%)			
- Arthralgia	43/55 (78.2%)	75/105 (71.4%)	0.233
- Arthritis	27/53 (50.9%)	58/105 (55.2%)	0.366
- Fulfil rheumatoid arthritis criteria ACR/EULAR 2010	22/55 (40%)	4/119 (3.4%)	**<0.001**
- Radiographic erosions	11/48 (22.9)	2/23 (8.7%)	0.129
- Ultrasound erosions	7/47 (14.9%)	1/17 (5.9%)	0.313
Extra-articular involvement, n (%)			
- Constitutional	21/36 (58.3%)	49/102 (48.0%)	0.087
- Lymphadenopathy	11/56 (19.6%)	25/112 (22.3%)	0.426
- Cutaneous	8/35 (22.9%)	29/108 (26.9%)	0.647
- Pulmonary (1)	8/34 (23.5%)	9/105 (8.6%)	**0.028**
- Renal	2/35 (2.9%)	4/106 (3.8%)	0.282
- Muscular	1/35 (2.9%)	6/106 (5.7%)	0.284
- Central Nervous System	1/57 (1.8%)	2/119 (1.7%)	0.683
- Peripheral Nervous System	1/35 (2.9%)	7/107 (6.5%)	0.495
- Hematologic involvement	9/35 (25.7%)	41/107 (38.3%)	0.516
- Vasculopathy (2)	5/56 (8.9%)	10/119 (8.4%)	0.557
- Hematological neoplasms	2/57 (3.5%)	0/119 (0%)	0.104
- Solid neoplasms	1/57 (1.8%)	4/119 (3.4%)	0.478

Abbreviations: ACPA - Anticyclic-citrullinated protein antibody; CRP - C-reactive Protein; ESR - Erythrocyte sedimentation rate; ESSPRI - Eular Sjögren's Syndrome Patient Reported Index; ESSDAI - EULAR Sjögren's syndrome disease activity index; ESS - EULAR sicca score; MGUS - monoclonal gammopathy of undetermined significance; PROFAD-SSI - Profile of Fatigue and Discomfort Sicca Symptoms Inventory; pSS - Sjögren's syndrome; SD - Standard Deviation.

(0) Continuous variables presented as mean ± sd (range); categorical variables presented as n (%) or n/N (%).
(1) Pulmonary - Nonspecific interstitial pneumonia, ground-glass pattern, pulmonary amyloid tumour, pulmonary micronodules and bronchiectasis.
(2) Vasculopathy - Raynaud's Phenomenon.

Background/Purpose: Extraglandular manifestations may occur in up to 40-50% of patients with SS, including inflammatory arthralgia and chronic polyarthritis (1-3). ACPA are prototypical markers of RA, but have also been described in 4-10% of patients with SS (3,4). Although ACPA have been associated with articular and lung involvement, their clinical relevance remains to be fully clarified (3,4).

Objective: To evaluate the prevalence of ACPA in SS patients and assess their associations with clinical, laboratorial and radiographic features.

Methods: We screened patients from the Observational Lisbon Sjögren's Syndrome Prospective (OLISSIPO) and University of Pisa (UNIPI) cohorts, included until May 2023, for the presence of ACPA. For each ACPA-positive, two ACPA-negative patients matched for age and sex were selected. We collected demographic, clinical and laboratorial variables. t-student or Mann-Whitney tests were used, as appropriate, for continuous variables and chi-square or Fisher tests for categorical variables.

Results: From 438 patients tested for ACPA, 176 patients (95.5% women) were selected (Table 1), 57 of them ACPA-positive (94.7% female), corresponding to a prevalence of 13.0%. Age at pSS diagnosis and disease duration were similar between groups. There were no differences in systemic disease activity, as assessed by the EULAR Sjögren's Syndrome disease activity index (ESSDAI), nor in dryness, pain and fatigue assessed by the EULAR Patient Reported Index (ESSPRI), EULAR sicca score (ESS), and Profile of Fatigue and Discomfort Sicca Symptoms Inventory (PROFAD-SSI). Similarly, xerostomia, xerophthalmia, salivary gland swelling and objective measures of reduced glandular function or inflammation (focus score) were also comparable between ACPA-positive and ACPA-negative patients. However, ACPA-positivity was associated with a significantly lower frequency of anti-Ro52 (52.6% vs 70.6%, $p< 0.001$), anti-Ro60 (50.9% vs 63.0%, $p=0.009$), and anti-SSB (29.8% vs 58.0%, $p< 0.001$) antibodies, but no differences in RF positivity (71.9% vs 81.5%, $p=0.107$). In accordance, markers of B cell hyperactivation such as C3 consumption (14.0% vs 35.7%, $p=0.024$), hypergammaglobulinemia (30.9% vs 54.8%, $p=0.026$) and IgG elevation (21.2% vs 74.2%, $p< 0.001$) were also less commonly associated with the presence of ACPA. Of note, articular involvement or erosive disease was not more frequent in ACPA-positive patients. Nonetheless, a higher number of ACPA-positive patients met the ACR/EULAR 2010 classification criteria for RA (40.0% vs 3.4%, $p< 0.001$). Finally, lung disease was significantly more common in the ACPA-positive group (23.5% vs 8.6%, $p=0.028$), whereas involvement of additional organs was not.

Conclusion: In patients with SS, ACPA is not associated with joint involvement, but, surprisingly, seems to define a subgroup of patients with lower markers of B cell activation (such as circulating anti-SSA/B, complement consumption and raised immunoglobulins). Furthermore, ACPA was associated with lung involvement, despite a similar distribution of known markers of pulmonary disease in SS such as RF. These findings deserve further confirmation in larger cohorts.

Disclosure: A. Silva: None; **F. Costa**: None; **M. Silva**: None; **G. Fulvio**: None; **M. Bandeira**: None; **M. Silvério-António**: None; **N. Khmelinskii**: None; **C. Baldini**: GlaxoSmithKlein(GSK), 6, Horizon, 6, Sanofi, 6; **V. Romão**: None.

Abstract Number: 2194

Association of Self-perceived Oral Health Status with ESSPRI Reported by Sjögren's Syndrome Patients

Oscar E. Alvarez-González[1], Hector Guerra[2], Elena A. Quintana-Aguilar[2], Sandra P. Arroyo-Sánchez[2], Jesus S. Cortez-Gutierrez[2], Jesus Alberto Cardenas-De la Garza[3], Francisco J. Torres-Quintanilla[4], Janett Riega-Torres[5], Cassandra Michele Skinner-Taylor[5] and Dionicio A. Galarza-Delgado[6], [1]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, Mexico, [2]Hospital Universitario "Dr. José Eleuterio González", Monterrey, Mexico, [3]Hospital Universitario "Dr. José Eleuterio González", San Nicolas, Mexico, [4]Hospital Universitario

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Salivary gland hypofunction, manifested as xerostomia in Sjögren's syndrome (SS), causes dental, language, and nutritional problems, leading to a detriment in oral health. The Geriatric/General Oral Health Assessment Index Spanish Version (GOHAI-SP) is a useful tool that has been used to assess the self-perception of oral status in SS patients (1). This study aims to associate and correlate the subjective EULAR SS Patient Reported Index (ESSPRI) and GOHAI-SP results with objective data from unstimulated salivary flow in 15 minutes (USF/15min).

Methods: A cross-sectional and observational study was conducted from October to December 2022 in the rheumatology service at Hospital Universitario "Dr. José Eleuterio González", Mexico. Patients meeting ACR/EULAR criteria for pSS and sSS were included and assessed with ESSPRI and GOHAI-SP during their follow-up appointment or reached by telephone. The latter index consists of 12 questions on a 1 to 5 Likert-type scale. The lowest obtainable score is 12 and the maximum is 60. Scores ≤ 44 were classified as poor oral health, moderate from 45 to 50, and good ≥ 51. Questions 1-4 assess oral functionality, 6, 7, 9-11 psychosocial status; 8 and 12 for pain. Data of USF/15min was obtained from patients' charts.

Results: A total of 41 patients were included: 31 (75.6%) with pSS and 10 (24.4%) with sSS most of whom were women (n=40, 97.6%) with a mean age of 53.41 (SD: 12.58). The median score of GOHAI-SP was 50 [IQR 43.5-52], medians for dryness, fatigue, and pain reported in ESSPRI domains were: 3 [0-7], 2 [0- 6.5] and 1 [0-5]; for USF/15min 1.5 [0.5-2.25]. The self-perceived health status was classified as good in 19 (46.3%), moderate and poor both in 11 (26.8%). We found that the worse the self-perceived oral condition, the higher ESSPRI medians for dryness ($p < 0.001$), fatigue (p 0.003), and pain (p 0.002) were reported. No significant differences were found when compared to USF/15min. Results of Spearman's correlation model are shown in Table 1. No significant differences were found between pSS and sSS groups.

Conclusion: The greater the severity of dryness, fatigue, and muscular or joint pain, the greater the functional impairment of mouth and oral pain; as well as the worse the psychosocial aspect manifested as concern, nervousness, discomfort, and limitation of interaction with people due to the dental appearance.

Table 1. Correlation between GOHAI-SP, ESSPRI and USF/15min.

		GOHAI-SP domains							
	Media n, [IQR]	Oral functionality 4 [3.5-4.37]		Psychosocial 4.2 [4-4.5]		Pain 4 [3-4.75]		Total 50 [43.5-52]	
		r =	*p =*	*r =*	*p =*	*r =*	*p =*	*r=*	*p=*
ESSPRI dryness	3 [0-7]	.655*	**<.001**	.649*	**<.001**	.512*	**<.001**	.654*	**<.001**
ESSPRI fatigue	2 [0-6.5]	.773*	**<.001**	.748*	**<.001**	.587*	**<.001**	.758*	**<.001**
ESSPRI pain	1 [0-5]	.786*	**<0.001**	.735*	**<0.001**	.546*	**<.001**	.772*	**<.001**
USF/15 min	1.5 [0.5-2.25]	-.167	.29	-.08	.585	.085	.59	-.107	.50

GOHAI-SP: Geriatric/General Oral Health Assessment Index Spanish Version, ESSPRI: EULAR Sjögren's Syndrome Patient Reported Index, USF: Unstimulated salivary flow

1. Leung KC, McMillan AS, Wong MC, Leung WK, Mok MY, Lau CS. The efficacy of cevimeline hydrochloride in the treatment of xerostomia in Sjögren's syndrome in southern Chinese patients: a randomised double-blind, placebo-controlled crossover study. Clin Rheumatol. 2008;27(4):429-436. doi:10.1007/s10067-007-0723-x

Disclosure: O. Alvarez-González: None; **H. Guerra**: None; **E. Quintana-Aguilar**: None; **S. Arroyo-Sánchez**: None; **J. Cortez-Gutierrez**: None; **J. Cardenas-De la Garza**: None; **F. Torres-Quintanilla**: None; **J. Riega-Torres**: None; **C. Skinner-Taylor**: None; **D. Galarza-Delgado**: None.

Abstract Number: 2195

Regional Differences in Clinical Phenotype of Axial Spondyloarthritis. Results from the International Map of Axial Spondyloarthritis (IMAS)

Denis Poddubnyy[1], Fernando Sommerfleck[2], Victoria Navarro-Compán[3], Christine Bundy[4], Souzi Makri[5], Shashank Murlidhar Akerkar[6], Lillann Wermskog[7], Elie Karam[8], Jose Correa Fernandez[9], Asif Siddiqui[10] and **Marco Garrido-Cumbrera**[11], [1]Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany, [2]Sanatorio Julio Mendez, Buenos Aires, Argentina, [3]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain, [4]Cardiff University, Cardiff, United Kingdom, [5]Cyprus League for People with Rheumatism (CYLPER), Nicosia, Cyprus, [6]Mumbai Arthritis Clinic, Mumbai, India, [7]Spondyloarthritis Association of Norwary (SPAFO);Axial Spondyloarthritis International Federation (ASIF), Oslo, Norway, [8]Canadian Spondylitis Association (CSA), Toronto, ON, Canada, [9]Universidad de Sevilla, Health & Territory Research (HTR), Sevilla, Spain, [10]Novartis Pharma AG, Basel, Switzerland, [11]University of Seville, Sevilla, Spain

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA

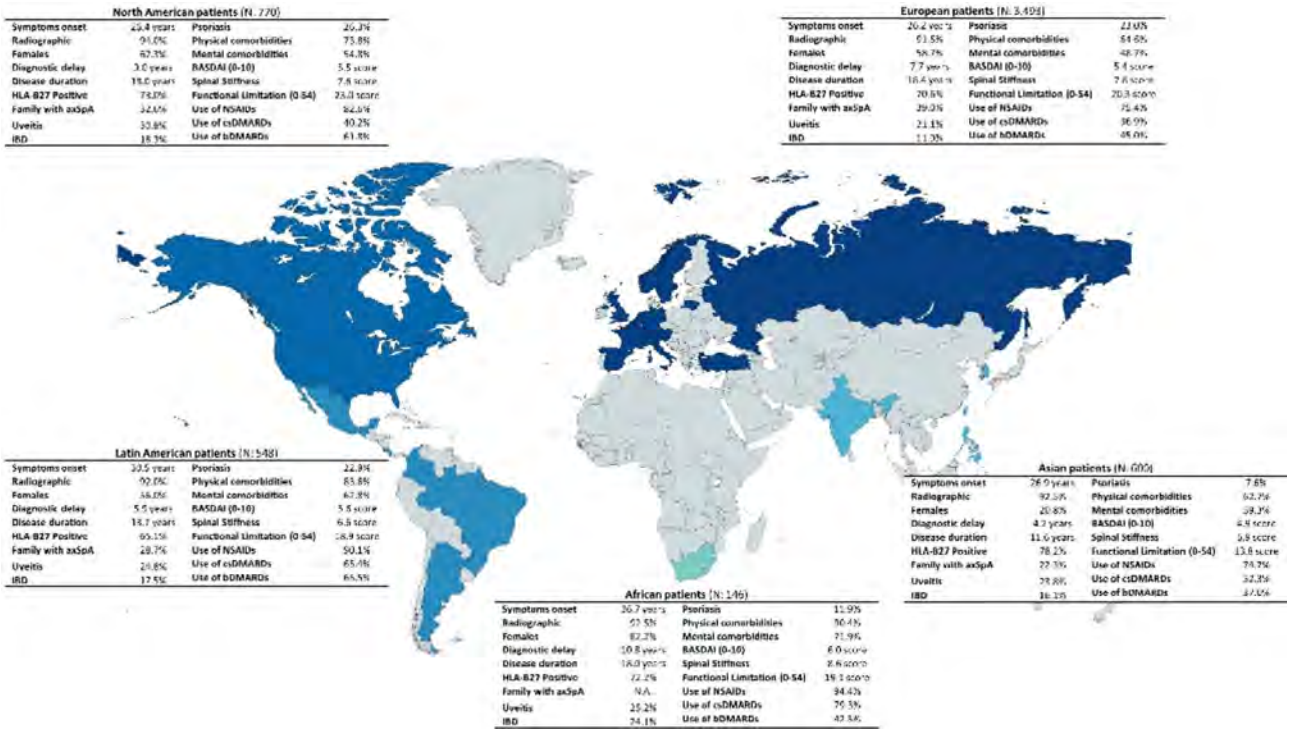
Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies have suggested there could be regional differences in clinical phenotype of axial spondyloarthritis (axSpA). This analysis aims to explore differences in axSpA clinical phenotype around the world in a large sample of patients included in the International Map of Axial Spondyloarthritis (IMAS).

Methods: IMAS was a cross-sectional online survey (2017-2022) of 5,557 unselected axSpA patients from 27 countries. We analysed across 5 geographic regions the age at onset of symptoms, classification as radiographic or non-radiographic, gender, HLA-B27, axSpA family history, extra-musculoskeletal manifestations (uveitis, inflammatory bowel disease and psoriasis), presence of comorbidities, disease activity (BASDAI), level of spinal stiffness, and treatment (NSAIDs, csDMARDs and bDMARDs). Kruskal-Wallis and chi-square test were used to compare axSpA characteristics across the regions.

Results: 5,557 patients participated in IMAS survey of which 3,493 were from Europe, 770 from North America, 600 from Asia, 548 from Latin America, and 146 from Africa. Results showed statistically significant differences between regions, except for the classification status (radiographic or non-radiographic). Age at onset of symptoms ranged between 25-30 years, and was higher in Latin America as compared to other regions. Diagnostic delay was longest in South Africa and lowest in Asia. The lowest frequency of HLA-B27 positivity was observed in Latin America and the highest in Asia. Family history of SpA was most often recorded in Europeand less often in Asia. All extra-musculoskeletal manifestations included were lowest in Europe compared with other regions. Physical and mental comorbidities were frequent in African patients and less common in Europe and Asia. Mean disease activity (BASDAI) was 5.4, with highest values in South Africa and lowest in Asia. Spinal stiffness was highest in South Africa and lowest in Latin America. Functional limitation was higher in North America and Europe and lower in Asia. Most of the patients had used NSAIDs for their condition and less than half had ever



Map 1. Regional Differences in Clinical Phenotype of Axial Spondyloarthritis

taken csDMARDS; both were more frequent in Latin America and South Africa. Almost half of the patients had ever taken bDMARDs, more frequent being in the Americas (Map 1).

Conclusion: There is great heterogeneity of axSpA clinical phenotype presentation around the world. Further understanding of these differences is needed to achieve early diagnosis and initiation of disease treatment in axSpA.

Disclosure: D. Poddubnyy: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, MoonLake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 2, UCB Pharma, 2, 6; **F. Sommerfleck**: AbbVie/Abbott, 2, 6, Eli Lilly, 6, Janssen, 2, 6, Novartis, 2, 6; **V. Navarro-Compán**: AbbVie, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, Janssen, 6, MoonLake, 2, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6; **C. Bundy**: AbbVie/Abbott, 6, Celgene, 6, Eli Lilly, 6, Janssen, 6, Novartis, 6, Pfizer, 6; **S. Makri**: GlaxoSmithKlein(GSK), 2, Novartis, 2; **S. Murlidhar Akerkar**: Eli Lilly, 6, Janssen, 6, Novartis, 6, Pfizer, 6; **L. Wermskog**: AbbVie/Abbott, 12, Have not received money, have received money Spondyloarthritis associated of Norway received the support, Eli Lilly, 12, Have not received money, have received money Spondyloarthritis associated of Norway received the support, Novartis, 3, 12, Have not received money, have received money Spondyloarthritis associated of Norway received the support, Pfizer, 12, Have not received money, have received money Spondyloarthritis associated of Norway received the support, UCB, 3, 12, Have not received money, have received money Spondyloarthritis associated of Norway received the support; **E. Karam**: None; **J. Correa Fernandez**: None; **A. Siddiqui**: Novartis, 3, 8; **M. Garrido-Cumbrera**: Novartis, 5.

Abstract Number: 2196

Females with Axial Spondyloarthritis Report Higher Burden of Disease and Worse Patient-reported Outcomes. Results from the International Map of Axial Spondyloarthritis (IMAS)

Victoria Navarro-Compán[1], **Marco Garrido-Cumbrera**[2], Denis Poddubnyy[3], Christine Bundy[4], Souzi Makri[5], Jose Correa Fernandez[6], Shashank Murlidhar Akerkar[7], Lillann Wermskog[8], Elie Karam[9], Asif Siddiqui[10] and Fernando Sommerfleck[11], [1]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain, [2]University of Seville, Sevilla, Spain, [3]Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany, [4]Cardiff University, Cardiff, United Kingdom, [5]Cyprus League for People with Rheumatism (CYLPER), Nicosia, Cyprus, [6]Universidad de Sevilla, Health & Territory Research (HTR), Sevilla, Spain, [7]Mumbai Arthritis Clinic, Mumbai, India, [8]Spondyloarthritis Association of Norwary (SPAFO);Axial Spondyloarthritis International Federation (ASIF), Oslo, Norway, [9]Canadian Spondylitis Association (CSA), Toronto, ON, Canada, [10]Novartis Pharma AG, Basel, Switzerland, [11]Sanatorio Julio Mendez, Buenos Aires, Argentina

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: There is increasing evidence of differences between males and females in axial spondyloarthritis (axSpA), but the source is restricted to specific geographic locations or populations. This analysis aims to assess gender differences in a large sample of patients included in the International Map of Axial Spondyloarthritis (IMAS) study from around the globe.

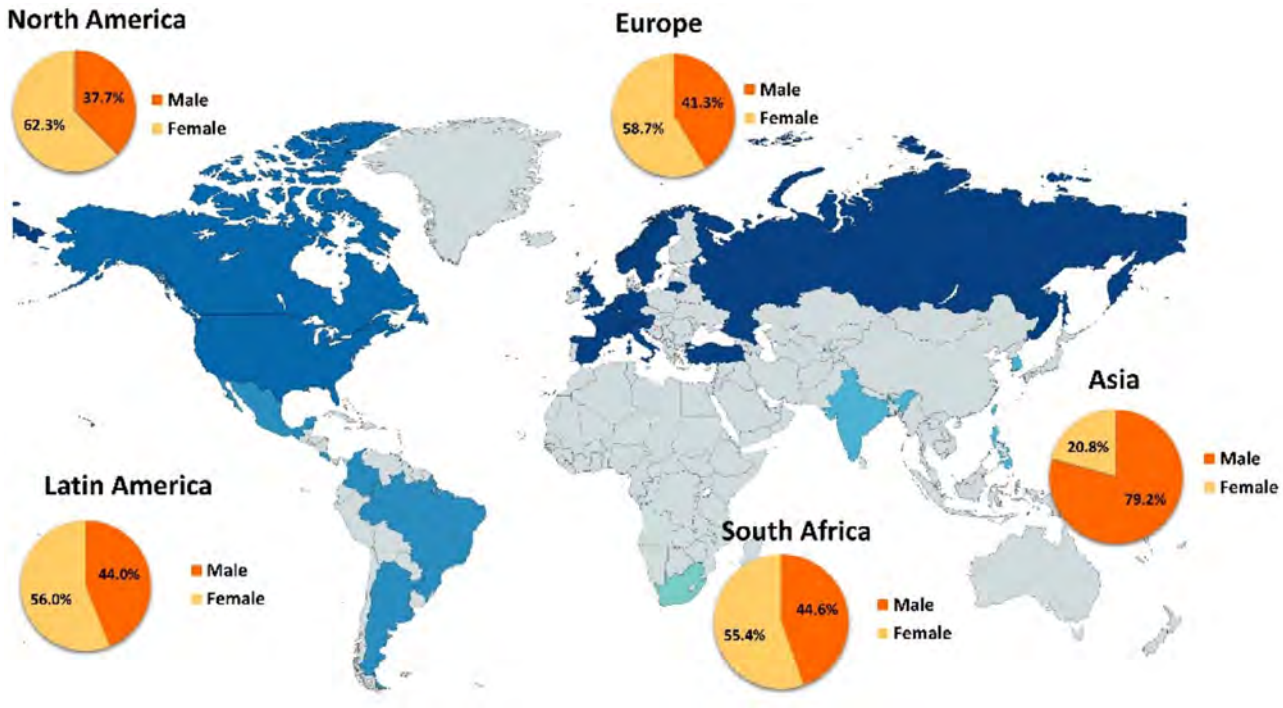


Figure 1. Gender proportion by region (N= 5,555)

Table 1. Patient and disease characteristics in males and females with axSpA (N= 5,555)

	Mean ± SD or n (%)		P-value
	Male 2,475 (44.6%)	Female 3,080 (55.4%)	
Sociodemographic			
Age	44.9 ± 13.6	43.2 ± 12.1	**<0.001**
Patient organization membership	1113 (45.0)	1293 (42.0)	**0.025**
Lifestyle			
Smoking	548 (23.3)	580 (19.7)	**0.002**
Alcohol consumption	823 (33.8)	808 (26.7)	**<0.001**
Disease characteristics			
Diagnostic delay	6.1 ± 7.8	8.5 ± 9.7	**<0.001**
HLA-B27 Positive	1115 (78.9)	1348 (65.8)	**<0.001**
Family history of axSpA	459 (31.4)	752 (39.8)	**<0.001**
Uveitis	564 (25.3)	607 (21.5)	**0.002**
Psoriasis	172 (17.3)	289 (22.7)	**0.002**
Patient-reported outcomes			
Disease activity (0-10)	5.0 ± 2.2	5.7 ± 2.0	**<0.001**
Functional limitation (0-54)	18.1 ± 15.2	21.2 ± 15.3	**<0.001**
Mental health (0-12)	4.2 ± 4.0	5.1 ± 4.1	**<0.001**
Mental comorbidities			
Anxiety	623 (27.0)	1149 (39.2)	**<0.001**
Depression	620 (26.8)	1007 (34.4)	**<0.001**
Sleep disorders	696 (30.3)	1206 (41.4)	**<0.001**
Treatment			
NSAIDs	1729 (75.5)	2190 (81.2)	**<0.001**
csDMARDs	933 (41.3)	1206 (45.5)	**0.003**
bDMARDs	1093 (47.1)	1362 (50.2)	**0.030**

Methods: IMAS is a cross-sectional online survey (2017-2022) of 5,557 unselected axSpA patients from 27 countries. The current analysis looked at the differences in a variety of patient and disease characteristics/assessments between males and females. The factors evaluated were: sociodemographic (age, educational level, marital status, employment status, and patient organization membership), health behaviours (smoking, alcohol consumption, and physical activity), disease characteristics (age at symptom onset, diagnostic delay, HLA-B27, family history of axSpA, uveitis, inflammatory bowel disease), patient-reported outcomes (disease activity [0-10] on the BASDAI scale, spinal stiffness [3-12], functional limitation [0-54], and mental health [0-12] using GHQ-12 scale), mental comorbidities (anxiety, depression, and sleep disorders), and treatments (NSAIDs, csDMARDs and bDMARDs).

Results: Data from 5,555 patients reporting gender were analyzed: 3,492 from Europe, 769 from North America, 600 from Asia, 548 from Latin America, and 146 from Africa. Globally, 55.4% were females, with higher proportions in South Africa (82.2%) and lower in Asia (20.8%; Figure 1). Compared to males, females were of a younger age, more frequently university educated, more often divorced, more commonly on permanent sick leave, and less often members of patient organizations. With respect to health behaviours, male participants smoked and drank more than females.Compared to males, diagnostic delay was significantly longer (by 2.4 years) while the rate of HLA-B27 positivity and family history with axSpA were lower in females. With respect to patient-reported outcomes, females presented with higher disease activity, greater functional limitation, and poorer mental health. The use of axSpA drug treatment was more common in females with a higher proportion having ever taken NSAIDs, csDMARDs and bDMARDS (Table 1).

Conclusion: Globally, females with axSpA practiced better health behaviors and reported lower frequency of HLA-B27 positivity but had longer diagnostic delay. Despite more frequently receiving medication, females presented with higher disease activity, greater functional limitation, and worse mental health. Reducing the disease burden and diagnostic delay in females is crucial to improving axSpA care around the world.

Disclosure: V. Navarro-Compán: AbbVie, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, Janssen, 6, MoonLake, 2, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6; **M. Garrido-Cumbrera**: Novartis, 5; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, MoonLake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 2, UCB Pharma, 2, 6; **C. Bundy**: AbbVie/Abbott, 6, Celgene, 6, Eli Lilly, 6, Janssen, 6, Novartis, 6, Pfizer, 6; **S. Makri**: GlaxoSmithKlein(GSK), 2, Novartis, 2; **J. Correa Fernandez**: None; **S. Murlidhar Akerkar**: Eli Lilly, 6, Janssen, 6, Novartis, 6, Pfizer, 6; **L. Wermskog**: AbbVie/Abbott, 12, Have not received money, have received money Spondyloarthritis associated of Norway received the support, Eli Lilly, 12, Have not received money, have received money Spondyloarthritis associated of Norway received the support, Novartis, 3, 12, Have not received money, have received money Spondyloarthritis associated of Norway received the support, Pfizer, 12, Have not received money, have received money Spondyloarthritis associated of Norway received the support, UCB, 3, 12, Have not received money, have received money Spondyloarthritis associated of Norway received the support; **E. Karam**: None; **A. Siddiqui**: Novartis, 3, 8; **F. Sommerfleck**: AbbVie/Abbott, 2, 6, Eli Lilly, 6, Janssen, 2, 6, Novartis, 2, 6.

Abstract Number: 2197

Diagnostic Delay in Patients Included in the International Map of Axial Spondyloarthrtis: Associations with Geographic, Socio-demographic and Disease-related Factors

Denis Poddubnyy[1], **Marco Garrido-Cumbrera**[2], Fernando Sommerfleck[3], Victoria Navarro-Compán[4], Christine Bundy[5], Souzi Makri[6], Jose Correa Fernandez[7], Shashank Murlidhar Akerkar[8], Jo Davies[9], Laura Christen[10] and Elie Karam[11], [1]Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany, [2]University of Seville, Sevilla, Spain, [3]Sanatorio Julio Mendez, Buenos Aires, Argentina, [4]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain, [5]Cardiff University, Cardiff, United Kingdom, [6]Cyprus League for People with Rheumatism (CYLPER), Nicosia, Cyprus, [7]Universidad de Sevilla, Health & Territory Research (HTR), Sevilla, Spain, [8]Mumbai Arthritis Clinic, Mumbai, India, [9]Axial Spondyloarthritis International Federation (ASIF), London, United Kingdom, [10]Novartis Pharma AG, Basel, Switzerland, [11]Canadian Spondylitis Association (CSA), Toronto, ON, Canada

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Despite efforts for early detection, delayed diagnosis in axial spondyloarthritis (axSpA) remains an unresolved challenge. This analysis aimed to assess diagnostic delay and its associated factors around the world in a large sample of patients included in the International Map of Axial Spondyloarthritis (IMAS).

Methods: IMAS is a cross-sectional online survey (2017-2022) including 5,557 unselected axSpA patients from 27 countries. Diagnostic delay was calculated as the difference between age at diagnosis and age at symptom onset reported by patients. The independent factors evaluated were: age at symptom onset, disease duration, gender, education level, diagnosed by rheumatologist, number of HCPs seen before diagnosis, HLA-B27, uveitis, and inflammatory bowel disease. The factor world region was introduced as a dummy variable taking Europe as the reference region due to its larger sample size and diagnostic delay close to the overall mean. The Mann-Whitney, Kruskal-Wallis test and Pearson correlation were used to evaluate the differences in diagnostic delay and independent variables. Associations between diagnostic delay and regions, sociodemographic characteristics, as well as disease-related factors were explored through univariable and multivariable linear regression analysis.

Results: Data from 5,327 patients who reported data to calculate diagnostic delay in IMAS survey were analyzed: 3,231 were from Europe, 770 from North America, 600 from Asia, 548 from Latin America, and 146 from Africa. Overall, patients reported a diagnostic delay of 7.4 years (median: 4.0) since symptom onset, with substantial variation across regions, being the highest in South Africa and the lowest in Asia (Figure 1). Furthermore, mean disease duration was 17.1 ± 13.3. Patients with longer diagnostic delay were more frequently female, younger at symptom onset, with more years with the condition, more commonly diagnosed by the rheumatologist, with a higher number of HCPs seen before diagnosis, had experienced uveitis, and inflammatory bowel disease. The variables independently associated with longer diagnostic delay in the final multivariable regression model were: younger age at symptom onset (b=-0.100), more disease duration (b=0.363), female gender (b=2.274), being diagnosed by rheumatologist (b=1.163), higher number of healthcare professionals (HCPs) seen before diagnosis (b=1.033), and presence of uveitis (b=1.286; Table 1).

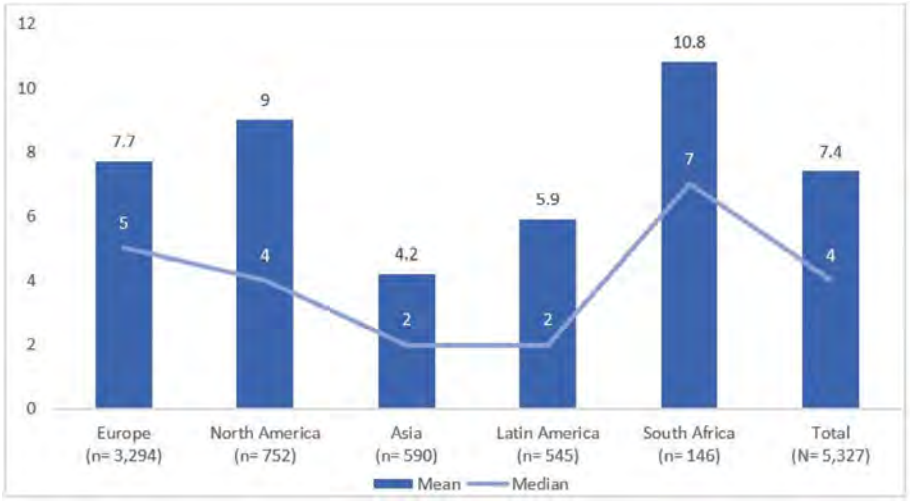


Figure 1. Mean and median diagnostic delays by region (N= 5,327)

Table 1. Univariable and multivariable linear regression analysis of the association between diagnostic delay and independent variables in patients with axial spondyloarthritis (N= 4,595)

Variables	Ref.	Univariable analysis		Multivariable analysis	
		B	95% CI	B	95% CI
Age at symptom onset, years	-	**-0.306**	**-0.326, -0.287**	**-0.100**	**-0.120, -0.080**
Disease duration	-	**0.401**	**0.386, 0.416**	**0.363**	**0.346, 0.380**
Female gender	Male	**2.324**	**1.843, 2.804**	**2.274**	**1.860, 2.687**
Diagnosed by rheumatologist, yes	No	**2.410**	**1.868, 2.952**	**1.163**	**0.710, 1.615**
No. of HCPs seen before diagnosis	-	**1.696**	**1.520, 1.873**	**1.033**	**0.877, 1.189**
Uveitis	No	**1.580**	**0.996, 2.165**	**1.286**	**0.808, 1.764**
Inflammatory bowel disease	No	**0.834**	**0.117, 1.550**	-0.043	-0.610, 0.525
Region, Asia	Europe	**-3.511**	**-4.241, -2.781**	**1.003**	**0.334, 1.673**
Region, North America		**1.228**	**0.499, 1.958**	**1.470**	**0.902, 2.039**
Region, Latin America		**-1.792**	**-2.583, -1.000**	0.626	-0.045, 1.297
Region, South Africa		**3.015**	**1.549, 4.481**	**3.356**	**2.170, 4.541**

Conclusion: In this global sample of axSpA patients, the mean diagnostic delay was 7.4 years, and had significant differences across regions. Younger age at symptom onset, longer disease duration, female gender, diagnosed by rheumatologist, higher number of HCPs seen before diagnosis, and the presence of uveitis were the parameters associated with a longer diagnostic delay in axSpA patients.

Disclosure: D. Poddubnyy: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, MoonLake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 2, UCB Pharma, 2, 6; **M. Garrido-Cumbrera**: Novartis, 5; **F. Sommerfleck**: AbbVie/Abbott, 2, 6, Eli Lilly, 6, Janssen, 2, 6, Novartis, 2, 6; **V. Navarro-Compán**: AbbVie, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, Janssen, 6, MoonLake, 2, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6; **C. Bundy**: AbbVie/Abbott, 6, Celgene, 6, Eli Lilly, 6, Janssen, 6, Novartis, 6, Pfizer, 6; **S. Makri**: GlaxoSmithKlein(GSK), 2, Novartis, 2; **J. Correa Fernandez**: None; **S. Murlidhar Akerkar**: Eli Lilly, 6, Janssen, 6, Novartis, 6, Pfizer, 6; **J. Davies**: AbbVie/Abbott, 12, No personal funding, but ASIF has received funding from Abbvie, Boehringer-Ingelheim, 12, No personal funding, but ASIF has received funding from Boehringer Ingleheim, Eli Lilly, 12, No personal funding, but ASIF has received funding from Lilly, Janssen, 12, No personal funding, but ASIF has received funding from Janssen, Novartis, 12, No personal funding, but ASIF has received funding from Novartis, Pfizer, 12, No personal funding, but ASIF has received funding from Pfizer, UCB, 12, No personal funding, but ASIF has received funding from UCB; **L. Christen**: Novartis, 3; **E. Karam**: None.

Abstract Number: 2198

Which Factors Are Associated with Clinically High Disease Activity in Axial Spondyloarthritis? Results from the International Map of Axial Spondyloarthritis (IMAS)

Marco Garrido-Cumbrera[1], Victoria Navarro-Compán[2], Fernando Sommerfleck[3], Christine Bundy[4], Souzi Makri[5], Jose Correa Fernandez[6], Shashank Murlidhar Akerkar[7], Jo Davies[8], Elie Karam[9], Asif Siddiqui[10] and Denis Poddubnyy[11], [1]University of Seville, Sevilla, Spain, [2]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain, [3]Sanatorio Julio Mendez, Buenos Aires, Argentina, [4]Cardiff University, Cardiff, United Kingdom, [5]Cyprus League for People with Rheumatism (CYLPER), Nicosia, Cyprus, [6]Universidad de Sevilla, Health & Territory Research (HTR), Sevilla, Spain, [7]Mumbai Arthritis Clinic, Mumbai, India, [8]Axial Spondyloarthritis International Federation (ASIF), London, United Kingdom, [9]Canadian Spondylitis Association (CSA), Toronto, ON, Canada, [10]Novartis Pharma AG, Basel, Switzerland, [11]Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Active axial spondyloarthritis (axSpA) is associated with poorer physical and mental health outcomes. This study aims to assess the prevalence of clinically active disease in axSpA and its associated factors in a large sample of patients from the International Map of Axial Spondyloarthritis (IMAS) study from around the globe.

Methods: IMAS is a cross-sectional online survey (2017-2022) including 5,557 unselected axSpA patients. Patients were divided between those with active disease (BASDAI < 4) and those without active disease (BASDAI ≥ 4). The factors evaluated were: age, gender, physical activity engagement, work-related issues, work choice and difficulty finding a job due to axSpA, number of self-reported symptomatic body regions, diagnostic delay, HLA-B27, extra-musculoskeletal manifestations, spinal stiffness (3-12), functional limitation (0-54), mental health using GHQ-12 scale (0-12), and treatments

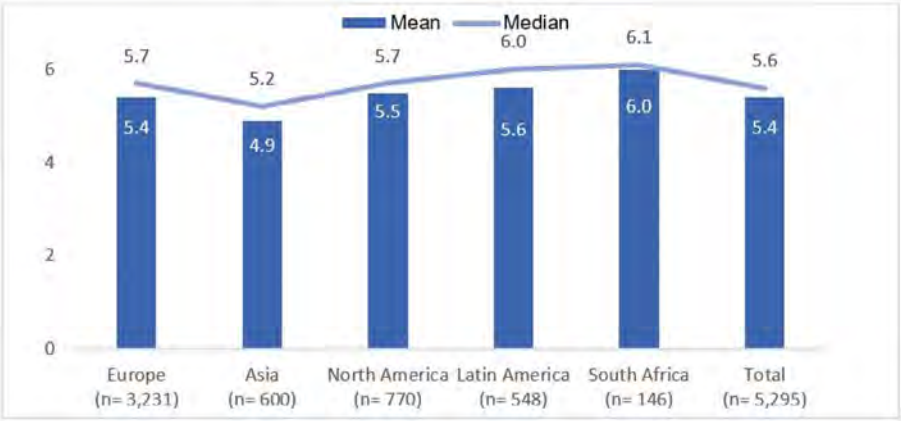


Figure 1. Mean and median of disease activity by region (N= 5,295)

(NSAIDs, csDMARDs and bDMARDs). Mann-Whitney, chi-square test and logistic regression analysis were used to evaluate the possible association of the investigated factors with active disease in axSpA patients.

Results: 5,295 patients who had responded to the BASDAI scale in IMAS survey were included in the present study: 3,231 were from Europe, 770 from North America, 600 from Asia, 548 from Latin America, and 146 from Africa. The mean age was 43.8±12.9 years and 55.4% were females. Patient reported a mean BASDAI of 5.4 (median 5.6; Figure 1) with 75% having active disease (BASDAI≥4). In South Africa, 87.0% of patients reported having active disease, compared to 68.5% in Asia. Compared to patients with non-active disease, patients with active disease were more likely to be older, female, physically inactive, experience work-related issues, have greater difficulty finding a job and faced limited work choice due to axSpA, had higher number of self-reported symptomatic body regions, longer diagnostic delay, higher proportion of HLA-B27 negative, presence of inflammatory bowel disease, greater spinal stiffness, higher functional limitation, worse mental health, and greater use of csDMARDs. In the multivariable logistic regression, the factors associated with active disease were the presence of work-related issues due to axSpA, difficulty finding a job due to axSpA, higher number of self-reported symptomatic

Table 1. Logistic regression analysis to determine factors associated with active disease (N= 2,630)

	Univariable logistic regression		Multivariable logistic regression	
	OR	CI 95%	OR	CI 95%
Age	0.99	**0.98, 0.99**	0.99	0.98, 1.01
Gender, Female	1.95	**1.72, 2.21**	1.14	0.84, 1.56
Physical activity engagement, No	1.34	**1.12, 1.59**	1.19	0.77, 1.85
No. of self-reported symptomatic body regions	1.12	**1.11, 1.14**	1.08	**1.04, 1.11**
Spinal Stiffness (3-12)	1.39	**1.35, 1.43**	1.37	**1.27, 1.47**
Functional Limitation (0-54)	1.05	**1.04, 1.05**	1.02	**1.01, 1.03**
Diagnostic Delay	1.01	**1.01, 1.02**	0.98	**0.96, 0.99**
HLA-B27, Negative	1.47	**1.22 1.76**	1.48	**1.06, 2.08**
Inflammatory bowel disease, Yes	1.82	**1.48, 2.23**	1.43	0.90, 2.28
Difficulty finding a job due to axSpA, Yes	5.08	**4.38, 5.90**	1.92	**1.38, 2.68**
Work-related issues due to axSpA, Yes	3.16	**2.70, 3.69**	1.73	**1.22, 2.44**
Work choice due to axSpA, Yes	2.10	**1.84, 2.41**	1.03	0.75, 1.41
Mental health GHQ-12 scores (0-12)	1.27	**1.24, 1.29**	1.20	**1.14, 1.26**
Use of csDMARDs	1.18	**1.03, 1.35**	1.11	0.82, 1.49

body regions, greater spinal stiffness, higher functional limitation, longer diagnostic delay, HLA-B27 negative, and worse mental health (Table 1).

Conclusion: Globally, three in four patients with axSpA reported clinically active disease, with higher proportion of patients with active disease in South Africa and lower in Asia. The causal relationship between the identified factors and clinical disease activity is complex and may vary from patient to patient. Our results underline the complexity of the clinical disease activity concept in axSpA and underline the need of a holistic approach in the patient management.

Disclosure: M. Garrido-Cumbrera: Novartis, 5; **V. Navarro-Compán**: AbbVie, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, Janssen, 6, MoonLake, 2, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6; **F. Sommerfleck**: AbbVie/Abbott, 2, 6, Eli Lilly, 6, Janssen, 2, 6, Novartis, 2, 6; **C. Bundy**: AbbVie/Abbott, 6, Celgene, 6, Eli Lilly, 6, Janssen, 6, Novartis, 6, Pfizer, 6; **S. Makri**: GlaxoSmithKlein(GSK), 2, Novartis, 2; **J. Correa Fernandez**: None; **S. Murlidhar Akerkar**: Eli Lilly, 6, Janssen, 6, Novartis, 6, Pfizer, 6; **J. Davies**: AbbVie/Abbott, 12, No personal funding, but ASIF has received funding from Abbvie, Boehringer-Ingelheim, 12, No personal funding, but ASIF has received funding from Boehringer Ingleheim, Eli Lilly, 12, No personal funding, but ASIF has received funding from Lilly, Janssen, 12, No personal funding, but ASIF has received funding from Janssen, Novartis, 12, No personal funding, but ASIF has received funding from Novartis, Pfizer, 12, No personal funding, but ASIF has received funding from Pfizer, UCB, 12, No personal funding, but ASIF has received funding from UCB; **E. Karam**: None; **A. Siddiqui**: Novartis, 3, 8; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, MoonLake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 2, UCB Pharma, 2, 6.

Abstract Number: 2199

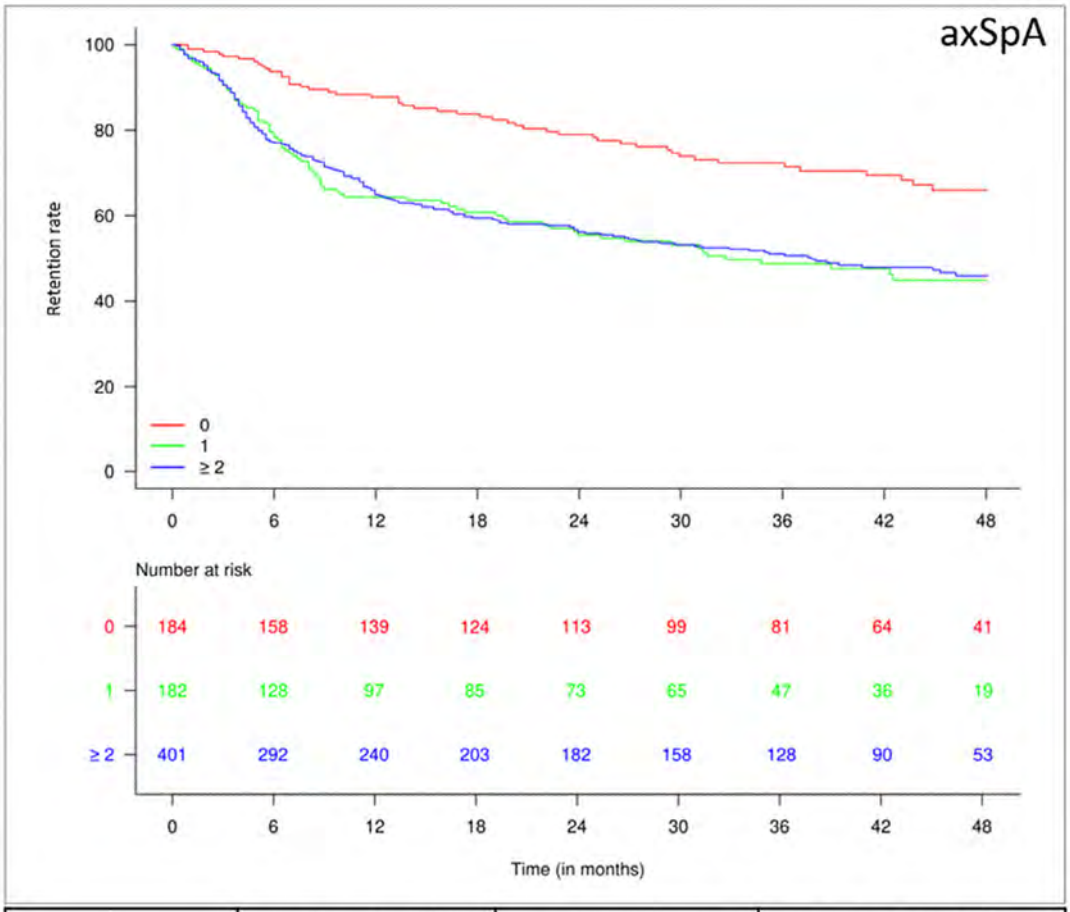
Four-year Secukinumab Treatment Outcomes in Axial Spondyloarthritis and Psoriatic Arthritis Patients Treated in Routine Care: Results from the EuroSpA Collaboration

Marion Pons[1], Stylianos Georgiadis[1], Zohra Faizy Ahmadzay[2], Mikkel Østergaard[3], Bente Glintborg[1], Jette Heberg[1], Sara Nysom Christiansen[1], Simon Horskjær Rasmussen[1], Isabel Castrejon[4], Fernando Alonso[5], Karin Laas[6], Sigrid Vorobjov[7], Nikita Khmelinskii[8], Jakub Zavada[9], Adrian Ciurea[10], Michael Nissen[11], Brigitte Michelsen[12], Pawel Mielnik[13], Anne Gitte Loft[14], Ziga Rotar[15], Katja Perdan Pirkmajer[16], Gary Macfarlane[17], Gareth T. Jones[17], Dan Nordstrom[18], Anna-Mari Hokkanen[19], Irene van der Horst-Bruinsma[20], Johan Karlsson Wallman[21], Bjorn Gudbjornsson[22], olafur Palsson[23], Merete Hetland[1] and Lykke Ørnbjerg[1], [1]Copenhagen Center for Arthritis Research, Rigshospitalet, Copenhagen, Denmark, [2]Rigshospitalet Glostrup, University of Copenhagen, Glostrup, Denmark, [3]Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Centre for Head and Orthopaedics, Rigshospitalet; University of Copenhagen, Copenhagen, Denmark, [4]Hospital Universitario Gregorio Marañón, Madrid, Spain, [5]Spanish Society of Rheumatology, Madrid, Spain, [6]Department of Rheumatology, East-Tallinn Central Hospital, Tallinn, Estonia, [7]National Institute for Health Development, Tallinn, Estonia, [8]Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal, [9]Institute of Rheumatology; Charles University, Prague, Czech Republic, [10]University Hospital Zurich, Zürich, Switzerland, [11]Geneva University Hospitals, Geneva, Switzerland, [12]Rigshospitalet Glostrup; Diakonhjemmet Hospital; Sørlandet Hospital, Copenhagen, Denmark, [13]Section for Rheumatology, Helse Førde, Førde, Norway, [14]Aarhus University, Horsens, Denmark, [15]University Medical Centre Ljubljana, Ljubljana, Slovenia, [16]University Medical Centre Ljubljana; University of Ljubljana, Ljubljana, Slovenia, [17]Aberdeen Centre for Arthritis and Musculoskeletal Health (Epidemiology Group), University of Aberdeen, Aberdeen, United Kingdom, [18]Helsinki University Hospital, Helsinki, Finland, [19]Departments of Medicine and Rheumatology, Helsinki University Hospital, Helsinki, Finland, [20]Rheumatology, Radboud University Medical Center, Nijmegen, Netherlands, [21]Lund University and Skåne University Hospital, Lund, Sweden, [22]Centre for Rheumatology Research, University Hospital, Reykjavik, Iceland, [23]Faculty of Medicine, University of Iceland, Reykjavik, Iceland

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) are part of the spondylarthritis spectrum that can be treated with secukinumab, a fully human IgG1 monoclonal antibody targeting interleukin-17A. Real-word data on long-term secukinumab effectiveness in these two diseases are limited. In separate cohorts of axSpA and PsA patients treated with secukinumab in routine care, we aimed to assess a) 24-, and 48-month retention rates; and b) proportions of patients achieving 24-, and 48-month composite scores of remission and response.

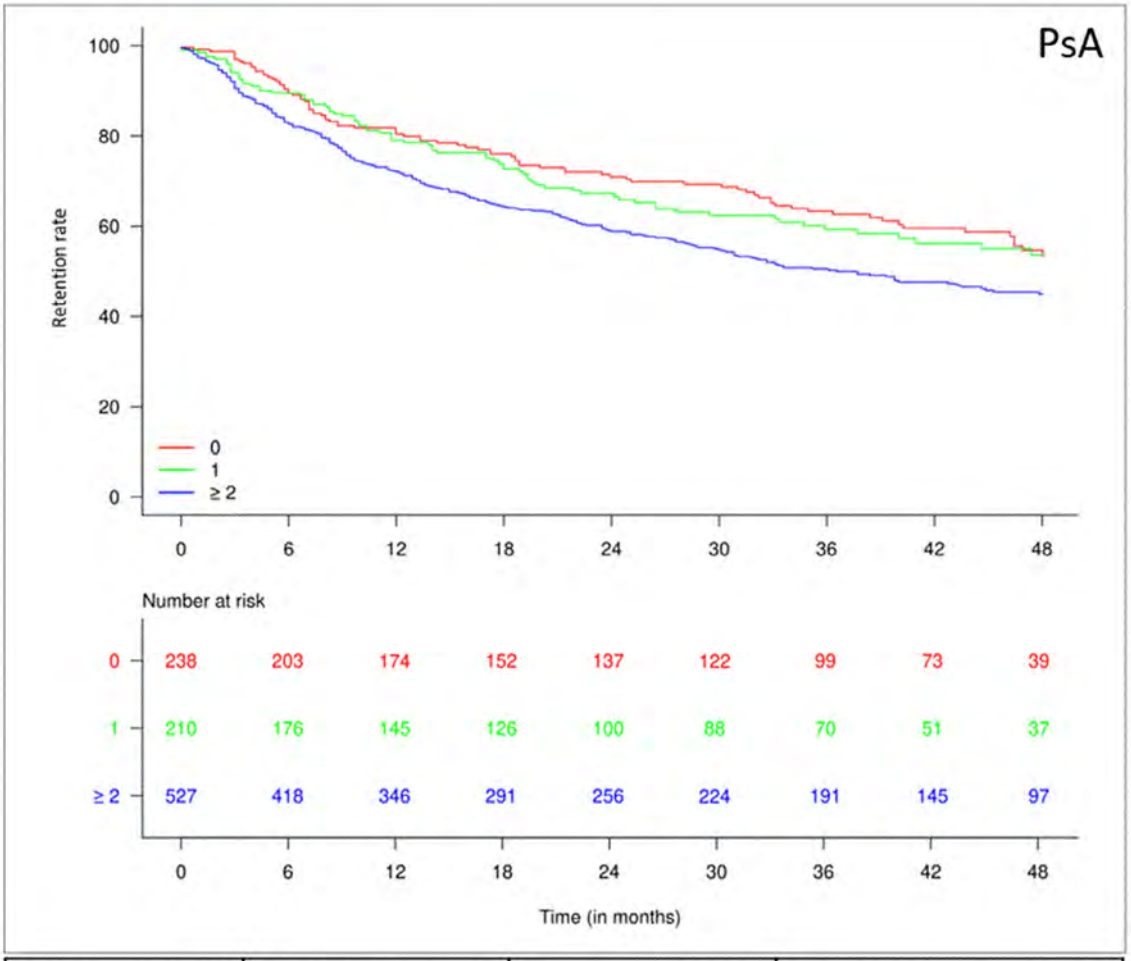


	Number of previous b/tsDMARDS	Retention rates	Fully adjusted* HR ref. b/tsDMARD naïve
24 months	b/tsDMARD naïve	79.0%	
	1 prior b/tsDMARD	55.5%	**2.59 [1.69-3.96], p<0.001**
	≥2 prior b/tsDMARDs	56.1%	**2.38 [1.58-3.59], p< 0.001**
48 months	b/tsDMARD naïve	66.0%	
	1 prior b/tsDMARD	44.8%	**2.13 [1.47-3.08], p<0.001**
	≥2 prior b/tsDMARDs	46.0%	**1.92 [1.35-2.73], p<0.001**

* Values adjusted for age, gender, register, time since diagnosis and baseline ASDAS-CRP. Values in bold indicate statistically significant results.

Figure 1: The 48-month retention rate for secukinumab in axSpA patients, stratified according to the number of previous b/tsDMARDs

Methods: Patients with axSpA and PsA who initiated secukinumab were included from 13 registriesparticipating in the European Spondyloarthritis (EuroSpA) Research Collaboration Network [1]. Kaplan-Meier plots with log-rank tests and Cox regression analyses were performed to assess 24-, and 48-month secukinumab retention rates overall, and compared by prior b/tsDMARD status (0/1/≥2). Comparisons of remission and response rates according to b/tsDMARDs status, were performed by logistic regression adjusted for age, gender, register, time since diagnosis and disease activity at treatment start (baseline). Missing baseline data were imputed by multivariate imputation by chained equations.



	Number of previous b/tsDMARDS	Retention rates	Fully adjusted* HR ref. b/tsDMARD naïve
24 months	b/tsDMARD naïve	70.9%	
	1 prior b/tsDMARD	67.2%	0.81 [0.46-1.44], p=0.47
	≥2 prior b/tsDMARDs	58.9%	1.32 [0.83-2.10], p=0.25
48 months	b/tsDMARD naïve	53.2%	
	1 prior b/tsDMARD	53.6%	0.94 [0.58-1.52], p=0.79
	≥2 prior b/tsDMARDs	44.9%	1.23 [0.81-1.86], p=0.33

** Values adjusted for age, gender, register, time since diagnosis and baseline DAPSA28.

Figure 2: The 48-month retention rate for secukinumab in PsA patients, stratified according to the number of previous b/tsDMARDs

Table 1: Composite score remission and response rates in axSpA and PsA patients treated with secukinumab

axSpA patients N=767					PsA patients N= 975				
Composite score remission and response rate		Crude (%)	N available	Fully adjusted* OR [95% CI] ref. b/tsDMARDs naive	Composite score remission and response rate		Crude (%)	N available	Fully adjusted** OR [95% CI] ref. b/tsDMARDs naive
ASDAS-CRP LDA (<2.1) 24 months	b/tsDMARD naïve (n=184)	60	70	Reference	DAPSA28 LDA (≤14) 24 months	b/tsDMARD naïve (n=238)	49	85	Reference
	1 prior b/tsDMARD (n=182)	51	45	0.79 [0.32-1.98], p=0.62		1 prior b/tsDMARD (n=210)	42	77	0.61 [0.30-1.26], p=0.18
	≥ 2 prior b/tsDMARD (n=401)	25	123	**0.33 [0.14-0.78], p=0.01**		≥2 prior b/tsDMARD (n=527)	38	203	0.73 [0.39-1.36], p=0.32
ASDAS-CRP LDA (<2.1) 48 months	b/tsDMARD naïve (n=184)	59	41	Reference	DAPSA28 LDA (≤14) 48 months	b/tsDMARD naïve (n=238)	57	42	Reference
	1 prior b/tsDMARD (n=182)	37	19	**0.23 [0.05-0.98], p=0.05**		1 prior b/tsDMARD (n=210)	53	30	0.86 [0.28-2.65], p=0.79
	≥ 2 prior b/tsDMARD (n=401)	37	52	0.30 [0.09-1.03], p=0.06		≥2 prior b/tsDMARD (n=527)	41	92	0.76 [0.29-2.01], p=0.58
ASDAS-CRP CII (≥1.1) 24 months	b/tsDMARD naïve (n=184)	75	53	Reference	DAPSA28 moderate response (75%) 24 months	b/tsDMARD naïve (n=238)	49	61	Reference
	1 prior b/tsDMARD (n=182)	48	33	0.81 [0.21-3.04], p=0.75		1 prior b/tsDMARD (n=210)	15	54	1.17 [0.24-5.57], p=0.85
	≥ 2 prior b/tsDMARD (n=401)	32	93	0.43 [0.13-1.41], p=0.16		≥2 prior b/tsDMARD (n=527)	15	166	0.31 [0.08-1.25], p=0.10
ASDAS-CRP CII (≥1.1) 48 months	b/tsDMARD naïve (n=184)	81	31	Reference	DAPSA28 moderate response (75%) 48 months	b/tsDMARD naïve (n=238)	39	33	Reference
	1 prior b/tsDMARD (n=182)	54	13	0.22 [0.02-1.97], p=0.17		1 prior b/tsDMARD (n=210)	24	21	3.50 [0.43-28.26], p=0.23
	≥ 2 prior b/tsDMARD (n=401)	40	40	0.21 [0.03-1.39], p=0.10		≥2 prior b/tsDMARD (n=527)	18	78	0.95 [0.19-4.82], p=0.95

* Values adjusted for age, gender, register, time since diagnosis and baseline ASDAS-CRP. ** Values adjusted for age, gender, register, time since diagnosis and baseline DAPSA28. OR, Odds Ratio; CI, Confidence Interval; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score- C reactive protein; DAPSA28, Disease Activity index for PSoriatic Arthritis in 28 joints; bDMARD, biologic Disease-Modifying Anti-Rheumatic drugs; tsDMARD, targeted synthetic Disease-Modifying Anti-Rheumatic drugs; LDA, Low Disease Activity; CII, Clinically Important Improvement. Values in bold indicate statistically significant results. N, number.

Results: A total of 767 axSpA and 975 PsA patients from 13 and 12 countries, respectively, were included. At baseline, axSpA patients had a median (IQR) age of 47 (38-55) years, were predominantly male (60%), and had high disease activity (median (IQR)Ankylosing Spondylitis Disease Activity Score (ASDAS)-CRP 3.6 (2.9-4.2)). PsA patients had a median (IQR) age of 52 (44-59) years, were predominantly female (56%), and had moderate disease activity (median (IQR) Disease Activity index for PSoriatic Arthritis in 28 joints (DAPSA28) 25.1 (16.7-37.3)). The overall 24-/48-month secukinumab retention rates were 61%/51% in axSpA, and 63%/49% in PsA patients, respectively. The 24-/48-month secukinumab retention rates in axSpA were significantly higher in bio-naïve patients than in patients treated with 1 or ≥2 prior b/tsDMARDs (Figure 1). In PsA patients, both 24-/48-month secukinumab retention rates were similar between bio-naïve patients and patients who previously received 1 prior b/tsDMARD, and numerically lower in patients having received ≥2 b/tsDMARDs (Figure 2). In axSpA patients, ASDAS-CRP low disease activity (LDA) and ASDAS-CRP clinically important improvement (CII) crude rates were numerically higher in the bio-naïve group at 24 and 48 months. After confounder adjustment, bio-naïve patients had higher rates of ASDAS-CRP LDA than patients who had previously received one or more b/tsDMARDs (Table 1). Similarly, the crude proportions of PsA patients achieving DAPSA28 LDA or moderate response were numerically (but not statistically significantly) higher in the bio-naïve group (Table 1).

Conclusion: This large real-life study showed that secukinumab retention rates after four years wereapproximately 50% in patients with axSpA and PsA. Bio-naïve patients had higher retention, remission and response rates than patients with prior b/tsDMARD exposure, particularly in axSpA.

References 1 https://eurospa.eu/.

Disclosure: M. Pons: Novartis, 5; **S. Georgiadis**: Novartis, 5; **Z. Faizy Ahmadzay**: Novartis, 5; **M. Østergaard**: AbbVie, 2, 5, 6, Amgen, 5, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Hospira, 2, 6, Janssen, 2, 6, MEDAC, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Novo Nordisk, 2, 6, Orion, 2, 6, Pfizer, 2, 6, Regeneron, 2, 6, Roche, 2, 6, Sandoz, 2, 6, Sanofi, 2, 6, UCB, 2, 6; **B. Glintborg**: AbbVie/Abbott, 5, Pfizer, 5, Sandoz, 5; **J. Heberg**: Novartis, 5; **S. Nysom Christiansen**: Novartis, 5, 6; **S. Horskjær Rasmussen**: Novartis, 5; **I. Castrejon**: Bristol Myers Squibb, 1, 6, Galapagos, 2, GlaxoSmithKline, 1, 6, Lilly, 1, 6, Merck Sharp & Dohme, 6, Pfizer, 1, 2, 6; **F. Alonso**: None; **K. Laas**: None; **S. Vorobjov**: None; **N. Khmelinskii**: None;

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Abstract Number: 2200

Sensitivity to Change of Structural Outcomes in Early Axial Spondyloarthritis After 10 Years of Follow Up. Data from DESIR Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The change over time of the structural damage of axial spondyloarthritis (axSpA) is important to consider since it may reflect the severity of the disease. In axSpA this structural damage can be evaluated either at the sacroiliac joints (SIJ) or spine level, and also either on conventional radiographs or Magnetic Resonance Imaging (MRI). The

Table. Sensitivity of change of the structural lesions.

	Imaging outcome	Standardized RoC per year	Relative standardized RoC	Relative standardized RoC per anatomic site
SIJ radiographs	mNY dichotomous	0.043	1 (reference)	1 (reference)
	mNY 1-grade change	0.045	1.047	1.047
	mNY 1-grade change and value >=2	0.048	1.116	1.116
	mNY continuous grade (range 0-8)	0.107	2.488	2.488
SIJ MRI	≥5 fatty lesions and/or erosions	0.165*	3.837	3.837
	≥3 erosions	0.030	0.670	0.670
	≥3 fatty lesions	0.227*	5.279	5.279
	No. of erosions (range 0-40)	0.038	0.884	0.884
	No. of fatty lesions (range 0-40)	0.192	4.465	4.465
	Total structural lesions (range 0-144)	0.099	2.302	2.302
Spine radiographs	≥1 syndesmophyte	0.076	1.767	1 (reference)
	mSASSS score (range 0-72)	0.134	3.116	1.763
Spine MRI	≥5 fatty lesions	-0.068*	1.581	0.089
	Total structural lesions (range 0-322)	0.059*	1.372	0.776
	No. of fatty lesions (range 0-92)	0.064*	1.488	0.842
	No. of corner erosions (range 0-92)	0.020*	0.465	0.263
	No. of corner bone spurs (range 0-92)	0.057	1.326	0.750

*Quadratic distribution

objective of this study was to evaluate the sensitivity to change of different structural imaging outcomes over 10 years of follow-up in patients with early axSpA.

Methods: Patients from the DESIR inception cohort (≤3 years of symptoms) axSpA (according to the treating rheumatologist) from the DESIR cohort were included. Radiographs and MRI of the SIJ and spine were obtained at baseline, 1, 2, 5 and 10 years. Images were scored in four separate reading waves by 3 trained central readers (wave 1 only 2 readers with one adjudicator) unaware of chronology. The yearly rate of change (RoC) of each outcome was analyzed using generalized estimation equations (GEEs) including all patients with ≥1 score from ≥1 reader from ≥1 wave and using time (years) as explanatory variable and adjusting for reader and wave. All outcomes (Table) were standardized (difference between the individual's value and the population mean divided by the population SD). In addition, the relative standardized RoC (i.e., the standardized yearly RoC of an outcome divided by the corresponding rate of a reference imaging outcome) was calculated, with a value >1 reflecting larger sensitivity, and < 1 lower sensitivity compared to the reference. Finally, the relative standardized ROC per anatomic site was calculated.

Results: A total of 704 patients (46% males and mean age 33.7 years) were included. Among all locations and modalities, the change in ≥3 fatty lesions was the outcome with the highest sensitivity to change (standardized RoC 0.227 per year). The two most sensitive to change outcomes in SIJ (both MRI and radiographs) were ≥3 fatty lesions, with a standardized RoC per year of 5.279, which is 5.3 times higher than the RoC of the definitive damage on pelvic radiographs according to the modified New York criteria (mNY) criteria (reference), followed by the absolute number of fatty lesions also 4.5 times more sensitive than the reference. Similarly, the most sensitive to change lesion in the spine (both MRI and radiographs) was the mSASSS score, which was 1.8 times more sensitive than the reference, i.e. ≥1 syndesmophyte.

Conclusion: MRI structural outcomes in the SIJ, in particular fatty lesions, are more sensitive to change than radiographic outcomes. On the other hand, mSASSS remains the most sensitive method, even if compared to MRI of the spine.

Disclosure: C. López Medina: AbbVie, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 6, MSD, 6, Novartis, 2, 5, 6, UCB Pharma, 2, 5, 6; **A. Molto**: None; **A. Sepriano**: None; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, Galapagos, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, UCB Pharma, 2, 5; **M. Dougados**: AbbVie, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Roche, 2, 5, UCB, 2, 5.

Abstract Number: 2201

When Usual Care Is Not so Usual: Facing the Challenges of Protocol Violations and Generalisability When Running a Strategy Trial. the Example of the Cluster-Randomized TICOSPA Trial

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Despite the ASAS-HI (primary outcome) did not reach statistical significance in the TICOSPA trial, other secondary outcomes were numerically higher in the treat-to-target (T2T) strategy in comparison to Usual Care (UC). Three hypotheses have been considered to explain this: a lack of power, the risk of protocol violations in the T2T arm and the potential optimal care in the UC arm. *Objectives:* a) to evaluate the proportion of patients (pts) who violated the protocol in the T2T arm during the 48 weeks (48W) of follow up as well as the impact and predictive factors of such violation; b) to compare the proportion of pts treated according to the ASAS/EULAR 2016 management recommendations for axSpA over the first 12W of follow-up period in both arms.

Methods: *Study design:* pragmatic, prospective, cluster-randomized controlled, 48W trial (NCT03043846). *Inclusion criteria*: Pts with a diagnosis of axSpA and fulfilling ASAS criteria, non-optimally treated with NSAIDs, bDMARD-naïve and ASDAS >2.1. *Study treatment regimens:*SpA expert centers were randomly allocated (1:1) to the treatment arm: a) T2T: pre-specified management strategy (Q4W visits), with a target of ASDAS< 2.1; b) UC: treatment decisions at the rheumatologist's discretion (Q12W). *Outcome:* Protocol violations in the T2T arm were evaluated at every visit by a specific question. *Statistical analysis*: Factors associated with at least one protocol violation over the study were evaluated using multivariate logistic regression. Outcomes at 48W were compared between T2T violators (T2T-V) vs. T2T non-violators (T2T-NV) vs. UC using GEE models adjusted by country and sex; b) *optimal care in UC:* proportion of pts treated according to the 2016 ASAS/EULAR recommendations over the first 12W in both arms were compared.

Table. Impact of protocol violation on the efficacy outcomes at week 48.

	T2T-NV N = 39	T2T-V N = 41	UC* N = 80	T2T-NV vs. T2T-V P-value	T2T-NV vs. UC P-value	T2T-V vs. UC P-value
ASAS-HI improvement W48	14 (35.9%)	16 (39.0%)	21 (26.6%)	0.773	0.299	0.160
ASAS20 W48	33 (84.6%)	33 (80.5%)	61 (77.2%)	0.640	0.340	0.650
ASAS40 W48	14 (35.9%)	16 (39.0%)	19 (24.1%)	0.773	0.180	0.089
BASDAI50 W48	24 (61.5%)	21 (51.2%)	25 (31.6%)	0.314	**0.002**	**0.037**
ASDAS-CII W48	22 (56.4%)	16 (39.0%)	26 (32.9%)	0.149	**0.022**	0.500
ASDAS-MI W48	6 (15.4%)	8 (19.5%)	9 (11.4%)	0.442	0.709	0.190
ASDAS-LDA W48	24 (61.5%)	19 (46.3%)	32 (40.5%)	0.377	0.081	0.451
ASDAS-ID W48	11 (28.2%)	8 (19.5%)	10 (12.7%)	0.730	0.130	0.299

*79 patients as denominator in the UC group. Generalized Estimating Equation (GEE) models using the group as dependent variable and the disease activity outcome as covariate. All comparisons have been adjusted by country and sex.

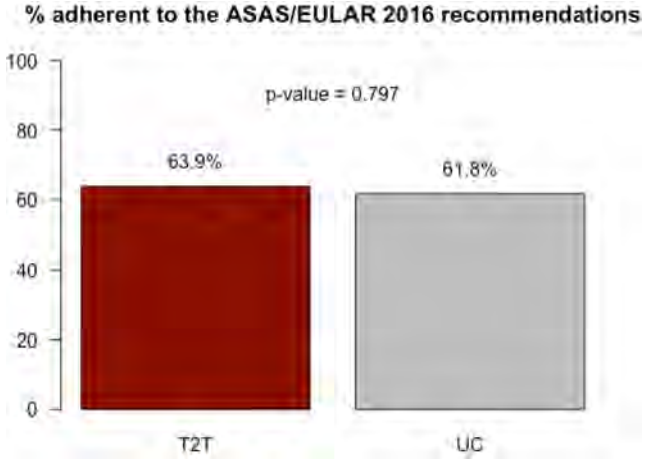

Figure. Proportion of patients treated according to the ASAS/EULAR 2016 management recommendations for axSpA in both groups during the first 12 weeks of follow-up.

Results: 160 pts initiated the trial (T2T:80 and UC:80). *a) Protocol violations:* In the T2T arm, 41/80 (51.2%) pts violated the protocol during at least one visit, with a total of 119 violations (27.7% represented by an intensification of bDMARD and 62.2% by a maintenance or reduction of the treatment against protocol). Baseline predictive factors independently associated with the protocol violation were the country (France vs. others; OR 3.8 (95%CI 1.1-15.0)), female sex (OR 4.4 (1.5-15.1)), diagnosis delay ≤7 years (OR 3.4 (1.1-11.9)), HLA-B27 negative (OR 6.4 (1.6-32.2)) and CRP≥6mg/L (OR 4.2 (1.3-15.9)). After 48W of follow-up, T2T-NV vs. T2T-V showed similar ratios of ASAS-HI improvement. ASDAS-LDA, ASDAS-ID and ASDAS-CII outcomes were more prevalent in T2T-NV vs. T2T-V, although they did not reach statistical significance (Table). b) *Optimal care in UC*: the proportion of pts managed according to the 2016 ASAS/EULAR recommendations during the first 12W of follow-up was similar in both arms (63.9% in T2T vs. 61.8% in UC, p=0.490) (Figure).

Conclusion: These results confirm that protocol violations in the T2T arm in the TICOSPA trial were frequent, although they did not have an impact on the rate of the primary outcome. The proportion of patients managed according to the 2016 ASAS/EULAR recommendations in the UC arm was very high, suggesting that the UC group was optimally treated and explaining the non-achievement of the primary objective in the TICOSPA trial.

Disclosure: C. López Medina: AbbVie, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 6, MSD, 6, Novartis, 2, 5, 6, UCB Pharma, 2, 5, 6; **F. Van den Bosch**: AbbVie, 2, 6, Amgen, 2, BMS, 6, Celgene, 6, Eli Lilly, 2, Galapagos, 2, Janssen, 2, 6, Merck, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB Pharma, 2, 6; **D. van der Heijde**: AbbVie, 2, Bayer, 2, BMS, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GSK, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; **M. Dougados**: AbbVie, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Roche, 2, 5, UCB, 2, 5; **A. Molto**: None.

Abstract Number: 2202

Deucravacitinib, an Oral, Selective, Allosteric Tyrosine Kinase 2 Inhibitor, in Patients with Moderate to Severe Psoriasis: Long-Term Efficacy in Placebo Crossovers

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Deucravacitinib, a first-in-class, oral, selective, allosteric tyrosine kinase 2 inhibitor, is approved in multiple countries for the treatment of adults with plaque psoriasis; it is currently being investigated in several immune-mediated diseases and has shown efficacy in phase 2 trials for SLE and PsA (NCT03252587 and NCT03881059, respectively). Deucravacitinib was superior to placebo and apremilast in the global, 52-week, phase 3 POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751) trials in moderate to severe plaque psoriasis. Patients who completed

PSO-1 and PSO-2 could enroll in the ongoing POETYK long-term extension (LTE) trial (NCT04036435). Patients treated with continuous deucravacitinib in PSO-1 maintained long-term efficacy responses through week 112. In the present analysis, we assessed the efficacy of deucravacitinib for up to 112 weeks among patients from PSO-1 who crossed over from placebo to deucravacitinib at week 16.

Methods: Patients in PSO-1 were randomized 1:2:1 to oral placebo, deucravacitinib 6 mg once daily (QD), or apremilast 30 mg twice daily. Patients randomized to placebo at baseline crossed over to deucravacitinib at week 16. At week 52, patients who completed the parent trial were able to enroll in the LTE trial and receive open-label deucravacitinib 6 mg QD. Efficacy outcomes included ≥ 75%/≥ 90% reductions from baseline in Psoriasis Area and Severity Index (PASI 75/90) and static Physician's Global Assessment (sPGA) score of

0 (clear) or 1 (almost clear) with a ≥ 2-point improvement from baseline. Efficacy is reported using modified nonresponder imputation; patients who had not reached the week 112 assessment or had not discontinued as of October 1, 2021, were excluded. As-observed data and results by treatment failure rule imputation were also analyzed.

Results: At week 16, PASI 75, PASI 90, and sPGA 0/1 response rates in patients treated with placebo were 12.7%, 4.2%, and 7.2%, respectively. A total of 126 patients randomized to placebo at baseline crossed over to deucravacitinib at week 16 and received open-label deucravacitinib in the LTE through week 112. At week 112, PASI 75 and PASI 90 response rates were 81.4% and 50.6%, respectively, and the sPGA 0/1 response rate was 58.2%. These results were similar to those at week 112 in patients who were treated with deucravacitinib from day 1.

Conclusion: Deucravacitinib treatment is associated with long-term efficacy in patients who originally received placebo and crossed over to deucravacitinib after 16 weeks in PSO-1, with results replicating those with continuous deucravacitinib treatment from day 1. These findings further indicate that the once-daily, oral treatment of deucravacitinib is an effective long-term therapy for moderate to severe plaque psoriasis.

Disclosure: R. Warren: AbbVie, 2, 5, 6, Almirall, 2, 5, 6, Amgen, 2, 5, 6, Arena, 2, 6, Astellas, 2, 6, Avillion, 2, 6, Biogen, 2, 6, BMS, 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 5, DiCE, 6, Eli Lilly, 2, 5, 6, GSK, 2, 6, Janssen, 2, 5, 6, LEO Pharma, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sanofi, 2, 6, Sun Pharma, 6, UCB Pharma, 2, 5, 6, Union, 6; **M. Lebwohl**: Mark Lebwohl is an employee of Mount Sinai and receives research funds from Abbvie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Cara therapeutics, 2; **S. Imafuku**: AbbVie, 5, Amgen (Celgene), 12, Personal fees, Boehringer Ingelheim, 12, Personal fees, Bristol Myers Squibb, 12, Personal fees, Daiichi Sankyo, 12, Personal fees, Eisai, 5, Eli Lilly, 12, Personal fees, GSK, 12, Personal fees, Janssen, 5, Kyowa Kirin, 5, Leo Pharma, 5, Maruho, 5, Novartis, 12, Personal fees, Sun Pharma, 5, Taiho Yakuhin, 5, Tanabe Mitsubishi, 5, Torii Yakuhin, 5, UCB, 12, Personal fees; **J. Bagel**: AbbVie, 2, 6, 12, Research funds, Amgen, 2, 12, Research funds, Arcutis, 12, Research funds, Boehringer-Ingelheim, 12, Research funds, Bristol-Myers Squibb(BMS), 12, Research funds, Celgene, 2, 6, 12, Research funds, CorEvitas' (Corrona) Psoriasis Registry, 12, Research funds, Dermavant, 12, Research funds, Dermira/UCB, 12, Research funds, Eli Lilly, 2, 6, 12, Research funds, Glenmark, 12, Research funds, Janssen Biotech, 2, 6, 12, Research funds, Kadmon, 12, Research funds, Leo Pharma, 12, Research funds, Lycera, 12, Research funds, Menlo Therapeutics, 12, Research funds, Novartis, 2, 6, 12, Research funds, Pfizer, 12, Research funds, Regeneron, 12, Research funds, Sun Pharma, 2, 12, Research funds, Taro, 12, Research funds, Valeant, 2, 12, Research funds; **A. Armstrong**: AbbVie, 5, Almirall, 1, 6, Arcutis, 1, 6, Aslan Pharmaceuticals, 1, 1, 6, 6, Beiersdorf, 1, 6, Boehringer Ingelheim/Parexel, 12, Personal fees, Bristol-Myers Squibb(BMS), 5, Celgene, 12, Personal fees, Dermavant, 1, 6, 12, Personal fees, Dermira, 1, 5, 6, Eli Lilly, 5, EPI Health, 1, 6, Genentech, 12, Personal fees, GSK, 12, Personal fees, Incyte, 1, 6, Janssen, 5, Kyowa Kirin, 5, Leo Pharma, 5, Lilly, 1, 6, Menlo Therapeutics, 12, Personal fees, Merck, 12, Personal fees, Mindera Health, 1, 6, Modernizing Medicine, 12, Personal fees, Nimbus, 1, 6, Novartis, 5, Ortho Dermatologics, 12, Personal fees, Pfizer, 12, Personal fees, Regeneron, 12, Personal fees, Sanofi Genzyme, 12, Personal

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Abstract Number: 2203

Self-Reported and Physician's Assessment of Inflammatory Back Pain According to ASAS Criteria: Is It the Same?

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammatory back pain (IBP) is the core symptom in patients with axial spondyloarthritis (axSpA). For its assessment, experts recommend using the Assessment of SpondyloArthritis International Society (ASAS) criteria. Advances in telemedicine and online screening strategies require to evaluate whether self-reported perform equally to

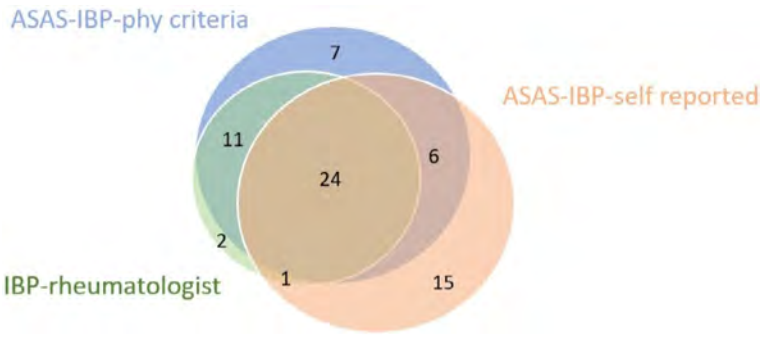

Figure. Number of patients showing IBP by each method of assessment

Table. Utility measures for each IBP assessment method to capture IBP according to rheumatologist judgement

	ASAS-IBP-phy criteria	ASAS-IBP-self reported
Accuracy	0.89	0.78
Sensitivity	0.89	0.81
Specificity	0.92	0.66
Negative Predictive Value	0.73	0.54
Positive Predictive Value	0.97	0.87

physicians' assessment.The objective of this study is to assess the agreement and correlation between self-reported and physician´s assessments of ASAS IBP criteria and evaluate their performance compared with rheumatologist´s judgement for IBP.

Methods: The "Strategy for a Hospital Early Referral in Patients with Axial Spondyloarthritis" (SHERPAS) is a prospective ongoing study recruiting young patients (18 to 40 years) with chronic back pain asked to undergo an MRI of the spine by other specialists different than rheumatologists in a tertiary hospital, starting in September 2021. After inclusion, an additional MRI of the sacroiliac joints (SIJ), followed by a rheumatology visit and eligible blood tests were performed. IBP was assessed in 3 different independent ways: i) ASAS criteria asked verbatim by the rheumatologist (ASAS-IBP-phy criteria), ii) ASAS criteria embedded in a self-reported questionnaire (ASAS-IBP-self reported), and iii) according to rheumatologist judgement in the interview (IBP-rheumatologist). Dataset for this interim analysis was locked in October 2022. Kappa statistic (κ) and tetrachoric correlation coefficient (rt) were calculated to assess the agreement and correlation between ASAS-IBP-phy criteria and ASAS-IBP-self reported. Overall accuracy, sensitivity, specificity, positive and negative predictive values for each IBP assessment method were calculated, using IBP-rheumatologist as gold standard.

Results: Among 152 recruited patients, 85 (55.9%) were female; mean (SD) age was 34.2 (5.3) years. 66/152 (43.4%) patients reported IBP by at least one of the three assessments, and 24 (15.8%) patients presented back pain as assessed by the three methods altogether. Venn diagrams representing the overlap between the different IBP assessments are shown in Figure. A moderate agreement (κ =0.48) and strong correlation (rt=0.7) were found between ASAS-IBP-self reported and ASAS-IBP-phy criteria. While ASAS-IBP-phy criteria showed a strong level of agreement and very strong correlation with IBP- rheumatologist (κ = 0.74, rt= 0.94), ASAS-IBP-self reported showed a moderate agreement and moderate correlation with this outcome (κ = 0.44, rt=0.67). ASAS-IBP-phy criteria showed better performance than ASAS-IBP-self reported for capturing IBP- rheumatologist [accuracy of 0.89 (95%CI 0.83- 0.94) vs 0.77 (95%CI 0.70- 0.84)] (Table).

Conclusion: ASAS criteria to define IBP show higher level of agreement and correlation with IBP rheumatologist overall judgement when assessed by physician as compared to a self-reported assessment. These results call for caution when extrapolating use of experts IBP criteria from clinical to online setting and suggest that clinicians should prioritize physician assessment over self-report to define this.

Disclosure: D. Benavent: Abbvie, 5, Galapagos, 6, Janssen, 6, Novartis, 5, Roche, 6; **M. Tapia**: None; **D. Bernabeu**: None; **V. muley**: None; **C. Plasencia-Rodríguez**: Abbvie, 5, 6, Eli Lilly, 6, Novartis, 5, Pfizer, 5, 6, Roche, 6; **A. Balsa**: AbbVie/Abbott, 1, 2, 5, 6, Bristol-Myers Squibb(BMS), 1, 5, Eli Lilly, 1, 5, 6, Merck/MSD, 1, 5, Novartis, 5, Pfizer, 1, 5, 6, UCB, 1, 5, 6; **V. Navarro-Compán**: AbbVie, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, Janssen, 6, MoonLake, 2, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 6.

Abstract Number: 2204

Residual Disease Activity in Canadian Patients with Axial Spondyloarthritis: Results from a Multi-registry Analysis (UNISON-Axial SpA)

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Session Time: 9:00AM–11:00AM

Background/Purpose: In patients with axial spondyloarthritis (axSpA), treatment goals consist of achieving remission or low disease activity (LDA) to alleviate symptoms, improve function, decrease disease complications, and forestall skeletal damage. Notably, it has been shown that failure to achieve Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) < 3 leaves significant disease activity for patients. No studies have yet used patient information from multiple Canadian rheumatology registries to better understand outcomes and unmet needs in patients with axSpA. The objective of this study was to describe residual disease activity in Canadians with axSpA treated with currently available therapies.

Methods: This is a multi-registry, observational, retrospective analysis of data extracted from the Rhumadata™ (Quebec), SPARCC (East/Atlantic and West regions, and Ontario), and FORCAST (Alberta) registries. Data were extracted for up to 12 months of the latest axSpA therapy initiation in adult patients between January 2010 and December 2020. The primary endpoint was the proportion of patients who failed to achieve sustained LDA at 12 months; LDA was defined as a BASDAI score < 3, and sustained LDA defined as achieving LDA at both 6 and 12 months. A secondary endpoint further described the proportion of patients who failed to achieve sustained LDA with a definition of BASDAI score < 4. Analyses included outcomes by treatment class (NSAIDs, TNFi, or IL-17i) and number of prior advanced therapies. Data from each registry and region were analyzed separately using a standard set of inclusion/exclusion criteria and statistical analysis plan.

Results: A total of 980 patients (Rhumadata™, N=488; SPARCC, N=239; FORCAST, N=253) were included. The mean age of patients ranged from 40.9 to 44.2 years, with a majority of male and HLA-B27 positive patients overall (Table 1). Mean time since diagnosis ranged from 5.1 to 10.6 years. In all 3 registries, most patients had failed NSAIDs and were receiving their first advanced therapy. The most common current advanced therapy class used was TNFi (Table 1) with less than 10% of patients receiving IL-17i.Nearly half of all patients from Rhumadata™ and FORCAST and 66% of those from SPARCC failed to achieve LDA (BASDAI < 3) at 6 months. At 12 months, failure to achieve sustained LDA ranged from 62.0% in Rhumadata to 81.0% in SPARCC (Table 1). This trend persisted even when using a less stringent definition to measure sustained LDA (BASDAI < 4). Small sample sizes from the West (n=12) and East/Atlantic (n=6) in SPARCC prevented reliable assessments in these regions.

Conclusion: This analysis demonstrated that most Canadians with axSpA failed to achieve sustained LDA after 12 months of initiating therapy. The variations seen in this analysis may reflect distinct regional patient profiles, differing prior biologic treatments at study entry, different provincial reimbursement criteria, or lack of standardized measurements. There is significant residual disease activity and a high unmet need for improved therapeutic approaches and patient outcomes for Canadians living with axSpA.

Table 1. Patient Demographics, Baseline Characteristics, and Response to Treatment, by Registry

	Rhumadata	SPARCC			FORCAST
	Quebec (N=488)	West (N=12)	Ontario (N=221)	East/Atlantic (N=6)	Alberta (N=253)
Age, mean (SD), years	44.1 (12.9)	44.2 (16.7)	43.5 (12.8)	40.9 (16.3)	41.3 (12.8)
Male, n (%)	282 (57.8)	8 (66.7)	123 (55.7)	3 (50.0)	185 (73.1)
BMI, mean (SD), kg/m^2	27.2 (6.0)	24.7 (2.8)	28.2 (6.5)	32.0 (6.6)	28.5 (5.9)
N	375	8	102	5	253
Time since diagnosis, mean (SD), years	6.2 (8.6)	7.4 (8.8)	10.6 (11.1)	5.1 (4.8)	8.3 (10.6)
N	488	12	196	5	253
HLA-B27 positive, n (%)	293 (60.0)	10 (83.3)	160 (74.4)	5 (83.3)	192 (75.9)
N	488	12	215	6	253
Current therapy class, n (%)					
NSAIDs	23 (4.7)	3 (25.0)	72 (32.6)	3 (50.0)	38 (15.0)
TNFi (original/brand)	383 (78.5)	9 (75.0)	122 (55.2)	3 (50.0)	211 (83.4)
TNFi (biosimilar)	41 (8.4)	0 (0.0)	8 (3.6)	0 (0.0)	0 (0.0)
IL-17i	41 (8.4)	0 (0.0)	19 (8.6)	0 (0.0)	3 (1.2)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Number of prior advanced therapies, n (%)					
0	289 (59.2)	10 (83.3)	129 (58.4)	6 (100.0)	223 (88.1)
1	116 (23.8)	2 (16.7)	35 (15.8)	0 (0.0)	27 (10.7)
2	50 (10.3)	0 (0.0)	28 (12.7)	0 (0.0)	2 (0.8)
>3	33 (6.8)	0 (0.0)	29 (13.1)	0 (0.0)	1 (0.4)
Failure to achieve LDA (BASDAI<3) at 6 months, n (%)	99 (49.5)	0 (0.0)	52 (65.8)	0 (0.0)	89 (55.3)
N	200	0	79	0	161
Failure to achieve LDA (BASDAI<3) at 12 months, n (%)	127 (52.7)	6 (54.6)	129 (63.9)	0 (0.0)	40 (46.5)
N	241	11	202	5	86
Failure to achieve sustained LDA (BASDAI<3) at 12 months, n (%)*	85 (62.0)	0 (0.0)	64 (81.0)	0 (0.0)	56 (65.1)
N	137	0	79	0	86
Failure to achieve sustained LDA (BASDAI<3) at 12 months, by therapy class, n (%)					
NSAIDs	3 (3.5)		17 (26.6)		1 (1.8)
N	85	-	64	-	56
TNFi (original/brand)	62 (72.9)		32 (50.0)		54 (96.4)
N	85	-	64	-	56
TNFi (biosimilar)	10 (11.8)		4 (6.2)		0 (0.0)
N	85	-	64	-	56
IL-17i	10 (11.8)		11 (17.2)		1 (1.8)
N	85	-	64	-	56
Failure to achieve LDA (BASDAI<4) at 6 months, n (%)	75 (37.5)	0 (0.0)	43 (54.4)	0 (0.0)	74 (46.0)
N	200	0	79	0	161
Failure to achieve LDA (BASDAI<4) at 12 months, n (%)	92 (38.2)	3 (27.8)	97 (48.0)	0 (0.0)	25 (29.1)
N	241	11	202	5	86
Failure to achieve sustained LDA (BASDAI<4) at 12 months, n (%)*	66 (48.2)	0 (0.0)	54 (68.4)	0 (0.0)	41 (47.7)
N	137	0	79	0	86

Abbreviations: BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index; HLA, human leukocyte antigen; IL, interleukin; LDA, low disease activity; N/A, not available; NSAID, nonsteroidal anti-inflammatory drug; SD, standard deviation; TNFi, tumor necrosis factor inhibitor.
* Not all patients had assessment of disease activity.

Disclosure: D. Choquette: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Eli Lilly, 2, 5, 6, Fresenius-Kabi, 2, 5, 6, JAMP pharma, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sandoz, 2, 5, 6, Tevapharm, 2, 5, 6; **W. Maksymowych**: AbbVie, 2, 5, 6, BMS, 2, 6, Boehringer-Ingelheim, 2, CARE Arthritis Ltd, 4, CARE Arthritis Ltd., 4, Celgene, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **P. Rahman**: AbbVie, 2, Amgen, 2, Bristol Myers Squibb, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, UCB, 2; **R. Inman**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Sandoz, 2; **M. Laliberté**: AbbVie, 3, 11; **P. Fournier**: AbbVie, 3, 11; **T. Girard**: AbbVie, 3, 11; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, Gilead Sciences, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5.

Abstract Number: 2205

Disease Activity and Widespread Pain Are the 2 Key Drivers of Global Health in Axial Spondyloarthritis, with Similar Findings in Different Patient Populations: An Analysis of 4 Databases and 6064 Patients

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Axial Spondyloarthritis (axSpA) is a chronic inflammatory disease affecting global functioning and health (GH). GH, a concept linked to health-related quality of life, is multifactorial in axSpA. On top of the disease itself, chronic widespread pain, comorbidities, and patient-related factors seem to play a role in GH [1]. Our objective was to assess the relative importance of factors associated with GH in axSpA.

Methods: This was a post-hoc cross-sectional analysis of 4 databases, for patients fulfilling ASAS criteria for axSpA, and with available GH scores: COMOSPA (N= 2756 patients analysed) and PERSPA (N= 2651) international cross-sectional studies; DESIR at 7 years (N= 284), a French inception cohort, and COMEDSPA (N= 373) at baseline, a French randomized

Table 1: Multivariable logistic models of factors associated to GH in axSpA.

Dataset	COMOSPA	PERSPA	COMEDSPA	DESIR
N patients	2756	2651	373	284
ASDAS	4.48 [3.80; 5.32]	2.60 [2.25; 3.01]	3.42 [1.96; 6.30]	3.90 [1.51; 11.39]
Widespread pain construct	2.19 [1.39; 3.56]	4.39 [3.35; 5.76]	4.11 [1.96; 8.78]	8.39 [2.07; 38.08]
Currently unemployed	1.67 [1.33; 2.13]	1.69 [1.33; 2.17]	4.76 [2.22; 10.00]	NS
Depression construct	1.93 [1.28; 2.92]	6.04 [3.83; 9.77]	NS	NS
b/ts DMARD intake	1.56 [1.22; 1.99]	NS	4.37 [1.59; 14.43]	NS
Current enthesitis	1.44 [1.03; 2.00]	1.34 [1.06; 1.70]	NS	NS
Current arthritis	2.25 [1.65; 3.07]	NS	NS	NS
Comorbidities RDCI	1.43 [1.22; 1.67]	NA	NS	NS
Obesity (BMI≥ 30kg/m²)	NS	NS	2.61 [1.13; 6.01]	NS
Age, years	1.01 [1.00; 1.03]	NS	NS	NS
CRP (per 10 mg/L increase)	0.54 [0.48; 0.61]	0.92 [0.88; 0.96]	NS	0.05 [0.00; 0.57]

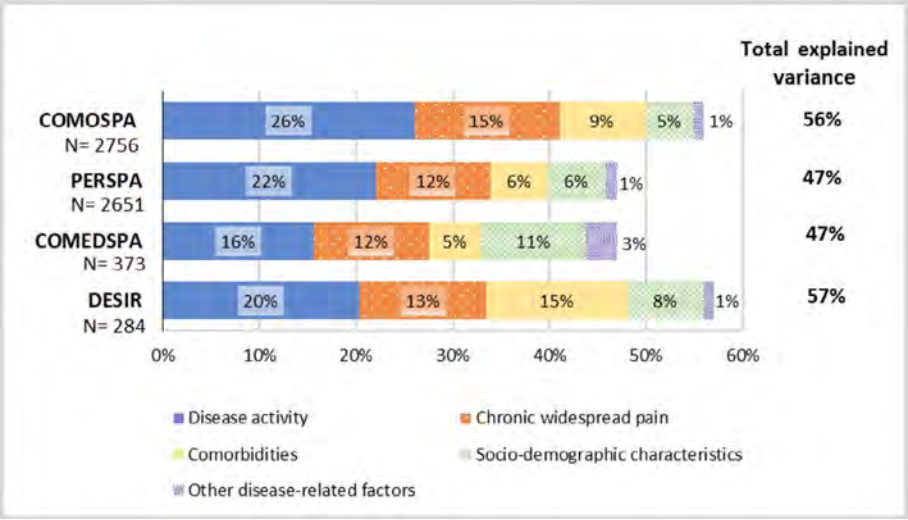

Figure 1: Relative variance of GH explained by each group of variables in the 4 datasets. RDCI was not available in PERSPA, diagnostic delay was not available in COMEDSPA and bamboo spine was not included in DESIR. Percentages are the proportion of the partial variance explained by each group of variables, relative to the total explained variance.

control trial. GH was assessed through the ASAS Health Index (ASAS-HI), range 0-17; in COMOSPA we used the EuroQoL-5D-3L (EQ-5D) since ASAS-HI was not available. Altered GH was defined by ASAS-HI ≥ 10 according to its graphical distribution and quartiles distribution in the datasets; a ROC curve of EQ-5D corresponding to this cut-off was obtained, and the Youden index that maximizes sensitivity and specificity was computed: thus, altered GH was defined by EQ-5D< 0.597. Disease-related factors included (a) disease activity: ASDAS, CRP, current psoriasis, current arthritis, current enthesitis; (b) other disease-related factors: disease duration, diagnostic delay, structural damage (bamboo spine), and bDMARD use. Non-disease-related factors included (a) sociodemographic data (sex, age, employment status and educational level), (b) comorbidities (Rheumatic Disease Comorbidity Index RDCI, obesity and depression) and (c) the construct of chronic widespread pain. Bivariate and multivariate logistic and linear regression were performed in each dataset. Partial R^2 explored the proportion of variance explained by groups of variables, relative to the total explained variance, in each dataset.

Results: In 6064 patients, mean age ranged from 38.9 to 45.8 years, 51.1%- 67.7% were male, 42.0%- 66.1% were in high disease activity, and 14.2%- 24.2% were screened positively for chronic widespread pain. GH was generally moderate to good: median ASAS-HI ranged from 5.0 to 7.0. In all, 47.0%, 29.1%, 23.1% and 16.5% patients had altered GH in COMOSPA, PERSPA, COMEDSPA and DESIR respectively. Altered GH was explained in all databases (multivariable logistic regression) by: ASDAS (odds ratio, OR, ranging 2.60-4.48) and chronic widespread pain (OR 2.19-8.39) **(Table1)**, and 47%-57% of GH was explained by the models (total variance of GH, linear regression). Disease activity (partial $R^{2,}$ 16%-26%) and chronic widespread pain (partial R^2 12%- 15%) were the key variables explaining GH (**Figure 1**).

Conclusion: Overall, 16 to 47% axSpA patients reported altered GH in this large population. Two elements were consistently associated to altered GH and together were the key variables explaining GH: higher ASDAS and chronic widespread pain. Our results allow to attribute a relative role to groups of variables to explain GH in axSpA. These results may be helpful for patient-physician communication and shared decision-making. (1) MacFarlane et al, Ann Rheum Dis 2020 ;79 :202-8

Disclosure: J. Drouet: None; **C. López Medina**: AbbVie, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 6, MSD, 6, Novartis, 2, 5, 6, UCB Pharma, 2, 5, 6; **B. Granger**: Bristol-Myers Squibb(BMS), 2; **B. Fautrel**: AbbVie, 2, BMS, 2, Chugai, 2, Fresenius Kabi, 2, Galapagos, 2, Lilly, 2, Medac, 2, Nordic Pharma, 2, Novartis, 2, Pfizer, 2, Sobi, 2, UCB, 2; **A. Molto**: None; **C. Gaujoux Viala**: AbbVie/Abbott, 2, Amgen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, Janssen, 2, Medac, 2, Merck-Serono, 2, Mylan, 2, Nordic Pharma, 2, Novartis,

2, Pfizer, 2, Roche-Chugai, 2, Sandoz, 2, Sanofi, 2, UCB Pharma, 2; **U. Kiltz**: AbbVie, 2, 5, 6, Amgen, 5, Biocad, 2, 6, Biogen, 5, Bristol-Myers Squibb(BMS), 2, 5, Chugai, 2, 6, Eli Lilly, 2, 6, Fresenius, 5, Gilead, 2, 5, GlaxoSmithKline (GSK), 5, Grünenthal, 2, 6, Hexal, 5, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, onkowiessen.de, 2, 5, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Viatris, 2, 5; **M. Dougados**: AbbVie, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Roche, 2, 5, UCB, 2, 5; **L. Gossec**: AbbVie, 2, 12, Personal fees, Amgen, 2, Biogen, 5, BMS, 12, Personal fees, Celltrion, 12, Personal fees, Eli Lilly, 5, 12, Personal fees, Galapagos, 12, Personal fees, Janssen, 12, Personal fees, MSD, 12, Personal fees, Novartis, 5, 12, Personal fees, Pfizer, 12, Personal fees, Sandoz, 5, 12, Personal fees, UCB Pharma, 5, 12, Personal fees.

Abstract Number: 2206

Increased Frequency of Activated MAIT Cells Expressing the Gut Homing Receptor CCR9 in Patients with Radiographic Axial Spondyloarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: MAIT (mucosal associated invariant T) cells are involved in mucosa defense against bacteria. This cellular subset is characterized by a semi-invariant αβ TCR and the expression of CD161. In patients with axial spondyloarthritis (ax SpA), previous works reported a decreased frequency of circulating MAIT cells compared to normal subjects. IL-17A is a relevant cytokine involved in SpA pathophysiology. MAIT cells are a cellular source of IL-17 and IL-17$^+$ MAIT cells were found increased in ax SpA. We have previously reported an increased frequency of IFNγ$^+$/IL-17$^+$ MAIT cells as well as IL-22$^+$ MAIT cells in ax SpA.

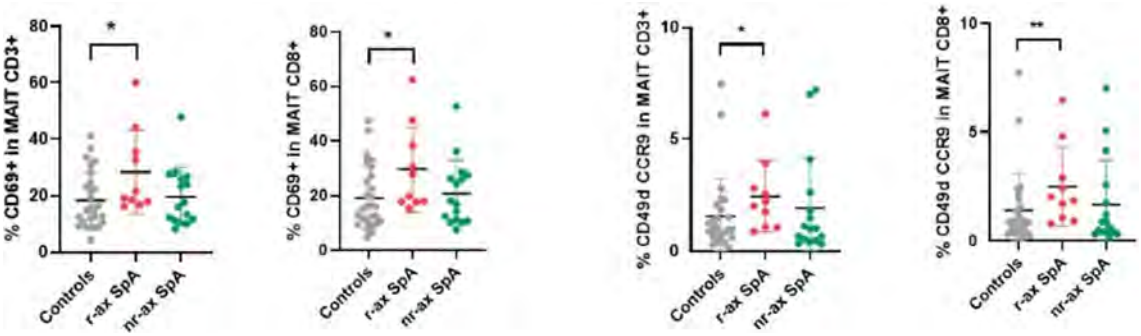
In this study, we aimed to complete our previous results by evaluating activation markers and chemokine receptor/integrin expression, especially those for gut homing, in MAIT cells.

Methods: patients exhibited ax SpA (ASAS criteria) with a radiographic (r-ax SpA) or non-radiographic (nr-ax SpA) form. They all were under NSAIDs and biologic naïve. Healthy subjects were recruited as controls (HC). Circulating CD4$^+$and CD8$^+$T cells and MAIT cells were determined on blood samples by single platform flow cytometry (Cytoflex, Beckman Coulter). MAIT cells were identified by the co-expression of CD3, CD161 and TCRα7.2. In each subpopulation, we examined the expression of CD26, CD69, CCR9 and CD49d integrin.

Results: 26 patients were included (11 r-ax SpA: 9 males [M]; mean age 54.1 ± 19.6 years; disease duration: 16.2 years; ASDAS score: 4.1; and 15 nr-ax SpA: 7 M; age: 36.4 ± 1.3; ASDAS: 5.6) and 27 HC (16 M; age: 43 ± 12.7). In patients with r-ax SpA, we observed an increased frequency of activated CD3$^+$ CD69$^+$ MAIT cells and CD3$^+$ MAIT cells expressing the gut

Table

	Healthy Controls	r-ax SpA	nr-ax SpA
% CD69$^+$ MAIT CD3$^+$	18.4 ± 9.9	**28.3** ± 14.7 *	19.7 ± 10.3
% CD69$^+$ MAIT CD8$^+$	19.1 ± 11.4	**29.5** ± 15.6 *	20.8 ± 12.0
% CD49d$^+$CCR9$^+$ MAIT CD3$^+$	1.6 ± 1.7	**2.5** ± 1.6 *	1.9 ± 2.3
% CD49d$^+$CCR9$^+$ MAIT CD8$^+$	1.4 ± 1.7	**2.5** ± 1.8**	1.7 ± 2



homing markers CCR9 and CD49d, as compared to HC ($p < 0.05$). These higher frequencies were not observed in patients with nr-ax SpA. In addition, when examining the $CD8^+$ MAIT population, similar higher frequencies of cells positive for CD69, CCR9 and CD49d were observed in patients with r-ax SpA compared to HC and patients with nr-ax SpA ($p< 0.01$ and $p< 0.05$, respectively).These modifications were specific for MAIT cells and were not observed in conventional $CD4^+$ or $CD8^+$ T lymphocytes.

Conclusion: patients with r-ax SpA are characterized by an increased frequency of activated MAIT cells that expressed homing receptors (chemokine and integrin) for the gut. These results suggest an involvement of this cellular population in the gut-joint axis that is well described in the pathophysiology of SpA.

these results confirm that MAIT cells are altered in ax SpA and highlight the relationships between ax SpA and gut inflammation, especially for the radiographic form.

Disclosure: E. Toussirot: None; **C. Laheurte**: None; **E. Gravelin**: None; **C. Vauchy**: None; **M. Puyraveau**: None; **P. Saas**: None.

Abstract Number: 2207

Knowledge, Awareness, and Attitudes Regarding Inflammatory Back Pain Among Non-Rheumatology Physicians in the United States

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammatory back pain (IBP) is the defining feature of axial spondyloarthritis (axSpA). However, it may be difficult for non-rheumatology physicians (non-rheums) to distinguish between mechanical and inflammatory back pain (IBP) thus contributing to delayed and missed diagnosis. This study aims to systematically survey non-rheums in the US to gain insights into their knowledge, awareness, and attitudes towards IBP. The objective is to identify barriers for timely referral and opportunities for intervention.

Methods: An online survey questionnaire was developed and refined using input from previous smaller regional studies, methodologies, and pilot testing. The survey included demographic information, practice patterns, and questions about the knowledge and approach toward IBP and axSpA. The survey was distributed to non-rheums taking care of chronic back pain (CBP) patients, namely Family/Internal Medicine, Spine Surgery/Orthopedics, Pain Medicine, and Physical Medicine/ Physiatry/Rehabilitation across the US using third-party vendors. The survey was also sent to rheumatologists (rheums), who served as the comparator group. Descriptive statistics was used to summarize the results.

Results: Of 3136 physicians who received the survey, 750 completed it (response rate 24%). **Table 1** presents information regarding physician specialty, demographics, and practice details. Physicians with variable years of practice experience were included (40% < 5-15 years, 40% 15-30 years, and 10% > 30 years). Respondents reported CBP as a common symptom among the patients; 72% of physicians reported CBP in 15% of their patients and 44% in 30% of patients. Seventy percent of non-rheums reported that 15 to 50% of their CBP patients have onset before age 50 years. About 75% of non-rheums are either moderately or very familiar with the term IBP; an additional 15% are somewhat familiar. Only 21% of non-rheums could identify all 8 IBP items, but 87% could recognize more than 4 of 8 IBP items (**Figure 1**). Among rheums, 69 % could recognize all eight features, and 27% could recognize 7 of 8 features. About 60% of non-rheums do not routinely

Table 1: Respondent demographics and practice details.

	N (%) Completers	N (%) Contacted	Response Rate (%)
Specialty			
Total	750	3136	24%
Family Medicine or Internal Medicine	225 (30%)	1008 (32%)	22%
Rheumatology	75 (10%)	321 (10%)	23%
Orthopedist or Spine Surgery	180 (24%)	799 (26%)	23%
Pain Management	100 (13%)	351 (11%)	28%
Physiatrist/Rehabilitation/Physical Medicine	170 (23%)	657 (21%)	26%
Gender			
Male	536 (72%)	-	-
Female	196 (26%)	-	-
Prefer Not to Self-Identify	18 (2%)	-	-
Practice Setting			
Single-Specialty	311 (41%)	-	-
Multi-Specialty	214 (29%)	-	-
Academic	153 (20%)	-	-
Community Health Center	36 (5%)	-	-
Veterans Affairs	20 (3%)	-	-
Other	16 (2%)	-	-
Geographic Region			
Northeast	202 (27%)	746 (24%)	27%
Midwest	142 (19%)	626 (20%)	27%
South	246 (33%)	1066 (34%)	23%
West	160 (21%)	698 (22%)	23%
Patients Seen Per Week			
<30 to 59 patients	267 (36%)	-	-
60-90 patients	248 (33%)	-	-
> 90 patients	235 (31%)	-	-
Percentage of Patients with Chronic Back Pain			-
< 5%-14%	211 (28%)	-	-
15-29%	210 (28%)	-	-
30-50%	167 (22%)	-	-
> 50%	162 (22%)	-	
Percentage of CBP Patients Younger than 50 Years			
< 5%-14%	177 (24%)	-	-
15-29%	307 (41%)	-	-
30-50%	220 (29%)	-	-
> 50%	46 (6%)	-	-

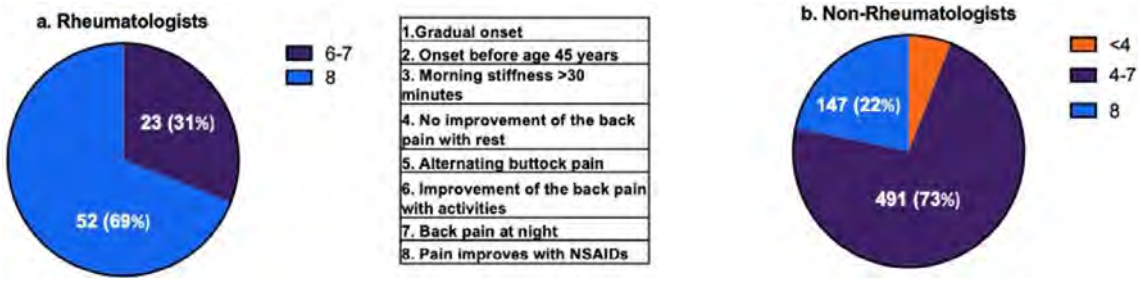

Figure 1: Percentages of rheumatology (a) and non-rheumatology (b) respondents who selected correct answer choices (shown in Figure) describing inflammatory back pain out of 16 choices, with 8 being highest score possible.

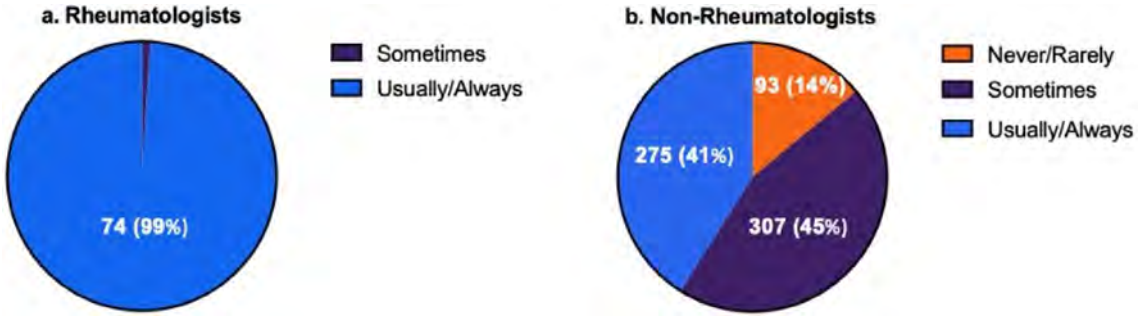

Figure 2: Percentages of rheumatology (a) and non-rheumatology (b) respondents who consider or assess for inflammatory back pain in practice for patients with chronic back pain

assess CBP patients for IBP; 14% rarely/ never assess, and 45% assess for IBP sometimes (**Figure 2**). In contrast, 99% of rheums are routinely assessed for IBP. Data about the IBP and response rates remained consistent across the non-rheums surveyed.

Conclusion: In this large nationwide survey study involving physicians from different specialties who manage CBP, we found that non-rheums are familiar with the term IBP, and the majority may have optimal knowledge about the IBP items, but fewer actually assess the CBP patients for the presence of IBP in routine practice. The use of computerized Clinical Decision Support Systems (CDSS) and improved education regarding the true prevalence of axSpA may help to wind down this barrier.

Disclosure: W. Odell: None; **S. Alexander**: None; **N. Page**: None; **N. Maheshwari**: Moderna, 12, Part of clinical trial by Moderna; **A. Danve**: Abbvie, 2, Amgen, 2, Janssen, 2, Lilly, 5, Medscape, 6, Novartis, 2, 5, Spondylitis Association of America, 5, Spondyloarthritis Research and Treatment Network, 5, UCB, 1.

Abstract Number: 2208

Awareness and Attitudes Regarding Axial Spondyloarthritis Among Non-Rheumatology Physicians in the United States

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Average diagnostic delay for axial spondyloarthritis (axSpA) is 7 to 10 years. Lack of timely referral of inflammatory back pain (IBP) patients by non-rheumatology physicians (non-rheums) is an important contributor. We systematically surveyed non-rheums in the US to assess their knowledge, awareness, and attitudes towards axSpA. The objective is to identify barriers for referral and opportunities for intervention.

Methods: An online survey questionnaire was developed and refined using input from previous smaller regional study, methodologists and pilot testing. Survey included demographic information, practice patterns, questions about the knowledge and approach towards IBP and axSpA. Survey was distributed to non-rheums taking care of chronic back pain (CBP) patients namely Family/Internal Medicine, Spine Surgery/Orthopedics, Pain Medicine, and Physical Medicine/Physiatry/Rehabilitation across the US using third party vendor. Survey was also sent to rheumatologists (rheums) who served

Table 1: Respondent demographics and practice details.

	N (%) Completers	N (%) Contacted	Response Rate (%)
Specialty			
Total	750	3136	24%
Family Medicine or Internal Medicine	225 (30%)	1008 (32%)	22%
Rheumatology	75 (10%)	321 (10%)	23%
Orthopedist or Spine Surgery	180 (24%)	799 (26%)	23%
Pain Management	100 (13%)	351 (11%)	28%
Physiatrist/Rehabilitation/Physical Medicine	170 (23%)	657 (21%)	26%
Gender			
Male	536 (72%)	-	-
Female	196 (26%)	-	-
Prefer Not to Self-Identify	18 (2%)	-	-
Practice Setting			
Single-Specialty	311 (41%)	-	-
Multi-Specialty	214 (29%)	-	-
Academic	153 (20%)	-	-
Community Health Center	36 (5%)	-	-
Veterans Affairs	20 (3%)	-	-
Other	16 (2%)	-	-
Geographic Region			
Northeast	202 (27%)	746 (24%)	27%
Midwest	142 (19%)	626 (20%)	27%
South	246 (33%)	1066 (34%)	23%
West	160 (21%)	698 (22%)	23%
Patients Seen Per Week			
<30 to 59 patients	267 (36%)	-	-
60-90 patients	248 (33%)	-	-
> 90 patients	235 (31%)	-	-
Percentage of Patients with Chronic Back Pain			-
< 5%-14%	211 (28%)	-	-
15-29%	210 (28%)	-	-
30-50%	167 (22%)	-	-
> 50%	162 (22%)	-	
Percentage of CBP Patients Younger than 50 Years			
< 5%-14%	177 (24%)	-	-
15-29%	307 (41%)	-	-
30-50%	220 (29%)	-	-
> 50%	46 (6%)	-	-

Table 2: Risk factor assessment and lab testing by rheumatology (n=75) and non-rheumatology (n=675) physicians. **P<0.01 and **** P<0.0001

For younger (age <50 years) patients with chronic back pain, how often do you ask or examine for the presence of following risk factors for ankylosing spondylitis/axial spondyloarthritis?			
	Never/Rarely n (%)	Sometimes n (%)	Usually/Always n (%)
Peripheral Arthritis			
Total Non-Rheumatology	113 (17%)	212 (31%)	350 (52%)
Rheumatology	0 (0%)	0 (0%)	75 (100%)****
Heel Pain			
Total Non-Rheumatology	232 (34%)	234 (35%)	209 (31%)
Rheumatology	0 (0%)	1 (1%)	74 (99%)****
Skin Psoriasis			
Total Non-Rheumatology	140 (21%)	223 (33%)	312 (46%)
Rheumatology	0 (0%)	0 (0%)	75 (100%)****
Uveitis or Iritis			
Total Non-Rheumatology	229, (34%)	188 (28%)	258 (38%)
Rheumatology	0 (0%)	0 (0%)	75 (100%)****
Inflammatory Bowel Disease (Crohn's disease or ulcerative colitis)			
Total Non-Rheumatology	131 (20%)	239 (35%)	305 (45%)
Rheumatology	0 (0%)	0 (0%)	75 (100%)****
Family History of Psoriasis, Anterior Uveitis, or Inflammatory Bowel Disease			
Total Non-Rheumatology	112 (16%)	193 (29%)	370 (55%)
Rheumatology	0 (0%)	1 (1%)	74 (99%)****
For patients with chronic back pain suggestive of inflammatory back pain, how often do you order the following tests?			
	Never/Rarely n (%)	Sometimes n (%)	Usually/Always n (%)
HLA-B27			
Total Non-Rheumatology	168 (25%)	180 (27%)	32 (48%)
Rheumatology	3 (4%)	10 (13%)	62 (83%)****
C-reactive protein			
Total Non-Rheumatology	101 (15%)	168 (25%)	406 (60%)
Rheumatology	0 (0%)	3 (4%)	72 (96%)****
ANA			
Total Non-Rheumatology	181 (27%)	181 (27%)	313 (46%)
Rheumatology	40 (53%)	15 (20%)	20 (27%)****
Rheumatoid Factor			
Total Non-Rheumatology	150 (22%)	174 (26%)	351 (52%)
Rheumatology	28 (37%)	21 (28%)	26 (35%)**
Erythrocyte Sedimentation Rate			
Total Non-Rheumatology	94 (14%)	160 (24%)	421 (62%)
Rheumatology	2 (3%)	5 (7%)	68 (90%)****

as comparator group. Descriptive statistics was used, and Pearson's chi-squared test was used to compare categorical variables

Results: Of 3136 physicians who received the survey, 750 completed it (response rate 24%). **Table 1** shows baseline information of respondents. Physicians were in various practice settings (42 % single specialty, 29% multi-specialty, 20% academics) and varying post-training experience (40% < 5-15 years, 40% 15-30 years, and 10% > 30years). CBP was

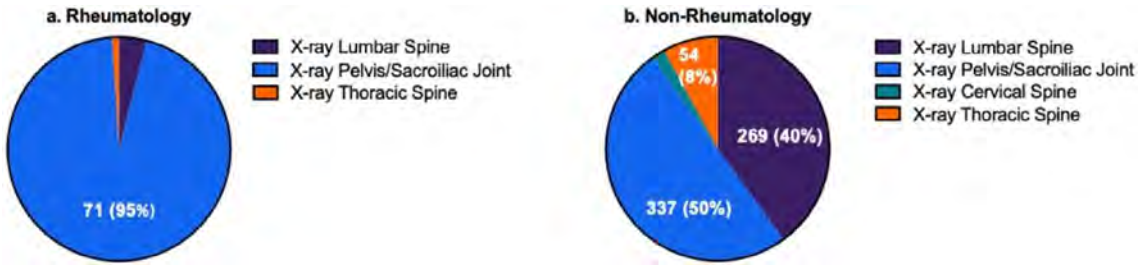

Figure 1: Rheumatology (a) and non-rheumatology (b) responses to question "Select the most appropriate initial imaging test that you would order in a patient with suspected ankylosing spondylitis/axial spondyloarthritis presenting to you with chronic back pain?"

commonly reported; 72% physicians reported CBP in >15% of their patients and 44% in >30% patients. While majority (75%) of non-rheums were familiar with IBP and 87% recognized >4 of 8 IBP items, only 40% routinely assess for IBP in clinical practice. Non-rheums screen CBP patients for inflammatory arthritis, IBD and family history of SpA for only 50% of the times and even less often for heel enthesitis, uveitis and psoriasis (see Table 2) as compared to rheums. Non-rheums also order the CRP and HLA-B27 significantly less often in CBP patients compared to rheums. Non-rheums usually/always order ANA and RF in 47% and 52% IBP patients; rheums order these in 27% and 35% patients respectively. Only 50% of non-rheums correctly answered x-ray SI/pelvis as initial imaging test of choice in suspected axSpA. MRI pelvis was selected as next imaging test by only 37% non-rheums. Non-familiarity with term axSpA and nr-axSpA was reported by 11% and 35% non-rheums respectively. Non-rheums less often (p value < 0.0001) consider axSpA/AS as a possible diagnosis in CBP patients; 20% never or rarely do it and 49% do it sometimes. Formal referral guidelines for axSpA patients were felt important or very important by 81% non-rheums and 97% rheums.

Conclusion: In this large nationwide survey study involving different specialists caring for CBP patients, we found that there is lack of knowledge and awareness about nomenclature, lab testing, and proper imaging in suspected axSpA patients. Unnecessary lab tests are commonly ordered in CBP patients by non-rheumatologists and also to an extent by rheumatologists. Formal referral guidelines and improved education may help in reducing the diagnostic delay of axSpA.

Disclosure: W. Odell: None; **S. Alexander**: None; **N. Page**: None; **N. Maheshwari**: Moderna, 12, Part of clinical trial by Moderna; **A. Danve**: Abbvie, 2, Amgen, 2, Janssen, 2, Lilly, 5, Medscape, 6, Novartis, 2, 5, Spondylitis Association of America, 5, Spondyloarthritis Research and Treatment Network, 5, UCB, 1.

Abstract Number: 2209

Prevalence and Clinical Characteristics of Late Onset Axial Spondyloarthritis: Results from a Multicentre Nationwide Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA

Session Type: Poster Session C

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Background/Purpose: Axial spondyloarthritis (axSpA) typically starts before the fourth decade of life. Consistent with that, the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA should be applied only in patients with chronic back pain starting before 45 years of age. It has, however, been suggested that axSpA can sometimes start later in life with a distinctive phenotype, the so-called 'late onset axSpA' (lo-axSpA). There is, nevertheless, only limited data in support of the existence of such phenotype. We aimed to evaluate the occurrence of lo-axSpA and if these patients differ from those with early onset axSpA (eo-axSpA).

	All patients (N=2165)	**Late onset axSpA** age at symptom onset ≥ 45 years **(N=273)**	**Early onset axSpA** age at symptom onset <45 years **(N=1892)**	**p-value***
Current age – years (mean, SD)	49.0 (12.8)	62.3 (8.8)	47.1 (12.2)	**<0.001**
Age at symptom onset - years (mean, SD)	31.7 (10.3)	51.4 (6.0)	28.9 (7.3)	**<0.001**
Age at diagnosis† - years (mean, SD)	38.0 (11.7)	55.1 (7.1)	35.5 (10.0)	**<0.001**
Diagnostic delay† - years (mean, SD)	6.3 (7.8)	3.7 (4.9)	6.6 (8.1)	**<0.001**
Symptom duration – years (mean, SD)	17.3 (11.6)	10.9 (6.9)	18.19 (11.9)	**<0.001**
Male gender (n, %)	1209 (56)	150 (55)	1059 (56)	0.749
Current Smokers$^{\Phi}$ (n, %)	393 (26)	22 (12)	371 (26)	**<0.001**
Current employment status$^{\Phi}$ (n, %)	1047 (67)	91 (48)	956 (70)	**<0.001**
Damage on X-SIJ (mNY)$^{\cup}$ (n, %)	1489 (85)	172 (82)	1317 (85)	0.284
HLA-B27† (n, %)	1346 (63)	136 (51)	1210 (65)	**<0.001**
Elevated CRP (ever)† (n, %)	1343 (63)	166 (62)	1177 (63)	0.073
Family history of SpA† (n, %)	289 (14)	21 (8)	268 (14)	**0.003**
Inflammatory back pain (ever)† (n, %)	1850 (87)	216 (81)	1634 (88)	**0.001**
Acute anterior uveitis (ever)† (n, %)	413 (19)	34 (13)	379 (20)	**0.003**
Good response NSAIDs (ever)† (n, %)	1169 (55)	141 (53)	1028 (55)	0.435
Peripheral arthritis (ever)† (n, %)	621 (29)	96 (36)	525 (28)	**0.010**
Heel enthesitis (ever)† (n, %)	444 (21)	56 (21)	388 (21)	0.976
Dactylitis (ever)† (n, %)	87 (4)	14 (5)	73 (4)	0.312
Psoriasis (ever)† (n, %)	54 (3)	7 (3)	47 (3)	0.930
IBD (ever)† (n, %)	45 (2)	7 (3)	38 (2)	0.542
BASDAI (0-10)$^{\theta}$ (mean, SD)	2.1 (2.5)	2.5 (2.8)	2.1 (2.5)	0.051
ASDAS$^{\Phi}$ (mean, SD)	2.1 (1.0)	2.2 (1.1)	2.1 (1.0)	0.208
BASFI (0-10)$^{\Phi}$ (mean, SD)	3.3 (2.5)	3.5 (2.9)	3.3 (2.8)	0.351
Treatment with csDMARDs (n, %)	524 (24)	64 (23)	460 (24)	0.754
Treatment with NSAIDs (n, %)	1059 (49)	135 (50)	924 (49)	0.850
Treatment with bDMARDs (n, %)	1662 (77)	213 (78)	1449 (77)	0.599

† Missing data <5%. θ Missing data <10%. Ʊ Missing data <25%. Φ Missing data <35%.
* Independent samples t-test for continuous variables and Chi2 for categorical variables.

Comparison of patient and disease characteristics between patients with late and early onset axSpA.

Methods: We performed a cross-sectional, multicentre, nationwide study using data from Reuma.pt, the Portuguese registry of patients with rheumatic diseases. Adult patients with the clinical diagnosis of axSpA, according to their treating rheumatologist, and with available information on the age of symptom onset were included. Lo-axSpA was defined as axSpA with a symptom onset ≥ 45 years of age. Demographic characteristics (e.g., age, gender, smoking status, and employment), SpA features [12 features (see Table) recorded as ever present, i.e., any time in the past or at the current study visit], measures of disease activity (ASDAS and BASDAI), disability (BASFI) and treatment with NSAIDs, csDMARDs and bDMARDs were compared between patients with lo-axSpA and eo-axSpA at the last available visit at the time of data extraction (13/12/2022).

Results: In total, 2165 patients with axSpA were included. The mean (standard deviation; SD) age at symptom onset was 32 (10) years and the mean (SD) symptom duration was 17 (12) years. The majority of the patients were male (56%), most had definite damage on pelvic radiographs according to the modified New York criteria (85%) and were treated with bDMARDs (77%). Out of the total 2165 patients, 273 (13%) had symptom onset ≥ 45 years and were therefore labelled as lo-axSpA. There were no differences in disease activity, disability or treatment between patients with lo-axSpA and eo-axSpA (Table). There were, however, some notable differences between the two groups. Patients with lo-axSpA were less often positive for HLA-B27 (51% vs 65%), less likely to have family history of SpA (8% vs 14%), acute anterior uveitis (13% vs 20%) and inflammatory back pain (81% vs 88%) than patients with eo-axSpA. On the contrary, patients with lo-axSpA had more peripheral arthritis (36% vs 28%) than patients with eo-axSpA.

Conclusion: This study shows that axSpA indeed starts before 45 years of age in the vast majority of the patients. Even though recall bias cannot be entirely ruled out, clinicians should however be aware that late-onset disease, though infrequent, may in some cases exist. This minority phenotype has a weaker association with HLA-B27, a lower probability of family history, inflammatory back pain or uveitis but more peripheral involvement.

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Abstract Number: 2210

Antibodies to Four Novel Peptides in New Onset Axial Spondyloarthritis

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SESSION INFORMATION
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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Diagnosis of axial spondyloarthritis (axSpA) is challenging and a specific laboratory diagnostic test is lacking. Previously, an axSpA cDNA phage display library, constructed from axSpA hip synovium, was screened to identify novel antibodies in early axSpA patients. This resulted in the identification of novel immunoglobulin G (IgG) and IgA

antibodies to 4 Hasselt University (UH)-axSpA peptides (UH-axSpA-IgG 4, 8 and UH-axSpA-IgA 1,10), corresponding to non-physiological peptides and to a novel axSpA autoantigen, Double homeobox protein 4 (DUX4). Validation of antibody reactivity in plasma samples of early axSpA patients (disease duration < 5 years) from 2 independent cohorts revealed antibody reactivity against at least one of these 4 peptide targets in 21.1% of early axSpA patients (30/142). Here we aim to validate the diagnostic potential of these 4 antibodies in a third independent cohort of new onset axSpA patients and controls.

Methods: Using ELISA, presence of antibodies to the 4 peptides was determined in 187 serum samples of the Belgian Inflammatory Arthritis and Spondylitis (Be-Giant) cohort and 74 controls with chronic low back pain (CLBP) and 101 age and gender-matched healthy controls (HC) from the UH cohort.

Results: The presence of antibodies against the 4 UH-axSpA peptides was confirmed in the Be-Giant cohort. Antibody reactivity against this panel of 4 antigens was present in 13.4% of newly diagnosed axSpA patients (25/187) compared to 6.2% (4/65, *p=0.1740*) in CLBP. The positive likelihood ratio (LR+) for confirming axSpA using antibodies to these 4 peptides was 2.2, which is comparable to the currently used laboratory marker C-reactive protein (CRP) with a LR+ of 2.5. So far, no correlation between these antibodies and clinical disease characteristics could be identified.

Conclusion: The presence of antibodies to 4 UH-axSpA peptides was confirmed in the Be-Giant of newly diagnosed axSpA patients and could be of added value for axSpA diagnosis.

Disclosure: P. Ruytinx: None; **E. Luyten**: None; **A. De Craemer**: None; **F. Van den Bosch**: AbbVie, 2, 6, Amgen, 2, BMS, 6, Celgene, 6, Eli Lilly, 2, Galapagos, 2, Janssen, 2, 6, Merck, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB Pharma, 2, 6; **D. Elewaut**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 2, galapagos, 5, Janssen, 6; **V. Somers**: None.

Abstract Number: 2211

A Two-year Comparison of Back Pain and Morning Stiffness in Axial Spondyloarthritis and Non-axial Spondyloarthritis Chronic Back Pain Patients in the Spondyloarthritis Caught Early (SPACE) Cohort

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SESSION INFORMATION

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Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Treatment of axial spondyloarthritis (axSpA) has been shown to improve symptoms of the disease such as back pain (BP) and morning stiffness (MS). As a result, early referral of patients suspected of having axSpA is strongly recommended. However, little data is available on the disease course of early axSpA in clinical practice, and particularly in comparison to referred patients who have chronic BP (CBP) but not axSpA. We set out to compare spinal symptoms at baseline and after 2 years (2y) in early axSpA and non-axSpA CBP patients in clinical practice.

Table 1. Baseline and two-years back pain and morning stiffness in early axSpA and non-axSpA chronic back pain patients.

	AxSpA			Non-axSpA		
	Baseline	2-years	p-value (overtime)	Baseline	2-years	p-value (overtime)
Back pain at any time, N		249			94	
mean (SD)	4.0 (2.4)	2.6 (2.3)	**p<0.001***	5.5 (2.2)	3.9 (2.6)	**p<0.001***
Change overtime, mean (SD)		-1.4 (2.5)			-1.6 (2.4)	
Present (score >2), n (%)	168 (67%)	107 (43%)		85 (90%)	63 (67%)	
Back pain at night, N		247			94	
mean (SD)	3.6 (2.9)	2.2 (2.5)	**p<0.001***	4.6 (2.7)	3.6 (2.8)	**p=0.001***
Change overtime, mean (SD)		-1.4 (2.9)			-1.0 (2.7)	
Present (score >2), n (%)	147 (60%)	82 (33%)		71 (76%)	56 (60%)	
Morning stiffness severity, N		261			106	
mean (SD)	4.7 (2.9)	3.1 (2.6)	**p<0.001***	6.0 (2.8)	4.0 (3.0)	**p<0.001***
Change overtime, mean (SD)		-1.6 (3.2)			-1.9 (2.9)	
Present (score >2), n (%)	186 (71%)	126 (48%)		89 (84%)	66 (62%)	
Morning stiffness duration#, N		260			107	
mean (SD)	3.6 (2.8)	2.3 (2.4)	**p<0.001***	4.6 (2.9)	3.1 (2.9)	**p<0.001***
Change overtime, mean (SD)		-1.2 (3.0)			-1.5 (3.1)	
Present (score >2), n (%)	159 (61%)	97 (37%)		82 (77%)	51 (48%)	

* Statistical significance (p-value <0.05). # Morning stiffness duration was assessed using a numeric rating scale (NRS) ranging from 0 (0 hours) to 10 (≥2 hours); for the other outcomes, a NRS ranging from 0 (no symptom) to 10 (unbearable symptom) was used.

Methods: The population consisted of adults (≥16 years) with CBP of unknown origin lasting more than 3 months and less than 2y, starting before 45 years, included in the SPondyloArthritis Caught Early (SPACE) cohort. Patients had a diagnosis of axSpA or non-axSpA at 2y with a high level of confidence by the treating rheumatologist (Marques ML, *Ann Rheum Dis* 2023;82:3-4). Patients reported the severity of BP (total and at night) and MS in the previous week on a numeric rating scale (NRS) ranging from 0 (no symptom) to 10 (unbearable symptom), both at baseline and 2y. For MS duration, a NRS ranging from 0 (0 hours) to 10 (≥2 hours) was used. For the assessment of each outcome, only patients with data at both timepoints were included. Wilcoxon signed-rank tests (for not normally distributed data) were used to compare baseline and 2y results within groups. For the comparison between groups, linear regression models were built, adjusting for the baseline value of the respective outcome, gender, age and use of NSAID.

Results: A total of 434 patients (303 axSpA; 131 non-axSpA) had undergone baseline and 2y visits. Data was available for both timepoints on at least one of the four questions related to BP and MS in 266 (88%) axSpA and 110 (84%) non-axSpA patients. Compared to non-axSpA, axSpA patients were more frequently male (52% vs 25%) and had more SpA features (mean (SD): 5 (2) *vs* 3 (1)), including HLA-B27 positivity (73% *vs* 29%). Age (mean (SD): 29 (8) *vs* 31 (8) years) and symptom duration (mean (SD): 13 (7) *vs* 13 (7) months) were similar between groups.

Overall, lower levels of BP and MS were observed in axSpA (*vs* non-axSpA) patients at baseline and 2y (Table 1). After 2y, BP (total and at night) and MS severity and duration significantly improved in both groups (all p≤0.001), even though symptoms persisted in a considerable number of patients (mainly in the non-axSpA group). A mean improvement ranging from 1.4 to

Table 2. Comparison of two-year outcomes of axSpA (vs non-axSpA) chronic back pain patients.

Outcome	Adjusted Coefficient (95% CI)#	p-value
Back pain at any time	-0.5 (-1.1; 0.1)	p=0.088
Back pain at night	**-0.8 (-1.5; -0.2)**	**p=0.012***
Morning stiffness severity	-0.5 (-1.2; 0.1)	p=0.082
Morning stiffness duration	-0.5 (-1.1; 0.1)	p=0.114

* Statistical significance (p-value <0.05). # Linear regression models, adjusted for the baseline value of the respective outcome, gender, age and use of NSAID.

1.6 points for axSpA patients and 1.0 to 1.9 points for non-axSpA patients was reported for each outcome. In adjusted multivariate analysis, axSpA (*vs* non-axSpA) was an independent predictor of a lower BP at night at 2y (Table 2, adjusted coefficient = -0.8, 95% CI (-1.5; -0.2); p=0.012), with no significant differences found for total BP or MS severity and duration.

Conclusion: Over 2y, BP and MS significantly improve in early axSpA. Although a similar improvement is seen in non-axSpA patients, at 2y most patients have persisting symptoms. AxSpA (*vs* non-axSpA) is an independent predictor of larger improvement in BP at night but not of the observed improvements in total BP and MS.

Disclosure: A. Bento da Silva: None; **M. Van Lunteren**: None; **M. marques**: None; **K. Fagerli**: None; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, Galapagos, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, UCB Pharma, 2, 5; **D. van der Heijde**: AbbVie, 2, Bayer, 2, BMS, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GSK, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; **F. Van Gaalen**: AbbVie, 12, Personal fees, BMS, 12, Personal fees, Eli Lilly, 12, Personal fees, Jacobus Stichting, 5, MSD, 12, Personal fees, Novartis, 5, 12, Fees, Stichting ASAS, 5, Stichting Vrienden van Sole Mio, 5, UCB Pharma, 5.

Abstract Number: 2212

Interpretation of Disease-specific Questionnaires on Disease Activity, Functional Capacity and Quality of Life in Daily Practice in Axial Spondyloarthritis

Styliani Tsiami[1], Kalliopi Klavdianou[2], Imke Redeker[3], Yaren Elif Özdemir[4], Philipp Sewerin[1], David Kiefer[1], Ioana Andreica[5], Uta Kiltz[6] and **Xenofon Baraliakos**[4], [1]Ruhr-Universität Bochum and Rheumazentrum Ruhrgebiet, Herne, Germany, [2]Asklepieion' General Hospital, Department of Rheumatology, Voula, Kaisariani Athens, Greece, [3]Ruhr Universität Bochum, Bochum, Germany, [4]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [5]Rheumazentrum Ruhrgebiet Herne, Herne, Germany, [6]Rheumazentrum Ruhrgebiet, Herne, Germany

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: In axial spondyloarthritis (axSpA), assessment of disease activity and physical function in clinical studies relies on patient-reported outcomes (PRO) such as patient's global, BASDAI, ASDAS and BASFI. However, it still remains unclear how response criteria adequately reflects the patients' opinion on disease status in daily practice. We aimed to investigate whether the results of PROs used in clinical studies with axSpA are indeed related to patient's opinion on disease status as reported in daily clinical routine.

Methods: Data were retrieved from the very first and from the last five visits within a timeframe of 5 years. Patient´s clinical characteristics, physician's global assessment and PROs (ASDAS, BASDAI, BASFI) were assessed at each visit. Status and change of all assessed information during follow-up were compared with patient´s opinion on symptoms related to axSpA, categorized into absent, mild, severe or very severe.

Results: 3,120 visits with median follow-up (IQR) 4.7 (4.3) years from 557 axSpA patients were analyzed. Mild symptoms were stated in 98.7% and 90.0% of visits with inactive or low ASDAS disease status, while 67.9% and 39.3% of visits showing association to high or very high ASDAS disease activity status, respectively (Fig.). In comparison, BASDAI < 4 was found in 90.8% of visits with mild symptoms, while BASDAI≥4 showed severe symptoms in 76.4% of visits (Fig.).

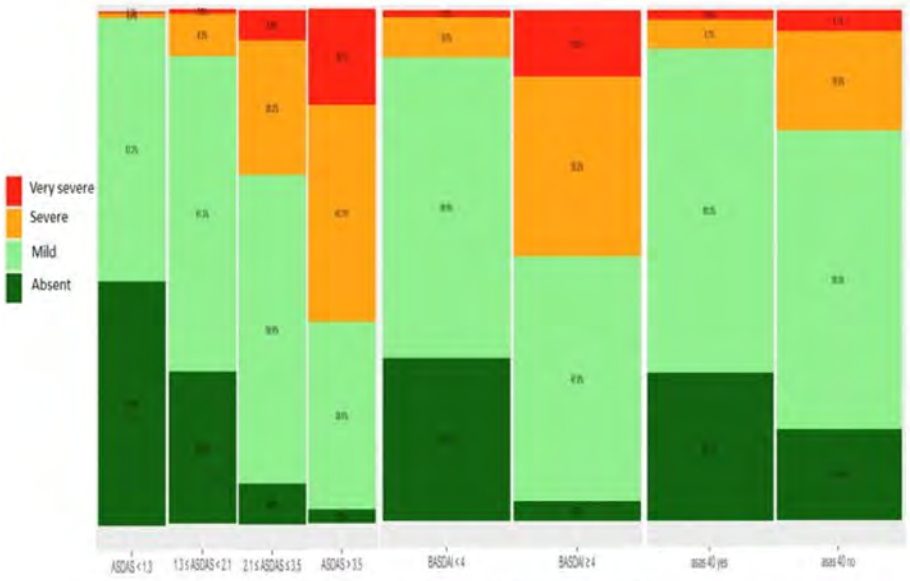

Figure: Percentages of visits with patients' subjective assessment of their symptoms sorted by disease activity

Achievement of ASAS40 was associated with 92.4% visits reporting absent/mild symptoms, while this was the case in 76.4% visits despite not reaching ASAS40. Similar data were observed for ASAS20. Severe symptoms were reported in 0.6% patients achieving vs. 30.1% patients not achieving ASAS partial remission (PR). BASFI correlated with patients' opinion regarding symptoms at each visit.

Conclusion: Low disease activity as assessed by ASDAS or BASDAI were associated with mild symptoms in the majority of visits over a period of up to 5 years. Interestingly, a large proportion of visits showed low disease activity even when not achieving ASAS20 or ASAS40 responses or ASAS-PR.

Disclosure: S. Tsiami: None; **K. Klavdianou**: None; **I. Redeker**: None; **Y. Özdemir**: None; **P. Sewerin**: AbbVie, 2, 5, 6, Biogen, 2, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 5, 6, Chugai, 2, 5, 6, Hexal, 2, 6, Janssen-Cilag, 2, 5, 6, Lilly, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, Sanofi-Genzyme, 2, 6, Swedish Orphan Biovitrum, 2, 6, UCB, 2, 5, 6; **D. Kiefer**: None; **I. Andreica**: AbbVie/Abbott, 1, 6, Amgen, 1, 6, AstraZeneca, 1, 6, Chugai, 6, Novartis, 1, 6, Sobi, 1, 6, UCB, 1, 6; **U. Kiltz**: AbbVie, 2, 5, 6, Amgen, 5, Biocad, 2, 6, Biogen, 5, Bristol-Myers Squibb(BMS), 2, 5, Chugai, 2, 6, Eli Lilly, 2, 6, Fresenius, 5, Gilead, 2, 5, GlaxoSmithKline (GSK), 5, Grünenthal, 2, 6, Hexal, 5, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, onkowiessen.de, 2, 5, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Viatris, 2, 5; **X. Baraliakos**: AbbVie, 2, 6, BMS, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, 6, UCB, 2, 6.

Abstract Number: 2213

Identification of a Diagnostic Model for Axial Spondyloarthritis in Daily Clinical Practice Using a Random Forest Machine Learning Approach

Imke Redeker[1], Styliani Tsiami[2], Jan Eicker[3], Uta Kiltz[4], David Kiefer[2], Ioana Andreica[5], Philipp Sewerin[2] and **Xenofon Baraliakos**[6], [1]Ruhr Universität Bochum, Bochum, Germany, [2]Ruhr-Universität Bochum and Rheumazentrum Ruhrgebiet, Herne, Germany, [3]Rheumazentrum Ruhrgebiet Herne and Ruhr-University Bochum, Herne, Germany, [4]Rheumazentrum Ruhrgebiet, Herne, Germany, [5]Rheumazentrum Ruhrgebiet Herne, Herne, Germany, [6]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
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Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In axial spondyloarthritis (axSpA), early diagnosis plays a key role in preventing disease progression. However, a validated diagnostic algorithm does not exist, while classification criteria are frequently misused diagnostically.

This study aimed at identifying which decision model is being used for diagnosing patients with axSpA based on evaluations made in daily practice.

Table 1. Patient characteristics

	no axSpA, N = 216[1]	**axSpA**, N = 183[1]
Male	105 (49%)	111 (61%)
Age	35 (28, 43)	36 (27, 47)
Symptom duration	1.5 (0.5, 5.0)	2.0 (1.0, 5.0)
Insidious onset of back pain	94 (44%)	177 (97%)
Improvement with exercise of back pain	119 (55%)	140 (77%)
Morning stiffness of back pain	61 (28%)	103 (56%)
Awakening at second half of night due to back pain	87 (40%)	24 (13%)
Arthritis	24 (11%)	52 (28%)
Uveitis	4 (1.9%)	33 (18%)
Dactylitis	15 (6.9%)	9 (4.9%)
Psoriasis	18 (8.3%)	21 (11%)
Inflammatory bowel disease	6 (2.8%)	11 (6.0%)
Good NSAID response	100 (46%)	151 (83%)
Elevated CRP	36 (17%)	108 (59%)
HLA-B27 positivity	35 (16%)	125 (68%)
Bone marrow edema on SIJ MRI	76 (35%)	140 (77%)
Erosion on SIJ MRI	4 (1.9%)	88 (48%)
Sclerosis on SIJ MRI	71 (33%)	110 (60%)
Fat metaplasia on SIJ MRI	17 (7.9%)	81 (44%)
Ankylosis on conventional radiograph	1 (0.5%)	28 (15%)
Family history for axSpA	18 (8.3%)	59 (32%)

[1] n (%); Median (IQR). axSpA: axial spondyloarthritis; MRI: magnetic-resonance-imaging; NSAID: non-steroidal anti-inflammatory drug; SIJ: sacroiliac-joints

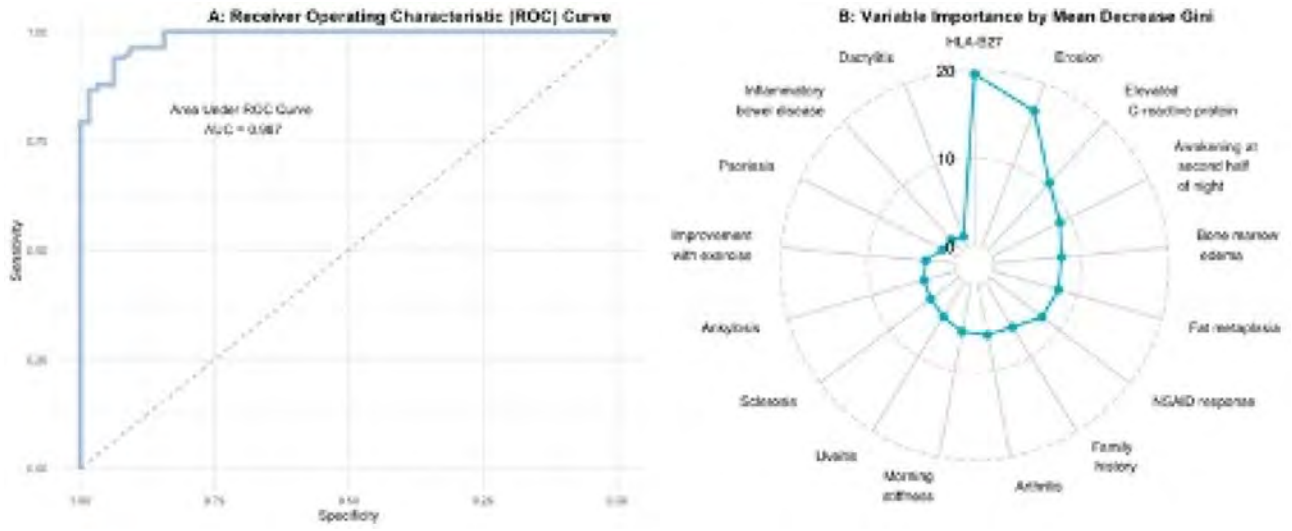

Figure 1

Methods: Complete clinical data of 399 patients who presented with chronic back pain in a specialized university clinic were retrospectively evaluated. All patients received complete rheumatologic examination. The total dataset was randomly split into training and test datasets at a 7/3 ratio. A model was built to classify patients into axSpA and non-axSpA based on the random forest algorithm, an ensemble machine learning technique which allows computing the importance of each variable in the statistical modelling process. The Mean Decrease Gini measure was used for the variable importance. The overall accuracy, sensitivity, specificity, and the area under the receiver operating characteristic (ROC) curve (AUC) in the test dataset were calculated.

Results: In total, 183 patients were diagnosed with axSpA and 216 with non-SpA (Table 1). In the test dataset, the model reached an accuracy of 0.9315, a sensitivity of 0.9634, a specificity of 0.8906, and an AUC of 0.9868 (Fig. 1A). HLA-B27 positivity, erosion on SIJ MRI, and elevated CRP played the most important role in the statistical modelling process followed by awakening at second half of night due to back pain and bone marrow edema and fat metaplasia on SIJ MRI (Fig. 1B).

Conclusion: Machine learning-based random forest classifier revealed a high performance in diagnosing patients with chronic back pain with axSpA and excluding patients with non-SpA using clinical, laboratory and imaging characteristics as evaluated in a daily practice scenario of a SpA-specialized clinic. External validation of the model is needed to investigate its clinical utility as a diagnostic decision support tool.

Disclosure: I. Redeker: None; **S. Tsiami**: None; **J. Eicker**: None; **U. Kiltz**: AbbVie, 2, 5, 6, Amgen, 5, Biocad, 2, 6, Biogen, 5, Bristol-Myers Squibb(BMS), 2, 5, Chugai, 2, 6, Eli Lilly, 2, 6, Fresenius, 5, Gilead, 2, 5, GlaxoSmithKline (GSK), 5, Grünenthal, 2, 6, Hexal, 5, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, onkowiessen.de, 2, 5, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Viatris, 2, 5; **D. Kiefer**: None; **I. Andreica**: AbbVie/Abbott, 1, 6, Amgen, 1, 6, AstraZeneca, 1, 6, Chugai, 6, Novartis, 1, 6, Sobi, 1, 6, UCB, 1, 6; **P. Sewerin**: AbbVie, 2, 5, 6, Biogen, 2, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 5, 6, Chugai, 2, 5, 6, Hexal, 2, 6, Janssen-Cilag, 2, 5, 6, Lilly, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, Sanofi-Genzyme, 2, 6, Swedish Orphan Biovitrum, 2, 6, UCB, 2, 5, 6; **X. Baraliakos**: AbbVie, 2, 6, BMS, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, 6, UCB, 2, 6.

Abstract Number: 2214

Systematic Literature Review and Meta-analysis Informing the Development of 2023 Spondyloarthritis Research and Treatment Network (SPARTAN) Referral Recommendations for Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA

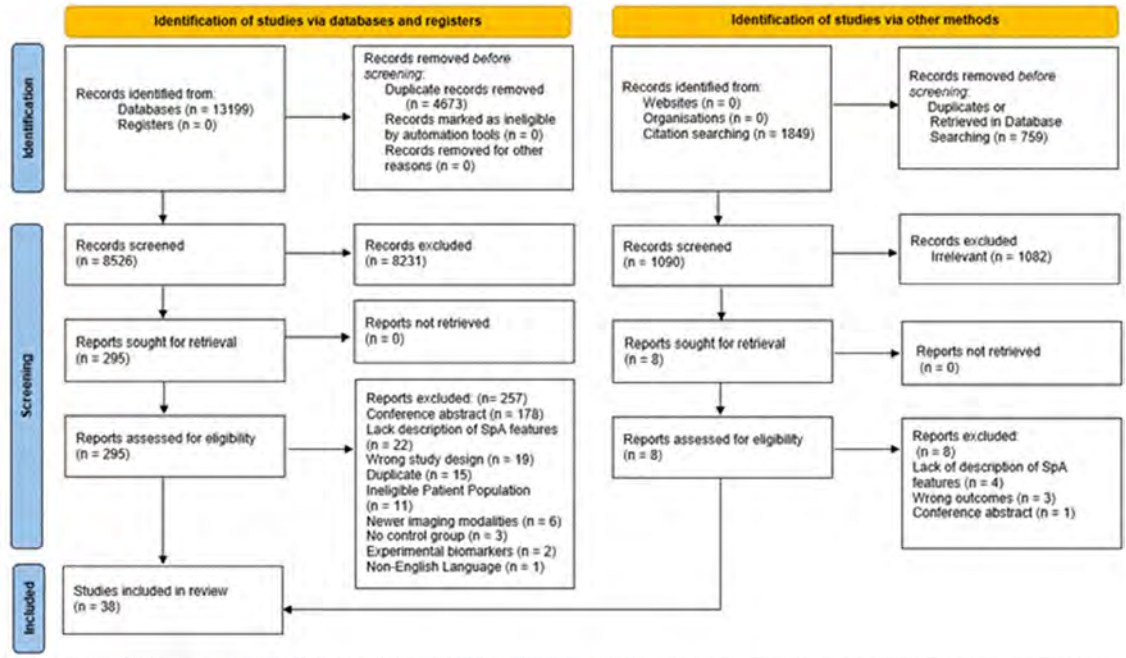
Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Lack of timely referral of suspected axSpA patients to rheumatologists contributes to misdiagnosis, delayed treatment, and poor outcomes. Currently there are no formal guidelines in the United States (US) to guide which chronic back pain (CBP) patients should be referred to rheumatology for evaluation of axSpA. To synthesize the evidence for the Spondyloarthritis Research and Treatment Network (SPARTAN) 2023 referral recommendations, we performed a systematic literature review (SLR) and meta-analysis to calculate predictive values of spondyloarthritis (SpA) features.

Methods: We generated Population, Intervention, Control and Outcome (PICO) questions using the framework "Are patients with CBP with SpA feature XYZ more likely to be diagnosed (or classified) as axSpA compared to those without SpA feature XYZ?" The list of SpA features was developed with input from research team members as well as stakeholders including patient partners. Databases including Cochrane Library, Google Scholar, Ovid Embase, Ovid Medline, PubMed, Scopus, and Web of Science Core Collection were searched from inception to April 2022 using relevant keywords to find observational studies in which CBP patients were referred to rheumatologists with suspicion of axSpA and which included information about SpA features in those diagnosed with axSpA and comparators. We followed PRISMA guidelines to report the SLR findings. Two reviewers from a team of 13 reviewers screened abstracts and full-length articles and abstracted the data from eligible studies. Conflicts were resolved by a senior author. Risk of bias was assessed using the QUADAS2 tool. A meta-analysis was performed to calculate and pool sensitivity, specificity, positive likelihood ratios (LR+), and positive predictive values for each SpA feature.

Results: We screened the title and abstracts of 8526 articles and 295 full-length articles were selected for full text review. Thirty-eight full text publications were included for data abstraction and evidence synthesis **(Figure 1)**. **Table 1** shows the test characteristics of 28 individual SpA features. LR+ ranged from 0.5 to 10. Objective SpA features including imaging evidence of sacroiliitis (6.4), elevated CRP (3.77) and positive HLA B27 (4.20) had higher LR+ followed by uveitis (3.25) and family history of spondyloarthritis (2.32). Except for good response to NSAIDs (2.32), individual items of inflammatory back pain as well as peripheral inflammatory arthritis, psoriasis, enthesitis had LR+ less than 2.



Adapted from: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372: n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Figure 1- PRISMA flowchart

Table 1. Test characteristics for SpA features derived from meta-analysis of studies included in t

	N studies	Sensitivity	Specificity	Positive predictive value	LR Positive	P pr o
Inflammatory back pain						
IBP as a concept	20	79%	58%	59%	1.87	
Good response to NSAIDs	16	67%	71%	57%	2.32	
Insidious onset	4	85%	24%	27%	1.67	
No improvement with rest	4	72%	50%	56%	1.45	
Improvement with exercise	6	80%	40%	48%	1.34	
Morning stiffness	6	67%	48%	55%	1.27	
Nocturnal pain	6	62%	46%	45%	1.15	
Pain sites						
Chest wall pain	1	21%	93%	67%	3.16	
Alternating buttock pain	7	43%	77%	63%	1.88	
Thoracic spine pain	3	20%	78%	23%	0.90	
Neck pain	3	8%	83%	17%	0.49	
Extra-axial features						
Uveitis	15	11%	97%	66%	3.25	
IBD	12	4%	98%	64%	2.20	
Psoriasis	14	9%	95%	52%	1.82	
Enthesitis symptoms	14	31%	80%	48%	1.53	
Peripheral arthritis	13	27%	71%	33%	0.92	
Dactylitis	10	9%	86%	27%	0.65	
Family history of Spondyloarthritis	16	23%	90%	57%	2.32	
Lab studies						
Elevated ESR	3	46%	89%	80%	4.33	
Elevated CRP	15	35%	91%	72%	3.77	
Positive HLA-B27	23	59%	86%	76%	4.20	
Imaging						
Sacroiliitis by any imaging	4	69%	89%	84%	6.40	
Sacroiliitis by X-ray	14	24%	98%	91%	10.02	
Sacroiliitis by MRI	18	49%	93%	86%	7.07	

*Post-test probability calculated using pre-test probability axSpA of 5%[1]

1. Reveille et al The Epidemiology of Back Pain, Axial Spondyloarthritis and HLA-B27 in the United States Am J Med Sci. 2013 Jun 431–436.

IBP= Inflammatory Back Pain FH= Family History, IBD = inflammatory bowel disease, ESR = erythrocyte sedimentation rate, CRP = C-reactive protein, axSpA: Axial Spondyloarthritis LR positive= Positive Likelihood Ratio

Conclusion: Our SLR and meta-analysis reveal important information about predictive values of individual SpA features and provide a foundation for formulating evidence-based referral recommendations in a data-driven process –first such effort in North America. The ultimate goal of this endeavor is to facilitate early and appropriate referral of patients with suspected axSpA to rheumatologists. Low LR+ for individual SpA features may necessitate using combinations of SpA features in the referral strategy.

Disclosure: A. Danve: Abbvie, 2, Amgen, 2, Janssen, 2, Lilly, 5, Medscape, 6, Novartis, 2, 5, Spondylitis Association of America, 5, Spondyloarthritis Research and Treatment Network, 5, UCB, 1; **M. Dubreuil**: Amgen, 2, Pfizer, 5, UCB Pharma, 2; **S. Alexander**: None; **Y. afinogenova**: None; **M. Bittar**: None; **A. Grimshaw**: None; **L. Fraenkel**: None; **M. LaValley**: None; **A. Kumthekar**: None; **J. liew**: None; **M. Magrey**: AbbVie, 2, Bristol Myers Squibb, 2, Eli Lilly, 2, Novartis, 2, Pfizer Inc, 2, UCB, 5; **V. Majithia**: AbbVie/Abbott, 2, Novartis, 2, UCB, 2; **S. Merjanah**: None; **H. Norton**: AbbVie/Abbott, 1, 5, 6, Amgen, 1, AstraZeneca, 1, Eli Lilly, 1, 5, 6, Horizon, 5, Janssen, 1, 6, Novartis, 1, 5, Pfizer, 1, 6, UCB, 1, 6; **J. Walsh**: AbbVie, 5, Amgen, 2, Eli Lilly, 2, Janssen, 2, Merck, 5, Novartis, 2, Pfizer, 2, 5, UCB Pharma, 2; **A. Deodhar**: AbbVie, 2, 5, Amgen, 2, Aurinia, 2, Bristol Myers Squibb, 2, 5, Celgene, 5, Eli Lilly, 2, 5, Janssen, 2, 6, MoonLake, 2, 5, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5.

Abstract Number: 2215

Can Axial Spondyloarthritis Unequivocally Be Diagnosed by Rheumatologists in Patients with Chronic Back Pain of Less Than Two Years Duration? The Primary Outcome of the Two-year SPondyloArthritis Caught Early (SPACE) Cohort

Mary Lucy marques[1], Sofia Ramiro[2], Miranda Van Lunteren[3], Rosalinde Stal[3], Robert BM Landewé[4], Marleen van de Sande[5], Karen Minde Fagerli[6], Inger Jorid Berg[6], Maikel van oosterhout[7], Sofia Exarchou[8], Roberta Ramonda[9], Désirée van der Heijde[2] and Floris Van Gaalen[3], [1]Leiden University Medical Center; Centro Hospitalar e Universitário de Coimbra (Department of Rheumatology), Coimbra, Portugal, [2]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [3]Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands, [4]Amsterdam Rheumatology & Clinical Immunology Center, Amsterdam and Zuyderland MC, Herleen, Netherlands, [5]Amsterdam UMC, University of Amsterdam, Department of Rheumatology & Clinical Immunology and Department of Experimental Immunology, Amsterdam Infection & Immunity Institute; Amsterdam Rheumatology & Immunology Center (ARC), Academic Medical Center, Amsterdam, Netherlands, [6]Center for Treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway, [7]Groene Hart Ziekenhuis, Gouda, Netherlands, [8]Lund University, Åkarp, Sweden, [9]University of Padova, Department of Rheumatology, Padova, Italy

SESSION INFORMATION

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Background/Purpose: Unacceptable diagnostic delay in axial Spondyloarthritis (axSpA) remains an issue. In 2008, the longitudinal SPondyloArthritis Caught Early (SPACE)-cohort started to assess the prevalence of axSpA and the reliability of an early diagnosis in patients with chronic back (CBP) of unknown origin. Here we present the primary outcomes of SPACE. We aimed to assess the two-year (2y) prevalence of an axSpA diagnosis in patients with recent onset CBP referred to the rheumatologist; the sustainability of a baseline (BL) diagnosis of axSpA when reviewed after 2y; and to explore BL patient differences of those with and without an axSpA diagnosis at 2y.

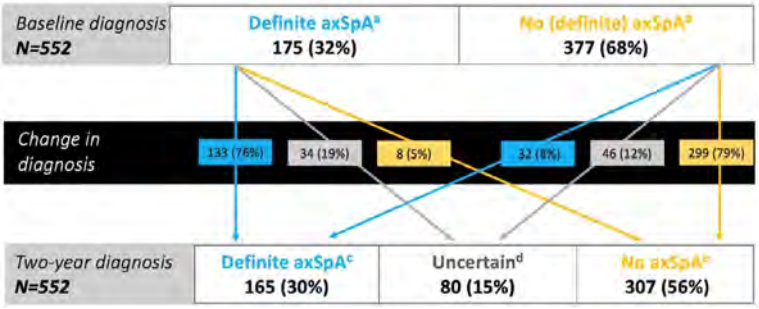

Figure 1. Diagnosis course from baseline (BL) to the two-year (2y) anchor visit. a. patients diagnosed at BL with axSpA with a Level of Confidence (LoC) ≥7; b. patients diagnosed at BL with axSpA (LoC <7) or with no axSpA (any LoC); c. patients diagnosed with axSpA with LoC ≥7 at 2y (if complete follow-up) or at the last two available visits (if missing the 2y visit); d. patients diagnosed with axSpA with LoC <7 at 2y (or LoC ≥7, if only baseline observation available), and patients with axSpA with LoC <7 at the last available observation and no consistent diagnosis at the last two observations nor alternative no axSpA diagnosis given at the last observation; e. patients with no axSpA at the last observation over 2y with LoC ≥7 (or if <7, plus an alternative no axSpA diagnosis reported, e.g. fibromyalgia or aspecific back pain). axSpA: axial Spondyloarthritis.

Methods: We analysed the 2y data from SPACE, a European inception cohort of patients (< 45y) with CBP of recent onset (≥3 months, ≤2y) and unknown origin. The full diagnostic work-up included clinical SpA features, acute phase reactants, HLA-B27, radiographs and MRI of the sacroiliac joints (SI-CR and SI-MRI) and spine (data not shown). Patients with an increased likelihood of having axSpA (≥1 major or ≥2 minor prespecified SpA features) were eligible for follow-up. The clinical diagnosis at 2y was the main outcome of this study. At each visit, the treating rheumatologist judged on the presence or absence of axSpA (axSpA or no-axSpA) with a level of confidence (LoC) on a numeric rating scale (0: *not confident at all* to 10: *very confident)*. The main outcome was the presence of 'definite axSpA' at 2y, defined by a clinical diagnosis of axSpA with LoC ≥7 at 2y (complete follow-up) or at the two last available visits (missing at 2y). 'No axSpA' was defined as not having axSpA at 2y (LoC ≥7; or if LoC < 7, plus an alternative diagnosis for CBP reported). All other patients were considered to have 'uncertain' diagnosis (***Figure 1***). ASAS classification criteria were computed using sacroiliitis local reading in *definite axSpA* patients. We assessed the prevalence of *definite axSpA* at 2y as well as changes in diagnosis over time, and descriptively summarised BL characteristics.

Table 1. Baseline characteristics by two-year (2y) diagnosis of patients with chronic back pain duration of ≥3 months but ≤2y, < 45y of age. # Currently present or past presence (if confirmed/reported by a physician). § Local data. axSpA: axial Spondyloarthritis; MRI: magnetic resonance imaging.

	Definite axSpA N=165	*Uncertain* N=80	*No axSpA* N=307
Age at inclusion, years	29.8 (7.6)	30.9 (8.7)	31.0 (8.4)
Male	52%	38%	26%
Symptom duration, months	12.8 (7.0)	13.4 (7.2)	13.4 (7.2)
HLA-B27 +	81%	60%	15%
Family history of SpA	48%	61%	39%
Inflammatory back pain[§]	76%	63%	55%
Good response to NSAIDs	43%	40%	24%
Peripheral arthritis[#]	16%	16%	7%
Dactylitis[#]	7%	9%	3%
Heel pain[#]	19%	15%	8%
Anterior uveitis[#]	13%	13%	3%
Inflammatory bowel disease[#]	7%	6%	7%
Psoriasis[#]	11%	9%	8%
Increased acute phase reactants[§]	37%	20%	19%
Sacroiliitis on radiographs[§]	23%	9%	0%
Sacroiliitis on MRI[§]	67%	26%	6%

Results: We included 552 CBP patients (Leiden n=383, Oslo n=94, Amsterdam n=48, and Gouda n=27).A diagnosis of definite axSpA was given to 175 (32%) patients at BL and 165 (30%) at 2y (***Figure 1***). The mean (SD) LoC were 8.1 (2.0) and 8.7 (1.0), with 155/175 (89%) and 145/165 (87%) fulfilling ASAS classification criteria, respectively. BL diagnostic judgments were relatively unequivocal and remained rather stable: At 2y, 5% of the BL diagnoses of definite axSpA were refuted; and -*vice versa*: 8% of those who did not obtain a BL diagnosis of axSpA 'gained' one at 2y. Diagnostic uncertainty remained in 15% of CBP-patients. Expectedly, BL SpA features were more prevalent in the 2y definite axSpA group (***Table 1***). HLA-B27 status and (presence or absence of) imaging-detected sacroiliitis at BL appeared the best discriminator(s) between *definite axSpA* and *no axSpA* at 2y.

Conclusion: One third of patients with CBP of recent onset referred to the rheumatologist has definite axSpA. Most patients can be unequivocally and reliably diagnosed at first assessment, though residual diagnostic uncertainty persisted after 2y. None of the many SpA features suffices alone, but HLA-B27 positivity andsacroiliitis on imaging best discriminate the 2y diagnostic groups.

Disclosure: M. marques: None; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, Galapagos, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, UCB Pharma, 2, 5; **M. Van Lunteren**: None; **R. Stal**: None; **R. Landewé**: AbbVie, 2, 5, AstraZeneca, 2, BMS, 2, Eli Lilly, 2, Novartis, 2, 5, Pfizer, 2, 5, Rheumatology Consultancy BV, 12, Owner, UCB Pharma, 2, 5; **M. van de Sande**: AbbVie, 2, Eli Lilly, 5, Janssen, 6, Novartis, 2, 5, 6, UCB Pharma, 2, 5, 6; **K. Minde Fagerli**: None; **I. Jorid Berg**: None; **M. van oosterhout**: None; **S. Exarchou**: Amgen, 2, Janssen, 2, Novartis, 2, UCB Pharma, 2; **R. Ramonda**: None; **D. van der Heijde**: AbbVie, 2, Bayer, 2, BMS, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GSK, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; **F. Van Gaalen**: AbbVie, 12, Personal fees, BMS, 12, Personal fees, Eli Lilly, 12, Personal fees, Jacobus Stichting, 5, MSD, 12, Personal fees, Novartis, 5, 12, Fees, Stichting ASAS, 5, Stichting Vrienden van Sole Mio, 5, UCB Pharma, 5.

Abstract Number: 2216

Hierarchy of Determinants of Work Impairment in Spondyloarthritis: Data from the Assessment of Spondyloarthritis International Society Health Index (ASAS-HI) International Validation Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Spondyloarthritis (SpA) is a disease of the working-age individual, with diverse economic and societal implications, including decreased employment rates. Our aim was to investigate the hierarchy of determinants contributing to work impairment in SpA.

Methods: Data was retrieved from the Assessment of SpondyloArthritis international Society (ASAS)-Health Index (HI) international validation study, a cross-sectional international observational study with a longitudinal component for reliability and responsiveness. Patients >60y reporting to be retired were excluded from the analyses (according to usual retirement ages across the 23 participating countries: www.oecd-ilibrary.org). The Work Productivity and Activity Impairment (WPAI) questionnaire was used to assess work productivity loss outcomes: absenteeism, presenteeism, overall work impairment, overall activity impairment. Initial univariable analyses using generalised estimated equations (GEE) explored the association between work-related outcomes (dependent variables) and sociodemographic and clinical variables (independent variables). A manual forward stepwise variable selection procedure was used for the selection of best-fit multivariable models. To avoid collinearity, separate models were built using ASDAS and BASDAI+CRP as independent variables. Lastly, a decision tree was built using Chi-square Automatic Interaction Detector (CHAID), a method of unbiased hierarchical multivariable analysis.

Results: From the original 1548 patients, a total of 1450 patients were included in the analysis, 345 of which had a follow-up reliability/responsiveness visit. Most patients were male (65%), mean age was 40 (±12) years and mean disease duration was 13 (±10) years. Most patients had axial SpA (84%) and a minority had peripheral SpA (16%). Medication use was: NSAIDs 64%, csDMARDs 26% and bDMARDs 38%. Most patients worked full-time (57.1%). Levels of absenteeism were 16% (±32%), presenteeism 29% (±26%), overall work impairment 39% (±34%), and overall activity impairment 41% (±29%). Worse physical function (measured by BASFI) and higher disease activity (measured by ASDAS or by BASDAI +CRP) were independently and consistently associated with all work productivity loss outcomes (Tables). Other variables less consistently associated with work productivity loss outcomes were bDMARD and NSAID use, history of uveitis and peripheral arthritis, disease duration, presence of radiographic sacroiliitis, and level of education (Tables). In the CHAID analysis (Figure), BASFI was the variable with higher discriminative power in predicting overall work impairment; ASDAS was the second-level discriminative variable. University education, disease duration, sex, radiographic sacroiliitis and history of arthritis were the third-level parameters. Similar results were observed for other work productivity loss outcomes (data not shown).

Conclusion: Loss of physical function and higher disease activity are major contributors to work productivity loss and are hierarchically superior to the contribution provided by other demographic and clinical variables.

Table 1. Best-fit multivariable model (adjusted B and 95%CI, p-values) for work productivity loss outcomes (GEE analysis), using ASDAS as independent variable. p-values in bold reflect significant associations. Variables tested in the univariable analyses and considered for multivariable models included: sex, age, symptom duration, disease duration, university education, history of arthritis, history of dactylitis, history of enthesitis, history of uveitis, history of psoriasis, history of inflammatory bowel disease, HLA-B27 status, CRP, NSAID use, cDMARD use, bDMARD use, number of comorbidities, radiographic sacroiliitis (modified New York criteria), anterior syndesmophytes (radiography), ASDAS-CRP, BASDAI and BASFI. Abbreviations: ASDAS, axial spondyloarthritis disease activity score-C-reactive protein; BASDAI, Bath ankylosing spondylitis disease activity index; BASFI, Bath ankylosing spondylitis function activity score; bDMARD, biological disease-modifying antirheumatic drug; GEE, generalised estimated equations.

Covariates	Work productivity loss outcomes							
	Absenteeism	p-value	Presenteeism	p-value	Overall work impairment	p-value	Overall activity impairment	p-value
ASDAS-CRP	0.39 (0.13, 0.65)	**0.003**	0.44 (0.36, 0.52)	**<0.001**	0.39 (0.30, 0.49)	**<0.001**	0.32 (0.28, 0.36)	**<0.001**
BASFI	0.20 (0.10, 0.30)	**<0.001**	0.12 (0.09, 0.16)	**<0.001**	0.12 (0.08, 0.16)	**<0.001**	0.11 (0.10, 0.13)	**<0.001**
bDMARD use	-0.29 (-0.81, 0.23)	0.27	0.25 (0.10, 0.40)	**0.001**	0.19 (0.01, 0.37)	**0.04**	-0.01 (-0.09, 0.08)	0.86
History of uveitis	____	____	-0.34 (-0.50, -0.17)	**<0.001**	____	____	____	____
Disease Duration	____	____	-0.01 (-0.02, 0.002)	0.10	-0.01 (-0.02, -0.001)	**0.03**	-0.01 (-0.01, -0.004)	**<0.001**
Radiographic sacroiliitis	-0.63 (-1.12, -0.15)	**0.01**	-0.16 (-0.30, -0.02)	**0.03**	-0.29 (-0.46, -0.12)	**0.001**	____	____
Number of comorbidities	____	____	____	____	0.11 (0.06, 0.17)	**<0.001**	0.04 (0.01, 0.06)	**0.003**

Table 2. Best-fit multivariable model (adjusted B and 95%CI, p-values) for work productivity loss outcomes (GEE analysis), using BASDAI and CRP as independent variables. p-values in bold reflect significant associations. Variables tested in the univariable analyses and considered for multivariable models included: sex, age, symptom duration, disease duration, university education, history of arthritis, history of dactylitis, history of enthesitis, history of uveitis, history of psoriasis, history of inflammatory bowel disease, HLA-B27 status, CRP, NSAID use, cDMARD use, bDMARD use, number of comorbidities, radiographic sacroiliitis (modified New York criteria), anterior syndesmophytes (radiography), ASDAS-CRP, BASDAI and BASFI. Abbreviations: ASDAS, axial spondyloarthritis disease activity score-C-reactive protein; BASDAI, Bath ankylosing spondylitis disease activity index; BASFI, Bath ankylosing spondylitis function activity score; bDMARD, biological disease-modifying antirheumatic drug; GEE, generalised estimated equations.

Covariates	Work productivity loss outcomes							
	Absenteeism	p-value	Presenteeism	p-value	Overall work impairment	p-value	Overall activity impairment	p-value
BASDAI	0.20 (0.06, 0.33)	**0.004**	0.27 (0.23, 0.31)	**<0.001**	0.23 (0.18, 0.28)	**<0.001**	0.22 (0.20, 0.24)	**<0.001**
CRP	0.01 (0.01, 0.03)	**0.05**	0.001 (-0.004, 0.01)	0.71	0.01 (-0.001, 0.01)	0.09	0.001 (-0.001, 0.003)	0.31
BASFI	0.21 (0.10, 0.31)	**<0.001**	0.07 (0.03, 0.10)	**<0.001**	0.09 (0.05, 0.12)	**<0.001**	0.08 (0.06, 0.10)	**<0.001**
History of arthritis	0.33 (-0.14, 0.90)	0.17	———	———	———	———	———	———
Disease duration	———	———	-0.01 (-0.02, -0.01)	**0.01**	-0.01 (-0.02, -0.002)	**0.02**	———	———
bDMARD use	———	———	———	———	———	———	-0.10 (-0.17, -0.02)	**0.02**
NSAID use	———	———	———	———	0.27 (0.10, 0.45)	**0.002**	———	———
Radiographic sacroiliitis	-0.46 (-0.95, 0.02)	0.06	———	———	———	———	———	———
University education	———	———	-0.22 (-0.34, -0.09)	**<0.001**	———	———	-0.10 (-0.17, -0.02)	**0.01**

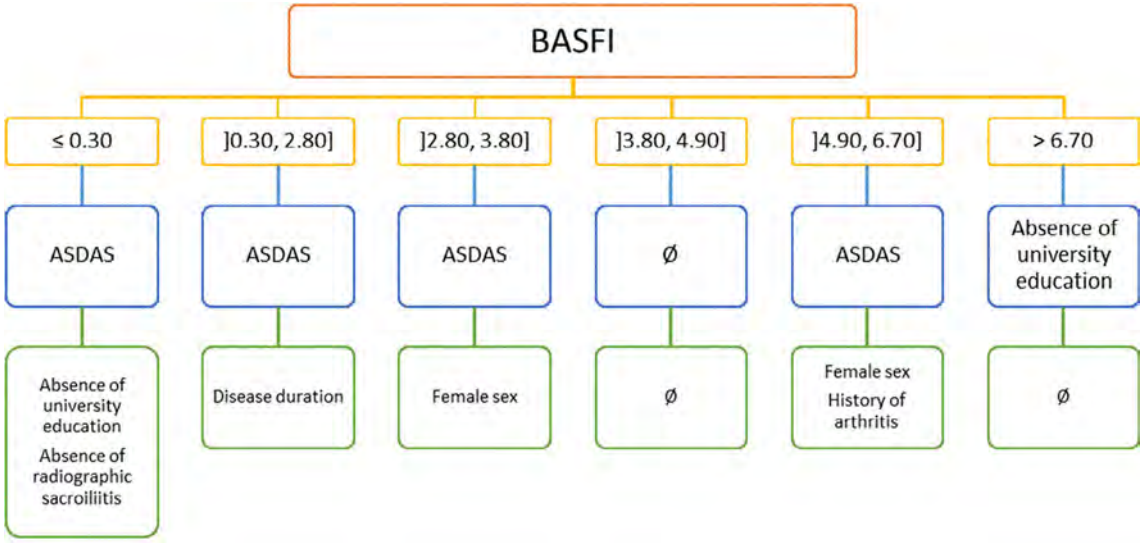

Figure. Decision tree (CHAID) analysis for overall work impairment. ASDAS, axial spondyloarthritis disease activity score-C-reactive protein; BASFI, Bath ankylosing spondylitis function activity score; bDMARD, biological disease-modifying antirheumatic drug; GEE, generalised estimated equations. Ø – no covariate included in this level of analysis.

Disclosure: F. Rajão Martins: None; **P. Carvalho**: Amgen, 6, Bial, 6, Novartis, 6, Pharmakern, 6; **D. van der Heijde**: AbbVie, 2, Bayer, 2, BMS, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GSK, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; **M. de Hooge**: UCB, 6; **A. Boonen**: AbbVie, 2, 5, 6, Galapagos, 2, 6, Novartis, 2, 6, Pfizer, 5, 6, UCB Pharma, 2, 6; **J. Braun**: None; **U. Kiltz**: AbbVie, 2, 5, 6, Amgen, 5, Biocad, 2, 6, Biogen, 5, Bristol-Myers Squibb(BMS), 2, 5, Chugai, 2, 6, Eli Lilly, 2, 6, Fresenius, 5, Gilead, 2, 5, GlaxoSmithKline (GSK), 5, Grünenthal, 2, 6, Hexal, 5, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, onkowiessen.de, 2, 5, Pfizer, 2, 5, 6, Roche,

2, 6, UCB, 2, 6, Viatris, 2, 5; **P. Machado**: AbbVie/Abbott, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Orphazyme, 2, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 6.

Abstract Number: 2217

Gender Disparities in Disease Activity Scores and Treatment Response Among Patients with Axial Spondyloarthritis

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The assessment of disease activity in axial spondyloarthritis (axSpA) heavily relies on patient-reported outcomes. It is well-established that gender can influence these outcomes. Accordingly, our study aimed to investigate gender-based differences in disease activity scores before and after treatment with biologic disease-modifying antirheumatic drugs (bDMARDs).

Methods: We conducted a retrospective analysis utilizing data from the Korean College of Rheumatology Biologics therapy (KOBIO) registry, encompassing axSpA patients treated between December 2012 and August 2021. We compared the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS) at the initial visit after commencing bDMARDs between male and female patients. Generalized linear model analyses were performed to assess the relationship between changes in disease activity scores and gender with the correction of other clinical variables.

Results: A total of 1,753 patients (1,343 males and 410 females) were included in the analyses. Baseline characteristics revealed that male patients were younger, exhibited longer disease duration, and had a higher proportion of HLA-B27 positive and radiographic disease cases. Additionally, male patients presented lower BASDAI scores and higher C-reactive protein (CRP) levels. At the first follow-up visit (after an average duration of 11.2 months from the initial visit), a significantly

	Gender	Age	Disease duration	HLA-B27	Radiographic disease	Smoking	Ex-smoker	Current smoker	Baseline value
BASDAI									
beta	0.4054	0.0190	0.0036	-0.4990	0.1918	.	0.1025	0.4557	-0.7609
SE	0.1377	0.0041	0.0089	0.1712	0.1758	.	0.1439	0.1298	0.0257
p	0.0033	0.0000	0.6888	0.0036	0.2752	0.0016	0.4764	0.0005	0.0000
ASDAS									
beta	0.1030	0.0079	0.0103	-0.2953	0.1022	.	0.0652	0.2964	-0.8320
SE	0.0680	0.0020	0.0045	0.0857	0.0880	.	0.0713	0.0647	0.0237
p	0.1303	0.0001	0.0214	0.0006	0.2459	0.0000	0.3609	0.0000	0.0000

BASDAI, Bath ankylosing spondylitis disease activity index; *ASDAS*, ankylosing spondylitis disease activity score; *SE*, standard error

The results of the multivariate generalized linear model of the relationship between the change in disease activity scores and clinical variables, including gender.

greater proportion of male patients achieved a BASDAI score < 4 compared to female patients (79.57% vs. 71.54%, p < 0.0010). However, there were no significant differences between genders in the proportion of patients achieving low disease activity (ASDAS < 2.1) or inactive disease (ASDAS < 1.3) in terms of ASDAS disease activity score (71.14% vs. 71.5%, p = 0.8892; 38.82% vs. 39.44%, p = 0.8265, respectively). After adjusting for baseline clinical information, a statistically significant association was observed between gender and the difference in BASDAI scores between the first follow-up visit and baseline (p = 0.0033, Table 1). Conversely, no significant relationship was found between gender and the difference in ASDAS scores (p = 0.1303, Table 1).

Conclusion: Our findings highlight the potential impact of gender on the interpretation of treatment response to bDMARDs in axSpA, emphasizing the need to consider diverse methods of calculating disease activity when assessing therapeutic outcomes in male and female patients.

Disclosure: S. Lee: None; **S. Kang**: None; **H. Kim**: None; **J. Lee**: None; **J. kim**: None; **E. Koh**: None; **H. Cha**: None.

Abstract Number: 2218

Exploring Metabolite Markers Associated with Treatment Response of Biologic Disease Modifying Antirheumatic Drugs in Psoriatic Arthritis Patients

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: The use of biologic disease-modifying anti-rheumatic drugs (bDMARDS) is the current standard of care for severe diseases like psoriatic arthritis (PsA) which affects approximately 25% of psoriasis patients. However, randomized controlled trials demonstrate a difference in the ACR20 response rate of only 20-30% in patients receiving treatment vs placebo. Thus, choosing the appropriate type of bDMARDS to administer targeted therapy of PsA remains challenging. Predictive biomarkers may help facilitate precision medicine. The objective of this study was to apply a global metabolomics approach to identify small molecules associated with treatment efficacy in PsA patients treated with either tumour necrosis factor inhibitors (TNFi) or Interleukin 17A inhibitors (IL-17Ai).

Methods: Serum samples were obtained from PsA patients satisfying the CASPAR criteria. Patients were treated with either TNFi (n = 20; infliximab, adalimumab, etanercept, certolizumab or golimumab) or IL-17Ai (n = 20; secukinumab or ixekizumab). Patients were evaluated at baseline and 3 months post-therapy and determined as responders or non-responders

Table 1: Demographic and disease characteristics of patients at baseline.

	IL-17i	TNFi
# of patients	20	20
Gender (% female)	55%	75%
Age (Years) (Mean)	55.95	56.85
Age (SD)	9.46	12.63
Disease Duration (Years) (Mean)	10.45	7.35
Disease Duration (SD)	6.91	7.89
Response status (% responder)	35%	65%

based on the Disease Activity Index for PsA (DAPSA) wherein responders had DAPSA < 14. Solid phase microextraction (SPME), a novel high throughput technique was used to prepare all samples simultaneously followed by liquid chromatography – high-resolution mass spectrometry (LC-HRMS) analysis. Data processing and feature identification was performed using 2 platforms – Metaboanalyst R and Compound Discoverer 3.3 respectively. Various Machine Learning (ML) algorithms including Naïve-Bayes (NB), logit boost, adaptive boosting, linear regression, support vector machine (SVM), linear discriminant analysis (LDA), and random forest (RF), was used for predictive feature analysis. Only features in models with an area under the curve of 0.7 or greater were considered as candidate metabolite markers.

Results: Table 1 provides the demographic and disease characteristics of the patients at baseline. 7/20 (35%) of patients treated with TNFi and 13/20 (65%) of patients treated with IL17Ai were responders. As little as 5 features from an SVM model produced an AUROC value of 0.732, while as many as 20 features using NB produced a value of 0.812 between responders and non-responders for both treatments combined at baseline. When considering a single treatment option (TNFi or IL-17Ai only), less than 5 features were required to produce AUROC scores of > 0.9 in both positive and negative mode data. Several exposome-related metabolites were identified via MS level 2 spectral matching including cotinine, adipic acid, toluic acid, monobutylphthalate and tridecylic acid. Glycochenodeoxycholic acid, an endogenous metabolite was also identified.

Conclusion: The identification of cotinine – a metabolite found in tobacco, could indicate that a risk behaviour such as smoking, or an exposure to second hand smoke as well as glycochenodeoxycholic acid – a metabolite that stimulates the mitochondrial pathway to cell death, may indicate that multiple mechanisms of action affects response to treatment. Validation of these results is required.

Disclosure: J. Koussiouris: None; **N. Looby**: None; **M. Kotlyar**: None; **V. Kulasingam**: None; **I. Jurisica**: None; **A. Mathew**: None; **P. Rahman**: AbbVie, 2, Amgen, 2, Bristol Myers Squibb, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, UCB, 2; **V. Chandran**: AbbVie, 1, 5, 6, Amgen, 1, 5, 6, AstraZeneca, 3, Bristol-Myers Squibb (BMS), 1, 6, Eli Lilly, 1, 5, 6, Janssen, 1, 6, Novartis, 1, 1, 6, UCB, 1, 2.

Abstract Number: 2219

Comparing the Construct Validity Among Measures of Pain and Stiffness in Patients with Axial Spondyloarthritis

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In the context of the recent update of the ASAS core outcomes set (COS), the preferred comparative validity of the measurement instruments to assess the domains 'Pain' and 'Stiffness' has been questioned as for each domain responsiveness of instruments was comparable. Group discrimination across various external constructs can help provide useful insights and represents unmet need.

Our objective was to compare the group discriminatory capacity, as part of the construct validity, of three instruments to assess pain and three questions of morning stiffness.

Methods: Data from the 8-year visit of patients with axSpA from the multinational OASIS cohort was assessed. The available instruments for pain assessment were: i) total spinal pain, ii) spinal pain at night, iii) spinal pain from BASDAI Q2 (addressing neck, back or hip pain); and for morning stiffness: i) severity of morning stiffness (BASDAI Q5), ii) duration of morning stiffness (BASDAI Q6), iii) the combined score between severity and duration of morning stiffness (average BASDAI Q5/6). Data from 8 year-visit were used as the first time-point where all the instruments were obtained on a 0–10 numeric rating scale (as currently used). The discriminatory capacity was assessed through the standardised mean difference (SMD) that is calculated as the difference of the group means divided by the pooled SD of the group means, with a higher value reflecting a higher discriminatory capacity. The external constructs used to compare the ability to discriminate between subgroups of patients were: ASDAS, BASDAI (dichotomized into inactive/active disease), PGA, PhGA, fatigue, BASFI, BASMI and mSASSS (dichotomized by the median).

Results: 98 patients were included: 71% males, mean age 54 (SD 11), with a mean symptom duration of 31 (11) years. The mean scores for pain were 3.7 (2.3), 2.9 (2.3) and 4.6 (2.6) for spinal pain, spinal pain at night and BASDAI Q2, respectively. The mean scores of morning stiffness were 3.7 (2.6), 3.3 (3.1) and 3.5 (2.7) for BASDAI Q5, Q6 and Q5/6, respectively. Spinal pain by BASDAI Q2 and total spinal pain had higher SMDs compared to spinal night pain across all group comparisons, with spinal pain BASDAI Q2 performing mostly slightly better (Table). Regarding morning stiffness, the severity question (BASDAI Q5) had consistently higher SMDs across all the clinical external constructs, while duration of morning stiffness (BASDAI Q6) performed worse.

Conclusion: Spinal pain from BASDAI Q2 and severity of morning stiffness (BASDAI Q5) are, respectively, the pain and morning stiffness instruments that best discriminate subgroups of patients classified according to disease activity, functional ability, fatigue or spinal mobility. The recommended ASAS COS pain instrument spinal pain BASDAI Q2, was confirmed to discriminate best. In the case of stiffness, the ASAS COS stiffness measure (BASDAI Q5/6) performed well although slightly less than the severity of morning stiffness (BASDAI Q5).

Table. Discrimination between subgroups of patients

Assessment measure	ASDAS <2.1 vs ≥2.1 SMD	BASDAI <4 vs ≥4 SMD	Fatigue <5 vs ≥5 SMD	BASFI <4 vs ≥4 SMD	BASMI <4 vs ≥4 SMD	mSASSS <15 vs ≥15 SMD
Total spinal pain	1.57	1.92	1.62	0.92	0.27	-0.32
Spinal night pain	1.07	1.39	1.27	0.78	0.07	-0.20
Spinal pain BASDAI Q2	1.88	2.37	1.65	0.89	0.31	-0.29
Morning stiffness severity BASDAI Q5	1.52	2.14	1.58	0.99	0.26	-0.11
Morning stiffness duration BASDAI Q6	1.18	1.80	1.09	0.83	0.09	-0.14
Morning stiffness average BASDAI Q5/6	1.40	2.14	1.38	0.95	0.17	-0.13

Disclosure: D. Capelusnik: None; **E. Nikiphorou**: AbbVie/Abbott, 6, Celltrion, 6, Eli Lilly, 6, fresenius, 6, Galapagos, 6, Gilead, 1, 6, Pfizer, 6, Sanofi, 6; **A. Boonen**: AbbVie, 2, 5, 6, Galapagos, 2, 6, Novartis, 2, 6, Pfizer, 5, 6, UCB Pharma, 2, 6; **D. van der Heijde**: AbbVie, 2, Bayer, 2, BMS, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GSK, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; **R. Landewé**: AbbVie, 2, 5, AstraZeneca, 2, BMS, 2, Eli Lilly, 2, Novartis, 2, 5, Pfizer, 2, 5, Rheumatology Consultancy BV, 12, Owner, UCB Pharma, 2, 5; **A. van Tubergen**: MSD, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, UCB Pharma, 2, 5; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, Galapagos, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, UCB Pharma, 2, 5.

Abstract Number: 2220

Factors Associated with Achieving Remission in Patients with Early Peripheral Spondyloarthritis: 10-Year Results from the German Spondyloarthritis Inception Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA

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Background/Purpose: Depending on leading manifestation, Spondyloarthritis (SpA) is classified as axial (axSpA) or peripheral SpA (pSpA). Achieving of remission/inactive disease is key goal in treatment of SpA, including pSpA. Results from recent worldwide ASAS PerSpA study showed that nearly 10% of SpA patients were identified as having pSpA (as opposed to other forms of SpA) by rheumatologist, but there are still no long-term observational studies focusing on outcomes including

Table. Univariable GEE analysis of association between clinical parameters and disease activity/remission.

	DAPSA	ASDAS	Clinical Remission
	B (95% CI)	β (95% CI)	OR (95% CI)
Male Sex	-2.12(-4.69;0.46)	-0.29(-0.63;0.05)	1.54(0.96;2.47)
Age	**0.12(0.03;0.21)**	**0.02(0.01;0.03)**	1.00(0.98;1.02)
HLA-B27 Positivity	**-3.95(-6.46; -1.45)**	**-0.56(-0.90; -0.23)**	**1.63(1.01;2.62)**
Symptom duration	-0.27(-0.60;0.05)	0.01(-0.03;0.05)	**1.14(1.03;1.26)**
Current psoriasis	**4.29(1.34;7.23)**	**0.39(0.05;0.73)**	**0.27(0.13;0.53)**
Ever psoriasis	**3.13(-0.01;6.26)**	0.38(-0.03;0.79)	0.67(0.38;1.18)
Current IBD	-0.79(-2.66;1.08)	**-0.73(-1.01; -0.46)**	0.26(0.03;2.01)
Ever IBD	-0.94(-5.31;3.43)	**-0.67(-1.00; -0.34)**	0.65(0.11;3.93)
Current Uveitis	3.68(-4.64;12.00)	0.54(-0.61;1.70)	0.28(0.05;1.59)
Ever uveitis	-2.81(-6.62;1.00)	-0.31(-0.86;0.24)	**1.74(0.99;3.07)**
CRP, mg/L	**0.15(0.12;0.19)**	**0.03(0.02;0.03)**	**0.96(0.93;0.99)**
Steroid intake	**3.96(1.62;6.30)**	0.25(-0.02;0.52)	**0.35(0.19;0.66)**
csDMARDs intake	1.52(-0.25;3.29)	0.05(-0.17;0.27)	**0.48(0.31;0.75)**
TNF intake	-0.50(-3.17;2.18)	-0.13(-0.48;0.22)	**0.37(0.16;0.82)**
NSAID intake score, (0-100)	**0.08(0.06;0.11)**	**0.01(0.01;0.01)**	**0.97(0.97;0.98)**

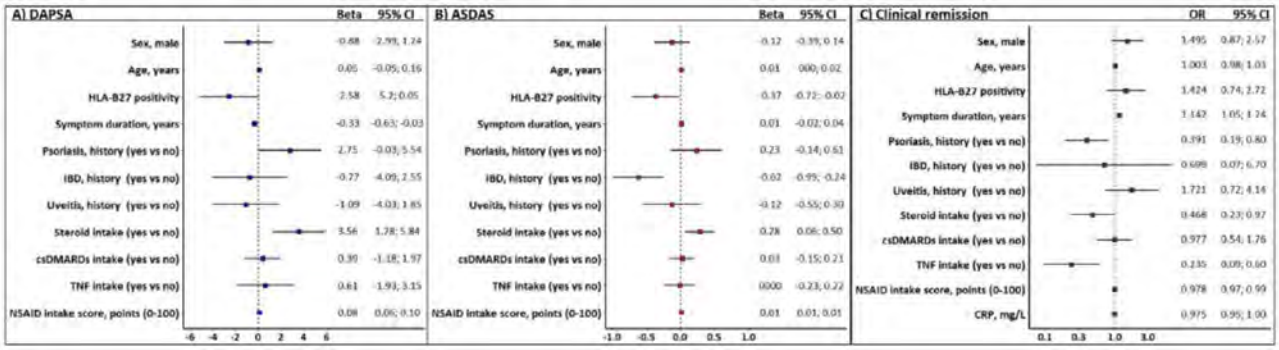

Figure. Multivariable GEE analyses show associations between parameters and outcomes A) DAPSA, B) ASDAS, and C) Clinical remission

disease activity/remission in pSpA. The aim of this study is to investigate factors associated with disease activity and achievement of remission over a period of up to 10 years of clinical observation in early pSpA patients.

Methods: Data from patients diagnosed with pSpA in GESPIC (with predominant peripheral manifestations, symptom duration of up to 5 years and not classified as axSpA) according to rheumatologist were used for this study. Visits were scheduled every 6 months for 2 years, then annually up to year 10. Clinical characteristics, examination (arthritis, enthesitis), and activity (questionnaires and laboratory) were collected at visits. Association between parameters and disease activity/remission [defined by Disease Activity in Psoriatic Arthritis (DAPSA), Axial SpA Disease Activity Score (ASDAS), and clinical remission (complete absence of arthritis or enthesitis)], was analysed by generalized estimating equations (GEE).

Results: The mean age of 115 pSpA patients (51.3% male) was 37.3 ± 12.2 years, and 71 (61.7%) patients were HLA-B27 positive. Baseline DAPSA and ASDAS were 13.3 ± 8.1 and 2.4 ± 0.9. During follow up 48 (41.7%), 46 (41.7%), and 94 (81.9%) patients reached at least once DAPSA remission (DAPSA < 4), ASDAS-Inactive disease (ASDAS< 1.3), and clinical remission, respectively. In univariable analyses, female sex, older age, HLA-B27 negativity, current and history of psoriasis, steroid, csDMARDs and higher NSAID intake were associated with higher DAPSA and lower odds of remission. Similar results were observed regarding ASDAS and clinical remission (Table). Multivariable analyses showed that history of psoriasis, HLA-B27 negativity, steroid intake, and higher NSAID intake were associated with higher DAPSA and ASDAS scores (Fig A,B), while longer symptom duration, psoriasis history, steroid, TNFi and higher NSAID intake, and higher CRP were associated with lower odds of remission (Fig C).

Conclusion: Several parameters associated with higher disease activity and absence of remission were identified. Psoriasis and higher CRP were associated with lower odds of achieving clinical remission, while an association with drug usage is likely a consequence of high disease activity.

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Abstract Number: 2221

Clinical and Molecular Patterns Associated with Persistence of Inflammation in Spondyloarthritis Patients: Unveiling Potential Biomarkers

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SESSION INFORMATION

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Background/Purpose: Chronic inflammation is closely associated with an increased risk of cardiovascular diseases (CVD) through the activation of the immune system and the release of inflammatory molecules like C-reactive protein (CRP). In Spondyloarthritis (SpA), prolonged inflammation can harm the vascular system, further raising the likelihood of developing CVD. Currently, there is a lack of tools available to identify patients who had persistent inflammation and its connection to CVD. The aim of this study was to analyze the clinical and molecular characteristics associated with persistent inflammation and to identify potential plasma protein biomarkers for an easy identification of patients with prolonged inflammation over the years in SpA patients

Methods: A study involving 136 patients diagnosed with SpA was conducted. Clinical and laboratory parameters, as well as CVD risk factors were recorded. To assess the presence of persistent inflammation, levels of CRP were retrospectively collected for a period of 5 years. A patient was classified as having persistent inflammation if increased CRP levels were detected in at 100% of the measurements taken during the preceding 5-year timeframe. Radiographs of the cervical spine, lumbar spine, and sacroiliac joints were obtained. Lateral views of the cervical and lumbar spine were scored according to the mSASSS index. Sacroiliitis was scored from right side and left side pelvic radiographs using the modified New York criteria. The plasma levels of 92 proteins related to CVD were analyzed using proximity extension assay (PEA) technology (Olink Target 96 CVD III panel, Cobiomic Biosciences).

Results: 36% of SpA patients had persistence of inflammation. Clinically, these patients showed higher levels of disease activity (ASDAS), peripheral forms, structural damage (mSASSS), acute phase reactants, altered metabolic profile, activation of complement component and higher rates of cardiometabolic comorbidities compared to non-persistent SpA patients. At molecular level, 16 CVD-related plasma proteins were significantly associated with presence of persistence of inflammation: MMP-9, RETN, PGLYRP-1, UPAR, PRTN-3, TR, RARRES-2, AZU-1, GP-6, TNF-R1, MPO, GDF-15, CCL-16, IL-2RA, PI3 and PDGF. The most contributing proteins to differentiate groups of SpA patients with persistent and non-persistent inflammation were MMP-9, RETN, PGLYRP-1 and UPAR. The combination of these proteins could predict the presence of constant persistent inflammation with an AUC=0.865. These proteins exhibit specific biological functions such as neutrophil degranulation, immune response, leukocyte migration and apoptosis.

Conclusion: 1) persistent inflammation over five years was associated with peripheral forms, increased disease activity and radiographical damage in SpA patients. 2) SpA patients with persistent inflammation display a pronounced alteration in their plasma CVD protein profile, indicating a connection between subclinical CVD risk and chronic inflammation. 3) we identified novel biomarkers that have the potential to differentiate SpA patients with persistent inflammation, offering valuable insights for therapeutic approaches.

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Abstract Number: 2222

Association Spondyloarthritis and Inflammatory Bowel Disease, More Severe Diseases on Both Sides

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Background/Purpose: There is a pathophysiological link between spondyloarthritis (SpA) and Inflammatory Bowel Disease (IBD), so that 10% of IBD is estimated to have SpA and 10% of SpA is estimated to have IBD. Recently, Luchetti *et al* demonstrated an increased level of bacterial translocation in cases of co-diagnosis of SpA and IBD compared to patients with IBD alone. These data suggest that coexistence of IBD with SpA is associated with more inflammation and therefore more active diseases. The aim of this study is to describe and to evaluate the characteristics of this population in comparison with SpA and IBD alone.

Methods: A single-centre retrospective observational study was conducted. We included all consecutive patients followed between 2019 and 2022 for spondyloarthritis (SpA) meeting the ASAS 2009 criteria and IBD histologically proven. For each patient, we collected demographics, smoking, extrarticular manifestations, imaging data and the number of bDMARDs used. We compare these patients with single diagnosis patients from the MISTIC cohort. The MISTIC cohort, a monocentric cohort, included 2000 patients aged 18–80 years who had SpA, rheumatoid arthritis or IBD and who were regularly followed-up. The MISTIC cohort was approved by the appropriate ethics committee and was conducted according to good clinical practice guidelines. Fischer's exact test was used for comparison between categorical variables and Student's t test for quantitative variables.

Results: A total of 62 patients with SpA/IBD, 51% male and 67% HLA B27+, were included (table). In 61% of the cases, IBD was diagnosed first, mainly Crohn's disease (68%), with a mean age at diagnosis of 31.1 (±15.6) years. Concerning SpA, it was mostly axial (95%), with radiographic sacroiliitis (55%) and with a mean age at diagnosis of 36.8 (±13.4) years. Patients

Table : patients characteritics

	SpA/IBD (n=62)	SpA (n=100)	IBD (n=100)	P value
Gender (% male)	51%	58%	54%	0.5
Age at diagnosis of IBD	**35.7 (±12.9)**		**31.1 (±15.6)**	**0.05**
Age at diagnosis of SpA	**36.8 (±13.4)**	**32.4 (±10.8)**		**0.02**
Disease duration IBD (years)	17.1 (±10.5)		14.5(±10.6)	0.13
Disease duration SpA (years)	14.0 (±9.84)	15.2 (±11.7)		0.17
HLA B27+	**63%**	**80%**		**0,002**
axSpA	95%			1
Number of bDMARDs	**2.8 (±1.7)**	**2 (±1.15)**	**1.65 (±0.8)**	**0.01**
Association bDMARDs	9.5 %			
Psoriaisis	**27%**	**17%**	**20%**	**0.04**
uveitis	**27%**	**18%**	**1%**	**0.087**
Sacroiliitis (Rx)	**55%**	**70%**		**0.24**
Syndesmophytes (Rx)	27%	27%		1
Crohn disease	68%		68%	1
Smoking	66%	44.9%	51.5%	0.01
Physical work	20%			
HBI score at diagnosis	**8.2 (±5.7)**		**2.6 (±3.1)**	**0.0006**
HBI score at last cinsultation	**4.2 (±3.4)**		**2.4 (±2.5)**	**0.0074**

had used an average of 3 bDMARDs and 10% were treated with a combination of bDMARDs. When comparing patients with SpA/IBD to those with a single diagnosis of SpA patients were older at diagnosis (36.8 (±13.4) VS 32.4 (±10.8) years old; p= 0.02), had more uveitis (27% VS 18%, p= 0.08) and psoriasis (27% VS 17%, p= 0.04), were more smoker (66% VS 44.9%; p= 0.01) but less HLA B27 positive (63% VS 80%, p= 0.002). They used more bDMARDs for the same disease duration (2.8 (±1.7) VS 2 (±1.15); p= 0.01). When comparing patients with a co-diagnosis to those with a single diagnosis of IBD, patients were older at diagnosis (35.7 (±12.9) VS 31.1 (±15.6) years old; p=0.05), had more uveitis (27% VS 1%, p= 0.08) and psoriasis (27% VS 20%, p= 0.04), were more smoker (66% VS 44.9%; p= 0.01). They used more bDMARDs for the same disease duration (2.8 (±1.7) VS 1.65 (±0.8); p= 0.01). Interstingly, patients with a codiagnosis have a higher endoscopic severity score (HBI) at diagnosis (8.2 (±5.7) VS 2.6 (±3.1) p= 0.0006) and at last follow-up (4.2 (±3.4) VS 2.4 (±2.5); p= 0.0074).

Conclusion: The population of patients with a co-diagnosis of SpA and IBD is a more severe both on the rheumatological and intestinal side. This population showed more frequent extraarticular manifestations and represent a cluster more difficult to treat.

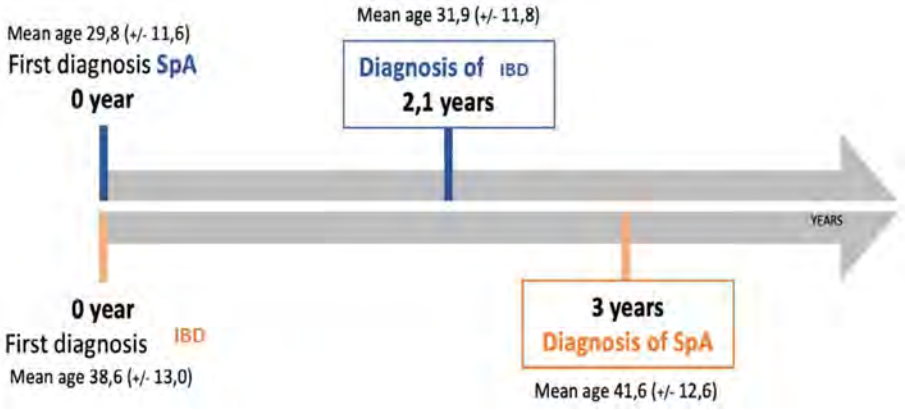

Figure: age at diagnoses according to the first diagnosis

Disclosure: J. Michel: None; **C. Prati**: None; **L. Vuitton**: None; **E. Toussirot**: None; **C. Vauchy**: None; **D. Wendling**: None; **f. Verhoeven**: None.

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Relationship Between Sleep Quality, Disease Activity, and Psychological Factors in Patients with Axial Spondyloarthritis: A Cross Sectional Study

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Background/Purpose: Sleep problems are prevalent in 30-70% of patients with axial Spondyloarthritis (SpA), negatively impacting their quality of life. Poor sleep quality in these patients has been associated with reduced exercise tolerance, worsened pain and fatigue, decreased functional status, and compromised response to therapy. While previous studies have

Table 34. Correlation between PSQI score and various variable

Sr. No	Variable	Correlation Coefficient (r)	P value
1.	Age	0.38	<0.001
2.	Duration of SpA	0.27	0.003
3.	ESR	0.4	<0.001
4.	CRP	0.48	<0.001
5.	WHOQoL- BREF: Domain 1 – Physical health Domain 2 – Psychological Domain 3 – Social Domain 4 – Environmental	 -0.82 -0.73 -0.74 -0.53	 <0.001 <0.001 <0.001 <0.001
6.	HADS D	0.79	<0.001
7.	HADS A	0.69	<0.001
8.	Fatigue (BASDAI Q1)	0.75	<0.001
9.	Pain (BASDAI Q2)	0.71	<0.001
10.	ASDAS CRP	0.69	<0.001
11.	BASDAI	0.72	<0.001
12.	BASFI	0.78	<0.001
13.	BASMI	0.71	<0.001

Correlation coefficients between the PSQI and demographic, clinical variables and PROs and index of disease activity, functionality, and Metric indices

explored the determinants of sleep problems in axial SpA patients, our study is the first in India to assess sleep quality and its components, as well as the influence of various factors on sleep in this population.

Methods: This prospective, cross-sectional study was conducted from March 2021 to September 2022 at the Department of Rheumatology, Indraprastha Apollo Hospital, Delhi. A total of 119 axial SpA patients participated, and sleep quality was measured using the PSQI questionnaire. Bivariate correlations were performed to examine the relationships between sleep quality (PSQI score) and various factors, including age, gender, disease duration, inflammatory markers, quality of life, disease activity, functionality, spinal mobility, anxiety, depression, fatigue, pain, socioeconomic status, and biological usage. Significant variables were included in a multiple linear regression model. Additionally, univariate analysis compared baseline variables and disease activity between patients with good sleep quality (PSQI < 5) and poor sleep quality (PSQI ≥ 5).

Results: Among the participants, 53% experienced poor sleep quality, with a mean global PSQI score of 5.54±4.03. As many as, 73% were not receiving treatment for insomnia. Patients with poor sleep quality had significantly higher scores across all seven dimensions of the PSQI. Sleep latency and subjective sleep quality were the most affected components, while the use of sleep medication was the least affected. Factors associated with poor sleep quality included older age, longer disease duration, smoking, radiographic evidence of sacroiliitis, hip disease, elevated inflammatory markers, low back pain, fatigue, high disease activity, poor functional status, increased spinal mobility limitation, anxiety, and depression (table 1). Gender, socioeconomic status, use of conventional DMARDs and biological therapy, enthesitis, and daytime sleepiness did not significantly influence sleep quality. Multivariate analysis revealed that limitations in spinal and hip mobility (OR: 3.76 [1.53-9.24]), fatigue (OR: 1.99 [1.27-3.11]), and depression (OR: 1.63 [1.10-2.41]) were independent risk factors for poor sleep quality.

Conclusion: Our study highlights the high prevalence of poor sleep quality in patients with axial SpA, despite limited utilization of insomnia treatments. Emotional factors such as fatigue and depression, as well as limitations in spinal and hip mobility, were identified as contributors to sleep problems in these patients. The complex relationship between sleep quality, emotional disorders, and disease activity underscores the importance of a multidisciplinary approach to managing axial SpA.

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Abstract Number: 2224

Difficult to Treat Axial Spondyloarthritis. Predictors of Poor Outcomes

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The term "Difficult-to-Treat" (D2T) defines those patients who remain active despite having undergone various treatments within the established recommendations. This concept is defined by EULAR for rheumatoid arthritis (RA)[1], and is yet to be presented in axial spondyloarthritis (ax-SpA) by the ASAS group, although it is proposed by some studies as those who require three or more biological drugs[2].

Table 1. Proposal of an extrapolated definition of D2T ax-SpA.	
To be classified as D2T the patient must meet one of the following:	
1. Treatment as recommended and failure of ≥ 4 b/tsDMARD or;	
2. Treatment as recommended and failure of ≥ 3 b/tsDMARD regardless of the MoA and evidence of disease activity.	
3. Treatment as recommended and failure of ≥ 2 b/tsDMARDs with different mechanisms of action and evidence of disease activity.	
Evidence of disease activity defined as:	ASDAS-CRP ≥ 2.1
	BASDAI ≥ 4/10
b/tsDMARD: Biologic and targeted synthetic disease-modifying antirheumatic drugs. D2T ax-SpA: Difficult-to-treat axial spondyloarthritis. MoA: Mode of Action.	

Our objectives are to determine the prevalence of D2T-ax-SpA in our Spondyloarthritis hospital registry cohort and to determine predictive factors prior to first b/ts DMARD in D2T-ax-SpA patients.

Methods: Single-center, retrospective study using a longitudinal cohort of patients with ax-SpA from a third level hospital registry in Cataluña who met the criteria for axial spondyloarthritis according to ASAS, from January 2000 to September 2022 and had a follow-up of more than 6 months with valid baseline information.

Sociodemographic, clinical, radiographic and treatment variables were collected. Patients in our study were classified as D2T according to a series of variables to achieve the most specific definition (Table 1). The comparator group included patients with axial spondyloarthritis with use of at least one b/tsDMARDs and who did not meet our D2T criteria.

For the bivariate analysis, the categorical variables were analyzed using the chi-square test and Fisher's test, the quantitative variables through the student's t test and U Mann Whitney.

For the multivariate analysis, we used logistic regression using imputations of missing values through a multiple imputation by chained equations.

Results: Five hundred and ten patients met the ASAS criteria for the diagnosis of AxSpA, 161 of whom had received treatment with at least one ts/bDMARD. Thirty-four (21.12%) met our definition of D2T, of which 55.9% were men, mean age 59.82 years (+/- 10.13).

No significant differences were found in the presence of comorbidities such as arterial hypertension, hyperlipidemia, diabetes mellitus, ischemic heart disease, and cerebrovascular disease. Nor in disease activity index or clinical manifestations such as uveitis, inflammatory bowel disease, enthesitis, arthritis, dactylitis. These results are summarized in Table 2.

Female sex (p= 0.0083), presence of psoriasis (p= 0.0007), onset as psoriatic axial spondyloarthritis (p= 0.0096) were found as risk factors for D2T AxSpA (Table 2). These findings were confirmed in the multivariate analysis (Table 3).

We also found a tendency to greater cervical involvement (SASSSmCC p= 0.025; BASRI CC p= 0.069; FLECHE p= 0.061), and being an active smoker in these patients, although this could not be demonstrated in the multivariate analysis.

Table 2. Sociodemographic, clinical and treatment variables.			
	Non D2T ax-SpA n = 126	D2T ax-SpA n = 34	p
Age (years):			
Mean age	53,4 ± 15,05	59,8 ± 10.1	0,006
Age onset of symptoms	33,7 ± 11,8	35,1 ± 11,9	0,322
Age at diagnosis	28 ± 10,3	27,8 ± 11,2	0,757
Sex			
Male	98 (78,4%)	19 (55,9%)	0,0083
Female	27 (21.6%)	15 (44,1 %)	
HLA B27			
Positive	88 (73,3%)	24 (70,6%)	0,7510
Negative	32 (26,7%)	10 (29,4%)	
High CRP			
Yes	87 (71.3%)	23 (67,6%)	0,6786
No	35 (28,7%)	11 (32,4%)	
Uveitis			
Yes	25 (19,8%)	8 (23,5%)	0,6372
No	101 (80,2%)	26 (76,5%)	
Psoriasis			
Yes	8 (6,3%)	9 (26,5%)	0,0007
No	118 (93,7 %)	25 (73.5%)	
Family history of SpA			
Yes	27 (23,3%)	6 (17.6%)	0,4860
No	89 (76,6%)	28 (82.4%)	
Enthesitis.			
Yes	42 (34,1%)	10 (29,4%)	0,6036
No	81 (65,9%)	24 (70,6%)	
Dactylitis			
Yes	5 (4%)	4 (11,8%)	0,0848
No	119 (96%)	30 (88,2%)	
Type of SpA:			
r-axSpA	90 (71,4%)	25 (73.5%)	0,8089
nr-axSpA	10 (7,9%)	1 (2,9%)	0,3070
PsA	4 (3,2%)	5 (14,7%)	0,0096
EnA	19 (15,1%)	3 (8,8%)	0,3472
JSpA	3 (2,4%)	0 (0%)	0,3637
History of tobacco:			
Non smoker	81	19	0,0092 0,0105
Ex-smoker	77	16	0,0465 0,0731
Smoker			0,4070 0,4519

AxPsA axial psoriatic arthritis.
Crp c reactive protein.
D2T ax-SpA: difficult-to-treat axial spondyloarthritis.
EnA: Enteropathic Arthritis.
JSpA: Juvenile Spondyloarthritis.
nr-axSpA: Non-Radiographic Axial Spondyloarthritis.
r-axSpA: Radiographic Axial Spondyloarthritis.

Table 3. Multivariate analysis.				
D2T ax-SpA	Haz. Ratio	P>|t|	[95% Conf. Interval]	
Female sex	4,009071	0,010	1,385541	11,60027
Psoriasis	5,689253	0,009	1,546198	20,93368
Active smoking	3,417687	0,071	,9002546	12,97475
Current age	1,034044	0,044	1,00097	1,068211
SASSSmCC	1,031436	0,364	,9645992	1,102904
D2T ax-SpA: difficult-to-treat axial spondyloarthritis. SASSS: Stoke Ankylosing Spondylitis Spine Score.				

Conclusion: Female sex, presence of psoriasis, onset as psoriatic axial spondyloarthritis prior to bDMARD seem to act as risk factors for D2T AxSpA.

References: 1.Nagy G, Roodenrijs NMT, Welsing PM, et al. (2021) EULAR definition of difficult-to-treat rheumatoid arthritis. Ann Rheum Dis 80 (1):31-5 2. Wendling D, Verhoeven F, Prati C (2022) Is the Difficult-to-Treat (D2T) concept applicable to axial spondyloarthritis? Joint Bone Spine 90 (3):105512

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Abstract Number: 2225

Long-term Evolution of Spondyloarthritis Patients Included in REGISPONSER, 17 Years Later (REGISPON-3 Study)

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: SpA
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Background/Purpose: The cross-sectional REGISPONSER study was conducted in 2004 in 31 centers from Spain, including a total of 2367 patients who met the European Spondyloarthropathy Study Group (ESSG) criteria for Spondyloarthritis (SpA). To date, the evolution/progression of SpA is not clearly defined due to the significant heterogeneity in the clinical profiles of patients and the challenges of conducting long-term prospective studies. Therefore, in this REGISPON-3 study, patients who participated in REGISPONSER from 8 out the 31 centers were reevaluated in a single visit 17 years after their initial assessment in REGISPONSER. The objective of this study is to describe, 17 years later, the confirmation or not of the initial diagnosis, clinical and radiographic evolution/progression, treatments used, and disease burden of these patients.

Methods: This is a longitudinal and multicenter study in which the REGISPONSER dataset has been combined with the REGISPON-3 data. In a single face-to-face visit, the following is carried out: a) interview with the patient; b) physical examination; c) plain X-ray of the spine, sacroiliac and hip; d) blood sample. Firstly, a descriptive analysis has been carried out to evaluate the change in the diagnosis of the patients 17 years later. The different treatments used in REGISPONSER and subsequently in REGISPON-3 have been described. Among the deceased patients, the different causes of death and diagnoses have been analysed. Finally, the average age of death has been calculated. The study was carried out in accordance with the Good Clinical Practice guidelines and after approval of the Ethics Committee in each center.

Results: From the total patients evaluated in REGISPONSER in the 8 participating centers (n=1151), we were able to recruit 437 patients (37.9%), of whom 339 were alive and 83 deceased. Table 1 shows the description of the REGISPONSER diagnoses and how they have changed 17 years later. Interestingly, among the 59 patients with undifferentiated SpA,

Table 1: Description of the evolution of the diagnosis of spondyloarthritis over 17 years from REGISPONSER I-II to REGISPON-3

REGISPONSER		REGISPON-3 final diagnosis	
Diagnosis	N (%) N = 339	Diagnosis	N (%) N=339
AS	225 (66.3)	r-AxSpA (AS)	192/225 (85.3)
		nr-AxSpA	4/225 (1.7)
		AxPsA	9/225 (4)
		p-SpA	1/225 (0.4)
		PsA	3/225 (1.3)
		Others	11/225 (4.8)
PsA	55 (16.2)	r-AxSpA (AS)	3/55 (5.4)
		nr-AxSpA	2/55 (3.6)
		PsA	43/55 (78.1)
		AxPsA	7/55 (12.7)
u-SpA	59 (17.4)	r-AxSpA (AS)	37/59 (62.7)
		Not SpA	4/59 (6.7)
		nr-AxSpA	9/59 (15.2)
		p-SpA	4/59 (6.7)
		PsA	1/59 (1.6)
		AxPsA	2/59 (3.3)
		u-SpA	2/59 (3.3)

Table 2: Description of the different treatments used in REGISPONSER y REGISPON-3

Treatments	Regisponser N=355	Regispon-3 N=306
DMARDs	92/355 (25.9)	156/306 (50.9)
TNFi	40/355 (11.3)	142/306 (46.4)
JAKi	0/355 (0)	7/306 (2.2)
IL-17i	0/355 (0)	35/306 (11.4)
IL-23i	0/355 (0)	13/306 (4.2)
Rituximab	0/355 (0)	3/306 (0.9)
Vedolizumab	0/355 (0)	2/306 (0.6)

37 developed r-axSpA, 9 nr-axSpA and 4 finally did not have SpA. Table 2 shows the treatments used in REGISPONSER and later in REGISPON-3. In general, the use of biologics increased after 17 years in the REGISPON-3 study. Among the 83 patients who died, the most frequent causes were infection (29.3%), cardiovascular (CV) events (24%), and cancer (22.7%). The mean age of death was 72.6 (10.1) years. The most frequent diagnoses of deceased patients were axial SpA (AxSpA) (69.1%), psoriatic arthritis (PsA) (19.8%) and axial PsA (AxPsA) (4.9%).

Conclusion: This study shows the preliminary results of the REGISPON-3 project. It has been observed that over the years some diagnoses changed and there are even patients whose diagnosis is not confirmed. The treatments have also evolved with a greater use and a greater variety of biological treatments, which has allowed to improve the prognosis of the disease. Finally, the causes of death in SpA have been studied, being infection, CV events and cancer the most frequent causes.

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Abstract Number: 2226

How Do Spondyloarthritis Start? Identification of the First Signs or Symptoms According to Diagnosis and HLA-B27. Data from REGISPONSER and RESPONDIA Registries

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SESSION INFORMATION

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Background/Purpose: The definition for early spondyloarthritis (SpA) implies the correct identification of the initial symptom of SpA. There is currently no consensus on whether only musculoskeletal manifestations (MM) or also extra-MM (EMM) should be considered as the onset of SpA.

Objectives: a) To describe the initial symptom (either MM or EMM) in the different SpA subtypes; b) to describe the initial symptom stratified by the clinical diagnosis and by the presence of HLA-B27; c) to analyze the clinical factors associated with different forms of initiation.

Methods: Observational, cross-sectional and multicenter study, including patients with a diagnosis of SpA (Ankylosing Spondylitis (AS), AS associated with Psoriasis (AS-Pso), AS associated with Inflammatory Bowel Disease (AS-IBD), Psoriatic Arthritis (PsA), Reactive Arthritis (ReA), Juvenile Spa (Juv-SpA), Arthritis associated with IBD (A-IBD) and undifferentiated SpA (u-SpA)) from REGISPONSER and RESPONDIA registries. Investigators responses to the question "Indicate the first sign or symptom attributable to the disease" have been recorded. The date of appearance of each MM and EMM feature was collected, allowing to determine the first symptom(s) in each patient. Differences in the first symptom across diagnosis and between HLA-B27 carriers were compared using the chi-square test. Finally, factors associated with the most prevalent initial symptom were evaluated.

Results: A total of 4411 patients were included. AS (54.9%), PsA (18.7%) and uSpA (11.1%) were the most prevalent diagnosis. In the overall population, low back pain (60.3%) was the most prevalent initial symptom followed by buttock pain (35.3%) and lower limbs arthritis (39.9%). The percentage of patients who started the disease with each symptom according to the diagnosis is represented in Figure 1.

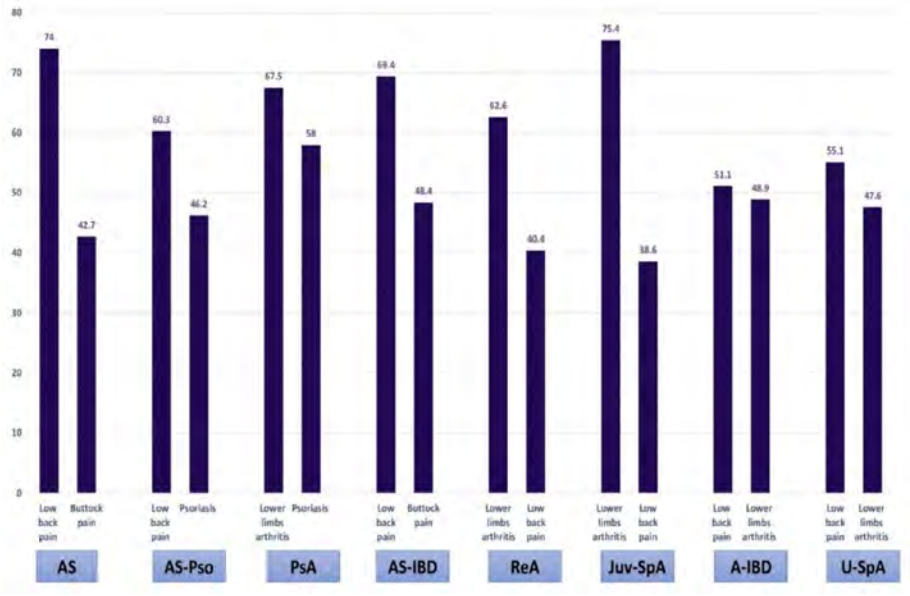

Figure 1: Description of the first symptoms according to the SpA diagnosis.

In AS patients, the absence of HLA-B27 lead to an increment in the probability of initiating the disease with cervical pain (25.6% vs. 15.5%), enthesitis (18.8% vs. 12.4%) and coxitis (15.7% vs. 8.4%) in comparison with HLA-B27 positives. In PsA, the initiation with upper limb arthritis (61% vs. 38.4%) and psoriasis (62.1% vs. 37%) was more prevalent in HLA-B27 negatives, while the initiation with low back pain (22.1% vs. 38.4%) and buttock pain 13.6% vs. 28.8%) was more prevalent in HLA-B27 positives. In AS-Pso, the absence of HLA-B27 was more frequently associated with peripheral features and psoriasis as first symptom.

In the whole population, factors associated with cervical pain vs. low back pain as first symptom were cutaneous psoriasis, negative HLA-B27 and peripheral involvement (arthritis, enthesitis and dactylitis). On the other hand, factors associated with upper limbs arthritis vs. lower limbs arthritis as first symptom were female gender, cutaneous psoriasis, HLA-B27 negative and absence of axial symptoms.

Conclusion: In this SpA population, the most prevalent initial symptoms were musculoskeletal, with differences across diagnosis and depending on the presence of HLA-B27 antigen. In AS patients the absence of the HLA-B27 seems to be associated with cervicalgia and peripheral involvement as first symptom, while in PsA it was associated with upper limbs involvement as initial symptom.

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Abstract Number: 2227

The Impact of Smoking Status on One Year Secukinumab Retention Rate in 1,684 Patients with PsA: Real-World Results from the EuroSpA Collaboration

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SESSION INFORMATION

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Background/Purpose: Smoking has been associated with higher disease activity, poorer treatment response, and drug retention rate among psoriatic arthritis (PsA) patients treated with Tumor Necrosis Factor inhibitors. However, few studies have investigated the impact of smoking on secukinumab (an IL17A inhibitor) treatment outcomes. In this study, we therefore aimed to investigate the association between smoking status and 12-month secukinumab retention rate in patients with PsA treated in routine care.

Methods: Patients with PsA, initiating secukinumab between January 1st, 2015 and December 31st, 2020, with available smoking data were identified in 10 European registries participating in the European Spondyloarthritis Research Collaboration Network (EuroSpA RCN). Patients were stratified according to their smoking status (never/former/current) at treatment start (baseline). Kaplan-Meier estimation with log-rank tests and Cox regression with hazard ratios (HR) were performed to assess and compare 12-month secukinumab retention rates. Three regression models were assessed: Model A) unadjusted analyses, Model B) adjusted for baseline age and gender and Model C) further adjusted for registry, time since

Table 1 Baseline characteristics of never, former, and current smokers.

	Never smoked N = 778	Former smoker N = 535	Current smoker N = 371	Data availability n(%)
Patient age, years	53 (44-60)	52 (45-60)	50 (41-57)	1683 (100)
Gender, male	358 (46)	244 (46)	158 (43)	1684 (100)
BMI, kg/m²	27.8 (24.8-31.9)	28.1 (24.6-32.0)	27.2 (24.5-31.1)	1268 (75)
Years since diagnosis	7 (3-14)	7 (3-14)	6 (3-12)	1627 (97)
PhGA, 0-100	40 (18-62)	40 (19-60)	32 (16-52)	1002 (60)
28 Swollen joint count	2 (0-5)	2 (0-4)	1 (0-4)	1328 (79)
28 Tender joint count	5 (2-10)	4 (1-8)	4 (1-9)	1332 (79)
CRP, mg/l	7 (2-18)	5 (2-15)	5 (2-14)	1316 (78)
DAS28 CRP, 0-10	4.3 (3.3-5.2)	4.1 (3.2-4.9)	4.1 (3.0-5.0)	1168 (69)
DAPSA28, 0-75	27.8 (17.9-41.7)	27.6 (18.1-38.0)	25.8 (17.1-37.5)	945 (56)
PGA, 0-100	70 (50-83)	70 (50-80)	70 (50-84)	1334 (79)
HAQ, 0-3	1.1 (0.8-1.6)	1.1 (0.6-1.5)	1.2 (0.8-1.8)	929 (55)
Number of previous b/tsDMARDs: 0/1/≥2	30%/25%/45%	26%/22%/52%	25%/27%/48%	1684 (100)

Data are as observed, median (IQR) or percentage. Pooled data from 11 registries participating in the EuroSpA Research Collaboration Network. b/tsDMARD, biologic/targeted Disease-Modifying Antirheumatic Drug; BMI, Body Mass Index; CRP, C-reactive protein; DAS28, Disease Activity Score in 28 joints; DAPSA Disease Activity index for PSoriatic Arthritis; DAPSA28, Disease Activity index for PSoriatic Arthritis in 28 joints; HAQ, Health Assessment Questionnaire; IQR, Interquartile Range; N, number of patients in cohort; n, total number of patients with available data; PGA, Patient Global Assessment; PhGA, Physician Global Assessment

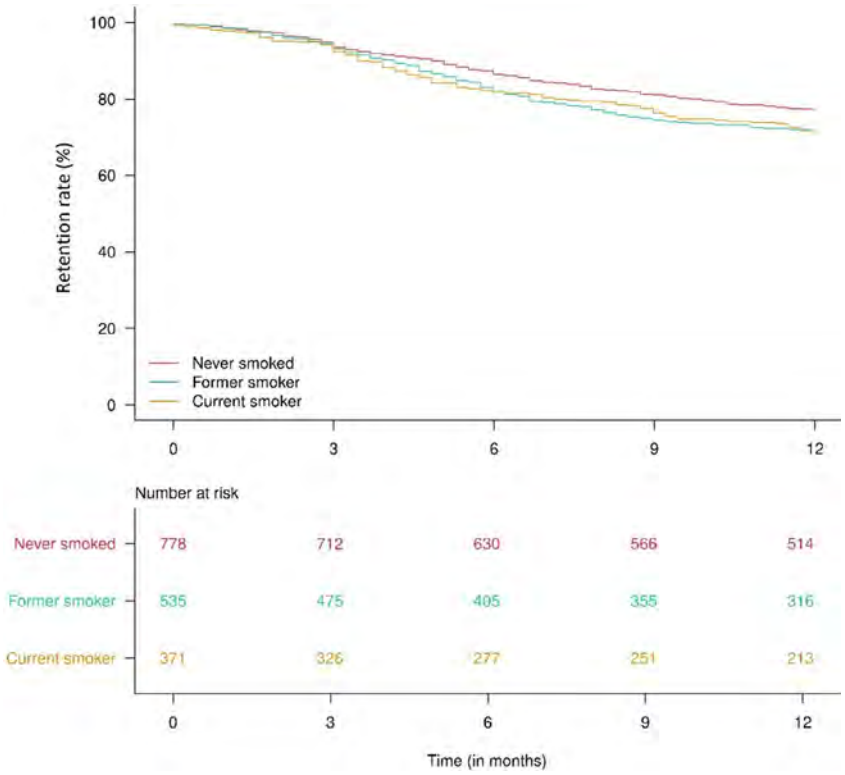

Figure 1 Kaplan-Meier curves of 12-months secukinumab retention rates in PsA patients according to smoking status (Log-rank test, p=0.039).

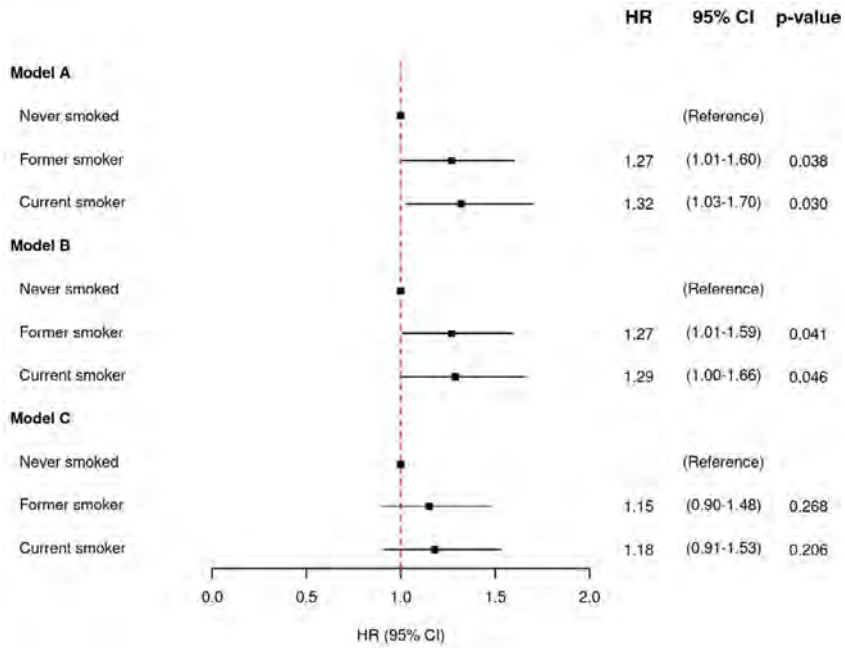

Figure 2 Secukinumab retention rates at 12-months according to smoking status. Forest plots of Cox regression analyses.

diagnosis, and line of treatment with biologic/targeted disease-modifying antirheumatic drugs(b/tsDMARD). Missing baseline covariates were imputed using multiple imputation with chained equations.

Results: Of 2,325 patients starting secukinumab treatment, 1,684 had available data on smoking status and were included. At baseline, never smokers compared to former and current smokers were older and scored higher in Disease Activity index for PSoriatic Arthritis in 28 joints (DAPSA28), C-reactive protein (CRP), and Physician Global Assessment, table 1. The 12-month retention rates were 77%, 72% and 71% among never, former, and current smokers, respectively, figure 1. For both former and current smokers, the hazard rates of withdrawal were significantly higher compared to never smokers in unadjusted, and in age and gender-adjusted analyses, figure 2. A similar trend was found in the fully adjusted Model C (HR 1.15 (95% confidence interval 0.90-1.48) and HR 1.18 (0.91-1.53), respectively), figure 2.

Conclusion: In PsA, current and former smokers, who initiate secukinumab treatment appear at increased risk of withdrawing therapy within 12 months as compared to never smokers. Studies of effectiveness should include smoking status, and further studies are needed to investigate if smoking cessation improves treatment outcomes.

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Abstract Number: 2228

Early Improvement in 3 Visual Analogue Scale (3VAS)/4VAS Predicts Reduced Rates of Radiographic Change in Bio-naive Active Psoriatic Arthritis Patients Receiving Guselkumab Treatment

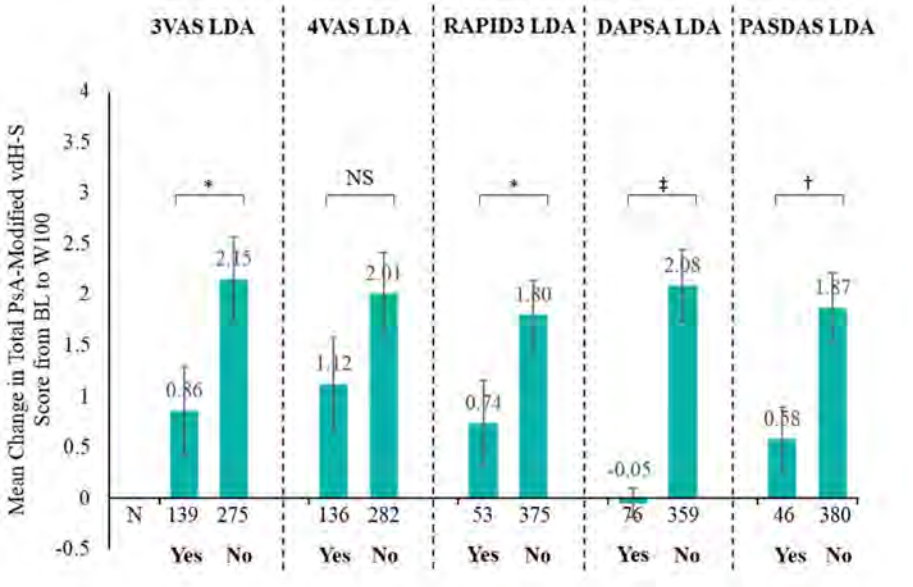
William R Tillett[1], **Laura Coates**[2], marijn vis[3], Enrique Soriano[4], Joseph F. Merola[5], Miriam Zimmermann[6], May Shawi[7], Mohamed Sharaf[8], Peter Nash[9] and Philip Helliwell[10], [1]Department of Rheumatology, Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom, [2]University of Oxford, Oxford, United Kingdom, [3]Erasmus Medical Center, Rotterdam, Netherlands, [4]Rheumatology Section, Internal Medicine Services, Hospital Italiano de Buenos Aires, and University Institute Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, [5]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [6]Immunology, Janssen Medical Affairs, LLC, Zug, Switzerland, [7]Immunology, Janssen Research & Development, LLC, Titusville, NJ, [8]Immunology, Janssen MEA, Dubai, United Arab Emirates, [9]School of Medicine, Griffith University, Brisbane, Australia, [10]University of Leeds, Leeds, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Guselkumab (GUS), a fully human IL-23p19 subunit inhibitor, was shown to reduce mean changes in radiographic progression vs placebo (PBO) by week (W)24 and to be associated with low rates of radiographic progression through W100 among GUS-treated patients (pts) with PsA, irrespective of dosing regimen (every [Q] 4W or Q8W). Furthermore, earlier clinical response predicted improved long-term radiographic outcome in GUS-treated pts with active PsA. The recently developed 3 Visual Analogue Scale (3VAS) and 4VAS scores are the first short multidimensional composite measures specifically for use in PsA routine clinical care. Here we determined whether early improvement in 3VAS/4VAS predicts radiographic change through W100.

Methods: DISCOVER-2 included bio-naive pts with active PsA (≥5 swollen and ≥5 tender joint counts [SJC/TJC]; CRP ≥0.6 mg/dL) randomized (1:1:1) to GUS 100 mg Q4W; GUS 100 mg at W0, W4, then Q8W; or PBO with crossover to GUS 100 mg Q4W at W24. In the current analysis, only pts randomized to GUS (Q4W and Q8W) were included (N=493). Response at W8 was defined as achievement of low disease activity (LDA) in 3VAS (≤3.4), 4VAS (≤3.5), routine assessment of pt index data 3 (RAPID3; ≤6), Disease Activity in PsA (DAPSA; ≤14), and PsA Disease Activity Score (PASDAS; ≤3.2). Association of W8 response with change from baseline (BL) to W100 in total PsA-modified van der Heijde-Sharp (vdH-S) score was assessed with the independent samples t-test and generalized linear models adjusting for known BL determinants of radiographic progression (vdH-S score, age, gender, and CRP). Pairwise correlations and agreement in LDA classification between the endpoints were assessed with Pearson's correlation coefficient and the kappa statistic, respectively.



*p<0.05; †p<0.01; ‡p<0.001.
BL, baseline; DAPSA, disease activity in psoriatic arthritis; LDA, low disease activity; NS, not significant; PASDAS, psoriatic arthritis disease activity score; PsA, psoriatic arthritis; RAPID3, routine assessment of patient index data 3; VAS, visual analogue scale; vdH-S, van der Heijde-Sharp; W, week.

Mean Change in Total PsA-Modified vdH-S Score from BL to W100 by Achievement of LDA in Outcomes of Interest

Results: Among GUS-treated pts not meeting the respective endpoints at BL, 32.9%, 31.6%, 12.4%, 17.8%, and 10.8% achieved LDA in 3VAS, 4VAS, RAPID3, DAPSA, and PASDAS, respectively, at W8. LDA achievement in 3VAS (0.86 vs 2.15, p=0.03), RAPID3 LDA (0.74 vs 1.80, p=0.049), DAPSA LDA (-0.05 vs 2.08, p< 0.001), and PASDAS LDA (0.58 vs 1.87, p=0.006) at W8 were associated with significantly less radiographic progression through W100 **(Figure)**. For 4VAS, achievement of remission (≤2.1; 0.71 vs 1.84, p=0.045), but not LDA (1.12 vs 2.01, p=0.142), was also associated with improved radiographic outcome. In multivariate analyses, improved response to GUS treatment at W8 in all endpoints assessed was associated with numerically less radiographic progression through W100. At W8, 3VAS and 4VAS showed strong correlations with RAPID3 (r_{3VAS}=0.787; r_{4VAS}=0.877) and PASDAS (r_{3VAS}=0.795; r_{4VAS}=0.790) and moderate correlations with DAPSA (r_{3VAS}=0.466; r_{4VAS}=0.524), whereas fair to moderate agreement (kappa range: 0.325-0.545) in LDA classification was noted.

Conclusion: Approximately one-third of GUS-treated pts achieved early response (W8 LDA) in 3VAS/4VAS, which was associated with reduced rates of radiographic change, as was early response in the other outcomes assessed. These results suggest that, in addition to their usefulness in assessing disease activity in routine clinical care, 3VAS and 4VAS, the former being more sensitive, may predict long-term radiographic changes.

Disclosure: W. Tillett: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, GSK, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Ovo Pharma, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma, 2, 5, 6; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, Bristol Myers Squibb, 2, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead Sciences, 2, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake, 2, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **m. vis**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Dutch Arthritis Foundation, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **E. Soriano**: AbbVie, 2, 5, 6, Amgen, 6, Bristol-Myers Squibb, 6, Eli Lilly, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Roche, 2, 5, 6, UCB, 5, 6; **J. Merola**: AbbVie, 12, Consultant and/or investigator, Amgen, 2, Biogen, 12, Consultant and/or investigator, Bristol Myers Squibb, 2, Dermavant, 12, Consultant and/or investigator, Eli Lilly, 12, Consultant and/or investigator, Janssen, 12, Consultant and/or investigator, LEO Pharma, 12, Consultant and/or investigator, Novartis, 12, Consultant and/or investigator, Pfizer, 12, Consultant and/or investigator, Regeneron, 12, Consultant and/or investigator, Sanofi, 12, Consultant and/or investigator, Sun Pharmaceuticals, 12, Consultant and/or investigator, UCB Pharma, 12, Consultant and/or investigator; **M. Zimmermann**: Janssen, 3, Johnson & Johnson, 11; **M. Shawi**: Immunology Global Medical Affairs, Janssen Pharmaceutical Companies of Johnson & Johnson, 3, Johnson & Johnson, 11; **M. Sharaf**: Janssen, 3, Johnson & Johnson, 11; **P. Nash**: AbbVie, 5, 6, Bristol Myers Squibb, 5, 6, Celgene, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, GSK, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer Inc, 5, 6; **P. Helliwell**: Janssen, 12, fees for educational services, Novartis, 12, fees for educational services.

Abstract Number: 2229

Individual Entheseal Points Have Differential Frequency of Involvement and Impact on Patient Reported Outcomes in Patients with Active Psoriatic Arthritis: Pooled Analysis of Two Phase 3, Randomized, Double-Blind, Placebo-Controlled Studies

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In patients with mono/oligoarticular psoriatic arthritis (PsA), swelling or tenderness of specific joints can be associated with poorer patient-reported outcomes (PROs) and physician global assessment[1]. We hypothesize that location of affected entheseal points may also have differential impact on PROs or time to enthesitis resolution with guselkumab (GUS). The objectives of this post-hoc analysis were: (1) to describe the distribution of affected entheseal points in patients with active polyarticular PsA; (2) to evaluate the impact of anatomical location of enthesitis and Leeds enthesitis index (LEI) score on patient-reported pain (PtP), patient global assessment (PtGA), and functional status; and (3) to compare the time to resolution of each entheseal point following treatment with GUS.

Methods: This post-hoc analysis used pooled data from adults with active PsA, despite standard therapies, from the DISCOVER-1 and DISCOVER-2 studies who were randomized to GUS 100 mg every 4 weeks (Q4W) or at W0, W4, then Q8W. Only patients with baseline enthesitis were included (N=473). Proportions of patients with enthesitis were determined for each entheseal point assessed by LEI score. Longitudinal impact of LEI score and location of individual entheseal points on PtP, PtGA, and health assessment questionnaire disability index (HAQ-DI), upon adjusting for potential confounders (age, sex, body mass index, prior use of tumor necrosis factor inhibitors, baseline PsA duration, swollen joint count, tender joint count), was assessed with mixed models for repeated measures through W52. Time to resolution of enthesitis at each anatomical location was assessed with Kaplan-Meier survival analysis.

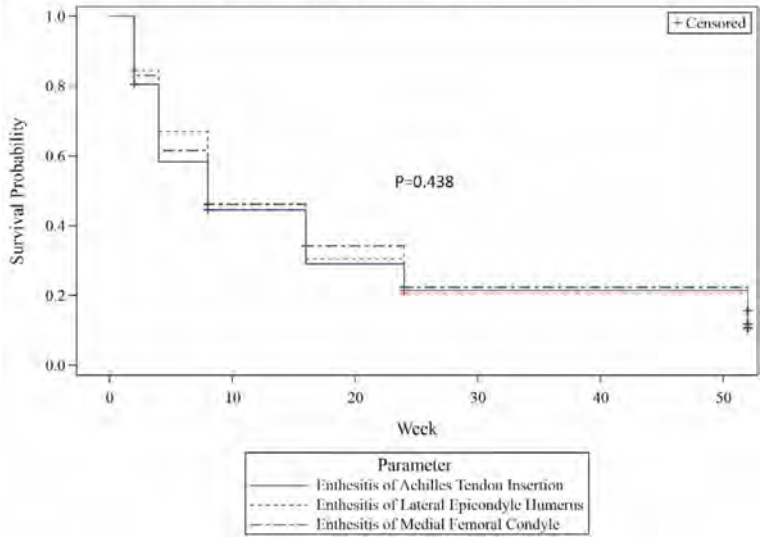
Results: Approximately half (49.5%) of GUS-randomized patients with baseline enthesitis had an LEI score of 1 or 2. The most commonly affected entheseal point was Achilles tendon insertion among both patients with baseline enthesitis and patients with an LEI score of 1 or 2. Through W52, higher baseline LEI score was associated with increased PtP, PtGA, and HAQ-DI scores (**Table**). Of the individual entheseal points assessed, enthesitis of Achilles tendon insertion had the

Table. Parameter Estimates[§] (95% Confidence Limits) of Association of LEI Score or Individual Entheseal Points with PROs (Higher Parameter Estimates Indicate Greater Association)

Determinant	Presence / # of points	PtP (0-100)	PtGA (0-100)	HAQ-DI (0-3)
LEI Score		**0.8 (0.3, 1.2)[†]**	**1.7 (1.1, 2.3)[‡]**	**0.01 (0.004, 0.02)[†]**
Enthesitis of Achilles Tendon Insertion	Yes vs. No[¥]	**3.7 (1.8, 5.6)[†]**	2.0 (-0.5, 4.6)	0.04 (-0.001, 0.08)
	2 vs. 0[¥]	**2.3 (0.7, 4.0)[†]**	**4.6 (2.4, 6.8)[‡]**	**0.04 (0.01, 0.08)[*]**
	1 vs. 0[¥]	**3.5 (1.9, 5.1)[‡]**	**3.2 (1.1, 5.4)[†]**	**0.05 (0.02, 0.08)[†]**
Enthesitis of Lateral Epicondyle Humerus	Yes vs. No[¥]	**3.0 (1.0, 4.9)[†]**	0.9 (-1.6, 3.4)	0.02 (-0.02, 0.06)
	2 vs. 0[¥]	**1.8 (0.1, 3.6)[*]**	**3.8 (1.6, 6.1)[†]**	0.02 (-0.02, 0.05)
	1 vs. 0[¥]	**2.5 (0.9, 4.0)[†]**	1.8 (-0.2, 3.8)	**0.03 (0.001, 0.07)[*]**
Enthesitis of Medial Femoral Condyle	Yes vs. No[¥]	1.0 (-1.0, 3.0)	-0.04 (-2.7, 2.6)	-0.01 (-0.05, 0.03)
	2 vs. 0[¥]	0.3 (-1.4, 1.9)	2.0 (-0.2, 4.1)	0.02 (-0.01, 0.06)
	1 vs. 0[¥]	0.1 (-1.5, 1.8)	1.6 (-0.5, 3.7)	-0.02 (-0.05, 0.01)

[§]Parameter estimates correspond to the incremental increase in each PRO for 'Yes vs No', '2 vs 0', and '1 vs 0' or for every increase in LEI score by one unit.
[¥]Categories 'No' and '0' correspond to pts with BL enthesitis who do not have enthesitis of the individual entheseal point.
[*]p <0.05; [†]p <0.01; [‡]p ≤0.0001. Bold text=statistical significance.
BL, baseline; HAQ-DI, health assessment questionnaire disability index; LEI, Leeds enthesitis index; PRO, patient-reported outcome; PtGA, patient global assessment; PtP, patient-reported pain.

Figure. Time to Resolution of Enthesitis by Anatomical Location



greatest impact on all PROs and enthesitis of medial femoral condyle the least. Following GUS treatment, median time to enthesitis resolution was W8 for each of the three anatomical locations assessed by the LEI (**Figure**).

Conclusion: In this population of patients with active polyarticular PsA, Achilles tendon insertion was the most commonly affected entheseal point and more highly associated with worse PtP, PtGA, and functional status. GUS treatment was associated with rapid enthesitis resolution, including resolution of Achilles enthesitis.

References: 1. Ayan G. *Int J Rheum Dis*. 2020;23(8):1094-9.

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Abstract Number: 2230

Bimekizumab Treatment in Patients with Active PsA and Prior Inadequate Response to TNF Inhibitors: Sustained Efficacy and Safety Results from a Phase 3 Study and Its Open-Label Extension up to 1 Year

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A, has shown superior efficacy to 16 weeks (wks) vs placebo (PBO) and tolerability in patients (pts) with active PsA in the phase 3 BE OPTIMAL and BE COMPLETE studies.1,2 Efficacy of BKZ to 52 wks has also been demonstrated in the

Table. BKZ efficacy at Weeks 16 and 52 [NRI and MI]

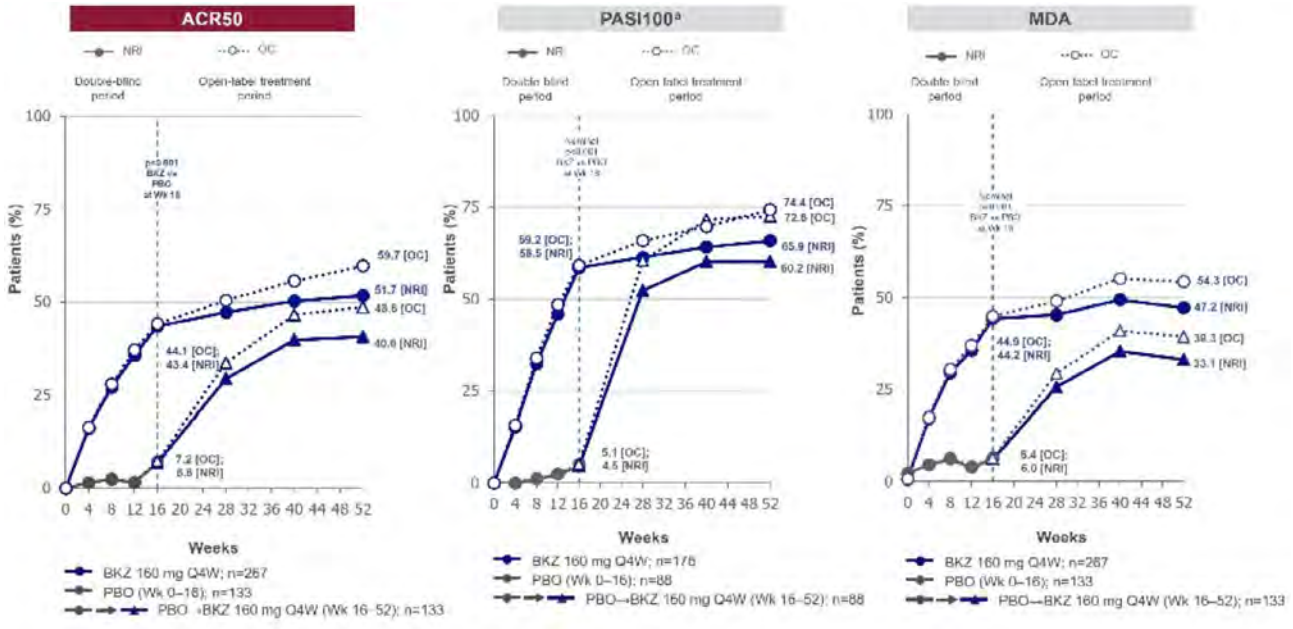
	Week 16		Week 52	
	PBO n=133	BKZ 160 mg Q4W n=267	PBO/BKZ 160 mg Q4W n=133	BKZ 160 mg Q4W n=267
ACR20 [NRI]	21 (15.8)	179 (67.0)	80 (60.2)	182 (68.2)
ACR70 [NRI]	1 (0.8)	71 (26.6)	34 (25.6)	95 (35.6)
PASI75[a] [NRI]	9 (10.2)	145 (82.4)	71 (80.7)	148 (84.1)
PASI90[a] [NRI]	6 (6.8)	121 (68.8)	65 (73.9)	131 (74.4)
MDA responder rate [NRI]	8 (6.0)	118 (44.2)	44 (33.1)	126 (47.2)
HAQ-DI CfB [MI], mean (SE)	−0.07 (0.04)	−0.38 (0.03)	−0.35 (0.05)	−0.39 (0.03)
mNAPSI resolution[b] [NRI]	12 (14.5)	73 (45.9)	51 (61.4)	107 (67.3)
Enthesitis resolution[c] [NRI]	8 (22.2)	52 (49.1)	21 (58.3)	60 (56.6)
Dactylitis resolution[d] [NRI]	6 (42.9)	24 (70.6)	12 (85.7)	29 (85.3)

Randomized set. n (%) unless otherwise specified. [a] In patients with psoriasis affecting ≥3% of body surface area at BL. [b] In patients with mNAPSI >0 at BL, PBO n=83, BKZ n=159; [c] In patients with LEI >0 at BL, PBO n=36, BKZ n=106; [d] In patients with LDI >0 at BL, PBO n=14, BKZ n=34. ACR20/70: ≥20/70% improvement in ACR criteria; BKZ: bimekizumab; HAQ-DI: HAQ – Disability Index; MDA: minimal disease activity; LDI: Leeds Dactylitis Index; LEI: Leeds Enthesitis Index; MI: multiple imputation; mNAPSI: modified Nail Psoriasis Severity Index; NRI: non-responder imputation; PASI: Psoriasis Area and Severity Index; PASI75/90: 75/90% improvement in PASI; PBO: placebo; Q4W: every four weeks; SE: standard error.

BE OPTIMAL study in biologic-naïve pts with PsA.3 Here, the efficacy and safety of BKZ treatment in pts with active PsA and prior inadequate response or intolerance to TNF inhibitors (TNFi-IR) are reported up to Wk 52 in the BE COMPLETE study.

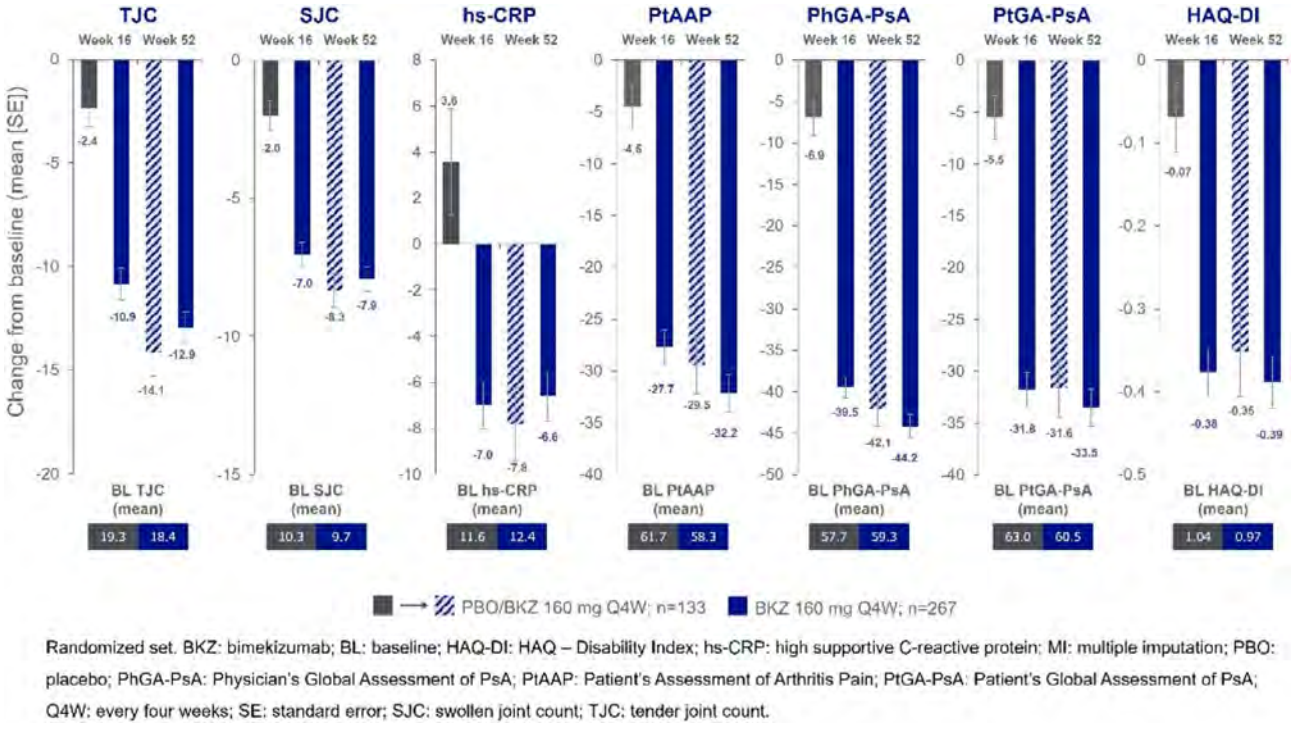
Methods: BE COMPLETE (NCT03896581) included a 16-wk double-blind, PBO-controlled period. Wk 16 completers were eligible for entry into BE VITAL (NCT04009499; open-label extension). Pts were randomized 2:1 to subcutaneous BKZ 160 mg every 4 wks or PBO. At Wk 16, PBO pts switched to BKZ (PBO/BKZ; received 36 wks of BKZ treatment up to Wk 52). BE VITAL included pts from BE OPTIMAL and BE COMPLETE; data here are for pts randomized at baseline (BL [Wk 0]) of BE COMPLETE only, up to 52 wks. Efficacy data are reported as observed case (OC) or using non-responder imputation (NRI; binary) or multiple imputation (MI; continuous). The number of treatment-emergent adverse events (TEAEs) to Wk 52 are reported for pts who received ≥1 dose of BKZ.

Results: 388/400 (97.0%) pts completed Wk 16; 377 (94.3%) entered BE VITAL and 347 (86.8%) completed Wk 52. Improved joint and skin efficacy responses with BKZ treatment were sustained from Wk 16 to Wk 52 (Table). At Wk 52, 138/267 (51.7%) of BKZ and 54/133 (40.6%) of PBO/BKZ pts achieved ACR50 (Figure 1). Improvements from BL in all ACR components were seen at Wk 16 and sustained to Wk 52 in BKZ-treated pts (Figure 2). In pts with BL psoriasis (≥3% body surface area), 116/176 (65.9%) of BKZ and 53/88 (60.2%) of PBO/BKZ pts achieved complete skin clearance (Psoriasis Area Severity Index [PASI]100) at Wk 52. At Wk 52, 126/267 (47.2%) of BKZ and 44/133 (33.1%) of PBO/BKZ pts achieved minimal disease activity (MDA; Figure 1). To Wk 52, 243/388 (62.6%) pts had ≥1 TEAE whilst receiving BKZ (exposure-adjusted incidence rate per 100 pt-years [EAIR/100 PY]: 126.0); 23 (5.9%) pts reported a serious TEAE (7.0/100 PY). Malignancies (excluding nonmelanoma skin cancers) were reported by 2 (0.7%) pts receiving BKZ (0.77/100 PY). Candida infections were reported by 25 (6.4%) pts receiving BKZ (7.7/100 PY); all were reported as mild or moderate by investigators and none were systemic. Two cases of oral candidiasis led to study discontinuation. There was one death (sudden death; pt with history of cardiac events), two adjudicated major adverse cardiac events and no definite or probable adjudicated inflammatory bowel disease.



Randomized set. [a] In pts with psoriasis affecting ≥3% of body surface area at BL. For binary variables, p values were obtained from logistic regression with treatment, prior TNFi exposure, and region as factors. Nominal p values are not powered or adjusted for multiplicity and should not be used to assess statistical significance. ACR50 responders using OC (n/Nsub) at Wk 16: BKZ 116/263, PBO 9/125; at Wk 52: BKZ 138/231, PBO/BKZ 54/111. PASI100 responders (OC: n/Nsub) at Wk 16: BKZ 103/174, PBO 4/79; at Wk 52: BKZ 116/156, Wk 52 PBO →BKZ 53/73. ACR50: ≥50% improvement in ACR criteria; BKZ: bimekizumab; MDA: minimal disease activity; NRI: non-responder imputation; OC: observed case; PASI: Psoriasis Area and Severity Index; PASI100: 100% improvement in PASI; PBO: placebo; Q4W: every four weeks; Wk: Week.

Figure 1. ACR50, PASI100 and MDA responses over time up to Week 52 [NRI and OC]



Randomized set. BKZ: bimekizumab; BL: baseline; HAQ-DI: HAQ – Disability Index; hs-CRP: high supportive C-reactive protein; MI: multiple imputation; PBO: placebo; PhGA-PsA: Physician's Global Assessment of PsA; PtAAP: Patient's Assessment of Arthritis Pain; PtGA-PsA: Patient's Global Assessment of PsA; Q4W: every four weeks; SE: standard error; SJC: swollen joint count; TJC: tender joint count.

Figure 2. Change from BL in the ACR components to 52 weeks [MI]

Conclusion: In pts with PsA and TNFi-IR, BKZ demonstrated sustained clinical efficacy from Wk 16 up to Wk 52. The safety profile was consistent with previous reports.1–3

References: 1. McInnes IB. Lancet 2023; 401(25–37); 2. Merola JF. Lancet 2023; 401(38–48); 3. Ritchlin C. Arthritis Rheumatol 2022;74(S9).

Disclosure: L. Coates: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, Bristol Myers Squibb, 2, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead Sciences, 2, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake, 2, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **R. Landewé**: AbbVie, 2, 5, AstraZeneca, 2, BMS, 2, Eli Lilly, 2, Novartis, 2, 5, Pfizer, 2, 5, Rheumatology Consultancy BV, 12, Owner, UCB Pharma, 2, 5; **I. McInnes**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Bristol Myers Squibb, 2, 5, Cabaletta, 2, 11, Causeway Therapeutics, 2, 11, Celgene, 2, 5, Compugen, 2, 11, Dextera, 11, Eli Lilly, 2, EveloBio, 1, 2, 4, 11, Gilead, 2, Janssen, 2, 5, Moonlake, 2, NHS GGC, 4, Novartis, 2, 5, Pfizer, 2, Sanofi, 2, UCB, 2, 5, Versus Arthritis, 12, Trustee Status; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2; **C. Ritchlin**: AbbVie, 2, 5, 6, Amgen, 2, BMS, 2, Eli Lilly, 2, Gilead, 2, Janssen, 2, Novartis, 2, Pfizer, 2, 5, 6, UCB, 2, 6; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer-Ingelheim, 6, Chugai, 5, 6, Eisai, 5, 6, Eli Lilly, 6, Gilead, 6, GSK, 6, Mitsubishi-Tanabe, 5, Pfizer, 6, Taiho, 6, Taisho, 5, 6; **A. Asahina**: AbbVie, 5, Amgen, 5, BMS, 5, Boehringer Ingelheim, 5, Eisai, 5, Eli Lilly, 5, Kyowa Kirin, 5, LEO Pharma, 5, Maruho, 5, Mitsubishi Tanabe Pharma, 5, Pfizer, 5, Sun Pharma, 5, Taiho Pharma, 5, Torii Pharmaceutical Co., 5, UCB Pharma, 5; **F. Behrens**: AbbVie, 2, 6, Affibody, 2, Amgen, 6, Boehringer-Ingelheim, 2, Celgene, 5, Chugai, 5, Eli Lilly, 6, Genzyme, 6, Gilead Sciences, 2, GSK, 2, 6, Janssen, 2, 5, MoonLake, 2, 6, MSD, 2, 6, Novartis, 6, Pfizer, 2, 5, 6, Roche, 5, Sandoz, 2, 6, Sanofi, 2, 6; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, Gilead Sciences, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5; **L. Gossec**: AbbVie, 2, 12, Personal fees, Amgen, 2, Biogen, 5, BMS, 12, Personal fees, Celltrion, 12, Personal fees, Eli Lilly, 5, 12, Personal fees, Galapagos,

12, Personal fees, Janssen, 12, Personal fees, MSD, 12, Personal fees, Novartis, 5, 12, Personal fees, Pfizer, 12, Personal fees, Sandoz, 5, 12, Personal fees, UCB Pharma, 5, 12, Personal fees; **A. Gottlieb**: Amgen, 1, 2, AnaptysBio, 1, 2, 5, Avotres Therapeutics, 1, 2, Boehringer Ingelheim, 1, 2, Bristol Myers Squibb, 1, 2, 5, Dice Therapeutics, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, MoonLake Immunotherapeutics, 5, Novartis, 1, 2, 5, Sanofi, 1, 2, UCB Pharma, 1, 2, 5, XBiotech, 1, 2; **R. Warren**: AbbVie, 2, 5, 6, Almirall, 2, 5, 6, Amgen, 2, 5, 6, Arena, 2, 6, Astellas, 2, 6, Avillion, 2, 6, Biogen, 2, 6, BMS, 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 5, DiCE, 6, Eli Lilly, 2, 5, 6, GSK, 2, 6, Janssen, 2, 5, 6, LEO Pharma, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sanofi, 2, 6, Sun Pharma, 6, UCB Pharma, 2, 5, 6, Union, 6; **B. Ink**: AbbVie, 11, GSK, 11, UCB Pharma, 3, 11; **R. Bajracharya**: UCB Pharma, 3, 11; **J. Coarse**: UCB Pharma, 3, 11; **J. Merola**: Abbvie, 2, 12, Investigator, Amgen, 2, 12, Investigator, Biogen, 2, 12, Investigator, Bristol-Myers Squibb, 2, 12, Investigator, Dermavant, 2, 12, Investigator, Eli Lilly, 2, 6, 12, Investigator, Janssen, 2, 12, Investigator, Leo Pharma, 2, 12, Investigator, Novartis, 2, 12, Investigator, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, 12, Investigator, Sun Pharma, 2, 12, Investigator, UCB Pharma, 2, 12, Investigator.

Abstract Number: 2231

Ixekizumab Significantly Improves Nail Disease and Adjacent Joint Tenderness and Swelling in Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Nail psoriasis (PsO) is a strong predictor for the development of psoriatic arthritis (PsA) and has been reported in 63–83% of patients with PsA[1]. Psoriatic nails are linked to arthritis in the adjacent distal interphalangeal joint (DIP) of fingers or interphalangeal joint of thumbs[2], and both can lead to severe functional impairment. In the SPIRIT-H2H study of adults with PsA, 354 of 566 participants had nail PsO and adjacent joint disease in at least one digit at baseline[3-4]. At the group level, SPIRIT-H2H patients treated with ixekizumab (IXE) achieved significantly greater improvements in nail PsO compared to those treated with adalimumab (ADA)[5]. This analysis aimed to assess the treatment effects of IXE and ADA at the individual digit level among patients with PsA, nail PsO, and adjacent joint disease.

Methods: This post hoc analysis included 354 patients from SPIRIT-H2H (NCT03151551) treated with either IXE (N=186) or ADA (N=168) who had nail PsO (Nail Psoriasis Severity Index (NAPSI) total score >0) and adjacent joint disease (tenderness and/or swelling) in at least one digit at baseline. Treatment effects were assessed for each individual finger unit displaying nail PsO and adjacent joint disease; here, finger unit defines the nail and adjacent joint of an individual digit; adjacent joint refers to the DIP of fingers or the interphalangeal joint of thumbs. Nail PsO was measured using NAPSI in the fingers only. Joint involvement was measured by tender/swollen joint count scores (TJC68/SJC66). Patients were evaluated for both nail and joint involvement at baseline and Weeks 12, 16, 24, 32, 40, and 52. Proportions of finger units with resolution of nail PsO, and proportions of finger units with resolution of adjacent joint disease were analyzed using Chi-square tests. Non-responder imputation was used to handle missing data.

Table 1.
Baseline demographics and disease characteristics of patients treated with either IXE or ADA who had psoriatic arthritis with nail psoriasis and adjacent joint disease at baseline.

	IXE	ADA
Number of patients	186	168
Affected finger units (n)	639	670
Age, years	47.4 (11.8)	48.7 (12.5)
Male, n (%)	115 (61.8)	96 (57.1)
Duration of symptoms since PsA diagnosis, years	7.4 (7.8)	6.4 (6.7)
TJC68	20.5 (13.2)	22.6 (15.5)
SJC66	10.9 (7.6)	11.3 (8.9)
NAPSI, fingers only	19.5 (18.2)	19.3 (16.5)
PASI	8.6 (8.7)	8.9 (8.2)

Data are mean (standard deviation) unless stated otherwise.
Abbreviations: ADA=adalimumab; IXE=ixekizumab; NAPSI=Nail Psoriasis Severity Index; PASI=Psoriasis Area and Severity Index; PsA=psoriatic arthritis; SJC66=Swollen Joint Count, 66 joints; TJC68=Tender Joint Count, 68 joints.

Results: There were 1309 (IXE=639, ADA=670) finger units affected by nail and adjacent joint disease at baseline (Table 1). Resolution of psoriatic nail disease (Figure 1A) and resolution of adjacent tenderness and/or swelling (Figure 1B) of the finger unit was significantly higher with IXE vs ADA at all post-baseline assessments over 52 weeks. Joint tenderness was resolved in a significantly larger proportion of IXE-treated finger units vs ADA at all post-baseline assessments over 52 weeks (Figure 2A). Joint swelling was resolved in a larger proportion of IXE-treated finger units vs ADA, and these differences reached statistical significance at all visits except Week 16 and Week 40 (Figure 2B). The tenderness and/or swelling of the finger unit resolved more rapidly than the adjacent nail disease (Figure 1).

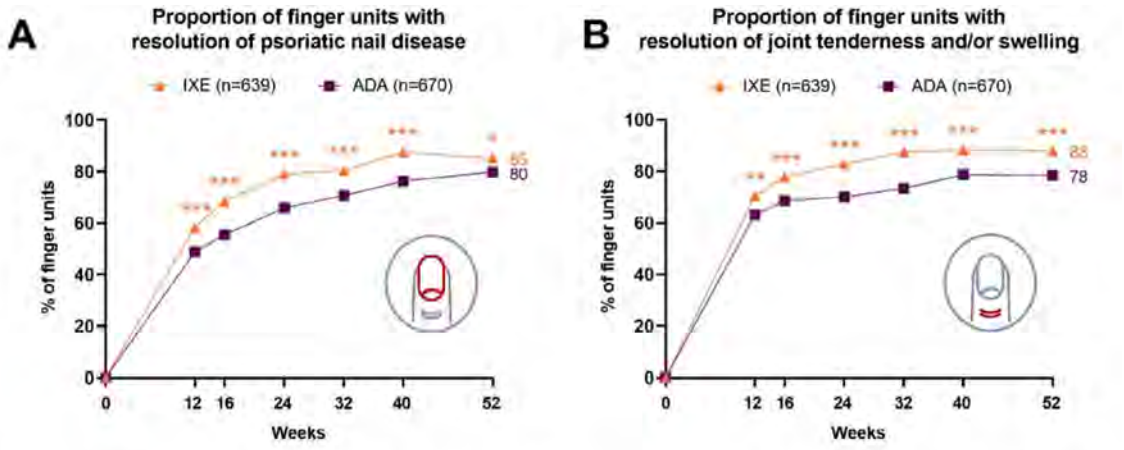

Figure 1. Proportion (%) of finger units with (A) resolution of psoriatic nail disease, and (B) resolution of joint tenderness and/or swelling, among patients treated with IXE or ADA who had psoriatic arthritis with nail psoriasis and adjacent joint disease at baseline.
Finger unit defines the nail and adjacent joint of an individual digit; adjacent joint refers to the DIP of fingers or the interphalangeal joint of thumbs. Data are nonresponder imputation mean. Significant difference between IXE vs ADA treatment denoted by *($p < 0.05$), **($p < 0.01$), and ***($p < 0.001$).
Abbreviations: ADA=adalimumab; IXE=ixekizumab.

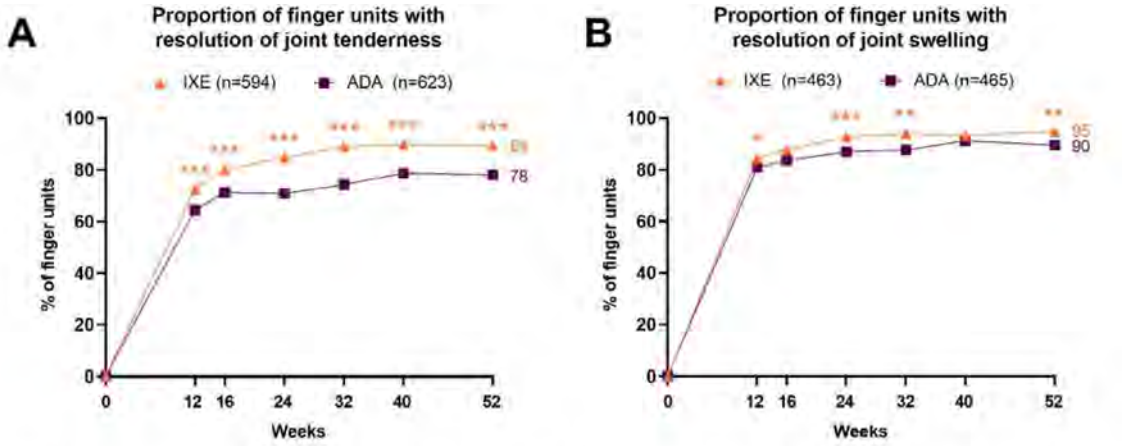

Figure 2. Proportion (%) of finger units with (A) resolution of joint tenderness, and (B) resolution of joint swelling, among patients treated with IXE or ADA who had psoriatic arthritis with nail psoriasis and adjacent joint disease at baseline.
Finger unit defines the nail and adjacent joint of an individual digit; adjacent joint refers to the DIP of fingers or the interphalangeal joint of thumbs. Data are nonresponder imputation mean. Significant difference between IXE vs ADA treatment denoted by *(p <0.05), **(p <0.01), and ***(p <0.001).
Abbreviations: ADA=adalimumab; IXE=ixekizumab.

Conclusion: IXE treatment showed a significant advantage over ADA in resolving nail PsO, joint tenderness, and joint swelling among the finger units with nail and adjacent joint disease of patients with PsA.

References

1. Elkayam O et al. Clin Rheumatol. 2000; 19(4): 301-305.
2. Lai TL et al. Clin Rheumatol. 2016; 35(8): 2031-2037
3. McGonagle D et al. British Society for Rheumatology. 2023; P169
4. McGonagle D et al. European Alliance of Associations for Rheumatology. 2023; POS1526
5. Smolen JS et al. Rheumatol Ther. 2020;7(4):1021-35

Disclosure: D. McGonagle: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, 6, 12, Paid Instructor, Janssen, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **A. Kavanaugh**: Amgen, 2, BMS, 2, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2; **I. McInnes**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Bristol Myers Squibb, 2, 5, Cabaletta, 2, 11, Causeway Therapeutics, 2, 11, Celgene, 2, 5, Compugen, 2, 11, Dextera, 11, Eli Lilly, 2, EveloBio, 1, 2, 4, 11, Gilead, 2, Janssen, 2, 5, Moonlake, 2, NHS GGC, 4, Novartis, 2, 5, Pfizer, 2, Sanofi, 2, UCB, 2, 5, Versus Arthritis, 12, Trustee Status; **L. Erik**: AbbVie, 2, 5, 6, Amgen, 2, 6, Biogen, 2, 6, Bristol-Myers Squibb, 2, 6, Eli Lilly, 2, 5, 6, Gilead, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 5, 6; **J. Merola**: Abbvie, 2, 12, Investigator, Amgen, 2, 12, Investigator, Biogen, 2, 12, Investigator, Bristol-Myers Squibb, 2, 12, Investigator, Dermavant, 2, 12, Investigator, Eli Lilly, 2, 6, 12, Investigator, Janssen, 2, 12, Investigator, Leo Pharma, 2, 12, Investigator, Novartis, 2, 12, Investigator, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, 12, Investigator, Sun Pharma, 2, 12, Investigator, UCB Pharma, 2, 12, Investigator; **B. Strober**: AbbVie, 6, 6, Alamar, 6, Almirall, 6, Alumis, 6, Amgen, 6, Arcutis, 6, 6, Arena, 6, Aristea, 6, Asana, 6, Boehringer Ingelheim, 6, Bristol Myers Squibb, 12, Consultancy honoraria, Connect Biopharma, 6, 11, CorEvitas, 6, CorEvitas Psoriasis Registry, 12, Scientific Co-Director (consulting fee), 12, Investigator, Dermavant, 6, 6, Dermira, 12, Investigator, Eli Lilly, 6, 6, Evelo Biosciences, 6, Immunic Therapeutics, 6, Incyte, 6, Janssen, 6, 6, Journal of Psoriasis and Psoriatic Arthritis, 6, Leo, 6, Maruho, 6, Meiji Seika Pharma, 6, Mindera Health, 6, 11, Novartis, 6, Pfizer, 6, Protagonist, 6, Regeneron, 6, 6, Sanofi-Genzyme, 6, 6, Sun Pharma, 6, UCB Pharma, 6, Union

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Abstract Number: 2232

Guselkumab, an IL-23p19 Subunit–specific Monoclonal Antibody, Is Able to Bind CD64$^+$ Myeloid Cells, Potently Neutralize IL-23 Produced from the Cells, and Mediate Internalization of IL-23

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Monoclonal antibodies (mAbs) targeting the interleukin (IL)-23p19 subunit are effective in treating psoriatic disease; however, their molecular attributes may translate to differences in clinical efficacy. Guselkumab (GUS) is a fully human anti-IL-23p19 subunit IgG1 mAb with a native Fc region, whereas risankizumab (RZB) is a humanized anti-IL-23p19 subunit IgG1 mAb with a mutated Fc region. Binding of mAbs to Fcγ receptors (FcγRs) is of particular interest, because FcγRI (CD64)$^+$ IL-23–producing myeloid cells are increased within inflamed tissue of patients with psoriatic disease. Furthermore, in psoriatic arthritis, joint disease activity is positively correlated with the frequency of peripheral CD64$^+$ monocytes. Here, *in vitro* functional characteristics of the antigen-binding and Fc regions of GUS and RZB, as well as implications of CD64 binding for mAb function and IL-23 neutralization, were explored.

Methods: IL-23 binding affinity of GUS and RZB was evaluated using a kinetic exclusion assay. Cellular potency was measured by mAb impact on IL-23–induced STAT3 phosphorylation in human peripheral blood mononuclear cells. Binding of GUS and RZB to FcγRs was assessed in cells transfected with individual FcγRs. Primary human monocytes differentiated into an inflammatory state were utilized in flow cytometry assays to assess GUS and RZB binding to CD64 and capture of locally produced endogenous IL-23. Cellular activation following mAb binding to CD64 on inflammatory monocytes was assessed using a 41-plex cytokine bead assay. Internalization of IL-23, GUS, and RZB within CD64$^+$ macrophages was assessed using live cell confocal imaging.

Results: GUS and RZB displayed comparable picomolar binding affinity for IL-23 and similar high potency for inhibiting IL-23–induced STAT3 phosphorylation. GUS showed the strongest binding to CD64 versus other FcγRs; RZB had negligible binding to any FcγR. GUS, but not RZB, showed dose-dependent Fc-mediated binding to CD64 on inflammatory monocytes, and CD64-bound GUS was able to capture endogenous IL-23 secreted from the same cells. GUS binding to CD64

on inflammatory monocytes did not induce or enhance cytokine production. GUS, but not RZB, bound to the cell surface of $CD64^+$ macrophages and mediated internalization of IL-23 to low pH intracellular compartments.

Conclusion: Compared with RZB, GUS has unique attributes that allow it to simultaneously bind $CD64^+$ myeloid cells via its native Fc region and neutralize IL-23 with high affinity and potency. These data suggest a potential mechanistic benefit through enrichment of GUS within inflamed tissue of patients with psoriatic disease, where $CD64^+$ IL-23–producing myeloid cells are increased, enabling potent neutralization of IL-23 at its source and removal of IL-23 from inflamed tissue via internalization.

Disclosure: D. McGonagle: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Janssen, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **r. atreya**: AbbVie, 2, 6, Amgen, 2, 6, Arena Pharmaceuticals, 2, 6, Biogen, 2, 6, Boehringer Ingelheim, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Celltrion Healthcare, 2, 6, Dr. Falk Pharma, 2, 6, Ferring, 2, 6, Fresenius Kabi, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, GlaxoSmithKline, 2, 6, InDex Pharmaceuticals, 2, 6, Janssen, 2, 6, Kliniksa Pharmaceuticals, 2, 6, Merk Sharp & Dohme, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Samsung Bioepsis, 2, 6, Stelic, 2, 6, Sterna Biologicals, 2, 6, Takeda, 2, 6, Tillotts, 2, 6; **M. Abreu**: AbbVie, 2, 6, Alimentiv, 2, 6, Amgen, 2, 6, Arena Pharmaceuticals, 2, 6, Bristol Myers Squibb, 2, 6, Celsius Therapeutics, 2, 6, Eli Lilly and Company, 2, 6, Gilead Sciences, 2, 6, Janssen Pharmaceuticals, 2, 6, Microba Life Sciences, 2, 6, Pfizer Pharmaceutical, 2, 6, Prometheus Biosciences, 2, 6, Takeda Pharmaceuticals, 2, 6, UCB Biopharma SRL, 2, 6, WebMD Global LLC, 2, 6; **J. Krueger**: AbbVie, 2, 5, 6, Aclaris, 2, 6, Akros, 5, Allergan, 2, 5, 6, Almirall, 2, 6, Amgen, 2, 5, 6, Arena, 2, 6, Aristea, 2, 6, Asana, 2, 6, Aurigene, 2, 6, Avillion, 5, Biogen, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Bristol Myers Squibb, 2, 5, 6, Eli Lilly, 2, 5, 6, Escalier, 2, 6, Exicure, 5, Galapagos, 2, 6, Incyte, 5, Innovaderm, 5, Janssen, 2, 5, 6, Kyowa Kirin, 5, MoonLake Immunotherapeutics, 2, 6, Nimbus Lackshmi, 2, 5, 6, Novan, 5, Novartis, 2, 5, 6, Parexel, 5, Pfizer, 2, 5, 6, Regeneron, 5, Sanofi, 2, 6, Sienna Biopharmaceuticals, 2, 6, Sun Pharma, 2, 6, Target-Derm, 2, 6, UCB, 2, 5, 6, Valeant, 2, 6, Ventyx, 2, 6, Vitae Pharmaceuticals, 5; **K. Eyerich**: AbbVie, 1, 6, Almirall, 1, 6, Boehringer Ingelheim, 1, 6, Bristol Myers Squibb, 1, 6, Eli Lilly, 1, 6, Hexal, 1, 6, Janssen, 1, 6, LEO Pharma, 1, 6, Novartis, 1, 6, Pfizer, 1, 6, Sanofi, 1, 6, UCB, 1, 6; **R. Bissonnette**: AbbVie, 1, 2, 5, 6, Almirall, 1, 2, 5, 6, Alumis, 1, 2, 5, 6, Amgen, 1, 2, 5, 6, AnaptysBio, 1, 2, 5, 6, Arcutis, 1, 2, 5, 6, Aristea, 1, 2, 5, 6, Bausch Health, 1, 2, 5, 6, Boehringer Ingelheim, 1, 2, 5, 6, Boston, 1, 2, 5, 6, Bristol Myers Squibb, 1, 2, 5, 6, Dermavant, 1, 2, 5, 6, Eli Lilly, 1, 2, 5, 6, Escalier, 1, 2, 5, 6, Innovaderm Research, 3, 11, Janssen, 1, 2, 5, 6, Kyowa Kirin, 1, 2, 5, 6, LEO Pharma, 1, 2, 5, 6, Nimbus, 1, 2, 5, 6, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, 6, Regeneron, 1, 2, 5, 6, Sienna, 1, 2, 5, 6, UCB, 1, 2, 5, 6, Ventyx Biosciences, 1, 2, 5, 6, Xencor, 1, 2, 5, 6; **K. Sachen**: Janssen, 3, Johnson & Johnson, 11; **C. Greving**: Janssen, 3, Johnson & Johnson, 11; **B. Stoveken**: Janssen, 3, Johnson & Johnson, 11; **D. Hammaker**: Janssen, 3, Johnson & Johnson, 11; **K. Leppard**: Janssen, 3, Johnson & Johnson, 11; **J. Hartman**: Janssen, 3, Johnson & Johnson, 11; **P. Bao**: Janssen, 3, Johnson & Johnson, 11; **E. Lacy**: Janssen, 3, Johnson & Johnson, 11; **I. Sarabia**: Janssen, 3, Johnson & Johnson, 11; **J. Deming**: Janssen, 3, Johnson & Johnson, 11; **M. Duprie**: Janssen, 3, Johnson & Johnson, 11; **J. Brown**: Janssen, 3, Johnson & Johnson, 11; **C. Ritchlin**: AbbVie, 2, 5, 6, Amgen, 2, BMS, 2, Eli Lilly, 2, Gilead, 2, Janssen, 2, Novartis, 2, Pfizer, 2, 5, 6, UCB, 2, 6; **I. McInnes**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Bristol Myers Squibb, 2, 5, Cabaletta, 2, 11, Causeway Therapeutics, 2, 11, Celgene, 2, 5, Compugen, 2, 11, Dextera, 11, Eli Lilly, 2, EveloBio, 1, 2, 4, 11, Gilead, 2, Janssen, 2, 5, Moonlake, 2, NHS GGC, 4, Novartis, 2, 5, Pfizer, 2, Sanofi, 2, UCB, 2, 5, Versus Arthritis, 12, Trustee Status; **M. Allez**: AbbVie, 2, 6, Amgen, 2, 6, Biogen, 2, 6, Boehringer Ingelheim, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Celltrion, 2, 6, Eli Lilly, 2, 6, Ferring, 2, 6, Galapagos, 2, 6, Genentech/Roche, 2, 5, 6, Gilead, 2, 6, IQVIA, 2, 6, Janssen, 2, 5, 6, Novartis, 2, 6, Pfizer, 2, 6, Takeda, 2, 5, 6, Tillotts, 2, 6; **A. Fourie**: Janssen, 3, Johnson & Johnson, 11.

Abstract Number: 2233

Neutrophil Levels Associate with Early Improvement in Spinal Pain and Week 24 Multi-Domain Disease Control During Guselkumab Treatment in Active Psoriatic Arthritis: Post Hoc Pooled Analyses of Two Phase 3 Randomized Controlled Trials

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

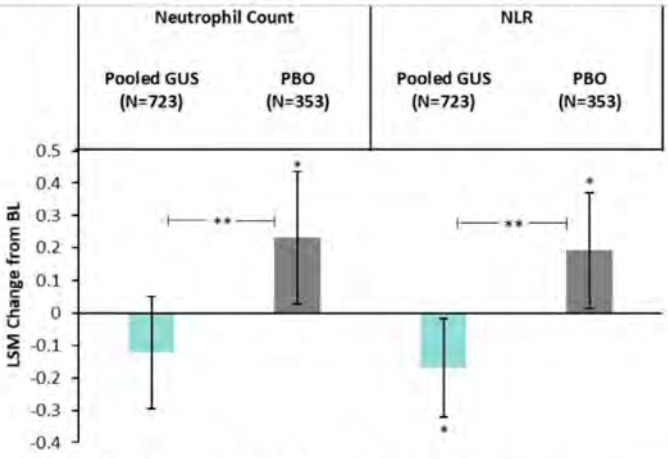
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Neutrophils have potential pathogenic roles in chronic inflammatory diseases (e.g., neutrophilic cutaneous microabscesses in psoriasis, and neutrophils in the synovial fluid/tissue in PsA and early sacroiliac joint biopsies in ankylosing spondylitis [AS]).[1] An amplification mechanism involving neutrophilic IL-23 production, as part of the T-cell-neutrophil axis, has been theorized to associate with rapid-onset action of IL-23 pathway inhibition seen in some pts.[2]In these post hoc analyses of the Phase 3 DISCOVER-1&2 studies, we explored relationships between blood neutrophils and clinical outcomes during treatment with the fully human IL-23p19-subunit inhibitor guselkumab (GUS).

Figure 1. Effect† of GUS vs. PBO on Change from BL to W4 in Neutrophil Levels



*p<0.05 vs. BL; **p<0.0001 for GUS vs. PBO. LSM: least squares mean.

†Upon adjustment for age; sex; obesity; smoking; prior TNFi use; and BL use of conventional synthetic DMARDs, corticosteroids, and NSAIDs.

Table. Association of W4 Changes in Neutrophil Levels with Achievement of Clinical Outcomes at W24 in GUS-Treated Pts

Achievement at W24	$\Delta_{BL \rightarrow W4}$Neutrophil Count OR† (95% CI)	$\Delta_{BL \rightarrow W4}$NLR OR† (95% CI)
BASDAI20 (in 194 pts with axPsA)	1.15 (0.93, 1.41)	1.34 (1.03, 1.73)**
ACR50	1.11 (1.00, 1.24)**	1.14 (1.02, 1.28)**
PASDAS LDA/VLDA (in 740 pts with BL PASDAS>3.2)	1.12 (1.00, 1.25)*	1.07 (0.95, 1.21)
Dactylitis resolution (in 319 pts with BL dactylitis)	1.22 (1.02, 1.46)**	1.18 (0.98, 1.43)*
Enthesitis resolution (in 473 pts with BL enthesitis)	1.08 (0.95, 1.23)	0.97 (0.85, 1.10)

†ORs>1 indicate an association between greater reductions in neutrophil levels and higher likelihood of achieving clinical outcomes at W24. Adjusted for BL levels, GUS regimen, prior TNFi use, and BL use of conventional synthetic DMARDs. *p<0.1, **p<0.05.

Methods: Adults in DISCOVER-1&2 (90% bio-naive) with active PsA were randomized 1:1:1 to GUS 100 mg every 4weeks (Q4W); GUS 100 mg at W0, W4, Q8W; or placebo (PBO). GUS effect (vs PBO) on early (W4) neutrophil (assessed as absolute count and neutrophil-to-lymphocyte ratio [NLR]) reduction was assessed using mixed models adjusting for potential confounders. In GUS patients (pts), associations between early (W4) neutrophil reduction and W24 achievement of 20% improvement in Bath AS Disease Activity Index (BASDAI20), ACR50, PsA Disease Activity Score (PASDAS) low/very low disease activity (LDA/VLDA), and enthesitis or dactylitis resolution were assessed with multivariate logistic regression. Associations between BL neutrophils and early clinical improvements (1st timepoint assessed) in swollen/tender joint counts (SJC/TJC at W4); skin visual analogue scale (VAS at W8); Leeds enthesitis index (LEI at W4); dactylitis severity score (DSS at W4); and spinal pain, BASDAI, and ASDAS in pts with axial involvement (axPsA; all at W8) were assessed in GUS pts using multivariate mixed models.

Results: GUS significantly reduced neutrophils (absolute count and NLR) vs PBO as early as W4 **(Figure 1)**. Early (W4) reductions in neutrophils with GUS were associated with significantly higher odds of achieving BASDAI20; ACR50; PASDAS LDA/VLDA; and dactylitis, but not enthesitis, resolution at W24 **(Table)**.However, no associations were observed between BL neutrophils in GUS-treated pts and early improvements in SJC, TJC, skin VAS, LEI, or DSS **(Figure 2A)**; lower BL neutrophil levels, conversely, were associated with a significantly greater improvement in spinal pain, and numerically greater improvements in BASDAI and ASDAS, at W8 in axPsA pts **(Figure 2B)**.

Conclusion: GUS rapidly (W4) reduced neutrophil levels, which in turn associated with greater likelihood of W24 achievement of important measures of disease control across PsA domains, e.g., ACR50, PASDAS LDA/VLDA, and dactylitis. The association between lower BL neutrophil levels and greater W8 improvement in spinal pain, but not with peripheral PsA domains, with GUS may signal a potential role of neutrophil reduction in mediating rapid improvements in axial symptoms and suggests a more impactful role for neutrophils in driving axial over peripheral symptoms. Such relationships thus require further study.

References:

1. Gong Y. *Arthritis Rheum*.2012;64:1399.
2. Macleod T. *Lancet Rheumatol*. 2023;5:47.

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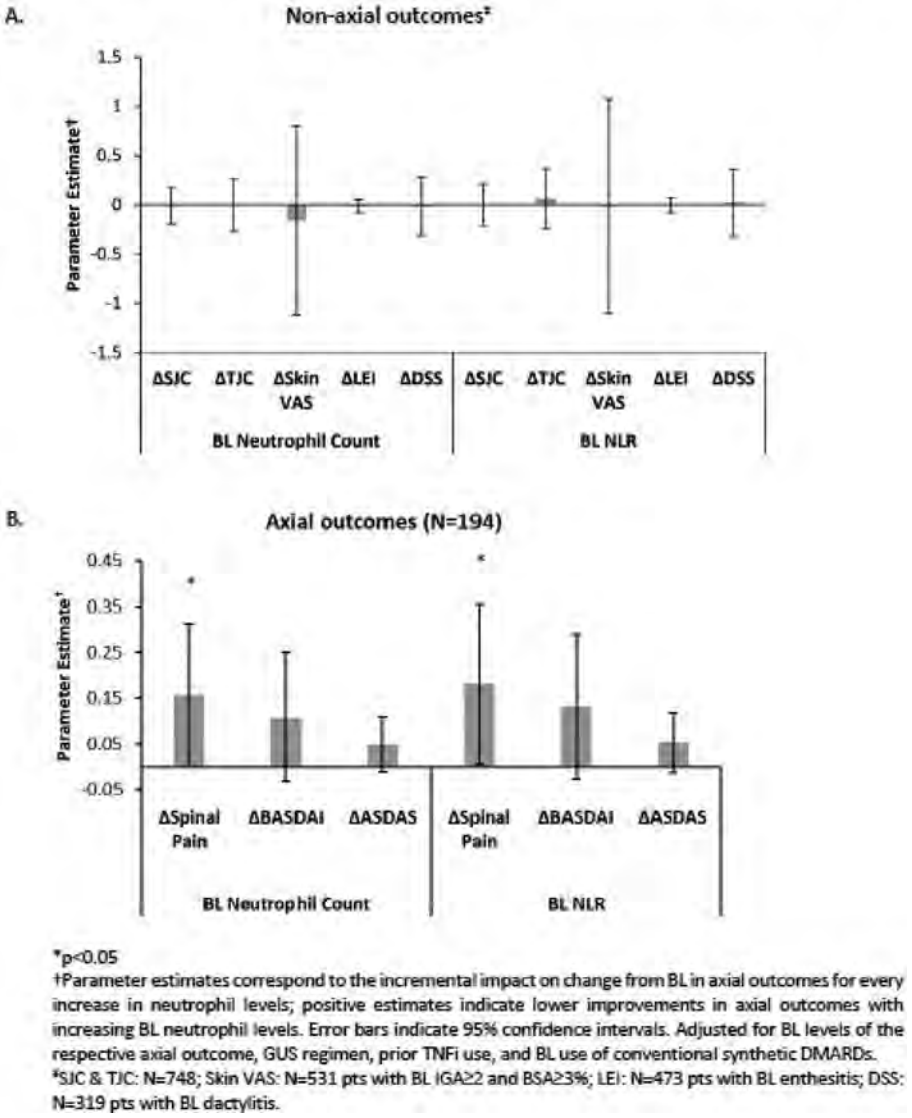
Figure 2. Association of BL Neutrophil Levels with Change from BL to First Assessment Timepoint† (W4 for Non-Axial Outcomes / W8 for Axial Outcomes) in Clinical Outcomes in GUS-Treated Pts



*p<0.05

†Parameter estimates correspond to the incremental impact on change from BL in axial outcomes for every increase in neutrophil levels; positive estimates indicate lower improvements in axial outcomes with increasing BL neutrophil levels. Error bars indicate 95% confidence intervals. Adjusted for BL levels of the respective axial outcome, GUS regimen, prior TNFi use, and BL use of conventional synthetic DMARDs.

‡SJC & TJC: N=748; Skin VAS: N=531 pts with BL IGA≥2 and BSA≥3%; LEI: N=473 pts with BL enthesitis; DSS: N=319 pts with BL dactylitis.

Pfizer, 12, Consultant and/or investigator, Regeneron, 12, Consultant and/or investigator, Sanofi, 12, Consultant and/or investigator, Sun Pharmaceuticals, 12, Consultant and/or investigator, UCB Pharma, 12, Consultant and/or investigator; **P. Rahman**: AbbVie, 2, Amgen, 2, Bristol Myers Squibb, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, UCB, 2; **D. McGonagle**: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Janssen, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 2234

Disagreement Between Patient and Physician Global Assessment over Time in Psoriatic Arthritis: Insight into Treatment Priorities

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The PsA core domain set developed by the Outcome Measures in Rheumatology working group includes musculoskeletal disease, fatigue, physical function, and structural damage, of which arthritis activity, pain, and fatigue were identified as essential by both patients (Pts) and physicians (Phs).[1-2] Assessing agreement between Pt and Ph global assessments (GA) may provide valuable insight into differential importance of specific PsA manifestations to Pts vs Phs. Although previous studies have assessed Pt/Ph disagreement, they have not evaluated potential variation over time.[3] This study assessed the agreement of PtGA and PhGA through week (W) 24 and identified factors driving disagreement between PtGA and PhGA using pooled data (N=1120) from the phase 3 DISCOVER (D)1 & 2 studies of the fully human IL-23p19 subunit inhibitor, guselkumab (GUS).

Table. Factors Associated with PhGA>PtGA and PtGA>PhGA Through W24

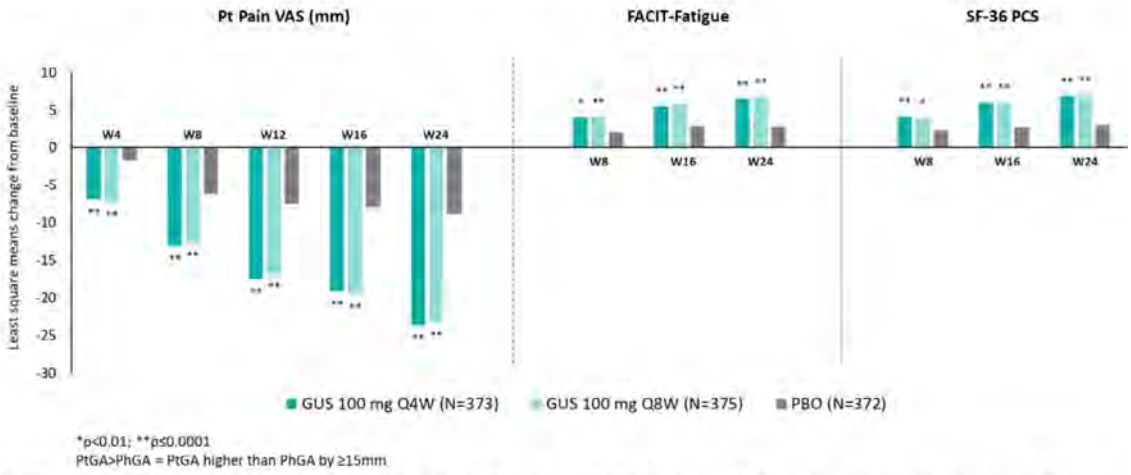
Visit	Predictors of Interest[¥]	Odds Ratio (95% CI)	
		PhGA>PtGA	PtGA>PhGA
BL (N=434)	CRP (mg/dL)	1.13 (1.00-1.27)*	
	Pt Pain (VAS mm)		0.94 (0.92-0.95)‡
	SF-36 PCS		1.04 (1.00-1.08)*
	SJC66	1.04 (1.00-1.07)*	
W8 (N=524)	CRP (mg/dL)	1.24 (1.04-1.47)*	
	Pt Pain (VAS mm)		0.92 (0.90-0.93)†
	SJC66	1.14 (1.08-1.20)‡	
	TJC68	1.06 (1.03-1.09)‡	
W16 (N=528)	CRP (mg/dL)	1.40 (1.14-1.71)†	
	Pt Pain (VAS mm)		0.91 (0.89-0.93)‡
	SJC66	1.14 (1.07-1.21)‡	
	TJC68	1.08 (1.04-1.11)‡	
W24 (N=548)	Pt Pain (VAS mm)		0.92 (0.91-0.94)‡
	SJC66	1.14 (1.08-1.21)‡	
	TJC68	1.07 (1.04-1.10)‡	
	FACIT-Fatigue		1.05 (1.02-1.09)†

*p <0.05, †p <0.01, ‡p ≤0.0001

¥Variables retained after backward selection; prior TNFi use was significant for W8/W24 but not shown. Other variables considered were age, sex, obesity, BL PsA duration, axial involvement, enthesitis, dactylitis, psoriasis, physical function, SF-36 MCS.

BL, baseline; CI, confidence interval; CRP, C-reactive protein; FACIT, Functional Assessment of Chronic Illness Therapy; MCS, mental component summary; PCS, physical component summary; PhGA, physician global assessment; PsA, psoriatic arthritis; Pt, patient; PtGA, patient global assessment; SF-36, 36-item Short-Form; SJC, swollen joint count; TJC, tender joint count; TNFi, tumor necrosis factor inhibitor; VAS, visual analogue scale; W, week

Figure. Effect of GUS on Disease Parameters Associated with PtGA>PhGA



FACIT, Functional Assessment of Chronic Illness Therapy; GUS, guselkumab; PBO, placebo; PCS, physical component summary; PhGA, physician global assessment; Pt, patient; PtGA, patient global assessment; Q4W, every 4 weeks; Q8W, every 8 weeks; SF-36, 36-item Short-Form; VAS, visual analogue scale; W, week

Methods: Pts with active PsA despite standard therapies (D1: ≥3 swollen/tender joint counts [SJC/TJC], CRP ≥0.3 mg/dL, ~30% with prior TNF inhibitors [TNFi]; D2: ≥5 SJC/TJC, CRP ≥0.6 mg/dL, biologic-naïve) were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, Q8W; or placebo. Pt/Ph agreement was defined as a difference of -15< PhGA-PtGA< 15. Determinants of PhGA exceeding PtGA by ≥15 (PhGA >PtGA) and PtGA exceeding PhGA by ≥15 (PtGA >PhGA) among Pts with PtGA/PhGA disagreement were assessed with the same logistic regression model considering Pt demographics, disease characteristics, and Pt-reported outcomes (PROs). The effect of GUS on disease parameters identified as determinants of PtGA vs PhGA disagreement was assessed with repeated measures mixed models adjusting for treatment group, baseline (BL) levels, prior TNFi use, and BL DMARD use.

Results: At BL, mean (SD) SJC=11.5 (7.4), TJC=20.6 (13.3), Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score=29.9 (10.0), PtGA=66.9 (19.9), and PhGA=64.8 (15.9) were consistent with moderate to high disease activity. Agreement between PtGA and PhGA was seen in most instances (61.2%); 23.2% of cases were characterized by PtGA >PhGA and 15.7% by PhGA >PtGA. The proportion of Pts with PtGA >PhGA increased to 39.1% at W24, while that with PhGA >PtGA decreased to 11.2%. The main determinant of PtGA >PhGA was higher Pt Pain (all time points); additional factors included worse physical health-related quality of life at BL and worse fatigue at W24 (**Table**). Conversely, Phs emphasized objective disease measures, namely higher SJC (all time points) and TJC (W8 to W24), and elevated CRP (BL to W16). GUS treatment was associated with prompt and sustained significant improvements in all identified determinants, including those driving PtGA >PhGA (**Figure**).

Conclusion: PtGA and PhGA were aligned in most encounters. PtGA >PhGA disagreement was driven by pain, fatigue, and physical health being weighed more by Pts than Phs. These findings have important implications in shared decision making and highlight the need to prioritize treatments addressing the full spectrum of PsA symptoms, including PROs.

References

1. Leung YY, et al. *J Rheum*. 2020 (Suppl);96:46
2. Mease PJ, et al. *Ann Rheum Dis*. 2022;81:879
3. Desthieux C, et al. *Arthritis Care Res*. 2017;69:1606

Disclosure: P. Rahman: AbbVie, 2, Amgen, 2, Bristol Myers Squibb, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, UCB, 2; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, Bristol Myers Squibb, 2, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead Sciences, 2, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake, 2, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **P. Nash**: AbbVie, 5, 6, Bristol Myers Squibb, 5, 6, Celgene, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, GSK, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer Inc, 5, 6; **A. Deodhar**: AbbVie, 2, 5, Amgen, 2, Aurinia, 2, Bristol Myers Squibb, 2, 5, Celgene, 5, Eli Lilly, 2, 5, Janssen, 2, 6, MoonLake, 2, 5, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5; **F. Nantel**: Janssen, 2, Johnson & Johnson, 11; **E. Rampakakis**: Janssen, 2, JSS Medical Research, Inc, 3; **L. Bessette**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol Myers Squibb, 2, 5, 6, Eli Lilly, 2, 5, 6, Fresenius Kabi, 2, 6, Gilead, 2, 5, 6, JAMP Pharma, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Organon, 2, 6, Pfizer, 2, 5, 6, Sandoz, 2, 6, Sanofi, 2, 5, 6, Teva, 2, 6, UCB, 2, 5, 6, UCBA, 5; **A. Marrache**: Janssen, Inc., 3, Johnson & Johnson, 11; **F. Lavie**: Janssen, 3, Johnson & Johnson, 11; **M. Shawi**: Immunology Global Medical Affairs, Janssen Pharmaceutical Companies of Johnson & Johnson, 3, Johnson & Johnson, 11; **W. Tillett**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, GSK, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Ovo Pharma, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma, 2, 5, 6.

Abstract Number: 2235

Identifying Differentially Expressed Genes to Predict TNF-Alpha and IL-17A Inhibitor Response in Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Approximately 30 to 40% of patients are primary non-responders, and the response rate declines after each successive biological therapy. The primary aim is to determine if cell type-specific transcriptomic data obtained at baseline can predict response to biologics at three months.

Methods: Ethics approval was obtained, and all patients consented to participate. Consecutive patients initiating TNFi or IL-17Ai therapy were assessed using a standardized protocol before initiation of biologic therapy and three months after treatment initiation. Responders were defined as patients with low DAPSA disease activity (≤14). CD8+ T cells were super paramagnetically isolated from PBMCs with Dynabeads (TM) CD8 kit (Cat#11147D). Total RNA was extracted from the CD8+ cells using Lexogen's Split RNA Kit (Cat#008.48). Libraries were pooled and sequenced on the NovaSeq 6000 for 2 x 150bp reads. STAR (v 2.6) package was used to align raw FASTQ reads and Cufflinks tool (v 2.2.1) was used to quantify the gene expression and then normalized within-sample to transcripts per million (TPM) reads. Differentially expressed genes (DEGs) were detected using limma (v 3.38.3) package. To identify biological pathways that related with drug treatment, the differential expressed genes were ranked by fold change and then to perform Gene Set Enrichment Analysis (GSEA) using MSigDB HALLMARK 2020.

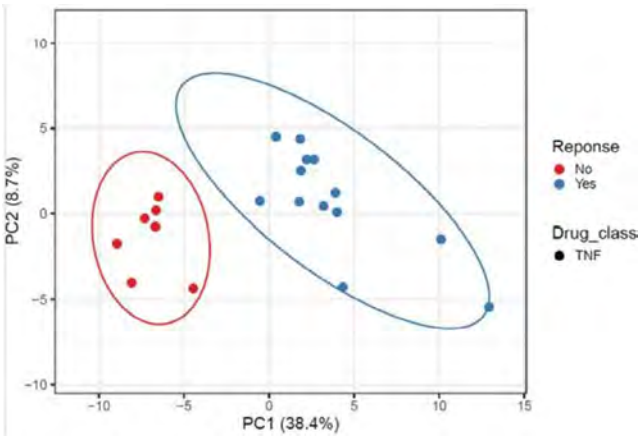


Figure 1: PCA plot of TNFi responder vs non responders of PsA patients at baseline

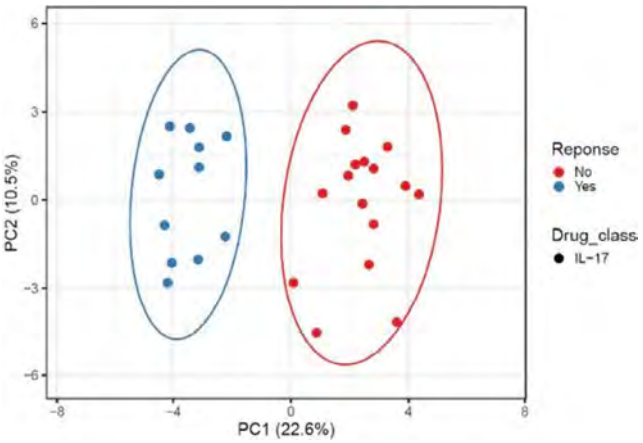


Figure 2: PCA plot of IL-17Ai among responders vs non responders of PsA patients at baseline

Results: We interrogated 49 PsA patients initiating either TNFi or interleukin-17A inhibitors. Of the 21 TNFi patients the mean age was 56, 14 were females (67%), and 13 (61%) were TNFi responders. For IL-17Ai, there were 28 PsA patients with a mean age of 56, 18 females (64%) and 11 (40%) were responders. PCA analysis discriminated responders vs. non-responder for both TNFi and IL-17Ai. The top five differentially expressed genes for TNFi response were *PM20D1, CLIC6, OR1L8, KLHL12, GPALPP1* and for IL-17Ai response were *C19orf81, NMI, RPIA, ALG1L, TUBA3E*. Using these DEGs, GSEA with the Hallmark gene sets identified MITOTIC_SPINDLE, E2F, G2M as the top down-regulated pathway after IL-17 treatment response, whereas INFLAMMATORY_RESPONSE, INTERFERON_GAMMA_RESPONSE and IL6_JAK_-STAT3_SIGNALING remained the top up-regulated pathways before TNFi treatment.

Conclusion: Genomic heterogeneity among PsA patients and cytokine led to differences in expressed genes in different biologic classes. Integration of cell-type-specific DEGs with protein-protein interactions and further comprehensive pathway enrichment analysis is pending.

Disclosure: Q. Li: None; **D. O'Rielly**: None; **K. Jenkins**: None; **D. Codner**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, Gilead Sciences, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5; **A. Dohey**: None; **I. Jurisica**: None; **V. Chandran**: AbbVie, 1, 5, 6, Amgen, 1, 5, 6, Astra-Zeneca, 3, Bristol-Myers Squibb (BMS), 1, 6, Eli Lilly, 1, 5, 6, Janssen, 1, 6, Novartis, 1, 1, 6, UCB, 1, 2; **P. Rahman**: AbbVie, 2, Amgen, 2, Bristol Myers Squibb, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, UCB, 2.

Abstract Number: 2236

Guselkumab Provides Rapid Clinically Meaningful Improvements in Clinical and Patient Reported Outcomes and Sustained Disease Control of Psoriatic Arthritis

Jeffrey R Curtis[1], Atul Deodhar[2], Enrique Soriano[3], Emmanouil Rampakakis[4], May Shawi[5], Natalie shiff[6], Marcie Strauss[7], Chenglong Han[8], William R Tillett[9] and Dafna Gladman[10], [1]Division of Clinical Immunology and Rheumatology, University of Alabama, Birmingham, AL, [2]Division of Arthritis and Rheumatic Disease, Oregon Health & Science University, Portland, OR, [3]Rheumatology Section, Internal Medicine Services, Hospital Italiano de Buenos Aires, and University Institute Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, [4]McGill University, Department of Pediatrics / JSS Medical Research, Scientific Affairs, Montreal, QC, Canada, [5]Immunology, Janssen Research & Development, LLC, Titusville, NJ, [6]Immunology, Janssen Scientific Affairs, LLC / Adjunct, Community Health and Epidemiology, University of Saskatchewan, Horsham, PA, [7]MEDASOURCE, Medical Group, Indianapolis, IN, [8]Immunology, Janssen Global Services, LLC, Malvern, PA, [9]Department of Rheumatology, Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom, [10]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Department of Medicine, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

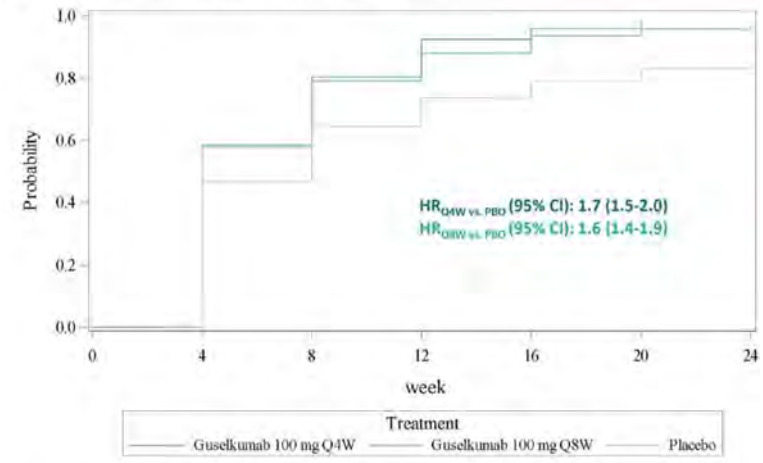
Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Guselkumab (GUS) has demonstrated robust efficacy across key PsA domains at Week (W) 24, with effects sustained or further enhanced through 2 years. Timing of clinically meaningful improvement in disease activity (DA), functional status, and health-related quality of life is of interest to PsA patients (pts) and providers. Here we 1) evaluated effect of GUS on time to minimal clinically important improvements (MCII) in pt reported outcomes and composite measures of DA; 2) assessed association between W4/W8 MCII achievement and later disease control (W24/W52).

Methods: This post hoc analysis evaluated 1120 adults with active PsA despite standard therapies from DISCOVER-1 (D1) (swollen & tender joint counts [SJC/TJC] ≥3 each, CRP ≥0.3 mg/dL, 1-2 prior TNF inhibitors [TNFi] in 31% of pts) and D2 (SJC/TJC ≥5 each, CRP ≥0.6 mg/dL, biologic-naïve). Pts were randomized 1:1:1 to GUS 100 mg every

Figure. Time to MCII in cDAPSA (Δ ≤ -5.7) Through W24



cDAPSA, clinical disease activity index for psoriatic arthritis; CI, confidence interval; HR, hazard ratio; MCII, minimal clinically important improvements; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; W, week.

Figure. Time to MCII in cDAPSA (Δ ≤ -5.7) Through W24

Table. Proportions of Pts Achieving MCII

Table. Proportions of Pts Achieving MCII

Endpoint with MCII	Week	GUS Q4W	GUS Q8W	PBO
cDAPSA	4[¥]	58.5%[†]	57.9%[†]	46.8%
	8	73.9%[‡]	72.1%[‡]	56.8%
Joint VAS	4[¥]	31.9%[†]	34.1%[‡]	21.1%
	8	45.3%[‡]	45.7%[‡]	30.7%
Pt Pain	4[¥]	27.8%[†]	29.4%[†]	18.9%
	8	44.7%[‡]	44.1%[‡]	28.1%
HAQ-DI	4[¥]	33.9%[†]	30.5%[*]	22.7%
	8	41.7%[‡]	42.6%[‡]	27.6%
PASDAS	8[¥]	68.4%[‡]	64.9%[‡]	44.0%
PtGA	8[¥]	53.4%[‡]	53.7%[‡]	32.9%
Skin VAS	8[¥]	64.0%[‡]	62.1%[‡]	35.2%
FACIT-F	8[¥]	51.1%[*]	53.1%[†]	43.4%
SF-36 PCS	8[¥]	43.2%[†]	41.6%	35.8%

[*]nominal p<0.05; [†]p<0.01; [‡]p≤0.0001 vs PBO. [¥]First time point assessed.
cDAPSA, clinical disease activity index for psoriatic arthritis; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; GUS, guselkumab; HAQ-DI, Health Assessment Questionnaire-Disability Index; MCII, minimal clinically important improvements; PASDAS, Psoriatic Arthritis Disease Activity Score; PBO, placebo; PCS, physical component summary; PtGA, Patient Global Assessment; Pts, patients; Q4W, every 4 weeks; Q8W, every 8 weeks; SF, Short Form; VAS, Visual Analogue Scale.

4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or placebo (PBO)®GUS 100 mg Q4W at W24. Time to MCII in outcomes of interest, i.e., improvement in clinical DA Index for PsA (cDAPSA) ≥5.7, Joint Visual Analogue Scale (VAS) ≥15mm, Pt Pain ≥15mm, HAQ-DI ≥0.35, PsA DA Score (PASDAS) ≥0.8, Pt Global Assessment (PtGA) ≥15mm, Skin VAS ≥15mm, Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F) ≥4, Short Form (SF)-36 physical component summary (PCS) ≥5, was compared between GUS vs PBO with Cox regression adjusting for baseline (BL) levels of respective outcome, treatment group, prior TNFi use, and BL DMARD use. MCII achievement was determined using non-responder imputation and compared between GUS and PBO using logistic regression adjusting for the above covariates. The association between MCII achievement at W4/W8 and stringent clinical response at W24/W52 amongst GUS-treated pts was assessed with logistic regression adjusting for prior TNFi use and BL DMARD use.

Results: Time to achieve MCII in all studied outcomes was significantly shorter (hazard ratio range: 1.3-2.5; all p< 0.01) for both GUS Q4W and Q8W vs PBO, including cDAPSA as a representative example (**Figure**), with curve separation occurring at the first timepoint assessed. MCII rates also were significantly higher with GUS vs PBO at the first timepoint assessed, i.e., W4 for cDAPSA, Joint VAS, Pt Pain, and HAQ-DI and W8 for PASDAS, PtGA, Skin VAS, FACIT-F, and SF-36 PCS (**Table**). W4 achievement of MCII in cDAPSA, Joint VAS, Pt Pain, and HAQ-DI was associated with greater odds of achieving future disease control, defined as ACR50, ACR70, cDAPSA ≤13, PASDAS ≤3.2, and minimal DA (MDA), at W24 (odds ratio [OR]: 1.5-3.6) and W52 (OR: 1.2-2.4). W8 achievement of MCII in all studied outcomes was also associated with greater odds of achieving disease control at W24 (OR: 1.4-17.2) and W52 (OR: 1.2-5.4).

Conclusion: In pts with active PsA, treatment with GUS was associated with more rapid MCII in both clinical and pt reported outcomes compared with PBO. As early as W4, achievement of MCII vs non-achievement in each studied outcome, particularly PASDAS and cDAPSA, was associated with greater odds of longer-term stringent DA control. Findings highlight the impact of these rapid improvements with GUS (as early as W4) on the trajectory of long-term pt outcomes.

Disclosure: J. Curtis: AbbVie, 2, 5, Amgen, 2, 5, BMS, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Genentech, 2, 5, Janssen, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB Pharma, 2, 5; **A. Deodhar**: AbbVie, 2, 5, Amgen, 2, Aurinia, 2, Bristol Myers Squibb, 2, 5, Celgene, 5, Eli Lilly, 2, 5, Janssen, 2, 6, MoonLake, 2, 5, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5; **E. Soriano**: AbbVie, 2, 5, 6, Amgen, 6, Bristol-Myers Squibb, 6, Eli Lilly, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Roche, 2, 5, 6, UCB, 5, 6; **E. Rampakakis**: Janssen, 2, JSS Medical Research, Inc, 3; **M. Shawi**: Immunology Global Medical Affairs, Janssen Pharmaceutical Companies of Johnson & Johnson, 3, Johnson & Johnson, 11; **N. shiff**: AbbVie, 11, Gilead, 11, Iovance, 11, Janssen Scientific Affairs, LLC, 3, Johnson & Johnson, 11, Novo-Nordisc, 11, Pfizer, 11; **M. Strauss**: Janssen Scientific Affairs, LLC, 2, MEDASOURCE, 3; **C. Han**: Janssen Research & Development, LLC, a wholly owned subsidiary of Johnson & Johnson, 3, Johnson & Johnson, 11; **W. Tillett**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, GSK, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Ovo Pharma, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma, 2, 5, 6; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, Gilead Sciences, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5.

Abstract Number: 2237

Upadacitinib in Refractory Psoriatic Arthritis. Multicenter Study of 134 Patients in Clinical Practice

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The EMA authorized Upadacitinib (UPA) in PsA in January 2021. UPA has shown efficacy in PsA refractory to anti-TNF in a clinical trial (RCT). Our objectives are: **a)** to study the effectiveness and safety of UPA in the 1st clinical practice (RWE) cases in Spain and **b)** to compare RWE patients with those of RCT.

TABLE 1. Baseline characteristics

	CLINICAL PRACTICE n=134	CLINICAL TRIAL n=211	p
Baseline demographic characteristics			
Age, years (mean ± SD)	51.82± 11.22	53.0 ± 12.0	0.362
Sex, n (%) women	97(72.4)	113 (53.6)	**< 0.001**
Disease Characteristics			
Duration of PsA, years (mean ± SD)	9.94 ± 7.72	9.5 ± 8.4	0.625
HAQ-DI	1.00 ± 0.63	1.10 ± 0.6	0.140
Swollen joints, mean ± SD	4.33 ± 5.01	11.3 ± 8.2	**< 0.001**
Painful joints, mean ± SD	6.10 ± 5.6	24.9±17.3	**< 0.001**
Enthesitis, n (%)	29 (21.6) (MASES)	172 (81.5) (SPARCC)	**< 0.001**
Dactylitis, n (%)	14 (10.5)	55(26.1)	**< 0.001**
PASI score, mean ± SD	0.95 ±1.65	10.1± 9.2	**< 0.001**
PCR (mg/L), mean ± SD	8.36 ± 14.47	11.2±18.5	0.133
Oral glucocorticoid, n (%)	58 (43.28)	22 (10.4)	**< 0.001**
Previous b-DMARDs			
Previous use of b-DMARD, n (%)	123 (91.8)	195 (92.4)	0.833
Number of previous b-DMARDs, n (%)			
0	11 (8.2)	18 (8.5) *	0.916
1	22 (16.4)	135 (63.7)	**< 0.001**
2	21 (15.7)	35 (16.5)	0.822
≥3	80 (59.7)	24 (11.3)	**< 0.001**
UPA at the beginning			
Monotherapy, n (%)	70 (52.24)	113 (53.6)	0.811
Combined with conventional DMARDs, n (%)	64 (47.76)	98 (46.4)	0.811

TABLE 1. Baseline characteristics

Methods: Multicenter study of 134 patients with PsA treated with UPA in Spain. The diagnosis of PsA was made using CASPAR criteria. Patients with refractory PsA from 29 Rheumatology Services (January 2021-January 2023) who had received ≥1 dose of UPA (15 mg/d) with at least 1 follow-up visit were included. Refractory PsA was defined if low clinical activity or remission had not been achieved with biological (b) and/or targeted synthetic (ts) DMARDs.

Table 2. Evolution

	Baseline (n=134)	1 month (n=89)	3 months (n=84)	6 months (n=55)	12 months (n=25)
Prednisone, n (%)	58 (43.28)	32 (35.95)	33 (39.28)	16 (29.09)	6 (24)
Dose, mg/day, mean ± SD	8.26±5.58	7.73±4.18	5.60±3.41	6.16±3.52	5.42±2.45
		p=0.049	**p=0.003**	**p=0.031**	p=0.141
Skin improvement					
Improvement n (%)	34 (25.37)	10 (52.63)	14 (87.50)	9 (69.23)	3 (50)
Onychopathia improvement					
Improvement n (%)	15 (11.28)	2 (20)	4 (57.14)	0 (0.0)	
Joint count					
swollen joints					
median [IQR]	3 [1.00;6.00]	1 [0.00; 4.00]	0 [0.00; 2.00]	0 [0.00; 2.00]	0 [0.00; 2.00]
p (vs baseline)		**p<0.001**	**p<0.001**	**p<0.001**	**p=0.003**
painful joints					
median [IQR]	5 [2.00; 8.00]	2 [0.00; 4.00]	2 [0.00; 6.00]	1 [0.00; 2.00]	2 [1.00; 4.00]
p (vs baseline)		**p<0.001**	**p<0.001**	**p<0.001**	**p=0.014**
Axial involvement improvement, n (%)	39 (29.10)	9 (52.94)	10 (45.45)	5 (35.71)	3 (33.33)
Enthesis improvement, n (%)	29 (21.64)	9 (64.29)	10 (50)	7 (53.85)	4 (44.44)
Dactylitis improvement, n (%)	14 (10.53)	7 (77.78)	4 (66.67)	4 (80)	1 (50)
PCR mg/L					
median [IQR]	2.90 [1.00; 8.95]	1.50 [0.43; 4.90]	2.02 [0.59; 5.12]	1.00 [0.3; 5.60]	1.00 [0.50; 5.50]
p (vs baseline)		**p=0.001**	p=0.235	**p< 0.001**	**p=0.006**
DAS28					
median [IQR]	4.7 [3.97; 5.38]	3.77 [2.87; 4.76]	3.17 [2.16; 4.06]	2.38 [1.73; 3.68]	2.50 [1.76; 3.09]
p (vs baseline)		**p<0.001**	**p<0.001**	**p<0.001**	**p=0.011**
DAPSA					
median [IQR]	25 [18.06;30.60]	17 [10.10;22.60]	13.29 [7.32;21.27]	12 [7.27;16.00]	10.06 [7.00;20.30]
p (vs baseline)		**p<0.001**	**p<0.001**	**p<0.001**	**p=0.015**

TABLE 2. Evolution

The outcomes were the effectiveness, safety and saving of corticosteroids (CS). A comparative study was carried out between this RWE cohort and those of the SELECT-PsA 2 RCT.

Results are expressed as percentages, mean±SD or median [IQR] depending on the distribution of the variable.

Results: 134 patients (97 women) were studied, mean age 51.8±11.2 years **(Table 1)**. The joint pattern was: peripheral (61.9%), mixed (30.6%) and axial (7.5%). During the evolution, they had also presented enthesitis (35.3%), dactylitis (25.4%), skin involvement (73.9%) and onychopathy (24.4%).

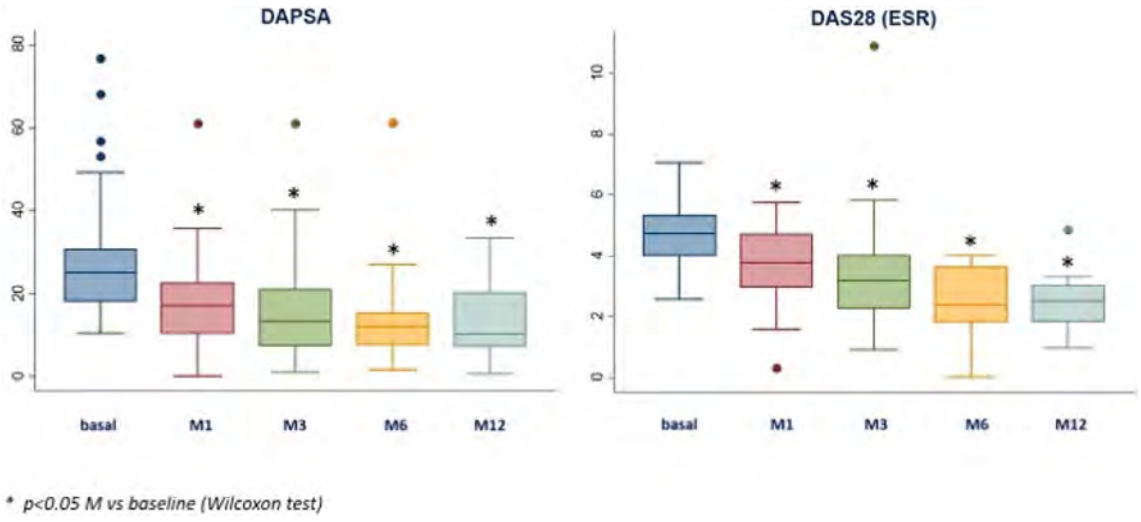
Prior to the UPA, they had received oral CS (68.7%) (mean maximum dose of prednisone 13.4±9.3) and a mean per patient of csDMARDs (1.8±1.0) and b-DMARD (3.3±2.2). The b-DMARDs were: Adalimumab (n=101), Secukinumab (66), Etanercept (53), Ixekizumab (44), Ustekinumab (44), Certolizumab (37), Infliximab (30), Golimumab (26), Guselkumab (2), Abatacept (2), Brodalumab (1). In addition, they received the following ts-DMARDs: Tofacitinib (n=29), Apremilast (27), Filgotinib (1).

UPA at baseline was associated with: **a)** prednisone (43.3%; mean dose 8.3±5.6 mg/d). **b)** csDMARDs (n=64; 47.8%): MTX (n=39), LEF (19), SSZ (10). At the start of the UPA they presented peripheral arthritis (78.4%), axial activity (29.1%), skin involvement (25.4%), onychopathy (11.3%), enthesitis (21.6%) and dactylitis (10.5%). After a mean follow-up of 5.9 ±5.1 months, a rapid and sustained improvement was observed in the activity indices **(table 2, figure)** and in the laboratory tests **(table 2)**.

At the 6th month, an improvement in axial involvement (35.7%) and extra-articular manifestations was observed: dactylitis (80%), enthesitis (53.8%) and skin involvement (69.2%), as well as a CS-sparing effect (p=0.031) **(table 2)**.

The RWE patients compared to the RCT were mostly women, refractory to a greater number of previous b-DMARDs and received more concomitant CS **(Table 1)**.

No serious adverse effects (AE) were observed. Minor AE were reported in 23 (17.2%) patients. UPA was discontinued in 44 (32.8%) (28 ineffectiveness, 4 patient decision, 4 infection, 2 de novo anterior uveitis episodes, 1 thrombosis, 1 surgery, 1 pregnancy, 1 urticaria and 1 diarrhea).



Figure

Conclusion: In this study, the first patients treated with UPA in PsA in RWE in Spain received more CS simultaneously and were refractory to a greater number of b-DMARDs than those in the RCT. As in the RCT, UPA was effective, fast, and relatively safe in refractory APs in RWE.

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Abstract Number: 2238

Longitudinal Effect of Guselkumab on Biomarkers of Inflammation and Cardiovascular Risk in Bionaive Patients with Active Psoriatic Arthritis and High Systemic Inflammatory Burden: Post-hoc Analysis of a Phase 3, Randomized, Double-blind, Placebo-Controlled Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) has been associated with an increased risk of cardiovascular (CV) disease, likely due to accelerated atherosclerosis secondary to chronic inflammation.[1] As such, patients (pts) and their health care providers have high interest in modification of CV risk. Neutrophil-to-lymphocyte ratio (NLR) and high-sensitivity (hs) CRP are biomarkers of systemic inflammation that can be followed over time and may serve as markers of CV risk. Guselkumab (GUS), a fully human IL-23p19-subunit inhibitor, has demonstrated efficacy in treating multiple PsA domains and a favorable safety profile.[2,3] This analysis assessed the impact of GUS on NLR and hsCRP as markers of CV risk in subsets of pts with active PsA and high systemic inflammatory burden.

Methods: DISCOVER-2 enrolled bionaïve adults with active PsA (≥5 swollen and ≥5 tender joints, and hsCRP ≥0.6 mg/dL) despite standard therapies; pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, Q8W; or placebo (PBO) with crossover to GUS 100 mg Q4W at W24 (PBO àGUS). The cohorts of DISCOVER-2 pts included in this analysis had baseline (BL) NLR values >2.5 (High NLR)[4] or BL hsCRP levels >10 mg/L (High hsCRP).[5] Changes from BL through W24 in NLR and hsCRP were assessed with mixed models for repeated measures adjusting for BL values of NLR and hsCRP, respectively, and BL use of conventional synthetic DMARDs, corticosteroids, and NSAIDs. Systolic (SBP) and diastolic (DBP) blood pressure as well as body mass index (BMI) through W100 were assessed descriptively.

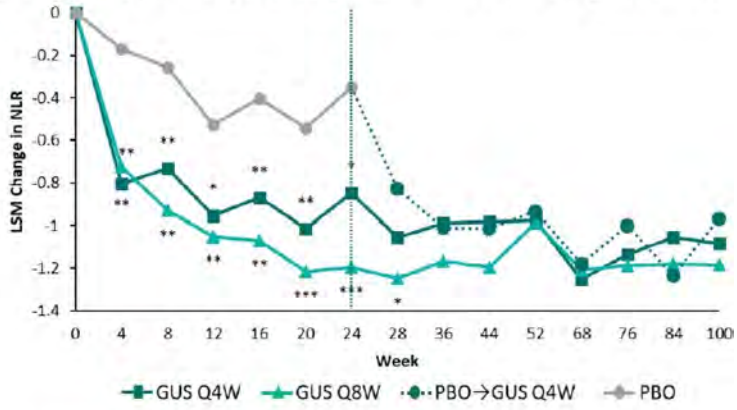
Results: The High NLR and High hsCRP cohorts comprised 445 and 393 patients, respectively, with approximately 60% of pts in each cohort also meeting the criteria for the other; BL characteristics (other than NLR/hsCRP) were generally consistent both between cohorts and across randomized treatment groups **(Table)**. Upon adjusting for BL values and concomitant PsA medications, GUS-treated pts exhibited significantly greater reductions compared with PBO in both NLR **(Figure 1)** and hsCRP **(Figure 2)** as of the first timepoint assessed (W4) and through W24, with PBOà GUS quickly (W28) converging following crossover to GUS. Reduced NLR and hsCRP levels ($p< 0.0001$ vs BL) were sustained through 2 years of GUS treatment. In both cohorts, mean BMI, SBP, and DBP remained stable through up to 2 years of GUS treatment, irrespective of GUS dosing regimen (data not shown).

Table. BL Characteristics of High NLR and High hsCRP Cohorts in DISCOVER-2

	High NLR Cohort			High hsCRP Cohort		
Parameter	**GUS Q4W (N=144)**	**GUS Q8W (N=147)**	**PBO (N=154)**	**GUS Q4W (N=129)**	**GUS Q8W (N=135)**	**PBO (N=129)**
Age (years)	46.6 (11.6)	44.2 (12.5)	45.2 (12.2)	45.8 (12.0)	44.3 (12.0)	44.4 (11.5)
Male sex, n (%)	91 (63.2)	87 (59.2)	81 (52.6)	91 (70.5)	71 (52.6)	72 (55.8)
PsA duration (years)	5.9 (5.7)	5.1 (5.4)	6.2 (6.1)	6.1 (6.3)	5.7 (6.1)	5.6 (5.1)
csDMARD use, n (%)	109 (75.7)	102 (69.4)	112 (72.7)	92 (71.3)	94 (69.6)	87 (67.4)
Corticosteroid use, n (%)	31 (21.5)	30 (20.4)	39 (25.3)	24 (18.6)	32 (23.7)	26 (20.2)
NSAID use, n (%)	106 (73.6)	96 (65.3)	102 (66.2)	95 (73.6)	98 (72.6)	89 (69.0)
NLR	4.1 (1.9)	4.1 (1.6)	4.2 (2.1)	3.5 (2.2)	3.4 (1.8)	3.6 (2.2)
>2.5	Def	Def	Def	82 (63.6)	89 (65.9)	90 (69.8)
hsCRP (mg/L)	19.7 (23.1)	22.0 (23.4)	25.5 (30.1)	29.3 (25.8)	32.5 (26.3)	35.9 (29.9)
>10 mg/L, n (%)	82 (56.9)	89 (60.5)	90 (58.4)	Def	Def	Def
BMI (kg/m^2)	28.4 (5.9)	28.2 (6.0)	28.1 (6.1)	28.8 (6.4)	28.8 (6.8)	28.3 (6.0)
SBP (mmHg)	125.8 (9.9)	125.6 (11.8)	126.3 (10.1)	126.9 (9.8)	126.0 (11.4)	126.3 (10.5)
DBP (mmHg)	78.8 (7.0)	78.6 (7.3)	79.6 (6.7)	80.1 (6.6)	78.7 (6.8)	79.3 (6.8)
DAPSA score	51.6 (22.1)	47.5 (19.6)	49.9 (20.6)	52.7 (23.1)	49.9 (19.6)	50.8 (19.5)
SJC (0-66)	13.7 (8.4)	12.1 (7.5)	12.5 (7.4)	13.7 (9.2)	12.4 (6.7)	12.2 (7.5)
TJC (0-68)	23.3 (13.8)	20.2 (11.7)	22.0 (14.0)	23.1 (14.0)	20.8 (12.0)	21.6 (12.5)
Pain (VAS, 0-100)	62.4 (19.7)	64.1 (20.2)	63.6 (17.3)	64.0 (18.8)	66.4 (18.9)	65.8 (17.6)
PtGA (VAS, 0-100)	66.9 (20.2)	69.8 (20.6)	69.0 (18.4)	70.7 (17.7)	71.5 (20.0)	71.3 (18.6)
HAQ-DI (0-3)	1.3 (0.5)	1.3 (0.6)	1.3 (0.5)	1.4 (0.5)	1.5 (0.6)	1.3 (0.6)
PhGA (VAS, 0-100)	66.2 (15.8)	66.1 (16.0)	67.1 (16.0)	69.2 (14.9)	69.1 (15.0)	67.4 (15.9)
% BSA affected by PsO	19.4 (20.9)	19.2 (22.8)	19.6 (21.9)	19.5 (20.4)	16.5 (20.7)	20.2 (22.7)
PASI score (0-72)	11.4 (12.5)	11.0 (13.1)	10.4 (11.0)	12.5 (13.2)	9.7 (12.1)	11.4 (11.6)
Pts with enthesitis, n (%)	104 (72.2)	94 (63.9)	111 (72.1)	101 (78.3)	90 (66.7)	90 (69.8)
LEI score (1-6)	3.0 (1.7)	2.7 (1.6)	2.9 (1.6)	2.9 (1.7)	2.6 (1.4)	2.8 (1.5)
Pts with Dactylitis, n (%)	74 (51.4)	67 (45.6)	70 (45.5)	74 (57.4)	63 (46.7)	57 (44.2)
DSS (1-60)	8.6 (10.2)	7.7 (9.2)	8.6 (9.9)	8.2 (9.6)	8.4 (10.0)	8.5 (10.3)

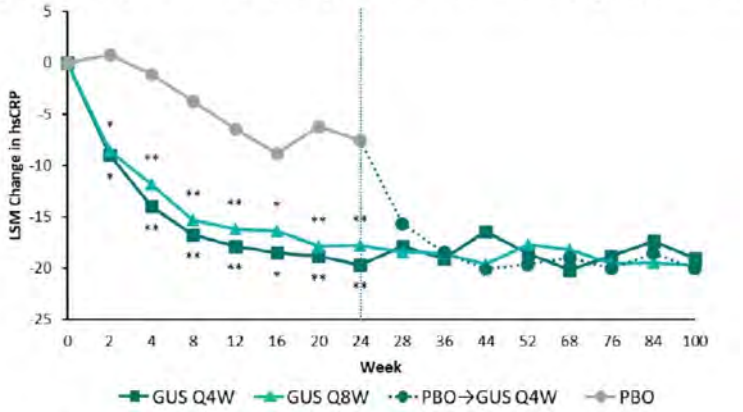
Data are presented as mean (SD) unless stated otherwise.
BMI: body mass index; BSA: body surface area; csDMARD: conventional synthetic disease-modifying antirheumatic drugs; DAPSA: Disease Activity in PSoriatic Arthritis; DBP: diastolic blood pressure; Def: by definition; DSS: dactylitis severity score; HAQ-DI: health assessment questionnaire-disability index; hsCRP: high-sensitivity C-reactive protein; LEI: Leeds enthesitis index; NLR: neutrophil-to-lymphocyte ratio; NSAID: non-steroidal anti-inflammatory drug; PASI: Psoriasis Area Severity Index; PhGA: physician global assessment; PsO: psoriasis; PtGA: patient global assessment (joint and skin); SBP: systolic blood pressure; SJC: swollen joint count; TJC: tender joint count.

Figure 1. Least Square Mean (LSM) Changes from BL to W24 in NLR (High NLR Cohort)



*p<0.05, **p<0.01, ***p<0.0001 for GUS Q4W/Q8W vs. PBO

Figure 2. Least Square Mean (LSM) Changes from BL to W24 in hsCRP (High hsCRP Cohort)



*p<0.001, **p<0.0001 for GUS Q4W/Q8W vs. PBO

Conclusion: In these two subgroups of bionaïve PsA pts with high levels of biomarkers of inflammation and CV risk, GUS led to rapid and sustained reductions in NLR and hs-CRP. In addition, traditional CV risk factors remained stable for 2 years. These findings highlight the potential utility of GUS to ameliorate systemic inflammation associated with elevated CV risk and support a consistent guselkumab safety profile in patients with PsA and high systemic inflammatory burden.

References

1. Zheng Z. *Front Cardiovasc Me*d. 2022 Apr 6;9:83543
2. Deodhar A. *Lancet*. 2020 Apr 4;395:1115
3. Mease PJ. *Lancet*. 2020 Apr 4;395:1126
4. Qiao S. *Ther Clin Risk Manag*. 2020; 16: 437
5. Merola JF. *Rheumatol Ther*. 2022 Jun;9:935

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Abstract Number: 2239

Achievement of Disease Control in PsA Patients Treated with Upadacitinib at Week 152: Post Hoc Analysis of the Long-term Extensions of Two Phase 3 Trials

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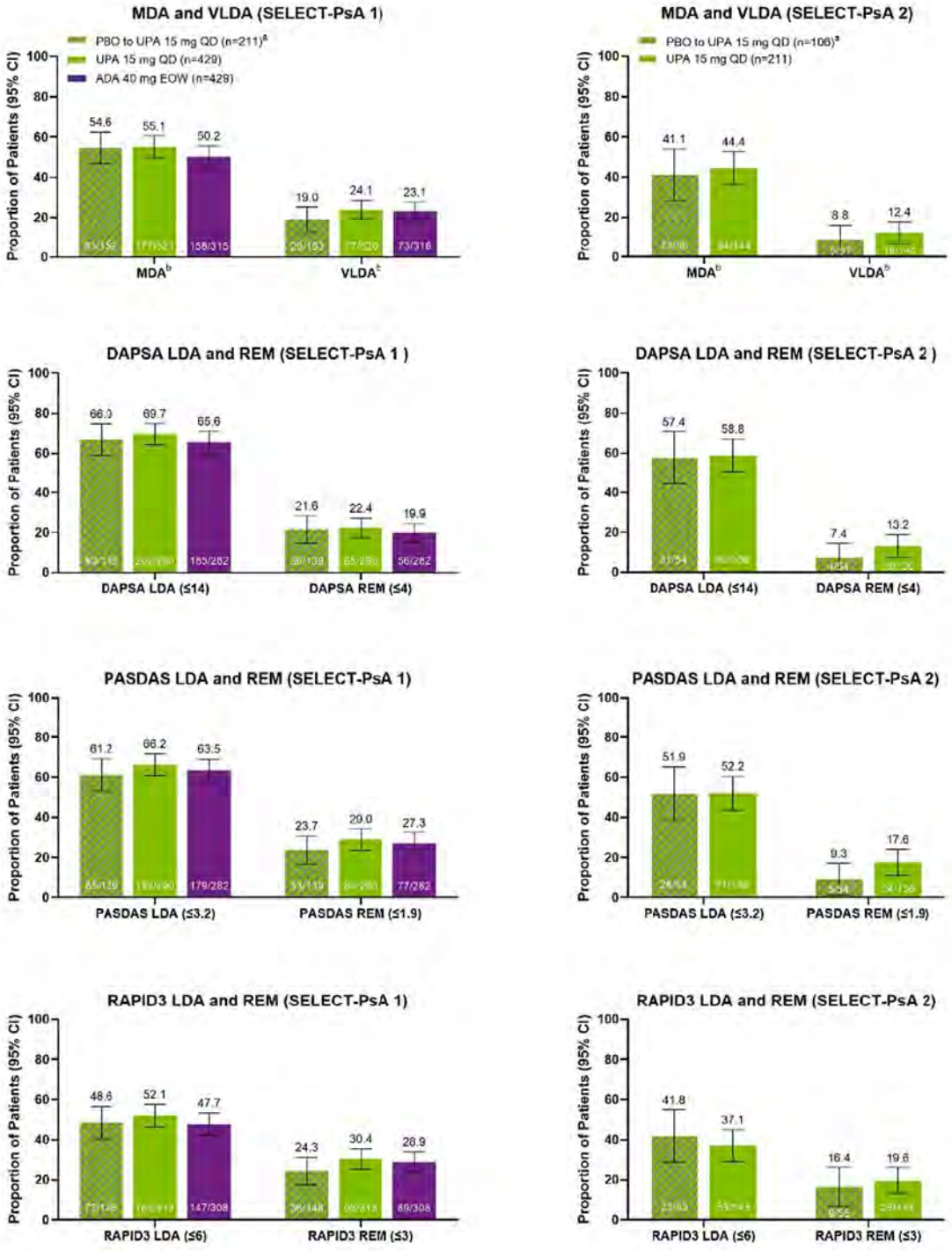
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: A main goal of therapy for patients (pts) with PsA is to achieve and maintain the lowest possible level of disease activity across domains.[1] Composite measures used to assess disease activity include Minimal Disease Activity (MDA)/Very Low Disease Activity (VLDA), as well as achievement of low disease activity (LDA) or remission (REM) using the Disease Activity index for PsA (DAPSA), PsA Disease Activity Score (PASDAS), and/or Routine Assessment of Patient Index Data 3 (RAPID3). Here, we assess the achievement of goals according to these measures in pts with PsA following long-term treatment with upadacitinib (UPA), an oral JAK inhibitor, at week (wk) 152 from two phase 3 trials.

Methods: Post hoc analysis of pts from the SELECT-PsA 1 (N=1704; inadequate response to non-biologic DMARDs [non-bDMARD-IR]) and SELECT-PsA 2 (N=641; bDMARD-IR) studies was performed.[2,3] Pts randomized to once daily UPA 15 mg (UPA15), placebo (switched to UPA15 at wk 24), or every other wk adalimumab (ADA; SELECT-PsA 1 study only) were evaluated. Proportions of pts achieving MDA (≥5/7 criteria)/VLDA (7/7 criteria), DAPSA LDA (≤14)/REM (≤4), PASDAS LDA (≤3.2)/REM (≤1.9), or RAPID3 LDA (≤6)/REM (≤3) at wk 152 were assessed. Additionally, proportions of pts achieving individual MDA components among those who did (responder) or did not (non-responder) achieve MDA at wk 152 are shown. As observed (AO) data are presented.

Results: At 3 years, ~50-70% of pts remained in the studies. In SELECT-PsA 1, similar proportions of pts treated with UPA15, PBO switched to UPA15, or ADA achieved MDA (range: 50-55%) or VLDA (range: 19-24%) at wk 152 (**Figure 1**). In SELECT-PsA 2, similar response rates were observed for MDA (range: 41-44%) and VLDA (range: 9-12%) amongst pts receiving UPA15 or PBO switched to UPA15. The proportions of pts achieving LDA or REM for DAPSA, PASDAS, and RAPID3 were similar between UPA15, PBO switched to UPA15, and ADA. As expected, pts identified as responders had higher response rates for all individual MDA components compared to non-responders across both studies (**Figure 2**). High proportions of responders and non-responders treated with UPA15 achieved SJC66 ≤1, PASI ≤1 or Body Surface Area-Psoriasis (BSA-Ps) ≤3%, and Leeds Enthesitis Index (LEI) ≤1; similar rates were observed with PBO switched to UPA15

Figure 1. Proportion of Patients Achieving LDA and REM at Week 152 (AO)

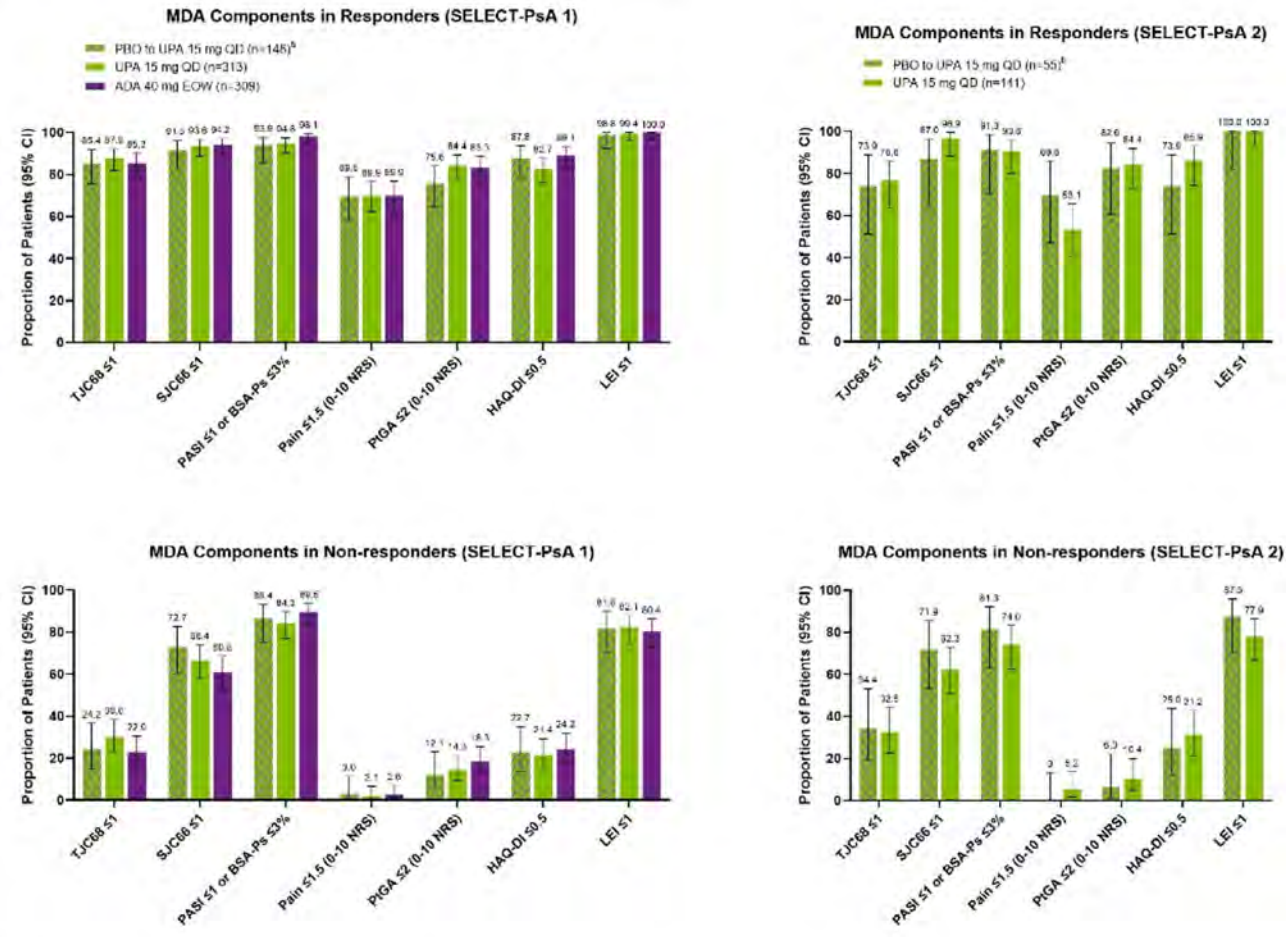


ADA, adalimumab; AO, as observed; BSA-Ps, body surface area with psoriasis; CI, confidence interval; DAPSA, Disease Activity index for PsA; EOW, every other week; LDA, low disease activity; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; NRS, numeric rating scale; PASDAS, PsA Disease Activity Score; PBO, placebo; PtGA, patient global assessment of disease activity; QD, once daily; RAPID3, Routine Assessment of Patient Index Data 3; REM, remission; UPA, upadacitinib; VLDA, very low disease activity.

[a]Patients randomized to PBO were switched to UPA 15 mg QD at week 24.

[b]MDA (≥5/7 criteria) or VLDA (7/7 criteria): SJC66 ≤1, TJC68 ≤1, PASI ≤1 or BSA-Ps ≤3%, pain ≤1.5 (0-10 NRS), PtGA ≤2 (0-10 NRS), HAQ-DI ≤0.5, and LEI ≤1.

Figure 2. Proportion of Patients Achieving MDA Components at Week 152 (AO)[a]



ADA, adalimumab; AO, as observed; BSA-Ps, body surface area with psoriasis; EOW, every other week; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; NRS, numeric rating scale; PBO, placebo; PtGA, patient global assessment of disease activity; QD, once daily; UPA, upadacitinib.
[a]Results exclude patients with at least one missing component of MDA.
[b]Patients randomized to PBO were switched to UPA 15 mg QD at week 24.

and ADA. In contrast, TJC68 ≤1, pts assessment of pain ≤1.5, pts global assessment of disease activity ≤2, and HAQ-DI ≤0.5 appeared to be more difficult to achieve across all treatments.

Conclusion: Among pts who remained in the studies with data at wk 152, high rates of LDA and REM were reported in pts treated with UPA15, which were similar to PBO switched to UPA15 and ADA, across several measures of disease activity irrespective of prior DMARD exposure. Across measures of LDA and REM, response rates were numerically lower in SELECT-PsA 2, likely due to the treatment refractory population, compared to SELECT-PsA 1. Even in pts who did not achieve MDA at wk 152, treatment with UPA15 led to a high proportion of pts achieving SJC66 ≤1, PASI ≤1 or BSA-Ps ≤3%, and LEI ≤1 in both studies.

References:

1. Coates LC, et al. *Nat Rev Rheumatol*. 2022;18:465-79.
2. McKinnes IB, et al. *N Engl J Med*. 2021;384:1227-39.
3. Mease PJ, et al. *Ann Rheum Dis*. 2021;80:312–320.

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Abstract Number: 2240

Persistence to Therapy Among Patients with Psoriatic Arthritis Treated with IL-17A or TNFα Inhibitors (IL-17Ai or TNFi)

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The treatment paradigm for psoriatic arthritis (PsA) has changed over the last two decades, with increasing numbers of therapy options that target a variety of inflammatory pathways. This analysis sought to examine treatment patterns among patients with PsA initiating either IL-17Ai or TNFi in order to understand patterns of persistence across biologics that utilize different mechanisms of action to treat PsA.

Methods: Adult patients newly initiating an IL-17Ai (ixekizumab or secukinumab) or TNFi biologic (adalimumab, certolizumab pegol, etanercept, golimumab, or infliximab) between April 1, 2016 and June 30, 2021 were identified in the MarketScan Commercial and Medicare Database. The first biologic claim served as the index date and patients were required to have continuous eligibility for 6 months prior and 12 months following index. Patients also had ≥1 PsA diagnosis claim in the pre-period or on index and could not have claims for other indicated conditions, except psoriasis. Biologic treatment patterns, including persistence and switching, were examined over the 12-month follow-up within the IL-17Ai and TNFi cohorts.

Results: A total of 4,338 IL-17Ai and 7,753 TNFi treated patients were eligible for the analyses. The majority of patients in both cohorts were female and aged 45-64 at index; mean±SD Charlson Comorbidity Index was 0.5±1.0 in the TNFi cohort and 0.7±1.2 in the IL-17Ai cohort (Table 1). Prior biologic use was observed in the baseline period for 29.0% of TNFi patients and 61.8% of IL-17Ai patients, while baseline conventional disease-modifying antirheumatic drug (cDMARD) use was observed for 43.3% and 37.6% of the respective cohorts (Figure 1; Table 1). TNFi or IL-17Ai treatment was initiated as combination therapy with cDMARDs in 22.6% of the TNFi cohort and 17.3% of the IL-17Ai cohort. Over the post-period, IL-17Ai patients remained on an IL-17Ai for a mean persistence of 261±126 days; TNFi patients remained on drug for 243 ±127 days (Figure 2). Rates of biologic switching over the post-period were 25.3% in the IL-17Ai cohort and 29.3% in the TNFi cohort.

Table 1. Cohort Demographics and Baseline Clinical Characteristics

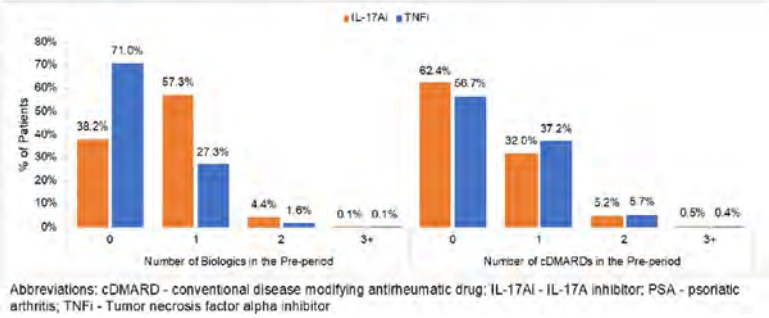
Table 1. Cohort Demographics and Baseline Clinical Characteristics

	IL-17Ai N = 4,338		TNFi N = 7,753	
	N/Mean	%/SD	N/Mean	%/SD
Age (Mean, SD)	49.72	10.25	48.52	10.88
Age category (N, %)				
18-34	335	7.7%	910	11.7%
35-44	892	20.6%	1,659	21.4%
45-54	1,543	35.6%	2,664	34.4%
55-64	1,421	32.8%	2,247	29.0%
65+	147	3.4%	273	3.5%
Sex (N, %)				
Male	1,813	41.8%	3,410	44.0%
Female	2,525	58.2%	4,343	56.0%
Charlson Comorbidity Index (Mean, SD)	0.7	1.2	0.5	1.0
Comorbidities and related conditions (N, %)				
Alcohol abuse	17	0.4%	43	0.6%
Anxiety	621	14.3%	1,039	13.4%
Depression	523	12.1%	886	11.4%
Dyslipidemia	1,063	24.5%	1,697	21.9%
Elevated transaminase	40	0.9%	104	1.3%
Cardiovascular diseases	303	7.0%	448	5.8%
Atherosclerosis	30	0.7%	34	0.4%
Peripheral arterial disease	93	2.1%	133	1.7%
Cerebrovascular disease	63	1.5%	109	1.4%
Coronary artery disease	168	3.9%	243	3.1%
Cirrhosis of the liver	27	0.6%	31	0.4%
Lymphoma	8	0.2%	4	0.1%
Metabolic syndrome	29	0.7%	55	0.7%
NAFL/NASH	100	2.3%	183	2.4%
Obesity[1]	1,082	24.9%	1,745	22.5%
Osteoarthritis	938	21.6%	1,718	22.2%
Osteoporosis	78	1.8%	104	1.3%
Psoriasis	3,041	70.1%	4,587	59.2%
Skin cancer	42	1.0%	67	0.9%
Type 2 diabetes	639	14.7%	924	11.9%
Pre-Index Medication Use (N, %)				
Biologic utilization	2,681	61.8%	2,248	29.0%
cDMARD utilization	1,114	37.6%	2,350	43.3%

[1] Obesity diagnoses are known to be under-reported in administrative claims.

Abbreviations: NAFL/NAFLD - nonalcoholic fatty liver/nonalcoholic steatohepatitis; cDMARD - conventional disease modifying antirheumatic drug; IL-17Ai - IL-17A inhibitor; SD - standard deviation; TNFi - tumor necrosis factor alpha inhibitor

Figure 1. PsA Medication Use Over the 6-Month Pre-period



Abbreviations: cDMARD - conventional disease modifying antirheumatic drug; IL-17Ai - IL-17A inhibitor; PSA - psoriatic arthritis; TNFi - Tumor necrosis factor alpha inhibitor

Figure 1. PsA Medication Use Over the 6-Month Pre-period

Figure 2. Persistence to Index Biologic Over the 12-Month Post-period

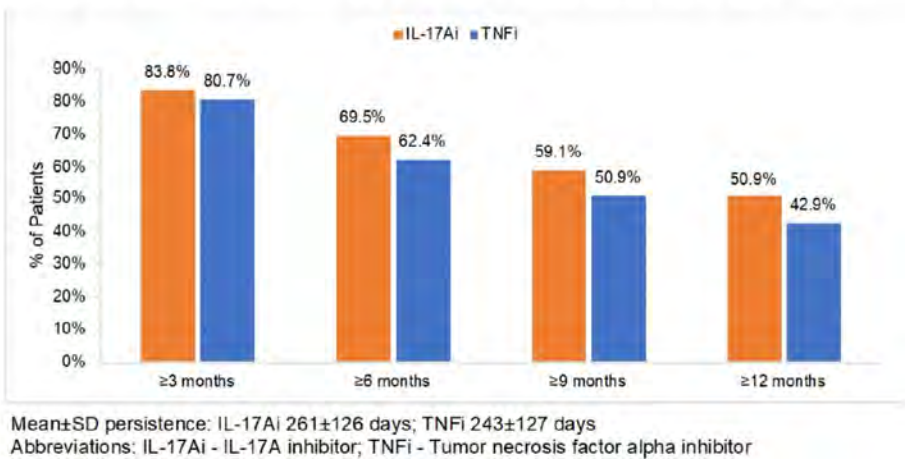


Figure 2. Persistence to Index Biologic Over the 12-Month Post-period

Conclusion: Persistence to therapy can be especially important in chronic, progressive diseases like PsA where patients will likely have to change treatment regimens over the course of disease. Results from this study indicate that IL-17Ai biologics can represent a viable, long-lived treatment choice even among patients with prior biologic experience and high comorbidity burden.

Disclosure: A. Vadhariya: Eli Lilly and Company, 3, 11; **S. Ross**: Eli Lilly and Company, 3, 11; **B. Brady**: Merative, 3, 12, Brenna Brady is an employee of Merative who received funding from Lilly to conduct this study; **H. Varker**: Merative, 3, 12, Employee of Merative. Merative was contracted by Eli Lilly to conduct the PSA study that is the basis of this manuscript/abstract; **A. Thu Tran**: Merative, 3; **J. Walsh**: AbbVie, 5, Amgen, 2, Eli Lilly, 2, Janssen, 2, Merck, 5, Novartis, 2, Pfizer, 2, 5, UCB Pharma, 2.

Abstract Number: 2241

Guselkumab Efficacy in Active Psoriatic Arthritis Patients with or Without Hyperuricemia: Post-hoc Analysis of Two Phase 3, Randomized, Double-blind, Placebo-Controlled Studies

Renaud FELTEN[1], Laura Widawski[2], Lionel Spielman[2], Jacques-Eric Gottenberg[3], Pierre-Marie Duret[2], Emmanouil Rampakakis[4], Mohamed Sharaf[5], Caren Constantin[6], vincenza campana[6] and Laurent Messer[7], [1]Hôpital de Hautepierre, Strasbourg, France, [2]Hôpitaux civils de Colmar, Colmar, France, [3]Rheumatology Department, Strasbourg University Hospital, Strasbourg, France, [4]JSS Medical Research, Saint-Laurent, QC, Canada, [5]Immunology, Janssen MEA, Dubai, United Arab Emirates, [6]Janssen Cilag Medical Affairs, Issy les Moulineaux, France, [7]Laboratoire Interdisciplinaire en études culturelles (LinCS), Strasbourg, France

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients (pts) with psoriasis (PsO) or PsA are at increased risk for developing gout; and hyperuricemia (HU) prevalence is higher in PsO/PsA pts than the general population[1,2]. A previous analysis showed that the profile of pts with vs without HU was distinct and that the efficacy of secukinumab (SEC) was comparable in hyper- and normo-

uricemic pts except for PsO Area Severity Index response (PASI90), which was lower with SEC 150mg in HU pts[3]. These post hoc analyses sought to contrast PsA pts with vs without HU and evaluate the efficacy of guselkumab (GUS) through 1y in both cohorts.

Methods: Adults in DISCOVER 1&2 (90% bionaive) with active PsA despite standard therapies were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, Q8W; or placebo. HU was defined as baseline (BL) serum urate levels of ≥360 μmol/L. Pts without HU (no HU) but with history of gout or uric-lowering therapies were excluded. Among GUS-randomized pts, the effect of HU vs no HU on changes from BL through W52 in Disease Activity (DA) Index for PsA (DAPSA), PsA DA Score (PASDAS), PASI, Health Assessment Questionnaire Disability Index (HAQ-DI), Short Form 36-item physical component summary (SF-36 PCS) score, and BASDAI (in pts with axial involvement) was assessed with mixed models for repeated measures adjusting for BL outcome levels, GUS regimen, prior TNFi use, and BL conventional synthetic DMARD use. The effect of HU vs no HU on achievement of ACR50, DAPSA low disease activity (LDA; ≤14), PASDAS LDA (≤3.2), PASI90, Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) response (Δ≥4), and enthesitis/dactylitis resolution in pts not in response/with condition at BL (all non-responder imputation for missing data) was assessed with logistic regression adjusting for the same covariates.

Table. Baseline Characteristics of Patients With vs. Without HU (≥360 μmol/L)

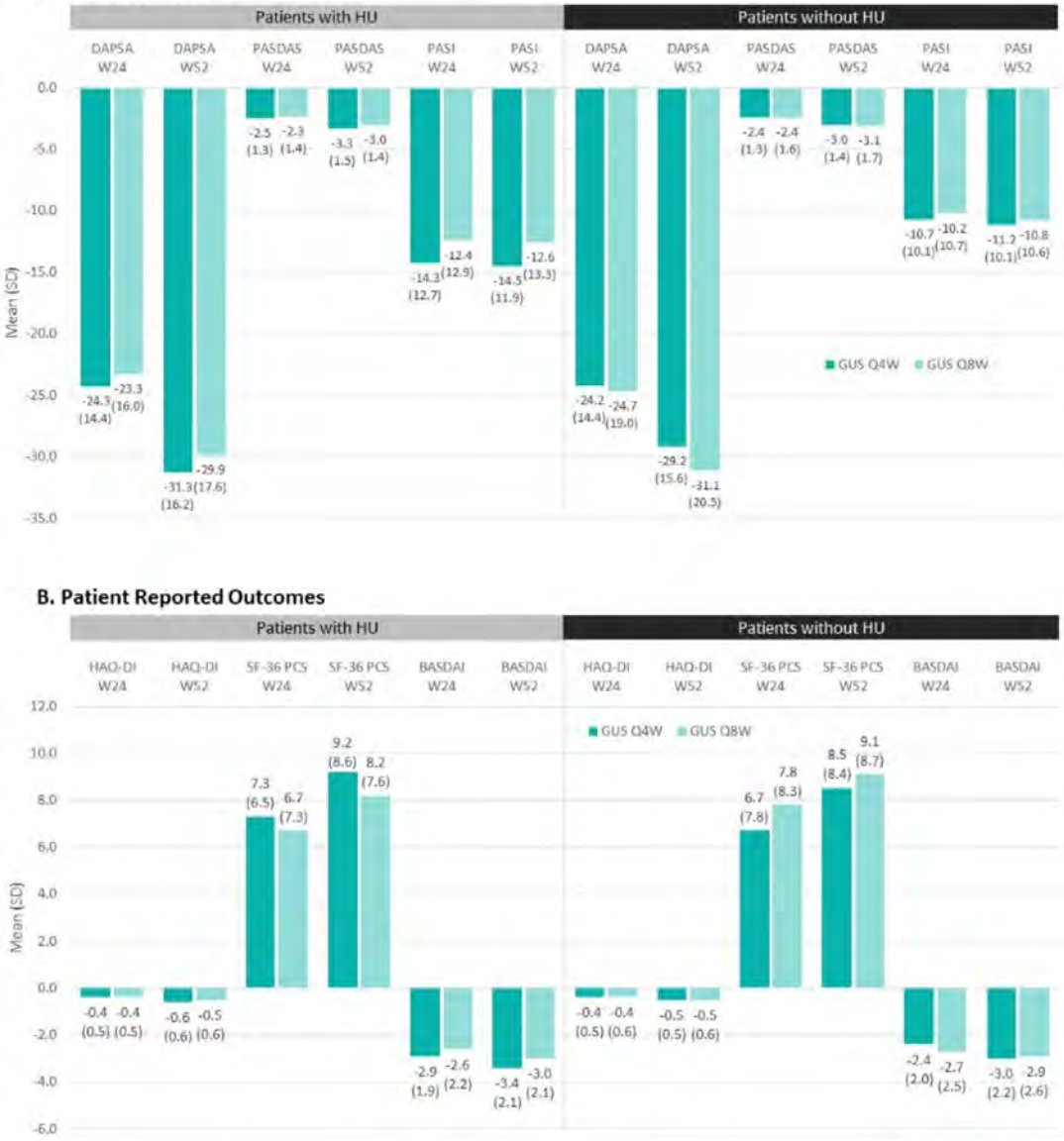
	HU (≥360 μmol/L) (N=425)	No HU (N=689)	Nominal P-value
Age at study BL (yrs)	47.8 (11.9)	45.8 (11.4)	**0.005**
Male sex, n (%)	312 (73.4)	269 (39.0)	**<0.001**
PsA disease duration (yrs)	5.9 (6.3)	5.8 (5.9)	0.819
Age at PsA diagnosis (yrs)	42.4 (12.1)	40.5 (11.6)	**0.009**
Prior TNFi use, n (%)	52 (12.2)	65 (9.4)	0.139
Concomitant csDMARD(s), n (%)	264 (62.1)	491 (71.3)	**0.002**
# of cardiovascular risk factors	1.8 (1.5)	1.4 (1.6)	**<0.001**
Hypertension, n (%)	199 (46.8)	215 (31.2)	**<0.001**
Diabetes, n (%)	45 (10.6)	57 (8.3)	0.193
Hyperlipidemia, n (%)	80 (18.8)	87 (12.6)	**0.005**
BMI≥30 kg/m², n (%)	217 (51.1)	226 (32.8)	**<0.001**
Current tobacco use	77 (18.1)	131 (19.0)	0.710
DAPSA	45.3 (19.7)	46.9 (21.0)	0.220
PASDAS	6.4 (1.1)	6.5 (1.1)	0.467
SJC (0-66)	11.2 (6.8)	11.6 (7.7)	0.416
TJC (0-68)	20.1 (13.1)	20.9 (13.4)	0.339
% BSA with psoriasis*, n (%)			**<0.001**
<3%	69 (16.2)	164 (23.8)	
≥3% to <10%	123 (28.9)	235 (34.1)	
≥10% to <20%	84 (19.8)	138 (20.0)	
≥20%	147 (34.6)	150 (21.8)	
PASI score (0-72)	11.3 (12.0)	8.4 (9.6)	**<0.001**
Presence of enthesitis, n (%)	266 (62.6)	457 (66.3)	0.210
LEI score (1-6)	2.8 (1.6)	2.8 (1.6)	0.572
Presence of Dactylitis, n (%)	175 (41.2)	296 (43.0)	0.566
Dactylitis Severity Score (1-60)	9.5 (11.0)	7.5 (8.7)	**0.041**
Pain VAS	60.3 (19.7)	61.8 (19.9)	0.214
Axial involvement (axPsA), n (%)	113 (26.6)	198 (28.7)	0.437
BASDAI (0-10) in pts with axPsA	6.4 (1.6)	6.5 (1.7)	0.527
HAQ-DI (0-3)	1.2 (0.6)	1.3 (0.6)	0.273
CRP (mg/dL)	1.7 (2.2)	1.8 (2.3)	0.349

Data are presented as mean (SD) unlessstated otherwise.

*Two pts in each group had missing information.

BSA: body surface area; csDMARDs: conventional synthetic DMARDs; LEI: Leeds enthesitis index; SJC: swollen joint count; TJC: tender joint count; VAS: visual analogue scale.

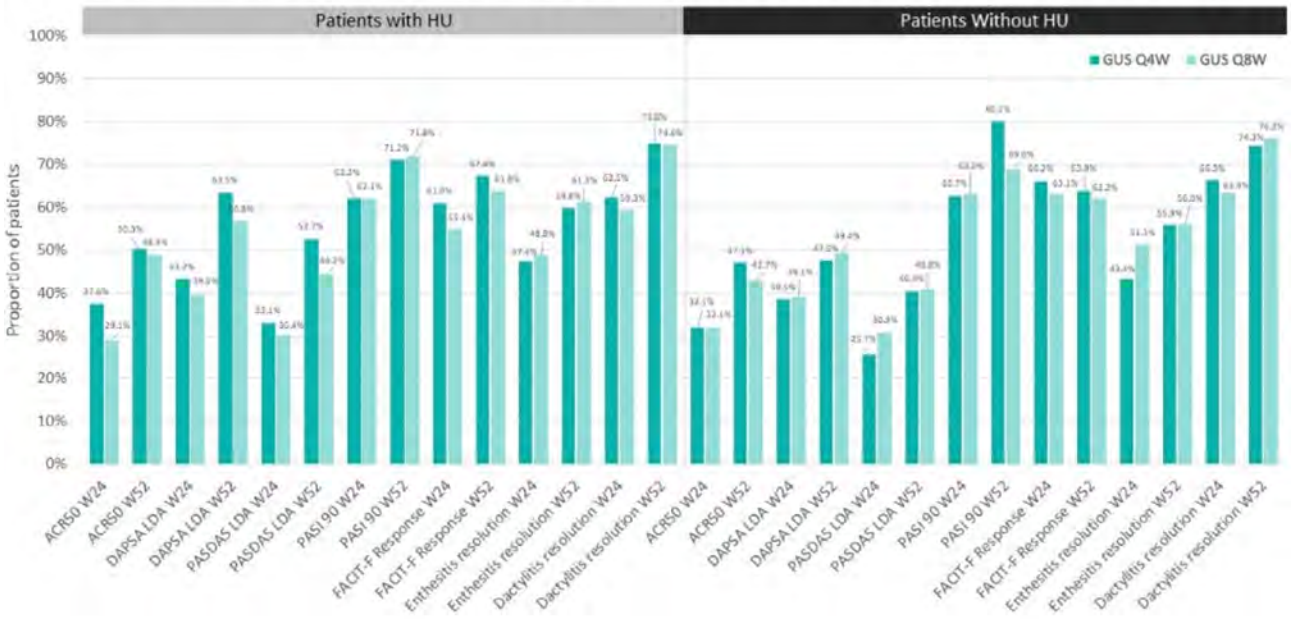
Figure 1. Changes from BL in Outcomes By Treatment Group and Presence of HU Through W52



Results: Relative to no HU pts (n=689), those with HU (n=425) were older at study BL and PsA diagnosis, and more likely to be male and have hypertension, hyperlipidemia, BMI ≥30 kg/m2 and more severe PsO and dactylitis (in pts with dactylitis) (**Table 1**). The two cohorts had generally comparable severity of joint disease, enthesitis and axial symptoms. In multivariate analysis (not shown), male sex, hypertension, high BMI, and PsO severity were associated with HU. Clinically meaningful and comparable improvements in all studied continuous outcomes were observed at W24 across HU cohorts and GUS regimens (**Figure 1**); further improvements were generally seen through W52 regardless of HU. Endpoint achievement was also comparable between HU cohorts and GUS regimens (**Figure 2**).

Conclusion: In this pooled analysis of mainly bio-naïve pts with active PsA, HU pts were more likely to be male and have high BMI, hypertension, and more severe PsO and dactylitis. The observed differential clinical profile and comorbidities, confirmed in previous studies[3], underscore the value of assessing serum urate levels in PsA pts. GUS was associated with clinically meaningful improvements across key PsA domains, with further enhancements generally seen through W52, irrespective of HU presence or GUS regimen.

Figure 2. Proportion of Patients Achieving Efficacy Endpoints By Treatment Group and Presence of HU Through W52



References

1. Tripolino C. Front Med. 2021;8:737573
2. AlJohani R. J Rheum. 2018;45:213
3. Felten R. Ann Rheum Dis. 2022;81:855

Disclosure: R. FELTEN: Janssen, 1, 2; **L. Widawski**: None; **L. Spielman**: None; **J. Gottenberg**: AbbVie, 2, BMS, 2, 5, Galapagos, 2, Gilead, 2, Lilly, 2, MSD, 2, Novartis, 2, Pfizer, 2, 5; **P. Duret**: None; **E. Rampakakis**: Janssen, 2, JSS Medical Research, 3; **M. Sharaf**: Janssen, 3, Johnson & Johnson, 11; **C. Constantin**: Janssen, 3, 11; **v. campana**: Janssen, 3, 11; **L. Messer**: None.

Abstract Number: 2242

Irrespective of the Number of Erosions at Baseline, Patients with Psoriatic Arthritis Treated with Ixekizumab Show Improved Clinical Outcomes

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic and progressive disease characterized by high rates of early joint erosions, which have been associated with impaired quality of life and increased mortality rates[1,2]. However, the relationship between the number of erosions at baseline (BL) and response to biological disease-modifying antirheumatic drugs (bDMARD) therapy has not been thoroughly investigated. In this post-hoc analysis, we assessed the efficacy of placebo (PBO), ixekizumab (IXE) or adalimumab (ADA) on patients (pts) with erosions visible on hand radiographs at BL.

Methods: Biologic-naïve pts with PsA (SPIRIT-P1, NCT01695239) were randomly assigned to PBO, IXE 80-mg every 2 weeks (Q2W) or 4 weeks (Q4W) after a 160-mg starting dose, or ADA 40-mg Q2W. Pts were stratified into two groups based on the number of BL erosions (erosion component of the modified total sharp scores ≤4 and >4). At week 24, outcomes analyzed for different baseline erosion score (BES) groups included American College of Rheumatology (ACR) 20%, 50%, 70%, Disease Activity index for PSoriatic Arthritis-Low Disease Activity (DAPSA-LDA), Health Assessment Questionnaire-Disability Index (HAQ-DI) and Minimal Disease Activity-Psoriasis Area Severity Index (MDA-PASI). Missing data were imputed using non-responder imputation (NRI) for categorical, and modified baseline observation carried forward (mBOCF) for continuous outcome variables. Comparisons between PBO and treatment within each BES group used logistic models for categorical, and ANCOVA for continuous outcome variables, adjusting for BL values, disease duration, geographic region, and prior conventional DMARD (cDMARD) experience.

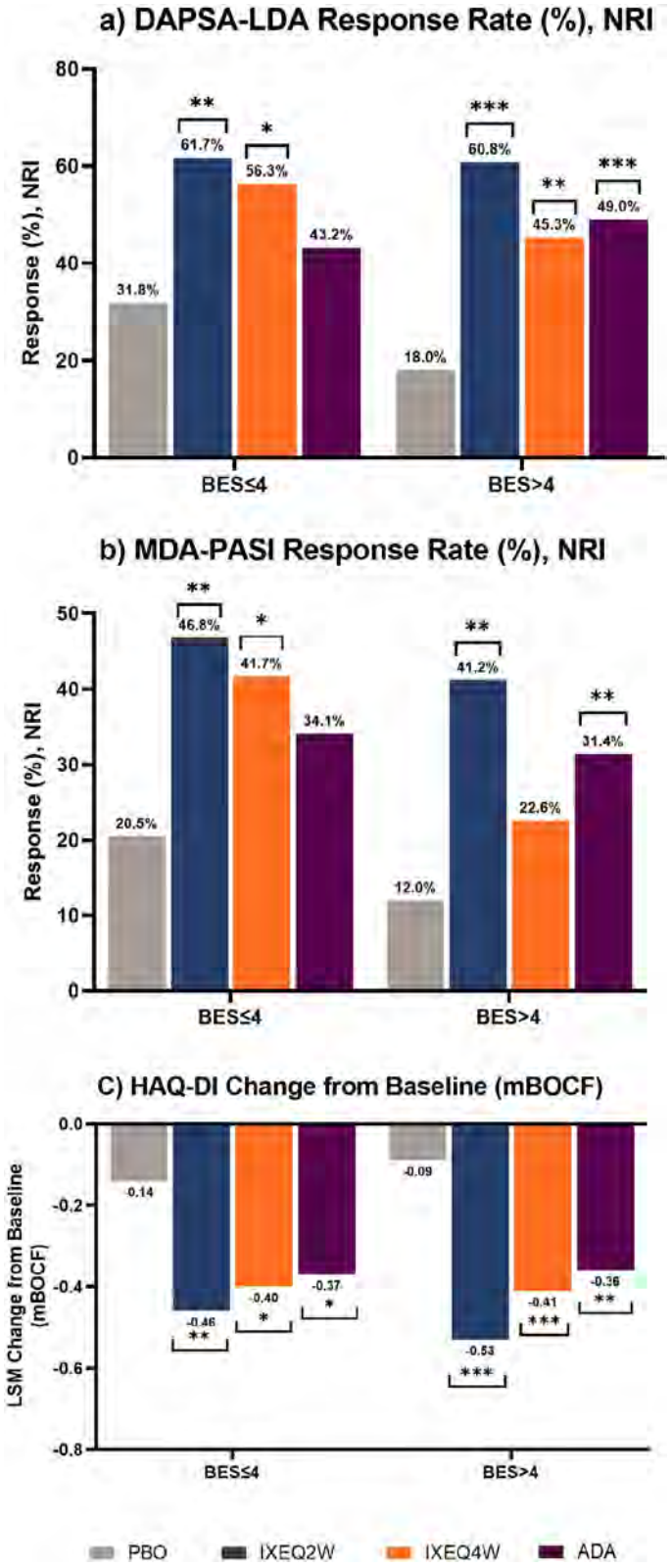
Results: 183 pts with BES≤4 and 205 pts with BES >4 at BL were included. At week 24, pts with BES >4 on PBO had worse outcomes across all parameters compared to those with BES≤4. There was significant improvement in DAPSA-LDA response rates in pts treated with IXE regardless of BES, whereas significant response rates were seen in ADA treated pts with BES >4 (**Figure 1a**). MDA-PASI response rates were significant in patients treated with IXEQ2W and IXEQ4W who had BES≤4, whereas pts with BES >4 demonstrated a significant response rate with IXEQ2W and ADA (**Figure 1b**). Change from baseline in HAQ-DI was significant for all pts treated with bDMARDS, regardless of BES (**Figure 1c**). Similarly, regardless of BES, significant differences in ACR50 and ACR70 response rates versus PBO were seen for pts treated with bMDARDS (**Figure 2b and 2c**).

Conclusion: Pts with higher BES in the PBO group experienced worse outcomes. Higher response rates (e.g., ACR50/70) were also harder to achieve in pts with higher BES. Irrespective of BES, IXE treated pts showed greater improvement compared to PBO in the achievement of LDA and functional outcomes.

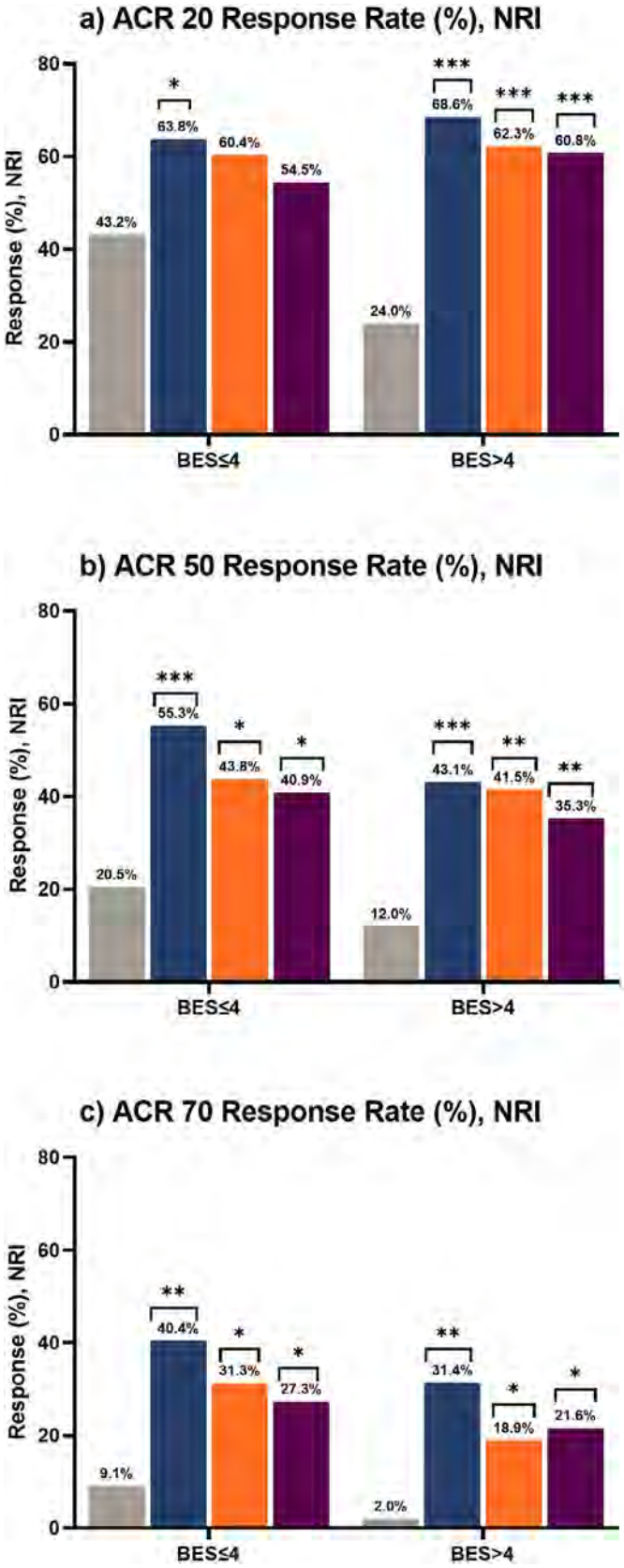
Table 1.0 Patient demographics and baseline characteristics

	BES≤4				BES>4			
	PBO (N=44)	IXEQ2W (N=47)	IXEQ4W (N=48)	ADA (N=44)	PBO (N=50)	IXEQ2W (N=51)	IXEQ4W (N=53)	ADA (N=51)
Age, yrs	46.8 (12.2)	46.3 (12.2)	45.6 (8.9)	45.8 (10.7)	53.5 (11.3)	52.6 (12.6)	52.1 (10.1)	50.8 (13.4)
Male, n (%)	23 (52.3)	21 (44.7)	17 (35.4)	18 (40.9)	20 (40)	25 (49)	25 (47.2)	31 (60.8)
Time since PsA onset, yrs	9.6 (9.7)	7.9 (6.7)	6.5 (5.3)	7.2 (6.6)	11.5 (8.5)	13.5 (13.0)	13.1 (11.4)	10.6 (7.7)
Time since PsA diagnosis, yrs	5.9 (7.4)	5.6 (6.2)	4.3 (4.7)	5.2 (6.1)	7.1 (6.8)	8.9 (9.5)	8.0 (7.4)	7.9 (7.3)
Bone Erosions Score	2.1 (1.2)	2.1 (1.2)	1.9 (1.4)	1.6 (0.9)	18.4 (20.9)	16.7 (20.8)	20.3 (20.9)	17.2 (19.9)
DAPSA Score	40.5 (17.9)	50.2 (22.9)	43.0 (15.2)	40.9 (16.6)	43.2 (19.5)	44.8 (19.0)	46.9 (22.5)	41.5 (20.4)
HAQ-DI Score	1.2 (0.6)	1.1 (0.6)	1.2 (0.6)	1.1 (0.6)	1.0 (0.5)	1.2 (0.5)	1.3 (0.5)	1.1 (0.5)
PASI Total Score	7.0 (8.3)	6.9 (8.4)	7.4 (7.2)	4.1 (5.1)	5.5 (7.3)	5.1 (5.0)	6.8 (6.3)	6.7 (7.4)

Data are mean(±SD) unless otherwise stated. Abbreviations: PBO=placebo, ADA=adalimumab, IXE=ixekizumab, Q2W=every 2 weeks, Q4W=every 4 weeks, yrs=years, N=number of responders, n=number of patients in specified category, PsA=psoriatic arthritis, BL=baseline, DAPSA=Disease Activity index for PSoriatic Arthritis, PASI= Psoriasis Area Severity Index, BES=Baseline Erosion Score, HAQ-DI= Health Assessment Questionnaire-Disability Index.



a) DAPSA-LDA Response Rate (%), NRI, b) MDA-PASI Response Rate (%), NRI and c) HAQ-DI Change from Baseline (mBOCF) at Week 24. Significantly greater response versus PBO denoted by * ($p \leq 0.05$), ** ($p \leq 0.01$), *** ($p \leq 0.001$). Abbreviations: PBO=placebo, ADA=adalimumab, IXE=ixekizumab, Q2W=every 2 weeks, Q4W=every 4 weeks, NRI=non-responder imputation, DAPSA-LDA= Disease Activity index for PSoriatic Arthritis-Low Disease Activity, MDA-PASI= Minimal Disease Activity-Psoriasis Area Severity Index, BES=Baseline Erosion Score, LSM= Least-squares Means, mBOCF= modified Baseline Observation Carried Forward, HAQ-DI= Health Assessment Questionnaire-Disability Index.



a) ACR 20, b) ACR 50, c) ACR70 Response Rate (%), NRI at Week 24. Significantly greater response versus PBO denoted by * ($p \leq 0.05$), ** ($p \leq 0.01$), *** ($p \leq 0.001$). Abbreviations: PBO=placebo, ADA=adalimumab, IXE=ixekizumab, Q2W=every 2 weeks, Q4W=every 4 weeks, NRI=-non-responder imputation, ACR=American College of Rheumatology, BES=Baseline Erosion Score.

References:

Touma, Z., et al. J. of Rheumatology. 2016; 43(6)
Gladman, D. D. et al. Arthritis & Rheumatism. 1998; 41(6)

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Abstract Number: 2243

Ultrasound Enthesitis Responsiveness versus Clinical Enthesitis Responsiveness: Week 52 Results of an Exploratory Analysis from a Phase 3b Study in Patients with Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Enthesitis is a key clinical and imaging hallmark in psoriatic arthritis (PsA). ULTIMATE (NCT02662985) demonstrated responsiveness of ultrasound (US) detected synovitis and enthesitis in PsA and confirmed rapid and long-lasting benefits of secukinumab (SEC) through 52 weeks.[1,2] Little is known about the relationship between US-detected enthesitis vs clinical enthesitis over time. We evaluated the responsiveness of US enthesitis to SEC over 52 weeks and the correlation with clinical response of enthesitis.

Methods: This was a 52-week study with a 12-week double-blind, placebo-controlled treatment period, a 12-week open-label (OL) treatment period and a 6-month extension period. Patients with ≥1 clinical enthesitis site, defined by the Spondyloarthritis Research Consortium of Canada (SPARCC) index,were randomized to weekly SEC (300 or 150 mg according to severity of skin psoriasis) or placebo. Placebo patients switched to OL SEC at Week 12 ('placebo-SEC'). Enthesitis was assessed by Power Doppler (PD) performed bilaterally across 6 sites (enthesitis-level), and at patient level with the novel global Outcome Measures in Rheumatology (OMERACT) enthesitis score, which included 2 definitions of activity: definition 1 combinedB-mode morphological abnormalities (0–1) and PD vascularization abnormalities (0–3); definition 2 focused on PD signal alone (0–3). Clinical response was assessed by SPARCC enthesitis index (0–16). We report observed data on the distribution of US and clinical enthesitis, enthesitis resolution over 52 weeks, and the correlation between US and clinical enthesitis from baseline (BL) to Week 12.

Table 1. Distribution of clinical and ultrasound assessed enthesitis by site over time from Baseline to Week 52

Enthesitis site*	SEC			Placebo-SEC		
	Distribution of ultrasound detected enthesitis		Distribution of clinical (SPARCC) enthesitis	Distribution of ultrasound detected enthesitis		Distribution of clinical (SPARCC) enthesitis
	Definition 1	Definition 2		Definition 1	Definition 2	
Lateral epicondyle, n (%)						
Baseline	41 (49)	17 (21)	39 (47)	38 (46)	17 (21)	36 (43)
Week 12	33 (40)	11 (13)	15 (18)	32 (39)	9 (11)	20 (24)
24	34 (41)	10 (12)	14 (17)	27 (33)	6 (7)	9 (11)
52	27 (33)	8 (10)	7 (8)	22 (27)	7 (8)	9 (11)
Quadriceps tendon insertion, n (%)						
Baseline	46 (55)	10 (12)	28 (34)	33 (40)	2 (2)	16 (19)
Week 12	33 (40)	8 (10)	10 (12)	25 (30)	2 (2)	9 (11)
24	35 (42)	6 (7)	7 (8)	22 (27)	2 (2)	8 (10)
52	32 (39)	6 (7)	7 (8)	16 (19)	1 (1)	2 (2)
Achilles tendon insertion, n (%)						
Baseline	41 (49)	10 (12)	40 (48)	37 (45)	2 (2)	46 (55)
Week 12	39 (47)	8 (10)	19 (23)	32 (39)	4 (5)	22 (27)
24	35 (42)	7 (8)	13 (16)	32 (39)	3 (4)	9 (11)
52	28 (34)	5 (6)	11 (13)	22 (27)	4 (5)	2 (2)
Patellar ligament proximal insertion, n (%)						
Baseline	28 (34)	8 (10)	23 (28)	15 (18)	3 (4)	20 (24)
Week 12	24 (29)	5 (6)	12 (14)	15 (18)	2 (2)	13 (16)
24	20 (24)	6 (7)	11 (13)	9 (11)	0 (0)	7 (8)
52	19 (23)	4 (5)	7 (8)	5 (6)	1 (1)	1 (1)
Patellar ligament distal insertion, n (%)						
Baseline	28 (34)	7 (8)	23 (28)	24 (29)	3 (4)	20 (24)
Week 12	24 (29)	6 (7)	12 (14)	16 (19)	2 (2)	13 (16)
24	22 (27)	5 (6)	11 (13)	18 (22)	3 (4)	7 (8)
52	13 (16)	4 (5)	7 (8)	10 (12)	1 (1)	1 (1)
Plantar fascia insertion, n (%)						
Baseline	30 (36)	0 (0)	16 (19)	23 (28)	0 (0)	26 (31)
Week 12	24 (29)	0 (0)	5 (6)	14 (17)	1 (1)	14 (17)
24	19 (23)	0 (0)	2 (2)	19 (23)	1 (1)	6 (7)
52	13 (16)	0 (0)	3 (4)	11 (13)	1 (1)	2 (2)

*n (%), number (percentage) of patients with enthesitis at the corresponding site, irrespective of left or right side

Composite OMERACT ultrasound enthesitis score at site level:
definition 1: range 0–4; sum of Power Doppler (0–3) and B mode (0–1) scores
definition 2: range 0–3; Power Doppler only

OMERACT, Outcome Measures in Rheumatoid Arthritis Clinical Trials; PDUS, power Doppler ultrasonography; SEC, secukinumab; SPARCC, Spondyloarthritis Research Consortium of Canada enthesitis index

Results: Overall, 166 patients were randomized; 90% (75/83) in the SEC group and 83% (69/83) in the placebo-SEC group completed 52 weeks. The mean number of clinical enthesitis sites at BL was 4 in both the SEC and placebo groups. Mean (SD) global OMERACT enthesitis scores were 6 (4.7) and 5 (3.2) (definition 1) and 3 (3.4) and 3 (1.6) (definition 2), for SEC and placebo-SEC, respectively. The proportion of patients with US-detected and clinical enthesitis decreased for most enthesitis sites in both treatment groups from BL to Week 24 and remained stable up to Week 52; definition 2 generally performed more closely to SPARCC clinical index than definition 1 **(Table 1).** According to the global OMERACT enthesitis score (definition 1 or 2), resolution of enthesitis was observed in a higher proportion of patients in the SEC vs placebo-SEC group at Week 12; the difference between SEC and placebo-SEC was similar at Week 52 **(Table 2).** No correlations were observed between the OMERACT score (definition 1 or 2) and SPARCC index regarding change from BL to Week 12 (**Table 3**).

Conclusion: A long-term stable response was observed with SEC and placebo-SEC in both US and clinical enthesitis up to Week 52. We found no correlation between US and clinically detected enthesitis, likely because the former assesses inflammation based on morphological/functional tissue changes while the SPARCC index evaluates inflammation based on tenderness of the entheseal site.

Table 2. Enthesitis resolution for SEC and placebo-SEC at Week 12 and Week 52

	Enthesitis resolution	SEC (150+300mg) n/m (%)	Placebo-SEC n/m (%)
Week 12	SPARCC resolution	39/81 (48)	22/76 (29)
	Global OMERACT enthesitis score definition 1 = 0	10/72 (14)	5/53 (9)
	Global OMERACT enthesitis score definition 2 = 0	14/34 (41)	6/19 (32)
Week 52	SPARCC resolution	36/65 (55)	37/56 (66)
	Global OMERACT enthesitis score definition 1 = 0	12/58 (21)	6/38 (16)
	Global OMERACT enthesitis score definition 2 = 0	15/28 (54)	8/16 (50)

SPARCC: range 0–16
Global OMERACT ultrasound enthesitis score:
definition 1: Sum of the 12 site level scores (6 sites bilaterally, each 0–4, see Table 1). Range 0–48
definition 2: Sum of the 12 site level scores (each 0–3). Range 0–36
m, number of patients with enthesitis assessment; n, number of patients with enthesitis resolution
Abbreviations, see Table 1

Table 3. Correlation (with 95% CI) between global OMERACT (PDUS) enthesitis score (Definition 1 or Definition 2) and SPARCC index with regards to change from Baseline to Week 12

Correlation analysis of ultrasound enthesitis vs. clinical enthesitis	SEC	Placebo-SEC
Global OMERACT PDUS enthesitis score (Definition 1) vs SPARCC index	–0.15 (–0.36 to 0.08)	0.15 (–0.10 to 0.38)
Global OMERACT PDUS enthesitis score (Definition 2) vs SPARCC index	–0.02 (–0.24 to 0.20)	0.08 (–0.16 to 0.32)
Abbreviations, see Table 1		

References:

1. D'Agostino MA, et al [abstract]. *Arthritis Rheumatol*. 2021; 73 (suppl 9).
2. D'Agostino MA, et al. *Rheumatology (Oxford)*. 2022;61(5):1867–1876.

Disclosure: M. D'Agostino: AbbVie/Abbott, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **C. Gaillez**: Bristol-Myers Squibb(BMS), 11, Novartis, 3, 11; **G. Schett**: None; **M. Boers**: Celltrion, 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **P. Carron**: AbbVie/Abbott, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Merck/MSD, 2, 5, 6, Novartis, 2, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **P. Mandl**: AbbVie/Abbott, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Celgene, 5, 6, Eli Lilly, 5, 6, Janssen, 5, 6, Merck/MSD, 5, 6, Novartis, 5, 6, Roche, 5, 6, UCB, 5, 6; **J. ROSA**: AbbVie/Abbott, 6, Eli Lilly, 6, Janssen, 6, Novartis, 6, Pfizer, 6; **E. Naredo**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 6, Eli Lilly, 5, 6, Janssen, 6, Novartis, 6, Pfizer, 6, Roche, 6, UCB, 6; **C. Bakewell**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Sanofi, 2, 6, UCB, 2, 6; **W. Bao**: Novartis, 3, 11; **P. Conaghan**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, Genascense, 2, GlaxoSmithKlein(GSK), 2, Grunenthal, 2, Janssen, 2, Levicept, 2, Merck/MSD, 2, Moebius Medical, 2, Novartis, 2, 6, Stryker, 2, Takeda, 2, TrialSpark, 2.

Abstract Number: 2244

Switching Between Biologics and Targeted Synthetic Therapies Due to Inefficacy in Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Biological and targeted synthetic therapies (ts/bDMARDs) have transformed the management ofP-soriatic arthritis (PsA).However, PsA might experience ts/bDMARD failure, (mainly due to inefficacy), and switching to another ts/bDMARD is the recommended strategy. In this aspect, there is a gap of knowledge regarding the correct

Table 1. Incidence rate (IR) of switching related to inefficacy by sociodemographic and clinical variables.

Variable	Patient-years	Events	IR per 100	CI (95%)
Sex				
Male	**460.90**	**26**	**5.64**	**3.84-8.28**
Female	**432.20**	**77**	**17.81**	**14.24-22.27**
Age, years				
<40	228.12	18	7.89	4.97-12.52
41-50	262.77	37	14.08	10.20-19.43
51-60	222.03	26	11.70	7.97-217.19
61-70	129.67	18	13.88	8.74-22.03
≥71	50.49	4	7.92	2.97-21.10
Cardiovascular comorbidity				
Yes	**484.43**	**49**	**10.11**	**7.64-13.38**
No	**367.98**	**45**	**12.22**	**9.13-16.37**
History of psoriasis				
Yes	607.01	63	10.37	8.10-13.28
No	231.81	29	12.51	8.69-18.00
Clinical symptoms				
Inflammatory back pain				
Yes	**147.73**	**26**	**17.44**	**11.88-25.62**
No	**745.37**	**77**	**10.33**	**8.26-12.91**
Anterior uveitis				
Yes	**12.15**	**2**	**16.46**	**4.11-65.84**
No	**880.94**	**101**	**11.46**	**9.43-13.93**
Peripheral arthritis				
Yes	**571.89**	**70**	**12.24**	**9.68-15.47**
No	**304.21**	**28**	**9.20**	**6.35-13.33**
Enthesitis				
Yes	**51.94**	**15**	**28.87**	**17.41-47.90**
No	**840.78**	**87**	**10.34**	**8.38-12.76**
Dactylitis				
Yes	**14.14**	**5**	**35.38**	**14.72-85.01**
No	**878.96**	**98**	**11.15**	**9.14-13.59**
Concomitant Glucocorticoids				
Yes	393.36	63	16.01	12.51-20.50
No	499.74	40	8.00	5.87-10.91
ts/bDMARDs				
TNFi	**793.00**	**77**	**9.47**	**7.55-11.87**
Anti-IL17	**69.66**	**16**	**23.00**	**14.09-37.54**
Anti-IL23	**10.28**	**5**	**48.59**	**20.22-116.7**
JAKi	**14.05**	**4**	**28.45**	**10.67-75.81**
Abatacept	**5.91**	**1**	**16.94**	**2.38-120.28**
Concomitant csDMARDs				
Methotrexate				
Yes	**606.35**	**61**	**10.05**	**7.82-12.92**

ts/bDMARDs: Targeted synthetic and Biologic Disease Modifying anti-rheumatic drugs; TNFi: TNF-alpha inhibitors. anti-Interlukine17 biological agent; anti-Interlukine-23 biological agent; JAKi: Janus kinase inhibitors

Table 2. Factors associated with switching due to inefficacy. Multivariate analysis			
Variable	HR	CI (95%)	p
Sex, female	2.57	1.55-4.26	0.000
Age at 1st ts/bDMARDs	0.99	0.98-1.01	0.6
Calendar time, years:			
<2019	1	-	-
2019-2022	2.49	1.49-4.18	0.000
Inflammatory back pain	1.49	1.03-2.17	0.03
Concomitant glucocorticoids	2.05	1.35-3.10	0.001
ts/bDMARDs:			
TNFi	1	-	-
Anti-IL17 agents	1.05	0.54-1.99	0.88
Others: Anti-IL23, JAKi, Abatacept	1.55	0.69-3.48	0.28
Concomitant Sulfasalazine	2.25	1.26-4.01	0.006
Courses of ts/bDMARDs	1.22	1.04-1.43	0.010

ts/bDMARDs: Targeted synthetic and Biologic Disease Modifying anti-rheumatic drugs; TNFi: TNF-alpha inhibitors. anti-Interlukine17 biological agent; anti-Interlukine-23 biological agent; JAKi: Janus kinase inhibitors

treatment algorithms that can be followed after ts/bDMARDfailuredue to inefficacy.**Objectives:** To assess the incidence rate of switching between ts/bDMARDs due to inefficacy, and to analyze the role of the different types of ts/bDMARDs in the risk of switching due to inefficacy. Other factors were also evaluated.

Methods: A longitudinal retrospective study (2015-2022) of PsA patients with ts/bDMARDs from an outpatient rheumatology clinic of a tertiary hospital was conducted. Main outcome: switching between ts/bDMARDs due to inefficacy.Independent variable:exposure to ts/bDMARDs during follow-up: a) anti-TNF; b) Other Biologics: abatacept; anti-IL17; anti-IL-23; c)Janus kinase inhibitors(JAKi). Covariables: Sociodemographic, clinics, and treatment.Statistical analysis:To estimate ts/bDMARDsswitchingdue to inefficacy rates, survival techniques were used, expressing the incidence rate (IR) per 100 patients*year with their confidence interval at 95% [CI 95%].Cox bivariate and multivariate regression analyses were run to assess the role of the different ts/bDMRADs in switching due to inefficacy. Results wereexpressed ashazard ratio(HR) and 95%CI.

Results: 141 PsA on ts/bDMARDs were included, with an 893.09 patients*year follow-up. 52.48% were female and the mean age was 48.06±13.21 years. 262 courses of treatment were recorded andTNFi was the ts/bDMARDsmost used, flowed byanti-IL-17. 92% were associated to a conventional DMARD, being MTX the most frequent (76.1%). Duringthe study period, 56 patients (40%) presented 121 switches between ts/bDMARDs, and 103 were related to inefficacy. The IR of switching due to inefficacy was 11.53 [9.51-13.98] and anti-TNF was the drug with the lowest incidence (Table 1). In the bivariate analysis of switching due to inefficacy, all types of ts/bDMARDs but TNFi had more risk of switching, in the comparing analysis (HR IL-17 vs TNFi: 2.26 [1.17-4.36], p=0.014; others vs TNFi: 3.21 [1.59-6.45], p=0.001); however, this statistical significance was lost in the multivariate analysis after adjustment for age, sex, year of ts/bDMARDs prescription, and comorbidity: none type of ts/bDMARD had more or less risk compared to each other (Table 2). The model also showed the effect of gender, specific clinical symptoms, prescription year, therapy courses, and the negative influence of glucocorticoids or sulfasalazine on switching due to inefficacy.

Conclusion: This study suggests that long-term control of PsA requires therapeutic switching due to inefficacy. This investigation is able to give us useful information about the comparative effectiveness of ts/bDMARDs, not finding any statistical difference in switching due to inefficacy among different ts/bDMARDs in the multivariate analysis. This studyconfirms previously identified risk factors of switching due to inefficacy and proposes new ones.

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Abstract Number: 2245

Drug Survival of Risankizumab vs Other Biologics After 13 Months of Treatment Among Patients with PsA in the Multicountry Postmarketing Observational VALUE Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

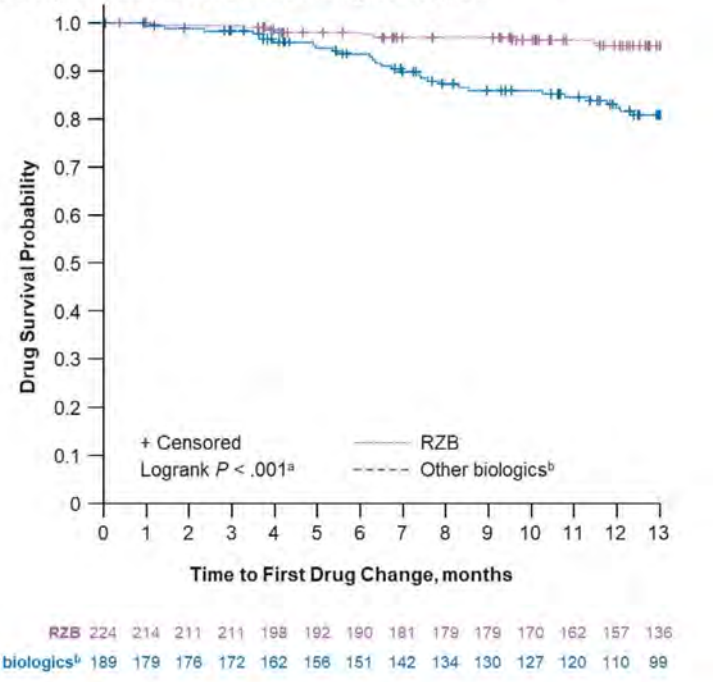
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

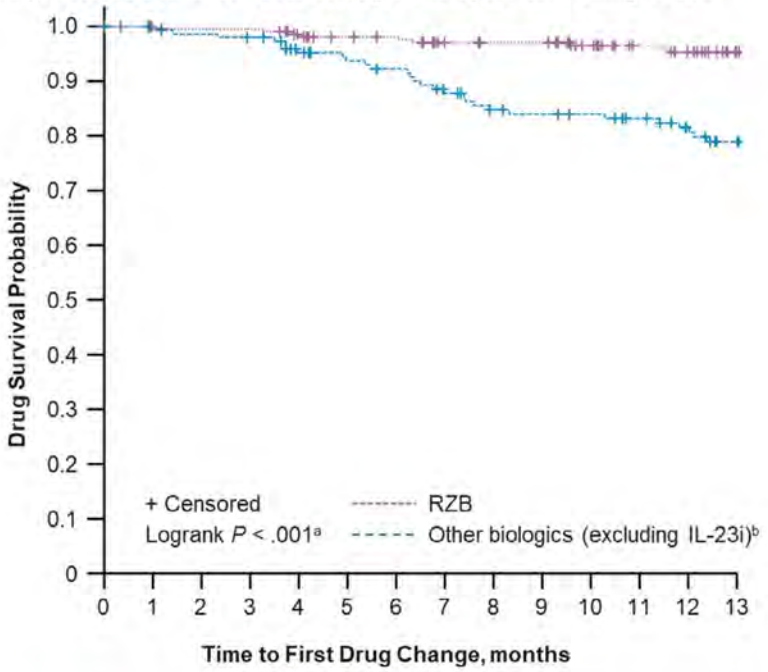
Background/Purpose: Risankizumab (RZB) is an optimized IL-23 inhibitor (IL-23i) currently approved for the treatment of plaque psoriasis (PsO), PsA, and Crohn's disease. In a post hoc analysis of data from the postmarketing VALUE study in patients with PsO who were treated with RZB or other biologic therapies, we assessed real-world drug survival for a subgroup of patients also diagnosed with PsA.

Figure 1. Kaplan-Meier estimate of drug survival among patients who were prescribed RZB or other biologic therapies.



RZB, risankizumab.
[a]Logrank *P* value based on available data through month 25.
[b]Includes secukinumab (n = 51), adalimumab (n = 38), ixekizumab (n = 37), guselkumab (n = 30), certolizumab pegol (n = 14), brodalumab (n = 7), ustekinumab (n = 6), tildrakizumab (n = 3), etanercept (n = 2), and infliximab (n = 1).

Figure 2. Kaplan-Meier estimate of drug survival among patients who were prescribed RZB or other biologic therapies excluding IL-23i.



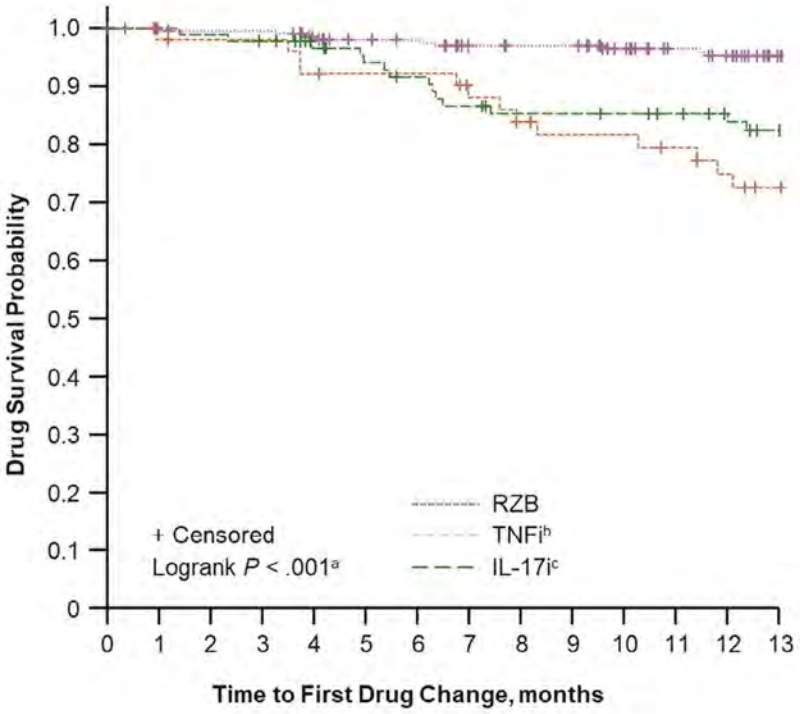
RZB	224	214	211	211	198	192	190	181	179	179	170	162	157	136
Other biologics (excluding IL-23i)[b]	156	147	145	143	133	128	125	117	110	108	106	102	94	86

IL-23i, IL-23 inhibitors; RZB, risankizumab.
[a]Logrank *P* value based on available data through month 25.
[b]Includes all other biologic therapies prescribed for psoriasis/PsA excluding the IL-23i guselkumab and tildrakizumab; secukinumab (n = 51), adalimumab (n = 38), ixekizumab (n = 37), certolizumab pegol (n = 14), brodalumab (n = 7), ustekinumab (n = 6), etanercept (n = 2), and infliximab (n = 1).

Methods: The ongoing, multicountry, prospective observational cohort VALUE study (NCT03982394) enrolled adults (aged ≥ 18 years) who were diagnosed with moderate-to-severe PsO and prescribed RZB or another biologic therapy in accordance with local labeling in a 2:1 ratio. All treatment decisions were made solely by the treating physician. This post hoc analysis included data from the subset of patients with PsO who were also diagnosed with PsA by a rheumatologist and was based on an interim database lock (data cutoff, September 26, 2022). Drug survival was compared for patients receiving RZB vs all other biologics, vs biologics excluding IL-23i, vs TNF-α inhibitors (TNFi), and vs IL-17 inhibitors (IL-17i). The probability of drug survival was estimated from Kaplan-Meier curves of time to first drug change (defined as discontinuation of the prescribed biologic treatment or changing to a different biologic treatment). Chi-squared tests were used to evaluate the proportion of patients who had drug changes by month 13. Analyses were repeated after propensity score matching (PSM) with a 1:1 ratio using greedy algorithm and exact match for biologic-naive/biologic-experienced status to account for baseline imbalances between comparison groups.

Results: A total of 244 (RZB) and 189 (other biologics) patients diagnosed with PsO and PsA were included in this analysis. Baseline demographics and characteristics were generally comparable between groups, except patients prescribed RZB vs other biologics were older (median age, 55 vs 51 years, $P = .02$) and more likely to have prior biologic therapy experience (67.4% vs 43.4%, $P < .001$). At month 13, fewer patients prescribed RZB had drug changes (5.5%) vs patients prescribed other biologics (19.0%), other biologics excluding IL-23i (20.5%), TNFi (26.7%), and IL-17i (16.4%; $P < .001$ for all comparisons). The estimated probability of drug survival [95% CI] at 13 months was higher among patients receiving RZB (95.3% [91.1%, 97.5%]) vs other biologics (80.9% [73.7%, 86.3%]; **Figure 1**); RZB vs biologics excluding IL-23i (78.9% [70.9%,

Figure 3. Kaplan-Meier estimate of drug survival among patients who were prescribed RZB, TNFi, or IL-17i.



RZB	224	214	211	211	198	192	190	181	179	179	170	162	157	136
TNFi[b]	55	51	50	50	47	46	46	42	39	37	37	35	32	28
IL-17i[c]	95	90	89	87	80	76	73	69	66	66	65	63	58	54

IL-17i, IL-17 inhibitors; RZB, risankizumab; TNFi, TNFα inhibitors.

[a]Logrank *P* value based on available data through month 25.
[b]Includes adalimumab (n = 38), certolizumab pegol (n = 14), etanercept (n = 2), and infliximab (n = 1).
[c]Includes secukinumab (n = 51), ixekizumab (n = 37), and brodalumab (n = 7).

85.0%]; **Figure 2**), or RZB vs TNFi and IL-17i (72.5% [57.3%, 83.1%] and 82.4% [72.0%, 89.2%]; **Figure 3**). Similar results were observed after PSM (estimated probability of drug survival [95% CI] at 13 months for RZB, 94.8% [88.7%, 97.6%]; other biologics, 84.8% [76.3%, 90.4%]; biologics excluding IL-23i, 82.4% [72.4%, 89.0%]; TNFi, 82.7% [63.2%, 92.4%]; and IL-17i, 82.8% [69.5%, 90.7%]).

Conclusion: Patients with PsO and PsA who were treated with RZB in the real-world setting experienced fewer drug changes and a higher probability of drug survival compared with those treated with other biologic therapies. These results can help inform clinician decision making when initiating biologic treatment in patients with PsA.

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5, 6, Merck-Serono, 1, 2, 5, 6, Mitsubishi Pharma, 1, 2, 5, 6, Moberg Pharma, 1, 2, 5, 6, MSD, 1, 2, 5, 6, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, 6, PRCL Research, 1, 2, 5, 6, Regeneron, 1, 2, 5, 6, Roche, 1, 2, 5, 6, Sanofi-Aventis/Genzyme, 1, 2, 5, 6, Sun Pharma, 1, 2, 5, 6, Takeda, 1, 2, 5, 6, UCB, 1, 2, 5, 6; **A. Östör**: AbbVie, 12, has served as a consultant and/or on advisory boards and/or undertaken clinical trials, GSK, 12, has served as a consultant and/or on advisory boards and/or undertaken clinical trials, Janssen, 12, has served as a consultant and/or on advisory boards and/or undertaken clinical trials, Lilly, 12, has served as a consultant and/or on advisory boards and/or undertaken clinical trials, Novartis, 12, has served as a consultant and/or on advisory boards and/or undertaken clinical trials, Pfizer, 12, has served as a consultant and/or on advisory boards and/or undertaken clinical trials; **V. Stakias**: AbbVie, 3, 11; **T. Madihlaba**: AbbVie, 3, 11; **R. Lippe**: AbbVie, 3, 11; **R. Liu**: AbbVie, 3, 11; **D. Thaçi**: AbbVie, 1, 2, 5, 12, Investigator, Almirall, 1, 2, 12, Investigator, Amgen, 1, 2, 12, Investigator, Boehringer-Ingelheim, 1, 2, 12, Investigator, Bristol-Myers Squibb(BMS), 1, 2, 12, Investigator, Celltrion, 1, 2, 12, Investigator, Eli Lilly, 1, 2, 12, Investigator, Galapagos, 1, 2, 12, Investigator, Galderma, 1, 2, 5, 12, Investigator, Janssen-Cilag, 1, 2, 12, Investigator, LEO Pharma, 1, 2, 5, 12, Investigator, Novartis, 1, 2, 5, 12, Investigator, Pfizer, 1, 2, 12, Investigator, Regeneron, 1, 2, 12, Investigator, Samsung, 1, 2, 12, Investigator, Sandoz, 1, 2, 12, Investigator, Sanofi, 1, 2, 12, Investigator, Target-Solution, 1, 2, 12, Investigator, UCB, 1, 2, 12, Investigator.

Abstract Number: 2246

Real-World Switching and Discontinuation Patterns for Biologic Disease-Modifying Antirheumatic Drugs in Patients with Active Psoriatic Arthritis in Japan

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

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Session Time: 9:00AM–11:00AM

Background/Purpose: The national prevalence of PsA among patients (pts) with psoriasis (PsO) in Japan is estimated to be 14.3%. Risankizumab (RZB) was approved for the treatment of PsO and PsA in Japan in March 2019. Real-world data on treatment persistence for PsA does not fully include recently approved biologic DMARDs (bDMARDs). This analysis

Table 1. Kaplan-Meier Rates of Switching and Discontinuation of Different PsA Treatments

Drug	N	Switching		Discontinuation		Switching or Discontinuation	
		12m	24m	12m	24m	12m	24m
RZB	74	21.00%	35.00%	21.60%	31.80%	25.90%	35.70%
GUS	115	30.30%	35.30%	37.40%	48.60%	41.20%	49.30%
ADA	264	20.50%	28.60%	49.00%	59.10%	50.40%	60.40%
CZP	108	24.70%	36.60%	34.70%	55.60%	44.70%	60.40%
SEC	188	18.90%	32.60%	36.10%	53.20%	36.50%	54.20%
IXE	156	21.30%	26.30%	31.20%	38.20%	36.40%	42.30%
BRO	53	27.10%	35.60%	48.00%	53.30%	47.90%	55.90%
UST	53	23.90%	31.10%	24.20%	35.80%	29.80%	41.50%

ADA, adalimumab; BRO, brodalumab; CZP, certolizumab pegol; GUS, guselkumab; IXE, ixekizumab; RZB, risankizumab; SEC, secukinumab; UST, ustekinumab.

Source: Japan Medical Data Center (JMDC) claims data from January 1, 2005 to August 31, 2022

Table 2. Adjusted Switching/Discontinuation Hazard Ratios by Treatment

Drug (reference: RZB)	Switching				Discontinuation				Switching or Discontinuation			
	Hazard Ratio	95% CI		P-Value	Hazard Ratio	95% CI		P-Value	Hazard Ratio	95% CI		P-Value
GUS	1.13	0.63	2	0.686	1.97	1.13	3.43	0.017	1.76	1.04	2.96	0.034
ADA	1.05	0.62	1.77	0.854	2.69	1.62	4.47	0	2.43	1.52	3.89	0
CZP	1.02	0.56	1.87	0.941	1.62	0.9	2.91	0.11	1.82	1.07	3.12	0.028
SEC	1.02	0.6	1.74	0.951	2.01	1.19	3.38	0.009	1.76	1.08	2.86	0.024
IXE	0.82	0.47	1.44	0.492	1.44	0.83	2.49	0.189	1.42	0.85	2.36	0.176
BRO	1.04	0.53	2.03	0.917	2.29	1.24	4.23	0.008	2.03	1.13	3.62	0.017
UST	1.1	0.59	2.07	0.766	1.34	0.72	2.51	0.359	1.36	0.76	2.44	0.301

ADA, adalimumab; BRO, brodalumab; CZP, certolizumab pegol; GUS, guselkumab; IXE, ixekizumab; RZB, risankizumab; SEC, secukinumab; UST, ustekinumab.

Cox proportional hazards models were used to estimate treatment-specific adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for switching and discontinuation; covariates included patient demographics, treatment history, and baseline comorbidities and healthcare charges.

quantified real-world treatment switching and discontinuation rates for pts with PsA in Japan initiating bDMARDs over 24 months, accounting for recent advancements in treatment.

Methods: A retrospective database study conducted using administrative claims from the Japan Medical Data Center Payer-Based Database from January 2005 through August 2022 included pts who had ≥ 1 medical claim for PsA preceding a claim for an approved bDMARD. Pts had ≥ 6 months of continuous eligibility prior to the first claim for a bDMARD (index date) and were evaluated for all treatments for which they had a qualifying index date. Treatment switch, defined as a claim for another bDMARD approved for PsA after the index date, and treatment discontinuation, defined as a gap in treatment without refill equal to 150% of the assumed days supply of the last prescription fill, were assessed up to 24 months past treatment initiation and rates were evaluated using Kaplan-Meier time-to-event analyses censored for loss of follow-up. bDMARD-specific adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using multivariate Cox proportional hazards models. HRs were adjusted for pt demographics, treatment history, and baseline comorbidities and healthcare charges.

Results: A total of 779 unique pts met the inclusion criteria for the study, and were treated with adalimumab (ADA; n = 264), bimekizumab (BIM; n = 5), brodalumab (BRO; n = 53), certolizumab pegol (CZP; n = 108), guselkumab (GUS; n = 115), ixekizumab (IXE; n =156), risankizumab (RZB; n = 74), secukinumab (SEC; n = 188), tildrakizumab (TIL; n = 5), and ustekinumab (UST; n = 53). Owing to small sample sizes, results are not shown for BIM and TIL. At 12/24 months following treatment initiation, 37.5%/49.0% of pts had discontinued their index bDMARD, while 22.2%/31.2% of pts had switched treatment. Switch rates varied across bDMARDs from 18.9-30.3% at 12 months, and 26.3%-36.6% at 24 months (**Table 1**). Discontinuation rates at 12/24 months were lowest for RZB (21.6%/31.8%), followed by UST (24.2%/35.8%), IXE (31.2%/38.2%), GUS (37.4%/48.6%), SEC (36.1%/53.2%), BRO (48.0%/53.3%), CZP (34.7%/55.6%), and ADA (49.0%/59.1%) [**Table 1**]. Adjusting for baseline pt characteristics, HRs of switching or discontinuation over 24 months were higher among CZP, SEC, ADA, BRO, and GUS, relative to RZB ($p < 0.05$) [**Table 2**].

Conclusion: Treatment switching and discontinuation were common in the first 24 months of treatment with bDMARDs for PsA in Japan. While treatment switch rates varied across bDMARDs, discontinuation rates were lowest for RZB at each timepoint that was examined. Hazards of switching or discontinuation relative to RZB were generally higher across most bDMARDs, indicating higher treatment persistence rates for RZB.

Disclosure: L. Erik: AbbVie, 2, 5, 6, Amgen, 2, 6, Biogen, 2, 6, Bristol-Myers Squibb, 2, 6, Eli Lilly, 2, 5, 6, Gilead, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 5, 6; **A. Soliman**: AbbVie/Abbott, 3, 10, 11; **D. Nunag**: AbbVie/Abbott, 5; **R. Lippe**: AbbVie, 3, 11; **M. Davis**: AbbVie/Abbott, 5; **M. Kishimoto**: AbbVie, 2, 6, Amgen, 2, 6, Asahi-Kasei Pharma, 2, 6, Astellas, 2, 6, Ayumi Pharma, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene, 2, 6, Chugai, 2, 6, Daiichi-Sankyo, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Ono Pharma, 2, 6, Pfizer, 2, 6, Tanabe-Mitsubishi, 2, 6, UCB, 2, 6.

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Gender Differences in Switching Biological and Targeted Synthetic Therapies in Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

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Background/Purpose: The impact of gender on biological and targeted synthetic therapies (ts/bDMARDs) used in PsA patients has been scarce studied. Our main objective was to explore gender differences in the incidence rate and causes of switching between ts/bDMARDs.

Methods: A retrospective longitudinal observational study was performed. Subjects: All patients who visited the outpatient rheumatology clinic from January 2007 to December 2021, and followed up to June 2022, diagnosed with PsA meeting CASPAR classification and on treatment with biological and targeted therapies (ts/bDMARDs). Main outcome: Switching of the ts/bDMARDs. Covariables: sociodemographic, clinics, and treatments. Statistical analysis: descriptive analysis of the switching, stratified by gender. To estimate ts/bDMARDs switching rates, survival techniques were used, expressing the incidence rate (IR) per 100 patients*year with their respective CI at 95% [CI 95%].

Results: A total of 141 patients with a diagnosis of PsA and under treatment with ts/bDMARDs were included, with a follow-up of 893.09 patients*year. The mean age was 48.06 ± 13.22 years and a 52.48% were females. PsA females showed some baseline disease characteristics: more depression, diabetes mellitus and thyroid disease and higher BMI. Regarding treatment characteristics, PsA males required more often concomitant corticosteroids and conventional synthetic DMARDs. A total of 262 treatment courses were recorded. Throughout follow-up, TNFi were the most used DMARDs in both genders,

Table 1: Total courses of ts/bDMARDs of the PsA patients

	Total courses (n=262)	Males courses (n=98)	Females courses (n=164)
ts/bDMARDs: n (%)			
TNFi	192 (73.28)	78 (79.59)	114 (69.51)
Adalimumab	81 (30.92)	39 (39.80)	42 (25.61)
Etanercept	41(15.75)	14 (14.29)	27 (16.46)
Certolizumab	36(13.74)	11(11.22)	25 (15.24)
Golimumab	16 (6.11)	6 (6.12)	10 (6.10)
Infliximab	18 (6.87)	8 (8.16)	10 (6.10)
Anti-IL17	43 (16.41)	16 (16.33)	27 (16.46)
Secukinumab	35(13.36)	13 (13.27)	22 (13.41)
Ixekizumab	8 (3.05)	3(3.06)	5(3.05)
Anti-IL12/IL23			
Ustekinumab	7 (2.67)	1(1.02)	6 (3.66)
JAKi	14 (5.35)	2 (2.04)	12 (7.32)
Tofacinib	4 (1.53)	0	4 (2.44)
Baricitinib	5 (1.91)	0	5 (3.05)
Upacitinib	5 (1.91)	2 (2.04)	3 (1.83)

* TNFi tumor necrosis factor inhibitor; JAKi: janus kinasa inhibitor

Table 2: Incidence rate (IR) of switching by gender

	Males (460.8 patients*year)		Females (432.7 patients*year)	
	Events	IR per 100 (CI 95%)	Events	IR per 100 (CI 95%)
Global switch	31	6.72(4.73-9.56)	91	21.02 (17.12-25.82
Switch due to inefficacy	25	5.42(3.66-8.02)	78	18.02 (14.4-22.5)
Primary failure	8	1.73 (0.86-3.47)	40	9.24 (6.78-12.60)
Secondary failure	18	3.90 (2.40-6.19)	38	8.78(6.38-12.06)
Switch due to adverse events	4	0.86 (0.32-2.31)	11	2.54 (1.40-4.58)
Switch due to other reasons	1	0.21 (0.30-1.54)	2	0.46 (0.11-1.84)

* Primary failure is defined as no clinical response within the initial treatment while secondary failure is defined as loss of efficacy of the drug after initial remission.

with 192 courses (73.28%), followed by Anti-IL17, with 43 (16.41%) courses of treatment, nevertheless, females used more Anti-IL12/23 and JAKi (Table 1). Of these 262 treatment courses, 122 (46.5%) were switched, with significative differences between gender (91 for females and 31 for males, p=0.001). About provider-reported reasons for switching, the most common reasons were primary inefficacy, loss of efficacy and adverse effects. The overall ts/bDMARDs switch rate in our study was IR (95% CI): 13.65 per 100 patients*year, with a much higher rate in females (21. 02 vs 6. 72), mainly due to primary failure. Table 2 show incidence rate (IR) of switching by gender and causes.

Conclusion: PsA female patients have distinct sociodemographic and clinic features that might contribute to the differences in therapy switching. Our results suggest that female patients are likely to change more their treatments. The overall ts/bDMARDs switch rates for females were significantly higher compared to males, mainly due to lack of efficacy. Gender differences in PsA are determined by biological and psychological factors (including gestational counselling reasons), influencing in the response to treatments and trends to switching.

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Primary Non-response in Psoriatic Arthritis Treated with Biologics and Targeted Synthetic Therapies in Daily Clinical Practice

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Background/Purpose: In Psoriatic arthritis (PsA), patients who fail to respond to biologics and targeted synthetic therapies (ts/bDMARDs), switching to another ts/bDMARD should be considered. Failure can be classified as primary non-response (without initial response probably due to therapeutic target failure), or secondary non-response (initial response achieved, but effectiveness is lost over time). Focusing in primary non-response, it seems reasonable to consider a different mode of action for the next treatment rather than switching within class, but studies addressing the best possible strategy are still lacking. Our purpose was obtain information from clinical practice regarding failures due to primary non-responsein PsA on ts/bDMARDs: 1) to assess the incidence rate of switching due to primary non-response; and 2) in those who have experienced primary non-response, to assess the risk of subsequent treatment failure by switching between classes compared to switching within class.

Methods: A longitudinal retrospective study (2015-2022) of PsA patients meeting CASPAR criteria on treatment with ts/bDMARDs from an outpatient rheumatology clinic was conducted. Main outcomes: 1) ts/bDMARD failure due to primary non-response; 2) subsequent discontinuation of ts/bDMARD due to lack of efficacy. Ourindependent variable wasswitching between classes compared to switching within class. To estimate bDMARDs switching rates, survival techniques were used, expressing the incidence rate (IR) per 100 patients*year with their CI at 95%. Cox multivariate regression analyses was run to assessthe role of switching between/within classes in the subsequent treatment failure.

Results: 141 PsA patients on treatment with ts/bDMARDs with a maximum follow-up of 16 years were included. Of these, 30 in 48 treatment courses developed primary non-response with an IR of 5.37 [4.04-7.12]. The IR was higher in women, and in those that started ts/bDMARDs after 2018. Regarding ts/bDMARDs those on TNF developed lower IR compared to the others (Table1). Focusing in those with primary non-response, there were 26 subsequent treatment failures with an IR of 22.09 [15.04-32.44]. The IR was higher in women, mainly after 2018 and in those patients who switched between classes (Table 2). In the multivariate adjusted model we found that switching within class increased the risk of subsequent failure compared switching between class (HR:3.26 [1.23-8.62], p=0.017).

Conclusion: In clinical practice, the IR of ts/bDMARDs failures due to primary non-response is 5.37% patients*year, but their subsequent failures are higher. This study provides a support to consider switching between classes a better alternative rather than switching within class after primary non-response.

Table 1: Incidence rate of switching due to primary non-response rate by covariables.

	Patients/year	N	IR	95%CI
Total	893.62	48	5.37	4.05-7.12
By gender				
Female	432.75	40	9.24	6.78-42.605
Male	460.87	8	1.73	0.86-3.47
By age at first ts/bDMARD, years				
< 40	228.12	9	3.94	2.05-7.58
40-50	262.77	12	4.56	2.59-8.04
50-60	222.56	13	5.84	3.39-10.06
60-70	129.68	12	9.25	5.25-16.29
>70	50.49	2	3.96	0.99-15.83
By year of ts/bDMARD start				
2007-2012	478.24	12	2.51	1.42-4.41
2013-2017	206.21	4	1.93	0.73-5.16
2018-2022	209.17	32	15.30	10.82-21.63
By bDMARDs				
TNF-alpha	793.69	31	3.90	2.74-5.55
IL-17	69.67	11	15.78	8.74-28.51
IL-23	10.28	4	38.87	14.59-103.58
JAKi	14.05	1	7.11	1.0-50.49
Abatacept	5.93	1	16.94	2.38-120.28

Table 2: In those with primary non-response, incidence rate of subsequent failure by covariables

	Patients/year	N	IR	95%CI
Total	117.69	26	22.09	15.04-32.44
By gender				
Female	87.75	22	25.07	16.50-38.07
Male	29.94	4	13.36	5.01-35.58
By age at first ts/bDMARD, years				
< 40	10.13	4	39.49	14.82-105.21
40-50	44.84	10	22.30	11.99-41.44
50-60	11.34	5	44.07	18.34-105.87
60-70	27.51	6	21.80	9.79-48.54
>70	23.87	1	4.19	0.59-29.74
By year of ts/bDMARD start				
2007-2012	56.57	7	12.37	5.89-25.95
2013-2017	31.24	4	12.80	4.80-34.11
2018-2022	29.88	15	50.19	30.26-83.27
By bDMARDs switching				
Within class	73.71	14	18.99	11.25-32.06
Between class	43.98	12	27.28	15.49-48.04

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Bimekizumab-Treated Patients with Active PsA Showed Sustained Improvement in Disease Symptoms Assessed by the PsA Impact of Disease (PsAID)-12 Questionnaire: 1-Year Results Reported from Two Phase 3 Studies

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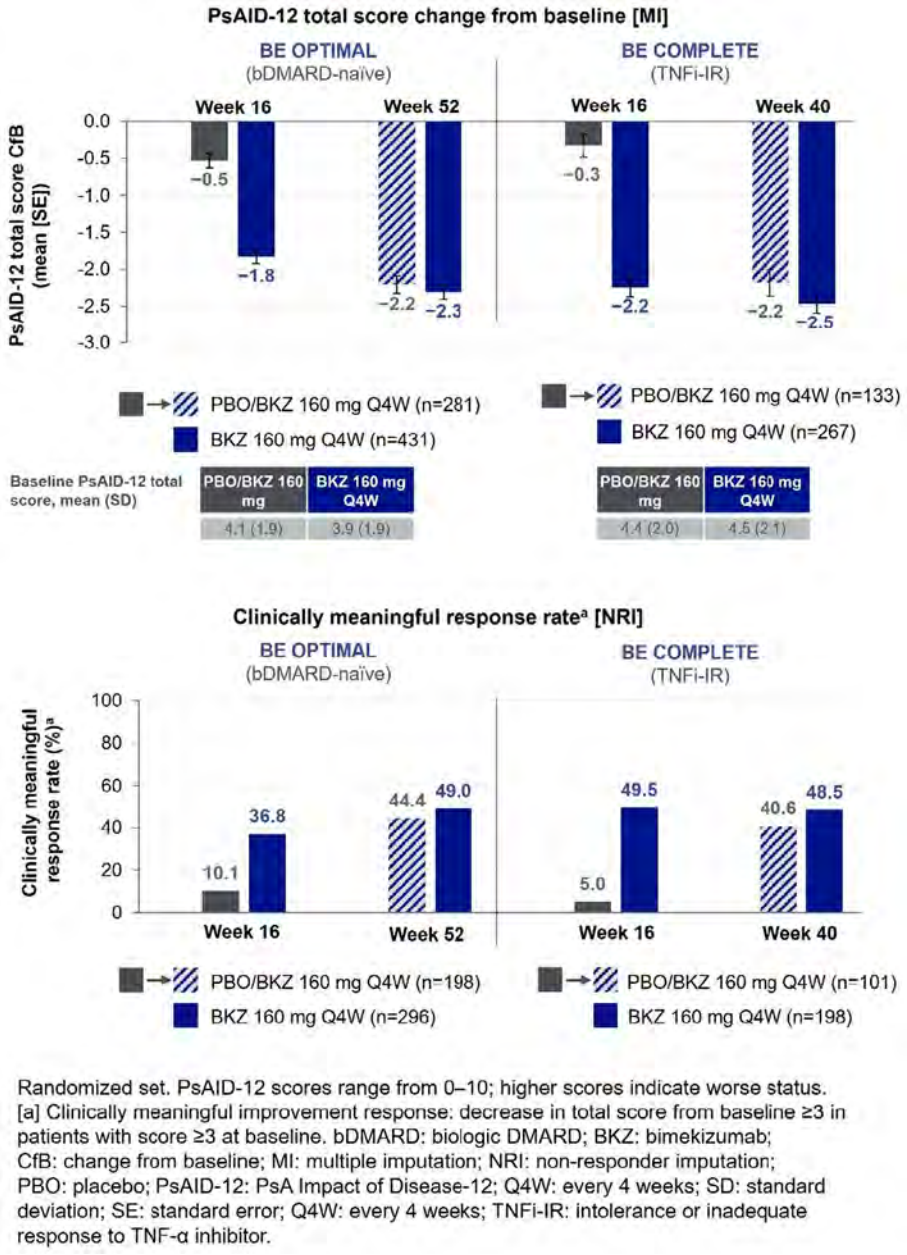
Background/Purpose: The PsA Impact of Disease-12 (PsAID-12) questionnaire is a patient (pt)-reported outcome measure assessing the impact of PsA on 12 physical, social, and psychological domains. OMERACT provisionally endorsed PsAID-12 as a core outcome measure for health-related quality of life (HRQoL) in clinical trials.[1] Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A, has demonstrated efficacy and tolerability to 52 weeks (wks) in pts with active PsA.[2,3] Here, the impact of BKZ on pt-reported symptoms and HRQoL, assessed by PsAID-12, is reported to 1 year.

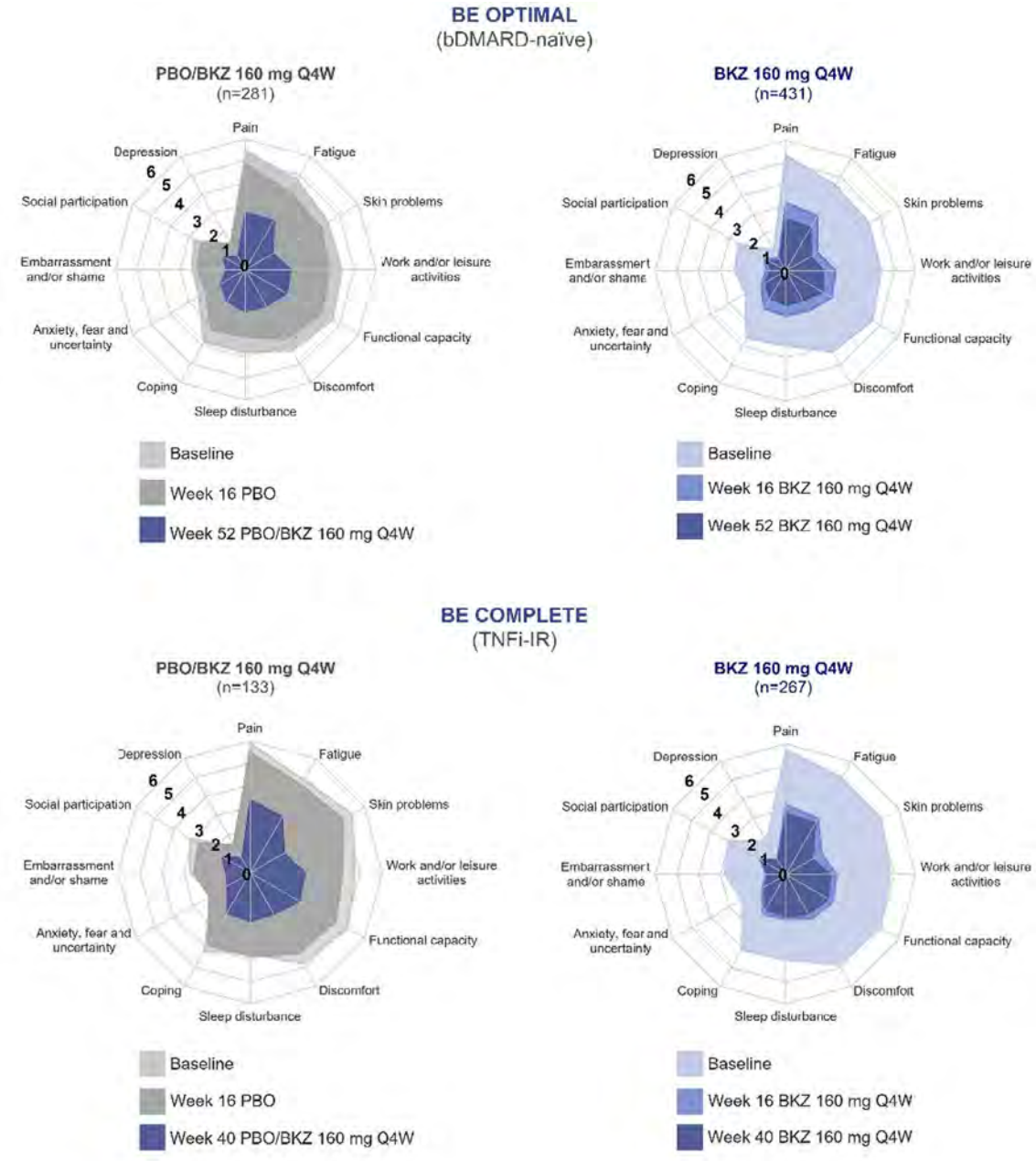
Methods: The phase 3 BE OPTIMAL (NCT03895203) and BE COMPLETE (NCT03896581) trials, both with a 16-wk double-blind, placebo (PBO)-controlled phase, assessed BKZ in pts with PsA who were biologic DMARD (bDMARD)-naïve or had intolerance or inadequate response to 1–2 TNF-α inhibitors (TNFi-IR), respectively. Pts in BE OPTIMAL were randomized 3:2:1 to subcutaneous (sc) BKZ 160 mg every 4 wks (Q4W), PBO, or reference (sc adalimumab 40 mg Q2W; data not reported here). At Wk 16, PBO pts switched to receive BKZ (PBO/BKZ). Pts in BE COMPLETE were randomized 2:1 to sc BKZ 160 mg Q4W or PBO; Wk 16 completers were eligible to enter an open-label extension, BE VITAL (NCT04009499), when PBO pts switched to BKZ (PBO/BKZ). BE COMPLETE plus BE VITAL is referred to as 'BE COMPLETE' hereafter. PsAID-12 total and single-item domain scores range from 0–10; higher scores indicate worse status.[1] Change from baseline (BL; CfB) and clinically meaningful improvement responses (decrease ≥3 from BL when respective PsAID-12 score ≥3 at BL) were collected to Wk 52 in BE OPTIMAL and Wk 40 in BE COMPLETE. Missing data imputed using multiple imputation (MI; continuous) or non-responder imputation (NRI; binary).



Randomized set. PsAID-12 scores range from 0–10; higher scores indicate worse status.
[a] Clinically meaningful improvement response: decrease in total score from baseline ≥3 in patients with score ≥3 at baseline. bDMARD: biologic DMARD; BKZ: bimekizumab; CfB: change from baseline; MI: multiple imputation; NRI: non-responder imputation; PBO: placebo; PsAID-12: PsA Impact of Disease-12; Q4W: every 4 weeks; SD: standard deviation; SE: standard error; Q4W: every 4 weeks; TNFi-IR: intolerance or inadequate response to TNF-α inhibitor.

Figure 1. PsAID-12 total score CfB [MI] and clinically meaningful improvement response rate [NRI] at Week 16 and Week 52/40

Results: 770/852 (90.4%) and 347/400 (86.8%) pts completed Wk 52 of BE OPTIMAL and BE COMPLETE, respectively. BKZ pts showed sustained improvements in PsAID-12 total score, with a mean CfB of –1.8 at Wk 16 and –2.3 at Wk 52 in BE OPTIMAL and –2.2 at Wk 16 and –2.5 at Wk 40 in BE COMPLETE. In both trials, PBO/BKZ pts achieved similar improvements to BKZ pts at Wk 52/40 (**Figure 1**). Clinically meaningful improvement response in PsAID-12 total score was achieved by 44.4% PBO/BKZ and 49.0% BKZ pts at Wk 52 in BE OPTIMAL, and 40.6% PBO/BKZ and 48.5% BKZ pts at Wk 40 in BE COMPLETE (**Figure1**). In both trials, improvements from BL in PsAID-12 individual domain mean scores were observed across all domains at Wk 16 and sustained to Wk 52/40 on BKZ (**Figure 2**). The greatest improvements were



Randomized set. PsAID-12 scores range from 0–10; higher scores indicate worse status.
bDMARD: biologic DMARD; BKZ: bimekizumab; PBO: placebo; PsAID-12: PsA Impact of Disease-12; Q4W: every 4 weeks; TNFi-IR: intolerance or inadequate response to TNF-α inhibitor.

Figure 2. PsAID-12 individual domain mean scores at baseline, Week 16, and Week 52/40 [MI]

observed in domains with the highest PsA impact at BL: pain, functional capacity, fatigue, and skin problems. Clinically meaningful improvement responses were achieved by around half of BKZ-treated patients across most individual domains, including pain, functional capacity, fatigue, and skin problems, at Wk 52/40.

Conclusion: Improvements in PsAID-12 total and most single-item domain scores at Wk 16 were sustained up to 1 year of BKZ treatment. Results were similar between the two trials, demonstrating consistent responses in bDMARD-naïve and TNFi-IR pts with active PsA.

References: 1. Orbai AM. J Rheumatol 2019;46:990–5. **2.** Ritchlin CT. Arthritis Rheumatol. 2022;74 (S9); **3.** Coates L. EULAR 2023;82 (S1).

Disclosure: D. Gladman: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, Gilead Sciences, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, Bristol Myers Squibb, 2, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead Sciences, 2, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake, 2, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **M. de Wit**: Celgene, 2, Eli Lilly, 2, Janssen, 2, Pfizer, 2, UCB Pharma, 2; **A. Ogdie**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CorEvitas, 2, Eli Lilly, 2, Gilead, 2, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, UCB, 2; **A. Orbai**: AbbVie, 5, Amgen, 5, BMS, 2, Janssen, 2, 5, Sanofi, 2, UCB Pharma, 2; **B. Ink**: AbbVie, 11, GSK, 11, UCB Pharma, 3, 11; **V. Taieb**: UCB Pharma, 3, 11; **J. Lambert**: UCB Pharma, 3, 11; **L. Gossec**: AbbVie, 2, 12, Personal fees, Amgen, 2, Biogen, 5, BMS, 12, Personal fees, Celltrion, 12, Personal fees, Eli Lilly, 5, 12, Personal fees, Galapagos, 12, Personal fees, Janssen, 12, Personal fees, MSD, 12, Personal fees, Novartis, 5, 12, Personal fees, Pfizer, 12, Personal fees, Sandoz, 5, 12, Personal fees, UCB Pharma, 5, 12, Personal fees.

Abstract Number: 2250

Bimekizumab Impact on Health-Related Quality of Life and Physical Function in Patients with Active Psoriatic Arthritis Who Were Biologic DMARD-Naïve or Had Inadequate Response or Intolerance to TNF-α Inhibitors: 1-Year Results from Two Phase 3, Randomized Studies

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

Session Type: Poster Session C

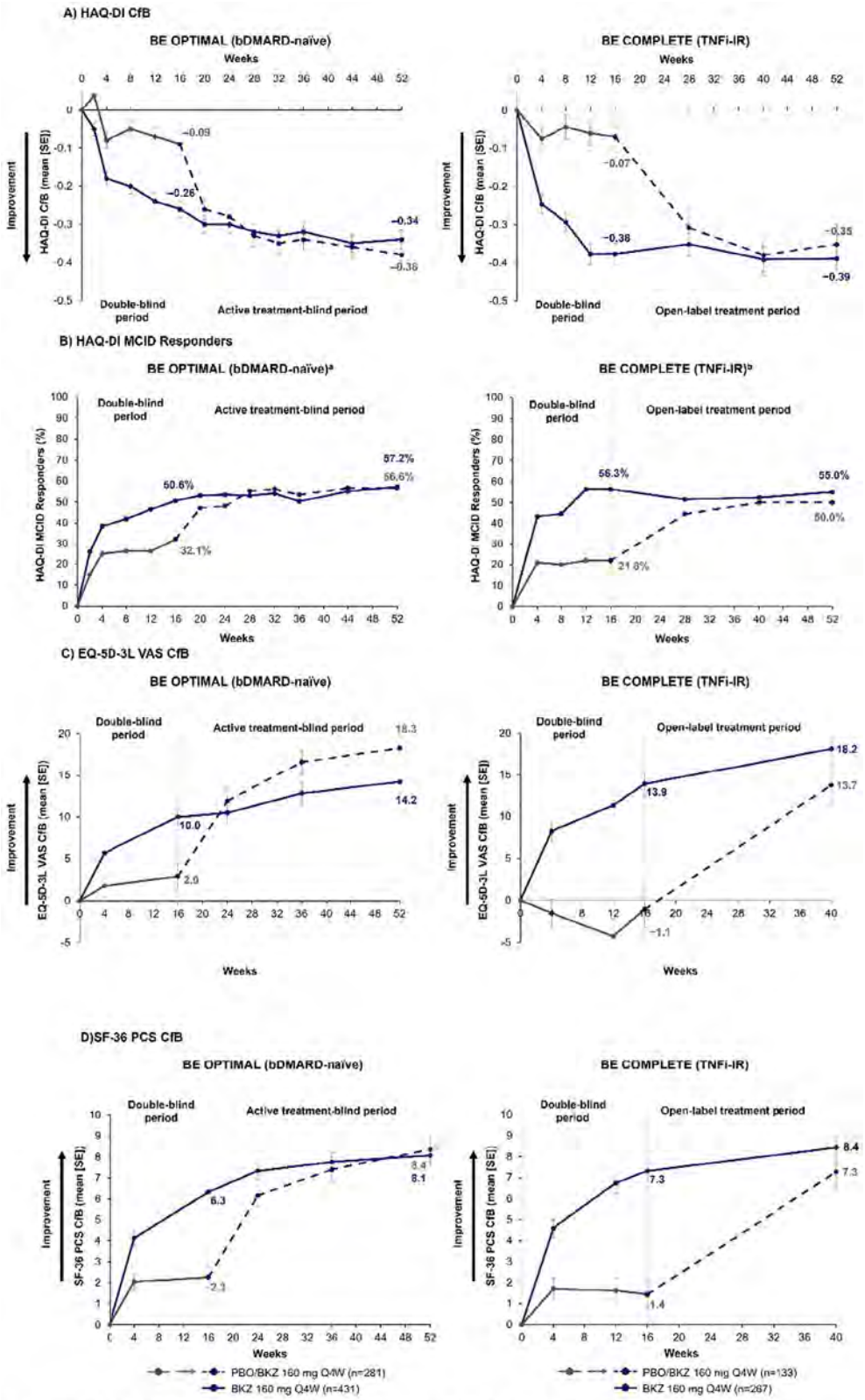
Session Time: 9:00AM–11:00AM

Background/Purpose: PsA has a substantial negative impact on patient (pt) health-related quality of life (HRQoL);[1] symptom control, preventing structural damage, and normalizing physical and social function to maximize HRQoL are key treatment goals.[2] Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A, has

Table. Health-related quality of life, physical function, and health status measures at baseline, Week 16, and Week 40/52 (MI, NRI, OC)

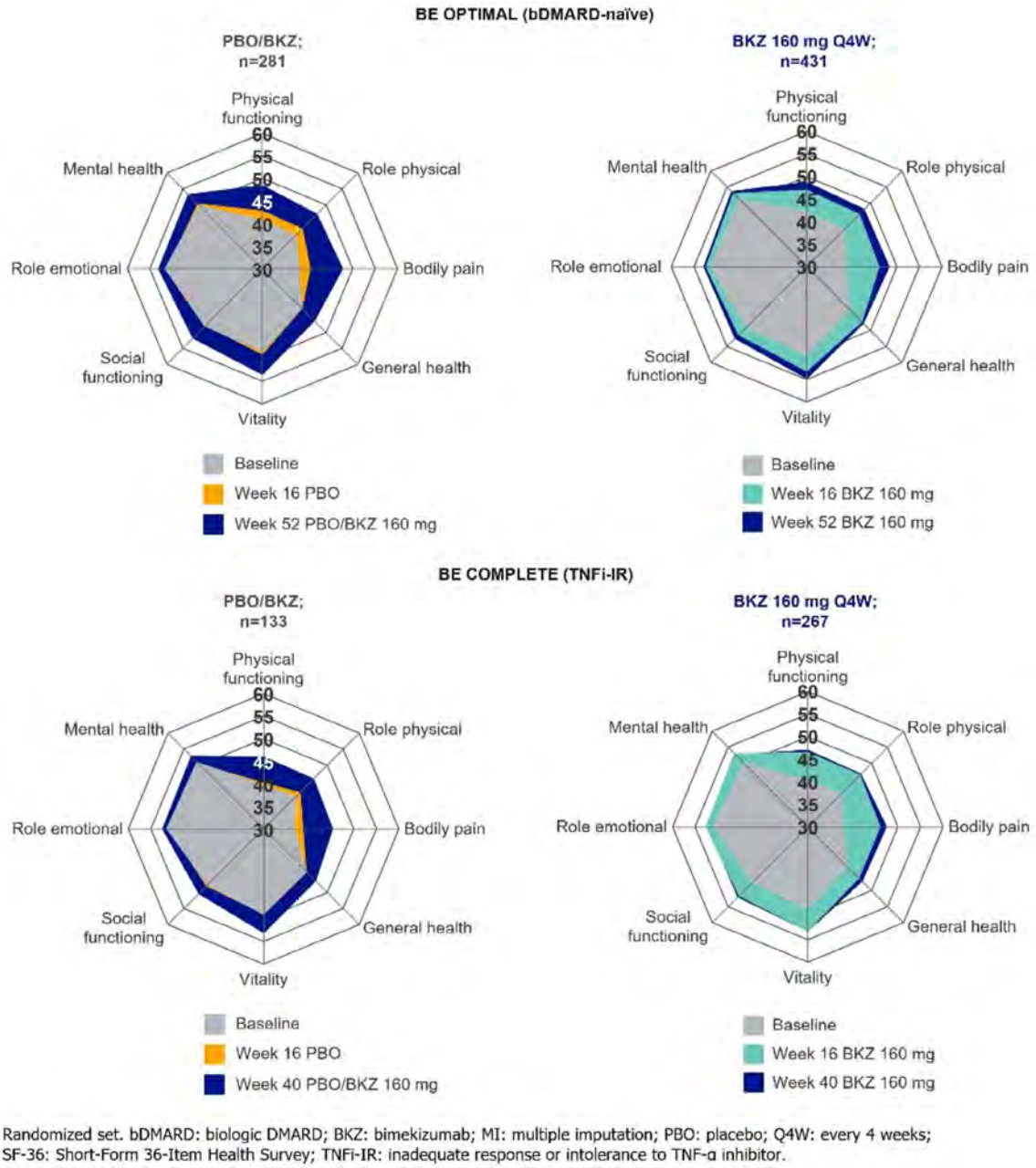
	BE OPTIMAL (bDMARD-naïve)				BE COMPLETE (TNFi-IR)			
	PBO (up to Week 16) → BKZ 160 mg Q4W (n=281)		BKZ 160 mg Q4W (n=431)		PBO (up to Week 16) → BKZ 160 mg Q4W (n=133)		BKZ 160 mg Q4W (n=267)	
	Week 16	Week 52	Week 16	Week 52	Week 16	Week 40	Week 16	Week 40
SF-36 PCS								
Baseline [OC], mean (SD)[a]	36.9 (9.7)		38.1 (9.4)		35.9 (10.2)		36.4 (9.0)	
CfB [MI], mean (SE)	+2.3 (0.5)	+8.4 (0.6)	+6.3 (0.4)	+8.1 (0.5)	+1.4 (0.7)	+7.3 (0.9)	+7.3 (0.5)	+8.4 (0.6)
SF-36 MCS								
Baseline [OC], mean (SD)[a]	54.3 (8.8)		54.7 (8.8)		55.3 (10.1)		54.0 (9.3)	
CfB [MI], mean (SE)	−0.8 (0.5)	+0.8 (0.5)	+0.3 (0.4)	+0.7 (0.4)	−0.9 (0.6)	−0.2 (0.7)	+1.3 (0.5)	+0.7 (0.5)
PsAID-12 total score								
Baseline [OC], mean (SD)[a]	4.1 (1.9)		3.9 (1.9)		4.4 (2.0)		4.5 (2.1)	
CfB [MI], mean (SE)	−0.5 (0.1)	−2.2 (0.1)	−1.8 (0.1)	−2.3 (0.1)	−0.3 (0.2)	−2.2 (0.2)	−2.2 (0.1)	−2.5 (0.1)
PsAID-12 total score responders [NRI][b]								
% (n/N)	10.1 (20/198)	44.4 (88/198)	36.8 (109/296)	49.0 (145/296)	5.0 (5/101)	40.6 (41/101)	49.5 (98/198)	48.5 (96/198)
EQ-5D-3L VAS								
Baseline [OC], mean (SD)[a]	54.1 (20.2)		58.1 (19.7)		54.5 (20.8)		54.3 (20.3)	
CfB [MI], mean (SE)	+2.9 (1.5)	+18.3 (1.7)	+10.0 (1.1)	+14.2 (1.3)	−1.1 (2.1)	+13.7 (2.5)	+13.9 (1.5)	+18.2 (1.7)
PsAQoL								
Baseline [OC], mean (SD)[a]	6.4 (5.1)		5.5 (4.6)		6.4 (5.1)		6.7 (5.2)	
CfB [MI], mean (SE)	−0.3 (0.3)	−2.6 (0.3)	−1.8 (0.2)	−2.5 (0.2)	0.0 (0.4)	–	−2.7 (0.3)	–
HAQ-DI								
Baseline [OC], mean (SD)[a]	0.89 (0.61)		0.82 (0.59)		1.0 (0.7)		1.0 (0.6)	
CfB [MI], mean (SE)	−0.09 (0.03)	−0.38 (0.03)	−0.26 (0.02)	−0.34 (0.02)	−0.07 (0.04)	−0.35 (0.05)	−0.38 (0.03)	−0.39 (0.03)
HAQ-DI MCID [NRI][c]								
% (n/N)	32.1 (71/221)	56.6 (125/221)	50.6 (161/318)	57.2 (182/318)	21.8 (24/110)	50.0 (55/110)	56.3 (130/231)	55.0 (127/231)
HAQ-DI normative state [NRI][d]								
Baseline, % (n/N)	32.4 (91/281)		36.7 (158/431)		29.3 (39/133)		28.8 (77/267)	
% (n/N)	39.9 (112/281)	57.7 (162/281)	56.4 (243/431)	57.3 (247/431)	30.8 (41/133)	42.9 (57/133)	58.1 (155/267)	53.2 (142/267)

Randomized set. PsAQoL scores collected only to Week 16 in BE COMPLETE; SF-36 PCS, SF-36 MCS, PsAID-12, and EQ-5D-3L scores collected only to Week 40 in BE COMPLETE. [a] BE OPTIMAL BKZ 160 mg Q4W: n=430. [b] PsAID-12 total score decrease of ≥3 from baseline in patients with PsAID-12 total score ≥3 at baseline. [c] HAQ-DI decrease from baseline ≥0.35 in patients with HAQ-DI ≥0.35 at baseline. [d] HAQ-DI ≤0.5. bDMARD: biologic DMARD; BKZ: bimekizumab; CfB: change from baseline; EQ-5D-3L: EuroQol-5 Dimensions-3 Level; HAQ-DI: HAQ-Disability Index; MCID: minimum clinically important difference; MCS: Mental Component Summary; MI: multiple imputation; NRI: non-responder imputation; OC: observed case; PBO: placebo; PCS: Physical Component Summary; PsAID-12: PsA Impact of Disease 12-item; PsAQoL: Psoriatic Arthritis Quality of Life; Q4W: every 4 weeks; SD: standard deviation; SE: standard error; SF-36: Short-Form 36-Item Health Survey; TNFi-IR: inadequate response or intolerance to TNF-α inhibitor; VAS: visual analog scale.



Randomized set. [a] PBO/BKZ 160 mg Q4W n=221, BKZ 160 mg Q4W n=318; [b] PBO/BKZ 160 mg Q4W n=110, BKZ 160 mg Q4W n=231.
bDMARD: biologic DMARD; BKZ: bimekizumab; CfB: change from baseline; EQ-5D-3L: EuroQol-5 Dimensions-3 Level; HAQ-DI: HAQ-Disability Index; MCID: minimal clinically important difference; MI: multiple imputation; NRI: non-responder imputation; PCS: Physical Component Summary; PBO: placebo; Q4W: every 4 weeks; SE: standard error; SF-36: Short-Form 36-Item Health Survey; TNFi-IR: inadequate response or intolerance to TNF-i inhibitor; VAS: visual analog scale.

Figure 1. Change from baseline HAQ-DI (A), proportion of HAQ-DI MCID responders (B), change from baseline EQ-5D-3L VAS (C), and change from baseline SF-36 PCS (D) to Week 40/52 (MI/NRI)



Randomized set. bDMARD: biologic DMARD; BKZ: bimekizumab; MI: multiple imputation; PBO: placebo; Q4W: every 4 weeks; SF-36: Short-Form 36-Item Health Survey; TNFi-IR: inadequate response or intolerance to TNF-α inhibitor.

Figure 2. SF-36 single-item subscale scores at baseline, Week 16, and Week 40/52 (MI)

demonstrated clinically relevant improvements in HRQoL measures to Week (Wk) 16 vs placebo (PBO) in pts with PsA in two phase 3 trials.[3,4] In this study, the impact of BKZ treatment on HRQoL is reported up to 1 year.

Methods: The phase 3 BE OPTIMAL (NCT03895203) and BE COMPLETE (NCT03896581) trials, both with a 16-wk double-blind, PBO-controlled phase, assessed BKZ in pts with PsA who were biologic DMARD (bDMARD)-naïve or had intolerance or inadequate response to TNF-α inhibitors (TNFi-IR), respectively. BE OPTIMAL pts were randomized 3:2:1 to subcutaneous (sc) BKZ 160 mg every 4 wks (Q4W), PBO, or reference (sc adalimumab 40 mg Q2W; data not reported). At Wk 16, PBO pts switched to BKZ (PBO/BKZ). BE COMPLETE pts were randomized 2:1 to sc BKZ 160 mg Q4W or PBO. Pts completing Wk 16 were eligible to enter an open-label extension, BE VITAL (NCT04009499), when PBO pts switched to BKZ (PBO/BKZ). BE COMPLETE plus BE VITAL is referred to as 'BE COMPLETE' hereafter.

Endpoints reported for HRQoL, health status, and physical function included Short-Form 36-Item Health Survey (SF-36) Physical and Mental Component Summaries (PCS; MCS) and subscale norm-based scores; PsA Impact of Disease 12-item (PsAID-12); EuroQol-5 Dimensions-3 Level Visual Analog Scale (EQ-5D-3L VAS); PsA Quality of Life (PsAQoL); HAQ-Disability Index (HAQ-DI). BE COMPLETE outcomes were collected to Wk 40/52 as stated in the **Table**. Non-responder and multiple imputation (NRI; MI) were used for missing binary and continuous variables.

Results: Overall, 770/852 (90.4%) and 347/400 (86.8%) pts completed Wk 52 of BE OPTIMAL and BE COMPLETE. Across both trials, Wk 16 improvements in HRQoL, health status, and physical function were sustained to Wk 52 on BKZ (**Table**). PBO/BKZ pts achieved comparable improvements to BKZ-randomized pts by Wk 52/40, including PsAID-12 total score response (decrease from baseline ≥3; bDMARD-naïve/TNFi-IR BKZ: 49.0/48.5%, PBO/BKZ: 44.4/40.6%), HAQ-DI minimal clinically important difference (MCID; decrease from baseline ≥0.35; BKZ: 57.2/55.0%, PBO/BKZ: 56.6/50.0%; **Figure 1**), and reaching HAQ-DI normative state of ≤0.5 (BKZ: 57.3/53.2%, PBO/BKZ: 57.7/42.9%). SF-36 PCS improved to a greater extent at Wk 16 in BKZ vs PBO pts (**Figure 1**); responses were sustained to Wk 52 on BKZ. SF-36 physical functioning, role physical, and bodily pain subscales showed the most improvement over the other subscales (**Figure 2**). Similar improvement trends were seen in EQ-5D-3L VAS (**Table**; **Figure 1**).

Conclusion: Clinically meaningful improvements in measures of HRQoL, health status, and physical function were observed up to 1 year with BKZ treatment, irrespective of prior bDMARD use.

References:1. Gudu T. Expert Rev Clin Immunol 2018;14:405–17; **2.** Gossec L. Ann Rheum Dis 2020;79:700–12; **3.** McInnes IB. Lancet 2023;401:25–37; **4.** Merola JF. Lancet 2023;401:38–48.

Disclosure: D. Gladman: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, Gilead Sciences, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5; **L. Gossec**: AbbVie, 2, 12, Personal fees, Amgen, 2, Biogen, 5, BMS, 12, Personal fees, Celltrion, 12, Personal fees, Eli Lilly, 5, 12, Personal fees, Galapagos, 12, Personal fees, Janssen, 12, Personal fees, MSD, 12, Personal fees, Novartis, 5, 12, Personal fees, Pfizer, 12, Personal fees, Sandoz, 5, 12, Personal fees, UCB Pharma, 5, 12, Personal fees; **M. Husni**: AbbVie, 1, 2, Amgen, 1, 2, Bristol-Myers Squibb, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, UCB, 1, 2; **L. Erik**: AbbVie, 2, 5, 6, Amgen, 2, 6, Biogen, 2, 6, Bristol-Myers Squibb, 2, 6, Eli Lilly, 2, 5, 6, Gilead, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, UCB, 2, 5, 6; **P. Gisondi**: AbbVie, 2, Abiogen, 2, Almirall, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, LEO Pharma, 2, Merck, 2, MSD, 2, Novartis, 2, Otsuka, 2, Pfizer, 2, Pierre Fabre, 2, Sanofi, 2, UCB Pharma, 2; **A. Gottlieb**: Amgen, 1, 2, AnaptysBio, 1, 2, 5, Avotres Therapeutics, 1, 2, Boehringer Ingelheim, 1, 2, Bristol Myers Squibb, 1, 2, 5, Dice Therapeutics, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, MoonLake Immunotherapeutics, 5, Novartis, 1, 2, 5, Sanofi, 1, 2, UCB Pharma, 1, 2, 5, XBiotech, 1, 2; **D. Thaçi**: AbbVie, 1, 2, 5, 12, Investigator, Almirall, 1, 2, 12, Investigator, Amgen, 1, 2, 12, Investigator, Boehringer-Ingelheim, 1, 2, 12, Investigator, Bristol-Myers Squibb(BMS), 1, 2, 12, Investigator, Celltrion, 1, 2, 12, Investigator, Eli Lilly, 1, 2, 12, Investigator, Galapagos, 1, 2, 12, Investigator, Galderma, 1, 2, 5, 12, Investigator, Janssen-Cilag, 1, 2, 12, Investigator, LEO Pharma, 1, 2, 5, 12, Investigator, Novartis, 1, 2, 5, 12, Investigator, Pfizer, 1, 2, 12, Investigator, Regeneron, 1, 2, 12, Investigator, Samsung, 1, 2, 12, Investigator, Sandoz, 1, 2, 12, Investigator, Sanofi, 1, 2, 12, Investigator, Target-Solution, 1, 2, 12, Investigator, UCB, 1, 2, 12, Investigator; **B. Ink**: AbbVie, 11, GSK, 11, UCB Pharma, 3, 11; **R. Bajracharya**: UCB Pharma, 3, 11; **J. Lambert**: UCB Pharma, 3, 11; **N. Lyris**: UCB Pharma, 3; **J. Coarse**: UCB Pharma, 3, 11; **W. Tillett**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, GSK, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Ovo Pharma, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma, 2, 5, 6.

Abstract Number: 2251

Direct and Indirect Effects of Upadacitinib or Adalimumab on Pain in Psoriatic Arthritis: Results from a Randomized Phase 3 Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

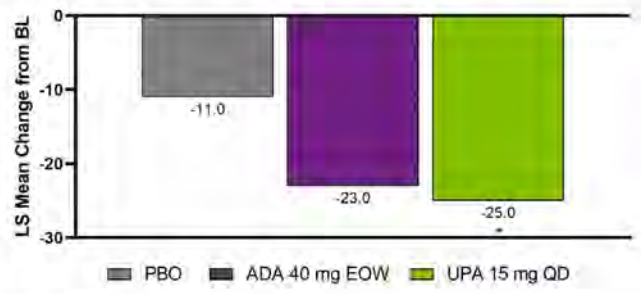
Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Pain, including inflammatory joint pain, may be debilitating in patients with psoriatic arthritis (PsA). Pain in PsA is multidimensional and can be influenced via reduction of inflammation and potentially by other means, such as a direct analgesic drug effect. The objective of this analysis of the SELECT-PsA 1 study was to assess the direct and indirect (ie, by changes in inflammation surrogates) effects of treatment with upadacitinib (UPA), a selective and reversible Janus kinase (JAK) inhibitor, or adalimumab (ADA), a TNF inhibitor, vs placebo (PBO) on pain in patients with PsA.

Methods: SELECT-PsA 1 was a randomized, double-blind phase 3 study in patients with PsA who had active disease at baseline. Adults (≥18 years) were randomized 1:1:1:1 to UPA 15 mg once daily, UPA 30 mg once daily, ADA 40 mg every other week, or PBO; for UPA, only UPA 15 mg data are reported here. As observed analysis was used for change from baseline to week 16 in Patient's Global Assessment (PtGA) of pain (1–100 mm) or tender joint count based on 28 joints (TJC28). Observed case multiple mediation analysis[1] for effect of UPA vs PBO and ADA vs PBO on pain (pain assessed as PtGA of pain or TJC28) was conducted. Indirect effect of treatment on pain was assessed based on inflammatory factors including itch, total enthesitis, Leeds Enthesitis Index (LEI), and CRP.

Figure 1. Change from Baseline in PtGA of Pain (mm) at Week 16



As observed analysis.
ADA, adalimumab; BL, baseline; EOW, every other week; LS, least squares; PBO, placebo; PtGA, Patient's Global Assessment; QD, once daily; UPA, upadacitinib.
*Statistically significant UPA vs PBO; $P<0.05$.

Figure 1. Change from Baseline in PtGA of Pain (mm) at Week 16

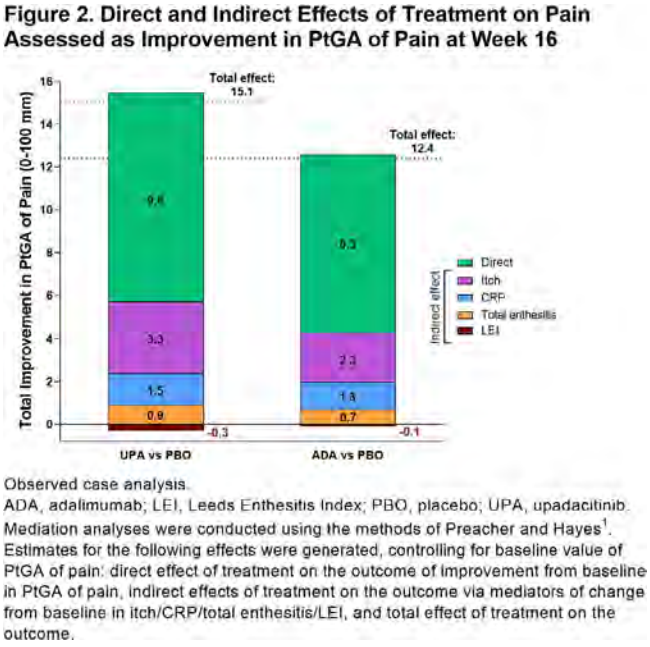


Figure 2. Direct and Indirect Effects of Treatment on Pain Assessed as Improvement in PtGA of Pain at Week 16

Results: 1281 patients were included in this analysis (UPA, n=429, ADA, n=429, PBO, n=423).PtGA of pain significantly improved with UPA vs PBO from baseline to week 16 (–25.0 [n=404] vs –11.0 [n=390]; *P*< 0.05; **Figure 1**). Improvements in pain were also observed with ADA at week 16 (–23.0 [n=408]). Total effects (15.1 and 12.4) and direct effects (9.8 and 8.3) on improvement in PtGA of pain were significantly greater with both UPA vs PBO and ADA vs PBO, respectively at week 16 (all *P*< 0.001; **Figure 2**); numerically greater reductions in total effect on pain were observed with UPA vs ADA. Direct and indirect effects on pain assessed as improvement in PtGA of pain were numerically greater with UPA vs ADA (**Figure 2)**. Improvement in elicited pain assessed asTJC28 was also significantly greater with UPA and ADA vs PBO (all *P*< 0.05;

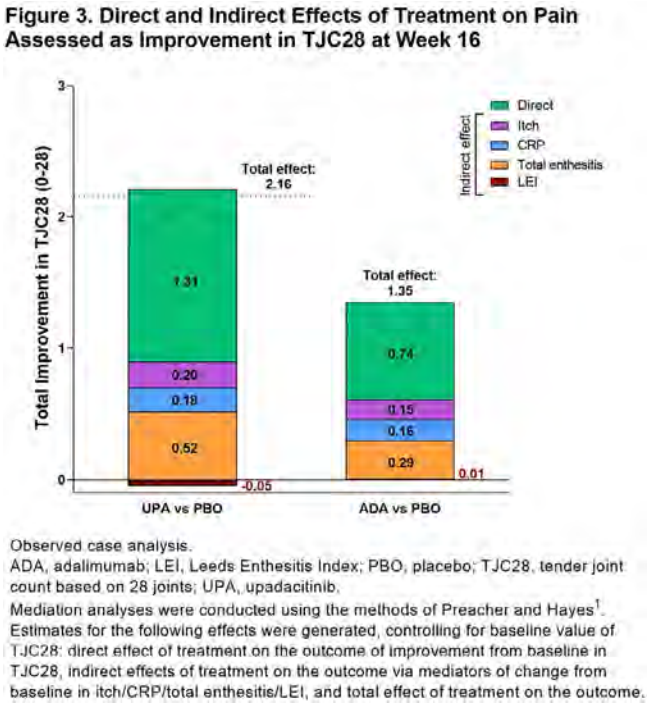


Figure 3. Direct and Indirect Effects of Treatment on Pain Assessed as Improvement in TJC28 at Week 16

Figure 3). Furthermore, UPA reduced pain assessed as TJC28 numerically more than ADA when examining the total effect explained by direct effects and the inflammatory mediators (indirect effects).

Conclusion: UPA and ADA produced relevantly higher mean improvements in pain via inflammatory or non-inflammatory mechanisms vs PBO in patients with PsA. Total effects on pain improvement were numerically greater with UPA vs ADA when assessed as PtGA of pain and TJC28.

Reference: [1]Preacher, KJ & Hayes, AF. *Behavior Research Methods,2008;40*(3), 879–891.

Disclosure: P. Taylor: AbbVie, 2, Biogen, 2, Eli Lilly, 2, Fresenius, 2, Galapagos, 2, 5, Gilead Sciences, 2, GSK, 2, Janssen, 2, Nordic Pharma, 2, Pfizer Inc, 2, Sanofi, 2, UCB, 2; **D. Walsh**: AbbVie, 2, Contura International A/S, 2, Eli Lilly, 5, GlaxoSmithKline Research & Development Limited, 5, Orion Corporation, 5, Pfizer, 5; **T. Takeuchi**: AbbVie, 2, 5, 6, AYUMI, 5, Bristol-Myers Squibb, 6, Chugai, 2, 5, 6, Daiichi Sankyo, 5, Eisai, 5, 6, Eli Lilly Japan, 2, 6, Gilead, 2, 6, Janssen, 6, Mitsubishi-Tanabe, 2, 5, 6, ONO, 5, Pfizer Japan, 6, Taiho, 2; **B. Fautrel**: AbbVie, 2, BMS, 2, Chugai, 2, Fresenius Kabi, 2, Galapagos, 2, Lilly, 2, Medac, 2, Nordic Pharma, 2, Novartis, 2, Pfizer, 2, Sobi, 2, UCB, 2; **J. Pope**: AbbVie, 1, 2; **K. Kato**: AbbVie/Abbott, 3, 11; **A. Setty**: AbbVie, 3, 11; **T. Gao**: AbbVie, 3, 11; **D. Caballero**: AbbVie, 3, 11; **R. Lippe**: AbbVie, 3, 11; **A. Kavanaugh**: AbbVie, 1, 2, Amgen, 1, 2, BMS, 1, 2, Eli Lilly, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, UCB, 1, 2.

Abstract Number: 2252

Bimekizumab Maintained Efficacy Responses Through 52 Weeks in Patients with Psoriatic Arthritis and Inadequate Response or Intolerance to TNF-α Inhibitors Who Were Responders at Week 16: Results from a Phase 3, Randomized Study

William R Tillett[1], Joseph Merola[2], Yoshiya Tanaka[3], Ennio G Favalli[4], Dennis McGonagle[5], Diamant Thaçi[6], Jessica A Walsh[7], Barbara Ink[8], Rajan Bajracharya[8], Jason Coarse[9] and Christopher T Ritchlin[10], [1]Department of Rheumatology, Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom, [2]Harvard Medical School, Brigham and Women's Hospital, Newton, MA, [3]University of Occupational and Environmental Health, Kitakyushu, Japan, [4]ASST Gaetano Pini-CTO, University of Milan, Department of Rheumatology, Milan, Italy, [5]Leeds Biomedical Research Centre, University of Leeds, Leeds, United Kingdom, [6]Institute and Comprehensive Center for Inflammation Medicine, University of Lübeck, Lübeck, Germany, [7]Salt Lake City Veterans Affairs Health and University of Utah Health, Division of Rheumatology, Salt Lake City, UT, [8]UCB Pharma, Slough, United Kingdom, [9]UCB Pharma, Morrisville, NC, [10]University of Rochester Medical School, Rochester, NY

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

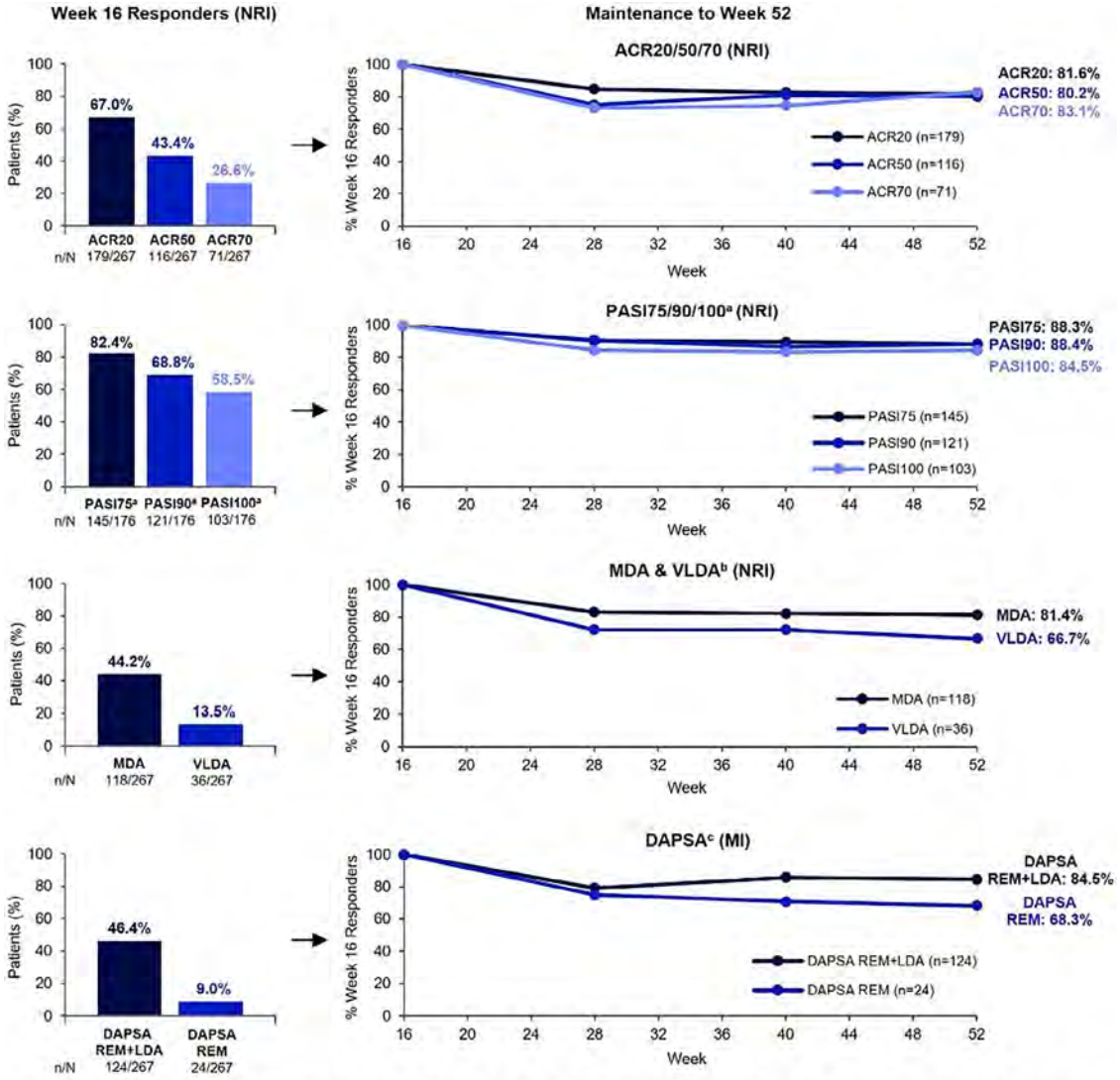
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: PsA is a chronic disease affecting multiple domains; however, patients (pts) can experience loss of response with long-term therapy.[1] Therefore, maintaining long-term treatment responses is important. Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A, demonstrated rapid and clinically meaningful improvements in joint and skin efficacy outcomes to Week (Wk) 16, vs placebo (PBO), that were sustained to Wk 52.[2–4] The objective of this analysis was to report maintenance of response in joint, skin, and composite efficacy outcomes to 52 wks in BKZ-treated pts with PsA who were Wk 16 responders.

Methods: BE COMPLETE (NCT03896581), a 16-wk double-blind phase 3 study, included pts with active PsA who had inadequate response or intolerance to 1–2 TNF-α inhibitors (TNFi-IR). Pts were randomized 2:1 to subcutaneous BKZ 160 mg every 4 wks (Q4W) or PBO. Pts completing Wk 16 were eligible to enter an open-label extension, BE VITAL (NCT04009499). Maintenance of response is reported as the percentage of BKZ-treated pts who achieved a response at Wk 16 and maintained response at Wk 52. ACR20/50/70, Psoriasis Area and Severity Index (PASI)75/90/100, minimal/very low disease activity (MDA/VLDA), and Disease Activity Index for PsA (DAPSA) remission/low disease activity (REM+LDA; ≤14) and remission (REM; ≤4) responses are presented. Data are reported as observed case (OC) and using non-responder



Randomized set. All data reported as NRI, except for DAPSA maintenance reported as MI. [a] In patients with psoriasis affecting ≥3% BSA at baseline. [b] Patients are considered to achieve MDA and VLDA when they meet 5/7 and 7/7 of the following criteria, respectively: TJC ≤1, SJC ≤1, PASI ≤1 or BSA ≤3%, patient pain (VAS ≤15 mm), patient global assessment (VAS ≤20), HAQ-DI ≤0.5, and tender entheseal points (LEI) ≤1. [c] DAPSA score is the sum of SJC (range: 0–66), TJC (range: 0–68), patient pain (VAS 0–10), patient global assessment (VAS 0–10), and C-reactive protein (mg/L). DAPSA REM+LDA is defined as DAPSA total score ≤14; DAPSA REM is defined as DAPSA total score ≤4.
ACR20/50/70: ≥20/50/70% improvement in ACR criteria; BSA: body surface area; DAPSA: Disease Activity Index for PsA; HAQ-DI: HAQ–Disability Index; LDA: low disease activity; LEI: Leeds Enthesitis Index; MDA: minimal disease activity; MI: multiple imputation; NRI: non-responder imputation; PASI: Psoriasis Area and Severity Index; PASI75/90/100: ≥75/90/100% improvement in PASI; REM: remission; SJC: swollen joint count; TEAE: treatment-emergent adverse events; TJC: tender joint count; VAS: visual analogue scale; VLDA: very low disease activity.

Figure. Maintenance of efficacy responses to Week 52 in Week 16 responders (NRI, MI)

imputation (NRI) or multiple imputation (MI). Treatment-emergent adverse events (TEAEs) to Wk 52 are reported for pts who received ≥1 dose of BKZ, including those who entered BE VITAL (PBO/BKZ).

Results: Overall, 267 pts were randomized to BKZ 160 mg Q4W; 263 (98.5%) and 236 (88.4%) completed Wks 16 and 52, respectively. Of BKZ-treated pts who were Wk 16 responders, ≥80% maintained response across all joint and skin outcomes, as well as MDA and DAPSA REM+LDA. At Wk 16, 179 (67.0%), 116 (43.4%), and 71 (26.6%) pts achieved ACR20/50/70, respectively. Over 80% of those responders maintained an ACR20/50/70 response at Wk 52: 81.6%, 80.2%, 83.1% (NRI); 89.6%, 86.1%, 85.5% (OC) (**Figure**). Of 176 pts with psoriasis affecting ≥3% body surface area (BSA) at baseline, 145 (82.4%), 121 (68.8%), and 103 (58.5%) achieved PASI75/90/100 at Wk 16. Of those responders, 88.3%, 88.4%, 84.5% (NRI); 97.0%, 96.4%, 91.6% (OC) maintained a PASI 75/90/100 response at Wk 52 (**Figure**). Similar results were observed for composite measures; 118 (44.2%) pts achieved MDA at Wk 16 and, of those, 81.4%/87.3% (NRI/OC) maintained their response at Wk 52. A high proportion of Wk 16 responders also maintained their VLDA, DAPSA REM+LDA, and DAPSA REM response at Wk 52 (**Figure**). To Wk 52, 243/388 (62.6%) BKZ-treated pts reported ≥1 TEAE and 23 (5.9%) reported serious TEAEs.

Conclusion: BKZ demonstrated robust maintenance of response at Wk 52 in TNFi-IR pts with PsA who responded to BKZ treatment at Wk 16. The safety profile was consistent with previous reports.[2,3]

References: 1. Boehncke WH. Am J Clin Dermatol 2013;14:377–88; **2.**McInnes IB. Lancet 2023;401:25–37; **3.** Merola JF. Lancet 2023;401:38–48; **4.**Coates LC. Ann Rheum Dis 2023;82(suppl 1):346.

Disclosure: W. Tillett: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, GSK, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Ovo Pharma, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma, 2, 5, 6; **J. Merola**: Abbvie, 2, 12, Investigator, Amgen, 2, 12, Investigator, Biogen, 2, 12, Investigator, Bristol-Myers Squibb, 2, 12, Investigator, Dermavant, 2, 12, Investigator, Eli Lilly, 2, 6, 12, Investigator, Janssen, 2, 12, Investigator, Leo Pharma, 2, 12, Investigator, Novartis, 2, 12, Investigator, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, 12, Investigator, Sun Pharma, 2, 12, Investigator, UCB Pharma, 2, 12, Investigator; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer-Ingelheim, 6, Chugai, 5, 6, Eisai, 5, 6, Eli Lilly, 6, Gilead, 6, GSK, 6, Mitsubishi-Tanabe, 5, Pfizer, 6, Taiho, 6, Taisho, 5, 6; **E. Favalli**: AbbVie, 2, 6, Bristol-Myers Squibb (BMS), 2, 6, Celltrion, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB Pharma, 2, 6; **D. McGonagle**: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Janssen, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **D. Thaçi**: AbbVie, 1, 2, 5, 12, Investigator, Almirall, 1, 2, 12, Investigator, Amgen, 1, 2, 12, Investigator, Boehringer-Ingelheim, 1, 2, 12, Investigator, Bristol-Myers Squibb(BMS), 1, 2, 12, Investigator, Celltrion, 1, 2, 12, Investigator, Eli Lilly, 1, 2, 12, Investigator, Galapagos, 1, 2, 12, Investigator, Galderma, 1, 2, 5, 12, Investigator, Janssen-Cilag, 1, 2, 12, Investigator, LEO Pharma, 1, 2, 5, 12, Investigator, Novartis, 1, 2, 5, 12, Investigator, Pfizer, 1, 2, 12, Investigator, Regeneron, 1, 2, 12, Investigator, Samsung, 1, 2, 12, Investigator, Sandoz, 1, 2, 12, Investigator, Sanofi, 1, 2, 12, Investigator, Target-Solution, 1, 2, 12, Investigator, UCB, 1, 2, 12, Investigator; **J. Walsh**: AbbVie, 5, Amgen, 2, Eli Lilly, 2, Janssen, 2, Merck, 5, Novartis, 2, Pfizer, 2, 5, UCB Pharma, 2; **B. Ink**: AbbVie, 11, GSK, 11, UCB Pharma, 3, 11; **R. Bajracharya**: UCB Pharma, 3, 11; **J. Coarse**: UCB Pharma, 3, 11; **C. Ritchlin**: AbbVie, 2, 12, Research, Amgen, 2, Eli Lilly, 2, Gilead, 2, Janssen, 2, Novartis, 2, Pfizer, 2, UCB Pharma, 2.

Abstract Number: 2253

Deucravacitinib, an Oral, Allosteric, Selective Tyrosine Kinase 2 Inhibitor, in Patients with Plaque Psoriasis Who Screened Positive for Psoriatic Arthritis in POETYK PSO-1 and POETYK PSO-2: Effect on Joint Pain and Peripheral Joint Disease vs Placebo and Apremilast

Joseph Merola[1], Philip J. Mease[2], April W. Armstrong[3], Vibeke Strand[4], Thomas Lehman[5], Jiyoon Choi[6], Brandon Becker[6], Yichen Zhong[7], Matthew J. Colombo[7], Diamant Thaçi[8], Androniki Bili[7] and Alice B. Gottlieb[9], [1]Harvard Medical School, Brigham and Women's Hospital, Newton, MA, [2]Swedish Medical Center/Providence St. Joseph Health and University of Washington School of Medicine, Seattle, WA, [3]Keck School of Medicine of University of Southern California, Los Angeles, CA, [4]Stanford University, Portola Valley, CA, [5]Bristol Myers Squibb, Philadelphia, PA, [6]Bristol Myers Squibb, Lawrenceville, NJ, [7]Bristol Myers Squibb, Princeton, NJ, [8]Institute and Comprehensive Center for Inflammation Medicine, University of Lübeck, Lübeck, Germany, [9]Icahn School of Medicine at Mount Sinai, New York, NY

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

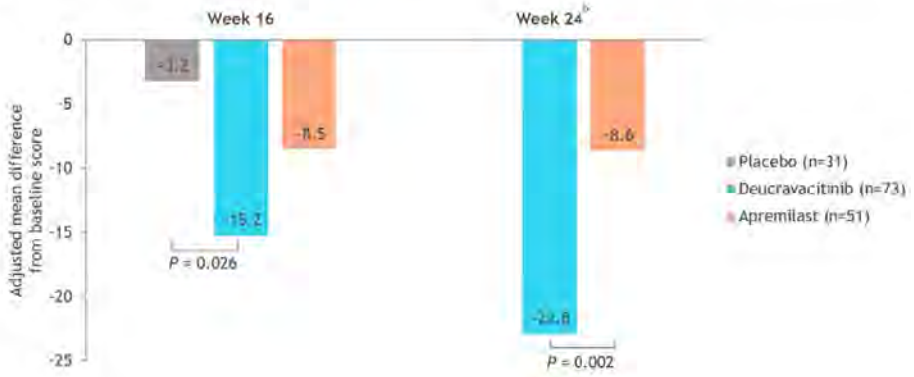
Background/Purpose: As 41% of patients with psoriasis may be undiagnosed for psoriatic arthritis, treatments must relieve both dermatologic and musculoskeletal symptoms. Deucravacitinib (DEUC), an oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor, is approved in the US, EU, and other countries for treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy. In the pivotal phase 3, randomized, controlled POETYK PSO-1 and PSO-2 trials, significantly greater proportions of patients receiving DEUC achieved 75% improvement from baseline in Psoriasis Area and Severity Index scores and static Physician Global Assessment scores of 0/1 at Week 16 vs patients receiving placebo (PBO) or apremilast (APR). The efficacy and safety of deucravacitinib in patients with active psoriatic arthritis was demonstrated in a phase 2 trial (NCT03881059), with significant improvements vs PBO observed in all key musculoskeletal, functional, and dermatologic outcomes. This analysis compared the effects of DEUC vs PBO and vs APR on peripheral joint disease, joint pain, and health-related quality of life using the 36-item Short Form (SF-36) physical component summary (PCS) score at Weeks 16 and 24 in patients from POETYK PSO-1 and PSO-2 who self-reported joint symptoms.

Methods: POETYK PSO-1 and PSO-2 randomized patients with moderate to severe psoriasis 1:2:1 to PBO, DEUC 6 mg once daily, or APR 30 mg twice daily. The self-administered Psoriatic Arthritis Screening and Evaluation (PASE) questionnaire (≥47 indicates psoriatic arthritis [PASE positive]) was completed by patients with peripheral joint complaints at baseline. Peripheral joint pain and joint disease activity were measured by a visual analog scale (VAS; range, 0–100), with changes from baseline VAS scores assessed only in patients with a baseline of ≥30 for pain and disease. All patients completed the SF-36. Higher scores indicate worse disease burden on VAS measures and better health-related quality of life on the SF-36 PCS.

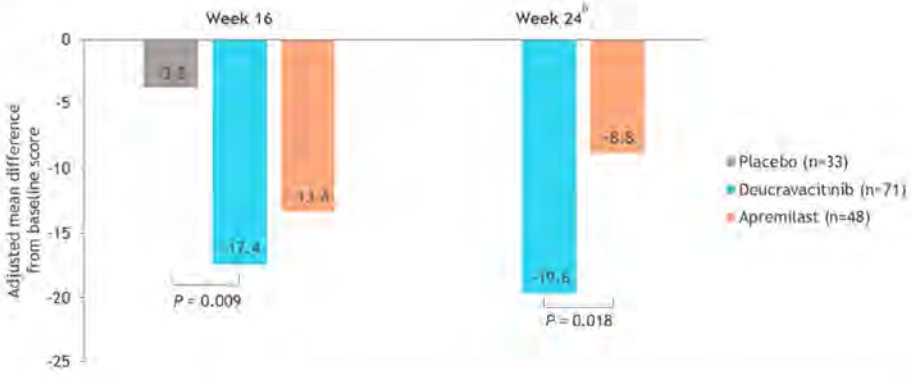
Results: This pooled analysis included 185 PASE-positive patients (11% of 1686 patients in the combined POETYK PSO-1 and PSO-2 trials). The improvement, assessed by adjusted mean change from baseline (CFB), was greater in patients treated with deucravacitinib vs placebo at Week 16 for joint pain VAS, joint disease VAS, and SF-36 PCS scores. Adjusted mean CFBs were greater in patients treated with deucravacitinib at Week 24 vs apremilast for joint pain VAS and joint disease VASscores, and were similar for SF-36 PCS scores (**Figures 1, 2**). A greater percentage of patients treated with DEUC reported 30% and 50% improvements on the joint pain VAS at Week 16 vs APR and PBO, and at Week 24 vs APR (**Figure 3**).

Figure 1. Mean change from baseline in (A) joint pain VAS scores[a] and (B) joint disease activity VAS scores[a] in the POETYK PSO-1 and PSO-2 pooled analysis

A.

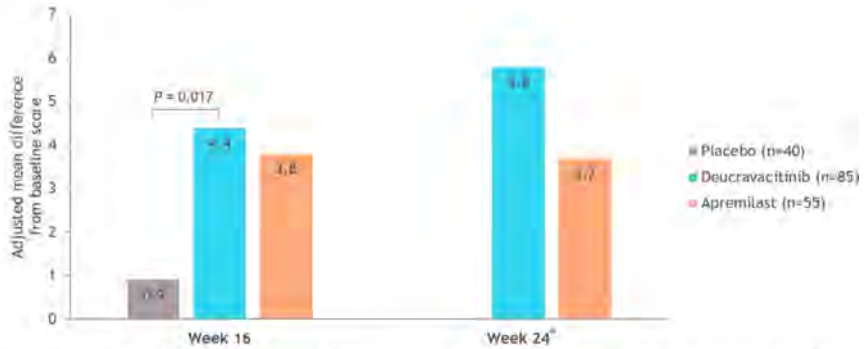


B.



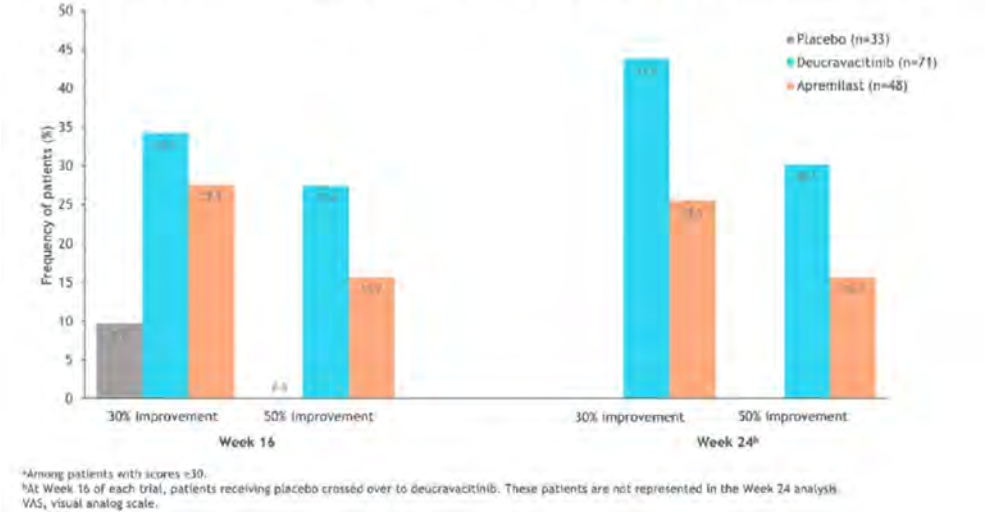
[a]Among patients with scores ≥30.
[b]At Week 16 of each trial, patients receiving placebo crossed over to deucravacitinib. These patients are not represented in the Week 24 analysis.
VAS, visual analog scale.

Figure 2. Change from baseline in SF-36 PCS score in the POETYK PSO-1 and PSO-2 pooled analysis



[a]At Week 16 of each trial, patients receiving placebo crossed over to deucravacitinib. These patients are not represented in the Week 24 analysis.
PCS, physical component summary; SF-36, 36-Item Short Form health survey.

Figure 3. Percentage of patients demonstrating 30% and 50% improvement in joint pain VAS scores[a] in the POETYK PSO-1 and PSO-2 pooled analysis



[a]Among patients with scores ≥10.
[b]At Week 16 of each trial, patients receiving placebo crossed over to deucravacitinib. These patients are not represented in the Week 24 analysis.
VAS, visual analog scale.

Conclusion: PASE-positive patients in POETYK PSO-1 and PSO-2 treated with DEUC reported greater improvements in the impact of joint disease and joint pain vs APR and PBO, and in SF-36 PCS scores vs those receiving PBO. Additionally, a greater percentage of patients treated with DEUC reported 30% and 50% improvements in joint pain vs patients receiving APR and patients receiving PBO. The magnitude of effect among DEUC-treated patients appeared to continue to improve through the 24-week active-controlled period.

Disclosure: J. Merola: Abbvie, 2, 12, Investigator, Amgen, 2, 12, Investigator, Biogen, 2, 12, Investigator, Bristol-Myers Squibb, 2, 12, Investigator, Dermavant, 2, 12, Investigator, Eli Lilly, 2, 6, 12, Investigator, Janssen, 2, 12, Investigator, Leo Pharma, 2, 12, Investigator, Novartis, 2, 12, Investigator, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, 12, Investigator, Sun Pharma, 2, 12, Investigator, UCB Pharma, 2, 12, Investigator; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, Aclaris, 2, Amgen, 2, 5, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Inmagene, 2, Janssen, 2, 5, 6, MoonLake Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 5, 6, Ventyx, 2, Xinthera, 2; **A. Armstrong**: AbbVie, 5, Almirall, 1, 6, Arcutis, 1, 6, Aslan Pharmaceuticals, 1, 1, 6, 6, Beiersdorf, 1, 6, Boehringer Ingelheim/Parexel, 12, Personal fees, Bristol-Myers Squibb(BMS), 5, Celgene, 12, Personal fees, Dermavant, 1, 6, 12, Personal fees, Dermira, 1, 5, 6, Eli Lilly, 5, EPI Health, 1, 6, Genentech, 12, Personal fees, GSK, 12, Personal fees, Incyte, 1, 6, Janssen, 5, Kyowa Kirin, 5, Leo Pharma, 5, Lilly, 1, 6, Menlo Therapeutics, 12, Personal fees, Merck, 12, Personal fees, Mindera Health, 1, 6, Modernizing Medicine, 12, Personal fees, Nimbus, 1, 6, Novartis, 5, Ortho Dermatologics, 12, Personal fees, Pfizer, 12, Personal fees, Regeneron, 12, Personal fees, Sanofi Genzyme, 12, Personal fees, Science 37, 12, Personal fees, Sun, 1, 6, Sun Pharma, 12, Personal fees, UCB, 5, Valeant, 12, Personal fees; **V. Strand**: Abbvie, 2, Alpine Immune Sciences, 2, Amgen, 2, Arena, 2, AstraZeneca, 2, Bayer, 2, Biosplice, 2, Bioventus, 2, Blackrock, 2, 2, BMS, 2, Boehringer Ingelheim, 2, Celltrion, 2, Chemocentryx, 2, EMD Serono, 2, Equillium, 2, Ermium, 2, Eupraxia Pharmaceuticals, 2, Flexion, 2, Galapagos, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon, 2, Ichnos, 2, Inmedix, 2, Janssen, 2, Kiniksa, 2, 2, Kypha, 2, Lilly, 2, Merck, 2, MiMedx, 2, Novartis, 2, Omeros, 2, Pfizer, 2, Regeneron, 2, Rheos, 2, R-Pharm, 2, Samsung, 2, Sandoz, 2, Sanofi, 2, Scipher, 2, Setpoint, 2, Sorrento, 2, Spherix, 2, Tonix, 2, UCB, 2, Urica, 2; **T. Lehman**: Bristol-Myers Squibb(BMS), 3; **J. Choi**: Bristol Myers Squibb, 3; **B. Becker**: Bristol-Myers Squibb(BMS), 3; **Y. Zhong**: Bristol-Myers Squibb(BMS), 3; **M. Colombo**: Bristol-Myers Squibb(BMS), 3, 11; **D. Thaçi**: AbbVie, 1, 2, 5, 12, Investigator, Almirall, 1, 2, 12, Investigator, Amgen, 1, 2, 12, Investigator, Boehringer-Ingelheim, 1, 2, 12, Investigator, Bristol-Myers Squibb(BMS), 1, 2, 12, Investigator, Celltrion, 1, 2, 12, Investigator, Eli

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Abstract Number: 2254

The Effects of Interleukin 17 Inhibitors on Major Adverse Cardiovascular Events in Patients Naïve to Biologic Agents with Psoriasis or Psoriatic Arthritis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Ruoning Ni[1], Jiayi Zheng[2], Ruru Guo[3] and Bharat Kumar[4], [1]University of Iowa Hospitals and Clinics, Coralville, IA, [2]The Wright Center for Graduate Medical Education, Scranton, PA, [3]Department of Rheumatology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China, [4]University of Iowa Hospitals and Clinics, Iowa City, IA

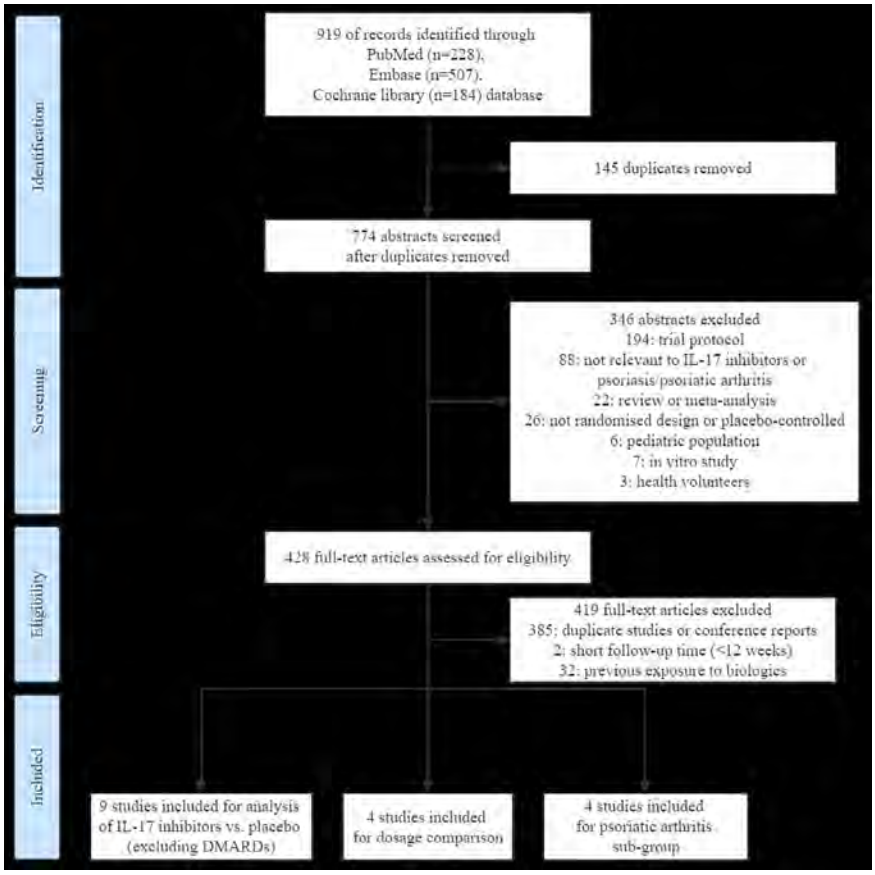
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The aim of this systematic review is to determine the effects of IL-17 inhibitors on major adverse cardiovascular events (MACEs) in patients with psoriasis (PsO) or psoriatic arthritis (PsA).

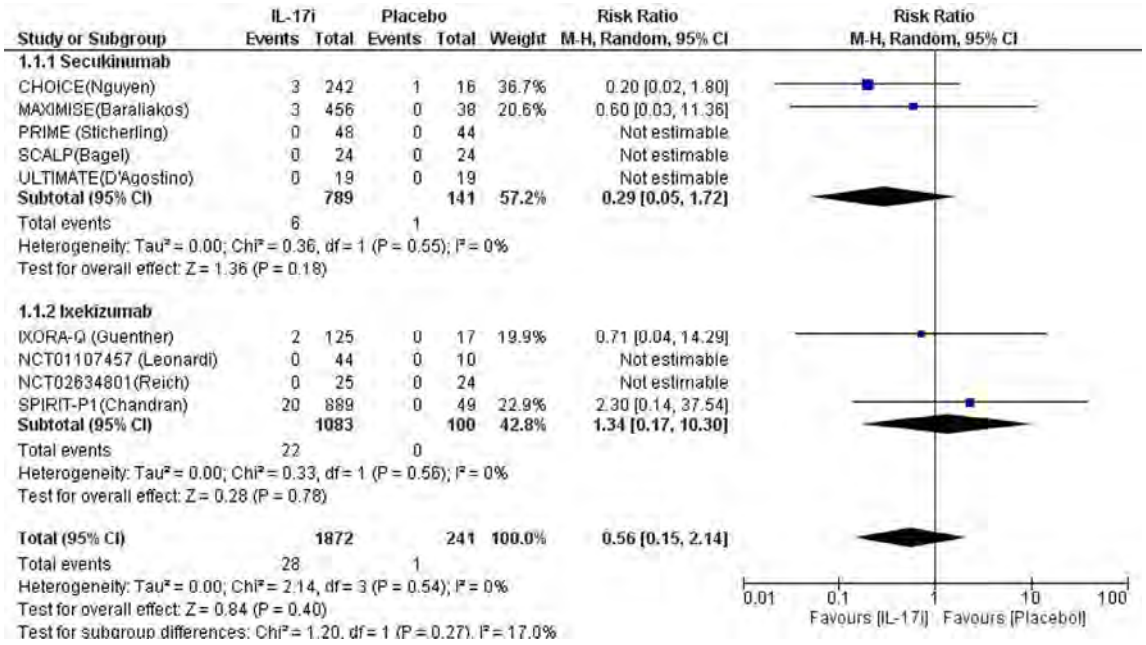
Methods: A search for randomized controlled trials of patients with PsO/PsA treated with IL-17 inhibitors that reported confirmed MACEs was conducted on December 7, 2022, in Medline, Embase, and the Cochrane Library for Randomized Controlled Trials. Two reviewers screened titles and abstracts and selected papers for full-text review. Trials that included the previous use of biologic disease modifying anti-rheumatic drugs were excluded. Risk ratios were calculated by the Mantel-Haenszel random-effect method. Heterogeneity across studies was measured by χ^2 test and I^2 statistics. Funnel plot analysis was produced to detect potential publication bias.

Results: Of the 919 references identified, 9 RCT studies were eligible for quantitative synthesis (n=2096 patients). The use of IL-17 inhibitors was not correlated with a statistically significant change in the risk of MACEs (Risk Ratio 0.56; 95% CI 0.15 to 2.14; p= 0.40). Subgroup analysis of secukinumab or ixekizumab also did not demonstrate changes in the risk for MACEs. Additionally, there was no detectable dose-dependent effect of IL-17 inhibitors on the risk of MACEs.

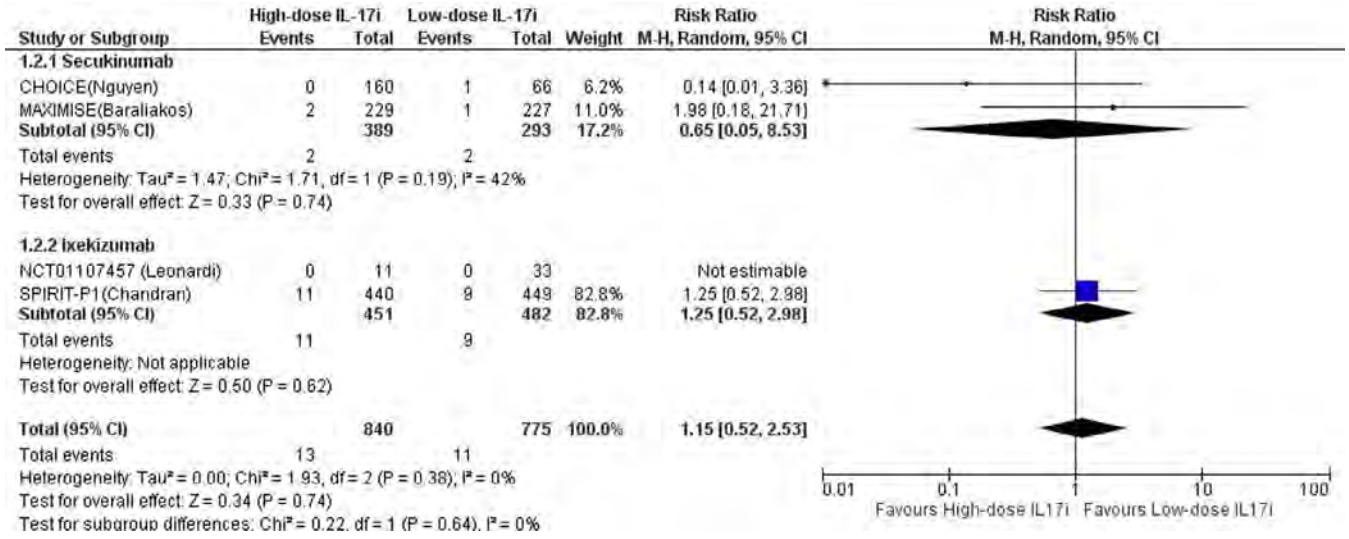
Conclusion: IL-17 inhibitor use is not correlated with a change in risk for major adverse cardiovascular in patients with PsO/PsA that have not previously received biologic disease-modifying anti-rheumatic drugs.



Flow chart of included randomized controlled trials.



Relative Risks (RRs) of all major adverse cardiovascular events (MACEs) in patients with psoriasis (PsO) and/or psoriatic arthritis (PsA) treated with interleukin 17 (IL-17) inhibitors compared with placebo or disease-modifying antirheumatic drugs (DMARDs) in randomized controlled trials (RCTs) using the Mantel-Haenszel (M-H) random-effect method. P-Y, patient-year.



RRs of all MACEs in patients with PsO/PsA treated with different dosages of IL-17 inhibitors in RCTs using the M-H random-effect method. P-Y, patient-year.

Disclosure: R. Ni: None; **J. Zheng**: None; **R. Guo**: None; **B. Kumar**: None.

Abstract Number: 2255

Bimekizumab versus Secukinumab for the Treatment of Nail Psoriasis in Patients with Moderate to Severe Plaque Psoriasis: Results from the BE RADIANT Phase 3b Trial

Kilian Eyerich[1], Alice B. Gottlieb[2], Stefano Piaserico[3], Stefan Beissert[4], Melinda Gooderham[5], Brian Kirby[6], Nicola Tilt[7], Cynthia Madden[8], Susanne Wiegratz[9], Dirk de Cuyper[10], **Joseph F. Merola**[11] and Boni Elewski[12], [1]Department of Dermatology, Medical Center, University of Freiburg, Freiburg, Germany, [2]Icahn School of Medicine at Mount Sinai, New York, NY, [3]Dermatology Unit, Department of Medicine, Università di Padova, Padova, Italy, [4]Department of Dermatology, University Hospital Carl Gustav Carus, TU Dresden, Dresden, Germany, [5]SKiN Centre for Dermatology, Probity Medical Research, Peterborough, ON, Canada, and Queen's University, Kingston, ON, Canada, [6]Elm Park and the Charles Institute, St Vincent's University Hospital, University College Dublin, Dublin, Ireland, [7]UCB Pharma, Slough, United Kingdom, [8]UCB Pharma, Morrisville, NC, [9]UCB Pharma, Monheim am Rhein, Germany, [10]UCB Pharma, Brussels, Belgium, [11]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [12]Department of Dermatology, University Hospitals of Cleveland, Case Western Reserve University, Cleveland, OH

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic lesions in highly visible areas, including the nails, disproportionately affect patients' health-related quality of life.[1] Here, we compare the efficacy of bimekizumab (BKZ) vs secukinumab (SEC) through 48 weeks (wks) for the treatment of nail psoriasis in patients with moderate to severe plaque psoriasis who had moderate to severe nail involvement at baseline.

Methods: In BE RADIANT, patients were randomized to BKZ 320mg every 4 wks (Q4W) or SEC 300mg weekly to Wk4 then Q4W. From Wk16, BKZ-randomized patients received BKZ Q4W or Q8W.[2] In this analysis, BKZ Q4W/Q4W and Q4W/Q8W were combined (BKZ Total). Modified Nail Psoriasis Severity Index (mNAPSI; total fingernail on a 0–130 scale) and mNAPSI sub-scores from Wks16–48 among patients with baseline mNAPSI >10 were assessed. Missing data were imputed as non-response (NRI).

Results: In total, 116 BKZ-treated and 99 SEC-treated patients had baseline mNAPSI >10; 37.1% and 40.4% achieved mNAPSI≤2 at Wk16; 75.0% and 59.6% achieved mNAPSI≤2 at Wk48. From Wks16–48, mNAPSI=0 (clear) response rates increased from 26.7% to 70.7% (BKZ), and 33.3% to 53.5% (SEC). 101 BKZ-treated and 86 SEC-treated patients had both baseline mNAPSI >10 and baseline nail pitting >0; 36.6% and 41.9% achieved nail pitting=0 (clear) at Wk16; 78.2% and 59.3% achieved nail pitting=0 at Wk48. 69 BKZ-treated and 56 SEC-treated patients had both baseline mNAPSI >10 and baseline nail plate crumbling >0; 65.2% and 69.6% achieved nail plate crumbling=0 (clear) at Wk16; 85.5% and 75.0% achieved nail plate crumbling=0 at Wk48. 59 BKZ-treated and 58 SEC-treated patients had both baseline mNAPSI >10 and baseline leukonychia >0; 69.5% and 70.7% achieved leukonychia=0 (clear) at Wk16; 79.7% and 69.0% achieved leukonychia=0 at Wk48.

Conclusion: From Wks16–48, BKZ-treated patients showed numerically greater improvements in nail psoriasis than SEC-treated patients, including complete nail clearance.

Funding: This study was funded by UCB Pharma. Medical writing provided by Costello Medical and funded by UCB Pharma.

References: 1. Augustin M et al. Br J Dermatol 2019;181(2):358–65; **2.** Reich K et al. N Engl J Med 2021;385(2):142–52, NCT03536884. Abstract previously submitted to AAD 2023.

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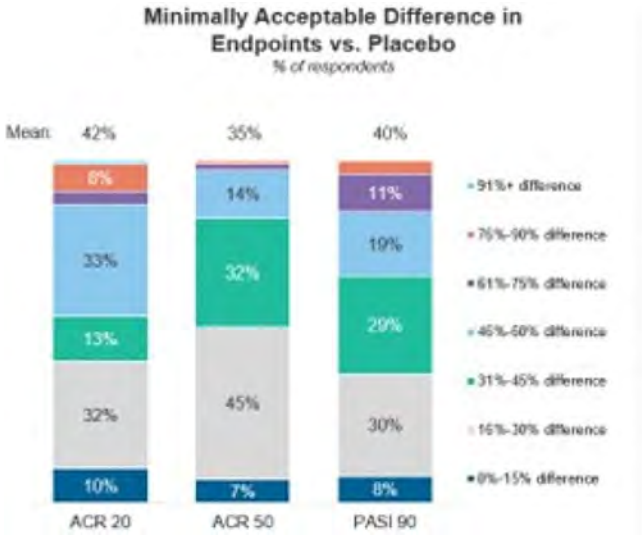
Abstract Number: 2256

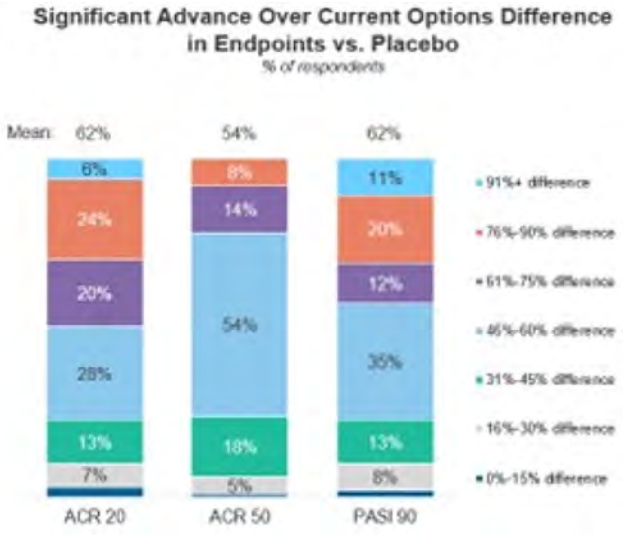
The Impact of Clinical Trial Metrics in Psoriatic Arthritis

Maxine Yarnall and **Kara Murray**, Spherix Global Insights, Exton, PA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment: SpA Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM



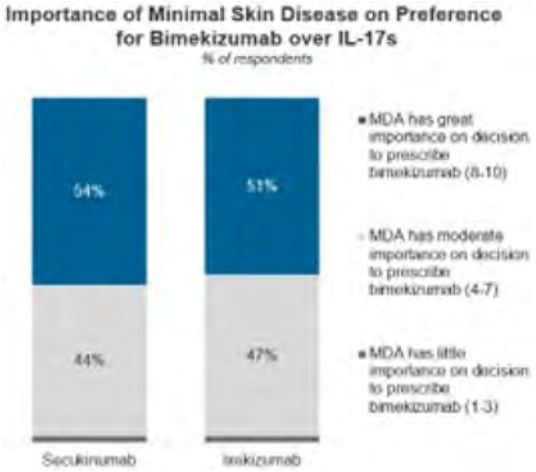


Background/Purpose: Rheumatologists have access to a plethora of advanced biologic and small molecule agents for the treatment of psoriatic arthritis (PsA). Prior to FDA approval, products undergo extensive clinical trial research vital in determining various outcome measures, such as a product's safety and efficacy. The knowledge gleaned from trial metrics empowers physicians to make informed treatment decisions for their patients. This research sought to understand brand performance, prescribing habits, and the influence of various clinical trial response criteria in treatment decisions.

Methods: An independent market analytics firm collaborated with US rheumatologists (n=101) to conduct analysis of the PsA market. Data were collected via an online survey fielded May 11 through May 23, 2023, including physician demographics, product usage, and attitudinal survey responses.

Results: Tumor necrosis factor (TNF) inhibitors continue to dominate the psoriatic arthritis market, capturing the majority of share in the first and second-line settings. Physicians reach for alternative mechanisms of action more frequently in second and later lines, led by Interleukin-17 (IL-17) inhibitors.

Two-fifths of surveyed rheumatologists indicate head-to-head studies comparing pipeline assets to adalimumab would be the most compelling as opposed to trials comparing any other pharmacologic treatment; preference for adalimumab as a comparator is unsurprising given physicians' experience, as well as the agent's long-term safety and efficacy data.



When reviewing placebo-controlled clinical trials, rheumatologists consider 42% ACR20, 35% ACR50, and 40% PASI90 responses as a minimally acceptable improvement. Although physicians do not indicate a strong preference towards one primary clinical trial endpoint, ACR50 responses and minimal disease activity (MDA) are most favorable. ACR70 responses are preferred as secondary endpoints.

With the upcoming launches of secukinumab IV and bimekizumab, physicians express the most interest in gaining access to an IV IL-17 inhibitor. Rheumatologists report having an IV formulation available will fill a number of unmet needs in PsA, most notably access for Medicare patients.

Bimekizumab's long-term data released from the BE OPTIMAL-3 study has an extremely positive impact on physician perceptions as well as their willingness to prescribe the IL-17A/F inhibitor. Half of those surveyed cite MDA as very influential in determining whether to prescribe bimekizumab over the currently available IL-17 inhibitors for the treatment of PsA.

Conclusion: Physicians express most interest in ACR50 and minimal disease activity as primary endpoints and prefer adalimumab as a comparator in head-to-head studies. The composition of clinical trials, from their primary endpoints to their outcome measurements, influence rheumatologists' prescribing habits in the PsA market.

Disclosure: M. Yarnall: None; **K. Murray**: None.

Abstract Number: 2257

Outcomes and Clinical Features of Acute Coronary Syndrome in Patients with SLE: A 14-Year Real-World Study (2006-2019)

Konstantinos Parperis[1] and Bikash Bhattarai[2], [1]University of Cyprus Medical School, Nicosia, Cyprus, [2]Valleywisehealth, Phoenix, AZ

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is an autoimmune inflammatory disease associated with an increased risk of cardiovascular complications, including acute coronary syndrome (ACS). However, there is limited real-world data available to comprehensively analyze the outcomes of ACS in patients with SLE over an extended period. This study aimed to compare the characteristics and outcomes of hospitalized patients with ACS, stratified by the presence or absence of SLE. The primary outcome was to examine the inpatient mortality, hospital length of stay, total hospital charges.

Methods: A retrospective observational analysis was conducted utilizing data from the US National Inpatient Sample (NIS) spanning the period from 2006 to 2019. Patients admitted with a diagnosis of ACS were categorized into two groups: those with International Classification of Diseases, Ninth and Tenth Revision (ICD-9 and -10) codes defining SLE and those without any SLE code. Demographics, clinical characteristics, and comorbidities were recorded. Furthermore, outcomes such as in-hospital mortality, complications, length of stay, and total hospital charges were analyzed and compared between the two groups. Associations between SLE and specific morbidity were assessed using chi-square tests, while t-tests were employed for continuous variables.

Results: A total of 17,322,365 (adjusted for sampling weight) ACS hospitalizations were identified in the NIS database, of which 70,901 (0.41%) were in patients with SLE (Table 1). Patients with SLE were more likely to be younger (mean age 61 vs 68 years; p < 0.0001), under 50 (21% vs 9%), female (82% vs 41%), and African American (25% vs 11%) compared to non-SLE patients. In addition, SLE patients were more statistically significant to have Medicaid (12% vs 7; p< 000.1) and live in the Southern region of the USA (43% vs 40%, p< 0.0001). Regarding comorbidities, SLE patients with ACS exhibited a higher prevalence of certain conditions, including antiphospholipid syndrome, chronic renal disease, ESRD and a history of thromboembolism (Table 1). Conversely, non-SLE patients with ACS had higher rates of comorbidities such as diabetes, hypertension, and dyslipidemia. Significant differences were observed in outcomes and resource utilization (Table 2). ACS in SLE patients was associated with longer length of stay (mean 6.2 vs 5.5 days; p< 0.0001) and higher cost (mean total charges $80,444 vs $74,321; p < 0.0001). No difference in the in-patient mortality was observed among the 2 groups.

Table 1: Demographics and comorbidities of SLE and non-SLE patients admitted with acute coronary syndrome from 2006 to 2019.

Variable	Non-SLE N=17,251,463	SLE N=70,901	P-value*
Age at hospitalization mean ± SD year	68.34±31.11	61.16±32.32	<.0001
Age less than 50	1678707 (9.73)	15187.8 (21.42)	<.0001
Gender			<.0001
Female	7151007 (41.46)	58246.2 (82.16)	
Race			<.0001
African American	1697337 (11.11)	16072.9 (25.05)	
Hispanic	1153951 (7.56)	5682.2 (8.86)	
Asian or Pacific Islander	367471 (2.41)	1246.66 (1.94)	
Native American	92235.9 (0.6)	320.587 (0.5)	
Other	467774 (3.06)	1702.24 (2.65)	
Primary payer			<.0001
Medicaid	1257105 (7.3)	8707.19 (12.29)	
Region			<.0001
South	6917065 (40.1)	30958.8 (43.66)	
Comorbidities, (%)			
Antiphospholipid syndrome	40351 (0.23)	2917.36 (4.11)	<.0001
Diabetes	6263973 (36.31)	18626 (26.27)	<.0001
Obesity (BMI >30)	1692857 (12.72)	6903.93 (12.97)	0.0947
Dyslipidemia	8685102 (50.34)	28017.1 (39.52)	<.0001
Hypertension	8218280 (47.64)	29308.7 (41.34)	<.0001
Chronic renal disease	3758878 (21.79)	20804.2 (29.34)	<.0001
ESRD, Maintenance dialysis	348289 (2.02)	3565 (5.03)	<.0001
History of venous thromboembolism	315022 (1.83)	3396.19 (4.79)	<.0001

*Chi-square P

Table 2. Outcomes and resource utilization of SLE and non-SLE patients admitted with acute coronary syndrome from 2006 to 2019.

Outcomes/Resource utilization			
	Non-SLE patients	SLE patients	P-value†
Length of stay, (mean ± SD)	5.51±15.74	6.29±16.74	<0.0001†
Total hospital charges, (mean ± SD)	$ 74321–228757	80444–237676	<0.0001†
Death during hospitalization(%)	1,196,400 (6.94)	4958(7)	0.5527

†t-test

Conclusion: Patients with SLE and ACS were younger, more likely to be female and African American. In addition, hospitalization of SLE patients with ACS is associated with longer hospital stay, and higher total cost compared to non-SLE. Further research is needed to optimize the prevention and management of ACS in the SLE population.

Disclosure: K. Parperis: None; **B. Bhattarai**: None.

Abstract Number: 2258

Brain Activity Patterns and Behavioural Performance in SLE Patients During a Spatial Working Memory and Sustained Attention Task

Michelle Barraclough[1], Shane McKie[2], Alex Kafkas[2], Ben Parker[3], Juan Pablo Diaz Martinez[4], Andrea Knight[5], Kathleen Bingham[1], Jiandong Su[1], Mahta Kakvan[6], Carolina Munoz-Grajales[7], Carmela Tartaglia[8], Lesley Ruttan[9], Joan Wither[1], Dennisse Bonilla[1], Daniela Montaldi[2], Rebecca Elliott[2], Patti Katz[10], Dorcas Beaton[11], Robin Green[9], Ian Bruce[2] and Zahi Touma[12], [1]University Health Network, Toronto, ON, Canada, [2]University of Manchester, Manchester, United Kingdom, [3]Manchester University Hospitals NHS Foundation Trust, Manchester, United Kingdom, [4]Schroeder Arthritis Institute, University Health Network, Toronto, ON, Canada, [5]The Hospital for Sick Children, Toronto, ON, Canada, [6]University Health Network, University of Toronto, Toronto, ON, Canada, [7]UHN/TWH, Toronto, ON, Canada, [8]Krembil Brain Institute, University Health Network, University of Toronto, Toronto, ON, Canada, [9]University Health Network, Toronto Rehabilitation Institute, Toronto, ON, Canada, [10]University of California San Francisco, San Rafael, CA, [11]Institute for Work & Health, Toronto, ON, Canada, [12]University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Cognitive impairment (CI) is a significant problem in SLE but there is a disconnect between objective and subjective CI. This makes it difficult to fully understand and treat CI. Functional magnetic resonance imaging (fMRI) has shown compensatory brain mechanisms may help to maintain cognitive function but potentially cause fatigue leading to subjective CI. This in part could explain the objective/subjective CI disconnect but ways to measure this are needed. We devised a new fMRI paradigm examining attention, working memory, learning and long-term associative memory. The aim was to assess this new task by examining whether attentional performance and working memory decreases over repeated trials in an SLE cohort using our preliminary data.

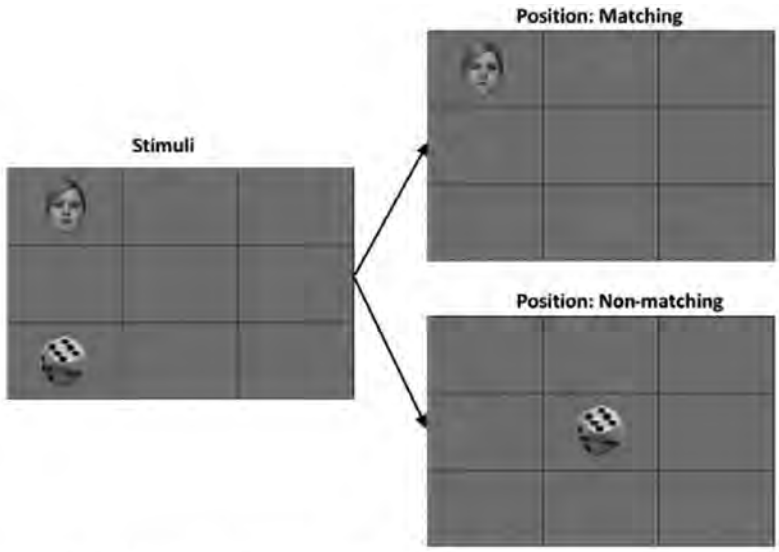


Figure 1: Stage 1 - Spatial working memory/sustained attention task
Participants saw a 3x3 matrix in which a face and an object were presented concurrently, but each in a single square. A series of face-object pairs were presented in this way in an adapted n-back design. In each trial, after a 1-sec delay participants were asked to respond if either a face or an object was presented in the same position as in the original array. In some trials the same face/object was presented in the original location (matching) or in a different one (non-matching). This provided a measure of **working memory** with a spatial emphasis. There were 3 blocks of 45 stimuli. There was a rest after the first block and fixations points within the trials. Altogether there were 135 stimuli.

Methods: Recruited adult SLE patients met EULAR/ACR criteria. Demographic, clinical and psychiatric data and patient reported outcome measures were collected. Cognitive function was assessed using a modified version of the ACR Neuropsychological Battery. MR scans included two structural scans and two functional MRI scans done during stage 1 and 2 of a cognitive task. Stage 1 (working memory and attention, Figure 1) was split into three trial blocks of equal length and performance over the trials was examined using mean number correct (maximum of 45 per trial), mean response time per trial (ms) and fMRI blood-oxygen-level-dependent (BOLD) response signal to stage 1 of the task. Differences between the trial performances were examined using repeated measures ANOVA and the fMRI data was modelled using SPM12. fMRI interference was done at a cluster extent correction threshold of family-wise error-corrected (pFWEc)< 0.05.

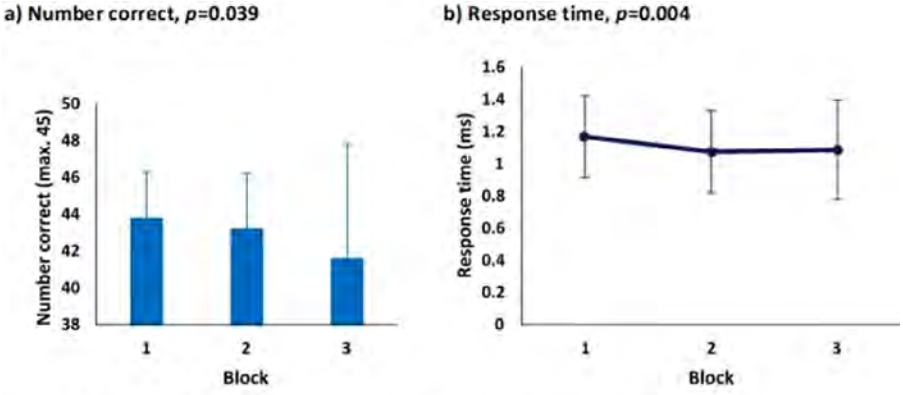


Figure 2. Stage 1 task performance across the three trial blocks, n=36

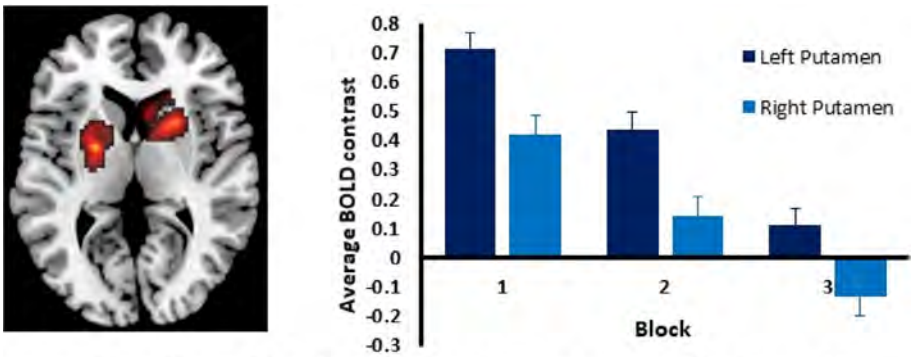


Figure 3. Significant BOLD signal response change over time for the working memory and attention task within a cluster containing the left and right putamen, n=10.

Results: Participants characteristics (n=36) were as follows; mean age 40 ±13, SLE disease duration 15 years ±10, SLEDAI-2K 4.3 ±4.8 and SDI 1 ±1.8. The majority were female (n=27, 75%), Caucasian (n=23, 63%) and educated to college level or higher (n=28, 78%). Current medication use was as follows; immunosuppressants (n=23, 64%), antimalarials (n=29, 81%), glucocorticoids (n=15, 42%) and biologics (n=6, 17%). Mean scores on the Beck Depression Inventory-II and Beck Anxiety Inventory were 14 ±12 and 33 ±11 respectively. CI was seen in 9 (35%). Participant performance on the working memory task worsened over time; response time was slowest during the first trial and quickest during the second (Figure 2). A significant cluster (900 voxels; pFWEc=0.006) containing the left and right putamen was found for the task BOLD response change over time. Within this cluster the BOLD response decreased from trial 1 to trial 3 (Figure 3).

Conclusion: Our new cognitive task is working as expected, with participants' performance worsening over time as participants become less engaged/cognitively fatigued. These results were mirrored by the fMRI results. Response time improved from trial one to two/three as the task was learnt. Final results will include data from healthy controls enabling us to determine if the decrease in performance is similar to healthy controls or if SLE patients become cognitively fatigued more quickly. We will also, examine the results from stage 2, the learning and long-term associative memory task.

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Abstract Number: 2259

The Effects of Systematic Lupus Erythematosus Related Cognitive Impairments on Activities of Daily Living and Life Role Participation: A Qualitative Framework Study

Michelle Barraclough[1], Aaron Howe[2], Ana Soberanis[2], Mahta Kakvan[3], Vijay Chattu[2], Ali Bani-Fatemi[2], Lisa Engel[4], Michelle Vitti[5], Emily Nalder[2], Yael Groverover[6], Monique Gignac[7], Dennisse Bonilla[1], Wils Nielsen[8], Nicole Anderson[9], Carmela Tartaglia[10], Behdin Nowrouzi-Kia[2] and Zahi Touma[2], [1]University Health Network, Toronto, ON, Canada, [2]University of Toronto, Toronto, ON, Canada, [3]University Health Network, University of Toronto, Toronto, ON, Canada,

[4]University of Manitoba, Institute for Work & Health, Winnipeg, MB, Canada, [5]Michelle Vitti Psychotherapy and Counselling, Toronto, ON, Canada, [6]NYU Steinhardt, New York, NY, [7]Institute for Work & Health, Toronto, ON, Canada, [8]University of Toronto, Markham, ON, Canada, [9]Schroeder Arthritis Institute, Krembil Research Institute, University Health Network and University of Toronto, Toronto, ON, Canada, [10]Krembil Brain Institute, University Health Network, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Cognitive impairment (CI) in systemic lupus erythematosus (SLE) negatively impacts health-related quality of life leading to activity limitations. This qualitative study aimed to (1) explore the effect of SLE-related CI on activities of daily living and life role participation; and (2) describe factors influencing activity restriction and life role participation.

Methods: Semi-structured, in-depth interviews probing living with CI in SLE were conducted with 24 adults living with SLE. Sociodemographic and clinical data, objective cognitive function (ACR-NB), and subjective cognitive function (PDQ-20) were collected. Participants were categorized into four groups of CI to perform a qualitative thematic analysis guided by a framework analytical approach. The groupings were defined as objective and subjective CI (Group 1), objective CI (Group 2), subjective CI (Group 3), and no CI (Group 4). Themes emerged using both inductive and deductive methods of data analysis.

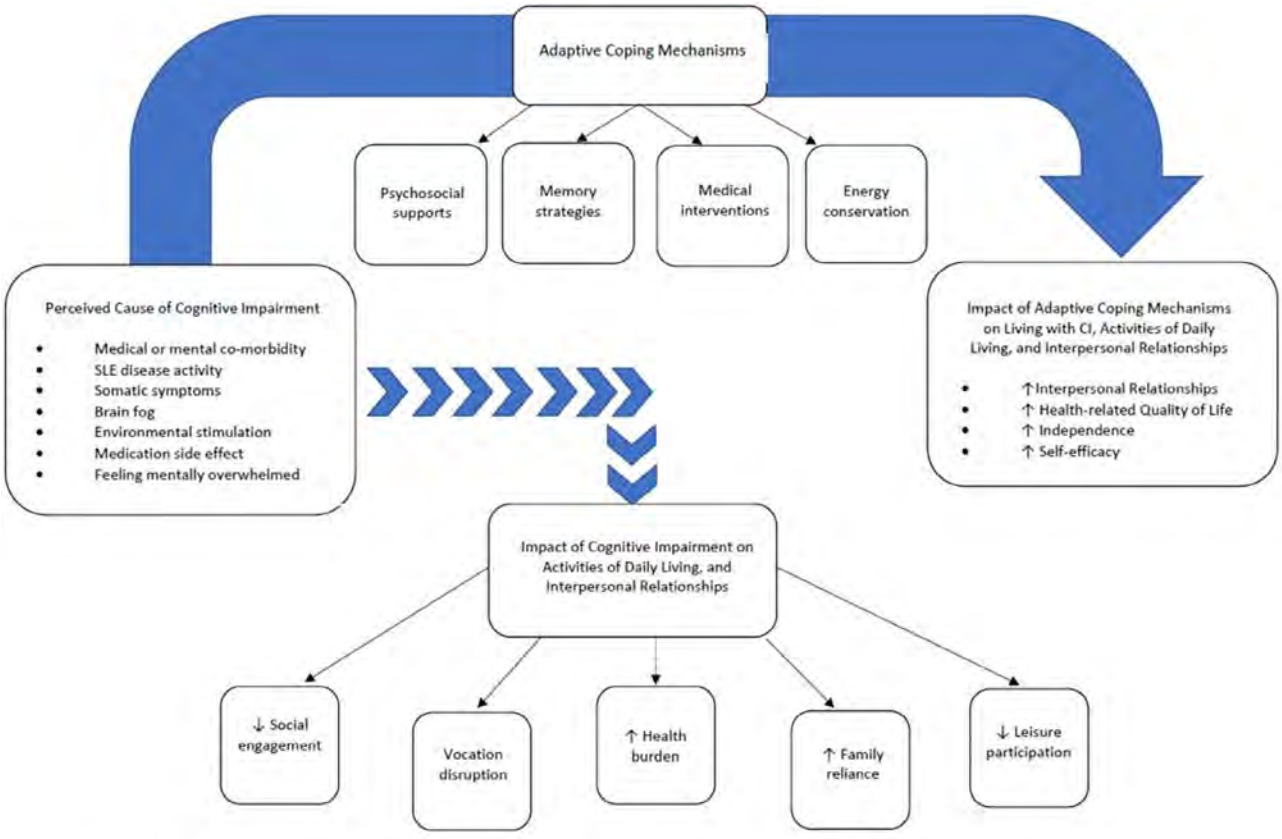

Figure 1. Relationship between SLE-related CI, activities of daily living, and life role participation.

Results: All participants met ACR classification criteria for SLE with a mean age of 42 ±13 years, SLE disease duration 13 ±10 years, SLEDAI (disease activity index) of 2.2 ±2.5, SDI (disease damage index) of 1.0±1.3, and prednisone daily dose of 3.4 mg/d ±6.0. Group sample sizes consisted of 11 participants in group 1, five in group 2, six in group 3, and 2 in group 4. Participants reported ongoing problems in multiple cognitive domains (memory, language, etc.) with multiple perceived causes. CI was felt to impact work, social, domestic and family life, health, and independence. Five overarching themes were represented in the data: (1) characterization of SLE-reported CI; (2) perceived cause of CI; (3) perceived impact of CI on activities of daily living and life role participation (4) adaptations for managing CI; (5) influence of CI adaptations on activities of daily living and life role participation. Figure 1 summarises the five identified themes and how they interact.

There were few between-group descriptive differences in the themes that emerged from the thematic and framework analyses. However, those within a subjective CI group (either group 1 or 3) characterized the involvement of mental health difficulties in perpetuating or exacerbating their self-reported experience of CI. Those within a subjective CI group also employed more frequent and diverse adaptations to manage their mental health difficulty, which had a secondary effect on their experience of CI.

Conclusion: This study provides a better understanding of the patient experience of CI in SLE, how it impacts their lives, and what coping strategies they employ. It highlights the long-term challenges those with CI in SLE undergo and provides evidence for the urgent need to implement multidisciplinary treatment options. The lack of descriptive differences between the study's CI groupings suggests that regardless of the "type" of CI defined, subjective or objective, the impact and challenges experienced by the patients remain the same.

When managing CI, it may be beneficial to evaluate and understand available psychosocial support resources to help identify and reinforce relevant adaptations to improve health-related quality of life.

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Abstract Number: 2260

Right Insular Cortex-Thalamic Functional Connectivity as a Potential Marker for Fatigue in Systemic Lupus Erythematosus and Primary Sjögren's Syndrome

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

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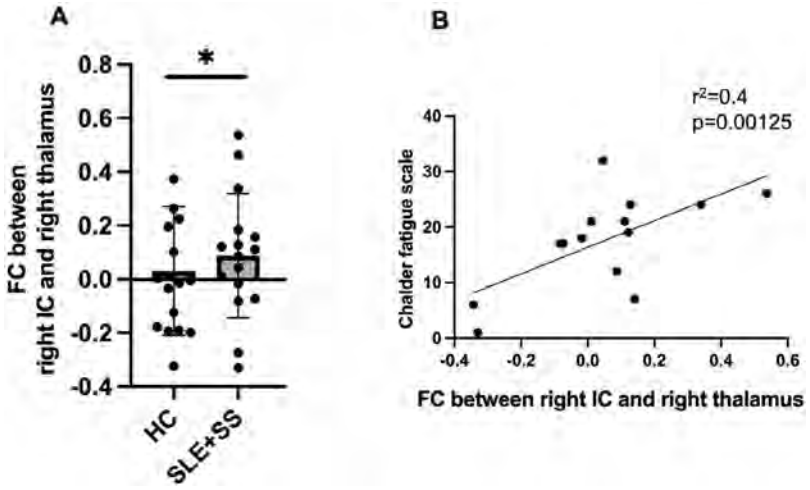

The specific functional connectivity (FC) between the right insular cortex (IC) and right thalamus in patients with systemic lupus erythematosus (SLE) and primary sjögren's syndrome (pSS). (A) FC value between right IC and right thalamus in healthy controls (HCs) and SLE/pSS. *p<0.05, ANCOVA, adjusted for age and sex. (B) Correlation analysis between the FC and Chalder fatigue scale in SLE/pSS.

Background/Purpose: Fatigue is a common symptom in patients with systemic lupus erythematosus (SLE) and primary Sjögren's syndrome (pSS). Resting-state functional magnetic resonance imaging (rs-fMRI) has emerged as a powerful tool for mapping large-scale networks in the human brain. Several studies have investigated the functional connectivity (FC) between brain regions of interests (ROIs) of fatigue using rs-fMRI. However, the evidence concerning patients with SLE and pSS remains unclear.The objective of this study is to identify the specific FC of fatigue in patients with SLE and pSS.

Methods: rs-fMRI data were acquired from SLE, pSS, and healthy controls. Demographic, clinical, and laboratory data were extracted from patients' electronic medical records. Disease activity was assessed by SLE Disease Activity Index score with the Safety of Estrogens in SLE National Assessment modification (SELENA-SLEDAI), and EULAR Sjögren's syndrome disease activity index (ESSDAI). In addition, the Chalder fatigue scale (CFS) and fatigue assessment questionnaire were collected. FCs were analyzed and compared among SLE, pSS, and HCs by ANCOVA, adjusted for age and sex. The association among SELENA-SLEDAI, ESSDAI, questionnaire scores, and FCs was evaluated by correlation analysis.

Results: A total of 9 SLE patients (90% female; median age: 44 years, IQR: 33-61), 5 SS patients (100% female; median age: 48 years, IQR: 44-49) and 16 HCs (63% female; median age: 41 years, IQR: 34-46) were enrolled. The median SELENA-SLEDAI was 4 (IQR: 0-10) and the median prednisolone dose was 4 mg/day (IQR: 0-10), the median ESSDAI was 3 (IQR: 2-4). In SLE and pSS patients with fatigue, higher FC was observed between the right insular cortex (IC) and right thalamus compared to HCs (p=0.049). There was a significant correlation between FC of the right IC and right thalamus and CFS, a fatigue evaluation index, in patients with SLE/pSS (r^2=0.4, p=0.0125). CFS did not correlate with SELENA-SLEDAI and ESSDAI either.

Conclusion: We identified a specific FC between right IC and right thalamus which may be associated with fatigue in SLE and pSS patients.

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Abstract Number: 2261

Burden of Flare and Organ Damage in Systemic Lupus Erythematosus (SLE) in the Asia Pacific Region: A Multicenter Cohort Study

Rangi Kandane-Rathnayake[1], Dominique Milea[2], Worawit Louthrenoo[3], Alberta Hoi[4], Vera Golder[1], Jiacai Cho[5], Aisha Lateef[5], Shue-Fen Luo[6], Yeong-Jian J Wu[7], Laniyati Hamijoyo[8], Sargunan Sockalingam[9], Zhanguo Li[10], Sandra Navarra[11], Leonid Zamora[11], Masayoshi Harigai[12], Yasuhiro Katsumata[12], Madelynn Chan[13], Yanjie Hao[14], Zhuoli Zhang[15], Sean O'Neill[16], Fiona Goldblatt[17], Shereen Oon[18], Xiaomeng Xu[2], Aldo Amador Navarro Rojas[19], Sang-Cheol Bae[20], Chak Sing Lau[21], Mandana Nikpour[22] and **Eric Morand**[23], [1]Monash University, Department of Medicine, Sub-faculty of Clinical and Molecular Medicine, Clayton, Australia, [2]GlaxoSmithKline, Value Evidence and Outcomes, Singapore, Singapore, [3]Chiang Mai University Hospital, Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai, Thailand, [4]Monash University, Department of Medicine, Sub-faculty of Clinical and Molecular Medicine, Melbourne, Australia, [5]National University Hospital, Rheumatology Division, Department of Medicine, Singapore, Singapore, [6]Chang Gung University, Department of Rheumatology, Allergy and Immunology, Chang Gung Memorial Hospital, Taoyuan, Taiwan, [7]Chang Gung University, Department of Rheumatology, Allergy and Immunology, Chang Gung Memorial Hospital, Keelung, Taiwan, [8]Padjadjaran University/Hasan Sadikin General Hospital, Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Bandung, Indonesia, [9]University of Malaya, Department of Medicine, Faculty of Medicine Building, Kuala Lumpur, Malaysia, [10]Peking University Health Science Center, Department of Rheumatology and Immunology, People's Hospital, Beijing, China, [11]University of Santo Tomas Hospital, Joint and Bone Center, Manila, Philippines, [12]Tokyo Women's Medical University, Division of Rheumatology, Department of Internal Medicine, Tokyo, Japan, [13]Tan Tock Seng Hospital, Department of Rheumatology, Allergy & Immunology, Singapore, Singapore, [14]St Vincent's Hospital Melbourne, Department of Rheumatology, Melbourne, Australia, [15]Peking University First Hospital, Rheumatology and Immunology Department, Beijing, China, [16]Department of Medicine, University of New South Wales, Kensington, Australia, [17]Royal Adelaide Hospital and Flinders Medical Centre, Adelaide, Australia, [18]University of Melbourne at St Vincent's Hospital, Departments of Rheumatology and Medicine, Fitzroy, Australia, [19]GlaxoSmithKline, Medical Affairs, Singapore, Singapore, [20]Hanyang University Hospital for Rheumatic Diseases and Hanyang University Institute for Rheumatology Research, Department of Rheumatology, Seoul, South Korea, [21]University of Hong Kong, Division of Rheumatology & Clinical Immunology, Department of Medicine, Queen Mary Hospital, Hong Kong, Hong Kong, [22]The University of Melbourne at St. Vincent's Hospital Melbourne, Departments of Medicine and Rheumatology, Melbourne, Australia, [23]Monash University, Centre for Inflammatory Diseases, Melbourne, Australia

SESSION INFORMATION

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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Up to 50% of patients with SLE develop irreversible organ damage within 10 years of diagnosis, and most experience recurrent disease flares of varying severity. Both the prevalence and severity of SLE are known to be higher in patients living in the Asia Pacific region, but few data on flare and damage rates are available. We examined the prevalence of organ damage and flare and estimated the magnitude of longitudinal associations between flares and subsequent organ damage accrual using real-world data from the Asia Pacific region.

Methods: Adult patients with SLE enrolled in a multinational cohort with a minimum of 3 years of observational data, captured prospectively between 2013 and 2020, were studied. Flares were assessed at each clinic visit using the Safety of Estrogens in Lupus National Assessment-SLE Disease Activity Index (SELENA-SLEDAI). Flare Index and organ damage was assessed annually using SLICC/ACR Damage Index (SDI). Organ damage was defined as present if the SDI was greater than zero (SDI >0) while damage accrual was defined if the change in SDI was greater than zero (ΔSDI >0). Multivariable, multifailure survival analyses were carried out to quantify the association between flares and organ damage accrual.

Table. Longitudinal associations between flares and organ damage accrual (ΔSDI>0) at tn. *HRs adjusted patients age at tn-1, disease duration at tn-1, gross domestic product of patients' country, cumulative prednisolone dose at tn-1, immunosuppressant use at tn-1, time-adjusted SLEDAI score at tn-1, and for the presence of existing organ damage at tn-1.

	HR*	(95% CI)	p value
Flares at t_{n-1}			
Any (mild/moderate [M/M] or severe) flare present	1.42	(1.17, 1.72)	<0.001
Cumulative number of any flares	1.07	(1.02, 1.13)	0.011
M/M flare present	1.41	(1.14, 1.75)	0.001
Cumulative number of M/M flares	1.08	(1.01, 1.14)	0.015
Severe flare present	1.52	(1.14, 2.03)	0.004
Cumulative number of severe flares	1.05	(0.98, 1.13)	0.13

Results: Overall, 1556 patients with SLE, recruited from Australia, China, Indonesia, Japan, Korea, Malaysia, Philippines, Singapore, Taiwan and Thailand, and followed for a median (interquartile range) of 5.7 (3.9, 7.0) years were studied. The prevalence of organ damage at study enrollment (baseline) was 39% (n=614/1556) and the incidence of damage accrual during observation was ~58 per 1000 patient-years (PY) (n=496/8569.86 PY). 40% (n=247/614) of patients with baseline organ damage and 26% (n=249/942) of patients without baseline organ damage accrued damage during the study period. 74% (n=1153) of patients experienced a flare of any severity (mild/moderate or severe) at least once during the study period; 57% (n=885) experienced recurrent (≥2) flares. Flares independently increased the risk of damage accrual; after controlling for confounders, the risk of organ damage accrual at subsequent visits in patients who experienced any flare was 42% greater than in patients without flares (adjusted hazard ratio [HR] [95% confidence interval, CI]: 1.42 [1.17, 1.72]; **Table**). The risk of damage accrual was greater if patients had severe flares (HR [95% CI]: 1.52 [1.14, 2.03]). For each additional flare, the risk of damage accrual increased by 7% (HR [95% CI]: 1.07 [1.02, 1.13]).

Conclusion: The burden of organ damage and flares in SLE is substantial, and flares quantifiably increase the risk of damage accrual. Prevention of flares should be a major goal of SLE disease management to minimize permanent organ damage.

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Abstract Number: 2262

Identifying Important Domains for Inclusion in a Novel Treatment Response Measure for Systemic Lupus Erythematosus (TRM-SLE): Results of a Modified Delphi Study

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SESSION INFORMATION

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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The Treatment Response Measure for Systemic Lupus Erythematosus (TRM-SLE) is a novel clinical outcome assessment (COA) for SLE randomized controlled trials (RCTs), being developed by an international clinician-industry-patient taskforce. Current COA development guidelines require that outcome measures used in RCTs should capture treatment effects relevant to how patients "feel, function or survive" to support regulatory approval (1). The aim of this study was to identify domains to be considered for inclusion in TRM-SLE from the perspective of expert SLE clinicians and patients based on this paradigm.

Methods: Candidate domains were identified via surveying a multinational panel of clinicians, patients and industry representatives. Domains were then rated in a modified Delphi study (two online survey rounds separated by a discussion meeting) in which clinicians with SLE expertise and patient advisory panellists were invited to rate the "importance" of candidate domains on a 1-9 scale (where 1 = not important and 9 = critically important). Importance was defined as domain activity having an impact on how a patient "feels, functions or survives", when assessing response to treatment in an SLE RCT. A literature review summarising associations of each candidate domain with key SLE symptoms, functional impact, damage and mortality was provided to participants to support participant ratings. The consensus threshold was prespecified as a rating of at least 7 by 70% of participants in both clinician and patient groups.

Table 1: Results of clinician and patient ratings of candidate domain importance, defined as domain activity impact on how a patient "feels, functions or survives" when assessing response to treatment in an SLE RCT.

Table 1: Results of clinician and patient ratings of candidate domain importance, defined as domain activity impact on how a patient "feels, functions or survives" when assessing response to treatment in an SLE RCT.

		% Rated Highly Important (7-9)	
Consensus on importance	**Candidate Domain**	**Clinician Group**	**Patient Group**
Consensus (≥70% participants scoring ≥7) in both clinician and patient groups	Lupus nephritis	99%	100%
	Neuropsychiatric lupus	98%	92%
	Rash	96%	73%
	Haemolytic anaemia	93%	82%
	Arthritis	90%	85%
	Thrombocytopenia	88%	91%
	Ophthalmic lupus	88%	82%
	Myositis	86%	91%
	Vasculitis	83%	75%
	Fatigue	76%	100%
	Serositis	77%	75%
	Brain fog	73%	100%
	Antiphospholipid syndrome	74%	91%
	Pulmonary lupus	71%	92%
Consensus (≥70% participants scoring ≥7) achieved in patient group only	Constitutional symptoms	69%	82%
	Mucosal ulcers	66%	82%
	Alopecia	64%	73%
	Gastrointestinal lupus	64%	73%
	Depression/anxiety	47%	82%
	Osteoporosis	35%	82%
	Fibromyalgia	35%	91%
	Hypertension	24%	82%
	Raynaud's/poor circulation	24%	82%
	Sjogren's syndrome/dryness	18%	91%
	Overlap autoimmune disease	8%	80%
Consensus not achieved in either group	Complement	27%	36%
	Anti-dsDNA antibodies	47%	0%
	Leukopenia	54%	36%
	Anaemia of chronic disease	15%	20%
	Lymphadenopathy	27%	0%
	Erythrocyte sedimentation rate	41%	36%
	Anti-Smith antibodies	7%	38%
	Costochondritis	1%	10%
	Serum iron	0%	0%

Results: The domain generation survey yielded 64 nominations, grouped into a core list of 34 candidate domains. Of 118 invitees to the modified Delphi study, 87 clinicians with a median (interquartile range; IQR) of 21 (11, 30) years' experience and 13 patients/representatives with a median (IQR) disease duration of 19 (16,33) years participated, with representation from six continents. Of the 34 candidate domains, 6 met the consensus threshold after Round 1 of voting, increasing to 14 after Round 2 (Table 1). An additional 11 domains met consensus in the patient group only. Notably, some domains meeting consensus on importance (e.g. fatigue) are not measured in current primary SLE trial endpoints, while others (e.g. anti-dsDNA, complement) included in current response measures did not reach consensus for inclusion.

Conclusion: When rated for importance, consensus was reached in both SLE clinician and patient groups on multiple candidate domains for inclusion in a novel COA for SLE trials. Discrepancies between clinician and patient perspectives were also identified. Important domains will next be rated on other characteristics relevant to inclusion in a COA (appropriateness, representation and measurability), with selected domains to proceed to definition of response measurement.

References:

1. FDA Patient Focused Drug Development Guidance: Selecting, Developing or Modifying Fit-for-Purpose Clinical Outcome Assessments. https://www.fda.gov/media/159500/download

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Abstract Number: 2263

Disease Activity Progression in Systemic Lupus Erythematosus: An Analysis of the SLE Prospective Observational Cohort Study (SPOCS)

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The international, multicenter SLE Prospective Observational Cohort Study (SPOCS) collected data on patients with SLE in relation to their type 1 interferon gene signature (IFNGS) status. Here, we report SLE disease activity progression over time—overall and by IFNGS category.

Table 1

Table 1. Disease activity (SLEDAI-2K total score) by baseline IFNGS status[a]

Timepoint	Overall (N = 826)	High IFNGS (N = 531)	Low IFNGS (N = 219)	*P*-value[b]
Baseline, mean (SD)	n = 591 9.8 (4.6)	n = 397 9.8 (4.3)	n = 137 9.2 (5.2)	
Score <10, n (%)	344 (58.2)	227 (57.2)	91 (66.4)	0.057
Score ≥10, n (%)	247 (41.8)	170 (42.8)	46 (33.6)	
6 months, mean (SD)	n = 440 6.4 (5.8)	n = 301 6.7 (5.9)	n = 104 5.5 (5.3)	
Score <10, n (%)	348 (79.1)	236 (78.4)	86 (82.7)	0.351
Score ≥10, n (%)	92 (20.9)	65 (21.6)	18 (17.3)	
12 months, mean (SD)	n = 333 5.7 (5.1)	n = 210 5.8 (5.1)	n = 89 5.6 (5.3)	
Score <10, n (%)	275 (82.6)	176 (83.8)	72 (80.9)	0.541
Score ≥10, n (%)	58 (17.4)	34 (16.2)	17 (19.1)	
18 months, mean (SD)	n = 313 6.0 (6.3)	n = 216 5.7 (4.9)	n = 64 6.1 (5.6)	
Score <10, n (%)	261 (83.4)	182 (84.3)	53 (82.8)	0.782
Score ≥10, n (%)	52 (16.6)	34 (15.7)	11 (17.2)	
24 months, mean (SD)	n = 266 5.4 (6.5)	n = 174 6.1 (7.5)	n = 72 4.0 (4.1)	
Score <10, n (%)	229 (86.1)	149 (85.6)	64 (88.9)	0.495
Score ≥10, n (%)	37 (13.9)	25 (14.4)	8 (11.1)	
30 months, mean (SD)	n = 278 5.2 (4.8)	n = 185 5.4 (4.8)	n = 65 4.7 (5.3)	
Score <10, n (%)	240 (86.3)	158 (85.4)	58 (89.2)	0.439
Score ≥10, n (%)	38 (13.7)	27 (14.6)	7 (10.8)	
36 months, mean (SD)	n = 245 5.7 (7.7)	n = 168 5.9 (8.4)	n = 58 5.4 (6.5)	
Score <10, n (%)	205 (83.7)	142 (84.5)	47 (81.0)	0.536
Score ≥10, n (%)	40 (16.3)	26 (15.5)	11 (19.0)	

[a]The IFNGS status was missing for 76 patients.

[b]Comparison of the total score by category (<10 or ≥10) between low and high baseline type 1 IFNGS categories using the chi-square test.

Methods: Eligible patients (aged ≥18 years) had physician-confirmed SLE (ACR or SLICC classification), ≥1 lifetime positive serology of ANA or dsDNA, a ≥6-month treatment duration with systemic SLE treatment beyond non-steroidal anti-inflammatory drugs and analgesics, and moderate-to-severe activity at enrollment. Disease activity was assessed by the modified Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), as well as by instances of flares, the Lupus Low Disease Activity State (LLDAS), and remission according to the 2021 Definition of Remission In Systemic Lupus Erythematosus (DORIS). IFNGS tests were conducted in a central laboratory; each sample was compared to pre-established cutoffs and given a qualitative diagnostic score, denoting low or high IFNGS. Comparisons between low and high IFNGS categories were performed with the chi-square test.

Results: A total of 826 patients were enrolled; 70.8% (n = 531) and 29.2% (n = 219) of patients had high and low baseline IFNGS, respectively, and the IFNGS status was missing for 76 patients. At baseline, the mean (standard deviation [SD]) SLEDAI-2K was 9.8 (4.6; n = 591); 58.2% (n = 344) of patients had a score of < 10. The mean (SD) SLEDAI-2K total scores at baseline were slightly lower in patients with a low IFNGS (9.2 [5.2]) compared with those with a high IFNGS (9.8 [4.3]; **Table 1**). Furthermore, a greater percentage of patients with a low IFNGS had SLEDAI-2K total scores of < 10 compared

Table 2

Table 2. Disease activity by incidence of flares, LLDAS, and remission status by baseline IFNGS status[a,b]

Timepoint	Overall (N = 826)	High IFNGS (N = 531)	Low IFNGS (N = 219)	*P*-value
Baseline, n (%)	n = 826	n = 531	n = 219	
≥1 flare within the last 6 months	421 (51.0)	277 (52.2)	107 (48.9)	
6 months, n (%)	n = 663	n = 427	n = 177	
≥1 flare since prior visit	120 (18.1)	81 (19.0)	29 (16.4)	
LLDAS	n = 435	n = 298	n = 104	
	31 (7.1)	20 (6.7)	7 (6.7)	0.995[c]
Remission	n = 544	n = 347	n = 148	
	13 (2.4)	6 (1.7)	6 (4.1)	0.197[d]
12 months, n (%)	n = 542	n = 327	n = 161	
≥1 flare since prior visit	100 (18.5)	62 (19.0)	26 (16.1)	
LLDAS	n = 326	n = 206	n = 89	
	25 (7.7)	16 (7.8)	5 (5.6)	0.510[c]
Remission	n = 431	n = 255	n = 132	
	13 (3.0)	10 (3.9)	2 (1.5)	0.234[d]
18 months, n (%)	n = 480	n = 319	n = 120	
≥1 flare since prior visit	78 (16.3)	55 (17.2)	16 (13.3)	
LLDAS	n = 299	n = 209	n = 60	
	14 (4.7)	8 (3.8)	4 (6.7)	0.475[d]
Remission	n = 362	n = 246	0	
	11 (3.0)	11 (4.5)	0	0.073[d]
24 months, n (%)	n = 428	n = 276	n = 113	
≥1 flare since prior visit	60 (14.0)	36 (13.0)	15 (13.3)	
LLDAS	n = 256	n = 168	n = 69	
	19 (7.4)	12 (7.1)	5 (7.2)	1.000[d]
Remission	n = 318	n = 204	n = 83	
	19 (6.0)	14 (6.9)	2 (2.4)	0.165[d]
30 months, n (%)	n = 443	n = 276	n = 123	
≥1 flare since prior visit	61 (13.8)	37 (13.4)	16 (13.0)	
LLDAS	n = 265	n = 175	n = 63	
	15 (5.7)	10 (5.7)	4 (6.3)	1.000[d]
Remission	n = 311	n = 199	n = 81	
	16 (5.1)	14 (7.0)	2 (2.5)	0.165[d]
36 months, n (%)	n = 409	n = 257	n = 114	
≥1 flare since prior visit	60 (14.7)	34 (13.2)	21 (18.4)	
LLDAS	n = 233	n = 158	n = 56	
	23 (9.9)	18 (11.4)	5 (8.9)	0.609[c]
Remission	n = 284	n = 181	0	
	15 (5.3)	15 (8.3)	0	0.007[d]

[a]Remission status is according to the 2021 Definition of Remission In Systemic Lupus Erythematosus (DORIS).

[b]The IFNGS status was missing for 76 patients.

[c]Comparison between low and high baseline IFNGS using the chi-square test.

[d]Comparison between low and high baseline IFNGS using Fisher's exact test.

to those with a high IFNGS (66.4% [n = 91] vs 57.2% [n = 227], respectively). At baseline, 51.0% (n = 421) of patients reported having had ≥1 flare within the last 6 months; these were reported in similar percentages of patients with high and low IFNGS (52.2% [n = 277] vs 48.9% [n = 107], respectively; **Table 2**). Across the first 6 months, the percentage of patients reporting ≥1 flare since baseline was 18.1% (n = 120; high IFNGS, 19.0% [n = 81]; low IFNGS, 16.4% [n = 29]). At 6 months, the same percentage of patients with low IFNGS and high IFNGS achieved LLDAS (6.7% [n = 7] and 6.7% [n = 20], respectively), but a numerically higher percentage of patients with low IFNGS versus high IFNGS achieved remission (4.1% [n = 6] vs 1.7% [n = 6], respectively). The mean SLEDAI-2K total scores and percentages of patients reporting new flares changed little after 6 months, regardless of the baseline IFNGS status. Less than 10% of patients achieved LLDAS and less than 10% achieved remission during the entire 36 months of follow-up.

Conclusion: Although flare rates observed prospectively were lower than those reported by patients at enrollment, patients continued to have flares over the course of 36 months. There was no significant improvement in disease activity, and there were low rates of LLDAS and remission. Altogether, these indicate an unmet need for improved treatment outcomes.

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Abstract Number: 2264

Proposal for Defining Moderate and Severe Activity States in Systemic Lupus Erythematosus. Impact on Flares and Other Outcomes

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: In systemic lupus erythematosus (SLE), there is no definition of states of moderate and severe SLE activity. How these states may influence different disease outcomes is unknown.

To propose a definition for states of moderate and severe activity in SLE and using the largest Spanish national cohort of SLE patients, to describe the prevalence of both states of activity and to analyze the impact of this classification on flare-ups, achieving low disease activity state (LLDAS), hospital admissions, health-related quality of life (HRQoL), damage accrual and mortality.

Table 1. Criteria and proposals for the definition of states of moderate and severe activity in SLE.

Table 1. Criteria and proposals for the definition of states of moderate and severe activity in SLE.

Criteria \ Definition	**SLE Moderate activity status (at each visit):** meets at least 2 of the 3 following criteria: Definition Criteria	**SLE Severe activity status (at each visit):** meets at least 2 of the 4 following criteria:
SELENA-SLEDAI (*Safety Of Estrogens In Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index*) **cSLEDAI: clinical SLEDAI,** i.e., not considering hypocomplementaemia nor the positivity of anti-dsDNA antibodies	4 < SLEDAIc ≤ 8	SLEDAIc > 8
PGA (*Physician Global Assessment*) on a 0-3 scale	1 < PGA ≤ 2	PGA >2
Glucocorticoid dose	• 7.5mg/day < prednisone < 30mg/day, or • Methylprednisolone pulses ≤125mg/day	• Prednisone ≥ 30mg/day, or • Methylprednisolone pulses >125 mg/day
Severe Non-SLEDAI manifestations: • Haemolytic anemia, autoimmune with Hb <10 g/L, • Microangiopathic haemolytic anemia and thrombotic microangiopathy (PTT), • Pure red cell aplasia, • Alveolar hemorrhage, • Lupus pneumonitis with hypoxemia, • Pulmonary hypertension, • Shrinking lung syndrome, • Gastrointestinal (vasculitis, protein-losing enteropathy), • Myocarditis, • Libman-Sacks endocarditis with valve dysfunction, • Transverse myelitis.		≥ 1 severe manifestation of non-SLEDAI SLE

Table 2. Mean number of flares (total, severe and mild-moderate) over the follow-up period (4 years) according to the activity status.

Table 2. Mean number of flares (total, severe and mild-moderate) over the follow-up period (4 years) according to the activity status.

	Moderate activity ≥ 1 time	Moderate (or severe) activity never	p	Severe activity ≥ 1 time	Severe activity never	p
Mean number (±SD) of **total flares** (V1-V5: 4 years)	3,2 (±2,5)	1,3 (±2,0)	**<0,001**	2,6 (±3,0)	1,3 (±2,0)	**<0,001**
Mean number (±SD) of **mild-moderate flares** (V1-V5: 4 years)	2,4 (±2,4)	1,0 (±1,8)	**<0,001**	1,4 (±2,3)	1,1 (±1,9)	**0,442**
Mean number (±SD) of **severe flares** (V1-V5: 4 years)	0,7 (±1,0)	0,2 (±0,6)	**<0,001**	1,2 (±1,4)	0,2 (±0,5)	**<0,001**

Methods: We propose definitions for states of moderate and severe activity in SLE (Table 1). To analyze the impact of this classification, available data from the prospective phaseof the Spanish Society of Rheumatology SLE Registry (RELESSER-PROS) were used, with 5 annual visits (V1-V5) over 4 years. Patients were required to have at least 3 consecutive visits. At each visit, the number of flares and their severity (according to the SELENA Flare Index), visits in LLDAS, hospital admissions, HRQoL according to the Lupus Impact Tracker (LIT), damage accrual (using the SLICC/ACR Damage Index [SDI]) and mortality was collected. T-test was used for group comparisons.

Results: A total of 1463 patients (90% women) were included, with a mean age (±SD) of 56 (±13.5) years. The mean disease duration of SLE (±SD) at V1 was 14 (±8.5) years. Patients had a mean (±SD) of 4.2 (±1.2) visits and a mean (±SD) follow-up of 2.5 (±0.7) years. Moderate activity was shown by 54 patients (3.7%) at V1, 20 patients (1.4%) at V2, 27 patients (1.8%) at V3, 5 patients (0.3%) at V4, and 11 patients (0.8%) at V5. On the other hand, 40 patients (2.7%) at V1, 15 patients (1.0%)

Table 3. Comparative results in LLDAS status, admissions, HRQoL, damage accrual and mortality over the follow-up period (4 years) in patients who have ever been in a situation of moderate or severe activity compared to those who have not.

Table 3. Comparative results in LLDAS status, admissions, HRQoL, damage accrual and mortality over the follow-up period (4 years) in patients who have ever been in a situation of moderate or severe activity compared to those who have not.

	Moderate activity ≥ 1 time	Moderate (or severe) activity never	p	Severe activity ≥ 1 time	Severe activity never	p
LLDAS status[a]	2,5 (±1,1)	3,7 (±1,3)	**<0,001**	2,3 (±1,3)	3,6 (±1,3)	**<0,001**
Admissions	2,4 (±3,5)	0,85 (±1,7)	**<0,001**	3,2 (±3,8)	0,86 (±1,7)	**<0,001**
Quality of life (Mean LIT[b])	40 (±21,1)	28,9 (±20,3)	**<0,001**	41,3 (±20,8)	29,1 (±20,4)	**<0,001**
Quality of life (Highest LIT[b])	54,5 (±24,6)	39,1 (±24,0)	**<0,001**	54,0 (±24,3)	39,5 (±24,1)	**<0,001**
Cumulative damage[c] (V5-V1)	0.88 (±1.19)	0.42 (±0.88)	**<0,001**	1.18 (±1.82)	0.42 (±0.83)	**<0,001**
Mortality[d]	0,029 3/105 (2,86%)	0,029 40/1358 (2,95%)	**0,959**	0,06 4/67 (5,97%)	0,028 39/1396 (2,79%)	**0,285**

Mean values ± SD.

[a] Number of visits in LLDAS.
[b] Higher LIT score means a greater deterioration in quality of life.
[c] SDI in V5 minus SDI in V1.
[d] Annual (at each visit) mortality rate. Number of deceased patients (%).

at V2, 13 patients (0.9%) at V3, 6 patients (0.4%) at V4 and 3 patients (0.2%) at V5 showed severe activity. Patients who presented both moderate and severe activity in at least 1 of the 5 visits had a significantly higher mean total number of flares over the 4-year follow-up period (V1-V5)than those who did not ($p< 0.001$). These same results occur in the case of severe flares. Regarding mild-moderate flares, patients with moderate and severe activity in at least 1 visit, had a higher mean number than patients without these activities, being statistically significant for moderate activity. More detailed information about flares can be seen in Table 2. On the other hand, patients who presented both moderate and severe activity in at least 1 of the 5 visits had significantly less number of visits in LLDAS, higher number of hospital admissions, worse HRQoL and greater damage accrual in the period V1-V5 than those who did not ($p< 0.001$ for all comparisons). Patients with severe activity in ≥1 visit had higher mortality (p=n.s.) (Table 3).

Conclusion: Patients who were in a state of moderate and/or severe activity at least on 1 occasion had worse outcomes at the end of follow-up in terms of number/severity of flares, hospital admissions, deterioration in HRQoL and damage accrual. These results emphasize the importance of setting achievable objectives in the Treat to Target (T2T) strategy for the treatment of SLE.

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Abstract Number: 2265

Lupus Damage Index Revision - Item Generation and Reduction Phase

Burak Kundakci[1], Megan Barber[2], Ann Clarke[2], Sindhu Johnson[3], Ian Bruce[4] and On behalf of the revised SLE organ damage index (SDI) collaborators[4], [1]Centre for Epidemiology Versus Arthritis, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, United Kingdom, [2]University of Calgary, Division of Rheumatology, Cumming School of Medicine, Calgary, AB, Canada, [3]Division of Rheumatology, Department of Medicine, Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western and Mount Sinai Hospitals; Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada, [4]University of Manchester, Manchester, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The SDI is a robust instrument, but is limited by incomplete items, restricted applicability in paediatric patients, and outdated item definitions1. The SLICC, ACR and LFA have embarked on a data- and expert/patient-driven project to develop a revised SDI. Our objective was to report the item generation and reduction phases of a five-phase process for developing a revised SDI.

Methods: Item generation and reduction involved a thorough literature review, a three-round Delphi exercise, and a subsequent revision by a 14-member steering committee. A group of lupus experts conducted a literature review to identify items that reflect the construct of damage in SLE and grouped the items into organ domains. A large international group of expert lupus clinicians was established by snow-ball sampling amongst SLICC members. Patient and caregiver partners were nominated through the LFA, Lupus UK, Lupus Europe, and Lupus Canada.

Participants generated and rated candidate items based on their appropriateness for inclusion in a revised SDI using a Delphi exercise. The 14-member steering committee then reviewed the items for further refinement.

Results: We assembled a diverse group of 146 individuals (mean age 50.6, ranging from 28 to 79 years; 60.3% females; 58.9% white; clinical experience ranging from 1 to 51 years) from 35 countries, representing the lupus research and patient community extensively. There were 135 medical doctors, 2 allied health professionals and 9 patients.

Item generation resulted in a total of 220 items across 14 organ systems. The literature review identified 4 unique items (1.8%), while 103 unique items (46.8%) were derived from the Delphi exercise alone, and 113 items (51.4%) appeared in both exercises. In the second round of the Delphi exercise, participants suggested an additional 6 unique items. Overall, 226 items were subjected to re-rating for appropriateness for inclusion in the revised SDI. Completion rates for the first, second, and third Delphi rounds were 97.9%, 95.0%, and 91.7%, respectively. Thirty-six items received a median score of 4 out of 9 and these were removed. All original 1996 SDI items were retained with median appropriateness scores of 7, 8, and 9, except for upper gastrointestinal tract surgery (median appropriateness score 5) and osteomyelitis (median appropriateness score 5). The steering committee further eliminated 126 items due to redundancy, limited availability or feasibility for assessment, overlap, lack of reflection of damage construct or association with lupus disease activity, and rarity. Figure 1 shows the number of candidate items identified at different stages during revised SDI development.

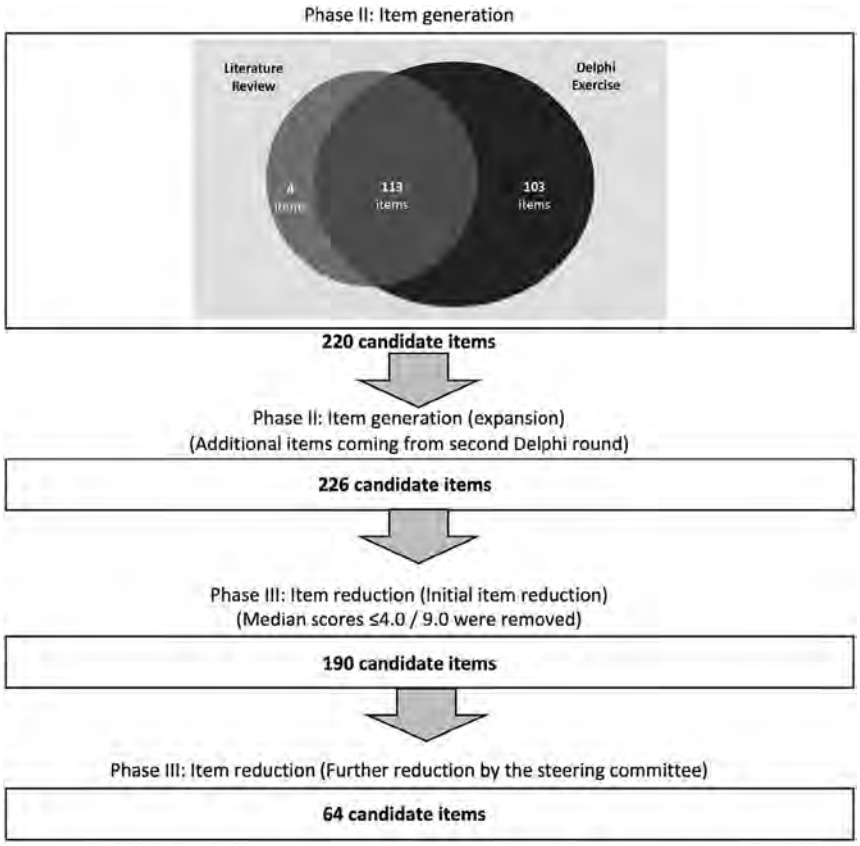

Figure 1. Number of candidate items identified at different stages of Phase II/III during revised SDI development

Conclusion: Using a combined data-driven and expert/patient-based approach, items and domains that comprise damage in SLE have been expanded. The item generation and reduction phase resulted in 64 candidate items for consideration. All original SDI items were retained in this step. Further steps are now underway to agree upon definitions for those items, including extent and duration of item presence, based on the best current evidence and internationally accepted norms.

1) Barber M, et al. Evolving concepts in SLE damage assessment. Nat Rev Rheumatol. 2021;17(6):307-8

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Abstract Number: 2266

Direct Health Care Costs Differ by SLE Autoantibody Machine Learning Clusters in an International Inception

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SESSION INFORMATION

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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Using machine learning, we identified 4 patient clusters based on longitudinal autoantibody profiles in an international SLE inception cohort, which were predictive of disease outcomes (*Ann Rheum Dis 2023*). We now compare direct and indirect costs between these SLE clusters to elucidate healthcare utilization patterns in SLE.

Table 1. Enrolment demographics and clinical characteristics of SLE Autoantibody Clusters in an international inception cohort (only statistically significant differences shown for clinical characteristics, indicated by bolded values[1])

	Cluster 1 N=137[2]	Cluster 2 N=376[3]	Cluster 3 N=80[4]	Cluster4 N=212[5]	FDR[1]
% Female	89.8 (30.4)	89.4 (30.9)	81.2 (39.3)	89.6 (30.6)	0.588
Mean Age of Diagnosis (SD), yrs	31.5 (10.8)	36.5 (13.9)	32.5 (13.9)	34.4 (14.1)	**0.014**
% Ethnicity					
White	32.1	61.7	68.8	42.5	**<0.001**
Asian	30.7	20.5	13.8	31.1	**0.014**
African	27.0	9.6	6.2	14.6	**<0.001**
Hispanic	5.1	4.8	10.0	8.5	0.571
Other	5.1	3.5	1.3	3.3	0.954
% Country					
North America	48.6	51.8	54.9	45.5	0.859
Europe	27.0	32.8	29.6	29.4	1.000
Asia	24.3	15.4	15.5	25.1	0.114
Mean BMI (SD), kg/m^2	24.3 (4.9)	25.6 (6.1)	26.1 (5.8)	24.1 (4.8)	**0.029**
% Smoker					
Former smoker	19.0	24.5	26.3	15.6	0.232
Current smoker	11.7	14.4	21.2	9.0	0.206
% Alcohol Abuse	0.7	1.3	2.5	1.4	1.000
% Post-Secondary Education	68.4	65.5	64.6	62.8	1.000
% Nephritis	56.2	32.1	50.9	46.9	**0.001**
Mean SLEDAI-2K Score (SD)					
Total Score	3.2 (3.2)	2.3 (2.9)	3.0 (2.1)	3.5 (3.4)	**0.020**
Adjusted Mean Score	4.2 (2.7)	2.6 (2.2)	3.5 (1.7)	3.9 (2.2)	**<0.001**
Immunological Subscale	1.64 (1.60)	0.90 (1.31)	1.96 (1.33)	2.01 (1.61)	**<0.001**
Mean SLICC Damage Index (SD)					
Seizures	0.01 (0.10)	0.02 (0.16)	0.11 (0.31)	0.01 (0.8)	**0.004**
Skin Domain	0.25 (0.53)	0.08 (0.29)	0.07 (0.32)	0.07 (0.28)	**0.002**
% Immunosuppressives/ Biologics, Ever	83.8	63.8	68.4	73.8	**0.014**
% Immunosuppressives/ Biologics, Current	72.3	45.5	47.4	53.8	**0.001**
% Mortality[6]	4.7	3.2	7.9	3.7	0.71

1. Comparison between cluster groups using one-way ANOVA test (null hypothesis that there is no difference between the means of the groups) and a Benjamini-Hochberg correction with false discovery rate (FDR) alpha = 0.05
2. Cluster 1 was characterized by high frequency of anti-Smith, anti-U1RNP
3. Cluster 2 was characterized by low anti-double stranded DNA (dsDNA) and ANA titres
4. Cluster 3 was characterized by high frequency of all five antiphospholipid antibodies
5. Cluster 4 had multiple autoantibody reactivity including to anti-histone, anti-dsDNA, anti-ribosomal P, anti-Sjögren syndrome antigen A or Ro60, anti-Sjögren syndrome antigen B or La, anti-Ro52/Tripartite Motif Protein 21, anti-proliferating cell nuclear antigen and anti-centromere B.
6. Cluster 1 n=106, cluster 2 n=250, cluster 3 n=63, cluster 4 n=163. Patients with less than 10-years of follow up who are still alive were excluded. Hazards of survival, adjusted for age at disease onset in a multivariable Cox regression demonstrates that patients in clusters 1 (adjusted HR 2.60 (95% CI 1.12 to 6.05), p=0.03) and 3 (adjusted HR 2.87 (95% CI 1.22 to 6.74), p=0.02) had lower survival compared with patients in cluster 2.

Methods: Patients fulfilling the 1997 Revised ACR SLE Classification Criteria from 33 centres (11 countries) were enrolled within 15 months of diagnosis and clustered by k-means using longitudinal 29 ANA immunofluorescence pattern and 20 autoantibody profiles. Data were collected annually on health care use (i.e., hospitalizations, medications, dialysis, and selected procedures, as well as SLE antibodies, organ involvement, activity [adjusted mean SLEDAI-2K] and medication use), supplemented by data on additional resource use and lost work-force/non-work-force productivity in a patient subset. Multiple imputation was used to predict all missing values for the patients in the full cohort who did not provide direct/indirect costs for all observations. Health care use was costed using 2023 Canadian prices and lost productivity using Statistics Canada age-and-sex specific wages. Average annual costs over follow up were compared between clusters using multivariable regressions, adjusting for significant predictors for direct and indirect costs.

Results: Of 1800+ patients enrolled in the SLICC cohort, 805 subjects were included in the SLE clusters and provided cost data (**Table 1**). Mean follow-up time for the entire cohort was 12.3 years (range 2.9-21.6 years) and similar across clusters. There were no clear differences in direct and indirect costs and component costs between clusters 1 (high frequency of anti-Sm/anti-U1RNP, predictive of high cumulative disease activity and immunosuppressant/biologic use), 2 (low autoantibody reactivity, predictive of low disease activity and immunosuppressant/biologic use), and 4 (multiple autoantibody reactivities, predictive of high disease activity). Thus, these 3 clusters were combined and compared with cluster 3 (highest frequency of all antiphospholipid antibodies [IgM/IgG anti-cardiolipin, -ß2GP1, -PS/PT, IgG anti-ß2GP1D1, lupus anticoagulant], predictive of seizures and mortality) using multivariable regressions. Cluster 3 had higher total direct costs than clusters 1, 2, and 4 combined ($9288 vs $7061; adj. diff. $2852 [95%CI $196, $5510]), particularly for hospitalizations ($2134 vs $1320; adj. diff. $1158 [95%CI $455, $1860]) (**Table 2**). Cluster 3 had significantly more hospitalizations for thrombotic/cardiovascular (CVD) events compared to combined clusters (2-sample test of proportions, 22.7% vs. 4.1%, diff. 18.6% [95%CI 6.0%, 31.3%]) (**Fig1**).

Table 2. Average annual complete direct and indirect health care costs (2023 Canadian Dollars)[1], n=805, comparing Cluster 3 and Combined Clusters 1, 2, and 4

	Cluster 3 N=80	Combined Clusters 1, 2, and 4 N=725	Difference (95% CI)[2]	Adjusted Difference (95% CI)[3]
Direct Costs				
Total	9288 (7338, 11238)	7061 (6572, 7551)	**2226 (219, 4233)**	**2852 (196, 5510)**
Hospital Visits[4]	2134 (1466, 2802)	1320 (1173, 1467)	**814 (131, 1497)**	**1158 (455, 1860)**
Medications	2803 (1232, 4373)	2270 (1899, 2640)	533 (-1079, 2144)	659 (-1039, 2356)
Dialysis	1265 (574, 1956)	610 (452, 767)	656 (-52, 1363)	591 (-876, 2056)
Other[5]	3086 (2575, 3597)	2862 (2643, 3081)	224 (-291, 738)	368 (-323, 1059)
Indirect Costs				
Total	30872 (24728, 37016)	30186 (25826, 34546)	686 (-6146, 7517)	-199 (-4817, 4420)

Bolded values indicate statistically significant result, p<0.05.

1. Potential predictors for imputing complete direct and indirect costs included age at diagnosis, sex, race and ethnicity, education, geographic location (i.e., residing inside vs outside North America [includes Canada, the US, and Mexico]), and the time-varying covariates: disease duration, smoking, high-risk alcohol use, and partial direct costs. Partial direct costs and geographic location remained in all models as final covariates, with the direct cost model also including age at diagnosis and education, and the indirect cost model also including disease duration. Ten sets of imputations were derived from these models, and all subsequent analyses involved pooling and averaging all estimates across imputed sets; variances were computed by applying standard combination rules.
2. The difference between Cluster 3 and others. These are the unadjusted analysis.
3. Potential predictors for adjusting cost differences included all potential predictors for the imputation models (see footnote 1) with the exception of partial costs. Direct cost differences were adjusted for disease duration and race/ethnicity, and for panel structure (multiple observations per patient); indirect cost differences were adjusted for disease duration and geographic location (residing within vs outside of North America), and multiple observations per patient.
4. Only 18.5% of the n=805 cohort had reasons for hospitalization; 12.6% for cluster 1; 19.1% for cluster 2; 25.0% for cluster 3; 19.3% for cluster 4.
5. Other costs in the complete direct cost analysis included physicians, non-physician healthcare professionals, emergency room visits, laboratory tests, radiological and other diagnostic procedures, outpatient surgeries, and help obtaining medical care over the year preceding the assessment.

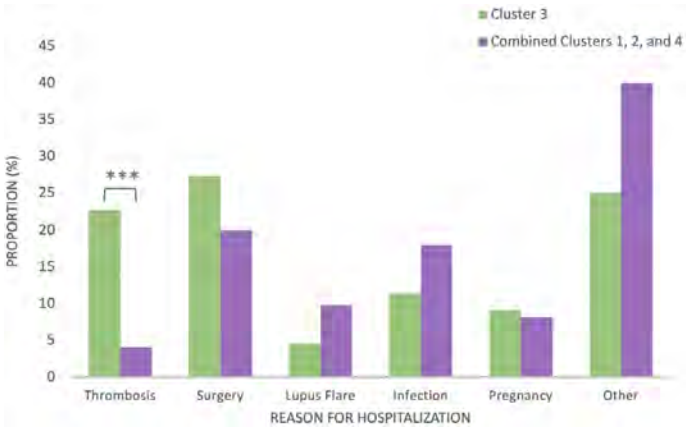

Figure 1. Reasons for Hospitalization Cluster 3 vs. Combined Clusters 1, 2, and 4. There was a higher proportion of hospitalizations for thrombotic events (e.g., myocardial infarction, stroke, pulmonary embolism) for Cluster 3 (*** $p<0.001$) compared to Combined Clusters 1, 2, and 4.

Conclusion: Machine learning based on autoantibodies alone identified a patient cluster with high antiphospholipid antibody frequency who incurred the greatest direct costs, a high proportion driven by hospitalizations due to thrombosis/CVD-related events. Even clusters with severe SLE did not incur such high cost, suggesting thrombotic and antiphospholipid-related complications are important contributors to the economic burden of SLE.

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C. Peschken: AstraZeneca, 2, 5, GSK, 2, 5, Roche, 1, 2; **D. Kamen**: None; **A. Askanase**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb, 2, Celgene, 2, Eli Lilly, 2, Genentech, 2, GSK, 2, Idorsia, 2, Janssen, 2, Mallinckrodt, 2, Pfizer, 2, UCB Pharma, 2; **J. Buyon**: Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, Related Sciences, 1; **A. Clarke**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, 5, Otsuka, 2, Roche, 2.

Abstract Number: 2267

Explainable Machine Learning to Predict Hospitalized Infection in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) have a 1.85-fold higher risk of all-cause mortality and a 2.74 fold higher risk of infection-related mortality compared with controls. In addition, infection is responsible for up to 45% of hospitalization and 65.8% of death. However, few studies had developed a prediction tool for hospitalized infection in patients with SLE using electronic medical records (EMR). Therefore, we aimed to develop predictive models for hospitalized infection in patients with SLE in a medical center in central Taiwan.

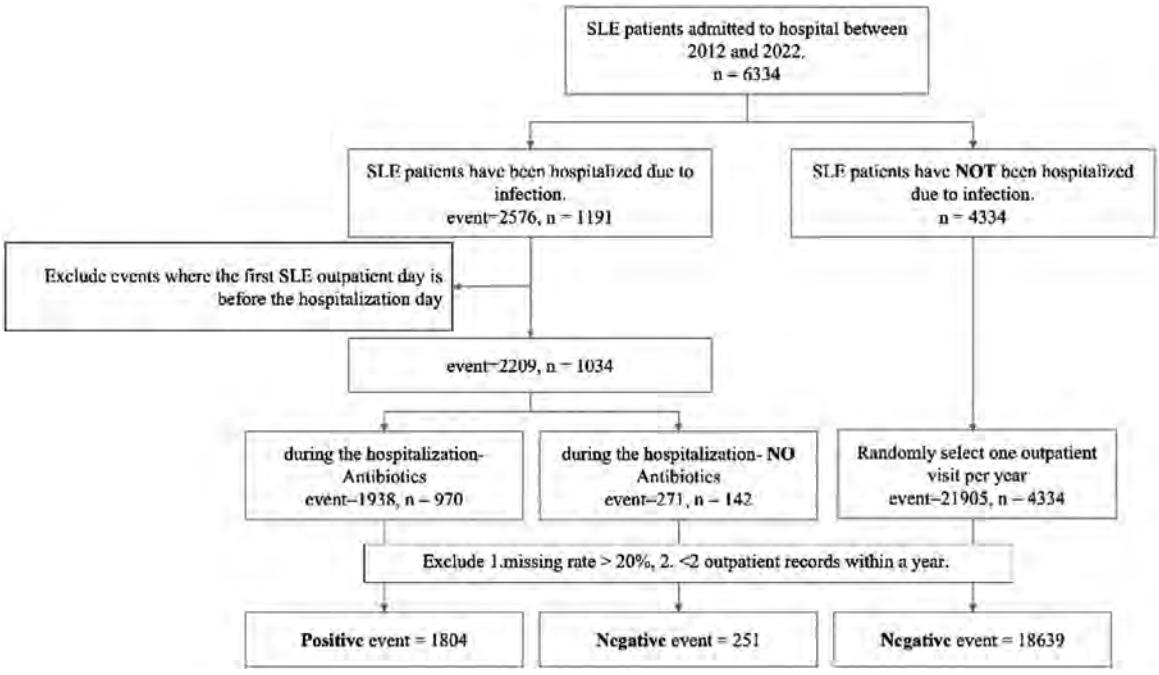

Fig 1. Flowchart of study subjects enrollment.

Methods: Using EMR data of patients with SLE from the Taichung Veterans General Hospital during the period of 2012–2022, we conducted five machine learning (ML) models, including extreme boosting (XGBoost), random forest (RF), logistic regression (LR), support vector machine (SVM) and K nearest neighbor (KNN). The ratio between training/testing was 80/20. We used the SHAP summary plot to illustrate the strength and the direction of associations between key features and 30-day risk of hospitalized infection. We performed the receiver operating characteristic (ROC) analysis, calibration curve and decision curve analysis to determine discrimination, accuracy and applicability of the predictive ML modes in the testing datasets.

Results: Figure 1 showed the flowchart of subject enrollment. A total of 5368 patients with SLE with at least two ambulatory visits were included. Table 1 summarizes characteristics of patients with and without hospitalized infection. We finally included 28 features of four domains (demographics, laboratory data within one year before the index date, comorbidities in prior one year, and cumulative dose of medications in prior 3 months [9 months for rituximab]) based on feature importance in the ML models (Fig 2A). Fig 2B showed cumulative relative feature importance of top 28 features categorized by main clinical domains in predicting 30-day hospitalized infection. As shown in Fig 2C, XGBoost showed the best performance among the five ML models with a sensitivity of 83.15%, a specificity of 94.09%, an accuracy of 93.11% and an area under curve (AUC) in ROC analysis of 95.9% in the testing datasets. Because laboratory data domain provides the largest portion of feature importance, after exclusion of 11 medication domain features, we re-conducted ML models using 15 laboratory data domain features and 2 demographic domain features and found the XGBoost model still revealed the best performance with an accuracy of 91.91% and an AUC in ROC of 93.94% (data not shown).

Conclusion: We developed explainable ML models to predict hospitalized prediction in patients with SLE using 10-year EMR data from a medical center in Taiwan.

Table 1. Characteristics of patients with SLE with and without hospitalized infection.

	All N = 20694	Non_Infection N = 18890	Infection N = 1804	p-value
Demographic data				
Age (years)	47.31±3.15	47.26±3.16	47.81±2.99	<0.001
Sex (male)	2242 (10.83%)	1941 (10.28%)	301 (16.69%)	<0.001
CCI categories				<0.001
CCI: 0	960 (4.64%)	933 (4.94%)	27 (1.5%)	
CCI: 1-2	16920 (81.76%)	15906 (84.2%)	1014 (56.21%)	
CCI>=3	2814 (13.6%)	2051 (10.86%)	763 (42.29%)	
Medication (mg)				
Rituximab (Mabthera)	12.02±157.82	8.19±119.76	52.10±365.86	<0.001
Belimumab (Benlysta)	5.90±368.44	5.86±384.46	6.30±97.37	0.9619
Abatacept (Orencia)	4.07±72.47	4.07±72.38	4.06±73.41	0.9946
MTX: Methotrexate	4.21±41.10	4.07±22.39	5.61±118.90	0.5843
LEF: Leflunomide	8.29±99.73	8.39±101.54	7.18±78.33	0.622
AZA: Azathioprin	931.18±1993.44	966.29±2024.06	563.55±1593.32	<0.001
HCQ: Hydroxychloroquine	11846.81±11741.33	11857.12±11763.14	11738.82±11513.05	0.6773
CSA: CICLOSPORIN	266.24±1386.99	255.09±1361.15	383.05±1629.09	0.0013
Corticosteroid	63.28±139.70	55.18±123.07	148.16±239.59	<0.001
Cyclophosphamide_01	350 (1.69%)	240 (1.27%)	110 (6.1%)	<0.001
MPA_01	2062 (9.96%)	1768 (9.36%)	294 (16.3%)	<0.001
Laboratory				
GPT_max (U/L)	36.24±59.73	33.72±53.05	62.51±103.31	<0.001
GPT_var (U/L)	461.88±10940.59	416.52±11349.82	923.07±5170.92	<0.001
CREAT_max (mg/dL)	1.21±1.77	1.05±1.30	2.87±3.87	<0.001
CREAT_var (mg/dL)	0.12±1.31	0.07±1.15	0.63±2.29	<0.001
WBC_max (/μL)	8109.79±3840.97	7770.20±3134.56	11667.49±7248.33	<0.001
WBC_var (/μL)	2223212.27±9722238.14	1791068.34±4611038.08	6660746.34±28733572.34	<0.001
PLT_min (*10^3/μL)	201.12±71.03	205.67±68.27	153.57±81.27	<0.001
PLT_var (*10^3/μL)	908.19±2219.35	772.20±1905.28	2296.40±4005.12	<0.001
C3_var (mg/dL)	78.97±140.10	72.15±118.40	155.08±275.57	<0.001
C3_latest (mg/dL)	94.62±25.60	94.93±24.95	91.10±31.78	<0.001
C4_var (mg/dL)	8.98±19.90	7.99±16.77	20.06±39.28	<0.001
C4_max (mg/dL)	24.32±10.94	24.05±10.62	27.39±13.66	<0.001
HGB_min (g/dL)	11.67±2.00	11.86±1.83	9.66±2.52	<0.001
HGB_var (g/dL)	0.45±0.83	0.39±0.77	1.02±1.18	<0.001
DSDNA_latest01	6643 (37.59%)	6092 (37.51%)	551 (38.61%)	0.4241

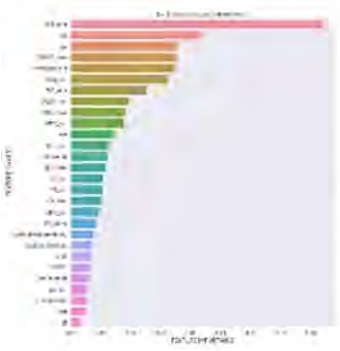

Fig 2A

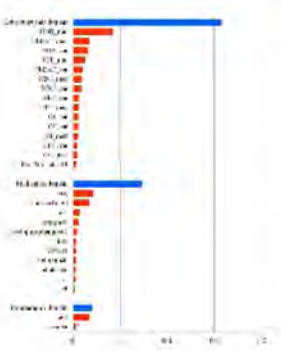

Fig 2B

	Classifier	Sens	Spec	Accuracy	AUROC
Validation	Xgboost	82.53% (3.31%)	94.50% (0.57%)	93.46% (0.48%)	95.87% (0.60%)
	RF	76.47% (3.23%)	84.39% (0.86%)	83.71% (0.55%)	88.14% (0.78%)
	LR	76.05% (2.79%)	84.55% (1.03%)	83.28% (0.71%)	84.30% (1.22%)
	SVM	71.80% (2.77%)	83.83% (1.04%)	82.78% (0.79%)	85.12% (0.90%)
	KNN	76.26% (2.93%)	98.66% (0.23%)	92.66% (0.45%)	76.45% (1.48%)
Testing	Xgboost	83.15%	94.09%	93.11%	95.90%
	RF	77.72%	84.46%	83.86%	87.71%
	LR	73.37%	84.83%	83.81%	83.13%
	SVM	75.00%	84.17%	83.35%	84.49%
	KNN	27.99%	98.57%	92.29%	77.27%

Fig 2C

Fig 2. XGBoost feature importance (2A), cumulative relative feature importance of top 28 features categorised by main clinical domains (2B) and performance of various machine learning models (2C).

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Abstract Number: 2268

Mental Illness and Outcomes of COVID-19 in Patients with Systemic Lupus Erythematosus: A Global Multicenter Cohort Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Poor COVID-19 outcomes in patients with systemic lupus erythematosus (SLE) has been found to be associated with glucocorticoid dose, male sex, older age, mycophenolate, rituximab, cyclophosphamide, moderate or high SLE disease activity, and comorbidities including kidney disease and cardiovascular disease/hypertension. However, the influence of mental illness on COVID-19 outcomes had not been addressed.TriNetX, a global federated health research network, has been used in several studies to investigate the outcomes and clinical features. Therefore, we aimed to assess the association of mental illness and COVID-19 outcomes in patients with SLE using electronic medical records (EMR) in the TriNetX Network. The aim of the study was to assess the association of short-term outcomes of COVID-19 with mental illness in patients with SLE.

Methods: The study identified SLE patients aged 20–89 years who got COVID-19 between January 1, 2020 and April 28, 2023 with and without a history of mental illness before COVID-19 infection. The diagnoses of SLE and mental illness (mental and behavioral disorders due to psychoactive substance use, mood [affective] disorders, or anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders) were based on International Classification of Diseases tenth revision (ICD-10), while the diagnosis of COVID-19 was based on ICD-10, Current Procedural Terminology (CPT) Codes, or Logical Observation Identifiers Names and Codes (LOINC). Propensity score was used to match COVID-19 infected SLE patients with and without a history of mental illness for potential confounders, we conducted Cox regression analyses to examine the association between mental illness and COVID-19 outcomes shown as hazard ratios (HRs) with 95% confidence intervals (CIs).

Results: We finally included 12,485 patients with SLE who had a history of mental illness and 12,485 matched SLE patients without a history of mental illness. The mean ± standard deviation (SD) age was 51.5 ± 15.8 years in the mental illness group and 51.6 ± 17.4 years in the non-mental illness group, respectively. The proportion of females was 89.2% in the mental illness group and 88.4% in the non-mental illness group. SLE patients with mental illness had a higher risk of hospitalization (HR, 1.26; 95% CI, 1.17–1.35), Intensive Care Unit (ICU) admission (HR, 1.47; 95% CI, 1.24–1.73), mechanical ventilation (HR, 1.50; 95% CI, 1.11–2.03), sepsis (HR, 1.24; 95% CI, 1.03–1.51) and cerebral vascular accident (CVA) (HR, 1.66; 95% CI, 1.41–1.96) than SLE patients without mental illness. However, the risk of mortality was lower in SLE patients with mental illness than in SLE patients without mental illness (HR, 0.73; 95% CI, 0.57–0.93).

Conclusion: This global multicenter matched cohort study showed that mental illness was associated with an increased risk of hospitalization, ICU admission, mechanical ventilation, sepsis and CVA, but a decreased risk of death within 30 days after the date of COVID-19 diagnosis in patients with SLE.

Disclosure: H. Chen: None.

Abstract Number: 2269

Evaluating Global Patterns in Treatment and Prevalence of Glucocorticoid Related Comorbidities in Systemic Lupus Erythematosus: An International Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

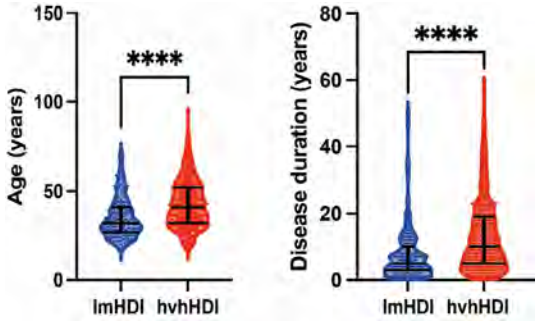

Figure 1. Patients from low/medium HDI (lmHDI) countries were significantly younger and had shorter disease duration than those from high/very high HDI (hvhHDI) countries (p<0.0001)

Background/Purpose: Regional disparities in the management of SLE are frequently described. Governance, funding, logistic barriers, and physician choice may be important determinants though data is scare from many underrepresented regions thus limiting our understanding and ability to appraise this. Steroids are a key contributor to damage and the use of steroid sparing medication has an important role in reducing these complications. In this study, we sought to evaluate global patterns in the treatment of SLE and identify the prevalence of steroid related comorbidities.

Table 1. Differences observed between patients from low/medium HDI (lmHDI) and high/very high HDI (hvhHDI) countries. Corticosteroid and anti-malarial treatment was more frequently used in the treatment of patients in low/medium HDI (lmHDI) countries, whilst biologic use was used more frequently in high/very high HDI (hvhHDI) countries.

Table 1	Low HDI (n=50)		Medium HDI (n=163)		High HDI (n=265)		Very High HDI (n=689)		All SLE Patients (n=1167)		p value (SLE lmHDI vs hvhHDI)
Immunosuppressants, n (%)	**36 (72)**		**104 (64)**		**169 (64)**		**339 (49)**		**648 (56)**		**0.0009*** **
Methotrexate, n (%)	5 (10)		27 (17)		35 (13)		91 (13)		158 (14)		ns
Mycophenolate Mofetil, n (%)	*9 (18)*		*45 (28)*		*70 (26)*		*127 (18)*		*251 (22)*		ns
Azathioprine, n (%)	*21 (42)*		*32 (20)*		*65 (25)*		*113 (16)*		*231 (20)*		***0.049****
Cyclophosphamide, n (%)	**0 (0)**		**3 (2)**		**2 (1)**		**9 (1)**		**14 (1)**		ns
Corticosteroids, n (%)	**37 (74)**		**119 (73)**		**159 (60)**		**404 (59)**		**719 (62)**		**0.0002*** **
No Steroids, n (%)	7 (14)		20 (12)		50 (19)		92 (13)		169 (15)		ns
<10 mg/day, n (%)	*17 (34)*		*58 (36)*		*89 (34)*		*184 (27)*		*348 (30)*		*0.057 (ns)*
10-20 mg/day, n (%)	*9 (18)*		*19 (12)*		*20 (8)*		*47 (7)*		*95 (8)*		***0.003****
>20 mg/day, n (%)	*3 (6)*		*7 (4)*		*10 (4)*		*16 (2)*		*36 (3)*		*ns*
Antimalarials, n (%)	**40 (80)**		**133 (82)**		**182 (69)**		**469 (68)**		**824 (71)**		**0.0002*** **
Biological treatments, n (%)	**1 (2)**		**3 (2)**		**19 (7)**		**48 (7)**		**71 (6)**		**0.005****
Comorbidities	**SLE**	**HC**	**SLE**	**HC**	**SLE**	**HC**	**SLE**	**HC**	**SLE**	**HC**	
Chronic Kidney Disease, n (%)	***5**** *(10)*	*0 (0)*	***13**** *(8)*	*7 (0.8)*	***31**** *(12)*	*5 (0.4)*	***76**** *(11)*	*4 (0.4)*	***125**** *(11)*	*16 (0.5)*	*ns*
Coronary Heart disease, n (%)	*1 (2)*	*1 (0.5)*	*2 (1)*	*8 (0.9)*	***11**** *(4)*	*6 (0.4)*	*15 (2)*	*15 (1.6)*	***29**** *(2)*	*30 (1)*	*ns*
Diabetes, n (%)	*2 (4)*	*11 (0.5)*	*4 (2)*	*51 (5.5)*	*7 (3)*	*33 (3)*	*28 (4)*	*29 (3)*	*41 (4)*	*124 (4)*	*ns*
Hypercholesterolaemia, n (%)	*2 (4)*	*5 (2)*	*6 (4)*	*48 (5)*	*17 (6)*	*91 (7)*	*75 (11)*	*77 (8)*	***100**** *(9)*	*221 (7)*	***0.0055****
Hypertension, n (%)	*8 (16)*	*28 (13)*	*24 (15)*	*95 (10)*	***37**** *(14)*	*122 (10)*	***122**** *(18)*	*77 (8)*	*191 (16)*	*212 (6)*	*ns*

Methods: We identified SLE patients from the COVAD 2 database, an international study of over 20,000 respondents. Data collection included, demographics, comorbidities, treatment including; corticosteroids (CS), antimalarials, immunosuppressants (IS), cyclophosphamide and biologics. Country Human Development Index (HDI) classification, a composite index formulated by the United Nations to rank countries into tiers of development, was utilised. Statistical analysis comprised of Chi square for comparison of categorical values and t-test for comparison between groups. Significance was defined as $p< 0.05$.

Results: A total of 1167 patients with SLE were included in analysis. As shown in Figure 1, patients from low/medium HDI (lmHDI) countries were significantly younger than those from high/very high HDI (hvhHDI) countries (median age 32, IQR 27-41 vs 41, IQR 32-52 years, $p< 0.0001$). In addition, disease duration was shorter in lmHDI countries (median 5, IQR 3-10 vs 10, IQR 5-19 years, $p< 0.0001$). As shown in Table 1, a higher proportion of SLE patients from lmHDI countries were on CS (73% vs 59%, p=0.0002), antimalarials (81% vs 68%, p=0.0002) and IS (66% vs 53%, p=0.0009) compared with patients from hvhHDI countries. Biologic use was more common in hvhHDI countries (7% vs 2%, p=0.0055). Comorbidity prevalence was similar between groups, however when adjusted for age, these were observed in younger patients from lmHDI countries than hvhHDI countries (with shorter disease durations), thus suggesting earlier steroid related complications. Patients with chronic kidney disease were significantly younger patients in lmHDI countries than hvhHDI countries (36.67 vs 44.64 years, p=0.015). Those with coronary artery disease (35.7 vs. 44.6 years, p=0.015) and hypertension (41.5 vs 49.8 years, p=0.003) were also younger in lmHDI countries.

Conclusion: In this large international study evaluating treatment and steroid related comorbidity incidence in SLE populations based on country HDI we identified several differences in pharmacological management globally. Whilst there was no significant difference in the incidence of comorbidities, these occurred in younger patients and earlier in the disease course in those from lmHDI countries. CS use was higher in lmHDI countries and may be a key contributor to the increased incidence in these comorbidities. Interestingly, Hydroxychloroquine, which has frequently been shown to reduce damage and cardiovascular comorbidities was more commonly used in lmHDI countries but these comorbidities persisted. Further studies are required to identify other factors contributing to this earlier development of comorbidities.

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Abstract Number: 2270

Factors Associated with Discordance Between Patient and Physician Perception of Disease Activity Among Patients with Systemic Lupus Erythematosus: An International Collaborative Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The management of SLE relies on regular assessment of disease activity. However, patient perception of disease activity can be highly variable and may be discordant with physician assessment. This problem has recently become a more important consideration due to the rise in virtual or telephone consultations, in which physicians may be guided by patient reported symptoms and perceived disease activity. In this study, we sought to evaluate factors associated with discordance between physician and patient perception of disease activity in SLE in a global cohort of patients.

Methods: Data was collected from an international collaborative research survey of more than 17,000 participants (of which 1292 had SLE). Variables such as disease duration, symptoms, comorbidities, medication and validated Patient Reported Outcome Measures (PROMs) were included. Patient perception of disease activity was self-reported. Physician defined disease activity was classified as the presence of at least one symptom of active SLE (including joint swelling, active rash, oral ulcers, alopecia, active renal disease) in addition to the need for a change or increase in lupus treatment within the last 6 months. Patients were classified into three groups; 1. Concordant active (both physician and patient in agreement of active disease); 2. Discordant (patient reported disease to be active but did not fulfil definition of physician confirmed active disease); 3. Concordant inactive (both physician and patient in agreement that the disease is inactive). Differences between groups was evaluated using Chi Square and t-test. Cramer's phi was used to assess strength on concordance between patient and physician reported disease activity. Predictors of discordance were analysed in regression models. Statistical significance was defined as $p< 0.05$.

Results: Of the 1292 patients with SLE, 5.1% were defined as Concordant Active disease, 49.46% had Concordant Inactive disease, and 45.43% were Discordant (patient perceived active with physician defined inactive disease). Cramer's phi between Physician Active and Patient Active disease was 0.16 (weak association). As summarised in Table 1, there was no difference in age, gender or disease duration between groups. In patients with inactive disease, Caucasian patients were

Table 1. Summary of key differences between Concordant Active, Discordant (patient perceived active disease and physician defined inactive disease), and Concordant Inactive patients with SLE

	Concordant Active n=66	Discordant (Patient Active, Clinician Inactive) n=587	Concordant Inactive n=639	P value
Demographics				
Age (years, mean ± SD)	38.56 ± 10.85	42.18 ± 13.30	40.83 ± 12.51	ns
Female, n (%)	65 (98.4)	559 (95.2)	606 (95.4)	ns
Ethnicity				
Caucasian	20 (30.3)	212 (36.1)	165 (25.8)	**<0.0001**
Black	8 (12.1)	68 (11.6)	62 (9.7)	ns
Asian	19 (28.8)	154 (26.2)	214 (33.5)	**0.006**
Hispanic	8 (12.1)	81 (13.8)	73 (11.4)	ns
Native American / Pacific Islander	6 (9.1)	26 (4.5)	29 (4.5)	ns
Mixed	2 (3.1)	27 (4.6)	49 (7.7)	**0.026**
Other	3 (4.5)	19 (3.2)	47 (7.4)	**0.001**
Disease Duration (years, mean ± SD)	10.42 ± 8.57	12.14 ± 10.33	12.33 ± 10.27	ns
Comorbidities				
Asthma	10 (15.2)	53 (9.1)	39 (6.1)	**0.013**
Chronic Kidney Disease	7 (10.6)	71 (12.1)	65 (10.2)	ns
Chronic Liver Disease	1 (1.6)	7 (1.2)	8 (1.3)	ns
Thyroid Disease	7 (10.6)	56 (9.5)	52 (8.1)	ns
Type 2 Diabetes Mellitus	1 (1.6)	24 (4.1)	13 (2.1)	ns
Chronic Obstructive Pulmonary Disease	2 (3.1)	10 (1.7)	20 (3.1)	ns
Interstitial Lung Disease	1 (1.6)	10 (1.7)	12 (1.9)	ns
Ischaemic Heart Disease	1 (1.6)	10 (1.7)	16 (2.5)	ns
Epilepsy	1 (1.6)	11 (1.9)	11 (1.7)	ns
Raised Cholesterol	4 (6.1)	51 (8.7)	58 (9.1)	ns
Hypertension	8 (12.1)	103 (17.6)	94 (14.7)	ns
Stroke	2 (3.1)	8 (1.3)	7 (1.1)	ns
Anxiety	10 (15.2)	89 (15.2)	99 (15.5)	ns
Depression	10 (15.2)	95 (16.2)	102 (15.9)	ns
Insomnia	7 (10.6)	59 (10.9)	72 (11.2)	ns
Treatment				
Methotrexate	15 (22.7)	82 (13.9)	42 (6.6)	**<0.0001**
Mycophenolate	13 (19.7)	145 (24.7)	97 (15.2)	**<0.0001**
Azathioprine	19 (28.8)	112 (19.1)	104 (16.3)	**<0.0001**
Hydroxychloroquine	50 (75.8)	423 (72.1)	328 (58.2)	**<0.0001**
Rituximab	1 (1.6)	24 (4.1)	10 (1.6)	**0.02**
Steroid Dose				
None	24 (36.4)	200 (34.1)	367 (57.4)	**<0.0001**
<10 mg / Day	30 (45.5)	280 (47.7)	220 (34.4)	**<0.0001**
10-20 mg / Day	8 (12.1)	82 (13.9)	42 (6.6)	**<0.0001**
>20 mg / Day	4 (6.0)	25 (4.3)	10 (1.6)	**0.005**
Symptoms / Signs				
Rash	30 (45.5)	6 (1.1)	3 (0.5)	**<0.0001**
Joint Swelling	41 (62.1)	28 (4.8)	11 (2.7)	**<0.0001**
Oral / Nasal Ulcers	20 (30.3)	6 (1.1)	4 (0.6)	**<0.0001**
Alopecia	30 (45.5)	7 (1.2)	4 (0.6)	**<0.0001**
Active Renal Disease	20 (30.3)	2 (0.3)	0 (0)	**<0.0001**
Raised ESR or CRP	21 (31.8)	8 (1.4)	3 (0.5)	**<0.0001**
Fatigue 4a, median (IQR)	12 (8.75-15)	11 (8-15)	9 (7-12)	**<0.0001**
Pain VAS, median (IQR)	4 (2-6.25)	3 (2-6)	2 (0-5)	**<0.0001**
Global Physical Health, median (IQR)	13 (12-14)	13 (12-15)	13 (12-14)	ns
Global Mental Health, median (IQR)	12 (10-14)	12 (10-14)	13 (11-16)	**<0.0001**
PROMIS Physical Function, median (IQR)	39.5 (32-45)	41 (36-46)	44 (28-48)	**<0.0001**

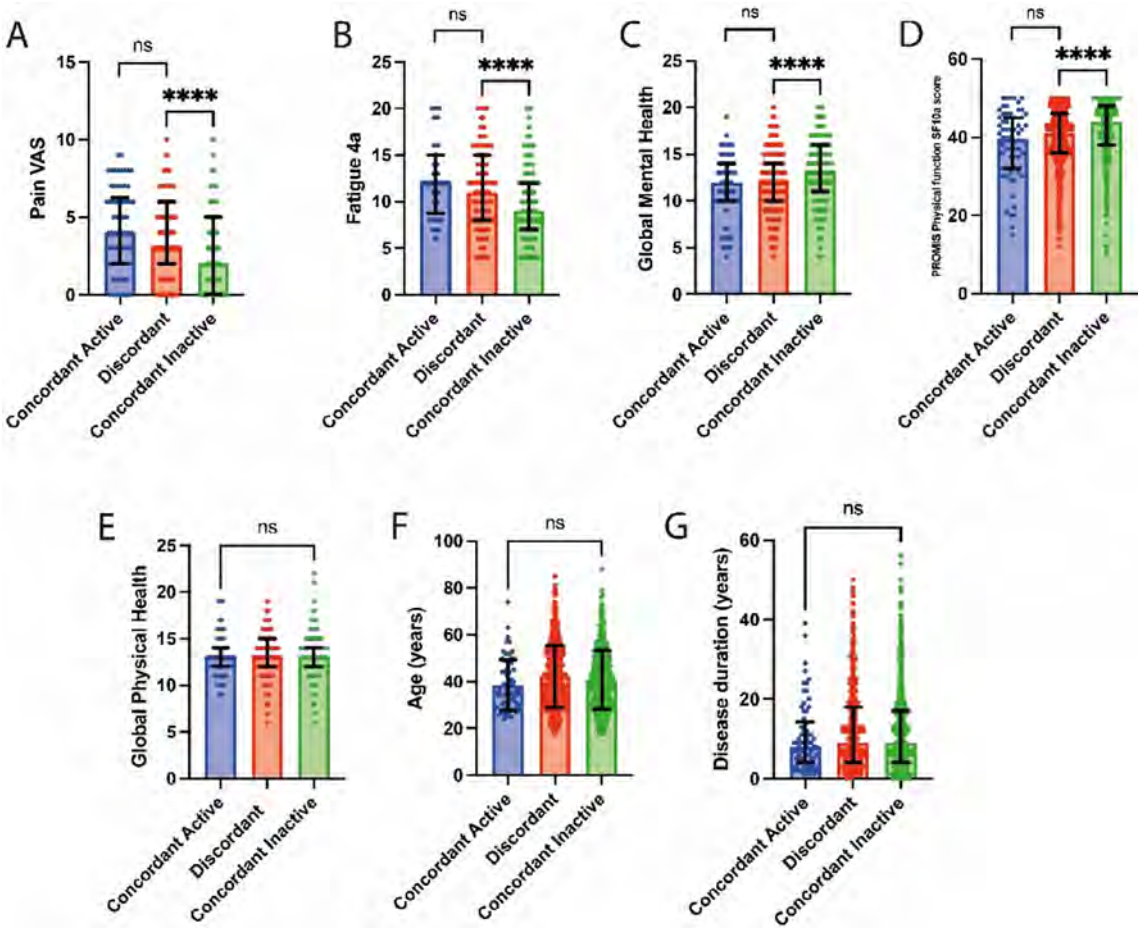

Figure 1. Patients who reported active disease (in the context of physician defined inactive disease, i.e. discordant) reported high levels of Pain (A), Fatigue (B) and had poorer mental health (C) and physical function (D) than those with concordant inactive disease (in which both patient and physician agreed the disease was not active). There was no significant difference in PROMIS Physical Health Score (E), Age (F) or Disease Duration (G) ns, not significant; **** p<0.0001

more likely to be discordant ($p < 0.0001$), with Asian, Mixed and Other ethnicities more likely to be concordant. In terms of treatment, those on steroids and immunosuppressive agents were more likely to be discordant in their assessment of disease activity, whilst those on no treatment were more likely to be in agreement with physicians that their disease was inactive. As shown in Figure 1, key symptomatic drivers of discordance included fatigue, pain and Global Mental Health scores ($p < 0.0001$). Patients were more likely to agree that their disease was inactive in the context of lower levels of pain, fatigue and better mental health scores whilst being on less treatment.

Conclusion: This study highlights that nearly half of patients perceive their disease to be active when their physicians feels it is inactive. In particular this was observed in those who reporting from high levels of fatigue, pain and poorer mental health.

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H. Chinoy: AstraZeneca, 1, Biogen, 2, Eli Lilly, 5, GlaxoSmithKlein(GSK), 6, Novartis, 2, Orphazyme, 2, Pfizer, 1, UCB, 6; **C. Study Group**: None; **R. Aggarwal**: Actigraph, 2, Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella Bioscience, 2, Corbus, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Mallinckrodt, 5, Merck, 2, Octapharma, 2, Pfizer, 2, 5, Q32, 5, Roivant, 2, Sanofi, 2, Teva, 2; **V. Agarwal**: None; **L. Gupta**: None; **C. Wincup**: None.

Abstract Number: 2271

Longitudinal Changes in Type 1 & Type 2 SLE Activity

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SESSION INFORMATION
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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The Type 1 & 2 SLE Model encompass symptoms classically attributed to inflammation, including arthritis, rash, serositis and nephritis (Type 1 SLE), and symptoms of fatigue, widespread pain, mood disturbance, and cognitive dysfunction (Type 2 SLE). Our preliminary data suggest there are at least two distinct sub-types of Type 2 SLE, one that is related to active inflammation and another that exists regardless of inflammation. The objective of this study was to use longitudinal measures of Type 1 and Type 2 SLE activity to identify distinct subgroups of Type 2 SLE.

Methods: SLE patients meeting SLICC criteria with ≥2 visits at a university rheumatology clinic over a 36-month period between February 2018 and August 2022 were included. At each visit, rheumatologists scored Type 1 and 2 SLE activity separately by Physician's Global Assessments, visual analog scales of 0-3 (0=no activity, 3=severe activity). Growth mixture models derived classes of patients based on their Type 1 and Type 2 PGA trajectories. We postulated quadratic trajectories and different number of classes were assessed based on objective model criteria and interpretability of the classes. Once the number of classes was selected, posterior probabilities assigned patients to the class with the highest probability. Patients were then classified according to their classes of Type 1 and Type 2 PGA trajectories into different "groups". Differences in clinical and demographic characteristics across groups were estimated using simple statistics.

Results: We included 297 patients with 2,011 visits. The best model fit of trajectories for both the Type 1 and Type 2 PGA included three classes. When patients were grouped according to their Type 1 and Type 2 PGA classes, the majority (73%) fell into one of four groups (Figure 1): 29% had low Type 1 and Type 2 activity (Minimal); 19% had constant high Type 2 but low Type 1 activity (Type 2); 7% had constant high Type 1 but low Type 2 activity (Type 1); and 18% had constant high Type 1 and Type 2 activity (Mixed). The remaining 27% of patients had variable Type 1 and Type 2 changes over time that did not fit into a distinct group. Patients in the Type 2 SLE group were older and more likely to be on disability (Table 1). While the SLEDAI and Type 1 PGA scores were similar between the Type 1 and Mixed groups, the disease manifestations were somewhat different, with more nephritis in the Type 1 group and higher LFA-REAL Musculoskeletal PGA scores in the Mixed group. While overall Type 2 PGA scores were similar for those in the Type 2 and Mixed groups, there was more depression, pain, and symptom severity among those in the Mixed group. In a descriptive analysis to determine if Type 1 and Type 2 PGA changed concordantly, 39% of patients had Type 1 and Type 2 SLE PGAs that consistently changed together.

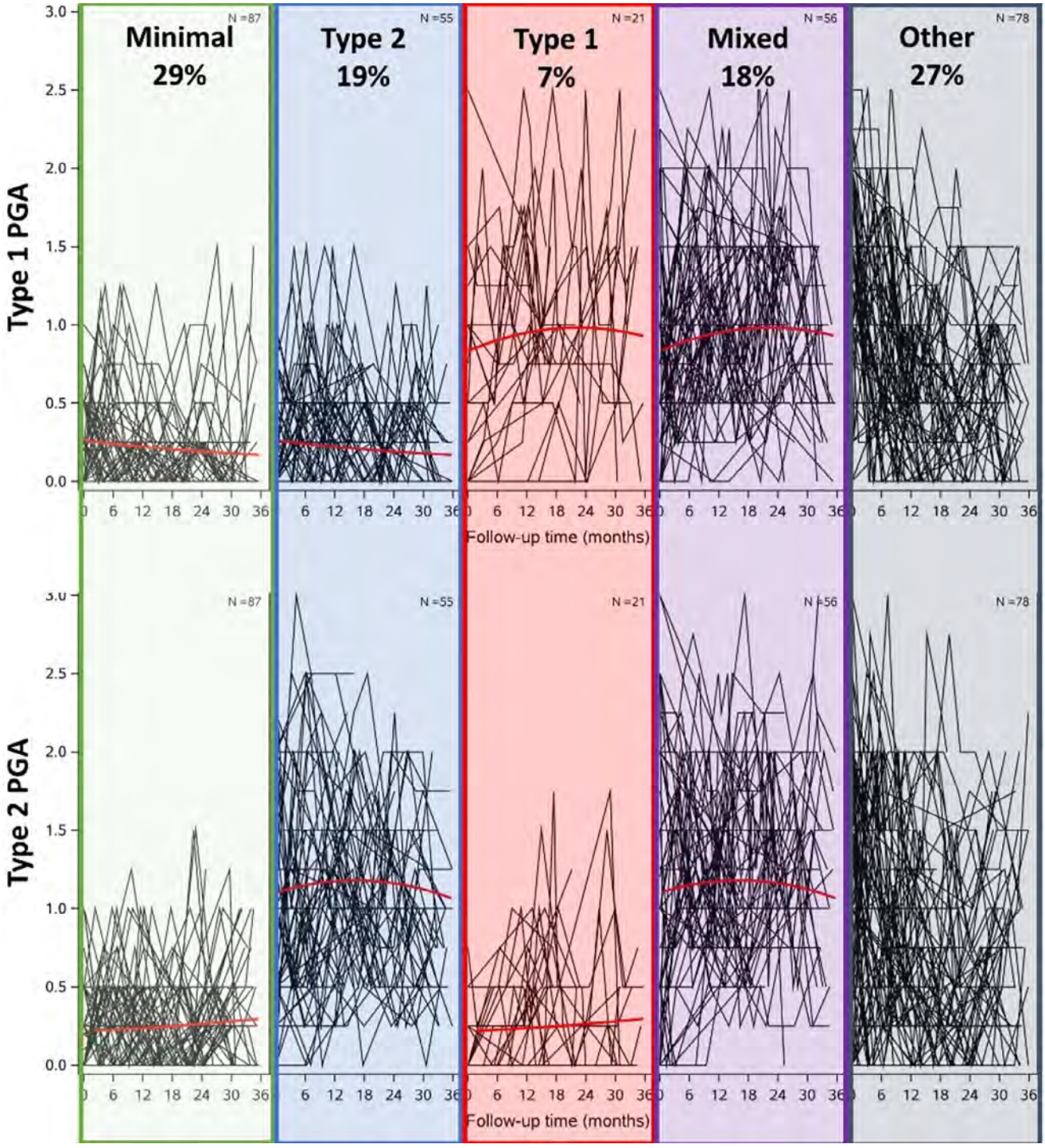

Figure 1. Spaghetti plots showing the individual trajectories of Type 1 and 2 PGAs for patients in each group.

Conclusion: We identified 4 main longitudinal subgroups of patient trajectories. Supporting our prior qualitative work, we found changes in Type 1 and Type 2 occurred together in almost 40% of patients. Future work is needed to understand the underlying etiology of each subgroup, allowing us to target these groups with appropriate medical and non-medical treatment plans.

Table 1. Cohort characteristics.

	Minimal	Type 2 SLE	Type 1 SLE	Mixed SLE	Not classified	p-value
	n=87	n=55	n=21	n=56	n=78	
Age	45.8 (13.9)	48.0 (12.8)	37.8 (13.3)	40.1 (13.4)	40.3 (12.2)	0.0005
Female	78 (89.7%)	54 (98.2%)	18 (85.7%)	53 (94.6%)	72 (92.3%)	0.2486
Black	49 (56.3%)	27 (49.1%)	13 (61.9%)	34 (60.7%)	44 (57.1%)	0.1820
Hispanic Ethnicity	1/87 (1.1%)	3/54 (5.6%)	4/21 (19.0%)	1/56 (1.8%)	4/76 (5.3%)	0.0071
Disability	13/84 (15.5%)	23/51 (45.1%)	3/19 (15.8%)	20/50 (40.0%)	22/71 (31.0%)	0.0010
Medicare/Medicaid	30/83 (36.1%)	29/51 (56.9%)	7/19 (36.8%)	29/53 (54.7%)	28/72 (38.9%)	0.0583
Depression	12/76 (15.8%)	18/46 (39.1%)	4/18 (22.2%)	28/45 (62.2%)	29/61 (47.5%)	<.0001
Total areas of widespread pain across visits	1.6 (1.7)	4.4 (3.1)	1.7 (1.7)	6.0 (3.6)	3.8 (3.1)	<.0001
Symptom severity score across visits	2.5 (1.7)	6.4 (2.2)	2.6 (1.7)	7.3 (2.2)	5.7 (3.0)	<.0001
Total FSS (also known as PSD) across visits	4.3 (3.1)	11.2 (4.7)	4.5 (2.9)	14.5 (5.4)	10.2 (6.0)	<.0001
Active lupus nephritis during study period	8/87 (9.2%)	10/55 (18.2%)	13/21 (61.9%)	19/56 (33.9%)	29/78 (37.2%)	<.0001
Clinical SLEDAI across visits	0.3 (0.8)	0.5 (1.1)	1.5 (2.2)	2.3 (2.4)	3.5 (2.8)	<.0001
SELENA-SLEDAI across visits	1.2 (1.4)	1.4 (1.6)	4.7 (2.1)	4.7 (2.8)	3.6 (2.5)	<.0001
Musculoskeletal PGA across visits	0.0 (0.1)	0.2 (0.2)	0.2 (0.3)	0.6 (0.4)	0.3 (0.3)	<.0001
Mucocutaneous PGA across visits	0.1 (0.1)	0.1 (0.1)	0.5 (0.5)	0.4 (0.5)	0.3 (0.4)	<.0001
Type 1 PGA across visits	0.1 (0.1)	0.3 (0.2)	0.9 (0.3)	1.0 (0.4)	0.8 (0.3)	<.0001
Type 2 PGA across visits	0.2 (0.2)	1.1 (0.4)	0.3 (0.2)	1.2 (0.4)	0.9 (0.5)	<.0001

Numbers are presented as n (%) or mean (SD)

Disclosure: A. Eudy: Amgen, 2, Exagen, 5, GlaxoSmithKlein(GSK), 5, Immunovant, 5, Pfizer, 5; **J. Rogers**: Amgen, 2, Ampel Biosolutions, 1, AstraZeneca, 6, Aurinia, 1, Eli Lilly, 1, Exagen, 5, GlaxoSmithKlein(GSK), 2, Immunovant, 2, 5; **D. Wojdyla**: None; **K. Sun**: AstraZeneca, 6; **R. Sadun**: None; **M. Maheswaranathan**: AstraZeneca, 6; **J. Doss**: None; **L. Criscione-Schreiber**: GlaxoSmithKlein(GSK), 5, UCB, 5; **M. Clowse**: Exagen, 5, GlaxoSmithKlein(GSK), 2, 5, Immunovant, 5, UCB, 2, 5.

Abstract Number: 2272

Age and Race-Based Differences in Emergency Department Utilization for Systemic Lupus Erythematosus in the United States

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) frequently visit the emergency department (ED) due to the complex disease course. Previous research highlights infection and pain as key reasons for ED use in SLE. Our previous study using the US National Emergency Department Sample (NEDS) found that SLE ED visits consisted of

Table 1. Baseline demographic characteristics and clinical comorbidities of ED encounters in SLE by age categories: National Emergency Department Sample (NEDS), 2019: National Emergency Department Sample (NEDS), 2019

ED visits with SLE: N= 414,139		18-30 years	31-50 years	51-64 years	≥ 65 years	p-value
N (weighted estimate), (%)		59,694	169,087	108,994	76,364	
Baseline Demographic Characteristics (%)						
Race/Ethnicity (%)	White	26.39	39.27	48.48	64.70	<0.001
	Black	47.11	37.73	33.02	21.56	
	Hispanic	19.17	16.71	13.06	8.69	
	Other	5.55	5.21	4.48	4.32	
Primary Payer (%)	Medicare	13.87	26.59	39.61	89.68	<0.001
	Medicaid	41.70	30.38	20.69	1.16	
	Private	30.08	30.17	31.87	7.65	
	Self	10.7	9.56	4.79	0.73	
	Others	3.4	3.19	2.92	0.7	
Clinical Comorbidities (%)						
Chronic kidney disease (CKD)		20.78	15.78	17.64	26.75	<0.001
Overweight and obesity		6.13	11.04	13.72	11.51	
Hyperlipidemia (HLD)		3.00	10.48	25.17	40.44	
Hypertension (HTN)		33.02	43.41	61.94	76.42	
Diabetes mellitus (DM)		5.30	14.61	24.79	27.86	
Ischemic heart disease		2.37	7.02	17.90	30.08	
Cerebrovascular disease		4.53	7.79	13.39	18.16	
Peripheral vascular disease (PVD)		2.96	3.68	4.71	6.68	
Heart failure		6.32	8.82	14.53	25.87	
VTE (DVT + PE)		11.28	13.41	12.67	12.98	0.01
Mood disorders		12.79	17.34	18.91	16.76	<0.001

Table 2. Baseline demographic characteristics and clinical comorbidities of ED encounters in SLE by racial/ethnic categories: National Emergency Department Sample (NEDS), 2019

ED visits with SLE: N= 414,139		White	Black	Hispanic	Other	p-value
N (weighted estimate), (%)		184,391	144,365	60,573	20,308	
Baseline Demographic Characteristics (%)						
Age, Mean (SE)		53 (0.22)	45 (0.25)	45 (0.37)	47 (0.45)	<0.001
Age categories (%)	18-30 years	8.54	19.48	18.9	16.31	<0.001
	31-50 years	36.01	44.19	46.64	43.38	
	51-64 years	28.65	24.93	23.5	24.06	
	≥ 65 years	26.8	11.4	10.96	16.25	
Primary Payer (%)	Medicare	44.45	39.31	30.21	31.87	<0.001
	Medicaid	18.65	27.51	31.44	26.76	
	Private	28.5	23.43	25.40	31.35	
	Self	5.76	7.38	9.13	5.81	
	Others	2.55	2.24	3.64	4.17	
Clinical Comorbidities (%)						
Chronic kidney disease (CKD)		13.14	24.60	22.92	21.55	<0.001
Overweight and obesity		11.77	11.48	9.63	8.11	
Hyperlipidemia		22.18	15.98	15.80	18.08	
Hypertension		47.74	61.46	50.08	48.59	
Diabetes mellitus (DM)		17.81	19.05	19.28	17.00	0.02
Ischemic heart disease		16.14	11.99	9.79	11.76	<0.001
Cerebrovascular disease		11.49	10.72	8.36	10.38	
Peripheral vascular disease (PVD)		5.33	3.45	3.78	4.31	
Heart failure		12.33	15.51	10.67	11.54	
VTE (DVT + PE)		12.49	14.23	11.24	11.03	0.001
Mood disorders		21.60	12.93	13.95	12.68	<0.001

more young patients, of Black race, with publicly funded insurance and a higher comorbidity burden, but Black patients were less likely to be admitted from the ED. This study aims to further investigate age and race-based variations in ED utilization.

Methods: Using NEDS (2019) discharge data for 989 hospitals, which approximates a 20% sample of US hospital-owned EDs, SLE visits were identified using ICD-10 codes (M32.xx) and categorized by age (18-30, 31-50, 51-64, and ≥ 65 years) and race (White, Black, Hispanic, Others). Demographic features, clinical comorbidities, and the top ten primary diagnoses associated with ED visits were compared across groups.

Results: We identified 414,139 ED SLE visits, 41% of which were visits by adults aged 31-50 years. Young SLE adults (18-30 years) visiting the ED were predominantly Black (47.10%), and had Medicaid (41.70%), while older adults (≥ 65 years) were mostly White (64.70%). Older adults had higher rates of chronic kidney disease (CKD), hyperlipidemia

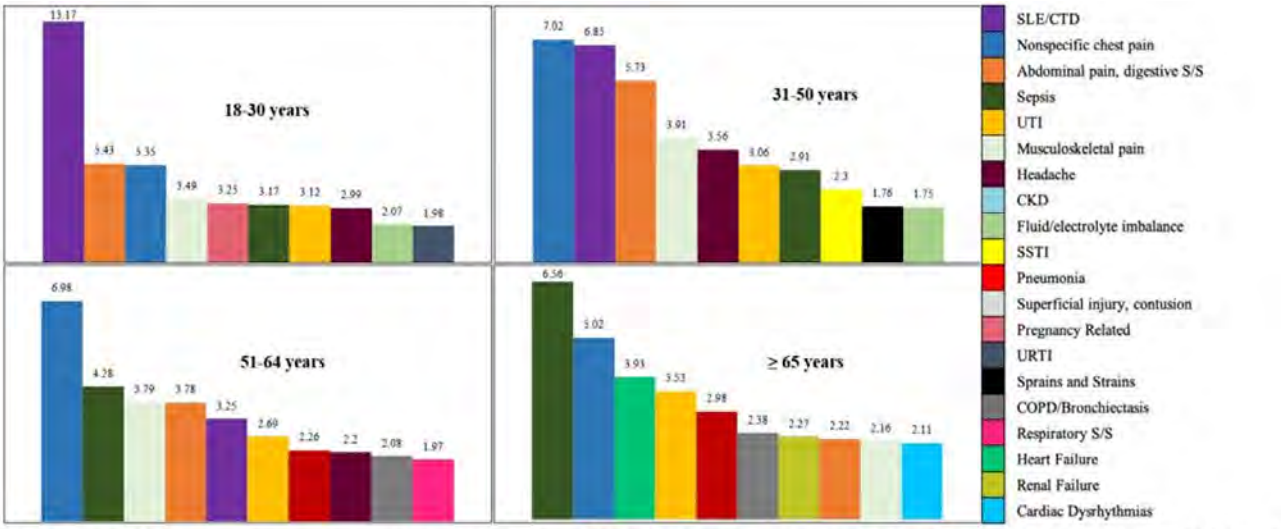

Figure 1a. Top ten primary diagnoses associated with ED visits in patients with SLE by age categories: National Emergency Department Sample (NEDS), 2019

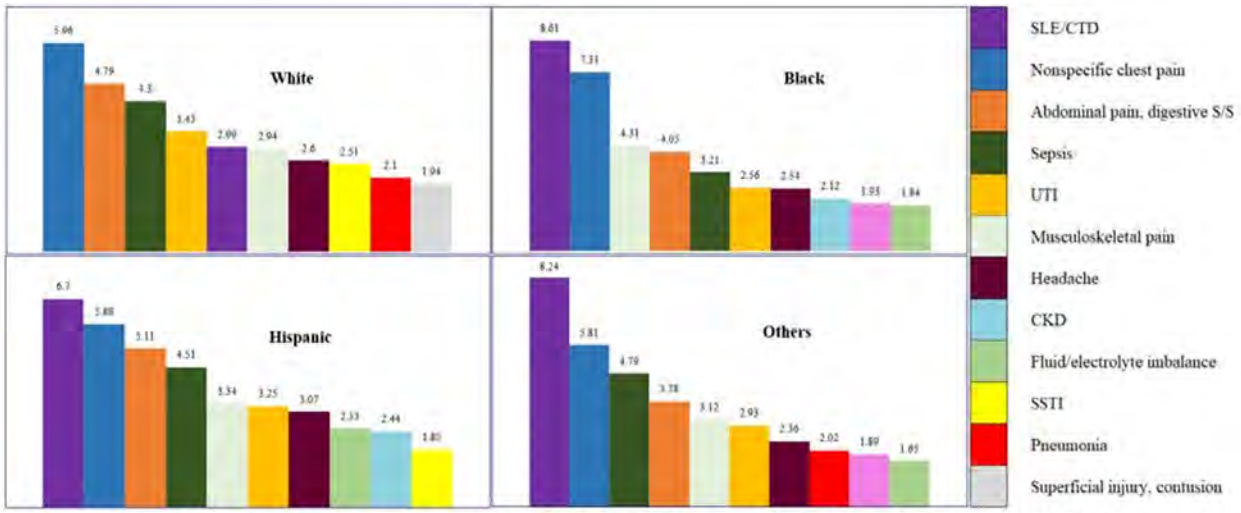

Figure 1b. Top ten primary diagnoses associated with ED visits in patients with SLE by racial/ethnic categories: National Emergency Department Sample (NEDS), 2019

Figure 1. Top ten primary diagnoses associated with ED visits in SLE by age and race categories, National Emergency Department Sample (NEDS), 2019

(HLD), hypertension (HTN), diabetes, and cardiovascular diseases (CVDs), but young SLE adults (18-30 years) also exhibited significant comorbidity burdens (CKD: 20.78%, HTN: 33.02%). Analyzing by race, more ED visits by Black and Hispanic SLE patients were in the 18-30 age group (~20%) compared to White patients (< 10%). Medicaid use was notably higher among non-White (27-32%) versus 19% in White patients. Comorbidity patterns varied, with White patients having higher HLD, ischemic heart disease (IHD), and mood disorders while Black patients had higher CKD and HTN (25% vs 13% and 61% vs 48%, respectively). The most common primary diagnosis for ED visits in young SLE adults (18-31 years) was "SLE/Connective tissue disease (CTD)", whereas sepsis was the most common diagnosis for older adults (≥ 65 years). Heart failure and arrhythmias were among the top 10 diagnoses for adults ≥ 65 years, but not in younger groups. The primary ED diagnosis of SLE/CTD was more common in Black (8.61%) and Hispanic (6.70%) than in White patients (2.99%), with no other major differences in other reasons for ED visits based on race.

Conclusion: In a previous study of general population ED visits, Black patients were less likely to be admitted from the ED, and our study suggested a similar pattern among SLE ED visits. Discriminating determinants appear to be younger age, higher Medicaid use, CKD, HTN, and heart failure amongst Black SLE patients, and higher prevalence of older age groups, and baseline CVDs among White patients. While it appears that increased age and/or more severe CVDs in the White patients may explain the disparate admission rates, further study is needed to confirm whether these discriminating factors are replicated in other datasets and whether other factors such as ED reliance as a primary source of care and insurance coverage affect the lower admission rate amongst Blacks.

Disclosure: R. Dhital: None; **I. Karageorgiou**: None; **A. Pokharel**: None; **K. Kalunian**: AbbVie/Abbott, 2, Amgen, 5, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EquilliumBio, 2, Genentech, 2, Gilead, 2, Janssen, 2, KezarBio, 1, Merck/MSD, 2, Novartis, 2, Pfizer, 2, Remegene, 2, Roche, 2, UCB, 5.

Abstract Number: 2273

Predicting SLE Disease Activity with Blood Biomarkers: A Step Towards Precision Medicine

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
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Background/Purpose: Systemic lupus erythematosus (SLE) is the prototypical autoimmune disease with diverse clinical manifestations and variable treatment response. Conventional biomarkers of SLE activityprovide modest correlation with disease activity and suffer from several confounding factors that limit their utility as treat-to-target surrogates.The SLEDisease Activity Index 2000 (SLEDAI-2K) is often employed to monitor disease activity, but the administrative burden it requires has limited its real-world adoption.Modeling the values of serum biomarkers to predict patients'clinical SLEDAI-2Kscores (cSLEDAI-2K; which excludes its immunologic lab components, i.e., anti-dsDNA and complement), holds potential to advance the developmentof individualized treatment plans, thus advancing the field of precision medicine. Therefore, the aim of this study was to investigate the correlation of serum biomarkers with cSLEDAI-2K scores and to evaluate their potential to stratify patients in active and inactive disease states.

Table 1: Cohort demographics

	Total (N=128)
Sex	
F	116 (90.6%)
M	12 (9.4%)
Race	
White	59 (46.1%)
Black	40 (31.3%)
Asian	18 (14.1%)
Other	7 (5.5%)
Hispanic	4 (3.1%)
Age	
Mean (SD)	44.3 (1.28)
Median [Min, Max]	44.0 [43.0, 47.0]
SLEDAI-2K	
Mean (SD)	4.35 (4.49)
Median [Min, Max]	4.00 [0, 26.0]
Clinical SLEDAI-2K	
Mean (SD)	2.79 (3.98)
Median [Min, Max]	1.00 [0, 22.0]
Physician's Global Assessment	
Mean (SD)	0.822 (0.899)
Median [Min, Max]	1.00 [0, 3.00]
Anti-dsDNA	
Mean (SD)	122 (171)
Median [Min, Max]	48.0 [9.80, 667]
EC4d	
Mean (SD)	19.1 (32.8)
Median [Min, Max]	10.7 [0.540, 264]
Anti-C1q	
Mean (SD)	21.4 (27.2)
Median [Min, Max]	8.50 [3.00, 145]
C3	
Mean (SD)	104 (36.1)
Median [Min, Max]	98.0 [6.00, 276]
C4	
Mean (SD)	19.3 (9.71)
Median [Min, Max]	17.0 [2.00, 49.0]

Methods: A total of 128 patients (90.6% female) with a mean age of 44.3 were included in the analysis. The patients sampled were raciallydiverse,as detailed in Table 1. The mean cSLEDAI-2K score was 4.35. The association of blood biomarkers, including anti-dsDNA, EC4d, PC4d, anti-C1q, C3, and C4with the cSLEDAI-2Kscore was evaluated using multiple 10-fold cross-validated regression models. The most predictive model was identified and used for further stratification of patients based on cSLEDAI-2Kscores of <4 (low activity) and >4 (high activity) groups.Significant differences in blood levels between patient groups were estimated using the Wilcoxon test.

Results: The best-performing regression model (RuleFit Regressor) had an R2 of 0.57. Despite the modest correlation, the average absolute residual between actual and predicted cSLEDAI-2Kwas only 1.3. Moreover,when the predicted scores were used to categorize patients into cSLEDAI-2K <4 or >4, the model achieved an accuracy of 84.5% in cross-validation and 72% in the unseen holdout partition (Figure 1). Biomarkers were ranked in order of predictive importance showing C3 at the top, with 100% of relative model importance, followed by the other biomarkerspresentedin relation to C3 (Figure 2,B). Finally, comparing blood levels of the ranked biomarkers confirmed a statistically significant difference between

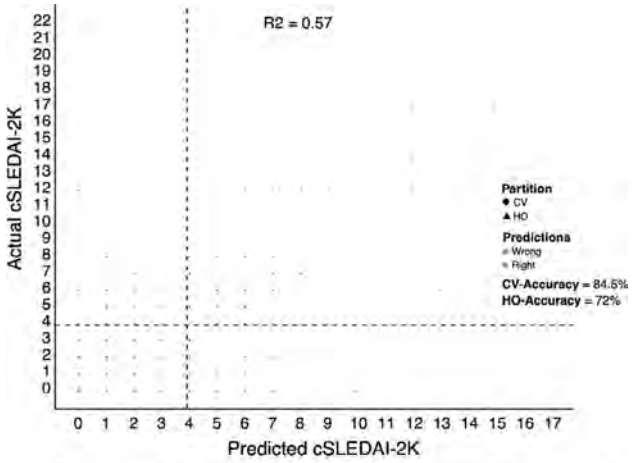

Figure 1. Scatterplot of Actual vs. Predicted stratified CSLEDAI-2k scores. The plot illustrates the top model's (RuleFit classifier) accuracy in predicting SLEDAI-2k scores derived from blood biomarkers only. Actual CSLEDAI-2k scores are reported on the Y-axis, while predicted scores are on the X-axis. The overall model R2 = 0.57 for samples included in both 10-fold cross-validation (CV) and hold out (HO) unseen partitions. After stratifying patients based on actual CSLEDAI-2k scores < 4 and those with >= 4, the model was able to correctly classify 84.5% of patients in CV and 72% of patients in the unseen HO. Red/blue dots represent wrong vs right model classification on a per sample basis.

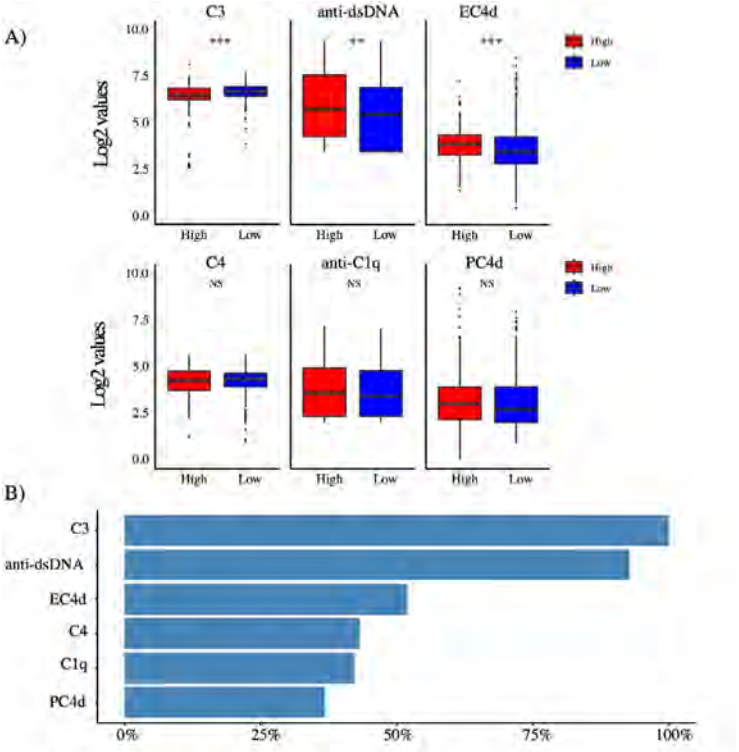

Figure 2. Blood biomarkers levels and their respective predictive power
A) Box plot showing log2 blood levels of top biomarkers required for model prediction. Whisker plots depict the interquartile range, median, minimum, and maximum for each group. Outliers, if present, are represented as individual points beyond the whiskers. A significant difference between groups is indicated by ***P< 0.0001; **P< 0.001 (Wilcoxon test). B) Biomarker importance rank score from top model. The predictive biomarkers are listed on the Y-axis, with their corresponding importance scores displayed on the X-axis. The scores are calculated in relation to the top important feature (C3; 100% importance). Higher scores indicate a greater influence on the model's predictive performance. This ranking provides insights into the relative importance of each feature in predicting cSLEDAI-2k scores, further informing our understanding of key factors contributing to disease activity in SLE.

SLE patients stratified bycSLEDAI-2K scores for C3 (P<0.001), anti-dsDNA (P= 0.005), and EC4d (P<0.001)(Figure 2, A), while differences inC4, anti-C1q, and PC4d were non-significant.

Conclusion: These results highlightthe potential of applying machine learning toselectedblood biomarkers to predict the cSLEDAI-2K score to monitor disease activity in clinical practice.EC4d emergedas anindependentpredictor,additive to the predictive power of conventional biomarkers across our top models, suggesting its potential use in a precision medicine approachto guide individualized treatment strategies in SLE. Further research is required to validate these findings and better understand their implications for individualized SLE management.

Disclosure: V. Kyttaris: AbbVie/Abbott, 5, AstraZeneca, 2, Aurinia, 1, EMD Serono, 5, Exagen, 2, 5, Fresenius Kabi, 1, Horizon Pharmaceuticals, 1, Novartis, 5, Scipher, 1, Takeda, 5, Vertex, 2; **T. O'Malley**: Exagen, 3, 11, 12, Shareholder; **G. Casaburi**: Exagen Inc., 3; **S. Kumar**: Exagen, Inc., 3; **A. Concoff**: Exagen, 3, 4, 12, Shareholder, Pacira Biosciences, Inc., 2, United Rheumatology, 4.

Abstract Number: 2274

Lupus Low Disease Activity State as an Attainable Target in Lupus Nephritis Associated with Reduced Risk of Relapse

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis (LN) is a significant comorbidity affecting approximately up to 50-60% of patients with systemic lupus erythematosus (SLE). Complete renal response (CRR) and partial renal response (PRR) have been recommended as treatment targets in LN. Lupus low disease activity state (LLDAS) is an important target associated with improved clinical outcome in SLE. Its role in patients in LN has not been fully evaluated. This study aims to investigate the attainment rate, predictors and outcomes associated with LLDAS attainment in patients with LN.

Methods: Patients with biopsy-proven LN during 2010-2020 in Queen Mary Hospital were included. Baseline demographics, blood parameters and urinalysis results were recorded. Renal response and LLDAS attainment were assessed at 12 months after LN diagnosis. CRR was defined as proteinuria ≤0.5g/day with normal estimate glomerular filtration rate (eGFR); PRR was defined as a reduction in proteinuria by ≥50% with near normal eGFR. LLDAS was attained by meeting: (1) SLE Disease Activity Index ≤4 with no major organ activity; (2) no new lupus disease; (3) physician global assessment ≤1; (4) prednisolone dose ≤7.5mg; (5) standard maintenance immunosuppressants1. Treatment response was defined as proteinuria reduction of ≥50% or to sub-nephrotic range. Relapse was defined as a biopsy-proven active LN on histology after an initial treatment response. Time-to-relapse survival analysis was performed to compare the significance of CRR/PRR and LLDAS attainment.

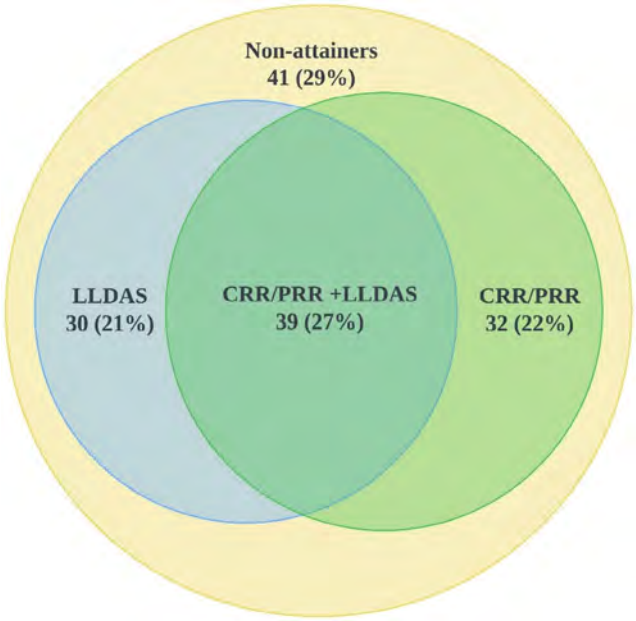

Figure 1: Attainment of CRR/PRR and/ or LLDAS at 12 months.

Results: A total of 143 LN patients were included with a median follow-up duration of 10.4 years (Table 1). At 12 months, 57 (40%), 14 (10%) and 69 (48%) patients achieved CRR, PRR and LLDAS, respectively. Although 39 (27%) patients attained both CRR/PRR and LLDAS, a significant number of 30 (21%) patients reached LLDAS without meeting CRR/PRR (Figure 1). Among 136 patients who achieved the pre-defined treatment response, 30 (22%) patients developed LN relapse after a median of 2.98 years. Patients reaching either CRR/PRR or LLDAS had a significantly lower risk of relapse (CRR/PRR: HR = 0.34, p = 0.02 ; LLDAS: HR = 0.28, p = 0.003). The attainment of both CRR/PRR and LLDAS was associated with the lowest risk of relapse (Figure 2).

Conclusion: We advocate LLDAS as a target for LN patients as LLDAS attainment lowers the risk of future relapse.

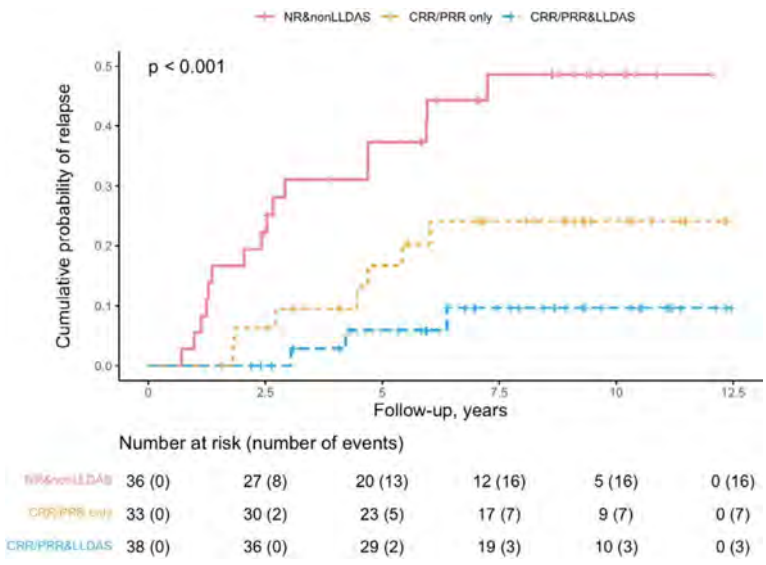

Figure 2: Risk of LN relapse.

Table 1: Baseline characteristics of 143 patients with biopsy-proven lupus nephritis

Characteristics	Number (%) or median (IQR)
Sex (female)	131/143 (92%)
Age of SLE at diagnosis	27 (15)
Follow up duration	10.44 (4.38)
24huP(g) or UPCR (mg/mg)	1.6 (1.2)
Serum albumin (g/L)	32 (7)
Serum creatinine (μmol/L)	64 (35)
eGFR (mL/min/1.73m²)	98 (56)
History of Lupus Nephritis	55/143 (38%)
WHO classes	
Class III (+/- V)	38/143 (27%)
Class IV (+/- V)	68/143 (48%)
Pure Class V	24/143 (17%)
CKD categories	
CKD1	83/143 (56%)
CKD2	35/143 (24%)
CKD3	19/143 (13%)
CKD4	3/143 (2%)
CKD5	3/143 (2%)
Presence of antibodies	
Anti-dsDNA	119/143 (83%)
Anti-Smith	23/129 (18%)
Anti-Ro	63/129 (49%)
Anti-La	13/129 (10%)
Anti-RNP	41/129 (32%)
Titre of immunological factors	
C3 (mg/dL)	51 (29)
C4 (mg/dL)	10 (9)
Anti-dsDNA (IU/mL)	190 (256)
Induction medication	
Mycophenolate Mofetil	105/143 (73%)
Azathioprine	13/143 (9%)
Calcineurin inhibitors	6/143 (4%)
Cyclophosphamide	2/143 (1%)
Hydroxychloroquine	78/143 (55%)

C3= Complement 3, C4= Complement 4, CKD= Chronic Kidney Disease, dsDNA= double stranded DNA, eGFR=estimated glomerular filtration rate, UPCR= Urinary protein-creatinine ratio, 24huP=24-hour urine protein,
eGFR calculated by MDRD formula

Disclosure: C. Cheung: None; **C. Lau**: AstraZeneca, 6, 12, external expert for SLE sterring committee 11.2022; **S. Chan**: None.

Abstract Number: 2275

Lupus Low Disease Activity State Ameliorates the Poor Prognosis in Lupus Nephritis Patients with anti-Sm Autoantibody

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-Sm autoantibody has been a known specific biomarker of systemic lupus erythematosus (SLE). There have been reports about its correlation with higher disease activity, renal involvement, and lower lupus low disease activity state attainment (LLDAS) among SLE patients. However, its exact role in renal outcome among patients with known lupus nephritis (LN) has been uncertain. This study adds to the literature in the role of Anti-Sm in relation to its prognostic value among patients with lupus nephritis. We also investigate the effect of LLDAS among patients with anti-Sm.

Methods: Patients with biopsy-proven LN during 2010-2020 were included. Baseline demographics, blood parameters and urinalysis results were recorded. Immunological markers such as autoantibodies profile were also documented. Complete or partial renal response (CRR/PRR) and LLDAS was assessed at 12 months post-LN, and any future relapses were recorded. LLDAS was attained by meeting: (1) SLE Disease Activity Index ≤4 with no major organ activity; (2) no new lupus disease; (3) physician global assessment ≤1; (4) prednisolone dose ≤7.5mg; (5) standard maintenance immunosuppressants. Relapse was a biopsy-proven LN after an initial treatment response of proteinuria reduction of ≥50% to sub-nephrotic range. Predictors of LLDAS and relapse were tested by logistic regression and COX regression respectively.

Table 1: Predictors of LN relapse

Table 1. Predictors of LN relapse

Predictors	Number (%) with relapse	Univariable COX regression		Multivariable COX regression	
		CHR (95% CI)	*p*-value	AHR (95% CI)	*p*-value
Sex					
female	27/125 (22%)	ref			
male	3/11 (28%)	1.33 (0.40-4.39)	0.64		
Age at LN onset		1.00 (0.97-1.03)	0.99		
History of LN					
first LN	12/66 (18%)	ref			
relapse LN	18/70 (26%)	1.32 (0.64-2.75)	0.45		
ISN/RPS LN classes					
class III (+/- V)	10/37 (27%)	ref			
class IV (+/- V)	15/64 (23%)	0.89 (0.34-1.97)	0.77		
pure class V	4/23 (17%)	0.56 (0.18-1.79)	0.33		
24huP(g) or UPCR (mg/mg)					
<3g	20/109 (18%)	ref			
≥3g	10/27 (37%)	2.23 (1.06-4.83)	**0.04**	1.68 (0.74-3.82)	0.22
Serum albumin (g/L)		0.94 (0.88-1.00)	0.05	0.96 (0.89-1.03)	0.20
Serum creatinine (μmol/L)		1.00 (0.98-1.01)	0.53		
Immunological factors					
Anti-Sm					
never	20/104 (19%)	ref			
ever	9/25 (36%)	2.26 (1.03-4.98)	**0.04**	2.34 (1.06-5.20)	**0.04**
Anti-dsDNA (IU/mL)					
normal	6/25 (24%)	ref			
elevated	24/111 (22%)	1.04 (0.43-2.55)	0.93		
C3 (mg/dL)					
normal	5/20 (25%)	ref			
low	25/116 (22%)	0.87 (0.33-2.27)	0.77		
Induction medication					
CNI					
no	30/131 (23%)	ref			
yes	0/5 (0%)	0.47 (0-395)	0.51		

AHR=adjusted hazard ratio; CHR=crude hazard ratio; CI=Confidence Interval; CNI=Calcineurin inhibitors; C3=Complement 3; ISN/RPS= International Society of Nephrology/Renal Pathology Society, LLDAS=Lupus low disease activity state; LN=Lupus nephritis; SLE=Systemic lupus erythematosus; Sm=Smith.
Significant *p* values are in bold.

Table 2: Predictors of LLADAS attainment at 12 months

Table 2. Predictors of LLDAS attainment at 12 months

Predictors	Number (%) in 12m LLDAS	Univariable logistic regression		Multivariable logistic regression	
		COR (95%CI)	*p*-value	AOR (95%CI)	*p*-value
Sex					
female	64/131 (49%)	ref			
male	5/12 (42%)	0.75 (0.23-2.48)	0.63		
Age at LN onset		1.00 (0.98-1.02)	0.88		
History of LN					
first LN	37/69 (54%)	ref			
relapse LN	32/74 (43%)	0.66 (0.34-1.28)	0.22		
ISN/RPS LN classes					
class III (+/- V)	18/38 (47%)	ref			
class IV (+/- V)	32/68 (47%)	0.99 (0.45-2.19)	0.98		
pure class V	11/24 (46%)	0.94 (0.34-2.62)	0.91		
24huP(g) or UPCR (mg/mg)					
<3g	58/116 (50%)	ref			
≥3g	11/27 (40%)	0.69 (0.29-1.61)	0.39		
Serum albumin (g/L)		1.04 (0.98-1.11)	0.20		
Serum creatinine (μmol/L)		1.00 (0.99-1.00)	0.25		
Immunological factors					
Anti-Sm					
never	55/111 (52%)	ref			
ever	7/25 (28%)	0.36 (0.14-0.92)	**0.03**	0.34 (0.13-0.89)	**0.03**
Anti-dsDNA (IU/mL)					
normal	16/27 (59%)	ref			
elevated	53/116 (46%)	0.58 (0.25-1.35)	0.21		
C3 (mg/dL)					
normal	14/21 (67%)	ref			
low	55/122 (45%)	0.41 (0.16-1.09)	0.07	0.45 (0.16-1.26)	0.13
Induction medication					
CNI					
no	64/137 (47%)	ref			
yes	5/6 (83%)	5.70 (0.65-50)	0.12		

AOR=adjusted odds ratio; COR=crude odds ratio; CI=Confidence Interval; CNI=Calcineurin inhibitors; C3=Complement 3; ISN/RPS= International Society of Nephrology/Renal Pathology Society, LLDAS=Lupus low disease activity state; LN=Lupus nephritis; SLE=Systemic lupus erythematosus; Sm=Smith.
Significant *p* values are in bold.

Results: A total 143 patients were included in this study. Anti-Sm positivity was present in 25 patients. Nephrotic range proteinuria and the presence of anti-Sm autoantibody were significant predictors of relapse in the univariable COX model. Only anti-Sm autoantibody was significant ($p = 0.04$) at the multivariable analysis. Anti-Sm autoantibody was the only variable found to predict LLDAS attainment ($p = 0.03$). Patients with anti-Sm had lower chance of LLDAS attainment (odds ratio = 0.34) with higher risk of subsequent relapse (hazard ratio = 2.34) compared to anti-Sm negative patients. Despite this, LLDAS attainment complementary to CRR/PRR was still found to be protective from future relapse ($p < 0.001$).

Conclusion: Patients with anti-Sm belonged to a high-risk subgroup with worse prognosis, yet LLDAS attainment could still prevent subsequent relapse among them.

Disclosure: C. Cheung: None; **C. Lau**: AstraZeneca, 6, 12, external expert for SLE sterring committee 11.2022; **S. Chan**: None.

Abstract Number: 2276

Patient Reported Impact of Lupus on Quality of Life

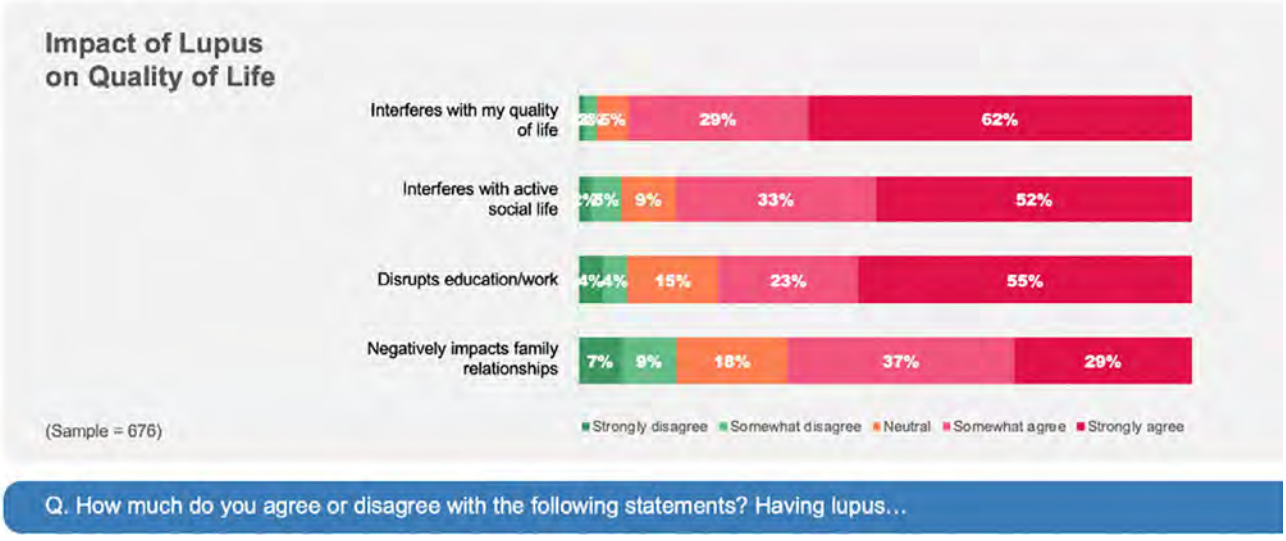
Beth Schneider, MyHealthTeam, San Francisco, CA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

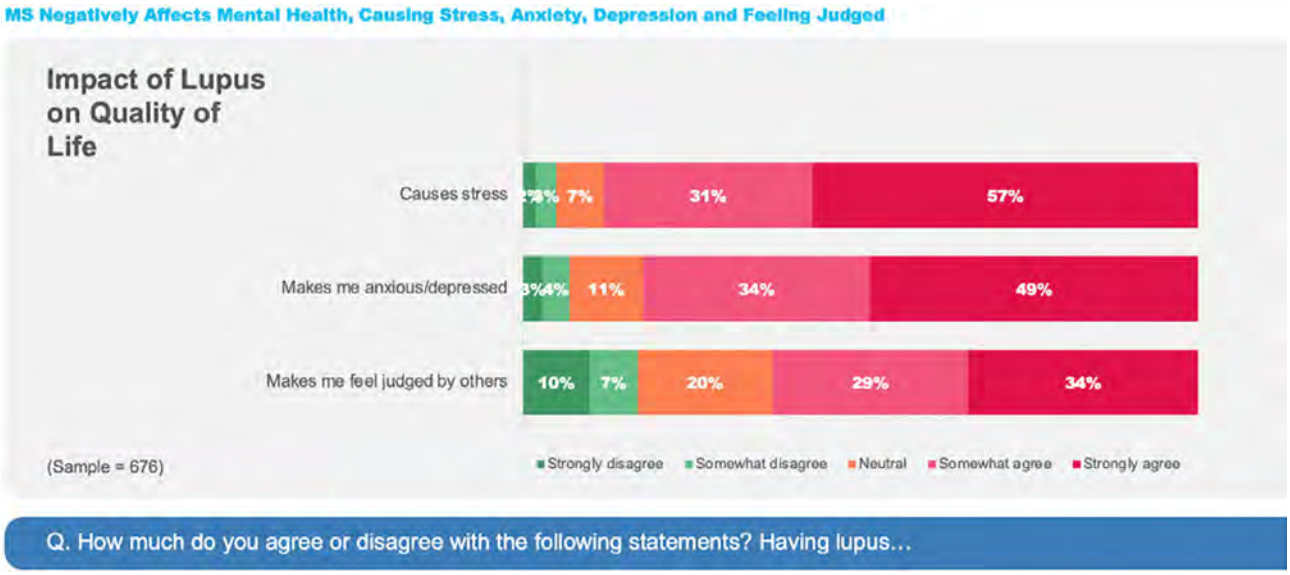
Background/Purpose: Research was undertaken to better understand how people living with lupus describe its sum total impact on their lives including work, challenges with relationships and its toll on mental health.

Methods: In August 2022, an email invitation to an online survey was sent to US members of MyLupusTeam, a social network of over 218,000 members. In total, 676 members diagnosed with *systemic lupus*erythematosus completed the 31-question survey regarding experiences with lupus and impact of the disease on everyday life.

Results: The far-reaching impact of lupus was evident in that most reported that lupus had a negative impact on overall quality of life (91%), interferes with their social life (84%), disrupts education/work (78%), and negatively impacts family relationships (66%). These lupus patients also found it hard to do everyday chores (89%) and hard to get around physically (79%). In total, only 7% felt their lupus related health was excellent or very good. "*The pain that I have means I can't do anything.*"The emotional toll of lupus manifested in feeling stressed (88%), anxious/depressed (83%) or judged by others (63%). In fact, a large number indicated depression (52%), or anxiety (55%) as diagnosed comorbidities. "*Visible symptoms appear on our faces or bodies that cause us to feel so low and embarrassed to show our faces in public.*" Despite the many obstacles, respondents were proactive in managing lupus.Most were able to stay on their prescribed medications (83%). And only 12% are not on any medication to treat lupus and its symptoms.However, 32% struggled to afford their medical expenses and these patients were much more likely be in poor health (75% versus 55% among those who could easily afford their medications).



Impact of Lupus on Quality of Life



Impact of Lupus on Mental Health

Conclusion: Understanding the physical, emotional, and quality of life impact of lupus, can help rheumatologists provide a more holistic approach to treating lupus patients. This includes listening to patient concerns and addressing the symptoms of lupus, including pain, depression, and fatigue, and not just disease progression. Importantly, by addressing the mental health aspects of lupus, rheumatologists can help create better health outcomes, including effective self-care regimens and an improved quality of life.

Disclosure: B. Schneider: None.

Abstract Number: 2277

Patients with Systemic Lupus Erythematosus: A Comparative Study Between Two Large, Multi-centric, Spanish and Argentinian Registers, Focused on Outcomes Differences

Iñigo Rúa-Figueroa[1], Rosana M Quintana[2], JULIA MARTINEZ BARRIO[3], Mercedes García[4], Maria Galindo-Izquierdo[5], Lucila Garcia[6], Jaime Calvo- Alén[7], Carla Gobbi[8], Esther Uriarte Isacelaya[9], Paula Alba[8], Eva Tomero Muriel[10], Verónica Bellomio[11], Mercedes Freire González[12], Susana Roverano[6], Victor Martinez-Taboada[13], Analia Patricia Alvarez[14], Eva Salgado-Pérez[15], Cesar Enrique Graf[16], Paloma Vela[17], Cecilia Pisoni[14], Antonio Fernandez-Nebro[18], Valeria Arturi[19], Clara Sanguesa Gomez[20], Catalina Gomez[14], Javier Narvaez[21], Zulema Plaza[22], Gregorio Santos Soler[23], Silvia Papasidero[24], José Ángel Hernández Beriain[25], Raul Paniego[6], Angela Pecondón[26], Maria Celina De La Vega[6], Oihane Ibarguengoitia-Barrena[27], Emma Civit[8], Gema Bonilla[28], Luciana Gonzalez Lucero[14], Vicente Torrente-Segarra[29], Maria Victoria Martire[6], Ana Paula Cacheda[30], Rodrigo Aguila Maldonado[14], Maria J. García-Villanueva[31], Sergio Gordon[14], Clara Moriano Morales[32], Marina Micelli[6], Loreto Horcada[33], Romina Nieto[34], Nuria Lozano Rivas[35], Gretel Rausch[14], Guillermo Pons-Estel[34] and Jose-Maria Pego-Reigosa[36], [1]Rheumatology, Hospital de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain, [2]Centro Regional de Enfermedades Autoinmunes y Reumticas (CREAR), Grupo Oroño, Rosario, Argentina, [3]Rheumatology, Gregorio Marañon University Hospital, Madrid, Spain, [4]Hospital Interzonal General de Agudos José de San Martín, La Plata, Argentina, [5]Rheumatology, University Hospital of 12 de Octubre, Madrid, Spain, [6]RELESSAR, CABA, Argentina, [7]Rheumatology, Bioaraba Research Unit, Hospital Universitario Araba, Vitoria, Spain, [8]RELESSAR, Cordoba, Argentina, [9]Rheumatology, University Hospital of Donosti, San Sebastián, Spain, [10]Rheumatology, Hospital La Princesa, Madrid, Spain, [11]RELESSAR, Tucuman, Argentina, [12]Rheumatology department, Complexo Hospitalario Universitario A Coruña (CHUAC). Instituto de Investigación Biomédica A Coruña (INIBIC), A Coruña, Spain, [13]Rheumatology, Hospital Marqués de Valdecilla, Santander, Spain, [14]Study Group of the Argentine Society of

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by multi-organ involvement, associated with substantial morbidity and mortality. A characteristic that distinguishes lupus patients is the aggressiveness of the disease, associated with worse outcomes, especially in certain ethnic groups. Patients of Afro-American ethnicity or Hispanics present more frequency of renal disease and higher damage accrual, as compared to Caucasians, and there is certain controversy regarding the factors that explain these differences and the relevance of the socio-economic status on there. **OBJETIVES:** To compare the clinical and serological features, treatments, outcomes and comorbidities of SLE patients from the cross-sectional phase of the Spanish lupus registry (RELESSER), those Latin American patients residing in Spain, who belong to the RELESSER register and patients from the Argentinian register (RELESSAR).

Methods: RELESSER and RELESSAR are large multicenter registries and share the same database, with identical definitions of the variables. Likewise, both include patients who meet the ACR /1997 classification criteria. The variables collected were: demographics, clinical, serology, comorbidities and treatments; disease activity index (SELENA-SLEDAI), damage (SLICC/ACR Damage Index (SDI). The Charlson Comorbidity Index was performed as well as Katz score. In RELESSER, Latin American patients were defined as those born in Latin American countries, whose Latin American parents have emigrated to Spain. Other ethnic groups of RELESSER were excluded from this analysis. The categorical variables were compared using Chi-square test or Fisher's test, and for the continuous variables, ANOVA or the Kruskal Wallis test were carried out. In cases where significant differences were found between the groups, and multiple comparisons were performed. The significance level < 0.05 was considered. R software was used for data analysis.

Results: A total of 5423 patients were included: 1475 in the RELESSAR group, 3627 in the Caucasian RELESSER, and 208 Latin-American from RELESSER. Table 1 shows the multiple comparisons between the groups. Latin-American patients irrespective of the country in which they live have a younger age, shorter duration of the disease with a shorter time to diagnosis, higher severity as measured by Katz Index, more frequency of nephritis, higher SLEDAI and higher use of corticosteroids treatment. However, RELESSER patients had showed higher frequency of comorbidities and hospitalizations.

Conclusion: Latin-American patients had severe disease, with higher frequency of renal involvement and use of corticosteroids, no matter the countryof residence suggesting that health resources would not be a good explanation for these differences. However, Spanish Caucasian patients have more mortality and infection, probably linked to lesser use of antimalarials and high degree of comorbidity.

Table 1. Comparison between RELESSAR patients, Latin-American RELESSER and Caucasian RELESSER.

	RELESSAR (N=1475)	Caucasian RELESSER (N=3627)	Latin-american RELESSER (N=208)	p-value	Total (N=5423)	RELESSAR vs Caucasian RELESSER	RELESSAR vs Latin American RELESSER	Caucasian RELESSER vs Latin-American RELESSER
Age at last evaluation, median [Q1, Q3]	37.6 [28.4, 48.0]	46.0 [36.7, 58.0]	36.3 [30.2, 46.0]	<0.001	43.6 [34.0, 54.9]	<0.001	0.300	<0.001
Female, n(%)[*2]	1352 (91.7)	3239 (89.4)	195 (93.8)	0.009	4887 (90.2)	0.047	0.369	0.087
Time to diagnosis (months), median [Q1, Q3][*864]	5.5 [2.2, 14.2]	9.2[3.0, 34.8]	5.9 [2.0, 17.5]	<0.001	7.4 [2.5, 24.7]	<0.001	0.928	0.003
Disease duration(months), median [Q1, Q3][*864]	73.5 [30.0, 144]	123 [60.7, 204]	71.1 [22.2, 127]	<0.001	107 [47.5, 187]	<0.001	0.200	<0.001
Charlson Comorbidity Index, median [Q1, Q3]	1.0 [1.0, 3.0]	2.0 [1.0, 3.0]	1.0[1.0, 2.0]	<0.001	2.0 [1.0, 3.0]	0.001	0.289	0.004
Clinical features, n (%)								
Malar rash [*258]	1134 (77.1)	1786 (51.2)	98 (50.3)	<0.001	3079 (58.5)	<0.001	<0.001	0.860
Discoid lupus [*206]	198 (13.6)	691 (19.9)	33 (17.2)	<0.001	937 (18.0)	<0.001	0.331	0.405
Photosensitivity [*227]	1077 (73.7)	1972 (57.3)	101 (52.9)	<0.001	3210 (61.8)	<0.001	<0.001	0.259
Oral ulcers [*224]	761 (52.2)	1480 (43.1)	78 (40.2)	<0.001	2361 (45.5)	<0.001	0.003	0.480
Arthritis [*170]	1204 (82.5)	2601 (74.7)	159 (79.5)	<0.001	4053 (77.2)	<0.001	0.354	0.222
Serous Involvement [*248]	820 (56.5)	1431 (41.7)	94 (48.2)	<0.001	2392 (46.2)	<0.001	0.047	0.086
Nephritis [*275]	624 (42.7)	965 (27.8)	78 (39.6)	<0.001	1709 (32.4)	<0.001	0.442	0.009
Neurological involvement [*200]	136 (9.3)	268 (7.7)	17 (8.7)	0.165	435 (8.3)			
Hematological Involvement [*184]	925 (62.8)	2659 (75.2)	151 (75.5)	<0.001	3816 (71.7)	<0.001	0.001	1.000
Anti DNA [*220]	975 (67.3)	2430 (70.3)	146 (75.6)	0.021	3636 (69.9)	0.061	0.061	0.135
Anti Sm [*193]	847 (66.7)	2732 (81.1)	133 (69.3)	<0.001	3790 (76.9)	<0.001	0.531	<0.001
ANA [*121]	42 (2.8)	47 (1.3)	2 (1.0)	<0.001	92 (1.7)	0.001	0.290	0.910
Hypocomplementemia	1197 (81.3)	2612 (75.5)	163 (84.5)	<0.001	4057 (78.3)	<0.001	1.000	0.006
SELENA-SLEDAI, Mean (SD)	3.14 (4.4)	2.39 (3.4)	3.69 (5.3)	<0.001	2.64 (3.8)	<0.001	0.134	<0.001

Continuation Table 1. Comparison between RELESSAR patients, Latin-American RELESSER and Caucasian RELESSER.

SDI, median [Q1, Q3]	1.0 [0, 1.0]	1.0 [0, 1.0]	0 [0, 1.0]	0.179	1.0 [0, 1.0]			
Corticosteroids use [*280]	1322 (96.1)	2929 (86.9)	174 (94.6)	<0.001	4520 (89.8)	<0.001	0.066	0.0009
Antimalarials use [*411]	1334 (97.4)	2748 (81.9)	148 (81.8)	<0.001	4321 (86.2)	<0.001	<0.001	1.000
Hospitalization [*253]	795 (53.9)	1918 (56.2)	123 (62.8)	0.044	2891 (55.7)	0.143	0.070	0.127
Hospitalization due to SLE [*285]	755 (52.1)	1805 (52.1)	121 (62.4)	0.019	2734 (52.4)	1.000	0.013	0.013
Serious infection [*367]	201 (14.3)	681 (20.3)	41 (21.2)	<0.001	936 (18.5)	<0.001	0.023	0.820
Refractory lupus	243 (16.5)	813 (22.4)	50 (24.0)	<0.001	988 (18.2)	<0.001	0.014	0.645
Katz Index, median [Q1, Q3]	3.0 [2.0, 4.0]	2.0 [1.0, 4.0]	3.0 [2.0, 5.0]	<0.001	3.0 [1.0, 4.0]	<0.001	0.618	0.012
Mortality [*445]	39 (2.7)	207 (6.3)	8 (4.4)	<0.001	<0.001	<0.001	0.371	0.371

SELENA-SLEDAI (disease activity index); SDI (Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index); ANA (Antinuclear antibodies); anti-Sm (Smith antibodies); Hypocomplementemia (C3 and/or C4 low); Anti DNA (anti-DNA antibodies)

Disclosure: I. Rúa-Figueroa: AstraZeneca, 5, GSK, 1, 6; **R. Quintana**: None; **J. MARTINEZ BARRIO**: None; **M. García**: GSK, 6, Janssen, 6, Pfizer, 6; **M. Galindo-Izquierdo**: None; **L. Garcia**: None; **J. Calvo- Alén**: AbbVie, 2, AstraZeneca, 2, Biogen, 6, BMS, 5, Galapagos, 6, GSK, 2, 6, Lilly, 2, 6, Novartis, 2, 6, Roche, 5, Sanofi, 2; **C. Gobbi**: None; **E. Uriarte Isacelaya**: None; **P. Alba**: None; **E. Tomero Muriel**: None; **V. Bellomio**: None; **M. Freire González**: None; **S. Roverano**: None; **V. Martinez-Taboada**: None; **A. Alvarez**: None; **E. Salgado-Pérez**: None; **C. Graf**: None; **P. Vela**: None; **C. Pisoni**: None; **A. Fernandez-Nebro**: None; **V. Arturi**: None; **C. Sanguesa Gomez**: None; **C. Gomez**: None; **J. Narvaez**: None; **Z. Plaza**: None; **G. Santos Soler**: None; **S. Papasidero**: None; **J. Hernández Beriain**: None; **R. Paniego**: None; **A. Pecondón**: None; **M. De La Vega**: None; **O. Ibarguengoitia-Barrena**: None; **E. Civit**: None; **G. Bonilla**: None; **L. Gonzalez Lucero**: None; **V. Torrente-Segarra**: None; **M. Martire**: None; **A. Cacheda**: None; **R. Aguila Maldonado**: None; **M. García-Villanueva**: AstraZeneca, 6, GSK, 6, Otsuka, 1; **S. Gordon**: None; **C. Moriano Morales**: None; **M. Micelli**: None; **L. Horcada**: None; **R. Nieto**: None; **N. Lozano Rivas**: None; **G. Rausch**: None; **G. Pons-Estel**: None; **J. Pego-Reigosa**: None.

Abstract Number: 2278

Pregnancy in Connective Tissue Diseases: A 30 Year Follow-up Study of 465 Pregnancies from a Spanish Monocentric Registry

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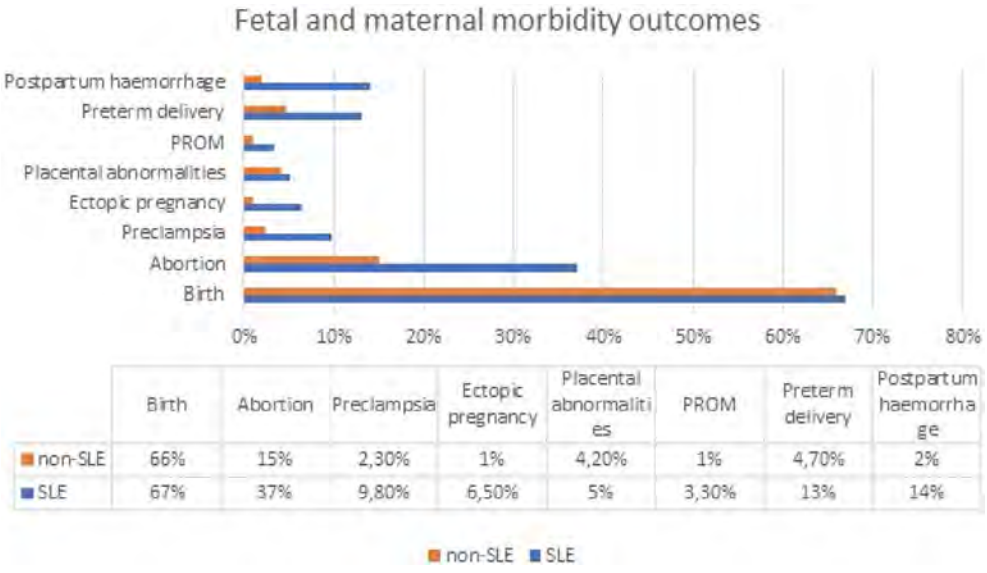
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Pregnancy in patients with connective tissue diseases are known to be at high risk for the occurrence of adverse pregnancy outcomes. We aim toevaluate the pregnancy outcomes in patients with systemic autoimmune diseases, including systemic lupus erythematosus (SLE), systemic sclerosis (SSc), primary Sjögren's syndrome (pSS) and undifferentiated connective tissue disease (UCTD).

	SLE	SSc	pSS	UCTD	P value
Total of pregnancies	192	88	120	65	
Age at pregnancy	32.4±4.5	29.5±7.2	30.4±3.5	33.5±2.7	0.45
Smokers	32 (26%)	17 (34%)	25 (31%)	12 (30%)	0.27
Birth	103 (67%)	68 (77%)	90 (75%)	47 (72%)	0.28
Abortion	57 (37%)	12 (14%)	18 (15%)	10 (15%)	**0.03**
Mean abortion number	2.7±0.7	1.1±0.6	2.4±0.3	0.9±0.5	**0.03**
Preeclampsia	15 (9.8%)	3 (3%)	2 (2%)	2 (3%)	**0.04**
Ectopic pregnancy	10 (6.5%)	0	1 (1%)	1 (2%)	**0.03**
Placental abnormalities	8 (5%)	5 (5.7%)	2 (2%)	3 (5%)	0.21
Premature rupture of membranes (PROM)	5 (3.3%)	0	2 (2%)	1 (2%)	0.24
Preterm delivery	20 (13%)	0	8 (6%)	5 (8%)	**0.02**
Postpartum haemorrhage	21 (14%)	0	4 (4%)	1 (2%)	**0.01**



	Birth	Abortion	Preclampsia	Ectopic pregnancy	Placental abnormalities	PROM	Preterm delivery	Postpartum haemorrhage
non-SLE	66%	15%	2,30%	1%	4,20%	1%	4,70%	2%
SLE	67%	37%	9,80%	6,50%	5%	3,30%	13%	14%

Methods: A retrospective and descriptive study was conducted from 1990 to 2020. All data were collected from the medical records of childbearing age women with SLE, SSc, SS and UTCD enrolled in our clinic at the time of their pregnancy and childbirth. The obstetric, maternal and fetal outcomes were collected and compared regarding diagnosis and adverse outcomes.

Results: The study group included 295 patients, 125 patients (42%) with SLE, 50 patients (17%) with SSc, 80 patients (27%) with Sjogren's, 40 patients (14%) with UCTD.A total of 465 pregnancies were registered. The maternal and fetal outcomes are detailed in table 1 and figure 1. The mean age at delivery was 31.5±8.5 years and the mean duration of disease was 7.2±5.6 years. Pregnancy loss occurred in 21% of patients, live births in 66% of pregnancies, preterm delivery in 8%, postpartum haemorrhage in 6%, preeclampsia in 5%, placental abnormalities in 4%, ectopic pregnancy in 3%, premature rupture of membranes in 2%.Treatment with HCQ was received in 115 pregnancies in SLE (59%), 21 pregnancies in SSc (24%) 62 pregnancies in pSS (52%) and 32 pregnancies in UCTD (49%). Exposure to corticosteroids and biologics during pregnancy was 23 (18.4%), 6 (12%), 15 (19%) and 3 (7.5%), respectively. Patients with SLE had a higher risk of fetal morbidity, including abortion (p=0.03), mean abortion rate (p=0.03), preeclampsia (p=0.04), ectopic pregnancy (p=0.03), preterm delivery (p=0.02) and postpartum haemorrhage (p=0.01) than patients without SLE. The multivariate model adjusted for age, nulliparity, active disease activity during pregnancy, smoking and exposure to biologics, HCQ and corticosteroids found an association between unfavourable pregnancy outcomes and disease activity (OR 2.4 95% CI (1.3-7.2), p 0.003), whilst HCQ during pregnancy (OR 0.23 95% CI (0.03-0.82) had a protective effect.

Conclusion: 66% of pregnancies in patients with autoimmune diseases resulted in live births. Patients with SLE had higher rates of fetal and maternal morbidity than SSc, pSS and UCTD. Disease activity was associated with unfavourable pregnancy outcomes. Exposure to HCQ had a protective effect during pregnancy. Pregnancy planning and counselling prior to conception of patients with connective tissue diseases leads to a reduction in maternal and perinatal complications.

Disclosure: C. Sieiro Santos: None; **P. Pérez García**: None; **J. Ordas Martínez**: None; **C. Moriano**: None; **C. Álvarez Castro**: None; **E. Díez Álvarez**: None.

Abstract Number: 2279

Sociodemographic Features, Health-Related Quality of Life (HRQoL), Previous General Self-Efficacy and Corticosteroids (CS) Are Associated with General Self-Efficacy in Systemic Lupus Erythematosus (SLE) Patients. Data from a Prevalent Latin American Lupus Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Self-efficacy is the belief that one can carry out a behavior necessary to reach a desired goal. A better self-efficacy has been reported as a predictor of better clinical outcomes in SLE patients such as a better HRQoL. However, predictors of a better self-efficacy in SLE patients remain to be identified. The aim of this study is to determine the predictors of a better general self-efficacy in SLE patients.

Methods: Patients from a single-center Peruvian lupus cohort were included. General self-efficacy was measured with the Patient-Reported Outcomes Measurement Information System (PROMIS) general self-efficacy instrument. For this instrument, a score of 50 is the average for a clinical population, a higher score indicates a greater self-efficacy. Potential predictors examined were gender, age at diagnosis, ethnicity, socioeconomic status, educational level, disease duration, disease activity (ascertained with the SLEDAI-2K), damage (ascertained with the SLICC/ACR damage index, SDI), Charlson comorbidity index, CS as prednisone daily dose, antimalarials and immunosuppressive drugs use, HRQoL (assessed with the LupusQoL), fatigue (ascertained with the FACIT-F) and previous general self-efficacy. Univariable and multivariable generalized estimating equations (GEEs) were performed using general self-efficacy in the subsequent visit, and the potential predictive factors in the previous visit. A multivariable model was done using a backward selection procedure with an alpha to stay in the model of 0.05.

Results: 820 visits from 274 patients were included; 256 (93.4%) were women with a mean age at diagnosis of 35.5 (13.3) years. General self-efficacy at baseline was 47.0 (10.0) and during the follow-up it was 46.6 (10.1). In the multivariable model, age at diagnosis, non-White ethnicity, lower socioeconomic status and the daily prednisone dose were negatively associated with general self-efficacy; better physical health and previous general self-efficacy were positively associated with general self-efficacy (table 1)

Conclusion: Age at diagnosis, lower socioeconomic status, non-White ethnicity and the daily prednisone dose predicted a worse self-efficacy; a better physical health and previous general self-efficacy predicted a better general self-efficacy. Further studies are needed to define the best strategies to improve general self´-efficacy in SLE patients.

Table 1: Factors associated with general self-efficacy. Univariable and multivariable models

Variables*	B (SE)	p value	B (SE)	p value
Female gender	-1.33 (1.8)	0.465		
Age at diagnosis	-0.14 (0.04)	<0.001	-0.05 (0.02)	0.026
Ethnicity				
White	Ref.			
Black	-16.80 (3.17)	<0.001	-10.89 (1.31)	<0.001
Mestizo	-11.34 (1.81)	<0.001	-8.56 (0.54	<0.001
Socioeconomic status				
High	Ref.		Ref.	
Middle	-4.52 (1.01)	<0.001	-2.57 (0.55)	<0.001
Low	-5.35 (1.49)	<0.001	-2.00 (0.98)	0.042
Educational level, years	0.54 (0.20)	0.006		
Disease duration, years	-0.02 (0.07)	0.824		
SLEDAI-2K	0.19 (0.09)	0.044		
SDI	-0.30 (0.31)	0.332		
Charlson comorbidity index	-0.38 (0.25)	0.136		
Prednisone daily dose, mg/d	-0.26 (0.09)	0.002	-0.14 (0.05)	0.002
Antimalarials use				
Never	Ref.			
Past	-1.18 (1.74)	0.498		
Current	-2.38 (1.56)	0.127		
Immunosuppressive drugs use				
Never	Ref.			
Past	-1.49 (2.19)	0.496		
Current	-4.09 (1.45)	0.005		
General self-efficacy	0.54 (0.04)	<0.001	0.40 (0.05)	<0.001
LupusQol.				
Physical health	0.19 (0.02)	<0.001	0.08 (0.02)	<0.001
Pain	0.13 (0.02)	<0.001		
Planning	0.15 (0.02)	<0.001		
Intimate relationships	0.03 (0.01)	0.004		
Burden to others	0.08 (0.01)	<0.001		
Emotional health	0.13 (0.02)	<0.001		
Body image	0.04 (0.01)	0.003		
Fatigue	0.14 (0.02)	<0.001		
FACIT-F	0.41 (0.04)	<0.001		

*All variables were ascertained in the previous visit. SE=standard error. SDI: SLICC/ACR damage index

Disclosure: M. Ugarte-Gil: AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Janssen, 5, Pfizer, 5; **R. Gamboa-Cárdenas**: None; **C. Reategui-Sokolova**: None; **V. Pimentel-Quiroz**: None; **C. Elera-Fitzcarrald**: None; **J. Cucho-Venegas**: None; **C. Pastor-Asurza**: None; **Z. Rodriguez-Bellido**: None; **R. Perich-Campos**: None; **G. Alarcón**: None.

Abstract Number: 2280

The LFA-REAL Clinician Reported Outcome Predicts Damage in Patients with Systemic Lupus Erythematosus (SLE). Data from a Prevalent Latin American Lupus Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The Lupus Foundation of America Rapid Evaluation of Activity in Lupus (LFA-REAL) clinician-reported outcome (ClinRO) correlates well with other disease activity indices such us the SLEDAI-2K and the PGA; however, its predictive value remains to be evaluated. The aim of this study was to evaluate the predictive value of the LFA-REAL and damage accrual in SLE patients.

Methods: We evaluated SLEs patients from the Almenara Lupus Cohort, Lima, Peru. The LFA-REAL ClinRO includes nine domains: mucocutaneous, musculoskeletal, cardiorespiratory, neuropsychiatric, renal, hematological, constitutional, vasculitis and other. Mucocutaneous includes one global scale and three subdomains (rash, alopecia and mucosal ulcers), and musculoskeletal includes one global scale and two subdomains (arthralgia/arthritis and myalgia/myositis). For each manifestation, a Visual Analogue Scale (VAS) from 0 to 100 mm is used, with anchors separating mild, moderate and severe disease. Additionally, two possible summary results can be reported. The first one includes only individual manifestations and does not include the global measurement of mucocutaneous and musculoskeletal involvement; it ranges from 0 to 1400 (the sum of 14 VAS). The alternative option is to include only the global domains and not the individual manifestations; it ranges from 0 to 1100 (the sum of 11 VAS). Damage was assessed with the SLICC/ACR damage index (SDI). Generalized estimating equations were performed, using as the outcome any increase in the SDI and the LFA-REAL ClinRO in the previous visit; multivariable models were adjusted for possible confounders measured at the same visit as the self-efficacy instrument. Incidence Rate Ratio (IRR) was reported per 10 units increase in the LFA-REAL ClinRO. The main model was done using the first global LFA-REAL ClinRO; the alternative model was done using the alternative method to calculate the LFA-REAL ClinRO.

Results: A total of 456 patients and 1536 visits were included. The mean LFA-REAL ClinRO (0-1400) was 18.2 (SD 30.7); the mean alternative LFA-REAL ClinRO (0-1100) was 16.9 (SD 27.4) and the mean SLEDAI-2K was 2.5 (4.2). During the follow-up visits, 63 (13.8%) patients accrued damage once and four (0.9%) accrued damage twice. In the univariable and multivariable models, both LFA-REAL ClinRO predicted damage accrual (Table 1).

Conclusion: The LFA-REAL ClinRO is predictive of damage accrual, even after adjusting for possible confounders. Larger studies are needed to determine the relevance of this index for SLE patients

Table 1 The predictive value of LFA-REAL ClinRO on damage accrual in SLE patients

	Univariable model		Multivariable model	
	IRR (CI 95%)	p value	IRR (CI 95%)	p value
Main analyses				
LFA-REAL ClinRO (0-1400)	1.08 (1.02-1.14)	0.018	1.08 (1.02-1.14)	0.009
Alternative analyses				
LFA-REAL ClinRO (0-1100)	1.09 (1.02-1.17)	0.018	1.10 (1.02-1.18)	0.010

* Adjusted for age at diagnosis, gender, socioeconomic status, SLICC/ACR damage index, disease duration, prednisone daily dose, antimalarial and immunosuppressive drugs use in the previous visit.

Disclosure: M. Ugarte-Gil: AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Janssen, 5, Pfizer, 5; **R. Gamboa-Cárdenas**: None; **V. Pimentel-Quiroz**: None; **C. Reategui-Sokolova**: None; **C. Elera-Fitzcarrald**: None; **E. Noriega**: None; **C. Pastor-Asurza**: None; **Z. Rodriguez-Bellido**: None; **R. Perich-Campos**: None; **G. Alarcón**: None.

Abstract Number: 2281

Epidemiology and Risk of Brain Abscess in Patients with Systemic Lupus Erythematosus in Taiwan: A Nationwide Population-based Study

Ke-Hung Lin[1], Tzu-Min Lin[1] and Chi-Ching Chang[2], [1]Taipei Medical University Hospital, Taipei, Taiwan, [2]Taipei Medical University, Taipei, Taiwan

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune systemic disorder with high morbidity and mortality. Although CNS infections account for only 0.53–2.25% of all infections in patients with SLE, the mortality rate associated with infections of the central nervous system (CNS) such as meningitis and brain abscess (BA) has been reported to be 26.3–52.2%.However, in spite of increased understanding of SLE, many questions (such as epidemiology and risk factors of BA) remain unanswered. Up to date, no study has specifically examined the risk of BA in patients with SLE.We conducted a nationwide population-based cohort study to determine trends in the incidence, mortality and potential risk factors of brain abscess among patient with SLE in Taiwan from 2006 through 2018.

Methods: We identified systemic lupus erythematosus patients from the National Health Insurance research-oriented database, and compared the incidence rate of brain abscess with that among non-systemic lupus erythematosus controls. A Cox multivariable proportional hazards model was employed to evaluate the risk of BA the systemic lupus erythematosus cohort

Results: We included 11,457 SLE patients and 57,285 non-SLE (mean age 42.36 yr, standard deviation 16.66yr; 85.46 % were women). After a mean follow-up of more than six years, the systemic lupus erythematosus cohort had a significantly higher incidence rate of BA (28.83 vs 3.08 per 100,000 person-years, incidence rate ratio 9.36, p<0.001, Table 1) than that

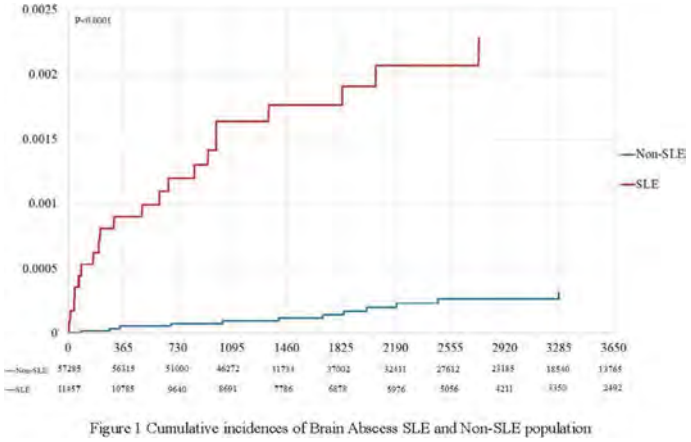

Figure 1 Cumulative incidences of Brain Abscess SLE and Non-SLE population

Figure 1 Cumulative incidences of Brain Abscess SLE and Non-SLE population

Table 1 Cox regression analysis for the adjusted risk of brain abscess

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				Univariate analysis			Multivariate analysis		
	event	Person-year*	IR	HR	95% CI	P-value	HR	95% CI	P-value
Non-SLE	12	389999.21	3.08	1			1		
SLE	21	72841.37	28.83	9.23	4.54~18.77	<.0001	7.33	3.45~15.58	<.0001
Gender									
Male	12	59959.65	20.01	1			1		
Female	21	402880.9	5.21	3.67	1.8~7.46	0.0003	2.84	1.37~5.91	0.0051
Age									
<40	10	249713.3	4.00	1			1		
40-65	14	174352.5	8.03	1.93	0.86~4.34	0.1137	1.53	0.66~3.56	0.3190
≥65	9	38774.77	23.2	4.95	2.00~12.34	0.0005	2.57	0.87~7.62	0.0878
Comorbidity									
No Alcoholism	33	462483.1	7.1	1			1		
Alcoholism	0	357.44	0	NA	NA	0.9867	NA	NA	0.9916
No Diabetes mellitus	28	439486.9	6.4	1			1		
Diabetes mellitus	5	23353.72	21.4	3.18	1.23~8.23	0.0173	1.63	0.58~4.57	0.3551
No Hypertension	24	410934.3	5.8	1			1		
Hypertension	9	51906.3	17.3	2.71	1.26~5.84	0.0109	0.75	0.3~1.86	0.5350
No Chronic kidney disease	28	455899.6	6.1	1			1		
Chronic kidney disease	5	6940.96	72.0	9.90	3.80~25.75	<.0001	2.20	0.77~6.28	0.1417
No Heart failure	29	458843.1	6.3	1			1		
Heart failure	4	3997.45	100.1	13.70	4.80~39.08	<.0001	3.47	1.1~10.93	0.0339
No Ischemia heart disease	29	448126.8	6.5	1			1		
Ischemia heart disease	4	14713.78	27.2	3.90	1.37~11.09	0.0108	1.25	0.39~3.93	0.7088
No Stroke	NA	NA	6.8	1			1		
Stroke	NA	NA	21.8	2.87	0.69~12.00	0.1489	0.93	0.21~4.1	0.9251
No HIV	33	462409.9	7.1	1			1		
HIV	0	430.64	0	NA	NA	0.9864	NA	NA	0.9938
No Liver disease	27	448289.1	6.0	1			1		
Liver disease	6	14551.44	41.2	6.43	2.65~15.57	<.0001	2.09	0.83~5.27	0.1197
No Cancer	28	443752.9	6.3	1			1		
Cancer	5	19087.69	26.2	3.95	1.52~10.23	0.0047	2.35	0.87~6.35	0.0914

1: adjust for SLE, age, sex, alcoholism, diabetes mellitus, hypertension, chronic kidney disease, heart failure, ischemia heart disease, stroke, HIV, liver disease.

of the control cohort.Kaplan–Meier analysis also revealed a significantly higher cumulative incidence of BA in the SLE patients than in the matched controls (p<0.001; Figure 1). Multivariate Cox regression analysis of the SLE and control cohorts (Table 2) revealed that SLE remained a significant risk factor even after other variables were adjusted (adjusted hazard ratio [HR] 7.33, 95% confidence interval [CI] 3.45∼15.58,p<0.001). Cox multivariate proportional hazards analysis revealed heart disease (adjusted HR 4.21, [CI] 1.23∼14.44), and receiving a mean prednisolone dose >7.5mg (adjusted HR 23.92, [CI] 2.97∼192.44) were independent risk factors for brain abscess in systemic lupus erythematosus patients.

Conclusion: A higher risk of BA was observed in systemic lupus erythematosus patients. Risk factors for BA in the systemic lupus erythematosus cohort included heart disease, and receiving a mean prednisolone dose >7.5mg

Table 2 Cox regression analysis for the risk of Brain Abscess among systemic lupus erythematosus patients.

Table 2 Cox regression analysis for the risk of Brain Abscess among systemic lupus erythematosus patients.

	Crude HR	95% CI	P-value	Adjust HR*	95% CI	P-value
Gender						
Female	2.01	0.74~5.5	0.1722			
Age (ref: 40-49)						
<20	0.87	0.11~7.23	0.8978			
20-29	0.58	0.16~2.06	0.4025			
30-39	0.41	0.1~1.65	0.2091			
50-59	0.49	0.1~2.42	0.3810			
60-69	1.03	0.21~5.12	0.9684			
70-79	1.52	0.31~7.54	0.6092			
≥80	1.91	0.23~16.03	0.5498			
Comorbidity						
Alcoholism	NA	NA	0.9907			
DM	0.90	0.12~6.69	0.9160			
Hypertension	1.27	0.47~3.47	0.6389			
Chronic kidney disease	3.11	1.04~9.27	0.0416			
Heart failure	4.48	1.32~15.24	0.0163	4.21	1.23~14.44	0.0222
IHD	1.84	0.43~7.92	0.4110			
Stroke	1.07	0.14~7.99	0.9465			
HIV	NA	NA	0.9912			
Liver disease	2.69	0.99~7.35	0.0534			
Cancer	2.14	0.5~9.18	0.3062			
Predisposing factors						
Congenital heart disease	NA	NA	0.9927			
Head trauma	NA	NA	0.9899			
Septicemia /Sepsis	3.72	1.09~12.68	0.0357			
Renal transplantation	NA	NA	0.9923			
ENT infections	0.95	0.37~2.45	0.9147			
Dental infection	0.89	0.38~2.12	0.7948			
Infections of prosthetic devices, implants and grafts	7.74	1.04~57.71	0.0459			
Treatment						
Azathioprine	0.40	0.16~0.99	0.0483			
Cyclosporine	0.39	0.05~2.87	0.3522			
Cyclophosphamide-oral	0.61	0.08~4.52	0.6250			
Cyclophosphamide-IV	1.36	0.46~4.06	0.5763			
Hydroxychloroquine	0.36	0.12~1.08	0.0685			
Methotrexate	NA	NA	0.9893			
Mycophenolate mofetil	0.64	0.15~2.76	0.5529			
Mean Prednisolone dose>7.5mg	27.73	3.52~218.54	0.0016	23.92	2.97~192.44	0.0028
Steroid-IV	0.74	0.25~2.19	0.5805			

*Adjust for SLE, age, sex, alcoholism, diabetes mellitus, hypertension, chronic kidney disease, heart failure, ischemia heart disease, stroke, HIV, liver disease, select variable by Stepwise model

Disclosure: K. Lin: None; **T. Lin**: None; **C. Chang**: None.

Abstract Number: 2282

Increased Risk of Systemic Lupus Erythematosus Flare After COVID-19

Arthur Mageau[1], Christel Gerardin[2], Kankoe Sallah[2], Jean-Francois Timsit[1], Thomas Papo[1] and Karim Sacre[1], [1]Université Paris Cité, Paris, France, [2]Assistance Publique Hopitaux de Paris, Paris, France

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The SARS-CoV2 pandemic reopened the unresolved question of whether and how a viral infection can trigger flares of immune-mediated inflammatory diseases such as systemic lupus erythematosus (SLE). We aimed to analyze the risk of lupus flare after admission for COVID-19.

Methods: We performed a matched cohort study using the Assistance Publique - Hôpitaux de Paris Clinical Data Warehouse which collects medical, biological and administrative information from 11 million patients in Paris area. Each SLE patient hospitalized with COVID-19 between March 2020 and December 2021 was matched to one SLE control patient on age ±3years,gender,chronickidneydisease,end-stage renal disease, and lupus biology. The main outcome was a lupus flare during the 6 months follow-up. A flare was considered if a) documented by the treating physician and b) justifying a change in SLE treatment. The electronic health records were individually checked for data accuracy.

Results: Among 4,533 SLE patients retrieved from the database, 81 have been admitted for a COVID-19 between March 2020 and December 31, 2021 from whom 79 (n=79/81,97.5%) were matched to 79 unique unexposed SLE patients (Table 1). A flare occurred in 14 (17.7%) SLE patients from the COVID-19 group as compared to 5 (6.3%) in the unexposed control group, including 4 lupus nephritis in the exposed group and 1 in the control group. After adjustment for HCQ use at index date and history of lupus nephritis, the risk of flare was higher in exposed SLE patients (hazard ratio [95% confidence interval] of 3.79 [1.49-9.65]).

Table 1 Characteristics of the matched populations Q1: first quartile; Q3: third quartile; CKD: Chronic kidney disease defined as an eGFR < 60mL/min and no end-stage renal disease; ESRD: End-stage renal disease defined as chronic dialysis or renal transplantation; IS: immunosuppressive; SMD: standardized mean differences. Lupus nephritis classes refer to the ISN/RPSWG classification (25). ┼C3 levels and anti-dsDNA IgG titers measured in the serum at the latest 6 months prior the index date were considered. When performed, lupus biology was defined as either normal - when both C3 level and anti-dsDNA IgG titer were into the normal range – or abnormal – when C3 level was low and/or anti-dsDNA IgG titer was high. * Matching variables. ǂ SLE treatment modification during the six months before the index date or during COVID episode.

	COVID-19 n = 79	No COVID-19 n=79	Absolute SMD
Age, in years*, median (Q1-Q3)	56.3 (40.6-68.3)	55.9 [39.7-68.2]	0.003
Female gender*, n (%)	76 (96.2)	76 (96.2)	0.000
Black ethnicity, n (%)	30 (45.4)	24 (36.4)	0.185
Comorbidities			
CKD*, n (%)	22 (27.9)	22 (27.9)	0.000
ESRD*, n (%)	15 (18.9)	15 (18.9)	0.000
SLE disease			
Years from SLE diagnosis, median [Q1-Q3]	14.2 [5.6-22.3]	11.8 [6.8-24.8]	0.035
History of lupus nephritis, n (%)	37 (48.1)	31 (39.7)	0.153
class III/IV nephritis, n (%)	24 (31.2)	22 (28.6)	0.056
Lupus biology during the last 6 months*‡, n (%)			0.022
Normal	29 (36.7)	30 (36.7)	
Abnormal	35 (44.3)	34 (43.0)	
Not performed	15 (18.9)	15 (18.9)	
SLE treatment at index date			
Hydroxychloroquine, n (%)	51 (65.4)	60 (75.9)	0.251
Steroids, n (%)	53 (67.9)	54 (68.3)	0.027
Prednisone equivalent daily dose, if any (mg/d)	5 [5-9]	7 [5-10]	0.109
IS drug, n (%)	31 (39.2)	32 (40.5)	0.025
Mycophenolate mofetil	22 (28.2)	20 (25.3)	
Azathioprine	5 (6.4)	9 (11.4)	
Rituximab	6(7.7)	5(6.4)	
Recent modification of SLE treatment ǂ, n (%)	24 (30.4)	23 (29.1)	0.028
Follow-up			
Death during follow-up, n (%)	11 (14.0)	3 (3.8)	

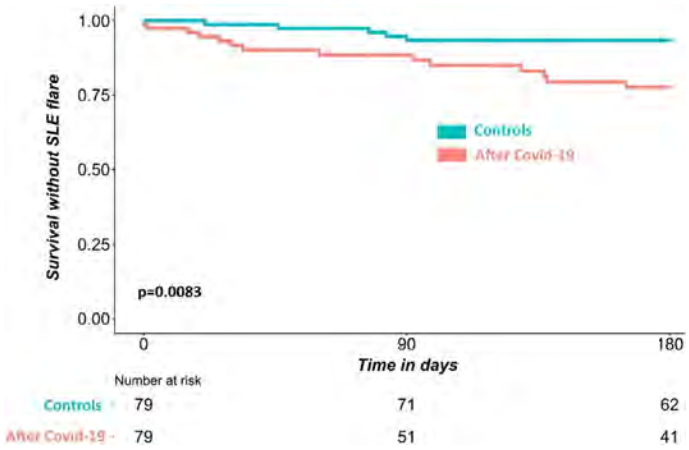

Figure 1 Kaplan-Meier curves of the survival without flare among the matched populations P value was calculated with the log rank test.

Conclusion: COVID-19 increases the risk of lupus flare.

Disclosure: A. Mageau: None; **C. Gerardin**: None; **K. Sallah**: None; **J. Timsit**: None; **T. Papo**: None; **K. Sacre**: None.

Abstract Number: 2283

Anti-SARS-CoV-2 Vaccination Among Patients Living with Systemic Lupus Erythematosus in Sweden: Coverage and Clinical Effectiveness

Arthur Mageau[1], Julia Simard[2], Elisabet Svenungsson[3] and Elizabeth Arkema[4], [1]Department of Medicine Solna, Clinical Epidemiology Division, Karolinska Institutet, Stockholm, Sweden / Internal Medicine Unit, Hopital Bichat, Paris, France, [2]Department of Epidemiology & Population Health, Stanford University School of Medicine, Stanford, CA, [3]Department of Medicine Solna, Unit of Rheumatology, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden, [4]Department of Medicine Solna, Clinical Epidemiology Division, Karolinska Institutet, Stockholm, Sweden

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Real-world data assessing the effectiveness of the anti-SARS-CoV2 vaccination in patients living with systemic lupus erythematosus (SLE) are currently lacking. We aimed to describe the uptake of the anti-SARS-CoV2 vaccination in 2021 and to investigate its clinical effectiveness in SLE patients living in Sweden.

Methods: First, we described the cumulative incidence of first anti-SARS-CoV2 vaccination among SLE patients and matched comparators living in Sweden on January 1, 2021 using the nationwide Swedish National Patient Register (NPR) and the National Vaccination Register. To assess vaccine effectiveness, we restricted the population to SLE patients and comparators i) with no COVID-19 diagnosis code before the 2nd vaccine dose and ii) who received two doses of anti-SARS-CoV2 mRNA vaccines before January 1st, 2022. The main outcome was a first hospitalization with COVID-19 as main diagnosis in the NPR. The secondary outcome was defined as first COVID-19 diagnosis in inpatient or outpatient care, as main or secondary diagnosis. Rates of main and secondary outcomes were compared between SLE patients and comparators. Multivariable-adjusted marginal Cox models estimate hazard ratios and 95% confidence intervals (HR;95%CI) overall and stratified by immunosuppressive (IS) treatment received during the year before second vaccine dose.

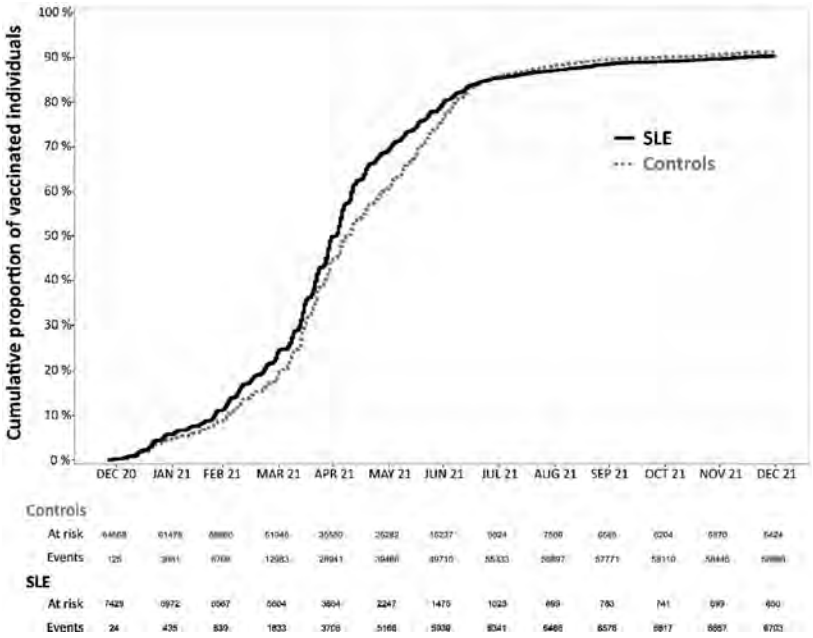

Figure 1: Uptake of the anti-SARS-CoV2 vaccine in SLE patients and matched comparators in Sweden, December 2020 to December 2021

Results: To describe the vaccine coverage, we included 7,429 SLE patients and 64,568 comparators matched on age, sex and county of residence. Vaccination uptake was similar over 2021 between SLE patients and comparators (**Figure 1**). By the end of 2021, around 10% of both SLE and comparators received no vaccine doses. Among 5,585 SLE patients and 37,102 comparators included in the effectiveness analysis, we observed 11 hospitalizations with COVID-19 listed as the primary diagnosis in the SLE group and 20 in the comparator group (**Table 1**). SLE was associated with a higher risk of COVID-19 hospitalization (HR 3.47; 95%CI 1.63-7.39). Rates of events were higher in both groups using the secondary outcome (SLE N=29, comparators N=57) but the HR was similar to the main outcome (HR 3.58; 95%CI 2.30-5.59). There were 2,802 SLE patients (50.2%) who were treated with IS during the year before second vaccine dose. The HR of COVID-19

Table 1: SLE patients and matched general population comparators who received 2 doses of mRNA anti-SARS-CoV2 vaccine in Sweden before January 1st, 2022.

	Non-SLE n=37,102	SLE n=5,585
First hospitalization with COVID as main diagnosis		
Events	20	11
Patient-years	22 745	3 339
Incidence per 1000 patient-years [95%CI]	0.88 [0.57-1.36]	3.29 [1.82-6.00]
Unadjusted HR [95%CI]	ref	3.76 [1.80-7.85]
Adjusted* HR [95%CI]	ref	3.47 [1.63-7.39]
First COVID-19 diagnosis in inpatient or outpatient care as main or secondary diagnosis		
Events	57	29
Patient-years	22 734	3 333
Incidence per 1000 patient-years [95%CI]	2.51 [1.93-3.25]	8.70 [6.05-12.5]
Unadjusted HR [95%CI]	ref	3.52 [2.26-5.48]
Adjusted* HR [95%CI]	ref	3.58 [2.30-5.59]

HR: hazard ratio; SLE = systemic lupus erythematosus; ref: reference; [95%CI]: 95% confidence interval.

*HRs are calculated using a marginal Cox model adjusting for age, sex, household composition and administrative health region.

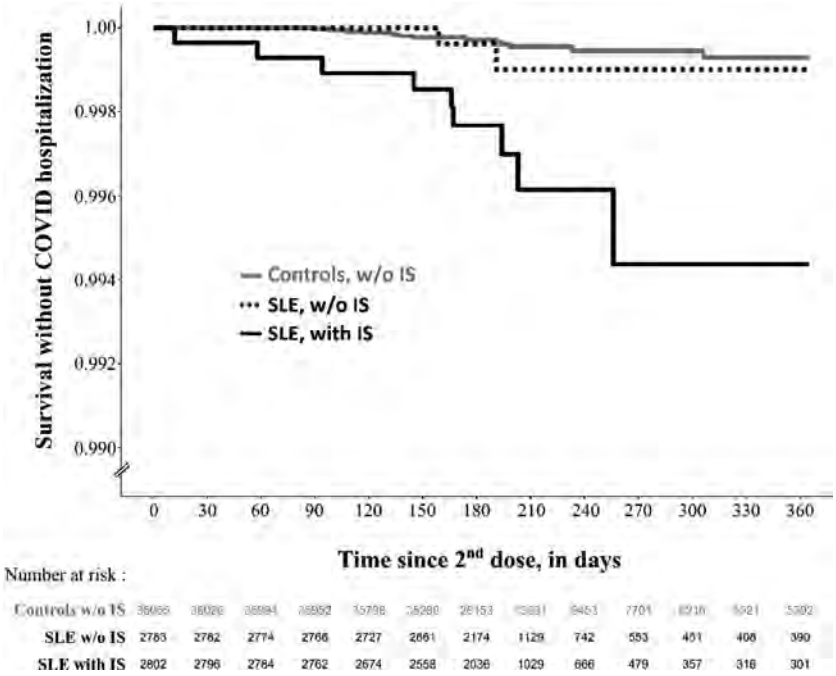

Figure 2: Survival without COVID-19 as a main diagnosis in inpatient care January 1st, 2021 among SLE patients treated with immunosuppressants, SLE patients not treated with immunosuppressants and comparators from general population who received 2 doses of mRNA anti-SARS-CoV2 vaccine in Sweden before January 1st, 2022.

hospitalization was higher for IS-treated SLE (HR 7.03; 95%CI 3.00-16.5) than for IS-untreated (HR 1.50; 95%CI 0.34-6.60; **Figure 2**) compared to the general population.

Conclusion: Anti-SARS-CoV2 vaccination coverage was similar between SLE patients and the general population in Sweden, but it could still be improved. Even though the incidence of post-vaccination COVID-19 hospitalization was very low, vaccine effectiveness was diminished in SLE patients and lowest in those treated with immunosuppressants.

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Abstract Number: 2284

Effect of Air Pollutant Exposure on Disease Activity of Systemic Lupus Erythematous: A Prospective Longitudinal Study from Korea

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Exposure to air pollutants is associated with an increased risk of pulmonary and cardiovascular disease and death. Because few studies have investigated the effects of air pollution on systemic lupus erythematosus (SLE), we investigated the association between exposure to air pollutants, including particulate matter (PM), and disease activity over 1 year in a prospective, longitudinal cohort of Korean patients with SLE.

Methods: The study enrolled 386 patients from three metropolitan regions in Korea. The daily average PM_{10}, $PM_{2.5}$, NO_2, CO, SO_2, and O_3 concentrations were measured using portable air quality monitors and data from the National Ambient Air Monitoring System. Disease activity was evaluated using the SLE Disease Activity Index 2000 (SLEDAI-2K) and Physician Global Assessment (PGA), every 3 months for 1 year. Lupus flares, a damage index, and 36-Item Short Form Health Survey (SF-36) scores were also assessed. A generalized estimating equation was used to evaluate the impact of air pollutants on clinical outcomes, including disease activity.

Results: Changes in PM_{10} and $PM_{2.5}$ were significantly associated with changes in SLEDAI-2K scores of > 8 over 1 year in SLE patients ($\beta = 0.097$, 95% confidence interval [CI]: 0.048–0.146, $p < 0.001$; $\beta = 0.100$, 95% CI: 0.054–0.146, $p < 0.001$, respectively). Changes in PM_{10} and $PM_{2.5}$ were also significantly associated with the development of lupus flares ($\beta = 1.603$, 95% CI: 1.067–2.408, $p = 0.023$; $\beta = 1.777$, 95% CI: 1.048–3.011, $p = 0.033$, respectively). However, there were no significant associations between the changes in NO_2, CO, SO_2, and O_3 and lupus activity.

Conclusion: In this study, PM_{10} and $PM_{2.5}$ exposure increased disease activity and the risk of lupus flares in SLE patients living in metropolitan regions.

Disclosure: J. Kang: None; **H. Jeong**: None; **S. Choi**: None; **D. Park**: None; **H. Baek**: None; **H. Choi**: None; **J. Jung**: None; **S. Lee**: None.

Abstract Number: 2285

Vaccine Uptake in Women with Systemic Lupus Erythematosus (SLE) - Study Update

J. Patricia Dhar[1], Hannah Forsythe[2], Louis Saravolatz[1] and Susanna Szpunar[3], [1]Ascension St. John Hospital and Wayne State University School of Medicine, Detroit, MI, [2]Michigan Department of Human and Health Services, Lansing, MI, [3]Ascension St. John Hospital, Detroit, MI

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
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Background/Purpose: Infections are a major cause of morbidity & mortality in patients with systemic lupus erythematosus (SLE), including vaccine-preventable infections. SLE patients are considered to be immunocompromised & thus fall into the Advisory Committee on Immunization Practice's (ACIP) immunosuppressed category. Vaccines for influenza, pneumococcus, pertussis, varicella, & HPV are safe & immunogenic in patients with SLE. Despite the availability of vaccines, vaccine uptake has been generally low in this population, with one reason being that physicians fail to recommend them. We sought to assess vaccine update in SLE patients seen in our large Detroit area community hospital compared to that of the adult Michigan Care Improvement Registry (MCIR) population. MCIR is an immunization database that documents immunizations given to Michigan residents.

Table 1: Demographic characteristics of female patients with systemic lupus erythematosus (SLE) at Ascension St. John's, compared to female Michigan residents age 18-70, as of the 2020 census. NH Black women and women age 45-49 are over-represented in the SLE group.

Characteristic	SLE females		MI females (census)	
Age as of 12/31/2020				
18-24	9	2.4%	461,906	13.5%
25-29	28	7.6%	338,436	9.9%
30-34	28	7.6%	315,612	9.3%
35-39	27	7.3%	301,855	8.9%
40-44	32	8.6%	292,452	8.6%
45-49	57	15.4%	302,231	8.9%
50-54	39	10.5%	322,098	9.4%
55-59	39	10.5%	352,803	10.3%
60-64	34	9.2%	355,788	10.4%
65-70	45	12.1%	366,902	10.8%
>70	33	8.9%		
Mean (SD)	51.0 (15.0) years		43.7 years	
Race				
NH Black	161	43.4%	474,729	13.9%
NH White	124	33.4%	2,482,471	72.8%
Other	30	8.1%	453,128	13.3%
Unknown	56	15.1%	*NA*	
Total	371		3,410,328	

Methods: We performed a retrospective chart review of adult patients ages 18-70 with SLE who received care at Ascension St. John Hospital to obtain clinical information on SLE. ACR, SLICC, and 2019 ACR/EULAR criteria were used for the diagnosis of SLE. Comparison of vaccine rates of the Ascension St. John SLE cohort recorded in MCIR & the overall adult MCIR population were performed. Vaccine target goals for the SLE & adult MCIR populations were as per the CDC/AICP

Table 2: Characteristics of SLE women

Variable	Percent (n) or Mean (± sd)
Mean ACR criteria count	4.2 ± 2.1
Mean SLICC criteria count	5.6 ± 2.9
Mean 2019 EULAR/ACR score	19.7 ± 10.0
Lupus Nephritis history	29.6% (81/274)
Lupus Cerebritis history	3.0% (11/262)
Smoking history	43.7% (153/350)
Corticosteroid use	76.7% (253/330)
Hydroxychloroquine use	84.3% (284/337)
Immunosuppressives other than corticosteroids & hydroxychloroquine	49.1% (182/371)
Reproductive history	
Sexually transmitted disease	34.6% (71/205)
Gravidity	2.7 ± 2.0
Mean Parity	1.8 ± 1.5
Median No. Stillbirths (range)	0 (0,3)
Median No. Miscarriages (range)	0 (0,7)
Median No. voluntary terminations (range)	0 (0,5)
Mean years to last pap smear	6.2 ± 4.3
History of abnormal pap smear	32.2% (85/264)
History of abnormal cervical biopsy	73.5% (25/34)
+HPV test documented	30.2% (39/129)

recommended vaccine schedule for immunosuppressed and immunocompetent persons. Deceased SLE patients and males were excluded from the analysis for both groups since there were very few male SLE patients to allow for comparison.Data were analyzed using the chi-squared test.

Results: The study groups included 371 SLE women & 3,410,328 Michigan (MI) females. The mean age was slightly older for SLE (51.0 yrs.) vs. MI females (43.7 yrs.), with Black women ages 45-49 yrs. over-represented in the SLE group (Table 1).The SLE group characteristics are seen in Table 2 based on available documentation. Most were on immunomodulatory drugs, ~ 1/3 had history of lupus nephritis, almost 1/2 had history of smoking, ~1/3 had a history sexually transmitted diseases, & ~1/3 had abnormal pap smears. Target vaccine uptake in the SLE group was statistically lower than the MCIR population for HPV, Prevnar13, Pneumovax 23, Tdap, Shingrix®, the COVID primary series completion (#1&2) and booster shot (#3). Similar uptake rates were seen for both groups for Prevnar 13 after age 65, influenza (some years), Shingrix after age 50, & and the first dose of COVID vaccination. (Table 3). Vaccine uptake for SLE women was higher than the MCIR population for pneumovax 23 after age 65, influenza during some years and the bivalent COVID booster.

Conclusion: Vaccine uptake in women with SLE was subpar for most of the adult vaccines recommended for immunosuppressed persons. A gap exists with respect to vaccination for HPV, Pneumococcus (Prevnar13, Pneumovax 23), Tdap, Shingrix®, the COVID series & booster completion where uptake was lower for SLE women. HPV-related cervical disease and serious infections are preventable morbidities in these high-risk women. Increased awareness of the importance of these vaccinations for women with SLE is needed, particularly in childbearing years.

Table 3: Uptake of 7 different vaccines by female SLE patients and MI residents found in the Michigan Care Improvement Registry (MCIR). Uptake is defined as the proportion of eligible persons receiving vaccines as recommended by ACIP (age and dosing recommendations may differ for immunocompromised patients).

Vaccine	Uptake SLE females	Uptake MCIR females	p value
HPV	16/92 = **17.4%**	495,313/1,417,809 = **34.9%**	0.0004
Prevnar13	19+: 91 / 371 = **24.5%** 65+: 32 / 59 = **54.2%**	65+: 172,367/366,902 = **47.0%**	<0.0001 0.27
Pneumovax23	19+: 135 / 371 = **36.4%** 65+: 40 / 59 = **67.8%**	65+: 167,037/366,902 = **45.5%**	0.0004 0.0006
Influenza			
2012-13	61 / 371 = **16.4%**	580,861/3,410,083 = **17.0%**	0.76
2013-14	57 / 371 = **15.4%**	639,018/3,410,083 = **18.7%**	0.10
2014-15	76 / 371 = **20.5%**	689,017/3,410,083 = **20.2%**	0.89
2015-16	96 / 371 = **25.9%**	755,740/3,410,083 = **22.2%**	0.09
2016-17	112 / 371 = **30.2%**	803,369/3,410,083 = **23.6%**	0.003
2017-18	127 / 371 = **34.2%**	896,711/3,410,083 = **26.3%**	0.0005
2018-19	147 / 371 = **39.6%**	995,228/3,410,083 = **29.2%**	<0.0001
2019-20	146 / 371 = **39.4%**	1,076,988/3,410,083 = **31.6%**	0.001
2020-21	138 / 371 = **37.2%**	1,191,180/3,410,083 = **34.9%**	0.35
2021-22	135 / 371 = **36.4%**	1,125,987/3,410,083 = **33.0%**	0.16
2022-23	151 / 371 = **40.7%**	1,084,711/3,410,083 = **31.8%**	0.0002
Tdap	190 / 371 = **51.2 %**	2,076,627/3,410,083 = **60.9%**	0.01
Shingrix			
• 1+ dose	19+: 67 / 371 = **18.1%** 50+: 51 / 170 = **30.0%**	50+: 455,821/1,397,591= **32.6%**	<0.0001 0.47
• 2 doses	19+: 49 / 371 = **13.2%** 50+: 38 / 170 = **22.4 %**	50+: 353,618/1,397,591= **25.3%**	<0.0001 0.38
COVID			
• 1+ dose	271 / 371 = **73.0%**	2,404,422/3,410,083 = **70.5%**	0.39
• primary	181 / 371 = **48.8%**	2,228,723/3,410,083 = **65.4%**	<0.0001
• boost	95 / 371 = **25.6%**	1,306,692/3,410,083 = **38.3%**	<0.0001
• bivalent	89 / 371 = **24.0%**	601,710/3,410,083 = **17.6%**	0.001

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Systemic Lupus Erythematosus and Functional Work Disability: A Qualitative Perspective Using a Work Disability Prevention Approach

Aaron Howe[1], Anson Li[2], Kevon Jules[2], Jeremy Tan[2], Malek Sadek[2], Mahta Kakvan[3], Vijay Chattu[1], Ali Bani-Fatemi[1], Dennisse Bonilla[4], Wils Nielsen[5], Nicole Anderson[6], J. Antonio Avina-Zubieta[7], Mary Fox[8], William Shaw[9], Derek Haaland[10], Janet Pope[11], Paul R. Fortin[12], Kathleen Bingham[4], Nathalie Rozenbojm[4], Christine Peschken[13], Jiandong Su[4], Jennifer Reynolds[14], Catherine Ivory[15], Dafna Gladman[16], Murray Urowitz[17], Francisco Sanchez-Guerrero[18], Lily Lim[13], Stephanie Keeling[19], Ana Soberanis[1], Patti Katz[20], Zahi Touma[1] and Behdin Nowrouzi-Kia[1], [1]University of Toronto, Toronto, ON, Canada, [2]University of Toronto, Restore Lab, Toronto, ON, Canada, [3]University Health Network, University of Toronto, Toronto, ON, Canada, [4]University Health Network, Toronto, ON, Canada, [5]University of Toronto, Markham, ON, Canada, [6]Schroeder Arthritis Institute, Krembil Research Institute, University Health Network and University of Toronto, Toronto, ON, Canada, [7]Arthritis Research Canada, Vancouver, BC, Canada, [8]York University, Toronto, ON, Canada, [9]University of Connecticut School of Medicine, Farmington, CT, [10]The Waterside Clinic, Oro Medonte, ON, Canada, [11]University of Western Ontario, London, ON, Canada, [12]Centre ARThrite - CHU de Québec - Université Laval, Quebec City, QC, Canada, [13]University of Manitoba, Winnipeg, MB, Canada, [14]University of British Columbia, Vancouver, BC, Canada, [15]The Ottawa Hospital Research Institute, Ottawa, ON, Canada, [16]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Department of Medicine, University of Toronto, Toronto, ON, Canada, [17]Schroeder Arthritis Institute, Krembil Research Institute; University of Toronto Lupus Clinic; Division of Rheumatology, Toronto, ON, Canada, [18]University Health Network/Sinai Health system, Toronto, ON, Canada, [19]University of Alberta, Edmonton, AB, Canada, [20]University of California San Francisco, San Rafael, CA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

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Session Time: 9:00AM–11:00AM

Background/Purpose: Work participation meaningfully influences mental wellbeing, health-related quality of life, and disease-related outcomes in individuals with systematic lupus erythematosus (SLE). Previous studies estimate that 20-50% of SLE patients experience some form of work disability (WD) yet there is limited understanding of the integrative effects of the psychosocial and workplace factors associated with WD. The objective of this study was to identify psychosocial and workplace factors associated with WD to create an SLE-related functional profile that is grounded in a WD prevention framework.

Methods: SLE patients (n=28) were purposively recruited from multiple medical centers across Canada. Guided by the WD prevention framework, semi-structured interviews were conducted with patients to explore their perspectives of factors associated with WD. The guide contained questions corresponding to the framework's proposition that disability in the workplace is not only due to the workers' characteristics but also due to environmental factors. Interview data were transcribed verbatim. Thematic analysis was utilized to analyze the data.

Results: Four themes emerged from the data: a) *modifiable workplace factors*, b) *workplace expectations and stigma with work performance*, c*) availability of workplace support and accommodations*, d) *physical limitations and feelings of safety at work* (Figure 1). Neurocognitive symptoms, fatigue, and physical limitations were frequently reported as factors associated with WD in SLE. Participants reported that participation in work increased their personal control, and reduced their physical and mental demands were more desirable and which in turn, subjectively prevented WD (Figure 2).

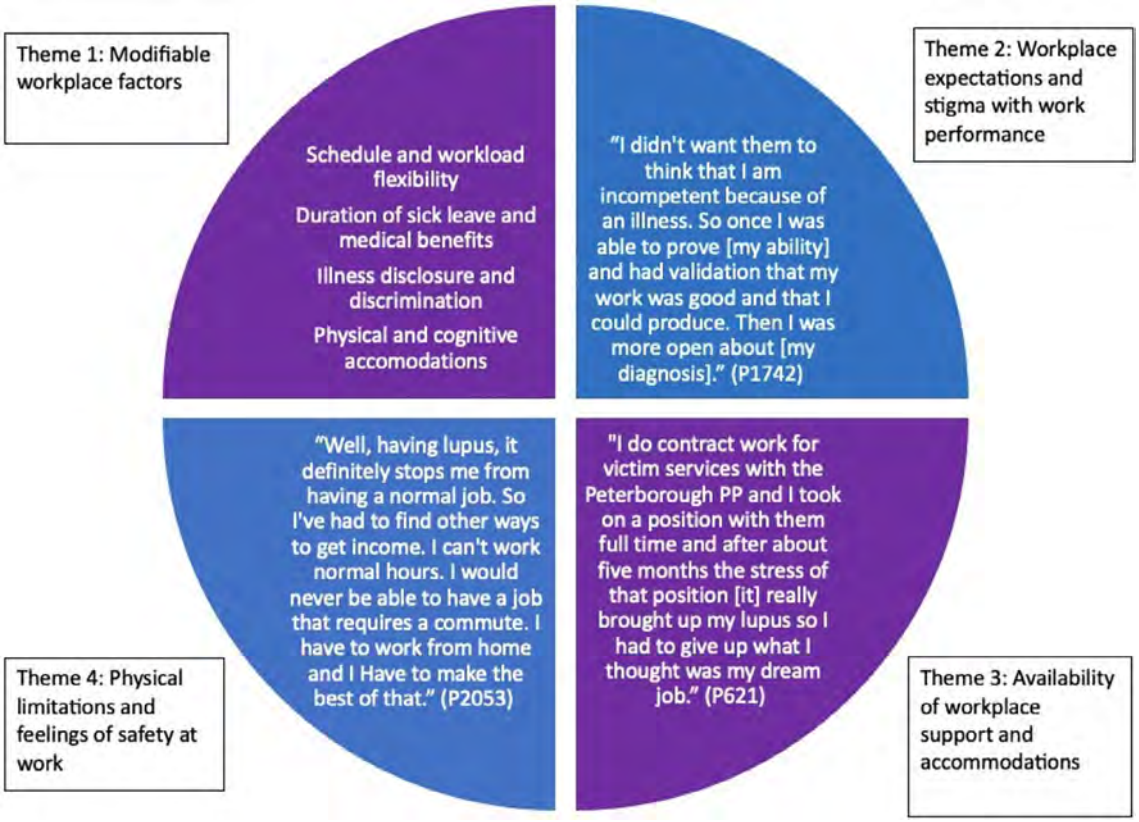

Figure 1. Thematic analysis diagram

Figure 2. Word frequency diagram

Conclusion: WD in SLE necessitates the recognition of the dynamic symptom fluctuations and multidimensionality of the disease, in the context of its relationship to work. Future studies should examine the psychosocial and workplace factors identified to establish a goal-oriented preventative framework that could improve WD outcomes in individuals with SLE.

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Abstract Number: 2287

Mental Health of Lupus Erythematosus Patients Managed in an Academic Safety-Net Clinic

Reina Gonzalez, Eleni Pilitsi, Hanni Menn, Monica Crespo-Bosque, Michael York and Christina Lam, Boston University, Boston, MA

SESSION INFORMATION
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Background/Purpose: Lupus erythematosus (LE) is a complex autoimmune disease with heterogeneous manifestations ranging from life-threatening multi-organ inflammation in systemic lupus erythematosus (SLE) to limited skin disease in cutaneous LE (CLE).Comorbid mental health disorders have been extensively reported in SLE patients, and some limited data suggests a similar trend for those with CLE. A recent meta-analysis reported a depression and anxiety pooled prevalence in SLE of 35.2% and 24.2%, respectively, while a Danish nationwide cohort study found a two-fold increased risk of depression in patients with cutaneous or systemic LE compared with the general population. A study in the U.S. indicated that 34.7% of patients with CLE seen in a dermatology clinic had depressive and/or anxiety symptoms in need of psychiatric intervention. Although studies suggest a high rate of depressive and anxiety symptoms among people living with SLE, none have reported potential differences in depression and anxiety risk among those with cutaneous involvement. We aim to identify the prevalence of depression and anxiety symptoms in need of further evaluation in patients with lupus erythematosus and perform subset analysis based on cutaneous involvement.

Methods: Patients of 18 years of age and older with a diagnosis of lupus erythematosus, systemic, cutaneous or both, managed at a Multidisciplinary Lupus Clinic, were invited to participate in the study and complete the PHQ-9 and GAD-7 questionnaire. Chart review was performed to extract sociodemographic data, lupus related history, work-up and management as well as medical history. Translated versions of the questionnaires were available in Spanish, French and Portuguese. For both PHQ-9 and GAD-7, a score equal or higher to 10 was considered a positive screen prompting further intervention. For patients with a positive screen on either questionnaire, result was discussed with them and, if patient was not actively followed by a mental health provider, a referral was placed to behavioral health services. If patient responded positive to PHQ-9's item concerning suicidal ideation, same-day psychiatric evaluation was pursued. The prevalence of anxiety and depressive symptoms in patients with lupus erythematosus was analyzed. We then analyzed patients with isolated CLE vs. SLE with CLE using chi-square test.

Results: A total of 110 patients received the PHQ-9 and GAD-7 questionnaires. Of these, 29 patients (28.4%) screened positive for anxiety and 42 patients (38.2%) for depression. When comparing patients with isolated CLE vs. SLE with CLE, we found a statistically significant increase of 50% (p-value=0.0077) in depressive symptoms among patients with SLE and CLE. Anxiety symptoms did not differ among the compared groups.

Conclusion: The results are consistent with previous prevalences described for LE patients with anxiety and depressive symptoms. Subset analysis by cutaneous involvement suggests that patients with both systemic and cutaneous involvement suffer from more depressive symptoms than those with isolated cutaneous involvement. This study highlights the importance of screening for mood disorders in patients with lupus, in particular patients with systemic disease.

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Abstract Number: 2288

Scoping Literature Review and Focus Groups Interviews to Identify Candidate Domains for the SLE OMERACT Core Domain Set

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SESSION INFORMATION

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Background/Purpose: We established the OMERACT SLE Working Group in 2021 which includes over 150 members representing over 25 countries and 5 continents to develop a new SLE Core Domain Set (CDS) and measurement instrument set. A CDS is essential for standardizing the measurement and reporting of domains in clinical trials and longitudinal studies in SLE. Domains in a CDS are selected from a candidate domain list through consensus voting exercises with stakeholders including patients, clinicians, researchers, pharmaceutical representatives, and others. The first CDS development

stage is generating a preliminary list of candidate domains. To inform the development of the new OMERACT SLE CDS, we have conducted a scoping literature review of systematic reviews and clinical trials of SLE, and focus groups with SLE patients about living with SLE.

Methods: ***Scoping Review***: We searched 5 databases (Medline, Embase, Cochrane, CINALH, PsycINFO) since 2010 and used Covidence for article screening. 3 reviewers performed an agreement test on the first 100 articles for title and abstract screening with a 98% agreement. Due to the large volume of studies, the 1st screening of title and abstract was conducted by a single reviewer. A 2nd agreement test on 100 articles was performed for full-text screening with the same reviewers with a 99% agreement. The 2nd screening of full-texts and data extraction of domains required 2 reviewers per article. ***Focus Groups***: We developed an interview guide of 11 open-ended questions asking about the pathophysiological manifestations and life impact of SLE. Patients were recruited by the University of Toronto from around the world representing 5 continents and 13 countries. Six focus groups were held virtually ranging from 3 to 10 participants per group. Transcripts have been developed and thematically coded using an open coding framework. ***Advisory Group***: An advisory group was established

Table 1 – Candidate Domains and Sub-Themes Generated from the Scoping Literature Review and Focus Groups

DOMAINS	SUB-THEMES
Adverse Events	Treatment side effects, glucocorticoid side effects
Anxiety	Anxiety about coping with disease uncertainty
Appearance	Body image, physical changes (weight gain), swollen body
Cognitive Function	Brain fog, cognitive impairment, Episodic memory, working Memory, attention, cognitive flexibility, prospective memory, cognition, awareness, memory
Control Over Disease	Loss of health status, controls of SLE with Covid, vulnerability
Damage	Disease-related
Depression	Depressed feelings, depressed about no longer being the same, depression about coping with disease uncertainty
Disability	
Disease Activity	Disease activity state/status/remission
Disease Severity	
Dizziness	
Economic Cost	Financial strain of illness, cost (medication, time off work, impact on employment, non-medical like lotion, alternative medicine)
Emotional Health	Emotions, mood changes, mood swings
Fatigue	Physical fatigue, emotional fatigue, lack of energy, tiredness
Flares	
Fever	
Frailty	
Health Related Quality of Life	Quality of life
Intimacy	
Isolation	Social isolation, social exclusion
Mortality	
Musculoskeletal	Swollen joints
Pain Severity	
Pain Interference	
Participation	Role participation, lifestyle impact, changes in basic needs, planning activities based on energy, understanding limitations
Physical Function	Loss of physical ability, functional ability
Pregnancy	
Satisfaction	
Self-Esteem	Guilt, self-efficacy, self-concept
Self-Management	Coping mechanisms
Sexuality	Drive, sexual dissatisfaction
Sleep	
Stiffness	
Stress	
Weakness	Muscle weakness
Work Status	Employment

with members from the OMERACT SLE Working Group Steering Committee, Patient Research Partners, and additional SLE Expert Stakeholders. This group reviewed all domains and themes and sorted them into domains.

Results: The literature search yielded 4113 articles. The 1st screening reduced the number of articles to 1421. The 2nd screening reduced the number of articles to 597. The scoping review and focus group transcripts yielded over 200 themes/domains. Duplicate and related themes/domains were grouped, and contextual factors were removed yielding a preliminary total of 36 domains (**Table 1**) which included domains such as disease activity, cognitive function, sleep, fatigue, anxiety, depression, stress, participation, pain interference, intimacy, and more.

Conclusion: Many candidate domains have been identified through the scoping literature review and focus group interviews. Further work is in process to finalize the list of the candidate domains to continue with a 4 round Delphi consensus voting exercise to achieve consensus on the new SLE CDS. The future goal for the SLE OMERACT Working Group is the instruments selection for each domain of the new CDS and appraisal of instruments measurement properties.

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Abstract Number: 2289

Short and Long Term Outcomes of Patients with Pure Membranous Lupus Nephritis Compared to Patients with Proliferative Disease

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SESSION INFORMATION
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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
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b>Background/Purpose: Patients with pure membranous lupus nephritis (LN) are known to have a different disease course than those with proliferative disease. The aim of this study is to determine the differences in short and long term outcomes between patients with pure membranous LN and those with proliferative LN, in terms of achieving complete proteinuria recovery (CPR), time to CPR and a composite of poor renal outcome.

Methods: This is a retrospective analysis of patients followed prospectively at a single large Lupus cohort who had biopsy-proven Class V, Class IV+V or III+V or isolated class III or IV LN. We included only first patient-biopsy. The baseline visit corresponds to the visit with highest level of proteinuria in relation with the kidney biopsy visit. Baseline characteristics of patients (demographic data, laboratory results, clinical features and treatment protocols) were analyzed. The primary endpoint, CPR, was defined as proteinuria < 500 mg/24 h. CPR was evaluated at 1 year and 2 years for the different LN classes. The time to CPR was assessed with a Kaplan-Meier curve. Time to a composite of poor renal outcome (eGFR ≤ 15 mL/min/1.73m^2, chronic dialysis or kidney transplant) was also evaluated. These outcomes were compared between patients with pure membranous LN and those with proliferative disease (including mixed biopsies; class III+V or IV+V).

Results: 209 patients fulfilled the above criteria with at least 2 years of follow up after the baseline visit. Of these, 53 had pure membranous LN, 41 had mixed disease (class IV+V or III+V), and 115 had pure proliferative disease (class III or IV). Overall, 156 patients had proliferative disease on biopsy. Patients with pure membranous LN were slightly older at baseline than those with proliferative disease (38.89 Vs 34.53 years, p= 0.016). They also had a higher eGFR (102.69 Vs 86.16 mL/min/1.73 m^2, p= 0.008) and a lower SLEDAI-2K score (11.64 Vs 15.96, p < 0.001) at baseline. Proliferative LN patients tended to be more serologically active (p= 0.001 for anti-dsDNA and < 0.001 for low complements) and had more hematuria (p< 0.001) and urinary casts (p=0.002). There were no significant differences in the baseline proteinuria levels between the two groups. Mycophenolate was the most commonly used drug in the standard of care therapy. Less patients with pure membranous LN received corticosteroids during the first year after the baseline visit (p= 0.004) **(Table 1)**.

There were no differences in the CPR at 1 year (51% for both groups) or at 2 years (66% for membranous and 62% for proliferative disease, p= 0.660) between the 2 groups. Time to CPR was also comparable (**Figure 1**). Time to the composite of poor renal outcome showed a trend in favor of pure membranous patients, but did not meet statistical significance (**Figure 2**).

Conclusion: CPR at one and two years, and time to CPR were similar in patients with pure membranous LN and those with proliferative disease. Time to a composite of poor renal outcome was not significantly different between the two groups. These results show that pure membranous lupus nephritis may be associated with ominous long term outcomes.

Table 1. Baseline demographic, clinical, and laboratory characteristics, as well as treatment regimens in patients with pure membranous LN and those with proliferative diseases

Variables at baseline visit		Membranous LN (n= 53)	Proliferative LN (including mixed cases) (n=156)	p-value
Class V	n (%)	53 (100)	0	<0.001
Class III+V or IV+V	n (%)	0	41 (26)	
Class III or IV	n (%)	0	115 (74)	
Age in years	(mean ± SD)	38.89 ± 12.55	34.53 ± 10.79	0.016
Sex, female	n (%)	45 (85)	138 (89)	0.662
Ethnicity	Black, n (%)	23 (43)	31 (20)	0.171
	Caucasian, n (%)	19 (37)	87 (56)	
	Chinese, n (%)	7 (14)	18 (11)	
	Others, n (%)	3 (6%)	20 (13)	
SLE duration in years	(mean ± SD)	6.91 ± 8.38	5.47 ± 6.02	0.177
Hypertension	n (%)	30 (57)	108 (69)	0.094
Diabetes mellitus	n (%)	3 (6%)	14 (9%)	0.522
Creatinine, umol/L	(mean ± SD)	77.81 ± 31.88	94.60 ± 58.75	0.051
eGFR, mL/min/1.73 m2	(mean ± SD)	102.69± 38.26	86.16 ± 38.00	0.008
Serum albumin, g/L	(mean ± SD)	32.87 ±7.00	31.44 ± 7.05	0.226
SLEDAI-2K	(mean ± SD)	11.64 ±7.17	15.96 ± 6.85	<0.001
SDI	(mean ± SD)	0.62 ±1.24	0.51 ± 1.12	0.525
Low complement	n (%)	22 (42%)	114 (73%)	<0.001
Positive ant-dsDNA	n (%)	25 (48%)	112 (72%)	0.001
Proteinuria in grams/24 hour urine collection or UPCR	(mean ± SD)	2.84 ± 2.21	3.43 ± 2.60	0.140
Hematuria	n (%)	12 (23%)	94 (60%)	<0.001
Active sediment (urinary casts)	n (%)	7 (13%)	56 (36%)	0.002
Immunosuppressives at 1 year	Azathioprine, n (%)	14 (26%)	64 (41%)	0.058
	Cyclosporine, n (%)	2 (4%)	5 (3%)	0.651
	Mycophenolate Mofetil, n (%)	22 (42%)	80 (51%)	0.253
	Other (including Tacrolimus, Rituximab, or Belimumab), n (%)	2 (4%)	6 (4%)	0.981
Corticosteroids during 1st year	n (%)	48 (91%)	154 (99%)	0.004
Antimalarials during 1st year	n (%)	38 (72%)	98 (63%)	0.278
ACE-I or ARB during 1st year	n (%)	27 (51%)	87 (56%)	0.492

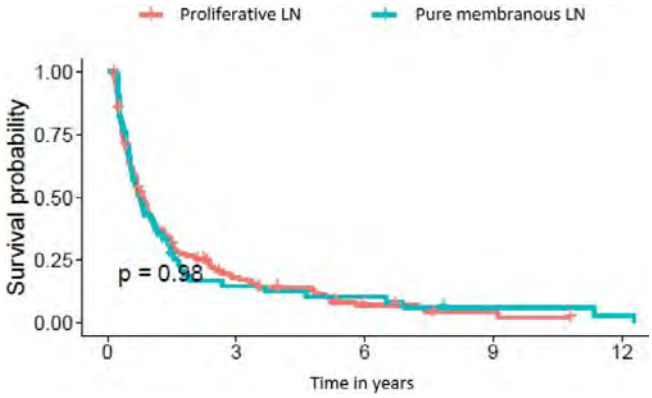

Figure 1. Time to CPR showing no difference between pure membranous and proliferative LN.

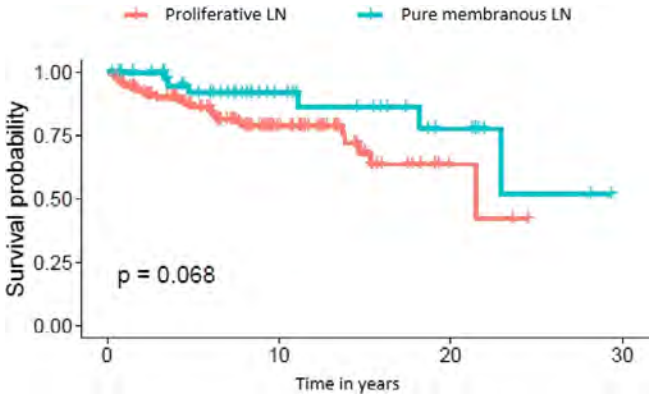

Figure 2. Time to a composite of poor renal outcome (eGFR ≤ 15 mL/min/1.73m2, chronic dialysis or kidney transplant) showing trends in favor of pure membranous LN, but with no statistical significance.

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Abstract Number: 2290

Association of Mycophenolate and Azathioprine Use with Cognitive Function in Systemic Lupus Using a Bayesian Longitudinal Item-response Theory Model

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Cognitive dysfunction (CD) is a common and often deleterious manifestation of systemic lupus erythematosus (SLE). CD is usually operationalized on the American College of Rheumatology Neuropsychological Battery (ACR-NB) as any z-score of ≤-1.5 on ≥2 domains or z ≤-2 in ≥1 domain; this approach necessarily omits information regarding affected cognitive domains. Using each individual ACR-NB z-scores, the aim of this study was to assess in further detail the association of azathioprine (AZA) and mycophenolate (MMF) use with performance in specific cognitive domains given that these medications have demonstrated overall neuroprotective qualities in prior studies.

Methods: Consecutive, adult SLE patients presenting to a single tertiary care center were considered for participation, providing demographic, clinical and psychiatric data, at multiple visits (0, 6, 12 months). Bayesian longitudinal item response theory (IRT) modelling using the cumulative dose of AZA and MMF, demographic and clinical variables as fixed effects and tests/domains and time/participant as random effects were undertaken to assess ACR-NB z-scores over time. Model One was fitted with an easiness parameter that was estimated for each domain and for each test nested within each domain (higher values represent a higher mean z-scores which represents better cognition). Model Two used the same structure as Model One but added a random slope for the cumulative dose of AZA to vary amongst domain and tests. Finally, leave-one-out cross-validation (loo-cv) was used to determine the best statistical model for our data.

Results: Three hundred participants representing 676 patient visits completed the study. The mean overall z-score with all covariates set to zero (ie. intercept) was -0.84 (95% CrI -1.73, 0.04). Cumulative AZA dose (decigrams/kg) was associated with a z-score increase of 0.34 (95% CrI -0.08, 0.61) on average (Figure 1). Time was also associated with a z-score increase, meaning that on average, z-scores improved as time passed. MMF use was not associated with a protective effect against CD (Figure 1). The easiness parameters for visual-spatial construction domain had the lowest estimate (Figure 2). On average, this domain decreased the z-score by -0.69 (95% CrI -1.77, 0.11). Of note, we found that simple attention and processing speed had a null effect on the mean z-score (Figure 2) but when examining each test within this domain we found

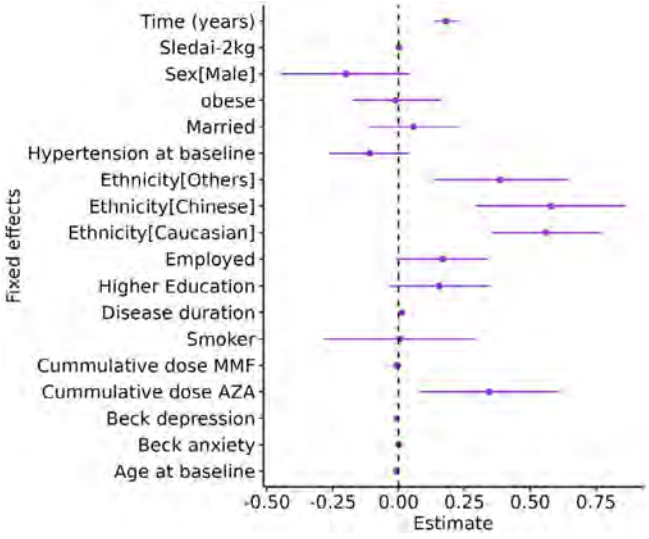

Figure 1. Posterior uncertainty intervals for the fixed effects in our model. X axis represents the distribution of the beta coefficients. Y axis represents the parameters where inference is made. The dark shaded region represents the point estimate from a frequentist point of view and the light shaded region represents the 95% uncertainty interval (CrI), i.e., with 95% of probability the estimate would lie in that region.

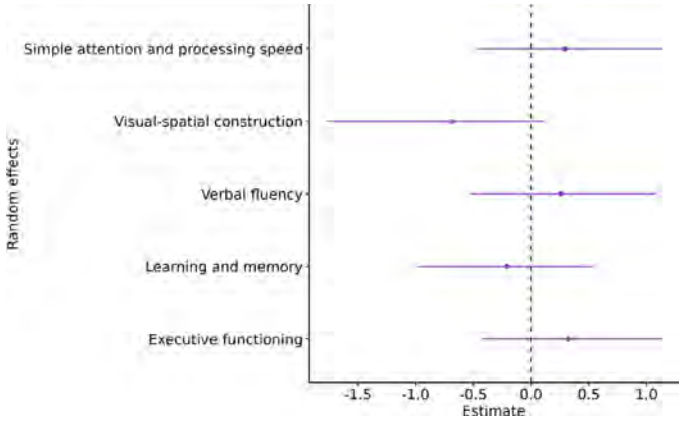

Figure 2. Posterior uncertainty intervals for the ACR Neuropsychiatric Battery domains (as random effects). X axis represents the mean z-score change and Y axis represents the parameters where inference is made. The dot on the graph represents the point estimate and the line represents the 95% CrI.

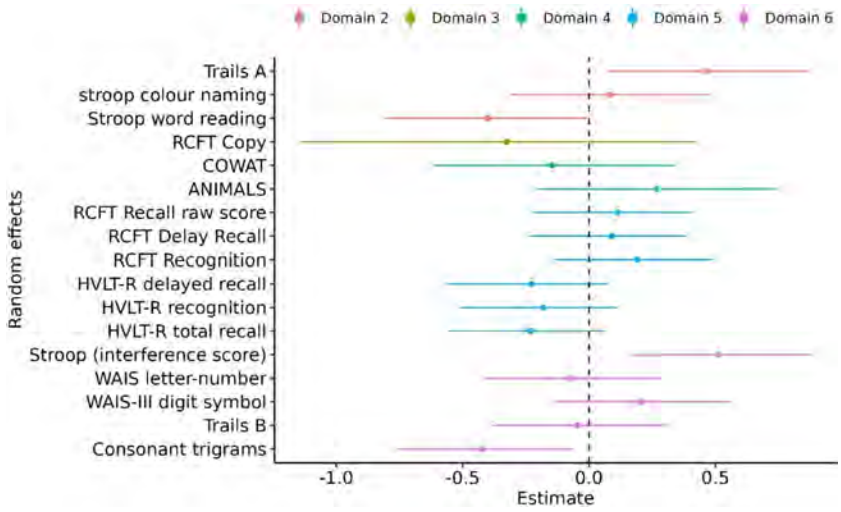

Figure 3. Posterior uncertainty intervals for the ACR Neuropsychiatric Battery tests (as random effects). X axis represents the estimated mean z-score change over time and Y axis represents the cognitive test parameters where an inference is made. Each color represents the cognitive domain where the test is nested. The dot on the graph represents the point estimate and the line represents the 95% CrI.

that Trails A had a positive effect while STROOP word reading decreased the mean z-score (Figure 3). Loo-cv showed Model One (without adding cumulative AZA dose as a random slope) to be the best fit for our data.

Conclusion: This analysis demonstrated that cognition may improve over time in patients with SLE. It also highlighted which cognitive domains and tests on the ACR-NB are more likely to be affected. Similar to our prior study, increasing cumulative AZA dose was associated with a protective effect against CD, while MMF use was not. This is the first longitudinal IRT model that examines trajectories of individual ACR-NB z-scores and relationship with immunosuppressant use. Additional studies are warranted to further investigate visual-spatial function in SLE, as well as the relationship of AZA and SLE-CD.

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Abstract Number: 2291

Therapeutic Drug Monitoring (TDM) of Hydroxychloroquine in Whole Blood: Analysis of over 10,000 Patient Results Using Lab Developed Liquid Chromatography Tandem Mass Spectrometry

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SESSION INFORMATION
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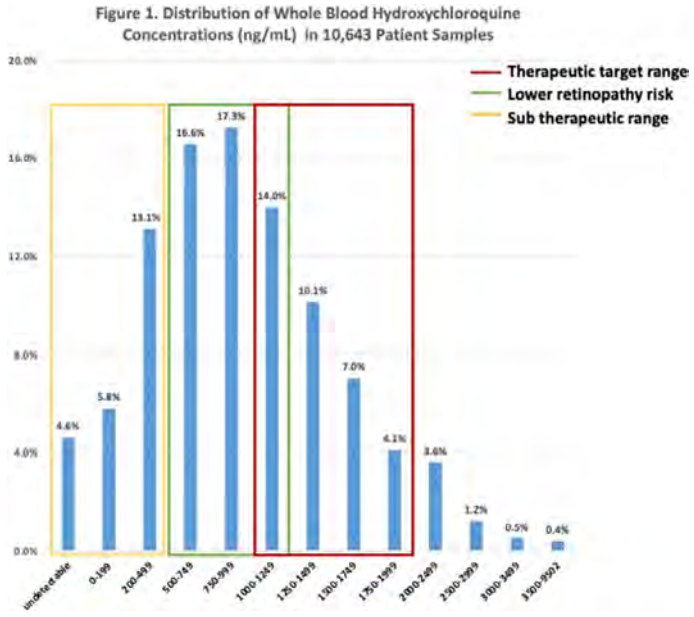
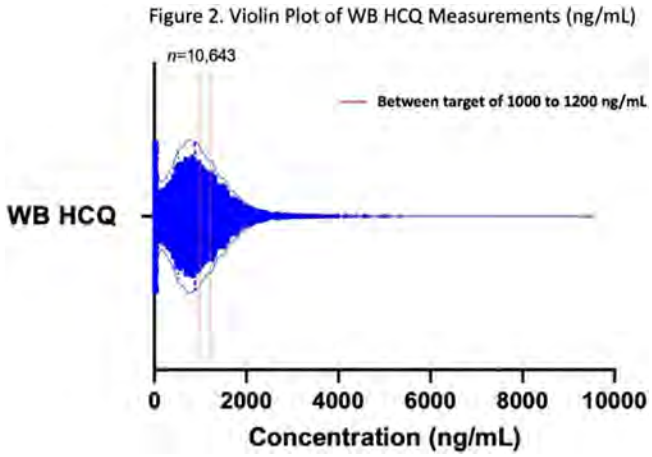
Background/Purpose: Hydroxychloroquine (HCQ), a mainstay SLE therapy, improves survival and reduces flares. Therapeutic drug monitoring (TDM) may be useful in 1) identifying and improving adherence issues, 2) titrating daily dose to achieve therapeutic benefits associated with whole blood HCQ >1000 ng/mL while 3) minimizing cumulative exposure by keeping levels < 2000 ng/mL.[1,2]*Whole blood* (WB) is the correct specimen because WB HCQ levels are higher than serum or plasma levels, more stable and reflective of the last month of HCQ ingestion, and are better correlated to efficacy and retinopathy risk.[2] Here, we report WB HCQ of 10,463 clinical patient samples and their distribution according to therapeutic targets.

Methods: HCQ in whole blood is quantitated by liquid chromatography tandem mass spectrometry (LC-MS/MS). Recommended sample collection is ~ 3 - 6 months into regular stable dosing to reach steady state and correlate with clinical efficacy.

Results: Distribution of WB HCQ in 10,463 patient samples showed more than one-third (3752, 35.9%) were within the target range of > 1000 and < 2000 ng/mL (Figure 1); About one-quarter (2568, 24.5%) were within a tighter therapeutic target window of 1000 to 1500 ng/mL. The vast majority (9852, 94.2%,) of all WB HCQ were < 2000 ng/mL with a small



Distribution of Whole Blood Hydroxychloroquine Concentrations in over 10,000 patients



Violin Plot Showing WB HCQ Concentrations over a Wide Range

percentage >2000 ng/mL (611, 5.8% between 2000 – 9502 ng/mL). About one-third (31.3%) were higher than 1177 ng/mL which corresponds to the upper tertile with higher retinopathy risk described by Petri *et al*.[1] Adherence issues were evident in 10.5% (1102) with undetectable (483, 4.6%) and very low (< 200 ng/mL) drug (619, 5.9%) . Depending upon the target threshold, levels < 500 ng/mL or < 1000 ng/mL may be considered subtherapeutic as seen in 2498 (23.9%) and 4263 (40.7%) samples, respectively.

Conclusion: Due to wide pharmacokinetic variability and adherence issues, a given prescribed dose of HCQ does not correspond to WB HCQ, e.g. following 4, 5 or 6 mg/kg/day, levels are known to vary widely from subtherapeutic < 500 to >2000 ng/mL.[2] Here, our clinical database reiterates this wide range in WB HCQ levels from undetectable (< 25) to 9502 ng/mL in 10,463 patient samples. One-quarter or one-third were within the therapeutic target range of 1000-1500 or 1000-200 ng/mL where >1000 has been associated with better disease control and survival. At the same time, levels less than 1177 avoid higher retinopathy risk (seen in green on Figure 1).1 A small percentage of samples, 5.8%, were higher than 2000 ng/mL, suggesting usefulness of TDM to fine tune daily dose. In 10%, there was evidence of poor adherence, with very low or nil drug, and one-quarter to 40% were subtherapeutic (< 500 or < 1000). The potential benefits of HCQ are many and include reduced flares and improved lupus nephritis, thrombosis risk, and long-term survival. At the same time, prescribed dose does not predict therapeutic levels. TDM-based counseling and dose adjustment may be instrumental in optimizing HCQ benefits while minimizing retinopathy risk.[1,2] In conclusion, our analysis demonstrates the growing use of HCQ TDM to facilitate dose titration to safe and most effective target levels.

References 1)Durcan L, et al. J Rheumatol 2015, 42:2092–2097. 2)Petri M, et al. Arthritis Rheumatol 2020, 72:448–453.

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Abstract Number: 2292

Is Machine Learning Useful to Predict Flare During Pregnancy in Systemic Lupus Erythematosus?

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SESSION INFORMATION
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Session Type: Poster Session C
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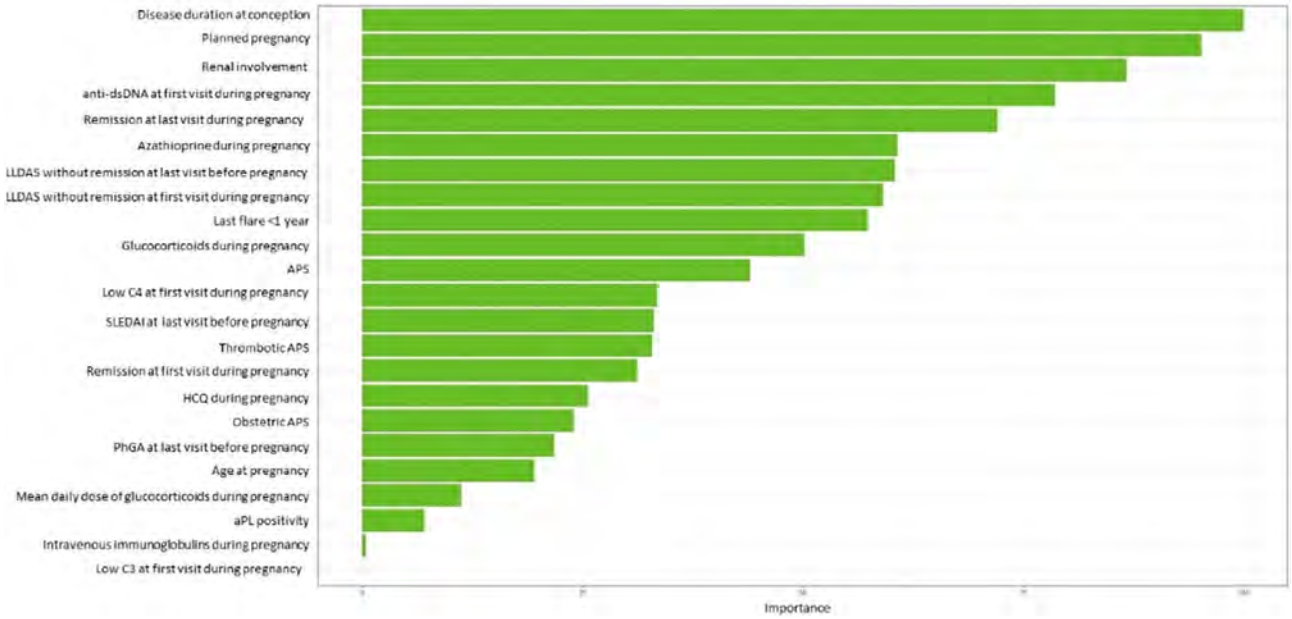
Background/Purpose: Systemic Lupus Erythematosus (SLE) patients are at risk of disease flare during pregnancy; risk stratification is crucial for personalized treatment and monitoring. Our hypothesis is that a machine learning (ML) approach could improve the flare prediction accuracy, enabling early identification of high-risk pregnancies. In this study, we aimed to build a ML model capable of predicting disease flares based on clinical and serological data obtained early in pregnancy.

Methods: 105 pregnancies in 84 SLE patients were prospectively followed at 4-week intervals during pregnancy and puerperium. At the first visit during pregnancy, demographic and clinical data, treatments as well as disease state at the last visit before pregnancy were gathered. At each visit, disease activity was assessed by means of the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and Physician Global Assessment (PhGA). Disease state was defined according to the LLDAS and DORIS definitions. Flares were defined as the emergence or worsening of symptoms requiring therapeutic adjustments or hospitalization. Classical inferential statistics by means of multivariate logistic regression were paralleled by a ML approach to predict the risk of flare based on baseline variables. After missing data imputation and variable filtering, the dataset was subdivided into training and test set, with 70-30% split. A Generalized Linear Model (GLM) with repeated cross-validation was then fitted on the training set, with the aim of predicting "the emergence of flares".

Table 1: characteristics of the cohort

	Overall	Patients with flare during pregnancy (N=25)	Patients without flare during pregnancy (N=80)	P value
Age at conception (years, mean±SD)	32.5±4.6	31.6±4.7	32.7±4.6	ns
Disease duration at conception (years, mean±SD)	10.1±5.9	6.8±4.0	11.2±6.0	0.001
Planned pregnancy (%)	65 (61.9)	32%	70%	<0.01
Time between last flare and pregnancy (year, mean±SD)	4.6±3.8	3.9±3.1	4.8±4.0	ns
aPL (%)	51 (48.6)	52%	46.8%	ns
APS (%)	13 (12.4)	16%	10.1%	ns
Patient characteristics at last visit before pregnancy				
SLEDAI (mean±SD)	2 ± 2.1	2.6±2.8	1.8±1.7	ns
Remission (%)	74 (70.5)	52.3%	87.5%	<0.01
LLDAS but not remission (%)	13 (12.4)	27.3%	9.7%	0.045
Patient characteristics at first pregnancy visit				
SLEDAI (mean ± DS)	1.8±2.5	3.1±1.5	1.3±3.1	0.003
Remission (%)	84 (80)	56.5%	91%	<0.01
LLDAS but not remission (%)	9 (8.6)	26%	3.8%	<0.01
Physician global assessment (mean±SD)	0.1 ± 0.5	0.34±0.7	0.04±0.2	<0.01
C3 hypocomplementemia (%)	46 (43.8)	66.6%	47.7%	ns
C4 hypocomplementemia (%)	28 (26.7)	47.6%	26.8%	0.07
Anti-dsDNA positivity (%)	22 (20.9)	42.8%	19.1%	0.03

Figure 1



Results: 25 flares occurred among the 105 pregnancies examined (26.25%). Patients' demographic and clinical data are shown in Table 1. At univariate analysis, the variables significantly associated with flare were LLDAS without remission at last evaluation (p=0.045) and at first visit during pregnancy (p< 0.01), shorter disease duration (p< 0.01), anti-dsDNA positivity (p=0.03), higher SLEDAI (p=0.02) and higher PGA (p=0.02) at first visit during pregnancy. Remission status at both last (p< 0.01) and first visit during pregnancy (p< 0.01) and planned pregnancy (p< 0.01) were protective. In the multivariate analysis, planned pregnancy and disease duration remained significant (OR 0.84 CI 0.72 to 0.98 p=0.02 and OR 0.18 CI 0.45 to 0.78 p=0.02, respectively). The ML model achieves a high accuracy of 96.3% in predicting the target, unlocking the possibility to enact prevention measures on fragile subjects. Additionally, the model identifies key parameters for patient information collection. The model's optimization gives different weights and statistical importance to each variable (Figure 1), confirming the importance of the two previously recognized predictors, including renal involvement, among others.

Conclusion: The constructed ML model has demonstrated remarkable accuracy in identifying flare occurrences during pregnancy based on baseline data. It is worth noting that both the statistical analysis and the ML model emphasized parameters such as proper pregnancy planning and disease duration at conception as the most influential in predicting the likelihood of a flare during gestation.

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Abstract Number: 2293

Recurrent Intracellular Infections Cluster Together in Patients of SLE with Lymphopenia and Active Disease

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
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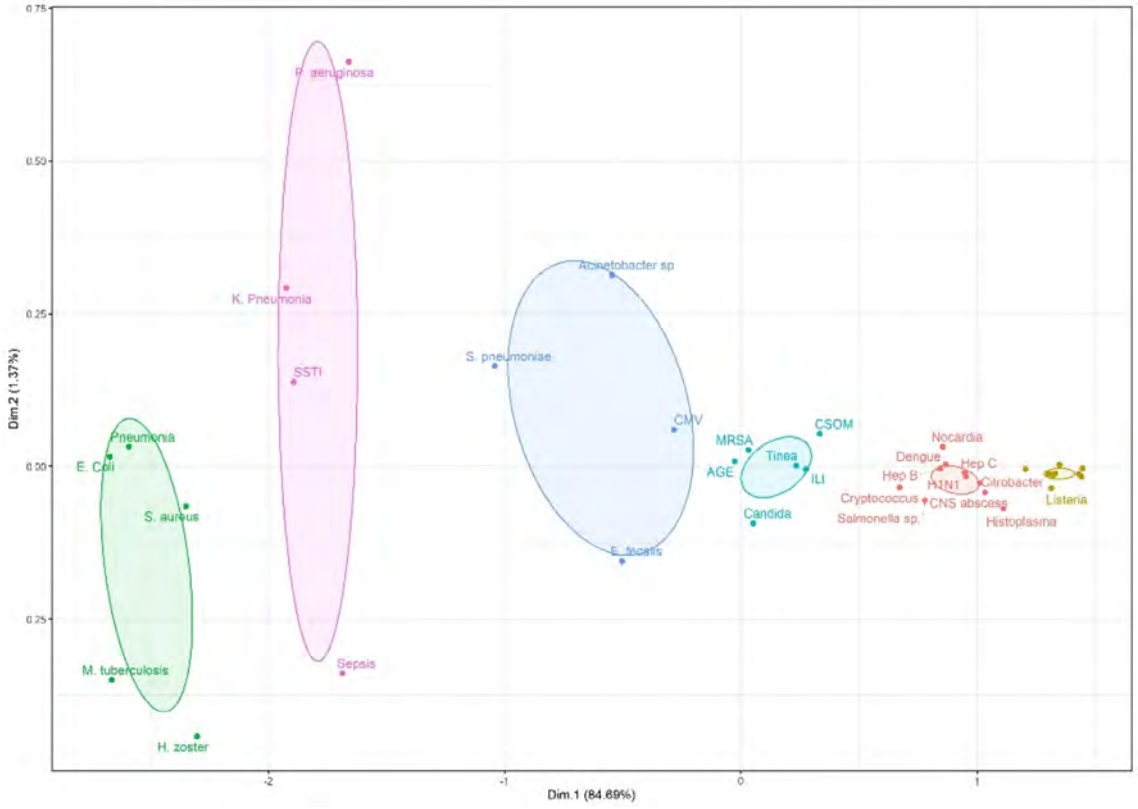
Background/Purpose: Infections are a major cause of morbidity and mortality in systemic lupus erythematosus (SLE). We studied whether infections cluster together and which patients are susceptible to recurrent infections.

Methods: Adult and juvenile SLE (ACR 1997 criteria) from 2000-2020 were reviewed retrospectively for minor and serious infections. Clusters were determined by principal coordinate analysis of a distance matrix from a random forest model.

Results: Of 1576 patients(1452 Female, mean age 27.98±10.53 years) with 8281.34 person-years of follow-up, 663 infections occurred in 490 individuals. Gram-negative bacteria were the most common, followed by mycobacteria (Table 1).

We identified 3 major and 3 minor clusters(Figure 1). Cluster 1 included predominantly intracellular infections: M. tuberculosis, S.aureus, H.zoster, E.coli, and pneumonia(microbiologically unconfirmed). Cluster 2 included bacterial infections: P.aeruginosa, K.pneumoniae, soft tissue infection, and sepsis(microbiologically unconfirmed). Cluster 3 included S.pneumoniae, E.fecalis, Acinetobacter, and Cytomegalovirus.

Cluster 1 was associated with fever(OR 1.95,1.39-2.73), nephritis(OR 1.6,1.23-2.06), myositis and serositis(OR 1.51,1.10-2.06), higher SLE disease activity index (SLEDAI) (14 vs 10), anti dsDNA(192 vs 150), low absolute lymphocyte counts(1296 vs 1512/cumm), C3(52.5 vs 61.8 mg/dl) and albumin(3 vs 3.5 g/dl). Cluster 2 was associated with



The plot shows principal coordinate analysis with the identification of 3 major and 3 minor clusters. The ellipses represent the 95% confidence interval for the centroid of the respective clusters.

Table 1. Prevalence of infections in the cohort.

Infection	Number (prevalence)		Number (prevalence)
Bacterial infections		Viral infections	
Escherichia coli	101 (6.4%)	*Herpes zoster*	44 (2.79%)
Pseudomonas aeruginosa	29 (1.84%)	*CMV*	13 (0.82)
Klebsiella pneumoniae	32 (2.03%)	*Parvovirus*	1 (0.06%)
Proteus mirabilis	2 (0.12%)	*Hepatitis B*	3 (0.19%)
Acinetobacter	12 (0.76%)	*Hepatitis C*	3 (0.19%)
Citrobacter	3 (0.19%)	*H1N1 influenza*	3 (0.19%)
Helicobacter pylori	1 (0.06%)	*Dengue*	4 (0.25%)
Staphylococcus aureus	53 (3.36%)	*Influenza like illness*	9 (0.57%)
MRSA	9 (0.57%)		
Streptococcus pneumoniae	20 (1.26%)	Fungal infections	
Listeria monocytogenes	1 (0.06%)	*Candida*	9 (0.57%)
Enterococcus	15 (0.95%)	*Cryptococcus*	5 (0.31%)
Nocardia	4 (0.25%)	*Histoplasma*	2 (0.12%)
Mycobacterium tuberculosis	93 (5.9%)	*Aspergillus*	1 (0.06%)
		Tinea	10 (0.63%)
Not microbiologically confirmed			
Acute gastroenteritis	9 (0.57%)	Parasitic infections	
Skin/soft tissue infection	36 (2.28%)	*Toxoplasma gondii*	1 (0.06%)
ENT infections	9 (0.57%)	*Neurocysticercosis*	1 (0.06%)
Pneumonia	66 (4.18%)	*Giardia lamblia*	1 (0.06%)
Sepsis	28 (1.77%)	*Plasmodium falciparum*	1 (0.06%)
CNS abscess	3 (0.19%)		

MRSA: methicillin resistant Staphylococcus aureus, ENT: ear, nose and throat. CMV: cytomegalovirus.

nephritis(OR 2.02, 1.33-3.06), gastrointestinal manifestations(OR 2.76, 1.13-6.75) and antiphospholipid syndrome(OR 1.87, 1.03-3.39), higher SLEDAI(14 vs 11), higher anti dsDNA antibodies(200 vs 150), low total leukocyte counts(5750 vs 6400) with similar absolute lymphocyte counts(1368 vs 1476), low C3(51.8 vs 61) and albumin(3.1 vs 3.5 g/dl). Cluster 3 was associated with low total leucocyte count(5100 vs 6400) and similar lymphocyte counts(1181 vs 1470), low C3(43.5 vs 60 mg/dl), and albumin(2.8 vs 3.4 g/dl).

Conclusion: A subset of patients prone to intracellular infections have lower lymphocytes. Patients prone to bacterial infections have lower total leukocyte counts with similar lymphocytes suggesting neutrophil deficiency. We hypothesize that functional assay of these cell lines in may predict future infection risk.

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Organ Damage Progression in Systemic Lupus Erythematosus: An Analysis of the SLE Prospective Observational Cohort Study (SPOCS)

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SESSION INFORMATION

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Background/Purpose: The SLE Prospective Observational Cohort Study (SPOCS) is an international, multicenter study collecting data on patients with SLE, including in relation to oral corticosteroid (OCS) use and type 1 interferon gene signature (IFNGS) status. Here, we report SLICC/ACR Damage Index (DI) progression over 3 years in the overall population, as well as by baseline IFNGS category and average daily OCS use.

Methods: Eligible patients (aged ≥18 years) had physician-confirmed moderate-to-severe SLE (ACR or SLICC classification), a ≥6-month treatment duration with systemic SLE treatment beyond non-steroidal anti-inflammatory drugs and analgesics, and ≥1 lifetime positive serology of ANA or dsDNA. Disease organ damage burden was assessed using the SLICC/ACR DI score. IFNGS tests were performed in a central laboratory. The chi-square test was used to compare score categories and the proportions of patients with ≥1 new damage observation since the prior visit; the Kruskal–Wallis test was used for comparisons of the mean (standard deviation [SD]).

Results: Among 826 patients overall, 70.8% (n = 531) and 29.2% (n = 219) of patients had high and low IFNGS statuses, respectively; IFNGS status was missing for 76 patients. At baseline, 52.0% (n = 426) of patients grouped by high or low IFNGS status and 52.1% (n = 400) of patients grouped by OCS use had organ damage (DI score ≥1). The mean (SD) SLICC/ACR DI score was higher in patients with a low IFNGS than those with a high IFNGS; this trend continued throughout follow-up (**Table 1**). Average DI scores and percentages of patients with ≥1 new organ damage increased from baseline to 36 months in each category. Among patients stratified by daily OCS use (n = 768), 40.5% (n = 311), 44.0% (n = 338), and 15.5% (n = 119) of patients had no OCS use, low OCS use (0 – ≤7.5 mg/day), and high OCS use (>7.5 mg/day) at baseline, respectively. Baseline mean (SD) DI scores were also similar in the overall, no OCS use, and low OCS use categories and higher in the high OCS use category (P = 0.209 for the no OCS use, low OCS use, and high OCS use categories; **Table 2**). The proportion of patients with ≥1 new organ damage increased from baseline to 12 months in each category (P = 0.611 for no OCS use, low OCS use, and high OCS use); a greater percentage of patients had ≥1 new organ

Table 1

Table 1. SLICC/ACR Damage Index by category and type 1 IFNGS test status[a]

Timepoint	Overall (N = 826)	High type 1 IFNGS (N = 531)	Low type 1 IFNGS (N = 219)	*P*-value
Baseline, mean (SD)	n = 820 1.1 (1.6)	n = 525 1.1 (1.6)	n = 219 1.3 (1.6)	
By category, n (%)				0.072[b]
Score 0	394 (48.0)	269 (51.2)	92 (42.0)	
Score 1	191 (23.3)	116 (22.1)	57 (26.0)	
Score >1	235 (28.7)	140 (26.7)	70 (32.0)	
12 months, mean (SD)	n = 499 1.4 (1.7)	n = 296 1.2 (1.7)	n = 151 1.6 (1.8)	
≥1 new damage since prior visit, n (%)	96 (19.2)	57 (19.3)	28 (18.5)	0.831[c]
24 months, mean (SD)	n = 314 1.6 (1.8)	n = 198 1.4 (1.7)	n = 86 1.8 (1.7)	
≥1 new damage since prior visit, n (%)	36 (11.5)	20 (10.1)	12 (14.0)	0.470[c]
36 months, mean (SD)	n = 326 1.8 (1.9)	n = 204 1.7 (1.9)	n = 90 2.0 (1.9)	
≥1 new damage since prior visit, n (%)	34 (10.4)	19 (9.3)	12 (13.3)	0.346[c]

[a]The IFNGS status was missing for 76 patients.
[b]Comparison by score category between low and high baseline type 1 IFNGS categories using the chi-square test.
[c]Comparison of proportions of patients with ≥1 new damage since prior visit between low and high baseline type 1 IFNGS categories using the chi-square test.

Table 2

Table 2. SLICC/ACR Damage Index by category and baseline average daily dose of OCS prednisolone-equivalent categories

Timepoint	Overall (N = 768)	No OCS (N = 311)	Low OCS[a] (N = 338)	High OCS[b] (N = 119)	*P*-value
	n = 768	n = 311	n = 338	n = 119	
Baseline, mean (SD)	1.1 (1.6)	1.1 (1.5)	1.1 (1.6)	1.4 (1.7)	0.209[c]
By category, n (%)					0.298[d]
Score 0	368 (47.9)	145 (46.6)	174 (51.5)	49 (41.2)	
Score 1	180 (23.4)	79 (25.4)	70 (20.7)	31 (26.1)	
Score >1	220 (28.6)	87 (28.0)	94 (27.8)	39 (32.8)	
	n = 461	n = 183	n = 206	n = 72	
12 months, mean (SD)	1.4 (1.7)	1.3 (1.7)	1.3 (1.8)	1.6 (1.6)	0.148[c]
≥1 new damage since prior visit, n (%)	89 (19.3)	33 (18.0)	39 (18.9)	17 (23.6)	0.611[e]
	n = 281	n = 106	n = 121	n = 54	
24 months, mean (SD)	1.6 (1.8)	1.7 (1.7)	1.5 (1.9)	1.7 (1.7)	0.551[c]
≥1 new damage since prior visit, n (%)	34 (12.1)	14 (13.2)	15 (12.4)	5 (9.3)	0.881[e]
	n = 300	n = 122	n = 133	n = 45	
36 months, mean (SD)	1.8 (2.0)	1.8 (1.8)	1.7 (2.1)	2.2 (1.9)	0.182[c]
≥1 new damage since prior visit, n (%)	33 (11.0)	13 (10.7)	10 (7.5)	10 (22.2)	0.036[e]

[a]Average >0 – ≤7.5 mg/day OCS use.
[b]Average >7.5 mg/day OCS use.
[c]Comparison of the mean (SD) between no OCS, low OCS dose, and high OCS dose using the Kruskal–Wallis test.
[d]Comparison by score category between no OCS, low OCS dose, and high OCS dose using the chi-square test.
[e]Comparison of proportions of patients with ≥1 new damage since prior visit between no OCS, low OCS dose, and high OCS dose using the chi-square test.

damage in the high OCS category compared to the no or low OCS categories. Moreover, the mean (SD) DI score was higher in the high OCS category compared to the no OCS and low OCS categories after 12 months.

Conclusion: Results from the SPOCS study will enhance our understanding of the progression of SLE organ damage and will help improve clinical outcomes for patients with moderate-to-severe SLE. Nearly 20% of patients had new organ damage after 12 months. Patients with low IFNGS had greater organ damage than those with high IFNGS, and compared to no OCS or low daily average OCS use, organ damage is higher in patients with high average daily OCS use. Together, these indicate an unmet need for new treatment options for all patients with SLE, especially steroid-sparing treatments.

Disclosure: R. Furie: Biogen, 2, 5; **E. Morand**: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 2, 5, 6, Biogen, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, EMD Serono, 2, 5, Galapagos, 2, Genentech, 2, 5, GlaxoSmithKline, 2, 5, IgM, 2, Janssen, 2, 5, Novartis, 2, Servier, 2, Takeda, 2, UCB, 5; **C. Peschken**: AstraZeneca, 2, 5, GSK, 2, 5, Roche, 1, 2; **M. Aringer**: AbbVie/Abbott, 1, 6, Boehringer-Ingelheim, 1, 6, Bristol-Myers Squibb(BMS), 1, 6, Chugai Pharma, 6, Eli Lilly, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Merck/MSD, 6, Novartis, 1, Otsuka Pharma, 1, 6, Pfizer, 1, 6, Roche, 1, 6, Sanofi Aventis, 1, 6, UCB, 1, 6; **L. Arnaud**: AbbVie, 6, Alexion, 6, Alpine, 2, 6, Amgen, 6, AstraZeneca, 1, 2, 6, Biogen, 6, Boehringer Ingelheim, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 1, 2, 6, Grifols, 6, Janssen, 6, Kezar Life Sciences, 2, 6, LFB, 6, Medac, 6, Novartis, 2, 6, Pfizer, 6, Roche-Chugaï, 6, UCB, 6; **B. Desta**: AstraZeneca, 3; **T. Grünfeld Eén**: AstraZeneca, 3, 11; **A. Sorrentino**: AbbVie/Abbott, 12, Own stocks, AstraZeneca, 3, Galapagos, 12, Own stocks, Gilead, 12, Own stocks, Moderna, 12, Own stocks; **S. Chen**: AstraZeneca, 3, 11; **B. Ding**: AstraZeneca, 3.

Abstract Number: 2295

Predictors of Adherence to Cervical Cancer Screening Guidelines Among Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Women with systemic lupus erythematous (SLE) are at increased risk for cervical dysplasia and cervical cancer. In our jurisdiction, current guidelines recommend that average-risk women aged 25-69 years should undergo Pap tests for cervical cancer screening once every 3 years. Lifelong annual screening is recommended for immunocompromised women, including those with a history of HIV infection or prior organ transplant. Recent Canadian guidelines have suggested that women with SLE should be considered as part of this high-risk group. However, the uptake of these recommendations in clinical practice is unclear.

In this study, we evaluated the provision of cervical cancer screening in a Canadian cohort of women with SLE. Specifically, we measured adherence with current guidelines for the frequency of cervical cancer screening. We also sought to identify SLE-specific predictors of adherence to cervical cancer screening guidelines.

Methods: This was a longitudinal study of women aged 25-69 years followed in the Lupus clinic at a single academic medical centre in Canada between January 2014 and December 2019. All participants met the 1997 revised ACR classification criteria for SLE. Women were excluded from the analysis if they were not eligible for routine cervical cancer screening due to prior total hysterectomy, HIV infection, organ transplant, or history of cervical dysplasia/cancer. During the study period, participants underwent standardized clinical and laboratory assessments on an annual basis. Information regarding cervical cancer screening practices was obtained retrospectively through electronic chart review. We measured adherence with general population guidelines (i.e., Pap test once every 3 years) and SLE-specific guidelines (i.e., Pap test once annually)

Table 1. Sample characteristics of SLE patients

	One-year time periods	Three-year time periods
Number of eligibility periods	557	154
Number of SLE patients	131	98
Age (years), mean (SD)	47.6 (11.7)	46.4 (11.2)
White race (%)	88.6%	91.6%
Marital status		
Married/Common-Law (%)	76.7%	76.0%
Single/Divorced/Widowed (%)	23.3%	24.0%
Education level		
Did not complete high school (%)	10.0%	5.2%
Completed high school (%)	24.4%	29.2%
Post-secondary education (%)	65.6%	65.6%
Cigarette smoking		
Current or past smoker (%)	40.6%	38.3%
SLE disease duration (years), mean (SD)	15.4 (9.4)	14.3 (9.0)
SLE disease activity (SLEDAI-2K)		
Median (IQR) score	2 (0 – 4)	2 (0 – 4)
SLICC/ACR Damage Index (SDI)		
Median (IQR) score	0 (0 – 2)	0 (0 – 2)
Score ≥ 1 (%)	42.5%	40.1%
SLE Organ Manifestations		
Renal disease (%)	29.3%	30.5%
Neuropsychiatric disease (%)	4.6%	3.1%
SLE Medications		
Antimalarial use (%)	68.8%	70.1%
Corticosteroid use (%)	10.2%	10.4%
Immunosuppressive use (%)	59.4%	50.7%

SD = standard deviation; IQR = interquartile range; SLE = Systemic Lupus Erythematosus; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000; SLICC = Systemic Lupus International Collaborating Clinics; ACR = American College of Rheumatology.

Table 2. Univariable generalized estimating equation (GEE) models for the association of demographic and clinical characteristics with adherence to cervical cancer screening guidelines among women with systemic lupus erythematosus (SLE)

	SLE-specific guidelines (1-year time periods) Odds ratio, 95% CI	General population guidelines (3-year time periods) Odds ratio, 95% CI
Number of eligibility periods	557	154
Number of SLE patients	131	98
Age, per 1-year increase	**0.97 (0.95 – 0.99)**	**0.96 (0.93 – 0.99)**
SLE disease duration, per 1-year increase	**0.97 (0.94 – 1.00)**	**0.96 (0.92 – 1.00)**
Marital status		
Single/Divorced/Widowed	Reference	Reference
Married/Common-Law	1.19 (0.65 – 2.15)	1.85 (0.81 – 4.21)
Education level		
Did not complete high school	Reference	Reference
Completed high school (%)	0.92 (0.31 – 2.77)	2.25 (0.35 – 14.3)
Post-secondary education (%)	1.80 (0.66 – 4.87)	3.76 (0.63 – 22.4)
Cigarette smoking		
Never smoker	Reference	Reference
Current or past smoker (%)	**0.59 (0.35 – 0.99)**	0.63 (0.31 – 1.31)
SLE disease activity (SLEDAI-2K), per 1-unit increase	1.00 (0.92 – 1.10)	1.01 (0.90 – 1.14)
SLICC/ACR Damage Index (SDI), per 1-unit increase	0.88 (0.73 – 1.05)	0.83 (0.65 – 1.05)
SLE Organ Manifestations		
Renal disease	**1.64 (1.00 – 2.80)**	1.41 (0.64 – 3.12)
Neuropsychiatric disease	0.78 (0.20 – 3.01)	0.66 (0.07 – 6.04)
SLE Medications		
Antimalarial use	1.43 (0.83 – 2.46)	2.00 (0.93 – 4.27)
Corticosteroid use	0.87 (0.41 – 1.85)	0.75 (0.26 – 2.16)
Immunosuppressive use	1.24 (0.75 – 2.03)	1.39 (0.69 – 2.80)

Bolded values indicated statistically significant associations ($p < 0.05$).

CI = confidence interval; SLE = Systemic Lupus Erythematosus; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000; SLICC = Systemic Lupus International Collaborating Clinics; ACR = American College of Rheumatology.

for the frequency of cervical cancer screening. To achieve this, two separate analyses were conducted, whereby follow-up was divided into 1) one-year eligibility periods; and 2) three-year eligibility periods. For each analysis, adherence was defined as the proportion of time periods where ≥ 1 Pap test was performed. Pre-specified demographic and clinical variables were evaluated as predictors of adherence to screening guidelines using generalized estimating equation (GEE) models.

Results: There were 557 one-year eligibility periods contributed by 131 SLE patients; and 154 three-year eligibility periods contributed by 98 SLE patients. Participant characteristics are summarized in **Table 1**. Pap tests were performed in 125/557 (22.4%) of 1-year eligibility periods and in 79/154 (51.3%) of 3-year eligibility periods. Mean adherence rates were 49.5% for general population screening guidelines and 23% for SLE-specific guidelines.

Predictors of adherence to general population screening guidelines included age and SLE disease duration, while predictors of adherence to annual screening included the above variables, as well as cigarette smoking status and history of lupus nephritis **(Table 2)**.

Conclusion: Adherence to cervical cancer screening guidelines was suboptimal in SLE patients. Future work should aim to identify barriers to routine cervical cancer screening in this population.

Disclosure: L. Cho: None; **A. Legge**: None.

Abstract Number: 2296

Association Between EQ-5D-5L and SLEDAI Scores in Patients with Systemic Lupus Erythematosus in the United States and Europe: A Real-world Survey

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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

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Session Time: 9:00AM–11:00AM

Background/Purpose: The EQ-5D-5L is validated for estimating health related quality of life (HRQoL) across a variety of different disease areas, including rheumatic diseases. However, its ability to effectively capture HRQoL in patients with complex conditions such as systemic lupus erythematosus (SLE) is debated. While disease-specific instruments may more robustly quantify HRQoL and disease burden in these patients, they cannot be used for cross-disease comparisons. Divergence of results between disease-specific instruments and the EQ-5D-5L may indicate an inability of the latter to completely capture the impact of disease manifestation in patients with SLE. In this study, we measured the correlation between the EQ-5D-5L and the SLE Disease Activity Index (SLEDAI) – a disease-specific instrument used to quantify SLE disease activity and severity.

Methods: Data were drawn from the 2021 Adelphi Real World Lupus Disease Specific Programme (DSP)™, a cross-sectional survey with retrospective data collection. Rheumatologists in France, Germany, Italy, Spain, the United Kingdom and the United States provided demographic and clinical information for their next 5-6 consecutively consulting patients with SLE. SLEDAI scores were derived from physicians' clinical assessment of their SLE patients. The same patients were then invited to complete a questionnaire that included an EQ-5D-5L form. We assessed the correlation between EQ-5D-5L and SLEDAI scores, and EQ-5D-5L subdomains and SLEDAI scores using Pearson's and Spearman's correlations, respectively.

Table 1: Patient demographics, clinical characteristics and treatment (n=211)	
Demographics	
Age, mean (SD)	42.9 (13.4)
Sex, female, n (%)	188 (89.1)
Ethnicity, White, n (%)	168 (79.6)
Years since SLE diagnosis (n=203), mean (SD)	5.6 (5.1)
Charlson Comorbidity Index, mean (SD)	0.3 (0.8)
Clinical Characteristics	
Physician-perceived current severity, n (%)	
Mild	134 (63.5)
Moderate/Severe	77 (36.5)
Physician-perceived flaring status, n (%)	
Currently flaring	19 (9.0)
Not currently flaring	192 (91.0)
Number of flares in the last 12 months, mean (SD)	0.7 (1.1)
Current number of symptoms, mean (SD)	3.7 (3.1)
Total SLEDAI Score	
Mean (SD)	10.4 (10.3)
≥6, n (%)	99 (46.9)
<6, n (%)	112 (53.1)
Current Treatments, n (%)	
Advanced therapy: (including biologics and JAK inhibitors)	69 (32.7)
Corticosteroids	145 (68.7)

Abbreviations: standard deviation (SD); systemic lupus erythematosus (SLE); SLE Disease Activity Index (SLEDAI); janus kinase (JAK).

Table 2: EQ-5D-5L correlations with SLEDAI (n=211)		
Total EQ-5D-5L and SLEDAI		
	Pearson's Rho (correlation)	**p-value**
Total EQ-5D-5L	-0.3637	<0.001
EQ-5D-5L subdomains and SLEDAI		
	Spearman's Rho (correlation)	**p-value**
Mobility	0.2031	0.003
Self-care	0.3076	<0.001
Usual activities	0.2532	<0.001
Pain/discomfort	0.1968	0.004
Anxiety/depression	0.3092	<0.001
Higher total EQ-5D-5L scores equate to higher quality of life; Higher scores on EQ-5D-5L subdomains equate to lower quality of life. EQ-5D-5L US tariff was used for the total utility score. Abbreviations: SLE Disease Activity Index (SLEDAI)		

Results: A total of 211 patients were included in this analysis. Mean (SD) age was 42.9 (13.4) years, 89% of patients were female and 80% were White. The mean (SD) SLEDAI score was 10.4 (10.3) and mean (SD) EQ-5D-5L score was 0.75 (0.24). Pearson's Rho correlation between SLEDAI scores and total EQ-5D-5L was r=-0.3637 (p< 0.001) while Spearman's Rho correlations between SLEDAI scores and each EQ-5D domain were: Mobility r=0.2031 (p=0.003); Self-care r=0.3076 (p< 0.001); Usual activities r=0.2532 (p< 0.001); Pain/discomfort r=0.1968 (p=0.004); Anxiety/depression r=0.3092 (p< 0.001).

Conclusion: Weak correlations were observed between SLEDAI and EQ-5D-5L and between SLEDAI and the EQ-5D-5L subdomains, suggesting a patient's clinical status may not be fully reflected in the EQ-5D-5L. More sensitive disease-specific instruments or HRQoL estimation tools may be required to fully capture the burden of disease in patients with SLE.

Disclosure: E. Igho-Osagie: Merck/MSD, 3; **R. Khandker**: Merck/MSD, 3; **J. Milligan**: None; **E. Goddard**: AbbVie/Abbott, 2, Adelphi Real World, 3; **S. Barlow**: AbbVie/Abbott, 2, Adelphi Real World, 3.

Abstract Number: 2297

Interferon-α as a Biomarker to Predict Flares in Lupus Nephritis

Laura Patricia Whittall Garcia[1], Dafna Gladman[2], Murray Urowitz[3], Zahi Touma[4] and Joan Wither[1], [1]University Health Network, Toronto, ON, Canada, [2]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Department of Medicine, University of Toronto, Toronto, ON, Canada, [3]Schroeder Arthritis Institute, Krembil Research Institute; University of Toronto Lupus Clinic; Division of Rheumatology, Toronto, ON, Canada, [4]University of Toronto, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Type I Interferons (IFN-I) play a role in SLE and Lupus Nephritis (LN) pathogenesis. We have recently shown that IFN-I gene expression predicts the risk of SLE flares and a more severe disease course in SLE patients. Furthermore, recently it has been suggested that patients with higher IFN-I gene expression in their renal tubular cells are less likely to respond to conventional therapy.

The aim of this study was to determine if the amount of IFN-α in serum at the time of an LN flare predicts response to therapy, subsequent LN flares, and decline in kidney function.

Table 1. Logistic Regression analysis and Multivariable Cox Regression analysis*. IFN-α predicts renal outcomes (N=95)

Table 1. Logistic Regression analysis and Multivariable Cox Regression analysis*. IFN-α predicts renal outcomes (N=95)		
Outcomes		
Failure to achieve a complete response		
	Odds Ratio (95% CI)	P value
Failure to achieve a CR at 1 year	1.14 (0.94-1.42)	0.16
Failure to achieve a CR at 2 years	1.25 (1.02-1.54)	0.03
LN Flares [a]		
	Hazard Ratio (95% CI)	P value
Time to first LN flare	1.12 (0.96-1.29)	0.14
Time to second LN flare	1.35 (1.07-1.71)	0.01
Decline in eGFR		
	Hazard Ratio (95% CI)	P value
Stage 3A CKD (eGFR ≤59)	1.23 (1.08-1.40)	0.001
Stage 3B CKD (eGFR ≤44)	1.22 (1.07-1.39)	0.003
Stage 4 CKD (eGFR ≤29)	1.27 (1.09-1.48)	0.001
Stage 5 CKD (eGFR <15)	1.17 (1.03-1.34)	0.01
[a] Development of end-stage renal disease (eGFR≤15) and death were used as competing risks for this analysis.		
[*] Logistic Regression analysis and Cox regression analysis were adjusted for ethnicity, adherence to treatment, history of a prior LN flare, serum creatinine at the time of the LN flare and the time in months from the sample collection to the IFN-α quantification.		

Methods: Patients with active LN were included in this study. All patients had 1) active LN, defined as a 24H urine protein >500mg/day with a subsequent modification in therapy by the treating physician, 2) stored serum sample ±3 months from the renal flare and 3) baseline estimated glomerular filtration rate (eGFR) ≥60ml/min (3 months prior to the flare).

The following outcomes were ascertained: 1) Complete Response (CR), defined as proteinuria < 500 mg/day and a serum creatinine within 15% of the baseline at 1 and 2 years after the flare, 2) number of LN flares during follow-up (defined by an increase in proteinuria of at least 1000 mg/d if the baseline was < 500 mg/d or doubling of proteinuria in baseline was ≥500 mg/d and a change in therapy by the treating physician, and 3) decline in eGFR to ≤59ml/min, ≤44ml/min,≤29ml/min and < 15ml/min during follow-up.

Serum IFN-α was measured by Simoa®

Table 2. Logistic Regression analysis and Multivariable Cox Regression analysis*. IFN-α cut-offs predicts renal outcomes (N=95)

Table 2. Logistic Regression analysis and Multivariable Cox Regression analysis*. IFN-α cut-offs predicts renal outcomes (N=95)		
Outcomes		
Failure to achieve a complete response		
IFN-α levels ≥0.6	Odds Ratio (95% CI)	P value
Failure to achieve a CR at 1 year	1.53 (0.60-3.94)	0.37
Failure to achieve a CR at 2 years	2.86 (1.05-7.00)	0.03
LN Flares [a]		
IFN-α levels ≥0.6	Hazard Ratio (95% CI)	P value
Time to first LN flare	1.12 (1.05-3.99)	0.03
Time to second LN flare	1.35 (1.12-8.03)	0.03
Decline in eGFR		
IFN-α levels ≥1.3	Hazard Ratio (95% CI)	P value
Stage 3A CKD (eGFR ≤59)	2.13 (1.06-4.02)	0.03
Stage 3B CKD (eGFR ≤44)	2.21 (1.04-4.67)	0.03
Stage 4 CKD (eGFR ≤29)	2.62 (1.10-6.00)	0.02
Stage 5 CKD (eGFR <15)	2.57 (1.02-6.04)	0.04
[a] Development of end-stage renal disease (eGFR≤15) and death were used as competing risks for this analysis.		
[*] Logistic Regression analysis and Cox regression analysis were adjusted for ethnicity, adherence to treatment, history of a prior LN flare, serum creatinine at the time of the LN flare and the time in months from the sample collection to the IFN-α quantification.		

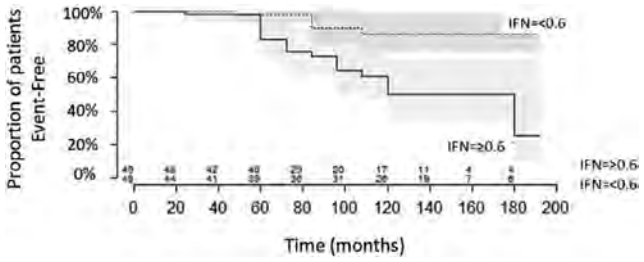

Figure 2. Time to ≥2 LN flares or end-stage renal disease (eGFR ≤15). Kaplan-Meier survival curves stratified by IFN-α levels ≥ 0.6 and <0.6, P=0.04.

Results: A total of 95 patients with active LN were included in the study. The median (IQR) age of the patients was 29 (23-41) years, 79 (83.7%) were women, and the disease duration was 6.0 (0.2-10.0) years. Forty (42.1%) were Caucasian, 21 (22.1%) were Afro-Caribbean, and 22 (23.1.%) were Asian. The baseline eGFR was 112 (98.7-127) ml/min, and the median (IQR) follow-up was 132 (96-156) months.76.8% had a kidney biopsy at the time of the LN flare, of whom 54.7% had a proliferative or mixed class, 17.8% class V, and 4.2% class I or II. The median (IQR) of prednisone was 40mg (30-38mg), 89 (93%) received antimalarial and all patients received immunosuppressive therapy.

The serum baseline levels of IFN-α predicted CR at 2 years from the LN flare. Furthermore, patients with higher baseline levels of IFN-α had a greater risk of having 2 or more subsequent renal flares. Every increase in 1 unit of IFN-α increased the risk of having 2 or more flares by 35%, and the risk of having a decline in kidney function during follow-up (**Table 1**).

Using ROC analysis, two IFN-α cut-offs were identified, 0.6 and 1.3 for predicting ≥2 LN flares and progression to eGFR ≤15, respectively. Even though the areas under the curve suggested that IFN-α is only a weak predictor (AUC=0.62 (0.51-0.74) and 0.60 (0.47-0.73) for ≥2 LN flares and progression to eGFR ≤15, respectively), these cutoffs continued to predict renal outcomes on Cox regression analysis, as seen in **Figure 2** and **Table 2.**

Conclusion: IFN-α serum levels predicted failure to respond to treatment at year 2 after the renal flare, the development of ≥2 LN flares, and decline in kidney function during follow-up.

Disclosure: L. Whittall Garcia: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, Gilead Sciences, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5; **M. Urowitz**: None; **Z. Touma**: AstraZeneca, 2, GSK, 2; **J. Wither**: AstraZeneca, 1, 6, Pfizer, 12, Indirect salary support through a Chair award to the Division of Rheumatology at the University of Toronto.

Abstract Number: 2298

SLE Patients Are at High Risk for Tuberculosis Infection: Data from a Lupus Center of an Endemic Country

Victor Leda[1], Andreia Sousa[1], **Fernanda Lopes**[1], Emily Neves[1], Sandra Pasoto[2], Danieli Andrade[2], Michelle Ugolini[1], Eloisa Bonfa[2], Eduardo Borba[1], Adriana Tonacio[1] and Luciana Seguro[1], [1]Hospital das Clinicas HCFMUSP, University of São Paulo, São Paulo, Brazil, [2]University of São Paulo, São Paulo, Brazil

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE patients are at high risk for tuberculosis (TB) infection especially in endemic countries. Despite the importance of this infection condition, there are still some uncertainties regarding a better characterization of this subgroup of SLE patients which variesamong different series. Screening for TB is routinely performed before immunobiological therapy but this procedure is not always considered for SLE patients starting glucocorticoid or immunosuppressive therapies, and is still under discussion. The aim of the present study was to evaluate clinical and epidemiological characteristics of SLE patients that developed TB after SLE onset.

Methods: SLE patients (2012 SLICC criteria) regularly followed in a single tertiary Lupus center in Brazil who were diagnosed with TB after SLE onset between 2000-2023 were included. Data of SLE patients were obtained from a direct interview and physical examination, and also confirmed in our ongoing prospective electronic chart database established in 2000 that consisted of an extensive clinical and laboratorial evaluation of each patient, including variables of this study, at one to six months intervals.

Results: Sixty-seven (5.3%) SLE patients with TB were identified in a total of 1,254. These SLE patients had a mean age of 48 (**±13.6)** years. Median time between SLE onset and TB diagnosis was 10 (±7.42) years. Regarding infection site, 33 patients (49.3%) had pulmonary tuberculosis and 34 (50.7%) with extrapulmonary tuberculosis (EPTB). Twelve patients (18%) were diagnosed with disseminated infection. The most frequent EPTB sites were lymph nodes (10.4%) and osteoarticular (8.9%), followed by similar rates of gastrointestinal tract (3%), pleural (3 %), skin and soft tissue (3%) and central nervoussystem (3%). At time of TB diagnosis, 51 patients (76%) were in use of glucocorticoid therapy with a median dose of prednisone of 7.5 mg/day (min. 0 mg/day - max. 60 mg/day). The most common DMARD agents used at TB onset were hydroxychloroquine (55%), azathioprine (31%), mycophenolate mofetil (25%), and methotrexate (12%). Adverse events to TB therapy occurred in 22 patients (32%), with most frequently reported side effects being hepatotoxicity and gastrointestinal intolerance.

Conclusion: Our results demonstrated that SLE patients have a high prevalence of tuberculosis, especially extrapulmonary tuberculosis.The use of glucocorticoid therapy was frequently observed at time of TB diagnosis but other immunossupressive drugs could also contribute to increase the risk of this infection.Further studies should be performed in order to define the role of screening of latent TB in SLE patients living in endemic areas.

Disclosure: V. Leda: None; **A. Sousa**: None; **F. Lopes**: None; **E. Neves**: None; **S. Pasoto**: None; **D. Andrade**: None; **M. Ugolini**: None; **E. Bonfa**: None; **E. Borba**: None; **A. Tonacio**: None; **L. Seguro**: None.

Abstract Number: 2299

Medication-related Hospitalizations in Systemic Lupus Erythematosus

Michele Stanciu[1], Evelyne Vinet[2], Emily Gibson McDonald[3], Gregory Clark[3], Christian Pineau[2], Fares Kalache[4], Louis-Pierre Grenier[5], Sasha Bernatsky[6] and Arielle Mendel[3], [1]McGill University, Montreal, QC, Canada, [2]McGill University Health Centre, Montréal, QC, Canada, [3]McGill University Health Centre, Montreal, QC, Canada, [4]McGill University Health Centre, Carignan, AB, Canada, [5]Montreal General Hospital, Montréal, QC, Canada, [6]Research Institute of the McGill University Health Centre, Montreal, QC, Canada

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Background/Purpose: Adverse drug events (ADEs; harm from use of a drug) cause a significant burden to the healthcare system, with an estimated 5% of hospitalizations being drug-related. Up to 80% of ADEs may be preventable; and up to 20% of medication-related events may be related to non-adherence or drug omissions (including non-use of an indicated medication, i.e. prophylactic therapies). People with systemic lupus erythematosus (SLE) take multiple medications, increasing risk of ADEs and other medication-related adverse events. Within the McGill University Health Centre (MUHC) SLE cohort, we estimated the frequency and preventability of hospitalizations related to ADEs and medical omissions.

Methods: All patients in the SLE cohort satisfy the 1997 American College of Rheumatology (ACR) classification criteria and were enrolled after diagnosis. We identified consecutive MUHC admissions among SLE cohort participants between 2015-2020. For each hospitalization, we recorded home medications, admission diagnosis, and outcomes of ADEs and drug omissions. Two adjudicators independently evaluated each hospitalization using the Leape and Bates method, to rank confidence that an ADE or drug omission contributed to the admission (1=little/no confidence; 6=virtually certain). We computed a kappa statistic to assess inter-rater reliability. A third adjudicator helped resolve 7 unclear cases. Medication-related events were then classified as potentially preventable or ameliorable, or not, and potentially modifiable factors were identified.

Results: Among 481 SLE cohort members followed between 2015-2020 (2303 person-years), 67 hospitalizations occurred (3 hospitalizations/100 person-years) among 45 participants. At first admission, median age was 38 years (interquartile range, IQR 27-53), median disease duration was 12 years (IQR 6-20), and participants' home medications numbered a median of 8 (IQR 4-11). Forty one (91%) were female, and >50% were non-Caucasian. Over a quarter (n=19, 28%) of hospitalizations were likely due to one or more ADE (Leape and Bates scores 4-6). Initial unweighted kappa for adjudication was 0.7. ADEs (n=22) included infections (n=13, 59%), cutaneous hypersensitivity reactions (n=2, 9%), adrenal insufficiency (n=1, 5%), drug toxicity (n=4, 18%), and thrombosis (n=2, 9%). Prednisone (n=10, 45%) and/or other immunosuppressants

Table 1. Characteristics of all participants and study population subgroups according to presence/absence of medication-related event

Characteristic	All participants (n=45)	No medication-related hospitalizations (n=23)	≥ 1 medication-related hospitalization (n=22)		
			Total medication-related hospitalizations (n=22)	≥ 1 preventable or ameliorable medication-related event (n=12)	No preventable medication-related event (n=10)
Age, median years (IQR)	38 (27-53)	47 (37-59)	28.5 (22-40)	32 (21-46)	28 (23-34)
SLE duration, median years (IQR)	12 (6-20)	17 (9-24)	9 (2-14)	8 (4-18)	10 (2-12)
Age at diagnosis, median years (IQR)	27 (18-33)	31 (26-35)	20 (15-27)	20 (16-29)	21 (13-27)
Female sex, n (%)	41 (91)	21 (91)	20 (91)	11 (92)	9 (90)
Past/present smoker, n (%)	16 (36)	9 (39)	7 (32)	5 (42)	2 (20)
Years of education, median (IQR)	13 (11-16)	16 (11-16)	12 (11-16)	12 (11-16)	14 (11-16)
Race/Ethnicity, n (%)					
Caucasian	21 (47)	12 (52)	9 (41)	4 (33)	5 (50)
Indigenous	6 (13)	1 (4)	5 (23)	4 (33)	1 (10)
Asian	6 (13)	3 (13)	3 (14)	2 (17)	1 (10)
Black	7 (16)	5 (22)	2 (9)	0 (0)	2 (20)
Other	5 (11)	2 (8)	3 (14)	2 (17)	1 (10)
Renal involvement, n(%)[a]	19 (42)	9 (39)	10 (45)	5 (42)	5 (50)
SLICC damage index[b], mean (SD)	1.6 (2.1)	2 (2.2)	1 (1.7)	1.7 (2.1)	0.2 (0.4)
≥1 SLICC damage item, n (%)	26 (58)	17 (74)	10 (45)	8 (67)	2 (20)
SLEDAI[c], median (IQR)	4.0 (2-8)	4 (2-7)	4 (4-9)	4 (3-8)	6 (4-12)
Number of medications, median (IQR)	8 (4-11)	8 (4-13)	8 (6-10)	10 (7-14)	7 (6-8)
≥5 current medications, n (%)	33 (73)	15 (65)	19 (86)	10 (83)	9 (90)
Current medications, n (%)					
Prednisone	20 (44)	7 (30)	15 (68)	8 (67)	7 (70)
Mean prednisone dose, mg/day (SD)	22.6 (17)	11 (9)	34 (23)	30 (20)	40 (25)
Antimalarial	39 (87)	22 (96)	17 (77)	9 (75)	8 (80)
Aspirin	9 (20)	5 (22)	4 (18)	3 (25)	1 (10)
Anticoagulant	7 (16)	5 (22)	3 (14)	2 (17)	1 (10)
Mycophenolate mofetil	17 (38)	6 (26)	12 (55)	6 (50)	6 (60)
Azathioprine	5 (11)	2 (9)	4 (18)	2 (17)	2 (20)
Methotrexate	1 (2)	0 (0)	1 (5)	0 (0)	1 (10)
Tacrolimus	2 (4)	1 (4)	1 (5)	0 (0)	1 (10)
Cyclophosphamide	1 (2)	0 (0)	1 (5)	1 (8)	0 (0)
Biologics (belimumab, rituximab)	3 (7)	1 (4)	2 (9)	2 (17)	0 (0)
Length of hospital stay, median (IQR)	4 (2-8)	4 (2-6)	6 (3-11)	7 (4-12)	4 (2-11)

[a]ACR criteria at first study visit
[b]At most recent study visit prior to admission (data available for 44/45 participants)
[c]At most recent study visit

Table 2: Characteristics of adverse drug events according to preventability

	Preventable and ameliorable events (n=10), n(%)	Non preventable nor ameliorable events (n=12), n(%)
Adverse drug event		
Infection	6 (60)	7 (58)
Opportunistic	2 (20)	2 (17)
Thrombosis	1 (10)	1 (8)
Cutaneous hypersensitivity reaction	1 (10)	1 (8)
Adrenal insufficiency	0	1 (8)
Cytopenias	2 (20)	0
Gastrointestinal toxicity	0	2 (17)
Medications involved		
Prednisone	5 (50)	5 (42)
Non-corticosteroid immunosuppressants	8 (80)	10 (83)
Cyclophosphamide	3 (30)	0
Mycophenolate mofetil	2 (20)	7 (58)
Rituximab	2 (20)	0
Azathioprine	5 (5)	2 (17)
Methotrexate	0	1 (8)
Tacrolimus	0	1 (8)
Aspirin/anticoagulation	1 (10)	0
Blood products (IVIg)	0	1 (8)
Antibiotics[a]	1 (10)	1 (8)

[a]Dapsone, trimethoprim-sulfamethoxazole

(n=18, 82%) were commonly involved. Eight (12%) hospitalizations related to drug omissions, of which 7 (10%) were flares due to non-adherence. Excluding these flares, 11 medication-related events (48%) were potentially preventable/ameliorable. Modifiable factors included timely glucocorticoid tapering (n=3, 25%), promptly acting on laboratory results (n=4, 33%), and preventative strategies (thromboprophylaxis, vaccination, infection screening; n=3, 25%).

Conclusion: In our SLE cohort, 40% of hospitalizations were medication-related, most often due to ADEs. At least half of medication-related hospitalizations were potentially preventable or ameliorable. Infection prevention should be a priority in this group.

Disclosure: M. Stanciu: None; **E. Vinet**: None; **E. McDonald**: None; **G. Clark**: None; **C. Pineau**: None; **F. Kalache**: None; **L. Grenier**: None; **S. Bernatsky**: None; **A. Mendel**: None.

Abstract Number: 2300

Outcomes of COVID-19 Before and During the Omicron Variant Period in Patients with Systemic Lupus Erythematosus: A Global Multicenter Cohort Study Using the TriNetX Network

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The global dominance of the SARS-CoV-2 Omicron variant ensued shortly after its initial identification in South Africa on November 24, 2021. The outcomes of COVID-19 Omicron variant period had been found to be better than those of COVID-19 before the Omicron variant period. Patients with systemic lupus erythematosus (SLE) have been

found to have a worse COVID-19 outcomes. However, whether the short outcomes of COVID-19 during the Omicron variant period are different from those before the Omicron period is still unclear. Utilizing the TriNetX Network, a worldwide federated health research network that leverages electronic medical records (EMR) from multiple centers, the study aimed to compare COVID-19 outcomes prior to and following the emergence of the Omicron variant in patients with SLE.

Methods: Using the EMR from the Global Collaborative Network database of TriNetX with 101 large health care organizations (HCOs) , we identified 22,782 and 20,668 COVID-19 patients with SLE aged 20–89 years before (between January 1, 2020 and October 31, 2021) and during (between January 1, 2022 and April 29, 2023) the Omicron variant dominance period predominance, respectively. The diagnoses of SLE and comorbidities were based on International Classification of Diseases tenth revision (ICD-10), while the diagnosis of COVID-19 was based on ICD-10, Current Procedural Terminology (CPT) Codes, or Logical Observation Identifiers Names and Codes (LOINC). The two groups of COVID-19 infected SLE patients were matched for age, sex, ethnicity, tobacco use, diabetes mellitus, chronic kidney disease, hypertensive diseases, chronic lower respiratory diseases, ischemic heart diseases, heart failure, neoplasms, anxiety, dissociate, stress-related somatoform and other nonpsychotic mental disorders, mood disorders, mental and behavioral disorders due to psychoactive substance use, and use of immune suppressants. We performed Cox regression analyses to compare the incidences of various COVID-19 outcomes within 30 days after COVID-19 diagnosis date in the pre-Omicron period group compared with those in the Omicron period group, shown as hazard ratios (HRs) with 95% confidence intervals (CIs).

Results: We finally included 20,155 matched SLE patients in both groups. The mean ± standard deviation (SD) age was 52 ± 16 years, and 89% of study subjects were females. Patients of SLE who got COVID-19 before the Omicron period had a higher risks of hospitalization (HR, 1.43; 95% CI, 1.26–1.64), ICU admission (HR, 1.37; 95% CI, 1.21–1.55), sepsis (HR, 1.33; 95% CI, 1.16–1.53), use of mechanical ventilation (HR, 1.64; 95% CI, 1.33–2.03), mental illness (HR, 1.59; 95% CI, 1.26–2.00), hemodialysis (HR, 1.54; 95% CI, 1.17–2.02), atrial fibrillation (HR, 1.44; 95% CI, 1.000–2.085; p = 0.049), acute kidney injury (HR, 1.16; 95% CI, 1.04–1.29), and death (HR, 1.56; 95% CI, 1.30–1.89). However, the risks of stroke and venous thromboembolism/pulmonary embolism were not significantly different between both groups.

Conclusion: This global multicenter cohort study revealed that most short-term (30-day) COVID-19 outcomes were better during the Omicron period than before the Omicron period in patients with SLE.

Disclosure: W. Huang: Novartis, 12, Received PI fee; **H. Chen**: None.

Abstract Number: 2301

Relapse in Japanese Patients with Newly Diagnosed SLE and Its Clinical Characteristics in Daily Clinical Practice: A Single Center Experience in Recent 10 Years

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
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Background/Purpose: SLE patients often experience relapse in the course of treatment, in spite of the progress of therapeutic strategy in SLE. The purpose of this study is to elucidate clinical features, outcome, and risk factors of relapse in patients with SLE who were newly diagnosed and treated at our hospital in recent 10 years.

Methods: This study is a retrospective cohort study. Newly diagnosed SLE patients who were treated in the department of Rheumatology, Fukushima Medical University hospital between 2011 and 2022 were collected. Patients who experienced relapse during observation period were regarded as Relapse-group (relapse was defined as BILAG grade B flare or more), and its clinical features including age, sex, disease duration, SLE symptoms, laboratory data and treatment such as the use of hydroxychloroquine (HCQ) and immunosuppressants (ISs), were compared with non-relapse SLE group. Cumulative relapse free survival in certain clinical items were also compared between the 2 groups using Kaplan-Meier curves.

Results: Among 382 SLE patients who received treatment in our department from 2011 to 2022, 83 newly diagnosed SLE patients were included. The mean age was 37.9 years old, and 75 patients were female (90.4%). The mean SLEDAI scores were 17.8. In 83 patients, 29 patients experienced relapse during the study period. The comparison of clinical characteristics between Relapse group (29 patients) and Non-relapse group (54 patients) were shown in Figure 1. General characteristics were similar between the 2 groups including age, sex, SLE symptoms and serology tests except for observation period ($p< 0.01$) and anti-SS-A antibody positive (P=0.01). In therapy, significantly increased frequency of HCQ intake and combination immunosuppressive therapy (steroids and HCQ plus IS, or more than 2 ISs) were observed (P=0.024 and 0.049, respectively) in non-relapse group. Kaplan-Meier analysis showed significantly higher cumulative relapse-free survival in anti-SS-A negative group and combination immunosuppressive therapy group (P=0.012 and 0.045, respectively) (Figure 2).

Figure 1

Clinical items mean SD, (%)	Relapse (n=29)	Non-relapse (N=54)	P
Age	35.5 ± 14.2	39.2 ± 16.2	NS
M/F	2/27 (93.1)	6/48 (88.9)	NS
Observation period (M)	79.4 ± 34.1	40.9 ± 37.1	<0.01
Diagnostic delay (M)	5.34 ± 5.18	3.74 ± 3.38	NS
Lupus symptoms			
Lupus nephritis	18/29 (62.1)	32/54 (59.3)	NS
NPSLE	6/29 (20.7)	12/54 (22.2)	NS
arthritis	14/29 (48.3)	26/54 (48.1)	NS
cytopenia	15/29 (51.7)	29/54 (53.7)	NS
skin lesions	14/29 (48.3)	29/54 (53.7)	NS
SLEDAI	16.6 ± 7.1	18.5 ± 8.65	NS
Anti-DNA Ab positive	23/29 (79.3)	47/54 (87.0)	NS
SS-A positive	25/29 (86.2)	32/54 (59.3)	0.01
Low C3/C4	24/29 (82.8)	48/54 (88.9)	NS
PSL doses	45.9 ± 15.0	43.4 ± 17.6	NS
Immunosuppressant	(Until relapse)		
HCQ	5/29 (17.2)	22/54 (40.7)	0.024
TAC	4/29 (13.8)	17/54 (31.5)	0.06
CYP	11/29 (37.9)	14/54 (25.9)	NS
BLM	0 (0)	6/54 (11.1)	NS
MMF	1/29 (3.4)	7/54 (13.0)	NS
More than 2IS or HCQ+IS (combination therapy)	5/29 (17.2)	20/54 (37.0)	0.049
LLDAS (end of follow up)	12/29 (41.4)	26/54 (48.1)	NS
Outcome (alive)	27/29 (93.1)	51/54 (94.4)	NS
Severe infections	9/29 (31.0)	9/54 (16.7)	0.11

Figure 1. Clinical features of SLE patients with relapse compared to non-relapse SLE patients

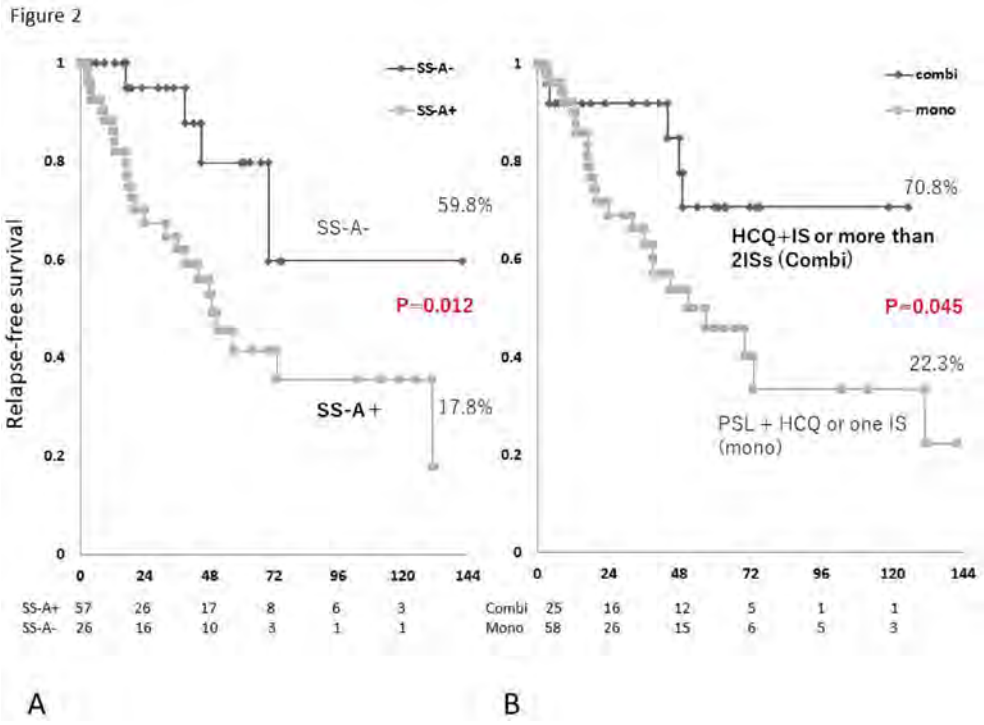

Figure 2. Cumulative relapse-free survival in patients with SLE: (A) anti-SS-A positive or negative, (B) Combination immunosuppressive therapy or mono therapy

Conclusion: Anti-SS-A positive, no HCQ use may be associated with SLE relapse in newly diagnosed SLE patients. Combination immunosuppressive therapy using steroids and HCQ plus IS, or more than 2 ISs may suppress new relapse of SLE in daily clinical practice.

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Abstract Number: 2302

Persistently Active Disease in Adult Patients with Childhood Onset Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies in childhood-onset systemic lupus erythematosus (cSLE) have suggested that cSLE patients have more severe disease, compared to those with adult-onset disease (aSLE). These reported associations are mostly based on cross-sectional observational studies. We compared longitudinal disease characteristics, medication use, and outcomes in cSLE versus aSLE patients in adulthood.

Methods: We followed adult patients who fulfilled ACR or SLICC classification criteria for SLE, enrolled in the Australian Lupus Registry and Biobank (ALRB), a multicentre observational cohort, between 2007 and 2022. Patients who were aged < 18 at diagnosis were grouped as cSLE, and patients aged ≥18years were grouped as aSLE. Patients' disease activity assessed using SLEDAI-2K, SFI and PGA, and medication details were captured at each routine visit while organ damage (using SDI) and HRQoL (using SF36v2) were captured annually. Lupus low disease activity state (LLDAS) and high disease activity status (HDAS, ever SLEDAI-2K score ≥10) are derived as previously published. Triple therapy is defined as concurrent use of immunosuppressant, hydroxychloroquine and corticosteroid. Comparisons were made using appropriate bivariate tests.

Results: The cohort consisted of 519 patients from 9 ALRB centres, with a median age of diagnosis of 29 [IQR: 22,42] years. 68 patients (13%) had cSLE. Despite their younger age at enrolment (25 vs 41 years, p< 0.001), a higher proportion of patients with cSLE already had damage present (SDI≥1) at enrolment (53% vs 40%, p=0.05) consistent with their longer disease duration (median length of disease for cSLE 13.2 vs aSLE 4.2, p< 0.001). cSLE patients had more renal involvement at enrolment (62% cSLE vs 37% aSLE, p< 0.001). The median (IQR) observation period was 4.8 (2.6, 9.3) years. Disease activity, as measured by enrolment SLEDAI-2K (median (IQR) of 8 (4,12) vs 4 (2,8), p=0.013) and time-adjusted mean SLEDAI (AMS) (median (IQR) of 5.0 (3.0, 6.4) cSLE vs 3.6 (1.9,5.1) aSLE, p< 0.001) were significantly higher in cSLE patients, and the difference persisted in each year of observation (Table 1). A higher proportion of cSLE patients had AMS >4, or had HDAS. Only 36% cSLE vs 51% aSLE (p=0.03) spent ³50% time in LLDAS. The domains of disease activity and visit frequency were similar between the two groups. A high proportion of cSLE patients had been treated with triple therapy at enrolment (50% vs 35.5%, p=0.021), and have used mycophenolate (58.8% vs 38.8%, p=0.002). Exposure to Rituximab was seen in 14.7% cSLE vs 8.7% aSLE (p=0.111) whereas exposure to cyclophosphamide was seen in 8.8% cSLE vs 6.0% aSLE (p=0.371).

Table 1. Pattern of visit frequency, disease activity, and medication use in each year of followup between cSLE vs aSLE patients.

Clinical Parameter	Descriptive Statistics by Year of Follow Up											
	Year 1			Year 2			Year 3			Year 4		
	cSLE (n=68)	aSLE (n=451)	P value*	cSLE (n=58)	aSLE (n=401)	P value*	cSLE (n=53)	aSLE (n=348)	P value*	cSLE (n=38)	aSLE (n=295)	P value*
Number of visits per year, median (IQR)	5 (3 - 6)	5 (3 - 7)	0.1406	3 (2 - 5)	4 (3 - 6)	0.01	4 (2 - 5)	4 (3 - 6)	0.076	5 (3 - 7)	4 (3 - 6)	0.513
Maximum SLEDAI-2K score, median (IQR)	8 (4 - 14)	6 (4 - 11)	0.1618	7.5 (4 - 12)	4.5 (2 - 8)	0.005	8 (4 - 10)	5 (2 - 8)	0.019	8 (4 - 10)	5 (2 - 8)	0.032
Experienced HDAS	24 (41.4%)	122 (30.3%)	0.089	16 (33.3%)	74 (20.8)	0.05	14 (34.4%)	68 (21.5%)	0.177	10 (28.6%)	55 (20.2%)	0.25
AMS, median (IQR)	4.8 (2.3 - 8.4)	3.8 (2 - 5.9)	0.0342	5.4 (3.8 - 6.4)	3.5 (2 - 5.3)	0.001	5.7 (4.5 - 7.6)	3.6 (1.5 - 5.4)	<0.001	5.0 (4 - 6.8)	3.6 (2 - 5.5)	0.002
AMS>4	34 (61.8%)	180 (45.3%)	0.022	29 (72.5%)	125 (38.7%)	<0.001	28 (75.7%)	112 (37.8%)	<0.001	20 (62.5%)	91 (38.1%)	0.008
Time in LLDAS (%), median (IQR)	0 (0 - 66)	36.5 (0 - 72)	0.1222	22.8 (0 - 76.9)	52.8 (0 - 85)	0.063	2.8 (0 - 40)	50.9 (0 - 100)	<0.001	20.3 (0 - 62.1)	47.8 (0 - 81.1)	0.063
Spent >=50% of time in LLDAS	16 (33.3%)	142 (37.9%)	0.541	17 (43.6%)	166 (53.6%)	0.241	7 (20.6%)	150 (51.4%)	0.001	9 (30%)	117 (49.2%)	0.048
Took triple therapy*	40 (58.8%)	223 (49.5%)	0.149	29 (50%)	183 (45.6%)	0.533	29 (54.7%)	152 (43.7%)	0.132	21 (55.3%)	128 (43.4%)	0.166
TAM Prednisolone (mg/day), median (IQR)	4.9 (0 - 9.4)	4.3 (0 - 7.9)	0.7	3.8 (0 - 7.2)	2.5 (0 - 5.8)	0.71	4 (0 - 6.2)	1.5 (0 - 5.4)	0.1613	4.2 (0 - 6.3)	1.6 (0 - 6)	0.382

AMS = Time-adjusted mean SLEDAI-2K score, aSLE = adult-onset Systemic Lupus Erythematosus, cSLE = childhood-onset Systemic Lupus Erythematosus, LLDAS = Lupus Low Disease
*Defined as concurrent treatment with hydroxychloroquine, prednisolone and an immunosuppressant (including Azathioprine, Cyclosporin, Cyclophosphamide, Leflunomide, Methotrexate,

Conclusion: cSLE patients had severe disease that was discernible at enrolment and persisted during follow-up. This difference was not due to fewer review visits, disproportionate involvement of certain organ domains, or undertreatment with conventional immunosuppressants. These findings should raise awareness amongst clinicians to consider early aggressive control of disease, including earlier consideration of biologic therapy.

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Abstract Number: 2303

Are Neuropsychiatric Symptoms in Systemic Lupus Erythematosus (NPSLE) Associated with More Frequent Hospitalizations or Exposure to a Greater Number of Immunosuppressive Medications?

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Neuropsychiatric (NP) symptoms occur in >50% of patients with systemic lupus erythematosus (SLE). A major barrier to research includes the non-specific nature of neuropsychiatric syndromes and the uncertainty of attribution to SLE activity. Unmet needs in NPSLE research include recognizing neuropsychiatric symptoms in lupus, diagnostic biomarkers, diagnostic imaging, prognostication, and novel therapies.

Methods: Charts of patients at a large academic center registry were reviewed to record the prevalence of the 19 NP symptoms described by the ACR in 1999. Patient demographics (gender, age, race, disease phenotype, disease duration), SLEDAI 2k score, autoantibody status, C3/C4 levels, and proteinuria >0.5 mg/mmol were collected from chart review. The number of hospitalizations, number and type of current and past immunosuppressive therapies as well as non-immunosuppressive therapies for patients with NP symptoms were compared to those without. Subgroup analysis was performed for those patients with seizure/cerebrovascular disease/polyneuropathy.

Results: 334 charts were reviewed, 327 were included in statistical analysis. 89% of patients were female, 11% male. By race, 65.9% White, 30.6% African American, 2.19% Asian, and 1.25% Hispanic/Latino. NP symptoms were present in 86.5% of the cohort, the most common were: headache (59.3%), anxiety (55.1%), mood disorder (49.8%), cognitive dysfunction (42.5%), polyneuropathy (20.3%), seizure (9.2%), and cerebrovascular disease (8%). There was no statistically significant difference in hospitalizations or immunosuppressive therapies utilized in patients with NP symptoms compared to

those without. However, patients with NP symptoms were more often hospitalized between 2-10 times compared to those without NP symptoms (not statistically significant). Patients with NP symptoms were more often on current steroid therapy and less often on current azathioprine, mycophenolate, or anifrolumab, and less often received *past* azathioprine or mycophenolate therapy (not statistically significant). Patients with NP symptoms were statistically more likely to be on antiepileptics (p=0.002), antidepressants (p< 0.001), or benzodiazepines (p=0.007). In subgroup analysis, patients with seizure/cerebrovascular disease/polyneuropathy were less likely to have low C3 (p=0.005) or proteinuria >0.5 (p=0.070) but were more likely to have leukopenia (p=0.011), be hospitalized (p=0.318), receive IVIG (p=0.04), antiepileptics (p< 0.001), antipsychotics (p=0.034), antidepressants (p< 0.001), and benzodiazepines (p=0.003).

Results

Table1 Descriptive table for demographics and neuropsychiatric events

Table1 Summarizes the demographics and neuropsychiatric events. 282 patients had NP symptoms, the prevalence rate for NP symptoms is 86.5%. 271 (84.7%) of the study cohort had ANA by IFA.

Table 1. Descriptive table for demographics and NP events

Variable	Level	All (n=327)	N
Sex	Male	36 (11.0%)	327
	Female	291 (89.0%)	
Race	African-American	98 (30.6%)	320
	Asian	7 (2.19%)	
	Hispanic/Latino	4 (1.25%)	
	White	211 (65.9%)	
Disease Duration	<1 Year	2 (0.62%)	322
	>=1 Year	320 (99.4%)	
Baseline SLEDAI 2K Score		2.00 [0.25;6.00]	274
NP Symptom		282 (86.5%)	326
NP Manifestation	Cognitive Dysfunction	139 (42.5%)	327
	Mood Disorder	162 (49.8%)	325
	Anxiety	179 (55.1%)	325
	Headache	192 (59.3%)	324
	Seizure	30 (9.20%)	326
	Cerebrovascular Disease	26 (8.00%)	325
	Psychosis	15 (4.62%)	325
	Acute Confusional State	3 (0.92%)	327
	Mononeuropathy	7 (2.15%)	326

Conclusion: There was no statistical difference in hospitalizations or immunosuppression between patients with NP symptoms versus those without. However, patients with NP symptoms were more often hospitalized between 2-10 times compared to patients without NP symptoms and were more often on current steroid therapy, and statistically more often on an antiepileptic, antidepressant, or benzodiazepine therapy. Patients with seizure/cerebrovascular disease/polyneuropathy were statistically less likely to have low C3 (p=0.005) but were more likely to have leukopenia (p=0.011).

Table 6. Subgroup Analysis for Seizure/Cerebrovascular/Polyneuropathy vs without any NP Symptoms

Variable	Level	All (n=151)	No Symptom (n=44)	Seizure/Cerebrovascular/ Polyneuropathy (n=107)	P-value	N
dsDNA Positivity		89 (58.9%)	28 (63.6%)	61 (57.0%)	0.569	151
dsDNA Value		53.0 [17.8;163]	53.0 [24.5;168]	46.5 [16.5;163]	0.529	88
Lupus Anticoagulant Positivity	Yes	25 (19.7%)	7 (17.9%)	18 (20.5%)	0.127	127
	No	94 (74.0%)	32 (82.1%)	62 (70.5%)		
	Indeterminate	8 (6.30%)	0 (0.00%)	8 (9.09%)		
aCL IgG Positivity		12 (9.30%)	2 (5.41%)	10 (10.9%)	0.507	129
aCL IgM Positivity		11 (8.53%)	4 (10.8%)	7 (7.61%)	0.728	129
B2GP IgG Positivity		15 (11.8%)	4 (10.8%)	11 (12.2%)	1.000	127
B2GP IgM Positivity		14 (11.1%)	5 (13.5%)	9 (10.1%)	0.550	126
Low C3		55 (36.4%)	24 (54.5%)	31 (29.0%)	**0.005**	151
Low C4		57 (37.7%)	21 (47.7%)	36 (33.6%)	0.151	151
Proteinuria >0.5	Absent	96 (67.6%)	22 (55.0%)	74 (72.5%)	0.070	142
	Present	46 (32.4%)	18 (45.0%)	28 (27.5%)		
Leukopenia	Absent	69 (46.6%)	13 (29.5%)	56 (53.8%)	**0.011**	148
	Present	79 (53.4%)	31 (70.5%)	48 (46.2%)		
Anemia	Absent	58 (39.5%)	14 (32.6%)	44 (42.3%)	0.360	147
	Present	89 (60.5%)	29 (67.4%)	60 (57.7%)		

Subgroup analysis for seizures/cerebrovascular disease/polyneuropathy

Table 1. Multivariable analysis for factors associated with the risk of infection requiring antibiotics.Subgroup analysis for non-immunosuppressive therapies utilized in seizures/cerebrovascular disease/polyneuropathy

Variable	Level	All (n=151)	No Symptom (n=44)	Seizure/Cerebrovascular/ Polyneuropathy (n=107)	P-value	N
Anticoagulation		26 (17.2%)	5 (11.4%)	21 (19.6%)	0.325	151
Antiplatelet Therapies		55 (36.4%)	11 (25.0%)	44 (41.1%)	0.092	151
Antiepileptics		52 (34.7%)	3 (6.82%)	49 (46.2%)	**<0.001**	150
Antipsychotics		10 (6.71%)	0 (0.00%)	10 (9.52%)	**0.034**	149
Antidepressants		58 (38.4%)	6 (13.6%)	52 (48.6%)	**<0.001**	151
Benzodiazepines		16 (10.7%)	0 (0.00%)	16 (15.1%)	**0.003**	150

Disclosure: J. Vondenberg: None; **C. Zhang**: None; **E. Littlejohn**: Aurinia, 6, GlaxoSmithKlein(GSK), 2.

Abstract Number: 2304

Disparity in Healthcare in Systemic Lupus Erythematosus: A Single-Center Study

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is variable in clinical presentation and has fluctuating disease severity. Health outcomes in SLE have been linked to both genetic and social factors related to differences in gender, ethnicity, education, income, and occupation. This cross-sectional study aims to evaluate the relationship between the access to primary care, social determinants of health (SDH), and disease outcome a single Canadian tertiary center.

Methods: Patients with 2019 EULAR/ACR SLE diagnosis were recruited consecutively and informed consent obtained after ethics board approval. Information on patient demographics, SDH and quality of life (Lupus QoL) was collected through a Patient Questionnaire. A chart review was conducted to document disease activity by SLE-Disease Activity Index (SLEDAi-2k) at the consenting visit, emergency department visits, ACR damage index and adverse outcomes.

Results: 93 patients with a confirmed diagnosis of SLE have been recruited and analyzed at this interim stage. 87.1% (n=81) had access to a General Practionner (GP group) and 12.9% (n=12) did not have access to a GP (Non-GP group). The Non-GP group had a mean SLEDAI-2K score of 4.2 ± 4.9 compared to 2.6 ± 3.6 in the GP group (p=0.21). The SLICC/ACR Damage Index score was 0.7 ± 1.2in Non-GP group and 1.2± 1.6 in GP group (p=0.21). Lupus QoL was similar with 61.2 ±20.5 compared to 64.8±19.5 (p=0.49) for the Non-GP group compared to GP group respectively. History of lupus related pregnancy complications were more frequent in non-Caucasian participants (32.4% vs 9.4%, p=0.010) compared to Caucasians and with a trend to occur more frequently in the Non-GP group (33.3% vs 15.8%). Compared to Caucasians, more

oral corticosteroids use was seen in the non-Caucasian group (51.4% vs 22.6% p=0.010), but similar rates of cardiovascular events and major infections.There is a trend, but not statistically significant, towards more osteoporosis in the non-Caucasian group (13.5% vs 1.9%) and a trend towards more fractures in that group (8.1% vs 0%). Equal rates of employment, education, smoking and emergency visits were recorded between GP an non-GP groups as well as between non-Caucasian and Caucasians.

Conclusion: Our interim results suggests that there remain discrepancies in health outcomes in our SLE cohort, despite our universal health care system. Preliminary results suggest SLE patients without access to primary care and non-Caucasians may have an increased risk of pregnancy complications, increased corticosteroid use and more osteoporosis. The sample size is small, and the study is ongoing. Further multivariate analysis is planned to elaborate on health determinants.

Disclosure: J. Reed: None; **A. Nazir**: None; **K. Alghamdi**: None; **C. Ivory**: None.

Abstract Number: 2305

Infection Vulnerability in Pregnant Women with and Without Systemic Lupus Erythematosus

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SESSION INFORMATION
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Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that predominantly affects women of childbearing age. Pregnant women with SLE have higher rates of adverse maternal and fetal outcomes than the general population. There is limited research on the risk of infection during pregnancy among women with SLE. This study aims to contribute to a better understanding of the incidence of infection in this population, the factors associated with increased infection risk, and compare the risk of infection among pregnant women with and without SLE.

Methods: Medical records from Tawam Hospital were reviewed retrospectively to identify patients with SLE (diagnosed based on ACR criteria) and pregnancy history. We collected data on demographics, clinical variables, and maternal (including infection). We randomly selected a one-to-one age-matched healthy control group and collected their pregnancy history. In cases of infection, we recorded the number and type of infection. We compared the infection odds ratios between pregnant women with and without SLE. Using multivariate analysis, we examined factors associated with infection in pregnant women with SLE.

Results: The outcomes of 78 pregnancies in 39 women with SLE and 107 pregnancies in 39 without SLE were analyzed. The mean age of both groups was similar (*P*=0.5). Infection episodes occurred in 55.8% of SLE pregnancies and 27% of non-SLE pregnancies (odds ratio 3.2, 95%CI 1.7-5.9). Among SLE pregnancies, we have a total of 98 infection episodes. In 51% of the SLE infections, patients received antibiotics. Most common infection was respiratory infection (43.9%), genitourinary (31.6%), skin and soft-tissue (9.2%), gastrointestinal (9.2%), and others (6.1%). In multivariate analysis, we

examined demographic, SLE disease activity, and symptoms for association with increased risk of infection. We found no factors to increase the risk of infection among SLE pregnancies. However, hydroxychloroquine was protective against infection (table 1).

Conclusion: Pregnant women with SLE have a significantly higher risk of infection compared to their non-SLE counterparts. The most common infection in SLE pregnancies was respiratory. No particular factors were identified to increase the infection risk among the SLE pregnancies. Interestingly, hydroxychloroquine use during pregnancy was found to be protective against infection. This finding highlights the importance of medication management in mitigating infection risks for pregnant women with SLE. However, further research is warranted to investigate the mechanisms involved in the increased risk of infection in pregnancies among women with SLE.

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Abstract Number: 2306

Changes in Rheumatology Disease Measures After Initiation of Belimumab Treatment in Patients with Systemic Lupus Erythematosus

Karen Worley[1], Christopher Bell[2], **Bernard Rubin**[3], Guillaume Germain[4], François Laliberté[4], Sean MacKnight[4], Ana Urosevic[4] and Mei Sheng Duh[5], [1]GlaxoSmithKline, US Value Evidence and Outcomes, Cincinnati, OH, [2]GlaxoSmithKline, US Value Evidence and Outcomes, Durham, NC, [3]GlaxoSmithKline, US Medical Affairs and Immuno-inflammation, Durham, NC, [4]Groupe d'analyse, Ltée, Montreal, QC, Canada, [5]Analysis Group, Boston, MA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Real-world benefits of belimumab (BL) in patients with SLE have been shown using SLE-specific measures.[1,2] As SLE disease activity measurement is challenging,[3] assessment of treatment effectiveness using other measures is important. Routine Assessment of Patient Index Data 3 (RAPID3) questionnaire assesses SLE in patients with RA and is a valid measure of SLE disease[4]. This study used real-world data from United Rheumatology Normalized Integrated Community Evidence (UR-NICE) to assess intravenous (IV) BL in improving outcomes.

Methods: Adults with SLE in UR-NICE database who initiated IV BL between January 1, 2012–December 3, 2019, and had ≥5 subsequent BL infusions were included. Patients had SLE clinical activity recorded in the database for ≥12 months before and ≥24 months after first IV BL. Primary objective was time to minimally important difference (MID) from 12 months before index to 24 months post index, measured by Patient Pain Index (PPI), RAPID3, Tender Joint Count (TJC), Swollen Joint Count (SJC), Complement (C)3, C4, and anti-dsDNA. Outcomes were assessed in patients with ≥1 record of that measure during baseline/follow-up. MID was 0.5x the standard deviation of mean baseline values for each disease measure.[5] Kaplan–Meier rates of time to first decrease below/increase above MID were reported during follow-up (3, 6, 12, 18, and 24 months).

Variable	B	Odds ratio	*P*-value
Hydroxychloroquine during pregnancy	-1.73	.18	.05
Pulse steroids during pregnancy	1.32	3.73	.3
Conception at≥ 35 years	1.52	4.59	.09

Results: Of the 495 patients, >50% were in the PPI, C3, and C4 subgroups, ∼30% in the TJC, SJC, and anti-dsDNA subgroups, and 21% in the RAPID3 subgroup.

Improvements in PPI were observed early and continued; 42.6% reached decrease below MID at 3 months, 55.0% at 6 months, and 76.4% at 24 months. For RAPID3 scores, decreases below MID were achieved by 36.5% at 3 months and 61.5% at 24 months. Decrease below MID in TJC was 16.7% at 3 months, which more than doubled to 35.4% at 12 months, and improved through 24 months. Decrease below MID in SJC almost doubled between 3 and 24 months (11.5% to 21.6%), although swollen joints were not as prevalent as tender joints at baseline.

Increase above MID for C3 and C4 levels, respectively, was 8.7% and 8.8% ≤3 months of treatment, increasing to 55.2% and 46.4% at 24 months. Anti-dsDNA levels improved after treatment initiation, with decrease below MID doubling between 3 and 6 months (7.8% to 15.6%).

Conclusion: Among patients initiating IV BL therapy, meaningful improvement in outcomes assessed with multiple rheumatology disease measures, including RAPID3, can be seen as early as 3 months, incrementally increasing over time. While laboratory measures are used to show the rapid effect of BL treatment, this study demonstrated symptomatic improvement in patient pain, physical function, and tender/swollen joints among BL-treated patients with SLE.

References

1. Collins CE, et al. *Rheumatol Ther*. 2020;7(4):949–65.
2. Levy RA, et al. *Lupus*. 2021;30(11):1705–21.
3. Mikdashi J, et al. *Arthritis Res Ther*. 2015;17(1):1–10.
4. Annapureddy N, et al. *Lupus*. 2018;27(6):982–90.
5. Ousmen A, et al. *Health Qual Life Outcomes*. 2018;16(1):1–12.

Content reprinted from the STAR Annual Meeting, February 3–5, 2023. Worley K, et al. Changes in Rheumatology Disease Measures after Initiation of Belimumab Treatment in Patients With Systemic Lupus Erythematosus.

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Pfizer has provided research funding to my employer, Analysis Group, Inc. for previous studies, Sanofi, 5, 12, Sanofi has provided research funding to my employer, Analysis Group, Inc. for previous studies, Takeda, 5, 12, Takeda has provided research funding to my employer, Analysis Group, Inc. for previous studies.

Abstract Number: 2307

Comparing Social Vulnerability Index to Area Deprivation Index to Patient Outcomes in SLE and Glucocorticoid Utilization

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: As shown in previous studies, outcomes in SLE are affected by social determinants of health which influence health care disparities. Evaluating health disparities through the lens of spatial context is an evolving field. Various indices have been developed to categorize the vulnerability of an area. Two such measures are the Center for Disease Control Social Vulnerability Index (SVI) and the Area Deprivation Index (ADI) by the University of Wisconsin-Madison. SVI was created with the intention of identifying vulnerable areas in times of disaster, while ADI was specifically created to inform healthcare delivery in disadvantaged neighborhoods. In addition, SVI is reported by census tract, versus ADI which is reported by census block (subdivision of census tract). Given the difference in intention behind each index and difference in area studied, we sought to understand whether SVI and ADI would have consistent associations with SLE disease activity and prednisone utilization. We also hypothesized that prednisone overutilization is prevalent across vulnerability indices, and that differences in prednisone use will be seen even between neighborhoods.

Methods: Patients from the Washington University Lupus Center who met either ACR or SLICC classification criteria for SLE were longitudinally assessed from April 2014 to August 2020. The patient's census tract and census block were determined using the address listed for each patient's index visit. Only patients with available SVI, ADI, disease activity assessments (SLEDAI 2000 Responder Index-50, S2K RI-50), and prednisone dose data were included. Census tracts corresponded to SVI from the CDC database, and census blocks corresponded to ADI from the Neighborhood Atlas. SVI ranges from 0 to 1, with 1 being most socially vulnerable, while ADI ranges from 0 to 100 with the 100th percentile being most disadvantaged. Any patient living in an area above the mean of 0.5 or 50th percentile can be seen as living in a socially vulnerable or disadvantaged area. SLE disease activity was assessed using the S2K RI-50, where scores > 4 correlated with active SLE. Prednisone prescribed at the index visit was divided into 4 categories (none, 0-7.5 mg, 8-20 mg, >20 mg).

Table 1. Patient Demographics

Patient Demographics	N
Gender	
Female	202
Male	18
Race	
White	97
Black or African American	115
American Indian or Alaska Native	2
Asian	3
Multiple Race	1

Table 2. Patients prescribed prednisone

Prednisone dosing	Number of Patients
None	135
>0-7.5 mg	20
>7.5-20 mg	40
>20 mg	10

Table 3. Number of patients in each quartile of SVI and ADI

SVI	Number of Patients
0-0.25	58
0.26-0.5	55
0.5-0.75	55
0.75-1	52
ADI	
0-25	13
26-50	64
51-75	54
76-100	89

Results: 220 patients were analyzed. There was no significant correlation between cumulative SVI and disease activity (OR 1.09, 95% CI=0.607-1.975, p=0.7635). Patients living in more disadvantaged areas per ADI were more significantly likely to have active disease (OR 1.65, 95% CI=0.864-3.161, p=0.129), although this was not statistically significant. Both those with vulnerable cumulative SVI (OR 2.23, 95% CI=1.24-3.99, p=0.006) and disadvantaged ADI were also more likely to be prescribed higher doses of prednisone (OR 3.57, 95% CI=1.73-7.36, p=0.0002).

Conclusion: Patients living in vulnerable areas determined by either SVI or ADI are likely to be prescribed higher doses of prednisone, despite having no statistically significant correlation with disease activity. This strongly suggests that those in more vulnerable or disadvantageous areas leverage prednisone utilization to control disease activity, which we hypothesize worsens long-term outcomes for this population.

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Abstract Number: 2308

The Association Between Poverty and SLE Disease Burden: Experiences from a Saint Lucian Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Poverty increases non-communicable disease risk, however its influence on systemic lupus erythematosus (SLE) burden is poorly understood. Non-White racial/ethnic groups, particularly of African origin, disproportionately suffer both from SLE and poverty, making disentangling racial/ethnic vs socioeconomic influences on SLE outcomes a challenge. Saint Lucia is a Caribbean island with a predominantly African ancestry population and variable socioeconomic dynamics. We therefore tested the association between poverty and SLE severity in a unique African ancestry SLE cohort.

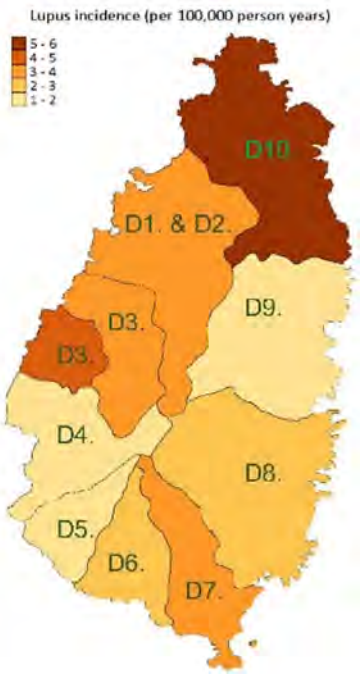
Methods: A 143-patient SLE cohort seeking care with the single practicing rheumatologist in Saint Lucia were included. All participants were at least 18 years old and met SLE classification criteria. Given that all rheumatology care is performed at this center, the cohort is expected to represent near-enumeration of SLE for the island population. Clinical data, demographics, and socioeconomic factors were obtained via chart review. Addresses identified district of residence, and area level poverty percentages in 2016 were obtained from the Saint Lucia National Report of Living Conditions. Incidence rates were calculated as the number of cases per 100,000 person-years of observation. The primary outcome was the Lupus Severity Index (LSI); calculated as a summation of ACR 1997 criteria multiplied by validated regression coefficients. Covariates that associated with LSI were identified by simple linear regression. Multiple regression was used to test the association between key covariates and LSI.

Results: The 2015-2018 incidence of SLE was 8 per 100,000 person-years (95% CI: 5.1-11.9). Incidence by district is shown in Figure 1. Of the 143 participants, 47 were below and 96 were above the poverty threshold. Impoverished patients were diagnosed 10 years earlier than non-impoverished patients, had lower BMIs, were more likely to live in impoverished districts, to take glucocorticoids at higher doses, and had higher lupus severity indexes than non-impoverished patients (**table 1**). Survival over the observation period was 85% in impoverished and 94% in non-impoverished participants (p=0.09). Linear regression models revealed associations between poverty status (p=0.002), younger age at onset (p=0.02), residence in an area with greater poverty level in 2016 (p=0.04), and higher glucocorticoid dose (p< 0.001), and greater LSI.

A.

District		Poverty headcount rate 2006	Poverty headcount rate 2016
D1.	Castries	13.1	27.6
D2.	Castries sub-urban	22.2	19.0
D3.	Anse La Raye/Canaries	44.9	38.0
D4.	Soufriere	42.5	25.5
D5.	Choiseul	38.4	16.9
D6.	Laborie	42.1	23.4
D7.	Vieux Fort	23.1	34.6
D8.	Micoud	43.6	31.2
D9.	Dennery	34.2	45.0
D10.	Gros-Islet	24.4	11.8
	Total	28.8	25.0

B.



A. The distribution of area level poverty by district in 2006 and 2016. D denotes district followed by the corresponding number. B. A map of Saint Lucia districts is shown with the SLE incidence by district indicated by the shading.

Demographics and Comorbidities	Below Poverty		P Value	Total
	Yes N=47	No N=96		All N =143
Age, mean years (SD)	35.7 (12.9)	46.6 (13.9)	<0.01	43.3 (14.4)
Gender, female N (%)	89	94	0.36	92
Age at Diagnosis (SD)	26.4 (10.3)	35.4 (11.7)	<0.01	32.5 (11.9)
Time to Diagnosis (SD)	1.2 (2.6)	1.8 (3.4)	0.33	1.6 (3.2)
Lupus Severity Index (SD)	1.2	0.78	<0.01	0.93
BMI, mean (SD)	21.9 (3.9)	24.5 (4.4)	<0.01	23.6 (4.4)
Osteoporosis or Osteopenia (%)	14	35	0.23	32
Osteonecrosis (%)	11	2	0.03	5
Pulmonary HTN (%)	4	1	0.31	2
Hypertension (%)	28	35	0.34	33
Cataracts (%)	0	2	0.32	1
Pulmonary Fibrosis (%)	2	1	0.61	1
DVT/Thrombosis (%)	2	10	0.03	8
Diabetes (%)	4	5	0.80	5
Hyperlipidemia (%)	21	29	0.33	26
Glucocorticoid (%)	85	57	<0.01	66
Glucocorticoid dose	11.2 (11.9)	5.4 (7.9)	<0.01	7.4 (9.8)
Antimalarial (%)	96	91	0.22	92
DMARD (%)	62	45	0.06	50
District poverty (%)	29	24	<0.01	26

Values are expressed as % for categorical variables and mean ± standard deviation (SD) for continuous variables. Categorical variables compared using Fisher's exact test; continuous variables compared using the two-sample T-test or Mann Whitney U Test. DMARDs include non-biologic agents (azathioprine, cyclophosphamide, mycophenolate mofetil, mycophenolic acid, sirolimus, tacrolimus) and biologic agents (anakinra, abatacept, belimumab, rituximab, tocilizumab). Antimalarial drugs include hydroxychloroquine or chloroquine. Glucocorticoid doses are expressed in prednisone equivalent doses. District poverty % reflects data as of 2016.

Conclusion: In this predominantly African ancestry SLE cohort, poverty associated with early onset SLE, higher Lupus Severity Index, and heavier reliance on glucocorticoid therapy. There were trends toward higher case fatality in impoverished participants. These data implicate socioeconomic stress in SLE disease burden and support further studies into the mechanis

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Abstract Number: 2309

Enterococcus Gallinarum Prevalence in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is associated with epithelial defects and disrupted intestinal barrier, risking bacterial translocation, and promoting systemic inflammation, known as dysbiosis, which is associated with increased disease activity (1). *Enterococcus gallinarum* has been previously linked to gastrointestinal autoimmune diseases, like autoimmune hepatitis and primary sclerosing cholangitis. (2) However, little is known about E. gallinarum prevalence in SLE. Our objective was to analyze the frequency of E. gallinarum in stool samples from SLE individuals and examine its association with clinical and laboratory characteristics.

Methods: A cross-sectional, descriptive study was conducted at the University Hospital "Dr. José Eleuterio González" in northern Mexico. We included adult patients who met the current criteria for systemic lupus erythematosus (SLE) and had recent (< 3 months) routine paraclinical tests, including acute phase reactants. Patients with other autoimmune diseases, chronic infections, pregnancy, cancer, abdominal surgery, or gastrointestinal bleeding were excluded. Demographic and clinical data, as well as anti-nuclear antibodies and complement levels, were obtained from medical records. No participant

Table 1. Sociodemographic, clinical and paraclinical features

	E. gallinarum Positive n = 7	E. gallinarum Negative n = 75	p value
Sociodemographic, mean ± SD			
• Age in years	37.14 ± 20.6	42.3 ± 13.8	0.10
• Months since diagnosis	75.85 ± 59.3	112.72 ± 99.5	0.23
• Weight in kg	58.88 ± 9.16	68.19 ± 15.98	0.06
• Size in m	1.61 ± 0.08	1.59 ± 0.06	0.20
• BMI, kg/m²	23.02 ± 4.02	26.65 ± 5.89	0.22
Clinical features, n (%)			
• Oral ulcers	0 (0.0)	5 (9.43)	0.42
• Alopecia	2 (28.57)	11 (20.75)	0.51
• Arthritis	3 (42.85)	31 (58.49)	0.61
• Serositis	4 (57.14)	4 (7.54)	**0.001**
• Nephritis	1 (14.28)	8 (15.09)	0.95
• CNS	0 (0.0)	2 (3.77)	0.62
• Hemolytic anemia	0 (0.0)	6 (11.32)	0.37
• CKD	0 (0.0)	1 (1.88)	0.72
• Chronic liver disease	0 (0.0)	2 (3.77)	0.62
• MEX-SLEDAI, mean ± SD	1.71 ± 2.92	1.83 ± 2.12	0.89
Laboratories, mean ± SD			
• Hemoglobin	13.87 ± 1.46	13.29 ± 1.04	0.19
• Leukocytes	6.46 ± 1.73	6.23 ± 2.49	0.81
• Lymphocytes	5.98 ± 10.16	5.69 ± 11.24	0.94
• Platelets	217.71 ± 31.7	250.47 ± 79.1	0.28
• BUN	16.38 ± 8.8	13.15 ± 5.4	0.23
• Creatinine	0.98 ± 0.29	0.72 ± 0.29	**0.03**
• Albumin	4.24 ± 0.47	4.16 ± 0.34	0.62
• TGO	21.42 ± 6.5	25.21 ± 10.8	0.37
• TGP	23.71 ± 22.2	23.14 ± 15.4	0.93
• CRP	0.78 ± 1.35	2.81 ± 7.56	0.55
• ESR	11.14 ± 7.6	19.49 ± 13.18	**0.03**
• ANAS	2248 ± 2653	730 ± 1499	0.27
• Anti-SM	13.93 ± 24.13	29.11 ± 122.47	0.83
• C3	42.62 ± 36.19	54 ± 52.85	0.48
• C4	9.12 ± 9.32	10.4 ± 10.95	0.77

Table 2. Demographic features and prevalence of *Enterococcus gallinarum* in patients with SLE vs healthy controls

	SLE n = 58	Healthy non-related controls n = 72	p value
Female, n (%)	51 (87.9)	65 (90.3)	0.440§
Age, mean ± SD	41.79 (14.60)	40.62 (14.21)	0.64†
Smoking, n (%)	9 (15.5)	2 (2.8)	0.011§
BMI (kg / m^2), mean ± SD	20.91 (4.59)	25.42 (4.32)	< 0.01†
Enterococcus gallinarum. n (%)	6 (10.3)	2 (2.8)	0.07§

BMI, body mass index; SD, standard deviation

† Student's t test.

§ Chi-Square Test

had received antibiotics, probiotics, or synbiotics within 3 months prior to the study. DNA was extracted using the DNeasy PowerLyzer PowerSoil DNeasy kit from Qiagen (Hilden, Germany) according to the manufacturer's specifications. E. gallinarum was detected using endpoint polymerase chain reaction assay in both SLE patients and age- and sex-matched healthy controls.

Results: Sixty subjects with systemic lupus erythematosus (SLE) were included in the study, with the majority being women (51, 85%). The mean age was 41.79 (±16.6) years, and the average time since diagnosis was 107.03 months (±95.46). E. gallinarum and Enterococcus spp were detected in 7 (11.6%) cases. The most common MEX-SLEDAI parameter observed was arthritis, present in 34 (56.6%) cases, followed by acute cutaneous lupus in 23 (38.3%) cases. Detailed clinical manifestations and laboratory findings can be found in Table 1. A significant difference was found in E. gallinarum-positive patients regarding creatinine levels (0.98 vs. 0.72, p=0.032), erythrocyte sedimentation rate (11.14 vs. 19.49, p=0.031), and the frequency of serositis (57.14% vs. 7.54%, p=0.001). However, when analyzing erythrocyte sedimentation rate using the age-adjusted upper limit, the significance was no longer present (p=0.4). When comparing the prevalence of E. gallinarum in age and sex matched healthy controls (2.8%) with subjects with systemic lupus erythematosus (SLE) (10.3%), E. gallinarum was found to be slightly higher, approaching statistical significance (Table 2)

Conclusion: E. gallinarum was found to have a slightly higher prevalence in patients with systemic lupus erythematosus (SLE) compared to healthy controls, indicating a potential association with the disease. Significant associations were observed between E. gallinarum-positive SLE patients and certain clinical and laboratory parameters.

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Abstract Number: 2310

Machine Learning Approaches for Prediction of Renal Flares in Systemic Lupus Erythematosus: Knowledge-Driven Models Outperformed Data-Driven Models

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
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Session Time: 9:00AM–11:00AM

Background/Purpose: Renal flares in patients with SLE result in significant nephron loss. Thus, identification of reliable early signals of impending renal flares is anticipated to improve the prognosis for these patients. Machine learning (ML) has witnessed growing utilisation in managing extensive, heterogeneous datasets, and non-linear relationships. In this study, we implemented two different approaches of ML algorithms to identify baseline clinical and laboratory determinants of renal flare occurrence in a large cohort of SLE.

Methods: We analysed data from five phase III trials (BLISS-52, BLISS-76, BLISS-NEA, BLISS-SC, EMBRACE) after exclusion of patients with baseline renal flare BILAG A or B (N=3169). Renal flares were defined as a change from C, D, or E to A or B in the renal domain of the classic BILAG index within a 52-week long follow-up. Following construction of panels of variables using either (i) knowledge or (ii) feature selection methods, we developed ML classifiers including extreme gradient boosting (XGBoost), least absolute shrinkage and selection operator (LASSO), random forest (RF), and multivariable logistic regression. A stratified split was applied to the data to partition the study population into a training (90%; N=2853) and a test set (10%; N=316). The training set was used in model development while the internal validation was developed by a 10 times 10-fold cross validation. The test set was used for external validation of the built model, and the performance of the models was demonstrated using area under the curve (AUC) of the receiver operating curves (ROC), accuracy with a 95% confidence interval (CI), sensitivity, and specificity metrics.Both approaches yielded final models that utilised the minimal number of features while maintaining optimal model performance.

Results: Of 3169 patients, 899 (28.3%) developed a renal flare during follow-up. XGBoost yielded the greatest accuracy both in the hypothesis-driven (0.97 and the data-driven approach (0.88), as well as the highest performance metrics (AUC: 0.97 and 0.91; sensitivity: 1.00 and 0.82; specificity: 0.94 and 0.94, respectively) and an adequate calibration on the test dataset. LASSO (accuracy: 0.95 and 0.86 ; AUC: 0.97 and 0.96; sensitivity: 1.00 and 0.86; specificity: 0.91 and 0.86, respectively) demonstrated similar performance. The final model successfully reduced the number of features to five parameters: renal BILAG C or D score, urine protein creatinine ratio, serum albumin, blood urea nitrogen, and C3 levels. These models exhibited encouraging performance, with AUC values of 0.88, 0.88, 0.88, and 0.87 for XGBoost, LASSO, logistic regression, and RF, respectively.

Conclusion: The knowledge-driven approach based on clinical expertise outperformed the unsupervised data-driven approach which solely relied on feature selection methods. Through utilisation of five routine clinical parameters, we developed a robust and highly accurate prediction tool for forecasting renal flares in patients with SLE. Our ML-based model holds substantial value in guiding clinical decision-making to personalise patient management and possesses potential for practical application in clinical settings.

Disclosure: N. Cetrez: None; **J. Lindblom**: None; **R. Da Mutten**: None; **D. Nikolopoulos**: None; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia Pharmaceuticals, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Elli Lilly and Company, 5, 6, F. Hoffmann-La Roche AG, 5, 6, Gilead Sciences, 5, 6, GSK, 5, 6, Janssen Pharmaceuticals, 5, 6, Novartis, 5, 6, Otsuka Pharmaceutical, 5, 6.

Abstract Number: 2311

Effect on Lupus Outcomes of the Protective Allele at rs1876453 in the Complement Receptor 2 Gene

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus is a heterogenous autoimmune disease characterized by inflammatory damage to multiple organ systems. We have shown that the single-nucleotide polymorphism (SNP) rs1876453 is associated with decreased risk of lupus, with a preferential effect on anti-double stranded (ds) DNA antibodies. Since anti-dsDNA antibodies develop prior to clinically apparent disease and are associated with more severe disease, we hypothesized that the minor A allele at rs1876453 would delay disease onset and improve clinical outcomes. We demonstrated a delay in lupus onset associated with the SNP using a large lupus association study [Large Lupus Association Study 2 (LLAS2)], and herein we explore the effects of the SNP on clinical outcomes using a longitudinal inception cohort.

Methods: Subjects genotyped using the Illumina platform from a longitudinal inception cohort [Systemic Lupus International Collaborating Clinics (SLICC), n=977] were studied. Age of onset was determined, and damage, disease activity, steroid exposure, and survival were assessed.

Results: As with the subjects in the LLAS2 cohort, the median age of diagnosis for subjects with the protective A allele at rs1876453 was significantly greater in the SLICC cohort [median (IQR), 33 (20) for GG, 36 (20) for AG, and 50 (31.5) for AA, p = 0.0167]. Subjects with the protective allele had similar scores for damage at 5 years, but their likelihood of developing damage by then was greater (41.6% for AG/AA vs 31.8% for GG at Year 5, p = 0.0270). This was not due to more severe disease, since they had lower disease activity [median SLEDAI (IQR) 2.5 (3.6) for GA/AA, 3.3 (3.8) for GG; p = 0.0163] and comparable steroid exposure. Although this was likely due in part to their older age at disease onset, there was a trend towards early damage even in patients younger than age 50 (p = 0.0762). Despite their older median age, their mortality rates were lower (p = 0.0414).

Conclusion: The minor allele at rs1876453 is associated with delayed onset, reduced overall disease activity, and lower mortality despite the increased probability of early damage. This increased risk of early damage may result from older age at disease onset or from a specific pathogenic mechanism in subjects with the protective SNP who develop lupus and will require further study.

Disclosure: A. Oganesyan: None; **R. Sharp**: None; **P. O'Neill**: None; **C. Aranow**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, 5, kezar Inc, 2; **L. Arnaud**: AbbVie, 6, Alexion, 6, Alpine, 2, 6, Amgen, 6, AstraZeneca, 1, 2, 6, Biogen, 6, Boehringer Ingelheim, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 1, 2, 6, Grifols, 6, Janssen, 6, Kezar Life Sciences, 2, 6, LFB, 6, Medac, 6, Novartis, 2, 6, Pfizer, 6, Roche-Chugaï, 6, UCB, 6; **A. Askanase**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb, 2, Celgene, 2, Eli Lilly, 2, Genentech, 2, GSK, 2, Idorsia, 2, Janssen, 2, Mallinckrodt, 2, Pfizer, 2, UCB Pharma, 2; **S. Bae**: None; **S. Bernatsky**: None; **I. Bruce**: AstraZeneca, 1, 2, 5, 6, Aurinia, 2, GSK, 1, 2, 5, 6, Janssen, 5, 6, Lilly, 1, UCB, 6; **J. Buyon**: Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, Related Sciences, 1; **W. Chatham**: None; **A. Clarke**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, 5, Otsuka, 2, Roche, 2; **N. Costedoat-Chalumeau**: None; **M. Dooley**: None; **P. Fortin**: AbbVie, 1, AstraZeneca, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Roche-Genentech, 1; **E. Ginzler**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, Gilead Sciences, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5; **C. Gordon**: AbbVie, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, Sanofi, 2, UCB Pharma, 2; **J. Hanly**: None; **M. Inanç**: Boehringer-Ingelheim, 6, Pfizer, 6, UCB, 6; **D. Isenberg**: None; **S. Jacobsen**: None; **A. Jonsen**: None; **K. Kalunian**: AbbVie/Abbott, 2, Amgen, 5, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EquilliumBio, 2, Genentech, 2, Gilead, 2, Janssen, 2, KezarBio, 1, Merck/MSD, 2, Novartis, 2, Pfizer, 2, Remegene, 2, Roche, 2, UCB, 5; **D. Kamen**: None; **S. Lim**: None; **A. Mak**: None; **E. Morand**: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 2, 5, 6, Biogen, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, EMD Serono, 2, 5, Galapagos, 2, Genentech, 2, 5, GlaxoSmithKline, 2, 5, IgM, 2, Janssen, 2, 5, Novartis, 2, Servier, 2, Takeda, 2, UCB, 5; **C. Peschken**: AstraZeneca, 2, 5, GSK, 2, 5, Roche, 1, 2; **M. Petri**: Alexion, 1, Amgen, 1, AnaptysBio, 1, Annexon Bio, 1, Argenx, 1, Arhros-Focus Med/Ed, 6, AstraZeneca, 1, 5, Aurinia, 1, 5, 6, Axdev, 1, Biogen, 1, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CVS Health, 1, Eli Lilly, 1, 5, Emergent Biosolutions, 1, Exagen, 5, Exo Therapeutics, 2, Gilead Biosciences, 2, GlaxoSmithKlein(GSK), 1, 5, 6, Horizon Therapeutics, 2, Idorsia Pharmaceuticals, 2, IQVIA, 1, Janssen, 1, 5, Kira Pharmaceuticals, 2, MedShr, 6, Merck/EMD Serono, 1, Momenta Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Proviant, 2, Sanofi, 2, Sinomab Biosciences, 2, Thermofisher, 5, UCB, 2; **B. Pons-Estel**: None; **A. Rahman**: None; **R. Ramsey-Goldman**: Ampel Solutions, 2, Calabetta, 2, Exagen, 2, Immunocor, 6; **J. Reynolds**: None; **J. Romero-Diaz**: None; **G. Ruiz-Irastorza**: None; **J. Sanchez-Guerrero**: None; **K. Steinsson**: None; **M. Urowitz**: None; **R. van Vollenhoven**: AbbVie, 2, 6, AstraZeneca, 2, 5, 6, Biogen, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Galapagos, 2, 5, 6, GlaxoSmithKline, 6, Janssen, 2, 6, MSD/Merck Sharp and Dohme, 5, Novartis, 5, Pfizer, 2, 5, 6, RemeGen, 2, Roche, 5, Sanofi, 5, UCB, 2, 5, 6; **E. Vinet**: None; **A. Voskuyl**: None; **D. Wallace**: None; **S. Manzi**: AbbVie, 5, Allegheny Singer Research Institute, 10, AstraZeneca,

2, 5, Exagen Diagnostics, Inc, 2, 9, 10, GSK, 2, 5, Lilly, 2, Lupus Foundation of America, 4, Novartis, 2, UCB Advisory Board, 2, Univiersity of Pittsburgh, 10; **K. Jones**: None; **S. Boackle**: None.

Abstract Number: 2312

Fungal Infections in Hospitalized Patients of Systemic Lupus Erythematosus: A Nationwide Cohort Analysis

Saman Tanveer and Chun Pan, John H. Stroger Jr. Hospital of Cook County, Chicago, IL

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Immunosuppressive therapy is the cornerstone of management in patients with systemic lupus erythematosus (SLE). Patients on immunosuppressive therapy are at increased risk of developing opportunistic fungal infections. We conducted this analysis to describe the epidemiology of fungal infections in this cohort.

Methods: We analyzed the National Inpatient Sample (NIS) 2016-2020 for all patients with discharge diagnosis of SLE & Fungal infections (Histoplasmosis, Pneumocystosis, Cryptococcosis, Aspergillosis, Blastomycosis, candidiasis, Coccidioidomycosis) as primary or secondary diagnosis via ICD-10 codes. Frequencies, demographics and trends were determined and compared between hospitalized patients with SLE and without SLE. A p-value of ≤0.05 was considered statistically significant.

Results: In hospitalized SLE patients, there was higher risk of developing fungal infections in male gender and in Hispanics & Asian populations. Steroid use, concomitant HIV infection and the presence of leukemias & lymphomas in hospitalized SLE patients were significant predictors of fungal infection (Figure 1). There were also differences in the incidence of different fungal infections based on geographical areas in the US, with Blastomycosis being more common in the Midwest. From 2016 to 2020, there was a decline in the incidence rate of hospitalization per 100,000 for non-SLE patients with fungal infections whereas this rate remained steady for the SLE cohort (Figure 2).

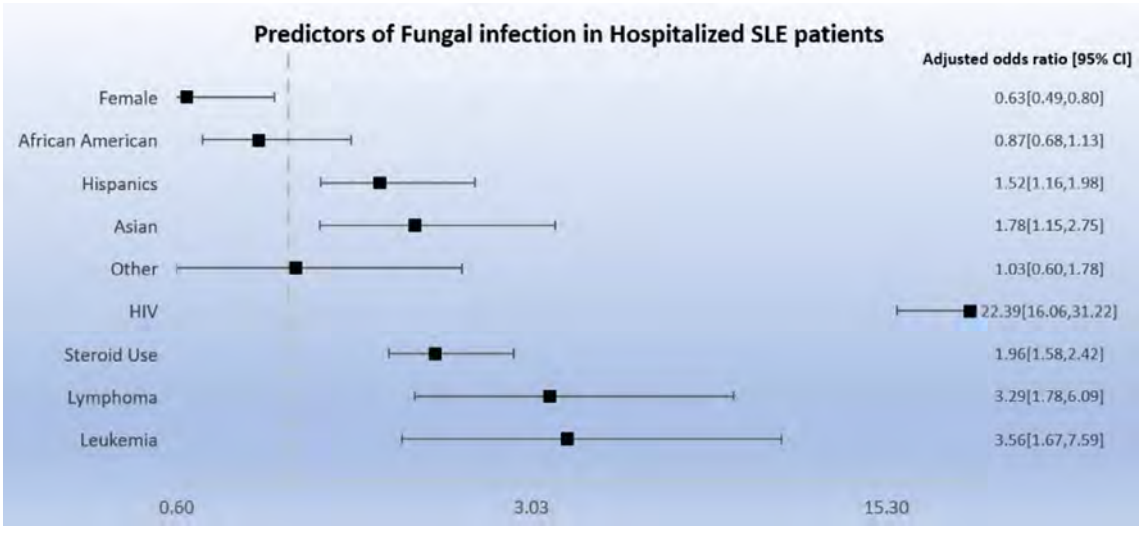


Figure 1 - Various predictors of fungal infections in hospitalized SLE patients (CI: Confidence Interval)

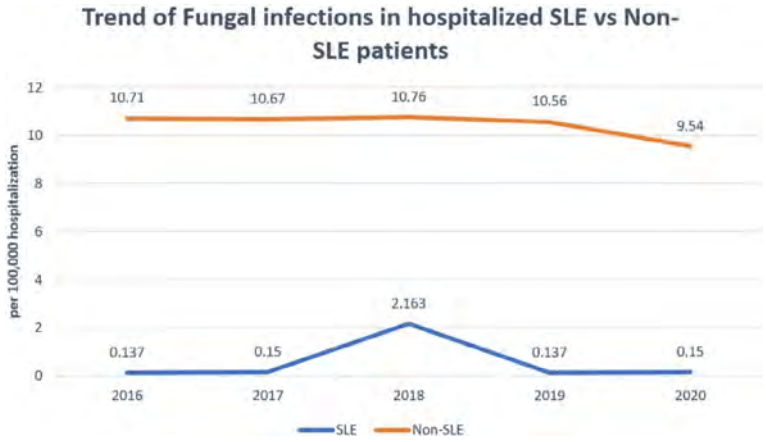


Figure 2 - Decrease in incidence rate of hospitalization per 100,000 for non-SLE patients with fungal infections; incidence rate of hospitalization per 100,000 for SLE patients with fungal infections has remained stable

Conclusion: The frequency of hospitalized SLE patients with fungal infections has remained stable between 2016 to 2020 compared to non-SLE patients for which this rate has decreased. This difference could be explained by the use of immunosuppressive therapy in SLE patients. Further studies can be done to explain the increased risk of fungal infections in hospitalized SLE patients who are males, Hispanics and Asians.

Disclosure: S. Tanveer: None; **C. Pan**: None.

Abstract Number: 2313

Utilization of Palliative Care in Hospitalized Patients with Systemic Lupus Erythematosus: A Nationwide Cohort Analysis

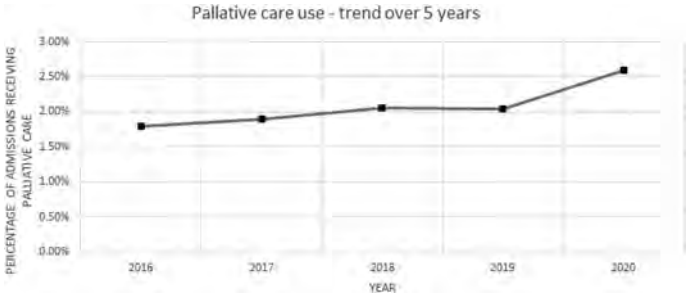
Saman Tanveer[1], Hema Pinnam[2], Fatima Tanveer[3] and Daksh Ahluwalia[1], [1]John H. Stroger Jr. Hospital of Cook County, Chicago, IL, [2]J.S.S. Medical College, Mysore, India, [3]CMH Lahore Medical College, Lahore, Pakistan

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: We aimed to investigate trends in utilization of hospital palliative care services among hospitalized patients with systemic lupus erythematosus (SLE) and analyze its impact on length of hospital stay, hospital charges, and in-hospital mortality.

Methods: The National Inpatient Sample (NIS) 2016-2020 was used to identify hospitalizations for SLE, and these were further stratified based on inpatient palliative care use. Univariate logistic regression analysis was used for yearly trends, with year of admission as the independent variable and palliative care use as the dependent variable. Length of stay and total hospitalization charges were compared using multivariate linear regression, adjusting for potential confounders. A p-value of ≤ 0.05 was considered statistically significant.



Graph 1 - Increase in utilization of palliative care among hospitalized patients with SLE from 2016 to 2020

Results: The overall proportion of utilization of hospital palliative care services for patients with SLE over five years, ranging from 2016 to 2020, was 2.07%. There was a rise in the trend of utilization of palliative care services in patients with SLE, increasing from 1.8% in 2016 to 2.60% in 2020 (P-value for trend < 0.001). Older age, higher Charlson comorbidity index,

Table 1 - Predictors of palliative care utilization in hospitalizations for SLE

PREDICTORS OF PALLIATIVE CARE USE IN HOSPITALIZATIONS FOR SLE		
VARIABLE	aOR (95% CI)	P-value
Gender		
Male	Referent	
Female	0.95 (0.86-1.05)	0.361
Age categories		
18 - 34	Referent	
35 - 49	1.80 (1.49-2.18)	<0.001
50 - 64	3.30 (2.76-3.94)	<0.001
65 - 79	5.28 (4.36-6.38)	<0.001
=80	10.95 (8.92-13.4)	<0.001
RACE		
White	Referent	
Black	0.89 (0.81-0.97)	0.014
Hispanic	0.87(0.77-0.98)	0.032
Asian	1.08(0.87-1.33)	0.472
Other race	0.86(0.69-1.07)	0.181
Charlson Comorbidity Index		
CCI 0	Referent	
CCI 1	No sample in this stratum	
CCI 2	1.79 (1.53-2.10)	<0.001
CCI 3 or more	3.96 (3.46-4.54)	<0.001
Hospital Region		
Northeast	Referent	
Midwest	1.32 (1.17-1.49)	<0.001
South	1.13(1.01-1.27)	0.027
West	1.25(1.10-1.41)	<0.001
Hospital Bed Size		
Small	Referent	
Medium	1.36 (1.21-1.53)	<0.001
Large	1.47(1.32-1.64)	<0.001
Hospital Location and Teaching Status		
Rural	Referent	
Urban non-teaching	1.21 (0.98-1.49)	0.065
Urban teaching	1.78(1.47-2.16)	<0.001
Insurance		
Medicare	Referent	
Medicaid	1.07 (0.94-1.21)	0.28
Private insurance	1.06(0.95-1.18)	0.253
Self-pay	1.15(0.88-1.51)	0.29

admission in urban teaching hospitals and large-size hospitals were associated with more frequent use of inpatient palliative care. Age less than 35 years, Black and Hispanic race were identified as independent predictors of lower use of inpatient palliative care. Patients with SLE who received palliative care services experienced a longer hospital stay (mean difference [MD]: 4.04 days, 95 % Confidence interval [CI]: 3.62-4.46 days, $p < 0.001$] as well as higher hospital charges (MD: $61287, 95% CI: $53914-$68660 $p < 0.001$), compared to SLE admissions that did not receive palliative care.

Conclusion: Utilization for palliative care services has increased over the last five years for hospitalized SLE patients, with a significant rise in utilization during the COVID-19 pandemic. Utilization of palliative care services is associated with increased length of stay in the hospital and increased hospitalization charges. Most importantly, significant disparities exist in palliative care utilization based on racial differences and medical comorbidities. Further efforts are needed for equitable access to palliative care in patients with rheumatological diseases.

Disclosure: S. Tanveer: None; **H. Pinnam**: None; **F. Tanveer**: None; **D. Ahluwalia**: None.

Abstract Number: 2314

Comparison of Disease Severity and Outcomes in Adolescent-Onset and Young Adult-Onset Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
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Background/Purpose: Adolescent-onset SLE is associated with more severe disease than adult-onset SLE, but young adults may also experience adverse outcomes. We sought to compare disease and damage-related outcomes between adolescent-onset and young adult-onset SLE.

Methods: We conducted a comparative cohort study to assess potential differences in outcomes between patients with adolescent-onset (ages 12-17) vs. young adult-onset (ages 18-23) SLE. Using observational data from a US multi-center electronic health record database, we identified patients with incident SLE (enrolled for ≥ 2 years prior to the first SLE code and met the SLE definition: > 2 SLE ICD codes > 30 days but < 2 years apart). We assessed demographics, SLE severity, early onset lupus nephritis (LN) and baseline comorbidities. We examined kidney outcomes including LN, chronic kidney disease (CKD), end-stage kidney disease (ESKD), transplantation. Among the subset with LN, we also assessed persistent proteinuria, defined as >500mg/day more than one year after LN onset among the subset with LN. We also assessed cardiovascular (CV) events (including major adverse cardiac events and venous thrombosis), psychiatric illness (including hospitalization for depression/suicidality), and SLICC damage index progression. Since LN can occur at SLE onset, kidney outcomes were compared using logistic regression; other outcomes were compared using cox regression to assess incidence rates and hazard ratios. We adjusted for sex, race/ethnicity, and geographic region.

Results: We identified 2866 patients with adolescent-onset and 5589 with young adult-onset SLE **(Table 1).** Adolescents were less likely to be non-Hispanic White (26 vs. 36%) than young adults. Adolescents had higher rates of moderate and severe SLE disease index scores and higher frequency of early onset LN compared to young adults (35 vs. 25%). Over

Baseline Characteristics	Adolescent onset (n=2866)	Young adult onset (n=5589)
Age of Onset, mean (SD)	15.0 (1.6)	20.7 (1.7)
Female sex, n (%)	2458 (85.8)	4973 (89.0)
Race/Ethnicity, n (%)		
African American	838 (29.2)	1852 (33.1)
Asian	145 (5.1)	203 (3.6)
White	752 (26.2)	1984 (35.5)
Unknown/Other	548 (19.1)	695 (12.4)
Hispanic	583 (20.3)	855 (15.3)
Geographic Region, n (%)		
East	399 (13.9)	1016 (18.2)
Midwest	528 (18.4)	998 (17.9)
South	1771 (61.8)	2920 (52.2)
West	168 (5.9)	655 (11.7)
SLE severity index, n (%)		
Mild	1447 (50.5)	3128 (56.0)
Moderate	1016 (35.5)	1714 (30.7)
Severe	403 (14.1)	747 (13.4)
Medication Use, n (%)		
Hydroxychloroquine	1485 (51.8)	2816 (50.4)
Glucocorticoids	1459 (50.9)	2741 (49.0)
Mycophenolate	739 (25.8)	1079 (19.3)
Cyclophosphamide	167 (5.8)	193 (3.5)
Belimumab	12 (0.4)	96 (1.7)
ACEi or ARB'	462 (31.2)	666 (28.8)
Early-Onset Lupus Nephritis*, n (%)	996 (34.8)	1420 (25.4)
CKD stage ≤2, n (%)	20 (0.7)	269 (4.8)
Depression, n (%)	56 (2.0)	186 (3.3)
Cardiovascular disease, n (%)	31 (1.1)	105 (1.9)
Healthcare Utilization, mean (SD)		
Outpatient visits	2.0 (4.5)	2.3 (5.3)
ER/Inpatient visits	0.5 (1.3)	0.6 (1.9)

Assessed in the one year prior to diagnosis unless otherwise specified. * Lupus nephritis defined as ≥1 specific lupus nephritis code (ICD-10 M32.14/15) or ≥2 ICD 9 or ICD 10 nephritis codes (Chibnik 2010). Patients with a lupus nephritis code within 6 months after the first SLE code were classified as early lupus nephritis. SLE severity index derived from ICD codes and medications, adapted from Garris et al. J Med Econ 2013.

Baseline Characteristics of Patients with Adolescent and Young Adult-Onset SLE

	Adolescent onset (n=2866)			Young adult onset (n=5589)				
	N	Follow up time, y (mean)	Incidence (%)	N	Follow up time, y (mean)	Incidence (%)	Unadjusted Odds Ratio (95% CI)	Adjusted* Odds Ratio (95% CI)
Kidney Outcomes								
Lupus Nephritis	1481	5.7	51.7	2309	5.4	41.3	1.52 (1.39-1.66)	1.43 (1.30-1.57)
End-Stage Kidney Disease	249	5.7	8.7	665	5.4	11.9	0.70 (0.60-0.82)	0.64 (0.55-0.75)
Chronic Kidney Disease stage ≥ 2	628	5.7	21.9	2270	5.4	40.6	0.41 (0.37-0.45)	0.42 (0.38-0.46)
Chronic Kidney Disease stage ≥ 3	381	5.7	13.3	1147	5.4	20.5	0.59 (0.52-0.67)	0.56 (0.49-0.64)
Kidney Transplant	101	5.7	3.5	234	5.4	4.2	0.84 (0.66-1.06)	0.76 (0.59-0.96)
Proteinuria >500mg/day† >1 year after LN onset	394	2.6	56.2	702	2.7	60.1	0.85 (0.71-1.03)	0.89 (0.73-1.08)

*Adjusted for sex, race/ethnicity, and geographic region. Young-adult onset SLE is the reference group. †Among patients with lupus nephritis and urine protein assessed ≥ 1 year after LN onset (n=701 with adolescent-onset SLE and n=1169 with young adult-onset SLE).

Kidney Outcomes in Adolescent-Onset Versus Young Adult-Onset Systemic Lupus Erythematosus

	Adolescent onset (n=2866)			Young adult onset (n=5589)				
	N	Follow up time, y (mean)	Incidence Rate (per 1000 PY)	N	Follow up time, y (mean)	Incidence Rate (per 1000 PY	Unadjusted Hazard Ratio (95% CI)	Adjusted* Hazard Ratio (95% CI)
Cardiovascular Outcomes								
Major Adverse Cardiac Events	149	5.4	9.7	429	5.1	15.2	0.64 (0.53-0.78)	0.59 (0.49-0.71)
Venous Thromboembolism	205	5.3	13.5	619	4.9	22.8	0.60 (0.52-0.71)	0.59 (0.50-0.69)
Psychiatric Outcomes								
Anxiety	461	5.1	31.3	1358	4.6	53.1	0.60 (0.54-0.67)	0.64 (0.58-0.71)
Depression	556	4.8	40.3	1479	4.3	61.8	0.67 (0.61-0.74)	0.71 (0.64-0.78)
Hospitalization for Depression/Suicide Attempt	201	5.4	13.1	480	5.1	16.9	0.78 (0.66-0.92)	0.80 (0.67-0.94)
SLICC Damage Index Accumulation (SDI ≥1)	1192	3.6	114.9	2533	3.2	142.6	0.84 (0.78-0.90)	0.81 (0.76-0.87)

PY, person-years; MACE includes hospitalizations for myocardial infarction, stroke, and heart failure. *Adjusted for sex, race/ethnicity, and geographic region. Young-adult onset SLE is the reference group.

Morbidity and Damage Progression in Adolescent-Onset Versus Young Adult-Onset Systemic Lupus Erythematosus

2/3 of each group used hydroxychloroquine and glucocorticoids. Over mean 5.7 and 5.4 years follow up, LN was more common in adolescents than young-adult onset SLE patients (adjusted HR 1.43 (1.30-1.57), but CKD, ESRD, and kidney transplant were less frequent than in young adults **(Table 2)**. There was a trend towards a lower risk of persistent proteinuria in adolescents, but this outcome was frequent in both groups with LN (56 vs. 60%). Adolescent-onset SLE was associated with a lower risk of CV events, psychiatric outcomes, and damage accumulation than in young-adult onset SLE **(Table 3)**.

Conclusion: In this comparative cohort study of patients with adolescent and young adult-onset SLE, we found that adolescents have more severe disease at SLE onset, with a higher risk of LN, but they have a lower risk of kidney damage and overall damage progression than young adults, as well as a lower risk of CV and psychiatric morbidity. Among those with LN in both age groups of SLE onset, more than half had persistent proteinuria, which suggests the need to improve outcomes.

Disclosure: E. Materne: None; **B. Zhou**: None; **H. Choi**: Ani, 2, Horizon, 2, 5, LG, 2, Protalix, 2, Shanton, 2; **Y. Zhang**: None; **A. Jorge**: None.

Abstract Number: 2315

Assessing Lupus Disease Activity Following the Onset of End-Stage Kidney Disease Within a Single Tertiary Centre in South London

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III

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Table 1 - Mean values before and after the onset of ESKD (n=30)

	Before	After
SLEDAI-2K score	4.8	2.6
dsDNA titre (IU/mL)	64.6	25.2
C3 level (g/L)	0.96	1.03
C4 level (g/L)	0.26	0.3
Prednisolone dose equivalent (mg/day)	15.7	11.5

Background/Purpose: Lupus nephritis represents a severe manifestation of SLE and is associated with a risk of progression to end-stage kidney disease (ESKD) if untreated, leading to significant morbidity and high healthcare-related costs. Once patients with SLE reach ESKD and are initiated on renal replacement therapy (RRT), in the form of either dialysis or transplantation, it has previously been suggested that the disease becomes quiescent. However, our experience suggests that patients continue to exhibit active disease even after reaching ESKD. In this study we describe the temporal trends in disease activity for patients with SLE before and after ESKD from a single tertiary centre in South London. We also sought to identify whether there was a greater risk of ongoing disease activity across ethnic groups.

Methods: We conducted a retrospective observational study of consecutive adult patients with biopsy-proven lupus nephritis and ESKD who were under regular follow up in our unit from May 2004 to May 2023. Clinical electronic records were examined from the first point of entry until the end of the study period, transfer or death. Medication, SLE Disease Activity Index 2000 (SLEDAI-2K), dsDNA and complement levels were checked at 6-monthly intervals before and after the onset of ESKD. The primary outcome was disease activity using the SLEDAI-2K score, before and after the onset of ESKD. A SLEDAI-2K score ≤4 was considered low disease activity and >4 as active or flaring disease. Mean scores were compared using Wilcoxon's signed-rank test.

Results: Thirty patients were included (90% female, 67% of Black ethnicity, 20% Caucasian and 13% Asian) with a combined 369 years of follow up. The mean age at SLE diagnosis was 29 years (±11.7) and the mean interval from SLE diagnosis to ESKD was 11.8 years (±7.4). During this period 12 patients underwent renal transplantation, 18 patients received dialysis only and 7 patients died (4 with active SLE). SLEDAI-2K fell on average after the onset of ESKD although this did not reach statistical significance (Figures 1 and 2). Immunological markers of disease activity did appear to improve, as shown in Table 1. Of the 29 patients with >6 months of data after ESKD onset, 15 achieved consistently low disease activity within an average of 1.4 years (±2.5). However, 14 of the 29 patients exhibited active disease with an average time to flare of 2.6 years (±3.4). Nine of these 14 patients showed active disease within 18 months of ESKD onset and all were of Black

Figure 1 - Mean SLEDAI-2K Scores Before and After ESKD

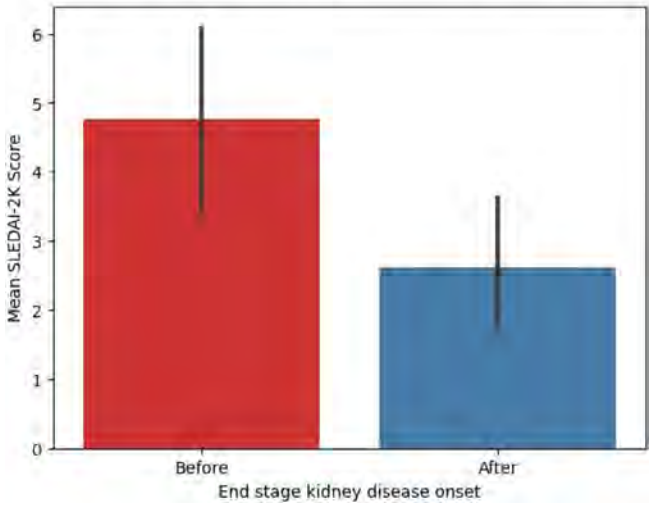
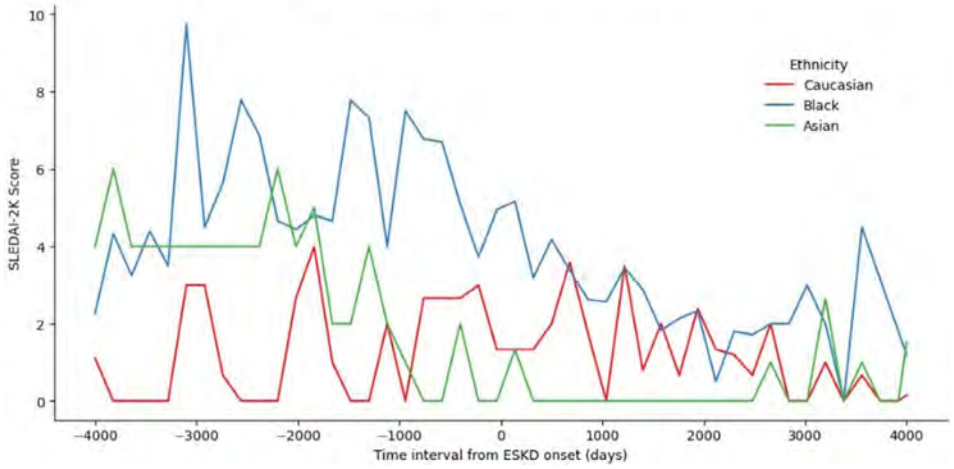


Figure 2 - SLEDAI-2K Scores In Relation To ESKD



ethnicity. Clinical manifestations after ESKD involved rashes, synovitis, serositis, myocarditis and neuropsychiatric involvement. Five patients ultimately required induction therapy with cyclophosphamide or rituximab.

Conclusion: Despite a fall in mean SLEDAI scores after the onset of ESKD, SLE disease activity persisted or flared in 48% of cases, often within 18 months of ESKD diagnosis. Our cohort were primarily of Black ethnicities, who are known to have more frequent and aggressive renal involvement. Our data contradicts the notion that SLE "burns out" in ESKD and supports a need for vigilance in the monitoring of patients with SLE and ESKD, particularly in those of Black ethnicities and within the first 18 months of RRT.

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Abstract Number: 2316

Effect of SARS-CoV2 Infection on Disease Flares in Patients with Systemic Lupus Erythematosus: A Case-control Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
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Background/Purpose: To study the effect of SARS-CoV2 infection on disease flares in patients with systemic lupus erythematosus (SLE).

Methods: Patients who fulfilled the ACR or SLICC criteria for SLE and were followed in our rheumatology clinics were retrospectively studied. We identified patients who had documented COVID-19 (Omicron and its variants) between February and November 2022 and a group of SLE controls who did not have COVID-19 randomly matched for age, sex, and the time period of COVID-19 in a 1:2 ratio. The primary outcomes of interest were SLE flares (clinical or serological) within 90 days of SARS-CoV2 infection.SLE flares were assessed by the SELENA flare instruments, with modifications (mild/moderate or severe). The rates of SLE flares were compared between SARS-CoV2-infected SLE patients and controls.

Results: 91 SLE patients with COVID-19 (age 48.6±14.0 years; 95.6% women; SLE duration 14.2±8.3 years; 53% history of lupus nephritis) and 182 SLE controls not infected by COVID-19 (age 48.7±13.8 years; 95.6% women; SLE duration 15.2 ±9.0 years) were studied. Eleven of 90 (12.2%) SARS-CoV2-infected patients had serious manifestations (oxygen requirement, use of mechanical ventilator, lung infiltrates on imaging studies or admission to the intensive care unit). Patients with mild COVID-19 were treated symptomatically or oral anti-viral agents whereas those with serious COVID-19 was treated with intravenous remdesivir, dexamethasone, and/or biologic/targeted agents. One (1.1%) of our patients died and 7 (7.7%) patients developed severe complications. Within 90 days of SARS-CoV2 infection, 14 (15.4%) patients developed mild/moderate SLE flares, and 2 (2.2%) patients had severe SLE flares. The incidence of SLE flares in SARS-CoV2-infected patients was significantly higher than those without (17.6% vs. 5.5%; p=0.001). The changes in anti-dsDNA and complement C3 levels, however, were not significantly different between the two groups. Among SARS-CoV2-infected SLE patients, those with clinical SLE flares had significantly lower C3 values (p=0.004) but non-significantly higher anti-dsDNA titer (p=0.32) before SARS-CoV2 infection than those without SLE flares. Herpes zoster (HZ) reactivation occurred in 2 patients (2.2%) with COVID-19, which was numerically higher than those not infected by COVID-19 (2 patients, 1.1%; p=0.48). No particular risk factors were identified for HZ reactivation after COVID-19 infection.

Conclusion: In this retrospective case-control study, clinical flares within 90 days were significantly more common in patients infected with SARS-CoV2 than age and gender-matched non-infected SLE controls.SLE patients with lower C3 levels were more likely to flare after COVID-19. The results from our study support the hypothesis for a viral trigger for disease exacerbation in SLE.

Disclosure: C. Mok: None; **C. Cheung**: None; **C. To**: None; **K. Chan**: None; **S. TSE**: None.

Abstract Number: 2317

Effect of SLE-DAS Remission on Quality of Life in Patients with Systemic Lupus Erythematosus: A Cross-sectional Validation Study

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Background/Purpose: The SLE Disease Activity Score (SLE-DAS) has been developed and validated in Italian patients with SLE. The objective of this study was to evaluate the effect of disease remission as defined by SLE-DAS on health-related quality of life (HRQoL) in Chinese patients with SLE.

Methods: Consecutive patients who fulfilled the 1997 ACR or 2012 SLICC criteria for SLE between March and May 2023 were recruited from our clinics. Participants were asked to complete the validated Chinese version of the LupusPRO (v1.8) HRQoL questionnaire and Fatigue Severity Score (FSS) before consultation. Attending physicians were asked to grade the SLE disease activity according to the Physicians' Global Assessment (PGA [0-3]), SLE-DAS and SLEDAI-2K. Remission, mild, and moderate/severe disease activity of SLE was defined as SLE-DAS ≤2.08, < 2.08-≤7.64 and >7.64 respectively. SLE-DAS Boolean-based remission was defined as all clinical items of SLE-DAS equal to zero and prednisolone usage ≤5mg/day. The effects of SLE-DAS remission on LupusPRO were studied by statistical analyses.

Results: At interim, a total of 216 SLE patients were studied (age 45.8±13.6 years; 96.2% women; SLE duration 16.0 ±7.8 years). All were ethnic Chinese. At baseline visit, 84 (38.9%) patients had clinically active SLE, defined by a PGA score ≥0.5.Active organ manifestations, in decreasing order of frequency, were proteinuria (17.2%), mucocutaneous lesions (11.0%), leukopenia (7.9%), arthritis (4.7%) and thrombocytopenia (2.8%). The distribution of PGA score was: < 0.5 (60.6%); 0.5-1.0 (16.2%), ≥1.0-2.0 (19.0%) and 2.0-3.0 (3.70%).There were 135 (62.5%) patients who scored zero in the clinical SLEDAI-2K.A total of 135 (62.5%) patients had SLE-DAS≤2.08, and 132 (61.1%) patients achieved SLE-DAS Boolean-based remission; 34 (15.7%) and 47 (21.6%) patients, respectively, had SLE-DAS mild and moderate/severe activity. SLE-DAS correlated significantly with PGA (r=0.802, p< 0.001), SLEDAI-2K (r=0.798, p< 0.001) and LupusPRO score (r=-0.285, p< 0.001).Patients with SLE-DAS Boolean-based remission, compared to non-remission, had significantly higher total LupusPRO score (73.1±15.1 vs 65.9±17.4; p < 0.001), particularly in the domains of lupus symptoms (72.0±17.7 vs 61.5±20.7; p< 0.001), procreation (88.3±19.6 vs 76.8±28.9; p< 0.001), lupus medications (68.2±23.6 vs 58.2±28.2; p=0.003), physical health (81.2±18.9 vs 76.5±21.4; p=0.03), emotional (64.5±22.5 vs 57.0±25.3; p=0.01), and body image (80.3±22.7 vs 74.3±27.6, p=0.01).Similarly, significantly higher LupusPRO score was observed in patients who achieved clinical SLEDAI-2K=0 (vs >0) (72.7±15.4 vs 66.3±17.3; p=0.005) and PGA< 0.5 (vs ≥0.5) (73.5±15.4 vs 65.2±16.7; p< 0.001). SLEDAI-2K and PGA also correlated significantly with LupusPRO score (r=-0.247; p< 0.001; r=-0.265; p< 0.001 respectively), with similar correlation coefficients with the SLE-DAS.

Conclusion: SLE-DAS remission is associated with significantly better HRQoL in Chinese patients with SLE in this interim cross-sectional analysis.Similar performance of SLE-DAS was observed with the SLEDAI-2K and PGA.Further longitudinal studies on the sensitivity of the SLE-DAS to change in disease activity are in progress.

Disclosure: F. Lam: None; **C. To**: None; **C. Mok**: None.

Abstract Number: 2318

The Association Between Systemic Lupus Erythematosus (SLE) and Bone Mineral Density (BMD) Polygenic Risk Scores with Lumbar Spine BMD Z-score: A Retrospective Cohort Study

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SESSION INFORMATION

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Background/Purpose: Childhood-onset systemic lupus erythematosus patients < 18 years (cSLE) are at risk for reduced bone mineral density (BMD) due to disease activity and chronic glucocorticoid exposure. Genetics play a role in SLE susceptibility. Our aim was to assess the genetic contribution to BMD among a multi-ethnic cSLE cohort.

Methods: All patients were diagnosed and followed at the SickKids and had baseline Lumbar Spine (LS) BMD scan, defined as 1 month prior, or up to one year post cSLE diagnosis. The main outcome of interest was LS (L1-L4) BMD z scores. Two weighted polygenic risk scores (PRSs)- 1) BMD PRS 2) SLE PRS were calculated based on largest GWASs to date. Both PRSs were regressed with BMD z-scores in linear models adjusted for demographics, glucocorticoid exposure, height percentile, BMI, and an indicator for lupus nephritis and/or neuropsychiatric lupus.

Results: The study included 284 patients, 82% female, 29% of European, and 28% of East Asian ancestry. The median age of cSLE diagnosis was 13.5 years [IQR 11.1, 15.3]. In multivariate model, a higher BMD PRS was significantly associated with low BMD z-score (β: -0.75; 95%CI: -1.32, -0.18; *P*=0.01) as was prior steroids use (β: -0.34; 95%CI: -0.63, -0.04; *P*=0.02). No association was found between SLE PRS and LS BMD z-scores. Height percentile and BMI were significantly associated with BMD z-score, however presence of LN and/or NPSLE was not.

Conclusion: High BMD PRS was significantly associated with lower LS BMD z-score in cSLE patients at baseline. BMD PRS may be an effective tool to stratify cSLE patients.

Disclosure: V. Mehra: None; **D. Dominguez**: None; **N. Gold**: None; **A. Knight**: Pfizer, 6; **D. Levy**: None; **F. Liao**: None; **E. Pullenayegum**: None; **A. Shammas**: None; **e. Sochett**: None; **R. vali**: None; **D. Webber**: None; **E. Silverman**: None; **L. Hiraki**: None.

Abstract Number: 2319

Changes in the Causes and Predictors of Lupus Mortality in Spain Through the Last Decades: Data from the RELESSER Registry

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SESSION INFORMATION
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Background/Purpose: The mortality in Systemic Lupus Erythematosus (SLE) varies largely across different countries most probably due to social, healthcare and ethnic differences. We need to identify demographic, clinical and serological predictors of mortality in SLE in our country, to improve the prognosis of SLE patients.

Objectives: To analyze the causes and identify predictive factors of mortality of SLE, and to assess the time evolution and chronological changes in Spain.

Methods: We performed a cross-sectional and retrospective study analyzing data from RELESSER cohort. Sociodemographic, clinical and serological variables, comorbidities and treatments, as well as indicators of disease activity, damage and severity were recorded. We excluded patients with lost information about the death variable and analyzed the differential features of deceased patients in comparisons with survivors through different time stages according to the date of diagnosis: until the 1980's; the 1990's and the first decade of the 21st century. Variables associated with mortality in univariate analysis were entered into different multivariate models to determine which ones were independently associated with the outcome of the disease in each decade.

Results: A total of 3665 patients were included, mostly caucasian female with similar general features regardless of the different time stages analyzed.18.4% until the 1980´s, the 5.97% in the 1990´s and up to 2.84% of the individuals in first decade of the 21st century, had died. The main age of death was similar in the different groups, around 55-58 years old (Table). The vascular events were the leading cause of death until the 1980´s, while in the last two decades, were infections.

The older age at diagnosis was predictor of mortality. Neither gender nor delay in diagnosis was independently associated with mortality, with the exception of the female sex, which behaved as a protective factor until the 1980´s.

The mortality predictors in our cohort were the presence of hypocomplementemia and organ damage until the 1980´s; thrombocytopenia, antiphospholipid syndrome and valve disease in the 1990´s; serositis, organ damage and depression in the first decade of the 21st century. Conversely, skin involvement was related to greater survival over the last two decades

Table. General Features

	Until 1980´s	1990´s	21st Century
N (3665)	539	1122	2004
Age at diagnosis, years, mean±SD	28.7 ± 12.6	33.4 ± 14.2	38.3 ± 15.3
Sex, female n (%)	491 (91.1%)	1025 (91.5%)	1770 (88.6%)
Caucasian race (%)	98.5%	96%	90.4%
Delay in diagnosis, months, mean±SD	20.8 ± 52.7	26.2 ± 53.6	28.9 ± 52.6
ACR criteria (≥ 4) (%)	98%	93.9%	88.1%
DECEASED n (%)	99 (18.4%)	67 (5.97%)	57 (2.84%)
Age of death, years, mean±SD	55.21 ± 15.59	57.74 ± 18.61	58.32 ± 19.73
Main cause of death	Vascular events	Infections	Infections

and comorbidities were associated with mortality in all periods of the study. The use of high doses of corticosteroids was predictor of mortality in each time stage, as well as the use of cyclophosphamide and rituximab from the year 2000. Antimalarial treatment was linked to improved survival in all the decades analyzed.

Conclusion: In the RELESSER cohort, the main cause of death in the last decades were infections. However, until the 1980´s, vascular events were predominant. Older age at diagnosis, use of corticosteroids and comorbidities were associated with significant increase in mortality in SLE, while antimalarial treatment was linked to improved survival. Data indicate that organ damage is a risk factor and skin involvement is a protective factor against mortality. Differentially, female sex until the 1980´s was independently associated with improved survival, and depression at the beginning of the 21st century was linked to mortality.

Disclosure: C. Moriano Morales: None; **J. Calvo- Alén**: AbbVie, 2, AstraZeneca, 2, Biogen, 6, BMS, 5, Galapagos, 6, GSK, 2, 6, Lilly, 2, 6, Novartis, 2, 6, Roche, 5, Sanofi, 2; **I. Rúa-Figueroa**: AstraZeneca, 5, GSK, 1, 6; **M. DIEZ ALVAREZ**: None; **C. Bermúdez**: None; **J. MARTINEZ BARRIO**: None; **M. Galindo-Izquierdo**: None; **A. Olivé-Marqués**: None; **E. Tomero Muriel**: None; **A. Fernandez-Nebro**: None; **M. Freire González**: None; **O. Fernandez-Berrizbeitia**: None; **A. Pérez Gómez**: None; **E. Uriarte Isacelaya**: None; **c. Marras Fernández-Cid**: None; **C. Montilla-Morales**: None; **G. Santos Soler**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6; **M. Rodríguez-Gómez**: None; **P. VELA**: AbbVie/Abbott, 5, AstraZeneca, 5, Eli Lilly, 5, 6, GlaxoSmithKlein(GSK), 6, Novartis, 5, Pfizer, 5; **A. Boteanu**: GSK, 5, 6; **J. Narvaez**: None; **V. Martinez-Taboada**: None; **B. Hernández-Cruz**: None; **J. Andreu-Sánchez**: None; **J. Hernández Beriain**: None; **L. Expósito**: None; **R. Menor-Almagro**: None; **M. Ibáñez-Barceló**: None; **I. Castellvi**: None; **C. Galisteo**: None; **E. Raya**: None; **V. Quevedo-Vila**: None; **T. Vazquez-Rodriguez**: None; **j. Ibáñez**: None; **J. Pego-Reigosa**: None.

Abstract Number: 2320

Predicting Remission and Low Disease Activity Attainment in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
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Background/Purpose: Response to therapy in SLE varies significantly and presents a considerable challenge in terms of predictability. Development of predictive models with ability to accurately foresee attainment of remission or low disease activity would be of major clinical value.

Methods: We extracted 288 baseline features from five phase III trials of belimumab, comprising 3645 patients. Using a recursive regression and partitioning tree, the top 20 most important factors were identified. Next, clinical expertise was integrated to narrow down the features qualified for the final model to only three. To investigate a potentially differential predictive

ability of the model with different treatment regimens, we stratified the study population into placebo and belimumab recipients. Outcomes were attainment of sustained remission as defined by the Definitions of Remission in SLE (DORIS) criteria and sustained lupus low disease activity state (LLDAS), maintained through week 52. Remission or LLDAS was considered sustained if present at two or more consecutive visits. Different predictive models i.e., least absolute shrinkage and selection operator (LASSO), neural network (NNet), support vector machine (SVM), and extreme gradient boosting (XGBoost) were trained 10 times in a 10-fold cross-validation. Performance was assessed using 20% of the data not used in training. Area under the curve (AUC), confusion matrix, and calibration plots were generated.

Results: In total, 11% met the criteria for sustained LLDAS and 5% those for sustained remission. Lower urinary protein/creatinine ratio (UPCR), lower prednisone dose, and increasing C3 levels were the features yielding the greatest predictive ability. The largest AUC was achieved for predicting sustained LLDAS in the placebo group (LASSO with AUC: 0.80, sensitivity: 0.73, specificity: 0.67, accuracy 0.70) while the belimumab subgroup yielded inferior performance (LASSO with AUC: 0.71, sensitivity: 0.77, specificity: 0.57, accuracy: 0.67). Although calibration seemed satisfactory, class imbalance and the small positive sample size overall might be a reason underlying the superior performance of the first model. Sustained remission was more challenging to predict among belimumab-treated patients (NNet with AUC: 0.63, sensitivity: 0.62, specificity: 0.60, accuracy: 0.61) compared with the placebo group (LASSO with AUC: 0.76, sensitivity: 0.63, specificity: 0.63, accuracy: 0.63). Prediction of sustained LLDAS yielded superior results (LASSO with AUC: 0.76, sensitivity: 0.68, specificity: 0.65, accuracy: 0.67) compared with remission (SVM with AUC: 0.71, sensitivity: 0.61, specificity: 0.71, accuracy: 0.66).

Conclusion: The models developed to predict attainment of sustained remission or LLDAS yielded moderate sensitivity and specificity. Overall, sustained LLDAS was more precisely predicted than sustained remission and accuracy in the placebo population was superior to that in belimumab-treated patients. By reducing the complexity to only 3 factors (UPCR, prednisone dose, C3 levels), our approach enabled a quick estimation of the probability to attain sustained remission or LLDAS in this SLE population.

Disclosure: R. Da Mutten: None; **N. Cetrez**: None; **J. Lindblom**: None; **S. Oon**: None; **D. Nikolopoulos**: None; **M. Nikpour**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, GSK, 2, 6, Janssen Pharmaceuticals, 2, 5, 6; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia Pharmaceuticals, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Elli Lilly and Company, 5, 6, F. Hoffmann-La Roche AG, 5, 6, Gilead Sciences, 5, 6, GSK, 5, 6, Janssen Pharmaceuticals, 5, 6, Novartis, 5, 6, Otsuka Pharmaceutical, 5, 6.

Abstract Number: 2321

Does the Perspective of SLE Patients Match the Expert Opinion and Definitions of Remission and Low Disease Activity State? Prospective Analysis of 500 Patients from a Spanish Multicenter Cohort

CORAL Mourino Rodriguez[1], Jose-Maria Pego-Reigosa[2], Iñigo Rúa-Figueroa[3], Francisco Rubino[4], Iñigo Hernández-Rodríguez[5], Raúl Menor-Almagro[6], Esther Uriarte Isacelaya[7], Eva Tomero Muriel[8], TAREK CARLOS SALMAN MONTE[9], MARIA IRENE CARRION BARBERA[9], Maria Galindo[10], Esther Rodriguez almaraz[10], Norman Jiménez[11], Luis Ines[12] and Irene Altabas Gonzalez[13], [1]Complejo Hospitalario Universitario de Vigo. IRIDIS (Investigation in Rheumatology and Immune-Mediated Diseases) Group, Galicia Sur Health Research Institute, Vigo, Spain, [2]Rheumatology, Hospital do Meixoeiro, Vigo, Spain, [3]Rheumatology, Hospital de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain, [4]Hospital Universitario de Gran Canaria Dr. Negrín, Las Palmas de Gran Canaria, Spain, [5]Hospital do Meixoeiro. Complejo Hospitalario Universitario de Vigo, Vigo, Spain, [6]Rheumatology, Hospital Jerez, Puerto De Santa María, Spain, [7]Hospital Universitario de Donostia, Donostia, Spain, [8]Rheumatology, Hospital La Princesa, Madrid, Spain, [9]Hospital del Mar/Parc de Salut Mar-IMIM, Barcelona, Spain, [10]Hospital Universitario 12 de Octubre, Madrid, Spain, [11]IIRIDIS (Investigation in Rheumatology and Immune-Mediated Diseases) Group, Galicia Sur Health Research Institute., Vigo, Spain, [12]Centro Hospitalar e Universitario de Coímbra, Coimbra, Portugal, [13]Complejo Hospitalario Universitario de

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SESSION INFORMATION
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Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: There is no information available regarding whether the patient's perception of disease activity aligns with current definitions of DORIS 2021 remission and Lupus Low Disease Activity State (LLDAS), nor whether there is concordance between the patient's perception and that of the physician.

Aim: To compare the SLE activity perceived by the patient using the Patient Acceptable Symptom State (PASS) question with the global assessment of activity by the physician, as well as with the definitions of LLDAS/DORIS2021.

Methods: Cross-sectional multicenter study of SLE patients from seven Spanish Rheumatology Departments. DORIS 2021 remission definition and LLDAS were applied and the rheumatologists were asked to classify the activity of the disease in 5 different categories: remission, SACQ, low, moderate or high activity. The patients were asked about their clinical SLE

Table 1. Patient demographics and disease characteristics.

	Number (%) or mean (± SD) (n = 503 patients)
Female gender	463 (92%)
Age at diagnosis (years)	40.7 (±21)
Disease duration at enrolment (years)	10,8 (± 9.9)
Age at enrolment (years)	50.4 (± 13.71)
ACR criteria [(a)]	
ANA	495 (96.5%)
Immunologic	398 (77.6%)
Arthritis	382 (74.5%)
Haematologic	291 (56.7%)
Malar rash	231 (45.0%)
Photosensitivity	229 (44.6%)
Mouth ulcers	178 (34.7%)
Renal	168 (32.7%)
Serositis	100 (19.5%)
Discoid rash	69 (13.5%)
Neurologic	28 (5.5%)
SLE activity	
SLEDAI-2K score at enrolment	2.8 (± 3.3)
SLICC/ACR-DI score at enrolment	0.96 (± 1.4)
Damage present at enrolment, n (%)	253 (49.8%)
Clinical SLEDAI-2 K (no complement or a-dsDNA)	1.6 (±2.7)
Treatment	
Prednisone	200 (39.7%)
Prednisone dose (mean ± SD)	5 (±6.27)
Antimalarials	366 (72.5%)
Immunosuppressants and/or biologic	219 (44%)

Abbreviations: SLE, systemic lupus erythematosus; ACR, American College of Rheumatology; SLEDAI, SLE disease activity index; PGA, physician global assessment; ANA, antinuclear antibody; ds DNA, double stranded DNA. SLICC/ACR-DI: Systemic Lupus International Collaborating Clinics (SLICC/American College of Rheumatology (ACR) damage index (SDI). (a) Ever present based on ACR criteria, LLDAS: Lupus Low Disease Activity State

condition through the PASS question: "Considering all the different ways your disease is affecting you, if you were to stay in this state for the next few months, do you consider your current state satisfactory?": PASS yes/PASS no. Statistical analysis: descriptive cross-sectional analysis. Analysis of the level of agreement between the PASS question and categorical classification (remission-low activity/ moderate-high activity) using Cohen's kappa.

Results: A total of 503 patients were included in the study (92% female, mean age 50.4 years). Table 1 shows in detail the patient´s characteristics at baseline. Of the 503 patient, 386 (77.4%) had an acceptable symptom state according to the PASS question. Mean (±SD) patient global assessment (PtGA) in a scale of 0-100 scale was 29.62 (±24.38) and mean (±SD) physician global assessment (PGA) in a scale of 0-3 was 0.46 (±0.59).A total of 236 (47.6%) patients met DORIS 2021 remission and 289 (59%) met LLDAS. According to the categorical classification of the rheumatologist: 435 (86.8%) patients were in remission or low disease; 56 (11.2%) in moderate activity and 10 (2%) in high activity state (Table 2). Among the patients who answered "yes" to the PASS question, 245 (65.5%) were in LLDAS and 220 (57.9%) were in remission according to the DORIS 2021 criteria. Mean PtGA in these patients was 19.7 (±18) and PGA 0.29 (±0.4). On the other hand, among non-PASS group, 71 (62.8%) patients were not in the LLDAS and 99 (87.6%) did not meet the criteria for DORIS 2021 remission state. Mean PtGA in these patients was 58 (±19) and PGA 1 (±0.7) (Table 3) Overall level of agreement between PASS question and categorical classification by the rheumatologist, was 82% (IC95%: 79.9, 82.9) with a Cohen's kappa of 0.43.

Table 2. SLE activity: patient and expert´s perspective

	Number (%) or mean (± SD) (n = 503 patients)
SLE disease state classification by expert	
Remission of SLE	205 (40.9%)
Serologically active, clinically inactive	74 (14.8%)
Low SLE activity	156 (31.1%)
Moderate SLE activity	56 (11.2%)
Severe SLE activity	10 (2%)
PGA at enrolment	0.46 (± 0.59)
Positive PASS question	386 (77.4%)
PtGA at enrolment	29.62 (±24.38)

Abbreviations: SLE, systemic lupus erythematosus; PGA, physician global assessment; PASS: Patient acceptable symptoms state; PtGA: patient global assessment.

Table 3. LLDAS and DORIS 2021 remission states according to PASS yes/no perspective by patient.

PASS (n, %)				**non-PASS (n, %)**			
LLDAS		**DORIS**		**LLDAS**		**DORIS**	
YES	NO	YES	NO	YES	NO	YES	NO
245 (65.5%)	129 (34.5%)	220 (57.9%)	160 (42.1%)	42 (37.2%)	71 (62.8%)	14 (12.4%)	99 (87.6%)
PtGA, mean, SD 19.76 (±18)				**PtGA, mean, SD** 58.04 (±19)			
PGA, mean, SD 0.29 (±0.4)				**PGA, mean, SD** 1.01 (±0.72)			

Abbreviations: PASS: Patient acceptable symptoms state; LLDAS: lupus low disease activity state; PGA: physician global assessment; PtGA: patient global assessment.

Conclusion: The majority of SLE patients reported being in an acceptable symptom state according to the PASS question, with similar results reported with the PtGA scale. SLE activity is similarly perceived by the physician perspective valued by the PGA and categorical classification. However, more than a third of patients in the PASS group were not in remission/LLDAS, and approximately 10-35% of the non-PASS group are in a state of remission/LLDAS. It seems that patient perspective is similar to the physician perspective in terms of subjective classification, but some differences are seen in terms of LLDAS and DORIS.

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Abstract Number: 2322

Identifying SLE Patients with Depression Using a Zero-Inflated Hidden Markov Model and Predicting Factors Associated with Transition from a Non-depressed State to a Depressed State

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Depression is one of the most common neuropsychiatric disorders in patients with SLE. The Centre for Epidemiologic Studies Depression Scale (CES-D) has been used to determine depressive symptomatology with a score of 24 serving as the cut-off for depression in SLE. Instead of using this cut-off, we aimed to: 1) classify patients into one of two states representing being depressed or not using a hidden Markov model, and 2) identify socioeconomic factors that predict patients' transition from a non-depressed state to a depressed state.

Methods: Data from the Lupus Outcomes Study at the University of California, San Francisco were analysed. Depressive symptoms were assessed with the CES-D annually providing up to 6 waves of observation. Patients with at least 2 waves of data were included. Under a Bayesian perspective, a contiguous-time hidden Markov model was fitted to the data, assuming that patients can be divided into two different states (non-depressed and depressed) over time. We assumed that CES-D scores follow a zero-inflated negative binomial distribution (excess of zeroes and integer outcome), and its means depend linearly on clinically relevant factors (**Figure 2**). Moreover, we included socioeconomic factors (below poverty line, employment and higher education) that could potentially be associated with the transition between the non-depressed and the depressed state.

Results: 763 adults with SLE followed over 7 years were included. We found that the non-depressed state had a mean CES-D rate (μ_{ND}) of 6.05 (95% CrI 5.61 – 6.55) whereas the depressed state mean rate (μD) was 18.3 (95% CrI 17.7 – 18.9) (**Figure 1**). The mean CES-D score rate decreased (improvement of depressive symptoms) by 2% for one-unit increase in SF-36 bodily pain score (higher scores means less pain), and it increased (worsening of depressive symptoms)

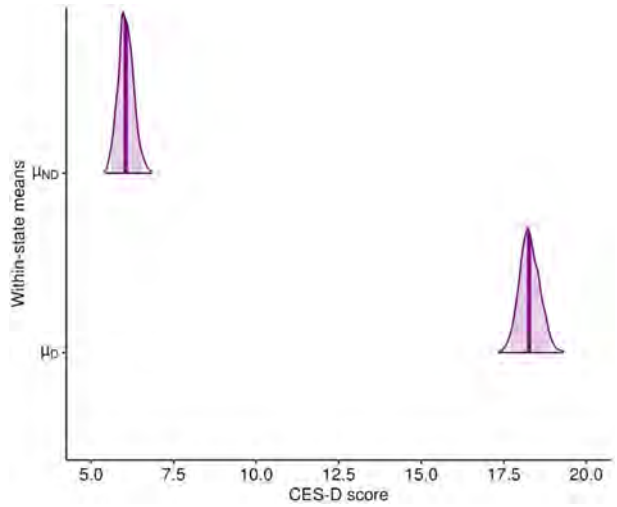

Figure 1. Posterior estimates for the within-state means of the two hidden states. X axis represents the distribution of the parameters of interest. Y axis represents the parameters where inference is made. The dark shaded region represents the point estimate from a frequentist point of view and the light shaded region represents the 95% uncertainty interval, i.e., with 95% of probability the estimate would lie in that region. As an example μ_ND represents the inference made on the unknown mean of the observed CES-D score given that it comes from the non-depressed state after adjusting for other clinical variables described in Figure 2.

by 12%, 26% and 28% for those with lupus related kidney disease, on anti-depressant, and current smokers versus those who did not smoke, respectively (**Figure 2**). Moreover, having higher education (college or more) decreased the rate of transitioning between the non-depressed state and the depressed state by 86% (**Figure 3**). For a patient who is not below the poverty line, nor employed and does not have higher education (i.e. transition covariates set to zero), the probability of transitioning between the non-depressed state and the depressed state was low (3%).

Conclusion: Using HMMs, we classified patients with SLE into two different states, depressed and non-depressed. Bodily pain, smoking, lupus related kidney disease and use of antidepressants drugs were associated with worsening depressive symptoms as measured by the CES-D. Transitioning between states was predicted by different factors over time, where higher education and employment significantly decreased the rate of transitioning between the non-depressed state and the depressed state.

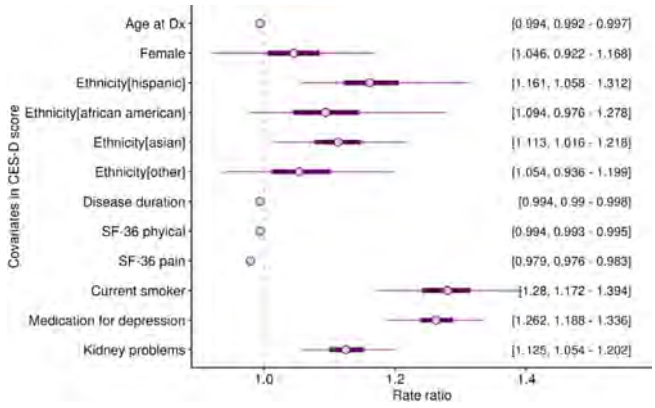

Figure 2. Posterior uncertainty intervals for the covariates in the CES-D score. X axis represents the rate ratio and Y axis represents the parameters where inference is made. For example, those who have kidney problems due to lupus have a 12.5% rate increase in their mean CES-D score compared to those without kidney problems. The dot on the graph represents the point estimate and the line represents the 95% CrI

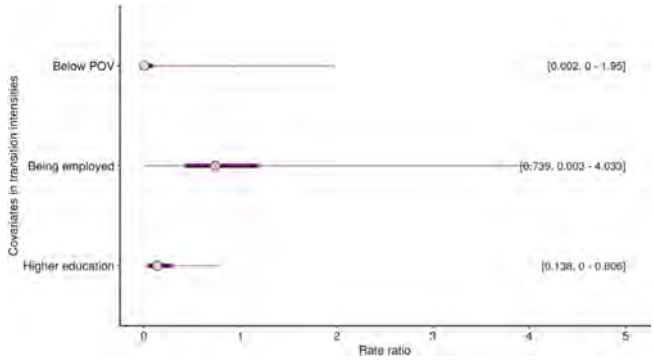

Figure 3. Posterior uncertainty intervals for the covariates in the transition between the non-depressed state and the depressed state X axis represents the hazard ratio and Y axis represents the parameters where inference is made. As an example, being below the POV had a protective effect (Rate ratio .002, 95% CrI 0 – 1.95), although this effect size was not significant. The dot on the graph represents the point estimate and the line represents the 95% CrI

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Abstract Number: 2323

An Electronic Health Record-Based Algorithm for Predicting Systemic Lupus Erythematosus Flares: Integrating Clinical Factors and Social Determinants of Health

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
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Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (**SLE**) has a relapsing-remitting course, with patients experiencing disease activity flares over time. Flares and prolonged disease activity are associated with progressive multi-system organ damage, poor quality of life, high healthcare costs, and increased mortality. Disparities have also been widely reported in the health care access and health outcomes among patients with SLE, and social determinants of health (**SDoH**) are often considered as the root causes of health disparities. However, existing studies evaluating SLE flares and disease activities have not yet considered SDoH or patients' social risks. The objective of this study is to incorporate both patients' clinical characteristics and SDoH and develop an electronic health record (**EHR**)-based machine learning prediction algorithm for SLE flares to support real-time clinical decision-making, address social risks and SDoH, and ultimately reduce health disparities of SLE.

Methods: OneFlorida+ network is part of the national Patient-Centered Clinical Research Network (PCORnet), collating EHR data from 17 million residents in Florida, 2.1 million in Georgia, and 1.1 million in Alabama. We identified adult SLE patients using 2013-2021 OneFlorida+ data and spatiotemporally linked the cohort with 486 neighborhood SDoH (e.g., neighborhood unemployment rate and median income). A validated surrogate measure of SLE Disease Activity Score 2000 (SLEDAI-2K) based on the EHR data was calculated for each 30-day period over the baseline year and follow-up year.

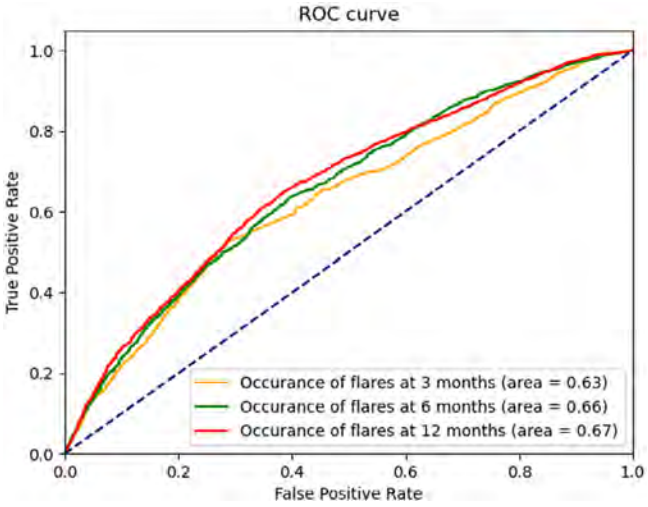

Figure. C statistics of gradient boosting machine algorithm to predict SLE flares.

The median score for the first 12 months was used to establish a baseline level of disease activity; and a flare was defined as an increase of at least 4 from the baseline score. We incorporated SDoH and patients' clinical characteristics (e.g., medical diagnoses, prescriptions, and lab results) collected at baseline year and employed a gradient boosting machine to predict the occurrence of flares at 3 months, 6 months and 12 months after baseline.

Results: We identified 33,151 eligible SLE patients; the mean age was 45 (std: 16) years, 89% were females, and 39%, 26%, and 25% were non-Hispanic White, non-Hispanic Black, and Hispanic race/ethnicity, respectively. Of the cohort, over one-third (39%) developed at least one flare during the follow-up year; 19%, 9%, 4%, and 6% experienced 1, 2, 3, and 3+ time(s) flares during the follow up year. Our algorithm showed a good utility for predicting individuals' risk of flares, achieving a C statistic (standard deviation) of 0.63 (0.01), 0.66 (0.01), and 0.67 (0.01) at the 3- month, and 6- month, and 12-month period, respectively (**Figure**).

Conclusion: By incorporating both SDoH and clinical data, our EHR-based algorithm shows promise for identifying likely flares in real-world patients with SLE. Future studies are needed to identify key SDoH causally associated with flares occurrence to identify intervention targets that improve both health outcomes and health disparities in patients with SLE.

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Abstract Number: 2324

Leveraging ChatGPT for Real-World Systematic Lupus Erythematosus Data Curation from Electronic Health Records: A Feasibility Study

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SESSION INFORMATION
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Background/Purpose: Epidemiologists, health services researchers, and health outcome investigators have begun utilizing real-world data (RWD) to gain valuable insights into disease patterns, treatment outcomes, and healthcare utilization and economics. Similarly, biopharmaceutical and medical device manufacturers utilize RWD to identify medical gaps, enhance patient care, and drive innovative therapeutic interventions. However, a significant portion (~80%) of essential clinical data is trapped in unstructured text within clinical notes, thereby remaining inaccessible in existing RWD for systemic lupus erythematosus (SLE).

Methods: To address this challenge, we leveraged the cutting-edge Natural Language Processing (NLP) model, ChatGPT 4.0, to analyze clinical notes to identify potential diagnosis of SLE. We evaluated:1) the adequacy of unstructured clinical notes in capturing essential clinical details (i.e., 22 clinical and immunologic variables) to support meeting the 2019 European League Against Rheumatism and American College of Rheumatology (EULAR/ACR) classification criteria for SLE; 2) the efficacy of the ChatGPT model in identifying those variables outlined in the EULAR/ACR criteria.

De-identified medical records were obtained from Temple University Health System's EHR system (Epic), comprised patients aged 18 years or above, with at least at least one rheumatology visit and one ICD-10-CM code of M32.* (SLE) between 1/1/2012 and 5/31/2022. Using a Python script, we conducted an automatic search for various mentions of SLE in rheumatology visit notes. We then identified those with a positive anti-nuclear antibody (ANA) test. A thorough manual review of the rheumatology notes were conducted to determine if patients met the EULAR/ACR classification criteria. Subsequently, we employed ChatGPT 4.0 to extract the EULAR/ACR clinical variables.

Results: The initial Python search yielded 16,124 rheumatology notes from 445 unique patients. The follow-up search for positive ANA tests returned 1,147 rheumatology notes from 187 unique patients. The manual review by trained medical professionals revealed that 116 of the 187 patients met the EULAR/ACR criteria. There was a remarkably high level of agreement between the assessments made by ChatGPT 4.0 and those made by trained medical professionals (830 out of

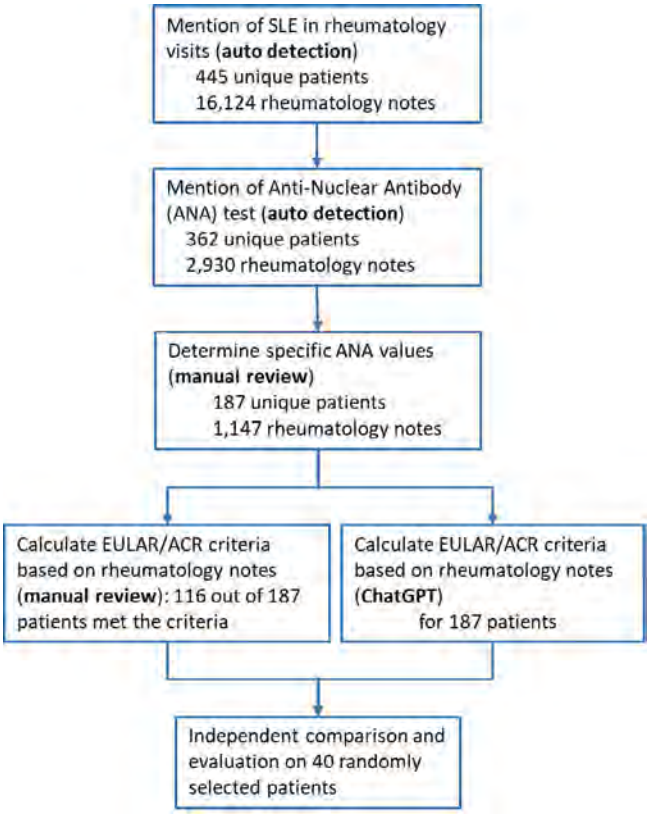

Figure 1. The overall study workflow

Table 1. Analysis of disagreements of annotations by medical professionals and ChatGPT

Clinical variables included in EULAR/ACR classification of SLE	Discrepancy between medical professional and chatGPT	Rightness by chatGPT	Rightness by medical professional
Alopecia	4	3	1
Oral ulcer	1	0	1
Subacute cutaneous or discoid lupus	8	3	5
Acute cutaneous lupus	5	3	2
Pleural or pericardial effusion	2	1	1
Joint involvement	12	10	2
Proteinuria	4	4	0
Antiphospholipid antibodies	4	2	2
Low C3 or low C4	1	1	0
Low C3 and low C4	3	1	2
anti-dsDNA antibody/anti-smith antibody	6	1	5
Total	50	29	21

880 clinical and immunologic variables across 40 randomly selected patients). Among the 50 annotations of disagreement (see Table 1), ChatGPT's interpretations were found to be accurate in 29 cases. In some cases, the differentiation between acute cutaneous lupus vs. subacute cutaneous lupus was not clearly documented in the visit notes. In other cases, ChatGPT and human annotators had to infer the classification based on certain patient-reported symptoms like rash and photosensitivity.

Conclusion: Our findings confirm that unstructured clinical notes contain sufficient clinical details into SLE patient care, including 22 clinical and immunologic variables specified in the established classification criterion for SLE. Moreover, the utilization of state-of-the-art NLP techniques has significant promise in identifying those with SLE, potentially enhancing existing SLE research using RWD.

Disclosure: L. Yao: Merck/MSD, 3; **L. Gebru**: None; **B. Aweke**: None; **J. Patel**: None; **E. Vina**: None; **D. Fleece**: None; **H. Wu**: None.

Abstract Number: 2325

Longitudinal ANA Titers in SLE and ANA-associated Rheumatic Diseases

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Antinuclear antibodies (ANAs) are a hallmark of systemic lupus erythematosus (SLE) and also a marker of subclinical autoimmunity. While a seminal study using the US Department of Defense Serum Repository suggested a progressive accumulation of autoantibodies before the onset of SLE, there have been no large-scale studies to

Table 1. International Classification of Diseases (ICD) codes used for classifying ANA-associated diseases

Diagnosis	ICD-9	ICD-10
Lupus	710.0	M32.9, M 32.10
Scleroderma	710.1	M34.0, M34.1, M34.9
Sjogren's Syndrome	710.2	M35.0
Dermatomyositis	710.3	M33.9
Polymyositis	710.4	M33.20
Mixed Connective Tissue Disease	710.8	M35.1
Undifferentiated Connective Tissue Disease	710.9	M35.8, 35.9

assess changes in ANA titers within individuals over time. We performed this study to characterize longitudinal, intra-individual variation in ANAs in persons with SLE or other ANA-associated rheumatic diseases, as well as ANA-positive persons without rheumatic disease, in a large healthcare system in the Midwestern US.

Methods: We performed an exploratory analysis of electronic health record data from an academic health system between 1999-2020. Among the patients with at least one positive ANA, we screened their electronic medical records for ANA-associated rheumatic disease diagnoses, based on International Classification of Diseases (ICD) coding. We categorized the study population into four groups:(1) SLE according to ICD coding; (2) A "validated" SLE subset of patients enrolled in our institutions IRB-approved Lupus Cohort; (3) "Other" ANA-associated rheumatic disease, and (4) ANA-positive controls without a history of ANA-associated rheumatic disease. The ICD codes utilized are listed in Table 1.

For group comparisons, ANOVA was utilized for continuous variables, and chi-square test for categorical variables. Multivariable generalized linear mixed effects models were utilized for analyses with ANA positivity (binary) as the outcome. For analyses with ANA titer strength (magnitude of positivity) as the outcome, linear mixed effects models were used. As laboratory measurement of ANA titers is based on the detection of"doubling" of levels (eg, 1:80, 1:160, 1:320, etc.), we took a log transformation on the ANA titer to normalize the skewness in the distribution of the variable.

Results: SLE patients had a higher odds of a positive ANA titer compared to other ANA-associated rheumatic diseases [OR 2.05, 95% CI(1.77, 2.37)] (Figure 1). Compared to the ANA+ control group, the average ANA titer magnitude for the ANA-associated rheumatic diseases group was 0.44 units [95% CI (0.33, 0.55)] higher on the log scale controlling for age,

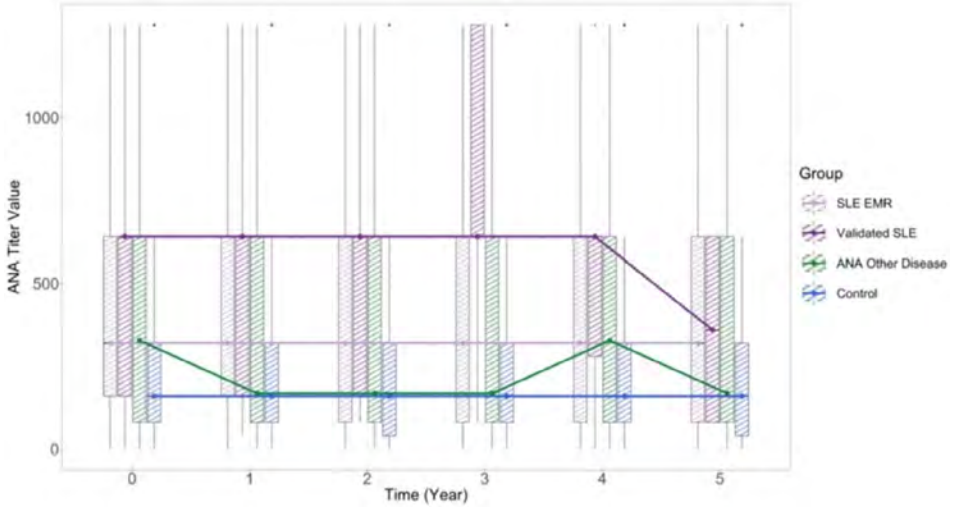

Figure 1. Boxplot of ANA titer among groups. (SLE-EMR, validated SLE patients, ANA-associated other rheumatic disease, ANA control group). Y-axis denotes the measure of ANA titer closest to each year point, X-axis denotes time (count in year), time is from baseline to 5-year follow-up. Dots and lines denote group median and its change over time. The upper and lower bound of each box is the 75% quantile and 25% quantile respectively.

Table 2. Results from linear mixed effects models, with log of ANA titer as the outcome.

Variable	Coefficient (95% CI)	P-value
Age	-0.0007 (-0.003, 0.002)	0.53
Female (Male referent)	0.18 (0.07, 0.29)	0.001**
Race (White referent)		
Black	0.07 (-0.04, 0.18)	0.20
Other/unknown	-0.01 (-0.17, 0.14)	0.86
Time (month)	-0.0002 (-0.002, 0.001)	0.74
Diagnostic group (ANA control referent)		
ANA other diagnosis	0.44 (0.33, 0.55)	<0.001***
SLE	0.77 (0.66, 0.88)	<0.001***
Time*ANA Other Disease	0.001 (-0.0007, 0.003)	0.21
Time*SLE	-0.003 (-0.004, -0.0008)	0.004**

sex and time, and 0.77 units [95% CI (0.66, 0.88)] higher for the SLE group, with both statistically significant (p< 0.001) (Table 2).

Longitudinally, in the validated SLE group, the likelihood of having a positive ANA decreased by 0.3% with each month [OR 0.997,95% CI (0.995, 0.998)]. ANA titer strength significantly decreased over time in the SLE group; after one year, the magnitude of ANA titer among patients in the SLE group was 0.033 units on the log scale lower than patients in the control group (95% CI 0.01, 0.04, p< 0.01).

Conclusion: Based on this large longitudinal dataset, ANA titers may be more dynamic than previously accepted in patients with SLE and ANA+ rheumatic diseases. Even in SLE, where titers were on average higher than for other ANA-associated diseases, declining ANA titers are seen over time, which might reflect aspects of disease states or flare risk that are beginning to be appreciated given accumulating evidence in other longitudinal studies.

Disclosure: E. Littlejohn: Aurinia, 6, GlaxoSmithKlein(GSK), 2; **L. Kong**: None; **L. Wang**: None; **E. Somers**: None.

Abstract Number: 2326

Efficacy and Safety of Voclosporin in Patients with Proteinuria > 2 G/g

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

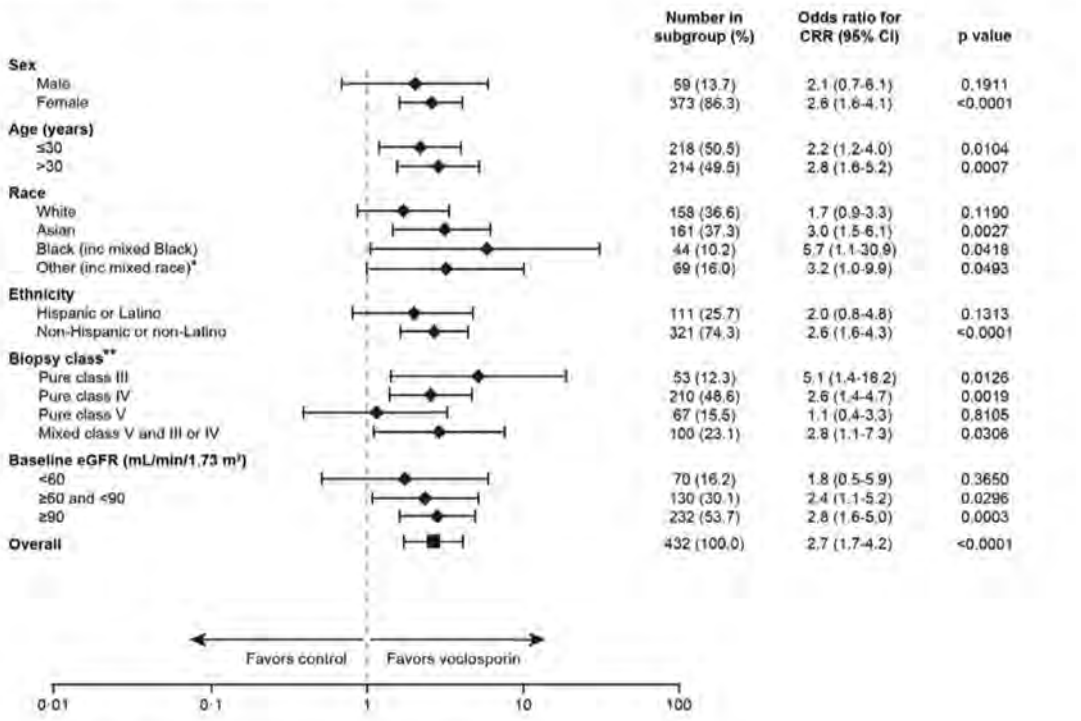
Background/Purpose: Proteinuria is the most common manifestation of lupus nephritis and is a mediator of progressive kidney damage. Early reductions in urine protein creatinine ratio (UPCR) have shown to be predictive of improved long-term outcomes in LN. However, recent studies with monoclonal antibody therapies have demonstrated a lack of efficacy in patients with moderate to high proteinuria (UPCR ≥2 to ≥3 g/g), potentially due to an increase in renal excretion of drug. In a pooled analysis of the Phase 2 AURA-LV and Phase 3 AURORA 1 studies, the addition of voclosporin to mycophenolate mofetil (MMF) and low-dose glucocorticoids resulted in earlier and greater reductions in proteinuria, regardless of baseline

demographics or disease characteristics. To further characterize the efficacy and safety of voclosporin in patients with moderate to high proteinuria, we have analyzed outcomes in patients with UPCR ≥2 g/g using the pooled dataset.

Methods: Both studies enrolled patients with biopsy-proven LN (Class III, IV, or V ± III/IV) within 6 months (or up to 2 years in AURORA 1) and proteinuria ≥1.5 g/g (≥2 g/g for Class V). Patients were randomized to voclosporin (23.7 mg BID) or placebo and treated for up to one year (48 weeks [AURA-LV], 52 weeks [AURORA 1]); all patients received MMF and low-dose glucocorticoids. For this post hoc analysis, complete renal response (CRR) rates were evaluated in patients with baseline UPCR ≥2 g/g. Complete renal response was defined as UPCR ≤0.5 g/g with stable renal function, low-dose steroids, and no rescue medication; partial renal response (PRR) was defined as a ≥50% reduction in UPCR from baseline. Adverse events (AEs) and measures of renal function were also assessed.

Results: Of the 268 and 266 patients included in the voclosporin and control arms of the pooled analysis, 217 and 215 patients had a baseline UPCR ≥2 g/g (mean [SD], 5.2 [3.4] vs. 4.6 [2.9] g/g). At one year, the change from baseline in least squares (LS) mean UPCR was significantly greater in the voclosporin arm (p=0.0003). A significantly greater percentage of voclosporin-treated patients achieved CRR at one year compared to the control arm (41.0% vs. 21.9%; odds ratio [OR] 2.48, p< 0.0001; Figure 1). Significantly more patients in the voclosporin arm (69.6%) than control arm (50.0%) achieved a PRR at one year (OR 2.3, p< 0.0001). Similar rates of AEs were reported in both arms. Measures of renal function, including mean eGFR, were similar and stable over one year of treatment (Figure 2, Table 1).

Figure 1. Complete Renal Response at One Year

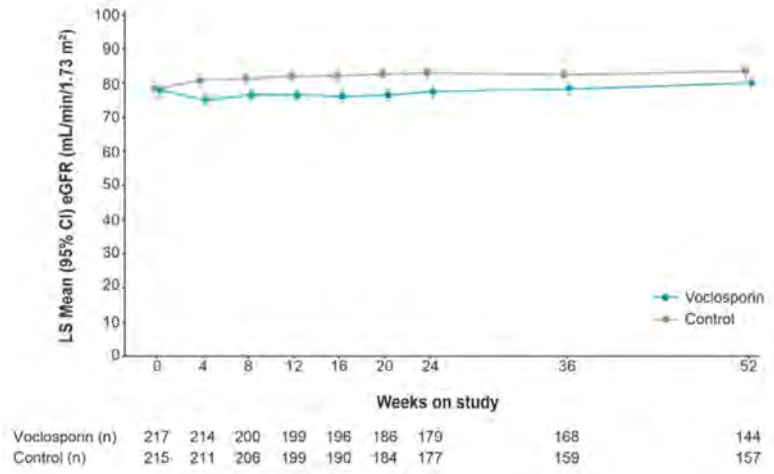


*Other races includes other or mixed races except Black race

**Two patients with Mixed Class III/IV and Mixed Class II/V disease are not included in the biopsy class subgroup analysis but are included in all other subgroup analyses and the overall analysis.

Post hoc analysis of patients with baseline UPCR ≥2 g/g includes pooled data from the 23.7 mg BID voclosporin arms and control arms in AURA-LV and AURORA 1. Analysis includes data from up to 48 weeks in AURA-LV and up to 52 weeks in AURORA 1. Complete renal response defined as UPCR of ≤0.5 g/g, eGFR ≥60 mL/min/1.73 m², or no decrease >20% from baseline, low-dose glucocorticoids, and no rescue medications. Odds ratio (OR) >1 demonstrates treatment benefit of voclosporin. CRR, complete renal response; estimated glomerular filtration rate; SD, standard deviation; UPCR, urine protein creatinine ratio.

Figure 2. LS Mean eGFR over Time



Post hoc analysis of patients with baseline UPCR ≥2 g/g includes pooled data from the 23.7 mg BID voclosporin arms and control arms of AURA-LV and AURORA 1. Data include up to 48 weeks from AURA-LV and up to 52 weeks from AURORA 1. Renal function was assessed with corrected eGFR (Chronic Kidney Disease Epidemiology Collaboration equation) using a prespecified ceiling of 90 mL/min/1.73 m². CI, confidence interval; eGFR, estimated glomerular filtration rate; LS Mean, least squares mean.

Table 1. Laboratory Parameters over Time

	Voclosporin n=217		Control n=215	
	Baseline	**One Year**	**Baseline**	**One Year**
Systolic BP, mean (SD) mmHg	126.0 (15.6)	120.0 (11.9)	125.8 (15.6)	118.2 (13.4)
Diastolic BP, mean (SD) mmHg	84.1 (11.3)	78.3 (8.8)	82.3 (11.6)	77.1 (10.4)
eGFR, mean (SD), mL/min/1.73 m²	77.7 (16.0)	79.8 (15.5)	78.0 (15.8)	83.1 (13.1)
UPCR, g/g	5.2 (3.4)	1.0 (1.7)	4.6 (2.9)	1.7 (1.9)
Magnesium, mean (SD) mg/dL	2.1 (0.2)	2.0 (0.2)	2.0 (0.2)	2.1 (0.2)
Potassium, mean (SD) mmol/L	4.1 (0.6)	4.2 (0.4)	4.0 (0.6)	3.9 (0.4)
Glucose, mean (SD) mg/dL	85.5 (24.6)	87.7 (21.3)	87.6 (37.5)	85.8 (11.8)
Creatinine, mean (SD) mg/dL	0.8 (0.3)	0.9 (0.3)	0.8 (0.3)	0.7 (0.3)

Post hoc analysis of patients with baseline UPCR ≥2 g/g includes pooled data from the 23.7 mg BID voclosporin arms and control arms of AURA-LV and AURORA 1. Data include up to 48 weeks from AURA-LV and up to 52 weeks from AURORA 1. Renal function assessed with corrected eGFR (Chronic Kidney Disease Epidemiology Collaboration equation) using a prespecified ceiling of 90 mL/min/1.73 m². BP, blood pressure; eGFR, estimated glomerular filtration rate; SD, standard deviation, UPCR, urine protein creatinine ratio.

Conclusion: Consistent with results from the overall pooled study population, patients with UPCR ≥2 g/g treated with voclosporin achieved significantly higher renal response rates than patients treated with MMF and low-dose glucocorticoids alone while renal function in both arms remained comparable. This is clinically relevant given the lack of safe and effective therapies for patients with high proteinuria.

Disclosure: E. Littlejohn: Aurinia, 6, GlaxoSmithKlein(GSK), 2; **S. Almaani**: Amgen, 2, Aurinia, 2, Chemocentryx, 2, Kezar, 2, Otsuka, 2; **V. Birardi**: Aurinia, 3, 11; **E. Yap**: Aurinia Pharmaceuticals, 3, 11; **C. Collins**: Aurinia Pharmaceuticals Inc., 12, Former employee and stockholder.

Abstract Number: 2327

Hydroxychloroquine Improves Low Complement Levels

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Low complement is associated with clinical disease activity and future organ damage in patients with systemic lupus erythematosus (SLE). Prior studies from Japan, although inconsistent, supported improvement in complement levels after hydroxychloroquine (HCQ) introduction. We studied HCQ whole blood levels and C3 and C4 levels in a US cohort.

Methods: In the first paired-visit analysis, to mimic the Japanese studies, we identified patients with low complement and low levels of HCQ in their blood.Then at their next clinic visit, we compared those whose HCQ whole blood levels increased to over 50 ng/mL to those whose HCQ whole blood levels did not with respect to changes in complement. In a second analysis, we considered all clinical visits in our cohort among patients who sometimes had low complement, and sometimes did not, and we examined the association between HCQ whole blood levels and low complement using conditional logistic regression.

Results: Although the numbers varied between analyses, approximately 68% of the patients included in these analyses were African American, and 93% were female. Table 1 shows the results of the analysis of paired visits with respect to C3.Among those whose HCQ whole blood levels increased to be above 50 ng/mL, there was a greater mean increase in mean C3 (p=0.022) compared to those whose HCQ whole blood levels did not increase.Similarly, with respect to C4, among those HCQ whole blood levels increased, there was a significantly greater probability of achieving normal C4 levels (p=0.0030) and of having a higher increase in mean C4 (p=0.0037) (Table 2).Table 3 shows the results considering all clinic visits among those with variable complement levels. In this analysis, we did not observe a strong relationship between HCQ whole blood levels and C3. However, there was a consistently higher probability of achieving normal C4 levels as HCQ whole blood levels increased.

Conclusion: Both C3 and C4 levels increased significantly with HCQ whole blood levels >50 ng/mL. The percentage of patients who achieved a normal C4 level with a HCQ whole blood level >50 ng/mL (44%) was statistically significant. Surprisingly, even a low HCQ whole blood level was able to achieve an increase in complement. In the second analysis, we found a strong dose response between HCQ whole blood levels and C4 (but not C3). Improving complement levels may be one mechanism by which HCQ prevents poor outcomes in SLE. As low complement is part of the SLEDAI, this effect can contribute to an SRI-4 response in clinical trials.

HCQ Whole Blood levels at 2nd visit (ng/mL)	Number (%) with complement in the normal range at 2nd visit	P-value[1]	Mean (SD) change in complement (mg/dL)	P-value[1]
<50 ng/mL (n=67)	9 (13%)	0.36	2.2 (12.9)	0.022
50+ ng/mL (n=84)	18 (21%)		8.3 (17.1)	

[1] Based on a GEE model to account for multiple measures from the same patient.

C3 changes between the two consecutive visits with a HCQ whole blood level of lower or higher than 50 ng/mL

HCQ Whole Blood levels at 2nd visit (ng/mL)	Number (%) with complement in the normal range on the 2nd visit	P-value[1]	Mean (SD) change in complement (mg/dL)	P-value[1]
<50 ng/mL (n=56)	9 (13%)	0.0030	0.7 (2.7)	0.0037
50+ ng/mL (n=61)	27 (44%)		3.0 (4.2)	

[1] Based on a GEE model to account for multiple measures from the same patient.

C4 changes between the two consecutive visits with a HCQ whole blood level of lower or higher than 50 ng/mL

HCQ Blood Level	Proportion (%) of visits with low C3	Odds Ratio (95% CI)	P-value[1]
HCQ<50 ng/mL (or patient reports no HCQ and HCQ was not measured	63/168 (38%)	1.00 (Ref)	
HCQ 50-199 ng/mL	33/88 (38%)	0.90 (0.63, 1.31)	0.59
HCQ 200-499 ng/mL	76/211 (36%)	0.74 (0.54, 1.00)	0.37
HCQ 500-999 ng/mL	100/302 (33%)	0.88 (0.67, 1.16)	0.37
HCQ 1000+ ng/mL	64/214 (30%)	0.88 (0.67, 1.16)	0.38
HCQ Blood Level	**Proportion (%) of visits with low C4**	**Odds Ratio (95% CI)**	**P-value[1]**
HCQ<50 ng/mL (or patient reports no HCQ and HCQ was not measured)	64/125 (51%)	1.00 (Ref)	
HCQ 50-199 ng/mL	36/72 (50%)	0.63 (0.41, 0.99)	0.045
HCQ 200-499 ng/mL	104/173 (40%)	0.55 (0.38, 0.80)	0.0015
HCQ 500-999 ng/mL	25/228 (20%)	0.39 (0.28, 0.54)	<0.0001
HCQ 1000+ ng/mL	24/147 (16%)	0.38 (0.28, 0.53)	<0.0001

[1] Based on conditional logistic regression.

Association between HCQ whole blood levels and risk of having low complement

Disclosure: M. Petri: Alexion, 1, Amgen, 1, AnaptysBio, 1, Annexon Bio, 1, Argenx, 1, Arhros-Focus Med/Ed, 6, AstraZeneca, 1, 5, Aurinia, 1, 5, 6, Axdev, 1, Biogen, 1, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CVS Health, 1, Eli Lilly, 1, 5, Emergent Biosolutions, 1, Exagen, 5, Exo Therapeutics, 2, Gilead Biosciences, 2, GlaxoSmithKlein(GSK), 1, 5, 6, Horizon Therapeutics, 2, Idorsia Pharmaceuticals, 2, IQVIA, 1, Janssen, 1, 5, Kira Pharmaceuticals, 2, MedShr, 6, Merck/EMD Serono, 1, Momenta Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Proviant, 2, Sanofi, 2, Sinomab Biosciences, 2, Thermofisher, 5, UCB, 2; **R. Jacobson**: None; **A. Fava**: Annexon Biosciences, 2, Sanofi, 1; **L. Magder**: None.

Abstract Number: 2328

Deucravacitinib, an Oral, Allosteric, Tyrosine Kinase 2 (TYK2) Inhibitor, in Patients with Active Systemic Lupus Erythematosus: Patient-Reported Outcomes in a Phase 2 Trial

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Treatment Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Table 1. Demographics and baseline disease activity

Characteristic	Placebo n = 90	Deucravacitinib 3 mg BID n = 91	Deucravacitinib 6 mg BID n = 93	Deucravacitinib 12 mg QD n = 89
Age, mean, years	40.1	40.2	40.9	39.0
BMI, mean, kg/m^2	27.5	26.5	26.1	27.1
Sex, female, n (%)	80 (88.9)	85 (93.4)	88 (94.6)	81 (91.0)
Race, White, n (%)	60 (66.7)	62 (68.1)	55 (59.1)	57 (64.0)
Use of CS, antimalarials, and immunosuppressants, n (%)				
CS	74 (82.2)	74 (81.3)	73 (78.5)	71 (79.8)
≥10 mg/day prednisone or equivalent	47 (52.2)	45 (49.5)	46 (49.5)	43 (48.3)
Antimalarial	75 (83.3)	81 (89.0)	84 (90.3)	75 (84.3)
Immunosuppressant	46 (51.1)	53 (58.2)	43 (46.2)	46 (51.7)
Antimalarial, immunosuppressant, and CS	26 (28.9)	38 (41.8)	26 (28.0)	27 (30.3)
SLEDAI-2K score, mean (SD)	10.8 (3.1)	11.1 (3.2)	10.8 (3.2)	10.7 (3.0)
Overall BILAG-2004, ≥1 A, n (%)	51 (56.7)	51 (56.0)	44 (47.3)	51 (57.3)
PGA, mean (SD)	1.82 (0.4)	1.80 (0.3)	1.84 (0.4)	1.86 (0.4)
CLASI-A score, mean (SD)	8.0 (5.1)	8.6 (7.6)	8.2 (6.5)	8.4 (5.8)
Active joint count, mean (SD)	9.2 (6.0)	8.6 (4.8)	8.8 (6.1)	9.4 (5.7)
Pain assessment score, mean (SD)	6.0 (2.3)	5.8 (2.4)	6.0 (2.0)	5.8 (2.4)
PROMIS Fatigue 7a T-score, mean (SD)	57.8 (8.4)	58.4 (8.5)	58.5 (7.9)	59.2 (7.5)
SF-36 PCS score, mean (SD)	36.5 (10.1)	38.8 (8.5)	36.8 (9.5)	36.6 (8.6)
SF-36 MCS score, mean (SD)	43.7 (9.8)	43.7 (12.0)	43.0 (12.1)	42.7 (10.1)

BID, twice daily; BILAG-2004, British Isles Lupus Assessment Group 2004 index; BMI, body mass index; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; CS, corticosteroids; MCS, mental component summary; PCS, physical component summary; PGA, Physician Global Assessment; PROMIS, Patient-Reported Outcomes Measurement Information System; QD, once daily; SD, standard deviation; SF-36, 36-Item Short Form Health Survey; SLEDAI-2K, SLE Disease Activity Index 2000.

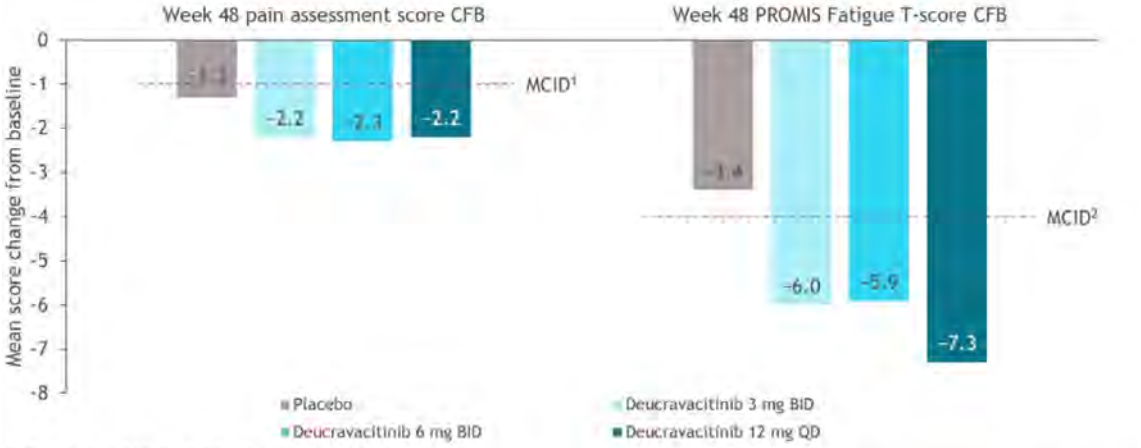
Background/Purpose: Deucravacitinib is a first-in-class, oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor approved in the US, EU, and other countries for treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy. In PAISLEY, a 48-week, phase 2, randomized controlled trial that assessed deucravacitinib in patients with active systemic lupus erythematosus (SLE), a greater proportion of patients receiving deucravacitinib treatment achieved SLE Responder Index-4 (SRI[4]) responses at Weeks 32 and 48 vs placebo. Patient-reported outcomes (PROs) were collected as exploratory endpoints.

Table 2. Patients reporting clinically meaningful response at Week 48

Assessment	Placebo, n (%)	Deucravacitinib 3 mg BID, n (%)	Deucravacitinib 6 mg BID, n (%)	Deucravacitinib 12 mg QD, n (%)
Pain NRS score[a]	30 (33.3)	47 (51.6)	41 (44.1)	34 (38.2)
PROMIS Fatigue T-score[b]	20 (22.2)	33 (36.3)	34 (36.6)	32 (36.0)
SF-36 PCS score[c]	26 (28.9)	36 (39.6)	45 (48.4)	35 (39.3)
SF-36 MCS score[c]	25 (27.8)	33 (36.3)	27 (29.0)	29 (32.6)

[a]Patients achieving 1-point improvement.
[b]Patients achieving 4-point improvement.
[c]Patients achieving 2.5-point improvement, scores range from 0–50.
BID, twice daily; MCS, mental component summary; NRS, numeric rating scale; PCS, physical component summary; PROMIS, Patient-Reported Outcomes Measurement Information System; QD, once daily; SF-36, 36-Item Short Form Health Survey.

Figure 1. Mean changes from baseline on the pain NRS and in the PROMIS Fatigue T-score at Week 48



1. Salaffi F, et al. *Eur J Pain*. 2004;8:283-91.
2. Strand V, et al. *Lupus Sci Med*. 2020;7:e000373.

BID, twice daily; CFB, change from baseline; MCID, minimal clinically important difference; NRS, numeric rating scale; PROMIS, Patient-Reported Outcomes Measurement Information System; QD, once daily.

Methods: All patients met Systemic Lupus International Collaborating Clinics classification criteria, were seropositive for antinuclear antibody, anti-double-stranded DNA, or anti-Smith antibody, and had Systemic Lupus Erythematosus Activity Index 2000 total score ≥6 points and clinical score ≥4 points. Patients (N=363) were randomized 1:1:1:1 to placebo (n=90) or deucravacitinib 3 mg twice daily (BID; n=91), 6 mg BID (n=93), or 12 mg once daily (QD; n=89). Patients assessed pain levels on a numeric rating scale (NRS) and completed the Patient-Reported Outcome Measurement Information System (PROMIS) Fatigue 7a Short Form and 36-Item Short Form Health Survey (SF-36). Missing data were imputed using control-based pattern imputation. Results were descriptive.

Results: Baseline characteristics were comparable across groups (**Table 1)**. At Week 48, greater mean changes from baseline in pain and fatigue were reported with deucravacitinib 3 mg BID, 6 mg BID, and 12 mg QD vs placebo, including achievement of the minimal clinically important differences (MCID) of −1 and −4 for both pain and fatigue with all doses of deucravacitinib vs for pain only with placebo (**Figure 1**). Patients treated with deucravacitinib reported greater achievement of changes associated with MCID for pain (−1), fatigue (−4), and SF-36 MCS and PCS (−2.5) vs placebo (**Table 2**). Mean scores (SD) at Week 48 numerically improved with deucravacitinib 3 mg BID, 6 mg BID, and 12 mg QD vs placebo, respectively: Pain NRS: 3.6 (2.7), 3.7 (2.6), 3.6 (2.8), and 4.7 (2.7); PROMIS Fatigue: 52.4 (10.2), 52.6 (10.0), 51.9 (10.6), and 54.4 (10.9); SF-36 PCS: 44.7 (10.0), 44.6 (9.3), 45.1 (11.0), and 41.5 (10.5); and SF-36 MCS: 46.7 (12.6), 46.3 (13.1), 47.3 (12.6), and 45.2 (12.9).

Conclusion: Patients with SLE who received deucravacitinib reported improvements over patients who received placebo on pain and fatigue, and in health-related quality of life at Week 48.

Disclosure: M. Mosca: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, GlaxoSmithKlein(GSK), 2, Otsuka, 2, UCB, 2; **L. Arnaud**: AbbVie, 6, Alexion, 6, Alpine, 2, 6, Amgen, 6, AstraZeneca, 1, 2, 6, Biogen, 6, Boehringer Ingelheim, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 1, 2, 6, Grifols, 6, Janssen, 6, Kezar Life Sciences, 2, 6, LFB, 6, Medac, 6, Novartis, 2, 6, Pfizer, 6, Roche-Chugaï, 6, UCB, 6; **A. Askanase**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb, 2, Celgene, 2, Eli Lilly, 2, Genentech, 2, GSK, 2, Idorsia, 2, Janssen, 2, Mallinckrodt, 2, Pfizer, 2, UCB Pharma, 2; **C. Hobar**: Bristol-Myers Squibb(BMS), 3; **B. Becker**: Bristol-Myers Squibb(BMS), 3; **S. Singhal**: Bristol-Myers Squibb(BMS), 3; **S. Banerjee**: Bristol-Myers Squibb(BMS), 3, 11;

S. Pomponi: Bristol-Myers Squibb(BMS), 3; **J. Choi**: Bristol Myers Squibb, 3; **A. Coles**: Bristol-Myers Squibb(BMS), 3; **V. Strand**: Abbvie, 2, Alpine Immune Sciences, 2, Amgen, 2, Arena, 2, AstraZeneca, 2, Bayer, 2, Biosplice, 2, Bioventus, 2, Blackrock, 2, 2, BMS, 2, Boehringer Ingelheim, 2, Celltrion, 2, Chemocentryx, 2, EMD Serono, 2, Equillium, 2, Ermium, 2, Eupraxia Pharmaceuticals, 2, Flexion, 2, Galapagos, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon, 2, Ichnos, 2, Inmedix, 2, Janssen, 2, Kiniksa, 2, 2, Kypha, 2, Lilly, 2, Merck, 2, MiMedx, 2, Novartis, 2, Omeros, 2, Pfizer, 2, Regeneron, 2, Rheos, 2, R-Pharm, 2, Samsung, 2, Sandoz, 2, Sanofi, 2, Scipher, 2, Setpoint, 2, Sorrento, 2, Spherix, 2, Tonix, 2, UCB, 2, Urica, 2.

Abstract Number: 2329

AMTX-100, a Nuclear Transport Inhibitor, Attenuates Inflammatory Cytokine Production in vitro and Following UV Mediated Skin Inflammation in a Mouse Model of Cutaneous Lupus Erythematosus in vivo

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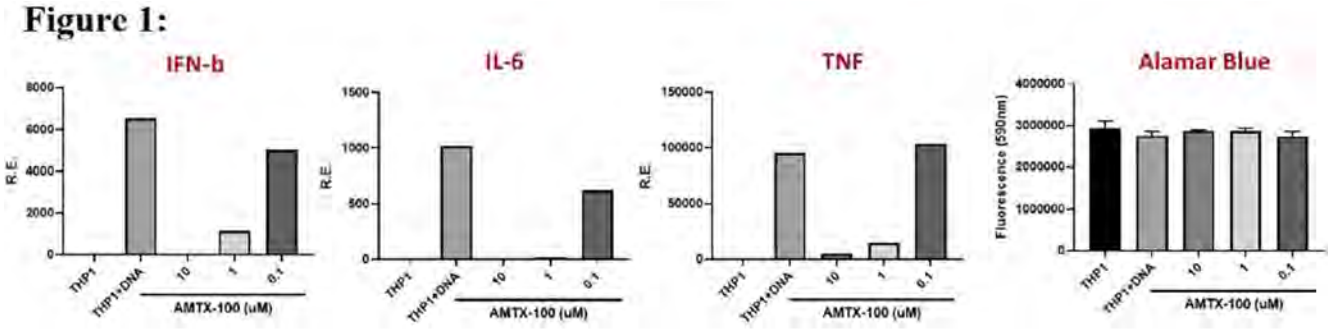
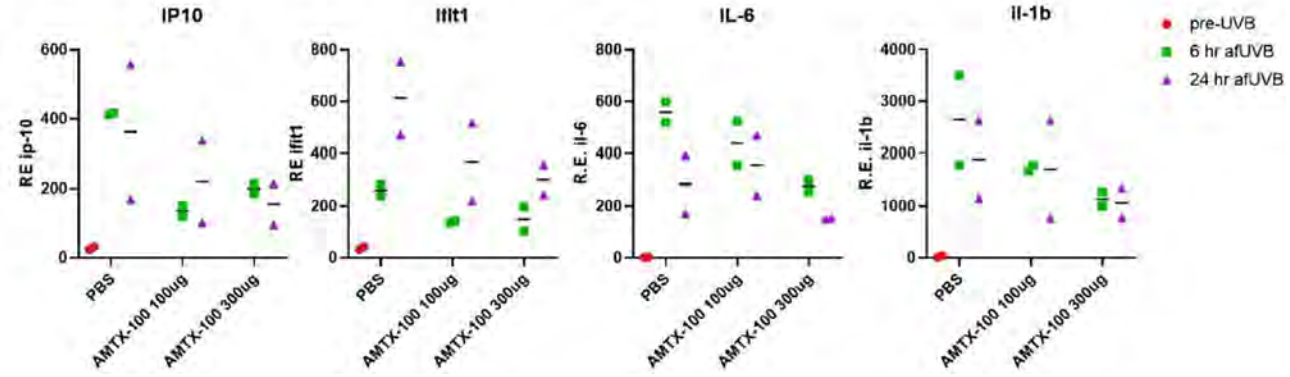
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammatory stimuli induce transcription factors (TFs) such as NF-kB and interferon regulatory factors (IRFs). TFs are transported from cytosol to nucleus to activate genes encoding chemokines and cytokines. Nuclear transport of TFs is performed by importins that comprise a beta chain and different alpha chains that confer substrate specificity for TF nuclear localization sequences (NLS). The alpha-5-containing importin (Impα5) is of particular interest because it transports STAT1, NF-kB, and other stress responsive TFs containing a NLS. AMTX-100 is a 28 amino acid chimeric peptide containing a huFGF4 domain and NF-kB p50 NLS that function to facilitate leukocyte cell penetration and as a nuclear transport checkpoint inhibitor (NTCI), respectively. AMTX-100 is currently in a Phase 2b clinical trial to treat inflammation in eczema. Since Impα5 binds to the NLS of NF-kB p50 as well as STAT1 & 3, we examined the effects of AMTX-100 on inflammatory pathways and Type I interferons (IFN-I), in vitro and in vivo.



AMTX-100 inhibits IFN-b and inflammatory cytokine production in vitro. The THP-1 monocyte cell line was incubated with serial 10-fold dilution of AMTX-100 as shown on the X-axis. Left three panels: After 1 hr, cells were transfected with ds-DNA and 6 hrs later the cells were harvested and the RNA expression of IFN-b, IL-6 and TNF quantified by qPCR. The results are shown as expression of the cytokine relative to 18S RNA (R.E. on the Y-axis). Right Panel: The Alamar blue test for viability revealed that the AMTX-100 peptide was non-toxic at the doses used in these experiments.

Figure 2:



AMTX-100 attenuates the skin IFN and inflammatory response to UV light exposure. C57BL/6 mice were exposed to a single dose of 500 mJ of UV light on the shaved dorsum. As shown on the X-axis, mice received either saline (PBS) or 100 or 300 ug AMTX-100 peptide in PBS before and after UV exposure. Biopsies were obtained at time 0 and at 6 and 24 hr after UV exposure. RNA was extracted and the relative expression of representative ISGs (IP10 and Ifit1) and the inflammatory cytokines (IL-6 and IL-1b) shown on the Y axis. Relative expression of genes prior to UV is shown in orange.

Methods: The human monocyte cell line, THP-1 was transfected with 0.1 ug dsDNA in the presence or absence of AMTX-100 and cytokine mRNA expression quantified by qPCR. Neutrophils from healthy volunteers were isolated by density gradient and exposed to either PMA, the ionophore A23187 or immune complexes (IC) containing the lupus antigen SmRNP. NET formation was quantified by release of DNA and MPO as determined by fluorimetry. Female C57BL/6 (B6) mice aged 8-12 weeks were exposed to a single dose of UV (500mJ/cm^2) on the dorsal skin. Skin biopsies were obtained before and at 6 and 24 hr post UV exposure. Cytokine gene expression was determined by qPCR. Statistical significance between groups was determined by Student's t-test.

Results: In vitro studies with THP-1 cells revealed that 1 uM AMTX-100 inhibited IFN-b expression by 82% , and IL-6, TNF and IL-1b by 98%, 84% and 95% respectively (Fig. 1). In neutrophils incubated with NET-inducing stimuli, AMTX-100 (3 uM) inhibited DNA and MPO release by ~40% in PMA or A23187 stimulated cells but did not affect NET release induced by IC. To determine whether AMTX-100 attenuated the IFN-I response following UV induced inflammation of mouse skin, we applied either 100 or 300 ug AMTX-100 in saline onto the skin before and once daily after UV exposure. As shown in Fig. 2, ISGs, as well IL-1 and IL6 were all reduced in an apparent dose dependent fashion. Similar results were obtained in a second in vivo experiment (not shown).

Conclusion: We conclude that AMTX-100 reduces Type I IFN and NF-kB-dependent inflammatory cytokines from DNA activated human monocytes *in vitro*. While AMTX-100 had a modest inhibitory effect on NET formation in response to PMA and ionophore stimulation, it did not attenuate NET formation induced by ICs in vitro. When tested *in vivo* using the lupus-relevant UV skin exposure, we observed a dose-dependent inhibition of several NF-kB-dependent cytokines as well as ISGs. Since AMTX-100 is in clinical trials for inflammatory skin disease, these findings suggest a novel therapeutic approach utilizing importin NTCIs that may be useful for prevention or treatment of cutaneous lupus erythematosus.

Disclosure: X. Sun: None; **J. An**: None; **T. Wang**: None; **A. Rathee**: None; **V. Alvarez**: Amytrx Therapeutics, 2; **M. Gonda**: Amytrx Therapeutics, Inc, 3, 4; **C. Lood**: Amytryx, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Citryll, 2, Eli Lilly, 5, Gilead, 5, Horizon Therapeutics, 5, Pfizer, 5, Redd Pharma, 5, 11; **K. Elkon**: None.

Abstract Number: 2330

Disease-Related Outcomes of Cognitive Behavioral Therapy in Randomized Control Trial for Youth with Childhood-onset SLE: A Secondary Analysis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Treatment Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Childhood-onset systemic lupus erythematosus (cSLE) is associated with symptoms such as fatigue, pain, and depressive symptoms that contribute to poor health-related quality of life. The Treatment and Education Approach for Childhood-Onset Lupus (TEACH; a cognitive behavioral therapy (CBT) program) has been shown in our prior work to significantly reduce fatigue and depressive symptoms when compared with standard care. The current study is a secondary data analysis of this recently completed trial which explores disease-related outcomes following TEACH, including disease activity, medication adherence, and health-related quality of life.

Methods: We conducted a randomized controlled trial of 59 youth ages 12-22 years meeting the ACR diagnostic classification criteria for SLE, from six rheumatology sites across the U.S. and Canada. Eligible participants had elevations in at least one target symptom area (e.g., fatigue, pain, or depression). Participants completed a baseline assessment, were randomized to 1) TEACH, a remotely delivered six-week CBT program with medical treatment as usual (TAU), or 2) TAU alone, then completed a post-assessment 8 weeks later. The current study explored: i) physician-reported disease activity via the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) and a Visual Analog Scale (VAS, range 0-100); ii) medication adherence measured by the Medication Adherence Self-Report Inventory (MASRI, range 0-100%); and iii) health-related quality of life measured by Pediatrics Quality of Life – Adolescent version (PedsQL-A, 0-100). Independent samples *t*-tests compared changes from baseline to post-assessment between those who received TEACH+TAU vs. those who received TAU alone.

Results: Twenty-eight (47.5%) participants received TEACH+TAU, and 31 (52.5%) received TAU alone. Participant characteristics are shown in Table 1. At baseline, disease activity (SLEDAI-2K) and health-related quality of life (general core score) were higher in the TEACH+TAU group. The change in disease activity (SLEDAI-2K) scores between groups significantly

Table 1

Baseline Characteristics	TEACH+TAU group (n=28)	TAU alone group (n=31)	p-value
Age (mean)	16.9	16.6	0.61
Female sex, n (%)	26, (92.9%)	30, (96.8%)	0.50
Race, n (%)	African American/Black, 5 (25%) White, 10 (35.7%) Asian, 8 (28.6%) Multiracial, 5 (17.9%)	African American/Black, 6 (19.4%) White, 15 (48.4%) Asian, 9 (29%) Other, 1 (3.2%)	0.10
Ethnicity, n (%)	Hispanic, 8 (28.6%)	Hispanic, 3 (9.7%)	
Disease duration (months)	66.19 ± 47.74	60.0 ± 44.5	0.62
Disease manifestations			
Neuropsychiatric lupus, n (%)	4 (14.3%)	2 (6.5%)	0.27
Presence of disease damage, n (%)	23 (82.1%)	19 (61.3%)	0.10
Disease activity			
SLEDAI-2K (mean ± SD)	5.96 ± 5.62	2.85 ± 3.7	0.02
Physician VAS (mean ± SD)	20.95 ± 21.77	18.44 ± 19.22	0.67
Medication Adherence (MASRI) (mean ± SD)	82.65 ± 16.41	83.90 ± 19.48	0.80
Health-related QOL (Peds QL-A)			
General core score (mean ± SD)	65.34 ± 15.63	51.30 ± 15.34	0.04
Rheumatology core score (mean ± SD)	68.63 ± 15.83	64.45 ± 16.07	0.53

Baseline characteristics of the TEACH+TAU group and TAU alone group.

Table 2

Disease-related Outcomes	Pre-post difference		Test statistic [95% CI], p-value
	TEACH+TAU	TAU alone	
Disease activity			
SLEDAI-2K	-2.11	0.67	T 2.47 [0.5-5.05], 0.02
Physician VAS	-9.81	1.21	T 2.24 [0.07-1.37], 0.03
Medication Adherence (MASRI)	7.5	2.22	T -1.27 [13.59-3.04], 0.21
Health-related QOL (Peds QL-A)			
General core score	14.05	10.03	T -0.93 [-12.92-4.89], 0.36
Rheumatology core score	12.81	10.07	T -.55 [-13.08-7.61], 0.59

Between group pre-post differences of disease-related outcomes.

Figure 3 A and B

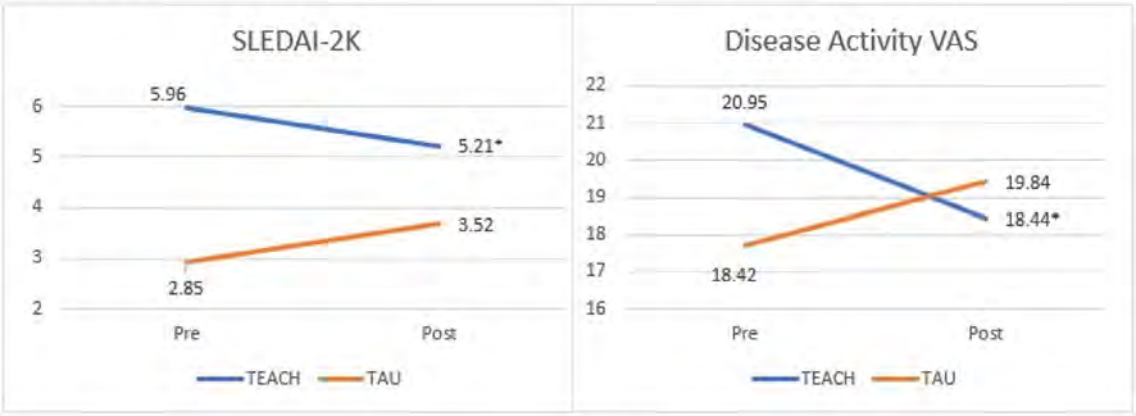

Figure 3A *Figure 3B*

Changes in SLEDAI-2K and Disease Activity VAS among TEACH and TAU participants from pre to post assessment.

differed, with the TEACH+TAU group demonstrating a significant decrease in disease activity scores ($t(40) = 2.47$, $p = 0.02$; Table 2, Figure 3A). There was also a statistically significant decrease in physician-reported disease activity VAS for the TEACH+TAU group vs the TAU group, ($t(38) = 2.24$, $p = 0.031$; Figure 3B). There were no other statistically significant differences between groups for changes in medication adherence or health-related quality of life.

Conclusion: TEACH may be associated with short-term improvement in disease activity, in addition to reducing depressive symptoms and fatigue. TEACH represents a promising treatment modality to mitigate mental health symptoms and improve disease outcomes. Future research will examine the long-term effectiveness of TEACH when implemented into real-world pediatric rheumatology clinics.

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Abstract Number: 2331

Molecular Predictors of Treatment Response in Two Trials of Abatacept in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Abatacept (ABA) is a fusion protein that disrupts T cell co-stimulation by inhibiting interactions between CD28 and CD80/86. ABA is effective in RA, but SLE clinical trials have been disappointing. Exploratory analyses have suggested that ABA might benefit some SLE patients depending on disease severity or outcome definitions, but identification of reproducible predictors of response remains elusive. This study applied a systems-based approach to developing a predictive model of abatacept response in SLE.

Methods: Pre-treatment peripheral blood mononuclear cells were obtained from the screening visits of the Clarification of Abatacept Effects in SLE with Integrated Biologic and Clinical Approaches (ABC; n=19) and the Abatacept and Cyclophosphamide Combination Therapy for Lupus Nephritis (ACCESS; n=40) clinical trials evaluating ABA in SLE patients without

organ-threatening disease or lupus nephritis, respectively. Genomic DNA and total RNA were extracted from isolated T cells, B cells, and monocytes, followed by DNA methylation microarray and RNA sequencing analyses. Machine learning was applied to methylation data using generalized linear modeling and 40 bootstrapped re-samplings split between 70% training and 30% testing.

Results: A total of 29 ABA responders (R) and 30 non-responders (NR) were identified from both clinical trials. Bootstrapped models of all cell types separated responders and non-responders robustly, with an average AUC of 0.976 (Fig 1A-B). Four CpGs were shared in at least 80% of the re-samplings (Fig 1C), and a model using these 4 CpGs on T cells alone revealed an average ROC of 0.935 (Fig. 1D-E). Applying this model to B cells and monocytes yielded similarly robust results (Fig. 1F-G),

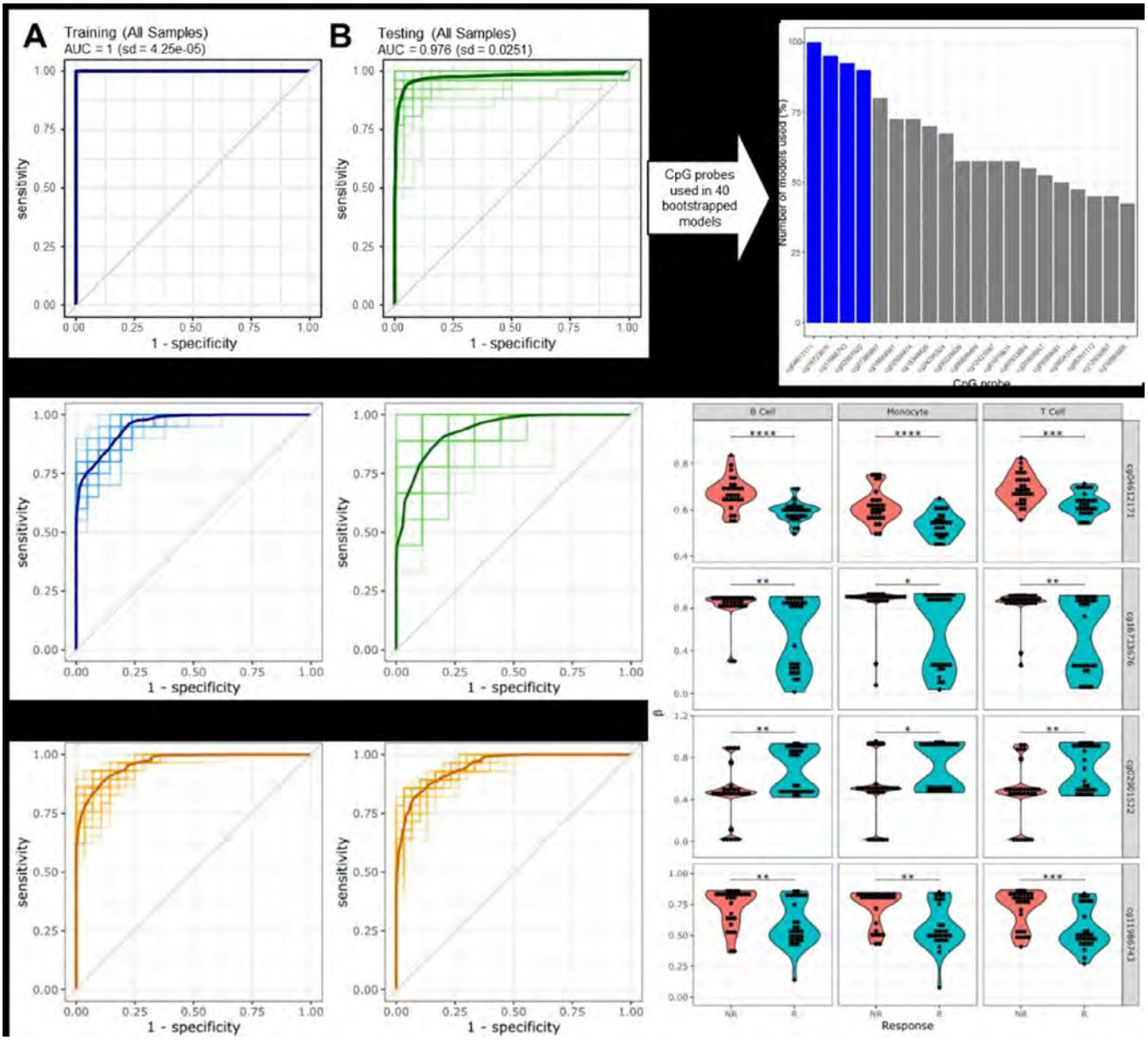

Figure 1. Machine learning identifies a 4-marker methylation signature distinguishing abatacept responders and non-responders at screening. ROC curves of 40 bootstrapped re-samplings of all cell type-specific epigenome profiles split between (A) 70% training and (B) 30% testing. (C) Percent of models using each of the top 20 most frequently utilized features across the models. (D-E) ROC curves of 40 bootstrapped re-samplings of T cell epigenome profiles. Models were developed with only the top 4 CpGs. (F-G) ROC curves of 40 models developed on T cells applied to B cells and monocytes. (H) Violin dot plots of methylation differences by abatacept response of the top 4 CpGs. Asterisks indicate significance of Benjamini-Hochberg corrected p-value of Mann-Whitney U-Tests: * < 0.05, ** < 0.01, *** < 0.001, **** < 0.0001.

and the 4 CpGs were differentially methylated in each cell type (Fig. 1H). In T cells, the 4 CpGs positively correlated with TCR activation, CTLA-4 regulation, and IL-2 production (Fig 2A-B), while BCR activity and phagosome activity and cytokine production are correlated with these CpGs in B cells and monocytes, respectively (Fig 2C-F). Unbiased principal component analysis on global T cell methylation profiles separated R and NR patients (Fig 3A), and most sites were hypermethylated in R patients (Fig 3C). The most hypermethylated transcription start sites revealed associations with cytokine storm and IL-17 signaling in NR patients (Fig 3D-E).

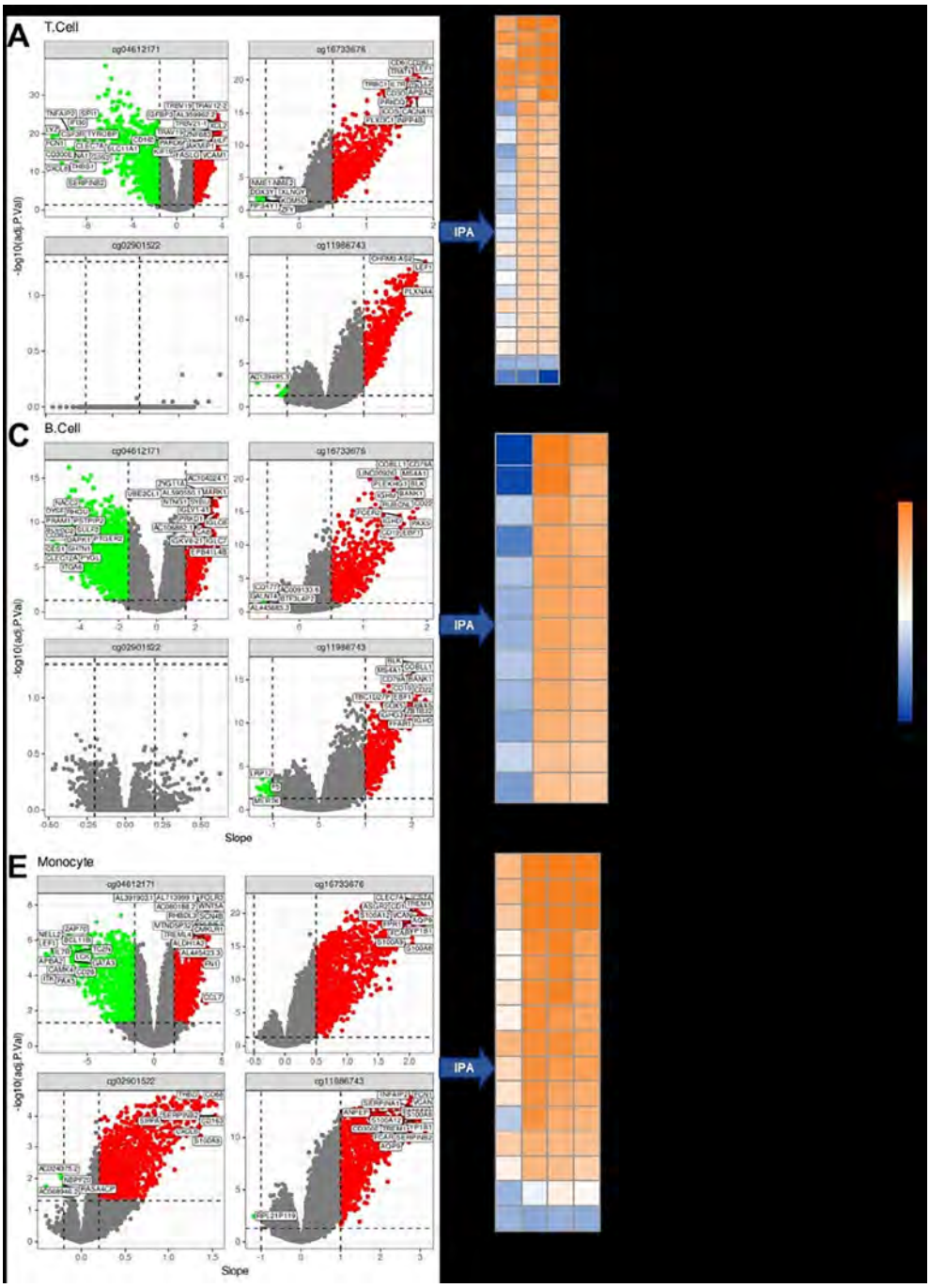

Figure 2. Correlation of RNA transcripts with methylation at CpGs predictive of abatacept response. Volcano plots and ingenuity pathway analysis (IPA) results of correlation analyses of methylation at each of the 4 predictive CpGs with RNA-seq data in (A-B) T cells, (C-D) B cells, and (E-F) monocytes. (A, C, E) The slope of each correlation is plotted on the x-axis, and the negative log transforms of p-values adjusted for multiple comparisons on the y-axis. (B, D, F) The most significantly correlated transcripts at each CpG of interest were input into IPA with previously noted cutoffs.

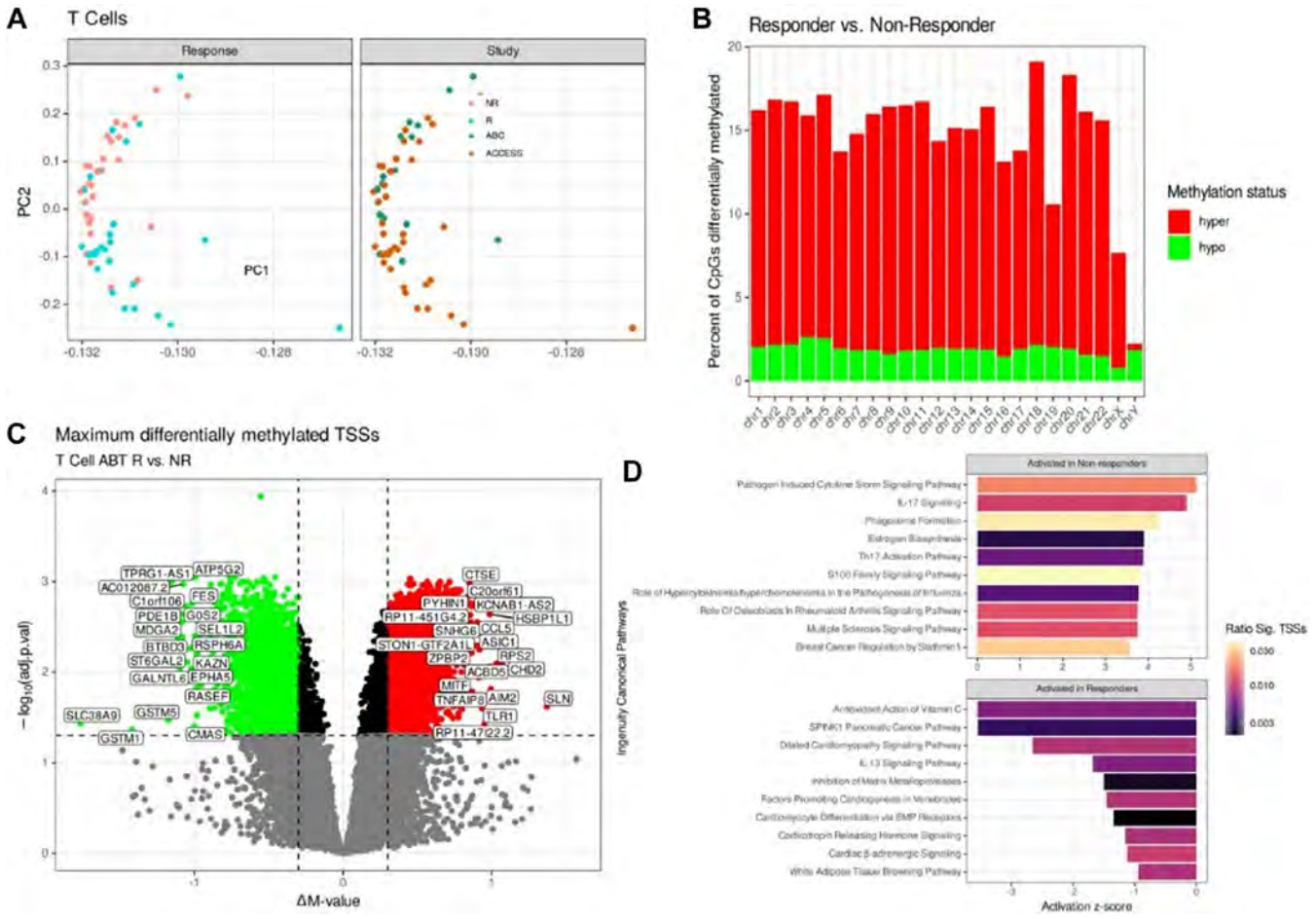

Figure 3. Global epigenetic landscape of T cells contributing to future abatacept response. (A) Principal component analyses of global DNA methylation profiles of T cells. (B) Bar graph of per-chromosome methylation comparison between T cells from abatacept responders and non-responders. (C) Volcano plot of maximum differential methylation at transcription start sites for annotated genes between T cells from abatacept responders and non-responders. (D) Bar graph of the top 10 canonical pathways from IPA by predicted activation in abatacept responders and non-responders. IPA results were filtered for Benjamini-Hochberg adjusted p-value < 0.05 by Fisher's exact test and selected for the top 10 positive and negative activation z-scores.

Conclusion: We determined a robust 4 CpG methylation signature that predicts ABA response across two disparate SLE trials. Parallel transcriptomic profiling linked this signature to cell lineage-specific activation pathways. Comparative epigenomic analysis of T cells revealed a hypomethylated signature in NR patients, likely driving continued proinflammatory responses despite abatacept treatment.

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Abstract Number: 2332

Dapirolizumab Pegol Efficacy by Subgroups in Patients with SLE: A Post Hoc Analysis of Phase 2b Clinical Trial Data

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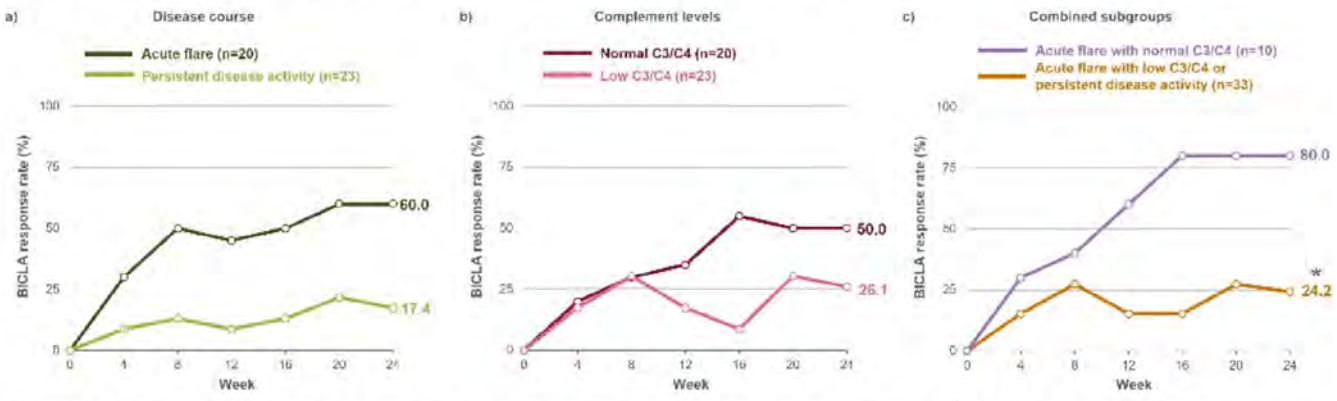
SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: SLE – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) clinical trials are challenged by high standard of care plus placebo (SOC+PBO) response rates.[1] Previous post hoc analyses of the phase 2b RISE trial in SLE (NCT02804763) identified acute flare and normal complement as potential predictors of SOC+PBO response.[2] This analysis aims to evaluate the treatment effect of dapirolizumab pegol (DZP; a polyethylene glycol-conjugated antigen-binding fragment lacking a functional Fc domain that inhibits CD40L) in subgroups of patients (pts) from the phase 2b RISE trial based on the previously identified potential predictors of SOC+PBO response.[2,3]

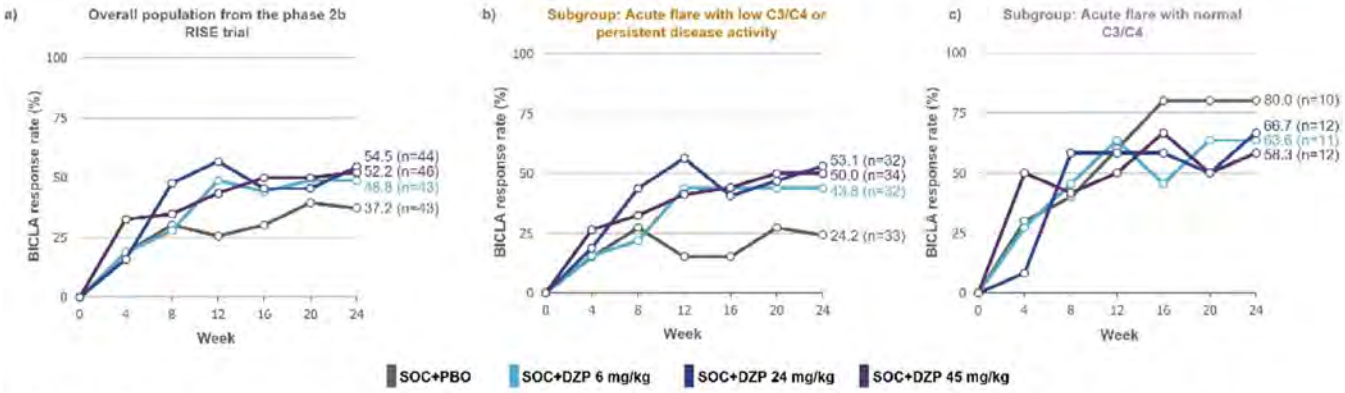
Methods: Post hoc analyses were performed on data from the phase 2b RISE trial, in which pts received PBO or DZP (6/24/45 mg/kg), alongside SOC, for 24 weeks (wks).[3] Adults with moderately to severely active SLE, receiving stable doses of corticosteroids, antimalarial or immunosuppressant drugs were included in the trial.[3] Pts from the trial were divided into subgroups based on previously identified potential predictors of SOC+PBO response.[2] Disease course at screening was defined using British Isles Lupus Assessment Group (BILAG) 2004 item level scores as acute flare (worsening/new symptoms) or persistent (symptoms rated as the same) based on the past 4 wks compared with the 4 wks prior to those. Low C3/C4 was defined as below the lower limit of normal at screening. Outcomes to Wk 24 were evaluated in subgroups and compared with the overall population. Outcomes assessed were BILAG-based Composite Lupus Assessment (BICLA) response, SLE Responder Index-4 (SRI-4) response, and change from baseline in Physician's Global Assessment (PGA).

Figure 1. BICLA response to Wk 24 in pts receiving SOC+PBO by subgroups



Full analysis set. *p=0.005 for the odds ratio (95% CI) of acute flare with low C3/C4 or persistent disease activity vs acute flare with normal C3/C4 at Wk 24 (0.1 [0.0, 0.5]). Missing data were imputed using modified non-responder imputation. **Abbreviations:** BICLA: British Isles Lupus Assessment Group-based Composite Lupus Assessment; CI: confidence interval; PBO: placebo; pts: patients; SOC: standard of care; Wk: Week.

Figure 2. BICLA response to Wk 24 in pts receiving SOC+PBO and SOC+DZP in the overall population and by combined subgroups



Full analysis set. Missing data were imputed using modified non-responder imputation. **Abbreviations:** BICLA: British Isles Lupus Assessment Group-based Composite Lupus Assessment; CI: confidence interval; DZP: dapirolizumab pegol; PBO: placebo; pts: patients; SOC: standard of care; Wk: Week.

Results: A higher proportion of pts receiving SOC+PBO with acute flare (vs persistent disease activity) and with normal C3/C4 (vs low C3/C4) achieved BICLA response at Wk 24 (**Figures 1a&1b**). When the subgroups were combined, a significantly higher proportion of pts receiving SOC+PBO with acute flare and normal C3/C4 achieved BICLA response at Wk 24 compared with pts receiving SOC+PBO with either acute flare with low C3/C4 or persistent disease activity (**Figure 1c**). BICLA responses to Wk 24 in the combined subgroups for pts receiving SOC+PBO and SOC+DZP are presented in **Figure 2b&2c**, alongside BICLA response in the overall population from the RISE trial in **Figure 2a**. Similar patterns were seen for SRI-4 response and change from baseline in PGA in the combined subgroups (data not shown). Baseline characteristics in the combined subgroups are presented in **Table 1**.

Table 1. Baseline characteristics of all pts in the phase 2b RISE trial by combined subgroups

	Acute flare with low C3/C4 or persistent disease activity (n=135)	Acute flare with normal C3/C4 (n=47)
Region, n (%)		
Western/Central Europe	24 (17.8)	4 (8.5)
Eastern Europe	26 (19.3)	18 (38.3)
North America	37 (27.4)	16 (34.0)
Latin America	48 (35.6)	9 (19.1)
Time since first diagnosis of SLE (years), mean (SD)	8.2 (7.1)	8.1 (7.0)
≥1 BILAG Grade A, n (%)	55 (40.7)	27 (57.4)
≥2 organ systems with BILAG Grade B and no organ system with BILAG Grade A, n (%)	80 (59.3)	20 (42.6)
SLEDAI-2K total score <10[a], n (%)	33 (24.4)	21 (44.7)
SLEDAI-2K total score ≥10[a], n (%)	101 (74.8)	25 (53.2)
Pts taking systemic corticosteroids, n (%)	121 (89.6)	38 (80.9)

Safety set. [a]SLEDAI-2K total score was calculated counting anti-dsDNA as positive if >10 iU. **Abbreviations:** BILAG: British Isles Lupus Assessment Group; dsDNA: double-stranded DNA; iU: international units; pts: patients; SD: standard deviation; SLE: systemic lupus erythematosus; SLEDAI-2K: SLE Disease Activity Index 2000.

Conclusion: Albeit in a limited sample size, pts with acute flare and normal complement were more likely to achieve response to SOC+PBO than pts with acute flare and low complement or persistent disease activity. These data suggest that SLE trial design may need to consider baseline clinical and serologic activity patterns to adequately assess treatment efficacy. **References:1.** Durcan L. Lancet. 2023;S0140-6736(23)00342-2. **2.** Stach C. Presented at LUPUS & KCR 2023, Abstract 2023-0801, ePoster LP-198. **3.** Furie RA. Rheumatology (Oxford). 2021;60:5397–407.

Disclosure: A. Askanase: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb, 2, Celgene, 2, Eli Lilly, 2, Genentech, 2, GSK, 2, Idorsia, 2, Janssen, 2, Mallinckrodt, 2, Pfizer, 2, UCB Pharma, 2; **C. Stach**: UCB Pharma, 3, 11; **C. Brittain**: UCB Pharma, 3, 11; **G. Stojan**: UCB Pharma, 3, 11; **R. Furie**: Biogen, 2, 5.

Abstract Number: 2333

Dapirolizumab Pegol Impacts Important Immunologic Pathways in SLE: Pharmacodynamic Analysis of B Cell and Type I Interferon Pathways from a Phase 2b Trial

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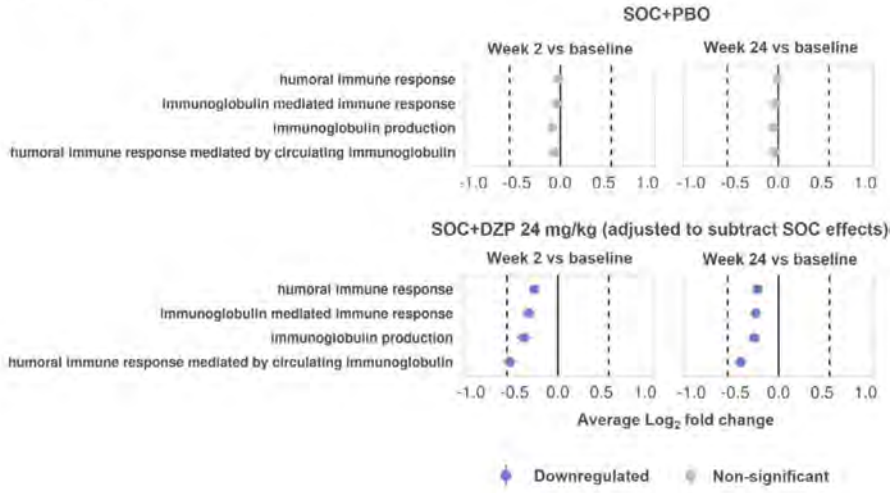
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The pivotal role of CD40-CD40L interactions in systemic lupus erythematosus (SLE) pathogenesis stems from the orchestration of a range of immune and inflammatory responses involving B cells, T cells, antigen-presenting cells, and type I interferon (IFN) production.[1,2] Dapirolizumab pegol (DZP) is a polyethylene glycol-conjugated antigen-binding fragment lacking a functional Fc domain that inhibits CD40L.[3] This post hoc pharmacodynamic analysis explored the impact of DZP on B cell and type I IFN pathways using data from the phase 2b RISE trial in SLE (NCT02804763).[3]

Methods: In RISE, patients (pts) received placebo (PBO) or DZP (6/24/45 mg/kg) alongside standard of care (SOC) for 24 weeks (wks); adults with moderately to severely active SLE, receiving stable doses of SOC treatments, were included in the trial.[3] Analyses presented here used a subgroup of patients from RISE (n=131) that is analogous to the phase 3 trial population(NCT04294667);[4] results are shown for the PBO and DZP 24 mg/kg arms. RNA sequencing (RNAseq) was performed on available blood samples at baseline and Wks 2 and 24; samples were not available for all pts at all timepoints. Gene expression changes were analyzed and competitive gene set analyses were carried out on pathways relevant to SLE immunopathology, selected from Gene Ontology Biological Processes and augmented with gene signatures that discriminate immune cell types in SLE.[5,6] Differential expression results for DZP treatment were corrected for SOC effects. To assess effects of DZP on type I IFN biology, pts were stratified post hoc by baseline type I IFN expression levels using a 4-gene type I IFN signature.[7]

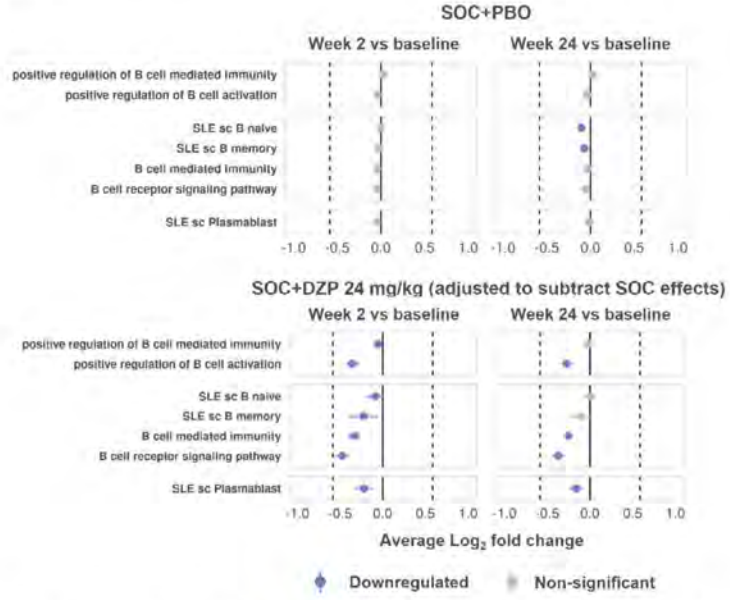
Results: DZP significantly downregulated genes related to immunoglobulin production compared with PBO, and this effect was observed as early as Wk 2 following a single dose (**Figure 1**). A similar trend was observed in clinical levels of autoantibodies (anti-dsDNA), which has been previously reported.[3]Compared with PBO, DZP also significantly downregulated genes that play a critical role in B cell biology, specifically those involved in B cell mediated immunity and B cell receptor

Figure 1. Effect of SOC+DZP compared with SOC+PBO on the expression of genes related to immunoglobulin production at Wk 2 and Wk 24



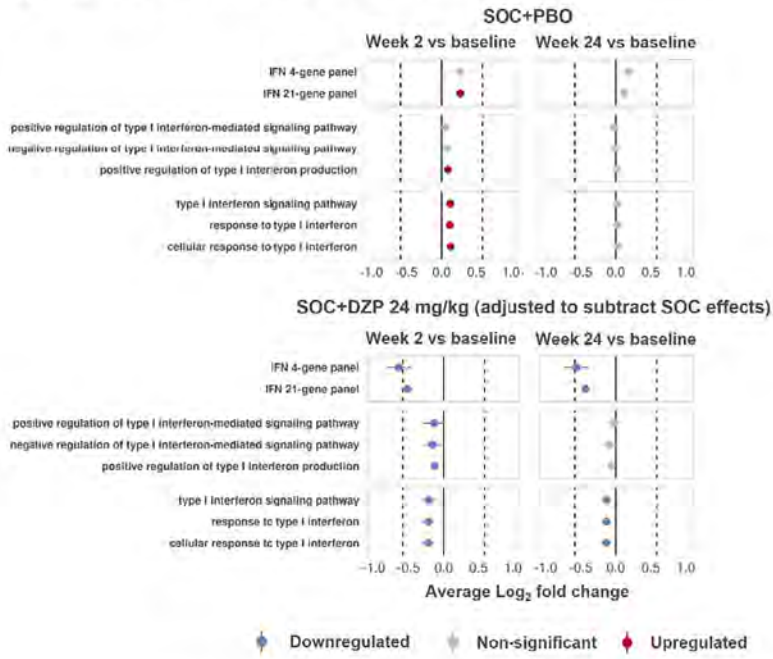
SOC+PBO: baseline: n=31; Wk 2: n=31; Wk 24: n=30. SOC+DZP 24 mg/kg: baseline: n=27; Wk 2: n=30; Wk 24: n=29. Each dot is a gene set, blue dots indicate statistically significant downregulated gene sets, grey dots represent non-significant changes. Dashed lines represent 1.5-fold change, block lines at 0 represent 1-fold change. Only significant datapoints after treatment with DZP 24 mg/kg are shown (FDR<0.05). **Abbreviations:** DZP: dapirolizumab pegol; FDR: false discovery rate; PBO: placebo; SOC: standard of care; Wk: Week.

Figure 2. Effect of SOC+DZP compared with SOC+PBO on the expression of genes related to B cell biology and regulators at Wk 2 and Wk 24



SOC+PBO: baseline: n= 31; Wk 2: n=31; Wk 24: n=30. SOC+DZP 24 mg/kg: baseline: n=27; Wk 2: n=30; Wk 24: n=29. Each dot is a gene set, blue dots indicate statistically significant downregulated gene sets, grey dots represent non-significant changes. Dashed lines represent 1.5-fold change, block lines at 0 represent 1-fold change. Only significant datapoints after treatment with DZP 24 mg/kg are shown (FDR<0.05). **Abbreviations:** DZP: dapirolizumab pegol; FDR: false discovery rate; PBO: placebo; sc: subcutaneous; SLE: systemic lupus erythematosus; SOC: standard of care: Wk: Week.

Figure 3. Effect of SOC+DZP compared with SOC+PBO on the expression of type I IFN gene signatures at Wk 2 and Wk 24 in pts with high type I IFN expression at baseline



SOC+PBO: baseline: n= 18; Wk 2: n=17; Wk 24: n=17. SOC+DZP 24 mg/kg: baseline: n=18; Wk 2: n=17; Wk 24: n=16. Each dot is a gene set, blue dots indicate statistically significant downregulated gene sets, red dots indicate statistically significant upregulated gene sets, and grey dots represent non-significant changes. Dashed lines represent 1.5-fold change, block lines at 0 represent 1-fold change. Only significant datapoints after treatment with DZP 24mg/kg are shown (FDR<0.05). **Abbreviations:** DZP: dapirolizumab pegol; FDR: false discovery rate; IFN: interferon; PBO: placebo; pts: patients; SOC: standard of care: Wk: Week.

signaling pathways (**Figure 2**). At baseline, 76/120 pts (63.3%) with RNAseq samples available across all treatment arms showed high type I IFN gene expression. In pts with high expression, DZP caused down-modulation of a variety of type I IFN gene signatures compared with PBO, with inhibitory effects observed as early as Wk 2 (**Figure 3**).

Conclusion: DZP exerts a broad suppressive effect on B cell biology, decreasing the expression of numerous gene sets involved in B cell activation and immunoglobulin production. Moreover, DZP decreases expression of type I IFN signatures in pts with high baseline type I IFN expression. The impacts of DZP were seen as early as Wk 2. These findings underscore the potent immunomodulatory role of DZP in SLE pathology.

References:1. Ramanujam M. Autoimmun Rev. 2020;19(11):102668. **2.** Rönnblom L. Lupus Sci Med. 2019;6(1): e000270. **3.** Furie RA. Rheumatology (Oxford). 2021;60:5397–407. **4.** Askanase A. Ann Rheum Dis. 2023;82(Suppl 1):272. **5.** Wu D. Nucleic Acids Res. 2012;40(17):e133. **6.** Mandric I. Nat Commun. 2020;11(1):5504. **7.** Felten R. Drug Des Devel Ther. 2019;13:1535–43.

Disclosure: I. Cutcutache: UCB Pharma, 3, 11; **A. Powlesland**: UCB Pharma, 3, 11; **A. Skelton**: UCB Pharma, 3, 11; **Y. Sun**: UCB Pharma, 3; **M. Page**: UCB Pharma, 3, 11; **G. Stojan**: UCB Pharma, 3, 11; **P. Lipsky**: None; **A. Skowera**: UCB Pharma, 3, 11; **C. Stach**: UCB Pharma, 3, 11.

Abstract Number: 2334

Remission Attainment in Patients with Systemic Lupus Erythematosus Treated with Anifrolumab Compared with Placebo over a 4-Year Period

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Treatment Poster III

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Session Time: 9:00AM–11:00AM

Background/Purpose: In patients with SLE, remission is an established therapeutic goal associated with reduced damage accrual and flares, and improved health-related quality of life.[1] Here, we evaluated attainment of DORIS (Definition of Remission in SLE) during anifrolumab treatment in the double-blind randomized phase 3 TULIP long-term extension (LTE) trial.[2]

Methods: Patients with moderate to severe SLE (1997 ACR criteria) despite standard therapy who completed the 52-week TULIP-1 or TULIP-2 trials (NCT02446912, NCT02446899) could reconsent to participatein the randomized, placebo-controlled, double-blind, 3-year extension (NCT02794285). Here, we analyzed patients randomized to receive intravenous anifrolumab 300 mg or placebo for the TULIP-1/TULIP-2 and LTE periods. DORIS attainment was defined as all the following: total clinical SLEDAI-2K score =0, physician global assessment (0–3) < 0.5, prednisone/equivalent dosage ≤5 mg/day, and no use of restricted medications (TULIP-1/TULIP-2 period only). Time to first DORIS was compared using Cox

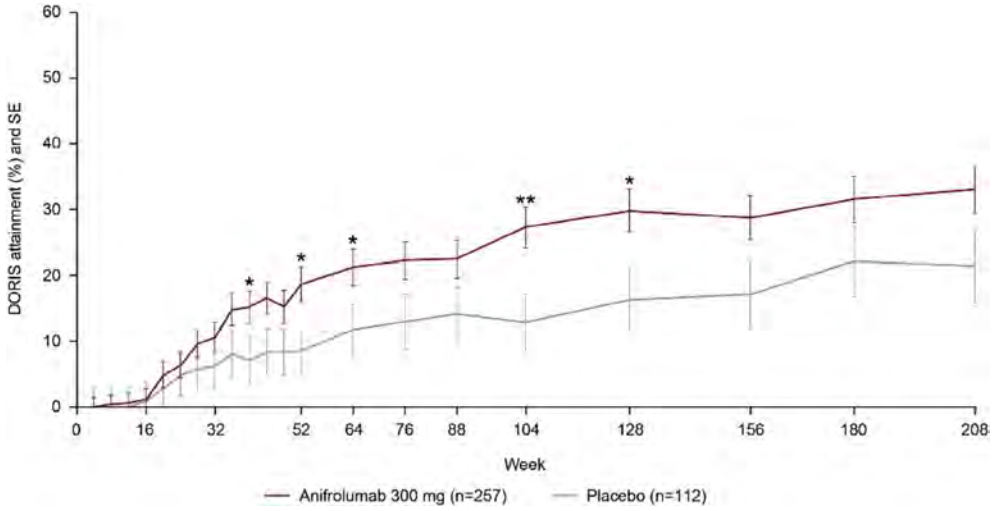

Figure. DORIS Attainment by Randomized Treatment in Patients With SLE in the TULIP and LTE Study Periods. DORIS attainment was defined as all the following: total clinical SLEDAI-2K score =0, physician global assessment (0–3) <0.5, prednisone/equivalent dosage ≤5 mg/day, and no use of restricted medications (TULIP-1 and TULIP-2 period only). Clinical SLEDAI-2K is a variant of the SLEDAI-2K, in which the serological descriptors (anti-dsDNA and complement) are omitted. DORIS attainment rates were calculated using a stratified Cochran–Mantel–Haenszel approach, with stratification factors of SLEDAI-2K at screening, Day 1 glucocorticoid dosage, type I interferon gene signature at screening, and study; response rates were compared using logistic regression. DORIS, Definition of Remission in SLE; LTE, long-term extension; SE, standard error. Nominal P: *<0.05; **<0.01.

regression. DORIS attainment rates were calculated using a Cochran–Mantel–Haenszel approach and compared using logistic regression. Total time and percentage of time in DORIS was analyzed using analysis of covariance. Patients who discontinuedinvestigational product prematurely and/or withdrew from the study due to lack of efficacy and/or disease worsening were considered nonresponders from that visit on. All *P*-values are nominal.

Results: Overall, 369 patients (anifrolumab 300 mg, n=257; placebo, n=112) who continued treatment in the LTE were analyzed for the 4-year TULIP+LTE period. Time to first DORIS remission was shorter in anifrolumab-treated patients compared with placebo (hazard ratio 1.49, 95% CI 1.04–2.19, *P*=0.034). DORIS remission attainment increased from TULIP baseline to Week 208; at the first LTE visit (Week 64), 21.2% of anifrolumab-treated patients achieved DORIS compared with 11.8% of the placebo group (odds ratio [OR] 2.1, 95% CI 1.0–4.1, *P*=0.036); a similar trend was seen up to Week 208 (33.0% vs 21.4%; OR 1.8, 95% CI 0.9–3.5, *P*=0.089) (Figure). Greater cumulative time (*P*=0.002) and percentage of time (*P*=0.002) were spent in DORIS by patients receiving anifrolumab compared with placebo. A greater proportion of patients treated with anifrolumab were in DORIS ≥20% of the time compared with placebo (OR 2.9, 95% CI 1.6–5.2, *P*=0.001) and ≥50% of the time (OR 2.3, 95% CI 1.1–5.0, *P*=0.030). Compared with placebo, anifrolumab-treated patients were more likely to sustain DORIS for ≥3 consecutive visits (OR 2.1, 95% CI 1.2–3.6, *P*=0.013) and ≥5 visits (OR 2.3, 95% CI 1.1–4.8, *P*=0.022).

Conclusion: Treatment with anifrolumab, in addition to standard therapy, was associated with more frequent, prolonged, and sustained DORIS remission attainment compared with placebo during the 4-year TULIP+LTE period. Our results suggest that DORIS, a definition of remission associated with improved clinical outcomes,[1] is an attainable therapeutic goal with long-term anifrolumab use.

References: 1.van Vollenhoven RF, et al. *Lupus Sci Med*. 2021;8:e000538.

2.Kalunian KC, et al. *Arthritis Rheumatol*. 2023;75:253–65.

Disclosure: R. van Vollenhoven: AbbVie, 2, 6, AstraZeneca, 2, 5, 6, Biogen, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Galapagos, 2, 5, 6, GlaxoSmithKline, 6, Janssen, 2, 6, MSD/Merck Sharp and Dohme, 5, Novartis, 5, Pfizer, 2, 5, 6, RemeGen, 2, Roche, 5, Sanofi, 5, UCB, 2, 5, 6; **E. Morand**: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 2, 5, 6, Biogen, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, EMD Serono, 2, 5, Galapagos, 2, Genentech, 2, 5, GlaxoSmithKline, 2, 5, IgM, 2, Janssen, 2, 5, Novartis, 2, Servier, 2, Takeda, 2, UCB, 5; **R. Furie**: AstraZeneca, 2, 5, 6; **K. Kalunian**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Biogen, 2, Bristol-Myers Squibb, 2, Eli Lilly, 2, Genentech/Roche, 2, GlaxoSmithKline, 2, Janssen, 2, Pfizer, 2; **R. Tummala**: AstraZeneca, 3; **G. Abreu**: AstraZeneca, 3; **H. Al-Mossawi**: AstraZeneca, 3; **C. Lindholm**: AstraZeneca, 3.

Abstract Number: 2335

Defining a Basket Population for ANA+ Arthritis Trials

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: SLE – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Musculoskeletal (MSK) manifestations are common in systemic lupus erythematosus (SLE) and other ANA-associated rheumatic musculoskeletal diseases (ANA-RMDs). Presently clinical trials recruit patients from individual diagnoses. Recruitment is often difficult, effect sizes are small and licensed therapies are only available to patients with the most common ANA-RMD, SLE.

Objectives:

1. To compare the symptom impact and immunophenotype of arthritis associated with a range of ANA-associated autoimmune diseases

2. To explore alternative classifications of the spectrum of ANA-associated arthritis to define basket populations for trials

3. To validate the MSK-BILAG across multiple diagnoses

Methods: We used analysis of flow cytometry for major subsets, gene expression (signatures for interferon, plasma blast, neutrophil, myeloid inflammation and erythropoiesis) and patient reported data from a mixed cohort of ANA-associated autoimmune diseases. 215 patients with MSK symptoms were included, 90 with SLE and 125 with an another diagnosis (UCTD, pSS, IM, MCTD and SSc).

The implications of legacy diagnosis membership were compared using QoL measures (SF36, EQ5D-5L, Patient VAS, ICECAP-A, FACIT-F, WPAI and ICECAP-A. Gaussian mixture modelling was used to explore alternative classifications more suitable for basket trials. The association of BILAG-MSK with physician VAS was tested in SLE and the non-SLE group.

Results: Legacy diagnosis was a poor indicator of the patient experience with Kruskal Wallis testing revealing only 2 significant differences (EQ5D Mobility and EQ5D-5l index domains) between diagnoses. Flow cytometric and gene expression data showed no significant differences between legacy diagnoses.

Better predictors of the patient experience were chromatin antibody positivity and non-European ancestry which were associated with worse EQ5D-5l index scores ($P < 0.05$ in both).

Preliminary gaussian mixture modelling analysis of this population based on variables identified as important within the principle component analysis identified 4 clusters. A biologically active MSK symptom dominant cluster (n=140), a biologically active non MSK symptom dominant cluster (n=43), a biologically and symptom quiescent cluster (n= 24) and a biologically and symptom quiescent cluster (n=65).

The application of the BILAG-MSK domain across ANA-RMDs correlated well with the Physician General Assessment scores of MSK disease activity suggesting it may be reasonable to apply this measure in any future basket trial.

Conclusion: Inflammatory arthritis is similar in both clinical impact and immune phenotype across ANA-associated RMDs, suggesting similar benefits of therapy for this feature within each disease. Machine learning reveals an alternative basket of patients suitable for clinical trials who have clinical synovitis, high symptom burden and consistently increased markers of immune activation, and a mixture of legacy diagnoses, who are more numerous than MSK SLE alone. A further smaller basket of patients have high symptom burden but little evidence of active inflammation.

Disclosure: J. Arnold: None; **M. Md Yusof**: Novartis, 6, Roche, 6, UCB, 1; **L. Carter**: UCB, 1; **Z. Wigston**: None; **E. Vital**: F. Hoffmann-La Roche Ltd, 2, Genentech, Inc., 2, Sandoz, 5.

Abstract Number: 2336

Identification of Urine Metabolites Linked to Disease Activity That Are Modulated by Anifrolumab in a Phase 2 LN Trial Using Untargeted Metabolomics Analysis

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SESSION INFORMATION

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Background/Purpose: LN is a severe complication of SLE, affecting 21%–48% of patients.[1] Development of noninvasive diagnostic tests for LN is ongoing; urinary biomarkers have good tissue proximity with minimal invasivity.[2] Anifrolumab, a type I IFN receptor mAb approved for the treatment of moderate to severe SLE,[3] is being evaluated in a phase 3 trial for patients with LN.[4] We conducted untargeted metabolomics profiling on urine samples from the phase 2 trial to identify markers associated with LN disease activity that were modulated by anifrolumab.

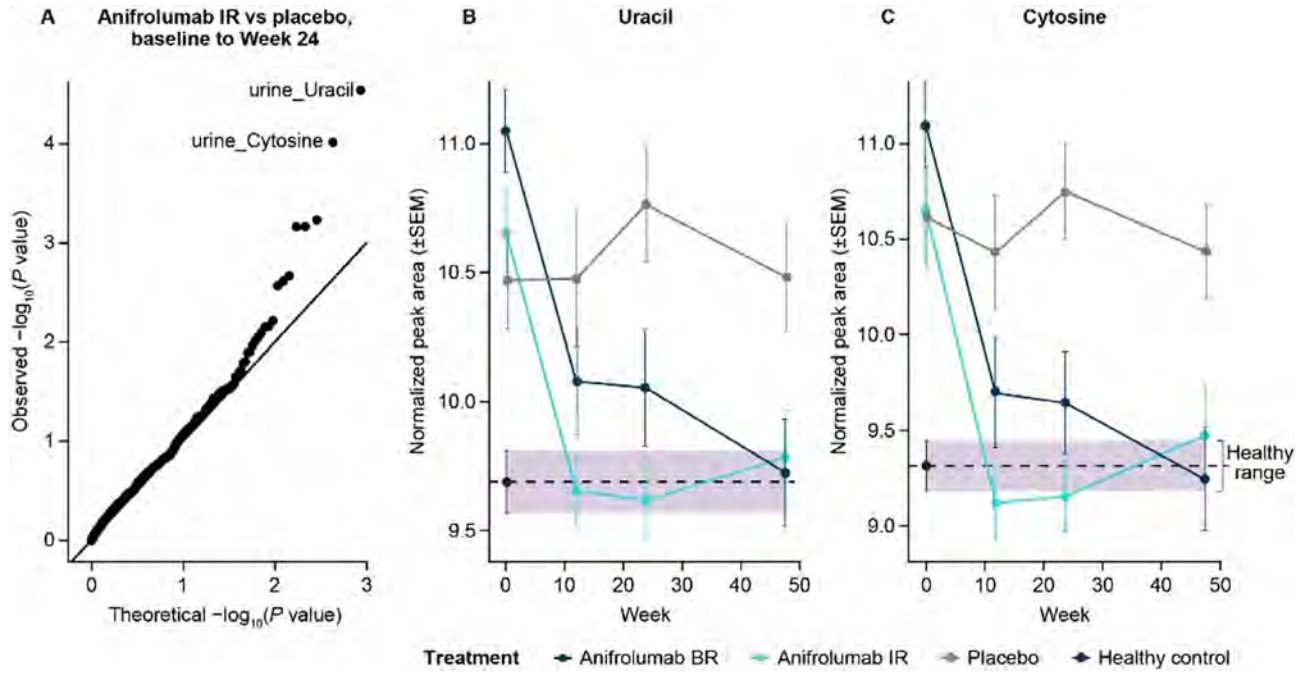

Figure: A. Untargeted urine metabolomics identified uracil and cytosine as the metabolites most impacted by anifrolumab treatment from BL to Week 24. B. Uracil and C. cytosine levels in urine were reduced by anifrolumab to within healthy ranges. BL, baseline; BR, basic regimen; IR, intensified regimen; SEM, standard error of the mean. For panel A, a linear mixed effects model evaluated the interaction of metabolite levels with treatment group and time.

Methods: The phase 2 TULIP-LN (NCT02547922) trial included adults with active LN (+ SLE per ACR 1997 criteria) who were randomized 1:1:1 to receive IV anifrolumab Q4W at standard SLE dosing (basic regimen [BR], 300 mg), intensified regimen (IR, 900 mg x3 doses, 300 mg thereafter), or placebo, in addition to standard therapy (including MMF and/or glucocorticoids). Metabolomics analysis (856 putatively identified metabolites) was conducted on patients with LN and healthy donors without renal involvement using an unbiased liquid chromatography–mass spectrometry-based approach in urine collected at baseline (BL) and Weeks 12, 24, and 48. Differentially modulated metabolites in the anifrolumab IR vs placebo groups were identified using a linear mixed effects model, adjusted for IFN gene signature (IFNGS, high/low) in blood and 24-hour urine protein–creatinine ratio (UPCR >3/≤3 mg/mg). Relationships between metabolite levels and serologic measures of disease activity (anti-dsDNA, complement C3), IFNGS, and UPCR were assessed with repeated measures correlation; nominal *P* values were adjusted for multiple comparisons (q).

Results: We analyzed urine metabolomics in 117 patients with LN (anifrolumab BR, n=36; IR, n=43; placebo, n=38) and 40 healthy donors. We identified 2 pyrimidine bases, uracil and cytosine, impacted by anifrolumab IR vs placebo from BL to Week 24 ($P< 0.05$; Figure A). Uracil and cytosine levels at BL were greater in patients with LN compared with healthy donors, and anifrolumab reduced their levels to within healthy ranges (Figures B, C). Within individual patients, uracil and cytosine levels correlated ($q< 0.05$) with IFNGS (R=0.59; R=0.65), anti-dsDNA levels (R=0.28; R=0.29), complement C3 levels (R=–0.19; R=–0.22), and UPCR (R=0.24; R=0.25).

Conclusion: Urine uracil and cytosine levels were elevated in patients with LN, consistent with studies showing upregulated pyrimidine metabolism in LN.[5] Uracil and cytosine levels were associated with IFNGS and measures of disease activity, indicating a previously unrecognized metabolomic link to type I IFN activity. Treatment with anifrolumab, in addition to standard therapy, normalized uracil and cytosine levels. Further studies are required to understand the role of uracil and cytosine in LN pathology, their association with type I IFN, and their potential as noninvasive biomarkers.

References:

1. Wang H, et al. *Arch Rheumatol*. 2017;33:17–25.
2. Qi S, et al. *Lupus*. 2018;27:1582–90.
3. AstraZeneca. Saphnelo prescribing information. 2021.
4. ClinicalTrials.gov. clinicaltrials.gov/ct2/show/NCT05138133.
5. Panousis N, et al. *Ann Rheum Dis*. 2019;78:1079–89.

Disclosure: D. Jayne: AstraZeneca, 2, Aurinia, 4, Boehringer Ingelheim, 2, Chinook, 2, CSL Vifor, 2, Roche, 2; **E. Mysler**: AbbVie, 1, 2, 6, Amgen, 6, AstraZeneca, 1, 5, 6, Bristol Myers Squibb, 5, GSK, 2, 5, Janssen, 1, 5, 6, Lilly, 5, 6, Novartis, 5, Pfizer, 1, 2, 6, Roche, 5, Sandoz, 6; **Z. Amoura**: Amgen, 5, AstraZeneca, 1, 5, 6, GSK, 1, 5, 6, Novartis, 1, 5, Roche, 5; **P. Gavin**: AstraZeneca, 3; **E. Allman**: AstraZeneca, 3, 10, 11; **C. Di Poto**: AstraZeneca, 3, 10, 11; **X. Tian**: AstraZeneca, 3; **S. Hess**: AstraZeneca, 3; **E. Csomor**: AstraZeneca, 3, GSK, 3; **P. Brohawn**: AstraZeneca, 3, 11; **D. Muthas**: AstraZeneca, 3, 11; **A. Platt**: AstraZeneca, 3, 11; **H. Al-Mossawi**: AstraZeneca, 3; **C. Lindholm**: AstraZeneca, 3; **N. Ferrari**: AstraZeneca, 3.

Abstract Number: 2337

Safety and Tolerability of NIM-1324, an Oral, Once-daily LANCL2 Agonist, in a Randomized, Double-Blind, Placebo-Controlled Phase 1 Study in Normal Healthy Volunteers

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus is a complex disease in which the immune system is dysfunctional at multiple levels including impaired regulatory responses, altered self-antigen processing and increased autoantibody production. LANCL2 is a novel therapeutic target that has been first targeted by a gut-restricted compound, omilancor, currently in clinical development for inflammatory bowel diseases. NIM-1324 functions through similar LANCL2-dependent immunometabolic mechanisms, increasing the suppressive capacity and stability of regulatory CD4+ T cells (Treg) while also supporting the metabolic demands of autophagy in phagocytes. The preclinical efficacy of NIM-1324 has been validated in NZB/W, MRL, and pristane-induced models of lupus and the preclinical safety has been demonstrated up to a NOAEL of 1,000 mg/kg/d.

Methods: Oral NIM-1324 was evaluated for safety and tolerability in normal healthy volunteers (n = 56) in a randomized, double-blind, placebo-controlled trial. Volunteers were randomized into five single ascending dose cohorts (250 – 1500 mg, p.o.) and three multiple ascending dose cohorts (250 – 1500 mg QD for seven days, p.o.). Safety and tolerability were assessed by adverse event (AE) reporting, vital signs, ECG, hematology, and clinical chemistry. Blood concentrations of NIM-1324 were measured. Whole blood gene expression and serum cytokines were analyzed as markers of target engagement.

Results: Single and seven-day dosing with NIM-1324 did not result in and SAEs or increases in total AE rates in individual dose cohorts and overall pooled active group relative to placebo. Oral NIM-1324 dosing did not result in any clinically significant findings by biochemistry, coagulation, ECG, hematology, or urinalysis. NIM-1324 was rapidly absorbed after oral dosing and did not accumulate over the seven-day dosing period. Plasma exposure of NIM-1324 was observed to scale in a dose-proportional manner within the range of 250 to 1000 mg/d. Using a whole blood transcriptomic signature developed during preclinical efficacy testing, NIM-1324 upregulated the mRNA expression of genes associated with mitochondrial metabolism and downregulated markers of phagocyte activation. The magnitude of effect in the 250 mg cohort was like those observed preclinically at maximally effective doses.

Conclusion: Oral treatment with NIM-1324 is well tolerated and safe in humans up to the tested limit dose of 1500 mg/d. Based on the observed safety, pharmacokinetics and target engagement profile, a first-in-patient clinical trial of NIM-1324 in systemic lupus erythematosus is currently planned.

Disclosure: A. Leber: None; **R. Hontecillas**: None; **N. Tubau Juni**: None; **J. Bassaganya-Riera**: Landos Biopharma, 3, 4, 8.

Abstract Number: 2338

Results of Single-Arm, Phase 1b Study of Anti-C1q Treatment (ANX009) Show That the Classical Pathway Is a Key Driver of Complement Activation and Consumption in Patients with Active Lupus Nephritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Treatment Poster III
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Background/Purpose: Lupus nephritis (LN) is an autoantibody-mediated disease involving glomerular deposition of immune complexes containing pathogenic anti-C1q antibodies, leading to C1q binding and activation of the classical complement pathway. ANX009 is a subcutaneously administered antigen-binding fragment of a humanized antibody that inhibits C1q interaction with immune complexes. Plasma measures of classical complement activation (C4d/C4 ratio) strongly correlate with disease activity in LN patients, suggesting that these patients may benefit from anti-C1q therapy.

Methods: LN-01 is an ongoing, single-arm, phase 1b study evaluating safety and tolerability of ANX009 in patients (N≤8) with class III or IV LN and a diagnosis of systemic lupus erythematosus according to EULAR/ACR 2019 criteria. Patients also exhibited high plasma C4d/C4 ratio and urine protein creatinine ratio >0.5 g/g at study enrollment. Patients undergo an 8-week screening period, a 3-week treatment period, and an 11-week off-treatment follow-up period. Primary and secondary endpoints are the percentage of patients with treatment-emergent adverse events (TEAEs) and change in complement biomarkers, respectively.

Results: To date, 4 patients completed treatment, one patient discontinued treatment, and screening is ongoing. Among 3/5 patients, 29 TEAEs occurred. All AEs were non-serious, except fever of unknown diagnosis in one patient. Injection site reactions arose in 3/5 patients—mild, mostly erythema. C4d/C4 ratio decreased with treatment in all 5 patients and returned to baseline after treatment cessation. Inhibition of C1q also resulted in normalization of downstream complement markers of activation and consumption for the entire pathway.

Conclusion: In this interim analysis, ANX009 administered subcutaneously was well tolerated and demonstrated C1q target engagement and complement inhibition in 5/5 patients. Normalization of all downstream activation markers and primary components, notably C3 and C5b-9, suggests the classical pathway, not the alternative pathway, is a key driver of complement activation in these LN patients. These interim results support further study of anti-C1q therapy in LN patients.

Disclosure: M. Dall'Era: Annexon Biosciences, 2, 5, AstraZeneca, 2, Aurinia, 2, Biogen, 2, GlaxoSmithKlein, 2, 5, Pfizer, 2; **J. Lichauco**: Annexon Biosciences, 5; **H. Chen**: Annexon Biosciences, 5; **H. Gomez**: Annexon Biosciences, 5, Johnson & Johnson, 5, Merck, 5; **M. Tee**: Annexon Biosciences, 5, AstraZeneca, 5, Biogen, 5, Celltrion, 6, Pfizer, 6, ZP Therapeutics, 6; **C. Arroyo**: Annexon Biosciences, 5; **J. Lan**: Annexon Biosciences, 5; **Y. Fang**: Annexon Biosciences, 5; **E. Chang**: Annexon Biosciences, 3, 8; **N. Yousefpour**: Annexon Biosciences, 3, 8; **J. Low**: Annexon Biosciences, 3, 8; **M. Bao**: Annexon Biosciences, 3, 8, Roche/Genentech, 3, 8; **Q. Chang**: Annexon Biosciences, 3, 8; **J. Osterloh**: Annexon Biosciences, 3, 8, FibroGen, Inc., 3; **A. Mongan**: Annexon Biosciences, 3, 8; **T. Yednock**: Annexon Biosciences, 3, 8; **D. Artis**: Annexon Biosciences, 3, 8; **Y. Andrews-Zwilling**: Annexon Biosciences, 3, 8; **H. Kroon**: Annexon Biosciences, 3, 8.

Abstract Number: 2339

Fragility of Randomized Clinical Trials of Systemic Lupus Erythematosus and Lupus Nephritis Therapies

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Randomized controlled trials (RCTs) in systemic lupus erythematosus (SLE) for novel therapeutics have frequently failed to meet criteria for regulatory approval. Even among drugs that were recently approved, trials been mixed in their conclusions or have had small effect sizes for outcomes that matter. The Fragility Index (FI) is a recently described method for assessing the robustness of RCTs findings, which calculates the minimum number of patients whose status would be required to change from an event to a non-event to make the study lose statistical significance ($p< 0.05$). We aimed to assess the robustness of pivotal phase 3 RCTs for SLE and LN treatments using the FI, the reverse FI (RFI), and the fragility quotient (FQ) scores to aid the interpretation of these RCTs.

Methods: To identify all RCTs, we searched on ClinicalTrials.gov for all phase 3, placebo-controlled RCTs, including patients with active SLE or LN. Trials were excluded if they were unpublished, phase 2 or 4 RCTs, or terminated due to reasons other than futility. Data on pre-specified primary endpoints, total participants, participants within each trial arm, and the number of events in the intervention and placebo groups were obtained from the full publications. FI score was calculated using an online calculator (available at https://clincalc.com/Stats/FragilityIndex.aspx), the RFI was calculated for RCTs with non-statistically significant results by modifying the number of events in the intervention arm until a p-value < 0.05 is reached while keeping the total number of participants constant. The FQ score was calculated by dividing the FI (or RFI) score by the total sample size of the trial. We used descriptive statistics to present the results.

Results: We evaluated 20 RCTs (16 in SLE, 4 in LN). The mean FI/RFI score of the 20 studies was 13.6±6.6. There were 9 studies with statistically significant results (7 in SLE, 2 in LN), and the mean FI score was 10.2±6.2. Twelve studies showed non-statistically significant results (9 in SLE, 2 in LN) with a mean RFI score of 15.6±6.1. The lowest FI was for the ILLUMINATE-2 trial (score: 2, Tabalumab), and the highest FI was found in the BLISS-52 trial (score: 17, Belimumab). The lowest RFI (non-significant trials) was for the ILLUMINATE-1 trial (score: 4, Tabalumab), and the highest RFI was for the TULIP-1 trial (score: 27, Anifrolumab). The RCT that granted FDA approval to anifrolumab was the TULIP-2 trial, with a FI score of 11. Voclosporin trial (AURORA-1) had an FI score of 15. Regarding the belimumab studies, BLISS-52 had an FI score of 17, BLISS-76 had an FI score of 4, BLISS-SC had an FI score of 16, and BLISS-LN had a FI score of 3. The lowest FQ scores were found in the ILLUMINATE trials and the highest in the Rituximab trials (LUNAR & EXPLORER) and the early terminated LOTUS trial.

Conclusion: The evidence supporting the recent approval of therapies for patients with SLE and LN is derived mostly from fragile RCTs, both among trials that met thresholds for statistical significance and among those that did not.

Table 1. Fragility evaluation of phase 3, randomized placebo-controlled trials involving patients with active systemic lupus erythematosus (SLE)

Study drug, trial	First author, year	Condition	Primary endpoints	Sample size	Events in intervention	Events in Placebo	FI or RFI score	FQ score
Anifrolumab								
TULIP 1*, NCT02446912	Furie RA et al., 2019	Adults with active SLE	SRI 4 response rate at week 52	Anifrolumab 300mg (n=180) Placebo (n=184)	65	74	27*	0.074
TULIP-2, NCT02446899	Morand EF et al., 2020	Adults with active SLE	BICLA response at week 52	Anifrolumab 300mg (n=180) Placebo (n=182)	86	57	11	0.030
Atacicept								
APRIL-SLE*, NCT00624338	Isenberg D et al., 2015	Active SLE	Proportion of patients experiencing flare BILAG A or B at week 52	Atacicept 75mg (n=159) Ataticept 150mg (n=145) Placebo (n=157)	92 54 (discontinued)	85	13*	0.041
Baricitinib								
SLE-BRAVE-I*, NCT03616912	Morand EF et al., 2023	Adults with active SLE	SRI-4 response at week 52	Baricitinib 2mg (n=255) Baricitinib 4mg (n=252) Placebo (n=253)	126 142	116	15* 4	0.030 0.008
SLE-BRAVE-II*, NCT03616964	Petri M et al., 2023	Adults with active SLE	SRI-4 response at week 52	Baricitinib 2mg (n=261) Baricitinib 4mg (n=258) Placebo (n=256)	120 121	116	22* 19*	0.043 0.037
Belimumab								
BLISS-52, NCT00424476	Navarra SV et al., 2011	Adults with active SLE	SRI-4 response at week 52	Belimumab 10mg/kg (n=290) Placebo (n=287)	167	125	17	0.029
BLISS-76, NCT00410384	Furie R et al., 2011	Adults with active SLE	SRI-4 response at week 52	Belimumab 10mg/kg (n=273) Placebo (n=275)	118	92	4	0.007
BLISS-SC, NCT01484496	Stohl et al., 2017	Adults with active SLE	SRI-4 response rate at week 52	Belimumab 200mg SC (n=556) Placebo (n=280)	341	136	16	0.019
BEL113750, NCT01345253	Zhang F et al., 2018	Adults with active SLE	SRI-4 response rate at week 52	Belimumab 10mg/kg (n=451) Placebo (n=226)	240	87	15	0.022
Blisibimod								
CHABLIS-SC1*, NCT01395745	Merrill JT et al., 2018	Adults with active SLE	SRI-6 response at week 52	Blisibimod (n=245) Placebo (n=197)	115	83	13*	0.029
Epratuzumab								
EMBODY1*, NCT01262365	Clowse MEB et al., 2017	Active SLE	BICLA response rate at week 48	Epratuzumab 600mg QW (n=248) Epratuzumab 1200mg Q2W (n=244) Placebo (n=249)	93 97	85	14* 9*	0.028 0.018
EMBODY2*, NCT01261793	Clowse MEB et al., 2017	Active SLE	BICLA response rate at week 48	Epratuzumab 600mg QW (n=264) Epratuzumab 1200mg Q2W (n=261) Placebo (n=263)	93 89	88	18* 21*	0.034 0.040
Rituximab								
EXPLORER*, NCT00137969	Merrill JT et al., 2010	Active SLE	Major clinical response at week 52	Rituximab (n=169) Placebo (n=88)	50	25	20*	0.078
Tabalumab								
ILLUMINATE-1*, NCT01196091	Isenberg DA et al., 2016	Active SLE	SRI-5 response at week 52	Tabalumab 120mg Q2W (n=381) Tabalumab 120mg Q4W (n=378) Placebo (n=379)	121 133	111	17* 4*	0.022 0.005
ILLUMINATE-2, NCT01205438	Merrill JT et al., 2016	Active SLE	SRI-5 response at week 52	Tabalumab 120mg Q2W (n=372) Tabalumab 120mg Q4W (n=376) Placebo (n=376)	143 131	104	15 2	0.020 0.002
Ustekinumab								
LOTUS*†, NCT03517722	van Vollenhoven RF et al., 2022	Active SLE	SRI-4 response at week 52	Ustekinumab (n=173) Placebo (n=116)	76	51	22*	0.076

BICLA: BILAG-based composite lupus assessment; BILAG: British Isles Lupus Assessment Group; FI: fragility index; FQ: fragility quotient; RFI: reverse FI; SLE: systemic lupus erythematosus; SRI: SLE responder index. *Trials with non-significant results. Results represents RFI scores. †Study terminated early due to futility.

Table 2. Fragility evaluation of phase 3, randomized placebo-controlled trials involving patients with active lupus nephritis (LN)

Study drug, trial	First author, year	Condition	Primary endpoints	Sample size	Events in intervention	Events in control	FI or RFI score	FQ score
Abatacept								
NCT00430677*	Furie RA et al., 2014	LN	Time to complete response. Complete response at week 52	Abatacept 30/10 (n=99) Abatacept 10/10 (n=99) Placebo (n=100)	9 11	8	9* 7*	0.045 0.035
Belimumab								
BLISS-LN, NCT01639339	Furie R et al., 2020	Adults with active LN	Primary efficacy renal response at week 104	Belimumab 10mg/kg (n=223) Placebo (n=223)	96	72	3	0.007
Rituximab								
LUNAR*, NCT00282347	Rovin BH et al., 2012	Active LN	Renal response rate at week 52	Rituximab (n=72) Placebo (n=72)	19	22	16*	0.111
Voclosporin								
AURORA-1, NCT03021499	Rovin BH et al., 2021	Adults with active LN	Complete renal response at week 52	Voclosporin (n=179) Placebo (n=178)	73	40	15	0.042

FI: fragility index; FQ: fragility quotient; RFI: reverse FI; LN: lupus nephritis. *Trials with non-significant results, Results represents RFI scores.

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Abstract Number: 2340

Multi-targeted Therapy Better in Achieving Complete Response in Lupus Nephritis: A Systematic Review and Meta-analysis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Treatment Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The overall management of SLE and Lupus Nephritis (LN) has significantly improved over the last four decades.Recently great therapeutic strides have been made in management of LN using newer agents alone or combination of older therapies. With the availability of increased number of options choosing the optimal treatment regimen for LN has become challenging. Identifying the treatment regimen most effective in achieving complete response while minimizing adverse events is crucial for improving patient outcomes.We performed a systematic review and meta-analysis of clinical trials to explore optimal treatment regimen for LN.

Methods: The systematic review and meta-analysis were performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The literature search was conducted using public databases, such as the Cochrane Library, Web of Science and PubMed. Only randomized controlled clinical trials with either active comparator or placebo arms were included. Studies were excluded if they were retrospective, with no comparative drug arm, or less than 20 subjects per treatment response arm. Due to lack of agreed upon outcome measures, complete response (CR) and partial response (PR) criteria were determined as per the definition used by individual studies. Severe adverse

reaction (SAE) frequencies were determined for each study for safety evaluation. Data from each study were evaluated for consistency. Publication bias was detected by using funnel plots. Forest plots were used to summarize data, generate frequencies, odds ratio (OR), relative risks (RR) and corresponding 95% confidence intervals (CI) for each subgroup. Heterogeneity was evaluated using the I^2statistic, and labelled as low (25%), moderate (50%) and high (75%). All analyses were performed using R Statistical Software meta package (v4.2.1; R Core Team 2022).

Results: 31 eligible studies comprising 5495 SLE patients were included in analyses, the study characteristic features are shown in Table 1. Overall significant OR for achieving CR was reported by 10 studies (Figure 1). The highest effect was reported from study by Bao et.al using a combination of tacrolimus(TAC) and mycophenolate mofetil (MMF) compared to cyclophosphamide (CYC) (OR=10.5, 95% CI 2.27; 48.76), another study using TAC+MMF combo reported OR=2.49, 95% CI 1.59;3.88. The study by Ginzler et.al reported OR= 5.06 (95% CI 1.6:16.02) in favor of using MMF. Studies using

Table 1. Main features of eligible clinical trials.

Study/year	Drug arms	Study design	Duration	Primary outcome
Furie 2022	OBI vs. Placebo	RCT-DB	104 weeks	Confirmed complete response
Zheng 2022	TAC vs. CYC	RCT-Open	24 weeks	Complete renal response
Ye 2022	TAC+MMF vs. CYC	RCT	72 weeks	Renal remission
Jayne 2021	ANIF vs. Placebo	RCT - DB	52 weeks	change in baseline 24-hour UPCR
Atisha-Fregoso 2021	RTX+BEL+CYC vs. RTX+CYC	RCT-Open	96 weeks	Safety (Phase II), Complete remission
Rovin 2021	VOC vs. Placebo	RCT-DB	52 weeks	Complete renal response
Furie 2020	BEL vs Placebo	RCT-DB	104 weeks	Primary efficacy renal response
Zhang 2020	MMF+TAC vs. MMF+CYC	RCT	6 months	Cystatin C, TGF-B levels
Rovin (low dose) 2019	VOC-low vs. Placebo	RCT-DB	48 weeks	Complete renal response
Rovin (high dose) 2019	VOC-High vs. Placebo	RCT-DB	48 weeks	Complete renal response
An 2019	CYC+MMF/AZA/LEF vs. CYC	RCT-Open	24 week	Complete remission
Sedhain 2018	MMF vs. CYC	RCT-Open	6 months	Treatment response
Mehra 2018	CYC-Low vs. CYC-High	RCT-Open	52 weeks	Complete renal response
Kamanamool 2018	TAC vs. MMF	RCT- Open	12 months	SLEDAI-2K
Rathi 2016	MMF vs. CYC-Low	RCT	24 weeks	Treatment response
Liu 2015	TAC+MMF vs. CYC	RCT- Open	24 week	Complete remission
Furie 2014	ABA 10/10 vs. Placebo	RCT-DB	12 months	Time to confirmed complete response
Furie 2014	ABA 30/10 vs. Placebo	RCT-DB	12 months	Time to confirmed complete response
Access 2014	ABA+CYC vs. EuroLN	RCT-DB	52 week	Complete response
Mok 2014	MMF vs. TAC	RCT-Open	6 months	Complete renal response
Mysler (Low) 2013	OCR-Low vs. Placebo	RCT-DB	48 week	Complete renal response
Mysler (High) 2013	OCR-High vs. Placebo	RCT-DB	48 week	Complete renal response
Rovin 2012	RTX vs. Placebo	RCT- DB	52/78 weeks	Complete renal response
Dooley 2011	MMF vs. AZA	RCT-DB	36-month	Time to treatment failure
Chen 2011	TAC vs. CYC	RCT-Open	6-month	Complete remission
Merrill 2010	RTX vs. Placebo	RCT- DV	52 weeks	Major clinical response
Appel 2009	MMF vs. CYC	RCT-Open	24 week	Change in UPCR and creatinine
Bao 2008	TAC+MMF vs. CYC	RCT-Open	9 months	Complete remission
Ginzler 2005	MMF vs. CYC	RCT-Open	24 week	Complete remission
Chan 2000	MMF vs. AZA	RCT	12 months	Complete remission
Austin 1986	CYC/AZA vs. PRD	RCT-Open	Not specified	Stable renal function

OBI: obinutuzumab, TAC: tacrolimus, CYC: cyclophosphamide, MMF: Mycophenolate, ANIF: anifrolumab, VOC: voclosporine, BEL: belimumab, AZA: azathioprine, LEF: leflunomide, ABA: abatacept, OCR: ocrelizumab, RTX: rituximab, PRD, prednisone

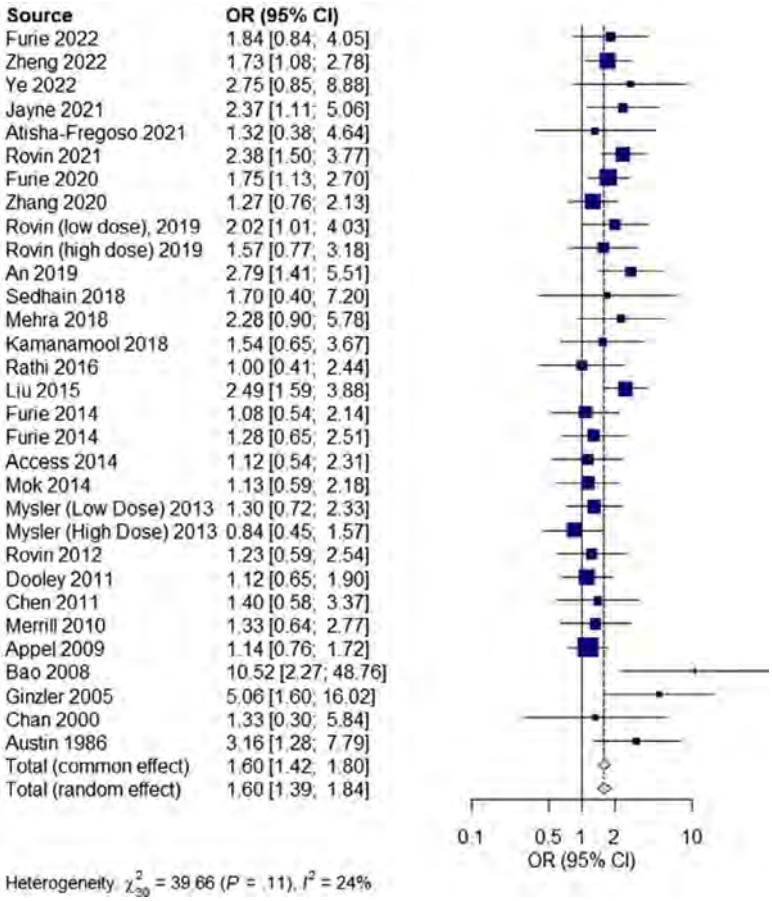

Figure 1. Odd ratios for complete remission in lupus nephritis studies.

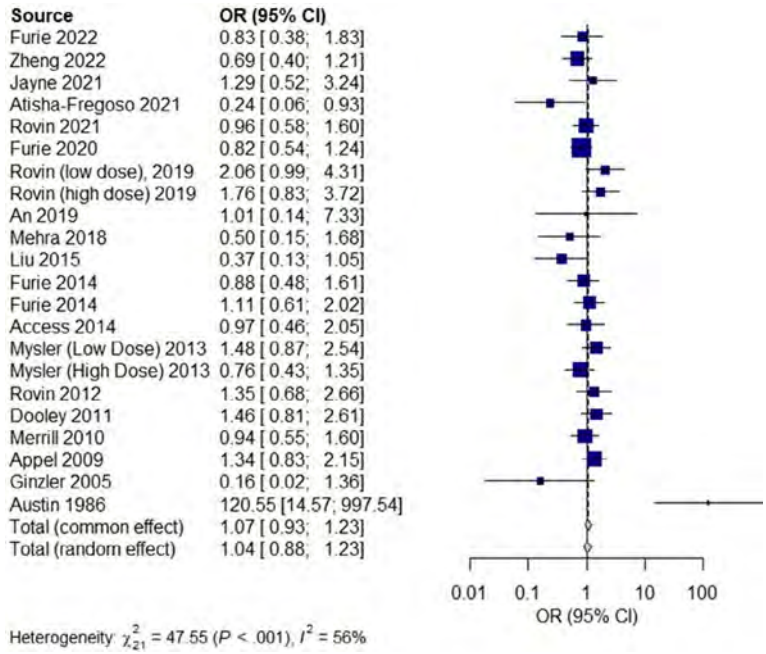

Figure 2. Odd ratios for severe adverse events in lupus nephritis trials.

CYC, voclosporin + MMF, and belimumab also reported significant OR for achieving CR. Data for the frequency of SAE were available in 22 studies. The frequency of SAE was not significantly different between treatments arms (OR: 1.07, 95%CI: 0.93-1.23, p >0.05)

Conclusion: Our meta-analysis suggests multi-target treatment strategies, by adding calcineurin inhibitors to MMF may be better for achieving complete response in LN. Furthermore, using this combination treatment did not seem to increase the risk of side effects. Heterogenous treatment response criteria and variable comparator arms were major limiting factors of this study.

Disclosure: O. Pamuk: None; **B. Shaikh**: None; **S. Khan**: None; **A. Abbas**: None; **S. Abi Doumeth**: None; **s. Hasni**: AstraZeneca, 5.

Abstract Number: 2341

Spanish National Registry of Belimumab in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: SLE – Treatment Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Belimumab (BLM) is a monoclonal antibody that inhibits B-lymphocyte stimulating factor (BlyS), approved in 2011 as a treatment for systemic lupus erythematosus (SLE). We present the experience with BLM in this spanish cohort.

Methods: Descriptive, retrospective, multicenter study in patients diagnosed with SLE according to EULAR/ACR 2019, SLICC and/or ACR 1997 diagnostic criteria. Data regarding SLE patients treated with BLM were collected from medical records (2011-2023). Demographic features, analytical variables, SLEDAI, renal involvement, steroid dose, administration routes, efficacy, remission and safety were assessed.

Results: Five hundred and twenty one patients were included with a mean age at diagnosis of 35.1 (13.9) years. 85.8% were women. The mean age at BLM begins was 44.5 (13.3) years and the median time from SLE diagnosis to BLM begin was 6.5 (2.4-14.3) years. Regarding administration route 50.2% were on intravenous (IV), 34.6 % on subcutaneous (SC) and 15.2% change from IV to SC route. The mean time of follow-up was 24.0 (21.4) months.

Baseline characteristics are summarized in Table 1 and patients in remission are shown in figure 1.

The median number of pre-BLM cDMARD use was 2.0 (2.0-3.0), being hydroxychloroquine (HCQ) the most used (94.2%). 93 patients received bDMARD before BLM begins, being Rituximab (RTX) the most used (79.6%), and 59 patients were treated with IV cyclophosphamide (CFM) with a median of 6 (4.5-8) IV bolus received. 75.6% and 21.5% of patients were on treatment with HCQ and methotrexate when BLM was started respectively.

Table 1: Baseline characteristics of patients included in Belimumab Spanish registry.

Table 1: Baseline characteristics of patients included in Belimumab Spanish registry.

Age at SLE diagnosis (years)*	35.1 (13.9)
Age at BLM starts (years)*	44.5 (13.3)
Gender (female) n, (%)	447 (85.8)
Time from diagnosis until BLM start (years)**	6.5 (2.4-14.3)
ANA title**	1/640 (1/320-1/1280)
ANA positive, n (%)	466 (89.4)
DNA positive, n (%)	408 (82.1)
Antiphospholipidic syndrome, n (%)	52 (10.8)
Antiphospholipidic antibodies, n (%)	141 (27.1)
("aB2GPI-", "ACL-", "AL+")	38 (8.4)
("aB2GPI+", "ACL+", "AL-")	16 (3.5)
("aB2GPI+", "ACL+", "AL+")	42 (9.3)
("aB2GPI-", "ACL+", "AL-")	25 (5.5)
("aB2GPI-", "ACL+", "AL+")	7 (1.6)
("aB2GPI+", "ACL-", "AL-")	8 (1.8)
("aB2GPI+", "ACL-", "AL+")	5 (1.1)
Renal involvement, n (%)	137 (28.2)
Articular involvement, n (%)	412 (82.9)
Hematologic involvement, n (%)	251 (52.8)
Skin involvement, n (%)	261 (54.4)
Cyclophosphamide, n (%)	59 (11.3)
bDMARD, n (%)	93 (17.9)
- Rituximab	79 (84.9)
cDMARD pre BLM, n (%)	521 (100)
- Hydroxychloroquine	491 (94.2)
- Methotrexate	280 (53.7)
- Azathioprine	182 (34.9)
- Mycophenolate mofetil/mycophenolic acid	153 (29.4)
- Leflunomide	59 (11.3)

* Mean (SD)
** Median (IQR)

The main reasons of starting BLM were musculoskeletal and mucocutaneous disorders (table1).

503 patients were on prednisone at the time of BLM begin with a median dose of 7.5 (5-10) mg. A statistically significant decrease in prednisone dose, SLEDAI and DNA was observed from baseline until the last follow up. In the other hand complement C3 and C4 raised (figure2).

One hundred and thirty seven patients (28.2%) had renal involvement. The median 24 hours proteinuria was 1.0 (0.5-2.4) grams and renal biopsy was done in 114 out of 137 patients, being class IV (42%), III (18.8%), II (12.5%) and V (10.7%) the most reported. 72.2% improve after BLM begins with last 24 hour proteinuria median of 0.2 (0.1-0.8) grams. Prior to BLM, most of them had been treated with MMF, RTX or CFM.

One hundred and and fitty one patients (29%) discontinued treatment mostly due to inefficacy (57.1%) and infections (12.2%). 133 patients developed infections, most of them mild, being urinary infection the most reported. 3 patients died, 8 had COVID and 3 presented neoplasms requiring discontinuation of the drug. The median time on treatment of patients that had to stop BLM was 12.0 (6-24) months.

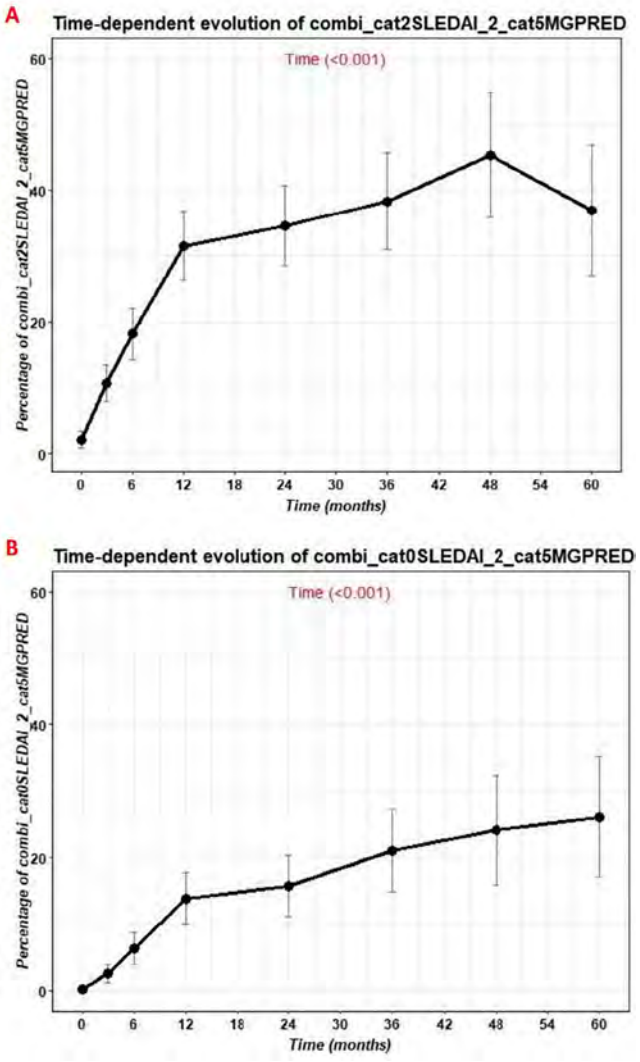

Figure 1: Remission define as SLEDAI ≤ 2 and ≤ 5 mg of prednisone (A) or SLEDAI ≤ 0 and ≤ 5 mg of prednisone (B).

Conclusion: Almost half of patients achieved remission after 4 years of BLM and a statistically significant improvement in prednisone dose reduction, SLEDAI, complement and antiDNA was demonstrated. Corticosteroids sparing effect with BLM was also observed.

BLM seems to be a good choice for patients with lupus nephritis since nearly three quarters of them normalized proteinuria values. No new safety alarms were reported.

This is the largest cohort of SLE patients treated with BLM reported in one country.

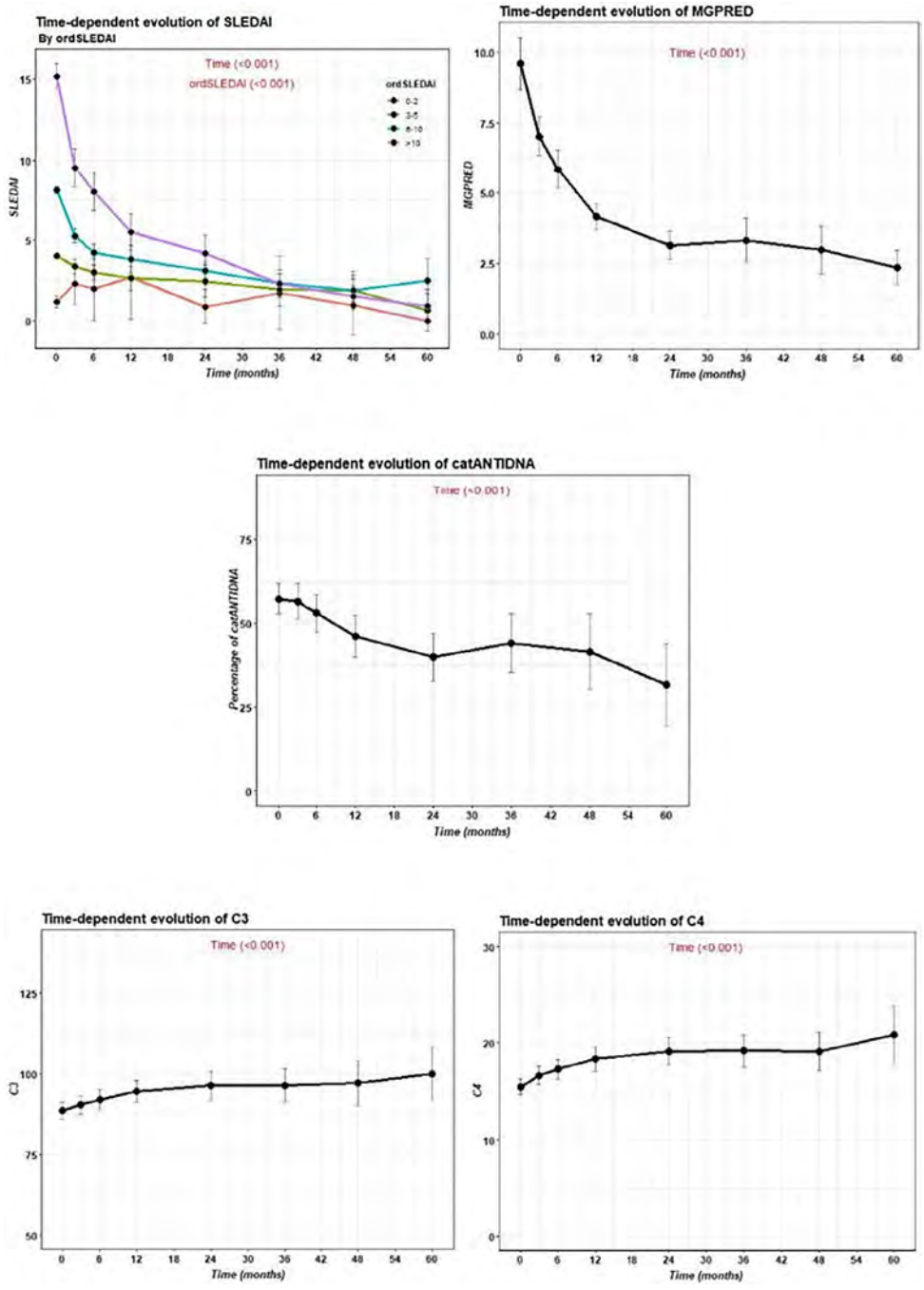

Figure 2: Time dependant evolution of SLEDAI, prednisone, antiDNA and complement C3 and C4.

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Abstract Number: 2342

Modulation of B Cell and Interferon Pathways by Ianalumab in Patients with Systemic Lupus Erythematosus: Findings from a Phase 2 Clinical Trial

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Ianalumab (VAY736) is an afucosylated monoclonal antibody targeting the B cell activating factor receptor (BAFFR) that depletes B cells via enhanced antibody dependent cellular cytotoxicity with concurrent blockade of BAFF:BAFFR mediated survival signals. BAFF is commonly overexpressed in systemic lupus erythematosus (SLE) and strongly linked to autoimmune pathogenesis. Here we assessed changes within the transcriptomic and proteomic landscape of SLE patients pre- and post-treatment with ianalumab to characterize pharmacodynamic (PD) biomarkers and biological pathways linked to the disease activity and clinical response.

Methods: A phase 2 clinical trial (NCT03656562) evaluated the PD and preliminary clinical efficacy of ianalumab in patients with moderate to severe SLE; a multicenter randomized, parallel group, double blind, placebo controlled trial with patients on monthly s.c. injection of ianalumab 300 mg or placebo. Blood samples were collected at baseline and week (W) 28 post treatment from placebo (n=28) and ianalumab treated patients (n=25). Blood samples from 40 healthy volunteers were included for baseline transcriptomics analysis. Targeted cellular analysis was done by flow cytometry, serum protein profiles were generated using the SomaScan v4.1 assay and transcriptome analysis was done with total RNA obtained from whole blood using an Illumina Stranded kit. Treatment and placebo groups were compared over time using multivariate linear regression models to identify cellular markers, proteins and genes that were differentially modulated by ianalumab.

Results: The analysis of changes to cellular subsets upon ianalumab treatment demonstrated a strong and statistically significant reduction in total B cells which was confirmed by changes in transitional, naïve and memory B cells as well as plasmablasts/plasma cells without reductions in $CD4^+$ and $CD8^+$ T cells or NK cells **(Fig 1).** Assessment of SLE molecular drivers through blood transcriptomics versus healthy volunteers confirmed a disease signature driven by type 1 interferon (IFN) and innate immunity pathways, correlating with immunoglobulin genes. Upon ianalumab treatment, a strong reduction in B cell

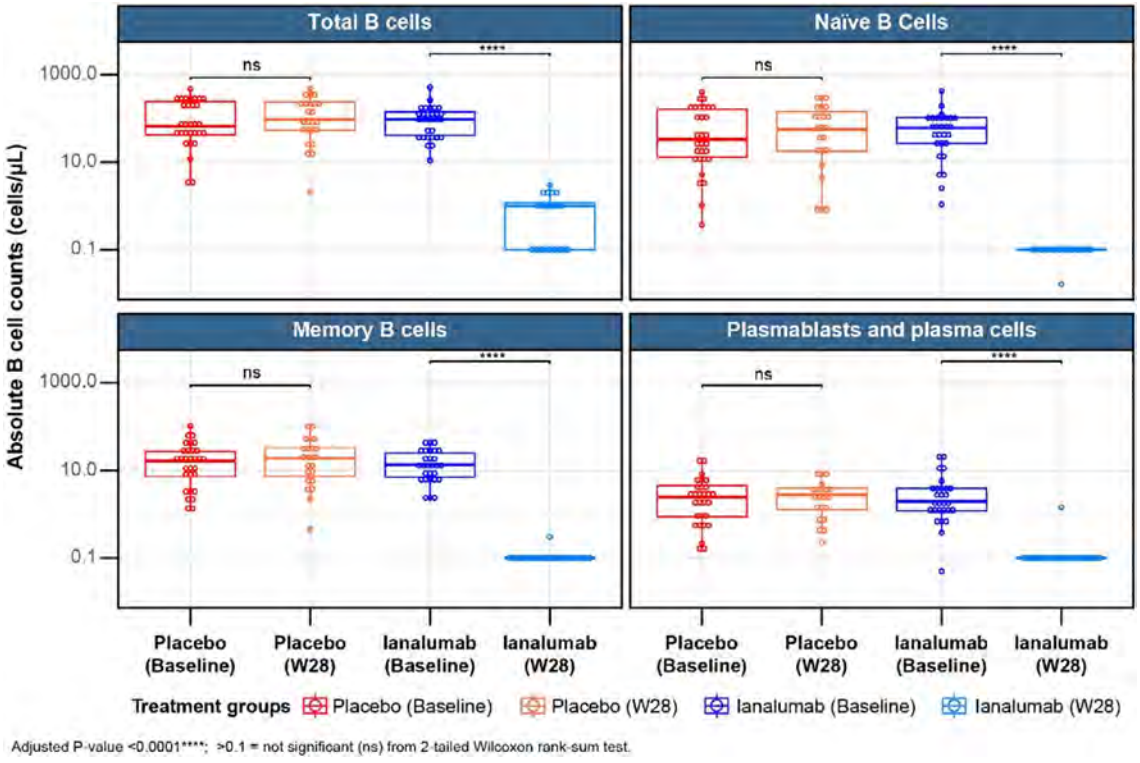

Fig 1. Depletion of B cell subsets (CD27+ memory cells and CD27high CD38high plasmablasts/plasma cells) upon ianalumab treatment measured by flow cytometry

related genes was seen at W28, accompanied by a significant decrease in IL-6 transcript and a modulation of the interferon gene signature (IFNGS) **(Fig 2)**. Broad serum protein profiling confirmed transcriptomics findings, showing reduction of multiple B cell markers on ianalumab treatment. Importantly, we observed that SRI-4 response to ianalumab was comparable in both baseline IFNGS-high and IFNGS-low patients, with a concomitant SLEDAI reduction.

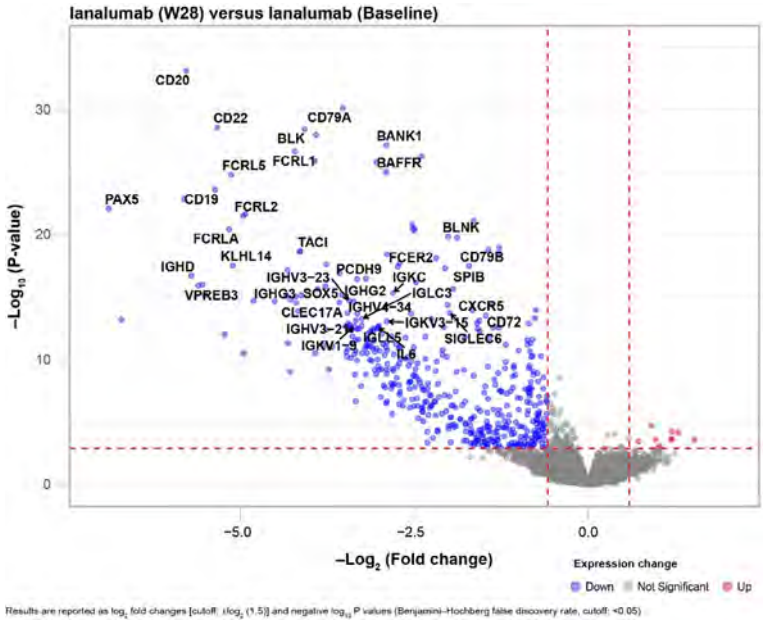

Fig 2. Volcano plot showing differentially expressed genes across time with ianalumab at W28 versus baseline

Conclusion: Ianalumab treatment of patients with SLE led to strong B cell depletion, including autoantibody-producing subsets, confirmed by transcriptomics and proteomics assessments. Initial evidence suggests that reductions in B cell numbers and autoantibodies levels observed clinically was accompanied by a decrease in IFNGS and clinical response to ianalumab was independent of baseline IFNGS status. Further molecular studies are ongoing to characterize the effects of ianalumab on these patients.

Disclosure: A. Santos da Costa: MiNK Therapeutics, 11, Novartis, 3, 11; **T. Dörner**: Eli Lilly, 1, 2, Janssen, 1, 2, Novartis, 1, 2, Roche, 1, 2, UCB, 1, 2; **A. Grioni**: Novartis, 3, 11; **A. Avrameas**: Novartis, 3, 11; **U. Sommer**: Novartis, 3; **R. Hillenbrand**: Novartis, 3, 11; **V. De Luca**: Novartis, 3, 11; **E. Ferrero**: Novartis, 3, 11; **A. Nogueira da Costa**: Novartis, 3, 11; **I. Isnardi**: Novartis, 3, 11; **S. J Oliver**: Novartis, 3, 11.

Abstract Number: 2343

Hydroxychloroquine Discontinuation in the Real World: Reasons, Predictive Factors and Clinical Implications

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: SLE – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by multisystemic involvement and difficult-to-predict disease flares. Hydroxychloroquine (HCQ) has long been recognized as a cornerstone of SLE management. However, the impact of discontinuing HCQ on disease activity and flare rates in SLE patients remains a subject of ongoing investigations. We aim to assess factors associated with flares in patients that discontinue HCQ.

Methods: This retrospective cohort study included SLE patients who met the 1997 ACR criteria for SLE. The study period was from 2012 to 2023. Patients were identified from our cohort and were required to have at least one year of follow-up before and after discontinuing HCQ. Thus, the time limit for discontinuation of HCQ was March 2022. Inclusion criteria stipulated consistent HCQ intake without erratic prescription patterns. HCQ discontinuation reason was documented. Patient data were collected on the electronic medical records through chart review. Local IRB approval was granted for it. We evaluated clinical and laboratory parameters historically (profile) and at the index visit, defined as within 3 months of HCQ discontinuation. Flares were evaluated 12 months before and after HCQ discontinuation according to the SLEDAI flare index. Statistical analysis was performed with STATA, group comparison by using t-test for continuous and a chi-square test for categorical variables.

Results: 42 patients were identified that met the established criteria. Ninety-five percent of patients were females. Blacks constituted 33% of the cohort and Hispanics 44%. The mean age at the index visit was 50 years old and were diagnosed, on average, 15 years before the index visit. Common clinical manifestations included mucocutaneous (69%), musculoskeletal (69%), and hematologic (69%). Class III/IV lupus nephritis was present in 21% and Class V in 17% of patients. The immunologic profile included dsDNA Ab positivity (76%), low C3 (67%), RNP antibody (38%), SSA Ab (36%), anticardiolipin Ab (33%), and Smith Ab (31%). ACR/EULAR 2019 classification criteria mean score was 24.4. 19%of patients had flared the

Table 1- Table 1- Clinical and serological profile of the SLE patients. Abbreviations: Ab: antibody, HCQ: hydroxychloroquine, LFT: liver function tests, RNP: ribonucleoprotein , dsDNA: double standed DNA,

year before HCQ discontinuation. The main reasons for discontinuation was retinal toxicity due to HCQ (57%), self-discontinuation (17%), and either other retinopathies or inability to perform eye exams (12%). At the index visit, mean C3 was 108 mg/dL and C4 20 mg/dL, and dsDNA Ab positivity in 38% (Table 1). 11/42 (26.1%) of patients flared the year after HCQ discontinuation, compared to 19% of flares the year before (p-value 0.433). Out of several parameters evaluated for association with flares, the strongest associations were: mean C3 at the index visit (79.4 mg/dL in flares versus 117.7 no flares, p-value < 0.001) and dsDNA positivity at index visit (83% flares versus 26% no flares, p-value 0.018). Other associations tested are available in Table 2.

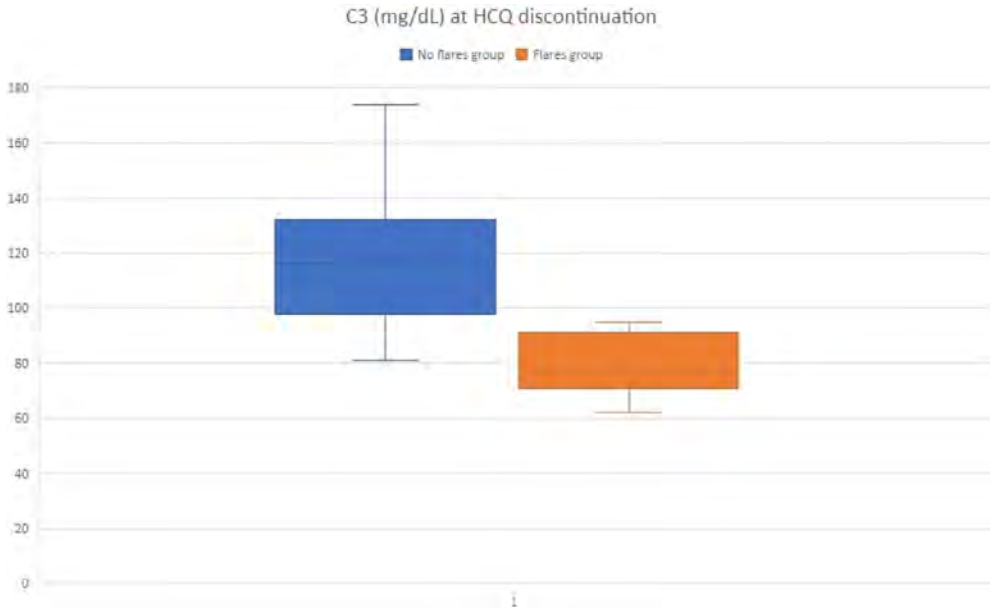
Conclusion: In a cohort of 42 SLE patients that had high ACR/EULAR 2019 classification scores (>20), older age, and prolonged disease duration, flares within 1 year of HCQ discontinuation did not have a higher incidence than the year before HCQ discontinuation but were associated with lower C3 levels and positive dsDNA antibody.

Table 2- Comparison of HCQ discontinuation flares vs no flares groups

Table 2- Comparison of HCQ discontinuation flares vs no flares groups

Factor	No flares after HCQ d/c	Flares after HCQ d/c	P-value
N	31	11	
Race			0.35
White	15 (48%)	3 (27%)	
Black	8 (26%)	6 (55%)	
Asian	5 (16%)	1 (9%)	
Other	3 (10%)	1 (9%)	
Ethnicity			1
Hispanic	3 (38%)	1 (100%)	
Chinese	2 (25%)	0 (0%)	
Indian	1 (12%)	0 (0%)	
Capeverdean	1 (12%)	0 (0%)	
Haitian	1 (12%)	0 (0%)	
Sex (Female)	29 (94%)	11 (100%)	1
Menopause (yes)	10 (32%)	3 (27%)	1
Family History of SLE (yes)	5 (16%)	3 (27%)	0.41
Ever smoker	5 (16%)	1 (9%)	1
Clinical Profile (Historical)			
Class III/IV LN	7 (23%)	2 (18%)	1
Class V LN	4 (13%)	3 (27%)	0.35
Leukopenia	18 (58%)	9 (82%)	0.27
Thrombocytopenia	7 (23%)	5 (45%)	0.24
Smith Ab	8 (26%)	5 (45%)	0.27
RNP Ab	10 (32%)	6 (55%)	0.28
SSA	10 (32%)	5 (45%)	0.48
SSB	5 (16%)	1 (9%)	1
dsDNA Ab	21 (68%)	11 (100%)	0.041
Low C3	15 (58%)	10 (91%)	0.067
Low C4	10 (32%)	5 (45%)	0.48
Lupus Anticoagulant	7 (23%)	2 (18%)	1
Anticardiolipin Ab	10 (32%)	4 (36%)	1
B2 Glycoprotein 1 Ab	5 (16%)	4 (36%)	0.21
EULAR total, mean (SD)	22.8 (12.5)	28.8 (6.3)	0.14
Constitutional	7 (23%)	3 (27%)	1
Hematologic	20 (65%)	9 (82%)	0.45
Neuropsychiatric	3 (10%)	0 (0%)	0.55
Mucocutaneous	19 (61%)	10 (91%)	0.13
Serositis	9 (29%)	2 (18%)	0.7
Musculoskeletal	21 (68%)	8 (73%)	1
Renal	13 (42%)	7 (64%)	0.3
Antiphospholipid Ab domain	16 (52%)	6 (55%)	1
Low Complements domain	18 (58%)	10 (91%)	0.067
Specific Ab domain	22 (71%)	11 (100%)	0.083
Index visit data			
Disease duration in years at index visit, mean (SD)	15.9 (9.2)	15.18 (10.5)	0.82
C3, mean (SD)	117.7 (24.5)	79.4 (12.3)	<0.001
C4, mean (SD)	22.0 (9.9)	14.2 (10.3)	0.08
Index visit dsDNA positivity	6 (26%)	5 (83%)	0.018

Abbreviations: Ab: antibody, HCQ: hydroxychloroquine, RNP: ribonucleoprotein , dsDNA: double standed DNA,



C3 levels and SLE flares after HCQ discontinuation

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Abstract Number: 2344

Telitacicept versus Belimumab for Patients with Active Systemic Lupus Erythematosus: A Retrospective, Multicenter, Real-world Observational Study

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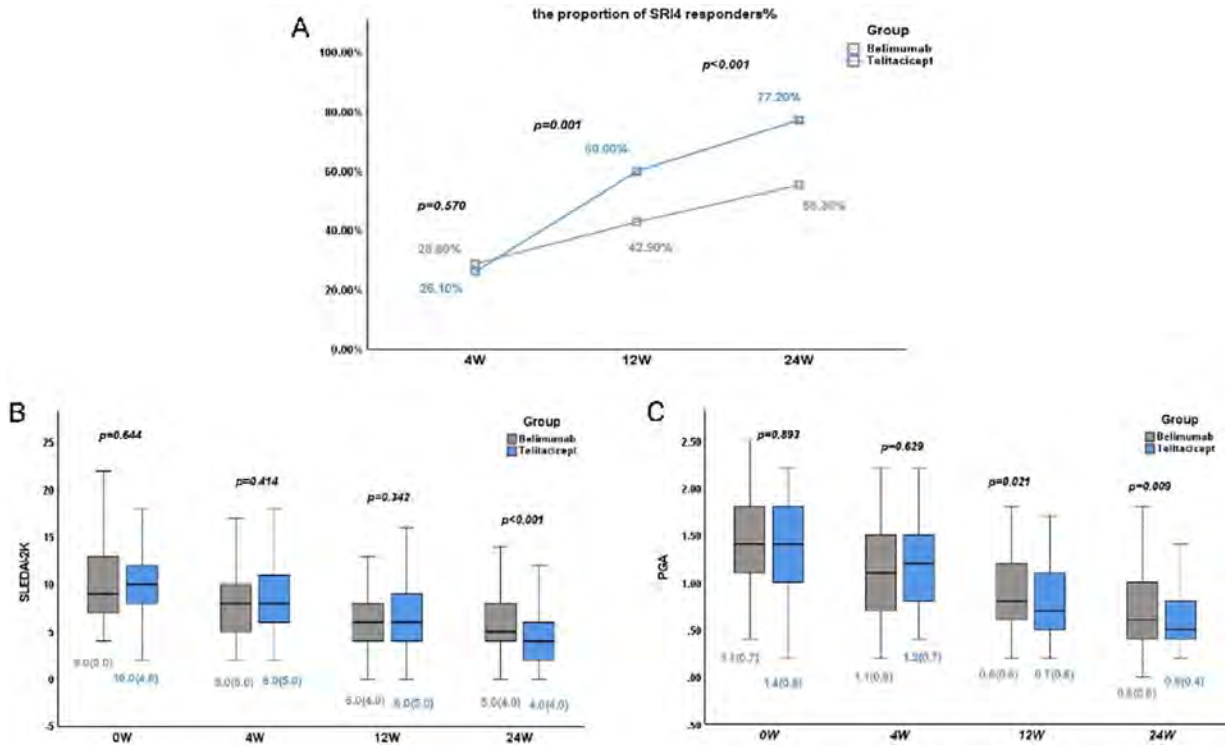
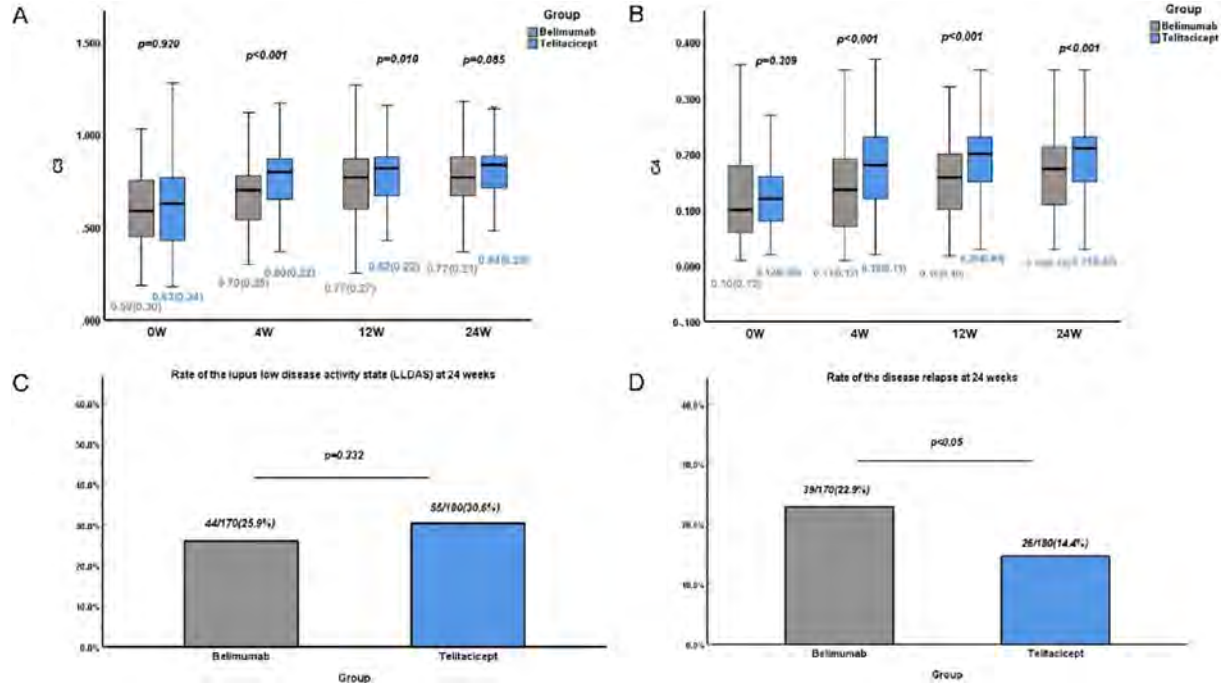
SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: SLE – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The past decade has witnessed the innovation of several biologics in the treatment of systemic lupus erythematosus (SLE), most of which target B cells, including B-cell activating factor/a proliferation-inducing ligand (BAFF/APRIL) inhibitors. Telitacicept is a TACI–immunoglobulin fusion protein that neutralizes the activity of BAFF and APRIL by competitively inhibiting the TACI site, thereby suppressing the development and survival of plasma cells and mature B cells. The aim of this study was to compare the efficacy and safety of two differentBAFF/APRIL inhibitors, telitacicept and belimumab, in treating patients with active SLE in real world clinical practice.



A-C Primary outcome in disease activity over a 24-week period following the introduction of BAFF/APRIL inhibitors after IPTW. (A) Comparison of changes in the proportion of SRI-4 responders after the treatment from 0 to 24 weeks between the belimumab and telitacicept groups. Comparison of changes in (B) Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score and (C) Physician Global Assessment (PGA) score after the treatment from 0 to 24 weeks with median (IQR).



A-D Complement changes and other outcomes in disease activity over a 24-week period following the introduction of BAFF/APRIL inhibitors after IPTW. Comparison of changes in (A) C3 and (B) C4 between the belimumab and telitacicept groups after the treatment from 0 to 24 weeks with median (IQR). Comparison of the rate of (C) Lupus Low Disease Activity State (LLDAS) and (D) relapse between the two groups at 24 weeks.

Methods: Patients with active SLE who received telitacicept (n=72) or belimumab (n=103) from 2019 to 2022 at multiple centers in China were retrospectively reviewed, and the efficacy of telitacicept and belimumab was compared. Patients with renal and hematologic abnormalities were separately selected to confirm the treatment efficacy in these systems. Propensity score-based inverse probability of treatment weighting (IPTW) was used to reduce selection bias. Multivariable logistic regression analysis was used to identify the factors contributing to limited response.

Results: No significant between-group differences in patient characteristics were observed after adjustment by IPTW. The proportion of SLE Responder Index 4 responders at 12 and 24 weeks was significantly higher in the telitacicept group ($p < 0.05$). Consistently, patients who received telitacicept had a significantly greater decrease in the SLEDAI-2K score and Physician Global Assessment score at 24 weeks ($p < 0.05$). No significant between-group difference in kidney efficacy was observed, but telitacicept produced greater improvement in patients with anemia, leukopenia, and thrombocytopenia at 24 weeks. Importantly, the telitacicept group had a lower incidence of adverse events, especially upper respiratory tract infections, than the belimumab group after the start of therapy ($p < 0.05$).

Conclusion: Telitacicept showed better efficacy and safety than belimumab for patients with active SLE in multiple clinical centers. Further investigations in larger cohorts and head-to-head clinical trials are required to verify these findings.

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Abstract Number: 2345

Paired Kidney Biopsies from the AURORA 2 Study of Voclosporin in Active Lupus Nephritis

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SESSION INFORMATION
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Background/Purpose: Voclosporin is approved for the treatment of adults with active lupus nephritis. Addition of voclosporin to mycophenolate mofetil (MMF) and low-dose glucocorticoids in the Phase 3 global AURORA 1 and AURORA 2 studies led to significantly earlier and greater reductions in proteinuria and an improved estimated glomerular filtration rate (eGFR) slope over time.To characterize the long-term renal impact of voclosporin at the histologic level, we analyzed paired kidney biopsies from a subset of patients in these studies.

Methods: Patients in AURORA 1 had biopsy-proven lupus nephritis, urine protein creatinine ratio (UPCR) ≥1.5 g/g (≥2 g/g for Class V), and estimated glomerular filtration rate (eGFR) >45 mL/min/1.73 m^2. Patients were randomized to voclosporin or control for 1 year in AURORA 1 and continued the same blinded therapy for 2 additional years in AURORA 2; all patients received MMF and low-dose glucocorticoids. A subset of patients had a kidney biopsy prior to screening and a repeat biopsy after approximately 18-months of therapy. Histopathologic grading according to National Institutes of Health indices for lupus nephritis activity and chronicity was conducted by Arkana Laboratories. Efficacy outcomes and measures of renal function over time, including eGFR were assessed.

Table 1. Laboratory parameters, clinical outcomes, and activity and chronicity index scores over time

	Voclosporin n=16		Control n=10	
	Baseline	**Month 36**	**Baseline**	**Month 36**
CRR, % (n/n)	-	62.5% (10/16)	-	40.0% (4/10)
PRR, % (n/n)	-	81.3% (13/16)	-	70.0% (7/10)
UPCR, mean (SD) g/g	4.59 (2.5)	0.99 (1.4)	4.71 (2.6)	2.1 (4.6)
eGFR, mean (SD), mL/min/1.73 m^2	80.3 (16.4)	82.7 (15.4)	82.6 (12.3)	85.8 (13.3)
Urine protein, mean (SD) mg/dL	413.7 (277.2)	135.7 (264.0)	350.2 (234.1)	128.0 (284.7)
Magnesium, mean (SD) mg/dL	2.0 (0.1)	2.0 (0.2)	2.1 (0.1)	2.1 (0.2)
Potassium, mean (SD) mmol/L	4.0 (0.3)	4.3 (0.2)	3.9 (0.4)	4.1 (0.5)
Glucose, mean (SD) mg/dL	84.4 (9.0)	93.5 (7.9)	93.5 (38.5)	89.1 (15.3)
Creatinine, mean (SD) mg/dL	0.8 (0.3)	0.8 (0.4)	0.8 (0.2)	0.8 (0.3)
Systolic BP, mean (SD) mmHg	121.7 (9.05)	118.3 (10.4)	121.1 (14.9)	110.8 (4.8)
Diastolic BP, mean (SD) mmHg	79.6 (8.7)	74.7 (7.7)	80.4	76.9 (4.5)
Histology	**Baseline**	**Follow-up**	**Baseline**	**Follow-up**
Activity Index, mean (SD)	1.8 (3.0)	0.4 (1.0)	2.8 (3.2)	0.4 (1.0)
Chronicity Index, mean (SD)	3.8 (3.5)	4.1 (3.3)	2.9 (2.3)	2.8 (2.7)

Renal function assessed with corrected eGFR (Chronic Kidney Disease Epidemiology Collaboration equation) using a prespecified ceiling of 90 mL/min/1.73 m^2. Histopathologic grading based on the National Institutes of Health indices for lupus nephritis activity (scale 0-24) and chronicity (scale 0-12). BP, blood pressure; CRR, complete renal response (UPCR ≤0.5 g/g, stable eGFR > 60 mL/min/1.73 m2, low-dose steroids, and no rescue medication); eGFR, estimated glomerular filtration rate; PRR, partial renal response (>50% reduction from baseline in UPCR); SD, standard deviation; UPCR, urine protein creatinine ratio.

Results: Paired biopsy samples were collected from sixteen patients in the voclosporin arm and ten patients in the control arm. Baseline mean activity scores were similar between arms, with scores improving with treatment in both arms (Table 1). Mean chronicity scores were also similar between arms at baseline and remained stable over time in most patients. Measures of renal function remained stable in both arms over the 3-year follow-up. Voclosporin-treated patients had numerically greater mean reductions from baseline in UPCR year-on-year compared to patients in the control arm, although the difference was not statistically significant. On-going research involving the above patients and others from AURORA 2 using multiplex immunohistochemistry and RNA-sequencing has been performed, and data are currently being analyzed.

Conclusion: As expected, mean activity scores improved in both treatment arms. Importantly, exposure to voclosporin was not associated with chronic injury, with the mean index remaining stable at follow-up. Similar to the overall population, patients treated with voclosporin saw greater reductions in UPCR over 3 years of treatment; safety outcomes from this small subgroup were also consistent with outcomes in AURORA 1. Multiplex immunohistochemistry and sequencing data will further illuminate the cellular and molecular underpinnings of disease and response to treatment.

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Abstract Number: 2346

SLE Medication Usage and Organ Damage Among Adult SLE Patients with SLE Treated with Belimumab (BEL): Pooled Data from Three Open-Label Extension Studies over 11+ Years

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SESSION INFORMATION
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Background/Purpose: A key treatment goal for patients (pts) with SLE is to reduce use of CS, due to their association with organ damage.[1] BEL is an approved treatment for active SLE and LN, in addition to standard therapy (ST).[1] BEL-treated pts were able to reduce CS dose and exhibited delayed organ damage progression during long-term extension studies (LTEs).[2–4] We evaluated use of SLE medications and change in organ damage over time in pts with SLE using data from three multicenter LTE studies.

Methods: This post hoc analysis pooled data from the LBSL02 LTE (Phase 2; GSK Study 112626),[2] BLISS-76 LTE (US pts only; Phase 3; GSK Study 112233),[3] and BLISS-52 + BLISS-76 LTE (excluding US pts from BLISS-76; Phase 3; GSK Study 112234)[4] studies. To enroll in LTEs, pts must have completed treatment through Week 72 of LBSL02 and BLISS-76, or Week 48 of BLISS-52; improvement in physician global assessment at Week 72 or 68 versus at first BEL dose was required in the LBSL02 LTE. Pts received BEL 10 mg/kg intravenously every 28 days plus ST at the start of each LTE, regardless of prior drug allocation. Maximum daily equivalent prednisone dose was summarized any time post–first BEL dose (in prior trial period or LTE) and in each year. SLICC/ACR Damage Index (SDI) score was assessed among eligible pts in the BLISS-76, and BLISS-52 + BLISS-76 LTE studies; the high disease activity (HDA) population (anti-dsDNA positive and low C3/C4); and the 5-year completer population (pts with ≥5 years of SDI data post–first BEL dose).

Results: Overall, 1304 pts enrolled in the LTE studies, 1299 (99.6%) received ≥1 dose of study drug (pooled safety population) and 604 (46.5%) completed their respective studies. Cumulative BEL-treated patient-years was 7040.1. At baseline (first BEL dose in prior trial period or LTE), 1054 (81.1%) pts received CS. Over time, the proportion of pts discontinuing CS (receiving an equivalent dose of 0 mg/day) increased; the proportion receiving >0 to ≤7.5 mg/day increased up to Year 4–5 (**Table 1**). Any use of CS decreased over time, while use of antimalarials and immunosuppressive/immunomodulatory agents remained stable (**Table 1**). At baseline, 580 (58.2%) and 416 (41.8%) pts had an SDI score of zero and ≥1, respectively. Mean (standard deviation [SD]) change over time in SDI score was similar and remained low for the total, HDA, and

Table 1. Use of SLE medication over time* (pooled safety population, N=1299; post hoc analysis). *Data are summarized at any time post–first BEL dose and in each year; †post–first BEL dose data include follow-up visits after the final dose of BEL; data from Year 0 up to last visit in the treatment period are shown by years of study participation; pts could be counted in more than one year interval; ‡CS were converted to a daily prednisone equivalent dose and the maximum dose was summarized in each interval; maximum daily prednisone dose applies to any time post–first BEL dose and for each year interval; baseline daily prednisone dose was calculated as the average daily dose for the 7 days pre–first BEL dose.

n (%)	Baseline (first BEL dose; N=1299)	Any time post–first BEL dose† (N=1299)	Year 0–1 (N=1299)	Year 1–2 (N=1254)	Year 2–3 (N=1140)	Year 3–4 (N=983)	Year 4–5 (N=867)	Year 5–6 (N=746)	Year 6–7 (N=541)	Year 7–8 (N=308)	Year 8–9 (N=175)	Year 9–10 (N=152)	Year 10–11 (N=131)	Year 11+ (N=88)
Maximum daily prednisone dose,‡ (mg/day)														
0	243 (18.7)	77 (5.9)	168 (12.9)	207 (16.6)	239 (21.0)	238 (24.3)	240 (27.7)	208 (28.0)	164 (30.4)	100 (32.5)	69 (39.7)	67 (44.4)	56 (42.7)	36 (40.9)
>0 to ≤7.5 mg/day	413 (31.8)	181 (14.0)	307 (23.6)	405 (32.4)	413 (36.3)	360 (36.7)	323 (37.3)	256 (34.4)	180 (33.3)	91 (29.5)	35 (20.1)	24 (15.9)	21 (16.0)	21 (23.9)
>7.5 to ≤40.0 mg/day	639 (49.3)	695 (53.6)	687 (52.9)	558 (44.6)	388 (34.1)	312 (31.8)	237 (27.4)	216 (29.0)	138 (25.6)	73 (23.7)	39 (22.4)	26 (17.2)	28 (21.4)	20 (22.7)
>40	2 (0.2)	343 (26.5)	137 (10.5)	80 (6.4)	98 (8.6)	71 (7.2)	65 (7.5)	64 (8.6)	58 (10.7)	44 (14.3)	31 (17.8)	34 (22.5)	26 (19.8)	11 (12.5)
Unknown	2	3	0	4	2	2	2	2	1	0	1	1	0	0
Any use of SLE medication														
Antimalarials	876 (67.4)	969 (74.6)	895 (68.9)	860 (68.6)	761 (66.8)	666 (67.8)	581 (67.0)	498 (66.8)	356 (65.8)	204 (66.2)	129 (73.7)	115 (75.7)	101 (77.1)	65 (73.9)
CS	1054 (81.1)	1222 (94.1)	1131 (87.1)	1047 (83.5)	901 (79.0)	745 (75.8)	627 (72.3)	538 (72.1)	377 (69.7)	208 (67.5)	106 (60.6)	85 (55.9)	75 (57.3)	52 (59.1)
Immunosuppressants/ immunomodulators	618 (47.6)	733 (56.4)	639 (49.2)	599 (47.8)	503 (44.1)	431 (43.8)	370 (42.7)	306 (41.0)	207 (38.3)	128 (41.6)	72 (41.1)	64 (42.1)	60 (45.8)	41 (46.6)

Table 2. Change in SDI score from baseline by belimumab visit* (N=1003; post hoc analysis). *Observed data are presented; the SDI score is cumulative, once an item is scored, it continues to be scored at subsequent visits; for years in which a patient withdraws from the study, the exit visit assessment is used in place of the Week 48 assessment for the year, but this value is not carried forward through later years; †number of pts with available data at baseline and Week 48 yearly visit; ‡HDA is defined as anti-dsDNA positive and low C3/C4; ¶the 5-year completer population is defined as pts with ≥5 years of SDI assessment data post–first BEL dose (in prior trial period or LTE).

	Baseline (first BEL dose)	Year 1, Week 48	Year 2, Week 48	Year 3, Week 48	Year 4, Week 48	Year 5, Week 48	Year 6, Week 48	Year 7, Week 48	Year 8, Week 48	Year 9, Week 48
Total, N=1003										
n†	996	977	921	817	698	616	517	339	130	6
Change in SDI score, mean (SD)	-	0.1 (0.3)	0.1 (0.4)	0.1 (0.4)	0.2 (0.5)	0.2 (0.5)	0.2 (0.5)	0.2 (0.6)	0.3 (0.6)	0.0 (0.0)
HDA‡, N=494										
n†	491	481	453	400	336	295	234	152	54	1
Change in SDI score, mean (SD)	-	0.1 (0.3)	0.1 (0.4)	0.2 (0.4)	0.2 (0.5)	0.2 (0.5)	0.2 (0.5)	0.2 (0.5)	0.3 (0.6)	0.0 (0.0)
5-year completers¶, N=522										
n†	522	521	517	511	512	508	517	339	130	6
Change in SDI score, mean (SD)	-	0.1 (0.3)	0.1 (0.3)	0.2 (0.4)	0.2 (0.4)	0.2 (0.5)	0.2 (0.5)	0.2 (0.6)	0.3 (0.6)	0.0 (0.0)

Table 3. Change in SDI score category from baseline by year* (5-year completer population,† N=522; post hoc analysis). * Observed data are presented; the SDI score is cumulative, once an item is scored, it continues to be scored at subsequent visits; for years in which a patient withdraws from the study, the exit visit assessment is used in place of the Week 48 assessment for the year, and this value is not carried forward through later years; †the 5-year completer population is defined as pts with ≥5 years of SDI assessment data post–first BEL dose (in prior trial period or LTE); ‡number of pts with available data at baseline and year interval.

	Year 0–1 (N=522)	Year 1–2 (N=522)	Year 2–3 (N=522)	Year 3–4 (N=522)	Year 4–5 (N=522)	Year 5–6 (N=522)	Year 6–7 (N=349)	Year 7–8 (N=130)	Year 8–9 (N=6)
n‡	341	491	512	512	508	518	340	129	6
SDI category, n (%)									
No increase	316 (93)	445 (91)	446 (87)	440 (86)	430 (85)	430 (83)	274 (81)	103 (80)	6 (100)
+1	23 (7)	42 (9)	57 (11)	61 (12)	63 (12)	71 (14)	52 (15)	19 (15)	0
+2	2 (<1)	4 (<1)	8 (2)	10 (2)	13 (3)	15 (3)	12 (4)	6 (5)	0
+3	0	0	1 (<1)	1 (<1)	2 (<1)	1 (<1)	1 (<1)	1 (<1)	0
+4	0	0	0	0	0	1 (<1)	1 (<1)	0	0

5-year completer populations (**Table 2**). Among the 5-year completer population, ≤20% had SDI worsening (change ≥0) compared with baseline in any study year (**Table 3**).

Conclusion: Over time, more BEL-treated pts were able to reduce their daily equivalent prednisone dose and exhibited low change in SDI. Limitations include the open-label nature of the studies, lack of control arm, and increased number of withdrawals at later years. These data are consistent with previous observations of the steroid sparing–effect of BEL, and delayed organ damage progression among a large population of BEL-treated pts.[2–5]

References

1 Fanouriakis A et al. *Ann Rheum Dis* 2019;0:1–10
2 Wallace DJ et el. *Arthritis Rheumatol* 2019;7:1125–34
3 Furie RA et al. Arthritis Rheumatol 2018;6:868–77

4 van Vollenhoven RF et al. *Rheumatology(Oxford)* 2020;2:281–91
5 Urowitz MB et al. *Lupus Sci Med* 2020;7:e000412

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Abstract Number: 2347

Efficacy of Belimumab in Patients with Systemic Lupus Erythematosus by Race and Ethnicity: A Large Post Hoc Integrated Analysis of Five Clinical Trials

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Background/Purpose: Belimumab (BEL) is approved for the treatment of active SLE, and lupus nephritis, with standard therapy.[1] The prevalence and severity of SLE tend to be higher in patients of Black and Asian race, and Hispanic ethnicity, compared with Caucasians.[2] This large integrated analysis investigated BEL efficacy by race and ethnicity in patients with SLE.

Methods: This Belimumab Summary of Lupus Efficacy (Be-SLE) post hoc analysis pooled data from five BEL trials: BLISS-76[3] (GSK study BEL110751); BLISS-52[4] (BEL110752); NEA[5] (BEL113750); BLISS-SC[6] (BEL112341); EMBRACE[7] (BEL115471; study in patients of self-identified Black race). Included patients received BEL (10 mg/kg/month intravenously or 200 mg/week subcutaneously) or placebo (PBO), plus standard therapy. The proportion of patients with SLE Responder Index-4 (SRI-4) response at Week 52, and time to first severe Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA)-SLEDAI Flare Index (SFI) flare, SFI flare, and BILAG (1A/2B) flare over 52 weeks were analyzed by race (Asian, White, Black African ancestry) and ethnicity (Hispanic/Latino, non-Hispanic/Latino).

Results: Among 3086 patients (BEL, n=1869; PBO, n=1217), 35.7% (BEL, n=697; PBO, n=405) were Asian, 33.4% (BEL, n=596; PBO, n=436) were White, and 20.5% (BEL, n=405; PBO, n=229) were of Black African ancestry. For ethnicity, 27.4% (BEL, n=495; PBO, n=352) were Hispanic/Latino and 72.6% (BEL, n=1374; PBO, n=865) were not Hispanic/Latino. At Week 52, higher proportions of BEL-treated patients were SRI-4 responders and fewer BEL-treated patients experienced severe SFI flares in all subgroups versus PBO, with statistically significant differences in all subgroups except patients of Black African ancestry (**Table**). Greatest treatment differences were among Hispanic/Latino and White patients. Fewer BEL-treated patients experienced SFI and BILAG (1A/2B) flares in all subgroups versus PBO; however, statistical

significance was not reached for SFI in the Black African ancestry subgroup and for BILAG (1A/2B) among the White and Black African ancestry subgroups (**Table**).

Conclusion: BEL significantly increased SRI-4 response rates at Week 52 and decreased flares versus PBO in most subgroups by race and ethnicity, which was largely consistent with results from the overall populations of the primary trials. Numerical benefit only observed in Black African ancestry patients was consistent with the EMBRACE trial findings,[7] from which most patients in this subgroup originated. This analysis was limited by low power to detect statistically significant differences in the smallest subgroup. Collectively, this analysis in a large, diverse population of patients with SLE continues to support the efficacy of BEL

n/N (%)	BEL + standard therapy (N=1869)	PBO + standard therapy (N=1217)	OR/HR (95% CI)*	p value
SRI-4 response at Week 52				
Asian	367/684 (54)	160/395 (41)	1.78 (1.36, 2.32)	<0.0001
White	343/592 (58)	174/432 (40)	1.92 (1.48, 2.49)	<0.0001
Black African ancestry	188/400 (47)	96/229 (42)	1.23 (0.88, 1.71)	0.2249
Hispanic/Latino	311/493 (63)	168/352 (48)	1.86 (1.40, 2.48)	<0.0001
Non-Hispanic/Latino	700/1353 (52)	333/851 (39)	1.65 (1.38, 1.98)	<0.0001
Time to first severe SFI flare over 52 weeks†				
Asian	96/697 (14)	93/405 (23)	0.60 (0.45, 0.80)	0.0005
White	62/596 (10)	81/436 (19)	0.53 (0.38, 0.75)	0.0003
Black African ancestry	81/405 (20)	54/229 (24)	0.87 (0.61, 1.23)	0.4301
Hispanic/Latino	54/495 (11)	84/352 (24)	0.44 (0.31, 0.63)	<0.0001
Non-Hispanic/Latino	204/1374 (15)	186/865 (22)	0.68 (0.55, 0.83)	0.0001
Time to first SFI flare over 52 weeks†				
Asian	478/697 (69)	313/405 (77)	0.77 (0.66, 0.89)	0.0003
White	377/596 (63)	322/436 (74)	0.79 (0.68, 0.92)	0.0022
Black African ancestry	308/405 (76)	180/229 (79)	1.03 (0.85, 1.24)	0.7667
Hispanic/Latino	336/495 (68)	267/352 (76)	0.82 (0.70, 0.97)	0.0184
Non-Hispanic/Latino	947/1374 (69)	664/865 (77)	0.83 (0.75, 0.92)	0.0004
Time to first BILAG flare (1A/2B) over 52 weeks†				
Asian	150/697 (22)	135/405 (33)	0.60 (0.47, 0.76)	<0.0001
White	124/596 (21)	115/436 (26)	0.77 (0.60, 1.00)	0.0528
Black African ancestry	115/405 (28)	73/229 (32)	0.87 (0.65, 1.18)	0.3751
Hispanic/Latino	106/495 (21)	107/352 (30)	0.67 (0.51, 0.87)	0.0035
Non-Hispanic/Latino	320/1374 (23)	264/865 (31)	0.74 (0.62, 0.87)	0.0003

*OR (SRI-4 response at Week 52), 95% CI, and p value are from a logistic regression model for the comparison between BEL and PBO with covariates of treatment group, study, and baseline SELENA-SLEDAI score (less than or equal to 9 vs greater than or equal to 10). HR (all other outcomes), 95% CI, and p value from Cox proportional hazards model for the comparison between BEL and PBO adjusting for study and baseline SELENA-SLEDAI score (<=9 vs >=10). †n shown are the number of patients with severe SFI flare/SFI flare/BILAG (1A/2B) flare over 52 weeks. CI, confidence interval; HR, hazards ratio; OR, odds ratio.

Funding: GSK

References

1 GSK. Benlysta US prescribing information. 2023
2 Lewis MJ, Jawad AS. *Rheumatol* (Oxford) 2017;56:i67–i77
3 Furie R et al. *Arthritis Rheumatol* 2011;63(12):3918–30
4 Navarra SV et al. *Lancet* 2011;377(9767):721–31
5 Stohl W et al. *Arthritis Rheumatol* 2017;69(5):1016–27
6 Zhang F et al. *Ann Rheum Dis* 2018;77(3):355–63
7 Ginzler E et al. *Arthritis Rheumatol* 2021;doi:10.1002/art.41900

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Abstract Number: 2348

Incidence of Infections Among Adult Patients with SLE Treated with Belimumab (BEL): Pooled Data from Three Open-Label Extension Studies over 11+ Years

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SESSION INFORMATION
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Background/Purpose: BEL-treated patients (pts) in clinical trials and long-term extension (LTE) studies[1-7] experienced comparable incidence of infections versus those treated with standard therapy (ST) alone in clinical trials[1-4]; however, sample sizes were limited. We performed the most comprehensive analysis of infections among BEL-treated pts.

Methods: This post hoc analysis pooled data from three multicenter BEL LTE studies of adults with active SLE: LBSL02 LTE (Phase 2; GSK Study 112626),[5] BLISS-76 LTE (including US pts only; Phase 3; GSK Study 112233),[6] and BLISS-52 + BLISS-76 LTE (excluding US pts from BLISS-76; Phase 3; GSK Study 112234).[7] Eligibility for LTE studies required completion of treatment through Week 72 (LBSL02 and BLISS-76 trials), or Week 48 (BLISS-52 trial); improvement in physician global assessment at Week 72 or 68 versus at first BEL dose was also required in LBSL02 LTE. Pts received open-label BEL 10 mg/kg intravenously every 28 days plus ST at the start of each LTE for up to 8 years (BLISS-76 and BLISS-52 + BLISS-76 LTEs) or 13 years (LBSL02 LTE), regardless of prior study drug allocation. Adverse events (AEs) were assessed

Table 1. Proportion of patients experiencing AE reported infections over time* (pooled safety population, N=1299; post hoc analysis). *Infections occurred on or after first BEL dose (in prior trial period or LTE), summarized at any time post–first BEL dose and in each year (post hoc analysis); †post–first BEL dose data include follow-up visits (post–final BEL dose); data from Year 0 up to last visit in the treatment period are shown by years of study participation; pts could be counted in more than one year interval; ‡ infections of special interest are limited to opportunistic infections, active tuberculosis, herpes zoster, and sepsis; ¶per sponsor adjudication.

n (%)	Any time post–first BEL dose† (N=1299)	Year 0–1 (N=1299)	Year 1–2 (N=1254)	Year 2–3 (N=1140)	Year 3–4 (N=983)	Year 4–5 (N=867)	Year 5–6 (N=746)	Year 6–7 (N=541)	Year 7–8 (N=308)	Year 8–9 (N=175)	Year 9–10 (N=152)	Year 10–11 (N=131)	Year 11+ (N=88)
Any infection or infestation	1140 (87.8)	865 (66.6)	703 (56.1)	615 (53.9)	548 (55.7)	428 (49.4)	353 (47.3)	244 (45.1)	148 (48.1)	113 (64.6)	91 (59.9)	72 (55.0)	22 (25.0)
Infections of special interest‡	213 (16.4)	57 (4.4)	42 (3.3)	35 (3.1)	38 (3.9)	25 (2.9)	28 (3.8)	16 (3.0)	9 (2.9)	4 (2.3)	8 (5.3)	5 (3.8)	3 (3.4)
Serious infections of special interest	39 (3.0)	11 (0.8)	4 (0.3)	7 (0.6)	6 (0.6)	3 (0.3)	2 (0.3)	0	2 (0.6)	0	1 (0.7)	1 (0.8)	1 (1.1)
Opportunistic infections¶	44 (3.4)	6 (0.5)	7 (0.6)	9 (0.8)	4 (0.4)	5 (0.6)	9 (1.2)	6 (1.1)	1 (0.3)	0	3 (2.0)	1 (0.8)	1 (1.1)
Active tuberculosis	4 (0.3)	0	0	3 (0.3)	0	0	1 (0.1)	0	0	0	0	0	0
Herpes zoster	137 (10.5)	36 (2.8)	22 (1.8)	19 (1.7)	23 (2.3)	13 (1.5)	17 (2.3)	11 (2.0)	4 (1.3)	3 (1.7)	4 (2.6)	4 (3.1)	2 (2.3)
Sepsis	25 (1.9)	6 (0.5)	1 (<0.1)	4 (0.4)	2 (0.2)	2 (0.2)	3 (0.4)	1 (0.2)	2 (0.6)	0	1 (0.7)	1 (0.8)	1 (1.1)
Deaths due to infections	10 (0.8)	2 (0.2)	1 (<0.1)	1 (<0.1)	2 (0.2)	0	0	1 (0.2)	0	0	0	0	0

at each infusion visit until the follow-up visit (post–final BEL dose) and summarized any time post–first BEL dose (in prior trial period or LTE) and in each year.

Results: Of 1304 pts enrolled, 1299 (99.6%) received ≥1 dose of BEL plus ST (pooled safety population), five patients did not receive study treatment, and 604 (46.5%) pts completed their respective studies (cumulative BEL-treated patient-years [PY] on study: 7040.1). Most reported reasons for withdrawal were "withdrawal by patient" (18.3%) and "AE" (10.6%).

Infections and infestations were the most frequent AE (87.8%) and serious AE (16.9%) at any time post–first BEL dose; 1.9% of discontinuations due to AE were due to infections and infestations. The proportion of pts experiencing an infection of special interest was 16.4% any time post–first BEL dose and generally remained stable each year (**Table 1**).Herpes zoster was

Table 2. Event rates (number of events per 100 PY) of infections of special interest over time* (pooled safety population, N=1299; post hoc analysis). *Infections of special interest occurred on or after first BEL dose (in prior trial period or LTE), summarized at any time post–first BEL dose and in each year (post hoc analysis); †the rate is the number of events per 100 PY; ‡post–first BEL dose data include follow-up visits (post–final BEL dose); data from Year 0 up to last visit in the treatment period are shown by years of study participation; pts could be counted in more than one year interval; §infections of special interest are limited to opportunistic infections, active tuberculosis, herpes zoster, and sepsis; ¶per sponsor adjudication.

Number of events (rate†)	Any time post–first BEL dose‡ (PY=7236)	Year 0–1 (PY=1273)	Year 1–2 (PY=1203)	Year 2–3 (PY=1053)	Year 3–4 (PY=925)	Year 4–5 (PY=816)	Year 5–6 (PY=659)	Year 6–7 (PY=438)	Year 7–8 (PY=228)	Year 8–9 (PY=164)	Year 9–10 (PY=140)	Year 10–11 (PY=104)	Year 11+ (PY=36)
Infections of special interest§	367 (5.1)	75 (5.9)	57 (4.7)	55 (5.2)	47 (5.1)	35 (4.3)	40 (6.1)	18 (4.1)	10 (4.4)	4 (2.4)	9 (6.4)	5 (4.8)	3 (8.3)
Serious infections of special interest	52 (0.7)	13 (1.0)	5 (0.4)	9 (0.9)	7 (0.8)	3 (0.4)	2 (0.3)	0	2 (0.9)	0	1 (0.7)	1 (1.0)	1 (2.8)
Opportunistic infections¶	65 (0.9)	6 (0.5)	10 (0.8)	10 (0.9)	4 (0.4)	8 (1.0)	12 (1.8)	6 (1.4)	1 (0.4)	0	3 (2.1)	1 (1.0)	1 (2.8)
Active tuberculosis	4 (<0.1)	0	0	3 (0.3)	0	0	1 (0.2)	0	0	0	0	0	0
Herpes zoster	182 (2.5)	40 (3.1)	30 (2.5)	20 (1.9)	24 (2.6)	13 (1.6)	24 (3.6)	12 (2.7)	4 (1.8)	3 (1.8)	5 (3.6)	4 (3.8)	2 (5.5)
Sepsis	34 (0.5)	8 (0.6)	1 (<0.1)	4 (0.4)	3 (0.3)	2 (0.2)	4 (0.6)	1 (0.2)	2 (0.9)	0	1 (0.7)	1 (1.0)	1 (2.8)

the most frequent infection of special interest; all subcategories generally remained stable over time. The rate of infections of special interest was 5.1 events per 100 PY; all subcategories remained stable over time(**Table 2**).

Conclusion: In this large, pooled population of BEL-treated pts, incidence of infections was generally stable up to 11 years with no new infection types or increase in severity. Limitations include the open-label nature of the studies, lack of control arm, inclusion of pts who had not withdrawn from prior study periods, and low numbers of pts at later years. Infection incidence rates were similar to or lower than in the GLADEL cohort study[8], and among pts receiving ST in the double-blind period of BEL clinical trials.[1-4]

Funding: GSK

References

1 Sheikh SZ et al. Lancet Rheumatol 2021;3:e122–30
2 Wallace DJ et al. Arthritis Rheum 2009;61:1168–78
3 Furie RA et al. Arthritis Rheum 2011;12:3918–30
4 Navarra SV et al. Lancet 2011;2:721–31
5 Wallace DJ et el. Arthritis Rheumatol 2019;7:1125–34
6 Furie RA et al. Arthritis Rheumatol 2018;6:868–77
7 van Vollenhoven RF et al. Rheumatol (Oxford) 2020;2:281–91
8 Pimentel-Quiroz VR et al. Lupus 2019;28:1101–10

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Abstract Number: 2349

Selection of the Dose for Subcutaneous Administration to Non-Japanese Subjects and Intravenous Administration to Japanese Subjects in the First-in-Human Study of DS-7011a, an Anti-TLR7 Monoclonal Antibody for the Treatment of Systemic Lupus Erythematosus

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Background/Purpose: Toll-like receptor (TLR)7 is a pattern recognition receptor whose ligands include nucleic acids and whose gain-of-function mutations have been reported to result insystemic lupus erythematosus (SLE). DS-7011a is an anti-TLR7 monoclonal antibody (mAb), which inhibits *in vitro* production of cytokines and antibodies stimulated by TLR7. A surrogate anti-TLR7 mAb improved survival and reduced autoantibody production in murine lupus models. DS-7011a

was generally safe and well tolerated and showed optimal pharmacokinetic (PK) and pharmacodynamic (PD) characteristics in a first-in-human (FIH), single ascending intravenous (IV) and subcutaneous (SC) dose studyin healthy volunteers (HV), including HV of Japanese descent [NCT05203692]. We report here the analysis of the PK and PD data from the non-Japanese HV (mainly Caucasian and African American) that were initially administered in this study IV doses of DS-7011a to select the doses for later SC administration to non-Japanese HV and IV administration to Japanese HV.

Methods: DS-7011a clinical PK and PD data from single ascending dose (SAD) IV cohorts (from 0.1 to 20 mg/kg, N = 34) of non-Japanese HV enrolled in the first stage of DS-7011a FIH study was used for PK/PD model development under blinded analysis. PK exposure of SC doses to non-Japanese HV was predicted by assuming human SC bioavailability identical to that observed in monkeys (55.6%). PK exposure of IV doses to Japanese HV was predicted by assuming mean body weight of 66 kg. Dose selection for three SAD SC cohorts of non-Japanese HV and one IV cohort of Japanese HV was informed by benchmarking simulated PK and PD profiles with selected IV reference doses (1, 3, and 10 mg/kg for SC cohorts of non-Japanese HV; 3 mg/kg for the IV cohort of Japanese HV) after interim review of blinded data.

Results: DS-7011a PK linearity started at 3 mg/kg after IV infusion, while the elimination of lower doses was accelerated by target-mediated disposition. DS-7011a PK profile after IV infusion was well described by a 2-compartment model, with parallel linear and saturable, non-linear clearance (CL). Weight was a covariate on linear CL and central volume, as higher weight resulted in increased CL and volume of distribution. DS-7011a showed *ex vivo* inhibition of TLR7-stimulated IL-6 production that was of large extent, early onset, and lasting duration at 3 mg/kg and above.*Ex vivo* IL-6 profile after DS-7011a IV infusion was adequately described by DS-7011a concentration-derived inhibition of *ex vivo* IL-6 production. By benchmarking simulated PK and IL-6 profile with IV reference dose data, SAD SC doses for non-Japanese HV were proposed as 100, 300, and 600 mg, and SAD IV dose for Japanese HV as 3 mg/kg.

Conclusion: Model prediction of SAD SC doses for non-Japanese HV and IV dose for Japanese HV is confirmed by emerging clinical PK data and demonstrates the value of model-informed dose selection for DS-7011a FIH. Additional analysis will be conducted to select DS-7011a dose for future treatment of SLE patients.

Disclosure: L. Zhang: Daiichi Sankyo, 3, Regeneron, 3; **J. Tanaka**: Daiichi Sankyo, 3, The Japan Agency for Medical Research and Development, 5; **M. Dodds**: Certara Strategic Consulting, 3; **M. Trame**: Certara Strategic Consulting, 3; **S. Xu**: Daiichi Sankyo, 3; **M. Kumazaki**: Daiichi Sankyo, 3; **Y. Tomimori**: Daiichi Sankyo, 3; **S. Patel**: Daiichi Sankyo, 3; **A. Mohan**: Daiichi Sankyo, 3; **G. Senaldi**: Daiichi Sankyo, 3; **T. Leil**: Daiichi Sankyo, 3.

Abstract Number: 2350

Upregulation of Both APRIL and BAFF in Systemic Lupus Erythematosus Suggests Non-Redundant Roles, Further Revealed by Dual Inhibition with Povetacicept (ALPN-303; TACI vTD-Fc)

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SESSION INFORMATION
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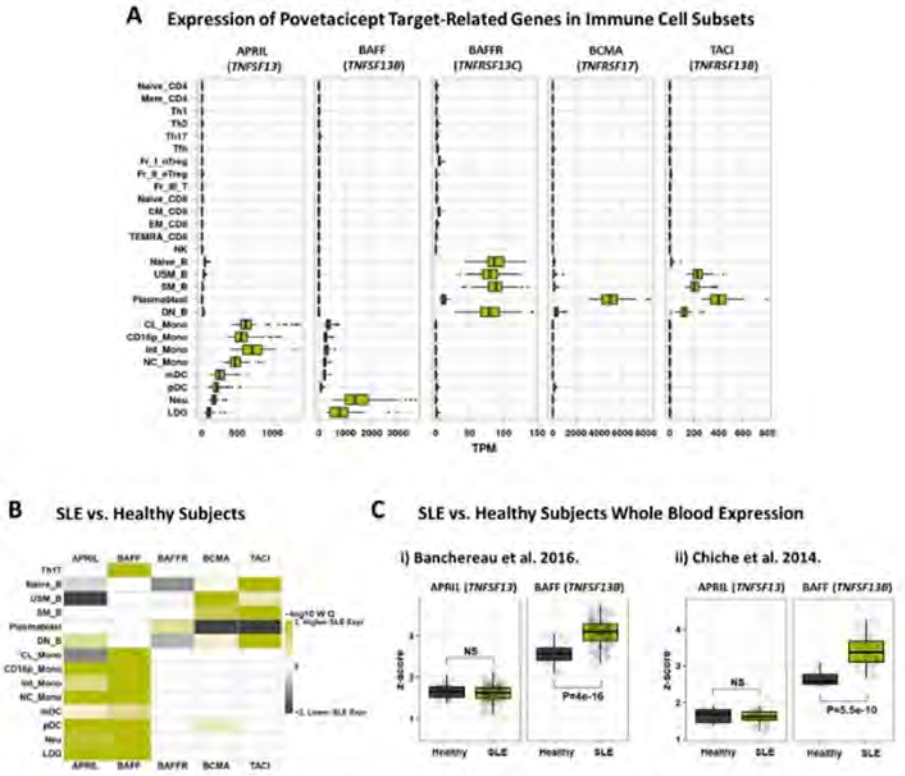

Figure 1: APRIL (*TNFSF13*) and BAFF (*TNFSF13B*) gene expression is upregulated in SLE. **A** Expression of povetacicept target-related genes from immune cell subsets sorted for RNASeq in healthy subjects[2]. **B** Transcript per million (TPM) values were $\log_2$ transformed and converted to z-scores for SLE vs. healthy comparison. Heatmap colors represent negative $\log_{10}$ q-values from Wilcoxon tests between SLE and healthy subjects. Positive (*green*) values represent higher SLE patient expression, and negative (*black*) values represent lower SLE patient expression. White values indicate either non-significance (q-values ≈ 1) or low expression (healthy subject median expression ≤ 10). TPM values displayed were upper quartile normalized. **C** BAFF expression in SLE vs. healthy subjects from publicly available transcriptional datasets from whole blood analyses: Banchereau et al., 2016[3] (SLE N=158) and Chiche et al., 2014[4] (SLE N=62).

Background/Purpose: B cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL) are cytokines that signal through transmembrane activator and CAML interactor (TACI), B cell maturation antigen (BCMA), and/or BAFF-Receptor (BAFF-R) and play important roles in B cell development, proliferation, function, and survival. Therapeutic agents targeting BAFF and/or APRIL have demonstrated promising clinical potential in systemic lupus erythematosus (SLE), lupus nephritis,

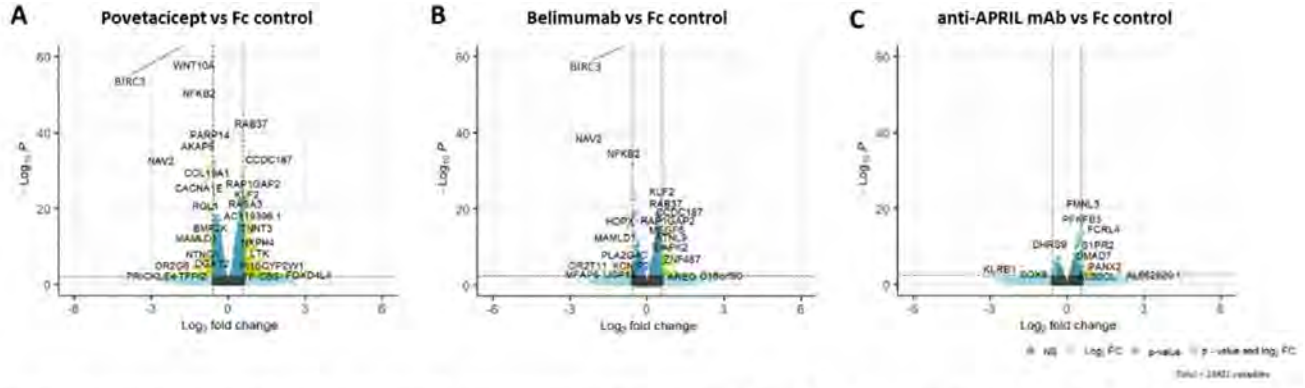

Figure 2: Povetacicept potently and more broadly downregulates genes associated with B cell activation than does anti-BAFF (belimumab) or anti-APRIL mAbs in primary human B cells stimulated with CD40L followed by BAFF+APRIL. Volcano plots demonstrate differentially expressed genes from B cells exposed to **A** povetacicept, **B** belimumab, or **C** anti-APRIL mAb vs Fc control in the presence of soluble BAFF and APRIL. Green dots represent differentially expressed genes that pass significance threshold with an adjusted p value > 0.005 and $\log_2$ fold cutoff value with an absolute value greater than 0.58. Light blue dots pass the p value cutoff but do not pass the $\log_2$ fold change threshold, dark blue dots represent genes that pass fold change cutoff, but not significantly, and gray dots pass neither $\log_2$ fold change nor p value cutoffs.

and other B cell-related diseases, but have generally targeted only BAFF, only APRIL, or predominantly BAFF. Due to the overlapping and non-redundant roles of BAFF and APRIL, more potent and/or complete inhibition of both cytokines is likely required for optimal efficacy. Povetacicept is an Fc fusion protein of a variant TACI domain engineered to have enhanced affinity for BAFF and APRIL, providing more potent dual inhibition of both BAFF and APRIL than wild type (WT) TACI-Fc or BAFF- or APRIL-specific antibodies. In preclinical mouse lupus models povetacicept suppressed autoantibodies, renal IgG deposition, and nephritis.[1]

Methods: Publicly available RNA Sequencing (RNA-Seq) datasets from healthy donors and SLE subjects were utilized to assess APRIL and BAFF gene expression.[2-4] Primary B cells isolated from healthy donor PBMCs were stimulated with CD40L for 72 hours, washed and then cultured for an additional 24 hours with 5 nM APRIL and 10 nM BAFF in the presence of either 100 nM of Fc control, povetacicept, anti-BAFF mAb (belimumab), or anti-APRIL mAb. Cultured B cells were then harvested for flow cytometry analysis or processed for bulk RNA-seq.

Results: In publicly available transcriptional datasets, SLE patients showed a significant elevation of only BAFF in whole blood compared to healthy adults, but specific analysis of cell types known to be associated with SLE pathogenesis revealed upregulation of both APRIL and BAFF (**Fig 1**). Genes associated with B cell activation, regulation of immunoglobulin production, and adaptive immunity were upregulated in primary B cells cultured with CD40L, BAFF, and APRIL. Povetacicept potently suppresses inflammatory pathways, significantly more broadly than mAbs targeting BAFF or APRIL alone (**Fig 2**).

Conclusion: Dual inhibition of both BAFF and APRIL may be required to achieve optimal suppression of pathogenic pathways associated with SLE and related diseases. When coupled with data from the literature, these results further support the clinical evaluation of dual BAFF/APRIL inhibitors such as povetacicept in SLE, as well as in other B cell- and/or autoantibody-related diseases. Clinical studies of povetacicept in autoimmune glomerulonephritis (NCT05732402) and cytopenias (NCT05757570) have been initiated; a study in SLE is in preparation.

1 Evans L, et al. 2023 Jan 27. Arthritis Rheumatol. Online ahead of print.
2 Ota M, et al. 2021. Cell. 184(11): 3006-21.
3 Banchereau R, et al. 2016. Cell. 165(6): 1548-1550.
4 Chiche L, et al. 2014. Arthritis Rheumatol. 66(6): 1583-95.

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Abstract Number: 2351

Health Outcomes Among Patients (Pts) with SLE Initiating Belimumab (BEL) with and Without the Use of Immunosuppressants in the Previous 2 Years

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SESSION INFORMATION

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Background/Purpose: BEL efficacy in pts with SLE has been previously demonstrated in clinical and real-world studies.[1] However, there are limited data on differences in outcomes for pts with SLE with different immunosuppressant (IS) treatment use before BEL initiation. This analysis assessed whether IS-naïve pts with SLE initiating BEL varied in their oral CS (OCS) use and clinical outcomes compared with those initiating BEL after the prior IS treatment.

Methods: This retrospective, longitudinal cohort study (GSK Study 217536) used data from the Komodo Health database of de-identified claims between Jan 2015 and Dec 2022. Eligible adults with SLE in the USA were identified from Jan 2017, allowing for ≥24 months of continuous enrollment before BEL initiation (index date). BEL initiators were categorized into 2 cohorts: BEL-0IS (pts who initiated BEL with no prior IS); BEL-1IS (pts who initiated BEL with 1 prior IS). Baseline (BL) was defined as 24 months pre-index. Pts were followed until the end of enrollment or up to 60 months post index. The incidence of SLE flares, organ damage (OD), OCS use, and healthcare resource utilization (HCRU) were stratified by BL moderate/severe disease severity and evaluated using descriptive statistics.

Results: At BL, of the 2719 BEL-0IS pts, 70.2% had moderate and 14.2% had severe SLE; of 4122 BEL-1IS pts, 78.9% had moderate, and 20.9% had severe SLE. BEL-1IS pts had higher BL flare rates (**Table**), partly due the moderate flare definition necessitating IS use. For both cohorts, BL OD was similar between pts with moderate (BEL-0IS: 67.6%; BEL-1IS: 68.4%) and severe SLE (BEL-0IS: 83.9%; BEL-1IS: 82.7%). All-cause BL HCRU was similar between pts with moderate SLE of both cohorts, but higher in BEL-1IS pts with severe SLE than in BEL-0IS pts. At 6 months post index, mean moderate flare rates (per-patient-year, PPY) were 2.2 for BEL-0IS and 4.7 for BEL-1IS in pts with moderate SLE, and 2.9 for BEL-0IS and 6.1 for BEL-1IS in pts with severe SLE; mean severe flare rates were 0.4 for BEL-0IS and 0.5 for BEL-1IS in pts with

Table. BL pt characteristics in the BEL-0IS and BEL-1IS cohorts stratified by disease severity. *Pts were classified into mutually exclusive groups of mild, moderate, or severe disease using a previously published algorithm, which is based on validated measures of SLE activity and the consensus of expert clinical opinion and considers medications of interest and HCRU associated with an SLE-related condition; †evaluated during the 24-month BL period excluding the index date; ‡SLE flare episodes were identified and classified by severity based on a previously published claims-based algorithm, which considers medications of interest and HCRU associated with an SLE diagnosis or SLE-related condition. SD, standard deviation.

	Moderate baseline SLE*		Severe baseline SLE*	
	BEL-0IS (N=1909)	BEL-1IS (N=3252)	BEL-0IS (N=386)	BEL-1IS (N=862)
Organ damage†, n (%)	1290 (67.6)	2223 (68.4)	324 (83.9)	713 (82.7)
SLE flares‡, pts with ≥1 flare, n (%)				
Mild	1727 (90.5)	3127 (96.2)	365 (94.6)	834 (96.8)
Moderate	1886 (98.8)	3252 (100.0)	361 (93.5)	860 (99.8)
Severe	254 (13.3)	490 (15.1)	301 (78.0)	724 (84.0)
All-cause HCRU†, mean ± SD (median)				
Inpatient visits	0.6 ± 1.4 (0.0)	0.6 ± 1.3 (0.0)	1.6 ± 2.6 (1.0)	1.9 ±2.8 (1.0)
Emergency department visits	1.1 ± 2.4 (0.0)	1.2 ± 2.6 (0.0)	2.5 ± 4.5 (1.0)	2.5 ± 4.8 (1.0)
OCS use at index, n (%)	1031 (54.0)	1916 (58.9)	264 (68.4)	632 (73.3)

moderate SLE, and 1.0 for BEL-0IS and 2.1 for BEL-1IS in pts with severe SLE. Notable difference persisted through 60 months post index. The median time to OD was 32.1 months for BEL-0IS and 26.7 months for BEL-1IS in pts with moderate SLE, and 22.7 months for BEL-0IS and 21.6 months for BEL-1IS in pts with severe SLE. In pts with BL OCS use, the median time to OCS discontinuation was 4.5 months for BEL-0IS and 8.9 months for BEL-1IS in pts with moderate BL SLE, and 6.2 months for BEL-0IS and 11.6 months for BEL-1IS in pts with severe BL SLE. Rates (PPY) of all-cause emergency room visits and inpatient stays were similar between pts with moderate SLE of both cohorts, but BEL-1IS pts with severe BL SLE had higher inpatient stay rates (0.7 vs 0.9).

Conclusion: While most BEL pts were able to discontinue OCS within 12 months post index, BEL-0IS pts were able to discontinue OCS in half the time of BEL-1IS pts. SLE flare rates were also notably lower in BEL-0IS pts, although some differences were observed in the cohorts during the BL. Future studies should further investigate optimal BEL placement in the SLE treatment pathway.

Funding: GSK

Reference: 1 Levy RA *et al*. *Lupus* 2021;30:1705–21

Disclosure: Y. Chen: Analysis Group, 3, GSK, 5; **K. Worley**: GSK, 3, 11; **B. Rabideau**: Analysis Group, 3, GSK, 5; **B. Rubin**: GSK, 3, 11; **B. Wu**: Analysis Group, 3, GSK, 5; **R. Chang**: Analysis Group, 3, GSK, 5; **M. DerSarkissian**: Analysis Group, 5, GSK, 5.

Abstract Number: 2352

High Serum C-X-C Motif Chemokine Ligand 10 (CXCL10) Potentially Predicts New Onset of Systemic Sclerosis-Interstitial Lung Disease

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis-interstitial lung disease (SSc-ILD) is the leading cause of death in SSc patients. There is an unmet need for predictive biomarkers of ILD to identify patients at risk, prior to clinical manifestations. Activated IFN-induced chemokines and proteins are implicated in the early inflammatory phase of SSc-ILD. CXCL10 is an IFN-induced chemokine that is important in the chemoattraction of CXCR3-expressing inflammatory cells in SSc-affected tissue.

Methods: One-hundred sixty-five SSc patients (SSc-ILD= 41) and 13 age- and sex-matched healthy controls were retrospectively followed for eight years. Furthermore, 15 SSc patients (SSc-ILD= 7) were prospectively recruited for bronchoalveolar lavage (BAL) procedure. CXCL10 mRNA and protein levels were measured on various levels (serum, BAL, and SSc-ILD lung tissues) by ELISA and nanoString transcriptomic assay. Spearman's correlations were performed between CXCL10 levels in serum and lungs. Kaplan-Meier analyses were performed to evaluate predictability of SSc-ILD using CXCL10 levels at baseline. Human primary lung fibroblasts were treated with BAL fluid or serum from SSc without ILD or SSc-ILD patients. After stimulation, inflammatory (IL-6 and CXCL10)/fibrotic (α-SMA and TGF-β) genes were assessed using qPCR.

TABLE 1: PATIENT CHARACTERISTICS AT BASELINE

	SSc patients without-ILD (n=124)	SSc patients with ILD (n=41)	HC (n=13)	P Value
AGE IN YEARS, MEDIAN (IQR)	61 (54-72)	65 (53-72)	53 (47-57)	p = 0·050
FEMALE, N (%)	102 (82·3)	28 (68·3)	8 (61·5)	p = 0·064
EXTENT OF SKIN INVOLVEMENT, n (%)				p = 0·312
LCSSC	114 (91·9)	35 (85·4)		
DCSSC	9 (7·3)	6 (14·6)		
OTHER	1 (0·8)	0 (0·0)		
PUFFY FINGERS OR SCLERODACTYLY, N (%)	103 (83·1)	35 (85·4)		p = 0·812
PITTING SCARS OR DIGITAL ULCERS, N (%)	66 (53·2)	17 (41·5)		p = 0·211
TELANGIECTASIA, N (%)	83 (74·1)	29 (78·4)		p = 0·704
RAYNAUD'S PHENOMENON, N (%)	124 (100·0)	40 (97·6)		p = 0·249
ANTIBODY PROFILE, N (%)				p = 0·001
ANTI-CENTROMERE	74 (59·7)	8 (19·5)		
ANTI-TOPOISOMERASE I	10 (8·1)	8 (19·5)		
ANTI-RNA POLYMERASE 3	1 (0·8)	0 (0·0)		
OTHER	39 (31·5)	25 (61·0)		
CALCINOSIS CUTIS, N (%)	40 (36·4)	11 (32·4)		p = 0·564
GASTROINTESTINAL INVOLVEMENT, N (%)	88 (73·9)	25 (62·5)		p = 0·249
PFTS, MEDIAN (IQR)				
% FVC	109·0 (95·5120·0)	94·5 (68·8-107·0)		**p < 0·0001**
% DLCO		54·0 (42·5-70·5)		**p < 0·0001**
COPD, N(%)	28 (22·6)	6 (14·6)		p = 0·374
MEDICATION, N(%)				
IMMUNOSUPPRESSION	17 (13·7)	15 (36·6)		**p = 0·0026**
VASODILATORS	16 (12·9)	3 (7·3)		p = 0·497
GLUCOCORTICOIDS	10 (8·1)	7 (17·1)		p = 0·136

lcSSc: limited cutaneous SSc; dcSSc: Diffuse cutaneous SSc; FVC: forced vital capacity, DL_{co}: capacity for diffusion of carbon monoxide, COPD: chronic obstructive pulmonary disease.

Results: At baseline, serum CXCL10 was significantly higher in SSc-ILD patients compared to SSc without ILD patients [Median (IQR): 126 (66-282) vs 79 (50-122), p=0.004] and healthy controls [Median (IQR): vs. 4 (4-9), p< 0.0001]. BAL fluid CXCL10 levels in SSc-ILD patients were not significantly higher than those in SSc without ILD [Median (IQR): 457 (42-725) vs 134 (72-333), p=0.2). However, BAL fluid CXCL10 levels significantly correlated with serum levels (r=0.7, p=0.007). The nanoString showed that CXCL10 gene expression is significantly higher in inflammatory lung tissue compared to fibrotic

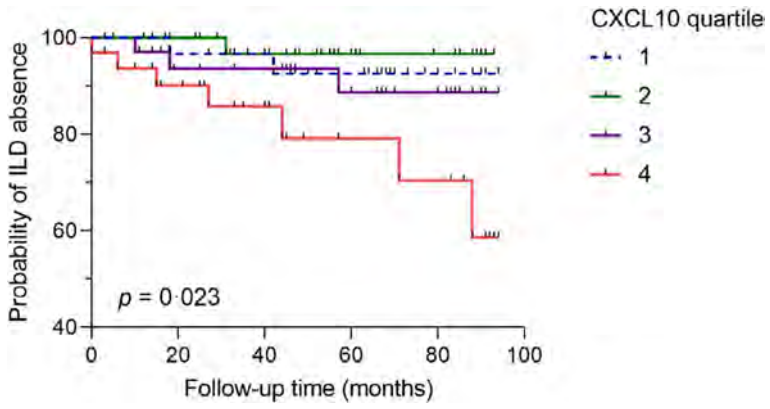

Figure 1: Capacity of CXCL10 to predict long-term ILD development. Kaplan-Meier survival curve according to baseline CXCL10 concentration quartiles. 1st quartile (N=34), 2nd quartile (N=35), 3rd quartile (N=35) and 4th quartile (N=34). CXCL10 levels in the 4th quartile significantly predicted the development of ILD in patients with SSc. p=0·023.

tissue (fold change=2.3, p=0.029). Kaplan-Meier survival analysis (figure 1) revealed that CXCL10 levels >3rd quartile at baseline in SSc patients significantly predicted new onset of ILD (p=0.023). The *in vitro* studies showed that CXCL10 and IL-6 were significantly overexpressed in lung fibroblasts treated with SSc-ILD BAL fluid or serum compared to SSc without

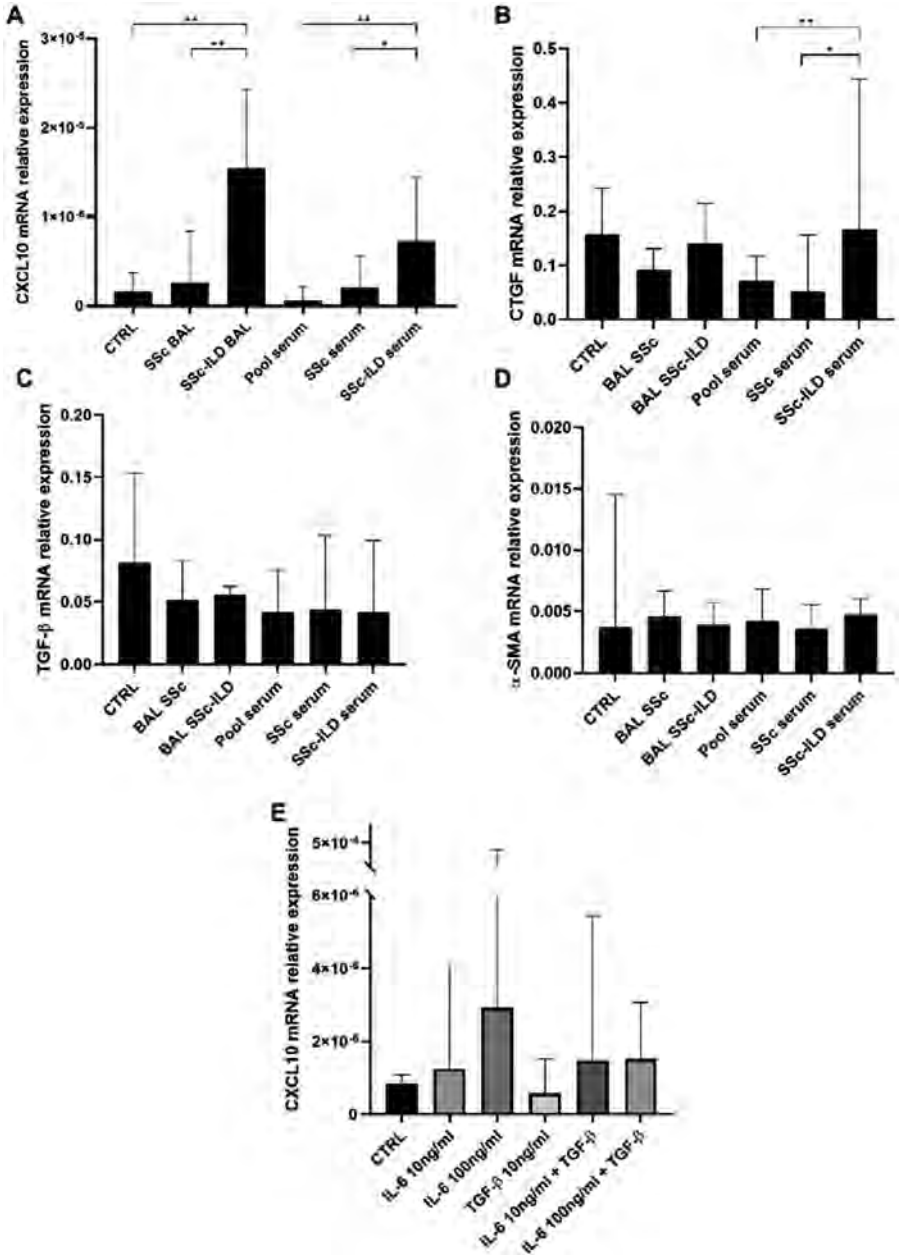

Figure 2: Stimulation of normal human lung fibroblasts with SSc fluids (A-D), or inflammatory or fibrotic cytokines (E). (A-D) 5% BAL supernatant from SSc without ILD (BAL SSc) or SSc-ILD (BAL SSc-ILD), or 1% serum from SSc without ILD (SSc serum) or SSc-ILD (SSc-ILD serum) or healthy control (Pool serum) was used to stimulate lung fibroblasts. (A) SSc-ILD BAL and serum significantly stimulated CXCL10 expression compared to SSc without ILD BAL (p = 0·0043) and serum (p = 0·0087). Also, SSc-ILD BAL significantly stimulated CXCL10 expression compared to CTRL (p = 0·0022) and SSc-ILD serum significantly stimulated CXCL10 compared to healthy serum (p = 0·0022). SSc-ILD serum significantly stimulated CTGF expression compared to SSc without ILD and pool sera (p = 0·026 and p = 0·0087, respectively). (C-D) No significant differences in TGF-β or α-SMA expression when treated with BAL or serum. The results are medians of three technical experiments (n=3) where 6 patients' biofluids were used (n=6). * $p < 0{\cdot}05$; ** $p < 0{\cdot}01$. (E) IL-6 (10ng/ml or 100ng/ml) or TGF-β (10ng/ml) or both were used to stimulate lung fibroblasts for 4h. IL-6 stimulated CXCL10 expression in a concentration-dependent manner. The higher concentration of IL-6 (100 ng/ml) showed increase of CXCL10 expression with a trend towards significance of p value = 0·055 vs CTRL. The results are medians with IQR of three technical experiments (n=3). CTRL: culture media without stimulant.

ILD [(CXCL10: p=0.0043; p=0.0087), (IL-6: p=0.0022; p=0.0043), respectively) and controls (all: p=0.0022). On the contrary, TGF-β and α-SMA expression did not change after treatment in all groups.

Conclusion: CXCL10 is a potential predictive biomarker for new onset of ILD in SSc patients. Further longitudinal studies with larger sample sizes are needed to verify the capability of CXCL10 to predict ILD. Additionally, our nanoString and *in vitro* data strongly suggest that CXCL10 may play a significant role in the early development of SSc-ILD which might be amenable to therapeutic interventions.

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Abstract Number: 2353

Role of Insulin-like Growth Factor Binding Protein-7 (IGFBP7) in Pulmonary Hypertension Pathogenesis and as a Biomarker Systemic Sclerosis-Associated Pulmonary Arterial Hypertension (SSc-PAH)

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc, scleroderma) is an autoimmune connective tissue disease that causes autoimmunity, vascular dysfunction, and fibrosis of the skin, lungs, and other organs. Pulmonary arterial hypertension (PAH) is a severe complication of SSc which can cause right heart failure and is associated with a high rate of morbidity and mortality. Insulin-like growth factor binding protein 7 (IGFBP7) has been shown to be a biomarker for heart failure, and to be elevated in SSc skin. This study assessed IGFBP7 in pulmonary arteries from mice with pulmonary hypertension, and then looked at the potential role of IGFBP7 as a serum biomarker in both mice and patients with SSc-PAH.

Methods: Single cell RNA sequencing was performed on wild-type (WT) and TNF transgenic (TNF-Tg) mice with pulmonary hypertension. After identification of cell types with Seurat, differential gene expression analysis was performed and volcano plots were generated to identify the most differentially regulated genes in each cell type. Trajectory analysis was performed with Monocle, and pseudotime was assessed with Tradeseq. Lungs from WT and TNF-Tg mice were subsequently stained for IGFBP7 (n=6 per genotype) and its binding partner collagen 4a1. Serum from WT and TNF-Tg mice was collected over a time-series (n=4 per condition) and ELISA was performed to determine serum IGFBP7 levels. Blood from SSc patients with pulmonary arterial hypertension (SSc-PAH, n = 26), interstitial lung disease (SSc-ILD, n = 44), no lung disease (SSc-NL, n=44), or healthy control (HC, n =28) were collected and ELISA was performed to determine serum IGFBP7 levels.

Results: TNF-Tg mice develop progressive pulmonary hypertension as they age, making the model suitable for identification of potential disease severity biomarkers. Volcano plots from single cell RNA-sequencing demonstrated that IGFBP7 was among the most overexpressed genes in general capillary cells (Fig.1A), arteriovenous endothelial cells (Fig.1B), Col14+

fibroblasts (Fig.1C), Col13+ fibroblasts (Fig.1D), and myofibroblasts (Fig.1E). Gene expression was elevated across multiple cell types and pseudotime analysis showed IGFBP7 was the gene most elevated in TNG-Tg vs WT lungs across all lineages (Fig. 1F-G). Elevation of IGFBP7 was also observed at the protein level with immunofluorescence staining demonstrating an increased number of perivascular IGFBP7+ cells in close proximity to Col4A1+ cells. Serum concentration of IGFBP7 was elevated in the TNF-Tg mice compared to the WT and showed an increase over time (Fig.2B). To confirm the relevance of these findings in human SSc lung disease, ELISA was performed for IGFBP7 and showed that patients with SSc-PAH had significantly higher serum IGFBP7 concentration compared to controls or SSc patients with ILD or without lung disease.

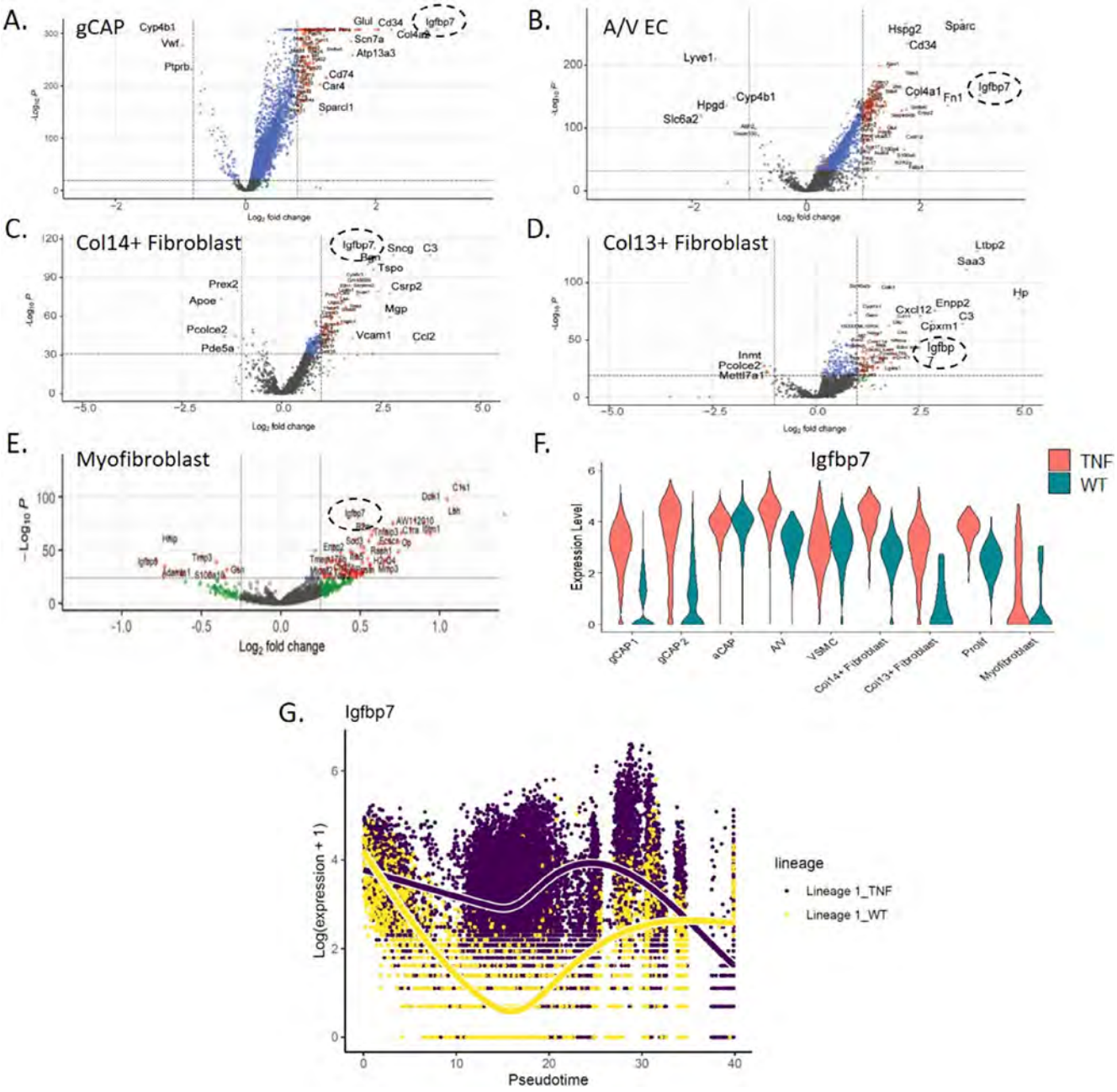


Figure 1. Single cell RNA sequencing of cells isolated from wild type (WT) and TNF transgenic mice (TNF). (A) General capillary endothelial cells, (B) Arteriovenous endothelial cells, (C) Collagen 14+ fibroblasts, (D) Collagen 13+ fibroblasts, and (E) Myofibroblasts. (F) Violin plot of individual cell type IGFBP7 expression and (G) Pseudotime analysis of Igfbp7 across all lineages.

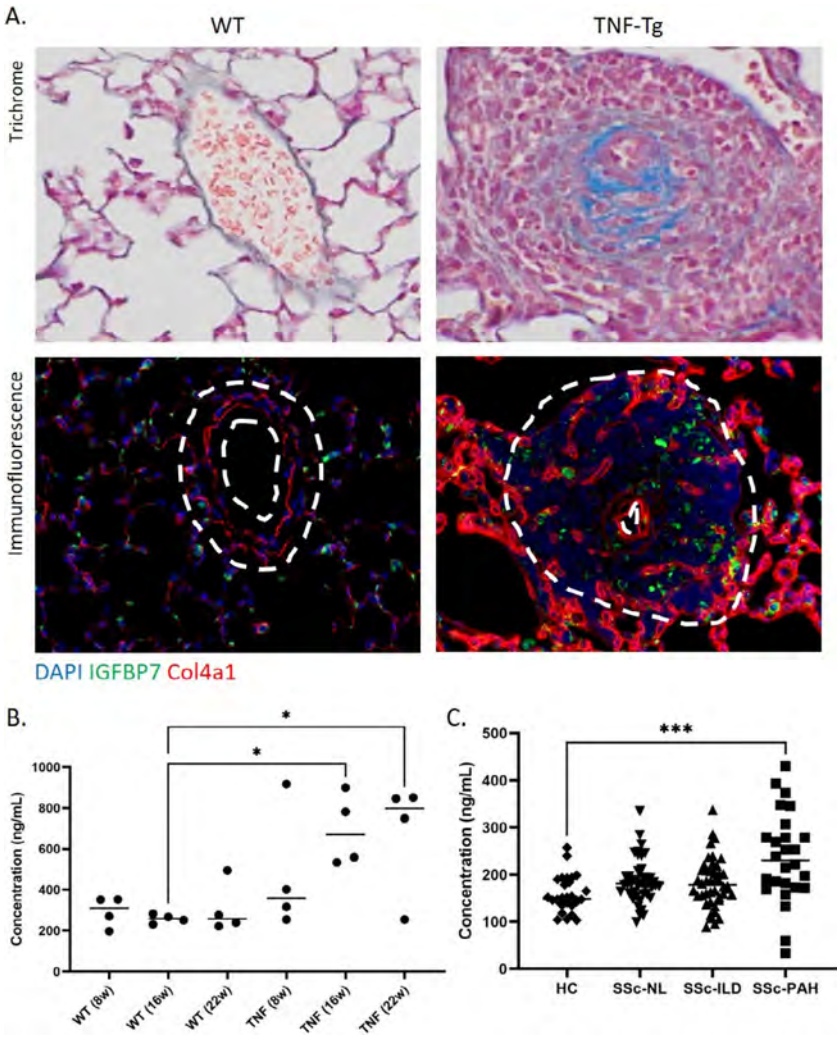


Figure 2. IGFBP7 protein level is elevated in tissue and serum. (A) Masson's trichrome (upper) and immunofluorescence staining (lower) images of pulmonary arteries from WT and TNF mice. Blood vessel lumen and adventitia are highlighted by white dashed lines. (B) Serum IGFBP7 concentration of the WT and TNF mice. *indicates p-value < 0.05. n=4 for per group. (C) Serum IGFBP7 concentration in patients with SSc associated PAH (SSc-PAH), SSc associated ILD (SSc-ILD), SSc with no lung disease (SSc-NL), or healthy control (HC). *** indicates p-value < 0.001. n=26 for PAH, n=44 for ILD, n=44 for NL, and n=28 for HC.

Conclusion: IGFBP7 is significantly upregulated in a TNF-Tg model of pulmonary hypertension across endothelial cells and fibroblasts, and serum levels increase as disease progresses. Patients with SSc-PAH have elevated levels of IGFBP7. Taken together, our data suggest that IGFBP7 is involved in PAH pathogenesis and may serve as a putative biomarker for SSc-PAH.

Disclosure: Y. Jeong: None; **S. Bhattacharya**: None; **M. Garcia-Hernandez**: None; **J. Rangel-Moreno**: None; **Q. Xu**: None; **B. Korman**: Teneofour, Inc, 2.

Abstract Number: 2354

Is Midkine a Novel Biomarker for Acro-osteolysis in Systemic Sclerosis?

Ganiat Adeogun[1], Venkateswara Gogulamudi[2], Meridith Balbach[1], Anthony Donato[2] and Tracy Frech[1], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Salt Lake Veterans Affairs Medical Center, Salt Lake City, UT

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Acro-osteolysis is a hand complication in systemic sclerosis (SSc) characterized by the destruction of distal digital bone possibly related to repetitive ischemia-reperfusion injury. Diagnosis typically involves a thorough medical history, physical examination, and imaging studies. Unfortunately, there is no reliable serological marker to diagnose SSc acro-osteolysis. The growth factor midkine is expressed during bone formation and fracture repair, and it is upregulated in hypoxia to promote angiogenesis. This study aims to develop a noninvasive and reliable biomarker for acro-osteolysis in patients with SSc.

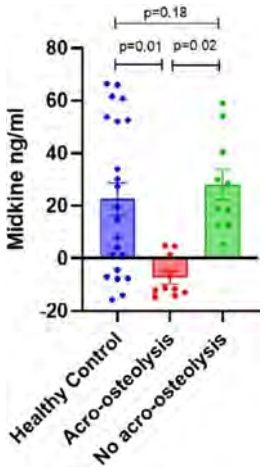
Methods: This study included SSc registry patients (IRB # 1618579) that had same day capillaroscopy, hand radiographs, and serum collection. Midkine levels were compared between SSc patients with and without acro-osteolysis detected on hand radiographs, and age-matched healthy controls. For all patients, plasma midkine concentrations were determined (MDK ELISA, Invitrogen, USA). An ANOVA test was used to assess differences between plasma midkine levels in SSc patients with acro-osteolysis, without acro-osteolysis and healthy controls.

Results: The clinical features of the 20 SSc patients are shown in Table 1. Most patients were white females with an antinuclear antibody (ANA), a SSc-specific autoantibody, limited cutaneous disease, and abnormal nailfold videocapillaroscopy (NVC). There were 10 SSc patients with acro-osteolysis on radiograph and 10 SSc patients without acro-osteolysis. These midkine levels were compared to 20 healthy control samples. The midkine levels were significantly higher in SSc patients with acro-osteolysis compared with no acro-osteolysis (p= 0.02) and healthy controls (p=0.01) (Figure 1). There were no significant differences between healthy controls and SSc patients without acro-osteolysis (p=0.18).

Conclusion: In this small, single-center study, serum level of midkine were significantly reduced in SSc patients with acro-osteolysis when compared to both healthy controls and SSc without acro-osteolysis. Higher levels were associated with intact digital tip on radiograph in SSc patients, which possibly indicates that this growth factor is necessary for maintaining

Clinical Feature:	SSc total population (n=20)	Acro-osteolysis (n=10)	No Acro-osteolysis (n=10)
Age (years), Mean (SD)	53 (12)	51 (9)	56 (14)
Sex: Female	17 (85%)	8	9
Race:			
• White	13 (65%)	8	5
• Black	5 (25%)	1	4
• Asian	1 (5%)	0	1
• Other	1 (5%)	1	0
Disease duration (years) for non-Raynaud's, Mean (SD)	11 (9)	12 (8)	9 (3)
Cutaneous Subset			
• Limited	12 (60%)	6	6
• Diffuse	8 (40%)	5	3
ANA positive	20 (100%)	10	10
SSc autoantibody Subset			
• Centromere	7 (35%)	4	3
• RNA polymerase III	3 (15%)	2	1
• Topoisomerase	2 (10%)	1	1
Digital Ulcers	5 (25%)	3	2
Nailfold Capillaroscopy:			
• Normal	2 (10%)	1	1
• Early	4 (20%)	0	4
• Active	5 (25%)	4	1
• Late	9 (45%)	4	5

Clinical Features of SSc Patients



Serum Levels of Midkine in Healthy Controls (n=20), Systemic Sclerosis (SSc) with acro-osteolysis (n=10), and SSc without acro-osteolysis (n=10)

digital health. Ongoing studies are planned to evaluate serial midkine levels as a novel, predictive biomarker for the development of acro-osteolysis in SSc patients.

Disclosure: G. Adeogun: None; **V. Gogulamudi**: None; **M. Balbach**: None; **A. Donato**: None; **T. Frech**: None.

Abstract Number: 2355

Proteome-based Stratification of Therapeutic Target Population for MT-6194 in Systemic Sclerosis with Pulmonary Arterial Hypertension

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: SSc-related pulmonary arterial hypertension (SSc-PAH) is the one of the leading causes of death in SSc. Early diagnosis and effective therapy for SSc-PAH may lead to improved outcomes. We have been developing MT-6194, a bispecific FynomAb targeting both human IL-17A and IL-6 receptor. To ensure that MT-6194 is used in appropriate patients, we attempted to stratify the patients using serum parameters.

Methods: SSc patients who met the 2013 ACR/EULAR classification criteria were eligible for study participation. We analyzed serum samples from 17 patients with diffuse cutaneous systemic sclerosis, 58 patients with limited cutaneous systemic sclerosis, and 38 healthy controls. PAH was defined as a mean pulmonary artery pressure of ≥25 mm Hg with pulmonary capillary wedge pressure of < 15 mm Hg by right-sided heart catheterization, and an absence of significant interstitial lung disease. The abundance ofserum proteins were analyzed using Proximity Extension Assay (PEA) technology (Olink).

Results: SSc patients were divided into 4 clusters according to their blood levels of IL-6 and IL-17A. SSc patients with high blood levels of both IL-6 and IL-17A had a high prevalence of PAH. We also identified 34 proteins that are upregulated in patients with high blood levels of both IL-6 and IL-17A, and that were significantly correlated with PAH prevalence. Unsupervised hierarchical clustering using the 34 proteins divided SSc patients into three clusters ("PAH cluster 1", "PAH cluster 2", and "PAH cluster 3" were defined). Almost all patients in "PAH cluster 3", where the identified proteins were highly elevated, had PAH. On the other hand, 4 of 30 patients in "PAH cluster 1", where the identified proteins were moderate elevated, had PAH, and there were no patients with PAH in "PAH cluster 2", which has low levels of identified proteins. A %FVC/%DLCO ratio > 1.6 is considered a risk factor for developing SSc-PAH. The %FVC/%DLCO ratio exceeded 1.6 not only in patients in "PAH cluster 3" but also in most patients in "PAH cluster 1". From these results, the 34 proteins can detect not only patients already suffering from PAH, but also patients at high risk of developing PAH. To identify predictive biomarkers of drug response, we evaluated the effects of MT-6194 on in vitro neutralization experiment using fibroblasts. As a result, eight molecules (IL-6, GDF15, LTBP2, CCL7, CHI3L1, EFEFMP1, PLAUR, and SPON1) were found to be upregulated in patients with high blood levels of both IL-6 and IL-17A, upregulated in fibroblast activation, and suppressed by MT-6194. The classification model using these biomarkers could classify not only "PAH cluster 3" but also "PAH cluster 1" with good performance.

Conclusion: Our study investigated the IL-6 and IL-17A-related classification of systemic sclerosis based on serum proteomics. Identified biomarkers stratified patients at increased risk of PAH. The 8-molecule signature identified in this study allowed us to select the appropriate patient population for MT-6194 treatment. Appropriately stratified clinical trials may yield additional treatment options for patients with systemic sclerosis.

Disclosure: Y. Ono: Mitsubishi Tanabe Pharma Corporation, 3; **A. Mogami**: Mitsubishi Tanabe Phama Corporation, 3; **R. Saito**: Mitsubishi Tanabe Pharma Corporation, 3; **N. Seki**: Mitsubishi Tanabe Pharama Corporation, 3; **S. Ishigaki**: None; **H. Takei**: None; **K. Yoshimoto**: None; **K. Chiba**: Mitsubishi Tanabe Pharma Corporation, 3; **T. Takeuchi**: AbbVie, 2, 5, 6, AYUMI, 5, Bristol-Myers Squibb, 6, Chugai, 2, 5, 6, Daiichi Sankyo, 5, Eisai, 5, 6, Eli Lilly Japan, 2, 6, Gilead, 2, 6, Janssen, 6, Mitsubishi-Tanabe, 2, 5, 6, ONO, 5, Pfizer Japan, 6, Taiho, 2; **Y. Kaneko**: AbbVie/Abbott, 1, 6, Ashai Kasei Pharma, 1, 6, Astellas Pharma, 1, 6, AstraZeneca, 1, 6, AYUMI Pharmacutia, 1, 6, Bristol-Myers Squibb(BMS), 1, 6, Chugai-Pharm, 1, 6, Eisai, 1, 6, Eli Lilly, 1, 6, Gilead Sciences Inc., 1, 6, GlaxoSmithKlein(GSK), 1, 6, Janssen Pharmaceutical KK, 1, 6, Novartis, 1, 6, Pfizer, 1, 6, Tanabe Mitsubishi Pharma, 1, 6, UCB Japan, 1, 6.

Abstract Number: 2356

A Macrophage-Specific Mechanism for Mycophenolate Mofetil in the Treatment of Systemic Sclerosis

Emily Morris, Rezvan Parvizi, Patricia Pioli and Michael Whitfield, Geisel School of Medicine at Dartmouth, Hanover, NH

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Sclerosis (SSc) is a rare autoimmune connective tissue disease characterized by inflammation and fibrosis. Treatment with mycophenolate mofetil (MMF), an inhibitor of lymphocyte guanine nucleotide synthesis that targets the enzyme inosine monophosphate dehydrogenase (IMPDH), is associated with clinical benefit in many SSc patients. Although MMF is thought to target lymphocytes exclusively, we have previously shown that MMF also reduces dermal myeloid cell numbers and CCL2 expression in the skin & sera of MMF-responsive SSc patients. Given macrophage

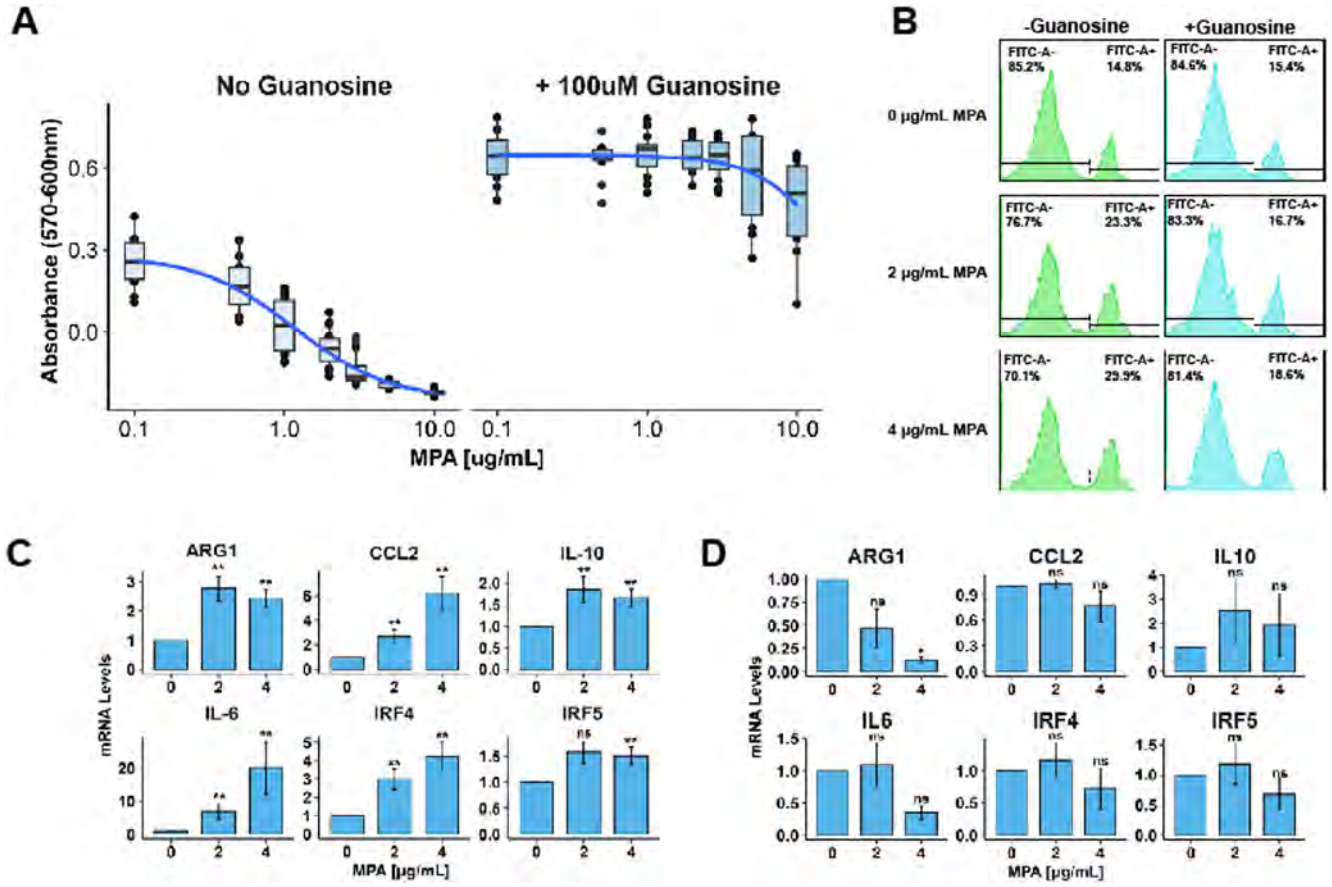

Figure 1: Mycophenolic acid reduces viability of primary human monocytes in vitro and upregulates mRNA expression of alternative activation markers through a guanosine dependent mechanism. (A) Primary human monocytes (n= 4 biological replicates; n = 4 technical replicates per biological replicate) were grown in the following concentrations of MPA for 7 days with or without guanosine supplementation (100µM): 0 µg/mL, 0.5 µg/mL, 1 µg/mL, 2 µg/mL, 3 µg/mL, 5 µg/mL, and 10µg/mL. A CellTiter Blue assay was performed viability of cells after 7 days in culture. Decreased absorbance indicates decreased mitochondrial function and viability; the average IC50 was 1.26 µg/mL MPA for unsupplemented monocytes. (B) Primary human monocytes were grown in 0 µg/mL, 2 µg/mL, or 4 µg/mL MPA for 4 days (n=3 biological replicates) with our without guanosine supplementation (100µM) and assessed for Annexin V (FITC) positivity via flow cytometry as an indicator of apoptosis; increasing concentrations of MPA induced higher levels of Annexin V positive monocytes only in the unsupplemented conditions (representative of 3 independent experiments). (C) and (D) Primary human monocytes were grown in 0 µg/mL, 2 µg/mL, or 4 µg/mL MPA for 4 days (n=4 biological replicates) without (C) and with (D) guanosine supplementation (100µM) for 4 days and assessed for mRNA expression of genes associated with classical and alternative activation. MPA dose-dependently upregulated expression of Arginase-1, CCL2, IL-10, IL-6, and IRF4 in unsupplemented monocytes (C). Supplementation with guanosine (D) consistently blocked this effect (significance of fold change in mRNA expression was assessed by Wilcoxon Ranked Sum test; * $p < 0.05$, ** $p < 0.005$).

plasticity, we hypothesized that, in addition to restricting macrophage skin infiltration, MMF might also mediate direct effects on dermal macrophage pro-fibrotic activation.

Methods: Clinical data from SSc patient cohorts were analyzed for myeloid gene signatures to identify changes in myeloid cell populations during MMF treatment. Primary human monocytes were cultured in clinically relevant serum concentrations of the active metabolite of MMF, mycophenolic acid (MPA), and analyzed for mRNA and surface marker expression, nitric oxide and cytokine production, cell viability and caspase activity in response to MPA. To assess MMF-mediated effects on pro-fibrotic macrophage activation, 3D tissue models of healthy and SSc skin were constructed and treated with or without MPA (0.5-10 µg/mL).

Results: SSc patients on MMF showed a significant decrease in myeloid cell populations in skin biopsies. The clinical target range for serum MPA levels are 1-3µg/mL for MMF patients; the IC_{50} of MPA in primary human monocytes in our experiments was found to be between 0.9-2.5 µg/mL (Fig. 1A), well within the clinical range. MPA dose-dependently induced

apoptosis in primary human monocytes at concentrations as low as 0.5 μg/mL (Fig. 1B). Intriguingly, a subset of monocytes not killed by MPA upregulated surface expression and mRNA levels of markers associated with alternative activation (Fig. 1C). MPA treatment of monocytes in 2D co-cultures with fibroblasts and 3D fabricated skin models showed similar results. Addition of guanosine to cultures significantly attenuated the ability of MPA to induce apoptosis in and modulate activation of monocytes (Fig. 1D).

Conclusion: We now demonstrate here that MMF inhibits primary human macrophage viability and alters macrophage function. Our work suggests that IMPDH activity is required for macrophage viability and mediates alternative activation, as treatment with guanosine rescues cell death and significantly attenuates macrophage phenotype. We thus propose that clinical benefit observed with MMF in the treatment of fibrotic diseases such as SSc may be attributable, at least in part, to effects on myeloid cells.

Disclosure: E. Morris: None; **R. Parvizi**: None; **P. Pioli**: Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 2, 5, Celdara Medical LLC, 2, 5, Pfizer, 5; **M. Whitfield**: Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 2, 5, Celdara Medical, 2, 5, 12, Scientific Founder.

Abstract Number: 2357

The Involvement of CCR3-CCL24 Axis in Endothelial to Mesenchymal Transition Process and Pulmonary Arterial Hypertension in Systemic Sclerosis Patients

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is an autoimmune disease characterized by vascular injury and extensive tissue fibrosis of the skin and internal organs. Endothelial cells (ECs), a predominant target of the autoimmune attack, may undergo proliferation arrest, apoptosis, or differentiation to myofibroblasts, leading to complications including pulmonary arterial hypertension (PAH). The differentiation of ECs into myofibroblasts through endothelial mesenchymal transition (EndMT) represents a critical step in the blood vessels remodeling. ECs in the dermal microvascular tissue of patients with SSc exhibit robust expression of CCR3, the cognate receptor of CCL24,which has been found to be elevated in the serum and skin biopsies of SSc patients. The objective of this study is to evaluate the association between serum CCL24 levels and clinical characteristics of SSc patients, as well as the involvement of the CCL24-CCR3 axis in EndMT process.

Methods: CCL24 levels were evaluated in the sera of 75 SSc patients using ELISA. In this cohort, Pearson correlation tests were conducted to determine the relationship between CCL24 levels and performance measures such as the 6-minute walk test (6MW test). To study the potential association of CCL24 and CCR3 with the processes underlying EndMT, we established an in-vitro system in which the combination of TGFβ TNFα induced EndMT in human umbilical vein endothelial cells (HUVECs) and explored the expression of CCR3 and the effect of CCL24 supplementation and anti CCL24 antibody to this

system. Studies included functional assessment of proliferation, cell death migration as well as evaluation of multiple markers of EndMT processes including αSMA, Vimentin, SNAIL, CD31 and VE-cadherin.

Results: The average level of CCL24 in the sera of patients with SSc with PAH (n=9) was significantly higher compared to the level of patients with SSc and without PAH (1136 vs 738 pg/ml, $p< 0.05$). Furthermore, a negative correlation was found between CCL24 levels and the 6MW test performance ($r=-0.3$, $p< 0.05$), reflecting reduced exercise capacity. The addition of TGFβ and TNFα resulted in EndMT in HUVECs, which was demonstrated by a significant increase in mesenchymal markers, reduced ECs markers, reduced cell number (52%, $p< 0.05$), and increased cell migration (112%, $p< 0.05$) relative to control. Furthermore, the EndMT process was associated with a significant increase in CCR3 levels (197%, $p< 0.05$). Notably, adding CCL24 in addition to TNFα and TGFβ further reduced cell count (from 52% to 33%, $p< 0.05$) and increased migration (from 112% to 127%, $p=0.07$). CCL24 neutralizing antibody (CM-101) completely inhibited cell migration and increased cell number.

Conclusion: This study provides evidence for the potential role of CCL24 in the pathogenesis of SSc and highlights its involvement in EndMT process resulting in disease complications such as PAH.

Disclosure: I. Amoyal: Chemomab Ltd, 5; **T. Hornik-Lurie**: Chemomab Ltd, 5; **T. Zitman-Gal**: Chemomab Ltd, 5; **H. Levy**: Chemomab Ltd, 3; **I. Vaknin**: Chemomab Ltd, 3; **L. Drucker**: Chemomab Ltd, 5; **I. Heusler**: Chemomab Ltd, 5; **Y. Levy**: Chemomab Ltd, 5; **S. Tartakover Matalon**: Chemomab Ltd, 5.

Abstract Number: 2358

Neutrophil Extracellular Traps Induce Endothelial-to-Mesenchymal Transition and Associate with Vascular Complications in Scleroderma

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (**SSc,** also known as scleroderma) is a disease characterized by fibrosis, autoimmunity, and vasculopathy. Many devastating complications such as digital ulcerations, scleroderma renal crisis, and pulmonary hypertension are the result of deranged vasculature. Neutrophils and neutrophil extracellular traps (**NETs**) have recently been revealed as drivers of diverse vasculopathies. Here, we investigated the potential role of NETs in SSc vascular complications.

Methods: Plasma from SSc patients (cohort 1: n=29, cohort 2: n=37) and healthy controls (n= 21) were evaluated for NET remnants (MPO-DNA complexes) and another marker of neutrophil activation (calprotectin) via ELISAs. For cohort 2, we compared diffuse SSc patients with known vascular complications (digital ulcers, pulmonary hypertension, and scleroderma renal crisis) to a cohort matched for age, sex, and disease duration but without vascular complications. To assess the effect of NETs on endothelial-to-mesenchymal transition (**EndoMT**), healthy human umbilical vein endothelial cells (**HUVECs**) or human dermal microvascular endothelial cells (**MVECs**) were treated with NETs (0.1-1 μg DNA/ml), TGF-β (10-100 ng/ml), or NETs + TGF-β. Gene expression of mesenchymal markers *ACTA2* and *S100A4* was measured by quantitative PCR.

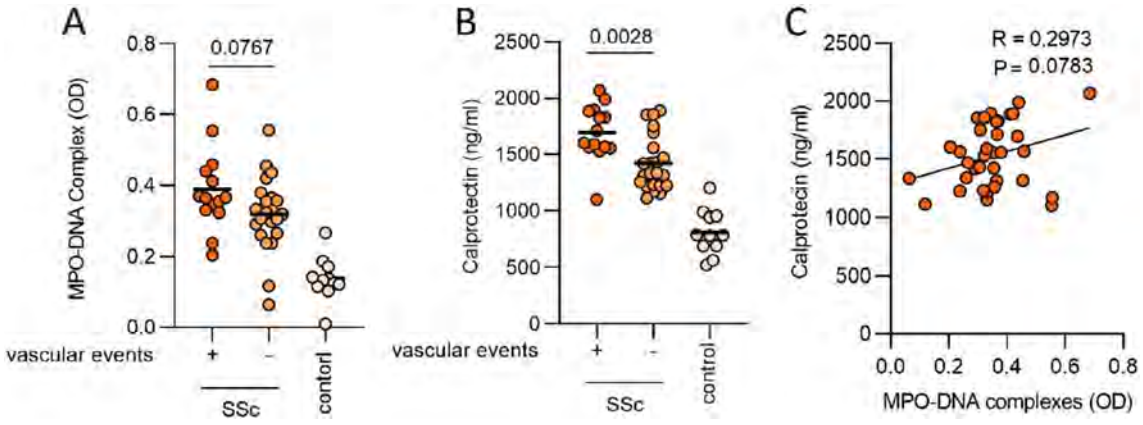

Fig 1: Plasma from SSc patients with vascular complications (n = 14), SSc patients without vascular complications (n = 23), and healthy controls (n = 11) were assessed for (A) MPO-DNA complexes and (B) calprotectin. Groups in A and B were compared by unpaired t-test, and Pearson correlation was computed for C.

Results: We tested cohort 1 (mixed SSc subtypes) and found higher levels of NET remnants in the plasma of patients with SSc compared to healthy controls (MPO-DNA complexes, mean 2.1 vs. 0.89 μg/ml, P=0.0018). At the same time, we found more plasma calprotectin in patients with diffuse SSc as compared with limited SSc (P=0.033). We then focused on patients with diffuse SSc (cohort 2), some with a history of vascular complications, and some without (**Figure 1**). We found more plasma calprotectin in patients with a history of vascular complications (P=0.0028); there was also a trend toward higher levels of NET remnants in the vascular patients although it missed statistical significance (P=0.0767). Interestingly, we found a positive correlation between circulating NETs and TGF-β (R=0.405, P=0.032), the latter a molecular determinant of fibrosis in SSc. We next assessed the potential role of NETs as inducers of EndoMT and the extent to which NETs might synergize with TGF-β in this induction. The combination of NETs and TGF-β (both at suboptimal concentrations) increased the expression of mesenchymal markers *ACTA2* (P=0.035) and *S100A4* (near significance at P=0.051) in HUVECs as compared with NETs or TGF-β alone. At higher concentrations (1 μg DNA/ml), NETs alone were also able to induce EndoMT (P=0.001). Notably, the addition of anti-NET therapies including anti-histone 4 (P=0.0007), DNase (P=0.034), and a neutrophil elastase inhibitor (P=0.0003) significantly reduced NET-mediated EndoMT (**Figure 2**).

Conclusion: Our data suggest that SSc patients with vascular complications have higher circulating markers of neutrophil activation than a matched cohort without vascular complications. Our data also suggest that NETs, similar to TGF-β, can contribute to EndoMT, and that anti-NET therapies might have potential for combatting EndoMT and vascular disease in SSc.

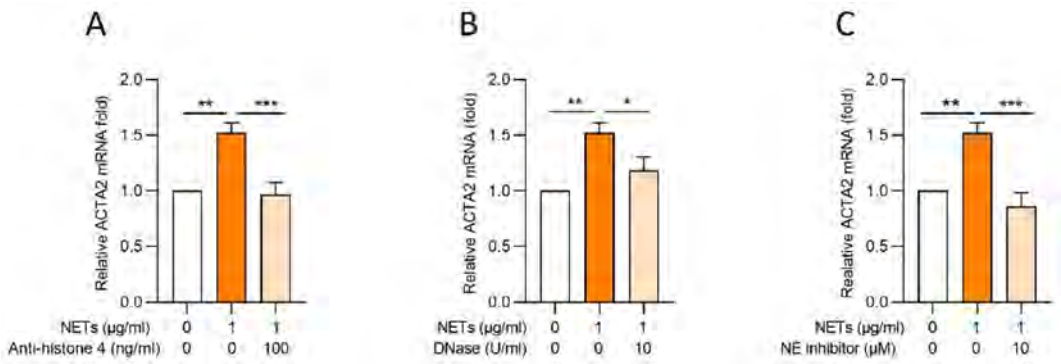

Fig 2: HUVECs were stimulated with NETs for 24 hours in the presence or absence of (A) anti-histone 4, (B) DNase, and (C) the NE inhibitor Sivelestat. The expression of mesenchymal markers was quantified by quantitative PCR. Groups were compared by unpaired ANOVA with correction for multiple comparisons.

Disclosure: R. Ali: None; **W. Liang**: None; **C. Shiple**: None; **R. Gedert**: None; **S. Huang**: None; **C. Sarosh**: None; **E. Tsou**: None; **D. Khanna**: AbbVie, 12, DSMB, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb, 2, 5, CSL Behring, 2, Genentech, 2, Horizon Therapeutics, 2, 5, Janssen, 2, 6, Pfizer, 5, Prometheus, 2; **J. Knight**: Jazz Pharmaceuticals, 2.

Abstract Number: 2359

Reversal of the Activation State of Pro-fibrotic CD206 Positive Macrophages by Therapeutic Peptide AUR300 in Systemic Sclerosis

Sandra Lopez[1], Bahja Ahmed Abdi[1], Linda Lei[1], Anas Al-Oweidi[1], Claire Macfadyen[1], Lydia Nagib[1], Sarah Ive[1], Anshul Kumar[1], Teresa Collins[1], Jennifer Cross[2], Christopher Denton[1], David Abraham[1], Clayton Yates[3], Charles Garvin[4], Henry Lopez[4], George Martin[5] and **Richard Stratton**[1], [1]University College London, London, United Kingdom, [2]Aurinia Pharmaceuticals Inc., Rockford, MD, [3]Tuskegee University, Tuskegee, AL, [4]Riptide Bioscience Inc., Valejo, CA, [5]Riptide Bioscience Inc., Bethesda, MD

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: A spectrum of macrophage activation is seen in human pathologic conditions; M2-like CD206 positive macrophages are pro-fibrotic and proresolution, while M1-like macrophages are proinflammatory, as identified by polarisation *in vitro*. CD206 positive macrophages are under study as potential targets for inflammatory fibrotic conditions

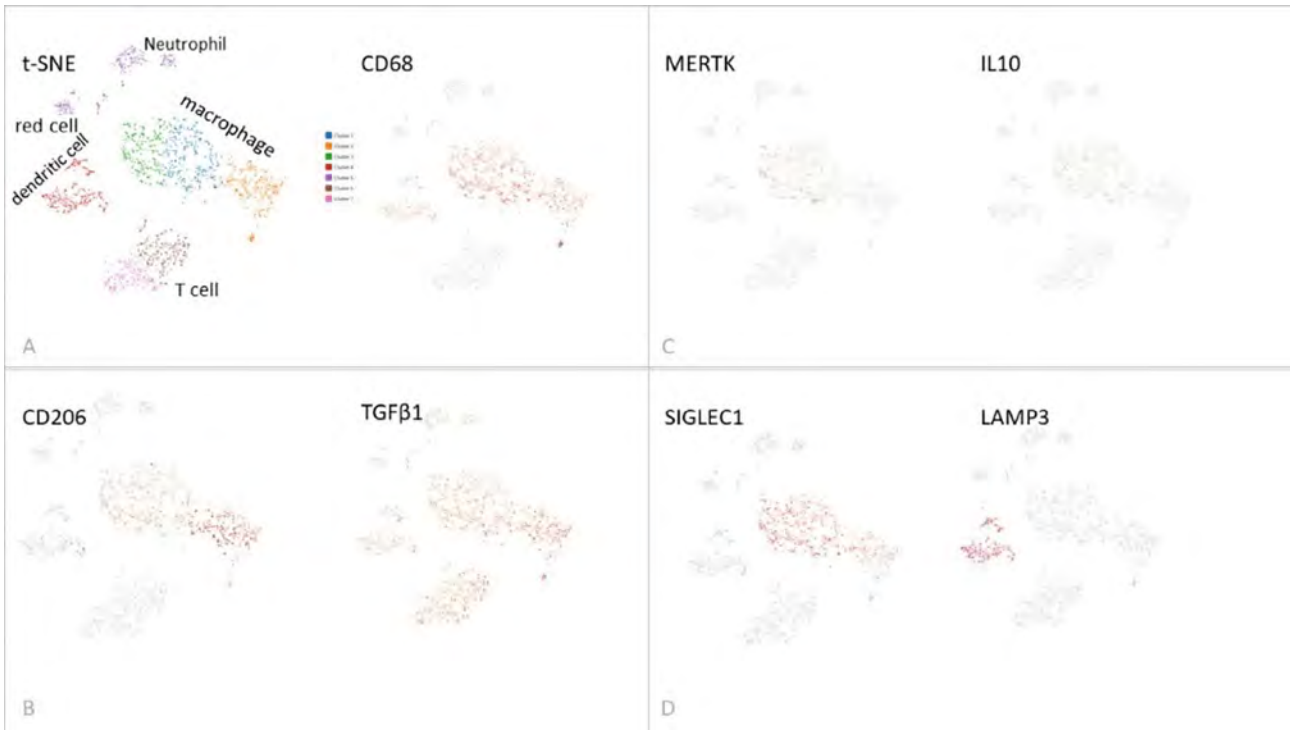

Figure 1 Single cell RNAseq of blister fluid derived cells from anti-Scl70 positive SSc patient. (A) Tissue derived immune cell populations and pan-macrophage marker CD68. (B) Pro-fibrotic CD206 cells. (C) Possible regulatory macrophages expressing MERTK and IL10. (D) Distinct tissue macrophage (SIGLEC1) and dendritic cell (LAMP3) cell populations.

including systemic sclerosis (SSc). We investigated SSc lesional macrophages by single cell profiling and Akoya Multiplex immunochemistry and evaluated the effects of AUR300, a novel peptide therapeutic that targets M2 macrophages via CD206, the mannose receptor.

Methods: Suction blister fluid-derived cells from lesional skin were profiled by 10X RNAseq matched to AKOYA antibody staining to characterise the tissue resident immune cells, including the CD206 positive macrophages of interest (n=12 SSc patients and controls).Tissue culture modelling with patients' blood monocyte-derived macrophages and disease fibroblasts (n=6 SSc cell lines), as well as bleomycin induced lung fibrosis as a model of organ involvement, were used to determine efficacy and mechanism of action of the therapeutic AUR300 peptide.Soluble CD206 (sCD206) (n=140 SSc and n=80 healthy control (HC) plasma samples) and cellular CD206 (n=17 SSc, n=9 HC macrophage lines) were investigated as potential biomarkers of SSc disease activity.

Results: CD206 positive macrophages were found in a spectrum of activation states varying from MERTK high CD206 low IL10 expressing regulatory cells, to CD206 high MERTK negative TGFβ expressing pathogenic cells (Figure 1) implicated in cross talk with fibroblasts, in the affected tissue and model systems. Exposure to disease microenvironments enhanced CD206 levels and triggered IL-6 release, reversed by the therapeutic AUR300 peptide ($p < 0.05$ for CD206, $p< 0.0013$ for IL-6, $p< 0.018$ for gel contraction, for effect of 10 μM AUR300) (Figure 2), which also attenuated inflammation and fibrosis in the bleomycin lung fibrosis model.Cross-talk with disease fibroblasts involved cytokines (IL-6, TSP-1) and growth factors (TGFβ and PDGF-BB) acting in concert. CD206 was elevated in plasma (HC 552±25, lcSSc 521±32, dcSSc 645±32, sCD206 pg/ml mean±SEM, $P< 0.026$ for dcSSc), tissue fluid (HC 31±3, SSc 48±6, pg/ml $P< 0.041$) and cells (HC 628, 485-729, SSc 663, 294-1932, median, range, fluorescence, P NS) as a biomarker, linked to severe resistant disease (highest in anti-Scl70 group).

Conclusion: In disease tissue, CD206 positive macrophages represent a spectrum of activation states, from pro-resolving MERTK IL-10 expressing cells, to pathogenic cells releasing profibrotic cytokines and growth factors in activating microenvironments. AUR300 reverses the activation state in SSc cell-based and murine *in vivo* models and represents a potential therapeutic for patients with strong CD206 positive signatures.

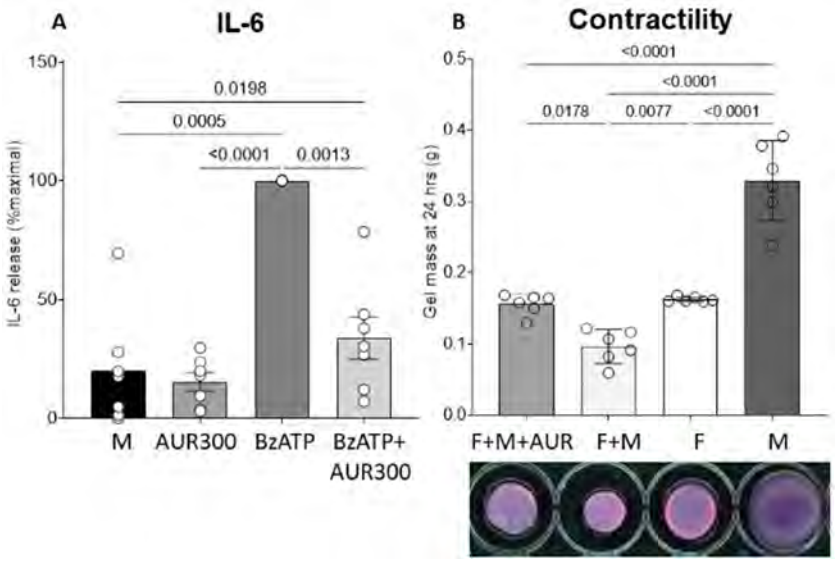

Figure 2 Effect of AUR300 on SSc macrophage activity in tissue culture models systems. (A) SSc blood monocyte-derived macrophage cultures were activated by stimulation with BzATP (0.1mM) with or without addition of AUR300 (10μM) which supressed the induction of IL-6 release. (B) In SSc macrophage-fibroblast co-cultures, macrophage induced fibroblast gel contraction was suppressed by the AUR300 compound (10μM). (AUR=AUR300 10μM, F= SSc fibroblasts, M=SSc macrophages,).

Disclosure: S. Lopez: None; **B. Ahmed Abdi**: None; **L. Lei**: None; **A. Al-Oweidi**: None; **C. Macfadyen**: None; **L. Nagib**: None; **S. Ive**: None; **A. Kumar**: None; **T. Collins**: Aurinia Pharmaceuticals Inc., 3; **J. Cross**: Aurinia Pharmaceuticals Inc., 3; **C. Denton**: AbbVie, 2, Acceleron, 2, Arxx Therapeutics, 5, Bayer, 2, Boehringer-Ingelheim, 2, 6, Corbus, 2, 6, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Horizon Therapeutics, 2, Inventiva, 2, 5, Janssen, 6, Roche, 2, Sanofi, 2, Servier, 5; **D. Abraham**: None; **C. Yates**: Riptide Bioscience Inc., 4; **C. Garvin**: Riptide Bioscience Inc., 4; **H. Lopez**: Riptide Bioscience Inc., 4; **G. Martin**: Riptide Bioscience Inc., 4; **R. Stratton**: Aurinia Pharmaceuticals Inc., 5, Riptide Bioscience Inc., 5.

Abstract Number: 2360

Systemic Sclerosis Macrophages Stimulate Calcinosis in Adipose Derived Mesenchymal Stem Cells via the Activin a Pathway

Tamara Searle[1], Ujvalla Kalluri[1], Sonia Ahmad[2], Bahja Ahmed Abdi[1], Sandra Lopez[1], Shiwen Xu[1], Teresa Collins[1], Jennifer Cross[3], George Martin[4], Henry Lopez[5], Clayton Yates[6] and **Richard Stratton**[1], [1]University College London, London, United Kingdom, [2]Holy Family Red Crescent Medical College, Dhaka, Bangladesh, [3]Aurinia Pharmaceuticals Inc., Rockford, MD, [4]Riptide Bioscience Inc., Bethesda, MD, [5]Riptide Bioscience Inc., Valejo, CA, [6]Tuskegee University, Tuskegee, AL

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Calcinosis may result from localised trans-differentiation of tissue resident stem cells in the subcutaneous layer of affected skin in systemic sclerosis (SSc), as a severe disabling manifestation linked to ischaemia and local trauma.Beyond SSc, inherited defects in Activin A responsive pathway (*ACTVAR1*) result in widespread calcinosis, as seen in Fibrodysplasia Ossificans Progessiva, where macrophages are implicated as the source of excess tissue Activin A.We investigated the possible induction of SSc calcinosis in a tissue culture model generated by stimulation of adipose derived mesenchymal stem cells (MSCs) with SSc patients' macrophages and explored the relevance of the Activin A pathway.

Methods: Clinical associations were screened in a database of well-characterised SSc patients with symptomatic calcinosis (n=28) and SSc without calcinosis (n=51). Human subcutaneous fat derived MSCs were cultured in osteogenic media, with or without SSc patients' monocyte-derived macrophages, with or without inhibitors, AUR300 10μM (peptide inhibitor of M2 macrophages) or SB431542 10μM (antagonist of Activin/ALK5 pathway). Cultures were stained with Alizarin red for osteogenesis on day 21. Macrophage secreted levels of Activin A under basal and ATP-stimulated conditions, were assayed by ELISA (Biotechne), as were plasma levels in n= 57 diffuse SSc patients (n=26 anti-Scl70, n=22 anti-RNA polymerase and 9 anti-U3RNP subgroup) and 21 healthy controls (HC).

Results: Most clinical characteristics did not differ significantly between patients with calcinosis and those without, including clinical subset, age, gender, disease duration, organ involvement or autoantibody subtype (all P values NS), whereas digital ulceration (DU) was associated with calcinosis (DU in 16/28 calcinosis and 13/51 no calcinosis, chi square P< 0.008). Notably, Activin A levels were increased in SSc patients' plasma samples when compared to controls, only in diffuse anti-Scl70 patient subgroup (plasma Activin A healthy controls 147, 80-249, anti-Scl70 SSc 261, 136-590 pg/ml, median, IQR, P< 0.05 Mann Whitney) (Figure 1A). Moreover, anti-Scl70 SSc patients' macrophages, released Activin A in tissue culture, enhanced by stimulation with BzATP (0.1 μM) and inhibited by AUR300 (10μM) (Figure 1B), and stimulated calcinosis in the MSC model, where addition of SSc macrophages (M) to the MSC cultures induced Alizarin red positive osteogenic foci

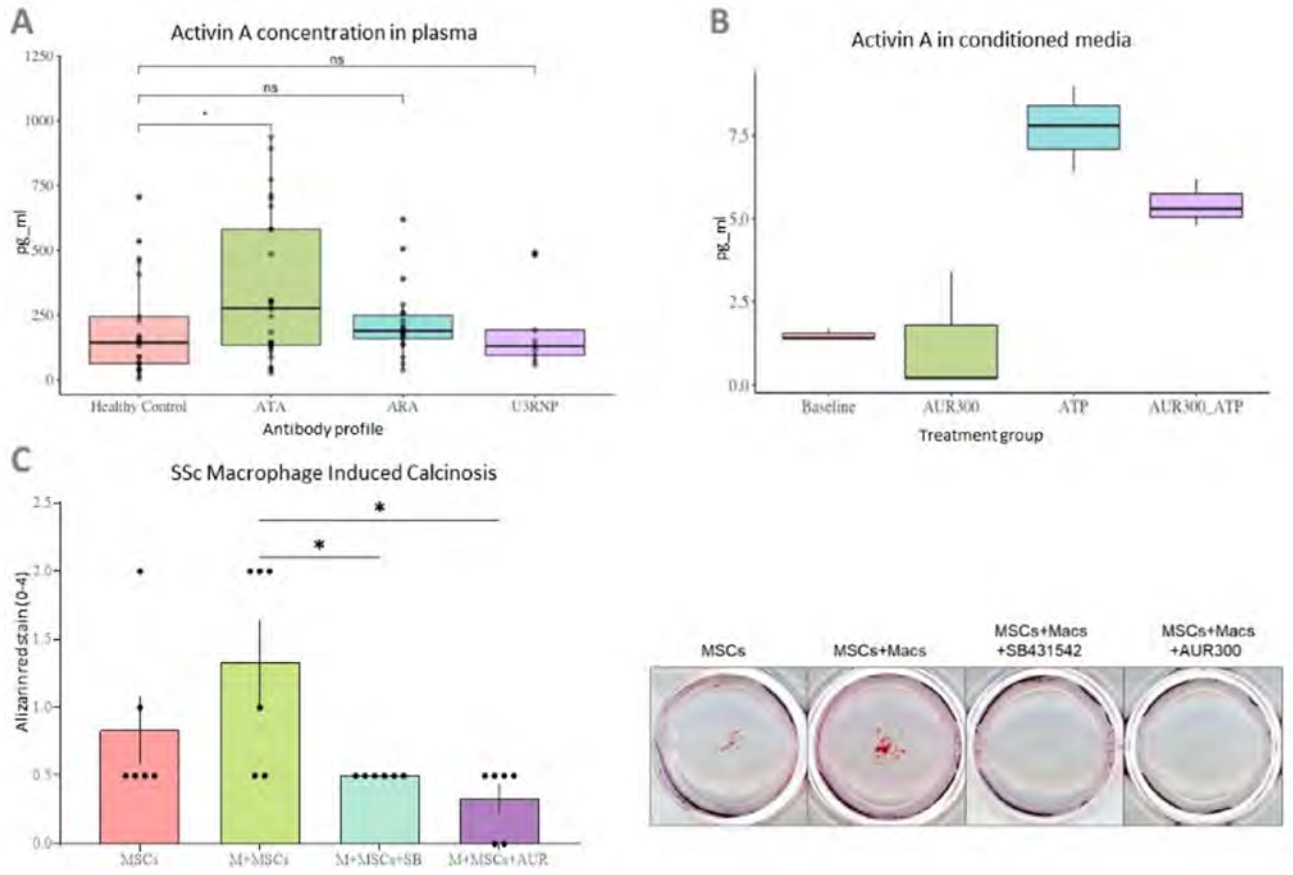

Figure 1 Role of activin A/ALK5 pathway in SSc macrophages induced calcinosis. (A) Plasma levels of Activin A are raised in diffuse SSc anti-Scl70 (ATA) group. (B) Release of Activin A by anti-Scl70 positive SSc patient's macrophages under basal and BzATP stimulated conditions: effect of peptide drug AUR300. (C) Role of activin A in anti-Scl70 SSc macrophage-induced MSC calcinosis model; antagonism by Activin/Alk5 signalling by inhibitor SB431542 and by M2 macrophage inhibitor. (ATP=0.1 μM BzATP, AUR=AUR300 10μM, M=macrophages, MSC=mesenchymal stem cells, SB=SB431542 10 μM, ARA=anti-RNA polymerase, ATA=anti-Scl70 subgroup, U3RNP=anti-U3RNP, *=P<0.05).

at 21 days, blocked by both AUR300 and SB431542 (MSCs 0.833+/-0.247, MSCs+M 1.33+/-0.307, MSCs+M+SB 0.5+/-0, MSCs+M+AUR300 0.33+/-0.105, Alizarin Red stain 0-4, P< 0.012 for AUR300 effect) (Figure 1C).

Conclusion: Calcinosis occurs in both diffuse and limited SSc subsets and across autoantibody subgroups and was associated with digital ulceration.Elevated plasma levels of Activin A, most notable in anti-Scl70 subgroup, is consistent with systemic upregulation of the Activin A pathway in SSc.Activated macrophages from SSc patients are a potential source of Activin A capable of stimulating MSCs via an osteogenic/calcinosis model.The AUR300 and SB431542 compounds as studied represent potential therapeutic inhibitors of this severe and currently resistant complication of SSc.

Disclosure: T. Searle: None; **U. Kalluri**: None; **S. Ahmad**: None; **B. Ahmed Abdi**: None; **S. Lopez**: None; **S. Xu**: None; **T. Collins**: Aurinia Pharmaceuticals Inc., 3; **J. Cross**: Aurinia Pharmaceuticals Inc., 3; **G. Martin**: Riptide Bioscience Inc., 4; **H. Lopez**: Riptide Bioscience Inc., 4; **C. Yates**: Riptide Bioscience Inc., 4; **R. Stratton**: Aurinia Pharmaceuticals Inc., 5, Riptide Bioscience Inc., 5.

Abstract Number: 2361

Optimal Combination of Circulating Biomarkers for Predicting the Progression of Interstitial Lung Disease in Patients with Systemic Sclerosis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: In patients with systemic sclerosis (SSc), progression of interstitial lung disease (ILD) is associated with an increased mortality. Since the course of SSc-ILD is highly variable, it is critical to predict the progression of ILD in clinical practice as well as in clinical trial setting. Previously reported risk factors for ILD progression include male, progression of skin thickness in diffuse cutaneous SSc (dcSSc), short SSc duration, anti-Scl-70, and elevated inflammatory markers and Krebs von den Lungen-6 (KL-6). The aim of this study was to examine performance of inflammatory markers and KL-6 to efficiently enrich patients who subsequently experience ILD progression in SSc patients using a single-center prospective cohort.

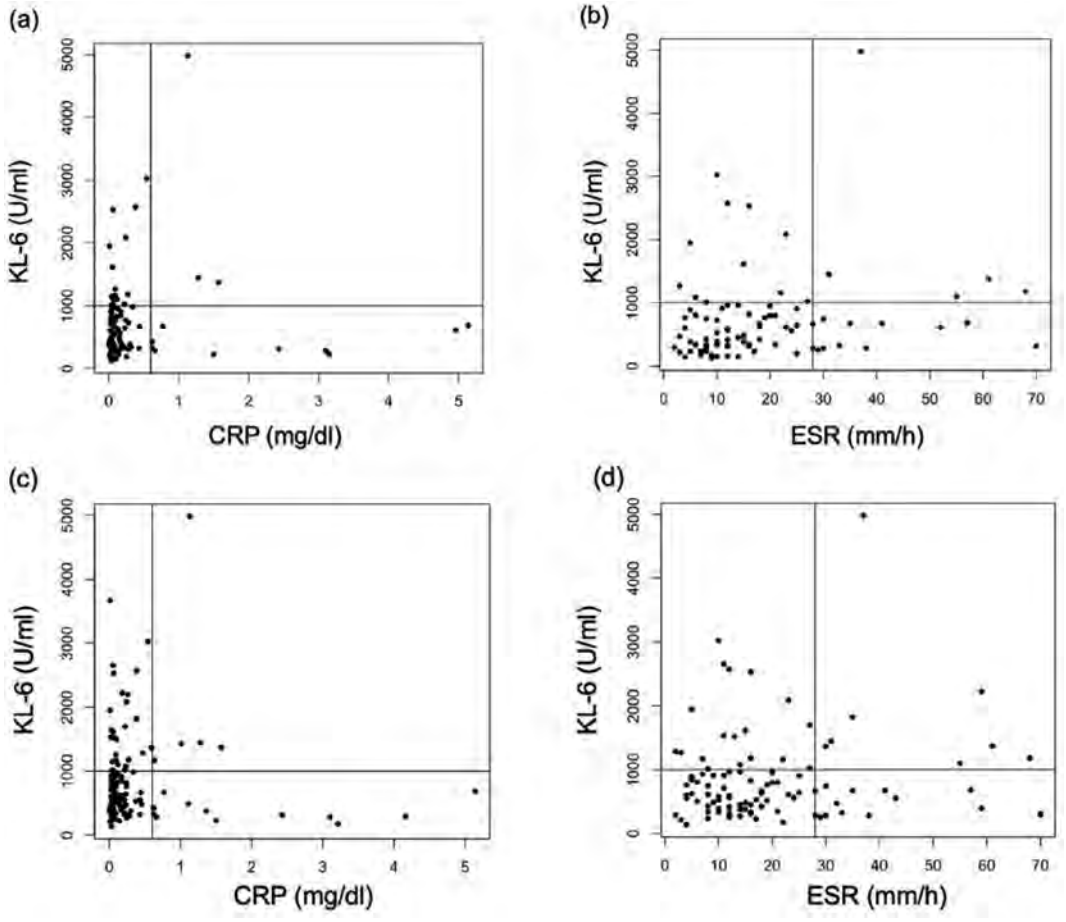

Figure 1. Scatter plot of CRP/ESR and KL-6 in dcSSc (a, b) and SSc-ILD cohorts (c, d).

Table 1. The AUC, sensitivity, and specificity of serum biomarkers and their combinations for predicting PF-ILD and PPF in dcSSc and SSc-ILD cohorts.

Variables	dcSSc						SSc-ILD					
	PFILD			PPF			PFILD			PPF		
	AUC	Sensitivity (CI)	Specificity (CI)	AUC	Sensitivity (CI)	Specificity (CI)	AUC	Sensitivity (CI)	Specificity (CI)	AUC	Sensitivity (CI)	Specificity (CI)
CRP≧0.6	0.51 (0.44-0.59)	0.15 (0.81-0.94)	0.88 (0.80-0.94)	0.48 (0.40-0.55)	0.09 (0.03-0.24)	0.86 (0.84-0.90)	0.51 (0.45-0.57)	0.14 (0.05-0.26)	0.88 (0.81-0.95)	0.49 (0.43-0.55)	0.11 (0.05-0.21)	0.87 (0.84-0.91)
ESR≧28	0.47 (0.38-0.55)	0.13 (0.05-0.28)	0.80 (0.77-0.85)	0.46 (0.37-0.54)	0.11 (0.03-0.29)	0.80 (0.78-0.84)	0.44 (0.36-0.52)	0.15 (0.07-0.27)	0.74 (0.70-0.79)	0.44 (0.36-0.53)	0.14 (0.06-0.28)	0.74 (0.71-0.79)
KL-6≧1000	0.57 (0.47-0.66)	0.27 (0.12-0.46)	0.86 (0.78-0.94)	0.54 (0.44-0.64)	0.24 (0.11-0.40)	0.85 (0.81-0.89)	0.64 (0.55-0.73)	0.45 (0.34-0.56)	0.83 (0.77-0.88)	0.61 (0.52-0.71)	0.43 (0.30-0.56)	0.80 (0.75-0.85)
CRP≧0.6 or ESR≧28	0.48 (0.38-0.58)	0.22 (0.10-0.38)	0.75 (0.71-0.80)	0.45 (0.35-0.55)	0.17 (0.06-0.36)	0.74 (0.71-0.78)	0.46 (0.37-0.55)	0.26 (0.15-0.39)	0.67 (0.62-0.73)	0.45 (0.36-0.55)	0.24 (0.13-0.39)	0.67 (0.63-0.72)
KL-6≧1000 or CRP≧0.6	0.57 (0.47-0.68)	0.38 (0.24-0.54)	0.76 (0.72-0.81)	0.54 (0.42-0.65)	0.33 (0.18-0.52)	0.74 (0.7-0.79)	0.62 (0.53-0.71)	0.52 (0.40-0.64)	0.72 (0.67-0.78)	0.59 (0.49-0.68)	0.49 (0.35-0.62)	0.69 (0.64-0.74)
KL-6≧1000 or ESR≧28	0.53 (0.42-0.64)	0.36 (0.22-0.52)	0.70 (0.65-0.76)	0.52 (0.40-0.64)	0.35 (0.19-0.54)	0.69 (0.65-0.74)	0.57 (0.47-0.66)	0.53 (0.40-0.64)	0.61 (0.54-0.67)	0.55 (0.45-0.66)	0.52 (0.38-0.65)	0.59 (0.54-0.65)
KL-6≧1000 or CRP≧0.6 or ESR≧28	0.54 (0.43-0.66)	0.44 (0.28-0.64)	0.64 (0.53-0.74)	0.51 (0.39-0.64)	0.40 (0.20-0.60)	0.63 (0.51-0.73)	0.56 (0.46-0.65)	0.58 (0.45-0.69)	0.54 (0.47-0.60)	0.53 (0.43-0.63)	0.55 (0.40-0.68)	0.52 (0.46-0.57)

Methods: Two cohorts, including patients with dcSSc (n=109) and those with SSc-ILD (n=136), were selected from our prospective SSc registry. 87 patients with dcSSc and ILD were included in both cohorts. C-reactive protein (CRP) ≥6 mg/L and erythrocyte sedimentation rate (ESR) ≥28 mm/hour were used as increased inflammatory markers, and a cutoff point of increased KL-6 was provisionally set at 1,000 U/mL. ILD progression was defined as the first event developing progressive fibrosing ILD (PF-ILD) or progressive pulmonary fibrosis (PPF). Receiver Operating Characteristic Curve (ROC) analysis was conducted to determine the sensitivity, specificity and area under the curves (AUCs) and the Youden index was used to identify the appropriate cutoff. Cumulative rates free from ILD progression were assessed using Kaplan-Meier analysis and statistical comparisons were made using log-rank test.

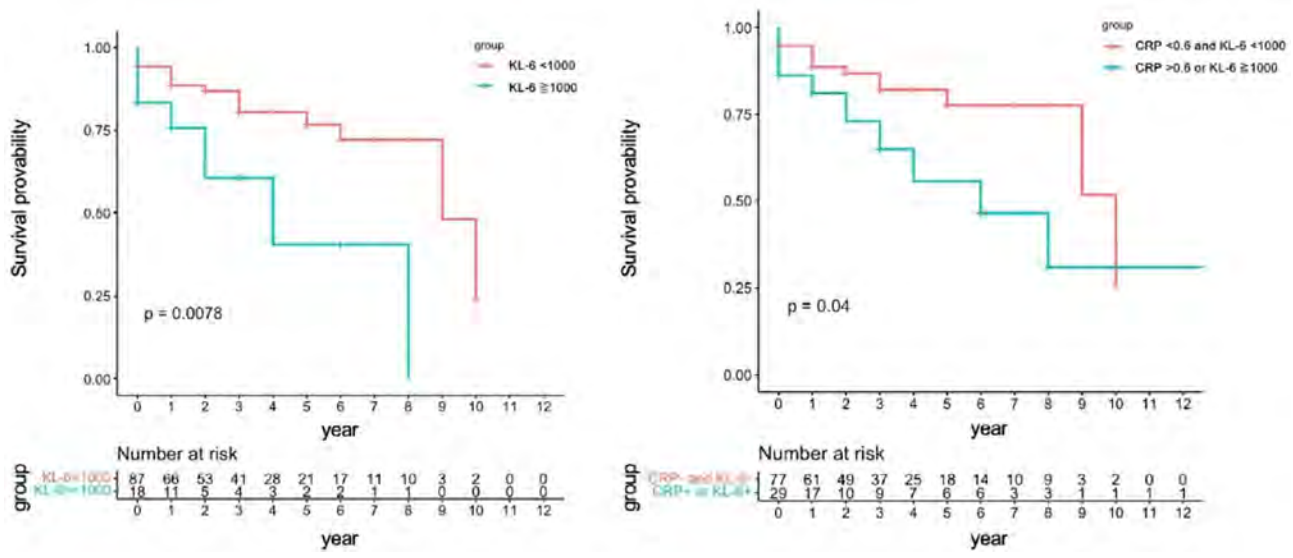

Figure 2. Kaplan-Meier analysis of cumulative PF-ILD-free survival rates in patients with dcSSc, stratified by the groups based on KL-6 or KL-6/CRP combination.

Results: Median disease duration at baseline was 15.0 and 23.5 months in dcSSc and SSc-ILD cohorts, respectively. In dcSSc cohort, 27 (25%) and 22 (20%) patients developed PF-ILD and PPF during median follow-up of 37 month, respectively; and 43 (31%) and 36 (26%) in SSc-ILD cohort developed PF-ILD and PPF during median follow-up of 43.5 months, respectively. There was no correlation between inflammatory markers and KL-6 (Figure 1). The specificity of CRP, ESR and KL-6 to predict ILD progression was favorable (74-88%), but sensitivity of CRP and ESR was low (9-15%). KL-6 provided better sensitivity (24-45%) (Table 1). The combination of CRP and KL-6 showed the best AUCs (0.54-0.62), with increased sensitivity (33-52%) while mainlining acceptable specificity (69-76%). Regardless of how ILD progression is defined, Kaplan-Meier analysis showed that the patients with increased KL-6 experienced ILD progression more frequently than those without. The same trend was observed for the KL-6/CRP combination (Figure 2). Optimal cut-offs of KL-6 to predict PF-ILD and PPF were found to be lower than provisional cut-off in dcSSc (∼610 U/mL) and SSc-ILD (820 U/mL) and the models using these data-driven cut-offs improved AUCs compared to provisional setting.

Conclusion: We propose use of combination of KL-6 and CRP in the inclusion criteria for enriching "at risk" patients in clinical trials for SSc, while optimal cut-off need to be further defined using different multicenter cohorts.

Disclosure: K. Yomono: None; **D. Khanna**: AbbVie, 12, DSMB, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb, 2, 5, CSL Behring, 2, Genentech, 2, Horizon Therapeutics, 2, 5, Janssen, 2, 6, Pfizer, 5, Prometheus, 2; **M. Kuwana**: AbbVie/Abbott, 6, Asahi-Kasei, 5, 6, Astellas, 6, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, 6, Chugai, 2, 5, 6, Corbus, 2, Eisai, 6, GlaxoSmithKlein(GSK), 2, Horizon, 2, Janssen, 6, Kissei, 2, MBL, 2, 5, Mitsubishi Tanabe, 2, 5, 6, Mochida, 2, 6, Nippon Shinyaku, 6, Ono, 5, 6.

Abstract Number: 2362

Identification of Protein Biomarkers Associated with the Severity and Risk of Progression of Interstitial Lung Disease in VEDOSS and Established Systemic Sclerosis Patients

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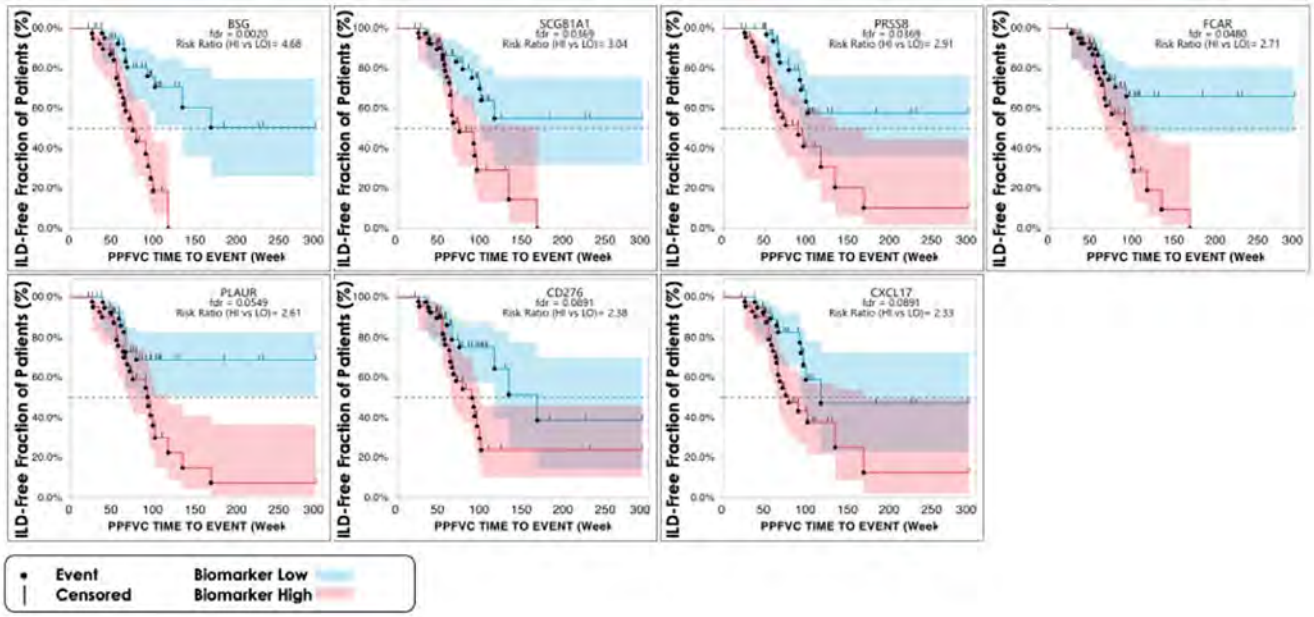
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Pulmonary Fibrosis (PF) is one of the primary causes of systemic sclerosis (SSc)-related death. Hence, monitoring and predicting the course of PF in SSc remains a critical need in patient management. Furthermore, the stratification of patients based on their risk of PF progression should be improved the feasibility of clinical studies. Here, we explore the relationships of a subset of protein biomarkers (pBMs), initially identified as prognostic of disease worsening in progressing fibrosing interstitial lung disease (ILD) (Bowman WS et al *Lancet Respir Medicine* 2022), with the severity and risk of PF in Very Early Diagnosis of SSc (VEDOSS) and established limited (lcSSc) and diffuse cutaneous SSc (dcSSc).

Methods: Hundreds one patients (33 VEDOSS, 21 lcSSc, and 47 dcSSc) were selected from the ongoing SSc registry at the University of Leeds. Using a proximity extension assay, we determined the relative levels of 34 PF-ILD-related pBMs in the serum samples. Association with the presence of ILD at baseline was calculated using a t-test, with the severity of ILD



(Percent Predicted FVC) at baseline using Pearson's correlation, and with the risk of FVC decline using a Proportional Hazard model based on the median-dichotomized pBM levels at baseline. All 101 patients were combined for these analyses, and Benjamini-Hochberg FDR correction for multiple comparisons was applied.

Results: Out of 34 pBMs, we identified 8 BMs differentially expressed between VEDOSS, lcSSc, and dcSSc patients with or without ILD at baseline. AGER was lower in patients with ILD, suggesting a positive beneficial relation with ILD. Conversely, the remaining 7 pBMs (ITGB6, KRT19, PRSS8, SCGB3A2, IL1RN, SERPINB8, and HGF) were higher in patients with ILD, suggesting a potentially detrimental link with ILD. Consistent with these observations, AGER correlated positively with baseline ppFVC, while the other 5 pBMs correlated negatively with baseline ppFVC. Finally, we identified 7 pBMs (BSG, SCGB1A1, PLAUR, FCAR, PRSS8, CD276, and CXCL17) associated with the relative risk of ILD progression (figure 1; as defined by a reduction of ppFVC of 0.05/week). PRSS8 was the only pBM shared across the three analyses, suggesting a possible role of this peptidase in lung fibrosis.

Conclusion: In this pilot study, we confirmed the association of a subset of the pBMs identified by Bowman et al. with the presence, severity, and risks of progression of ILD in VEDOSS, lcSSc, and dcSSc patients. Notably, the pBMs associated with the presence and severity of lung fibrosis differed from those associated with the risk of progression. While these results could lead to useful biomarker tools for the stratification and monitoring of lung fibrosis in VEDOSS and SSc patients, we need to confirm these results in an additional group of prospectively recruited VEDOSS and established SSc.

Disclosure: T. Sornasse: AbbVie, 3, 11; **V. Kakkar**: None; **R. Ross**: None; **S. Kim**: AbbVie/Abbott, 3, Merck/MSD, 11; **F. Del Galdo**: AbbVie/Abbott, 5, arxx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, capella, 2, Chemomab, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Mitsubishi-Tanabe, 2, 5.

Abstract Number: 2363

Increase in Macrophage Infiltration in Scleroderma Esophageal Mucosa Is Associated with Motility and Mucosal Complications

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science
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Session Time: 9:00AM–11:00AM

Background/Purpose: The macrophage activation is elevated in systemic sclerosis (SSc) patients, and is implicated in pathogenesis of tissue inflammation, fibrosis, and the development of skin disease and interstitial lung disease. The gastroesophageal manifestations are common in SSc, with significant motility and mucosal complications. In this study, we aimed to investigate the potential influence of macrophages in SSc esophagus.

Methods: In this single-center observational study, we prospectively enrolled patients with SSc and primary gastroesophageal reflux disease (GERD) patients to the study. The SSc patients fulfilled the 2013 ACR/EULAR Classification Criteria. The primary GERD patients were examined by gastroenterologist and rheumatologist by clinical and serology tests to exclude possible autoimmune diseases and other structural gastrointestinal disorders.

The patients underwent a series of esophageal and gastric examinations including upper gastroendoscopy, high-resolution esophageal manometry, and middle-portion esophageal endoscopic mucosal biopsy. The erosive esophagitis was graded with Los Angeles classification and the diagnosis of motility disorder was classified according to Chicago Classification version 4.0.

The esophageal biopsy specimens were examined using light microscopy with hematoxylin-eosin stain, and immunohistochemical stains with CD117, Desmin, CD3, CD20, and CD68.

The statistical significance was calculated using Fisher's exact test for binomial parameters and Wilcoxon rank sum exact test for continuous and categorical data.

Immunohistochemical stains	SSc (n=22)	GERD (n=6)	p-value
CD117	0 (0%)	0 (0%)	
Desmin	12 (55%)	0 (0%)	0.024
CD3	22 (100%)	3 (50%)	0.002
CD20	2 (9.1%)	0 (0%)	>0.9
CD68	15 (68%)	0 (0%)	0.005

GERD, gastroesophageal reflux disease; SSc, systemic sclerosis

Systemic sclerosis (n=22)	CD68-positive (n=15)	CD68-negative (n=7)	p-value
UES Resting Pressure (mmHg)	39 (13, 45)	19 (13, 33)	0.3
UES IRP 0.2s (mmHg)	7.7 (5.9, 9.7)	11.7 (10.3, 15.1)	0.007
UES IRP 0.8s (mmHg)	13.5 (10.5, 18.4)	18.8 (16.6, 24.3)	0.052
LES Resting Pressure (mmHg)	13 (8, 18)	13 (8, 22)	0.7
LES IRP 4s (mmHg)	3.8 (0.0, 12.8)	1.6 (0.3, 11.3)	>0.9
Erosive esophagitis (LA grade)			0.3
0	4 (27%)	5 (71%)	
1	7 (47%)	1 (14%)	
2	3 (20%)	1 (14%)	
3	1 (6.7%)	0 (0%)	
Erosive esophagitis	11 (73%)	2 (29%)	0.074

IRP: integrated relaxation pressure; LA grade: Los Angeles classification grading; LES, lower esophageal sphincter; UES, upper esophageal sphincter

Results: From September 2021 to March 2023, 22 SSc patients and 6 primary gastroesophageal reflux disease patients completed the study. The median ages and female sex were similar across both groups. The rates of erosive esophagitis (59% vs. 33%, p = 0.4) and the LA gradings (p = 0.6%) were comparable. On immunohistochemical stains, the SSc patients exhibited increased T cell (100% vs. 50%, p = 0.006) and macrophage (68% vs. 0%, p = 0.008) infiltrations.

In SSc patients, the presence of esophageal macrophage infiltration was not associated with age, female sex, GERD and dysphagia symptoms, the proportion of the absent contractility on manometry, the interstitial lung disease, the functional vital capacity, or the diffusion of carbon monoxide. However, the macrophage infiltration is associated with a decreased upper esophageal sphincter relaxation pressure (7.7 vs. 11.7 mmHg, p = 0.007) and numerically higher rates of erosive esophagitis (73% vs. 29%, p = 0.074.)

Conclusion: In this study, we found a higher proportion of T cell and macrophage infiltrations in SSc patients compared with primary GERD individuals, irrespective of the mucosal complications. The macrophage infiltration in SSc patients was associated with decreased esophageal sphincter pressure and numerically higher incidence of erosive esophagitis. The observation supported the pathological role of macrophages in SSc and indicated its significance in developing esophageal mucosal and functional complications.

Disclosure: T. Lee: None; **T. Lan**: None; **K. Li**: None; **S. Hsieh**: None; **P. Tseng**: None.

Abstract Number: 2364

Circulating CTHRC1 Levels Are Associated with Disease Severity and Predict Survival in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Despite recent advances in systemic sclerosis (SSc), there remains a paucity of clinically actionable biomarkers to assess disease severity and predict progression. Collagen triple helix repeat containing-1 (CTHRC1), a protein secreted during tissue-repair that regulates fibroblast function and vascular remodeling after arterial injury has been reported to be a marker for a subpopulation of fibroblasts uniquely found in lungs of SSc-ILD patients. The aim of this study was to determine whether serum levels of CTHRC1 are associated with specific disease manifestations and predict clinical outcomes in SSc.

Table 1: Demographic and clinical characteristics of SSc patients and healthy controls

	Normal (N=41)	SSc (N=377)
CTHRC1		
Mean (SD)	16300 (5750)	33300 (18600)
Median [Min, Max]	15100 [9360, 30900]	29500 [7670, 139000]
Age (years)		
Mean (SD)	60.4 (7.13)	54.7 (13.4)
Median [Min, Max]	59.0 [50.0, 74.0]	56.0 [19.0, 85.0]
Sex		
Male	18 (43.9%)	56 (14.9%)
Female	23 (56.1%)	321 (85.1%)
Race		
White	31 (75.6%)	214 (56.8%)
Hispanic	0 (0%)	72 (19.1%)
Black	3 (7.3%)	34 (9.0%)
Asian	6 (14.6%)	51 (13.5%)
Other	1 (2.4%)	6 (1.6%)
Disease Duration (years)		
Mean (SD)		9.77 (8.24)
Median [Min, Max]		7.56 [0.0400, 40.8]
SSc Subtype		
Limited		249 (66.0%)
Diffuse		128 (34.0%)
ACA positive (%)		
		99 (26.3%)
Scl70 positive (%)		
		97 (25.7%)
RNAPol III positive (%)		
		64 (17.0%)
mRSS		
Mean (SD)		6.03 (6.45)
Median [Min, Max]		3.00 [0, 36.0]
ILD Present (%)		
		196 (52.0%)
PAH Present (%)		
		76 (20.2%)
Severe Vascular Disease (%)		
		29 (7.7%)

Methods: Retrospective analysis of a prospectively collected longitudinal cohort was performed using a large, well characterized cohort of SSc patients, fulfilling the ACR/EULAR 2013 classification criteria, and healthy controls. Serum levels of CTHRC1 were measured by ELISA in 377 SSc patients and 40 healthy controls (Table 1). SSc patients were stratified by quartiles of CTHRC1 serum level for analysis. Quartile characteristics were compared using ANOVA/Chi-Square and mixed models were utilized to assess the association of CTHRC1 serum level with SSc disease manifestations and severity, including skin disease, interstitial lung disease (ILD), pulmonary arterial hypertension (PAH), and peripheral vascular disease. Survival analysis, as defined by time to death or lung transplantation, was assessed by Kaplan-Meier analysis between quartiles with long-rank test.

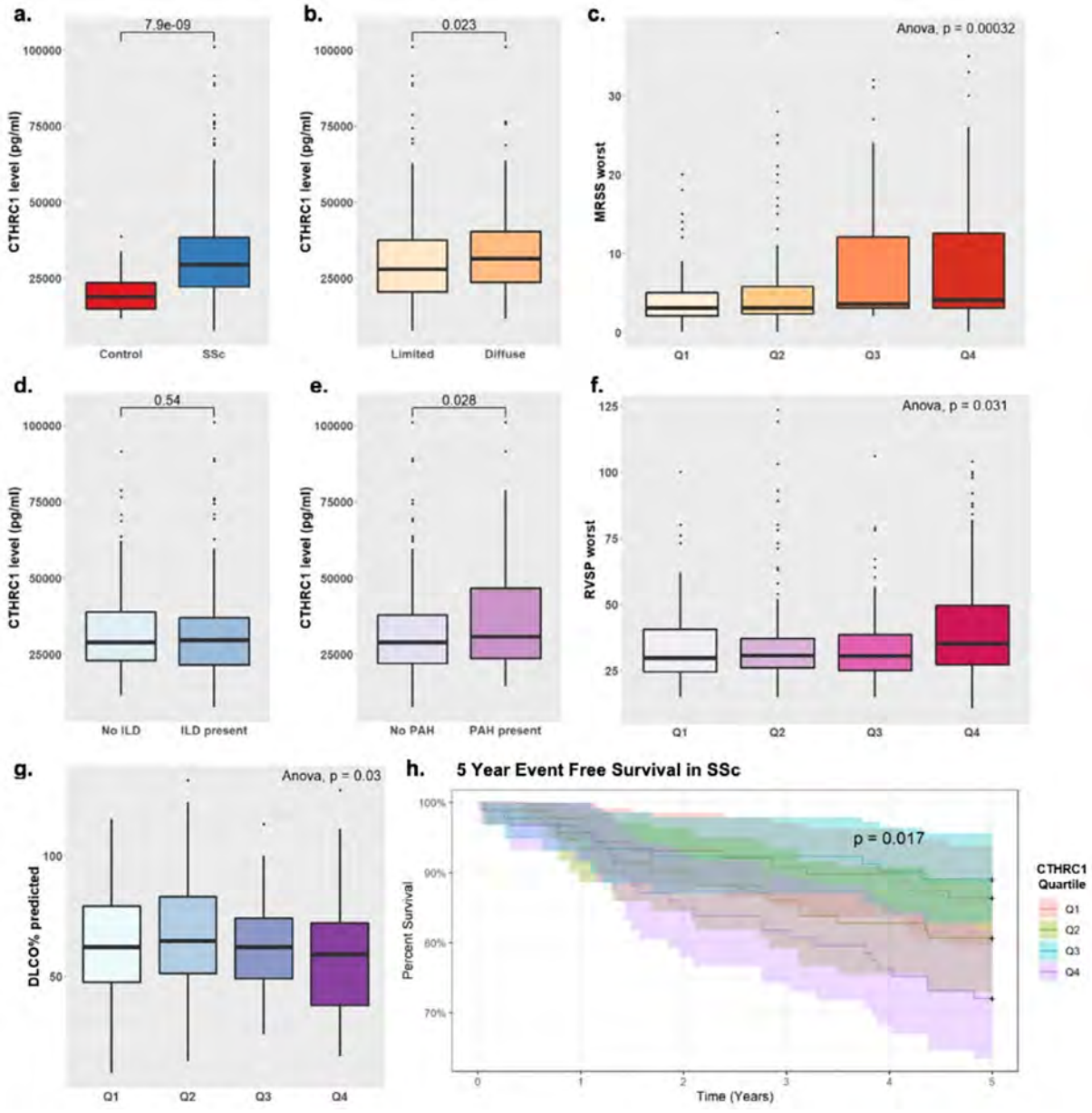

Figure 1: Serum CTHRC1 levels are elevated in SSc patients (a) and associated with skin disease severity (b-c), PAH severity (d-g) and 5 year event free survival (h). Q1 represents quartile of patients with lowest serum CTHRC1 level while Q4 represents highest.

Results: Serum CTHRC1 was significantly increased in SSc patients compared to healthy controls (Fig 1a). After controlling for age, sex, race, disease duration and SSc antibody status, elevated CTHRC1 was independently associated with skin disease severity ($p< 0.05$) and PAH (OR=1.43 per 10k pg elevation, p=0.005). Patient with diffuse skin disease had significantly higher CTHRC1 than limited skin disease (p=0.023) (Fig 1b) and elevated CTHRC1 was associated with both increased MRSS at time of serum measurement (p=0.003) and worst MRSS recorded (p=0.005) (Fig 1c). CTHRC1 was not associated with the presence of ILD, however was significantly elevated in subjects with PAH (Fig 1d-e). After controlling for covariates, higher CTHRC1 levels were significantly associated with markers of PAH severity, including decreased DLCO% predicted ($p< 0.001$) and elevated RVSP (p=0.003) at time of serum measurement as well as for worst recorded values (p=0.01) (Fig 1f-g). Elevated CTHRC1 serum level was associated with worse survival among SSc patients (Fig 1h).

Conclusion: Circulating CTHRC1 levels are increased in SSc patients and exhibit a significant association with more severe skin disease, PAH, and worse survival. While it remains to be determined whether CTHRC1 is directly implicated in the disease pathologic process, these findings suggest that circulating CTHRC1 may be further validated as a clinically actionable biomarker in SSc.

Disclosure: M. Yang: None; **S. Lee**: None; **L. Hazelwood**: AbbVie/Abbott, 3, 11; **D. Sheppard**: None; **F. Boin**: None; **P. Wolters**: None.

Abstract Number: 2365

Decoding the Peripheral Immune Landscape of Systemic Sclerosis to Investigate Disease Stages and Interstitial Lung Disease Progression

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a heterogenous autoimmune disease characterized by fibrosis, vascular abnormalities and immune dysregulation. Characterization of peripheral blood immune signatures in relation to disease stages and progression remains insufficiently defined. Understanding these immune signatures may shed light to SSc pathogenesis underpinning distinct disease stages and states.

Methods: The study included a cohort of SSc patients (n=15), age and sex matched to healthy controls (n=7). We compared immune signatures of SSc patients at different stages ("very early diagnosis of SSc" (VEDOSS), early < 3 years and late >5 years from disease onset) and ILD status (stable vs progressive). Clinical and laboratory parameters were recorded for auto-antibody profile, immunosuppressive treatment and disease activity including ILD status. Peripheral blood mononuclear cells of SSc patients were analysed by high dimensional Mass Cytometry (CyTOF) approach employing 73 unique markers to identify perturbations in SSc immunome in comparison to healthy controls. A high throughput analytical and discovery platform, EPIC (Extended Polydimensional Immune Characterization) was deployed for multi-dimensional data analysis and clustering to identify significantly perturbed immune cell subsets.

Results: Unsupervised clustering revealed significant differences in T and NK cell subsets. Supervised analysis revealed activated CD4+ cells expressing CXCR4 and type 1 IFNs (IFI44 and IFI44L) to be significantly increased in SSc compared to healthy controls. This was particularly more pronounced in the late stage of disease and for patients with stable ILD. CXCR4 are known to mediate migration of lymphocytes, endothelial progenitor cells and stem cells and may play a key role in tissue fibrosis. Conversely, a decreased number of cytotoxic NK cells expressing CX3CR1 were found in SSc. CX3CR1 is a mediator of chemotaxis for immune cells and a significant decrease could potentially indicate impaired immunosurveillance in SSc patients. This subset was significantly decreased in the early and late stages of disease and in stable ILD state.

Conclusion: These findings shed light on the heterogeneity of SSc and provide insights into the differential characteristics of disease stages. Understanding the mechanism underlying SSc disease progression and immune perturbations will aid in early diagnosis and intervention. This could contribute to the development of targeted therapeutic strategies and better management of this debilitating disease. Further investigations are warranted to explore the functional significance of increased activated CD4 cells expressing CXCR4 and decreased cytotoxic NK cells expressing CX3CR1 in SSc, as well as to identify potential therapeutic targets that could mitigate disease progression and restore immune homeostasis in affected individuals.

Disclosure: V. Chellamuthu: None; **M. Noviani**: None; **A. Lajam**: None; **A. Low**: Boehringer-Ingelheim, 6, Janssen, 6; **S. Albani**: None.

Abstract Number: 2366

Spatial Frequency Domain Imaging as a Novel Method to Quantify Longitudinal Skin Changes in Scleroderma

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science
Session Type: Poster Session C
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Background/Purpose: Systemic sclerosis (SSc) is an autoimmune disease characterized by excessive collagen deposition in the skin and internal organs, along with vascular dysfunction. The modified Rodnan skin score (mRSS) is the established gold standard for evaluating skin fibrosis in SSc. Nevertheless, mRSS is not objective, has significant interrater variability and may miss small but clinically significant changes. Spatial Frequency Domain Imaging (SFDI) is a non-invasive and optical technique that uses near-infrared light to generate widefield images of tissue optical properties (absorption (μ_a) and reduced scattering coefficients (μ_s')) at sub-surface depths. Our recent study showed that μ_s' is highly correlated with mRSS, suggesting that SFDI is a reliable method for assessing skin fibrosis in SSc patients (Fig. 1) (1). However, the sensitivity of SFDI to longitudinal changes has yet to be examined.

Methods: The SFDI data were collected from the left and right forearms in 2 healthy control (HC) subjects and 6 patients with diffuse SSc.Subjects were measured at two different time points, at least two months apart. Local forearm mRSS scores were performed by a trained physician, blinded to the SFDI measurements and using the averaging method. A rectangular region of interest (ROI) of dimensions 800 × 300 pixels (approx. 4.3 × 11.5 cm), aligned along the dorsal forearm was used

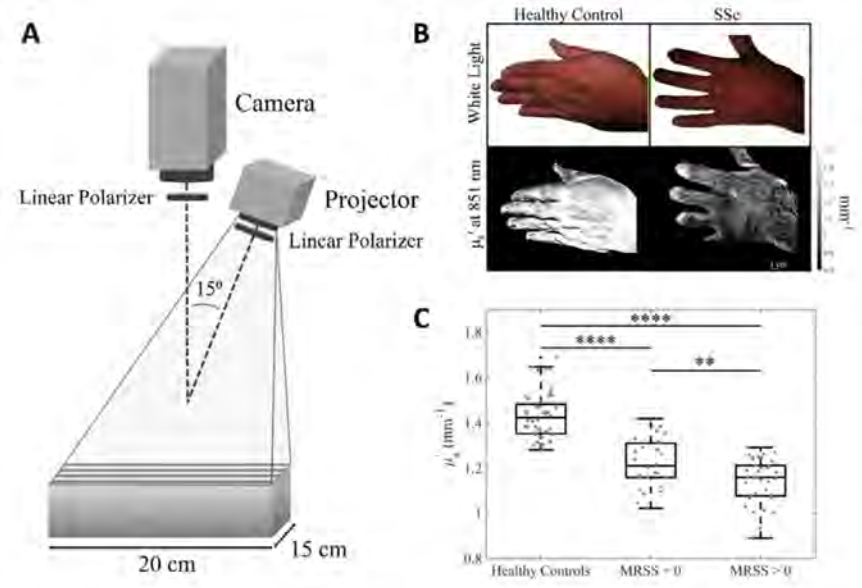

*Figure 1. A) Schematic diagram of a SFDI system. The target site is placed directly below the illumination source for data acquisition. B) The scleroderma patient exhibited a lower μ_s' value compared to the healthy subject at 851 nm as shown in the bottom row. C) μ_s' difference in healthy controls, versus mRSS = 0 and mRSS > 0 in SSc patients. ****p < 0.0001, **p ≤ 0.01. Panels A and C adapted from ref (1).*

Figure 1

to measure μ_s' at 851 nm .Differences between the sum of left and right forearms in each patient were plotted against differences in the sum ofμ_s' in each patient. Correlation between the absolute change of μ_s' versus absolute change of mRSS at the 2 time-points were evaluated using the Spearman test. A p-value < 0.05 was considered statistically significant. All data were analyzed with GraphPad Prism 9 software.

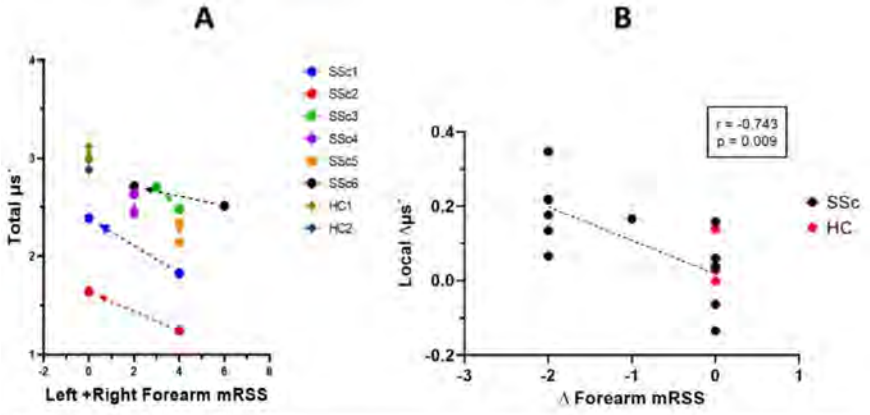

Figure 2. *A) Longitudinal associations of t1 and t2 total μ_s' (sum of left and R forearms) and t1 and t2 total mRSS (sum of left and R forearms) values for each individual patient. B) Correlation between the longitudinal change in μ_s' at each forearm and the corresponding change in mRSS at the same site r=-0.74 (**p < 0.01). t1-time of first measurements; t2-time of second measurements; SSc-scleroderma patient; HC- healthy controls*

Figure 2

Results: 83% of SSc patients were females, with a mean age of 44 ± 18.4 years. Mean disease duration was 4.3 ± 2.6 years and mean follow up interval between measurements was 23 months ± 4.8 months. In 3 patients the sum of forearm mRSS scores improved by 4 points (SSc1, 2 and 6), one patient had a modest improvement (1 point, SSc3), while two patients remained stable (SSc4 and 5, Fig 2A). No patient had an increase in the forearm skin score. As expected, the patients with no improvement showed minimal changes in the μs', similar to controls (0.0109 ± 0.1129 mm^{-1} in SSc compared to 0.0497 ± 0.0613 mm^{-1} in HC). However, when patients improved there was a proportionate increase in μs' that mirrored the degree of mRSS improvement (Fig 2A). Next we assessed correlation between change in mRSS and change in μs' at each site, and found a significant negative correlation ($r = -0.74$, $p < 0.01$, Fig 2B).

Conclusion: Our preliminary study indicates that SFDI is sensitive to longitudinal changes in the skin of SSc patients, further supporting this method as a highly promising new tool for scleroderma skin assessment and monitoring. Future studies are required to confirm these findings.

References:

1. Pilvar A, Mehendale AM, Karrobi K, El-Adili F, Bujor A, Roblyer D. Spatial frequency domain imaging for the assessment of scleroderma skin involvement. Biomed Opt Express. 2023;14(6):2955. doi:10.1364/BOE.489609

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Abstract Number: 2367

Characterization of the SFRP4+ PRG4+ Fibroblast Subpopulation in the Dermis of Healthy Skin and Its Relationship to SFRP4+ PRG4- Myofibroblasts in the Skin of Patients with Systemic Sclerosis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a debilitating autoimmune disease characterized by extensive fibrosis affecting multiple organs. The fibrosis arises from the excessive production of collagen by dysregulated myofibroblasts. Our recent single cell RNA-sequencing (scRNA-seq) studies have described several fibroblast subpopulations in the skin of SSc patients. We have previously shown that myofibroblasts derive from one of these populations that expresses secreted frizzled-related protein 2 (SFRP2) and DPP4, the most common subpopulation of dermal fibroblasts[1]. As these cells differentiate into myofibroblasts they show upregulated expression of another gene, secreted frizzled-related protein 4 (SFRP4). However, SFRP4 is also expressed by another fibroblast subpopulation found in healthy as well as SSc skin. ScRNA-seq indicates that this subpopulation also expresses PRG4. Thus, we sought to better understand the location of PRG4+ fibroblasts in healthy skin and their relationship to SFRP4+ myofibroblasts.

Methods: Dorsal forearm skin biopsies were obtained from a cohort of eight SSc patients and twelve healthy controls, following the approved protocol by the Institutional Review Board of the University of Pittsburgh School of Medicine. Paraffin-embedded skin samples were utilized for double and triple immunofluorescence staining, employing Tyramide

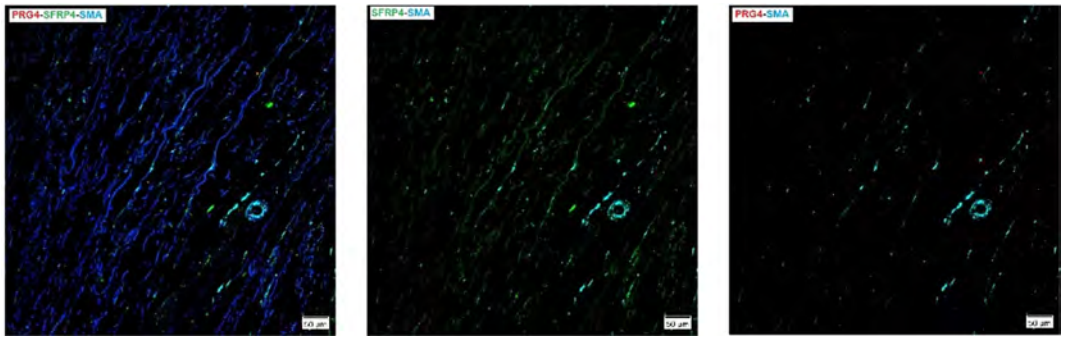

Figure 1 shows α-SMA+ SFRP4+ PRG4- myofibroblasts in the dermis of SSc patients

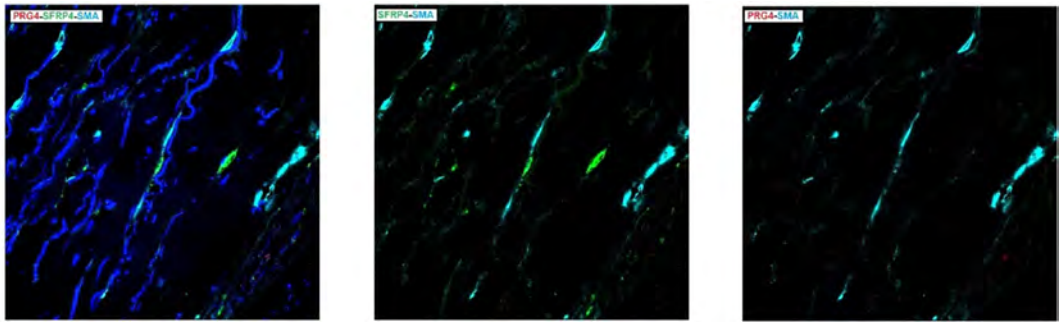

Figure 2 shows a higher magnification of α-SMA+ SFRP4+ PRG4- myofibroblast staining in the dermis of SSc patients

amplification and a range of antibodies targeting distinct fibroblast markers. High-resolution figures were generated using the Olympus FluoView 3000 confocal microscope.

Results: Our study uncovered a unique subpopulation of fibroblasts characterized by expression of proteoglycan 4 (PRG4) as well as (variable) expression of SFRP4 (and other markers). These cells were seen in both healthy and SSc skin. These cells were located in both papillary and reticular dermis. In contrast, myofibroblasts also expressed secreted frizzled-related protein 4 (SFRP4) and alpha-smooth muscle actin (α-SMA), while lacking the (PRG4) marker. Myofibroblasts were specifically identified in the deep dermis of SSc patients and were not observed in healthy skin.

Conclusion: This study clarifies the relationship between SFRP4-expressing fibroblast subpopulations. PRG4+ fibroblasts do not appear to be myofibroblast progenitors due to previous bioinformatics analyses, as well as their topological distribution in the skin. However, it is likely that they contribute to hydration of skin and intriguing to consider how they may contribute to loss of skin hydration and elasticity with aging, and possibly contribute to other skin pathology. This study also reinforces the importance of the distinct population of α-SMA+ SFRP4+ PRG4- myofibroblasts, which are key cells in driving skin fibrosis and tethering in SSc.

Disclosure: B. Nazari: None; **T. Tabib**: None; **R. Lafyatis**: None.

Abstract Number: 2368

Is Skin Disease a Local Manifestation of Systemic Tissue Turnover? Serological Collagen Biomarkers Provide Important Information on Skin Diseases Arising from Mutations in Collagen Genes

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science
Session Type: Poster Session C
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Background/Purpose: Collagens are the main constituents of the skin. Genetic mutations in type VI, VII, and XVII collagen cause skin diseases, such as atopic dermatitis, epidermolysis bullosa, and bullous pemphigoid. These are all characterized as systemic diseases, with local manifestations. Novel collagen biomarkers hold the potential to detect skin manifestations, monitor the disease course, as well as improve our understanding of the pathophysiology. The objective of this study was to develop blood-based biomarkers of type VI, VII, and XVII collagen, and investigate their diagnostic potential for skin pathologies, including systemic sclerosis.

Methods: Three novel immunoassays targeting the N-terminal of type VI collagen (C6A6), an MMP-generated neo-epitope fragment of type VII collagen (C7M), and type XVII collagen (PRO-C17) were developed and used to measure the aforementioned analyte levels in serum from healthy donors (n=25), patients with atopic dermatitis (n=20) and systemic sclerosis (n=5).

Differences between biomarker levels in healthy donors and patients with atopic dermatitis, and systemic sclerosis, were calculated by a Mann-Whitney U test. The diagnostic accuracy was evaluated by the area under the receiver operating characteristics (AUROC) curve between the individual dermatological indications and healthy controls. An AUC=0.85 was considered clinically relevant.

Results: Patients with atopic dermatitis presented higher levels of C6A6, C7M, and PRO-C17 compared to healthy donors ($p < 0.001$, $p< 0.001$, and $p=0.0005$, respectively), where C7M was significantly elevated in patients with systemic sclerosis compared to healthy donors ($p=0.0019$). Neither C6A6 or PRO-C17 could separate between healthy donors and patients with systemic sclerosis. The diagnostic accuracy of C6A6 for separating patients with atopic dermatitis from healthy controls was AUC=1.00, while the C7M biomarker presented an AUC=0.912, and PRO-C17 presented an AUC=0.842. The C7M presented a diagnostic accuracy of an AUC=0.908 for separating healthy donors and patients with systemic sclerosis.

Conclusion: There was a clear link between collagen genetic components and serological biomarkers in skin diseases. This study highlights the possible use of novel non-invasive biomarkers of collagens to describe the disease in patients with atopic dermatitis. In addition, C7M may be a useful biomarker in systemic sclerosis. These biomarkers reflect the downstream effect of different genetic mutations leading to skin disease and may be useful to determine skin involvement in rheumatic diseases, including systemic sclerosis and psoriatic arthritis.

Disclosure: S. Holm Nielsen: Nordic Bioscience, 3, 8; **M. Anđelić**: Nordic Bioscience, 3; **D. Sinkeviciute**: Nordic Bioscience, 3; **A. Bay-Jensen**: Nordic Bioscience, 3, 3, 8, 9; **M. Karsdal**: Nordic Bioscience, 3, 4, 8.

Abstract Number: 2369

Investigating Macrophage Heterogeneity in the Esophagus of SSc Patients

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III: Translational Science

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is characterized by an initial inflammatory phase followed by fibrosis. Esophageal dysfunction in SSc is associated with Gastroesophageal Reflux Disease (GERD), which can lead to severe complications and contribute to fibrosis. SSc patients exhibit increased numbers of specific immune cells, such as CD14+ monocytes, fibrocytes, and tissue macrophages, which are correlated with disease severity and reduced survival. However, the role of macrophage populations in the esophagus and affected tissues remains poorly understood. This study aims to investigate the transcriptional heterogeneity of macrophages in the esophagus of SSc patients.

Methods: Esophageal biopsies were obtained from SSc patients, GERD patients without SSc, and healthy control patients. scRNA-Seq was performed on 20 samples and Cellular Indexing of Transcriptomes and Epitopes by Sequencing (CITE-Seq) was performed on 7 samples where CD45+ immune cells were isolated using fluorescence-activated cell sorting (FACS). Data were processed and analyzed using the 10X Genomics 3' v3.0 pipeline and the Seurat package.

Results: Analysis of the integrated immune cell data identified 16 individual clusters from about 45,000 cells, including T cells, B cells, and various myeloid cell subsets. Within the myeloid subsets (18% of CD45+), 10 distinct clusters were identified, including multiple dendritic cell subsets ($LAMP3^+$ ~5%) and macrophages. RNA expression analysis and protein expression confirmation revealed heterogeneity among macrophage subsets, characterized by differential expression of specific markers such as FABP4, CD11b, CD11c, and CCR2, and APOE as well as varying expression of HLA-antigens, indicating differences in antigen presentation capabilities. The number of macrophages was found to be increased up to 2-fold in SSc compared to GERD patients and healthy controls.

Conclusion: This is the first study to evaluate immune cells in the esophagus of SSc patients. We demonstrate the presence of diverse macrophage subsets within the esophagus of SSc patients, each potentially contributing to distinct functions and mechanisms in the pathogenesis of SSc. These findings underscore the importance of precisely identifying immune cell populations within affected organs and targeting specific subsets to effectively intervene in the inflammatory process of SSc. Future research will investigate the differential characteristics of these macrophage subsets compared to control and GERD patients.

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Abstract Number: 2370

C5 as a Genetic Marker for Discriminating Between IgA Vasculitis and IgA Nephropathy?

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Vasculitis – ANCA-Associated Poster III: Biomarkers & Renal Outcomes

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Immunoglobulin-A vasculitis (IgAV) and IgA nephropathy (IgAN) are inflammatory conditions that share pathophysiological mechanisms[1,2]. Similar features are also described between IgAV nephritis (IgAVN) and IgAN[3]. However, whether IgAV is an extension of IgAN or a different disease entity is still inconclusive[3]. The complement system plays a crucial role in the development of immune-mediated disorders, being specifically associated with renal pathology and clinical phenotypes in patients with IgAV[4]. In this regard, C5 signalling blockage is described as a novel strategy to modulate inflammatory diseases, such as different types of vasculitis[5].

Methods: The main objective of this study was to determine the role of *C5* as a potential genetic biomarker for discriminating between IgAV and IgAN. For that purpose, 9 tag genetic variants within *C5* (rs10760128, rs74971050, rs4310279, rs7868761, rs10818495, rs2159777, rs10156396, rs3815467 and rs16910280) were genotyped in the largest series of Caucasian patients diagnosed with IgAV ever assessed for genetic studies (n=407) and in 98 Caucasian patients diagnosed with IgAN. 35.4% of our patients were IgAVN.

Results: Similar genotype distribution were observed in IgAV patients compared to those with IgAN, when *C5*variants were analyzed independently (**Table 1**). In addition, no statistically significant allele differences were disclosed between patients with IgAV patients and those with IgAN (**Table 1**). Moreover, when we compared patients with IgAVN and patients with IgAN, we did not observe genotype nor allele statistical differences (**Table 1**). Similar results were disclosed when haplotype frequencies of *C5* were compared between patients with IgAV and those with IgAN, as well as between patients with IgAV-Nand patients with IgAN (data not shown).

Table 1. Genotype and allele frequencies of *C5* in patients with IgAV and those patients with IgAN and IgAVN.

	Change		Genotypes, % (n)			Alleles, % (n)	
Polymorphism	1/2	Data set	1/1	1/2	2/2	1	2
rs10760128	T/C	IgAV	36.2 (147)	48.0 (195)	15.8 (64)	60.2 (489)	39.8 (323)
		IgAN	35.7 (35)	44.9 (44)	19.4 (19)	58.2 (114)	41.8 (82)
		IgAVN	37.3 (53)	47.2 (67)	15.5 (22)	60.9 (173)	39.1 (111)
rs7497050	C/T	IgAV	63.1 (257)	32.9 (134)	3.69 (16)	79.6 (648)	20.4 (166)
		IgAN	71.4 (70)	23.5 (23)	5.1 (5)	83.2 (163)	16.8 (33)
		IgAVN	59.2 (84)	35.2 (50)	5.6 (8)	76.8 (218)	23.2 (66)
rs4310279	A/G	IgAV	60.7 (246)	33.8 (137)	5.4 (22)	77.7 (629)	22.4 (181)
		IgAN	60.8 (59)	34.0 (33)	5.2 (5)	77.8 (151)	22.2 (43)
		IgAVN	59.4 (85)	32.2 (46)	8.4 (12)	75.5 (216)	24.5 (70)
rs7868761	T/C	IgAV	81.6 (328)	17.4 (70)	1.0 (4)	90.3 (726)	9.7 (78)
		IgAN	74.7 (71)	23.2 (22)	2.1 (2)	86.3 (164)	13.7 (26)
		IgAVN	83.3 (120)	16.7 (24)	0	91.7 (264)	8.3 (24)
rs10818495	C/A	IgAV	24.6 (99)	50.8 (204)	24.6 (99)	50.0 (402)	50.0 (402)
		IgAN	29.6 (29)	44.9 (44)	25.5 (25)	52.0 (102)	48.0 (94)
		IgAVN	24.1 (34)	49.7 (70)	26.2 (37)	48.9 (138)	51.1 (144)
rs2159777	G/T	IgAV	23.6 (95)	51.9 (209)	24.4 (98)	49.6 (399)	50.4 (405)
		IgAN	30.9 (30)	47.4 (46)	21.7 (21)	54.6 (106)	45.4 (88)
		IgAVN	22.4 (32)	51.8 (74)	28.9 (37)	48.3 (138)	51.8 (148)
rs10156396	C/T	IgAV	63.8 (259)	31.5 (128)	4.7 (19)	79.6 (646)	20.4 (166)
		IgAN	64.2 (61)	32.6 (31)	3.2 (3)	80.5 (153)	19.5 (37)
		IgAVN	62.0 (88)	32.4 (46)	5.6 (8)	78.2 (222)	21.8 (62)
rs3815467	G/A	IgAV	71.8 (293)	25.7 (105)	2.5 (10)	84.7 (691)	15.3 (125)
		IgAN	68.8 (66)	29.2 (28)	2.1 (2)	83.3 (160)	16.7 (32)
		IgAVN	76.2 (109)	23.1 (33)	0.7 (1)	87.8 (251)	12.2 (35)
rs16910280	C/T	IgAV	59.8 (238)	36.4 (145)	3.8 (15)	78.0 (621)	22.0 (175)
		IgAN	67.4 (66)	27.6 (27)	5.1 (5)	81.1 (159)	18.9 (37)
		IgAVN	56.9 (78)	40.2 (55)	2.9 (4)	77.0 (211)	23.0 (63)

Table 2. Haplotype analysis of *C5* in patients with IgAV and those patients with IgAN and IgAVN.

Haplotype*	IgAV, % (n)	IgAN, % (n)	p	IgAVN, % (n)	IgAN, % (n)	p
TCATCGCGC	35.2 (285)	37.6 (74)	0.51	34.4 (97)	37.6 (74)	0.47
TTATATCGT	16.8 (137)	13.5 (27)	0.28	18.8 (53)	13.5 (27)	0.13
CCGTATTGC	9.8 (79)	8.0 (16)	0.49	11.1 (32)	8.0 (16)	0.26
CCATATTGC	6.7 (55)	9.2 (18)	0.27	6.2 (18)	9.2 (189	0.22
CCATCTCAC	6.6 (54)	4.4 (9)	0.29	5.6 (16)	4.4 (9)	0.56
CCGCAGCAC	4.6 (37)	6.3 (12)	0.99	3.4 (10)	6.3 (12)	0.14

*The polymorphism order was: rs10760128, rs7497050, rs4310279, rs7868761, rs10818495, rs2159777, rs10156396, rs3815467 and rs16910280; Haplotypes frequencies higher than 5% are displayed in the table.

Conclusion: Our results reveal a similar *C5*genetic distribution in IgAV, IgAVN and IgAN, indicating that this gene may not be used as a genetic biomarkerfor discriminating between these entities.

References: [1] *N Engl J Med 2013;368:2402-14*; [2] *Autoimmun Rev 2018;17:301-15;* [3] *Front Immunol 2022;13:921864*; [4] *Front Immunol 2019;10:2166*.

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Abstract Number: 2371

Plasma and Urine Cytokine Profiles in Active ANCA-Associated Vasculitis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Vasculitis – ANCA-Associated Poster III: Biomarkers & Renal Outcomes
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: ANCA-associated vasculitis (AAV) is a multisystem autoimmune disease that often affects the kidneys. It is unclear why some patients with AAV have kidney involvement while others do not. To investigate the mechanisms underlying these phenotypes, this study examined plasma and urine cytokine profiles in patients with active renal and non-renal AAV (AAGN and NR-AAV, respectively), and healthy controls (HC).

Methods: Levels of 200 cytokines were measured in the plasma and urine of 6 patients with active AAGN, 9 patients with NR-AAV, and 3 HC using a human cytokine array. Urine cytokine levels were corrected to urine creatinine and an analyte-to-creatinine ratio was utilized for analysis. Levels in the three groups were compared using ANOVA. Analytes with false discovery rate (FDR)-corrected p-values < 0.05 were further compared using Tukey HSD post-hoc test.

Table 1. Patient Characteristics

Table 1. Patient and Disease Characteristics

Age at biopsy, median (IQR)	58 (41-68)
% Female	59%
% White	95%
Newly diagnosed	95%
ANCA ELISA*	
anti-PR3	45% (10/22)
anti-MPO	45% (10/22)
both positive	5% (1/22)
negative	5% (1/22)
ANCA IIF	
c-ANCA	52% (12/23)
p-ANCA	30% (7/23)
*negative***	17% (4/23)
Phenotype	
GPA	52% (12/23)
MPA	35% (8/23)
EGPA	13% (3/23)
Serum Creatinine, average ±SD	3.6 ±2.9

*not available in one patient
** all had detectable ANCAs by ELISA
Abbreviations: ANCA: antineutrophil cytoplasmic antibodies. PR3: proteinase 3. MPO: myeloperoxidase. c-ANCA: cytoplasmic ANCA. P-ANCA: perinuclear ANCA. GPA: granulomatosis with polyangiitis. MPA: microscopic polyangiititis. EGPA: eosinophilic GPA

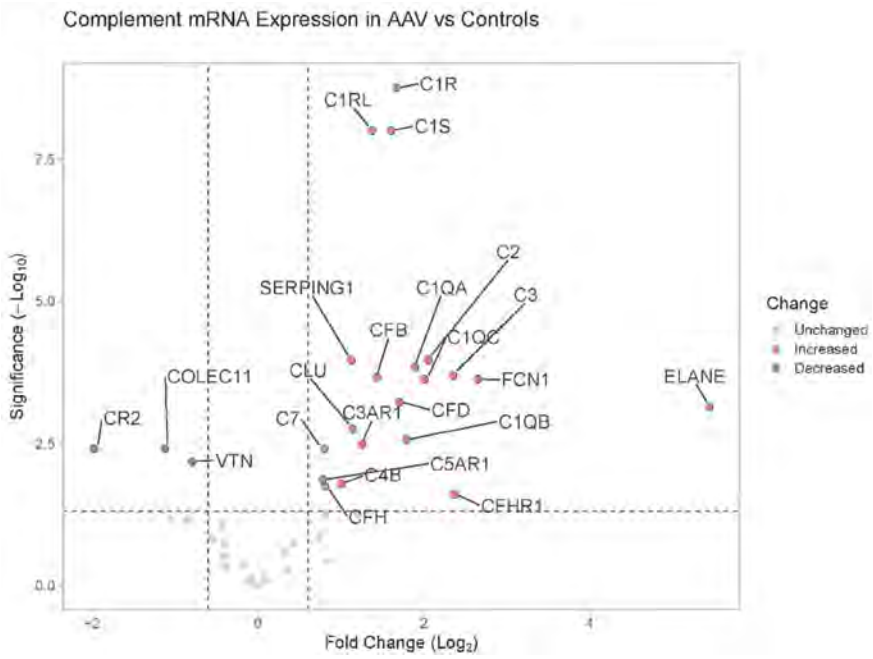

Figure 1. Difference in urine (a) and plasma (b) levels of cytokines in patients with active renal and non-renal vasculitis.

Results: Patient Characteristics are depicted in Table 1. Most cytokines measured were similar between HC and NR-AAV patients. Compared to patients with NR-AAV, patients with AAGN had higher levels of plasma and urine cytokines that are involved in involved in Th17 signaling (IL-17A, IL-17F, IL-17R, IL-23, IL-6), Th1 response (IL-12, GM-CSF, IFNg, TNFa), chemotaxis (especially for T-cells, monocytes, and dendritic cells - eotaxin-2, I-TAC, Lymphotactin, MCP-3, MIP-3a, CCL23), B and T-cell crosstalk (B7-1, CD40, CD40L), and angiogenesis (VEGFR1, FLT4, VEGF-C, VEGF-D, SDF1a) (Figure 1).

Conclusion: Compared to NR-AAV, AAGN is associated with an increase in plasma and urine levels of many pro-inflammatory cytokines. T-cell differentiation, signaling, and crosstalk seem to be the most prominent molecular processes that are active in patients with AAGN. These data suggest a prominent role of T-cells in AAGN which have the potential of being leveraged therapeutically.

Disclosure: S. Almaani: Amgen, 2, Aurinia, 2, Chemocentryx, 2, Kezar, 2, Otsuka, 2; **H. Song**: None; **S. Ardoin**: None; **L. Fussner**: Amgen, 2; **B. Rovin**: AstraZeneca, 2, 5, Aurinia, 2, 5, Biogen, 2, F. Hoffmann-La Roche Ltd, 2, Genentech, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2.

Abstract Number: 2372

Soluble Triggering Receptor Expressed on Myeloid Cell-1 Reflects the Cross-sectional Activity of Microscopic Polyangiitis and Granulomatosis with Polyangiitis

Jang Woo Ha[1], Jason Jungsik Song[2], Yong-Beom Park[2], Sung Soo Ahn[2] and Sang-Won Lee[3], [1]Yonsei University College of Medicine, Seodaemun-gu, Seoul, South Korea, [2]Yonsei University College of Medicine, Seoul, South Korea, [3]Yonsei University College of Medicine, Seoul, South Korea

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Vasculitis – ANCA-Associated Poster III: Biomarkers & Renal Outcomes
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: This study investigated whether the soluble triggering receptor expressed on myeloid cells-1 (sTREM-1) reflects the cross-sectional activity of microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA).

Methods: This study included 47 MPA and 32 GPA patients with well-documented clinical records and stored sera at diagnosis. The activity of vasculitis was assessed using the Birmingham vasculitis activity score (BVAS) The patients were arbitrarily divided into two groups according to BVAS at a frequency of 50% as the upper and lower halves of BVAS.

Results: The median age of the 79 patients was 67.0 years, and 58.2% were women. The median BVAS and sTREM-1 were 12.0 and 513.5 pg/mL. sTREM-1 was significantly correlated with BVAS along with five-factor score, short Form 36 health survey, and C-reactive protein. In the multivariable linear regression analysis, erythrocyte sedimentation rate (standardised β 0.241), and sTREM-1 (standardised β 0.288) were independently correlated with BVAS. Using the receiver operator characteristic curve, the cut-off of sTREM-1 for the upper half of BVAS was set as 474.1 pg/mL. When we divided patients into two groups based on sTREM-1 ≥474.1 pg/mL, MPA and GPA patients with sTREM-1 ≥474.1 pg/mL exhibited a significantly higher risk for the upper half of BVAS than those without (relative risk 5.932). In the multivariable logistic regression analysis with sTREM-1 ≥474 pg/mL, sTREM-1 ≥474 pg/mL (OR 5.662) was independently associated with the upper half of BVAS.

Table 1. Linear regression analysis of variables for BVAS in patients with MPA and GPA

Table 1. Linear regression analysis of variables for BVAS in patients with MPA and GPA

Variables	Univariable			Multivariable		
	Beta	95% CI	P value	Standardised Beta	95% CI	P value
Demographic data						
Age (years)	0.146	-0.045, 0.215	0.200			
AAV activity-, prognosis-, and function-related indices						
FFS	0.319	0.956, 4.921	0.004	0.153	-0.447, 3.260	0.135
SF-36 PCS	-0.482	-0.265, -0.110	<0.001	-0.231	-0.205, 0.026	0.128
SF-36 MCS	-0.434	-0.264, -0.095	<0.001	-0.190	-0.131, 0.116	0.902
Acute-phase reactants						
ESR (mm/hr)	0.419	0.040, 0.119	<0.001	0.241	0.001, 0.090	0.044
CRP (mg/L)	0.415	0034, 0.100	<0.001	0.032	-0.034, 0.045	0.798
sTREM-1 (pg/mL)	0.450	0.004, 0.009	<0.001	0.288	0.001, 0.007	0.010

BVAS: Birmingham vasculitis activity score; MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis; AAV: ANCA-associated vasculitis; ANCA: antineutrophil cytoplasmic antibody; FFS: five-factor score; SF36: 36-item short form survey; PCS: physical component summary; MCS: mental component summary; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; sTREM-1: Soluble triggering receptor expressed on myeloid cells 1.

Table 2. Logistic regression analysis of variables for the upper half of BVAS in patients with MPA and GPA

Table 2. Logistic regression analysis of variables for the upper half of BVAS in patients with MPA and GPA

Variables	Univariable			Multivariable (sTREM-1)			Multivariable (sTREM-1 ≥ 474.1 pg/mL)		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Demographic data									
Age (years)	1.037	0.996, 1.066	0.080						
AAV activity-, prognosis-, and function-related indices									
FFS	5.117	3.643, 5.915	0.001	3.858	1.230, 5.783	0.014	3.280	1.055, 4.930	0.035
SF-36 PCS	0.965	0.945, 0.980	0.004	0.936	0.844, 1.038	0.521	0.995	0.948, 1.039	0.771
SF-36 MCS	0.969	0.945, 0.993	0.012	1.010	0.961, 1.061	0.707	1.007	0.959, 1.056	0.789
Acute-phase reactants									
ESR (mm/hr)	1.021	1.009, 1.033	0.001	1.021	1.004, 1.038	0.016	1.024	1.002, 1.044	0.032
CRP (mg/L)	1.018	1.006, 1.031	0.003	1.005	0.989, 1.021	0.535	1.008	0.991, 1.024	0.362
sTREM-1 (pg/mL)	1.002	1.001, 1.004	0.006	1.001	0.999, 1.003	0.184			
sTREM-1 ≥ 474.1 pg/mL	5.932	2.245, 15.673	<0.001				5.662	1.548, 22.823	0.010

BVAS: Birmingham vasculitis activity score; MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis; AAV: ANCA-associated vasculitis; ANCA: antineutrophil cytoplasmic antibody; FFS: five-factor score; SF36: 36-item short form survey; PCS: physical component summary; MCS: mental component summary; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; sTREM-1: Soluble triggering receptor expressed on myeloid cells 1.

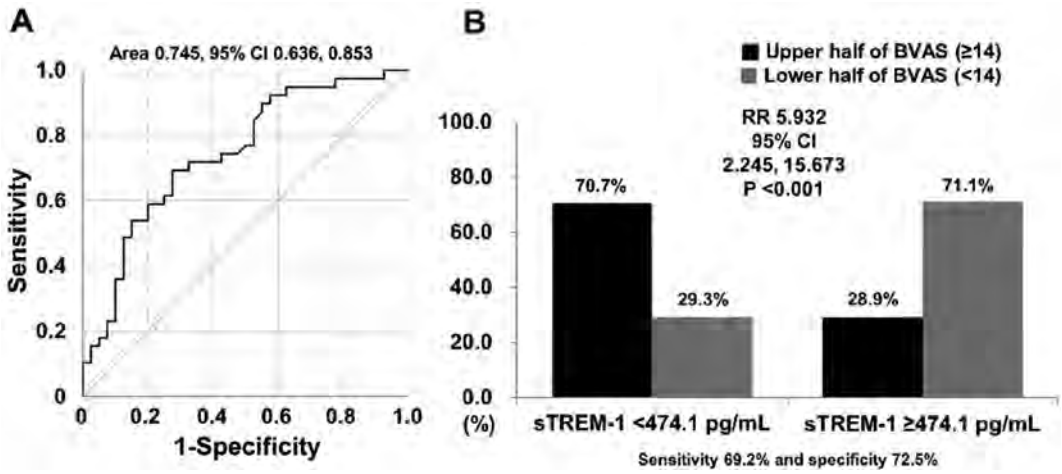

Figure 1. Optimal cut-off and relative risk. (A) Using the ROC curve, sTREM-1 of 474.1 pg/ml was set as the cut-off for the upper half of BVAS. (B) MPA and GPA patients with sTREM-1 ≥474.1 pg/mL exhibited a significantly higher risk for the upper half of BVAS than those without. ROC: receiver operator characteristic; sTREM-1: soluble triggering receptor expressed on myeloid cells-1; BVAS: Birmingham vasculitis activity score; MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis.

Conclusion: This study is the first to demonstrate that sTREM-1 reflects the cross-sectional activity of MPA and GPA.

Disclosure: J. Ha: None; **J. Song**: None; **Y. Park**: None; **S. Ahn**: None; **S. Lee**: None.

Abstract Number: 2373

SIRPα Expression in Systemic Vasculitis

Shubhasree Banerjee[1], Eileen Rose[2], Sandip Panicker[2], Nader Khalidi[3], Curry Koening[4], Carol Langford[5], Paul Monach[6], Christian Pagnoux[7], Carol McAlear[1] and Peter Merkel[1], [1]University of Pennsylvania, Philadelphia, PA, [2]Electra Therapeutics, Inc., South San Francisco, CA, [3]McMaster University, Hamilton, ON, Canada, [4]University of Texas Dell Medical School, Austin, TX, [5]Cleveland Clinic, Cleveland, OH, [6]VA Boston Healthcare System, Boston, MA, [7]Mount Sinai Hospital, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Vasculitis – ANCA-Associated Poster III: Biomarkers & Renal Outcomes
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Signal regulatory protein alpha (SIRPα) is primarily found on myeloid cells, including macrophages and neutrophils. Upon binding to CD47, SIRPa signaling regulates various cellular functions, including phagocytosis, antigen presentation, cell proliferation, cellular fusion, and cell migration. Therefore, SIRPamay be involved in the pathogenesis of autoimmune diseases including systemic vasculitis. This study aimed to assess SIRPa expression in tissue samples from patients with vasculitis.

Methods: Immunohistochemical staining for SIRPα was performed on kidney, lung, and temporal artery (TA) biopsy samples from patients with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), giant cell arteritis (GCA), and patients without vasculitis. Cells were grouped into 4 categories: i) monocytes/macrophages/dendritic cells; ii) neutrophils; iii) eosinophils; and iv) lymphocytes. Categories iii and iv were not analyzed because of positive isotype control staining and absence of SIRPα+ cells, respectively. A semiquantitative estimation of SIRPα+ cells in categories i and ii were reported

using the H-score system based on a visual estimate of the percentage of SIRPα+ cells and the staining intensities classified from 0 to 3 (H-score = 0 x [% with 0 intensity] + 1 x [% with 1 intensity] + 2 x [% with 2 intensity] + 3 x [% with 3 intensity]). Density of inflammatory infiltrate for individual cell categories were visually estimated and reported using an ordinal scale. Statistical analysis was done using GraphPad Prism 9.5.

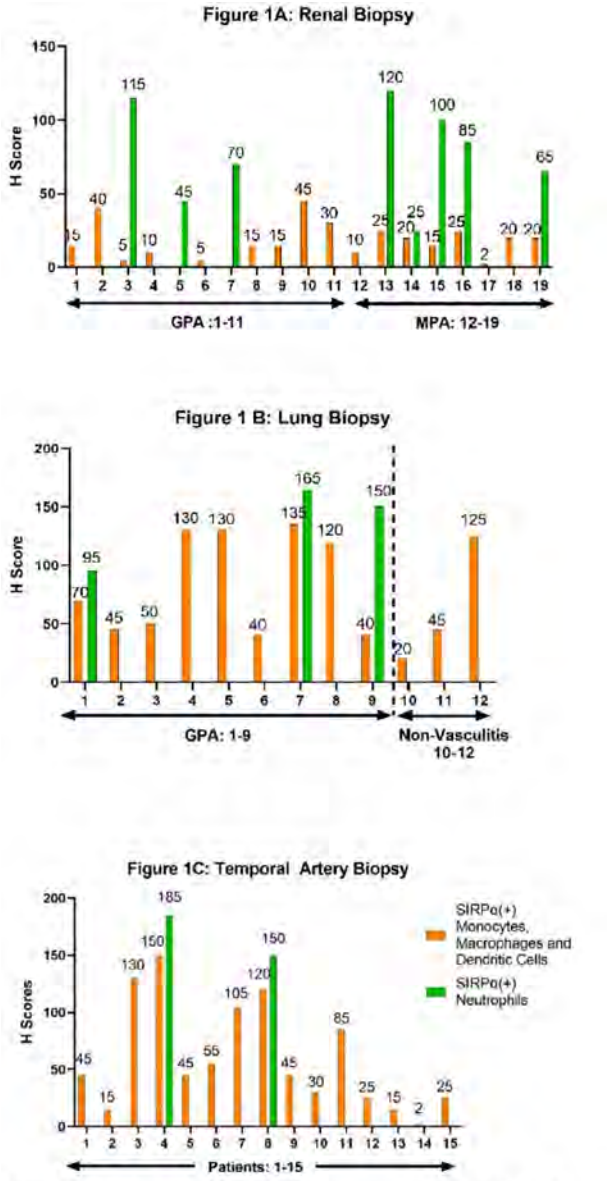

Figure 1: SIRPα expression on macrophages, monocytes, dendritic cells, and neutrophils, in tissues from patients with and without vasculitis.
Figure 1A: Three non-vasculitis kidney tissue samples had no SIRPα staining. Figure 1B: Non-vasculitis lung tissue samples (# 10, 11, 12 had macrophages and monocytes and thereby demonstrated SIRPα staining. Figure 1C: Three temporal artery biopsy samples without vasculitis had no SIRPα staining.

Figure 1: SIRPα expression on macrophages, monocytes, dendritic cells, and neutrophils, in tissues from patients with and without vasculitis. Figure 1A: Three non-vasculitis kidney tissue samples had no SIRPα staining. Figure 1B: Non-vasculitis lung tissue samples (# 10, 11, 12 had macrophages and monocytes and thereby demonstrated SIRPα staining. Figure 1C: Three temporal artery biopsy samples without vasculitis had no SIRPα staining.

Results: Samples from 43 patients (20 with GPA, 8 with MPA, and 15 with GCA) were included in the study. Tissue samples included kidney from 11 patients with GPA and 8 patients with MPA; lung from 9 patients with GPA; and TA from 15 patients with GCA. All renal biopsies demonstrated glomerulonephritis with crescents. Inflammation was found in all the lung tissue samples and 6/9 (67%) demonstrated granuloma formation. All 15 TA samples showed inflammation in the arterial wall consistent with the diagnosis of GCA and 9 (60%) demonstrated granuloma formation/multinucleated giant cell infiltration and disruption of the internal elastic lamina. **Figure 1** summarizes the data on SIRPa expression by tissue type. All tissue samples from patients with active vasculitis showed SIRPα staining. Due to absence of infiltrating immune cells, the kidney and TA samples from patients without vasculitis did not show any SIRPα staining. However, due to the presence of tissue-resident

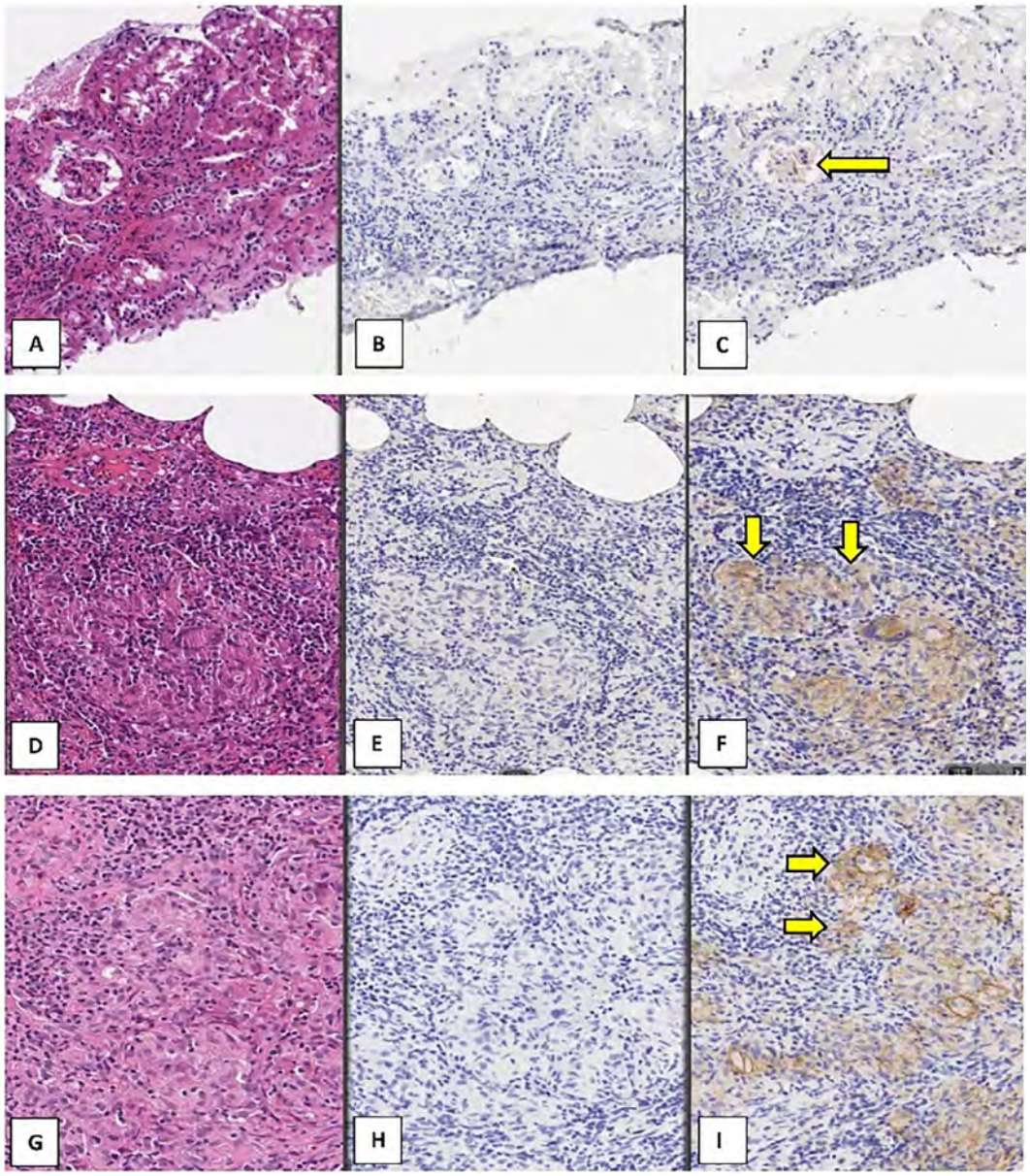

Figure 2: Tissue samples from patients with granulomatosis with polyangiitis, microscopic polyangiitis, and giant cell arteritis demonstrating SIRPα Expression. Figure: 2A-C: Renal biopsy from a patient with granulomatosis with polyangiitis; Figure 2D-F: Lung biopsy from a patient with granulomatosis with polyangiitis: Figure 2G-I: Temporal artery biopsy from a patient with giant cell arteritis. Figures A, D, and G: H&E staining; Figures B, E, and H: Control rabbit IgG monoclonal antibody (DA1E) stain which is the negative control stain for anti- SIRPα stain; Figures C, F , and I: anti-SIRPα antibody D613M stain. The yellow arrows demonstrate some areas of positive SIRPα stain. Magnification of all images was at 20X.

macrophages and monocytes, lung tissue from patients without vasculitis showed SIRPα staining. **Figure 2** provides examples of SIRPα staining in tissue samples from patients with vasculitis. **Figure 3** shows the overall density of inflammatory infiltrate of cell categories i and ii in the tissues.

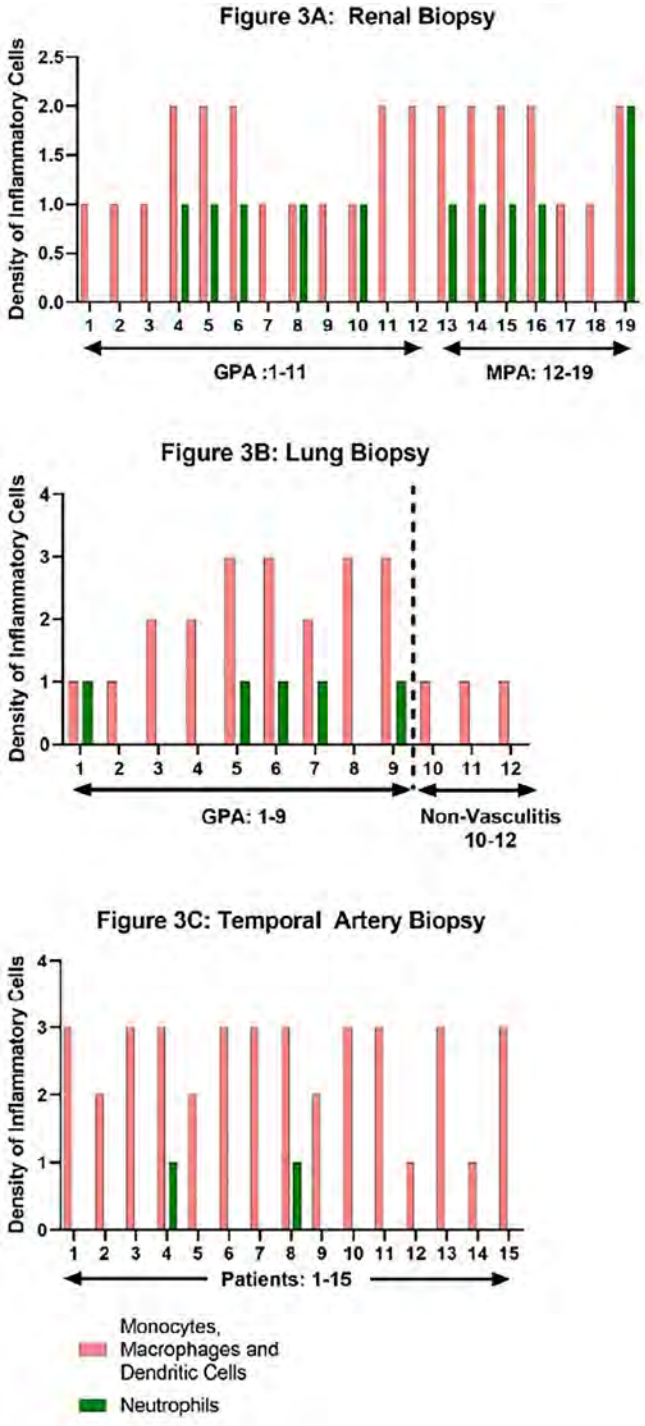

Figure 3: Density of infiltration of macrophages, monocytes, dendritic cells, and neutrophils, in tissues from patients with and without vasculitis. An ordinal scale ranging from 0 to 3+ (0 = none, 1+ = rare/mild, 2+ = moderate, 3+ = severe/dense inflammatory infiltrate) was used to represent the density of each cell type infiltrate. Figure 3A: Three non-vasculitis kidney tissue samples had no inflammatory infiltrate. Figure 1B: Non-vasculitis lung tissue samples (# 10, 11, 12) had infiltration of macrophages and monocytes. Figure 1C: Three temporal artery biopsy samples without vasculitis had no inflammatory infiltrate.

Conclusion: This study demonstrates high-level expression of SIRPα in macrophages and monocytes in affected tissues in systemic vasculitis. Some tissues also had SIRPα+ neutrophils. These findings pave the way for further studies exploring the role of the SIRPα/CD47 pathway in the pathogenesis of systemic vasculitis and the potential for blockade of SIRPα and/or the depletion of SIRPa+ cells as treatment of systemic vasculitis.

Disclosure: S. Banerjee: None; **E. Rose**: Electra Therapeutics, Inc., 11, Star Therapeutics, Inc., 3, 11; **S. Panicker**: Electra Therapeutics, Inc., 11, Star Therapeutics, Inc., 3, 11; **N. Khalidi**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 1, Otsuka, 1, 6, Roche, 1, 6; **C. Koening**: Amgen, 1; **C. Langford**: AbbVie, 12, Non-paid consultant, AstraZeneca, 5, 12, Non-paid consultant, Bristol-Myers Squibb(BMS), 5, 12, Non-paid consultant, GlaxoSmithKlein(GSK), 5; **P. Monach**: Genentech, 12, Lecture with honorarium, HI-Bio, 2; **C. Pagnoux**: AstraZeneca, 1, 2, 6, GlaxoSmithKlein(GSK), 1, 6, Otsuka, 1, 2, 5, 6, Pfizer, 5, Roche, 2; **C. McAlear**: None; **P. Merkel**: AbbVie/Abbott, 5, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos, 5, Electra, 5, Genentech, 5, GlaxoSmithKlein(GSK), 2, 5, HiBio, 2, InflaRx, 2, 5, Janssen, 2, Jubilant, 2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, Takeda, 2, 5, UpToDate, 9, Visterra, 2.

Abstract Number: 2374

Torque Teno Virus as a Potential Biomarker for Assessment of Immunocompetence in Patients with ANCA-associated Vasculitis

Balazs Odler[1], Regina Riedl[1], Jacinta Lee[2], Laura Cooney[3], Peter Merkel[4], William St.Clair[5], Duvuru Geetha[6], Paul Monach[7], David Jayne[2], Rona Smith[2], Paul A. Lyons[2], Mark Little[8], Salem Almaani[9], Alexander Rosenkranz[1], Ulrich Specks[10], John Stone[11] and Andreas Kronbichler[12], [1]Medical University of Graz, Graz, Austria, [2]University of Cambridge, Cambridge, United Kingdom, [3]Immune Tolerance Network, Seattle, WA, [4]University of Pennsylvania, Philadelphia, PA, [5]Duke University Medical Center, Durham, NC, [6]Johns Hopkins University, Baltimore, MD, [7]VA Boston Healthcare System, Boston, MA, [8]Trinity College Dublin, Dublin, Ireland, [9]Ohio State University Medical Center, Columbus, OH, [10]Mayo Clinic, Rochester, MN, [11]Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Concord, MA, [12]Department of Internal Medicine IV (Nephrology and Hypertension), Innsbruck, Austria

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Vasculitis – ANCA-Associated Poster III: Biomarkers & Renal Outcomes

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: ANCA-associated vasculitis (AAV) is a life-threatening disorder characterized by a relapsing-remitting disease course necessitating immunosuppression to control disease activity. Balancing the risks of infection against maintaining good disease control is crucial and yet often challenging. There is a lack of validated biomarkers to tailor immunosuppression to minimize therapy-related complications while maintaining a relapse-free period. The monitoring of Torque teno virus (TTV) has been successfully used in transplant medicine to predict the risk of organ rejection and infectious complications. However, the presence and role of TTV in association with clinical outcomes in AAV has yet to be reported.

Methods: Consecutive plasma samples (N=915) of 81 patients with AAV from the RAVE trial were used for assessment of the TTV load. Participants received either rituximab (RTX, N=40) or cyclophosphamide (CYC, N=41) followed by azathioprine (AZA). The TTV DNA was quantified using a real-time polymerase chain reaction method (TTV R-GENE®, BioMérieux) at multiple study visits. Change in TTV load and differences between non-relapsing and relapsing patients were investigated during a follow-up period of 1080 days.

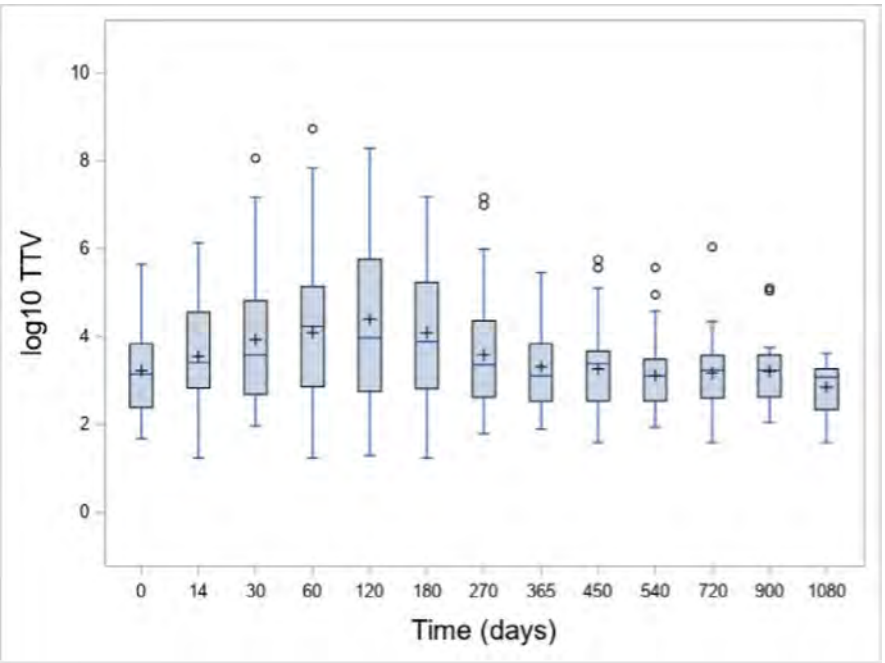

Figure 1. Change in TTV load after randomization in the study cohort of patients with ANCA-associated vasculitis. Box plots represent the interquartile range, while plus signs indicate the mean value.

Results: In total, 915 TTV quantifications were performed. At baseline, 72% (N=58) of patients had detectable TTV in the peripheral blood. The baseline median TTV load of all patients was 3 x 10^2 c/mL (interquartile range [IQR]: 0 – 3 x 10^3 c/mL). TTV load increased after initiation of immunosuppression and peaked at day 120 (median 2 x 10^3 c/mL, IQR: 2 x 10^2 – 5 x 10^5; Figure 1) and was detectable in 80% of the patients. Patients receiving RTX as a remission induction therapy showed a non-significant higher TTV load during the first 180 days in comparison to CYC/AZA-treated individuals at any visits. Patients with disease relapse had a lower TTV load at day 120 as compared to those without relapse (median 4 x

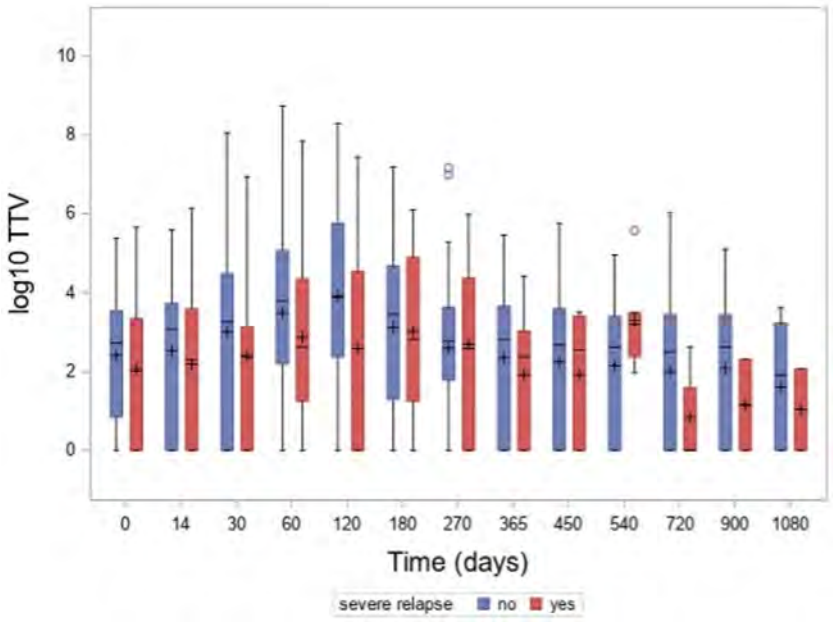

Figure 2. TTV load in the study cohort of ANCA-associated vasculitis patients with and without a disease relapse over time. Box plots represent the interquartile range, while plus signs indicate the mean value.

10^2 [IQR: 0 – 3 x 10^4] c/mL vs median 8 x 10^3 [IQR: 2 x 10^2 – 6 x 10^5] c/mL, p=0.036, respectively; Figure 2). For the 25 severe relapses, the median time to relapse was 339 (IQR: 232-516) days. Six relapses occured before 120 day, while 19 after day 120.

Conclusion: Among patients with AAV, TTV load reflects the intensity of immunosuppression and is associated with disease relapses. These results suggest that TTV might be a biomarker for the assessment of immunocompetence and identifying patients at risk of relapse in AAV.

Disclosure: B. Odler: CSL Vifor, 6, Delta4, 1, Otsuka Pharmaceuticals, 5, 6; **R. Riedl**: None; **J. Lee**: None; **L. Cooney**: None; **P. Merkel**: AbbVie/Abbott, 5, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos, 5, Electra, 5, Genentech, 5, GlaxoSmithKlein(GSK), 2, 5, HiBio, 2, InflaRx, 2, 5, Janssen, 2, Jubilant, 2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, Takeda, 2, 5, UpToDate, 9, Visterra, 2; **W. St.Clair**: CSL Behring, 2, Horizon Therapeutics, 2, 5, Related Sciences, 2, Resolve Therapeutics, 2, Sonoma biotherapeutics, 2, Up To Date, 9; **D. Geetha**: Amgen, 2, Aurinia, 2, calliditas, 2, chemocentryx, 2, GlaxoSmithKlein(GSK), 2; **P. Monach**: Genentech, 12, Lecture with honorarium, HI-Bio, 2; **D. Jayne**: AstraZeneca, 2, Aurinia, 4, Boehringer Ingelheim, 2, Chinook, 2, CSL Vifor, 2, Roche, 2; **R. Smith**: GlaxoSmithKlein(GSK), 5, Union Therapeutics, 5; **P. Lyons**: None; **M. Little**: Vifor, 5; **S. Almaani**: Amgen, 2, Aurinia, 2, Chemocentryx, 2, Kezar, 2, Otsuka, 2; **A. Rosenkranz**: None; **U. Specks**: Amgen, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 5, ChemoCentryx, 2, Genentech, 5, GlaxoSmithKlein(GSK), 5; **J. Stone**: Abvie, 2, Amgen, 1, 2, Argenx, 2, Aztrazeneca, 2, Bristol Myers Squibb, 2, 5, Celgene, 2, Chemocentryx, 2, Chugai, 2, GSK, 2, Horizon Therapeutics, 1, 2, 5, InflaRx, 2, IQVIA, 1, 2, Kyverna, 2, Mirabio, 2, NIH, 5, Novartis, 2, PPD, 2, Prometheus, 2, Q32, 2, Regeneron, 2, Roche-Genentech, 2, Roivant, 2, Sanofi, 2, 5, Spruce Biosciences, 2, Star Therapeutics, 2, Steritas, 12, Chair, Scientific Advisory Board (no fiduciary responsibilities), ZenasBio, 2; **A. Kronbichler**: Catalyst Biosciences, 2, CSL Vifor, 2, Delta4, 2, GlaxoSmithKlein(GSK), 2, Otsuka, 2, Waiden Biosciences, 2.

Abstract Number: 2375

Clinical Characteristics of ANCA-associated Vasculitis with High Levels of Serum Interleukin 7

Shoichi Fukui[1], Haruna Matsuo[2], Kanako Kojima[3], Shota Kurushima[1], Tohru Michitsuji[4], Yoshika Tsuji[5], Toshimasa Shimizu[3], Masataka Umeda[3], Remi Sumiyoshi[5], Takashi Igawa[1], Tomohiro Koga[5], Shin-ya Kawashiri[1], Naoki Iwamoto[1], Tomoki Origuchi[1] and Atsushi Kawakami[1], [1]Nagasaki University, Nagasaki, Japan, [2]Nagasaki University, Nagasaki City, Japan, [3]Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, [4]Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Medical Sciences, Nagasaki, Japan, [5]Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University, Nagasaki, Japan

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Vasculitis – ANCA-Associated Poster III: Biomarkers & Renal Outcomes

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Interleukin 7 (IL-7) is a hematopoietic growth factor produced by stromal cells in the bone marrow and thymus, which is indispensable in maintaining immune cells. The transcriptome analysis using CD8 positive T cells demonstrated genes involved in the IL-7 receptor pathway were the poor prognostic factor in anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) (McKinney EF, Nat Med 2010;16:586–91). However, the clinical utility of the

serum IL-7 levels in AAV is unknown. We aimed to elucidate the clinical characteristics of patients with AAV with high serum IL-7 levels.

Methods: We retrospectively analyzed 60 patients newly diagnosed with AAV (granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA)) from March 2010 to April 2022 with preserved sera. We collected medical records from baseline variables at diagnosis, including clinical symptoms, laboratory data, treatments, and outcomes. Multiplex cytokine and chemokine bead assays were performed using preserved serum supernatants. Serum samples from 101 healthy donors were used to define the normal serum IL-7 levels. We compared clinical indices between the patients with and without high levels of IL-7 defined by the median levels of serum IL-7.

Results: The median serum levels of IL-7 were 8.3pg/mL (IQR: 5.3pg/mL - 15.1pg/mL) and 22.4pg/mL (IQR: 11.9pg/mL - 46.6pg/mL) in healthy donors and patients with AAV, respectively. The median levels of IL-7 (22.4pg/mL) divided the patients with AAV into two groups (30 patients for each group). The IL-7 high group had significantly higher total Birmingham Vasculitis Activity Score (BVAS), higher white blood cell count, higher neutrophil count, higher platelet count, higher CRP level, lower lymphocyte count, and lower IgG levels compared to the IL-7 low group (Table). The serum levels of IL-7 correlated with the total BVAS score significantly (ρ=0.28 (Spearman's rank correlation coefficient), p=0.028). No significant differences were shown in the type of ANCA (MPO-ANCA or PR3-ANCA) and the diseases (GPA or MPA). There were no

Table: Clinical characteristics of AAV with low and high levels of serum IL-7

	Total	IL-7 Low	IL-7 High	p value
Number of patients	60	30	30	
Age (years)	75 [69, 82]	75 [68, 81]	76 [71, 83]	0.211
MPA (%)	39 (65.0)	19 (63.3)	20 (66.7)	1.000
BVAS 1	2.0 [1.0, 3.0]	2.0 [1.0, 3.0]	2.0 [2.0, 3.0]	0.191
BVAS 2	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	1.000
BVAS 3	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.483
BVAS 4	0.0 [0.0, 2.0]	0.0 [0.0, 1.5]	0.0 [0.0, 3.0]	0.701
BVAS 5	4.0 [3.0, 4.0]	4.0 [3.0, 4.0]	4.0 [3.0, 4.0]	0.623
BVAS 6	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	NA
BVAS 7	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	NA
BVAS 8	6.0 [0.0, 6.0]	3.0 [0.0, 6.0]	6.0 [0.0, 10.0]	0.285
BVAS 9	0.0 [0.0, 6.5]	0.0 [0.0, 3.0]	0.0 [0.0, 9.0]	0.251
Total BVAS	15.0 [10.0, 18.0]	12.5 [8.0, 17.0]	16.0 [12.5, 19.0]	0.04
ESR (mm/hour)	85 [66, 98]	90 [56, 99]	81 [68, 98]	0.838
White blood cell (*10^3/μL)	10.1 [7.2, 14.0]	7.7 [6.3, 11.0]	12.4 [9.9, 14.9]	<0.001
Hemoglobin (/μL)	10.2 [9.0, 11.3]	10.5 [8.6, 11.3]	10.0 [9.1, 11.3]	0.756
Platelet (*10^4/μL)	34.2 [28.8, 42.8]	30.4 [25.0, 34.9]	40.0 [33.9, 45.5]	<0.001
Neutrophil count (*10^3/μL)	9.0 [7.7, 9.6]	8.3 [7.2, 9.4]	9.4 [8.5, 9.8]	0.013
Lymphocyte count (*10^3/μL)	1.3 [0.9, 1.9]	1.7 [1.1, 2.6]	1.0 [0.8, 1.4]	0.008
CRP (mg/dL)	8.1 [2.9, 12.6]	3.7 [1.5, 8.5]	12.0 [7.5, 16.7]	<0.001
IgA (mg/dL)	324 [249, 401]	322 [244, 403]	324 [251, 401]	0.873
IgG (mg/dL)	1756 [1496, 1994]	1849 [1559, 2338]	1629 [1456, 1844]	0.047
IgM (mg/dL)	86 [60, 120]	86 [64, 123]	83 [52, 107]	0.477
CH50 (/mL)	47.3 [42.2, 53.9]	47.4 [44.4, 51.3]	46.8 [41.6, 54.0]	0.987
C3 (mg/dL)	111.4 [99.5, 138.3]	112.3 [98.8, 145.0]	109.8 [99.8, 134.3]	0.695
C4 (mg/dL)	26.3 [20.6, 30.8]	26.3 [20.2, 32.3]	26.4 [21.1, 30.6]	0.889
ferritin (ng/mL)	335 [214, 499]	281 [163, 447]	407 [266, 594]	0.142
MPO-ANCA positive (%)	53 (88.3)	27 (90.0)	26 (86.7)	1.000
PR3-ANCA positive (%)	10 (16.9)	5 (16.7)	5 (17.2)	1.000
mPSL pulse (%)	40 (66.7)	17 (56.7)	23 (76.7)	0.171
Intravenous cyclophosphamide (%)	17 (28.3)	11 (36.7)	6 (20.0)	0.252
Rituximab (%)	8 (13.3)	4 (13.3)	4 (13.3)	1.000
Relapse (%)	20 (33.3)	12 (40.0)	8 (26.7)	0.411
Dialysis (%)	1 (1.7)	1 (3.3)	0 (0.0)	1.000
Death (%)	8 (13.3)	2 (6.7)	6 (20.0)	0.255

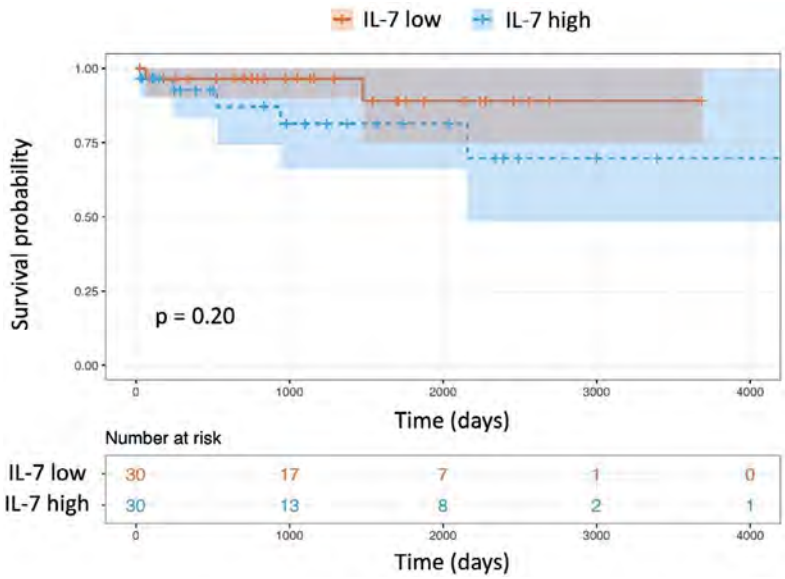

Figure: Survival provability of AAV with low and high levels of serum IL-7

differences in the treatments (initial prednisolone dose, methylprednisolone pulse therapy, intravenous cyclophosphamide, and rituximab) and the prognosis (relapse and death). The log-rank test demonstrated no significant differences in the survival rate (p=0.20, Figure).

Conclusion: The high serum levels of IL-7 at diagnosis demonstrated the high disease activity and distinct character with higher white blood cell count, platelet count, and CRP levels in AAV.

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Abstract Number: 2376

Eosinophil Activation as a Biomarker for Discriminating Active and Remission Phase in ANCA-Associated Vasculitis

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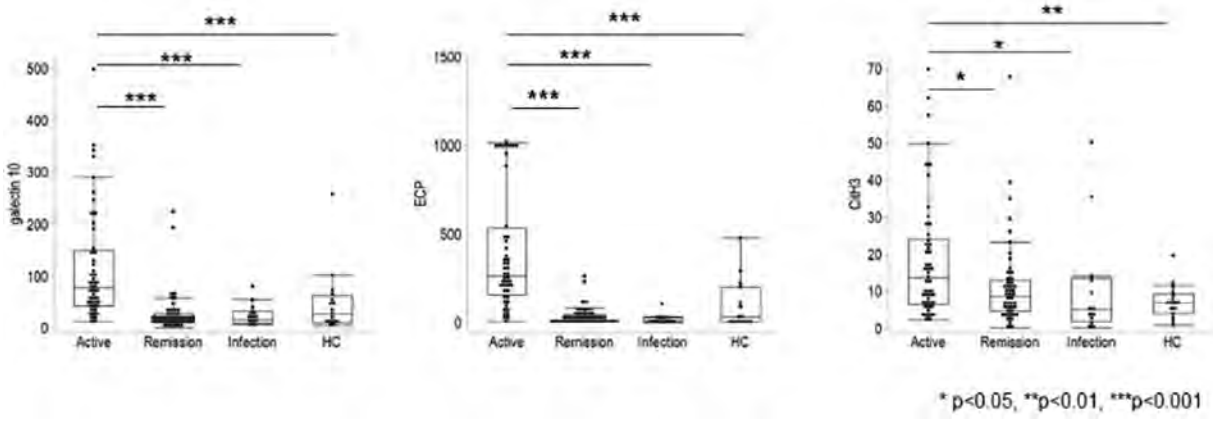
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Vasculitis – ANCA-Associated Poster III: Biomarkers & Renal Outcomes
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a life-threatening disease requiring complex management due to a lack of suitable biomarkers. Elevated or persistently positive ANCA titer as an indicator of disease activity or relapse in patients with AAV remains controversial. ANCA can activate eosinophils to induce cell

Figure 1



The serum concentrations of galectin-10, ECP, and CitH3 in active AAV, in remission AAV, remission with infection AAV, and HC groups. *p < 0.05. **p < 0.01, ***P < 0.001; (Mann–Whitney U test)

death, which in turn releases histone-coated filamentous DNA, referred to as eosinophil extracellular traps (EETs). Eosinophils play an important role in eosinophilic granulomatosis with polyangiitis, and galectin-10, which is released from EETs, is useful as a biomarker. However, the role of eosinophils in granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) remains unclear. Therefore, we investigated the association of galectin 10, eosinophil cationic protein (ECP), and citrullinated histone H3 (CitH3), which is a marker of EETs and neutrophil extracellular traps, with disease activity in GPA and MPA using Birmingham Vasculitis Activity Score (BVAS).

Methods: Serum concentrations of galectin-10, ECP, and CitH3 were retrospectively examined in 50 patients with AAV both in active and remission states, 13 patients with AAV in remission states with infection, and 16 age- and sex-matched healthy controls using ELISA kits. Additionally, the association between disease activity and conventional markers such as ANCA and CRP was also evaluated.

Results: The serum concentrations of galectin-10, ECP, and CitH3 in active AAV were significantly higher than those in remission AAV, remission with infection AAV, and HC groups (Figure 1). BVAS was associated with galectin-10 and ECP ($r=0.62$, $p< 0.001$ and $r=0.69$, $p< 0.001$, respectively), but only weakly associated with CitH3 ($r=0.21$, $p< 0.05$). ANCA titer was associated with the BVAS score ($r=0.71$, $p< 0.001$). Elevated serum galectin-10, ECP, and ANCA titers were identified as factors associated with the active phase using multivariate analysis with eosinophil count as a covariate. Receiver operating characteristic analyses for galectin-10, ECP, and ANCA titers for discriminating between active disease and remission revealed an area under the curve (AUC) of 0.886, with a sensitivity of 81.3% and specificity of 85%, AUC of 0.938, with a sensitivity of 83.3% and specificity of 95.1%, and AUC of 0.888, with a sensitivity of 69.4% and specificity of 93.5%, respectively.

Conclusion: Galectin-10 and ECP levels are elevated in patients with GPA and MPA, and can discriminate between active disease and remission independent of eosinophil counts. This suggests that the activation of both neutrophils and eosinophils is important for disease activity.

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Abstract Number: 2377

The Impact of Chronologic versus Biologic Age on the Risk of Severe Infection, End-Stage Renal Disease, and Death in Older Adults with ANCA-Associated Vasculitis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Vasculitis – ANCA-Associated Poster III: Biomarkers & Renal Outcomes

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Older adults with ANCA-associated vasculitis (AAV) have distinct clinical presentations and outcomes when compared to younger adults. Despite a high incidence of AAV in older adults, they are underrepresented in clinical trials. Studies have focused on age as a risk factor for poor outcomes. Frailty, a syndrome associated with increased

Table 1. Baseline Characteristics of patients with AAV by age group AAV = ANCA-associated vasculitis, SD = standard deviation, PR3 = Proteinase 3, MPO = myeloperoxidase, eGFR = estimated glomerular filtration rate, BVAS/WG = Birmingham Vasculitis Activity Score, CCI = Charlson Comorbidity Index, CFI = Claims-based Frailty index, RTX = rituximab, CYC = cyclophosphamide

Table 1. Baseline Characteristics of patients with AAV by age group

Characteristics	AAV 65-74 years old N = 142	AAV ≥ 75 years old N = 156
Age, mean (SD)	69 (2.6)	80.6 (4.7)
Sex, female	83 (58)	94 (60)
Race		
White	116 (82)	141 (90)
Black	3 (2)	1 (1)
Asian	2 (1)	3 (2)
Other	5 (4)	2 (1)
ANCA status		
PR3-ANCA+	30 (21)	27 (17)
MPO-ANCA+	112 (79)	129 (83)
Organ involvement		
Head and neck	49 (35)	40 (26)
Pulmonary	67 (47)	79 (51)
Renal	97 (68)	118 (76)
Neurologic	21 (15)	10 (6)
eGFR, ml/min/1.72m^2, median (IQR)	34.5 (13.7, 63.4)	20.9 (9.4, 45.5)
BVAS/WG at diagnosis, mean (SD)	5 (2)	5 (2)
CCI at diagnosis, mean (SD)	1.7 (2.3)	2.6 (2.7)
CFI, frailty classification		
Robust	17 (12)	11 (7)
Pre-frail	95 (67)	91 (58)
Mildly frail	23 (16)	43 (28)
Moderately/severely frail	7 (5)	11 (7)
Induction Treatment		
RTX	80 (56)	97 (62)
CYC	52 (37)	49 (31)
Other	10 (7)	10 (6)
Follow-up years, mean (SD)	5.9 (4.1)	4.4 (3.6)

Data presented as n (%), unless specified otherwise.
AAV = ANCA-associated vasculitis, SD = standard deviation, PR3 = Proteinase 3, MPO = myeloperoxidase, eGFR = estimated glomerular filtration rate, BVAS/WG = Birmingham Vasculitis Activity Score, CCI = Charlson Comorbidity Index, CFI = Claims-based Frailty index, RTX = rituximab, CYC = cyclophosphamide

morbidity and mortality, has not been adequately studied in older adults with AAV and provides a more holistic assessment.

The objective of this study was to compare the impact of age and frailty on early (≤ 2 years of diagnosis) end-stage renal disease (ESRD), severe infection, and death in adults with incident AAV who are ≥ 75 years old vs 65-74 years old.

Methods: Patients ≥ 65 years were included from the 2002-2019 Mass General Brigham AAV cohort, a consecutive inception cohort. EGPA patients were excluded. Covariates including demographics, disease characteristics, and the Charlson comorbidity index were assessed at baseline. Disease activity at diagnosis was assessed using the Birmingham Vasculitis Activity Score (BVAS/GPA). Baseline frailty was measured using the claims-based frailty index (CFI); pre-established cut-offs defined degrees of frailty (robust, pre-frail, mildly frail, and moderately/severely frail).[1]

Death and ESRD (composite outcome) were ascertained from linkage to national registries and/or medical records. Severe infections were identified utilizing inpatient data or as a code in death certificate. The cumulative incidence of the death/ESRD and severe infections at 2-years were estimated. Kaplan-Meier curves for the probability of composite outcome and severe infection by age and frailty were generated. Multivariable analysis was performed to compare the association of age and frailty with death/ESRD and severe infections within 2 years of treatment initiation.

Results: There were 298 patients included. Most were female (61%), white (86%), MPO-ANCA+ (80%), and had renal involvement (72%). Patients ≥ 75 years old (n=156) had a median age of 81 years, while median age was 69 years in the 65-74 years group (**Table 1**).

The cumulative incidence at 2 years of death/ESRD (23.1% [95% CI 16.5, 29.7]) vs 5.6% [95% CI 1.8, 9.4]) and severe infection (34.0% [95% CI 26.5, 41.4] vs 12% [95% CI 6.6, 17.3]) were higher in AAV patients ≥ 75 vs 65-74 years old. In the multivariable analysis, age ≥ 75 years was associated with an increased risk of composite outcome (hazard ratio (HR) 4.22, 95% CI 1.94-9.15); frailty was not (HR 2.02, 95% CI 0.46,8.81) (**Table 2, Figure 1**). In contrast, both frailty (HR 8.9, 95% CI 2.20,36.90) and age ≥ 75 years (HR 2.90, 95 CI% 1.73, 4.47) appeared to be independent risk factors for severe infections at 2-year follow-up; the association with frailty appeared greater.

Conclusion: AAV patients aged ≥ 75 vs 65-74 years had a higher incidence of death/ESRD and severe infections. Older age was associated with death/ESRD and severe infection risk. Frailty was a strong risk factor, independent of age, for severe infection. These findings highlight the need for innovative considerations beyond age when assessing outcome risks in older adults with AAV.

Table 2. Univariable and multivariable analyses for factors associated with outcomes in older adults with AAV at 2 years ESRD = end-stage renal disease, CFI = Claims-based frailty index, BVAS = Birmingham Vasculitis Activity Score, CYC = cyclophosphamide aAdjusted for sex, frailty, pulmonary involvement, renal involvement, and BVAS/GPA. bAdjusted for age, sex, pulmonary involvement, renal involvement, and BVAS/GPA.

Table 2. Univariable and multivariable analyses for factors associated with outcomes in older adults with AAV at 2 years

	Composite outcome (ESRD/Death)		Severe infection	
Factors	Univariable analysis HR (95% CI)	Multivariable analysis HR (95% CI)	Univariable analysis HR (95% CI)	Multivariable analysis HR (95% CI)
Age ≥ 75 years (Ref. 65-74 years)	**4.42 (2.05, 9.51)**	**4.22 (1.94, 9.15)[a]**	**3.21 (1.87, 5.52)**	**2.9 (1.73, 4.77)[a]**
CFI				
Robust	REF	REF	**REF**	REF
Pre-frail	1.85 (0.44-7.80)	1.68 (0.39, 7.13)[b]	4.01 (0.56-28.72)	2.7 (0.6, 11.2)[b]
Frail	2.71 (0.63-11.72)	2.02 (0.46, 8.81)[b]	**19.39 (2.77-135.66)**	**8.9 (2.2, 36.9)[b]**

ESRD = end-stage renal disease, CFI = Claims-based frailty index, BVAS = Birmingham Vasculitis Activity Score, CYC = cyclophosphamide
[a]Adjusted for sex, frailty, pulmonary involvement, renal involvement, and BVAS/GPA.
[b]Adjusted for age, sex, pulmonary involvement, renal involvement, and BVAS/GPA.

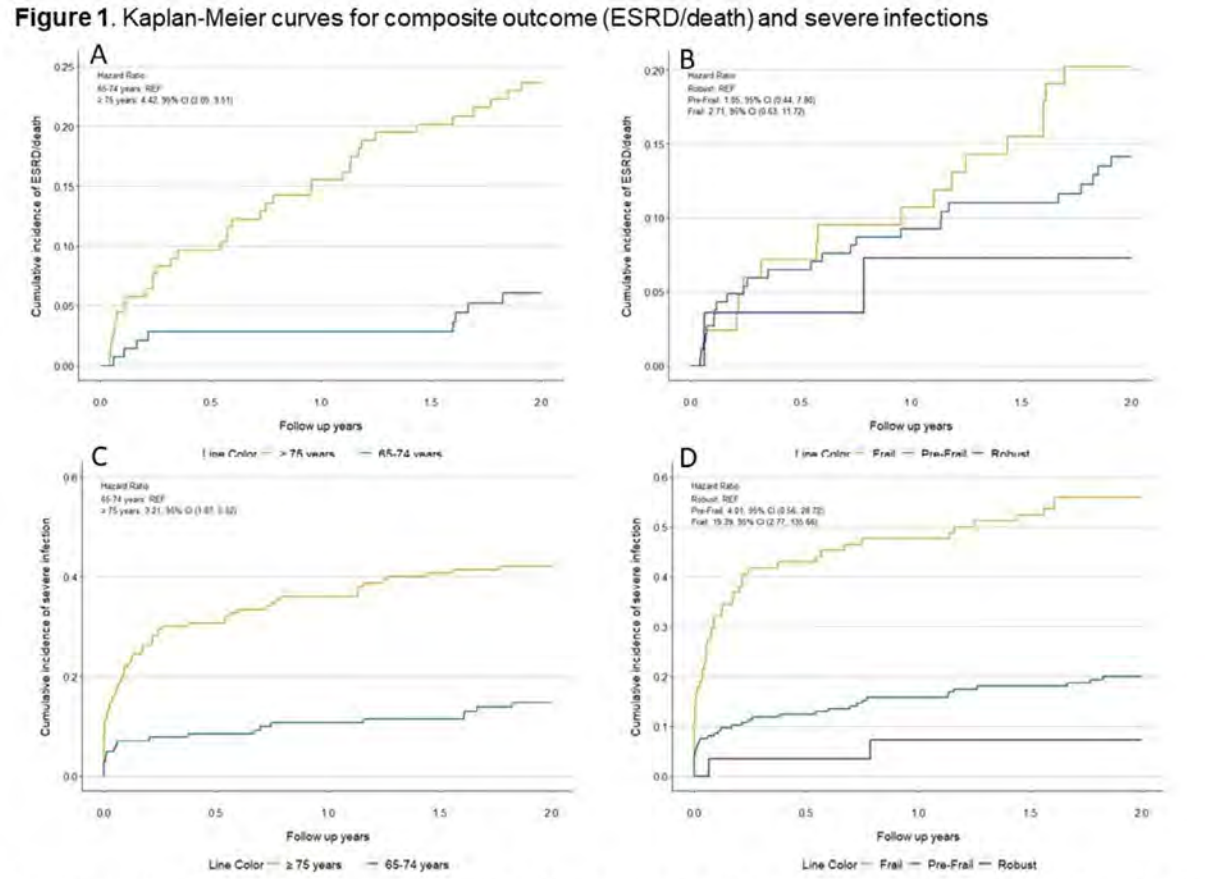

Figure 1. Kaplan-Meier curves for composite outcome (ESRD/death) and severe infections Composite outcome (ESRD/death) by age category (A) and frailty status (B), and severe infections by age (C) and frailty status (D).

References

1. Kim DH, et al. J Gerontol A Biol Sci Med Sci

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Abstract Number: 2378

Longitudinal Trajectories of Renal Function in ANCA-Associated Vasculitis: Findings from the Expanded Mass General Brigham Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Vasculitis – ANCA-Associated Poster III: Biomarkers & Renal Outcomes
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: ANCA-associated vasculitis (AAV) commonly causes renal damage, leading to a spectrum of chronic kidney disease (CKD) and end-stage renal disease (ESRD). Quantitative descriptions of the longitudinal course of renal dysfunction in AAV have recently been published from the 2002-2017 Mass General Brigham (MGB) AAV cohort. We aimed to further investigate these findings in an expanded cohort with additional years of follow-up.

Table 1. Baseline Characteristics of the Study Cohort

	Overall (N=375)	Rapid decline (N=23, 6%)	Impaired (N=109, 29%)	Preserved (N=216, 58%)	Improvement (N=27, 7%)	p-value
Probability of group membership (mean, SD)	0.99 (0.96-1.0)	1.0 (1.0-1.0)	0.99 (0.86-0.99)	0.99 (0.97-0.99)	1.0 (0.99-1.0)	
Number of visits*	8 (5-12)	6 (3-9)	9 (6-13)	8 (5-12)	9 (3-12)	0.20
Demographics						
Age at diagnosis (mean, SD)	62 (17)	65 (17)	64 (16)	61 (17)	64 (18)	0.22
Female sex (N, %)	226 (60)	13 (57)	63 (58)	136 (63)	14 (52)	0.60
Race/ethnicity						0.91
White	332 (89)	21 (91)	97 (89)	190 (88)	24 (89)	
Black	10 (3)	0 (0)	4 (4)	5 (2)	1 (4)	
Hispanic	5 (1)	0 (0)	1 (1)	4 (2)	0 (0)	
Asian	3 (1)	1 (4)	0 (0)	2 (1)	0 (0)	
Multiple	1 (0.3)	0 (0)	0 (0)	1 (0.5)	0 (0)	
Other	12 (3)	1 (4)	3 (3)	7 (3)	1 (4)	
Not recorded	9 (2)	0 (0)	3 (3)	6 (3)	0 (0)	
Clinical characteristics at baseline						
ANCA Type						0.53
MPO	252 (67)	17 (74)	78 (72)	139 (64)	18 (67)	
PR3	123 (33)	6 (26)	31 (28)	77 (36)	9 (33)	
BVAS/GPA (median, IQR)	5 (4-6)	6 (4-7)	5 (4-6.5)	4 (3-6)	6 (4-9)	<0.001
Renal	242 (65)	23 (100)	92 (84)	100 (46)	27 (100)	<0.001
Mucosal/ocular	36 (10)	0 (0)	6 (6)	29 (13)	1 (4)	0.03
Otolaryngological	135 (36)	4 (17)	30 (28)	93 (43)	8 (30)	0.01
Pulmonary	195 (52)	13 (57)	41 (38)	131 (61)	10 (37)	<0.001
Neurological	40 (11)	3 (13)	8 (7)	28 (13)	1 (4)	0.26
Comorbidities						
Charlson Comorbidity Index (median, IQR)	3 (1-5)	5 (3-7)	4 (2-6)	2 (1-5)	3 (2-5)	<0.001
Baseline DM	50 (13)	3 (13)	16 (15)	29 (14)	2 (7)	0.80
Baseline HTN	135 (36)	13 (57)	40 (37)	69 (32)	13 (48)	0.06
Baseline eGFR (±30d)	51 (21-88)	7 (6-10)	27 (18-39)	82 (56-97)	10 (8-16)	<0.001
Induction treatment						0.52
CYC-based	107 (29)	8 (35)	35 (32)	54 (25)	10 (37)	
RTX-based	220 (59)	14 (61)	64 (59)	127 (59)	15 (56)	
Other	48 (13)	1 (4)	10 (9)	35 (16)	2 (7)	
Plasma Exchange	77 (21)	16 (70)	24 (22)	21 (10)	16 (59)	<0.001

SD: standard deviation. MPO: anti-myeloperoxidase. PR3: anti-proteinase 3. BVAS/GPA: Birmingham Vasculitis Activity Score for Granulomatosis with Polyangiitis. DM: diabetes mellitus. HTN: hypertension. eGFR: estimated glomerular filtration rate. CYC: cyclophosphamide. RTX: rituximab.
*Number of months in the 36-month observation period in which the patient had a clinical renal function measurement.

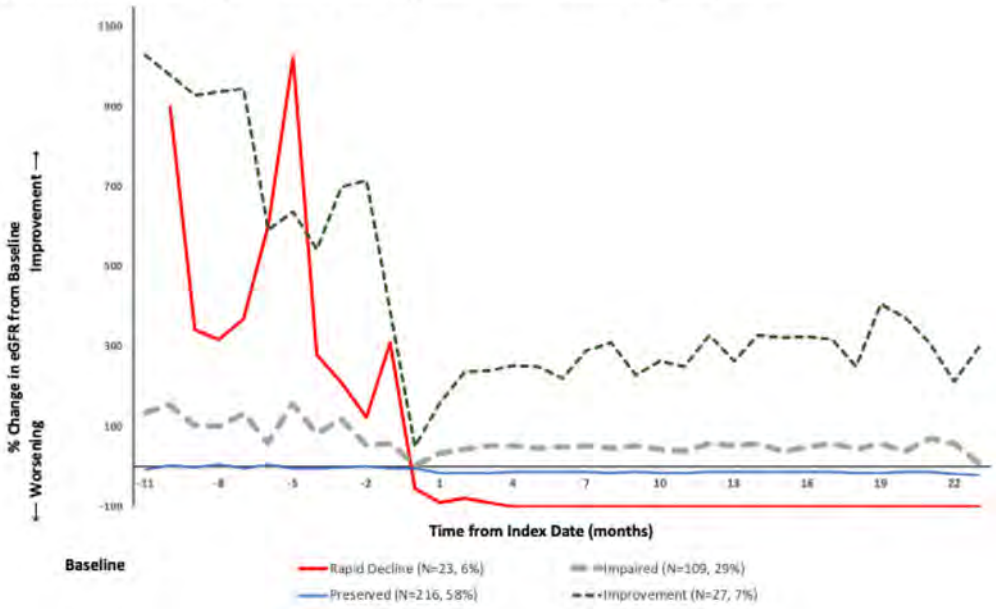
Table 2: Renal outcomes and mortality

	Overall (N=375)	Rapid decline (N=23, 6%)	Impaired (N=109, 29%)	Preserved (N=216, 58%)	Improvement (N=27, 7%)	p-value
Treatment resistance						<0.001
Yes	73 (20)	19 (83)	26 (24)	23 (11)	5 (19)	
No	143 (38)	1 (4)	60 (56)	63 (29)	19 (70)	
Renal outcomes						
Permanent ESRD*	49 (13)	22 (96)	11 (10)	15 (7)	1 (4)	<0.0001
Active vasculitis as cause of ESRD**	30 (61)	20 (91)	5 (45)	5 (33)	0 (0)	0.01
Time to ESRD (y)***	0.1 (0.0-3.5)	0.01 (0-0.1)	3.5 (0-6.8)	2.5 (0-5.6)	10 (10-10)	<0.001
eGFR at 1 year	51 (27-84)	2 (1-6)	35 (24-48)	77 (52-94)	26 (20-32)	<0.001
eGFR at 2 years	61 (36-84)	0 (0-0)	45 (28-62)	75 (53-92)	51 (36-64)	<0.001
eGFR at 5 years	62 (34-83)	0 (0-0)	49 (28-67)	73 (46-89)	64 (48-76)	<0.001
CKD III+ at 1 year	210 (56)	23 (100)	93 (85)	67 (31)	27 (100)	<0.001
CKD III+ at 2 years	144 (49)	13 (100)	62 (70)	58 (33)	11 (69)	<0.001
CKD III+ at 5 years	88 (48)	10 (100)	37 (69)	36 (34)	5 (38)	<0.001
Mortality						
Death	105 (28)	14 (61)	31 (28)	54 (25)	6 (23)	0.004
Follow-up time to death or censorship	5.7 (2.2-8.7)	5.2 (0.7-7.5)	5.7 (1.9-8.5)	5.7 (2.4-8.7)	5.9 (2.0-10)	0.01

CKD: Chronic kidney disease. ESRD: End-stage renal disease.
*Defined as (1) need for dialysis for >12 weeks, (2) dialysis until death if the patient died between 14-84 days of follow up, or (3) renal transplant.
** Among those with determined cause of ESRD.
***Among those who experienced ESRD.

Methods: We included patients from the MGB AAV cohort (2002-2022). A "baseline" measurement (±30 d from treatment initiation, the index date) of renal function was required along with one additional test. Renal function was assessed at up to monthly intervals, from -12 m to +24 m relative to the index date. Group-based trajectory modeling was used to identify distinct renal function trajectories. We assessed between-group differences (between all trajectory groups) with the chi-square and Kruskall-Wallis tests. Time to ESRD was compared using the log-rank test.

Figure: Observed Renal Trajectories in the Expanded Mass General Brigham Cohort



Results: We identified 4 renal trajectory groups among 375 patients: rapid decline (N=23 [6%]), impaired (N=109 [29%]), preserved (N=216 [58%]), and improvement (N=27 [7%]) (Figure). The median posterior probability of group membership was >0.98 in all groups, indicating excellent fit. Age, sex, race and ANCA type were not statistically different between groups. Renal vasculitis was found in all patients in the rapid decline (N=23 [100%]) and improvement (N=27 [100%]) groups, and in a majority of the impaired (N=92 [84%]), compared to a minority of the preserved group (N=100 [46%]; p< 0.001). Pulmonary vasculitis was more common among the rapid decline (N=13 [57%]) and preserved (N=131 [61%]) groups, compared to the impaired (N=41 [38%]) and improvement (N=10 [37%]) groups (p< 0.001). Otolaryngological and mucosal manifestations were most common in the preserved group (Table 1). The rapid decline group had the greatest baseline comorbidity, followed by the impaired group (p< 0.001; Table 1). Diabetes was equally common between groups, but there was a strong trend toward a higher rate of hypertension among the rapid decline and improvement groups vs the impaired and preserved groups (p=0.06). Disease activity by baseline Birmingham Vasculitis Activity Score was higher in the rapid decline (6 [4, 7]) and improvement (6 [4, 9]) groups, compared to the impaired (5 [4, 6.5]) and preserved (4 [3, 6]) groups (p< 0.001). ESRD occurred in 49 patients. In the rapid decline group, 22 patients (96%) experienced ESRD, compared to 11 (10%) in impaired, 15 (7%) in preserved and 1 (4%) in the improvement group (Table 2). ESRD occurred at a median of < 1 m from the index date in rapid decline vs 3.5 y (IQR 0, 6.8) in impaired and 2.5 y (IQR 0, 5.6) in the preserved group (log-rank p< 0.001). The cause of ESRD was active AAV in 91% of cases in the rapid decline, vs 45% in the impaired and 33% in the preserved group (p=0.01; Table 2).

Conclusion: We identified 4 distinct renal trajectory groups in an expanded AAV cohort. Trajectory groups were distinguished by variation in baseline comorbidity, rates of ESRD and CKD, and timing and cause of ESRD. Confirmation in a separate cohort will be required.

Disclosure: J. Hanberg: None; **C. Cook**: None; **X. Fu**: None; **H. Choi**: Ani, 2, Horizon, 2, 5, LG, 2, Protalix, 2, Shanton, 2; **Y. Zhang**: None; **Z. Wallace**: BioCryst, 2, Bristol-Myers Squibb(BMS), 5, Horizon, 1, 2, 5, MedPace, 2, Novartis, 1, PPD, 2, Sanofi, 1, 5, Shionogi, 1, Visterra, 1, 2, Zenas, 1, 2.

Abstract Number: 2379

A Real-World Descriptive Study of Renal Outcomes Among Patients with ANCA-Associated Vasculitis Initiating Remission Induction Therapy

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Vasculitis – ANCA-Associated Poster III: Biomarkers & Renal Outcomes
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Session Time: 9:00AM–11:00AM

Background/Purpose: ANCA-associated vasculitis (AAV) is a group of rare autoimmune diseases characterized by inflammation and necrosis of small- to medium-sized blood vessels, commonly affecting the kidneys. Clinical characteristics have been used to categorize AAV into different subtypes, including microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA). This study describes baseline characteristics and renal outcomes among patients with GPA or MPA who initiated remission induction therapy (RIT).

Methods: An observational retrospective cohort study using data from the MarketScan® Commercial and Medicare Supplemental claims database was conducted among patients diagnosed with GPA (ICD-10-CM M31.3, M31.30, M31.31) or MPA (M31.7) between April 1, 2016 and January 31, 2023. Patients must have been ≥18 years old on the GPA or MPA

diagnosis date (index date) and had ≥6 months of continuous medical and prescription enrollment prior to the index date (the baseline period). The study period was chosen to coincide with the availability of ICD-10 diagnosis codes for GPA and MPA. All available data prior to the index date were used to determine whether AAV diagnosis was prevalent based on the presence of claims for AAV prior to the index date, or presumptive incident based on the absence of AAV claims before the index date. Renal outcomes during follow-up were examined among the subset of presumed incident GPA or MPA patients initiating RIT, based on their first use of rituximab or cyclophosphamide. Renal outcomes included moderate-to-severe chronic kidney disease (CKD), defined as Stage 3 or higher, end-stage renal disease (ESRD), dialysis, and kidney transplant. The cumulative incidence for all available follow-up was estimated for each renal outcome.

Results: A total of 4,878 patients with GPA or MPA were identified. Among these, 33% (n=1,604) were prevalent cases, and 67% (n=3,274) were presumptive incident cases, with a higher proportion of prevalent cases among patients with GPA (35%, n=1,477) than MPA (18%, n=127). RIT was initiated among 23% (n=625) and 32% (n=185) of patients with presumptive incident GPA and MPA, respectively. These patients were primarily female (54% for GPA, and 68% for MPA) and age (mean ± standard deviation [SD]) at diagnosis was 51.9 ± 13.8 for GPA, and 57.7 ± 13.2 for MPA, respectively (Table 1). The prevalence of comorbidities between patients with GPA or MPA was generally similar, though comorbidities with renal or vascular involvement tended to be more frequent in patients with MPA than with GPA (Table 1). Claims for systemic steroids and immunosuppressive drugs were similar for patients with GPA (77% and 24%) and MPA (76% and 33%),

Table 1: Baseline and clinical characteristics of patients with presumptive incident AAV who initiated RIT

Characteristic	GPA or MPA (n = 810)	GPA (n = 625)	MPA (n = 185)
Mean age at diagnosis, years (SD)	53.2 (13.9)	51.9 (13.8)	57.7 (13.2)
Female patients (%)	465 (57.4%)	339 (54.2%)	126 (68.1%)
Selected comorbidities, n patients (%)			
Metabolic			
Hyperlipidemia	283 (34.9%)	205 (32.8%)	78 (42.2%)
Type 2 diabetes	119 (14.7%)	94 (15.0%)	25 (13.5%)
Obesity	163 (20.1%)	122 (19.5%)	41 (22.2%)
Vascular			
Hypertension	390 (48.1%)	285 (45.6%)	105 (56.8%)
Peripheral vascular disease	421 (52.0%)	305 (48.8%)	116 (62.7%)
Pulmonary/airway			
Interstitial lung fibrosis	63 (7.8%)	31 (5.0%)	32 (17.3%)
Chronic sinusitis	188 (23.2%)	170 (27.2%)	18 (9.7%)
Allergic rhinitis	128 (15.8%)	112 (17.9%)	16 (8.6%)
Renal/urologic			
Hematuria	220 (27.2%)	157 (25.1%)	63 (34.1%)
Proteinuria	181 (22.3%)	118 (18.9%)	63 (34.1%)
Glomerulonephritis	112 (13.8%)	76 (12.2%)	36 (19.5%)
Immune			
Rheumatoid arthritis	81 (10.0%)	63 (10.1%)	18 (9.7%)
Systemic lupus erythematosus	42 (5.2%)	27 (4.3%)	15 (8.1%)
Medications of interest, n patients (%)			
Systemic steroids	623 (76.9%)	482 (77.1%)	141 (76.2%)
Immunosuppressive drugs	214 (26.4%)	153 (24.5%)	61 (33.0%)
Mycophenolate mofetil	38 (4.7%)	29 (4.6%)	9 (4.9%)
Azathioprine	33 (4.1%)	23 (3.7%)	10 (5.4%)
Methotrexate	61 (7.5%)	49 (7.8%)	12 (6.5%)
Rituximab	95 (11.7%)	60 (9.6%)	35 (18.9%)
Cyclophosphamide	20 (2.5%)	13 (2.1%)	7 (3.8%)

AAV: ANCA-associated vasculitis. GPA: granulomatosis with polyangiitis. MPA: microscopic polyangiitis. RIT: remission induction therapy. SD: standard deviation.

Table 2: Cumulative incidence of selected renal outcomes among presumptive incident patients with GPA or MPA after initiating RIT

Outcome	Number of events	Patients at risk[1]	Cumulative incidence
Moderate to severe CKD (Stage 3 to 5)			
GPA or MPA	161	604	161 (26.7%)
GPA	128	491	128 (26.1%)
MPA	33	113	33 (29.2%)
End-stage renal disease			
GPA or MPA	74	758	74 (9.8%)
GPA	58	589	58 (9.8%)
MPA	16	169	16 (9.5%)
Dialysis			
GPA or MPA	89	722	89 (12.3%)
GPA	69	563	69 (12.3%)
MPA	20	159	20 (12.6%)
Kidney transplant			
GPA or MPA	22	801	22 (2.7%)
GPA	18	618	18 (2.9%)
MPA	4	183	4 (2.2%)

[1]Excludes patients who had claims for an outcome prior to initiating RIT.

CKD: chronic kidney disease. GPA: granulomatosis with polyangiitis. MPA: microscopic polyangiitis. RIT: remission induction therapy.

respectively. The cumulative incidences of CKD, dialysis, ESRD, and kidney transplant among patients with GPA or MPA were 27%, 12%, 10%, and 3%, respectively, and were similar across AAV subtypes (Table 2).

Conclusion: This study indicates that there remains a substantial burden of renal disease among patients with presumptive incident GPA or MPA after initiating RIT in a real-world setting.

Disclosure: S. Oh: Amgen, 3, 11; **S. Inguva**: Amgen, 3, 11; **P. Rane**: Amgen, 3, 11; **B. Tumminello**: Amgen, 3, 11, ChemoCentryx, 3, 11, Equillium, 3, 11.

Abstract Number: 2380

Renal Survival Rate of ANCA-associated Vasculitis in Korea: A Nationwide Population-Based Study Using Claims Data

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Vasculitis – ANCA-Associated Poster III: Biomarkers & Renal Outcomes

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: ANCA-associated vasculitis (AAV) is a rare systemic autoimmune disease with varying reports of incidence rates and clinical manifestations. Renal involvement is one of the most common manifestations and it can potentially progress to end-stage renal disease (ESRD). This study investigated the incidence rate and renal survival rate of patients with AAV using national health database in Korea.

Methods: Data were collected from the Korean National Health Insurance Claims Database. Incident AAV cases, according to the previously validated case-finding algorithm of AAV, between January 2010 to December 2019 were identified. Inverse probability treatment weights based on propensity scores and Cox's regression analysis were used to calculate the renal survival rate of patients with AAV and compared to that of the patients with primary glomerulonephritis (PGN) and among disease subgroups.

Results: We identified a total of 2,048 AAV patients, consisting of 876 granulomatosis with polyangiitis (GPA), 646 eosinophilic granulomatosis with polyangiitis (EGPA) and 526 microscopic polyangiitis (MPA) and 57,549 patients with PGN. The percentage of patients with renal replacement treatment (RRT) in AAV was 20.5% (n=419), consisting of 18.7%, 4.5%, and 43% in GPA, EGPA and MPA, respectively. A total of 33,931 (59%) patients underwent RRT in PGN. The overall risk of ESRD was significantly lower in AAV group (hazard ratio [HR] 0.3, $p< 0.001$) compared to the PGN group after adjusting for age and sex. Among AAV subtypes, renal survival rate was superior in the order of EGPA, GPA and MPA (HR 0.08, 0.29, and 0.9, respectively and all p-values were < 0.001) compared to that of PGN.

Conclusion: A considerable number of AAV patients required RRT. Renal survival rate of AAV was favorable compared to PGN.

Disclosure: C. Choi: None; **J. Shin**: None; **N. Choi**: None; **S. Ryu**: None.

Abstract Number: 2381

ANCA-associated Vasculitis and Renal Disease in a Multidisciplinary Outpatient Clinic in Northern Spain

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SESSION INFORMATION
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Background/Purpose: The severity of clinical features and outcomes in previous series of patients reported with renal disease related to ANCA-associated vasculitis (AAV) vary greatly, probably due to selection bias.

To establish the actual clinical spectrum of renal disease due to AAV in a multidisciplinary outpatient clinic in Northern Spain.

Methods: Review of 132 patients classified as having AAV between 1994 to 2022; Granulomatosis with polyangiitis (GPA), Microscopic polyangiitis (MPA) or Eosinophilic Granulomatosis polyangiitis (EGPA) was classified according to 2022 ACR/EULAR classification criteria.

Results: Renal disease was observed in 82 of 132 (62.1%) AAV (38 men/44 women), median age 61.37 years (24-87 years). Table reflects the main clinical findings and outcomes.

Renal biopsy was performed in 44 patients (36 patients showing a pauci-immune crescentic glomerulonephritis). The remaining 38 patients were not biopsied due to patient disagreement, mild renal disease or contraindication for biopsy.

The most frequent ANCA antibody specificity was MPO (64.6%) followed by PR3 (26.8%) and double positivity in 3 patients (2 MPO and PR3 and 1 MPO and MBG).

43 patients were classified as MPA (52.4%), of those, 18 patients (21.9%) had renal limited vasculitis, 27 GPA (32.9%), and 4 EGPA (4.9%). The rest of the patients had other renal disease (5 microhematuria, 1 amyloidosis, 1 diabetes nephropathy and 1 nephroangiosclerosis).

Nephritic syndrome was the most common renal manifestation when the vasculitis was fully established (56.1%).

The most frequent therapies used were corticosteroids (68.3%), Cyclophosphamide (46.3%), Azathioprine (35.4%), Rituximab (34.1%) and mycophenolate mofetil (23.2%).

After a median follow-up of 6.23 years (7 days-22.9 years) the last median creatinine and glomerular filtration rate (GFR) was 1.4 mg/dl and 43 ml/min, respectively.

Renal function worsened compared to baseline in 78.3% of MPO positive and only in 33% of PR3 positive (p=0.005).

During the first 12 months follow-up, stabilization or normalization GFR (median GFR at 1 year: 50 ml/min) was observed in 47.1% with no statistical differences among ANCA groups (p=0.303).

Table. Main clinical findings and outcomes of patients with AAV and renal disease. Abbreviations: ANCA-associated vasculitis (AAV), Granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA) or microscopic polyarteritis (MPA)

	AAV with renal disease (n=82)
Renal biopsy; n, (%)	44, (53.66%)
ANCA; n, (%)	
MPO	53, (64.6%)
PR3	22, (26.8%)
double positivity	3, (3.65%)
Diagnosis; n, (%)	
MPA	43, (52.4%)
GPA	27, (32.9%)
EGPA	4, (4.9%)
Other diseases	8, (9.8%)
Renal involvement; n, (%)	
nephritic syndrome	46 (56.1%)
proteinuria > 3.5 g/24h	3 (3.6%)
isolated hematuria	5 (6.1%)
Outcome; n, (%)	
dialysis	16, (19.5%)
total remission	25, (30.5%)
relapses	17, (20.7%)

Renal outcome at the end of follow-up was poorer in MPA than GPA or EGPA (76.3%, 47.4% and 50% respectively worsened GFR from baseline).

16 patients (19.5%) needed dialysis at any moment. Total remission was achieved in 25 patients (30.5%) while relapses were observed in 17 patients (20.7%).

Severe infectious was the main severe side-effect, reported in 26 patients (31.7%).

Conclusion: Most AAV patients had some grade of renal disease during follow-up and almost 20% ended up needing dialysis. Therefore this multi-systemic disease should be managed in a multidisciplinary way to establish an early diagnosis and adequate treatment, limiting chronic disease.

Disclosure: S. Al Fazazi: None; **F. Benavides**: None; **V. Calvo Río**: None; **m. rodriguez Vidriales**: None; **c. escagedo Cagigas**: None; **m. renuncio garcia**: None; **l. martin penagos**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6.

Abstract Number: 2382

Relapse of Patients with ANCA-associated Vasculitis Who Are on Dialysis

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Background/Purpose: It is known that disease activity of ANCA-associated vasculitis (AAV) is decreased after dialysis. However, most studies have been conducted on Caucasians, and factors associated with relapse during dialysis have not been well-studied. Therefore, this study aimed to elucidate the clinical manifestation of AAV relapse during dialysis, and identify factors associated with relapse, in an Asian country.

Methods: We retrospectively reviewed the data of patients diagnosed with AAV who were on dialysis due to renal involvement during follow-up from July 2005 to March 2021 at a single tertiary center in Seoul, Korea. Diagnosis of AAV was based on the International Chapel Hill Consensus Conference on the Nomenclature of Systemic Vasculitides. The patients on dialysis at the time of AAV diagnosis or during follow-up period were included in our study. Cox regression analysis was performed with the relapse as the dependent variable for the univariable and multivariable analysis.

Results: A total of 38 patients were included in the present study. Median age of participants was 64.0 (52.5–71.3) years, 28 (73.7%) were female, and 92.1% had microscopic polyangiitis (MPA). At diagnosis, mean BVAS was 18.3 (± 4.0), and 66.3% of patients had pulmonary manifestations. Of them, 12 patients were relapsed during followed up for 59.7 (± 50.4) months after dialysis. Among patients who experienced relapse, 9 had diffuse alveolar hemorrhage (DAH), and interstitial

Table 1. Baseline characteristics of patients with or without relapse

	All (n = 38)	Relapse		p-value
		Yes (n = 12)	No (n = 26)	
At time of diagnosis				
Age, years	64.0 (52.5–71.3)	58.0 (50.3–67.8)	64.0 (57.5–72.3)	0.353
Female, n (%)	28 (73.7)	9 (75.0)	19 (73.1)	0.900
BVAS at diagnosis	18.3 ± 4.0	18.5 ± 3.4	18.3 ± 4.3	0.871
Renal involvement	38 (100)	12 (100)	26 (100)	0.179
Pulmonary involvement	29 (66.3)	11 (91.7)	18 (69.2)	0.130
ENT	3 (7.9)	1 (8.3)	2 (7.7)	>0.999
Neurologic involvement	3 (7.9)	1 (8.3)	2 (7.7)	0.946
AAV type				0.946
MPA	35 (92.1)	11 (91.7)	24 (92.3)	
GPA	3 (7.9)	1 (8.3)	2 (7.7)	
ANCA type by ELISA				0.687
Anti-PR3	2 (5.3)	0 (0)	2 (7.7)	
Anti-MPO	35 (92.1)	12 (100)	23 (88.5)	
ANCA type by IF				>0.999
p-ANCA	18 (90.0)	7 (100)	11 (84.6)	
c-ANCA	1 (5.0)	0 (0)	1 (7.7)	
Laboratory data				
WBC, /uL	9800 (7400–14300)	9500 (7450–12300)	10250 (7400–15125)	0.379
Neutrophil, %	79.1 ± 10.5	81.5 ± 12.7	78.0 ± 9.3	0.352
Lymphocyte, %	13.4 ± 8.1	11.7 ± 8.7	14.1 ± 7.8	0.412
Hb, g/dL	8.4 ± 1.6	8.8 ± 2.2	8.3 ±1.3	0.417
Platelet, x10^3/uL	299.3 ± 129.5	233.3 ± 90.4	329.7 ± 134.8	0.031
ESR, mm/h	74.9 ± 31.0	58.2 ± 29.3	80.2 ± 30.3	0.132
CRP, mg/dL	11.0 ± 9.2	5.3 ± 5.0	13.0 ± 9.6	0.039
Albumin, g/dL	2.7 ± 0.6	3.0 ± 0.6	2.6 ± 0.5	0.039
Creatinine, mg/dL	5.8 ± 3.0	5.0 ± 2.6	6.2 ± 3.2	0.250

Values are mean (±standard deviation) or median (interquartile range), or n (%).

BVAS: Birmingham Vasculitis Activity Score, ENT: ear, nose, and throat, AAV: ANCA-associated vasculitis, ANCA: antineutrophil cytoplasmic antibody, MPA: microscopic polyangiitis, GPA: granulomatosis polyangiitis, ELISA: enzyme-linked immunosorbent assay, Anti-PR3: anti-proteinase 3, Anti-MPO: anti-myeloperoxidase, IF: immunofluorescence, WBC: white blood cell, Hb: hemoglobin, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein

Table 2. Uni- and multi-variable analysis of factors associated with relapse

	Univariable		Multivariable	
Variable	HR (95% CI)	p-value	HR (95% CI)	p-value
At the time of diagnosis				
Age, years	1.019 (0.972–1.069)	0.440		
Female	0.378 (0.098–1.451)	0.156		
BVAS at diagnosis	1.032 (0.898–1.185)	0.659		
Pulmonary involvement	5.574 (0.713–43.561)	0.101		
Lung infiltration	5.580 (1.168–26.659)	0.031		
DAH	4.594 (1.449–14.562)	0.010	5.509 (1.569–19.339)	0.008
ENT	0.946 (0.120–7.479)	0.958		
Neurologic involvement	0.578 (0.074–4.508)	0.601		
WBC, /uL	1.000 (1.000–1.000)	0.846		
Hb, g/dL	1.080 (0.794–1.468)	0.624		
Platelet, x10^3/uL	0.992 (0.986–0.999)	0.031		
ESR, mm/h	0.981 (0.956–1.006)	0.141		
CRP, mg/dL	0.917 (0.822–1.022)	0.117		
Albumin, g/dL	1.752 (0.695–4.414)	0.235		
Treatment				
Corticosteroid pulse for induction	0.281 (0.080–0.990)	0.048		
Plasma exchange for induction	0.655 (0.142–3.026)	0.588		
Mean corticosteroid doses, mg/day	1.360 (1.155–1.602)	<0.001	1.381 (1.161–1.642)	<0.001
Cumulative cyclophosphamide doses, g	0.977 (0.908–1.051)	0.533		
Maintenance therapy	1.762 (0.529–5.873)	0.356		

HR: hazard ratio, CI: confidence interval,

BVAS: Birmingham Vasculitis Activity Score, DAH: diffuse alveolar hemorrhage, ENT: ear, nose, and throat, WBC: white blood cell count, Hb: hemoglobin, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein

lung disease (ILD) aggravation (n = 2) and DAH (n =1) were found. There were no significant differences in age, sex, or mean BVAS at baseline between relapse and non-relapse group. Treatment regimen including cyclophosphamide, plasmapheresis, and maintenance therapy with azathioprine did not show statistical differences between the two groups. However, in univariable analysis, significant associations were observed between lung infiltration [HR 5.580 (1.168–26.659), p=0.031], DAH [HR 4.594 (1.449–14.562), p=0.010], corticosteroid pulse for induction [HR 0.281 (0.080–0.990), p=0.048], and mean corticosteroid doses [HR 1.360 (1.155–1.602), p< 0.001] with AAV relapse. Multivariable analysis showed that DAH [5.509 (1.569–19.339), p=0.008] and mean corticosteroid doses [1.381 (1.161–1.642), p< 0.001] were significantly associated with relapse.

Conclusion: Pulmonary manifestation, including DAH at baseline, was significantly associated with AAV relapse, and a significant association between mean corticosteroid doses and relapse was found.

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Abstract Number: 2383

Clinical Characteristics, Treatment Patterns, and Clinical Outcomes in Patients with Dual Positive Anti-Neutrophil Cytoplasmic Antibody and Anti-Glomerular Basement Membrane Antibody: A Single Center Experience

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Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Knowledge of disease characteristics and long-term outcomes of dual-positive patients (DPP) exhibiting anti-neutrophil cytoplasmic antibodies (ANCA) and anti-glomerular basement membrane (GBM) antibodies is limited to small studies in European cohorts. Data regarding disease characteristics, treatment modalities, and disease outcomes from North American populations are limited to case reports.

Methods: We performed a comparative retrospective chart review from a single center of adult DPP with both ANCA and anti-GBM antibodies and Single-positive patients (SPP) with only anti-GBM antibodies presenting between 1/1/2014 – 2/8/2023. The follow-up period ranged from 1- 84 months. 9 DPP and 17 SPP were identified. 14 patients not meeting the clinical criteria for ANCA vasculitis or GBM disease as determined by treating physicians were excluded.

Results: 50% (n=6) of the patients with anti-GBM antibodies also tested positive for ANCA at the time of diagnosis. 5 of these patients had myeloperoxidase (MPO) antibodies, none had anti-proteinase-3 (PR-3) antibodies. The median age was 70 years for DPPand 67 years for SPP. DPP presented with acute renal failure (ARF) (n=5), pulmonary-renal syndrome (n=2), and isolated diffuse alveolar hemorrhage (DAH) (n=1). 6 SPP presented with ARF and 2 with pulmonary-renal syndrome. A similar number of DPP and SPP required dialysis at initial presentation however more SPP had GFR< 15 (n=5) as compared to DPP (n=4). Median serum creatinine was 8.5 mg/dL for SPP and 7.8 mg/dL for DPP. 11/12 patients underwent renal biopsy, 10/12 showed crescentic glomerulonephritis (CGN) and 8/12 had linear IgG staining on

immunofluorescence. Pulmonary disease was more severe in DPP with 2 patients requiring stay in the intensive care unit (ICU) and 1 patient requiring mechanical ventilation as compared to 1 SPP requiring ICU stay. DPP pulmonary diagnoses include pulmonary fibrosis (n=2), and pulmonary nodules (n=1), which were not seen in SPP. All 5 DPP requiring dialysis at presentation remained dialysis dependent.1 SPP requiring dialysis at diagnosis was able to stop dialysis after 11 months. All patients received plasmapheresis except for 2 SPP;1 with sepsis and 1 with 100% crescents. All patients received pulse dose steroids. DPP were mostly treated with rituximab (n=5) while most SPP patients received cyclophosphamide (n=4). DPP received maintenance immunosuppression with rituximab (n=2) and mycophenolate mofetil (n=2) for a duration ranging from 3-18 months. Only 1SPPreceived maintenance steroids over 4 years until renal transplant. 1 DPP and 1 SPP who did not receive immunosuppression due to comorbidities died. 5/6 DPP had no relapse in the study period. One patient who developed DAH2 years after initial presentation was successfully treated with steroids and Rituximab.

Table 1.

Clinical Characteristics	DPP ANCA/ GBM (n=6)	SPP Anti-GBM (n=6)
Age at presentation-years (Median, range)	70.5 (65-86)	67 (30-77)
Gender, n (%)		
Male	3 (50%)	4 (66.6%)
Female	3 (50%)	2 (33%)
Race, n (%)		
White or Caucasian	6 (100%)	5 (83%)
Black or African American	0	1 (16.7%)
Ethnicity, n (%)		
Not Hispanic or Latino	6 (100%)	6 (100%)
Hispanic or Latino	0 (0%)	0 (0%)
Antibody Profile, n (%)		
c-ANCA	5 (83%)	0 (0%)
P- ANCA	5 (83%)	0 (0%)
PR-3	0 (0%)	0 (0%)
MPO	5 (83%)	0 (0%)
C-ANCA/PR3	0 (0%)	0 (0%)
P-ANCA/MPO	4 (66%)	0 (0%)
C-ANCA/P-ANCA	4 (66%)	0 (0%)
GBM	6 (100%)	6 (100%)
GBM checked with ANCA	6 (100%)	5 (83%)
Disease manifestations, n (%)		
Renal	5 (83%)	6(100%)
GFR<15	4 (66%)	5 (83%)
GFR 15-29	0 (0%)	1 (16.7%)
GFR 30-59	1 (16%)	0 (0%)
GFR>60	1 (16%)	0 (0%)
Requiring dialysis at presentation	5 (83%)	5 (83%)
Pulmonary	4 (66%)	2 (33%)
Hemorrhage	3 (50%)	2 (33%)
Pulmonary nodules	1(16%)	0 (0%)
Pulmonary fibrosis	2 (33%)	0 (0%)
Requiring ICU stay	2 (33%)	1 (16%)
Requiring intubation	1 (16%)	0 (0%)
Constitutional	6 (100%)	2 (33%)
Polyarthralgia	2 (33%)	0 (0%)
ENT(sinus disease)	2 (33%)	0 (0%)

Conclusion: Half (50%) of this cohort of anti-GBM-positive patients also had positive ANCA serology, highlighting the importance of testing for both antibodies in CGN. DPP presented with mixed clinical features of ANCA vasculitis and anti-GBM disease. Patients with dual positivity may have an increased risk of disease relapse upon discontinuation of immunosuppression.

Disclosure: Z. Shahid: None; **M. Lucke**: AbbVie/Abbott, 2; **S. Arora**: Aurinia, 1, 6, Calliditas, 6, Gsk, 6, Travere, 1.

Abstract Number: 2384

Major Cardiovascular Adverse Events in Patients with ANCA Vasculitis Compared with Hypertension Control Group

Lisa Rosenberg[1], Larabe Farrukh[1], Simrin Kooner[1], Moiz Ehtesham[1], Sumbal Wajid[1], Ruben Peredo-Wende[2] and Shannon Murawski[1], [1]Albany Medical Center, Albany, NY, [2]Stratton VA Medical Center, Albany, NY

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Vasculitis – ANCA-Associated Poster III: Biomarkers & Renal Outcomes
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Vascular damage from inflammation in ANCA vasculitis leads to a sustained procoagulant state causing accelerated atherosclerosis. A population-based cohort study found that the risk of cardiovascular disease is more than 3-fold higher in patients with ANCA-associated vasculitis. We hypothesize that those with ANCA vasculitis are more likely to have a major adverse cardiovascular event (MACE) compared to those in the hypertension control group.

Methods: We retrospectively reviewed patients with ANCA vasculitis (n=125) between 2017-2020. Charts were reviewed to assess cardiovascular (CV) risk factors which included history of smoking, hypertension, hyperlipidemia, diabetes mellitus and chronic kidney disease. Incidence of MACE such as myocardial infarction (MI), stroke, heart failure (HF) was calculated retrospectively after the diagnosis of ANCA vasculitis. Chi square and modified Poisson regression were used to calculate the incidence rate ratio (IRR) for MACE. We also retrospectively reviewed patients with hypertension without ANCA-associated vasculitis (n=100) between 2017-2020. The associations of each of the ANCA vasculitis categories and hypertension group with outcomes of MACE were examined by logistic regression. Minitab statistical software was used with significance accepted at $p < 0.05$.

Table 1

MACE	ANCA	Control	Odds Ratio	95% Confidence Interval
Stroke	EGPA	Hypertension	4.7647	(1.6858, 13.4671)
	GPA	Hypertension	10.2857	(4.4984, 23.5188)
	MPA	Hypertension	5.4000	(1.1196, 26.0439)
MI	EGPA	Hypertension	17.6000	(4.9577, 62.4804)
	GPA	Hypertension	8.7273	(2.7577, 27.6193)
	MPA	Hypertension	8.0000	(1.2122, 52.7971)
HF	EGPA	Hypertension	3.7251	(1.2344, 11.2419)
	GPA	Hypertension	6.7407	(2.8587, 15.8944)
	MPA	Hypertension	3.3704	(0.5912, 19.2155)

Table 2

MACE	ANCA	Size (Percentage)	Unadjusted IRR`	p-value	Adjusted IRR	p-value
Stroke	GPA	48 (62.3%)	1.00 (Reference)		1.00 (Reference)	
	EGPA	14 (37.8%)	0.61 (0.31 – 0.95)	0.03	0.65 (0.41 – 0.72)	0.04
	MPA	4 (36.4%)	0.68 (0.36 – 0.80)	0.02	0.67 (0.67 – 0.71)	0.01
MI	GPA	26 (33.7%)	1.00 (Reference)		1.00 (Reference)	
	EGPA	16 (43.2%)	1.28 (0.71 – 2.11)	0.31	1.34 (0.82 – 2.18)	0.23
	MPA	4 (36.4%)	1.07 (0.44 – 2.51)	0.86	1.18 (0.51 – 2.76)	0.71
HF	GPA	32 (41.5%)	1.00 (Reference)		1.00 (Reference)	
	EGPA	25 (67.6%)	1.23 (1.11 – 1.45)	0.04	1.21 (1.08 – 1.32)	0.04
	MPA	4 (36.4%)	0.87 (0.38 – 2.00)	0.75	1.05 (0.47 – 2.31)	0.89

Results: The mean age of the hypertension group was 62 years with a mean BMI of 30.1 kg/m². Females were 48%. The odds of having a stroke and MI were significantly higher amongst EGPA, GPA, and MPA patients than hypertension patients ($p< 0.05$). The odds of having HF were significantly higher amongst EGPA and GPA patients than hypertension patients ($p< 0.05$) [Table 1].

Of 125 total ANCA vasculitis patients, 77 (61.6%) had granulomatosis with polyangiitis (GPA), 37 (29.6%) had eosinophilic granulomatosis with polyangiitis (EGPA), and 11 (8.8%) had microscopic polyangiitis (MPA). Females were 68%. Mean age of the cohort was 58 years with a mean BMI of 29.4 kg/m². The unadjusted and adjusted (for age, gender, and CV risk factors) IRR for stroke was significantly lower in patients with EGPA and MPA vs. GPA ($p< 0.05$). The IRR for HF was significantly higher in EGPA vs. GPA ($p< 0.05$) [Table 2].

Conclusion: ANCA-associated vasculitis is a significant risk factor of MACE. The hypertension control group may not be a true matched control group. The ANCA vasculitis group may have other comorbidities including, diabetes, hyperlipidemia, chronic kidney disease, and tobacco abuse. More studies are needed to show that control of ANCA disease activity can decrease the risk of MACE and death. More studies are needed to show that treatment of modifiable risk factors including, glucocorticoid use, chronic kidney disease (CKD), proteinuria, respiratory infections, dyslipidemia, hypertension, metabolic syndrome, and insulin intolerance is necessary to optimize long-term outcomes.

Disclosure: L. Rosenberg: None; **L. Farrukh**: None; **S. Kooner**: None; **M. Ehtesham**: None; **S. Wajid**: None; **R. Peredo-Wende**: None; **S. Murawski**: None.

Abstract Number: 2385

Risk of Major Adverse Cardiovascular Events in ANCA-associated Vasculitis

Jon Idoate[1], Morgane Mourguet[1], Thomas Villeneuve[1], Grégoire Prevot[1], Laurent Guilleminault[2], Ribes David[1], Stan Faguer[1], Antoine Huart[1], Dominique Chauveau[1], Laurent Alric[1], Martin Michaud[1], Laurent Sailler[1], Sébastien De Almeida Chavez[1], Emmanuelle Mouchon[1], Olivier Lairez[1] and **Gregory Pugnet**[3], [1]CHU Toulouse, Toulouse, France, [2]Department of respiratory and allergic diseases, Toulouse University Hospital Center, Toulouse, France, [3]CHU Toulouse Rangueil Service de Medecine Interne et Immunologie Clinique, Toulouse, France

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Vasculitis – ANCA-Associated Poster III: Biomarkers & Renal Outcomes
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The aim of this study was to investigate the risk of major adverse cardiovascular events (MACE) in patients with ANCA-associated vasculitis (AAV).

Methods: We conducted a retrospective study using the ANCA-associated vasculitis Toulouse cohort (AAVT). The incidence of MACE, defined as myocardial infarction (MI) and/or stroke and/or death, as well as survival, were compared between groups using the Chapel Hill Consensus Conference classification criteria. We also applied Cox regression models adjusted for traditional cardiovascular risk factors and sex to assess the risk of MI, stroke and MACE occurrence.

Results: A total of 454 patients were included, including 266 (50%) with granulomatosis with polyangiitis (GPA), 167 (37%) with microscopic polyangiitis (MPA), and 61 (13%) with eosinophilic granulomatosis with polyangiitis (EGPA). Of these, 249 (55%) were men and 205 (45%) were women. The mean age at diagnosis was 61 (SD: 16.49) years, and the mean follow-up duration was 7.185 (SD: 6.72) years. We identified 19 MI and 13 strokes during the study period. The incidence rate of MACE was 23.77 per 1000 patient-years in the GPA group, compared to 35.51 per 1000 patient-years in the MPA group and 20.03 per 1000 patient-years in the EGPA group. The mean time to occurrence of a MACE was 8.07 (SD: 6.19) years in the GPA group, 4.59 (SD: 4.63) years in the MPA group and 13.58 (SD: 11.51) years in the GEPA group (p=0.0001). At 5 and 10 years from diagnosis, the probability of survival without MACE was 93.3% and 81.57%, respectively, in the GPA group, 83.98% and 67.15% in the MPA group, and 94.33% and 86.83% in the EGPA group (p=0.037). The incidence rate of MI was 4.10 per 1000 patient-years in the GPA group, compared to 8.44 per 1000 patient-years in the MPA group and 5.37 per 1000 patient-years in the EGPA group. The mean time to occurrence of an MI was 3.72 (SD: 5.74) years in the GPA group, compared to 3.04 (SD: 2) years in the MPA group and 7.52 (SD: 5.28) years in the EGPA group (p=0.0001). At 5 and 10 years from diagnosis, the incidence of MI was 2% and 3%, respectively, in the GPA group, 4% and 5% in the MPA group, and 2% and 5% in the EGPA group (p=0.48). The incidence rate of stroke was 4.08 per 1000 patient-years in the GPA group, compared to 5.26 per 1000 patient-years in the MPA group and 1.73 per 1000

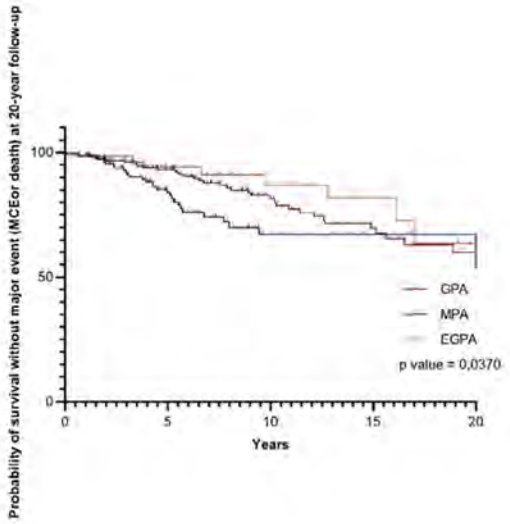

Figure 1. Kaplan Meier estimate of event-free survival where major adverse cardiovascular event were counted as events in ANCA-associated vasculitis.

patient-years in the EGPA group. The mean time to occurrence of a stroke was 7.19 (SD: 5.11) years in the GPA group, compared to 3 (SD: 2.14) years in the MPA group and 17.83 (SD not applicable) years in the EGPA group (0;0001). At 5 and 10 years from diagnosis the incidence of stroke was 1% and 2% respectively in the GPA group, 2% and 3% in the MPA group, and 0% in the EGPA group (p=0;49).

Conclusion: Patients classified as MPA appear to be at higher risk of MACE and have a lower probability of MACE-free survival.

Disclosure: J. Idoate: None; **M. Mourguet**: None; **T. Villeneuve**: None; **G. Prevot**: None; **L. Guilleminault**: None; **R. David**: None; **S. Faguer**: None; **A. Huart**: None; **D. Chauveau**: None; **L. Alric**: None; **M. Michaud**: None; **L. Sailler**: None; **S. De Almeida Chavez**: None; **E. Mouchon**: None; **O. Lairez**: None; **G. Pugnet**: None.

Abstract Number: 2386

Impact of ANCA Specificity on Risk of Major Adverse Cardiovascular Events in ANCA-associated Vasculitis

Jon Idoate[1], Morgane Mourguet[1], Ribes David[1], Stan Faguer[1], Antoine Huart[1], Dominique Chauveau[1], Thomas Villeneuve[1], Grégoire Prevot[1], Laurent Guilleminault[2], Emmanuelle Mouchon[1], Laurent Balardy[1], Laurent Sailler[1], Sébastien De Almeida Chavez[1], Laurent Alric[1], Martin Michaud[1], Olivier Lairez[1] and **Gregory Pugnet**[3], [1]CHU Toulouse, Toulouse, France, [2]Department of respiratory and allergic diseases, Toulouse University Hospital Center, Toulouse, France, [3]CHU Toulouse Rangueil Service de Medecine Interne et Immunologie Clinique, Toulouse, France

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Vasculitis – ANCA-Associated Poster III: Biomarkers & Renal Outcomes
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The aim of this study was to investigate the relationship between ANCA specificity and the risk of major adverse cardiovascular events (MACE) in patients with ANCA-associated vasculitis (AAV).

Methods: We conducted a retrospective study using the ANCA-associated vasculitis Toulouse cohort (AAVT). The incidence of MACE, defined as myocardial infarction (MI) and/or stroke and/or death, as well as survival, were compared among patients according to their ANCA specificity. We also applied Cox regression models adjusted for traditional cardiovascular risk factors and sex to assess the risk of MI, stroke and MACE occurrence.

Results: A total of 402 patients were included, of whom 166 (41%) had anti-PR3 ANCA and 236 (59%) had anti-MPO ANCA. Among them, 220 (55%) were male and 182 (45%) were female. The mean age at diagnosis was 61.22 (SD: 16.05) years, and the mean follow-up duration was 7.51 (SD: 6.41) years. During the study period, 15 cases of MI and 12 cases of stroke were identified.

The incidence rate of MACE was 33.11 per 1000 patient-years in the anti-MPO ANCA group, compared to 21.37 per 1000 patient-years in the anti-PR3 ANCA group. The mean time to MACE occurrence was 3.29 (SD: 2.74) years in the anti-MPO ANCA group and 7.33 (SD: 5.68) years in the anti-PR3 ANCA group (p=0.0001). At 5 and 10 years from diagnosis, the probability of MACE-free survival was 89.39% and 68.77% respectively in the anti-MPO ANCA group, and 93.39% and 83.36% in the anti-PR3 ANCA group (p=0.0001) (figure 1).

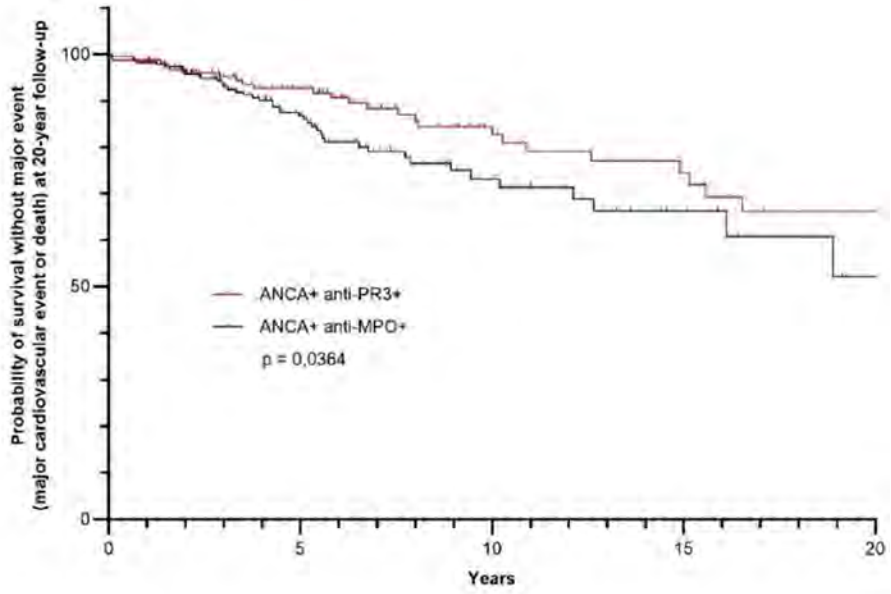

Figure 1. Kaplan Meier estimate of event-free survival where major adverse cardiovascular event were counted as events in ANCA-associated vasculitis.

The incidence rate of MI was 6.16 per 1000 patient-years in the anti-MPO ANCA group, compared to 4.09 per 1000 patient-years in the anti-PR3 ANCA group. The mean time to MI occurrence was 2.21 (SD: 1.81) years in the anti-MPO ANCA group, while it was 4.24 (SD: 6.11) years in the anti-PR3 ANCA group (p=0.0001). At 5 and 10 years from diagnosis, the incidence of MI was 4% in the anti-MPO ANCA group, compared to 2% and 3%, respectively, in the anti-PR3 ANCA group (p=0.31).

The incidence rate of stroke was 6.13 per 1000 patient-years in the anti-MPO ANCA group, compared to 2.72 per 1000 patient-years in the anti-PR3 ANCA group. The mean time to stroke occurrence was 4.39 (SD: 2.99) years in the anti-MPO ANCA group, while it was 7.69 (SD: 7.42) years in the anti-PR3 ANCA group (p=0.0009). At 5 and 10 years from diagnosis, the incidence of stroke was 2% and 3%, respectively, in the anti-MPO ANCA group, and 1% and 2% in the anti-PR3 ANCA group (p=0.18).

The Cox regression model found an association between the presence of anti-MPO ANCA and the risk of MACE (HR: 1.77; 95% CI: 1.13-2.8; p=0.0134). A similar trend was observed for the risk of stroke (HR: 3.05; 95% CI: 0.88-10.6; p=0.0795). There was no association found between the presence of anti-MPO ANCA and the risk of MI.

Conclusion: Patients with anti-MPO ANCA appear to be at higher risk of MACE.

Disclosure: J. Idoate: None; **M. Mourguet**: None; **R. David**: None; **S. Faguer**: None; **A. Huart**: None; **D. Chauveau**: None; **T. Villeneuve**: None; **G. Prevot**: None; **L. Guilleminault**: None; **E. Mouchon**: None; **L. Balardy**: None; **L. Sailler**: None; **S. De Almeida Chavez**: None; **L. Alric**: None; **M. Michaud**: None; **O. Lairez**: None; **G. Pugnet**: None.

Abstract Number: 2387

Large Vessel Involvement and the Risk of Severe Infections in Patients with Giant Cell Arteritis – a Population-based Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Manifestations of giant cell arteritis (GCA) include large vessel involvement (LVI) of the aorta and its branches. Aortic aneuryms are more common compared to the general population. GCA is complicated by an increased risk of infections, likely due to treatment and/or the systemic nature of the disease. There is limited information on the impact of

Table 1

Table 1. Characteristics and prevalent comorbidities at diagnosis in patients with biopsy-proven giant cell arteritis

	GCA patients N= 516
Age at diagnosis, mean [SD]	75.3 [8.30]
Female sex, n (%)	377 (73.0)
Large vessel involvement, n (%)	100 (19.4)
Aortic involvement, n (%)	62 (12)
Charlson Comorbidity Index (CCI)	
CCI groups, n (%)	
0	227 (43.8)
1	210 (40.7)
2	43 (8.3)
≥3	37 (7.2)
Cardiovascular disease (CVD), n (%)	
Coronary artery disease	62 (12)
Heart failure	117 (22.7)
Cerebrovascular disease	84 (16.3)
Peripheral arterial disease	None
CVD, any	189 (36.6)
Diabetes mellitus (DM), n (%)	
Type I	26 (5.0)
Type II	83 (16.1)
DM, any	86 (16.7)
Pulmonary disease, n (%)	
Chronic obstructive pulmonary disease	54 (10.5)
Kidney disease, n (%)	
Chronic kidney disease with renal failure	17 (3.3)
Renal failure, non-specified	17 (3.3)
Osteoporosis related fractures, n (%)	
Hip fracture	54 (10.5)
Vertebral fracture	12 (2.3)
Wrist fracture	41 (7.9)
Proximal humeral fracture	19 (3.7)

SD: Standard deviation

the disease phenotype on the risk of infection among patients with GCA. No previous study has investigated LVI in GCA as a risk factor for severe infections. Such investigations need to take into account demographics and comorbidities. The objective of this study was to assess the influence of age, sex, LVI and pre-existing comorbidities on the risk of severe infection in GCA.

Methods: Patients with biopsy-proven GCA, diagnosed between 2002 and 2010, were identified from a regional pathology register, and followed through the end of study December 2011.

Data on infections requiring hospitalization were obtained from linkage to the regional healthcare registry. Twenty categories of infections were identified based on ICD-10 codes.

Five categories of pre-existing comorbidities were based on diagnoses registered within four years before the date of GCA diagnosis, and the Charlson comorbidity index (CCI) was calculated. Information on LVI was obtained through structured review of all relevant radiological and clinic-physiological studies. LVI was defined as presence of aneurysm, ectasia, or stenosis of the aorta and/or its main branches or positive 18fluoro-2-deoxy-d-glucose positron emission tomography–computed tomography or other nuclear imaging methods indicating vasculitis. Patients with LVI findings after or ≤1 year before the GCA diagnosis were classified as having the LVI phenotype. Cox regression analysis was used to identify possible predictors of severe infections among patients with GCA. Patients were followed from time of GCA diagnosis and censored at death or migration from the region. Covariates were excluded from multivariate models based on co-linearity.

Results: Among 516 patients with biopsy-proven GCA (Table 1), 19.4% had confirmed LVI, and 12% had aortic involvement (aneurysm, ectasia, dissection or signs of vasculitis on nuclear imaging) with or without concomitant distributary artery affection. There were 118 patients with ≥1 severe infection during the study period.

Table 2

Table 2. Cox regression analyses of the potential predictors of severe infections

	Crude HR (95% CI)	Age- adjusted HR (95% CI)
Age, per SD	**1.79 (1.45 - 2.21)**	NA
Male sex	1.38 (0.93 - 2.04)	1.47 (1.00 - 2.18)
Charlson comorbidity index		
0	1.00 (ref)	NA
1	0.89 (0.60 - 1.33)	0.83 (0.56 - 1.24)
2	1.03 (0.51 - 2.09)	0.94 (0.47 - 1.92)
≥3	1.74 (0.88 - 3.41)	1.48 (0.76 - 2.92)
Any large vessel involvement	1.30 (0.85 - 1.97)	**1.61 (1.05 - 2.46)**
Aortic involvement	1.39 (0.85 - 2.27)	**1.97 (1.19 - 3.27)**
Coronary artery disease	**2.83 (1.84 - 4.42)**	**2.30 (1.48 - 3.59)**
Heart failure	**3.19 (2.21 - 4.60)**	**2.40 (1.64 - 3.54)**
Cerebrovascular disease	1.52 (0.97 - 2.38)	1.31 (0.83 - 2.05)
Cardiovascular disease, any	**2.82 (1.59 - 4.07)**	**2.22 (1.52 - 3.24)**
Diabetes mellitus, type I	**1.92 (1.01 - 3.67)**	**1.97 (1.03 - 3.78)**
Diabetes type II	1.44 (0.92 - 2.25)	**1.69 (1.08 - 2.66)**
Diabetes mellitus, any	**2.03 (1.31 - 3.15)**	**1.81 (1.17 - 2.82)**
Chronic obstructive pulmonary disease	**2.38 (1.50 - 3.79)**	**2.19 (1.38 - 3.48)**
Chronic kidney disease with renal failure	**4.40 (2.30 - 8.43)**	**3.39 (1.75 - 6.58)**
Renal failure un specified	**3.21 (1.68 - 6.13)**	**2.51 (1.31 - 4.82)**
Hip fracture	1.36 (0.79 - 2.34)	0.80 (0.46 - 1.38)
Vertebral fracture	1.54 (0.57 - 4.19)	0.97 (0.36 - 2.62)
Wrist fracture	0.77 (0.37 - 1.57)	0.63 (0.31 - 1.29)
Proximal humeral fracture	2.03 (0.99 - 4.16)	**2.16 (1.05 - 4.44)**

HR: Hazard ratio, CI: Confidence interval; SD: Standard deviation; NA: Not applicable

Table 3

Table 3. Predictors of severe infections in patients with GCA – Cox regression, multivariate analysis

Variables	HR (95% CI)
Age, per SD	**1.82 (1.46 - 2.28)**
Male sex	1.45 (0.97 - 2.18)
Aortic involvement	**1.75 (1.04 - 2.94)**
Diabetes	**1.82 (1.16 - 2.84)**
Chronic obstructive pulmonary disease	**1.89 (1.18 - 3.03)**
Chronic kidney disease with renal failure	**2.90 (1.48 - 5.67)**
Proximal humeral fracture	**2.29 (1.08 - 4.86)**

SD: Standard deviation

Higher age at diagnosis and several pre-existing comorbidities, i.e. coronary artery disease, heart failure, diabetes, chronic obstructive pulmonary disease and renal failure were significant predictors for severe infections (Table 2). LVI overall and aortic involvement were associated with significantly increased risk of severe infections in age-adjusted analyses (Table 2**)**. In the multivariate analysis, aortic involvement was predictive of severe infections (Hazard ratio 1.75; 95% confidence interval 1.04-2.94, adjusted for age and comorbidities) (Table 3**)**.

Conclusion: In patients with GCA, age and specific pre-existing medical conditions are predictors of severe infections. LVI, in particular of the aorta, may also be associated with a higher risk for severe infection.

Disclosure: N. Naderi: None; **A. Mohammad**: None; **K. Wadström**: None; **U. Bergström**: None; **C. Turesson**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, Pfizer, 6.

Abstract Number: 2388

Increased Risk of Severe Infections in Early Giant Cell Arteritis: A Population- based Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
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Background/Purpose: Giant cell arteritis (GCA) is the most common type of vasculitis in adults aged 50 years or older. Although the substantial morbidity from infections in patients with GCA, partly due to immunosuppressive treatment, is well recognized, few studies have evaluated the incidence of severe infections compared to the general population. Even fewer have investigated the incidence of severe infection by time from GCA diagnosis compared to a reference population.

The objective of this study was to compare the risk of severe infection in different time intervals after GCA diagnosis to the general population.

Table 1

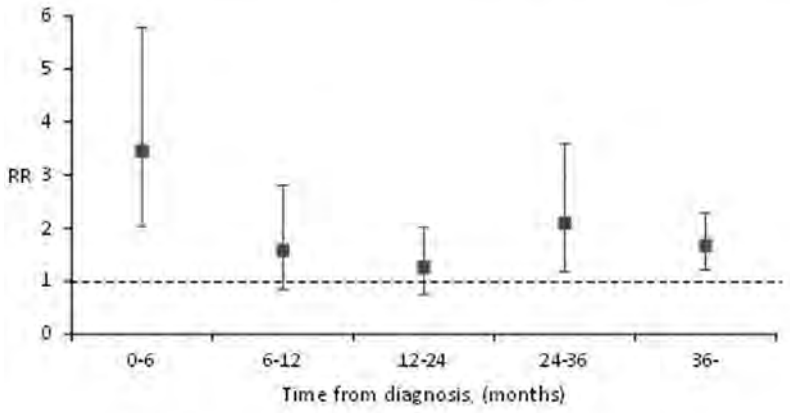
Table 1. Rates of severe infections in patients with giant cell arteritis and reference subjects

	Cases			Reference subjects		
Follow-up interval (months)	Infections (n)	Follow-up (pyr)	Rate/100 pyr (95% CI)	Infections (n)	Follow-up (pyr)	Rate/100 pyr (95% CI)
All severe infections						
0-6	37	250.5	14.8 (10.4; 20.4)	45	995.9	4.5 (3.3; 6.1)
6-12	21	240.2	8.7 (5.4; 13.4)	63	972.6	6.5 (5.0; 8.3)
12-24	40	441.7	9.1 (6.5; 12.3)	116	1806.7	6.4 (5.3; 7.7)
24-36	29	357.0	8.1 (5.4; 11.7)	65	1484.2	4.4 (3.4; 5.6)
36-	95	1011.4	9.4 (7.6; 11.5)	287	4155.0	6.9 (6.1; 7.8)

n; number; pyr: person years; CI: Confidence interval.

Methods: Patients with biopsy-proven GCA, diagnosed between 2002 and 2010 were retrieved from a regional pathology register. They were compared with four reference subjects per case from the corresponding area, matched for age, sex and area of residence. Data on infections requiring hospitalization were obtained from linkage of the cases and the references to the regional healthcare register, through 2011. Using ICD-10 codes, twenty categories of infections were identified. Patients and reference subjects were censored at death or migration from the area. Incidence rates of severe infections in patients with GCA and reference subjects, stratified by follow-up time (0-6 months, 6-12 months, 1-2 years, 2-3 years, > 3 years), were estimated by dividing the number of severe infections in each time interval with the corresponding follow-up time (in years). The follow-up time started at date of diagnosis for patients (index-date for reference subjects) and ended at death or December 31, 2011. Rate Ratios (RRs) regarding severe infections, stratified by category of follow-up time, were calculated for patients with GCA vs. reference subjects. The 95% confidence intervals (CI) for incidence rates and RRs were estimated using the Poisson distribution ratio.

Figure 1.
Incidence of severe infections in patients with GCA vs reference subjects



RR: Rate ratios. Whiskers indicate 95% confidence intervals

Figure 1

Results: Five hundred and sixteen patients with GCA were identified and compared to 3335 matched reference subjects. A total of 222 severe infections occurred in 118 patients with GCA. The cumulative incidence rate of severe infections was 8.5 % during the first year and 22.9 % over the entire follow-up.

The incidence rate in patients with GCA was highest during the first six months, 14.8/100 person-years (Table 1**)**.

During this period, the rate was significantly increased compared to reference subjects (RR 3.27; 95% CI 2.06; 5.11) (Figure 1**).**

The rate of severe infections was numerically higher than that for the general population during the entire follow-up, but the difference reached statistical significance only during the first six months and after > 2 years of follow-up (Table 1, Figure 1**)**.

Conclusion: The risk for severe infection is increased in patients with GCA compared to the general population, in particular during the first 6 months after diagnosis.

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Calprotectin (S100A8/S100A9) and Serumamyloid A Are Not Superior to C Reactive Protein and Erythrocyte Sedimentation Rate in Monitoring Disease Activity in Giant Cell Arteritis – Treated with or Without Tocilizumab

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Background/Purpose: Monitoring disease activity in giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) remains challenging as standard inflammation parameters, i.e., C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), are not specific for rheumatic disease activity. Furthermore, tocilizumab (TCZ), meanwhile a cornerstone of GCA treatment, inhibits interleukin-6 (IL-6)-dependent synthesis of CRP. Calprotectin (CALPR) and serum amyloid A (SAA) are promising alternatives, especially since they are at least largely independent of IL-6. However, there are few prospective data on large cohorts. Our aim was to evaluate the value of CALPR and SAA for indicating disease activity in GCA/PMR.

Methods: In a prospective cohort study, CRP, ESR, CALPR, and SAA were measured repeatedly at each visit in 98 patients with confirmed GCA (N=81) or PMR (N=17). A total of 576 visits (=measurements) were performed with a mean of 5.9 ± 2.7 visits for each patient. Patients were classified as "active disease" by clinical evaluation according to current guidelines at 131 visits (=22.7% of all visits). TCZ was administered at 140 visits. To test the predictive power of patients' active status based on all measurements, we performed univariate logistic regression. For the resulting receiver operator curves (ROC), 99% confidence intervals of the area under the curve (AUC) were calculated based on a bootstrap approach (9999 replicates). Because patients were measured multiple times, we modeled the log value of all measurements using a mixed-effects model with the random factor "patient." These values were modeled using the numeric factors BMI and age and the binary factors sex (male/female), prednisolone (yes/no), MTX (yes/no), diagnosis (GCA/PMR), and active (yes/no).

Results: ROC analysis of examinations without TCZ showed the best AUC for CRP (0.76; 0.69-0.83), followed by SAA (0.74; 0.66-0.82), ESR (0.7; 0.63-0.78), and CALPR (0.66; 0.59-0.73). For visits with TCZ, SAA showed the best AUC (0.73; 0.5-0.9), then CRP (0.58; 0.41-0.77), CALPR (0.55; 0.32-0.74), and ESR (0.48; 0.31-0.68). In the adjusted model for visits without TCZ, CRP, ESR, and SAA showed highly significant mean change in active disease ($p > 0.001$), CALPR showed significant change ($p < 0.05$). For visits with TCZ, no parameter showed significant mean change with active disease.

Conclusion: SAA shows better AUC than the other seromarker in patients treated with TCZ. In patients without TCZ treatment, the AUC of CRP and SAA are almost equal. However, after multivariate regression, no significant effect is detectable for any of the tested parameters.

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Characterization of Senescent Cells in Temporal Arteries of Patients with Giant Cell Arteritis Reveal an Inflammatory Phenotype and Strong Dependence from IL-6

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Background/Purpose: Age is the strongest risk factor of giant cell arteritis (GCA), implying a possible pathogenetic role of cellular senescence. So far, no studies have investigated adequately this question. The current study aims to identify the various senescent cell types in temporal artery biopsies (TABs) of GCA and polymyalgia rheumatica (PMR) patients by applying the novel multi-marker algorithm, define the secretory associated senescent phenotype (SASP) key molecules and explore possible implications of senescence in GCA pathogenesis.

Methods: Seventy five positive TABs from GCA patients and 22 negative from PMR patients were retrospectively analyzed. Senescent cells and their histologic origin were identified after staining for specific cellular markers including GL13, p21, vimentin, CD68, CD3 and aSMA, following the established multi-marker algorithm(1,2); IL-6 and MMP-9 were investigated as components of the (SASP) by triple co-staining. Twenty-four hour GCA or PMR artery culture supernatants were applied to primary skin fibroblasts with or without IL-6 blocking agent to explore the induction of IL-6 associated cellular senescence.

Results: Senescent cells were present in GCA arteries at higher proportion compared to PMR (9.50% vs 2.66% respectively, $p< 0.0001$) adjacent to the inflammatory cells and were mainly originated from fibroblasts (29.6%), macrophages (16.2%) and endothelial cells (14.3%) (Figure 1). IL-6 was expressed mainly by senescent fibroblasts and macrophages while MMP-9 by fibroblasts only (Figure 2). IL-6 positive senescent cells were associated with the extension of vascular wall

Figure 1. Detection of senescent cells in tissue artery biopsies of GCA patients. (A) Representative images for single GL13 staining with immunohistochemistry (upper panel) and immunofluorescence (lower panel) in TABs of GCA and PMR patients, showing higher proportion of GL13 positive cells adjacent to the inflammatory cells in GCA arteries compared to PMR. (B) Graphical representation of the proportion of GL13 positive senescent cells, after immunohistochemical evaluation by two independent readers and quantification analysis in 75 GCA and 22 PMR TABs (GCA vs PMR): 9.50% vs 2.66%, $p<0.001$. (C) Confirmation of senescent cells by co-staining for GL13 and p21WAF1/Cip1 in a TAB of a GCA compared to a PMR patient (representative image). (D) Electron micrographs of senescent cells in artery of GCA patients showing Lipofuscin (LF) granules in their cytoplasm (Di,ii). (E) Electron micrographs of cells in artery of PMR patient without lipofuscin granules (Ei,ii). Higher magnification of the area in the black box of (Ei). N: nucleus. Staining: uranyl acetate/lead citrate. Objectives (A) 20x, (C) 63x. Scale bars: 50μm (A) 10μm (C). 1μM (Di,ii, Eii), 2μM (Ei). ****$p < 0.0001$

Figure 2. Characterization of senescent cells per cell type in tissue artery biopsies of GCA patients. Representative images of double positive senescent cells after staining for GL13 and (A) Vimentin(+) (fibroblasts), (B) CD68(+) (macrophages), (C) CD34(+) (endothelial cells) or (D) aSMA (+) (smooth cells) in a TAB of one GCA and one PMR patient (double staining immunofluorescence). Squares depict magnified cells with presence of double positive staining. (E) Quantification analysis by two independent observers, showing significantly higher proportion of senescent fibroblasts (GL13(+)/Vimentin(+)), macrophages (GL13(+)/CD68(+)) and endothelial cells (GL13(+)/CD34(+)) in 13 GCA compared to 13 PMR biopsies. Objectives 20x. Scale bars: 50 μm. n.s. not significant, *$p < 0.05$, **$p < 0.01$, $p < 0.001$

Figure 3. Senescent cells in GCA express SASP that includes IL-6 and MMP-9. Representative images of IL-6 expression by senescent cells of different origin: (A) GL13(+)/Vimentin(+) (senescent fibroblasts, (B) GL13(+)/CD68(+) (senescent macrophages), (C) GL13(+)/CD34(+) (senescent endothelial cells)) and (D) GL13(+)/aSMA(+) (senescent smooth muscle cells) in a TAB of n=10 GCA and n=10 PMR patients (triple staining immunofluorescence). (E) Graphical representation of the proportion of IL-6 positive senescent cells in 10 GCA and 10 PMR biopsies, showing significantly higher proportion of IL- 6 positive senescent fibroblasts (GL13(+)/Vimentin(+)) and macrophages (GL13(+)/CD68(+)). Representative images of MMP-9 expression by GL13/vimentin double positive (senescent fibroblasts) cells in a TAB of one GCA and one PMR patient (triple stainingimmunofluorescence). (F-G) Graphical representation showing higher proportion of MMP-9 positive senescent fibroblast (GL13(+)/vimentin(+)) in the 3 GCA compared to 3 PMR specimens. Objectives (A), (D) 20x, (B), (C), 63x. Scale bars: (A), (D) 50 μm, (B), (C), 10μm. n.s. not significant, *$p < 0.05$, **$p < 0.01$

inflammation (adventitial limited disease vs transmural inflammation: 10.02% vs 4.37% respectively, p< 0.0001) (Figure 3). Giant cell arteritis but not PMR artery culture supernatant induced IL-6-associated senescence that was partially inhibited by IL-6 blockade.

Conclusion: Senescent cells with inflammatory phenotype are present in GCA arteries and are associated with the inflammatory burden of the vascular wall. These findings suggest a potential implication of senescent cells in disease pathogenesis by perpetuating inflammation and affecting vascular remodeling via IL-6 dependent mechanisms.

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Epidemiology and Predictors of Relapse in Giant Cell Arteritis: Results of the ARTESER Register

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	3 months	1 year	2 year	3 year	4 year	5 year
Total number of patients	1607	1284	872	532	281	126
Relapse	51	232	114	55	28	6
No relapse	1556	1052	758	477	253	120
Relapse rate	3,2%	18%	13%	10%	10%	4,8%
Number of relapses per patient	1=47 2=4	1=192 2=36 3=5 4=0 5=1	1=101 2=11 3=4	1=50 2=5	1=23 2=5	1=5 2=1
Percentage of patients with ≥ 1 relapse	8%	18%	13%	9%	18%	17%
Total number of relapses	55	284	135	60	33	7
Cumulative relapse rate		18% (232/1052)	27,9% (243/872)	37,6% (200/532)	44,8% (126/81)	42% (53/126)

Background/Purpose: The relapse rate of treated patients with giant cell arteritis (GCA) varied widely in observational series and randomized controlled trials. This study aimed to estimate the frequency and timing of relapse, the prevalence of multiple relapses, the characteristics of flares, and the predictors of relapse in a large cohort of Spanish patients with GCA.

Methods: All patients in the ARTESER (Registry of Giant Cell Arteritis Patients of the Spanish Society of Rheumatology) were reviewed. ARTESER is a multicentre observational retrospective longitudinal study conducted in 26 hospitals that included all consecutive patients diagnosed with GCA between 1 June 2013 and 29 March 2019. All cases were aged 50 years or older and had a confirmed diagnosis of GCA, that is, they met at least one of the following criteria: objective confirmation of the presence of vasculitis in a diagnostic test, at least three 1990 ACR criteria for GCA satisfied, and/or a diagnosis made based on the clinical judgment of the investigator. We diagnosed disease relapses if all the following criteria were satisfied: 1) reappearance of signs/symptoms of GCA and/or polymyalgia rheumatica (PMR); 2) resolution of signs/symptoms after increasing glucocorticoids; 3) presence of raised acute-phase reactants ESR and/or CRP, and 4) exclusion of other causes. The data were obtained by review of medical records.

Results: In total, 1675 patients were included. They were predominantly female (70.3%), with a mean (±SD) age at diagnosis of 76.9±8.1 years. Of them, 1284 patients were followed up for one or more years. During follow-up, 574 relapses were observed in 334 (26%) patients. One-year, 2-year, 3-year, and 4-year cumulative relapse rates were 18%, 27.9%, 37.6%, and 44.8%, respectively (see Table 1). Most relapses (81.2%) occurred within the first two years after diagnosis (55.3% in the first year and 26% during the second). The mean dose of prednisone at the first relapse was 13.95 mg/day (IQR25%-75%: 5-20 mg). Fifteen percent (34/232) of patients experienced > 1 flare within the first year of treatment and 10.5% (12/114) during the second year. The majority of flares corresponded to a minor relapse according to the EULAR consensus definitions for disease activity states in GCA (minor relapses 73% / major relapses 27%) In the multivariate analysis, we did not identify any clinical factor at diagnosis that was a predictor of relapse during the first three years of evolution: nor the age, sex, presence of cranial manifestations, severe ischemic complications, large vessel involvement, or a strong initial systemic inflammatory response. By contrast, the administration of intravenous (IV)methylprednisolone (MP) boluses was negatively associated with the occurrence of relapses (OR: 0.356, 95% CI 0.182 to 0.696; p< 0.01).

Conclusion: Relapses among patients with GCA are common, mainly during the first two years after diagnosis. Between 8 and 18% of patients had multiple relapses. Despite the relevance of this problem, we do not yet have any predictive factors to identify patients with a higher risk of flare. Induction treatment with high-dose IV MP boluses appears to decrease the risk of relapses.

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Characterization of Arterial Dendritic Cells in Polymyalgia Rheumatica and Giant Cell Arteritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
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Background/Purpose: Polymyalgia rheumatica (PMR) is associated with giant cell arteritis (GCA) in 16 to 21% of cases. This raises the question of a pathophysiological continuum between PMR and GCA, especially since a study reported mature arterial wall dendritic cells (DC) in patients with GCA or PMR. There are 3 main types of DC: plasmacytoid DC (expressing CD123), conventional DC (cDC) expressing CD141 (cDC1) or CD1c (cDC2), and monocyte-derived DC (mo-DC) expressing CD209 and CD14.This study aimed to identify, localize and characterize the phenotype of arterial DC in PMR and GCA.

Methods: Using temporal artery biopsies (TAB) from patients with PMR, GCA and healthy controls, bulk RNA-sequencing and RT-PCR analyses were performed to assess the level of expression of myeloid DC genes (*CD141*, *CD1C*, *CD209*, *ITGAX*), DC maturation genes *(CD83, CD80/86, CCR7)* and mature DC chemokine expression *(CCL18, CCL19, CCL20, CCL21)*. Expression of markers of DC lineage (CD209), DC maturation state (CD83 and CCR7) and DC origin (CD14, CD68, CD1c, CD141) were also studied in TABs by immunofluorescence (IF).

Results: Forty-three patients were included (14 GCA, 15 PMR, 14 controls). TAB from GCA patients were characterized by a strong mature DC signature with high level of expression of DC associated genes (*CD1C*, *ITGAX* [coding CD11c] and *CD209 [coding DC-SIGN])*, DC maturation genes (*CD83, CCR7, CD80/CD86)* and DC chemokine genes *(CCL18, CCL19,*

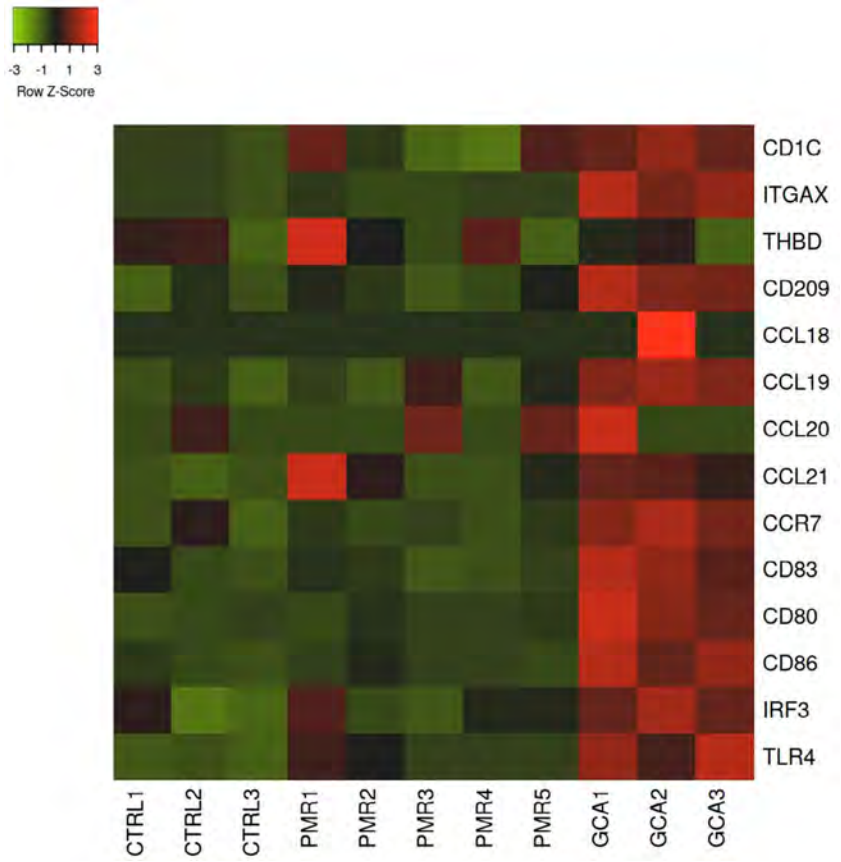

Figure 1: "DC signature" in GCA, PMR and control arteries. Myeloid dendritic cell genes are defined as genes that characterize human dendritic cells: CD1C (coding CD1c), THBD (coding CD141), CD209, ITGAX (coding CD11c). DC maturation associated genes are defined by the process in which antigen-activated dendritic cells acquire the specialized features of a mature conventional dendritic cell. Mature conventional dendritic cells upregulate the surface expression of MHC molecules, chemokine receptors and adhesion molecules, and increase the number of dendrites (cytoplasmic protrusions) in preparation for migration to lymphoid organs where they present antigen to T cells: CD83, CD80, CD86, CCR7, CCL18, CCL19, CCL20, CCL21, TLR4, IRF3.

CCL20). In PMR arteries, the DC signature was more heterogeneous: a few arteries expressed *CD1C* and *CD141* but none expressed DC maturation genes. Healthy arteries were characterized by the absence of expression of DC associated genes and mature DC genes (figure 1). In GCA arteries, IF analysis revealed that the three arterial layers were heavily infiltrated by $CD209^+$ cells. These cells also expressed CD14 and often CD68, thus fitting with mo-DC ($CD209^+CD14^+CD68^-$) or macrophages ($CD209^+CD14^+CD68^+$). Some of these cells expressed maturation markers of DC (CD83 and CCR7). However, no CD1c or CD141 cells were found in the arterial wall by IF. In PMR and control arteries, no DC were found by IF. Transcriptomic analysis revealed that GCA arteries expressed many genes involved in the differentiation of monocytes into mo-DC, including *CSF2*, *CYBA*, *IRF4*, *AHR*, *WNT5A*, and *FZD2*.

Conclusion: This work demonstrates the presence of mature $CD209^+CD83^+CCR7^+$ DCs within the arterial wall in GCA but not in PMR or healthy arteries. The phenotype of these DCs mainly fits with mo-DCs. In PMR, the DC signature is more heterogeneous without expression of DC maturation markers.

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Abstract Number: 2393

CXCL9/IL-6 and MMP3/CD141 Ratio Allow to Discriminate Between Isolated PMR and GCA/PMR Overlap

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SESSION INFORMATION
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Background/Purpose: Polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) are frequently overlapping conditions. It is estimated that 16 to 21% of PMR patients have GCA. In PMR, the presence of cranial features of GCA easily lead the clinician to diagnose GCA. However, the diagnosis of isolated large vessel (LV) GCA is more challenging and requires the use of vascular imaging techniques that are costly and/or irradiating. It is currently not recommended to perform vascular imaging or temporal artery biopsy to rule out GCA in PMR patients without features of GCA. Therefore, the identification of biomarkers able to rule out GCA in PMR patients could be helpful to select PMR patients in whom these exams should be performed. The aim of this study was to assess the performance of several biomarkers to identify GCA in PMR patients.

Methods: Patients were prospectively enrolled at the Dijon University Hospital (France). At inclusion, all patients were free of glucocorticoids or immunosuppressive drugs. All isolated PMR patients fulfilled the 2012 ACR/EULAR classification criteria and GCA was ruled out by at least one exam evaluating the temporal arteries (biopsy and/or doppler US scan) and an evaluation of large vessels by angio-CT or ^{18}FDG-PET-CT. All PMR/GCA overlap patients fulfilled the 2022 ACR/EULAR classification criteria for GCA. For all patients, vascular remodeling markers (MMP2, MMP3, MMP9, ANGPTL4, ANGPTL6), endothelial markers (CD141, CD31, CD146, vWFA2, ICAM-1, VCAM-1), cytokines (IL-6, CXCL-9, IL-27, IL-11) and CD163 were determined by Luminex assay in serum samples. Mann-Whitney tests were performed to compare PMR and PMR/GCA patients. Receiving operator characteristic (ROC) with area under the curve (AUC) were used to assess the performance of the tested biomarkers. Optimal cut off were identified according to Youden Index.

Results: Fifty isolated PMR and 29 GCA/PMR patients were included. GCA/PMR patients had higher serum levels of CD141 ($p = 0.004$) and CXCL9 ($p = 0.004$) than isolated PMR patients. By contrast, serum levels of MMP3 ($p = 0.02$) and IL-6 ($p = 0.003$) were lower in GCA/PMR patients compared to isolated PMR patients. There was no difference between groups for the other markers. AUC were calculated for CD141, CXCL9, IL-6 and MMP3. Separately, none of them reached an AUC > 0.7. However, when combined, high accuracy performance was revealed for the CXCL9/IL-6 ratio, which was significantly increased in GCA/PMR patients ($p < 0.0001$) with an AUC of 0.75 (cutoff > 35.06) while the MMP3/CD141 ratio was significantly lower in GCA/PMR patients ($p < 0.0001$; AUC = 0.77, cutoff < 5.1).

Conclusion: This study demonstrated that combining serum markers such as MMP3/CD141 and CXCL9/IL-6 could help to discriminate between individuals with isolated PMR and those with GCA/PMR. These markers warrant prospective evaluation in larger cohorts of PMR and PMR/GCA patients.

Disclosure: a. ramon: None; **h. Greigert**: None; **a. guilloteau**: None; **c. cladière**: None; **m. ciudad**: None; **S. Audia**: None; **p. ornetti**: None; **j. Maillefert**: None; **B. Bonnotte**: None; **M. Samson**: ARGENX, 2, Boehringer-Ingelheim, 2, CHUGAI, 2, CSL Vifor, 2, GlaxoSmithKlein(GSK), 2, NOVARTIS, 2, 5.

Abstract Number: 2394

18f-FDG-PET/CT for Giant Cell Arteritis Detection of Large Vessel Vasculitis: What Should We Take into Consideration? Analytical Study of the Arteser Registry

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SESSION INFORMATION

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Background/Purpose: Imaging studies in patients with giant cell arteritis (GCA) and suspected large vessel vasculitis (LVV) are sensitive, increasingly available, and less aggressive than temporal artery biopsy. Positron emission tomography/computed tomography (PET/CT) with 18-fluorodeoxyglucose (18F-FDG) allows for the evaluation of mural inflammation in extracranial arteries and supports the diagnosis of LVV. This study aimed to analyze in which patients with GCA the use of 18F-FDG-PET/CT is useful for detecting LVV.

Methods: ARTESER is a large Spanish registry promoted by the Spanish Society of Rheumatology, including patients with a new diagnosis of GCA, from June 2013 to March 2019. A selection of patients who underwent an 18F-FDG-PET/CT was carried out. The main variable of the study was the presence of vasculitis detected by this imaging technique. The diagnosis of LVV was based on expert opinion. Demographic variables, comorbidities, acute phase reactants, cumulative dose of glucocorticoids prior to the test, and the number of days elapsed before performing the test were considered. The clinical phenotypes were defined as cranial or extracranial, depending on the main symptom at the moment of diagnosis. Results are presented as a bivariable model to analyze differences between patients with positive and negative results, a regression model to approach the association between variables in those with a positive test, and a ROC area under the curve analysis.

Table 1: General characteristics of GCA patients with an 18F-FDG-PET/TC.

	Negative 18F-FDG-PET/CT N= 132	Positive 18F-FDG-PET/CT N= 245	p-value*	Total N= 377
Demographic data				
Women, n (%)	93 (70.5)	176 (71.8)	0.78	269 (71.4)
Age, years (SD)	76.2 (8.1)	71.9 (9.0)	0	73.4 (9.0)
Laboratory parameters				
Erythrocyte sedimentation rate, mm/h (SD)	76.3 (30.9)	77.5 (36.9)	0.764	77.1 (34.9)
C-reactive protein, mg/L (SD)	92.0 (106.8)	116.0 (205.8)	0.23	107.67 (177.9)
Hemoglobin, g/dL (SD)	11.8 (1.6)	11.4 (1.7)	0.032	11.6 (1.7)
Platelets, $x10^3$/L (SD)	306.43 (140.3)	343.6 (323.25)	0.22	330.2 (271.9)
Comorbidities, n (%)				
Hypertension	92 (70.8)	137 (57.1)	**0.01**	229 (61.9)
Diabetes mellitus	33 (25.8)	38 (16.0)	**0.024**	71 (19.4)
Dyslipidemia	71 (54.6)	115 (48.3)	0.248	186 (50.5)
Smoking	7 (17.5)	34 (39.1)	**0.016**	41 (32.3)
Obesity	15 (23.4)	15 (10.6)	**0.015**	30 (14.6)
Cardiovascular disease	40 (31.5)	30 (13.5)	**<0.001**	70 (20)
Days (%) passed from the clinical suspicion up to the 18F-FDG-PET/CT				
0-3 days	29 (26.9)	159 (64.9)	**<0.001**	188 (53.3)
4-10 days	16 (14.8)	25 (10.2)		41 (11.6)
11-100 days	39 (36.1)	38 (15.5)		77 (21.8)
More than 101 days	24 (22.2)	23 (9.4)		47 (13.3)
Glucocorticoids received before the 18F-FDG-PET/CT, n (%)				
Glucocorticoids (oral or iv)	113 (85.6)	146 (59.6)	**<0.001**	259 (68.7)
No glucocorticoids	19 (14.4)	99 (40.4)		118 (31.3)

*p-value refers to the statistical difference between patients with the listed characteristics, to those who do not present them.

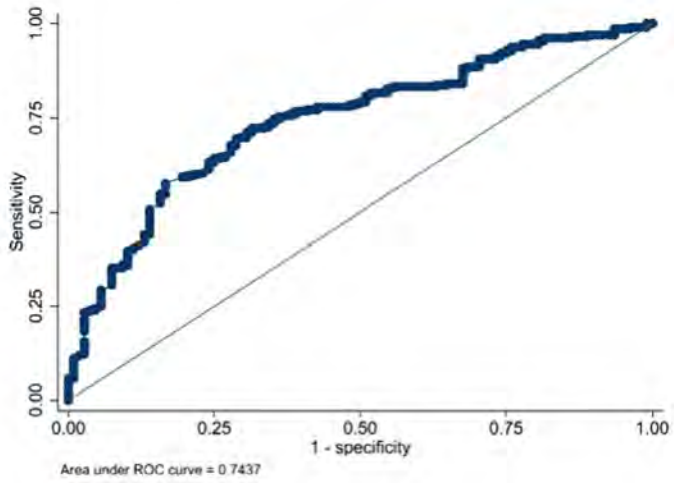
Results: From a total of 1675 GCA patients, included in ARTESER registry, 377 met the inclusion criteria of having an 18F-FDG-PET/CT done during the diagnostic process. **Table 1** shows the bivariable analysis. 67.4% of patients presented as a cranial-GCA phenotype and 29.1% as extracranial-GCA variant, 18 patients could not be classified as either phenotype. Sixty-five percent of patients in our registry had LVV, as detected by 18F-FDG-PET/CT (n=245). In those patients with a positive PET/TC, the vascular territory most frequently affected was the thoracic aorta (85.7%), followed by supra-aortic vessels (78.8%), and abdominal aorta (57.6%). Cardiovascular risk factors were more frequent in patients with a negative 18F-FDG-PET/CT **(Table 1)**. The regression model (**Table 2**) shows a negative association with a positive 18F-FDG-PET/CT for older patients, patients with diabetes mellitus and cardiovascular disease and, the *odds ratio* for having a positive 18F-FDG-PET/TC is lower, as days go by. No variables were found to have a positive association with a positive 18F-FDG-PET/TC. Depending on the cumulative dosage of glucocorticoids, 18F-FDG-PET/CT had an area under the curve of 0.74 **(Figure 1).**

Conclusion: Younger patients have a higher probability of presenting a LVV detected by 18F-FDG-PET/CT. Patients with cardiovascular risk factors (hypertension, diabetes mellitus, smoking), have a higher probability of a negative 18F-FDG-PET/CT. The most frequent large vessel affected was the thoracic aorta. As days go off, and the cumulative glucocorticoid

Table 2: Regression model for patients with GCA and a positive 18F-FDG-PET/TC.

Variable	OR [95% CI]
Age	**0.949*** [0.914-0.986]**
Gender	0.610 [0.316-1.179]
Hypertension	1.065 [0.550-2.064]
Diabetes Mellitus	**0.482** [0.238-0.978]**
Dyslipidemia	0.926 [0.512-1.1675]
Cardiovascular disease	**0.439** [0.211-0.914]**
Cranial GCA	1.206 [0.333-4.371]
Extracranial GCA	1.854 [0.455-7.554]
Oral glucocorticoids	0.984 [0.661-1.467]
Intravenous glucocorticoids	0.559 [0.222-1.409]
Days until the 18F-FDG-PET/TC was done	
4-10 days$	**0.335** [0.143-0.783]**
11-100 days$	**0.255*** [0.125-0.523]**
More than 101 days$	**0.189*** [0.610-0.587]**

Figure 1: Area under ROC curve analysis.



dose is higher, vascular wall uptake of 18F-FDG is reduced, the reason why 18F-FDG-PET/CT should be performed as soon as possible.

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Abstract Number: 2395

Recommendations for Early Referral of Patients with Suspected Polymyalgia Rheumatica: An Initiative from the International Giant Cell Arteritis and Polymyalgia Rheumatica Study Group

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SESSION INFORMATION

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Background/Purpose: Existing EULAR/ACR guidelines on polymyalgia rheumatica (PMR) are focused on the management by rheumatologists. However, there is no consensus regarding early referral and evaluation in secondary care for patients with suspected PMR. It is well known that important differential diagnosis such as giant cell arteritis may be missed in general practice. In addition, a recently conducted worldwide survey suggested a wide heterogeneity in the referral of patients with suspected PMR from primary to secondary care [1]. The aim of this project was to develop evidence-based guidelines for the early referral of patients with suspected PMR.

Methods: A task force formed by members from the international giant cell arteritis (GCA)/PMR study group consisting of 38 participants (29 rheumatologists, 4 general practitioners, 4 patients with PMR, and a health care professional) drafted the guideline. Task force activities were led in accordance with the EULAR standard operating procedures. After 3 virtual meetings during 2022, 70 clinical questions were initially identified. These were later reduced to 10 and finally 6 questions following the Population, Intervention, Comparator, Intervention (PICO) format. The protocol for the systematic literature review was published at the PROSPERO database, search were performed on February 14th 2023, and data extraction and evaluation were

Table 1. Questions for the systematic literature review in Population, Intervention, Comparator, Intervention format.

1: What is the diagnostic value of strategy A (I), compared with strategy B (C), to make an accurate diagnosis (O), in people with suspected PMR (P)?

A specific strategy cannot be defined. Therefore, the terms strategy A and strategy B is used. Search will focus on papers comparing different strategies for diagnosis.

2: What is the outcome (O) of patients with suspected PMR (P) undergoing screening for GCA (I) as compared to not undergoing screening (C)?

A specific outcome cannot be defined (glucocorticoid free survival, relapse free survival, vision loss, quality of life etc.). Search will focus on all available outcomes.

3: Is assessment with diagnostic strategy A for giant cell arteritis (GCA) efficient (I), compared to diagnostic strategy B (C), on the ability to diagnose GCA (O) in people with suspected PMR at diagnosis (P)?

A specific diagnostic strategy will not be defined. Therefore, the terms strategy A and strategy B is used. Search will focus on papers comparing different strategies including but not limited to ultrasound, PET-CT, MRI and clinical evaluation.

4: What is the value of shared care (I) compared to sole management in primary care (C), in patients with suspected PMR (P1) or established PMR (P2), on outcomes (O).

All available outcomes will be gathered.

5: What is the effect of initiating glucocorticoids before referral to secondary care (I), compared with not initiating glucocorticoids (C), on the ability to make an accurate diagnosis (O), in people with suspected PMR (P)?

6: Does a fast-track diagnostic pathway for PMR (I), compared to standard care (C), influence diagnostic accuracy of PMR (O) in people with suspected PMR referred to secondary care for evaluation (P)?

performed by two investigators. Full text papers with more than 20 participants with suspected PMR evaluating the 6 PICOs were included. The results of the SLR were discussed during 3 online meetings, formulating the draft of the guideline.

Results: The PICO questions are shown in Table 1. The SLR yielded 14 papers, concerning PICO 1, 3, 4, and 6 (Figure 1). For PICO 2 and 5 no studies were identified. Guideline draft included 3 overarching principles and 6 recommendations: mandatory evaluations of patients with suspected PMR in primary care before referral, which patients with suspected PMR to refer for evaluation in secondary care, when to start glucocorticoids in patients referred to secondary care for evaluation of suspected PMR, and when to use rapid refer strategies in patients suspected of PMR, which patients seen in secondary care with suspected PMR should be evaluated for GCA, and which patients could be managed in primary care after the diagnosis.

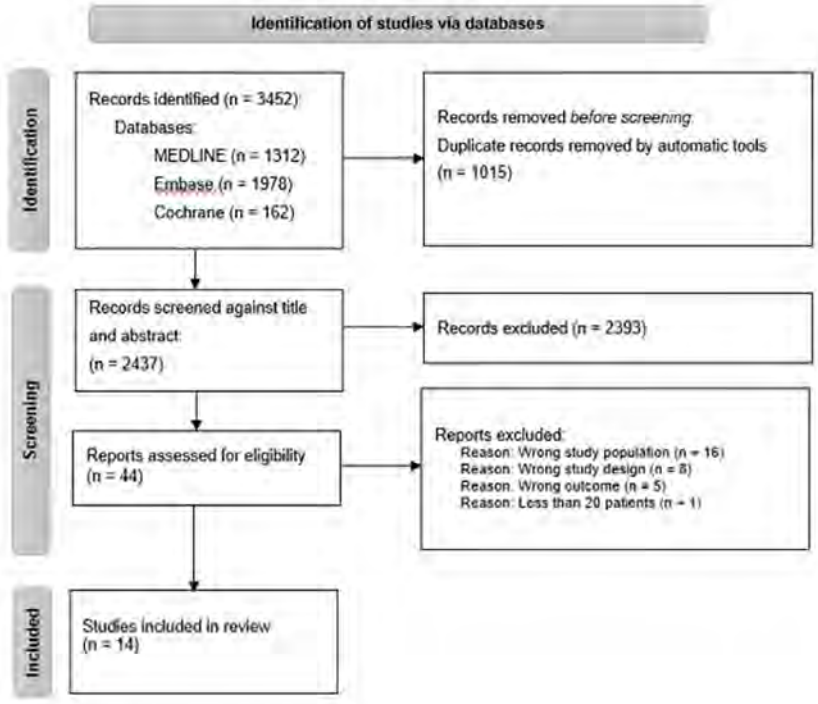

Figure 1. Prisma flow diagram of study selection

Conclusion: This is the first international consensus of the management of referral of patients with suspected PMR. The recommendations will ensure a more uniform management in the future, with a decreased risk of misdiagnosis. Moreover, the work will also define the future research agenda in the field.

References [1] Donskov AO, Mackie SL, Hauge EM, et al. An international survey of current management practices for polymyalgia rheumatica by general practitioners and rheumatologists. Rheumatology (Oxford) 2023.

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Abstract Number: 2396

Diagnostic Performance of a Newly-Launched Canadian Fast-Track Ultrasound Clinic Performed by Rheumatologists for Diagnosis of Giant Cell Arteritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Giant Cell Arteritis (GCA) poses diagnostic challenges for clinicians as there is no universal gold standard. We hypothesize that launching a Fast-Track Ultrasound (US) clinic by rheumatologists may spare the need for a biopsy. Therefore, we aimed to assess the diagnostic performance of temporal artery (TA) US in this setting.

Table 1 : Diagnostic performance of the ultrasound of the temporal and axillary arteries for GCA diagnosis

		Sensitivity		Specificity		PPV		NPV	
	N	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Total	99	80.0	59.3-93.2	91.7	83.2-97.0	76.9	60.2-88.0	93.2	86.1-96.7
GCA Probability score									
Low risk	28	100.0	2.5-100	88.5	69.9-97.6	25.0	10.3-49.1	100.0	n/a
Medium risk	42	71.4	29.0-96.3	94.3	80.8-99.3	71.4	37.6-91.2	94.3	83.6-98.2
High risk	29	82.4	56.6-96.2	91.7	61.5-99.8	93.3	68.0-98.9	78.6	56.4-91.2
Disease course									
New-onset	88	78.3	56.3-92.5	90.8	81.0-96.5	75.0	57.6-86.9	92.2	84.4-92.3
Relapse	11	100.0	15.8-100	100.0	66.4-100	n/a	n/a	n/a	n/a
Biopsy	45	73.7	48.8-90.9	80.8	60.7-93.5	73.7	54.9-86.6	80.8	65.9-90.1

Methods: In this Canadian monocentric retrospective cross-sectional analysis, 106 subjects were identified from the Fast-Track clinic between 05/2020-05/2022 (99 after exclusion). Each subject had an US of the temporal and axillary arteries according to a standardized protocol for either suspicion of new-onset or relapse of GCA. The pretest probability was calculated using the *Southend probability score (*high, medium or low*)*. The sensitivity (Sn), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) were calculated using the rheumatologist final diagnosis as the gold standard.

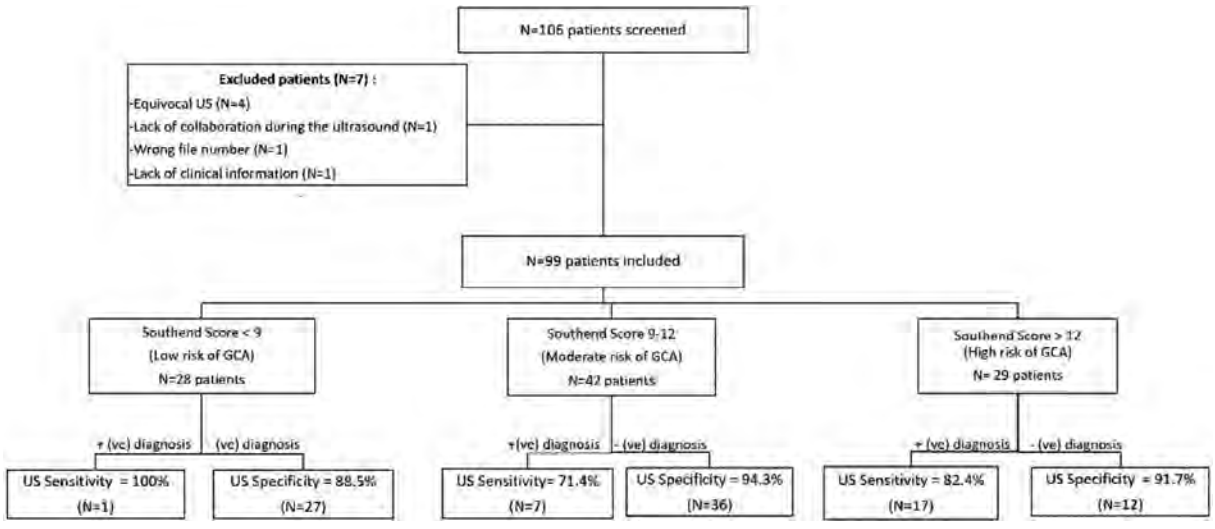

Figure 1 : Workflow of the exclusion criteria and summary of the diagnostic performance of US in GCA

Results: TA US demonstrated a sensitivity of 80.0% [95% confidence interval (CI) 59.3; 93.2%], a specificity of 91.7% (95% CI 83.2; 97.0%), a PPV of 76.9% (95% CI 60.2; 88.0%), and a NPV of 93.2% (95% CI 86.1; 96.7%). 30, 44, 29 subjects were at high, medium, and low risk, respectively. Of those subgroups, subjects at high risk had higher PPV with a lower NPV, while similar Sn/Sp were observed between all three subgroups (see Table).

Conclusion: Our findings confirm the validity of TA US as a diagnostic tool for GCA and highlight the importance of Fast-Track US clinics. Future studies will inform on the role of TA biopsy in the setting of increasing use of US.

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Abstract Number: 2397

Impact of Exposure to Environmental Air Pollution on the Onset of Giant Cell Arteritis

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SESSION INFORMATION

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Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Environmental air pollution (AP) has been found to affect vascular inflammation and to contribute to the risk of onset and flare of autoimmune diseases[1,2]. Giant cell arteritis (GCA) has been reported to be more prevalent in urban than in rural areas[3], indicating a possible link between AP and disease onset. The objective of this study is to investigate whether there is an association between exposure to AP and the risk of developing GCA and its ischemic complications.

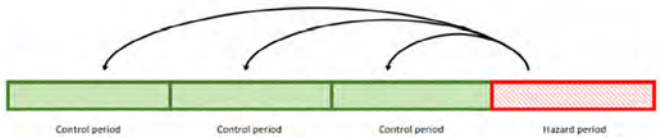
Methods: Charts of consecutive patients with GCA followed between June 2013 and December 2021 in three hospitals (Bozen, Milan, Verona) of Northern Italy were reviewed. Only patients who were resident in Italy at the time of diagnosis and who had confirmed GCA, a follow-up ≥ 6 months and precise information on disease onset were included. Data collection included demographics, clinical information, and ZIP code of residency. Patients were linked to their daily particulate matter (PM10, mass concentration, particles with aerodynamic diameter ≤10μm), exposure derived from a spatio-temporal interpolation process using a Bayesian hierarchical model that included 11 spatial and spatio-temporal predictors, such as meteorological variables and Aerosol Optical Depth. The model was cross-validated, showed good performance and provides a 1km x 1km spatial resolution for daily exposure to PM10. A case-crossover study with conditional logistic regression was conducted to investigate the acute effect of PM10 exposure on disease onset and the development of ischemic

Table 1. Study population *(n = 232)*

Age at diagnosis (IQR)	73 (66-79)	
Female (%)	160 (69)	
Season of symptoms onset (%)		
Autumn	58 (25)	
Summer	57 (24.6)	*p= NS*
Spring	52 (22.4)	
Winter	65 (28)	
Year of diagnosis (%)		
2013-2017	102 (44)	
2018-2021	130 (56)	
Follow-up in months (IQR)	32 (18-51)	
Comorbidities at baseline (%)		
≥1 cardiovascular comorbidity*	132 (57)	
Cancer	20 (9)	
Disease phenotype (%)		
Cranial	121/226 (53)	
LV	34 (15)	
Cranial + LV	71 (31)	
Laboratory parameters at onset (IQR)		
CRP mg/L	58 (34-103)	
ESR mm/h	72 (54-130)	
Haemoglobin g/dL	12.5 (11.7-13)	
Thrombocytes x 1000/µL	343000 (273000-430000)	
Mean PM10 concentration 60 days before symptoms onset, mean ±SD (µg/m³)		
Cohort of Bozen (32 pts)	20±13.1†	
Cohort of Milan (177 pts)	27±13.7†	
Cohort of Verona (23 pts)	25.8±14†	

Legend. CRP, C-reactive protein; ESR: erythrocyte sedimentation rate; IQR, interquartile range; LV, large vessel; NS, non-significant; pts: patients; SD, standard deviation. *Coronary artery disease, Diabetes mellitus, Dyslipidaemia, Hypertension, Peripheral vascular disease, Stroke; †PM10 exposure was determined based on the residential address of each patient, utilizing a 1km x 1km grid (*Fioravanti et al., 2021*).

Figure 1. Case-crossover study design

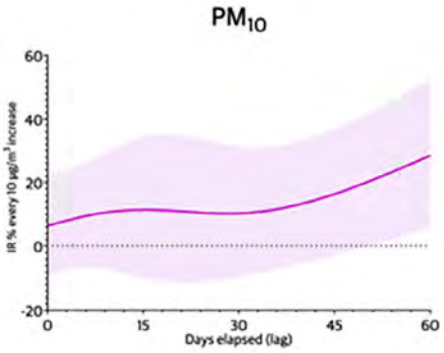


complications. Several lag exposures before symptoms onset were selected (hazard periods) and compared to 3 same-length periods prior to symptoms onset (control periods) (**Figure 1**).

Results: Two hundred and thirty-two patients were included. **Table 1** summarizes their main demographic and clinical features. **Figure 2** shows the exposure-response association between air pollutants and the risk of developing GCA. Incremental odds (%) of GCA every 10 µg/m³ increase in PM10 concentration at different lag-exposure were found. Specifically, the incremental risk (every 10 µg/m³ increase in PM10) for 60-day lag was27,08 (95% CI 5,81-52,63); at shorter lags we found no significant association. There was no significant difference after adjusting for seasonality. Fifty-nine patients (25%) suffered from a GCA-related ischemic complication. No significant association between exposure to PM10 and ischemic complications was found (p=.198).

Conclusion: Conclusion. Acute exposure to environmental AP PM10 seems to be associated with a higher risk of developing GCA but not with GCA-related ischemic complications. Further studies on larger cohorts are needed to confirm these preliminary results.

Figure 2. Exposure-response association between air pollutants and risk of GCA.



The curve was interpolated using the conditional logistic regression model. The curve was smoothed with restricted cubic splines with knots at 1, 7, 15, 30 and 60 days.

PM10

Lag	beta	se	IR%	95%CI		OR	UL	LL
1	0,005498	0,007507	5,652	-8,804	22,399	1,006	1,020	0,991
7	0,008659	0,007767	9,045	-6,354	26,975	1,009	1,024	0,993
15	0,009509	0,01021	9,976	-9,970	34,340	1,010	1,030	0,990
30	0,008614	0,009439	8,996	-9,413	31,146	1,009	1,027	0,990
60	0,023967	0,009346	27,083	5,811	52,631	1,024	1,043	1,006

Bibliography

Ke Wei, Gen Biol 2007; 2. Adami, Rheumatology 2021; 3. Reinhold-Keller, Rheumatology 2000

Disclosure: M. Bond: AbbVie/Abbott, 5; **A. Tomelleri**: Novartis, 1; **M. Reatini**: None; **C. Campochiaro**: Boehringer Ingelheim, 1, 6, Janssen, 1, 6, Novartis, 1, 6; **G. Cattani**: None; **L. Dagna**: AbbVie, 2, AstraZeneca, 2, Biogen, 2, BMS, 2, 5, Boehringer Ingelheim, 2, Celltrion, 5, Eli Lilly, 2, Galapagos, 2, GSK, 1, Janssen, 2, Kiniksa Pharmaceuticals, 2, 5, Novartis, 2, 6, Pfizer, 2, 5, Sobi, 2, 5, 6; **M. Rossini**: None; **C. Dejaco**: AbbVie/Abbott, 1, 5, 6, Eli Lilly, 6, Galapagos Pharma, 1, 6, Janssen, 1, 6, Novartis, 1, 6, Pfizer, 6, Sparrow, 1; **G. Adami**: None.

Abstract Number: 2398

FDG Uptake in Limb Arteries at Diagnosis of Giant Cell Arteritis and Risk of Relapse: An Observational Cohort Study

Geoffroy Peyrac[1], Arthur Mageau[2], Augustin Gaudemer[2], Khadija Benali[1], Jean-Francois Alexandra[1], Andrey Strukov[1], Sebastien Ottaviani[1], Thomas Papo[2] and Karim Sacre[2], [1]Assistance Publique Hopitaux de Paris, Paris, France, [2]Université Paris Cité, Paris, France

SESSION INFORMATION
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Background/Purpose: Steroids and anti-IL6 biotherapy are highly effective in obtaining remission in patients with giant cell arteritis (GCA) but the risk of relapses remains high, especially once treatments are withdrawn. Predictors of relapse in GCA are missing. We aimed to identify predictors of relapse in GCA.

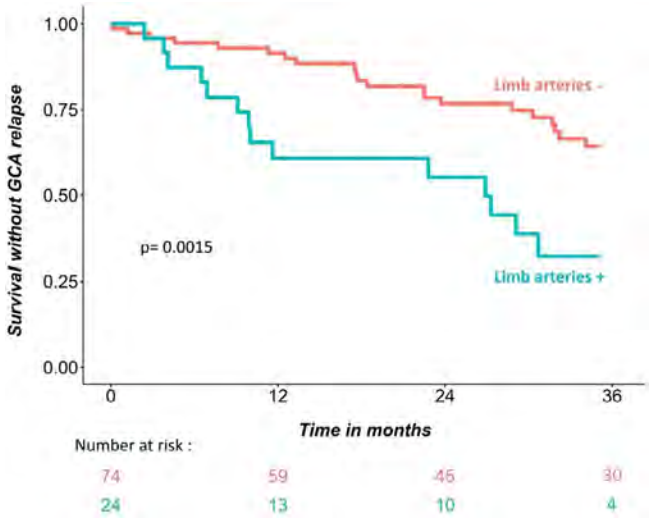

Figure 1Kaplan-Meier Curves of Study Population Patients with FDG uptake in limb arteries (limb arteries +) at diagnosis had higher rates of relapse than patients without FDG uptake in limb arteries (limb arteries -) at diagnosis (log-rank; p = 0.0015).

Methods: All consecutive patients admitted with a new diagnosis of GCA in our national center for rare immune-mediated inflammatory diseases (Bichat hospital, Paris, France) between January 2011 to December 2021 were eligible for this study. Patients were included if the 2022 American College of Rheumatology/EULAR classification criteria for GCA were met. GCA relapse was defined by the presence of recurrent or new-onset disease related symptoms, an increase of CRP value >10mg/L and the necessity for an increase in the prednisone dose. The primary outcome was the GCA relapse rate over the 36-months follow up. Factors associated with the primary outcome were identified and time to first relapse was studied with a multivariable Cox model.

Results: One hundred and eight patients (74 [69-81] years, 65% of women) with a new diagnosis of GCA were studied. At diagnosis, 87 (81%) patients had cranial symptoms. CRP was high (> 10 mg/L) in all but 5 cases (90%) with a median level of 64 [34-132] mg/L. GCA was biopsy-proven in 65 (64%) cases. Ninety-eight (91%) FDG/PET CT performed at diagnosis were available for a systematic review of FDG uptake in aorta, supra-aortic trunks, and limb (axillary and iliofemoral) arteries. Unequivocally strong linear large vessels wall FDG uptake was found in 74 (73%) cases. All patients received steroids given for 21.0 [18.0-28.5] months, associated with methotrexate or tocilizumab in 1 (1%) and 2 (2%) cases, respectively. During a median follow-up of 27.5 [11.4 - 35.0] months, 40 (37%) patients experienced GCA relapse. Univariate analysis showed that FDG uptake in limb arterie sat diagnosis was associated with GCA relapse: relapse occurred in 58% (n=14/24) of patients with FDG uptake in limb arteries and in 28% (n=21/74) of patients without FDG uptake in limb arteries(p=0.008). Multivariable Cox regression model, including age, gender, thickened aortic wall, FDG uptake in limb arteries and IV steroid pulse as covariates, showed that FDG uptake in limb arterie sat diagnosis was the unique identified risk factor for relapse (HR 3.05 [1.48-6.25], p=0.002) (Figure 1).

Conclusion: FDG uptake in limb arteries at diagnosis of GCA is associated with relapse. FDG/PET CT may help to better tailor therapy in GCA.

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Abstract Number: 2399

Ultrasound Is Comparable to Computed Tomography Angiography in Identifying Aortic Aneurysms in Patients with Giant Cell Arteritis

Anne Bull Haaversen[1], Tanaz Kermani[2], Lene Kristin Brekke[3], Oyvind Molberg[4] and Andreas Diamantopoulos[5], [1]Martina Hansens Hospital, Hosle, Norway, [2]Rheumatology, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, [3]Haugesund Hospoital For Rheumatic Diseases, Haugesund, Nepal, [4]Dept of Rheumatology, University Hospital Oslo, Oslo, Norway, [5]Akershus University Hospital, Lørenskog, Norway

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III

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Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with Giant cell arteritis (GCA) face an elevated risk of aneurysm formation. Despite this, consensus regarding optimal aortic visualization methods and aneurysm monitoring frequency is still lacking. Low-frequency transducer ultrasound offers a potential solution, capable of visualizing the ascending aorta and aortic arch. We conducted a study to compare this ultrasound technique against Computed Tomography Angiography (CTA), the current gold standard for aortic evaluation.

Methods: We conducted our study at Martina Hansens Hospital in Bærum, Norway. We included patients diagnosed with GCA who also met the ACR/EULAR classification criteria for GCA. The ascending aorta's diameter was measured using both ultrasound and CTA. Aortic aneurysm was defined as an ascending aorta diameter of ≥40 mm. The Student's t-test was used to compare the results.

Results: Our pilot study included thirteen patients, twelve females, and one male, with an average disease duration of 4.6 years (95%CI 3.7-5.5). The mean diameter of the ascending aorta was 35.4 mm (95%CI 32.3-38.4) measured by ultrasound and 36.5 mm (95%CI 33.0-40.0) by CTA. The mean difference between the two methods was 1.15 mm (95%CI -0.07 to 2.38, p-value = 0.06). CTA identified four patients with an ascending aorta aneurysm, while ultrasound identified three. (Table 1). No aneurysms were found in the descending aorta by CTA.

Patient	Sex	Age	GCA type	Ultrasound measurements at the aortic root	CT measurements at the aortic root	Aneurysm	Years from GCA diagnosis to ultrasound/CT
1	Female	81	Mixed	28	27	No	4
2	Female	78	Cranial	31	30	No	5
3	Female	87	Mixed	31	34	No	4
4	Female	87	Mixed	32	32	No	8
5	Female	64	Cranial	33	38	No	5
6	Female	78	Mixed	34	34	No	5
7	Female	71	Mixed	34	34	No	2
8	Female	74	LV	34	34	No	4
9	Female	76	Mixed	38	39	No	6
10	Female	82	Mixed	40	41	Yes	4
11	Female	69	Mixed	42	42	Yes	4
12	Female	60	LV	46	48	Yes	4
13	Male	74	Mixed	37	42	Yes	4

LV; Large Vessel only involvement; Mixed: Large vessel and cranial vessels involvement

Conclusion: Our preliminary findings suggest that ultrasound provides results comparable to CTA in assessing the ascending aorta diameter in GCA patients. This positions ultrasound as a potential tool for monitoring aortic aneurysm development in this patient group.

Disclosure: A. Bull Haaversen: None; **T. Kermani**: None; **L. Brekke**: None; **O. Molberg**: None; **A. Diamantopoulos**: None.

Abstract Number: 2400

Applanation Tonometry of the Temporal Arteries in Participants with Suspected Giant Cell Arteritis: A Proof of Concept

Jean-Paul Makhzoum[1], Stephanie Ducharme-Benard[2], Samer Hussein[2], Rosalie-Selene Meunier[2], Carolyn Ross[3], Alik Chamlian[4], Jonathan Ducharme[5], Leia Chamlian[4], Alae Dhahbi[4], Christian Pagnoux[6] and Remi Goupil[7], [1]Vasculitis Clinic, Hopital du Sacre-Coeur de Montreal, Canadian Network for Research on Vasculitides, Montreal, QC, Canada, [2]Vasculitis Clinic, Hopital du Sacre-Coeur de Montreal, Montreal, QC, Canada, [3]Vasculitis Clinic, Canadian Network for Research on Vasculitides, Hopital du Sacre-Coeur de Montreal, Montreal, QC, Canada, [4]Laval University, Montreal, QC, Canada, [5]University of Sherbrooke, Montreal, QC, Canada, [6]Mount Sinai Hospital, Toronto, ON, Canada, [7]Hopital du Sacre-Coeur de Montreal, University of Montreal, Montreal, QC, Canada

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Applanation tonometry (ATn) is a non-invasive, point-of-care tool used to capture arterial pressure waveforms. It can measure arterial pulse wave velocity (PWV), a marker of arterial wall stiffness. Arterial inflammation increases vessel-wall stiffness and PWV, as previously demonstrated in patients with Takayasu arteritis. ATn on temporal arteries has not yet been studied, and it may help detect vasculitis in patients with active giant cell arteritis (GCA). The objective of this study is to investigate the feasibility of ATn on temporal arteries, assess the quality of the waveform/PWV obtained, and explore if PWV is increased in patients with GCA.

Methods: A cross-sectional study was performed in our quaternary vasculitis clinic from June to December 2022. Participants referred for suspected GCA, without prior temporal artery biopsy, were eligible. At baseline, participants had a clinical assessment, color doppler ultrasound (CDUS) and ATn of temporal arteries. ATn was performed by dedicated, blinded research personnel in a separate room. GCA specialists who completed the clinical assessment and CDUS were blinded to ATn results. Final diagnosis was established based on expert opinion at the 6-month follow-up. We used the Sphygmo Cor system to perform ATn. PWV were measured in five arterial segments on the right side: carotid to superficial temporal artery (C-S), carotid to parietal temporal artery (C-P), carotid to frontal temporal artery (C-F), superficial to parietal temporal artery (S-P), and superficial to frontal temporal artery (S-F). The quality of the waveform was confirmed visually. The coefficient of variation (CV = standard deviation/transit time) of the proximal and distal arterial points was assessed. A CV ≤ 6% denoted good capture quality as per the manufacturer's recommendations. Descriptives statistics were performed for baseline characteristics and ATn quality assessment. Mann-Whitney U test was used to explore a potential difference in PWV in patients with and without GCA.

Results: Fifteen participants were enrolled, including 3 patients with a final diagnosis of GCA who satisfied the 2022 ACR/EULAR classification criteria (Table 1). A total of 69 arterial segments were assessed (PWV measures could not be obtained in 1 C-F, 3 S-P and 2 S-F segments). Quality assessment of the ATn waveform was satisfactory for the C-S,

Table 1: Baseline characteristics of 15 participants undergoing applanation tonometry of temporal arteries.

Baseline characteristics	Results	
Age (in years), median (IQR)	77	(73 – 79)
Female, n (%)	9	(60)
Caucasian ethnicity, n (%)	14	(93)
Smoking status, n (%)		
Previous smoker	8	(53)
Active smoker	1	(7)
Vascular medical history, n (%)		
Coronary artery disease	2	(13)
Atrial fibrillation	3	(20)
Peripheral vascular disease	1	(7)
Hypertension	10	(67)
Dyslipidemia	9	(60)
Diabetes	4	(27)
Baseline vascular medication, n (%)		
Calcium channel blockers	6	(40)
ACE inhibitors	3	(20)
Angiotensin receptor antagonists	6	(40)
Alpha-blockers or nitrates	1	(7)
Diuretics	3	(21)
Statins	7	(47)
Suspected GCA clinical assessment, n (%)		
Headache	11	(73)
Scalp tenderness	2	(13)
Jaw claudication	3	(20)
Visual symptoms	3	(20)
Polymyalgia rheumatica	5	(33)
Constitutional symptoms	6	(40)
Abnormal temporal arteries	3	(20)
C-reactive protein (mg/L), median (IQR)	27.5	(3.2 – 117.0)
ESR (mm/hr), median (IQR)	48	(23 – 68)
Prior empiric GC initiated, n (%)	10	(67)
Days on GC at baseline, median (IQR)	6	(4 - 7)
GCA confirmed at month 6, n (%)	3	(20)

IQR (interquartile range), ACE (angiotensin converting enzyme), GCA (giant cell arteritis), ESR (erythrocyte sedimentation rate), GC (glucocorticoids).

C-F, S-F arterial segments (Table 2). Parietal temporal arteries had a high proportion of low-quality waveforms, likely due to their small size relative to the probe. In patients with GCA, median PWV of the C-S, C-P, C-F and S-P segments were numerically but not statistically higher than in patients without GCA (Table 3).

Conclusion: ATn of temporal arteries is feasible, and PWV measures were of quality for 3 arterial segments (C-S, C-F, S-F). Median PWV was higher in patients with active GCA than in subjects without confirmed GCA; however, this study was underpowered to detect statistical difference. This proof-of-concept study allowed the identification of arterial segments that are now further evaluated in a larger trial of ATn in GCA (Clinicaltrials.gov id: NCT05703763).

Table 2: Quality assessment of the waveform obtained for 5 arterial segments in 15 participants undergoing applanation tonometry of temporal arteries.

ATn of 5 temporal artery segments	Results
Adequate signal quality, n (%)	
Carotid to superficial TA	N=15
Proximal waveform	15 (100)
Distal waveform	14 (93)
Carotid to parietal TA	N=15
Proximal waveform	15 (100)
Distal waveform	7 (47)
Carotid to frontal TA	N=14
Proximal waveform	13 (93)
Distal waveform	10 (71)
Superficial to parietal TA	N=12
Proximal waveform	11 (92)
Distal waveform	7 (58)
Superficial to frontal TA	N=13
Proximal waveform	12 (92)
Distal waveform	10 (77)

ATn (applanation tonometry), TA (temporal artery)

Table 3: Comparison of pulse wave velocity measured by applanation tonometry in patients with and without GCA.

	Pulse wave velocity results (in meters/second), median (IQR)				
Temporal artery segment	No GCA		GCA		p-value*
Carotid to superficial TA	4.5	(2.9-6.7)	6.4	(4.2-33.7)	0.23
Carotid to parietal TA	1.9	(0.5-5.5)	4.3	(1.0-5.7)	0.47
Carotid to frontal TA	2.9	(1.0-4.6)	5.4	(1.1-9.1)	0.31
Superficial to parietal TA	1.3	(0.4-2.7)	1.6	(0.2-2.9)	1.00
Superficial to frontal TA	3.3	(1.9-6.6)	2.1	(0.2-4.2)	0.34

*Hypothesis test used was Mann-Whitney U test

IQR (interquartile range), GCA (giant cell arteritis), TA (temporal artery)

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Abstract Number: 2401

A Study Defining the Optimal Sonographic Parameters for Intima-Media Thickness in Diagnosing Giant Cell Arteritis

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SESSION INFORMATION

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Session Type: Poster Session C
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Background/Purpose: In recent years, Temporal Artery US (TAUS) incorporating Axillary Artery US (AAUS) has become a reliable alternative to biopsy for diagnosing GCA but studies have shown heterogenous results for its' diagnostic performance for this purpose (1,2). Published values for Intima-Media Thickness (IMT) exist which can differentiate an inflamed vessel from a normal one but have not yet been validated (Table 1). We aimed to establish what IMT values in each vascular territory could reliably support or refute a diagnosis of GCA.

Methods: We performed a prospective study of all newly diagnosed GCA patients (clinical diagnosis, verified by 2 rheumatologists after 6 months) who had a positive baseline vascular US (n= 57) presenting to our Rapid Access GCA clinic over 18 months. US of all 6 branches of the Superficial Temporal Arteries (STA) and both Axillary Arteries (AA) were performed on all patients using a GE P9 device. Sonographic abnormalities considered indicative of vasculitis in the temporal arteries included the halo sign and non-compressible arteries with a thickened IMT (3). In the axillary arteries, a halo sign and an

Table 1: IMT Cut-off values used to diagnose GCA on vascular US (4).

Vessel	IMT Cut-off Value
Common STA	0.42 mm
Frontal STA	0.34 mm
Parietal STA	0.29 mm
Axillary Artery	1.0 mm

Table 2: Baseline Intima-Media Thickness (IMT) values in each Superficial Temporal (STA) and Axillary Artery (AA) branch that give 100%, >95% and >90% sensitivity and specificity for a clinical diagnosis of GCA. Rt=right, Lt=left.

Vessel, IMT in mm	100% sensitivity	>95%	>90%	100% specificity	>95%	>90%
Rt Common STA	0.20	0.25	0.25	0.85	0.60	0.41
Rt Frontal STA	0.15	0.20	0.20	0.46	0.44	0.33
Rt Parietal STA	0.01	0.15	0.15	0.45	0.35	0.29
Rt Axillary Artery	0.40	0.49	0.50	2.70	1.10	0.91
Lt Common STA	0.20	0.30	0.30	0.75	0.65	0.44
Lt Frontal STA	0.15	0.20	0.20	0.55	0.43	0.35
Lt Parietal STA	0.15	0.18	0.20	0.55	0.35	0.26
Lt Axillary Artery	0.34	0.50	0.50	2.00	1.10	0.90

intima-media thickness of >1.0mm was considered positive. We performed Chi-Square test with ROC analysis to determine the sensitivity and specificity of each measured IMT value in each branch of the STA and AA.

Results: 66/124 patients had a clinical diagnosis of GCA at 6 months. 57 of these patients had a positive baseline vascular US. Our cohort consisted of 61% males (n=35) with a mean age of 74.4 years. Overall, US had a sensitivity of 86.4% and a specificity of 82.8% for a clinical diagnosis of GCA. Table 2 demonstrates the sonographically-defined IMT values in our cohort for each branch of the STA and AA which can irrefutably exclude (i.e. sensitivity 100%) or diagnose (i.e. specificity 100%) GCA.

Conclusion: Our data provides a template which can guide clinician-sonographers when interpreting vascular US images in cases of suspected GCA. The conventional method of identifying a halo with a non-compressible artery is somewhat limited due to conflicting results of its diagnostic performance in clinical studies to date. By incorporating IMT measurement into the routine US protocol for GCA, clinicians can attain increased diagnostic accuracy if the above thresholds are met.

Disclosure: C. Kirby: None; **S. Cowley**: None; **R. Flood**: None; **R. Mullan**: None; **G. Murphy**: None; **D. Kane**: None.

Abstract Number: 2402

A Retrospective Analysis of Prevalence of Positive Temporal Artery Biopsies in African American Patients with Giant Cell Arteritis (GCA) in a Large Academic Health Center

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Background/Purpose: Giant Cell Arteritis (GCA) is a systemic vasculitis reportedly more common in Caucasian older adults**.** Studies suggest that GCA is very rare in African American patients. There is paucity of data on positivity of temporal artery biopsy (TAB) in African American patients. The primary aim of our study is to assess the prevalence of positive TAB in AA patients in a large academic center. Our secondary outcome is to describe the presenting symptoms of GCA in AA patients.

Methods: We conducted retrospective chart reviews of patients who underwent TAB at a large academic health center between 2010 and 2021. Adult patients with self-reported race as AA were included in the study. Analyses were performed using Microsoft Excel.

Results: A total of 77 patients' charts were reviewed. Only 8 patients (10.4 %) had positive temporal artery biopsies. Their mean age was 79 years. In those patients with positive TAB, headache was reported in all cases, while only 4/8 patients presented with visual symptoms. Additionally, 3/8 patients reported jaw claudication and only 2/8 patients complained of scalp tenderness. The duration of steroid treatment prior to biopsy did not exceed 10 days.

Clinical suspicion was high enough after a multidisciplinary discussion to decide to treat 10/77 patients for GCA despite negative TAB. Vision changes were observed in 7/10 patients. 9/10 patients had elevated erythrocyte sedimentation rate (ESR). Only one patient presented with normal ESR, however, due to vision loss with evidence of ischemic optic neuropathy and concurrent cilioretinal artery occlusion, providers decided to treat for GCA. Notably, one patient had a PET scan that showed increased metabolic activity along the thoracic and abdominal aorta and was subsequently treated for extracranial GCA. In our study, rheumatology was consulted for 76.6% (59/77) of the patients, including all 18 patients who were treated for GCA; 8 with positive biopsies and 10 with negative biopsies.

The mean score for the 2022 ACR/EULAR GCA criteria was 8 among patients who had positive biopsies, while the mean score for GCA probability score (GCAPS) was 13. In contrast, patients with negative biopsies who continued to receive treatment for GCA had average scores on the ACR/EULAR and GCAPS of 5 and 11 respectively. Higher scores of ACR/EULAR and GCAPS were observed in the positive biopsy groups. Among the total cohort of 77 patients, 12 patients had symptoms of Polymyalgia Rheumatica. None of them had positive temporal artery biopsy, however 2 patients were treated as GCA cases despite negative biopsy results per provider high clinical suspicion.

Conclusion: Our study shows that the rate of positive TAB in African Americans is 10.4 % which is higher than 8.4% previously reported in the study by *Greuneret al*. Headache was found to be the most common presenting symptom of GCA in our cohort. In our study, a total of 23.4% (18 out of 77) of the patients were diagnosed and treated as GCA, 76.6% of them had negative biopsy and were not treated as GCA. Further research is needed to better stratify the risk of temporal artery inflammation in AA patients prior to the decision to pursue TAB.

Disclosure: L. Al saleh: None; **H. Haddad**: None; **s. Dia**: None; **F. Constantinescu**: None.

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Systole and Diastole Ultrasound Wall Thickness Shows Significant Differences That Affect the Diagnosis and Assessment of Giant Cell Arteritis

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Background/Purpose: In the last few years, several cut-off points for the intima-media thickness (IMT) of temporal arteries (TA) and large vessels (LV) have been proposed for the ultrasound (US) diagnosis of giant cell arteritis (GCA). It has usually been recommended to use the average measure of the higher IMT, but there is currently a lack of consensus on this. We have observed some changes in the IMT measurements depending of if they are performed in systole or diastole. To confirm if there are differences in the IMT measurement taken in systole or diastole and if they are clinically relevant.

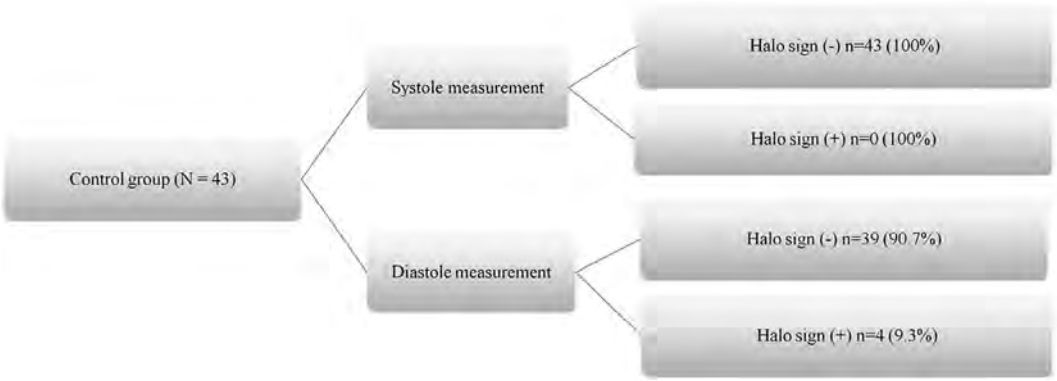
Methods: Observational study that included recorded videos of the US examination performed in consecutive patients referred to our GCA fast track clinic with suspicion of GCA. The gold standard diagnosis was the clinical diagnosis of the doctor after at least 6 months of follow-up. All the videos of every explored vessel (TA with their common trunk -CT- and their

Category	No GCA			GCA		
N	43			41		
Sex ♂ / ♀ (n)	15/28			19/22		
Age years (mean ± SD)	75.1±9.1			81.1±6.9		
	Systole	Diastole	p	Systole	Diastole	p
TA Frontal (right)	0.21±0.57	0.22±0.5	0.001	0.36±0.14	0.39±0.15	0.001
TA Frontal (left)	0.21±0.04	0.22±0.04	0.001	0.38±0.19	0.39±0.19	0.001
TA Parietal (right)	0.19±0.05	0.22±0.04	0.001	0.44±0.20	0.44±0.20	0.001
TA Parietal (left)	0.20±0.04	0.22±0.04	0.001	0.36±0.19	0.39±0.20	0.001
TA Common (right)	0.25±0.08	0.26±0.08	0.002	0.49±0.24	0.52±0.28	0.001
TA Common (left)	0.23±0.06	0.26±0.06	0.001	0.43±0.20	0.46±0.20	0.001
Axillary (right)	0.56±0.13	0.58±0.14	0.001	0.74±0.32	0.79±0.32	0.001
Axillary (left)	0.52±0.13	0.56±0.12	0.001	0.71±0.29	0.75±0.31	0.001
Subclavian (right)	0.65±0.15	0.68±0.15	0.001	0.77±0.25	0.82±0.27	0.001
Subclavian (left)	0.58±0.19	0.60±0.19	0.017	0.78±0.31	0.82±0.33	0.001

GCA = giant cell arteritis; N = number of patients; SD = standard deviation; TA temporal artery. Measures are showed in mm).

frontal -FR- and parietal -PAR-branches, subclavian -SC- and axillary -AA- arteries) were reviewed and the IMT of each of them was measured in systole and diastole peaks. We define an US result as positive with cut-off values of IMT ≥ 0.34 mm for FR and PAR, ≥ 0.42 mm for CT, and ≥ 1 mm for AA and SC. Demographic data were also collected. Reliability was tested by two independent readers in 40 patients using the of intraclass correlation coefficient mixed model absolute agreement (ICC).

Results: We have included 84 cases, 41 with GCA and 43 without GCA (controls). The mean values of age and sex, as well as the IMT in systole and diastole of each vessel are shown in Table 1. There were not significant differences in sex but patients without GCA were younger ($p < 0.01$). US IMT measurements in systolic and diastolic times showed statistically significant differences in all the explored vessels, both in patients with GCA and in the control non GCA group (Table 1). All the IMT measured in diastole showed higher and statistically significant values than those measured in systole, with a mean increment of measurement of 5.7% and 6.83 % in TA and 5.02% and 4.95% in LV, respectively in the GCA and control group. These results can have clinical relevance since if we used diastolic measurements, instead of systolic measurements, 4/43 (9.3%) cases in controls had halo sign in one isolated vessel (1 case in right FR, 1 in right CT, 1 in right SC, 1 in left SC) (Figure 1). However, in GCA patients, the number of patients with halo sign did not change, but the number of pathological vessels increased in 15 branches when the measurement was performed in diastole (2 in right FR, 3 in right PAR, 1 in right CT, 3 in left FR, 4 in left CT and 2 in right AA)(Fig 1), so it could influence the assessment of the disease with OGUS or other scores. The result of the interrater analysis, between two readers, revealed an ICC between 0.845 and 0.992 for the different arteries.



Conclusion: There are significant differences between the IMT measured in systolic and diastolic peaks, as in GCA as in normal controls, with higher values in diastole. The differences are relatively small but may increase the number of false positives in 9.3% cases in controls, and the number of affected vessels in the GCA group. This should be considered in the diagnosis and assessment of GCA.

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Abstract Number: 2404

Subclinical Giant Cell Arteritis in Polimialgia Rheumatica: A Biomarker of High Relapse Risk

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SESSION INFORMATION

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Background/Purpose: Around 20% of polymyalgia rheumatica (PMR) patients without clinical symptoms of giant cell arteritis (GCA) have subclinical GCA by image or byopsy[1]. However, there is not data about its natural evolution and how these patients should be treated.Our main objective was to compare the outcomes of patients with PMR and subclinical GCA with those with isolated PMR over a 2-year period.

Methods: We included PMR patients with a complete vascular ultrasound examination at basal visit, recruited from nine European rheumatology centers. We analyzed longitudinal data from baseline, 3, 6, 12, 18 and 24 months. Only patients followed for at least one year were included. All patients fulfilled the 2012 EULAR/ACR Provisional Classification Criteria for PMR. Patients were stratified into two groups: isolated PMR and PMR with subclinical GCA with ultrasound positive halo sign. The outcomes (relapses, prednisone use and treatments needed) were compared between groups, using Chi^2, student t test and logistic regression analysis. PMR relapse was defined as clinical and/or laboratory worsening after initial remission requiring change in treatment after excluding other causes. Relapses were classified as minor or major according to the EULAR definition[2].

Results: We included 150 PMR patients (50 with subclinical GCA, 100 withisolated PMR) with a median (IQR) follow-up of 22 (20; 24) months without significant differences betweenisolated PMR and subclinical GCA. 47 patients (29%) had a relapse, 31 (62%) in the PMR with subclinical GCA group and 16 (14.3%)in the isolated PMR group ($p< 0.001$).In patients with pure PMR all relapses were minor, whereas in patients with subclinical GCA there was one major relapse. Prednisone starting dose was significantly higher in patients with PMR with subclinical GCA than in patients with isolated PMR

	Pure PMR (n=100)	Subclinical GCA/PMR (n=50)	p
Age, mean ± SD years	71.7±8.4	74.1±7.8	0.080
Female sex, n (%)	66 (59%)	25 (50%)	0.302
CRP, mean ± SD mg/L	55.3±52.4	34.6±37.2	0.008
ESR, mean ± SD mm/hr	63.2±31.2	62.7±33.1	0.936
Follow-up time, median (IQR)	22.5 (21; 24)	22 (18; 25)	0.895
Relapses, n/n total (%)			
Total	16/112 (14.3%)	31/52 (59.6%)	0.001
Minor	16/112 (14.3%)	30/52 (57.7%)	0.001
Major	0	1 (2%)	
Glucocorticoid dose, mean ± SD mg of prednisone (or equivalent)			
Baseline	19.5±7.4	33.6±14.3	0.001
Month 3	10.0±5.2	15.2±7.9	0.001
Month 6	5.1±2.7	8.9±6.4	0.001
Month 12	2.4±3.4	7.5±13.5	0.016
Month 18	1.6±4.3	3.3±5.4	0.147
Month 24	0.4±4.9	1.6±6.6	0.296
Adjunctive DMARDs	13 (13%)	25 (50%)	0.001
Adjunctive biological therapy or new small molecules	2 (2%)	14 (28%)	0.001

(Table 1). Among patients with subclinical GCA, no differences were found in the prednisone starting dose between those who relapsed and those who did not (mean, 32.4±15.6 vs 35.5±12.1 mg, p=0.722). Patients who relapsed had a faster prednisone dose reduction in the first 3 months in compared to the non-relapsing patients (mean dose at 3 months, 13.0 ±7.4 vs 18.8±7.5 mg, p< 0.01). Five patients in the PMR with subclinical GCA group received tozilizumab therapy at diagnosis; one of them had a minor relapse. No differences were found between relapsing and non-relapsing patients with subclinical GCA regarding age, sex, CPR and ESR.

Conclusion: Patients with PMR and subclinical GCA had a significantly higher number of relapses during a 24-month follow-up than patients with isolated PMR (62 vs 16%). Our results suggest that patients with PMR with subclinical GCA should be treated in the same manner as patients with clinically overt GCA without ischemic symptoms.

References. 1 De Miguel et al.Prevalence and characteristics of subclinical giant cell arteritis in polymyalgia rheumatica. Rheumatology (Oxford). 2023 May 2:kead189. doi: 10.1093/rheumatology/kead189. Online ahead of print. 2 Hellmich B et al. 2018 Update of the EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis. 2020 Jan;79:19-30.

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Abstract Number: 2405

Role of Mitochondria in Activation of Platelets in Giant Cell Arteritis

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SESSION INFORMATION

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Background/Purpose: We recently found extracellular mitochondrial-derived N-formyl methionine in patients with giant cell arteritis (GCA. Extracellular mitochondria can be extruded by several mechanisms, including platelet activation, and are highly immunogenic, leading to formation of anti-mitochondrial antibodies (AMAs), such as anti-cardiolipin antibodies that have also been observed in GCA. The purpose of this study was to determine the presence of additional AMAs, including anti-mitofusin 1 (MFN1) antibodies, in patients with GCA. We also sought to determine whether extracellular mitochondria are capable of mediating platelet activation in patients with GCA.

Methods: Anti-MFN1 IgG levels were measured using an in-house ELISA in the plasma from patients with GCA (n=65 in remission, n=14 with active disease), and 30 healthy controls (HC). Ultrapure mitochondria, isolated from HepG2 cells, were incubated with plasma from 65 patients with GCA in remission, and 16 HC, and assessed for IgA and IgG binding to the mitochondrial outer membrane using flow cytometry. Mitochondria were also opsonized with patient (n=58) or healthy control (n=10) plasma (6%), and subsequently incubated with platelets to determine the capacity of plasma factors, including AMAs, to promote mitochondrial-mediated platelet activation.

Results: Levels of anti-MFN1 IgG antibodies, a specific AMA, were elevated both in active disease ($p< 0.0001$) and in remission ($p< 0.0001$) in patients with GCA (**Figure 1A**). No differences in levels of anti-MFN1 antibodies were found between patients in remission and active disease for GCA (**Figure 1B**).No association was observed between anti-MFN1 antibodies and ESR levels (**Figure 1C**). Though total levels of IgG AMA did not reach statistical significance (p=0.38) in GCA patients compared to HC, IgA AMA levels were significantly higher in patients with GCA as compared to healthy individuals (p=0.003, **Figure 2A**). Levels of IgA AMA correlated with levels of IgG AMA in patients with GCA (**Figure 2B**), but not with levels of anti-MFN1 (data not shown). Finally, to investigate a potential pathogenic role of AMAs in GCA, exogenous mitochondria, derived from HepG2 cells, were opsonized with patient plasma and, upon washing, incubated with platelets from healthy individual. Plasma from patients with GCA had enhanced capacity to promote mitochondrial-mediated platelet activation as measured by P-selectin expression on platelet cell surface by flow cytometry, as compared to plasma from HC ($p< 0.0001$, **Figure 3A**). Platelet levels of P-selectin were associated with levels of anti-MFN1 IgG in patients with GCA (r=0.43, p=0.0012, **Figure 3B**).

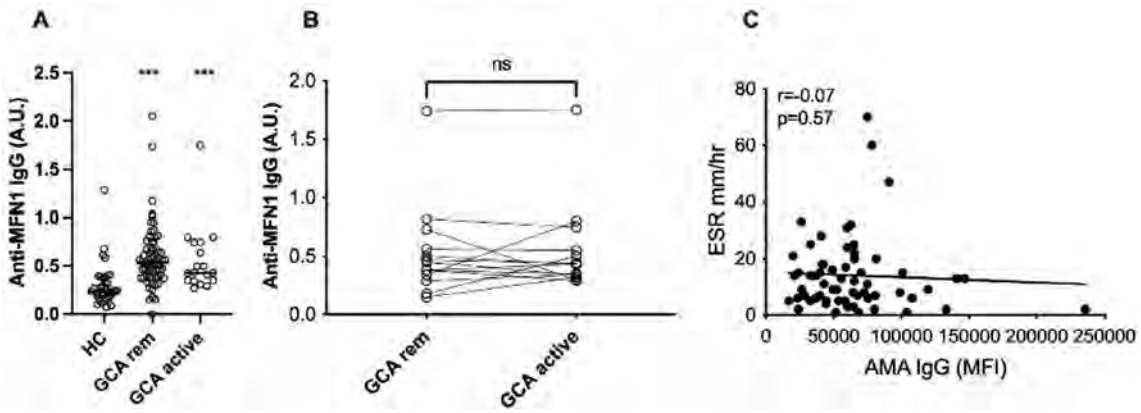

Figure 1. Anti-mitochondrial antibodies in giant cell arteritis. A) Levels of anti-MFN1 IgG antibodies were analyzed in the plasma of patients with giant cell arteritis (GCA) both in active disease and in remission (rem) and compared to healthy controls (HC). B) Anti-MFN1 IgG levels in patients at time-point of remission (rem) as well as matched active disease (active) as assessed by physician global assessment (PGA) in GCA. C) Correlation between levels of anti-MFN1 IgG antibodies and ESR. For statistical analyses, Mann-Whitney U test (A), Wilcoxon (B), and Spearman's correlation (C) were used. *** p<0.001.

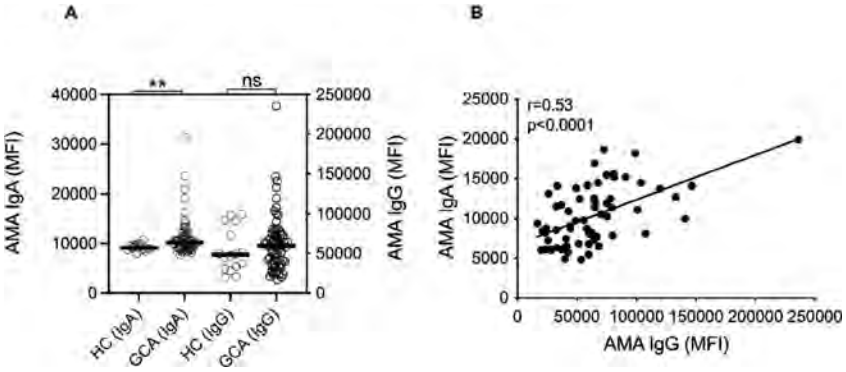

Figure 2. IgA and IgG anti-mitochondrial antibodies in giant cell arteritis. A) Levels of IgA and IgG anti-mitochondrial antibodies (AMA) were measured in the plasma of patients with giant cell arteritis (GCA) and health controls (HC) by flow cytometry. Results are presented as the mean fluorescence intensity (MFI). B) Correlation analysis between IgA AMA levels and IgG AMA levels in patients with GCA. Statistical analyses were done by Mann-Whitney U test (A) and Spearman's correlation (B). ** p<0.01.

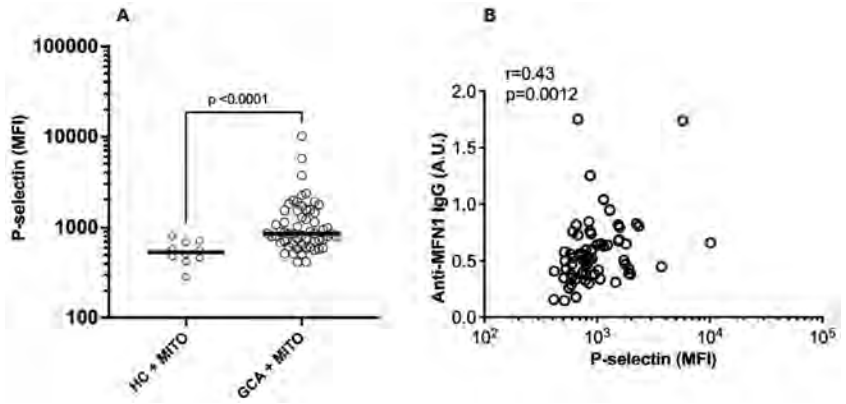

Figure 3. Mitochondrial-mediated platelet activation in giant cell arteritis. A) Platelet rich plasma (PRP) from a healthy individual was exposed to mitochondria (mito) in the presence of plasma of patients with giant cell arteritis (GCA, (n=58) and healthy controls (HC, n=10), and P-selectin expression on platelet measured by flow cytometry. Results are presented as the mean fluorescence intensity (MFI). B) Correlation analysis between levels of anti-MFN1 IgG and in vitro-induction of P-selectin on platelets in patients with GCA. Statistical analyses by Mann-Whitney U test (A) and Spearman's correlation (B).

Conclusion: We report the presence of AMAs in GCA. Presence of autoantibodies targeting mitochondria supports the hypothesis of antigenic mitochondrial components being present in GCA. Our data suggest that mitochondrial targeting by AMAs results in immune complex formation, potently activating platelets, possibly partaking in the thromboembolic morbidity and mortality of the disease. Targeting key drivers of mitochondrial extrusion in GCA could lead to new therapeutic interventions, including suppression of platelet activation.

Disclosure: D. Michailidou: Chemocentryx, 1; **P. Grayson**: None; **P. Hermanson**: None; **J. Armando Gonzalez-Chapa**: None; **D. Cuthbertson**: None; **N. Khalidi**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(-GSK), 1, Otsuka, 1, 6, Roche, 1, 6; **C. Koening**: Amgen, 1; **C. Langford**: AbbVie, 12, Non-paid consultant, AstraZeneca, 5, 12, Non-paid consultant, Bristol-Myers Squibb(BMS), 5, 12, Non-paid consultant, GlaxoSmithKlein(GSK), 5; **C. McAlear**: None; **L. Moreland**: Boehringer-Ingelheim, 12, member of independent Data Safety Monitoring Board, Celltrion, 12, member of independent Data Safety Monitoring Board; **C. Pagnoux**: AstraZeneca, 1, 2, 6, GlaxoSmithKlein(GSK), 1, 6, Otsuka, 1, 2, 5, 6, Pfizer, 5, Roche, 2; **P. Seo**: Amgen, 1, Janssen, 1; **A. Sreih**: Bristol Myers Squibb, 3; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Chemocentryx, 1, 6, Eli Lilly, 5, kiniksa, 5; **P. Monach**: Genentech, 12, Lecture with honorarium, HI-Bio, 2; **P. Merkel**: AbbVie/Abbott, 5, Amgen, 2, 5, ArGenx,

2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos, 5, Electra, 5, Genentech, 5, GlaxoSmithKlein(GSK), 2, 5, HiBio, 2, InflaRx, 2, 5, Janssen, 2, Jubilant, 2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, Takeda, 2, 5, UpTo-Date, 9, Visterra, 2; **C. Lood**: Amytryx, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Citryll, 2, Eli Lilly, 5, Gilead, 5, Horizon Therapeutics, 5, Pfizer, 5, Redd Pharma, 5, 11.

Abstract Number: 2406

Risk of Large Vessel Complications in Patients with Giant Cell Arteritis, a Population-based Study

Mohanad Elfishawi[1], Mahmut Kaymakci[1], Sara Achenbach[2], Cynthia Crowson[1], Tanaz Kermani[3], Cornelia M. Weyand[4], Matthew Koster[1] and Kenneth Warrington[1], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Rochester, MN, Rochester, MN, [3]University of California Los Angeles, Los Angeles, CA, [4]Mayo Clinic School of Medicine and Stanford University, Rochester, MN

SESSION INFORMATION
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Background/Purpose: Large vessel (LV) complications are known to occur in patients with giant cell arteritis (GCA). The magnitude of risk compared to the general population remains unclear.

In this study, we aimed to estimate the incidence of LV manifestations in a population-based cohort of patients with GCA compared with a non-GCA cohort from the same population.

Methods: The patient cohort included cases with incident GCA between 2000-2016 in defined geographical area. Incident LV complications were defined as aortic aneurysm, aortic dissection, stenosis in the aorta or any of its main branches diagnosed within 1 year prior to the diagnosis of GCA or anytime afterwards. A comparator cohort (age- and sex- matched) of individuals without GCA was assembled from the same population. Each subject was given an index date corresponding to an incidence date in the GCA cohort. All subjects were followed through December 31st, 2020, death, or migration. Cumulative incidence of large artery complications was adjusted for the competing risk of death. Cox proportional hazards models were used to assess the association of clinical characteristics with large artery complications.

Table 1. Large Vessel Complications in Patients with GCA Compared to Matched Comparators without GCA.

Event Type	HR (95% CI)*	HR (95% CI)**
Any Large Vessel Involvement	2.67 (1.59-4.51)	3.22 (1.83-5.68)
Large artery stenosis	2.98 (1.62-5.48)	4.20 (2.16-8.16)
Aortic Aneurysm/Dissection	2.41 (0.94-6.18)	1.86 (0.71-4.88)
Thoracic Aneurysm	13.46 (1.78-101.98)	--
Abdominal Aneurysm	1.08 (0.33-3.55)	--
*Age and sex adjusted **Adjusted for age, sex, hypertension, hyperlipidemia, diabetes mellitus, stroke, heart failure. Comorbid conditions were analyzed as time-dependent variables.		

Results: The patient cohort included 119 cases with GCA. Majority were female (88, 74%); mean age at diagnosis was 77.7 ± 8.1 years. Mean follow up for GCA cohort was 8.9 ± 4.7 years and 7.7 ± 4.9 years for the comparator cohort. LV complications occurred in 49 patients in the GCA cohort Vs 20 in non-GCA (HR: 2.67, 95% CI: 1.59-4.51). Large artery stenosis occurred in 40 patients in GCA cohort vs. 14 in non-GCA (HR: 2.98, 95% CI: 1.62-5.48). This included subclavian artery stenosis (17/40 GCA vs 1/14 non-GCA), axillary artery stenosis (9/40 GCA vs 0 non-GCA), vertebral artery stenosis (13/40 GCA Vs 3/14 non-GCA) and carotid artery stenosis (6/40 GCA Vs 4/14 non GCA).

On the other hand, aortic aneurysm/dissection occurred in 16 patients in the GCA cohort vs. 6 in non-GCA (HR: 2.41, 95% CI: 0.94-6.18). Furthermore, GCA was found to be a significant risk factor for the development of thoracic aortic aneurysm (HR: 13.46, 95% CI:1.78-101.98) but not for abdominal aortic aneurysm (HR: 1.08, 95% CI: 0.33-3.55) (Table 1). This elevated risk for any LV complication, large-artery stenosis and aneurysms persisted even when adjusted for age, sex, and comorbid conditions (Table 1). Interestingly, the incidence rates of any LV complication at 5 and 15 years were 27.8%

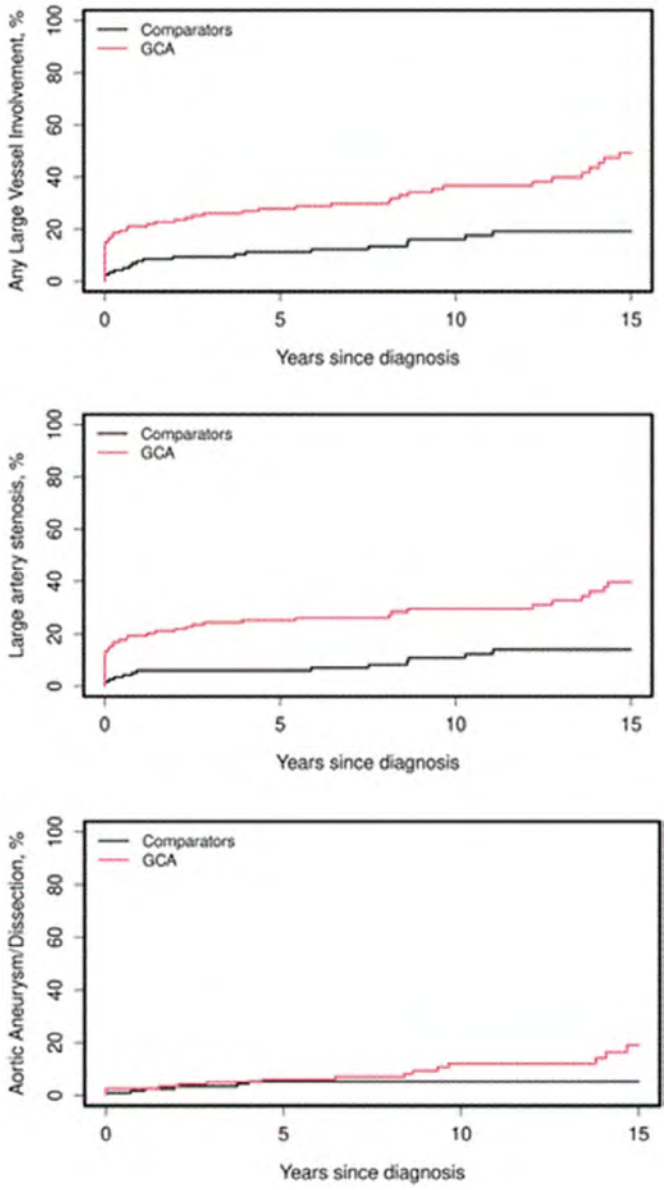

Figure 1. Cumulative incidence trends of any LV complication (upper panel), Large artery stenosis (middle panel) and Aortic aneurysm/dissection (lower panel) diagnosed within 1 year prior to incidence/index date or anytime thereafter during follow up.

(95% CI: 20.8-37.2%) and 49.2% (95% CI: 39.3-61.7%) respectively for the GCA cohort compared to 11.2% (95% CI: 6.7-18.7%) and 19.2% (95% CI: 12.5-29.4%) in the comparator cohort (Figure 1). Among individuals who developed LV complications, presence of GCA was not a significant predictor for death (HR: 0.82, 95% CI: 0.41-1.61).

Conclusion: In this study, large-artery stenosis and thoracic but not abdominal aortic complications were higher in patients with GCA. The pattern of involvement of large-artery and aortic manifestations differed in patients with GCA. Compared to the general population, the incidence of LV complications in patients with GCA increased over time which has implications for the long-term follow-up. GCA did not significantly increase risk of death in subjects with LV complications.

Disclosure: M. Elfishawi: None; **M. Kaymakci**: None; **S. Achenbach**: None; **C. Crowson**: None; **T. Kermani**: None; **C. Weyand**: None; **M. Koster**: None; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Chemocentryx, 1, 6, Eli Lilly, 5, kiniksa, 5.

Abstract Number: 2407

Immuno-permissive Antigen-presenting Cells in Giant Cell Arteritis

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SESSION INFORMATION
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Background/Purpose: Giant cell arteritis (GCA) is a medium and large vessel vasculitis with pathognomonic granulomatous infiltrates in the vessel wall. During the early stages of vasculitis, the bone marrow accelerates myelopoiesis, providing critical effector cells that control T cell immunity via antigen-presenting function. GCA macrophages are distinguished from healthy cells by the low expression of the checkpoint molecules PD-L1 and CD155. Here, we have defined macrophage profiles of co-stimulatory and co-inhibitory ligands and have tested the functional implications of co-stimulation/co-inhibition on T cell differentiation.

Methods: Monocytes from the peripheral blood of GCA patients and age-matched controls were differentiated into monocyte-derived macrophages (MDM) with M-CSF and polarized with LPS/IFN-γ. Patients with granulomatosis with polyangiitis (GPA) served as disease controls. Ligand expression was measured by flow cytometry or by immunofluorescence staining in granulomatous tissue lesions. Cellular protein expression was analyzed by immunoblotting and immunoprecipitation.

Results: Compared to age-matched controls and GPA patients, MDM from GCA patients were strongly positive for CD80/CD86 but expressed low levels of PD-L1 (p=0.0035) and CD155 (p=0.0005). Healthy MDM were consistently double positive for PD-L1 and CD155, but GCA patients had a population of PD-L1^{low} CD155^{low} and of PD-L1^{neg} CD155^{low} MDM. Combined PD-L1/CD155 low expression was maintained in tissue macrophages in inflamed arteries. PD-L1 and CD155 mRNA transcripts were equally abundant in patients and controls and immunoblotting demonstrated similar amounts of total CD155 protein in GCA and control MDM. Subcellular mapping studies with organelle specific markers placed CD155

into the endoplasmic reticulum in GCA MDM and immunoprecipitation experiments confirmed that CD155 protein was retained by ER membranes (p=0.004 GCA vs. control). Transcriptomic studies identified an ER stress signature in GCA MDM, and tunicamycin-induced ER stress was sufficient to cause CD155 retention in healthy MDM (p=0.008). We explored whether the low surface expression of PD-L1 and CD155 had functional consequences. $CD155^{low}$ MDM shifted the differentiation of interacting $CD4^+$ T cells, favoring the expansion of poorly differentiated multifunctional memory T cells.Anti-CD155 blocking antibodies produced a similar bias in T cell differentiation (p< 0.001). Defective expression of the inhibitory ligands was resistant to immunosuppressive therapy and persisted in steroid treated patients.

Conclusion: Patients with GCA generate abnormal antigen-presenting cells that are characterized by the lack of inhibitory ligands. The defect is shared by at least two checkpoints, involving PD-L1- and CD155-dependent signaling. Underlying molecular defects map to the endoplasmic reticulum, which traps PD-L1 and CD155 in the cytosol and prevents surface translocation. $PD\text{-}L1^{low}$ $CD155^{low}$ macrophages function as immuno-permissive antigen-presenting cells, supporting the unopposed expansion of multifunctional, pro-inflammatory effector T cells.

Disclosure: S. Ohtsuki: None; **C. Wang**: None; **R. Watanabe**: None; **H. Zhang**: None; **M. Akiyama**: None; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Chemocentryx, 1, 6, Eli Lilly, 5, kiniksa, 5; **G. Berry**: None; **J. Goronzy**: AbbVie/Abbott, 1, Bristol-Myers Squibb(BMS), 1, Gilead, 1; **C. Weyand**: AbbVie/Abbott, 1, Bristol-Myers Squibb(BMS), 1, Gilead, 1.

Abstract Number: 2408

The Use of the Southend GCA Probability Score (GCAPS) in Assessing the Risk of Giant Cell Arteritis in Australian Ophthalmological and General Medical Hospital Cohorts

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SESSION INFORMATION
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Background/Purpose: The rate of positive temporal artery biopsies (TAB) in patients with suspected giant cell arteritis (GCA) varies widely, indicating the need for better pre-test probability evaluation. The Southend Probability Score (GCAPS) has been developed as a GCA risk stratification tool and low scores (< 10), can exclude the diagnosis without the need for further investigation. It has not been studied in ophthalmology specific hospitals, where patients may present with a higher frequency of ophthalmic symptoms and have a greater risk of vision loss if the diagnosis is missed.

Methods: Medical records of patients who underwent temporal artery biopsy (TAB) between 2010-2020 at the quaternary Sydney and Sydney Eye Hospital (SSEH) and 2010-2017 at the tertiary Prince of Wales Hospital (POWH) were reviewed and stratified into low (score < 10), intermediate (score 10-12) and high risk (score ≥13) according to the GCAPS score.

Results: Two hundred and thirty-three patients were assessed: 160 from SSEH and 73 from POWH. All 39 patients classified as low-risk had a negative TAB result (table 1). Amongst low-risk patients, the most reported symptoms were headache (69.2%) and cranial ischemia (38.5%), which included jaw claudication, transient monocular vision disturbance and diplopia.

The most frequently noted examination findings were temporal artery abnormalities (15.4%) and isolated relative-afferent pupillary defect (5.1%). None of the low-risk patients had findings consistent with arteritic anterior ischemic optic neuropathy.

Conclusion: The GCAPS reliably predicted negative biopsy results in all patients with a low-risk score. This study supports its use as a risk stratification tool in both ophthalmological and general medical settings and help to exclude the diagnosis and need for temporal artery biopsy in patients with GCAPS of less than 10.

Table 1: Characteristics and clinical features of patients with suspected giant cell arteritis risk stratified by Southend GCA Probability Score (GCAPS).

		Risk Category (Score)			
	All (n=233)	Low (n=39) GCAPS < 10	Intermediate (n=77) GCAPS 10-12	High (n=117) GCAPS ≥ 13	P-value[a]
% total		16.7	33.0	50.2	
Female, n (%)	148 (63.5)	26 (66.7)	47 (61.0)	75 (64.1)	0.824
Positive biopsy n (%)	63 (27.0)	0 (0.0)	14 (18.2)	49 (41.9)	<0.001
Age, mean (SD) (yr.)	73.6 (9.4)	69.1 (11.2)	72.4 (8.4)	75.9 (8.7)	<0.001
CRP, mg/L n (%)					
0-5	90 (38.6)	28 (71.8)	34 (44.2)	28 (23.9)	<0.001
6-10	29 (12.4)	2 (5.1)	12 (15.6)	15 (12.8)	0.269
11-25	31 (13.3)	2 (5.1)	11 (14.3)	18 (15.4)	0.251
≥ 25	83 (35.6)	7 (17.9)	20 (26.0)	56 (47.9)	<0.001
Symptoms, n (%)					
Headache	159 (68.2)	27 (69.2)	56 (72.7)	76 (65.0)	0.518
Polymyalgic	33 (14.2)	6 (15.4)	6 (7.8)	21 (17.9)	0.135
Constitutional	30 (12.9)	1 (2.6)	12 (15.6)	17 (14.5)	0.329
Ischemic[b]	171 (73.4)	15 (38.5)	47 (61.0)	109 (93.2)	<0.001
Visual[c] n (%)					
AION	44 (18.9)	1 (2.6)	3 (3.9)	40 (17.2)	<0.001
*AAION**	21 (9.0)	0 (0.0)	0 (0.0)	21 (17.9)	<0.001
*NAION**	23 (9.9)	1 (2.6)	3 (3.9)	19 (16.2)	0.005
CRAO	10 (4.3)	0 (0.0)	2 (2.6)	8 (6.8)	0.127
RAPD	13 (5.6)	2 (5.1)	3 (3.9)	8 (6.8)	0.677
VF defect	12 (5.2)	1 (2.6)	3 (3.9)	8 (6.8)	0.481
Temporal artery examination abnormality n (%)	47 (20.2)	6 (15.4)	17 (22.1)	24 (20.5)	0.692
Extra-cranial artery abnormalities n (%)	1 (0.4)	0 (0.0)	1 (1.3)	0 (0.0)	0.362
Cranial nerve palsy[d] n(%)	13 (5.6)	0 (0.0)	4 (5.2)	9 (7.7)	0.190

[a] Comparison of low, intermediate, and high-risk groups using Chi-square test (categorical data) or one-way analysis of variance (continuous data) using SPSS (IBM Corp. Released 2021. IBM SPSS Statistics for Macintosh, Version 28.0. Armonk, NY: IBM Corp) Statistical significance defined as P<0.05. [b] Ischemic symptoms: jaw claudication, transient monocular vision disturbance or diplopia [c] Visual abnormalities: central retinal artery occlusion (CRAO), visual field (VF) defect, arteritic anterior ischaemic optic neuropathy (AAION), non-arteritic anterior ischaemic optic neuropathy (NAION), or relative afferent pupillary defect (RAPD) [d] CNIII = 23.1% (3/13), CNIV = 15.4%(2/13), CNVI = 61.5% (8/13) *Diagnosis of AAION or NAION made retrospectively according to temporal artery biopsy result

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Abstract Number: 2409

Concordance of Relapse Symptoms with Initial Baseline Presentation Features Among Patients with Giant Cell Arteritis

Max Guarda[1], Andrew Hanson[2], Hannah Langenfeld[2], Cynthia Crowson[1], Jigisha Rakholiya[3], Cristian Labarca[4], Cornelia M. Weyand[5], Kenneth Warrington[1] and Matthew Koster[1], [1]Mayo Clinic, Rochester, MN, [2]Department of Quantitative Health Sciences, Mayo Clinic, Rochester, MN, [3]Mayo Clinic, Pueblo, CO, [4]Clinica Alemana de Santiago, Santiago, Chile, [5]Mayo Clinic School of Medicine and Stanford University, Rochester, MN

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

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Background/Purpose: Relapse is common in giant cell arteritis (GCA) with 40-75% of patients having at least one flare during course of disease. A clinically relevant question for both patients and providers is whether the initial symptoms at GCA diagnosis will be present at time of relapse or whether other clinical features may manifest. Given most cohorts describe both baseline and relapse symptoms in aggregate, evaluation of patient level concordance between initial symptoms and relapse has not been delineated. The purpose of this study was to evaluate the concordance between initial GCA symptoms at diagnosis and first relapse in patients with GCA.

Methods: Two previously described cohorts of patients with GCA were utilized. Cohort 1: 286 patients with biopsy-proven GCA treated with prednisone (no tocilizumab) and Cohort 2: 114 patients with biopsy-proven or imaging-proven GCA treated with tocilizumab. Clinical symptoms at diagnosis and first relapse were grouped into the following categories:

Table 1: Odds ratios for presence of symptoms at relapse associated with presence of given symptom at baseline. Cohort 1 (biopsy-proven, non-tocilizumab), Cohort 2 (tocilizumab treated)

Cohort 1 (n=183 patients with 1 or more relapses)					
	First relapse				
Baseline	*Constitutional*	*Musculoskeletal*	*Cranial*	*Visual*	*Large vessel*
Constitutional	1.85 (0.89, 3.86)	**0.54 (0.30, 0.98)**	1.21 (0.67, 2.18)	2.21 (0.23, 21.7)	0.84 (0.27, 2.60)
Musculoskeletal	0.91 (0.45, 1.84)	**3.94 (2.04, 7.62)**	**0.32 (0.17, 0.60)**	0.63 (0.09, 4.56)	3.76 (0.81, 17.5)
Cranial	0.88 (0.32, 2.38)	1.07 (0.45, 2.56)	2.30 (0.93, 5.67)	-	**0.14 (0.04, 0.46)**
Visual	1.01 (0.47, 2.17)	0.68 (0.35, 1.32)	1.32 (0.69, 2.52)	-	0.74 (0.28, 2.81)
LV	0.77 (0.24, 2.42)	0.49 (0.18, 1.32)	0.44 (0.17, 1.15)	2.65 (0.26, 26.7)	**48.2 (11.6, 201)**
Cohort 2 (n=58 patients with 1 or more relapses)					
	First relapse				
Baseline	*Constitutional*	*Musculoskeletal*	*Cranial*	*Visual*	*Large vessel*
Constitutional	0.81 (0.05, 13.6)	1.67 (0.57, 4.84)	0.76 (0.27, 2.13)	0.39 (0.03, 4.53)	0.97 (0.26, 3.62)
Musculoskeletal	-	**9.12 (2.66, 31.2)**	**0.15 (0.05, 0.46)**	0.48 (0.04, 5.63)	0.50 (0.13, 1.95)
Cranial	-	0.51 (0.12, 2.13)	**10.7 (1.24, 92.0)**	-	0.39 (0.08, 1.89)
Visual	-	**0.20 (0.06, 0.71)**	1.57 (0.53, 4.62)	-	0.60 (0.14, 2.58)
LV	-	1.37 (0.47, 3.94)	0.42 (0.14, 1.23)	0.70 (0.06, 8.14)	3.09 (0.79, 12.1)

constitutional, musculoskeletal (MSK), cranial (non-visual), visual, and large-vessel (LV). Patients could have more than one category present at each time event. Odds ratios and conditional probabilities were calculated.

Results: In cohort 1 (C1), 183/286 (64%) patients had at least one relapse, whereas cohort 2 (C2) had 58/114 (51%) with at least one relapse. In C1, at first relapse 73% had symptoms in a single category, compared to 13% at baseline. At first relapse, 31% had cranial only, 30% MSK only, 9% constitutional only, 8% cranial plus constitutional, 7% cranial plus MSK. In C2, at first relapse 79% had symptoms in a single category, compared to 10% at baseline. At first relapse 33% had cranial only, 31% MSK only, 12% LV only, 9% cranial plus MSK. Odds ratios for presence of symptoms at first relapse based on presence of symptoms at baseline for C1 and C2 are shown in **Table 1**. In C1, patients with MSK symptoms at baseline were near 4 times more likely to have MSK features at first relapse but more than 3 times less likely to have cranial symptoms. Presence of LV symptoms at baseline resulted in a 48-fold increased odds of LV symptom at first relapse. In C2, patients with MSK at baseline had 9-fold greater odds of MSK at relapse but near 7-fold lower odds of cranial relapse symptoms. In C1, 21% and C2, 19% of patients went on to have new symptom categories at first relapse that were not present at baseline. Conditional probabilities of symptoms at first relapse according to presence or absence of baseline symptoms are shown in **Table 2**. No patient without visual symptoms at baseline developed visual symptoms at first relapse in either cohort. At first relapse new constitutional symptoms (17% C1, 4% C2), MSK (24% C1, 17% C2), cranial (33% C1, 11% C2), LV (2% C1, 12% C2) features were seen among patients that did not have these at baseline.

Conclusion: Relapse in GCA is common. Patients with MSK features at onset have greater odds of MSK but lower odds of cranial symptoms at relapse. New GCA symptoms not present at baseline occur in approximately 20% of first relapses, therefore providers should educate patients on the spectrum of GCA symptoms to be aware of, even beyond those present at a patient's diagnosis.

Table 2: Conditional probabilities of given symptom category at first relapse according to presence or absence of baseline symptom.

Cohort 1										
Probability	*Pr(Relapse 1 symptom | baseline = No)*					*Pr(Relapse 1 symptom | baseline = Yes)*				
Baseline symptom	*Con.*	*Msk.*	*Cran.*	*Vis.*	*LV*	*Con.*	*Msk.*	*Cran.*	*Vis.*	*LV*
Constitutional	**17%**	52%	48%	1%	8%	**27%**	37%	53%	3%	7%
Musculoskeletal	24%	**24%**	68%	3%	3%	22%	**55%**	40%	2%	10%
Cranial	25%	42%	**33%**	0%	25%	23%	43%	**53%**	3%	4%
Visual	23%	46%	49%	**0%**	8%	23%	37%	56%	**8%**	6%
LV	23%	45%	53%	2%	**2%**	19%	29%	33%	5%	**48%**
Cohort 2										
Probability	*Pr(Relapse 1 symptom | baseline = No)*					*Pr(Relapse 1 symptom | baseline = Yes)*				
Baseline symptom	*Con.*	*Msk.*	*Cran.*	*Vis.*	*LV*	*Con.*	*Msk.*	*Cran.*	*Vis.*	*LV*
Constitutional	**4%**	35%	54%	8%	19%	**3%**	47%	47%	3%	19%
Musculoskeletal	7%	**17%**	72%	7%	24%	0%	**66%**	28%	3%	14%
Cranial	0%	56%	**11%**	0%	33%	4%	39%	**57%**	6%	16%
Visual	5%	54%	46%	**0%**	22%	0%	19%	57%	**14%**	14%
LV	6%	38%	59%	6%	**12%**	0%	46%	38%	4%	**29%**

Values are percentages and represent the observed risk for the given symptom in those without (baseline=no) and with (baseline=yes) each symptom category at baseline. For example in cohort 1, 17% of patients without constitutional symptoms at baseline went on to have constitutional symptoms at first relapse, whereas 27% of patients with constitutional symptoms at baseline went on to have constitutional symptoms at first relapse.

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Abstract Number: 2410

Tocilizumab versus Methotrexate in Giant Cell Arteritis: A Retrospective Study to Compare Efficacy and Rapidity of These Steroid-sparing Agents in GCA Patients

Luca Quartuccio Quartuccio[1], **Elena Treppo**[2], Maria De Martino[3], Maria Pillon[1], Simone Perniola[4], Dario Bruno[4], Miriam Isola[3] and Elisa Gremese[4], [1]Rheumatology Division, Department of Medicine, University of Udine, Udine, Italy, [2]Physician, Moimacco, Italy, [3]Institute of Statistics, Department of Medicine, University of Udine, Udine, Italy, [4]Division of Rheumatology, Institute of Rheumatology and Affine Sciences, School of Medicine, Catholic University of the Sacred Heart, Roma, Italy

SESSION INFORMATION

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Background/Purpose: Glucocorticoids (GCs) are still the mainstay of treatment of Giant Cell Arteritis (GCA). Although GCs are highly effective in GCA, it is well documented the high burden of toxicity of GCs as well as the disease relapse during GC tapering. Therefore, patients with GCA may benefit from GC-sparing treatments. The aim of this retrospective study was to compare the efficacy and rapidity of TCZ and MTX as steroid-sparing agents in a real-life cohort of GCA patients.

Methods: A retrospective analysis was conducted including patients with newly diagnosed GCA from the Rheumatology Units of Udine and Rome. The diagnosis of GCA was based on the presence of symptoms and signs and confirmed by temporal artery biopsy, temporal artery ultrasound, or PET/CT imaging. The inclusion criterion was the treatment with TCZ or MTX as first steroid-sparing drug.

Results: 112 GCA patients (81 female) with a median age of 70 (IQ 65-75) years were collected. Thirty-one out of 112 (27.7%) patients were treated with TCZ (162mg/week), while 81/112 (72.3%) patients received MTX (up to 20mg/week) as a GC-sparing agent.

The median time of follow up in the TCZ and MTX group was 28 (18.5-44) and 67 (42-99) months (**p < 0.001**), respectively. At the last medical examination, 110/112 (98.2%) patients were in sustained remission, and 25/31 (80.6%) patients in TCZ group and 60/81 (74.1%) patients in MTX group were on steroid-free therapy.

At month 6 after GCA onset, 5/31 (16.1%) patients in TCZ group and none in MTX group were in GC-free sustained remission (**p-value=0.001**). Similarly, at month 12, 64.5% (20/31) and 11.1% (9/81) of patients were in sustained GC-free remission in TCZ and MTX group, respectively (**p-value < 0.001**). The median time to discontinued GCs was 10 (IQR 7-12) months (TCZ group) and 24 (IQR 18-45) months (MTX group) (**p-value < 0.001**).

During the follow up period, at least one relapse of the disease occurred in 7/31 (22.6%) in TCZ-treated and 43/81 (53.8%) in MTX-treated patients, respectively (**p-value=0.003**).

The number of overall complications (including infectious events, new-onset of hypertension, new-onset diabetes mellitus, fragility fractures, secondary osteoporosis, ischemic events and malignancies) was not statistically different between the two groups over the follow up, even if a trend towards a lower incidence of secondary osteoporosis was recorded, and the total number of adverse events under TCZ was numerically lower than on MTX (p-value=0.086).

Conclusion: TCZ allowed a faster discontinuation of steroid therapy and a lower relapse rate than MTX in GCA patients.

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Abstract Number: 2411

C-X-C Motif Chemokine Receptor 4-targeted Molecular Imaging in Giant Cell Arteritis – a Head-to-head Comparison with FDG PET

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Background/Purpose: 2-[^{18}F]fluoro-2-deoxy-D-glucose(FDG) is the reference PET radiotracer for detecting inflammation in giant cell arteritis (GCA). C-X-C motif chemokine receptor 4 (CXCR4)-directed PET, however, allows for targeting leukocyte subsets, thereby providing a direct visualization of active inflammation. We aimed to report initial results from a Phase II trial applying chemokine receptor-targeted imaging in patients with newly diagnosed GCA (NCT05604482).

Methods: Nine treatment-naïve individuals with confirmed GCA underwent PET/CT imaging with both FDG and [^{68}Ga] PentixaFor (PXF). For each PET, a total of 13 arterial segments per patient were analyzed. In addition, eight joints were examined for concurrent polymyalgia rheumatica. We compared both scans on a visual (using PETVAS) and quantitative level

(by calculating the target-to-background ratio [TBR], with blood pool as reference). Flow cytometry determined quantitative CXCR4 expression on leukocytes in peripheral blood by calculating a normalized median fluorescence intensity (NMFI) scoring (with CXCR4 antibody isotype serving as control). Quantitative PET results were then correlated with NMFI.

Results: At the visual level, PETVAS of FDG (25.62 ± 5.61) was comparable with PXF (21.33 ± 3.5, P=0.07). The TBR of FDG (2.41 ± 0.96) was also not significantly different from that of PXF (1.8 ± 0.8, P=0.11). The interquartile ranges (IQR) for PEN (IQR, 0.48), however, were lower than for FDG (IQR, 1.5), suggesting lower scatter and improved accuracy for PXF-based quantitative read-outs. Comparable results were also recorded for joints (PEN: IQR, 0.25; FDG: IQR, 0.5). Flow cytometry showed broad expression of CXCR4 on leukocytes. Subpopulations with the highest CXCR4 expression were naive B and T cells, followed by basophils. NMFI and PXF-based quantification showed significant correlations with basophils in the aorta, with the most prominent association for the abdominal segment (r=0.85, P=0.03).

Conclusion: Quantification of the CXCR4-targeted PET radiotracer PXF was comparable to FDG for assessing vessel wall and joint inflammation. Thus, PXF PET may be incorporated for image-guided, anti-inflammatory strategies in patients with newly diagnosed GCA.

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Abstract Number: 2412

Evaluation of the Pretest Probability Score, Ultrasound and Biopsy on GCA Diagnose: Data from Real Clinical Practice

María del Carmen San José Méndez[1], Uxía Couto Lareo[1], Vanesa Balboa Barreiro[2], Francisco J. Blanco[1], Bruno de aspe de la iglesia[1], Antonio Atanes Sandoval[3], Diego Dios Santos[1], Jesús Carlos Fernández López[1], Mercedes Freire González[1], Guillermo González Arribas[1], Genaro Graña Gil[1], Natividad Oreiro Villar[1], Jose Antonio Pinto Tasende[1], Francisco Javier De Toro Santos[1], Clara Ventin Rodriguez[1], Maite silva díaz[3] and Ana Lois Iglesias[1], [1]Rheumatology department, Complexo Hospitalario Universitario A Coruña (CHUAC). Instituto de Investigación Biomédica A Coruña (INIBIC), A Coruña, Spain, [2]Clinic epidemiology and biostatistics department. Complejo Hospitalario Universitario A Coruña (CHUAC). Instituto de Investigación Biomédica A Coruña (INIBIC), A Coruña, Spain, [3]Rheumatology department, Complexo Hospitalario Universitario A Coruña (CHUAC). Instituto de Investigación Biomédica A Coruña (INIBIC)., A Coruña, Spain

SESSION INFORMATION
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Background/Purpose: Giant cell arteritis (GCA) affects large and medium size arteries. Biopsy was considered the gold standard in the diagnosis[1], but in the last years other techniques are being implemented like temporal and axillar arteries ultrasound (US) with a good performance being included in the 2022 ACR GCA classification criteria[2]. To improve the diagnosis of these patients a Pretest Probability Score (Southend) (PPS) has been developed[3],stratifying patients into 3 different risk groups. The aim was to study the performance of the different tools available for the diagnosis of GCA: PPS, vascular ultrasound, and biopsy of Temporal Artery.

Table 1. Descriptive analysis of the sample (n=97) comparing the main characteristics in GCA and non-GCA.

		GCA (n=23)		Non-GCA (n=74)		p
		n (%)	Mean (SD)	n (%)	Mean (SD)	
Age at diagnosis			77.35 (7.27)		74.32 (10.27)	0.262
Sex	Men	11 (47.83)		28 (37,84)		0.393
	Women	12 (52.17)		46 (62.16)		
Time symptoms to diagnosis (weeks)			5.26 (4.85)		16.79 (23.60)	0.030
Headache		20 (86.96)		39 (52.7)		0.003
Scalp hypersensitivity		9 (39.13)		6 (8.11)		0.001
Jaw claudication		14 (60.87)		7 (9.46)		< 0.001
Visual symptoms		11 (47.83)		20 (27.03)		0.062
Polymyalgia rheumatica		10 (43.48)		31 (41.89)		0.831
Temporal artery alteration	Right	7 (31.82)		3 (4.62)		< 0.001
	Left	4 (18.18)		4 (6.15)		
	Bilateral	7 (31.82)		7 (10.77)		
CRP mg/L			68.5 (57.66)		73.76 (87.82)	0.321
Positive ultrasound		21 (91.30)		6 (8.22)		0.415
Biopsy		21		34		
Positive biopsy		13 (61.90)		0 (0.00)		< 0.001
Pretest score	Low	0 (0.00)		26 (35.14)		< 0.001
	Medium	5 (21.74)		32 (43.24)		
	High	18 (78.26)		16 (21.62)		

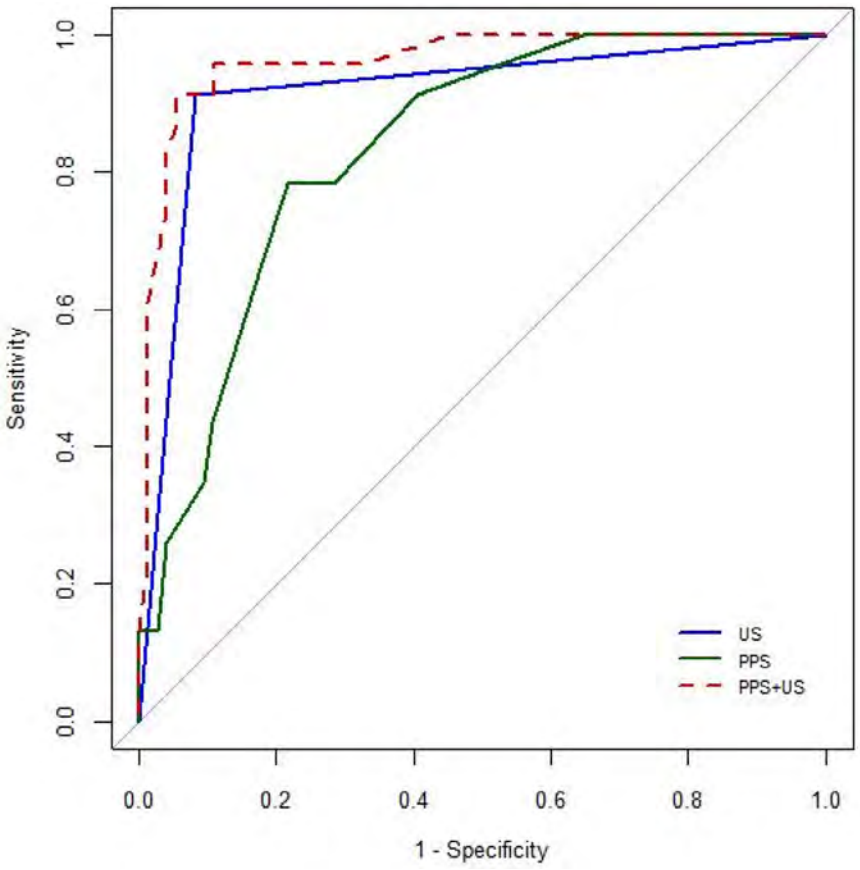

Figure 1. AUC of the different diagnostic tests studied (probability pretest score, ultrasound of temporal artery and combination).

Methods: Retrospective study of the patients referred to our Rheumatology Department with GCA suspicion from January 2019 to October 2022. Demographic and clinical variables including the ones from the PPS were collected.Exploration of the 3 branches of temporal artery and axillar artery bilaterally was performed by grey scale and Color Doppler US (Esaote MylabSix probe 10-22 Hz) evaluating the halo sign and the intima-media thicknes[4].PPS and US were carried out in all patients referred. Biopsy was performed in the necessary cases. Final GCA diagnosis was performed according to the rheumatologist decision (clinical diagnosis). A descriptive analysis of the sample was performed. Quantitative variables are expressed as mean (±SD) and qualitative ones as absolute frequencies and percentage. A comparative analysis was performed according to clinical diagnosis. The comparison of means was carried out using the Student's T or Mann-Whitney U test. The association between qualitative variables was analyzed using Chi-square test. The agreement between the different tests was analyzed using Kappa index. The predictive capacity of the different diagnostic tests is evaluated using ROC curves, providing their AUC, and the sensitivity and specificity values.

Results: Patients (97) with suspected GCA were included, 59.79% women, with a mean age of 74.4 (±9.69). Final diagnosis attending to clinical criteria and other tests was made in 23 patients (23.7%). In GCA compared with non GCA patients showed more frequently and statistical significance: headache, scalp hypersensitivity, facial pain, jaw claudication and changes on temporal artery. Ultrasound was positive in 91.3% (n=21) GCA patients, from them 61.90% had a positive biopsy (Table 1). Area under ROC curve (AUC), sensitivity and specificity for PPS were 0.83 (0.75-0.92), 78.3% and 78.4%, respectively, for US were 0.91 (0.84-0.99), 91.3% and 91.8%, and for biopsy, 0.81 (0.67-0.94), 61.9% and 100%. Data from the combination of PPS+US showed an AUC of 0.96 (0.92-1) (sensitivity 91.3% and specificity 94.5%). Combination of PPS+biopsy showed an AUC of 0.90 (sensitivity 71.4% and specificity 91.2%) (Figure 1).

Conclusion: The combination of US with PPS value improves the individual predictive capacity of each these diagnostic techniques.

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Abstract Number: 2413

Janus Kinase Inhibitors in Giant Cell Arteritis in Clinical Practice. Real-World Clinical Practice Study and Literature Review

Fernando López[1], Javier Loricera[2], Toluwalase Tofade[3], Diana Prieto-Peña[2], Susana Romero Yuste[4], Eugenio De Miguel[5], Anne Riveros-Frutos[6], Ivan Ferraz Amaro[7], Santos Castañeda[8], Eztizen Labrador-Sánchez[9], Olga Maiz[10], Elena Becerra-Fernández[11], Javier Narvaez[12], Eva Galindez-Agirregoikoa[13], Ismael González[14], Ana Urruticoechea[15], Sebastian Unizony[16] and Ricardo Blanco[17], [1]Rheumatology, Hospital Universitario Marqués de Valdecilla, Santander, Spain, [2]Hospital Universitario Marqués de Valdecilla, Santander, Spain, [3]Neurology Department, Massachusetts General Hospital, Boston, MA, [4]Complexo Hospitalario Universitario, Pontevedra, Spain, [5]Hospital Universitario La Paz, Madrid, Spain, [6]Hospital Universitario Germans Trias i Pujol, Barcelona, Spain, [7]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [8]Hospital Universitario de la Princesa, Madrid, Spain, [9]Hospital Universitario San Pedro, Laguardia, Spain, [10]Hospital Universitario de Donostia. San Sebastián, Spain., Donosti, Spain, [11]Department of Rheumatology, Hospital Universitario de Torrevieja, London, United Kingdom, [12]Hospital Universitario de Bellvitge, Barcelona, Spain, [13]Basurto University Hospital, Bilbao, Spain, [14]Hospital Universitario de León, León, Spain, [15]Hospital Can Misses, Ibiza, Spain, [16]Massachusetts General Hospital, Winchester, MA, [17]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain

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Background/Purpose: Patients with giant cell arteritis (GCA) can relapse despite glucocorticoids, methotrexate and tocilizumab treatment. The JAK/STAT signalling pathway is involved in the pathogenesis of GCA, and JAK inhibitors (JAKi) are a potential treatment alternative. Baricitinib showed positive results in a small uncontrolled study **(1)**.

The objective of this study is to evaluate the effectiveness of JAKi in GCA.

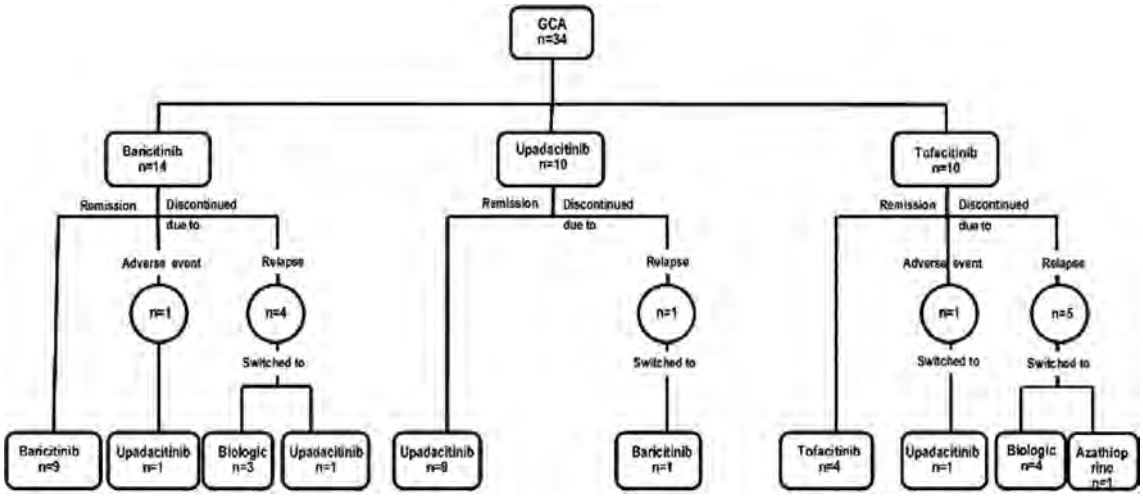
Methods: Real-world, retrospective clinical practice study of patients with GCA treated with JAKi. Outcomes assessed included disease relapse and safety. A literature search for other JAKi-treated GCA cases was conducted in PubMed, Embase and the Cochrane library from inception to 04/30/2023. We compared results of the previous baricitinib study **(1)** and the baricitinib recipients in our series.

Results: We present 34 patients (29 females[85%], mean age, 72.2 years, relapsing disease 34 [100%]) that received JAKi **.** The initial JAKi was baricitinib (n=14), tofacitinib (n=10) and upadacitinib (n=10) **(Table and Figure)**. After a median [IQR] follow-up of 9.5 [4.2-12.7] months, 22 (64.7%) achieved and maintained remission, and 12 (35.3%) patients discontinued

TABLE. Current series and literature review of patients with GCA treated with JAKi.

Reference	Cases	Sex	Age, mean±SD	JAKi	Previous csDMARDs	Previous bDMARDs	Follow-up (months), mean±SD	Outcome
Hershy. Br J Haematol. 2019	1	Female	75	Ruxolitinib	Methotrexate, mycophenolate mofetil	None	9	No data
Prigent. Clin Nucl Med. 2021	1	Female	76	Baricitinib	Methotrexate	Tocilizumab	12	Clinical improvement
Camellino. Ann Rheum Dis 2022	3	Female (3)	74±11.5	Baricitinib (3)	Methotrexate (2), hydroxychloroquine (1),sulfasalazine (1),cyclosporine (1), mycophenolate mophetil (1)	Tocilizumab (2)	8.5±4.9; no data(1)	Clinical improvement (1); no data (2)
Koster. Ann Rheum Dis. 2021	15	Female (11), male (4)	72.4±7.2	Baricitinib (15)	Methotrexate (2), Cyclophosphamide (1)	Sirukumab (1)	11.3±2.5	Clinical improvement (13);no improvement(1);no data (1)
Sanada. Rheumatology (Oxford). 2022	1	Female	72	Upadacitinib	Sulfasalazine	None	7.5	Clinical improvement
Current series	34	Female (29), male (5)	72.2±7.8	Baricitinib(14), tofacitinib(10), upadacitinib(10)	Methotrexate (20), hydroxychloroquine (3), leflunomide(1)	Tocilizumab (26),sarilumab(3),abatacept (6), azathioprine (2), ustekinumab (2)	9.7±7.2	Clinical improvement (22), no improvement(10)

Current series and literature review of patients with GCA treated with JAKi.



Flow chart of the 34 GCA patients treated with JAKi

the initial JAKi due to relapse (n=10, 29.4%) or severe adverse events (SAEs) (n=2, 5.9%) including liver dysfunction and dyspnea/palpitations. The 12 patients failing the initial JAKi were switched to an alternative [JAKi (n=4), biologic therapy (n=7) and azathioprine (n=1)]. The literature review identified another 21 GCA patients (17 females, mean age 74.2 years) treated with JAKi, mostly with baricitinib (n=18). Most of these patients benefited from JAKi therapy **(Table).** Patients in our series receiving baricitinib had longer disease duration (median [IQR]31 [12-51] vs 9 [7-21] months; p=0.001) and had received biologics (71% vs 6.7%; p< 0.001) more frequently than those in the previous baricitinib study **(1)**. Remaining baseline features were similar.

Conclusion: This real-world analysis suggest that JAKi could be effective in GCA, including patients failing other immunosuppressive therapies. The results of an ongoing phase 3 randomized controlled trial are awaited to confirm or rule out this observation.

References:

1. Koster MJ, et al. Ann Rheum Dis. 2022

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Abstract Number: 2414

Relapse in Giant Cell Arteritis Treated with Tocilizumab. Predictive Factors

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SESSION INFORMATION

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Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III

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Background/Purpose: Tocilizumab (TCZ) is the only biologic therapy approved for giant cell arteritis (GCA). Clinical trial with TCZ in GCA was performed with intravenous (iv) TCZ in a phase 2 trial **(1)**, and with subcutaneous (sc) TCZ in the phase 3 GiACTA **(2)**. There is general agreement on the initial/maintenance dose, but duration of TCZ therapy is not well established. In GiACTA trial, after one year on TCZ, most patients had GCA relapse after withdrawal.

This study aims to assessthe predictive factors of relapse in GCA in a clinical practice scenario.

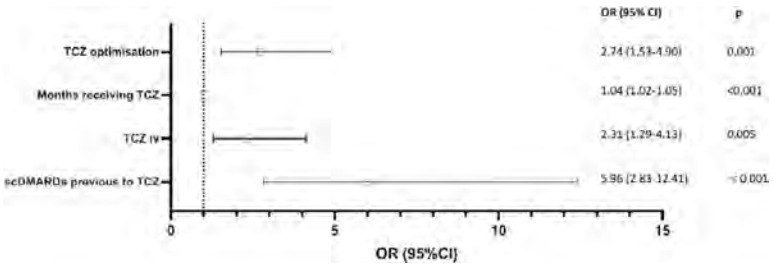
Methods: Multicentre observational study of 471 patients with GCA. The diagnosis of GCA was performed between 2016 and 2021 according to: **a)** ACR criteria, and/or **b)** temporal artery biopsy, and/or **c)** imaging techniques. Relapse was defined according to EULAR consensus definition **(3)**. From the 471 patients, we selected the patients who had available the data on relapse during follow-up. Multivariable study was conducted to identify the best set of predictors for the appearance of a relapse.

TABLE. Main features of the patients with GCA according to relapses.

	No relapsing GCA (n=342)	Relapsing GCA (n= 63)	p
Age at GCA diagnosis (mean±SD)	72±9	70±9	0.12
Women/Men (% de women)	246/96 (72)	47/16 (75)	0.57
Phenotype			
cGCA	152 (44)	31 (48)	0.63
ecGCA	62 (18)	12 (18)	0.95
mixGCA	128 (37)	22 (34)	0.58
Cardiovascular risk factors			
High blood pressure, n (%)	212 (63)	37 (60)	0.65
Dyslipidemia, n (%)	193 (57)	33 (53)	0.57
Diabetes, n (%)	63 (19)	12 (19)	0.89
Previous or current smoking history, n (%)	33 (10)	9 (14)	0.28
Ischemic manifestations			
Headache, n (%)	189 (55)	36 (58)	0.70
Jaw claudication, n (%)	84 (26)	11 (19)	0.25
Visual manifestations, n (%)	56 (16)	13 (20)	0.48
Systemic manifestations			
Fever, n (%)	39 (11)	12 (19)	0.11
Constitutional syndrome, n (%)	139 (41)	27 (42)	0.83
PmR, n (%)	210 (62)	43 (68)	0.32
Laboratory			
ESR, mm/1a hora, median [IQR]	36 [14-56]	14 [6-42]	0.85
CRP (mg/dL), median [IQR]	1.6 [0.3-3.0]	0.8 [0.4-2.9]	0.21
Previous treatment			
scDMARDs, n (%)	171 (50)	53 (82)	<0.001
bDMARDs, n (%)	4 (1)	4 (6)	<0.001
Prednisone dose (mg/day), median [IQR]	20 [10-40]	20 [10-30]	0.86
TCZ			
IV/SC, (%IV)	171/171 (50)	45/18 (69)	0.004
Mono/combo, (%mono)	263/79 (77)	43/20 (66)	0.066
Optimization, n (%)	123 (39)	38 (62)	<0.001
Months receiving TCZ	27 [18-43]	4 [2-12]	<0.001

Abbreviations: bDMARDs: biologic disease-modifying antirheumatic drugs,GCA, CRP: C-reactive protein, giant cell arteritis, ESR: erythrocyte sedimentation rate, IQR: interquartile range [25th-75th], scDMARDs: synthetic conventional disease-modifying antirheumatic drugs, SD: standard deviation

Main features of the patients with GCA according to relapses.



Results: GCA relapses were observed in 63 of 405 (15%) patients for whom such data was available**(Table).** No significant differences were observed between the two groups in demographic, clinical and laboratory characteristics or in prednisone dose at initiation of TCZ. The set of variables associated with GCA relapses were prior use of synthetic conventional disease-modifying antirheumatic drugs (scDMARDs), use of iv.TCZ, shorter time on TCZ therapy and optimization of TCZ dose **(Figure).**

Conclusion: GCA relapse seems related mainly to TCZ schedule and was associated with iv TCZ, and a shorter treatment time and optimization.

References:

1. Villiger PM, et al. Lancet. 2016. PMID: 26952547
2. Stone JH, et al. N Engl J Med. 2017. PMID: 28745999
3. Hellmich B, et al. Ann Rheum Dis. 2020. PMID: 31270110

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Abstract Number: 2415

Giant Cell Arteritis Is Associated with Worse Hospital Outcomes in Aortic Aneurysm/Dissection Hospitalizations: A Nationwide United States Population-Based Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
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Session Time: 9:00AM–11:00AM

Background/Purpose: Giant Cell Arteritis (GCA) is a known risk factor for Aortic Aneurysm/Dissection (AAD). However, it is unclear if patients with GCA have worse hospital outcomes when hospitalized for AAD compared to patients without GCA hospitalized for AAD. We queried the largest inpatient hospitalization database in the United States (U.S.) to answer this question.

Methods: Data were abstracted from the National Inpatient Sample (NIS) from 2016 to 2020 Database. NIS is a nationally representative approximate 20-percent stratified sample of all discharges from U.S. community hospitals, excluding rehabilitation and long-term acute care hospitals. The numbers in the databases are weighted to optimize national estimates. The NIS was searched for hospitalizations for patients aged ≥ 50 years with a principal diagnosis of AAD ("I71") with and without a coexisting secondary diagnosis of GCA ("M315" and "M316") using ICD-10 codes. The principal diagnosis is the main reason for hospitalization. Any diagnosis other than the principal is a secondary diagnosis. Each hospitalization in the NIS has only 1 principal diagnosis and can have up to 40 secondary diagnoses. The chi-square test was used to compare baseline characteristics between the GCA and non-GCA groups. The primary outcome was inpatient mortality. Hospital length of stay (LOS) and total hospital charges were secondary outcomes. Multivariable logistic and linear regression analyses were used to adjust for confounders for the primary and secondary outcomes, respectively. We adjusted for age, gender, race, insurance type, income, Charlson co-morbidity index, and hospital characteristics. STATA version 16 was used for analysis. Since NIS contains publicly available depersonalized data, Institutional Review Board (IRB) review was waived.

Results: There were about 175 million hospitalizations in the combined 2016-2020 database. We obtained 314,215 hospitalizations for patients aged ≥ 50 years with a principal diagnosis of AAD. 685 (0.2%) of these had a secondary diagnosis of GCA, while 313,530 (99.8%) did not have co-existing GCA. The GCA group was older (mean age of 74.6 vs 71.8 years, $p < 0.0001$) and had more females (76.6% vs 29.5%, $p < 0.001$) compared to the non-GCA group. The GCA group had similar inpatient mortality compared to the non-GCA group (6.4% vs 6.6%, p=0.627). The GCA group had longer LOS (9.4 vs 5.5 days, $p < 0.0001$) and higher total hospital charges ($224,540 vs 180,356, p=0.002) compared to the non-GCA group. See table 1.

Conclusion: GCA patients admitted for AAD have worse hospital outcomes (longer LOS and higher total hospital charges) compared to non-GCA patients admitted for AAD. Adequate treatment of GCA to prevent complications such as AAD is needed. In addition, screening, early detection, and prompt management of AAD via a multidisciplinary approach are essential in optimizing the outcomes of GCA patients.

Table 1: Hospital outcomes of Aortic Aneurysm/Dissection hospitalizations with and without Giant Cell Arteritis

Hospital Outcomes	AAD with GCA (n=685)	AAD without GCA (n=313,530)	Adjusted odds ratio (95% CI)	P-value
Inpatient mortality, %	6.6	6.4	1.5 (0.3-6.9)	0.627
			Adjusted mean difference	
Hospital length of stay, days	9.4	5.5	7.7 (3.8-11.7)	<0.0001
Total Hospital charges, USD	224,540	180,356	177,239 (64,678-289,800)	0.002

Abbreviations: AAD: Aortic Aneurysm/Dissection hospitalizations, GCA: Giant cell arteritis, USD United States dollars, 95% CI: 95% Confidence Interval

Disclosure: A. Minalyan: None; **C. Hino**: None; **E. He**: None; **O. Idolor**: None; **C. Osuorji**: None; **N. Chukwu**: None; **E. Edigin**: None; **V. Sandhu**: Exagen, 2, 5.

Abstract Number: 2416

Comparison of Clinical, Laboratory and Imaging Features of Relapses Between Takayasu and LV-GCA Patients. an Italian Monocentric Study

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SESSION INFORMATION

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Background/Purpose: No previous study has compared clinical, laboratory and imaging features of relapses in Takayasu (TAK) and large vessel giant cell arteritis (LV-GCA). The aim of our study was to compare relapses characteristics in these 2 group of pts.

Methods: We retrospectively evaluated 171 pts LVV (119 LV-GCA and 52 TAK) seen at the Rheumatology Unit of Reggio Emilia Hospital (Italy) between 01.01.2005 and 31.12.2016 and followed-up for at least 2 years. Data of the pts collected at relapses included demographic, clinical, laboratory and imaging (PET/CT scan, MRI/CT angiography and/or arterial US). GCA was diagnosed according to ACR1990 criteria and LV-GCA in the presence of LVV involvement seen at CT and/or MRI and/or ultrasonography and/or PET examinations according to GIACTA criteria. TAK was diagnosed using Ishikawa's10 diagnostic criteria and its modification by Sharma et al. and ACR classification criteria for TAK. Disease-related signs/symptoms, ESR and CRP levels, and GC dosages were recorded at every follow-up visit. The presence of clinical disease relapses or long term remission were evaluated at every visit. We also evaluated the appearance of new structural lesions (SL) (stenosis, occlusion, and/or vessel dilatation at CTA/MRA and/or US examination) or new inflammatory lesions (IL)(new/increased FDG uptake at PET/TC or parietal thickening increase at US or CTA).

Results: During a median follow-up duration of 76 months we observed 86 TAK relapses and 89 LV-GCA relapses. TAK relapses presented more frequently carotidodynia (8.1 vs 1.1%, p = 0.032), chest pain (10.5 vs 1.1 %, p=0.009), large vessel vasculitis (89.4 vs 59.8%, p=0.001), had higher ESR (45+32 vs 32+29 p=0.009). TAK relapse caused the introduction of BIO therapy more frequently (48.8% vs 16.8%, p=0.001). LV-GCA relapses were characterized by cranial symptoms (16.9 vs 3.5, p=0.005), polymyalgia rheumatica (27.0 vs 0, p=0.001) and appeared after a shorter time from diagnosis (37.4+42 vs 52.8+48.3 months, p= 0.025). At vessel imaging TAK relapses had more anonymous artery involvement (30.7 vs 15.1 %, p =0.043), LV-GCA relapses had more thoracic and abdominal aorta involvement (89.6 vs 54.1, p< 0.001 and 45.8 vs 14.9, p=0001, respectively) At vessel imaging LV-GCA relapses had higher prevalence of IL (4.31 (1.98) vs 2.0 (1.84), p < 0.001). TAK relapses had higher new SL at common carotid artery (20.3 vs 1.9%, p =0.002), anonymous artery (9.5 vs 0, p=0.041) and subclavian artery (23.3 vs 1.9%, p=0.001). LV-GCA relapses had higher prevalence of common carotid(59.6 vs 28.4%, p=0.001) aortic (89.6 vs 56.8%, p< 0.001) and femoral (10.9 vs 1.5%, p=0.038) new IL.

Conclusion: TAK and LV-GCA relapses have different clinical, laboratory and imaging features. In particular TAK relapses were characterized by higher prevalence of new arterial SL while LV-GCA by new arterial IL.

Disclosure: L. BOIARDI: None; **P. MACCHIONI**: None; **F. Muratore**: None; **E. Galli**: None; **c. marvisi**: None; **G. Besutti**: None; **L. Spaggiari**: None; **A. Versari**: None; **C. Salvarani**: CSL Vifor, 1, 2, 6, Eli Lilly, 1, 2, 6.

Abstract Number: 2417

Influence of Histological Tempol Artery Biopsy Findings on Outcomes of Biopsy-proven Giant Cell Arteritis in Italian Patients : A Long Single Center Follow-up Study

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Few studies have evaluted the influence of histological features of temporal artery biopsy (TAB) on disease outcome in giant cell arteritis (GCA) patients. Our aim was to investigate potential associations between TAB histological characterstics and outcomes of GCA in a long term single center retrospective follow-up study.

Methods: Two hundred and four Italian patients with biopsy-proven GCA resident in Reggio Emilia area (Italy) followed up for at least 12 months entered the study (median duration of FU 130 months(range 13-435 months). The following histological findings of TAB were recorded : localisation of inflammatory infiltrate (peri-adventitial and vasa vasorum small vessel vascultis (SVV+VVV), inflammation limited to adventitia (ILA), trans mural inflammation TMI), presence of giant cells (GC), presence of infiltrating neutrophils, plasma cells, histiocytes, eosinophils, presence of laminar necrosis (LN), vessel wall calcifications, luminal trombosis (LT) and intimal hyperplasia (IH). The severity of inflammation (SI) was graded on a semiquantitative scale (mild, moderate and severe), the severity of i IH (was graded as mild < 25% reduction in lumen diameter, moderate from 25% to 75%, and severe >75%).

The following data were recorded during follow up : presence of relapses, long term remission (LTR), cumulative steroid dose at 6, 12 months and at end of FU, duration of treatment and of LTR and mortality. Survival curve were compared with K-M method using log rank test.

Results: Relapses were recorded by 42.5% of the patients during a median FU period of 130 months (13-435). Factors which influenced the time of first relapse were : presence of GC (140 vs 207 months, p=0.025), presence of LT (91 vs 171 months, p=0.036) and histological subtype (80 vs 156 vs 249 months for SVV+VVV, ILA and TMI respectively, p=0.017). Fifty-seven % of patients were able to withdraw steroids for at least 12 month. Histological subtypes influenced the duration of treatment (SVV+VVV 2.7 months, ILA 17.9 months, TMI 32.0 months, p=0.019). Seventy % of patients died during the follow up period. Factors with impact on survival time were : SI severe vs mild infiltrate (107 months vs 155 months, p=0.006), presence of GC (112 vs 154 months, p=0.049), presence of LN (96 months vs 132 months, p=0.029), histological subtypes (TMI 115 months vs ILA 161 months vs SVV+VVV 195 months, p= 0.017).

Conclusion: Histological findings of TAB influenced survival time, first relapse time and duration of steroid treatment in GCA pts.

Disclosure: L. BOIARDI: None; **P. MACCHIONI**: None; **F. Muratore**: None; **E. Galli**: None; **c. marvisi**: None; **c. Ricordi**: None; **f. Macaluso**: None; **a. cavazza**: None; **S. Croci**: None; **C. Salvarani**: CSL Vifor, 1, 2, 6, Eli Lilly, 1, 2, 6.

Abstract Number: 2418

Effectiveness of Dose Spacing with Tocilizumab in Giant Cell Arteritis Treatment

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Background/Purpose: The only steroid sparing agent approved for treatment of Giant Cell Arteritis (GCA) is the anti-interleukin-6 receptor antagonist tocilizumab. There remains uncertainty regarding treatment duration of tocilizumab and the optimal approach to medication withdrawal.

Methods: Patients who met the 2022 ACR/EULAR GCA classification criteria with a clinical diagnosis of GCA were prospectively enrolled. As per ACR/ Vasculitis Foundation guidelines all patients with a new diagnosis of GCA were started on tocilizumab if there were no contraindications. All patients had a 26-week glucocorticoid taper as per the GiACTA protocol. Tocilizumab was administered weekly for the first 12 months, and then every-other-week for an additional 12 months. Relapse of disease on tocilizumab was managed with temporary increases in systemic glucocorticoids.

Results: 55 patients with newly-diagnosed GCA were included. Of these, 27 patients did not receive tocilizumab treatment for a variety of reasons; recent or active treatment for malignancy (7), history of diverticulitis (3), patient preference not to start (5), co-existing inflammatory condition for which other biologic treatment was preferred (1), patient frailty and/or recurrent infections (9), death before start of tocilizumab (1). 1 further patient only had one month of treatment before discontinuation for a drug reaction. 27 patients (49%) had weekly treatment with tocilizumab for 1 year. Of these only 17 had every second week tocilizumab at one year. 5 remained on a weekly dose due to previous visual loss and concern about preserving the remaining eye. 2 had other coexisting inflammatory diseases for which weekly dosing was required. 1 died of natural causes before dose spacing, and 2 stopped tocilizumab before spacing due to side effects. 27 patients had tocilizumab weekly for a mean of 15.7 months and 17 of had tocilizumab every-other-week at one year for a mean of 8.1 months. 2 patients (11.7%)

	Tocilizumab weekly (27)	Tocilizumab two-weekly (17)
Mean duration tocilizumab (months)	15.7	8.1
Number of minor relapses	1	1
Number of major relapses	0	2
Overall relapse free remission	26 (96%)	14 (82%)
Number of minor infections not requiring hospital admission	1	2
Number of major infections requiring hospital admission	1	0
Infection free remission	25 (92.5%)	15 (88%)

Figure 1: Results

had a major relapse on every-other-week tocilizumab (one aortic dissection and one with monocular visual loss). There were two minor relapses, one in the weekly dosing group and one in the two-weekly dosing group.

While on weekly tocilizumab, 1 patient had a minor infection treated in the community and 1 had a major infection (diverticulitis) requiring hospital admission. In the every-other-week tocilizumab group, two patient had minor infections treated in the community and no patient had a major infection requiring hospitalisation.

Conclusion: In a real-world prospective study cohort, only 49% (27/55) of patients were eligible for tocilizumab therapy (with GIACTA protocol steroid). 17/27 were eligible for dose reduction to every other week with 2/17 (11.7%) having major relapses of GCA at 24 months. In a real-life cohort tocilizumab therapy was only possible in 1 in 2 patients and when initiated was continued beyond the recommended period of 12 months in the majority of patients. Overall, 96% of patients in the weekly dosing group had relapse-free remission compared to 82% in the every-other-week treatment group. A dose reduction in tocilizumab after 12 months of weekly treatment maintained most patients in remission, had comparable safety outcomes and was cost effective.

Disclosure: S. Cowley: None; **C. Kirby**: None; **P. Harkins**: Janssen, 5; **R. Conway**: AbbVie/Abbott, 5, 6, Celltrion, 5, Fresenius Kabi, 6, Galapagos, 6, Janssen, 5, 6, Nordic Pharma, 5, Novartis, 5, UCB, 6, Viatris, 6; **G. Murphy**: None; **D. Kane**: None.

Abstract Number: 2419

Visual Manifestations in Giant Cell Arteritis: Identification of Risk Factors from the ARTESER Registry

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SESSION INFORMATION

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Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III

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Background/Purpose: Visual loss is one of the most feared complications in giant cell arteritis (GCA). Some factors have been previously associated with visual loss, as lower levels of inflammatory markers, jaw claudication or thrombocytosis, although some of these studies showed contradictory results. Our objective was to identify predictive factors of visual involvement in a large cohort of patients with GCA.

Methods: ARTESER is a large Spanish multicenter registry promoted by the Spanish Society of Rheumatology, including patients with GCA diagnosis from June 2013 to March 2019. The following variables were collected at diagnosis per protocol: demographics, symptoms (including all visual manifestations reported by clinicians), laboratory test results, temporal artery biopsy and imaging techniques (ultrasound, PET, MRI, CT).Patients with and without visual involvement were compared in a bivariate analysis. Multivariate logistic regression model was performed to determine potential predictive factors of visual manifestations.

Table 1. Clinical, laboratory and imaging variables of patients with GCA according to presence of visual manifestations.

	All patients n=1636	Patients with visual symptoms n=599	Patients without visual symptoms n=1037	p
Demographics				
Female, n (%)	1151 (70.4%)	405 (67.6%)	746 (71.9%)	0.065
Age, mean (SD)	76.9 (8.10)	78.6 (7.56)	76.1 (8.18)	<0.001
Clinical variables				
Symptoms, duration up to diagnosis (months), mean (SD)	2.9 (5.67)	1.9 (5.22)	3.5 (5.84)	<0.001
Headache, n (%)	1307 (80.3%)	465 (77.9%)	842 (81.7%)	0.065
Jaw claudication, n (%)	590 (37.6%)	256 (44.7%)	334 (33.5%)	<0.001
Scalp tenderness, n (%)	446 (31.3%)	183 (31.5%)	283 (31.1%)	0.877
Upper limb claudication, n (%)	149 (10.1%)	53 (9.9%)	96 (10.2%)	0.885
Lower limb claudication, n (%)	153 (10.4%)	47 (8.8%)	106 (11.2%)	0.141
Polymyalgia rheumatica, n (%)	683 (43.5%)	190 (33.7%)	493 (48.9%)	<0.001
Fever, n (%)	355 (24%)	71 (13.2%)	284 (30.2%)	<0.001
Abnormal TA clinical examination, n (%)	807 (53.1%)	313 (56.3%)	494 (51.2%)	0.055
Smoking, n (%)	127 (8.3%)	46 (8.2%)	81 (8.3%)	0.112
Previous antiplatelet use, n (%)	308 (19.4%)	144 (24.9%)	164 (16.3%)	<0.001
Previous cardiovascular disease, n (%)	356 (22.6%)	142 (24.5%)	214 (21.5%)	0.164
Hypertension, n (%)	1057 (65.3%)	425 (71.5%)	632 (61.7%)	<0.001
Diabetes Mellitus, n (%)	344 (21.4%)	152 (25.9%)	192 (18.8%)	<0.001
Dyslipidemia, n (%)	783 (48.6%)	301 (51.5%)	482 (47%)	0.078
Temporal artery biopsy positive n=1204, n (%)	753 (62.5%)	302 (65.2%)	451 (60.9%)	0.128
Cranial-GCA, n (%)	1305 (79.8%)	515 (86%)	790 (76.2%)	<0.001
LV-GCA, n (%)	331 (55.3%)	84 (39.8%)	247 (63.6%)	<0.001
Mixed (cranial + LV) GCA, n (%)	197 (19%)	281 (17.2%)	84 (14%)	0.010
Imaging findings				
Positive FDG-PET/CT n=368, n (%)	240 (65.2%)	50 (48.5%)	190 (71.7%)	<0.001
Positive CT angiography n=184, n (%)	61 (33.2%)	16 (24.2%)	45 (38.1%)	0.055
Positive TA US n=701, n (%)	478 (68.2%)	179 (67.8%)	299 (68.4%)	0.865
Positive LV US n=177, n (%)	60 (33.9%)	24 (31.6%)	36 (35.6%)	0.572
Laboratory variables				
CRP (mg/L), mean (SD)	96.2 (177.2)	85 (190.69)	102.7 (171.29)	0.066
ESR (mm/h), mean (SD)	75.9 (33.57)	72.5 (32.41)	77.7 (34.07)	0.003
Haemoglobin (g/dL), mean (SD)	11.8 (1.61)	12 (1.59)	11.8 (1.62)	0.019
Platelets 10^3/L, mean (SD)	326.6 (180.03)	315.5 (142.97)	332 (200)	0.083

Abbreviations: GCA: giant cell arteritis; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; TA: temporal artery; US: ultrasound; LV: large-vessel; SD: standard deviation; CT: computed tomography

Table 2. Logistic regression analysis of factors associated with visual manifestations.

Variables	OR	95% CI
Female	0.887	0.670 - 1.173
Age	1.029	1.011 - 1.048
Jaw claudication	1.747	1.343 - 2.271
Polymyalgia rheumatica	0.498	0.383 - 0.648
Fever	0.393	0.274 - 0.563
Abnormal TA clinical examination	1.042	0.806 - 1.348
LV-GCA	0.724	0.512 - 1.023
ESR	0.993	0.989 - 0.998
Hb	0.971	0.883 - 1.069
Previous antiplatelet use	1.292	0.939 - 1.778
Hypertension	1.191	0.894 - 1.586
Diabetes Mellitus	1.358	0.994 - 1.854

Abbreviations: GCA: giant cell arteritis; ESR: erythrocyte sedimentation rate; LV: large-vessel; TA: temporal artery

Results: A total of 1636 GCA patients were included for analysis, of whom 599 (36.6%) presented visual involvement. The most frequent visual manifestation was anterior ischemic optic neuropathy (45.7%), followed by transient monocular vision loss (45.1%). Clinical, laboratory and imaging variables of patients with and without visual symptoms are shownin Table 1. Older age (OR 1.029; 95% CI 1.011-1.048), jaw claudication (OR 1.747; 95% CI 1.343-2.271) and diabetes mellitus (OR 1.358; 95% CI 0.994-1.854) were the only independent predictors of visual symptoms in our cohort. The presence of polymyalgia rheumatica (OR 0.498; 95% CI 0.383-0.648), fever (OR 0.393; 95% CI 0.274-0.563) and higher erythrocyte sedimentation rate (ESR) (OR 0.993; 95% CI 0.989-0.998) were associated with a reduced risk of developing visual involvement (Table 2).

Conclusion: One out of every three GCA patients present visual manifestations at diagnosis. Older age, jaw claudication and diabetes mellitus are independent predictors of visual manifestations, whereas polymyalgia rheumatica, fever and high ESR reduces the risk of visual involvement.

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Abstract Number: 2420

Sex Differences in Giant Cell Arteritis: Data from the ARTESER Registry

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SESSION INFORMATION

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Background/Purpose: Giant cell arteritis (GCA) is the most common vasculitis in North America and Western Europe. GCA is more likely to occur in women (1). However, there are scarce data on the epidemiology, clinical presentation, comorbidities, treatment and outcomes between men and women. Our aim was to assess the previous differential features between gender found in ARTESER registry.

Methods: ARTESER is a large Spanish multicenterepidemiological registry of GCA promoted by the Spanish Society of Rheumatology in which 26 national hospitals participated. Patients were included according to whether they met the 1990 ACR criteria, had a positive diagnostic test (biopsy or imaging test) or by the clinical judgement of the investigator. The recruitment period was between 2013 and 2019 and standardized data were included for all patients diagnosed with GCA in these centers. Differences between sexes were compared in a bivariate analysis.

Table 1. Main epidemiologic features and comorbidities at diagnosis.

	Total n=1675	Women n=1178	Men n=497
Annual incidence, Incidence rate x10^5 inhabitants ≥50 years (95% CI)	7.4 (6.6-8.3)	10.1 (8.1-11.5)	4.8 (3.8-5.9)
Age at diagnosis, years, mean (SD)	76.9 (8.1)	76.9 (8.0)	76.9 (8.3)
Comorbidity			
Arterial hypertension, n (%)	1079 (64.6)	749 (63.7)	330 (66.8)
Dyslipidemia, n (%)	801 (48.0)	563 (47.9)	238 (48.3)
Smoking status			
Former, n (%)	132 (8.4)	69 (6.3)	63 (13.4)
Current, n (%)	300 (19.1)	84 (7.7)	216 (46.0)
Never, n (%)	1135 (72.4)	944 (86.1)	191 (40.6)
Cardiovascular disease, n (%)	367 (22.0)	204 (17.4)	163 (33.1)
Diabetes mellitus, n (%)	351 (21.1)	217 (18.6)	134 (27.2)
Osteoporosis, n (%)	282 (17.0)	260 (22.3)	22 (4.5)
History of cancer, n (%)	204 (12.3)	109 (9.3)	95 (19.3)
Chronic kidney failure, n (%)	167 (10.0)	112 (9.6)	55 (11.2)
Obesity, n (%)	149 (9.0)	115 (9.8)	34 (7.0)
Alcohol consumption, n (%)	119 (7.1)	26 (2.2)	93 (18.9)

Results: A total of 1675 patients with GCA were included, 1178 women and 497 men. The annual incidence of GCA was higher in the female group (10.07; 95%CI: 8.7-11.5) than in the male group (4.83; 95%CI: 3.8-5.9) with a similar mean age at diagnosis and symptom onset between the two groups of 76.9 and 76.7 years, respectively. Among the comorbidities presented at diagnosis, male had a higher presentation of diabetes mellitus, tobacco use, alcohol consumption, cardiovascular disease and neoplasms than female, in which only osteoporosis was more frequent. The results are shown in **table 1.** Clinical manifestations were divided into cranial, extracranial and general. Among the cranial manifestations, headache (79.9%), temporal (49.2%) and visual (36.1%) disturbances were the most frequent. Polymyalgia rheumatica was the predominant extracranial manifestation (41.8%) and asthenia the most general symptom reported (52.2%). Main data are shown in **table 2.** We analyzed the distribution according to sex and observed a higher frequency of headache (p=0.028), polymyalgia rheumatica (p=0.003) and asthenia (p=0.035) in the female group. In contrast, we found a higher frequency of dysphasia in the male group (p=0.013) and visual symptoms, with no statistically significant differences in the latter. In terms of laboratory findings, elevated glomerular sedimentation rate (ESR) (p=0.039) and platelet count (p< 0.001) were higher in female. Treatment and outcome data are shown in **table 3.** Regarding the use of glucocorticoids and related adverse effects no differences between the two groups were detected. The use of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) was more frequent in males (p=0.005), but no differences were found regarding tocilizumab administration. There were no differences in the number of relapses or disease remission. However, the proportion of deaths during follow-up was higher in women (13.8% vs. 6.6%, p< 0.001).

Conclusion: GCA was more frequent in females, with more than twice as many cases as males. Some of the classic manifestations, such as headache, polymyalgia rheumatica and asthenia, were more common in women. In addition, women had higher ESR and platelet levels than men. The use of csDMARDs was higher in the male group but mortality was increased in females.

Table 2. Differences in clinical manifestations and laboratory abnormalities at diagnosis and during follow-up according to sex in ARTESER Registry.

	Total n=1675	Women n=1178	Men n=497	p(women vs men)
Clinical manifestations (phenotypes)				
Cranial				
Recent-onset headache, n (%)	1337 (79.9)	955 (81.1)	382 (76.9)	**0.028***
Temporal artery tenderness or decreased pulsation, n (%)	824 (49.2)	593 (50.4)	231 (46.5)	0.079
Visual symptoms, n (%)	605 (36.1)	411 (34.9)	194 (39.0)	0.101
Jaw claudication, n (%)	597 (35.7)	425 (36.1)	172 (34.6)	0.621
Hypersensitive scalp, n (%)	451 (26.9)	324 (27.5)	127 (25.6)	0.290
Facial pain, n (%)	213 (12.7)	158 (13.4)	55 (11.1)	0.169
Vertigo, n (%)	127 (7.6)	89 (7.6)	38 (7.6)	0.994
Dysphagia, n (%)	56 (3.3)	31 (2.6)	25 (5.0)	**0.013***
Hearing loss, n (%)	45 (2.7)	29 (2.5)	16 (3.2)	0.404
Transitory ischemic attack, n (%)	32 (1.9)	19 (1.6)	13 (2.6)	0.176
Extracranial				
Polymyalgia rheumatica, n (%)	699 (41.8)	521 (44.3)	178 (35.8)	**0.003***
Claudication-lower limbs, n (%)	157 (9.4)	104 (8.8)	53 (10.7)	0.269
Claudication-upper limbs, n (%)	152 (9.1)	114 (9.7)	38 (7.6)	0.173
Peripheral synovitis, n (%)	86 (5.2)	59 (5.1)	27 (5.5)	0.641
General				
Asthenia, n (%)	873 (52.2)	634 (53.9)	239 (48.1)	**0.035***
Anorexia, n (%)	608 (36.3)	428 (36.4)	180 (36.2)	0.824
Weight loss, n (%)	541 (32.3)	367 (31.2)	174 (35.0)	0.106
Fever/low-grade fever, n (%)	367 (21.9)	254 (21.6)	113 (22.7)	0.728
Laboratory findings at diagnosis				
High ESR, n (%)	1409 (84.12)	1005 (85.3)	404 (81.3)	**0.039***
ESR, mm/h, mean (SD)	75.9 (33.6)	77.4 (33.0)	72.3 (34.7)	**0.005***
Hemoglobin, g/dL, mean (SD)	11.9 (1.6)	11.6 (1.5)	12.3 (1.8)	0.892
Platelets, (x10^9/L), mean (SD)	326.6 (180.0)	337.0 (192.5)	302.3 (144.3)	**<0.001***

Abbreviations: ESR: erythrocyte sedimentation rate. *Significant differences (= p-value <0.05) in bold.

Table 3. Differences in treatment and outcomes during follow-up according to sex in ARTESER Registry.

	Total n=1675	Women n=1178	Men n=497	p(men vs women)
Treatment				
Glucocorticoids therapy, n (%)	1636 (97.7)	486 (97.8)	1150 (97.6)	0.839
IV boluses of glucocorticoids, n (%)	424 (25.3)	132 (26.6)	292 (24.8)	0.741
Oral glucocorticoids, n (%)	1633 (97.5)	485 (97.6)	1148 (97.5)	0.97
Adverse effect associated with steroids, n (%)	387 (23.1)	110 (22.1)	277 (23.5)	0.481
Immunosuppressive treatment csDMARDs, n (%)	556 (33.2)	140 (28.2)	416 (35.3)	**0.005***
Immunosuppressive treatment with csDMARDs since baseline, n (%)	263 (15.7)	65 (13.1)	198 (16.8)	0.055
Tocilizumab treatment, n (%)	161 (9.6)	37 (7.4)	124 (10.5)	0.147
Tocilizumab treatment since baseline, n (%)	47 (2.8)	13 (2.6)	34 (2.9)	0.527
Outcomes				
Relapses, n (%)	33 4 (19.9)	96 (19.3)	238 (20.2)	0.678
Remission, n (%)	197 (11.8)	61 (12.3)	136 (11.5)	0.672
Death, n (%)	142 (8.5)	65 (13.8)	77 (6.6)	**<0.001***

Abbreviations: csDMARDs: conventional synthetic disease-modifying antirheumatic drugs. *Significant differences (= p-value <0.05) in bold.

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Optic Nerve Sheath Measurement on Ultrasound: A Novel Diagnostic Test for Giant Cell Arteritis

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SESSION INFORMATION

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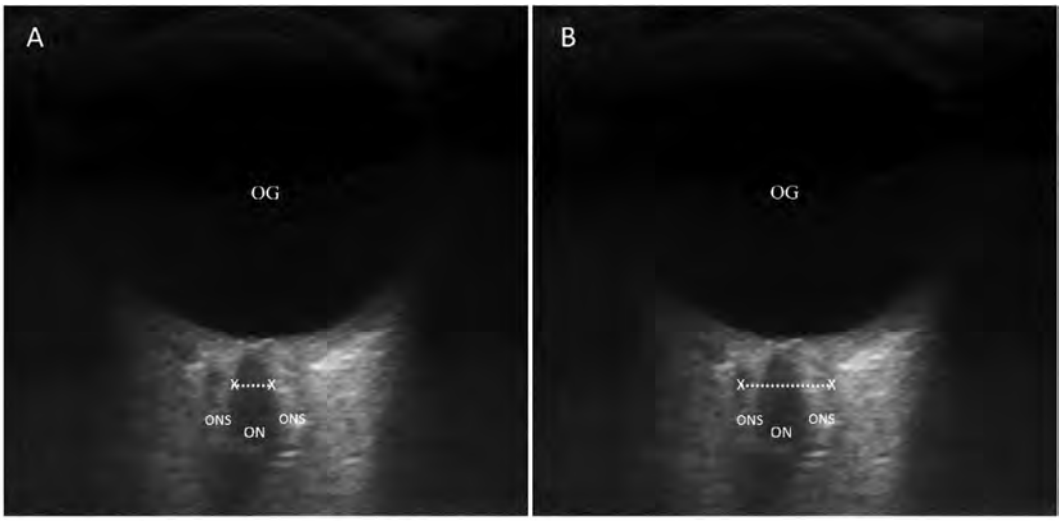
Background/Purpose: Confirming the diagnosis of giant cell arteritis (GCA) remains challenging. Available diagnostic tests have limited accuracy and availability. Recently, optic nerve sheath enhancement on magnetic resonance imaging has been reported in patients with GCA. Whether this finding can be documented on ultrasound is unknown. Optic nerve

(ON) ultrasound is non-invasive, easy to learn and does not require sophisticated equipment. This study aims to investigate if ON sheath measurement on ultrasound may be used to identify patients with active, new-onset GCA.

Methods: A cross sectional study was performed in our GCA Fast-Track clinic from June to December 2022. Adult patients were included if: (1) they were referred for suspected new-onset GCA, (2) had received < 14 days of glucocorticoids, and (3) had no prior history of intracranial hypertension, retinal disorder, or demyelinating disease. Study procedures were completed during the same visit: clinical assessment, bloodwork, ultrasound of temporal/axillary arteries and of the ON. Ultrasound measurements were performed for both eyes, 3mm distal to the posterior aspect of the ocular globe. Optic nerve sheath diameter (ONSD, includes ON and its sheath) and optic nerve diameter (OND) were measured. Optic nerve sheath thickness (ONST) was obtained by subtracting OND from ONSD (Figure 1). Final diagnosis of GCA was confirmed clinically after 6-month follow-up. Independent sample t-test was used to compare mean differences in ONSD, OND and ONST in patients with and without GCA at baseline. Paired-sample t-test was used to compare measurements between both eyes. Multivariable analysis was conducted for clinical baseline characteristics and ON ultrasound measurements. A significance level of 0.05 with Bonferroni correction (n=6) for multiple comparisons was used.

Results: A total of 30 participants were enrolled, including 9 participants with a final diagnosis of GCA (all of whom also satisfied 2022 ACR/EULAR classification criteria (Table 1)). Patients with GCA had a higher mean ONSD (5.98mm) compared to those without GCA (4.02mm); with a mean difference of 1.96mm (95% confidence interval [CI]: 1.11–2.82, p< 0.001). Mean ONST was higher in patients with GCA (3.01mm) than those without GCA (1.54mm), with a mean difference of 1.46mm (95%CI: 0.85–2.07, p< 0.001). Mean OND was numerically but not statistically higher in patients with GCA (Table 2). Paired measurement comparisons of ONSD, OND, ONST did not differ between the right and left eyes. On multivariable analysis, there was no significant association between age, sex, hypertension, diabetes, anterior ischemic optic neuropathy and ONSD, OND, ONST ultrasound measurements.

Conclusion: Patients with GCA had significantly wider optic nerve sheaths on ultrasound than patients without GCA. ON ultrasound may represent a novel, rapid, bedside diagnostic test in GCA. A large prospective cohort study is ongoing to confirm these findings and evaluate if ONSD-ONST are dynamic disease markers in GCA (ClinicalTrials.gov id: NCT05749094).



OG, ocular globe; ON, optic nerve; ONS, optic nerve sheath.
Panel A dotted line : measurement of the optic nerve diameter (OND), 3mm distal to the posterior aspect of the OG.
Panel B dotted line: measurement of the optic nerve sheath diameter (ONSD, includes the optic nerve and its sheath), 3mm distal to the posterior aspect of the OG.

Figure 1: Optic Nerve Diameter and Optic Nerve Sheath Diameter Measurement on Ultrasound.

Table 1: Characteristics of 30 Participants with Suspected GCA undergoing Optic Nerve Sheath Ultrasound.

Characteristics	GCA N = 9	No GCA N = 21
Demographics		
Age in years, median (IQR)	79 (79-82)	73 (64-75)
Female patients, n (%)	2 (22)	15 (71)
Caucasian, n (%)	9 (100)	19 (90)
Past medical history, n (%)		
History of smoking	5 (56)	12 (57)
Active smoking	2 (22)	2 (10)
Hypertension	5 (56)	10 (48)
Diabetes	2 (22)	5 (24)
Dyslipidemia	4 (44)	10 (48)
Clinical features, n (%)		
Headache	7 (78)	17 (81)
Scalp tenderness	4 (44)	3 (14)
Jaw claudication	5 (56)	3 (14)
Constitutional symptoms	4 (44)	11 (52)
Polymyalgia rheumatica	3 (33)	6 (29)
Diplopia	1 (11)	3 (14)
Amaurosis fugax	1 (11)	0
Vision loss	4 (44)	0
Abnormal TA examination	5 (56)	4 (19)
Confirmed AION	4 (67)	0
Inflammatory markers, median (IQR)		
CRP (mg/L)	60.0 (41.0-88.0)	22.5 (3.2-109.7)
ESR (mm/h)	62.5 (58.0-64.0)	48.5 (23.0-56.0)
Therapy received prior to study visit		
Any glucocorticoids, n (%)	8 (89)	13 (62)
IV glucocorticoids, n (%)	5 (56)	2 (10)
Days on glucocorticoids, median (IQR)	5 (2-6)	4 (2-7)

GCA, giant cell arteritis; SD, standard deviation; TA, temporal artery; AION, anterior ischemic optic neuropathy; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IQR, interquartile range; IV, intravenous.

Table 2: Optic Nerve Sheath Ultrasound Results in 30 Participants with Suspected GCA

	Mean, in mm (SD)		MD (mm)	95% CI	*p**
	Right Eye N=30	**Left Eye** N=30			
ONSD	4.66 (1.41)	4.55 (1.49)	0.11	(-0.24, 0.45)	0.52
OND	2.78 (0.64)	2.47 (0.69)	0.31	(0.08, 0.53)	0.01
ONST	1.88 (1.01)	2.08 (1.11)	-0.20	(-0.45, 0.06)	0.12
	GCA N = 9	**No GCA** N = 21			
ONSD	5.98 (1.17)	4.02 (0.99)	1.96	(1.11, 2.82)	**<0.001**
OND	2.97 (0.46)	2.47 (0.58)	0.50	(0.05, 0.95)	0.03
ONST	3.01 (1.00)	1.54 (0.62)	1.46	(0.85, 2.07)	**<0.001**

*Significance level used for interpretation of hypothesis tests was 0.00833 (Bonferroni correction: $\alpha = 0.05$, n=6).

GCA, giant cell arteritis; SD, standard deviation; MD, mean difference; CI, confidence interval; ONSD, optic nerve sheath diameter; OND, optic nerve diameter; ONST, optic nerve sheath thickness.

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Abstract Number: 2422

Magnetic Resonance Imaging Reflects Disease Activity in the "Giant Cell Arteritis Treatment with Ultra-short Glucocorticoids and Tocilizumab" Trial (The GUSTO Trial)

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Magnetic resonance imaging (MRI) is well established for diagnosing giant cell arteritis (GCA). Its role in monitoring disease activity has yet to be determined. We investigated vascular and musculoskeletal inflammation using MRI in the patients of the GUSTO trial.

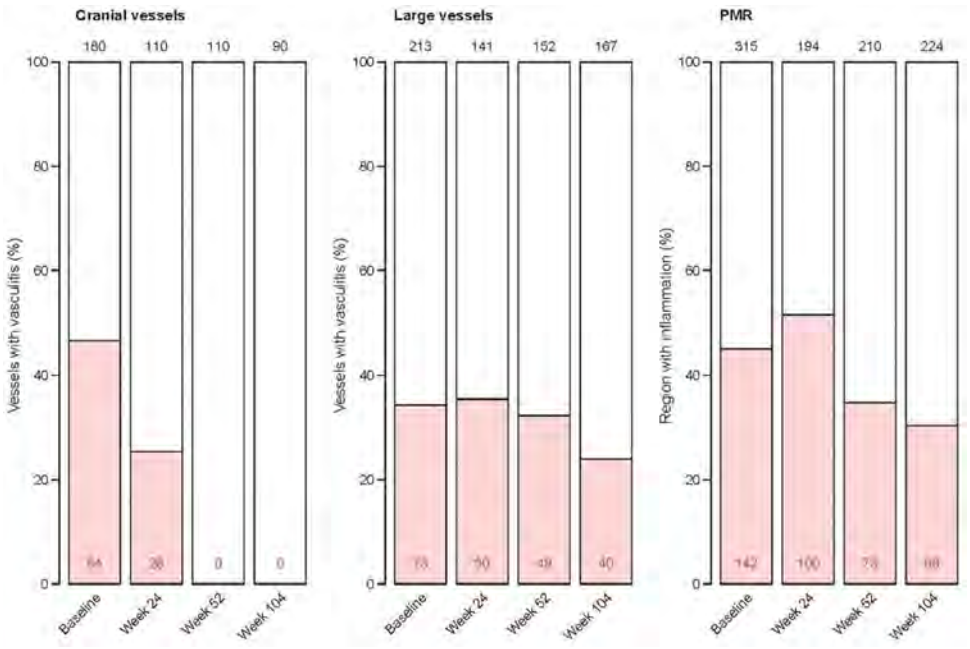

Figure 1: Proportion of segments with inflammatory findings (red numbers) summarized over all patients (black numbers=number of segments or regions assessed).

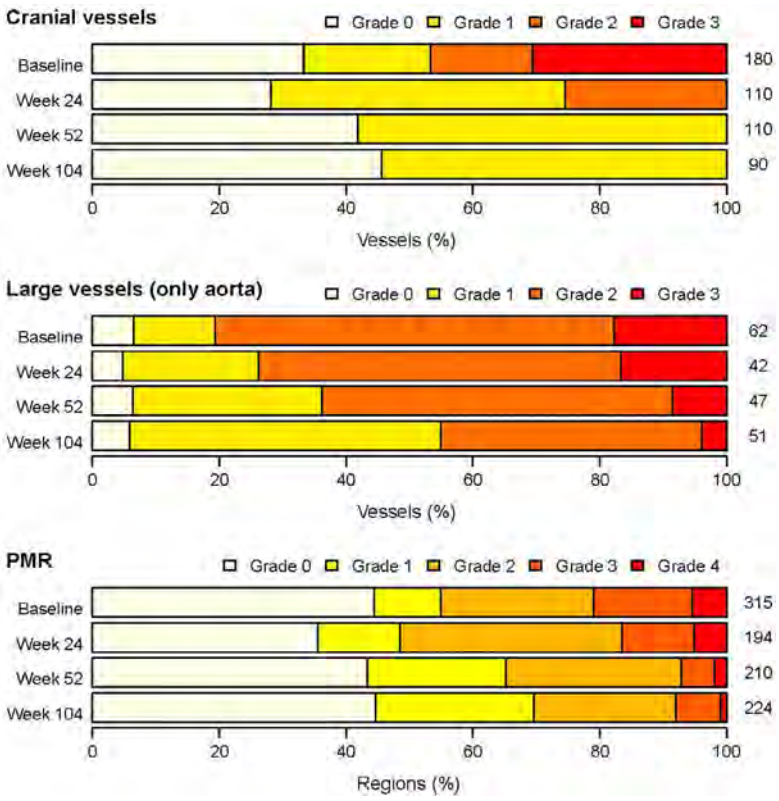

Figure 2: Grading of vessels and PMR findings summarized over all patients. Numbers refer to the total number of segments or regions assessed.

Methods: Eighteen patients with newly diagnosed GCA received 500 mg methylprednisolone intravenously for 3 consecutive days [1]. After that, GC treatment was discontinued, and a single dose of tocilizumab (TCZ) was administered intravenously, followed by weekly subcutaneous TCZ injections from day 10 until week 52. Cranial, thoracic and abdominal MR exams were performed at baseline (active, new-onset disease), and at weeks 24, 52 (remission on-treatment), and 104 (remission off-treatment). Polymyalgia rheumatica (PMR) findings as well as vasculitic disease extent and intensity were rated by experienced radiologistsand one board-certified neuroradiologist as previously reported (grade 0-3, grade ≥ 2 considered as vasculitis) [2,3]. Up to 10 cranial, 13 large vessel and 18 musculoskeletal segments were assessed.

Results: In total, 673 vascular segments and 943 musculoskeletal regions in 56 thoracic/abdominal MR and 490 vascular segments in 49 cranial MR scans of 18 patients were analyzed. Cranial vessels displayed dynamic changes. At weeks 52 and 104, no cranial vascular segment displayed vasculitic findings. Vasculitic signal alterations were still detectable in every 4th cranial segment at week 24. Large vessels, except for the ascending aorta, displayed no or only a slight decrease in vasculitic findings upon remission on- and off-treatment. PMR findings persisted in most patients. Results are displayed in Figures 1 - 3.

Conclusion: Whereas signals of cranial vessels normalized upon a 52-week treatment, large vessel signals and PMR findings persisted. Remission of vasculitic activity in cranial arteries took more than 24 weeks, which was longer than time to clinical symptom resolution and normalization of serum proteins but paralleled intima-media thickness measurements using ultrasound [4]. Thus, in contrast to large vessel signals and PMR findings, the dynamic of cranial vessel signals suggests that MRI of these arteries is a very promising monitoring tool for suspected relapse after 52 weeks of treatment.

References:

1. Christ et al. Lancet Rheumatology, 2021

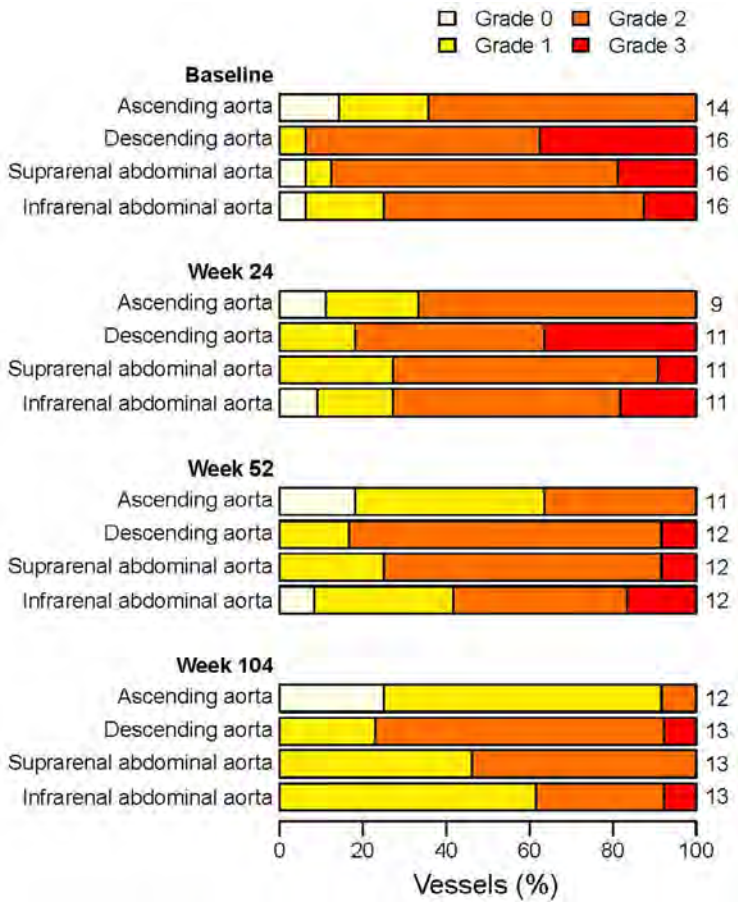

Figure 3: Grading of aortic segments. Numbers refer to the total number of patients with assessment.

2. Klink et al. Radiology, 2014.
3. Reichenbach et al. Rheumatology, 2018.
4. Seitz et al. Rheumatology, 2021.

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Abstract Number: 2423

Concordance Between the 1990 ACR Classification Criteria and the New 2022 ACR/EULAR 2022 Criteria in Giant Cell Arteritis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Classification criteria for vasculitis, including giant cell arteritis (GCA) are under constant revision. In 2022, the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) criteria were presented, renewing those published by ACR in 1990. They include wider range of clinical criteria and imaging tests, such as ultrasonography (US) and **Positron emission tomography** (PET), which has contributed to the diagnosis of a higher number of cases.

The objective of this study was to assess the concordance between recent 2022 ACR/EULAR giant cell arteritis classification criteria and the criteria of ACR 1990 **(1,2)**.

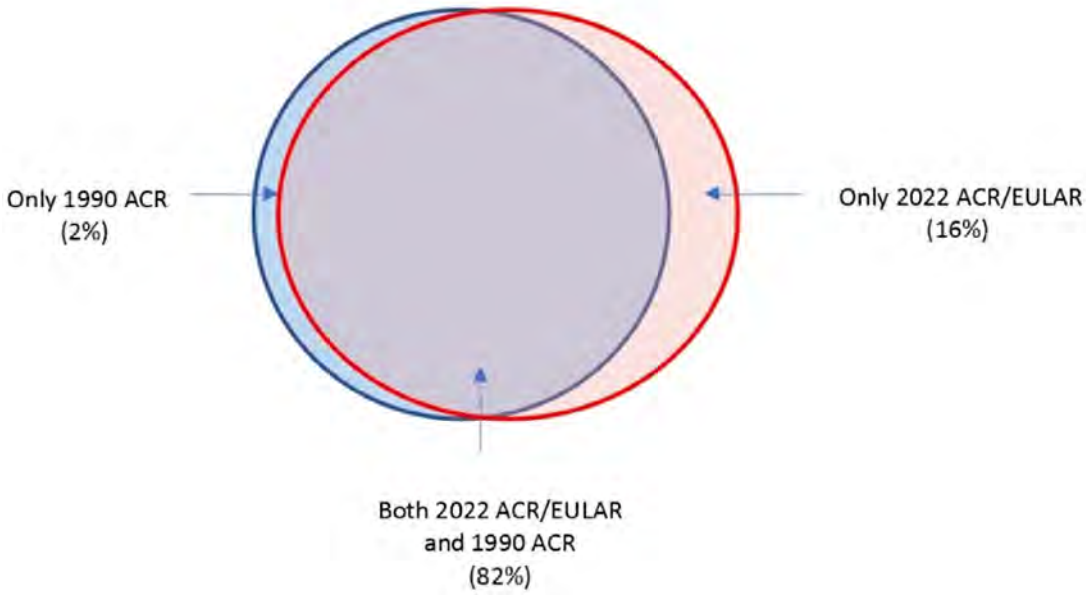
Methods: Observational study of patients diagnosed with GCA who underwent temporal artery biopsy (TAB) between 2016 and 2022 in an university hospital. Concordance between both sets of criteria were analyzed with Cohen's kappa index.

TABLE. Main characteristics according to TAB result

	Suspected diagnosis of GCA (n=191)	ACR 1990 Criteria (n=128)	ACR/EULAR 2022 Criteria (n=155)	Negative ACR1990 Criteria Positive ACR/EULAR 2022 Criteria (n=30)
Age (years), mean±SD*¶	75 ± 10	75 ± 10	75 ± 10	73 ± 10
Sex, female/male	120/71	78/50	96/59	10/20
TAB+, n (%) *¶	52 (27)	51 (39)	52 (34)	1 (3)
Halo sign on temporal artery US, n (%) ¶	37 (19)	29 (23)	37 (24)	10 (59)
Bilateral axillary involvement on US, n (%) ¶	12 (18)	8 (19)	12 (20)	4 (24)
FDG-PET activity throughout aorta, n (%) ¶	43 (43)	30 (48)	37 (44)	7 (33)
GCA Phenotype, n (%)				
Cranial GCA	127 (66)	95 (74)	108 (70)	16 (53)
Extracranial GCA	28 (15)	6 (5)	14 (9)	8 (27)
Mixed GCA	36 (19)	27 (21)	33 (21)	6 (20)
Ischemic manifestations, n (%)				
Headache*¶	152 (80)	117 (91)	134 (86)	20 (67)
Scalp tenderness¶	48 (25)	39 (30)	46 (30)	7 (23)
Jaw/lingual claudication¶	50 (26)	39 (30)	49 (32)	10 (33)
Visual symptoms	76 (40)	58 (45)	66 (43)	8 (27)
Sudden visual loss ¶	44 (23)	35 (27)	40 (26)	5 (17)
Blindness	16 (8)	12 (9)	14 (9)	2 (7)
Abnormal examination of TA*¶	89 (47)	81 (63)	85 (55)	6 (20)
Systemic manifestations, n (%)				
Fever	27 (14)	20 (16)	20 (13)	1 (3)
PmR¶	113 (59)	71 (55)	91 (59)	20 (67)
Laboratory				
CRP, mg/dL, median [IQR] ¶	2.5 [0.5-7.7]	4.2 [1.3-9.0]	3.4 [0.7-7.8]	0.6 [0.4-2.2]
ESR 1h, median [IQR]* ¶	52 [29-82]	63 [41-88]	57 [33-84]	29 [10-44]
Hb, mean ±SD	12.4 ± 1.4	12.3 ± 1.4	12.4 ± 1.3	12.6 ± 1.3
* Criteria evaluated in ACR1990				
¶ Criteria evaluated in ACR/EULAR 2022				

Abbreviations: ACR: American College of Rheumatology, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, EULAR: European League Against Rheumatism, FDG-PET: fluorodeoxyglucose positron emission tomography, GCA: giant cell arteritis, Hb: Hemoglobin, PmR: polymyalgia rheumatica, TA: temporal artery, TAB: temporal artery biopsy, US: ultrasound.

Figure. % of patients who met the different classification criteria.



Results: We present 191 patients (120 female/71 male) (mean±SD; 75±10 years). The main characteristics of the patients are shown in **Table**. The Kappa index between both criteria weighted by prevalence and bias was 0.654 (moderate-high degree of agreement). Global agreement of 83% was observed, with a higher specific agreement for negative results (88%) than for positive results (67%). Disagreement was observed in 16% of patients who were considered negative for ACR 1990 criteria but positive for ACR/EULAR 2022 criteria and in 2% who were considered positive for ACR 1990 criteria but negative for ACR/EULAR 2022. 2022 ACR/EULAR showed a higher sensitivity, and 27 additional patients were classified as GCA with these classification criteria.

Conclusion: Moderate-high concordance was found between 2022 ACR/EULAR and 1990 ACR classification criteria. However, the 2022 ACR/EULAR criteria consider a wider range of factors than the 1990 ACR criteria by introducing US and PET findings, thus increasing sensitivity and allowing a larger number of patients to be diagnosed. Cranial GCA was the most frequent phenotype observed.

References:

Ponte C, et al. Arthritis Rheumatol. 2022. PMID: 36350123
Hunder GG, et al. Arthritis Rheum. 1990. PMID: 2202311

Disclosure: J. Sanchez Martin: None; **J. Medina Valle**: None; **J. Loricera**: None; **M. Garcia Reija**: None; **R. Blanco**: AbbVie, 5, 6, Amgen, 6, AstraZeneca, 2, BMS, 6, Eli Lilly, 6, Galapagos, 2, 6, Janssen, 2, 6, MSD, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 5, 6, Sanofi, 6.

Abstract Number: 2424

Exploring the Limit of Image Resolution for Human Expert Classification of Vascular Ultrasound Images in Giant Cell Arteritis and Healthy Subjects: The GCA-US-AI Project

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Giant cell arteritis (GCA) is the most common form of vasculitis in adults, necessitating prompt diagnosis to prevent severe complications. However, access to expert GCA ultrasonography is often limited to larger medical centers. The utilization of artificial intelligence (AI)-based assistance for ultrasound image classification holds significant potential. The development of such AI systems involves selecting a neural network architecture from a wide range of options, each with distinct characteristics, including limitations in processing image size, resolution, result quality, and resource

efficiency. This project aims to address the minimum resolution required for human experts to reliably classify ultrasound images of commonly affected arteries, distinguishing between GCA and normal.

Methods: In this study, a blinded classification task was conducted, involving 42 international experts from the OMERACT subgroup on ultrasound in large vessel vasculitis. A set of 250 vascular ultrasound images from both GCA patients and healthy individuals were presented to the experts. The image selection process initially comprised 10 B-mode scans each of the common temporal artery, its frontal branch, parietal branch, and the axillary artery (all in cross-section), as well as the axillary artery in longitudinal scan. These 50 images were presented in a random order at five distinct resolution levels: 32x32, 64x64, 128x128, 224x224, and 512x512 pixels (refer to Figure 1). The survey and image classification tasks were conducted using REDCap version 13.2.5, while data interim analysis was performed utilizing R (version 4.3.0).

Results: This interim analysis includes data from 30 study group members with an average of 10.5±6.4 years (mean±standard deviation) of experience in ultrasound in GCA. Across all artery categories, the proportion of images considered unclassifiable decreased as the image resolution increased. The mean percentage of unclassifiable images was 91% at 32x32 pixels and reduced to 26% at 512x512pixels (refer to Table 1). Similarly, lower image resolution resulted in less frequent correct classifications (see Figure 2). The chance of correct image classification was comparable at image resolutions of 512x512 pixels (highest resolution level) and 224x224 pixels (odds ratio = 0.99, p=0.891), while it was significantly lower at image sizes of 128x128 pixels (OR=0.79, p=0.01), 64x64 pixels (OR = 0.42, p< 0.001), and 32x32 pixels (OR=0.24, p< 0.001).

Conclusion: As the image resolution increases, the proficiency of human experts in GCA ultrasound improves, enabling more confident and accurate classification of vascular ultrasound images. At a resolution of 224x224 pixels and above, classification accuracy exceeded 50%. The best classification performance was achieved at a resolution of 512x512 pixels

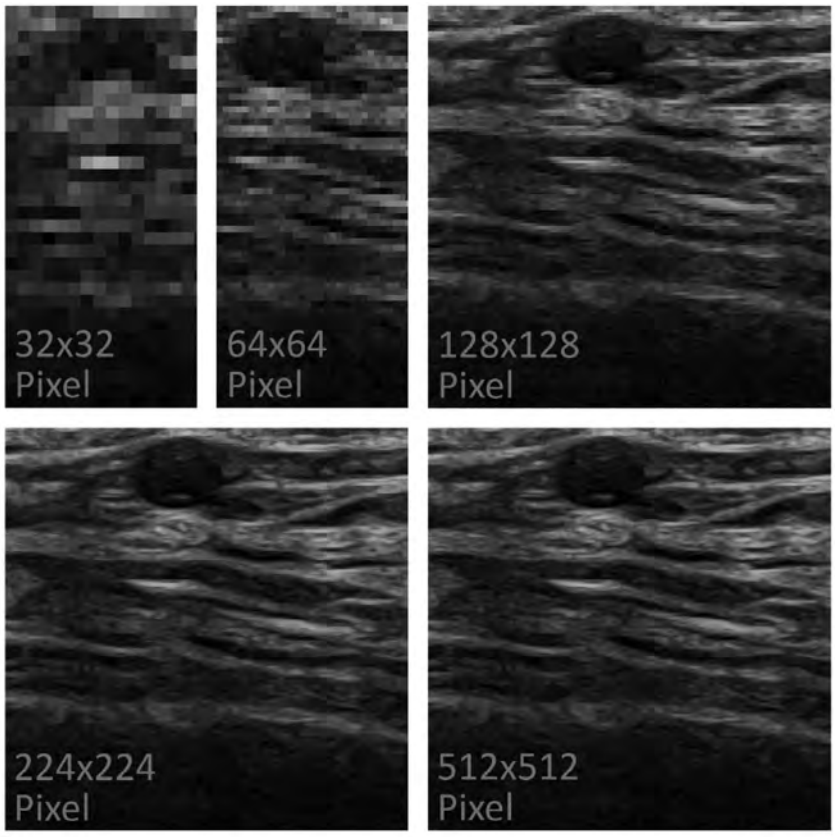

Figure 1: Shown is an exemplary ultrasound image of the common temporal artery (cross-section, B-mode), presented to study participants at five different resolution levels.

Table 1: Frequency of the selected response category "Meaningful classification is not possible" depending on the image resolution level.

Proportion of ultrasound images that were rated as unclassifiable by human experts at different resolution levels

Image resolution (pixels)	Overall		Vessel-specific proportions				
	Total number of images rated as unclassifiable (any vessel)	Proportion of images rated as unclassifiable (any vessel)	Axillary artery (Transverse section)	Axillary artery (Longitudinal section)	Common temporal artery (Transverse section)	Frontal branch (Transverse section)	Parietal branch (Transverse section)
32x32	1365/1500	91.00 %	91.33%	91.33%	88.33%	91.67%	92.33%
64x64	1228/1500	81.87 %	79.33%	84.33%	80.00%	85.00%	80.67%
128x128	835/1500	55.67 %	52.00%	57.00%	55.67%	62.67%	51.00%
224x224	484/1500	32.27 %	28.67%	26.67%	33.00%	42.33%	30.67%
512x512	394/1500	26.27 %	21.67%	19.00%	25.67%	37.67%	27.33%

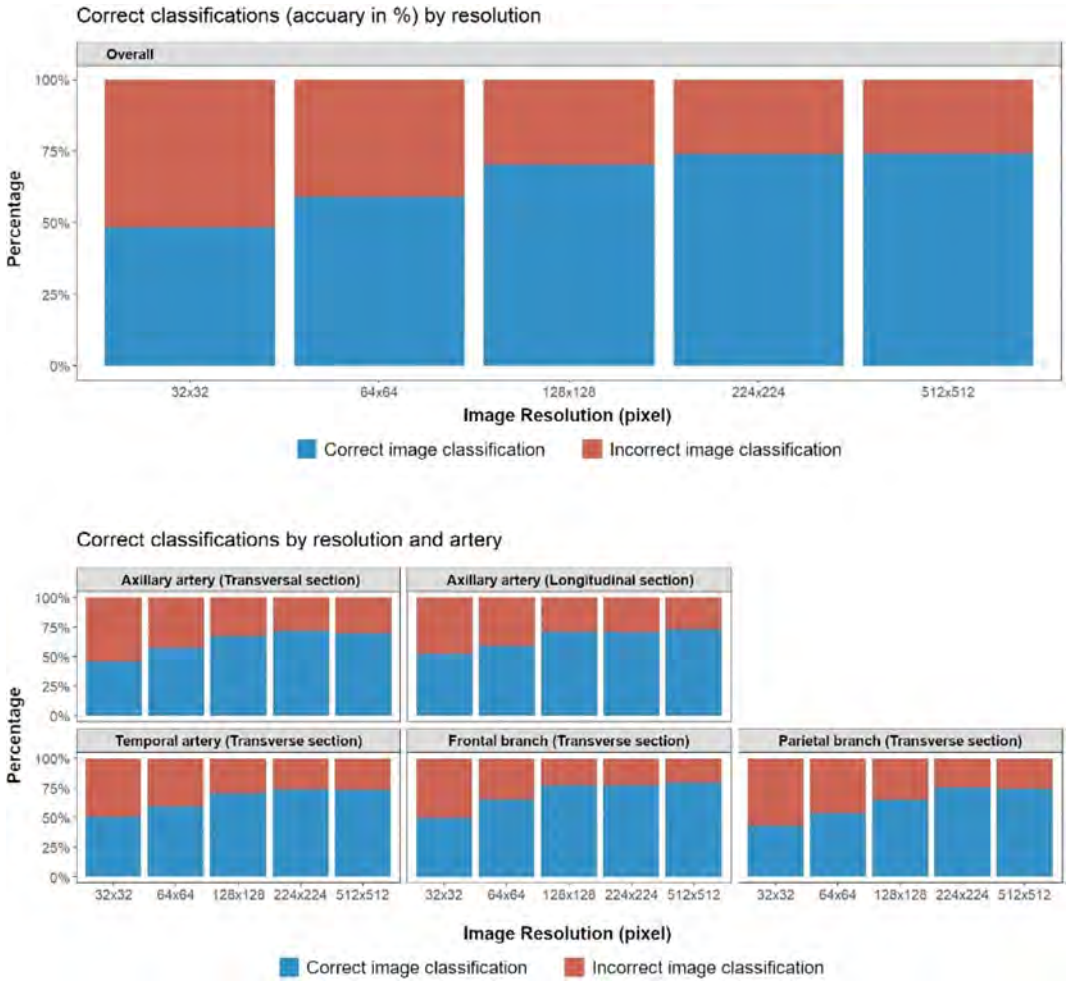

Figure 2: Frequency of correct image classification as "GCA patient" or "healthy individual" depending on image resolution level.

(74.13% of all single-image classifications correct). Yet given the comparable performance at a resolution level of 224x224 pixels (73.93% of all single-image classifications correct), this opens up a variety of perspectives in neural network architecture selection for the development of an AI based assistance for GCA ultrasound image classification.

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Abstract Number: 2425

Pregnancy Outcomes Among Patients with Vasculitis Using Administrative Claims Data

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SESSION INFORMATION
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Background/Purpose: Systemic vasculitides are rare, heterogeneous, inflammatory disorders associated with high morbidity and mortality. Recent management and therapeutic advances have improved life expectancy and reproductive opportunities for vasculitis patients. Research on the risk of preterm delivery and maternal complications in these patients is limited. Therefore, we investigated pregnancy outcomes among patients with vasculitis leveraging large, administrative claims data.

Methods: Using administrative claims data from private health insurance providers we identified all pregnancies regardless of outcome for patients with and without vasculitis from 2007 to 2021. Vasculitis was defined as ≥2 ICD coded outpatient visits or ≥1 ICD coded inpatient visit occurring before the estimated last menstrual period (LMP). Vasculitis was further categorized by vessel size: large, medium, small, and variable based on Chapel Hill Consensus Conference criteria. As a referent population we included those without vasculitis or other rheumatic disease, defined as no ICD coded outpatient or inpatient visits for vasculitis, systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis, or juvenile idiopathic

Table 1. Pregnancy outcomes for patients without vasculitis and with vasculitis stratified by vessel size (2007-2021).

Characteristics	Non-vasculitis (n= 4,209,034)	All vasculitis (n= 665)	Large Vessel[1] (n= 60)	Medium vessel [2] (n= 160)	Small vessel [3] (n= 217)	Variable vessel [4] (n= 250)
Maternal age, median (IQR)[5]	31 (27, 35)	33 (29, 36)	35 (32, 37)	32 (26, 35)	33 (30, 37)	32 (28, 35)
Gestational age in weeks, mean (SD)	39 (16, 39)	38 (13, 42)	39 (11, 39)	38 (11, 41)	37 (11, 41)	39 (35, 39)
Observed time with vasculitis in years, mean (SD)[6]		2 (2.0)	1.8 (1.9)	2.7 (2.5)	1.6 (1.7)	1.9 (1.8)
Pregnancy outcomes						
Livebirth	3,044,907 (72%)	461 (69%)	44 (73%)	107 (67%)	136 (63%)	191 (76%)
Spontaneous abortion	810,512 (19%)	139 (21%)	13 (22%)	38 (24%)	55 (25%)	38 (15%)
Elective termination	191,903 (5%)	41 (6%)	<11	12 (8%)	14 (6%)	14 (6%)
Stillbirth, Mixed birth[7]	27,747 (<1%)	0	0	0	0	0
Ectopic & molar pregnancy	118,683 (3%)	24 (4%)	<11	<11	12 (6%)	<11
Unspecified abortion	15,282 (<1%)	0	0	0	0	0
Preterm delivery[8]	250,124 (6%)	62 (13%)	<11	<11	23 (17%)	28 (15%)

[1]Large vessel size includes Takayasu Arteritis
[2]Medium vessel size includes Polyarteritis Nodosa and Kawasaki Disease
[3]Small vessel size includes anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides, Cryoglobulinemic Vasculitis, IgA Vasculitis, Hypocomplementemic Urticarial Vasculitis, and Primary Angiitis of the central nervous system (PACNS)
[4]Variable vessel size includes Behçet's disease and Cogan's syndrome
[5]Maternal age at delivery
[6]From observed date of Vasculitis diagnosis to estimated last menstrual period (LMP)
[7]Mixed birth is a Multifetal pregnancy resulting in stillbirth and livebirth
[8]Restricted to pregnancies that result in livebirth, mixed birth, or stillbirth
IQR = interquartile range
SD = Standard deviation

arthritis before LMP or during pregnancy. We described pregnancy outcomes in patients with vasculitis compared to the referent population. We also explored pregnancy characteristics and complications in patients with vasculitis stratified by parity (nulliparous vs multiparous).

Results: There were 665 pregnancies among 527 patients with vasculitis and 4,209,034 pregnancies among 2,932,379 patients from the referent population. Patients with vasculitis had a higher frequency of spontaneous abortion, elective termination, ectopic and molar pregnancy, and nearly two times as much preterm delivery compared to the referent population. Approximately 12% of pregnancies among patients with vasculitis were complicated by preeclampsia. Multiparous pregnancies compared to nulliparous had a slightly higher frequency of preterm delivery and were more often comorbid with gestational diabetes, pre-pregnancy hypertension, obesity, and hypothyroidism. Patients with small vessel vasculitis had higher frequencies of spontaneous abortion, preterm delivery, and comorbidities among vasculitis subtypes.

Conclusion: Pregnancies among patients with vasculitis had a higher frequency of spontaneous abortion and preterm delivery. Risk of maternal complications associated with vasculitis were observed to vary by vessel size and parity. These findings further the knowledge base and provide patients with up-to-date statistics on outcomes and complications.

Table 2. Pregnancy characteristics and complications for patients with vasculitis stratified by parity and vessel size (2007-2021).

	All Vasculitis		Large vessel[1]		Medium vessel[2]		Small vessel[3]		Variable vessel[4]	
	Nullip (n=227)	Multip (n=438)	Nullip (n=18)	Multip (n=42)	Nullip (n=42)	Multip (n=118)	Nullip (n=53)	Multip (n=164)	Nullip (n=117)	Multip (n=133)
Pregnancy outcomes[5]										
Livebirth	147 (65%)	314 (72%)	10 (56%)	34 (81%)	31 (74%)	76 (64%)	24 (45%)	112 (68%)	83 (71%)	108 (81%)
Spontaneous abortion	59 (26%)	80 (18%)	8 (44%)	<11	<11	30 (25%)	21 (40%)	34 (21%)	24 (21%)	14 (11%)
Elective termination	11 (5%)	30 (7%)	0	<11	<11	<11	<11	13 (8%)	<11	<11
Maternal complications/features										
Cesarean section[6]	60 (41%)	130 (41%)	<11	16 (47%)	11 (36%)	24 (32%)	<11	51 (46%)	36 (43%)	49 (45%)
Preeclampsia/ Eclampsia[6]	19 (13%)	38 (12%)	<11	<11	<11	15 (20%)	<11	16 (14%)	<11	<11
Preterm delivery[6]	19 (13%)	43 (14%)	<11	<11	<11	<11	<11	18 (16%)	11 (13%)	17 (16%)
Spontaneous	15 (79%)	29 (67%)	0	<11	<11	<11	<11	11 (61%)	<11	15 (88%)
Medically indicated	<11	14 (33%)	<11	<11	0	<11	0	<11	<11	<11
Multifetal gestation	<11	22 (5%)	0	<11	<11	10 (9%)	<11	<11	<11	<11
Gestational diabetes	13 (6%)	49 (11%)	<11	<11	<11	12 (10%)	<11	21 (13%)	<11	15 (11%)
Gestational hypertension	<11	<11	0	0	<11	<11	0	<11	<11	<11
Prior preeclampsia		30 (7%)		<11		16 (14%)		13 (8%)		<11
Pre-pregnancy comorbidities										
Hypertension	30 (13%)	102 (23%)	<11	13 (31%)	<11	36 (31%)	<11	55 (34%)	<11	12 (9%)
Diabetes (type 1 & 2)	<11	11 (3%)	0	0	<11	<11	<11	<11	<11	<11
Renal disease	11 (5%)	16 (4%)	0	<11	<11	<11	<11	11 (7%)	0	0
Obesity (BMI > 30 kg/m^2)	<11	79 (18%)	0	<11	0	18 (15%)	0	49 (30%)	<11	11 (8%)

[1]Large vessel size includes Takayasu Arteritis
[2]Medium vessel size includes Polyarteritis Nodosa and Kawasaki Disease
[3]Small vessel size includes anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitides, Cryoglobulinemic Vasculitis, IgA Vasculitis, Hypocomplementemic Urticarial Vasculitis, and Primary Angiitis of the central nervous system (PACNS)
[4]Variable vessel size includes Behçet's disease and Cogan's syndrome
[5]There were no stillbirths or mixed births and there were very few molar and ectopic pregnancies
[6]Restricted to pregnancies that result in livebirth, mixed birth, or stillbirth
Nullip=nulliparous (pregnancies with no prior birthing history), Multip=multiparous (pregnancies with prior birthing history)

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Abstract Number: 2426

The Role of β-catenin in Synovial Lining Fibroblast Differentiation

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SESSION INFORMATION
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Session Time: 11:00AM–12:30PM

Background/Purpose: In healthy synovium, lining fibroblasts promote joint health by secreting proteoglycans that lubricate the joint cavity. In rheumatoid arthritis (RA), sublining fibroblasts undergo marked expansion while lining fibroblasts are relatively diminished[1–4]. We have previously demonstrated the role of vascular endothelial-derived Notch signaling as a driver of

perivascular sublining fibroblast differentiation[4]. Here, we seek to identify the transcriptional regulators of synovial lining fibroblast differentiation using synovial patient-derived organoids.

Methods: We developed two 3D tissue culture approaches to study fibroblast differentiation. First, we developed patient-derived organoids from synovial tissue explants that maintain fibroblast heterogeneity ex vivo. We leveraged an in vitro micromass system[5] to examine the stability and reversibility of fibroblast differentiation. Fibroblast differentiation in organoids were examined via confocal microscopy, histology, and single-cell RNA sequencing (scRNAseq). A targeted transcription factor screen was performed using siRNA and CRISPR gene-editing to identify candidate transcription factors driving fibroblast differentiation.

Results: Addition of a GSK3 inhibitor leads to compaction within patient-derived organoids, resembling a synovial lining-like layer **(Fig 1A-B)**. We identified cadherin-23 (CDH23), an atypical cadherin, as a novel cadherin that is specific to lining fibroblasts **(Fig 1C)**. Inhibition of GSK3 results in profound changes in gene expression, including upregulation of CDH23 and other lining fibroblast marker genes **(Fig 1E)**. This GSK3i-induced gene expression program is reversible suggesting active signaling is required to maintain this phenotype **(Fig 1F-G)**. We performed a targeted screen against transcription factors that are induced by GSK3 inhibition. This screen identified β-catenin as a necessary factor for mediating key transcriptional changes consistent with a lining-like phenotype in synovial fibroblasts **(Fig 2A)**. Consistent with β-catenin's potential role as a co-transcription factor, we observed increased β-catenin expression and nuclear localization in GSK3i-treated fibroblasts **(Fig 2B-C)**.

Conclusion: Inhibition of GSK3 induces a reversible lining-like phenotype in synovial fibroblasts. β-catenin is necessary for upregulation of lining fibroblast marker genes in the context of GSK3 inhibition. Further work is required to confirm direct transcriptional effects of β-catenin on synovial fibroblasts and upstream mechanisms. Understanding the mechanism underlying fibroblast differentiation could lead to identification of novel therapeutic targets for restoring synovial lining function in RA patients.

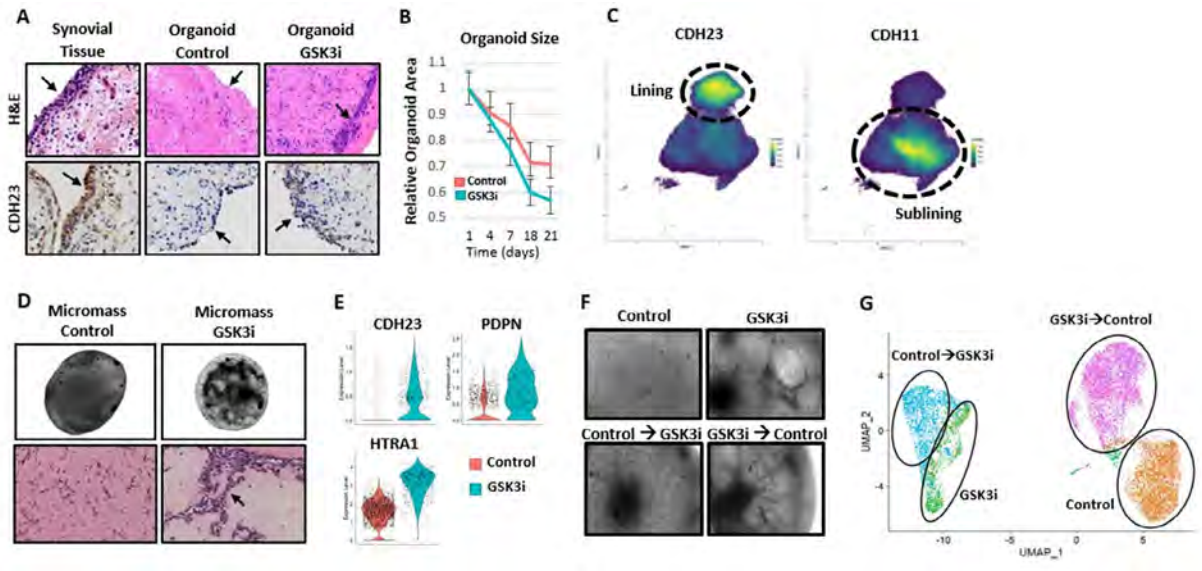

Figure 1: Synovial lining-like phenotype recapitulated in 3D culture. (A) IHC staining of synovial organoids displaying compaction and upregulation of CDH23 when treated with GSK3i, which resembles synovial lining. (B) Organoid size decreases more drastically when exposed to GSK3i indicating a compaction phenotype (C) Density plot of CDH23 and CDH11 mRNA expression in synovial fibroblasts from the Accelerating Medicines Partnership scRNAseq dataset (D) Micromass generated from synovial fibroblasts. (E) RNA expression of lining marker genes upregulated by GSK3 inhibition. (F) Live imaging of micromass that were either grown in control media, exposed to GSK3i, exposed to GSK3i after initially grown in control media, or grown in control media after initially exposed to GSK3i. (G) UMAP depicting scRNAseq data on micromass fibroblasts showing partial reversibility of GSK3i-induced transcriptional profile.

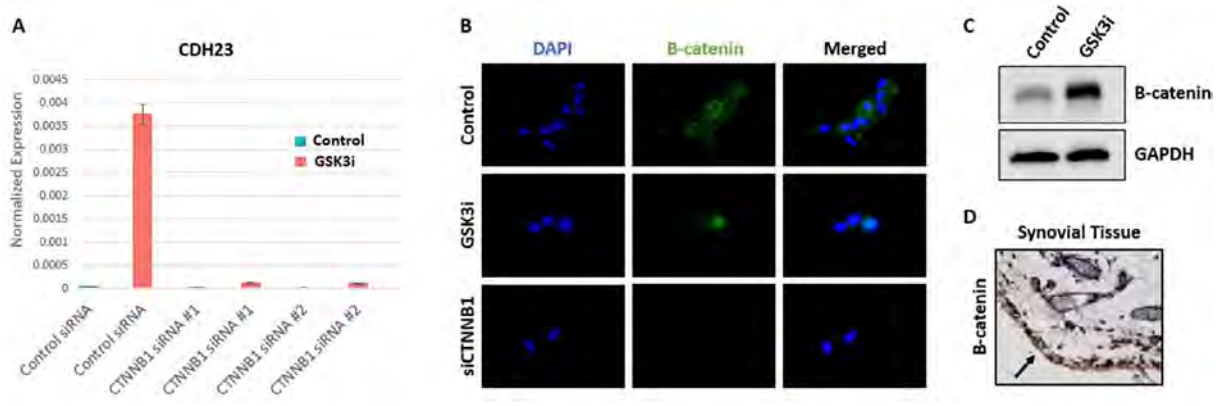

Figure 2: β-catenin is necessary for lining-like transcriptional changes in the context of GSK3 inhibition. (A) Normalized mRNA expression of CDH23 with siRNA knockdown against CTNNB1, which encodes β-catenin. (B) Immunofluorescent images of β-catenin (green) in synovial fibroblasts treated with either a GSK3 inhibitor or CTNNB1 siRNA. (C) Western blot showing upregulation of β-catenin in synovial fibroblasts treated with GSK3i. (D) High expression of β-catenin detected in synovial lining.

1. F. Mizoguchi et al., Nat. Commun.9, 789 (2018).
2. F. Zhang et al., Nat. Immunol.20, 928–942 (2019).
3. A. P. Croft et al., Nature. 570, 246–251 (2019).
4. K. Wei et al., Nature. 582, 259–264 (2020).
5. H. P. Kiener et al., Arthritis Rheum.62, 742–752 (2010).

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Degranulating PR3+ Myeloid Cells Characterize Proliferative Lupus Nephritis

Alessandra Ida Celia[1], Xiaoping Yang[2], Hana Minsky[2], Silvia Malvica[2], Michelle Petri[3], the Accelerating Medicines Partnership in RA/SLE[4], Avi Rosenberg[5] and Andrea Fava[2], [1]John Hopkins University of Medicine, Rome, Italy, [2]Johns Hopkins University, Baltimore, MD, [3]Department of Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Timonium, MD, [4]Multiple, Multiple, [5]Department of Pathology, The Johns Hopkins University School of Medicine, Baltimore, MD

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Background/Purpose: As part of the Accelerating Medicines Partnership (AMP), we discovered that urinary PR3, a neutrophil degranulation product, is associated with histological activity, indicating the involvement of neutrophil degranulation in proliferative LN, the most aggressive type of LN. Although mature neutrophils with classical polylobate nuclei are rare in LN kidney biopsies, recent evidence suggests that immature myeloid cells undergoing degranulation play a role in the

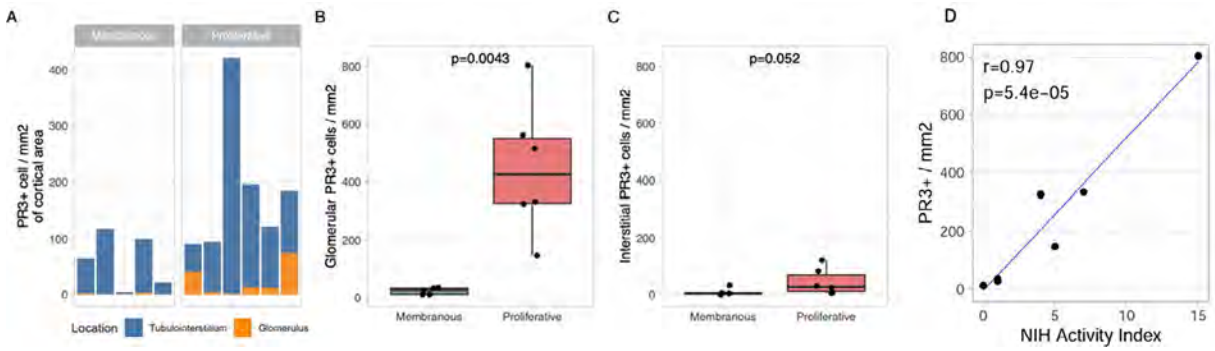

Figure1. Clinicopathological associations of intrarenal PR3+ cells. The majority of PR3+ cells were in the tubulointersitium (A). However, accounting for the smaller glomerular area, there was a higher density of PR3+ cells in the glomeruli (B-C). PR3+ cell abundance was higher in proliferative LN, especially in the glomeruli (A-C). Glomerular PR3+ cell density very strongly correlated with histological activity measured by the NIH Activity Index (Pearson's r=0.97, p=5*10-5; panel D. The analysis was limited to renal cortex.

pathogenesis of LN. Our aim is to investigate the presence of PR3+ cells in LN kidney, their association with histopathological features and to define their immunophenotype.

Methods: We performed multiplexed histology using serial immunohistochemistry (sIHC) on LN kidney biopsies to quantify the expression of PR3 and multiple cell lineage markers (20-plex). Image analysis including deconvolution, cell segmentation, glomerular annotation, and quantitative histology was performed using Indica HALO. The analysis was limited to renal cortex.

Results: A total of 11 patients with LN who underwent a clinically indicated kidney biopsy were enrolled: 6 (55%) with pure proliferative LN (ISN/RPS class III or IV) and 5 (45%) with pure membranous LN. PR3+ cells were identified in all biopsies (range 343-7625 per sample) and most of them did not show a polylobate nucleus. The majority of PR3+ cells were in the tubulointersitium **(Figure 1A).** However, when present, there was a higher density of PR3+ cells in the glomeruli due to their smaller area**(Figure 1A-C)**. PR3+ cell abundance was higher in proliferative LN, especially in the glomeruli **(Figure 1A-C)**. Glomerular PR3+ cell density very strongly correlated with histological activity measured by the NIH Activity Index (Pearson's r=0.97, $p=5*10^{-5}$; **Figure 1D)**. PR3+ cells displayed a unilobate nucleus (**Figure 2**). Most PR3+ cells coexpressed MPO. We identified 2 subsets of PR3+ cells based the coexpression of other lineage markers **(Figures 2 and 3**).

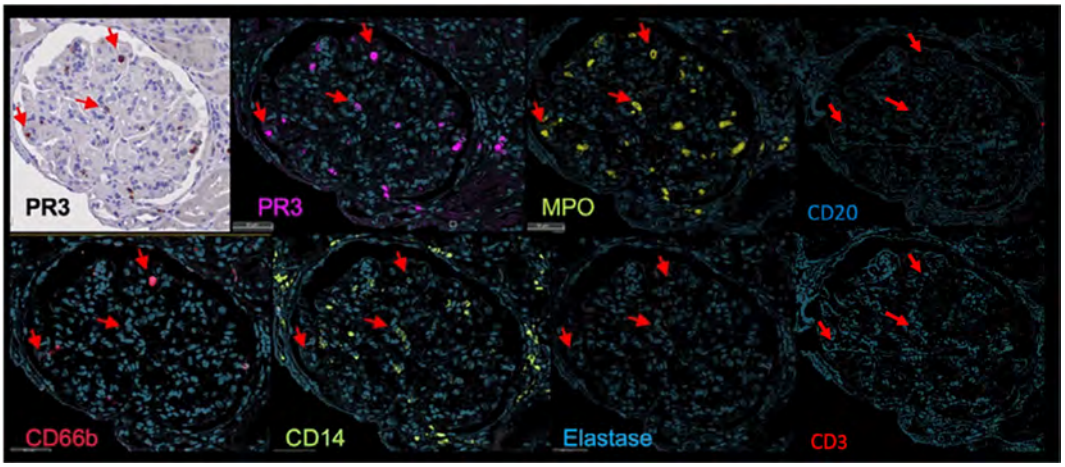

Figure2. Surface markers expression in PR3+ cells. The original and deconvoluted IHC images are shown for a representative glomerulus, with arrows indicating three identical representative cells. Markers indicated at the bottom with matching false colors.

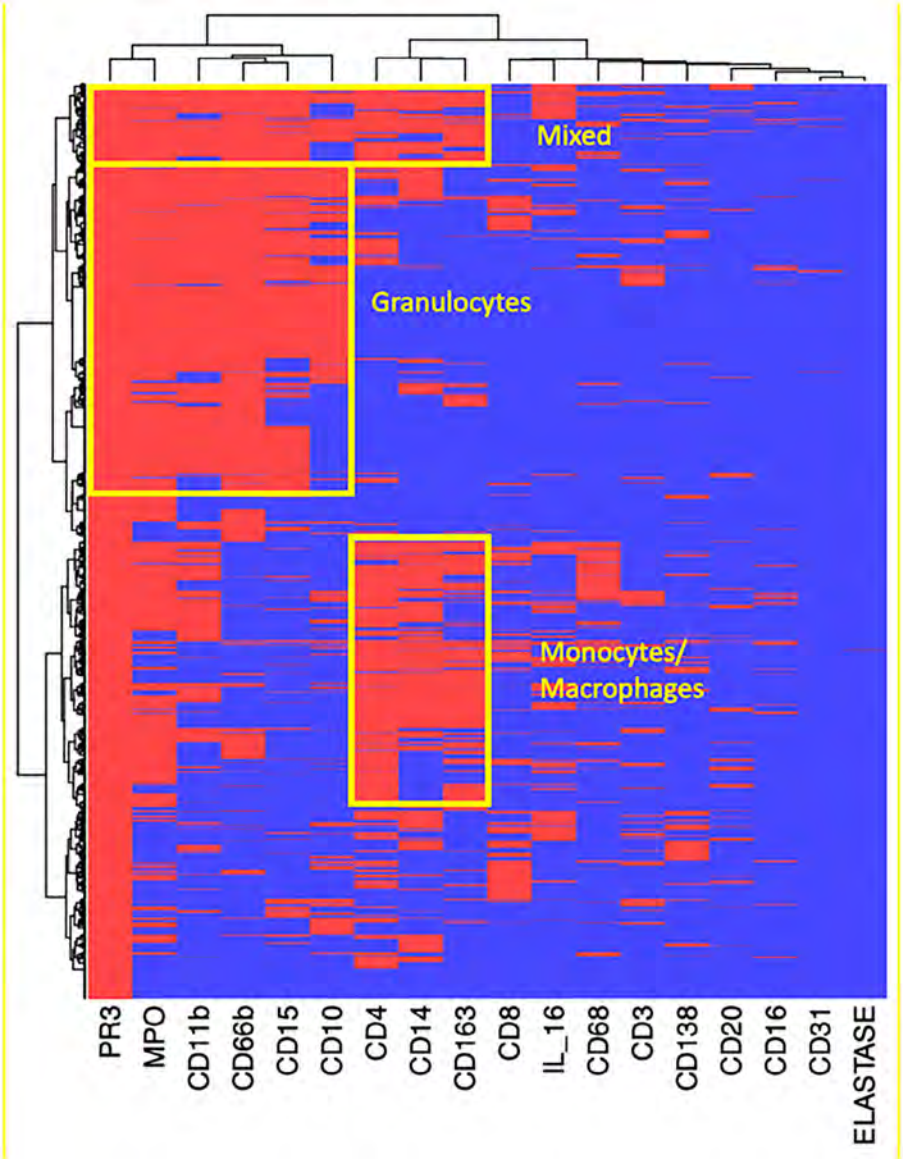

Figure3. Cell phenotypes Heatmaps displays the heterogeneity of marker coexpression at the single cell level fo PR3+ cells. Three distinct subsets of PR3+ cells infiltrating the kidney were identified. Data from one representative kidney biopsy (class IV lupus nephritis, NIH Activity Index 8/24, Chronicity Index 6/12).

One group coexpressed CD66b, CD11b, CD15, and (variably) CD10 indicating a degranulating phenotype (**Figure 3**). The other group expressed CD14, CD163, and CD4 indicating a phagocytic phenotype **(Figure 3).** The was a smaller subset with features of both groups.

Conclusion: PR3+ cells are abundant in LN, increased in proliferative LN and are strongly associated with histological activity thereby characterizing a more aggressive phenotype. This population densely infiltrated the glomeruli emphasizing a potential role in the endothelial pathogenic process. There were two subsets of kidney-infiltrating PR3+ cells characterized by a phagocytic or a degranulating phenotype; both were mononucleated suggesting a monocyte or nonsegmented neutrophil lineage. We previously showed the association between urinary PR3 and histological activity suggesting that intrarenal PR3+ cells are actively degranulating and therefore likely inducing kidney damage. These findings nominate PR3+ cells as a potential therapeutic target. Spatial transcriptomics and proteomic studies are ongoing to define the lineage and function of these cells.

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Abstract Number: 2428

Unclosing Premature Mortality Gap Among Gout Patients in the US General Population, Independent of Serum Urate and Atherosclerotic Cardiovascular Risk Factors

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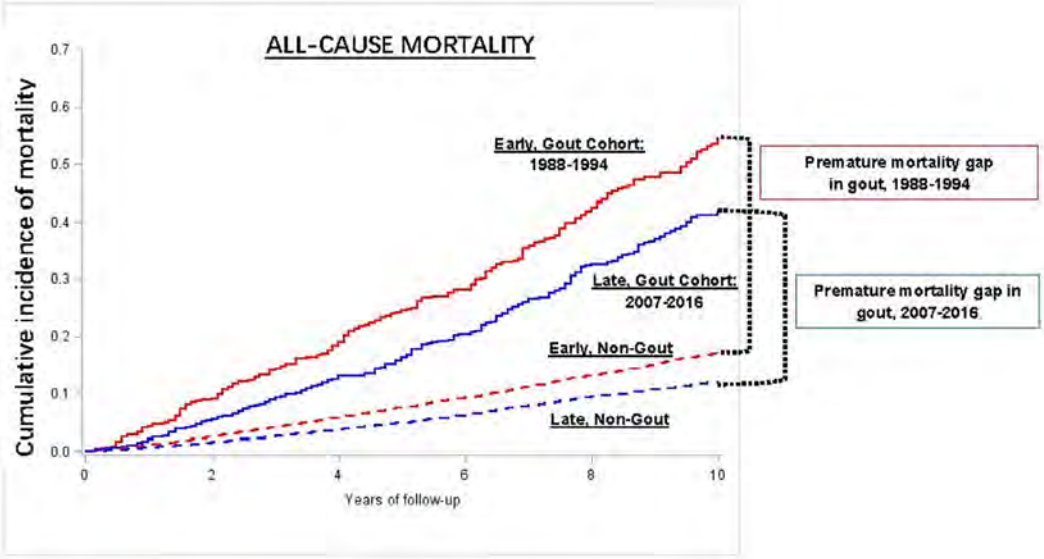
Background/Purpose: A recent UK study reported a transient increased cardiovascular risk after gout flare episodes [Cipolletta et al. *JAMA* 2022], which may translate to premature mortality for gout patients over the long term. Prior studies reported premature mortality in gout; however, it is unknown whether this mortality gap has improved over recent years at a national level.We prospectively evaluated the association between gout and the risk of all-cause and cardiovascular (CVD) mortality fully adjusting for serum urate (SU) and atherosclerotic cardiovascular disease (ASCVD) risk factors in the latest US general population data (as well as the UK).

Methods: Using nationally representative samples of US adults in the National Health and Nutrition Examination Survey (NHANES), linked prospectively with vital statistics data, we examined the independent association of prevalent gout with mortality risk and compared Early (NHANES III: 1988-1994 baseline) and Late cohorts (2007-2016 baseline), as well as key demographic subgroups defined by sex and self-reported race/ethnicity (Black vs. White).Hazard ratios (HRs) were calculated over 10 years adjusting for SU, ASCVD risk factors, cardiometabolic comorbidities, kidney function, and relevant medications. We replicated the Late cohort findings among incident gout in a nationwide UK cohort (2006-2010 baseline).

Results: US adults with gout had higher 10-year all-cause mortality rates than those without gout, in both the Early and Late cohorts, with similar magnitudes of excess mortality (**Figure**) and adjusted hazard ratios (HR) between the two cohorts (HR, 1.20; 1.03–1.40 and 1.19; 1.04–1.37, respectively; p for gout*time interaction=0.69).HRs changed minimally with further adjustment for SU (HR, 1.19; 1.02–1.38 and 1.19; 1.03–1.37, respectively) (**Table 1**).Late cohort findings were replicated among incident gout in the UK (adjusted HR, 1.61; 1.47–1.75).In both countries, associations were larger among women than men (HR 1.32 (1.10 to 1.58) in US and 1.90 (1.55 to 2.32) in UK; p for interaction=0.04) and prominent among Black individuals (**Table 2**).



Cumulative incidence of all-cause mortality by time period and gout status in the nationwide US cohort. Solid red line=Gout, Early Cohort (1988-1994), Dashed red line=Non-Gout, Early Cohort (1988-1994), Solid blue line=Gout, Late Cohort (2007-2016), Dashed blue line=Non-Gout, Late Cohort (2007-2016). The premature mortality gap in gout (difference between the solid and dashed lines) did not improve between the Early and Late cohorts.

Adjusted HR for cardiovascular mortality in the late US cohort was 1.39 (1.09–1.78); those for circulatory, cardiovascular, and coronary heart disease deaths among Britons with incident gout were 1.48 (1.24–1.76), 1.49 (1.20–1.85) and 1.59 (1.26–1.99), respectively.

Conclusion: Premature mortality in gout (beyond SU and ASCVD risk factors) has not improved over time in the US at a national level, despite improved survival in the general population, and is worse among women and possibly among Black individuals, among whom gout is already more prevalent compared to White individuals [PMID 35969396].Mortality gap was replicated among incident gout patients in the UK. This unclosing premature mortality gap suggests shortcomings in current gout care, particularly among women and possibly among Black patients and a potential role for targeted anti-inflammatory therapies such as daily colchicine for dual purposes of gout and CVD prevention, as is promoted in CVD prevention in European and Canadian cardiology guidelines.

Table 1. Association between prevalent gout and all-cause mortality according to Early and Late nationwide US cohorts.

	All		Early Cohort (NHANES III: 1988-1994 baseline)		Late Cohort (NHANES 2007–2016 baseline)		P for interaction
	Gout	Non-gout	Gout	Non-gout	Gout	Non-gout	
No. of deaths	439	4127	192	2418	247	1709	-
Person-years	10,060	293,432	3590	142,552	6470	150,881	-
Model 1	1.37 (1.24 to 1.52)	1.00 (ref)	1.31 (1.13 to 1.52)	1.00 (ref)	1.43 (1.25 to 1.64)	1.00 (ref)	0.30
Model 2	1.29 (1.16 to 1.42)	1.00 (ref)	1.25 (1.08 to 1.46)	1.00 (ref)	1.30 (1.13 to 1.50)	1.00 (ref)	0.42
Model 3	1.20 (1.08 to 1.33)	1.00 (ref)	1.20 (1.03 to 1.40)	1.00 (ref)	1.19 (1.04 to 1.37)	1.00 (ref)	0.69
Model 3 + SU	1.19 (1.08 to 1.32)	1.00 (ref)	1.19 (1.02 to 1.38)	1.00 (ref)	1.19 (1.03 to 1.37)	1.00 (ref)	0.63

Model 1 was adjusted for age (time scale), sex (male or female), race/ethnicity (White, Black, Hispanic, or Other), and NHANES cycle (III, 2007-2008, 2009-2010, 2011-2012, 2013-2014, or 2015-2016).
Model 2 was further adjusted for body mass index, education (some high school or lower, high school, college, graduate school or higher, or missing), smoking (former, current, never, or missing), alcohol consumption (times/month), and total cholesterol, HDL, systolic BP, diastolic BP (continuous), diuretic use, statin use, aspirin use, prescription use for hypertension, and for women, post-menopausal status (yes, no, or missing).
Model 3 was further adjusted for coronary heart disease (yes or no), diabetes (yes or no), and estimated glomerular filtration rate (continuous).
SU = serum urate

Table 2. Association between prevalent gout and all-cause mortality according to demographic subgroups, nationwide US and UK cohorts. * Adjusted for age, sex, race, NHANES cycle/year of enrolment, body mass index, education, smoking status, alcohol intake, total cholesterol, HDL, systolic and diastolic blood pressure (continuous), aspirin, diuretic, statin, and anti-hypertensive medication use, post-menopausal status (women), heart disease, diabetes, and estimated glomerular filtration rate (continuous)

UNITED STATES					
Sex	**Female**		**Male**		**P for interaction**
	Gout	**Non-gout**	**Gout**	**Non-gout**	
No. of deaths	137	1844	302	2283	-
Person-years	2944	157490	7116	135942	-
Adjusted HR*	1.33 (1.11 to 1.60)	1.00 (ref)	1.13 (1.00 to 1.28)	1.00 (ref)	0.03
+ serum urate adjusted HR	1.32 (1.10 to 1.58)	1.00 (ref)	1.13 (1.00 to 1.28)	1.00 (ref)	0.04
Race	**Black**		**White**		**P for interaction**
	Gout	**Non-gout**	**Gout**	**Non-gout**	
No. of deaths	106	799	290	2498	-
Person-years	2437	67469	5701	123247	-
Adjusted HR*	1.40 (1.12 to 1.74)	1.00 (ref)	1.13 (1.00 to 1.28)	1.00 (ref)	0.18
+ serum urate adjusted HR	1.36 (1.09 to 1.70)	1.00 (ref)	1.13 (1.00 to 1.29)	1.00 (ref)	0.22
UNITED KINGDOM					
Sex	**Female**		**Male**		**P for interaction**
	Gout	**Non-gout**	**Gout**	**Non-gout**	
No. of deaths	229	420	804	2113	-
Person-years	10,458	54,091	36,396	176,751	-
Adjusted HR*	1.96 (1.63 to 2.36)	1.00 (ref)	1.61 (1.47 to 1.75)	1.00 (ref)	0.03
+ serum urate adjusted HR	1.90 (1.55 to 2.32)	1.00 (ref)	1.55 (1.41 to 1.71)	1.00 (ref)	0.04
Race	**Black**		**White**		**P for interaction**
	Gout	**Non-gout**	**Gout**	**Non-gout**	
No. of deaths	20	25	983	2449	-
Person-years	639	2745	44,385	220,422	-
Adjusted HR*	2.79 (1.38 to 5.63)	1.00 (ref)	1.66 (1.53 to 1.79)	1.00 (ref)	0.12
+ serum urate adjusted HR	2.18 (1.00 to 4.78)	1.00 (ref)	1.60 (1.46 to 1.75)	1.00 (ref)	0.12

* Adjusted for age, sex, race, NHANES cycle/year of enrolment, body mass index, education, smoking status, alcohol intake, total cholesterol, HDL, systolic and diastolic blood pressure (continuous), aspirin, diuretic, statin, and anti-hypertensive medication use, post-menopausal status (women), heart disease, diabetes, and estimated glomerular filtration rate (continuous)

Disclosure: N. McCormick: None; **K. Lin**: None; **C. Yokose**: None; **N. Lu**: None; **Y. Zhang**: None; **H. Choi**: Ani, 2, Horizon, 2, 5, LG, 2, Protalix, 2, Shanton, 2.

Abstract Number: 2429

Romosozumab versus Denosumab in High-risk Patients Treated with Glucocorticoids: Interim 12-month Results from a Pilot Randomized Controlled Trial

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Plenary III
Session Type: Plenary Session
Session Time: 11:00AM–12:30PM

Background/Purpose: To compare the efficacy and safety of romozosumab (ROMO) and denosumab (DEN) in high-risk patients treated with glucocorticoids (GCs).

Methods: Adult patients (≥18 years) who were receiving prednisolone ≥5mg/day for ≥12 months and had moderate/high risk of osteoporotic fracture (history of fracture, DEXA T score ≤-2.5 [age ≥40 years] or Z scores ≤-3.0 [age < 40 years] or high 10-year major fracture risk by FRAX) were included. Participants were randomized to receive either ROMO (210mg SC monthly) or DEN (60mg SC every 6 months) for 12 months, followed by DEN for 2 more 6-month doses in both arms. The primary efficacy end point was the change in bone mineral density (BMD) at the lumbar spine from baseline to month 12.Secondary end points included BMD change at the non-dominant hip and femoral neck at month 12, change in bone turnover markers, new vertebral fractures, change in BMD at the hip and spine at month 24 and adverse events (AEs).

Results: 70 patients were recruited and 63(90%) completed the study (age 62.6±9.1 years; 96% women; 35 each assigned to ROMO or DEN).The mean prednisolone dose at entry was 6.6±3.5mg/day. Osteoporosis at spine/hip/femoral neck and a history of fragility fracture was present in 34(48.6%) and 35(50%) patients, respectively. Oral bisphosphonates were being used in 33(47%) patients prior to first dose of the study drugs. While the baseline demographics and osteoporosis risk factors were not significantly different between the two groups, ROMO-treated patients had lower hip/femoral neck BMD and serum vitamin D3 levels than those treated with DEN. At month 12, a significant increase in spine BMD was observed in both the ROMO (+7.3±4.5%; p< 0.001) and DEN (+2.3±3.1%; p< 0.001) groups of patients. The inter-group difference in spine BMD at month 12 was statistically significant after adjustment for baseline BMD values, age, sex, osteoporosis risk factors and the cumulative prednisolone doses in 12 months (p < 0.001).The corresponding increase in hip BMD were +1.6% ±3.3% (p=0.01) in the ROMO group and +1.6%±2.6% (p=0.003) in the DEN group. No significant inter-group difference in hip BMD was observed after adjustment for the same factors. The increase in femoral neck BMD from baseline to 12m was not significant in both groups. In DEN-treated patients, both serum CTX (-34.7±54.8%; p=0.002) and P1NP (-35.1 ±43.3%; p< 0.001) dropped significantly from baseline to 12m.However, in the ROMO group, a non-significant drop in CTX (-18.1±76.9%; p=0.18) but increase in P1NP (+1.7±70.3%; p=0.89) was observed. Only one new vertebral fracture developed in the ROMO group at 12m.The commonest AE was self-limiting injection site pain/redness, which was significantly more common in ROMO-treated patients. Post-injection musculoskeletal pain was reported in 2 and 3 patients in the ROMO and DEN group of patients, respectively. Mild hypocalcemia and hypercalcemia were observed in 2 DEN-treated patients. No serious AEs were reported. Complete 24-month data are pending in September 2023.

Conclusion: Romosozumab was superior to denosumab in raising the spine BMD at month 12 in chronic GC users with high fracture risk. Romosozumab may offer a new treatment option for GIOP in high-risk patients.

Disclosure: C. Mok: None; **S. TSE**: None; **K. Chan**: None; **W. Ma**: None.

Abstract Number: 2430

Time-Dependent Evaluation of Weighted Cumulative Glucocorticoid Exposure and Major Adverse Cardiovascular Events in a Cohort of Veterans with Rheumatoid Arthritis

Beth Wallace[1], Yuqing Gao[2], H. Myra Kim[1], Bryant England[3], Joshua Baker[4], Brian Sauer[5], Grant Cannon[6], Punyasha Roul[3], Ted R Mikuls[7], Shirley Cohen-Mekelburg[1], Daniel Clauw[8], Wyndy Wiitala[2], Rodney Hayward[1], Jeremy Sussman[1] and Akbar Waljee[9], [1]VA Ann Arbor; University of Michigan, Ann Arbor, MI, [2]VA Ann Arbor, Ann Arbor, MI, [3]University of Nebraska Medical Center, Omaha, NE, [4]University of Pennsylvania, Philadelphia, PA, [5]Salt Lake City VA/University of Utah, Salt Lake City, UT, [6]University of Utah and Salt Lake City VA, Salt Lake City, UT, [7]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE, [8]Department of Anesthesiology, University of Michigan, Ann Arbor, MI, [9]VA Ann Arbor, University of Michigan, Ann Arbor, MI

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Plenary III

Session Type: Plenary Session

Session Time: 11:00AM–12:30PM

Background/Purpose: Three-quarters of RA patients use glucocorticoids (GC) to manage RA symptoms. Prior work suggests recent GC use is associated with major adverse cardiovascular events (MACE) in RA, but these studies did not adequately consider the effect of prior GC exposure on current risk.

Methods: In this retrospective cohort study, we used national VA administrative data to identify RA patients with an initial VA rheumatology visit in 2010-2018 (index date) and a one-year lookback period prior to this. Exclusions included age < 40 or >90, non-RA rheumatologic disorder, prior MACE, or CHF. We used a Cox proportional hazards model to estimate the

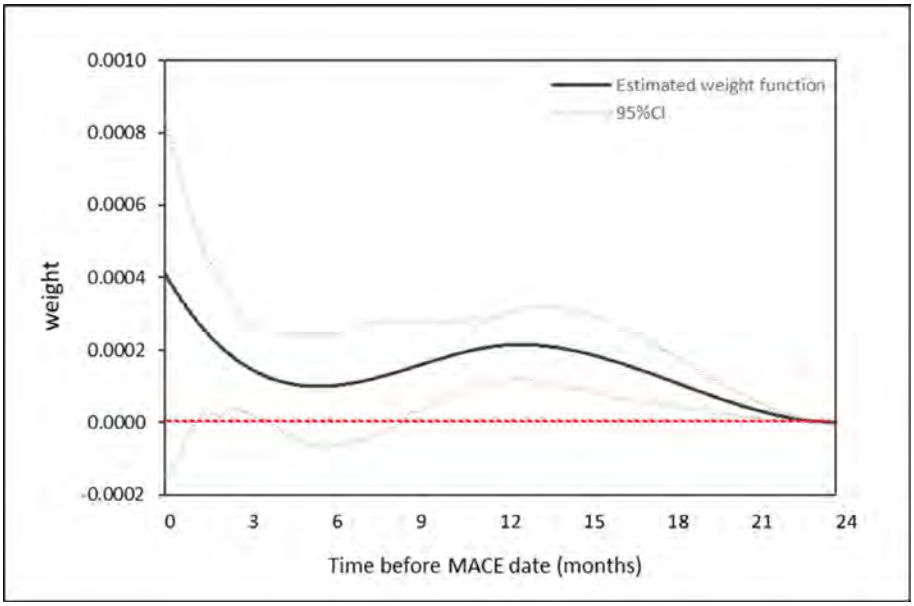

Table 1: Baseline characteristics by 5-year risk of major adverse cardiovascular events (MACE). Values are median and interquartile range (IQR) unless specified otherwise.

	Overall cohort (N= 18,882)	Low VARS (N= 4,675)	Medium VARS (N= 10,453)	High VARS (N= 3,754)
Age in years, mean (SD)	62.5 (10.0)	52.2 (6.8)	63.4 (7.1)	72.8 (8.1)
Male, N (%)	15,775 (84%)	2,357 (50%)	9,759 (93%)	3,659 (97%)
Years of follow-up	4.8 (2.8 - 7.3)	4.7 (2.8 - 7.2)	4.9 (2.9 - 7.4)	4.4(2.5 - 7.0)
Adjusted Elixhauser count[2]	2 (1 - 3)	2 (1 - 3)	2 (1 - 3)	2 (1 - 3)
Office visits/past year	9 (5 - 16)	10 (5 - 18)	9 (5 - 16)	9 (5 - 17)
Rheumatology visits/past year	3 (2 - 5)	3 (2 - 5)	3 (2 - 5)	3 (2 - 5)
Outpatient prescriptions/past year	9 (5 - 14)	8 (5 - 14)	9 (5 - 14)	10 (6 -14)
MTX use/past year, N(%)	7,018 (37.2%)	1,668 (35.7%)	3,947 (37.8%)	1,403 (37.4%)
bDMARD use/past year (y/n), N (%)	2,463 (13.0%)	648 (13.9%)	1,383 (13.2%)	432 (11.5%)
5-year MACE risk[3]	5.3% (3.0%-8.1%)	1.7% (1.0%-2.4%)	5.5% (4.2% - 7.0%)	11.4% (10.1%-13.6%)
≥1 MACE during study period, N(%)	766 (4.1%)	66 (1.4%)	436 (4.2%)	264 (7.0%)

[1]Veterans' Affairs Risk Score for Cardiovascular Disease (VARS-CV) score <3%, 3-9%, and >9%, respectively

[2]Excluding RA, diabetes, hypertension, congestive heart failure which were inclusion/exclusion criteria or part of VARS-CV score

[3]Estimated using VARS-CV score

effect of time-varying cumulative weighted oral GC use (primary exposure) on risk of MACE defined as MI, stroke/TIA, cardiac arrest, coronary revascularization, or death from CV cause (primary outcome). We estimated the primary exposure using a weighted cumulative dose (WCD) model representing GC exposure as a weighted sum of past doses (Sylvestre et al, 2009). Weights estimated using cubic regression splines reflect the relative impact of GC exposure at different times. Since the time period over which prior GC exposure affects MACE risk is not well defined, we fit potential WCD models evaluating exposure over the 30 days, 90 days, 180 days, 1 year, 2 years, and 3 years prior to MACE. The best-fitting model, using a 2-year exposure window prior to MACE, was selected (**Fig 1**).

Results: Among 18,882 patients (mean age 62.5 years, 84% male), median 5-year MACE risk at baseline was 5.3%; 3,754 patients (19.9%) had high baseline MACE risk (**Table 1**). Incident MACE occurred in 4.1% of patients, with median time to MACE of 2.67 (IQR 1.26-4.45) years. **Table 2** shows adjusted hazard ratios (aHRs) for several temporal patterns of GC exposure compared to no use for the 2 years prior to MACE. Using 5mg, 7.5mg, and 10mg/day prednisone equivalent for 90 days prior to MACE is associated with a 13%, 19%, and 27% increase in MACE, respectively (aHR [95% CI] 1.13 [1.01-1.24], 1.19 [1.02-1.38], 1.27 [1.02-1.54]). aHRs and 95% CI for use of 5mg/day for 15 and 30 days prior to MACE were 1.03 (0.99-1.06) and 1.05 (0.99-1.11) respectively. Use of 5mg, 7.5mg, and 10mg for 30 days, with last use 1 year pre-MACE, were associated with 3%, 5%, and 7% increases in MACE (aHR [95% CI] 1.03 [1.02-1.05], 1.05 [1.03-1.07], 1.07 [1.04-1.10]. Similar use for 90 days was associated with 10%, 15%, and 21% increases, respectively (aHR [95% CI] 1.10 [1.05-1.15], 1.15 [1.08-1.23], 1.21 [1.11-1.32]).

Conclusion: In this national RA cohort, we observed a dose-, duration-, and recency-dependent relationship between previous GC use and MACE. GC doses as small as 5mg/day, durations as short as 30 days, and use as long as one year prior to MACE were all associated with an increased risk of MACE. Future work will examine the effect of time-varying covariate adjustment, and potential effect modification of prior GC exposure on risk associated with current use.

Patients with active GC use at time of MACE		
Pattern of use	**HR**	**95% CI**
Currently using 5mg/day, ongoing for the past 15 days	1.03	0.99 - 1.06
Currently using 7.5mg/day, ongoing for the past 15 days	1.04	0.99 – 1.09
Currently using 10 mg/day, ongoing for the past 15 days	1.06	0.98 – 1.12
Currently using 5mg/day, ongoing for the past 30 days	1.05	0.99 - 1.11
Currently using 7.5mg/day, ongoing for the past 30 days	1.08	0.98 - 1.17
Currently using 10mg/day, ongoing for the past 30 days	1.11	0.97 - 1.23
Currently using 5mg/day, ongoing for the past 90 days	**1.13**	1.01 – 1.24
Currently using 7.5mg/day, ongoing for the past 90 days	**1.19**	1.02 – 1.38
Currently using 10mg/day, ongoing for the past 90 days	**1.27**	1.02 – 1.54
Currently using 5mg/day, ongoing for the past 180 days	**1.18**	1.05 -1.33
Currently using 7.5mg/day, ongoing for the past 180 days	**1.29**	1.08 – 1.53
Currently using 10mg/day, ongoing for the past 180 days	**1.40**	1.10 – 1.76
Patients with Gaps in GC before MACE		
Pattern of use	**HR**	**95% CI**
Took 5mg/day for 30 days, last use 90 days ago	**1.02**	1.00 - 1.04
Took 7.5mg/day for 30 days, last use 90 days ago	**1.03**	1.00 – 1.06
Took 10mg/day for 30 days, last use 90 days ago	**1.04**	1.00 – 1.08
Took 5mg/day for 30 days, last use 365 days ago	**1.03**	1.02 - 1.05
Took 5mg/day for 30 days, last use 365 days ago	**1.05**	1.03 - 1.07
Took 5mg/day for 30 days, last use 365 days ago	**1.07**	1.04 - 1.10
Took 5mg/day for 90 days, last use 90 days ago	1.05	0.99 - 1.12
Took 5mg/day for 90 days, last use 90 days ago	1.08	0.99 – 1.18
Took 5mg/day for 90 days, last use 90 days ago	1.11	0.98 – 1.24
Took 5mg/day for 90 days, last use 365 days ago	**1.10**	1.05 - 1.15
Took 7.5mg/day for 90 days, last use 365 days ago	**1.15**	1.08 – 1.23
Took 10mg/day for 90 days, last use 365 days ago	**1.21**	1.11 – 1.32

*Adjusted for age, sex, race, and the following assessed over the year prior to index date: smoking status, BMI, adjusted Elixhauser index, VARS-CV score, claim for malignancy, use of lipid-lowering medications, opioid use, methotrexate use, biologic use, hydroxychloroquine, hospitalization for infection, number of rheumatology clinic visits.

*95% CIs are calculated from 200 bootstrap resamples

Adjusted HR* (with 95% bootstrap CI**) for the association between clinical patterns of glucocorticoid use during the past 2 years and MACE, compared to non-use for the past 2 years.

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Abstract Number: 2431

Integrated Single Cell Multi-omics Analysis in At-Risk for Future Rheumatoid Arthritis (RA) and Early RA Reveals Shared Transcription Factor Profiles in Multiple Cell Lineages

Cong Liu[1], David Boyle[1], Adam Savage[2], Marie Feser[3], Kristen Demoruelle[3], kristine Kuhn[4], Michael Holer[3], kevin Deane[3], Palak Genge[2], Morgan Weiss[2], Veronica Hernandez[2], Julian Reading[2], Jane Buckner[5], Tom Bumol[2], Mark Gillespie[2], Peter Skene[2], Wei Wang[6] and Gary Firestein[1], [1]University of California San Diego, San Diego, CA, [2]Allen Institute for Immunology, Seattle, WA, [3]University of Colorado Anschutz Medical Campus, Aurora, CO, [4]University of Colorado School of Medicine, Aurora, CO, [5]Benaroya Research Institute at Virginia Mason, Seattle, WA, [6]University of California San Diego, La Jolla, CA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: RA – Etiology & Pathogenesis
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Identifying molecular signatures associated with anti-citrullinated protein antibody (ACPA) positive individuals who are 'at-risk' for future RA (At-Risk) and early RA (ERA) requires comprehensive datasets to integrate multi-omics platforms to define personalized mechanisms. In this study, we measured single cell epigenomic and transcriptomic profiles from peripheral blood mononuclear cells (PBMCs) of At-Risk individuals, ERA patients and controls (CON). We performed a cross-sectional analysis using a novel bioinformatic tool to integrate the large-scale multi-omics single cell data.

Methods: Three cohorts were studied including 26 At-Risk with elevated ACPA, 6 ERA, and 35 controls (CON). scRNA-seq and scATAC-seq data were paired for each participant (pt). Seurat and ArchR packages identified co-embedded clusters between scRNA and scATAC cells for each sample, which were annotated to identify cell types. Each cluster was processed through the Taiji pipeline (Nat Commun 2022;13:6221) to create regulatory networks and PageRanks for transcription factors (TFs). Groups were identified using K-means clustering with Pearson correlation as the distance metric. Chi-square test was applied and K-means group-specific TFs were identified by Wilcoxon test.

Results: 1613 clusters from 67 samples spanning 21 cell types were identified and grouped into 5 K-means groups displaying distinct TF regulatory patterns. 4 groups were enriched for individual cell lineages, such as CD4 and CD8 T cells, B cells and monocytes. Group 2 (G2) was multilineage and was significantly enriched in the At-Risk and ERA (8.2 clusters/pt)

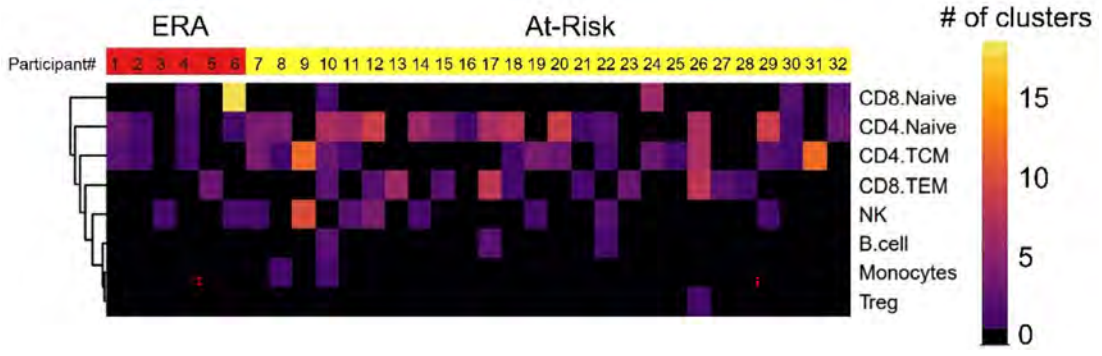

Figure 1. Heatmap across cell lineages of G2 clusters for participants in At-Risk and ERA . The color represents number of clusters for each participant in specific cell type. The horizontal axis shows the individual participants and the vertical axis shows the number clusters for each lineage. Some controls also displayed these clusters although the number was significantly less than At-Risk/ERA, particularly for certain T cell subsets.

compared to CON (5.5 clusters/pt) ($p< 0.001$). 344 TFs were G2-specific, such as embryonic development TFs SP7, FOXL2, and TFAP2C ($p< 0.001$ each). Reactome pathway analysis in G2 showed enrichment in RUNX2, SUMOylation, and YAP1 pathways, each of which have been previously implicated in RA. Remarkably, the G2 signatures were shared by multiple lineages in individual At-Risk and ERA participants. CD4 T naïve, CD4 TCM, and CD8 T naïve cells had greatest enrichment (47% vs 24% of total clusters in G2, $p< 0.0001$; 38% vs 22%, $p< 0.01$; 55% vs 27%, $p< 0.05$, respectively for At-Risk/ERA vs CON). In many cases, more than one cell lineage displayed the signature in an individual participant. Of interest, MAIT cells with the TF signature were only found in CON (49% vs. 0% in At-Risk/ERA, $p=0.01$). Figure 1 shows a heatmap illustrating the cell lineages with the At-Risk/ERA signature.

Conclusion: Distinctive TF profiles are enriched in PBMCs from ACPA+ At-Risk and ERA compared to controls, especially in CD8 and CD4 T cells. These TFs involve pathogenic pathways that have been identified in RA. Furthermore, PageRanks and pathways were similar between At-Risk and ERA suggesting that these mechanisms antedate classifiable disease. Moreover, the cell lineages with these TFs and pathways varied between individual participants, suggesting common mechanisms can occur across multiple cell types. These findings could explain the diversity of clinical responses in RA to targeted therapies because each patient can have an unique combination of pathogenic cell types displaying the RA TF signature.

Disclosure: C. Liu: None; **D. Boyle**: None; **A. Savage**: Adaptive Biotechnologies, 3, 11, Eli Lilly, 2, 5; **M. Feser**: None; **K. Demoruelle**: Boehringer-Ingelheim, 5, Gilead, 5, Pfizer, 5; **k. Kuhn**: pfizer, 5, ucb, 2; **M. Holer**: None; **k. Deane**: Bristol-Myers Squibb(BMS), 1, Gilead, 5, Janssen, 5, Werfen, 1, 12, Biomarker kits; **P. Genge**: None; **M. Weiss**: None; **V. Hernandez**: None; **J. Reading**: None; **J. Buckner**: Bristol-Myers Squibb(BMS), 2, gentibio, 1, 10, 11, hotspot therapeutics, 2, Janssen, 2; **T. Bumol**: Omeros Corporation, 4; **M. Gillespie**: Eli Lilly, 2, 5, Novo Nordisk, 3, 12, Stock; **P. Skene**: Eli Lilly, 2, 5; **W. Wang**: None; **G. Firestein**: Eli Lilly, 5.

Abstract Number: 2432

Wnt Signaling Drives Pathogenic Stromal Inflammation in Inflammatory Arthritis

Alisa Mueller[1], Angela Zou[2], Lucy-Jayne Marsh[3], Samuel Kemble[4], Saba Nayar[3], Emily Taylor[3], Triin Major[3], David Gardner[5], Gerald F.M. Watts[1], Cassandra Murphy[1], Roche Fibroblast Network Consortium[6], Adam Croft[3], Andrew Filer[3], Christopher Buckley[7], Kevin Wei[8], ilya Korsunsky[1], Soumya Raychaudhuri[1] and Michael Brenner[8], [1]Brigham and Women's Hospital, Boston, MA, [2]Harvard Medical School, Boston, MA, [3]University of Birmingham, Birmingham, United Kingdom, [4]University Birmingham, Rugeley, United Kingdom, [5]University of Birmingham, Havelock North, New Zealand, [6]Roche, Basel, Switzerland, [7]University of Oxford, Oxford, United Kingdom, [8]Brigham and Women's Hospital and Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: RA – Etiology & Pathogenesis

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Synovial fibroblasts are a promising therapeutic target in rheumatoid arthritis (RA) where they can adopt inflammatory or destructive phenotypes and directly promote bone and cartilage degradation. In our prior analyses, we found that non-canonical Wnt activation induces robust inflammatory gene expression in these cells. Moreover, two Wnt modulators, RSPO3 and DKK3, are reciprocally expressed and form a transcriptional gradient associated with increased and decreased Wnt activation, respectively. Strikingly, RSPO3 and Wnt activation signatures are enhanced in

synovial fibroblasts in RA, suggesting the potential relevance of the Wnt pathway *in vivo*. Here, we explore the clinical impact of Wnt signaling in mouse models of inflammatory arthritis where we demonstrate that Wnt activation worsens the severity and prolongs the course of arthritis.

Methods: Single-cell RNA sequencing (scRNA-seq) libraries were generated from enzymatically digested, sort-purified CD45- synovial tissue dissected from K/BxN serum recipient mice at the indicated time points. To generate Wnt activation signatures, human RA synovial fibroblasts were stimulated *in vitro* with a combination of Wnt ligands, doses, and time points, and we performed RNA-seq and differential gene expression analysis. RSPO3 signatures were developed from scRNA-seq data of synovial fibroblasts from the Roche Fibroblast Network Consortium. In the antigen-induced arthritis (AIA) model, C57Bl/6 mice underwent subcutaneous (day -21) and knee intra-articular (day 0) injections of methylated BSA (mBSA) followed by knee intra-articular injections of PBS or Wnt5a (days 2 and 4). Knee diameters were measured using calipers, and synovial samples were collected at day 7 for scRNA-seq.

Results: Synovial tissues were processed at baseline, peak inflammation, resolving and resolved time points in K/BxN serum transfer recipient mice (Figure 1A). scRNA-seq analyses reveal reciprocal expression of RSPO3 and DKK3, similar to the pattern in human RA synovium (Figure 1B and 1C). Likewise, Wnt activation scores are enriched in cells that show high expression of the Wnt agonist RSPO3 (Figure 1D). Strikingly, RSPO3 and Wnt activation signatures are increased in synovial fibroblasts isolated at the peak of arthritis compared to those from control and resolution time points (Figure 1E). To determine how the activation of Wnt signaling would impact clinical arthritis, we used the AIA model where non-canonical Wnt5a ligand could be directly injected into the knee (Figure 2A). Strikingly, we found that Wnt activation induces a profound increase in the severity and duration of arthritis (Figure 2B) associated with increased expression of cytokines, chemokines, and other inflammatory mediators in synovial fibroblasts (Figure 2C).

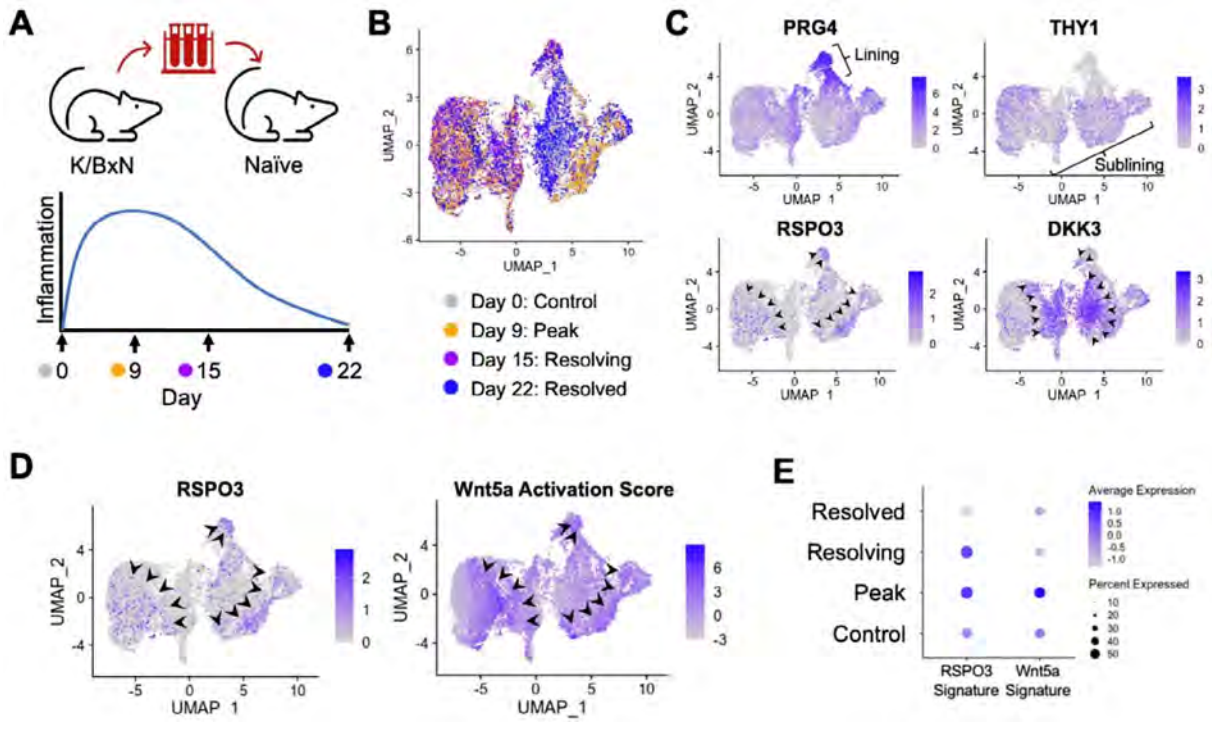

Figure 1: Stromal Wnt activation observed in rheumatoid arthritis is recapitulated in a murine model of inflammatory arthritis. A) Schematic depicting the methodology and time course of inflammation in the K/BxN serum transfer mouse model of inflammatory arthritis. (B) UMAP showing synovial fibroblasts from scRNA-seq analysis of joint tissues harvested at the indicated time points from C57BL/6 mice undergoing serum transfer arthritis. N=3 mice per time point. (C) UMAP of synovial fibroblasts depicting expression of the indicated genes. Arrowheads highlight regions of high expression of RSPO3 or DKK3. (D) UMAP showing the expression of RSPO3 alongside the non-canonical Wnt5a activation score, with arrowheads highlighting regions of high expression. (E) Dot plot exhibiting the level of expression of the RSPO3 and Wnt5a activation signatures at the indicated time points.

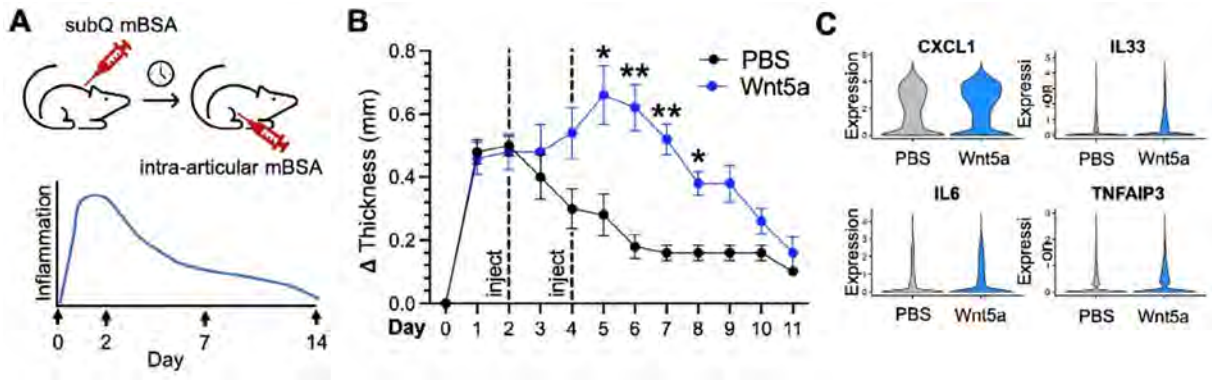

Figure 2: Wnt pathway activation increases the severity and duration of arthritis in a murine model of inflammatory arthritis. A) Schematic illustrating the methodology and time course of the antigen-induced arthritis (AIA) mouse model. Here, mice undergo subcutaneous (subQ) mBSA injection (day -21) followed by intra-articular mBSA injection in the knee (day 0). (B) Change in knee thickness over time in mice undergoing AIA with either Wnt5a (blue) or PBS control (black) knee intra-articular injection at days 2 and 4. N=11 mice each in PBS control and Wnt5a injection groups. (C) Violin plots depicting expression of the indicated genes derived from scRNA-seq of synovial tissue harvested at day 7 from AIA mice treated with PBS or Wnt5a. N=3 mice each in PBS control and Wnt5a injection groups.

Conclusion: Here, we demonstrate that stromal activation of Wnt signaling identified in human RA is recapitulated in mouse models of inflammatory arthritis and that non-canonical Wnt activation is associated with worsening severity of clinical arthritis. This work provides evidence supporting a new molecular target for treatments directed at synovial fibroblasts in RA.

Disclosure: A. Mueller: None; **A. Zou**: None; **L. Marsh**: None; **S. Kemble**: None; **S. Nayar**: None; **E. Taylor**: None; **T. Major**: None; **D. Gardner**: None; **G. Watts**: None; **C. Murphy**: None; **R. Fibroblast Network Consortium**: Roche, 3; **A. Croft**: None; **A. Filer**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 5, Janssen, 5, Nascient, 5, Sonoma Biotherapeutics, 2; **C. Buckley**: Bristol-Myers Squibb(BMS), 5, Mestag, 11; **K. Wei**: 10X Genomics, 5, capital one, 6, Gilead sciences, 5, horizon therapeutics, 6, Mestag, 2; **i. Korsunsky**: Mestag Therapeutics, 2; **S. Raychaudhuri**: AbbVie, 6, Janssen, 1, Mestag, Inc, 2, 8, Pfizer, 1, Sanofi, 1, Sonoma, 1, 8; **M. Brenner**: 4FO Ventures, 2, GlaxoSmithKlein(GSK), 2, Mestag Therapeutics, 2, 11, Third Rock Ventures, 2.

Abstract Number: 2433

Longitudinal Multi-Omics Single Cell Analysis Reveals Abatacept Treatment Shifts Peripheral Lymphocyte Subpopulations in Seropositive RA with Reduction of Mature B Cells and Retention of Transitional and Naive B Cells

Gregg Silverman[1], William Rigby[2], Helena Jun[1], Jasmine Shwetar[1], Katie Tumang[1], Sergei Koralov[3], Ellie Ivanova[1], David Mieles[1], Sladjana Skopelia-Gardner[4] and Kelly Ruggles[1], [1]NYU Grossman School of Medicine, New York, NY, [2]Hitchcock-Dartmouth Medicine Center, Hanover, NH, [3]NYU Grossman Schoolof Medicine, New York, NY, [4]Hitchcock-Dartmouth Medicine Center, Lebanon, NH

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: RA – Etiology & Pathogenesis

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

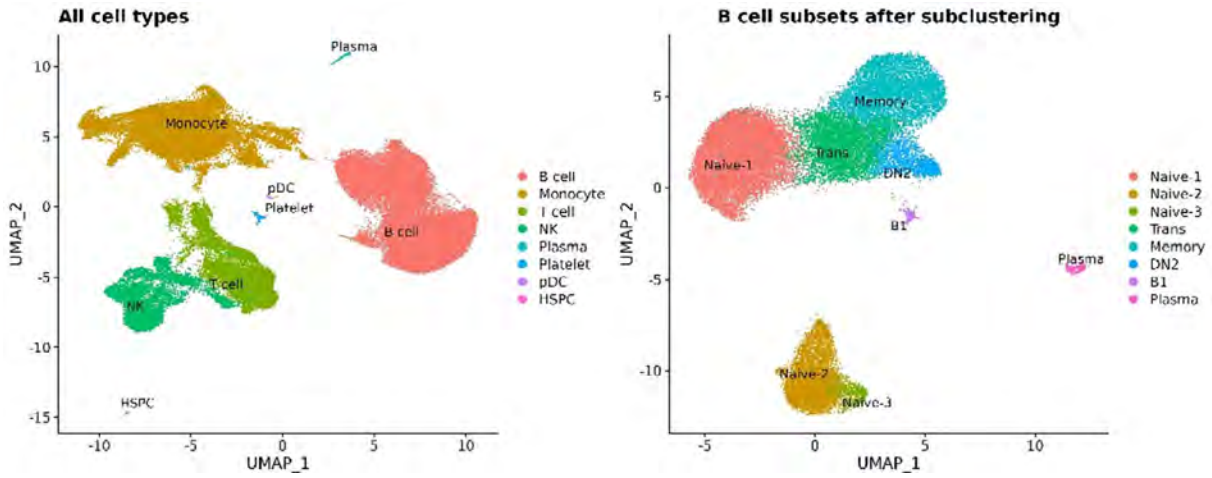

Figure 1. Cell type clustering based on UMAP analysis for 7 RA patients. Data pooled from samples obtained at baseline (0month), and 3 months and 6 months after abatacept initiation, with discontinuation after month 5 infusion, and follow-up at 9 months.

Background/Purpose: Biologic agents of diverse molecular mechanisms of action are approved for RA, but we do not have a full understanding of the implications of treatment and we do not know who will best respond to an agent. Abatacept (CTLA4-Ig) was designed to block a co-stimulation pathway involved in T-cell activation, yet other effects have been suspected. We therefore designed the open-label study, RA and memory B cells (RAMBA trial), to investigate the cellular and transcriptomic consequences of abatacept treatment.

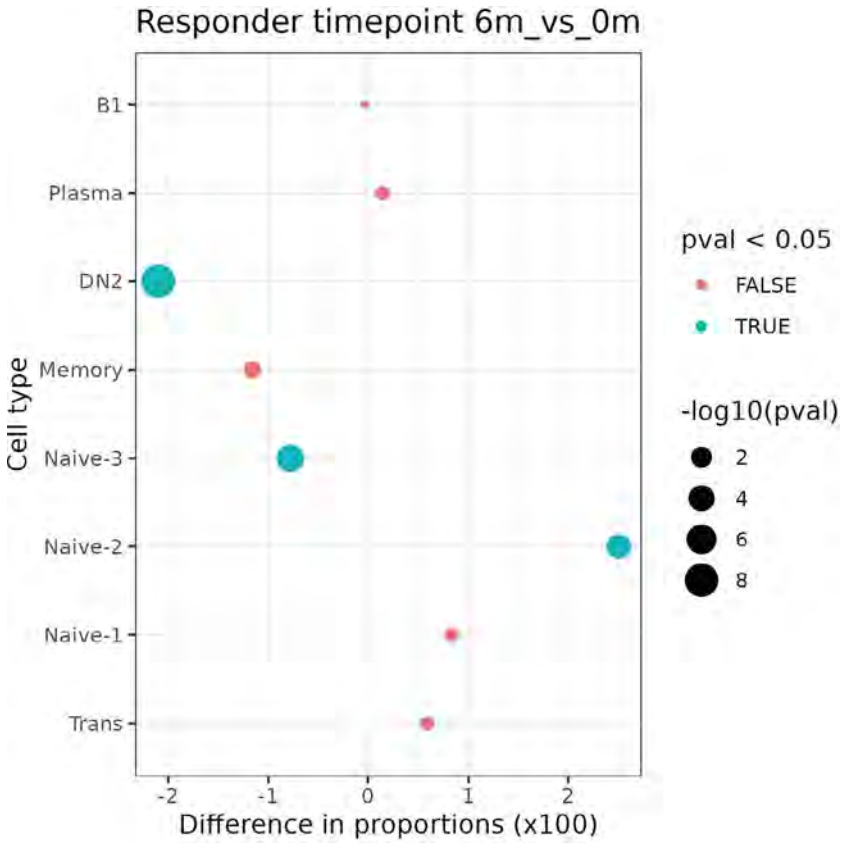

Figure 2. Distribution of B-cell subsets in clinical responders over time. Results are for Chi-squared test on the counts of responder B cell subsets between baseline and 6 month time points.

Methods: Biologic-naïve patients with seropositive RA were enrolled, and received the standard IV regimen of abatacept that was then discontinued after the month 5 infusion. Clinical evaluation and biospecimen collection were performed at baseline, 3, 6, and 9 months or when a flare occurred. In addition to routine clinical lab testing, autoantibody responses were evaluated in a multiplex assay with IgM-RF, and IgM- and IgG- to 4 ACPA fine specificities including CCP3. PBMCs or samples of negatively selected B-lineage cells were interrogated at a single cell level for high-dimensional surface phenotype and transcriptomic profiles, by Expanded Cellular Indexing of Transcriptomes and Epitopes (ExCITE) sequencing.

Results: 21 enrolled patients had two or more follow-up visits, with 18 completing to 9 months or post-treatment flare.12 patients achieved low disease activity by DAS28-CRP (< 3.2) or CDAI (< 10). Clinical responses were mirrored by reductions in serum RF and/or ACPA levels (not shown). Initial single cell analyses of 7 patients, of 70,790 PBMCs and 33,160 B-lineage cells Abatacept treatments induced increases in naïve CD4+ T cells over time (not shown). CD19+ B-lineage cells were resolved into 8 subsets (Fig.1). Treatment was associated with significant reductions of Naïve-3, and CD19+ sIgD- CD27- (DN2) B cells linked to autoimmune B-cell responses. In contrast, treatment was also associated with significant increases in the accumulation of Naïve-2 B cells, and a trend towards increases in the peripheral accumulation of transitional and Naïve-1 B cells (Fig.2).

Conclusion: Complete clinical response to abatacept in RA was associated with cellular shifts in peripheral B-cell subsets identified based on surface phenotype and transcriptomic profiles, with a return to a state dominated by newly emergent transitional and early naïve B cells. These findings elucidate previously unsuspected aspects of MOA of abatacept, that we postulate reflects a reversion in balance towards the preimmune natural state of clonal ignorance unaffected by autoimmune disease.

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Disclosure: G. Silverman: None; **W. Rigby**: None; **H. Jun**: None; **J. Shwetar**: None; **K. Tumang**: None; **S. Koralov**: None; **E. Ivanova**: None; **D. Mieles**: None; **S. Skopelia-Gardner**: None; **K. Ruggles**: None.

Abstract Number: 2434

Acetylated Bacterial Proteins as Potent Antigens Inducing an Anti-modified Protein Antibody Response

Mikhail Volkov, Arieke Kampstra, Karin van Schie, Joanneke Kwekkeboom, Arnoud de Ru, Peter van Veelen, Thomas Huizinga, René Toes and Diane van der Woude, Leiden University Medical Center, Leiden, Netherlands

SESSION INFORMATION
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Session Title: Abstracts: RA – Etiology & Pathogenesis
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Gut-residing bacteria, such as *E.coli*, can acetylate their proteome under conditions of amine starvation. It is postulated that the (gut) microbiome is involved in the breach of immune tolerance to modified self-proteins leading to the anti-modified protein antibodies (AMPA), hallmarking seropositive RA. Our aim was to determine whether acetylated bacterial proteins can induce AMPA-responses cross-reactive to modified self-proteins and be recognized by human AMPA (hAMPA).

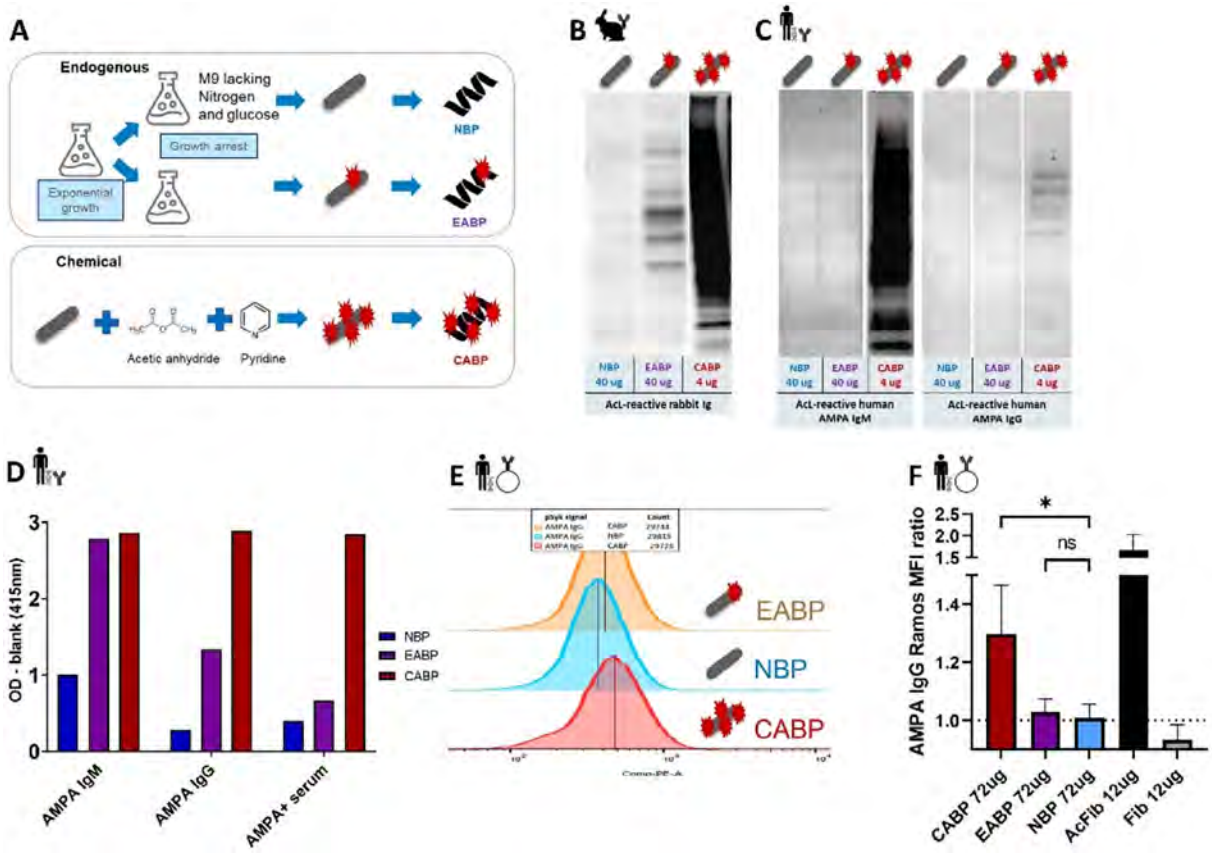

Figure 1. Recognition of acetylated bacterial antigens by hAMPA (A) Schematic overview of the generation of NBP, EABP and CABP. (B) Western blotting with NBP, EABP and CABP stained with anti-acetyllysine polyclonal rabbit antibody. (C) Western blotting with NBP, EABP and CABP stained with hAMPA mAbs, recognizing acetylated proteins: 7E4 IgG and 1E3 IgM. (D) ELISA with 1E3 IgM, 7E4 IgG and polyclonal IgG from an RA patient serum isolated with CAcP4 peptide. (E) pSyk MFI, visualizing BCR activation of Ramos B cells expressing 7E4 IgG after incubation with acetylated E. coli antigens. (F) Summary of three BCR activation experiments with 7E4 Ramos B cells. Statistical differences are indicated with asterisks, indicating p-value: * < 0.05, ** < 0.01, **** < 0.0001.

Methods: *E. coli*-bacteria were grown under amine starvation to generate endogenously acetylated bacterial proteins. Furthermore, *E. coli* proteins were acetylated chemically (Figure 1A). Recognition of these proteins by hAMPA was analysed by western blotting and ELISA; recognition by B cells carrying a modified protein-reactive B cell receptor (BCR) was analysed with a pSyk activation assay. C57BL/6 mice were immunized with (modified) bacterial protein fractions, and sera were analysed by ELISA (Figure 2A).

Results: Chemically modified bacterial protein fractions contained high levels of acetylated proteins (Figure 1B) and were readily recognized by hAMPA (Figure 1C) and able to activate B cells carrying modified protein-reactive BCRs (Figure 1E-F). Likewise, although expressing lower levels of acetylation, also endogenously acetylated protein fractions were recognized by hAMPA in ELISA (Figure 1D). Immunizing mice with chemically modifed protein fractions induced a strong cross-reactive AMPA response, targeting various modified antigens including citrullinated proteins (Figure 2B-C). Interestingly, highly acetylated bacterial proteins could induce an AMPA response even without an adjuvant (Figure 2D).

Conclusion: Acetylated bacterial proteins are recognizable by hAMPA and capable of inducing a cross-reactive AMPA response in mice. These observations provide first evidence for a novel mechanism, involving the (endogenous) acetylation of the bacterial proteome, allowing a breach of tolerance to modified proteins and the formation of cross-reactive AMPA.

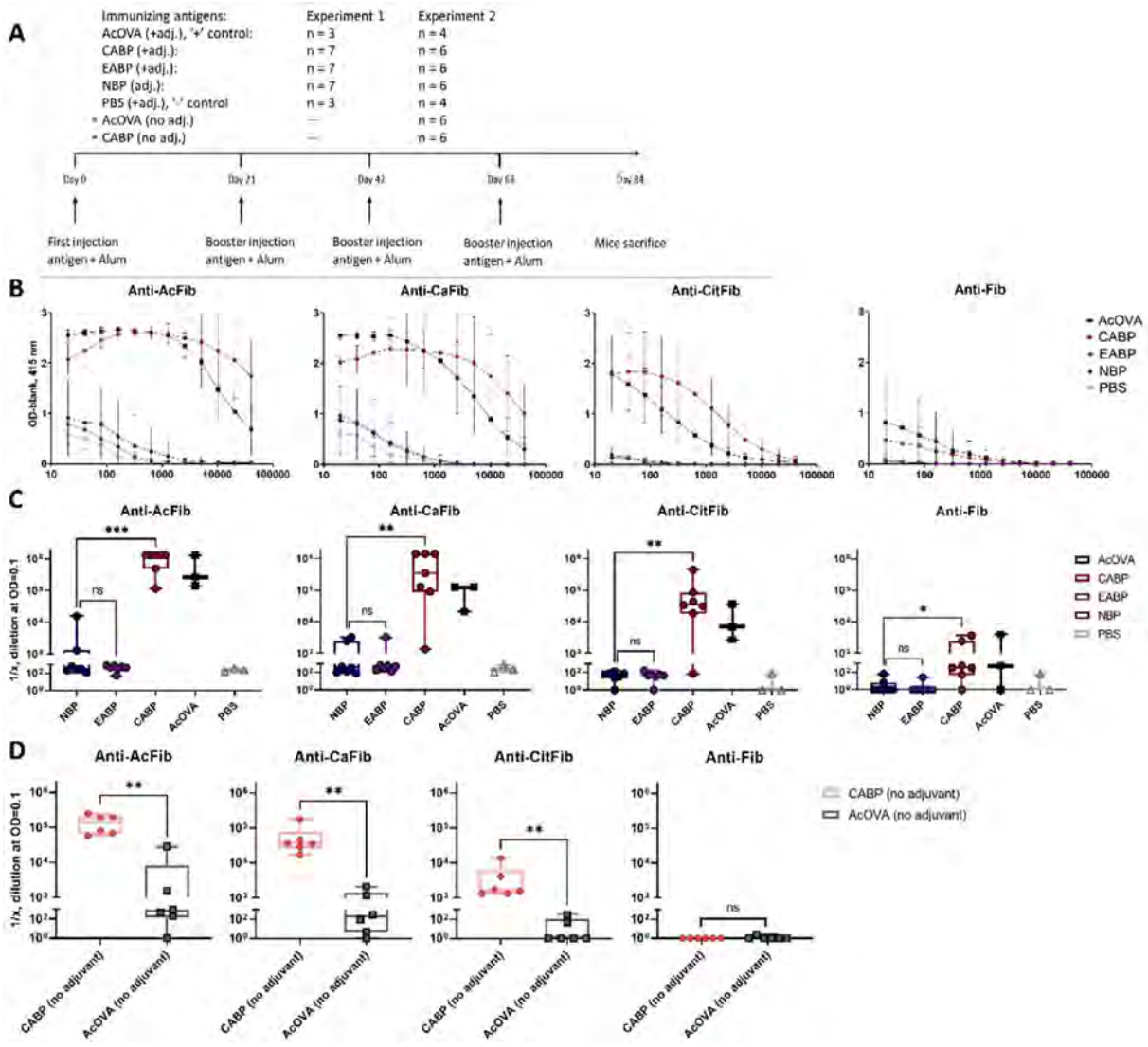

Figure 2. Immunization of mice with bacterial acetylation proteins (A) Immunization scheme of the performed mouse experiments. (B) Reactivity of titrated mouse serum to modified and unmodified versions of fibrinogen, per immunizing antigen. (C) Mice immunized with the antigens with the adjuvant: titers at OD = 0.1, as determined by ELISA to modified and native versions of fibrinogen. (D) Mice immunized with CABP or AcOVA without the adjuvant: reactivity of individual mouse serum samples to modified and unmodified versions of fibrinogen. Statistical differences are indicated with asterisks, indicating p-value: * < 0.05, ** < 0.01, **** < 0.0001. A-C: data are representative of two experiments. AcOVA: acetylated ovalbumin, CABP: chemically acetylated bacterial proteins; EABP: endogenously acetylated bacterial proteins; NBP: non-acetylated bacterial proteins; PBS: phosphate buffer saline.

Disclosure: M. Volkov: Pfizer, 3, 11; **A. Kampstra**: None; **K. van Schie**: None; **J. Kwekkeboom**: None; **A. de Ru**: None; **P. van Veelen**: None; **T. Huizinga**: None; **R. Toes**: Bristol-Myers Squibb(BMS), 5; **D. van der Woude**: None.

Abstract Number: 2435

Deciphering Rheumatoid Arthritis Disease Activity-Associated Gene Signatures and Cell Subsets Through Single Cell Transcriptomics

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CA, [3]Aarhus University, Aarhus, Denmark, and University of California San Francisco, San Francisco, CA, [4]University of California San Francisco, San Francisco, CA, [5]Bakar Computational Health Sciences Institute, University of California San Francisco, San Francisco, CA, [6]NIH/NHGRI, Bethesda, MD, [7]Sorbonne Université APHP, Paris, France, [8]UCSF/SFVAHCS, San Francisco, CA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: RA – Etiology & Pathogenesis

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Single cell transcriptional profiling (scRNA-Seq) is valuable in identifying gene signatures and cell subpopulations associated with rheumatoid arthritis (RA). However prior studies have often overlooked important demographic confounders and not focused on non-remission and difficult to treat RA. The aim of this study is to identify peripheral blood mononuclear cells (PBMCs) of RA and disease-activity cell subsets and gene signatures in a diverse population of patients.

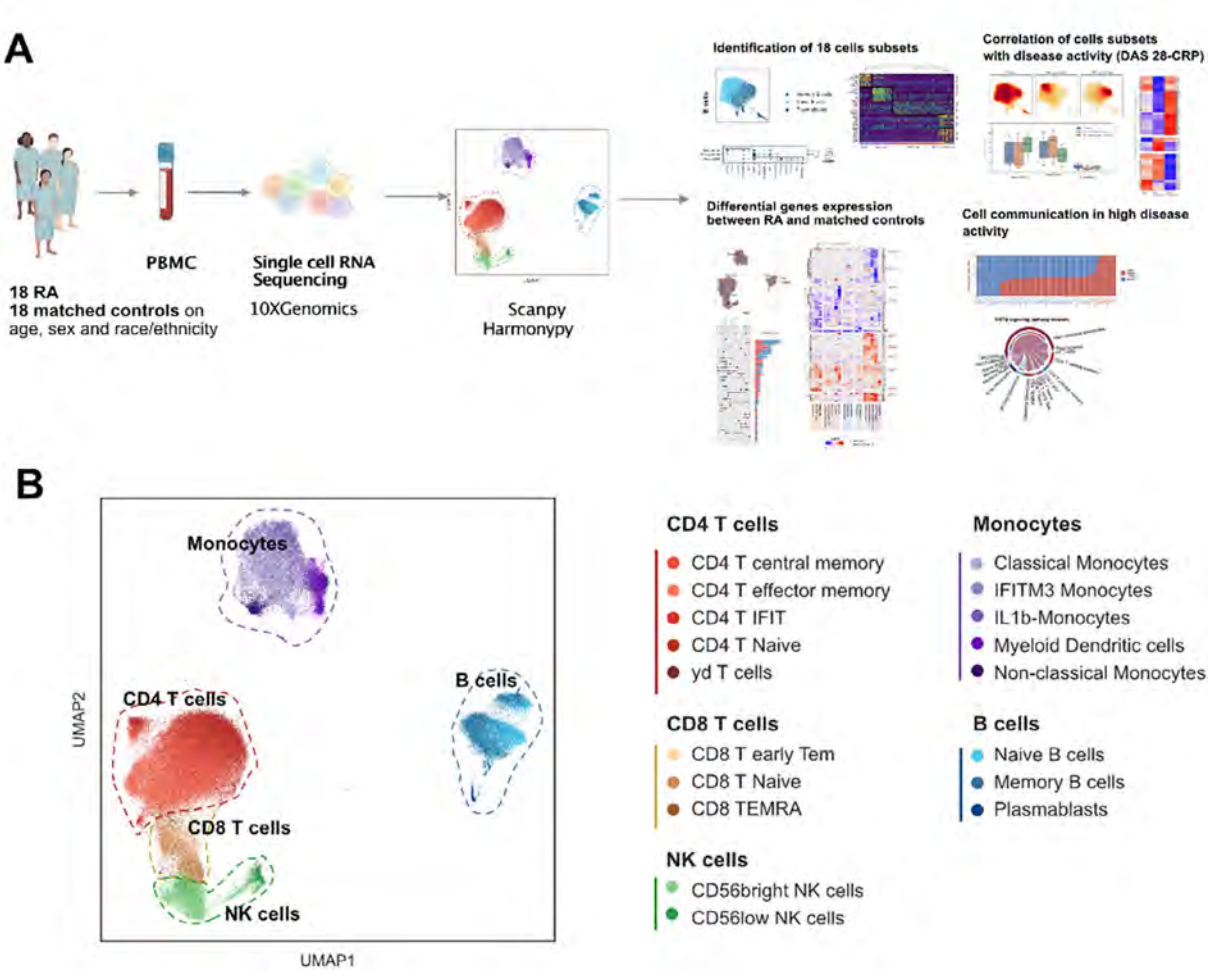

Figure 1 | A. Graphical Abstract. B. UMAP embeddings and subset annotations of single cell RNAseq dataset from patients with rheumatoid arthritis (n=18) and healthy controls (n=18) matched on age, sex, and ethnicity. CD, Cluster differentiation; DCs, Dendritics cells; IFIT, Interferon Induced proteins with Tetratricopeptide repeats; IFITM, interferon-induced transmembrane; Tem: T effector memory, TEMRA: Terminally differentiated effector memory. RA Rheumatoid ArthritisTem: T effector memory, TEMRA: Terminally differentiated effector memory. RA Rheumatoid Arthritis

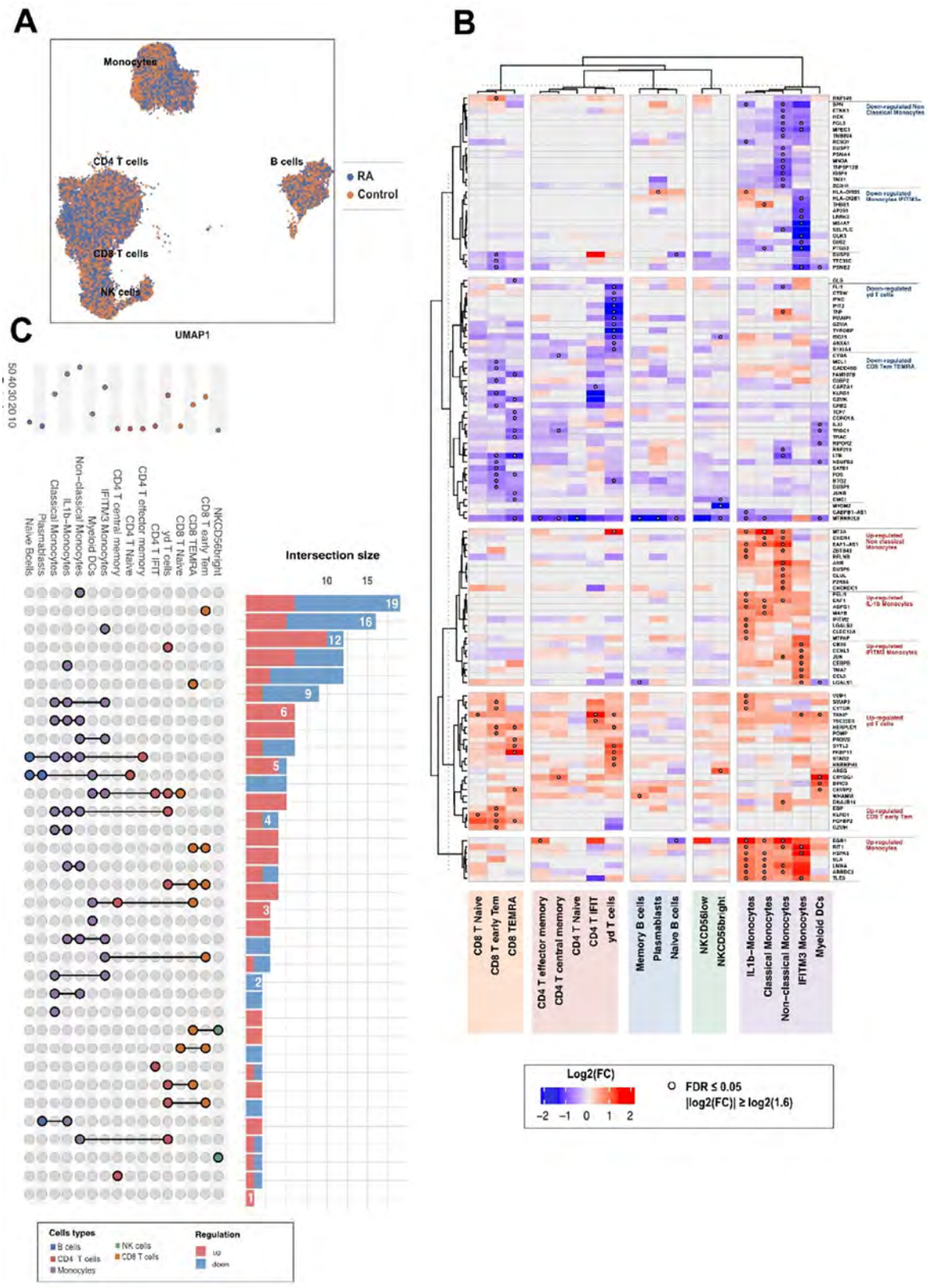

Figure 2 | A. Single cell UMAP projection of patients with rheumatoid arthritis and matched controls. B Differentially expressed genes between patients with RA and matched controls. C. Upsets pot of upregulated and downregulated genes. CD, Cluster differentiation; DCs, Dendritics cells; IFIT, Interferon Induced proteins with Tetratricopeptide repeats; IFITM, interferon-induced transmembrane; Tem: T effector memory, TEMRA: Terminally differentiated effector memory. RA Rheumatoid Arthritis

Methods: 10X Chromium single cell sequencing was performed on peripheral blood mononuclear cells (PBMC) from 18 early RA patients and 18 healthy controls matched on age, sex, race and ethnicity. Data were processed using standard CellRanger and Scanpy pipelines, with HarmonyPy for batch correction. Differential expression (DE) was computed using pseudobulk analysis and DESeq2. Pathway analysis was carried out with over-representation analysis (ORA). Mann-Whitney tests were used to assess differences in cell proportions between matched RA and control samples, as well as between RA patients with low disease activity or remission (DAS28-CRP< 3.2; n=9) versus moderate or high disease activity (DAS28 CRP≥3.2;n=7). Ligand-receptor interaction analysis was performed using Cellchatdb.

Results: The final dataset consisted of 22,159 genes across 125,698 cells. We identified 18 PBMC subsets, including 5 CD4+ T cell subsets, 3 CD8+ T cell subsets, 2 Natural Killer cell subsets, 3 B cell subsets, and 5 monocyte subsets (Figure 1). Within these subsets, IFIT CD4 T+ cells and IFITM3 monocytes were associated with Interferon-gamma response. 168 genes were DE between RA and matched controls (FDR≤0.05, foldchange >1.6). We identified up-regulation of pro-inflammatory genes associated with monocyte subsets and downregulation of inflammatory genes in gamma-delta T cells. Several genes associated with RA predisposition such as HLA-DRB5 and HLA-DQB1 were specifically downregulated in IFITM3 monocytes (Figure 2). Functional analysis and ORA highlighted significant enrichment of B cell activation and B cell receptor signaling pathways. Differences in cell subset proportions between patients with high and moderate activity, patients in low disease activity and remission, and healthy controls (n=18, Figure 3) were also observed. Non classical

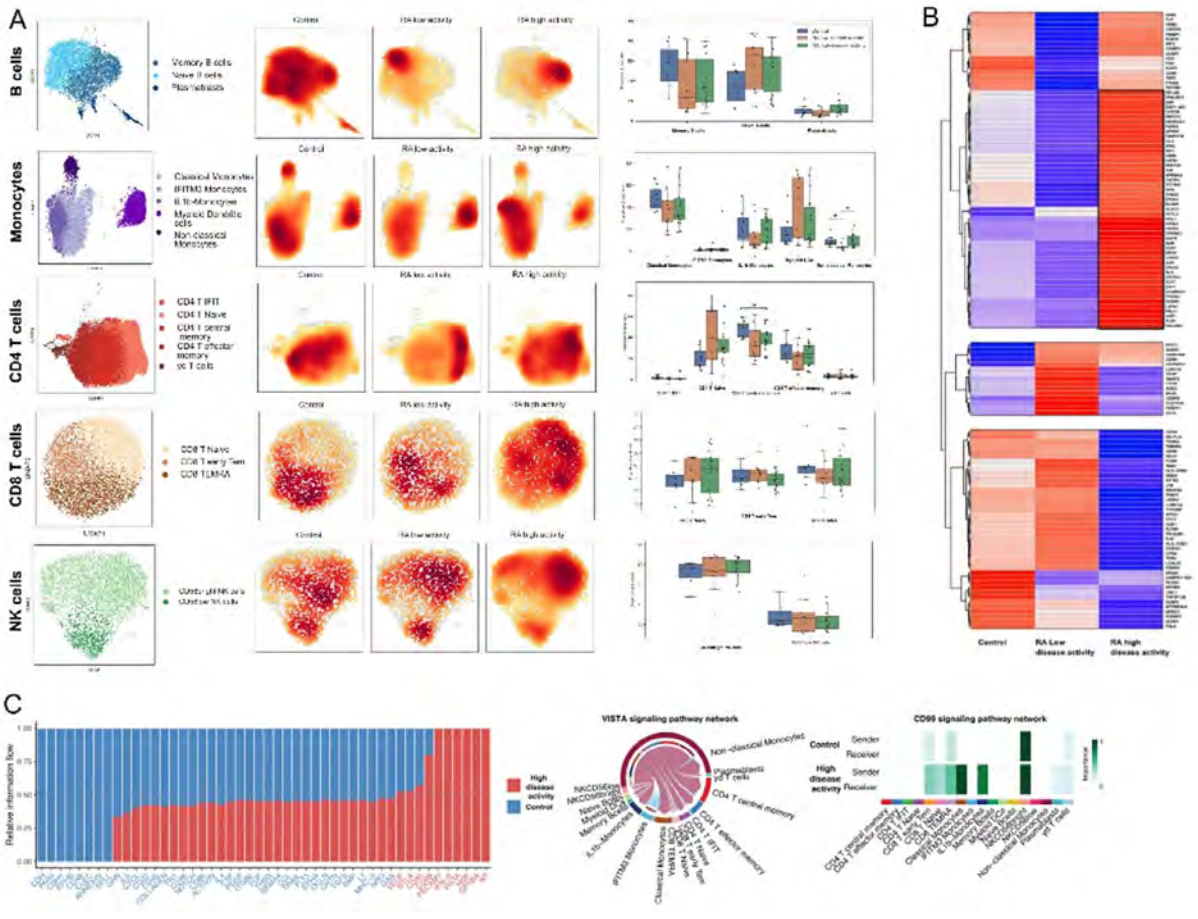

Figure 3 | A. Compositional, density and cell proportion analysis between control patients with low disease and high activity (Mann-Whitney - Wilcoxon p≤ 0.05). B. Genes expression heatmap between controls and RA with low and high disease activity and average expression across cell subtypes C. Communication pathway significantly up and downregulated in high disease activity and controls, overview of cell communication within the VISA and the CD99 pathway. CD, Cluster differentiation; DCs, Dendritics cells; IFIT, Interferon Induced proteins with Tetratricopeptide repeats; IFITM, interferon-induced transmembrane; Tem: T effector memory, TEMRA: Terminally differentiated effector memory. RA Rheumatoid Arthritis

monocytes and T central memory were decreased in patients with high disease activity compared to control and high disease activity (p=0.022; p=0.034). We also identified a specific signature of 49 genes, including IFNG, TNF, KLRD, EGR1, CBX6, CXCR4, JUN, and TLE3, that was significantly associated with disease activity. Finally, cell communication analysis between patients with high disease activity and controls revealed upregulation of IFN-II, VEGF, VISTA, BTLA, and CD40 pathway signaling.

Conclusion: Here we describe a dataset of scRNA-Seq PBMCs from a diverse population of patients with RA and matched healthy controls. We identify differentially expressed genes and cell subsets linked to disease activity, providing insights into RA pathophysiology and potentially new therapeutic targets.

Disclosure: M. Binvignat: None; **B. Miao**: None; **C. Wibrand**: AMBU, 11, GenMab, 11, Lundbeck, 11, NovoNordisk, 11; **M. Yang**: None; **D. Rychkov**: None; **E. Flynn**: None; **U. Khan**: None; **J. Nititham**: None; **A. Carvidi**: None; **M. Krueger**: None; **E. Niemi**: None; **Y. Sun**: None; **G. Fragiadakis**: None; **D. Klatzmann**: None; **J. SELLAM**: None; **E. Mariotti-Ferrandiz**: None; **A. Gross**: None; **C. Ye**: Chan Zuckerberg Initiative, 5, Genentech, 5, ImmunAI, 1, 8, Maze Therapeutics, 2, 8, Related Sciences, 1, 8, TReX Bio, 2; **A. Butte**: 10X Genomics Health, 2, Genentech, 1, Mango Tree, 2, Merck/MSD, 1, Novartis, 1, NuMedii, 2, 8, personalis, 2, 4, 8, Roche, 1, samsung, 2, Verinata (Illumina), 2; **L. Criswell**: None; **M. Nakamura**: None; **M. Sirota**: Exxagen, 1.

Abstract Number: 2436

Characterizing Spatial Organization of Immune Infiltrates in Rheumatoid Arthritis Synovia Using Spatial Transcriptomic Analysis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: RA – Etiology & Pathogenesis
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Session Time: 2:00PM–3:30PM

Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune disease characterized by immune infiltration of the synovial tissue lining joints. RA is clinically heterogenous, with patients having varied responses to therapies, likely reflecting distinct pathogenic mechanisms. To begin to define the heterogeneity in RA, a recent study showed that the fractional abundances of 5 cell types can help predict treatment response in some subsets of RA (1). With the goal of better understanding the spatial organization of cells in RA synovial tissues and mapping cell-cell interactions, we sought to take a key next step in defining RA heterogeneity and its relation to treatment response

Methods:

Spatial transcriptomic profiling

We used CosMx Spatial Molecular Imager to measure the RNA expression levels of 960 genes in 10 paraffin-embedded inflamed synovial tissue samples.

Cell segmentation and annotation

We developed a segmentation pipeline to map transcripts to cells, and then classified each cell into one of 10 major cell types. We used the single-cell RNA seq synovial atlas to map these cells further into fine-grained cell-states.

Niche detection and characterization

We performed spatial tissue segmentation to identify contiguous and transcriptionally homogeneous sections of the tissue called "niches". We split tissues into tiles and performed spatial clustering of the tiles to detect niches.

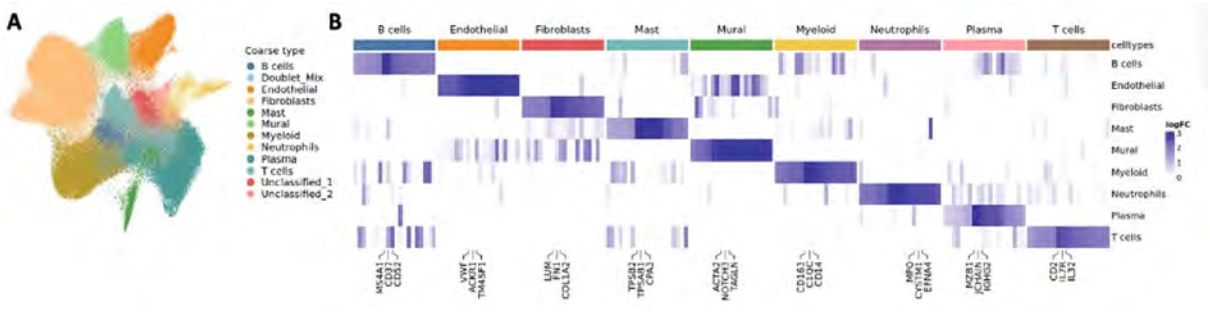
Results:

1. Identification of major and fine-grain cell types *in situ*. We segmented and labeled 333,966 high quality cells across 10 RA synovial tissue samples. We identified 10 major cell lineages (Figure 1A-B), including 2 absent in single-cell RNA-seq studies: mast cells and neutrophils. We subclassified cells into 54 subtypes and activation states based on prior definitions from the AMP single-cell RNA-seq atlas of inflamed synovium (1). We detected 2 cell states of mast cells (resting and activated) and 3 cell states of neutrophils (resting, activated, and proliferating) based on key gene expression markers.

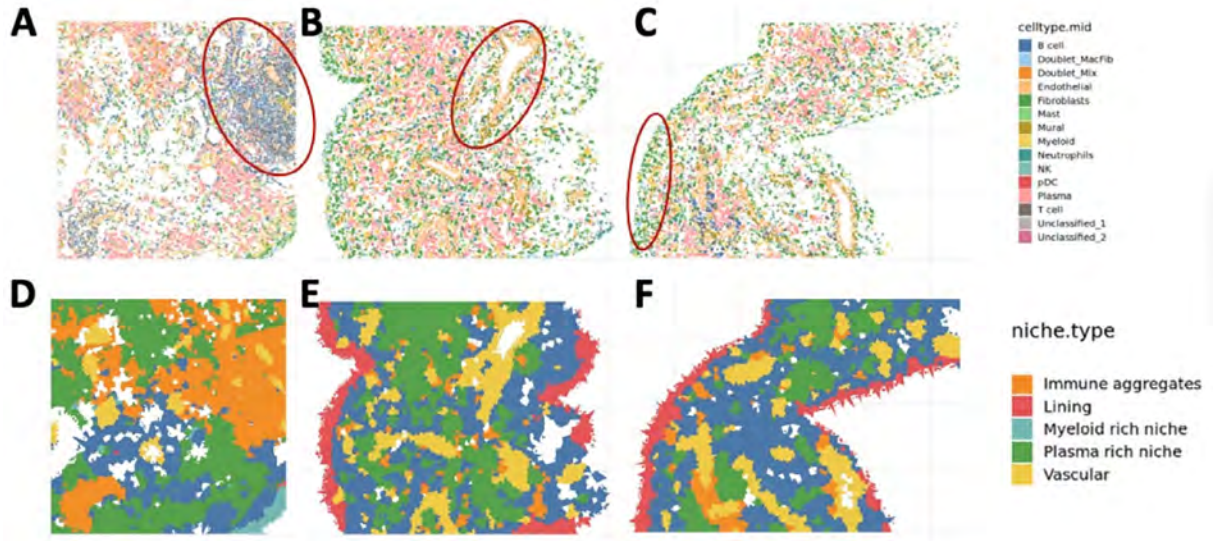
2. Quantification of anatomic niches. We mapped annotated cells into tissue space, where they organized into anatomic structures: vasculature (endothelial and mural cells), lining (lining fibroblasts and MERTK+ macrophages), and immune aggregates (T, B, and plasma cells) (Figure 2A-C). We quantified the boundaries of these niches and identified all niches in most samples. We next quantified the relative composition of niches within and across donors and observed significant heterogeneity of niches within samples (Figure 2D-F).

3. Validation with independent cohort. We validated our spatial organization results in an independent inflamed synovial tissue cohort from 3 patients with treatment naïve RA. Using our pipeline, we found similar proportions of cell types and organization of cells into the canonical niches defined in our spatial atlas (Figure 3A, B).

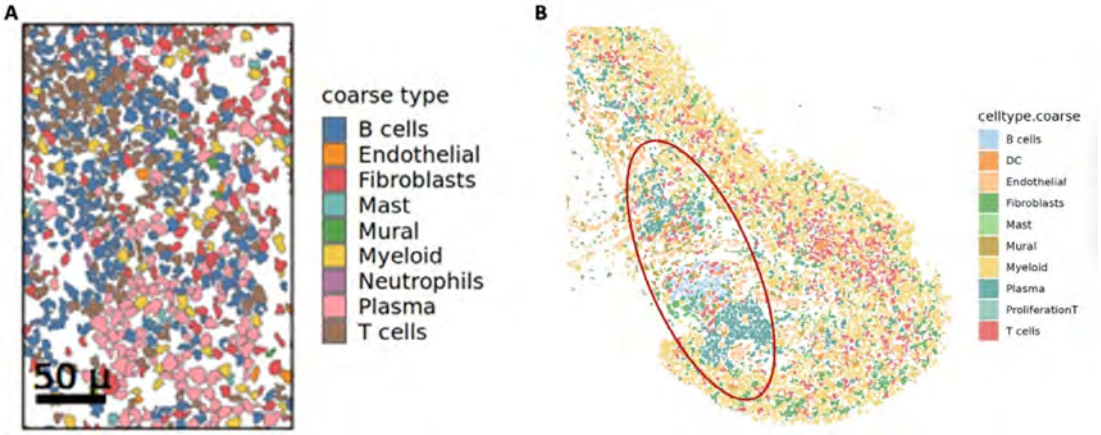
Conclusion: We established a draft spatial atlas of RA synovium and provided spatial context for 54 cell types, subtypes, and activation states observed in dissociated tissue assays. This atlas will serve as a reference to map the cellular organization in different cohorts as demonstrated and eventually enable us to compare the effects of different therapeutics on the RA tissue.



Identification of major cell types in situ (A) Cells projected in UMAP space, colored by their major cell type. (B) Heatmap of gene log fold-changes for each of the major cell types. Top 3 marker genes for each cluster are annotated on the x-axis.



Identification of anatomical niches (A-C) Cells in tissue space in active RA synovium. Each panel shows an FOV from a tissue sample. Red ovals in each FOV highlight an anatomical niche (A) immune aggregate, (B) vascular niche, (C) lining. (D-F) Niches in space: each panel shows detected niches in the FOVs shown in A-C. FOV: Field of view



Anatomical niches across cohorts (A) Cells in tissue space in active RA synovium organized into an immune aggregate (B) Cells in tissue space in treatment naïve RA synovium. Red oval highlights the immune aggregate niche.

Disclosure: R. Madhu: None; **K. Bhamidipati**: None; **A. Jonsson**: None; **F. Zhang**: None; **L. MacDonald**: None; **Y. Kim**: NANOSTRING, 3; **Y. Cui**: NANOSTRING, 3; **S. BWH**: Mestag Therapeutics, 2; **A. RA SLE Network**: None; **M. Kurowska-Stolarska**: None; **S. Alvernini**: None; **E. Gravallese**: Associate Editor, New England Journal of Medicine, 3, Co-editor of the textbook Rheumatology, 9, UptoDate, 9; **M. Brenner**: 4FO Ventures, 2, GlaxoSmithKlein(GSK), 2, Mestag Therapeutics, 2, 11, Third Rock Ventures, 2; **S. Raychaudhuri**: AbbVie, 6, Janssen, 1, Mestag, Inc, 2, 8, Pfizer, 1, Sanofi, 1, Sonoma, 1, 8; **K. Wei**: 10X Genomics, 5, capital one, 6, Gilead sciences, 5, horizon therapeutics, 6, Mestag, 2; **i. Korsunsky**: Mestag Therapeutics, 2.

Abstract Number: 2437

Translocation of Intestinal Bacteria to Axial and Peripheral Joints in a Model of Spondyloarthropathy

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Basic Science

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: In spondylarthropathy (SpA), such as psoriatic arthritis (PsA) and ankylosing spondylitis (AS), arthritis is often associated with gut inflammation. After systemic β-1,3-glucan (curdlan) injection, ZAP70^{W163C} SKG mice develop IL23-dependent SpA-like spondylarthritis, ileitis and faecal dysbiosis with enrichment in Gram-negative pathobionts over commensals, recapitulating human SpA disease spectrum. Spondylitis in AS patients does not respond to anti-IL-23. To assess the interaction of intestinal dysbiosis and spondyloarthritis, we treated diseased SKG mice with anti-IL-23p19.

Methods: Specific-pathogen-free SKG or BALB/c control mice were injected i.p. with curdlan followed by anti-IL-23p19 antibody or isotype three weeks later. At eight weeks, ileum, ankle and sacroiliac joints were collected, paraffin-embedded for histology and scored for arthritis and ileitis. Tissue sections were analysed by fluorescence imaging using universal bacterial DNA EUB338 and non-sense EUB338 control probes, combined with anti-MPO or anti-IBA-1 antibodies for neutrophils and macrophages.

Results: At 8 weeks post-curdlan, isotype-treated SPF SKG mice developed ileitis, enthesitis, axial and peripheral arthritis while anti-IL-23p19-treated SKG mice had much less severe disease, and BALB/c mice remained healthy. In inflamed ileum of isotype-treated SKG mice, EUB338+ bacteria translocated from the lumen to the gut lamina propria, where they colocalised with infiltrating MPO+ neutrophils and IBA-1+ resident macrophages. In arthritic axial and ankle joints, EUB338+ bacterial DNA was detected in the blood vessels, tendon entheses, ligaments and the bone marrow, associated with bone and cartilage destruction. MPO+ neutrophils and IBA-1+ resident macrophages infiltrated the areas of inflammation. In anti-IL-23p19-treated SKG mice, bacterial signals were detected in entheses but not the bone marrow. No bacterial signal was detected in BALB/c tissues.

Conclusion: In SKG mice, curdlan triggers IL-23-dependent gut permeability and ileitis that allows mucosal invasion of bacteria, and dissemination of intestinal bacterial DNA to axial and peripheral joints' bone marrow and entheses through the vasculature, similar to reactive arthritis. While anti-IL-23 blocks bone marrow entry of bacterial DNA, it fails to limit the entheseal spread after disease onset. This suggests a potential mechanism by which inflammation is perpetuated in ankylosing spondylitis.

Disclosure: B. Cai: None; **R. Giri**: None; **H. Benham**: None; **L. Rehaume**: None; **G. Strutton**: None; **A. Bergot**: None; **R. Thomas**: CSL, 2, 5, Janssen-Cilag, 6, Sandoz, 6.

Abstract Number: 2438

Synovial Tissue Single-Cell Analysis Demonstrates Differential Fibroblast Populations Between RA and PsA Which Display Distinct Function

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Basic Science

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Synovial fibroblasts (FLS) are key contributors to joint inflammation and damage in patients with Rheumatoid (RA) and Psoriatic Arthritis (PsA). Recent studies have identified FLS subsets with distinct pro-inflammatory roles in RA. However, there is a scarcity of data regarding the contribution of FLS in PsA pathogenesis and overall lack of unifying nomenclature. Therefore, the aim is to identify the phenotypic and functional characteristics that define distinct FLS populations and function in RA vs PsA, with implication for disease pathogenesis and therapeutic response.

Methods: Single cell (Sc) RNAseq was performed on 88,953 RA and PsA FLS from intact synovial biopsies and FLS populations were defined by advanced bioinformatic analysis. Subsequently, multiparametric flow cytometric analysis (22 markers) was performed on RA and PsA patient synovial biopsies to examine FLS phenotype and function. Further characterization of differences in the invasive activity of RA and PsA FLS was conducted ex vivo through quantification of matrix metalloproteinases using MSD multiplex-assays/RT-PCR, whilst metabolism was assessed by Seahorse-XFe-technology. Additionally, flow cytometric analysis of key FLS activation/functional markers was performed on RA and PsA FLS across passages 0-3 (P0-3) to define phenotypic alterations once removed from the joint microenvironment.

Results: ScRNAseq analysis demonstrated 11 distinct FLS populations in RA and PsA, with differential frequency of clusters observed with $THY1^+$ FLS dominant in RA vs THY1- FLS dominant in PsA. Flow analysis of $PDPN^+$ FLS demonstrated significant increases in $HLADR^+$, YAP^+, $Cad11^+$, and $pS6^+$ FLS in RA (all $p< 0.05$), whilst PsA FLS demonstrated a significant increase in CD55 expression ($p=0.0079$). Further flow analysis identified 6 FLS populations that could be matched to 6 main populations in the scRNAseq. When compared directly between diseases, patients with RA displayed significant enrichment in $THY1^+CD34^-CD55^-FAP^+$ and $THY1^+CD34^+CD55^-FAP^+$ FLS ($p=0.0093$), while patients with PsA displayed enrichment in $THY1^+CD34^-CD55^+FAP^+$($p=0.02$) and $THY1^-CD34^-CD55^+FAP^+$ FLS ($p=0.0013$). HLADR and Cad11 were significantly higher in RA subpopulations, compared to increased metabolic markers in PsA subpopulations by flow cytometry. In parallel, single-cell analysis of these populations demonstrated immune/inflammatory responses in RA dominant populations in contrast to matrix degrading and metabolic markers in PsA populations. Expanded RA and PsA FLS (P0) confirmed these differences in matrix degrading/metabolic pathways, matching the single cell/flow cytometric analysis. While P0 FLS maintained similar phenotypic profiles to ex vivo FLS, once expanded to P3, FLS started to lose specific phenotypic characteristics. Specifically, the expression of HLADR and CD55 reduced across passages 0-3, while CD34 and CD54 increased, supporting their transient nature.

Conclusion: Distinct FLS populations with unique functional properties were identified in RA and PsA. However, once removed from the joint microenvironment, FLS subset stability appears transient with convergence towards common phenotypes.

Disclosure: Ó. Tynan: None; **M. Canavan**: None; **A. Floudas**: None; **C. Smith**: None; **A. O' Rourke**: None; **D. Anton**: None; **C. Orr**: None; **D. Veale**: None; **U. Fearon**: None.

Abstract Number: 2439

Proteomic and Genomic Profiling of Plasma Exosomes from Ankylosing Spondylitis Patients

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Basic Science
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Recent advances in understanding the biology of Ankylosing Spondylitis (AS) using innovative genomic and proteomic approaches offer the opportunity to address current challenges in AS diagnosis and management. Altered expression of genes, microRNAs (miRNAs), or proteins may contribute to immune dysregulation and play a significant role in the onset and persistence of inflammation in AS. The ability of exosomes to transport miRNAs across cells and alter the phenotype of recipient cells has implicated exosomes in perpetuating inflammation in AS. This study reports the first proteomic and miRNA profiling of plasma-derived exosomes in AS using comprehensive computational biology analysis.

Methods: Plasma samples from AS patients and healthy controls (HC) were isolated via ultracentrifugation and subjected to extracellular vesicle (EV) flow cytometry analysis to characterize exosome surface markers by a multiplex immunocapture assay. Cytokine profiling of plasma-derived exosomes and cell culture supernatants was performed. Next-generation sequencing was used to identify miRNA populations in exosomes enriched from plasma fractions. CD4+T cells were sorted, and the frequency and proliferation of CD4+T cell subsets were analyzed after treatment with AS-exosomes using flow cytometry.

Results: The expression of exosome-marker proteins CD63 and CD81 was elevated in the AS patients compared to HC ($q < 0.05$). Cytokine profiling in plasma-derived AS-exosomes demonstrated downregulation of interleukin (IL)-8 and IL-10 ($q < 0.05$). AS-exosomes co-cultured with HC CD4+ T cells induced significant upregulation of IFNα2 and IL-33 ($q < 0.05$). Exosomes from AS patients inhibited the proliferation of regulatory T cells (Treg), suggesting a mechanism for chronically activated T cells in this disease. Culture of CD4+T cells from healthy individuals in the presence of AS-exosomes reduced the proliferation of FOXP3+Treg cells and decreased the frequency of FOXP3+IRF4+Treg cells. miRNA sequencing identified 24 differentially expressed miRNAs found in circulating exosomes of AS patients compared with HC; 22 of which were upregulated, and 2 were downregulated.

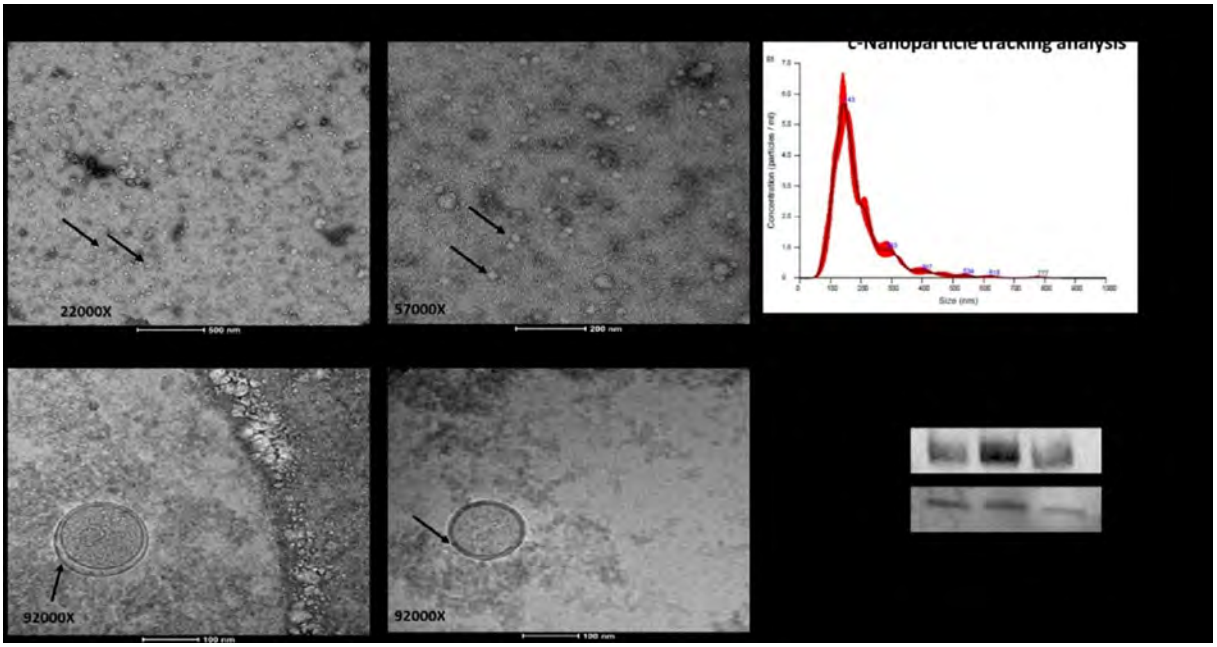

Figure 1. (a) Exosome characteristics with morphology, size, and markers. Exosomes display a round-shaped morphology in negative TEM. It is on 22000x magnification, demonstrating the density of isolated exosomes in plasma (b)and are bilayer and spherical by cryo-TEM imaging. (c) Exosome sizes can be determined using nanoparticle tracking. NTA was used to examine the exosome size and concentration, and the results showed that the exosomes had an average size of 147 nm. (d) Expression of the exosomal markers CD63 and CD9 was confirmed with Western blot.

Conclusion: Individuals with AS have different immunological and genetic profiles, as determined by evaluating the exosomes of these patients. The inhibitory effect of exosomes on Treg in AS suggests a mechanism contributing to chronically activated T cells in this disease.

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Abstract Number: 2440

Synovial Shaping of Skin-derived Migrating Immune Cells Determines Initiation of Inflammation in Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Basic Science

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Around 30% of the patients with psoriasis (PsO) develop psoriatic arthritis (PsA) overtime, suggesting the existence of a disease mediated skin-joint crosstalk. To date, it is still obscure why the inflammatory process in some patients with PsO is restrained to the skin, whereas in other patients it spreads to the joints. Using a pre-clinical model of PsA and PsO, we aimed to untangle the skin-joint axis and to address its role in PsA pathogenesis.

Methods: The IL-23 overexpression (IL-23OE) mouse model of PsO was performed in different genetic backgrounds of KAEDE-transgenic mice expressing a photo-convertible fluorescent reporter to assess cell trafficking from inflamed skin to the joints. Photoswitch from $KAEDE^{GREEN}$ to $KAEDE^{RED}$ of psoriatic skin lesions was obtained upon UV light irradiation. Skin-derived cell trafficking to the joints was detected by light sheet fluorescence microscopy (LSFM) and flow cytometry. Imaging flow cytometry was used to determine the immune nature of the migrating cells. Phenotypical characteristic of skin-derived migrating cells in joints was addressed by single-cell RNA-sequencing (scRNAseq) and functional assays. Data were validated in synovial biopsies from PsO and PsA patients by imaging mass cytometry.

Results: Psoriatic skin lesions were induced upon IL-23OE independently from the mouse strain, whereas the initiation of joint inflammation was dependent on the genetic background of the mice, as assessed by MRI scan and histological analysis. Immune cell migration from psoriatic skin to the joints was observed in both protected and non-protected mice from arthritis. ScRNAseq and computational analysis with RNA velocity approach indicates CD2+ MCHII+ monocytes as predominant cell type evading from the inflamed skin and entering the synovial tissue, with no frequency differences between PsO and PsA mice. No phenotypical differences were observed in the pre-differentiated stage of those monocytes in both, arthritis-protected and non-protected animals. However, once in the synovial tissue their further differentiation into macrophages resulted into two different phenotypes, with pro-inflammatory signatures in mice developing PsA. Interactome analyses between local differentiated skin-derived macrophages and tissue resident synovial cells highlighted the role of synovial sublining fibroblasts in shaping the fate of skin-derived macrophages into a protective phenotype without capacity to initiate the joint inflammatory process in PsO mice without arthritis. Imaging mass cytometry of synovial biopsies from patients with PsO and PsA identified niches of the synovial membrane that were either or not protected from inflammation by a similar fibroblastic fate as observed in the murine setting.

Conclusion: Skin derived monocytes play a major role in spreading the inflammation from psoriatic skin to the joints. However, it is upon interaction with the stromal-resident cells that the fate of the migrating monocytes is shaped towards joint protection or joint inflammation resembling PsA. These data might provide completely new diagnostic insights in assessing the risk of PsO patients to develop PsA.

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Abstract Number: 2441

Upregulation of RANKL in the Skin of Patients with Psoriatic Arthritis

Maria de la Luz Garcia-Hernandez[1], Takeshi Yoshida[2], Javier Rangel-Moreno[2], Alicia Lieberman[3], Ananta Paine[4], Joshua Weitz[2], Francisco Tausk[5], Lisa A Beck[2] and Christopher T Ritchlin[6], [1]University of Rochester, West Henrietta, NY, [2]University of Rochester, Rochester, NY, [3]University of Rochester, Batavia, NY, [4]ORNA Tx, Southborough, MA, [5]Universiy of Rochester, Rochester, NY, [6]University of Rochester Medical School, Allergy, Immunology & Rheumatology Division, Canandaigua, NY

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Basic Science

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic inflammatory disease that affects the skin and joints. Circulating Osteoclast precursors (OCP) are elevated in the blood of PsA patients and express Dendritic Cell-Transmembrane Protein (DC-STAMP), a protein essential for cell-cell fusion. Receptor Activator of Nuclear Factor kB Ligand (RANKL) is a pivotal effector driving osteoclastogenesis and is elevated in psoriatic synovium. Herein, we examined skin from PsO and PsA patients to determine if events in the skin trigger the differentiation of monocytes to OCPs.

Methods: We collected lesional (L) and non-lesional (NL) skin biopsies from 23 patients with Ps and 16 patients with PsA. We applied immunofluorescence to visualize and enumerate DC-STAMP$^+$ monocytes, CD3$^+$ TNF$^+$ IL17$^+$ cells and RANKL expression by dermal-infiltrating immune cells and keratinocytes. We also evaluated RANKL expression in CD45$^-$ skin cell suspension by flow cytometry and the induction of RANKL in keratinocytes activated with IL-17 and TNF by western blot analysis.

Results: We found significantly higher RANKL mRNA expression (PsA: 16.67-fold vs PsO: 1.7-fold, p = 0.001) and infiltration by RANKL$^+$ cells in PsA compared to PsO skin (PsA: 4.8% vs PsO: 2% p = 0.022). In addition, 43.75% of PsA L skin have RANKL expression in the epidermal cells but not PsO lesional skin biopsies. Skin cell suspensions showed higher RANKL$^+$ non-hematopoietic cells in L skin, compared to NL skin. We also found an increased number of dermal DC-STAMP$^+$CD14$^+$ OCP in the dermis of PsA plaques. CD3$^+$ T and IL17$^+$ cells were less abundant in PsA, compared to PsO L skin. We detected a higher TNF concentration in sera from PsA patients than Ps. Furthermore, incubation with both TNF and IL17, but not TNF or IL-17 alone, strongly induced RANKL expression on keratinocytes.

Conclusion: We find infiltration of DC-STAMP$^+$CD14$^+$ OCP in the skin of PsA but not Ps patients. Also, increased systemic TNF levels in PsA patients combined with IL17 upregulates RANKL$^+$ protein expression by non-hematopoietic cells. Thus, expression of RANKL by monocytes and keratinocytes in plaques of PsA patients demonstrate the ability to promote RANKL-dependent priming of OCP.

Disclosure: M. Garcia-Hernandez: None; **T. Yoshida**: None; **J. Rangel-Moreno**: None; **A. Lieberman**: None; **A. Paine**: None; **J. Weitz**: None; **F. Tausk**: None; **L. Beck**: None; **C. Ritchlin**: AbbVie, 2, 5, 6, Amgen, 2, BMS, 2, Eli Lilly, 2, Gilead, 2, Janssen, 2, Novartis, 2, Pfizer, 2, 5, 6, UCB, 2, 6.

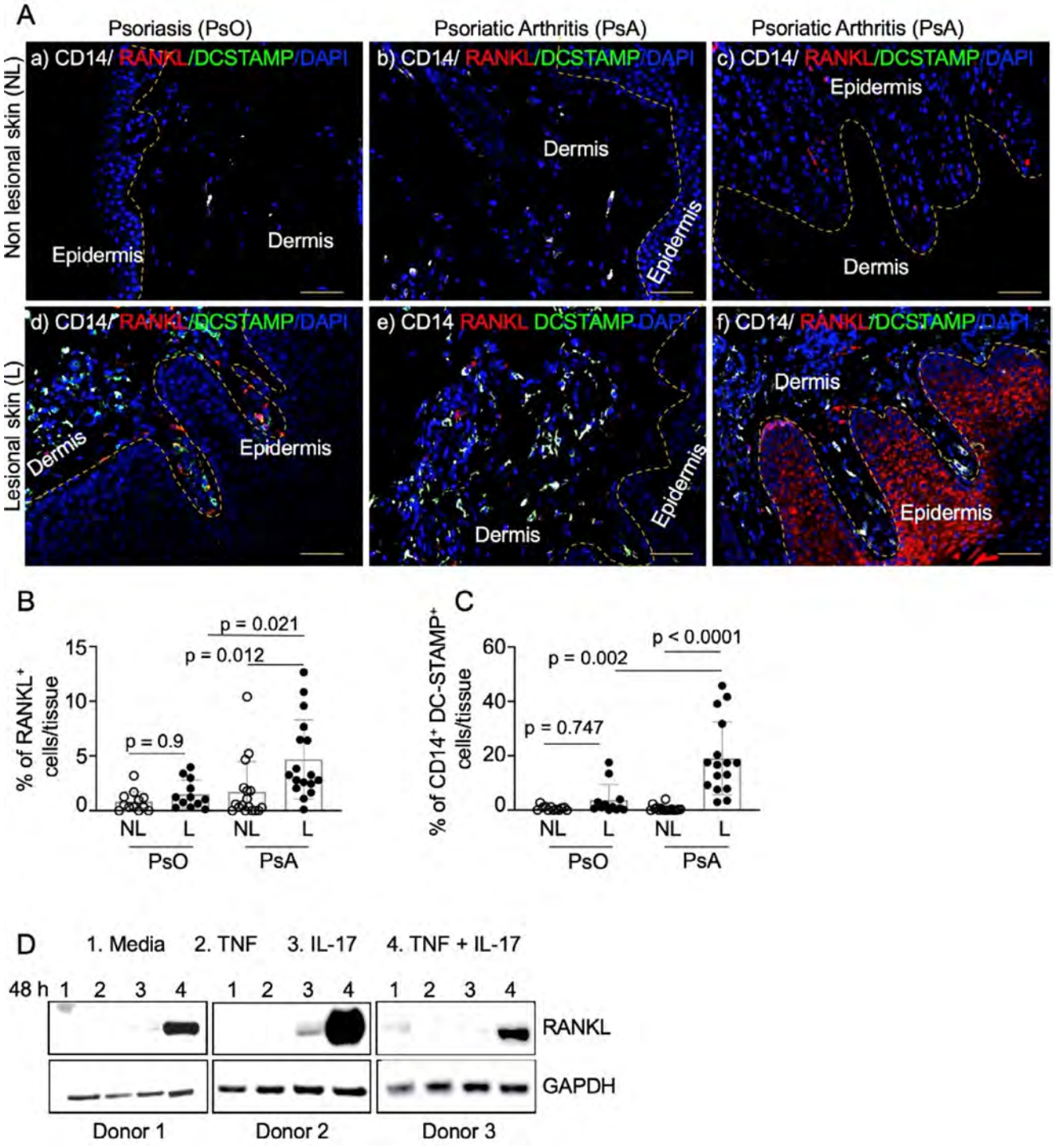

Figure 1. A) Exclusive RANKL ligand expression in PsA skin. A) Tissue sections from lesional and non-lesiona l skin biopsies were stained with antibodies against RANKL (red), CD14 (white) and DC-STAMP (green). Representative 200x magnification mosaic pictures taken with a Zeiss Axioplan microscope and recorded with Hamamatsu camera are shown. B) The morphometric analysis shows higher percentage of RANKL+ and C) higher percentage of DC-STAMP+ CD14+ cells (OCP) in PsA skin biopsies. Graphs show mean ± standard of 12 PsO and 16 PsA lesional and non-lesional skin biopsies. D) TNF and IL-17 cytokines induced the production of RANKL in vitro. Keratinocytes were isolated from neonatal foreskins. Cells were incubated during 48 hours with 20 ng/ml of human TNF and/or IL-17. Total protein was extracted and a western blot was performed with antibodies against RANKL or GAPDH as an internal control.

Abstract Number: 2442

Neutrophils Induce Contact-Dependent Expansion of Arthritogenic Th17 Cells and Are Necessary for Disease in Experimental Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Basic Science
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Ankylosing spondylitis (AS) patients have irregular neutrophil responses, as indicated clinically by neutrophilia and increased neutrophil to lymphocyte ratios that positively associate with disease activity. $CD4^+$ T helper cells that produce IL-17 (Th17 cells) drive the pathogenesis of AS, and IL-17 blockade is an effective therapy for this disease. Yet, a causative connection between neutrophils and induction of pathogenic Th17 responses in AS remains unknown.

Methods: Arthritis was induced by intraperitoneal injection of 1.5mg zymosan to female SKG mice pre-treated with neutrophil-depleting mAb 1A8 or an isotype control, and onset and severity of peripheral arthritis and axial disease was measured clinically. Neutrophils and CD4+ T cells were isolated from the bone marrow and spleen, respectively, of naïve SKG and WT mice. Zymosan-stimulated neutrophils and TCR-activated CD4+ T cells were co-cultured, together or separated by a 0.4-um pore transwell. IL-17A in supernatants was quantified by ELISA after 72h of co-culture. N=2-4 mice/experiment/genotype, experiments were repeated 3 times each. Statistical significance was calculated by multiple unpaired parametric student T tests.

Results: SKG mice developed Th17 responses and clinical arthritis as early as 5d post-zymosan exposure (pze). SKG mice-deplete of neutrophils showed decreased Th17 responses and undetectable arthritis 5d pze; thereby revealing neutrophils as a requirement for the onset of AS. SKG T cells co-cultured with stimulated neutrophils at a 1:2 (T cell:neutrophil) ratio produced 4.5-fold more IL-17A than SKG T cells cultured in the absence of neutrophils. While SKG neutrophils increased IL-17A production in a dose-dependent manner, WT neutrophils did not. Collectively, these data indicate that neutrophils are alone sufficient to expand Th17 cells. Intriguingly, the capacity of co-cultured neutrophils to potentiate Th17 cells was mitigated when physically separated in transwell plates, indicating that neutrophil-induced Th17 expansion works through a contact-dependent mechanism.

Conclusion: Our study suggests that activated SKG neutrophils interact physically with CD4+ T cells to induce potent arthritogenic Th17 responses. Understanding the intersection between innate and adaptive cellular mechanisms in AS pathogenesis will elucidate novel therapeutic targets for treatment of disease.

Disclosure: H. Struthers: None; **E. Vance**: None; **K. Asare-Konadu**: None; **H. Rosenzweig**: None; **R. Napier**: None.

Abstract Number: 2443

Blockade of OX40/OX40L Signaling Using anti-OX40L Ameliorates Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: SLE – Animal Models
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Genetic variations in the OX40 ligand (OX40L) locus have been implicated in the susceptibility to systemic lupus erythematosus (SLE). Notably, the blockade of OX40L has demonstrated promising effects in mitigating renal damage and suppressing autoantibody production in NZB/W F1 mice, a commonly used model for SLE. Despite these encouraging findings, the precise mechanisms by which OX40L blockade exerts its delaying effect on the lupus phenotype remain elusive, warranting further investigation and exploration.

Methods: In the present study, we conducted an investigation to assess the effects of OX40L blockade using anti-OX40L in the MRL/lpr murine model of lupus, a well-established experimental system. The mice were categorized into three groups, each consisting of 9-11 individuals: IgG treatment, Cyclophosphamide (CTX) treatment, and anti-OX40L treatment. Following the respective treatments, the mice were sacrificed, and samples of serum, kidney, and spleen were collected for comprehensive outcome evaluation.

Subsequently, we explored the impact of anti-OX40L treatment on immunosuppression in 8-week-old C57BL/6J mice that were immunized with KLH. This was accomplished through the measurement of serum immunoglobulins (Igs) and flow cytometry analysis of splenocytes. Additionally, *in vitro* experimentation involving the treatment of anti-OX40L in $CD4^+$ T cells and $CD19^+$ B cells was conducted to elucidate the roles of OX40L in the pathogenesis of SLE.

Results: In the current study, we have made significant observations regarding the impact of blocking OX40L in MRL/lpr mice, a murine model of lupus. Notably, treatment with anti-OX40L resulted in a remarkable delay in disease progression, as evidenced by reduced production of anti-dsDNA antibodies, decreased proteinuria, and diminished Ig deposition in the kidney. Additionally, we observed lower frequencies of Th1 and Tfh cells in the spleen of anti-OX40L-treated mice compared to the IgG-treated group.

Furthermore, our *in vitro* experiments revealed that anti-OX40L treatment promoted the up-regulation of polyclonal $CD4^+$ T cell differentiation into regulatory T cells (Tregs). This finding suggests a potential mechanism through which anti-OX40L exerts its beneficial effects. In KLH-immunized mice, the administration of anti-OX40L resulted in decreased levels of immunoglobulins (Igs) and reduced numbers of plasmablast cells, further supporting the immunosuppressive effects of OX40L blockade.

Interestingly, we also found that blocking OX40/OX40L signaling inhibited the TLR7-mediated differentiation of antibody-secreting cells (ASCs) and antibody production. This effect was accompanied by the up-regulation of SPI-B, IRF8, and PAX5, as well as the down-regulation of Xbp-1 in B cells, indicating the involvement of multiple regulatory factors in this process.

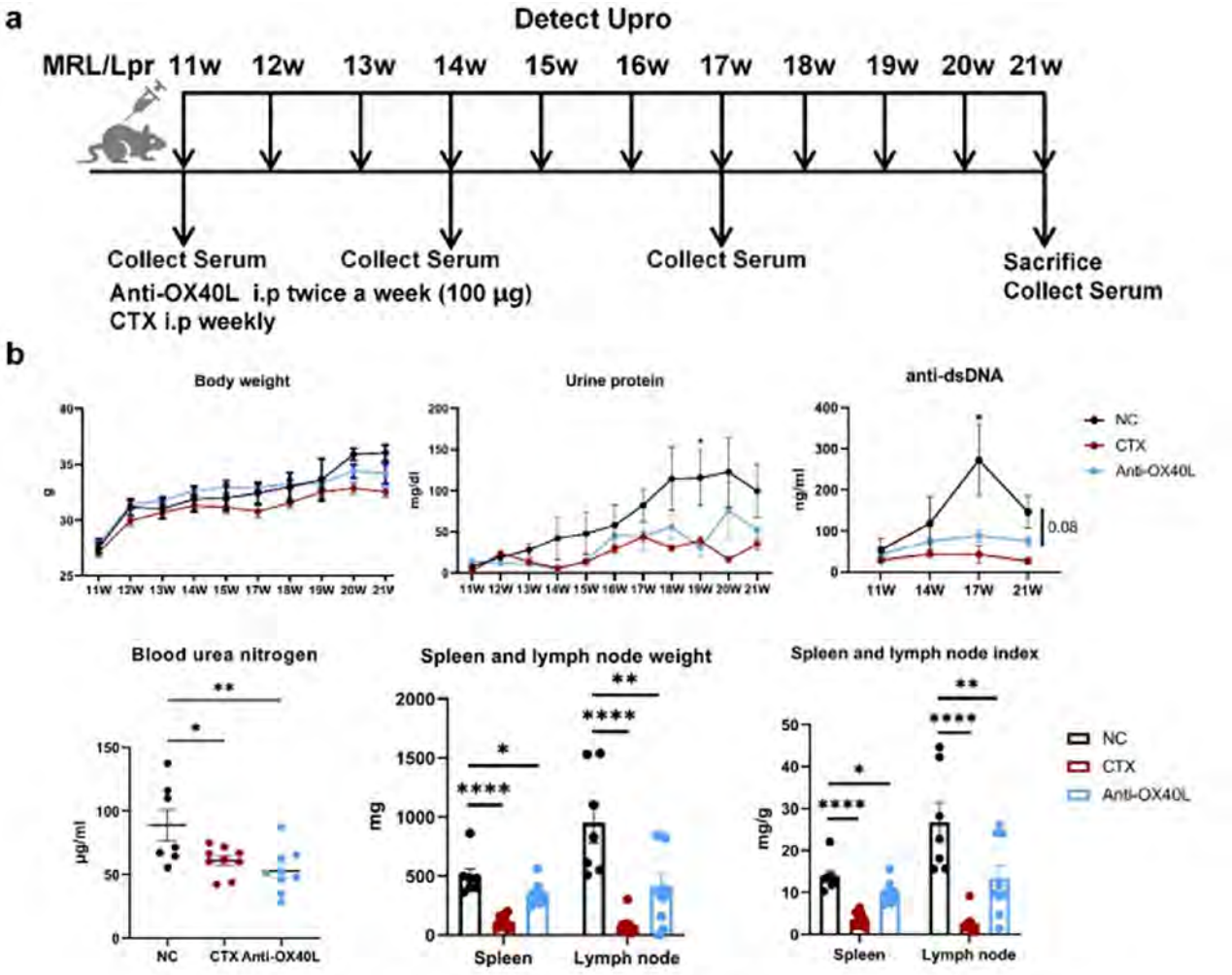

Fig. 1. Anti-OX40L ameliorates the lupus progression. **(a)** A schematic of the treatment of anti-OX40L in MRL/Lpr mice. **(b)** Body weight, urine protein, anti-dsDNA (IgG), blood urea nitrogen, spleen and lymph node weigh, as well as spleen and lymph node index were shown. Horizontal bars represent the mean ± SEM. n = 11 in MRL/Lpr group+ IgG isotype control (NC) (4 mice died); n = 10 in MRL/Lpr + CTX treated group (1 mouse died); n = 11 in MRL/Lpr + Anti-OX40L treated group (2 mice died). $*p < 0.05$, $**p < 0.01$, $***p < 0.001$, $****p < 0.0001$.

Conclusion: The results obtained from our study, along with the extensive evidence from previous investigations, underscore the potential of blocking OX40L as an effective strategy to mitigate disease progression and alleviate the pathological manifestations of SLE.

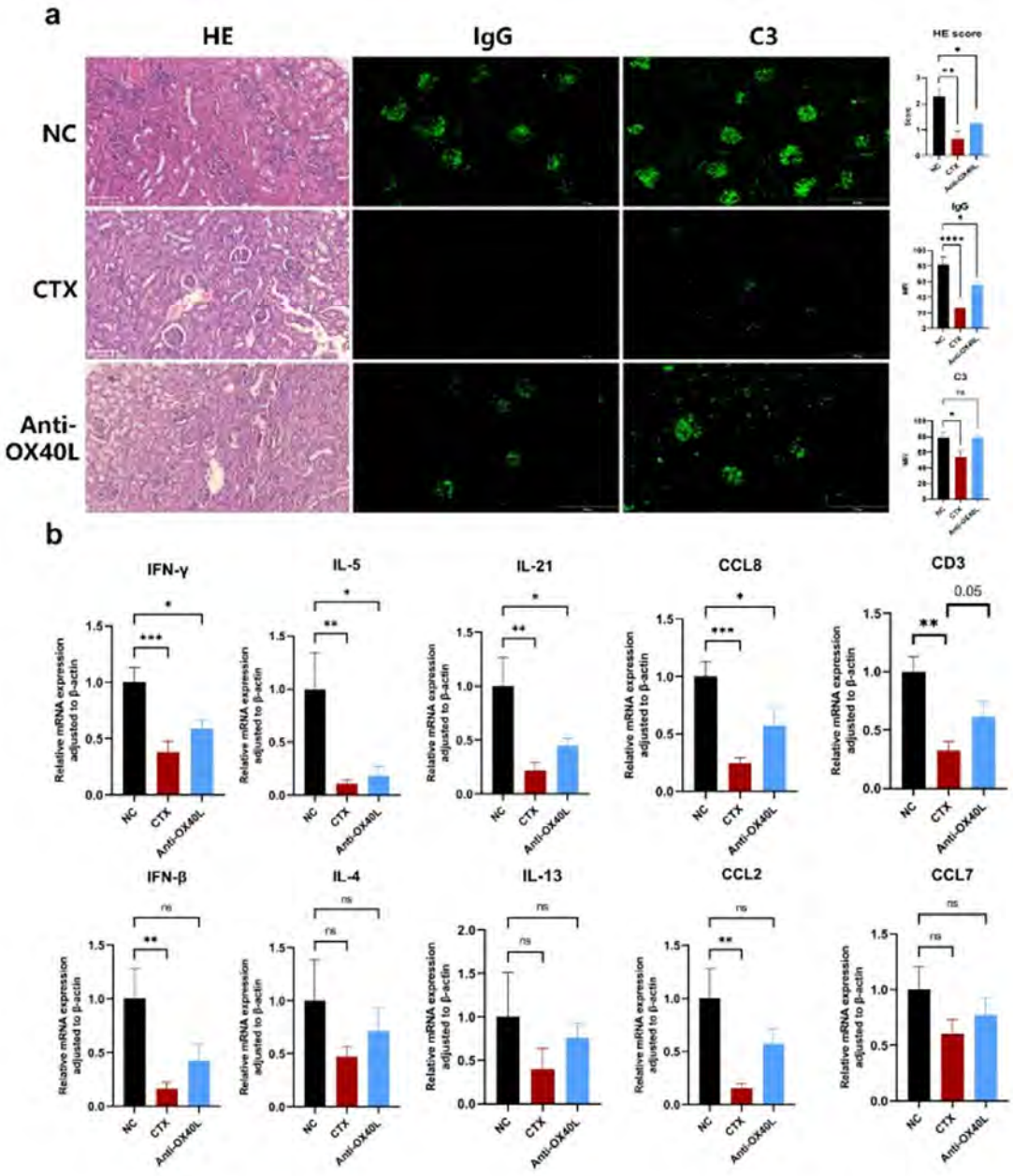

Fig. 2. Anti-OX40L improves histological damage, reduces immune-complex deposition, and controls inflammatory response in MRL/Lpr mice. **(a)** H&E staining, IgG and C3 deposition in the of kidney MRL/lpr mice. **(b)** Anti-OX40L treatment reduced renal mRNA levels of pro-inflammatory cytokines (INF-γ, IL-5, IL-21), chemokine (CCL8), and marker of inflammatory cell (CD3) in MRL/Lpr mice. Horizontal bars represent the mean ± SEM. n = 11 in MRL/Lpr group+ IgG isotype control (NC) (4 mice died); n = 10 in MRL/Lpr + CTX treated group (1 mouse died); n = 11 in MRL/Lpr + Anti-OX40L treated group (2 mice died). $*p < 0.05$, $**p < 0.01$, $***p < 0.001$.

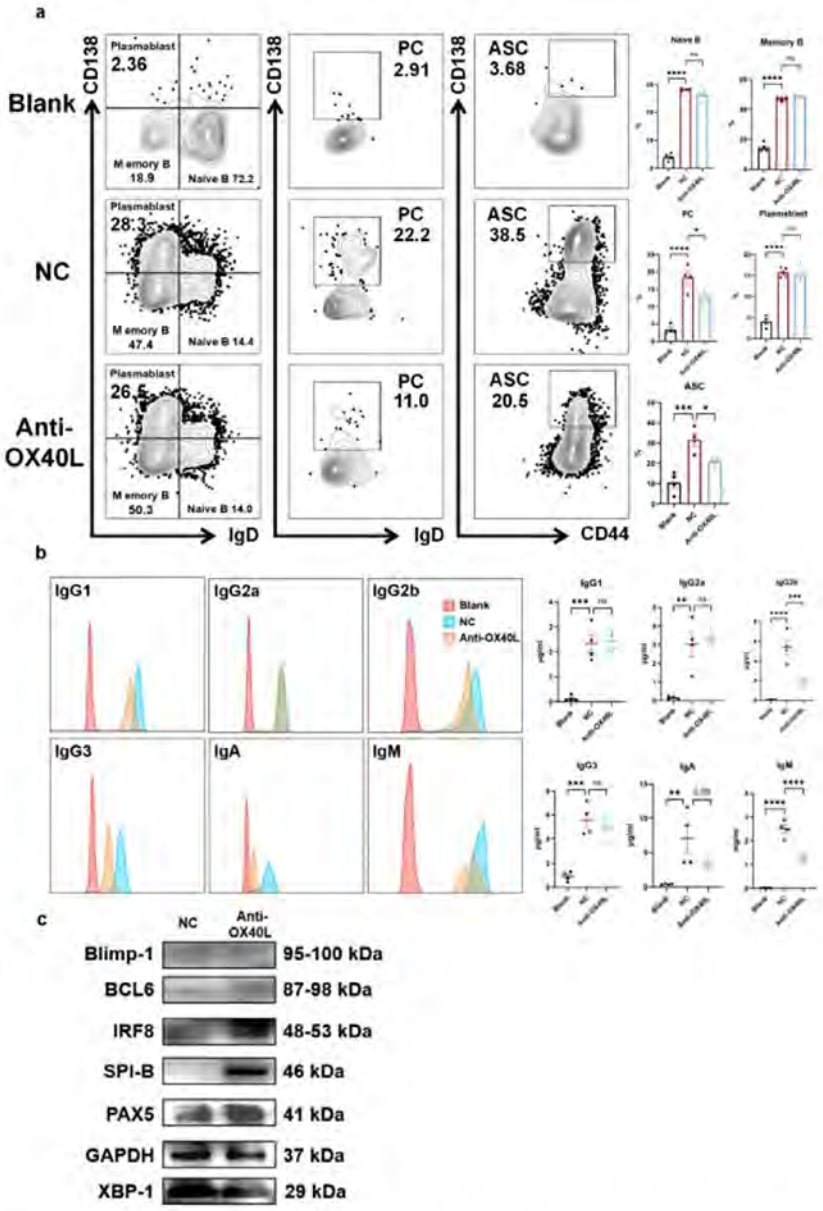

Fig. 6. Anti-OX40L inhibits TLR7-mediated differentiation of ASCs and antibody production through up-regulation of SPI-B, IRF8, and PAX5, and down-regulation of Xbp-1. **(a)** Representative flow cytometry diagrams and statistical analysis of the percentages of naïve B cells, memory B cells, plasmablast cells, plasma cells, and ASCs ($CD44^{hi}$ $CD138^{-}$) in the splenic B cells stimulated by R848 and IL-4. **(b)** The levels of IgG1, IgG2a, IgG2b, IgG3, IgA, and IgM from the splenic B cell supernatant after 72 h of culture. **(c)** Regulation of key transcription factors related to B-cell proliferation and differentiation after anti-OX40L treatment for 48 h. Horizontal bars represent the mean + SEM. $*p < 0.05$, $**p < 0.01$, $***p < 0.001$, $****p < 0.0001$.

Disclosure: J. Zhao: None; **L. Li**: None; **X. Feng**: None; **H. Yin**: None; **Q. Lu**: None.

Abstract Number: 2444

Development of Engineered Smith-Specific Regulatory T Cells to Treat Lupus Nephritis

Eric Morand[1], Rachel Cheong[2], Peter Eggenhuizen[2], Janet Chang[2], Ashraf Broury[2], Boaz Ng[2], Khai Loh[2], Elean Tay[2], Chanjuan Shen[3], Julie Monk[2], Yong Zhong[4], Steven Lim[2], Jia Xi Chung[2], Rangi Kandane-Rathnayake[5], Rachel Koelmeyer[2], Alberta Hoi[6], Sarah Snelgrove[2], Yi Tian Ting[2] and Joshua Ooi[2], [1]Monash University, Centre for Inflammatory Diseases, Melbourne, Australia, [2]Monash University, Clayton, Australia, [3]Central South University, Changsha, China, [4]Xiangya Hospital, Central South University, Changsha, China, [5]Monash University, Department of Medicine, Sub-faculty of Clinical and Molecular Medicine, Clayton, Australia, [6]Monash University, Department of Medicine, Sub-faculty of Clinical and Molecular Medicine, Melbourne, Australia

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: SLE – Animal Models

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Regulatory T cells (Tregs) play an important role in maintaining immune system homeostasis. Antigen-specific Tregs potently and specifically suppress autoreactivity, suggesting their potential to be engineered to treat autoimmune diseases. Lupus nephritis (LN) is a severe manifestation of SLE associated with the presence of anti-Smith (Sm) autoantibodies as well as the HLA haplotypes DR15 and DR3, with the majority of patients DR15. Due to the strong association of LN with anti-Sm and HLA-DR15, we developed Sm-specific Tregs for potential treatment of LN.

Methods: We identified DR15-restricted Sm T cell epitopes using a physical affinity binding assay. T cell receptors (TCRs) specific for Sm epitopes were identified by co-culturing CD4+ T cells with dendritic cells from HLA-DR15+ healthy donors and Sm epitopes, and sequencing proliferating CD4+ T cells using high-throughput 10X single cell V(D)J sequencing. TCRs were ranked based on clonal expansion, cloned into a lentiviral vector then transduced onto primary SLE patient Tregs. Sm-specific Tregs were evaluated for suppression of T effector cell function in vitro and in a humanised model of LN created by the transfer of PBMCs from anti-Sm positive HLA-DR15+ SLE patient into NSG-MHC-null mice.

Results: The top three Sm epitopes identified were SmB/B'$_{58\text{-}72}$, SmB/B'$_{1\text{-}15,}$ and SmD3$_{43\text{-}57}$; the respective stability indices (SI) were 16.0, 1.4 and 1.2. Highly reactive TCRs specific for SmB/B'$_{58\text{-}72}$ were identified and the highest ranked SmB/B'$_{58\text{-}72}$ reactive TCR was cloned into a lentiviral vector then transduced onto primary SLE patient Tregs, resulting in Sm-Tregs. In *in vitro* co-cultures of SLE patient PBMCs with SmB/B'$_{58\text{-}72}$, Sm-Tregs, but not polyclonal Tregs induced 90% suppression of pro-inflammatory cytokine secretion (IFN-g (pg/mL): control 39.7±11.4, polyclonal Tregs 37.3±12.6, Sm-Tregs 2.7±1.0, $p< 0.05$; IL-17A (pg/mL): control 26.3±2.9, polyclonal Tregs 17.0±2.7, Sm-Tregs 2.4±0.6, $p< 0.01$) while Sm-Tregs produced significantly more IL-10 ($p< 0.01$). Transfer into NSG-MHC-null mice of Sm+ HLA-DR15+SLE patient PBMCs, but not healthy HLA-DR15+ PBMC, induced an LN phenotype characterised by proteinuria and histological glomerular necrosis. Treatment with Sm-Tregs halted the progression of functional and histological injury in this model (proteinuria: control 3.6±0.2, polyclonal Tregs 3.2±0.2, Sm-Tregs 1.2±0.2, $p< 0.01$; glomerular segmental necrosis: control 75.2±2.9%, polyclonal Tregs 61.2±6.3%, Sm-Tregs 14.4±1.9%, $p< 0.001$).

Conclusion: Antigen-specific Tregs generated against an immunodominant Sm peptide were highly efficient at suppressing Sm-specific T effector responses. HLDA-DR15+Sm+ SLE patient PBMC induced a model of LN, in which Sm-Tregs were therapeutic. Autologous Sm-Treg cell therapy is a promising treatment for LN, and other antigen-specific autoimmune diseases could be similarly targeted.

Disclosure: E. Morand: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 2, 5, 6, Biogen, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, EMD Serono, 2, 5, Galapagos, 2, Genentech, 2, 5, GlaxoSmithKline, 2, 5, IgM, 2, Janssen, 2, 5, Novartis, 2, Servier, 2, Takeda, 2, UCB, 5; **R. Cheong**: None; **P. Eggenhuizen**: Amgen, 5; **J. Chang**: None; **A. Broury**: None; **B. Ng**: None; **K. Loh**: None; **E. Tay**: None; **C. Shen**: None; **J. Monk**: None; **Y. Zhong**: None; **S. Lim**: Bio-Rad, 6, Sony Biotechnology, 6; **J. Chung**: None; **R. Kandane-Rathnayake**: None; **R. Koelmeyer**: None; **A. Hoi**: Abbvie, 6, AstraZeneca, 5, Australian Rheumatology Association, 4, Eli Lilly, 6, EUSA Pharma (UK) Limited, 2, Limbic, 6, Moose Republic, 6, Novartis, 6; **S. Snelgrove**: None; **Y. Ting**: None; **J. Ooi**: Amgen, 5, 10.

Abstract Number: 2445

Targeting of Endothelial Dysfunction in Lupus Nephritis: Effect on Human Renal Endothelial Cell Gene Expression and Outcomes in Murine Lupus Nephritis

Dayvia Russell[1], Sandra Sanchez[2], Evelyn Bruner[2] and Jim Oates[2], [1]Ralph H. Johnson VA Medical Center, Charleston, SC, [2]Medical University of South Carolina, Charleston, SC

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: SLE – Animal Models
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Lupus nephritis (LN) constitutes one of the most severe manifestations of systemic lupus erythematosus (SLE). Evidence points to endothelial nitric oxide synthase (eNOS) uncoupling, which induces oxidation-mediated changes in gene transcription, as a mechanism leading to chronic endothelial cell dysfunction (ECD) and damage in LN. Treatment with sepiapterin (L-Sep), which induces coupling of eNOS, restores endothelial function in lupus serum-treated endothelial cells. The aim of this study was to determine whether treatment with L-Sep could improve outcomes in a murine model of LN, and to better understand the protective mechanism of L-Sep by identifying genes involved in inflammatory redox pathways in human LN that are regulated by L-Sep.

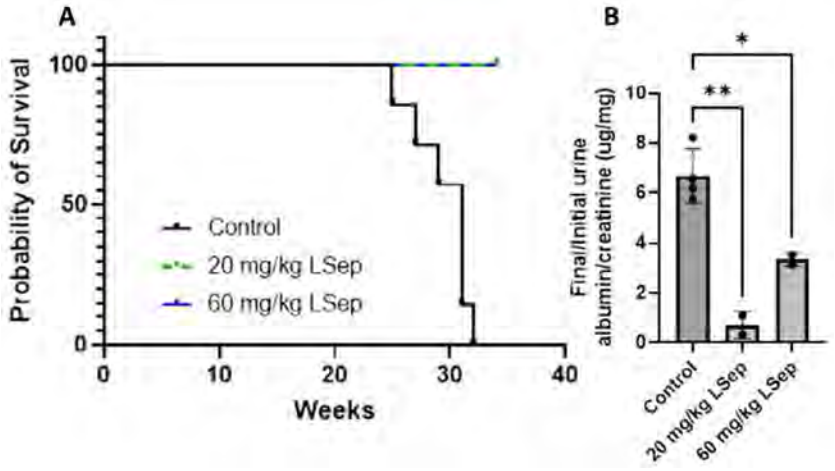

Figure 1. Survival and proteinuria in mice treated with vehicle or L-sepiapterin (LSep). Mice were treated (0, 20, or 60 mg/kg/day L-Sep) at the onset of trace proteinuria for five weeks. A) Survival (lack of death or severe illness requiring euthanasia) by age of mouse and treatment group B) 24-hour urine albumin/creatinine were collected at baseline and 5 weeks of therapy and reported as a ratio of 5wk/baseline values.

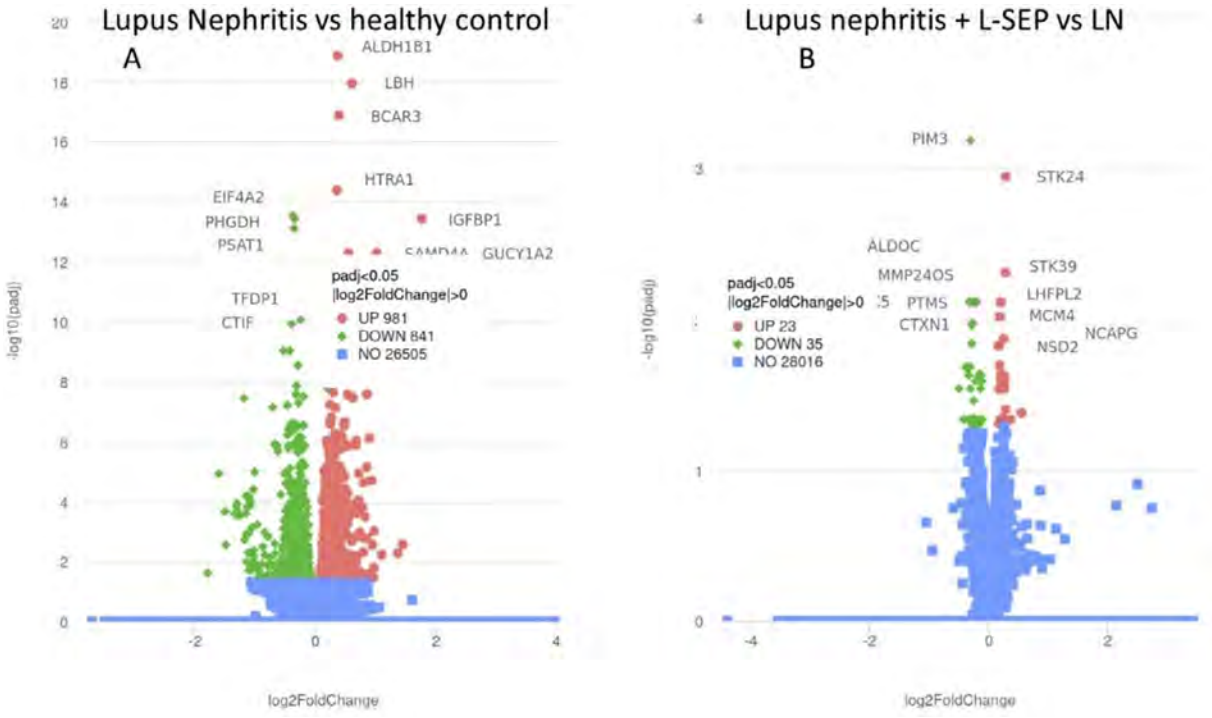

Figure 2. Volcano plot from human glomerular endothelial cell gene expression fold change versus -log10(p value adjusted). Human glomerular endothelial cells were treated with 10% serum for 3 hours. A) volcano plot of differential gene expression of cells treated with lupus nephritis (LN) flare serum versus healthy control serum (n=5) B) volcano plot of differential gene expression from cells treated with either LN flare serum or LN flare serum with L-Sep.

Methods: Female NZM2410/J mice, a model of lupus nephritis, were examined for the onset of trace proteinuria, at which time mice were randomized into treatments groups of vehicle, 20 mg/kg/day L-Sep, or 60 mg/kg/day L-Sep. Urine proteinuria was assessed weekly, and histopathological grading of kidneys using NIH activity and chronicity indices, along with C3 and IgG renal expression were examined after five weeks of treatment. Kaplan-Meier curves and log-rank test were applied to assess survival. One-way ANOVA with Tukey's multiple comparisons test was used to determine differences in proteinuria.

Human renal glomerular endothelial cells (HRGECs) were grown to confluence in media containing 10% human healthy control (HC) serum (n=5, negative for connective tissue disease), or lupus nephritis serum (n=5, class IV LN, collected at the time of induction of therapy) +/- 5 μM L-Sep. After three hours of culture, RNA was extracted, and RNA sequencing, using NovaSeq PE 150, was performed to determine differentially expressed genes between LN and HC treated cells and between LN and LN + LSep treated cells.

Results: Mice receiving L-Sep showed improved urine albumin/creatinine from five weeks/start of treatment compared to those receiving vehicle (p=0.001 for vehicle vs. 20 mg/kg L-Sep; p=0.017 for vehicle vs. 60 mg/kg L-Sep), along with enhanced survival as demonstrated by Kaplan-Meier curves and log rank test. Kidney sections from mice receiving L-Sep (n=3) had lower renal activity (0.0 ± 0.0 vs. 4.6 ± 1.1, p = 0.004) and chronicity scores (2.3 ± 2.1, p = 0.23) than mice treated with 20 (n=2) or 60 (n=2) mg/kg/day L-Sep.

RNA sequencing revealed that genes involved in oxidative-stress and hypertension were differentially upregulated in HRGECs cultured with LN serum compared to Healthy Control (HC) serum (STK24, padj= 0.001; STK39, padj= 0.005). PIM3, which increases eNOS expression, was the most significantly downregulated gene in LN compared to HC

(padj=0.0006). HRGECs treated with L-Sep had increased expression of syndecan-4 (SDC4) (padj=2.49E-11), a component of the glycocalyx that functions to protect ECs.

Conclusion: This study suggests L-Sep, a drug that restores eNOS coupling, may be beneficial in the treatment of LN, in part by preventing activity and fibrosis in the kidney. Differential gene expression analysis suggests that redox-regulated genes are increased with LN serum treatment, while L-Sep may improve endothelial barrier function by inducing syndecan 4 expression.

Disclosure: D. Russell: None; **S. Sanchez**: None; **E. Bruner**: None; **J. Oates**: None.

Abstract Number: 2446

Intermittent Fasting Attenuates Cognitive Dysfunction in Murine Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: SLE – Animal Models
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Cognitive dysfunction is one of the most common manifestations of neuropsychiatric systemic lupus erythematosus (NPSLE) and severely affects patients' health-related quality of life. Intermittent fasting (IF) has been shown promising therapeutic effects in neurodegenerative diseases. In this study, we evaluated the impact of intermittent fasting on cognitive function in lupus-prone mice.

Methods: MRL/lpr mice, as an animal model for studying NPSLE, can spontaneously exhibit cognitive dysfunction. After 8 weeks of alternate-day fasting, novel object recognition and Morris water maze tests were used to assess cognitive manifestation. The number of microglia (IBA-1^{+}) was evaluated by immunofluorescence staining. Expression levels of IL-1β, IL-6 and TNF-α were detected by qRT-PCR. The blood-brain barrier permeability and autophagy levels were evaluated by western blotting.

Results: We found that IF improves cognitive function of MRL/lpr mice in the behavioral tests. IF also decreased hippocampal microglia activation and expression of inflammatory cytokines in MRL/lpr mice. In addition, we demonstrated that IF reduced blood-brain barrier permeability. Furthermore, IF inhibited mTOR signaling and increased autophagy levels.

Conclusion: These data indicate that IF improves cognitive function in lupus-prone mice.

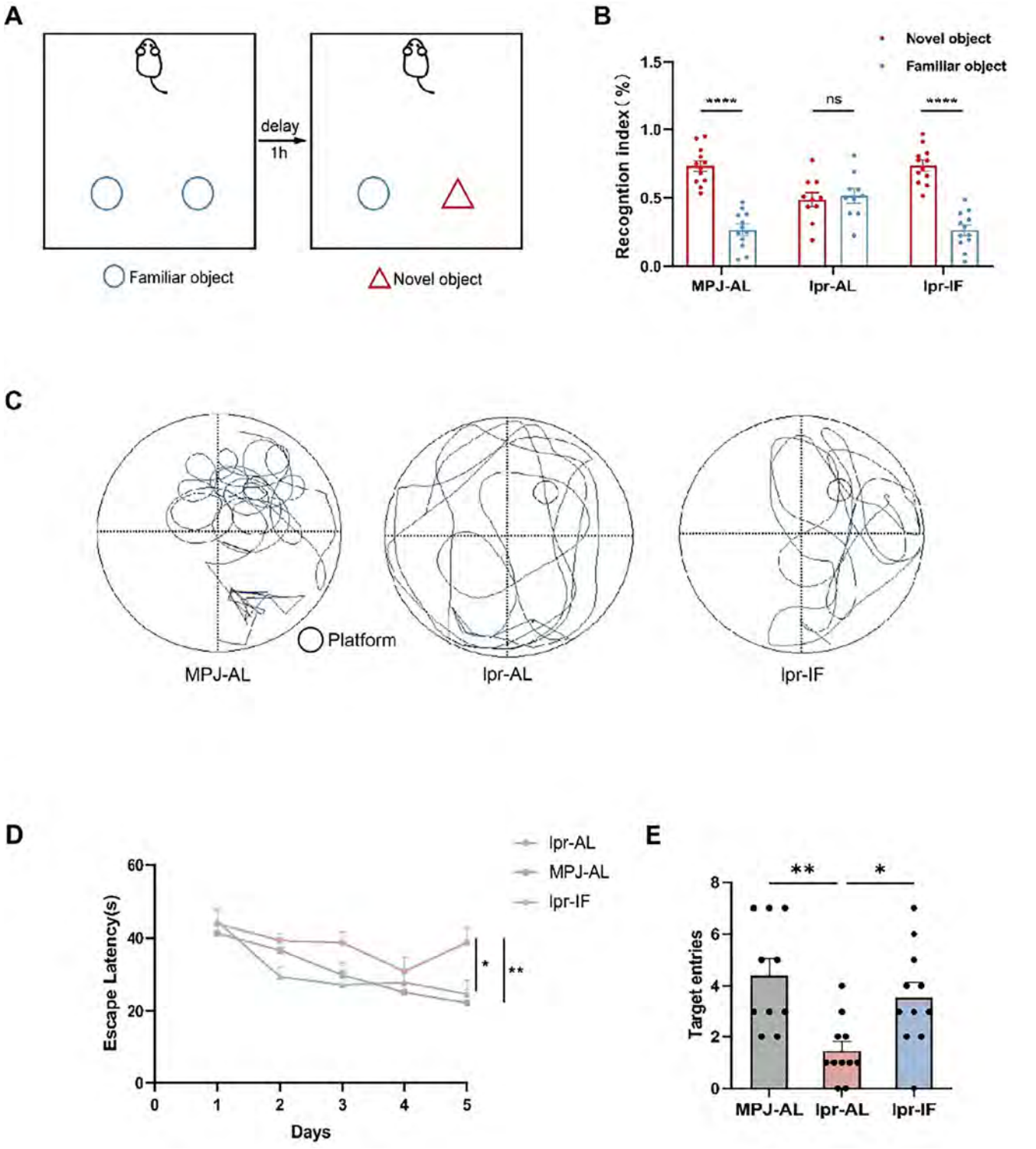

Fig.1 IF improves cognitive function of MRL/lpr mice.A:The experimental procedure of the novel object recognition test.B: The test recognition index of mice (n = 10-12 mice per group).C:The represent image of day6 in the Morris water maze test.D:The escape latency to the platform of day1-5.E:The target entries of day6.The data are represented as the mean ± standard error of the mean. *P < 0.05, **P < 0.01, ***P < 0.001 and ****P < 0.0001; NS, not significant.

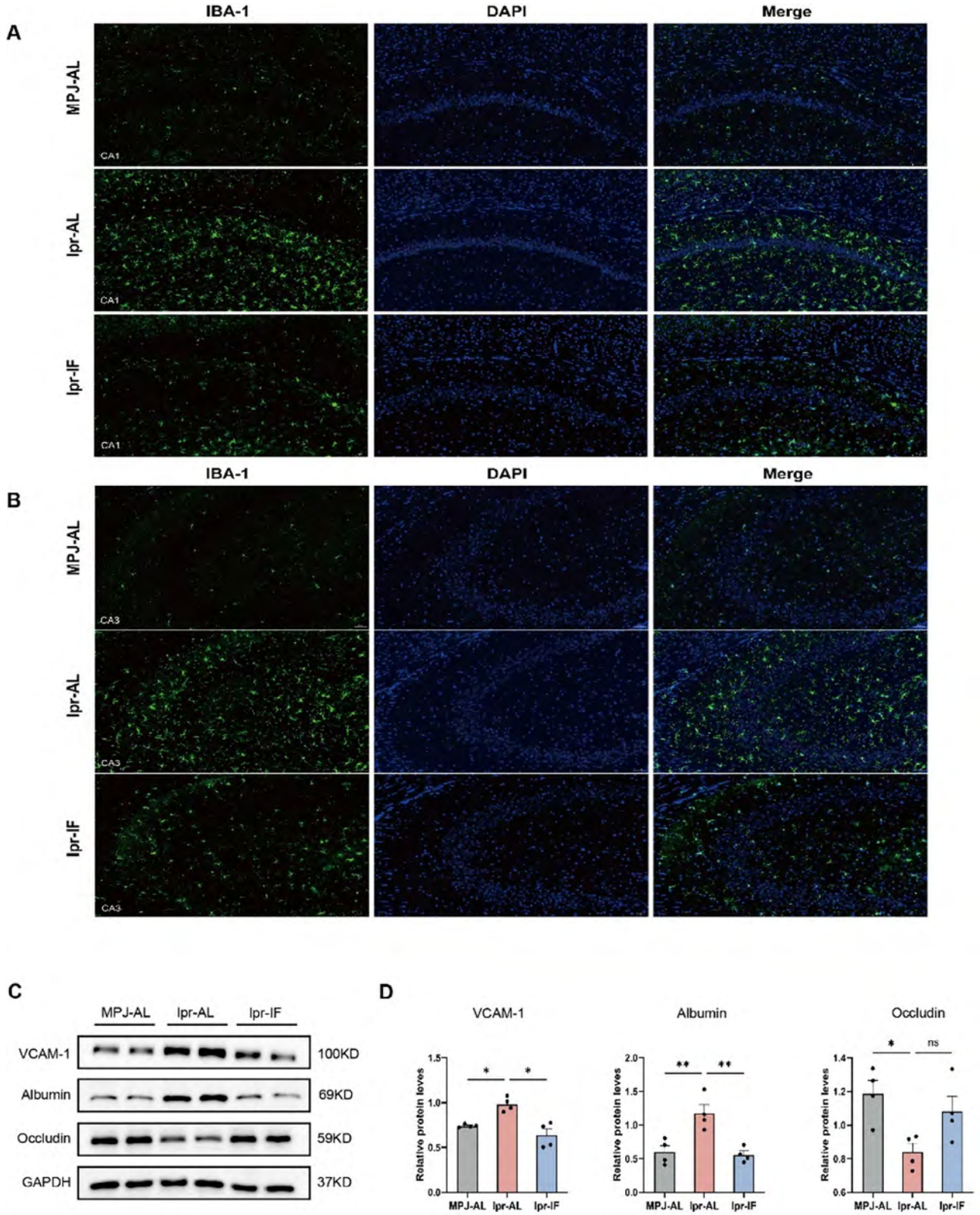

Fig.2 IF decreased hippocampal microglia activation and blood-brain barrier permeability of MRL/lpr mice.A-B:The represent image of microglia (IBA-1+) in the CA1 and CA3 of hippocampal.C:Western blotting analysis of proteins in the brain of mice.D:The quantification of indicated protein levels shown in A (n = 4 mice per group).

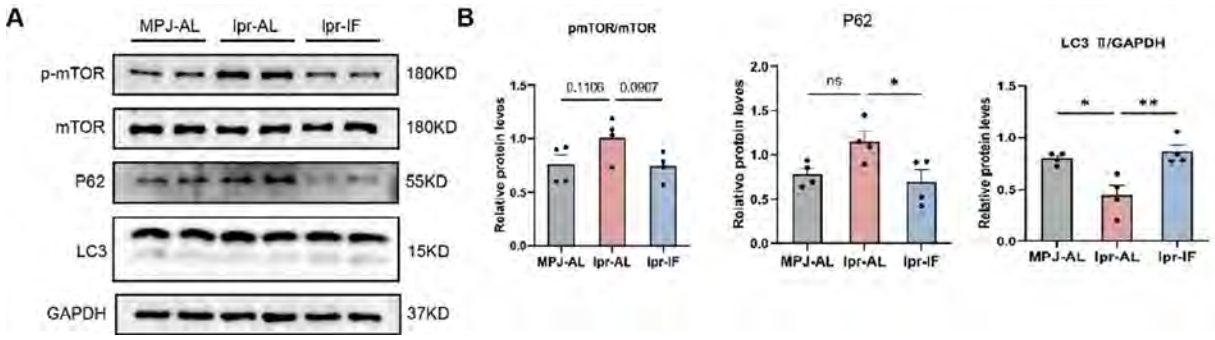

Fig.3 IF inhibited mTOR signaling and increased autophagy levels of MRL/lpr mice.A:Western blotting analysis of proteins in the hippocampal of mice.B:The quantification of indicated protein levels shown in A (n = 4 mice per group).

Disclosure: Y. Feng: None; **J. Qin**: None; **L. Zheng**: None; **H. Ren**: None; **M. Yang**: None; **Q. Huang**: None.

Abstract Number: 2447

Interleukin-6 Activates Glial Cells and Induces Cognitive Dysfunction in Murine Neuropsychiatric Lupus

Joshua Reynolds[1], Michelle Huang[1], Myriam Meineck[2], Tamara Möckel[2], Andreas Schwarting[2] and **Chaim Putterman**[1], [1]Albert Einstein College of Medicine, Bronx, NY, [2]University Medical Center of the Johannes Gutenberg University of Mainz, Mainz, Germany

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: SLE – Animal Models
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Up to 50% of SLE patients experience neuropsychiatric involvement (neuropsychiatric lupus, or NPLSE) in the form of cognitive deficits, memory loss, depression, and anxiety. The pathogenic mechanisms of NPSLE have yet to be firmly established. Since current non-specific treatment regimens in NPSLE often fail to improve symptoms, identifying novel and more targeted interventions is necessary to improve patient care. Cerebrospinal fluid and serum levels of the inflammatory cytokine interleukin-6 (IL-6) are increased in NPSLE patients and lupus mice. Excessive IL-6, possibly entering the brain from the serum, could promote neuroinflammation by activating glial cells, including astrocytes and microglia. We aimed to assess this putative mechanism, hypothesizing that knocking out IL-6 in lupus mice would ameliorate NPSLE.

Methods: Female MRL/lpr mice exhibit severe lupus-like disease and neuropsychiatric deficits. To investigate the association of IL-6 with NPSLE, we compared serum levels of IL-6 with behavioral testing scores in 18-week-old MRL/lpr mice. Object placement (OP) and object recognition (OR) tests measured novelty preference to assess cognition and memory (increased scores indicate improved performance). Social preference (SP), Porsolt swim, tail suspension, and elevated plus maze (EPM) measured murine correlates of anxiety and depression. We repeated this battery in two separate cohorts of 14- to 18-week-old IL-6 knockout (KO; n = 7 + 8) and age-matched wildtype (WT; n = 7 + 8) MRL/lpr mice. Systemic disease was assessed by serum levels of anti-dsDNA antibodies. We measured gene expression of *gfap*, an astrocytic activation marker, and *aif1*, a microglial marker, in right-hemispheric cortical tissue by real-time qPCR. Results were compared between KO and WT using two-tail Mann-Whitney u- or Student's t-tests when appropriate, with a p-value threshold of 0.05.

Results: Elevated serum IL-6 correlated with worse spatial memory as measured by the OP task (n = 8; r = -0.76, p = 0.037; Fig 1A), but not with the depression or anxiety tasks. Serum anti-dsDNA antibody titers (Fig 1B) did not significantly differ between IL-6 KO mice and WT controls (p = 0.130). MRL/lpr IL-6 KO mice showed significantly increased novelty preference on OP (KO: 57.87 +/- 3.15; WT: 45.37 +/- 2.29, p = 0.002; Fig 1C) and OR (KO: 67.91 +/- 3.62; WT: 48.93 +/- 4.34; p = 0.003; Fig 1D). No difference was found on SP (p = 0.838), Porsolt swim (p = 0.161; Fig 1E), tail suspension (p = 0.325), or EPM (p = 0.890). Expression of both glial genes, *gfap* (KO: 1.03 +/- 0.15; WT: 1.49 +/- 0.16; p = 0.037) and *aif1* (KO: 0.59 +/- 0.05; WT: 0.84 +/- 0.09; p = 0.036), were decreased in whole cortex samples from IL-6 KO mice compared to WT (Fig 1F).

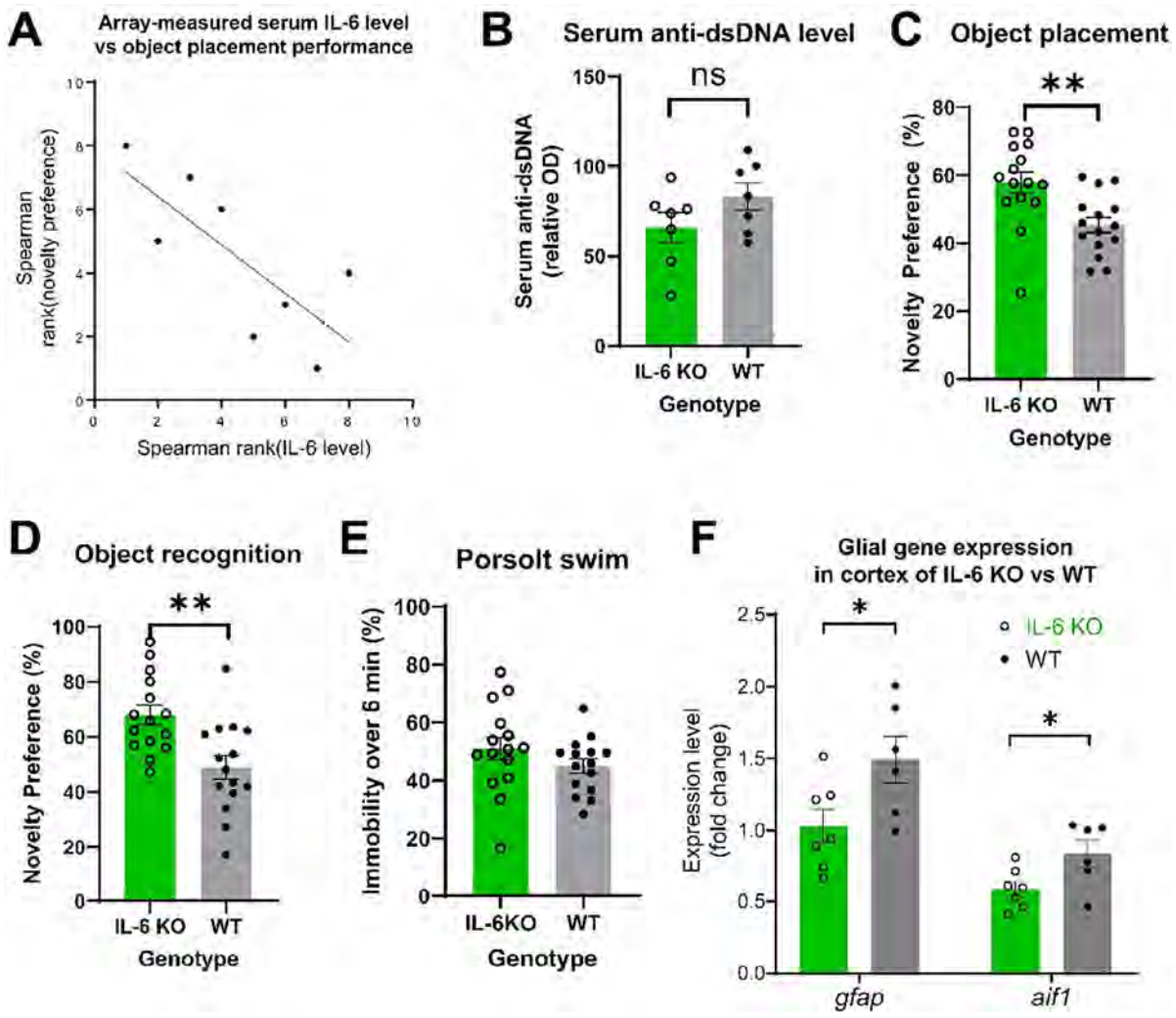

Figure 1. Role of IL-6 in murine neuropsychiatric lupus. To explore the pathogenic potential of IL-6 in NPSLE, we measured serum IL-6 in unmanipulated MRL/lpr mice (panel A). Cognitive and affective features of murine neuropsychiatric lupus were studied in IL-6 knockout (IL-6 KO) and littermate control (WT) MRL/lpr mice using a standard neurobehavioral battery (panel C-F). Object placement and object recognition tasks assess a mouse's preference for a novel object. Each task relies on intact spatial memory or identification memory, respectively; less novelty preference equates to worse cognitive performance. Porsolt swim is a validated measure of murine depressive-like behavior, wherein a mouse with worse disease spends more time immobile when placed in a tank of water (behavioral despair). A) There is a significant correlation between serum IL-6 levels and object placement novelty preference in unmanipulated MRL/lpr mice (n = 8; r = -0.76; p = 0.037). B) Systemic disease burden, as measured by serum anti-dsDNA antibody levels determined by ELISA (OD: optical density), did not differ between IL-6 KO and WT (n = 7; p = 0.1297). IL-6 KO lupus mice showed improved novelty preference on both object placement (C) (n = 15; p = 0.002) and object recognition (D) (n = 15; p = 0.003) tasks. E) Depressive-like behavior did not differ between genotypes (n = 15; p = 0.161). F) Whole cortex expression of astrocyte (gfap; n = 6-7; p = 0.037) and microglia (aif1; n = 6-7; p = 0.036) marker genes was significantly decreased in IL-6 KO lupus mice. * $p < 0.05$; ** $p < 0.01$; the "n" provided is the number of mice for each genotype.

Conclusion: In conclusion, we found that serum IL-6 levels correlate with worse cognition and memory in lupus mice. Moreover, knocking out IL-6 ameliorates those deficits without altering affective features or systemic disease. Whether pharmacologic inhibition of IL-6 would similarly attenuate murine NPSLE remains to be determined. IL-6 KO mice also demonstrated decreased cortical expression of inflammatory glial genes. Therefore, IL-6 may play a specific, glia-mediated role in the cognitive and memory deficits of NPSLE.

Disclosure: J. Reynolds: None; **M. Huang**: None; **M. Meineck**: None; **T. Möckel**: None; **A. Schwarting**: GlaxoSmithKlein(GSK), 5, 6; **C. Putterman**: Equillium, 2, KidneyCure, 1, Progentec, 2.

Abstract Number: 2448

UV Light Exposure Induces a Type I Interferon Dependent Activation and Migration of Inflammatory Dendritic Cells to Local Lymph Nodes

Xizhang Sun, Jaime Chao, Michael Gerner and Keith Elkon, University of Washington, Seattle, WA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: SLE – Animal Models
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Photosensitivity occurs in ~ 75% of lupus patients. Although ultraviolet (UV) light stimulates Type I interferon (IFN-I) in the skin, why lupus patients are sensitive to UV skin injury and how systemic immune responses are generated are poorly understood. Following skin inflammation in other contexts, DC migrate to draining lymph nodes (dLN) and activate adaptive immune cells. In virus infections that induce Type I interferon (IFN-I), a unique inflammatory DC subset (infl-cDC2) that are potent antigen presenting cells are generated. To explore the links between UV mediated skin inflammation and innate responses, we examined myeloid cell migration, including DC subsets (cDC1, cDC2, infl-cDC2) to dLNs in normal and a lupus prone mouse strain. We also examined the influence of Type-I IFN in migratory DC differentiation.

Methods: Mice were females aged 8-12 weeks of the strains C57BL/6 (B6); KiKR (photoactivatable); interferon receptor deficient (Ifnar KO); and Trex1 mutant mice (knock in of the lupus mutant allele, D18N, Trex1m). Mice were exposed to a single dose of UV (500mJ/cm^2) on the dorsal skin. In some experiments, the skin was painted with TRITC prior to UV to determine the origin of cells in the dLN. Brachial and axillary dLN were harvested at 1- or 2-days post UV exposure. Flow cytometry using the Symphony A3 cytometer identified myeloid cells as described previously. Statistical significance between groups was determined by Student's t-test.

Results: Skin painted with TRITC confirmed that skin derived DC migrated to dLN after UV. When compared to non-UV exposed mice and control non-draining LN, UV caused an increase in TRITC+CD64+ and TRITC+ Ly6Ghi (neutrophils) cells in dLN. UV of KiKR mouse skin revealed that both cDC1 and cDC2 cells migrated to dLN following UV. Higher numbers of neutrophils as well as CD64+ myeloid cells, that included monocytes as well as infl-cDC2 (CD26+MAR-1+), were detected in the dLN after UV, compared to non-UV exposed control mice (Fig.1). We observed a significant reduction of infl-cDC2 cells in Ifnar KO mice indicating that their development was IFN-I dependent. Finally, we quantified myeloid cell populations in the dLN of lupus-prone Trex1m mice. Although UV did not increase cDC1 nor cDC2 in dLN, we observed a significant increase in the infl-cDC2 in the dLN in this lupus prone strain (Fig.1). Curiously, monocyte and neutrophil migration to dLN were reduced in Trex1m mice compared to B6 after UV.

Figure 1:

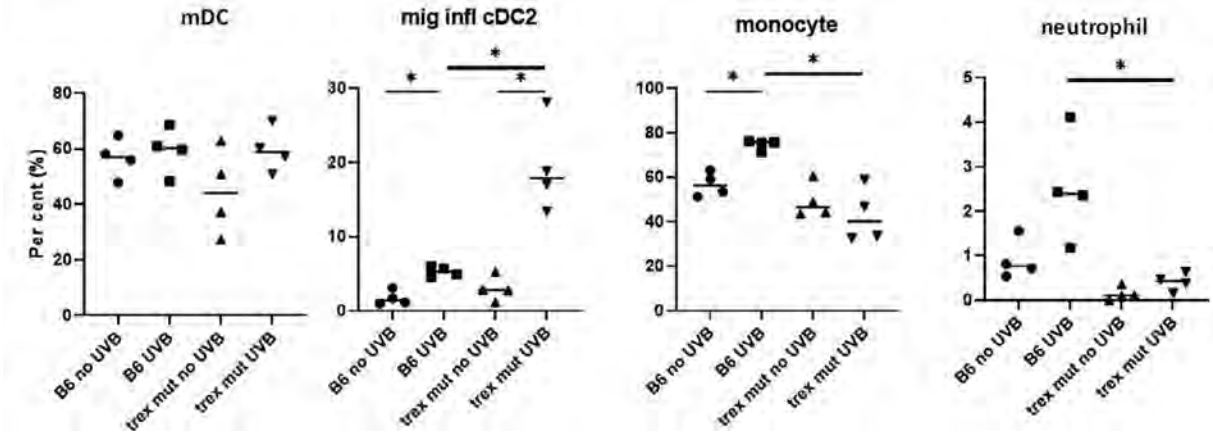

Fig 1. Percentage of cells in the draining Lymph Nodes (dLN). B6 or Trex1 mutant (mut) mice were exposed to 500 mJ/cm2 UV light on the dorsum. 48 hours after UV exposure, the brachial and axillary LN were harvested. The dissociated cells were analyzed by flow cytometry using 15 markers to distinguish different myeloid population on the Symphony A3 cytometer. The percentage of each cell type was calculated and comparisons made by Student's t test. mDC = migratory DC. * $p<0.05$.

Conclusion: We conclude that exposure of normal skin to UV light causes migration of many different types of myeloid cells to dLN, including skin-derived migratory DC, neutrophils, and monocytes. A subset of CD64+ infl-cDC2 is also induced and is dependent on UV-induced IFN-I. Of interest, Trex1m mice exhibit altered myeloid cell responses in the dLNs, including increased representation of infl-DCs and reduced neutrophil and monocyte cellularity. Overall, these findings show marked and non-equivalent IFN-I dependent effects of UV on myeloid cell responses in the dLN in wild type vs lupus-prone mice, implicating a link between IFN-I and the development of APCs that promote the adaptive immune response.

Disclosure: X. Sun: None; **J. Chao**: None; **M. Gerner**: None; **K. Elkon**: None.

Abstract Number: 2449

Cognitive Functioning Among Individuals with Systemic Lupus Erythematosus: A Population-Based Study

Laura Plantinga[1], C. Barrett Bowling[2], Charmayne Dunlop-Thomas[1], Courtney Hoge[1], Bradley Pearce[1], Cristina Drenkard[1] and S. Sam Lim[1], [1]Emory University, Atlanta, GA, [2]Duke University, Durham, NC

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Epidemiology & Public Health II
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Studies of objectively measured cognitive dysfunction in SLE are often limited by small sample size, limited generalizability, and lack of diversity. We sought to comprehensively describe cognitive functioning and its correlates among participants recruited from a population-based, primarily Black U.S. cohort.

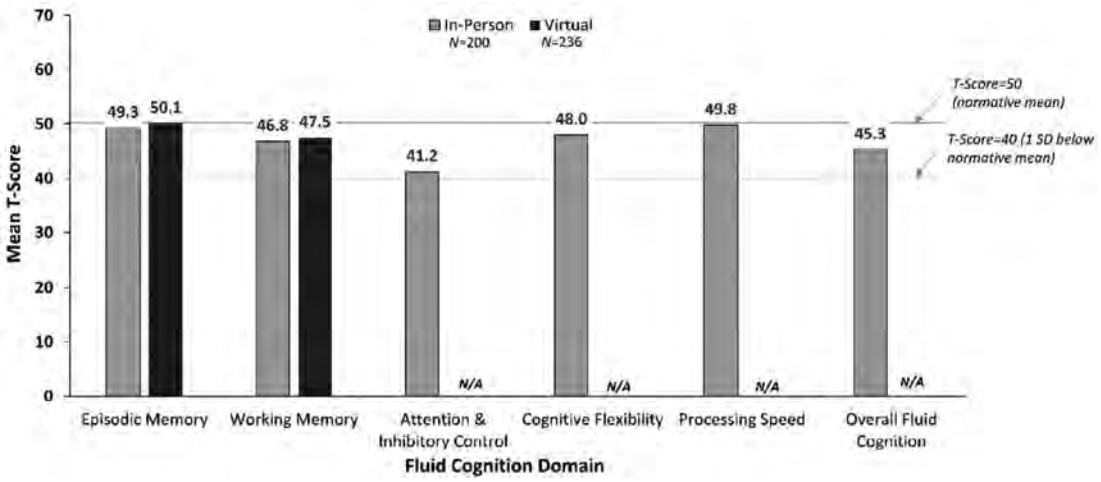

Figure 1. Mean fully adjusted* NIH Toolbox Fluid Cognition Battery T-scores among individuals with SLE, by visit type.

Methods: Participants (*n*=200; mean age, 42.6; 87.5% female, 86.5% Black, 5.0% Hispanic) completed in-person study visits (10/2019-5/2022), which included: (1) the NIH Toolbox Fluid Cognition Battery (episodic memory, working memory, attention and inhibitory control, cognitive flexibility, processing speed, overall composite measure; expressed as T-scores, adjusted for age, gender, race/ethnicity, and education); and (2) two brief screening tests, (a) a clock-drawing task (score range, 0-15; higher score=better performance) and (b) the Trail Making Test (TMT) B task (time in seconds, faster time=better performance). An additional 236 participants completed virtual study visits (10/2020-11/2021), which included NIH Toolbox episodic and working memory modules only. Descriptive statistics were calculated for all measures and the adjusted associations of various participant characteristics with the overall fluid cognition score were assessed with multivariable linear regression. Scatterplots and pairwise correlations were used to estimate relationships between cognitive functioning measures.

Results: The mean adjusted overall fluid cognition T-score was 45.3, ~0.5 SD below the general population mean; 31% participants scored < 40 (>1 SD below the mean), suggesting impairment. The mean score for attention and inhibitory control was nearly 1 SD below average (**Figure 1**). Adjusted fluid cognition T-scores were not associated with age, race, ethnicity, or gender, but those who had a high school education or less *vs*. having a college degree or higher had 5.3 points (>0.5

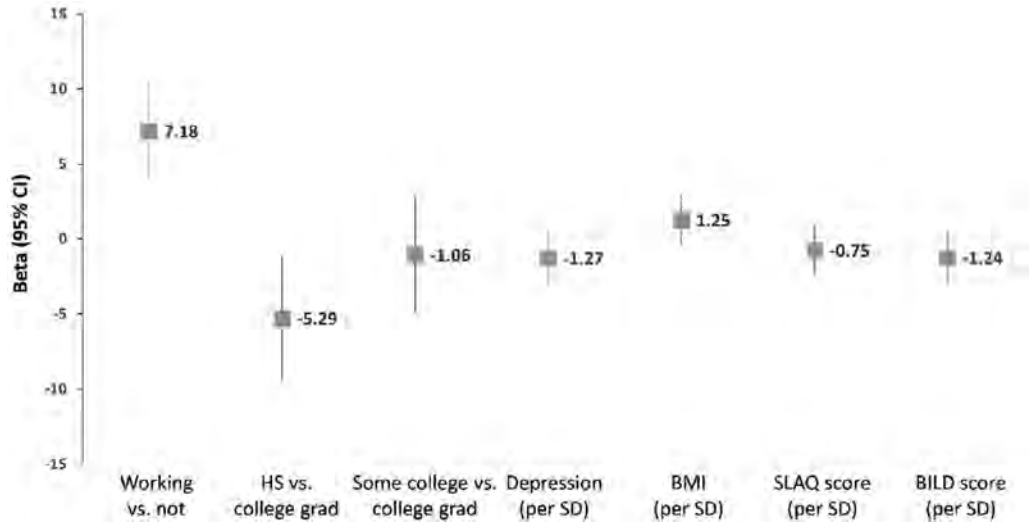

Figure 2. Adjusted differences in fluid cognition T-score by individual characteristics. HS, high school; BMI, body mass index; SLAQ, SLE Activity Questionnaire; BILD, Brief Index of Lupus Damage.

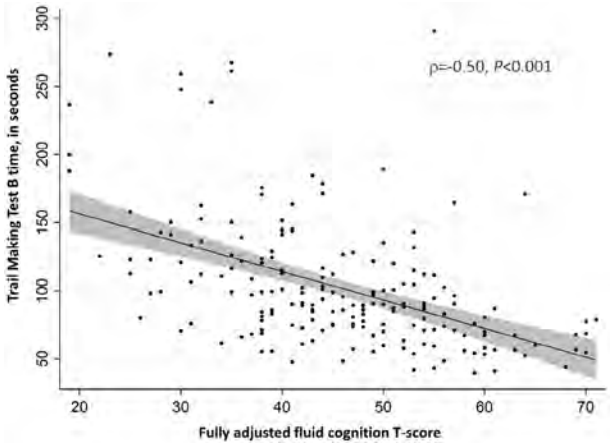

Figure 3. Scatterplot of Trail Making Test B time vs. fully adjusted fluid cognition T-Score. Line, fitted values; shaded area, 95% CI.

SD) lower score. Current working status was associated with a 7.2-point higher adjusted T-score, while higher depression, SLE activity, and SLE damage scores were associated with slightly lower T-scores (not statistically significant; **Figure 2**). Clock score (median=14, interquartile range, 13-15) was weakly correlated with fluid cognition T-score (r=0.17, *P*=0.01), while TMT B time (median=90.3, interquartile range, 71.9-121.1 s) was moderately correlated with fluid cognition T-score (**-Figure 3**). Moreover, 2.5% of individuals did not complete the TMT B within 300 s, suggesting impairment.

Conclusion: Our results suggest individuals with SLE commonly suffer from deficits in fluid cognition, particularly attention and inhibitory control. Higher educational attainment and working status may be protective against impairment, but reverse causality may contribute to this observed pattern. Additionally, we found that multi-domain measurement of global fluid cognition among these individuals may provide nuanced information beyond that available from screening tasks that are designed primarily to detect impairment among older adults. Together, these results inform potential interventions to support cognitive function among individuals with SLE.

Disclosure: L. Plantinga: None; **C. Bowling**: None; **C. Dunlop-Thomas**: None; **C. Hoge**: None; **B. Pearce**: None; **C. Drenkard**: None; **S. Lim**: None.

Abstract Number: 2450

Gene by Respiratory Disease Interactions Associated with Developing Rheumatoid Arthritis

Vanessa Kronzer[1], Keigo Hayashi[2], Cynthia Crowson[1], John Davis[1], Gregory McDermott[2], Jing Cui[3], Elena Losina[3], Pierre-Antoine Juge[4], James Cerhan[1] and Jeffrey Sparks[5], [1]Mayo Clinic, Rochester, MN, [2]Brigham and Women's Hospital, Boston, MA, [3]Brigham and Women's Hospital, Boston, MA, [4]Division of Rheumatology, Inflammation, and Immunity Brigham & Women's Hospital, Boston, MA, [5]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Epidemiology & Public Health II

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Cigarette smoking, textile dust, and occupational inhalants all strongly interact with the Human Leukocyte Antigen (*HLA*) shared epitope for risk of seropositive RA. Recently, we found preceding respiratory tract diseases including asthma, sinusitis, and interstitial lung disease (ILD) are associated with increased risk of RA. In addition, the *MUC5B* promoter variant was found to increase risk of RA-ILD. Therefore, we aimed (1) to identify gene by respiratory tract disease interactions associated with developing RA and (2) to determine the interaction between *MUC5B* and respiratory tract diseases for RA risk.

Methods: In this case-control study using a single center biobank, we identified incident RA cases, all confirmed by ACR/EULAR criteria. We matched each RA case to four controls on age, sex, and electronic health record (EHR) duration at index date of RA diagnosis (or assigned date for controls). Genetic exposures included an overall genetic risk score (GRS) including all genetic factors previously associated with RA, an *HLA* GRS for RA, and the *MUC5B* promoter variant. We dichotomized the GRSs into "high" and "low" risk by the highest tertile in controls. We obtained preceding respiratory tract diseases from diagnosis codes (positive predictive value 86%). We estimated attributable proportions (AP) and multiplicative odds ratios (OR) with 95% confidence intervals (CI) for RA for each genetic and preceding respiratory disease using conditional logistic regression models, adjusting for age, sex, EHR duration, enrollment year, genetic ancestry by principal components, education, body mass index, and smoking status and pack-years.

Results: We identified 653 incident RA cases and 2,607 matched controls (mean age 54 years, 76% female, Table 1). The highest tertile of the overall GRS and the *HLA* GRS were each associated with increased RA risk (OR 2.28, 95% CI 1.89,2.74; OR 2.02, 95% CI 1.67,2.45). ILD and high *HLA* interacted synergistically for RA risk (OR for both factors 4.30, 95% CI 1.28,14.38 vs. neither; AP 0.51, 95% CI-0.16,1.18; Figure 1). Asthma and the *MUC5B* promoter variant also interacted synergistically for seropositive RA risk (OR for both factors 2.58, 95% CI 1.10,6.07 vs. neither; AP 0.62, 95% CI 0.24,1.00; Figure 2). Aside from these two synergistic interactions, each GRS exhibited a negative, or "antagonistic,"

Table 1. Characteristics of the 653 incident RA cases and 2,607 matched controls with GWAS data and at least 5 years of EHR history

Characteristic	RA cases (n=653)	Controls (n=2607)	p-value
Age, years, mean (SD)	54 (13)	54 (12)	*
Female sex, n (%)	494 (76)	1971 (76)	*
EHR history in years, median (IQR)	12 (9,17)	12 (8,16)	*
Education college or higher, n (%)**	377 (58)	1882 (72)	<0.001
BMI, kg/m², mean (SD)	29 (7)	28 (6)	<0.001
Smoking status, n (%)**			<0.001
Never	320 (49)	1526 (59)	
Past	274 (42)	949 (36)	
Current	59 (9)	132 (5)	
Smoking pack-years, mean (SD)**	10 (20)	6.6 (13)	<0.001

BMI = body mass index, CI = confidence interval, EHR = electronic health record, GWAS = genome-wide association study, IQR = interquartile range, kg = kilograms, m = meters, RA = rheumatoid arthritis, SD = standard deviation
*Matching factors
**As of biobank enrollment

Figure 1. High HLA genetic risk score (GRS) and interstitial lung disease (ILD) interact synergistically for RA risk (reference group=low GRS/ILD absent).

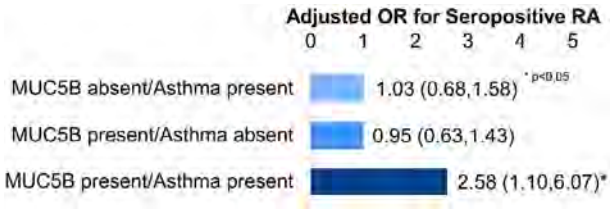

Figure 2. MUC5B promoter variant and asthma interact synergistically for seropositive RA risk (reference group=MUC5B absent/asthma absent).

multiplicative interaction with any respiratory tract disease and sinusitis for RA risk (multiplicative ORs 0.80, 95% CI 0.68,0.94 and 0.73, 95% CI 0.55,0.96, respectively, for the overall GRS).

Conclusion: In summary, ILD in the presence of *HLA* risk alleles and asthma in the presence of the *MUC5B* promoter variant were both synergistically associated with developing RA. Future studies should replicate these findings, as they may prove useful for RA screening (i.e. testing for *HLA* in individuals with ILD) and prevention (i.e. close monitoring for RA in people with asthma who have the *MUC5B* promoter variant).

Disclosure: V. Kronzer: None; **K. Hayashi**: None; **C. Crowson**: None; **J. Davis**: Girihlet, 9, Pfizer, 5, Remission Medical, 9; **G. McDermott**: None; **J. Cui**: None; **E. Losina**: None; **P. Juge**: None; **J. Cerhan**: None; **J. Sparks**: AbbVie, 2, Amgen, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, 5, Gilead, 2, Inova Diagnostics, 2, Janssen, 2, Optum, 2, Pfizer, 2, ReCor, 2.

Abstract Number: 2451

TET2 Clonal Hematopoiesis and Incident Rheumatoid Arthritis: Results from the UK Biobank

Karen Costenbader[1], Zhi Yu[2], Emily G. Oakes[3], Michelle Robinette[4], Mridul Agarwal[5], Buu Truong[6], Md Mesbah Uddin[6], Alexander Bick[7], Abhishek Niroula[6], Daniel Solomon[3] and Pradeep Natarajan[8], [1]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [2]Broad Institute; Massachusetts General Hospital, Cambridge, MA, [3]Brigham and Women's Hospital, Boston, MA, [4]Brigham and Women's Hospital; Dana-Farber Cancer Institute, Boston, MA, [5]Dana-Farber Cancer Institute, Boston, MA, [6]Broad Institute, Cambridge, MA, [7]Broad Institute; Vanderbilt University Medical Center, Nashville, TN, [8]Broad Institute; Massachusetts General Hospital, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Epidemiology & Public Health II
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Clonal hematopoiesis (CH), the clonal expansion of somatically mutated blood cells in people without hematologic malignancy, is found in ~10% of people age ≥ 70 years. CH genetic mutations confer selective advantage to stem cells. Several have been associated with aging and increased production of inflammatory cytokines, as well as with increased risk of cardiovascular disease (CVD) and malignancy. In population studies, somatic mutations in the epigenetic regulatory genes *DNMT3A, TET2,* and *ASXL1* predominate. We hypothesized that CH may be related to risk of rheumatoid arthritis (RA), which increases with age and is characterized by systemic inflammation.

Table 1. Characteristics of the UK Biobank study population with Whole Exome Sequencing Data (N= 189,947)[a]			
	RA n=1,592	No Incident RA N = 188,355	p[c]
Age in years, mean (SD)[b]	59.61 (7.28)	56.45 (8.06)	***
Male, (%)	531 (33.4)	85,412 (45.3)	***
White race, (%)	846 (53.1)	83181 (44.2)	**
Ever smoked, %	28.96 (5.61)	27.35 (4.72)	***
Body mass index in kg/m², mean (SD)	59.61 (7.28)	56.45 (8.06)	***
Diabetes Mellitus, (%)	93 (5.8)	4,394 (2.3)	***
Cardiovascular disease, (%)	68 (4.3)	4,976 (2.6)	***
Hypercholesterolemia (%)	584 (36.7)	39,793 (21.1)	***
C-reactive protein, mean (SD)	4.48 (6.69)	2.49 (4.16)	***
Creatinine, mean (SD)	0.07 (0.01)	0.07 (0.01)	ns
Any clonal hematopoiesis mutation, (%)	122 (7.7)	11,026 (5.9)	**
DNMT3A >2%	63 (4.0)	6,699 (3.6)	ns
TET2 >2%	32 (2.0)	1,894 (1.0)	**
ASXL1 >2%	11 (0.7)	906 (0.5)	ns

[a] Restricted to unrelated individuals in 200K UK Biobank exomes tranche with unrelatedness defined as < 3rd degree relatedness
[b] Metrics represented as mean (standard deviation, SD) for continuous variables; % (n) for categorical variables. Clinical conditions occurring prior to enrollment.
[c] t-test or Chi square test, *p< 0.05, **p < 0.01, ***p < 0.001, ns= p> 0.05

Methods: We tested this hypothesis in the UK Biobank *Exomes* dataset. The UK Biobank prospective study consists of 502,543 adults recruited 2006-2010 from 22 UK centers. All participants provided consent for linkage to medical records and blood samples. At baseline visit, demographic and clinical variables were collected, as was blood for DNA. Both genome-wide genotyping and whole exome sequencing (WES) were performed on ~ 200,000 participants' DNA. We identified the 3 most common CH somatic mutations: *DNMT3A, TET2,* and *ASXL1*. We assessed both variant allele fraction (VAF) > 2% and >10%. We identified RA by a validated billing code algorithm and tested associations with incident RA (individuals without prevalent RA and not taking any RA disease-modifying drugs at enrollment). We compared baseline characteristics of individuals who developed incident RA to those who did not. Cox regression models estimated hazards ratios

Table 2. Clonal Hematopoiesis Mutation and Risk of Incident RA among unrelated Participants in the UK Biobank study population with Whole Exome Sequencing Data (N= 189,947)[a]			
		Incident RA vs. non-RA[a]	
	Model[b]	HR (95% CI)	p[c]
CH VAF > 2%	1	1.10 (0.91, 1.33)	ns
	2	1.10 (0.91, 1.33)	ns
DNMT3A >2%	1	0.92 (0.71, 1.18)	ns
	2	0.92 (0.71, 1.19)	ns
TET2 >2%	1	1.60 (1.13, 2.27)	**
	2	1.49 (1.03, 2.18)	*
ASXL1 >2%	1	1.22 (0.68, 2.22)	ns
	2	1.11 (0.60, 2.07)	ns
CH VAF >10%	1	1.27 (1.02, 1.58)	*
	2	1.30 (1.04, 1.63)	*
DNMT3A >10%	1	1.09 (0.79, 1.50)	ns
	2	1.15 (0.83, 1.58)	ns
TET2 >10%	1	1.54 (1.01, 2.34)	*
	2	1.41 (0.90, 2.22)	ns
ASXL1 >10%	1	1.46 (0.76, 2.81)	ns
	2	1.27 (0.63, 2.54)	ns

[a] Study population included 189,947 unrelated individuals in UK Biobank without RA at baseline. Logistic regression models were used for calculating the ORs for all cases
[b] Model 1 adjusted for age at baseline, sex, race, genotyping array and first 10 genetic principal components
Model 2 adjusted for covariates in model 1 and smoking status, body mass index, history of diabetes mellitus and cardiovascular disease at baseline
[c] *p< 0.05, **p < 0.01, ***p < 0.001, ns= p> 0.05
VAF: variant allele frequency; HR: hazard ratio; CI: confidence interval

(HR) for incident RA according to the presence of the 3 most common CH mutations. Model 1 adjusted for baseline age, sex, race, and 1st 10 genetic principal components. Model 2 additionally adjusted for baseline smoking, body mass index (BMI), CVD, and type 2 diabetes.

Results: We studied 189,947 unrelated individuals in UK Biobank without RA at baseline and identified 1,592 who developed incident RA. **Table 1** shows the baseline characteristics of those with and without incident RA. Those with incident RA were more likely to be female, more frequently reported a smoking history, had higher median BMIs, and were more likely to have prevalent CVD, type 2 diabetes, and hypercholesterolemia. *TET2* mutations were present in significantly higher proportions of the incident RA population. **Table 2** presents the results of adjusted regression models: *TET2* (VAF >2%) was associated with increased HR of developing RA (model 1 HR 1.60 [1.13, 2.27]). Further adjustment for lifestyle risk factors and comorbidities was associated with attenuated HR for RA (model 2 HR 1.49 [95%CI 1.03, 2.18]). Having *TET2* mutation with VAF >10% was also associated with increased RA risk (model 1 HR 1.54 [1.01, 2.34]).

Conclusion: The CH mutation *TET2* may be related to risk of RA, as it is for other diseases of inflammation and aging. As *TET2* increases interleukin-1beta (IL-1β) expression in mouse models, it may accelerate RA onset. *TET2* CH may also be related to the increased risk of cancer and CVD among patients with RA. These findings are being pursued and analyses replicated in other cohorts.

Disclosure: K. Costenbader: Amgen, 2, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Eli Lilly, 2, Exagen Diagnostics, 5, Gilead, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5; **Z. Yu**: None; **E. Oakes**: None; **M. Robinette**: None; **M. Agarwal**: German Accelerator Life Sciences, 2, iuvando Health, 4, 8; **B. Truong**: None; **M. Uddin**: None; **A. Bick**: None; **A. Niroula**: None; **D. Solomon**: CorEvitas, 5, Janssen, 5, moderna, 5, Novartis, 5, UpToDate, 9; **P. Natarajan**: Allelica, 2, 5, Amgen, 5, Apple, 2, 5, AstraZeneca, 2, Blackstone Life Sciences, 2, Boston Scientific, 5, Esperion Therapeutics, 4, Foresite Labs, 2, Genentech / Roche, 2, 5, GV, 2, HeartFlow, 2, Magnet Biomedicine, 2, Novartis, 2, 5, Preciseli, 4, 12, equity, TenSixteen Bio, 4, 12, equity, Vertex, 12, spouse employment and equity.

Abstract Number: 2452

Assessment of Association Between Hydroxychloroquine Use and Toxic Retinopathy, Overall and by Indication, in a Large Cohort of Rheumatology Patients Within the US Department of Defense Military Healthcare System

Rachel Robbins[1], Toni Rush[2] and Jess Edison[3], [1]Walter Reed National Military Medical Center, Germantown, MD, [2]Health Research Tx, Pace, FL, [3]Uniformed Services University of the Health Sciences / National Capital Consortium-Walter Reed Bethesda, Bethesda, MD

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Epidemiology & Public Health II
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: While generally believed to be a safe, well-established treatment, hydroxychloroquine (HCQ) use is associated with irreversible retinal toxicity requiring regular monitoring. The objective of the study was to assess the association between HCQ and retinopathy in a rheumatology cohort and by indication utilizing a large longitudinal database.

Methods: Between January 1, 2011, to December 31, 2019, all rheumatology patients 18 years of age and older were identified within the DoD healthcare system. Patients were assigned exposure status by defining hydroxychloroquine (HCQ) utilization accessing pharmacy dispensing data using an intent-to-treat approach. Prior toxic retinopathy was an exclusion criteria. Propensity score (PS) matching (1:1) was used to create study cohorts balanced on baseline covariates, including indication in the overall cohorts. In the indication specific analyses, PS estimation and matching were performed in cohorts stratified by indication. Cox proportional regression modeling was used to estimate the hazard ratios of toxic retinopathy after exposure to HCQ among overall rheumatology cohorts as well as for rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). All analyses were stratified by sex. A systematic algorithm was used to assign rheumatologic HCQ indication based on ICD-9/10 diagnostic codes assessed in claims data. Patients with diagnostic codes for a single rheumatologic condition were assigned that indication. If a patient had diagnostic codes for more than one rheumatologic condition, the indication with the most diagnostic codes was the defined indication. If one of the conditions was Sjögren's, then the condition other than Sjögren's, e.g., RA, was the assigned indication regardless of the count of diagnostic codes. SLE took precedence as the indication when diagnostic codes for both SLE and discoid lupus were present.

Results: All HCQ patients were matched to non-HCQ users. In the overall female cohort (n=88,120), patients had a mean age 55.7 (sd 16.6) and a median follow-up time 3.9 yr (IQR 1.9-6.2) and patients in the male cohort (n=19,946) had a mean age 60.8 (sd 16.0) and a median follow-up time 3.7 yr (IQR 1.8-6.1). In both cohorts, HCQ use was significantly associated (p< .0001) with retinopathy (Figure 1 & 2) with events occurring consistently more frequently in the HCQ cohorts. Female and male patients exposed to HCQ had a higher risk of retinopathy compared to non-exposed (HR 1.49, 95% 1.39,1.60; p< .0001; HR 1.47, 95% 1.26,1.72; p< .0001; respectively). For indications, HCQ use was significantly associated with retinopathy with variability seen within sex. The female RA cohort had an HR 1.41 (95% CI 1.28, 1.54; p< .0001) while the female SLE cohort had an HR 1.68 (95% CI 1.46, 1.94; p< .0001).A similar pattern was seen in the male cohorts, RA with HR 1.45 (95% CI 1.21, 1.74; p< .0001) and SLE with HR 2.02(95% CI 1.37, 2.96;p=0.0004) (Table 1).

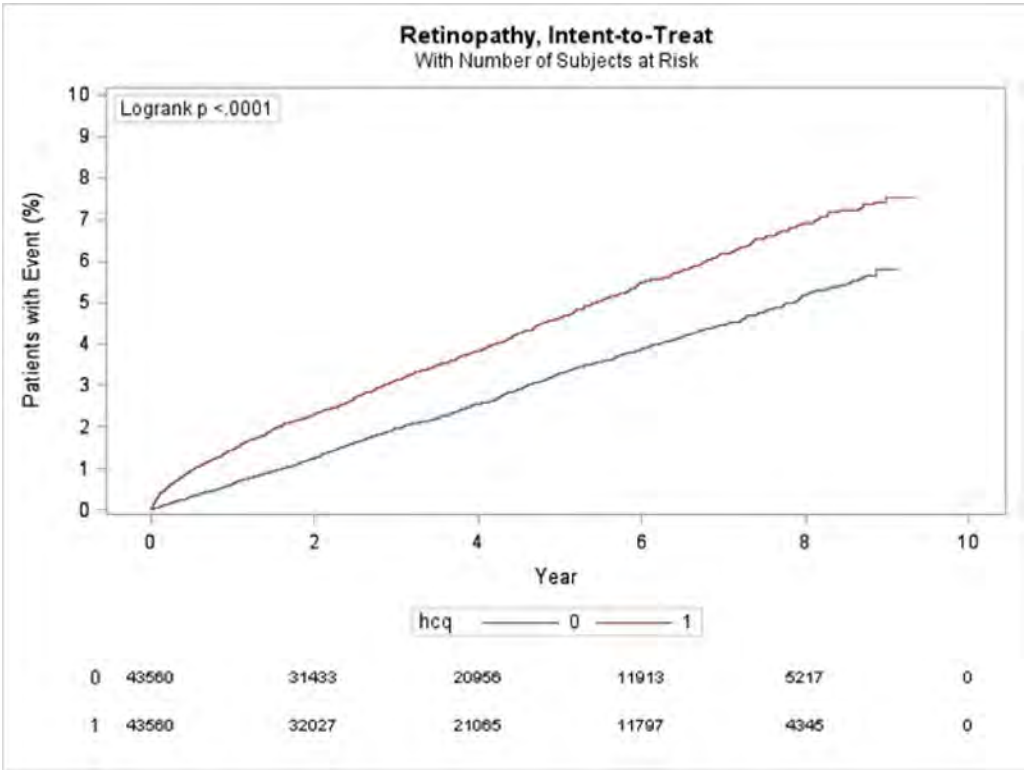

Figure 1.Kaplan Meier curve for Toxic Retinopathy in Overall Rheumatology Female Cohort by HCQ status

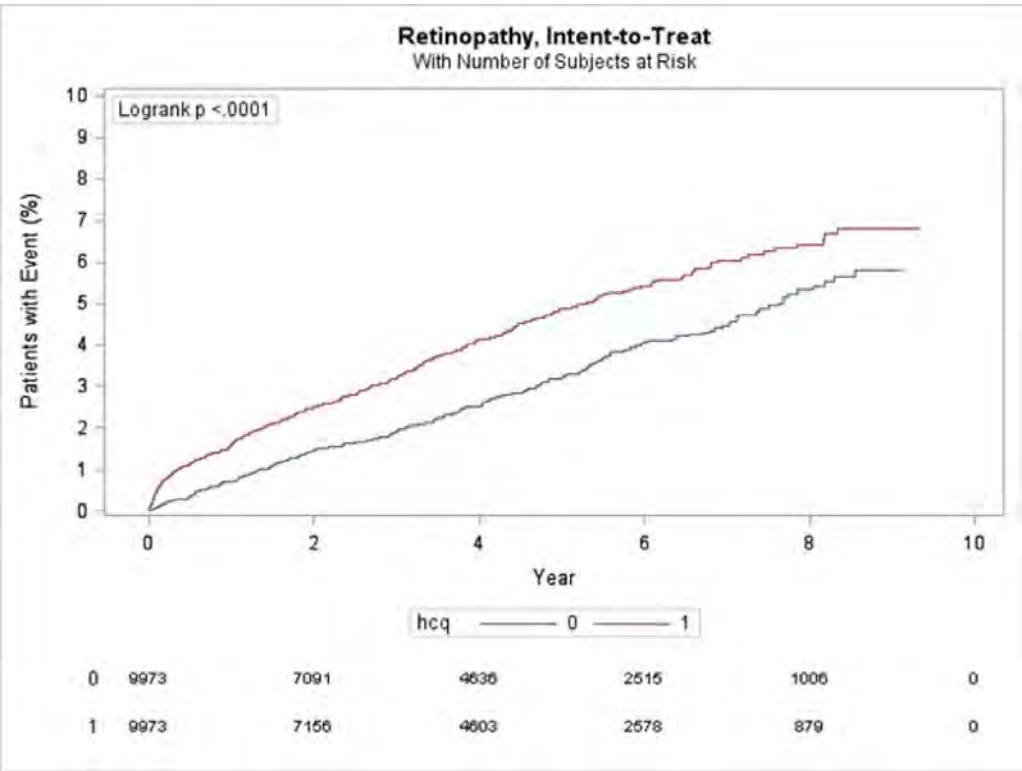

Figure 2. Kaplan Meier curve for Toxic Retinopathy in Overall Rheumatology Male Cohort by HCQ status

Conclusion: This uniquely large cohort of HCQ users reveals a risk of retinopathy that varies by sex and indication. The potential for serious ophthalmologic toxicity over the period studied emphasizes the importance of close ophthalmologic monitoring in the context of rheumatic disease where long term use is common.

Table 1.

Hazard Ratio of Toxic Retinopathy Associated with HCQ Utilization in a Cohort of Adult FEMALE Rheumatology MHS Patients DoD Database Jan 01, 2011 – Dec 31, 2019

		HCQ				Hazard Ratio			
		No		Yes					
Model	Matched Cohort	n	%	n	%	HR	95% CI		p-value
Overall	87,120	1,180	*2.71*	1,754	*4.03*	1.49	1.39	1.60	<.0001
Rheumatoid Arthritis	51,720	799	*3.09*	1,123	*4.34*	1.41	1.28	1.54	<.0001
Systemic Lupus	28,812	302	*2.10*	510	*3.54*	1.68	1.46	1.94	<.0001

Hazard Ratio of Toxic Retinopathy Associated with HCQ Utilization in a Cohort of Adult MALE Rheumatology MHS Patients DoD Database Jan 01, 2011 – Dec 31, 2019

		HCQ				Hazard Ratio			
		No		Yes					
Model	Matched Cohort	n	%	n	%	HR	95% CI		p-value
Overall	19,946	269	*2.70*	397	*3.98*	1.47	1.26	1.72	<.0001
Rheumatoid Arthritis	14,324	199	*2.78*	292	*4.08*	1.45	1.21	1.74	<.0001
Systemic Lupus	3,944	39	*1.98*	78	*3.96*	2.02	1.37	2.96	0.0004

Disclosure: R. Robbins: None; **T. Rush**: None; **J. Edison**: None.

Abstract Number: 2453

Development of a Hydroxychloroquine Retinopathy Prediction Score

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Epidemiology & Public Health II
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Hydroxychloroquine (HCQ) is an important medication for SLE and other rheumatic diseases, but its major adverse event is HCQ retinopathy. Weight-based HCQ dose is known to influence the risk of retinopathy, but other risk factors have also been identified. We explored predictive models for HCQ retinopathy and developed a clinical risk score.

Methods: We used a longitudinal cohort of incident HCQ users enrolled in the United States integrated health network Kaiser Permanente Northern California. HCQ retinopathy outcomes were obtained by masked expert-adjudication of optical coherence tomography screening studies, as previously described (Melles RB, Jorge A, *Ann Int Med* 2023). Among patients using HCQ for at least 5 years, we assessed candidate predictors at 5 years of use including the weight-based HCQ dose, cumulative dose in the first 5-years, age, sex, race/ethnicity, biometrics, indication for HCQ use, comorbidities including diabetes, liver disease, estimated glomerular filtration rate (eGFR), tamoxifen use, and use of inhibitors of cytochrome P450 CYP2D6, CYP2C8, or CYP3A4. We used Cox proportional hazards regression, using backwards stepwise selection to develop a parsimonious model, and an alternate method of random survival forest (RSF) to identify predictors of the 10-year risk of HCQ retinopathy (i.e., risk within 15 years from HCQ initiation). We created a comparator model using HCQ dose alone (weight-based dose at 5 years: > or ≤ 5 mg/kg). We assessed model discrimination with c-statistics, assessed model calibration using the Hosmer-Lemeshow statistic, and graphed deciles of predicted vs observed risk. We then developed an integer-based risk score from the optimal Cox model. Continuous variables were converted to categorical variables. We assessed net reclassification improvement and integrated discrimination improvement between the integer-based risk score and comparator model with HCQ dose alone.

Results: Of 4,151 patients who initiated HCQ and continued for ≥5 years, 119 developed HCQ retinopathy within 15 years (**Table 1**). The final Cox model had better discrimination than the RSF model and than HCQ dose alone (C-statistic 0.80 [95% CI 0.77-0.83] versus 0.62 (95% CI 0.53-0.70) for the RSF model and 0.72 [95% CI 0.68-0.77] for the HCQ dose-only model. From the identified predictors in this model, an integer-based risk score for 10-year risk of HCQ retinopathy was created: B-SAFE (Body weight [kg], Sex, Age, glomerular Filtration rate, Exposure (cumulative dose in first 5 years since initiation [g] and current weight-based dose [mg/kg/day]). The B-SAFE model c-statistic was 0.78 (95% CI 0.75=0.82) with acceptable calibration (**Figure 1**). Compared with the HCQ dose-only model, the net reclassification index was 0.34 (95% CI 0.20-0.46). The risk score ranged from 0-33 points and can identify patients with HCQ retinopathy risk ranging from < 1% to >20% (**Figure 2**).

Conclusion: In addition to weight-based HCQ dose, we identified additional predictors of HCQ retinopathy. These clinical and laboratory variables were incorporated into a novel risk score that performs better than HCQ dose alone in predicting the 10-year risk of HCQ retinopathy among long-term users.

Table 1. Characteristics of the Study Participants With and Without Incident Hydroxychloroquine Retinopathy Within 15 Years of Use, Assessed at 5 Years of Use

Characteristics	Overall (N =4151)	No Retinopathy During Follow-up (N= 4032)	Incident Retinopathy During Follow-up (N= 119)	P value
Age, years, mean (SD)	58.0 (14.1)	57.8 (14.1)	63.4 (11.6)	<0.001
Age category, n (%)				<0.001
Age <50	1119 (27.0)	1108 (27.5)	11 (9.2)	
Age 50-59	1037 (25.0)	1010 (25.0)	27 (22.7)	
Age 60-69	1083 (26.1)	1040 (25.8)	43 (36.1)	
Age ≥70	912 (22.0)	874 (21.7)	38 (31.9)	
Female, n (%)	3442 (82.9)	3330 (82.6)	112 (94.1)	<0.001
Race/Ethnicity, n (%)				0.184
White, non-Hispanic	2168 (52.2)	2102 (52.1)	66 (55.5)	
Hispanic	709 (17.1)	689 (17.1)	20 (16.8)	
Asian	561 (13.5)	540 (13.4)	21 (17.6)	
Black	416 (10.0)	411 (10.2)	5 (4.2)	
Other	297 (7.2)	290 (7.2)	7 (5.9)	
Indication for HCQ, n (%)				0.011
RA/Other inflammatory arthritis	2414 (58.2)	2348 (58.2)	66 (55.5)	
SLE/Other CTD	1385 (33.4)	1351 (33.5)	34 (28.6)	
Other/unknown	352 (8.5)	333 (8.3)	19 (16.0)	
Weight, kg, mean (SD)	77.9 (20.7)	78.2 (20.8)	69.4 (15.0)	<0.001
BMI, mean (SD)	28.6 (6.9)	28.7 (6.9)	26.4 (5.6)	<0.001
Ideal Body Weight (kg), mean (SD)	57.4 (9.4)	57.5 (9.4)	54.4 (7.7)	<0.001
eGFR, mean (SD)	85.9 (20.5)	86.2 (20.4)	75.9 (18.9)	<0.001
Liver disease, n (%)	86 (2.1)	83 (2.1)	3 (2.5)	0.737
Diabetes, n (%)	290 (7.0)	284 (7.0)	6 (5.0)	0.399
Tamoxifen use, n (%)	17 (0.4)	14 (0.3)	3 (2.5)	0.012
CYP Inhibitor use, n (%)	775 (18.7)	759 (18.8)	16 (13.4)	0.138
Cumulative Dose at 5 years, g, mean (SD)	490.6 (170.3)	486.8 (170.2)	618.7 (117.5)	<0.001
Current Weight-Based Dose >5 mg/kg/day, n (%)	1608 (38.7)	1515 (37.6)	93 (78.2)	<0.001

HCQ, hydroxychloroquine; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; CTD, connective tissue diseases; BMI, body mass index; eGFR, estimated glomerular filtration rate; CYP, cytochrome P450

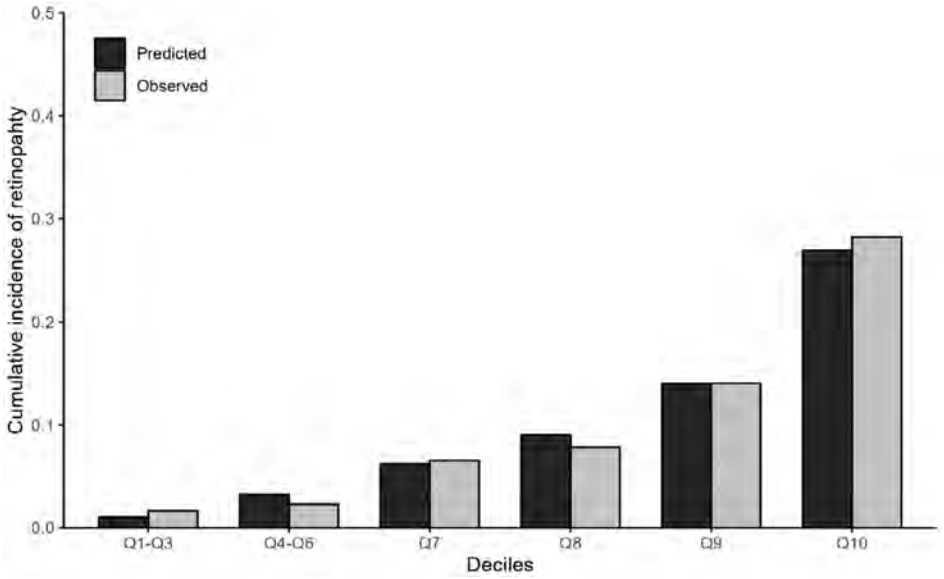

Figure 1. Calibration of the B-SAFE risk score model. Predicted vs. observed 10-year incidence of hydroxychloroquine retinopathy based on deciles of predicted risk. Hosmer-Lemeshow statistic x2 =3.19, P =0.67. Q1 to Q10 refer to deciles of risk score.

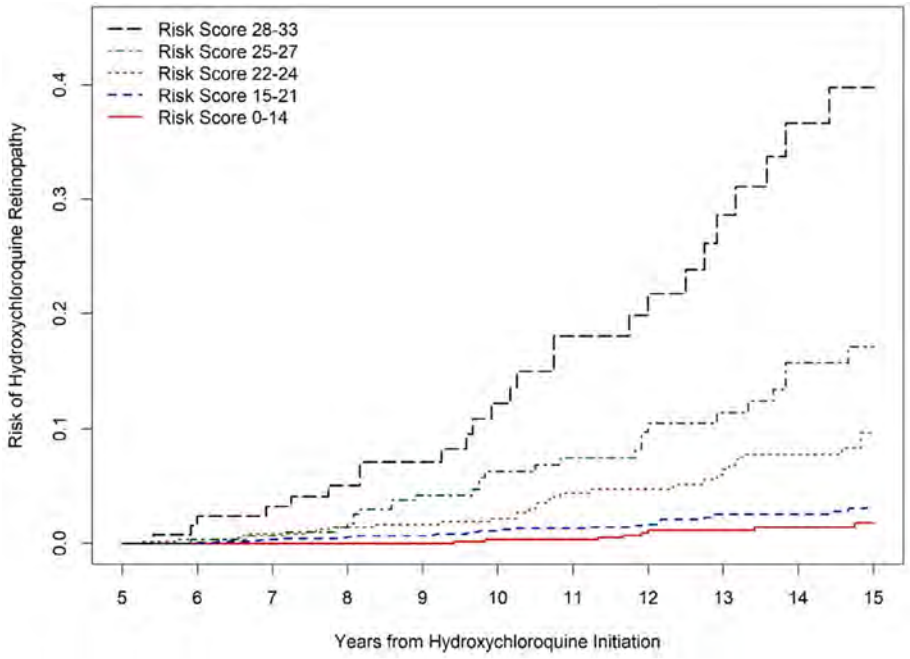

Figure 2. Cumulative Incidence of HCQ Retinopathy According to Risk Score Groups. Risk scores were divided into 5-groups based on 10-year retinopathy risk, ranging from <1% corresponding with scores 0-14, 1-5% corresponding with scores 15-21, >5-10% corresponding with scores 22-24, >10-20% corresponding with scores 25-27, and >20% corresponding with scores 28-33.

Disclosure: A. Jorge: None; **R. Melles**: None; **B. Zhou**: None; **Y. Zhang**: None; **H. Choi**: Ani, 2, Horizon, 2, 5, LG, 2, Protalix, 2, Shanton, 2.

Abstract Number: 2454

Endometriosis Increase Risk of Antiphospholipid Syndrome: A Propensity Score Matched Cohort Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Epidemiology & Public Health II

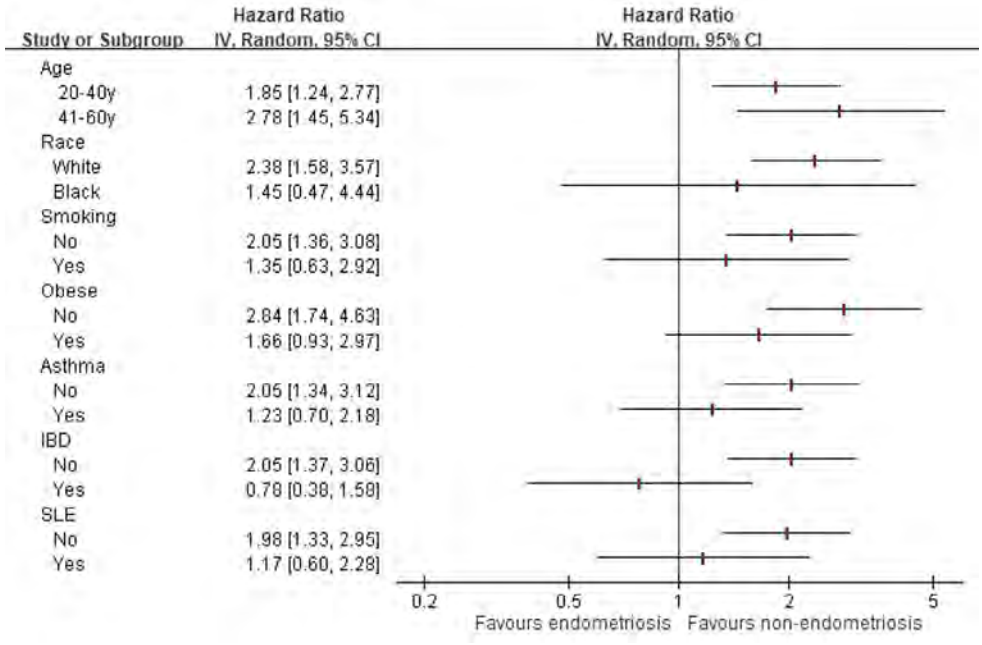
Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Patients with endometriosis have a variety of autoimmune abnormalities. Our objective was to investigate the risk of incident antiphospholipid syndrome (APS) in patients with endometriosis.

Methods: A retrospective cohort study was conducted using the US TriNetX (Cambridge, MA), a global federated health research network that provides real-time electronic medical record datasets. Propensity score matching was performed to adjust for demographic variables, comorbidities, and medication use. Cox proportional hazards models and subgroup analyses were used to estimate hazard ratios (HRs) for APS. The Kaplan–Meier method was used to plot the cumulative incidence curves. Subgroup analyses were also conducted, including age, obesity, and systemic lupus erythematosus (SLE). A sensitive analysis stratified by surgery confirmed endometriosis was performed.

Results: We identified50,078 patients with endometriosis among 16,602,603 female adults (20-60y) patients in the database. After propensity matching, 50,078 patients without endometriosis were analyzed for comparison. Compared to individuals without endometriosis, patients with endometriosis had a significantly higher risk of incident APS throughout the



Forest plot of subgroup analysis

course of endometriosis (log rank test, $p < 0.001$). The HRs ranged from 1.82 (APS within 30 days to 1 year after index date, 95% confidence intervals [CI] 1.40–2.53) to 2.44 (APS within 30 days to any time after the index date, 95% CI 1.65–3.61). In the subgroup analyses, an increased risk of APS was observed in all ages, white race, and subgroups without smoking, obesity, asthma, inflammatory bowel disease, and SLE (HR range 1.85–2.84). Sensitivity analyses revealed that risk of APS increased significantly in patients with surgery confirmed endometriosis, but not in patients without surgery confirmed endometriosis.

Conclusion: Patients with endometriosis had a significantly higher risk (up to 284%) of APS. Our study provides strong evidence for the screening of APS in patients with endometriosis.

Disclosure: Z. Chen: None; **S. Wang**: None; **J. Wei**: Abbvie, 2, 5, 6, Amgen, 5, AstraZeneca, 6, BMS, 2, 5, 6, Celgene, 2, Chugai, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 5, 6, Gilead, 5, GSK, 2, 5, Janssen, 2, 5, 6, Novartis, 2, 5, Pfizer, 2, 5, 6, Sanofi-Aventis, 2, SUN pharma, 5, TSH Taiwan, 2, UCB pharma, 2, 5; **S. Dai**: None.

Abstract Number: 2455

Addressing Native American Health Disparities in Rheumatoid Arthritis by Training Primary Care Providers: Expanding the Reach of the RAE Initiative

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Healthcare Disparities in Rheumatology
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: The United States faces a critical shortage of rheumatology providers. This shortage is especially dire in rural areas, such as Navajo Nation, where primary care providers (PCPs) are often in the position of managing their patients' rheumatologic conditions with little or no specialist support. Rheumatology training programs for front-line PCPs are an important and under-utilized strategy to help address the workforce crisis. In 2021, the Rheumatology Access Expansion (RAE) Initiative launched the Rheumatoid Arthritis (RA) ECHO, a remote 12-week training program to teach Navajo Area PCPs about the diagnosis and management of RA. We successfully offered the RA ECHO curriculum three times on Navajo Nation from 2021-2022. For our fourth cohort (spring 2023), we greatly expanded our target audience, inviting healthcare workers serving American Indian communities all across the country. Here, we present data from the first four cohorts of the RA ECHO, including the impact of the program on PCPs' knowledge, confidence, and clinical behaviors related to the diagnosis and management of RA.

Methods: Between September 2021 and April 2023, we offered the RA ECHO Curriculum four times ("cohorts 1-4"). PCPs completed surveys before and after the course, including a RA medical knowledge test, as well as questions about their self-reported confidence in RA diagnosis and management on a Likert scale (1 = not at all confident, to 5 = extremely confident). Beginning with cohort 3, we also included questions about participants' self-reported changes in clinical behaviors related to RA (for example, the frequency with which they perform a screening joint exam for tenderness and synovitis, or check hepatitis serologies prior to starting immunosuppression). Pooling data across the cohorts, we used paired t-tests to assess mean changes in PCPs' knowledge and confidence scores post-intervention.

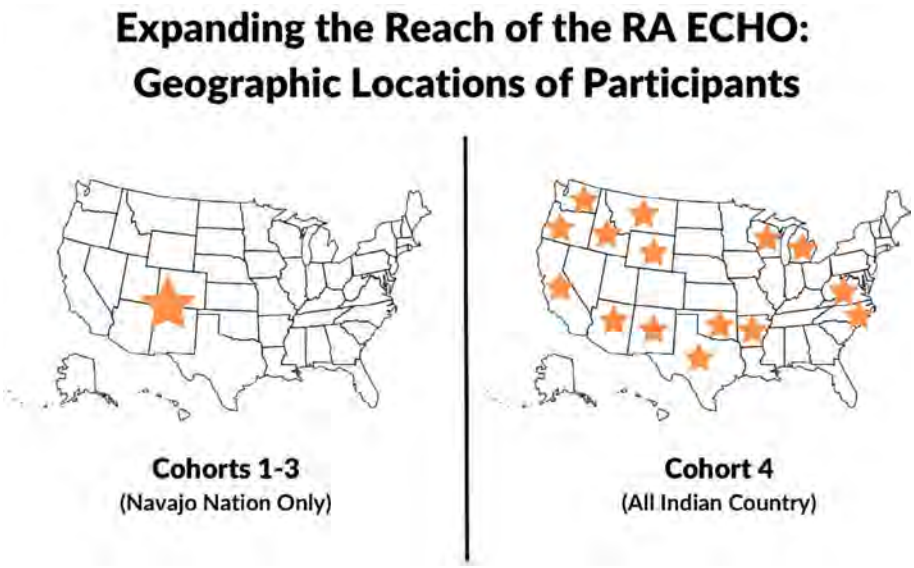

Figure 1: Geographic locations of PCP participants, separated by cohort.

Results: In total, 93 healthcare providers participated in the RA ECHO. Participants in cohorts 1-3 were all from Navajo Nation, while participants in cohort 4 came from 15 different states (Figure 1). Across all cohorts, paired pre- and post-intervention scores were available for a total of 32 and 34 PCPs for the knowledge and confidence surveys, respectively. Statistically significant improvements were observed in participants' knowledge (test scores increased by 26%, 95% CI: 19%-33%) and confidence (1.08 points on the Likert scale, 95% CI: 0.75-1.41) (Figure 2). Additionally, 79% of respondents

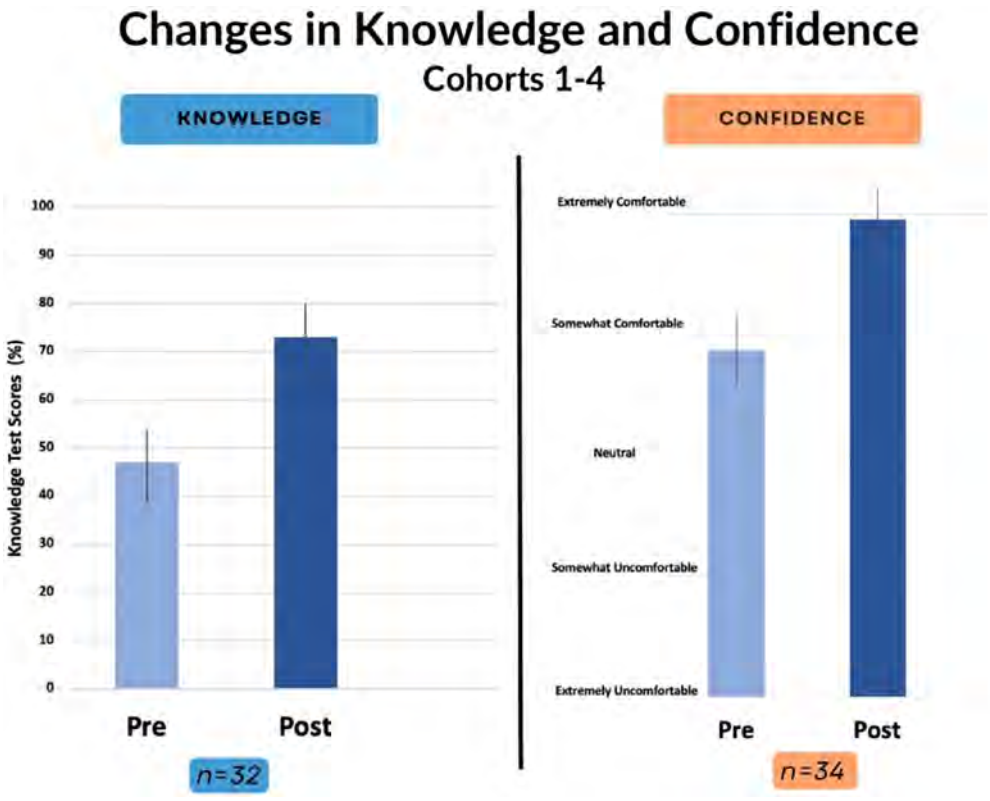

Figure 2: Changes in participants' knowledge and confidence related to RA diagnosis and management (pooled data for cohorts 1-4).

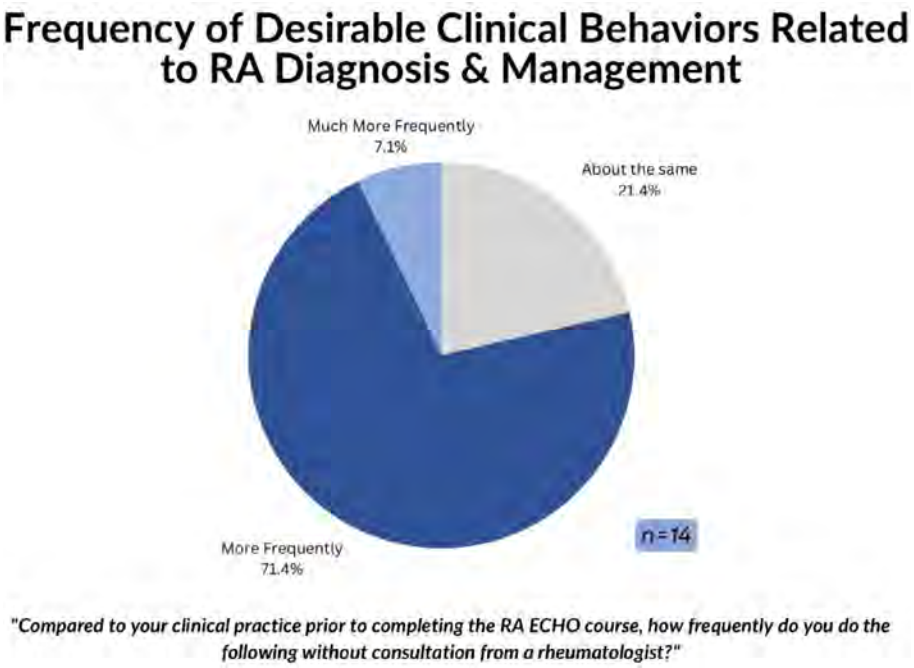

Figure 3: Self-reported changes in the frequency of desirable clinical behaviors related to RA diagnosis and management, from participants in cohorts 3 and 4.

reported performing desirable clinical behaviors related to RA diagnosis and management "more frequently" or "much more frequently" after completing the course (Figure 3).

Conclusion: Since 2021, the RAE Initiative has successfully trained 4 cohorts of PCPs through the RA ECHO Curriculum, and we've expanded the reach of the program far beyond Navajo Nation. Participants improved their medical knowledge, confidence, and self-reported frequency of desirable clinical behaviors related to the diagnosis and management of RA. Future research will focus on the impact of the RA ECHO on patient outcomes. The RA ECHO can serve as a scalable model for the development of similar programs in other communities with limited access to rheumatology providers.

Disclosure: J. Mandal: None; **Z. Izadi**: Bristol-Myers Squibb(BMS), 3; **T. Carroway**: None; **G. Grant**: None; **M. Margaretten**: None; **J. Yazdany**: Astra Zeneca, 2, 5, Aurinia, 5, Gilead, 5, Pfizer, 2.

Abstract Number: 2456

Lupus Patient Navigator Program to Improve Healthcare Barriers for Minority Patients

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Healthcare Disparities in Rheumatology
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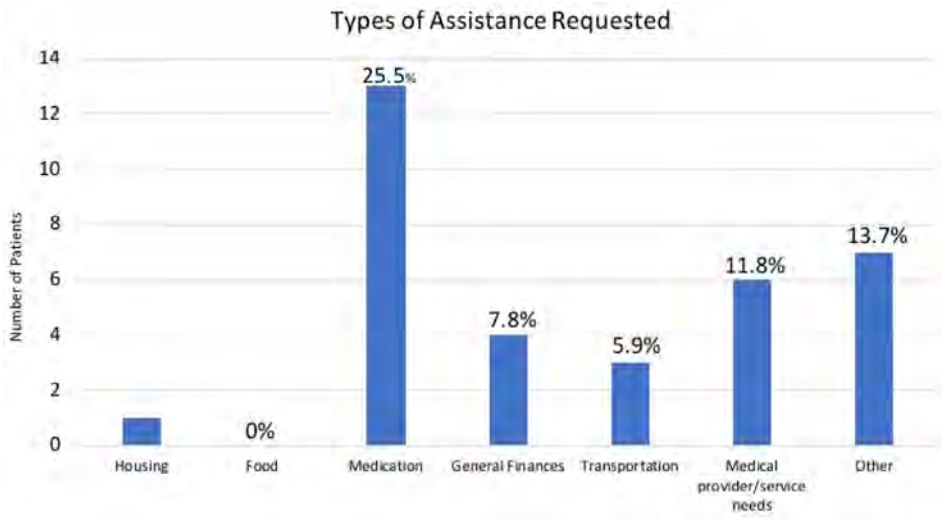

Figure 1. Participants in the LPNP requested multiple types of assistance from the PN during baseline visit. 56.9% patients asked for assistance, all of which asked for assistance for themselves rather than for their spouse or family. 25.5% requested assistance with medications followed by the other category, which included including help with appointment and medication reminders.

Background/Purpose: Despite recent progress in diagnosis and treatment of SLE minorities continue to bear the greater burden of disease with disproportionately higher morbidity and mortality. Barriers to care include access to preventive and specialty healthcare, economic resources, and health literacy. The goal of this study is to measure the impact and acceptability of a Lupus Patient Navigator Program (LPNP) providing interventions to reduce barriers to care for patients at high risk of poor outcomes.

Methods: Self-identified minority patients with SLE ≥18 years old at Medical University of South Carolina or University of Alabama were invited to participate if they were prescribed ≥1 immunosuppressant, and: 1) had ≥1 missed clinic or lab visit in the past 6 months, or 2) nonadherence to medical therapy, or 3) newly diagnosed SLE. The LPNP is modeled after the CDC STEPS to CARE toolkit. Participants had visits with the patient navigator (PN) every 3 months with monthly and as-

Table 1: There is a greater positive improvement in patient's QoL in those that are unemployed/disabled compared to employed/student.

Employment Effects on LupusPro Over 6 months

	Employed/Student	Unemployed/Disability	P-value
HRQoL	2.8±10.2	5.61±10.4	0.42
Lupus Symptoms	12.5±19.0	11.43±15.5	0.85
Cognition	8.13±20.4	5.71±17.8	0.70
Lupus Medications	-3.13±26.5	5.24±19.1	0.27
Procreation	0.63±21.4	5.71±11.6	0.36
Physical Health	3.13±19.5	4.24±12.0	0.83
Pain Vitality	2.5±17.5	0.52±21.0	0.76
Emotional health	-1.21±21.1	3.81±22.5	0.49
Body Image	-3.25±20.3	8.19±15.1	0.06
NHRQoL	-2.76±14.7	0.85±10.1	0.38
Desires-Goals	-5.63±26.3	0.24±24.6	0.49
Social Support	3.75±29.2	2.38±17.9	0.86
Coping	4.58±29.7	-1.11±16.5	0.46
Satisfaction with Care	-13.75±24.4	1.9±11.9	*0.014

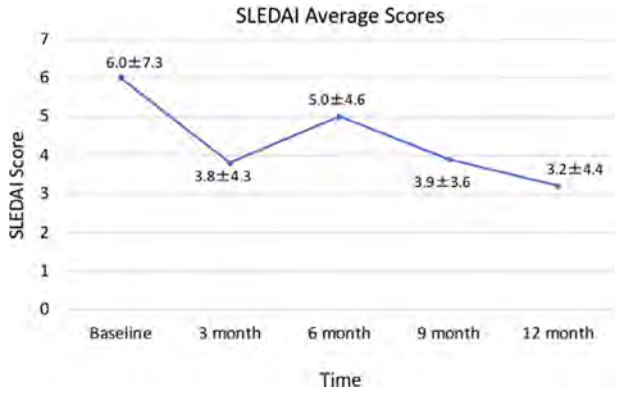

Figure 2. 42 patients at baseline visit completed SLEDAI questionnaires. SLEDAI scores from baseline to 1 year, visits are still ongoing. P-value 0.06 from baseline to 1 year.

needed check-ins by phone or email, with resources provided throughout the 12-month study duration. Patient-reported questionnaires included Type of Assistance Requested, LupusPRO for quality of life (QoL), SLEDAI, and Patient Satisfaction with Logistical Aspects of Navigation / Interpersonal Relationship with Navigator (PSN-L, PSN-I) Scales.

Results: 51 patients (96% female, 96% Black) with SLE completed at least 6-months, and 44 to date have completed 12-month assessments. Of the 51 patients, 90% were high school graduates, 86% had health insurance, 48% were unemployed/disabled, 33% were currently employed. A wide range of types of PN assistance were requested (**Figure 1**), with assistance with medications being most common at 25%. In addition, LupusPRO measures improved from baseline to the 6-month visit in most QoL domains. Results demonstrated a greater positive improvement in patient's QoL in those that are unemployed/disabled compared to employed participants (**Table 1**). SLEDAI scores from baseline to 1 year also improved from an average of 6.0 to 3.2 (**Figure 2**). Lastly, patients were satisfied with assistance received from the patient navigator in areas such as receiving/interpreting medical information and obtaining resources as indicated in the PSN-L, PSN-I Scales.

Conclusion: Implementation of a LPNP shows promise in addressing significant barriers to care for patients with SLE at high risk for poor outcomes, with participants to date reporting improved QoL and high satisfaction with the PN.

Disclosure: S. Karim: None; **G. Link**: None; **D. Wilson**: None; **J. Oates**: None; **G. Gilkeson**: None; **J. Singh**: None; **D. Kamen**: None.

Abstract Number: 2457

Ageism in Rheumatology: The Health Care Professional's Perspective

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Healthcare Disparities in Rheumatology
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Ageism (stereotypes, prejudice or discrimination based on age) is highly prevalent and has been linked to reduced lifespan, prolonged disability, and accelerated cognitive decline in older adults. Very little is known about ageism within the field of rheumatology. The aim of this study is to understand ageism among rheumatology health care professionals and to assess how ageism affects rheumatologic care.

Methods: An English language REDcap survey, distributed over social media and email, included Likert scaled, multiple-response and free response questions related to the clinical care of older adults and the validated Expectations Regarding Aging (ERA-12) scale where higher scores indicate reduced stereotypical beliefs regarding aging. Spearman's rank correlation coefficients were calculated for the ERA-12 scores and the responses to the other Likert questions to assess the effects of ageism on self-reported rheumatologic care decisions.

Table 1: Demographics

Table 1: Demographics (n=183)	
Age	
<30	15 (8.2%)
30-44	61 (33.3%)
45-64	87 (47.5%)
>65	20 (10.9%)
Gender	
Female/Woman	112 (61.2%)
Male/Man	70 (38.3%)
Transgender/Non-Binary Gender/Other	0 (0%)
Prefer not to say	1 (0.5%)
Race/ethnicity	
Asian	39 (21.3%)
Black or African American	0 (0%)
White	134 (73.2%)
Other	11 (5.9%)
Hispanic race	
Yes	13 (7.1%)
No	169 (92%)
Prefer not to say	1 (0.5%)
Occupation	
Advanced practice provider	17 (9.3%)
Physician	145 (79.2%)
Other	21 (11.3%)
Specialty	
Internal Medicine	19 (11.7%)
Rheumatology	140 (86.4%)
Other	3 (1.8%)
Community Type	
Urban	121 (66%)
Suburban	50 (27.3%)
Rural	12 (6.6%)
Practice setting	
Academic medicine	119 (65.0%)
Private practice	34 (18.6%)
Large group practice	19 (10.4%)
Government	11 (6.0%)
% of Practice >65	
<25%	21 (11.5%)
25-50%	90 (49.2%)
51-75%	68 (37%)
>75%	4 (2.2%)
Years in practice	
In training	27 (14.8%)

Table 2: What are some of the ways you treat older adults with rheumatic disease differently than younger adults (in general)?

Table 2: What are some of the ways you treat older adults with rheumatic disease differently than younger adults (in general)? (n=162)	
Decreased use of NSAIDs in older adults compared to younger adults	136 (83.4%)
Decreased use of opioids in older adults compared to younger adults	70 (42.9%)
I manage older adults the same way I manage younger adults	29 (17.8%)
Increased use of oral glucocorticoids in older adults compared to younger adults	25 (15.3%)
Decreased use of biologics in older adults compared to younger adults	23 (14.1%)
Decreased use of DMARDS (MTX, leflunomide, plaquenil) in older adults compared to younger adults	16 (9.8%)
Decreased use of intra-articular steroids in older adults compared to younger adults	1 (0.6%)
Other	13 (8.0%)

n (%)

Table 3: Likert scaled and yes/no questions with ERA-12 Spearman's Rank Correlation Coefficients

Table 3: Likert scaled and yes/no questions with ERA-12 Spearman's Rank Correlation Coefficients (n=183)						
	Strongly Agree	Agree	Disagree	Strongly Disagree	Spearman Rank Correlation Coefficient	p-value
I am confident managing the care of older adults with rheumatic disease.	66 (36%)	105 (57%)	11 (6.0%)	1 (0.5%)	-0.04849	0.51447
Older adults experience rheumatic disease differently than younger adults.	13 (7.1%)	102 (56%)	63 (34%)	5 (2.7%)	0.16492	0.02569
Older adults with rheumatic disease have a negative attitude towards the aging process.	3 (1.6%)	41 (22%)	124 (68%)	15 (8.2%)	0.12358	0.09558
Other healthcare professionals express negative attitudes about older people.	4 (2.2%)	32 (17%)	114 (62%)	33 (18%)	0.0083	0.91124
Older adults are more likely to minimize their symptoms than younger adults.	11 (6.0%)	81 (44%)	80 (44%)	11 (6.0%)	0.04346	0.55916
Older adults are more demanding of attention than younger adults.	1 (0.5%)	14 (7.7%)	129 (70%)	39 (21%)	0.21522	0.00344
One way I treat older adults differently than younger adults is that I tend to focus my prescribing efforts more on symptom relief than disease modifying therapy.*	0 (0.0%)	28 (17%)	94 (58%)	40 (25%)	0.27618	0.00037
One way I treat older adults differently than younger adults is that I tend to emphasize the risks of aggressive medical intervention rather than the possible benefits.*	1 (0.6%)	40 (25%)	95 (59%)	26 (16%)	0.24653	0.00156
Older adults are typically more concerned about the risks of aggressive medical intervention than they are interested in the possible benefits.	5 (2.7%)	67 (37%)	93 (51%)	18 (10%)	0.20864	0.00459
I enjoy caring for older adults with rheumatic disease.	72 (39%)	106 (58%)	5 (2.7%)	0 (0.0%)	-0.20841	0.00464
	No		Yes		Spearman Rank Correlation Coefficient	p-value
Are you familiar with the Geriatric SMs?	126 (69%)		57 (31%)		0.25049	0.00063
Have you received any training specific to the care of older adults?	123 (67%)		60 (33%)		0.13581	0.06678

*n=162 for questions presented only to prescribers, n (%)

Results: Over 3 months, 183 surveys were completed by respondents around the world but predominantly in the US. The survey respondent median age was between 45-64, 61% were women, 73% were white and 51% had been in practice for >11 years (Table 1). Most respondents were physicians (79%), specializing in rheumatology (86%), and practicing in academic medicine (65%). The most challenging aspects of caring for older adults were reported to be multi-complexity (90%), polypharmacy (79%), insufficient visit time (53%) and patient financial limitations (45%). The most frequently reported differences in the care of older adults included reduced use of NSAIDs (83%) and decreased use of opioids (42%), with a minority of providers reporting that they manage older and younger adults the same (18%) (Table 2). The median ERA-12 score was 36 out of 48 indicating that respondents on average disagreed with the stereotypes regarding aging but did not strongly disagree. Table 3 shows higher ERA-12 scores (less ageist beliefs) were associated with greater enjoyment of the care of older adults (p=0.0046) and awareness of the Geriatrics 5Ms (p=0.00063). Lower ERA-12 scores were associated with believing that older adults are more demanding of attention (p=0.0034) and more concerned about the risks of medical therapy (p=0.0046) than younger adults. Lower ERA-12 scores were also associated with a shift from disease modifying therapy to symptom relief in older adults (p=0.00037).

Conclusion: Increased stereotypical thinking regarding aging is associated with self-reported changes to patient counseling, medical decision making, and perception of patient goals. This suggests that our biases regarding aging may affect how we care for older patients. Knowledge of the Geriatrics 5Ms was correlated with increased ERA-12 scores suggesting that increased awareness of aging principles may reduce these stereotypes and ultimately improve care for older adults. Further studies to quantify the effects of ageism on patient care and to assess the patient perspective on ageism in rheumatology are needed to identify interventions that can improve outcomes for this patient population.

Disclosure: A. Smith: None; **P. Achanta**: None; **U. Makris**: None.

Abstract Number: 2458

The Impact of Social Inequities on Presentation of Childhood-Onset Systemic Lupus Erythematosus (cSLE) at a Large Tertiary Center

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Healthcare Disparities in Rheumatology
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: The prevalence of childhood-onset SLE (cSLE) differs by racial/ethnic group. Yet, the role of social determinants of health (SDoH) in disease severity is not understood. We hypothesized that in an urban center with a large, diverse catchment area, SDoH influence the severity of cSLE at diagnosis.

Methods: We completed an IRB-approved retrospective review of 136 children newly diagnosed with cSLE between 1/1/18-5/31/22 at Texas Children's Hospital (TCH). We abstracted demographic, clinical severity characteristics (SLEDAI at diagnosis, inpatient or ICU admission, CNS, CYC therapy) and SDoH variables such as State Area Deprivation Index

(ADI; higher quartiles indicate greater deprivation), insurance status, distance to care, pollution burden, food accessibility, and social work consultation. Statistical analyses performed in Stata v15.1 and ArcGIS Pro2.2.

Results: Mean age at diagnosis was 13.4 years ± 3 SD, with 82.4% female, 52.9% Hispanic White (HW) and 25.7% non-Hispanic Black (NHB). Fourteen patients (10.3%) were uninsured (UI) and 50% had Medicaid (M) or Children's Health Insurance Program (CHIP). Half were diagnosed during inpatient admission (14% in the ICU). Average SLEDAI at diagnosis was 12.5 ± 7.1

Table 1. Patient and Social Characteristics (N=136)

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Patient Characteristics		Social Characteristics	
Age at Diagnosis	13.4 years ± 3 SD	**Primary Language**	
Sex		English	92 (67.6%)
Female	Female 112 (82.4%)	Spanish	42 (30.9%)
Male	Male 24 (17.6%)	Other	2 (1.5%)
Race/Ethnicity		**PCP**	
Non-Hispanic White	8 (5.9%)	Yes	91 (66.9%)
Non-Hispanic Black	35 (25.7)	No	20 (14.7%)
Non-Hispanic Asian	11 (8.1%)	Unknown	25 (18.4%)
Biracial	10 (7.4%)	**Insurance**	
Hispanic White	72 (52.9%)	Medicaid/CHIP	68 (50%)
Organ Involvement		Private	54 (39.7%)
Hematologic	122 (89.7%)	None	14 (10.3%)
Joint	78 (57.4%)	**Referral Source**	
Cutaneous	63 (46.3%)	PCP	36 (26.5%)
Renal	48 (35.3%)	ED/Hospital	67 (49.3%)
Mucosal	35 (26.5%)	Subspecialty	33 (24.3%)
Pulmonary	14 (10.3%)	**Diagnosis Location**	
Cardiac	12 (8.8%)	Outpatient	68 (50%)
Gastrointestinal	10 (7.4%)	Inpatient Floor	49 (36%)
CNS	8 (5.9%)	Inpatient ICU	19 (14%)
Muscle	5 (3.7%)	**Social Work Consulted**	109 (80.1%)
SLICC Criteria	7 ± 2.4 SD	Insurance	31 (28.4%)
ACR Criteria	4.5 ± 1.4 SD	Psychiatric	28 (25.7%)
SLEDAI Score	12.5 ± 7.1 SD	Transportation	21 (19.3%)
Medications Used		Transition	19 (17.4%)
IV Steroids	82 (60.3%)	Financial	8 (7.3%)
PO Steroids	45 (33.1%)	Legal Assistance	5 (4.9%)
Hydroxychloroquine	132 (97.1%)	School Needs	5 (4.9%)
Azathioprine	23 (16.9%)	Death Support	4 (3.7%)
Methotrexate	16 (11.8%)	Food Insecurity	4 (3.7%)
Cyclophosphamide	14 (10.3%)	Medical Noncompliance	3 (2.8%)
Rituximab	43 (31.6%)	Unstable Employment	2 (1.8%)
MMF	50 (36.8%)	Other	3 (2.8%)
ASA	51 (37.5%)	No Needs Identified	27 (24.8%)
Enoxaparin	4 (2.9%)	**State ADI Percentile (N=129)**	45.7 ± 25.2 SD
Plasmapheresis	3 (2.2%)	**Low Food Access (N=133)***	33 (24.8%)
Other	4 (2.9%)		Median (IQR)
Deaths	3 (2.2%)	**Distance to TCH (miles)**	26.1 (17.1-48.1)
		Distance to FQHC (miles)	3.7 (2.3-5.7)
		Pollution Burden (decile)**	7 (5-9)

*Based on USDA 2019 Flag for low-access tract: a tract with at least 500 people or 33% of the population living more than 1 mile (urban areas) or 10 miles (rural areas) from the nearest supermarket, supercenter or large grocery store
**Based on 2020 Environmental Protection Agency State-Based pollution scores
Abbreviations: ADI: Area Deprivation Index, TCH: Texas Children's Hospital, FQHC: Federally Qualified Health Center

SD; 48.5% had SLEDAI ≥12 (severe disease). Average ADI (%) was 45.7 ± 25.2 SD. Twenty-five percent lived in a census tract with low-access to supermarkets. The median pollution burden score decile was 7 (IQR 5-9). Social work was consulted in 80.1% (Table 1).

SLEDAI scores were higher in NHB and Biracial (BR) patients at presentation (BR 17.1, NHB 14.8, HW 11.5, Asian (A) 10.6, Non-Hispanic White (NHW) 8.5; *P*=0.01), Table 2. CNS involvement was highest among NHB children (NHB 17.1%, BR 10%, A 9.1%, HW 0%, NHW 0%; *P*=0.004). CYC was most often used in NHB and BR patients (NHB 25.7%, BR 20%, A 9.1%, HW 2.8%, NHW 0%; *P*=0.003). HW patients had the highest ADI (HW 54.3, NHW 42.7, BR 37.6, NHB 37.5, A 28.5; *P*=0.001) and live in lower food accessible neighborhoods (HW 35.7%, NHW 25%, NHB 11.4%, BR 11.1%, A 9.1%; *P*=0.035). NHWs travel further to TCH (NHW 99.3 miles, A 26.2, NHB 25.2, HW 24.1, BR 20.7; P< 0.001), live in less polluted neighborhoods (burden score BR 8, HW 8, NHB 7, A 6, NHW 3; *P*=0.021), and were less likely to have a social work consult (BR 100%, NHB 85.7%, HW 81.9%, A 63.6%, NHW 37.5%; *P*=0.01).

Table 2. Summary Statistics by Race/Ethnicity

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	Non-Hispanic White (N=8)	Non-Hispanic Black (N=35)	Non-Hispanic Asian (N=11)	Biracial (N=10)	Hispanic White (N=72)	*P*-value
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Age at Diagnosis	13.7 (2.5)	13.4 (3.4)	13 (3.0)	11.9 (2.4)	13.6 (2.8)	0.531
SLICC	6.4 (2.4)	7.5 (2.7)	6.8 (2.3)	7.8 (2.7)	6.8 (2.3)	0.424
SLEDAI	8.5 (6.1)	14.8 (7.7)	10.6 (5.9)	17.1 (6.7)	11.5 (6.6)	**0.010**
ACR	4.5 (1.5)	4.9 (1.4)	4.2 (1.3)	5.4 (1.4)	4.2 (1.3)	**0.021**
State ADI (Percentile)	N=8 42.7 ± 18.4	N=35 37.5 ± 24.9	N=11 28.5 ± 23.1	N=9 37.6 ± 26.2	N=66 54.3 ± 23.4	**0.001**
Low Food Access N (%)*	2 (25%)	4 (11.4%)	1 (9.1%)	1 (11.1%)	25 (35.7%)	**0.035**
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	
Travel to TCH (miles)	99.3 (63-105.4)	25.2 (15.8-33.9)	26.2 (23.3-28.5)	20.7 (14.7-28)	24.1 (17.2-43.2)	**<0.001**
Travel to FQHC (miles)	9.5 (4-11.6)	3.2 (1.9-6)	4.4 (3.7-5.8)	3.2 (2.4-4.4)	3.1 (2.1-5.1)	**<0.001**
Pollution Burden (decile)**	3 (2.5-4)	7 (5-8)	6 (5-7)	8 (6-8)	8 (5-9)	**0.021**
Diagnosis Location	N (%)	N (%)	N (%)	N (%)	N (%)	0.222
Outpatient	5 (62.5)	12 (34.3)	9 (81.8)	4 (40)	38 (52.8)	
Inpatient Floor	3 (37.5)	16 (45.7)	1 (9.1)	4 (40)	25 (34.7)0	
Inpatient ICU	0	7 (20)	1 (9.1)	2 (20)	9 (12.5)	
Referral Source	N (%)	N (%)	N (%)	N (%)	N (%)	0.082
PCP	2 (25)	5 (14.3)	5 (45.5)	3 (30)	21 (29.2)	
ED/Hospital	3 (37.5)	25 (71.4)	2 (18.2)	5 (50)	32 (44.4)	
Subspecialty	3 (37.5)	5 (14.3)	4 (36.4)	2 (20)	19 (26.4)	
Social Work Consult	N (%)	N (%)	N (%)	N (%)	N (%)	**0.010**
Yes	3 (37.5)	30 (85.7)	7 (63.6)	10 (100)	59 (81.9)	
No	5 (62.5)	5 (14.3)	4 (36.4)	0	13 (18.1)	
Severe Disease Characteristics	N (%)	N (%)	N (%)	N (%)	N (%)	
Renal Disease	2 (25)	17 (48.6)	1 (9.1)	5 (50)	23 (31.9)	0.102
CNS Disease	0	6 (17.1)	1 (9.1)	1 (10)	0	**0.004**
CYC Use	0	9 (25.7)	1 (9.1)	2 (20)	2 (2.8)	**0.003**

*Based on USDA 2019 Flag for low-access tract: a tract with at least 500 people or 33% of the population living more than 1 mile (urban areas) or 10 miles (rural areas) from the nearest supermarket, supercenter or large grocery store

**Based on 2020 Environmental Protection Agency State-Based pollution scores

Abbreviations: ADI: Area Deprivation Index, TCH: Texas Children's Hospital, FQHC: Federally Qualified Health Center

UI patients were most likely to be diagnosed on an inpatient floor and those with M had the highest proportion of ICU admissions (Floor: UI 64.3%, M 33.8%, Private (P) 31.5%; ICU: M 19.1%, UI 14.3%, P 7.4%; *P*=0.034), Table 3. UI and M patients had higher ADI (UI 57.4%, M 50.4%, P 36.8%; P=0.003), more social work consults (UI 100%, M 88.2%, P 64.8%; *P*=0.001) and live in more polluted neighborhoods (burden score UI 8, M 8, P 6; *P*=0.041).

Table 3. Summary Statistics by Insurance Status

Table 3. Summary Statistics by Insurance Status

	None (N=14)	Medicaid/CHIP (N=68)	Private (N=54)	*P*-value
	Mean (SD)	Mean (SD)	Mean (SD)	
Age at Diagnosis	14.1 (2.5)	13.2 (3.1)	13.3 (2.9)	0.613
SLICC Criteria	7.9 (2.1)	7.1 (2.2)	6.6 (2.6)	0.166
SLEDAI	15.1 (8.9)	13.1 (6.7)	11.1 (6.8)	0.100
ACR Criteria	4.8 (1.1)	4.6 (1.4)	4.4 (1.4)	0.472
State ADI (Percentile)	N=12 57.4 ± 24.0	N=66 50.4 ± 26.1	N=51 36.8 ± 21.6	**0.003**
Low Food Access N (%)*	5 (35.7%)	18 (16.5%)	10 (19.6%)	0.413
	Median (IQR)	Median (IQR)	Median (IQR)	
Travel (Miles) to TCH	24.3 (20.1-96.8)	25.5 (15.3-40.3)	26.5 (17.2-51.8)	0.958
Travel (Miles) to FQHC	4 (2.9-5.7)	3.1 (1.8-5.0)	4.4 (2.9-6.2)	**0.049**
Pollution Burden (Decile)**	8 (4-10)	8 (5-9)	6 (4-8)	**0.041**
Diagnosis Location	N (%)	N (%)	N (%)	**0.034**
Outpatient	3 (21.4)	32 (47.1)	33 (61.1)	
Inpatient Floor	9 (64.3)	23 (33.8)	17 (31.5)	
Inpatient ICU	2 (14.3)	13 (19.1)	4 (7.4)	
Race/Ethnicity	N (%)	N (%)	N (%)	**0.007**
Non-Hispanic White	1 (7.1)	2 (2.9)	5 (9.3)	
Non-Hispanic Black	0	21 (30.9)	14 (25.9)	
Non-Hispanic Asian	0	3 (4.4)	8 (14.8)	
Biracial	0	4 (5.9)	6 (11.1)	
Hispanic White	13 (92.9)	38 (55.9)	21 (38.9)	
Referral Source	N (%)	N (%)	N (%)	**0.011**
PCP	1 (7.1)	19 (27.9)	16 (29.6)	
ED/Hospital	12 (85.7)	36 (52.9)	19 (35.2)	
Subspecialty	1 (7.1)	13 (19.1)	19 (35.2)	
Access to PCP	N (%)	N (%)	N(%)	**0.001**
Yes	5 (35.7)	45 (66.2)	41 (75.9)	
No	8 (57.1)	8 (11.8)	4 (7.4)	
Unknown	1 (7.1)	15 (22.1)	9 (16.7)	
Primary Language English	N (%)	N (%)	N (%)	**0.026**
Yes	5 (35.7)	47 (69.1)	40 (74.1)	
No	9 (64.3)	21 (30.9)	14 (25.9)	
Social Work Consulted	N (%)	N (%)	N (%)	**0.001**
Yes	14 (100)	60 (88.2)	35 (64.8)	
No	0	8 (11.8)	19 (35.2)	
Transportation Difficulty	N (%)	N (%)	N (%)	**0.001**
Yes	14 (100)	9 (13.2)	8 (14.8)	
No	0	59 (86.8)	46 (85.2)	

*Based on USDA 2019 Flag for low-access tract: a tract with at least 500 people or 33% of the population living more than 1 mile (urban areas) or 10 miles (rural areas) from the nearest supermarket, supercenter or large grocery store
**Based on 2020 Environmental Protection Agency State-Based pollution scores
Abbreviations: ADI: Area Deprivation Index, TCH: Texas Children's Hospital, FQHC: Federally Qualified Health Center

Conclusion: In children with cSLE drawn from a large urban catchment area, we observed an impact of non-modifiable (e.g., race/ethnicity) and modifiable (e.g, insurance status, access to care, food accessibility) factors on disease severity at presentation. Next steps include geospatial mapping to identify high-risk neighborhoods with a discordant number of cSLE patients, and targeting modifiable risk factors in these communities to improve patient experiences and outcomes.

Disclosure: E. Beil: None; **E. Muscal**: Sobi, 1, 11; **A. Oluyomi**: None; **O. Rosales**: None; **D. Guffey**: None; **M. DeGuzman**: None; **C. Yildirim-Toruner**: None; **A. Ramirez**: None; **E. Peckham-Gregory**: None.

Abstract Number: 2459

Reporting of Race and Ethnicity in Lupus Publications in High-impact Rheumatology Journals

Idil Eroglu, Hailey Baker, Mario Felix and Lisa Suter, Yale School of Medicine, New Haven, CT

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Healthcare Disparities in Rheumatology
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Reporting of race and ethnicity as social constructs is critical to highlight equity and diversity of study participants, with the knowledge that socio-economic factors can affect systemic lupus erythematosus (SLE) outcomes[1-3]. Currently, reporting of race and ethnicity in rheumatology journals is not standardized. Studies often report majority White populations without discussing racial disparities or how inequities lead to worse outcomes[4]. Recent guidance on reporting of race and ethnicity by JAMA highlights the importance of specifying who identified participant race and ethnicity, including the federal Office of Management and Budget (OMB) minimum categories (American Indian or Alaska Native, Asian, Black, or African American, Native Hawaiian or Other Pacific Islander, and White), and reasons for assessing race. Reviewing current reporting practices on race and ethnicity in rheumatology journals is essential to potentially identify areas of improvement, especially in SLE which has high proportions of racial and ethnic disparities[5]. Here, we assess the reporting of race and ethnicity in recent high-impact rheumatology publications on SLE research to analyze for adherence to these reporting recommendations.

Methods: Using the Scimago Journal & Country Rank, we identified *Annals of Rheumatic Diseases* and *Arthritis and Rheumatology as* the two highest-ranked rheumatology journals according to the Scimago Journal Rank. We identified all studies involving human subject data published between January 2020 – December 2022 with at least one author based in the U.S. using the following search terms to identify our publications: systemic lupus erythematosus (Libman sacks or Libman-sacks), (lupus or lupovisceritis or erythematodes visceralis or SLE), (United Status or USA), "2020", "2021", "2022". Manuscripts were excluded if they did not involve human subjects. A single researcher (I.E.) reviewed all studies on reporting of race, ethnicity, and various other socioeconomic variables.

Results: A total of 103 articles met our inclusion criteria and six studies were excluded. There were 24 prospective cohort studies, 22 retrospective cohort/case-control studies, 20 randomized control trials, 5 cross-sectional studies, 22 laboratory studies with patient samples, 9 genomic analyses using patient sequences, and one machine learning study using patient data. Among included studies, 96 (93%) included any demographic data, 70 (68%) reported race, 59 (57%) reported ethnicity. Of those that reported race, 56 (80%) had majority White participants and only 4 studies met OMB minimum reporting

criteria for race. Only 13 studies (13%) mentioned that racial and ethnic categories were patient-reported. Additionally, we observed that 24 studies included any comorbidities and 16 studies included various other SES factors.

Conclusion: Reporting of race and ethnicity is not standardized across SLE research in high-impact rheumatology journals, and the majority of publications are not meeting the JAMA guidelines for reporting race and ethnicity.

Disclosure: I. Eroglu: None; **H. Baker**: None; **M. Felix**: None; **L. Suter**: Centers for Medicare Medicaid Services, 12, Salary support from unrelated CMS ontract, unrelated NIH grant to Elena Losina/BWH, 1.

Abstract Number: 2460

Health Care Segregation, but Not Metropolitan Area Segregation, Magnifies Racial Disparities in Hospital Outcomes of Pediatric Lupus

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Healthcare Disparities in Rheumatology
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Racial disparities and hospital-level variation in pediatric SLE (pSLE) outcomes are well described, but it is not known how the racial and ethnic composition of the populations hospitals serve contributes to these disparities. Using de-identified data, we evaluated whether hospital minority composition, a measure of health care segregation, or metropolitan statistical area (MSA)-level racial or ethnic segregation modify racial disparities in pSLE outcomes.

Methods: We linked data from the Pediatric Health Information System (2006–2021) for patients 5-26 years old hospitalized for SLE to MSA-level 2020 U.S. Census and American Community Survey data. Primary outcomes assessed at the patient level were intensive care unit (ICU) stays and adverse renal outcomes (end stage renal disease, dialysis, or transplant). Hospital Black racial composition and Hispanic ethnic composition were based on % of all admissions (any indication) reported by each hospital. MSA segregation was measured by census-derived Dissimilarity Index (DI) for Black/Non-Hispanic White (NHW) or Hispanic/Non-Hispanic segregation, reflecting evenness of spatial distribution of two groups across census tracts within an MSA. We compared indices using mixed effects logistic models with hospital-level random effects, adjusted for calendar period, sociodemographics, severity indicators, and hospital volume. We stratified hospitals by above or below the median for Black or Hispanic composition and by high or low Black/NHW segregation.

Results: Of 8125 patients (at 47 hospitals), 2293 (28%) ever required ICU care and 698 (9%) had an adverse renal outcome (Table 1). Higher hospital Hispanic composition, but not Black racial composition, associated with lower overall odds of ICU stay (OR 0.99 [0.986-0.996] per % increase). Significant Black vs. NHW disparity in ICU care was observed only at hospitals with high Black racial composition, whereas Hispanic vs. NHW disparities in ICU stay did not differ by hospital Hispanic composition (Fig 1).

Similarly, the magnitude of Black vs. NHW disparity in renal outcomes was larger at hospitals with high Black racial composition (OR 2.0 [1.4-2.8] vs. 1.7 [1.1-2.4]). Moreover, disparities in renal outcomes for Hispanic White vs. NHW children were only observed at hospitals with high Black racial composition (Fig 2A). We observed the opposite for Hispanic composition, where Hispanic White, Asian, and American Indian/Other vs. NHW disparities were only apparent at hospitals with low Hispanic composition (Fig 2B).

MSA-level DI was not significantly associated with either outcome. Black vs. NHW disparities did not differ by high (DI >0.6) vs. low MSA Black/NHW segregation (Fig 1C, 2C). No MSAs met criteria for high Hispanic/Non-Hispanic segregation.

Table 1. Patient, Hospital, and Metropolitan Area-Level Characteristics of Hospitalized Children with SLE

Patient-Level Covariates		N=8125
Race and Ethnicity, n(%)	American Indian/Other Non-Hispanic*	622 (8)
	Asian or Pacific Islander	605 (7)
	Black	2673 (33)
	Hispanic Other race	1012 (12)
	Hispanic White	1279 (16)
	Unknown race and ethnicity	156 (2)
	White, Non-Hispanic	1778 (22)
Age in years, median (min, max)		15 (5, 26)
Female Sex, n(%)	Female	6701 (82)
Insurance, n(%)	Commercial	2991 (37)
	Public Insurance	4556 (56)
	Other/Self-Pay	475 (6)
	Unknown	103 (1)
Median Household Income for zip code, n(%)	1st Quartile	1978 (24)
	2nd Quartile	1978 (24)
	3rd Quartile	1978 (24)
	4th Quartile	1978 (24)
	Unknown	213 (3)
Calendar Period, n(%)	2005-2010	2495 (31)
	2011-2015	2389 (29)
	2016-2021	3241 (40)
Nephritis diagnosis code		4735 (58)
Seizure diagnosis code		871 (11)
Stroke diagnosis code		445 (5)
APR-DRG Illness Severity, n(%)	Minor	835 (10)
	Moderate	2955 (36)
	Major	2961 (36)
	Extreme	1374 (17)
*Hospital-Level Covariates^*		N=47
Annualized Inpatient Admission Volume, median (min, max)		5338 (1787, 13825)
Annualized SLE Inpatient Volume, median (min, max)		77 (11, 864)
Hospital Black Racial Composition (%), median (min, max)		19 (2, 67)
Hospital Hispanic Ethnic Composition (%), median (min max)		12 (1, 59)
Metropolitan Area-Level Covariates[Ł]		N=41
Highly Segregated Dissimilarity Index (>0.6) (Black vs. Non-Hispanic White), n(%)		3620 (45)
Less Well Integrated Dissimilarity Index (≥0.3) (Hispanic vs. Non-Hispanic), n(%)		7485 (92)
ICE[ǂ] Race (Black vs. Non-Hispanic White), median (min, max)		0.53 (-0.003, 0.79)
ICE Ethnicity (Hispanic vs. Non-Hispanic), median (min, max)		0.64 (0.03, 0.85)
ICE Income (Highest 80%ile vs. Lowest 20%ile), median (min, max)		0.06 (-0.07, 0.42)

*Includes 94 individuals with hospital-reported American Indian race

^Black racial composition could be determined for N=46 out of 47 hospitals (one withdrew data); Hispanic ethnic composition could be determined for N=45 hospitals (one outlier excluded for incomplete reporting of ethnicity)

Ł N=41 hospital city names could be mapped to a metropolitan statistical area (MSA)

ǂ Index of Concentration at the Extremes (ICE) ranges from -1 to 1, with more positive values representing a higher proportion of residents belonging to the most privileged group relative to the least privileged group

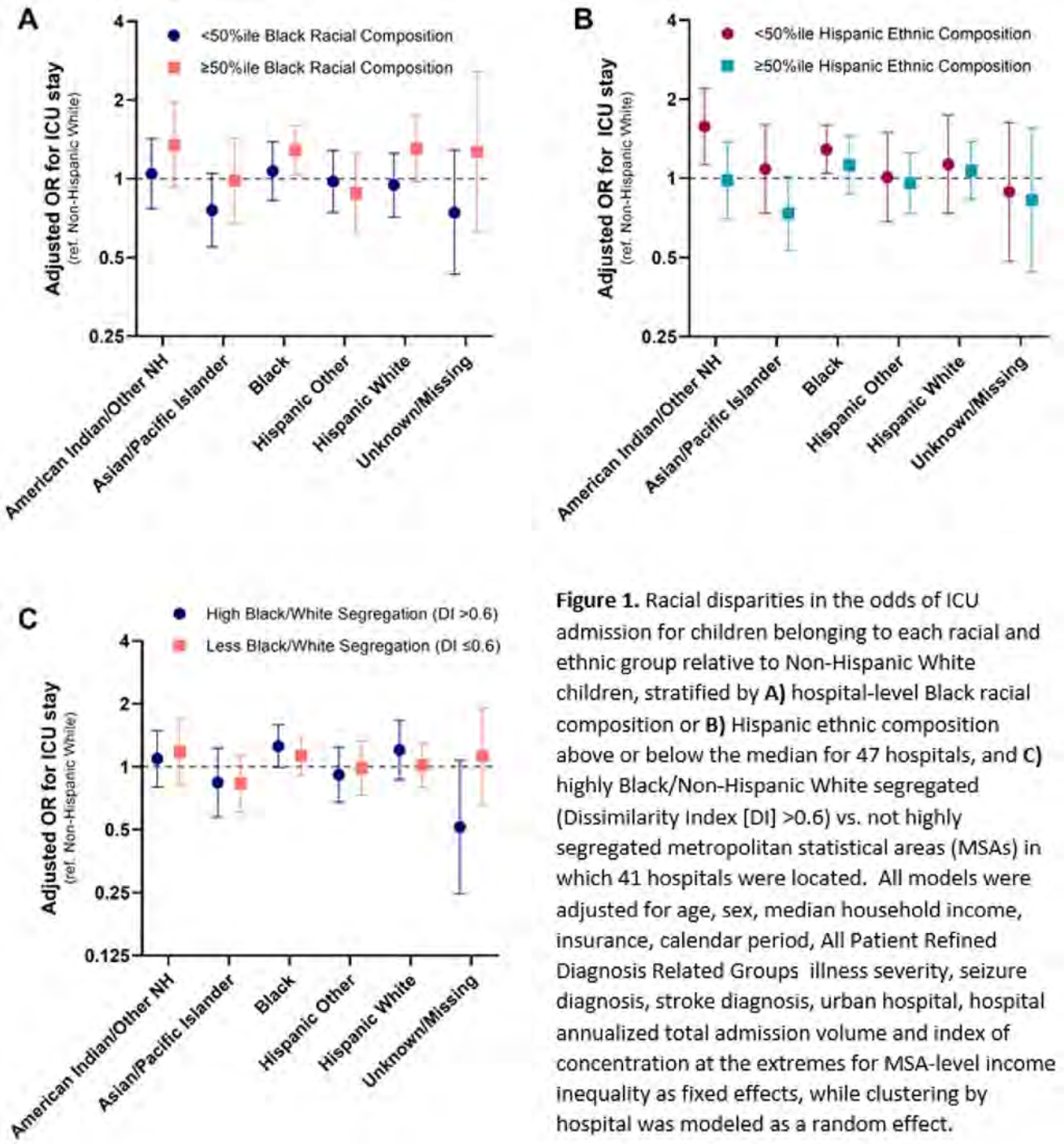

Figure 1. Racial disparities in the odds of ICU admission for children belonging to each racial and ethnic group relative to Non-Hispanic White children, stratified by **A)** hospital-level Black racial composition or **B)** Hispanic ethnic composition above or below the median for 47 hospitals, and **C)** highly Black/Non-Hispanic White segregated (Dissimilarity Index [DI] >0.6) vs. not highly segregated metropolitan statistical areas (MSAs) in which 41 hospitals were located. All models were adjusted for age, sex, median household income, insurance, calendar period, All Patient Refined Diagnosis Related Groups illness severity, seizure diagnosis, stroke diagnosis, urban hospital, hospital annualized total admission volume and index of concentration at the extremes for MSA-level income inequality as fixed effects, while clustering by hospital was modeled as a random effect.

Conclusion: Racial disparities in pSLE outcomes are magnified at hospitals serving a greater proportion of Black patients, which may reflect negative effects of health care segregation and inequitable hospital resources. Metropolitan level measures of segregation explain little variance in hospital outcomes, therefore linkages to small geographic units must be included in health care databases to understand local factors that contribute to poor outcomes.

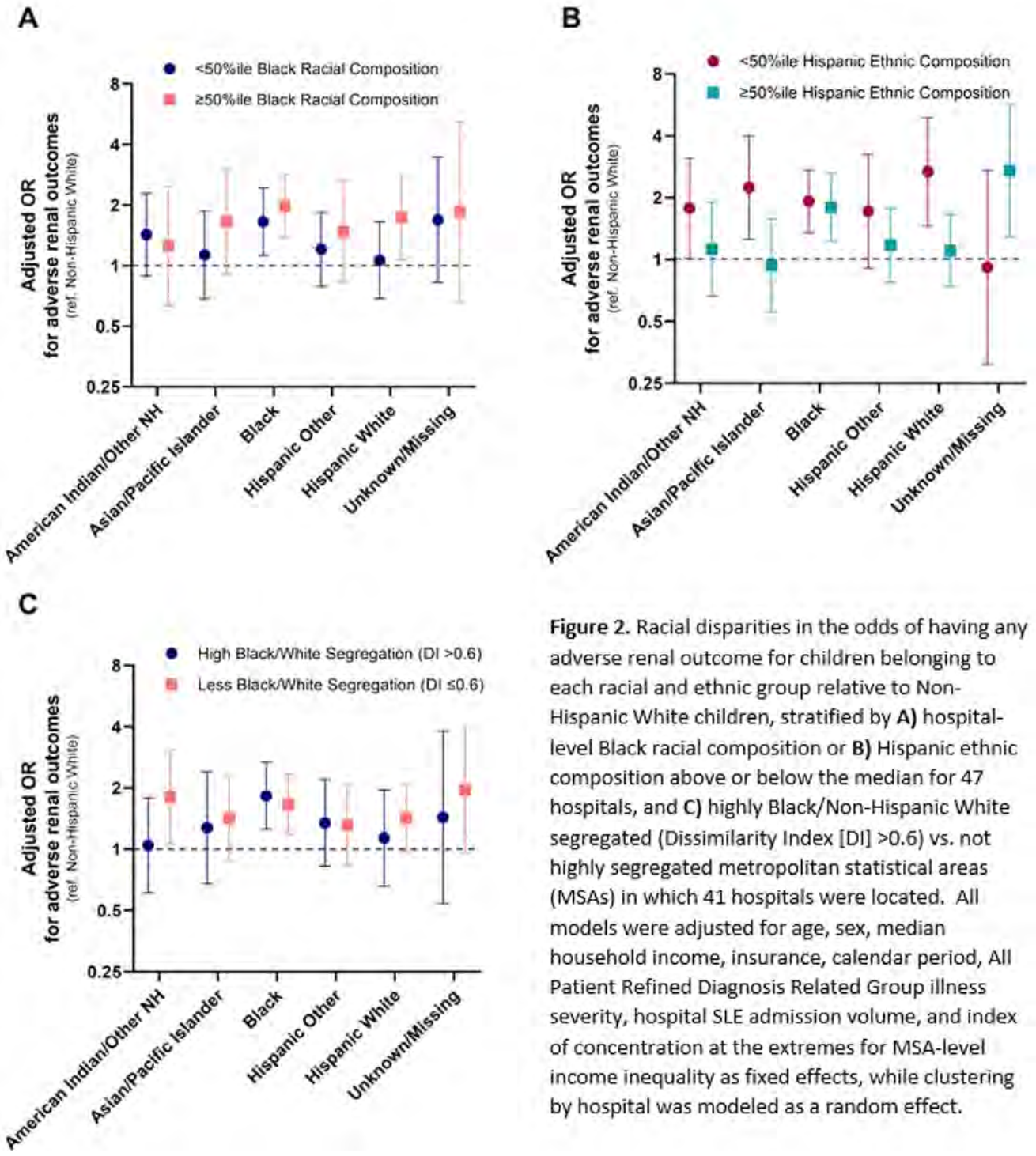

Figure 2. Racial disparities in the odds of having any adverse renal outcome for children belonging to each racial and ethnic group relative to Non-Hispanic White children, stratified by **A)** hospital-level Black racial composition or **B)** Hispanic ethnic composition above or below the median for 47 hospitals, and **C)** highly Black/Non-Hispanic White segregated (Dissimilarity Index [DI] >0.6) vs. not highly segregated metropolitan statistical areas (MSAs) in which 41 hospitals were located. All models were adjusted for age, sex, median household income, insurance, calendar period, All Patient Refined Diagnosis Related Group illness severity, hospital SLE admission volume, and index of concentration at the extremes for MSA-level income inequality as fixed effects, while clustering by hospital was modeled as a random effect.

Disclosure: J. Chang: None; **J. Liu**: None; **L. Berbert**: None; **E. Weller**: None; **G. Alonzi**: None; **E. Smitherman**: None; **P. Patel**: AbbVie/Abbott, 12, Site Principal Investagator, Pfizer, 12, Site Principal Investigator; **M. Son**: None; **K. Costenbader**: Amgen, 2, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Eli Lilly, 2, Exagen Diagnostics, 5, Gilead, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5.

Abstract Number: 2461

Transcriptional Derepression of CHD4/NuRD-regulated Genes in the Muscle of Patients with Dermatomyositis and anti-Mi2 Autoantibodies

Iago Pinal-Fernandez[1], Jose Cesar Milisenda[2], Katherine Pak[1], Sandra Muñoz-Braceras[3], Maria Casal-Dominguez[3], Jose Jiram Torres-Ruiz[3], Stefania Dell´Orso[4], Faiza Naz[4], Gustavo Gutierrez-Cruz[4], Yaiza Duque-Jaimez[2], Ana Matas-Garcia[2], Joan Padrosa[5], Francesc J Garcia-Garcia[2], Mariona Guitart-Manpel[2], Gloria Garrabou[2], Ernesto Trallero-Araguas[6], Brian Wallit[7], Julie Paik[8], Jemima Albayda[8], Lisa Christopher-Stine[8], Tom Lloyd[9], Josep Maria Grau[2], Albert Selva-O'Callaghan[6] and Andrew Mammen[10], [1]National Institutes of Health, Bethesda, MD, [2]Muscle Research Unit, Internal Medicine Service, Hospital Clinic, Barcelona, Spain, [3]Muscle Disease Unit, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [4]National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [5]CIBERER, Barcelona, Spain, Barcelona, Spain, [6]Systemic Autoimmune Disease Unit, Vall d'Hebron Institute of Research, Barcelona, Spain, [7]National Institute of Neurological Diseases and Stroke, National Institutes of Health, Bethesda, MD, [8]Johns Hopkins University, Baltimore, MD, [9]Johns Hopkins University School of Medicine, Baltimore, MD, [10]NIH, Bethesda, MD

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science I

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Myositis is a heterogeneous family of diseases including dermatomyositis (DM), immune-mediated necrotizing myopathy (IMNM), antisynthetase syndrome (AS), and inclusion body myositis (IBM). Myositis-specific autoantibodies define different subtypes of myositis. For example, patients with anti-Mi2 autoantibodies targeting the CHD4/NuRD complex (a transcriptional repressor) have more severe muscle disease than other DM patients. This study aimed to define the transcriptional profile of muscle biopsies from anti-Mi2-positive DM patients.

Methods: RNA sequencing was performed on muscle biopsies (n=171) from patients with anti-Mi2-positive DM (n=18), DM without anti-Mi2 autoantibodies (n=32), AS (n=18), IMNM (n=54), and IBM (n=16) as well as 33 normal muscle biopsies. Genes specifically upregulated in anti-Mi2-positive DM were identified. Muscle biopsies were stained for human immunoglobulin and protein products corresponding to genes specifically upregulated in anti-Mi2-positive muscle biopsies.

Results: A set of 135 genes, including SCRT1 and MADCAM, was specifically overexpressed in anti-Mi2-positive DM muscle. This set was enriched for CHD4/NuRD-regulated genes and included genes that are not otherwise expressed in skeletal muscle. The expression levels of these genes correlated with anti-Mi2 autoantibody titers, markers of disease activity, and with the other members of the gene set. In anti-Mi2-positive muscle biopsies, immunoglobulin was localized to the nucleus, MADCAM protein was present in the cytoplasm of perifascicular fibers, and SCRT1 protein was localized to myofiber nuclei.

Conclusion: Based on these findings, we hypothesize that anti-Mi2 autoantibodies could exert a pathogenic effect by entering damaged myofibers, inhibiting the CHD4/NuRD complex, and subsequently derepressing the unique set of genes defined in this study.

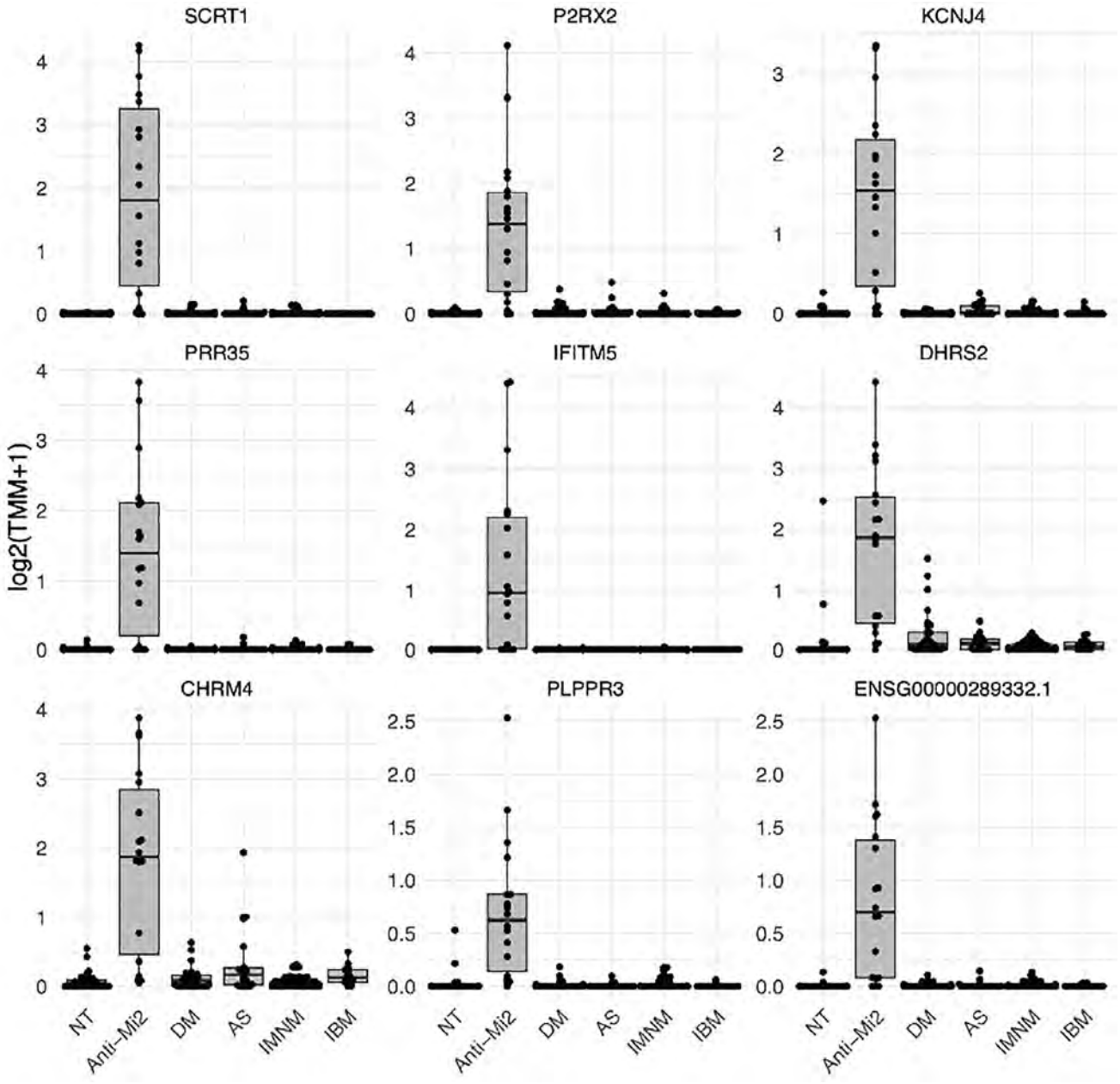

Figure 1. The most differentially overexpressed genes in anti-Mi2 dermatomyositis muscle compared to all the other muscle biopsies included in the study (histologically normal muscle biopsies [NT], non-anti-Mi2 dermatomyositis [DM], antisynthetase syndrome [AS], immune-mediated necrotizing myositis [IMNM], and inclusion body myositis [IBM]).

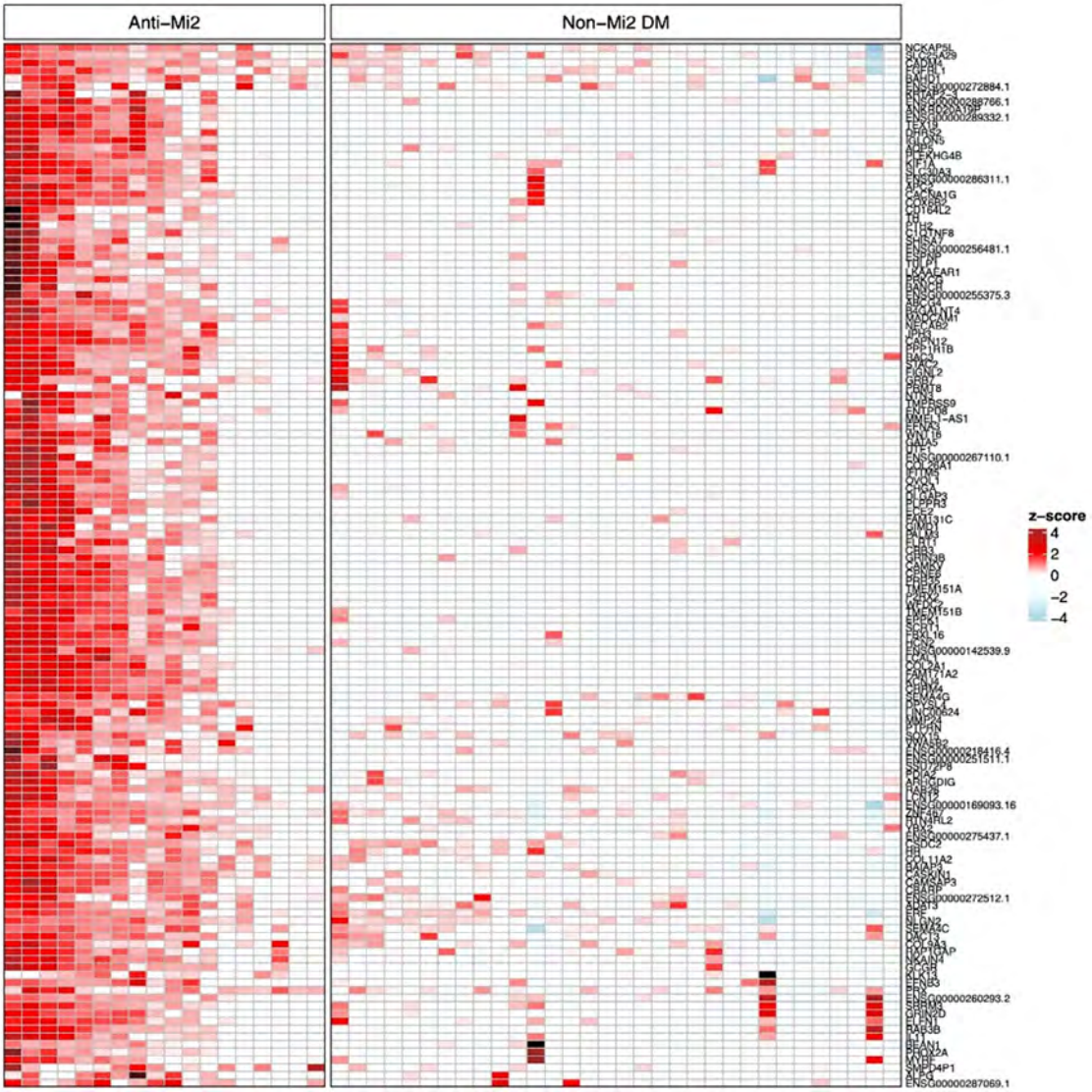

Figure 2. Normalized expression (z-score) of the specifically overexpressed genes in patients with anti-Mi2-positive dermatomyositis (DM) compared with non-Mi2-positive DM.

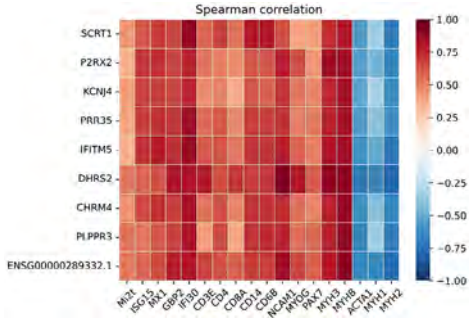

Figure 3. Correlation of the most differentially specifically overexpressed genes in patients with anti-Mi2-positive dermatomyositis and: titer of anti-Mi2 autoantibodies by ELISA (Mi2t), type 1 interferon-inducible genes (ISG15, MX1), type 2 interferon-inducible genes (GBP2, IFI30), T-cell markers (CD3E, CD4, CD8), macrophages (CD14, CD68), markers of muscle differentiation (NCAM1, MYOG, PAX7, MYH3, MYH8), and structural mature muscle proteins (ACTA1, MYH1, MYH2).

Disclosure: I. Pinal-Fernandez: None; **J. Milisenda**: None; **K. Pak**: None; **S. Muñoz-Braceras**: None; **M. Casal-Dominguez**: None; **J. Torres-Ruiz**: None; **S. Dell´Orso**: None; **F. Naz**: None; **G. Gutierrez-Cruz**: None; **Y. Duque-Jaimez**: None; **A. Matas-Garcia**: None; **J. Padrosa**: None; **F. Garcia-Garcia**: None; **M. Guitart-Manpel**: None; **G. Garrabou**: None; **E. Trallero-Araguas**: None; **B. Wallit**: None; **J. Paik**: None; **J. Albayda**: Amgen, 5, Janssen, 5; **L. Christopher-Stine**: None; **T. Lloyd**: None; **J. Grau**: None; **A. Selva-O'Callaghan**: None; **A. Mammen**: None.

Abstract Number: 2462

Mitochondrial-Mediated Neutrophil Activation in Dermatomyositis (DM) and Inclusion Body Myositis (IBM): Insights into Pathogenesis and Therapeutic Implications

Jorge Armando Gonzalez-Chapa[1], Jemima Albayda[2], Begum Horuluoglu[3], Despina Michailidou[1], Marina Barguil Macedo[1], Lisa Christopher-Stine[2], Ingrid Lundberg[4] and Christian Lood[1], [1]University of Washington, Seattle, WA, [2]Johns Hopkins University, Baltimore, MD, [3]Karolinska Institutet, Stockholm, Sweden, [4]Division of Rheumatology, Department of Medicine, Karolinska Institutet; Department of Gastroenterology, Dermatotology, Rhematology, Karolinska Universitetssjukhuset, Stockholm, Sweden

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science I

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Dermatomyositis (DM) and inclusion body myositis (IBM) are characterized by muscle weakness and inflammation, with emerging evidence of mitochondrial and neutrophil involvement. Prior work from our group has demonstrated the important role of mitochondrial-derived danger-associated molecular patterns to promote neutrophil activation in inflammatory conditions. In the current study, we aimed to investigate whether patients with myopathies had elevated levels of extracellular mitochondrial biomarkers promoting neutrophil-mediated inflammation.

Methods: Plasma samples were obtained from patients with inclusion body myositis (IBM, n=46), dermatomyositis (DM, n=40), and healthy individuals (HC, n=40) from Karolinska Institutet, Stockholm, Sweden; Johns Hopkins, Baltimore, USA; and University of Washington, Seattle, USA. DM patients were further categorized based on the presence of autoantibodies towards MDA5 (n= 19) and TIF1-gamma (n=21). Plasma levels of neutrophil-derived calprotectin and neutrophil elastase (NE)-DNA complexes, as well as mitochondrial-derived GDF-15, and N-formyl methionine (fMET), which are valuable indicators of potential mitochondrial driven-pathological processes, cellular stress, and/or tissue damage, were measured using ELISA. Statistical analysis was performed using GraphPad Prism 9.4.0.

Results: Calprotectin levels were significantly elevated in DM patients, with the highest concentrations observed in those with MDA5 subtype **(Figure 1A)**. Patients with IBM had similar levels of calprotectin as compared to HC. In contrast, levels of neutrophil extracellular traps, NETs (NE-DNA), were elevated in both DM and IBM patients, as compared to HC **(Figure 1B)**. Both IBM and DM patients exhibited higher levels of mitochondrial-derived fMET and GDF-15 as compared to HC **(Figures 1C and D)**, supporting a role for mitochondrial dysfunction and extrusion in these myopathies. Levels of GDF-15 and fMET were strongly correlated in DM but surprisingly no association was found in IBM (**Figures 2A and B)**. Of note, consistent with other inflammatory conditions, levels of mitochondrial-derived fMET correlated strongly with neutrophil activation marker calprotectin in both IBM and DM (**Figures 2C and D**) suggesting that similar mechanisms, e.g. activation of neutrophils through fMET receptor FPR1, may operate in these subgroups of myopathies.

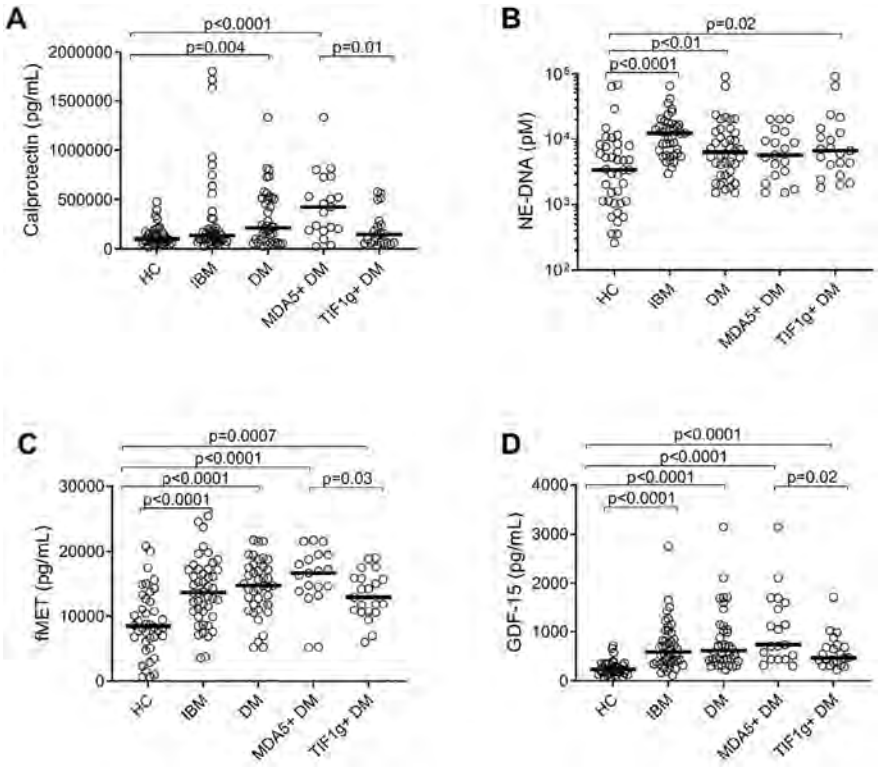

Figure 1. Neutrophil and mitochondrial biomarkers in IBM and DM. Levels of A) Calprotectin, B) NE-DNA, C) fMET, and D) GDF-15 in patients with Inclusion Body Myositis (IBM), Dermatomyositis (DM), and Healthy Controls (HC). DM patients were subdivided into MDA5 (n=19) and TIF-1 gamma (n=21) subgroups. Mann-Whitney U test was used for statistical analyses.

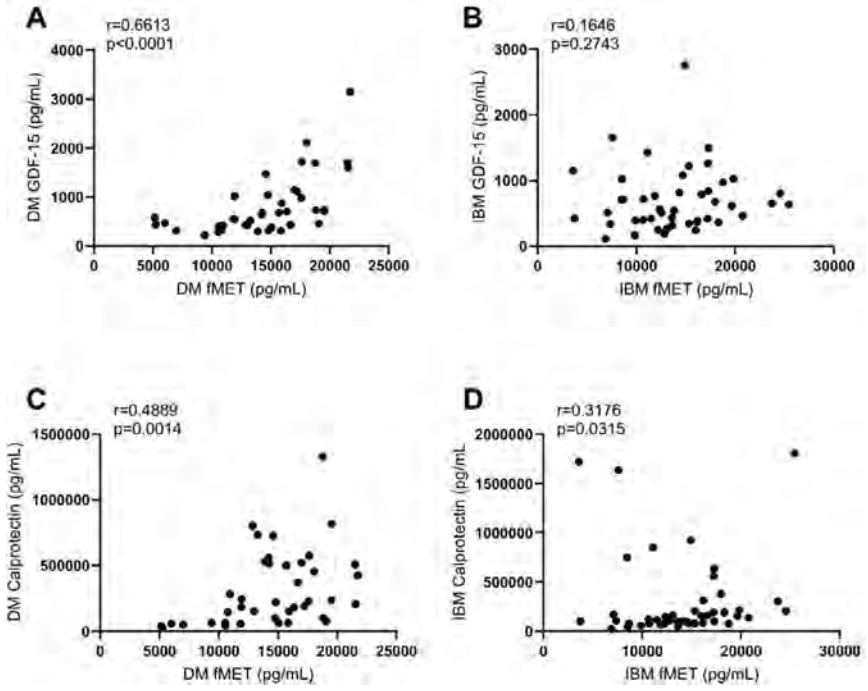

Figure 2. DM and IBM correlations between neutrophil and mitochondrial biomarkers Correlations between GDF-15 and fMET in A) DM and B) IBM patients. Correlations between calprotectin and fMET in C) DM and D) IBM patients. Spearman's correlation coefficient test.

Conclusion: Our findings reveal distinct biomarker profiles in DM and IBM, highlighting the potential roles of mitochondria and neutrophils in myopathies. The differences and similarities observed between the subgroups suggest that calprotectin and NETs may play distinct roles in DM and IBM, while elevated levels of mitochondrial-derived fMET and GDF-15 indicate the potential involvement of mitochondrial dysfunction suggesting a common pathological mechanism. Further studies are warranted to determine the role of mitochondria and neutrophils in disease pathogenesis, as well as their clinical implications in monitoring disease activity.

Disclosure: J. Armando Gonzalez-Chapa: None; **J. Albayda**: Amgen, 5, Janssen, 5; **B. Horuluoglu**: None; **D. Michailidou**: Chemocentryx, 1; **M. Barguil Macedo**: None; **L. Christopher-Stine**: None; **I. Lundberg**: Argenx, 6, Astra-Zeneca, 5, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 1, Corbus Pharmaceutical, 6, EMD Serono Research & Development Institute, 6, Janssen, 6, Kezar, 6, Novartis, 11, Octapharma, 6, Orphazyme, 6, Pfizer, 1, Roche, 11, Xencor, 6; **C. Lood**: Amytryx, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Citryll, 2, Eli Lilly, 5, Gilead, 5, Horizon Therapeutics, 5, Pfizer, 5, Redd Pharma, 5, 11.

Abstract Number: 2463

Efficacy and Safety of Car-T-Cell Treatment in Refractory Antisynthetase Syndrome – Data of the First Three Patients

Jule Taubmann[1], Johannes Knitza[2], Fabian Müller[3], Sebastian Boeltz[1], Simon Voelkl[4], Michael Aigner[4], Arnd Kleyer[5], Ioanna Minnopoulou[1], Regina Gary[4], Sascha kretschmann[4], Andreas Mackensen[4] and Georg Schett[6], [1]Department of Internal Medicine 3, Rheumatology and Immunology, Universitätsklinikum Erlangen and Friedrich-Alexander-Universität Erlangen Nürnberg, Erlangen, Germany, [2]Department of Internal Medicine 3 Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg, University Hospital Erlangen, Erlangen, Germany, [3]Friedrich Alexander Universität Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany, [4]Department of Internal Medicine 5, Hematology and Oncology, Universitätsklinikum Erlangen and Friedrich-Alexander-Universität Erlangen Nürnberg, Erlangen, Germany, [5]University Hospital Erlangen, Erlangen, Germany, [6]Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science I

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Antisynthetase syndrome (ASS) can be very severe affecting the lungs, the skin and the joints next to the muscles. ASS can take a refractory life-threatening course, necessitating the development of new treatment strategies. We recently reported the first case of successful rescue therapy of ASS with CD19-targeted CAR-T-cells [1]. Herein, we present efficacy and safety data for the first three patients with refractory ASS treated with autologous CD19 CAR-T-cells. The objective of this study was to test whether administration of CD19 CAR-T-cells is tolerable and effective in patients with severe refractory ASS.

Methods: Autologous CD19 CAR-T-cells were prepared and given as described previously [1,2,3]. All immunosuppressive treatments were stopped before CD19 CAR-T-cell administration. Tolerability was assessed by monitoring for Cytokine-Release Syndrome (CRS) and Immune-related effector Cell Neurotoxicity Syndrome (ICANS). Efficacy was assessed by CK levels, good response according 2016 ACR/EULAR total improvement score (TIS), imaging of muscles and lungs and successful cessation of all immunosuppressive treatments including glucocorticoids.

Results: Three ASS patients were treated with CD19 CAR-T-cells (table 1). All patients presented with active myositis and elevated CK levels. Patient 1 showed involvement of the muscles, skin and lungs, patient 2 showed involvement of muscles, skin, joints and lungs, patient 3 showed involvement of muscles and lungs. All patients did not respond to a minimum of 5 different immunosuppressive treatments (table 1). CAR-T-cell treatment was well-tolerated. Mild CRS (grade I) was observed in the first two patients. Patient 3 showed signs off increased O2 requirement (temporarily 10l/min by mask), chills and fever (39.0°C) defined as CRS grade II. All patients were treated with tocilizumab and CRS resolved quickly. Patient 2 had signs of mild self-limited ICANS (grade I discrete ataxia for a few days) two weeks after CAR-T treatment. Expansion of CAR-T-cells

	Pat #1	Pat #2	Pat #3
Age (ys)	43	44	42
Sex (F/M)	M	F	F
Disease Duration (ys)	2	6	1
autoantibodies	Jo 1	Jo 1	PI 7, Ro 52
Lung involvement; oxygen requirement (liter per minute at rest)	yes; 4L /min	no	yes; 3L /min
Nb. failed treatments	5 (incl CYC, RTX)	10 (inlc. CYC, RTX, OCR)	5 (incl CYC, RTX, OCR)
Baseline MMT8	115/150	103/150	137/150
Baseline CK (<170 U/l)	9305	4298	766
Conditioning Dose (%)	100	100	100
Peak CAR T (cells/µl)	60	1524	66,2
Peak CAR T (% of T cells)	3,5	56,45	11,05
Duration of B cell Aplasia (days)	128	93	ongoing
Follow-up (months)	12	8	2
Seroconversion	yes	no	not yet
TIS (6 months after Car-T-Cell therapy)	98 major	97,5 major	Follow up
CRS (grade 0-4)	1	1	2
Tocilizumab (Nb. of applications)	3	1	1
ICANS (grade 0-4)	0	1	0

Table 1 contains baseline demographic data from three antisynthetase syndrome patients treated with CD19 CAR T-cell therapy. Patient number one to three, age in years (ys), sex in female (F) and male (M). Disease duration in years (ys). Characterization of autoantibody positivity; data on lung involvement and oxygen requirement in liter per minute under rest; number (Nb.) of failed treatments (including CYC=cyclophosphamide, RTX=rituximab, OCR=ocrelizumab). Baseline muscle strength with a manual muscle test (MMT8) score of maximum 150. Baseline creatine kinase (CK) levels (norm value <170 U/l). Conditioning dose referred to 1x cyclophosphamide 1g/m2 and 3x fludarabine 25mg/m2. Maximum of CAR-T-cell expansion after administration of 1 million CAR-T-cells /kg body weight given as peak of CAR-T cells absolute and percent CAR+ of CD3+ T cells. Period of follow up in months after Car-T-cell application. Serconversion reached (yes/no) defined as disappearance of ASS specific antibodies (e.g. anti-Jo1). Efficacy criteria according to the 2016 ACR/EULAR total improvement score (TIS) 6 months after Car-T-cell therapy. Adverse events listed at Cytokine-release syndrome (CRS), application of tocilizumab regarding CRS in numbers of applications (Nb. Of applications) and Immune-related effector Cell Neurotoxicity Syndrome (ICANS) in grade 0-4.

paralleled with the complete depletion of circulating B cells. The first two patients experienced normalization of CK levels (patient 1: CK+150 days: 70 U/l, patient 2: CK+150 days: 99 U/l), major clinical improvement according to the 2016 TIS and could stop all immunosuppressive therapy. Follow-up CT scans of the lung done in patient 1 showed resolution of alveolar inflammation. Follow-up MRI of patient 1 and 2 revealed abrogation of inflammatory changes in the thigh muscles and hamstrings. At the latest follow up (365days and 150days) both patients were in drug-free remission, while patient 3 awaits follow up assessment.

Conclusion: Taken together, these data suggest that CD19 CAR-T-cell therapy provides a possibility to intercept with severe ASS leading to drug-free remission and resolution of muscle and lung inflammation.

Disclosure: J. Taubmann: None; **J. Knitza**: None; **F. Müller**: AbbVie, 6, AstraZeneca, 1, 5, 6, Bristol Myers Squibb, 1, 6, Janssen, 6, KITE, 1, 6, Miltenyi Biomedicine, 1, 6, Novartis, 1, 6, Sobi, 6; **S. Boeltz**: None; **S. Voelkl**: None; **M. Aigner**: Kosmas Therapuetics, 8, Kyverna, 5, Miltenyi Biomedicine, 2, 7, Miltenyi Biotec, 6; **A. Kleyer**: None; **I. Minnopoulou**: None; **R. Gary**: None; **S. kretschmann**: None; **A. Mackensen**: BioNTech, 1, Bristol-Myers Squibb(BMS), 1, KITE/Gilead, 1, 6, Kyverna, 5, Miltenyi Biotech, 5; **G. Schett**: None.

Abstract Number: 2464

B Cells in Anti-tRNA Synthetase Syndrome Patients Show an Activated, Interferon Responsive Signature

Erin Wilfong[1], Leslie Crofford[2] and Rachel Bonami[1], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Vanderbilt University Medical Center, Melbourne, AR

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science I
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Autoantibodies directed against various tRNA synthetases defines the anti-tRNA synthetase syndrome (ARS). While it is unclear if the autoantibodies are directly pathogenic, the efficacy of rituximab in ARS implies that B cell dysregulation is critical in disease pathogenesis. We investigate how B cell transcriptomics varies in patients with active ARS versus healthy controls (HCs).

Methods: Ten patients with active ARS and HCs were identified from the MYSTIC cohort (VUMC IRB 141415). We thawed cryopreserved peripheral blood mononuclear cells (PBMCs) and isolated live CD19+ B cells using fluorescence activated cytometry sorting. Single cell RNA-Seq was performed using the 10X chromium platform with a target depth of 50,000 reads/cell. Data were de-multiplexed and processed using the CellRanger pipeline, and single-cell analysis was performed using Seurat v4.0.0. Immunoglobulin, MHC, and Y-chromosome genes were removed to prevent them driving transcriptionally defined clusters. B cell subset identities were assigned to clusters based on prior literature transcriptional profiles. Differential gene expression analysis comparing was performed in Seurat, subjected to GSEA pathway analysis, and visualized with CytoScape.

Results: Table 1 shows baseline participant characteristics. Eleven unique transcriptional clusters were identified and collapsed into five B cell subsets (transitional, naïve, activated, memory, plasmablast (**Fig. 1A**)) for downstream analysis based on isotype switching and gene expression (**Fig. 1B-C**). Initial visual examination of Jo-1 ARS, non-Jo-1 ARS, and healthy

Table 1. Baseline Characteristics

	Anti-tRNA Synthetase Patients (n=10)	Healthy Controls (n=5)
Age at enrollment (years)†	55 (41.5,58)	53 (43,59)
Female sex	5/10	3/5
Black, Indigenous, and Persons of Color	5/10	2/5
Disease duration (years)†	1.2 (0.9,3.8)	
Anti-tRNA synthetase antibody		
Jo1	5	
PL7	1	
PL12	4	
Muscle involvement		
Proximal weakness	4/10	
Elevated CK/aldolase/LDH	7/10	
Skin involvement		
Mechanic's hands	6/10	
Heliotrope rash	3/10	
Gottron's sign/papules	2/10	
Inflammatory arthritis	7/10	
Interstitial lung disease	10/10	
Therapies at enrollment		
Prednisone	7/10	
Mycophenolate	1/10	
Azathioprine	1/10	

†expressed as median(interquartile range)

control groups on UMAP plots suggested potential B cell subset skewing across participant groups (**Fig. 1D**). Jo-1 ARS patients showed an increase in naïve B cells, Non-Jo-1-ARS patients had increased activated B cells, and both ARS patient groups tended to have a lower frequency of memory B cells than HCs (**Fig. 1F**). Results of the GSEA analysis are shown in **Fig. 2**. Notably, the gene ontology term "defense response to symbiont," which contains the interferon genes IFI6, IFI44L, IFITM1, IFITM2, IRF7, ISG20, MX2, STAT1, was the most overrepresented term for transitional (FDR p=0.009) and activated (FDR p< 0.001) subsets. The Reactome term "Eph-ephrin signaling," which contains the critical B cell activation/migration genes ACTB, AP2M1, CDC42, CFL1, RAC1, and RHOA, was the most overrepresented term for memory cells (FDR p=0.01).

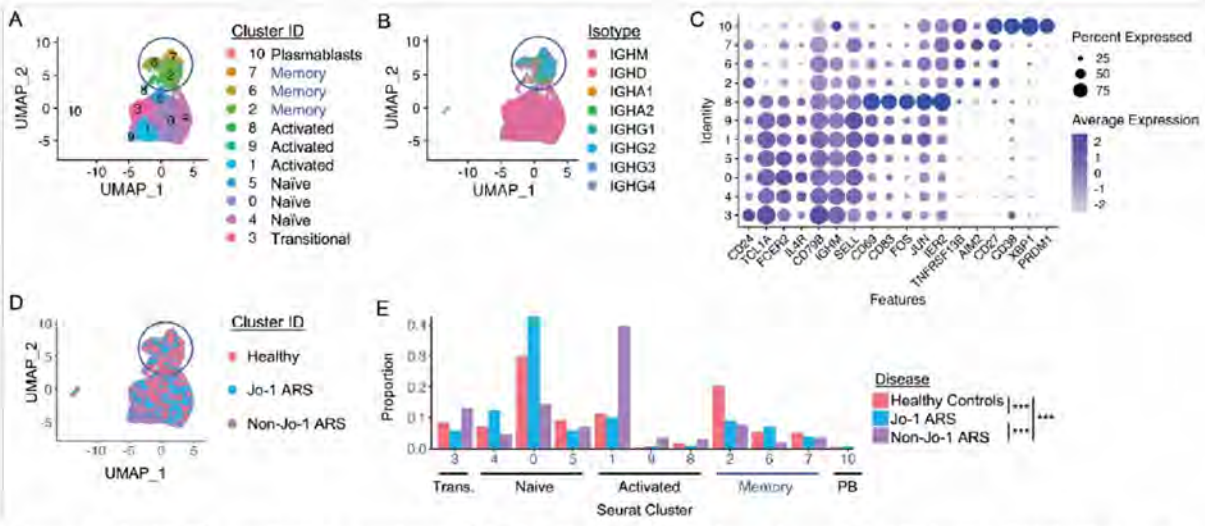

Figure 1. Anti-tRNA synthetase syndrome (ARS) patient subsets show skewed B cell cluster distribution from each other and healthy controls. Single-cell RNA-seq technology was used to profile 2,000-5,000 purified CD19+CD3- cells isolated from Jo1 ARS patients (n=5), non-Jo1 ARS patients (n=5), and healthy controls (n=5). Seurat was used to identify 11 clusters which were further grouped as naive, transitional, activated, memory, or plasmablast subsets based on manual inspection of isotype and gene expression profiles of each cluster. Blue circles highlight the memory subset. **A)** RNA-seq-based B cell subsets, **B)** BCR isotype, and **C)** manually selected gene expression profiles for cells grouped by B cell subset. **D)** UMAP is colored for each disease groups. **E)** Boxplots show the mean frequency of each B cell subset by disease group.

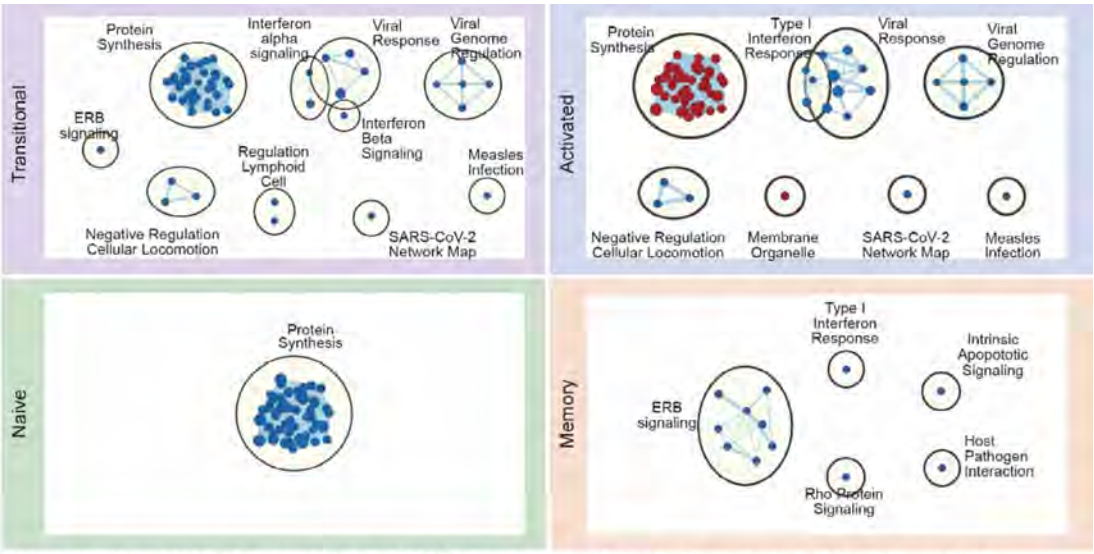

Figure 2. Annotated visualization of GSEA enrichment analysis. A rank list for differentially expressed genes for the transitional, naive, activated, and memory subsets was fed into the GSEA algorithm using an FDR Q-value of 0.1 and Jaccard overlap combined setting of 0.375. GSEA output files were visualized in CytoScape v.3.9.1 and automatically annotated using Enrichment Map and AutoAnnotate plugins.

Conclusion: B cell subset frequencies are skewed in ARS compared to HCs. ARS patients have altered B cell and interferon signaling compared to healthy controls. Future work will dissect how ARS B cell activation differs from normal immune responses.

Disclosure: E. Wilfong: Boehringer-Ingelheim, 1, 5, 6, Cabaletta Bio, 1; **L. Crofford**: None; **R. Bonami**: Argenx, 5.

Abstract Number: 2465

Clonally Expanded B Cells in Anti-Histidyl-tRNA Synthetase Syndrome Patients Exhibit an Autoreactive-Prone Memory Phenotype and Bind Jo-1 Autoantigen

Lindsay Bass[1], Dena Liu[1], Alberto Cisneros[2], Jennifer Young-Glazer[2], Leslie Crofford[3], **Erin Wilfong**[2] and Rachel Bonami[2], [1]Vanderbilt University, Nashville, TN, [2]Vanderbilt University Medical Center, Nashville, TN, [3]Vanderbilt University Medical Center, Melbourne, AR

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science I
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Anti-histidyl-tRNA synthetase syndrome (Jo-1 ARS) is defined by the presence of autoantibodies against histidyl tRNA synthetase (Jo-1). Clinically, Jo-1 ARS can involve multiple tissues including muscle, lung, skin, and joints. Previously, we identified that Jo-1 binding B cells show skewing towards specific phenotypic subsets in the peripheral blood of Jo-1 ARS patients, but the mechanisms that promote B cell recognition of Jo-1 autoantigen are unknown.

Methods: Five patients with active anti-Jo-1 ARS were identified from the Vanderbilt MYSTIC cohort (VUMC IRB 141415). We isolated live CD19+ B cells from cryopreserved peripheral blood mononuclear cells (PBMCs) using fluorescence activated cytometry sorting. Five-thousand cells were targeted for sequencing per sample. Single cell RNA-Seq, V(D)J sequencing, and Cite-Seq were performed using the 10X Chromium platform (5'-RNA, V(D)J, and CITE-Seq) demultiplexed and processed using the CellRanger pipeline and analyzed with Seurat v4.0.0. V(D)J gene identities and % somatic hypermutation were determined for B cell receptors (BCR) using IMGT/HighV-QUEST. Seurat was used to merge these outputs with RNA-seq and CITE-seq data to enable integrated analysis of BCRs with transcriptomic and phenotypic profiling. Clonally expanded BCRs were identified and recombinantly expressed as monoclonal antibodies. Total IgG, Jo-1, LPS, dsDNA, and insulin binding were measured by ELISA.

Results: Five B cell subsets (transitional, naïve, activated, memory, plasmablast) were assigned based on isotype switching and gene expression **(Fig. 1A-B)**. We identified 21 expanded clonotypes (defined as n ³ 3 per donor) amongst the five donors (**Fig. 1C**). Clonally expanded cells were CD27+ and CD21lo (**Fig. 2**) and were primarily IgM+ (non-class-switched) (**Fig. 3A**). Somatic hypermutation was highly variable and ranged from germline to very high (25%) (**Fig. 3B**). Recombinant expression of clonally expanded BCRs as IgG1 antibodies and ELISA binding studies revealed that 5/21 (24%) bound Jo-1. All Jo-1 binding clones exhibited some binding of dsDNA, LPS, or insulin, confirming polyreactivity. Multiple Jo-1 binding B cells expressed the VH4-34 heavy chain gene, which has been previously associated with autoimmunity.

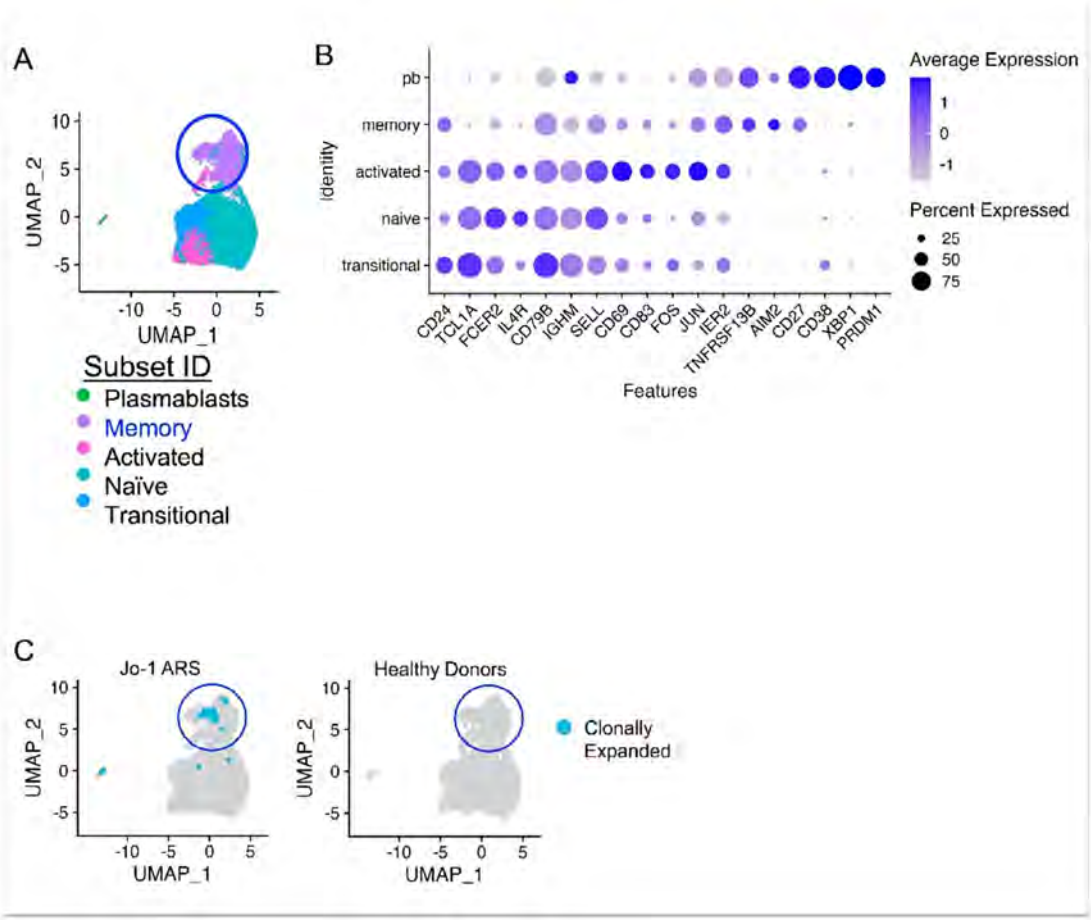

Figure 1. Transcriptionally defined memory B cell subsets and clonally expanded cells are identified in ARS patients. The 10X Genomics single-cell platform was used to perform transcriptomic (RNA-seq) profiling of purified B lymphocytes isolated from n=5 Jo-1 ARS patients, n=5 non-Jo-1 ARS patients, and n=5 healthy donors (age and sex-matched). A) Transcriptionally defined clusters and B) selected gene expression were identified using Seurat. C) Integrated Seurat/IMGT/HighV-QUEST analysis identified clonally expanded B cells (teal) through single-cell immune repertoire profiling (BCR-seq) in Jo-1 ARS (left) and healthy donors (right).

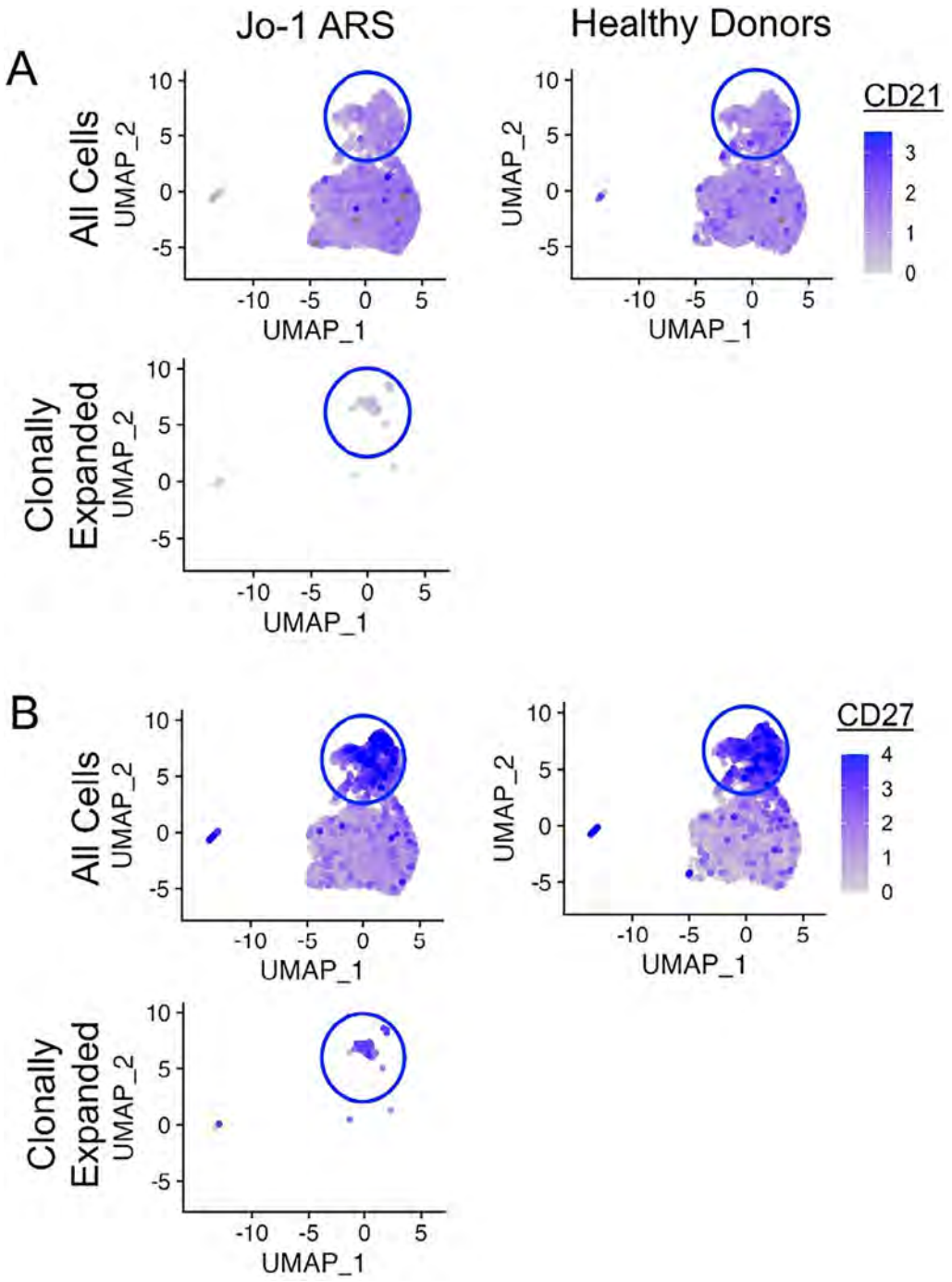

Figure 2. Clonally expanded B cells isolated from Jo-1 ARS patients exhibit an autoreactive-prone memory (CD21lo CD27+) phenotype. CITE-seq was used to measure A) CD21 and B) CD27 expression in total B cells (top panels) or clonally expanded B cells (bottom panels) in Jo-1 ARS or healthy donors. Heatmaps indicate expression levels.

Conclusion: Clonally expanded B cells in patients with Jo-1 ARS are enriched for anti-Jo1 B cells, which display an autoreactive-prone (CD21lo) memory phenotype. Somatic hypermutation analysis shows that germline recognition of Jo-1 autoantigen is possible, and that Jo-1-binding B cells can undergo extensive somatic hypermutation. Future studies will be required to determine if somatic hypermutation is associated with affinity maturation of Jo-1-binding B cells, and presumably enhanced pathogenicity.

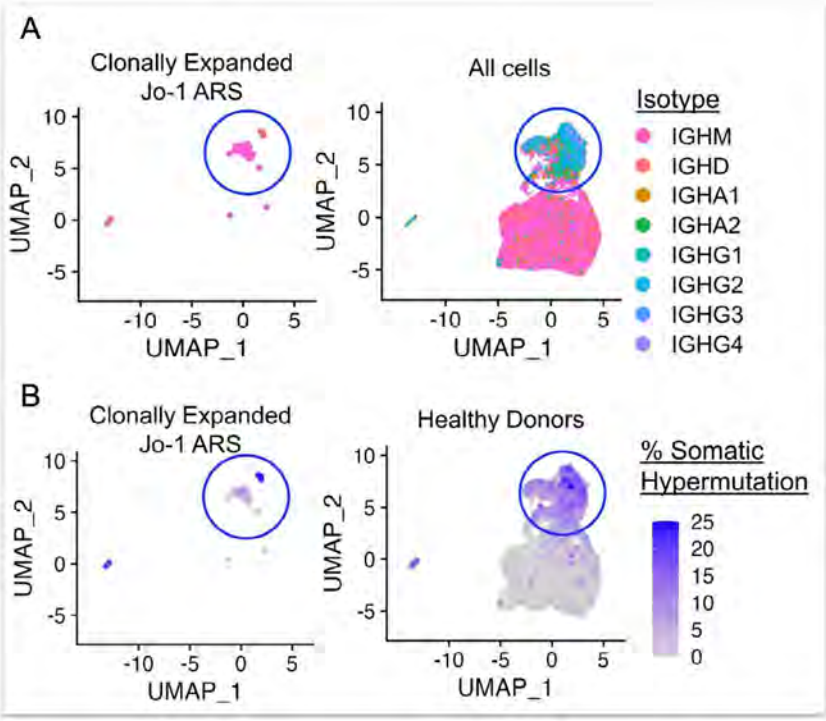

Figure 3. Clonally expanded B cells isolated from Jo-1 ARS patients underwent limited class switching and ranged from minimally to highly mutated BCRs. Integrated Seurat/IMGT/HighV-QUEST analysis of single-cell RNA-seq/BCR-seq data identified clonally expanded B cells from Jo-1 ARS patients (left) or total cells (right). A) isotype and B) percent variable heavy chain (VH) gene somatic hypermutation is shown. Heatmap indicates % somatic hypermutation.

Disclosure: L. Bass: None; **D. Liu**: None; **A. Cisneros**: None; **J. Young-Glazer**: Argenx, 5; **L. Crofford**: None; **E. Wilfong**: Boehringer-Ingelheim, 1, 5, 6, Cabaletta Bio, 1; **R. Bonami**: Argenx, 5.

Abstract Number: 2466

Monoclonal Anti-MDA5 Autoantibodies Derived from a Patient with Dermatomyositis Target the Hel2i Domain of the MDA5 Protein

Eveline Van Gompel[1], Ragnhild Stålesen[2], Caroline Grönwall[2], Annika van Vollenhoven[2], Lena Israelsson[2], Ingrid Lundberg[3], Vivianne Malmström[2], Karine Chemin[4] and Vijay Joshua[2], [1]Karolinska Institutet - KU Leuven, Leuven, Belgium, [2]Karolinska Institutet, Stockholm, Sweden, [3]Division of Rheumatology, Department of Medicine, Karolinska Institutet; Department of Gastroenterology, Dermatology, Rhematology, Karolinska Universitetssjukhuset, Stockholm, Sweden, [4]Division of Rheumatology, Department of Medicine Solna, Center for Molecular Medicine, Karolinska University Hospital, Karolinska Institutet, Stockholm, Sweden

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science I

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: The strong clinical association between the anti-MDA5 autoantibodies and the development of severe lung disease in patients with dermatomyositis (DM) suggests an active role for the autoantibodies in the pathogenesis. The MDA5-specific autoreactive immune cells are understudied and it remains unclear if (and how) the autoantibodies contribute to the pathogenesis.

We aimed to get insight in the repertoire of the antigen-specific autoreactive B cells from patients with anti-MDA5(+) DM and confirm their antigen-specificity by producing anti-MDA5 monoclonal autoantibodies (mAb).

Methods: Circulating lymphocytes were available from MDA5(+) patients (n=3) at Karolinska Institutet (Sweden). All patients satisfy the EULAR/ACR IIM classification criteria. B cells were enriched using a negative selection kit and stained with a live/dead dye, with Streptavidin (SA)-PE-DL755 decoy probe to label non-specific B cells and with MDA5- SA-PE to label MDA5-specific B cells. Other B cell markers included CD19, IgD, CD27 and CD38. Single MDA5-SA-PE(+) B cells were index sorted using Influx (BD Bioscience) and recombinant mAbs were generated from the B cell receptor sequences as described previously and expressed as IgG1. Quality controls included SDS-PAGE, ELISA, and size-exclusion chromatography. Unspecific autoreactivity was assessed in a soluble membrane protein polyreactivity assay. MDA5-specificity of the produced mAbs was evaluated with ELISA and Western Blot. Apparent affinity was determined using a competition ELISA.

Results: Out of 234 MDA5(+)B cells sorted, 23 paired heavy and light chain sequences were selected to be expressed whereof 9 were originally IgGs, 3 IgAs and 11 IgMs. Two out of 23 mAbs were highly reactive towards the MDA5 protein in ELISA. The sequences originated from IgG-producing switched memory B cells (CD19+CD27loIgD-CD38+) and contained a low number of heavy and light variable region somatic hypermutations (SHM, 4 and 1 resp.). ELISA moreover showed that both mAbs specifically recognize the Hel2i domain of the MDA5 protein, but they differ in apparent affinity. Notably, one clone displayed sub-nanomolar apparent affinity, despite low SHM. The patient from whom the mAbs originated showed radiographic signs of ILD, had skin involvement and was lymphopenic.

Conclusion: We successfully cloned anti-MDA5 mAbs from two different B cell receptor sequences from an MDA5(+) patient with DM. Both mAbs specifically recognize the Hel2i domain of the MDA5 protein, but with different apparent affinity. These results are in line with previous findings, where we found the helicase domains to be the main immunogenic domains in 30 MDA5(+) serum samples. Therefore we hypothesize the anti-MDA5 autoantibodies potentially compete with the natural ligand of the MDA5 protein and interfere with the canonical function of MDA5 as a sensor of viral RNA. The successful production of anti-MDA5 mAbs allows us to further investigate this hypothesis, starting with setting up an *in vitro* competition assay to assess if the presence of anti-MDA5 mAbs can affect the downstream MDA5-signalling in lung fibroblasts.

Disclosure: E. Van Gompel: None; **R. Stålesen**: None; **C. Grönwall**: None; **A. van Vollenhoven**: None; **L. Israelsson**: None; **I. Lundberg**: Argenx, 6, Astra-Zeneca, 5, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 1, Corbus Pharmaceutical, 6, EMD Serono Research & Development Institute, 6, Janssen, 6, Kezar, 6, Novartis, 11, Octapharma, 6, Orphazyme, 6, Pfizer, 1, Roche, 11, Xencor, 6; **V. Malmström**: Eli Lilly, 1, Janssen, 5, ONO, 1, Pfizer, 5; **K. Chemin**: Janssen, 5; **V. Joshua**: None.

Abstract Number: 2467

Quadriceps Muscle Fat Composition but Not Muscle Energetics Is Associated with Knee Osteoarthritis: Initial Results from the Study of Muscle, Mobility, and Aging

Giovanna Distefano[1], Daniel Evans[2], Peggy Cawthon[2], John Lynch[2], Thomas Link[2], Philip Kramer[3], Stephanie Harrison[2], Bret Goodpaster[4], Jane Cauley[5], Theresa Mau[2], Paul Coen[4], Lauren Sparks[4] and **Nancy Lane**[6], [1]AventisHealth, Orlando, FL, [2]University of California San Francisco, San Francisco, CA, [3]Wake Forest, Winston-Salem, NC, [4]Aventis Health, Orlando, FL, [5]University of Pittsburgh, Pittsburgh, PA, [6]University of California, Hillsborough, CA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Osteoarthritis II: Novel Insights from Observational Studies
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Osteoarthritis (OA) remains the most common cause of joint pain and disability with age, and to date, effective treatments to reduce pain and slow disease progression remain elusive. Nonpharmacologic therapies, including physical therapy and walking, are reported to be effective in reducing knee pain and maintaining function in subjects with knee OA (KOA). Deep phenotyping of the thigh muscle was performed in older adults from the Study of Muscle, Mobility, and Aging (SOMMA) with the goal of determining the relationship between measures of muscle health and KOA in older adults.

Methods: Men and women aged >70 yrs. recruited from two study sites (University of Pittsburgh and Wake Forest University) based on their ability to walk ¼ mile at >= 0.6m/s and perform study related activities. Muscle mass and composition were assessed by MRI of the thigh, and D3Cr muscle mass by D3-creatine dilution. Knee extensor leg power was assessed using a Keiser exercise machine. Muscle mitochondrial energetics were assessed by P^{31} MRS (ATP_{max}) and high resolution respirometry of permeabilized myofibers collected from a muscle biopsy of the vastus lateralis (Oxidative phosphorylation, OXPHOS). At one-year post-enrollment, knee x-rays and standardized knee pain assessments were completed, and knee OA was defined by Kellgren and Lawrence (KL) grade >= 2. Participants were grouped NoKOA, NoPain; NoKOA, Pain; KOA, NoPain, and KOA, Pain. Differences between groups were assessed by ANOVA with parametric post-hoc tests and associations between participants with knee OA and muscle variables were analyzed by linear regression adjusted for age, gender, study site/technician, and race.

Table 1. Study Subject Characteristics (mean ± SD)

Variables	NoKOA, NoPAIN	NoKOA, Pain	KOA, NoPain	KOA, PAIN	P value
	(N= 212)	(N= 50)	(N= 203)	(N= 193)	
Age (Yrs.)	75.8±4.7	74.5 ± 4.0	76.6 ± 5.1	76.2 ± 5.1	0.04
Female, N (%)	109 (51.4)	29 (58.0)	113 (55.7)	125 (64.8)	0.05
BMI (kg/m^2)	26.2 ± 4.0	26.8 ± 4.6	27.9 ± 4.5	28.5 ± 4.2	<0.01
Walk speed from 400m walk in m/s	1.12 ± 0.16	1.10 ± 0.17	1.04 ± 0.18	1.01 ± 0.18	<0.01
% D3Cr muscle mass (kg)	0.31 ± 0.06	0.30 ± 0.08	0.29 ± 0.06	0.28 ± 0.07	<0.01
Mean Anterior Thigh Muscle Fat Infiltration (%)	0.067 ± 0.018	0.069 ±0.021	0.076 ±0.022	0.081 ± 0.023	<0.01
Total Thigh Fat Free Muscle vol (L)	9.09 ± 2.28	8.83 ± 2.28	9.19 ± 2.26	8.87 ± 2.29	0.52
P^{31} MRS (ATP_{max}) (mM/sec)	0.550 ± 0.1425	0.574 ± 0.177	0.53 ± 0.15	0.54 ± 0.15	0.41
OXPHOS (pmol/(s*mg))	61.4 ± 16.8	63.6 ± 23.0	62.1 ± 20.6	56.6 ± 17.0	0.02
Knee Extensor Leg Power (watts/kg)	5.3 ± 1.8	5.0 ± 1.8	4.7 ± 1.7	4.3 ± 1.5	<0.01

Table 2. Muscle mass, composition, function, and mitochondrial energetics in subjects with and without knee osteoarthritis

	D3Cr muscle mass (kg)	Mean Anterior Thigh muscle fat infiltration (%)	Total thigh fat free mass (L)	P^{31} MRS (ATP_{max}) (mM/sec)	OXPHOS (pmol/(s*mg))	Knee extensor leg power (watts/kg)
NoKOA, NoPain	0.0 (referent)	0.0 (referent)	0.0 (referent)	0.0 (referent)	0.0 (referent)	0.0 (referent)
NoKOA, Pain	-0.006 (-0.025, 0.013)	0.002 (-0.004, 0.008)	-0.127 (-0.509, 0.254)	0.018 (-0.029, 0.064)	2.81 (-2.59, 8.22)	-0.226 (-0.647, 0.195)
KOA, NoPAIN	-0.013 (-0.026, -0.001) *	0.008 (0.004, 0.012) *	0.299 (0.058, 0.539) *	-0.006 (-0.035, 0.020)	2.08 (-1.47, 5.62)	-0.482 (-0.744, -0.219)
KOA,Pain	-0.022 (-0.034, -0.010)*	0.012 (0.008, 0.016)*	0.294 (0.047, 0.541)*	0.004 (-0.025, 0.034)	2.33 (-5.93, 1.28)	-0.774 (-1.05, -0.502)*

Data represent beta coefficients (95% CI). *p<0.05 when compared to No KOA ,No Pain group. All linear models are adjusted for age, gender, site or technician, and race,

Results: This analysis was performed on 658 SOMMA participants who had knee x-rays obtained, with a mean age of 76.1 yrs. Subjects with KOA tended to be older, with more anterior intramuscular fat, lower knee extension leg power and lower mitochondrial energetics (Table 1). After adjustment for age, gender, race, BMI and study site, KOA with and without pain groups showed lower % functional muscle mass by D_3Cr enrichment, lower knee extensor leg power, and greater anterior thigh intramuscular fat compared to the NoKOA, NoPain group (Table 2). No significant differences between groups were observed for the muscle mitochondrial energetics measures.

Conclusion: Older adults with KOA, with and without knee pain, have lower D3Cr muscle mass, lower knee extension leg power, similar mitochondrial function, and higher amounts of intramuscular fat than those without knee OA and without pain. The association of KOA with increased intramuscular fat is now under investigation.

Disclosure: G. Distefano: None; **D. Evans**: None; **P. Cawthon**: None; **J. Lynch**: None; **T. Link**: None; **P. Kramer**: None; **S. Harrison**: None; **B. Goodpaster**: None; **J. Cauley**: None; **T. Mau**: None; **P. Coen**: None; **L. Sparks**: None; **N. Lane**: None.

Abstract Number: 2468

Association Between Gut Microbiome-related Metabolites and Symptomatic Hand Osteoarthritis in Two Independent Cohorts

Jie Wei[1], Zidan Yang[2], Jiatian Li[3], Yuqing Zhang[4], Weiya Zhang[5], Michael Doherty[5], Tuo Yang[6], Yuanheng Yang[3], Hui Li[3], Yilun Wang[3], Ziying Wu[3], Changjun Li[7], Guanghua Lei[3] and Chao Zeng[3], [1]Health Management Center, Xiangya Hospital Central South University, Changsha, China, [2]Key Laboratory of Aging-related Bone and Joint Diseases Prevention and Treatment, Ministry of Education, Xiangya Hospital, Central South University, Changsha, China, [3]Department of Orthopaedics, Xiangya Hospital, Central South University, Changsha, China, [4]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, MA, [5]Academic Rheumatology, Clinical Sciences Building, University of Nottingham, City Hospital, Nottingham, United Kingdom, [6]Department of Health Management Center, Xiangya Hospital, Central South University, Changsha, China, [7]National Clinical Research Center for Geriatric Disorders, Xiangya Hospital, Central South University, Changsha, China

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Osteoarthritis II: Novel Insights from Observational Studies

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Since gut microbiome dysbiosis can cause inflammatory disorders by affecting host metabolism, we postulate that the gut microbiome and related metabolites could play a role in the pathogenesis of hand osteoarthritis. We characterised gut microbiome-related metabolites in people with symptomatic hand OA (SHOA) in two independent cohorts.

Methods: Using data collected from a large-sample community-based observational study (discovery cohort) (n=1,359), the Xiangya OA (XO) Study, we first performed shotgun metagenomic sequencing of stool samples for gut microbial function. We then performed targeted metabolomics analysis of plasma samples for metabolites related to altered microbial function in SHOA and compared the metabolites between participants with and those without SHOA. We also applied a multi-omics analysis approach to examine the associations between SHOA-related microbial function and SHOA-related plasma metabolites. Finally, we then replicated the findings from the XO Study among 71 SHOA patients and 71 age (±1 year), sex and BMI (±2 kg/m^2) matched controls (validation cohort) (Figure 1).

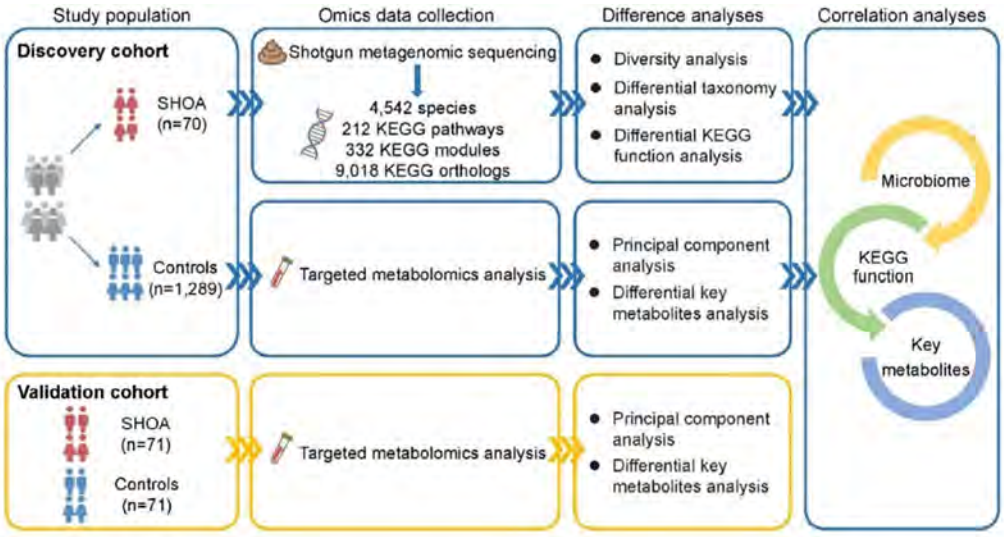

Figure 1. Summary of the present study. SHOA, symptomatic hand osteoarthritis; KEGG, Kyoto Encyclopedia of Genes and Genomes.

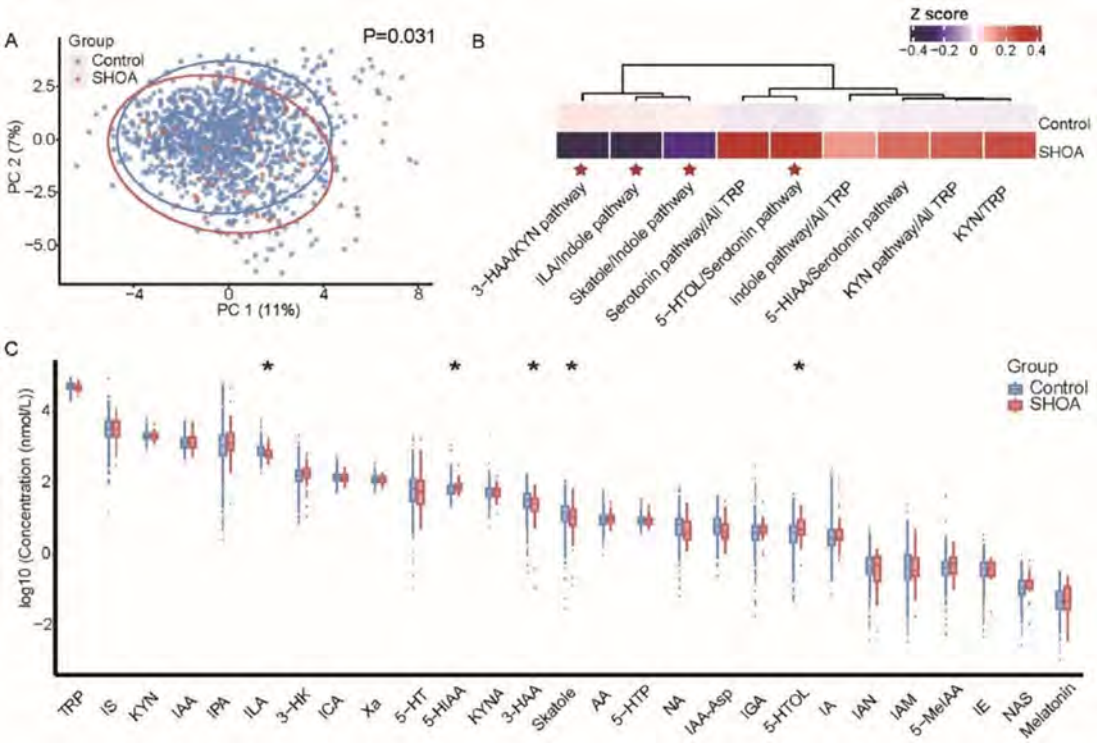

Figure 2. Associations of plasma tryptophan metabolites with SHOA in the discovery cohort. (A) Principal Component Analysis (PCA) plot compared the composition of plasma tryptophan metabolites between participants with SHOA and those without SHOA. Associations of ratios of tryptophan metabolites concentration in their related pathway (B) and individual plasma tryptophan metabolites (C) with SHOA adjusting for age, sex, body mass index, smoking status, alcohol consumption, and frequency of dietary intake of meat/eggs, dairy, and vegetables. Significant ratios are marked with red stars. SHOA, symptomatic hand osteoarthritis; TRP, tryptophan; KYN, kynurenine; ILA, indole-3-lactic acid; 3-HAA, 3-hydroxyanthranilic acid; 5-HIAA, 5-hydroxyindoleacetic acid; 5-HTOL, 5-hydroxytryptophol; 3-HK; 3-hydroxykynurenine; 5-HT, serotonin; 5-HTP, L-5-hydroxytryptophan; 5-MeIAA; 5-methoxy-3-indoleacetic acid; AA, anthranilic acid; IA; indole acrylic acid; IAA, indole-3-acetic acid; IAA-Asp, indole-3-acetyl-aspartate; IAM, indole-3-acetamide; IAN, indole-3-acetonitrile; ICA, indole-3-carboxaldehyde; IE, indole ethanol/tryptophol; IGA, 3-indoleglyoxylic acid; IPA, 3-indolepropionic acid; IS, indoxylsulfate; KYNA, kynurenic acid; NA, nicotinic acid; NAS, N-acetyl-5-hydroxytryptamine; Xa, xanthurenic acid.

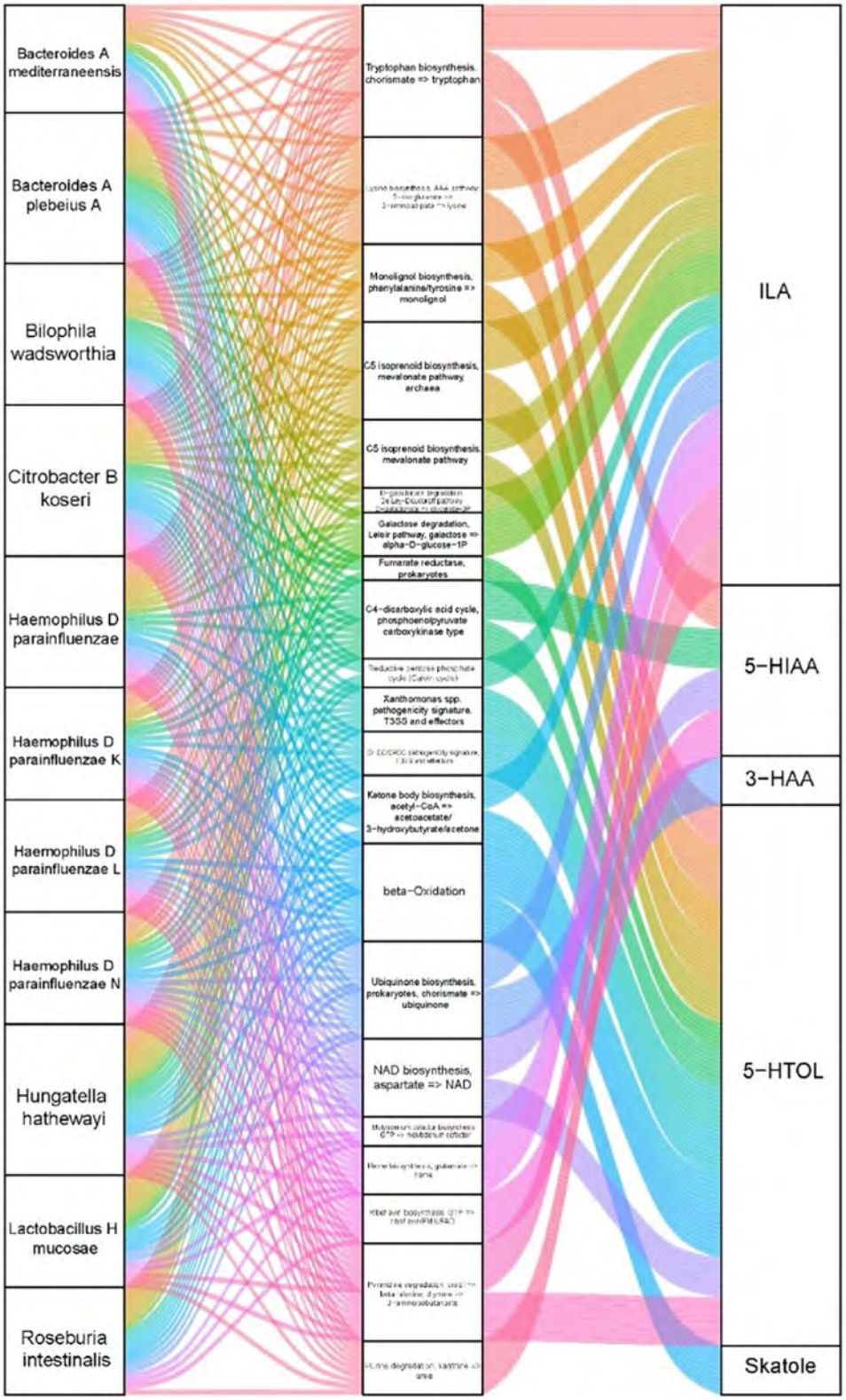

Figure 3. Correlations of microbial species to the microbial modules, and correlations of microbial modules to the tryptophan metabolites. The Sankey plot shows the significant correlations of classified microbial species with KEGG modules and KEGG modules with differential tryptophan metabolites. Shown are microbial species (left), KEGG modules (middle), and plasma tryptophan metabolites (right). The curved lines connecting the panels indicate the correlations, with colors corresponding to different modules. ILA, indole-3-lactic acid; 5-HIAA, 5-hydroxyindoleacetic acid; 3-HAA, 3-hydroxyanthranilic acid; 5-HTOL, 5-hydroxytryptophol.

Results: In the discovery cohort, compared with those without SHOA (n=70), participants with SHOA had significantly altered microbial functions related to tryptophan metabolism. Then we measured the plasma tryptophan metabolites and found that participants with SHOA had higher levels of 5-hydroxytryptophol and 5-hydroxyindoleacetic acid, but lower levels of indole-3-lactic acid (ILA), 3-hydroxyanthranilic acid and skatole (Figure 2). The multivariable-adjusted odd ratios of SHOA per one log10 unit increase for 5-HIAA, 5-HTOL, ILA, skatole, and 3-HAA were 8.97 (95% CI: 2.37 to 33.98), 3.44 (95% CI: 1.44 to 8.18), 0.19 (95% CI: 0.04 to 0.99), 0.51 (95% CI: 0.28 to 0.90) and 0.36 (95% CI: 0.19 to 0.70), respectively. Moreover, the multi-omics analysis suggested that the lower level of ILA in SHOA was related to the microbial function of tryptophan biosynthesis, which was further correlated with the microbiome species *Bacteroides A mediterraneensis* (Figure 3). Finally, we verified the associations between plasma tryptophan metabolites and SHOA in the validation cohort. Consistent with the findings in the discovery cohort, we observed a lower level of the ILA in the SHOA group compared with controls, with the multivariable adjusted ORs of SHOA per one log10 unit increase for ILA being 0.03 (95% CI: 0.002 to 0.46).

Conclusion: Alterations of the microbial function of tryptophan biosynthesis and tryptophan metabolites, especially lower levels of ILA, are associated with SHOA. Our novel findings suggest potential pathways and targets for further treatment of SHOA.

Disclosure: J. Wei: None; **Z. Yang**: None; **J. Li**: None; **Y. Zhang**: None; **W. Zhang**: None; **M. Doherty**: None; **T. Yang**: None; **Y. Yang**: None; **H. Li**: None; **Y. Wang**: None; **Z. Wu**: None; **C. Li**: None; **G. Lei**: None; **C. Zeng**: None.

Abstract Number: 2469

Associations Between Body Composition Measurements of Obesity and the Radiographic Progression of Hand Osteoarthritis: Data from the Dong-gu Study

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Osteoarthritis II: Novel Insights from Observational Studies
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Previous studies have found that obesity is a risk factor for hand osteoarthritis (OA), but most have been cross-sectional studies and thus causality is uncertain. Longitudinal studies are instead needed to explore the association between obesity-related characteristics, including fat deposition/distribution and hand OA. The present study examined the association between changes in body composition measurements and the radiographic progression of hand OA in a longitudinal cohort.

Methods: In the Dong-gu Study population, 1,277 patients had hand radiographs at baseline and at the 4-year follow-up. X-rays of the hand joints were scored using a semi-quantitative grading method. Body composition was simultaneously measured in a bioelectrical impedance analysis using an InBody 520 analyzer. The relationship between changes in body composition measurements and the radiographic progression of hand OA was assessed in a multiple linear regression analysis.

Results: Total hand joint scores increased from 16.3 ± 5.74 at baseline to 18.8 ± 8.11 at year 4 (P < 0.001). Changes of body mass index, hip circumference (HC), waist-to-hip circumference (WHC), and fat mass were significantly associated with changes in the total hand joint scores (P = 0.012, P < 0.001, P = 0.017, P = 0.008, respectively). HC and WHC were significantly associated with radiographic progression of the hand joints, after adjusting for age, sex, physical activity, education status, smoking, alcohol consumption, hypertension, diabetes mellitus, dyslipidemia, chronic pulmonary disease, chronic liver disease, cardiovascular disease, cerebrovascular disease, and malignancy (P < 0.001, P = 0.001, respectively).

Conclusion: Changes in fat distribution were significantly associated with the radiographic progression of hand OA over 4 years, suggesting a role for the systemic effect of adipose tissue.

Disclosure: S. Choi: None; **H. Jeong**: None; **D. Park**: None; **J. Kang**: None; **M. Shin**: None; **S. Lee**: None.

Abstract Number: 2470

Low Serum Adiponectin Levels Were Associated with Radiographic Progression of Hand Osteoarthritis in a 6-year Follow-up of the Dong-gu Study

Sung-Eun Choi[1], Hyemin Jeong[1], Dong-Jin Park[1], Ji-Hyoun Kang[2], Min-Ho Shin[3] and Shin-Seok Lee[1], [1]Chonnam National University Medical School & Hospital, Gwangju, South Korea, [2]Chonnam National University Hospital, Gwangju, South Korea, [3]Chonnam National University Medical School, Gwangju, South Korea

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Osteoarthritis II: Novel Insights from Observational Studies
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: The association between serum adiponectin levels and hand osteoarthritis (OA) has been studied cross-sectionally, but longitudinal studies on the radiographic progression of hand OA are lacking. Thus, we investigated the relationship between serum adiponectin levels and radiographic features of hand OA in a prospective longitudinal cohort.

Methods: A total of 1,356 subjects were enrolled from the Dong-gu study. Baseline serum adiponectin levels were measured by enzyme linked immunosorbent assay, and hand joint radiographs were assessed using a semi-quantitative grading system at the first visit and 6 years later. Multiple linear regression analysis was used to investigate the association between serum adiponectin levels and radiologic changes in hand OA.

Results: Total hand joint scores increased from 16.5 ± 5.74 at baseline to 19.4 ± 8.11 at year 6 ($p < 0.001$). The baseline adiponectin levels were negatively associated with the changes in total hand joint score ($p = 0.019$), subchondral cyst score ($p = 0.006$), and malalignment score ($p = 0.026$) after adjusting for age, gender, body mass index, smoking, alcohol consumption, education, physical activity, hypertension, diabetes mellitus, dyslipidemia, chronic pulmonary disease, chronic liver disease, cardiovascular disease, cerebrovascular disease, and malignancy. When serum adiponectin levels above and below the median were compared with the total score for hand OA based on the median radiographic scores, subjects with serum adiponectin levels below the median exhibited radiographic progression in hand joints after adjustment (odds ratio = 0.618, 95% confidence interval: 0.477–0.801, $p < 0.001$).

Conclusion: In this longitudinal population-based study, decreased serum adiponectin levels were associated with progression of radiographic hand OA.

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Abstract Number: 2471

Higher Pain and Functional Impairment in Erosive Hand Osteoarthritis Than in Treated Rheumatoid Arthritis: A Comparative Study Between DIGICOD and ESPOIR Cohorts

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Osteoarthritis II: Novel Insights from Observational Studies

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Hand osteoarthritis (HOA) is considered as a less severe disease with a better functional prognosis and a lower global burden than rheumatoid arthritis (RA). This paradigm may no longer be true considering the efficacy of targeted therapies in RA compared to the weak efficacy of therapies in the most severe form of HOA, namely erosive HOA (EHOA) (1).

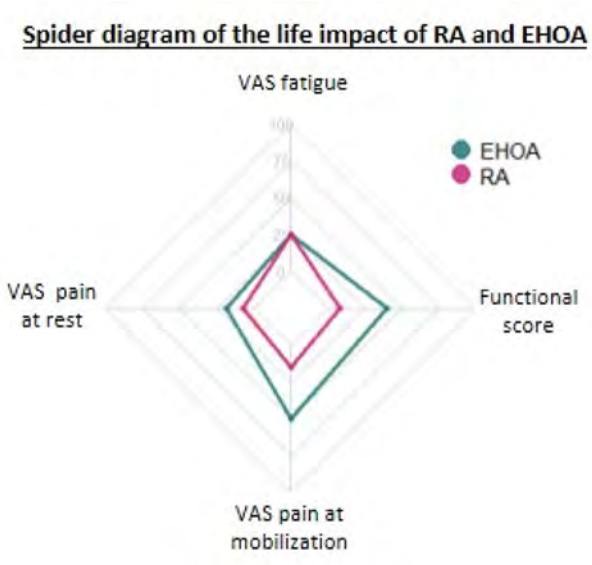

Figure 1: Spider diagram of the life impact of RA and EHOA VAS = visual analogical scale, EHOA = erosive hand osteoarthritis; RA : rheumatoid arthritis

Methods: We aimed to compare the burdens of established EHOA and RA. The objectives were to compare pain, functional impairment and the prevalence of comorbidities and of cardiovascular diseases (CVD).

This study involved EOHA patients, defined by at least 1 erosive joint according to the Verbruggen score (3)from inclusion visit of DIGital Cohort Osteoarthritis Design (DIGICOD), a French cohort of symptomatic HOA. RA patients fulfilling ACR/EULAR 2010 criteria at the 10th year visit were selected from the ESPOIR cohort (*Étude et Suivi des Polyarthrites Indifférenciées Récentes*), a French cohort of early RA (4).

Pain intensity at rest or mobilization (0-100mm visual analogical scale (VAS)³40/100), fatigue (VAS fatigue³25/100), function (normalized (0-100) scores of Health assessment questionnaire for RA, and AUStralian CANadian Osteoarthritis Hand Index for EHOA > 16.7) were analyzed and compared between EHOA and RA using logistic regression models adjusted on age, gender, BMI, comorbidities and socio-educational level. The risk to have ³ 2 comorbidities (among CVD, cancer, hemopathy, fracture) or at least 1 CVD (among high blood pressure, diabetes, dyslipidemia, myocardial infarction, stroke) were compared and adjusted on age, gender, BMI and socio-educational level. Odds ratios (OR) and their 95% confidence intervals (CIs) were reported (EOHA vs RA).

Results: We selected 138 EHOA patients and 379 with RA. The median [interquartile] age for EHOA patients was 67.3 [64.3; 72.2] years vs 48.6[39.9 ; 55.6] years for RA patients (p< 0.001). The disease duration, at the evaluation time, was 13.5 [7.0; 20.0] for EHOA and 10.5 years [10.3 ; 10.7] for RA patients. RA was anti-CCP antibodies positive for 56% of patients and in remission for 61%. RA patients received methotrexate (82%), biologics (37%) and corticosteroids (25%) while 20% of EHOA patients received oral non-steroidal anti-inflammatory drugs.

The number of painful joints in the hands was higher for EHOA than RA patients (4.0 [2.0;8.8] vs 0.0 [0.0;3.0], p< 0.001).

In the adjusted analysis, EHOA was associated with more pain at mobilization (OR = 3.13 95% CI [1.74 to 5.68] p< 0.001) and functional impairment (OR = 2.27 CI 95% [1.26 to 4.17], p = 0.007) (Figure 1). There was no difference for pain at rest and for fatigue.

For comorbidities, the proportions of EHOA patients with ³ 2 comorbidities were higher than RA patients (37.7% vs 27.5%). However, in adjusted analysis, the risk to have ³ 2 comorbidities was lower in EHOA than in RA (OR = 0.25 CI 95% [0.13 to 0.48]; p< 0.001) while there was no difference for CVD risk

Conclusion: After more than 10 years of disease duration, EHOA is associated with more pain and functional impairment but less comorbidities than RA. This study highlights the significant need for effective therapies EHOA.

1. Kwok WY, Ann Rheum Dis, 2011
2. Sellam J, Joint Bone Spine, 2021
3. Combe B, Rheumatology (Oxford),2021

Disclosure: S. Berkani: None; **A. Aparicio Monforte**: None; **S. tuffet**: None; **a. rousseau**: None; **n. rincheval**: None; **e. maheu**: None; **b. combe**: None; **A. SARAUX**: None; **B. Fautrel**: AbbVie, 2, BMS, 2, Chugai, 2, Fresenius Kabi, 2, Galapagos, 2, Lilly, 2, Medac, 2, Nordic Pharma, 2, Novartis, 2, Pfizer, 2, Sobi, 2, UCB, 2; **L. Gossec**: AbbVie, 2, 12, Personal fees, Amgen, 2, Biogen, 5, BMS, 12, Personal fees, Celltrion, 12, Personal fees, Eli Lilly, 5, 12, Personal fees, Galapagos, 12, Personal fees, Janssen, 12, Personal fees, MSD, 12, Personal fees, Novartis, 5, 12, Personal fees, Pfizer, 12, Personal fees, Sandoz, 5, 12, Personal fees, UCB Pharma, 5, 12, Personal fees; **F. Berenbaum**: None; **J. SELLAM**: None; **a. courties**: None.

Abstract Number: 2472

Synovitis and the Risk of Incident Hand Osteoarthritis: Data from the Xiangya Osteoarthritis Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Osteoarthritis II: Novel Insights from Observational Studies

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Synovitis is a modifiable pathological lesion of hand osteoarthritis (HOA). Although synovitis has been related to the prevalence and symptoms of HOA, it remains unclear whether the presence of synovitis increases the risk of incident HOA. We aimed to examine the association between baseline synovitis and incident HOA.

Methods: We conducted a prospective cohort study among participants from the Xiangya OA (XO) Study. Rdiographic and ultrasound examinations were performed on both hands and reliability has been described in previous studies. Hands without baseline radiographic HOA (Kellgren-Lawrence grade $\geq$2 in any joint of a hand) or symptomatic HOA (Kellgren-Lawrence grade $\geq$2 plus self-reported symptoms in the same joint of a hand) were included in the analyses. Incident HOA was defined as the development of radiographic HOA or symptomatic HOA during the three-year follow-up. Hand synovitis was defined as grey-scale synovitis $\geq$2 grade by ultrasound. The inflammatory activity of the synovitis was assessed by the Power Doppler signal (PDS) detected in the synovium. We used generalized estimating equations to examine the relation of synovitis to the risk of incident radiographic and symptomatic HOA, respectively. We assessed the dose-response relationship between the synovitis load (number of hand joints affected by synovitis) and synovitis inflammatory activity (i.e., no synovitis, synovitis without PDS, and synovitis with PDS) at baseline and the risk of HOA. We quantified the impact of synovitis on incident HOA risk by population attributable fractions (PAF).

Results: Included in the analysis were 4,022 hands (2,280 participants) for incident radiographic HOA and 5,016 hands (2,600 participants) for incident symptomatic HOA, respectively (**Figure 1**). During three years of follow-up, 857 (21.3%) hands developed incident radiographic HOA and 111 (2.2%) hands developed symptomatic HOA. As shown in **Table 1**, baseline hand synovitis was associated with an increased risk of radiographic HOA (OR=2.69, 95% CI: 2.06-3.53, P <0.01) and symptomatic HOA (OR=1.73, 95% CI: 1.05-2.85, P=0.03). **Figure 2** shows there was a strong dose-response relationship between the number of hand joints with synovitis and the risk of radiographic and symptomatic HOA (P for trend <0.05). Compared with hands without synovitis, the risk of radiographic HOA was 2.6-fold higher among hands with synovitis but without PDS (OR=2.56, 95% CI: 1.95-3.36, P <0.01), and 10.4-fold higher among hands with both synovitis and PDS (OR=10.42, 95% CI: 1.51-71.81, P=0.03), with the P for trend being statistically significant. We could not assess the relationship between baseline synovitis activity and the risk of symptomatic HOA because of the limited sample size. Approximately 12.5% of incident radiographic HOA and 13.3% of incident symptomatic HOA were attributed to hand synovitis.

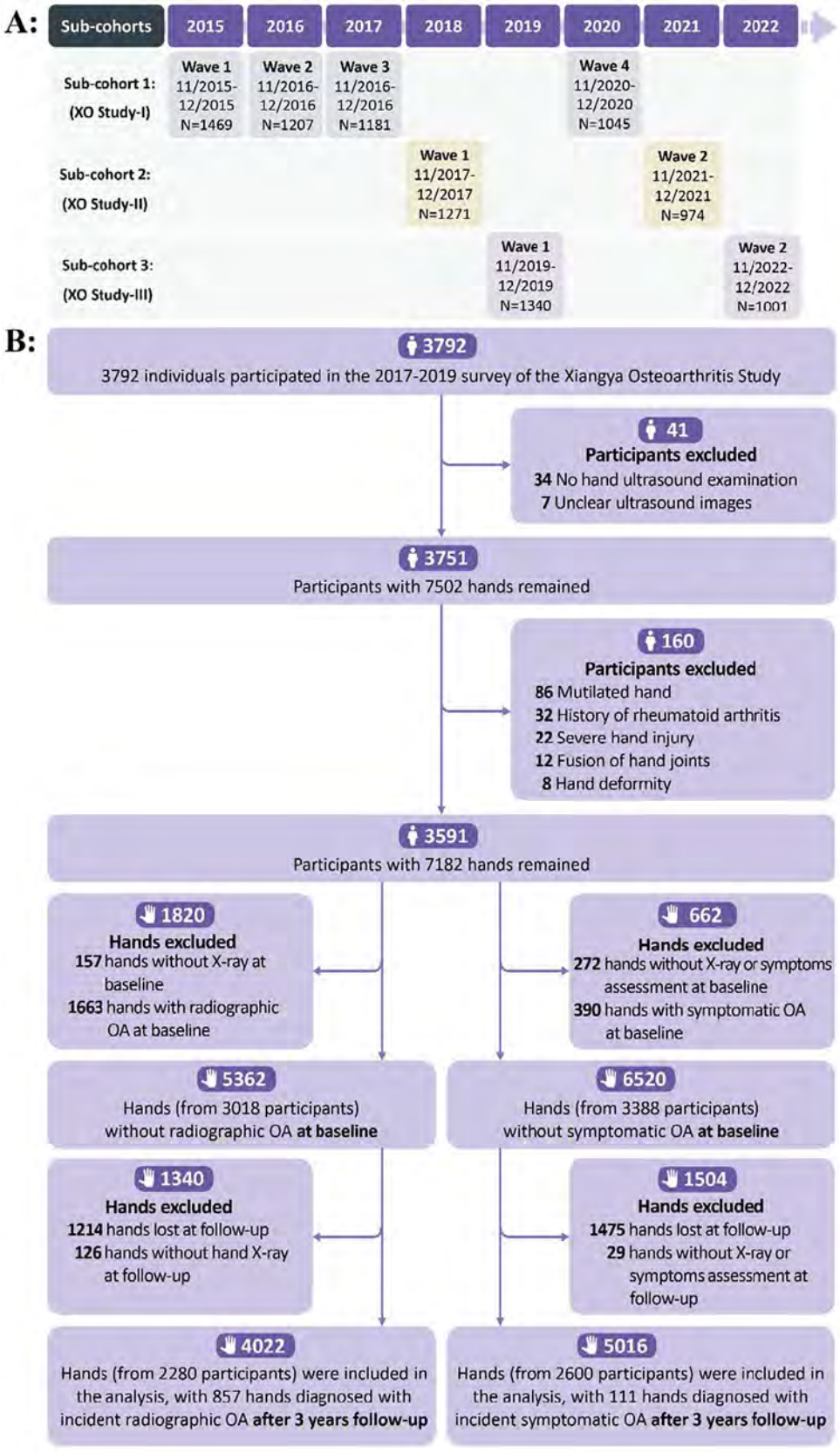

Figure 1. (A) diagram of examination cycles of the Xiangya Osteoarthritis Study (XO Study); (B) flow chart of participants in the study according to new onset of radiographic or symptomatic HOA. HOA, hand osteoarthritis.

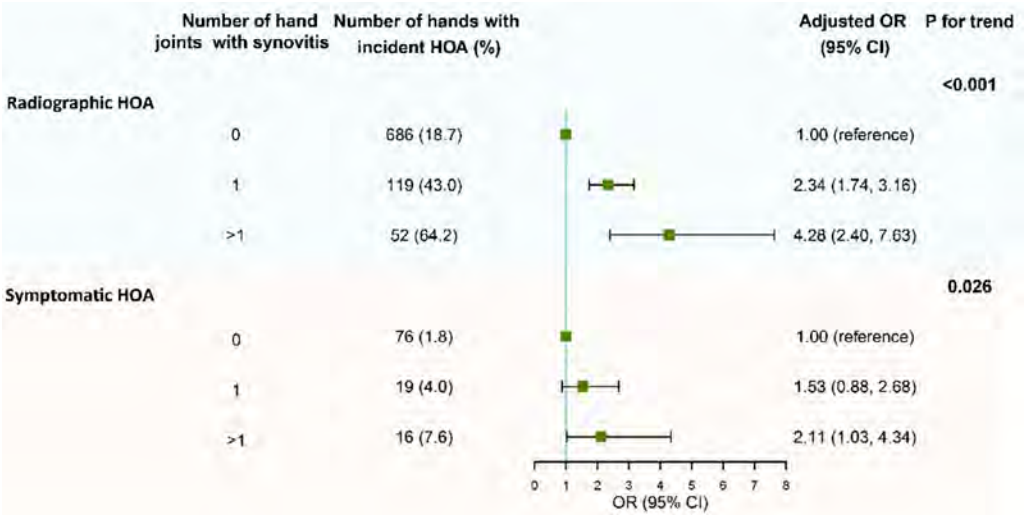

Figure 2. Associations between baseline synovitis load and incident radiographic or symptomatic HOA over three years of follow-up. Adjusted for age, sex, body mass index, smoking status, alcohol consumption, educational level, hand injury history and Kellgren/Lawrence grade at baseline. CI, confidence interval; HOA, hand osteoarthritis; OR, odds ratio.

Table 1. Associations between baseline hand synovitis and incident radiographic or symptomatic HOA over three years of follow-up

	Baseline hand synovitis	
	No	Yes
Incident radiographic HOA		
No, number (%)	2,978 (81.28)	187 (52.23)
Yes, number (%)	686 (18.72)	171 (47.77)
Crude OR (95% CI)	1.00 (reference)	3.97 (3.15, 5.00)
Adjusted OR (95% CI)[a]	1.00 (reference)	2.69 (2.06, 3.53)
Incident symptomatic HOA		
No, number (%)	4,251 (98.24)	654 (94.92)
Yes, number (%)	76 (1.76)	35 (5.08)
Crude OR (95% CI)	1.00 (reference)	2.99 (1.91, 4.70)
Adjusted OR (95% CI)[a]	1.00 (reference)	1.73 (1.05, 2.85)

CI, confidence interval; HOA, hand osteoarthritis; OR, odds ratio.

[a] Adjusted for age, sex, BMI, smoking status, alcohol consumption, educational level, hand injury history and Kellgren–Lawrence grade at baseline.

Conclusion: Synovitis is associated with an increased risk of both incident radiographic and symptomatic HOA in the general population. The strength of the associations increases with the load and inflammatory activity of synovitis. These results support synovitis as a risk factor for HOA and a prospective target for disease prevention.

Disclosure: t. Jiang: None; **Q. Weng**: None; **J. Li**: None; **Y. Zhang**: None; **W. Zhang**: None; **M. Doherty**: None; **T. Yang**: None; **Z. Yang**: None; **K. Liu**: None; **Q. Chen**: None; **J. Wei**: None; **G. Lei**: None; **C. Zeng**: None.

Abstract Number: 2473

A Consensus Based Algorithm to Screen for Lung Disease in Children with Systemic Juvenile Idiopathic Arthritis

Holly Wobma[1], Ronny Bachrach[2], Joseph Farrell[2], Margaret Chang[3], Megan Day-Lewis[1], Fatma Dedeoglu[1], Martha Fishman[4], Olha Halyabar[1], Claudia Harris[1], Daniel Ibanez[1], Liyoung Kim[1], Timothy Klouda[4], Katie Krone[4], Pui Lee[1], Mindy Lo[1], Kyle McBrearty[1], Esra Meidan[1], Susan Prockop[5], Aaida Samad[4], Mary Beth Son[1], Peter Nigrovic[3], Alicia Casey[4], Joyce Chang[3] and Lauren Henderson[3], [1]Division of Immunology, Boston Children's Hospital, Boston, MA, [2]Community Member, Boston, MA, [3]Boston Children's Hospital, Boston, MA, [4]Division of Pulmonary Medicine, Boston Children's Hospital, Boston, MA, [5]Division of Hematology-Oncology, Boston Children's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Pediatric Rheumatology – Clinical III: Potpourri

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Over the last decade, lung disease (LD) has become an increasingly recognized complication of systemic juvenile idiopathic arthritis (sJIA). Children with sJIA-LD may be asymptomatic (diagnosed based on chest imaging) or present with a rapidly progressive disease course that can be fatal. Currently, the true burden of disease is unknown due

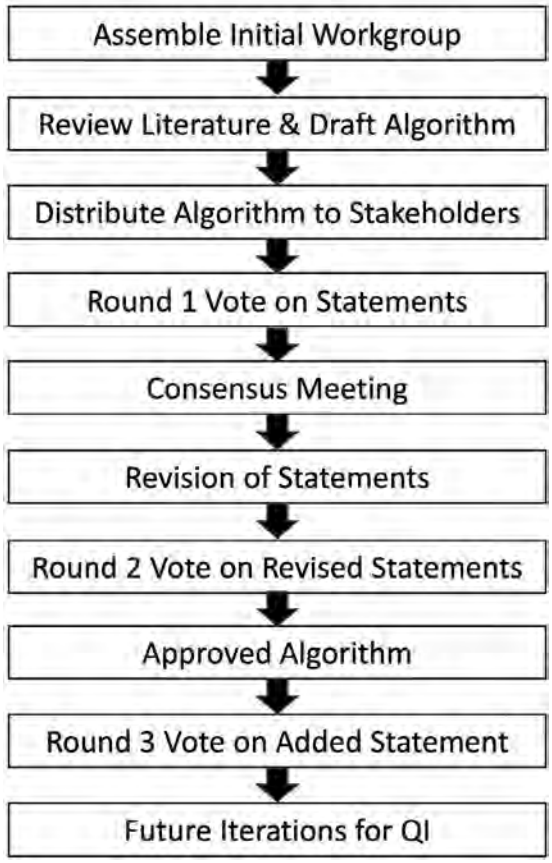

Figure 1. Steps used to develop the sJIA-LD screening algorithm. Through a modified Delphi approach, statements were voted upon, discussed, refined, and re-evaluated by a collaborative workgroup containing diverse stakeholders. Approved statements were rated as appropriate with a moderate or high level of consensus and were organized into the final version of the algorithm. sJIA-LD, systemic juvenile idiopathic arthritis lung disease; QI, quality improvement

to the variability of clinical symptoms and lack of a standardized approach to pulmonary screening in sJIA patients. Here, we sought to develop an algorithm to evaluate for LD in patients with sJIA at our institution.

Methods: A multidisciplinary workgroup was assembled and included members representing rheumatology (n=14), pulmonary (n=5), stem cell transplantation (n=1), and patients and their families (n=2). Four workgroup leaders drafted an initial algorithm based on review of the published literature and experience at our center. A modified Delphi approach was used to achieve agreement through 3 rounds of anonymous, asynchronous voting and a consensus meeting held in the Fall of 2022 (Figure 1). Approved statements were rated as appropriate by the workgroup with moderate or high levels of consensus. These approved statements were organized into the final version of the screening algorithm for LD in sJIA.

Results: The workgroup ultimately rated 21 statements as appropriate with a moderate or high level of consensus. The final algorithm recommends pulmonary screening for newly diagnosed sJIA patients with clinical features that the workgroup agreed may confer increased risk for LD (Figure 2). These "red flag" features include: baseline characteristics (young age

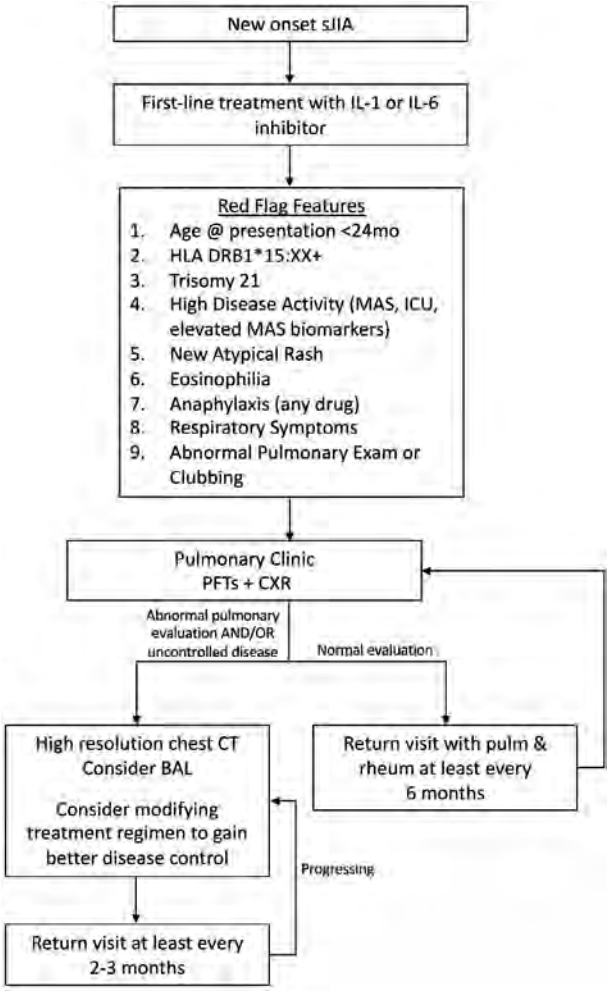

Figure 2. Pulmonary screening algorithm for lung disease in patients with sJIA. The approved algorithm outlines a consensus-based approach to pulmonary screening for LD in sJIA patients at our center. Patients with newly diagnosed sJIA and at least one red flag feature are referred for pulmonary evaluation and follow up. MAS biomarkers include CXCL9, IL-18, ferritin, sIL-2R. Eosinophilia is defined as two consecutive AEC >500/uL or a doubling of baseline AEC. PFTs include spirometry, lung volumes, DLCO, and 6-minute walk test. In younger children who cannot perform these PFTs, a 3-minute walk test can be used. This algorithm was developed for educational purposes only and for use in the Rheumatology and Pulmonary Programs at Boston Children's Hospital. Decisions about evaluation and treatment are the responsibility of the treating clinician and should always be tailored to individual clinical circumstances. sJIA, systemic juvenile idiopathic arthritis; ICU, intensive care unit; MAS, macrophage activation syndrome; AEC, absolute eosinophil count; sIL-2R, soluble IL-2 receptor; PFTs, pulmonary function tests; CXR, chest x-ray, CT, computed tomography; BAL, bronchoalveolar lavage; DLCO, diffusing capacity of the lungs for carbon monoxide

at sJIA disease onset, presence of HLA-DRB1*15 alleles, trisomy 21), high disease activity (history of MAS, sJIA-related ICU admission, elevated MAS biomarkers such as ferritin, soluble IL-2 receptor, IL-18 and CXCL9), respiratory symptoms or abnormal pulmonary examination findings, and features of drug hypersensitivity-like reactions (eosinophilia, new non-evanescent rash without identifiable cause, anaphylaxis to any drug). The presence of any red flag feature prompts an initial pulmonary evaluation, which includes pulmonary function tests (3-minute walk test for young children who cannot perform PFTs), chest x-ray, and referral to the pulmonary clinic. For patients with an abnormal initial pulmonary evaluation and/or persistently active sJIA disease, a high-resolution chest CT is recommended. Bronchoalveolar lavage should also be considered in these patients to evaluate for infectious causes of respiratory decline. The workgroup recommended that all patients with red flag features should be followed closely in the pulmonary clinic.

Conclusion: We used a multidisciplinary, consensus-based approach to develop a strategy to screen for LD in children with sJIA. This approach is intended to reduce practice variation and identify pulmonary complications earlier in the disease course when interventions may be more successful. The algorithm will form the foundation upon which iterative changes can be made as our understanding of sJIA-LD improves.

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Abstract Number: 2474

Uveitis as Predictor of Disease Flare After the First Course of Anti-TNF Withdrawal in Oligo and Polyarticular Juvenile Idiopathic Arthritis: A Multicentric Italian Experience

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SESSION INFORMATION
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Session Title: Abstracts: Pediatric Rheumatology – Clinical III: Potpourri
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: TNF inhibitors (TNFi) have dramatically changed the prognosis of Juvenile Idiopathic Arthritis (JIA). However, once achieved disease remission, it is not clear how and when withdraw the therapy. We aim to describe a multicentric cohort of JIA treated with Adalimumab or Etanercept who discontinued the treatment for persistent remission and identify factors associated with relapse.

Methods: In a multicentric Italian retrospective cohort study (Florence, Brescia, Trieste and Bari), medical records of patients with oligoarticular and polyarticular JIA were evaluated if they stopped therapy for persistent remission after the first course of TNFi. We collected demographic, clinical and laboratory data at onset and during biologic treatment.

Results: 136 patients were enrolled (102 female, median age at onset 3 years (R1-15)), of whom 76 (55.9%) had oligoarticular JIA, 55 (40.4%) uveitis and 99 (72.8%) ANA positivity. Adalimumab (59.3%) and Etanercept (40.7%) were started at a median age of 6 years (R1-16). Remission was achieved after a median time of 4 months (R 1-32) and TNFi were discontinued after a median time of 30 months (R 6-90), increasing the interval of administration in 76.5%, reducing the dose in 18.4% and abrupt discontinuation in16.9%. The 79.4% of patients relapsed after a median time of 5 months (R 0.5-66) and they were more likely female (X^2 5.9 p< 0.014), younger at onset (p< 0.001) and TNFi initiation (p 0.002), to have uveitis

Table 1: Characteristics of the population according to the event of flare after biologic withdrawal. M: median, N: nu mber, R: range, pOligo: persistent oligoarthritis, eOligo: extended oligoarthritis, Poli: polyarticular, JIA: Juvenile Idiopathic arthritis, JADAS10: Juvenile Arthritis Disease Activity Score 10, CHAQ: Childhood Health Assessment Questionnaire, ESR: erytrosedimentation rate, CRP: C reactive protein, B: biologics, Tp therapy

	Entire cohort (136)	*No relapse (28)*	*Relapse (108)*	*Odds ratio (CI)*	*Test and p value*
Female n	102	16	86	1.3 (1.03-1.69)	?² 5.9 p 0.014
Age at diagnosis m ®	3 (1-15)	7 (1-15)	3 (1-11)		p<0.001
Uveitis history, n	55	5	50	3.97 (1.4-11.2)	?² 7.4 p<0.006
Type of JIA *pOligo n* *eOligo n* *Poli n*	 55 21 60	 12 3 13	 43 18 47	-	ns
ANA positivity	99	16	83	2.49 (1.04-5.95)	?² 4.3 p 0.03
FR positivity	3	1	2	0.57 (0.05-6.6)	ns
Comorbdity n	29	10	19	0.38 (0.15-0.962)	?²4.35 p 0.037
ESR mm/h (median R)	45 (2-120)	42.5 (2-120)	45 (2-120)		ns
CRP mg/dl m ®	1.29 (0-17)	1.17 (0-10.2)	1.34 (0-17)		ns
JADAS10	17.3 (2-41.7)	20.5 (3.7-41)	16.9 (2-34)		ns
Type of Biologics	ADA 79 ETA 57	ADA 13 ETA 15	ADA 66 ETA 42	0.552 (0.239-1.27)	ns
Characteristics of population when the biologic was started					
Age m, R	6 (1-16)	9.5 (1-15)	6 (1-16)		p0.002
Concomitant therapy	111 MTX	20	91	-	?² 6.58 p 0.03
Systemic Corticosteroids	28 (20.6%)	7	21	0.724 (0.27-1.9)	ns
Active uveitis at B initiation	36	5	31	1.87 (0.6-5.3)	ns
ESR mm/h m (R)	21.5 (0-120)	11 (0-120)	23 (0-120)		Ns
CRP mg/dl m (R)	0.41 (0.02-32)	0.4 (0.08-12.5)	0.42 (0.02-32)		Ns
JADAS10	17.2 (0-34.4)	12 (0-34)	17.5 (0-28.9)		Ns
Time between diagnosis and B (months)	12 (0-127)	8.5 (0-117)	13 (1-127)		p0.021
Time to achieve remission on therapy	4 (1-32)	3 (1-30)	4 (1-32)		Ns
Duration of therapy	30 (6-90)	30 (9-81)	30 (6-90)		Ns
Duration of remission on therapy	23 (3-64)	23.5 (10-64)	23 (3-60)		ns
Time free from relapse out of therapy months	6 (0.5-96)	Duration FU 16 (4-96)	5 (0.5-66)		
Type of flare *Arthritis* *Uveitis* *Both*	 71 19 18	-	 71 19 18	-	ns
Continuation of concomitant therapy after stop bio	39	6	33		ns
N of months to stop B	6 (0-22)	9 (0-22)	6 (0-22)		p 0.005
Modality to stop B *Lengthening intervals* *Reduction of dose* *Abrupt*	 104 25 16	 26 4 1	 78 21 15	 0.2 (0.045-0.89) 1.48 (0.4 -4.6) 4.35 (0.55-34.4)	?² 5.2 p0.02

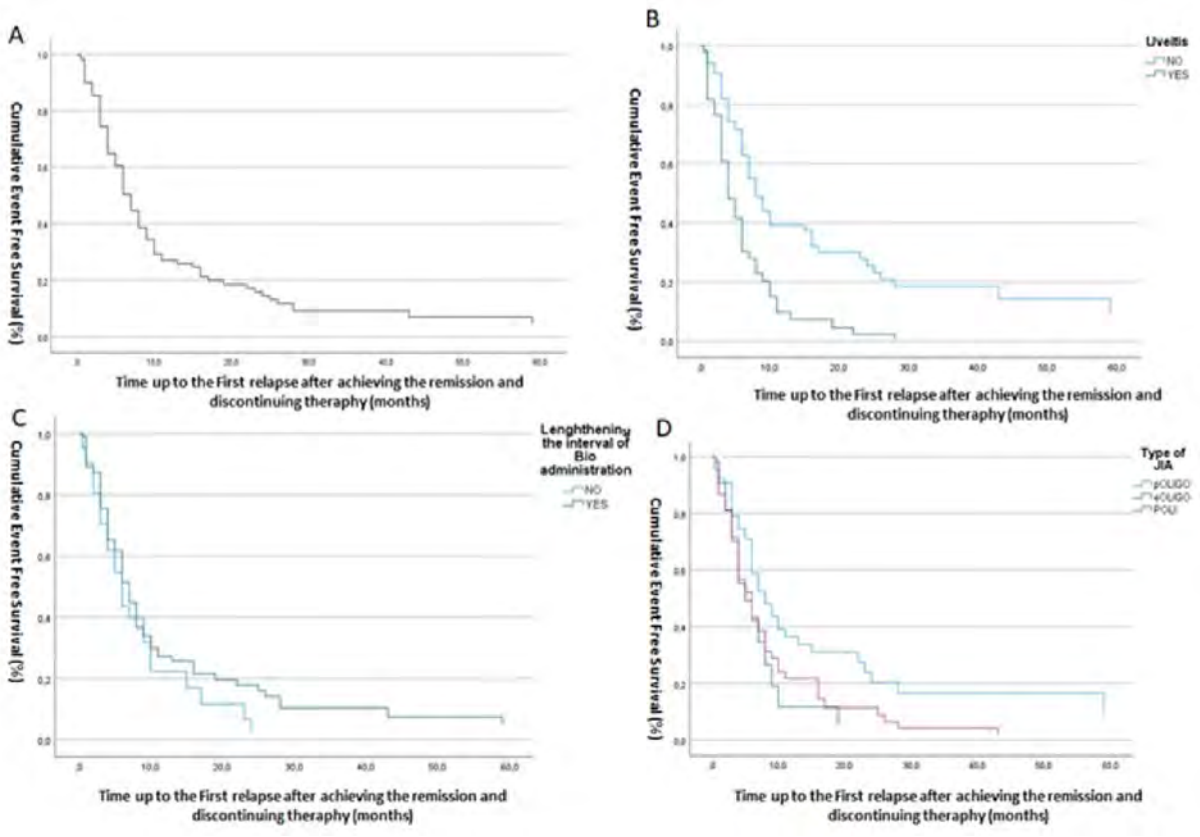

Figure 1: Survival functions from Cox regression, showing the time up to the first relapse after discontinuing therapy among enrolled patients (A), by uveitis (Log Rank $\chi_2$20.54 p0.025) (B), by drug withdrawal modality lengthening the interval of biologic administration (LogRank χ_2 30.3 p 0.001) (C), and by JIA subtypes (LogRank χ_2 31.9 p<0.001) (D)

(X^2 7.4 p< 0.006), longer time to TNFi initiation (p0.02), shorter time of weaning therapy (p0.005) and discontinued therapy not lengthening intervals of administration (X^2 5.2 p0.015). Moreover, patients with uveitis and who not lengthening the interval of administration have earlier relapse evaluated with Kaplan-Meier curve (Log Rank χ^2 = 16.4 p < 0.0001 and χ^2 = 6.95 p 0.008). Cox regression showed as independent predictors for time to relapse uveitis (HR 2.25 CI 1.41 – 3.57), age at onset (HR 0.907 CI 0.830-0.991), duration of tapering (HR 0.928 CI 0.875 -0.985) and to have a pOligo (HR 0.59 CI 0.361-0.978) (χ^2 = 32.9 p0.001). Stratifying the curve by uveitis, JIA categories and tapering modalities the curves showed respectively that patients with uveitis and who do not lengthened the interval of administration relapsed earlier compared to the others (respectively Log Rank χ^2 = 20.54 p0.025 and Log Rank χ^2 = 30.3 p0.001), while patients with pOligo relapse later compared to the other (Log Rank χ^2 = 31.9 p< 0.001)

Conclusion: Early age at onset, uveitis, duration of tapering and to have pOligo seem to be independent risk factors for earlier relapse after first Anti-TNF withdrawal.

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Abstract Number: 2475

Elevation of the IL-17 Cytokine Family Distinguishes Kawasaki Disease from Other Pediatric Inflammatory Disorders

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Pediatric Rheumatology – Clinical III: Potpourri

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Kawasaki disease (KD) is a systemic vasculitis of young children that can lead to the development of coronary artery aneurysms (CAA) in up to 20% of patients. As KD shares overlapping clinical features with other pediatric inflammatory conditions, we aimed to identify diagnostic markers to distinguish KD using the proximity extension assay (PEA) proteomics platform that accurately quantifies protein targets in small volumes of biological fluids (Figure 1A).

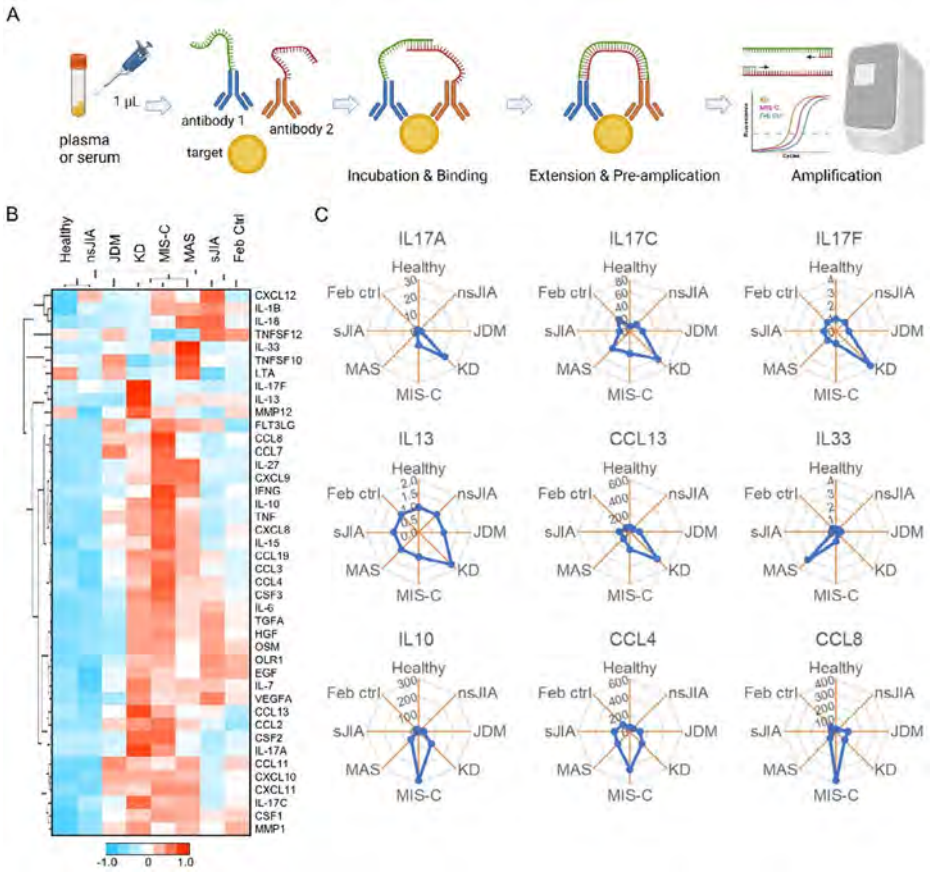

Figure 1. Profiling proinflammatory markers in pediatric inflammatory diseases using proximity extension assay (PEA). A) Schematic illustrating the key steps of PEA. B) Hierarchical clustering and heatmap display of normalized PEA data in healthy controls (n=30), febrile controls (n=26), and patients with Kawasaki disease (KD; n=23), multisystem inflammatory syndrome in children (MIS-C; n=25), macrophage activation syndrome (MAS, n=13), systemic- and non-systemic juvenile idiopathic arthritis (n=14 and n=10, respectively), and juvenile dermatomyositis (n=9). C) Radar plots of median expression values of key cytokines and chemokines upregulated in KD, MAS, and MIS-C. Units represent pg/mL in panel C.

Methods: We used PEA to profile proinflammatory mediators in plasma samples from healthy pediatric controls (n=30), febrile controls (n=26), and patients with KD (n=23), multisystem inflammatory syndrome in children (MIS-C; n=25), macrophage activation syndrome (MAS; n=13), systemic- and non-systemic juvenile idiopathic arthritis (n=14 and n=10, respectively), and juvenile dermatomyositis (n=9). We validated the key findings using serum samples from additional patients with KD (n=37) and febrile controls (n=28).

Results: High-fidelity proteomic profiling by PEA revealed distinct patterns of cytokine and chemokine expression across pediatric inflammatory diseases (Figure 1B). Although KD and MIS-C exhibited many similarities, KD differed from MIS-C and other febrile diseases in that most patients exhibited elevation in one or more members of the IL-17 cytokine family, IL-17A, IL-17C, and IL-17F (Figure 1C). In contrast, the MIS-C group showed elevated levels of IL-10, CCL4 and CCL8, while IL-33 elevation was specifically observed in the MAS group.

IL-17A, IL-17C, and IL-17F levels were significantly higher in patients with KD compared to those with MIS-C and febrile controls (Figure 2A). IL-17A was particularly sensitive and specific in discriminating KD from febrile controls with an area under the receiver operator characteristics (ROC) curve of 0.95 (95% CI: 0.89–1.00) in the derivation set and 0.91 (0.85–0.98) in the validation set. Concurrent elevation of all three IL-17-family cytokines was observed in >50% of KD patients (Figure 2B), including 19 of 20 with CAA, but was rare in other comparator groups. IL-17A and IL-17F levels were significantly higher in KD patients with CAA compared to those without CAA, whereas the levels of IL-1β, IL-6, and TNF were comparable between the groups.

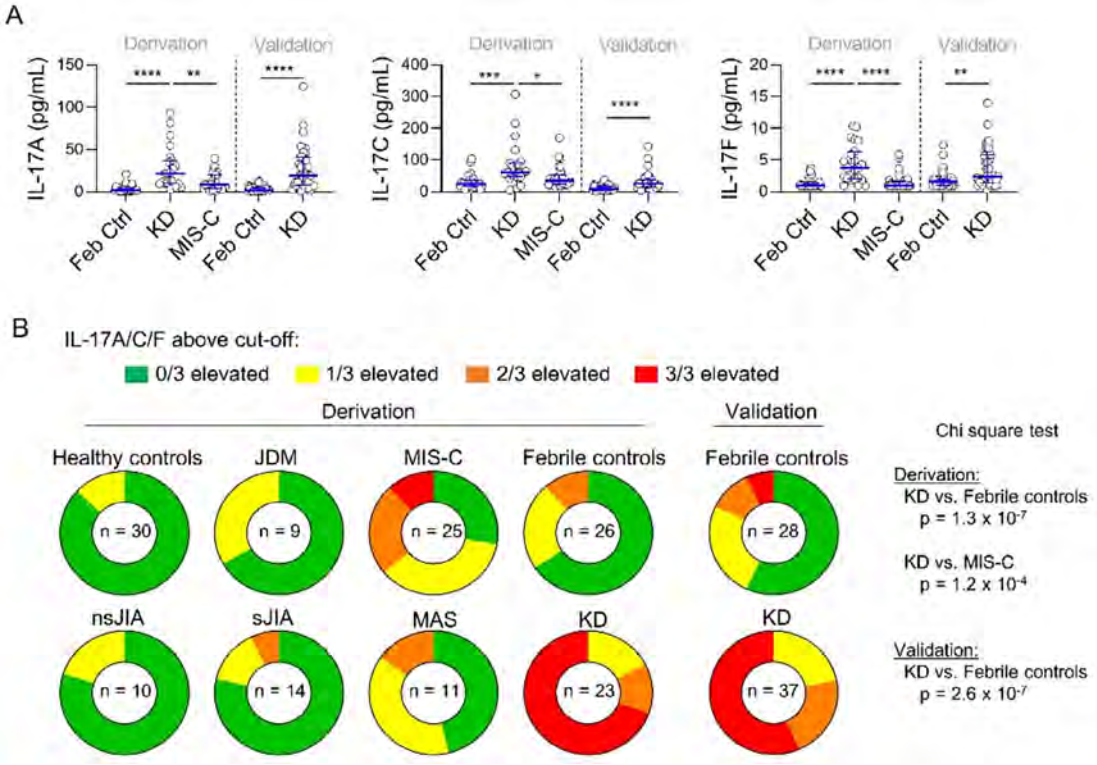

Figure 2. Identification of inflammatory mediators associated with KD. A) Comparison of IL-17 cytokine levels in febrile controls (n=26 in derivation cohort; n=28 in validation cohort), patients with KD (n=23 in derivation cohort; n=37 in validation cohort), and patients with MIS-C (n=25). Median and interquartile range are displayed by blue lines. B) Circle diagrams illustrating the proportion of patients with elevated levels of IL-17A, IL-17C, and/or IL-17F. Mann-Whitney U test was used for statistical analysis in panel A. Chi square test was used for panel B. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.

Conclusion: Data from a single center demonstrated that elevation of IL-17-family cytokines is a hallmark of KD and may help to distinguish this pediatric vasculitis from its clinical mimics. Future multicenter studies are needed to validate these findings.

Disclosure: K. Brodeur: None; **M. Liu**: None; **Y. Du**: None; **L. Henderson**: Adaptive Biotechnologies, 2, 5, Bristol-Myers Squibb(BMS), 5, Pfizer, 2, Sobi, 1, 2, 5; **J. Chang**: None; **J. Newburger**: None; **P. Nigrovic**: None; **P. Lee**: None.

Abstract Number: 2476

Defining Cutoffs for Disease Activity States in Systemic Juvenile Idiopathic Arthritis Based on the Systemic Juvenile Arthritis Disease Activity Score

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SESSION INFORMATION

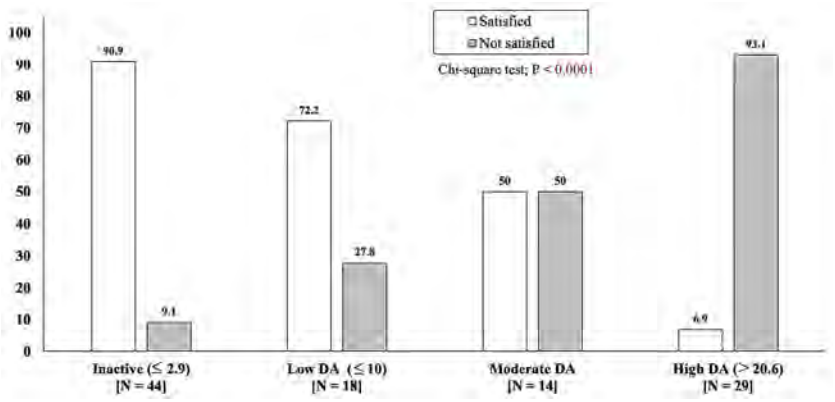
Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Pediatric Rheumatology – Clinical III: Potpourri

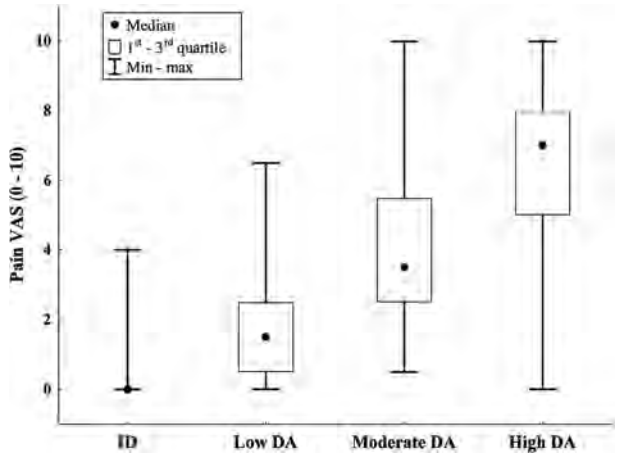
Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: The systemic Juvenile Arthritis Disease Activity Score (sJADAS) is a composite disease activity (DA) score specifically validated for use in systemic JIA (sJIA), whose range is 0-50. The sJADAS10 is obtained as the simple sum of the scores of the following 5 items: 1) physician global assessment of overall DA, measured on a 10-cm visual analog scale (VAS), where 0 = no activity and 10 = maximum activity; 2) parent/patient global assessment of child's well-being, measured on a 10-cm VAS, where 0 = very well and 10 = very poor; 3) count of joints with active disease in a maximum of 10 joints; 4) ESR or CRP level, normalized to a 0-10 scale; and 5) modified Systemic Manifestation Score (mSMS), ranging from 0 to 10, where 0 = absence of systemic manifestations and 10 = maximum activity of systemic manifestations. Our aim was to develop and validate the cutoffs in the sJADAS10 that define the states of inactive disease (ID), low (or minimal) DA (LDA), moderate DA (MDA) and high DA (HDA) in sJIA.

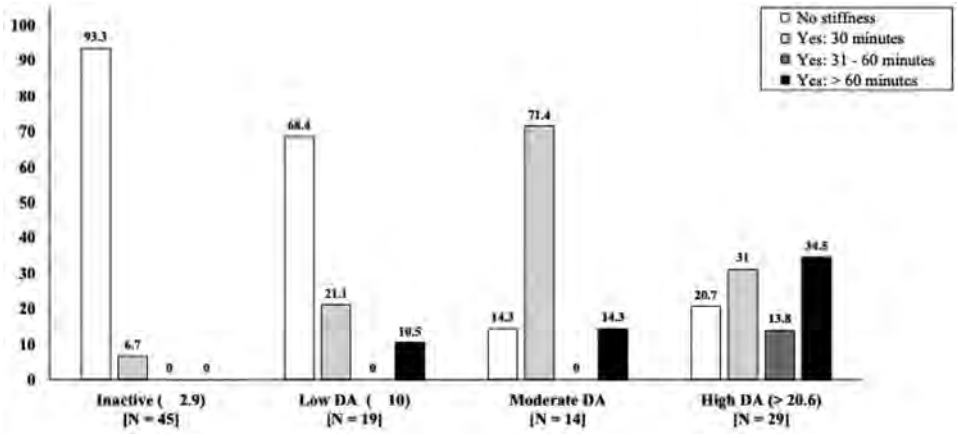


Discriminant Ability: sJADAS total score by category of Parent Acceptable Symptom State (PASS).



Discriminant Ability: sJADAS total score by level of pain VAS.

Methods: A multinational cross-sectional sample of 378 patients with definite or probable sJIA was enrolled. Each patient was categorized subjectively by the caring physician at study visit as being in the state of ID, LDA, MDA, or HDA. A total of 400 visits were collected, that were randomly divided into two samples: a developmental (n=240) and a validation sample (n=160). Optimal cutoff values were determined in the developmental sample against the subjective physician rating of DA state, that was used as external criterion, by multiple methods (calculation of percentiles of cumulative score distribution,



Relationship between sJADAS categories (as defined by the selected cutoff values) and categories of morning stiffness.

ROC curve analysis, Youden index, 90% fixed specificity and kappa agreement). The choice of final cutoffs was based on clinical and statistical grounds. Cutoff validation was conducted in the validation sample by assessing discriminative ability.

Results: The selected sJADAS10 cutoffs were < = 2.9 for ID, < = 10 for LDA, 10-20.6 for MDA, and >20.6 for HDA. In validation analyses, the cutoffs showed strong ability to discriminate among DA states defined subjectively by the parents, parents' satisfaction/dissatisfaction with illness outcome (Fig. 1), level of child's pain (Fig. 2), presence/absence of functional impairment, presence/absence of morning stiffness (Fig. 3), and normal/reduced quality of life.

Conclusion: We developed the cutoffs in the sJADAS10 that define the main DA states in sJIA. The cutoffs revealed good metrologic properties in the validation sample, and are therefore suitable for application in clinical practice and research.

Disclosure: S. Rosina: None; **A. Rebollo Gimenez**: None; **L. Tarantola**: None; **Y. Vyzhga**: None; **L. Carlini**: None; **E. Patrone**: None; **M. Katsikas**: Novartis, 6, Pfizer, 6; **C. Saad-Magalhaes**: None; **D. El-Ghoneimy**: None; **Y. El Miedany**: None; **R. Khubchandani**: None; **P. Pal**: None; **G. Simonini**: Novartis, 5, SOBI, 5; **G. Filocamo**: None; **M. Gattinara**: None; **F. De Benedetti**: Abbvie, Novimmune, Novartis, Roche, Sanofi-Aventis, Sobi, Regeneron, Elixiron and Zydus, 5; **D. Montin**: None; **A. Civino**: None; **M. Alsuweiti**: None; **V. Stenevicha**: None; **V. Chasnyk**: None; **E. Alexeeva**: AbbVie, 5, 6, AMGen, 5, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 5, Merck/MSD, 5, Novartis, 5, 6, Pfizer, 5, 6, Roche, 5, 6, Sanofi, 5, USB Pharma, 5; **S. Al-Mayouf**: None; **S. Vilayuk**: None; **A. Pistorio**: None; **A. Ravelli**: AbbVie/Abbott, 12, honoraria for consultancies or speaker bureaus from, Novartis, 12, honoraria for consultancies or speaker bureaus from, Pfizer, 12, honoraria for consultancies or speaker bureaus from.

Abstract Number: 2477

Anifrolumab Normalizes the Type I Interferon Signature in a Cohort of Patients with Type I Interferonopathies

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Pediatric Rheumatology – Clinical III: Potpourri
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Autoinflammatory Type I Interferonopathies (IFNopathies) include SAVI (STING-associated vasculopathy with onset in infancy), CANDLE/PRASS (Chronic atypical neutrophilic dermatosis, with lipodystrophy and elevated temperature), and AGS (Aicardi-Goutieres syndrome). A high blood IFN-I signature/score correlates with disease activity and response to treatment[2] and is used together with a ratio (IFN-I score/NFKB score) to characterize patients with yet genetically uncharacterized diseases[3]. JAK inhibitors (JAKi), which block the signaling of the IFN receptor, have been the

mainstay of treatment,[1] but suppression of the IFN-I score is only achieved in a subset of CANDLE/PRAAS patients. We treated patients with ongoing active disease and elevated IFN-I scores with the anti- type I IFN receptor (IFNAR) monoclonal antibody, anifrolumab to achieve better disease control and reduce side effects from high-dose JAKi treatment.

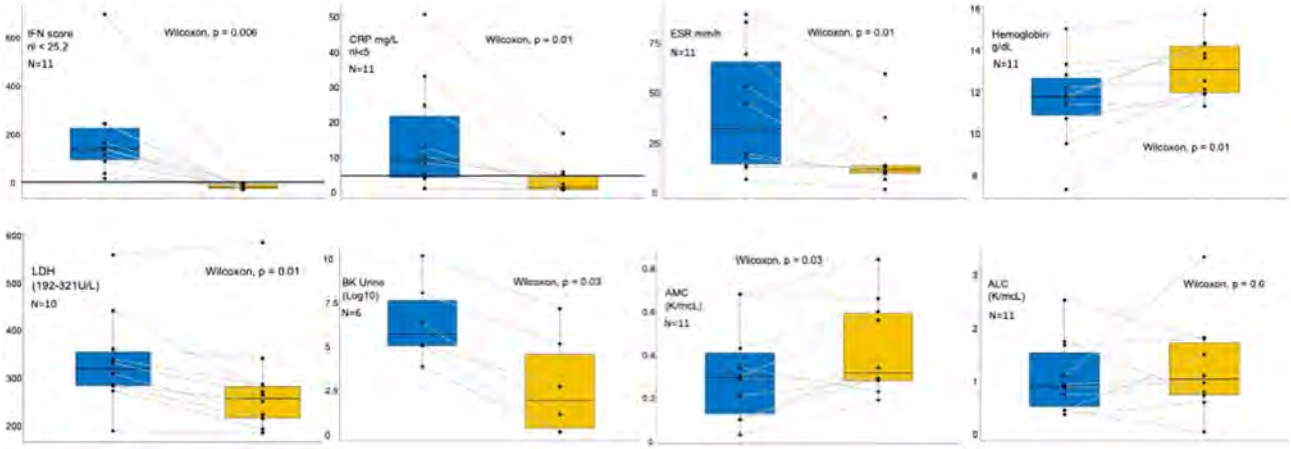
Methods: Pts (n=12), enrolled in NCT02974595, with type I IFNopathies (SAVI=3, CANDLE=6, Undifferentiated=3) and persistently elevated type I IFN score in the blood on optimized treatment with the JAKinhibitor, baricitinib, (n=11), were started on anifrolumab infusions every 4 wks (300 mg or 5.5 mg/kg) either as monotherapy (n=1) or in combination with the baseline JAKi treatment (n=11). The median length of treatment with anifrolumab (range 2-20, median 8 months). Table 1. All patients received zoster prophylaxis. Patient-reported outcomes (daily diaries and questionnaires, n=10) and clinical biomarkers, safety labs including BK viral titers were monitored (n=12).

Table 1: Characteristics of the IFNopathy cohort who received anifrolumab

	N=12
Age, Median (Range, yrs.)	17 (2-42)
Female, n (%)	4 (34%)
White, n (%)	10 (84%)
Interferonopathy type, (n)	SAVI (3) CANDLE (6) Undifferentiated (3)
Concomitant Baricitinib, n (%)	11 (92%)
Baricitinib dose at baseline, median (range, mg/day)	7 (4-12)
Baricitinib dose on anifrolumab, median (range, mg/day)	10 (60%)
Corticosteroid Use, n (%)	9 (75%)
Prednisone dose at baseline, median (range, mg/kg/day)*	0.2 (0.1-1)
Prednisone dose reduction on anifrolumab, n (% reduction)	6 (22%)
Anifrolumab	
Anifrolumab dose, every 28 days (range, mg)**	5.5/kg-300
Anifrolumab treatment duration, median (range, months)	8 (2-20)

*One patient is on methylprednisolone monthly infusion. The dose is reduced from 80 mg to 60 mg on anifrolumab.
**in patients >40kg the full dose of anifrolumab was administered

Figure 1:
Changes in the biomarkers before and after treatment with anifrolumab (n=11)
The blue box represent the value immediately before the first dose and the yellow box is the most recent lab value available on anifrolumab.
In one patient the recent labs were not available at the time of analysis. The same patient had IFN score measured in a different scale.
Paired Wilcoxon rank sum test was used for analysis.



Results: Treatment with anifrolumab resulted in a median change in IFN-I score from 142 to -16 and normalized in all patients treated (n=12) (Figure1). Clinical flares did not occur. The baricitinib dose was tapered down by median of 3 mg/day (0.2 mg/kg/day) in 10/11 pts of the starting dose. Pts on systemic steroids (n=9) could taper down by median of 0.5 mg/kg (n=7) or discontinued steroids (n=2). Inflammatory markers, CRP, and ESR significantly improved on anifrolumab (2/3 SAVI patients continue to have high CRP). Anemia resolved in all patients. Urine BK viral load dropped in (n=6) who had baseline high BK viral titers. Two pts on the combination of anifrolumab and JAKi developed systemic viral infections (Enterovirus n=1, Human Herpesvirus-6 =1 complicated with encephalopathy), and two patients had a long course of rhinovirus and parainfluenza infections that were resolved after tapering down the dose of JAKi and supportive therapy. Evaluation of cytokines and biomarkers is ongoing.

Conclusion: Anifrolumab effectively suppressed the IFN-1 signature/score in all patients, including in SAVI pts; this was associated with improved serum CRP and ESR in the context of tapering doses of baricitinib and corticosteroids. BK viral titers dropped. Long-term follow-up to assess treatment efficacy in controlling inflammatory organ manifestations and progression of organ damage is critical in determining the impact of IFN-I blockade on the diseases manifestations of the autoinflammatory interferonopathies.

Disclosure: S. Alehashemi: None; **A. Baumgardner**: None; **B. Shakoory**: None; **A. Almeida de Jesus**: None; **S. Park**: None; **K. Uss**: None; **M. Robles**: None; **K. Palmblad**: None; **A. Horne**: None; **P. Brodin**: None; **S. Akoghlanian**: None; **R. Abraham**: None; **P. Mustillo**: None; **L. Barillas-Arias**: None; **A. Heras**: None; **T. Wampler Muskardin**: None; **M. Lawrence**: None; **H. Mannem**: None; **B. Nolan**: None; **S. Canna**: Apollo Therapeutics, 2, Novartis, 12, Site PI for industry-sponsored trial, PracticePoint CME, 6, Simcha Therapeutics, 2, Sobi, 6; **A. Reinhardt**: None; **B. Binstadt**: Sobi, Inc., 5; **R. Goldbach-Mansky**: None.

Abstract Number: 2478

Effect of Conventional and Biologic Disease-Modifying Anti-Rheumatic Drugs on the Antibody Response to Four Doses of COVID-19 mRNA Vaccines in Children with Autoimmune and Rheumatic Diseases

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Pediatric Rheumatology – Clinical III: Potpourri

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Children with rheumatic and autoimmune diseases are often treated with conventional or biologic disease-modifying antirheumatic drugs (cDMARDs and bDMARDs) to control disease. While effective, DMARDs may impact antibody responses to COVID-19 vaccination, leading to a risk of breakthrough infections. Here, we compared the effect of different treatments for rheumatic and autoimmune diseases on the antibody response to COVID-19 vaccination in children.

Methods: A prospective observational study was conducted across Canada. Serum or dried blood spots were collected from children with autoimmune or rheumatic diseases after each COVID-19 vaccine dose. Antibodies against the SARS-CoV-2 spike (SmT1) and receptor-binding domain (RBD) were measured using an automated ELISA platform and results are reported in binding antibody units per mL (BAU/mL). Children who had evidence of a SARS-CoV-2 infection prior to sample collection were excluded, except for the hybrid immunity analysis. The magnitude and kinetics of the antibody response after each vaccine dose were compared between treatment groups using mixed-effects linear regression models. Disease activity was measured in a subset of participants using the Childhood Health Assessment Questionnaire (CHAQ) and the Visual Analog Scale (VAS).

Results: For this interim analysis, 1751 potential participants were identified. Of these, 1748 were contacted and 192 enrolled in the study. Data are currently available for 126 participants, including from 94 individuals without evidence of prior COVID-19 infection. Participants contributed 1-6 samples, resulting in total of 187 samples collected pre-vaccination, and following 1-4 vaccine doses (Table 1). The median age of participants was 12 years and most patients had a primary diagnosis of either JIA (57%) or vasculitis (19%). There was a relatively even distribution between the three treatment groups (none, cDMARDs, and bDMARDs), with a slight over-representation of bDMARD-treated patients (42%).

Following the second dose of the COVID-19 vaccine, IgG responses were both reduced in magnitude and waned faster for participants treated with bDMARDs than for those treated with cDMARDs or who were treatment naïve (Figures 1 & 2). Post-dose 3, differences in the magnitude of response between treatment groups were attenuated, but responses continued to wane at a faster rate in those treated with bDMARDs (Figures 1 & 2). Differences between treatment groups were not significant, however, among children with evidence of a prior SARS-CoV-2 infection. After dose 4, antibody responses were similar in all treatment groups (Figures 1 & 2). As measured by CHAQ and VAS scores reported by parents and participants, vaccination was not associated with increased disease activity.

Conclusion: Antibody responses to COVID-19 vaccination in children with autoimmune and rheumatic diseases were lowest in individuals treated with bDMARDs, with third and fourth vaccine doses necessary to yield robust and durable antibody responses. Given that vaccination did not impact underlying disease activity, additional work is needed to optimize vaccine strategies in this population.

Table 1. Characteristics of participants without evidence of prior COVID-19 infection

	Total	Pre-vaccination	Post dose 1	Post dose 2	Post dose 3	Post dose 4
N						
Observations	187	49	7	45	55	25
Individuals	94	49	7	35	41	17
Female - N (%)	109 (58.3)	27 (55.1)	5 (71.4)	27 (60.0)	36 (65.5)	12 (48.0)
Age[a]						
Mean (min-max)	12 (2 - 19)	10 (2 - 17)	8 (4 - 12)	11 (5 - 17)	13 (6 - 18)	14 (8 - 18)
Median (IQR)	12 (9 - 14)	11 (8 - 14)	8 (5 - 11)	10 (9 - 12)	13 (11 - 15)	14 (13 - 16)
Primary diagnosis - N (%)						
JIA	106 (56.7)	32 (65.3)	6 (85.7)	27 (60.0)	27 (49.1)	13 (52.0)
Vasculitis	36 (19.3)	11 (22.4)	1 (14.3)	9 (20.0)	9 (16.4)	4 (16.0)
Other rheumatic	19 (10.2)	3 (6.1)	0 (0.0)	3 (6.7)	8 (14.5)	4 (16.0)
Other autoinflammatory	26 (13.9)	3 (6.1)	0 (0.0)	6 (13.3)	11 (20.0)	4 (16.0)
Treatment[a] **- N (%)**						
None	61 (32.6)	23 (46.9)	3 (42.9)	18 (40.0)	17 (30.9)	0 (0.0)
cDMARDs	42 (22.5)	10 (20.4)	1 (14.3)	12 (26.7)	15 (27.3)	3 (12.0)
bDMARDs	79 (42.2)	16 (32.7)	3 (42.9)	15 (33.3)	21 (38.2)	19 (76.0)
Days since vaccination						
Mean (min-max)			48 (28 - 81)	141 (13 - 396)	117 (7 - 399)	63 (6 - 196)
Median (IQR)			36 (34 - 72)	119 (46 - 207)	109 (52 - 179)	32 (21 - 93)

[a] At time of collection for pre-vaccination samples, at time of vaccination for post-vaccination samples

* Denominator for all rows is the number of observations (not the number of individuals)

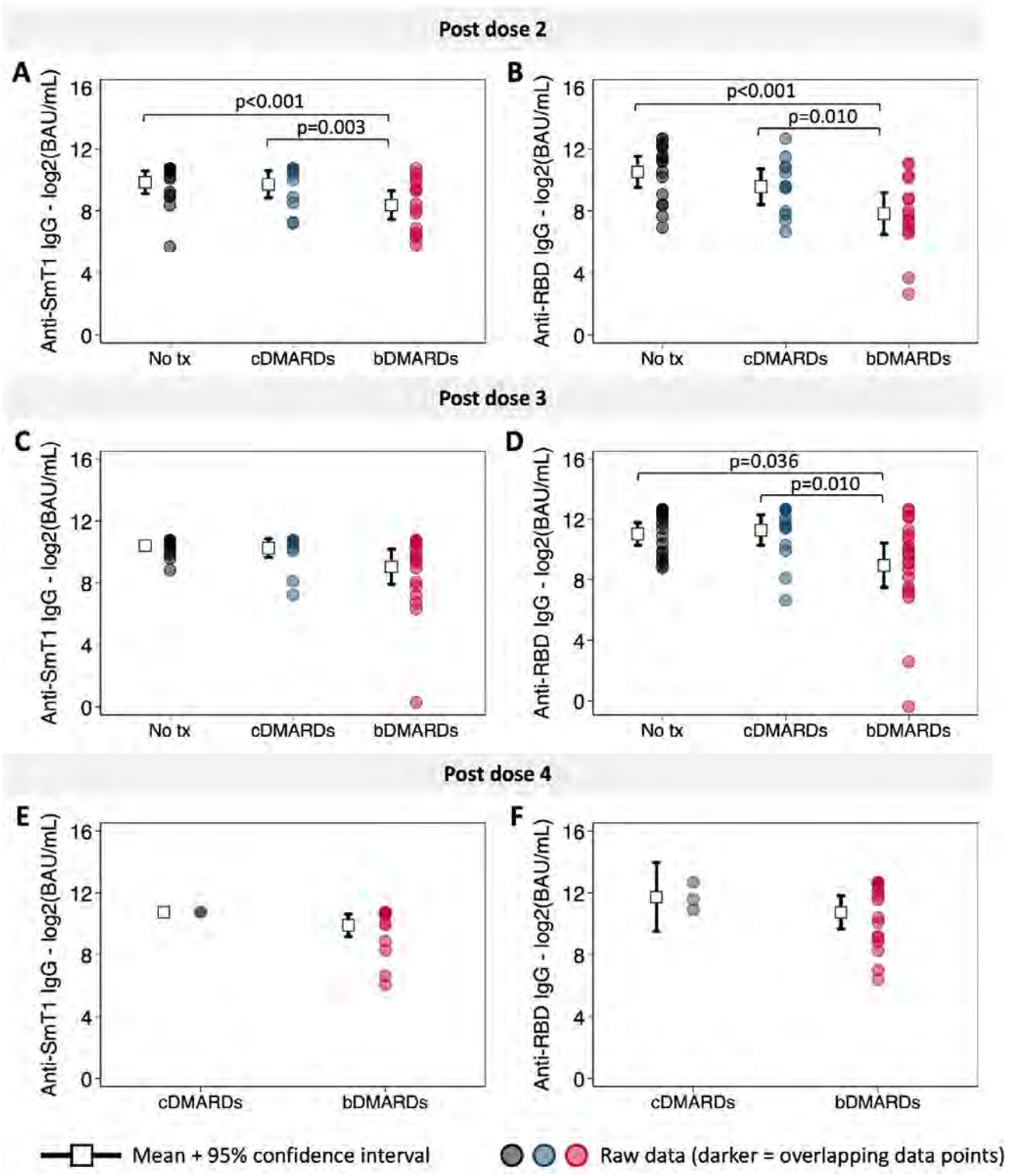

Figure 1. Effect of treatment on the magnitude of the antibody response to the COVID-19 vaccine in children with autoimmune and rheumatic disease

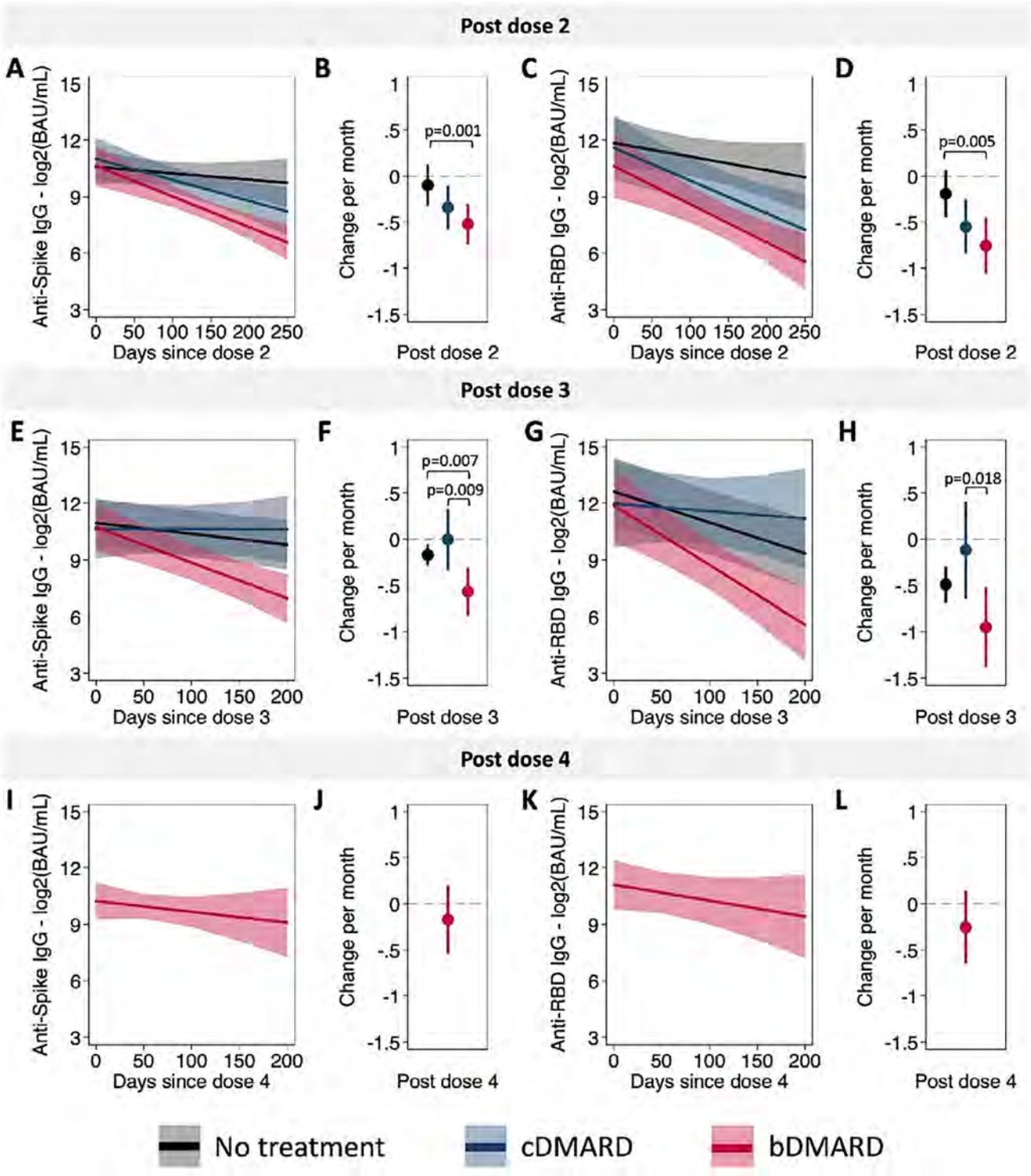

Figure 2. Effect of treatment on the durability of the antibody response to the COVID-19 vaccine in children with autoimmune and rheumatic disease

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Abstract Number: 2479

Tolerability and Effectiveness of Antifibrotics in Rheumatoid Arthritis-associated Interstitial Lung Disease

Pierre-Antoine Juge[1], Keigo Hayashi[2], Gregory McDermott[2], Kathleen Vanni[2], Emily Kowalski[2], Grace Qian[2], Katarina Bade[3], Alene Saavedra[2], Philippe Dieudé[4], Paul Dellaripa[3], Tracy J. Doyle[2] and Jeffrey Sparks[5], [1]Division of Rheumatology, Inflammation, and Immunity Brigham & Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital, Boston, MA, [3]Brigham and Women's Hospital, Boston, MA, [4]Assistance Publique-Hôpitaux de Paris, Bichat-Claude Bernard University Hospital, INSERM UMR1152, University de Paris Cité, Department of Rheumatology, Paris, France, [5]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes III: Predicting & Optimizing Outcomes

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Nintedanib and pirfenidone are antifibrotic drugs indicated for the treatment of idiopathic pulmonary fibrosis (IPF) and other forms of progressive pulmonary fibrosis. Antifibrotics have also been tested in RA-associated interstitial lung disease (ILD) within two recent randomized clinical trials (RCT). However, there are limited real-world studies regarding the use of antifibrotics, and none in RA-ILD. RA-ILD patients may be different from IPF patients since they often need concomitant immunosuppression for articular disease. Our aim was to investigate the tolerability and effectiveness of antifibrotics in a real-world cohort of patients with RA-ILD.

Methods: In this retrospective cohort study, we identified RA-ILD patients initiating antifibrotics at a large multi-hospital healthcare system. We used electronic query to find all patients with at least two RA diagnosis codes and a prescription for either nintedanib or pirfenidone (2014-2023). We then performed medical record review to confirm all patients met 2010 ACR/EULAR classification criteria for RA and had definite RA-ILD by Bongartz criteria. Data regarding adverse events (AEs), tolerability, pulmonary function test (PFT) results, and clinical data were collected. Drug retention was estimated using a Kaplan-Meier curve. A linear mixed model with random intercept was used to compare the within-patient trajectory of the percent predicted forced vital capacity (%FVC) within 18-months before to 18-months after antifibrotic initiation among those with these PFT data.

Results: We analyzed 74 patients with RA-ILD that initiated antifibrotics (mean age 67.8 years, 53% male); 40 patients initiated nintedanib and 34 initiated pirfenidone (**Table 1**). Median follow-up was 89 weeks (min 4, max 387). AEs were reported in 41 (55%) patients, with gastrointestinal (GI) AEs (n=30) being most common, followed by disease progression (n=6), rash (n=3), and hepatitis (n=2). The initial antifibrotic was discontinued in 34 (46%) patients due to: GI AEs (n=19), rash (n=3), transaminitis (n=2), and financial reasons (n=1). The median drug survival was 147.7 weeks (95%CI 79.1, NA; **Figure 1**). There was no difference in drug retention between nintedanib and pirfenidone (p=0.68). A second antifibrotic was prescribed in 14 patients, with 4 discontinuations. Change of %FVC trajectory was analyzed for 49 patients with available PFTs within 18 months pre- and post-antifibrotic (median number of PFT/patient = 4). There was a statistical difference in the estimated %FVC slope after initiation (-0.3% per year compared to -6.2% per year before initiation, p=0.031, **Figure 2**). Twenty-six patients (35%) died (17 due to ILD) and 4 (5%) had lung transplantation during follow-up.

Conclusion: In this first real-world study of antifibrotic use in RA-ILD, AEs were frequently reported, particularly GI, and discontinuation was common (46% compared to 20% for nintedanib and 24% for pirfenidone in their respective RCTs). However, antifibrotic initiation was associated with a modestly improved trajectory in %FVC. Death and/or lung transplant were frequent, emphasizing the need for additional safe and effective RA-ILD treatment options.

Table 1. Characteristics of patients with RA-ILD at initiation of initial antifibrotic medication. ACPA: anti-citrullinated peptides proteins, cs and bDMARDs: conventional and biologic disease modifying drugs, DLCO: diffusing lung capacity of the lungs for carbon monoxide, FVC: forced vital capacity, HRCT: high resolution computed tomography, ILD: Interstitial lung disease, NSIP: non-specific interstitial pneumonia, RA: rheumatoid arthritis, RF: rheumatoid factor, UIP: usual interstitial pneumonia.

	Nintedanib n=40 (54%)	Pirfenidone n=34 (46%)	Overall n=74
Demographics and lifestyle			
Mean age, years (SD)	69.2 (9.1)	66.3 (7.9)	67.8 (8.6)
Male sex	19 (48%)	20 (59%)	39 (53%)
Race			
- White	34 (85%)	27 (79%)	61 (82%)
- Black	2 (5%)	5 (15%)	7 (9%)
- Asian	1 (3%)	1 (3%)	2 (3%)
- Other	3 (8%)	1 (3%)	4 (5%)
Smoking status			
- Never	11 (28%)	12 (36%)	23 (31%)
- Past	28 (70%)	20 (59%)	48 (65%)
- Current	1 (3%)	2 (6%)	3 (4%)
Median smoking, pack-years (IQR)	15 (0, 30)	9.5 (0, 35)	14.5 (0, 30)
RA characteristics			
Mean RA duration, years (SD)	11.1 (12.1)	6.1 (8.7)	8.8 (10.9)
ACPA-positive (%)	22 (59%)	18 (58%)	40 (59%)
RF-positive (%)	29 (76%)	18 (56%)	47 (67%)
RA disease activity			
- Remission	24 (71%)	20 (65%)	44 (68%)
- Low	7 (21%)	5 (16%)	12 (19%)
- Moderate	3 (9%)	5 (16%)	8 (12%)
- High	0 (0%)	1 (3%)	1 (2%)
Concomitant DMARDs			
Methotrexate	2 (5%)	3 (9%)	5 (7%)
Other csDMARDs	9 (23%)	8 (24%)	17 (23%)
Rituximab	8 (20%)	2 (6%)	10 (14%)
Other biologic DMARDs	2 (5%)	4 (12%)	6 (8%)
JAK inhibitors	0 (0%)	1 (1%)	1 (1%)
Mycophenolate mofetil	1 (3%)	3 (9%)	4 (5%)
Glucocorticoids	24 (60%)	13 (38%)	37 (50%)
Median glucocorticoid dose, mg pred (IQR)	10 (5, 10)	20 (7.5, 20)	10 (5, 10)
ILD characteristics			
Mean ILD duration, years (SD)	5.4 (5.3)	5.3 (4.7)	5.3 (5.0)
Fibrotic ILD (%)	40 (100%)	34 (100%)	74 (100%)
HRCT ILD pattern			
- UIP (%)	28 (70%)	20 (59%)	48 (65%)
- Probable UIP (%)	3 (8%)	1 (3%)	4 (5%)
- Fibrotic NSIP (%)	6 (15%)	7 (21%)	13 (18%)
- Unknown (%)	3 (8%)	6 (18%)	9 (12%)
Mean %FVC (SD)	73.4 (23.0)	72.8 (16.4)	73.1 (20.1)

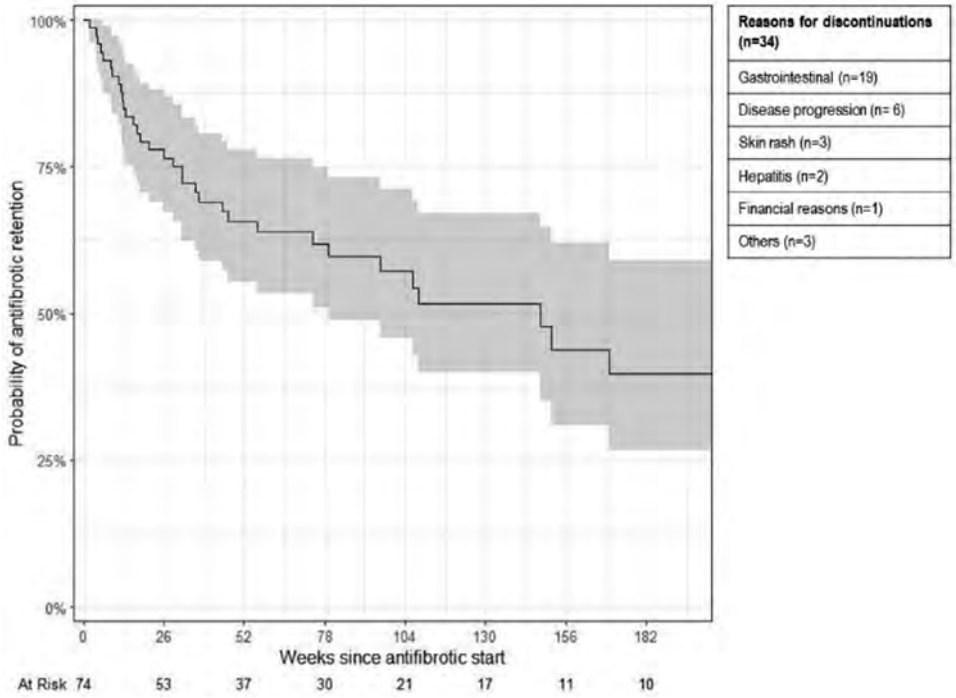

Figure 1. Kaplan-Meier curve for retention of initial antifibrotic used to treat RA-ILD.

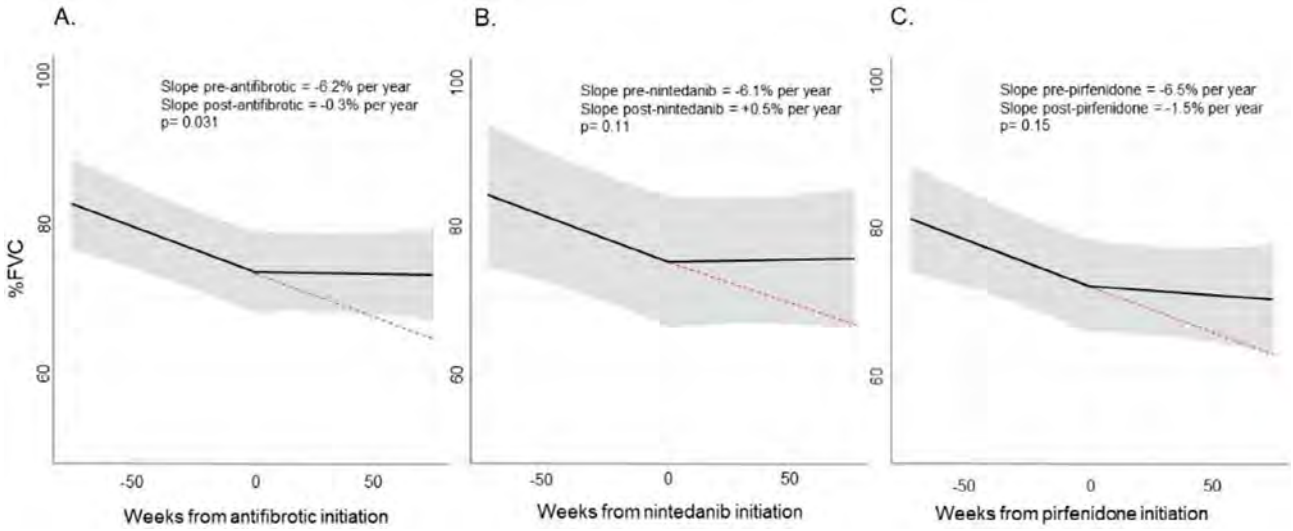

Figure 2. Trajectories of %FVC before and after initial antifibrotic prescription for RA-ILD. The shaded grey represents the 95%CI of the %FVC trajectory. The dotted line represents the hypothetical decline in %FVC based on %FVC values prior to antifibrotic initiation. Panel A represents patients that initiated either antifibrotic (nintedanib or pirfenidone), Panel B represents patients that initiated nintedanib, and Panel C represents patients that initiated pirfenidone. Trajectories were estimated using a linear mixed model with random intercept with a knot at initial antifibrotic prescription (time 0). FVC: forced vital capacity.

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Abstract Number: 2480

Definition of Rheumatoid Arthritis Flare Based on SDAI and CDAI

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes III: Predicting & Optimizing Outcomes

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Measures of improvement and state of disease activity are well-established in rheumatoid arthritis (RA), whereas distinct classifiers for worsening ("flare") are lacking to date. Definitions of flare are highly warranted for novel treatment strategies that aim for drug tapering or withdrawal in patients on treatment target. We therefore aim to provide preliminary definitions of flare, based on the Simplified and Clinical Disease Activity Indices (SDAI, CDAI).(1)

Table 1 Baseline, three- and six-month data from the NOR-DMARD main analysis cohort and the Vienna RA validation cohort (no. of treatment cycles: 4256 and 2557, respectively); values are given in percent, or as mean and standard deviation

	NOR-DMARD COHORT			Vienna RA COHORT		
	Baseline	Month 3	Month 6	Baseline	Month 3	Month 6
Years of patient inclusion	2002-2022			1996-2021		
Female (%)	71.5%			77.8%		
Age (years)	54.1 (14.1)			54.1 (14.6)		
Disease duration (years)	7.9 (9.5)			6.2 (9.2)		
csDMARD/ btsDMARD (%)	50.6/49.4%			72.2/27.8%		
SDAI	24.7 (13.8)	14.1 (11.1)	13.7 (11.9)	18.9 (13.1)	14.8 (12.4)	13.4 (11.8)
CDAI	22.6 (12.9)	13.0 (10.4)	12.5 (11.1)	17.0 (12.0)	13.5 (11.5)	12.4 (11.2)
CRP (mg/l)	20.1 (27.3)	10.6 (16.8)	10.6 (17.7)	17.3 (28.2)	11.9 (22.2)	9.9 (16.5)
ESR (mm/h)	27.0 (21.8)	18.4 (16.7)	18.1 (16.7)	33.2 (25.8)	26.9 (21.2)	25.7 (21.5)
SJC28	6.4 (5.5)	3.3 (3.9)	3.0 (4.0)	4.6 (4.6)	3.6 (4.3)	3.2 (3.8)
TJC28	7.5 (6.7)	4.3 (5.4)	4.1 (5.4)	5.2 (6.5)	4.2 (6.1)	3.9 (6.1)
PGA (mm)	49.6 (24.4)	33.1 (23.6)	33.8 (24.7)	43.8 (25.5)	36.6 (25.9)	33.4 (25.7)
EGA (mm)	37.6 (18.5)	21.1 (15.5)	20.6 (17.0)	28.6 (20.1)	21.8 (18.9)	20.3 (18.5)
Pain (VAS mm)	46.3 (24.7)	31.0 (23.3)	31.6 (24.3)	39.3 (25.2)	32.2 (25.4)	31.2 (25.1)
HAQ (0-3)	0.7 (0.5)	0.4 (0.4)	0.5 (0.4)	1.0 (0.8)	0.9 (0.8)	0.8 (0.8)

csDMARDs=conventional synthetic disease-modifying anti-rheumatic drug; btsDMARD=biologic/targeted synthetic disease-modifying anti-rheumatic drug; SDAI=Simplified Disease Activity Index; CDAI=Clinical Disease Activity Index; CRP=C-reactive protein; ESR=Erythrocyte sedimentation rate; SJC28=Swollen joint count of 28 joints; TJC=Tender joint count of 28 joints; PGA=Patient global assessment of disease activity; EGA=Evaluator global assessment of disease activity; HAQ=Health assessment questionnaire

Methods: We analysed RA treatment courses from the Norwegian DMARD registry (NOR-DMARD) and the Vienna RA cohort. In a receiver operating curve (ROC) analysis, we determined distinct cut points for absolute worsening in SDAI and CDAI based on a semiquantitative patient anchor (for details see legend figure 1). We separated the NOR-DMARD dataset into a training and test cohort by 8:2 random sampling. For internal validation, we performed bootstrapping in the training cohort and evaluated performance in the test cohort. We then validated the definitions externally in the independent Vienna RA cohort, and determined their performance on content, construct, longitudinal, and face validity.

Results: We analyzed 4256 treatment courses in the NOR-DMARD registry and 2557 in the Vienna RA cohort (table 1). The preliminary definitions for absolute changes in SDAI and CDAI for flare are an increase of 4.7 and 4.5, respectively (figure 1). These cut points performed well in the NOR-DMARD test cohort and the external validation cohort. When flaring, patients showed worsening in all disease activity core set variables, including both patient reported and objective measures (figure

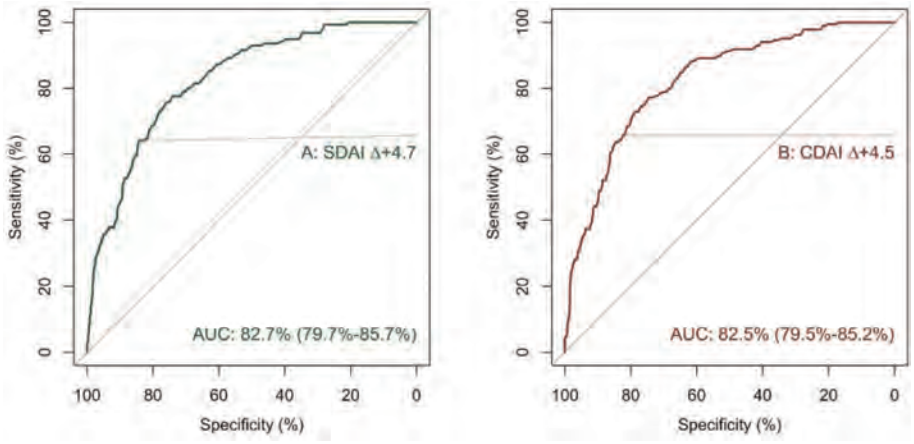

Figure 1 Receiver operating curves (ROC) to derive cut points for absolute changes in SDAI (A) and CDAI (B); based on a semiquantitative patient anchor from NOR-DMARD, where patients reported their perception of response to DMARD treatment compared to baseline on a five-point Likert scale (much worse – worse – unchanged – better – much better). Flare was defined as worsening of at least two points on the Likert scale, compared to the assessment at month three; 95%-confidence intervals for the area under the receiver operating curve (AUC) were estimated using bootstraps with 1000 resamples.

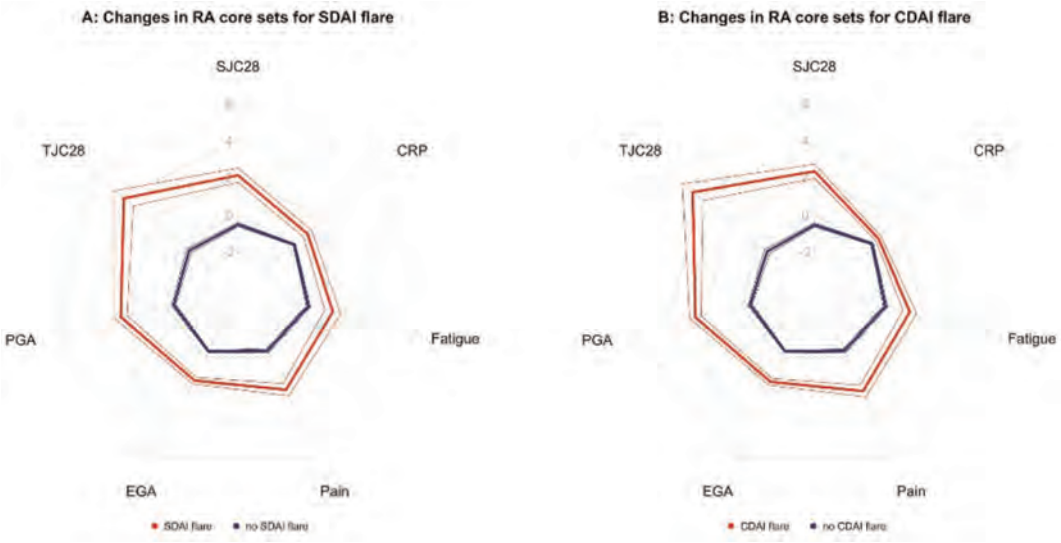

Figure 2 Content validity analysis; spider charts illustrate internal consistency of the novel definitions (A: SDAI Δ+4.7; B: CDAI Δ+4.5) across all rheumatoid arthritis core sets, tested in 1252 visits of 329 patients in the Vienna RA cohort; evaluator global (EGA), patient global (PGA), pain, and fatigue are given in cm; C-reactive protein (CRP) in mg/dl; thin borders mark 95%-confidence intervals

2), and were more frequently subjected to subsequent treatment changes (p< 0.001). Flares substantially impacted both functional and structural disease outcomes (increase in Health Assessment Questionnaire score, ΔHAQ,(2) for flare vs. no flare +0.44, p< 0.001; radiographic progression, Δmodified Sharp Score,(3) 43% higher after flare vs. no flare visits, 95%-CI 1.04-1.96, p< 0.001). This underlines clinical face and construct validity of the novel definitions.

Conclusion: We here provide novel preliminary definitions for flare in RA based on changes in SDAI and CDAI. In times of highly effective treatments available for RA, and consideration of treatment tapering or withdrawal, these definitions will be useful for guiding decision making in clinical practice and designing clinical trials.

References

1. Smolen JS, Aletaha D. Scores for all seasons: SDAI and CDAI. Clin Exp Rheumatol. 2014;32(5 Suppl 85):S-75-9.
2. Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. Arthritis Rheum. 1980;23 (2):137-45.
3. van der Heijde D. How to read radiographs according to the Sharp/van der Heijde method. J Rheumatol. 2000;27 (1):261-3.

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Abstract Number: 2481

Pre-pregnancy Gene Expression Signatures Among Women with Rheumatoid Arthritis May Represent Predictive Biomarkers for Subsequent Improvement or Worsening During Pregnancy

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes III: Predicting & Optimizing Outcomes
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Rheumatoid arthritis (RA) can improve naturally during pregnancy in a substantial proportion of women (50-75%), while it may worsen or remain unchanged in others. Thus far, there are no biomarkers to predict, at the pre-pregnancy stage, whether a woman with RA will improve or worsen during pregnancy. We examined pre-pregnancy gene

expression profiles among women with RA to identify prediction biomarkers for improvement/worsening during pregnancy. We also aimed to identify genes that demonstrated altered expression during pregnancy when RA improved or worsened.

Methods: Blood samples were collected before pregnancy (T0) and at the 3rd trimester (T3) from 19 women with RA and 14 healthy women enrolled in our prospective pregnancy cohort. RA improvement/worsening during pregnancy was assessed using the Clinical Disease Activity Index (CDAI). Total RNA from whole blood was sequenced to examine gene expression, and differences between groups or time-points were evaluated using differential expression analysis, using FDR < 0.05 and fold-change >=1.5 for significance. Co-expression network analysis and functional enrichment were also performed.

Results: Of the 19 women with RA, 14 improved during pregnancy ($RA_{improved}$) and 5 worsened ($RA_{worsened}$). At the T0 baseline, although both groups had similar disease activity (CDAI) [$RA_{improved}$ (mean±S.D.): 16.8±11.5 and $RA_{worsened}$: 16.9±7.6; p=0.9], their gene expression profiles were significantly different. The $RA_{improved}$ T0 gene expression signature showed increased expression of neutrophil-related genes. Additionally, one gene co-expression module related to B cell function was significantly correlated with the worsening of RA during pregnancy (r=0.65, FDR=$5E^{-5}$). This module was also significantly enriched (21-fold, FDR=$1.7E^{-118}$) in genes differentially expressed between the 2 RA groups at T0. At T3, the expression profile of the $RA_{improved}$ group became similar to those of the healthy women, and for most (86%) of the genes in the $RA_{improved}$ T0 RA signature, their T3 expression were no longer associated with the disease. In the $RA_{worsened}$ group, several genes became newly differentially expressed at T3, including some candidates known to be expressed in the RA synovium. Further, additional candidate genes (e.g. PADI4) previously reported to be involved in RA demonstrated longitudinal expression patterns that were associated with pregnancy, and those associations were influenced by clinical outcome during pregnancy.

Conclusion: Pre-pregnancy gene expression profiles in RA appear to be predictive of the subsequent improvement or worsening of RA during pregnancy, and they suggest that the $RA_{improved}$ and $RA_{worsened}$ groups may represent two distinct RA endotypes.

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Abstract Number: 2482

Preinflammatory Mesenchymal (PRIME) Cell Signature Genes Enrichment Predicts Treatment Response and Joint Prognosis in Rheumatoid Arthritis

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SESSION INFORMATION

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Session Type: Abstract Session

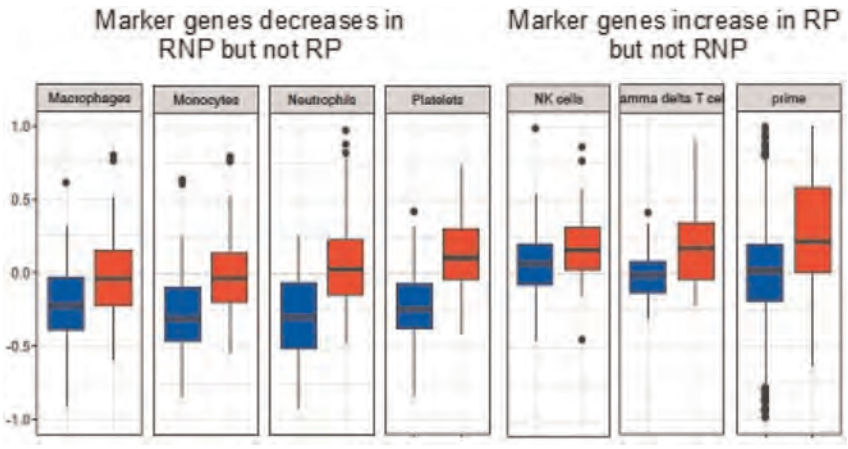
Session Time: 2:00PM–3:30PM

Background/Purpose: This study aimed to determine predictors of treatment response and radiographic progression following the initiation of biological disease-modifying antirheumatic medications (bDMARDs) in patients with rheumatoid arthritis (RA).

Methods: RNAseq was performed on peripheral blood mononuclear cells (PBMCs) taken before and 3 months after bDMARD initiation. Treatment response was defined as good EULAR response (change in DAS28 >1.2 if the DAS28 was >3.2) and radiographic progression was defined as increase in modified total sharp score (mTSS) of more than 0.5, 3.4, or 5.

Results: A total of 41 patients with RA were evaluated (meanage: 63.1 years; 75.6% are females). Radiographic progression was observed 60% of patients and was significantly less common in patients with a good EULAR response. Innate immune pathways, were significantly enriched at baseline in patients without radiographic progression, while genes atypical of immune cells, such as genes related to GO_mesoderm_developement, were upregulated in radiographic progressors, using various thresholds of mTSS change, suggesting enrichment of mesenchymal signature genes. In longitudinal analysis, Preinflammatory mesenchymal (PRIME) cell signature genes showed signifcant enrichment in radiographic progressors and poor treatment responders. In patients with no radiographic progression, innate immune cell, such as neutrophil, monocyte, and platelet, marker genes decreased significantly at 3 months compared to baseline, while they remained unchanged in patients with radiographic progression. On the other hand, in patients with radiographic progression, PRIME cell genes as well as NK and gdT cell genes increased significantly at 3 months compared to baseline, while they remained unchanged in those without radiographic progression (Figure 1).

Conclusion: PBMC innate immune gene signature are increased at baseline and decrease with treatment in patients no radiographic progression. On the other hand, PRIME cell genes are increased at baseline and increase further with treatment in patients with radiographic progression.



Gene expression changes after 3 months of treatment compared to baseline in radiographic nonprogressors (RNP; blue) and radiographic progressors (RP; red).

Disclosure: T. Fujii: AbbVie/Abbott, 6, Asahi Kasei Pharma, 6, Chugai Pharma, 6, Janssen, 6, Tanabe Mitsubishi Pharma, 6; **D. Orange**: Rockefeller University, 10; **C. Hale**: None; **K. Murata**: None; **H. Onizawa**: None; **A. Onishi**: None; **M. Tanaka**: AbbVie GK, 6, Asahi Kasei Pharma Corp., 5, Astellas Pharma Inc., 6, Ayumi Pharmaceutical Corp., 5, Chugai Pharmaceutical Co., Ltd., 6, Eisai Co., Ltd., 6, Eli Lilly Japan K.K., 6, Kyowa Kirin Co., Ltd., 5, Pfizer Inc., 6, Taisho Pharmaceutical Co., Ltd., 5, Tanabe Mitsubishi Pharma Corp., 6, Teijin Pharma, Ltd., 6, UCB Japan Co., Ltd., 6; **A. Morinobu**: None; **S. Matsuda**: None.

Abstract Number: 2483

CD68 and Fibrinoid Necrosis Are Synovial Biomarkers of Severity in Early Rheumatoid Arthritis and Are Associated with a Better Response to Methotrexate: Analysis of the UCLouvain Brussels ERA Cohort

Francesco Natalucci[1], clement triaille[2], Emilie Sapart[2], Cécile VAN MULLEM[2], Tatiana Sokolova[3], Laurent MERIC de BELLEFON[2], Adrien NZEUSSEU TOUKAP[2], Christine GALANT[4], Bernard Lauwerys[5] and Patrick Durez[2], [1]UCLouvain University, Sermoneta, Italy, [2]Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCLouvain) – Institut de Recherche Expérimentale et Clinique (IREC), Rheumatology, Brussels, Belgium, [3]Université Catholique de Louvain, Brussels, Belgium, [4]Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCLouvain), Anatomie pathologique, Brussels, Belgium, [5]UCB Pharma, Brussels, Belgium

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes III: Predicting & Optimizing Outcomes

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Rheumatoid Arthritis (RA) is a chronic autoimmune disease with persistent synovial inflammation. Despite early diagnosis and the treatment-to-target strategy in ERA, the treatment response rate is not optimal. Analyzing synovial tissue in ERA may help to find useful biomarkers to optimize the remission rate. Therefore, this study aimed to analyze the histology features together with the presence and distribution of cells by immunohistochemistry (IHC) of ERA synovial biopsies, to better characterize the disease and identify the presence of predictive factors of treatment response.

Methods: According to ACR/EULAR 2010, ERA patients were enrolled as part of the UCLouvain Arthritis Cohort at Cliniques Universitaires Saint Luc, Brussels. All patients were naïve to steroids and DMARDs therapy. Patients underwent ultrasound (US)-guided or mini-arthroscopy synovial biopsy. After the biopsy, patients started DMARD therapy and were evaluated every 3-4 months. Synovial samples were analyzed for histology (Synovial Hyperplasia, Fibrinoid Necrosis, Hypervascularization, Inflammatory Infiltrate), pathotypes (lymphoid, myeloid, or pauci-immune), and IHC (CD3, CD20, CD138, and CD68) with a semiquantitative score from 0 to 3 for each feature.

Results: 140 patients were included. Clinical and demographic features are reported in Table 1. CD68 and Fibrinoid Necrosis score were strongly associated [r= 0,44 (0,27-0,56); p< 0,0001]. CD68 score showed a good correlation with CRP [r=0.31 (0.13-0.46); p=0.0013], DAS28 [r=0,26 (0,07-0,43); p=0,005], SDAI [r=0,28 (0,07-0,47); p=0,008] and CDAI

Table 1. Clinical and Demographic characteristics of the cohort

Median, (IQR) / (%)	Whole Cohort N=140	CD68Necrosis^{HIGH}	CD68Necrosis^{LOW}	p
Age	52.7 (21.4)	56.4 (25.6)	48.32 (22.1)	0.08
Time to Biopsy	6 (9)	4 (9)	6 (10.75)	0.33
BMI	20.3 (6.8)	21.35 (7.9)	23.15 (4.9)	0.30
TJC (28)	6 (8.5)	6 (8)	5 (8.5)	0.69
SJC (28)	6 (8)	8 (7)	5 (8.5)	0.16
TJC (44)	7 (10)	8.5 (10.25)	6 (9.5)	0.31
SJC (44)	7 (10)	8 (9.25)	6 (9.75)	0.33
CRP (mg/dL)	1.59 (3.3)	2.5 (4)	0.92 (2.96)	0.02
HAQ	1.5 (1.125)	1.75 (1.06)	1.5 (1.22)	0.19
DAS 28	5.19 (1.73)	5.48 (1.6)	4.8 (1.7)	0.03
SDAI	28.8 (20.1)	33.10 (17.4)	25.65 (21.4)	0.03
CDAI	26 (19.25)	29.25 (14.35)	23.85 (17.9)	0.25
VASm	4 (2)	5 (3)	3.3 (8.87)	0.03
VASp	7 (3.1)	7.3 (2.65)	7 (3.4)	0.53
Female (%)	75%	77.5%	75%	0.99
RF (%)	51.1%	60.3%	47.8%	0.16
anti-CCP (%)	52.6%	58.4%	49.2%	0.31

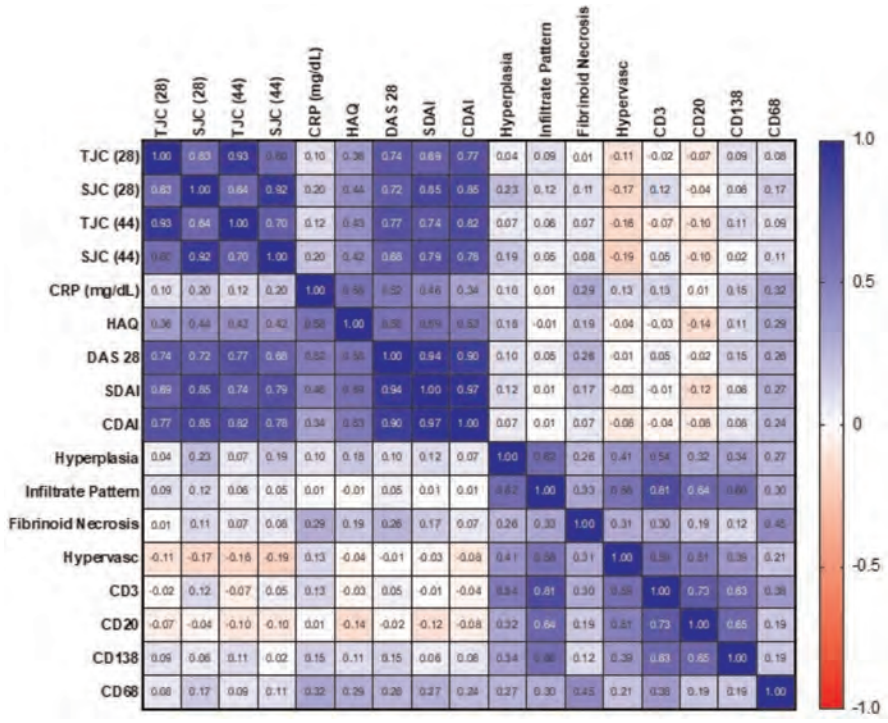


Figure 1. Correlation Matrix Each cell represents the r Spearman correlation value between clinical features and histology/IHC semiquantitative scores.

[r=0,25 (0,03-0,44); p=0,018]. The Fibrinoid Necrosis score showed a good correlation with CRP [r=0,29 (0,11-0,45); p=0,001] and DAS28 [r=0,26 (0,06-0,43); p=0,009].Based on the sum of the CD68 and Necrosis semiquantitative score [0-6], patients were then categorized as CD68Necrosis^{HIGH} (≥3) and CD68Necrosis^{LOW} (< 3). CD68Necrosis^{HIGH} patients had higher CRP values [2.5 mg/dL (4) *versus* 0.92 mg/dL (2.96); p=0.02], DAS28 [5.48 (1.6) *versus* 4.8 (1.7); p=0.03] and SDAI [33.10 (17.4) *versus* 25.65 (21.4); p=0.03). At three months of observation, CD68Necrosis^{HIGH} patients, compared to CD68Necrosis^{LOW} showed a greater fall of DAS28 [1.99 (2.06) *versus* 1.1 (2.27), p=0.03], SDAI [21.45 (IQR 23.3) *versus* 11.65 (IQR 17.5); p=0.003] and CDAI [16 [14.9] *versus* 10.5 (20.1), p=0.04].Moreover, CD68Necrosis^{HIGH} patients had a higher EULAR Moderate/Good Response rate compared to CD68Necrosis^{LOW} (90% versus 71.43%; p=0.036). CD68Necrosis score was then included in a predictive matrix model together with baseline disease features (SJC44 and DAS28) with

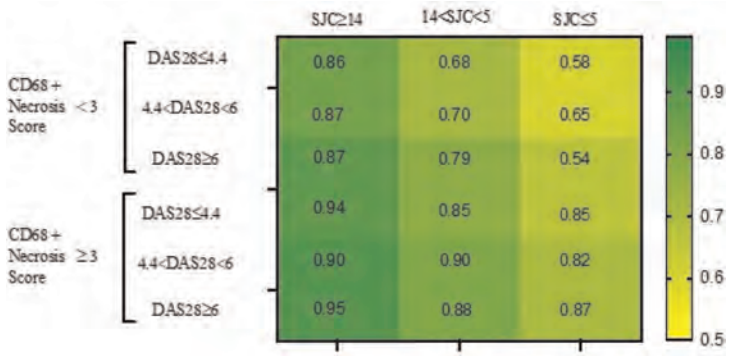


Figure 2. Three Months EULAR Moderate/Good Response Probability Prediction Matrix: The values reported expressing the 3 months predictive probability of reaching a Moderate/Good EULAR Response [0-1 = 0% - 100%] for each combination of included categorized variables. For example, a patient with CD68 + Necrosis Score <3, SJC ≥ 14, and DAS28 ≥ 6 has a 3-month predicted probability of reaching at least a Moderate EULAR Response of 87%.

a Moderate/Good EULAR Response Criteria at 3 months as the outcome (AUC 0.724, 95%CI [0.58-0.86]; p=0.0028, Figure 2). Classification into pathotypes did not identify patients with better responses to treatment or requiring therapy with bDMARDs/tsDMARDs.

Conclusion: The evaluation of Macrophages and Fibrinoid Necrosis in ERA synovial biopsies identifies patients with higher disease activity and with a better DAS28 fall at three months. The semiquantitative score can predict the achievement of EULAR Response Criteria, alone or with clinical baseline features.

Disclosure: F. Natalucci: None; **c. triaille**: None; **E. Sapart**: None; **C. VAN MULLEM**: None; **T. Sokolova**: None; **L. MERIC de BELLEFON**: None; **A. NZEUSSEU TOUKAP**: None; **C. GALANT**: None; **B. Lauwerys**: UCB Pharma, 3, 11; **P. Durez**: None.

Abstract Number: 2484

Optimizing the Care of the Rheumatic Patient with Rheumatologist-Pharmacist Co-management

Ruchi Patel[1], Kristen Salava[1], Eric Newman[2], Joseph Chronowski[1], Dante Grassi[1], Hillary Harris[3], Amanda Young[1], Idorenyin Udoeyo[2], Lisa Schroeder[2], David Bulbin[4], David Pugliese[5] and Jonida Cote[6], [1]Geisinger Medical Center, Danville, PA, [2]Geisinger, Danville, PA, [3]Geisinger, Wilkes Barre, PA, [4]Geisinger Health System, Danville, PA, [5]Geisinger Health System, Wilkes-Barre, PA, [6]Geisinger Medical Center, Orefield, PA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes III: Predicting & Optimizing Outcomes
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: More effective teamwork can improve patient care. We studied the effect of a Rheumatologist-Pharmacist Co-management program on the quality of care of rheumatology patients starting DMARDs.

Methods: The Rheumatologist-Pharmacist Co-management team used ACR guideline-driven protocols to manage rheumatic patients starting methotrexate (MTX).Interventions included Rheumatologist-Pharmacist visits, laboratory monitoring, medication tolerability assessment, treat-to-target (T2T) dose titration and disease monitoring. Electronic health record (EHR) data was compared for 3 groups -Rheumatologists at baseline, Rheumatologists at intervention and Co-management at intervention. Patient demographics, adherence with monthly visits and laboratories for the first 3 months after MTX initiation, MTX dose escalation, cumulative prednisone use within 6 months and biologic initiation within 12 months of MTX initiation were analyzed using appropriate statistical measures. Disease activity among the 3 groups was compared by descriptive analysis.

Results: Demographic evaluation showed that the Co-management group was more likely to be RF+ (80.6% vs 63.2% vs 72.4%) and had higher disease activity by CDAI (93.8% vs. 71.1% vs 75.6%) compared to the baseline and intervention period rheumatologist groups (Table 1). For the first 3 months post MTX intervention, the Co-management group was more adherent to all visits and all laboratories versus the baseline rheumatologist group (15% vs 2.2%, p=0.002; 70% vs 31.5%, p< 0.001) and the intervention rheumatologist group (15% vs 1.2%, p=0.001; 70% vs 24.8%, p< 0.001) (Table 2).When compared to the baseline and the intervention period rheumatologist groups, the Co-management group had a higher number of patients who escalated MTX dose to target (77.8% vs 36.6%, p< 0.001; 77.8% vs 34%, p< 0.001) and maximized MTX dose by 6 months (median 20mg vs 15 mg, p=0.01; 20 mg vs 15 mg, p=0.02).Additionally, the Co-management group had lower cumulative prednisone exposure (mean 144.6mg vs 493mg, p< 0.0001; 144.6mg vs 268.5mg, p< 0.58) and fewer patients

Table 1. Patient Demographics and Health History

Patient Characteristics	Total N=472	Rheumatologists alone – Baseline 1/2018 -12/2020 Group 1 (N=267)	Rheumatologists alone - Intervention 1/2021 -9/2022 Group 2 (N=165)	Co-management 1/2021 - 9/2022 Group 3 (N=40)	P-value Group 1 vs 3	P-value Group 2 vs 3
Age, mean (SD)	58.1 (13.7)	58.0 (13.7)	57.7 (14.2)	60.3 (11.6)	0.31[a]	0.29[a]
Gender, n (%)					0.03[b]	0.10[b]
Male	134 (28.4%)	69 (25.8%)	48 (29.1%)	17 (42.5%)		
Female	338 (71.6%)	198 (74.2%)	117 (70.9%)	23 (57.5%)		
Rheumatoid Factor, n (%)					0.06[b]	0.35[b]
Negative: <14	125 (32.2%)	82 (36.8%)	37 (27.6%)	6 (19.4%)		
Positive: ≥14	263 (67.8%)	141 (63.2%)	97 (72.4%)	25 (80.6%)		
CCP Antibody, n (%)					0.80[b]	0.66[b]
Positive: ≥20	225 (60.2%)	129 (60.6%)	74 (58.7%)	22 (62.9%)		
Negative: <20	149 (39.8%)	84 (39.4%)	52 (41.3%)	13 (37.1%)		
CRP at baseline, n (%)					0.22[c]	0.24[c]
Negative: ≤5	49 (34.0%)	18 (31.6%)	24 (32.9%)	7 (50.0%)		
Positive: >5	95 (66.0%)	39 (68.4%)	49 (67.1%)	7 (50.0%)		
ESR at baseline, n (%)					0.24[b]	0.40[b]
Negative: <20	71 (46.7%)	27 (42.9%)	34 (47.2%)	10 (58.8%)		
Positive: ≥20	81 (53.3%)	36 (57.1%)	38 (52.8%)	7 (41.2%)		
Baseline CDAI, n (%)					0.06[c]	0.16[c]
≤10 (low disease activity)	36 (25.0%)	24 (28.9%)	11 (24.4%)	1 (6.3%)		
>10 (moderate/high disease activity)	108 (75.0%)	59 (71.1%)	34 (75.6%)	15 (93.8%)		
Primary Insurance, n (%)					0.29[b]	0.69[b]
Commercial	233 (49.4%)	123 (46.1%)	88 (53.3%)	22 (55.0%)		
Medicare/Medicare Advantage Plans	174 (36.9%)	108 (40.4%)	55 (33.3%)	11 (27.5%)		
Medicaid Plans	65 (13.8%)	36 (13.5%)	22 (13.3%)	7 (17.5%)		

(a) Independent two-sample t-test (b) Chi-square test (c) Fisher's Exact test

Table 2. Comparison of Adherence to Touch Point and Lab Visits between Groups.

Patient Management	Rheumatologists alone – Baseline 1/2018 -12/2020 Group 1 (N=267)	Rheumatologists alone - Intervention 1/2021 -9/2022 Group 2 (N=165)	Co-management 1/2021 -9/2022 Group 3 (N=40)	P-value Group 1 vs 3	P-value Group 2 vs 3
Patients with all 3 visits, n (%)					
No	261 (97.8%)	163 (98.8%)	34 (85.0%)	0.002[c]	0.001[c]
Yes	6 (2.2%)	2 (1.2%)	6 (15.0%)		
Patients with all 3 monthly CBC visits, n (%)					
No	177 (66.3%)	113 (68.5%)	12 (30.0%)	<0.0001[b]	<0.0001[b]
Yes	90 (33.7%)	52 (31.5%)	28 (70.0%)		
Patients with all 3 monthly Cr[1] visits, n (%)					
No	170 (63.7%)	110 (66.7%)	11 (27.5%)	<0.0001[b]	<0.0001[b]
Yes	97 (36.3%)	55 (33.3%)	29 (72.5%)		
Patients with all 3 monthly LFT[2] visits, n (%)					
No	176 (65.9%)	120 (72.7%)	11 (27.5%)	<0.0001[b]	<0.0001[b]
Yes	91 (34.1%)	45 (27.3%)	29 (72.5%)		
All laboratories* n (%)					
No	183 (68.5%)	124 (75.2%)	12 (30.0%)	<.0001[b]	<.0001[b]
Yes	84 (31.5%)	41 (24.8%)	28 (70.0%)		

(a) Independent two-sample t-test (b)Chi-square test (c) Fisher's Exact test [1]Cr: Creatinine; [2]LFTs: Liver function tests *All laboratories: Collective month 1, month 2 and month 3 creatinine, liver function tests and CBC.

Table 3. Comparison of Clinical Characteristics between Groups.

Patient Management	Rheumatologists alone – Baseline 1/2018 -12/2020 Group 1(N=267)	Rheumatologists alone – Intervention 1/2021 -9/2022 Group 2 (N=165)	Co-management 1/2021 -9/2022 Group 3 (N=40)	P-value Group 1 vs 3	P-value Group 2 vs 3
Patients on Methotrexate at 6 months (%)					
No	95 (35.6%)	62 (37.6%)	13 (32.5%)	0.70[a]	0.55[b]
Yes	172 (64.4%)	103 (62.4%)	27 (67.5%)		
Methotrexate Dose Escalation from baseline, n (%)					
N (comparable MTX)	172	103	27		
No	109 (63.4%)	68 (66.0%)	6 (22.2%)	<0.0001[b]	<0.0001[b]
Yes	63 (36.6%)	35 (34.0%)	21 (77.8%)		
Methotrexate Dose at 6 months					
N	172	103	27		
Mean (SD)	17.2 (4.0)	17.4 (3.8)	19.6 (4.4)	0.01[d]	0.02[d]
Median (IQR)	15.0 (15.0,20.0)	15.0 (15.0, 20.0)	20.0 (15.0,25.0)		
Patients prescribed biologic within 12 months n (%)					
No	220 (82.4%)	156 (94.5%)	38 (95.0%)	0.04[b]	>0.99[c]
Yes	47 (17.6%)	9 (5.5%)	2 (5.0%)		
Total steroid usage 0 - 6 month (mg)					
Mean (SD)	493.0 (572.5)	268.5 (563.5)	144.6 (251.9)	<0.0001[d]	0.58[d]
Median (IQR)	304.0 (0, 845.0)	0 (0, 305.0)	0 (0, 276.5)		
***CDAI improved, n (%)**					
Yes	31 (64.6%)	19 (73.1%)	9 (90.0%)	(N/A)	(N/A)
No	17 (35.4%)	7 (26.9%)	1 (10.0%)		
***Post intervention low disease activity (CDAI ≤ 10), n (%)**					
≤10	28 (58.3%)	10 (38.5%)	7 (70.0%)	(N/A)	(N/A)
>10	20 (41.7%)	16 (61.5%)	3 (30.0%)		

(b) Chi-square test (c) Fisher's Exact test (d) Wilcoxon test (Mann-Whitney) *The values reflected are for patients who had a complete pre and post CDAI.

starting biologics by 12 months of MTX initiation (5% vs 17.6%, p=0.04) when compared to the baseline rheumatologist group. CDAI evaluation post intervention suggested a trend toward more patients with CDAI improvement (90% vs 64.6% vs 73.1%) and low disease activity (CDAI ≤ 10) (70% vs 58.3% vs 38.5%) achieved in the Co-management group vs rheumatologist managed groups respectively, however this analysis is underpowered due to the small Co-management population (Table 3).

Conclusion: Adherence to guideline-driven care is directly correlated with improved patient outcomes. In our study, despite having increased disease severity (higher RF+ and higher CDAI scores pre-intervention), the Co-management group had greater adherence with visits, laboratories and T2T disease management compared to the rheumatologist only groups. Additionally, they used less cumulative steroids within a 6-month period and had better control of their rheumatoid arthritis disease activity. Our Co-management care model shows improved care delivery when compared to usual care and is a model that can be easily replicated.

Disclosure: R. Patel: None; **K. Salava**: None; **E. Newman**: None; **J. Chronowski**: None; **D. Grassi**: None; **H. Harris**: None; **A. Young**: None; **I. Udoeyo**: None; **L. Schroeder**: None; **D. Bulbin**: AbbVie/Abbott, 2, 6, Alexion, 2, 6, Amgen, 2, 6, Novartis, 2, Sanofi Genzyme, 6; **D. Pugliese**: None; **J. Cote**: None.

Abstract Number: 2485

Comparative Risk of Serious Psychiatric Events with Belimumab versus Oral Immunosuppressant Use in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: SLE – Treatment II: Nonrenal
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: In randomized placebo-controlled trials, including the phase 4 Belimumab Assessment of Safety in SLE study, belimumab use was associated with a higher incidence of serious depression and suicidality than placebo. (Sheikh S et al, Lancet Rheumatol. 2020). However, the comparative risk of psychiatric outcomes between belimumab versus oral immunosuppressants is unknown.

Methods: We conducted a comparative cohort study of adult patients with SLE who initiated treatment with belimumab versus an oral immunosuppressant (azathioprine [AZA], methotrexate [MTX], or mycophenolate [MMF]) between 2011-2021 using observational data from TriNetX, a United States multi-center electronic health records database. We excluded patients with lupus nephritis prior to the index date of treatment initiation. The outcomes of interest were hospitalization for depression and attempted suicide. We designed and emulated a hypothetical target trial to estimate the cumulative incidence and hazard ratios (HRs) of these outcomes associated with belimumab initiation versus each of the oral immunosuppressants. In three parallel analyses, we used propensity score overlap weighting to balance covariates, including age, sex, race/ethnicity, geographic region, year of initiation, use of concomitant SLE medications (glucocorticoids, hydroxychloroquine, rituximab, cyclophosphamide, other immunosuppressants), Charlson comorbidity index, SLE severity index, chronic kidney disease, healthcare utilization, and prior diagnoses of mood disorders. In a secondary population excluding patients with prior mood disorders, we also assessed the outcome of new onset depression. Patients were followed until the earliest of the outcome, death, end of the study period (August 31, 2021), or two years after treatment initiation. In a per-protocol analysis, patients were additionally censored for discontinuation of the assigned treatment or initiation of the comparator, and we adjusted for adherence to assigned treatment using inverse probability of treatment weighting.

Results: Of 91,425 patients with SLE, we compared 2,434 and 5,644 initiators of belimumab and AZA, (**Table 1**), 2,163 and 7,224 initiators of belimumab and MTX, and 2,431 and 6,350 initiators of belimumab and MMF, respectively. After propensity score overlap weighting, covariates were balanced in each comparison. 95% were female; the mean age was 44 years. Attempted suicide was rare, with fewer than 10 events in each treatment group. There were no differences in the risk of hospitalized depression among belimumab initiators and initiators of AZA or MTX (**Table 2**). The risk of hospitalization for depression was lower for belimumab than MMF users (HR 0.70 [95% CI 0.52-0.95]). There was no difference in the risk of new onset depression among patients without a prior history of mood disorders (**Table 3**).

Conclusion: In this multi-center observational SLE cohort, we found that belimumab use was not associated with an increased risk of serious psychiatric events compared with oral immunosuppressants for SLE. This provides real-world reassurance of the safety of this medication for the treatment of SLE.

Table 1. Baseline Characteristics of Belimumab and Azathioprine Initiators with Non-Renal Systemic Lupus Erythematosus

	Before overlap weighting			After overlap weighting		
	Belimumab (n=2434)	AZA (n=5644)	Std. Diff.	Belimumab	AZA	Std. Diff.
Age, years, mean (SD)	44.2 (12.6)	44.7 (14.6)	0.0377	44.3	44.3	<0.001
Female, n (%)	2322 (95.4)	5218 (92.5)	0.1236	94.8	94.8	<0.001
Race/Ethnicity, n (%)			0.2828			<0.001
White	1438 (59.1)	2603 (46.1)		54.4	54.4	
Black	587 (24.1)	1869 (33.1)		27.0	27.1	
Asian	51 (2.1)	139 (2.5)		2.3	2.3	
Hispanic	169 (6.9)	593 (10.5)		8.2	8.2	
Other	189 (7.8)	440 (7.8)		8.0	8.0	
Geographic Region, n (%)			0.4104			<0.001
East	808 (33.2)	969 (17.2)		25.5	25.5	
Midwest	300 (12.3)	1011 (17.9)		14.7	14.7	
South	915 (37.6)	2827 (50.1)		42.4	42.4	
West	411 (16.9)	837 (14.8)		17.4	17.4	
Treatment initiation year, median	2018	2017	0.4990	2018	2018	<0.001
SLE duration year, mean (SD)	2.4 (3.0)	2.0 (3.3)	0.1305	2.3	2.3	<0.001
CKD stage ≥3, n (%)	228 (9.4)	468 (8.3)	0.0379	8.6	8.6	<0.001
Charlson Comorbidity Index, mean (SD)	1.0 (0.8)	1.0 (0.9)	0.0375	1.0	1.0	<0.001
SLE Severity Index, n (%)			0.0930			<0.001
Mild	1360 (55.9)	3123 (55.3)		56.0	56.0	
Moderate	802 (32.9)	1772 (31.4)		32.3	32.3	
Severe	272 (11.2)	749 (13.3)		11.7	11.7	
Medication Use, n (%)						
Glucocorticoids	1561 (64.1)	3189 (56.5)	0.1564	61.3	61.3	<0.001
Hydroxychloroquine	1503 (61.8)	2875 (50.9)	0.2193	57.2	57.2	<0.001
Methotrexate	584 (24.0)	628 (11.1)	0.3431	18.0	18.0	<0.001
Mycophenolate	419 (17.2)	477 (8.5)	0.2643	13.5	13.5	<0.001
Other oral immunosuppressant	258 (10.6)	310 (5.5)	0.1886	8.3	8.3	<0.001
Rituximab	51 (2.1)	86 (1.5)	0.0429	1.9	1.9	<0.001
Cyclophosphamide	16 (0.7)	49 (0.9)	0.0242	0.7	0.7	<0.001
Healthcare Utilization						
Outpatient visits, median (IQR)	5 (9)	4 (10)	0.0751	5.0	4.0	<0.001
ER/Inpatient visits, n (%)	602 (24.7)	1699 (30.1)	0.1206	27.1	27.1	<0.001
Prior mood disorder, n (%)	275 (11.3)	604 (10.7)	0.0191	11.7	11.7	<0.001

Covariates assessed within the six months prior to the index date. Non-renal lupus defined by meeting SLE definition (≥2 SLE ICD codes ≥2 months and ≤2 years apart) and not meeting lupus nephritis definition (defined by ≥1 LN code (ICD-10 M32.14) or ≥2 nephritis codes (e.g., ICD-9 580-586, 791.0 or ICD-10 N00, N04-5, N17-18, R80.9) prior to the index date. MTX, methotrexate. CKD, chronic kidney disease, defined by ≥1 ICD codes or GFR <60 on ≥2 occasions. ER, emergency room. SLE Severity Index is adapted from Garris algorithm for administrative data, based on ICD codes and not including medication dosing. Other oral immunosuppressant use includes leflunomide, sulfasalazine, cyclosporine, tacrolimus, abatacept, tocilizumab, TNF inhibitors, IL17 inhibitors, IL12/23 inhibitors, and JAK inhibitors

Table 2. Comparative Risk of Hospitalization for Depression with Belimumab versus Oral Immunosuppressant use

Treatment arms	Events (n)	Two-Year Cumulative Incidence (%)	Hazard Ratio (95% CI)
Per-protocol analysis			
Belimumab vs Azathioprine			
Azathioprine	236	5.5	1.00(ref)
Belimumab	74	4.7	0.85 (0.64-1.12)
Belimumab vs Methotrexate			
Methotrexate	241	4.4	1.00(ref)
Belimumab	70	4.3	0.97 (0.73-1.30)
Belimumab vs Mycophenolate			
Mycophenolate	269	5.2	1.00(ref)
Belimumab	61	3.7	0.70 (0.52-0.95)
Intention-to-treat analysis			
Belimumab vs Azathioprine			
Azathioprine	277	5.4	1.00 (ref)
Belimumab	92	5.2	0.96 (0.75-1.24)
Belimumab vs Methotrexate			
Methotrexate	300	5.0	1.00 (ref)
Belimumab	89	5.2	1.04 (0.81-1.34)
Belimumab vs Mycophenolate			
Mycophenolate	321	5.5	1.00 (ref)
Belimumab	80	4.5	0.82 (0.63-1.06)

Patients are followed until the earliest of the event, death, 2-years follow-up, or the end of the study period. The per-protocol analysis uses inverse probability of treatment weighting and censors at the time of deviation from assigned treatment strategy.

Table 3. Comparative Risk of Depression with Belimumab versus Oral Immunosuppressant use in Non-Renal Systemic Lupus Erythematosus without Prior Mood Disorder

	Hospitalization for Depression			Depression		
Treatment arms	**Events (n)**	**Two-Year Cumulative Incidence (%)**	**Adjusted Hazard Ratio (95% CI)**	**Events (n)**	**Two-Year Cumulative Incidence (%)**	**Adjusted Hazard Ratio (95% CI)**
Per-protocol analysis						
Belimumab vs Azathioprine						
Azathioprine	128	3.5	1.00(ref)	564	14.4	1.00(ref)
Belimumab	41	3.8	1.09 (0.75-1.59)	202	15.4	1.09 (0.91-1.30)
Belimumab vs Methotrexate						
Methotrexate	132	3.1	1.00(ref)	639	13.0	1.00(ref)
Belimumab	35	3.0	0.98 (0.65-1.47)	184	13.4	1.03 (0.86-1.24)
Belimumab vs Mycophenolate						
Mycophenolate	147	3.5	1.00(ref)	623	13.1	1.00(ref)
Belimumab	31	3.1	0.88 (0.58-1.35)	179	13.8	1.06 (0.88-1.27)
Intention-to-treat analysis						
Belimumab vs Azathioprine						
Azathioprine	155	3.3	1.00 (ref)	667	14.6	1.00 (ref)
Belimumab	48	3.5	1.07 (0.76-1.50)	230	15.5	1.07 (0.91-1.25)
Belimumab vs Methotrexate						
Methotrexate	162	3.2	1.00 (ref)	777	15.0	1.00 (ref)
Belimumab	46	3.4	1.06 (0.75-1.50)	215	15.0	1.00 (0.85-1.18)
Belimumab vs Mycophenolate						
Mycophenolate	181	3.4	1.00 (ref)	749	14.5	1.00 (ref)
Belimumab	41	3.1	0.92 (0.64-1.31)	212	14.9	1.03 (0.87-1.21)

Patients are followed until the earliest of the event, death, 2-years follow-up, or the end of the study period. The per-protocol analysis uses inverse probability of treatment weighting and censors at the time of deviation from assigned treatment strategy.

Disclosure: A. Jorge: None; **B. Zhou**: None; **Y. Zhang**: None; **H. Choi**: Ani, 2, Horizon, 2, 5, LG, 2, Protalix, 2, Shanton, 2.

Abstract Number: 2486

Should SLE Patients Entering Clinical Trials Be Required to Have at Least One BILAG a And/or Two BILAG B Scores?

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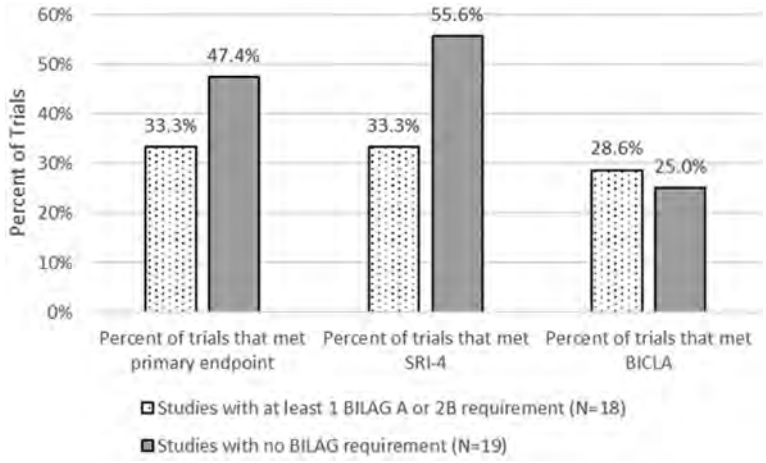
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: SLE – Treatment II: Nonrenal
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

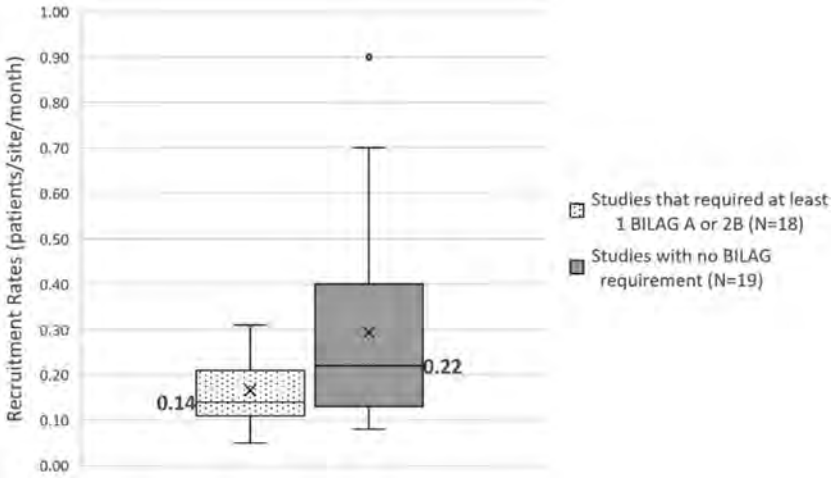
Background/Purpose: High placebo response rates have challenged interpretation of clinical trial results in SLE and may have contributed to failure of some effective treatments. One hypothesis to explain inflated placebo responses is that patients may not have sufficient disease activity at baseline. Most study designs require at entry a score of ≥6 on the SLE Disease Activity Index (SLEDAI). Some have attempted to enrich for more active disease by adding an additional inclusion criterion using BILAG: score of A (severe) in ≥1 organ system and/or B (moderate) in ≥2 organ systems (BILAG restricted studies). However, the impact of this requirement on enrollment and study outcomes, including placebo responses, has not previously been examined.

Methods: Data from all reported phase II & III SLE trials with ≥100 subjects enrolled, at least 24 weeks treatment duration, and SLE responder index (SRI) and/or BILAG-based combined lupus assessment (BICLA) results were analyzed. In studies that did not require BILAG 1A or 2B at entry (BILAG non-restricted studies), the proportion of patients who nevertheless had at least 1 BILAG A or 2B was examined. BILAG restricted trials were compared to non-restricted for meeting primary endpoints, SRI-4, BICLA, placebo responses, and recruitment rates.

Results: Of 40 trials that met the initial search criteria, 3 were excluded from the analysis for not allowing BILAG A at screening (2 trials) and for major changes in entry criteria during study (1 trial). Of the 37 remaining studies (21 phase II and 16 phase III), 18 were BILAG-restricted and 19 non-restricted. In non-restricted studies, the mean percent of patients with at least 1 BILAG A or 2B scores was 62.7%.



Impact of at least 1 BILAG A or 2B inclusion criterion on study results: comparison between trials with and without this requirement in meeting the primary endpoint, SRI-4 and BICLA (p=NS).



Impact of at least 1 BILAG A or 2B inclusion criterion on recruitment rates: comparison of recruitment rates between trials with and without this requirement (p = 0.047; Mann Whitney test)

Fifteen of 37 trials (41%) met the primary endpoint, including 6 of 18 (33%) restricted and 9 of 19 (47%) non-restricted studies (Figure 1). Of 36 studies with available SRI-4 data, this endpoint was met by 16 (44%) overall, 6 (33%) of 18 restricted and 10 (56%) of 18 non-restricted studies. Nineteen studies measured BICLA, which was met by 5 (26%) overall, including 4 (29%) of 14 restricted and 1 (25%) of 4 non-restricted.

Mean SRI-4 and BICLA placebo responses in all the studies were 43% and 36%: 44.3% and 36% in restricted studies, 41.7% and 35.9% in non-restricted studies.

Mean and median recruitment rates for all studies combined were 0.23 and 0.17 patients/site/month (p/s/m). BILAG restricted trials enrolled significantly slower than non-restricted with mean/median 0.17/0.14 p/s/m versus 0.29/0.22 p/s/m (p=0.047, Mann-Whitney test, Figure 2).

Conclusion: Phase II and III SLE studies that require at least 1 BILAG A or 2B at screening are not more likely to meet their primary endpoint. BILAG-restriction does not decrease placebo responses. Furthermore, this entry criterion decreases the eligible patient pool by almost 40% significantly slowing recruitment rates.

Disclosure: E. Olech: AbbVie/Abbott, 2, 6, IQVIA, 3, Pfizer, 6, UCB, 6; **J. Merrill**: AbbVie, 2, Alexion, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, Bristol Myers Squibb, 2, 5, EMD Serono, 2, Genentech, 2, Gilead, 2, GlaxoSmithKline, 2, 5, Lilly, 2, Merck, 2, Pfizer, 2, Provention, 2, Remegen, 2, Sanofi, 2, UCB Pharma, 2, Zenas, 2.

Abstract Number: 2487

Phase 2 Safety and Efficacy of Subcutaneous (s.c.) Dose Ianalumab (VAY736; Anti-BAFFR mAb) Administered Monthly over 28 Weeks in Patients with Systemic Lupus Erythematosus (SLE) of Moderate-to-Severe Activity

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Hiroshi Kaneko[24], Bernadette Rojkovich[25], Lingyun Sun[26], Eugeny Zotkin[27], Jean-Francois Viallard[28], Masao Katayama[29], Berta Paula Magallares-Lopez[30], Tirtha Sengupta[31], Carol Sips[32] and Stephen J Oliver[32], [1]Shanghai Institute of Rheumatology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University (SJTUSM), Shanghai, China, [2]Charité Research Organisation GmbH, Berlin, Germany, [3]SM Kirov Military Medical Academy, St. Petersburg, Russia, [4]Lupus Unit, Rheumatology Department, Vall d'Hebron Hospitals, Barcelona, Spain, [5]Yabludowicz Center for Autoimmune Disease, Sheba Medical Center, Tel Aviv University, Tel Aviv, Israel, [6]Rheumatic Disease Unit, Department of Internal Medicine, Phramongkutklao Hospital and College of Medicine, Bangkok, Thailand, [7]Department of Systemic Connective Tissue Diseases, National Institute of Geriatrics, Rheumatology and Rehabilitation, Warsaw, Poland, [8]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic, [9]Department of Dermatology, Japan Community Healthcare Organization Chukyo Hospital, Nagoya, Japan, [10]Chung Shan Medical University Hospital, Department of Rheumatology, Taichung, Taiwan, [11]Department of Internal Medicine, Poznan University of Medicine Sciences, Poznan, PL, Poznań, Poland, [12]China Medical University Hospital, Taichung, Taiwan, [13]Organizacion Medica de Investigacion, Buenos Aires, Argentina, [14]Department of Rheumatology and Systemic Connective Tissue Diseases, University Hospital No. 2, Bydgoszcz, Poland, [15]Division of Clinical Immunology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary, [16]LLC Family Clinic, Yekaterinburg, RU, Yekaterinburg, Russia, [17]Taichung Veterans General Hospital, Taichung, Taiwan, [18]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, [19]Department of Rheumatology and Clinical Immunology, University Medical Center Freiburg, University of Freiburg, Freiburg, Germany, [20]Monash University, Department of Medicine, Subfaculty of Clinical and Molecular Medicine, Melbourne, Australia, [21]Division of Rheumatology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [22]Chonnam National University Medical School & Hospital, Gwangju, South Korea, [23]Department of Rheumatology, Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, China, [24]Division of Rheumatic Disease, National Center for Global Health and Medicine, Tokyo, Japan, [25]Department of Rheumatology and Physiotherapy, Polyclinic of the Hospitaller Brothers of St. John of God, Semmelweis University, Budapest, Hungary, [26]Department of Rheumatology and Immunology, The Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China, [27]VA Nasonova Research Institute of Rheumatology, Moscow, Russia, [28]CHU de Bordeaux, Hôpital Haut-Lévêque, Pessac, France, [29]National Hospital Organization, Nagoya Medical Center, Nagoya, JP, Nagoya, Japan, [30]Department of Rheumatology, Hospital de la Santa Creu I Sant Pau, Barcelona, Spain, [31]Novartis Pharma India, Hyderabad, Hyderabad, India, [32]Novartis Pharma AG, Basel, Switzerland

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: SLE – Treatment II: Nonrenal

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Ianalumab is a novel defucosylated human IgG1 mAb targeting the receptor for *B* cell *A*ctivating *F*actor belonging to the TNF *F*amily (BAFF-R) providing potent B cell depletion by enhanced antibody-dependent cellular cytotoxicity along with BAFF:BAFF-R signaling blockade.We report safety and efficacy of ianalumab in patients with active SLE.

Methods: This multi-center randomized, parallel group, double-blind placebo-controlled umbrella trial (NCT03656562) enrolled patients (19 Dec 2018 to 31 Jan 2022) having ANA ≥1:80 and meeting ≥4 of 11 ACR 1997 SLE classification criteria, with SLEDAI-2K score ≥6 and BILAG-2004 ≥1 A or ≥2 B scores that included activity in either mucocutaneous and/or musculoskeletal domains. This report is limited to interim analysis results for the fully enrolled ianalumab treatment cohort (active n=34; placebo n=33) completing 28-week blinded treatment period (monthly s.c. injection ianalumab 300 mg or placebo), with measured outcomes at baseline and weeks (w) 4, 8, 12, 16, 24 & 28. Primary w28 outcome was proportion patients meeting composite endpoint requirements consisting of those achieving SLE-Responder Index (SRI)-4 who also tapered predniso(lo)ne to ≤5 mg/d or ≤ baseline dose, whichever was lower, by w16 and kept within that range to w28.Secondary/exploratory outcomes included safety/tolerability, incidence BILAG-2004 moderate or severe flares (≥1 A or ≥2 B), proportion patients achieving Lupus Low Disease Activity State (LLDAS), patient and physician global assessments, and laboratory markers of B cell-associated autoimmune activity.

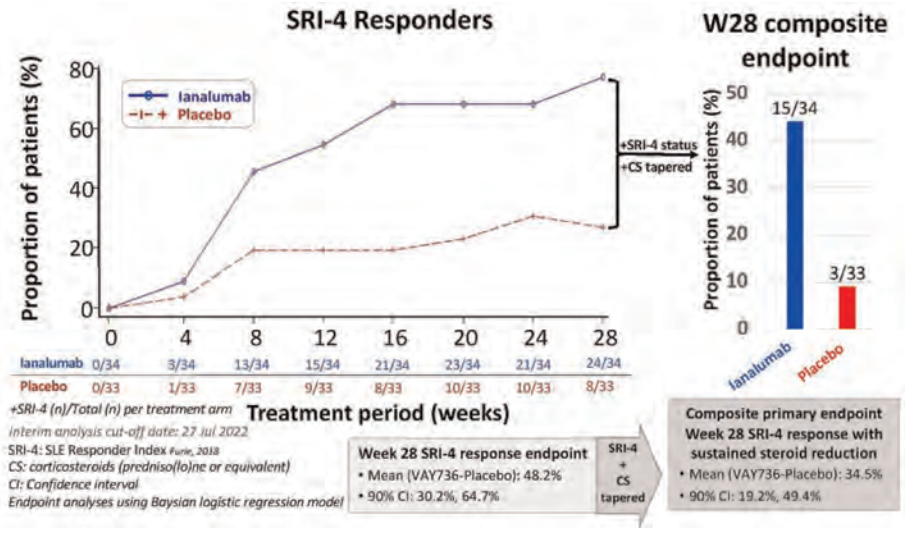

Figure 1. Primary endpoint: SRI-4 responders with sustained tapered corticosteroids

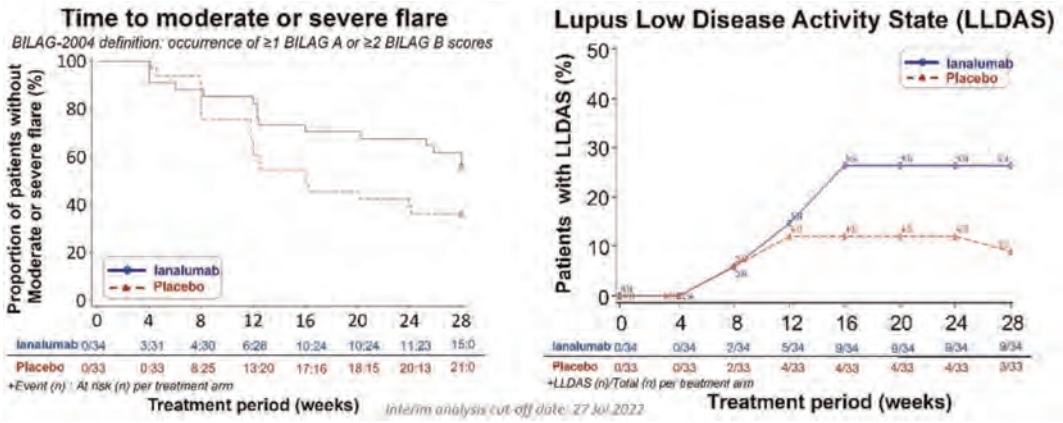

Figure 2. Ianalumab treatment effects on time to disease flare and achievement of LLDAS

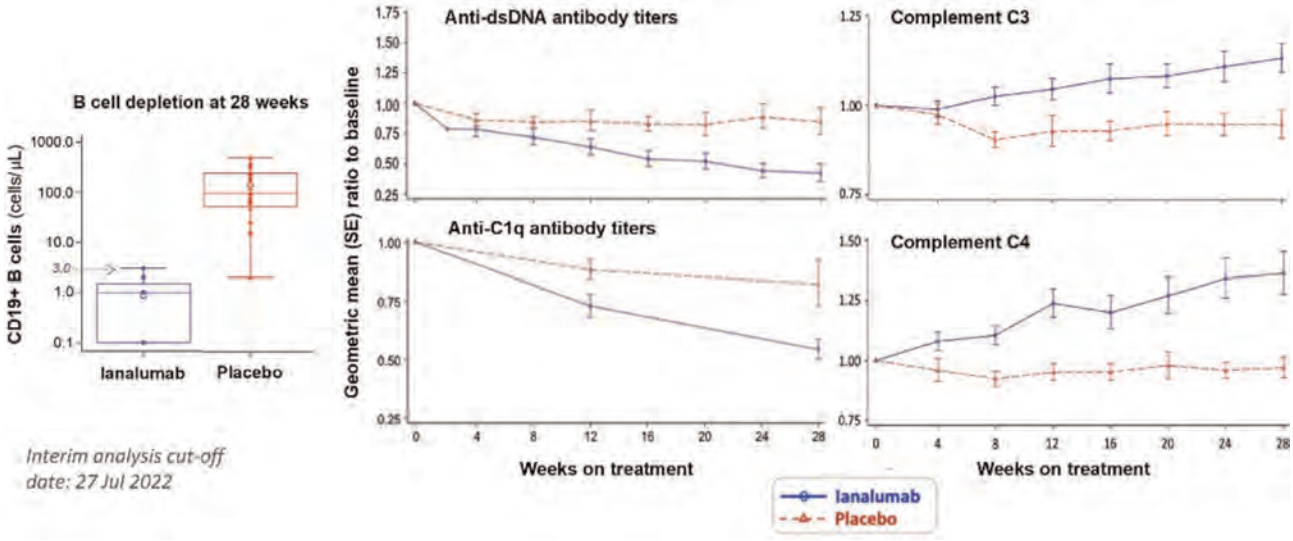

Figure 3. Ianalumab effects on laboratory markers of B cell autoimmune activity

Results: VAY736 was safe and well-tolerated with no drug-related SAE or dropouts, and one pandemic-related discontinuation in placebo arm. Baseline median(*range*) values for ianalumab and placebo arms, respectively, were: SLEDAI-2Kscore 10 (*6-32*) and10 (*4-18*), and predniso(lo)ne 10 mg (*0-30*) and 10 mg (*0-27.5*). Marked depletion of circulating CD19+ B cells was consistently achieved in all ianalumab-treated patients: w28 median 1 cell/uL; range *0-3* (Fig. 3). The mean w28 SRI-4 treatment effect of ianalumab (n=24) over placebo (n=8) was 48.2% (Fig. 1), and that also met the composite primary endpoint was 34.5% (ianalumab n=15; placebo n=3). Reduced incidence of moderate or severe flare was noted for patients treated with ianalumab 44% (n=15) vs placebo 64% (n=21). Benefits of ianalumab over placebo were observed for time-to-moderate or -severe flare and for achieving w28 LLDAS (Fig. 2). Therapeutic responses were also observed for ianalumab- vs placebo-treated subjects on laboratory markers of autoimmune activity (Fig. 3).

Conclusion: Potent B cell depletion was consistently achieved in ianalumab-treated SLE patients that was well tolerated, achieving the primary endpoint of SRI-4 response with sustained steroid reduction, along with substantial treatment benefits on overall SRI-4 response, LLDAS and reductions in moderate and severe flares, and on laboratory markers of autoimmune activity. These positive phase 2 study results support ongoing phase 3 development in lupus of the dual mechanisms of action of ianalumab (SIRIUS-SLE 1 & 2, and SIRIUS-LN).

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Abstract Number: 2488

Efficacy and Safety of ABBV-599 High Dose (Elsubrutinib 60 mg and Upadacitinib 30 mg) and Upadacitinib Monotherapy for the Treatment of Systemic Lupus Erythematosus: A Phase 2, Double-blind, Placebo-controlled Trial

Joan Merrill[1], Yoshiya Tanaka[2], David D'Cruz[3], Karina Vila-Rivera[4], Daniel Siri[5], Xiaofeng Zeng[6], Kristin D'Silva[7], Ling Cheng[7], Thierry Sornasse[7], Thao Doan[7], Denise Kruzikas[7] and Alan Friedman[7], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]University of Occupational and Environmental Health, Kitakyushu, Japan, [3]King's College London, London, United Kingdom, [4]GCM Medical, San Juan, PR, [5]CAICI SRL, Rosario, Argentina, [6]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China, [7]AbbVie, Inc., North Chicago, IL

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: SLE – Treatment II: Nonrenal
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: ABBV-599 is a novel combination of elsubrutinib (ELS; a selective BTK inhibitor) and upadacitinib (UPA; a JAK inhibitor) that targets non-overlapping signaling pathways associated with systemic lupus erythematosus (SLE). The objective of this analysis is to report results from SLEek, a phase 2, randomized, placebo (PBO)-controlled, parallel-group, multicenter study evaluating efficacy and safety of ABBV-599 and UPA monotherapy in adults with moderately to severely active SLE (NCT03978520).

Methods: Patients (pts) were randomized 1:1:1:1:1 to once daily (QD) ABBV-599 high dose (HD; ELS 60 mg + UPA 30 mg), ABBV-599 low dose (LD; ELS 60 mg + UPA 15 mg), ELS 60 mg, UPA 30 mg, or PBO. The primary endpoint was the proportion of patients at W24 achieving SLE Responder Index-4 (SRI-4) and steroid dose ≤ 10 mg QD; additional efficacy and safety endpoints through W48 are also reported. The pre-specified 2-sided alpha level was 0.1.

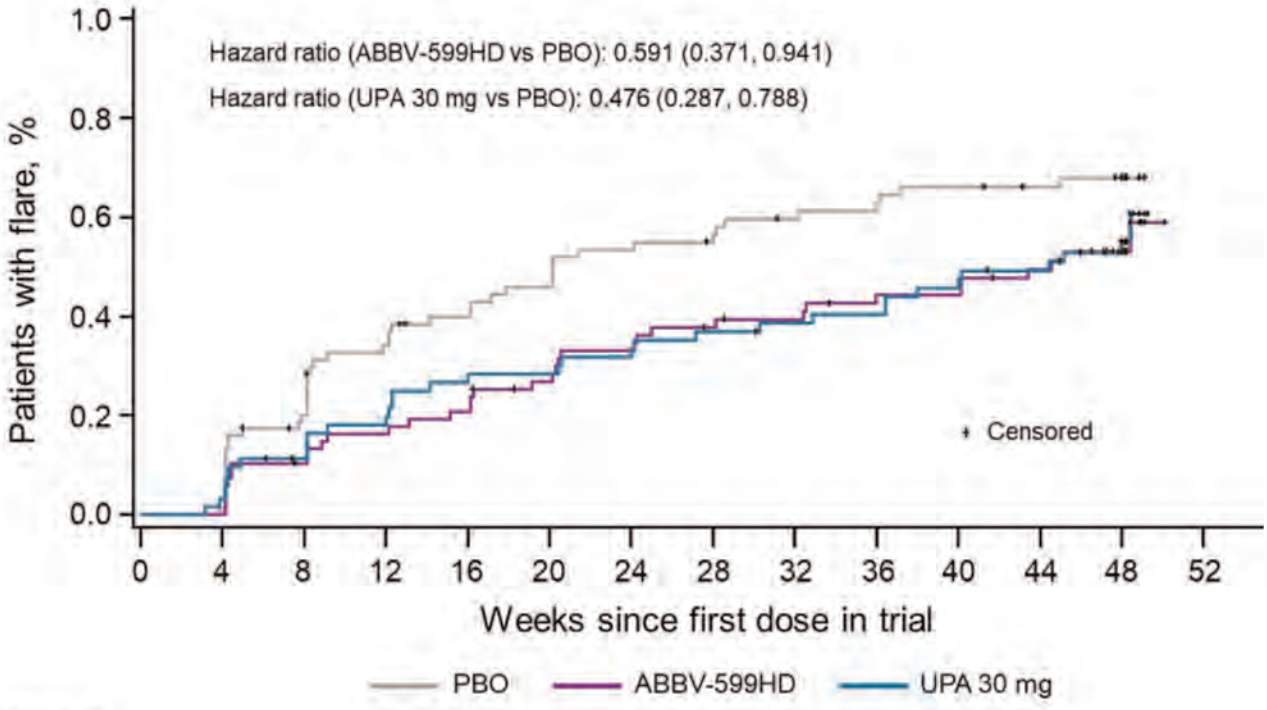
Results: 341 patients were enrolled. After a planned interim analysis when 50% of pts reached W24, the ABBV-599LD and ELS 60 mg arms were discontinued for lack of efficacy (no safety concerns). Of 205 continuing pts (ABBV-599HD n = 68, UPA 30 mg n = 62, PBO n = 75), baseline characteristics were well balanced. The primary endpoint (proportion achieving SRI-4 and steroid dose ≤ 10 mg QD at W24 vs PBO) was met by ABBV-599HD and UPA 30 mg. Key secondary endpoints were also achieved at W48 in both groups (**Table**). Overall flares and time to first flare were substantially reduced in the ABBV-599HD and UPA 30 mg groups through W48 (**Figure**). Anti-double stranded DNA antibodies were significantly decreased with both treatments. TEAEs considered related to study drug were 42.6% ABBV-599HD, 32.3% UPA 30 mg,

Table. Key Endpoints at Week 48

	PBO (n = 75)	ABBV-599HD (n = 68)	UPA 30 mg (n = 62)
SRI-4 and steroid dose ≤ 10 mg QD, n (%) [95% CI][a]	24 (32.0) [21.4, 42.6]	33 (48.5) [36.7, 60.4]*	27 (43.5) [31.2, 55.9]
SRI-4, n (%) [95% CI][a]	24 (32.0) [21.4, 42.6]	35 (51.5) [39.6, 63.3]*	28 (45.2) [32.8, 57.5]*
BICLA, n (%) [95% CI][a]	19 (25.3) [15.5, 35.2]	33 (48.5) [36.7, 60.4]***	33 (53.2) [40.8, 65.6]***
LLDAS, n (%) [95% CI][a]	18 (24.0) [14.3, 33.7]	27 (39.7) [28.1, 51.3]*	31 (50.0) [37.6, 62.4]***
Joint-Count 50 in patients with ≥ 6 affected joints at baseline, n/n (%) [95% CI][a]	26/59 (44.1) [31.4, 56.7]	37/58 (63.8) [51.4, 76.2]*	34/59 (57.6) [45.0, 70.2]*
CLASI-50 in patients with baseline CLASI ≥ 10, n/n (%) [95% CI][a]	5/14 (35.7) [10.6, 60.8]	6/12 (50.0) [21.7, 78.3]	5/8 (62.5) [29.0, 96.0]*
Change from baseline in steroid dose, mg, LS mean (SE)[b]	−1.5 (0.5)	−1.5 (0.5)	−1.2 (0.5)
SFI, events/patient-years (95% CI)[c]			
Overall flares	2.8 (2.4, 3.3)	1.5 (1.2, 1.9)***	2.0 (1.6, 2.4)**
Mild/moderate flares	2.5 (2.1, 2.9)	1.3 (1.0, 1.6)***	1.9 (1.5, 2.3)*
Severe flares	0.3 (0.2, 0.5)	0.2 (0.1, 0.3)	0.2 (0.1, 0.3)*
Time to first flare by SFI, days, median (Q1, Q3)[c]	141 (57, NE)	312 (114, NE)*	311 (99, NE)**
BILAG-based flare rate, estimated incidence rate[c]	0.57	0.19*	0.26

Data are presented for the full analysis set.
[a]Missing data imputed using NRI incorporating multiple imputation to handle missing data due to COVID 19.
[b]Missing data imputed using MMRM.
[c]Observed data w/o imputation.
*$P < .1$; **$P < .05$; ***$P < .01$, ***$P < .001$ vs PBO.
ABBV-599HD, elsubrutinib 60 mg QD and UPA 30 mg QD; CLASI-50, ≥ 50% reduction in CLASI activity score; Joint-Count 50, ≥ 50% improvement in tender or swollen lupus joints; LLDAS, Lupus Low Disease Activity State; NE, not estimated; PBO, placebo; SFI, SELENA SLEDAI Flare Index; UPA, upadacitinib.

Figure. Time to First Flare by SELENA SLEDAI Flare Index.



Patients, n														
PBO	75	74	58	46	40	36	31	29	25	24	21	19	17	0
ABBV-599HD	68	68	60	56	53	47	43	39	37	34	33	29	22	0
UPA 30 mg	62	60	52	48	43	42	40	37	35	34	31	28	22	0

Missing data imputed using AO.

ABBV-599HD, elsubrutinib 60 mg QD and UPA 30 mg QD; AO, as observed; PBO, placebo; SELENA, Safety of Estrogens in Lupus Erythematosus National Assessment; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; UPA, upadacitinib.

and 33.3% PBO. There were no malignancies or VTE. There were 3 non-fatal CV events (1 MI on PBO and 2 ruptured cerebral aneurysms [1 each on ABBV-599HD and UPA 30 mg]); all were assessed as unrelated to study drug by investigators. No new safety signals were observed beyond previously known data for UPA or ELS.

Conclusion: ABBV-599HD (ELS 60 mg + UPA 30 mg) and UPA 30 mg demonstrated significant improvements in SLE disease activity and flares with acceptable safety through 48 weeks.

Disclosure: J. Merrill: AbbVie, 2, Alexion, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, Bristol Myers Squibb, 2, 5, EMD Serono, 2, Genentech, 2, Gilead, 2, GlaxoSmithKline, 2, 5, Lilly, 2, Merck, 2, Pfizer, 2, Provention, 2, Remegen, 2, Sanofi, 2, UCB Pharma, 2, Zenas, 2; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer-Ingelheim, 6, Chugai, 5, 6, Eisai, 5, 6, Eli Lilly, 6, Gilead, 6, GSK, 6, Mitsubishi-Tanabe, 5, Pfizer, 6, Taiho, 6, Taisho, 5, 6; **D. D'Cruz**: Eli Lilly, 2, GlaxoSmithKlein(GSK), 2, UCB, 2; **K. Vila-Rivera**: AbbVie/Abbott, 2; **D. Siri**: AbbVie/Abbott, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 5, Gilead, 5, GlaxoSmithKlein(GSK), 5, Hoffman Laroche, 5, Janssen, 5, Sanofi, 5; **X. Zeng**: None; **K. D'Silva**: AbbVie/Abbott, 3, 11; **L. Cheng**: AbbVie/Abbott, 3, 11; **T. Sornasse**: AbbVie, 3, 11; **T. Doan**: AbbVie/Abbott, 3, 11; **D. Kruzikas**: AbbVie/Abbott, 3, 11; **A. Friedman**: AbbVie, 3, 11.

Abstract Number: 2489

Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) Achievement and Sustained Response with Deucravacitinib, an Oral, Selective, Allosteric Tyrosine Kinase 2 Inhibitor, in a Phase 2 Trial in SLE

Cristina Arriens[1], Ronald van Vollenhoven[2], Alice B. Gottlieb[3], Coburn Hobar[4], Samantha Pomponi[4], Ravi Koti[5], Thomas Wegman[6] and Victoria P. Werth[7], [1]Oklahoma Medical Research Foundation and University of Oklahoma Health Sciences Center, Department of Arthritis & Clinical Immunology, Oklahoma City, OK, [2]Amsterdam University Medical Centers, Amsterdam, Netherlands, [3]Icahn School of Medicine at Mount Sinai, New York, NY, [4]Bristol Myers Squibb, Princeton, NJ, [5]Syneos Health, Morrisville, NC, [6]Bristol Myers Squibb, Beaver Falls, PA, [7]University of Pennsylvania, Wynnewood, PA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

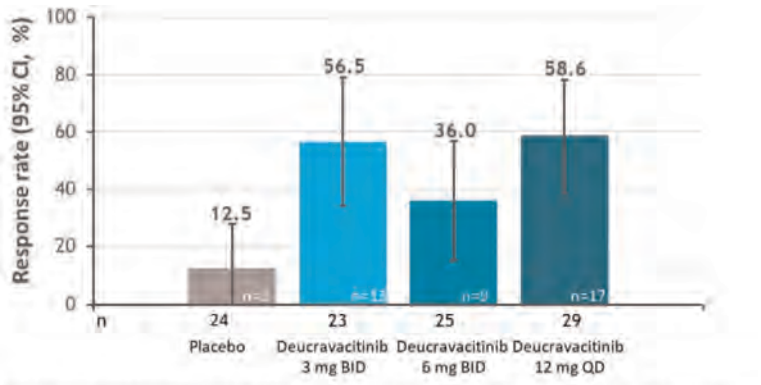
Session Title: Abstracts: SLE – Treatment II: Nonrenal

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

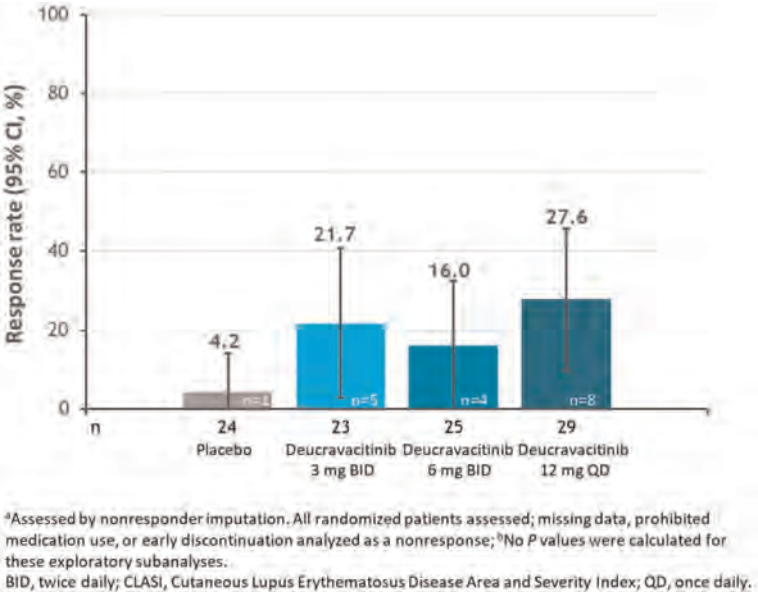
Background/Purpose: Deucravacitinib is a first-in-class, oral, selective, allosteric tyrosine kinase 2 inhibitor approved in multiple countries for the treatment of adults with plaque psoriasis. A 48-week, double-blind phase 2 trial (NCT03252587) in patients with SLE showed that deucravacitinib demonstrated greater efficacy compared with placebo across multiple endpoints, including the primary endpoint of Systemic Lupus Erythematosus Responder Index-4 (SRI[4]) at week 32 and the secondary endpoint of ≥50% reduction in CLASI activity (CLASI-50) for patients with moderate to severe skin involvement at baseline (CLASI score ≥10).[1] Here, we explored whether patients could sustain CLASI-50 over time and achieve 100% reduction in CLASI activity. CLASI-50 was also evaluated by SLE cutaneous manifestation subtype.

Methods: Patients with active SLE and a baseline CLASI score ≥10 who received placebo (n=24), deucravacitinib 3 mg twice daily (BID) (n=23), 6 mg BID (n=25), or 12 mg once daily (n=29) were included in these analyses. Exploratory outcomes were the proportion of patients that sustained CLASI-50 for the 5 consecutive visits from weeks 32 through 48, achieved 100% reduction in CLASI activity at week 48, and achieved CLASI-50 by SLE cutaneous manifestation subtype. For the subtype analysis, patients were classified as acute, subacute, chronic, or discoid at the discretion of investigators using SLICC classification criteria at screening without biopsy confirmation. Patients could be in ≥1 subcategory based on



[a]Assessed by nonresponder imputation. All randomized patients assessed; missing data, prohibited medication use, or early discontinuation analyzed as a nonresponse; [b]CLASI-50 is defined as a decrease of ≥50% from baseline in CLASI score at week 48 in patients with a CLASI score ≥10 at baseline; [c]No *P* values were calculated for these exploratory subanalyses; [d]A sustained response was defined as patients who were responders through 5 consecutive visits from weeks 32 through 48. Number of responders at each visit is the number of responders at that visit and at all previous visits from week 32.
BID, twice daily; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; QD, once daily.

Figure 1. Sustained CLASI-50 response among patients with CLASI ≥10 at baseline (a, b, c, d)

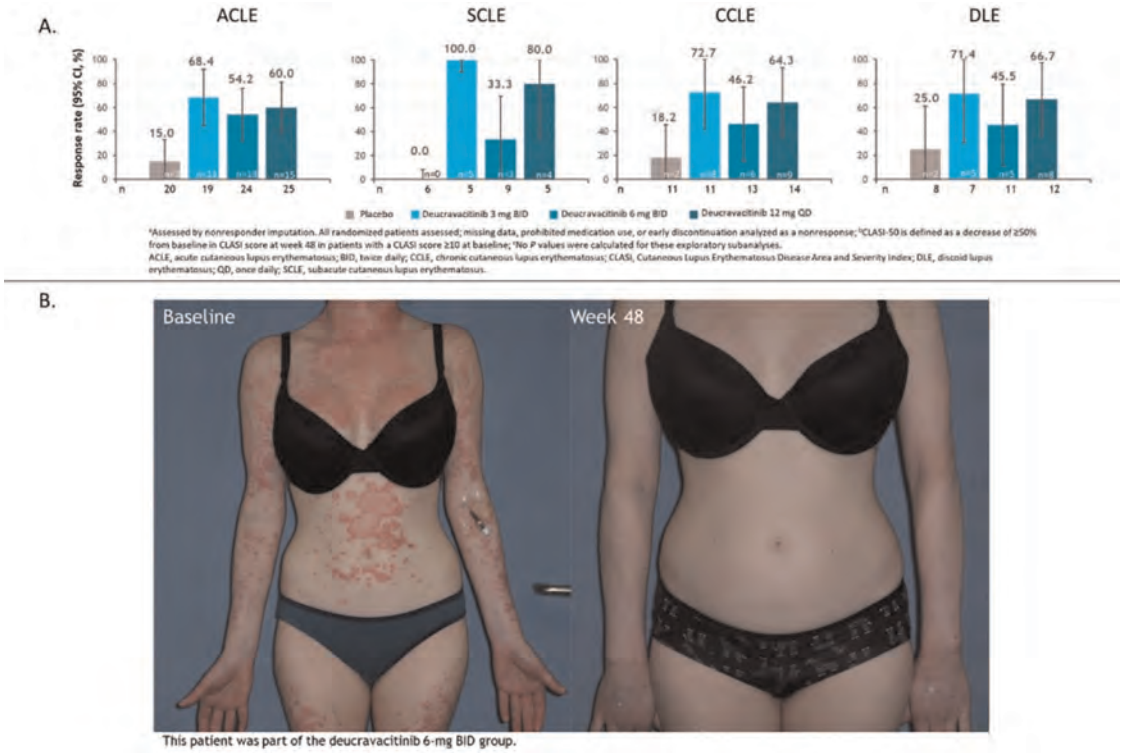


[a]Assessed by nonresponder imputation. All randomized patients assessed; missing data, prohibited medication use, or early discontinuation analyzed as a nonresponse; [b]No *P* values were calculated for these exploratory subanalyses.
BID, twice daily; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; QD, once daily.

Figure 2. Proportion of patients with CLASI ≥10 at baseline achieving a 100% reduction in CLASI at week 48 (a, b)

classification criteria; all patients classified as discoid were included in the chronic subgroup. All analyses were descriptive.

Results: Among patients with a baseline CLASI score ≥10, a numerically higher proportion of patients treated with deucravacitinib had a sustained response for the 5 consecutive visits between weeks 32 and 48 compared with placebo (**Figure 1**). Furthermore, a higher proportion of these patients treated with deucravacitinib achieved 100% reduction in CLASI activity at



[a]Assessed by nonresponder imputation. All randomized patients assessed; missing data, prohibited medication use, or early discontinuation analyzed as a nonresponse; [c]CLASI-50 is defined as a decrease of ≥50% from baseline in CLASI score at week 48 in patients with a CLASI score ≥10 at baseline; [b]No *P* values were calculated for these exploratory subanalyses.
ACLE, acute cutaneous lupus erythematosus; BID, twice daily; CCLE, chronic cutaneous lupus erythematosus; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; DLE, discoid lupus erythematosus; QD, once daily; SCLE, subacute cutaneous lupus erythematosus.

This patient was part of the deucravacitinib 6-mg BID group.

Figure 3. Proportion of patients with CLASI ≥10 at baseline achieving CLASI-50 at week 48 by cutaneous manifestation subtype (a, b, c) (A) and exemplary patient photographic data (B)

week 48 (**Figure 2**). Analysis by cutaneous manifestation suggested that a numerically higher proportion of patients treated with deucravacitinib achieved CLASI-50 at week 48 compared with placebo in all subtypes assessed (**Figure 3**).

Conclusion: Among patients with moderate to severe skin involvement at baseline, more patients treated with deucravacitinib were able to achieve improvements in skin overall, and a greater proportion of patients were able to sustain a CLASI-50 response from weeks 32 through 48 compared with placebo. CLASI-50 achievement was more frequent among patients treated with deucravacitinib regardless of cutaneous subtype.

Reference:

1. Morand E, et al. *Arthritis Rheumatol* 2023;75:242–252.

Disclosure: C. Arriens: AstraZeneca, 1, 5, 6, Aurinia, 6, Bristol-Myers Squibb, 1, 5, Cabaletta, 1, GSK, 1, Kezar, 1, UCB, 1; **R. van Vollenhoven**: AbbVie, 2, 6, AstraZeneca, 2, 5, 6, Biogen, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Galapagos, 2, 5, 6, GlaxoSmithKline, 6, Janssen, 2, 6, MSD/Merck Sharp and Dohme, 5, Novartis, 5, Pfizer, 2, 5, 6, RemeGen, 2, Roche, 5, Sanofi, 5, UCB, 2, 5, 6; **A. Gottlieb**: Amgen, 1, 2, AnaptysBio, 1, 2, 5, Avotres Therapeutics, 1, 2, Boehringer Ingelheim, 1, 2, Bristol Myers Squibb, 1, 2, 5, Dice Therapeutics, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, MoonLake Immunotherapeutics, 5, Novartis, 1, 2, 5, Sanofi, 1, 2, UCB Pharma, 1, 2, 5, XBiotech, 1, 2; **C. Hobar**: Bristol-Myers Squibb(BMS), 3; **S. Pomponi**: Bristol-Myers Squibb(BMS), 3; **R. Koti**: Bristol-Myers Squibb(BMS), 12, providing statistical services, Syneos Health, 3; **T. Wegman**: Bristol-Myers Squibb(BMS), 3, 12, Shareholder; **V. Werth**: AbbVie, 2, Amgen, 2, 5, Anaptysbio, 2, Argenx, 5, AstraZeneca, 2, Biogen, 2, 5, Bristol Myers Squibb, 2, Celgene, 2, 5, Corbus, 5, CSL Behring, 2, 5, EMD Serono, 2, Galderma, 2, Genentech, 5, Gilead, 2, 5, GlaxoSmithKline, 2, Horizon Therapeutics, 5, Idera, 2, Incyte, 2, Janssen, 2, Kyowa Kirin, 2, Lilly, 2, MedImmune, 2, Medscape, 2, Merck, 2, Nektar, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Principia, 2, Regeneron, 5, Resolve, 2, 2, Rome Therapeutics, 2, 5, Sanofi, 2, Ventus, 5, Viela, 2, 5, Xencor, 2.

Abstract Number: 2490

Safety and Efficacy of Mycophenolate Mofetil in New-onset Systemic Lupus Erythematosus with High Titer of Anti-dsDNA Antibody and Without Major Organ Involvement: A Multicenter Randomized Controlled Trial

Junna Ye[1], Yijun You[2], Zhuochao Zhou[2], Jingyi Wu[2], Fan wang[2] and Chengde Yang[2], [1]Ruijin Hospital affiliated to Shanghai Jiaotong University School of Medicine, Shanghai, China, [2]Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

SESSION INFORMATION

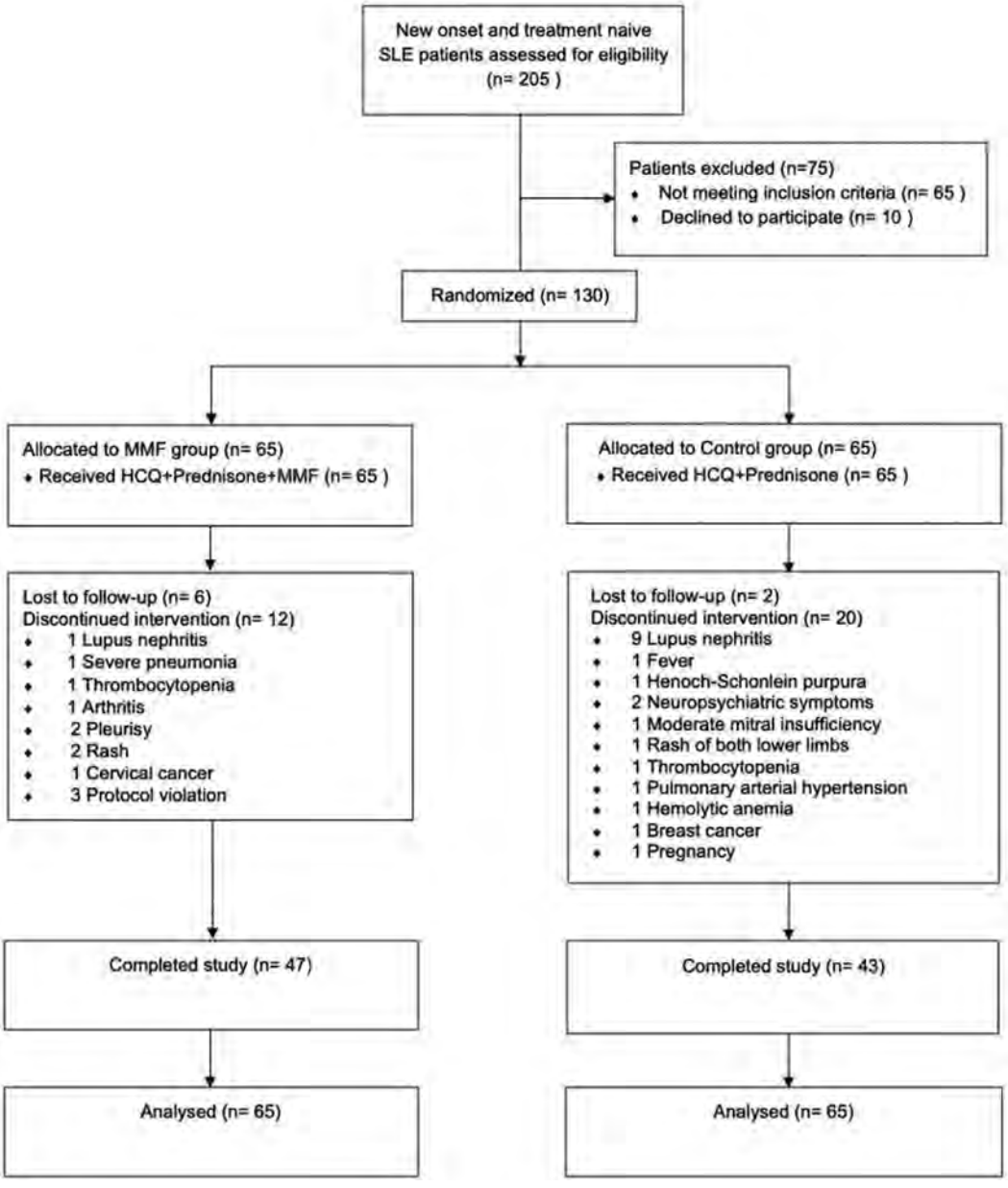
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: SLE – Treatment II: Nonrenal
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Previous clinical trials of mycophenolate mofetil (MMF) in SLE were mainly focused on lupus nephritis (LN) (patients have been diagnosed with LN). In the pathogenesis of LN as well as other organ damages, anti-dsDNA antibody plays an important role.

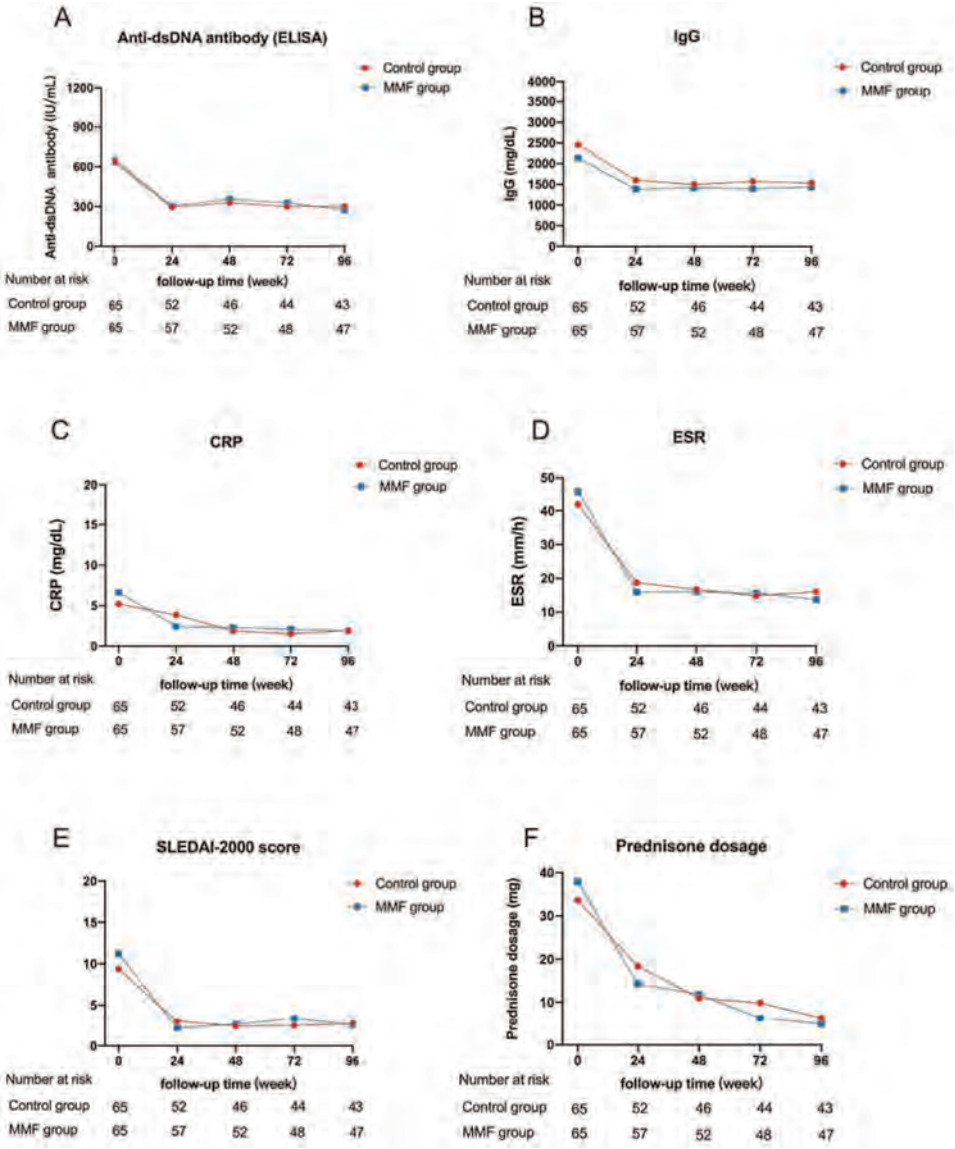
To assess the efficacy and safety of MMF plus hydroxychloroquine (HCQ) and prednisone compared with HCQ and prednisone alone in newly diagnosed and treatment-naïve SLE patients with high titer of anti-dsDNA antibody and without major organ involvement.

Methods: This investigator-initiated multicenter, open-label, randomized, controlled trial which enrolled 130 patients was conducted in three hospitals across China between September 2018 and September 2021. Inclusion criteria were newly diagnosed and treatment-naïve SLE patients with high titer of anti-dsDNA antibody (anti-dsDNA (ELISA) ≥ 300 IU/mL; (CLFT) ≥1:10) and without major organ involvement (brain, heart, liver, kidney, lung, muscle, and gastrointestinal tract).

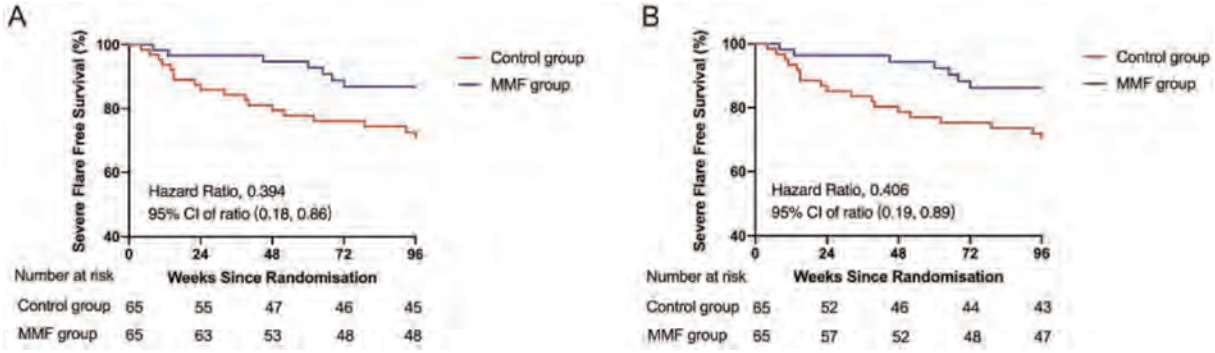
Participants were randomly assigned to received HCQ (5mg/kg/day) and prednisone (0.5mg/kg/day) (n=65) or HCQ (5mg/kg/day) and prednisone (0.5mg/kg/day) plus MMF 500mg twice daily (n=65).



Flowchart of this study.



Changes in clinical parameters in the control and MMF groups during the follow-up.



Severe flare-free survival was analyzed by Kaplan-Meier analysis with a log rank test in the ITT and PP populations.The intention-to-treat (ITT) population included all the eligible patients who had undergone randomization and received the treatment. The per protocol (PP) population included who were adherent to trial treatment excluded patients with major protocol violations.

The primary endpoint was the proportion of SLE patients having flares according to SELENA-SLEDAI Flare Index. The secondary outcome included the proportion of lupus low disease activity state (LLDAS) at week 96, short form-36 (SF-36) score before and after treatment, the proportion of adverse events, changes in SLEDAI-2000 score and prednisone dose.

Results: During the follow-up, 10.76% of patients in MMF group and 27.69% of patients in Control group showed severe flares (RR: 0.39, 95% CI: 0.17-0.87, p=0.014). 1.54% of patients in MMF group and 13.85% of patients in Control group manifested LN (RR: 0.11, 95% CI: 0.01-0.85, p=0.008). There was no significant differences in mild to moderate flares between the two groups (p=0.856). Besides, 33.85% of patients in MMF group and 16.92% of patients in Control group never had a relapse in the follow-ups (p=0.027). For the secondary outcomes, 41.54% patients in MMF group and 35.38% patients in Control group achieved LLDAS. SF-36 score of MMF group was better than Control group. Adverse events were reported in 49.23% patients in MMF group and 36.92% patients in Control group (p=0.157). Prednisone dosage was decreased gradually from baseline (mean [SD]: 33.66 [11.89] mg in Control group; 37.93 [13.56] mg in MMF group) to Week 96 (6.30 [6.82] in Control group; 4.88 [3.65] mg in MMF group) (prednisone dose change, p=0.087).

Conclusion: Low dose of MMF might decrease the rate of severe flare and lower the incidence of LN in new-onset SLE patients with high titer of anti-dsDNA antibody and without major organ involvement. Further research is needed to confirm efficacy of longer term outcomes in more diverse patient populations.

Disclosure: J. Ye: None; **Y. You**: None; **Z. Zhou**: None; **J. Wu**: None; **F. wang**: None; **C. Yang**: None.

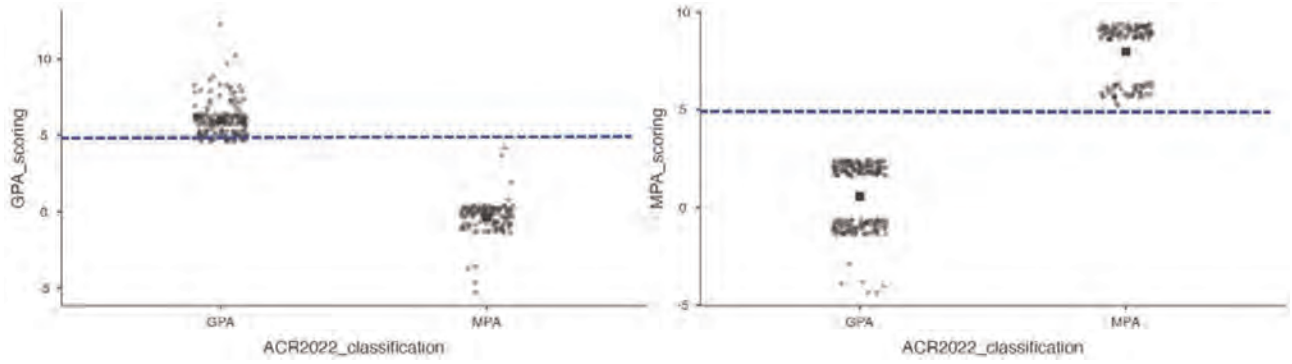
Abstract Number: 2491

Alignment Between the Novel 2022 ACR/EULAR Classification Criteria for ANCA-associated Vasculitis (AAV), Clinical Diagnosis and Organ Manifestations in a European AAV Cohort

Stefan Krämer[1], Thomas Rauen[1], Kristian Vogt[1], Teresa Anslinger[1], Martin Busch[2], Tobias Schmitt[3], Raoul Bergner[4], Sebastian Mosberger[4] and **Thomas Neumann**[5], [1]RWTH, University Hospital Aachen, Department of Nephrology and Rheumatology, Aachen, Germany, [2]University Hospital Jena, Friedrich-Schiller University, Department of Internal Mediciine III, Jena, Germany, [3]University Hospital Jena, Friedrich Schiller University, Department of Nephrology, Jena, Germany, [4]Municipal Hospital Ludwigshafen, Department of Internal Medicine A, Nephrology and Rheumatology, Ludwigshafen, Germany, [5]Cantonal Hospital St. Gallen, Department of Rheumatology, St. Gallen, Switzerland

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Vasculitis – ANCA-Associated II
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

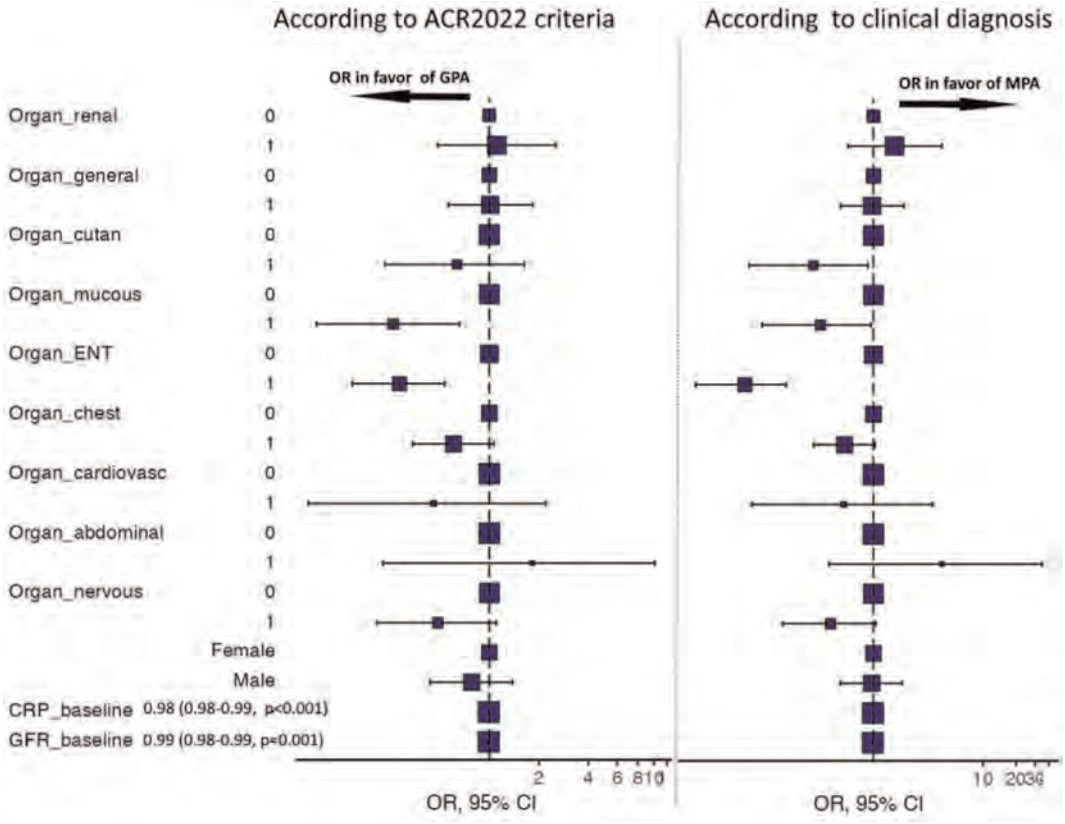
Background/Purpose: In 2022, ACR and EULAR proposed new classification criteria for granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) based on a numerical item scoring system for different manifestations in ANCA-associated vasculitis (AAV) emphasizing the role of laboratory findings. Recently, a low concordance rate of only 73% in comparison with former nomenclature and algorithm for classification was reported in a Korean cohort of 65 GPA patients [1]. We thought to (i) retrospectively re-classify patients from our multicentric AAV cohort using to the 2022 ACR/EULAR criteria for GPA and MPA using a computational algorithm that involved existing clinical, laboratory and histological data, (ii) to compare these results to prior clinical diagnoses and (iii) to investigate the predictive power of organ manifestations for both, classification and diagnosis.



Clustering of ACR/EULAR 2022 criteria scores for GPA (left) and GPA classified cases (right)

Methods: Data of AAV patients from four tertiary referral centers (Germany and Switzerland) were collected between 2000 and 2021. Cases without conclusive ANCA status were excluded from computed analysis. The 2022 ACR/EULAR criteria were applied by algorithmically analyzing BVAS entries for organ manifestation, laboratory results for ANCA/ELISA testing and histological data for detection of granuloma and/or pauci-immune glomerulonephritis. Results were compared to previously reported diagnoses and clinical manifestations were analyzed by their odds ratio (OR) to be either diagnosed or classified as GPA or MPA.

Results: The final dataset included a total of 305 cases, 294 (96.4%) of Caucasian ethnicity, 161 males (52.8%), median age 61 years (IQR 50-70). Based on the 2022 ACR/EULAR criteria, 299 (98%) cases could be unambiguously categorized. The overall concordance was found to be higher in GPA with 93.1% (vs. 88.2% in MPA) as previously reported [2]. Within all cases classified as MPA, the ACR/EULAR itemized score sums up to an average of 7.99 points (±1.42) in MPA cases



OR for either MPA or GPA classification (left) and previous clinical diagnosis (right)

1 Pyo JY, Ahn SS, Song JJ, *et al*. Reclassification of previously diagnosed GPA patients using the 2022 ACR/EULAR classification criteria. *Rheumatology (Oxford)* Published Online First: 4 May 2022. doi:10.1093/RHEUMATOLOGY/KEAC267

2 Krämer S, Rauen T, Pruin K, et al. POS1162 Evaluation of the 2022 ACR/EULAR classification criteria for GPA and MPA in a European ANCA-associated vasculitis (AAV) cohort. Ann Rheum Dis 2023; 82:913–913. doi:10.1136/ANNRHEUMDIS-2023-EULAR.3899

Literature

vs. -0.201 points (±1.36) for GPA cases (fig. 1). Classification as GPA sums up to an average score of 5.87 points (±1.21) vs. 0.548 points (±1.68). Overall, the distance of 9.41 points is higher in MPA cases, indicating a better selectivity as compared to GPA than vice versa with 5.32 points. ENT/mucous membrane involvement showed significant association with GPA for both classification and even more in clinical diagnosis (fig. 2). In addition to BVAS, baseline CRP (100 vs. 56 mg/L) and estimated GFR levels (57 vs. 36 ml/min/1.73 m²) were more elevated in GPA. GPA was more common among males than MPA.

Conclusion: The computational algorithm performed well to categorize 98% of all cases. Our findings demonstrated positive and negative concordance rates above 88% and suggest a higher specificity for GPA, but higher sensitivity for MPA classification criteria as well as better selectivity in MPA. Concerning clinical manifestations, ENT and mucous membrane involvement showed highest and significant association to GPA in our European cohort, reflecting their strong weighting in scoring.

Disclosure: S. Krämer: None; **T. Rauen**: None; **K. Vogt**: None; **T. Anslinger**: None; **M. Busch**: AstraZeneca, 6, Boehringer-Ingelheim, 2, 6, GlaxoSmithKline(GSK), 2, 6, Novartis, 6, Pfizer, 6, Vifor, 2, 6; **T. Schmitt**: None; **R. Bergner**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 6, Chugai, 6, Galapagos, 2, 6, GlaxoSmithKlein(GSK), 6, Merck/MSD, 6, Novartis, 6, Vifor, 2; **S. Mosberger**: None; **T. Neumann**: GlaxoSmithKlein(GSK), 1, 6, Janssen, 12, Travel support, Novartis, 6, Pfizer, 12, Travel support, Vifor Pharma Switzerland, 1, 5, 6.

Abstract Number: 2492

The Impact of Neurologic Involvement in ANCA-Associated Vasculitis on Self-Reported Health-Related Quality of Life

Rula Hajj-Ali[1], Chao Zhang[2], Renee Borchin[3], Jenn Gordon[4], David Cuthbertson[3], Carol McAlear[5], Christine Yeung[5], David Badenoch[6], Cristina Burroughs[3] and Peter Merkel[5], [1]Cleveland Clinic, Cleveland, OH, [2]Cleveland Clinic Foundation, Cleveland, OH, [3]University of South Florida, Tampa, FL, [4]Vasculitis Patient Powered Research Network (VPPRN), Philadelphia, PA, [5]University of Pennsylvania, Philadelphia, PA, [6]Vasculitis Patient Powered Research Network (VPPRN), Los Angeles, CA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Vasculitis – ANCA-Associated II
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Neurologic involvement (NI) is a common manifestation in patients with ANCA-associated vasculitis (AAV) and can lead to chronic pain and disability. This project assessed the impact of NI on health-related quality of life (HRQoL) in AAV.

Methods: Retrospective analysis of data provided from 2014-2022 by patients ≥18 years old with AAV [eosinophilic granulomatosis with polyangiitis (EGPA), granulomatosis with polyangiitis (GPA), or microscopic polyangiitis (MPA)] enrolled in the Vasculitis Patient-Powered Research Network (VPPRN), an online registry. The VPPRN collects data regarding type of

PROMIS measures in patients with ANCA-associated vasculitis with (light blue) and without (dark blue) neurologic involvement: Compared to patients without neurologic involvement, patients with neurologic involvement had higher scores for fatigue, depression, sleep disturbance, and pain interference, and lower scores for anxiety, social role, and physical function

vasculitis, disease manifestations, information on how and when the diagnosis of vasculitis was established, and measures of HRQoL, including from multiple Patient-Reported Outcome Measurement Information System (PROMIS) domains. PROMIS measures generate T-scores with the mean T-score = 50 with a standard deviation of 10 in the reference population (U.S. general population). Data were analyzed according to NI involvement.

Results: Data from 1465 patients with AAV with available information on NI were included in this analysis; 901 of 1465 (61.5%) patients reported NI. Table 1 summarizes the demographic and clinical characteristics of patients with or without NI. Compared to patients without NI, those with NI were older at the time of diagnosis of AAV, were more likely to be diagnosed with GPA (vs. EGPA or MPA), be positive for ANCA, and more likely to have constitutional, musculoskeletal, skin, mucous membranes, ear/nose/throat, cardiovascular, pulmonary, and thrombotic manifestations of disease. The rate of renal involvement was the same among patients with or without NI. Patients with NI reported greater severity of vasculitis. There was no significant difference in the medications ever received among patients with NI vs patients with no NI.

Overall, patients with AAV reported reduced HRQoL in almost all domains compared to a reference population. Compared to patients without NI, patients with NI report higher scores for fatigue, depression, sleep disturbance, and pain interference, and lower scores for anxiety, social role, and physical function (Figure2).

Conclusion: NI, as reported directly by patients, is common in AAV, occurring in approximately two-thirds of patients. This rate is higher than has been reported through clinician-documented data, implying that physicians may be underappreciating the extent of NI in AAV. NI is more common in GPA, compared to EGPA or MPA. Patients with NI have involvement of more organ systems than patients without NI. NI in patients with AAV has a negative impact on multiple domains of illness and health-related quality of life. These patient-reported data are informative for clinicians and patients with AAV and should raise the awareness of the impairment in patients with NI in AAV

Disclosure: R. Hajj-Ali: Amgen, 2, GlaxoSmithKlein(GSK), 2, uptodate, 9; **C. Zhang**: None; **R. Borchin**: None; **J. Gordon**: Excision Biotherapeutics, 3; **D. Cuthbertson**: None; **C. McAlear**: None; **C. Yeung**: None; **D. Badenoch**: None; **C. Burroughs**: None; **P. Merkel**: AbbVie/Abbott, 5, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos, 5, Electra, 5, Genentech, 5, GlaxoSmithKlein(GSK), 2, 5, HiBio, 2, InflaRx, 2, 5, Janssen, 2, Jubilant, 2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, Takeda, 2, 5, UpToDate, 9, Visterra, 2.

Abstract Number: 2493

Renal Prognosis of Dialysis-dependent Patients at Baseline in ANCA-associated Vasculitis

Maxime Vignac[1], Dorian Nezam[2], François Grolleau[3], Pauline Morel[4], Dimitri Titeca-Beauport[5], Stanislas Faguer[6], alexandre Karras[7], Justine Solignac[8], Noémie Jourde-Chiche[9], Francois Maurier[10], Hamza Sakhi[1], Khalil El Karoui[1], Rafik Mesbah[11], Pierre Louis Carron[12], Vincent Audard[1], Didier Ducloux[13], Romain Paule[14], Jean-François Augusto[15], Julien Aniort[16], Aurélien Tiple[16], Cédric Rafat[1], Xavier Puéchal[17], Pierre Gobert[18], Catherine Hanrotel[19], Stéphane Bally[20], Nihal Martis[21], Cécile-Audrey Durel[22], Pascal Godmer[23], Aurélie Hummel[24], François Perrin[25], Antoine Néel[26], Claire De Moreuil[27], Tiphaine Goulenok[28], Dominique Guerrot[29], Aurelie Foucher[30], Alban DEROUX[12], Loic Guillevin[31], Alexis REGENT[32], Raphaël Porcher[3] and Benjamin Terrier[33], [1]APHP, Paris, France, [2]CH du Havre, Havre, France, [3]Université Paris Cité, Paris, France, [4]AURA Paris Plaisance, Paris, France, [5]CHU Amiens, Amiens, France, [6]CHU Toulouse, Toulouse, France, [7]HEGP - APHP, Paris, France, [8]APHM, Marseille, France, [9]AP-HM, Marseille, France, [10]Hôpitaux privés de Metz, Vaux / Frankreich, France, [11]Boulogne Hospital (CH), Boulogne, France, [12]CHU de Grenoble, Grenoble, France, [13]CHU de Besançon, Besançon, France, [14]Hôpital Foch, Paris, France, [15]CHU d'Angers, Angers, France, [16]CHU de Clermont Ferrand, Clermont Ferrand, France, [17]National Referral Center for Rare Systemic Autoimmune Diseases, Paris, France, [18]Clinique Rhône Durance, Avignon, France, [19]CHU Brest, Brest, France, [20]CH Métropole Savoie, Chambery, France, [21]CHU de Nice, Nice, France, [22]CHU Lyon, Lyon, France, [23]CH Bretagne Atlantique, Vannes, France, [24]CHU Necker, Paris, France, [25]CH

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SESSION INFORMATION
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Background/Purpose: Renal involvement in ANCA-associated vasculitides (AAV) is an organ- and life-threatening manifestation and therefore an important prognostic factor. However, the identification of predictive factors for renal failure remains a major challenge. Indeed, it may influence the intensity of induction treatment strategies. Furthermore, the benefit of plasma exchange (PLEX) has been questioned in recent years. The aim of this study is to describe the clinical outcome of patients requiring renal replacement therapy (RRT) at baseline and to identify clinical, biological and histological factors at baseline associated with their prognosis at one year.

Methods: This retrospective multicentre study included patients with anti-myeloperoxidase or proteinase 3 AAV with biopsy-proven renal involvement. Characteristics were evaluated stratified by dialysis requirement at baseline to identify determinants of renal prognosis. The primary composite outcome was the occurrence of death or end-stage renal disease at one year. Prognostic outcomes were modelized by generalized linear models to quantify the impact of predictors.

Results: Of the 395 patients enrolled, 106 (26.8%) were on dialysis at baseline. The mean age was 63.1±13.6 years and age was not associated with RRT at baseline (p=0.521). PR3-ANCA was associated to a greater prevalence of renal failure.

Among patients with dialysis at baseline, 61 (57.5%) achieved the one-year composite outcome of death or end-stage kidney disease (ESKD), whereas only 29 (10.0%) patients RRT-free at baseline reached the outcome at one year (p< 0,001). Thirty (28.3%) patients with RRT at baseline had an eGFR at one year superior to 30 mL/min/1,73m², with a null median of eGFR recuperation at one year (0,00 [IQR 0.00-31.5 mL/min/1,73m²]).

Among patients requiring dialysis at baseline, age at diagnosis was not associated with the composite outcome at one year in multivariate analysis (p=0.744). MPO-ANCA were associated with a higher prevalence of RRT or death at one year (OR 3,08; 95%CI 1.21–8.14; p = 0.02). In addition, Brix score at baseline was associated with worse renal prognosis at one year (OR 1.40; 95%CI 1.16–1.73; p=0.001).

Of the patients requiring dialysis at baseline, 80 (75.5%) underwent PLEX. Plasma exchanges were independently associated with a higher estimated glomerular filtration rate (eGFR) at one year of 9.15 mL/min/1.73m² [95%CI 0.26-18.04] (p=0.044). In addition, 41 (91.1%) of the surviving patients who were weaned from RRT at one year had received PLEX, whereas only 39 (63.9%) of the patients with the composite outcome (death or RRT at one year) had received PLEX (p=0.003). Thus, PLEX was associated with a reduced risk of one-year RRT or death in patients receiving dialysis at baseline (OR 0.24, 95%CI 0.06-0.82).

Conclusion: This study describes the clinical evolution of patients with AAV requiring RRT at baseline. It shows a strong association between plasma exchange and improvement in renal function with a higher rate of dialysis weaning. It opens perspectives for further studies in patients who benefit more from PLEX therapy.

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Abstract Number: 2494

Complement mRNA Expression in Patients with ANCA-associated Glomerulonephritis

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SESSION INFORMATION
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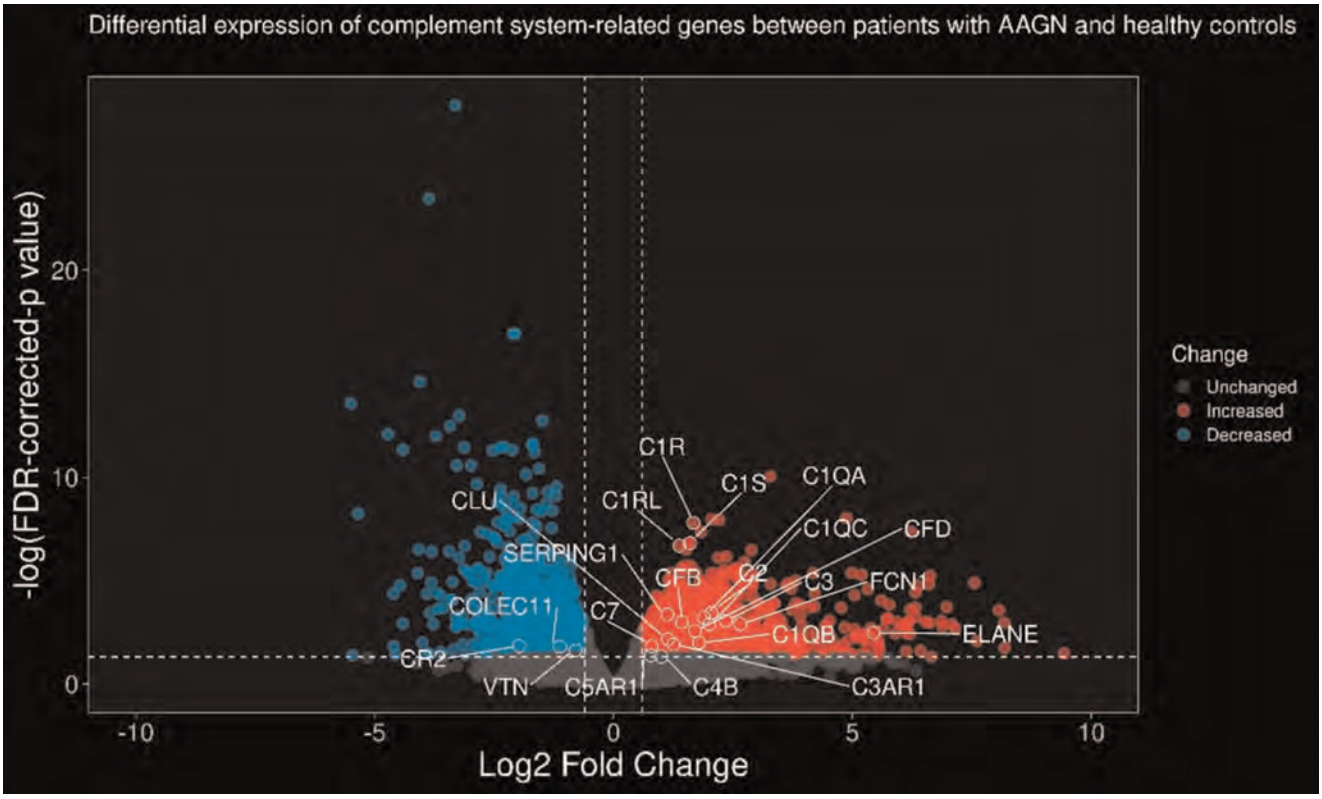
Background/Purpose: The role of complement in patients with ANCA-associated vasculitis (AAV) has been increasingly appreciated and led to the use of complement system antagonists as a therapeutic strategy. However, it is unclear whether complement system activation occurs in affected organs such as the kidneys. This study aimed to characterize complement gene expression in patients with AAV with renal involvement (AAGN).

Table 1. Patient and Disease Characteristics

Age at biopsy, median (IQR)	58 (41-68)
% Female	59%
% White	95%
Newly diagnosed	95%
ANCA ELISA*	
anti-PR3	45% (10/22)
anti-MPO	45% (10/22)
both positive	5% (1/22)
negative	5% (1/22)
ANCA IIF	
c-ANCA	52% (12/23)
p-ANCA	30% (7/23)
*negative***	17% (4/23)
Phenotype	
GPA	52% (12/23)
MPA	35% (8/23)
EGPA	13% (3/23)
Serum Creatinine, average ±SD	3.6 ±2.9

*not available in one patient
** all had detectable ANCAs by ELISA
Abbreviations: ANCA: antineutrophil cytoplasmic antibodies. PR3: proteinase 3. MPO: myeloperoxidase. c-ANCA: cytoplasmic ANCA. P-ANCA: perinuclear ANCA. GPA: granulomatosis with polyangiitis. MPA: microscopic polyangiititis. EGPA: eosinophilic GPA



Complement mRNA expression of AAGN vs controls

Methods: Whole-tissue RNA-sequencing was performed on kidney biopsy samples of 23 patients with AAGN, and 5 healthy kidney donors. After quality control, differential expression (DGE) analysis was performed using generalized linear models correcting for number of genes and batch effects. This abstract describes mRNA expression of 42 complement system proteins, receptors, and regulators. For this analysis, differential expression was considered statistically if the FDR-corrected p-value < 0.05, and the absolute value of log2 fold change between groups was > 0.6 ($|\log_2 FC| > 0.6$).

Results: Patients' clinical and demographic characteristics are depicted in **Table 1**. Most patients were female (13/23), White (21/23), and had a median age of 58 years. Most patients had c-ANCAs and a granulomatosis with polyangiitis phenotype. DGE analysis (**Figure 1)** revealed increased abundance of mRNA coding for proteins participating in the classical (C1q, C1r, C1s, C2, C4B), alternative (CFB, CFD), and common (C3, C7) complement pathways. In addition, there was an increase in abundance of the anaphylatoxin receptors (C3AR, C5AR). mRNA abundance of complement regulators (CFH, CD55, CD46, CR1) were not different compared to controls except for CR2 which was decreased in patients with AAGN.

Conclusion: Analysis of mRNA expression in kidneys of patients with AAGN reveals increased abundance of members of the classical and alternative complement pathways, anaphylatoxin receptors, without a concomitant increase in mRNA expression of complement regulatory proteins. Along with our previous finding of increased complement activation products in urine of patients with active AAGN, these data strongly suggest intra-renal complement system activation in patients with AAGN.

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Abstract Number: 2495

Unbiased Proteomic Approach to Identify Novel Biomarkers of Disease Activity in ANCA- Associated Vasculitis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
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Session Type: Abstract Session
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Background/Purpose: Identifying novel biomarkers of disease activity could improve outcomes by facilitating personalized approaches to treatment decisions in ANCA-associated vasculitis. Biomarkers of disease activity used in day-to-day practice include PR3- or MPO-ANCA, CRP, and ESR, but these are unreliable. Few studies have examined a limited number of circulating proteins as biomarkers, identifying some candidates (e.g., BCA-1, MMP-3, TIMP-1). We previously leveraged a high-throughput, unbiased approach to investigate 92 potential biomarkers in AAV patients and identified 5 potential biomarkers: MCP3, TNFSF-14, OSM, Flt3L, and SCF. The objective of this study was to further investigate the association of 5 novel protein biomarkers with AAV disease activity.

Methods: Serum samples from n=78 patients with AAV were retrieved from a large biobank. We classified disease activity as "Active" or "Remission" at sample collection. The Olink high-throughput proteomic assay was used to measure circulating protein levels. Measurements of ESR, CRP, white blood cell (WBC) count and platelets collected for clinical purposes were extracted from the electronic medical record. We compared the levels of these potential biomarkers in active disease vs remission. Using the median value of each biomarker in the cohort as cut-off values, we determined the odds ratio

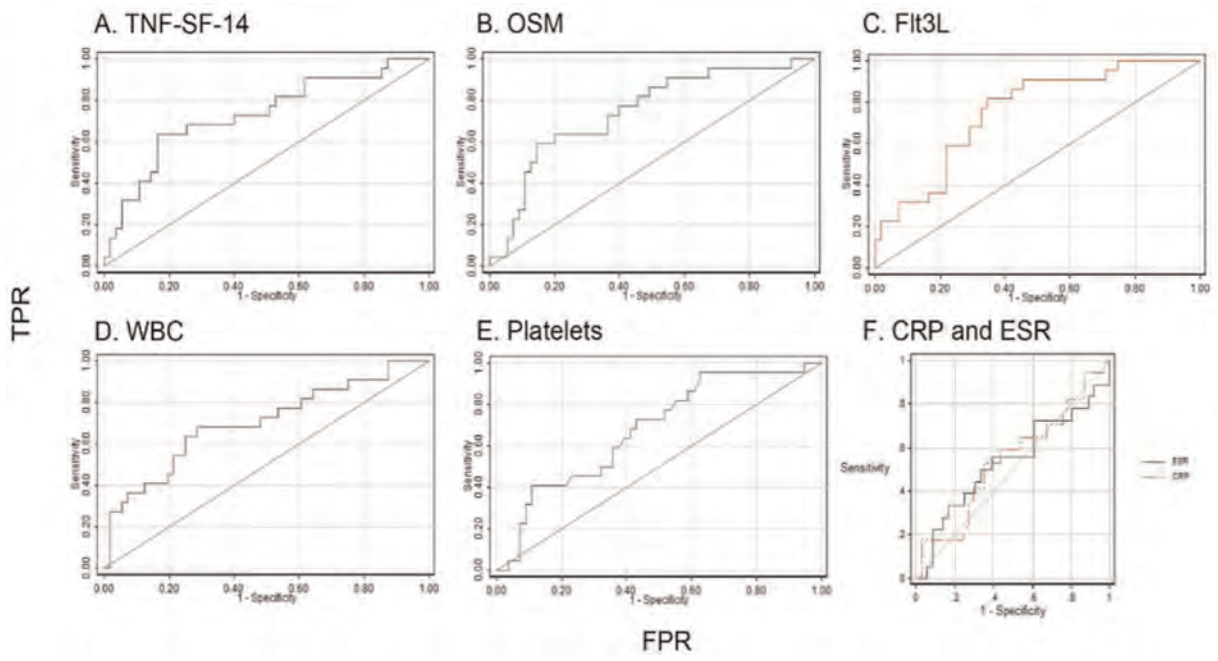

Figure 1: Receiver Operating Characteristic Curve (ROC) for the top performing biomarkers examining active vs inactive AAV disease. Note: TNF-SF-14=tumor necrosis factor super family-14; OSM=oncostatinM; Flt3L=FMS-like tyrosine kinase 3 ligand.

Table 1: AUC for top performing biomarkers in AAV disease status. Note: CI=confidence interval.

Biomarker	TNF-SF-14	OSM	Flt3L	WBC	Plt	CRP	ESR
AUC	0.731	0.745	0.757	0.703	0.680	0.549	0.547
CI	(0.601-0.862)	(0.622-0.867)	(0.644-0.871)	(0.566-0.840)	(0.551-0.809)	(0.376-0.721)	(0.372-0.722)

Table 2: Multivariate logistic regression for median biomarker levels and odds ratios for AAV active disease controlling for steroid use, ANCA type (PR3, MPO), age, and gender. Note: CI=confidence interval; MCP3=Monocyte chemotactic protein-3; SCF-Stem cell factor.

Biomarker	Odds Ratio (median cutoff, CI, p-value)
OSM	4.93 (≥ 6.96, 1.29-18.88, p=0.02)
TNF-SF-14	3.15 (≥ 7.07, 0.92-10.78, p=0.068)
MCP-3	1.38 (≥ 3.18, 0.48-.3.98, p=0.555)
Flt3L	0.11 (≥ 9.64, 0.03-0.46, p=0.002)
SCF	0.30 (≥ 10.13, 0.1-0.89, p=0.03)

(OR), the area under the receiver operating curve (AUC) of the association of abnormal biomarker with active disease, and a multivariate logistic regression to adjust for steroid use, sex, age and ANCA type.

Results: The mean age was 57.3 +/- 17.6, 55% were female, and 28% had active disease at sample collection. When comparing active disease vs remission, abnormal levels of OSM, TNF-SF-14, Flt3L, and SCF differentiated disease states: OR of 5.10 (p=0.005), 3.71 (p=0.017), 0.13 (p=0.001), and 0.34 (p=0.04), respectively. AUC analysis indicated that TNF-SF-14 (0.73, CI 0.60-0.86), OSM (0.75, CI 0.62-0.87), and Flt3L (0.76, CI 0.64-0.87) were more strongly associated with active disease than other biomarkers, including WBC (0.70, CI 0.57-0.84), platelets (0.68, CI 0.55-0.81), CRP (0.55, CI 0.38-0.72), and ESR (0.55, CI 0.37-0.72).After adjusting for steroid use, sex, age, and ANCA type, we found that only OSM and Flt3L differentiated active disease from remission.

Conclusion: Using a high-throughput, unbiased proteomics approach, we further investigated novel candidate markers differentiating active AAV disease from remission. These proteins likely reflect different states of immune activation during active disease and outperform conventional inflammatory markers (e.g., CRP, ESR) as well as WBC and platelets. Our study has certain limitations including sample size, a cross-sectional study design, and requires validation across diverse, longitudinal cohorts. The potential for biomarkers that accurately identify those individuals in remission compared to active disease may facilitate tailored, personalized therapeutic intervention, which avoids unnecessary exposure to the toxic side effects of immunomodulatory agents.

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Abstract Number: 2496

HXB-319, a New Generation Mesenchymal Stromal Cell (MSC) Therapy, Alleviates Neutrophilic Inflammation, and End-organ Damage in Pulmonary Renal Syndromes by Inducing FoxP3+ Tregs, and by Promoting TNFα-stimulated gene-6 (TSG-6) over Expression

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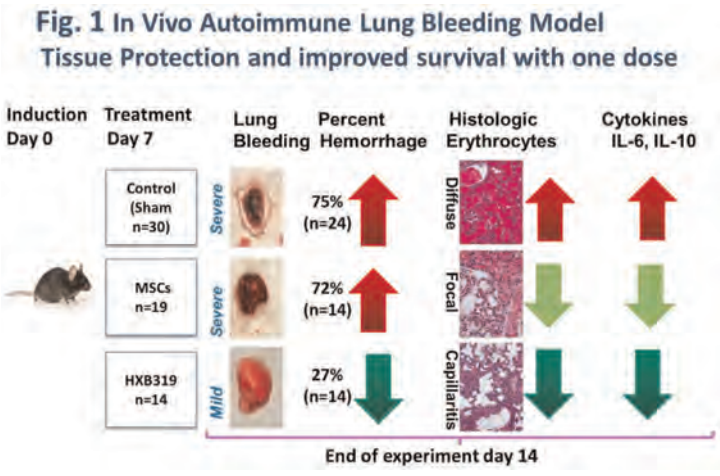
Background/Purpose: Mesenchymal stromal cells (MSCs) have been shown to be safe therapies in more than 100 human clinical trials. However, MSCs clinical efficacy is variable, and has been dependent on the severity of the inflammatory disease activity. MSC therapies have NOT been FDA approved for any disease indication, mostly due to lack of uniform potency and lack of specificity targeting the varying aspects of autoimmune diseases.

We developed a novel MSC-based cell therapy (HXB-319) that potently reduces inflammation and potentially halts organ damage in autoimmune pulmonary renal syndromes.

Methods: Using a combination of cytokines and growth factors that mimicked severe autoimmune disease microenvironment, we engineered a novel bone marrow derived MSC based cell therapy (HXB-319). We then verified its anti-inflammatory activity by flow cytometry, RT-PCR, and mass spectrophotometry *in vitro. Next, In vivo* efficacy was assessed by treating autoimmune induced DAH in C57Bl/6 mice by intraperitoneal (IP) injection of pristane. Seven days later, some mice were treated with either MSCs or HXB-319 ($2X10^6$ cells, IP). At day 14, peritoneal lavage fluid and lung tissue were sampled.

Results: HXB-319 cells showed significantly increased expression of anti-inflammatory genes (indoleamine 2,3-dioxygenase (IDO), TSG-6 and CD-274), and markers of angiogenesis (vascular endothelial growth factor A (VEGFA) and CD-146).



In vivo validation of HXB-319 mechanism of action

Table 1: Flow cytometry analysis of post mortem peritoneal lavage fluid of DAH model

Cell Population	DAH	MSC	HXB-319	Control
Neutrophils[a]	0.53 ± 0.05*	0.69 ± 0.10*	0.29 ± 0.10*¶^	0.004 ± 0.001
NK cells[a]	0.10 ± 0.02*	0.12 ± 0.03*	0.05 ± 0.01¶^	0.02 ± 0.01
Th17 $CD4^+$ $ROR\gamma T^{+c}$	83.3 ± 1.38*	77.8 ± 1.8*	75.0 ± 2.2*¶	59.0 ± 0.66
Th17 ($CD8^+ROR\gamma T$) $^{+c}$	92.3 ± 0.78*	86.9 ± 2.0*	82.3 ± 3.4*¶	59.7 ± 1.57
Tregs ($CD4^+FoxP3$) $^{+c}$	0.46 ± 0.67*	0.87 ± 0.10*¶	0.94 ± 0.15*¶^	0.29 ± 0.04
$FoxP3^+/ROR\gamma T^{+d}$	0.56 ± 0.09	1.14 ± 0.15*¶	1.27 ± 0.05*¶	0.48 ± 0.07

a data are millions of cells recovered from peritoneal lavage
b data are the dimensionless ratio of $CD3^+CD4^+$ cells compared to $CD3^+CD8^+$ cells
c data are the percentage of CD4 or CD8 cells that express the indicated cytosolic marker
d data are 100 times the dimensionless ratio of $CD3^+CD4^+FoxP3^+$ to $CD3^+CD4^+$ $ROR\gamma T^+$ cells
- significantly different from Control,
- ¶ significantly different from DAH,
- ^significantly different between the HXB-319 and MSCs

Protein pathway analysis of HXB-319 culture media (secretome) showed significant upregulation of protein pathways that reduce inflammation (IL1RN, IDO), and fibrosis with upregulation of HGF, c-MET signaling, matrix metalloproteinase secretion (MMP1, MMP13), and downregulation of TGF-β via Activin pathway, while inducing vascularization (VEGF).

Diffuse alveolar hemorrhage (DAH) model (C57bl/6 mouse induced by 0.5 cc IP pristane injection) was utilized for proof-of-concept *in vivo* studies. In the DAH model, the mortality is typically above 75% beyond 14 days after pristane injection.

When delivered *in vivo* to the DAH mice,HXB-319 significantly reduced lung inflammation and alveolar hemorrhage (27.2%) vs. naked MSC treatment (75%) (Fig.1). Pulmonary gene expression of IL-6 and 1L-10, and serum IL-1β levels were significantly reduced by HXB-319 when measured at day 14.

Peritoneal lavage fluid from DAH mice treated with HXB-319 showed reductions in total cells recovered, neutrophils, monocytes, and NK cells compared to mice given MSCs or untreated DAH mice, the reduction in neutrophils was the most statistically significant result (Table 1). DAH mouse treatment with HXB-319 cells, also significantly decreased the proportion of RORγT cells (Th17) in both CD4+ and CD8+ populations, and significantly increased the proportion of FoxP3+ cells among CD4+ cells (Tregs).

Conclusion: Novel HXB-319 cell therapy, phenotypically engineered to control inflammation, is a potent anti-inflammatory, anti-fibrotic, and angiogenic cell therapy. HXB-319 may suppress severe autoimmune disease activity, and end organ damage in DAH, particularly by excessive induction of anti inflammatory activity via IDO, and over expression of TSG-6, increased CD4+ Tregs and significant suppressive effects on neutrophil population.

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Abstract Number: 2497

Factors Influencing Time to Diagnosis in U.S. Patients with Systemic Lupus Erythematosus

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Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disease defined by its heterogeneity and cycles of flares and remissions. Owing to non-specific or incomplete sequelae, diagnosing lupus represents a considerable clinical challenge. Despite increased awareness among physicians and patients, considerable diagnostic delays in SLE persist. The objective of this study was to identify factors contributing to delays in SLE diagnosis.

Methods: We performed cross-sectional analysis of 925 US patients with SLE registered in the Lupus Foundation of America Research Accelerated by You (RAY®) registry from October 2020 to May 2023. The Accelerated Failure Time model was used to ascertain factors influencing time to diagnosis. Demographics variables including age, sex, race as well as onset of first symptoms and time of diagnosis were evaluated. The potential effect of income, educational attainment and US region were also determined.

Results: All participants included in the analysis were ultimately diagnosed with lupus. The average duration from symptom onset and diagnosis is 6.29±0.277 SE years. Using a multivariable log-logistic AFT model, we observed that age (β=.019, p< .001), residence in the southern region (β=0.227, p=.024) and identification as American Indian/Alaska Native (β=0.651,p=.008) were associated with prolonged time to SLE diagnosis. Conversely, Asian (β=-0.545, p=.006) and Black/African American race (β=-.366, p=.002) showed association with a shorter time to diagnosis. Evaluation of income indicated a potential association with a shorter time to diagnosis (β=-0.049, p=0.063); however, it was not statistically significant.

Conclusion: Diagnostic delays remain a considerable issue for individuals eventually diagnosed with lupus. Factors such as race, regional location, and age may contribute to time to diagnosis. Additional research is needed to explore the relationship between these variables and the timing of SLE diagnosis.

Disclosure: J. Buie: None.

Abstract Number: 2498

Does Physical Activity Modify the Relationship Between Pain and Corticosteroid Injection Utilization in Adults with or at High Risk for Knee Osteoarthritis?

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Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Knee osteoarthritis (OA) is a leading global cause of pain and disability, with no current cure. Knee pain is the most common symptom and a driving factor for patients to seek treatment for knee OA. Exercise and Corticosteroid (CS) injections are mainstays of treatment for knee OA, however, increased utilization of CS injections may increase the risk of radiographic knee OA progression and cartilage loss. Given this, physical activity (PA) may be an ideal first-line treatment, however, it is unknown if PA modifies the utilization of CS in those with varying levels of pain. Therefore, the purpose of this study was to determine if PA modifies the relationship between knee pain and utilization of CS injections during a 5-year follow-up period in adults with or at high risk for knee OA.

Methods: We used data from the Osteoarthritis Initiative (OAI). Our exposure was visual analogue scale (VAS) knee pain severity over the past 30 days, dichotomized using a patient acceptable symptom state (PASS) value into high (≥ 4) vs low pain (< 4) at the 48-month visit (analytic baseline, BL). Our outcome was receiving a CS injection. Participants were asked, "In the past 6 months, have you received a CS injection?" at the 48-, 60-, 72-, 84-, 96-, and 108-month follow-up visits. PA at BL was measured using an Actigraph GT1M and was examined as an effect measure modifier between pain and CS injection. We used 6000 steps/day to stratify the sample, as this cutoff was previously found to be associated with

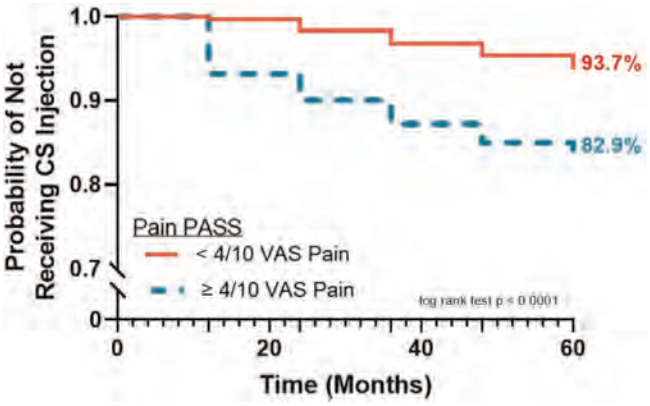

Figure 1: Kaplan-Meier survival curves for not receiving a CS injection by pain PASS exposure group in those who walked ≥ 6000 steps/day at baseline.

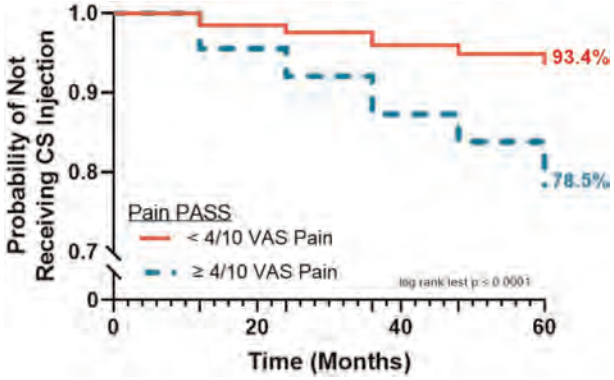

Figure 2: Kaplan-Meier survival curves for not receiving a CS injection by pain PASS exposure group in those who walked < 6000 steps/day at baseline.

Table 1: Hazard ratios and 95% confidence intervals for receiving a CS injection, by pain PASS exposure group, stratified by steps/day at baseline.

	CS Injection n/N (%)	HR [95% CI] (unadjusted)	HR [95% CI] (adjusted)
≥ 6000 steps/day			
Low pain (< 4/10)	32 / 523 (6.1%)	1.0 [REF]	1.0 [REF]
High pain (≥ 4/10)	54 / 321 (16.8%)	2.98 [1.92, 4.61]	1.48 [0.79, 2.78]
< 6000 steps/day			
Low pain (< 4/10)	36 / 580 (6.2%)	1.0 [REF]	1.0 [REF]
High pain (≥ 4/10)	90 / 444 (20.3%)	3.61 [2.45, 5.31]	2.72 [1.50, 4.94]

Note: models were adjusted for age, sex, BMI, race, education, comorbidity, function measured by the Knee Osteoarthritis Outcome Score (KOOS), and radiographic knee OA presence

developing functional limitation. We excluded participants who answered yes to the CS injection question at BL. We produced Kaplan-Meier survival curves for cumulative incidence of not receiving a CS injection and used Cox proportional hazards regression to calculate discrete-time hazard ratios (HR) and 95% confidence intervals (CI), adjusted for potential confounders.

Results: 1868 participants (mean age = 65.0 years old, 55% female, mean BMI = 28.5 kg/m^2) were included in the overall analytic sample. 212 participants received at least one CS injection over 5 years of follow-up. In the ≥ 6000 steps/day group, survival probability was 82.9% for those with high pain and 93.7% for those with low pain (Figure 1). In the < 6000 steps/day group, survival probability was 78.5% for those with high pain and 93.4% for those with low pain (Figure 2). Participants with ≥ 4/10 pain that walked < 6000 steps/day had a 2.72 times greater hazard of receiving a CS injection compared to those with < 4/10 pain (adjusted HR [95% CI] = 2.72 [1.50, 4.94]). Participants with ≥ 4/10 pain that walked ≥ 6000 steps/day had a 1.48 times greater hazard of receiving a CS injection compared to those with < 4/10 pain, which did not reach statistical significance (adjusted HR [95% CI] = 1.48 [0.79, 2.78]) (Table 1).

Conclusion: In adults with knee OA who walk less than 6000 steps per day, high pain is associated with greater corticosteroid utilization. However, in those who walk at least 6000 steps per day, pain is not related to CS injection utilization over the next 5 years. This initial look suggests that daily walking may modify the relationship between pain and receiving a CS injection, though further research is warranted.

Disclosure: S. Liles: None; **D. White**: Viatris, 6; **T. Bye**: None; **J. Jakiela**: None.

Abstract Number: 2499

Influence of Adiposity on Physical Function, Physical Activity, and Self-Reported Symptom Severity for Individuals with Arthritis Prior to Beginning a Physical Activity Promotion Intervention

Scott Jamieson, Sara Wilcox and Christine Pellegrini, The University of South Carolina, Columbia, SC

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Interprofessional OA & Lupus
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Engagement in moderate-vigorous physical activity (MVPA) is recommended for individuals with obesity to promote weight loss and mitigate severity of chronic diseases associated with higher levels of adiposity. However, limited research has examined the role that weight status plays on physical function, physical activity, and symptoms severity for individuals with arthritis. Therefore, this study compared differences in physical activity; physical function; and arthritis pain, stiffness, fatigue, and self-efficacy between individuals with and without obesity.

Methods: Participants ≥18 years with a diagnosis of arthritis from an ongoing study aimed to evaluate a phone-based version of the Walk with Ease program were included. Physical function was assessed with the 30-second chair stand and 6-minute walk. Participants wore an ActiGraph GT9x Link for 7 days. Total minutes/week of MVPA (≥2020 counts/min) and steps/day were calculated among participants with >4 valid days (≥10 hours of wear time). Weight status was calculated using body mass index (BMI); a BMI ≥30 kg/m^2 indicated obesity and < 30 kg/m^2 indicated absence of obesity. Self-efficacy in arthritis care was assessed with the Arthritis Self-Efficacy Scale (ASES). Symptom severity for pain, fatigue, and stiffness was assessed using a visual analog scale (VAS). Independent t-tests were used to compare mean differences in physical function; physical activity; and self-reported measures of pain, stiffness, fatigue, and self-efficacy between participants with and without obesity.

Results: A total of 140 participants were included in the analysis (91.4% female, 60.7% African American, 63.0 ± 9.7 years, BMI 34.5 ± 8.1 kg/m^2). Differences between those with and without obesity are shown in Table 1. Participants without obesity were on average older than participants with obesity. Both groups were predominantly female and African American, with osteoarthritis the most common arthritis diagnosis for each. Participants without obesity were more physically active in terms of MVPA/week, steps/day, and walked a greater distance in the 6-minute walk test ($p< 0.05$). Participants without obesity also reported lower levels of fatigue and stiffness ($p< 0.05$). Pain ($p=0.059$) and ASES ($p=0.071$) approached significance such that participants without obesity reported higher levels of arthritis self-efficacy and lower levels of pain. No significant differences between groups were seen on the 30-second chair stand test ($p=0.969$).

Conclusion: Participants with obesity had greater impairments on the majority of tests administered along with lower levels of physical activity as compared to those without obesity. Additional coaching strategies are warranted encouraging adults with arthritis who are obese to engage in regular physical activity to assist with health-related outcomes.

Table 1: Demographics & Group Differences on Physical Activity, Physical Function, & Self-Reported Symptom Severity (n=140)

Demographics	BMI < 30 kg/m^2 (n=47)	BMI ≥ 30 kg/m^2 (n=93)	
Sex	89.4% Female	92.5% Female	
Race	53.2% African American	64.5% African American	
Age (years)	63.62 ± 9.75	62.74 ± 9.64	
BMI (kg/m^2)	26.29 ± 2.77	38.61 ± 6.70	
Arthritis dx:	48.9% Osteoarthritis	61.3% Osteoarthritis	
Measurement	**BMI < 30 kg/m^2**	**BMI ≥ 30 kg/m^2**	**p-value**
6-minute walk test (ft)	1422.95 ± 280.21	1229.64 ± 281.72	p<0.001
30-second chair stand test (repetitions)	8.91 ± 2.47	8.94 ± 3.22	p=0.969
MVPA (minutes/week)	86.10 ± 109.83	46.16 ± 57.88	p=0.005
Steps/day	4999.26 ± 2596.52	3727.75 ± 1865.95	p=0.001
VAS pain (mm)	34.16 ± 25.48	43.10 ± 26.55	p=0.059
VAS fatigue (mm)	33.35 ± 26.52	47.59 ± 29.45	p=0.006
VAS stiffness (mm)	38.07 ± 27.23	51.59 ± 26.03	p=0.005
Arthritis self-efficacy scale	6.47 ± 1.90	5.83 ± 1.99	p=0.071

Disclosure: S. Jamieson: None; **S. Wilcox**: None; **C. Pellegrini**: None.

Abstract Number: 2500

Suicidal Ideation and Self-Efficacy in Systemic Lupus Erythematosus: Georgians Organized Against Lupus (GOAL) Cohort

Charmayne Dunlop-Thomas[1], Gaobin Bao[1], Jessica Williams[2], Hilton Mozee[1], Cristina Drenkard[1] and S. Sam Lim[1], [1]Emory University, Atlanta, GA, [2]Emory University School of Medicine, Atlanta, GA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Interprofessional OA & Lupus
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Suicidal ideation is more common in SLE than in other chronic diseases. Targeted interventions are needed to reduce morbidity and mortality. Bandura's theory of self-efficacy notes the importance of individual perception of capabilities as predictors of health and well-being. Patients working with healthcare professionals to understand and manage symptoms is crucial. This study aimed to identify health and psychosocial factors associated with SI among patients with SLE, which could serve as possible targets for intervention by healthcare professionals. We explored the possible association between self-efficacy (SE) for managing symptoms and treatments and suicidal ideation (SI) among SLE patients from the Georgians Organized Against Lupus (GOAL) Cohort.

Methods: We examined data from the GOAL Cohort, a large population-based cohort of adults from metropolitan Atlanta, Georgia, who fulfilled three or more ACR classification criteria with a final SLE diagnosis by a board-certified rheumatologist. GOAL participants responded to validated self-administered tools on health outcomes. This study included participants with completed surveys between 2017- 2020. We explored the following measures: Patient Health Questionnaire-9, PROMIS Self-efficacy for managing medications and treatments (SEMMT) and PROMIS Self-efficacy for managing symptoms (SEMS), PROMIS depression, the Systemic Lupus Activity Questionnaire (SLAQ), and the Self-administered Brief Index of Lupus Damage (SA-BILD). We examined an individual SEMS question for further examination: I can work with my doctor

Table: Logistic Regression of Suicidal Ideation in SLE

		Univariable		Multivariable	
	Characteristics	**Odds Ratio**	**P value**	**Odds Ratio**	**P value**
Self-efficacy	***Adequate confidence in working with a doctor to manage symptoms (per 1 scale ↓)**	**1.73 (1.43-2.09)**	**<0.0001**	**1.64 (1.25-2.14)**	**<0.001**
	SEMMT (per 5 units ↓)	**1.39 (1.22-1.58)**	**<0.001**		
	SEMS (per 5 units ↓)	**1.56 (1.35-1.81)**	**<0.001**		
Socio-demo	Age at survey completion (per 10 units ↑)	0.86 (0.74-1.01)	0.071	1.23 (0.90-1.69)	0.20
	Disease duration (per 5 units ↑)	0.91 (0.81-1.01)	0.087	1.14 (0.95-1.36)	0.16
	Education years (per 3 units ↑)	0.88 (0.70-1.10)	0.25	1.25 (0.87-1.80)	0.22
	Organ damage (BILD score) (per 3 units ↑)	1.08 (0.92-1.28)	0.35	0.90 (0.67-1.22)	0.50
Health	Disease Activity (SLAQ score) (per 3 units ↑)	**1.34 (1.25-1.45)**	**<0.0001**	1.00 (0.89-1.13)	0.97
	PROMIS Depression T-score (per 5 units ↑)	**2.66 (2.23-3.17)**	**<0.0001**	**2.98 (2.36-3.77)**	**<0.001**

*SEMS individual question - adequate is defined as quite or very confident in working with a doctor to manage symptoms. Inadequate is defined as not at all, a little or somewhat confident in working with a doctor to manage symptoms. Abbreviations: SEMMT - PROMIS Self-efficacy for managing medications and treatments, SEMS - PROMIS Self-efficacy for managing symptoms, SA-BILD – Self-administered-Brief Index of Lupus Damage, SLAQ – Systemic Lupus Activity Questionnaire. Multivariable adjustments: socio-demographics (age, race, education, marital status, work status), insurance, disease duration, disease severity, and depression.

to manage my symptoms with response choices on a Likert scale from 1 (I am not at all confident) to 5 (I am very confident). Logistic regression was used to examine factors associated with SI.

Results: This study includes data from 967 SLE participants (94% women, mean age 32 years [SD 11.8], 82% Black, mean disease duration 15 years [SD 10.3], 14% uninsured). The mean disease activity and organ damage scores were 15 (SD 8.8) and 4 (SD 3.7), respectively. The t-scores for SEMMT and SEMS were 46 [SD 8.9] and 48 [SD 8.7], respectively. Ninety participants (9.4%) endorsed suicidal ideation.

Univariate analyses showed that lower SE, higher SLE activity and higher depression scores were significantly associated with SI. In the multivariate analysis, only lower SE related to working with doctors to manage symptoms remained significantly associated with suicidal ideation after controlling for other factors (Table).

Conclusion: In a population-based, predominantly Black SLE cohort with considerable disease activity, there was a significant proportion of suicidal ideation. After controlling for other risk factors, such as socio-demographics and disease status, those with low self-efficacy for working with doctors to manage symptoms were at higher risk for SI. Health professionals can consider assessing and addressing perceptions of self-management capabilities among patients with SLE in order to improve outcomes in this vulnerable population.

Disclosure: C. Dunlop-Thomas: None; **G. Bao**: None; **J. Williams**: None; **H. Mozee**: None; **C. Drenkard**: None; **S. Lim**: None.

Abstract Number: 2501

WITHDRAWN

SESSION INFORMATION

Session Date: **Tuesday, November 14, 2023**
Session Title: Abstracts: Interprofessional OA & Lupus
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a common multisystem autoimmune disease with chronic inflammation. Many efficacy evaluation indicators of randomized clinical trials (RCTs) for SLE have been proposed but the comparability remains unknown. We aim to explore the preference and comparability of indicators reporting response rate and provide basis for primary outcome selection when evaluating the efficacy of SLE pharmaceutical treatment.

Methods: We systematically searched 3 databases and 3 registries to identify pharmacological intervention-controlled SLE RCTs. Relative discriminations between indicators were assessed by the Bayesian hierarchical linear mixed model.

Results: 33 RCTs met our inclusion criteria and we compared 8 of the most commonly used indicators reporting response rate (Figure 1). Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)-4and Systemic Lupus Erythematosus Responder Index(SRI)-4 were considered the best recommended indicators reporting response rate to discriminate the pharmacological efficacy. Indicator preference was altered by disease severity, classification of drugs and outcome of trials, but SLEDAI-4 had robust efficacy in discriminating ability for most interventions. Of note, British Isles Lupus Assessment Group (BILAG) Index-based Combined Lupus Assessment (BICLA) showed efficacy in trials covering all-severity patients, as well as non-biologics RCTs. BILAG response and Physician's Global Assessment (PGA) response were more cautious

in evaluating disease changes. Serious adverse events (SAE) was often applied to evaluate the safety and tolerability of treatments rather than efficacy (Figure 2).

Conclusion: The impressionable efficacy discrimination ability of indicators highlights the importance of flexibility and comprehensiveness when choosing primary outcome(s) (Table 1). As for trials that are only evaluated by SLEDAI-4, attention should be paid to outcome interpretation to avoid the exaggeration of treatment efficacy.

Abstract Number: 2502

Self-Reported Sleep Disorders Among Individuals with Systemic Lupus Erythematosus

Patti Katz[1], Maria Dall'Era[2], Jinoos Yazdany[3] and Kaleb Michaud[4], [1]University of California San Francisco, San Rafael, CA, [2]University of California San Francisco, San Francisco, CA, [3]University of California, General Department of Medicine, Division of Rheumatology, San Francisco, CA, [4]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Interprofessional OA & Lupus
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Research in the general population has linked sleep disorders to poor outcomes such as lower pain thresholds, fatigue, cognitive impairment, depression, and cardiovascular disease – important health outcomes relevant to lupus, as well as higher levels of systemic inflammation, which may influence SLE disease activity and symptoms. SLE-specific studies have linked self-reported sleep problems with greater disease activity and symptoms and even risk of lupus onset. Some sleep disorders are more common among older individuals. We examine the prevalence of self-reported sleep disorders in two SLE cohorts, one with greater representation from older adults with SLE.

Methods: Data are from participants with physician-confirmed SLE in the California Lupus Epidemiology Study (CLUES) and the FORWARD Databank. In one data collection period in each study, we examined two sleep disorders: obstructive sleep apnea (OSA) using the validated STOP-Bang questionnaire and self-reported OSA diagnosis, and restless legs syndrome (RLS) using validated self-reported questions and self-reported RLS diagnosis. We examined the prevalence of OSA and RLS and the overlap between the two in each cohort. Unadjusted analyses identified significant associations between OSA and RLS and sociodemographic (age, sex, income, education), general health (smoking, obesity, comorbidities [Rheumatic Disease Comorbidity Index, RDCI), and SLE-related (SLE duration, self-reported disease activity [Systemic Lupus Activity Questionnaire, SLAQ], and damage [Brief Index of Lupus Damage, BILD], 0-10 pain rating, glucocorticoid use, use of immunosuppressive medications) characteristics. Multivariable analyses to identify independent associations of sleep disorders included all variables significant at $p \leq 0.10$ in unadjusted analyses.

Results: Mean age was 50 ± 14 years in CLUES and 61 ± 12 years in FORWARD (Table 1). Prevalence of each sleep disorder was higher in the older FORWARD cohort and considerably higher in both cohorts than in the general population (Table 1). In CLUES and FORWARD, 36.7% and 53.8% of participants, respectively, had at least one sleep disorder. In multivariable analyses, SLAQ, pain, and a higher number of comorbid conditions were the most consistent factors associated with sleep disorders (Tables 2 and 3).Obesity (BMI ≥30 kg/m2) was also associated with OSA.

Table 1. Subject characteristics

	CLUES (n = 248)	FORWARD (n = 336)	
Sociodemographic			
Age	49.9 ± 13.9	60.5 ± 7.5	
Female	91.2 (229)	93.5 (314)	
General health			
Obese (BMI ≥ 30)	24.7 (62)	34.8 (117)	
Smoking			
Current	2.8 (7)	3.0 (10)	
Ever	27.4 (68)	32.7 (110)	
Comorbid conditions			
Rheumatic Disease Comorbidity Index (RDCI)	1.4 ± 1.4	2.7 ± 2.0	
SLE			
Duration, years	21.2 ± 11.2	25.2 ± 12.1	
Systemic Lupus Activity Questionnaire (SLAQ)	8.9 ± 7.1	11.1 ± 7.6	
Brief Index of Lupus Damage (BILD)	2.4 ± 2.3	3.7 ± 2.3	
Pain rating, 0 - 10	2.2 ± 2.6	3.8 ± 2.8	
Medications			
Glucocorticoids			
Any	45.0 (116)	34.2 (113)	
High dose	15.0 (38)	9.2 (31)	
Immunosuppressive use	53.8 (135)	31.3 (105)	
Prevalence of sleep disorders			Population estimates
Obstructive sleep apnea (OSA) risk	12.8 (32)	18.8 (63)	• general population 4.2%[1]
OSA diagnosis	13.1 (32)	23.5 (79)	• age 60-65: 8.2% females, 14.6% male[2]
OSA high risk or diagnosis	18.6 (46)	30.7 (103)	
Restless legs syndrome (RLS) symptoms	25.8 (64)	33.1 (109)	• <15%[3]
RLS diagnosis	7.2 (18)	19.5 (65)	
RLS symptoms or diagnosis	28.2 (70)	37.4 (123)	

Tabled values are mean ± SD or % (n)

[1]Ram S, Seirawan H, Kumar S, Clark G. Prevalence and impact of sleep disorders and sleep habits in the United States. Sleep Breath 2010; 14:63-70.
[2]Huang T, Lin B, Mark S, Stampfer M, Laden F, Hu F, Tworoger S, Redline S. Sex differences in the associations of obstructive sleep apnoea with epidemiological factors. Eur Resp J 2018; 51:1702421.
[3]Ohayon M, O'Hara R, Vitiello M. Epidemiology of restless legs syndrome: a synthesis of the literature. Sleep Med Rev 2012; 16:283-295

Table 2. Factors associated with Obstructive Sleep Apnea (OSA, high risk or diagnosis)

	CLUES				FORWARD			
	No OSA (n= 201)	OSA (n= 46)	P	Multivariable	No OSA (n= 233)	OSA (n= 103)	P	Multivariable
Sociodemographic characteristics								
Age, years	48.1 ± 14.1	58.5 ± 9.8	<0.0001	**1.04 (1.003, 1.08)**	60.1 ± 13.1	61.4 ± 9.5	.32	
Female	92.0 (185)	87.0 (40)	0.26		93.6 (218)	93.2 (96)	0.99	
General health-related								
Current smoker	2.0 (4)	1.2 (3)	0.12		3.4 (8)	1.9 (2)	0.73	
Ever smoke	28.6 (57)	37.0 (17)	0.29		31.8 (74)	35.0 (36)	0.61	
Obese (BMI ≥30)	19.4 (39)	47.8 (22)	<0.0001	**3.36 (1.47, 7.71)**	22.3 (52)	63.1 (65)	<0.0001	**5.12 (2.92, 8.97)**
Comorbidities (RDCI)	1.2 ± 1.3	2.3 ± 1.4	<0.0001	1.30 (0.96, 1.74)	2.3 ± 1.8	3.7 ± 2.1	<0.0001	**1.28 (1.09, 1.50)**
SLE-related								
Duration, years	19.6 ± 10.7	28.3 ± 10.6	<0.0001	**1.06 (1.02, 1.11)**	24.9 ± 12.2	25.8 ± 11.9	0.54	
SLAQ	7.8 ± 6.5	13.5 ± 7.9	<0.0001	**1.13 (1.06, 1.20)**	9.4 ± 6.8	14.8 ± 7.9	<0.0001	**1.08 (1.04, 1.13)**
BILD	2.2 ± 2.3	3.3 ± 2.3	0.0044	0.90 (0.75, 1.08)	3.4 ± 2.2	4.3 ± 2.6	0.0015	1.01 (0.89, 1.16)
Pain (0 – 10)	2.0 ± 2.4	3.3 ± 3.0	0.01	***[1.16 (1.004, 1.33)]***	3.3 ± 2.7	5.0 ± 2.6	<0.0001	***[1.18 (1.06, 1.31)]***
Medications								
Glucocorticoid use	44.8 (90)	43.5 (20)	0.99		32.6 (75)	38.0 (38)	0.38	
High dose GC (≥10 mg/day)	13.9 (28)	21.7 (10)	0.18		6.9 (16)	14.6 (15)	0.04	1.58 (0.66, 3.82)
Immunosuppressive	54.2 (109)	50.0 (23)	0.63		32.6 (76)	28.2 (29)	0.45	

RDCI = Rheumatic Disease Comorbidity Index; SLAQ = Systemic Lupus Activity Questionnaire; BILD = Brief Index of Lupus Damage

Table 3. Factors associated with restless legs syndrome (RLS, diagnosis or symptoms)

	CLUES				FORWARD			
	No RLS (n= 178)	RLS (n= 70)	P	Multivariable	No RLS (n= 206)	RLS (n= 118)	P	Multivariable
Sociodemographic characteristics								
Age, years	49.5 ± 14.5	50.9 ± 12.5	0.47		60.2 ± 13.1	60.5 ± 10.7	0.81	
Female	92.7 (165)	87.1 (61)	0.21		92.2 (190)	95.9 (118)	0.25	
General health-related								
Current smoker	2.8 (3)	2.9 (2)	0.99		1.5 (3)	4.9 (6)	0.08	
Ever smoke	27.7 (49)	36.2 (25)	0.22		27.2 (56)	43.0 (40)	0.02	1.45 (0.86, 2.44)
Obese (BMI ≥30)	20.8 (37)	35.7 (25)	0.02	1.47 (0.76, 2.83)	32.5 (67)	39.0 (48)	0.24	
Comorbidities	1.9 ± 1.6	2.9 ± 2.1	0.0003	**1.25 (1.004, 1.55)**	2.3 ± 1.9	3.3 ± 2.0	<0.0001	**1.23 (1.07, 1.41**
SLE-related								
Duration, years	20.8 ± 11.9	22.4 ± 9.1	0.28		27.2 ± 11.5	27.0 ± 14.5	0.90	
SLAQ	7.5 ± 6.4	12.4 ± 7.6	<0.0001	**1.08 (1.04, 1.13)**	9.6 ± 6.7	13.7 ± 8.1	0.0001	**1.06 (1.02, 1.11)**
BILD	2.4 ± 2.3	2.7 ± 2.5	0.31		3.5 ± 2.3	4.0 ± 2.5	0.048	0.95 (0.84, 1.07)
Pain (0 – 10)	1.9 ± 2.4	3.2 ± 2.8	0.0003	***[1.17 (1.05, 1.39)]***	3.5 ± 2.7	4.5 ± 2.8	0.0077	***[1.10 (1.00, 1.21)]***
Medications								
Glucocorticoid use	44.9 (80)	45.7 (32)	0.99		34.3 (70)	34.5 (41)	0.99	
High dose GC (≥10 mg/day)	14.0 (25)	18.6 (13)	0.43		9.2 (19)	8.9 (11)	0.93	
Immunosuppressive	55.1 (98)	50.0 (35)	0.48		32.0 (66)	30.1 (37)	0.81	

RDCI = Rheumatic Disease Comorbidity Index; SLAQ = Systemic Lupus Activity Questionnaire; BILD = Brief Index of Lupus Damage

Conclusion: High proportions of individuals in both of these SLE cohort had sleep disorders; prevalence was greater in the older cohort. Factors associated with sleep disorders – comorbid conditions, disease activity, and pain – were similar in the two cohorts. Given the association of sleep disorders with poor health outcomes, increased awareness of and screening for sleep disorders among SLE patients may be beneficial, particularly among older adults who may be more likely to have sleep disorders and be more sensitive to the negative impacts of sleep disorders.

Disclosure: P. Katz: None; **M. Dall'Era**: Annexon Biosciences, 2, 5, AstraZeneca, 2, Aurinia, 2, Biogen, 2, GlaxoSmithKlein, 2, 5, Pfizer, 2; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, Gilead, 5, Pfizer, 2; **K. Michaud**: None.

Abstract Number: 2503

Cytokines Regulate the Fibrotic Response of Growth Factors in Joint Fibroblast-like Synoviocytes

Sofie Falkenløve Madsen[1], Mikkel Rathsach Andersen[2], Alexander Scheller Madrid[2], Signe Holm Nielsen[3], Morten Karsdal[3], Christian Thudium[3] and Anne-Christine Bay-Jensen[3], [1]University of Copenhagen, Herlev, Denmark, [2]Herlev-Gentofte Hospital, Gentofte, Denmark, [3]Nordic Bioscience, Herlev, Denmark

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Cytokines & Cell Trafficking
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Rheumatoid arthritis (RA) and osteoarthritis (OA) are characterized by inflammation, joint swelling, stiffness, and pain. A fibroid phenotype has been identified in RA, where fibrosis is the key molecular feature, and inflammation is absent. Fibroblast-like synoviocytes (FLS) are located in the synovial membrane (SM), where they produce

extracellular matrix (ECM) components as a response to injury. The interplay between joint fibrosis and inflammation and its impact on ECM formation are poorly understood. We hypothesize that a fibro-inflammatory environment may affect the fibrotic response of FLS. Our objective was to characterize the fibrotic ECM profile of FLS in a fibro-inflammatory context to gain insights into the complex dynamics of fibrosis and inflammation in joint pathology.

Methods: Primary human FLS were isolated from the SM of patients undergoing total knee replacement surgery (n=8). The FLS were cultured in 0.4% fetal bovine serum DMEM with ficoll (to create a crowded environment) and ascorbic acid for 12 days. The growth factors, TGF-β1 [1 nM] and PDGF-AB [6 nM], and cytokines, IL-1β [0.5 nM] and TNF-α [0.5 nM] were added either alone or in combination. Non-treated FLS were used as control (w/o). Every 4 days, the supernatant was collected, and new treatments were added. PRO-C3, a type III collagen formation biomarker, was measured in the supernatant using a validated ELISA. 2-way ANOVA compared day-to-day differences with Tukey's multiple comparisons tests. In addition, the AUC for each patient was computed, and the treatment differences were compared using the Kruskal-Wallis test with Dunn's multiple comparisons tests.

Results: TGF-β increased the PRO-C3 formation from day 8 (D8) and PDGF from D4 compared to w/o ($p < 0.05$, Fig. 1A, 1B). Co-stimulation with TGF-β+IL-1β increased PRO-C3 on D4 compared to w/o ($p < 0.05$); however, it was not different from TGF-β or IL-1β alone (Fig. 1A). The AUC of co-stimulation with TGF-β+IL-1β were higher than w/o ($p < 0.05$, Fig. 1B).

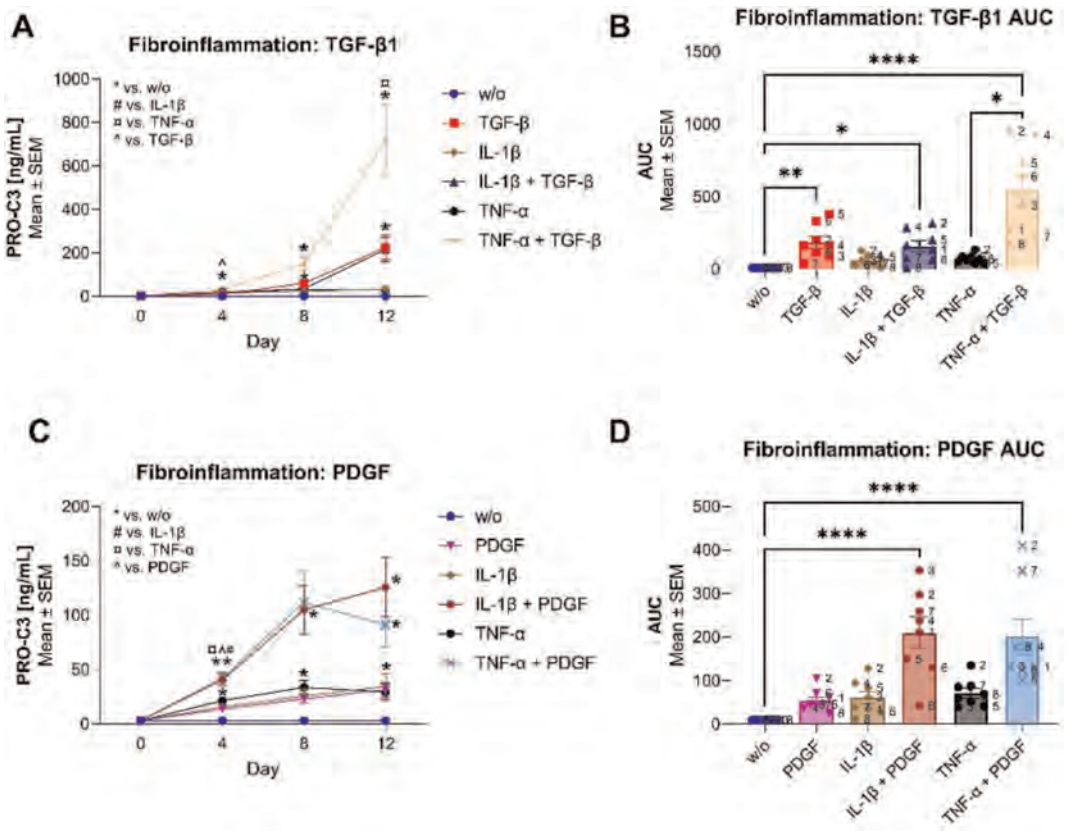

Figure 1 The effect of fibro inflammation on type III collagen formation (PRO-C3). A) PRO-C3 increases from single stimulation of TGF-β from D8, IL-1β on D4 and TNF-α on D4 and D8 compared to w/o. Co-stimulation of TGF-β+IL-1β increases PRO-C3 on D4 compared to w/o. Co-stimulation of TGF-β+TNF-α increases PRO-C3 compared to w/o from D4 and onwards, and to TGF-β on D4 and to TNF-α on D12. B) AUC increases from stimulation of TGF-β, TGF-β+IL-1β and TGF-β+TNF-α compared to w/o. Co-stimulation of TGF-β+TNF-α also increases AUC compared to TNF-α. No. indicates the different patients. C) PDGF and PDGF+IL-1β increases PRO-C3 from D4 and onwards compared to w/o. Co-stimulation of PDGF+IL-1β also increases PRO-C3 on D4 compared to PDGF and IL-1β. Co-stimulation of PDGF+TNF-α increases PRO-C3 compared to PDGF, TNF-α and w/o on D4, and to w/o on D12. D) Co-stimulation of PDGF+IL-1β and PDGF+TNF-α increases the AUC compared to w/o. No. indicates the different patients. A significance level of $p \leq 0.05$ was employed, and symbols denote the level * = $p<0.05$, ** =$p<0.01$, *** =$p<0.001$, **** =$p<0.0001$.

In contrast, co-stimulation with TGF-β+TNF-α increased PRO-C3 compared to w/o from D4 and onwards, and were higher than TGF-β on D4 and TNF-α on D12 ($p< 0.05$, Fig. 1A). The AUC of TGF-β+TNF-α was increased compared to w/o and TNF-α ($p< 0.0001$ and $p< 0.05$, respectively, Fig. 1B). Co-stimulation of PDGF+IL-1β, increased PRO-C3 from D4 and onwards compared to w/o, and to PDGF and IL-1β on D4 ($p< 0.05$, Fig. 1C). The AUC of the co-stimulation was increased compared with w/o ($p< 0.0001$, Fig. 1D). A similar trend was found for co-stimulation of PDGF+TNF-α. Here, PRO-C3 was increased on D4 and D12 compared to w/o and compared to PDGF and TNF-α on D4 ($p< 0.05$, Fig. 1C). The AUC of the co-stimulation was higher than w/o ($p< 0.0001$, Fig. 1D).

Conclusion: In conclusion, the combination of inflammatory cytokines and fibrotic growth factors induces a heightened fibrotic response, particularly increasing type III collagen formation, more than the fibrotic growth factors alone. These data suggest that the coexistence of fibrosis and inflammation could potentially influence the mechanisms driving joint damage in RA and OA. This underscores the potential need for therapeutic strategies targeting both fibrosis and inflammation in patients with arthritis.

Disclosure: S. Madsen: None; **M. Andersen**: None; **A. Scheller Madrid**: None; **S. Holm Nielsen**: Nordic Bioscience, 3, 8; **M. Karsdal**: Nordic Bioscience, 3, 4, 8; **C. Thudium**: Nordic Bioscience, 3, 11; **A. Bay-Jensen**: Nordic Bioscience, 3, 3, 8, 9.

Abstract Number: 2504

The Effect of Inflammatory Conditions on the Regulation of Canonical and Non-canonical NF-kB Pathways via Bcl11b

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Cytokines & Cell Trafficking
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: *Bcl11b*, a zinc finger bi-functional transcription factor, is highly expressed in various tissues during development and differentiation, including stromal cells. It has been shown that Bcl11b has an impact on Th17 responses. Recently we found using a bioinformatic analysis that *Bcl11b* is down-regulated in psoriatic skin. In addition to Bcl11b, other transcription factors, such as NF-kB, are also involved in immune-mediated diseases that can be activated by cytokine stimulation. However, the mechanism of activation and regulation of pathways related to these transcription factors has not been identified.

To investigate the role of *Bcl11b* in the regulation of NF-kB pathways in keratinocytes under naïve and inflammatory conditions.

Methods: : HaCaT keratinocytes were cultured and *Bcl11b* was knocked down in these cells using the CRISPRi approach. qPCR and WB were performed to analyze the RNA and protein levels of *Bcl11b*, control genes, and NF-kB pathway genes. In addition, the effect of IL-17A, IL-23, TNF, IL-23/TNF, and IL-17A/IL-23 on the activation of the canonical and non-canonical NF-kB pathways in HaCaT keratinocytes was investigated in the presence or absence of *Bcl11b*.

Results: To mimic the lower expression of Bcl11b that has been found in different autoimmune diseases, *Bcl11b* was knocked down in keratinocytes, which was confirmed using q-PCR and WB. Gene expression analysis and/or WB of NF-kB pathways including NF-kB1, TNF, NF-kB2, RELB, and NIK indicated an upstream role of *Bcl11b* in both the canonical and non-canonical NF-kB pathways. We further analyzed these pathways under inflammatory conditions. Cytokine stimulation showed that the IL-17A, IL-17/IL-23, and IL-23/TNF can rescue the down-regulation of *Bcl11b* expression. None of these cytokines are able to activate the canonical NF-kB pathway under Bcl11b knockdown condition. Interestingly, IL-17A and IL-23/TNF, but not IL-23 or TNF alone, are able to activate the non-canonical NF-kB pathway in the absence of Bcl11b.

Conclusion: Here, we showed for the first time the role of *Bcl11b* and its interaction with the canonical and non-canonical NF-kB pathways in keratinocytes. Our data suggest that pro inflammatory cytokines have different effects on *Bcl11b* dependent activation of NF-kB pathways. Since Bcl11b acts both directly, and indirectly to promoter regions, this may impact its effect on the NF-kB pathways in different inflammatory conditions. Further studies are warranted to unravel the interaction of Bcl11b and these two NF-kB pathways.

Disclosure: S. Parsa: None; **S. Rahmani**: None; **N. Davelaar**: None; **A. M.C.mus**: None; **E. Lubberts**: None.

Abstract Number: 2505

Discovery of First-in-Class IRAK4 Scaffolding Inhibitors for the Treatment of Inflammatory Disorders

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Cytokines & Cell Trafficking
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Interleukin-1 receptor-associated kinase 4 (IRAK4), is a key node that mediates inflammatory signaling in response to activation of toll-like receptor (TLR) and IL-1 receptor (IL-1R) activation making it an attractive target for treating inflammatory diseases. IRAK4 has multiple functions, including kinase activity and a scaffolding activity that bridges the interaction between MYD88 and IRAK1/2, which is a critical interaction for signal transduction from the myddosome. IRAK4 kinase inhibitors cannot block signaling in cells outside the myeloid compartment and reducing IRAK4 protein by targeted degradation fails to maximally block IRAK4 signaling. Thus, targeting scaffolding directly is an attractive approach to inhibit IRAK4 across a range of disease relevant cell types. Here, we describe compounds that bind to IRAK4, directly block scaffolding activity, and are effective at inhibiting IRAK4 signal transduction and cytokine production across a range of disease relevant cell types.

Methods: IRAK4 degraders, kinase inhibitors, and scaffolding inhibitors were tested for their ability to block scaffolding with recombinant proteins and in myeloid and non-myeloid cells and for their ability to inhibit cytokine production in primary cells responding to TLR ligands or IL-1 stimulation. The effect of scaffolding inhibitors in mice was determined by assessing TNF production following lipopolysaccharide (LPS) exposure, and chemokine production and neutrophil recruitment in a urate crystal model of gout.

Results: IRAK4 scaffolding inhibitors blocked recombinant IRAK4 binding both to IRAK1 and IRAK2 in vitro and in cells, whereas kinase inhibitors and protein degraders had no effect. To identify a relationship between scaffolding activity and proinflammatory signaling, the effect of these compounds on cytokine production was assessed in a panel of cells. In peripheral blood mononuclear cells (PBMCs) each compound blocked cytokine production. However, in certain disease relevant cell types, including fibroblasts, synoviocytes, osteoclasts, chondrocytes, and keratinocytes from healthy subjects or patients with inflammatory diseases only the scaffolding inhibitors blocked cytokine production in a robust fashion. Oral administration of the scaffolding inhibitor to mice dose-dependently reduced serum TNF produced in response to LPS and significantly reduced chemokine production and neutrophil recruitment in a model of gout.

Conclusion: Our data suggest that inhibiting IRAK4 scaffolding is an effective mechanism to inhibit IRAK4 signaling and unlike IRAK4 kinase inhibitors and degraders, has robust activity against disease relevant cell types. As such, blocking IRAK4 scaffolding represents a novel therapeutic approach to treat inflammatory diseases with the potential to achieve greater efficacy relative to previous approaches to drug this target.

Disclosure: K. Byth: Bicycle Therapeutics, 3, 4, 8; **R. Morgan**: Odyssey therapuetics, 11; **P. Michelys**: Novartis, 3, 11, odyssey therapeutics, 3, 11; **K. Demock**: None; **G. Kannan**: None; **Q. Chen**: None; **B. Sanchez**: None; **X. Lu**: None; **A. Telling**: None; **C. Lesch**: None; **C. Yu**: None; **S. Bradley**: None; **B. Andresen**: Merck/MSD, 3, Odyssey Therapeutics, Inc., 3; **S. Hassanien**: None; **C. Taylor**: None; **Z. Hou**: None; **K. Borrelli**: None; **A. Gardberg**: Morphosys, 3, Odyssey Therapeutics, 3; **E. Munschy**: None; **A. Schwaid**: None; **A. Opipari**: Odyssey Therapeutics, 3; **S. Pan**: None; **L. Franchi**: Odyssey Therapeutics, 3, 11.

Abstract Number: 2506

Role of TGF-β Activated Kinase 1 in Cytokine-Driven Juvenile Idiopathic Arthritis Synovial Fibroblasts Activation

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Cytokines & Cell Trafficking
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Chronic synovitis is a debilitating manifestation of juvenile idiopathic arthritis (JIA). Synovial fibroblast is a major preparator of inflammatory arthritis and has not been well studied in JIA. Thus, we aimed to study the involvement of TGF-β activated kinase 1 (TAK1) in cytokine-driven JIA synovial fibroblasts (JIASFs) activation and subsequent induction of inflammatory arthritis.

Methods: JIASFs were isolated from the synovial fluids aspirated from the knees of deidentified JIA patients. JIASFs were treated with TNF-α and IL-1β (0-120 minutes) to study the phosphorylation of TAK1 and downstream signaling pathways. To investigate the overall impact of TAK1 inhibition, RNA sequencing (RNA-seq) analysis of JIASFs following IL-1β stimulation with and without TAK1 inhibitor- 5Z-7-oxozeaenol (5Z) was conducted. JIASFs treated with NG-25 (reversible TAK1 inhibitor) and 5Z (irreversible TAK1 inhibitor) were also examined for the expression of p-TAK1, p-p38, p-ERK, and p-JNK via Western blotting. To study the involvement of TAK1 in inducing JIASF aggressive and inflammatory phenotype, the

expression of COX-2, podoplanin, IL-6, IL-8, CXCL5, and CCL5 following 5Z treatment were determined dose-dependently via ELISA and Western blotting. The statistical value of $p< 0.05$ was considered statistically significant.

Results: RNA-seq analysis identified 2,076 differentially expressed genes significantly regulated by IL-1β (10 ng/mL; n=3, $p< 0.05$). A total of 502 genes, mostly involved in inflammation and aberrant cell proliferation, were upregulated by IL-1β, and 1,574 genes primarily responsible for controlled cell proliferation and homeostasis were downregulated by IL-1β. Among those 2,076 genes, 707 genes were significantly altered following 5Z (1 μM) treatment, of which 389 genes were significantly upregulated whereas 318 genes were significantly downregulated by 5Z treatment. Gene Ontology studies on RNA-seq revealed that 5Z suppressed the genes involved in cytokine signaling in the immune system, and inflammation, and restored the genes involved in the negative regulation of centriole replication, and regulation of the cell cycle process. Furthermore, the treatment with 5Z or NG-25 (0.01 to 1 μM) followed by IL-1β (10 ng/mL) stimulation revealed that 5Z significantly inhibited the p-TAK1 at 0.01 μM ($p < 0.001$, n = 3) and p-p38, p-JNK and p-ERK at 0.1 μM ($p < 0.0001$, n= 3). Whereas NG-25 significantly suppressed p-TAK1 at 1 μM ($p < 0.05$, n=3) and its downstream p-p38 and p-JNK at 0.1 μM and 0.5 μM, respectively. 5Z also significantly downregulated the expression of COX-2 (at 0.05 μM, $p< 0.01$, n=3), IL-8 and CXCL5 (at 0.01 μM, $p< 0.01$, n=3). The expression of podoplanin, IL-6 and CCL5 also went down following 5Z treatment (at 0.25 μM, n=3) indicating the overall potential of TAK1 inhibition to limit JIASFs ability to exacerbate arthritis.

Conclusion: Our preliminary findings delineate the critical role of TAK1 in cytokine-driven hyperplasia and invasiveness of JIASFs, and the inhibition of TAK1 *in vitro* promises cessation of JIASF- mediated expression of inflammatory markers.

Disclosure: M. Shanta: None; **A. Singh**: None; **P. Panipinto**: Regeneron, 3; **S. Ahmed**: None.

Abstract Number: 2507

ZCCHC6 Modulates the Global Phosphorylation Landscape in TNF-a-induced Rheumatoid Arthritis Synovial Fibroblasts

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Cytokines & Cell Trafficking
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: ZCCHC6, also known as TUT7 or TENT2, plays a crucial role in RNA processing and metabolism through its uridylyl transferase function. This function involves adding uridine residues to the 3' ends of RNA molecules, including mRNA and microRNAs and is important for regulating RNA stability, decay, and turnover. However, its role in pro-inflammatory cytokines, such as IL-1β and TNF-α induced inflammatory function, remains elusive.

Methods: To investigate the role of ZCCHC6 in TNF-α-induced inflammation, RNA-seq analysis was performed in human rheumatoid arthritis synovial fibroblasts (RASFs) treated with TNF-α alone or with ZCCHC6 knockdown using siRNA method. Mass Spectrometry based untargeted phospho-proteomics analysis was conducted to determine changes in the global phosphorylation landscape of RASFs treated with ZCCHC6 siRNA in the presence of TNF-α stimulation. Additionally, Gene Ontology studies, ELISA, quantitative RT-PCR, and Western blot analyses were performed to determine the effect on inflammatory responses in TNF-α-activated RASFs with or without ZCCHC6 knockdown. The experiments were carried out using at least three RASF donor lines, with statistical significance set at $p< 0.05$.

Results: ZCCHC6 knockdown in human RASFs resulted in the differential regulation of 835 genes in the presence of TNF-α. Out of these genes, 384 genes were upregulated, whereas 451 genes were downregulated by at least 2-fold (N=3, p< 0.05). ZCCHC6 exhibited anti-inflammatory effects in TNF-α-stimulated RASFs, as its knockdown by targeted siRNA by enhanced the phosphorylation of signaling proteins important in MAPK-activated pathways, including ASK1, cJun, pERK, p38, pP65, and SAPK/JNK proteins (N=3, p< 0.05). The MS-based phospho-proteomic analysis confirmed that ZCCHC6 knockdown selectively influenced the phosphorylation of 263 unique proteins (N=3, p< 0.05). Gene Ontology studies revealed the upregulation of key pathways, such as mRNA metabolism, apoptosis, DNA damage, and cellular localization. Further analysis demonstrated critical changes in the cellular activity of phosphorylation events that are tightly regulated by Protein Phosphatase 2A (PP2A), a serine/threonine phosphatase. A loss of ZCCHC6 inhibited the TNF-α-induced expression of three regulatory subunits of PP2A, including the structural subunit (A), catalytic subunit (C), and regulatory subunit (B).

Conclusion: This study unveils a novel axis involving ZCCHC6 and TNF-α in the progression of RA. TNF-α utilizes ZCCHC6 to mediate internal phosphorylation signaling events, positively influencing Protein Phosphatase activity, and driving the pathological processes underlying inflammation in RA.

Disclosure: A. Singh: None; **F. Shaikh**: None; **S. Ahmed**: None.

Abstract Number: 2508

Chronic IL-6 Trans-Signaling Enhances Stem Cell-Like Characteristics of Rheumatoid Arthritis Synovial Fibroblasts

Anil Singh and Salahuddin Ahmed, Washington State university, Spokane, WA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Cytokines & Cell Trafficking
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Chronic exposure to IL-6 trans-signaling has been shown to significantly impact the characteristics of rheumatoid arthritis synovial fibroblasts (RASFs). Previous studies have demonstrated that this exposure increases heterogeneity markers, upregulates reprogramming factors, and transforms RASFs into cells with stem cell-like characteristics. Moreover, the transcription factor Ets2 has been identified as a crucial player in these effects, as it is upregulated and translocated to the nucleus of RASFs upon IL-6 trans-signaling stimulation.

Methods: To further explore the role of Ets2 in IL-6-induced inflammation, comprehensive analyses were performed. RNA-seq analysis was conducted on RASFs treated with IL-6 + IL6R, either alone or in combination with Ets2 knockdown using siRNA. Mass spectrometry-based untargeted phospho-proteomics analysis was utilized to evaluate global protein changes in RASFs. Additional RNA sequencing was carried out, and the data were evaluated using ELISA, quantitative RT-PCR, and Western blot analyses. The experiments involved multiple RASF donor lines, with statistical significance set at p< 0.05.

Results: Chronic IL-6 trans-signaling promotes stem cell-like characteristics in rheumatoid arthritis synovial fibroblasts (RASFs), as evidenced by the upregulation of Nanog, OCT4, Sox2, and Myc. This effect is also observed in normal synovial fibroblasts (NSFs), indicating a broader influence on cell differentiation. Proteomics analysis confirmed the upregulation of stemness markers and metabolic intermediates associated with glycolysis in IL-6 trans-stimulated RASFs. Inhibition of the

Ets2 transcription factor resulted in the downregulation of Nanog, Myc, and Sox2, suggesting that Ets2 drives the reprogramming of RASFs to a stem cell-like phenotype (N=3, $p< 0.05$). IL-6 trans-signaling induced the upregulation of CD90/Thy1, a marker of mesenchymal stem cells, which was reversed by Ets2 knockdown (N=3, $p< 0.05$). The downregulation of heterogeneity markers Thy1 and PDPN without Ets2 implies that IL-6 employs Ets2 to drive both inflammatory and differentiation functions in RASFs. RNA sequencing identified 506 differentially regulated genes (N=3, $p< 0.05$), with the enrichment of stem cell factors in the transcriptomics data. These findings shed light on the impact of chronic IL-6 trans-signaling on RASFs and highlight the role of Ets2 in regulating inflammatory and differentiation processes. Understanding these molecular events could lead to novel therapeutic strategies for rheumatoid arthritis.

Conclusion: To further explore the molecular changes induced by chronic IL-6 trans-signaling, we performed RNA sequencing on RASFs that were continuously stimulated with IL-6 + sIL6R. Our analysis identified 506 differentially regulated genes, with stem cell factors like Sox2, Myc, Oct4, Nanog, among others, showing enrichment in the transcriptomics data. The role of Ets2 as a key mediator in this process highlights its significance in regulating both inflammatory and differentiation functions.

Disclosure: A. Singh: None; **S. Ahmed**: None.

Abstract Number: 2509

Risk Factors and Mortality of Immune Checkpoint Inhibitor-Induced Flares of Pre-Existing Rheumatoid Arthritis: An Analysis Accounting for Competing Risk of Death and Immortal Time Bias

Kaitlin McCarter[1], Senada Arabelovic[1], Taylor Wolfgang[1], Xiaosong Wang[1], Kazuki Yoshida[1], Grace Qian[1], Emily Kowalski[1], Kathleen Vanni[1], Nicole LeBoeuf[1], Elizabeth Buchbinder[2], Lydia Gedmintas[1], Lindsey MacFarlane[1], Deepak Rao[1], Nancy Shadick[3], Ellen Gravallese[4] and Jeffrey Sparks[5], [1]Brigham and Women's Hospital, Boston, MA, [2]Dana-Farber Cancer Institute, Boston, MA, [3]Brigham and Women's Hospital, Boston, MA, [4]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [5]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Immunological Complications of Medical Therapy
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Immune checkpoint inhibitors (ICI) stimulate the immune system to treat cancer but may cause flares of pre-existing immune-mediated inflammatory diseases. Risk factors for ICI-induced RA flares are unknown. Some studies suggest that flare of pre-existing autoimmune disease after ICI may portend a mortality benefit, perhaps as a marker of immune activity against cancer, but this has not been investigated for ICI-induced RA flares. Evaluating a post-baseline outcome such as RA flare could be prone to immortal time bias where patients must survive long enough to flare, falsely showing an association with mortality. Therefore, we studied risk factors and outcomes of ICI-induced RA flares, considering competing risk of death and immortal time bias in the analysis.

Methods: We performed a retrospective cohort study of patients with pre-existing RA initiating ICI for cancer treatment at a large healthcare system (2011-2022). We performed medical record review on patients with a RA diagnosis code prior to ICI initiation to confirm patients met 2010 ACR/EULAR RA criteria. We collected data on demographics, cancer, RA, RA disease activity/flares after ICI initiation, ICI disruption, and mortality. We analyzed baseline risk factors for RA flare after ICI

initiation taking into account competing risk of death using the Fine and Gray method. We performed a landmark analysis to limit the potential for immortal time bias, where baseline was 3 months after ICI initiation. Among those who survived at least 3 months, we examined whether RA flare within 3 months after ICI initiation was associated with mortality using Cox regression.

Results: Among 11,901 patients who initiated ICI for cancer treatment, we analyzed 100 pre-existing RA patients (mean age 70.3 years, 63% female, 89% on PD-1 monotherapy, 50% lung cancer). At ICI initiation, 71% were seropositive, 82% had remission/low RA disease activity, 24% were on glucocorticoids, 35% were on conventional DMARDs, and 10% were on b/tsDMARDs (**Table 1**). RA flares occurred in 46% (incidence rate 1.84 per 1000 person-days, 95%CI 1.30, 2.37); 31/100 flared within 3 months of baseline. 72% died during follow-up, 21/100 within 3 months of baseline. Seropositive RA had an adjusted sdHR of 1.95 (95%CI 1.02, 3.71) for RA flare compared to seronegative, accounting for competing risk of death (**Table 2**). Otherwise, there were no baseline factors associated with RA flare, including cancer type, baseline disease activity, RA duration, and deformities. 9/46 (20%) patients had their ICI discontinued/paused due to RA flares. In the

Table 1. Baseline characteristics of pre-existing RA patients at index date of immune checkpoint inhibitor initiation (n=100).

	Pre-existing RA patients initiating ICI (n=100)
Demographics and smoking	
Mean age, years (SD)	70.3 (10.6)
Female sex, %	63%
White race, %	94%
Ever smoker, %	73%
Median pack-years (IQR)	20 (0, 40)
Cancer characteristics	
Target of ICI, %	
PD-1	89%
PD-L1	4%
CTLA-4	5%
Combination	2%
Type of cancer, %	
Lung	50%
Melanoma	20%
Genitourinary tract	9%
Gastrointestinal tract	5%
Head and neck	4%
Other	12%
Median cancer duration, years (IQR)	0.8 (0.1, 2.1)
Previous chemotherapy, hormonal therapy, radiation, or stem cell transplant, n (%)	76%
RA characteristics	
Median RA duration, years (IQR)	9.4 (4.8, 17.4)
Seropositive, %	59/83 (71%)
Anti-CCP+, %	41/67 (61%)
RF+, %	47/68 (69%)
RA disease activity, %	
Remission/low	63/77 (82%)
Moderate/high	14/77 (18%)
Bone erosions or other deformities, %	33%
Glucocorticoids and/or DMARD use, %	51%
Glucocorticoid use, %	24%
DMARD use, %	35%
csDMARD use, %	27%
b/tsDMARD use, %	10%

*Other cancers were hematologic, brain, breast cancer, mesothelioma, Merkel cell carcinoma, and neuroendocrine carcinoma.

Anti-CCP, anti-cyclic citrullinated peptide; b/tsDMARD, biologic or targeted synthetic disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; CTLA-4, cytotoxic T-lymphocyte-associated protein 4; DMARD, disease-modifying antirheumatic drug; ICI, immune checkpoint inhibitor; IQR, interquartile range; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; RA, rheumatoid arthritis; RA, rheumatoid arthritis; RF, rheumatoid factor; SD, standard deviation.

Table 2. Risk of RA flare after immune checkpoint inhibitor initiation by baseline factors, accounting for competing risk of death.

	RA flare cases	Person-days	Incidence rate (95%CI) per 1000 person-days	Unadjusted competing risk sdHR for RA flare (95%CI)	Age-adjusted competing risk sdHR for RA flare (95%CI)
Age (per year)	46	25,068	1.84 (1.30, 2.37)	0.98 (0.96, 1.01)	0.98 (0.96, 1.01)
Sex					
Female	26	14,162	1.84 (1.13, 2.54)	1.0 (Ref)	1.0 (Ref)
Male	20	10,906	1.83 (1.03, 2.64)	1.20 (0.67, 2.14)	1.11 (0.61, 2.01)
Pack-years (per unit)	46	25,068	1.84 (1.30, 2.37)	1.00 (0.98, 1.01)	1.00 (0.98, 1.01)
Type of cancer					
Lung	20	10,448	1.91 (1.08, 2.75)	1.0 (Ref)	1.0 (Ref)
Melanoma	13	6,842	1.90 (0.87, 2.93)	1.53 (0.75, 3.13)	1.53 (0.75, 3.12)
All others	13	7,778	1.67 (0.76, 2.58)	1.03 (0.52, 2.02)	1.03 (0.53, 2.02)
Cancer duration (per year)	46	25,068	1.84 (1.30, 2.37)	**1.18 (1.02, 1.35)**	1.15 (0.99, 1.33)
RA duration (per year)	46	25,068	1.84 (1.30, 2.37)	1.01 (0.99, 1.03)	1.02 (0.99, 1.04)
RA serostatus					
Seronegative	10	9,305	1.07 (0.41, 1.74)	1.0 (Ref)	1.0 (Ref)
Seropositive	32	10,722	2.98 (1.95, 4.02)	**2.01 (1.03, 3.91)**	**1.95 (1.02, 3.71)**
RA disease activity at ICI initiation					
Remission/low	33	16,578	1.99 (1.31, 2.67)	1.0 (Ref)	1.0 (Ref)
Moderate/severe	8	1,142	7.01 (2.15, 11.9)	1.57 (0.71, 3.44)	1.76 (0.81, 3.82)
RA treatment at ICI initiation					
No treatment	22	11,016	2.00 (1.16, 2.83)	1.0 (Ref)	1.0 (Ref)
Glucocorticoids and/or DMARD	24	14,052	1.71 (1.02, 2.39)	1.12 (0.63, 1.99)	1.29 (0.70, 2.37)
RA deformities					
No	30	18,488	1.62 (1.04, 2.20)	1.0 (Ref)	1.0 (Ref)
Yes	16	6,580	2.43 (1.24, 3.62)	1.17 (0.65, 2.14)	1.39 (0.74, 2.63)

CI, confidence interval; DMARD, disease-modifying antirheumatic drug; ICI, immune checkpoint inhibitor; RA, rheumatoid arthritis; sdHR, subdistribution hazard ratio.

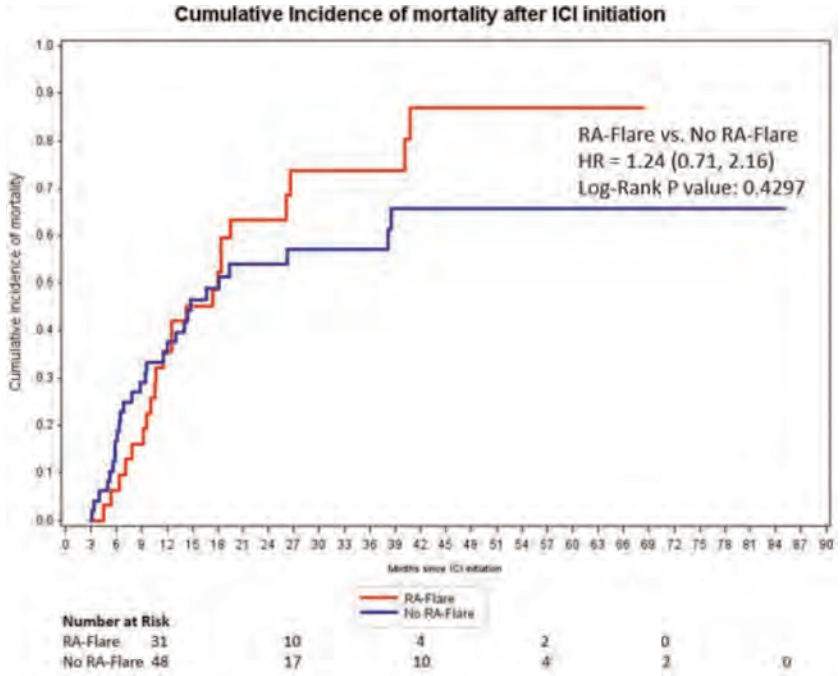

Figure 1. Cumulative incidence and hazard ratio for mortality by presence/absence of RA flare within 3 months of immune checkpoint inhibitor initiation. The landmark analysis was restricted to patients who survived at least 3 months after immune checkpoint inhibitor initiation (n=79). The model was adjusted for age, sex, cancer type (lung/melanoma/other), cancer duration, and Charlson comorbidity index.

landmark analysis among 79 patients who survived at least 3 months, RA flare in the first 3 months was not associated with lower mortality (adjusted HR 1.24, 95%CI 0.71, 2.16) compared to no RA flare (**Figure**).

Conclusion: RA flares and mortality were each common among pre-existing RA patients initiating ICI for cancer. Seropositivity was the only baseline factor associated with RA flare after accounting for the competing risk of death. RA flare after ICI may not have prognostic implications for mortality. Previous findings suggesting mortality benefit from flares of other autoimmune diseases after ICI may have been due to immortal time bias.

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Abstract Number: 2510

Autoantibody-positivity Before Treatment Is Associated with Immune-related Adverse Events in Melanoma Patients Treated with anti-PD-1

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Immunological Complications of Medical Therapy
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: PD-1 immune checkpoint inhibitors are able to re-activate restrained anti-tumor T-cell responses in melanoma patients. However, PD-1 inhibition may also activate auto-reactive T-cells leading to immune-related adverse events (irAEs). Autoantibodies might also play a role in anti-PD-1 induced irAEs and could potentially be used to identify patients at risk of developing these irAEs. Therefore, we investigated the association between autoantibody-positivity and treatment toxicity and response in melanoma patients treated with anti-PD-1.

Methods: This multicenter, retrospective study included 143 advanced melanoma patients treated with anti-PD-1. Until six months after treatment initiation, toxicities grade ≥2 and recurrences/responses were captured. Autoantibody measurements, comprising IgM rheumatoid factor (RF), antinuclear antibodies (ANA), anti-cyclic citrullinated peptide antibodies (anti-CCP2), anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-Tg) were performed in an ISO15189 accredited laboratory at baseline and after three months of treatment.

Table 1. Association of baseline autoantibodies with immune-related adverse events (irAE). In each cell, n/N indicates the number of patients who developed the irAE (n) out of the total number of patients who were either positive or negative at baseline for the indicated antibody (N). Anti-CCP2: anti-cyclic citrullinated peptide antibodies, RF: rheumatoid factor, anti-TPO: thyroid peroxidase, anti-TG: anti-thyroglobulin, ANA: antinuclear antibodies

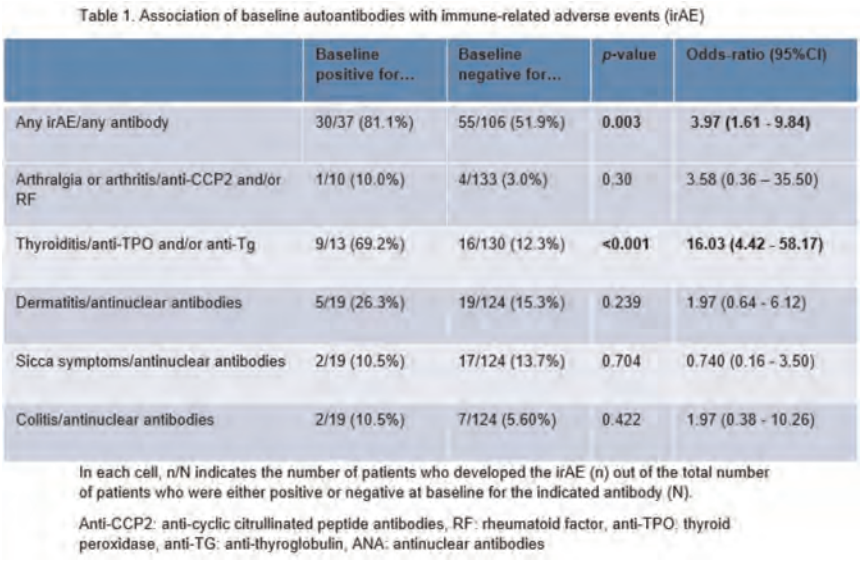

Table 1. Association of baseline autoantibodies with immune-related adverse events (irAE)

	Baseline positive for...	Baseline negative for...	p-value	Odds-ratio (95%CI)
Any irAE/any antibody	30/37 (81.1%)	55/106 (51.9%)	**0.003**	**3.97 (1.61 - 9.84)**
Arthralgia or arthritis/anti-CCP2 and/or RF	1/10 (10.0%)	4/133 (3.0%)	0.30	3.58 (0.36 – 35.50)
Thyroiditis/anti-TPO and/or anti-Tg	9/13 (69.2%)	16/130 (12.3%)	**<0.001**	**16.03 (4.42 - 58.17)**
Dermatitis/antinuclear antibodies	5/19 (26.3%)	19/124 (15.3%)	0.239	1.97 (0.64 - 6.12)
Sicca symptoms/antinuclear antibodies	2/19 (10.5%)	17/124 (13.7%)	0.704	0.740 (0.16 - 3.50)
Colitis/antinuclear antibodies	2/19 (10.5%)	7/124 (5.60%)	0.422	1.97 (0.38 - 10.26)

In each cell, n/N indicates the number of patients who developed the irAE (n) out of the total number of patients who were either positive or negative at baseline for the indicated antibody (N).

Anti-CCP2: anti-cyclic citrullinated peptide antibodies, RF: rheumatoid factor, anti-TPO: thyroid peroxidase, anti-TG: anti-thyroglobulin, ANA: antinuclear antibodies

Results: A total of 169 irAEs were experienced by 86 patients, the most common being thyroiditis (n=25), dermatitis (n=24), and sicca complaints (n=19). More irAE (30/37 [81%]) were observed in patients with pre-existing detectable autoantibodies than in patients without these autoantibodies (55/106 [52%], $p = 0.003$) (table 1). This was mainly due to the strong association of anti-thyroid antibodies and thyroid dysfunction (69% in anti-TPO and/or anti-Tg positive patients versus 12% in anti-TPO and/or anti-Tg negative patients, $p < 0.001$). No association between anti-CCP2, RF or ANA and arthritis, dermatitis, sicca or colitis was observed. The association with thyroid antibodies was strongest in female patients: of seropositive female patients 7/7 (100%) developed thyroiditis, compared to only 10/48 (21%) of anti-TPO and anti-Tg negative patients.

Seroconversion during anti-PD-1-treatment was only seen for thyroid antibodies. Here the combined positivity for anti-TPO and/or anti-Tg increased from 13/143 (9.1%) at baseline to 24/143 (17%) on treatment ($p = 0.003$). For the other autoantibodies the total number of seropositive patients stayed stable or decreased on treatment (table 2). Seroconversion of anti-Tg and/or anti-TPO was associated with thyroid dysfunction in female patients: 6/10 [60%] of seroconverted patients developed thyroid dysfunction compared to 3/38 [8%] patients that remained seronegative ($p = 0.001$). Autoantibody-positivity was not associated with disease recurrence ($p = 0.45$) or response ($p = 0.69$).

Table 2. Number of autoantibody-positive patients per antibody (RF, anti-CCP2, anti-TG, anti-TPO and ANA) at baseline and on treatment. Anti-CCP2: anti-cyclic citrullinated peptide antibodies, RF: rheumatoid factor, anti-TPO: thyroid peroxidase, anti-TG: anti-thyroglobulin, ANA: antinuclear antibodies

Autoantibody	Baseline (positive/total)	On treatment (positive/total)	Seroconversion (neg to pos)	Seroreversion (pos to neg)
RF	10/143 (6.99%)	10/143 (6.99%)	3	3
Anti-CCP2	0/143 (0%)	0/143 (0%)	0	0
Anti-Tg	7/143 (4.90%)	22/143 (15.4%)	15	0
Anti-TPO	7/143 (4.90%)	12/143 (8.39%)	6	1
ANA	19/143 (13.3%)	17/143 (11.9%)	2	4

Conclusion: Autoantibody-positivity prior to anti-PD-1 therapy is associated with the development of irAEs in melanoma patients, indicating that anti-PD-1 therapy not only leads to loss of tolerance to tumor antigens but also to nontumor autoantigens. Baseline positivity and seroconversion of anti-thyroid antibodies were associated with the development of thyroiditis.

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Abstract Number: 2511

Superior SARS-CoV-2 Antibody Response Achieved in Rituximab-treated Patients When Vaccinated Against COVID-19 Before Compared to After Rituximab Initiation – Guidance for Future Vaccination Strategies

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SESSION INFORMATION

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Session Title: Abstracts: Immunological Complications of Medical Therapy

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Background/Purpose: Rituximab (RTX) treatment significantly decreases the antibody response to COVID-19 vaccines, raising concerns about its use. However, unlike during the pandemic, most patients initiating RTX now, will receive COVID-19 vaccination before initiating RTX. Thus, the effect of RTX treatment on serological vaccine response in pre-vaccinated individuals remains unclear. We aimed to assess the antibody (abs) level and function by three different SARS-CoV-2 abs assays in COVID-19 vaccinated patients, depending on the timing of RTX treatment initiation, either before or after vaccination.

Methods: Patients treated with RTX at the Dep. of Rheumatology, Aarhus University Hospital, from 2017 to 2022 were eligible for inclusion (n=368). Patients were categorized based on the order of RTX treatment to their primary COVID-19 vaccination: *RTX pre* (RTX only prior to vaccination), *RTX pre+post* (RTX prior to and after vaccination), and *RTX post* (RTX only after vaccination). Additionally, we investigated the effect of vaccines administered ≥ 9 months since the last RTX treatment, "*RTX-free*" vaccinations. Serological response was evaluated by measuring 2 different SARS-CoV-2-IgGs (Spike and Nucleocapsid) and the concentration and activity of neutralizing antibodies. Blood donors (BDs) were enrolled as controls, n=113.

Results: We included 254 patients; 67% female, aged 62 years. The predominant diagnoses were ANCA-vasculitis (31%), rheumatoid arthritis (26%) and myositis (12%). Patients had on average four COVID-19 vaccinations and one infection, while BDs had respectively three and one.

The *RTX pre+post* group (n=132) had significantly lower concentrations of spike and neutralizing abs, neutralizing activity and seroconversion compared to the *RTX pre (n=54)* and *RTX post*group(n=68), Fig 1A-D. Only 65% of *RTX pre+post*developed neutralizing abs compared to 91% for the*RTX post* and 93% for the*RTX pre,* Fig 1C. There was no difference between the *RTX pre* or *RTX post* in seroconversion of the 3 abs measured (all p's ≥ 0.08).

Univariate and multivariate logistic regression analysis were performed with seroconversion of SARS-CoV-2-Spike IgG as the dependent variable, Table 1. The final model had number of "*RTX-free*" vaccinations (OR 1.93) and number of RTX infusions (OR 0.94) as the significant predictors.

There was a significant dose-dependent correlation between "*RTX-free*" vaccinations with both antibody concentrations and seroconversion (Fig 2A, P< 0.001). The patients with zero "*RTX-free*" vaccinations had a seroconversion rate of 50%, compared to 89% for patients with 3 "*RTX-free*" vaccinations and40-fold higher median ab levels.

Conclusion: Our study demonstrates that COVID-19 vaccination administered before initiating RTX will induce a superior serological response compared to vaccination after RTX treatment. This supports the continuous use of RTX in rheumatic diseases with an emphasis on administering vaccinations before initiating RTX. Additionally, our findings highlight the importance of timing vaccinations for individuals undergoing continuous RTX treatment. The concept of "*RTX-free*" vaccinations with a minimum gap of 9 months since last RTX treatment may be useful in guiding vaccination strategies.

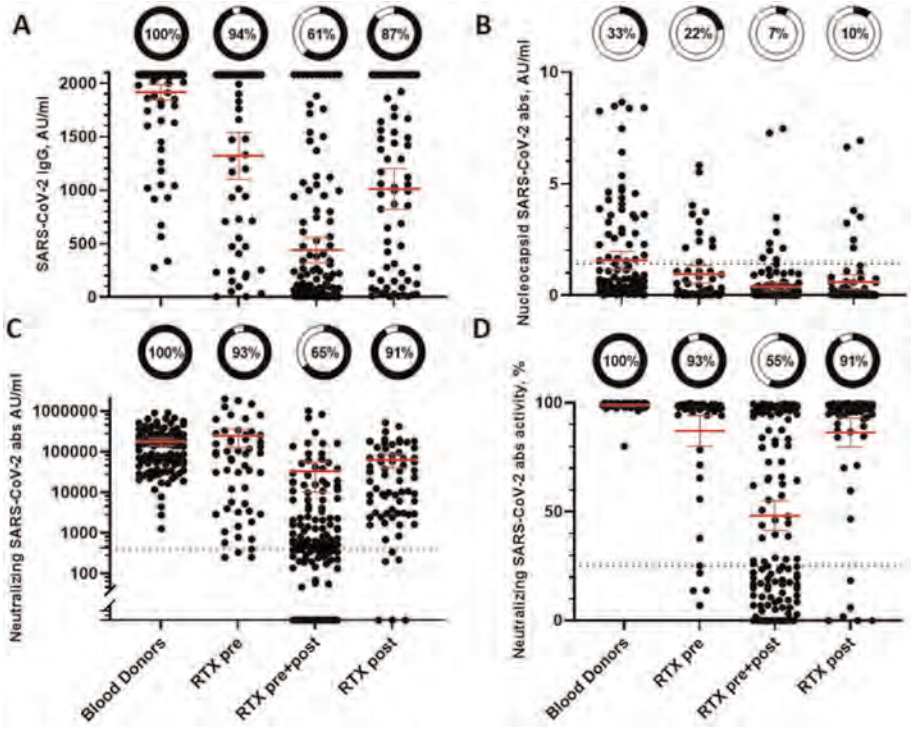

Figure 1. Concentrations of IgG (A), nucleocapside (B) and neutralizing (C) SARS-CoV-2 antibodies and neutralizing antibody activity (D) in Rituximab (RTX) treated patients and blood donors. RTX treated patients are divided according to sequence of primary COVID-19 vaccination and RTX treatment. ''RTX pre'' indicate RTX treatment were only given prior to vaccination, and not after. ''RTX pre+post'' RTX treatment were given prior to and after vaccination. ''RTX post'' RTX treatment were only given after primary COVID-19 vaccination. Pie charts indicate percentage of patients with measurabel antibodies/positive neutralizing antibody activity. Horizontal line indicate mean and whiskers 95% CI. Dotted lines indicate levels for positive test.

Table 1. Univariate and multivariate logistic regression analysis with presence of SARS-CoV-2 IgG antibodies as the dependent variable in RTX treated patients.

Univariate logistic regression analysis		Odds Ratio	95% Confidence Interval	P-value
Sex, female = ref.		0.59	0.33-1.05	0.08
Age, years		0.98	0.96-1.01	0.15
BMI		1.00	0.98-1.05	0.92
Diagnosis		1.04	0.98-1.11	0.17
COVID-19 vaccinations, n		0.85	0.60-1.21	0.38
"RTX-free" COVID-19 vaccinations, n		2.12	1.66-2.70	**<0.001**
COVID-19 infections, n		1.21	0.78-1.86	0.39
Recieved COVID-19 monoclonal abs, yes=ref		0.51	0.25-1.03	0.06
COVID-19 symptoms <6 weeks		1.10	0.46-2.67	0.82
Total RTX infusions, n		0.90	0.87-0.94	**<0.001**
Total RTX dose, mg		0.90	0.86-0.95	**<0.001**
Total RTX treatment time, months		0.99	0.98-.099	**<0.001**
RTX treatment in last 15 months		0.19	0.08-0.44	**<0.001**
RTX group				
	RTX pre+post	ref	ref	ref
	RTX pre	11.05	3.28-37.26	**<0.001**
	RTX post	4.26	1.95-9.33	**<0.001**
Prednisone treatment, mg		1.04	0.96-1.14	0.29
Initial model - Multiple logistic regression analysis - stepwise backward selection				
"RTX-free" COVID-19 vaccinations, n		1.80	1.23-2.62	**0.002**
Total RTX infusions, n		0.86	0.71-1.03	0.10
Total RTX dose, mg		1.09	0.90-1.31	0.40
Total RTX treatment time, months		1.00	0.99-1.02	0.78
RTX treatment in last 15 months		0.42	0.12-1.46	0.17
RTX group				
	RTX pre+post	ref	ref	ref
	RTX pre	0.84	0.13-5.71	0.86
	RTX post	0.77	0.22-2.62	0.67
Final model - Multiple logistic regression analysis - stepwise backward selection				
"RTX-free" COVID-19 vaccinations, n		1.93	1.51-2.48	**<0.001**
Total RTX infusions, n		0.94	0.89-0.98	**0.005**

All significant variables from the univariate analysis were included in the initial multiple logistic regression model. Stepwise backward selection, using the criterion of $P \geq 0.05$ for removal from the model. The first and final models of the multiple regression analyses are presented. "RTX-free" COVID-19 vaccinations are defined as no RTX treatment 9 months prior to and 1 months after vaccination. The final model had a LR chi2 = 58.03, $P < 0.001$

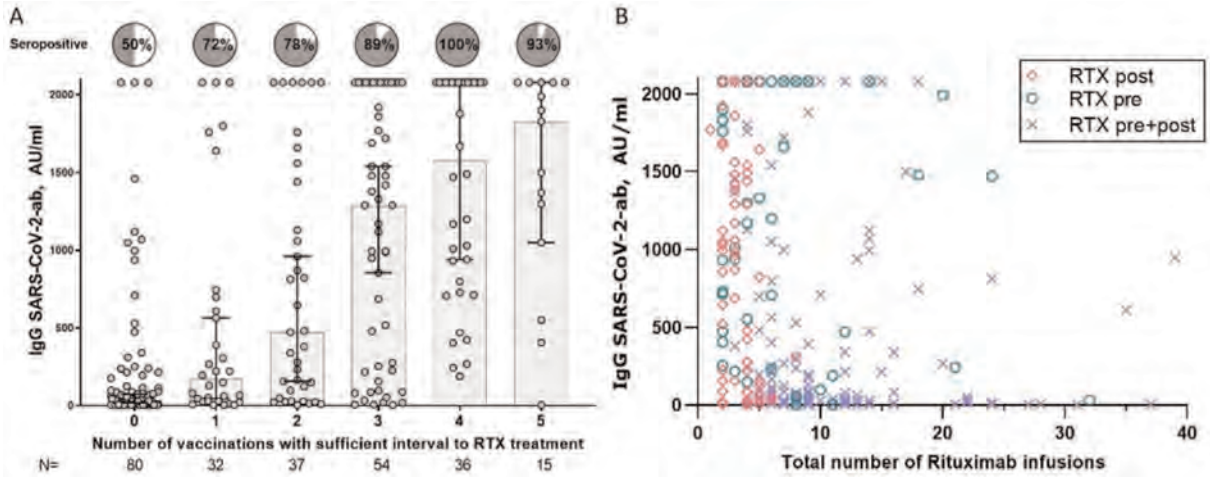

Figure 2. Graphical presentation of variables with explanatory power in multiple logistic regression analysis with precense of SARS-CoV-2 IgG antibodies as dependent variable. (A) Number of vaccinations with sufficient interval to latest RTX infusion, "RTX-free", e.g. no RTX given 9 months prior to and 1 month after COVID-19 vaccination. Bar indicate median, whiskers 95% CI, N total number of patients in each group (B) Total number of RTX infusions recieved.

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Abstract Number: 2512

Targeted Therapies for Severe Immune-related Adverse Events of Immune Checkpoint Inhibitors Are Not Associated with a Worse Prognosis

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SESSION INFORMATION

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Background/Purpose: In about 10% of patients, the immune response to immune checkpoint inhibitors (ICI) exceeds the anti-tumor response and leads to autoimmune complications (immune-related Adverse Events, irAEs), which can sometimes be severe and require the use of targeted therapies. Two studies recently reported a deleterious impact of targeted therapies on the survival of patients with irAEs. This work aims at comparing overall survival in patients treated for an hospitalized irAE with a biological or targeted synthetic DMARD (b/tsDMARD), conventional synthetic DMARD or exclusively with corticosteroids.

Methods: All adults included in the French national health database who initiated ICI for any type of cancer between 2014 and 2019 were retrospectively analyzed, with a a one-year look-back and one year look-ahead period. The occurrence of an irAE during ICI treatment or in the 12 following months was defined by the combination of (1) hospitalization for a cause

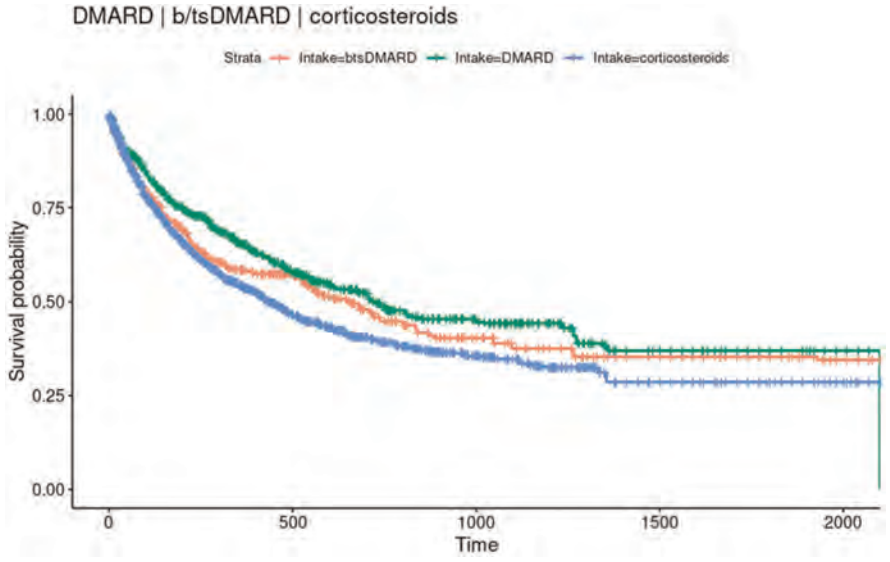

Figure. Overall survival in days in patients treated with a conventional DMARD (green), a b/tsDMARD (red), or corticosteroids (blue).

evoking an irAE of any nature, except endocrinopathy, and (2) initiation of corticosteroids, csDMARD or b/tsDMARD. Patients contributed from the time the 2 criteria were fulfilled until the end of follow-up or death. Treatment of IRAEs was considered as a time dependent variable with 3 classes: corticosteroids alone, csDMARD and b/tsDMARD. Because switches in treatment could occur during follow-up, propensity score (PS) was recalculated every 30 days using a multinomial logistic regression. PS included the current treatment, gender, age, type of cancer, ICI prescribed in monotherapy or as a combination, ICI year of beginning, time from cancer to initiation of ICI, use of corticosteroids, hospitalization in intensive care unit, type of irAE, number of LTDs, Charlson's index and FDep social deprivation index. Overall survival was compared between the three groups using a Cox model ponderated with overlap weights to ensure balance.

Results: 71,723 patients (men: 66.0%, median age: 66 years) initiating an ICI were analyzed. An hospitalized irAE occurred in 2575 patients at a median time of 232 days after ICI initiation and the 4 most frequent were gastrointestinal (inflammatory colitis, 1.7%), rheumatic (0.7%), cardiologic (0.5%) and pulmonary (0.4%). Global mortality was 66.0%. Median patient follow-up after irAE was 268 days. The weighted baseline populations consisted of 180 patients treated with b/tsDMARD, 263 patients treated with conventional DMARD and 341 patients exclusively with corticosteroids. Covariates were well-balanced between groups.

Overall mortality in patients treated with b/tsDMARD did not significantly differ from csDMARD (HR=1.13, CI=[0.97, 1.33]). Overall mortality in patients treated with corticosteroids was significantly higher than csDMARD (HR=1.30, CI=[1.04, 1.64]) but did not differ significantly from b/tsDMARD (HR=1.15, CI=[0.95, 1.39]).

Conclusion: In this large nationwide study, with one of the largest number of hospitalized irAEs and b/tsDMARD-treated patients, targeted therapies were not associated with a worse prognosis. The prognosis according to the underlying type of IRAEs is currently being investigated and will be presented at the meeting.

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Abstract Number: 2513

Latent Class Analysis Identifies 2 Clinical Phenotypes of Immune Checkpoint Inhibitor-induced Inflammatory Arthritis

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SESSION INFORMATION
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Session Type: Abstract Session
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Background/Purpose: : Immune checkpoint inhibitors (ICI) for cancer treatment can cause inflammatory arthritis (IA). ICI-IA is a heterogeneous entity affecting peripheral joints, tendons, and rarely the axial skeleton, and can be severe and persist even after ICI cessation. Since ICI-IA is a distinct entity with unique pathogenesis, applying categories of traditional IA is limited; thus, we used a data-driven approach to define clinically relevant subgroups within ICI-IA and examined differences between subgroups.

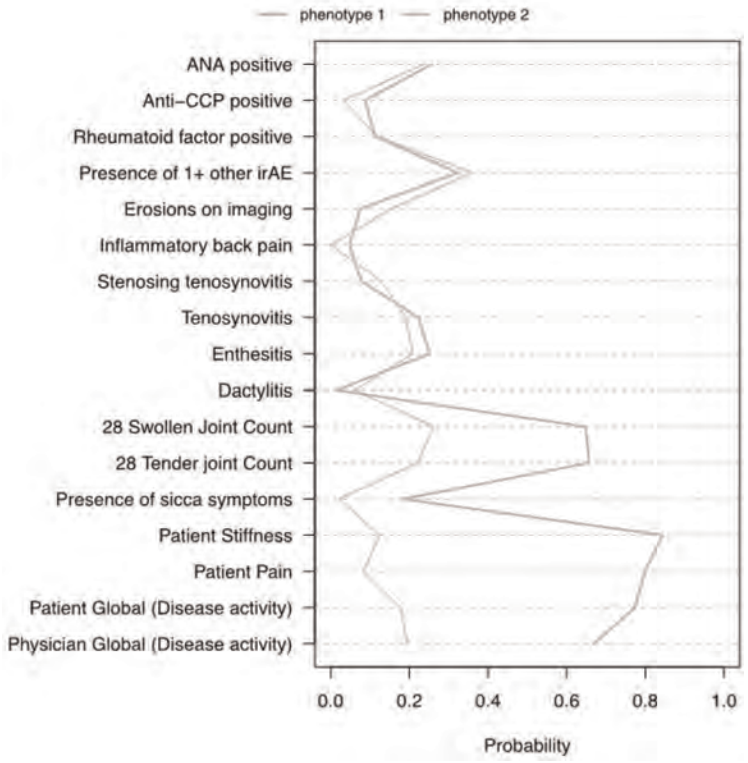

Figure 1. Predicted probabilities of features for two estimated phenotypes among 126 cancer patients receiving immune checkpoint inhibitors who developed inflammatory arthritis. For continuous variables (e.g. joint counts, disease activity ratings) probability is for being in the top 50% of values.

Table 1: Summary of inflammatory arthritis features by latent class group membership

			Phenotype 1 (N = 77)		Phenotype 2 (N = 49)		Difference
	N	N yes (%)	N	N yes (%)	N	N yes (%)	p*
High Physician Global	124	54 (44%)	75	15 (20%)	49	39 (80%)	**<0.001**
High Patient Global	123	59 (48%)	75	17 (23%)	48	42 (88%)	**<0.001**
High Patient Pain	119	54 (45%)	71	16 (23%)	48	38 (79%)	**<0.001**
High Patient Stiffness	105	52 (50%)	60	14 (23%)	45	38 (84%)	**<0.001**
Presence of sicca symptoms	126	13 (10%)	77	5 (6%)	49	8 (16%)	0.130
High tender joint count	125	55 (44%)	76	14 (18%)	49	41 (84%)	**<0.001**
High swollen joint count	125	57 (46%)	76	20 (26%)	49	37 (76%)	**<0.001**
Dactylitis	126	5 (4%)	77	4 (5%)	49	1 (2%)	0.648
Enthesitis	126	29 (23%)	77	15 (19%)	49	14 (29%)	0.280
Tenosynovitis	126	26 (21%)	77	16 (21%)	49	10 (20%)	1.000
Stenosing Tenosynovitis	126	13 (10%)	77	8 (10%)	49	5 (10%)	1.000
Inflammatory Back Pain	126	3 (2%)	77	2 (3%)	49	1 (2%)	1.000
Erosions on imaging	46	5 (11%)	24	4 (17%)	22	1 (5%)	0.349
Presence of 1+other irAE	126	43 (34%)	77	25 (32%)	49	18 (37%)	0.701
Rheumatoid factor positive	112	13 (12%)	68	8 (12%)	44	5 (11%)	1.000
Anti-CCP positive	114	7 (6%)	68	4 (6%)	46	3 (7%)	1.000
ANA positive	109	27 (25%)	64	13 (20%)	45	14 (31%)	0.260
Upper > lower joints (count)	126	59 (47%)	77	30 (39%)	49	29 (59%)	**0.030**
Small > large joints (count)	126	90 (71%)	77	48 (62%)	49	42 (86%)	**0.005**
Any hip or shoulder	126	34 (27%)	77	14 (18%)	49	20 (41%)	**0.007**

Methods: Participants were ³18 years old, treated with anti-PD-1, anti-PD-L1, and/or anti-CTLA-4 agents alone or in combination, and had ICI-IA diagnosed by a rheumatologist. We used information from the baseline rheumatology visit (patient reported symptoms, physical exam features, physician global arthritis rating, and laboratory studies) to cluster patients with latent class analysis (LCA). The Bayesian Information Criteria (BIC) was used to select the number of phenotypes with the lowest BIC. We then compared demographics, cancer type and treatments, and IA treatments and outcomes between

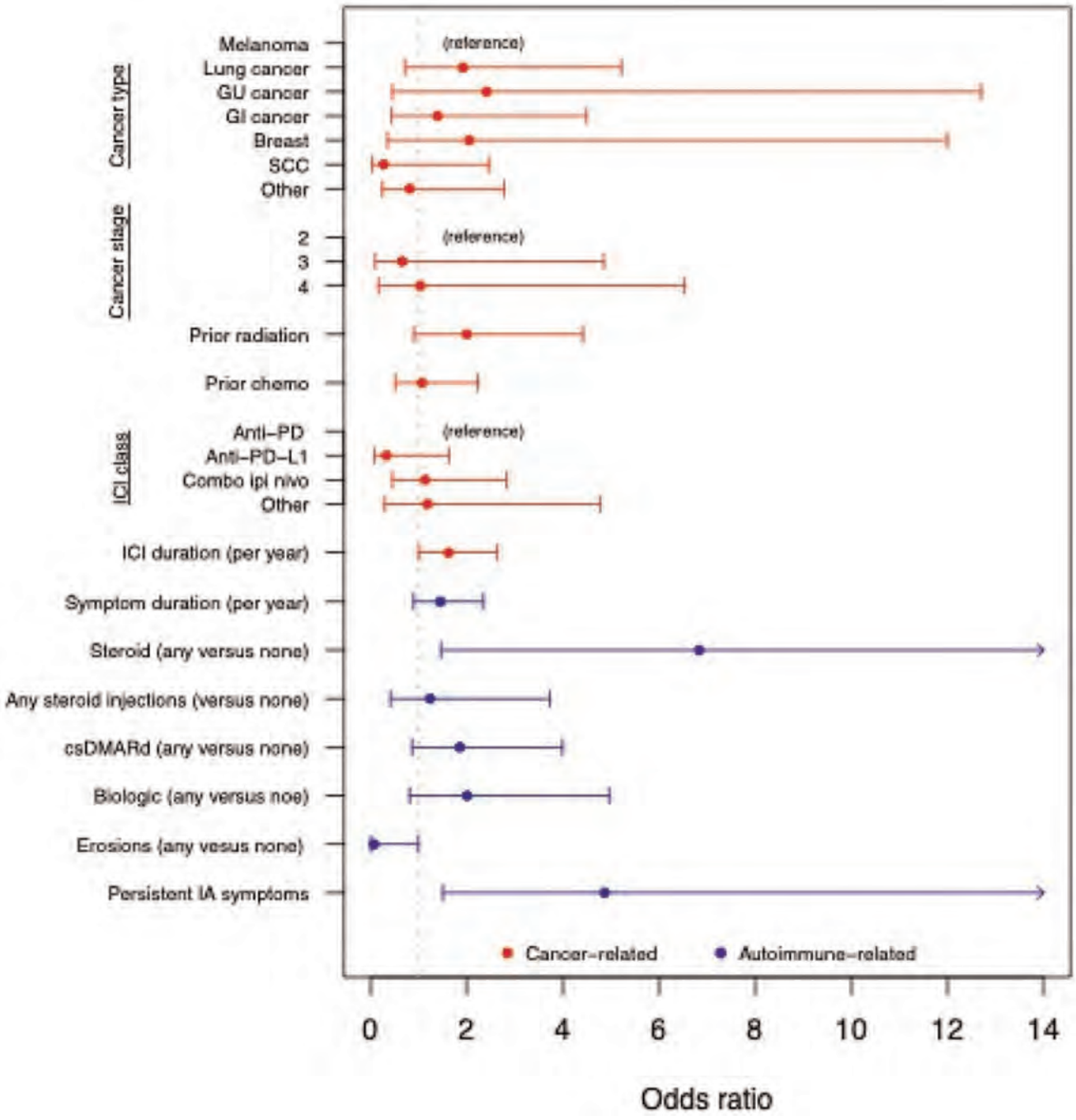

Figure 2: Associations between disease characteristics and latent class membership. Odds ratios greater than one are interpretable as a higher likelihood of being phenotype 2, the group with more severe IA symptoms. Odds ratios are adjusted for age and gender. Odds ratios in red represent potential risk factors for class membership (present before IA development) and those in blue represent IA-related outcomes that may be associated with class membership.

the estimated phenotypes. Next, we estimated the association between these features of interest and the likelihood of being in the group with the most severe IA symptoms using logistic regression.

Results: Of the 126 patients with ICI-IA, most participants were female (56%) and white (92%). Most patients had a moderate or high disease activity by CDAI. Mean CDAI was 16.98 (SD 10.2). Twenty variables were used to estimate latent classes. Two distinct phenotypes were indicated by the BIC; 77 patients are estimated to be the first phenotype and 49 in the second phenotype (Figure 1). The significantly different features of the phenotypes included higher levels of all components of the CDAI, more stiffness, and having more small and upper extremity joints involved for phenotype 2 (Table 1). Anti-CCP and RF positivity did not differ between groups. Patients in phenotype 2 were more likely to require steroids as compared to patients in phenotype 1 and were more likely to have persistent IA >6 months after ICI cessation (Figure 2). There was also a trend of longer ICI exposure prior to ICI-IA in phenotype 2, but no association with type of ICI or cancer.

Conclusion: Two separate phenotypes of ICI-IA were identified using LCA, the second having a more severe polyarthritis at baseline affecting the upper extremities. Those in the group with more severe features at baseline were more likely to need corticosteroids and to have persistent IA. There were no differences in terms of cancer type and treatment, thus future research can interrogate underlying genetic and immunologic differences between groups.

Disclosure: L. Cappelli: Bristol-Myers Squibb(BMS), 5, Mallincrkrodt, 2; **J. Perin**: None; **C. Bingham**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 2, Janssen, 2, Pfizer, 2, Sanofi, 2; **A. Shah**: Arena Pharmaceuticals, 5, Eicos Sciences, 5, Kadmon Corporation, 5, Medpace LLC, 5.

Abstract Number: 2514

Myositis Triad Subset Is Associated with High Mortality in Immune Checkpoint Inhibitor- Induced Myositis

Selene Rubino[1], Grant Cannon[2], Brian Sauer[3], Jorge Rojas Jr[4], Greg Stoddard[1], Gary Kunkel[1], Jessica A Walsh[5], Bryant England[6], Ted R Mikuls[7], Joshua Baker[8] and Tawnie Braaten[1], [1]University of Utah, Salt Lake City, UT, [2]University of Utah and Salt Lake City VA, Salt Lake City, UT, [3]Salt Lake City VA/University of Utah, Salt Lake City, UT, [4]Puget Sound VA and University of Utah, Seattle, WA, [5]Salt Lake City Veterans Affairs Health and University of Utah Health, Division of Rheumatology, Salt Lake City, UT, [6]University of Nebraska Medical Center, Omaha, NE, [7]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE, [8]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Immunological Complications of Medical Therapy
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Myositis is an infrequent but serious complication associated with immune check point inhibitor (ICI) treatment. Many patients with ICI-induced myositis will develop concurrent myocarditis and myasthenia gravis-like symptoms (ICI triad). We describe the prevalence and clinical characteristics of ICI-induced myositis and ICI triad among veterans receiving ICI.

Methods: Veterans enrolled in VHA who received ICI treatments between 6/6/2011 and 2/14/2023 were identified in the Corporate Data Warehouse. This analysis also employed data from the VA Central Cancer Registry for cancer diagnoses and Death Ascertainment File for all-cause mortality. Patients considered at high risk for ICI-induced myositis had medical records review via the Compensation and Pension Record Interchange (CAPRI) electronic medical records. Patients were

Table 1. Demographic characteristics of Veterans Treated with Immune Checkpoint Inhibitors (ICI)

	ICI Myositis alone (n=36)	ICI Myositis Triad Syndrome (n=24)	No Myositis (n= 29,501)	
Age at ICI infusion				
Years – Mean ± SD	70.3±10	76.6±7.5	70.0±8.7	p<0.001
Sex				
Male	36 (100%)	24 (100%)	28463 (96.5%)	P=0.712
Race				
White	24 (66.7%)	22 (92%)	22150 (75%)	p=0.331
Black	10 (28%)	0 (0%)	5120 (17%)	
Other	1 (2.9%)	2 (5.8%)	1919 (6.5%)	
Smoking Status				
Ever	12 (33%)	11 (46%)	15881 (54%)	p=0.1
Never	8 (22%)	4 (16.7%)	4001 (13.6%)	
Unknown	16 (44%)	9 (37.5%)	9619 (32.6%)	
Cancer Diagnosis				
Lung	15 (48.4%)	4 (20%)	13403 (53%)	p=0.004
Melanoma	6 (19%)	3 (15%)	2704 (10.7%)	
Genitourinary	5 (16%)	10 (50%)	4029 (16%)	
Gastrointestinal	5 (16%)	2 (10%)	3186 (12.6%)	
Other	0 (0%)	1 (5%)	1969 (7.8%)	
Initial ICI infusion Class				
PD-1	30 (83.3%)	20 (83.3%)	21690 (73.5%)	p=0.36
PD-L1	3 (8.3%)	2 (8.3%)	6082 (20.6%)	
CTLA-4	2 (5.5%)	2 (8.3%)	1018 (3.4%)	
Combination Therapy	1 (2.8%)	0 (0%)	711 (2.4%)	

considered at high risk if they met at least one of the following criteria: a creatine kinase (CK) value over 10-times the upper limit of normal (312 U/L) within six months of first ICI, the term "myositis" in a discharge summary any time after first ICI and/or term "myositis" in a progress note within six months after first ICI. ICI-induced myositis was defined by the presence of a provider diagnosis of ICI-induced myositis in CAPRI and laboratory or imaging evidence of myositis in the absence of alternate etiologies such as STEMI or septic shock. Mortality follow-up data was calculated in months from ICI initiation. Univariate testing by the Bartlett's test and multivariate analysis by Cox regressions performed in Stata.

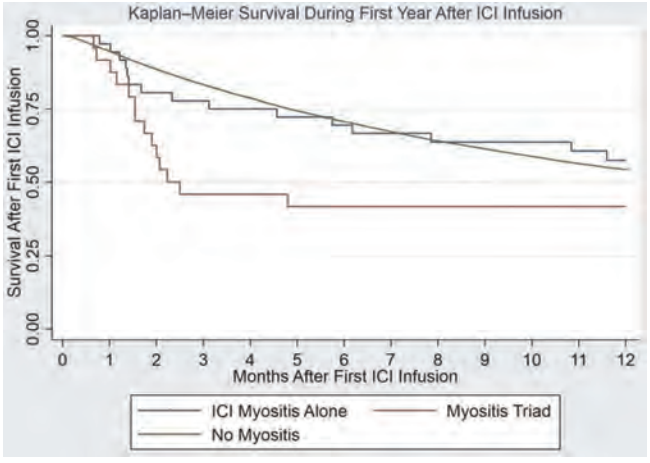

Figure 1. Kaplan-Meier Survival Curve of Veterans Treated with Immune Checkpoint Inhibitors by Myositis Category

Results: We identified 60 patients with ICI-induced myositis of which 24 (40%) had the ICI triad out of 29,561 treated with ICIs. All patients with ICI-induced myositis were male. Self-defined race, ethnicity, and smoking status were similar between veterans treated with ICI who did not develop myositis, those who developed myositis alone, or ICI triad. ICI triad patients were significantly older compared to myositis alone patients (76.6±7.5 vs 70±10 years, p< 0.001). While PD-1 use was higher in the ICI-induced myositis groups, this increase was not statistically significant (83.3% vs 73.5%, p=0.36) (Table 1).Genitourinary cancers were more common in ICI triad populations than myositis alone (50% vs 15.6%, p=0.002). ICI triad patients had increased mortality in the first year of treatment than myositis alone patients but this difference just outside range for statistically significant (HR 1.65 [0.77-3.5], p=0.077 by Cox). Myositis alone patients had no significant mortality differences in mortality compared to patients without myositis (HR 1.01 [0.61,1.68], p=0.967 by Cox (Figure 1). These results were not confounded by either age or genitourinary status.

Conclusion: The ICI triad is a severe subset of ICI-induced myositis which is associated with older age at initial ICI treatment. A signal for potential association with ICI triad subset was seen with genitourinary cancers that will require further investigation. A strong trend for increased early mortality in the ICI triad subset closely following ICI initiation was observed in comparison to patients with myositis alone and ICI-treated veterans without myositis.

Disclosure: S. Rubino: None; **G. Cannon**: None; **B. Sauer**: None; **J. Rojas Jr**: None; **G. Stoddard**: None; **G. Kunkel**: None; **J. Walsh**: AbbVie, 5, Amgen, 2, Eli Lilly, 2, Janssen, 2, Merck, 5, Novartis, 2, Pfizer, 2, 5, UCB Pharma, 2; **B. England**: Boehringer-Ingelheim, 2, 5; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **J. Baker**: CorEvitas, 2, Cumberland Pharma, 2, Horizon Pharmaceuticals, 5; **T. Braaten**: None.

Abstract Number: 2515

Machine Learning-Based Stratification of Mixed Connective Tissue Disease Using Immunophenotyping Data from Patients with Related Autoimmune Diseases

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases II

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Mixed connective tissue disease (MCTD) is a heterogenous autoimmune disorder with overlapping clinical features of systemic lupus erythematosus (SLE), polymyositis/dermatomyositis, and systemic sclerosis (SSc). Despite its unique clinical characteristics, some patients may develop other rheumatic diseases during a follow-up period [1]. To better understand the heterogeneity of MCTD and to stratify the patients, we developed machine learning models

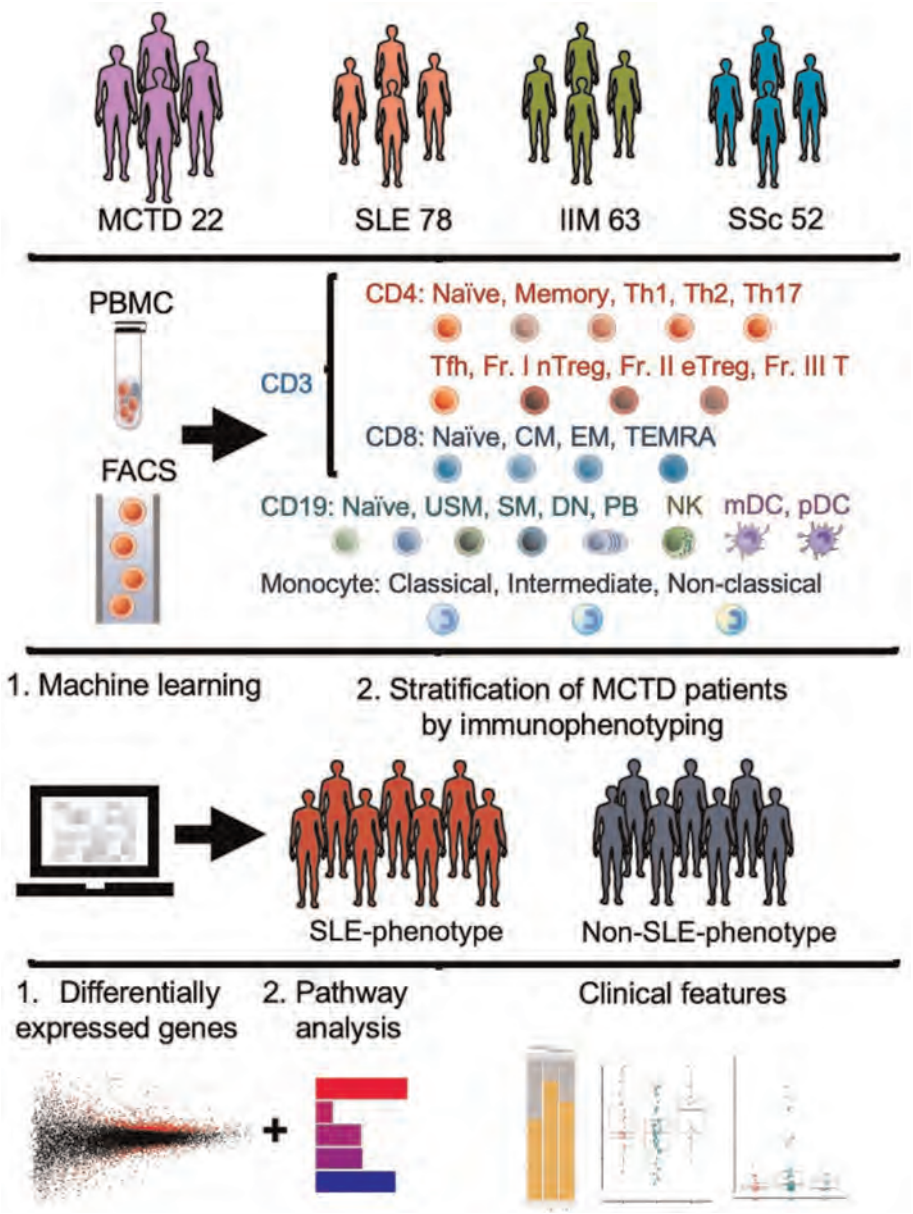

Figure 1. Workflow of this study

using immunophenotyping as a reference for SLE, idiopathic inflammatory myopathy (IIM), and SSc and identify differences in symptoms and transcriptome among the subgroups of MCTD.

Methods: We employed our large-scale database, Immune Cell Gene Expression Atlas from the University of Tokyo (ImmuNexUT) [2], to analyze the immunophenotyping (24 subsets) of patients with MCTD alongside SLE, IIM, and SSc. By utilizing the immunophenotyping data of SLE, IIM, and SSc, we developed machine learning models such as random forest, neural network, etc., to stratify MCTD patients. Following the stratification of the MCTD patients, we performed a transcriptome analysis, including a differentially expressed gene (DEG) analysis and pathway analysis. Finally, we compared the clinical features of the subgroup of MCTD patients (**Figure 1**).

Results: We enrolled a total of 215 patients with autoimmune diseases, consisting of 22 MCTD, 78 SLE, 63 IIM, and 52 SSc patients, and collected the data of immunophenotyping, bulk RNA-sequence on peripheral mononuclear blood cells, and clinical characteristics. We constructed machine learning models to classify patients with SLE, IIM, and SSc based on the

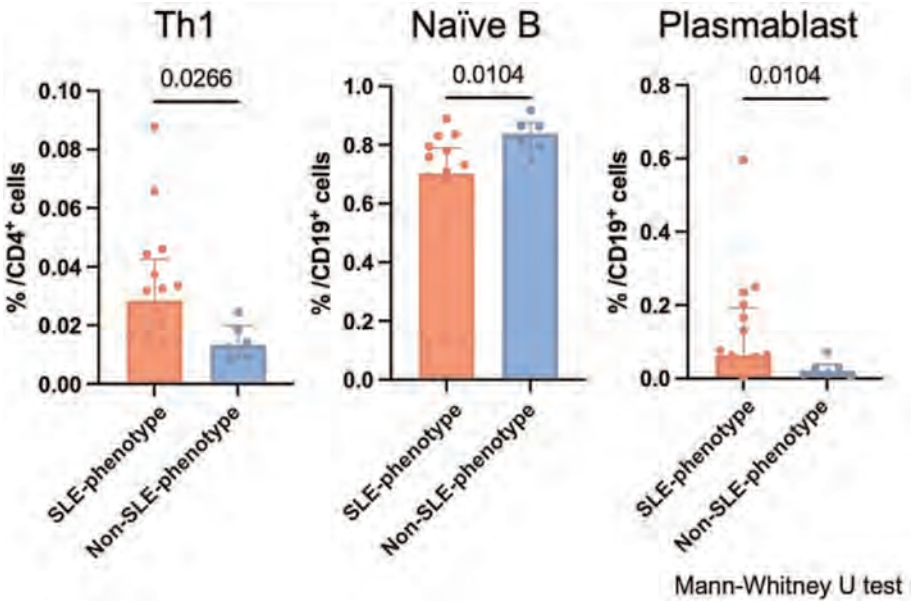

Figure 2. Comparison of immunophenotyping and clinical features of MCTD patients between SLE-phenotype and non-SLE-phenotype patients.

immunophenotyping and applied these models to the MCTD patients. Of the 22 patients with MCTD, 16 were classified as SLE-phenotype, and 6 were classified as non-SLE-phenotype (4 IIM-phenotype and 2 SSc-phenotype). Among the MCTD patients, SLE-phenotype patients had significantly higher proportions of Th1, naïve B cells, and plasmablast (p=0.03, 0.01, and 0.01, respectively) (**Figure 2**). Regarding clinical features, the proportions of having the SLE symptoms such as lymphadenopathy, malar rash, serositis, and cytopenia were significantly higher in SLE-phenotype patients (87.5% vs 33.3%, p=0.025). The number of DEGs across the cell types between SLE patients and MCTD patients (SLE-phenotype and non-SLE-phenotype) was comparable.

Conclusion: Our study suggested the potential stratification of MCTD patients based on their immunophenotyping. This approach may help distinguish clinical phenotypes in MCTD.

[1] Reiseter S *et al,* Arthritis Res Ther 2017
[2] Ota M *et al, Cell* 2022

Disclosure: S. Izuka: Eisai, 6; **T. Komai**: Amgen, 6, Asahi Kasei, 6, Chugai, 5, 6, Daiichi-Sankyo, 6, Eisai, 6, Eli Lilly, 1, 6, GlaxoSmithKlein(GSK), 5, 6, Janssen, 6, Novartis, 6, Tanabe Mitsubishi, 6; **T. Itamiya**: Chugai Pharmaceutical Co., Ltd., 5; **M. Ota**: Chugai Pharmaceutical., 12, belong to the Social Cooperation Program, Department of Functional Genomics and Immunological Diseases, supported by Chugai Pharmaceutical.; **S. Yamada**: Asahi Kasei, 6, Chugai Pharmaceutical., 6, Pfizer, 6; **Y. Nagafuchi**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, 6, Chugai Pharmaceutical., 12, belong to the Social Cooperation Program, Department of Functional Genomics and Immunological Diseases, supported by Chugai Pharmaceutical., GlaxoSmithKlein(GSK), 5, Novartis, 6; **H. Shoda**: AbbVie/Abbott, 6, Asahi Kasei, 6, Astellas, 6, AstraZeneca, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Chugai Pharmaceutical., 6, Daiichi-Sankyo, 6, Eisai, 6, Eli Lilly, 6, Gilead, 6, GlaxoSmithKline, 6, Jansen, 6, Novartis, 6, Pfizer, 6, Sanofi, 6, Taisho Pharmaceutical, 6, Takeda, 6; **K. Matsuki**: Chugai Pharmaceutical., 3; **K. Yamamoto**: AbbVie, 6, Pfizer Japan Inc, 12, Outsourcing contract, RegCell, 1, Sun Pharmaceutical Industries Ltd, 6; **T. Okamura**: Chugai Pharmaceutical., 12, belong to the Social Cooperation Program, Department of Functional Genomics and Immunological Diseases, supported by Chugai Pharmaceutical.; **K. Fujio**: AbbVie/Abbott, 6, Asahi Kasei, 5, 6, Astellas, 6, AstraZeneca, 6, Ayumi, 6, Bristol-Myers Squibb(BMS), 5, 6, Chugai Pharmaceutical., 5, 6, Daiichi-Sankyo, 6, Eisai, 5, 6, Eli Lilly, 5, 6, Janssen, 6, Novartis, 6, Ono, 6, Pfizer, 6, Sanofi, 6, Tanabe Mitsubishi, 5, 6, Tsumura, 5.

Abstract Number: 2516

The Effect of Starting Prednisone Dose on the Treatment of Polymyalgia Rheumatica

Katrina Nguyen[1], Jennifer Du[1], Jiaxiao shi[2] and **Antony Lin**[1], [1]Kaiser SCAL, Fontana, CA, [2]SCPMG, Pasadena, CA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases II
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Polymyalgia rheumatica (PMR) is a systemic inflammatory syndrome that is characterized by widespread pain and stiffness around the shoulders, pelvic girdle and neck. PMR is usually treated with oral glucocorticoids, most commonly prednisone. However, long-term use of prednisone has been associated with various serious side-effects. Some literature suggested minimum effective dose of prednisone is within the range of 12.5-25 mg of prednisone daily. However, there is limited data suggesting the ideal starting dose of prednisone. Our study is to evaluate the effect of starting prednisone dose on the treatment duration of PMR and to determine the ideal initial prednisone dose that will lead to the shortest time needed to achieve 12 months of prednisone-free period.

Methods: We performed a retrospective chart review on a cohort of 919 adult patients newly diagnosed with PMR who were started on prednisone between January 1, 2010 to December 31, 2018 from the Kaiser San Bernardino and Riverside, Southern California, USA. Patients were excluded if hey had prior conditions that require long-term glucocorticoid use before PMR diagnosed, existing diagnoses of giant cell arteritis, and patients who did not achieve 12 month of prednisone-free period. Potential risk factors (age, Duration and inflammatory markers) were also evaluated. The primary outcome was to compare the duration of prednisone treatment in groups with 4 different starting doses of prednisone. The secondary outcome was to evaluate the treatment duration in patients with added steroid-sparing agents and the incidence of re-treatment with prednisone after achieving 12-month prednisone-free period.

Results: Among 701 patients with PMR diagnosed and was treated with prednisone. Their mean age was 68.7 and 443 (63.2 %) were women. The mean ESR was 45.5. Prednisone at 15mg (n = 191) had the shortest duration (mean of 23.4 months) of treatment before achieving 12-month prednisone free period with p value of 0.019. Out of 191 patients giving prednisone 15mg daily, 171 (89.5%) were started by rheumatologists. Patients who were started at 10mg or less prednisone daily and required steroid-sparing agents (n = 7 out of 202) had the longest duration of treatment (with a mean of 94.3 months) with p value of 0.008. Our study also showed that the percentage of patients requiring re-treatment with prednisone decreased with higher starting doses of prednisone. However, this p-value was not significant.

Table 1. Durations of prednisone treatment (in months)

Duration of treatment		Prednisone dose, mg				
		≤10	11 - 15**	16 - 20**	21 - 80	p-value (p<0.05)
Total prednisone* (n = 701)	Mean ± Std. Dev, months	32.4 ± 34.4	23.4 ± 23.3	29.9 ± 28.1	28.4 ± 31.4	0.019[a]
	Median (IQR), months	20.8 (38.8)	13.8 (25.1)	19 (33.5)	13.8(35.3)	0.057[b]
Prednisone only (n = 658)	Mean ± Std. Dev, months	30.4 ± 32.5	23.3 ± 23.3	27.3 ± 25.5	27.4 ± 32.1	0.11
	Median (IQR), months	19.6 (33.8)	13.8 (25)	17.7 (29.8)	13.2 (32.5)	0.24
Prednisone + steroid sparing agents (n = 43)	Mean ± Std. Dev, months	94.3 ± 39.5	24.7 ± 26.8	55.2 ± 38.7	41.5 ± 20.1	0.0078
	Median (IQR), months	116.3 (61.5)	14.7 (42)	32.7 (61.6)	46.2 (28.2)	0.018

Conclusion: Based on a systemic literature review about PMR, our study has the largest study population with 701 patients. Out study showed the patients who were treated with medium dose of daily prednisone dose of 15mg achieved 12 months of prednisone-free period in the shortest time. Since the patients treated with both prednisone 10mg daily or less and steroid-sparing agents had a longer duration, we recommend against any starting daily doses of 10mg or less. Patients treated with high prednisone dose had the lowest rate of restarting prednisone after 12 months compared with the other dose groups. With the treatment duration appeared to be longer when taking prednisone 20mg or higher, this suggested that PMR may be a heterogenous diseases with various severity and co-morbid diseases.

Disclosure: K. Nguyen: None; **J. Du**: None; **J. shi**: None; **A. Lin**: None.

Abstract Number: 2517

The Relationship Between the NETosis Findings and Disease Activity in Behcet Disease

Erdem Bektas[1], Rabia Deniz[2], Zeliha Emrence[3], Sema Sırma Ekmekci[3], Neslihan Abacı[3], Shirkhan Amikishiyev[4], Yasemin Yalçınkaya[4], Bahar Artim Esen[4], Murat Inanç[5] and Ahmet Gul[6], [1]Istanbul University, Istanbul Faculty of Medicine, Department of Internal Medicine, Istanbul, Turkey, [2]University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Department of Rheumatology, Istanbul, Turkey, [3]Istanbul University, Aziz Sancar Institute of Experimental Medicine, Department of Genetics, Istanbul, Turkey, [4]Istanbul University, Istanbul Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, [5]Istanbul University, Istanbul, Turkey, [6]Division of Rheumatology, Department of Internal Medicine, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases II
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Behcet disease (BD) is a multisystemic inflammatory disease of unknown etiology. BD has been classified among the neutrophilic dermatosis, and neutrophil extracellular traps (NETs) have been claimed in the pathogenesis of BD [1]. We herein aimed to investigate the potential relationship between the NETosis findings and local and systemic disease activity in BD.

Methods: The study group was consisted of orally and/or systemically active BD patients who met the ISG criteria and healthy individuals. The patients with additional inflammatory conditions or using biologic agents were excluded. Serum and saliva samples were collected from the patients during their active (active oral ulcer and/or systemic manifestations) and remission (no manifestations, normal acute phase reactants) periods cross-sectionally. Some of them were followed also longitudinally. Cell-free DNA (cf-DNA), neutrophil elastase (NE), myeloperoxidase (MPO) and citrullinated histon-3 (cit-H3) levels were measured as NETosis findings, and the results were adjusted according to the peripheral blood neutrophil counts (as the amount of biomarker per 1 million neutrophils). Unadjusted and adjusted levels were evaluated.

Results: The study group consisted of 30 active and 18 inactive BD patients as well as 10 healthy controls. Serum samples were collected from all active patients, and saliva samples were obtained from 15 orally active patients, while 18 serum and 7 saliva samples were obtained when they were in remission. Demographic and cumulative clinical characteristics of the patients are shown in **Table 1**. In active BD, serum cf-DNA and serum NE levels were found to be high ($p \leq 0.001$, $p < 0.05$), whereas adjusted serum MPO and adjusted serum cit-H3 levels were found to be low ($p \leq 0.001$, $p \leq 0.01$). In inactive BD, serum NE level were higher than controls ($p < 0.05$), while serum MPO, adjusted serum MPO and adjusted serum cit-H3 levels were lower than controls ($p < 0.05$, $p \leq 0.001$, $p < 0.05$, respectively). No difference was found in salivary NETosis

Table 1. Demographic and cumulative clinical characteristics of the active and inactive patients. Data show median (IQR) or mean ± SD as appropriate. Abbreviations: BD, Behcet disease; CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; IQR, interquartile range; N, number of available patients; n, number of meet criteria; SD, standard deviation; TNFi, tumor necrosis factor inhibitor

	Active BD (N=30)	Inactive BD (N=18)
Sex, male, n (%)	21 (70)	11 (61.1)
Age, year	34.5 (26.5-42)	36.5 ± 9.1
Follow-up period, month	54 (10.5-150)	48 (10.25-70.5)
HLA B51, n (%)	10/13 (76.9)	9/12 (75)
Smoking, n (%)	8 (26.7)	7 (38.9)
ISG criteria, n (%)	29 (96.7)	17 (94.4)
Involvements, n (%)		
Mucocutaneous	30 (100)	18 (100)
Arthritis	12 (40)	8 (44.4)
Uveitis	8 (26.7)	2 (11.1)
Neurologic	2 (6.7)	1 (5.6)
Gastrointestinal	1 (3.3)	0 (0)
Vascular	7 (23.3)	6 (33.3)
Other	1 (3.3)	1 (5.6)
Treatments, n (%)		
Naive	7 (23.3)	0 (0)
Colchicium	23 (76.7)	18 (100)
Azathioprine	7 (23.3)	10 (55.6)
Corticosteroid	3 (10)	9 (50)
TNFi	0 (0)	1 (5.6)
Laboratory values		
Neutrophil count, $10^3/\mu l$	6.5 ± 2.6	4.7 (3.4-6.6)
CRP, mg/l	7.5 (3.16-26.5)	2.44 (0.6-4.46)
ESR, mm/h	10.5 (7-23.25)	9 (3-15)

findings between patient groups and controls (**Figure 1**). Serum cf-DNA and saliva cf-DNA levels showed a decrease in longitudinal follow-up towards remission ($p \leq 0.01$, $p < 0.05$) (**Figure 2**). Serum cf-DNA and saliva cf-DNA positively correlated with C-reactive protein and erythrocyte sedimentation rate, while adjusted serum MPO and adjusted serum cit-H3 negatively correlated ($p < 0.05$).

Conclusion: NETosis findings showed changes in association with systemic and/or local activity of BD patients in relation to the disease manifestations. Especially, serum and saliva cf-DNA levels potentially indicated the local and systemic disease activity, and serum NE levels were high in both active and inactive periods. The mechanism of the low serum MPO and cit-H3 levels, particularly in the active patients warrants further investigation. Changes of the findings after adjustment of the results according to the peripheral blood neutrophil counts may indicate that the NETosis findings detected in serum could be related to high neutrophil turnover in the active phase of the disease. Further studies are needed to clarify the biomarker potential of NETosis findings in BD.

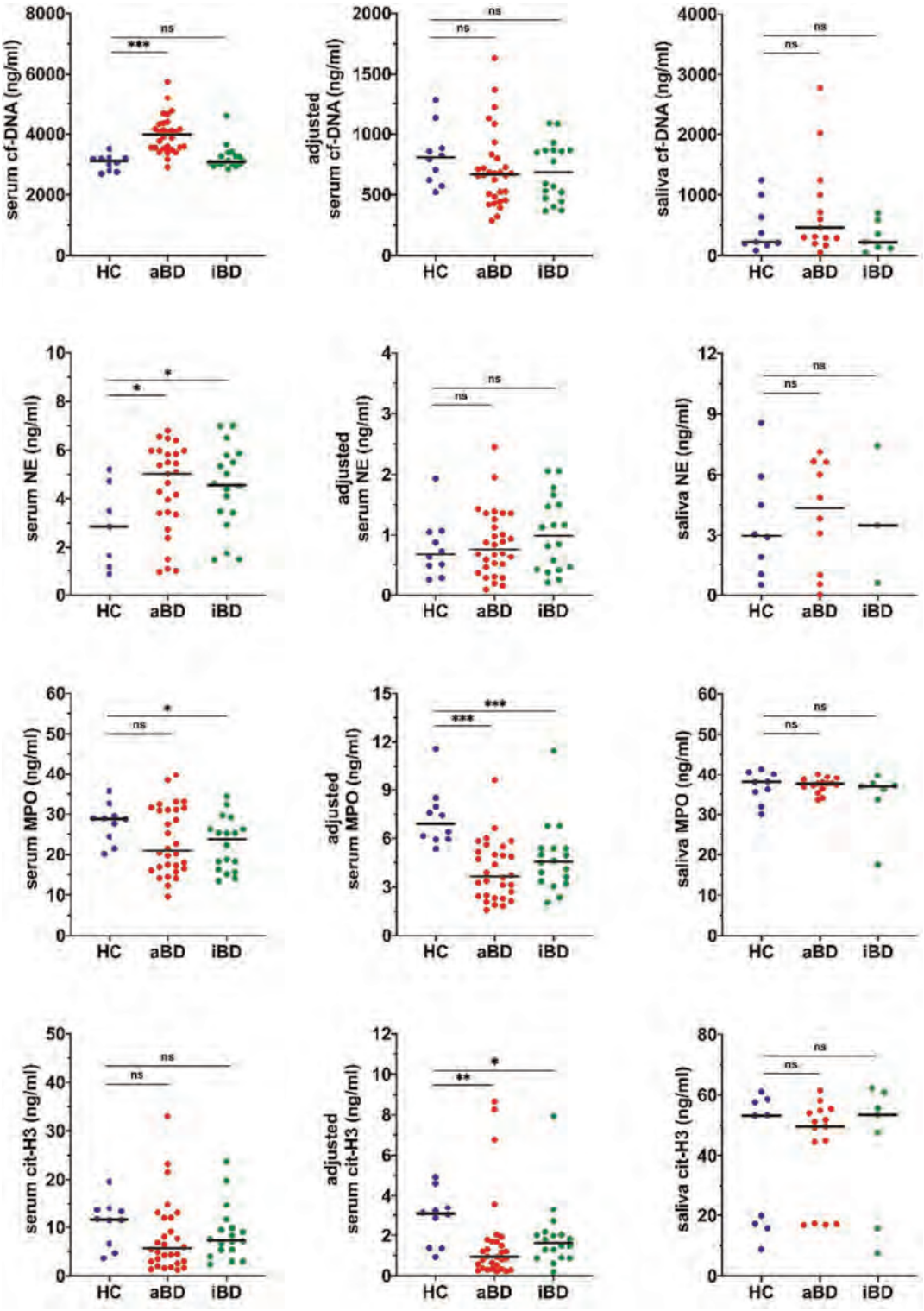

Figure 1. The levels of NETosis findings in control group, active BD and inactive BD. Data shows as median (IQR). Mann-Whitney-U test; *p<0.05, **p≤0.01, ***p≤0.001, ns: not significant. (HC: healthy control, BD: Behçet disease, aBD: active BD, iBD: inactive BD, cf-DNA: cell free-DNA, NE: neutrophil elastase, MPO: myeloperoxidase, cit-H3: citrullinated histon-3)

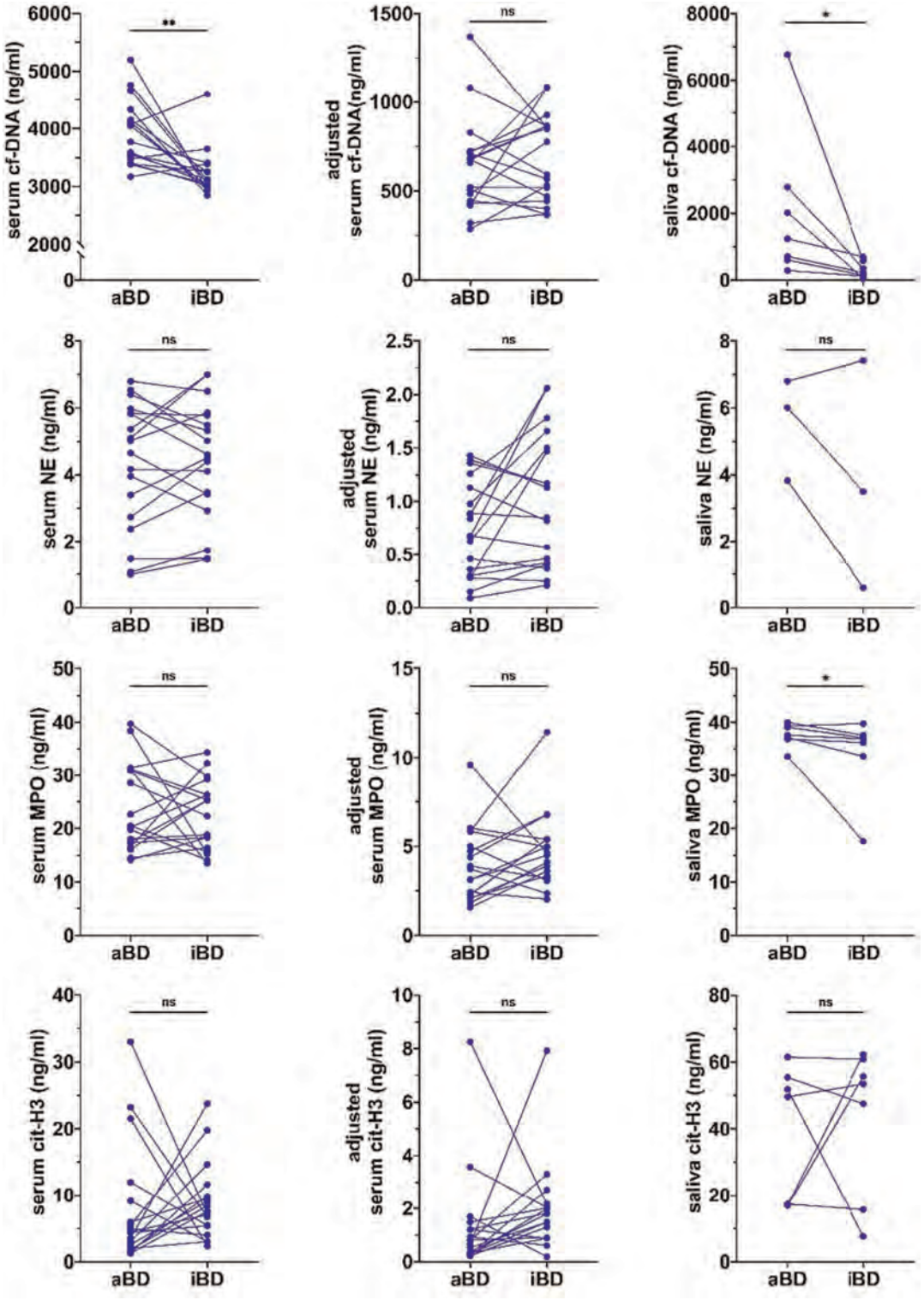

Figure 2. Change in the levels of NETosis findings in longitudinal follow-up. Wilcoxon test; *p<0.05, **p≤0.01, ns: not significant. (BD: Behçet disease, aBD: active BD, iBD: inactive BD, cf-DNA: cell free-DNA, NE: neutrophil elastase, MPO: myeloperoxidase, cit-H3: citrullinated histon-3)

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Abstract Number: 2518

Could the Adenosine Pathway Identify Cases with a Progressive Fibrosing Phenotype Between Patients with Autoimmune Interstitial Lung Disease? An Initial Approach

Olga Sanchez Pernaute[1], Cristina Vadillo-Font[2], Hilda Godoy[3], Laura Cebrian[4], Gema Bonilla[5], Rosario Garcia-Vicuna[6], Irene Llorente Cubas[6], Fredeswinda Romero[1], Rosalía Laporta[3], Belen Lopez-Muñiz[4], M Asunción Nieto[7], Luis Gomez-Carrera[5], Claudia Valenzuela[8], M Jesus Rodriguez-Nieto[9] and lydia Abasolo[10], [1]IIS-HU Fundación Jiménez Díaz, Madrid, Spain, [2]Hospital Clinico San Carlos, Madrid, Spain, [3]Hospital Universitario Puerta de Hierro, Madrid, Spain, [4]Hospital Universitario Infanta Leonor, Madrid, Spain, [5]Hospital Univ. La Paz, Madrid, Spain, [6]Hospital Universitario de la Princesa, Madrid, Spain, [7]Hospital Clínico S. Carlos, Madrid, Spain, [8]Hospital Universitario La Princesa, Madrid, Spain, [9]Pulmonology department, Hospital Fundación Jimenez Díaz, Madrid, Spain, [10]Hospital Clínico San Carlos, Madrid, Spain

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases II

Session Type: Abstract Session

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Background/Purpose: Interstitial lung diseases with an autoimmune background (AIP) are a heterogeneous group of processes. There is an unmet need to identify those cases with a progressive fibrosing phenotype in order to tailor therapeutics. Both of inflammation and hypoxia enhance ATP externalisation and increase synthesis of extracellular adenosine. In turn, increased adenosine promotes postinjury fibrotic remodelling, via A2A or A2B receptors. Netrin-1, which is also triggered by hypoxia has been found to activate A2B receptors, and is up-regulated during experimental and human lung fibrosis. We have explored activation of the adenosine pathway in patients with different subtypes of AIP.

Methods: We conducted a cross-sectional study in patients from the NEREA Register of autoimmune IP cases and in lung tissues from the IIS-HUFJD biobank. We measured adenosine and its metabolite inosine in plasma using HPLC. Serum levels of netrin 1 were determined by ELISA. Immunodetection of A2A, A2B and alpha-SMA was performed in the lung specimens. A descriptive analysis was carried out, and comparison between categories was done with parametric tests.

Results: The population comprised 126 subjects (115 cases, 74% women, and 11 controls). There were 64 newly diagnosed patients and 51 prevalent cases. Predominant radiographic patterns were NSIP (32p) and UIP (23p), while underlying autoimmune conditions included 9p with RA, 5 MCTD, 4 ARS, 16 SSc, 6 pSS, 3 IIM, and overlapping syndromes. Twenty six patients fulfilled IPAF criteria, while 11 patients were unclassifiable. At the time of biomarkers determination, 44p were considered to have a fibrotic process. Presence of RA-defining autoAb was found in 24 patients. ANA test was + in 69 out of 81 cases. There was a positive correlation between adenosine and netrin 1 (r 0.3, p 0.004), but not with the markers of epithelial injury lactate dehydrogenase (LDH) and Krebs von den Lungen 6 (KL6). Netrin 1 was enhanced in the patient population in comparison to healthy controls (p 0.005). Levels of adenosine, inosine and netrin 1 were higher in women than in men, and also tended to be higher in patients with established disease as compared with newly diagnosed ones, while in contrast KL-6 levels dropped in established disease as regarded to newly diagnosed patients (p 0.05). Netrin 1 levels were higher in those patients with fibrotic disease (p 0.08), and in RF+ cases (p 0.011). In contrast, we could not observe significant differences as concerned radiographic patterns or clinical diagnosis.

In the lung specimens, A2B receptors were enriched at the fibrotic interstitial areas and in alveolar epithelial cells. On the other hand, scattered infiltrating cells and some endothelial layers showed activation of the A2A receptors.

Conclusion: On the whole, our findings suggest that a subgroup or patients with AIP up-regulate the adenosine/netrin-1 pathway, in this way promoting the development of a profibrotic remodelling via A2BR and possibly modulating processes of immune cell activation and migration via A2A signaling. The role of netrin 1 as biomarker of the progressive fibrosing phenotype in these patients needs to be confirmed with longitudinal studies.

Disclosure: O. Sanchez Pernaute: None; **C. Vadillo-Font**: None; **H. Godoy**: None; **L. Cebrian**: None; **G. Bonilla**: None; **R. Garcia-Vicuna**: None; **I. Llorente Cubas**: None; **F. Romero**: None; **R. Laporta**: None; **B. Lopez-Muñiz**: None; **M. Nieto**: None; **L. Gomez-Carrera**: None; **C. Valenzuela**: None; **M. Rodriguez-Nieto**: None; **I. Abasolo**: None.

Abstract Number: 2519

A Phase II Clinical Study to Investigate the Efficacy and Safety of Hemay005 Tablets in Patients with Active Behçet`sDisease

Charles Jones[1], Zhanguo Li[2], Zhuoli Zhang[3], Jian Wu[4], Guixiu Shi[5], Wenjie Zheng[6], Jianping Tang[7], Xiaobing Wang[8], Lie Dai[9], Lin Chen[10], Yasong Li[11], Ling Wu[12], Yongfu Wang[13], Shengyun Liu[14], Yao Ke[15], Jin Lin[16], Zhenchun Zhang[17], Jiankang Hu[18], Wantai Dang[19], Songlou Yin[20], Xin Tang[21], Mingfei Zhu[22], Jinfeng Lin[22], Richard Jones[22], Weiguo Wan[23] and xianjun Hu[22], [1]Hemay Pharmaceuticals, Tianjin, China, [2]Peking University Health Science Center, Department of Rheumatology and Immunology, People's Hospital, Beijing, China, [3]Peking University First Hospital, Rheumatology and Immunology Department, Beijing, China, [4]Suzhou University Affiliated First Hospital, Suzhou, China, [5]the First Affiliated Hospital of Xiamen University, Xiamen, China, [6]Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, Beijing, China, [7]Shanghai Tongji Hospital, Shanghai, China, [8]The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China, [9]Department of Rheumatology, Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, China, [10]Jilin Provincial People's Hospital, Changchun, China, [11]11Zhejiang Provincial People's Hospital, Hangzhou, China, [12]University of Hong Kong Shenzhen Hospital, Shenzhen, China, [13]The First Affiliated Hospital of Baotou Medical College, Baotou, China, [14]The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China, [15]Jiangsu Provincial People's Hospital, Nanjing, China, [16]The First Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China, [17]Linyi People's Hospital, Linyi, China, [18]Pingxiang People's Hospital, PingXiang, China, [19]The First Affiliated Hospital of Chengdu Medical College, Chengdu, China, [20]Xuzhou Medical University Affiliated Hospital, Xuzhou, China, [21]Bestudy (Shanghai) Medical Technology Co., Ltd, Shanghai, China, [22]Clinical Department, Tianjin Hemay Pharmaceutical Co., Ltd., Tianjin, China, [23]Huashan Hospital Affiliated to Fudan University, Shanghai, China

SESSION INFORMATION

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Background/Purpose: Behçet's disease (BD) is a chronic and recurrent vascular inflammatory disease with major manifestations including oral ulcers, genital ulcers, skin damage and ophthalmitis, and it can also affect the nervous system, gastrointestinal tract, cardiovascular system, joints, and other vital organs. PDE IV inhibition is an approved therapy for BD. Hemay005 is a novel PDE IV inhibitor for treating chronic inflammatory diseases. Hemay005 significantly inhibits the activation of T lymphocytes, which play a vital role in the pathogenesis of Bechet's disease. It also inhibits Th1 type proinflammatory cytokines TNF-α, IFN-γ, IL-2, IL-12, and IL-23. Improvements in the side effect /efficacy ratio vs Apremilast are anticipated to improve on the efficacy of Apremilast, which was side effect limited at doses >30mg.

Methods: This was a multi-centre, randomized, double-blind, placebo-parallel-controlled, phase II clinical study. The study included four periods: a screening period, a 12-week core treatment period, a 12-week extension treatment period, and an off-drug observation period. All subjects completed the extension treatment period, followed by a 4-week off-drug observation period. It was planned to enrol a total of 252 patients, with randomization at 2:2:1:1 ratio. The study was terminated early

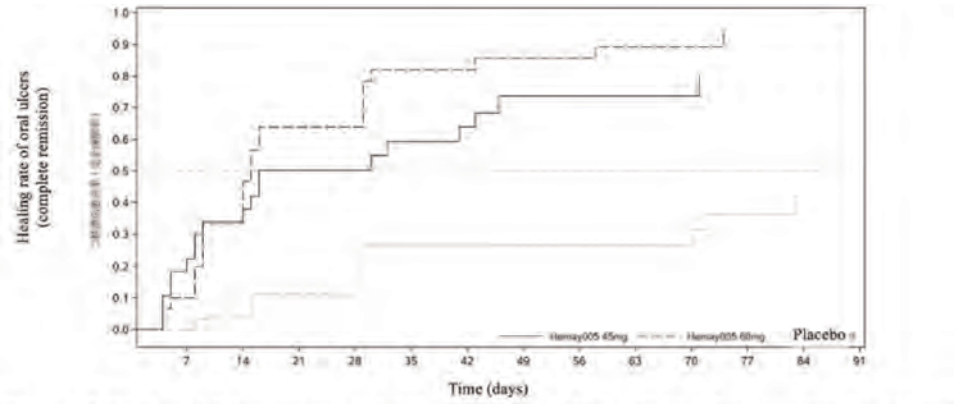

Figure 5 Kaplan-Meier curves - the time to first achieved complete remission of oral ulcer - FAS

Fig 1: Kaplan Meier curves: The time to first complete remission of oral ulcers -FAS

as the efficacy objective was achieved after 90 patients were recruited. The Area under the curve (AUC) for the number of oral ulcers in BD patients from baseline to Week 12 was the primary efficacy endpoint. Adverse Events were also recorded as primary safety endpoint.

Results: Overall, 90 subjects were recruited; 29 subjects were assigned to Hemay005 tablet 45 mg BID group, 31 to Hemay005 tablet 60 mg BID group, and 30 to placebo group. Results based on the FAS showed that the Hemay005 60 mg BID (1-sided, P <0.0001) and 45 mg BID (1-sided, P <0.0001) were statistically different from placebo in reducing the AUCs for the number of oral ulcers from baseline to Week 12. Analysis of the median healing time of oral ulcer estimated by KM was 16 days in 45 mg BID group, with 95% CI (8, 46); 15 days in 60 mg BID group, with 95% CI (9, 29); and the median healing time could not be estimated by KM method in placebo group Fig 1.

In the safety data set; (patients who received one dose or more of the drug or placebo), the incidence of TEAEs related to the study drug and leading to discontinuation of medication were higher in the 45 mg BID (6.9%) and 60 mg BID (6.7%)groups than that in the placebo group (0.0%) during the core treatment period. Most TEAEs reported during the core treatment period were mild; the incidence of severe TEAEs was dose-related, 3.3%, in the 60 mg BID and 0% in the 45 mg BID and placebo groups, respectively. No SAEs related to drug were reported throughout the study.

Table1 : The number of TEAS (MedDRA v 25); Percentages were calculated based on the number of subjects in the SS(Safety data set)

TEAEs reported in ≥ 5.0% of subjects in any treatment group, listed by SOC - SS

	45mg BID (N=29) n (%) E	60mg BID (N=30) n (%) E	Placebo (N=30) n (%) E
All TEAEs	26 (89.7) 129	29 (96.7) 186	21 (70.0) 75
Gastrointestinal disorders	20 (69.0) 52	20 (66.7) 58	12 (40.0) 19
Nervous system disorders	9 (31.0) 16	15 (50.0) 32	3 (10.0) 4
Infections and infestations	9 (31.0) 12	10 (33.3) 12	5 (16.7) 6
Musculoskeletal and connective tissue disorders	8 (27.6) 13	9 (30.0) 15	7 (23.3) 8
Metabolism and nutrition disorders	6 (20.7) 11	5 (16.7) 7	2 (6.7) 2
General disorders and administration site conditions	5 (17.2) 6	6 (20.0) 6	4 (13.3) 8
Investigations	3 (10.3) 7	8 (26.7) 31	11 (36.7) 14
Skin and subcutaneous tissue disorders	2 (6.9) 2	8 (26.7) 12	4 (13.3) 6
Respiratory, thoracic and mediastinal disorders	0	4 (13.3) 5	1 (3.3) 1
Cardiac Disorders	2 (6.9) 2	1 (3.3) 2	1 (3.3) 1
Reproductive system and breast disorders	2 (6.9) 3	1 (3.3) 1	0
Psychiatric disorders	0	3 (10.0) 3	1 (3.3) 1

Conclusion: Hemay005 60 mg BID and 45 mg BID for 12 weeks effectively reduced the AUC for the number of oral ulcers from baseline to Week 12 in BD patients. The study drug was safe and well-tolerated. A phase III clinical trial in patients with Bechet's disease is underway.

Disclosure: C. Jones: Hemay Pharmaceutical, 3; **Z. Li**: Abbott, 2, 9, Abbvie, 2, 9, BMS, 2, 9, Celgene, 2, 9, Eli Lilly, 2, 9, GSK, 2, 9, Janssen, 2, 9, MSD, 2, 9, Novartis, 2, 9, Pfizer, 2, 9, Roche, 2, 9, UCB Pharma, 2, 9; **Z. Zhang**: None; **J. Wu**: None; **G. Shi**: None; **W. Zheng**: None; **J. Tang**: None; **X. Wang**: None; **L. Dai**: None; **L. Chen**: None; **Y. Li**: None; **L. Wu**: None; **Y. Wang**: None; **S. Liu**: None; **Y. Ke**: None; **J. Lin**: None; **Z. Zhang**: None; **J. Hu**: None; **W. Dang**: None; **S. Yin**: None; **X. Tang**: None; **M. Zhu**: Hemay Pharmaceutical, 3; **J. Lin**: Hemay Pharmaceutical, 3; **R. Jones**: Hemay Pharmaceutical, 3; **W. Wan**: None; **x. Hu**: Hemay Pharmaceutical, 3.

Abstract Number: 2520

Identification of Clinical Phenotypes in Sarcoidosis Using a Cluster Analysis

Carmen Lasa[1], Raul Fernandez-Ramon[2], Jorge Javier Gaitán[2], Jose Luis Martin-Varillas[3], Rosalía Demetrio[2], Ivan Ferraz Amaro[4], Santos Castañeda[5] and Ricardo Blanco[6], [1]Hospital Universitario Marqués de Valdecilla, IDIVAL., La Cavada, Spain, [2]Hospital Universitario Marqués de Valdecilla, Santander, Spain, [3]Hospital de Laredo, Laredo, Spain, [4]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [5]Hospital de la Princesa, Madrid, Spain, [6]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain

SESSION INFORMATION
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Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases II
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Sarcoidosis is a disease with heterogeneous clinical presentation and course. The objective of this study is the identification of clinical phenotypes using cluster analysis.

Methods: A model-based clustering relaying on 19 clinical variables was performed in a retrospective cohort of 342 sarcoidosis patients, diagnosed and follow-up from 1999 to 2019 in a hospital at Northern Spain. Chi-square test and ANOVA were used to compare categorical and continuous variables among groups. Two-sample t-tests and the partition of Pearson's chi-square statistic were used in pairwise comparisons. The Wasfi severity score was calculated and compared among clusters.

Results: Cluster analysis identified five groups: C1: erythema nodosum and articular involvement (n=55; 16.1%), C2: miscellaneous extrapulmonary sarcoidosis (n=49; 14.3%), C3: ocular and/or neurological involvement (n=83; 24.3%), C4: isolated hiliar adenopathy (n=17; 5.0%), and C5: parenchymal lung involvement with dyspnea (n=138; 40.4%). Lung involvement was predominant in all clusters, ranging from 89.9% (C5) to 100% (C1 and C4), except for C2 (55.1%). Extrapulmonary involvement was significantly higher in C2 (96.4%) and C3 (98.0%). Demographic and clinical characteristics are shown in **Table 1**. A significant low mean FEV1 was detected in C5 (90.5±21.8) versus C1 (102.0±22.9), C3 (102.3 ±17.6) and C4 (105.8±20.8). The cluster 5 had a significantly lower mean FVC (96.6±18.9) than the other clusters, ranging from 108.1±18.0 (C3) to 111.5±21.7 (C4). The prescription of systemic steroids and non-corticosteroid immunosuppressants was significantly higher in the clusters 1, 3 and 5**.** Chronicity rates were significantly higher in C3 (31.3%) and C5

(32.6%) compared to C1 (9.1%) and C4 (0%). The clusters 3 and 5 also showed significantly higher severity score values. According to the clusters identified in the present study, we proposed an individualized "treat to target" schedule by subgroups (**Figure 1)**.

Table 1. Demographic and clinical characteristics of the study population.

Characteristics	Whole cohort	C1	C2	C3	C4	C5	p- value	q-value
Total	342 (100)	55 (16.1)	49 (14.3)	83 (24.3)	17 (5.0)	138 (40.4)		
Gender (female)	177 (51.8)	36 (65.5) ^{A}	35 (71.4) ^{B}	49 (59.0) ^{C}	9 (52.9)	48 (34.8) ^{A,B,C}	<0.001	<0.001
Follow-up period (years)	9.1±5.8	9.0±6.2	7.5±5.8 ^{A}	8.5±6.0 ^{B}	9.1±6.2	10.1±5.3 ^{A,B}	0.06	0.07
Age at diagnosis (years)	47.7±15.1	44.6±13.5 ^{A}	52.0±14.5 ^{A,B}	48.4±16.8	50.3±17.0	46.6±14.3 ^{B}	0.1	0.1
Pulmonary involvement	302 (88.3)	55 (100) ^{A,B}	27 (55.1) ^{A,C,D,E}	79 (95.2) ^{C}	17 (100) ^{D}	124 (89.9) ^{B,E}	<0.001	<0.001
Extra-pulmonary involvement	234 (68.6)	53 (96.4) ^{A,B,C}	48 (98.0) ^{D,E}	55 (66.3) ^{A,D,E}	0 ^{B,D,E}	78 (56.5) ^{C,E}	<0.001	<0.001
Skin	117 (34.2)	38 (69.1) ^{A,B,C}	32 (65.3) ^{D,E}	17 (20.5) ^{A,D}	0 ^{B,D}	30 (21.7) ^{C,E,F}	<0.001	<0.001
Nodosum erythema	70 (20.5)	35 (63.6) ^{A,B,C,D}	0 ^{A,E,F}	16 (19.3) ^{B,E}	0 ^{C}	19 (13.8) ^{D,F}	<0.001	<0.001
Granulomatous lesions	47 (13.8)	3 (5.5) ^{A}	32 (65.3) ^{A,B,C,D}	1 (1.2) ^{B,E}	0 ^{C}	11 (8.0) ^{D,E}	<0.001	<0.001
Eye	61 (17.8)	0 ^{A,B}	1 (2.0) ^{C,D}	30 (36.1) ^{A,C,E}	0 ^{E}	30 (21.7) ^{B,D,E}	0.02	0.02
Anterior uveitis	31 (9.1)	0 ^{A,B}	1 (2.0) ^{C}	19 (22.9) ^{A,C,D,E}	0 ^{D}	11 (8.0) ^{B,E}	<0.001	<0.001
Panuveitis	12 (3.5)	0	0	5 (6.0)	0	7 (5.1)	0.1	0.1
Liver	33 (9.6)	1 (1.8) ^{A}	17 (34.7) ^{A,B,C,D}	3 (3.6) ^{B}	0 ^{C}	12 (8.7) ^{D}	<0.001	<0.001
Joint	95 (27.8)	37 (67.3) ^{A,B,C,D}	8 (16.3) ^{A}	19 (22.9) ^{B,E}	0 ^{C,E,F}	33 (23.9) ^{D,F}	<0.001	<0.001
Hypercalcemia	17 (5.0)	1 (1.8) ^{A}	8 (16.3) ^{A,B,C}	2 (2.4) ^{B}	0	6 (4.3) ^{C}	0.002	0.002
Nervous system	29 (8.5)	1 (1.8) ^{A}	0 ^{B}	20 (24.1) ^{A,B,C,D}	0 ^{C}	8 (5.8) ^{D}	<0.001	<0.001
Heart	5 (1.5)	0	1 (2.0)	0	0	4 (2.9)	0.4	0.3
Lofgren's syndrome	43 (12.6)	24 (43.6) ^{A,B,C,D}	2 (4.1) ^{A}	9 (11.0) ^{B}	0 ^{C}	8 (5.8) ^{D}	<0.001	<0.001
Number of involved organs	2.0±1.0	2.4±0.7 ^{A,B,C,D}	1.9±0.8 ^{A,C}	2.1±1.1 ^{B,F}	1.0±0.0 ^{C,E,F,G}	1.8±1.1 ^{D,G}	<0.001	<0.001
Cough	51 (14.9)	3 (5.5) ^{A}	1 (2.0) ^{B,C}	14 (16.9) ^{B}	0 ^{D}	33 (23.9) ^{A,C,D}	<0.001	<0.001
Dyspnoea	94 (27.5)	11 (20.0) ^{A}	5 (10.2) ^{B}	17 (20.5) ^{C,D}	0 ^{D,E}	61 (44.2) ^{A,B,C,E}	<0.001	<0.001
Asthenia	96 (28.1)	1 (1.8) ^{A,B,C}	18 (36.7) ^{A,D}	42 (50.6) ^{B,E,F}	0 ^{D,E,G}	35 (25.4) ^{C,F,G}	<0.001	<0.001
Fever	38 (11.1)	16 (29.1) ^{A,B,C,D}	0 ^{A,E,F}	7 (8.4) ^{B,E}	0 ^{C}	15 (10.9) ^{D,F}	<0.001	<0.001
Treatment								
Corticosteroids	206 (60.2)	30 (54.5) ^{A,B,C}	17 (34.7) ^{A,D,E}	51 (61.4) ^{D,F}	3 (17.6) ^{B,F}	105 (76.1) ^{C,E,F}	<0.001	<0.001
Duration (weeks)	176.7±177.5	127.8.5±144.8	115.5±101.1	194.6±195.8	8.7±1.5	195.3±184.1	0.08	0.08
Maximum dose (mg/kg)	41.6±18.5	21.8±11.7 ^{A,B,C,D}	45.9±15.4 ^{A}	41.3±17.7 ^{B}	50.00±17.3 ^{C}	46.5±17.2 ^{D}	<0.001	<0.001
Immunosuppressants	96 (28.1)	13 (23.6) ^{A,B}	7 (14.3) ^{C,D}	35 (42.2) ^{A,C,E}	0 ^{B,E,F}	41 (29.7) ^{D,F}	<0.001	<0.001
CIS	87 (25.4)	13 (23.6) ^{A}	6 (12.2) ^{B,C}	32 (38.6) ^{B,D}	0 ^{A,D,E}	36 (26.1) ^{C,E}	0.001	0.002
Biological therapy	44 (12.9)	2 (3.6) ^{A,B}	1 (2.0) ^{C,D}	18 (21.7) ^{A,C,E}	0 ^{E}	23 (16.7) ^{B,D}	0.001	0.002
Chronicity	87 (26.5)	5 (9.1) ^{A,B}	10 (20.4)	26 (31.3) ^{A,C}	0 ^{C,D}	45 (32.6) ^{B,D}	0.001	0.002
Sequelae / irreversible organ damage	47 (13.7)	2 (3.6) ^{A}	6 (12.2)	11 (13.3)	0 ^{B}	27 (19.6) ^{A,B}	0.02	0.03

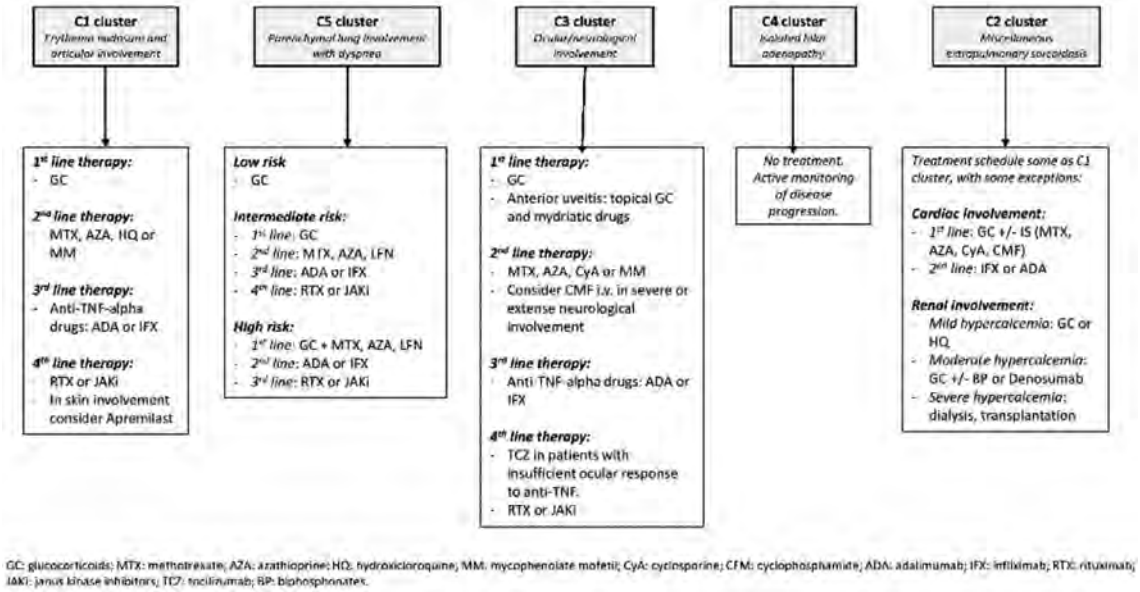
CIS: conventional synthetic immunosuppressant agents; SD: standard desviation.

Data presented: n (%) or mean ± SD

C1: erythema nodosum and articular involvement; **C2**: miscellaneous extrapulmonary sarcoidosis; **C3**: ocular and/or neurological involvement; **C4**: isolated hilar adenopathy; **C5**: parenchymal lung involvement with dyspnea.

Clusters sharing the same letter (*A, B, C, D, E, F, G*) means that they have statistically significant differences (q<0.05) in the pairwise comparison.

Figure 1. Proposed treat to target schedule according to patient cluster.



GC: glucocorticoids; MTX: methotrexate; AZA: azathioprine; HQ: hydroxicloroquine; MM: mycophenolate mofetil; CyA: ciclosporine; CFM: cyclophosphamide; ADA: adalimumab; IFX: infliximab; RTX: rituximab; JAKi: janus kinase inhibitors; TCZ: tocilizumab; BP: biphosphonates.

Conclusion: Five phenotypes of sarcoidosis with different clinical and prognostic characteristics are proposed in our study. Cluster analysis can be a useful tool for identifying clinical patterns in a disease as heterogeneous as sarcoidosis and facilitating its management.

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Abstract Number: 2521

Understanding Age as a Risk Factor for Complications After Total Knee Arthroplasty: What Can We Learn from Machine Learning?

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Orthopedics, Low Back Pain, & Rehabilitation
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Rates of total knee arthroplasty (TKA) in the United Stateshave risen, coupled with increasing demand for TKAs in younger patients.[1]Althoughrates of postoperative complications in TKA have decreased significantly,[2] they remaina significant concern for patients and clinicians. In light of these changing trends in TKA use and outcomes, we sought to understand how risk for adverse TKA outcomes changes with age using machine learning algorithms.

Methods: We studied patients undergoing TKA from the Pennsylvania Health Care Cost Containment Council (PHC4) Database, 2012-2018.Our primary variable of interest was age as a risk factor for the binary outcomes of 90-day readmission, 90-day mortality, 1-year revision, and the continuous outcome length of stay (LOS). Our model included patient-level demographics and covariates, including sex, race, discharge location, and insurance. We trained explainable boosting machines (EBMs)to predict risk (70% train:30% test) for the aforementioned outcomes.[3]For binary outcomes, we stratified the training data by outcome for balance. EBMs are highly accurate, interpretable models that are flexible in visualizing the dependent variables and handle collinearity well which is important in TKA. We report test AUROCs and R^2as evaluation metrics for predictive performance of the models, and further include partial dependency plots which explain the relationship of age with these outcomes.

Table 1: Cohort Characteristics by Outcome

	Cohort	90-Day Readmission	90-Day Mortality	1-Year Revision
Variable [a]	N=227,959	N=17,065	N=511	N=1,795
Age	66 [60, 73]	69 [62, 67] ***	75 [66, 81] ***	64 [57, 71] ***
Sex				
Female	141063 (61.9%)	10,050 (59%) ***	251 (49%) ***	983 (55%) ***
Race				
White	205364 (90.1%)	15,094 (89%) ***	448 (88%) *	1,586 (89%) ***
Black	14422 (6.3%)	1,456 (8.5%) ***	46 (9.0%) *	161 (9.0%) ***
Other	7917 (3.5%)	498 (2.9%) ***	17 (3.3%) *	43 (2.4%) ***
Discharge location				
HHC	57702 (25.3%)	3,652 (21%) ***	60 (12%) ***	610 (34%) ***
Home	27268 (12.0%)	1,497 (8.8%) ***	17 (3.3%) ***	269 (15%) ***
IRF	117982 (51.8%)	8,990 (53%) ***	341 (67%) ***	644 (36%) ***
SNF	25007 (11.0%)	2,926 (17%) ***	93 (18%) ***	272 (15%) ***
Insurance				
Commercial	90965 (39.9%)	4,505 (26%) ***	78 (15%) ***	733 (41%) ***
Government	1449 (0.6%)	100 (0.6%) ***	6 (1.2%) ***	15 (0.8%) ***
Medicaid	8780 (3.9%)	871 (5.1%) ***	22 (4.3%) ***	142 (7.9%) ***
Medicare	125419 (55.0%)	11,514 (67%) ***	403 (79%) ***	897 (50%) ***
Unknown/uninsured	1346 (0.6%)	75 (0.4%) ***	2 (0.4%) ***	8 (0.4%) ***
Diabetes	23443 (10.3%)	2,478 (15%) ***	76 (15%) ***	265 (15%) ***
Hypertension	76043 (33.4%)	6,634 (39%) ***	175 (34%)	820 (46%) ***
Obesity	31312 (13.7%)	2,856 (17%) ***	74 (14%)	380 (21%) ***
Elixhauser Comorbidity Index	0 [0,2]	1 [0, 3] ***	1 [0, 3] ***	1 [0, 3] ***

[a] Data presented as N (%) or Median [IQR].

* p-value < 0.05. ** p-value < 0.01. *** p-value < 0.001. p-value calculated via Chi-squared test, Fisher's exact test, and Wilcoxon rank sum test. p-values compares groups with and without the outcome for all the variables listed above.

HHC, health home care; IRF, inpatient rehabilitation facility; SNF, skilled nursing facility.

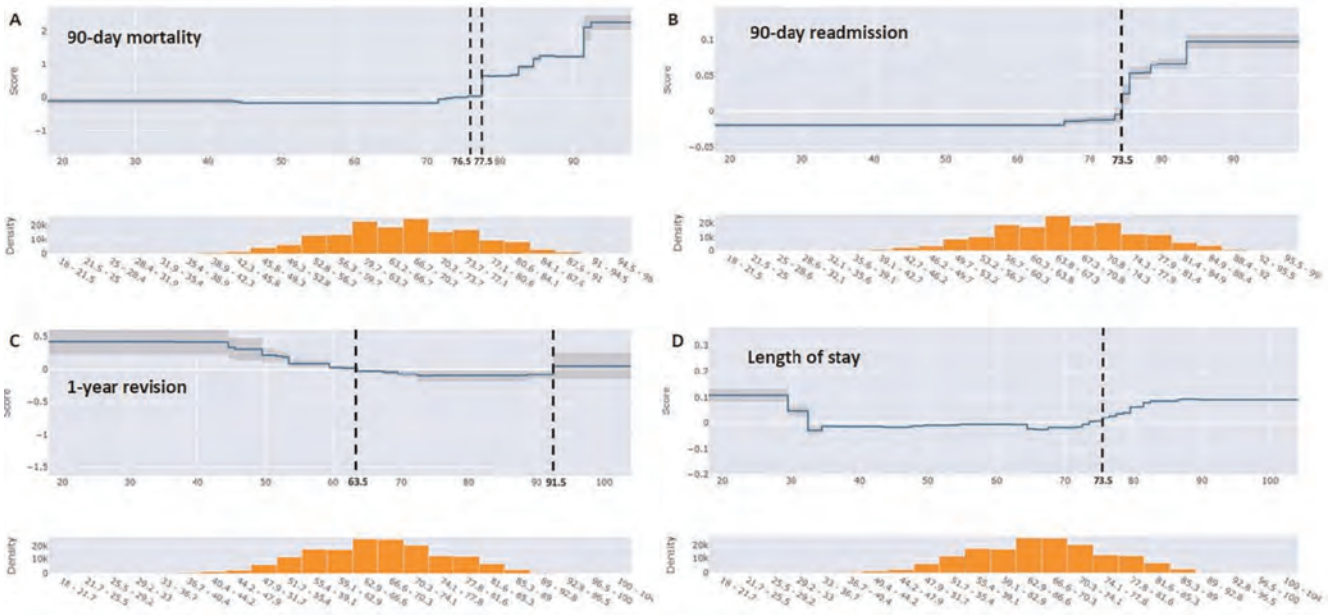

Figure 1: Partial dependency plots to understand the marginal effect of age (years) on (A) 90-day mortality, (B) 90-day readmission, (C) 1-year revision, and (D) length of stay from the supervised explainable boosting machine models. Y-axis score is shown in log scale. Vertical lines demonstrate where risk score is equal to 0, and show the age of the average contribution to risk.

Results: We had a cohort of 227,959TKA patients, with a median age of 65 years with 90.1% White and 55% Medicare-insured (Table 1).90-day readmission was observed in 7.49%, 90-day mortality in 0.22%, and 1-year revision in 0.79%. Predictive performance of adverse outcomes was strongest for 90-day mortality (AUROC=0.74), followed by 1-year revision (AUROC=0.64), 90-day readmission (AUROC=0.62), and LOS (RMSE=0.36, R^2=0.13). Age was among the most important factors for predicting all outcomes and its relationship with the outcomes is detailed in the partial dependency plots in Figure 1.Predicted risk of90-day mortality increases significantly after the age of 77.5 years, whereas90-day readmission increases after the age of 73.5 years, and LOS risk increases at 73.5 years. However, with 1-year revision the risk decreases after the age of 63.5 (Figure 1).

Conclusion: We determined that the effect of age as a risk factor for poor TKA outcomes changes dramatically at specific time points, thus demonstrating that there is a nonlinear relationship between age and TKA outcomes. Traditional regression models have always been understood to have a proportionate increase in risk as age increases. However, our study gives nuance to this understanding and can help physicians and patients in decision-making when trying to quantify risks related to aging as they consider TKA as a treatment option.

References

1. Ravi B et al. The changing demographics of total joint arthroplasty recipients in the United States and Ontario from 2001 to 2007. PMID:23218428
2. Singh JA et al. Rates of Total Joint Replacement in the United States: Future Projections to 2020–2040 Using the National Inpatient Sample. PMID:30988126
3. Nori H et al. InterpretML: A Unified Framework for Machine Learning Interpretability. arXiv:1909.09223

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Abstract Number: 2522

Diabetes Mellitus Impacts Primary Total Hip Arthroplasty Outcomes: A National Cohort Study

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Orthopedics, Low Back Pain, & Rehabilitation
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Primary total hip arthroplasty (THA) patients often have concomitant medical comorbidities. This study aims to identify the impact of diabetes mellitus (DM) on inpatient clinical and healthcare utilization outcomes in patients, and whether this association varies by the underlying primary diagnoses.

Methods: We identified patients over the age of 18 who underwent THA in the 2019 National Inpatient Sample (NIS). We stratified patients by primary diagnosis into hip osteoarthritis (OA; N=405691), avascular necrosis (AVN; N=17060), fracture (N=104265), inflammatory arthritis (IA; N=5720) (includes rheumatoid arthritis [RA], spondylarthritis [SpA], including ankylosing spondylitis, and psoriatic arthritis [PsA]), vs. other. We identified underlying diagnoses using primary diagnosis codes and diabetes and complications using secondary diagnosis codes. We performed multivariable-adjusted regression analyses for clinical and healthcare utilization outcomes as endpoints, adjusted for race, age, sex, hospital bed size, census region, and teaching status.

Results: Total cohort population was 591,891, with 101,385 classified as diabetic. Mean age was 68.75, mean length of stay (LOS) was 2.73 days, and 58.20% were female. Overall, DM was associated with increased LOS, non-routine discharge (i.e., to a facility), and acute renal failure (ARF) ($p \leq 0.05$ each). Patients in the OA or fracture cohorts with DM were more likely to have non-routine discharges ($p \leq 0.001$ each). DM was significantly associated with an increased risk of longer LOS and ARF in OA, fracture, and IA cohorts ($p \leq 0.03$ each). DM was associated with increased risk of blood transfusions ($p=0.031$), and a lower risk of pneumonia and prosthetic complications in the fracture cohort ($p \leq 0.016$ each).

Conclusion: DM was associated with increased healthcare utilization and ARF following primary THA, indicating associated healthcare resource and clinical burden. The variation in association of DM with outcomes post-primary THA for people with AVN or fractures, identifies differential effect in elective versus non-elective cases that needs further study.

Table-1: Baseline Hospital and Patient Characteristics with Diabetes Mellitus (DM) who underwent primary total hip arthroplasty (THA) in the National Inpatient Sample (2019, N=532736)

Variable	Non-Diabetic (N=490506; 82.9%)	Diabetic (N=101385; 17.1%)	Overall (N=591891)	p value
Age (mean ± SD years)	68.35 ± 0.09	70.68 ± 0.09	68.75 ±0.09	<.001
Length of Stay (mean ± SD days)	2.61 ± 0.03	3.28 ± 0.03	2.73 ±0.03	<.001
Total Charges (mean ± SD dollars)	71183.01 ± 965.5	76712.59 ± 1003.3	72130.27 ± 952.8	<.001
In-hospital mortality	1435 (0.30%)	410 (0.40%)	1845 (0.30%)	<.001
Underlying Condition (N,%)				<.001
Osteoarthritis	342045 (69.70%)	63645 (62.80%)	405691 (68.50%)	
Avascular necrosis	14855 (3.00%)	2205 (2.20%)	17060 (2.90%)	
Fracture	80865 (16.50%)	23400 (23.10%)	104265 (17.60%)	
Inflammatory arthritis[1]	4540 (0.90%)	1180 (1.20%)	5720 (1.00%)	
Other	48200 (9.80%)	10955 (10.80%)	59155 (10.00%)	
Sex (N,%)				<.001
Male	200350 (40.80%)	47105 (46.50%)	247455 (41.80%)	
Female	290150 (59.20%)	54280 (53.50%)	344430 (58.20%)	
Number of Obese Patients	92730 (18.90%)	31250 (30.80%)	123980 (20.90%)	0.788
Number of Morbidly Obese Patients	19660 (4.00%)	8070 (8.00%)	27730 (4.70%)	0.002
Race (N,%)				<.001
White	417215 (87.40%)	79425 (80.20%)	496641 (86.10%)	
Black	31565 (6.60%)	10390 (10.50%)	41955 (7.30%)	
Hispanic	15020 (3.10%)	5225 (5.30%)	20245 (3.50%)	
Asian or Pacific Islander	4715 (1.00%)	1755 (1.80%)	6470 (1.10%)	
Native American	7525 (1.60%)	1615 (1.60%)	9140 (1.60%)	
Other	1520 (0.30%)	570 (0.60%)	2090 (0.40%)	
Charlson Comorbidity (N,%)				<.001
0	312145 (63.60%)	0 (0.00%)	312145 (52.70%)	
1	113810 (23.20%)	41785 (41.20%)	155595 (26.30%)	
2	32835 (6.70%)	23535 (23.20%)	56370 (9.50%)	
3	11215 (2.30%)	16590 (16.40%)	27805 (4.70%)	
4	3420 (0.70%)	8600 (8.50%)	12020 (2.00%)	
≥5	17080 (3.50%)	10875 (10.70%)	27955 (4.70%)	
Insurance Type (N,%)				<.001
Medicare	301025 (61.40%)	71615 (70.70%)	372640 (63.00%)	
Medicaid	23120 (4.70%)	4450 (4.40%)	27570 (4.70%)	
Private Insurance	149425 (30.50%)	21835 (21.60%)	171260 (29.00%)	
Self-Pay	4575 (0.90%)	750 (0.70%)	5325 (0.90%)	
No Charge	180 (0.00%)	35 (0.00%)	215 (0.00%)	
Other	11625 (2.40%)	2610 (2.60%)	14235 (2.40%)	
Patient Disposition (N,%)				<.001
Routine	184065 (37.50%)	29760 (29.40%)	213825 (36.10%)	
Transfer to Short-term Hospital	1335 (0.30%)	430 (0.40%)	1765 (0.30%)	
Transfer Other[2]	121715 (24.80%)	37700 (37.20%)	159415 (26.90%)	
Home Health Care (HHC)	181535 (37.00%)	32955 (32.50%)	214490 (36.20%)	
Against Medical Advice (AMA)	360 (0.10%)	115 (0.10%)	475 (0.10%)	
Died	1435 (0.30%)	410 (0.40%)	1845 (0.30%)	
Median Household Income for ZIP Code (N,%)				<.001
0-25th percentile	99330 (20.50%)	25780 (25.80%)	125110 (21.40%)	
26th-50th percentile (median)	119955 (24.80%)	26620 (26.60%)	146575 (25.10%)	
51st to 75th percentile	132155 (27.30%)	26375 (26.40%)	158530 (27.20%)	
76th to 100th percentile	132195 (27.30%)	21150 (21.20%)	153345 (26.30%)	
Census Division of Hospital (N,%)				<.001
New England	28120 (5.70%)	4700 (4.60%)	32820 (5.50%)	
Middle Atlantic	65545 (13.40%)	12620 (12.40%)	78165 (13.20%)	
East North Central	80890 (16.50%)	18420 (18.20%)	99310 (16.80%)	
West North Central	40220 (8.20%)	7990 (7.90%)	48210 (8.10%)	
South Atlantic	96310 (19.60%)	21295 (21.00%)	117605 (19.90%)	
East South Central	31100 (6.30%)	8040 (7.90%)	39140 (6.60%)	
West South Central	45050 (9.20%)	10330 (10.20%)	55380 (9.40%)	
Mountain	39305 (8.00%)	6480 (6.40%)	45785 (7.70%)	
Pacific	63965 (13.00%)	11510 (11.40%)	75475 (12.80%)	
Location/teaching status of hospital (N,%)				0.481
Rural	42435 (8.70%)	9615 (9.50%)	52050 (8.80%)	
Urban nonteaching	105455 (21.50%)	21915 (21.60%)	127370 (21.50%)	
Urban teaching	342615 (69.80%)	69855 (68.90%)	412470 (69.70%)	
Complications (Post-operative)[3]				
Need for blood transfusion	21180 (4.30%)	6295 (6.20%)	27475 (4.60%)	<.001
Prosthetic complications	8565 (1.70%)	2015 (2.00%)	10580 (1.80%)	<.001
Post-procedural infection	1160 (0.20%)	300 (0.30%)	1460 (0.20%)	0.626
Complications (Cumulative)[4]				
Acute renal failure	19460 (4.00%)	9100 (9.00%)	28560 (4.80%)	<.001
Myocardial infarction	1920 (0.40%)	620 (0.60%)	2540 (0.40%)	<.001
Pulmonary embolism	1075 (0.20%)	290 (0.30%)	1365 (0.20%)	0.313
Deep vein thrombosis	2020 (0.40%)	540 (0.50%)	2560 (0.40%)	0.782
Pneumonia	21180 (4.30%)	6295 (6.20%)	27475 (4.60%)	0.131

[1]Includes rheumatoid arthritis, spondylarthritis, ankylosing spondylitis and psoriatic arthritis

[2]Includes Skilled Nursing Facility (SNF), Intermediate Care Facility (ICF), Another Type of Facility

Table-2: Multivariable-adjusted association of Diabetes Mellitus (DM) with clinical outcomes of patients who underwent primary total hip arthroplasty (THA), stratified by underlying diagnosis

	Osteoarthritis (N=405691; 68.5%)		Avascular necrosis (N=17060; 2.9%)		Fracture (N=104265; 17.6%)		Inflammatory arthritis[1] (N=5720; 0.9%)		Other (N=59155; 10.0%)		Total (N=591891)	
Variable	aOR (95% CI)	p	aOR (95% CI)	p	aOR (95% CI)	p	aOR (95% CI)	p	aOR (95% CI)	p	aOR (95% CI)	p
Length of Stay (> 2 days)	1.437 (1.357-1.522)	<.001	1.314 (1.000-1.725)	0.05	1.379 (1.188-1.600)	<.001	1.787 (1.059-3.014)	0.03	1.281 (1.128-1.456)	<.001	1.377 (1.320-1.437)	<.001
Total Cost (Charges above median)	0.985 (0.935-1.039)	0.582	0.928 (0.731-1.179)	0.543	1.016 (0.940-1.098)	0.686	1.433 (0.975-2.107)	0.067	1.141 (1.010-1.288)	0.034	1.007 (0.967-1.049)	0.743
Mortality	1.483 (0.530-4.149)	0.452	*		0.924 (0.659-1.296)	0.646	1.544 (0.511-4.666)	0.441	0.624 (0.361-1.079)	0.091	0.818 (0.626-1.069)	0.141
Non-routine discharge	1.136 (1.084-1.190)	<.001	1.142 (0.900-1.449)	0.275	1.622 (1.495-1.886)	<.001	1.275 (0.678-2.398)	0.451	1.226 (1.068-1.408)	0.004	1.156 (1.107-1.207)	<.001
Complications (Post-operative)[2]												
Need for blood transfusion	0.986 (0.859-1.131)	0.835	0.943 (0.559-1.590)	0.826	1.136 (1.011-1.275)	0.031	0.946 (0.621-1.440)	0.795	1.106 (0.953-1.285)	0.185	1.053 (0.977-1.134)	0.178
Prosthetic complications	0.991 (0.788-1.246)	0.94	0.338 (0.079-1.444)	0.143	0.665 (0.502-0.880)	0.004	0.797 (0.489-1.301)	0.364	1.086 (0.918-1.285)	0.337	0.948 (0.845-1.064)	0.368
Post-procedural infection	0.904 (0.227-3.603)	0.886	*		0.951 (0.449-2.016)	0.895	*		0.890 (0.630-1.257)	0.508	0.861 (0.634-1.169)	0.338
Complications (Cumulative)[3]												
Acute renal failure	1.901 (1.680-2.153)	<.001	1.732 (0.955-3.139)	0.07	1.809 (1.647-1.987)	<.001	1.626 (1.079-2.450)	0.02	1.580 (1.363-1.831)	<.001	1.699 (1.590-1.815)	<.001
Pneumonia	1.503 (0.914-2.473)	0.108	1.522 (0.361-6.422)	0.567	0.877 (0.652-1.180)	0.385	0.747 (0.243-2.294)	0.611	0.926 (0.555-1.547)	0.77	0.922 (0.742-1.144)	0.460
Pulmonary embolism	1.031 (0.506-2.102)	0.932	3.502 (0.191-64.194)	0.398	0.879 (0.567-1.363)	0.565	1.899 (0.346-10.429)	0.46	0.889 (0.471-1.677)	0.716	0.948 (0.697-1.288)	0.732
Deep vein thrombosis	1.074 (0.697-1.656)	0.746	0.961 (0.148-6.252)	0.967	0.727 (0.508-1.041)	0.081	1.025 (0.273-3.845)	0.971	0.860 (0.567-1.304)	0.689	0.878 (0.697-1.104)	0.265
Myocardial infarction	1.041 (0.982-1.103)	0.174	0.879-0.660-1.170)	0.376	0.985 (0.913-1.063)	0.696	0.846 (0.608-1.178)	0.322	0.944 (0.847-1.053)	0.303	1.007 (0.965-1.050)	0.75

[1]Includes rheumatoid arthritis, spondylarthritis, ankylosing spondylitis and psoriatic arthritis

*removed from multivariate regression due to quasi-complete separation

ICD-10 CM codes: Acute Renal Failure (N17.x), Myocardial Infarction (I21.x), Pneumonia (J18.9, J15.9, J22.x), Pulmonary Embolism (I26.x), Deep Venous Thrombosis (DVT; I82.x), Prosthetic Complication (T84.010A, T84.012A, T84.012A, T84.013A, T84.018A, T84.019A, T84.020A, T82.021A, T84.022A, T84.023A, T84.028A, T84.029A, T84.090A, T84.091A, T84.092A, T84.093A, T84.098A, T84.099A, M96.65, M96.661,M96.662, M96.669, M96.671, M96.672, M96.69, M97.02XA, M97.11X1, M97.12XA), Post-Procedural Infection (T84.50XA, T84.51XA, T84.52XA, T84.54XA, T84.59XA, T81.4)

ICD-10 PCS codes: Blood Transfusion (302*)

[2]Only initial encounter ICD-10 codes selected

[3]Complications may include pre-operative conditions

Disclosure: S. Chandrupatla: None; **K. Rumalla**: None; **J. Singh**: Other, 2, 6, 11, 11, 12, Adaptimmune Therapeutics, GeoVax Labs, Pieris Pharmaceuticals, Enzolytics Inc., Seres Therapeutics, Tonix, Charlotte's Web, 12, Atai life sciences, kintara therapeutics, Intelligent Biosolutions, Acumen pharmaceutical, TPT Global Tech, Vaxart pharmaceuticals, Atyu biopharma, 12, speaker's bureau of Simply Speaking, other, 12, received institutional research support from Zimmer Biomet Holdings. JAS received food and beverage payments from Intuitive Surgical Inc./Philips Elec, Other, 12, Schipher, Crealta/Horizon, Medisys, Fidia, PK Med, Two labs Inc., Adept Field Solutions, Clinical Care options, Clearview healthcare partners, Putnam.

Abstract Number: 2523

Region, Race, and Hospital Factors Impact Length of Stay and Hospital Charges Post-primary Total Knee Arthroplasty

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Orthopedics, Low Back Pain, & Rehabilitation

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Osteoarthritis (OA) affects nearly 33 million adults in the US and total knee arthroplasty (TKA) is an effective treatment. Outcomes can vary by regional and hospital level disparities. We sought to determine patient characteristics and hospital level factors of extended hospital stays and increased costs in patients with knee OA who underwent primary TKA in a nationally representative sample.

Methods: We examined patients from the 2019 National Inpatient Sample (NIS) with OA who underwent primary TKA using the International Classification of Disease 10th Edition (ICD-10) Diagnosis and Procedure codes. Patient and regional characteristics were assessed. Primary outcomes were extended length of stay (eLOS) and increased hospital charges (IHC), determined as the upper quartile of each outcome. Multivariable analysis determined independent predictors for each outcome. Area Under the Curve (AUC) analysis assessed classification ability.

Results: 543,291 patients underwent TKA in 2019; 61.7% were female and 81.3% were white. Independent predictors of IHC include hospital bed size ($p < 0.001$), location & teaching status ($p < 0.001$), and hospital control ($p < 0.001$). South and West region hospitals a significantly higher adjusted odds ratio (aOR 1.54 & 2.79, $p < 0.001$) of IHC when compared to Northeastern region hospitals. Significant independent predictors of eLOS include race & ethnicity ($p < 0.001$), payer

Table-1: Baseline Hospital and Patient Characteristics with Osteoarthritis who undergo Total Knee Replacement in the Nationwide Inpatient Sample (2019, N=543,291)	
Variables	
Age (standard error)	67 (0.1)
Sex	
Male	208140 (38.3)
Female	335150 (61.7)
Race & Ethnicity	
White	429561 (81.3)
Black	43385 (8.2)
Hispanic	32670 (6.2)
Asian or Pacific Islander	8550 (1.6)
Native American	2630 (0.5)
Other	11810 (2.2)
Region	
Northeast	111071 (20.4)
Midwest	139025 (25.6)
South	195575 (36.0)
West	97620 (18.0)
Payer	
Medicare	313045 (57.7)
Medicaid	22705 (4.2)
Private	184810 (34.1)
Self-pay or other	22195 (4.1)
Median Income Quartile by Patient ZIP Code	
1st (Highest Income)	119850 (22.3)
2nd	138670 (25.9
3rd	147335 (27.5)
4th (Lowest Income)	130155 (24.3)
Hospital Bed Size	
Small	195240 (35.9)
Medium	148875 (27.4)
Large	199175 (36.7)
Location & Teaching Status	
Rural	55375 (10.2)
Urban Non-Teaching	127891 (23.5)
Urban Teaching	360025 (66.3)
Hospital Control	
Government (Public)	45695 (8.4)
Private, Not-for-Profit (Voluntary)	397760 (73.2)
Private (Proprietary)	99836 (18.4)
Extended Length of Stay (> 3 days)	43740 (8.1)
Increased Total Charge (> $77,500)	135380 (25.0)
Non-Home Discharge	84580 (15.6)
Perioperative Complication	13825 (2.5)
Mortality	200 (0.0)
Data are reported as raw numbers with proportions (%) for comparison * Indicates values under the HCUP reporting limit	

Table-2: Multivariable analysis of regional characteristics for primary outcomes extended length of stay and increased hospital charge (2019, N=543,291)

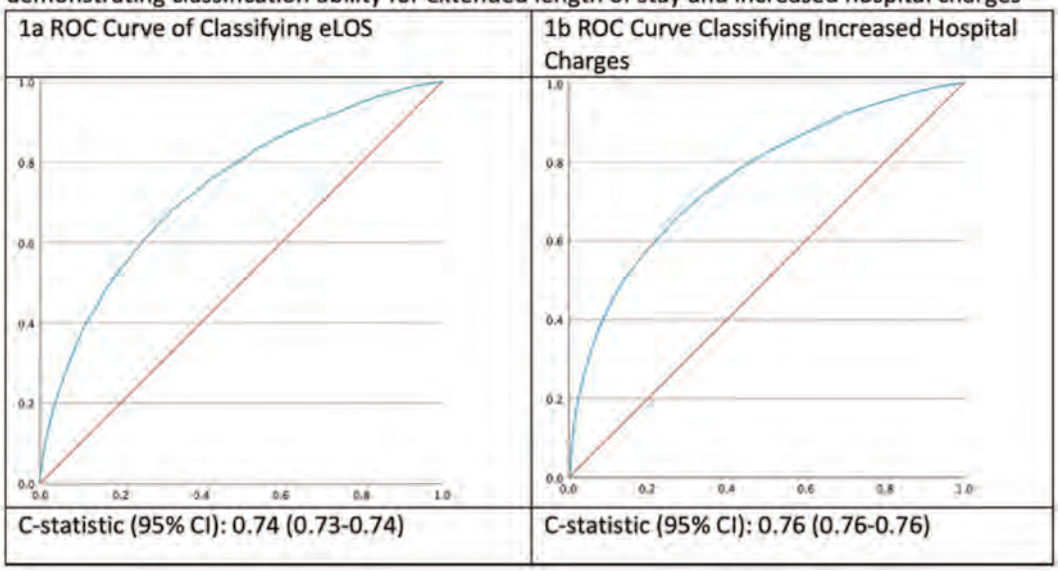
	Extended Hospital Length of Stay (LOS > 3 days)		Increased Hospital Charge (> $77,500)	
Variables	aOR (95% CI)	p-value	aOR (95% CI)	p-value
Age	1.41 (1.35-1.47)	<0.001	0.92 (0.89-0.96)	<0.001
Sex		<0.001		0.005
Male	Ref		Ref	
Female	1.18 (1.12-1.24)		0.94 (0.90-0.98)	
Race/Ethnicity		<0.001		<0.001
White	Ref		Ref	
Black	1.77 (1.61-1.95)		1.28 (1.12-1.47)	
Hispanic	1.10 (0.94-1.30)		1.84 (1.55-2.19)	
Asian or Pacific Islander	1.28 (0.92-1.78)		1.55 (1.25-1.92)	
Native American	1.35 (0.90-2.02)		0.48 (0.31-0.75)	
Other	1.20 (0.99-1.45)		1.92 (1.43-2.58)	
Region		<0.001		<0.001
Northeast	Ref		Ref	
Midwest	0.95 (0.79-1.13)		0.69 (0.46-1.02)	
South	0.85 (0.68-1.06)		1.54 (1.05-2.26)	
West	0.46 (0.36-0.58)		2.79 (1.86-4.19)	
Payer		<0.001		<0.001
Medicare	1.02 (0.89-1.16)		1.18 (1.08-1.29)	
Medicaid	1.84 (1.59-2.14)		1.27 (1.09-1.48)	
Private	Ref		Ref	
Self-pay or other	1.42 (1.21-1.67)		1.05 (0.89-1.24)	
Median Income Quartile by Patient ZIP Code		<0.001		0.278
1st (Lowest Income)	1.35 (1.19-1.52)		0.92 (0.76-1.10)	
2nd	1.25 (1.12-1.40)		0.90 (0.77-1.06)	
3rd	1.12 (1.02-1.24)		0.88 (0.76-1.01)	
4th (Highest Income)	Ref		Ref	
Hospital Bed Size		0.786		<0.001
Small	0.97 (0.80-1.18)		0.54 (0.39-0.74)	
Medium	0.94 (0.79-1.12)		1.02 (0.80-1.31)	
Large	Ref		Ref	
Location & Teaching Status		0.330		<0.001
Rural	1.08 (0.93-1.25)		0.39 (0.30-0.51)	
Urban Non-Teaching	0.94 (0.79-1.11)		0.73 (0.56-0.94)	
Urban Teaching	Ref		Ref	
Hospital Control		<0.001		<0.001
Government (Public)	1.49 (1.22-1.82)		0.64 (0.46-0.91)	
Private, Not-for-Profit (Voluntary)	Ref		Ref	
Private (Proprietary)	0.56 (0.44-0.70)		4.20 (3.08-5.73)	
Perioperative Complication	2.87 (2.58-3.18)	<0.001	1.16 (1.02-1.32)	0.026
Length of Stay	-	-	1.33 (1.18-1.50)	<0.001
Total Hospital Charge	1.18 (1.16-1.21)	<0.001	-	-

Data are reported as raw numbers with proportions (%) for comparison.
Unit of change for age = 10; Unit of Change for Total Hospital Charge = $10,000
Significance was determined a priori at $p < 0.05$.

($p < 0.001$), and hospital control ($p < 0.001$). Multivariable models for eLOS and IHC had AUC C-statistic scores of 0.74 and 0.76, respectively, demonstrating a modest classification ability.

Conclusion: Patient race/ethnicity, payer, regional and hospital level characteristics impacted outcomes and costs for the OA patients who underwent primary TKA in 2019. A stronger emphasis to address regional, hospital-level, and racial disparities can improve outcomes for the thousands of OA patients who undergo TKA every year.

Figure-1: Multivariable prediction models of geographic and regional level characteristics demonstrating classification ability for extended length of stay and increased hospital charges



Disclosure: K. Rumalla: None; **S. Chandrupatla**: None; **J. Singh**: Other, 2, 6, 11, 11, 12, Adaptimmune Therapeutics, GeoVax Labs, Pieris Pharmaceuticals, Enzolytics Inc., Seres Therapeutics, Tonix, Charlotte's Web, 12, Atai life sciences, kintara therapeutics, Intelligent Biosolutions, Acumen pharmaceutical, TPT Global Tech, Vaxart pharmaceuticals, Atyu biopharma, 12, speaker's bureau of Simply Speaking, other, 12, received institutional research support from Zimmer Biomet Holdings. JAS received food and beverage payments from Intuitive Surgical Inc./Philips Elec, Other, 12, Schipher, Crealta/Horizon, Medisys, Fidia, PK Med, Two labs Inc., Adept Field Solutions, Clinical Care options, Clearview healthcare partners, Putnam.

Abstract Number: 2524

Relation of Pain Sensitivity to Forces While Walking in Adults with and Without Knee Pain: The Multicenter Osteoarthritis (MOST) Study

Patrick Corrigan[1], Cara Lewis[2], Kerry Costello[3], Deepak Kumar[2], David Felson[2], Tuhina Neogi[4], Laura Frey Law[5], Michael LaValley[6], Michael Nevitt[7], Beth Lewis[8] and Joshua Stefanik[9], [1]Saint Louis University, St. Louis, MO, [2]Boston University, Boston, MA, [3]University of Florida, Gainesville, FL, [4]Boston University School of Medicine, Boston, MA, [5]University of Iowa, Iowa City, IA, [6]Boston University School of Public Health, Arlington, MA, [7]University of California San Francisco, San Francisco, CA, [8]University of Alabama at Birimingham, Birmingham, AL, [9]Northeastern University, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Orthopedics, Low Back Pain, & Rehabilitation

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Knee osteoarthritis (KOA) is a leading cause of pain and disability worldwide with no definitive treatment. There is a need to identify mechanisms that explain KOA progression so that targeted treatments can be developed. Increased forces while walking are associated with structural progression of KOA. Altered nociceptive signaling, a feature of KOA, could partially explain forces while walking. In this study, we aimed to characterize the relation of pain sensitization to ground reaction forces during walking. We hypothesized that lower pressure pain thresholds (PPTs) (i.e., greater

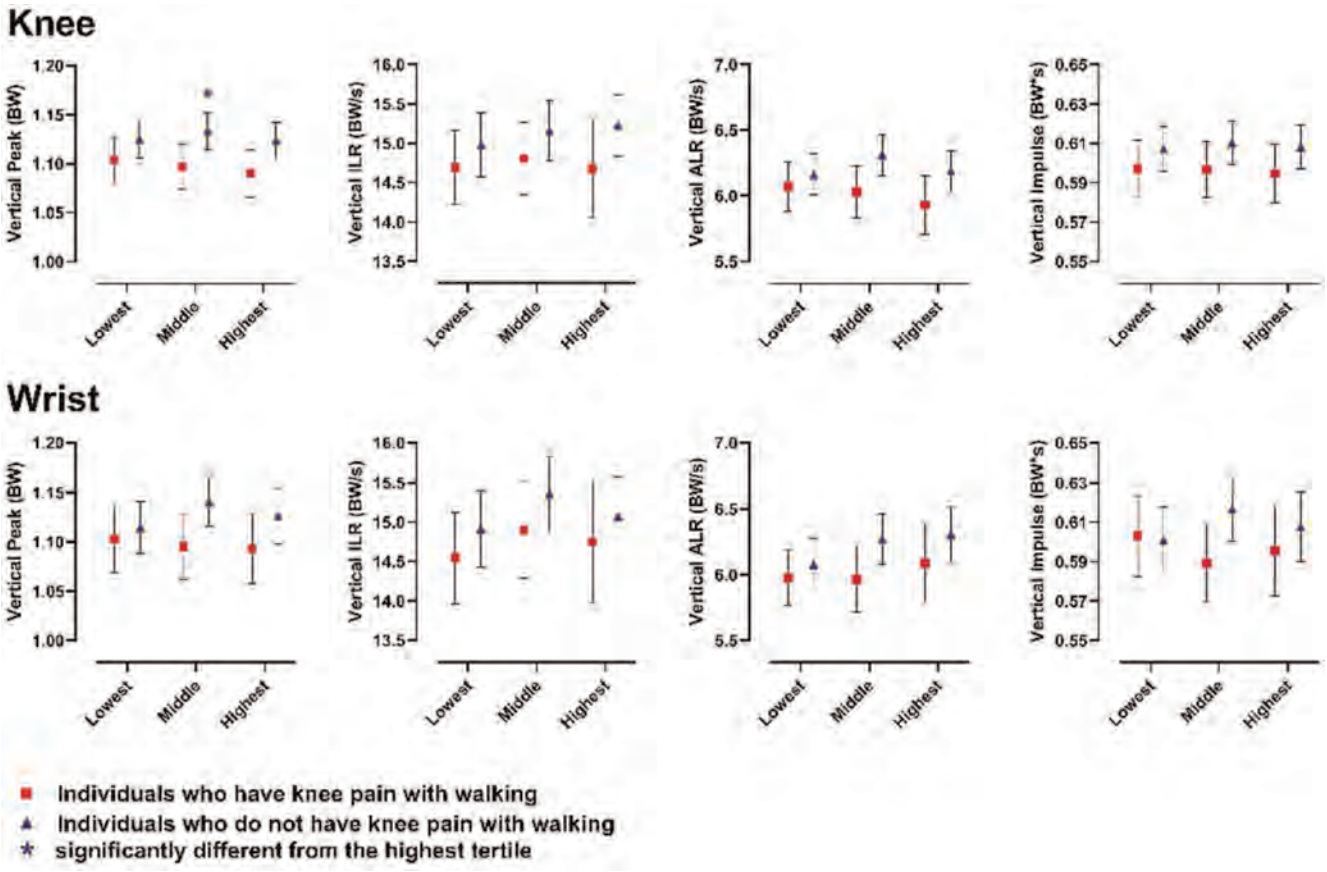
sensitization) would be associated with decreased vertical ground reaction forces (vGRF) in those with and without knee pain while walking.

Methods: We used data from the 12-year visit of the Multicenter Osteoarthritis (MOST) Study. MOST is a NIH-funded, prospective, cohort study of >3000 persons with or without KOA.

PPTs were assessed at the right wrist (unless contraindicated) and both patellae. For each trial, a hand-held pressure algometer with a 1 cm^2 tip was used to apply pressure at a rate of 0.5 kg/s. Pressure was recorded when pain was first perceived. PPTs for each anatomic site were determined as the average of three trials. Sex-specific tertiles were used to categorize PPTs because of known sex differences.

Three-dimensional force data were sampled (1000 Hz) while participants walked at a self-selected speed. With vGRF waveforms, we determined peak force, peak instantaneous loading rate (ILR), and average loading rate (ALR) during the first half of stance, as well as total impulse during stance (i.e., time integral). All vGRF metrics were averaged across at least 3 gait trials for each limb and normalized to body weight.

Generalized linear models, with generalized estimating equations to account for the correlation between limbs, characterized relations of PPT tertiles to vGRF metrics. Person-level covariates included age, sex, and race. Limb-level covariates included KOA status (Kellgren-Lawrence ≥2), knee pain severity (VAS; 0-100), and gait speed. For each vGRF metric, adjusted means and 95% confidence intervals were determined for each PPT tertile after stratifying by knee pain with walking. Knee pain was defined as at least mild pain in response to the question "how much pain do you have in your (right/left) knee while walking on a flat surface?"



Relation of sex-specific pressure pain threshold tertiles to vertical ground reaction force metrics during walking.

Results: 1944 MOST participants (57% female; 19% non-white; 38% with at least mild knee pain with walking), with a mean (SD) age of 62.4 (9.8) years and BMI of 29.9 (5.3) kg/m^2, were included. Of the 3399 limbs, 26% had KOA, and average walking speed and VAS were 1.31 (0.23) m/s and 12 (17), respectively.

All vGRF metrics are reported in Figure 1 by PPT tertile for those with and without knee pain with walking. Only the vGRF peak forces were significantly different between the middle and highest PPT knee tertiles; no other vGRF metrics differed across PPT tertiles. All vGRF metrics were numerically lower in those with knee pain with walking compared to those without knee pain with walking.

Conclusion: Pain sensitivity was not associated with limb-level loading in persons with or without knee pain during walking.

Disclosure: P. Corrigan: None; **C. Lewis**: None; **K. Costello**: None; **D. Kumar**: Eli Lilly, 5, Pfizer, 5; **D. Felson**: None; **T. Neogi**: None; **L. Frey Law**: None; **M. LaValley**: None; **M. Nevitt**: None; **B. Lewis**: None; **J. Stefanik**: None.

Abstract Number: 2525

Comparing Patellar Tendon Characteristics Between Adults with and Without Knee Pain

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Orthopedics, Low Back Pain, & Rehabilitation
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Knee pain is one of the most common types of joint pain leading to disability, limited physical activity, and reduced quality of life. While numerous risk factors for knee pain have been identified, extensor tendons have received limited attention. Altered patellar tendon structure and stiffness may contribute to knee pain through their effects on quadriceps muscle function and joint biomechanics. In this study, we aimed to determine if patellar tendon characteristics differed between adults with and without knee pain.

Comparing patellar tendon thickness (a), CSA (b), and shear wave speeds (c) between knees with and without pain.

Methods: Adults over the age of 45 with and without knee pain were recruited. Exclusion criteria included: history of traumatic knee joint injury in the past 6 months, knee joint injection in the past 3 months, knee replacement, or a diagnosis of rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, reactive arthritis, lupus, gout, bone cancer, connective tissue disorders, or neurologic condition.

Patellar tendon characteristics were assessed bilaterally with a GE LOGIQ *e*10 ultrasound scanner immediately distal to the proximal enthesis. Participants were resting in a seated position with their hips and knees flexed to 90 degrees. Brightness mode was used to assess patellar tendon thickness and cross-sectional area (CSA). Shear wave elastography was performed to estimate patellar tendon shear wave speed, a surrogate measure of tendon stiffness. For each measure, three trials were acquired and averaged.

For analysis, we compared the most symptomatic limb in those with knee pain to a randomly selected limb in those without knee pain. The most symptomatic limb was defined as the limb with the highest VAS pain score (0-100). If VAS scores were identical, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale was used to define the index knee. Patellar tendon thickness, CSA, and shear wave speeds were compared between groups using independent t-tests.

Results: A total of 42 adults were included, 24 with knee pain (VAS pain ≥1) and 18 without knee pain (VAS=0). Individuals with knee pain (14 female) had a mean (SD) age and BMI of 61 (10) years and 32.23 (5.28) kg/m^2, respectively. Individuals without knee pain (10 female) had a mean (SD) age and BMI of 63 (10) years and 30.95 (6.15) kg/m^2, respectively.

Mean (SD) patellar tendon thickness, CSA, and shear wave speeds for the entire sample were 3.25 (0.64) mm, 0.90 (0.22) cm^2, and 5.68 (1.79) m/s, respectively. Patellar tendon shear wave speeds were significantly slower in knees with pain compared to knees without pain (Figure 1). Patellar tendon thickness and CSA were not significantly different between groups (Figure 1).

Conclusion: Compared to knees without pain, those with knee pain have reduced patellar tendon stiffness. Further work in this area is needed to determine if treatments that target the patellar tendon are effective at reducing knee pain.

Disclosure: S. Price: None; **K. Silbernagel**: None; **D. Felson**: None; **J. Stefanik**: None; **P. Corrigan**: None.

Abstract Number: 2526

Single-cell RNA Sequencing Reveals the CRTAC1+ Population Actively Contributes to the Pathogenesis of Spinal Ligament Degeneration by Inducing Macrophage Activation

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Orthopedics, Low Back Pain, & Rehabilitation
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Spinal ligament degeneration is a chronic disease that affects the spine, ligaments, and associated bones, resulting in back pain and functional limitations in the world's aging population. Despite the significant burden on musculoskeletal medicine, there is a lack of research on preventive strategies for ligament degeneration. This study aims to establish a comprehensive transcriptomic atlas of ligament tissues and identify effective drug targets.

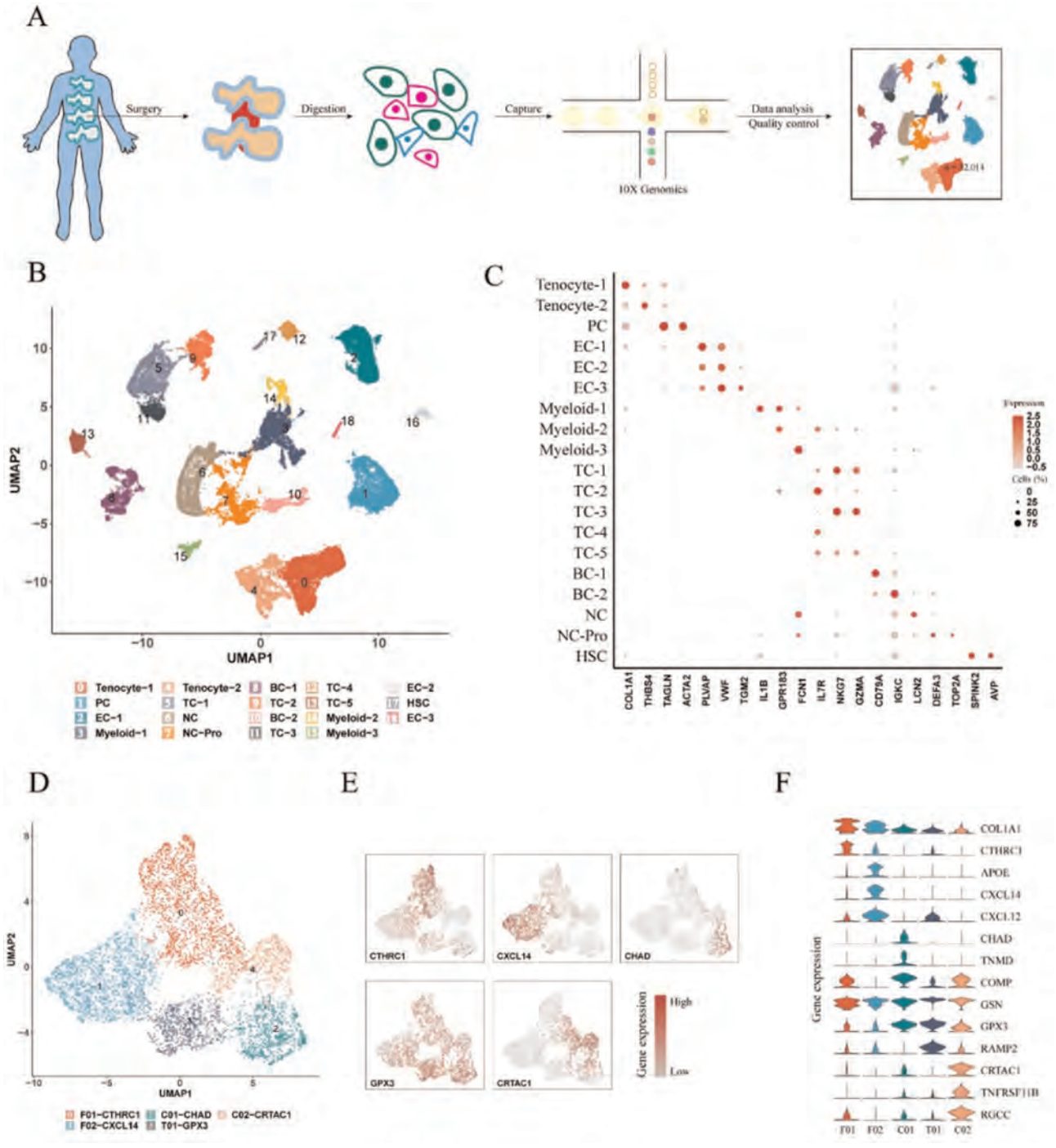

Figure 1 A, Workflow of ligament digestion and single-cell RNA sequencing. B, UMAP plot of total cells, 19 clusters were identified. C, Dotplot showed the marker genes of the 19 cell clusters. D, UMAP plot of stromal cell subpopulations. E, Feature plot of stromal cell subpopulations. F, Marker genes of the five stromal cell subpopulations.

Methods: Single-cell RNA sequencing was performed on six degenerative ligaments and three traumatic ligaments to decipher the heterogeneity of the tissues, followed by data analysis using various computational tools. Library preparation with 10X Genomics and sequencing on Illumina NextSeq instrument was performed. Immunohistochemistry and immunofluorescence analysis were performed to validate the molecular patterns and while in vitro models of primary ligament cells were isolated and utilized for the follow-up functional studies. Protein and mRNA levels were examined using western blot and

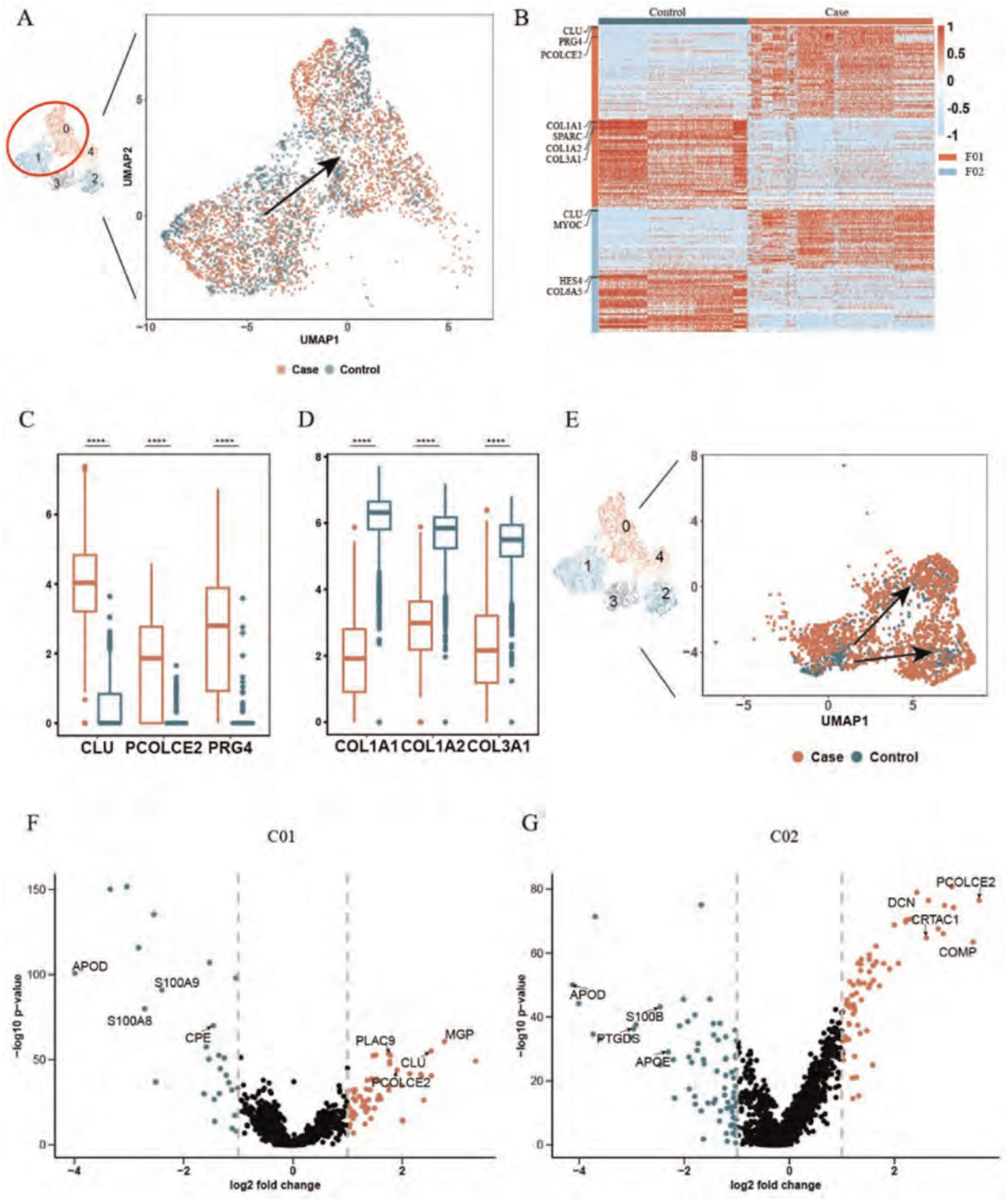

Figure 2 A, UMAP plot of the fibroblast-like cells. B, Heatmap of the differentially expressed genes of the two cell clusters. C, The expression level of chondrogenesis-related genes in fibroblast-like cells. D, The expression level of collagen-related genes in fibroblast-like cells. E, UMAP plot of the chondrocyte-like cells and tenocytes. F-G, Volcano plot showed the differentially expressed genes of the two chondrocyte-like cell clusters.

qPCR analysis. GW5074 (an inhibitor targeting ATF3) and si-ATF3 were used to silence ATF3 in ligament cells, and lentiviral transfection was conducted to overexpress ATF3. In addition, ligament cells were stimulated with recombinant SPP1 to evaluate its impact.

Results: After rigorous quality control, we obtained high-quality data from 32,014 cells for downstream analysis (Figure 1A). Our findings revealed distinct cell clusters comprising stromal and immune cells (Figures 1B-C). Stromal cells exhibited five cell subpopulations (Figures 1D-F), including GPX3+ tenocytes, two clusters of chondrocyte-like cells (CHAD+ and CRTAC1+), and two clusters of fibroblast-like cells (CTHRC1+ and CXCL14+). Notably, collagen degradation associated

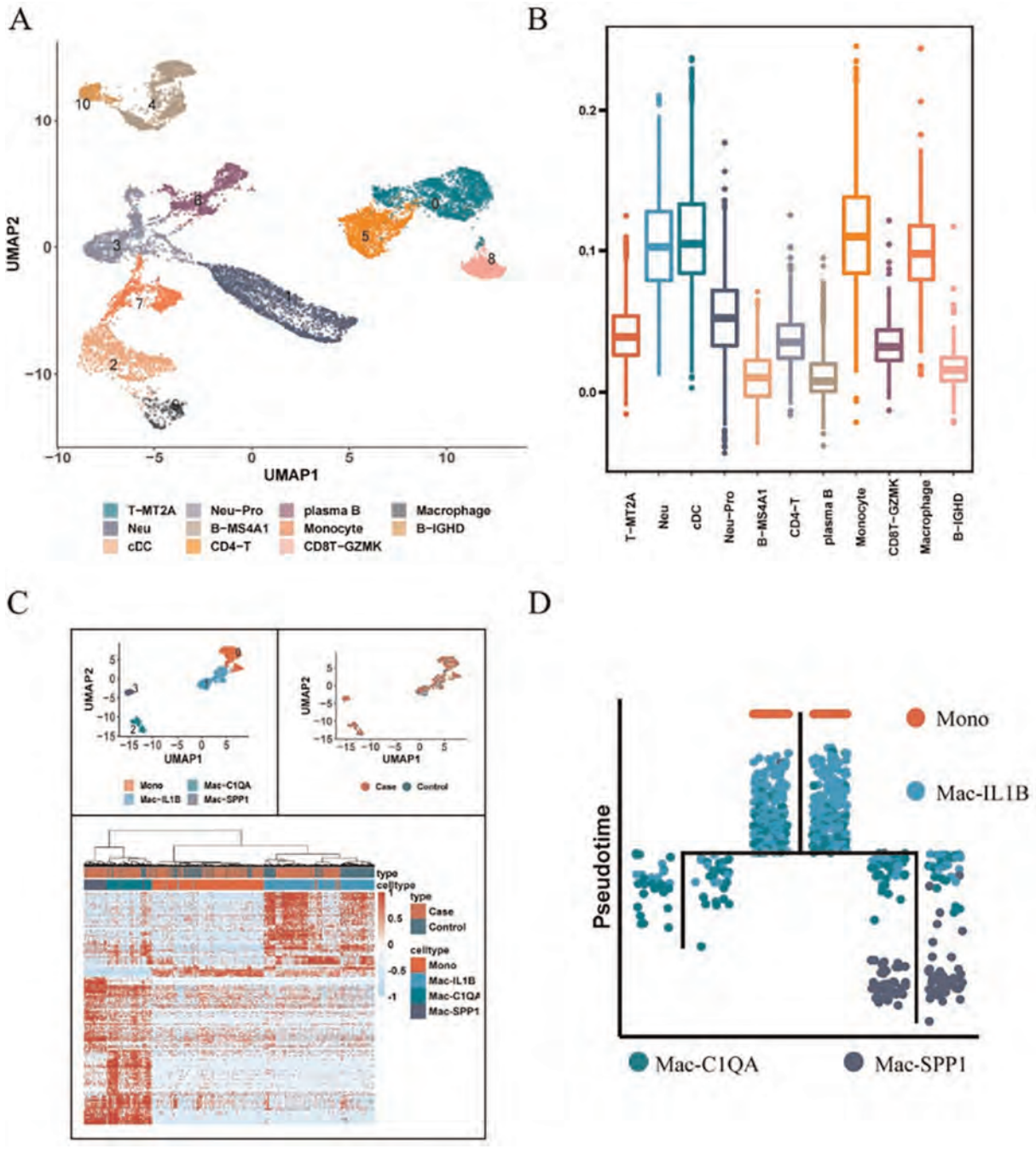

Figure 3 A, UMAP plot of immune cell subpopulations. B, The inflammation scores of the 11 immune cell subpopulations. C, UMAP plot of monocyte/macrophage subpopulations and Heatmap of the four cell clusters. D, Trajectory analysis of four cell clusters showed the evolutionary process of SPP1+ macrophage.

with CTHRC1+ fibroblast-like cells (Figures 2A-D) and ossification linked to CRTAC1+ chondrocyte-like cells (Figures 2E-G) were key features of ligament degeneration. Immune cells exhibited 11 cell subpopulations, including monocyte/macrophage, neutrophils, T cell, B cell, plasma B and cDC (Figure 3A). Among immune cells, myeloid cells demonstrated pathogenic activation, and degenerative ligaments showed enrichment of SPP1+ macrophages (Figures 3B-D). Further investigations unveiled the influence of ATF3, a core transcription factor, on the expression of CRTAC1/MGP/CLU in stromal cells, potentially mediating the interaction between SPP1+ macrophages and ligament degeneration (data not shown here).

Conclusion: SPP1+ macrophages contribute to the pathology of ligament degeneration through their interaction with the core transcription factor ATF3, resulting in enhanced expression of CRTAC1/MGP/CLU in stromal cells. Targeting SPP1+ macrophages and ATF3 in ligament stromal cells may hold promise for mitigating ligament degeneration.

Disclosure: Y. Tang: None; **D. Zhuo**: None; **L. Jin**: None; **Q. Zhu**: None; **Y. Chen**: None; **J. Wang**: None; **J. Liu**: None.

Abstract Number: 2527

Risk Factors for Bone Loss in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Osteoporotic fractures are the most common damage item from the Systemic Lupus Erythematosus International Collaborating Clinics (SLICC)/American College of Rheumatology (ACR) Damage Index. Previous studies reported conflicting results on risk factors for osteoporosis in systemic lupus erythematosus (SLE). The role of vitamin D in osteoporosis in the general population and in SLE remains controversial. We conducted this study to evaluate the risk factors for bone loss in SLE.

Methods: We used a longitudinal cohort that included body mass index (BMI), 25-hydroxy vitamin D levels, complement levels, SLE disease activity index (SLEDAI), and prednisone dose historically and at each visit. 4283 bone density results from 1476 different patients were abstracted from the medical record and included in the statistical analysis. We estimated the association between various patient characteristics and spinal BMD using generalized estimating equations.

Results: A spinal T-score of -2.5 or lower was reported in 9.8% of the measurements. Univariate analysis (Table 1) showed that age, lower BMI, higher SLEDAI, mean prednisone dose, and a history of low C3 or C4 were associated with a spinal T-score of < -2.5. A multivariate analysis (Table 2) controlling for age, race, BMI, and mean prednisone dose showed higher risk of spinal osteoporosis with increasing age >40 years, Black race, mean SLEDAI >2, and history of any prednisone dose. BMI of >25 was protective. Sex, history of anti-DNA, or low C3/C4 were not associated with spinal osteoporosis in the multivariate analysis. The mean 25-hydroxy vitamin D, the first measured 25-hydroxy vitamin D, and the 25-hydroxy vitamin D level measured within 30 days prior to the bone density test were not associated with spinal osteoporosis (Table 3); but the mean 25-hydroxy vitamin D >50ng/ml was associated with lower mean spinal T-score.

Table 1. Number (%) with spinal osteoporosis and mean (DS) spinal T-scores in subgroups.

Predictor	Subgroups	Number of BMD measures	Number (%) -2.5 or lower	P-value[3]	Mean (SD) T-score	P-value[3]
Age	<40	1276	92 (7%)	<0.0001	-0.57 (1.28)	<0.0001
	40-49	1080	83 (8%)		-0.56 (1.32)	
	50-59	1049	109 (10%)		-0.85 (1.34)	
	60-69	677	106 (16%)		-0.92 (1.54)	
	70+	201	31 (15%)		-0.72 (1.71)	
Sex	Female	3977	391 (10%)	0.99	-0.70 (1.37)	0.75
	Male	306	30 (10%)		-0.73 (1.53)	
Race	White	2271	190 (8%)	0.062	-0.70 (1.31)	0.49
	Black	1646	195 (12%)		-0.68 (1.49)	
	Others	366	36 (10%)		-0.80 (1.27)	
BMI	<24.9	1791	260 (15%)	<0.0001	-1.07 (1.28)	<0.0001
	25-29.9	1202	99 (8%)		-0.62 (1.36)	
	30-34.9	702	40 (6%)		-0.31 (1.43)	
	35+	563	17 (3%)		-0.18 (1.32)	
Mean SLEDAI[1]	<1.9	1847	133 (7%)	0.0010	-0.63 (1.35)	0.083
	2-3.9	1255	161 (13%)		-0.75 (1.46)	
	4+	799	98 (12%)		-0.82 (1.36)	
Mean vitamin D (ng/ml)[1]	<29	587	61 (10%)	0.43	-0.62 (1.47)	0.0006
	30-39	766	68 (9%)		-0.56 (1.40)	
	40-49	825	73 (9%)		-0.61 (1.42)	
	50+	501	58 (12%)		-0.92 (1.36)	
Mean prednisone dose (mg/day)[1]	None	1198	62 (5%)	0.0002	-0.44 (1.31)	<0.0001
	<4.9	1175	105 (9%)		-0.69 (1.37)	
	5-9.9	895	128 (14%)		-0.88 (1.46)	
	10+	636	98 (15%)		-1.00 (1.37)	
Prior anti-dsDNA[2]	No	1765	154 (9%)	0.054	-0.67 (1.33)	0.61
	Yes	2134	239 (11%)		-0.74 (1.44)	
Prior low C3[2]	No	1912	148 (8%)	0.041	-0.55 (1.40)	0.054
	Yes	1990	244 (12%)		-0.85 (1.36)	
Prior low C4[2]	No	2240	187 (8%)	0.0030	-0.65 (1.39)	0.53
	Yes	1662	205 (12%)		-0.77 (1.39)	

[1] Mean SLEDAI, vitamin D, and prednisone dose were defined as the mean from all cohort visits prior to the visit when BMD was measured.

[2] Prior anti-dsDNA, prior low C3 and prior low C4 were defined as the occurrence at any cohort visit prior to the visit when BMD was measured.

[3] P-values based on GEE to account for repeated observations on the same person.

Conclusion: Spinal osteoporosis in SLE was associated with age, African-American ethnicity, disease activity, and prednisone dose. Although African-Americans in the general population are protected against osteoporosis, in SLE they are at risk. Any prednisone dose – even low doses – increased osteoporosis. Vitamin D was not protective (and higher doses might have been harmful in the continuous analysis). Reduction of disease activity but without reliance on prednisone is key to osteoporosis reduction in SLE.

Table 2. Odds ratios for spinal osteoporosis based on multivariate analysis controlling for age, race, mean prednisone dose.

Predictor	Subgroups	Adjusted[1] Odds Ratio (95% CI)	Adjusted[1] p-values
Age	<40	1.00 (Ref. Group)	--
	40-49	1.63 (1.13-2.35)	0.0089
	50-59	3.19 (2.19-4.64)	<0.0001
	60-69	3.97 (2.61-6.05)	<0.0001
	70+	3.81 (2.31-6.28)	<0.0001
Sex	Female	1.00 (Ref. Group)	--
	Male	0.72 (0.37-1.38)	0.32
Race	White	1.00 (Ref. Group)	--
	Black	1.75 (1.21-2.53)	0.0031
	Others	1.18 (0.60-2.31)	0.64
BMI	<24.9	1.00 (Ref. Group)	--
	25-29.9	0.70 (0.55-0.88)	0.0028
	30-34.9	0.46 (0.31-0.66)	<0.0001
	35+	0.31 (0.20-0.48)	<0.0001
Mean SLEDAI[2]	<1.9	1.00 (Ref. Group)	--
	2-3.9	1.68 (1.19-2.37)	0.0034
	4+	1.72 (1.14-2.61)	0.010
Mean vitamin D (ng/ml)[2]	<29	1.00 (Ref. Group)	--
	30-39	1.14 (0.72-1.79)	0.58
	40-49	0.87 (0.53-1.43)	0.58
	50+	1.08 (0.61-1.90)	0.80
Mean prednisone dose (mg/day)[2]	None	1.00 (Ref. Group)	--
	<4.9	1.62 (1.09-2.42)	0.017
	5-9.9	2.35 (1.55-3.58)	<0.0001
	10+	2.65 (1.68-4.17)	<0.0001
Prior anti-dsDNA[3]	No	1.00 (Ref. Group)	--
	Yes	1.05 (0.78-1.40)	0.75
Prior low C3[3]	No	1.00 (Ref. Group)	--
	Yes	1.03 (0.78-1.37)	0.82
Prior low C4[3]	No	1.00 (Ref. Group)	--
	Yes	1.29 (0.94-1.77)	0.11

[1] Adjusted for age, race, BMI, and prednisone dose using a GEE logistic regression.
[2] Mean SLEDAI, mean vitamin D, and mean prednisone dose were defined as the mean from all cohort visits prior to the visit when BMD was measured.
[3] Prior anti-dsDNA, prior low C3, and prior low C4 were defined as the occurrence at any cohort visit prior to the visit when BMD was measured.

Table 3. Number (%) with spinal osteoporosis and mean (DS) spinal T-scores in 25-hydroxy vitamin D subgroups.

Predictor	Subgroups	Number of BMD measures	Number (%) with T-score -2.5 or lower	P-value[2]	Mean (SD) T-score	P-value[2]
First measured vitamin D	<19	974	122 (13%)	0.20	-0.69 (1.46)	0.15
	20-29	954	76 (8%)		-0.70 (1.30)	
	30-39	1072	85 (8%)		-0.59 (1.39)	
	40-49	697	69 (10%)		-0.77 (1.36)	
	50+	408	45 (11%)		-0.76 (1.42)	
Vitamin D measured right before BMD[1]	<19	140	11 (8%)	0.65	-0.34 (1.48)	0.075
	20-29	271	31 (11%)		-0.66 (1.39)	
	30-39	475	50 (11%)		-0.57 (1.48)	
	40-49	376	35 (9%)		-0.68 (1.41)	
	50+	441	42 (10%)		-0.75 (1.32)	

[1] Vitamin D measured within 30 days before the bone density test.
[2] Based on a GEE model

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Abstract Number: 2528

Current Trends in the Risk of Subsequent Fracture After Initial Fracture, and Post-Fracture Treatment Among Commercially Insured Postmenopausal Women in the United States

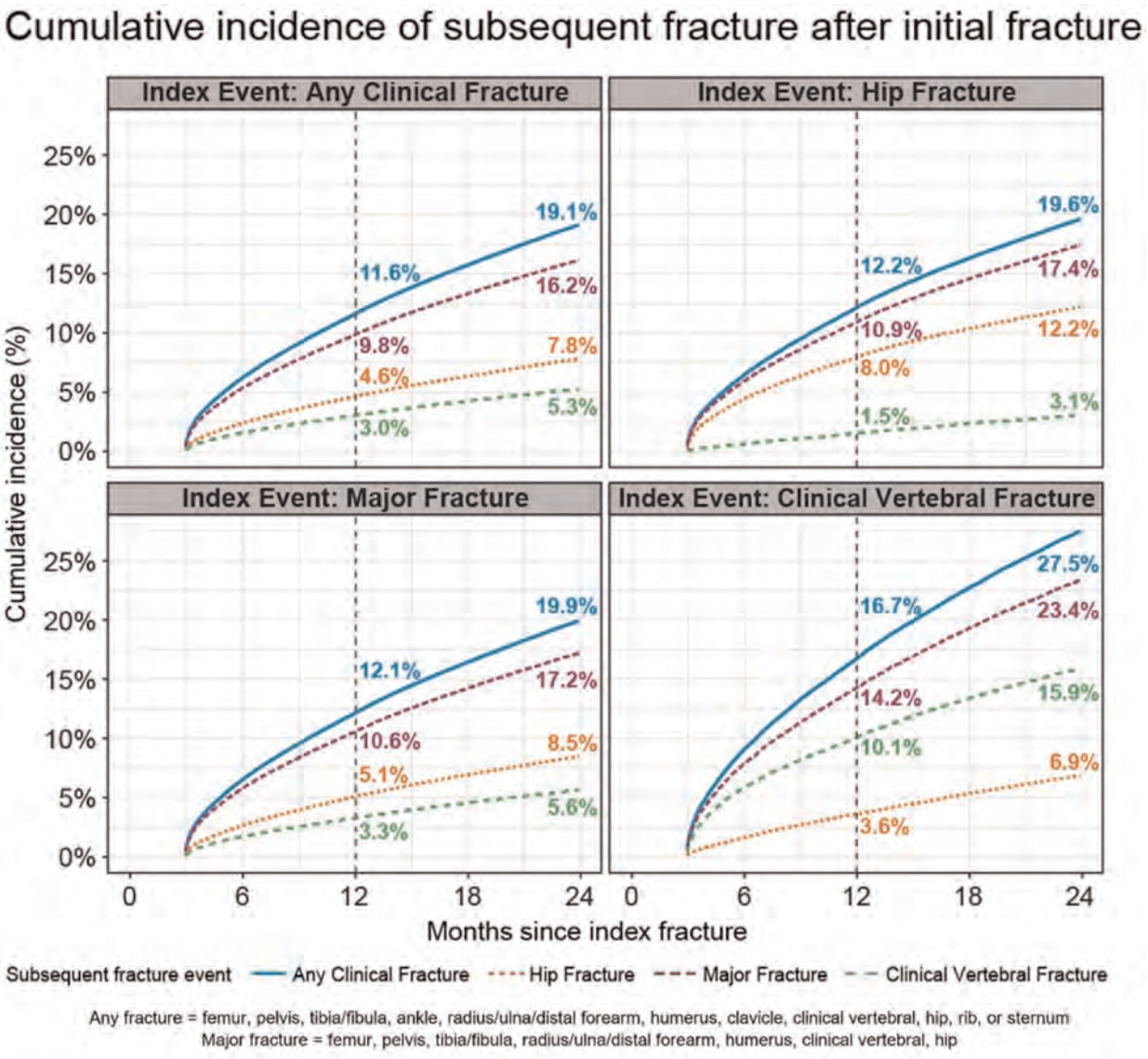
Min Kim[1], Vanessa C. Brunetti[1], Felicia Cosman[2], Jeffrey Curtis[3], E Michael Lewiecki[4], Matthew Phelan[5], Peter Samai[5], Michele McDermott[1], Tzu-Chieh Lin[1], M Alan Brookhart[6] and Kathleen Hurwitz[5], [1]Amgen, Inc., Thousand Oaks, CA, [2]Columbia University, New York, NY, [3]University of Alabama at Birmingham, Birmingham, AL, [4]New Mexico Clinical Research & Osteoporosis Center, Albuquerque, NM, [5]Target RWE, Durham, NC, [6]Department of Population Health Sciences, Duke University, Durham, NC

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Recent studies suggest that post-fracture pharmacologic management has been declining in the U.S. despite an increase in the burden of osteoporosis (OP). In light of this treatment gap, few studies have reported on the incidence of subsequent fracture risk among commercially insured postmenopausal women with a history of fracture.

Methods: We assembled a retrospective cohort of women aged ≥50 years from 2012-2021 using an administrative claims database of privately insured or employer-sponsored Medicare Advantage coverage. Osteoporotic fractures were identified by ≥1 insurance claims with a relevant diagnosis and/or procedure code for an open or closed fracture. Treatments for osteoporosis were identified by prescription fills or medical procedure claims. The cumulative incidence of a new, subsequent fracture at the same or a different anatomic site was estimated for any (clinical vertebral, hip, femur, pelvis, tibia, fibula, radius/ulna/distal forearm, humerus, clavicle, rib, sternum), major (any fracture excluding extremities, clavicle, rib, sternum), hip, and clinical vertebral fractures occurring ≥90 days of initial index fracture to up to 2 years. Women were followed from the index fracture for up to 2 years to estimate the cumulative incidence of any treatment uptake. All analyses used inverse probability weighting to adjust for differential censoring due to differences in demographics and clinical risk factors.

Results: Among the 483,564 women with any initial fracture (mean age 74.8), the 1-year cumulative incidence of a subsequent fracture at any site was 11.6%, which increased to 19.1% at 2 years (Figure). The same-site subsequent fracture risk was highest for women with an initial clinical vertebral fracture: 10.1% experienced a subsequent vertebral fracture at year 1 and 15.9% at year 2. Among women with an initial hip fracture, 12.2% and 19.6% experienced a subsequent fracture at any site after 1 and 2 years, respectively, while 8.0% and 12.2% experienced a subsequent hip fracture at 1 year and 2 years, respectively. Most patients did not receive pharmacological treatment one year (91.7%) and two years (89.4%) after their initial fracture.



Conclusion: Although clinical guidelines specify that OP is a lifelong, chronic disease requiring ongoing management, recent data over a 10-year period show that recurrent fracture rates within 2 years are high, while pharmacological treatment remains underutilized in this high-risk population.

Disclosure: M. Kim: Amgen, 3, 11; **V. Brunetti**: Amgen, 3, 11; **F. Cosman**: Amgen, 2, 5, 6, Biocon, 2, Enterabio, 2, Radius Health, 2, 5, 6, UCB, 2; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, 5, CorEvitas, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **E. Lewiecki**: Amgen, 2, 5, 6, Ascendis, 6, Radius Health, 2, 5; **M. Phelan**: Target RWE, 3, 11; **P. Samai**: NoviSci, 3, 11, Target RWE, 3, 11; **M. McDermott**: Amgen, 3, 11; **T. Lin**: Amgen, 3, 3, 3, 11, 11, 11; **M. Brookhart**: AbbVie/Abbott, 1, Amgen, 1, Atara Biosciences, 1, BlueCross BlueShield North Carolina, 1, Brigham and Women's Hospital, 1, Fibrogen, 1, Genentech, 1, Merck, 1, National Institutes of Health, 5, NoviSci, 3, 11, Sanofi Pasteur, 1, Target RWE, 3, 11; **K. Hurwitz**: National Institutes of Health, 5, Target RWE, 3, 11.

Abstract Number: 2529

Comparative Effectiveness of Denosumab versus Zoledronic Acid Among Postmenopausal Women with Osteoporosis in the U.S. Medicare Program

Jeffrey R Curtis[1], Tarun Arora[2], Ye Liu[3], Vanessa C. Brunetti[4], Tzu-Chieh Lin[4], Leslie Spangler[4], Robert K. Stad[4], Michele McDermott[4], Brian D. Bradbury[4] and Min Kim[4], [1]Division of Clinical Immunology and Rheumatology, University of Alabama, Birmingham, AL, [2]Foundation for Advancing Science, Technology, Education, and Research, Birmingham, AL, [3]University of Alabama at Birmingham, Birmingham, AL, [4]Amgen, Inc., Thousand Oaks, CA

SESSION INFORMATION

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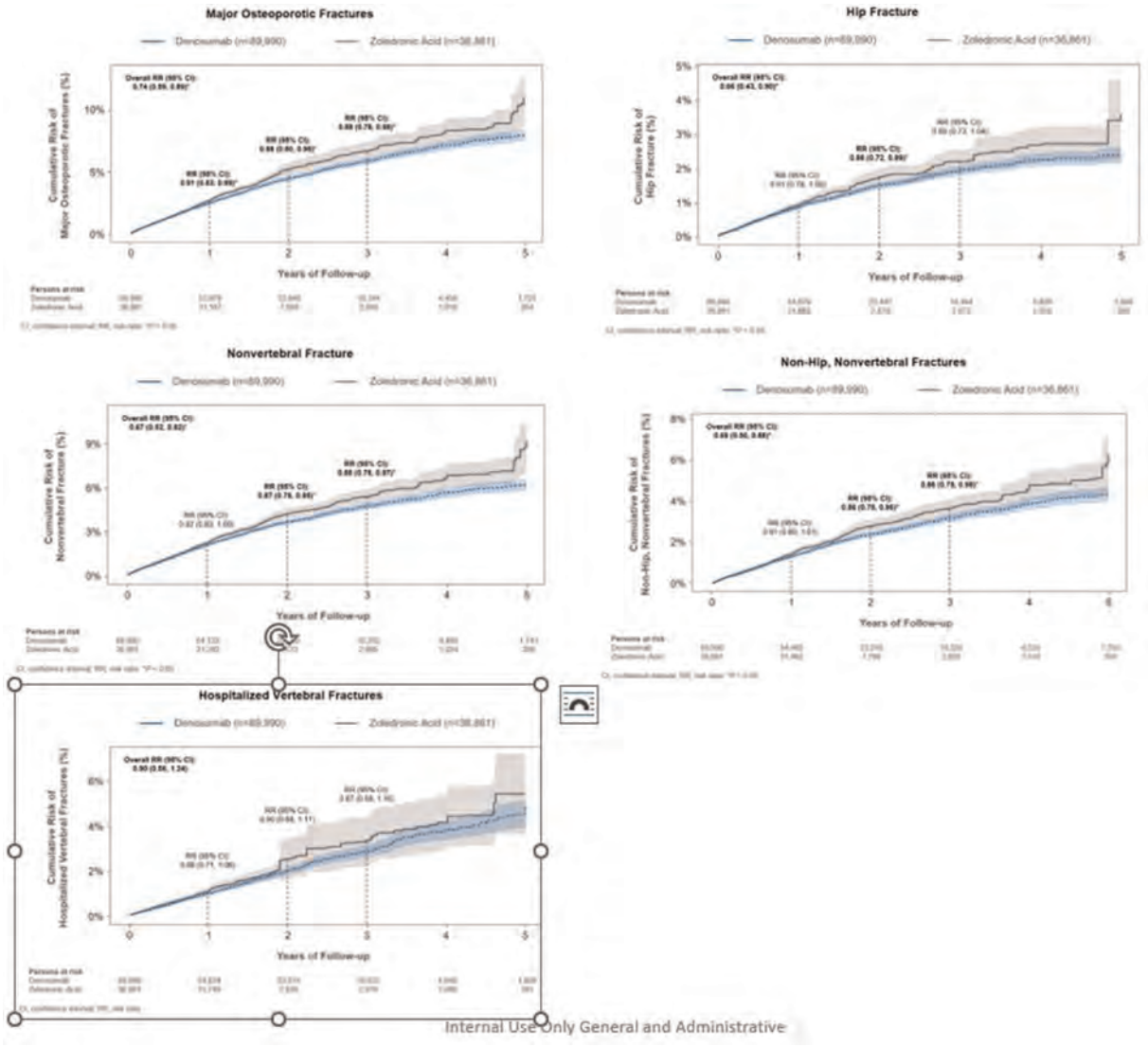
Background/Purpose: Although clinical trials have shown that denosumab (Dmab) significantly increases bone mineral density at key skeletal sites more than zoledronic acid (ZA), evidence from randomized trials evaluating fracture outcomes is lacking. This retrospective cohort study evaluated the comparative effectiveness of Dmab versus ZA in reducing fracture risk among women with postmenopausal osteoporosis (PMO) in the U.S.

Methods: Female Medicare fee-for-service beneficiaries ≥ 66 years of age who newly initiated Dmab (n=89,990) or ZA (n=36,861) between Jan 1, 2012 to Dec 31, 2018 with no prior history of osteoporosis treatment were followed from treatment initiation (index date) until the first instance of a given fracture outcome, treatment discontinuation (defined as the end of exposure according to usual dosing intervals + 60-day gap) or switch, Medicare disenrollment, death, end of available data (Dec 31, 2019), or 5 years post-index date. A doubly robust inverse-probability of treatment (weights estimated from multivariate logistic regression models) and censoring (weights estimated from multivariate Cox Proportional Hazards regression models) weighted function was used to estimate the relative risk (RR) associated with the use of Dmab compared with ZA for major osteoporotic (MOP; nonvertebral and hospitalized vertebral), hip, nonvertebral (NV; includes hip, humerus, pelvis, radius/ulna, other femur), non-hip, nonvertebral (NHNV), and hospitalized vertebral (HV) fractures for the overall study period and by year of follow-up.

Results: Over a maximum of 5 years of follow-up, Dmab reduced the risk of MOP by 26% (RR=0.74; 95% CI: 0.59-0.89), hip by 34% (0.66; 0.43-0.90), NV by 33% (0.67; 0.52-0.82), and NHNV by 31% (0.69; 0.50-0.88), and HV fractures by 10% (0.90; 0.56-1.24) compared with ZA (Figure). Over time, Dmab reduced the risk of MOP fractures by 9% (0.91; 0.83-0.99) at year 1, 12% (0.88; 0.80-0.96) at year 2, and 12% (0.88; 0.78-0.98) at year 3. An increase in the magnitude of fracture risk reduction with increasing duration of exposure was also observed for other NV outcomes.

Conclusion: In a cohort of over 125,000 treatment-naive women with PMO, we observed robust, clinically meaningful reductions in the risk of MOP, hip, NV, and NHNV fractures for patients on Dmab compared to ZA, with greater reductions in fracture risk with longer duration of exposure.



Disclosure: J. Curtis: AbbVie, 2, 5, Amgen, 2, 5, BMS, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Genentech, 2, 5, Janssen, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB Pharma, 2, 5; **T. Arora**: Amgen, 5; **Y. Liu**: None; **V. Brunetti**: Amgen, 3, 11; **T. Lin**: Amgen, 3, 3, 3, 11, 11, 11; **L. Spangler**: Amgen, 3, 11; **R. Stad**: Amgen, 3, 11; **M. McDermott**: Amgen, 3, 11; **B. Bradbury**: Amgen, 3, 11; **M. Kim**: Amgen, 3, 11.

Abstract Number: 2530

Risk Evaluation of Osteoporotic Fractures Following Lung Transplantation (LT): A Retrospective Cohort Study Conducted at an International Transplant Center

Sarah Keller[1], Adil Vural[2], Jennifer Varley[2], Komal Mushtaq[2], Walaa Abu Alya[3], Neel Tapryal[2], Hassan Shaheen[3], Marie Budev[2], Abby Abelson[2] and Chad Deal[1], [1]Cleveland Clinic Foundation, Cleveland, OH, [2]Cleveland Clinic, Cleveland, OH, [3]Cleveland Clinic Fairview Hospital, Cleveland, OH

SESSION INFORMATION

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Background/Purpose: Osteoporotic fractures are a well-known complication in LT recipients, significantly impacting their quality of life. Specific risk factors for these fractures in LT recipients are poorly understood, and universal guidelines are lacking. We aimed to assess the incidence of osteoporotic fractures in end-stage lung disease patients pre- and post-LT, while also identifying potential risk factors for post-LT fractures.

Methods: This retrospective cohort study was conducted at a large international transplant center, including adult patients who underwent LT between January 1, 2010, and April 14, 2018. Patients who expired within the first year post-LT or had prior LT were excluded. Endpoints comprised the incidence of vertebral and non-vertebral osteoporotic fractures post-LT, as well as potential risk factors for post-LT fractures, as determined by clinicians. Secondary endpoints included evaluating the impact of osteoporosis medications. Logistic regression modeling was employed to examine the relationships between potential risk factors and post-LT fractures.

Table 1. Summary of study population characteristics.

Table 1. Summary of study population characteristics.

Variable		Total (N=786)
Age at time of transplant, Median [25th;75th]		61.0 [54.0;67.0]
Sex, N (%)		
Male		526 (67%)
Female		259 (33%)
Race, N (%)		
White		683 (87%)
Black		60 (7.6%)
Other		42 (5.3%)
Pre-transplant BMI, Median [25th; 75th]		25.7 [22.2; 28.9]
Smoking, N (%)		
Current/Former		481 (61.3%)
Never		304 (38.7%)
Current alcohol use, N (%)		252 (32.1%)
Most common transplant indications, N (%)		
Idiopathic Pulmonary Fibrosis		386 (49.1%)
Chronic Obstructive Pulmonary Disease/Emphysema		181 (23%)
Cystic Fibrosis		67 (8.5%)
Pre-transplant oral steroid use >3 months, N (%)		439 (55.9%)
Pre-transplant bone metabolism medication use, N (%)		276 (35.3%)
Alendronate, N (%)		173 (62.7%)
Zoledronic Acid, N (%)		50 (18.1%)
Risedronate, N (%)		28 (10.1%)
Post-transplant 1 year prednisone dose, Median [25th;75th]		5.00 [5.00;5.00]
Post-transplant bone metabolism medication use, N (%)		433 (55.2%)
Alendronate, N (%)		222 (51.3%)
Denosumab, N (%)		143 (33%)
Zoledronic Acid, N (%)		81 (18.7%)
Post-transplant biopsy-proven acute lung rejection in 1st year, N (%)		471 (60%)
Number of rejection episodes:	1	226
	2	145
	3	58
	4	25

Table 2. Summary of osteopenia/osteoporosis prevalence and fragility fractures before and after transplant.

Table 2. Summary of osteopenia/osteoporosis prevalence and fragility fractures before and after transplant.

		Pre-transplant	*Post-transplant*
Diagnosis of osteopenia, N (%)		261 (33.2%)	232 (29.5%)
Diagnosis of osteoporosis, N (%)		186 (23.6%)	185 (23.5%)*
≥1 Fragility fracture, N (%)		90 (11.4%)	185 (23.5%)
Number of fragility fractures/patient, N (%):	1	72 (80%)	143 (77.2%)
	2	16 (20%)	28 (15.1%)
	3	1 (1.1%)	3 (1.6%)
Fragility fracture type			
Ankle, N (%)		5 (4.4%)	17 (7.5%)
Forearm, N (%)		2 (1.7%)	11 (4.8%)
Hip, N (%)		5 (4.4%)	22 (9.7%)
Other, N (%)		8 (7.1%)	23 (10.1%)
Ribs, N (%)		39 (34.8%)	44 (19.4%)
Vertebrae, N (%)		53 (47.3%)	109 (48.2%)
Time from transplant to 1st post-transplant fracture (days), Median [25th;75th]		N/A	655 [210;1331]
Fracture (pre- and post-transplant) while taking bone metabolism medications, N (%)		63 (14.5%)	

*Post-transplant osteoporosis data shows newly diagnosed osteoporosis, excluding pre-transplant osteoporosis patients.

Results: Out of 911 patients who underwent LT, 786 patients met the study inclusion criteria (median age: 61; 67% male; 87% white). The most common indication for LT was idiopathic pulmonary fibrosis (49.1%) **(Table 1)**. Pre-LT, 186 patients (23.6%) had osteoporosis (T-score < -2.5), and ≥1 fracture occurred in 90 patients (11.4%), with vertebral fractures being the most common (53, 47.3%). Following LT, 185 patients (23.5%) developed new-onset osteoporosis, and 185 patients (23.5%) experienced at least one fracture, with 109 of these fractures (48.2%) being vertebral in nature. The median time to post-LT fracture was 655 days **(Table 2)**. Post-LT, 55.2% received osteoporosis medications, with the most prescribed

Table 3. Post-transplant fragility fracture predictors assessment.

Table 3. Post-transplant fragility fracture predictors assessment.

	Post-transplant fragility fracture	
Predictors	*Odds Ratio [95%CI]*	*p-value*
Age (IQR Increase)*	1.31 (1.02 – 1.69)	0.036
Sex (Female vs Male)	1.53 (0.98 – 2.39)	0.062
Smoking (Never vs Current/Former)	0.72 (0.45 – 1.14)	0.158
Alcohol (Yes vs No)	1.43 (0.93 – 2.20)	0.099
Pre-transplant osteopenia	1.13 (0.73 – 1.73)	0.594
Pre-transplant osteoporosis	2.04 (1.11 – 3.75)	0.021
Pre-transplant fragility fracture	0.89 (0.39 – 2.02)	0.777
Pre-transplant oral steroid use >3 months	0.89 (0.59 – 1.35)	0.895
Post-transplant biopsy-proven acute lung rejection in 1st year	1.19 (0.79 – 1.81)	0.400

CI: confidence interval, IQR: interquartile range
*Comparing age Q3 (67) to Q1 (51)

medications being alendronate (51.3%) and denosumab (33%). Notably, 14.5% of patients on bone metabolism medications experienced fractures either before or after LT.

A pre-LT diagnosis of osteoporosis was associated with a 2.04-fold increased odds of post-LT fractures compared to individuals with normal bone mass (95% CI 1.11-3.75, p=0.021). Compared to patients with age of 53 years (Q1), individuals aged 67 years (Q3) have 32% higher odds of experiencing post-LT fractures (95% CI: 1.03-1.69). Conversely, acute lung rejection episodes within the first year post-LT did not significantly increase the odds of post-LT fractures (95% CI 0.79-1.81, p=0.4) **(Table 3)**.

Conclusion: Osteoporosis and fractures remain significant comorbidities in LT recipients. Pre-LT osteoporosis and age is a strong predictor of post-LT fractures, highlighting the importance of proactive management. Notably, pre-LT fractures, osteopenia, and long term pre-LT steroid use were not associated with an increased risk of post-LT fractures. Acute lung rejection episodes post-LT did not contribute significantly to post-LT fractures. The high incidence of fractures among patients on bone metabolism medications underscores the need for effective prevention and management strategies for LT recipients. These findings emphasize the importance of ongoing vigilance and the development of universal LT osteoporosis management guidelines.

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Abstract Number: 2531

Proton Pump Inhibitor Use Is Associated with Impaired Bone Mineral Density but Not Bone Microarchitecture in Patients with Inflammatory Rheumatic and Musculoskeletal Diseases Taking Glucocorticoids

Andriko Palmowski[1], Gabriela Schmajuk[2], Jinoos Yazdany[3], Patti Katz[4], Jing Li[5], Rachael Stovall[5], Emma Kersey[5], Sabrina Mai Nielsen[6], Robin Christensen[7], Henning Bliddal[8], Zhivana Boyadzhieva[9], Udo Schneider[9], Tobias Alexander[10], Burkhard Muche[11], Sandra Hermann[11], Edgar Wiebe[11] and Frank Buttgereit[11], [1]Charité - Universitätsmedizin Berlin, Berlin, Germany, [2]UCSF / SFVA, San Francisco, CA, [3]University of California, General Department of Medicine, Division of Rheumatology, San Francisco, CA, [4]University of California San Francisco, San Rafael, CA, [5]University of California San Francisco, San Francisco, CA, [6]The Parker Institute, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark, [7]Musculoskeletal Statistics Unit, The Parker Institute, Copenhagen, Denmark, [8]The Parker Institute, Bispebjerg and Frederiksberg Hospital, Frederiksberg, Denmark, [9]Charité Universitatsmedizine - Berlin, Berlin, Germany, [10]Charité Universiätsmedizin Berlin, Dept. Rheumatology, Berlin, Germany, [11]Charité Universitätsmedizin, Dept. Rheumatology, Berlin, Germany

SESSION INFORMATION

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Session Type: Abstract Session

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Background/Purpose: Patients with inflammatory rheumatic and musculoskeletal diseases (iRMDs) are at increased risk of osteoporosis and fragility fractures. For this population, whether proton pump inhibitor (PPI) intake contributes to that risk has not yet been definitively answered. Prior studies have yielded conflicting results, did not account for over-the-counter use of PPI, and major confounders were unmeasured. In addition, bone microarchitecture as a potential mediator of fracture risk has not been studied. We studied the effect of regular PPI intake on bone mineral density (BMD) and microarchitecture in patients with iRMDs.

Table. Bone mineral density and trabecular bone score in PPI users and non-users.

Table. Bone mineral density and trabecular bone score in PPI users and non-users.

	PPI use	No PPI use	Contrast	P-value
Crude (unadjusted)				
Left femoral neck T-score	-1.24 (-1.36 to -1.13)	-1.01 (-1.12 to -0.89)	-0.24 (-0.11 to -0.37)	<0.001
Lumbar spine T-score	-0.87 (-1.06 to -0.69)	-0.64 (-0.79 to -0.48)	-0.23 (-0.05 to 0.42)	0.01
Trabecular bone score	1.28 (1.24 to 1.31)	1.30 (1.26 to 1.33)	-0.02 (-0.06 to 0.02)	0.35
Adjusted				
Left femoral neck T-score	-1.24 (-1.36 to -1.13)	-1.08 (-1.27 to -0.88)	-0.17 (-0.35 to 0.01)	0.07
Lumbar spine T-score	-0.87 (-1.06 to -0.69)	-0.62 (-0.83 to -0.41)	-0.25 (-0.47 to -0.04)	0.02
Trabecular bone score	1.28 (1.24 to 1.31)	1.27 (1.24 to 1.31)	0.00 (-0.04 to 0.04)	0.97

Numbers are estimated marginal means and 95% confidence intervals.

Methods: Cross-sectional baseline data from the single center Rh-GIOP cohort were used. Briefly, patients with iRMDs were prospectively enrolled and assessed with DXA scans, laboratory testing, and bone-health-related questionnaires since 2015. Regular PPI and glucocorticoid (GC) use were ascertained by both chart review and patient self-report. Three co-primary outcomes (all reported as T-scores) were defined: BMD of the left femoral neck and the lumbar spine, and the trabecular bone score (TBS). The latter is a measure correlating with lumbar vertebrae's microarchitecture and is measured in a subset. Inverse probability of treatment weighting adjusted for the following confounders: age, sex, body mass index, iRMD type, C-reactive protein, current and cumulative GC dose, NSAID use, smoking, alcohol consumption, functional status (Health Assessment Questionnaire), disease duration, bisphosphonate use, chronic kidney disease stage, presence of diabetes mellitus, and frequency of exercise. We investigated whether dose-response relationships were present ("high dose" of >20mg/d vs. "low dose" of ≤20mg/d pantoprazole equivalent) and conducted an additional analysis with an interaction term for GC use. All analyses were based on linear regression models. Multiple imputation with 100 imputations was used to account for missing data (∼4%). A detailed prespecified statistical analysis plan with a gatekeeping procedure for statistical testing was followed.

Results: 1,495 patients (75.3% women; mean age 62.6 ± 13.1 years; 49.2% with regular PPI use [of those: 63.1% high dose]) were included. Most patients had a diagnosis of rheumatoid arthritis (37.5%), followed by 25.3% connective tissue diseases, 16% vasculitides, 14.2% spondyloarthropathies, and 7% others. 63.8% used GCs (median dose 5mg/d). In both adjusted and unadjusted analyses, PPI users had lower BMD at both the left femoral neck and the lumbar spine (**Table**). Interestingly, differences between PPI users and non-users were only present in the subset of patients concurrently using GCs (data not shown). There was no statistically significant difference in BMD when comparing high and low dose PPI users (all $P \geq 0.52$). TBS (n = 389) was similar in PPI users and non-users (**Table**).

Conclusion: Loss of BMD (seen at both lumbar spine and left femoral neck) rather than impairment of bone microarchitecture seems to be driving the increased fracture risk seen with PPI use in patients with iRMDs. The negative association between PPI use and BMD appears to be dependent on concurrent GC use.

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and Novartis., 2, 6, 12, Travel Expenses; **F. Buttgereit**: AbbVie/Abbott, 6, Horizon Therapeutics, 5, Pfizer, 5, 6, Roche, 6.

Abstract Number: 2532

Prevalence and Disease-Specific Factors Associated with Osteoporosis in Systemic Sclerosis: A Cross-Sectional Analysis of Two Large European Cohorts

Charles MIDOL[1], **Edgar Wiebe**[2], Elise Siegert[3], Dörte Huscher[4], Helene Behal[5], David Launay[6], Eric Hachulla[7], Eric Matteson[8], Vincent Sobanski[9] and Frank Buttgereit[2], [1]Lille University Hospital, Besançon, France, [2]Charité Universitätsmedizin, Dept. Rheumatology, Berlin, Germany, [3]Department of Rheumatology, Charité University Hospital, Charité Platz 1, D-10117, Berlin, Germany, [4]Institute of Biometry and Clinical Epidemiology and Berlin Institute of Health, Charité Universitätsmedizin Berlin, Berlin, Germany, [5]Univ. Lille, CHU Lille, Biostatistics Department, Lille, France, [6]Univ. Lille, Inserm, CHU Lille, Service de Médecine Interne, Lille, France, [7]CHU Lille, Département de Médecine Interne et Immunologie Clinique, Centre de Référence des Maladies Auto-immunes Systémiques Rares du Nord et Nord-Ouest de France (CeRAINO), Lille, France, [8]Mayo Clinic College of Medicine and Science, Rochester, MN, USA, Rochester, MN, [9]Univ. Lille, Inserm, CHU Lille, U1286 - INFINITE - Institute for Translational Research in Inflammation, Lille, France

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Session Time: 4:00PM–5:30PM

Background/Purpose: Patients with systemic sclerosis (SSc) are at increased risk for osteoporosis (OP) and associated fragility fractures. However, the risks factors and mechanisms driving bone loss in patients with SSc remain elusive. The role of "general" factors such as higher age and low body mass index (BMI) is well established but their interplay with disease-specific factors is unclear. Thus, our objectives in the present study were i) to evaluate the prevalence of clinical OP and fragility fractures in a large population of SSc patients, and ii) to identify potential disease-specific factors for OP in this population. The findings presented in this abstract represent an extended analysis of our previously submitted work, in order to investigate the association between disease severity and osteoporosis in patients with systemic sclerosis.

Methods: This cross-sectional study was based on two large European prospective cohorts of SSc patients with retrospective collection of bone health data. OP was defined as the presence of a T-score below -2.5 at femoral neck or lumbar spine and/or a previous major osteoporotic fracture and/or the prescription of anti-osteoporotic therapy. Long-term therapy with glucocorticoids (GCs) was defined by a daily prednisone equivalent dose above 2.5 mg for more than 3 months. Age, female sex, BMI and treatment with proton pump inhibitors (PPIs) as predefined risk factors according to published evidence, as well as clinically relevant factors associated with a p-value < 0.05 in univariable analyses, after correction for multiple comparison, were implemented into a multivariable logistic regression model.

Results: A total of 932 patients fulfilling the ACR/EULAR 2013 classification criteria were included in the study, followed forward in time at two university hospitals: Lille (n=485) and Berlin (n=447). The two cohorts were studied separately. The prevalence of OP was 32% in Berlin and 23% in Lille (p=0.003), fragility fractures occurred in 22% and 18%, respectively.

Multivariable analysis in the Berlin cohort indicated that higher age (OR 1.05 [95%CI 1.03 to 1.07], p< 0.001), female sex (OR 2.70 [95%CI 1.29 to 5.65], p=0.009), diffuse skin extent (OR 5.03 [95%CI 2.50 to 10.10], p< 0.001), low BMI (OR 0.94 [95%CI 0.88 to 0.99], p=0.009), WHO-FC III-IV dyspnea (OR 2.06 [95%CI 1.16-3.67], p=0.014), receiving GCs (OR 1.78 [95%CI 1.10 to 3.17], p=0.026) or PPIs (OR 1.87 [95%CI 1.10 to 3.17], p=0.020) were associated with OP.

A. Berlin

Determinants	OR	Lower 95CI	Upper 95CI	p value
Age	1.05	1.03	1.07	<0.001
Female sex	2.7	1.29	5.65	0.009
BMI	0.94	0.88	0.99	0.009
Cutaneous diffuse	5.03	2.5	10.1	<0.001
mRSS	0.97	0.93	1	0.11
ILD	1.39	0.83	2.35	0.21
WHO-FC II-IV	2.06	1.16	3.67	0.014
PPIs use	1.87	1.1	3.17	0.02
GCs use	1.78	1.1	3.17	0.026

B. Lille

Determinants	OR	Lower 95CI	Upper 95CI	p value
Age	1.06	1.04	1.08	<0.001
Female sex	1.32	0.7	2.52	0.39
BMI	0.98	0.93	1.02	0.30
Cutaneous diffuse	0.99	0.53	1.84	0.98
ILD	1.00	0.55	1.81	0.99
ATA	2.22	1.18	4.16	0.013
DMARDs use	1.06	0.59	1.92	0.85
PPIs use	1.25	0.68	2.23	0.47
GCs use	4.48	2.42	8.26	<0.001

Figure 1. Factors associated with OP in two cohorts of SSc patients. (A) Berlin (n=447), (B) Lille (n=485). Forest plots indicate Odds ratio (OR) with lower and upper 95%CI (confidence interval). ATA: Anti-topoisomerase I antibodies; BMI: body mass index; DLCO: diffusing capacity for carbon monoxide; GCs: Glucocorticoids; ILD: interstitial lung disease; mRSS: modified Rodnan Skin Score; PPIs: Proton pump inhibitors; WHO-FC: WHO functional class.

In the Lille cohort, multivariable analysis confirmed the association of OP with higher age (OR 1.06 [95%CI 1.04 to 1.08], p< 0.001), GCs use (OR 4.48 [95%CI 2.42 to 8.26], p< 0.001), and with anti-topoisomerase I antibody positivity (OR 2.22 [95%CI 1.18 to 4.16], p=0.013).

Conclusion: Our data support a multifactorial etiopathogenesis of OP in SSc: besides common risk-factors for OP such as higher age, female sex, and BMI, several disease specific characteristics were associated with OP, such as SSc severity as reflected by diffuse skin extent and presence of antitopoisomerase I antibodies as well as severe dyspnea and SSc treatment (PPIs and GCs). These findings help to identify patients with SSc at particular risk for OP in clinical practice.

Disclosure: C. MIDOL: None; **E. Wiebe**: EW reports consultancy fees, honoraria and travel expenses from Medac and Novartis., 2, 6, 12, Travel Expenses; **E. Siegert**: None; **D. Huscher**: None; **H. Behal**: None; **D. Launay**: Actelion, 5, Boehringer-Ingelheim, 5, CSL Behring and Biocryst, 5, GlaxoSmithKlein(GSK), 5, Takeda, 5; **E. Hachulla**: Bayer, 6, Boehringer-Ingelheim, 6, CSL Behring, 5, GlaxoSmithKlein(GSK), 5, 6, Johnson & Johnson, 5, 6, Roche, 5, 6, Sanofi-Genzyme, 6; **E. Matteson**: AbbVie, 5, Alvotech Inc., 2, American College of Rheumatology, 12, Committee member, Boehringer-Ingelheim, 2, 6, Horizon Therapeutics, 1, NIH/NIAMS, 1, Practice Point Communications, 6, UpToDate, 9; **V. Sobanski**: None; **F. Buttgereit**: AbbVie/Abbott, 6, Horizon Therapeutics, 5, Pfizer, 5, 6, Roche, 6.

Abstract Number: 2533

Real-world Evidence for Assessing Mortality Disparity Between the Patients with Rheumatoid Arthritis and the General Population in Japan: Results from the IORRA Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes II: Patient Experience

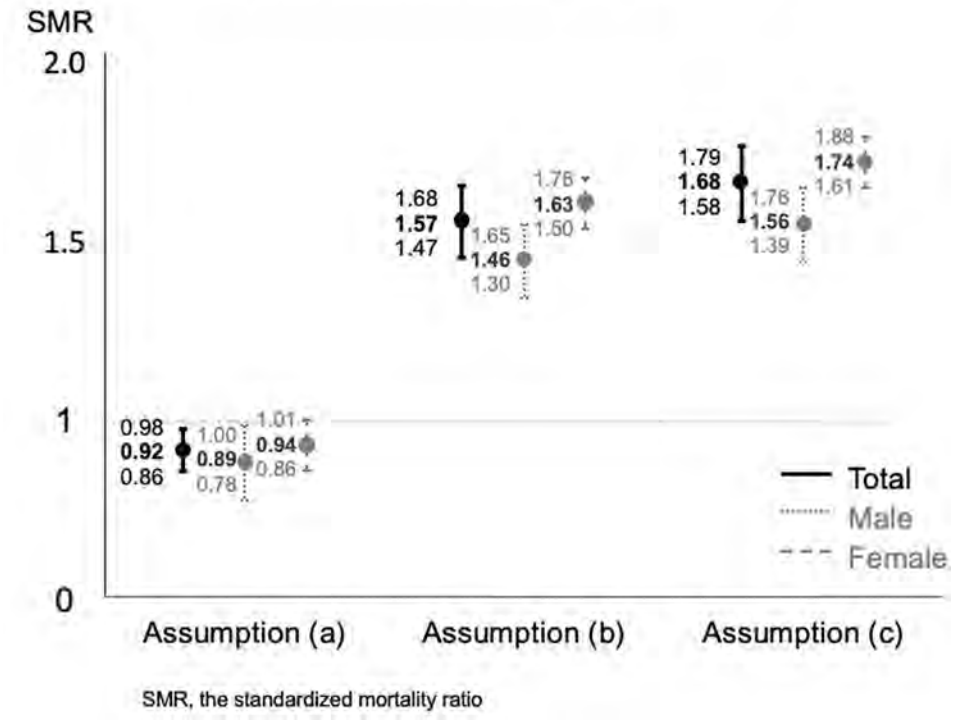
Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Patients with rheumatoid arthritis (RA) have been reported to have higher mortality rates than the general population. Our previous report showed that the standardized mortality ratio (SMR) of Japanese patients with RA registered in the Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort between 2000 and 2007 was 1.46-1.90 (Nakajima A. Scand J Rheumatol 2010). Since the introduction of various biological disease-modifying anti-rheumatic drugs (bDMARDs) in Japan after 2007, the mortality rates have declined(Abhishek A. Rheumatology 2018), but it is unclear if the mortality disparity with the general population has decreased. Our study aims to investigate the mortality and its risk factors of Japanese patients with RA since 2007.

Methods: The IORRA cohort is an observational study of patients with RA established in 2000 at Tokyo Women's Medical University. We observed RA patients who participated in the IORRA survey from October 2007 to September 2020 until October 1, 2021. Since there is no National Death Registry in Japan, we obtained death reports from residual families who responded to our mail query, from affiliated hospitals' physicians, and from police if a dead patient was found outside of a hospital. The primary endpoint was to calculate SMR using the person-year method with the Japanese general population data as a reference from the Ministry of Health, Labour, and Welfare, Japan. Cases lost to follow-up were treated using

Figure. 1 The results of the standardized mortality ratio (SMR) analysis.



These are the results of the sensitivity analysis of the standardized mortality ratio (SMR). The adjusted SMRs were calculated by taking into account the supplementation of lost-to-follow-up cases. (a) Adjusted SMR assumed that all untraceable cases were alive. (b) Adjusted SMR assumed that the untraceable cases had the same mortality rate as tractable cases. (c) Adjusted SMR assumed that the untraceable cases were 1.65 times more likely to die than the traceable cases.

multiple imputation methods as a sensitivity analysis of SMR. The secondary endpoints were to examine the risk factors for death using the time-dependent Cox proportional hazards model.

Results: Among 10,613 patients with RA (female, 83.7%; mean age, 57.1±14.1 years; mean disease duration, 9.8 ±9.6 years; mean observation period, 9.4±4.2 years) who enrolled in the IORRA survey from October 2007 to September 2020, 3,284 (30.9%))were lost to follow up. During the observation period, which covered 99,364.8 person-years, 915 deaths were reported. The leading causes of death were malignancies (28%), respiratory involvement (22%), and cardiovascular disorders (12%). The SMR (95% confidence interval), assuming that all lost-to-follow-up patients were alive, was 0.92 (0.86-0.98). When it was assumed that lost-to-follow-up patients had the same mortality rate as the remaining patients, the SMR was 1.57 (1.47–1.68). Alternatively, when it was assumed that the mortality rate of lost-to-follow-up patients was 1.65 times as high as that of the remaining patients based on the previous report (Kauppi M, J Rheumatol 2005), the SMR was 1.68 (1.58-1.79) (Figure 1). Factors associated with increased mortality included male sex, older age, history of smoking, higher disease activity score in 28 joints (DAS28), higher Japanese version of the health assessment questionnaire (J-HAQ) score, corticosteroid use, and presence of interstitial lung disease. Conversely, factors associated with decreased mortality included methotrexate (MTX) use and bDMARDs use (Table 1).

Conclusion: The mortality in patients with RA has remained consistently poor since 2007 when compared to the general population. MTX and bDMARDs use may reduce the risk of death.

Table. 1 Risk factors associated with mortality in patients with rheumatoid arthritis based on clinical, medication, and comorbidities.

Factor		HR	95% CI	P value
Male		2.30	1.88 – 2.81	< 0.01
Age (/10 year)		2.17	1.99 – 2.38	< 0.01
BMI (kg/m²)	18.5 – 24.9	reference	-	-
	< 18.5	1.50	1.26 – 1.79	< 0.01
	24.9<	0.97	0.76 – 1.23	0.79
Smoking	Never	reference	-	-
	Previous	1.25	1.03 – 1.51	0.03
	Current	1.44	1.07 – 1.93	0.02
DAS28-ESR	< 2.6	reference	-	-
	2 .6 ≤ – ≤ 3.2	1.69	1.33 – 2.13	< 0.01
	3.2 < – ≤ 5.1	2.10	1.68 – 2.62	< 0.01
	5.1 <	2.59	1.80 – 3.73	< 0.01
J-HAQ	0.0 – ≤ 0.50	reference	-	-
	0 .50 < – ≤ 1.00	1.44	1.13 – 1.83	< 0.01
	1.00 < – ≤ 2.00	1.40	1.12 – 1.74	< 0.01
	2.00 <	2.51	1.98 – 3.20	< 0.01
RF (IU/mL)	≤ 15	reference	-	-
	15 < – ≤ 45	0.85	0.68 – 1.07	0.16
	45 <	0.91	0.75 – 1.10	0.33
PSL use (mg/day)	0	reference	-	-
	0 < – ≤ 5	1.55	1.31 – 1.84	< 0.01
	5 < – ≤ 10	2.53	1.98 – 3.24	< 0.01
	10 <	3.68	2.39 – 5.67	< 0.01
MTX use (mg/week)	0	reference	-	-
	0 < – ≤ 8	0.72	0.61 – 0.85	< 0.01
	8 <	0.60	0.48 – 0.76	< 0.01
Biological DMARDs use	TNF inhibitor	0.63	0.45 – 0.88	< 0.01
	Non-TNF inhibitor	0.45	0.29 – 0.71	< 0.01
Comorbidity	Interstitial lung disease	1.31	1.02 – 1.69	0.04
	Cardiovascular disease	0.97	0.74 – 1.29	0.86
	Hypertension	0.78	0.65 – 0.94	< 0.01
	Diabetes mellitus	1.20	0.91 – 1.58	0.18
	Depression	1.47	0.90 – 2.38	0.12

BMI , body mass index; CI, confidence interval; DAS28-ESR, disease activity score in 28 joints with erythrocyte sedimentation rate; DMARDs, disease-modifying antirheumatic drugs; HR, hazard ratio; J-HAQ, Japanese version of Health Assessment Questionnaire; MTX, methotrexate; PSL, prednisolone; TNF, tumor necrosis factor

Risk factors associated with mortality in patients with rheumatoid arthritis based on clinical, medication, and comorbidities. A time-dependent multivariate Cox proportional hazards model was utilized to analyze sex, age, BMI, history of smoking, DAS28-ESR, J-HAQ, RF, medications used, and comorbidities as explanatory variables.

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Abstract Number: 2534

A Novel Approach for Mixed-methods Research Using Language Learning Models: A Report Using Patients' Perspectives on Barriers to Hip and Knee Replacement

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes II: Patient Experience
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: While qualitative research techniques provide valuable insights into patient experiences and perceptions, analyzing textual data from interviews can be time consuming and require multiple analysts for concept triangulation. Triangulation in qualitative data analysis minimizes potential biases that stem from relying on a single investigator. This approach enhances the credibility and validity of the findings by corroborating information from various perspectives and investigators. The capability of Large Language Model (LLM) technology to identify patterns and themes in textual data offers potential for conducting independent analysis of patients perceptions of care. This study explored a novel approach to triangulation in mixed-methods research (MMR) by employing ChatGPT-4, an LLM, for analyzing data from interviews of patients with advanced arthritis facing barriers to joint replacement.

Methods: We compared the thematic analysis and survey generation between investigators and ChatGPT-4, an AI-powered natural language processing tool that utilizes Generative Pre-trained Transformer (GPT), a type of large language model (LLM), as its core model. We used qualitative data from an existing qualitative study that explored patient perceptions of barriers to joint replacement utilization. Textual data from six semi-structured interviews were analyzed by human investigators and ChatGPT-4 independently. Human investigators used NVivo software to analyze the data and generate the codes and themes that emerged. Once the analysis was completed and it was determined that thematic saturation had been achieved, we proceeded to utilize ChatGPT-4 to directly generate themes from the interview transcripts. Both, human investigators and ChatGPT-4 independently, used the themes to create a survey. We compared the investigator-generated themes and survey with those generated by ChatGPT-4.

Results: ChatGPT-4 generated analogous dominant themes and a comprehensive corresponding survey as the human investigators but in significantly less time. (**Table 1**) Human-led thematic analysis produced 6 themes and 30 survey questions, taking significant time. ChatGPT-4 generated the same themes in under 45 minutes and created 17 survey questions in less than 1 minute. Themes generated by ChatGPT-4 covered the same topics as human-generated themes. However,

Table 1: Comparison of human- and ChatGPT-4 generated themes and surveys regarding barriers to arthroplasty. Check marks indicate matched and italicized lines indicate unmatched questions between groups. *

Human-Generated Themes and Survey Questions	ChatGPT-4 Generated Themes and Survey Questions
Theme 1: Cost	**Theme 1: Financial barriers**
✓ Cost of a joint replacement	✓ How concerned are you about the cost of arthroplasty surgery?
✓ Cost of the co-pay for a joint replacement	✓ How concerned are you about copays for specialist visits related to arthroplasty surgery?
✓ Cost of a co-pay for physical therapy after joint replacement	
Theme 2: Physician	**Theme 2: Lack of trust in healthcare system**
✓ Finding a surgeon I trust	✓ How much trust do you have in your surgeon's expertise and success rate?
o Figuring out how to find a qualified and experienced surgeon	
o Finding a surgeon who understands what I need	
Theme 3: Trust/pride	**Theme 3: Personal responsibility and social isolation**
✓ Not having trust in any doctors or hospitals	✓ How much assistance and support do you think you will need during recovery from arthroplasty?
o Having someone I know have a bad result from a joint replacement	✓ How much caregiving responsibility do you have for family members?
o Already had a bad experience with a joint replacement	o How difficult do you find it to accept help during recovery from arthroplasty surgery?
o Already having bad experiences with other surgery or medical procedures	o How satisfied are you with the social support you currently receive?
o Having people to see me using a cane or walker	
Theme 4: Timing	**Theme 4: Lack of information**
✓ Not having enough information to decide about having a joint replacement	o How much information do you have about the specific procedures involved in arthroplasty surgery?
o Having a joint replacement is the last resort, and I think I should wait longer	
o Having many medical problems and having a joint replacement is not a priority now	
o Being too young to undergo joint replacement surgery	
o Being too old to undergo joint replacement surgery	
o Not doing everything I can do (like lose weight) to avoid having a joint replacement	
o Not having bad enough joint pain to have a joint replacement	
Theme 5: Procedure-specific concerns	**Theme 5: Fear and uncertainty about procedure**
✓ Fear that I will need another joint replacement after the first one because I am young	✓ How uncertain are you about the potential complications of arthroplasty surgery?
✓ Fear that a joint replacement will not help me walk and function better	✓ How fearful are you about undergoing arthroplasty surgery?
✓ Fear that the joint replacement will not improve my pain	✓ How skeptical are you about the long-term benefits of arthroplasty surgery for managing pain?
o Fear of needles	o How satisfied are you with current treatments for managing arthritis?
Theme 6: Recovery	**Theme 6: Challenges during recovery**
✓ Availability of someone to help me recover from a joint replacement	✓ How concerned are you about the healing process after arthroplasty surgery?
✓ Availability to take care of my family/friends while I undergo joint replacement surgery	✓ How accessible do you think comprehensive physical therapy services are for arthroplasty patients?
✓ Accessing transportation to get to physical therapy appointments	✓ How concerned are you about the need for multiple surgeries every 20 years?
✓ Finding good physical therapy centers in my community	o How concerned are you about the duration of recovery after arthroplasty surgery?
✓ Concerns about how hard the recovery after a joint replacement will be	
o Concern of being healthy enough to undergo joint replacement surgery	
o Taking care of myself after a joint replacement because my building doesn't have an elevator	

*Check marks signify that the question was successfully matched in the alternative method of survey generation, whereas circles indicate that the question was not matched.

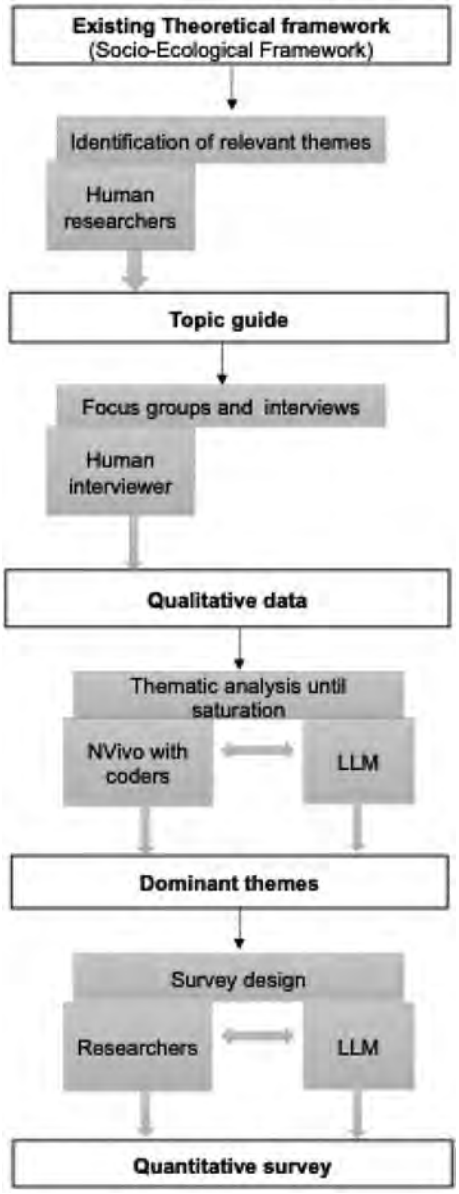

Figure 1: Mixed methods with Large Language Model (LLM) and human investigators for qualitative research

ChatGPT-4's survey questions were shorter and less specific compared to human-generated questions. The **Figure 1** mixed-methods flowchart proposes integrating LLMs alongside human investigators as a supplementary tool for the preliminary thematic analysis of qualitative data and survey generation.

Conclusion: The potential of ChatGPT-4 as a tool for assisting in triangulation was evident in both the qualitative portion of mixed methods research (MMR) by assisting with thematic analysis, and in the quantitative portion of MMR by facilitating survey development. This integration may improve the overall workflow efficiency of MMR. Given the novelty of LLM technology and the limited research on its embedded biases, investigators must consider the ethical and qualitative implications when using LLMs for research purposes.

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Abstract Number: 2535

Strategies to Embrace Living with Lupus Fearlessly (SELF): A Promising Digital Intervention for Lupus Self-Management

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes II: Patient Experience

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: The Lupus Foundation of America (LFA) has engaged in a 5-year cooperative agreement with the Centers for Disease Control and Prevention to implement a digital lupus self-management (SM) intervention based on the Transtheoretical Model of Change. Strategies to Embrace Living with Lupus Fearlessly (SELF) is designed to help users adopt 4 key lupus SM behaviors shown to have the highest impact on health and functional status: managing symptoms, managing stress, managing medications, and working with your healthcare team (each behavior includes 3-5 skills).

Methods: SELF offers user-tailored SM activities, symptom/medication trackers, a journal, links to LFA educators/peer support, and tailored text message tips. Onboarding and 90-day follow-up assessments collect demographics, stage of change for the 4 key SM behaviors , and patient-reported outcomes (PROs) such as measures of physical and mental health. Users select one SM behavior as a focus for a 2-week period. Activities are tailored to stage of change for that focus behavior. Users 'master a skill' if they improve from a skill-building stage at onboarding to a mastery stage at follow-up (Figure 1).

SELF was launched in January 2022 and promoted to people with lupus (PWL) via LFA and a patient registry. Utilization and outcomes were evaluated in January, 2023 for users who registered during the prior year.

Results: A total of 3,427 PWL registered for SELF, and 51% completed the onboarding assessment (n=1742) to gain access to the program.

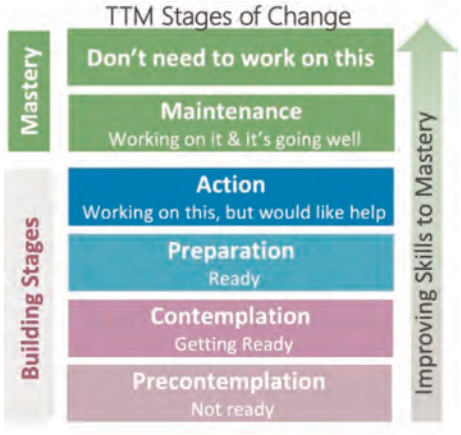

Figure 1. Transtheoretical Model of Change (TTM) is shown with stages of change and progression of improvement to mastery.

Table 1. User demographics are shown for three distinct groups: Enrollment disengagers (people who registered for SELF but did not complete the onboarding assessment), SELF users who did not complete a 90-day follow-up assessment and SELF users who completed a 90-day follow-up assessment.

	Enrollment Disengagers	SELF Users without Follow-up Assessment	SELF Users with Follow-up Assessment
N	1685	1569	173
Gender Identity	94.4% female 4.7% male 0.9% other	95.6% female 3.6% male 0.8% other	94.8% female 3.4% male 1.8% other
Age	46.5	45.9	51.4
Years Since Diagnosis	8.6	9.6	12.7
Race and Ethnicity			
White, non-Hispanic	51.7%	53.8%	44.2%
Black, non-Hispanic	21.8%	22.8%	38.4%
Hispanic	16.1%	13.9%	8.1%
Other/multi-racial	4.6%	4.8%	4.1%
Asian	2.3%	3.7%	2.9%
No answer	3.4%	1.0%	2.3%

Among SELF users for whom follow-up data were available (n=173), 46% (n=79) mastered 1 or more SM skills with many users mastering more (Figure 2); 52% experienced less fatigue ($p < .001$, $d = 0.33$); 37% reported better overall physical health ($p = .007$, $d = 0.22$); 41% reported better mental health ($p = .001$, $d = 0.28$); 59% improved medication adherence ($p = .004$, $d = 0.36$); and 59% improved doctor-patient communication ($p = .035$, $d = 0.16$). For those who did not complete a follow-up assessment (n-1569), the impact of SELF cannot be known, but users completed 8.1 SM activities on average (range = 0 - 224). Enrollment disengagers (n=1685) did not complete the onboarding assessment. The engagement groups were similar (demographics in Table 1), but those who completed follow-up assessments had a higher average age, longer duration since diagnosis, and a higher percentage of Black, non-Hispanic users.

Figure 2. Among SELF users who completed the follow-up assessment, 46% mastered one or more additional SM skills. Across the 4 key SM behaviors, SELF users improved the % of skills mastered from onboarding assessment to follow-up assessment in every category.

Conclusion: Improvements to SM skill development and PROs show that SELF is a promising program for building skills and impacting outcomes for PWL. Low engagement at onboarding and follow-up assessments indicates a need to ease response burden. While results need more study, it is notable that more users who completed the follow-up assessment were Black, a group historically experiencing greater health disparities.

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Abstract Number: 2536

DMARD Adherence During the COVID-19 Pandemic and Association with Risk of COVID-19 Infection

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes II: Patient Experience
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: The COVID-19 pandemic affected medication adherence in patients with autoimmune disease (AD) due to their fear of contracting COVID-19, financial hardship, and medication shortage. We compared adherence to disease-modifying antirheumatic drugs (DMARDs) before, during, and after the COVID-19 pandemic among patients with AD and evaluated whether adherence affected the risk of contracting COVID-19.

Methods: This retrospective study included patients aged ≥18 years in a large integrated healthcare system during 2019-2021, who had ICD-coded diagnoses of AD and ≥2 DMARDs prescriptions dispensed by outpatient pharmacy. DMARDs were classified as synthetic (sDMARDs) or biologic (bDMARDs). Medication adherence was measured by the Medication Possession Ratio (MPR), with adherence defined as MPR ≥80%. Adherence during the pre-pandemic year (March 19, 2019 to March 18, 2020), pandemic year (March 19, 2020 to March 18, 2021), and vaccine era (March 19, 2021 to September 18, 2021) were compared using the Wilcoxon test. Multivariable logistic regression was used to examine the association of treatment adherence and risk of COVID-19, reporting odds ratios (OR) and 95% confidence intervals (CI), adjusted for age, sex, race and ethnicity, primary language, smoking, weight category, and presence of other chronic health conditions.

Results: The cohort included 7959 patients with AD; 77.2% were female, 46.4% were White, 21.3% Hispanic, 19.2% Asian/Pacific Islander (PI), and 10.7% Black race. The most common AD diagnoses were rheumatoid arthritis (62.8%), psoriatic arthritis (12.8%), and lupus (18.3%). The most commonly prescribed sDMARDs were methotrexate (51.5%), hydroxychloroquine (45.8%), and leflunomide (17.3%), while the most commonly prescribed bDMARDs were tofacitinib (14.3%), TNF inhibitors (7.7%), and abatacept (2.9%). The majority were receiving sDMARD monotherapy (69.8%), followed by combination sDMARD and bDMARD therapy (24.4%), bDMARD monotherapy (3.6%), and sDMARD triple therapy (3.6%). Of patients prescribed sDMARDs, 72% were adherent in the pre-pandemic year, 66% in the pandemic year, and 68% in the vaccine era. Of patients prescribed bDMARDs, 48% , 44%, and 53% were adherent in the pre-pandemic, pandemic, and

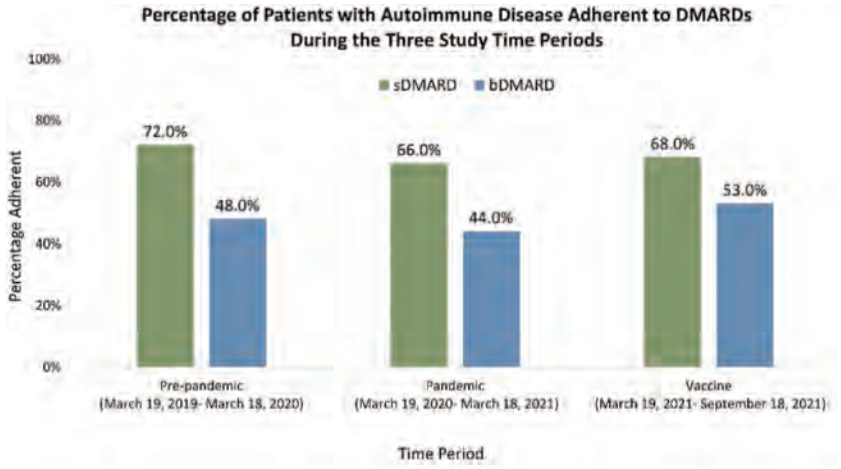

Figure 1. Percentage of Patients with Autoimmune Disease Adherent to DMARDs During the Three Study Time Periods

Table 1. Cohort Characteristics

Characteristics	N (%)
Female	6147 (77.2%)
Age (years)	
<40	1042 (13.1%)
40-49	1322 (16.6%)
50-59	2270 (28.5%)
60-69	1865 (23.4%)
70+	1460 (18.3%)
Race/Ethnicity	
Asian/Pacific Islander	1529 (19.2%)
Black	850 (10.7%)
Hispanic	1697 (21.3%)
Other/Unknown	192 (2.4%)
White	3691 (46.4%)
Rheumatologic Diagnosis	
Rheumatoid arthritis	4997 (62.8%)
Psoriatic arthritis	1022 (12.8%)
Spondyloarthritis	259 (3.3%)
SLE	1459 (18.3%)
Vasculitis	124 (1.6%)
Myositis	220 (2.8%)
Scleroderma	174 (2.2%)
Others	187 (2.5%)

vaccine era. Differences in adherence between the time periods were statistically significant ($p< 0.01$) for both sDMARDs and bDMARDs. Adherence to sDMARDs was associated with lower risk of COVID-19 infection (OR 0.73, 95% CI 0.60-0.88), adjusting for covariates. Similar findings were seen for adherence to bDMARDs (OR 0.56, 95% CI 0.34-0.94).

Conclusion: In a large population of patients with AD, medication adherence, particularly to bDMARDs, was low even pre-pandemic and decreased further during the pandemic, but subsequently increased in the vaccine era. Medication adherence was associated with lower risk of COVID-19 infection. These findings support efforts to reduce barriers to medication adherence, including addressing patient concerns regarding infection risk. Future studies should examine whether there is an association between poor medication adherence and severity of COVID-19 infection and outcomes.

Disclosure: T. Selvam: None; **K. Peterman**: None; **A. Haghshenas**: None; **L. Liu**: None.

Abstract Number: 2537

Implementation of a Best Practice Advisory to Improve Infection Screening Prior to New Prescriptions of Biologics and Targeted Synthetic Drugs

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes II: Patient Experience

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Biologic and targeted synthetic DMARDs (b/tsDMARDs) are widely used to treat patients with various autoimmune inflammatory diseases (ARD). Use of a b/tsDMARD in patients with pre-existing tuberculosis (TB), hepatitis B (HBV), or hepatitis C (HCV) can lead to significant morbidity and mortality. Many national and international societies recommend screening for one or all of these exposures prior to initiation of certain b/tsDMARDs. However, recommended timing intervals of screening are not clear and adherence to these recommendations varies widely. This quality improvement initiative focused on improving screening for TB, HBV, and HCV prior to new prescription of a b/tsDMARD using a best practice advisory (BPA) in the electronic health records (EHR).

Methods: Patients aged 18 years or older with at least one visit with a clinician (attending, fellow, or APRN) in the section of Rheumatology in the designated time frame were included. Upon a new prescription of a b/tsDMARD, clinicians were alerted via a BPA pop-up in the EHR about the last available results if any, for TB, HBV, and HCV, and allowed for quick ordering as appropriate. This BPA was implemented on December 1, 2020. Baseline screening proportions for TB (QuantiFERON), HBV, and HCV for patients prescribed a new b/tsDMARD from October 1, 2017 to November 30, 2020 (pre-BPA period) were compared with those of patients with prescriptions from December 1, 2020 to March 3, 2022 (post-BPA period).

Results: A total of 711 patients pre-BPA and 257 patients post-BPA implementation were included in the study. The BPA implementation was associated with statistically significant improvement in screening for TB, HBsAg, HBcAb, and HCV Ab or HCV viral load (Table 1). Partial hepatitis B testing (screening for HBcAb or HBsAg) was significantly changed by the BPA (pre-BPA 364 of 711 (51%) vs post-BPA 186 of 257 (72%), p=< 0.001). Complete hepatitis B testing (screening for both HBcAb and HBsAg) also improved after BPA implementation (pre-BPA 222 of 711 (31%) vs post-BPA 127 of 257 (49%), p< 0.001). A total of 154 patients (22%) in the pre-BPA and 117 patients (46%) in the post-BPA periods were appropriately screened for all three infectious diseases, which was statistically significant (p< 0.001). Multivariable logistic analysis revealed in the pre-BPA period, relative to attending physicians, fellows were significantly more likely to order testing (HBcAb p=< 0.001, HBsAb p=< 0.001, HBsAg p=0.005, partial Hep B testing p=0.006, complete Hep B testing p=< 0.001, HCV Ab or HCV RNA p=0.002, all four tests p=< 0.001) after accounting for multiple comparisons. In the pre-BPA period, each year of age decreased the adjusted odds of TB testing by 2% (OR 0.98; 95% CI 0.97, 1.0; p=0.006) and males had lower adjusted odds for HBcAb testing than females (OR 0.58; 95% CI 0.39, 0.85). In the post-BPA period, there were no statistically significant findings for any patient or clinician variable.

Conclusion: Implementation of a BPA in the EHR can improve infectious disease screening for patients with ARD initiating b/tsDMARDs and has potential to improve patient safety and eliminate screening discrepancies.

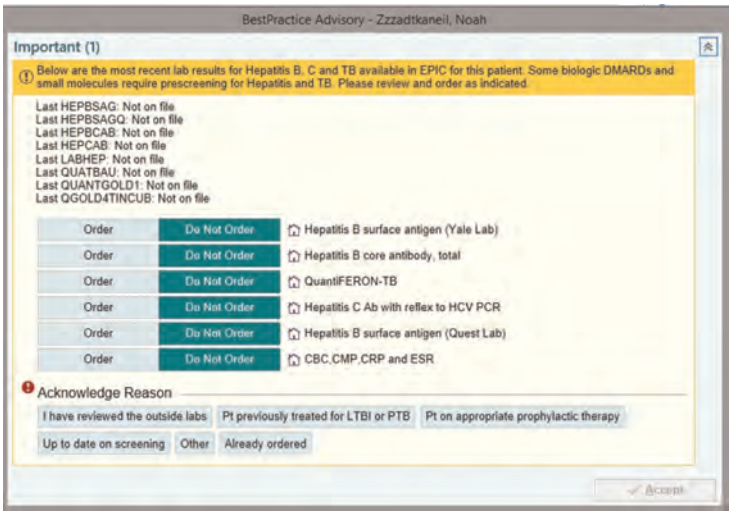

Figure 1 is a visualization of the finalized BPA after subsequent PDSA cycles identified areas of improvement in the clinical decision support system. This final version of the BPA includes seven lab result components at the top, five options for quick ordering of infectious disease screening, four lab components for general monitoring while on drug therapy (CBC, CMP, CRP, and ESR), and five acknowledgement reasons for why a clinician is or is not ordering the labs. TB= "Tuberculosis"; HCV="hepatitis C virus"; PCR= "polymerase chain reaction"; LTBI = "latent tuberculosis infection"; PTB = "pulmonary tuberculosis"; HEPBSAG= "Hepatitis B surface Antigen"; HEPBSAGQ= "Hepatitis B surface Antigen, Quest Diagnostics"; HEPBCAB="Hepatitis B core Antibody"; LABHEP= represents multiple test components for Hepatitis C; HEPCAB="Hepatitis C Antibody"; QUATBAU= "TB QuantiFERON Gold"; QUANTGOLD1= "TB QuantiFERON Gold"; QGOLD4TINCUB= "TB QuantiFERON Gold"

Table 1 includes descriptive statistics of the study population pre-BPA (10/1/2017 – 11/30/2020) and post-BPA (12/1/2020 – 3/3/2022) implementation. A Bonferroni correction was used to correct for multiple comparisons and reduce risk of false positive results, which is represented by the Q-values. BPA="best practice advisory"; TNF= "Tumor necrosis factor"; CTLA4= "cytotoxic T-lymphocyte associated protein 4"; IL-17= "Interleukin 17"; IL-6= "Interleukin 6"; JAK= "Janus kinase inhibitor". Inflammatory arthritides included rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, and Adult-onset Still's disease. Connective tissue diseases included were systemic lupus erythematosus, Sjogren's syndrome, mixed connective tissue disease, and systemic sclerosis. Vasculitides included anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis, Bechet's disease, giant cell arteritis, and Takayasu arteritis. The "Other" category included diagnoses for polymyalgia rheumatica and Familial Mediterranean Fever.

Table 1. Description of study population pre- and post-best practice advisory (BPA)

	Pre-BPA (N=711)	Post-BPA (N=257)	P-value	Q-value
Mean Age, Years (SD)	54 (14)	54 (15)	0.77	>0.9
Female N (%)	517 (73)	165 (64)	0.013	0.065
Race and Ethnicity			0.81	>0.9
American Indian or Alaska Native N (%)	2 (0)	2 (1)		
Asian N (%)	12 (2)	4 (2)		
Black or African American N (%)	67 (9)	24 (9)		
Other or Unknown N (%)	79 (11)	33 (13)		
Other Pacific Islander N (%)	2 (0)	0 (0)		
White or Caucasian N (%)	549 (77)	194 (75)		
Rheumatic Disease			0.4	>0.9
Inflammatory Arthritis N (%)	305 (43)	141 (55)		
Connective Tissue Disease N (%)	25 (4)	14 (5)		
Vasculitis N (%)	16 (2)	12 (5)		
Other N (%)	3 (0)	0 (0)		
Missing Diagnosis N (%)	362 (51)	90 (35)		
Class of Medication Prescribed			0.37	>0.9
TNF inhibitors N (%)	373 (52)	130 (51)		
IL-17 inhibitors N (%)	113 (16)	34 (13)		
Anti-CD20 N (%)	1 (0)	1 (0)		
IL-6 N (%)	42 (6)	22 (9)		
JAK N (%)	118 (17)	40 (16)		
CTLA-4 Agonists N (%)	25 (4)	9 (4)		
Other N (%)	39 (5)	21 (8)		

Table 2 displays observed screening rates of TB, HBV, and HCV before and after the initiation of the BPA on 12/1/2020. Partial Hep B testing was defined as having either HBsAg or HBcAb, but not both. Complete Hep B testing was defined as having both HBsAg and HBcAb. To be considered as having testing of "All Four Tests" a patient had to have QuantiFERON Gold, HBsAg, HBcAb, and HCV Ab or HCV quantitative RNA performed within the specified time. We used a Bonferroni correction to correct for multiple comparisons and reduce risk of false positive results, which is represented by Q-values. BPA= "Best Practice Advisory"; TB= "Tuberculosis"; HBsAb= "Hepatitis B surface antibody"; HBcAb= "Hepatitis B core antibody"; HBsAg= "Hepatitis B surface antigen"; HCV= "Hepatitis C virus"; HBV= "Hepatitis B virus." *Q-value=<0.001 **Q-value=>0.9

Table 2. Comparison of screening rates of TB, HBV and HCV tests captured pre-BPA and post-BPA

	Pre-BPA (N=711)	Post-BPA (N=257)	P-value
TB, N (%)	467 (66)	210 (82)	<0.001*
HBsAb, N (%)	196 (28)	73 (28)	0.8**
HBcAb, N (%)	224 (32)	132 (51)	<0.001*
HBsAg, N (%)	362 (51)	181 (70)	<0.001*
HCV Ab or HCV RNA, N (%)	424 (60)	202 (79)	<0.001*
Partial Hep B, N (%)	364 (51)	186 (72)	<0.001*
Complete Hep B, N (%)	222 (31)	127 (49)	<0.001*
All four tests, N (%)	154 (22)	117 (46)	<0.001*

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Abstract Number: 2538

Safety and Efficacy of Sodium-glucose Co-transporter 2 Inhibitors in Patients with Psoriasis and Concomitant Type 2 Diabetes Mellitus: A Population-based Cohort Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes II: Patient Experience

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Psoriasis and type 2 diabetes mellitus (T2D) may share common underlying pathophysiology, in which the pathogenesis of psoriasis is mediated by NOD-like receptor family pyrin domain-containing inflammasome (NLRP)-dependent inflammatory pathways that is a target of sodium-glucose co-transporter 2 inhibitors (SGLT2i). The aim of the present study was to investigate whether treating psoriasis patients with concomitant T2D using SGLT2i improves clinical outcomes compared to similar line oral antidiabetic medications.

Methods: This was a population-based cohort study between 2014 and 2023 that included psoriasis patients with concomitant T2D from 92 hospitals across the United States. The risk of psoriasis-related comorbidities and general medical outcomes in patients treated with SGLT2i was compared with that in 1:1 propensity score-matched psoriasis patients with T2D on dipeptidyl peptidase 4 inhibitors (DPP4i). Hazard ratios (HRs) were estimated using Cox proportional hazards regression.

Results: After propensity-score matching, there were 17,085 patients with psoriasis and concomitant T2D on SGLT2i. Compared to those using DPP4i, patients on SGLT2i presented with a significantly lowered risk of incident cardiorenal complications including myocardial infarction (HR: 0.84, 95% CI: 0.74, 0.95), acute kidney failure (HR: 0.68, 95% CI: 0.63, 0.73), and chronic kidney disease (HR: 0.73, 95% CI: 0.69, 0.77), and a significantly lowered risk of incident emergency visits (HR: 0.82, 95% CI: 0.78, 0.85) over a mean follow-up period of six years. The risk of psoriatic arthritis (HR: 1.04, 95% CI: 0.98, 1.10), metabolic syndrome (HR: 1.15, 95% CI: 0.96, 1.39), stroke (HR: 0.93, 95% CI: 0.83, 1.04), amputation of the lower limb (HR: 0.78, 95% CI: 0.42, 1.47), and hospitalization (HR: 0.88, 95% CI: 0.76, 1.02) was not significantly different between SGLT2i and DPP4i users. Diabetic ketoacidosis (HR: 1.602, 95% CI: 1.21, 2.12) was a potential adverse event of SGLT2i.

Conclusion: Among patients with psoriasis and concomitant T2D, SGLT2i use was associated with a significantly decreased risk of incident cardiorenal events and emergency visits and did not trigger psoriasis-related comorbidities including psoriatic arthritis. Further research, including clinical trials are warranted to validate the findings.

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Abstract Number: 2539

Baseline IL-10 Levels as a Predictive Biomarker for Achieving Clinical Response with Abatacept in ACPA+ Patients with Early RA

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: RA – Treatments III: Predictors of Response & Tapering

Session Type: Abstract Session

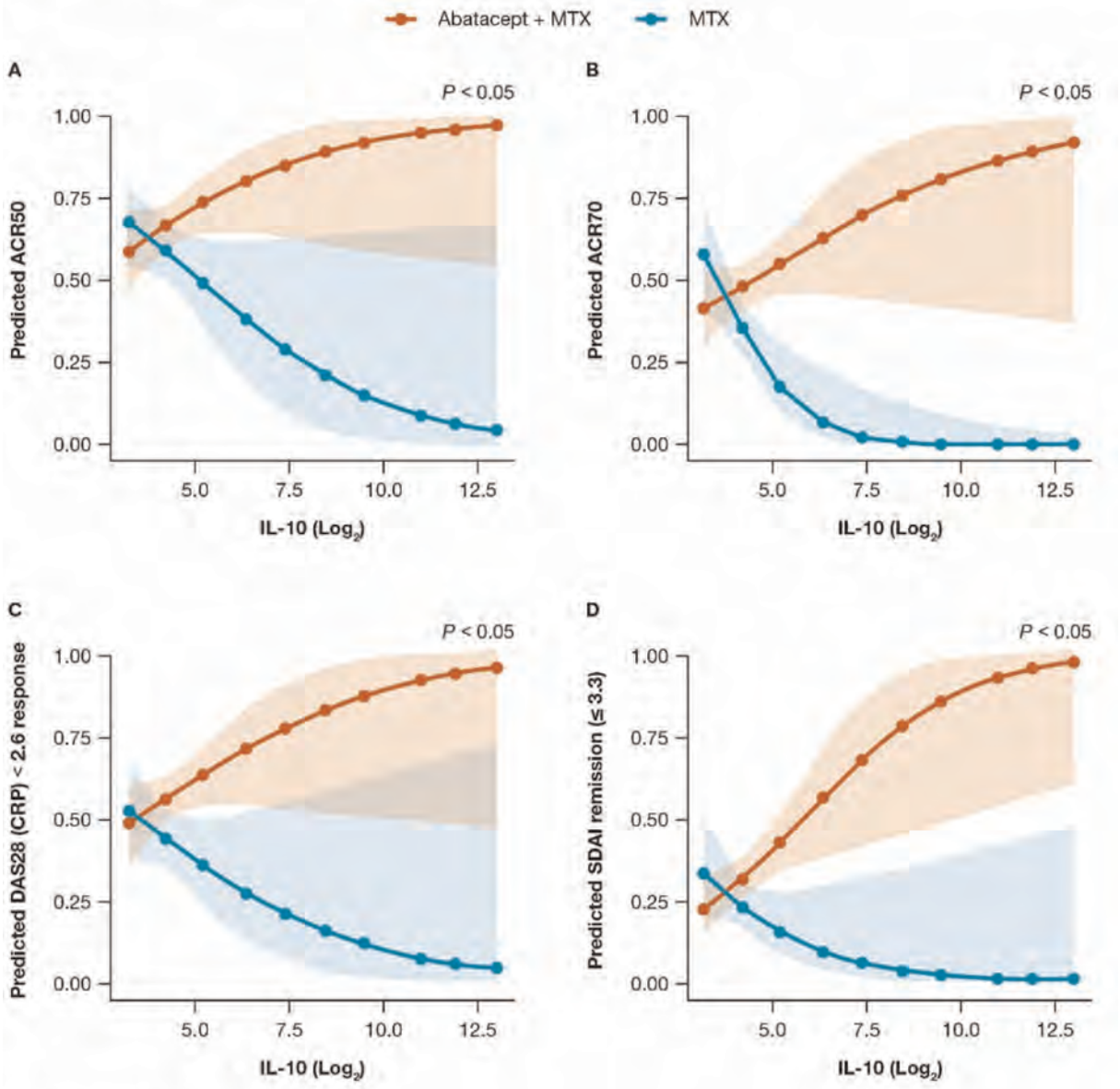
Session Time: 4:00PM–5:30PM

Background/Purpose: A key target of RA treatment is to achieve early and sustained remission in order to ensure lower levels of long-term structural joint damage and physical disability. Identifying predictive biomarkers may help guide treatment options to achieve this. Inflammatory biomarkers such as IL-10, a pleiotropic cytokine that drives B-cell responses and is associated with higher seropositivity for RF and anti-CCP in patients (pts) with RA,[1] may provide clinical value as predictive

biomarkers. We evaluated the association of baseline (BL) circulated biomarkers with disease activity (DA) measures and their ability to predict clinical response in MTX-naive, ACPA+ pts with early RA from a phase 3b study (AVERT-2; NCT02504268).[2]

Methods: Pts aged ≥ 18 years with early RA (≤ 6 months from diagnosis; ACR/EULAR 2010[3]) were randomized to abatacept + MTX or abatacept placebo + MTX (referred to as MTX). Serum samples were collected over a 56-week period, with endpoints assessed at weeks 24 and 52.A broad selection of 113 inflammatory and immune response–related proteins were analyzed using either the Olink Target 96 multiplex immunoassay inflammation panel or selected panels from Myriad Rules-Based Medicine. BL biomarker and clinical DA measures were analyzed using Spearman's correlation, with changes from BL in select biomarkers analyzed via repeated measures mixed-effects models. Logistic regression predicted response

Figure 1. Higher baseline IL-10 levels predicted greater response with abatacept + MTX versus MTX for (A) ACR50, (B) ACR70, (C) DAS28 (CRP) response, and (D) SDAI remission at week 52



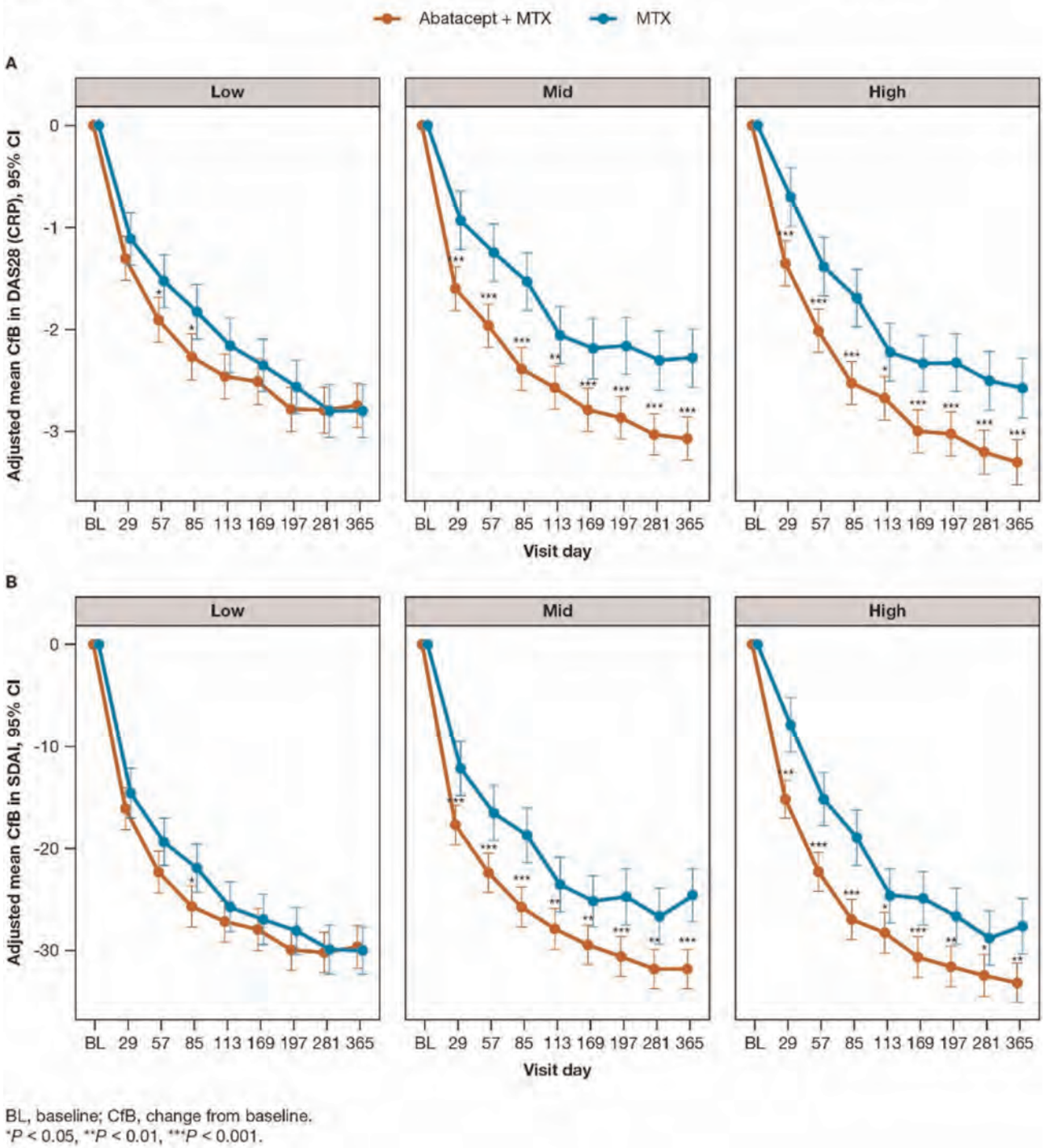
Shaded areas show 95% CIs.

ACR50/70, 50/70% improvement in ACR criteria.

to treatment with BL age, Simplified Disease Activity Index (SDAI), pain (measured via visual assessment scale), and ACPA positivity as covariates.

Results: Of 752 pts in the intent-to-treat population, 446 from the abatacept + MTX arm and 300 from the MTX arm were included in the biomarker analyses. BL characteristics were well-balanced between treatments. Of the 15 biomarkers significantly associated with ≥ 2 BL DA measures, at both weeks 24 and 52, pts receiving abatacept + MTX showed significantly

Figure 2. Higher baseline IL-10 tertile is associated with greater improvements in (A) DAS28 (CRP) and (B) SDAI over time for abatacept + MTX versus MTX



BL, baseline; CfB, change from baseline.
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

greater reductions in all biomarker levels compared with MTX ($P < 0.05$ to $P < 0.001$) with a change from BL in 13 biomarkers demonstrating significant associations with DA measure reduction ($P < 0.05$). Higher BL levels of IL-10 predicted greater clinical improvement, assessed by ACR and DAS28 (CRP) (< 2.6) responses and SDAI remission (≤ 3.3), with abatacept + MTX vs MTX ($P < 0.05$ at week 52) (**Figure 1**). Further, a higher BL IL-10 concentration tertile was significantly associated with greater improvements in DAS28 (CRP) and SDAI on abatacept + MTX vs MTX ($P < 0.05$ to $P < 0.001$ at days 29–365) (**Figure 2**).

Conclusion: Higher BL IL-10 levels predicted greater clinical response for pts treated with abatacept + MTX vs MTX. Increased IL-10 levels may reflect greater interactions between CD4+ T-helper cells and autoantibody-producing B cells. These findings may help clinicians to identify pts most likely to respond favorably to the abatacept mechanism of action. A prospective study is warranted to confirm whether screening for IL-10 in the clinical setting can help guide treatment options for pts with RA.

References

1. Hernández-Bello J, et al. *Cytokine* 2017;95:88–96.
2. Emery P, et al. *Rheumatol Ther* 2023;10:707–27.
3. Aletaha D, et al. *Arthritis Rheum* 2010;62:2569–81.

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Abstract Number: 2540

The Molecular Stratification of Rheumatoid Arthritis Using High-throughput Technologies Is Directly Associated with Disease Activity and Clinical Response

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
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Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a remarkably heterogeneous autoimmune disease whose clinical outcomes with disease-modifying antirheumatic drugs (DMARDs) remain unpredictable. The aim of this study was to characterize the molecular landscape of RA patients by using a multi-omic approach involving transcriptomics and proteomics and their association with disease status and clinical response.

Methods: Peripheral blood mononuclear cells from 123 RA patients were profiled by RNAseq on Illumina platforms. The RA cohort included 49 patients taking conventional DMARDs and 74 biologics-naïve patients before receiving biologic (TNFi) or targeted-synthetic DMARDs (JAKinibs). Clinical outcomes were evaluated after 6 months of treatment following EULAR criteria. A consensus cluster approach was used to identify patients' subgroups based on their transcriptomic profile. In parallel, a panel of 92 inflammatory mediators was analyzed in the RA serum using the Olink platform.

Results: Unsupervised hierarchical clustering identified 3 subgroups of RA patients displaying differential expression of 7 gene modules defining distinctive biological pathways. Cluster 1 included the inflamed-myeloid group, showing high expression in myeloid and inflammation genes modules. Cluster 2 defined the healthy-like RA patients, displaying low levels of all gene modules. Cluster 3, identified the B-cells group, exhibiting high levels of B cell gene-modules. The analysis of the serum proteome among these clusters identified 34 proteins showing differential expression levels, where a signature of chemokines, interleukins, and growth factors was found increased in C1 compared with C2 and C3.

Clinically, C1 grouped RA patients with more severe disease activity, higher number of circulating monocytes and neutrophils, and larger disease evolution compared with C2 and C3. On the contrary, C2 involved patients with the lowest disease severity and evolution time and included few patients starting b- or ts-DMARDs. Lastly, C3 included patients with disease activity and evolution time like C2 but showed the highest number of circulating lymphocytes.

Regarding the response to DMARDs, C1 grouped RA patients with the highest percentage of response to TNFi. Clinical response of patients treated with JAKinibs was independent of the cluster where patients were allocated. That data suggests that clinical response to each drug might be associated with a deregulated expression of specific modules of genes and inflammatory proteins at baseline. Accordingly, correlation studies among DAS28 variation at 6 months and basal levels of different gene modules and proteins showed specificity depending on the drug analyzed.

Conclusion:

1. RA patients conform distinctive subgroups based on altered transcriptomic and proteomic profiles, directly linked to their clinical status.
2. Clinical effectiveness of TNFi and JAKinibs was divergent among these molecular clusters and associated with specific transcriptomic and proteomic profiles before starting such therapies.

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Abstract Number: 2541

Differential Responses to Initial Treatment Strategies for Rheumatoid Arthritis Among Those with Lower Body Mass and Adiposity

Joshua Baker[1], James O'Dell[2], Bryant England[2], Jon Giles[3], Jefferey Newcomb[4], Michael George[1], Geoffrey Thiele[2], Larry Moreland[5], S. Louis Bridges[6], Jeffrey R Curtis[7] and Ted R Mikuls[8], [1]University of Pennsylvania, Philadelphia, PA, [2]University of Nebraska Medical Center, Omaha, NE, [3]Columbia University, New York, NY, [4]University of Nebraska, Omaha, NE, [5]University of Colorado, Denver, CO, [6]Hospital for Special Surgery, New York, NY, [7]Division of Clinical Immunology and Rheumatology, University of Alabama, Birmingham, AL, [8]Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: RA – Treatments III: Predictors of Response & Tapering

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: The identification of measures that help predict who is likely to benefit most from early escalation to biologic therapy would inform personalized care among patients with rheumatoid arthritis (RA) early in the course of the disease. While prior studies have assessed how body mass index (BMI) and adiposity might influence responses to therapy, these studies rarely have compared two active treatment strategies. We aimed to determine if BMI and circulating adipokines (peptide hormones produced by adipose tissue) can identify patients most likely to benefit from early initiation of tumor necrosis factor inhibitors (TNFi) as initial therapy compared to combination therapy with conventional DMARDs.

Methods: This is a secondary analysis of the Rheumatoid Arthritis Comparison of Active Treatments (RACAT) trial and the Treatment of Early Aggressive Rheumatoid Arthritis (TEAR) trial. Both trials evaluated strategies with conventional DMARDs (triple therapy) compared to strategies that included TNFi (etanercept), among patients with active RA. We compared response rates between TNFi and triple therapy among patients with different BMI (normal/underweight v. overweight/obese). Adipokines were also measured at enrollment in RACAT using validated assays and we explored the association

Table 1: Changes in RA outcomes at 24 weeks by BMI and treatment from regression models, adjusted for age, sex, and baseline DAS28.

	Under/Normal Weight N=71			Overweight/Obese N=232			
RACAT	**Triple** N=27	**Etanercept** N=44	**P**	**Triple** N=124	**Etanercept** N=108	**P**	***P**
ΔDAS28	-1.32 (0.24)	-2.47 (0.19)	<0.001	-1.88 (0.11)	-1.92 (0.12)	0.78	0.001
% ACR20	23%	64%	0.001	46%	42%	0.56	0.001
% ACR50	3%	40%	0.005	25%	24%	0.83	0.005
% ACR70	4%	21%	0.11	6%	8%	0.44	0.21
% LDA	25%	48%	0.04	25%	31%	0.25	0.21
% Switched	30%	23%	0.50	24%	28%	0.41	0.33
	Under/Normal Weight N=142			**Overweight/Obese** N=387			
TEAR	**Triple** N=46	**Etanercept** N=96	**P**	**Triple** N=128	**Etanercept** N=259	**P**	**P***
ΔDAS28	-1.88 (0.19)	-2.10 (0.13)	0.36	-1.80 (0.11)	-1.72 (0.08)	0.59	0.29
% ACR20	52%	67%	0.05	57%	55%	0.76	0.08
% ACR50	31%	43%	0.12	31%	29%	0.63	0.13
% ACR70	9%	17%	0.19	9%	10%	0.37	0.54
% LDA	48%	49%	0.86	40%	37%	0.58	0.66

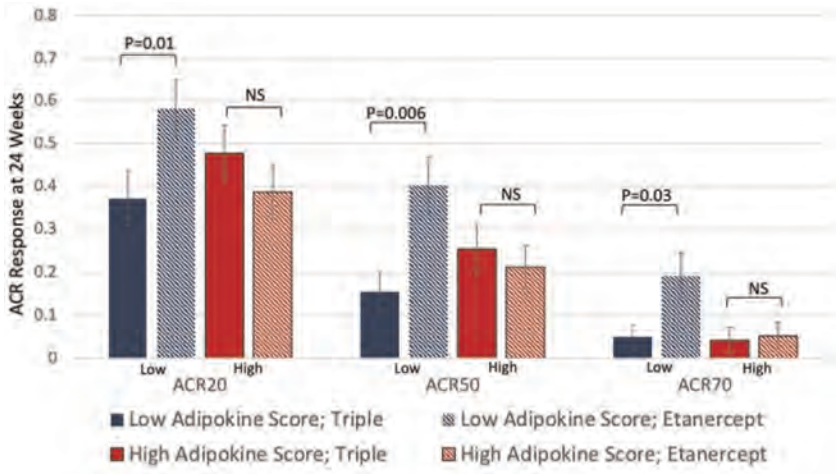

Figure 1: American College of Rheumatology Response rates in RACAT among 1) participants with a low adipokine score receiving triple therapy (blue solid bar); 2) participants with a low adipokine score receiving immediate etanercept (blue striped bar); 3) participants with a high adipokine score receiving triple therapy (red solid bar), and 4) participants with a high adipokine score receiving etanercept (red striped bar).

between an adipokine score (number of adipokines above/below the median, grouping those that directionally reflect greater adiposity) and response within the two treatment arms. Analyses were adjusted for age, sex, BMI, and baseline disease activity (DAS28).

Results: We included 306 participants that were eligible from RACAT and 601 from TEAR. In RACAT, greater change in DAS28 and greater ACR20 response was observed for TNFi initiators compared to triple therapy among participants that were normal or underweight (ACR 20: 64% v. 23%) while no differences between TNFi and triple therapy were observed among overweight and obese (p for interaction = 0.001) (Table). Similar patterns were observed in TEAR, though were more modest. The pattern in TEAR was similar among methotrexate-naïve initiators at baseline and methotrexate inadequate responders at 6-months (combined data are shown in Table). In RACAT, adipokine scores below the median (< 2) and a profile consistent with lower adiposity were associated with greater response to TNFi (ACR20: 58% v. 37%) (Figure). The addition of adipokines to the model resulted in better model fit compared to a model with BMI alone (p=0.01).

Conclusion: Low BMI and evidence of low adiposity based on adipokine profiles are both associated with a superior response to initiation of TNFi compared to the initiation of triple therapy. This is the first study, to our knowledge, to identify a meaningful difference between two active strategies based on weight and body habitus and may reflect phenotypic differences or pharmacodynamic effects. The results support earlier escalation to TNFi among thin patients that do not respond to methotrexate and have implications for future clinical trial design.

Disclosure: J. Baker: Bristol-Myers Squibb(BMS), 2, Burns-White, LLC, 2, CorEvitas, LLC, 2, Pfizer, 2; **J. O'Dell**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **J. Giles**: AbbVie, 2, Eli Lilly, 2, Gilead, 2, Novartis, 2, Pfizer, 2; **J. Newcomb**: None; **M. George**: AbbVie/Abbott, 2, GlaxoSmithKlein(GSK), 5, Janssen, 5; **G. Thiele**: None; **L. Moreland**: Boehringer-Ingelheim, 12, member of independent Data Safety Monitoring Board, Celltrion, 12, member of independent Data Safety Monitoring Board; **S. Bridges**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, BMS, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Genentech, 2, 5, Janssen, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB Pharma, 2, 5; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9.

Abstract Number: 2542

Impact of Concomitant Methotrexate on Disease Activity After Tapering Abatacept in Patients with Rheumatoid Arthritis: A Nationwide Cohort Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: RA – Treatments III: Predictors of Response & Tapering

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Recent randomized-controlled studies have suggested that tapering bDMARDs and/or csDMARDs after achieving sustained remission in patients with rheumatoid arthritis (RA) can be considered. However, the optimal tapering strategy is yet to be established, and it may differ between various circumstances. We investigated whether concomitant treatment of methotrexate (MTX) may influence the disease activity after tapering abatacept in patients with RA.

Methods: We utilized the data from the Korean College of Rheumatology Biologics and Targeted therapy Registry (KOBIO-RA) (NCT01965132). Patients were enrolled when initiating a bDMARD (defined as baseline) and were followed up annually thereafter. Follow-up data on disease activity, concomitant medications, and dose of bDMARDs were collected. We included patients who 1) were treated with abatacept at baseline and 2) had no missing data on the dose of abatacept and MTX. The observational unit in this study was a 1-year interval. Patients were divided into two groups according to whether the dose of abatacept was de-escalated or not compared with the preceding interval (tapering group vs. control group). The primary outcome of the study was DAS28-ESR-based remission in the 1-year interval. To minimize confounding by indication between the two groups, we used the marginal structural model in which inverse probability of treatment weights (IPTWs) for each interval was applied to control all baseline and time-varying confounders.

Table. Effect of tapering abatacept on disease activity with and without concomitant MTX treatment

Table. Effect of tapering abatacept on disease activity with and without concomitant MTX treatment

	OR (vs. control group)	95% CI	P for interaction
DAS28-remission			0.002
Without concomitant MTX	0.26	0.10 to 0.67	
With concomitant MTX	1.42	0.88 to 2.30	
DAS28-LDA			0.003
Without concomitant MTX	0.20	0.07 to 0.55	
With concomitant MTX	1.06	0.75 to 1.50	
Severe disability (HAQ > 2)			0.045
Without concomitant MTX	4.27	0.86 to 21.32	
With concomitant MTX	0.56	0.18 to 1.80	
SDAI-remission			0.446
Without concomitant MTX	0.50	0.15 to 1.62	
With concomitant MTX	0.85	0.46 to 1.57	

DAS, Disease activity score; HAQ, Health Assessment Questionnaire; LDA, Low disease activity; MTX, Methotrexate; OR, Odds ratio; SDAI, Simple Disease Activity Index

Results: A total of 505 intervals from 179 patients were analyzed. The mean (SD) age of the patients was 59.3 (12.9) years and 150 (83.8%) were females. Baseline DAS28-ESR was 5.7 (1.0) and the mean (SD) weekly dose of MTX was 12.5 (3.3) mg. Tapering abatacept was undergone in 146 (28.9%) intervals, with a mean dose quotient of 0.68. The DAS28-ESR measured in the interval before tapering abatacept was 3.4 (1.3) and DAS28 remission was achieved in only 51 (34.9%) intervals before tapering abatacept.

In the IPTW-applied pseudopopulation, the effect of tapering abatacept was significantly different based on concomitant use of MTX (P for interaction 0.002). In the subgroup of 1-year intervals without concomitant MTX, tapering abatacept significantly lower the odds for achieving DAS28-based remission, with an OR of 0.26 (95% CI 0.10 to 0.67). In contrast, with concomitant MTX, tapering abatacept did not have any significant effect (OR 1.42 [0.88 to 2.30]). This result was consistent when the effect of tapering abatacept was estimated using the outcome variable of achieving DAS28-low disease activity, or severe functional impairment (defined as HAQ >2). However, tapering abatacept with/without MTX did not significantly affect the odds for achieving SDAI-based remission (Table).

Conclusion: Tapering abatacept in the absence of concomitant MTX treatment is associated with a worse outcome in patients with RA.

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Abstract Number: 2543

Clinical and Radiographic Results of Tapering and Withdrawing CsDMARDs versus Stable Treatment in Patients with Rheumatoid Arthritis in Remission: 3-year Results from a Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

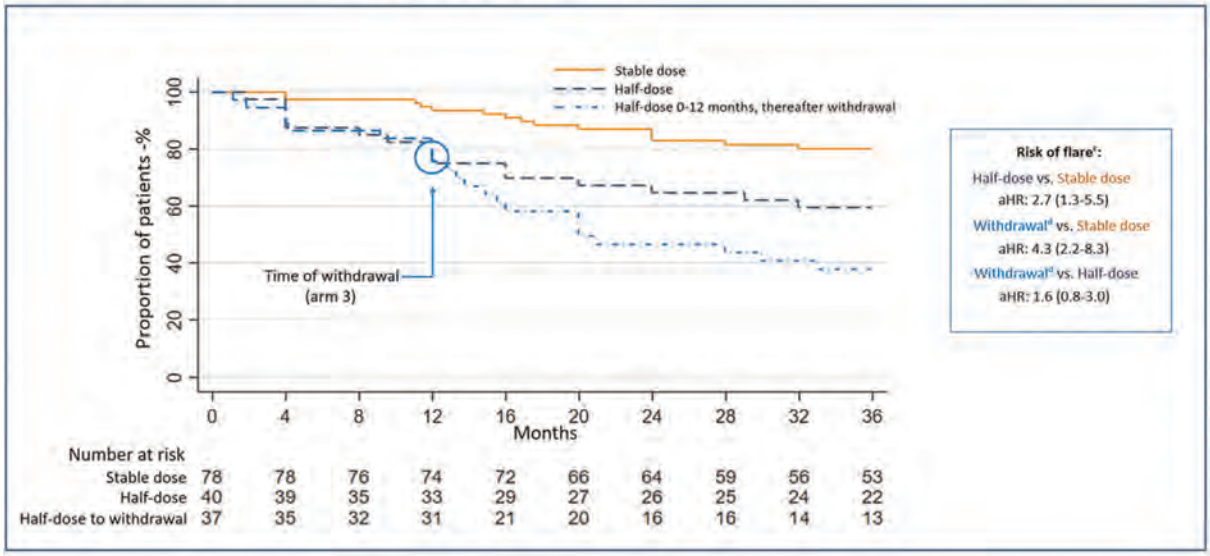
Session Title: Abstracts: RA – Treatments III: Predictors of Response & Tapering

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Tapering of disease-modifying antirheumatic drugs (DMARDs) to achieve drug-free remission is a potential goal for the growing group of patients with rheumatoid arthritis (RA) in remission, although long-term effects of such strategies remain unclear. The purpose of this study was to compare the 3-year clinical and radiographic outcomes of three conventional synthetic DMARD (csDMARD) treatment strategies (continued stable treatment, half-dose treatment and tapering to withdrawal) among patients in sustained RA remission.

Figure 1: Proportions of patients without a flare[a] over the study period[b]



[a] Flare was defined as a combination of Disease Activity Score (DAS) above the cut-off for remission (1.6), a change in DAS of at least 0.6, and at least 2 swollen joints, or that both the treating physician and the patient agreed that a clinically significant flare had occurred.
[b] The analyses were performed in a per protocol population (all randomized patients meeting the study entry criteria were included in the analysis up until the date of a major protocol violation (nine patients) or censored when lost to follow-up (eight patients)).
[c] The risk of flare was analyzed by Cox Proportional Hazard Regression, adjusted for study centre.
[d] Half-dose 0-12 months, thereafter withdrawal.

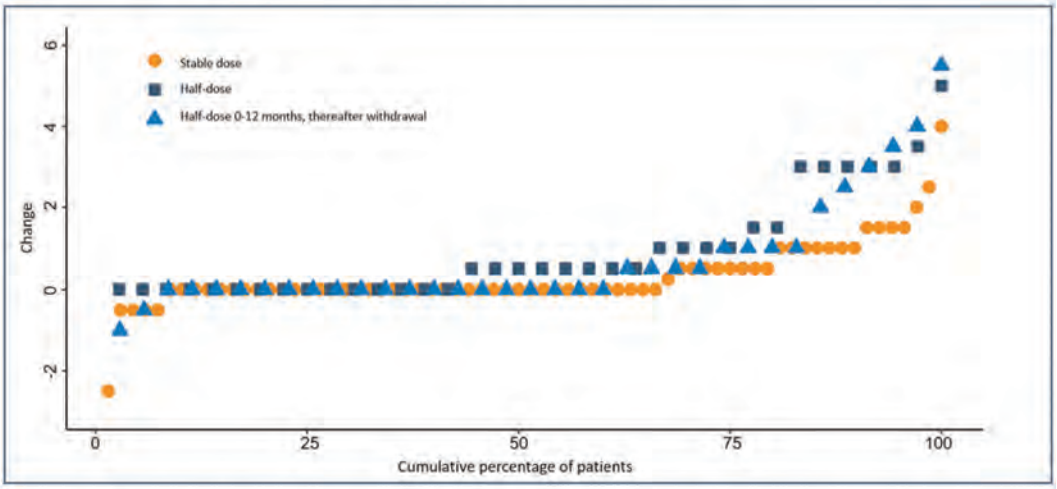
Methods: ARCTIC REWIND was a randomized, multicenter, open-label, clinical trial enrolling 160 RA patients in sustained remission for ≥1 year on stable csDMARD therapy (Lillegraven et al. JAMA 2021). Patients were randomized 2:1:1 to stable csDMARDs, half-dose csDMARDs, or half-dose csDMARDs for one year followed by withdrawal of all csDMARDs. The primary endpoint was absence of disease activity flare over 3 years. A flare was defined as a combination of DAS >1.6, an

Table: Remission at 12, 24 and 36 months[a]

	Remission, No./total No. (%)[b]				Absolute Risk Difference, % (95 % CI)[c]		
	Stable dose	Half-dose	Half-dose 0-12 months, thereafter withdrawal		Half-dose vs stable dose[d]	Half-dose 0-12 months, thereafter withdrawal vs stable dose[d]	Half-dose 0-12 months, thereafter withdrawal vs half- dose[d]
DAS remission				**DAS remission**			
12 months	71/77 (92%)	34/39 (87%)	29/36 (81%)	12 months[e]	-8.5 (-18.7-1.5)	NA	NA
24 months	64/73 (88%)	33/37 (89%)	33/35 (94%)	24 months	1.2 (-11.1-13.6)	6.0 (-5.0-17.0)	4.7 (-8.0-17.5)
36 months	64/67 (96%)	34/36 (94%)	31/34 (91%)	36 months	1.2 (-10.2-7.7)	-4.7 (-15.5-6.0)	-3.5 (-15.7-8.6)
ACR/EULAR 2011 Boolean remission				**ACR/EULAR 2011 Boolean remission**			
12 months	56/77 (73%)	25/39 (64%)	22/36 (61%)	12 months[e]	-11.3 (-26.2-3.5)	NA	NA
24 months	47/73 (64%)	21/37 (57%)	20/35 (57%)	24 months	-7.8 (-27.2-11.6)	-6.3 (-26.2-12.6)	1.0 (-21.5-23.4)
36 months	55/67 (82%)	25/36 (69%)	19/34 (56%)	36 months	-12.1 (-30.2-6.0)	-25.3 (-44.8—6.3)	-13.3 (-35.4-8.9)

[a] The analyses were performed in a per protocol population (all randomized patients meeting the study entry criteria were included in the analysis up until the date of a major protocol violation (nine patients in total). Furthermore, eight patients were lost to follow-up (one patient was lost to follow-up before 12 months, four patients were lost to follow-up before 24 months, and three patients were lost to follow-up before 36 months)).
[b] Crude remission rate.
[c] Absolute risk difference, calculated with mixed-effect logistic regression with random effects for both patient and study centre, in latter to account for the centre stratification.
[d] Reference group.
[e] The two groups using half-dose for the first year pooled in this analysis.
Abbreviation NA: Not applicable (same treatment the first 12 months).

Figure 2: Change in van der Heijde-modified Sharp score[a] at 36 months compared to baseline[b]



[a]The van der Heijde–modified Sharp scoring method assesses erosions in 16 joints of each hand and 6 joints of each foot, and the erosions are given a score of 1 to 5. Joint space narrowing is assessed in 15 joints for each hand and 6 joints for each foot. This gives scores for erosions on a scale from 0 to 280 and joint space narrowing on a scale from 0 to 168, thus the total van der Heijde–modified Sharp score ranges from 0 to 448, with higher scores indicating greater joint damage.
[b]The analyses were performed in a per protocol population (all randomized patients meeting the study entry criteria were included in the analysis up until the date of a major protocol violation (nine patients) or censored when lost to follow-up (eight patients)).

increase in DAS ≥0.6 units and ≥2 swollen joints, or if the physician and patient agreed that a clinically significant flare had occurred. Full-dose csDMARD treatment was reinstated upon flare. Secondary endpoints included remission (DAS, ACR/EULAR Boolean), and the 3-year change in radiographic joint damage (van der Heijde-Sharp score, vdHSS). Data were analyzed using Kaplan-Meier, Mann-Whitney test, Cox and mixed effect logistic regression, with stratification or adjustment for study center.

Results: Of 156 patients who received the allocated treatment strategy, 139 patients completed 3-years follow-up without major protocol violation. Mean baseline methotrexate dose/week was 19.0 mg in the stable group, 19.7 mg in the half-dose group, and 19.5 mg in the withdrawal group, and mean DAS at baseline was 0.8 in all groups. 80 % remained flare-free in the stable group, compared with 60 % in the half-dose group (adjusted HR (aHR) for flare 2.7 (95% CI: 1.3 to 5.5)), and 38 % in the tapering to withdrawal group (aHR for flare 4.3 (2.2 to 8.3)) (Figure 1). The aHR was 1.6 (0.8 to 3.0) in the tapering to withdrawal group compared to the half-dose group. A majority were in remission at 1, 2 and 3 years (Table), with the only significant group difference for ACR/EULAR Boolean remission at 3 years, with risk difference for tapering to withdrawal vs stable dose -25% (-45 to -6). Median (IQR) change in vdHSS after 3 years was 0.0 (0-0.5) in the stable group, 0.5 (0.0-1.3) in the half-dose group, and 0.0 (0.0-1.0) in the tapering to withdrawal group (Figure 2), with statistical significant difference between stable and half-dose group, $p< 0.01$. Sensitivity analyses in the full analysis population gave similar results.

Conclusion: These 3-year data show that 38% of patients in the tapering to withdrawal arm achieved long-term drug-free remission, indicating that this is a realistic option for some RA patients in sustained remission. The two tapering strategies were associated with an increased risk of flares compared to full-dose csDMARD, and the half-dose group had more radiographic change. However, there were no differences in DAS-remission at the end of the study period. Further research identifying prognostic factors for successful tapering is needed.

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5, Galapagos, 2, 5, Gilead, 2, grunenthal, 6, Janssen, 2, 6, Novartis, 5, Pfizer, 2, 5, sandoz, 2, 6, UCB, 2, 5, 6; **D. Solomon**: CorEvitas, 5, Janssen, 5, Moderna, 5, Novartis, 5; **D. van der Heijde**: AbbVie, 2, Bayer, 2, BMS, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GSK, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; **E. Haavardsholm**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Eli Lilly, 2, Gilead, 2, Pfizer, 6, UCB, 6; **S. Lillegraven**: Boehringer-Ingelheim, 5.

Abstract Number: 2544

Microbial Metabolism of Methotrexate Contributes to Its Pharmacokinetics in Vivo

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: RA – Treatments III: Predictors of Response & Tapering
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Methotrexate (MTX) is a first-line treatment drug used in rheumatoid arthritis (RA) patients. However, only 30-40% of patients tolerate the drug and achieve adequate therapeutic effects[1]. Risk factors such as smoking, age, and disease severity are associated with MTX non-responsiveness in patients[2]. Yet, these risk factors are limited in their ability to predict MTX non-responsiveness, and many of them are not modifiable. One hypothesis, pursued by our lab, is that the gut microbiome metabolizes MTX and interferes with its efficacy. This is significant because the gut microbiome can be both predictive and modifiable, and therefore can be leveraged to improve MTX efficacy and advance personalized medicine for patients with RA. In support of this hypothesis, we have previously shown that specific bacterial taxa and the abundance of bacterial genes are predictive of future MTX outcomes in RA patients[3].Yet, it remains to be seen whether the gut microbial community can directly affect MTX pharmacology and which microbes are responsible for MTX metabolism. Here, we examined the causal impact of the microbiome on MTX pharmacokinetics and surveyed the spectrum of RA-associated gut microbes that metabolize MTX.

Methods: To test the contribution of microbial metabolism of in MTX pharmacology *in vivo*, we orally dosed germ-free (GF) mice and specific-pathogen free mice (SPF) (N=6 per colonization state) with MTX 50 mg/kg. Plasma was collected at 0, 15, 30, 60, 120, 240, and 480 minutes; the concentration of MTX and its metabolites were quantified by HPLC-MS-MS (Sciex 6500 QTRAP). To survey the spectrum of RA-associated gut microbes that metabolize MTX, we collected stool samples from treatment-naïve RA patients (N= 5) and isolated individual strains on rich media. Each isolate was incubated with MTX 50 ug/mL or vehicle control (i.e., DMSO) for 72 hours and bacterial growth was measured by spectrometry (i.e., OD600). MTX metabolism was assessed by HPLC by: (1) quantifying a decrease in MTX levels and (2) detection of novel peaks.

Results: Peak plasma concentrations of MTX were significantly higher in GF mice as compared to SPF mice. In contrast, plasma concentrations of MTX metabolites were negligible in GF mice, whereas SPF mice showed increasing levels of MTX metabolites over 4 hours. To determine which RA-associated microbes might be responsible for MTX metabolism, we harvested 120 bacterial isolates from 5 RA patients. Of the profiled 120 isolates, 30.83% of isolates (37/120) metabolized MTX.

Conclusion: The presence of a microbiome in mice results metabolism of orally-administered MTX *in vivo* leading to altered pharmacokinetics. Furthermore, a significant percentage of isolates harvested from RA patient microbial communities are capable of metabolizing MTX *in vitro*. These findings support the overarching hypothesis that the gut microbiome contributes to MTX efficacy in RA patients.

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Abstract Number: 2545

Efficacy and Safety of Intravenous Secukinumab for the Treatment of Active Axial Spondyloarthritis: Results from a Randomized, Double-Blind, Phase 3 Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment III: AxSpA

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: While subcutaneous secukinumab (SEC) is approved for the treatment of axial spondyloarthritis (axSpA), some patients may benefit more from intravenous (IV) administration. This study investigated the long-term efficacy, safety, and tolerability of IV SEC in patients with active axSpA.

Methods: INVIGORATE-1 (NCT04156620) is a randomized, double blind, parallel group, phase 3 trial of patients with active axSpA (either radiographic [r]-axSpA or nonradiographic [nr]-axSpA). All patients had inflammatory back pain (ASAS criteria) for ≥6 months with onset before 45 years of age. Patients with r-axSpA fulfilled the modified New York criteria, and patients with nr-axSpA met ASAS criteria and had objective signs of inflammation at screening (positive MRI and/or elevated high-

Table 1. Patient demographics and baseline disease characteristics.

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Characteristic	Secukinumab (n=264)	Placebo/Secukinumab (n=262)
Age, mean (SD), years	39.8 (12.4)	39.1 (11.7)
Male, n (%)	165 (62.5)	178 (67.9)
Weight, mean (SD), kg	77.6 (18.0)	78.1 (18.4)
No previous TNFi exposure, n (%)	233 (88.3)	216 (82.4)
Time since axSpA diagnosis, mean (SD), years	5.5 (7.7)	4.6 (6.1)
Abnormal hsCRP, n (%)*	125 (47.3)	129 (49.2)
HLA-B27 positive, n (%)	210 (79.5)	215 (82.1)

* hsCRP ≥5 mg/L for nr-axSpA or ≥10 mg/L for r-axSpA.
AxSpA, axial spondyloarthritis; HLA-B27, human leukocyte antigen B27; hsCRP, high-sensitivity C-reactive protein; TNFi, tumor necrosis factor inhibitor.

sensitivity C-reactive protein (≥5 mg/L for nr-axSpA; ≥10 mg/L for r-axSpA). Patients were randomized 1:1 to receive IV SEC (6 mg/kg at baseline followed by 3 mg/kg every 4 weeks) or placebo (PBO) for 16 weeks. After Week 16, patients randomized to PBO were switched to IV SEC (3 mg/kg every 4 weeks), while patients randomized to SEC continued receiving IV SEC through Week 52. The primary endpoint was ASAS40 response at Week 16. Efficacy was assessed through Week 52 by the proportion of patients achieving ASAS40 response, ASDAS-CRP major improvement, and ASAS5/6 response, and by change from baseline in BASDAI, BASFI, and SF-36 PCS. Safety was evaluated through Week 60. Efficacy data through Week 16 are reported using nonresponder imputation; efficacy data from Week 20 through Week 52 are reported as observed.

Results: Demographics and baseline characteristics were balanced across treatment groups (**Table 1**). Among patients randomized to IV SEC (n=264) or PBO/IV SEC (n=262), 86.0% and 88.9% completed the entire study period, respectively. A total of 413 patients had r-axSpA and 113 patients had nr-axSpA. SEC treatment resulted in rapid and sustained improvement in ASAS40 response rates in patients randomized to SEC (**Figure 1**). By Week 24, patients who switched from PBO to SEC at Week 16 achieved comparable ASAS40 response rates to those of patients originally randomized to SEC. ASAS40 responses were maintained through Week 52 for both groups (SEC, 66.8%; PBO/IV SEC, 74.9% [observed data]). SEC treatment also resulted in rapid improvements in all other efficacy measures that were maintained through Week 52 (**Table 2**). Through Week 16, the incidences of adverse events (AEs; 38.6% vs 39.1%), serious AEs (2.7% vs 1.1%), and AEs leading to

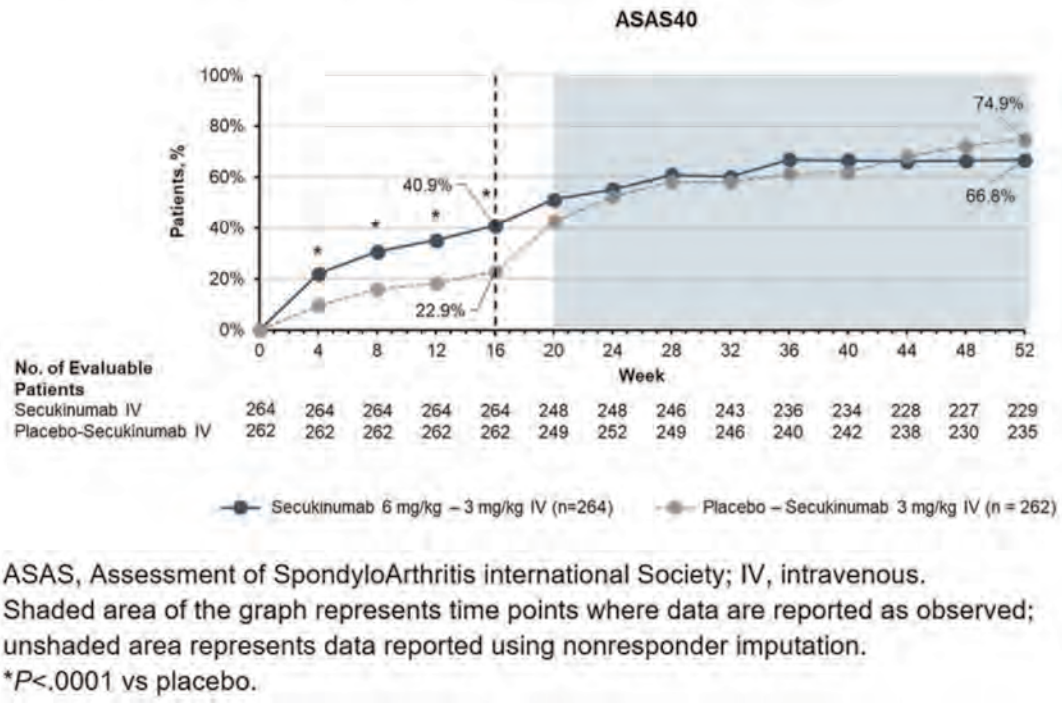
Table 2. Achievement of efficacy responses and improvements in disease measures from baseline at Week 52 (observed data).

Table 2. Achievement of efficacy responses and improvements in disease measures from baseline at Week 52 (observed data)

Efficacy measure	Secukinumab (n=264)	Placebo/Secukinumab (n=262)
Binary measures, n/M (%)		
ASAS40 response	153/229 (66.8)	176/235 (74.9)
ASDAS-CRP major improvement	97/224 (43.3)	117/223 (52.5)
ASAS5/6 response	143/224 (63.8)	147/223 (65.9)
ASAS20 response	187/229 (81.7)	197/235 (83.8)
ASDAS-CRP inactive disease	77/224 (34.4)	69/223 (30.9)
ASAS partial remission	74/229 (32.3)	75/235 (31.9)
Continuous measures, mean change from baseline (SD)		
BASDAI	-4.03 (2.30)	-4.22 (2.34)
BASFI	-3.65 (2.49)	-3.67 (2.52)
SF-36 PCS	10.13 (7.60)	9.70 (8.27)
ASQoL	-6.16 (5.06)	-6.22 (5.03)
hsCRP	-10.00 (21.01)	-9.38 (15.49)
PSQI	-3.2 (3.8)	-3.3 (3.6)

ASAS, Assessment of SpondyloArthritis international Society; ASDAS, Ankylosing Spondylitis Disease Activity Score; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score with CRP; ASQoL, Ankylosing Spondylitis Quality of Life Questionnaire; BASDAI, Bath Ankylosing Spondylitis Disease Activity Score; BASFI, Bath Ankylosing Spondylitis Functional Index; n/M, number of patients who achieved binary efficacy measure/number of evaluable patients; PSQI, Pittsburgh Sleep Quality Index; SF-36 PCS, Short Form 36 Physical Component Summary.

Figure 1. Proportions of patients with axSpA who achieved ASAS40 through Week 16 (nonresponder imputation) and through Week 52 (observed data)



ASAS, Assessment of SpondyloArthritis international Society; IV, intravenous.
Shaded area of the graph represents time points where data are reported as observed; unshaded area represents data reported using nonresponder imputation.
*P<.0001 vs placebo.

Figure 1. Proportions of patients with axSpA who achieved ASAS40 through Week 16 (nonresponder imputation) and through Week 52 (observed data).

treatment discontinuation (1.9% vs 0.4%) were similar for patients receiving SEC or PBO, respectively. Among patients receiving any IV SEC through the entire study period, 63.2%, 6.0%, and 3.5% reported any AE, serious AEs, and AEs leading to treatment discontinuation, respectively. One death occurred during SEC treatment due to a suspected myocardial infarction and was deemed not related to treatment.

Conclusion: IV SEC was safe and effective for treatment of adults with active axSpA over 52 weeks. The safety profile of IV SEC for patients with axSpA was consistent with that of previous reports for subcutaneous SEC, and no new safety signals were observed.

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Abstract Number: 2546

Anti-infliximab Antibodies as a Marker of Drug Survival and Tapering in Ankylosing Spondylitis Patients: 12 Years Follow-up

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SESSION INFORMATION
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Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Tumor necrosis factor inhibitors (TNFi) therapies were one of the major advances in the treatment of Ankylosing Spondylitis (AS) patients. For infliximab, anti-drug antibodies (ADA) seem to contribute to drug failure but it is not known its long term influence on tapering, drug survival and switching. We aim to evaluate the frequency and long-term kinetics of anti-infliximab antibodies (anti-IFX) and its influence on drug survival, treatment failure, infusion reaction, tapering strategy and in subsequent treatment with a second TNFi.

Methods: A prospective cohort of 60 AS patients under infliximab (IFX) as their first biological therapy were evaluated retrospectively regarding clinical and laboratorial data, IFX levels and anti-IFX, both by ELISA, at baseline and after 6, 12-14, 22-24, 48-54, 96-102 weeks and immediately before the switching, treatment withdrawal or the end of the study. The switching group (to another TNFi), were further evaluated after 3 and 6 months. For the tapering group, additional clinical and laboratory data were assessed before tapering strategy and at tapering failure or withdrawal of the drug. Biological agent and anti-IFX antibodies quantification was performed according to the manufacturer's protocol of the kits (Promonitor® IFX and Promonitor ®anti-IFX).

Results: Anti-IFX were detected in 27 (45%) patients during follow-up and 85.1% in the first year. The concomitant use of methotrexate was negatively associated with anti-IFX (5.0 [18.5%] vs. 14.0 [42.4%]; p=0.048). Infusion reactions were more often observed in positive anti-IFX patients at 22-24 weeks (3.0 [21.4%] vs. 1.0 [2.2%]; p=0.020) and at 48-54 weeks (3 [20.0%] vs. 0 [0.0%]; p=0.034). Anti-IFX at 48-54 weeks was associated with treatment failure (7.0 [46.7%] vs. 4.0 [13.8%]; p=0.028) and lower overall IFX survival (54.9 months [CI 95% 26.3-83.4] vs. 148.9 months [CI 95% 123.5-174.4]; p< 0.001). Of note, for the tapering group (n=24) anti-IFX was associated with shorter survival of this strategy (9.9 months [IC 95% 4.0-15.8] vs 63.4 months [IC 95% 27.9-98.8]; p=0.004). In contrast, for patients who failed to IFX (n=29), anti-IFX positivity at the switching was related to a better clinical response to the second TNFi at 3 months (15.0 [83.3%] vs. 3.0 [27.3%]; p=0.005) and at 6 months (15 [83.3%] vs. 4 [36.4%]; p=0.017).

Conclusion: This study demonstrates that in spite of anti-IFX association with worse IFX performance, this marker was a predictor of 2nd TNFi good clinical response. We also provided novel data that anti-IFX is a parameter for reduced tapering survival, reinforcing its detection to guide clinical decision in these two treatment strategies. Additionally, concomitant use of methotrexate (MTX) may be recommended to reduce anti-IFX formation in AS.

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Abstract Number: 2547

Characteristics of Difficult-To-Treat Axial Spondyloarthritis: Results of a Multicentric Retrospective Study

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SESSION INFORMATION

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Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment III: AxSpA

Session Type: Abstract Session

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Background/Purpose: The EULAR task force recently published the difficult-to-treat (D2T) RA definition[1], however, a definition of D2T axSpA is still lacking. To date, we have little data concerning D2T axSpA, especially in real-world. One of the limitations of the D2T RA EULAR definition is the lack of a temporal criterion. The primary endpoint of this work was to study

Table 1 – Baseline characteristics of D2T axSpA and nD2T axSpA patients

Parameters	N	D2T axSpA n = 88	N	nD2T axSpA n = 223	p value
Men	88	44 (50.0)	223	126 (56.5)	0.30
Age (years), mean ± SD	88	47.6 ± 12.5	223	46.4 ± 13.1	0.45
BMI, mean ± SD	88	27,0 ± 6,1	223	26,3 ± 5,5	0.41
axSpA duration (years), median (IQR)		9 (7 to 17)		8 (5 to 13)	**0.006**
Current smoker status	59	24 (40.7)	121	57 (47.1)	0.42
Clinical axSpA characteristics at baseline					
Enthesitis spondyloarthritis	66	14 (21.2)	207	33 (15.9)	0.32
Peripheral spondyloarthritis	86	30 (34.9)	215	46 (21.4)	**0.015**
Dactylitis	83	4 (4.8)	184	11 (6.0)	1.00
Psoriasis	81	17 (21.0)	208	43 (20.7)	0.88
r-axSpA	73	52 (71.2)	179	108 (60.3)	0.10
IBD	86	5 (5.8)	191	6 (3.1)	0.32
Positive HLA B27 status	78	58 (74.4)	190	131 (68.9)	0.38
Baseline CRP (mg/L), median (IQR)	78	11.1 (3.0 to 25.7)	168	12.4 (4.6 to 22.8)	0.78
BASDAI Baseline, mean ± SD	80	63.7 ± 16.5	163	58.8 ± 14.7	**0.015**
Charlson score					0.96
0	87	53 (60.9)	199	118 (59.3)	
1	87	14 (16.1)	199	34 (17.1)	
≥2	87	19 (23.0)	199	47 (23.6)	
Previous treatments					
Infliximab		40 (45.5)		26 (11.7)	<0.001
Etanercept		59 (67.0)		86 (38.6)	<0.001
Adalimumab		69 (78.4)		134 (60.1)	0.002
Golimumab		35 (39.8)		84 (37.7)	0.73
Certolizumab		41 (46.6)		43 (19.3)	<0.001
Secukinumab		79 (89.8)		62 (27.8)	<0.001
Ixekizumab		12 (13.6)		1 (0.4)	<0.001
JAKi		7 (8.0)		2 (0.9)	0.003
Main comorbidities					
Diabetes mellitus	86	3 (3.5)	198	7 (3.5)	1.00
Hypertension	86	10 (11.6)	198	29 (14.6)	0.50
Fibromyalgia	86	15 (17.4)	198	8 (4.0)	**<0.001**

Values are expressed as number (%) unless otherwise stated. axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; bDMARD: biological disease modifying antirheumatic drug; BMI: body mass index; CRP: C-reactive protein; (n)D2T: (non) difficult-to-treat; HLA: human leukocyte antigen; IBD: inflammatory bowel disease; IQR: interquartile range; JAKi: Janus Kinase inhibitors; N: number of available observations; NA: not applicable; SD: standard deviation;

the characteristics of D2T axSpA patients using the EULAR definition applied to axSpA. The second endpoint was to study a sub-group of patients with a predefined more stringent definition including a temporal criterion.

Methods: A retrospective multicentric study was performed. Patients with axSpA (radiographic or non-radiographic) ≥18 years old starting a b/tsDMARDs with at least 2-year follow-up were included. D2T axSpA was defined as failure of ≥ 2 b/tsDMARDs with different mechanism of action (MoA) among TNF inhibitors, IL-17 inhibitors and JAK inhibitors. Very D2T axSpA was defined as failure of ≥ 2 b/tsDMARDs in strictly less than 2 years. D2T and Very D2T axSpA patient's characteristics were compared with non-D2T patients.

Results: 311 axSpA patients were included: 88 D2T axSpA (28.3%) and 223 non-D2T (nD2T) axSpA (71.7%) (**Table 1**). Proportion of r-axSpA patients was 71.2% in the D2T group and 60.3% in the nD2T group (p=0.10). Disease duration was significantly higher in the D2T group (p=0.006). Peripheral involvement was more prevalent in the D2T group with 34.9% of patients vs. 21.4% in the nD2T group (p=0.015). BASDAI level at baseline was higher in the D2T group with a mean of 63.7 vs 58.8 in the nD2T group (p=0.015). Fibromyalgia was found to be more frequent in the D2T group vs nD2T group (p < 0.001). Among D2T patients, 12 (14%) presented a contraindication to TNF or IL-17 inhibitors (multiple sclerosis, inflammatory bowel diseases, recurrent uveitis, solid cancer < 5 years).

12 patients (3.8%) were categorized as very D2T axSpA. axSpA patient's characteristics were compared between the three groups (Very D2T, remaining D2T and nD2T) and in case of significant result, pairwise comparisons were performed (**-Table 2**). When compared to nD2T, Very D2T patients had a higher CRP level at baseline (42.0 ± 31.3 *vs* 17.8 ± 23.1; p=0.010). Inflammatory bowel disease (IBD) prevalence at baseline was higher in the Very D2T group with 41.7% vs 3.1% in the nD2T group (p< 0.001). Uveitis at baseline was more frequent (45.5% vs 11%; p=0.020). None of the Very D2T patients had a diagnosis of fibromyalgia.

Table 2 – Characteristics of Very D2T axSpA, remaining D2T axSpA and nD2T patients: comparison two-by-two

Parameters	*3 groups comparison* *p* value	*Very D2T vs nD2T* *p* value	*Very D2T vs rD2T* *p* value	*rD2T vs nD2T* *p* value
axSpA duration (years)	**0.016**	0.15	0.59	**0.045**
Peripheral spondyloarthritis	**0.042**	0.80	1.00	0.066
Uveitis	**0.007**	**0.020**	0.15	0.45
IBD	**<0.001**	**<0.001**	**<0.001**	0.57
Baseline CRP	**0.006**	**0.010**	**0.013**	0.413
Fibromyalgia	**<0.001**	1.00	0.35	**<0.001**

axSpA: axial spondyloarthritis; CRP: C-reactive protein; IBD: inflammatory bowel disease; rD2T: remaining difficult-to-treat (total D2T population minus patients categorized as Very D2T)

Definition of Difficult-to-treat axSpA. 3 criteria needed.

- Failure of treatments according to either of the following options:
  - ≥ 2 b/tsDMARDs with different mechanisms of action within less than 2 years

Or

  - ≥ 1 b/tsDMARDs within less than 2 years and a contra-indication to one therapeutic class *(i.e. contra-indication to TNF inhibitors (multiple sclerosis, severe heart insufficiency).*

- Suggestive evidence of disease activity/progression, defined as ≥ 1 of the following:
  - o At least moderate activity (ASDAS-CRP 1.3 or BASDAI 4/10),
  - o Signs (including biology and imaging) and/or symptoms suggestive of active disease (articular or extra rheumatological: uveitis, psoriasis, inflammatory bowel disease),
  - o Inability to reduce or discontinue NSAIDs,
  - o Disease controlled, but with persistent ax-SpA symptoms causing reduced quality of life,
- Management of signs and/or symptoms is perceived as problematic by the rheumatologist and/or patient.

Figure 1 - Proposal of D2T axSpA definition

Conclusion: D2T axSpA was associated with a longer disease duration, higher BASDAI at baseline, higher prevalence of peripheral involvement and more frequent fibromyalgia. Very D2T patients represented a minim proportion of patients after applying a more stringent definition and might be independent from fibromyalgia, with higher CRP level at baseline and higher prevalence of IBD and uveitis. This study highlights some characteristics that may help practitioners better identify D2T axSpA patients. Pending a consensual definition by the European and American societies, we propose a definition of D2T axSpA (**Figure 1**).

[1] Nagy G *et al*. EULAR definition of difficult-to-treat rheumatoid arthritis. *Ann Rheum Dis* 2021;**80**:31–5.

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Abstract Number: 2548

Low Uveitis Rates in Patients with Axial Spondyloarthritis Treated with Bimekizumab: Pooled Results from Phase 2b/3 Trials

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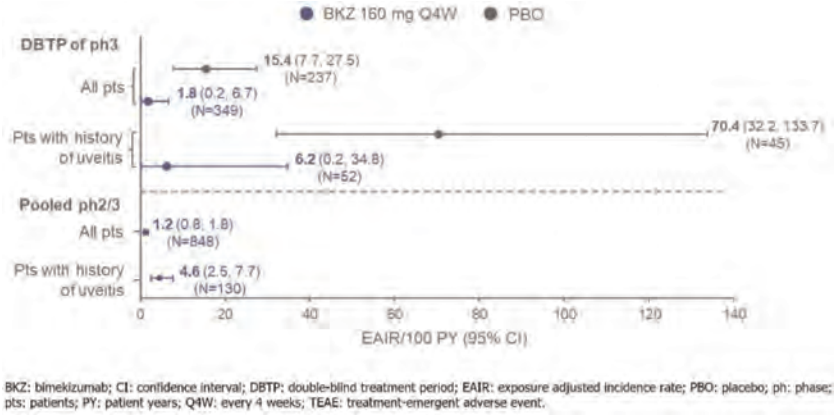
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Acute anterior uveitis (’uveitis’), or ’iritis’, is a common extra-musculoskeletal manifestation among patients (pts) with axial spondyloarthritis (axSpA).[1] IL-17 has been implicated in the pathogenesis of uveitis; however, inhibition of IL-17A alone may not be optimal for the management of uveitis.[2] Here, we report the incidence of uveitis following inhibition of IL-17A in addition to IL-17F with bimekizumab (BKZ) in pts with axSpA.

Methods: Data were pooled for pts randomized to BKZ or placebo (PBO) in the double-blind treatment period (DBTP) of the phase (ph)3 studies BE MOBILE 1 (NCT03928704; non-radiographic [nr]-axSpA) and 2 (NCT03928743; radiographic [r]-axSpA i.e., ankylosing spondylitis).[3,4] Data were pooled separately for all pts treated with BKZ 160mg every 4 weeks (Q4W) in BE MOBILE 1, BE MOBILE 2, BE MOVING (NCT04436640; open-label extension [OLE] of BE MOBILE 1 and 2), and the ph2b study BE AGILE (NCT02963506; r-axSpA)[5] and its OLE BE AGILE 2 (NCT03355573). Uveitis treatment-

emergent adverse events (TEAEs) were identified using the preferred terms "autoimmune uveitis", "iridocyclitis", "iritis", and "uveitis", and were reported as both incidence and exposure adjusted incidence rates (EAIRs) per 100 pt years (PY) for all pts who received ≥1 BKZ dose.

Results: Baseline characteristics were reflective of a pt population with moderate to severe axSpA (**Table**). In the DBTP of BE MOBILE 1 and 2, uveitis TEAEs occurred in 11/237 pts randomized to PBO (4.6%; EAIR/100 PY [95% CI]: 15.4 [7.7, 27.5]) and 2/349 (0.6%; 1.8 [0.2, 6.7]) pts randomized to BKZ (% difference [95% CI]: 4.07 [1.71, 7.60]); **Figure**). In the 45 PBO-randomized (19.0%) and 52 BKZ-randomized (14.9%) pts with history of uveitis, uveitis TEAEs occurred in 20.0% (EAIR/100 PY [95% CI]: 70.4 [32.2, 133.7]) and 1.9% (6.2 [0.2, 34.8]) of pts, respectively. In the pooled ph2b/3 trial data, total BKZ exposure was 2,034.4 PY (N=848); 130 (15.3%) pts had history of uveitis. Uveitis TEAEs occurred in 25 pts overall (2.9%; EAIR/100 PY [95% CI]: 1.2 [0.8, 1.8]) and 14 pts with history of uveitis (10.8%; 4.6 [2.5, 7.7]; **Figure**). All uveitis TEAEs were mild/moderate; one event led to discontinuation.



BKZ: bimekizumab; CI: confidence interval; DBTP: double-blind treatment period; EAIR: exposure adjusted incidence rate; PBO: placebo; ph: phase; pts: patients; PY: patient years; Q4W: every 4 weeks; TEAE: treatment-emergent adverse event.

Figure. Pooled incidence of uveitis TEAEs (EAIR/100 PY [95% CI]) stratified by history of uveitis in patients randomized to BKZ 160 mg Q4W or PBO in the DBTP (Weeks 0–16) of the phase 3 trials BE MOBILE 1 and 2, and all patients treated with BKZ 160 mg Q4W in phase 2b/3 trials.

Table. Baseline characteristics

	Pooled phase 3		Pooled phase 2b/3
	PBO (N=237)	BKZ 160 mg Q4W (N=349)	BKZ 160 mg Q4W (N=848)
Age (years), mean (SD)	38.8 (12.1)	40.0 (11.8)	40.3 (11.9)
Male, n (%)	145 (61.2)	233 (66.8)	606 (71.5)
HLA-B27 positive, n (%)	187 (78.9)	294 (84.2)	717 (84.6)[a]
Caucasian, n (%)	200 (84.4)	286 (81.9)	746 (88.0)
r-axSpA, n (%)	111 (46.8)	221 (63.3)	604 (71.2)
Time since first axSpA symptoms (years), mean (SD)	10.3 (8.9)	12.4 (10.5)	12.4 (9.9)
History of uveitis, n (%)	45 (19.0)	52 (14.9)	130 (15.3)
Baseline concomitant synthetic DMARDs, n (%)	51 (21.5)	77 (22.1)	197 (23.2)

[a] n=6 missing. axSpA: axial spondyloarthritis; BKZ: bimekizumab; HLA-B27: human leukocyte antigen B27; PBO: placebo; Q4W: every 4 weeks; r-axSpA: radiographic axSpA; SD: standard deviation.

Conclusion: The incidence rate of uveitis TEAEs was lower to Wk 16 in axSpA pts randomized to BKZ 160 mg Q4W vs PBO. In the largest pool of ph2b/3 data available at the time of this report, the incidence rate of uveitis with BKZ 160 mg Q4W remained low at 1.2/100 PY.

References: 1. Robinson PC. Arthritis Rheumatol. 2015;67(1):140–51; **2.** Dick AD. J Opthalmol 2013;120(4):777–87; **3.** Boel A. Ann Rheum Dis 2019;78:1545–9; **4.** Baraliakos X. Arthritis Rheumatol 2022;74 (suppl 9); **5.** van der Heijde D. Ann Rheum Dis 2020;79:595–604.

Disclosure: M. Rudwaleit: AbbVie, 2, 6, Boehringer Ingelheim, 6, Chugai, 6, Eli Lilly, 2, 6, Janssen, 6, Novartis, 2, 6, Pfizer, 6, UCB Pharma, 2, 6; **M. Brown**: Clementia, 2, Grey Wolf Therapeutics, 2, Incyte, 2, Ipsen, 2, Novartis, 6, Pfizer, 2, Regeneron, 2, UCB Pharma, 5, Xinthera, 2; **F. Van Gaalen**: AbbVie, 12, Personal fees, BMS, 12, Personal fees, Eli Lilly, 12, Personal fees, Jacobus Stichting, 5, MSD, 12, Personal fees, Novartis, 5, 12, Fees, Stichting ASAS, 5, Stichting Vrienden van Sole Mio, 5, UCB Pharma, 5; **N. Haroon**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, UCB Pharma, 2; **L. Gensler**: AbbVie, 2, Acelyrin, 2, Eli Lilly, 2, Fresenius Kabi, 2, Janssen, 2, Novartis, 2, 5, Pfizer, 2, UCB Pharma, 2, 5; **C. Fleurinck**: UCB Pharma, 3; **A. Marten**: UCB Pharma, 3; **U. Massow**: UCB Pharma, 3; **N. De Peyrecave**: UCB Pharma, 3; **T. Vaux**: UCB Pharma, 3; **K. White**: UCB Pharma, 3, 12, Shareholder; **A. Deodhar**: AbbVie, 2, 5, Amgen, 2, Aurinia, 2, Bristol Myers Squibb, 2, 5, Celgene, 5, Eli Lilly, 2, 5, Janssen, 2, 6, MoonLake, 2, 5, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5; **I. van der Horst-Bruinsma**: AbbVie, 2, 5, 12, Fees for lectures, BMS, 12, Fees for lectures, Eli Lilly, 2, MSD, 2, 5, 12, Fees for lectures, Novartis, 2, Pfizer, 5, UCB Pharma, 2, 5.

Abstract Number: 2549

Effect of Ixekizumab Treatment on MRI Structural Lesions in the Sacroiliac Joints of Patients with Radiographic Axial Spondyloarthritis; A Post-hoc Analysis of a Placebo and Active Controlled RCT

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment III: AxSpA
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: The effect of Ixekizumab (IXE) on structural lesions in the sacroiliac joints (SIJ) of patients (pts) with radiographic Axial Spondylarthritis (r-axSpA) assessed by magnetic resonance imaging (MRI) has not been analyzed. This analysis evaluated the effect of IXE versus placebo and active control, adalimumab (ADA), on structural lesions in SIJ assessed by MRI at week 16 in bio-naïve pts with r-axSpA.

Methods: COAST V (NCT02696785) is a phase 3, multicenter, randomized, double blind, placebo and active controlled study in bio-naïve adult pts (≥18 years) with active r-axSpA (1). Pts were randomly assigned 1:1:1:1 to placebo (PBO), 80 mg subcutaneous IXE, every 2 weeks (IXE Q2W) or 4 weeks (IXE Q4W), or 40 mg ADA Q2W (active reference group). Post-hoc analyses of pts with MRI available at baseline (BL) and week 16 for PBO, IXE Q2W, IXE Q4W and ADA groups are reported. Changes in MRI structural lesions were scored using the Spondyloarthritis Research Consortium of Canada

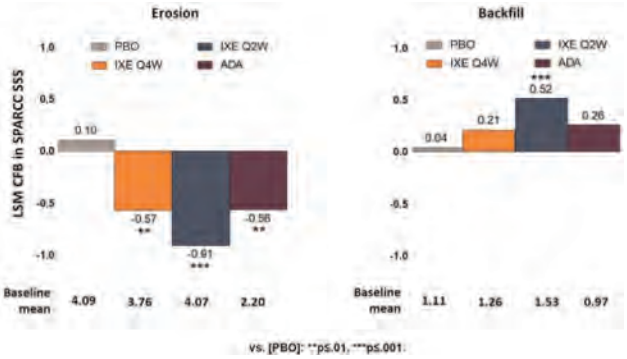

Figure 1: SPARCC SSS LSM Change from Baseline to Week 16

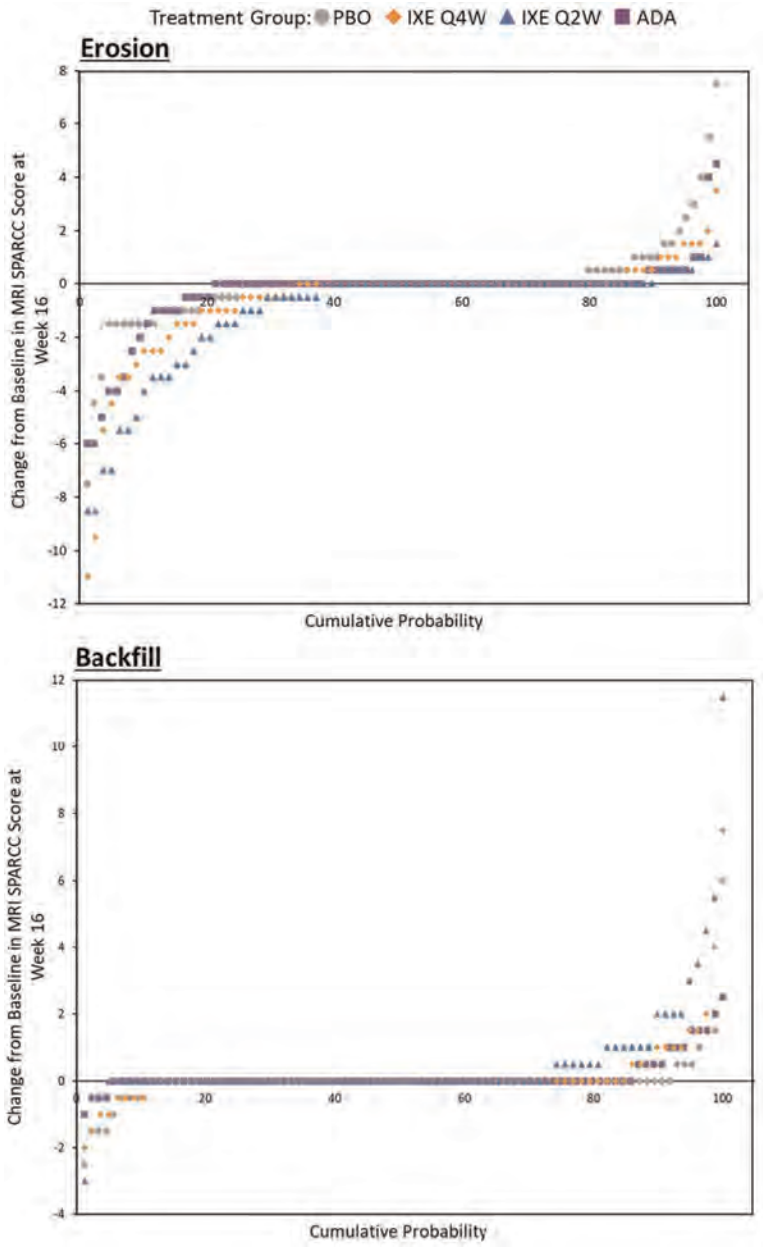

Figure 2: Cumulative Probability of Change from Baseline to Week 16 in SPARCC SSS

(SPARCC) sacroiliac joint structural scores (SSS) for erosion, backfill, fat lesion and ankylosis. For each of the 4 lesion types, analysis of covariance was utilized for treatment comparisons in observed cases after adjusting for BL values, BL SPARCC bone marrow edema (BME), and stratification factors (treatment, geographic region, BL CRP) and for backfill the analysis was also adjusted for BL erosion. Sensitivity analyses included adjustment of different factors and subsets of pts with less severe ankylosis scores. Subgroup analyses were conducted for changes in structural lesions by sex, HLA-B27 status, and SPARCC BME BL cutoffs ≥4, < 4.

Results: Of the 341 pts in the COAST V study, MRI scans were available for 325 pts at BL and week 16. At BL, the mean (std) scores for SPARCC SSS erosions for PBO, IXE Q4W, IXE Q2W and ADA were comparable. A significant decrease in SPARCC SSS erosion score, LSM (SEM), was observed in both IXE doses with the greatest decrease in IXE Q2W -0.91 (0.19). An increase in SPARCC SSS backfill score, LSM (SEM), was evident in both IXE doses, but a significant mean change was observed only in IXE Q2W 0.52 (0.12) (Figure 1). Cumulative probability of change from BL to week 16 in SPARCC SSS and sensitivity analyses confirmed the findings (Figure 2). SPARCC SSS erosions score, LSM (SEM), were significantly

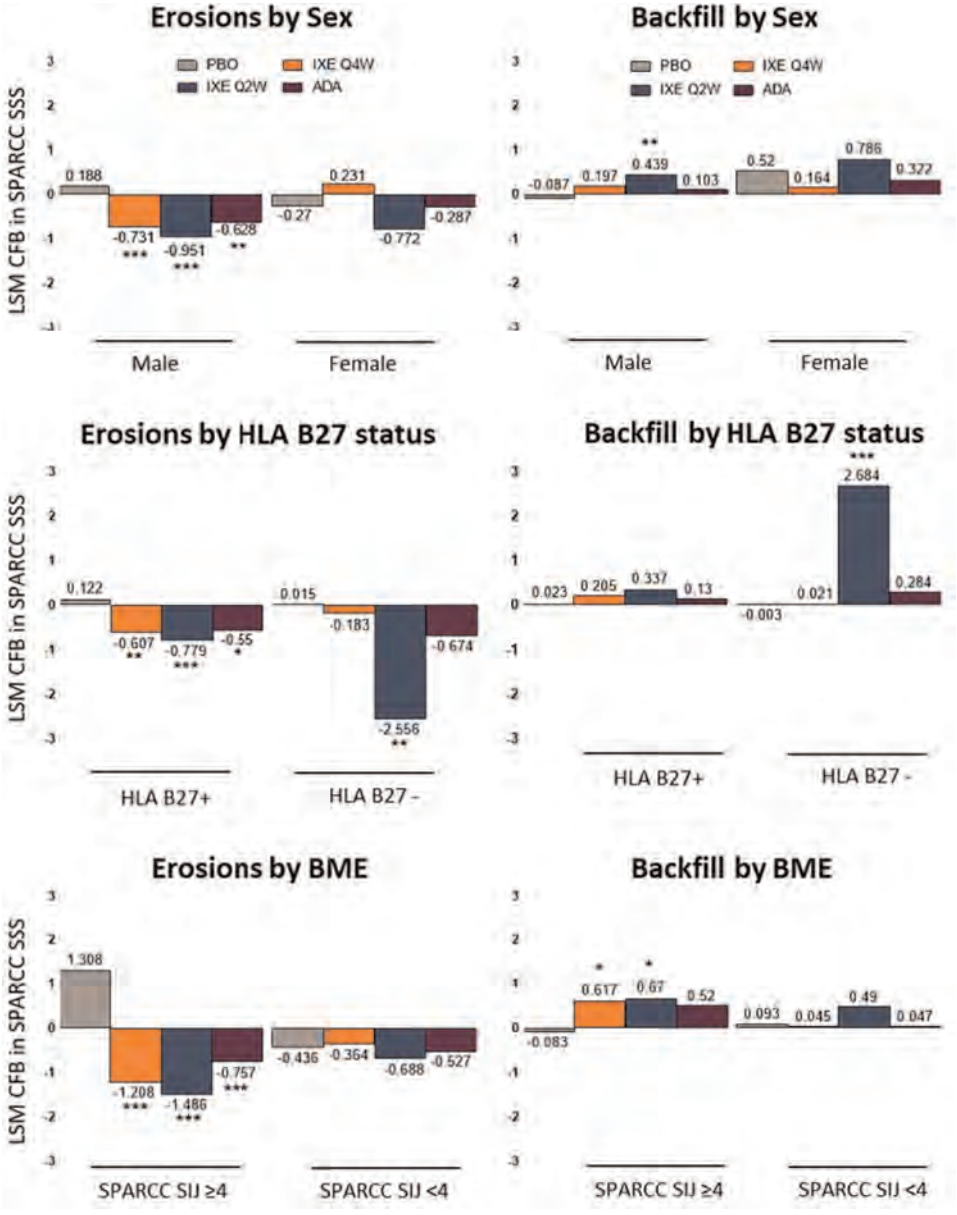

Figure 3: Subgroup Analyses for Changes in Structural Lesions

decreased in males for IXE Q4W -0.731 (0.199) and IXE Q2W -0.951 (0.207), in HLA B27 positive pts for IXE Q4W -0.607 (0.189) and IXE Q2W -0.779 (0.189), in HLA B27 negative pts for IXE Q2W -2.556 (0.656), and in pts with SPARCC SIJ BME ≥4 for IXE Q4W -1.208 (0.359) and IXE Q2W -1.486 (0.344) (Figure 3). SPARCC SSS backfill score, LSM (SEM), was significantly increased in males for IXE Q2W 0.439 (0.141), in HLA B27 negative pts for IXE Q2W 2.684 (0.434), and in pts with SPARCC SIJ BME ≥4 for IXE Q4W 0.617 (0.249) and IXE Q2W 0.67 (0.239).

Conclusion: In pts with bio-naïve r-axSpA, IXE treatment for 16 weeks decreased erosion scores and increased backfill scores, particularly in the IXE Q2W group, consistent with rapid tissue repair. Cumulative probability of change from BL to week 16 in SPARCC SSS and sensitivity analyses confirmed this. This documents that IXE may have an impact in structural damage progression and healing in pts with r-axSpA.

1. van der Heijde D et al. Lancet, 2018.

Disclosure: W. Maksymowych: AbbVie, 2, 5, 6, BMS, 2, 6, Boehringer-Ingelheim, 2, CARE Arthritis Ltd, 4, CARE Arthritis Ltd., 4, Celgene, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **R. Lambert**: Calyx, 2, CARE Arthritis Limited, 2, Image Analysis Group, 2; **E. Krishnan**: Eli Lilly, 3, 11; **B. Zhu**: Eli Lilly, 3, 11; **R. Bolce**: Eli Lilly and Company, 3, 11; **M. Østergaard**: AbbVie, 2, 5, 6, Amgen, 5, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Hospira, 2, 6, Janssen, 2, 6, MEDAC, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Novo Nordisk, 2, 6, Orion, 2, 6, Pfizer, 2, 6, Regeneron, 2, 6, Roche, 2, 6, Sandoz, 2, 6, Sanofi, 2, 6, UCB, 2, 6.

Abstract Number: 2550

The Incidence of Uveitis in Patients with Axial Spondylarthritis Treated with Biologics or Targeted Synthetics: A Systematic Review and Network Meta-analysis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment III: AxSpA
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Anterior uveitis (AU) is one of the commonly observed extraspinal manifestations in Axial spondyloarthritis (AxSpA). Data on the protective effects of targeted immunomodulatory therapies at reducing the frequency of AU flare is limited, particularly amongst more recently licensed drugs. The objective of this study was to investigate the incidence of AU in AxSpA patients treated with etanercept, anti-TNF, anti-IL17A and JAK inhibitors, and compare the protective effect between therapies.

Methods: Embase and MEDLINE were systematically searched to identify all RCTs assessing etanercept, anti-TNF, anti-IL17A and JAK inhibitors drugs in patients with AxSpA. The primary outcome of interest was AU events. Patient exposure years were calculated using a per-protocol analysis. Meta-analysis was performed to compare treatments with placebo. A fixed continuity correction of 0.1 was applied to each RCT arm with zero events. Crude incidence (IR) was calculated.

Relative risk between the treatment arm and placebo was estimated and expressed as incidence rate ratios (IRR). Network meta-analysis (NMA) was employed to allow indirect comparisons between the therapies.

Results: Forty-three studies with 9,184 participants met the inclusion criteria. The IR of AU per 100 patient-years were 1.0 [95% CI: 0.4, 1.8] for anti-TNF, 3.2 [1.2, 7.0] for etanercept, 2.2 [1.5, 3.0] for anti-IL17, 1.4 [0.5, 3.4] for JAK inhibitors, and 4.3 [3.3, 5.6] per 100-person years in the pooled placebo group. Compared with placebo, anti-TNF and JAK inhibitors

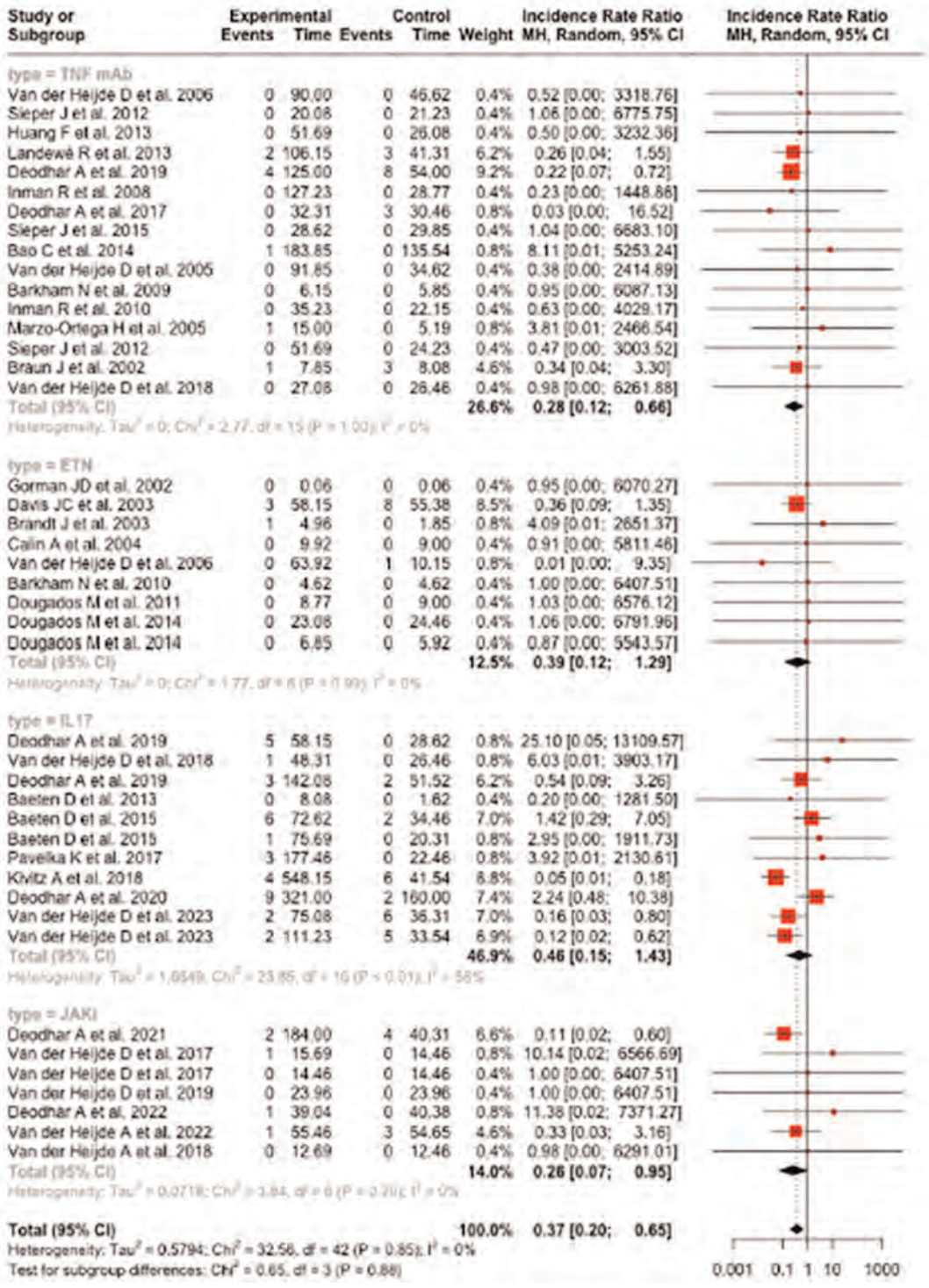

Figure 1. Pairwise meta-analysis, using a per protocol approach to calculated exposure.

had an IRR of uveitis: 0.28 [0.12, 0.66] for anti-TNF and 0.46 [0.07, 0.95] for JAK inhibitors. A lower but non-significant IRR was seen with etanercept (0.39 [0.12, 1.29]) and anti-IL17(0.46 [0.15, 1.43]) (Figure 1). Indirect comparisons between the treatment arms using network meta-analysis did not demonstrate any significant difference in risk of uveitis between different treatment arms.

Conclusion: Targeted immunomodulatory therapy is protective against AU flare. The greatest effects are seen with anti-TNF and JAK inhibitions, although indirect comparisons do not demonstrate any significant difference between treatment modalities.

Disclosure: Z. Yang: None; **M. Adas**: None; **B. Katie**: None; **D. Nagra**: AbbVie/Abbott, 6; **A. Uguzlar**: None; **M. Russell**: Eli Lilly, 6, Janssen, 6; **N. Wilson**: None; **S. Steer**: None; **S. Norton**: Janssen, 6, Pfizer, 6; **J. Galloway**: AbbVie, 2, 5, 6, AstraZeneca, 5, Biogen, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 2551

Remission and Low Disease Activity (LDA) in Patients with SLE Treated with Belimumab (BEL): Results from a Large Integrated Analysis

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes III: Disease Activity

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: A key treatment goal in SLE management is the attainment of remission or LDA,[1] for which various definitions exist, including "Definitions of Remission in SLE" (DORIS),[2] and "Lupus LDA State" (LLDAS).[3]Using DORIS and LLDAS criteria, we evaluated remission or LDA attainment in patients with SLE treated with BEL, an approved treatment for active SLE and LN, with standard therapy.

Methods: This is a post hoc analysis of pooled data for adults with SLE from five trials: BLISS-76, BLISS-52, NEA, BLISS-SC, and EMBRACE (GSK Studies BEL110751, BEL110752, BEL113750, BEL112341, and BEL115471). Included patients received BEL (10 mg/kg/month intravenously or 200 mg/week [wk] subcutaneously) or placebo (PBO), plus standard therapy. Attainment of LLDAS and DORIS was compared between BEL and PBO using logistic regression adjusted for trial variance, in the overall population and in the following baseline patient subgroups: SLEDAI 2000 (SLEDAI-2K)score ³10; anti-dsDNA positivity; anti-dsDNA positivity or low complement C3/C4 levels; glucocorticoid (GC) dose (prednisone-equivalent) >7.5 mg/day.

Results: Among 1869 BEL and 1217 PBO patients analyzed, 94.4% were female, mean (standard deviation, SD) age was 37 (12) years. In the overall population, significantly greater attainment of remission was observed for BEL vs PBO at Wk 20 (odds ratio, OR [95% confidence interval, CI]: 1.59 [1.01, 2.50]; p=0.047) and Wk 28 (1.83 [1.20, 2.79]; p=0.005), and BEL superiority was maintained from Wk 48 (1.45 [1.07, 1.95]; p=0.016) to Wk 52 (**Figure**). Statistically significantly greater attainment of LLDAS with BEL vs PBO was first observed at Wk 24 (1.35 [1.04, 1.74]; p=0.022) and was maintained through Wk 52 (**Figure**). Similar results were observed for the baseline patient subgroups, with greater remission/LLDAS attainment with longer treatment, except for the GC >7.5 mg/day dose subgroup, where no significant difference in remission attainment was seen with BEL vs PBO (**Figure**). The earliest superiority of BEL in attaining remission was seen for patients with baselineSLEDAI-2K ³10 at Wk 20 (2.34 [1.11, 4.96]; p=0.026), which was maintained to Wk 52 (**Figure**). Superiority of BEL in attaining LLDAS was first seen at Wk 16 for patients with baselineSLEDAI-2K ³10 (1.65 [1.01, 2.69]; p=0.045),

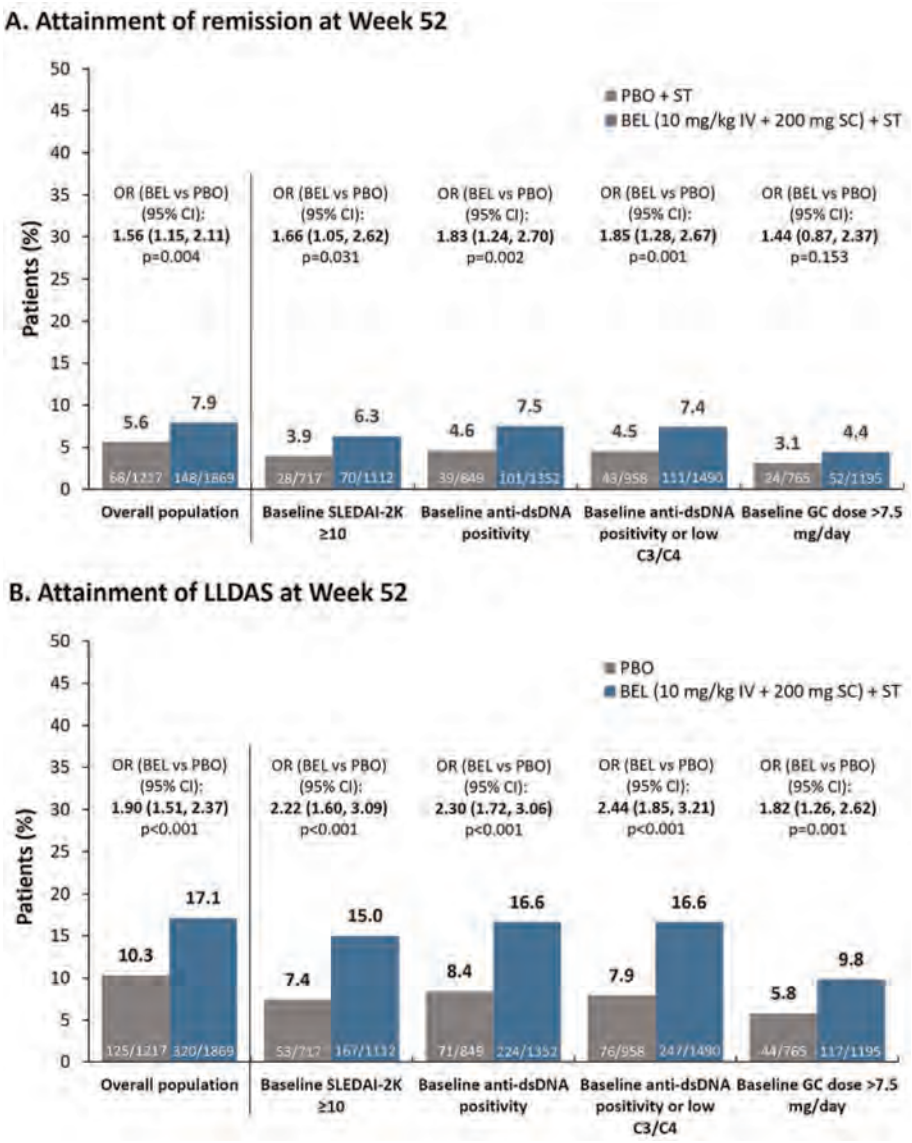

Figure. Remission* (A) and LLDAS† (B) rates in patients with SLE treated with BEL versus PBO, in the overall population, and in patient subgroups per baseline characteristics. Logistic regression (adjusted for the trials) was used for comparisons between BEL and PBO. *The DORIS remission definition requires a clinical SLEDAI-2K score=0 and a PGA score <0.5 (scale 0–3), while it allows serological activity and use of low-dose GCs (prednisone-equivalent <=5 mg/day) and immunosuppressive or biological agents at standard doses; †the LLDAS definition requires a SLEDAI-2K score <=4, excluding major organ activity and fever or new activity since the previous assessment, and PGA score <=1 (scale 0–3), and it allows a prednisone-equivalent dose <=7.5 mg/day and immunosuppressive or approved biological agents at standard doses. IV, intravenous; PGA, Physician Global Assessment; SC, subcutaneous; ST, standard therapy.

baseline anti-dsDNA positivity (1.48 [1.01, 2.18]; p=0.043), and baseline anti-dsDNA positivity/low C3/C4 (1.49 [1.04, 2.12]; p=0.029), and was maintained from Wk 24 (1.78 [1.20, 2.65]; p=0.004, 1.46 [1.05, 2.02]; p=0.025, and 1.49 [1.09, 2.02]; p=0.011, respectively) to Wk 52 (**Figure**).

Conclusion: In this large analysis, statistically significant differences in attainment of remission and LLDAS in favor of BEL vs PBO were seen as early as 24 wks after treatment, with 8% (vs 6%) and 17% (vs 10%) of BEL-treated patients achieving remission and LLDAS, respectively, at Wk 52. BEL appeared particularly beneficial for patients with baselineSLEDAI-2K ^{3}10 and baseline anti-dsDNA positivity/low C3/C4, in whom LLDAS was attained earlier than in the overall population.

Funding: GSK

References

1 Fanouriakis A et al. *Ann Rheum Dis* 2019;78:736–45
2 van Vollenhoven RF et al. *Lupus Sci Med* 2021;8:e000538
3 Franklyn K et al. *Ann Rheum Dis* 2016;75:1615–21

Disclosure: I. Parodis: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia Pharmaceuticals, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Elli Lilly and Company, 5, 6, F. Hoffmann-La Roche AG, 5, 6, Gilead Sciences, 5, 6, GSK, 5, 6, Janssen Pharmaceuticals, 5, 6, Novartis, 5, 6, Otsuka Pharmaceutical, 5, 6; **J. Lindblom**: None; **R. Levy**: GSK, 3, 11; **M. Zen**: Eli Lilly, 6, GSK, 6; **N. Cetrez**: None; **A. Gomez**: None; **S. Oon**: None; **C. Henning**: GSK, 3, 11; **M. Khamashta**: GSK, 3, 11; **H. Quasny**: GSK, 3, 11; **D. Chauhan**: GSK, 3, 11; **A. Askanase**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb, 2, Celgene, 2, Eli Lilly, 2, Genentech, 2, GSK, 2, Idorsia, 2, Janssen, 2, Mallinckrodt, 2, Pfizer, 2, UCB Pharma, 2; **R. van Vollenhoven**: AbbVie/Abbott, 2, 6, AstraZeneca, 2, Biogen, 2, Biotest, 2, Bristol-Myers Squibb(BMS), 2, Galapagos, 2, 6, Gilead, 2, GSK, 6, Janssen, 2, 6, Pfizer, 2, 5, 6, Roche, 5, 6, Sanofi, 2, Servier, 2, UCB, 2, 6, Vielabio, 2; **M. Nikpour**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, GSK, 2, 6, Janssen Pharmaceuticals, 2, 5, 6.

Abstract Number: 2552

Inflammatory Fibrosis Precedes Loss of Kidney Function in Lupus Nephritis

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes III: Disease Activity
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Interstitial fibrosis in lupus nephritis (LN) is often infiltrated by immune cells. However, this is typically regarded as nonspecific "scar reaction" rather than active disease requiring treatment. In contrast, scar inflammation in kidney allografts is associated with chronic rejection and treated with immunosuppression. The objective of this study was to investigate the relationship between inflammatory fibrosis and kidney disease progression in LN.

Table 1. Clinical and demographic characteristics.

	Overall
n	124
Age, years (mean (SD))	36.4 (12.7)
Female (%)	113 (84.9)
Race/Ethnicity (%)	
Asian	9 (12.3)
Black	38 (52.1)
White	21 (28.8)
Other	5 (6.8)
Hispanic	15 (20.5)
eGFR, ml/min (mean (SD))	82.8 (28.8)
UPCR, g/g (mean (SD))	2.07 (2.46)
ISN class (%)	
II	4 (4.9)
III	14 (17.3)
III+V	17 (21.0)
IV	6 (7.4)
IV+V	9 (11.1)
V	31 (38.3)
NIH Activity Index (mean (SD))	3.84 (4.36)
NIH Chronicity Index (mean (SD))	3.17 (2.50)

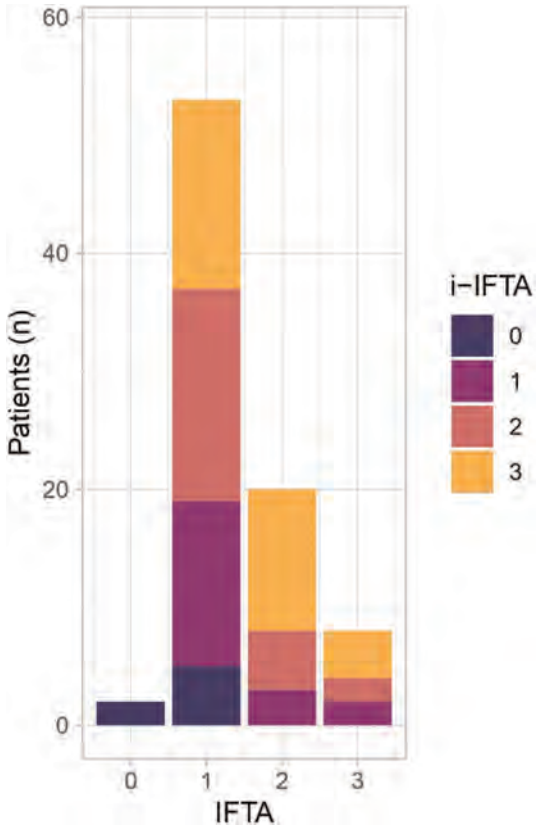

Figure 1. Distribution of i-IFTA groups according to the respective IFTA score. N=124.

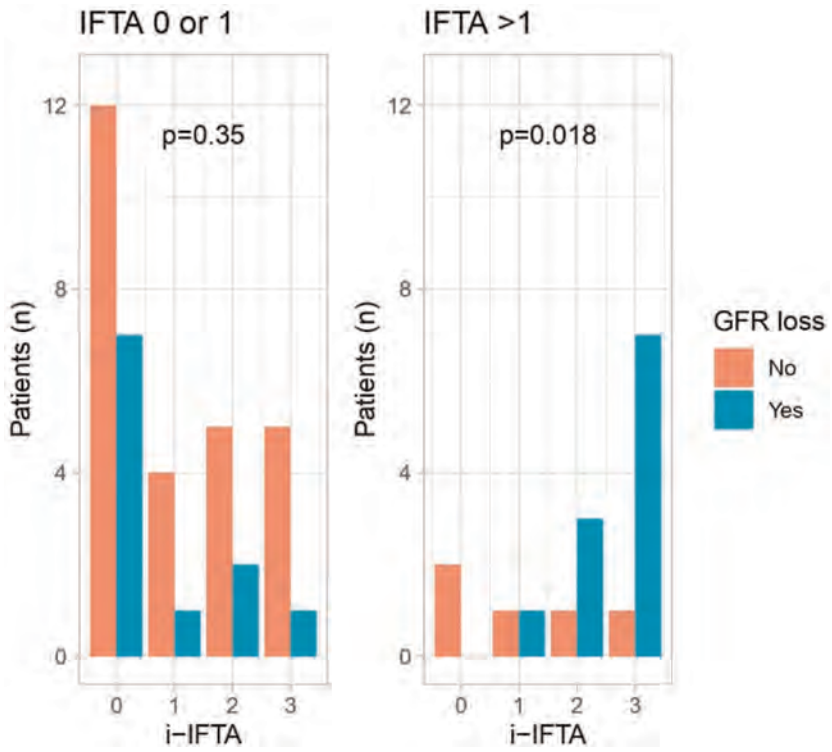

Figure 2. Significant GFR loss according to i-IFTA score. Bars display the frequency of GFR loss in patients with IFTA 0 or 1 (n=37) and IFTA >1 (n=16). Chi-square for trends.

Methods: Interstitial fibrosis and tubular atrophy (IFTA) were scored in 124 kidney biopsies from patients classified as LN according to the 2018 International Society of Nephrology/Renal Pathology Society criteria. Inflammation in areas of IFTA (i-IFTA) was graded 0-3 by 2 operators and reviewed by a senior renal pathologist based on extent according to the Banff Classification of Allograft Pathology (< 10%, 10-25%, 26-50%, >50%, respectively). Glomerular filtration rate (GFR) was estimated using the CKD-EPI equation. Significant GFR loss was defined as a decline of >15 ml/min at 3 years from biopsy or end-stage kidney disease (ESKD) by year 3 requiring dialysis or transplant.

Results: The clinical and demographic characteristics of the cohort are summarized in **Table 1.** IFTA was observed in 88/124 (71%) biopsies, and i-IFTA was identified in 76/88 (86%) cases. The distribution of i-IFTA grades according to the degree of IFTA is illustrated in **Figure 1**. Of the 53 IFTA cases with 3-year follow-up data available, significant GFR loss was observed in 22/53 (42%) cases. As expected, IFTA was associated with GFR loss (p for trend = 0.03). In patients with moderate-to-severe IFTA (grade 2 or 3), the degree of i-IFTA was associated with higher risk of significant GFR loss (**-Figure 2**). The risk of significant GFR loss in this subgroup was 0/2 (0%), 1/2 (50%), 3/4 (75%), and 7/8 (87.5%) for i-IFTA grades 0, 1, 2, and 3, respectively (p for trend = 0.018).

Conclusion: Inflammation in areas of IFTA is frequently observed in LN and exhibits substantial heterogeneity in its severity. For patients with baseline IFTA grades >1, the degree of i-IFTA emerged as a strong predictor of poor renal outcomes. These data support the routine scoring of i-IFTA in LN due to its prognostic implications and nominate i-IFTA as a potential therapeutic target.

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L. Magder: None; **M. Petri**: Alexion, 1, Amgen, 1, AnaptysBio, 1, Annexon Bio, 1, Argenx, 1, Arhros-Focus Med/Ed, 6, AstraZeneca, 1, 5, Aurinia, 1, 5, 6, Axdev, 1, Biogen, 1, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CVS Health, 1, Eli Lilly, 1, 5, Emergent Biosolutions, 1, Exagen, 5, Exo Therapeutics, 2, Gilead Biosciences, 2, GlaxoSmithKlein(GSK), 1, 5, 6, Horizon Therapeutics, 2, Idorsia Pharmaceuticals, 2, IQVIA, 1, Janssen, 1, 5, Kira Pharmaceuticals, 2, MedShr, 6, Merck/EMD Serono, 1, Momenta Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Proviant, 2, Sanofi, 2, Sinomab Biosciences, 2, Thermofisher, 5, UCB, 2; **t. Accelerating Medicines Partnership in RA/SLE**: None; **A. Rosenberg**: None; **A. Fava**: Annexon Biosciences, 2, Sanofi, 1.

Abstract Number: 2553

Prevalence, Determinants and Outcomes of Target Attainment in SLE Patients with Clinically Active Disease in a Large Multinational Prospective Lupus Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes III: Disease Activity

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: There is increasing interest in adopting the principle of treating to target (T2T) in systemic lupus erythematosus (SLE). Remission and low disease activity states have been demonstrated to have protective associations with adverse outcomes such as flare, damage accrual and mortality. However, knowledge gaps remain in relation to the timing and impact of target attainment. In this study, we aimed to identify (i) the proportion of patients achieving the lupus low disease activity state (LLDAS) and the definition of remission in SLE (DORIS-remission) subsequent to a visit with clinically active disease, (ii) time to attainment of LLDAS and DORIS-remission, (iii) determinants of attaining these targets, and (iv) frequency and time to flare and damage accrual following target attainment.

Methods: Patients in the Asia Pacific Lupus Collaboration (APLC) cohort, followed between 2013 and 2020 who had any clinical disease activity according to the clinical domains of SLEDAI-2K and did not fulfill LLDAS or DORIS-remission were followed from their first time fulfilling these criteria. SELENA-SLEDAI flare index and the SLICC/ACR Damage Index were used to assess flare and damage accrual, respectively. We used Multivariable Cox regression models to analyse factors associated with attainment of LLDAS and DORIS-remission. Generalized estimating equation (GEE) models were used to identify factors associated with flare after attainment of target.

Results: 2852 patients (92.4% female) were followed for a median of 3.3 (1.1-5.7) years. The mean (standard deviations) SLEDAI and PGA at the first visit with clinical activity were 7.0±4.3 and 0.9±0.7, respectively. 1858 (65.2%) of the patients achieved LLDAS, with median (interquartile ranges) time to first attainment of LLDAS being 0.5 (0.3-1.2) years (Figure 1). The proportion and median time to first attainment of DORIS-remission were 49.3% and 0.7 (0.4-1.6) years, respectively. Multivariable Cox model showed that nephritis, positive anti-dsDNA and low complement were associated with a longer time to attainment of LLDAS and DORIS-remission, and in addition non-Asian ethnicity was associated with a longer time taken to attain DORIS-remission (Table 1). After the first attainment of LLDAS, 887/1852 (47.9%) of patients experienced flare(s) with a median time to first flare of 0.7 (0.3-1.4) years. 679/1405 (48.3%) patients had flare(s) after the first attainment of DORIS-remission within a median time of 0.8 (0.3-1.6) years (Figure 1). In multivariable GEE model, factors associated with flare post attainment of LLDAS included tapering of corticosteroids and immunosuppressants (Table 2). 110/960 (11.5%) and 77/750 (10.2%) patients had damage accrual within 24 months of first attainment of LLDAS and DORIS-remission, respectively (Figure 1).

Table 1. Multivariable Cox regression model for determinants of LLDAS or DORIS-remission attainment after the first visit with clinical activity

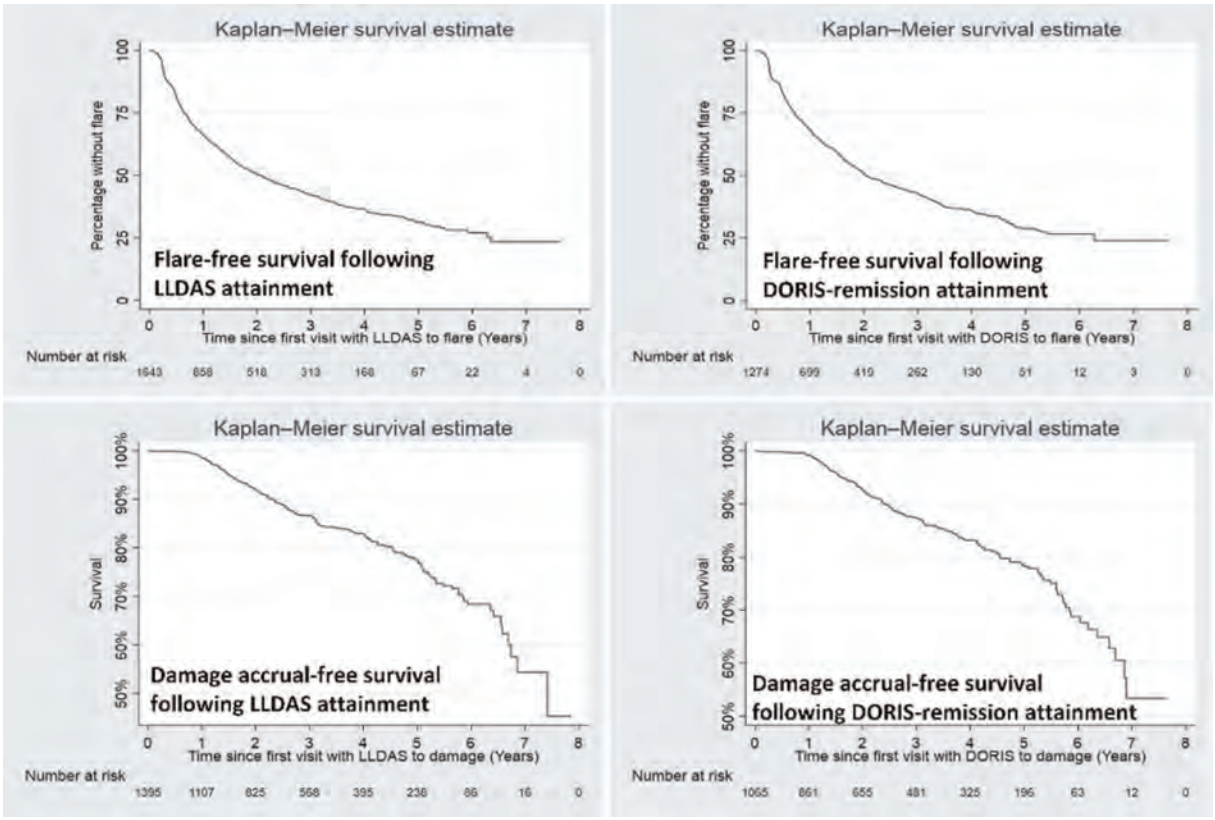
Model for LLDAS attainment			
Variables at first visit with clinical activity	**HR**	**95% CI**	**P value**
Nephritis	0.50	0.45-0.57	<0.001
Positive anti-dsDNA	0.79	0.72-0.87	<0.001
Low complements	0.84	0.76-0.92	<0.001
Immunosuppressants			
No immunosuppressant	Reference		
MMF/MPA	0.85	0.75-0.96	<0.001
Other immunosuppressant*	0.80	0.72-0.89	<0.001
Model for DORIS-remission attainment			
Variables at first visit with clinical activity	**HR**	**95% CI**	**P value**
Ethnicity			
Asian	Reference		
Non-Asian	0.71	0.60-0.83	<0.001
Nephritis	0.68	0.59-0.77	<0.001
Positive anti-dsDNA	0.80	0.71-0.89	<0.001
Low complements	0.72	0.64-0.80	<0.001
Immunosuppressants			
No immunosuppressant	Reference		
MMF/MPA	0.80	0.70-0.93	0.002
Other immunosuppressant*	0.69	0.61-0.78	<0.001

* Other immunosuppressants include Cyclophosphamide, Cyclosporin, Tacrolimus, Azathioprine, Methotrexate, Leflunomide

Abbreviation: LLDAS: lupus low disease activity state; DORIS: the definition of remission in SLE; anti-dsDNA: anti-double strain DNA; MMF: mycophenolate; MPA: mycophenolic acid

Table 2. Multivariable Generalized Estimating Equation Model for flare at the visit subsequent to LLDAS attainment

Variables	HR	95% CI	P value
Age at visit, per year	0.993	0.988-0.999	0.017
Time-adjusted mean SLEDAI at visit	1.07	1.04-1.10	<0.001
Cumulative duration of LLDAS, per day	0.9997	0.9996-0.9998	<0.001
Current anti-malarial use	0.81	0.72-0.92	0.001
Tapering prednisolone or Immunosuppressants since achieving LLDAS	1.13	1.01-1.25	0.026



Flare-free and damage accrual-free survival after first attainment of LLDAS or DORIS-remission

Conclusion: In patients with clinically active disease, LLDAS and DORIS-remission are both achievable goals. However, flares still occur in almost 50% of patients, and 10-11.5% of patients still accrue damage over two years following LLDAS or DORIS-remission attainment, suggesting that further research is needed to inform monitoring and treatment adjustment in SLE patients to maintain states associated with optimal outcomes.

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5; **Z. Zhang**: None; **M. Chan**: None; **J. Kikuchi**: None; **T. Takeuchi**: AbbVie, 2, 5, 6, AYUMI, 5, Bristol-Myers Squibb, 6, Chugai, 2, 5, 6, Daiichi Sankyo, 5, Eisai, 5, 6, Eli Lilly Japan, 2, 6, Gilead, 2, 6, Janssen, 6, Mitsubishi-Tanabe, 2, 5, 6, ONO, 5, Pfizer Japan, 6, Taiho, 2; **S. Bae**: None; **F. Goldblatt**: None; **S. O'Neill**: None; **K. Ng**: AbbVie/Abbott, 1; **A. Law**: None; **B. Basnayake**: None; **N. Tugnet**: None; **S. Kumar**: None; **C. Tee**: None; **M. Tee**: None; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer-Ingelheim, 6, Chugai, 5, 6, Eisai, 5, 6, Eli Lilly, 6, Gilead, 6, GSK, 6, Mitsubishi-Tanabe, 5, Pfizer, 6, Taiho, 6, Taisho, 5, 6; **C. Lau**: AstraZeneca, 6, 12, external expert for SLE sterring committee 11.2022; **V. Golder**: None; **A. Hoi**: Abbvie, 6, AstraZeneca, 5, Australian Rheumatology Association, 4, Eli Lilly, 6, EUSA Pharma (UK) Limited, 2, Limbic, 6, Moose Republic, 6, Novartis, 6; **E. Morand**: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 2, 5, 6, Biogen, 2, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, EMD Serono, 2, 5, Galapagos, 2, Genentech, 2, 5, GlaxoSmithKline, 2, 5, IgM, 2, Janssen, 2, 5, Novartis, 2, Servier, 2, Takeda, 2, UCB, 5; **S. Oon**: None; **M. Nikpour**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, GSK, 2, 6, Janssen Pharmaceuticals, 2, 5, 6.

Abstract Number: 2554

Validation of a Flare Risk Index Informed by Select Immune Mediators in Systemic Lupus Erythematosus in a Confirmatory Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes III: Disease Activity

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: SLE is marked by immune dysregulation linked to varied clinical disease activity. Using a unique confirmatory cohort of SLE patients, this study seeks to validate a recently refined Lupus Flare Risk Index (L-FRI; Munroe et al. Arthritis Rheumatol. 2023) reflecting altered immunity prior to clinical disease flare.

Methods: The L-FRI is the sum of log-transformed, standardized immune mediators, weighted by the Spearman r correlation coefficient for each preflare/prenonflare analyte vs. subsequent flare/nonflare hSLEDAI disease activity (flare is defined by the SELENA-SLEDAI Flare Index). SLE-associated plasma mediators (n=11) were evaluated by microfluidic immunoassay in 52 preflare and 52 prenonflare samples from patients with classified SLE. Hybrid SLEDAI (hSLEDAI) scores, clinical features, medication usage, and the presence of SLE-associated autoantibody (AutoAb) specificities, including dsDNA, chromatin, Ro/SSA, La/SSB, Sm, SmRNP, and RNP, were also compared at preflare (105 ± 62 days prior to flare) vs. prenonflare (105 ± 55 days prior to nonflare) time points. Data from this validation cohort were compared to development and merged development/validation cohorts.

Results: This validation (Val) cohort is enriched for African American (AA) SLE patients (44% preflare, 48% prenonflare vs. 11% preflare, 15% prenonflare in the development [Dev] cohort), with an associated increase in preflare hSLEDAI scores (4.0±3.4 preflare, 1.9±2.2 prenonflare, *p=0.0004* [Val] vs. 2.4±2.6 preflare, 2.8±3.8 prenonflare, *p=0.8953* [Dev]). Otherwise, after adjusting for multiple comparison, we did not observe differences with respect to clinical features, medication

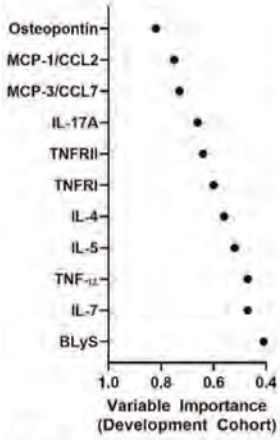


Figure 1

Development

L-FRI				
Pre-flare mean (95%CI)	Pre-nonflare mean (95%CI)	*p-value*	Effect Size	
3.1 (1.2 to 5.0)	-2.7 (-4.2 to -1.2)	*<0.0001*	0.907	
AUC			**Correlation with hSLEDAI @ FU**	
AUC	95% CI	p-value	Spearman r	95% CI	p-value
0.755	0.660 to 0.849	<0.0001	0.434	0.253 to 0.585	*<0.0001*

Validation

L-FRI				
Pre-flare mean (95%CI)	Pre-nonflare mean (95%CI)	*p-value*	Effect Size	
4.5 (2.3 to 6.8)	-1.5 (-3.5 to 0.5)	*<0.0001*	0.886	
AUC			**Correlation with hSLEDAI @ FU**	
AUC	95% CI	p-value	Spearman r	95% CI	p-value
0.707	0.609 to 0.806	*0.0003*	0.399	0.218-0.553	*<0.0001*

Combined

L-FRI				
Pre-flare mean (95%CI)	Pre-nonflare mean (95%CI)	*p-value*	Effect Size	
4.0 (2.5 to 5.5)	-2.3 (-3.6 to -1.1)	*<0.0001*	0.916	
AUC			**Correlation with hSLEDAI @ FU**	
AUC	95% CI	*p-value*	Spearman r	95% CI	p-value
0.742	0.675 to 0.809	*<0.0001*	0.420	0.294-0.531	*<0.0001*

Table 1. Univariate Analysis of Individual Soluble Mediators Informing the L-FRI

Development Cohort	Pre-Flare			Pre-Nonflare			
Variable	Mean	SEM	95%CI	Mean	SEM	95%CI	*p-value*[a]
Osteopontin (ng/ml)	84.4	6.8	70.7-98.1	64.4	3.7	56.9-71.9	***0.0086***
MCP-1/CCL2 (pg/ml)	337	26	285-390	320	13	294-346	*0.5283*
MCP-3/CCL7 (pg/ml)	4.4	1.6	1.3-7.5	2.7	0.7	1.3-4.1	*0.3846*
IL-17A (pg/ml)	4.4	3.6	3.7-5.1	3.5	2.5	3.0-4.0	***0.0334***
TNFRII (pg/ml)	3546	293	2956-4136	2738	120	2497-2979	***0.0087***
TNFRI (pg/ml)	1597	115	1366-1829	1298	54	1189-1406	***0.0156***
IL-4 (fg/ml)	550	225	93-1005	167	17	133-201	***0.0345***
IL-5 (fg/ml)	440	95	248-632	441	76	289-593	*0.2226*
TNF-α (pg/ml)	10.4	0.8	8.8-12.0	8.1	0.4	7.2-8.9	***0.0089***
IL-7 (pg/ml)	8.6	0.5	7.5-9.7	7.3	0.4	6.6-8.1	***0.0456***
BLyS (pg/ml)	1123	86	949-1297	1006	103	800-1211	*0.1851*
Validation Cohort	**Pre-Flare**			**Pre-Nonflare**			
Variable	Mean	SEM	95%CI	Mean	SEM	95%CI	*p-value*[a]
Osteopontin (ng/ml)	113.7	8.8	96.0-131.3	83.1	4.8	73.5-92.6	***0.0055***
MCP-1/CCL2 (pg/ml)	832	315	199-1466	357	35.9	284-429	***0.0124***
MCP-3/CCL7 (pg/ml)	13.5	5.6	2.3-24.7	5.7	2.2	1.2-10.2	***0.0482***
IL-17A (pg/ml)	1.1	0.1	0.9-1.5	1.1	0.1	0.9-1.4	*0.7561*
TNFRII (pg/ml)	4609	273	4062-5156	3487	182	3121-3852	***0.0040***
TNFRI (pg/ml)	1818	111	1595-2040	1433	65.9	1300-1565	***0.0129***
IL-4 (fg/ml)	279	52	173-384	463	70	323-603	***0.0373***
IL-5 (fg/ml)	776	223	328-1224	544	108	328-760	*0.6709*
TNF-α (pg/ml)	18.3	1.3	15.7-21.0	13.6	1.2	11.2-16.0	***0.0020***
IL-7 (pg/ml)	15	6.5	1.9-28.1	5.6	0.6	4.5-6.8	***0.0362***
BLyS (pg/ml)	1703	144	1414-1992	1288	101	1085-1491	***0.0391***
Combined Cohort	**Pre-Flare**			**Pre-Nonflare**			
Variable	Mean	SEM	95%CI	Mean	SEM	95%CI	*p-value*[a]
Osteopontin (ng/ml)	99.8	5.7	88.3-111	73.5	3.1	67.3-79.8	***0.0001***
MCP-1/CCL2 (pg/ml)	595	166	266-924	338	18.7	301-375	*0.0879*
MCP-3/CCL7 (pg/ml)	9.2	3	3.2-15.2	4.2	1.2	1.9-65	*0.1205*
IL-17A (pg/ml)	2.7	0.2	2.2-3.2	2.4	0.2	2.0-2.7	*0.2364*
TNFRII (pg/ml)	4609	192	4229-4989	3487	128	3233-3740	***≤0.0001***
TNFRI (pg/ml)	1818	77.9	1663-1972	1433	46.3	1341-1525	***0.0004***
IL-4 (fg/ml)	396	103	192-600	314	38.5	238-391	*0.5973*
IL-5 (fg/ml)	617	126	366-567	491	65.3	362-621	*0.7598*
TNF-α (pg/ml)	14.6	0.9	12.8-16.3	10.8	0.7	9.5-12.1	***0.0002***
IL-7 (pg/ml)	11.9	3.4	5.1-18.8	6.5	0.4	5.8-7.2	***0.0294***
BLyS (pg/ml)	1428	90.6	1248-1608	1144	73	999-1289	***0.0150***

[a]Mann-Whitney test. Unadjusted significant ***p≤0.05***; Bonferroni corrected significant ***p=0.0046***

SELENA-SLEDAI Flare Index (SFI) Flare Features	Development M/M Flare (n=41)	Development Severe Flare (n=5)	Development All Flare (n=46)	Validation M/M Flare (n=42)	Validation Severe Flare (n=10)	Validation All Flare (n=52)	Combined M/M Flare (n=83)	Combined Severe Flare (n=15)	Combined All Flare (n=98)
Mild to Moderate (M/M) Flare Features (n, %)									
Cutaneous	10 (24%)	N/A	10 (22%)	15 (36%)	N/A	15 (29%)	25 (83%)	N/A	25 (26%)
Nasopharyngeal	9 (22%)	N/A	9 (20%)	4 (10%)	N/A	4 (8%)	13 (16%)	N/A	13 (13%)
Pleuritis	3 (7%)	N/A	3 (7%)	1 (2%)	N/A	1 (2%)	4 (5%)	N/A	4 (4%)
Arthritis	25 (61%)	N/A	25 (54%)	21 (50%)	N/A	21 (40%)	46 (55%)	N/A	46 (47%)
Fever	1 (2%)	N/A	1 (2%)	1 (2%)	N/A	1 (2%)	2 (2%)	N/A	2 (2%)
Prednisone increase (not to >0.5 mg/kg/day)	5 (12%)	N/A	5 (11%)	19 (45%)	N/A	19 (37%)	24 (29%)	N/A	24 (24%)
Added NSAID or Plaquenil	0	N/A	0	6 (14%)	N/A	6 (12%)	6 (7%)	N/A	6 (6%)
PGA increase (>1, not more than 2.5)	3 (7%)	N/A	3 (7%)	2 (5%)	N/A	2 (4%)	5 (6%)	N/A	5 (5%)
Severe Flare Features (n, %)									
Prednisone doubling + CNS-SLE	N/A	0	0	N/A	1 (10%)	1 (2%)	N/A	1 (7%)	1 (1%)
Prednisone doubling + Nephritis	N/A	2 (40%)	2 (4%)	N/A	9 (90%)	9 (17%)	N/A	11 (73%)	11 (11%)
Prednisone doubling + Thrombocytopenia	N/A	1 (20%)	1 (2%)	N/A	0	0	N/A	1 (7%)	1 (1%)
Prednisone increase (>0.5 mg/kg/day)	N/A	1 (20%)	1 (2%)	N/A	3 (30%)	3 (6%)	N/A	4 (27%)	4 (4%)
New SLE Medication or Hospitalization	N/A	2 (40%)	2 (4%)	N/A	3 (30%)	3 (6%)	N/A	5 (33%)	5 (5%)
PGA Increase (>2.5)	N/A	3 (60%)	3 (7%)	N/A	2 (20%)	2 (4%)	N/A	5 (33%)	5 (5%)

Development

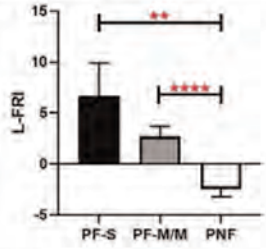
Pre-M/M vs PNF	AUC			Correlation with hSLEDAI @ FU		
Effect Size	AUC	95% CI	p-value	Spearman r	95% CI	p-value
0.730	0.730	0.635-0.825	<0.0001	0.441	0.256-0.594	*<0.0001*
Pre-Severe vs PNF	AUC			Correlation with hSLEDAI @ FU		
Effect Size	AUC	95% CI	p-value	Spearman r	95% CI	p-value
1.333	0.843	0.683-1.000	<0.0001	0.387	0.138-0.590	*0.0024*

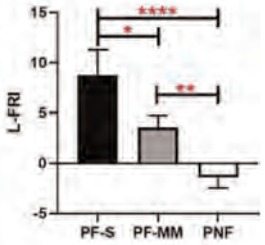
Validation

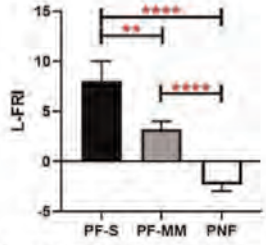
Pre-M/M vs PNF	AUC			Correlation with hSLEDAI @ FU		
Effect Size	AUC	95% CI	p-value	Spearman r	95% CI	p-value
1.111	0.668	0.560-0.776	*0.0052*	0.336	0.137-0.509	*0.0009*
Pre-Severe vs PNF	AUC			Correlation with hSLEDAI @ FU		
Effect Size	AUC	95% CI	p-value	Spearman r	95% CI	p-value
2.137	0.871	0.771-0.972	*0.0002*	0.462	0.233-0.643	*0.0002*

Combined

Pre-M/M vs PNF	AUC			Correlation with hSLEDAI @ FU		
Effect Size	AUC	95% CI	p-value	Spearman r	95% CI	p-value
0.824	0.718	0.646-0.790	*<0.0001*	0.377	0.242-0.497	*<0.0001*
Pre-Severe vs PNF	AUC			Correlation with hSLEDAI @ FU		
Effect Size	AUC	95% CI	p-value	Spearman r	95% CI	p-value
1.476	0.876	0.796-0.957	*<0.0001*	0.351	0.177-0.504	*<0.0001*







*p<0.05, **p<0.01, ****p<0.0001 Kruskal-Wallis test with Dunn's multiple comparison.

Figure 2

usage, or number and type of SLE-associated AutoAbs in preflare vs. prenonflare samples. The L-FRI, informed by 11 mediators (**Fig. 1**), significantly ($p< 0.0001$) differentiated preflare vs. prenonflare samples in the Val cohort, similar to that of the Dev and combined (Com) cohorts (**Fig. 1**), with a large (>0.8) Cohen's effect size, AUC >0.7 ($p\leq0.0003$), and Spearman r ≥0.399 ($p< 0.0001$) vs. hSLEDAI scores at disease flare/nonflare (**Fig. 1**). The inclusion of 11 mediators in the L-FRI allows for varied differences between preflare vs. prenonflare across cohorts, yet with consistent differences in osteopontin, TNFRII, TNFRI, and TNF-α (**Table 1**). Furthermore, the L-FRI differentiates SLE patients at risk of imminent severe (S) and mild-moderate (M/M) flares vs. nonflare (**Fig. 2**), with increased L-FRI scores ($p\leq0.05$), effect size (≥1.3), and AUC (≥0.843, $p\leq0.0002$) in pre-severe flare samples across the Val, Dev, and Com cohorts (**Fig. 2**).

Conclusion: We verified the utility of the L-FRI, informed by 11 immune mediators, to identify SLE patients at risk of imminent lupus disease flare. Of particular interest is the ability of the L-FRI to differentiate future M/M vs. severe flare risk. A subset of mediators consistently enhanced the L-FRI to identify SLE patients who may benefit from early intervention strategies. Such an approach would be advantageous in prospective clinical trials for study participant recruitment and assessment, as well as improved management of lupus

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Abstract Number: 2555

Cluster Analysis Reveals Subgroups in Patients with Serologically Active Clinically Quiescent Systemic Lupus Erythematosus: Implication for Long-term Prognosis Prediction

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes III: Disease Activity

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Serologically active clinically quiescent (SACQ) is a clinical state of systemic lupus erythematosus (SLE) characterized by high levels of serologic markers without clinical activity. SACQ patients are at potential risk of flares, even organ damage, and thus should be given closer monitoring according to the treat-to-target strategies. However, substantial phenotypic heterogeneity exists in SACQ patients hindering disease management. In this multi-center prospective study, we aimed to determine distinct subgroups among SACQ patients and identify their utility in organ damage prediction.

Methods: SACQ was defined as at least a 6-month period with persistent serologic activity (positive anti-dsDNA antibody, and/or hypocomplementemia), and without clinical activity. Partitioning around medoids (PAM) cluster analysis based on 18 independent components was performed to characterize the phenotypes. The flare was measured according to the SELENA-SLEDAI flare index. Organ damage is principally assessed using the SLICC damage index (SDI).

Results: Of 4107 enrolled SLE patients under standard treatment, 990 (17.1%) achieved the state as SACQ in 2.2 years. During the mean follow-up of 7246.8 patient years, 36.7% of SACQ patients experienced at least one flare in 1.7±0.8 years and 16.5% showed organ damage in 3.0±1.9 years. In SACQ patients, three distinct subgroups (Table) with markedly different features and outcomes were identified (Figure 1). Cluster 1 (n=219, 22.1%) was male, elderly patients, with neural involvement and hematological involvement, corresponding to the highest risk of organ damage accumulation (35.6%) (Figure 2). Cluster 2 (n=279, 28.2%) had the lowest rate of major organ involvements and autoantibodies positivity among the three subgroups and corresponded to mild risk of damage accrual (5.7%). Cluster 3 (n=492, 49.7%) was characterized by the highest proportion of lupus nephritis, corresponding to mild risk of flares (32.7%), moderate risk of organ damage (14.0%), and severe risk of renal damage (7.1%). For the management of SACQ, 224 patients tried tapering glucocorticoids. 86 (30.8%) patients in cluster 2 ("mild involvements" cluster) tapered glucocorticoids under tight control and 49 of them withdrawn successfully without flares. In contrast, only 31 (14.2%) patients in cluster 1 ("severe involvements" cluster) tried to withdraw glucocorticoids.

Table. Clinical features of the three clusters.

	Total (n=990)	Cluster1 (n=219)	Cluster 2 (n=279)	Cluster 3 (n=492)	P value
Clinical features and treatment at SACQ					
Male, n(%)	50(9.1)	37(16.9)	3(1.1)	10(2.0)	**<0.001**
Age at baseline, years	33.6±10.5	42.2±12.2	29.8±10.5	31.9±7.0	**<0.001**
Time to SACQ/SQCQ, years	2.0±2.3	2.0±2.5	1.6±1.6	2.2±2.3	**<0.001**
Skin involvements, n(%)	592(59.8)	128(58.4)	183(65.6)	281(57.1)	0.063
Arthritis, n(%)	558(56.4)	136(62.1)	149(53.4)	273(55.5)	0.130
Serositis, n(%)	90(9.1)	29(13.2)	13(4.7)	48(9.8)	**0.003**
Lupus nephritis, n(%)	329(33.2)	57(26.0)	16(5.7)	256(52.0)	**<0.001**
Neurological involvement, n(%)	44(4.4)	14(6.4)	3(1.1)	27(5.5)	**0.005**
Hematological involvement, n(%)	348(35.2)	91(41.6)	73(27.2)	184(37.4)	**0.001**
Anti-SSA/SSB antiboides, n(%)	319(32.2)	72(32.9)	85(30.5)	152(32.9)	0.760
Anti-RNP antibodies positive, n(%)	290(29.3)	56(25.6)	68(24.4)	166(33.7)	**0.009**
Antiphospholipid antiboides, n(%)	248(25.1)	82(37.4)	52(18.6)	114(23.2)	**<0.001**
Anti-nucleosome antibodies, n(%)	153(15.5)	42(19.2)	27(9.7)	84(17.1)	**0.005**
Hypocomplementemia	634(64.0)	150(68.5)	173(62.0)	311(63.2)	0.282
Anti-dsDNA positive	593(59.9)	123(56.2)	179(64.2)	291(59.1)	0.174
Hydroxychloroquine, n(%)	781(78.9)	166(75.8)	239(85.7)	376(76.4)	**0.005**
Immunosuppressant, n(%)	826(83.4)	211(96.3)	125(44.8)	490(99.6)	**<0.001**
SDI at SACQ/SQCQ =0, n(%)	852(86.1)	175(79.9)	271(97.1)	406(82.5)	**<0.001**
Prognosis after achieving SACQ					
Withdraw low-dose GCs	224(22.6)	31(14.2)	**86(30.8)**	107(21.7)	**0.031**
Success withdraw	125(12.6)	17(7.8)	**49(17.6)**	69(14.0)	**0.016**
Flare, n(%)	368(37.2)	85(38.8)	122(43.6)	161(32.7)	**0.008**
Time from SACQ to flare, years	1.7±0.8	1.8±0.9	1.5±0.8	1.9±0.8	**0.002**
Damage accumulation, n(%)	163(16.5)	**78(35.6)**	15(5.7)	69(14.0)	**<0.001**
Renal damage, n(%)	49(4.9)	10(4.6)	4(1.4)	**35(7.1)**	**0.002**
Interstitial lung disease, n(%)	9(0.9)	5(2.3)	3(1.1)	1(0.2)	**0.025**
Osteonecrosis, n(%)	61(6.2)	**39(17.8)**	3(1.1)	21(4.5)	**<0.001**
Death, n(%)	21(2.1)	6(2.7)	3(1.1)	12(2.4)	0.348

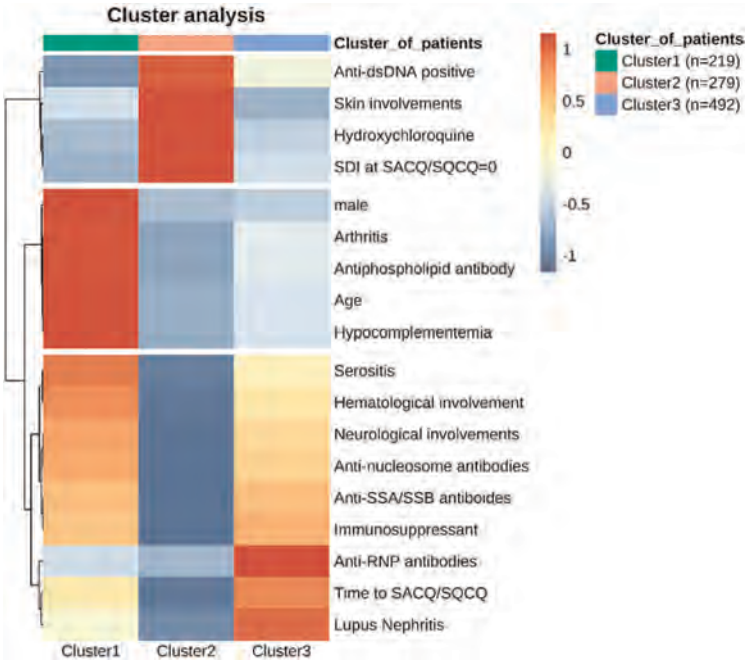

Figure 1. Heatmap of the cluster analysis.

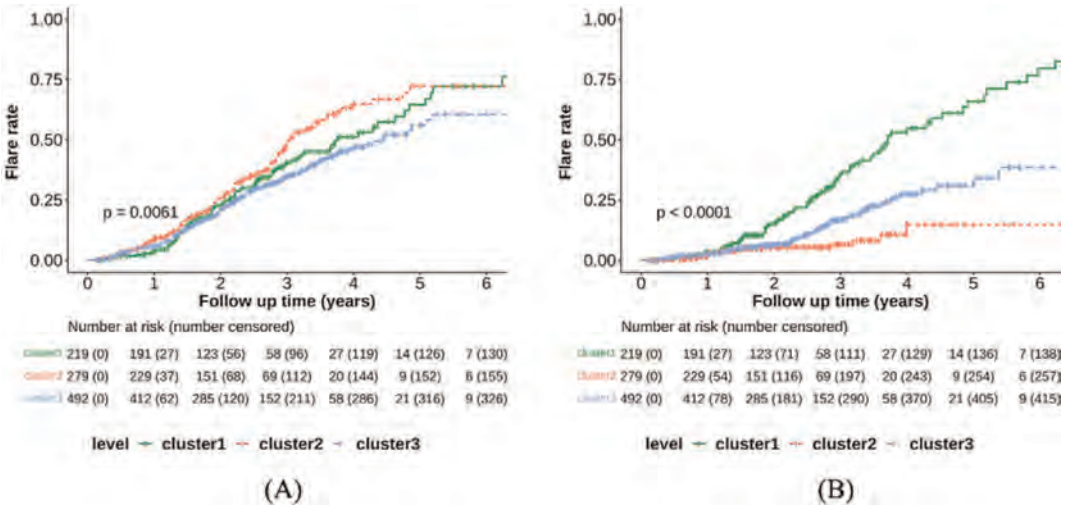

Figure 2. Cumulative probability of flares (A) and damage accrual rate (B) in the three clusters of SACQ patients

Conclusion: Our study distinguished three distinct clinical patterns and outcomes in SACQ patients. Low-dose glucocorticoid withdrawal under tight surveillance should be considered in SACQ patients without major organ involvement. Classification of SACQ patients into phenotypes with prognostic values may facilitate the individualized management of SACQ patients.

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Abstract Number: 2556

End-of-Life in Systemic Lupus Erythematosus Beset by Increased Flares and Higher Treatment Burden: Data from a Prospective Large Multinational Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes III: Disease Activity

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: SLE patients suffer high symptom burden at the end-of-life. However, the course of disease and treatment burden in the last year of life have not been described. Also, there remains few predictors to identify patients at risk of imminent death within a year that could trigger initiation of supportive care.

Methods: We collected data from SLE patients (ACR/SLICC criteria) prospectively between 2013 to 2020 from 13 Asia-pacific countries. Data at each visit included laboratory variables, SLEDAI and treatment. SLICC Damage Index (SDI) and 36-item Short Form Survey (SF-36) were administered annually. We captured causes of death, with each death possibly attributed to more than one cause. We computed a modified SLICC-frailty index that excluded Sjogren syndrome, hypothyroidism, BMI, hypertension and headache disorder. In order to build a model to identify patients in need of supportive care at the end-of-life, we used a generalized estimating equations (GEE) model that included variables at a given visit that could predict imminent death within a year. Next, we used GEE models to compare the course of disease in the last year of life versus before, with respect to (i) flares; (ii) use of immunosuppressive agents (IS); (iii) corticosteroid dose (CS); (iv) treatment escalation or tapering (any increase or decrease respecitvely, in IS/CS doses); (v) visit intervals; (vi) SF36 physical (PCS) and mental (MCS) scores.

Table 1. Multivariable Generalized Estimating Equation Model for Odds of Imminent Death Within One Year

	Odds Ratio (95% CI)	Standard coefficient	*p*
Age	1.02 (0.98-1.06)	0.02	0.32
Female vs male	1.89 (0.37-9.56)	0.63	0.44
Primary vs tertiary education	0.80 (0.24-2.73)	-0.22	0.72
Highest gross domestic product (GDP) category*	0.19 (0.07-0.49)	-1.68	<0.01
Anti-malarial (no vs yes)	1.29 (0.61-2.72)	0.25	0.51
Immunosuppressive therapy (no vs yes)	1.04 (0.54-1.98)	0.04	0.92
Prednisolone dose	1.00 (1.00-1.01)	<0.01	0.07
Haemoglobin	0.99 (0.98-1.00)	-0.01	0.07
Albumin	0.99 (0.95-1.03)	-0.01	0.61
Estimated glomerular filtration rate	1.00 (0.99-1.02)	<0.01	0.71
aPL positivity (no vs yes)	3.25 (1.13-9.37)	1.18	0.03
Disease duration	1.03 (0.97-1.08)	0.03	0.38
SLEDAI	1.04 (0.96-1.12)	0.04	0.35
SDI	1.52 (1.18-1.96)	0.42	<0.01
Frail*	0.55 (0.23-1.32)	-0.60	0.18

* GDP >$50000 per capita compared to <$20000 per capita

*Classified as frail on modified SLICC frailty index which excludes Sjogren syndrome, hypothyroidism, BMI, hypertension and headache disorder. Compared to other non-frail categories.

Results: We studied 4105 patients, of which 90 died at a median age of 43 (29.5-56.5) years and 7 (2-12) years after diagnosis. The most prevalent cause of death was infection (57/90, 63.3%) followed by SLE (40/90, 44.4%). The modified SLICC frailty index scores before death revealed that 73/90 (81.1%) were least fit or frail. In the last year of life, patients spent 56.9% of days on IS, the median CS dose was 10 (2.2-17.8) mg/day and visit interval was 85 (50-117) days; 41/90 (53.9%) had treatment escalated whereas 16/90 (21.1%) received treatment tapering.

A model that included age, sex, anti-malarial use, country gross domestic product (GDP), haemoglobin, albumin, CS dose, SDI, SLEDAI and modified SLICC frailty was not sensitive (65.6%) or specific (73.4%) in identifying patients who would demise in a year. (Table 1).

In multivariable GEE models, the odds of flare were higher in the last year of life (OR 1.59, 95% CI 1.09-2.31, p=0.016). Patients had higher odds of staying in low disease activity (LLDAS) before the last year of life (OR 3.63, 95% CI 2.17-6.05, p< 0.01). Patients had fewer days on IS in the year preceding death, as compared to other years (p= 0.047), but had higher daily CS doses (p< 0.01) and shorter visit intervals (p< 0.01). Patients in the last year of life received more treatment escalations (OR 2.30, 95% CI 1.29-4.13, p=0.005). There were no significant differences in treatment tapering, PCS or MCS scores before or during the year preceding death.

Conclusion: In the year leading up to demise, SLE patients suffer increased flares and higher treatment burden. Existing disease-related instruments, laboratory and clinical variables have limited utility in identifying patients who would die within a year. Our results highlight an urgent need to better identify and support SLE patients near the end-of-life.

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Abstract Number: 2557

Clinicopathologic Features of Patients with Giant Cell Arteritis and Thoracic Aorta Repair: A Single Center Experience over Two Decades

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders II: Clinical

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Patients with giant cell arteritis (GCA) are at increased risk of thoracic aortic aneurysm and dissection. This late complication of the disease is presumed to reflect damage from prior aortitis, however whether ongoing aortic inflammation contributes to aneurysm formation is largely unknown. The aim of this project was to investigate the clinicopathologic findings of patients with GCA who underwent thoracic aorta repair.

Methods: Patients who had thoracic aorta surgery at our institution between January 1, 2000, and December 31, 2021, were identified and screened for a prior diagnosis of GCA. The available data was manually abstracted from the medical records of all study subjects, and two cardiovascular pathologists reviewed available aorta tissue obtained during surgery. Grade 1 inflammation of the aorta was defined as inflammation limited to the peri-vasa vasorum or focal involvement, grade 2 was defined as inflammation beyond the peri-vasa vasorum or multifocal involvement but less than 50% of the medial thickness, grade 3 was defined as diffuse inflammation with involvement of equal or more than 50% of the medial thickness. Survival rates were estimated using Kaplan-Meier methods. Overall observed survival was compared with lifetable rates from the US population. The standardized mortality ratio was estimated as the ratio of the observed and expected number of deaths.

Results: Of the 4621 patients who underwent thoracic aorta surgery during the study period, 49 had a previous diagnosis of GCA (Table 1). Thirty-two (65%) were female, and 43 (88%) patients had either positive temporal artery biopsy or met the 1990 ACR or 2022 ACR/EULAR classification criteria for GCA. Forty-one patients had cranial symptoms at GCA diagnosis. All patients were considered in clinical remission at the time of aortic surgery. Ten (20%) patients had thoracic aortic dissection. Inflammatory markers (median [IQR]) were lower at the time of aortic surgery compared to initial diagnosis (erythrocyte sedimentation rate (mm/hr): 91 [54.0- 109.5] vs. 10 [5.0- 20.0]; C-reactive protein (mg/L): 76.5 [28.0- 139.0] vs. 3.1 [3.0- 8.0]). Histopathologic evaluation of the aortic tissue revealed active aortitis in most patients with GCA (40/49, 82%) after a median (IQR) of 6.0 (2.6- 10.3) years from GCA diagnosis. Healed aortitis was detected in 5 (10%) patients, and in 4 (8%) patients there was no evidence of active or healed aortitis. Nineteen (39%) patients were on immunosuppressive treatment at the time of aortic surgery. The detailed histopathologic re-evaluation of 43 out of 49 aortic samples revealed grade 1 aortitis in 17 (40%) patients, grade 2 in 12 (28%), and grade 3 in 5 (12%) (Table 2). The overall mortality compared to age and sex-matched general population was significantly increased with a standardized mortality ratio of 1.55 (95% CI, 1.05- 2.19) (Figure 1).

Conclusion: Histopathologic evaluation of the thoracic aorta obtained during surgery revealed active aortitis in most patients with GCA despite being considered in clinical remission several years after the initial diagnosis. Chronic, smoldering aortic inflammation likely contributes to the development of aortic aneurysm and dissection in GCA.

Table 1. Characteristics of the patients with giant cell arteritis who had thoracic aorta surgery.

	Total (n=49)	Active Aortitis (n=40)	Healed Aortitis (n=5)	No Evidence of Active or Healed Aortitis (n=4)
Age at GCA diagnosis, mean (SD) years	68.4 (7.66)	68.3 (7.52)	64.3 (7.90)	74.0 (7.12)
Age at aortic surgery, mean (SD) years	75.3 (7.25)	75.3 (7.42)	74.9 (7.90)	75.7 (6.42)
Sex, female	32 (65%)	28 (70%)	4 (80%)	0 (0%)
Race, white	48 (98%)	39 (98%)	5 (100%)	4 (100%)
Smoking, ever	27 (55%)	21 (53%)	3 (60%)	3 (75%)
Body mass index, mean (SD)	26.05 (4.22)	25.84 (3.93)	24.58 (5.80)	29.65 (4.77)
Polymyalgia rheumatica	20 (41%)	18 (45%)	0 (0%)	2 (50%)
Hypertension	43 (88%)	34 (85%)	5 (100%)	4 (100%)
Diabetes mellitus	6 (12%)	5 (13%)	0 (0%)	1 (25%)
Hyperlipidemia	37 (76%)	30 (75%)	4 (80%)	3 (75%)
Length of time between GCA diagnosis and aorta surgery, median (IQR) years	5.6 (2.5- 10.4)	6.0 (2.6- 10.3)	11.5 (9.5- 11.6)	1.9 (0.9- 2.6)
Follow-up duration, median (IQR) years	6.3 (2.8- 8.7)	6.4 (3.0- 8.6)	8.5 (2.5- 11.4)	4.3 (2.6- 8.9)
Positive Temporal Artery Biopsy	32/41 (78%)	27/35 (77%)	4/4 (100%)	1/2 (50%)
1990 ACR GCA Classification	39 (80%) [a]	33 (83%)	3 (60%)	3 (75%)
2022 ACR/EULAR GCA Classification	36 (73%) [b]	31 (78%)	4 (80%)	1 (25%)
Patients diagnosed with GCA at our institution	21 (43%)	19 (48%)	1 (20%)	1 (25%)
Duration of treatment with GCs prior to aortic surgery, median (IQR) years	2.0 (1.0- 3.9)	2.2 (1.0- 4.1)	2.5 (1.7- 6.3)	0.6 (0.4- 1.6)
Number of patients on immunosuppressive treatment at aortic surgery	19 (39%)	16 (40%)	1 (20%)	2 (50%)

[a] 6/10 patients who did not meet the 1990 ACR Criteria had limited data for at least one of the criteria questions.
[b] 7/13 patients who did not meet the 2022 ACR/EULAR Criteria had limited data for at least one of the criteria questions.

Table 2. Detailed histopathologic re-evaluation of 34 aorta specimens showing active aortitis.

Inflammatory Pattern	Total Active Aortitis (n=34)	Grade 1 Active Aortitis (n=17)	Grade 2 Active Aortitis (n=12)	Grade 3 Active Aortitis (n=5)
Granulomatous	15 (44%)	7 (41%)	6 (50%)	2 (40%)
Lymphoplasmacytic	12 (35%)	7 (41%)	4 (33%)	1 (20%)
Mixed (Both granulomatous and lymphoplasmacytic)	3 (9%)	0 (0%)	1 (8%)	2 (40%)
Other	4 (12%)	3 (18%) (lymphohistiocytic)	1 (8%) (predominantly granulomatous, focally suppurative)	0 (0%)

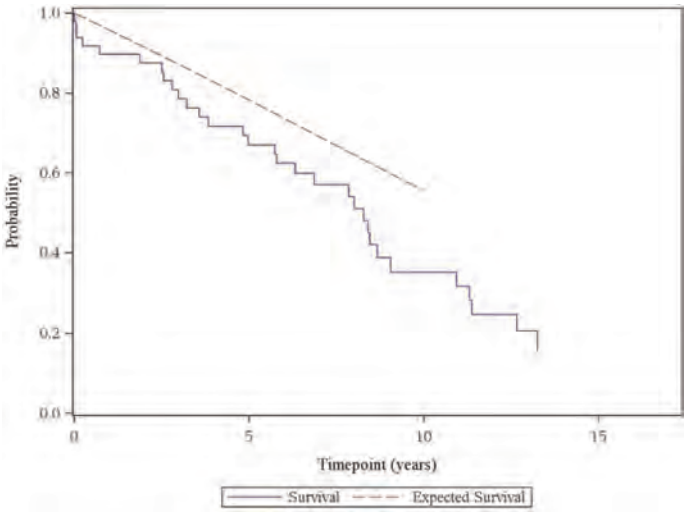

Figure 1. Overall survival of the patients with giant cell arteritis compared to expected rates from United States total lifetables (observed: solid blue line; expected: dashed red line).

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Abstract Number: 2558

Aortic Aneurysms in a Multicenter Cohort of 196 Patients with Aortitis Related to Giant Cell Arteritis Treated with Tocilizumab

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SESSION INFORMATION

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Background/Purpose: Aortic aneurysms is a serious complication that can occur in patients with giant cell arteritis (GCA) **(1-2)**. Tocilizumab (TCZ) is approved for GCA. Nevertheless, to date, the usefulness of TCZ in aortic aneurysms has not been evaluated.

Our aim was to assess the role of TCZ in **a)** prevention of development of aneurysms, and **b)** impairment of aneurysm if present.

Methods: Observational, multicenter study of 196 patients with aortitis related to GCA treated with TCZ. Patients were diagnosed with GCA accordingly to **a)** American College of Rheumatology criteria, and/or **b)** positive biopsy of temporal artery, and/or **c)** the presence of imaging techniques consistent with LVV.

TABLE 1. Main features of 196 patients with aortitis related to GCA.

	Overall N=196	GCA-aortitis with aneurysm (n=10)	GCA-aortitis without aneurysm with imaging follow-up test (n=95)	p
General features				
Age (mean±SD)	71.3± 9.5	68.1±9.7	67.7±9.4	0.840
Female/Male (% of female), n	148/ 48 (75.5)	7/3(70)	71/24(75)	0.500
Time from GCA diagnosis to TCZ onset (months), median	7 [2-18.7]	2 [3-15]	9 [3-18]	0.509
Positive TAB, n (%)	56 (50)	2 (29)	26 (46)	0.434
Clinical phenotype of GCA				
Extra-cranial, n (%)	70 (36)	6 (60)	38 (40)	0.188
Mixed, n (%)	126 (64)	4(40)	57(60)	0.188
Cardiovascular risk factors				
High blood pressure, n (%)	112 (57)	8 (80)	53 (56)	0.151
Dyslipidemia, n (%)	103 (53)	7 (70)	52 (55)	0.320
Diabetes, n (%)	26 (13)	1 (10)	12 (14)	0.627
Previous or current smoking history, n (%)	20 (10)	2 (20)	13 (14)	0.451
Ischemic manifestations				
Visual involvement, n (%)	16 (8)	2(20)	5 (5)	0.133
Headache, n (%)	74 (38)	2(20)	34 (36)	0.258
Jaw claudication	27 (14)	0 (0)	9 (9)	0.375
Systemic manifestations				
Fever, n (%)	24 (12)	2 (20)	8 (8)	0.208
Constitutional syndrome, n	87 (44)	5 (50)	39 (41)	0.309
PmR, n (%)	131 (67)	4 (40)	60 (63)	0.226
Acute phase reactants				
ESR, mm/1st hour, median	32 [14-54]	36 [12.5-97.5]	26 [13-48]	0.162
CRP (mg/dL), median [IQR]	1.5 [0.6-3.4]	3.2 [1.1-10.4]	1.4 [0.6-2.3]	**0.000**
Prednisone dose, mg/day, mean±SD	15 [10-30]	12.5 [9.4-35]	10 [7.5-20]	0.138
TCZ mono/TCZ combo, n (% TCZ mono)	136/60 (69)	8/2 (80)	56/39 (59)	0.170

Abbreviations: CRP: C-reactive protein; ESR: erythrocyte sedimentation rate, GCA: giant cell arteritis, IQR: interquartile range, PmR: polymyalgia rheumatica; SD: standard deviation, TCZcombo: tocilizumab in combination with synthetic immunosuppressants (besides corticosteroids), TCZmono: tocilizumab in monotherapy (besides corticosteroids)

Main features of 196 patients with aortitis related to GCA

TABLE 2. Characteristics and outcome of aortic aneurysms in treatment with TCZ

	AT TCZ INITIATION				FOLLOW-UP			
Case	Age/Sex	Localization of aneurysm	Imaging technique of aneurysm diagnosis	Maximum diameter of aneurysm (cm)	Follow-up imaging technique of aneurysm evaluation	Time from TCZ initiation (months)	Maximum diameter of aneurysm	Surgery due to aneurysm
1	60/Male	2 aneurysms in abdominal aorta	^{18}F-FDG PET/CT scan and CT-A	11 and 13	Not performed	–	–	yes
2	75/Male	Thoracic aorta	^{18}F-FDG PET/CT scan and CT-A	6.2	Not performed	–	–	yes
3	51/Female	Aortic arch	^{18}F-FDG PET/CT scan	7	Not performed	–	–	yes
4	78/Female	Aortic arch	^{18}F-FDG PET/CT scan and CT-A	5.9	Not performed	–	–	yes
5	69/Female	Thoracic aorta	CT-A	4.8	Not performed	–	–	yes
6	67/Male	Abdominal aorta	^{18}F-FDG PET/CT scan and CT-A	4.7	^{18}F-FDG PET/CT scan and CT-A	8	4.8	yes
7	54/Female	Supraaortic trunk	^{18}F-FDG PET/CT scan	5.1	CT-A	15	8	Yes (Died during surgery)
8	89/Female	Thoracic aorta	^{18}F-FDG PET/CT scan and CT-A	4.7	CT-A	14	5.4	yes
9	68/Female	Thoracic aorta	^{18}F-FDG PET/CT scan and CT-A	3.4	CT-A	10	3.3	No
10	78/Female	Thoracic aorta	^{18}F-FDG PET/CT scan	3.9	Not performed	–	–	No

Abbreviations: CT-A: computed tomography angiography; ^{18}F-FDG PET/CT: ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography

Characteristics and outcome of aortic aneurysms in treatment with TCZ

Patients with GCA-aortitis were divided into two subgroups: **a)** with, and **b)** without aortic aneurysms.

Results: We studied 196 (148 women/48 men; mean age 71.3±9.5 years) patients with aortitis related to GCA treated with TCZ. Aortitis was confirmed by PET in all cases. Aortic aneurysms were present in 10 of 196 (5%) patients when TCZ was initiated.

Imaging in follow-up was present in these 10 patients and in 95 of the remaining 186 patients, that were finally studied. Main general features of both groups are shown in **TABLE 1.** No significant differences were observed between the two groups except for the median serum CRP value, which was higher in the group of patients with aneurysms. After a mean follow-up of 25±19 months, none of the 95 GCA-aortitis patients without aneurysm at TCZ initiation developed any aneurysm.

In **TABLE 2** are summarized the characteristics and follow-up of the 10 patients with aneurysms. Aneurysms were more frequently located in thoracic segment (n=5; 50%). Early surgery was required in 5 cases at TCZ initiation, and the usefulness of TCZ in these cases could not be assessed. From the remaining 5 patients, 3 patients experienced aneurysm growth despite TCZ therapy and a surgery was required during follow-up. The other 2 patients remained stable and did not require surgery due to the small size of the aneurysm.

Conclusion: Aortic aneurysms is a rare, but not exceptional complication in patients with aortitis related to GCA. In these patients, although TCZ could prevent the development of new aneurysms, it does not appear to prevent aneurysm growth.

References.

1. Nuenninghoff DM, et al. Arthritis Rheum. 2003. PMID: 14674004
2. Loricera J, et al. Rev Esp Med Nucl Imagen Mol. 2015. PMID: 26272121

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Abstract Number: 2559

Clinical Manifestations and Immunomodulatory Treatment in Patients with Relapsing Polychondritis

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SESSION INFORMATION

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Session Type: Abstract Session

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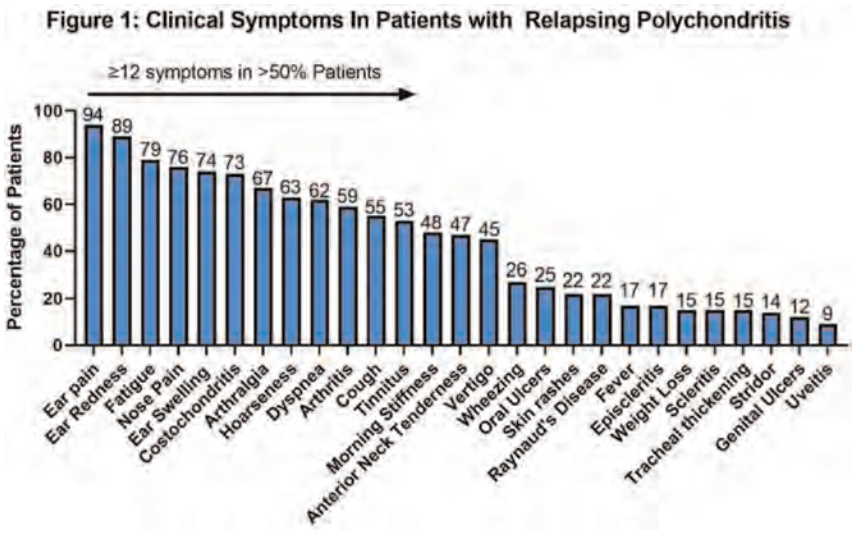
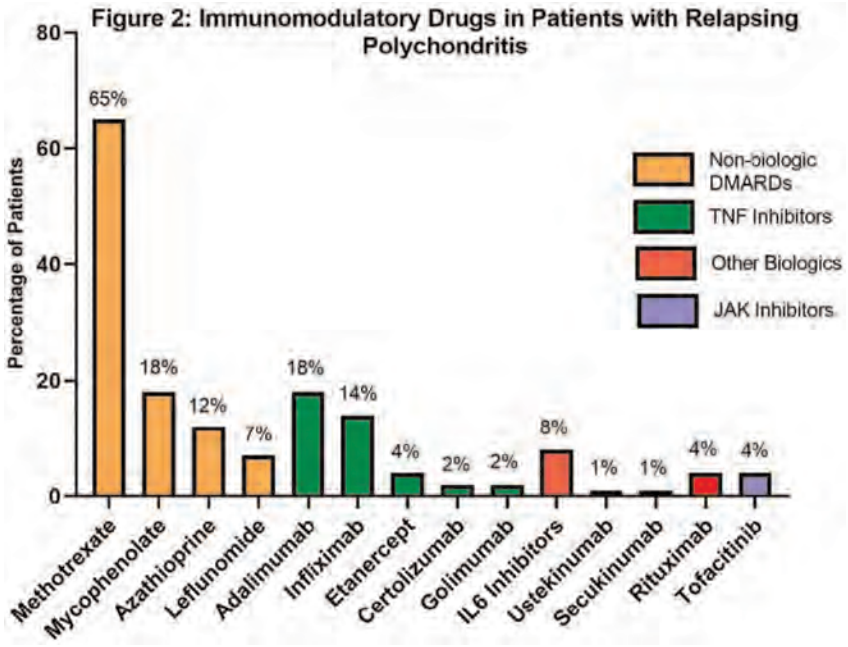
Background/Purpose: Relapsing polychondritis (RP) is a rare systemic inflammatory disease without standard treatment guidelines. This study aims to investigate the clinical characteristics, current treatment approaches, and association between clinical manifestations and immunomodulatory medication use in patients with RP.

Methods: This study included adult patients with physician-diagnosed RP enrolled in a multicenter prospective observational cohort. Data collected at baseline included demographics, clinical manifestations of RP ever experienced, disease damage indices, and immunomodulatory medications ever received. History of immunomodulatory treatment was categorized into three groups: I) no treatment or treatment only with glucocorticoids (GCs); II) treatment with non-biologic immunosuppressive (IS) drugs [other than Janus kinase inhibitors (JAKis)] with/ without GCs; III) treatment with JAKis and/or biologic IS with/without GCs/non-biologic IS. Chi-square test and logistic regression were used to determine the association between categorical and continuous independent variables.





Results: The study included 195 patients with RP. The clinical characteristics are detailed in **Figure 1**. Mean age was 49 (SD 13) years, with 86% (n=167) female, and 89% (n=174) Caucasians. Mean age at diagnosis was 43 (SD 13) years and mean disease duration was 5 (3-8) years.

All patients in the cohort had ear-nose-throat involvement and the majority (83%, n=163) had musculoskeletal manifestations. Clinical manifestations were heterogeneous and >50% (n=102) of patients had 12 or more symptoms (**Figure 1**). Permanent organ damage included sensorineural hearing loss in 26% (n=50), auricular deformity in 12% (n=23), saddle nose deformity 12% (n=23) and subglottic stenosis (SGS) in 9% (n=18). In subjects who underwent dynamic CT chest (n=162), tracheomalacia and bronchomalacia were found in 31% (n=50) and 20% (n=32), respectively.

Distribution per treatment group was: group I- 37 (19%) patients; group II- 55 (28%) patients; and group III- 103 (53%) patients. Most patients 95% (n=186) received treatment with GCs. The most frequently prescribed non-biologic drug was methotrexate in 65% (n=126) and the most prescribed class of biologic drugs was TNF inhibitors (29%, n=57) (**Figure 2**). Patients with arthritis were more likely to be in treatment group III (63%) compared to groups I and II (14% and 22%; P=0.01). Nasal inflammation was common in groups II and III (80% each) compared to group I (56%; P=0.02). Dry cough was associated with Group III (61%) vs Groups I and II (13% and 26%, P= 0.03). Patients with SGS were more likely to be in Group III (88%) vs group I and II (5%, P< 0.01). Tracheal thickening was also more common in Group III (76%) vs Groups I and II (16% and 8%; P=0.03).

Conclusion: Patients with RP have heterogeneous clinical presentations and are treated with a variety of immunosuppressive drugs. Arthritis, nasal inflammation, cough, SGS and tracheal thickening were associated with more frequent use of biologic drugs/JAKi or non-biologic IS. These findings highlight the absence of a consensus approach to treatment of RP and underscore the need for clinical trials and treatment guidelines in RP.

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Abstract Number: 2560

Risk of Gastrointestinal Perforation Among Patients with Giant Cell Arteritis Who Received Tocilizumab

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders II: Clinical
Session Type: Abstract Session
Session Time: 4:00PM–5:30PM

Background/Purpose: Exposure to the interleukin-6 inhibitor tocilizumab has been associated with an increased risk of gastrointestinal (GI) perforation in patients with rheumatoid arthritis. No studies to date have evaluated the risk of GI perforation in patients with giant cell arteritis (GCA) on treatment with tocilizumab. This study aimed to describe the incidence and risk factors associated with GI perforation among incident cases of GCA receiving treatment with tocilizumab.

Methods: We performed a retrospective cohort study of incident cases of GCA using the US-based TriNetX electronic health records database from 1/1/2010 to 4/23/2023. Patients were included if they had (1) 2 ICD-9CM/ICD10-CM codes for GCA separated by 30 days but within 1 year and (2) received any dose of prednisone within 30 days of the first GCA code. Gastrointestinal perforations were defined by ICD-9-CM/ICD-10-CM codes as described previously, and the incidence of gastrointestinal perforations as well as unadjusted incident rate ratios were calculated.1 Adjusted analysis using a Poisson regression was conducted. The clone-censor-weight approach was then used to account for immortal time bias. After cloning, censoring, and weighting using inverse probability of censoring, time-updated multivariable Cox proportional hazards models were used to calculate the hazard ratio (HR) and 95% confidence intervals for the risk of GI perforation.

Results: During the study period, 5,142 patients met the inclusion criteria (845 tocilizumab exposed and 4,297 tocilizumab unexposed), the majority of whom were female (3,624, 70.5%) and white (3,728, 72.5%) (Table 1). Incident GI perforations among tocilizumab exposed vs. unexposed were 2.0/1,000 person-years and 3.4/1,000 person-years, respectively, resulting in an incident rate ratio of 0.57 (95% CI 0.14-2.41). The adjusted rate ratio (RR) of GI perforation with tocilizumab use in a Poisson regression was RR 0.56 (95% CI 0.13-2.38). Factors associated with GI perforation included the history of diverticulitis (RR 3.51, 95% CI 1.55-7.96) and the use of intravenous methylprednisolone (RR 5.41, 95% CI 2.41-12.12). After implementing the clone-censor-weight approach, tocilizumab exposure was not associated with an increased risk of GI perforation (HR 1.05, 95% CI 0.30-1.65).

Conclusion: In this retrospective cohort study of patients with incident GCA, GI perforations were rare. When compared with steroid treatment, tocilizumab exposure was not associated with an increased risk of GI perforation. Risk factors for GI perforation included a history of diverticulitis and intravenous methylprednisolone use. These findings highlight the importance of judicious steroid use and will be useful for counseling patients considering initiation of IL-6 inhibitors.

Reference

1. Curtis JR. Arthritis Rheum. 2011 Feb;63(2):346

Table 1. Demographic and clinical characteristics, n = 5,142

Characteristic	Overall	Tocilizumab Exposed	Tocilizumab Unexposed
Total Number of Patients	5,142	845	4,297
Age at Diagnosis, mean (SD)	72.4 (8.9)	73.1 (8.0)	72.2 (9.0)
Gender	-	-	-
Female	3,624 (70.5%)	609 (72.1%)	3,015 (70.2%)
Male	1,518 (29.5%)	236 (27.9%)	1,282 (29.8%)
Race/Ethnicity	-	-	-
White	3,728 (72.5%)	691 (81.8%)	3,037 (70.7%)
Black or African American	720 (14.0%)	66 (7.8%)	654 (15.2%)
Hispanic or Latino	228 (4.4%)	19 (2.2%)	209 (4.9%)
Asian	83 (1.6%)	12 (1.4%)	71 (1.7%)
Other / NA	383 (7.4%)	57 (6.7%)	326 (7.6%)
Admissions during Prior Year, mean (SD)	0.9 (2.2)	0.5 (1.9)	0.9 (2.3)
Encounters during Prior Year, mean (SD)	21.6 (25.0)	19.5 (21.0)	22.1 (25.6)=
Comorbidities at Diagnosis	-	-	-
Charlson Comorbidity Index, mean (SD)	1.3 (1.8)	1.0 (1.6)	1.4 (1.9)
Diabetes	1,455 (28.3%)	179 (21.2%)	1,276 (29.7%)
Chronic Obstructive Pulmonary Disease	1,267 (24.6%)	177 (20.9%)	1,090 (25.4%)
Renal Disease	867 (16.9%)	102 (12.1%)	765 (17.8%)
Obesity	847 (16.5%)	103 (12.2%)	744 (17.3%)
Congestive Heart Failure	712 (13.8%)	87 (10.3%)	625 (14.5%)
Diverticulitis	613 (11.9%)	75 (8.9%)	538 (12.5%)
Liver Disease	308 (6.0%)	31 (3.7%)	277 (6.4%)
Smoking	219 (4.3%)	19 (2.2%)	200 (4.7%)
Diverticulosis	6 (0.1%)	0 (0%)	6 (0.1%)

*Diverticulitis and diverticulosis used a lookback period from the first recorded diagnostic code to the index date; the other comorbidities used 1 year prior to the index date
Data presented as n(%), unless specified otherwise.

Disclosure: D. Nepal: None; **S. Sattui**: AstraZeneca, 5, Bristol Myers Squibb Foundation, 5, Rheumatology Research Foundation, 5, Sanofi, 2, 5; **Z. Wallace**: BioCryst, 2, Bristol-Myers Squibb(BMS), 5, Horizon, 1, 2, 5, MedPace, 2, Novartis, 1, PPD, 2, Sanofi, 1, 5, Shionogi, 1, Visterra, 1, 2, Zenas, 1, 2; **M. Putman**: AbbVie/Abbott, 12, Trial participation, AstraZeneca, 12, Trial participation, Novartis, 2.

Abstract Number: 2561

The Prognostic Value of the "2022 ACR/EULAR Classification Criteria for Giant Cell Arteritis": Data from the Italian Society of Rheumatology Vasculitis Study Group

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders II: Clinical

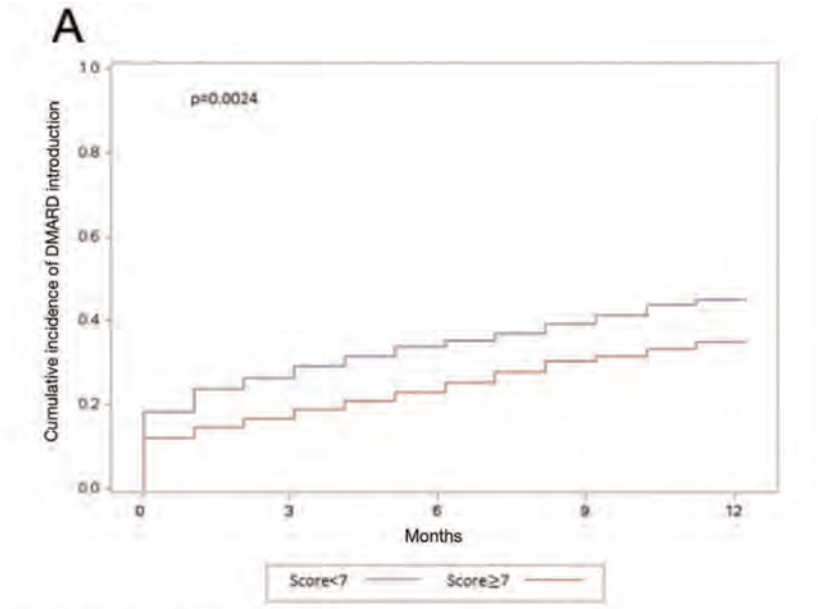
Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: The 2022 classification criteria for giant cell arteritis (GCA) have been recently published. The aim of this study is to investigate whether the score obtained by summing clinical and laboratory items and the fulfillment of each item correlate with prognosis.

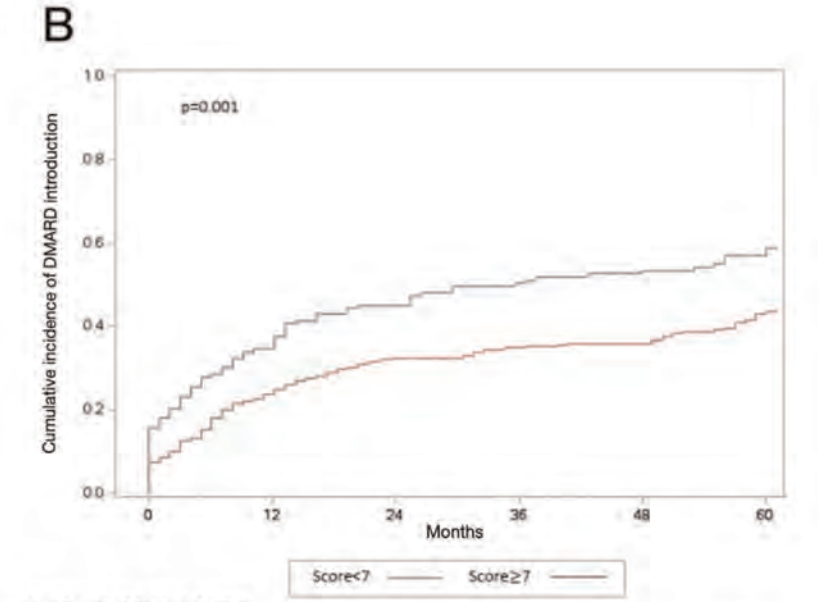
Methods: Data of GCA patients from centres belonging to the Italian Society of Rheumatology Vasculitis Group were retrospectively reviewed. Baseline clinical/laboratory items included in the 2022 GCA classification criteria were retrieved and summed to obtain a total score (from 0 to 16). Therapy-related complications, disease-related outcomes and need for disease-modifying drug (DMARD) introduction at baseline (only for visual loss [VL]), at 12 months and at 60 months were evaluated. Univariate and multivariate logistic analyses were performed.

Results: 873 patients (mean score, 8.1 ± 3.3; mean items fulfilled per-patient, 4.2 ± 1.6) were included. Follow-up data were available for all patients at 12 months and for 467 (53.4%) patients at 60 months. At GCA onset, 165 (18.9%) patients had VL. At 12 and 60 months, 41 (4.7%) and 28 (6.0%) patients developed ascending aorta aneurysm (AAA), 86 (9.9%) and



Number of subjects at risk (%)

Score<7	257 (100%)	189 (73.5%)	170 (66%)	156 (60.7%)	141 (55%)
Score≥7	616 (100%)	513 (83%)	475 (77%)	428 (69.5%)	401 (65%)



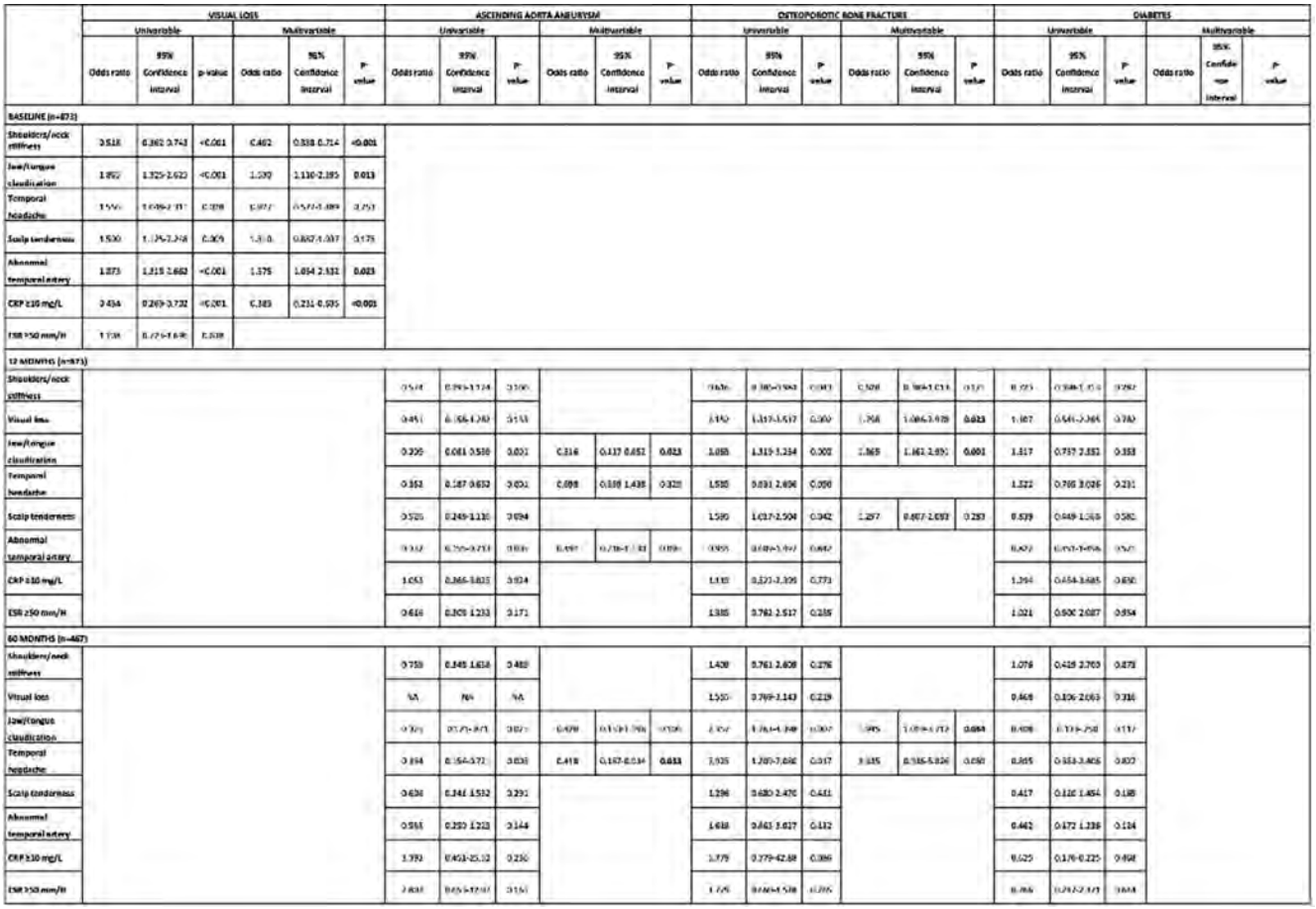
Number of subjects at risk (%)

Score<7	133 (100%)	87 (65.4%)	73 (55%)	66 (49.6%)	62 (46.6%)	55 (41%)
Score≥7	334 (100%)	254 (76%)	226 (67.6%)	217 (65%)	214 (64%)	188 (56%)

Figure legend. Cumulative incidence of DMARD introduction in patients with a score <7 (blue line) and in patients with a score ≥7 (red line) at 12 (A) and 60 months (B).

45 (9.6%) patients suffered from osteoporotic fractures (OF), 49 (5.6%) and 19 (4.1%) patients developed diabetes, respectively. 331 (38%) and 224 (48.0%) patients were prescribed ≥1 DMARD within 12 and 60 months, respectively.

Table legend. Univariate and multivariate logistic analyses evaluating the association of each item with different outcomes.



At univariate analysis, a higher score (excluding 'VL') was associated with VL (OR 1.551 [95%CI 1.439-1.672], p< 0.0001). A higher score was associated with AAA (OR 0.769 [0.687-0.860], p=0.0012; 0.814 [0.718-0.923], p=0.0014) at 12 and 60 months, OF (OR 1.102 [1.029-1.180], p=0.0057, 1.171 [1.064-1.290], p=0.0013) at 12 and 60 months, diabetes at 60 months (OR 0.856 [0.740-0.990], p=0.0364), and need for DMARD introduction at 12 (OR 0.948 [0.909-0.989], p=0.0135) and 60 months (OR 0.902 [0.853-0.955], p=0.0003). A score < 7 was associated with DMARD introduction at both timepoints (Figure).

At multivariate analysis, jaw/tongue claudication and temporal artery abnormality were directly associated with whereas polymyalgic symptoms and CRP ≥10 mg/L were inversely associated with VL. Jaw/tongue claudication was associated with a lower risk of AAA and higher risk of OF at 12 months and with a higher risk of OF at 60 months; headache with a lower risk of AAA at 60 months and VL with a higher risk of OF at 12 months (Table).

Conclusion: Considering only clinical and laboratory items, a higher score obtained from the 2022 GCA classification criteria is positively associated with VL and OF, and negatively with AAA and diabetes. A score < 7 is associated with a higher probability of receiving a DMARD. Cranial symptoms increase the risk of VL and OF but reduce the risk of AAA. PMR symptoms and high CRP levels are protective for VL.

Disclosure: A. Tomelleri: Novartis, 1; **C. Campochiaro**: Boehringer Ingelheim, 1, 6, Janssen, 1, 6, Novartis, 1, 6; **F. Muratore**: None; **S. Monti**: CSL Vifor, 6; **N. Farina**: None; **C. Marvisi**: None; **E. Galli**: None; **A. Milanesi**: None; **N. Viapiana**: None; **A. Berti**: None; **R. Bortolotti**: None; **M. Bond**: AbbVie/Abbott, 5; **R. Padoan**:

GlaxoSmithKlein(GSK), 6; **M. Felicetti**: None; **F. Schiavon**: None; **C. Nannini**: None; **F. Cantini**: None; **A. Giollo**: Eli Lilly, 6, galapagos, 2, 6, Novartis, 2, Sandoz, 2; **M. Rossini**: None; **E. Conticini**: None; **B. Frediani**: None; **F. Conti**: None; **R. Priori**: None; **M. Sebastiani**: None; **G. Cassone**: None; **L. Quartuccio**: None; **E. Treppo**: None; **S. Bettio**: None; **A. Hoxha**: None; **M. Lovisotto**: None; **G. Emmi**: AstraZeneca, 2, Boehringer-Ingelheim, 2, GlaxoSmithKlein(-GSK), 2, Novartis, 2, Sanofi, 2, Sobi, 2; **i. mattioli**: None; **P. Leccese**: None; **R. Caporali**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celltrion, 2, 6, Fresenius Kabi, 2, Galapagos, 2, 6, Janssen, 2, 6, Lilly, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, Sandoz, 2, 6, UCB, 2, 6; **L. Argolini**: None; **R. Foti**: None; **E. Visalli**: None; **M. Colaci**: None; **C. Montecucco**: None; **L. Dagna**: AbbVie/Abbott, 2, AstraZeneca, 2, biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, 5, Eli Lilly, 2, galapagos, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Kiniksa Pharmaceuticals, 2, Novartis, 2, 6, Pfizer, 2, 5, SOBI, 2, 5, 6; **C. Salvarani**: CSL Vifor, 1, 2, 6, Eli Lilly, 1, 2, 6.

Abstract Number: 2562

Immune Checkpoint Inhibitors-Induced Large Vessel Vasculitis: Data from a Multicenter Study

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders II: Clinical

Session Type: Abstract Session

Session Time: 4:00PM–5:30PM

Background/Purpose: Immune checkpoint inhibitors (ICIs) have dramatically improved the prognosis for many cancers. The therapeutic effect of ICIs is based on their ability to release the brakes on lymphocyte activation. However, this brake release can cause immune-related adverse events (IrAEs) in up to 60-80% of cases. Few observations of ICI-induced large vessel vasculitis (LVV) have been reported. We aimed to describe the characteristics and outcomes of LVV occurring after or during ICI therapy.

Methods: We conducted a European, multicenter, retrospective study of patients who received at least one infusion of ICI and subsequently presented with LVV between March 2018 and January 2023. The diagnosis of giant cell arteritis (GCA) among LVV patients was based on the 2022 ACR/EULAR classification criteria. Remission was defined by the absence of manifestations attributable to active vasculitis and normal acute phase reactants.

Results: Nineteen patients were included (median age 70 (IQR 61-75) years). Previous history of PMR or GCA was noted in 4 (21%) patients. The two most common cancers treated with ICIs were melanoma (32%) and renal cell carcinoma (26%). Five (26%) patients received a combination of nivolumab and ipilimumab, 7 (37%) pembrolizumab, 6 (32%) nivolumab, and 1 (5%) atezolizumab. First LVV manifestations occurred after a median of 5 (IQR 3-19) ICI infusions and a median time of 4 (IQR 2-15) months since the first ICI infusion.

Six (32%) patients had cephalic manifestations, 6 (32%) had vascular manifestations, and 7 (37%) had both. Four patients (21%) had visual loss. Nine (47%) patients had PMR symptoms and 5 (26%) had other IrAEs, mainly hepatitis. 18F-FDG PET/CT showed hypermetabolism of the aorta or its main branches in 12 (63%) patients. Temporal artery biopsy was positive in 3/6 cases. Overall, 13 (68%) of patients fulfilled ACR/EULAR criteria for GCA.

ICIs were still being used at the onset of LVV in 16 patients, while they were discontinued prior to LVV in 3 patients. For patients still on ICIs, management consisted of definitive discontinuation of ICIs in 10 (53%) patients and temporary discontinuation or continuation of ICIs in 6 (32%) patients.

All patients received oral glucocorticoids. The median initial prednisone dose was 0.7 g/kg/d (IQR 0.7-1). Two (11%) patients received tocilizumab as first-line therapy.

Median follow-up after LVV diagnosis was 8 months (IQR 4-14). Remission was achieved in 18 (95%) patients. Three patients relapsed during prednisone tapering, at a median dose of 10 mg/d (IQR 5-15). Overall, 4 (21%) patients did not respond or relapsed during prednisone tapering, including 1/13 (8%) of patients who discontinued ICIs and 3/6 (50%) of patients who continued to receive ICIs. At the end of follow-up, 4/18 (22%) patients had died, 3 of cancer and 1 of acute coronary syndrome.

Conclusion: LVV is a rare IrAE that usually occurs early after the initiation of ICI. Unexplained elevations in acute phase reactants in ICI-treated patients should prompt clinicians to look for signs of LVV, as severe ischaemic manifestations such as visual loss may occur. Patients with ICI-induced LVV who were maintained on ICI or rechallenged had a more refractory or relapsing course.

Disclosure: A. Cottu: None; **A. Tomelleri**: Novartis, 1; **C. Campochiaro**: Boehringer Ingelheim, 1, 6, Janssen, 1, 6, Novartis, 1, 6; **A. Forestier**: None; **J. Dion**: None; **M. Bond**: AbbVie/Abbott, 5; **A. Laparra-ramakichenin**: None; **A. Gury**: None; **X. Savary**: None; **R. Dhote**: None; **A. Betrains**: None; **L. Bouillet**: None; **E. Liozon**: None; **E. Bories**: None; **A. Petitdemange**: None; **P. Legendre**: None; **B. Crichi**: None; **P. Kerschen**: None; **L. Carneiro-Esteves**: None; **L. Grange**: None; **B. Terrier**: AstraZeneca, 5, CSL Vifor, 2, GlaxoSmithKlein(GSK), 2.

Abstract Number: 2563

Causal Associations Between Gut Microbiota and Rheumatic Diseases: A Mendelian Randomization Study

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SESSION INFORMATION

Session Date: Wednesday, November 15, 2023
Session Title: Abstracts: Epidemiology & Public Health III
Session Type: Abstract Session
Session Time: 9:00AM–10:30AM

Background/Purpose: Gut microbiota has been increasingly recognized as important and novel targets for rheumatic diseases. However, previous studies mostly examined the associations, leaving causality largely unknown, which hinders the clinical application of gut microbiota in preventing and treating rheumatic diseases.

Figure 1. Mendelian randomization results of the correlations between 141 gut microbiota taxa and 14 rheumatic diseases. The red color represents a detrimental effect, while blue represents a protective effect of the gut microbiota on the rheumatic disease. The shade of color represents the significance of associations. Statistically significant (FDR < 0·05) results are indicated by an asterisk (*).

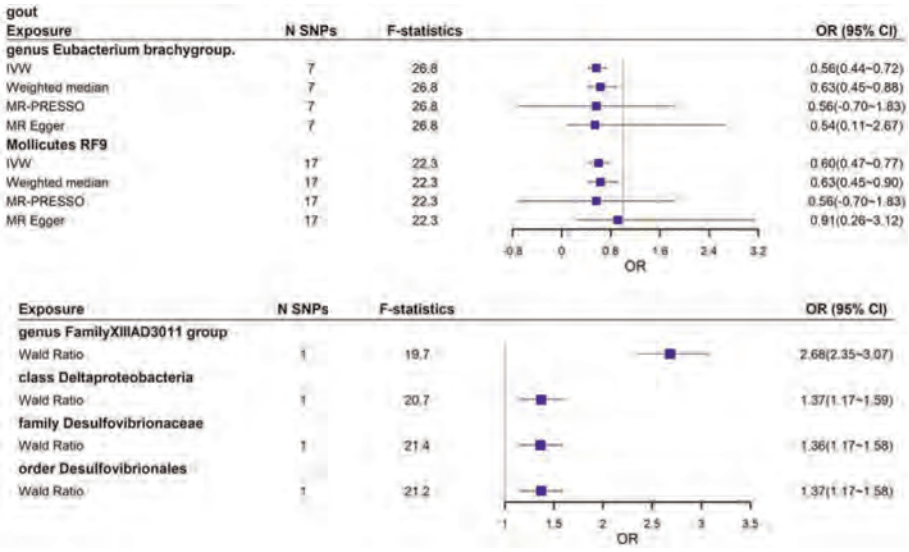
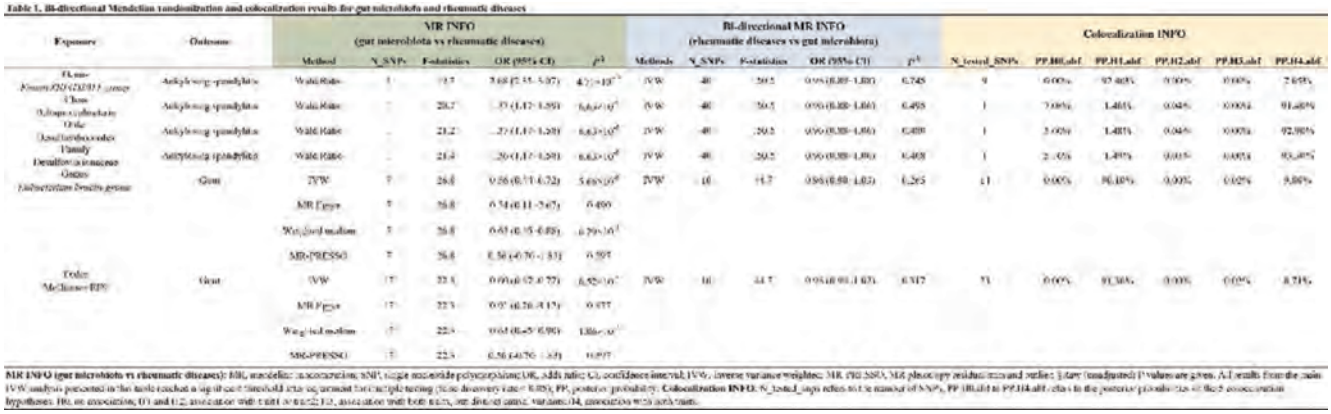


Figure 2. Forest plot for gout and ankylosing spondylitis N SNPs, number of genetic instruments; OR, odds ratio; CI, confidence interval; IVW, inverse-variance weighted; MR-PRESSO, MR pleiotropy residual sum and outlier. Wald ratio was calculated per SNP. If there were more than one SNP, IVW (primary), weighted median, and other MR methods were used to pool the result.

Methods: We performed Mendelian randomization (MR) analysis to investigate the causal associations between gut microbiota and rheumatic diseases. The genetic instruments for 141 gut microbiota taxa were extracted from the published genome-wide association study (GWAS) of individuals with European ancestry (N=18,340), and the summary statistics for 14 rheumatic diseases (sample size ranges from 6,190 to 417,596) were obtained from publicly available GWASs and the FinnGen database. Several MR methods (e.g., inverse-variance weighted and weighted median) were used to examine the causal association, and bi-directional MR and colocalization analyses were performed to examine the potential bi-directional causality and whether the gut microbiota and rheumatic disease share the same causal variant, respectively.

Results: Six pairs of relations between gut microbiota and rheumatic diseases remained statistically significant after multiple testing (FDR < 0.05), among which Genus *FamilyXIIIAD3011 group* (odds ratio [OR]=2.68, 95% CI=2.35-3.07), class Deltaproteobacteria (OR=1.37, 95% CI=1.17-1.59), family Desulfovibrionaceae (OR=1.36, 95% CI=1.17-1.58) and order Desulfovibrionales (OR=1.36, 95% CI=1.17-1.58) increased the risk of ankylosing spondylitis. Genus *Eubacterium brachy group* (OR=0.57, 95% CI=0.44-0.72), order Mollicutes RF9 (OR=0.61, 95% CI=0.48-0.77) decreased the risk of gout. Among them, the results were consistent across different MR methods. Using colocalization analysis, we identified that class

Table 1. Bi-directional Mendelian randomization and colocalization results for gut microbiota and rheumatic diseases



MR INFO (gut microbiota vs rheumatic diseases): MR, mendelian randomization; SNP, single nucleotide polymorphism; OR, odds ratio; CI, confidence interval; IVW, inverse-variance weighted; MR PRESSO, MR pleiotropy residual sum and outlier. P.raw (unadjusted) P values are given. All results from the main IVW analysis presented in the table reached a significant threshold after adjustment for multiple testing (false discovery rate< 0.05). PP, posterior probability. Colocalization INFO: N_tested_snps refers to the number of SNPs, PP.H0.abf to PP.H4.abf refers to the posterior probabilities of the 5 association hypotheses: H0, no association; H1 and H2, association with trait A (trait 1) and B, respectively, but distinct causal variants; H4, association with both traits, one shared causal variant.

Deltaproteobacteria, family Desulfovibrionaceae, and order Desulfovibrionales shared the same genetic variants with ankylosing spondylitis. No evidence of bi-directional causality was found between microbiota and rheumatic disease.

Conclusion: We identified and provided genetic evidence for six novel causal associations between gut microbiota taxa and rheumatic diseases. If confirmed by future animal studies or clinical trials, our results can serve as new clinical targets for rheumatic diseases and thus is conducive to the prevention and treatment of ankylosing spondylitis and gout.

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Abstract Number: 2564

The Effectiveness of a Fourth Dose of COVID-19 mRNA Vaccine in Patients with Systemic Autoimmune Rheumatic Diseases Using Immunomodulators: An Emulated Target Trial

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SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
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Background/Purpose: Many patients with systemic autoimmune rheumatic diseases (SARDs) using immunomodulators have blunted humoral responses to COVID-19 vaccines. As such, the initial mRNA vaccine series is defined as 3 doses for this population and a 4th (or first "booster") dose was recommended by the CDC in October 2021. However, 4th dose uptake among patients with SARDs has been low. In the general population, a 4th vaccine dose reduces the risk of breakthrough infection; its effectiveness in SARDs receiving immunomodulators has not been established.

Methods: We conducted an emulated target trial in a large US healthcare system, comparing receiving vs. not receiving a 4th vaccine. Eligible patients had SARDs by a validated algorithm including immunomodulator use and were eligible (by CDC guidelines) to receive a 4th dose of BNT162b2 or mRNA-1273 between 1/16/22-6/11/22. We excluded recipients of Ad26.COV2.S. To account for temporal changes in COVID-19 variants and guidance on 4th dose eligibility, the study period was divided into 1-week intervals. Cases were included in a 1-week interval if they received a 4th mRNA dose in that interval; comparators were eligible for a 4th dose but had not yet received it before or during the interval and had similar duration from 3rd dose to account for waning. The index date for cases was the date of 4th dose; for comparators, it was a random date within the interval.

The primary outcome was COVID-19 infection (positive COVID-19 PCR or antigen test or positive COVID-19 flag in the electronic record). Follow-up ended at the earliest of: (1) COVID-19; (2) bivalent vaccine availability (9/1/22); (3) "deviation" from the assigned arm (i.e., 5th dose for cases, 4th dose for comparators); (4) or non-COVID death as a competing risk. The

propensity score (PS) for receiving the 4th dose was calculated weekly using logistic regression. We performed time-stratified, overlap PS-weighted Cox regressions to examine the relation of the 4th dose to the risk of each outcome.

Results: We included a total of 4,010 patients who received ≥3 mRNA vaccines and were eligible for a 4th during the study period; of this group, 2994 received a 4th dose and 1014 did not. Baseline covariates before and after overlap weighting are shown in Table 1. The mean age was 67 years, 72% were female, 88% were White, and most had RA (54%). The most common treatments were conventional synthetic DMARDs (58%) and biologic DMARDs (39%). Prior to the 3rd dose, 599 (14.9%) had had COVID-19.

The incidence of COVID-19 was lower in the 4th dose cohort than comparator cohort (14.8 vs 23.7 per 1000 person-months) (Table 2). The rate difference between the two cohorts was -8.85 (95% CI: -13.37 to -4.33) per 1000 person-months with an HR of 0.59 (95% CI: 0.47-0.74), favoring a 4th dose (Figure). The risk of hospitalization or death within

Table 1: Baseline characteristics of the study cohort, before and after propensity score overlap weighting.

	Before PS Overlap Weighting			After PS Overlap Weighting		
	4 doses	3 doses	Standardized difference	4 doses	3 doses	Standardized difference
Age (mean, SD)	67 (13)	67 (13)	0.72	67 (12)	67 (4)	< 0.001
Female sex (%)	72.5	73	0.24	72.7	72.7	< 0.001
White (%)	87.7	87	0.23	87.5	87.5	< 0.001
Hispanic or Latino/a ethnicity (%)	3.2	4.02	0.34	3.2	3.2	< 0.001
Median zip code area-level income (SUSD, IQR)	92327 (73948, 114766)	90320 (73438, 111935)	0.47	92327 (73841, 114766)	92610 (75263, 113783)	< 0.001
BMI, kg/m² (mean, SD)	28.1 (6.4)	28.4 (6.6)	0.33	28.1 (6.0)	28.1 (1.7)	< 0.001
Ever smoker (%)	28.2	28.2	0.23	28.1	28.1	< 0.001
CCI (median, IQR)	1 (1, 3)	1 (1, 4)	0.31	1 (1,4)	2 (1,4)	< 0.001
Interstitial lung disease (%)	6.4	6.54	0.17	6.5	6.5	< 0.001
Rheumatic disease (%)						
Rheumatoid arthritis	52.4	50.4	0.37	54.3	54.3	< 0.001
Other inflammatory arthritis	24.1	21.8	0.27	24.6	24.6	< 0.001
Systemic lupus erythematosus	9.12	9.13	0.23	9.46	9.46	< 0.001
Vasculitis	8.45	7.92	0.26	8.67	8.67	< 0.001
Other rheumatic disease	15.1	15.8	0.19	15.55	15.55	< 0.001
Multiple rheumatic diseases	9.25	9.22	0.17	9.52	9.52	< 0.001
Immunomodulatory medication (%)						
bDMARD (except rituximab)	37.7	32.4	0.77	39.3	39.3	< 0.001
Rituximab	0.58	0.54	0.27	0.53	0.53	< 0.001
csDMARD	56	53.5	0.3	58.1	58.1	< 0.001
tsDMARD	3.68	3.29	0.23	3.8	3.8	< 0.001
Oral glucocorticoid	14.1	13.7	0.15	14.5	14.5	< 0.001
Prior COVID-19 infection (%)	8.67	8.9	0.41	8.9	8.9	< 0.001
BNT162b2 as initial 2-dose series	33.8	33.6	0.28	33.8	33.8	< 0.001

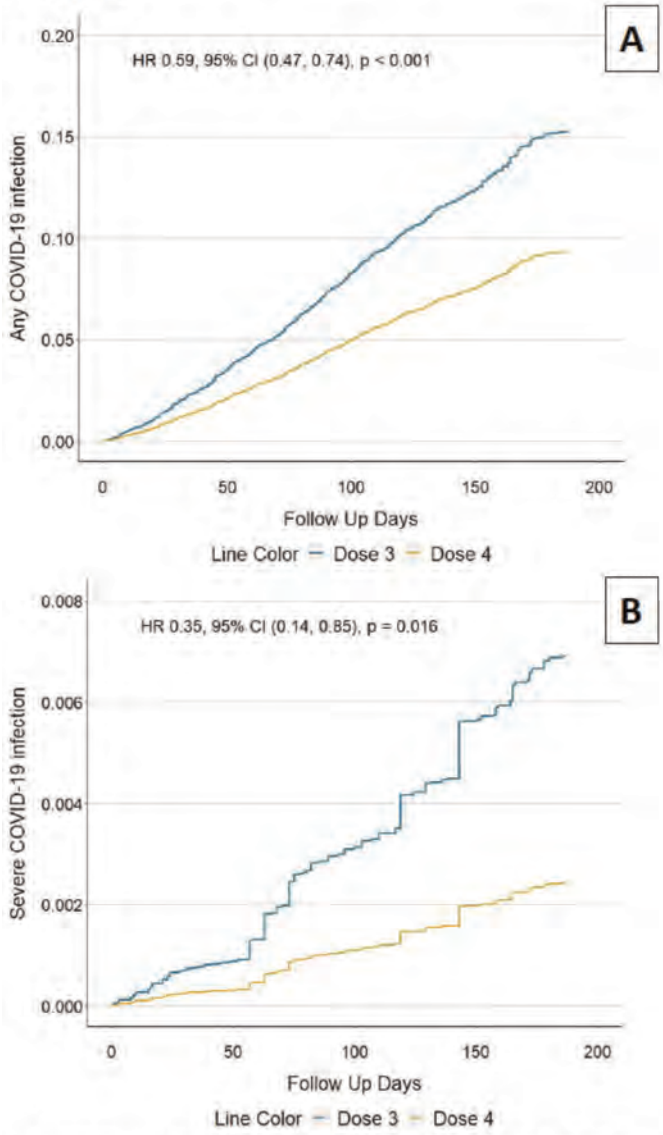
Variables shown were included as covariates in propensity score calculation. BMI: Body mass index. CCI: Charlson Comorbidity Index. bDMARD: biologic disease-modifying anti-rheumatic drug. csDMARD: conventional synthetic disease-modifying anti-rheumatic drug. tsDMARD: targeted synthetic disease-modifying anti-rheumatic drug.

Table 2: Frequency and risk of primary outcome (COVID-19 infection) and secondary outcomes (hospitalization or death within -3 to +14 or 30 days of positive COVID-19 test)

	Number of events		Median follow-up, d (IQR)		Incidence rate, per 1,000 person-months		Rate difference (95% CI), per 1,000 person-months	HR (95% CI)
Outcome	4 doses	3 doses	4 doses	3 doses	4 doses	3 doses	4 vs. 3 doses	4 vs. 3 doses
Primary analysis								
Any COVID-19 infection	196	2153	135 (112, 154)	65 (30, 156)	14.8	23.7	-8.85 (-13.37, -4.34)	0.59 (0.47, 0.74)
Secondary analysis								
Hospitalization/death within 14 days of positive COVID-19 test	10	160	136 (113, 157)	66 (31, 154)	0.36	0.93	-0.57 (-1.16, 0.02)	0.35 (0.14, 0.85)

HR: hazard ratio. IQR: interquartile range. CI: confidence interval.

Figure: Survival curves for those receiving a 4th dose vs not receiving a 4th dose of COVID-19 mRNA vaccine.



HR: hazard ratio. CI: confidence interval. **Panel A:** Survival curves for any COVID-19 infection in patients receiving a 4th vs no 4th dose of mRNA vaccine. **Panel B:** Survival curves for outcome of severe COVID-19 (hospitalization or death within 14 days) in patients receiving a 4th vs no 4th dose of mRNA vaccine.

14 days from COVID infection was lower in the 4th dose cohort than comparators (0.36 vs. 0.93 events/1000 person-months) with an HR of 0.35 (95% CI: 0.14-0.85).

Conclusion: In this emulated target trial, a 4th dose of mRNA vaccine reduced the risk of COVID-19 by 41% and severe COVID-19 by 65% among patients with SARDs using immunomodulators during the Omicron era. Patients with SARDs should be encouraged to receive at least 4 doses of mRNA vaccines.

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2, Amgen, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, 5, Gilead, 2, Inova Diagnostics, 2, Janssen, 2, Optum, 2, Pfizer, 2, ReCor, 2; **Z. Wallace**: BioCryst, 2, Bristol-Myers Squibb(BMS), 5, Horizon, 1, 2, 5, MedPace, 2, Novartis, 1, PPD, 2, Sanofi, 1, 5, Shionogi, 1, Visterra, 1, 2, Zenas, 1, 2.

Abstract Number: 2565

The Problem of Pain in Rheumatology: A Population-based Study of Annual Trends in Pain Management Modalities in Patients with Autoimmune Rheumatic Diseases in the United States, 2007-2021

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SESSION INFORMATION
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Background/Purpose: Autoimmune rheumatic diseases (ARD) such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are salient causes of disability, functional limitations, reduced quality of life and increased mortality. Pain remains the chief complaint among patients with ARD despite the advent of more effective therapies. Current guidelines recommend prioritizing non-opioid treatments in chronic pain. However, little is known about recent changes in the use of chronic pain treatment modalities in ARD. Such knowledge will be foundational for updating chronic pain treatment guidelines in rheumatology. The aim of this study is to examine annual trends among a national sample of privately insured adults diagnosed with ARD.

Methods: We used the IBM MarketScan Database (2007-2021) to identify patients in outpatient settings with ≥1 ARD diagnosis code by a specialist for ankylosing spondylitis (AS), psoriatic arthritis (PsA), RA, Sjogren's syndrome (SjS), systemic sclerosis (SSc), and SLE. Our primary outcome was opioid use and secondary outcomes were use of anticonvulsants, antidepressants, skeletal muscle relaxants, NSAIDS, topical pain medications and physical/occupational therapy. We extracted

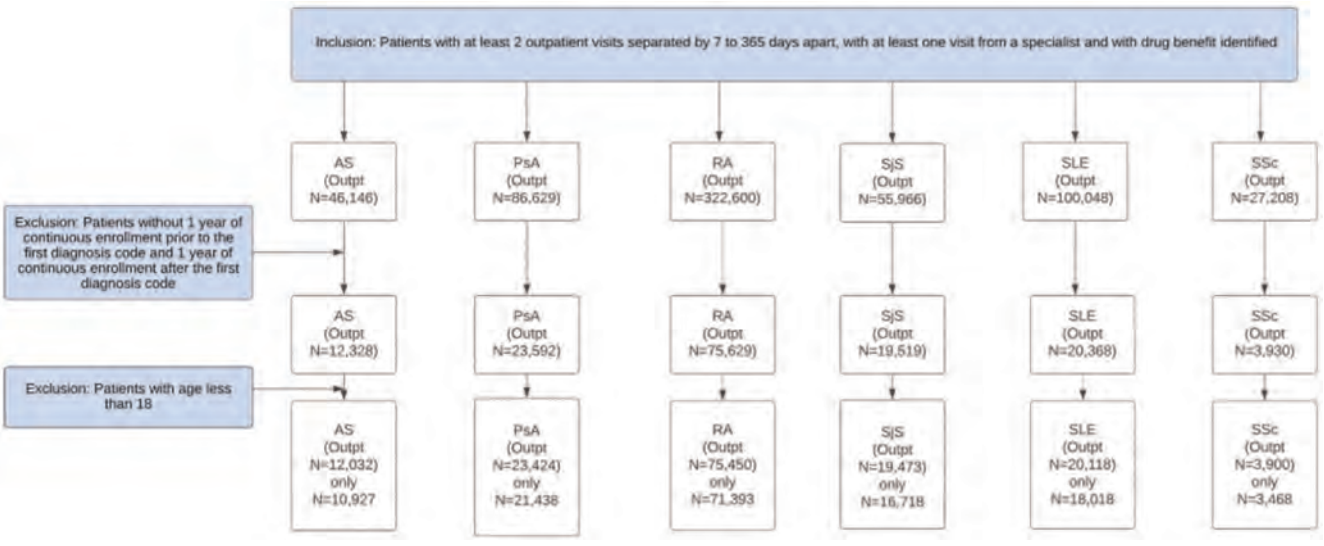

Figure 1. Consort Diagram

the proportion of patients who met the outcomes for each year. The numerator included patients receiving medications or non-pharmaceutical therapy within one year of their 1st ARD diagnosis. The denominator included patients with their 1st ARD diagnosis. We used logistic regression to estimate the association between calendar time and outcomes, adjusted for age, sex, and region. We included a spline knot to balance model fit by maximizing model likelihood and interpretation of results.

Results: There were 141,962 patients in our study (AS [n=10,927], PsA [n=21,438], RA [n=71,393], SjS [n=16,718], SLE [n=18,018], and SSc [n=3,468]) (Figure 1). Prevalence of opioid use increased from 26% in 2008 to 38% in 2014 and reduced to 24% in 2020. Prevalence of physical therapy use increased from 12% in 2008 to 24% in 2020. Prevalence of anticonvulsant use was 11% in 2008 and increased to 24% in 2020 (Figure 2). The odds of opioid use increased annually until 2014 by 3% [aOR, 1.03 (1.03, 1.04)] and decreased annually by 15% after 2014 [aOR, 0.85 (0.84, 0.86)] (Figure 3).

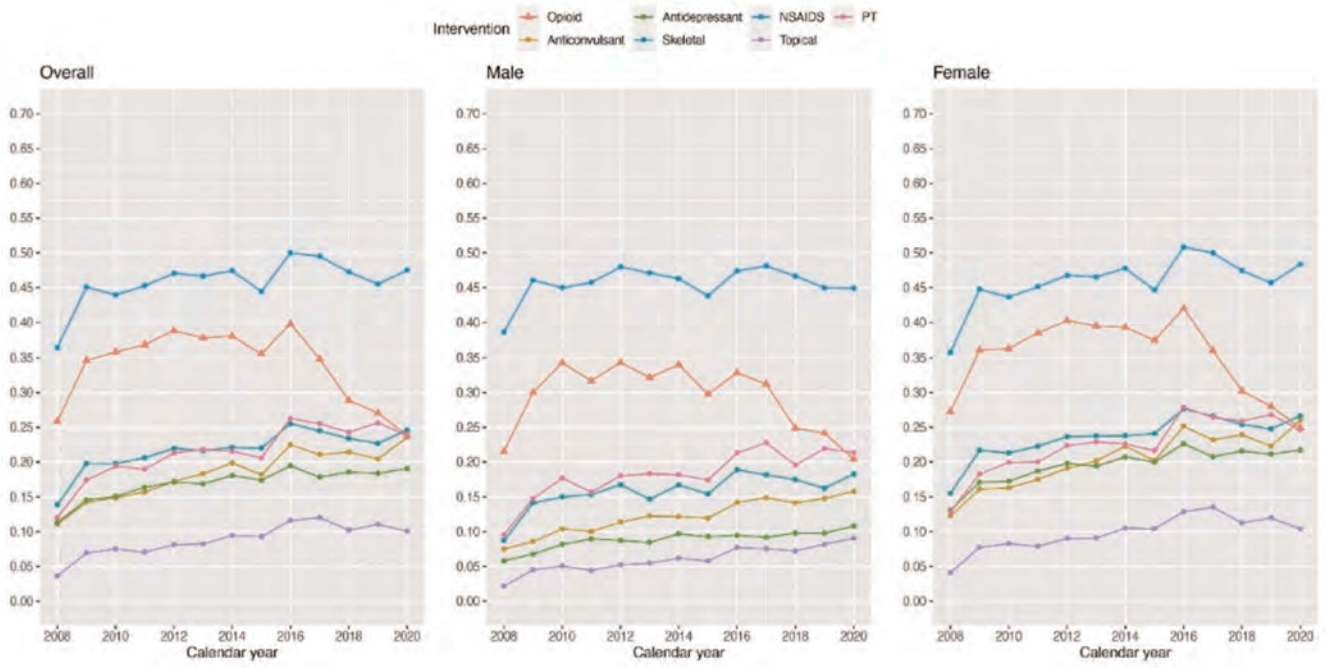

Figure 2. Trends of pain-related treatments among overall autoimmune patients, and stratified by sex

Outcomes	Unadjusted OR (95% CI)*	Adjusted OR (95% CI)**
Opioid (up to 2014)	1.03 (1.03, 1.04)	1.03 (1.03, 1.04)
Opioid (after 2014)	0.86 (0.85, 0.86)	0.85 (0.84, 0.86)
Anticonvulsant (up to 2014)	1.07 (1.06, 1.08)	1.08 (1.07, 1.09)
Anticonvulsant (after 2014)	1.00 (0.99, 1.01)	0.99 (0.99, 1.00)
Antidepressant (up to 2014)	1.05 (1.04, 1.05)	1.05 (1.04, 1.06)
Antidepressant (after 2014)	0.98 (0.97, 0.99)	0.98 (0.97, 0.99)
Skeletal (up to 2014)	1.04 (1.03, 1.05)	1.04 (1.04, 1.05)
Skeletal (after 2014)	0.97 (0.96, 0.98)	0.96 (0.96, 0.97)
NSAIDS (up to 2014)	1.02 (1.01, 1.03)	1.02 (1.02, 1.03)
NSAIDS (after 2014)	0.96 (0.95, 0.97)	0.96 (0.95, 0.96)
Topical (up to 2014)	1.09 (1.08, 1.10)	1.09 (1.07, 1.10)
Topical (after 2014)	0.98 (0.97, 0.99)	0.98 (0.97, 1.00)
PT (up to 2014)	1.05 (1.05, 1.06)	1.05 (1.04, 1.06)
PT (after 2014)	0.98 (0.98, 0.99)	0.99 (0.98, 1.00)

Abbreviation: OR, odds ratio.
*Per one-year increase
** Per one-year increase, adjusted for age, gender, and region.

Figure 3. Time trends of pain-related treatments among autoimmune patients

The odds of physical therapy use increased annually by 5% until 2014 [aOR, 1.05 (1.04, 1.06)] and with a slight decrease annually by 1% after 2014 [aOR, 0.99 (0.98, 1.00)]. The odds of anticonvulsant use increased annually by 8% until 2014 [aOR, 1.08 (1.07, 1.09)], with no statistically significant time trend after 2014 (aOR, 0.99 (0.99, 1.00). The use of topical analgesics increased annually by 9% up to 2014 [aOR, 1.09 (1.07, 1.10)], while the use of NSAIDs decreased annually by 4% after 2014 [aOR, 0.96 (0.95, 0.96)]. These trends did not differ by gender except for NSAID use before 2014 and topical analgesic use after 2014.

Conclusion: The use of various nonopioid pain management modalities has increased or stabilized in recent years, while opioid and NSAID use has declined since 2014. Future studies are needed to evaluate the effectiveness of these changes, and what possible effects they have had on outcomes such as quality of life, disability, and function.

Disclosure: T. Falasinnu: None; **D. Lu**: None; **M. Baker**: Mobility Bio, 8, Nēsos, 2.

Abstract Number: 2566

Comparisons of the Risk of Serious Infections Associated with the Different Classes of Targeted Therapies Used in Psoriatic Arthritis Patients: A Nationwide Cohort Study from the French Health Insurance Database

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Background/Purpose: Targeted therapies have demonstrated their efficacy in the treatment of psoriatic arthritis (PsA), with an increased risk of serious infections. However, a comparison of this risk according to the different classes of drugs, in real world settings, remains an unmet need. This study aimed to assess and compare the risk of serious infections associated with different targeted therapies used in PsA from a national healthcare database.

Methods: This nationwide cohort study used data from the French National Health Insurance Database (*SNDS*), which covers over 98.8% of the French population.

All adults aged over 18 years with PsA registered in the SNDS were eligible for inclusion between January 1, 2015 and June 30, 2021. New users of targeted therapies (adalimumab, etanercept, golimumab, certolizumab, infliximab [TNF_i], secukinumab and ixekizumab [$IL17_i$], ustekinumab [$IL12/23_i$], and tofacitinib [JAK_i]) were included, defined as patients who had no previous prescriptions of targeted therapies in the year prior the index date. Patients with HIV infection, a history of cancer, transplant or serious infection were excluded. The follow-up period extended to December 31, 2021. The primary end point was the occurrence of a serious infection in a time-to-event analysis using propensity score-weighted Cox proportional hazards regression models, with adalimumab as comparator, estimating weighted hazard ratios ($_wHR$) with their corresponding 95% confidence intervals (CIs). Other drugs used as add-on therapies (csDMARDs, NSAIDs and prednisone) were considered as time-dependant covariables.

Results: Between 2015 and 2021, 12,071 new users of targeted therapies were included (mean age 48.7 ± 12.7 years; 6,909 [57.8%] women; median follow-up 13.2 [interquartile range: 6.4-31.5] months).

Among new users, 8,946 (74.1%) were treated with a TNF_i, 1,796 (14.9%) with an $IL17_i$, 1,177 (9.8%) with an $IL12/23_i$, and 152 (1.3%) with a JAK_i.

The total number of serious infections was 367, with an overall crude incidence rate of 17.0 (95%CI, 15.2-18.7) per 1,000 person-years. The most frequent serious infections were pulmonary infections (94 [0.8%] patients) (*Table 1*).

After inverse propensity weighting and adjustment for time-dependent covariables, risk of serious infection appeared significantly lower for patients receiving etanercept ($_wHR$, 0.70; 95%CI, 0.54-0.93) or ustekinumab ($_wHR$, 0.56; 95%CI, 0.36-0.89) than for those receiving adalimumab. No significant difference in the risk of serious infection was detected for the other targeted therapies (*Figure 1*). Concomitant use of systemic corticosteroids was associated with an increased risk of serious infection ($_wHR$, 1.85; 95%CI, 1.48-2.31).

Conclusion: Overall, the incidence of serious infections associated with targeted therapies used in PsA patients in real world settings is low. Compared with new users of adalimumab, this risk was lower among new users of etanercept and ustekinumab, with no difference among new users of the other TNF_i, $IL17_i$ or JAK_i. Given the numerous therapeutic options available for PsA treatment, these findings could assist physicians in optimizing their therapeutic strategies based on individual patients' characteristics.

Table 1. Serious infections and deaths events according to the targeted therapy used among psoriatic arthritis (PsA) patients between 2015 and 2021 in France. No., number; Mo., months; IQR, interquartile range; ENT, ear nose throat; NA, not applicable.

Events	No. (%) of events	Incidence rate, per 1000 person-years (95%CI)	Time before event, median (IQR), Mo.
Total (n= 12,071)			
Serious infections	367 (3.0)	17.0 (15.2-18.7)	9.5 (3.2-23.4)
Pulmonary infections	94 (0.8)	4.3 (3.5-5.2)	11.6 (3.8-30.4)
Gastrointestinal infections	90 (0.8)	4.2 (3.3-5.0)	9.6 (3.7-22.8)
Skin and subcutaneous tissues infections	73 (0.6)	3.4 (2.6-4.1)	9.4 (3.0-22.7)
Urinary tract infections	28 (0.2)	1.3 (0.8-1.8)	6.8 (1.9-17.4)
ENT infections	24 (0.2)	1.1 (0.7-1.6)	6.9 (4.4-12.2)
Musculoskeletal infections	11 (0.09)	0.5 (0.2-0.8)	7.4 (1.4-18.0)
Other infections	47 (0.4)	2.2 (1.6-2.8)	11.8 (3.2-25.8)
Deaths	25 (0.2)	1.2 (0.7-1.6)	19.7 (8.9-24.1)
Adalimumab (n= 4616)			
Serious infections	150 (3.3)	18.9 (15.9-21.9)	7.6 (2.5-23.3)
Deaths	8 (0.2)	1.0 (0.3-1.7)	9.0 (3.0-34.9)
Etanercept (n= 2623)			
Serious infections	73 (2.8)	14.2 (11.0-17.5)	10.0 (3.9-22.8)
Deaths	9 (0.3)	1.8 (0.6-2.9)	22.9 (21.0-32.7)
Golimumab (n= 954)			
Serious infections	24 (2.5)	12.9 (7.7-18.1)	10.6 (4.2-33.9)
Deaths	3 (0.3)	1.6 (0-3.4)	19.7 (16.3-22.8)
Certolizumab (n= 683)			
Serious infections	17 (2.5)	15.2 (8.0-22.4)	15.2 (7.6-25.3)
Deaths	2 (0.3)	1.8 (0-4.3)	16.0 (15.7-16.4)
Infliximab (n= 70)			
Serious infections	5 (7.1)	41.1 (5.1-77.1)	19.4 (2.1-19.8)
Deaths	0	NA	NA
Secukinumab (n= 1452)			
Serious infections	55 (3.8)	22.0 (16.2-27.9)	11.9 (3.7-26.0)
Deaths	0	NA	NA
Ixekizumab (n= 344)			
Serious infections	10 (2.9)	22.1 (8.4-35.9)	7.9 (4.7-12.5)
Deaths	0	NA	NA
Ustekinumab (n= 1177)			
Serious infections	28 (2.4)	11.8 (7.4-16.2)	11.0 (6.5-28.1)
Deaths	3 (0.3)	1.3 (0-2.7)	10.6 (4.1-57.9)
Tofacitinib (n= 152)			
Serious infections	5 (3.3)	34.8 (4.3-65.2)	10.4 (8.1-11.8)
Deaths	0	NA	NA

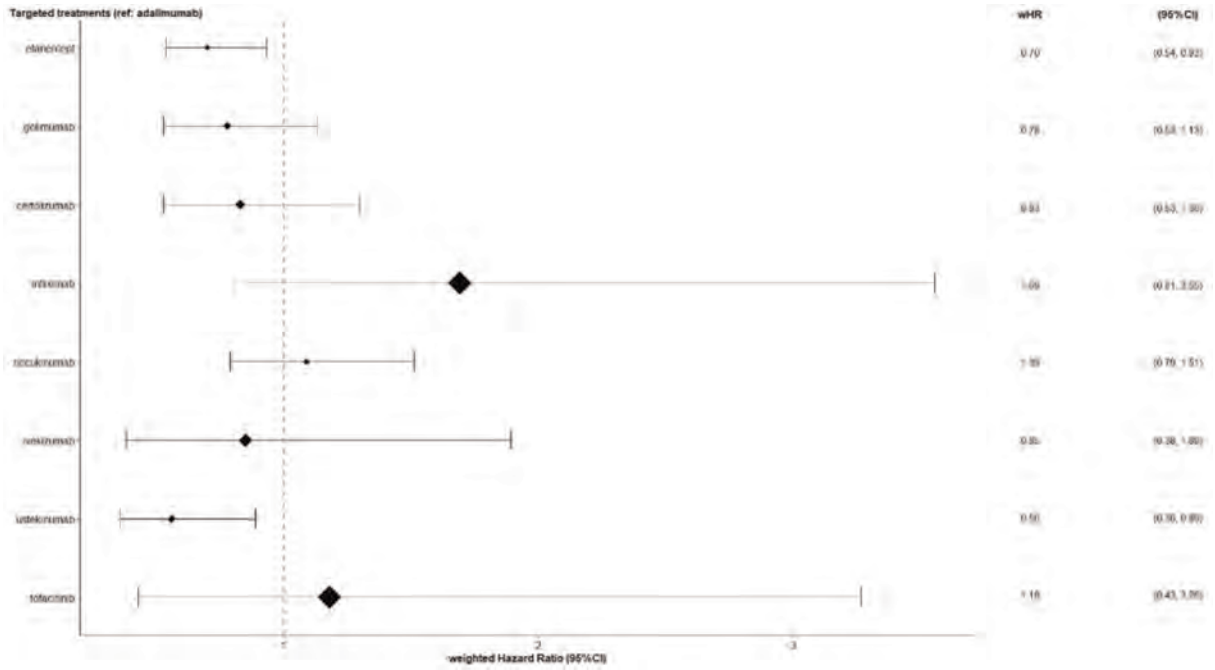

Figure 1. Forest plot of the risk of serious infection in patients with psoriatic arthritis (PsA), new users of targeted therapy, analysed by a time-to-event analysis using propensity score-weighted Cox proportional hazards regression models, estimating weighted hazard ratios (wHR) with their corresponding 95% confidence intervals (CIs). Ref, reference; wHR, weighted hazard ratio; CI, confidence interval.

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Abstract Number: 2567

An Extended Interval Between mRNA COVID-19 Booster Vaccinations Is Associated with an Increased Humoral Immune Response in Patients with Inflammatory Rheumatic Diseases

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SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Abstracts: Epidemiology & Public Health III
Session Type: Abstract Session
Session Time: 9:00AM–10:30AM

Background/Purpose: There is evidence that extending the interval between COVID-19 vaccination doses is associated with increased immunogenicity and neutralizing activity in healthy individuals (*1*, *2*). Previously, we reported higher humoral immune responses in patients with inflammatory rheumatic diseases (IRD) receiving mRNA-1273 vs BNT162b2 for their

2-dose primary immunization series (*3*). The same patients subsequently received a 3rd COVID-19 vaccine dose at varying intervals from the 2nd dose. The objectives of this study were to assess whether the interval or vaccine type (BNT162b2 vs mRNA-1273) affect the anti-SARS-CoV-2 Spike IgG levels up to 180 d post 3rd vaccine dose and the hazard of a positive SARS-CoV-2 test within 365 d post 3rd vaccine dose.

Methods: Patients from the Swiss cohort for patients with IRD (SCQM) who participated in the earlier phase of the study were recruited. They completed questionnaires using the mySCQM patient app and provided two self-collected capillary blood samples following the administration of the 3rd vaccine dose, that were tested for anti-S1-IgG levels. The analysis included patients who received a 3-dose homologous vaccination and reported no SARS-CoV-2 infection between the 2nd and 3rd doses. Mixed effects continuous outcome logistic regression and Cox proportional hazards regression models were employed to address the study aims. We adjusted for potential confounders at the time of the 1st vaccination.

Results: 344 IRD patients (67% female, mean age 52 y, 34% RA, 36% axSpA, 22% PsA, 8% UA) received their 3rd COVID-19 vaccination between 2021-08-13and 2022-03-04. The mean interval between the 2nd and 3rd vaccinations was 214 d (s.d. 25 d). The longer the interval to the booster dose was, the higher the antibody response to the 3rd dose up to 180 d post immunization. This result persisted after adjusting for confounders (Table 2). Indicatively, prolonging the vaccination interval by 30 d, led to a 1.9-fold increase (95% CI 1.2 – 3.0) of the odds of higher antibody levels post 3rd vaccination (Fig. 1).

Table 1. Patient demographics and clinical characteristics (n = 344)

	mRNA-1273	BNT162b2	All
Age at BL, years (mean (s.d.))	52.9 (10.8)	51.3 (12.9)	52.1 (12.9)
Females, n (%)	110 (67.1)	122 (67.8)	232 (67.4%)
Previous SARS-CoV-2 infection at BL, n (%)	15 (9.1)	20 (11.1)	35 (10.2)
Diagnosis, n (%)			
Rheumatoid Arthritis (RA)	57 (34.8)	61 (33.9)	118 (34.3)
Axial Spondyloarthritis (axSpA)	60 (36.6)	65 (36.1)	125 (36.3)
Psoriatic Arthritis (PsA)	41 (25.0)	34 (18.9)	75 (21.8)
Undifferentiated arthritis (UA)	6 (3.7)	20 (11.1)	26 (7.6)
Treatment at BL, n (%)			
No DMARD medication	31 (18.9)	30 (16.7)	61 (17.7)
Conventional synthetic disease-modifying antirheumatic drugs (csDMARD)	18 (11.0)	16 (8.9)	34 (9.9)
of which combination therapy[x]	*2*	*1*	*3*
Glucocorticoid monotherapy	2 (1.2)	1 (0.6)	3 (0.9)
Tumour Necrosis Factor inhibitors (TNFi)	75 (45.7)	91 (50.6.4)	166 (48.3)
of which combination therapy[x]	*19*	*27*	*46*
Janus Kinase Inhibitors (JAKi)	10 (6.1)	13 (7.2)	23 (6.7)
of which combination therapy[x]	*2*	*3*	*5*
Abatacept	3 (1.8)	5 (2.8)	8 (2.3)
of which combination therapy[x]	*1*	*2*	*3*
Interleukin inhibitors IL-1/IL-6/IL-17/IL-23	23 (14.0)	24 (13.3)	47 (13.7)
of which combination therapy[x]	*6*	*7*	*13*
PDE4i	2 (1.2)	0	2 (1.2)
Vaccine, 3-dose homologous n (%)			
BNT162b2			180 (52.3)
mRNA-1273*			164 (47.7)
Interval between 2nd and 3rd vaccination, days (mean (s.d.))	212 (24)	216 (25)	214 (25)

Patients on rituximab were excluded due to the high variability in the time since their last infusion.
[x]combination therapy = bDMARD with csDMARD and/or GC; *Available dosing info of 3rd mRNA-1273 vaccination: 31 patients ½ dose; 20 patients full dose; 113 patients NA

Table 2. The odds ratios of higher antibody levels and the hazard ratios of test-positive SARS-CoV-2 infection following the 3rd COVID-19 mRNA-based vaccination.

	Antibody model		Risk of test-positive infection model	
	OR (95% CI)	p value	HR (95% CI)	p value
Age	1.01 (0.97-1.05)	0.60	0.99 (0.98-1.01)	0.28
Past SARS-CoV-2 infection at BL	1.21 (0.42-3.48)	0.72	0.69 (0.39-1.22)	0.20
Sample time collection with respect to 3rd vaccination	0.95 (0.94-0.96)	<0.0001	N/A	N/A
mRNA-1273 vs BNT162b2	**3.3** (1.66-6.56)	**0.0007**	**0.64** (0.46-0.89)	**0.0085**
Interval between 2nd and 3rd vaccination*	**1.02** (1.01-1.04)	**0.0064**	1.0 (0.99-1.01)	0.64
Vaccine-age interaction	1.04 (0.98-1.11)	0.15	0.98 (0.96-1.01)	0.28

* Reported OR and HR are for an increase in interval of 1 day (for an increase in interval of 30 d see Fig. 1).

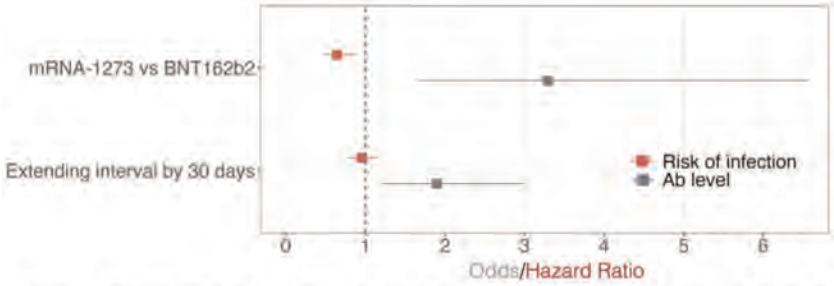

Figure 1. The odds ratios with 95% CI for higher anti-S1 antibody levels (Ab level) up to 180 d post 3-dose homologous mRNA vaccination (gray) and the hazard ratios with 95% CI for test-positive SARS-CoV-2 infection up to 365 d post 3-dose homologous mRNA vaccination (red).

154 patients reported a SARS-CoV-2 infection after the 3rd vaccine dose (between 2021-12-28and 2022-12-05, during the B.1.1.529 Omicron wave). We found no evidence of the vaccination interval affecting the hazard of test-positive SARS-CoV-2 infection up to 365 d post 3rd vaccination (Table 2).

After adjusting for confounders, the odds of higher anti-S1 levels were 3.3 times greater (95% CI 1.7 – 6.6; p< 0.001) in 3-dose homologous mRNA-1273 recipients compared toBNT162b2 recipients (Table 2, Fig. 1). Moreover, the hazard of a test-positive SARS-CoV-2 infection up to 365 d post 3rd vaccination was 36% lower (HR 0.64; 95% CI 0.46 – 0.89; p < 0.01) in 3-dose homologous mRNA-1273 vs BNT162b2 recipients (Table 2, Fig. 1).

Conclusion: A longer vaccination interval and a 3-dose homologous vaccination with mRNA-1273 were associated with higher anti-SARS-CoV-2 Spike IgG levels post 3rd vaccination in IRD patients. 3-dose homologous vaccination with mRNA-1273 was also associated with a lower risk of a test-positive SARS-CoV-2 infection post 3rd vaccination.

1. X. Zhao *et al*., *N. Engl. J. Med*.**386**, 894–896 (2022).
2. T. A. Bates *et al*., *JCI Insight*. **8** (2023)
3. C. E. Raptis *et al*., *Front. Immunol*.**13**, 1–11 (2022).

Disclosure: C. Raptis: None; **C. Berger**: None; **C. Polysopoulos**: None; **A. Ciurea**: None; **D. Andrey**: None; **T. Maletic**: None; **M. Riek**: None; **A. Scherer**: None; **I. von Loga**: None; **J. Safford**: None; **K. Lauper**: Eli Lilly, 5, Pfizer, 2; **B. Moeller**: None; **N. Vuilleumier**: None; **A. Finckh**: None; **A. Rubbert-Roth**: AbbVie/Abbott, 2, 6, Amgen, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, 6.

Abstract Number: 2568

First Breakthrough COVID-19 Infection Following Two SARS-CoV-2 Vaccinations Among Primary Systemic Vasculitis Patients

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SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
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Background/Purpose: Primary systemic vasculitis (PSV) patients on immunosuppression are at higher risk of adverse outcomes following COVID-19 infection and often mount suboptimal vaccine responses to SARS-CoV-2 vaccination. The aim of this study was to investigate risk factors for first breakthrough COVID-19 infection after two vaccine doses in this patient group, from 02 January 2021 to 01 April 2023.

Methods: PSV patients enrolled in a prospective, UK-based multicentre observational cohort study investigating serological responses to SARS-CoV-2 vaccination (ethics reference: 20/EM/0180) were included if they had two SARS-CoV-2 vaccine doses. Patients were excluded if they had a previous history of documented COVID-19 infection or if their SARS-CoV-2 anti-nucleocapsid antibody titre (anti-N IgG) was >6104 median fluorescence intensity (MFI) indicating previous infection[1]. First symptomatic breakthrough SARS-CoV-2 infection (PCR or lateral flow positive) >14 days after a second SARS-CoV-2 vaccination was the outcome of interest. SARS-CoV-2 IgG spike antibody (anti-S IgG) and anti-N IgG titres were measured using a Luminex assay, and seroconversion was defined as an anti-S IgG titre >1896 MFI[1]. Clinical details were obtained via electronic health records.

[1]Smith et al. BMC Nephrol. 2022 May 31;23(1):199

Results: 252 PSV patients were identified, with 13 of these excluded (n = 9 had COVID-19 prior to or within 14 days of their second vaccination, n = 4 withdrew consent), leaving 239 eligible patients (48.5% male, median age 58.8 years) for the analysis, mainly consisting of ANCA-associated vasculitis (AAV) patients (Table 1). Median follow-up was 400 (range 78–756) days. During follow-up, 117 patients (49.0%) had a first breakthrough COVID-19 infection, representing a crude incidence rate of 12.0 per 10,000 person-days. 14 required inpatient admission (12.0%), with two being admitted to intensive care. One patient died of COVID-19. Median time from second vaccination to first breakthrough infection was 350 (interquartile range 285–442) days. Univariable and multivariable analyses of first breakthrough infection were conducted using the Fine and Gray method to adjust for the competing events of death and study withdrawal. In the fully-adjusted model, seroconversion and third and subsequent vaccinations i.e., boosters were associated with a lower hazard of breakthrough infection, with hazard ratios of 0.48 (95% confidence interval [CI] 0.27–0.85; p=0.012) and 0.43 (95% CI 0.32–0.59; p< 0.001) respectively. Chronic kidney disease was also associated with reduced hazard in fully-adjusted analysis (p=0.01). Patients with a history of malignancy (p=0.033), and those with IgA vasculitis and large vessel vasculitis (relative to AAV) were all at higher hazard for breakthrough infection (p=0.002, and p=0.009 respectively, Table 2)

Conclusion: In this cohort of PSV patients on immunosuppression who had two SARS-CoV-2 vaccinations, a third and subsequent vaccine doses were independently associated with reduced risk of breakthrough COVID-19 infection. Our study highlights the importance of booster vaccinations and support anti-S IgG titres as a correlate of protection against COVID-19 in this group of patients.

Table 1. Demographic details of Primary Systemic Vasculitis cohort (n = 239)

Table 1. Demographic details of Primary Systemic Vasculitis cohort

Median age, years (interquartile range [IQR])	58.8 (44.3–71.0)
Male, n (%)	116 (48.5%)
Diagnosis, n (%)	
ANCA-associated vasculitis (AAV)	141 (59.0%)
Systemic lupus erythematosus (SLE)	29 (12.1%)
Medium vessel vasculitis	4 (1.7%)
Large vessel vasculitis	10 (4.1%)
Behcet's disease	20 (8.4%)
IgA vasculitis	9 (3.8%)
Other*	26 (10.9%)
Comorbidities, n (%)	
Hypertension	117 (49.0%)
Chronic kidney disease (CKD) ≥ stage 3	71 (29.7%)
Chronic lung disease	83 (34.7%)
Cardiac disease	37 (15.5%)
Diabetes	25 (10.5%)
History of malignancy	11 (4.6%)
Medications, n (%)	
Prednisolone	119 (49.8%)
Antiproliferatives‡	54 (22.6%)
Methotrexate	13 (5.4%)
Calcineurin inhibitors	5 (2.1%)
Rituximab within 6 months of vaccination	100 (41.8%)
Cyclophosphamide within 12 months	58 (24.2%)
Anti-TNF agents	15 (6.3%)
Primary vaccination course, n (%)	
ChAdOx1 nCoV-19 (AstraZeneca) x2	143 (59.8%)
Pfizer BioNTech (BNT162b2) x2	82 (34.3%)
Moderna (mRNA-1273) x2	1 (0.42%)
ChAdOx1 nCoV-19 and BNT162b2	2 (0.82%)
Missing	11 (4.6%)
Seroconversion after two vaccinations, n (%)	159 (70.0%)
Booster vaccination doses, n (%)	
1 booster	201 (84.1%)
2 boosters	152 (63.6%)
3 boosters	36 (15.0%)
4 boosters	3 (1.7%)

*Includes IgG4 disease, cryoglobulinaemic vasculitis, rheumatoid vasculitis, relapsing polychondritis, glomerulonephritis, VEXAS, Schnitzer syndrome, cutaneous vasculitis
‡Mycophenolate mofetil or Azathioprine

Table 2. Univariable and multivariable predictors of first breakthrough COVID- 19 infection

Table 2. Univariable and multivariable predictors of first breakthrough COVID-19 infection

	Univariable model		Fully-adjusted model*	
	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value
Age (years)	**0.98 (0.97, 0.99)**	**0.003**	1 (0.98, 1.02)	0.931
Sex				
Female	1.00 (Reference)		1.00 (Reference)	
Male	0.8 (0.56, 1.15)	0.234	0.97 (0.64, 1.46)	0.877
Diagnosis				
ANCA-associated vasculitis (AAV)	1.00 (Reference)		1.00 (Reference)	
Systemic lupus erythematosus (SLE)	1.39 (0.88, 2.18)	0.157	0.85 (0.33, 2.18)	0.729
Medium vessel vasculitis	0.77 (0.19, 3.15)	0.715	0.94 (0.16, 5.48)	0.948
Large vessel vasculitis	1.98 (0.85, 4.59)	0.111	**3.65 (1.38, 9.61)**	**0.009**
Behcet's disease	**2.6 (1.51, 4.47)**	**0.001**	1.9 (0.89, 4.08)	0.099
IgA vasculitis	1.4 (0.73, 2.66)	0.313	**4.17 (1.69, 10.31)**	**0.002**
Other	2.91 (1.22, 6.91)	0.016	1.04 (0.47, 2.27)	0.923
Comorbidities				
Hypertension	**0.61 (0.42, 0.88)**	**0.008**	0.64 (0.39, 1.05)	0.074
Chronic lung disease	1.11 (0.75, 1.64)	0.603	1.42 (0.86, 2.33)	0.166
Chronic kidney disease (CKD) ≥ stage 3	**0.78 (0.66, 0.91)**	**0.002**	**0.8 (0.67, 0.95)**	**0.01**
Diabetes	0.92 (0.48, 1.78)	0.813	1.35 (0.68, 2.68)	0.387
History of malignancy	1.23 (0.6, 2.5)	0.576	**2.35 (1.07, 5.15)**	**0.033**
Cardiac disease	0.91 (0.56, 1.47)	0.694	0.92 (0.47, 1.81)	0.819
Medications				
Prednisolone	1.15 (0.8, 1.64)	0.445	0.89 (0.59, 1.34)	0.575
Antiproliferatives	1.14 (0.78, 1.65)	0.499	1.28 (0.71, 2.32)	0.41
Methotrexate	1.3 (0.59, 2.87)	0.521	0.55 (0.15, 1.97)	0.355
Calcineurin inhibitors	1.31 (0.56, 3.04)	0.528	1.02 (0.31, 3.34)	0.972
Rituximab within 6 months of vaccination	0.78 (0.53, 1.14)	0.199	0.88 (0.52, 1.48)	0.621
Cyclophosphamide within 12 months	0.65 (0.4, 1.03)	0.069	0.83 (0.48, 1.43)	0.496
Anti-TNF agents	**2.05 (1.18, 3.54)**	**0.01**	1.51 (0.71, 3.18)	0.282
Seroconversion (anti-S IgG > 1896 MFI)	0.74 (0.49, 1.11)	0.141	**0.48 (0.27, 0.85)**	**0.012**
Booster vaccination doses	**0.48 (0.36, 0.64)**	**<0.001**	**0.43 (0.32, 0.59)**	**<0.001**

*n=237, competing risks regression using Fine and Gray model to adjust for competing events of death or withdrawal during study; adjusted for age (years), sex, diagnosis, comorbidities, medications, seroconversion and third and subsequent vaccination doses i.e., boosters

Disclosure: M. Chen-Xu: GSK, 5; **D. Cooper**: None; **R. Döffinger**: None; **D. Jones**: GSK, 1, 5, Roche, 5, Vifor Pharma, 1; **R. Smith**: GlaxoSmithKlein(GSK), 5, Union Therapeutics, 5.

Abstract Number: 2569

Efficacy and Safety of Therapeutic Interventions for the Treatment of Still's Disease: A Systematic Review and Meta-analysis Informing the EULAR/PReS Recommendations for the Diagnosis and Management of Systemic Juvenile Idiopathic Arthritis and Adult-Onset Still's Disease

Sara Bindoli[1], Arianna De Matteis[2], STEPHANE MITROVIC[3], Bruno Fautrel[4], Loreto Carmona[5], Fabrizio De Benedetti[6] and On Behalf Of The Eular/PreS QoC011 Task Force Member[7], [1]Rheumatology Unit, Dept of Medicine, University of Padova, Padova, Italy, [2]IRCCS Ospedale Pediatrico Bambino Gesu', Rome, Italy, [3]Pitie Salpetriere Hospital, Sorbonne University, APHP, Paris, France, [4]Sorbonne Université APHP, Paris, France, [5]Instituto de Salud Musculoesquelética (InMusc), Madrid, Spain, [6]Bambino Gesu Children's Hospital, Division of Rheumatology, Rome, Italy, [7]EULAR/PReS QoC011 Task Force members are: Jordi Anton, Alexandre Belot, Claudia Bracaglia, Tamas Constantin, Lorenzo Dagna, Alessandro De Bartolo, Eugen Feist, Dirk Foell, Marco Gattorno, Sophie Georgin-Lavialle, Roberto Giacomelli, Alexei Grom, Yvan Jamilloux, Katarina Laskari, Calin Lazar, Francesca Minoia, Peter Nigrovic, Filipa Oliveira Ramos, Seza Ozen, Pierre Quartier-dit-Maire, Piero Ruscitti, Erdal Sag, Sinisa Savic, Marie-Elise Truchetet, Bas Vastert, Tanita Wilhelmer, Carine Wouters., Paris, France

SESSION INFORMATION

Session Date: Wednesday, November 15, 2023

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases III

Session Type: Abstract Session

Session Time: 9:00AM–10:30AM

Background/Purpose: To investigate the efficacy and safety of therapies currently in use and under evaluation for systemic Juvenile Idiopathic Arthritis (sJIA) and Adult-Onset Still's disease (AOSD).

Methods: A systematic review (SR) was performed. Medline, Embase, and the Cochrane Library databases were searched up to October 2022 for clinical trials (randomised, RCT, and quasi-controlled, CCT), longitudinal observational studies (retrospective, LOR, and prospective, LOP) and SRs published after 2013. The research question was formulated according to the PICO format. Population: sJIA (fulfilling ILAR criteria) or AOSD (fulfilling either Yamaguchi's and/or Fautrel's criteria) patients; Intervention: any pharmacological treatment (in use or under evaluation for sJIA/AOSD); Comparator: any other active drug or placebo; Outcomes: any relevant efficacy and safety outcome. The risk of bias (RoB) of the included clinical studies was assessed with the Cochrane RoB tool, while AMSTAR-2 was used to critically assess SRs.

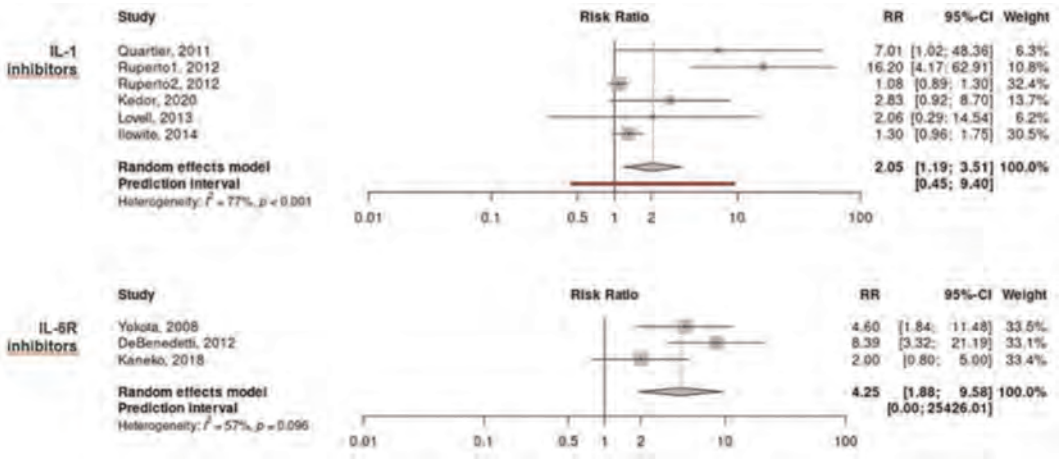

Figure: Meta-analysis of controlled clinical trials having assessed the efficacy of IL-1 and IL-6R inhibitors in Still's disease, based on ACR50 response.

Table: Studies having compared early (< 3 months) versus late (≥3 months) introduction of IL-1 and IL-6R inhibitors for the treatment of people with Still's disease.

		Study	Subtype	N	Time from disease onset to treatment start - months	Time of assessment	CID % (N)	other outcomes: %	Author, year
Comparison early vs late treatment	IL-1 (ANK)	LOR	sJIA	56	Early < 3 months	6 months	92 (35/37)	-	Pardeo 2021
					Late ≥ 3 months	6 months	37 (7/19)	-	
	IL-6 i (TCZ)	LOR	sJIA	23	Early 1 month (IQR 4)	12 months	54 (6/11)	ACR70: 91	Pacharapakornpon 2017
					Late 7.5 months (IQR 23)	12 months	0 (0/12)	ACR70: 50	

Results: Of 3,941 records, 115 full texts were finally included, representing 25 RCTs, 10 SRs published after 2013 and 80 LOR or LOP studies. Studies on glucocorticoids (GCs) and conventional synthetic DMARDs were mainly observational and displayed high RoB for the majority of them. Biologic DMARD (bDMARD) targeting IL-1 (IL-1i) or IL-6R (IL-6Ri) were the drugs with the highest level of evidence (6 clinical trials for IL-1i and 3 for IL-6Ri). A meta-analysis was conducted accordingly, using adapted ACR50 response as the outcome measure, and identified significant effect of both bDMARDs with RR 2.05 (95%CI 1.19, 3.51) and 4.25 (95%CI 1.88, 9.58) for IL1i and IL-6Ri respectively (Figure). Additionally, 2 retrospective longitudinal studies have demonstrated that the benefit of early bDMARD introduction, i.e. < 3 months, was associated with higher rates of clinically inactive disease (Table). This is consistent with data from other non-comparative studies in which clinically inactive disease (CID) achievement rates are between 59 to 100% when IL-1 or IL-6 inhibitors are initiated within 3 to 6 months, and 23 to 32% when they are started later on. Data on tsDMARDs (JAK-inhibitors), with promising findings, were limited to a few small case series.

Conclusion: Besides glucocorticoids, IL-1 and IL-6 inhibitors yielded the highest level of evidence for the treatment of sJIA and AOSD and their use early during the disease course was markedly efficacious.

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Abstract Number: 2570

Thrombosis in Patients with VEXAS Syndrome: A Retrospective Cohort Study

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SESSION INFORMATION

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Session Time: 9:00AM–10:30AM

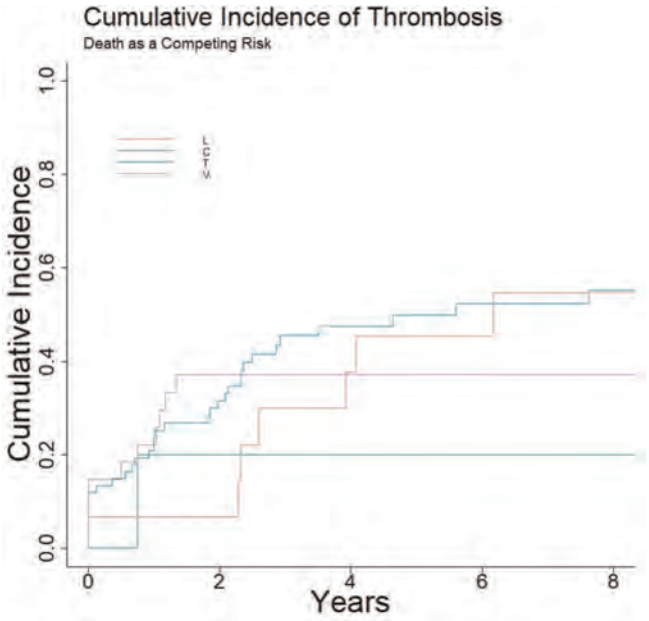
Background/Purpose: VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome, due to somatic mutations in the UBA1 gene, is an autoinflammatory disorder associated with an increased thrombotic risk. We investigated the frequency and characteristics of thrombotic events in patients with VEXAS syndrome, as well as their impact on survival.

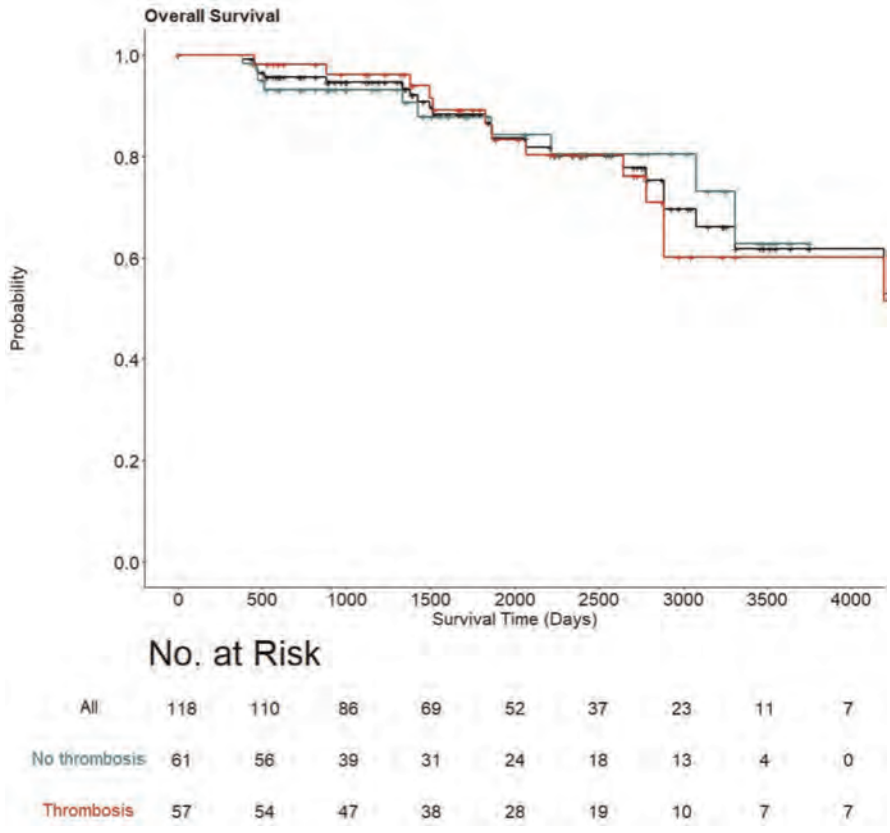
Methods: This retrospective, multi-center study utilized electronic medical records from the National Institutes of Health (NIH) Clinical Center and Mayo Clinic, along with referred outside records, to identify patients with VEXAS syndrome who had a confirmed *UBA1* somatic mutation and VEXAS clinical features. The time of symptom onset was used as the time of disease onset. Thrombosis was considered VEXAS disease onset if it occurred within two years of inflammatory symptom onset. SVT was excluded as a thrombotic event for analysis. Univariate and multivariate logistic regression analysis was used to identify predictors of thrombosis. Kaplan-Meier curve models were applied to estimate overall survival (OS). Statistical significance was $P < .05$. Lupus anticoagulant (LA) was assessed in 41 patients and other coagulation assays in 27.

Table 1. Demographic and clinical characteristics of patients with VEXAS syndrome and thrombotic events

Characteristic	Participants (N = 119)
Demographic characteristics	
Male sex, n (%)	119 (100)
Age (y), median (range)	64.5 (39.0, 86.0)
Somatic *UBA1* mutations	
p.Met41Val, n (%)	27 (23)
p.Met41Leu, n (%)	16 (13)
p.Met41Thr, n (%)	69 (58)
Splice motif mutation, n (%)	5 (4)
VEXAS phenotype	
Systemic symptoms (fever, fatigue, weight loss), n (%)	95 (80)
Skin involvement (rash), n (%)	89 (75)
Sweet's syndrome, n (%)	13 (11)
Inflammatory eye disease (episcleritis, uveitis), n (%)	35 (30)
Inner ear involvement (hearing loss, tinnitus, vertigo), n (%)	36 (30)
Chondritis (ear, nose), n (%)	50 (42)
Relapsing polychondritis, n (%)	49 (41)
Cardiac involvement (myocarditis, pericarditis, pericardial effusion), n (%)	7 (6)
Pulmonary involvement (lung infiltrates, pleural effusion), n (%)	60 (50)
Musculoskeletal involvement (arthritis, tenosynovitis), n (%)	76 (64)
Macrocytic anemia, n (%)	107 (90)
Myelodysplastic syndrome, n (%)	36 (30)
Plasma cell dyscrasia, n (%)	21 (18)
Venous thrombotic events	
DVT, n (%)	41 (34)
Proximal DVT, n (%)	27 (23)
Distal DVT, n (%)	12 (10)
PE, n (%)	17 (14)
Superficial thrombophlebitis, n (%)	23 (19)
Unprovoked event, n (%)	33 (28)
Recurrent event, n (%)	20 (17)
Event while on anticoagulation, n (%)	10 (8)
Time to event (mo), median (range)	33 (0, 553)
Arterial thrombotic events	
Stroke, n (%)	5 (4)
Myocardial infarction, n (%)	6 (5)
Recurrent event, n (%)	1 (1)
Time to event (mo), median (range)	29 (0, 232)

Results: A total of 119 VEXAS patients were included. All patients (100%) were male with a median age of 65 years (39-86 years). Hematologic manifestations included macrocytic anemia in 107 (90%), myelodysplastic syndrome (MDS) in 36 (30%), and plasma cell dyscrasia (PCD) in 21 (18%).





Of the 119 patients, 58/119 (49%) had a thrombotic event. Of those, 51 (43%) had VTE, and 9 (8%) had arterial events (AT), with a median time from disease onset of 33 and 29 months, respectively; seven patients (6%) had both venous and AT. The majority of VTE events were unprovoked 33 (28%) and over one-third 20 (17%) were recurrent, and 10 (8%) on anticoagulation (Table 1).

The cumulative incidence (CI) at a median follow-up of DVT, PE, and arterial thrombosis was 28.7%, 9.7%, and 8.7% respectively. CI at median follow-up of any thrombotic event was 22% for UBA1 M41L, 40% for M41T, and 37% for M41V, however, rising CI was seen with M41L over time while occurring early in M41T and M41V (Figure 1). The M41L UBA1 variant was positively associated with PE in univariate (OR: 4.58; p=0.02) and multivariate (OR: 16.94; p = 0.01) analyses but not with DVT or arterial thrombosis. The median OS from disease onset was 1740 days with no significant difference in OS between patients with (86.9%) or without (89.7%) thrombosis (Figure 2). In the univariate and multivariate Cox proportional hazard model, thrombosis was not associated with worse OS. The majority of VEXAS patients had high factor VIII levels (26/27; 96%) and VWF activity (16/27; 59%), while most had high VWF antigen (11/25; 44%), factor IX levels (12/27; 44%) and protein C activity (11/27; 41%). CRP and ESR were positively correlated with D-dimer and negatively correlated with VWF activity. LA was positive in 16/41 (40%) and correlated significantly with higher CRP (p< 0.01).

Conclusion: Patients with VEXAS syndrome are at high risk of VTE, which can recur despite anticoagulation therapy. Considering the high prevalence of thrombosis in VEXAS patients, it is crucial to assess their VTE risk carefully and consider prophylactic anticoagulation.

Disclosure: A. Ghorbanzadeh: None; **Y. Kusne**: None; **A. Dulau-Florea**: None; **R. Shalhoub**: None; **P. Alcedo**: None; **K. Nghiem**: None; **M. Ferrada**: None; **a. hines**: None; **S. Panicker**: None; **a. ombrello**: None; **K. Reichard**: None; **I. Darden**: None; **W. Goodspeed**: None; **L. wilson**: None; **H. Olteanu**: None; **T. Lasho**: None; **D. Kastner**: None; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Chemocentryx, 1, 6, Eli Lilly, 5, kiniksa, 5; **A. Mangaonkar**: None; **R. Go**: None; **D. Beck**: None; **M. Patnaik**: None; **N. Young**: None; **K. Calvo**: None; **A. Casanegra**: None; **P. Grayson**: None; **M. Koster**: None; **C. Wu**: None; **D. Houghton**: None; **B. Patel**: None; **Y. Kanthi**: None; **E. Groarke**: None.

Abstract Number: 2571

Identification of Biomarkers Predicting Steroid Resistance in Immune Checkpoint Inhibitor-Induced Arthritis

Rashmi Thimmapuram[1], Maryam Buni[2], Huifang Lu[3], Jean Tayar[4], Yuanteng Li[4], Maria Suarez-Almazor[5], Rene Rico[4], Naimah Turner[4], Roza Nurieva[4] and Sang Kim[6], [1]Baylor College of Medicine, Houston, TX, [2]MD Anderson Cancer Center, Bellaire, TX, [3]UT MD Anderson Cancer Center, Houston, TX, [4]The University of Texas, MD Anderson Cancer Center, Houston, TX, [5]MD Anderson Cancer Center, Houston, TX, [6]The Univesrity of Texas MD Andesron Cancer Center, Pearland, TX

SESSION INFORMATION

Session Date: Wednesday, November 15, 2023

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases III

Session Type: Abstract Session

Session Time: 9:00AM–10:30AM

Background/Purpose: Immune checkpoint inhibitors (ICIs) are revolutionizing cancer treatment. However, ICIs often lead to immune-related adverse events (irAEs). Approximately 5% of patients treated with ICIs develop arthritis (here, ICI-arthritis). ICI-arthritis not only causes joint destruction but also necessitates the discontinuation of ICI therapy. Importantly, steroids,

Table 1. Information of peripheral blood samples

Table 1. Information of peripheral blood samples

Characteristic	No. (%)		
	Steroid-sensitive, n=19	Steroid-resistant, n=20	Neg control, n=11
Duration (Median with range; weeks)			N/A
From the first ICI infusion to sample donation	36.9 [6, 134.4]	31.1 [1.3, 244]	
From the last ICI infusion to sample donation	6.1 [0.4, 84.4]	6.6 [0.1, 126]	
From development of symptoms to sample donation	10 [1.6,132.6]	6.7 [0.1, 22.1]	
Systemic steroids <4 weeks prior to sample donation	1 (5)	0 (0)	N/A
DMARDs < 12 weeks prior to sample donation	2 (10)	1 (5)	N/A
ESR (Median; Range)	14 [4, 77]	39 [7, 113]	N/A
CRP (Median; Range)	2.7 [0.4, 78.4]	15.4 [0.8, 173.9]	N/A
CDAI (Median; Range)	15 [0.6, 48]	19 [3, 47]	N/A

the first-line therapy for irAEs, significantly abrogate the antitumor efficacy of ICIs. Therefore, it is critical to identify biomarkers which predict steroid resistance in irAE patients. This is particularly important in managing ICI-arthritis, because it requires long-term therapy, often with disease modifying anti-rheumatic drugs (DMARDs) in addition to systemic steroids.

Methods: Between 2019 and 2022, we enrolled 39 patients who newly developed joint pain and swelling following ICI therapy and were diagnosed with ICI-arthritis at the MD Anderson Rheumatology clinic. From the time of ICI-arthritis diagnosis, we prospectively followed these patients for one year. Simultaneously, at the time of ICI-arthritis diagnosis, we collected peripheral blood (PB) samples for serum cytokine analysis. PB samples were collected 13.4 ± 22.1 (mean ± SD) weeks after the onset of arthritis symptoms. We also collected PB samples from 11 healthy volunteers as negative controls. Levels of serum cytokines were measured by a multiplex assay. Mean differences were determined using unpaired t-test for two groups or one-way ANOVA test for three groups.

Results: Nineteen patients responded well to steroid monotherapy (here, steroid sensitive [SS] group) while twenty patients required DMARDs during the one-year followup (here, steroid resistant [SR] group). In both groups, ICI-arthritis developed primarily with PD-1 inhibitor monotherapy (74% in the SS group vs. 65% in the SR group). Fifteen patients in the SS group and 18 patients in the SR group exhibited RA-like polyarthritis. In the SR group, DMARDs were initiated 3.5 ± 3.0 months after the onset of arthritis symptoms. Hydroxychloroquine was the most commonly prescribed DMARD, followed by tocilizumab, methotrexate, and sulfasalazine. Compared to the SS group, patients in the SR group required higher doses of steroids (cumulative dose of prednisone: 1,921 ± 1,382 mg in the SR group vs. 613 ± 741 mg in the SS group; P=0.0008). A higher percentage of patients in the SS group tested positive for antinuclear antibody (10% in the SR group vs. 42% in the SS group). Characteristics of the samples were comparable between the SS and SR groups (Table 1). Serum analyses revealed that the level of interleukin (IL)-10 was higher in the SR group (14.5 ± 3.4 pg/mL in the SR group vs. 10.3 ± 5.6 pg/mL in the SS group; P=0.03). The level of serum IL-17A was higher in patients with SR arthritis, but the difference did not reach statistical significance (11.0 ± 10.9 pg/mL in the SR group vs. 5.0 ± 6.9 pg/mL in the SS group; P=0.14).

Conclusion: Th17 cells might play an important role in steroid resistance in ICI arthritis while Treg signatures might be enhanced as a compensatory mechanism. In-depth cellular, molecular, and immunologic analyses of Th17 cells will enable us to identify a biomarker predicting steroid resistance in ICI arthritis.

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Abstract Number: 2572

Autoantibody Profile of Autoimmune Driven Interstitial Lung Disease as Compared to Idiopathic Pulmonary Fibrosis and Association of Autoantibodies with Survival

Elena Joerns[1], Chad Newton[2], Stanislav Kolenikov[3], Jeffrey Sparks[4] and David Karp[5], [1]University of Texas Southwestern Medical Center, Dallas, TX, [2]UT Southwestern, Dallas, TX, [3]NORC at the University of Chicago, Columbia, MO, [4]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [5]UT Southwestern Medical Center, Dallas, TX

SESSION INFORMATION

Session Date: Wednesday, November 15, 2023

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases III

Session Type: Abstract Session

Session Time: 9:00AM–10:30AM

Background/Purpose: The term interstitial pneumonia with autoimmune features (IPAF) describes patients with interstitial lung disease (ILD) and features of autoimmunity, that do not fulfill classification criteria for any of the defined rheumatic diseases (RD) or for other ILD subtypes. While cases of progressive ILD with clear autoimmune etiology such as those associated with RDs are usually treated with immunosuppression, IPAF, due to its heterogeneity and unclear pathophysiology, presents substantial difficulty in management. Our overarching hypothesis is that there are unique autoantibody profiles that can be identified in autoimmune forms of ILD reflecting the underlying inflammation-mediated damage. Understanding these signatures will allow us to identify an autoimmune endotype within poorly characterized ILD types such as IPAF with potential therapeutic implications.

Methods: We conducted a cross-sectional analysis of patients with RD-ILD (n=32) and idiopathic pulmonary fibrosis (IPF) (n=69) to evaluate autoantibodies correlating to autoimmune driven ILD (defined as RD-ILD). Autoantibody profiles were determined using a fluorescence-based multiplex assay for the detection of 124 IgM and IgG autoantibodies that detect autoantigens important in rheumatic diseases and ILD in the prior literature. T-test with False Discovery Rate (a=0.05) was performed to investigate significant mean differences between RD-ILD and IPF to identify autoantibodies characteristic of RD-ILD versus IPF, controlling for minimum detection level with censored regression methods. LASSO logistic regression was performed to identify autoantibodies predictive of RD-ILD subtype versus IPF subtype. A longitudinal cohort study

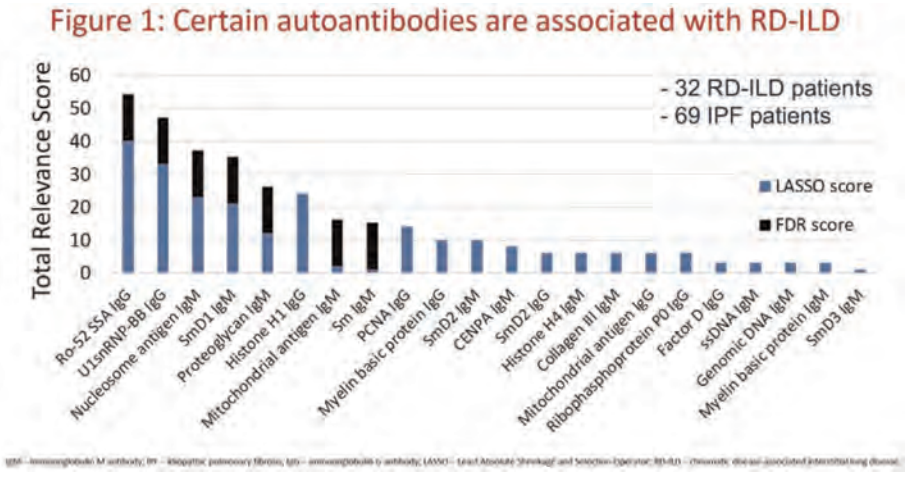


Figure 1: Certain autoantibodies are associated with RD-ILD

Table 1: Significant autoantibodies in RD-ILD progression

Table 1: Significant autoantibodies in RD-ILD progression

Autoantibody	HR (95% CI)	p-value
Histone H2-b IgM	2.3 (1.1-5.0)	0.031
Nucleolin IgM	2.10 (1.2-3.7)	0.01
Myelin basic protein IgM	2.29 (1.0-5.0)	0.039
Insulin IgM	24.6 (1.2-508.3)	0.038
Hemocyanin IgM	1.8 (1.1-3.0)	0.017
Ro-60 SSA IgG	2.4 (1.1-4.9)	0.022
Hemocyanin IgG	1.8 (1.1-3.0)	0.017
GP-210 IgG	1.4 (1.2-1.7)	0.001
Complement 4 IgG	4.6 (1.2-18.2)	0.028
Topoisomerase IgG	2.2 (1.1-4.2)	0.024
TNF-alpha IgG	2.6 (1.3-5.2)	0.009

Table 2: Significant autoantibodies in IPF progression

Table 2: Significant autoantibodies in IPF progression

Autoantibody	HR (95% CI)	p-value
Matrigel IgM	1.5 (1.0-2.1)	0.045
Decorin bovine IgM	2.4 (1.2-4.8)	0.019
TNF-alpha IgM	1.4 (1.0-2.0)	0.044
TIF-1-gamma IgM	1.5 (1.0-1.3)	0.038
Prothrombin IgM	1.5 (1.1-2.2)	0.023
Ro52-SSA IgG	1.6 (1.9-2.3)	0.02

was performed to evaluate association of autoantibodies with lung disease progression (defined as relative forced vital capacity (FVC) decline of 10% or more, death, or lung transplant). Cox logistic regression was utilized to assess the association of autoantibodies with time to progression within each ILD subtype.

Results: Seven autoantibodies were selected by both FDR and LASSO methods, with additional autoantibodies selected by one of the other two methods. Ro-52 SSA IgG, U1snRNP IgG, nucleosome antigen IgM, SM-D1 IgM, proteoglycan IgM, and histone H1 IgG autoantibodies showed highest relevance score for association with RD-ILD versus IPF subtype (Figure 1).

In RD-ILD, 11 autoantibodies were significantly associated with faster progression, while in IPF, six autoantibodies were significantly associated with the outcome.

Conclusion: Several autoantibodies appear to be associated with RD-ILD more than IPF. Greater autoantibody level elevation in RD-ILD than in IPF emphasizes the lack of autoimmunity in the IPF patients. Different autoantibodies were associated with progression in RD-ILD and IPF, suggesting different mechanisms of damage. Autoantibodies predicting faster progression in IPF patients emphasized potentially undiagnosed autoimmune ILDs among IPF patients and the need for broad testing in a variety of ILDs. Knowledge of autoantibody profiles associated with autoimmune lung disease and progression in various ILD subtypes has implications for management decisions in ILD.

Disclosure: E. Joerns: None; **C. Newton**: Boehringer-Ingelheim, 2; **S. Kolenikov**: None; **J. Sparks**: AbbVie, 2, Amgen, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, 5, Gilead, 2, Inova Diagnostics, 2, Janssen, 2, Optum, 2, Pfizer, 2, ReCor, 2; **D. Karp**: Ampel Biosciences, 2, Biogen, 5, Bristol-Myers Squibb(BMS), 5, Celgene, 5, Eli Lilly, 5, Genentech, 5, Provention Bio, 1, Rilite, 5, UCB, 5.

Abstract Number: 2573

Prevalence of Pulmonary Hypertension in a Cohort of Patients with Interstitial Pneumonia with Autoimmune Features and Its Effect on Lung Disease Progression and Mortality

Michelle Ghebranious, Elena Joerns, Traci Adams and Trushil Shah, University of Texas Southwestern Medical Center, Dallas, TX

SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases III
Session Type: Abstract Session
Session Time: 9:00AM–10:30AM

Background/Purpose: Interstitial pneumonia with autoimmune features (IPAF) is a subset of interstitial lung disease (ILD) that manifests with interstitial pneumonia and features of autoimmunity while not meeting classification criteria for a defined rheumatic disease. Recent studies have examined the clinical characteristics, common comorbidities, and outcomes of IPAF patients, but little is known regarding the presence of pulmonary hypertension (PH) in this population. Given the known effect of PH on decreased functional capacity and increased mortality in patients with underlying ILD, we characterize the effect of PH on lung disease progression and mortality in a cohort of patients with IPAF.

Methods: Using a retrospective study design, we evaluated the prevalence of PH in an institutional cohort of patients with IPAF at the University of Texas Southwestern Medical Center. Included patients were identified as having pre-capillary PH on right heart catheterization as defined by the European Society of Cardiology 2022 guidelines. Descriptive statistics were used to describe baseline data including demographic factors, radiographic patterns, pulmonary function tests, and 6-minute walk distance. In addition, right heart catheterization (RHC) and echocardiogram (TTE) data were collected and used to stratify patients according to disease severity (severe = mean pulmonary artery pressure (mPAP) ≥30 mmHg and pulmonary vascular resistance (PVR) ≥4 WU). Using Cox logistic regression, we evaluated the association of clinical variables on time to relative forced vital capacity (FVC) decline of ≥10% and survival.

Results: A cohort of 173 IPAF patients was analyzed, of which 46 patients (26.6%) met criteria for pre-capillary PH by RHC. Clinical characteristics of the patients with PH are summarized in Table 1. Among the patients with PH by RHC (n=46), 21 (46%) were classified as having mild or moderate PH, and 25 (54%) with severe PH. The average time between IPAF and PH diagnosis was 2.35 (SD ± 2.1) years. Following diagnosis, 92% of patients with severe PH were followed in PH clinic and started on treatment. There was not a statistically significant association between the severity of PH, being followed in PH clinic, or the number of PH medications and time to relative FVC decline ≥10% or mortality (Table 2). A trend was observed as patients with more severe PH had a faster decline in FVC of 10% or more (Figure 1).

Conclusion: PH was prevalent in our cohort of patients with IPAF and the severity of PH was associated with lung function decline and mortality, although this was not statistically significant. Clinicians taking care of patients with IPAF should be aware of the high prevalence of PH and its possible association with clinical outcomes in this population. Thus, a high index of suspicion for the condition should be maintained when a patient with IPAF is evaluated, and further screening and workup should be considered if PH is suspected.

Table 1: Baseline Characteristics of IPAF Patients at Time of PH Diagnosis

Table 1: Baseline Characteristics of IPAF Patients at Time of PH Diagnosis (n=46)				
Age, years	62.7 ± 11.1			
Sex	Male: 12 (26%)		Female: 34 (74%)	
Race	White: 26 (57%)	Black: 14 (30%)	Asian: 1 (2%)	Other: 5 (11%)
Ethnicity	Hispanic: 6 (13%)		Non-Hispanic: 40 (87%)	
Smoking Status	Current/Former Smoker: 19 (41%)		Non-Smoker: 27 (59%)	
Radiographic Pattern (n = 41)	Usual Interstitial Pneumonia: 11 (27%)		Non-Usual Interstitial Pneumonia: 30 (73%)	
FVC (% predicted) (n = 45)	55.9 ± 15.2			
DLCO (% predicted) (n = 34)	31.1 ± 14.8			
6-MWD, meters (n = 40)	222.6 ± 91.9			
NT-proBNP, pg/mL (n=20)	2656.9 ± 3538.5			
CCI (n = 46)	3.4 ± 2.5			
RDCI (n = 46)	3.7 ± 1.2			
Right Heart Catheterization (n = 46)	RA Pressure, mmHg		4.8 ± 4.3	
	Mean PA Pressure, mmHg		34.9 ± 11.8	
	Wedge Pressure, mmHg		7.9 ± 4.4	
	PVR, Wood units		5.6 ± 3.2	
	Cardiac Index, L/m2		2.8 ± 0.8	
	SVO2, %		68.3 ± 12.3	
Echocardiogram (n = 40)	TR Severity (n =39)		Normal/Mild	31 (79%)
			Moderate/Severe	8 (41%)
	RVSP (n = 40)		<45 mmHg	21 (53%)
			≥45 mmHg	19 (47%)
	RA Size (n = 37)		Normal	23 (62%)
			Dilated	14 (38%)
	Septal Flattening (n = 35)		Yes	16 (46%)
			No	19 (54%)
	RVDd, cm (n = 24)		4.21 ± 0.73	
	LVDd/RVDd (n = 24)		>1	7 (29%)
			≤1	17 (71%)
	RV Function (n = 40)		Normal	28 (70%)
			Reduced	12 (30%)
	Pulmonary Artery Acceleration Time, ms (n = 35)		0.08 ± 0.03	
	Pericardial Effusion (n = 39)		Yes	14 (36%)
			No	25 (64%)
	IVC Dilation (n = 30)		Yes	9 (30%)
			No	21 (70%)

FVC = forced vital capacity; DLCO = diffusing capacity of lung for carbon monoxide; 6-MWD = 6-minute walk distance; NT-proBNP = N-terminal pro-B-type natriuretic peptide; CCI = charlson comorbidity index; RDCI = rheumatic disease comorbidity index; RA = right atrium; PA = pulmonary arterial; PVR = pulmonary vascular resistance; SVO_2 = mixed venous oxygen saturation; TR = tricuspid regurgitation; RVSP = right ventricular systolic pressure; RVDd = right ventricular diastolic diameter; LVDd = left ventricular diastolic diameter; RV = right ventricular; IVC = inferior vena cava

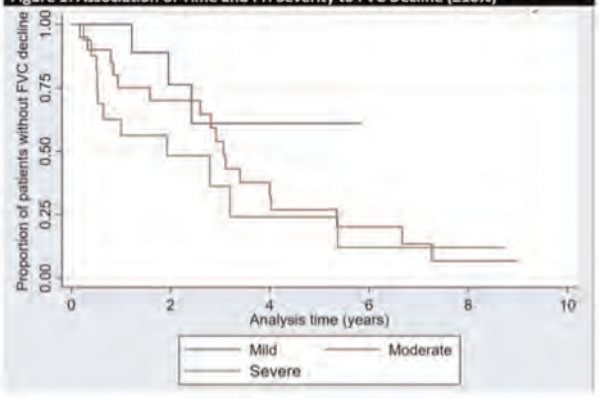
Table 2: Evaluation of Time to FVC Decline and Mortality

Table 2: Evaluation of Time to FVC Decline and Mortality

Evaluation of Time to FVC Decline from Initial PFTs at IPAF Diagnosis			
	HR	95% CI	p-value
PH Severity	1.62	0.95-2.77	0.077
• Mild	1.00		
• Moderate	2.36	0.69-8.10	0.173
• Severe	3.15	0.87-11.41	0.08
Treatment (Yes/No)	1.11	0.52-2.38	0.786
Number of Medications	1.02	0.78-1.35	0.852
Followed by PH Clinic	1.18	0.54-2.57	0.681
CCI	1.01	0.87-1.18	0.867
RDCI	0.96	0.68-1.35	0.813
Evaluation of Time to Mortality from Time of IPAF Diagnosis			
	HR	95% CI	p-value
PH Severity	1.23	0.66-2.29	0.507
• Mild	1.00		
• Moderate	0.68	0.20-2.33	0.535
• Severe	1.24	0.38-3.98	0.722
Treatment (Yes/No)	0.82	0.33-2.05	0.679
Number of Medications	1	0.73-1.38	0.999
Followed by PH Clinic	0.77	0.31-1.92	0.578
CCI	1.17	0.98-1.38	0.077
RDCI	1.25	0.86-1.81	0.249
Evaluation of Time to Mortality from Time of RHC			
	HR	95% CI	p-value
PH Severity	0.96	0.51-1.79	0.892
• Mild	1.00		
• Moderate	0.54	0.16-1.88	0.333
• Severe	0.75	0.23-2.46	0.633
Treatment (Yes/No)	0.73	0.29-1.83	0.503
Number of Medications	0.91	0.66-1.26	0.583
Followed by PH Clinic	0.62	0.25-1.55	0.309
CCI	1.09	0.92-1.29	0.312
RDCI	1.09	0.76-1.57	0.631

FVC = forced vital capacity; PFT= pulmonary function test; IPAF = interstitial pneumonia with autoimmune features; HR = hazard ratio; CI = confidence interval; PH = pulmonary hypertension; CCI = charlson comorbidity index; RDCI = rheumatic disease comorbidity index; RHC = right heart catheterization

Figure 1: Association of Time and PH Severity to FVC Decline (≥10%)



FVC = forced vital capacity; PH = pulmonary hypertension

Figure 1: Association of Time and PH Severity to FVC Decline (≥10%)

Disclosure: M. Ghebranious: None; **E. Joerns**: None; **T. Adams**: None; **T. Shah**: None.

Abstract Number: 2574

Are Patients Classified as IPAF More Likely to Also Meet SLE Criteria by 2019 EULAR/ACR Than by SLICC?: An Abstract

Gabriela Martinez Zayas[1], David Karp[1] and Elena Joerns[2], [1]UT Southwestern Medical Center, Dallas, TX, [2]University of Texas Southwestern Medical Center, Dallas, TX

SESSION INFORMATION

Session Date: Wednesday, November 15, 2023

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases III

Session Type: Abstract Session

Session Time: 9:00AM–10:30AM

Background/Purpose: Interstitial pneumonia with autoimmune features (IPAF) is a research classification proposed by the European Respiratory Society and American Thoracic Society Task Force for those patients with forms of interstitial lung disease (ILD) that have autoimmune features but that do not classify as having systemic rheumatic diseases such as systemic lupus erythematous (SLE).(1)

In 2012 the Systemic Lupus International Collaborating Clinics (SLICC) published criteria to identify and classify patients with SLE. (2) Subsequently, in 2019 the European Alliance of Association of Rheumatology/American College of Rheumatology (EULAR/ACR) published updated criteria SLE criteria. Sensitivities were similar, but 2019 EULAR/ACR criteria had superior specificity. (3)

We hypothesized that patients initially classified as IPAF may meet SLE by 2019 ACR/EULAR criteria more frequently than by SLICC criteria. The purpose of our study was to review data of patients classified as IPAF and assess if there is a difference in classification of SLE by both sets of criteria.

Methods: This observational, single-center cohort study included consecutive patients who had initially been classified as having IPAF between December 1st, 2005-August 31st, 2019. Two authors (GM-Z, EKJ) independently and retrospectively reviewed patients' charts and assigned SLE criteria by SLICC or 2019 EULAR/ACR classifications. Fisher's exact test was used to assess for significant difference in number of patients' meeting SLE criteria by SLICC criteria versus 2019 EULAR/ACR criteria.

Results: A total of 197 patients that had been initially classified as IPAF were included. Out of these 197 patients, 12 met SLE criteria by SLICC and 23 by 2019 EULAR/ACR. All but three patients that met SLE criteria SLICC also met 2019 EULAR/ACR criteria. The difference in eligibility for these three patients was due to lymphopenia (Figure 1). The most frequent SLE inclusion characteristics by either criteria and by 2019 EULAR/ACR criteria alone are shown in Figures 1 and 2, respectively. The difference in meeting SLE criteria between groups was statistically significant ($p< 0.001$, Table 1).

Conclusion: The difference in the number of patients originally classified as IPAF that met SLE criteria by SLICC and by 2019 EULAR/ACR upon re-review in 2023 was statistically significant (12 vs 23 patients, respectively, $p < 0.001$, Table 1). Based on our results, we conclude that 2019 ACR/EULAR criteria are superior for SLE classification in patients with ILD. ILD may be an underrecognized manifestation of SLE. Patients with ILD who have features seen in SLE, particularly dsDNA/Smith, arthritis and serositis should undergo full work-up to evaluate for other SLE clinical characteristics.

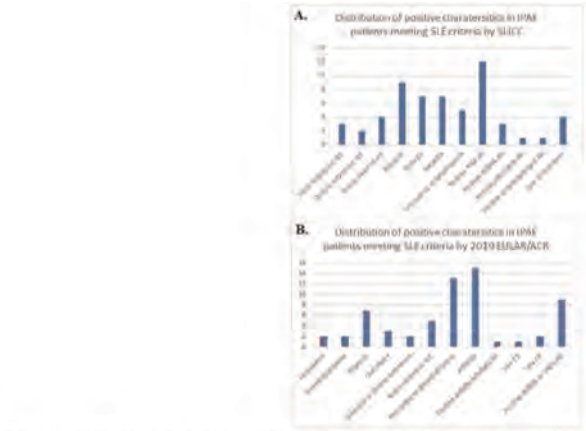


Figure 1. The figure shows the distribution of positive characteristics in IPAF patients meeting SLE criteria by A) SLICC and by B) 2019 EULAR/ACR. Characteristics that were not met by any patients were omitted from the figure. Abbreviations: IPAF: interstitial pneumonia with autoimmune features; SLE=systemic lupus erythematous; SLICC: Systemic Lupus International Collaborating Clinics; EULAR/ACR European Alliance of Association of Rheumatology/American College of Rheumatology; Ab=antibodies.

Figure 1. The figure shows the distribution of positive characteristics in IPAF patients meeting SLE criteria by A) SLICC and by B) 2019 EULAR/ACR

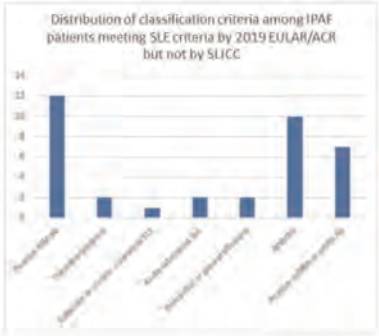


Figure 2. The figure shows the distribution of classification criteria among IPAF patients that met SLE criteria by 2019 EULAR/ACR but not by SLICC. Characteristics that were not met by any patients were omitted from the figure. Abbreviations: IPAF: interstitial pneumonia with autoimmune features; SLE=systemic lupus erythematous; SLICC: Systemic Lupus International Collaborating Clinics; EULAR/ACR European Alliance of Association of Rheumatology/American College of Rheumatology; Ab=antibodies.

Figure 2. The figure shows the distribution of classification criteria among IPAF patients that met SLE criteria by 2019 EULAR/ACR but not by SLICC.

Table 1. IPAF Patients Meeting SLE Criteria by SLICC and 2019 EULAR/ACR.

Table 1. IPAF Patients Meeting SLE Criteria by SLICC and 2019 EULAR/ACR.

	IPAF[a] patients found to meet SLE[b] criteria by 2019 EULAR[d]/ACR[e]	IPAF[a] patients found not to meet SLE[b] criteria by 2019 EULAR[d]/ACR[e]	Total number of patients	Fisher's exact (p-value)
IPAF[a] patients found to meet SLE[b] criteria by SLICC	9	3	12	<0.001
IPAF[a] patients found not to meet SLE[b] criteria by SLICC	14	171	185	
Total number of patients	23	174	197	

Note: [a]Interstitial pneumonia with autoimmune features, [b]Systemic lupus erythematous, [c]Systemic Lupus International Collaborating Clinics, [d]European Alliance of Association of Rheumatology, [e]American College of Rheumatology

Disclosure: G. Martinez Zayas: None; **D. Karp**: Ample, 2, Biogen, 5, Bristol myers, 5, Celgene, 5, Eli Lilly, 5, Genetech, 5, Prevention Bio, 1, Rilite, 5, UCB, 5; **E. Joerns**: None.

Abstract Number: 2575

Accurate Stratification of Cancer Risk in a Real-World Cohort Using the International Guideline for Idiopathic Inflammatory Myopathy-Associated Cancer Screening

Alexander Oldroyd[1], Francisca Bozan[1], Xia Lyu[2], Patrick Gordon[3], David Isenberg[4], Neil McHugh[5], Harsha Gunawardena[6], Patrick Kiely[7], Janine Lamb[1], Pedro Machado[8], James Miller[9], Sarah Tansley[5] and Hector Chinoy[10], [1]University of Manchester, Manchester, United Kingdom, [2]Department of Rheumatology, Shanghai Renji Hospital, School of Medicine, Shanghai Jiaotong University, Shanghai, China, [3]NHS, London, United Kingdom, [4]University College London, London, United Kingdom, [5]University of Bath, Bath, United Kingdom, [6]North Bristol NHS Trust, Bristol, United Kingdom, [7]St George's University Hospitals NHS Foundation Trust, London, United Kingdom, [8]Centre for Rheumatology & Department of Neuromuscular Diseases, University College London, London, UK. Department of Rheumatology, Northwick Park Hospital, London North West University Healthcare NHS trust, London, UK., London, United Kingdom, [9]Royal Victoria Infirmary, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle, United Kingdom, [10]The University of Manchester, Sale, United Kingdom

SESSION INFORMATION

Session Date: Wednesday, November 15, 2023

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science II

Session Type: Abstract Session

Session Time: 9:00AM–10:30AM

Background/Purpose: Adult-onset idiopathic inflammatory myopathy (IIM) is associated with an increased cancer risk within three years prior to or following IIM onset. The International Guideline for Idiopathic Inflammatory Myopathy-Associated Cancer Screening recommends individual patient risk stratification into "high", "moderate", and "standard" according to IIM subtype, antibody profile, and clinical features[1]. Application in a real-world IIM cohort could assess the accuracy of this risk stratification approach and guide future amendments.

Methods: The MyoProsp study recruited a UK-based cohort with adult onset IIM within 2 years of diagnosis between 2016 and 2020. Comprehensive demographic, disease activity, IIM subtype, myositis-specific/associated autoantibody (MSA/MAA), and cancer data (primary cancer site, date of diagnosis) were collected. Estimated cancer risk of each participant ("high", "moderate", and "standard") according to the International Guideline for Idiopathic Inflammatory Myopathy-Associated Cancer Screening was identified. "High disease activity" (a high risk factor) was defined as physician global and patient global assessment scores greater than 75 (range 0-100). As defined in the guideline, participants with two or more "high risk factors" (see Table 1) were assigned as high cancer risk; those with one "high risk factor" or two or more "intermediate risk factors" were assigned as moderate cancer risk; the remaining were assigned as standard risk. The concordance of risk stratification and actual cancer diagnosis was calculated across the cohort.

Results: Two hundred and ninety participants (72% female, mean age 54 years at time of recruitment) were included in the analysis (see Table 1 for a profile of IIM subtypes and presence of cancer risk factors). One hundred and twenty three participants (42%) fulfilled criteria for high cancer risk, 116 (40%) moderate risk, and 51 (17%) standard risk. Seventeen cancers (6% of whole cohort) were detected within the cohort, of which five (29%) were breast cancer, two (12%) cancer of unknown primary, two stomach (12%), and one (6%) each of bladder, endometrial, kidney, lung, lymphoma, oesophagus, ovarian, and prostate. The "high risk" group displayed the highest proportions of cancers (n=14, 11%), followed by the "moderate risk" group (n=3, 3%; one each of breast, endometrial, and kidney cancer); no participant with "standard risk" had a cancer diagnosis.

Table 1 – Demographics, profile of risk factors, and cancer diagnoses stratified by cancer risk category

Variable		Total cohort N = 290	Cancer risk group†		
			High N = 123	Moderate N = 116	Standard N = 51
Cancer diagnosis N (%)		17 (5.9)	14 (11.4)	3 (2.6)	0 (0.0)
Mean age / years (SD)		54.1 (14.8)	56.7 (13.3)	55.6 (14.1)	32.4 (6.1)
High risk factors N (%)	DM	76 (26.0)	66 (53.7)	10 (8.6)	0 (0.0)
	Anti-TIF1-gamma	4 (1.4)	4 (3.3)	0 (0.0)	0 (0.0)
	Anti-NXP2	1 (0.3)	1 (0.8)	0 (0.0)	0 (0.0)
	Age >40 years at time of IIM onset	204 (70.3)	113 (91.9)	91 (78.4)	0 (0.0)
	Persistent high disease activity*	19 (6.6)	15 (12.2)	4 (3.4)	0 (0.0)
	Dysphagia	86 (29.7)	80 (65.0)	6 (5.2)	0 (0.0)
	Cutaneous necrosis/ulceration	26 (9.0)	24 (19.5)	2 (1.7)	0 (0.0)
Intermediate risk factors N (%)	PM	45 (15.5)	5 (4.1)	20 (17.2)	20 (39.2)
	CADM	1 (0.3)	0 (0.0)	0 (0.0)	1 (2.0)
	IMNM	40 (13.8)	14 (11.3)	22 (19.0)	4 (7.8)
	Anti-SAE1	11 (3.8)	10 (8.1)	1 (0.9)	0 (0.0)
	Anti-HMGCR	5 (1.7)	2 (1.6)	3 (2.6)	0 (0.0)
	Anti-Mi2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Anti-MDA5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Male sex	81 (27.9)	44 (35.8)	35 (30.2)	2 (3.9)
Low risk factors N (%)	ASyS	59 (20.3)	14 (11.4)	33 (28.4)	12 (23.5)
	CTD-associated	39 (13.4)	17 (13.8)	15 (12.9)	7 (13.7)
	Anti-SRP	5 (1.7)	0 (0.0)	4 (3.4)	1 (2.0)
	Anti-Jo1	99 (34.1)	21 (17.1)	48 (41.4)	30 (58.8)
	Non-Jo1 ASSD antibody	11 (3.8)	3 (2.4)	7 (6.0)	1 (2.0)
	MAA	20 (6.9)	10 (8.1)	7 (6.0)	3 (5.9)
	Raynaud's phenomenon	92 (31.7)	45 (36.6)	34 (29.3)	13 (25.5)
	Inflammatory arthropathy	66 (22.8)	36 (29.3)	24 (20.7)	6 (11.8)
	Interstitial lung disease	94 (32.4)	31 (25.2)	37 (31.9)	26 (51.0)

IIM = idiopathic inflammatory myopathy
DM = dermatomyositis
PM = polymyositis
IMNM = immune-mediated necrotising myopathy
CADM = clinically amyopathic dermatomyositis
ASyS = anti-synthetase syndrome
CTD = connective tissue disease
NXP2 = nuclear matrix protein 2
TIF1-gamma = transcriptional intermediary factor 1
SAE1 = small ubiquitin-like modifier-1 activating enzyme
HMGCR = 3-hydroxy 3-methylutaryl coenzyme A reductase
MDA5 = melanoma differentiation-associated gene 5
SRP = signal recognition particle
MAA = myositis-associated autoantibody (PM-Scl, Ku, RNP, Ro/La [SSA/B])
† According to The International Guideline for Idiopathic Inflammatory Myopathy-Associated Cancer Screening – recommendations 5, 6, 7, and 8
* Defined as physician global and patient global assessment scores greater than 75 (range 0-100).

Conclusion: Risk stratification recommended by The International Guideline for Idiopathic Inflammatory Myopathy-Associated Cancer Screening clearly and appropriately stratified cancer risk in a real-world IIM cohort, thus demonstrating clinical utility. Future research should focus on investigating the impact of risk stratification upon stage at time of cancer diagnosis and outcomes, including survival.

[1] Oldroyd A, Callen J, Chinoy H, Chung L, Fiorentino D, Gordon P, Machado P, McHugh N, O'Callaghan A, Schmidt J, Tansley S, Vleugels R, Werth V, Aggarwal R. Cancer Screening Recommendations for Patients with Idiopathic Inflammatory Myopathy [abstract]. Arthritis Rheumatol. 2022; 74 (suppl 9).

Disclosure: A. Oldroyd: None; **F. Bozan**: None; **X. Lyu**: None; **P. Gordon**: Celltrion, 12, Support to attend EULAR conference 2023, Galapagos, 1; **D. Isenberg**: None; **N. McHugh**: None; **H. Gunawardena**: Boehringer-Ingelheim, 6; **P. Kiely**: None; **J. Lamb**: Eli Lilly, 5; **P. Machado**: AbbVie/Abbott, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Celgene,

2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Orphazyme, 2, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 6; **J. Miller**: None; **S. Tansley**: Boehringer-Ingelheim, 6; **H. Chinoy**: AstraZeneca, 1, Biogen, 2, Eli Lilly, 5, GlaxoSmithKlein(GSK), 6, Novartis, 2, Orphazyme, 2, Pfizer, 1, UCB, 6.

Abstract Number: 2576

Rapid Onset of Response in Adult Dermatomyositis Patients Receiving Anti-interferon β (PF-06823859): Results of a Phase 2, Double-blind, Randomized, Placebo-Controlled Study

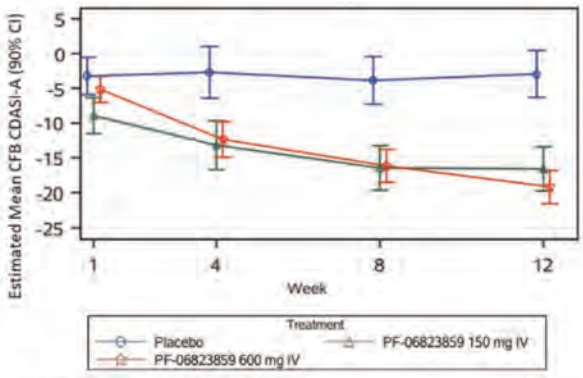
Rohit Aggarwal[1], Elena Peeva[2], Aaron Mangold[3], Abigail Sloan[2] and Myron Chu[2], [1]University of Pittsburgh, Pittsburgh, PA, [2]Pfizer, Cambridge, MA, [3]Mayo Clinic, Scottsdale, AZ

SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science II
Session Type: Abstract Session
Session Time: 9:00AM–10:30AM

Background/Purpose: Interferon (IFN) dysregulation is a key feature in the pathogenesis of Dermatomyositis (DM). PF-06823859 is a potent, selective, humanized IgG1 neutralizing antibody directed against IFNb. We examined the onset of efficacy of PF-06823859 in patients (pts) with moderate-to-severe refractory DM.

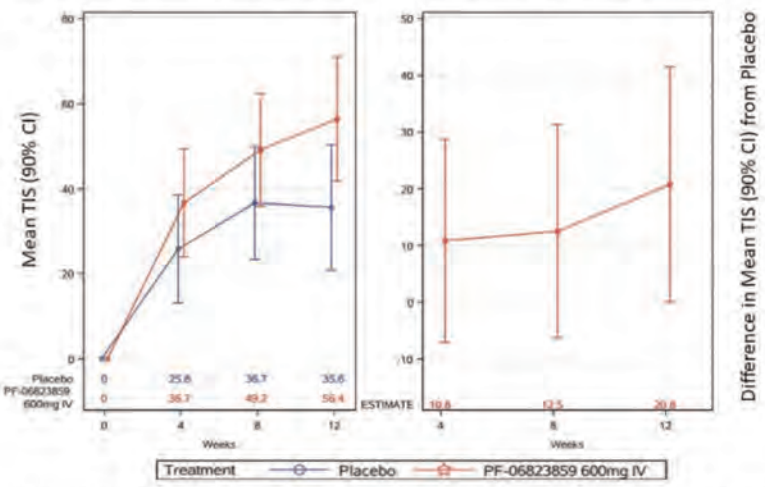
Methods: This double-blind, placebo (PBO)-controlled, Phase 2 study (NCT03181893) enrolled adult pts (18–75 years) with moderate-to-severe refractory DM.Pts with skin disease predominant (SP) DM and Cutaneous Dermatomyositis Disease Area and Severity Index activity [CDASI-A] score ≥14 who had failed ≥1 standard of care systemic treatment were randomized to PBO, PF-06823859 150 mg or 600 mg (intravenous administration on Day 0, wks 4 and 8). Pts with muscle disease predominant (MP) DM who met 1 of the following: (1) Manual Muscle Testing (MMT-8) ≤136/150 and Physician Global Assessment (PhGA) ≥3 cm on a 0–10 cm visual analogue scale (VAS) or (2) sum of PhGA, Patient Global Assessment (PtGA), Extra-muscular Global Assessment ≥10 cm (0–10 cm VA for each) and refractory disease, were randomized to PBO or IV PF-06823859 600 mg(Day 0, wks 4 and 8). Onset of efficacy was evaluated in the SP cohort using the CDASI-A, 5D-itch, Dermatology Quality of Life Index (DLQI), and SF-36 change from baseline to Wk 12. In the MP cohort, onset of efficacy was evaluated using the Total Improvement Score (TIS), Manual Muscle Testing (MMT-8), creatine kinase (CK) levels, PtGA, Health Assessment Questionnaire Disability Index (HAQ-DI) and FACIT-Fatigue change from baseline to Wk 12.

Change from Baseline of CDASI Activity Score (CDASI-A) in Skin Predominant Dermatomyositis Participants in Phase 2 Study C0251002 Receiving PF-06823859. Note: Lower CDASI-A score is better (improvement of disease)



Longitudinal ANCOVA Model, with baseline value as a covariate, treatment, visit as factor variables and treatment by visit as unstructured interaction effect

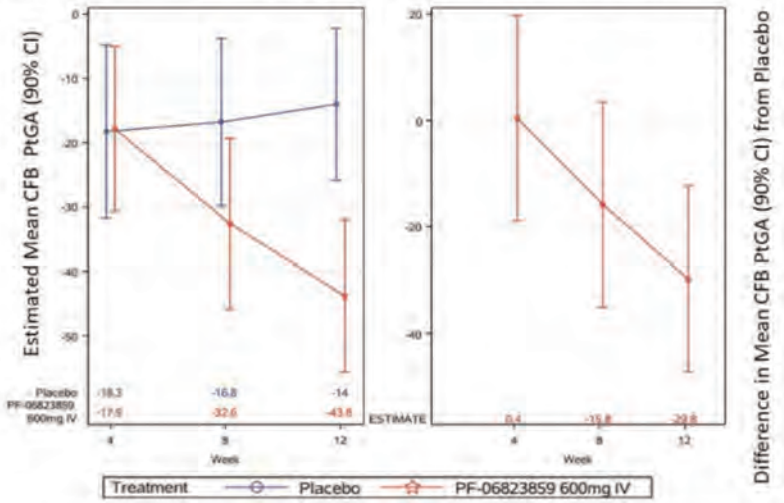
Total Improvement Score (TIS) in Muscle Predominant Dermatomyositis Participants in Phase 2 Study C0251002 Receiving PF-06823859 Following Sensitivity Analysis. Note: Higher TIS is better (improvement in disease)



MMRM Model with treatment, visit as factor variables, treatment by visit as unstructured interaction effect

Results: SP and MP cohorts had 57 and 18 pts respectively. In the SP cohort, differentiation from PBO in CDASI-A was observed at Wk 4 for both 150 mg (PBO-adjusted CFB -13.19 [p=0.0006]) and 600 mg (PBO-adjusted CFB -12.35 [p=0.0004]) doses. A reduction in CFB 5D-itch was observed for the 600 mg dose at Wk 1 (PBO-adjusted CFB 5D-itch 600 mg [p=0.0359]). PBO-adjusted CFB in DLQI and SF-36 mental component were observed for 150 and 600 mg (p=0.024, p=0.016 and p=0.009, p=0.0398, respectively) at Wk 4. In the MP cohort, a numerical advantage was observed in TIS scores at 600 mg compared to PBO with increasing trends from Wks 4-12 (PBO-adjusted CFB [p=0.0497] at Wk 12) following a sensitivity analysis that removed affected data following use of a prohibited medication by one pt. Significant reduction in CK and HAQ-DI was observed at Wk 4 and 8, respectively (PBO-adjusted CFB for 600 mg CK [p=0.044] and HAQ-DI [p=0.035]). A numerical differentiation in PtGA started at Wk 1 and reached significance at Wk 8 (PBO-adjusted CFB 600 mg [p=0.0470]). A numerical advantage in MMT-8 and FACIT-F were observed starting at Wk 4, but did not reach statistical significance.

Change from Baseline in Patient Global Assessment (PtGA) in Muscle Predominant Dermatomyositis Participants in Phase 2 Study C0251002 Receiving PF-06823859. Note: lower PtGA score is better (improvement of disease)



Longitudinal ANCOVA Model, with baseline value as a covariate, treatment, visit as factor variables and treatment by visit as unstructured interaction effect

Conclusion: PF-06823859 induced rapid improvement in 5D-itch (Wk 1), followed by CDASI-A, DLQI, and SF-36 (mental component) at Wk 4 in DM pts with SP disease. Rapid improvement in MP DM was observed at Wk 1 for PtGA, and at Wk 4 for MMT-8 and CK. The inhibition of IFNβ activity by PF-06823859 is a promising treatment in DM, with a more rapid onset of efficacy potentially allowing a faster taper of steroids than current DM therapies.

Disclosure: R. Aggarwal: Actigraph, 2, Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella Bioscience, 2, Corbus, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Mallinckrodt, 5, Merck, 2, Octapharma, 2, Pfizer, 2, 5, Q32, 5, Roivant, 2, Sanofi, 2, Teva, 2; **E. Peeva**: Pfizer, 3, Pfizer Inc, 3, 11; **A. Mangold**: Clarivate, 2, Corbus, 5, Horizon Therapeutics, 5, Merck/MSD, 5, Pfizer, 2, 5, Priovant, 5; **A. Sloan**: Pfizer, 3; **M. Chu**: Pfizer, 3, 11.

Abstract Number: 2577

Frequency of Atherosclerotic Cardiovascular Disease Following a Diagnosis of Idiopathic Inflammatory Myopathy: Data from a Large National Registry

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SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science II
Session Type: Abstract Session
Session Time: 9:00AM–10:30AM

Background/Purpose: Idiopathic inflammatory myopathies confer an increased risk of morbidity from cardiovascular disease. Prior work has noted more than double risk of cardiovascular events for patients with dermatomyositis (DM) and polymyositis (PM) when compared to the general population. Furthermore, in a single center study of patients with DM, one-fifth of hospitalizations were associated with an atherosclerotic cardiovascular (ASCVD) diagnosis or procedure. We investigated the incidence of new-onset ASCVD after International Classification of Disease (ICD) diagnosis code of DM, PM, dermatopolymyositis (DPM) or juvenile dermatomyositis (JDM).

Methods: This retrospective analysis used the TriNetX database, a national federated research network of de-identified data enrolling over 150 million patients. Patients were identified by entry of two ICD codes separated by at least 6 months, according to their first diagnosis code (i.e., DM, PM, DPM, or JDM). Patients with an ASCVD code that preceded the diagnosis code were excluded as we wanted to capture a new ASCVD event. We defined an ASCVD event as an ICD code entry for myocardial infarction, ischemic stroke, transient ischemic attack or peripheral arterial disease. Logistic regression modeling the odds of ASCVD outcome were used to produce adjusted odds ratios (OR) and 95% confidence intervals (95% CI) for differences among diagnosis codes.

Results: A total of 35,649 patients were identified, of whom 26% were male and the mean age at first IIM diagnosis code was 54 (table 1). In the sample, half of the patients had hypertension. The majority of patients (79%) were not on a cholesterol medication, and 20% had a prior dispensation for a statin medication. The ASCVD outcome occurred in 30% of patients with PM, 24% in patients with DM, 15% of patients with DPM and 4% of patients with JDM. The median time to ASCVD

Table 1: Demographics	n or mean or median	% or ±SD or (IQR)
Male, n %	9321	26.1
Age at first diagnosis, mean ± SD years, range=1 – 88	54.4	±17.2
Comorbidity history by 2 ICD codes within 90 days		
Overweight or obesity	8729	24.5
Obesity	6783	19.0
Hypertension	18194	51.0
Diabetes	8697	24.4
Smoking	6042	16.9
Alcohol	320	0.9
Cholesterol med history (not mutually exclusive)		
Statin	7025	19.7
Ezetimibe	622	1.7
PCSK9	162	0.5
Number of cholesterol meds per person		
None	28246	79.2
1	7012	19.7
2	376	1.1
all 3	15	0.0
ICD Diagnosis		
PM	16900	47.4
DM	10153	28.5
DPM	6501	18.2
JDM	2025	5.7
DM and PM same date	70	0.2
ASCVD at any time after diagnosis	8682	24.4
Median years to ASCVD (95% CI) after IIM diagnosis	12.4	(11.9, 13.6)

Abbreviations: SD=standard deviation, IQR= interquartile range, ICD=International Classification of Disease, PM=polymyositis, DM=dermatomyositis, DPM= dermatopolymyositis, IIM=Idiopathic inflammatory myopathy, JDM=Juvenile dermatomyositis, PCSK9=Proprotein convertase subtilisin/kexin type, CI= Confidence interval

event was 9.7 years for PM, 14.2 years for DM, and 16.7 years for DPM (Figure 1). There were higher odds of ASCVD outcome for all PM, DM, DPM patients compared to JDM (table 2). Compared to DM, patients with PM had 26% higher odds of ASCVD (table 2).

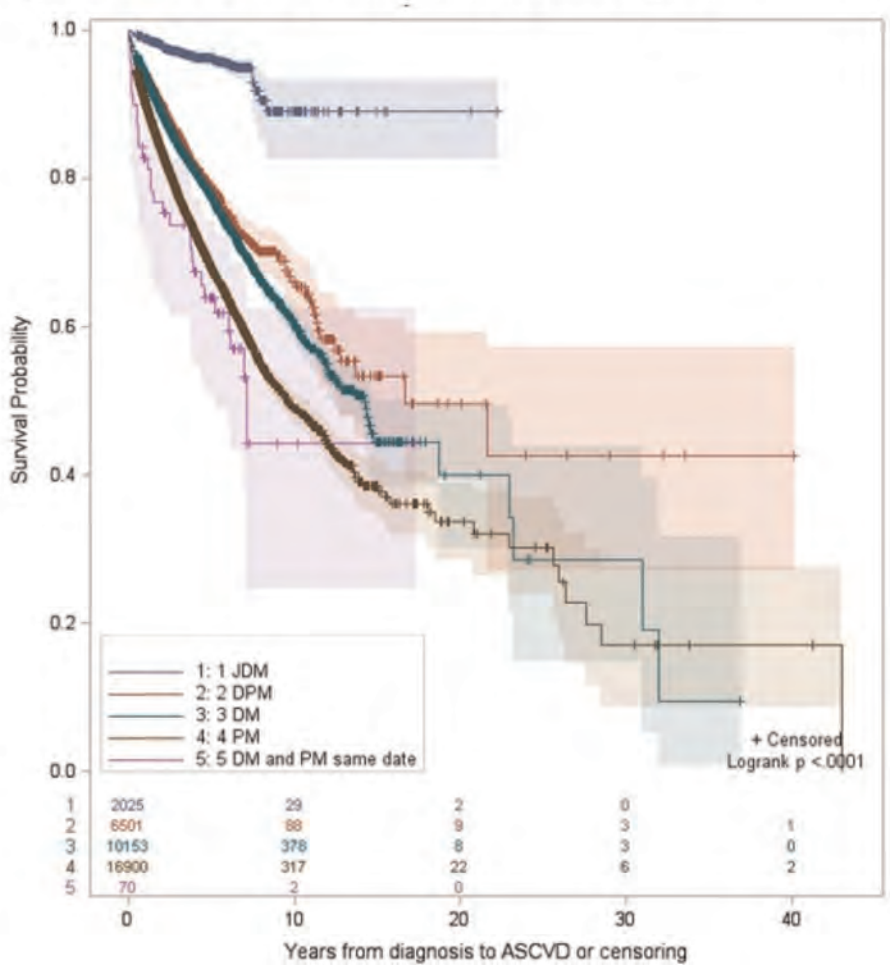
Conclusion: ASCVD is an important comorbidity that affects patients with IIM. Given the median time to event of 12 years, it appears to be a long-term complication after myositis diagnosis in patients who do not have concomitant ASCVD. This study also highlights the need for further evaluation into the use of the DPM code which represents a subset of patients seen in the US who have a longer time to ASCVD event compared to patients with ICD codes for DM or PM. Future study should investigate the shorter time-to-event observed in PM than other IIM. Additional study should evaluate whether special screening or intervention are necessary to reduce risk for ASCVD in IIM.

Table 2: Logistic regression modeling ICD diagnosis association with odds of ASCVD

Diagnosis type risk factor	*aOR (95% CI)*
PM (vs JDM)	**2.37 (1.77, 3.18)**
DM (vs JDM)	**1.88 (1.40, 2.52)**
DPM (vs JDM)	**1.87 (1.39, 2.53)**
PM (vs DPM)	**1.27 (1.15, 1.40)**
DM (vs DPM)	1.00 (0.90, 1.12)
PM (vs DM)	**1.26 (1.17, 1.37)**

Abbreviations: aOR=adjusted odds ratio; CI=confidence interval, PM=polymyositis, DM=dermatomyositis, DPM= dermatopolymyositis, JDM=Juvenile dermatomyositis, aOR shown in **BOLD** if statistically significant at alpha=0.05; adjusted for covariables: age at first diagnosis, year of birth, sex, overweight, obesity, hypertension, diabetes, smoking, alcohol, and follow-up time

Figure 1: Product-Limit Survival Estimate by IIM Diagnosis



Disclosure: A. Allenzara: Partner employed by Atai, 3, Partner employed by Latigo, 3; **C. Alvarez**: None; **A. Nelson**: None; **G. Foulke**: AstraZeneca, 2.

Abstract Number: 2578

Machine Learning Identifies New Sporadic Inclusion Body Myositis Endotypes Associated with Unique Autoantibody Profiles

Jenny Wei[1], Mark Tarnopolsky[2], Marie Hudson[3], Ross Mitchell[4], Katherine Buhler[5], Antoine Dufour[6], Luiz de Almeida[6], Paul R. Fortin[7], Eric Boilard[8], Yann Becker[8], Erin Hatcher[2], Mei Feng Zhang[6], Marvin Fritzler[6] and May Choi[6], [1]University of Toronto, Toronto, ON, Canada, [2]McMaster University, Hamilton, ON, Canada, [3]McGill University, Montréal, QC, Canada, [4]University of Alberta, Edmonton, AB, Canada, [5]University of Calgary; Cumming School of Medicine, Calgary, AB, Canada, [6]University of Calgary, Calgary, AB, Canada, [7]Centre ARThrite - CHU de Québec - Université Laval, Quebec City, QC, Canada, [8]Université Laval, Quebec City, QC, Canada

SESSION INFORMATION

Session Date: Wednesday, November 15, 2023

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science II

Session Type: Abstract Session

Session Time: 9:00AM–10:30AM

Background/Purpose: Sporadic inclusion body myositis (sIBM) is a subset of autoimmune inflammatory myopathies (AIM) that is often challenging to diagnose. The objective of this study was to use machine learning and a comprehensive profile of autoantibodies to: 1) examine sIBM endotypes, 2) differentiate sIBM from AIM. The primary goal was to identify an approach that would facilitate earlier and more precise diagnosis.

Table 1. Baseline Characteristics and Autoantibody Profiles of the Four sIBM Clinical Clusters

	Entire cohort (n=75)	Cluster 1 (n=22)	Cluster 2 (n=23)	Cluster 3 (n=23)	Cluster 4 (n=7)	P-value[1]	Adj. p-value[2]
Male, % (n)	62.2 (46)	0	100 (23)	100 (23)	0	**<0.001**	**<0.001**
Age, mean (SD) yrs	68.3 (9.2)	67.4 (8.3)	68.3 (9.9)	69.7 (9.9)	66.3 (8.3)	0.759	1.000
Creatine Kinase Level, mean (SD) U/L	504.4 (290.1)	574.8 (275.1)	533.4 (334.7)	460.0 (255.2)	385.1 (281.6)	0.081	0.317
Disease Severity, mean (SD)	1.93 (0.63)	2.14 (0.66)	1.76 (0.58)	2.07 (0.59)	1.43 (0.45)	0.106	0.343
Quad Atrophy, % (n)	94.6 (70)	100.0 (22)	95.7 (22)	91.3 (21)	71.4 (5)	**0.067**	0.317
Grip Weakness, % (n)	93.2 (69)	95.2 (20)	87.0 (20)	95.7 (22)	100.0 (7)	0.765	1.000
Dysphagia, % (n)	60.8 (45)	100.0 (22)	0.0 (0)	100.0 (23)	0.0 (0)	**<0.001**	**<0.001**
Knee Extension Weakness, % (n)	100 (74)	100.0 (22)	100.0 (23)	100.0 (23)	100.0 (7)	1.000	1.000
Autoantibodies, % (n)							
Anti-NTSc1A	73.0 (54)	68.2 (15)	60.9 (14)	91.3 (21)	57.1 (4)	0.055	0.317
Anti-RuvBL1	18.9 (14)	18.2 (4)	17.4 (4)	21.7 (5)	14.3 (1)	1.000	1.000
Anti-RuvBL2	1.4 (1)	0.0 (0)	4.3 (1)	0.0 (0)	0.0 (0)	1.000	1.000
Anti-PDHX	5.4 (4)	4.5 (1)	4.3 (1)	4.3 (1)	14.3 (1)	0.689	1.000
Anti-MFN1	8.1 (6)	9.1 (2)	8.7 (2)	4.3 (1)	14.3 (1)	0.780	1.000
Anti-MFN2	1.4 (1)	0.0 (0)	0.0 (0)	4.3 (1)	0.0 (0)	1.000	1.000
Anti-Jo-1	2.7 (2)	0.0 (0)	0.0 (0)	4.3 (1)	14.3 (1)	0.179	0.530
Anti-Mi2-α	2.7 (2)	4.5 (1)	4.3 (0)	0.0 (0)	0.0 (0)	0.809	1.000
Anti-Mi2β	10.8 (8)	13.6 (3)	8.7 (2)	13.0 (3)	0.0 (0)	0.871	1.000
Anti-NXP2	1.4 (1)	4.5 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.387	0.797
Anti-TIF1γ	2.7 (2)	0.0 (0)	0.0 (0)	8.7 (2)	0.0 (0)	0.445	0.889
Anti-PL7	4.1 (3)	9.1 (2)	0.0 (0)	0.0 (0)	0.0 (0)	0.490	0.953
Anti-PL12	5.4 (4)	4.5 (1)	8.7 (2)	4.3 (1)	0.0 (0)	1.000	1.000
Anti-PM75	1.4 (1)	4.5 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.689	1.000
Anti-PM100	2.7 (2)	9.1 (2)	0.0 (0)	0.0 (0)	0.0 (0)	0.387	0.797
Anti-Ku	1.4 (1)	0.0 (0)	0.0 (0)	4.3 (1)	0.0 (0)	1.000	1.000
Anti-SRP	2.7 (2)	4.5 (1)	4.3 (1)	0.0 (0)	0.0 (0)	0.809	1.000
Anti-EJ	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.000	1.000
Anti-OJ	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.000	1.000
Anti-Ro52/TRIM21	16.2 (12)	22.7 (5)	8.7 (2)	4.3 (1)	57.1 (4)	0.008	0.186
Anti-M2	6.8 (5)	9.1 (2)	0.0 (0)	8.7 (2)	14.3 (1)	0.380	0.797
Anti-LC-1	6.8 (5)	9.1 (2)	0.0 (0)	8.7 (2)	14.3 (1)	0.380	0.797
Anti-M2-3E	5.4 (4)	9.1 (2)	0.0 (0)	4.3 (1)	14.3 (1)	0.211	0.597
Anti-Sp100	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	14.3 (1)	0.093	0.317
Anti-gp210	5.4 (4)	9.1 (2)	0.0 (0)	8.7 (2)	0.0 (0)	0.569	1.000
Anti-SLA/LP	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.000	1.000
Anti-SLA	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.000	1.000
Anti-LKM-1	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.000	1.000
Anti-PML	2.7 (2)	0.0 (0)	0.0 (0)	4.3 (1)	14.3 (1)	0.179	0.530
Anti-VCP	27.0 (20)	18.2 (4)	34.8 (8)	30.4 (7)	14.3 (1)	0.559	1.000
ANA	60.8 (45)	63.6 (14)	56.5 (13)	47.8 (11)	100.0 (7)	0.090	0.317
AC1	18.9 (14)	18.2 (4)	13.0 (3)	26.1 (6)	14.3 (1)	0.769	1.000
AC2	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.000	1.000
AC3	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.000	1.000
AC4	44.6 (33)	45.5 (10)	47.8 (11)	34.8 (8)	57.1 (4)	0.694	1.000
AC5	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	14.3 (1)	0.093	0.317
AC6	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.000	1.000
AC7	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.000	1.000
AC8	1.4 (1)	4.5 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.387	0.797
AC9	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	14.3 (1)	0.093	0.317
AC10	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	14.3 (1)	0.093	0.317
AC11	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	14.3 (1)	0.093	0.317
AC12	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	14.3 (1)	0.093	0.317
AC13	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	14.3 (1)	0.093	0.317
AC14	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	14.3 (1)	0.093	0.317
AC15	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	14.3 (1)	0.093	0.317
AC16	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	14.3 (1)	0.093	0.317
AC17	1.4 (1)	0.0 (0)	4.3 (1)	0.0 (0)	0.0 (0)	1.000	1.000
AC18	6.8 (5)	4.5 (1)	0.0 (0)	8.7 (2)	28.6 (2)	0.053	0.317
AC19	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.000	1.000
AC20	20.3 (15)	31.8 (7)	21.7 (5)	4.3 (1)	28.6 (2)	0.081	0.317
AC21	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.000	1.000
AC22	1.4 (1)	4.5 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.387	0.797
AC23	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.000	1.000
AC24	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.000	1.000
AC25	1.4 (1)	0.0 (0)	0.0 (0)	4.3 (1)	0.0 (0)	1.000	1.000
AC26	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	14.3 (1)	0.093	0.317
AC27	1.4 (1)	4.5 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.387	0.797
AC28	4.1 (3)	4.5 (1)	0.0 (0)	4.3 (1)	14.3 (1)	0.278	0.728
AC29	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.000	1.000

Bolded values indicate statistically significant result.
1. Fisher's Exact test or one-way ANOVA
2. Benjamini-Hochberg correction with false discovery rate (FDR) alpha = 0.05

Table 2. Model Performance of Machine Learning Algorithms Based on Autoantibody Profiles to Differentiate Sporadic Inclusion Body Myositis (n=92) from Other Types of Autoimmune Inflammatory Myopathies[1] (n=129).

	Sensitivity	Specificity	Precision (PPV)	NPV	Accuracy	F1
Artificial Neural Network	57.6	87.6	78.3	74.6	75.1	65.6
Extreme Gradient Boosting (XGB)	71.3	81.1	72.7	79.5	76.5	71.1
Decision Tree	70.2	80.1	72.2	78.3	75.1	70.0
Logistic Regression	66.3	85.0	75.6	78.0	76.0	68.7
K-Nearest Neighbour	65.4	87.9	79.1	77.8	77.8	70.5
Support Vector Machine	59.9	89.7	80.9	75.7	76.4	67.0
Random Forest	71.3	75.9	67.0	79.1	73.3	67.9

1. Other autoimmune inflammatory myopathies included dermatomyositis, polymyositis, anti-synthase syndrome, immune-mediated necrotizing myositis, overlap myositis and other.
Abbreviations: NPV, negative predictive value; PPV, positive predictive value

Methods: Clinical and demographic information were obtained on sIBM patients and AIM disease comparators. Baseline sera from these patients were tested for conventional and novel autoantibodies that included anti-NT5c1A/Mup44 and anti-mitofusin (MFN)-1 and -2) using an addressable laser bead immunoassay, a multiplexed autoimmune liver disease array, and antinuclear antibodies (ANA) on HEp-2 substrates by an indirect immunofluorescence assay (IFA). Agglomerative hierarchical clustering based on clinical features (creatine kinase level, dysphagia, knee extension weakness, quadriceps atrophy, grip strength, and disease severity (graded by expert)) was performed to identify clinical sub-phenotypes of sIBM. Seven classification algorithms were trained using K-fold cross validation to differentiate sIBM from AIM based on the

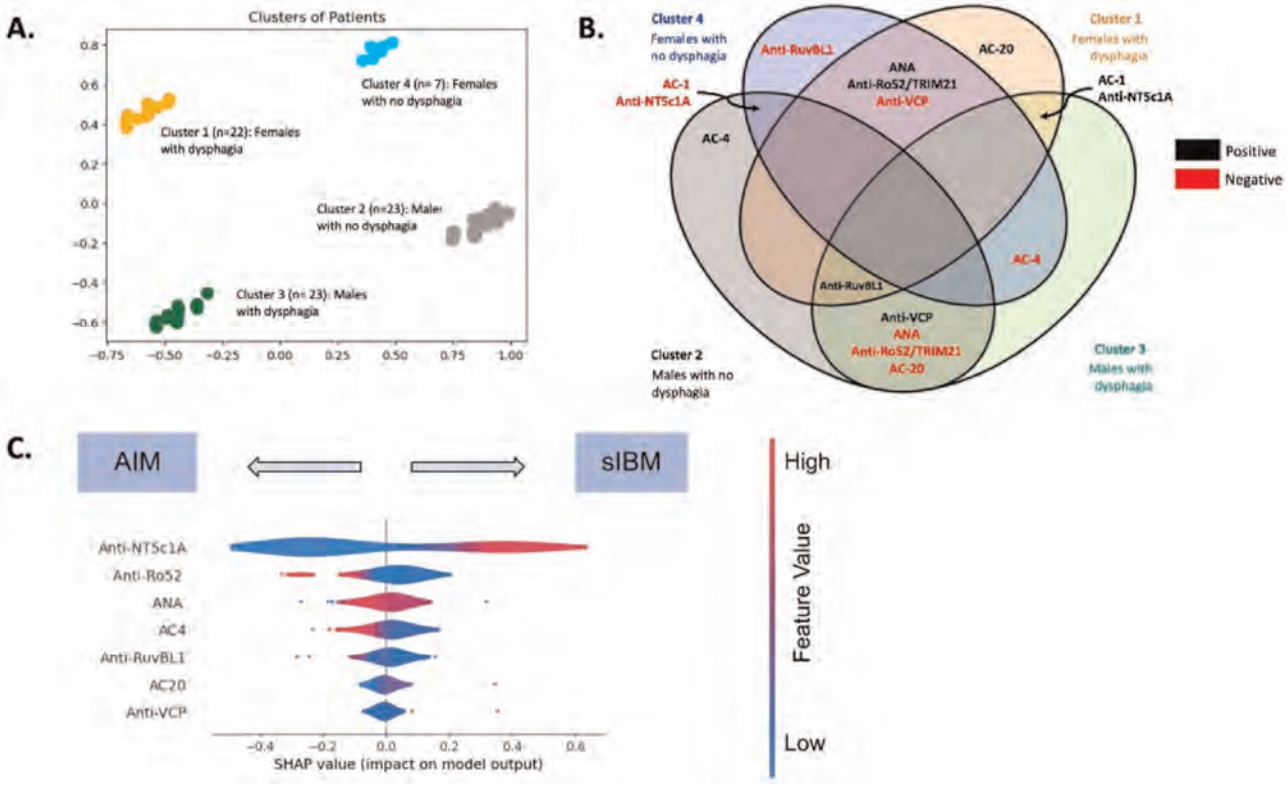


Figure 1. A) Four sIBM cluster identified by agglomerative hierarchical clustering based on clinical features (creatine kinase level, dysphagia, knee extension weakness, quadriceps atrophy, grip strength, and disease severity (graded by expert)). B) Autoantibody profile associated with each sIBM cluster determined by SHapley Additive exPlanation (SHAP). C) SHAP plots for the most important autoantibodies using Extreme Gradient Boosting machine learning model to differentiate sIBM from AIM (autoimmune inflammatory myopathies). Autoantibodies that had a frequency of less than 10% of the entire cohort are not shown on the SHAP plots.

autoantibodies and performance was assessed. SHapley Additive exPlanation (SHAP) plots identified the most important associated with each sIBM cluster and model used to different between sIBM vs. AIM.

Results: 75 sIBM patients were included in the cluster analysis (mean age 68.3 years (SD 9.2), 62.2% male) (**Table 1**). Four sIBM clinical clusters were identified: 1) females with dysphagia (n=22), 2) males with no dysphagia (n=23), 3) males with dysphagia (n=23), 4) females with no dysphagia (n=7) (**Figure 1a**). Based on the SHAP analysis, ANA and anti-Ro52/TRIM21 were more likely to be positive among female clusters (1 and 4), while anti-VCP was more likely to be positive among male clusters (2 and 3) (**Figure 1b**). Positive AC-1 (homogeneous pattern) and anti-NT5c1A were more likely to be found in clusters with dysphagia (1 and 3). Anti-RuvBL1 was less likely to be found among females with no dysphagia (cluster 4). Machine learning analysis based on autoantibody profile alone included an additional 17 sIBM patients (total 92) sIBM and 129 AIM disease controls. All the machine learning models used to differentiate sIBM vs. AIM, based on autoantibody profile alone, demonstrated high specificity (75.9%-89.7%) with fair sensitivity (57.6%-71.3%), accuracy (73.3%-77.8%) and F1 score (65.6%-71.1%) (**Table 2**). SHAP analysis revealed that positive anti-NT5c1A, AC-20 (cytoplasmic [speckled]) pattern, anti-VCP, but negative anti-Ro52/TRIM21, ANA, AC-4 (nuclear [fine speckled]) pattern, and anti-RuvBL1, favored a diagnosis of sIBM over AIM (**Figure 1c**).

Conclusion: In this comprehensive machine learning analysis of autoantibodies, ANA, anti-NT5c1A, anti-Ro52/TRIM21, anti-VCP, and anti-RuvBL1 were important biomarkers for both assessing sIBM clinical endotypes and differentiating sIBM from other AIMs. Future studies to study other novel biomarkers and validate our findings in larger cohorts are needed.

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Abstract Number: 2579

Validation of PROMIS in Adult and Pediatric Patients with Idiopathic Inflammatory Myopathies

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SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science II
Session Type: Abstract Session
Session Time: 9:00AM–10:30AM

Background/Purpose: This study aimed to validate the Patient Reported Outcome Measurement Information System (PROMIS) tools in patients with adult and juvenile idiopathic inflammatory myopathies (IIM/JIIM) to better assess quality of life (HR-QoL).

Table 1: Demographics, clinical, and autoantibody subgroups in patient populations

	Juvenile-Onset (N=85) Median (IQR) or n/N, %	Adult-Onset (N=50) Median (IQR) or n/N, %
Age at enrollment (years)	13.0 (8.5-17.0)	49.5 (36.5-58.3)
Disease duration (years)	2.8 (1.0-7.7)	1.6 (0.9-9.4)
Female	53/85, 62%	38/50, 76%
Race		
Caucasian	63/83, 76%	29/47, 62%
African American	11/83, 13%	11/47, 23%
Asian	4/83, 5%	2/47, 4%
Other	5/83, 6%	5/47, 11%
Ethnicity (Hispanic or Latino)	12/83, 14%	5/48, 10%
Diagnosis		
JDM/DM*	82/85, 97%	40/50, 80%
MSA		
anti-NXP2(MJ)	24/70, 34%	12/44, 27%
anti-p155/140	19/70, 27%	7/44, 16%
anti-MDA5	12/70, 17%	2/38, 5%
anti-synthetase‡	4/71, 6%	12/48, 25%
anti-Mi2	2/71, 3%	4/48, 8%
MAA positive †	24/72, 33%	7/48, 15%

JDM: Juvenile Dermatomyositis, DM: Dermatomyositis, JPM: Juvenile Polymyositis, PM: Polymyositis, MAA: Myositis Associated Autoantibody, MSA: Myositis Specific Autoantibody, NXP2: nuclear matrix protein-2, MDA5: melanoma differentiation associated protein-5, SRP: signal recognition particle
* non-JDM/DM subgroup included polymyositis and immune mediated necrotizing myositis
‡ anti-Jo-1, anti-PL7, anti-PL12, or anti-KS.
† MAAs included La/Ro, Ro, PMSCL, U1RNP, or U1RNP/Sm.
Antibody testing for signal recognition particle (SRP) was also performed; no patients tested positive.

Methods: Seventy-four children and 11 adults with juvenile-onset IIM (mean age 13 years, 62% female) and 50 adult-IIM patients (mean age 50 years, 76% female) with probable or definite Bohan and Peter criteria for IIM enrolled in a myositis natural history study (Table 1). Patients ≥ 18 years of age (n=61) completed PROMIS57, while patients < 18 years (n=49) and/or their parents (n=70) completed PROMIS49. PROMIS domains (Physical Function (PF), Pain Interference (PI), Fatigue, Social Role (SR), Peer Relations (PR), Anxiety, Depression, and Sleep Disturbance) were analyzed for content validity or

Table 2: PROMIS scores in myositis patients vs. healthy controls

Domains of PROMIS 49 – Patient	**Mean ± SD**	**p-value**
Physical Function T-score	44.3 ± 9.8	p < 0.001
Pain Interference T-score	49.6 ± 12.2	ns
Fatigue T-score	49.5 ± 12.6	ns
Peer Relations T-score	50.2 ± 11.3	ns
Anxiety T-score	47.0 ± 11.0	ns
Depression T-score	44.9 ± 10.9	p = 0.002*
Domains of PROMIS 49 – Parent		
Physical Function T-score	42.1 ± 9.9	p < 0.001
Pain Interference T-score	49.8 ± 11.2	ns
Fatigue T-score	51.7 ± 13.2	ns
Peer Relations T-score	49.2 ± 10.2	ns
Anxiety T-score	48.9 ± 11.5	ns
Depression T-score	45.7 ± 10.3	p < 0.001*
Domains of PROMIS 57		
Physical Function T-score	39.9 ± 8.5	p < 0.001
Pain Interference T-score	55.8 ± 10.6	p < 0.001
Fatigue T-score	55.1 ± 11.1	p < 0.001
Social Role T-score	45.6 ± 9.3	p < 0.001
Anxiety T-score	52.5 ± 9.5	p = 0.043
Depression T-score	50.0 ± 8.9	ns
Sleep Disturbance T-score	52.1 ± 9.0	ns

p-values are based on comparison with the PROMIS healthy reference population (T-scores = 50).
**Study participants reported less depression than general population.*

internal consistency and construct validity, using Pearson's r and Cronbach's α. Construct validity of PROMIS was examined in the correlation of PROMIS scores with HAQ/CHAQ and SF-36 as previously studied instruments of HR-QoL.

Results: When compared to the PROMIS healthy reference population, both JIIM patients and their parents reported significantly lower PF, while adult IIM patients reported lower PF, lower SR, and higher PI, Fatigue, and Anxiety scores (Table 2). Pediatric Anxiety scores increased with age (r=0.324, p=0.023), and adult female patients had higher Anxiety scores than adult males (53.9 vs 48.3, p=0.029); there were no other differences in PROMIS scores by demographics. In paired analysis of parent and patient PROMIS scores, parents reported lower PF (p< 0.001), and greater Fatigue (p=0.023) and Anxiety (p=0.032) than their children. All three PROMIS instruments demonstrated "Excellent" or "Good" internal consistency (Cronbach α=0.895 - 0.986) in all domains. None of the PROMIS instruments exhibited floor or ceiling effects, as the majority of patients scored within 2 standard deviations of the mean for all of the domains. PROMIS exhibited strong construct validity using both the HAQ and CHAQ disability index, especially in the PF, PI, and Fatigue domains (r=0.51 - 0.78, p< 0.001). PROMIS57 scores also showed significant correlations with many related SF-36 domains, including PF, PI, and Fatigue (r=|0.840| - 0.85, p< 0.001).

Conclusion: As the first study to analyze many domains of PROMIS in adults with IIM, patients with JIIM, and parents of children with JIIM, our findings emphasize the perceived burden of disease between these populations and suggest that parents perceive poorer health status than their children. Our findings of PROMIS demonstrated excellent internal consistency and correlations with related domains on the HAQ/CHAQ and SF-36. These findings support the incorporation of PROMIS into assessments of IIM/JIIM populations and emphasize the importance of PROMIS to address comprehensive well-being for pediatric and adult patients with these chronic conditions.

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Abstract Number: 2580

High-intensity Resistance Training Improves Quality of Life, Muscle Endurance and Strength in Patients with Myositis

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SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science II
Session Type: Abstract Session
Session Time: 9:00AM–10:30AM

Background/Purpose: Myositis is associated with muscle impairment, which impacts quality of life. The purpose of this study was to investigate the effects of high-intensity strength training on quality of life, functional capacity, muscle strength and disease-related measures in patients with myositis.

Methods: Using a randomized control trial design (**NCT04486261**), 32 patients with established and stable myositis, were randomly allocated to 16 weeks of high-intensity strength training (HRT) or 16 weeks of baseline activity levels (CON). The primary outcome was quality of life (Short Form-36, SF-36) - physical component summary (PCS). Secondary outcomes

included SF36 - mental component summary (MCS), functional capacity measures (e.g., 2-minute walk test (2MWT), 30-s Sit-To-Stand (30-STS), Timed-Up-&-GO (TUG) and Functional Index 3 (FI3)), maximal leg extensor power (LEP) and disease-related measures (Physician Global Activity (PhGA), Patient Global Activity (PtGA), Extramuscular Global Assessment (EMGA), Creatine Kinase (CK), Health Assessment Questionnaire (HAQ), Physician Global Damage (PhGD), Patient Global Damage (PtGD), and Manual Muscle Testing 8 (MMT8)).

Results: The primary outcome PCS showed an improvement in favour of HRT with a between-group difference of 5.33 (0.61;10.05) (p=0.03). Further, FI3 showed a between-group difference with greater gains of HRT (11.49 (3.37;19.60) (p=0.04)). Within-group increases in other functional capacity measures were observed with HRT (30-s STS, 6.5%, p=0.03; TUG, 12.9%, p< 0.0001; 2MWT, 4.9%, p=0.008; LEP, 14.2%, p=0.04). HRT also resulted in a between-group improvement in MMT8 (1.30 (0.09;2.51) (p=0.04)). Finally, IMACS's physician global damage decreased by 27.7% (p=0.02), and patient global damage decreased by 47.2% (p=0.03), within the HRT group (**Table 1**).

Conclusion: Improvement in physical component of quality of life was observed following 16 weeks of strength training in myositis patients. Likewise, improvements in muscle endurance by FI3 and strength by MMT8 were significantly higher in TRAIN compared to CON. No increases in disease activity or damage were observed. These results indicate that high-intensity strength training is well tolerated and positively impacts patients with established myositis.

Data are presented as means and 95% confidence intervals in parentheses. HRT: high-intensity resistance trained; CON: control; 2MWT: 2-minute walk test; 30 STS: 30 second Sit To Stand; TUG: Timed Up and Go; FI3: Functional Index 3; LEP: Leg Power; PhGA: physician global activity; PtGA: patient global Activity; EMGA: Extramuscular global assessment; MMT8: Manual muscle testing 8; HAQ: Health assessment questionnaire; CK: Creatine kinase; PhGD: physician global damage; PtGD: patient global damage. Bold font means significant. Significant levels set at p=0.05.

Table 1. Measure of function capacity and myositis disease activity/damage pre-to-post intervention.

	HRT Pre	HRT Post	Within-group (p-value)	CON Pre	CON Post	Within-group	Between-group (Time-by-group) (p-value)
Functional capacity and muscle power							
2MWT (Meters)	197.1 (182.1:212.0)	206.7 (191.7:221.7)	**0.008**	194.9 (178.2:211.6)	202.7 (186.0:219.4)	**0.02**	0.96
30-STS (Repetitions)	15.5 (13.3:17.7)	16.5 (13.8:19.1)	**0.03**	15.0 (13.0:17.0)	15.1 (12.7:17.6)	0.78	0.22
TUG (Seconds)	6.2 (5.3:7.0)	5.4 (4.7:6.1)	**<0.0001**	5.9 (4.9:6.9)	5.7 (4.8:6.6)	0.45	0.08
FI3 (Percentage)	**56.8** (41.4:72.2)	**73.6** (59.1:88.2)	**0.0004**	71.1 (57.9:84.4)	75.2 (63.5:86.9)	**0.10**	**0.007**
LEP (Watts/kg)	2.19 (1.81:2.58)	2.50 (1.95:3.05)	**0.04**	2.66 (2.41:3.17)	2.73 (2.16:3.30)	0.60	0.35
IMACS disease activity measures							
PhGA (0-100)	4.3 (1.8:6.8)	4.6 (1.1:8.1)	p=0.70	3.2 (1.6:4.9)	4.0 (1.3:6.7)	p=0.57	p=0.65
PtGA (0-100)	7.9 (3.4:12.4)	6.7 (1.2:12.2)	p=0.51	6.6 (3.4:9.7)	6.6 (2.0:11.1)	p=0.99	p=0.82
EMGA (0-100)	4.0 (1.3:6.7)	4.0 (0.5:7.6)	p=0.97	3.2 (1.6:4.9)	3.6 (0.9:6.4)	p=0.77	p=0.86
MMT8 (0-80)	**76.7** (74.8:78.7)	**78.5** (77.5:79.5)	**p=0.02**	**76.9** (75.7:78.2)	**77.2** (75.9:78.5)	**p=0.51**	**p=0.04**
HAQ (0-3)	0.208 (0.061:0.355)	0.094 (0.005:0.181)	p=0.08	0.294 (0.005:0.584)	0.241 (0.076:0.406)	p=0.51	p=0.12
CK (mmol/L)	276.7 (43.8:509.6)	146.1 (101.7:190.4)	p=0.22	161.8 (80.2:243.3)	222.0 (54.5:309.5)	p=0.50	p=0.33
IMACS disease damage measures							
PhGD (0-100)	17.0 (10.3:23.7)	12.3 (7.5:17.1)	**p=0.02**	15.0 (10.6:19.4)	13.9 (9.4:18.4)	p=0.49	p=0.12
PtGD (0-100)	19.7 (10.1:29.3)	10.4 (6.3:14.5)	**p=0.03**	18.2 (11.5:25.0)	13.9 (8.7:19.0)	p=0.07	p=0.07

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Abstract Number: 2581

Proteomic Signatures in Pre-Rheumatoid Arthritis Suggest Evolving Biological Pathways in Different Stages of Disease Development That May Inform Prediction and Prevention Strategies

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SESSION INFORMATION

Session Date: Wednesday, November 15, 2023

Session Title: Abstracts: RA – Diagnosis, Manifestations, and Outcomes IV: Pre-RA & RA Diagnosis

Session Type: Abstract Session

Session Time: 11:00AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) includes a stage of development that can be termed 'pre-RA' and defined as the presence of abnormal biomarkers and/or other features (e.g. articular symptoms) prior to the development of clinically-apparent synovitis (i.e. Clinical RA). In pre-RA, multiple interventions are being evaluated to prevent, delay or modulate future Clinical RA. However, the biologic pathways during the various stages of development in pre-RA are incompletely understood, and this 'gap' limits the ability to predict Clinical RA in at-risk populations as well as target the key pathways during disease development. To address this gap, we evaluated samples from the pre-RA period, and controls, from the Department of Defense Serum Repository (DoDSR) to test the hypothesis that proteomic testing can identify evolving biologic features in pre-RA that can ultimately be used to improve prediction for future Clinical RA and identify potential stage-specific targets for preventive interventions.

Table 1. Characteristics of individuals with RA and controls without RA

Table 1. Characteristics of individuals with RA and controls without RA

	RA Subjects	Healthy Controls	P value
Subjects (number of samples available), N	213 (608)	215 (614)	
Female, N (%)	116 (54%)	118 (55%)	0.98[#]
Age, mean (SD)			
Age at First Visit	26.5 (7.1)	25 (6.9)	**0.015***
Age at Last Visit	35.8 (8.1)	34.8 (7.8)	0.28*
Race & Ethnicity, N (%)			1.00[#]
Asian	8 (4%)	8 (4%)	
African-American	60 (28%)	60 (28%)	
Caucasian	102 (48%)	104 (48%)	
Hispanic or Latino	27 (13%)	27 (13%)	
Other	16 (8%)	16 (8%)	
Samples per subject, mean (SD)	2.85 (0.72)	2.86 (0.70)	0.78*
Autoantibodies (RA: post diagnosis, Control: last sample)			
CCP3 positive, N (%)	146 (69%)	6 (2.8%)	**<0.01[#]**
RFIgA positive, N (%)	101 (47%)	7 (3.2%)	**<0.01[#]**
RFIgM positive, N (%)	126 (59%)	8 (3.7%)	**<0.01[#]**

*Mann-Whitney test. [#]Fisher's exact test.

Methods: We evaluated 197 proteins on the Olink platform in serum from the DoDSR from the pre-RA period from 213 individuals with confirmed RA and 215 controls without RA (**Table 1**). Samples were also tested for ACPA and rheumatoid factor (RF) using anti-CCP3, RF-IgA and RF-IgM ELISA assays (Werfen).We applied linear mixed effect models and Mann-Whitney testing to evaluate participant-specific trajectories for pre-RA and controls in discrete time periods prior to RA diagnosis (i.e. pre-RA), and to identify biologic pathways through KEGG analyses. All p-values were adjusted for multiple testing with false discovery rate (FDR).

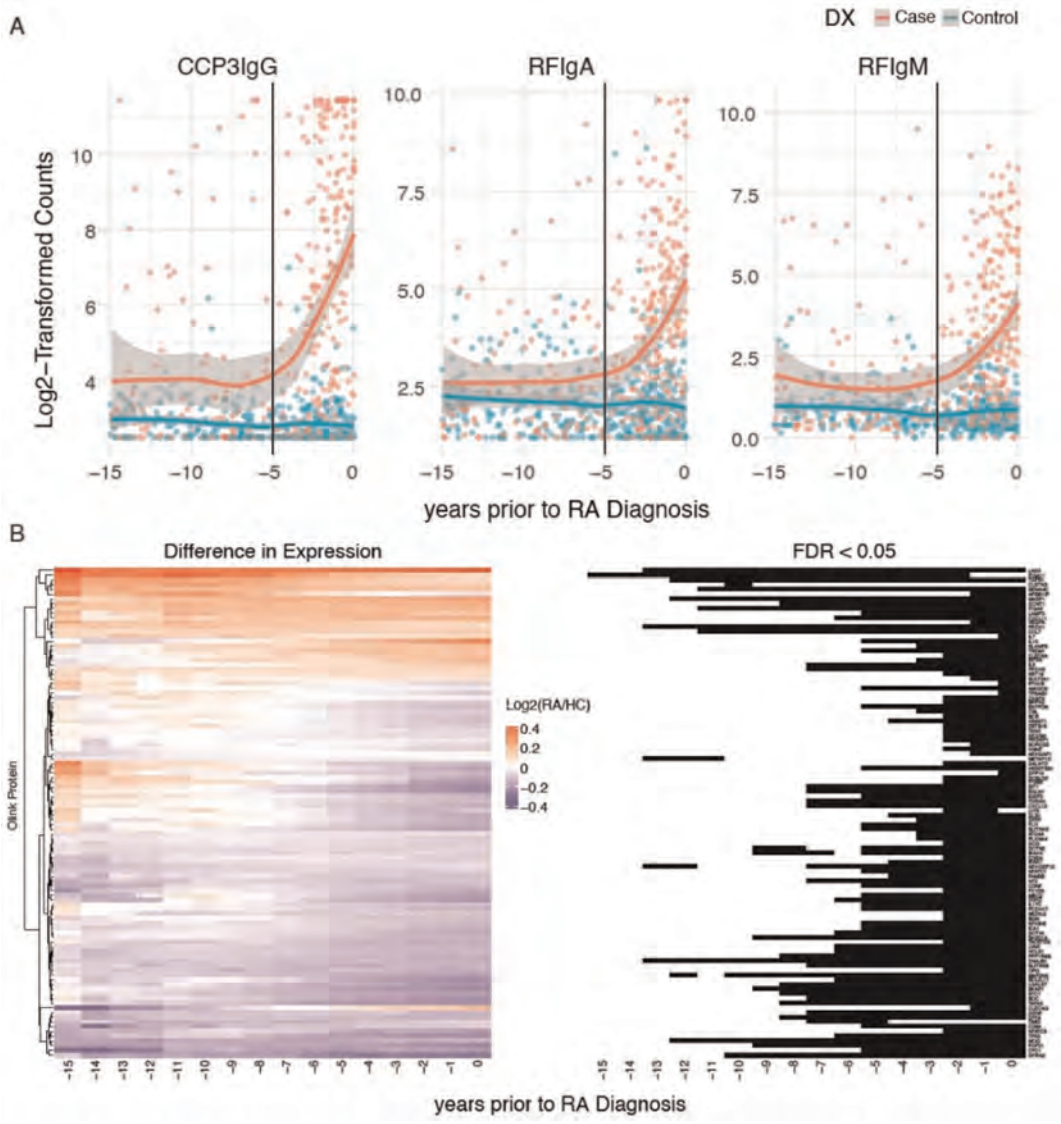

Figure 1. Autoantibody and proteomic findings in pre-RA. Panel A: Autoantibody levels for CCP3, RFIgA, and RFIgM for each sample from -15 to 0 years prior to RA diagnosis. LOESS regression curves were fit to show cohort trajectory, with confidence bands shown in gray. Overall, these autoantibodies increase in level with an inflection point of rise in RA cases ~5 years prior to diagnosis. Panel B: Heatmaps showing longitudinal signatures of 104 proteins that were differentially expressed between samples from the pre-RA period in individuals who developed RA compared to controls. Panel B/left side: Each cell denotes the Log2 fold change differences between individuals with RA and controls. Red cells denote higher normalized protein expression in RA, and blue/purple cells represent lower expression in RA. Panel B/right side: Each black cell denotes a protein that was differentially expressed in pre-RA samples versus controls at each time point and significant at a false-discovery rate (FDR) < 0.05. Overall, the differential expression of proteins appears to be in 'stages' with potential inflection point for many proteins approximately 5 years prior to the diagnosis of RA.

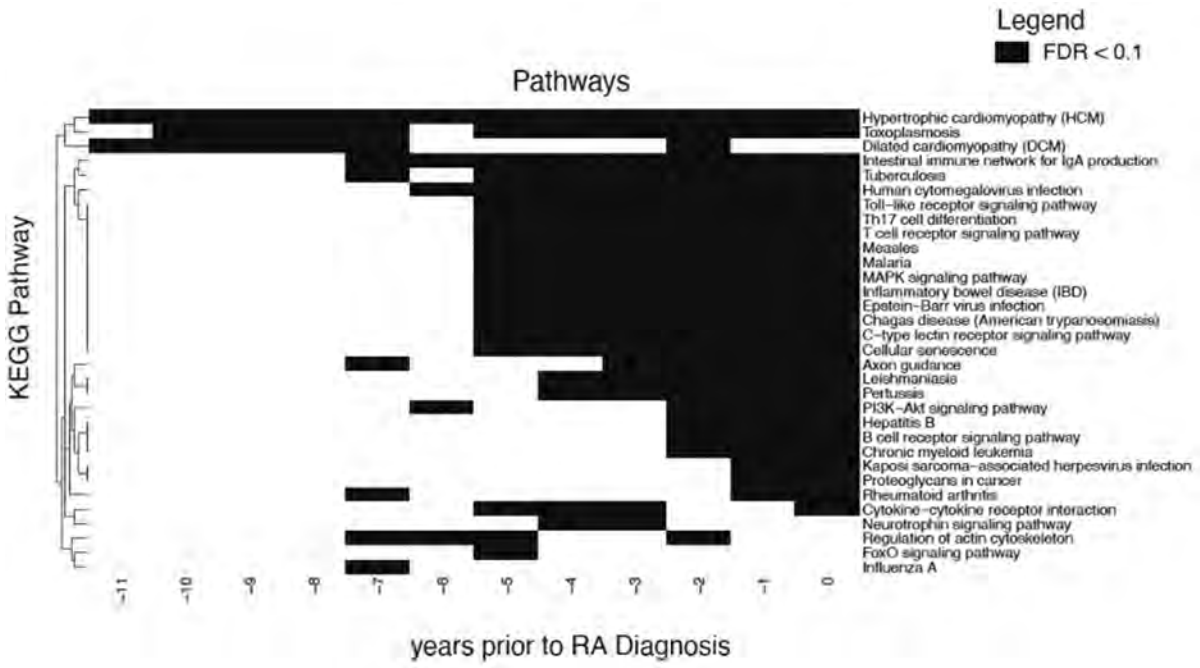

Figure 2. Biologic pathway enrichment in specific years prior to RA diagnosis. We applied KEGG analyses of the proteins that were differentially expressed in individuals in the pre-RA period compared to controls. The black cells indicate the enriched pathways in the pre-RA period in individuals with RA compared to controls, and significant at a false-discovery rate (FDR) <0.1. Overall, the pathways were differentially expressed at various time points in pre-RA, including a number of pathways predominately present <=5 years prior to RA diagnosis.

Results: Anti-CCP3, RFIgA, and RFIgM were significantly elevated in individuals in pre-RA compared to controls, with the highest levels observed ≤5 years prior to diagnosis (**Fig 1A**). We further identified 104 proteins that were differentially expressed in pre-RA samples compared to controls (**Fig 1B**). Of these, 60/104 proteins (e.g. IL7, IL10, NFKBIE) were differentially expressed ≤5 years prior to RA diagnosis in pre-RA samples vs controls, and enriched 21 biologic pathways including infection-related (e.g. Epstein-Barr virus, Malaria), mucosal (e.g. IBD) and cellular signaling pathways (e.g. Toll-like receptor and MAPK signaling). In contrast, only 2 proteins were differentially expressed >5 years prior to RA diagnosis. The remaining 42/104 proteins (e.g. LAG3, IL6, TGFB1) were differentially expressed over both time periods and enriched 10 pathways.

Conclusion: Our findings suggest that autoantibody and protein biomarkers evolve in pre-RA in distinct stages. In particular, the protein biomarkers may identify biologic pathways that are relevant to certain time points in pre-RA evolution. Notably, several pathways associated with infections and/or mucosal processes enriched in the period ≤5 years prior to clinical RA suggests these factors may play a role in increasing autoantibody levels and the transition from pre-RA to Clinical RA. These findings can be explored in future studies to improve prediction of future RA, as well as identify specific processes and pathways that could be targeted with preventive interventions.

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Abstract Number: 2582

Expansion of Circulating HLA-DR$^+$ Peripheral Helper T Cells and CXCR5$^-$CD38$^+$ Mature Naïve B Cells in ACPA-positive Individuals At-risk for and with Classified RA

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SESSION INFORMATION

Session Date: Wednesday, November 15, 2023

Session Title: Abstracts: RA – Diagnosis, Manifestations, and Outcomes IV: Pre-RA & RA Diagnosis

Session Type: Abstract Session

Session Time: 11:00AM–12:30PM

Background/Purpose: Production of ACPA following T and B cell interactions is a hallmark of ACPA+ RA. Recently identified peripheral helper T (Tph) cells have B cell-helper functions coupled with a migratory program targeting inflamed peripheral non-lymphoid tissues. Tph cells are expanded in the inflamed joint and blood of ACPA+ RA patients. However, it is not known whether immune dysregulation with an expansion of Tph cells occurs in a pre-disease stage of RA (i.e., ACPA+ at-risk individuals [ARI]).

Methods: We analyzed peripheral blood mononuclear cells (PBMC) from two independent and ethnically distinct cohorts to identify cell populations associated with serum ACPA positivity as well as eventual progression to classified RA. First, we employed mass cytometry with 38 markers in PBMCs from ARI, ACPA+ early RA patients, and healthy controls in a Japanese cohort (n = 17 in each group). Data were analyzed by computational analyses and biaxial gating. Next, the findings identified in the Japanese cohort were evaluated by flow cytometric analysis of PBMCs from a US-based cohort that included 11 healthy controls and 11 ACPA+ individuals who all subsequently developed RA (pre-RA), of which 9 had available post-RA diagnosis PBMC (post-RA), allowing for longitudinal analyses.

Results: In the Japanese cohort, FlowSOM analysis of CD4$^+$ T cells identified 10 metaclusters (i.e., cell populations). Of those, two metaclusters were significantly increased in ARI and RA compared to controls (**Figure 1A**). One of these metaclusters showed a high level of PD-1 expression and lack of CXCR5 expression, consistent with Tph cells (**Figure 1B**). t-SNE clustering visualized Tph cells composed of two distinct subpopulations based on HLA-DR expression (**Figure 1C**). Biaxial gating revealed that HLA-DR$^+$ Tph cells were significantly increased in ARI ($p = 0.002$) and RA ($p < 0.001$) compared to controls, while HLA-DR$^-$ Tph cells were increased only in RA (**Figure 1D**). In ARI, the frequency of HLA-DR$^+$ Tph cells was higher in 'progressors' (i.e., ARI who developed RA within one year after PBMC collection) compared to non-progressors ($p = 0.032$, **Figure 1E**). The FlowSOM analysis of B cells identified 15 metaclusters, and one of these metaclusters was significantly expanded in ARI and RA compared to controls (**Figure 2A**). Heatmap indicated that this metacluster was IgM$^+$IgD$^+$CD38$^+$CD27$^-$CXCR5$^-$ cells (CXCR5$^-$CD38$^+$ mature naïve B cells) (**Figure 2B**). Biaxial gating confirmed their expansion in ARI and RA ($p = 0.002$, $p < 0.001$, respectively; **Figure 2C**). In the US-based cohort, HLA-DR$^+$ Tph cells and CXCR5$^-$CD38$^+$ mature naïve B cells were also increased in pre-RA compared to controls ($p = 0.047$, $p = 0.040$, respectively; **Figure 3AB**). The frequencies of HLA-DR$^+$ Tph cells and CXCR5$^-$CD38$^+$ mature naïve B cells did not significantly differ between pre-RA and post-RA visits (**Figure 3CD**).

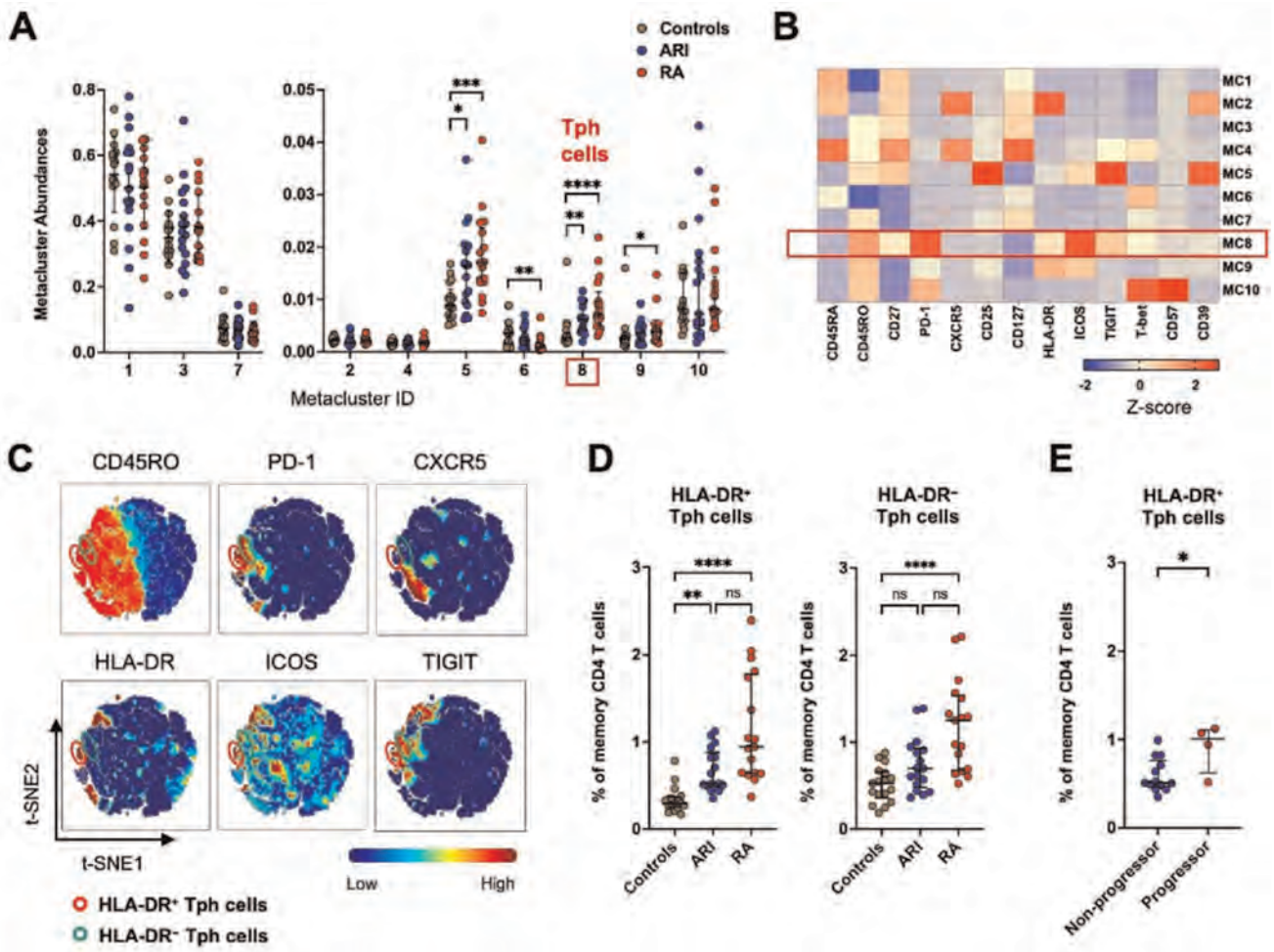

Figure 1. Identification of expanded HLA-DR⁺ Tph cells in blood of ACPA+ at-risk individuals and early RA patients in the Japanese at-risk cohort. (A) Abundance of FlowSOM metaclusters of CD4+ T cells. (B) Heatmap of normalized expression of mass cytometry markers in each metacluster (MC). (C) Visualization of CD4⁺ T cells by t-SNE, showing HLA-DR⁺ Tph cells (red circle) and HLA-DR⁻ Tph cells (green circle). (D) Frequencies of HLA-DR⁺ Tph cells and HLA-DR⁻ Tph cells. (E) Frequency of HLA-DR⁺ Tph cells in ARI who developed RA within one year after PBMC collection (progressor, n=4) and those who did not develop RA within that period (non-progressor, n=13). *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001 by Kruskal-Wallis test and Dunn's multiple comparisons test in A and D, and by Mann-Whitney test in E. Error bars show median with interquartile range. ARI, at-risk individuals; ns, not significant; Tph, peripheral helper T.

Conclusion: The expansion of HLA-DR$^+$ Tph cells and CXCR5$^-$CD38$^+$ mature naïve B cells in ACPA+ individuals, including those who develop classified RA, and the association of the former sub-type with 'progressors' supports a key role of these cells in ACPA positivity as well as a transition from pre-RA to classified RA. These cell sub-types may identify a mechanistic target for treatment and prevention in RA.

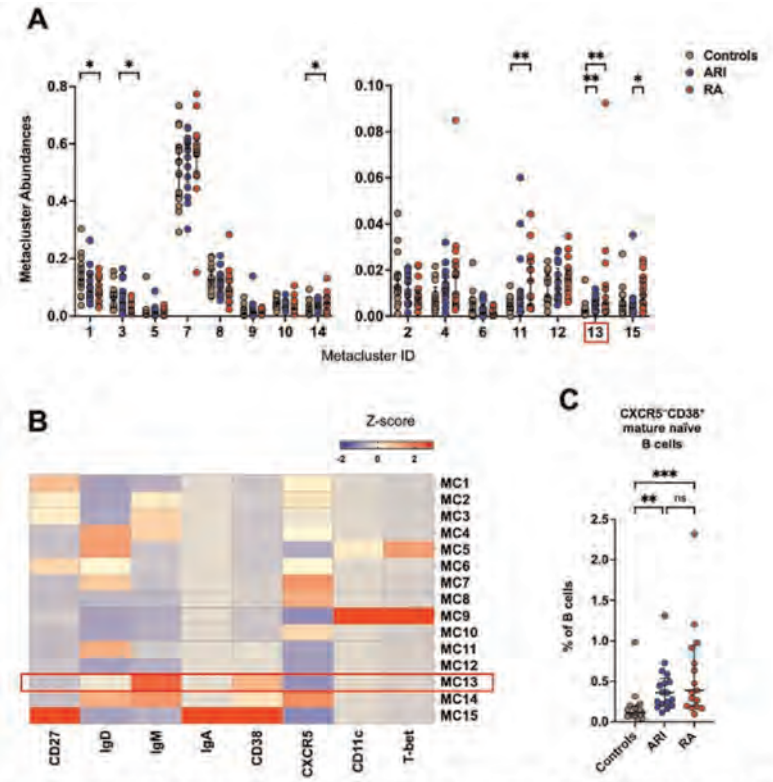

Figure 2. Expansion of CXCR5⁻CD38⁺ mature naïve B cells in blood of ACPA+ at-risk individuals and early RA patients in the Japanese at-risk cohort. (A) Abundance of FlowSOM metaclusters of B cells. (B) Heatmap of normalized expression of mass cytometry markers in each metacluster (MC). (C) Frequency of CXCR5⁻CD38⁺ mature naïve B cells by biaxial gating. *P < 0.05, **P < 0.01, ***P < 0.001 by Kruskal-Wallis test and Dunn's multiple comparisons test. Error bars show median with interquartile range. ARI, at-risk individuals.

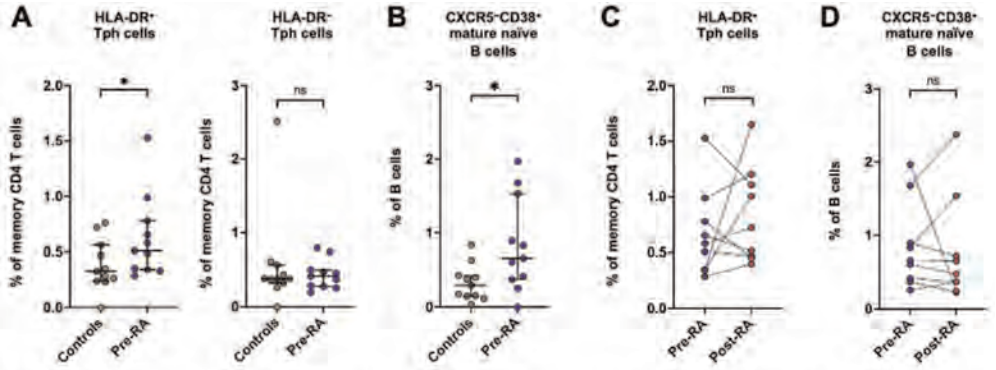

Figure 3. Cross-sectional and longitudinal analyses of T cell and B cell subsets in the US-based at-risk cohort. (A) Frequencies of HLA-DR⁺ Tph cells and HLA-DR⁻ Tph cells in memory CD4⁺ T cells. (B) Frequency of CXCR5⁻CD38⁺ mature naïve B cells. (C) Longitudinal change in frequency of HLA-DR⁺ Tph cells. (D) Longitudinal change in frequency of CXCR5⁻CD38⁺ mature naïve B cells. Comparison between HC and Pre-RA was performed by Mann-Whitney test, and comparison between Pre-RA and Post-RA was performed by Wilcoxon matched-pairs signed rank test. *P < 0.05. Error bars show median with interquartile range.

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Squibb(BMS), 2, gentibio, 1, 10, 11, hotspot therapeutics, 2, Janssen, 2; **W. Robinson**: None; **J. Seifert**: None; **M. Feser**: None; **L. Moss**: None; **J. Norri**: None; **M. Harigai**: Astellas Pharma, 6, AstraZeneca, 6, GlaxoSmithKlein(-GSK), 6, 12, Post marketing surveillence, Novartis, 5; **E. Hsieh**: None; **M. Holer**: None; **Y. Okamoto**: None.

Abstract Number: 2583

A Predictive Model for Progression to Clinical Arthritis Based on Lymphocyte Subsets and ACPA in At-risk Individuals with Arthralgia

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SESSION INFORMATION

Session Date: Wednesday, November 15, 2023

Session Title: Abstracts: RA – Diagnosis, Manifestations, and Outcomes IV: Pre-RA & RA Diagnosis

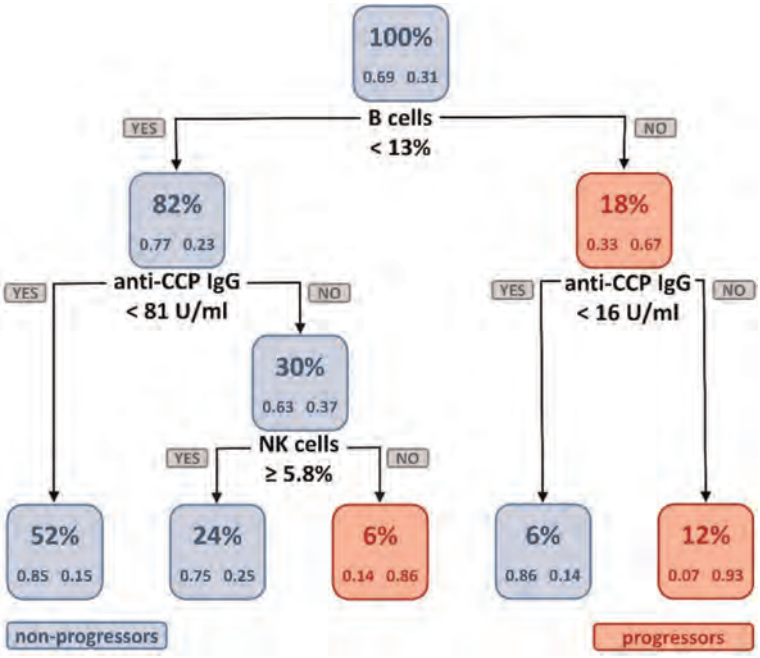
Session Type: Abstract Session

Session Time: 11:00AM–12:30PM

Background/Purpose: The positivity of antibodies against citrullinated proteins (ACPA) substantially increases the risk of developing rheumatoid arthritis (RA). The definition of individuals with arthralgia at risk of progression to RA (clinically suspect arthralgia, CSA) was established by EULAR based on clinical characteristics irrespective of the ACPA. Dysregulation of lymphocyte subpopulations (including B and NK cells) was previously described in early and established RA. We aimed to propose the predictive model for progression to arthritis based on peripheral lymphocyte subsets and ACPA in at-risk individuals with arthralgia.

Methods: Individuals from the At Risk of RA (ARRA) prospective observational cohort were defined at baseline as having arthralgia without arthritis on the examination of 66 joints and being either ACPA+ and/or meeting the EULAR definition of CSA. The percentage (%) of B cells, T cells, NK cells, NK-T cells, and γδ-T cells were detected within the peripheral blood lymphocyte population using flow cytometry. A logistic regression model was constructed to discriminate between progressors to arthritis and non-progressors and evaluated using ROC curves. Moreover, a classification decision tree was built to find segments with the highest risk of progression to arthritis.

Results: Out of 191 at-risk individuals with a median of 14 months follow-up and symptom duration 13 months at inclusion, 36 developed clinical arthritis (progressors) within a median of 9 months follow-up. For the construction of predictive models, 81 individuals who have not yet progressed to arthritis (non-progressors) with symptom duration longer than 12 months were included. A logistic regression model with baseline age, body mass index, % of peripheral blood lymphocyte subpopulations, and anti-CCP and anti-MCV serum levels as predictors was constructed for the discrimination between progressors and non-progressors. The resulting predictive model for arthritis development showed in a total cohort that high anti-CCP IgG levels, high % of B cells, and low % of NK cells increase the probability of developing arthritis, particularly in ACPA+ individuals, but not in the subset of ACPA- individuals. Evaluation of this model using the ROC curve showed AUC=0.732 ($p< 0.001$). When the identical set of predictors was applied to ACPA+ individuals, AUC was even higher (AUC=804,$p< 0.001$). However, we were not able to construct a well-performing model in ACPA- individuals. The CSA definition appears of no predictive value in our cohort. The proposed classification decision tree (Figure 1) showed, that individuals with B cells over 13% and anti-CCP IgG over 16 U/ml have a higher risk (93%) of progression to arthritis.



Classification decision tree

Conclusion: We propose here a predictive model to distinguish at-risk individuals with arthralgia who progress to arthritis from non-progressors based on baseline levels of lymphocyte subpopulations and ACPA levels, especially applicable in ACPA-positive individuals. The final model includes B cells and NK cells, which are involved in the pathogenesis of RA. This is a preliminary model that requires further validation in larger at-risk of RA cohorts.

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Abstract Number: 2584

Gut Microbiome and Intestinal Inflammation in Preclinical Stages of Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Wednesday, November 15, 2023

Session Title: Abstracts: RA – Diagnosis, Manifestations, and Outcomes IV: Pre-RA & RA Diagnosis

Session Type: Abstract Session

Session Time: 11:00AM–12:30PM

Background/Purpose: We attempted to replicate and expand previous findings of an increased abundance of Prevotellaceae in early untreated Rheumatoid Arthritis (RA) or its preclinical stages, in first-degree relatives of RA patients (FDRs).[1]

Methods: FDRs from the SCREEN-RA cohort (Evaluation of a SCREENing strategy for RA)[2] were categorized in four groups:

- Controls: healthy asymptomatic FDRs
- High genetic risk: asymptomatic FDRs with two shared epitope (SE) copies
- Autoimmunity: asymptomatic FDRs with RA-associated autoimmunity
- Symptomatic: clinically suspect arthralgias (CSA) or untreated new-onset RA

Fecal samples were collected and immediately frozen. DNA was extracted and V3-V4 16S regions were sequenced on a MiSeq platform. Output was processed with DADA2 pipeline on R, using Silva 138v database. Cells counts (cytometry) and calprotectin (ELISA) were obtained for each fecal sample. Microbial community composition and differential analysis were conducted using non-parametric tests, such as PERMANOVA, Wilcoxon and Kruskal-Wallis, or Aldex2 R-package to account for data compositionality.

Results: A total of 372 individuals were included (Table 1). Groups had similar age, gender, and BMI. We found no group-wise clustering of 16S sequence variants (PERMANOVA, R2 = 0.0073, p = 0.81) (Figure 1A) and we found no group-differences in Prevotellaceae abundance (Figure 1B; Kruskal-Wallis p = 0.14). Results were similar after fecal cell counts correction (not shown). Aldex2 found no significant differences between groups regarding other bacterial families.

Table 1 Legend SD: Standard Deviation. N: Negative. L: Low positivity (1 to 3x the norm). H: High positivity (>=3x the norm). ACPA: Anti-Citrullinated Protein Antibodies. RF: Rheumatoid Factor. Anti-ra33: anti-Ra33 autoantibodies. CSA: Clinical Suspect Arthralgia according to the EULAR definition – score ranges from 1 to 7, with cutoffs at 3 or 4. Shared Epitope: a group of MHC-II alleles conferring higher risk for RA. NA: Not Assigned.

Table 1 – Study population characteristics at sampling time, SCREEN-RA, 2019-2022

	Control	High Genetic risk	Autoimmunity	Symptomatic	p
n	227	50	50	45	
Female	78 %	82 %	74 %	89 %	0.264
Age – mean(SD)	52 (14)	53 (12)	55 (16)	54 (12)	0.590
BMI – mean(SD)	24 (4)	25 (3)	25 (5)	24 (5)	0.722
RA-autoimmunity	0 %	0 %	100 %	24 %	<0.001
ACPA					<0.001
N	100 %	100 %	66 %	84 %	
L	0 %	0 %	14 %	4 %	
H	0 %	0 %	20 %	11 %	
RF					<0.001
N	89 %	94 %	28 %	67 %	
L	11 %	6 %	2 %	16 %	
H	0 %	0 %	70 %	18 %	
Anti-ra33					<0.001
N	41 %	72 %	64 %	58 %	
L	9 %	20 %	22 %	11 %	
H	0 %	0 %	4 %	0 %	
NA	51 %	8 %	10 %	31 %	
Shared Epitope copies					<0.001
0	52 %	0 %	46 %	53 %	
1	48 %	0 %	40 %	36 %	
2	0 %	100 %	14 %	9 %	
NA	0 %	0 %	0 %	2 %	
Clinically Suspect Arthralgia (CSA)					<0.001
No	94 %	100 %	100 %	4 %	
Yes	0 %	0 %	0 %	93 %	
NA	4 %	0 %	0 %	2 %	

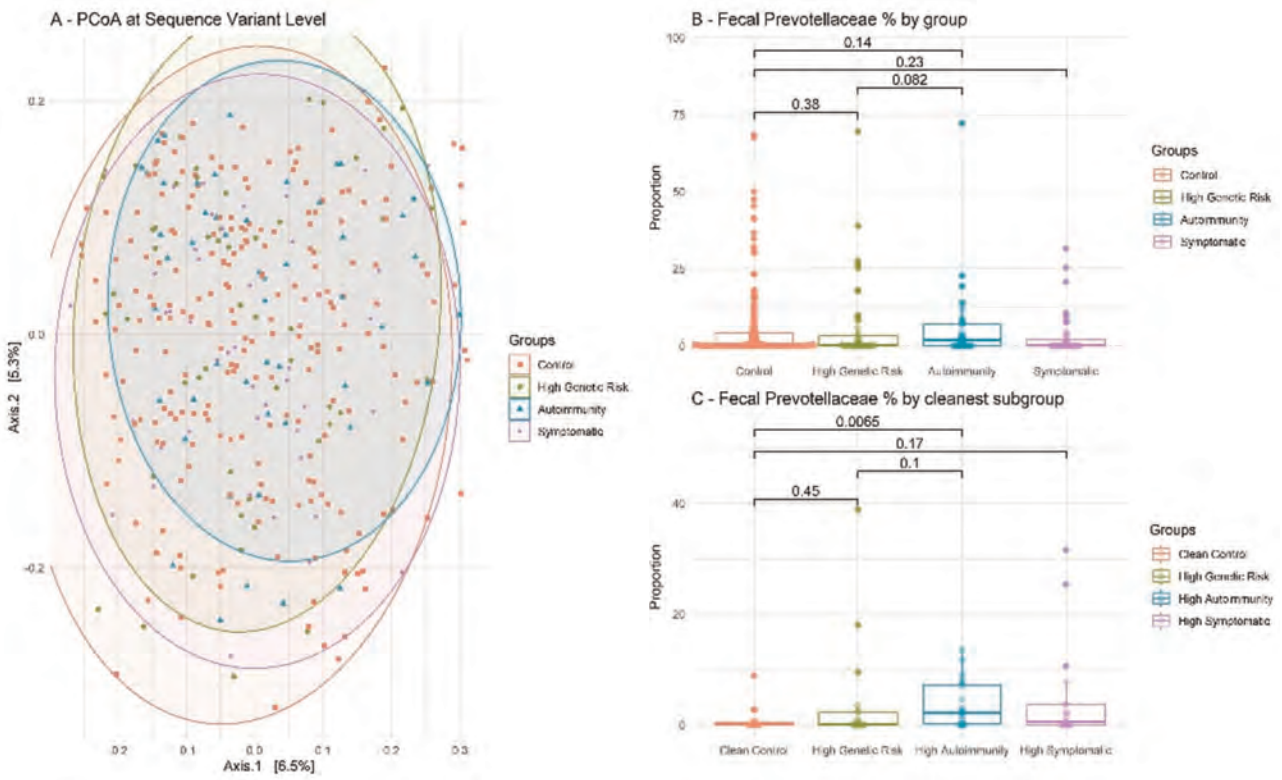

Figure 1: Microbiota 16S profiling by risk group, SCREEN-RA cohort A - PCoA : Principal Coordinate Analysis, performed at the Amplicon Sequence Variant level. On this figure, the more distant two point are, the more different they are in terms of 16S gene composition, based on Bray-Curtis index. B – Percentages of 16S sequences attributed to Prevotellaceae bacteria, per group. Wilcoxon test. C – Same panel as B, but restricted to cleaner subgroups, with high auto-antibody titers and/or high CSA scores. For readability Y-axis was cut (grey dotted line).

In a predefined subgroup analysis, selecting the most pronounced phenotypes in each group (i.e. highest autoantibody titers or arthralgia scores, n = 4x20) reproduced published results regarding Prevotellaceae (Figure 1C – Wilcoxon $p < 0.01$).

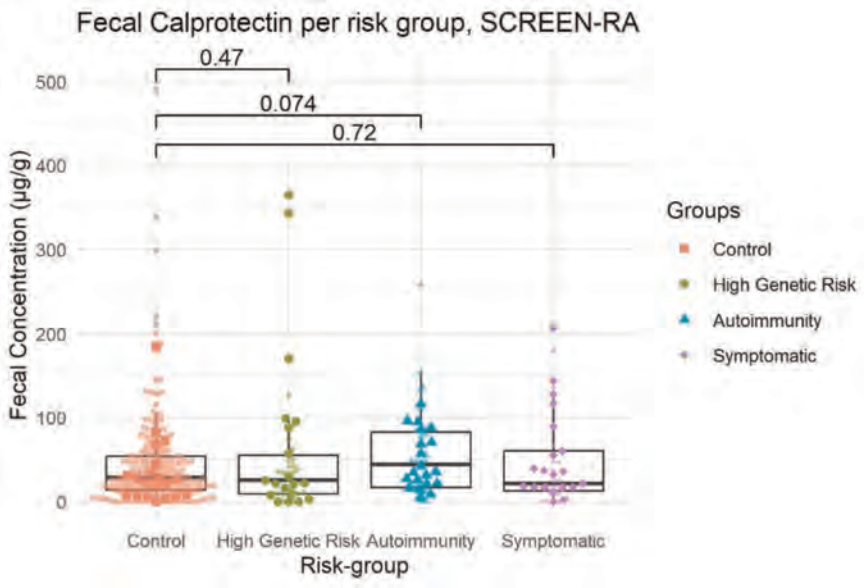

Figure 2: Fecal calprotectin by risk group, SCREEN-RA cohort Measured with ELISA in fresh frozen stool. Bold points are subjects presented on panel 1C.

Examining biomarkers of mucosal inflammation, we found a trend for fecal calprotectin elevation in the autoimmunity stage compared to controls (p = 0.074), which was no longer apparent in the symptomatic stage.

Specific bacterial cell counts, or abundances, failed to identify intestinal 'dysbiosis' in pre-clinical stages of RA and are most likely not usable as clinical biomarkers under these conditions. Still, a comparison of the most pronounced phenotypes retrieved the previously reported association, which suggests a weak signal in a distinct subgroup of patients. Accounting for lifestyle characteristics, such as diet, use of antibiotics or probiotics, may reduce confounding. Potentially increased fecal calprotectin in asymptomatic RA autoimmunity could suggests an ongoing low grade mucosal inflammation of the intestine.

Conclusion: Prevotellaceae abundance, or bacterial cell counts, are associated with RA-autoimmunity only in the most pronounced phenotypes of preclinical RA stages. But in the larger overall FDR population, specific bacterial taxa were not associated with pre-clinical RA stages.

References

1. Alpizar-Rodriguez, D. *et al.Ann. Rheum. Dis*.78,590–593(2019), www.doi.org/10.1136/annrheumdis-2018-214514
2. Gilbert, B. T. P. *et al.BMJ Open*11,e048409(2021), www.doi.org/10.1136/bmjopen-2020-048409

Disclosure: B. GILBERT: None; **R. TITO TADEO**: None; **C. LAMACCHIA**: None; **O. STUDER**: None; **D. COURVOISIER**: None; **J. RAES**: None; **A. Finckh**: None.

Abstract Number: 2585

Cytokine and Chemokine Elevations in ACPA+ Individuals Suggest Possible Viral, Mucosal and/or Innate Responses Are Related to the Transition to Future Clinical RA

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SESSION INFORMATION
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Session Title: Abstracts: RA – Diagnosis, Manifestations, and Outcomes IV: Pre-RA & RA Diagnosis
Session Type: Abstract Session
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Background/Purpose: Rheumatoid arthritis (RA) has a 'pre-RA' period definable as elevations of antibodies to citrullinated protein antibodies (ACPA) before clinically-apparent inflammatory arthritis (i.e. Clinical RA). ACPA elevations are highly associated with the future development of Clinical RA; in addition, biomarkers such as cytokines and chemokines in the pre-RA period may improve the prediction of future Clinical RA as well as identify biologic pathways related to disease development that could ultimately be targeted with preventive interventions. In this study, we evaluated 45 cytokines and chemokines in cohort of ACPA+ individuals without Clinical RA at baseline.

Methods: Through testing of first-degree relatives of patients with established RA, health-fair screening and clinic referral evaluations, we identified 85 ACPA+ individuals (CCP3, Werfen) who had no history or physical examination evidence of inflammatory arthritis. All ACPA+ individuals were followed prospectively for Clinical RA development. We tested their

Table 1. Characteristics of ACPA+ Converters and Nonconverters at Their Baseline Study Visit

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	Converters (n=23)	Nonconverters (n=62)	p-value
Days to Clinical RA (or duration of follow-up), median (range)	589 (23 to 1649)	689 (474 to 1094)	-
Age, mean (SD)	55 (12)	58 (13)	0.29
Female, n (%)	17 (74%)	42 (68%)	0.79
Non-Hispanic White, n (%)	16 (70%)	52 (84%)	0.22
RFIgM positive, n (%)	9 (39%)	14 (23%)	0.01
RFIgA positive, n (%)	8 (35%)	5 (8%)	<0.01
CRP positive (>3 mg/L), n (%)	7 (30%)	20 (32%)	0.62

Table 2. Cytokines and Chemokines Tested (n=45)

Table 2. Cytokines and Chemokines Tested (n=45)
CD40Ligand (cluster of differentiation 40 ligand), **CXCL13** (CXC motif chemokine ligand 13), **EGF** (epidermal growth factor), **Eotaxin**, **FGF Basic** (fibroblast growth factor basic), **Flt3 Ligand** (FMS-related tyrosine kindase-3 ligand), **GCSF** (granulocyte-colony stimulating factor), **GMCSF** (Granulocyte-macrophage colony-stimulating factor), **Granzyme B**, **GROα** (growth-regulated alpha), **GROβ** (growth-regulated beta), **IFNA** (interferon-lambda), **IFNα**, **IFNβ**, **IL-10** (interleukin-10), **IL-12p70**, **IL-13**, **IL-15**, **IL-17A**, **IL-17E**, **IL-1ra**, **IL-1α**, **IL-1β**, **IL-2**, **IL-3**, **IL-33**, **IL-4**, **IL-5**, **IL-6**, **IL-7**, **IL-8**, **IP-10**, **MCP1** (monocyte chemoattractant protein-1), **MIP1α** (macrophage inflammatory protein-1 alpha), **MIP1β**, **MIP3**, **MIPβ**, **PDGFAA** (platelet derived growth factor AA), **PDGFABBB** (platelet derived growth factor subunit B), **PDL1B7H1** (programmed death ligand 1-B7-H1), **RANTES** (regulated on activation, normal T cell expressed and secreted), **TGFα** (transforming growth factor-alpha), **TNFα** (tumor necrosis factor-alpha), **TRAIL** (tumor necrosis factor (TNF)-Related Apoptosis Inducing Ligand), **VEGF** (vascular endothelial growth factor)

baseline serum samples for 45 cytokines and chemokines (Table 2) using a Luminex platform and evaluated differences in log-transformed levels between ACPA+ individuals who did (or did not) later develop Clinical RA, including standard p-values as well as false discovery rate (FDR) corrected p-values to account for multiple comparisons.

Results: 85 ACPA+ individuals were followed longitudinally for a median of 639 days, and 23/85 (27%) developed Clinical RA ('Converters') a median of 589 days after their baseline visit (**Table 1**). At their baseline visit, the Converters had higher rates of positivity for RF-IgM and IgA than Nonconverters. In addition, Converters had higher levels of MCP1, IP10, IFN-

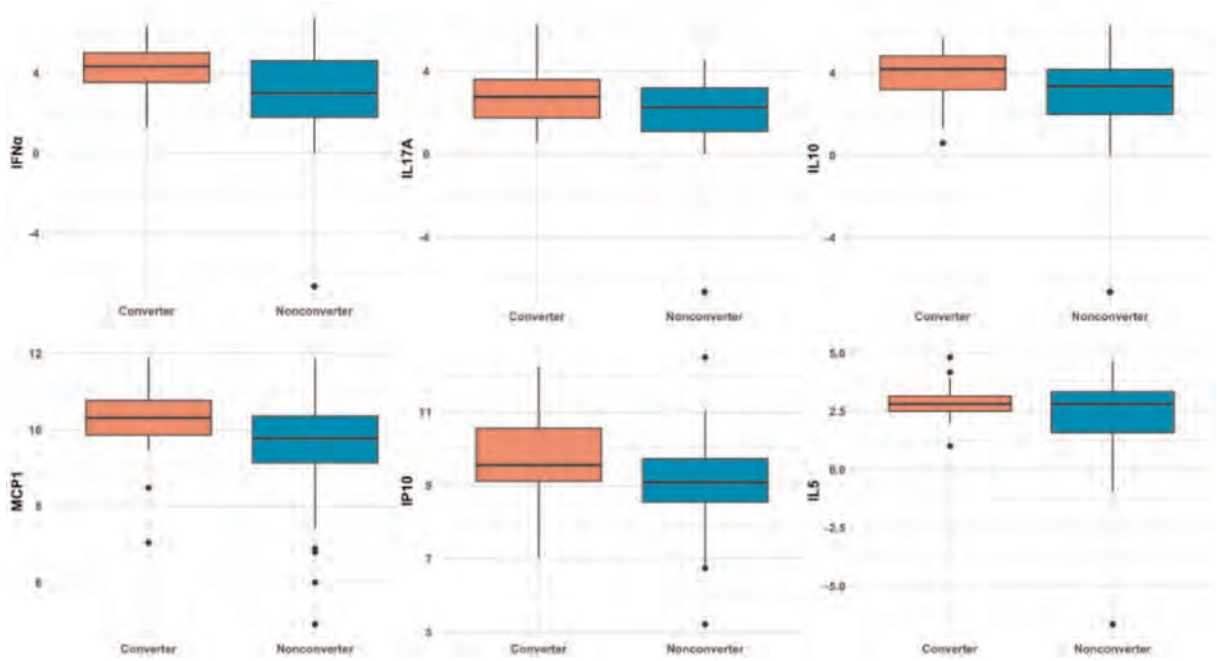

Figure 1. Multiple cytokines and chemokines are elevated at baseline in ACPA+ individuals who later develop Clinical RA (i.e. Converters) compared to ACPA+ individuals who do not (i.e. Nonconverters). IFN-alpha, IL17A, IL10, MCP1, IP10 and IL5 are all elevated in Converters compared to Nonconverters at a standard p-value of <0.05; however, only IFN-alpha remained significant at false discovery rate (FDR) corrected p-value of <0.05, although there were trends for elevations of IL17A and and IL10 (FDR p<0.10). These latter 3 cytokines have multiple biologic roles; their elevations may indicate a role for viral infections, mucosal and/or innate processes in the transition from ACPA+ state to Clinical RA.

alpha, IL10, IL17A and IL5 at a standard p< 0.05 level (Figure 1). Of these, IFN-alpha was significantly elevated in Converters compared to Nonconverters at an FDR-corrected p-value of < 0.05, with trends of higher levels of IL10 and IL17A in Converters vs Nonconverters (FDR p< 0.1).

Conclusion: Multiple cytokines and chemokines are elevated at baseline in ACPA+ individuals who develop clinical RA in a median of 589 days compared to those who do not. The most significant difference was the elevation of IFN-alpha, with trends of IL10 and IL17A. These 3 cytokines have multiple immunologic effects and in particular their elevations may indicate a role for viral infections and/or mucosal and innate immunologic processes in the transition from ACPA+ state to Clinical RA. Future studies will evaluate whether these cytokines improve the ability to predict future RA, as well as role of these cytokines and related biologic processes in the evolution from pre- to Clinical RA.

Disclosure: D. Carlson: None; **C. Carpenter**: None; **S. Goff**: None; **J. Seifert**: None; **L. Moss**: None; **M. Feser**: None; **J. Buckner**: Bristol-Myers Squibb(BMS), 2, gentibio, 1, 10, 11, hotspot therapeutics, 2, Janssen, 2; **W. Robinson**: None; **J. Kirschmann**: None; **G. Firestein**: Eli Lilly, 5; **M. Holer**: None; **k. Deane**: Bristol-Myers Squibb(BMS), 1, Gilead, 5, Janssen, 5, Werfen, 1, 12, Biomarker kits.

Abstract Number: 2586

A Novel Blood-Based Assay Differentiates Seropositive and Seronegative Rheumatoid Arthritis from Healthy Individuals and Those with Other Inflammatory Diseases or Osteoarthritis

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SESSION INFORMATION
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Session Title: Abstracts: RA – Diagnosis, Manifestations, and Outcomes IV: Pre-RA & RA Diagnosis
Session Type: Abstract Session
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Background/Purpose: Non-invasive differentiation of seropositive and seronegative rheumatoid arthritis (RA) from other conditions has been limited in the current practice. We aimed to evaluate the clinical feasibility of a novel blood-based assay to differentiate RA patents from healthy controls and those with other conditions, including osteoarthritis (OA) and inflammatory conditions.

Methods: We acquired plasma samples from 89 individuals meeting 2010 ACR/EULAR classification criteria for RA (89 samples), 29 healthy controls (66 samples), 12 individuals with osteoarthritis (12 samples) or 61 individuals with an inflammatory condition (62 samples; Table 1). Samples were processed via chromatin enrichment assay that enables access to tissue and disease specific genetic signatures. A machine learning algorithm (involving 5-repeat 10-fold cross-validation training and testing), trained to identify synovial signatures in blood plasma, was used to generate the probabilistic estimates for the presence and absence of RA.

For RA vs non-RA, we report the area under the curve (AUC), mean (standard deviation; SD) sensitivity, overall specificity, positive likelihood ratio and negative likelihood ratio. For comparator conditions, we report specificity alone.

Table 2. Test performance in differentiation individuals with RA from those who were healthy or had health conditions adjacent to rheumatoid arthritis

	Number of RA / Non-RA	Performance Averages Across 5-repeats				
		AUC	Sensitivity, %	Specificity, %	Positive Likelihood Ratio	Negative Likelihood Ratio
RA vs. Non-RA						
For all:	89 / 140	0.991 (0.0007)	90.8 (0.94)	96.1 (0.64)	24.13 (4.495)	0.10 (0.001)
For seronegative:	27/140	0.991 (0.0007)	83.7 (2.03)	–	21.46 (3.99)	0.17(0.002)
vs. Healthy controls	– / 66	–	–	100 (0)		
vs. Ankylosing spondylitis	– / 13	–	–	95.4 (4.2)		
vs. Crohn's Disease	– / 11	–	–	100 (0)		
vs. Psoriasis	– / 18	–	–	92.2 (3.00)		
vs. Psoriatic arthritis	– / 10	–	–	80.0 (0)		
vs. Ulcerative colitis	– / 10	–	–	100 (0)		
vs. Osteoarthritis	– / 12	–	–	88.3 (4.56)		

AUC: area under the curve; RA: rheumatoid arthritis

Table 1. Sample description

	Number of samples	Number of patients	White, % (race known**)	Female, %	Age, Median (Q1, Q3)
Overall, including:	229	191*	63.3% (n=188)	67.9%	56.0 (40.0, 66.0)
Rheumatoid Arthritis* **	89	89	58.4% (n=89)	86.5%	58.0 (48.0, 68.0)
Non-RA:	140	102	67.7% (n=99)	51.8%	51.0 (34.0, 65.0)
Healthy controls	66	29*	42.3% (n=26)	53.6%	41.0 (34.2, 51.8)
Ankylosing spondylitis	13	13	84.6% (n=13)	30.8%	59.0 (36.0, 63.0)
Crohn's Disease	11	10	80.0% (n=10)	30.0%	59.0 (37.2, 70.0)
Psoriasis	18	18	66.7% (n=18)	50.0%	44.5 (33.0, 56.8)
Psoriatic arthritis	10	10	70.0% (n=10)	50.0%	65.5 (63.0, 71.8)
Ulcerative colitis	10	10	70.0% (n=10)	50.0%	27.0 (23.2, 68.0)
Osteoarthritis	12	12	91.7% (n=12)	91.7%	75.5 (23.2, 41.0)

* One patient did not have demographic characteristics recorded but was included in the sample because plasma and healthy status were known.
** Race was known for some patients, the number of which is indicated in parentheses.
*** Among RA patients, 70% were seropositive, 30% were seronegative and 96% were biologic-naïve

Results: Table 1 describes the study sample. RA subjects were 70% seropositive, 30% seronegative, 96% biologic-naïve (Table 1).The test distinguished RA from non-RA with the following overall accuracy: AUC 0.991 (0.0007), sensitivity 90.8% (0.94%), and overall specificity 96.1% (0.64%), positive likelihood ratio 24.13 (4.495) and negative likelihood ratio 0.10 (0.001). For seronegative RA, the results included sensitivity 83.7% (2.03%), positive likelihood ratio 21.46 (3.99), and negative likelihood ratio 0.17 (0.002). In comparator groups, specificity was 80.0% (0 %) for psoriatic arthritis, 88.3% (4.56%) for osteoarthritis, 92.2% (3.04%) for psoriasis, 95.4% (4.21%) for ankylosing spondylitis, and 100% (0%) for healthy controls, Crohn's disease, and ulcerative colitis (Table 2).

Conclusion: A novel non-invasive assay differentiated individuals with RA from healthy controls and those with other inflammatory conditions without RA with high sensitivity and overall specificity. In comparator cohorts, the assay demonstrated high specificity for all groups, including healthy controls, osteoarthritis, and other inflammatory conditions. The sensitivity was maintained in seronegative individuals. Further research is needed to confirm these results in an independent study.

Note: Both Dr. Shadick and Dr. Weinblatt are last authors.

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Abstract Number: 2587

Measuring Frailty in SLE: Agreement Among Methods

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SESSION INFORMATION
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Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes IV: Outcomes & Comorbidity
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Background/Purpose: Frailty, conceptualized as an accumulation of deficits across multiple physiological systems, was first examined in SLE in 2017 using the Fried Frailty Phenotype criteria and showed associations with functional decline, cognitive impairment, and mortality. Frailty in SLE has since been measured with other methods, including the recently-developed Systemic Lupus International Coordinating Clinics (SLICC) Frailty Index. We examined the agreement between 3 frailty measurement methods and the associations of frailty by each measure with outcomes.

Methods: Data were from the California Lupus Epidemiology Study (CLUES), a longitudinal cohort with rheumatologist-confirmed SLE. Data are collected annually. In Year 3 (n=256), frailty was measured in 3 ways: SLICC Frailty Index (SLICC-FI), Short Physical Performance Battery (SPPB; n=166), and FRAIL scale (Figure 1). We also examined PROMIS Physical Function score ≤40 (1 SD below population mean) as a proxy for frailty (PF40). Kappa (k) analyses assessed agreement between frailty measures. Linear and logistic regressions examined cross-sectional associations between frailty and hospitalizations in the previous 12 months, cognitive impairment (≤ -1.5 SD below age- and education-adjusted norms on the Controlled Word Association Test, COWAT), distance walked in 6 minutes (6MWT), self-reported disease damage (Brief Index of Lupus Damage, BILD), disability (Short Valued Life Activities questionnaire, SVLA), fatigue (PROMIS Fatigue), and depressive symptoms (Patient Health Questionnaire, PHQ-8). Longitudinal outcomes examined were hospitalization, functional decline (SVLA score worsening ≥ 0.5 SD), and an increase in BILD ≥2 points at any point during the subsequent 3 years.

Results: Mean age was 48±14 years, SLE duration 19±11 years. The cohort was 90% female. Racial/ethnic representation was 37% Asian, 10% Black, 23% Hispanic, and 30% White (non-overlapping categories). Prevalence of frailty varied by measurement method: SLICC-FI, 45.9%; SPPB, 10.8%; FRAIL scale ≥3, 17.5%; FRAIL scale ≥2, 33.3%; PF40, 23.6%. Agreement among frailty measures was weak to moderate, with highest agreement between FRAIL≥2 and PF40 (k = 0.63), SLICC-FI and FRAIL≥2 (k = 0.62), and SLICC-FI and PF40 (k = 0.50). FRAIL≥3 and PF40 were significantly associated with all cross-sectional outcomes, FRAIL≥2 with all except hospitalization, SLICC-FI with all except cognitive impairment, and SPPB with SVLA, PHQ, 6MWD, and fatigue (Table 1). SLICC-FI was significantly associated with all longitudinal

Figure 1. Components of the three frailty measures: Short Physical Performance Battery, FRAIL scale, and SLICC Frailty Index

	Short Physical Performance Battery [1]	FRAIL scale [2]	SLICC Frailty Index [3]
General	Performance based	Questionnaire	Based primarily on SDI, SLEDAI, and SF-36 subscales
Components	• Standing balance • Time to complete 5 chair stands • Time to complete 4-meter walk	• Fatigue • Difficulty walking up 10 steps • Difficulty walking several hundred yards • Presence of ≥5 of 11 illnesses • Weight loss	48 health "deficits" identified • 14 related to organ damage • 14 reflect active inflammation • 6 reflect comorbid conditions •14 related to function, mobility, health attitude, and mental health
Scoring	Each component is scored 0 – 4, for a total score range of 0 – 12, with higher scores reflecting better status	Each component can receive 1 point. Points are summed for total score ranging from 0 – 5.	Each deficit is scored 0 – 1. The total number of deficits is summed and divided by 48.
Frailty definitions	Robust, ≥ 10 Pre-frail, 8 or 9 Frail, ≤7	Robust, 0 Prefrail, 1 or 2 Frail, ≥3 We also assessed FRAIL score ≥2.	Robust, 0 – 0.03 Less fit, >0.03 – 0.10 Least fit, >0.10 – 0.21 Frail, >0.21

Abbreviations: FRAIL = Fatigue, Resistance, Ambulation, Illnesses, and Loss of weight; SLICC = Systemic Lupus International Coorcinating Clinics; SDI = SLICC Damage Index; SLEDAI = Systemic Lupus Erythematosus Disease Activity Index; SF-36 = Short Form 36.

1. Guralnik J, Simonsick E, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol: Med Sci 1994; 49:M85-M94.
2. Morley J, Malmstrom T, Miller D. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. J Nutr Health Aging 2012; 16:601-608.
3. Legge A, Kirkland S, Rockwood K, et al. Evaluating the properties of a frailty index and its association with mortality risk among patients with systemic lupus erythematosus. Arthritis & Rheumatology 2019; 71:1297-1307.

Table 1. Association of frailty measures with cross-sectional outcomes

Frailty definition		Cross-sectional outcomes: Hospitalized*	Cognitive Impairment*		BILD†	PHQ†	SVLA†	PROMIS Fatigue†	6MWD† (n = 122)
FRAIL scale ≥3	OR (95% CI)	**2.2 (1.1, 4.7)**	**2.2 (1.1, 4.7)**	β (p-value)	**1.0 (0.0071)**	**7.0 (<0.0001)**	**0.84 (<0.0001)**	**13.3 (<0.0001)**	**-88.4 (0.0001)**
% (n) frail = 17.5 (43)	c (95% CI)	0.57 (0.50, 0.64)	0.57 (0.50, 0.64)	R^2	0.03	0.27	0.28	0.20	0.11
FRAIL scale ≥2	OR (95% CI)	**1.7 (0.9, 3.3)**	**2.2 (1.1, 4.1)**	β (p-value)	**1.4 (<0.0001)**	**6.4 (<0.0001)**	**0.87 (<0.0001)**	**11.6 (<0.0001)**	**-56.5 (0.002)**
% (n) frail = 33.3 (82)	c (95% CI)	0.56 (0.48, 0.64)	0.59 (0.51, 0.67)	R^2	0.10	0.35	0.47	0.24	0.07
SLICC Frailty Index	OR (95% CI)	**2.6 (1.4, 5.2)**	1.5 (0.8, 2.9)	β (p-value)	**1.7 (<0.0001)**	**5.8 (<0.0001)**	**0.80 (<0.0001)**	**12.4 (<0.0001)**	**-62.1 (0.0002)**
% (n) frail = 45.9 (113)	c (95% CI)	0.62 (0.54, 0.70)	0.55 (0.47, 0.63)	R^2	0.15	0.32	0.45	0.30	0.10
SPPB (n = 166)	OR (95% CI)	1.5 (0.5, 4.9)	2.5 (0.8, 7.2)	β (p-value)	**0.6 (0.2)**	**4.0 (0.0018)**	**0.45 (0.001)**	**5.9 (0.036)**	**-158.3 (<0.0001)**
% (n) frail = 10.8 (18)	c (95% CI)	0.52 (0.45, 0.59)	0.55 (0.48, 0.63)	R^2	0.01	0.06	0.06	0.03	0.12
PROMIS Physical Function T-score ≤ 40 (PF40)	OR (95% CI)	**2.6 (1.3, 5.1)**	**2.0 (1.0, 4.0)**	β (p-value)	**1.3 (<0.0001)**	**5.9 (<0.0001)**	**1.02 (<0.0001)**	**12.6 (<0.0001)**	**-84.0 (0.0002)**
% (n) frail = 23.6 (58)	c (95% CI)	0.60 (0.52, 0.67)	0.57 (0.49, 0.64)	R^2	0.06	0.24	0.52	0.23	0.10

* (OR, 95% CI) from logistic regression analysis

† (β, p-value) from linear regression analysis

Notes: c-statistic of 0.5 means no explanatory power greater than chance. Bolding represents statistical significance at $p<0.05$

FRAIL = Fatigue, Resistance, Ambulation, Illnesses, and Loss of weight ; PROMIS = Patient Reported Outcomes Measurement Information System; SLICC = Systemic Lupus International Coordinating Clinics Damage Index ; SPPB = Short Physical Performance Battery

Definitions of outcomes

Hospitalized: Report at Year 3 interview of any hospitalization during the previous 12 months

Cognitive impairment: ≤ -1.5 SD below age- and education-adjusted norms on the Controlled Word Association Test, COWAT

BILD = Brief Index of Lupus Damage. Self-reported validated measure of SLE damage

PHQ = Patient Health Questionnaire-8 depressive symptoms score. Scores ≥10 are suggestive of moderate-severe depression.

SVLA = Short Valued Life Activities disability questionnaire. Scores range from 0 – 3, with higher scores indicating more disability.

PROMIS = Patient Reported Outcomes Measurement Information System 4-item Fatigue scale. Population mean ± SD, 50 ± 10

6MWD = Six-minute walk distance, meters

Table 2. Association of frailty measures with longitudinal outcomes

Frailty definition		Longitudinal outcomes		
		Any follow-up hospitalization	Any SVLA decline	BILD increase
FRAIL scale ≥3	OR (95% CI)	1.8 (0.9, 3.5)	1.7 (0.8, 3.7)	2.2 (0.9, 4.9)
	c (95% CI)	0.54 (0.49, 0.60)	0.54 (0.48, 0.61)	0.56 (0.48, 0.64)
FRAIL scale ≥2	OR (95% CI)	**2.2 (1.2, 3.8)**	**2.6 (1.4, 5.0)**	1.4 (0.7, 2.9)
	c (95% CI)	**0.59 (0.52, 0.66)**	**0.62 (0.53, 0.69)**	0.54 (0.45, 0.63)
SLICC Frailty Index	OR (95% CI)	**2.2 (1.3, 3.9)**	**2.9 (1.5, 5.8)**	**4.9 (2.1, 11.3)**
	c (95% CI)	**0.60 (0.53, 0.67)**	**0.63 (0.55, 0.71)**	**0.68 (0.60, 0.76)**
SPPB	OR (95% CI)	1.0 (0.3, 3.0)	1.1 (0.3, 3.9)	1.4 (0.4, 5.1)
	c (95% CI)	0.50 (0.45, 0.55)	0.51 (0.44, 0.57)	0.52 (0.44, 0.59)
PROMIS Physical Function T-score ≤ 40 (PF40)	OR (95% CI)	1.5 (0.8, 2.8)	**2.2 (1.1, 4.5)**	**3.9 (1.9, 8.3)**
	c (95% CI)	0.54 (0.48, 0.60)	**0.58 (0.51, 0.65)**	**0.65 (0.56)**

* (OR, 95% CI) from logistic regression analysis.
† (β, p-value) from linear regression analysis
Note: c-statistic of 0.5 means no explanatory power greater than chance.

FRAIL = Fatigue, Resistance, Ambulation, Illnesses, and Loss of weight ; PROMIS = Patient Reported Outcomes Measurement Information System; SLICC = Systemic Lupus International Coordinating Clinics Damage Index ; SPPB = Short Physical Performance Battery

Definitions of outcomes
Follow-up hospitalization: Report of any hospitalization during follow-up period (Years 4, 5, or 6)
SVLA decline = Short Valued Life Activities disability questionnaire. Worsening of score ≥ 0.5 SD from Year 3 at Year 4, 5, or 6
BILD = Brief Index of Lupus Damage. Increase in score ≥2 points during follow-up period

outcomes, FRAIL≥2 with follow-up hospitalizations and SVLA decline, and PF40 with SVLA decline and BILD increase (Table 2).

Conclusion: Agreement between measures of frailty in SLE is moderate at best. The SLICC-FI was a robust predictor of all SLE cross-sectional and longitudinal outcomes examined in this study except cognitive impairment. The simple FRAIL≥2 performed almost as well. The PROMIS PF, which may already be incorporated into many studies or clinical workflows, also performed well and may be used as a reasonable proxy for frailty. These data should inform selection of frailty measures for future studies in SLE.

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Abstract Number: 2588

Updated Analyses of Cancer Incidence and Risk Factors in a Large International SLE Cohort

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SESSION INFORMATION

Session Date: Wednesday, November 15, 2023

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes IV: Outcomes & Comorbidity

Session Type: Abstract Session

Session Time: 11:00AM–12:30PM

Background/Purpose: Many studies of cancer risk in SLE are limited by small sample size or use of administrative data, which rely on billing code diagnoses instead of clinical data. We produced updated estimates cancer risk in the largest-ever cohort of clinically confirmed incident SLE patients.

Methods: Adults with SLE were enrolled (within 15 months of diagnosis) into the SLICC Inception Cohort, across 32 centres. Individuals were followed with annual assessments, where detailed data was collected on Disease Activity Index-2000 (SLEDAI-2K), lupus drugs in the past year, and documentation of cancer diagnoses (by the examining physician at yearly intervals).

We performed univariate and multivariate Cox regression, with baseline demographics (age at SLE onset, race/ethnicity, sex), and time-dependent variables for medications (antimalarials, biologics and other immunosuppressives, corticosteroids), smoking, and SLEDAI-2K. As well as cancer over-all, we evaluated risk factors for the most common cancer types.

Results: Of 1848 new-onset SLE patients enrolled between 1999-2011, 1675 had at least one follow-up; these were the sample for the current analysis. End date was the first of death, last visit, or end of study interval for this analysis (June 21,2021). Baseline demographics are shown in Table 1.

Over 16493 years of follow-up (median follow up, 10 years) 72 cancers occurred (incidence 4. 4 events per 1,000 patient-years). This included 16 breast cancers, 10 non-melanoma skin, 10 lung, 6 hematological, 6 prostate, 5 melanoma, 3 cervical, 3 renal, 3 head and neck, 3 thyroid, 2 gastric, 2 uterine, and one each rectal, sarcoma, thymoma. Adjusted and

Table 1. Baseline characteristics of the SLE sample

Baseline characteristics	No Cancer (N=1603)	Cancer (N=72)	Overall (N=1675)
Female sex	1434 (89.5)	53 (73.6)	1487 (88.8)
White race/ethnicity	778 (48.5)	49 (68.1)	827 (49.4)
Mean age at SLE diagnosis, years (SD)	34.1 (13.0)	45.5 (15.0)	34.6 (13.3)
Mean SLE duration, months (SD)	5.6 (4.2)	5.4 (3.7)	5.6 (4.2)
Ever top quartile SLE activity, N (%)	541 (33.7)	18 (25.0)	559 (33.4)
Ever smoking, N (%)	533 (33.3)	34 (47.2)	567 (33.9)
Ever cigarettes 15+/day, N (%)	131 (8.2)	18 (25.0)	149 (8.9)
Ever steroids, N (%)	1198 (74.7)	51 (70.8)	1249 (74.6)
Ever cyclophosphamide, N (%)	139 (8.7)	4 (5.6)	143 (8.5)
Ever azathioprine (Imuran), N (%)	462 (28.8)	21 (29.2)	483 (28.8)
Ever methotrexate, N (%)	188 (11.7)	9 (12.5)	197 (11.8)
Ever mycophenolate, N (%)	243 (15.2)	9 (12.5)	252 (15.0)
Ever antimalarial, N (%)	1264 (78.9)	53 (73.6)	1317 (78.6)
Ever NSAID, N (%)	321 (20.0)	11 (15.3)	332 (19.8)
Ever aspirin, N (%)	303 (18.9)	17 (23.6)	320 (19.1)
Ever biologic, N (%)	40 (2.5)	0 (0.0)	40 (2.4)
Ever dsDNA antibody, N (%)	536 (33.4)	15 (20.8)	551 (32.9)

unadjusted hazard ratios (HR) are shown in Table 2. Multivariate analyses of all cancer types (analyzed together) suggested a higher risk of cancer among patients of older age, males, and those who smoked more than 15 cigarettes a day.

In the multivariate analyses specifically for breast cancer, age at SLE diagnoses remained a risk factor, and antimalarials were associated with a decreased risk. This effect of antimalarials was not clearly seen for any other cancer type. For non-melanoma skin cancer, both age at SLE diagnosis and cyclophosphamide (albeit with a wide confidence interval) were associated with risk. For hematologic cancers, older age was a risk factor in univariate analyses (hazard ratio, HR 1.06, 95% confidence interval, CI 1.01 , 1.12) as was highest quartile of SLEDAI-2k (HR 10.3, 95% CI 1.31 , 81.7), but due to the low number of hematologic cancers, multivariate estimates were less precise and confidence intervals included the null value for all variables.

Conclusion: Our updated analyses of this large, international inception SLE cohort continues to illustrate how different cancer types in SLE might be associated with specific risk factors. Additional follow-up is still needed to precisely determine the potential effects of disease activity (particularly for hematologic malignancies) and medications on cancer risk in SLE.

Table 2. Hazard Ratio (HR) for cancer in SLE (Cox regression analysis)

ALL CANCERS	Unadjusted HR (95% CI)	Adjusted HR (95% CI)[a]
Age at SLE diagnosis (years)	**1.06 (1.04, 1.07)**	**1.05 (1.03, 1.06)**
Female sex	**0.34 (0.20, 0.57)**	**0.48 (0.28, 0.84)**
White race/ethnicity	**2.42 (1.47, 3.97)**	1.34 (0.76, 2.34)
Top quartile SLEDAI-2K	0.62 (0.37, 1.02)	0.83 (0.48, 1.45)
Ever cigarettes 15+/day	**3.34 (1.99, 5.60)**	**2.00 (1.16, 3.44)**
Ever steroids	0.62 (0.36, 1.06)	0.77 (0.42, 1.43)
Ever cyclophosphamide	0.89 (0.46, 1.74)	1.35 (0.64, 2.88)
Ever azathioprine	0.76 (0.47, 1.23)	1.00 (0.59, 1.72)
Ever methotrexate	1.30 (0.74, 2.27)	1.50 (0.84, 2.69)
Ever mycophenolate	0.86 (0.50, 1.47)	1.20 (0.66, 2.18)
Ever antimalarial	0.64 (0.35, 1.18)	0.63 (0.34, 1.19)
Ever biologic	0.79 (0.34, 1.84)	0.80 (0.32, 1.95)
BREAST CANCER	**Unadjusted HR (95% CI)**	**Adjusted HR (95% CI)[a]**
Age at SLE diagnosis (years)	**1.08 (1.04, 1.11)**	**1.07 (1.04, 1.11)**
White race/ethnicity	1.49 (0.56, 4.01)	0.71 (0.22, 2.24)
Top quartile SLEDAI-2K	0.48 (0.15, 1.48)	0.72 (0.20, 2.59)
Ever cigarettes 15+/day	2.27 (0.65, 7.99)	1.47 (0.38, 5.70)
Ever steroids	0.47 (0.16, 1.35)	0.65 (0.19, 2.21)
Ever cyclophosphamide	0.89 (0.20, 3.94)	2.06 (0.37, 11.6)
Ever azathioprine	0.33 (0.09, 1.17)	0.42 (0.11, 1.65)
Ever methotrexate	1.91 (0.66, 5.51)	2.30 (0.77, 6.89)
Ever mycophenolate	0.83 (0.26, 2.60)	1.31 (0.35, 4.93)
Ever antimalarial	0.37 (0.12, 1.16)	**0.31 (0.10, 0.97)**
NON-MELANOMA SKIN	**Unadjusted HR (95% CI)**	**Adjusted HR (95% CI)[a]**
Age at SLE diagnosis (years)	**1.08 (1.04, 1.13)**	**1.07 (1.02, 1.12)**
Female sex	0.29 (0.07, 1.11)	0.53 (0.12, 2.29)
White race/ethnicity	**10.3 (1.31, 81.7)**	5.40 (0.59, 49.2)
Top quartile SLEDAI-2K	0.16 (0.02, 1.23)	0.13 (0.01, 1.19)
Ever cigarettes 15+/day	3.66 (0.95, 14.2)	1.86 (0.46, 7.53)
Ever steroids	0.86 (0.18, 4.08)	0.89 (0.15, 5.26)
Ever cyclophosphamide	**3.61 (1.02, 12.8)**	**14.3 (2.88, 70.5)**
Ever azathioprine	0.63 (0.16, 2.45)	0.69 (0.14, 3.33)
Ever methotrexate	2.05 (0.53, 7.97)	2.92 (0.66, 12.8)
Ever mycophenolate	1.27 (0.32, 5.11)	1.41 (0.29, 6.81)
Ever antimalarial	0.38 (0.09, 1.51)	0.34 (0.08, 1.55)
Ever biologic	1.14 (0.14, 9.31)	0.83 (0.08, 8.92)
LUNG CANCER	**Unadjusted HR (95% CI)**	**Adjusted HR (95% CI)[a]**
Age at SLE diagnosis (years)	**1.11 (1.06, 1.15)**	**1.11 (1.05, 1.17)**
Female sex	**0.08 (0.02, 0.29)**	**0.17 (0.05, 0.64)**
Top quartile SLEDAI-2K	0.33 (0.07, 1.55)	0.28 (0.03, 2.33)
Ever cigarettes 15+/day	**20.5 (5.30, 79.4)**	**10.9 (2.75, 42.9)**
Ever steroids	0.74 (0.16, 3.51)	0.81 (0.13, 4.93)
Ever cyclophosphamide	1.33 (0.28, 6.28)	3.00 (0.43, 21.1)
Ever azathioprine	1.30 (0.37, 4.49)	1.99 (0.44, 9.13)
Ever mycophenolate	0.53 (0.11, 2.51)	0.59 (0.11, 3.35)
Ever biologic	1.73 (0.36, 8.30)	2.19 (0.25, 19.0)

[a] Adjusted for all variables shown; disease activity, smoking, and all drug variables were time dependent.

[b] For lung cancer the variables for race/ethnicity, cyclophosphamide, methotrexate, and antimalarials, were excluded because all lung cancer patients were white, all took antimalarials and none took cyclophosphamide or methotrexate.

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Abstract Number: 2589

Real-World Application of the Pediatric Glucocorticoid Toxicity Index in Children with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Wednesday, November 15, 2023

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes IV: Outcomes & Comorbidity

Session Type: Abstract Session

Session Time: 11:00AM–12:30PM

Background/Purpose: Chronic glucocorticoid (GC) morbidity is rarely captured as a standardized clinical outcome in pediatric rheumatic conditions. The pediatric glucocorticoid toxicity index (pGTI) (Brogan et al. 2022) is a new, pediatric-specific tool to measure GC toxicity in research and clinical care. Common clinically important toxicities are organized into domains

and weighted according to severity. We used the pGTI to quantify and identify risk factors for GC toxicity in children with pediatric-onset systemic lupus erythematosus (pSLE) with or without lupus nephritis (LN).

Methods: We conducted a single-center cohort study of patients with pSLE, stratified by LN. We included patients with rheumatology visits since January 2016 and ³6 months of systemic GC treatment and followed them through March 2023. We scored change in GC toxicity using a modified version of the pGTI, including steroid toxicity items in 12/15 subdomains, at visits every 6 months (+/-2) for up to 3 years. Glucose metabolism, dyslipidemia, and bone density domains could not be assessed due to sparse data. Index date was the visit at which GC were initiated. Positive scores indicate new/worsening toxicity and negative scores indicate improvement. We also calculated the Cumulative Worsening Score (CWS), an endpoint of the pGTI representing a continuous summation of any GC toxicity accrued over time. Mixed effects linear regression was used to estimate associations of baseline factors and GC exposure with CWS over time.

Table 1. Baseline characteristics of children with SLE by history of nephritis

	No nephritis (N=29)	With nephritis (N=48)
Demographic Characteristics		
Age at SLE diagnosis (years), median [IQR]	13.8 [11.4 - 16.2]	13.9 [11.9 - 16.4]
Disease duration at index visit (months), median [IQR]	0.0 [0.0 - 1.0]	0.0 [0.0 - 1.0]
Female, n (%)	25 (86%)	37 (77%)
Race		
Asian	3 (10%)	8 (17%)
Black	4 (14%)	11 (23%)
Other*	6 (21%)	9 (19%)
White	15 (52%)	14 (29%)
Unknown	1 (3%)	6 (13%)
Hispanic ethnicity	8 (28%)	13 (27%)
Insurance status		
Public	12 (41%)	22 (46%)
Private	17 (59%)	25 (52%)
Uninsured	0 (0%)	1 (2%)
Calendar year of index visit		
Before 2016	12 (41%)	19 (40%)
2016-2022	17 (59%)	29 (60%)
BMI at index visit		
Normal	25 (86%)	35 (73%)
≥ 85 and <95%ile	3 (10%)	9 (19%)
≥ 95ile	1 (3%)	4 (8%)
Disease Features		
SLEDAI-2K score at index visit, median [IQR]†	8.5 [5.0 - 14.5]	20.0 [14.0 - 24.0]
Nephritis Class		
Class III/IV	N/A	36 (75%)
Mixed Class III/IV and V	N/A	6 (13%)
Class V	N/A	4 (8%)
Unavailable	N/A	2 (4%)
Serositis	8 (28%)	16 (33%)
Neurologic Manifestations	6 (21%)	10 (21%)
Anti-dsDNA antibody positive	23 (79%)	45 (94%)
Medication use within 30 days of index visit		
Cyclophosphamide	3 (10%)	12 (25%)
Rituximab	6 (21%)	6 (13%)
Mycophenolate	3 (10%)	18 (38%)
Other non-biologic DMARD^	7 (24%)	8 (17%)

The index visit date was defined by the first encounter at which oral glucocorticoids were initiated for SLE. BMI = body mass index; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000. *Other includes Middle Eastern. †Index SLEDAI-2K scores were missing for 1 non-nephritis and 7 nephritis patients. ^Includes azathioprine, leflunomide, methotrexate, calcineurin inhibitors, and JAK-STAT inhibitors.

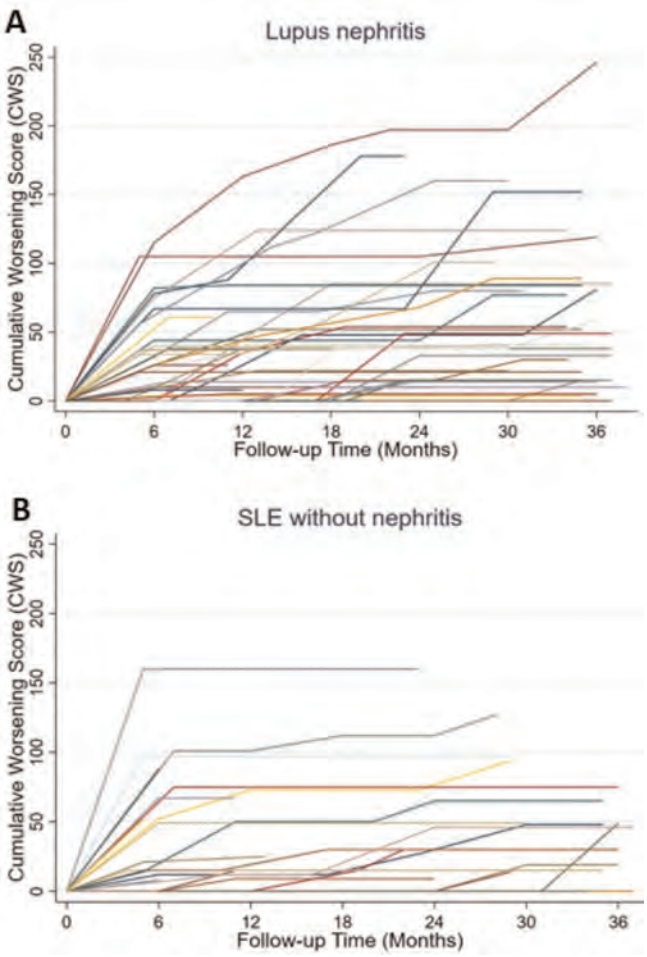

Figure 1. Individual Cumulative Worsening Score (CWS) trajectories over three years of follow-up in pediatric SLE patients (A) with (n=48) and (B) without nephritis (n=29). CWS is a continuous summation of any glucocorticoid (GC) toxicity accrued after the index visit. Each line represents the score trajectory of an individual patient. Following discontinuation of GCs, if there was no GC use during subsequent visit intervals, then further increase in toxicity could not be reliably attributed to GC use and did not contribute to the CWS.

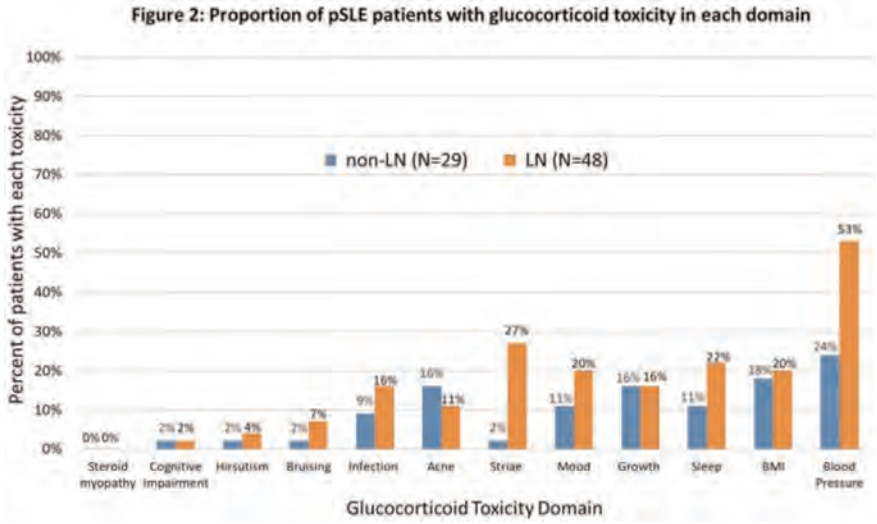

Figure 2. Proportion of patients with pediatric SLE (stratified by presence of LN) with new or worsening toxicity for each pediatric glucocorticoid toxicity subdomain at any time during follow-up.

Results: We included 425 visits by 77 pSLE patients (median 6 visits/patient [IQR 5-7]), of which 48 had LN (Table 1). In both groups, the most common toxicity was worsening blood pressure; this was more pervasive in the LN group (53% vs. 24% of patients), which also exhibited greater damage (24% vs. 8% developed hypertensive emergency or posterior reversible encephalopathy syndrome). Increased body mass index (BMI), sleep disturbance, and growth delay were also common. Compared to LN patients, those without LN had similar or less frequent toxicity in every subdomain except for acne (Fig 2). Median CWS at month 12 was 15 (IQR [0-47]; N = 47) in the LN subgroup and 15 (IQR [0-67]; N = 22) in those without LN. 46% of patients with LN and 34% without accrued new/worsening toxicity beyond 12 months (Fig 1).

Cumulative dose associated with greater CWS (1.5 unit increase in CWS for every 1000 mg higher cumulative prednisone dose, 95% CI [0.03 – 2.8]), adjusted for time, but there was large between-subject variance. Of baseline factors in Table 1, younger age of onset, need for initial treatment with rituximab, and baseline BMI >95th%ile were significantly associated with higher CWS over time.

Conclusion: Patients with pSLE exhibit significant GC toxicity captured by the pGTI, particularly in blood pressure, BMI, sleep, and growth subdomains. This cohort also demonstrated substantial between-subject variability in toxicity. We will further assess the construct validity and feasibility of the pGTI in upcoming multicenter analyses. Standardized, pediatric-specific assessment of GC toxicity may help facilitate reduction in GC-associated morbidity in children with SLE.

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Abstract Number: 2590

Association Between Frailty and Readmissions in Hospitalized Patients with Systemic Lupus Erythematosus (SLE)

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SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes IV: Outcomes & Comorbidity
Session Type: Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: SLE has one of the highest 30-day hospital readmission rates among chronic conditions[1]. Frailty is common[2] and associated with hospitalization[3] in SLE, but whether frailty is associated with worse outcomes after hospital admission, including readmissions, is unknown. Our objective was to evaluate the association between frailty status and risk of readmissions, inpatient mortality at readmissions, and cost of admission among patients with SLE.

Methods: Using ICD-10 codes, we identified adults >18 years of age within the National Readmissions Database who had a primary or secondary diagnosis of SLE and were hospitalized between January and June 2018. We excluded patients who died during the index hospitalization, had an elective hospitalization, were transferred from another hospital, or were missing length of stay (LOS) or total cost values. Using the validated claims-based Hospital Frailty Risk Score[4], we categorized individuals as either frail (score≥5) or non-frail (score<5) at the time of index hospitalization. Age, sex, insurance type, household income, Elixhauser Comorbidity Index (ECI), and LOS were extracted from the dataset. Primary outcome was readmission rates following discharge from the index hospitalization. Secondary outcomes included inpatient mortality, and the economic burden of hospitalizations. We compared baseline characteristics and primary and secondary outcomes between frail and non-frail patients with SLE using descriptive statistics. We used Cox proportional hazard models to estimate the association between frailty and risk of readmissions, after adjustment for relevant covariates.

Table 1: Baseline Patient, Hospital, and Hospitalization Characteristics of Patients with SLE at Time of Index Admission by Frailty Status

Outcomes at Index Hospitalization	Non-frail patients	Frail patients	P-Value
N	21,353	18,385	
Age	64.52±14.256	71.13±13.02	<0.01
Age categories (%)			<0.01
<40	29.33%	18.48%	
40-64	46.97%	44.14%	
>64	23.70%	37.38%	
Female	89.50%%	87.20%	<0.01
Urban	94.69%%	94.07%%	<0.01
Primary Expected Payer			
1. Medicare/Medicaid	43%	62%	<0.01
2. Medicaid	21%	17%	
3. Private Insurance	32%	19%	
4. Self-pay	3%	2%	
5. Other	1%	0%	
Median Household Income			
1. 0-25th percentile	31.9%	32.2%	0.012
($1-$45,999)			
2. 26th to 50th percentile	26.5%	27.1%	
($46,000-$58,999)			
3. 51st to 75th percentile	23.0%	22.8%	
($59,000-$78,999)			
4. 76th to 100th percentile	18.7%	17.8%	
($79,000 or more)			
Teaching Status			
1. Metropolitan non-teaching	20.9%	20.4%	<0.01
2. Metropolitan teaching	93.8%	73.7%	
3. Non-metropolitan non-teaching	5.3%	5.9%	
Bed size			
1. Small	14.4%	14.5%	0.20
2. Medium	26.5%	26.1%	
3. Large	59.1%	59.4%	
Elixhauser Index *	8.53	14.14	<0.01
Length of stay	3 (2-5)	5 (3-9)	<0.01
Comorbid Conditions			
Hypertension	43.40%	47.05%	<0.01
Heart Failure	12.81%	24.15%	<0.01
Diabetes mellitus	19.11%	26.56%	<0.01
COPD	26.24%	31.42%	<0.01

*Elixhauser Index ranges from -7 to +12.

Table 2: Longitudinal Hospitalization-Related Outcomes in Frail and Non-frail Patients with SLE

Outcomes	Non-frail patients	Frail patients	P-Value
Readmission	43.10%	59.80%	<0.01
Inpatient mortality	0.27%	2.88%	<0.01
Length of Stay > 7 days	9.11%	28.89%	<0.01
Average days to readmission	87.7	77.1	<0.01
Cost of hospitalization			
Median	$7,991.00	$11,087.00	<0.01
Interquartile Range	$4,755 - $14,010	$6,359 - $20,978	

Results: We identified 39,738 patients with SLE admitted during the study period. Over a median follow-up of 9 months, frail patients with SLE (n = 18,385, 46.3%) were older with Medicare/Medicaid coverage and had higher ECI scores and longer LOS compared to non-frail patients with SLE (n = 21,353, 53.7%) (**Table 1**). Frail patients with SLE had more prolonged hospitalizations defined by LOS > 7 days with higher costs per hospitalization. Readmission rates in frail patients with SLE were significantly higher. At index hospitalization, frail patients had significantly higher inpatient mortality and fewer days-to-readmission on average (**Table 2**). In multivariable Cox proportional hazard analysis, frailty was independently associated with a 10% higher risk of readmission after adjustment for covariates (**Table 3**).

Conclusion: Among patients with SLE who were hospitalized, frailty is associated with more readmissions, higher mortality, and greater economic burden of hospitalization as compared to non-frail SLE patients. Assessing frailty status may help risk stratify patients with SLE at higher risk for readmission. Further research is needed to determine strategies to reduce frailty in patients with SLE in order to decrease readmission rates and other adverse health outcomes.

Table 3: Cox Proportional Hazard Analysis Evaluating Risk of Readmission by Frailty Risk Score.

Variable	Hazard Ratio (95% Confidence interval)	P-value
Frailty risk score	1.10 (1.06-1.13)	<0.01
Age	1.00 (1.00-1.00)	<0.01
Female	0.95 (0.92-1.00)	0.03
Median Household Income	1.01 (0.99-1.02)	0.44
Hospital Teaching Status	0.99 (0.97-1.02)	0.68
Primary Expected Payer	1.01 (0.99-1.02)	0.41
Bed Size	1.01 (0.99-1.03)	0.52
Elixhauser Index	1.01 (1.01-1.01)	<0.01
Hypertension	0.97 (0.94-1.00)	0.04
Heart Failure	1.02 (0.98-1.06)	0.43
Diabetes	1.00 (0.97-1.04)	0.92
COPD	0.95 (0.92-0.98)	<0.01
Obesity	1.01 (0.97-1.04)	0.72

Model adjusted for age, gender, area code, hospital teaching status, and primary expected payer, frailty.

References

1. Yazdany, J., Marafino, B. J., Dean, M. L., Bardach, N. S., Duseja, R., Ward, M. M., & Dudley, R. A. (2014). Thirty-day hospital readmissions in systemic lupus erythematosus: predictors and hospital- and state-level variation. Arthritis & rheumatology (Hoboken, N.J.), 66(10), 2828–2836. https://doi.org/10.1002/art.38768
2. Legge A, Kirkland S, Rockwood K, Andreou P, Bae SC, Gordon C, et al. Construction of a Frailty Index as a Novel Health Measure in Systemic Lupus Erythematosus. J Rheumatol. 2020;47(1):72-81.
3. Legge A, Kirkland S, Rockwood K, Andreou P, Bae SC, Gordon C, et al. Prediction of hospitalizations in systemic lupus erythematosus using the Systemic Lupus International Collaborating Clinics Frailty Index (SLICC-FI). Arthritis Care Res (Hoboken). 2020.
4. Gilbert T, Neuburger J, Kraindler J, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. *Lancet* 2018; published online April 26. http://dx.doi.org/10.1016/S0140-6736(18)30668-8.

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Abstract Number: 2591

Under Assault: Ongoing Brain Dysfunction Identified on Resting State-functional MRI (rs-fMRI) in SLE Patients in Clinical Remission

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SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes IV: Outcomes & Comorbidity
Session Type: Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: There is substantial evidence that the brain is targeted early in SLE, likely from disease inception. Data from mouse models and human studies suggest that SLE-related pathogenic mechanisms contribute to brain injury through blood brain barrier disruption, autoantibody and cytokine-mediated injury and microglial synaptic pruning (1). It is unknown whether SLE-related brain abnormalities improve or persist during clinical disease remission. We used rs-fMRI to identify a candidate SLE-related functional network (SLE-Net) and measure individual SLE-Net expression levels in SLE and healthy control (HC) subjects.

Methods: rs-fMRI scans were obtained on 25 SLE and 14 HC enrolled in a prospective observational study. SLE subjects were determined to be in clinical remission (SLE-R; n=9), defined as no disease activity and off all SLE medications except Plaquenil for ≥3 years, or not in remission (SLE-NR).

Results: An automated algorithm, blind to group, was applied to rs-fMRI data. For independent components (IC) selection, logistic regression analysis was applied to each of 1,000 bootstrap iterations, revealing three component patterns (IC4 [hippocampus, parahippocampal gyrus, putamen, globus pallidus], IC20 [insula], and IC21 [motor, premotor cortex]), for which the SLE and HC groups differed significantly based on their respective subject scores ($p < 0.05$). The IC weights (coefficients), 0.35, 0.63, and 0.7, respectively, were determined with a second bootstrap procedure to identify the combination

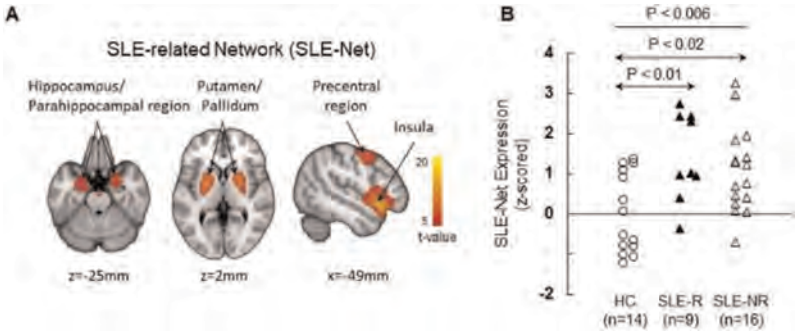

Figure 1. SLE-Net. A. SLE-Net identified in rs-fMRI scans from 25 SLE and 14 age- and gender-matched HC (p=0.001; Student t-test). SLE-Net characterized by bilateral contributions from the hippocampus and parahippocampal gyrus, insula, putamen, globus pallidus, motor and premotor cortex. B. SLE-Net expression levels (z-scored) for 9 SLE-R (filled triangles), 16 SLE-NR (open triangles), and 14 HC (open circles). SLE-Net expression differed across groups (p<0.006; ANOVA), with abnormal increases in both SLE-R and SLE-NR (p<0.02; post-hoc tests).

best discriminating SLE from HC. This resulted in a composite SLE-Net, for which the corresponding expression levels accurately discriminated the two groups (P< 0.005; permutation test, 5,000 iterations) (Fig. 1A). Regions contributing to SLE-Net were among the hypermetabolic regions previously identified in SLE with FDG PET (2). SLE-Net expression in individual subjects (Fig. 1B) were elevated in SLE compared to HC (P=0.006). In an exploratory analysis, we used the same approach to identify a candidate SLE-R-specific network (SLE-RNet). Despite the small n (9), a significant SLE-RNet was identified that discriminated SLE-R from HC (p < 0.005; Student t-test). The topography of SLE-RNet was closely related to that of SLE-Net (r=0.93, p< 0.001; voxel-wise correlation with SLE-Net).

Conclusion: In the absence of additional SLE-R subjects for validation, the SLE-NET is considered preliminary. However, our data support the hypothesis that there may be ongoing brain dysfunction despite the appearance of clinical remission and this may impact treatment considerations. 1. N. Kello, E. Anderson, B. Diamond, Cognitive Dysfunction in Systemic Lupus Erythematosus: A Case for Initiating Trials. Arthritis Rheumatol 71, 1413-1425 (2019). 2. M. Mackay et al., Metabolic and microstructural alterations in the SLE brain correlate with cognitive impairment. JCI Insight 4, (2019).

Disclosure: M. MacKay: None; **a. vo**: None; **E. Anderson**: None; **C. Aranow**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, 5, kezar Inc, 2; **B. Diamond**: Alpine, 12, DSMB, DBV, 2, 2, IMT, 2, Kyverna, 2, Nighthawk, 2, ONO, 2; **D. Eidelberg**: None.

Abstract Number: 2592

Trends, Sociodemographic and Clinical Factors Associated with Avascular Necrosis and Related Arthroplasties in Hospitalized Patients with Systemic Lupus Erythematosus and Rheumatoid Arthritis

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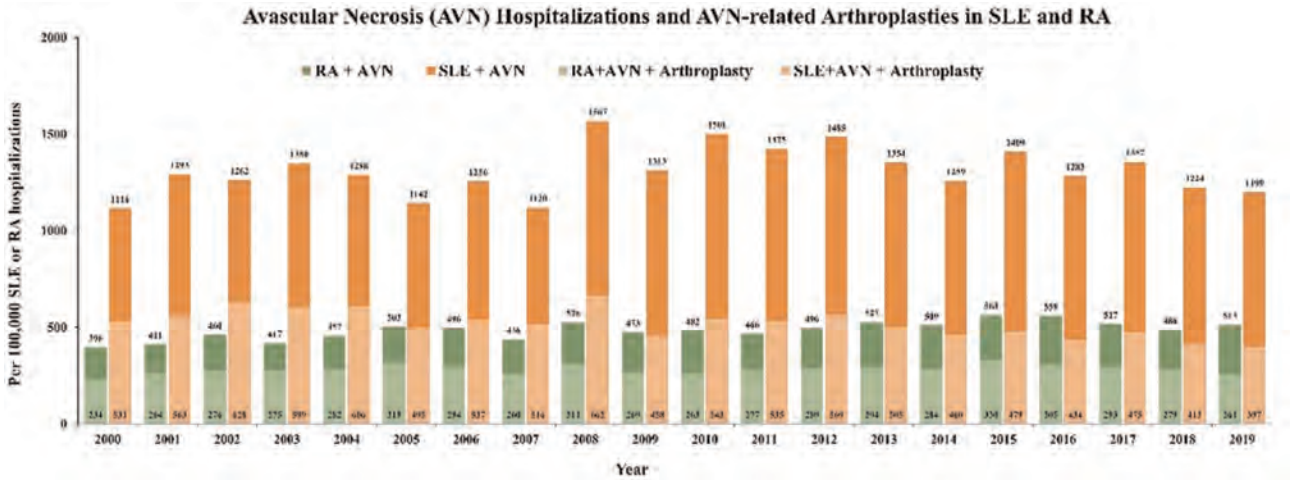
SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes IV: Outcomes & Comorbidity
Session Type: Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Avascular necrosis (AVN) can be a debilitating complication of autoimmune diseases and steroid treatment, with a higher prevalence in systemic lupus erythematosus (SLE) (0.8-33%) compared to rheumatoid arthritis (RA) (0.4%-12). AVN frequently leads to progressive joint destruction necessitating arthroplasty. Limited research exists on trends following the introduction of newer steroid-sparing agents as well as sociodemographic and clinical factors associated with AVN. We aimed to analyze rates, trends, and characteristics associated with AVN and AVN-related joint arthroplasties among SLE and RA hospitalizations using the largest publicly available all-payer inpatient US database, the National Inpatient Sample (NIS).

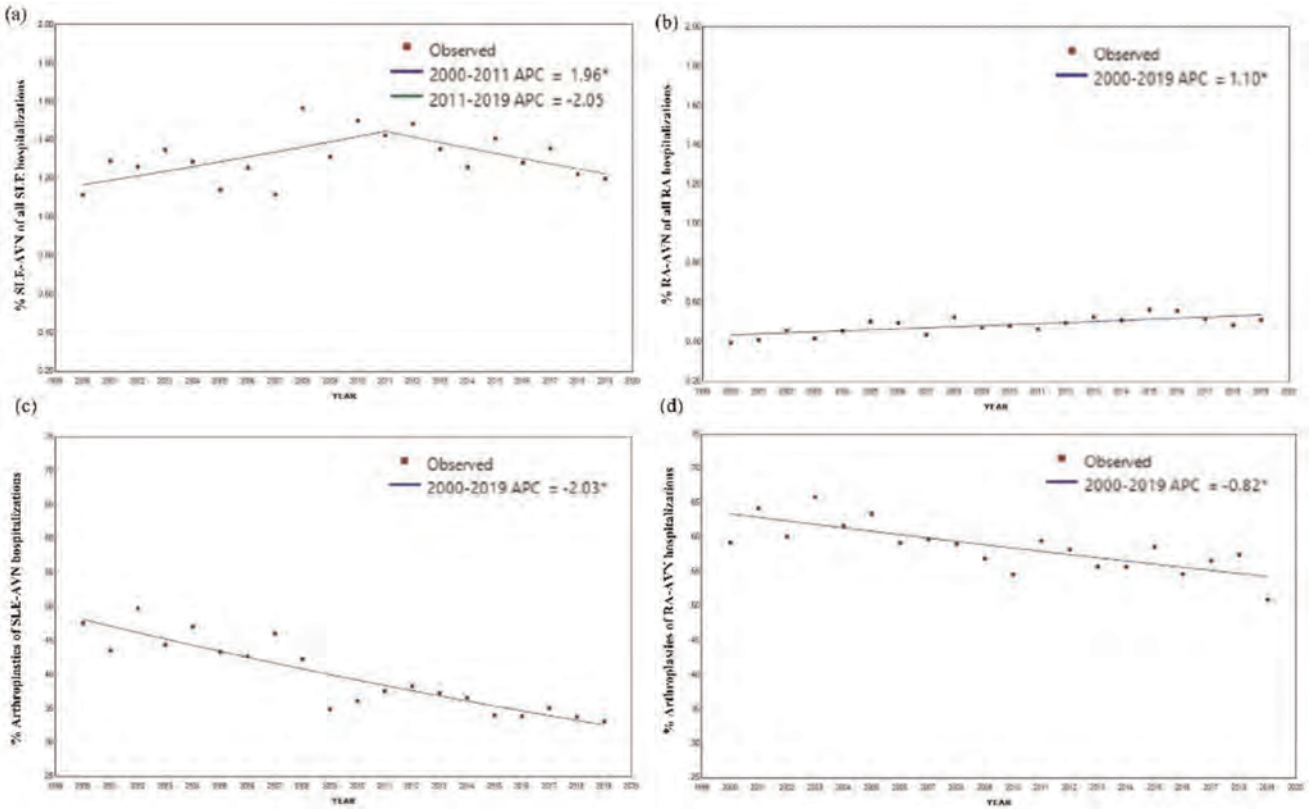
Methods: This cross-sectional study used NIS data (2000-2019) to identify hospitalized adults (≥18 years) with diagnoses of SLE and RA, and those with concomitant AVN diagnoses using validated International Classification of Disease (ICD) codes. AVN was further grouped into whether or not they had arthroplasties to examine trends. We compared SLE and RA hospitalizations with and without AVN, and arthroplasties using STATA and the Joinpoint regression program to calculate annual percent change (APC).

Results: From 2000-2019, there were 3,295,384 SLE and 8,983,521 RA hospitalizations, among which 43,339 (1.3%) and 44,148 (0.5%) had concomitant AVN (herein referred to as SLE-AVN and RA-AVN, respectively; **Table 1**). Of the SLE-AVN and RA-AVN, 16,941 (39%) and 25,509 (57%) underwent arthroplasties, respectively (**Table 1, Figure 1**). We observed an uptrend in RA-AVN (APC: 1.10*), with a decrease in the proportions of arthroplasties (APC: -0.82*; **Figure 2**). In contrast, there was an initial increase followed by a tendency to decline in SLE-AVN (APC 2000-2011: 1.96* APC 2011-2019 -2.05), with a decrease in the proportion of arthroplasties over time (APC -2.03*, **Figure 2**). Hospitalizations with AVN were younger [SLE (mean age: 43 vs 52 without), RA (mean age: 60 vs 68 without)] and more often Black race [SLE (41% Black with AVN, 26% without), RA (17% with AVN vs 10% without); Table 1]. SLE-AVN patients had higher rates of antiphospholipid syndrome (5% vs 3%) and end-stage renal disease (11% vs 9%); RA-AVN patients had higher nicotine use (15% vs 12%) compared to those without AVN. Among SLE-AVN and RA-AVN, encounters with arthroplasty (**Table 1**) were less likely to be Black (34% vs 46% in SLE-AVN and 13% vs 23% in RA-AVN) or have Medicaid coverage (15% vs 24% for SLE-AVN, and 9% vs 15% for RA-AVN) or most comorbidities than those without.

	SLE (N= 3,295,384)		SLE-AVN (N= 43,339)		RA (N= 8,983,521)		RA-AVN (N= 44,148)	
SLE and RA hospitalizations	**SLE without AVN**	**SLE with AVN**	**SLE-AVN without Arthroplasty**	**SLE-AVN with Arthroplasty**	**RA without AVN**	**RA with AVN**	**RA-AVN without Arthroplasty**	**RA-AVN with Arthroplasty**
Weighted estimate, N (%)	3,252,047 (98.7%)	43,339 (1.3%)	26,397 (61%)	16,941 (39 %)	8,939,368 (99.5%)	44,148 (0.5%)	19,013 (43%)	25,509 (57%)
Mean age, years ± SEM	52 ± 0.09	43 ± 0.20	41 ± 0.25	46 ± 0.29	68 ± 0.04	60 ± 0.19	59 ± 0.32	61 ± 0.21
Age categories, (%)								
< 45 years	35.86	55.63	61.22	46.91	7.21	15.24	19.75	11.95
≥ 45 years	64.14	44.37	38.78	53.09	92.79	84.76	80.25	88.05
Sex, (%)								
Female	88.94	86.91	86.77	87.13	74.82	74.36	75.28	73.68
Male	11.05	13.09	13.23	12.87	25.18	25.64	24.72	26.32
Race categories, (%)								
White	46.70	31.65	27.26	38.48	66.57	61.28	54.13	66.50
Black	25.66	41.20	46.21	33.39	10.38	17.06	23.22	12.57
Hispanic	10.77	8.58	9.73	6.79	6.65	6.02	7.36	5.04
Asian/Pacific Islander	1.90	2.91	2.46	3.62	1.23	1.18	1.38	1.02
Others	2.80	3.18	3.32	2.97	2.46	2.33	2.50	2.21
Missing	12.17	12.48	11.02	14.75	12.71	12.13	11.41	12.66
Income quartile, (%)								
1stQuart	30.61	32.25	34.74	28.38	26.16	27.69	30.17	25.88
2ndQuart	25.12	23.25	22.10	25.02	26.6	26.22	24.75	27.28
3rdQuart	22.88	22.58	22.30	23.03	24.66	23.95	22.70	24.86
4thQuart	21.38	21.92	20.86	23.57	22.59	22.14	22.38	21.98
Primary Payer, n (%)								
Medicare	46.56	43.96	46.86	39.43	68.34	58.32	61.07	56.30
Medicaid	17.77	20.47	23.87	15.17	7.33	11.19	14.76	8.57
Private insurance	29.34	31.45	25.05	41.44	20.75	26.69	20.74	31.03
Self-pay	3.48	1.76	2.17	1.13	1.59	1.22	1.74	0.84
Others	2.85	2.35	2.05	2.83	2.00	2.59	1.69	3.26
Clinical comorbidities, (%)								
APS	3.43	5.05	6.61	2.62	0.45	0.93	1.23	0.71
ESRD	8.49	10.92	15.89	3.17	1.63	1.78	3.39	0.60
COPD	12.51	6.92	7.17	6.53	21.11	15.39	18.75	12.94
Hypertension	56.09	55.95	58.45	52.06	62.77	57.12	56.86	57.31
Diabetes mellitus	19.24	11.00	13.23	7.54	25.26	16.77	20.46	14.07
Hyperlipidemia	18.63	14.12	13.61	14.90	30.31	24.92	22.12	26.96
IHD	18.02	10.41	11.27	9.07	26.48	14.75	17.65	12.63
PVD	5.89	7.33	7.84	6.54	4.86	4.37	5.66	3.43
HF, CMP, myocarditis	17.03	10.27	13.81	4.75	19.74	9.74	15.49	5.53
Alcohol related disorders	2.11	1.03	1.13	0.90	2.34	2.44	3.09	1.97
Nicotine dependence	12.27	13.07	12.19	14.44	11.39	15.01	15.16	14.91
Malignant neoplasm	4.56	1.67	2.49	0.39	7.00	3.31	5.74	1.54



Avascular necrosis (AVN) and related arthroplasties per 100,000 hospitalized adults with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), National Inpatient Sample, 2000-2019. Green represents RA, orange represents SLE, arthroplasties are represented by lighter shading.



Trends of avascular necrosis (AVN) and AVN-associated arthroplasties among hospitalized adults with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), National Inpatient Sample, 2000-2019. (a) The percentage of AVN among SLE hospitalizations shows an initial significant uptrend (APC 1.96*) with a peak around 2011 (b) The percentage of AVN among RA hospitalizations shows a modest significant uptrend over time (APC 1.10*), however, rates are lower compared to SLE-AVN. (c) AVN-related arthroplasties in both SLE-AVN (APC -2.03*) and (d) RA-AVN (APC -0.82*) show a significant decline over time. The rate of change from 2000 to 2019 was calculated using Joinpoint regression software and expressed as Annual Percent Change (APC). *Indicates significant difference at alpha = 0.05 level.

Conclusion: We report an initial increasing trend of SLE-AVN followed by a tendency to decline, which may relate to newer steroid-sparing therapies (i.e., Belimumab approval in 2011). There was an overall declining trend of AVN-associated arthroplasties in both SLE and RA. AVN hospitalizations were more likely to be younger and of the Black race. Yet, arthroplasty was less likely in encounters with patients who were Black or had Medicaid coverage. Our data indicate potential healthcare disparities that may influence surgical access. Further research should examine sociodemographic and treatment differences impacting AVN and arthroplasty rates.

Comparison of SLE and RA hospitalizations with and without diagnoses of AVN and with and without AVN-associated arthroplasties (hip, knee, shoulder), National Inpatient Sample, 2000-2019 *SLE: systemic lupus erythematosus, RA: rheumatoid arthritis, AVN: avascular necrosis, SEM: standard error of mean APS: Antiphospholipid syndrome ESRD: End-stage renal disease IHD: Ischemic heart disease PVD: Peripheral vascular disease HF: Heart failure, CMP: cardiomyopathy Differences in variables between groups are significant with $p < 0.05$ except for: SLE without AVN vs SLE with AVN: hypertension; SLE-AVN without and with arthroplasty: sex, COPD, hyperlipidemia, alcohol-related disorders; RA without AVN vs RA with AVN: sex, ESRD, alcohol-related disorders; RA-AVN without and with arthroplasty: sex, hypertension, nicotine dependence

Disclosure: R. Dhital: None; **N. Singh**: None; **B. Pedersen**: None; **C. Bartels**: Pfizer, 5.

Abstract Number: 2593

FT011 for the Treatment of Systemic Sclerosis. Results from a Phase II Study

Christopher Denton[1], Wendy Stevens[2], Nicole Kruger[3], Michelle Papadimitriou[4], Fay Khong[4], Michelle Bradney[3], Darren Kelly[4] and Robert Lafyatis[5], [1]University College London, London, United Kingdom, [2]Department of Rheumatology, St Vincent's Hospital Melbourne, Fitzroy, Australia, [3]Certa Therapeutics, Melbourne, Australia, [4]Certa Therapeutics and Melbourne University, Melbourne, Australia, [5]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Abstracts: Systemic Sclerosis & Related Disorders III: Clinical Trials
Session Type: Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Systemic Sclerosis (SSc) is an autoimmune disease characterized by vascular damage, inflammation, and fibrosis of the skin and organs, with no approved disease modifying treatments. The available treatment options are limited to systemic sclerosis-associated interstitial lung disease to slow the decline in lung function. Accordingly, there remains a serious unmet medical need for safe and effective therapeutics for the SSc population. FT011, a G protein-coupled receptor 68 (GPR68) proton sensing antagonist is being developed as a novel inhibitor of pro-fibrotic and inflammatory pathways.

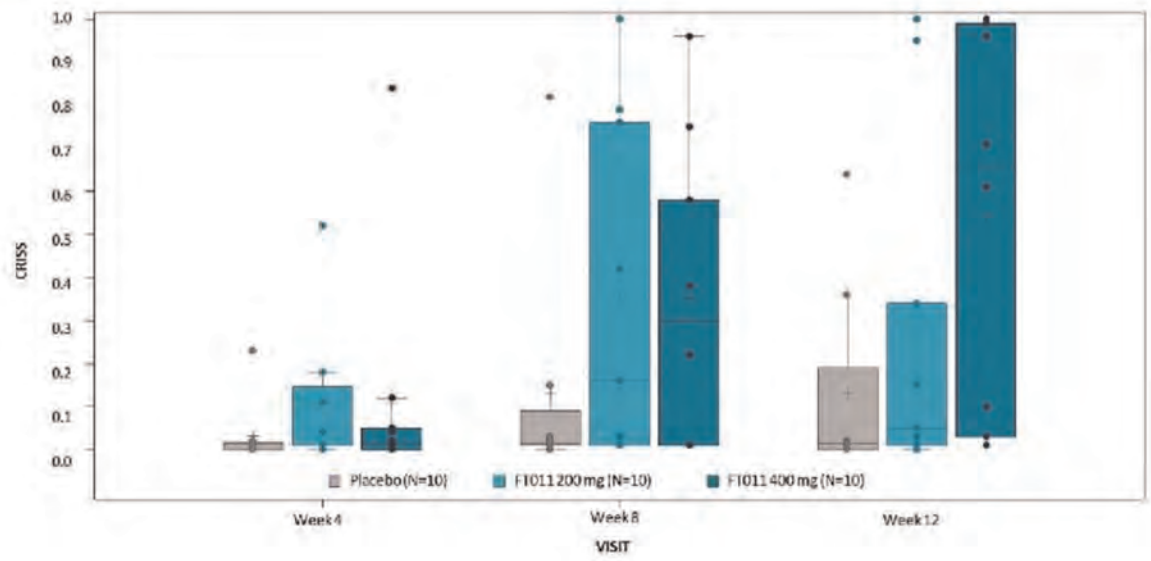
Methods: This was a Phase II, multi-center, randomized, double blind, placebo-controlled study of the pharmacokinetics, pharmacodynamic effects, and safety, of oral FT011 in patients with diffuse SSc (dSSc). The study randomized 30 participants (n = 10/group) to placebo, FT011 200 mg or FT011 400 mg taken once daily (OD) for 12 weeks. ClinicalTrials.gov Identifier: NCT04647890

Results: Patients were a mean age of 51 years, white and the majority (73%) female. Treatment with FT011 400 mg OD for 12 weeks resulted in significant and clinically meaningful improvements in the American College of Rheumatology Combined Response Index in Diffuse Cutaneous Systemic Sclerosis (ACR-CRISS) score and its composites.

By week 12, 60% of patients in the FT011 400 mg arm were classified as clinical responders with improvement in ACR-CRISS (defined by predicted probability ≥0.60)[1] vs 10.0% in the placebo arm (nominal p-value = 0.046). Median ACR-CRISS score was 0.660 vs 0.015, FT011 400 mg vs placebo, respectively. The mean ACR-CRISS score was 0.542 in the FT011 400 mg arm vs 0.131 in the placebo arm (nominal p-value = 0.019) (Figure 1).

FT011 also led to significant and clinically meaningful improvements across multiple efficacy measures including % predicted Forced Vital Capacity (FVC), Scleroderma Health Assessment Questionnaire-Disability Index (SHAQ-DI) and physician global assessments (Table 1).

Figure 1: Longitudinal Plots of Composite Response Index in Diffuse Cutaneous Systemic Sclerosis Scores Over Time



Notes: CRISS: Composite Response Index in Diffuse Cutaneous Systemic Sclerosis. IQR: Interquartile Range. The CRISS score is ranged from 0.0 to 1.0 where higher scores indicate greater improvement. Symbol inside the box: Mean. Horizontal line inside the box: Median. Bottom and top of box: 25th and 75th percentiles, respectively. Bottom and top whiskers: Extreme value within 1.5 IQR. Circle: individual participant's value.

Table 1: Efficacy Measure Changes from Baseline to Week 12

	Placebo	FT011 400 mg	FT011 400mg - Placebo	Nominal P-value
Parameter Visit	LS mean (95%CI)		LS Mean difference (95%CI)	
# mRSS	-1.8 (-4.57, 0.97)	-3.25 (-5.87, -0.62)	-1.45 (-5.27, 2.38)	0.443
ǂ % Predicted FVC	-1.64 (-5.49, 2.21)	4.9 (1.23, 8.56)	6.54 (1.23, 11.85)	0.018
# SHAQ-DI	0.0273 (-0.145, 0.200)	-0.2636 (-0.428, -0.100)	-0.291 (-0.529, -0.053)	0.019
ǂ Patient Global Assessment	8.14 (-5.60, 21.88)	9.03 (-3.70, 21.76)	0.89 (-18.01, 19.79)	0.924
# Physician Global Assessment	-4.83 (-19.52, 9.86)	-28.19 (-41.29, -15.10)	-23.36 (-43.03, -3.69)	0.022

Notes: ǂ Positive value indicates improvement and # Negative value indicates improvement. A formal sample size calculation for efficacy endpoints was not conducted for this study; the results are considered exploratory.

50% of patients in the FT011 400 mg arm exceeded the % predicted FVC minimally important clinically difference (MICD) (defined as a change of >3.3 - 5.3%)[2] vs no patients in the placebo arm meeting these criteria. Furthermore, 60% of patients in the FT011 400 mg arm met the MICD for SHAQ-DI (defined as a change of –0.13)[3] vs 22% in the placebo arm.

Compared to placebo, FT011 demonstrated numerically larger improvements from baseline to week 12 for mRSS and patient global assessment, however this was not significant.

FT011 was safe and well tolerated, with no differences in drug-related treatment-emergent adverse events between placebo and active treatment groups. There were no serious adverse events reported, nor any adverse events resulting in study drug interruption, withdrawal, or discontinuation.

Conclusion: These results demonstrate promising efficacy and safety data for FT011 OD after 12 weeks of treatment and therefore warrants a confirmatory phase III study to assess its potential to improve this debilitating condition.

References

[1] Khanna D et al. Arthritis Rheumatol. 2016 Feb;68(2):299-311.
[2] Kafaja S, et al. Am J Respir Crit Care Med. 2018 Mar 1;197(5):644-652.
[3] Daste C, et al. Semin Arthritis Rheum. 2019 Feb;48(4):694-700.

Disclosure: C. Denton: AbbVie, 2, Acceleron, 2, Arxx Therapeutics, 5, Bayer, 2, Boehringer-Ingelheim, 2, 6, Corbus, 2, 6, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Horizon Therapeutics, 2, Inventiva, 2, 5, Janssen, 6, Roche, 2, Sanofi, 2, Servier, 5; **W. Stevens**: None; **N. Kruger**: Certa Therapeutics Pty Ltd, 2; **M. Papadimitriou**: Certa Therapeutics, 3; **F. Khong**: Certa Therapeutics, 3; **M. Bradney**: None; **D. Kelly**: Certa therapeutics, 3, 4; **R. Lafyatis**: Advarra/GSK, 1, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, 5, Certa Therapeutics, 2, Corbus, 2, 5, EMD Serono, 2, Formation, 2, 5, Genentech, 1, 2, Merck/MSD, 2, Moderna, 5, Morphic, 2, Pfizer, 2, 5, Regeneron, 5, Third Rock Venture, 2, Thirona Bio, 2, 4, 11, Zag Bio, 2.

Abstract Number: 2594

Trajectories of Forced Vital Capacity (FVC) in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD)

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SESSION INFORMATION
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Session Type: Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: The SENSCIS trial enrolled patients with SSc-ILD without a requirement for them to have evidence of recent progression. During the trial, nintedanib reduced the rate of decline in FVC (mL/year) versus placebo. The open-label extension of the SENSCIS trial, SENSCIS-ON, assessed changes in FVC in patients treated with nintedanib over the longer term. We assessed the trajectory of FVC decline in patients who received placebo in the SENSCIS trial and then nintedanib in SENSCIS-ON.

Methods: In the SENSCIS trial, patients with SSc-ILD were randomized to receive nintedanib or placebo double-blind until the last patient reached week 52 but for ≤100 weeks. Patients who completed the SENSCIS trial on treatment (nintedanib or placebo) and attended a follow-up visit were eligible to enter SENSCIS-ON. The protocol allowed an off-treatment period between SENSCIS and SENSCIS-ON of ≤12 weeks. We calculated the trajectory of FVC in patients who received placebo in SENSCIS and initiated nintedanib in SENSCIS-ON. The baseline measurement in SENSCIS-ON was considered the anchor measurement (time point 0) (Figure 1). FVC was measured at time points before the anchor measurement (when patients were receiving placebo in SENSCIS or were off treatment between SENSCIS and SENSCIS-ON) and at time points after the anchor measurement (when patients were receiving open-label nintedanib in SENSCIS-ON). Analyses were descriptive and based on observed FVC values.

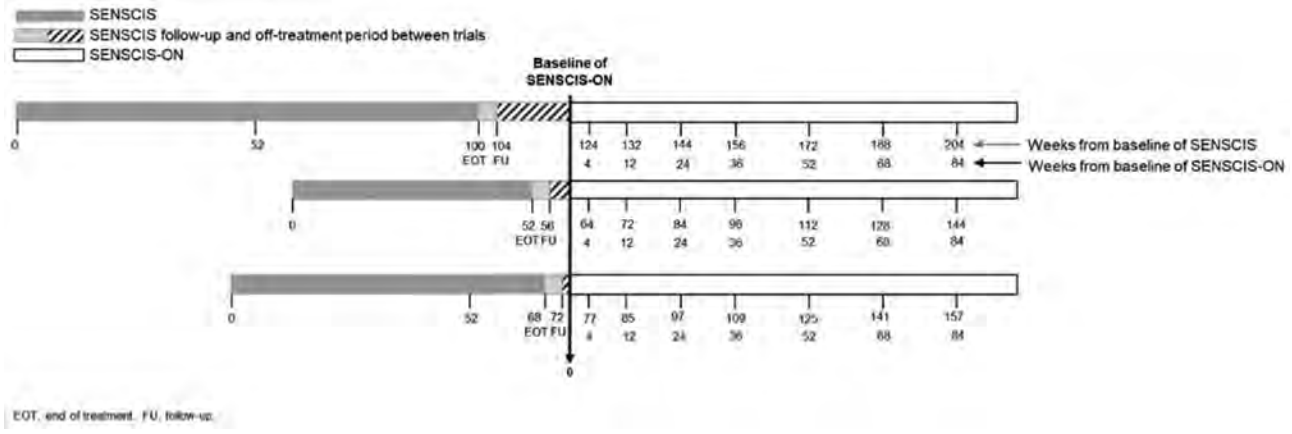

Figure 1. Method for pooling FVC data in SENSCIS and SENSCIS-ON

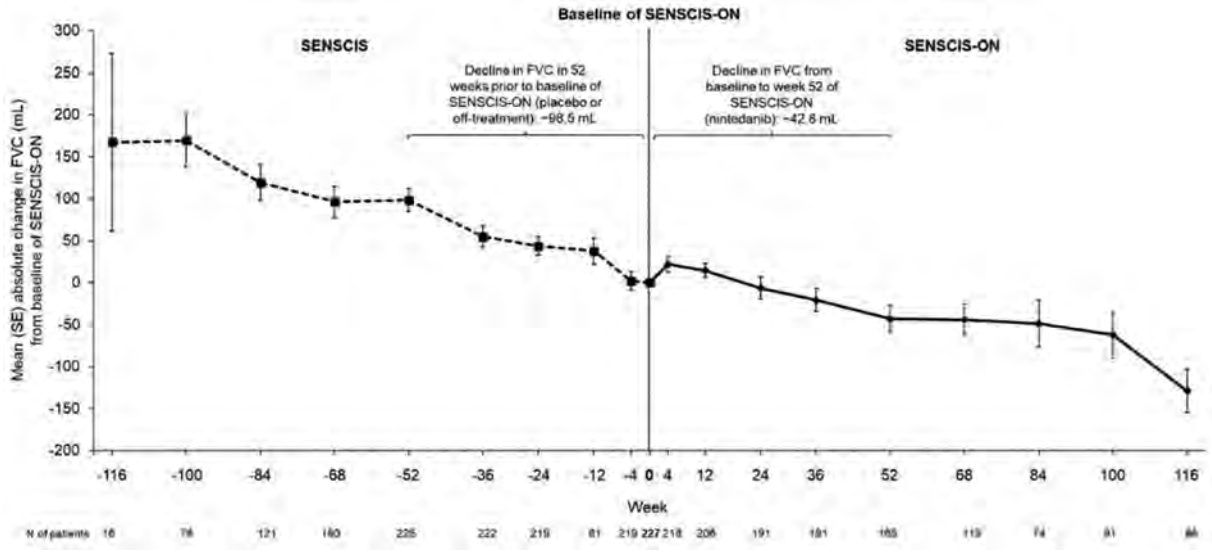

Figure 2. Trajectory of FVC in patients who received placebo in the SENSCIS trial followed by nintedanib in SENSCIS-ON

Results: In total, 231 patients received placebo in SENSCIS and then nintedanib in SENSCIS-ON. In these patients, mean (SD) FVC was 2593 (833) mL at baseline of SENSCIS and 2441 (833) mL at baseline of SENSCIS-ON. The mean decline in FVC in the 52 weeks prior to baseline of SENSCIS-ON (when patients were receiving placebo in SENSCIS or were off treatment) was −98.5 mL (Figure 2). The mean decline in FVC from baseline of SENSCIS-ON to week 52 of SENSCIS-ON (when patients were receiving nintedanib) was −42.8 mL (Figure 2).

Conclusion: In patients who received placebo in the SENSCIS trial, the decline in FVC over 52 weeks was reduced by approximately 57% following initiation of open-label nintedanib in SENSCIS-ON. These analyses illustrate the progressive nature of SSc-ILD in the population enrolled in SENSCIS and the effectiveness of nintedanib on slowing the progression of SSc-ILD.

Disclosure: O. Distler: 4P-Pharma, 2, 5, 6, AbbVie, 2, 5, 6, Acceleron, 2, 5, 6, Alcimed, 2, 5, 6, Altavant Sciences, 2, 5, 6, Amgen, 2, 5, 6, AnaMar, 2, 5, 6, Arxx, 2, 5, 6, AstraZeneca, 2, 5, 6, Bayer, 2, 5, 6, Blade Therapeutics, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Citus AG, 12, Co-Founder, Corbus Pharmaceuticals, 2, 5, 6, CSL Behring, 2, 5, 6, Galapagos, 2, 5, 6, Galderma, 2, 5, 6, Glenmark, 2, 5, 6, Gossamer, 2, 5, 6, Horizon Therapeutics, 2, 5, 6, Janssen, 2, 5, 6, Kymera, 2, 5, 6, Lupin, 2, 5, 6, Medscape, 2, 5, 6, Miltenyi Biotec, 2, 5, 6, Mitsubishi Tanabe, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143), 10, Prometheus Biosciences, 2, 5, 6, Redx Pharma, 2, 5, 6, Roivant, 2, 5, 6, Topadur, 2, 5, 6; **M. Vonk**: Boehringer Ingelheim, 5, 6, Corbus, 1, EUSTAR, 4, Ferrer, 5, Galapagos, 5, Janssen, 5, 6, MSD, 6, Systemic Sclerosis ERN ReCONNET, 4; **A. Azuma**: Boehringer Ingelheim, 2, 5, 6, Kyorin Pharma, 2, Taiho, 2, Toray, 2; **M. Mayes**: Boehringer Ingelheim, 1, 5, British Medical Journal, 9, Corbus, 5, EICOS, 1, 5, Horizon Pharma, 5, Medtelligence, 6, Mitsubishi Tanabe, 1, 5, Oxford University Press, 9, Prometheus, 5, Springer International Publishing, 9; **D. Khanna**: AbbVie, 12, DSMB, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb, 2, 5, CSL Behring, 2, Genentech, 2, Horizon Therapeutics, 2, 5, Janssen, 2, 6, Pfizer, 5, Prometheus, 2; **K. Highland**: Boehringer Ingelheim, 2, 5, 6, Scleroderma Foundation, 1; **G. Toenges**: Boehringer Ingelheim, 3; **M. Alves**: Boehringer Ingelheim, 3; **Y. Allanore**: AbbVie, 6, AstraZeneca, 1, Boehringer Ingelheim, 1, 2, 6, Chemomab, 1, Curzion, 1, Janssen, 6, Medsenic, 1, Menarini, 1, Prometheus, 1, Sanofi, 1, 2.

Abstract Number: 2595

A Randomized Controlled Trial to Compare the Efficacy and Safety of Tacrolimus with Mycophenolate Mofetil in Patients with Systemic Sclerosis - Interstitial Lung Disease (INSIST TRIAL)

Shefali Khanna Sharma[1], Jithin Mathew[1], Chirag Kopp[1], Varun Dhir[2], Sahajal Dhooria[3], Anindita Sinha[1] and Sanjay Jain[1], [1]Post Graduate Institute of Medical Education and Research, Chandigarh, India, [2]PGIMER, CHD, INDIA, Chandigarh, India, [3]PGI CHANDIGARH, Chandigarh, India

SESSION INFORMATION

Session Date: Wednesday, November 15, 2023
Session Title: Abstracts: Systemic Sclerosis & Related Disorders III: Clinical Trials
Session Type: Abstract Session
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Background/Purpose: Interstitial lung disease in systemic sclerosis(SSc-ILD) is heterogeneous with limited therapeutic options. Mycophenolate mofetil (MMF) is the most commonly used first line agent for SSc-ILD. Tacrolimus has shown promising efficacy in few small case series, and large cohorts of patients with non-SSC-ILD1,but has never been evaluated in the setting of a clinical trial in scleroderma.

Methods: In this single center open labelled, prospective, two-arm parallel group, randomized controlled pilot study (INSIST) conducted between November 2021 to December 2022, patients with progressive ILD (FVC decline >10%) due to SSc, aged between 18-65 years, disease duration < 10 years, without concomitant inflammatory myositis, with an FVC of 40-85%, and not having received active immunosuppression other than prednisolone < 10mg/day in the last 6 months were randomized to receive either MMF (target dose 2gm/day) or tacrolimus (Max dose-0.075 mg/kg/day; target trough levels-4- 10ng/ml) for 24 weeks. The primary endpoint was the difference in change in FVC% at 24 weeks; secondary outcomes included absolute change in FVC, skin scores, 6-minute walk distance, Mahler's transitional dyspnea index, ACR-CRISS and revised CRISS responses and adverse outcomes. (Trial Reg: CTRI/2021/11/037864)

Results: 25 out of 26 patients (13 in each group) completed 24 weeks follow up. Majority had Anti-Scl 70 positivity (73%) and limited skin disease. At 24 weeks, the mean change in FVC was 4.4% (10.6) and 6.92%(8.4) in the MMF and tacrolimus groups respectively (difference 2.52%, 95% CI (-10.3 to 5.18); p-0.500). All patients on tacrolimus and 85% of patients on MMF had stabilization (ΔFVC% -5% TO 5%) or improvement (ΔFVC% >10%) in lung function. Secondary outcomes were similar between two groups. Subgroup analyses stratified by ILD type, skin involvement at baseline, and early vs late SSc

Table 1: Primary and Secondary outcomes at 24 weeks

	MMF (n=13)	Tacrolimus (n=13)	P value
Change in FVC (% predicted), mean (SD)	+ 4.4 (10.6)	+ 6.92 (8.4)	Difference 2.52%, 95% CI (-10.3 to 5.18); p-0.500
Absolute change in FVC (ml), mean (SD)	+130.7 (164.6)	+176.8 (305.5)	0.636
Change in mRSS , median (IQR)	-1 (-3 to -0.5)	-1 (-1 to -0.5)	0.209
Change in 6MWD (metres), mean (SD)	63.15 (56.72)	32.67 (27.53)	0.094
Change in SGRQ score, mean (SD)	-14.83 (12.40)	-12.97 (11.78)	0.698
Focal Score TDI, median (IQR)	3 (2-4)	3 (2-4)	0.979
Change in SF-36 PCS, mean (SD)	5.59 (4.89)	4.72 (12.91)	0.823
Change in SF-36 MCS, mean (SD)	3.46 (7.86)	5.58 (5.54)	0.446
Change in PGA, median (IQR)	-2.0 (-2.5 to -1.5)	-2.0 (-2 to -1)	0.364
Change in HAQ-DI, median (IQR)	-0.23 (-0.25 to -0.19)	-0.125 (-0.25 to -0.125)	0.393
ACR-CRISS Improvement, n (%)	5 (38.5)	3 (23.1)	0.395
Revised ACR-CRISS responders; n (%)	10 (76.9)	7 (53.9)	0.416

FVC: Forced Vital Capacity; 6MWD- 6 minute walk distance; mRSS- Modified Rodnan Skin Score; SGRQ- St. George Respiratory Questionnaire; HAQ-DI- Health Assessment Questionnaire-Disability Index; TDI- Transitional Dyspnea Index; SF-36- Short Form 36; PCS- Physical component summary; MCS- Mental Component Summary; CRISS - Composite Response Index in Systemic Sclerosis

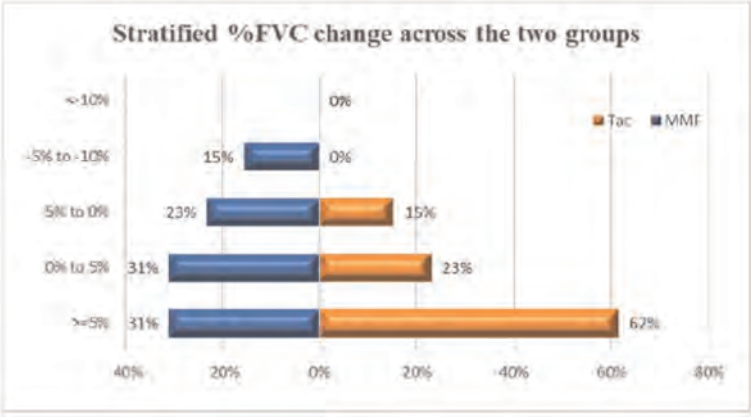

Figure 1: Changes in FVC% stratified by magnitude of change

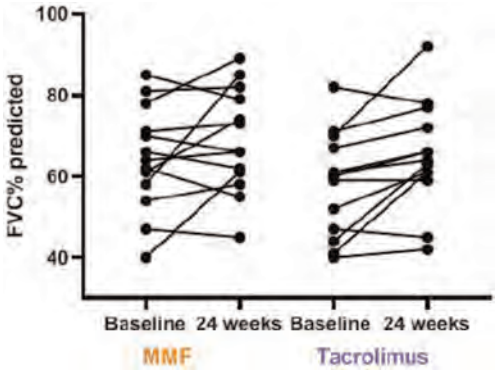

Figure 2: FVC changes at individual level between baseline and week 24 in both groups

yielded similar results. The mean tacrolimus levels were 4.9 ng/ml(1.47) and the median dose needed to achieve these levels was 4mg/d. No serious adverse events were noted in either group. Gastrointestinal disturbances was noted in 23% of patients of mycophenolate and new onset hypertension, minor infection and diarrhea in 1 patient each in the tacrolimus arm. Notably, tacrolimus did not result in renal dysfunction or renal crises.

Conclusion: Tacrolimus resulted in comparable improvement to MMF across primary and secondary outcome measures at 24 weeks with a favorable safety profile in patients with SSc ILD. Larger studies with longer follow up are needed to investigate the role of calcineurin inhibitors in SSc.

Disclosure: S. Sharma: None; **J. Mathew**: None; **C. Kopp**: None; **V. Dhir**: None; **S. Dhooria**: None; **A. Sinha**: None; **S. Jain**: None.

Abstract Number: 2596

Head-To-Head Comparison of the Effectiveness of Tocilizumab, Rituximab, Mycophenolate Mofetil, and Cyclophosphamide in Patients with SSc-ILD from the EUSTAR Database

Qingran Yan[1], Cosimo Bruni[2], Alexandru Garaiman[2], Carina Mihai[2], Suzana Jordan[2], Mike Becker[3], Muriel Elhai[4], Rucsandra Dobrota[2], liubov Petelytska[3], Anna-Maria Hoffmann-Vold[5], Joerg Henes[6], Eric Hachulla[7], Elise Siegert[8], Alexandra Balbir-Gurman[9], Giovanna Cuomo[10], Gabriela Riemekasten[11], Stefan Heitmann[12], valeria Riccieri[13], Susanne Ullman[14], Petros Sfikakis[15], Francesca Ingegnoli[16], Vera Bernardino[17], Marie-Elise Truchetet[18], Francesco Del Galdo[19], SHUANG YE[20] and Oliver Distler[2], [1]Department of Rheumatology, University Hospital Zurich, Zurich, Swaziland, [2]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [3]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zürich, Switzerland, [4]University Hospital zurich, University of Zurich, Zurich, Switzerland, [5]Oslo University Hospital, Oslo, Norway, [6]University Hospital Tuebingen, Tuebingen, Germany, [7]University of Lille, Lille, France, [8]Department of Rheumatology, Charité University Hospital, Charité Platz 1, D-10117, Berlin, Germany, [9]Rheumatology Institute, Rambam Health Care Campus and Rappaport Faculty of |Medicine, Technion, Haifa, Israel, [10]Department of Precision Medicine, "Luigi Vanvitelli" University of Campania, Naples, Italy, [11]University Clinic Schleswit-Holstein (UKSH), Lübeck, Germany, [12]Department of Rheumatology, Marienhospital Stuttgart, Böheimstrasse 37, D-70199, Stuttgart, Germany, [13]Department of Clinical, Internal and Cardiovascular Specialities, Sapienza University of Rome, Roma, Italy, [14]Department of Dermatology, University Hospital of Copenhagen, Hospital Bispebjerg, Copenhagen, Denmark, [15]National Kapodistrian University of Athens Medical School, Athens, Greece, [16]Universita' degli Studi di Milano, Milano, Italy, [17]Centro Hospitalar Lisboa Central, Lisbon, Portugal, [18]Bordeaux University Hospital, Bordeaux, France, [19]University of Leeds - Leeds Institute of Rheumatic and Muskuloskeletal Medicine, Leeds, United Kingdom, [20]Department of Rheumatology, Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China

SESSION INFORMATION

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Background/Purpose: Tocilizumab (TCZ), rituximab (RTX), mycophenolate mofetil (MMF), and cyclophosphamide (CYC) are the immunosuppressants (IS) with the current best evidence for the treatment of systemic sclerosis-associated interstitial lung disease (SSc-ILD)[1-4]. However, limited information is available from comparison studies, and these treatments have often been tested in diverse populations. This study aimed to compare the effectiveness of TCZ, RTX, MMF, and CYC in SSc-ILD patients from the EUSTAR database.

Methods: We included SSc patients from the EUSTAR database who fulfilled the following criteria: 1/ radiologically confirmed ILD; 2/ database record on the use of TCZ, RTX, MMF, or CYC; 3/ baseline and follow-up lung function associated with the treatment period. The primary endpoint was the change of forced vital capacity (FVC) % predicted from baseline to follow-up. Secondary endpoints included changes in diffusing capacity (DLCO) % predicted, modified Rodnan Skin Score (mRSS), and categorical changes in lung function tests and mRSS. Missing data were processed using multiple imputations with chained equations. Selection bias of the medications was reduced to a minimum using propensity score-based inverse probability of treatment weighting (IPTW). For paired therapy comparisons, we used average treatment effects (ATE). Subgroup analysis included previous IS use, background IS, and treatment duration (less than 18 months).

Results: 995 patients with 1050 treatment observations were included in this study. TCZ patients had more arthritis, higher baseline FVC and DLCO, more reticular change in chest CT, and less ground glass opacity. RTX and CYC patients had more elevations of C-reaction protein, and TCZ and RTX patients had higher baseline mRSS, more digital ulcers, and fewer IS naive cases (Table 1).

The median follow-up time was 11 months (interquartile range: 8-14 months). After IPTW, the changes of FVC % predicted were not significantly different between the four treatment arms by the Kruskal Wallis test (P=0.058, Figure 1). Among paired comparisons, only the treatment difference between CYC vs. RTX was significant (mean difference of FVC % predicted, 2.29; 95% CI, 0.18-4.40; P=0.034, Table 2).

In the multivariate logistic regression, only CYC was associated with stable or improved FVC among the four agents. The treatment differences in change of FVC% predicted among the four groups were not significant in patients with previous IS, background IS, or treatment duration > 18 months. Interestingly, MMF showed better FVC responses in patients with previous IS than in IS naive patients [Mean adjusted change of FVC % predicted (95% CI): 1.90 (0.36 to 3.45) vs. -0.04 (-1.35 to 1.26), P=0.047].

Conclusion: In this first large real-world observational study, the treatment effectiveness on FVC change of SSc-ILD patients was not statistically different between TCZ, RTX, MMF, and CYC. CYC showed clinically marginal but statistically significantly better effectiveness in some sub-analyses. Head-to-head randomized clinical trials on IS with longer follow-up are needed for SSc-ILD.

Table1. Patient parameters pre- and post-IPTW. IPTW, inverse probability of treatment weighting; CYC, cyclophosphamide; MMF, mycophenolate mofetil; RTX, rituximab; TCZ, tocilizumab; CRP, C-reaction protein; DU, digital ulcer; SRC, scleroderma renal crisis; ACA, anti-centromere antibody; ATA, anti-topoisomerase I antibody; ESR, erythrocyte sediment rate; LVEF, left ventricular ejection fraction; RHC, right heart catheter; PH, pulmonary hypertension; FVC, forced vital capacity; DLCO, diffusing capacity of the lungs for carbon monoxide; HRCT, high-resolution computational tomography; GGO, ground-glass opacity; AZA, azathioprine; LEF, leflunomide; MTX, methotrexate.

	Pre IPTW					Post IPTW				
	CYC	MMF	RTX	TCZ	P values	CYC	MMF	RTX	TCZ	P values
No. of patients	225	554	175	96		713.12	930.8	650.35	570.91	
Demographic & patient characters										
Age (year, median [IQR])	54.00 [47.00, 64.00]	55.00 [46.00, 64.00]	53.00 [44.50, 61.00]	55.50 [49.75, 62.00]	0.179	55.00 [47.00, 64.00]	55.00 [46.00, 64.00]	53.00 [45.00, 60.00]	55.00 [48.06, 62.15]	0.474
Non-RP durtaion (month, median [IQR])	32.00 [16.00, 102.00]	66.50 [30.25, 130.75]	58.00 [27.00, 120.00]	55.00 [28.75, 123.00]	<0.001	59.07 [24.00, 120.00]	60.00 [26.00, 125.74]	57.58 [29.36, 120.43]	54.05 [24.39, 121.69]	0.886
Female (%)	168 (74.7)	427 (77.1)	128 (73.1)	79 (82.3)	0.335	559.4 (78.5)	706.0 (75.8)	501.8 (77.2)	438.2 (76.7)	0.943
dcSSc (%)	144 (64.0)	314 (56.7)	111 (63.4)	65 (67.7)	0.065	440.6 (61.8)	557.5 (59.9)	402.6 (61.9)	401.0 (70.2)	0.376
Smoker ever (%)	80 (35.6)	196 (35.4)	74 (42.3)	44 (45.8)	0.113	255.5 (35.8)	351.3 (37.7)	243.2 (37.4)	271.4 (47.5)	0.28
mRSS (median [IQR])	10.00 [5.00, 20.00]	9.00 [4.00, 16.00]	12.00 [6.00, 19.00]	12.50 [5.00, 21.00]	<0.001	9.00 [5.00, 19.00]	9.00 [4.00, 16.00]	11.00 [6.00, 16.00]	9.30 [4.00, 20.63]	0.421
CRP elevation ever (%)	143 (63.6)	271 (48.9)	118 (67.4)	46 (47.9)	<0.001	413.2 (57.9)	490.2 (52.7)	387.5 (59.6)	283.5 (49.7)	0.427
Race (%)					<0.001					0.004
Unknown	36 (16.0)	55 (9.9)	35 (20.0)	8 (8.3)		111.9 (15.7)	95.5 (10.3)	130.0 (20.0)	29.4 (5.2)	
White	160 (71.1)	458 (82.7)	130 (74.3)	71 (74.0)		529.9 (74.3)	764.5 (82.1)	468.8 (72.1)	435.8 (76.3)	
Black	3 (1.3)	8 (1.4)	5 (2.9)	3 (3.1)		8.6 (1.2)	14.9 (1.6)	28.3 (4.4)	24.4 (4.3)	
Asian	17 (7.6)	15 (2.7)	2 (1.1)	10 (10.4)		36.7 (5.1)	28.3 (3.0)	2.9 (0.5)	69.3 (12.1)	
Hispanic	1 (0.4)	3 (0.5)	1 (0.6)	0 (0.0)		2.7 (0.4)	4.2 (0.5)	2.5 (0.4)	0.0 (0.0)	
Others	8 (3.6)	15 (2.7)	2 (1.1)	4 (4.2)		23.3 (3.3)	23.4 (2.5)	17.8 (2.7)	11.9 (2.1)	
DU ever (%)	86 (38.2)	205 (37.0)	94 (53.7)	40 (41.7)	0.001	272.8 (38.3)	354.9 (38.1)	317.9 (48.9)	270.6 (47.4)	0.175
SRC ever (%)	3 (1.3)	10 (1.8)	5 (2.9)	3 (3.1)	0.595	5.8 (0.8)	18.7 (2.0)	18.1 (2.8)	14.2 (2.5)	0.493
Autoantibodies										
ACA+ (%)	28 (12.4)	90 (16.2)	17 (9.7)	12 (12.5)	0.132	97.0 (13.6)	134.8 (14.5)	68.4 (10.5)	48.3 (8.5)	0.403
ATA+ (%)	149 (66.2)	341 (61.6)	101 (57.7)	62 (64.6)	0.337	457.2 (64.1)	586.7 (63.0)	375.0 (57.7)	403.3 (70.6)	0.27
Anti-U1RNP+ (%)	12 (5.3)	39 (7.0)	13 (7.4)	3 (3.1)	0.417	44.7 (6.3)	60.4 (6.5)	37.5 (5.8)	15.4 (2.7)	0.495
Anti-Pm3+ (%)	14 (6.2)	46 (8.3)	17 (9.7)	11 (11.5)	0.398	36.0 (5.0)	78.4 (8.4)	48.4 (7.4)	43.4 (7.6)	0.578
Anti-PM/Scl+ (%)	12 (5.3)	37 (6.7)	18 (10.3)	5 (5.2)	0.215	26.4 (3.7)	64.3 (6.9)	59.2 (9.1)	25.8 (4.5)	0.295
Baseline parameters										
ESR (mm/h, median [IQR])	31.00 [16.00, 50.00]	25.00 [12.00, 47.75]	26.00 [12.00, 50.00]	15.50 [4.00, 40.25]	<0.001	28.00 [14.86, 47.18]	26.00 [12.11, 46.60]	28.19 [12.00, 52.00]	18.00 [5.00, 40.69]	0.165
CRP (g/L)	0.50 [0.28, 1.40]	0.44 [0.21, 0.90]	0.60 [0.28, 1.65]	0.34 [0.06, 0.76]	0.002	0.48 [0.28, 1.20]	0.44 [0.22, 0.90]	0.50 [0.28, 1.33]	0.36 [0.03, 0.90]	0.102
Arthritis (%)	35 (15.6)	41 (7.4)	32 (18.3)	32 (33.3)	<0.001	98.1 (13.8)	95.0 (10.2)	110.0 (16.9)	91.0 (15.9)	0.263
Tendon friction (%)	34 (15.1)	46 (8.3)	24 (13.7)	11 (11.5)	0.025	88.9 (12.5)	81.7 (8.8)	76.6 (11.8)	68.5 (12.0)	0.671
Joint contraction (%)	73 (32.4)	198 (35.7)	95 (54.3)	48 (50.0)	<0.001	249.3 (35.0)	344.4 (37.0)	310.8 (47.8)	261.7 (45.8)	0.118
Mysositis (%)	30 (13.3)	36 (6.5)	23 (13.1)	9 (9.4)	0.006	62.4 (8.8)	66.4 (7.1)	60.3 (9.3)	67.7 (11.9)	0.537
LVEF<45% (%)	6 (2.7)	7 (1.3)	2 (1.1)	0 (0.0)	0.256	12.8 (1.8)	12.1 (1.3)	4.4 (0.7)	0.0 (0.0)	0.171
LVEF (%, median [IQR])	60.00 [53.00, 65.00]	60.00 [50.00, 65.00]	60.00 [53.00, 65.00]	60.00 [55.00, 63.25]	0.291	60.00 [54.00, 65.00]	60.00 [50.00, 65.00]	60.63 [55.00, 66.00]	60.00 [55.00, 63.00]	0.293
Pericardial effusion (%)	23 (10.2)	33 (6.0)	14 (8.0)	6 (6.2)	0.201	61.7 (8.7)	57.5 (6.2)	50.3 (7.7)	39.7 (7.0)	0.827
RHC confirmed PH (%)	9 (4.0)	34 (6.1)	22 (12.6)	2 (2.1)	0.001	38.3 (5.4)	54.7 (5.9)	43.7 (6.7)	25.5 (4.5)	0.855
FVC% predicted (median [IQR])	76.00 [63.00, 89.00]	80.00 [66.00, 94.75]	77.00 [62.00, 90.00]	84.00 [67.00, 94.00]	0.038	78.63 (19.25)	79.78 (20.39)	79.35 (20.50)	78.80 (18.12)	0.901
DLCO% predicted (median [IQR])	49.00 [35.00, 59.00]	51.50 [37.25, 65.00]	52.00 [40.00, 67.00]	54.50 [41.00, 68.25]	0.016	50.00 [36.10, 63.00]	52.00 [38.00, 65.00]	53.00 [38.00, 65.00]	51.00 [38.00, 65.88]	0.763
Esophageal symptoms (%)	138 (61.3)	353 (63.7)	113 (64.6)	65 (67.7)	0.736	432.7 (60.7)	592.9 (63.7)	390.0 (60.0)	406.4 (71.2)	0.307
HRCT pattern										
GGO (%)	139 (61.8)	322 (58.1)	117 (66.9)	47 (49.0)	0.026	438.8 (61.5)	542.9 (58.3)	390.7 (60.1)	287.7 (50.4)	0.371
Honey combing (%)	137 (60.9)	299 (54.0)	69 (39.4)	56 (58.3)	<0.001	453.6 (63.6)	495.6 (53.2)	255.1 (39.2)	319.2 (55.9)	0.004
Reticular change (%)	163 (72.4)	379 (68.4)	111 (63.4)	86 (89.6)	<0.001	502.6 (70.5)	644.4 (69.2)	461.4 (70.9)	459.9 (80.6)	0.287
Previous medications										
Previous IS (%)	59 (26.2)	226 (40.8)	131 (74.9)	57 (59.4)	<0.001	266.4 (37.4)	392.6 (42.2)	360.6 (55.5)	263.5 (46.2)	0.052
CYC (%)	0 (0.0)	147 (26.5)	63 (36.0)	14 (14.6)		0.0 (0.0)	256.9 (27.6)	167.8 (25.8)	82.1 (14.4)	
MMF (%)	14 (6.2)	0 (0.0)	57 (32.6)	19 (19.8)		69.3 (9.7)	0.0 (0.0)	162.0 (24.9)	87.8 (15.4)	
RTX (%)	0 (0.0)	7 (1.3)	0 (0.0)	7 (7.3)		0.0 (0.0)	11.4 (1.2)	0.0 (0.0)	41.8 (7.3)	
TCZ (%)	0 (0.0)	3 (0.5)	7 (4.0)	0 (0.0)		0.0 (0.0)	5.7 (0.6)	17.0 (2.6)	0.0 (0.0)	
AZA (%)	24 (10.7)	67 (12.1)	17 (9.7)	5 (5.2)		117.2 (16.4)	106.4 (11.4)	50.1 (7.7)	15.9 (2.8)	
LEF (%)	1 (0.4)	0 (0.0)	7 (4.0)	6 (6.2)		6.0 (0.8)	0.0 (0.0)	19.7 (3.0)	19.6 (3.4)	
MTX (%)	29 (12.9)	67 (12.1)	55 (31.4)	33 (34.4)		111.6 (15.6)	124.7 (13.4)	130.1 (20.0)	144.8 (25.4)	
No. of previous IS (median [IQR])	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	1.00 [0.50, 2.00]	1.00 [0.00, 1.00]	<0.001	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	1.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.005
Background medications										
Antifibrotic (%)	20 (8.9)	37 (6.7)	23 (13.1)	13 (13.5)	0.02	59.9 (8.4)	70.7 (7.6)	63.7 (9.8)	74.3 (13.0)	0.439
Background IS (%)	8 (3.6)	15 (2.7)	35 (20.0)	25 (26.0)	<0.001	26.5 (3.7)	45.7 (4.9)	68.7 (10.6)	61.3 (10.7)	0.006
CYC (%)	0 (0.0)	0 (0.0)	2 (1.1)	1 (1.0)		0.0 (0.0)	0.0 (0.0)	2.9 (0.4)	1.5 (0.3)	
MMF (%)	0 (0.0)	0 (0.0)	8 (4.6)	0 (0.0)		0.0 (0.0)	0.0 (0.0)	21.6 (3.3)	0.0 (0.0)	
RTX (%)	0 (0.0)	5 (0.9)	0 (0.0)	0 (0.0)		0.0 (0.0)	16.8 (1.8)	0.0 (0.0)	0.0 (0.0)	
TCZ (%)	0 (0.0)	5 (0.9)	0 (0.0)	0 (0.0)		0.0 (0.0)	16.8 (1.8)	0.0 (0.0)	0.0 (0.0)	
AZA (%)	4 (1.8)	5 (0.9)	8 (4.6)	4 (4.2)		11.9 (1.7)	13.1 (1.4)	11.9 (1.8)	8.2 (1.4)	
MTX (%)	4 (1.8)	5 (0.9)	18 (10.3)	15 (15.6)		14.6 (2.0)	15.8 (1.7)	33.7 (5.2)	37.6 (6.6)	
Any steroids (%)	159 (70.7)	361 (65.2)	134 (76.6)	54 (56.2)	0.002	472.2 (66.2)	608.1 (65.3)	436.0 (67.0)	305.4 (53.5)	0.18
Pred>10mg (%)	9 (4.0)	15 (2.7)	6 (3.4)	1 (1.0)	0.505	27.2 (3.8)	27.1 (2.9)	18.2 (2.8)	1.5 (0.3)	0.107
Follow-up parameters										
Follow-up duration (month) (median [IQR])	11.00 [8.00, 13.00]	12.00 [9.00, 15.00]	11.00 [7.00, 13.00]	11.00 [9.00, 13.00]	0.002	11.00 [9.00, 13.00]	11.00 [8.00, 14.00]	11.00 [8.00, 13.00]	11.00 [9.00, 13.00]	0.486
Treatment duration <18m	156 (69.3)	270 (48.7)	128 (73.1)	60 (62.5)	<0.001	448.5 (62.9)	515.7 (55.4)	448.8 (69.0)	327.5 (57.4)	0.145
Outcomes										
ΔFVC predicted (median [IQR])	1.00 [-3.00, 6.00]	0.00 [-5.00, 6.00]	0.00 [-5.00, 6.00]	-0.50 [-7.00, 4.00]	0.011	1.00 [-2.12, 7.35]	0.00 [-5.00, 6.00]	0.00 [-4.00, 5.00]	0.00 [-6.19, 4.00]	0.058
Δmrss (median [IQR])	0.00 [-4.00, 2.00]	0.00 [-4.00, 1.00]	0.00 [-5.00, 1.00]	-1.00 [-7.00, 0.00]	0.028	0.00 [-4.00, 2.00]	-1.00 [-4.00, 1.00]	0.00 [-4.00, 1.00]	-1.00 [-6.32, 0.00]	0.142
ΔDLCO% predicted (median [IQR])	2.00 [-4.00, 13.00]	1.00 [-4.00, 11.00]	0.00 [-6.50, 7.50]	3.50 [-5.00, 10.25]	0.074	2.00 [-3.53, 15.66]	1.00 [-4.00, 10.00]	1.00 [-5.00, 8.34]	4.00 [-8.80, 10.00]	0.769

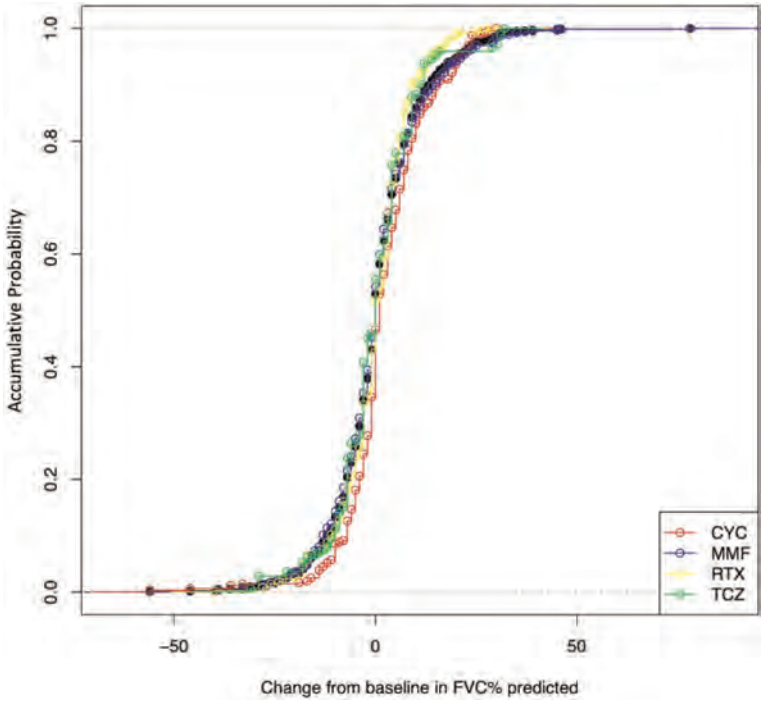

Figure 1. Post IPTW accumulative probability of the change of FVC% predicted with the treatment of cyclophosphamide (CYC), mycophenolate mofetil (MMF), rituximab (RTX), and tocilizumab (TCZ).

Table 2. Paired comparisons between the effectiveness of cyclophosphamide (CYC), mycophenolate mofetil (MMF), rituximab (RTX), and tocilizumab (TCZ) in ΔFVC% predicted from the baseline to the one-year follow-up. Average treatment effects were used for paired comparisons after IPTW.

	mean difference	std. error	P-value
MMF vs. CYC	-1.6600426	0.9132509	0.0694
CYC vs.RTX	2.314001414	1.0816927	0.0326
TCZ vs. CYC	-2.3196089	1.5316029	0.1302
MMF vs.RTX	0.653958802	0.9259617	0.4802
TCZ vs. MMF	1.660042613	1.81772896	0.0694
TCZ vs. RTX	-0.005607455	1.5392158	0.9971

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Fecal Microbiota Transplantation in Patients with Systemic Sclerosis and Lower Gastrointestinal Tract Symptoms: Data from the ReSScue Phase 2 Randomized Clinical Trial

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SESSION INFORMATION

Session Date: Wednesday, November 15, 2023

Session Title: Abstracts: Systemic Sclerosis & Related Disorders III: Clinical Trials

Session Type: Abstract Session

Session Time: 11:00AM–12:30PM

Background/Purpose: Lower gastrointestinal tract (GIT) complications are common in patients with systemic sclerosis (SSc), associate with a high disease burden, and current treatment alternatives are limited. Patients with SSc have also an altered intestinal microbiota composition. This provides a rational for the investigation of fecal microbiota transplantation (FMT) in SSc patients with lower GIT symptoms. In this randomized mutlicenter double-blind clinical trial (RCT) we assessed the safety and efficacy of a standardized intestinal microbiota infusion in SSc patients with lower GIT symptoms.

Methods: Patients with SSc and moderate to severe bloating and/or diarrhea assessed by the UCLA SCTC GIT score 2.0 were enrolled in a multicenter, double-blind, randomized, placebo-controlled phase 2 trial. Patients were randomized to receive FMT with an intestinal infusion of a standardized fecal microbiota culture (ACHIM) or placebo at weeks 0 and 2. At week 12, all patients received a FMT infusion and were followed in an open lable phase until week 20. The primary outcome was change between baseline and week 12 in UCLA GIT score item diarrhea or bloating measured as the average marginal effect (AME), depending on which was the worst symptom at baseline; evaluated separately for each patient. Comprehensive predefined subgroup analyses were conducted. Secondary outcomes were safety and tolerability and total UCLA GIT score. Other outcome measures included the change in UCLA GIT score from week 12 to week 20.

Results: A total of 65 patients were randomized to receive FMT or placebo. Baseline characteristics in the groups were comparable (Table). There was no significant difference in the change in lower GIT symptoms from week 0 to week 12 between the groups (AME=0.17 (-0.12, 0.47), p=0.25) and no significant differences in any of the predefined subgroup analyses (Figure 1A-C and 2). Similarly, no significant difference was observed in the total GIT score between the two groups (AME=0.09 (-0.04, 0.23), p=0.17). Furthermore, during the open lable period, there was no statistical difference in change

Table: Baseline characteristics of patients included in the randomized double-blimd placebo controlled ReSScue trial

Parameter	FMT with ACHIM (N=33)	Placebo (N=34)
Age, y (SD)	58 (11.5)	60 (11.7)
Female, n (%)	33 (100)	29 (85)
Worst symptom Bloating, n (%)	22 (67)	22 (65)
Disease duration, y (SD)	9 (7)	10 (8)
Limited cutaneous SSc, n (%)	31 (94)	28 (85)
FVC% (SD)	95 (13.7)	90 (19.2)
Immunosuppressives, n (%)	3 (9)	5 (15)
Proton pump inhibitors n (%)	27 (82)	21 (62)
Calcium channel blocker, n (%)	18 (58)	20 (59)
Total UCLA GIT score	0.9 (0.5)	0.7 (0.3)
UCLA GIT scale Diarrhea	0.8 (0.7)	0.5 (0.5)
UCLA GIT scale Bloating	1.8 (0.8)	1.7 (0.7)

between the ACHIM and the placebo group (AME= -0.04 (-0.32, 0.23), p=0.077) shown in Figure 1D. Participants treated with ACHIM, 16 (37%) and with placebo 19 (42%) experienced any side effects. These were in general mild and short-lasting, with abdominal pain as the most frequent side effect present in 5 (15%) in ACHIM and 2 (6%) in placebo. Time to resolved pain was 2days in both groups. One patient experienced an intramural perforation during gastroscopy and needed IV antibiotics but fully recovered.

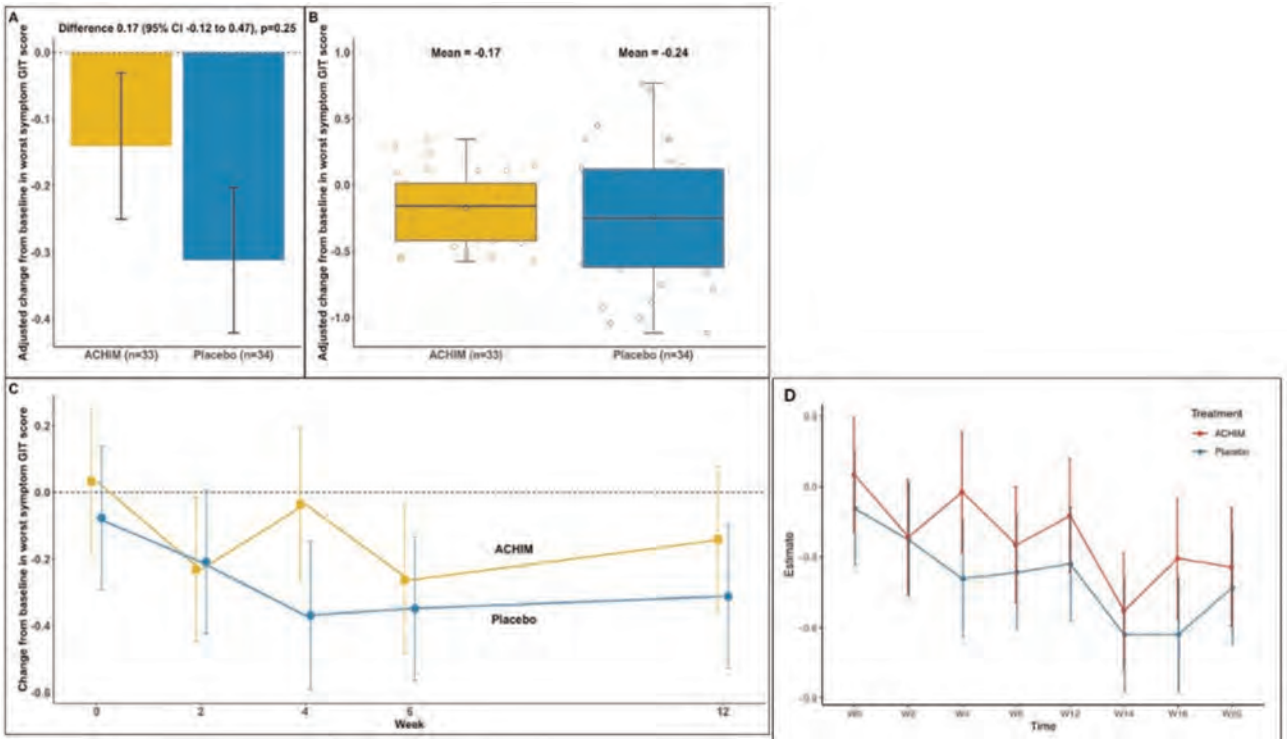

Figure 1: Change in worst symptom GIT score between baseline and week 12. Panel A shows the marginal means of the adjusted changes in the worst symptom GIT score over 12 weeks together with their standard errors for ACHIM and placebo groups as well as the adjusted between-group difference estimated from the primary model. Panel B shows the box-plots of the predicted (adjusted) individual changes in worst symptom GIT score over 12 weeks for both treatment groups given by the primary model. Panel C shows the mean change from baseline to 12 weeks in the worst symptom GIT score. The bars indicate 95% confidence intervals. Panel D shows the mean change from baseline to 20 weeks in the worst symptom GIT score. The bars indicate 95% confidence intervals

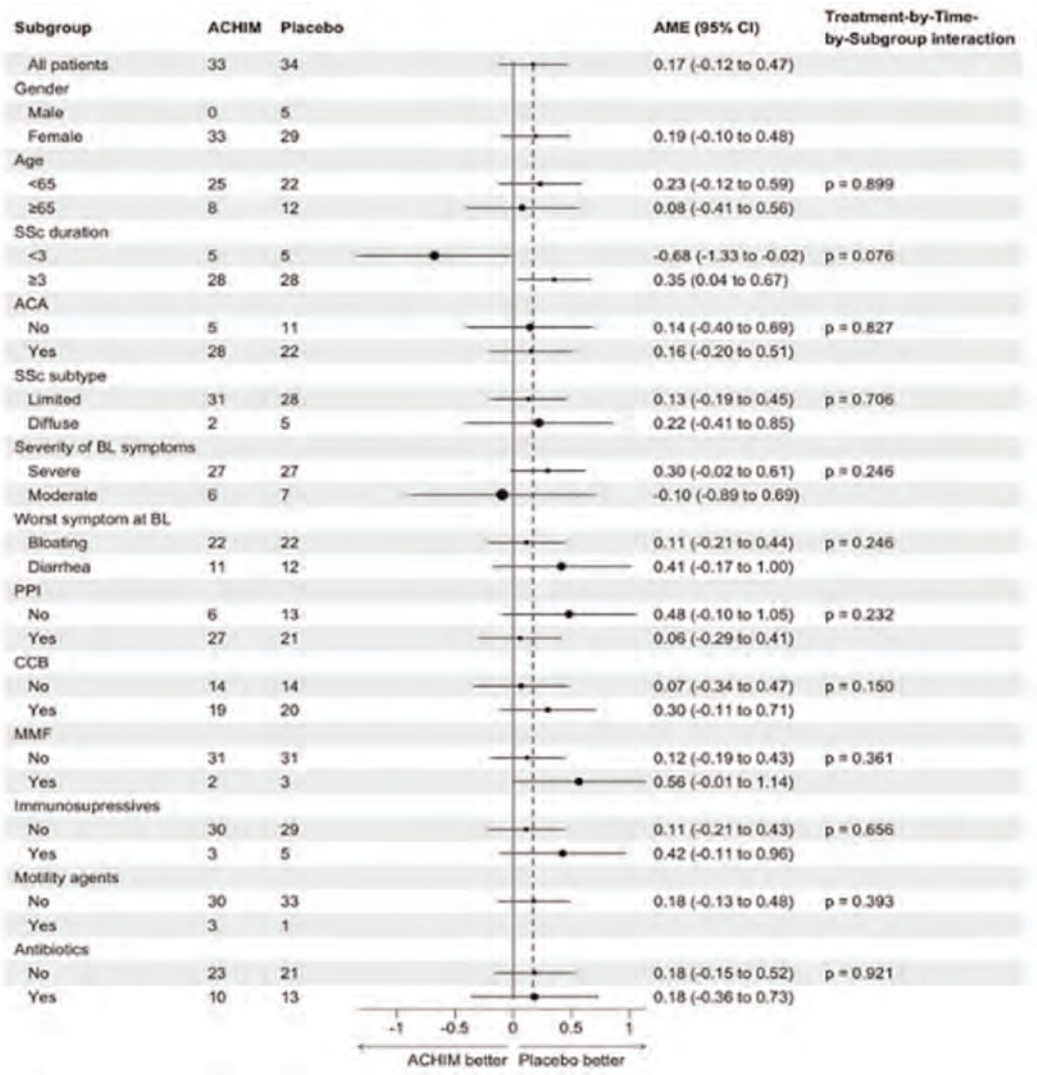

Figure 2: Pre-specified subgroup analyses of the change in the worst symptom GIT score from baseline to week 12 (primary endpoint) based on baseline characteristics and concomitant medication.

Conclusion: We were unable to find indications that FMT improves lower GIT symptoms in SSc patients, but the treatment was found to be safe.

Disclosure: A. Hoffmann-Vold: Arxx Therapeutics, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Support for travel, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, 12, Support for travel, Roche, 2, 6, 12, Support for travel; **H. Fretheim**: actelion, 5, bayer, 2, Boehringer-Ingelheim, 6, GlaxoSmithKlein(GSK), 5; **I. Barua**: None; **M. Nordgård Carstens**: None; **H. Didriksen**: None; **V. Sarna**: None; **K. Lundin**: Falk Pharma, 2, GSK, 2, Takeda, 2, 6, Topas, 2; **O. Distler**: 4P-Pharma, 2, 5, 6, AbbVie, 2, 5, 6, Acceleron, 2, 5, 6, Alcimed, 2, 5, 6, Altavant Sciences, 2, 5, 6, Amgen, 2, 5, 6, AnaMar, 2, 5, 6, Arxx, 2, 5, 6, AstraZeneca, 2, 5, 6, Bayer, 2, 5, 6, Blade Therapeutics, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Citus AG, 12, Co-Founder, Corbus Pharmaceuticals, 2, 5, 6, CSL Behring, 2, 5, 6, Galapagos, 2, 5, 6, Galderma, 2, 5, 6, Glenmark, 2, 5, 6, Gossamer, 2, 5, 6, Horizon Therapeutics, 2, 5, 6, Janssen, 2, 5, 6, Kymera, 2, 5, 6, Lupin, 2, 5, 6, Medscape, 2, 5, 6, Miltenyi Biotec, 2, 5, 6, Mitsubishi Tanabe, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Patent issued ‘‘mir-29 for the treatment of systemic sclerosis’’ (US8247389, EP2331143), 10, Prometheus Biosciences, 2, 5, 6, Redx Pharma, 2, 5, 6, Roivant, 2, 5, 6, Topadur, 2, 5, 6; **D. Khanna**: AbbVie, 12, DSMB, AstraZeneca, 2, Boehringer-Ingelheim,

2, Bristol-Myers Squibb, 2, 5, CSL Behring, 2, Genentech, 2, Horizon Therapeutics, 2, 5, Janssen, 2, 6, Pfizer, 5, Prometheus, 2; **E. Volkmann**: Boehringer-Ingelheim, 2, 5, 6, CSL Behring, 2, GlaxoSmithKline, 2, Horizon, 5, Prometheus, 5, Roche, 2; **O. Midtvedt**: None; **T. Midtvedt**: ACHIM, 8, 10, 11; **A. Dhainaut**: None; **A. Halse**: None; **G. Bakland**: UCB, 2; **I. Olsen**: None; **M. Pesonen**: None; **O. Molberg**: None.

Abstract Number: 2598

6 Months-follow up Data of Systemic Sclerosis Patients Treated with CD 19 Targeting CAR-T Cells

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SESSION INFORMATION

Session Date: Wednesday, November 15, 2023

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Background/Purpose: CD19-targeting CAR-T-cells showed remarkable improvements in autoimmune diseases including refractory lupus erythematodes (1,2) and inflammatory myopathy (3). Moreover, first data of a patient with diffuse Systemic Sclerosis (SSc) were recently reported (4). Here we present 6 months follow up data of the first three patients with severe diffuse SSc who received CAR-T-cell treatment.

Methods: T-cells were acquired by peripheral blood apheresis and transfected with a lentiviral vector encoding a CAR against CD19 (Miltenyi Biotec) using the CliniMacs Prodigy system (Miltenyi Biotec). Infusion of CAR-T-cells was performed upon lymphodepletion with fludarabine (25 mg/m^2 on days -5, -4, -3) and cyclophosphamide (1g/m2 on day -3, 50% dose reduction in patient 3 due to renal insufficiency) as single infusion. Immunosuppression was stopped before CAR-T-cell infusion. Outcomes were assessed before baseline and 6 months after CAR-T-cell infusion.

Results: Three SSc patients were treated with CAR-T-cells with a follow up of 6 months: patient 1 (male, baseline data: 60 yrs, disease duration 2 years (first non-Raynaud symptom), mRSS 24, myocardial- and lung fibrosis, anti RNAP3-antibodies), patient 2: male, 37 yrs, mRSS 27, disease duration 1.5 yrs, lung- and myocardial fibrosis, digital ulcerations (DU), anti-Scl70 antibodies) and patient 3 (female,38 yrs, disease duration 1.5 yrs, mRSS 32, scleroderma renal crisis, DU, anti-Scl70 antibodies). All patients had failed state of the art SSc treatments. The CAR-T-cell procedure was well tolerated: Patient 1 developed mild CRS (grade I; fever) and an episode of respiratory tract infection three months after CAR-T infusion, treated outpatient with antibiotics. B-cells were completely absent in peripheral blood within 7 days after CAR-T

cells administration in all patients. ANA titres were reduced by 10-fold in patients 2 and 3, patient 1 converted to negative ANA status within 3 months and anti-RNAP III antibodies turned negative. mRSS improved in all three patients until six-months follow up (median 6 points (5-7)). 2 patients suffered from multiple digital ulcerations despite bosentan- treatment before CAR-T cells, which were no longer detectable on follow up. All patients reported improvement of hand function (median reduction of Cochin Hand function scale of 8 points (8-20). Improvement of HAQ-DI ranged from 0.5 to 1.38 points and of EUSTAR activity from 3.62 to 4.37 points. Lung function parameters remained stable in patients 1 and 3 and improved in patient 2 (FVC increase by 390 ml (8%)). Myocardial ^{68}Ga-FAPI-04-uptake declined in patients 1 and 2 by 30% and 35% respectively. B-cells recurred after 84 days in patient 1 and 2 without signs of disease activity.

Conclusion: These data on the first three SSc patients receiving CD19 CAR-T cell treatment show that the procedure is well tolerated and can lead to stabilization of SSc disease activity without additional immunosuppression on 6 months follow up.

Disclosure: C. Bergmann: Boehringer-Ingelheim, 2, 5, Janssen, 2; **F. Müller**: AbbVie, 6, AstraZeneca, 1, 5, 6, Bristol Myers Squibb, 1, 6, Janssen, 6, KITE, 1, 6, Miltenyi Biomedicine, 1, 6, Novartis, 1, 6, Sobi, 6; **J. Auth**: None; **J. Taubmann**: None; **M. Aigner**: Kosmas Therapuetics, 8, Kyverna, 5, Miltenyi Biomedicine, 2, 7, Miltenyi Biotec, 6; **D. Werner**: None; **A. Wirsching**: None; **J. Knitza**: None; **H. Györfi**: Boehringer-Ingelheim, 6; **J. Distler**: None; **A. Mackensen**: BioNTech, 1, Bristol-Myers Squibb(BMS), 1, KITE/Gilead, 1, 6, Kyverna, 5, Miltenyi Biotech, 5; **G. Schett**: None.

Abstract Number: 2599

Study of the Role of interleukin-17 in Giant Cell Arteritis

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SESSION INFORMATION
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Session Time: 11:00AM–12:30PM

Background/Purpose: Giant cell arteritis (GCA) is a vasculitis in which Th17 cells have been identified in excess in lesions and in the blood of patients. While the efficacy of secukinumab has recently been reported in a phase II study, the role of interleukin-17 (IL-17) in the pathophysiology of GCA is not clearly understood. The aim of this study was to investigate the role of IL-17 in the pathogenesis of GCA.

Methods: Vascular myofibroblasts (MFs) were obtained from cultures of healthy arteries in MATRIGEL as previously described. After 3-6 doubling passages, MFs were treated with IL-17 (50 ng/mL), interferon-gamma (IFN-γ, 50 ng/mL), secukinumab (20 μg/mL) or the association of IL-17 and IFN- γ or IL-17 and secukinumab for 24 hours. mRNA expression was analyzed by RNA sequencing and RT-PCR. Proliferation was analyzed by impedancemetry and migration was assessed by scratch-wound healing assays. Fresh fragments of temporal artery biopsies (TAB) were prospectively

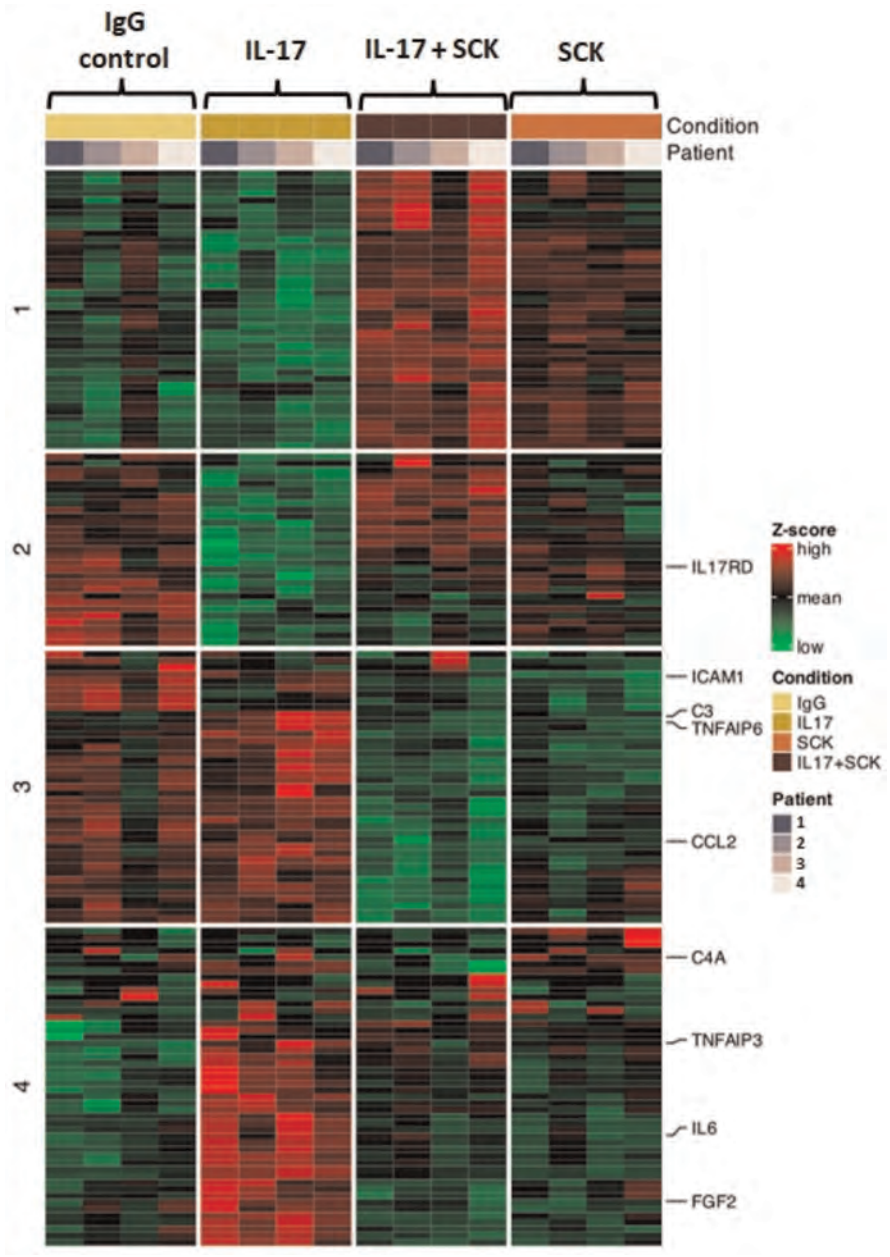

Figure 1: transcriptomic analysis (RNA sequencing) of MF cultivated during 24 hours with IL-17, secukinumab (SCK), IL-17 and SCK or IgG control.

collected, cut in 1-mm sections and cultured for 5 days in MATRIGEL®, as previously described, in the presence of IL-17, secukinumab or IgG control. Then, arterial sections were collected, homogenized and analyzed by RT-PCR.

Results: The transcriptome of MFs was dramatically modified when IL-17 was added to the culture, with increased expression of genes involved in vascular inflammation (*CCL2*, *IL6*), NFkB pathway activation (*TNFAIP6*, *TNFAIP3*), leukocyte adhesion (*ICAM1*), complement activation (*C3*, *C4A*) and MF proliferation (*FGF2*) (Figure 1). These changes were reversed in the presence of secukinumab (**Figure 1**).

RT-PCR analysis of 8 MF lines showed that in the presence of IL-17, the mRNA expression of the genes encoding for IL1-β, IL-6, IL-12p35, VEGF-A, GM-CSF, CCL2 and CCL20 was increased ($P < 0.01$). There was no significant effect on the mRNA expression of IL-23p19, IL-12p40, collagen alpha chains 1 and 3, PDGFA, PDGFB, CXCL9 or CXCL10. The addition

of IFN-γ to the culture increased the expression level of chains of the IL-17 receptor (*IL17RA* and *IL17RC*), creating a synergistic effect in the presence of IFN-γ and IL-17, thus resulting in a sharp rise in the expression of genes encoding for IL-1β, IL-6, IL-12p35, GM-CSF, VEGF-A, CCL2 and CCL20.

The study of MF migration and proliferation revealed that IL-17 had no direct effect on these MF functions.

Ex-vivo cultures of TAB revealed that treatment with IL-17 increased the expression of mRNA encoding for IL-6, VEGF-A, GM-CSF, CCL2 and CCL20 in negative TAB (n=8; $P< 0.05$) whereas treatment with secukinumab decreased the expression of mRNA encoding for IL-6 and CCL20 in positive TAB (n=12; $P < 0.05$).

Conclusion: IL-17 increases vascular inflammation and has a direct effect on MF synergistically with IFN-γ, which increases the production of pro-inflammatory cytokines (IL-1B, IL-6, GM-CSF), chemokines leading to the recruitment of T cells (CCL20) and monocytes (CCL2), and growth factors involved in neoangiogenesis (VEGF). In contrast, IL-17 does not appear to have a direct effect on MF proliferation and migration. These data explain why blocking the IL-17 signaling pathway could be useful in the treatment of GCA.

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Abstract Number: 2600

Clonal Hematopoiesis Is Associated with Giant Cell Arteritis

SESSION INFORMATION

Session Date: **Wednesday, November 15, 2023**
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Background/Purpose: Giant cell arteritis (GCA) is an age-related vasculitis of large and medium vessels. Prior population studies have identified an association between GCA and hematologic malignancy (HM). Clonal hematopoiesis describes the age-related expansion of blood cells carrying somatic mutations that drive development of HM, most frequently in the epigenetic modifiers *DNMT3A, TET2*, and *ASXL1*. When the variant allele fraction (VAF) is ≥ 0.02, the terms clonal hematopoiesis of indeterminant potential (CHIP) and clonal cytopenia of uncertain significance (CCUS) are used to refer to patients without and with unexplained cytopenia, respectively. Individuals with CHIP/CCUS, especially mutated in *TET2*, develop many other age-related inflammatory-spectrum disorders including ischemic cardiovascular disease, non-alcoholic fatty liver disease, and gout. How the presence of CHIP, CCUS, or specific somatic mutation genotypes may influence the developmental and/or clinical outcomes in GCA is not well understood.

Methods: We analyzed sequenced exomes of 470960 UK Biobank participants for the presence of CH and used multivariable Cox regression to associate the presence of CHIP, CCUS, and the top three mutated genes with incident GCA. We then performed CH-panel targeted sequencing of DNA from blood samples from 114 patients with GCA recruited from a large academic health system who had a positive temporal artery biopsy, positive imaging, or met 1990 ACR classification criteria for clinical diagnosis GCA, of which 99% met 2022 ACR/EULAR classification criteria post-hoc. Abstraction of clinical data from the electronic medical record was performed to test association of *TET2* with development of GCA-associated vision loss and to determine HM outcomes.

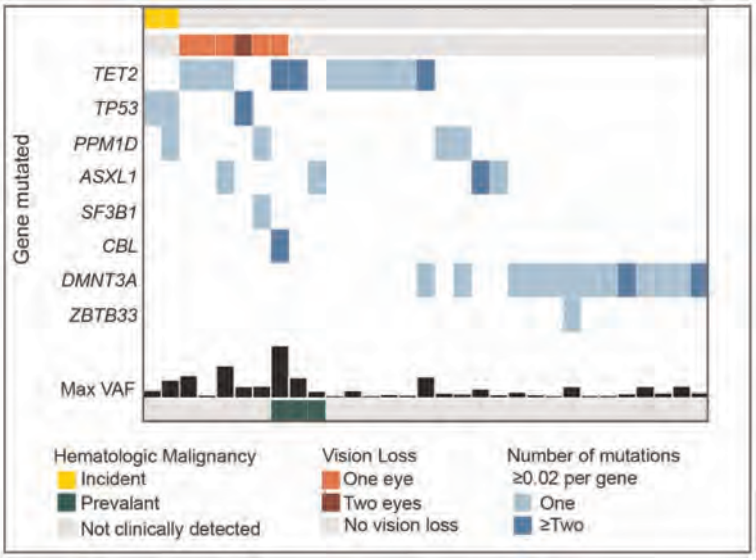

Figure 1: Co-mutation plot of adverse outcomes of hematologic malignancy and vision loss in individuals with GCA and CH. Each column represents one individual. Rows show mutated genes, color coded by number of mutations, and the maximum variant allele frequency (VAF) of largest mutation.

Results: We identified 779 UKB participants with incident GCA, of which 11.8% had CHIP/CCUS. CHIP/CCUS had a 1.48-fold increase in risk of incident GCA compared to UKB participants without CH. GCA risk was highest among individuals with CCUS (HR 2.98, p =0.0018) and with *TET2*-mutated CHIP/CCUS (HR 2.02, p =0.0012). Within the institutional GCA cohort, somatic mutations were detected in 27.2%, most commonly in *DNMT3A* (41.9%) and *TET2* 35.5%). *TET2*-mutated GCA was associated with vision loss (n = 4, OR 4.33, p = 0.047) (Figure 1). Overall, adverse outcomes (vision loss or incident HM) were associated with clones with larger VAF (median VAF 0.161 vs 0.049, p = 0.004). Cytopenia was common before and after GCA diagnosis, but few individuals underwent diagnostic evaluation for HM (7.2%) with abnormalities detected in most cases (87.5%). Compared to diagnosis of GCA, we observed prevalent HM in individuals with *TET2* (n =2) and *ASXL1* mutations (n=1) and incident HM only among individuals with *TP53*-mutant CH (n=2) (Figure 1).

Conclusion: CH increases risk for development of GCA in a genotype-specific fashion, with greatest risk being conferred by the presence of mutations in *TET2*. *TET2* mutations likewise increase the risk of GCA-associated vision loss. Features associated in large population studies with increased risk of HM, namely CCUS and larger clone size, were also associated with increased development of GCA and adverse outcomes, respectively.

Abstract Number: 2601

Identification of Giant Cell Arteritis Using Plasma Proteome Profiles Integrated with Machine Learning

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SESSION INFORMATION

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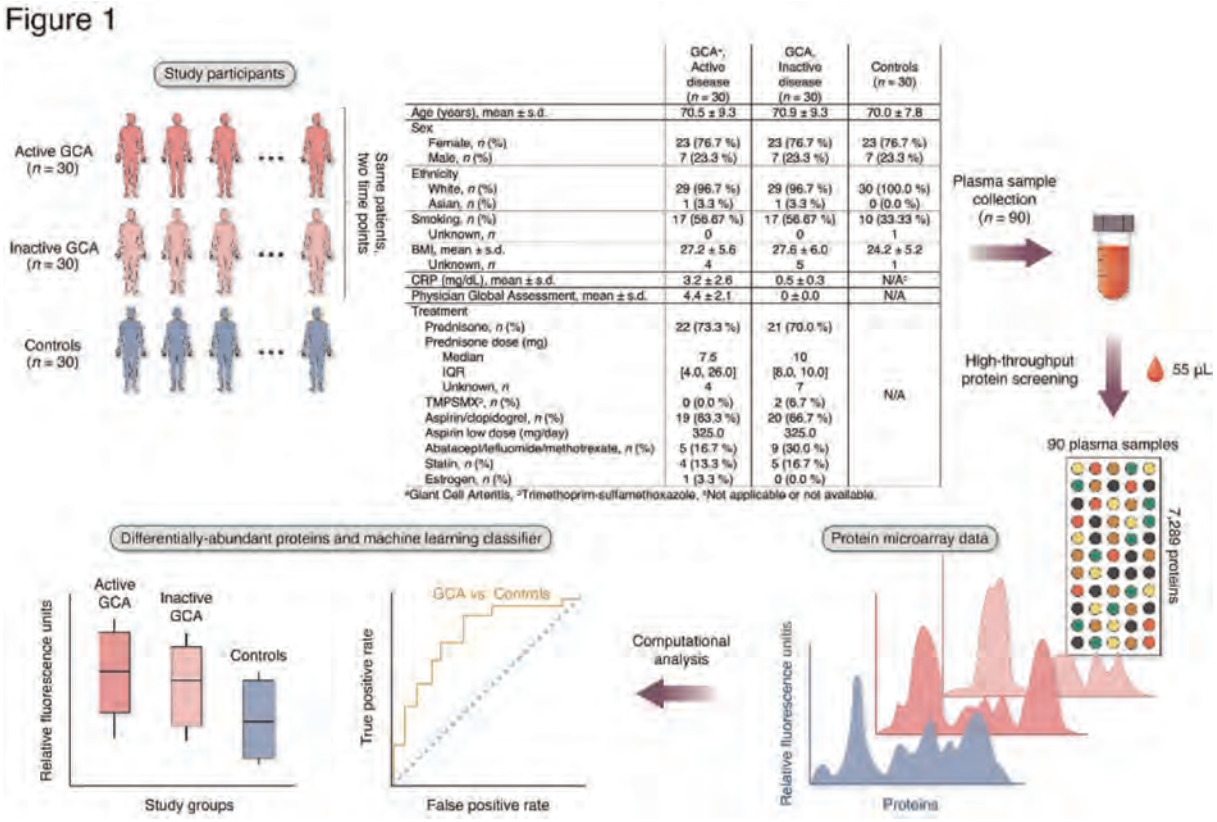
Background/Purpose: The availability of diagnostic laboratory tests and specific biomarkers of disease activity for giant cell arteritis (GCA) remains an area of unmet need. The purpose of this study was to utilize a high-throughput screening array to identify plasma proteins that 1) differentiate patients with GCA from controls; and 2) associate with disease activity in GCA.

Methods: This study included patients with GCA (n = 30) from a multi-institutional prospective longitudinal cohort study and 30 age-/sex-/race-matched healthy controls (**Figure 1**). Most patients with GCA were taking glucocorticoids at the time of sample collection (**Figure 1**). Plasma samples were collected from patients with GCA at two separate visits: 1) during active disease; and 2) during inactive disease. An aptamer-based, multiplex microarray platform (SomaScan® Assay, SomaLogic) measured semi-quantitative abundances of 7,289 proteins in relative fluorescence units (RFUs). Linear regression models identified differentially-abundant proteins between patients with GCA (at active or inactive disease state) compared with controls while adjusting for potential confounders ($P < 0.01$). Gene Ontology (GO) Biological Processes identified enriched functional categories of the differentially-abundant proteins. Proteins associated with disease activity (Physician Global Assessment, PGA) in patients with active GCA were also identified. A random forest model was trained on plasma proteomes to develop a classifier that distinguishes GCA (active or inactive state) from controls.

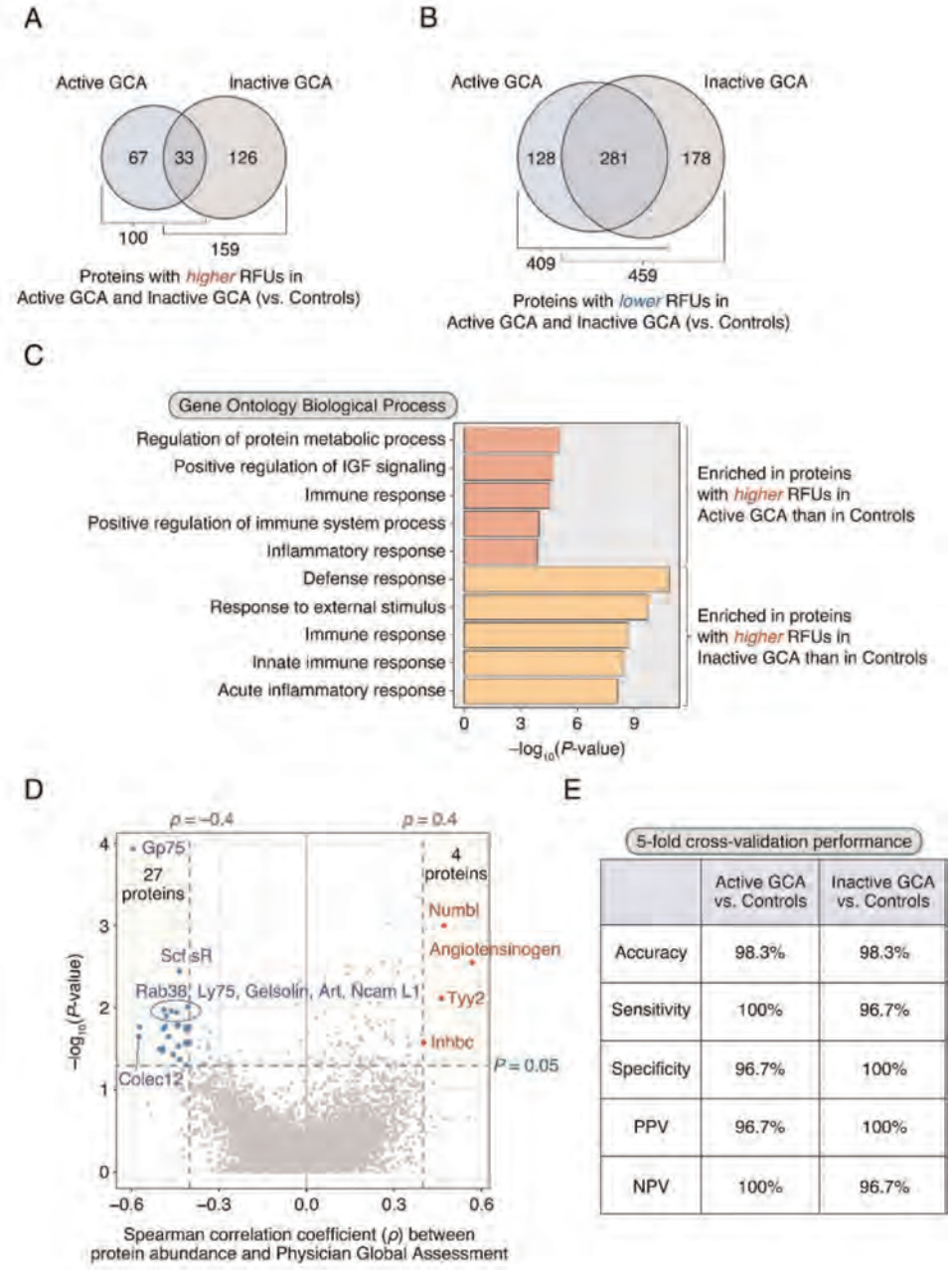


	GCA*, Active disease (n = 30)	GCA, Inactive disease (n = 30)	Controls (n = 30)
Age (years), mean ± s.d.	70.5 ± 9.3	70.9 ± 9.3	70.0 ± 7.8
Sex			
Female, n (%)	23 (76.7 %)	23 (76.7 %)	23 (76.7 %)
Male, n (%)	7 (23.3 %)	7 (23.3 %)	7 (23.3 %)
Ethnicity			
White, n (%)	29 (96.7 %)	29 (96.7 %)	30 (100.0 %)
Asian, n (%)	1 (3.3 %)	1 (3.3 %)	0 (0.0 %)
Smoking, n (%)	17 (56.67 %)	17 (56.67 %)	10 (33.33 %)
Unknown, n	0	0	1
BMI, mean ± s.d.	27.2 ± 5.6	27.6 ± 6.0	24.2 ± 5.2
Unknown, n	4	5	1
CRP (mg/dL), mean ± s.d.	3.2 ± 2.6	0.5 ± 0.3	N/A[2]
Physician Global Assessment, mean ± s.d.	4.4 ± 2.1	0 ± 0.0	N/A
Treatment			
Prednisone, n (%)	22 (73.3 %)	21 (70.0 %)	
Prednisone dose (mg)			
Median	7.5	10	
IQR	[4.0, 26.0]	[5.0, 10.0]	
Unknown, n	4	7	N/A
TMPSMX[2], n (%)	0 (0.0 %)	2 (6.7 %)	
Aspirin/clopidogrel, n (%)	19 (63.3 %)	20 (66.7 %)	
Aspirin low dose (mg/day)	325.0	325.0	
Abatacept/leflunomide/methotrexate, n (%)	5 (16.7 %)	9 (30.0 %)	
Statin, n (%)	4 (13.3 %)	5 (16.7 %)	
Estrogen, n (%)	1 (3.3 %)	0 (0.0 %)	

[1]Giant Cell Arteritis, [2]Trimethoprim-sulfamethoxazole, [3]Not applicable or not available.

Figure 1. Study design overview. Plasma samples were collected from 30 patients with GCA and 30 healthy controls. For each patient with GCA, one sample was collected at a time of active disease (physician global assessment [PGA] > 0) and another at a time of inactive disease (PGA = 0). Proteome profiling was performed on all samples using an aptamer-based, multiplex microarray platform. Proteins were compared between patients with GCA and controls to identify differentially-abundant proteins and enriched biological functions. The confounding factors adjusted for during linear regression modeling were age, sex, smoking status, and use of prednisone, aspirin, and methotrexate. A machine learning technique (random forests) was trained on the plasma proteome profiles to build a classifier that distinguishes between GCA and controls.

Figure 2



	Active GCA vs. Controls	Inactive GCA vs. Controls
Accuracy	98.3%	98.3%
Sensitivity	100%	96.7%
Specificity	96.7%	100%
PPV	96.7%	100%
NPV	100%	96.7%

Figure 2. Differences in plasma proteins between patients with GCA and healthy controls form the basis of a novel machine learning approach for identifying GCA. Plasma proteins found to have significantly higher (A) or lower (B) relative fluorescence unit (RFU) abundances in active GCA and inactive GCA compared with controls (P-value of the corresponding regression coefficient < 0.01). The intersection of the Venn diagram indicates proteins having higher (or lower) RFUs in both disease states. (C) Top 5 enriched (i.e., statistically over-represented) GO Biological Processes from proteins higher in active GCA and inactive GCA compared with controls. Enriched GO terms are rank-ordered in descending order based on modified one-tailed Fisher's exact test P-values. (D) A total of 31 proteins were significantly associated with physician's global assessment (PGA) in active GCA (P-value < 0.05 and |Spearman's rho| > 0.4): 4 and 27 proteins had positive and negative correlations with PGA, respectively. (E) Random forest classifiers could differentiate patients with GCA from controls with high accuracy (> 98%) in 5-fold cross-validation.

Results: 509 and 618 differentially-abundant proteins were identified between active GCA compared with healthy controls (**Figure 2A**) and inactive GCA compared with controls (**Figure 2B**), respectively. Among these, 100 and 159 proteins had significantly higher abundances in active GCA and inactive GCA, respectively. The observed enriched biological processes are shown in **Figure 2C**: 'Regulation of protein metabolic process' and immune-related processes were the most highly

enriched functions of plasma proteins found higher in active GCA. Interestingly, processes involving apoptosis, nucleotide metabolism, and EGFR, ErbB, and neurotrophin signaling were also significantly enriched. A paired analysis between active and inactive visits found 219 differentially abundant proteins. In addition, 31 proteins were found to be associated with disease activity (PGA) in patients with active GCA (**Figure 2D**). A random forest classifier correctly predicted active GCA vs. controls with an accuracy of 98.3% (sensitivity: 100%; specificity: 96.7%) in 5-fold cross-validation (**Figure 2E**). Similarly, in the case of inactive GCA vs. controls, a random forest classifier distinguished these two phenotypes at 98.3% accuracy (sensitivity: 96.7%; specificity: 100%).

Conclusion: Plasma proteome profiling in two different disease states of GCA produced highly accurate classification for distinguishing active and inactive disease states from controls. These results demonstrate the strong potential of integrating plasma proteomes with machine learning for future approaches to identify GCA. Future studies should include validating these findings in a larger independent cohort.

Disclosure: k. cunningham: None; **J. Sung**: None; **B. Hur**: None; **V. GUPTA**: None; **M. Koster**: None; **C. Weyand**: AbbVie/Abbott, 1, Bristol-Myers Squibb(BMS), 1, Gilead, 1; **D. Cuthbertson**: None; **N. Khalidi**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 1, Otsuka, 1, 6, Roche, 1, 6; **C. Koening**: Amgen, 1; **C. Langford**: AbbVie, 12, Non-paid consultant, AstraZeneca, 5, 12, Non-paid consultant, Bristol-Myers Squibb(BMS), 5, 12, Non-paid consultant, GlaxoSmithKlein(GSK), 5; **C. McAlear**: None; **P. Monach**: Genentech, 12, Lecture with honorarium, HI-Bio, 2; **L. Moreland**: Boehringer-Ingelheim, 12, member of independent Data Safety Monitoring Board, Celltrion, 12, member of independent Data Safety Monitoring Board; **C. Pagnoux**: AstraZeneca, 1, 2, 6, GlaxoSmithKlein(GSK), 1, 6, Otsuka, 1, 2, 5, 6, Pfizer, 5, Roche, 2; **R. Rhee**: None; **P. Seo**: Amgen, 1, Janssen, 1; **P. Merkel**: AbbVie/Abbott, 5, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos, 5, Electra, 5, Genentech, 5, GlaxoSmithKlein(GSK), 2, 5, HiBio, 2, InflaRx, 2, 5, Janssen, 2, Jubilant, 2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, Takeda, 2, 5, UpToDate, 9, Visterra, 2; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Chemocentryx, 1, 6, Eli Lilly, 5, kiniksa, 5.

Abstract Number: 2602

Spatially Resolved Cellular Signatures Predict Corticosteroid Treatment Response in Giant Cell Arteritis

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SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders III: Innovation
Session Type: Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Corticosteroids (CS) remain the mainstay of giant cell arteritis (GCA) therapy. Between ~30-70% patients relapse following CS taper and are consequently at risk of high toxicity due to prolonged CS exposure. Predictors of CS treatment response would enable a stratified approach to management but have yet to be established. Existing

mechanistic GCA research has mostly focussed upon a putative role for $CD4^+$ T cells in treatment non-response, however, GCA is characterised by a more expansive immune landscape. This study is the first to comprehensively characterise the spatial immunobiology of GCA and associate this with CS treatment response.

Methods: Archival formalin-fixed paraffin-embedded (FFPE) GCA temporal artery biopsies (TAB) from patients who fulfilled ACR GCA criteria were linked to their clinical record and sub-grouped according to those who fulfilled the EULAR definition for sustained remission (SR) at 1 year (n=6) and those who did not (non-response; NR, n=6). Non-GCA TAB (n=4) were included as controls. Tissue sections were analysed for the whole transcriptome atlas on the Nanostring GeoMx Digital Spatial Profiler. Specific topographic areas of interest (AOI) were defined by immunofluorescence in the adventitia, media, and intima layers within which $CD45^+$ (leukocytes), $CD68^+$ (macrophages and giant cells; Mϕ and GCs), $CD31^+$ (endothelial cells), and $CD45^-CD68^-CD31^-$ (stroma). Several bioinformatic tools were used to determine transcriptomic differences, including GeoMx NGS pipeline, DESeq2 package, Searchlight2 software, Gene Set Enrichment Analysis (GSEA), and CIBERSORT. The results informed a 28-plex antibody panel for spatial phenotypic cell analysis, which was applied to sections sourced from corresponding TABs using a PhenoCycler System (CODEX).

Results: Spatial transcriptomic analysis identified 2,275 differentially expressed genes between GCA and controls. The most significantly upregulated genes were immunoglobulin genes and genes associated with pathological Mϕ. GCA SR cases had greater $CD45^+$ and $CD68^+$ infiltrates towards the intima layer than NR cases. Differential expression signature analysis showed fundamental differences among $CD68^+$ adventitial/media Mϕ, intima Mϕ, and GCs. Deconvolution analysis indicated a mix of monocyte, M1 and M2 Mϕ in the adventitial transcriptomic signature, while a mainly M0 undifferentiated phenotype was observed in intima Mϕ and GCs. Notably, SR cases expressed an increased plasma cell molecular signature when compared to NR cases, both in adventitial $CD45^+$ AOI and stroma. In contrast, NR adventitial $CD45^+$ AOI demonstrated a pronounced $CD4^+$ T cell signature associated with INFγ response and other inflammatory pathways, including TNF and IL-6 signalling. CODEX imaging analysis revealed clear and abundant $CD138^+CD38^+$ plasma cells in the adventitia layer, which were visible in 6/6 of SR cases and only 1/5 of NR case.

Conclusion: Spatial analysis of GCA TAB tissue collected at diagnosis revealed strong plasma cell and pathological Mϕ signatures that correlated with CS treatment response at 1 year. In contrast, CS treatment non-response was characterised by a $CD4^+$ T cell signature.

Disclosure: C. Ansalone: None; **S. McAllister**: None; **E. Pickerill**: Eli Lilly, 3, 11; **L. Zhang**: Eli Lilly, 3; **A. Peacock**: None; **D. McGovern**: None; **H. Leslie**: None; **V. Kellior**: None; **E. Qian**: None; **D. Gemperline**: Eli Lilly, 3, 11; **A. Virlan**: None; **S. Wright**: None; **P. Cauchi**: None; **T. Beckman**: None; **L. Hutton**: None; **J. Cole**: None; **I. Wulur**: Eli Lilly, 3, 11; **R. Benschop**: Eli Lilly, 3; **N. Jamieson**: Galvani, 1; **C. Goodyear**: Abbvie, 6, AstraZeneca, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 5, Eli Lilly, 5, Galvani, 2, 5, GlaxoSmithKlein(GSK), 5, Istesso, 5, Janssen, 5, MedAnnex, 2, 5, Medincell, 2, MiroBio, 5, Revolo, 5, UCB, 5, 6; **N. Basu**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Pfizer, 5, Roche, 6, Vifor, 2, 5, 6.

Abstract Number: 2603

Impact of IL-6 Receptor Small Nucleotide Polymorphism Asp358Ala on T Cell Activity and Clinical Outcomes in Patients with Giant Cell Arteritis

Christopher Redmond[1], Robert Zorc[2], McKella Sylvester[3], Cameron Rankin[4], Rebecca Kuan[5], Kristina Wells[6], Lily Dai[7], Kaitlin Quinn[8], Massimo Gadina[9] and Peter Grayson[10], [1]National Institutes of Health, Hagerstown, MD, [2]National Institute of Arthritis and Musculoskeletal and Skin Diseases/National Institutes of Health, Bethesda, MD, [3]Colgate University, Bethesda, MD, [4]NIAMS, NIH, Washington, DC, [5]NIH, Bethesda, MD, [6]University of California Davis, Bethesda, MD, [7]NIH, Germantown, MD, [8]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National

Institutes of Health (NIH), Bethesda, MD, [9]National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD, [10]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Chevy Chase, MD

SESSION INFORMATION

Session Date: Wednesday, November 15, 2023
Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders III: Innovation
Session Type: Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Giant cell arteritis (GCA) is a large vessel vasculitis in adults that commonly involves the aorta and branching arteries, resulting in multiple symptoms including vision loss. IL-6 has been identified as key to GCA pathogenesis, and treatment with IL6 receptor (IL-6R) antibody, tocilizumab, induces steroid-free disease remission in many patients with GCA. Not all patients with GCA have favorable clinical response to tocilizumab. A relatively common SNP in IL-6R, Asp358Ala, results in increased solubilization of the IL-6R that then binds the ubiquitous IL-6 co-receptor, gp130, leading to more pro-inflammatory soluble IL-6 signaling, known as trans signaling. This contrasts with classical membrane bound IL-6R signaling, found on hepatocytes and lymphocytes, that results in anti-inflammatory effects and release of C-reactive protein. We hypothesized that the Asp358Ala IL-6R variant in patients with GCA impact IL-6 mediated T cell activity and response to tocilizumab.

Methods: Samples and clinical data were obtained from patients who met the 2022 ACR/EULAR Classification Criteria for GCA. Genetic sequencing was completed to identify GCA patients with the Asp358Ala variant. Serum from patients was used to quantitate serum soluble IL-6R levels by ELISA. Peripheral blood mononuclear cells (PBMCs) evaluated for

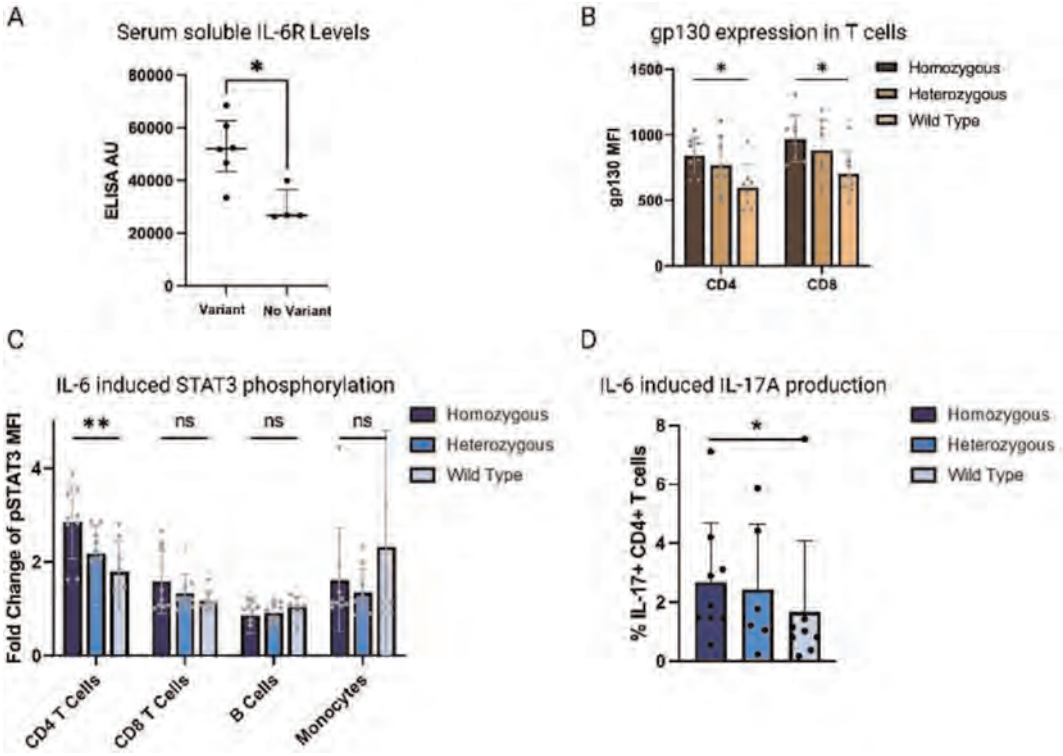

Figure 1. A) Serum samples from GCA patients were measured by ELISA for soluble IL-6R levels. sIL-6R levels from patients with the Asp358Ala variant (homozygous and heterozygous) were compared to those without the variant. B) PBMCs were analyzed by flow cytometry for gp130 expression on different T cell subsets. C) PBMCs were stimulated with IL-6 (100ng/ml) for 15mins and then analyzed for STAT3 phosphorylation. C) PBMCs from patients with GCA were stimulated with 50ng/ml of IL-6 and costimulatory molecules (CD3, CD28, anti-IL4, and anti-IFNy) for 3 days and then re-stimulated with PMA/Ionomycin.

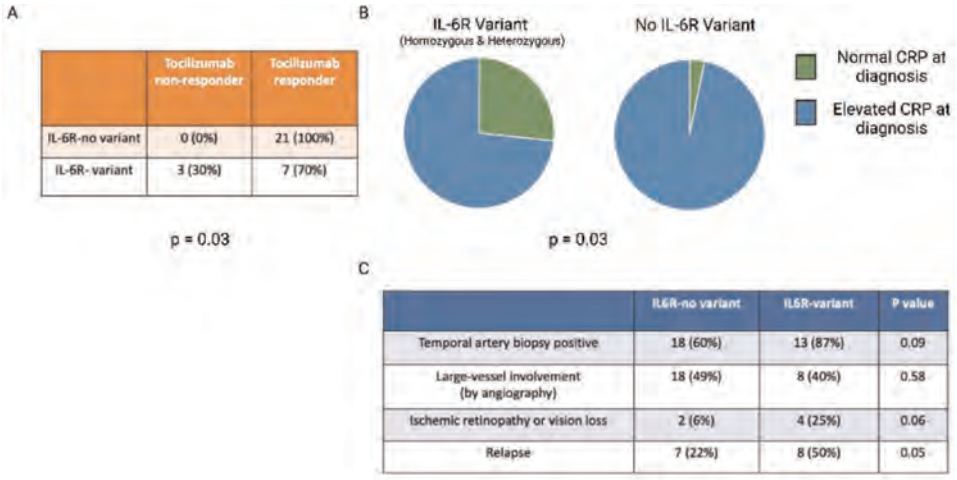

Figure 2. Clinical characteristics of a prospective observational cohort of patients with GCA. A) Tocilizumab non-response was identified as clinical signs or symptoms of active disease following treatment with tocilizumab. Response and non-response was compared between GCA patients with and without the IL6-R variant (Asp358Ala) B) CRP at time of diagnosis was compared between GCA patients with and without the IL6-R variant (Asp358Ala), normal range was determined by clinical laboratory standards. 3) Prospective chart review as conducted to identify clinical characteristics and complications commonly associated with GCA, before, during, or after treatment with tocilizumab.

expression of IL-6R and its co-receptor, gp130, using flow cytometry. The same PBMCs were stimulated ex vivo with IL-6 and evaluated for downstream targets of IL-6, STAT3 phosphorylation and IL-17A expression, also using flow cytometry. Clinical symptoms, laboratory values, and response to tocilizumab was identified by chart review. Active disease was defined by clinical signs and symptoms.

Results: Patients with GCA and the Asp358Ala IL-6R variant had increased serum soluble IL-6 receptor levels (Fig 1A) as well as higher lymphocyte expression of surface gp130 (Fig 1B). When stimulated ex vivo with IL-6, CD4+ T cells in patients with Asp358Ala had increased STAT3 phosphorylation and IL17A expression (Fig 1C and 1D). Similar associations were not seen in other leukocyte subsets or in CD4+ T cells from healthy controls by variant status. Clinically, patients with the Asp358Ala SNP had a higher likelihood of treatment failure to tocilizumab (Fig 2A), lower CRP values at diagnosis (Fig 2B), and a higher rate of relapse (Fig 2C).

Conclusion: The Asp358Ala IL6R variant may result in increased pro-inflammatory trans IL-6 signaling via increased soluble IL-6R and surface gp130 expression, leading to more robust STAT3 phosphorylation and IL-17A production in T cells. IL-6R inhibition via tocilizumab in patients with the Asp358Ala variant may be insufficient to achieve disease control. This variant may be a useful biomarker to predict treatment response to tocilizumab and to identify patients who may respond more favorably to alternative therapeutic approaches.

Disclosure: C. Redmond: None; **R. Zorc**: None; **M. Sylvester**: None; **C. Rankin**: None; **R. Kuan**: Colgate-Palmolive Company, 5; **K. Wells**: None; **L. Dai**: None; **K. Quinn**: None; **M. Gadina**: None; **P. Grayson**: None.

Abstract Number: 2604

Premature Vascular Smooth Muscle Cells Senescence Driven by Interleukin-6-Mitochondrial STAT3-Mitofusin 2 Signaling in Takayasu's Arteritis

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SESSION INFORMATION

Session Date: Wednesday, November 15, 2023

Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders III: Innovation

Session Type: Abstract Session

Session Time: 11:00AM–12:30PM

Background/Purpose: Takayasu's arteritis (TAK) is characterized by persistent vascular inflammation involving aorta and its main branches, which is an important prosenescent factor that in turn amplifies local inflammation via senescence-associated secretory phenotype (SASP). In this study, we aimed to explore the pathogenic role of vascular smooth muscle cells (VSMCs) senescence and the relevant prosenescent pathway in TAK.

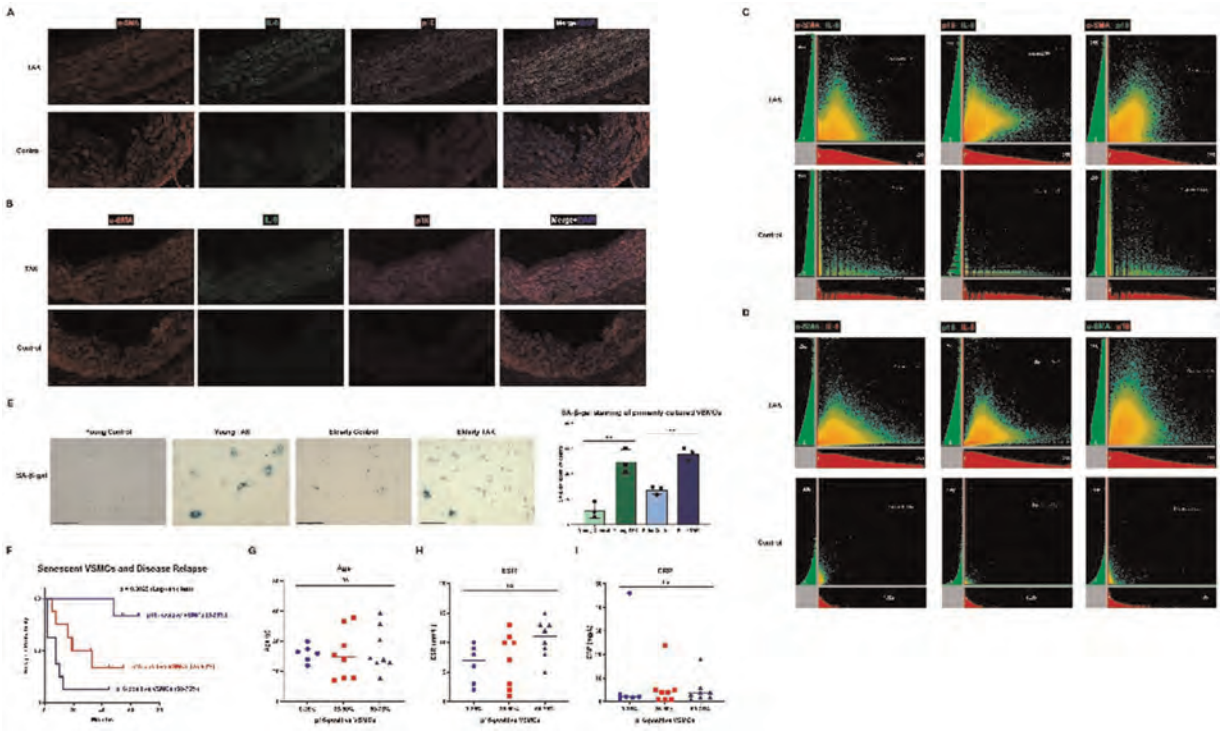

Figure 1. Premature VSMCs senescence in TAK patients and its association with disease parameters

Methods: Cellular senescence markers were tested in vascular samples from patients with TAK using immunofluorescence, western blot and SA-β-gal staining. The key prosenescent inflammatory cytokine and its downstream intracellular events were investigated in a series of in-vitro and ex-vivo experiments including coculture experiments, RNA-Seq, gene knock-down, mitochondrial assays, co-immunoprecipitation, and tissue culture.

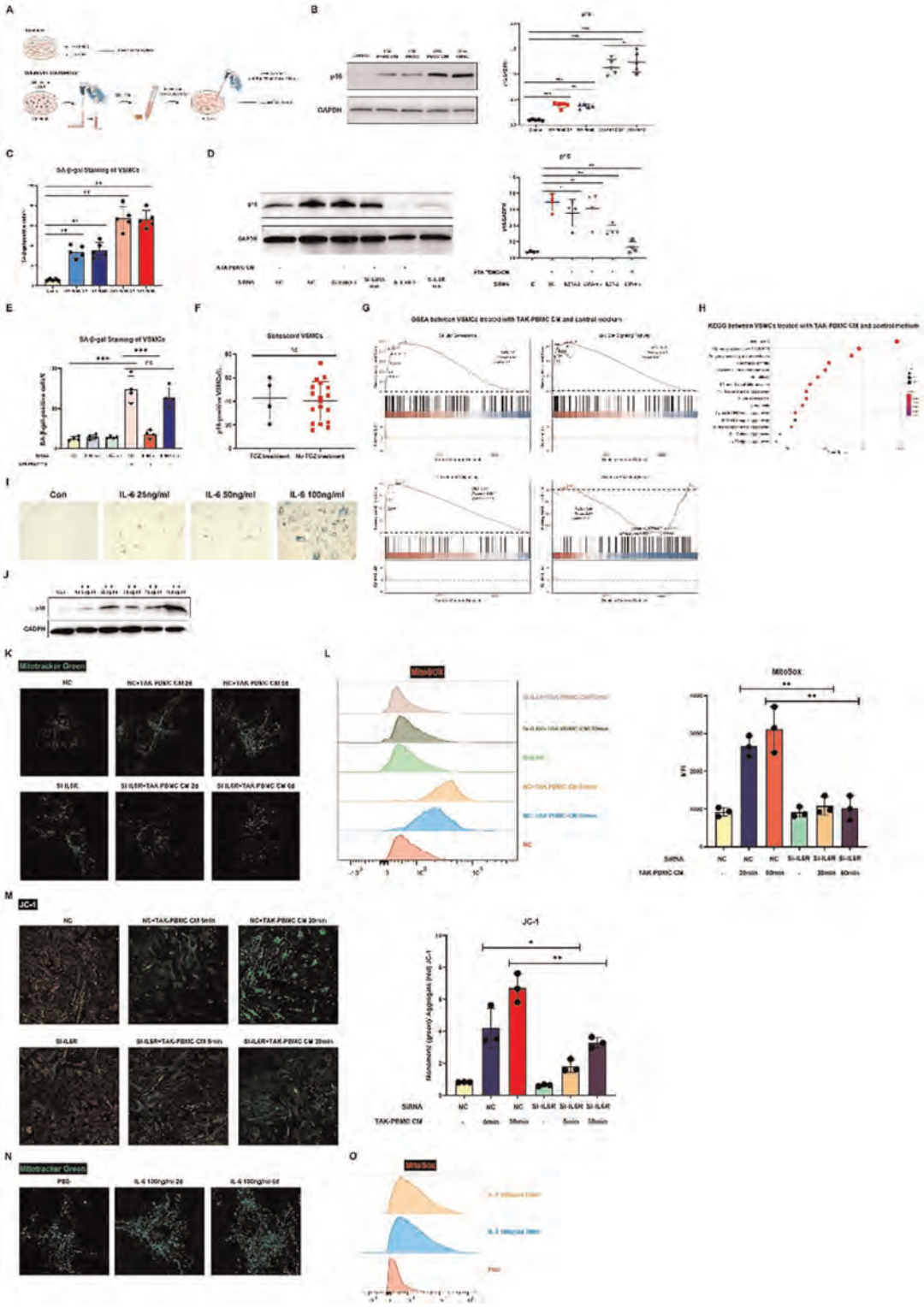

Figure 2. Prosenescent effects and senescence-associated mitochodrial dysfunctions driven by TAK inflammatory milieu via IL-6 signaling

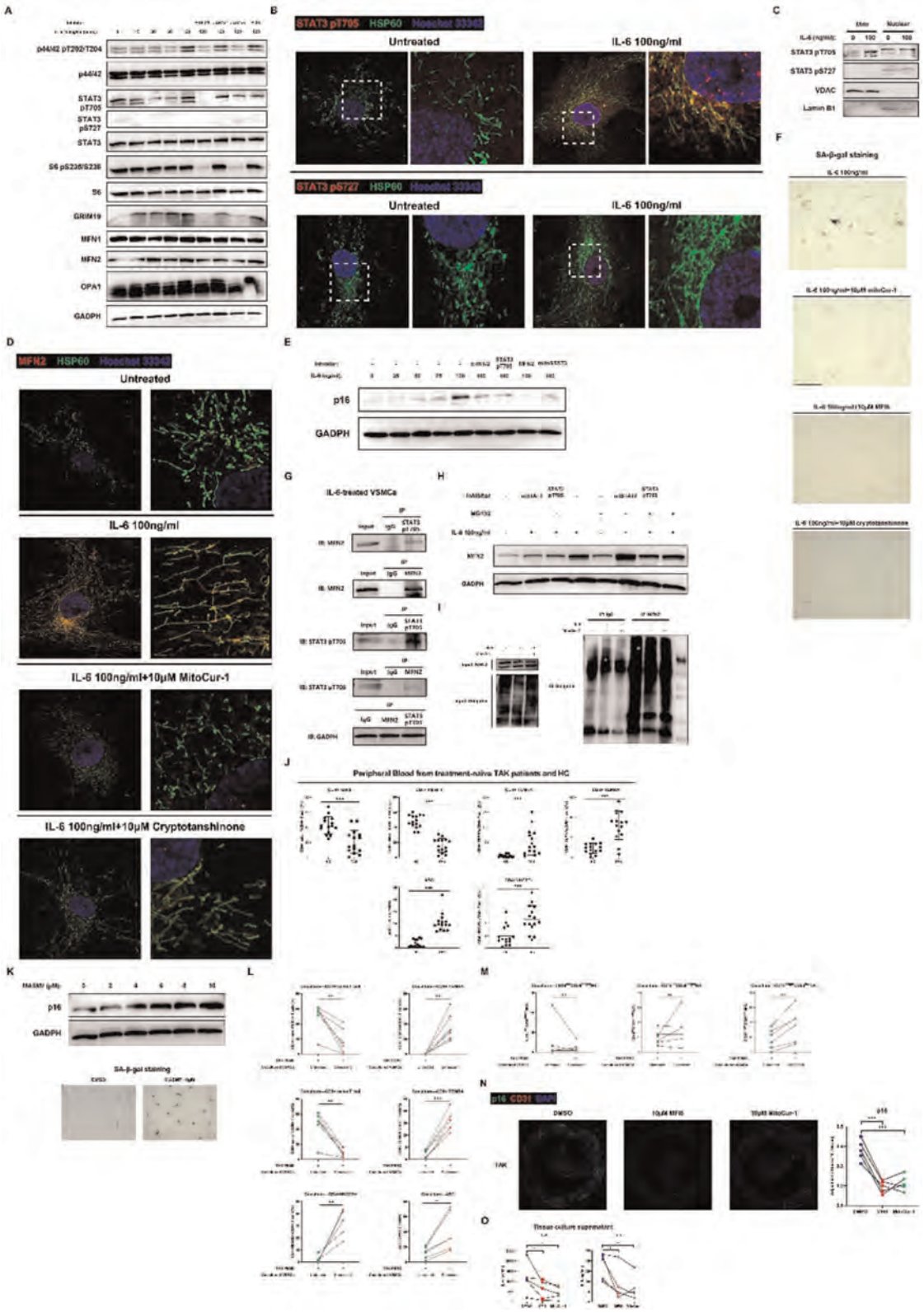

Figure 3. IL-6-induced prosenescent noncanonical mitochondrial-localized phosphorylated STAT3 (Tyr705) interact with MFN2 and prevented it from proteasomal degradation in VSMCs, resulting mitochondrial elongation in VSMCs. Coculture with senescent VSMCs lead to an immunosenescence-like and cytotoxic phenotype switch in cocultured TAK PBMCs. MitoCur-1 or MFI8 treatment ameliorates VSMCs senescence in ex vivo-cultured arteries from TAK patients.

Results: The features of premature VSMCs senescence, including upregulated p16 expression, more intense SA-β-gal staining, and SASP consisting of increased interleukin-6 (IL-6) and IL-8 expression, were detected in TAK patients, compared with age- and sex-matched control subjects (Figure 1). Treatment with conditioned medium of peripheral blood mononuclear cell (PBMC) from patients (TAK-PBMC CM) and coculture with TAK-PBMC exerted similar prosenescent effects on VSMCs via IL-6 signaling. RNA-Seq suggested that cellular senescence and IL-6-STAT3 pathway were upregulated, while oxidative phosphorylation pathway was downregulated in TAK-PBMC CM-treated VSMCs. TAK-PBMC CM treatment induced multiple senescence-associated mitochondrial dysfunctions that can be significantly improved by IL-6 receptor knockdown (Figure 2). IL-6-induced noncanonical mitochondrial localization of phosphorylated STAT3 (Tyr705) prevented mitofusin 2 (MFN2) from proteasomal degradation, and subsequently promoted mitochondrial elongation and cellular senescence in VSMCs. In addition, coculture with MFN2 activator MASM7-induced senescent VSMCs led to an immunosenescence-like and cytotoxic phenotype switch in TAK-PBMC that can be detected in treatment-naïve patients, including decreased frequencies of naïve T cells, increased frequencies of TEMRA cells, age-associated B cells and $CD16^{bright}CD56^{dim}$ NK cells, and upregulated NKG2D expression in CD4+ T cells (Figure 3). Of clinical relevance, although no significant difference of ESR and CRP levels was observed among patients with various senescent VSMCs proportions, patients with higher percentage of senescent VSMCs were more likely to relapse (Figure 1). However, senescent VSMCs proportions in vascular samples were comparable between patients taking long-term tocilizumab treatment (>1 year) and those receiving other therapies, which is contradicting our expectation. Instead, treatment with mitoCur-1 (mitochondrial STAT3 inhibitor) or MFI8 ameliorated (MFN2 inhibitor) VSMCs senescence in ex vivo cultured arteries of patients with TAK (Figure 3).

Conclusion: VSMCs of patients with TAK exhibited the features of cellular senescence. IL-6-mitochondrial STAT3-MFN2 signaling is an important driver of VSMCs senescence. This may provide new insights into the mechanisms governing inflammation in TAK.

Disclosure: C. Fang: None; **L. Du**: None; **L. Li**: None; **Y. Chen**: None; **Z. Chen**: None; **Y. Li**: None; **J. Li**: None; **M. Li**: None; **x. Zeng**: None; **X. Tian**: None.

Late-Breaking Abstracts

Abstract Number: L01

Analysis of 245,388 Diverse Participants in the NIH All of Us Cohort Identifies VEXAS Resiliency in UBA1 M41L Somatic Mutation Carriers

Robert Corty[1] and Alexander Bick[2], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Vanderbilt University, Nashville, TN

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Late-Breaking Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: VEXAS syndrome is a recently-discovered systemic auto-inflammatory disease caused by somatic mutation at position 41 in the X-linked gene *UBA1*.[1] First, 25 older men with M41T, M41V, or M41L with variant allele fraction (VAF) 35-80% were reported among quaternary referral populations of severely ill patients. A later study of 163,096 patients participating in a regional health system research cohort found 8 older men with the same *UBA1* M41X mutations, with VAF 9-74%.[2] Nearly all had severe anemia and macrocytosis, and five had a clinical diagnosis of VEXAS. This study population was >96% White and more than half of participants were >60 years old. Thus, there is a critical unmet need to define the prevalence and clinical consequences of somatic *UBA1* M41L mutation in a racially and geographically diverse population.

Methods: We analyzed 245,388 individuals with clinical-grade whole genome sequencing data in the NIH All of Us cohort v7 data release.[3] Somatic variants in *UBA1* were identified with *Mutect2* [4], annotated with *Annovar* [5], and filtered in R version 4.2.2 [6] based on published pragmatic guidelines.[7] VEXAS-associated SNOMED codes, laboratory abnormalities, and medications were defined by literature search of symptoms of confirmed cases.[1,2,8] Controls were identified in a 10:1 ratio based on matching age and sex.

Results: 74 participants in the NIH All of Us cohort harbor somatic mutation *UBA1* M41L and none have the other well-described variants, M41V or M41T. The M41L mutation was more common among women than men (n = 62 vs 12, $p < 0.001$) and no effect of age ($p = 0.17$) or ancestry ($p > 0.4$) was observed. The cases are age 20 to 83 and have VAF 4.5% to 33%. Their ancestry is 51% European, 27% African, and 19% admixed/Latino. The number of VEXAS-associated diagnosis codes was similar between cases and controls (4.3 vs 3.6, $p = 0.77$), but cases had an increased rate of asthma (27% vs 18%, $p < 0.001$), Tietze's syndrome (8% vs 2%, $p < 0.001$), and neutropenia (7% vs 2%, $p = 0.005$). The minimum observed hemoglobin was similar between cases and controls (11.5 vs 11.4 mg/dL) as was the maximum mean corpuscular volume (91.7 vs 91.4). Interestingly, cases were much more likely to be prescribed systemic steroids than matched controls (55% vs 0%, $p < 0.001$).

Conclusion: We describe the largest cohort of people with somatic mutation M41L in the *UBA1* gene and the largest cohort of women with a VEXAS-associated mutation. The diagnosis codes and laboratory values do not comport with the severe, systemic illness that has characterized our understanding of VEXAS to date. However, these cases were prescribed systemic steroids at a much higher rate than matched controls and are enriched for a few idiopathic inflammatory diagnoses suggesting an incompletely-appreciated inflammatory syndrome. These cases are younger, healthier, have lower VAF, and much better represent the demographic and geographic diversity of the United States than previous reports. We

hypothesize that many of the cases reported here will not develop VEXAS due to either somatic reversion or haplosufficiency of *UBA1*. Further characterization of the genetic and clinical trajectories in these individuals may permit strategies for risk stratification, monitoring, and treatment.

Table 1: Demographic characteristics of participants with somatic mutation M41L in UBA1 closely mirror their matched controls.

	case (n = 74)	control (n = 740)
age (mean (SD))	48.3 (16.3)	48.3 (16.2)
sex = Male (%)	12 (16%)	120 (16%)
genetic ancestry (%)		
African	20 (27%)	179 (24%)
American/Admixed	14 (19%)	164 (22%)
European	38 (51%)	367 (50%)
ethnicity (%)		
Hispanic or Latino	15 (20%)	164 (22%)
Not Hispanic or Latino	57 (77%)	557 (75%)

Figure 1: Participants with with somatic mutation M41L in UBA1 reside in geographically diverse parts of the United States.

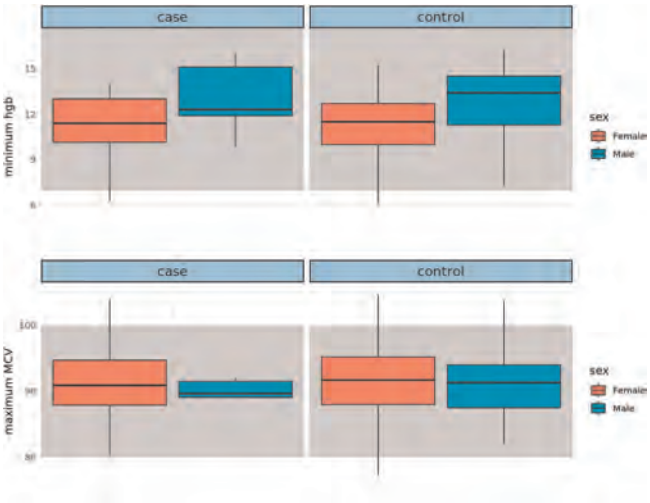

Figure 2: Participants with with somatic mutation M41L in UBA1 have similar minimum hemoglobin concentration and maximum mean corpuscular volume (MCV) as compared to matched controls.

Disclosure: R. Corty: None; **A. Bick**: None.

Abstract Number: L02

Mutational Analysis of UNC93B1 Identifies Regulatory Regions Mutated in Human SLE

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SESSION INFORMATION

Session Date: Tuesday, November 14, 2023

Session Title: Late-Breaking Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Endosomal nucleic acid-sensing toll-like receptors 3, 7 and 9 are key innate immune sensors of dsRNA, ssRNA and ssDNA, respectively, whose activities must be tightly regulated to prevent systemic autoimmune or autoinflammatory disease (TLR7, TLR9) or virus-associated immunopathology (TLR3). The 12-pass transmembrane protein UNC93B1 chaperones nascent TLR3, TLR7 and TLR9 molecules from the ER to endosomes that support ligand recognition and signaling. Release from UNC93B1 is required for TLR3 and TLR9 signaling, whereas a persistent association between UNC93B1 and TLR7 is important for limiting TLR7 responses to endogenous nucleic acids.

Methods: Here we undertook a systematic scanning mutagenesis screen of all cytosolic and endosomal loops of UNC93B1 in murine RAW macrophages, totaling 93 mutated single or triplet amino acid residues.

Results: We identified both negative and positive regulatory regions - in particular, 21, 31 and 17 of these mutations yielded a 2-fold or higher enhancement of TNFa production downstream of TLR3, TLR7 or TLR9, respectively. The number and effect size of negative regulatory UNC93B1 mutations was noted to be highest for TLR7 responses.

We were subsequently contacted by several groups of clinicians who had identified patients with coding mutations in UNC93B1, including: (i) a family of 3 adolescent siblings and with pediatric onset isolated cutaneous tumid lupus, harboring a heterozygous T93I mutation; (ii) an adolescent girl with pediatric onset extended oligoarticular JIA, chillblain and tumid lupus rashes and an ataxic/dystonic movement disorder with CNS basal ganglia calcifications reminiscent of Aicardis-Goutieres syndrome, harboring a heterozygous R336C mutation not present in either of her parents; and (iii) a young man diagnosed at age 10 with SLE complicated by aggressive class IV nephritis, harboring a homozygous G590E mutation. When introduced in to human THP-1 monocytes and murine RAW macrophages, these mutations enhanced cytokine responses to TLR7 (expressed in mouse and human cells), TLR8 (human cells only), and to a lesser extent TLR3 (mouse cells only) stimulation, phenocopying mutants in the same UNC93B1 regions from our original screen. Knock-in mice have been generated for all three human variant alleles, and to date analysis of Unc93b1^(R336C) mice has revealed a 30% reduction in body weight, splenomegaly, expansion of Age-Associated B cells and plasma cells, monocytes and neutrophils, and titers of serum ANA IgG comparable to TLR7.1 transgenic animals.

Conclusion: Altogether our results implicate the UNC93B1-TLR7/8 axis in human monogenic autoimmune disease and provide a functional resource and analysis pipeline to assess the impact of yet-to-be-reported UNC93B1 mutations.

Disclosure: J. Huizar: None; **V. Rael**: None; **J. Yano**: None; **L. Slayden**: None; **M. Weiss**: None; **R. Saxton**: None; **B. Liu**: None; **O. Majer**: None; **G. Barton**: None.

Abstract Number: L03

Efficacy and Safety of Targeted Therapies in VEXAS Syndrome: Retrospective Study from the French VEXAS Group

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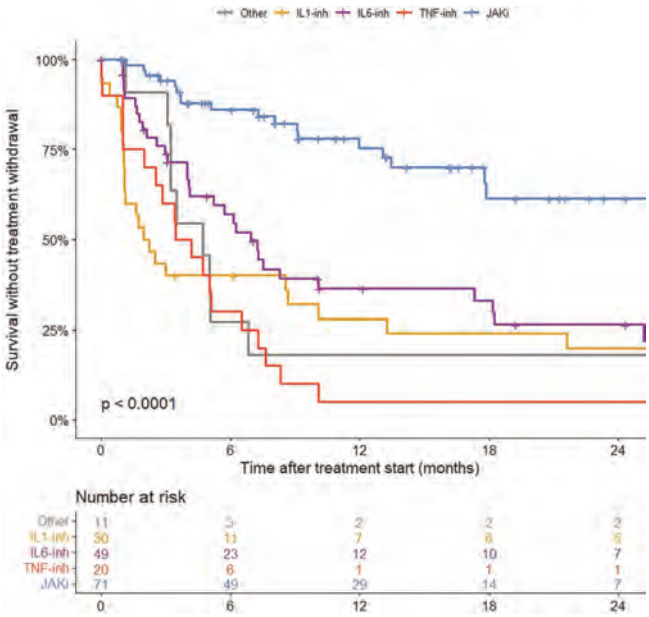
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Late-Breaking Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome is a monogenic disease of adults due to acquired somatic mutations of the *UBA1* gene. Patients present with a broad range of inflammatory and hematological manifestations, and the prognosis is severe. Due to its recent description, the therapeutic management is poorly codified and only based on small retrospective studies. The aim of this study was to evaluate the efficacy and safety of targeted therapies in a cohort of patients with VEXAS syndrome.

Methods: Multicenter retrospective study conducted within the French national VEXAS study registry between November 2020 and August 2023 including patients with genetically proven VEXAS syndrome who had received at least one targeted therapy. CR was defined by clinical remission, CRP < 10 mg/L and corticosteroid therapy less than 10 mg/day; partial response (PR) by clinical remission, CRP and corticosteroid therapy decreased by 50%; and no response by persistence of clinical activity and/or biological inflammatory syndrome and/or inability to decrease corticosteroid therapy.

Results: One hundred and ten patients (male 99%, median age 71 (68-79) years) who had received 194 targeted therapies were included. Treatments received were JAK inhibitor (JAKi) in 40% (n=78, ruxolitinib in 87%) of cases, anti-interleukin (IL)-6 antibody in 26% (n=51, tocilizumab in 92%), anti-IL-1 in 17% (n=33, anakinra in 91%), anti-TNFa in 10% (n=20), and another targeted therapy in 6% (n=12). Fifty-three patients (48%) received more than one targeted therapy. The main clinical features of VEXAS syndrome at the initiation of targeted therapy were constitutional symptoms (82%), skin involvement (76%) and inflammatory arthralgias (60%). Myelodysplastic syndrome was present in 28% of cases, without indication for specific hematological treatment. Median CRP at treatment initiation was 39 (19-57) mg/L and median prednisone dose received was 20 (10-35) mg/day. At 3 months, overall response (CR and PR) was 24% (CR 19% and PR 5%) with JAKi, 32% (CR 20% and PR 12%) with anti-IL-6, 9% with anti-IL-1, and 0% with anti-TNF or another targeted therapy. At 6 months, the overall response was 30% (CR 26% and PR 4%) with JAKi and 26% (CR 20% and PR 6%) with anti-IL-6. Corticosteroid withdrawal was similar between JAKi and anti-IL-6. Compared to JAKi, other therapies had significantly higher risk of treatment withdrawal during follow-up (P< 0.001, Figure 1). Treatment was stopped in 28% (n=22) of cases under JAKi with a median delay of 7.2 (3.4-12.4) months and in 69% of cases under anti-IL-6 with a median delay of 5.1 (2-9.1) months.



Survival without treatment withdrawal according to the targeted therapy used

The causes of discontinuation were primary failure, secondary failure, serious adverse event or death respectively in 43%, 14%, 19% and 19% with JAKi, 46%, 11%, 31% and 9% with anti-IL-6, 50%, 4%, 35% and 8% with anti-IL-1, and 74%, 5%, 16% and 5% with anti-TNFa.

Conclusion: This large multicenter cohort is the first to compare the efficacy and safety of targeted therapies in VEXAS syndrome. This study confirms the benefit of JAKi and tocilizumab with similar response rates, whereas the other targeted therapies appear to have lower efficacy. These results need to be confirmed in prospective therapeutic trials.

Disclosure: J. HADJADJ: AstraZeneca, 1; **Y. NGUYEN**: None; **D. MOULOUDJI**: None; **R. BOURGUIBA**: None; **M. HEIBLIG**: None; **A. HASSINA**: None; **V. LACOMBE**: None; **S. ARDOIS**: None; **C. CAMPOCHIARO**: None; **A. MARIA**: None; **T. COMONT**: None; **E. Lazaro**: None; **F. LIFERMANN**: None; **G. LE GUENNO**: None; **H. LOBBES**: None; **R. Outh**: None; **J. Campagne**: None; **C. COUSTAL**: None; **A. GARNIER**: None; **Y. Jamilloux**: None; **A. MEYER**: None; **N. Abisror**: None; **O. KOSMIDER**: None; **V. Jachiet**: None; **O. FAIN**: None; **B. Terrier**: AstraZeneca, 2, GlaxoSmithKline, 2, Pharma, 2, Vifor, 2; **A. Mekinian**: None; **S. Georgin-Lavialle**: None.

Abstract Number: L04

EP-104IAR (Extended-Release Fluticasone Propionate for Injectable Suspension): Topline and Key Secondary Results from a Phase 2 Randomized, Double-blind, Vehicle-Controlled Trial in Subjects with Knee Osteoarthritis

James Helliwell[1], **Amanda Malone**[1], Mark Kowalski[2], Asger Reinstrup Bihlet[3], Claire Miller[4], Alejandro Castillo Mondragon[5], Yanqi Li[6], Christine Dobek[7], Vik Peck[1], Mike Wilmink[8] and Lee Simon[9], [1]Eupraxia Pharmaceuticals, Victoria, BC, Canada, [2]Eupraxia Pharmaceuticals, Winchester, VA, [3]NBCD A/S, Soeborg, Denmark, [4]NBCD A/S, Copenhagen, Denmark, [5]NBCD, Copenhagen, Denmark, [6]NBCD A/S, Soborg, Denmark, [7]Eupraxia Pharmaceuticals, Edmonton, AB, Canada, [8]OrthoArizona, Phoenix, AZ, [9]SDG LLC, Cambridge, MA

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Late-Breaking Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: EP-104IAR is being developed to treat OA symptoms. Previous results from non-clinical studies evaluating local joint safety in beagle dogs, in contrast to other corticosteroid preparations, indicated that the prolonged local residence time of EP-104IAR had no impact on cartilage health.[1] Safety and PK data from a Phase 1 trial in 24 OA knee patients were consistent with nonclinical findings and supported continued development of EP-104IAR.[2] This report describes the results of a Phase 2b trial in subjects with Knee OA.

Methods: Subjects were randomized 1:1 to a single intraarticular dose of EP-104IAR 25 mg, or vehicle and followed for 24 weeks. Males and females, ≥40 years, with a diagnosis of primary knee OA, Kellgren-Lawrence Grade 2-3 and symptoms (WOMAC Pain scores ≥ 4.0 to ≤9.0 (out of 10)) were enrolled. Subjects recorded weekly WOMAC Pain and monthly

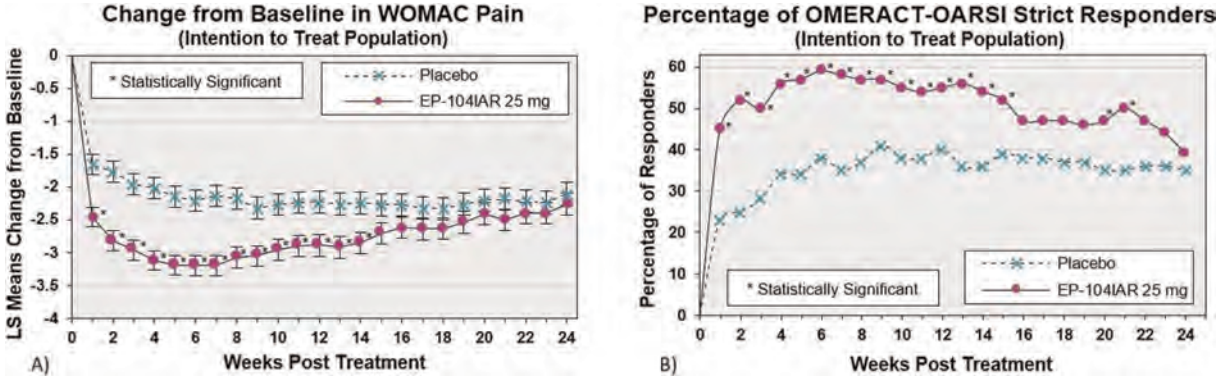


Figure 1: A) Least-squares mean change from baseline (and standard error) for the primary efficacy end point of Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)-A (pain) (n = 318). B) Percent of patients classified as OMERACT-OARSI strict responders (OMERACT-OARSI strict responder defined as a subject with a greater than 2-point change from baseline and a 50% reduction in baseline pain) (n=318).

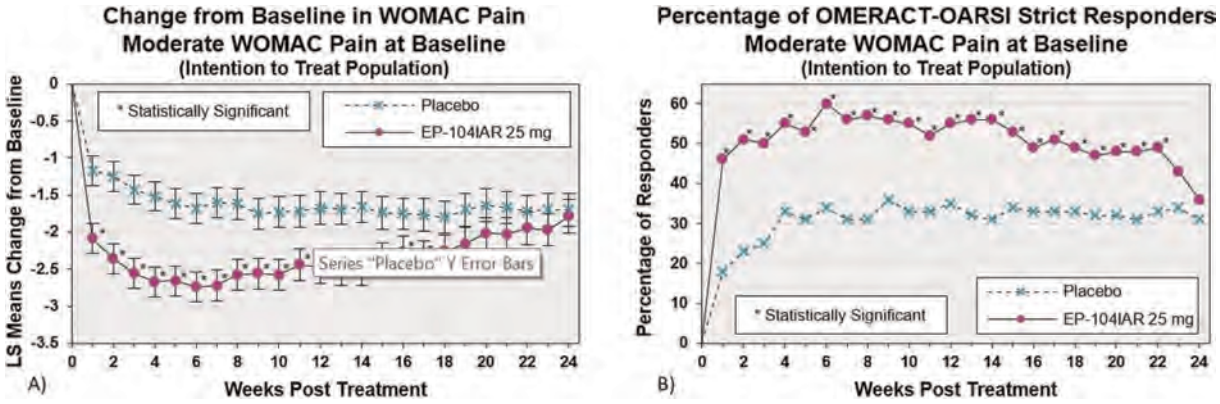


Figure 2: A) Least-squares mean change from baseline (and standard error) for the exploratory efficacy end point of Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)-A (pain) in the moderate sub-population (n = 214). B) Percent of patients classified as OMERACT-OARSI strict responders (OMERACT-OARSI strict responder defined as a subject with a greater than 2-point change from baseline and a 50% reduction in baseline pain) in the moderate sub-population (n=214). Moderate was defined as having an average baseline WOMAC-A score on entry between 3.5-6.5. Patients who's screening WOMAC-A scores were ≥4 but dropped below 4 on the day of injection were still eligible for the trial (potentially resulting in an average baseline pain <4).

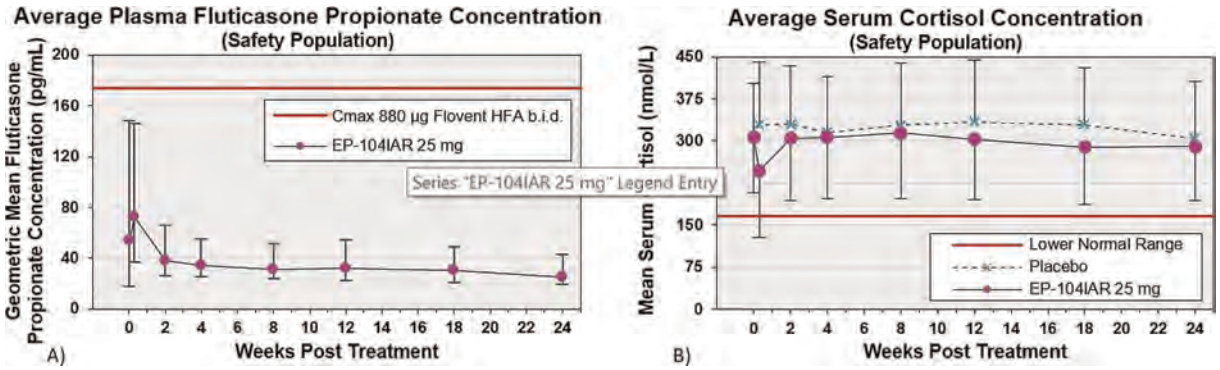


Figure 3: A) Geometric Mean ± SE plasma fluticasone concentrations following a single injection of EP-104IAR (n=163 received EP-104IAR). Red line demarcates the average Cmax fluticasone concentrations with b.i.d. dosing of 880 µg Flovent HFA. B) Geometric Mean ± SE serum cortisol concentrations. Red line demarcates lower bound of normal cortisol range (n=318).

WOMAC Total measurements on a diary device. Safety assessments included adverse events (AEs), vital signs, laboratory evaluations, and knee examinations. The primary endpoint was the change from baseline between treatments in WOMAC® Pain at Week 12.

Results: 318 subjects were dosed (163 EP-104IAR, 155 vehicle), median age = 64 years, 57.5% female. 68% had moderate OA pain (average baseline WOMAC Pain 3.5-6.5). Participants treated with EP-104IAR had significantly higher pain relief compared to vehicle in WOMAC Pain at Week 12 (change from baseline: -2.89 EP-104IAR, -2.23 vehicle; 95%CI -1.1, -0.2, p=0.004). This significant difference persisted until Week 14 in the full population and until Week 17 in subjects with moderate pain. A similar pattern was observed in the OMERACT-OARSI Strict Responders analysis: in allcomers % of OMERACT-OARSI Strict Responders was statistically different until Week 15 while in moderates there was statistical significance to Week 22 (both $p < 0.05$). Most AEs were mild/moderate. There were no EP-104IAR-related serious AEs or withdrawals. Mean serum cortisol and glucose values were similar in both treatment arms, no subjects developed adrenal insufficiency.

Conclusion: A single dose of EP-104IAR provided clinically and statistically significant pain relief for 14 weeks compared to vehicle. In subjects with moderate pain, significant pain-relief persisted for 17 weeks. Responder analyses in subjects with moderate pain demonstrated that clinically meaningful differences persisted for the majority of the study. This suggests EP-104IAR could offer clinically meaningful and safe benefit for substantially longer than any other currently marketed corticosteroids.

Disclosure: J. Helliwell: Eupraxia Pharmaceuticals, 3, 4, 10, 11; **A. Malone**: Eupraxia Pharmaceuticals, 3, 4, 8, 10, 11; **M. Kowalski**: Eupraxia Pharmaceuticals, 3, 11; **A. Bihlet**: NBCD A/S, 3, 11; **C. Miller**: None; **A. Mondragon**: None; **Y. Li**: None; **C. Dobek**: Eupraxia Pharmaceuticals, 3, 11; **V. Peck**: Eupraxia Pharmaceuticals, 3, 11; **M. Wilmink**: Eupraxia Pharmaceuticals, 4, NextStep Arthropedix, 9; **L. Simon**: 150 companies, I consult for, 2, eupraxia, 2.

Abstract Number: L05

DICKENS: A Multicentre Randomised Controlled Trial of Diacerein for Knee Osteoarthritis with Effusion-Synovitis

Guoqi Cai[1], Graeme Jones[2], Flavia Cicuttini[3], Anita Wluka[3], Yuanyuan Wang[3], Catherine Hill[4], Helen Keen[5], Benny Antony[2], barbara de Graaff[2], Michael Thompson[2], Tania Winzenberg[2], Kathy Buttigieg[2], Petr Otahal[2] and Dawn Aitken[2], [1]School of Public Health, Anhui Medical University, Hefei, China, [2]Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia, [3]Monash University, Melbourne, Australia, [4]The Queen Elizabeth Hospital, University of Adelaide, Adelaide, Australia, [5]Fiona Stanley Hospital, Murdoch, Australia

SESSION INFORMATION
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Session Title: Late-Breaking Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: There is an unmet need for treatments of knee OA. Diacerein is recommended for alleviating pain in OA patients for its anti-inflammatory effect by blocking interleukin-1β. Previous trials showed a small beneficial effect of diacerein on pain and joint space narrowing (JSN) in OA patients. However, none specifically targeted patients with an inflammatory OA phenotype who might benefit most from this therapy. Therefore, this trial aimed to determine the effect of diacerein on knee pain and effusion-synovitis over 24 weeks in patients with symptomatic knee OA and MRI-detected effusion-synovitis.

Methods: The DIaCerein for Knee osteoarthritis with EffusioN-Synovitis (DICKENS) study was a multicentre, randomised, double-blinded, placebo-controlled trial over 24 weeks. Patients aged 40-64 years who had significant knee pain (defined as a 0-100mm visual analogue scale (VAS) ≥ 40 mm) and MRI-detected effusion-synovitis were randomised to receive either diacerein (50 mg twice daily for the first 2 weeks, increasing to 100 mg twice daily afterwards if gastrointestinal side-effects acceptable) or identical placebo. Those with severe knee OA (Grade 3 JSN using the Osteoarthritis Research Society International (OARSI) atlas) were excluded. The primary outcome was improvement in knee pain on a 0-100mm VAS at 24 weeks. Secondary outcomes included improvements in effusion-synovitis, knee pain, function, and stiffness by the WOMAC, leg strength, and quality of life (the Assessment of Quality of Life (AQoL-8D) and the 5 level EuroQoL-5-dimensional version (EQ-5D-5L)). Pre-specified stratification analyses were conducted by effusion-synovitis (grade 1 or 2/3) at baseline.

Results: 262 patients (mean ± SD age 54.9±6.1 years, 147 females) were enrolled, and 88.5% completed the trial. At baseline, mean ± SD knee VAS pain (0-100) was 54.8±18.3, and median (interquartile range) effusion-synovitis volume was 4.6 (2.3 to 9.8) ml. After 24 weeks, there was no significant difference in changes in knee pain (VAS pain: -19.9 vs -18.6, p=0.77; WOMAC pain: -76.9 vs -70.4, p=0.64) or WOMAC function (-253.2 vs -234.0, p=0.68) and stiffness scores (-37.5 vs -31.4, p=0.34) between the diacerein and placebo groups. Between-group difference in change in effusion-synovitis volume was statistically significant (diacerein vs placebo: +0.4 ml vs -1.1 ml, p=0.002). There were no significant between-group differences in other secondary outcomes, except that improvement in AQoL-8D (0.03 vs 0.07, p=0.02) was significantly higher in the placebo group. Pre-specified analyses showed no between-group differences in change in knee symptoms in patients with either grade 1 or 2/3 effusion-synovitis at baseline. Adverse events were more frequent in the diacerein group, especially diarrhoea (38.6% vs 22.3%) and coloured urine (10.6% vs none).

Conclusion: In patients with symptomatic knee OA and effusion-synovitis, 50-100 mg twice daily of diacerein, compared to placebo, did not significantly improve knee pain or effusion-synovitis over 24 weeks. These findings do not support the use of diacerein in treating patients with knee OA and effusion-synovitis.

Disclosure: G. Cai: None; **G. Jones**: None; **F. Cicuttini**: None; **A. Wluka**: None; **Y. Wang**: None; **C. Hill**: None; **H. Keen**: None; **B. Antony**: None; **b. de Graaff**: None; **M. Thompson**: None; **T. Winzenberg**: None; **K. Buttigieg**: None; **P. Otahal**: None; **D. Aitken**: None.

Abstract Number: L06

Improvement in Clinical and Patient-Reported Outcomes for Refractory Juvenile-Onset Systemic Sclerosis (jSSc) 6 Months to 2 Years After Autologous Stem Cell Transplantation (ASCT)

Kathryn Torok[1], Paulina Horvei[1], Franziska Rosser[1], Kirsten Rose-felker[2], Vibha Sood[2], Adam Olsen[2], Nicole Hogue[2], Vickie Vandergrift[2], Lauren Farver[2], Devin Mcguire[2], Jonathan Li[3], Haley Havrilla[2], Jessie Alexander[4], Shawna McIntyre[2] and Paul Szabolcs[1], [1]University of Pittsburgh; UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA, [2]UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA, [3]University of Pittsburgh Medical Center, Pittsburgh, PA, [4]Stanford Children's Hospital, Palo Alto, CA

SESSION INFORMATION
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Session Title: Late-Breaking Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile-onset systemic sclerosis (jSSc) is an inflammatory, fibrotic, and vasculopathic disease that causes severe multi-organ dysfunction leading to significant morbidity and early mortality.When patients with adult SSc are refractory to available immunomodulatory therapies clinical studies support the use of autologous stem cell transplant (ASCT), but data is limited in jSSc. Herein, we report the outcomes of five jSSc patients 6 months to 2 years after receiving ASCT.

Methods: All patients were referred to our multidisciplinary pediatric scleroderma center, had disease refractory to ≥3 immunomodulatory therapies, and met criteria for ASCT by severity of lung or skin disease, or both (Table 1). Our ASCT protocol began with stem cell mobilization with cyclophosphamide and filgrastim, collected via pheresis. Conditioning chemoradiation was then administered per an IRB-approved individual treatment plan (Patients 1-3) or per our clinical trial NCT03630211 (Patients 4-5) with rituximab, anti-thymocyte globulin (ATG), total body irradiation 600 cGy with lung and kidney shielding, and cyclophosphamide or thiotepa +/- alemtuzumab. CD34+ selected cryopreserved autologous peripheral blood stem cell graft was infused on day 0. Antimicrobial prophylaxis and viral monitoring (EBV, CMV, adenovirus) followed institutional standards. Corticosteroids were discontinued by week 5 post-ASCT. Clinical outcomes and patient reported measures were collected at baseline (pre-ASCT), 6, 12 and 24 months-post ASCT.

Results: All 5 patients engrafted, with median neutrophil engraftment on day 10.8 (range 10-11) and median platelet engraftment (>50K) on day 18.8 (range 16-20). Patients globally improved across physician-measured and patient reported outcomes (Table 2). There was an average overall disease HAQ VAS improvement of 75% (range: 48-99%). In the skin/musculoskeletal domain, all 5 patients met the mRSS MCID by their 6-month visit, with an average of 87% improvement (range 74-100%), sustained at 1 and 2 years follow-up. In the gastrointestinal domain, four patients displayed improvement in their GIT by a mean 55% (range 38-68%) and one remained unchanged. Three had repeat lower esophageal manometry with an average improvement of 15 mmHg (range: 5-26 mmHg) associated with an average reduction in esophageal acid exposure by 67%. In the pulmonary domain, FVC overall remained relatively stable, however DLCO improved by >10% among two patients and 5-10% among two other patients. Global function, measured by the CHAQ from a rheumatology standpoint, demonstrated a significant mean reduction among all patients in CHAQ at 6 months by -0.60, surpassing the MCID threefold, and from a BMT standpoint, the performance functional score increased from a mean score of 68 (range: 50-80) to 86 (range: 70-100) toward healthy status.

Table 1. Baseline juvenile systemic sclerosis (jSSc) patient characteristics prior to autologous stem cell transplant (ASCT).

ID	Race	Ethnicity	Sex	Age at Onset (years)	Age at time of ASCT (years)	Disease Duration at time of ASCT (years)	Disease Subtype	Treatment Prior to ASCT	Major organ manifestations	Auto-antibody positivity	mRSS
Patient 1	White	Non-Hispanic	M	15	18	3	dcSSc	Cytoxan, Rituximab, Mycophenolate mofetil, Methotrexate	Progressive mod-severe ILD (DLCO 35%, FVC 52%), Mod-severe mRSS, joint contracture small to large joints, RP, GI esophageal dysmotility	Scl-70	24
Patient 2	Black	Non-Hispanic	F	7	15	8	lcSSc	Cytoxan, Mycophenolate mofetil, Methotrexate	Progressive ***severe*** ILD (DLCO 28%, FVC 48%), Skin thickening minimal after Cytoxan; GI esophageal dysmotility	ANA only	5
Patient 3	White	Hispanic	F	13	21	7	Overlap	Cytoxan, IVIG, Rituximab, Mycophenolate mofetil, Methotrexate, Baricitinib	Progressive skin thickening, weakness myositis, joint contracture small to large joints; restrictive lung disease from muscle weakness and ST; GI esophageal dysmotility	PM-Scl	23
Patient 4	White	Hispanic	F	11	18	7	dcSSc	Rituximab, Mycophenolate mofetil, IVIG, Prednisone	Progressive skin thickening, recent onset ILD, joint limitation, fatigue/endurance, mod-server RP with recurrent digital ulcers	Scl-70	28
Patient 5	Black	Non-Hispanic	F	16	18	2	Overlap	Rituximab, Mycophenolate mofetil, IVIG, Prednisone	Severe GI disease (TPN dependent), progressive skin thickening, myositis/myopathy, PHTN	U3-RNP	28

Abbreviations: dcSSc (diffuse cutaneous systemic sclerosis); lcSSc (limited cutaneous systemic sclerosis); Overlap (overlap SSc and dermatomyositis); Scl-70 (scleroderma-70 anti-topoisomerase antibody); PM-Scl (polymyositis-scleroderma overlap antibody); U3-RNP (U3 – ribonucleoprotein antibody, fibrillarin) ; ILD (interstitial lung disease); PHTN (pulmonary arterial hypertension)

Table 2. Baseline and post-ASCT Follow-up clinical variables and Patient reported outcomes (PROs).

	Patient 1			Patient 2			Patient 3			Patient 4		Patient 5	
	BL	1 yr	2 yr	BL	1 yr	2yr	BL	1 yr	2 yr	BL	1 yr	BL	6 mo
SKIN/MUSCULOSKELETAL													
mRSS	24	1	1	5	0	0	23	6	8	29	7	20	2
Finger to Palm distance (cm)	1.50	1.10	1.00	0.50	0	0	1.20	0.60	1.20	1.50	1.20	3.00	1.20
VAS scales HAQ*													
Pain (0-3)	0.78	0.00	0.00	0.73	0.00	0.10	1.90	1.44	2.56	1.35	0.63	0.42	0.21
Hand (0-3)	0.80	0.00	0.00	0.00	0.00	0.00	2.02	0.21	2.67	1.77	0.69	0.54	0.00
Disease (0-3)	2.69	0.10	0.04	1.53	0.30	0.19	0.56	0.13	0.98	1.65	1.17	2.31	0.90
Oral Aperture (cm)	6.00	6.00	6.50	4.00	5.00	5.00	4.00	5.00	4.50	4.50	5.00	2.50	3.50
VASCULAR													
Nailfold capillary change (dermatoscope)	Moderate dilation, drop out, hemorrhage	Mild dilation, hemorrhages, dropout	Mild dilation, hemorrhages, dropout	Mild dilation	Normal	Normal	Mild dilation, few spot hemorrhage	Few areas dilation	Digital pitting scarring	Drop out throughout, dilation	Three digital ulcers present	Dropoff and old dilation, disorganized	Dropoff and old dilation, disorganized
Raynaud's Vascular VAS HAQ (0-3)*	1.64	0.06	0.02	0.00	0.00	0.00	2.23	0.40	0.17	1.17	1.40	0.00	0.00
GASTROINTESTINAL													
LES pressure by manometry (mmHg) nl 13-43	8	13	-	14	27.6	-	15	41	-	4.5	-	6.5	-
24 hr pH probe													
% time esophageal exposed acid (nl <8%)	17	3	-	8	3	-	20	8.1	-	32	-	64	-
Longest acid reflux episode (mins)	48	2	-	14	17.5	-	106	27	-	43	-	183	-
GIT (GI scale) total (0-3)*	0.06	0.10	0.06	0.19	0.10	0.06	0.48	0.19	0.30	0.73	0.27	0.42	0.21
PULMONARY													
Pulmonary Function Tests													
FVC	52	53	58	48	50	46	40	46	41	84	79	76	81
DLCO	35	35	43	28	28	24	59	59	81	61	71	47	53
GLOBAL													
CHAQ (0-3)*	0.25	0.00	0.00	0.75	0.38	0.10	1.63	0.50	1.75	1.25	0.75	2.25	1.50
PERFORMANCE SCORE													
KPS (>16 yo)	80	90	100	N/A	N/A	N/A	70	90	70	80	90	60	80
LPS (<16 yo)	N/A	N/A	N/A	50	90	90	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Abbreviations: ASCT (autologous stem cell transplant); mRSS (modified Rodnan skin score); VAS (Visual Analog Scale); HAQ (Health Assessment Questionnaire); CHAQ (Childhood Health Assessment Questionnaire); LES (lower esophageal sphincter); GIT (scleroderma gastrointestinal tract instrument); FVC (forced vital capacity); DLCO (diffusing capacity for carbon monoxide); GLI2012 prediction equations used for both FVC and DLCO; KPS (Karnofsky Performance Scale); LPS (Lansky Play-Performance Scale). KPS and LPS scales are 0 to 100; higher number reflects normal function/ healthy status.

* Indicates a patient reported outcome. VAS scale on HAQ, GIT, CHAQ are 0 to 3; higher number reflects more interference of disease with function.

Conclusion: Among our cohort of refractory jSSc patients with moderate-severe disease, ASCT was a safe and effective intervention that provided sustained global disease modifying improvement throughout 2 years after transplant. Most notable improvements were in skin, gastrointestinal, pulmonary, and patient-reported functional domains.

Disclosure: K. Torok: None; **P. Horvei**: None; **F. Rosser**: None; **K. Rose-felker**: None; **V. Sood**: None; **A. Olsen**: None; **N. Hogue**: None; **V. Vandergrift**: None; **L. Farver**: None; **D. Mcguire**: None; **J. Li**: None; **H. Havrilla**: None; **J. Alexander**: None; **S. McIntyre**: None; **P. Szabolcs**: None.

Abstract Number: L07

3-year Results of Tapering TNFi to Withdrawal Compared to Stable TNFi Among Rheumatoid Arthritis Patients in Sustained Remission: A Multicenter Randomized Trial

Kaja Kjørholt[1], Nina Sundlisæter[1], Anna-Birgitte Aga[1], Joseph Sexton[1], Inge Christoffer Olsen[2], Åse Lexberg[3], Tor Magne Madland[4], Hallvard Fremstad[5], Christian A. Høili[6], Gunnstein Bakland[7], Cristina Spada[8], Hilde Haukeland[9], Inger Myrnes Hansen[10], Ellen Moholt[1], Karen Holten[1], Till Uhlig[1], Tore Kvien[1], Daniel Solomon[11], Désirée van der Heijde[12], Espen Haavardsholm[1] and **Siri Lillegraven**[1], [1]Center for treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway, [2]Department of Research Support for Clinical Trials, Oslo University Hospital, Oslo, Nepal, [3]Department of Rheumatology, Drammen Hospital, Vestre Viken HF, Drammen, Norway, [4]Department of Rheumatology, Haukeland University Hospital, Bergen, Norway, [5]Department of Rheumatology, Møre og Romsdal Hospital Trust, Ålesund, Norway, [6]Department of Rheumatology, Østfold Hospital Trust, Moss, Norway, [7]Department of Rheumatology, University Hospital of North Norway, Tromsø, Norway, [8]Department of Rheumatology, Revmatismesykehuset AS, Lillehammer, Norway, [9]Department of Rheumatology, Martina Hansens Hospital, Bærum, Norway, [10]Deptartment of Rheumatology, Helgelandssykehuset, Mo i Rana, Norway, [11]Division of Rheumatology, Brigham and Women's Hospital, Newton, MA, [12]Department of Rheumatology, Leiden University Medical Center, Meerssen, Netherlands

SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Late-Breaking Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Tapering of tumor necrosis factor inhibitor (TNFi) treatment in patients who have reached sustained remission is debated in current guidelines, and further data are needed regarding the long-term consequences of such strategies. Our aim was to assess the 3-year effect of tapering to withdrawal of TNFi versus continued stable TNFi on disease activity flare and remission status.

Methods: ARCTIC REWIND was a randomized, multicenter, open-label, non-inferiority trial including RA patients in sustained remission for ^{3}12 months on stable TNFi therapy, with no swollen joints at inclusion. Patients were randomized 1:1 to taper to withdrawal of TNFi (four months half-dose, thereafter withdrawal) or continue stable TNFi therapy, with scheduled visits every four months for 3 years. Full-dose TNFi therapy was reinstated if a flare occurred. The primary endpoint of the current study was disease activity flare over 3 years. A flare was defined as a combination of DAS >1.6 (loss of remission status), an increase in DAS ≥0.6 units (change above minimal detectable change) and ≥2 swollen joints, or if the physician and patient agreed that a clinically significant flare had occurred. Secondary endpoints included remission status (ACR/EULAR Boolean 2.0 and DAS), medication use and adverse events (AE). Flare-free survival was analyzed by Kaplan-Meier, flare by center adjusted Cox regression, and remission status by logistic regression adjusted for baseline status, analyzed in a per protocol population.

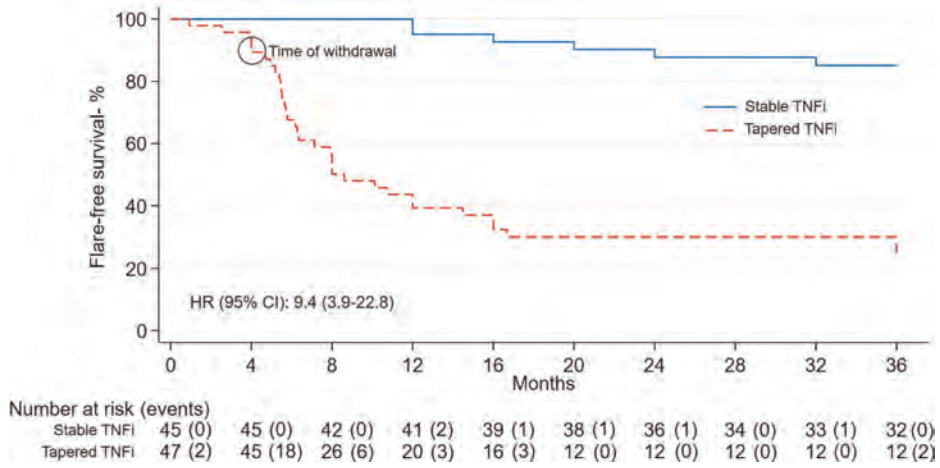
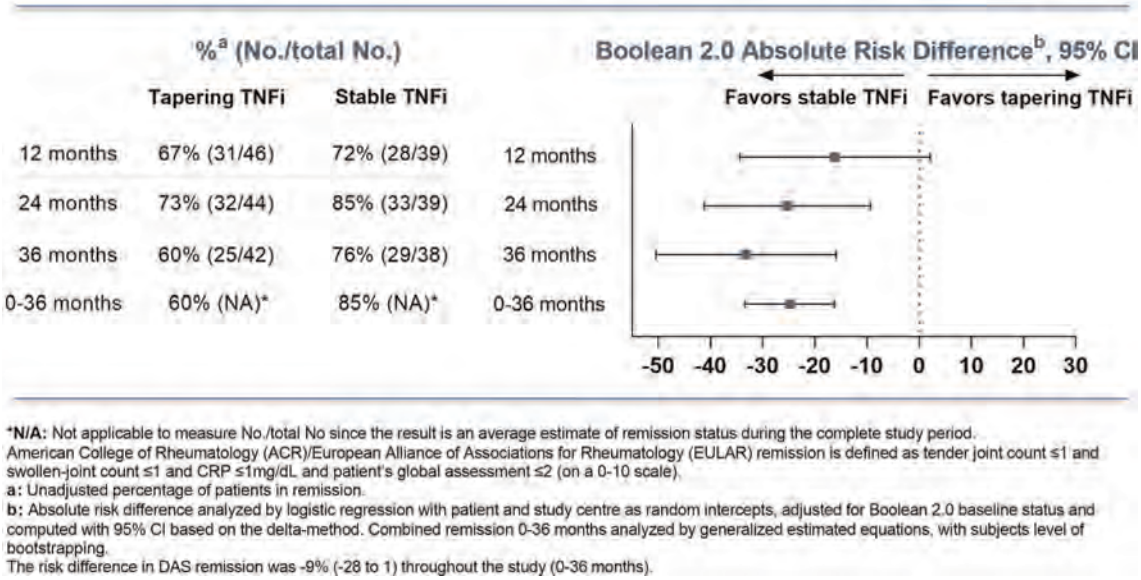


Figure 1: Proportions of patients without a flare over the study period



*N/A: Not applicable to measure No./total No since the result is an average estimate of remission status during the complete study period.
American College of Rheumatology (ACR)/European Alliance of Associations for Rheumatology (EULAR) remission is defined as tender joint count ≤1 and swollen-joint count ≤1 and CRP ≤1mg/dL and patient's global assessment ≤2 (on a 0-10 scale).
a: Unadjusted percentage of patients in remission.
b: Absolute risk difference analyzed by logistic regression with patient and study centre as random intercepts, adjusted for Boolean 2.0 baseline status and computed with 95% CI based on the delta-method. Combined remission 0-36 months analyzed by generalized estimated equations, with subjects level of bootstrapping.
The risk difference in DAS remission was -9% (-28 to 1) throughout the study (0-36 months).

Figure 2: ACR/EULAR Boolean 2.0 remission status

Table: Medication use

% (No./total No.)	Tapering TNFi	Stable TNFi
bDMARD/tsDMARD treatment at 3-year follow-up[1]:		
• No bDMARD/JAKi	29% (12/42)	0% (0/38)
• Same TNFi as baseline	62% (26/42)	89% (34/38)
• Other TNFi	10% (4/42)	5% (2/38)
• JAKi	0% (0/42)	5% (2/38)
csDMARD co-medication increase at 3-years follow-up compared to baseline[1]	8% (3/42)	3% (1/38)
Glucocorticoids during the study:		
- ≥1 treatment period with systemic glucocorticoids	23% (11/47)	13% (6/45)
- ≥1 intraarticular glucocorticoids injections	46% (21/47)	23% (10/45)

[1]The analyses were performed in patients that completed 3-years follow up in a per-protocol population

Abbrevations:
bDMARD: biological disease-modifying antirheumatic drug
tsDMARD: targeted synthetic disease-modifying antirheumatic drug
csDMARD: conventional synthetic disease-modifying antirheumatic drug
JAKi: Janus Kinase inhibitor

Results: Of 99 randomized patients, 92 received the allocated therapy, and 80 (87%) completed 3-year follow-up. Mean baseline DAS was 0.8 in the tapering TNFi group, and 0.9 in the stable TNFi group. csDMARD co-medication was used by 89% in the tapering group and 91% in the stable group. After 3 years, 25% (95% CI: 13 to 38) remained flare-free in the tapering TNFi group compared to 85% (70 to 93) in the stable TNFi group (Fig 1), with corresponding hazard ratio for flare of 9.4 (3.9 to 22.8). Most patients regained DAS remission within the next visit after a flare (81% in tapering group, 67% in stable group). We observed significantly lower Boolean 2.0 remission rates in the tapering TNFi group than the stable TNFi group throughout the study period (Fig 2), adjusted risk difference 0-36 months -25% (-33 to -16), p< 0.001 (Boolean 1.0 revealed similar results). Systemic glucocorticoids (≥1 treatment period during the study) were used by 23% in the tapering TNFi group and 13% in the stable TNFi group during the study, and 10% switched to other types of TNFi or JAK inhibitor treatment in the tapering group, and 11% in the stable group (Table). AE/serious AE occurred in 81%/21% of the patients in the tapering group, and 89%/11% of the patients in the stable group.

Conclusion: A large majority of RA patients in remission tapering TNFi to withdrawal experienced a flare within 3 years, while a minority of patients receiving stable TNFi treatment flared over the same time period. Even though most patients regained remission within the next visit after a flare, TNFi tapering was associated with significantly lower Boolean 2.0 remission rates throughout the study. These findings do not support tapering of TNFi treatment among RA patients in sustained remission.

Disclosure: K. Kjørholt: None; **N. Sundlisæter**: None; **A. Aga**: AbbVie, 6, Lilly, 6, Novartis, 6, Pfizer, 6; **J. Sexton**: None; **I. Olsen**: Dilafor AB, 2, European Clinical Research Infrastructure Network, 12, Attending meetings and/or travel, European Medicines Agency, 12, Support for attending meetings/and or travel; **Å. Lexberg**: None; **T. Madland**: None; **H. Fremstad**: None; **C. Høili**: None; **G. Bakland**: None; **C. Spada**: UCB, 1; **H. Haukeland**: UCB, 12, Advisory Board; **I. Hansen**: None; **E. Moholt**: None; **K. Holten**: None; **T. Uhlig**: Galapagos, Lilly, Pfizer, UCB, 1, 2; **T. Kvien**: AbbVie, 1, 2, BMS, 5, Galapagos, 2, 5, Grünenthal, 6, janssen, 2, Novartis, 5, Pfizer, 5, Sandoz, 6, UCB, 2; **D. Solomon**: CorEvitas, 5, Janssen, 5, moderna, 5, Novartis, 5; **D. van der Heijde**: AbbVie, 2, Argenx, 2, Bayer, 2, Bristol-Myers Squibb(BMS), 2, Galapagos, 2, Glaxo-Smith-Kline, 2, Imaging Rheumatology bv, 12, Director, Janssen, 2, Lilly, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; **E. Haavardsholm**: AbbVie, 1, Eli Lilly, 1, UCB, 1; **S. Lillegraven**: None.

Abstract Number: L08

Early Clinical Development of CIT-013, a First in Class NETosis Inhibitor, in a Randomized Phase I Dose Escalation Study in Healthy Volunteers Demonstrating Potent Inhibition of LPS Induced Neutrophil Extracellular Trap Formation

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Late-Breaking Poster
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Background/Purpose: Aberrant Neutrophil Extracellular Traps (NETs) production contributes to the pathophysiology of multiple inflammatory and autoimmune diseases such as Rheumatoid arthritis (RA) Hidradenitis suppurativa (HS), Systemic Lupus Erythematosus and ANCA-Associated Vasculitis. Here we report the first in human studies of a humanized

monoclonal antibody (CIT-013) with high affinity for citrullinated histones H2A and H4. CIT-013 inhibits NET formation and accelerates the clearance of NETs and netting neutrophils to lower NET tissue burden in vivo with significant anti-inflammatory consequences in pre-clinical studies (Chirivi et al 2021; DOI 10.1038/s41423-020-0381-3).

The objectives of the studies were:

- Part A: to assess safety, tolerability, andpharmacokinetics (PK) of intravenous (IV) single ascending doses of CIT-013.
- Part B: to assess safety, tolerability, PK, and pharmacodynamics (PD) by inducing systemic NET formation by nano-dosing lipopolysaccharide (LPS) after single IV doses of CIT-013.
- Part C: to evaluate safety, tolerability, bioavailability, and PK of single subcutaneous (SC) doses of CIT-013.

Methods: The study was a randomized, double-blind, placebo-controlled, phase I study with a single dose of CIT-013 in healthy volunteers. In part A, single ascending doses of 0.1, 0.3, 1.0, 1.8 and 3.0 mg/kg CIT-013 or placebo were administered IV. In part B, 0.3 or 0.9 mg/kg CIT-013 or placebo were given IV before 2ng/kg LPS. LPS will trigger the innate immune system resulting in measurable circulating NET components in the blood. In part C, 50 or 100 mg CIT-013 or placebo was administrated SC. Endpoints were safety, tolerability, and PK in all three parts, plus PD in part B.

Results: In total 73 healthy volunteers were dosed (Figure 1) and no severe, or Serious Adverse Events (SAEs) were reported. In part A, IV administration of CIT-013 was well tolerated up to 0.3 mg/kg alone, and 0.9 mg/kg with premedication. Dose limiting toxicity was seen at doses greater than 0.9 mg/kg with chest discomfort associated with elevated cytokines, CRP and temperature as the most common AEs. CIT-013 given SC at 50 mg or 100 mg was well tolerated. The only AEs of note were mild injection site reactions. PK was consistent with what would be expected from an IgG1 human monoclonal antibody with a half-life of approximately 7 days. The bioavailability of 100 mg given SC was 66% compared to IV administration and equated to approximately 0.7 mg/kg given IV (Figure 2). CIT-013 markedly reduced LPS induced levels of systemic NET components, equally well at 0.3 and 0.9 mg/kg, demonstrating effective target engagement (Figure 3).

Conclusion: CIT-013 is well tolerated up to 0.3 mg/kg intravenously and up to 0.9 mg/kg with pre-medication. Dose limiting toxicity was seen when given intravenously, with chest discomfort associated with elevated cytokines, CRP and temperature which was markedly reduced by subcutaneous administration. Near complete inhibition of circulating NET components at 0.3 and 0.9 mg/kg CIT-013 in the LPS challenge study showed effective target engagement. These data form the basis for further development of CIT-013 in RA and HS.

Part /Cohort	N	Gender		Age (years)		BMI (kg/m²)	
		Male	Female	mean	SD	mean	SD
Part A 0.1 mg/kg	n=3	3	0	34.3	15.70	23.5	4.86
Part A 0.3 mg/kg	n=6	6	0	29.0	9.67	24.6	4.60
Part A 0.9 mg/kg	n=12	4	8	35.4	10.85	23.7	2.30
Part A 1.8 mg/kg	n=3	2	1	36.7	15.01	21.5	1.51
Part A 3.0 mg/kg	n=1	1	0	55.0	NA	21.2	NA
Part A placebo	n=12	9	3	34.0	13.51	24.0	2.02
Part B 0.3 mg/kg	n=3	0	3	24.0	3.61	21.2	1.31
Part B 0.9 mg/kg	n=8	8	0	31.9	12.35	23.5	3.39
Part B placebo	n=9	7	2	27.6	9.61	23.6	3.16
Part C 50 mg	n=6	5	1	35.0	12.46	25.6	3.21
Part C 100 mg	n=6	2	4	29.3	8.16	22.7	1.90
Part C placebo	n=4	2	2	32.5	8.66	24.2	3.82

Figure 1. Baseline demographic characteristics

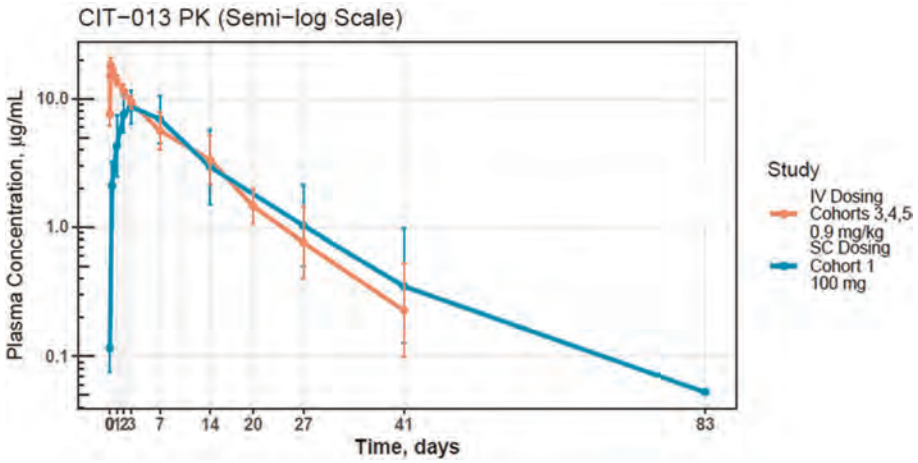

Figure 2. PK Intravenous and subcutaneous administration of CIT-013

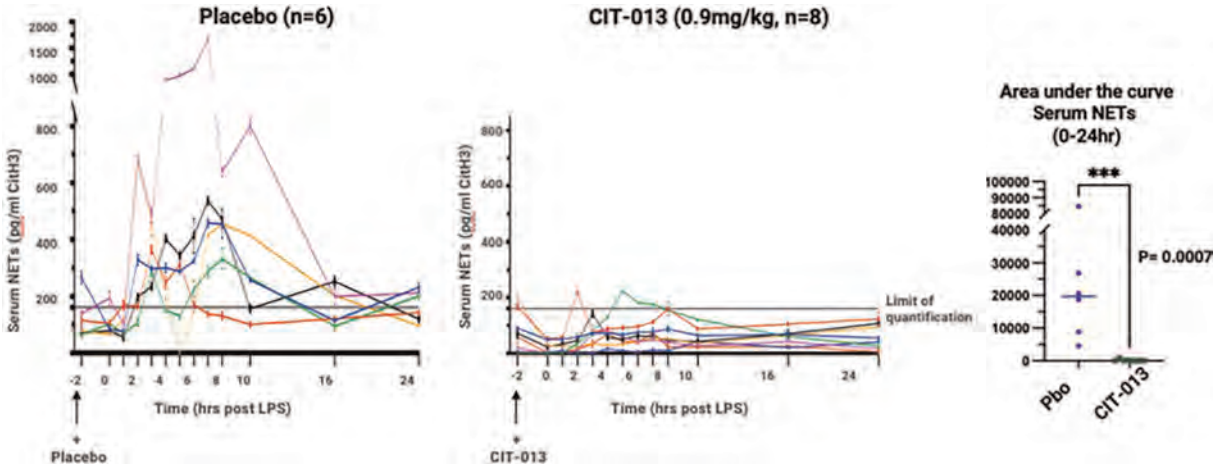

Figure 3. NET components in second LPS cohort

Disclosure: L. Middelink: Cityll BV, 2, 11; **R. Chirivi**: Cityll BV, 3, 4, 8, 11; **H. van Es**: Cityll BV, 1, 4, 8, 11; **E. Meldrum**: Cityll BV, 3, 4, 11; **P. van Zandvoort**: Cityll BV, 3, 11; **T. Bruurmijn**: Cityll BV, 3, 11; **M. Moerland**: None; **P. Round**: Cityll BV, 2, 4, 11.

Abstract Number: L09

Efficacy and Safety of LNK01001 in Chinese Patients with Moderate to Severe Active Rheumatoid Arthritis with an Inadequate Response to Conventional Synthetic DMARDs: 24-week Results from a Phase 2 Trial

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Hospital of Shanxi Medical University, Taiyuan, China, [6]Beijing Hospital, Beijing, China, [7]Jiujiang No. 1 People's Hospital, Jiujiang, China, [8]Hunan Provincial People's Hospital, Changsha, China, [9]Jining First People's Hospital, Jining, China, [10]Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, [11]First Affiliated Hospital of Jilin University, Changchun, China, [12]Qilu Hospital of Shandong University, Jinan, China, [13]Central Hospital of Xuzhou City, Xuzhou, China, [14]The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China, [15]The First Affiliated Hospital of Bengbu Medical College, Bengbu, China, [16]Chenzhou First People's Hospital, Binzhou, China, [17]Sun Yat-Sen Memorial Hospital, Guangzhou, China, [18]Shantou University Medical College No.1 Affiliated Hospital, Shantou, China, [19]Yanbian University Affiliated Hospital, Yanbian, China, [20]guangdong second provincial general hospital, Guangzhou, China, [21]Huai'an First People's Hospital, Huaian, China, [22]The First Affiliated Hospital of Baotou Medical College, Baotou, China, [23]The First Affiliated Hospital of Soochow University, Suzhou, China, [24]The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China, [25]Tianjin Medical University General Hospital, Tianjin, China, [26]Huizhou Central People's Hospital, Huizhou, China, [27]Peking University Shougang Hospital, Beijing, China, [28]The First Hospital of China Medial University, Shenyang, China, [29]Guangdong Provincial People's Hospital, Guangzhou, China, [30]Lynk Pharmaceuticals Co., Ltd., Hangzhou, China, [31]Lynk Pharma, Hangzhou, China, [32]Lynk Pharma, Saint Louis, MO, [33]Lynk Pharma, Nanjing, China

SESSION INFORMATION

Session Date: Tuesday, November 14, 2023
Session Title: Late-Breaking Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: LNK01001 is a selective oral JAK1 inhibitor in clinical development for treating autoimmune and inflammatory diseases, including rheumatoid arthritis (RA). Here, we report the 24-week efficacy and safety results of LNK01001 in patients with moderate to severe active RA who had an inadequate response to csDMARDs.

Methods: Eligible participants aged 18 to 75 with a diagnosis of moderate to severe active RA who met ACR/EULAR 2010 criteria and had an inadequate response to csDMARDs, were randomized (1: 1: 1) to receive LNK01001 12mg or 24mg twice daily (BID), or placebo for 12 weeks, followed by a 12-week extension treatment with LNK01001 12mg or 24mg. The primary endpoint was the proportion of patients achieving an ACR20 response at Week 12.

Results: All 156 patients randomized were included in the analysis. The mean age was 52.4 years, and 76.9% were female, mean DAS28-CRP score was 5.884. Baseline characteristics were similar across treatment groups. At week 12, a significantly higher proportion of patients achieved ACR20, ACR50 and ACR70 in LNK01001 12 mg and 24 mg groups compared with the placebo group (ACR20: 60.0% [95%CI: 45.2, 73.6], 73.1% [95%CI: 59.0, 84.4], vs 31.5% [95%CI: 19.5, 45.6], both doses $p< 0.01$; ACR50: 40.0% [95%CI: 26.4, 54.8], 42.3% [95%CI: 28.7, 56.8], vs 9.3% [95%CI: 3.1, 20.3], both doses $p< 0.001$; and ACR70: 12.0% [95%CI: 4.5, 24.3], 23.1% [95%CI: 12.5, 36.8], vs 1.9% [95%CI: 0.0, 9.9], both doses $p < 0.05$). A statistically significant difference was reached as early as Week 1 in ACR20 for both doses of LNK01001 vs placebo (18.0% [95%CI: 8.6, 31.4], 23.1% [95%CI: 12.5, 36.8], vs 0% [95%CI: 0, 6.6], both doses $p < 0.01$). Disease activity reduction measured by DAS28-CRP and functional ability improvement of HAQ-DI were significant in patients treated with LNK01001 compared to patients treated with placebo (-2.518, -2.614, vs -1.263, both doses $p < 0.0001$; and -0.64, -0.73, vs -0.34, both doses $P < 0.01$). During extension treatment, the proportion of patients achieving ACR20/50/70, DAS28 (≤ 3.2 and < 2.6), SDAI (≤ 11 and ≤ 3.3) and CDAI (≤ 10 and ≤ 2.8) response increased steadily over time. At week 24, 91.1% (95%CI: 78.8, 97.5) and 90.7% (95%CI: 77.9, 97.4) of patients achieved ACR20 in LNK01001 12mg and 24mg group, respectively.

The most frequently reported TEAE in patients receiving LNK01001 was hyperlipidemia. No serious infection, malignancy, venous thromboembolism or major adverse cardiovascular events were reported up to 24 weeks.

Conclusion: Treatment with LNK01001 12 mg or 24 mg BID up to 24 weeks in patients with moderate to severe active RA and an inadequate response to csDMARDs were generally safe, and well tolerated with most TEAEs being mild to moderate. Both doses were superior to placebo in reducing the severity of rheumatoid arthritis over a period of 12 weeks across multiple efficacy end points.

Disclosure: C. Wu: None; **X. Wang**: None; **J. Hu**: None; **X. Shi**: None; **X. Wang**: None; **X. Zhang**: None; **J. Liu**: None; **H. Rao**: None; **J. Zhao**: None; **R. Du**: None; **Z. Jiang**: None; **H. liu**: None; **L. Liu**: None; **S. Liu**: None; **C. Xie**: None; **X. Liao**: None; **L. Dai**: None; **Z. Hou**: None; **J. Jin**: None; **T. Li**: None; **D. Meng**: None; **Y. Wang**: None; **J. Wu**: None; **J. Gu**: None; **W. Wei**: None; **Y. Zhuang**: None; **K. Wang**: None; **R. Zhang**: None; **X. Zhang**: None; **H. Wei**: None; **Z. Wan**: Lynk Pharmaceuticals, 3, 4, 8, 10; **J. Wang**: None; **M. Vazquez**: None; **H. Wu**: None; **X. Zeng**: None.

Abstract Number: L10

Dazodalibep, a CD40L Antagonist, in a Phase 2, Randomized, Double-Blind, Placebo-Controlled, Crossover Trial of Subjects with Sjögren's Disease Having Unacceptable Symptomatic Burden but Limited Extraglandular Organ Involvement

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SESSION INFORMATION
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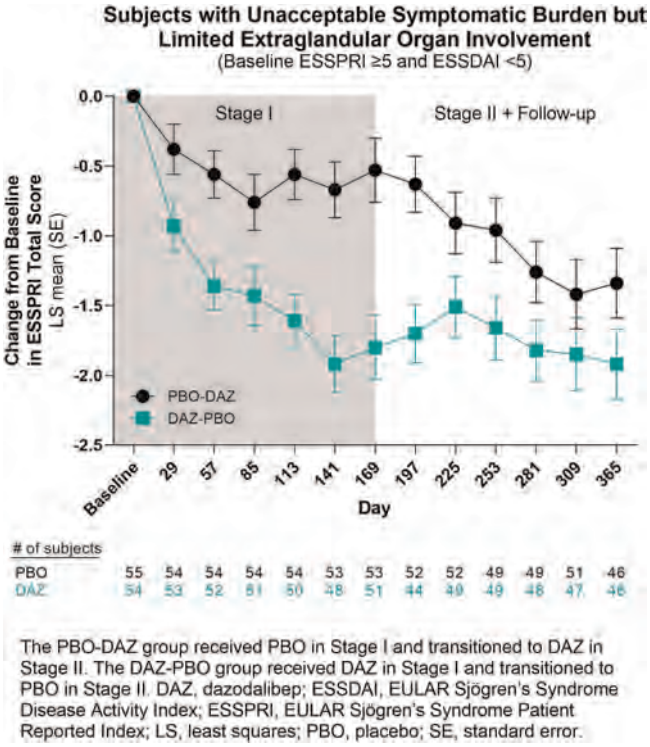
Background/Purpose: Dazodalibep (DAZ) is a non-antibody fusion protein that acts as a CD40L antagonist and blocks costimulatory signals between immune cells, including T cells, B cells, and antigen-presenting cells. Previously, we reported that the primary endpoint, the change from baseline to Day 169 in the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI), was achieved in the population of subjects with unacceptable symptomatic burden but limited extraglandular organ involvement (NCT04129164).[1] Here, we report the efficacy and safety of DAZ therapy in this population through the crossover period of the study.

Methods: We performed a randomized, double-blind, placebo-controlled, crossover study to evaluate DAZ therapy in adult subjects with Sjögren's Disease having an ESSPRI score ≥ 5 and EULAR Sjögren's Syndrome Disease Activity Index score < 5. Eligible subjects were randomized 1:1 to receive intravenous DAZ 1500 mg or PBO Q2W x 3 doses, and then Q4W x 4 additional doses (Stage I). Starting on Day 169, subjects initially randomized to DAZ transitioned to PBO Q4W x 5 doses (DAZ-PBO) and subjects randomized to PBO were switched to DAZ Q4W x 5 doses (PBO-DAZ); all were then followed for 12 weeks (Stage II).



Adjusted mean change from baseline in ESSPRI total score.

Treatment-emergent AEs in Stage II Preferred term, n (%)	PBO-DAZ N=52	DAZ-PBO N=48
Nasopharyngitis	2 (3.8)	6 (12.2)
COVID-19	9 (17.3)	5 (10.2)
Arthralgia	1 (1.9)	3 (6.1)
Constipation	0	3 (6.1)
Gastroesophageal reflux disease	0	3 (6.1)
Urinary Tract Infection	2 (3.8)	3 (6.1)
Headache	4 (7.7)	1 (2.0)

The PBO-DAZ group received PBO in Stage I and transitioned to DAZ in Stage II. The DAZ-PBO group received DAZ in Stage I and transitioned to PBO in Stage II. AE, adverse event; DAZ, dazodalibep; PBO, placebo.

Most frequently reported treatment-emergent AEs occurring in ≥5% of subjects.

Results: A total of 109 eligible subjects were randomized (DAZ, N=54; PBO, N=55), with 102 (93.6%) completing Stage I and 94 (86.2%) completing Stage II. In the PBO-DAZ group, the change from baseline in ESSPRI total score (LS mean ± SE) improved from –0.5 ± 0.2 at Day 169 to –1.3 ± 0.3 at Day 365. In the DAZ-PBO group, the change from baseline in ESSPRI total score achieved during Stage I was sustained during the crossover period through Day 365 (Day 169: –1.8 ± 0.3; Day 365: –1.9 ± 0.3). In the PBO-DAZ group, the proportion of subjects achieving an ESSPRI response (≥1 point or ≥15% improvement in ESSPRI total score) at Day 169 was 32.7% (18/55) and continued improvement was observed during the crossover period (Day 365: 50.0% [26/52]). In the DAZ-PBO group, the proportion of subjects achieving an ESSPRI response at Day 169 was 66.7% (36/54) and this treatment effect was largely sustained through the crossover period (Day 365: 57.1% [28/49]). During Stage II, the subjects in the PBO-DAZ group exhibited improvement in the Functional Assessment of Chronic Illness Therapy-Fatigue score, and Patient's Global Impression of Severity score during the crossover period.

In Stage II, 66 of 101 subjects reported an AE (DAZ-PBO: 32 [65.3%]; PBO-DAZ: 34 [65.4%]) and the majority were mild/moderate in severity. Two SAEs were reported in two subjects in the DAZ-PBO group (urinary tract infection, invasive ductal breast carcinoma), and one SAE was reported in the PBO-DAZ group (atrial flutter). One subject in the PBO-DAZ group discontinued the study during Stage II due to an AE (rash).

Conclusion: The results during Stage II provide further evidence of the clinical efficacy of DAZ in Sjögren's disease and support the primary endpoint result. DAZ was generally safe and well tolerated in Stage II, although larger trials of DAZ therapy for this indication are warranted to further explore its safety profile and confirm its clinical efficacy.

References:
1. St. Clair EW et al. *Ann Rheum Dis* 2023; 82(Suppl 1):201.

Disclosure: E. St. Clair: Bristol-Myers Squibb (BMS), 2, CSL Behring, 2, Horizon Therapeutics, 2, Resolve Therapeutics, 2, Sonoma Biotherapeutics, 2, UpToDate, 9; **L. Wang**: Horizon Therapeutics, 3, 11; **I. Alevizos**: Horizon Therapeutics, 3, 11; **W. Rees**: Horizon Therapeutics, 3, 11; **A. Baer**: Bristol-Myers Squibb (BMS), 2, iCell Gene Therapeutics, 2; **W. Ng**: Abbvie, 5, Argenx, 2, GlaxoSmithKlein (GSK), 5, Janssen, 2, Novartis, 2, Resolve Therapeutics, 2, Sanofi, 2; **G. Noaiseh**: Novartis, 2; **C. Baldini**: GlaxoSmithKlein (GSK), 2, Sanofi, 2.

Abstract Number: L11

Risk of Cardiovascular Events According to Biological Agent Exposure in Patients with Ankylosing Spondylitis: A Korean Population-based Study

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Late-Breaking Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with ankylosing spondylitis (AS) have a higher risk of cardiovascular events than controls. Although biological disease-modifying anti-rheumatic drugs (bDMARDs) are efficacious in treating AS, their effect on risk of cardiovascular events remains unclear. This study evaluated the risk of cardiovascular events according to tumour necrosis factor inhibitors (TNFis) and interleukin-17 inhibitors (IL-17is) exposures in patients with AS.

Methods: We extracted the data of 43,502 patients diagnosed with AS from 2010 onwards and without prior history of cardiovascular events from the Korean nationwide database. Cardiovascular events were defined as incident myocardial infarctions or strokes. Patients were followed-up through 2021. We used multivariable time-dependent Cox models to estimate the adjusted hazard ratios [HRs] and 95% confidence intervals [CIs] for cardiovascular events, comparing TNFis exposure (vs. bDMARDs non-exposure) and IL-17is exposure (vs. bDMARDs non-exposure and vs. TNFis exposure).

Results: The incidence rates of cardiovascular events in periods of bDMARDs non-exposure, TNFis exposure, and IL-17is exposure were 18.66, 8.92, and 12.87 per 10,000 person-years, respectively. TNFis exposure (vs. bDMARDs non-exposure) was significantly associated with a lower risk of cardiovascular events (adjusted HR 0.697, 95% CI 0.499–0.974), whereas IL-17is exposure (vs. bDMARDs non-exposure) was not (adjusted HR 0.958, 95% CI 0.133–6.888). The risk of cardiovascular events did not differ between IL-17is and TNFis exposures (adjusted HR 1.373, 95% CI 0.188–10.029).

Table 1. Characteristics of the study population

	N = 43,502
Demographics	
Age, years, mean ± SD	41.2±16.31
Male, n (%)	30,740 (70.7)
Comorbidities	
Hypertension, n (%)	8,696 (20.0)
Type 2 diabetes, n (%)	3,138 (7.2)
Dyslipidaemia, n (%)	6,765 (15.6)
Chronic kidney disease, n (%)	622 (1.4)
Medications	
Methotrexate, n (%)	6,793 (15.6)
Sulfasalazine, n (%)	25,400 (58.4)
Glucocorticoids, n (%)	36,042 (82.9)
Non-selective NSAIDs other than naproxen, n (%)	39,456 (90.7)
Naproxen, n (%)	6,827 (15.7)
Selective COX-2 inhibitors, n (%)	22,394 (51.5)
Anti-platelets, n (%)	5,180 (11.9)
Anticoagulants, n (%)	917 (2.1)
Statins, n (%)	12,345 (28.4)
ACE inhibitors or ARBs, n (%)	10,527 (24.2)
Beta-blockers, n (%)	3,319 (7.6)
SGLT2 inhibitors, n (%)	887 (2.0)
GLP1 receptor agonists, n (%)	125 (0.3)

ACE, angiotensin-converting enzyme; ARBs, angiotensin II receptor blockers; COX-2, cyclooxygenase-2; GLP1, glucagon-like peptide-1; NSAIDs, non-steroidal anti-inflammatory drugs; SD, standard deviation; SGLT2, sodium-glucose cotransporter-2

Table 2. Crude incidence rate of cardiovascular events

	Events	Person-years	Incidence rate per 10,000 person-years (95% CI)
MI or stroke			
Non-exposure	336	180,076.9	18.659 (16.665–20.652)
TNFis	42	47,074.2	8.922 (6.225–11.619)
IL-17is	1	777.2	12.866 (0.000–38.069)
MI			
Non-exposure	174	180,719.5	9.628 (8.198–11.058)
TNFis	20	47,152.4	4.242 (2.383–6.100)
IL-17is	1	777.5	12.862 (0.000–38.054)
Stroke			
Non-exposure	165	180,076.9	9.139 (7.745–10.533)
TNFis	22	47,074.2	4.666 (2.717–6.616)
IL-17is	0	777.2	0.000 (0.000–0.000)

CI, confidence interval; IL-17is, interleukin-17 inhibitors; MI, myocardial infarction; TNFis, tumour necrosis factor inhibitors

Table 3. Risk of cardiovascular events according to bDMARDs exposure

	Univariable model		Multivariable model	
	Crude HR(95% CI)	p	Adjusted HR*(95% CI)	p
MI or stroke				
TNFis (vs. non-exposure)	0.478 (0.347–0.660)	<0.001	0.697 (0.499–0.974)	0.034
IL-17is (vs. non-exposure)	0.734 (0.103–5.247)	0.758	0.958 (0.133–6.888)	0.966
IL-17is (vs. TNFis)	1.535 (0.211–11.183)	0.672	1.373 (0.188–10.029)	0.755
MI				
TNFis (vs. non-exposure)	0.429 (0.270–0.681)	<0.001	0.623 (0.388–0.999)	0.0499
IL-17is (vs. non-exposure)	1.149 (0.160–8.247)	0.890	1.406 (0.194–10.197)	0.736
IL-17is (vs. TNFis)	2.681 (0.338–20.053)	0.337	2.257 (0.300–16.974)	0.400
Stroke				
TNFis (vs. non-exposure)	0.527 (0.338–0.823)	0.0048	0.796 (0.500–1.266)	0.336
IL-17is (vs. non-exposure)	-		-	
IL-17is (vs. TNFis)	-		-	

*Adjusted for age, sex, hypertension, type 2 diabetes, dyslipidaemia, chronic kidney disease, methotrexate, sulfasalazine, glucocorticoids, non-selective non-steroidal anti-inflammatory drugs other than naproxen, naproxen, selective cyclooxygenase-2 inhibitors, anti-platelets, anticoagulants, statins, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, beta-blockers, sodium-glucose cotransporter-2 inhibitors, and glucagon-like peptide-1 receptor agonists

bDMARDs, biological disease-modifying anti-rheumatic drugs; CI, confidence interval; HR, hazard ratio; IL-17is, interleukin-17 inhibitors; MI, myocardial infarction; TNFis, tumour necrosis factor inhibitors

Conclusion: TNFis exposure (vs. bDMARDs non-exposure) was associated with approximately 30% lower risk of cardiovascular events in patients with AS. IL-17is exposure had no significant association with the risk of cardiovascular events compared to bDMARDs non-exposure or TNFis exposure.

Disclosure: O. Kwon: None; **H. Lee**: None; **J. Yang**: None; **Y. Park**: None; **M. Park**: None.

Abstract Number: L12

Efficacy and Safety Outcomes of TAK-279, a Selective Oral Tyrosine Kinase 2 (TYK2) Inhibitor, from a Randomized, Double-blind, Placebo-controlled Phase 2b Trial in Patients with Active Psoriatic Arthritis

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LLC, San Diego, CA, [10]Takeda Development Center Americas, Inc., Boston, MA, [11]Rheumazentrum Ruhrgebiet, Ruhr-University Bochum, Bochum, Germany

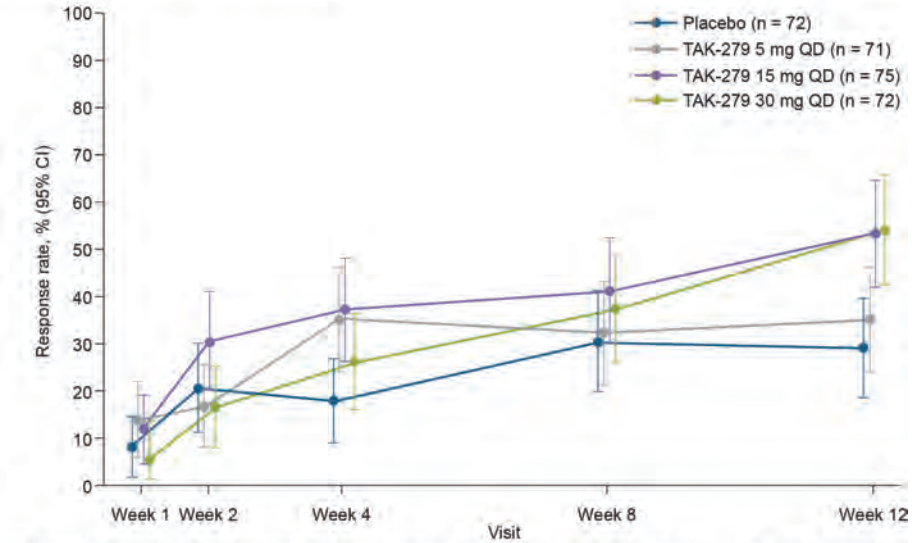
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Late-Breaking Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: TYK2 mediates signaling by key cytokines involved in the pathogenesis of immune-mediated inflammatory diseases such as psoriatic arthritis (PsA) and psoriasis (PsO). TAK-279 is a highly selective, oral, allosteric TYK2 inhibitor shown to be clinically effective with an acceptable safety profile in a phase 2b trial in patients with moderate-to-severe PsO (Armstrong *et al*. AAD 2023).The current study evaluated efficacy and safety of TAK-279 in patients with active PsA treated over 12 weeks.

Methods: This phase 2b randomized, multicenter, double-blind, placebo (PBO)-controlled, dose-ranging study (NCT05153148) was conducted at 45 sites in North America and Europe. Eligible patients were aged ≥ 18 years, with PsA symptoms for ≥ 6 months prior to screening, met CASPAR criteria, and had ≥ 3 tender and ≥ 3 swollen joint counts (TJC/SJC) at enrollment despite prior NSAID, DMARD or biologic treatment. Patients were randomized 1:1:1:1 to receive oral TAK-279 5 mg, 15 mg, 30 mg, or PBO, once daily for 12 weeks. Primary endpoint: ACR 20 response at Week 12. Secondary endpoints at Week 12 included: ACR 50, ACR 70, PASI 75 responses (in patients with ≥ 3% BSA), change from baseline in TJC/SJC, physician global assessment (PhGA) of PsA, and safety.

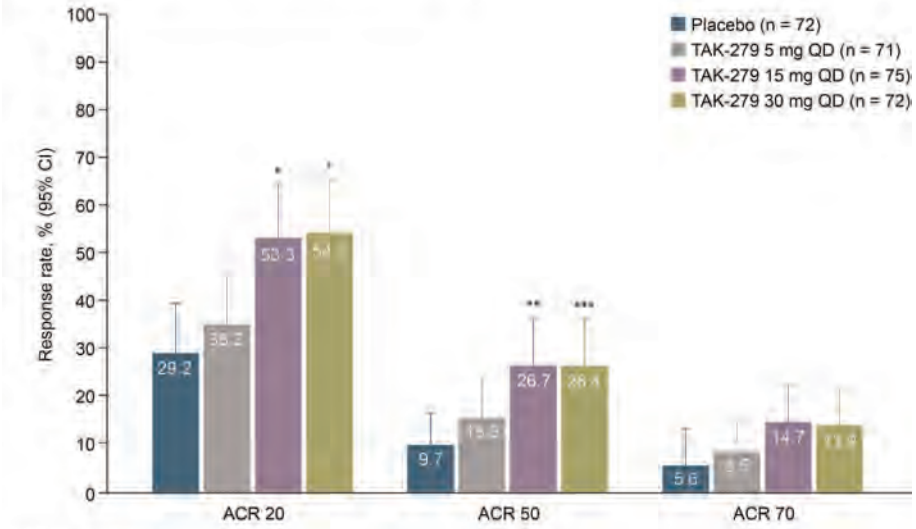
Results: In total, 290 patients were randomized and treated; 245 completed 12 weeks' treatment. Baseline characteristics were generally comparable across groups (except for a lower mean TJC in the 30 mg group); 58.6% had BSA ≥ 3% (of which mean baseline PASI score was 6.2), and 32.1% had prior biologic use (20.7% TNFis). Mean baseline hsCRP was 7.0 mg/L; 45.9% had hsCRP ≥ 3 mg/L. The primary endpoint was met with a significantly greater proportion of patients achieving ACR 20 with TAK-279 15 mg and 30 mg vs PBO (53.3% and 54.2% vs 29.2%, both $p = 0.002$; **Figure 1**). ACR

Figure 1. ACR 20 response over time.



The ACR20 is a composite measure defined as both improvement of 20% in the number of tender and number of swollen joints, and a 20% improvement in three of the following five criteria: patient global assessment of psoriatic arthritis, physician global assessment of psoriatic arthritis, patient global assessment of psoriatic arthritis pain, Health Assessment Questionnaire - Disability Index and high-sensitivity C-reactive protein.
CI, confidence interval.

Figure 2. ACR 20/50/70 responses at Week 12.



*ACR 20: $p = 0.002$ versus placebo.
p values for ACR 50 are nominal: **$p = 0.005$, ***$p = 0.009$ versus placebo.
CI, confidence interval; QD, once daily.

Table 1. Safety overview.

	Placebo (n = 72)	TAK-279 5 mg QD (n = 71)	TAK-279 15 mg QD (n = 75)	TAK-279 30 mg QD (n = 72)
Any TEAE, n (%)	39 (54.2)	42 (59.2)	45 (60.0)	56 (77.8)
Drug-related TEAEs, n (%)	11 (15.3)	15 (21.1)	20 (26.7)	29 (40.3)
TEAEs leading to study discontinuation, n (%)	1 (1.4)	0	3 (4.0)	5 (6.9)
Serious TEAEs, n (%)	4 (5.6)	4 (5.6)	3 (4.0)	2 (2.8)
At least one Grade 3 or higher TEAE	7 (9.7)	6 (8.5)	7 (9.3)	3 (4.2)
TEAEs leading to death, n	0	0	0	0
Most frequent TEAEs,* n (%)				
Nasopharyngitis	3 (4.2)	6 (8.5)	7 (9.3)	7 (9.7)
URTIs	2 (2.8)	8 (11.3)	3 (4.0)	7 (9.7)
Headache	3 (4.2)	2 (2.8)	6 (8.0)	4 (5.6)
Rash	0	3 (4.2)	6 (8.0)	4 (5.6)
Blood CPK increased	3 (4.2)	2 (2.8)	4 (5.3)	1 (1.4)
Dermatitis acneiform	0	0	2 (2.7)	6 (8.3)
Psoriatic arthropathy	5 (6.9)	0	2 (2.7)	1 (1.4)
Rash papular	0	1 (1.4)	3 (4.0)	4 (5.6)
Aphthous ulcer	0	0	1 (1.3)	6 (8.3)
Dermatitis allergic	0	1 (1.4)	1 (1.3)	4 (5.6)
Rash maculo-papular	0	0	2 (2.7)	4 (5.6)

*TEAEs occurring at ≥ 5% by preferred term in any treatment arm.
CPK, creatine phosphokinase; QD, once daily; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection.

50 response rates were also higher in the TAK-279 15 mg and 30 mg groups vs PBO ($p = 0.005$ and $p = 0.009$, respectively**; Figure 2).** PASI 75 response was highest in the 30 mg group vs other doses and PBO (45.7% [30 mg] and 28.3% [15 mg] vs 15.4% [PBO]; $p = 0.002$ and $p = 0.101$, respectively). A numerically higher proportion of patients treated with TAK-279 15 mg and 30 mg achieved ACR 70 than with PBO (**Figure 2**). Numerical reductions were observed in mean change from baseline in

the TJC/SJC in all groups, with higher reductions with the 15 mg and 30 mg doses vs PBO and 5 mg TAK-279. Improvements from baseline were seen in PhGA of PsA in all TAK-279 groups vs PBO (5 mg [p = 0.016]; 15 mg [p = 0.004]; 30 mg [p = 0.003]). Safety outcomes are summarized in **Table 1**. Nasopharyngitis, upper respiratory tract infections, headache and rash were the most common treatment-emergent adverse events (TEAEs) in TAK-279-treated patients. No opportunistic infections, major adverse cardiovascular events or differences in mean laboratory parameters of interest were observed, compared with PBO. Serious and grade 3 or higher TEAEs occurred infrequently and at a similar rate in the TAK-279 and PBO groups.

Conclusion: TAK-279 was well tolerated and demonstrated superior dose-dependent efficacy to PBO over 12 weeks of treatment in patients with active PsA. Its safety profile was consistent with that observed in the phase 2b PsO study.

Disclosure: A. Kivitz: AbbVie, 6, 12, Manuscript writing and educational events, Amgen, 6, 11, 12, Manuscript writing and educational events, Chemocentryx, 1, Eli Lilly, 6, Frescenius Kabi, 2, Genzyme, 2, Gilead, 2, 11, Grunenthal, 2, GSK, 2, 6, 11, 12, Manuscript writing and educational events, Horizon, 1, 2, Janssen, 1, 2, Novartis, 1, 11, Pfizer, 2, 6, 11, 12, Manuscript writing and educational events, Princeton Biopartners, 1, Selecta, 2, Synact, 2, Takeda, 2, UCB, 1, 6; **E. Muensterman**: Takeda, 3, 11; **A. Kavanaugh**: AbbVie, 2, Amgen, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB, 2; **D. van der Heijde**: AbbVie, 2, Argenx, 2, Bayer, 2, Bristol-Myers Squibb(BMS), 2, Galapagos, 2, Glaxo-Smith-Kline, 2, Imaging Rheumatology bv, 12, Director, Janssen, 2, Lilly, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; **P. Klimiuk**: None; **G. Valenzuela**: AbbVie, 2, 6, Alexion, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, BMS, 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, Centocor, 2, 6, Esaote, 2, 6, Exagen, 2, 6, Genentech, 2, 6, Gilead, 2, 6, Global Health Living, 2, 6, Horizon, 2, 6, Image Analysis Group, 2, 6, Janssen, 2, 6, Lilly, 2, 6, Mallinckrodt, 2, 5, 6, Merck, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Pharmacia, 2, 6, Radius, 2, 6, Regeneron, 2, 6, Sandoz, 2, 6, Sanofi, 2, 6, Takeda, 2, 6, UCB, 2, 6; **E. Dokoupilova**: AbbVie, 5, Eli Lilly, 5, Gilead, 5, Janssen-Cilag, 5, Nimbus, 5, Novartis, 5, UCB Biopharma SPRL, 5; **G. Poirier**: Nimbus, 3, 11; **B. Srivastava**: Nimbus, 3, 11; **S. Dasen**: Nimbus, 3, 11; **X. Zhang**: Nimbus, 3, 11; **M. Trivedi**: Takeda, 3, 11; **H. Weng**: HW MedAdvice LLC, 3, Takeda, 2; **T. Hong**: Takeda, 3, 11; **P. Pothula**: Takeda, 3, 11; **X. Baraliakos**: Abbvie, 1, 2, 6, Amgen, 1, 2, 6, BMS, 1, 2, 6, Chugai, 1, 2, 6, Galapagos, 1, 2, 6, Lilly, 1, 2, 6, MSD, 1, 2, 6, Novartis, 1, 2, 6, Pfizer, 1, 2, 6, Roche, 1, 2, 6, Sandoz, 1, 2, 6, UCB, 1, 2, 6.

Abstract Number: L13

An Open-label, Multicenter, Phase 1/2 Study to Assess Safety, Efficacy and Cellular Kinetics of YTB323, a Rapid Manufacturing CAR-T Cell Therapy Targeting CD19 on B Cells, for Severe Refractory Systemic Lupus Erythematosus: Preliminary Results

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SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Late-Breaking Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is characterized by pathogenic autoreactive B cells producing autoantibodies against multiple self-antigens. Recently, a series of clinical cases suggested that traditionally manufactured anti-CD19 chimeric antigen receptor T cell (CAR-T cell) therapies show potential to promote full clinical remission in severe refractory SLE (srSLE).[1,2] This is the first clinical trial to evaluate the preliminary safety and efficacy of anti-CD19 CAR-T cell therapy in patients with srSLE. YTB323 is a novel, rapidly manufactured, autologous CAR-T cell therapy that has shown preserved T cell stemness and enhanced CAR-T cell efficacy in hematological malignancies.[3]

Table 1: Patient baseline characteristics and exposure

Parameter	Patient 1	Patient 2	Patient 3
Age (years), sex, race	50, male, white	48, female, white	38, female, white
Lymphodepleting therapy	cyclophosphamide, fludarabine	cyclophosphamide, fludarabine	cyclophosphamide, fludarabine
YTB323 infusion	25-Apr-2023 (day 1)	08-Jun-2023 (day 1)	12-Jul-2023 (day 1)
Diagnosis (year)	SLE (2013)	SLE (2012)	SLE (2002), LN (2012)
Follow-up duration from YTB323 dosing (days)	106	62	28
Major organ involvement	pleuritis, vasculitis, arthritis, constitutional symptoms, skin rash, proteinuria	LN (Class III/IV), arthritis, pericarditis, skin rash	LN (Class IV-V), arthritis
Disease activity SLEDAI-2K	22	14	12
Urine protein/creatinine ratio (g/mol)	130.49 (H)	156.69 (H)	155.24 (H)

Normal ranges (local lab) for urine protein/creatinine ratio: 0-22.6. Values were within normal range, unless otherwise stated.
H, high; LN, lupus nephritis; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE Disease Activity Index 2000.

Figure 1: Adverse events by patients and severity over time

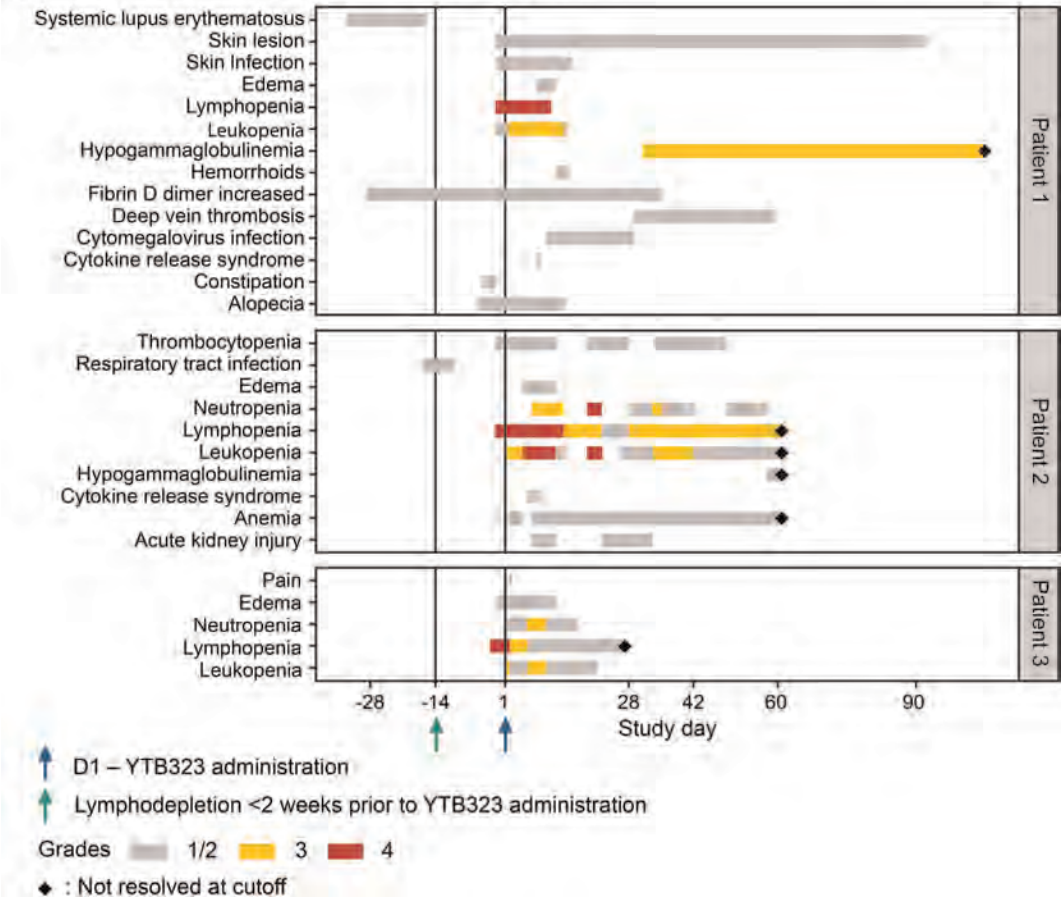
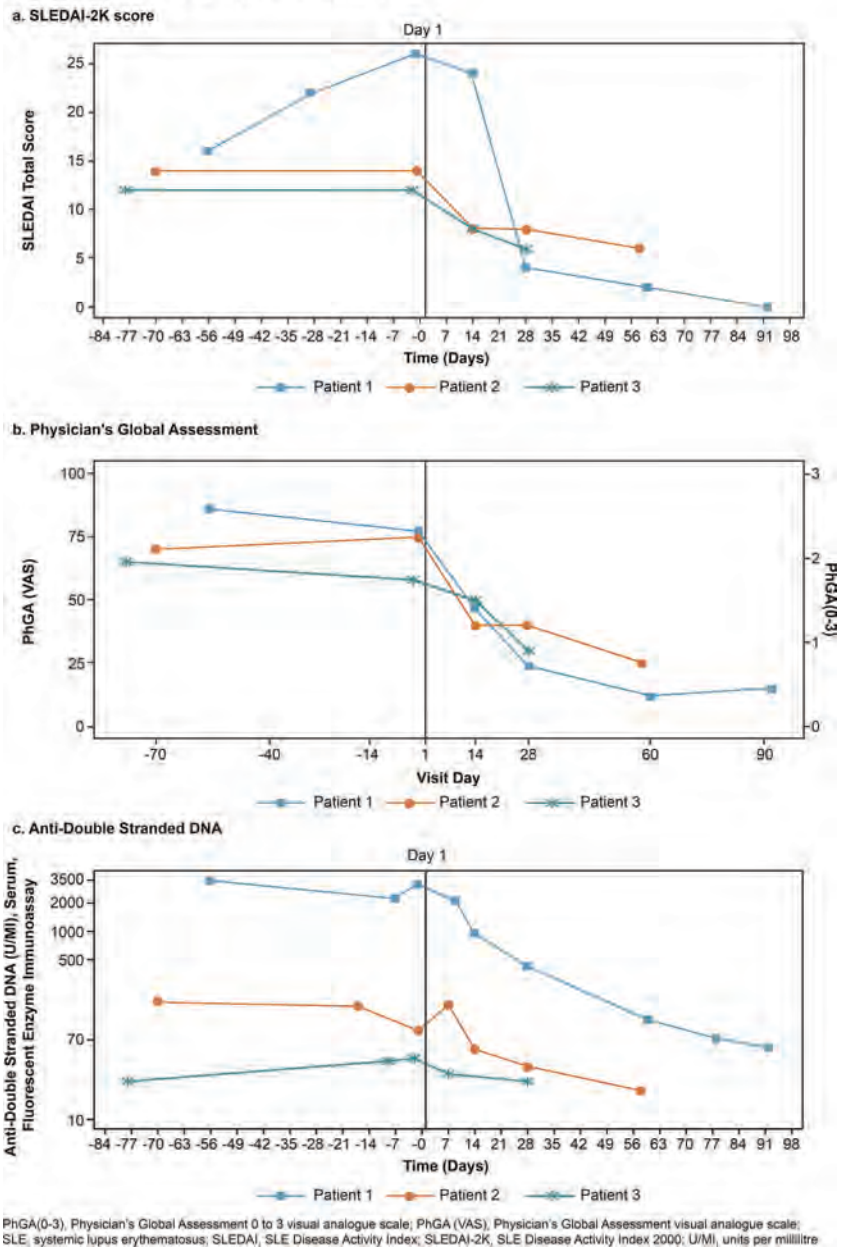


Figure 2: Individual efficacy parameters over time



PhGA(0-3), Physician's Global Assessment 0 to 3 visual analogue scale; PhGA (VAS), Physician's Global Assessment visual analogue scale; SLE, systemic lupus erythematosus; SLEDAI, SLE Disease Activity Index; SLEDAI-2K, SLE Disease Activity Index 2000; U/Ml, units per millilitre

Methods: An open-label, single-arm, multicenter phase 1/2 study, CYTB323G12101 (NCT05798117), to assess the safety, efficacy and cellular kinetics of YTB323 in participants with srSLE is currently ongoing. A sentinel cohort of patients with srSLE (n=3), dosed with $12.5x10^6$ cells at least 28 days apart, was enrolled. The primary endpoint was safety as measured by vital signs, adverse events, laboratory parameters and ECG evaluation. CAR-T cell kinetics were monitored by quantitative PCR and flow cytometry. Further relevant endpoints included changes from baseline levels in circulating B and T cells, autoantibody and complement levels, disease activity scores and renal outcome measures.

Results: Baseline characteristics of patients are summarized in **Table 1**. Adverse events are shown in **Figure 1**. No serious adverse events or deaths were reported. Following screening, the first patient experienced a worsening of disease during immunosuppressant washout prior to receiving lymphodepletion therapy. No immune effector cell-associated neurotoxicity syndrome (ICANS) occurred. A grade 1 cytomegalovirus reactivation occurred in one patient, which was subsequently resolved. Two patients had cytokine release syndrome (grade 1 or 2); both responded well to tocilizumab treatment and fully recovered. As expected,

grade 3 and 4 transient lymphodepletion-related cytopenias were observed in all patients. Grade 2 or 3 hypogammaglobulinemia was observed in two patients; neither event required intravenous immunoglobulin treatment. Cellular kinetics studies showed peak expansion (T_{max}) at 13 and 18 days post-infusion for the two patients with available data characterizing the expansion phase. Transient T cell and sustained B cell depletion were observed in all patients. Preliminary efficacy data **(Figure 2)** suggest substantial decreases in SLE Disease Activity Index (SLEDAI) **(Figure 2a)** and Physician's Global Assessment (PhGA) **(Figure 2b)**, in line with improvements in relevant disease biomarkers such as dsDNA **(Figure 2c)**, complement levels and proteinuria.

Conclusion: Preliminary data from this clinical trial including the first three sentinel patients suggest favorable safety, CAR-T cell expansion, B cell depletion and initial efficacy, supporting continuation of the study to evaluate YTB323 in srSLE.

References

1. Mackensen et al. *Nat Med* (2022) 28:2124-32.
2. Schett et al. *The EULAR Journal* (2023) 93.
3. Dickinson et al. *Cancer Discov* (2023) 13:1982-1997.

Disclosure: J. Cortés Hernández: GlaxoSmithKlein(GSK), 6; **P. Barba**: Allogene, 1, 2, Amgen, 1, 2, BMS/Celgene, 1, 2, Incite, 1, 2, Kite/Gilead, 1, 2, Miltenyi Biomedicine, 1, 2, Nektar, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, Pierre Fabre, 1, 2; **M. Linares Alberich**: None; **O. Fischer**: Novartis, 3; **B. Kovacs**: Novartis, 3; **T. Calzascia**: Novartis, 3; **D. Pearson**: Novartis, 3; **A. Jordán Garrote**: Novartis, 3; **T. Kirsilä**: Novartis, 3; **R. Siegel**: Novartis, 3; **T. Shisha**: Novartis, 3; **G. Cavalli**: Novartis, 3; **P. Gergely**: Novartis, 3.

Abstract Number: L14

Efficacy and Safety of Benralizumab Compared with Mepolizumab in the Treatment of Eosinophilic Granulomatosis with Polyangiitis in Patients Receiving Standard of Care Therapy: Phase 3 MANDARA Study

Michael Wechsler[1], Parameswaran Nair[2], Benjamin Terrier[3], Bastian Walz[4], Arnaud Bourdin[5], David Jayne[6], David Jackson[7], Florence Roufosse[8], Lena Börjesson Sjö[9], Ying Fan[10], Maria Jison[10], Christopher McCrae[11], Sofia Necander[9], Anat Shavit[12], Claire Walton[12] and **Peter Merkel**[13], [1]National Jewish Health, Denver, CO, [2]McMaster University, Hamilton, ON, Canada, [3]Cochin Hospital, Paris, France, [4]University of Tübingen, Kirchheim-Teck, Germany, [5]University of Montpellier, CHU Montpellier, INSERM, Montpellier, Montpellier, France, [6]Addenbrooke's Hospital, Cambridge, United Kingdom, [7]Guy's Severe Asthma Centre, School of Immunology & Microbial Sciences, King's College London,, London, United Kingdom, [8]Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium, [9]Late-stage Respiratory & Immunology, BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden, [10]Late-stage Respiratory & Immunology, BioPharmaceuticals R&D, AstraZeneca,, Gaithersburg, MD, [11]Translational Science & Experimental Medicine, Early Respiratory & Immunology, BioPharmaceuticals R&D, AstraZeneca, Gaithersburg, MD, [12]BioPharmaceutials Medical, AstraZeneca, Cambridge, United Kingdom, [13]University of Pennsylvania, Philadelphia, PA

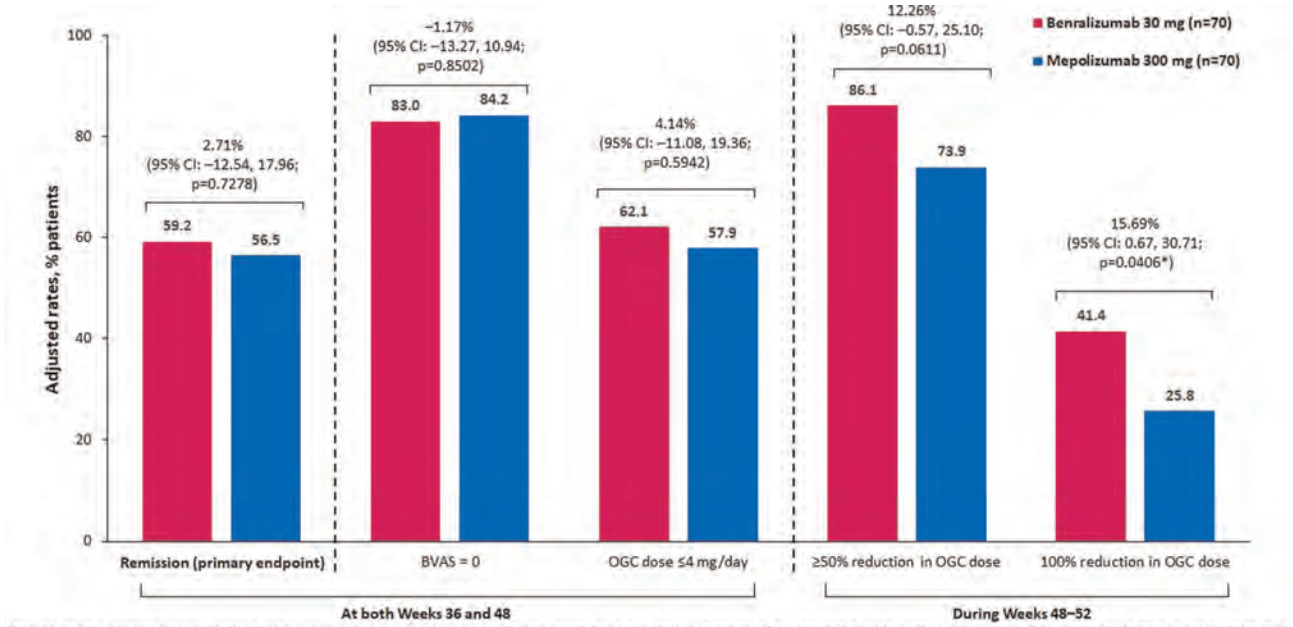
SESSION INFORMATION
Session Date: Tuesday, November 14, 2023
Session Title: Late-Breaking Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Eosinophilic inflammation is a key pathophysiological mechanism of eosinophilic granulomatosis with polyangiitis (EGPA). Oral glucocorticoids (OGCs) and immunosuppressants remain the basis for the standard of care (SoC),but their long-term use is associated withsignificantadverse effects, and relapses are frequently seen. The MANDARA

trial compared the efficacy and safety of benralizumab (a monoclonal antibody against the IL-5 receptor) and mepolizumab (an anti-IL-5 agent, and the only approved drug for EGPA) in patients with EGPA receiving SoC.

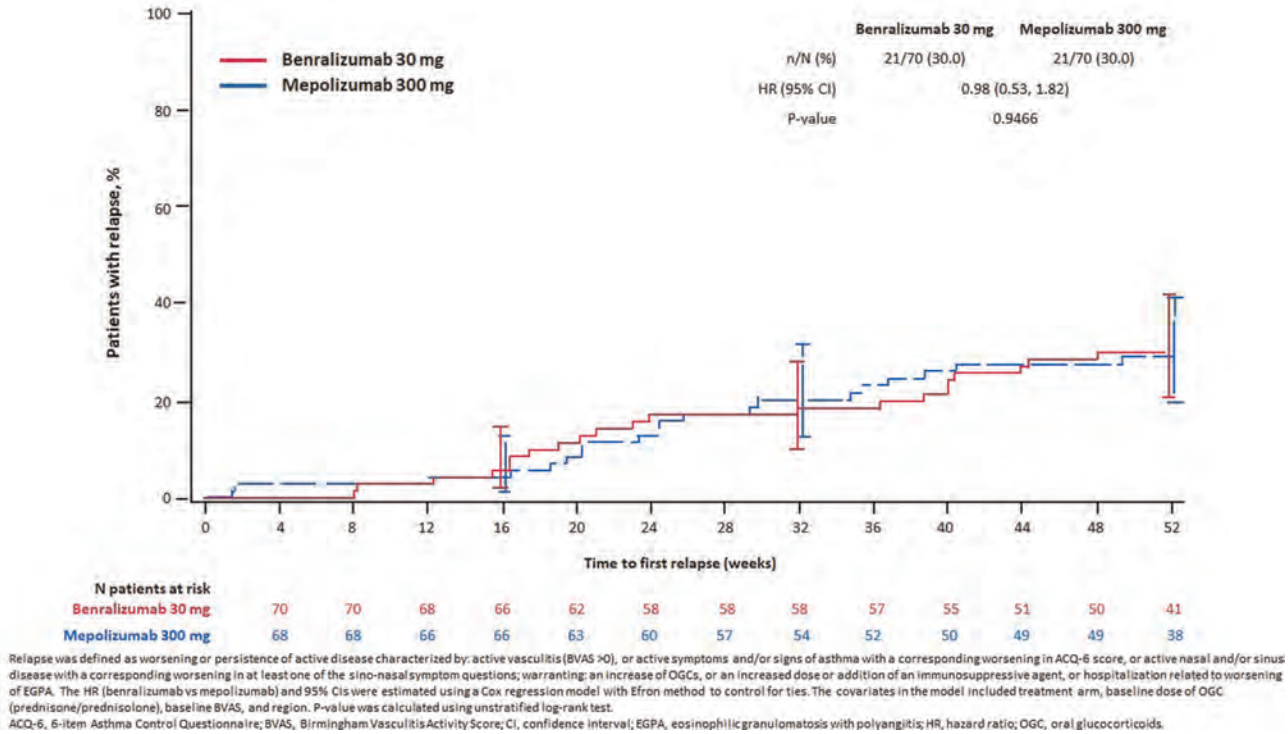
Methods: MANDARA was a randomized, active-controlled, parallel-group, multicenter, 52-week double-blind with open-label extension, Phase III non-inferiority study (NCT04157348). Patients (≥18 years) with documented EGPA based on asthma and blood eosinophilia plus ≥2 additional features of EGPA, and a history of relapsing/refractory disease requiring stable OGCs (≥7.5 mg prednisone/prednisolone daily) ± stable immunosuppressive therapy for ≥4 weeks before randomization, were included. Benralizumab 1 x 30 mg or mepolizumab 3 x 100 mg were administered by subcutaneous injection every 4 weeks for 52 weeks, and OGC was tapered if disease was controlled. The primary endpoint was the proportion of patients achieving remission (defined as Birmingham Vasculitis Activity Score [BVAS] = 0 and OGC dose ≤4 mg/day) at both Weeks 36 and 48. Secondary endpoints included accrued and maintained remission, OGC use, other clinical benefits, time to first relapse, and safety.

Results: 140 patients were randomized (mean [standard deviation; SD] age 52.3 [14.1] years; 60.0% women) to benralizumab (n=70) or mepolizumab (n=70). The adjusted remission rate at both Weeks 36 and 48 was 59.2% for the benralizumab group and 56.5% for the mepolizumab group (difference: 2.71%; 95% confidence interval [CI]: –12.54, 17.96; p=0.7278), confirming non-inferiority of benralizumab to mepolizumab (using the predefined margin of –25%; **Figure 1**). Secondary efficacy endpoints are shown in **Table 1**. The proportion of patients who relapsed was the same for benralizumab vs mepolizumab (both 30.0%; **Figure 2**). The mean (SD) OGC dose was 11.02 (5.25) mg/day at baseline. At Weeks 48–52, 86.1% vs 73.9% in the benralizumab and mepolizumab groups, respectively, had a reduction in OGC dose of ≥50% from baseline, and 41.4% vs 25.8% were fully tapered off OGC. Adverse events (AEs) were reported in 90.0% of benralizumab and 95.7% of mepolizumab recipients, most commonly COVID-19 (21.4% vs 27.1%), headache (17.1% vs 15.7%), and arthralgia (17.1% vs 11.4%). Serious AEs were reported in 5.7% of benralizumab and 12.9% of mepolizumab recipients. No benralizumab and 2 mepolizumab recipients experienced AEs leading to discontinuation of treatment.



*Nominal p-value. Patients received double-blind treatment with either one SC injection of benralizumab 30 mg plus three SC injections of mepolizumab placebo, or three SC injections of mepolizumab 100 mg plus one SC injection of benralizumab placebo every 4 weeks from baseline to Week 48. Remission was defined as BVAS=0 and OGC dose ≤4 mg/day (patients achieving remission who had, at any subsequent visit, a BVAS=1 that did not require an increase in OGC dose >4 mg/day or any other significant clinical intervention/investigation, were considered to be in continued remission). Remission rates and the between-treatment differences were estimated using marginal standardization method in a logistic regression model. The covariates in the model included treatment arm, baseline dose of OGC (prednisone/prednisolone), baseline BVAS and region (North America, Rest of World, and Japan). Baseline was defined as the last measurement on or prior to the date of randomization. The non-inferiority margin was predefined at –25%. P-values are shown for the superiority test. During the double-blind period of the study if patients reached BVAS=0 after Week 4 their OGCs were allowed to be tapered according to standard practice.
BVAS, Birmingham Vasculitis Activity Score; CI, confidence interval; OGC, oral glucocorticoid; SC, subcutaneous.

Figure 1. Efficacy outcomes and between-treatment differences in rates during the double-blind treatment period



Relapse was defined as worsening or persistence of active disease characterized by: active vasculitis (BVAS >0), or active symptoms and/or signs of asthma with a corresponding worsening in ACQ-6 score, or active nasal and/or sinus disease with a corresponding worsening in at least one of the sino-nasal symptom questions; warranting: an increase of OGCs, or an increased dose or addition of an immunosuppressive agent, or hospitalization related to worsening of EGPA. The HR (benralizumab vs mepolizumab) and 95% CIs were estimated using a Cox regression model with Efron method to control for ties. The covariates in the model included treatment arm, baseline dose of OGC (prednisone/prednisolone), baseline BVAS, and region. P-value was calculated using unstratified log-rank test.
ACQ-6, 6-item Asthma Control Questionnaire; BVAS, Birmingham Vasculitis Activity Score; CI, confidence interval; EGPA, eosinophilic granulomatosis with polyangiitis; HR, hazard ratio; OGC, oral glucocorticoids.

Figure 2. Time to first relapse

Table 1. Secondary endpoints during the double-blind treatment period

	Treatment	Patients with accrued remission duration up to Week 52, n (%)					Comparison between groups	
		0 weeks	>0 to < 12 weeks	12 to < 24 weeks	24 to <36 weeks	≥36 weeks	OR (95% CI)	P value
Accrued remission up to Week 52								
Remission	Benralizumab (n=70)	9 (12.9)	12 (17.1)	8 (11.4)	21 (30.0)	20 (28.6)	1.36 (0.75, 2.48)	0.3142
	Mepolizumab (n=70)	15 (21.4)	10 (14.3)	8 (11.4)	19 (27.1)	18 (25.7)		
Achieved remission by Week 24 and maintained remission until Week 52								
		Patients, n (%)			Adjusted remission rates, %		Difference in remission rates (95% CI)	P value
Remission	Benralizumab (n=70)	28 (40.0)			42.1		5.54 (−9.30, 20.37)	0.4643
	Mepolizumab (n=70)	27 (38.6)			36.5			
Achieved clinical benefit								
		Patients, n (%)			Adjusted response rates, %		Difference in response rates (95% CI)	P value
Clinical benefit (OGC dose ≤4 mg/day threshold)	Benralizumab (n=70)	66 (94.3)			94.4		4.60 (−4.22, 13.41)	0.3068
	Mepolizumab (n=70)	63 (90.0)			89.8			
Clinical benefit (OGC dose ≤7.5 mg/day threshold)	Benralizumab (n=70)	68 (97.1)			97.3		−1.13 (−5.85, 3.59)	0.6390
	Mepolizumab (n=70)	69 (98.6)			98.5			
Achieved complete response								
		Patients, n (%)			Adjusted response rates, %		Difference in response rates (95% CI)	P value
Complete response (OGC dose ≤4 mg/day threshold)	Benralizumab (n=70)	43 (61.4)			62.5		7.90 (−7.32, 23.12)	0.3088
	Mepolizumab (n=70)	39 (55.7)			54.6			
Complete response (OGC dose ≤7.5 mg/day threshold)	Benralizumab (n=70)	45 (64.3)			64.9		6.93 (−8.42, 22.28)	0.3762
	Mepolizumab (n=70)	41 (58.6)			57.9			

Secondary endpoints are not multiplicity-protected. All p-values are nominal. ORs and 95% CIs for benralizumab versus mepolizumab were estimated using a proportional odds model, with covariates including treatment arm, baseline OGC dose, baseline BVAS, and region. Rates and the difference in rates (benralizumab minus mepolizumab) and 95% CIs, were estimated using marginal standardization method from a logistic regression model, with covariates including treatment arm, baseline OGC dose, baseline BVAS, and region. Remission was defined as BVAS=0 and OGC dose ≤4 mg/day (patients achieving remission who had, at any subsequent visit, a BVAS=1 that did not require an increase in OGC dose >4 mg/day or any other significant clinical intervention/investigation, were considered to be in continued remission). Daily dose of OGCs: Baseline is defined as the last measurement on or prior to the date of randomization. Clinical benefit was defined as any of the following: remission (BVAS=0 and OGC dose ≤4 mg/day or ≤7.5 mg/day) at any time during the double-blind treatment period; ≥50% reduction in average daily OGC dose during Weeks 48 through 52; relapse free during the double-blind treatment period. Complete response was defined as all of the following: remission (BVAS=0 and OGC dose ≤4 mg/day or ≤7.5 mg/day) at any time during the double-blind treatment period; ≥50% reduction in average daily OGC dose during Weeks 48 through 52; relapse free during the double-blind treatment period.
BVAS, Birmingham Vasculitis Activity Score; CI, confidence interval; OGC, oral glucocorticoids; OR, odds ratio.

Conclusion: This study demonstrated non-inferiority of benralizumab vs mepolizumab over 52 weeks in patients with relapsing/refractory EGPA receiving SoC and provides evidence for the efficacy and utility of benralizumab, with more benralizumab-treated patients being fully tapered off OGC. Both study drugs were well tolerated with a similar proportion of patients reporting AEs.

Disclosure: M. Wechsler: Amgen, 2, AstraZeneca, 2, Boehringer Ingelheim, 2, Cohero Health, 2, Equillium, 2, Genentech, 2, GlaxoSmithKline, 2, Novartis, 2, Regeneron, 2, Sanofi–Genzyme, 2, Sentien Biotechnologies, 2, Teva, 2; **P. Nair**: Arrowhead, 6, AstraZeneca, 6, 12, institution received grant support, CSL Behring, 6, Cyclomedica, 12, institution received grant support, Equillium, 12, institution received grant support, Foresee, 12, institution received grant support, Genentech, 12, institution received grant support, GlaxoSmithKline, 6, Sanofi, 6, 12, institution received grant support, Teva, 12, institution received grant support; **B. Terrier**: AstraZeneca, 2, GlaxoSmithKline, 2, Pharma, 2, Vifor, 2; **B. Walz**: AB2Bio, 5, AbbVie, 5, Amgen, 2, 6, AstraZeneca, 2, 5, 6, Boehringer Ingelheim, 2, 6, ChemoCentryx, 5, GlaxoSmithKline, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 5; **A. Bourdin**: Amgen, 2, 6, AstraZeneca, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Chiesi, 2, 6, GlaxoSmithKline, 2, 5, 6, Novartis, 2, 6, Sanofi Regeneron, 2, 6; **D. Jayne**: Amgen, 2, 6, AstraZeneca, 2, 6, Aurinia, 4, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb (BMS), 2, 6, ChemoCentryx, 6, Chinook, 1, Chugai, 2, 6, CSL-Vifor, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Novartis, 2, 6, Roche, 2, 5, 6, Takeda, 1, 2, 6, Travere, 2, Vifor, 2, 6; **D. Jackson**: AstraZeneca, 2, 5, 6, Boehringer Ingelheim, 2, 6, Chiesi, 2, 6, GlaxoSmithKline, 2, 6, NAPP, 2, 6, Novartis, 2, 6, Sanofi Regeneron, 2, 6, TEVA, 2, 6; **F. Roufosse**: AstraZeneca, 2, GlaxoSmithKline, 2, Menarini, 2, Merck, 2, UpToDate, 9; **L. Börjesson Sjö**: AstraZeneca, 3, 11; **Y. Fan**: AstraZeneca, 3, 11; **M. Jison**: AstraZeneca, 3, 11; **C. McCrae**: AstraZeneca, 3, 11; **S. Necander**: AstraZeneca, 3, 11; **A. Shavit**: AstraZeneca, 3, 11; **C. Walton**: AstraZeneca, 3, 11; **P. Merkel**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta, 2, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein(GSK), 2, 5, HiBio, 2, InflaRx, 1, 5, Janssen, 2, Jubilant, 2, Kyverna, 2, 11, MiroBio, 2, Neutrolis, 5, Novartis, 2, NS Pharma, 2, Q32, 2, 11, Regeneron, 2, Sparrow, 2, 11, Takeda, 2, 5, Up-To-Date, 9, Visterra, 2.

Abstract Number: L15

AR882, an Efficacious and Selective URAT1 Inhibitor for Patients with Chronic Gouty Arthritis and Subcutaneous Tophi: Results from a Global, Prospective, Proof-of-Concept Trial Using Dual Energy Computed Tomography

Robert Keenan[1], James Cheng-Chung Wei[2], Sarah Morris[3], Pamella Mundell[3], Wen Wei[3], Ke Shi[3], Zancong Shen[3], Vijay Hingorani[4], Shunqi Yan[3], Bahram Kiani[5] and Litain Yeh[3], [1]Arthrosi Therapeutics, Inc., Chapel Hill, NC, [2]Chung Shan Medical University, Taichung, Taiwan (Republic of China), [3]Arthrosi Therapeutics, Inc., San Diego, CA, [4]Vanguard Healthsciences, Inc., San Diego, CA, [5]Wake Forest University School of Medicine, Winston-Salem, NC

SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 7:30AM–9:00AM

Background/Purpose: AR882 is a novel and selective URAT1 inhibitor currently in clinical stage development for the treatment of gout and tophaceous gout and has demonstrated robust and sustained serum urate (sUA) lowering in a 3-month Phase 2b trial. This proof-of-concept trial evaluates the effect of AR882 versus allopurinol on the reduction of clinically visible tophi in patients with gout using caliper measurements and Dual Energy Computer Tomography (DECT).

Methods: The phase 2 global trial recruited 42 gout patients with subcutaneous tophi. The patients were randomized into three treatment groups to receive once-daily AR882 75 mg, once-daily AR882 50 mg + allopurinol, or once-daily allopurinol up to 300 mg at a 1:1:1 ratio. Tophi measurements with calipers were completed every 4 weeks for 6 months; patients were imaged with DECT at baseline and 6 months. The primary efficacy endpoint was sUA change at month 3. Secondary endpoints included resolution of target tophus area and change from baseline in target tophus crystal volume at month 6. Safety assessments, including vital signs and electrocardiograms, were collected throughout the study.

Results: In the Intent-to-Treat population, the mean baseline sUA level ranged between 9.1-9.6 mg/dL across treatment groups. At month 3, the mean sUA levels were reduced to 4.5 (±1.2), 4.7 (±1.4), and 6.1 (±2.0) mg/dL, respectively for 75 mg, 50 mg + allopurinol and allopurinol. In the 75 mg AR882 group, 86% and 64% of patients achieved sUA < 6 and < 5 mg/dL, respectively; in the 50 mg AR882 + allopurinol group, 77% and 69% of patients achieved sUA levels < 6 and

Table 1. Mean (SD) sUA reduction, response rates and complete resolution of at least one target tophus.

Treatment	N	Baseline	sUA levels at Month 3 (ITT)		sUA (mg/dL) response, % at Month 3 (ITT)				n/N, % of subjects with ≥1 tophus completely resolved (Month 6)
		sUA mg/dL	sUA mg/dL	% change	< 6	< 5	< 4	< 3	
AR882 75 mg	14	9.1 (1.3)	4.5 (1.2)	-49.6 (12.5)	86	64	43	7	4/14 (29%)
AR882 50 mg + allopurinol	13	9.6 (1.2)	4.7 (1.4)	-49.9 (15.1)	77	69	23	8	1/13 (8%)
allopurinol	13	9.5 (2.0)	6.1 (2.0)	-34.9 (20.1)	46	23	15	8	1/13 (8%)

ITT: Intent-to-Treat population

Table 2. Mean (SE) change in DECT crystal volumes at Month 6.

Treatment	Visit	N	Crystal volume, cm^3	Absolute change, cm^3	Percent change
AR882 75 mg	Baseline	12	15.6 (9.9)		
	Month 6	11	8.7 (5.0)	-8.3 (5.8)	-30.7 (17.7)
AR882 50 mg + allopurinol	Baseline	12	4.7 (2.0)		
	Month 6	9	3.2 (1.8)	-0.9 (0.5)	-31.5 (13.9)
Allopurinol	Baseline	13	11.5 (5.8)		
	Month 6	13	10.3 (4.5)	-1.2 (3.8)	-16.8 (25.5)

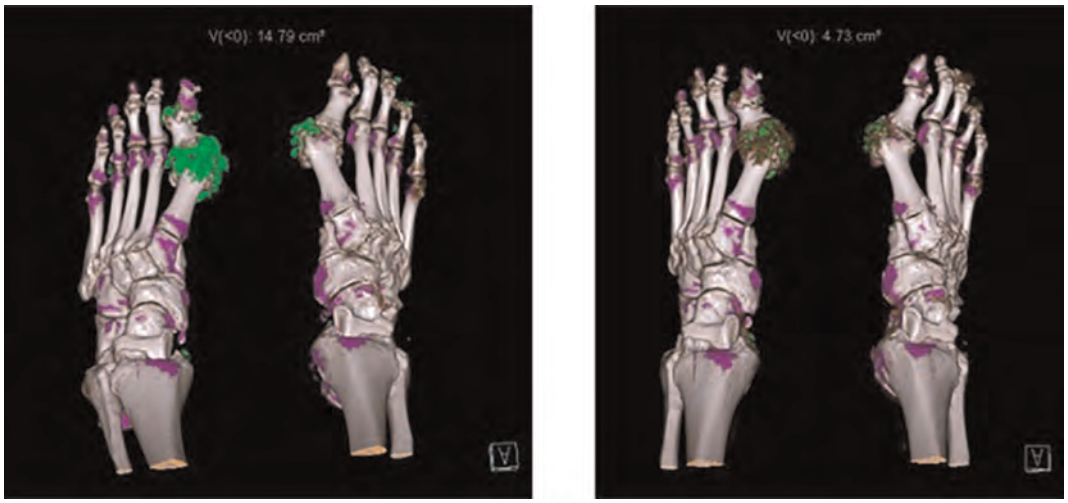


Figure 1. DECT image of gouty arthritis showing 68% reduction in total urate crystal volume from baseline (left) to Month 6 after taking AR882 75 mg once daily.

< 5 mg/dL, respectively. This was compared to patients in the allopurinol group, where 46% and 23% of patients achieved sUA levels < 6 and < 5 mg/dL, respectively (Table 1).

At Month 6, 4 patients (29%) in the AR882 75 mg group showed complete resolution of at least one tophus, compared to 1 patient (8%) in AR882 50 mg + allopurinol and 1 patient (8%) in allopurinol groups. The AR882 75 mg group showed a greater reduction of total urate crystal volume (-30.7%, -8.3 cm^3) vs. combination (-31.5%, -0.9 cm^3) or allopurinol (-16.8%, -1.2 cm^3) from baseline to month 6 on DECT (Table 2). Figure 1 shows a 68% decrease in total urate crystal volume of the feet and ankles after AR882 75 mg once daily treatment for 6 months.

There were no serious adverse events related to AR882 treatment. No kidney or liver abnormalities were observed. The most frequently reported adverse event was gout flare, mild or moderate adverse events including diarrhea, headache, and upper respiratory infection. Gout flare rate appeared less in the AR882 treatment groups than in the allopurinol group.

Conclusion: In this global study, six-month treatment of AR882 demonstrated safe and efficacious sUA lowering, tophus resolution and total crystal volume dissolution in gout patients with various demographics and baseline characteristics. AR882 may offer improved efficacy and better safety compared to existing therapies in the treatment of patients with gout, including those with both clinically visible and subclinical crystal deposition.

Disclosure: R. Keenan: Arthrosi Therapeutics, 3; **J. WEI**: Arthrosi Therapeutics, 5; **S. Morris**: Arthrosi Therapeutics, 3; **P. Mundell**: Arthrosi Therapeutics, 3; **W. Wei**: Arthrosi Therapeutics, 3; **K. Shi**: Arthrosi Therapeutics, 3; **Z. Shen**: Arthrosi Therapeutics, 3, 3; **V. Hingorani**: Arthrosi Therapeutics, 2; **S. Yan**: Arthrosi Therapeutics, 3, 8; **B. Kiani**: None; **L. Yeh**: Arthrosi Therapeutics, 3, 8.

Abstract Number: L16

Withdrawal of Immunosuppressant and Low-dose Steroids in IgG4-RD Patients with Stable Disease (WInS IgG4-RD): An Investigator-initiated, Multi-center, Open-label, Randomized Controlled Trial

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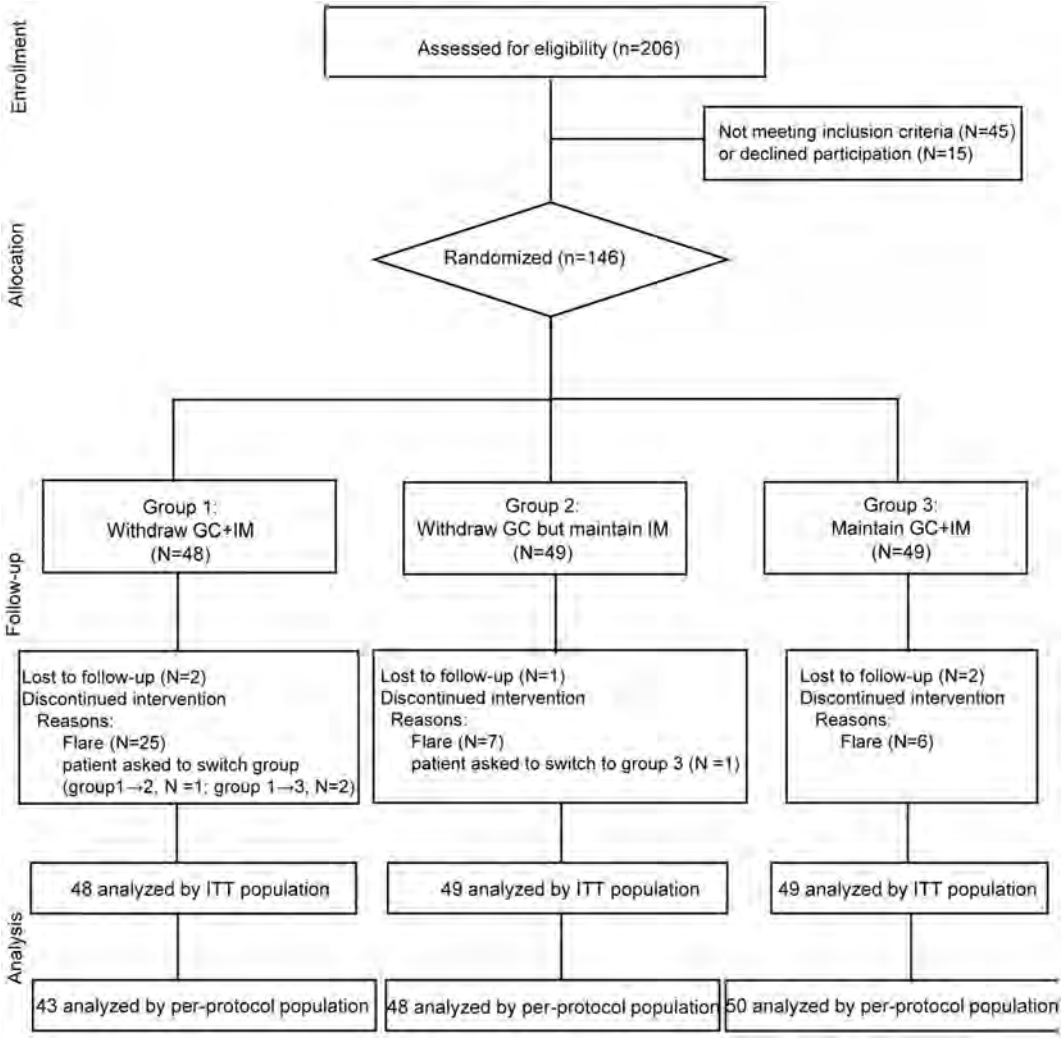
SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 7:30AM–9:00AM

Background/Purpose: IgG4-related disease (IgG4-RD) is a fibroinflammatory disease. Remission induction treatment with glucocorticoid (GC) is usually effective, but its tendency of relapse makes the strategy for maintenance treatment a challenge. The WInS IgG4-RD (withdraw immunosuppressants and steroid in stable IgG4-RD) trial tested whether discontinuation of GC and immunosuppressive agent (IM) were feasible in stable IgG4-RD.

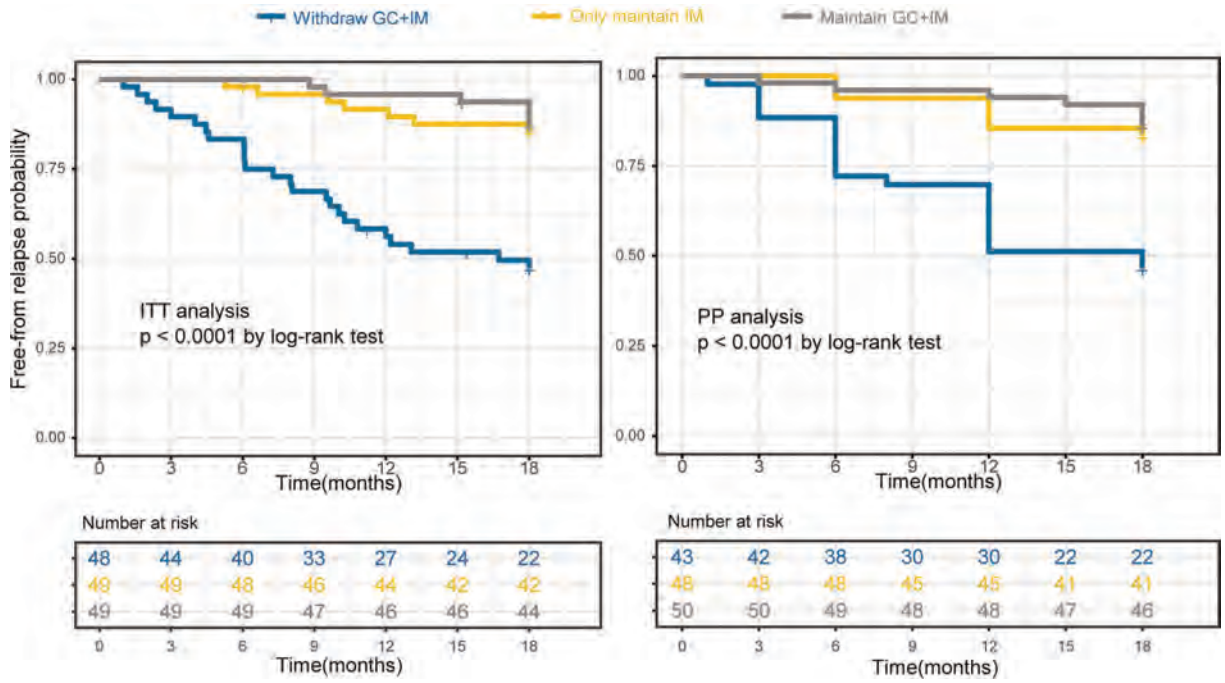
Methods: The WInS IgG4-RD trial was a multicentre, open-label, randomised controlled trial. IgG4-RD patients receiving GC+IM as maintenance treatment with clinically quiescent disease for at least 12 months were randomised (1:1:1) into three groups: (1) Group 1: withdraw GC+IM; (2) Group 2: withdraw GC but maintain IM; (3) Group 3: maintain GC +IM. The primary endpoint was the relapse rate of disease within 18 months. The secondary endpoints include the changes of responder index (RI), physician's global assessment (PGA), serum IgG4 and IgG, as well as adverse events.

Results: One hundred and forty-six patients were randomised, with 48 patients in Group 1, and 49 patients in Group 2 and Group 3 respectively. Within the 18-month follow-up period, disease relapse occurred in 25/48 (52.1%) patients in Group 1 versus 7/49 (14.2%) in Group 2 and 6/49 (12.2%) in Group 3 ($p< 0.001$). The changes in RI and PGA were significantly higher in Group 1 than Group 2 ($p< 0.001$) or Group 3 ($p< 0.001$).

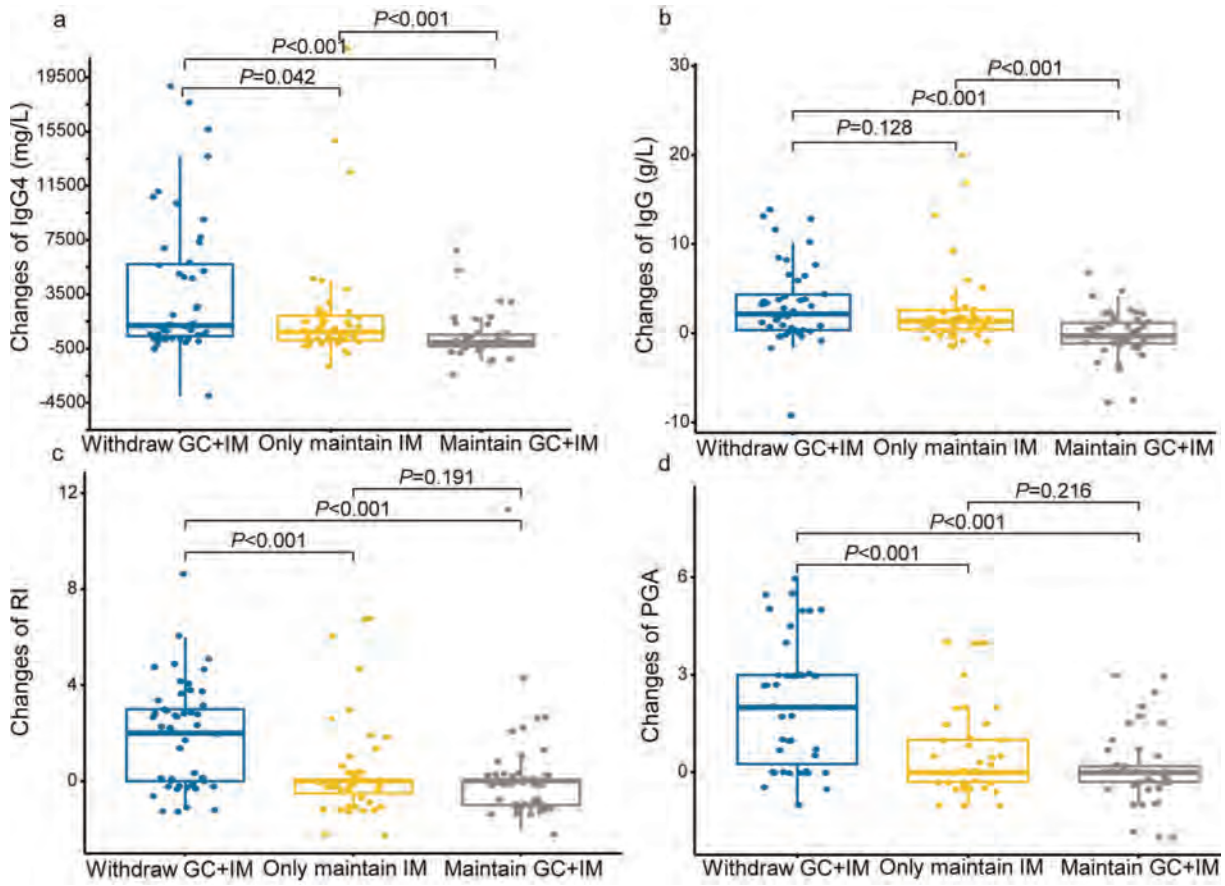
Conclusion: The maintenance of IMs, with or without low-dose GC, was found to be superior to withdraw GC+IM in preventing relapse for long-time stable IgG4-RD.



Flowchart of WInS IgG4-RD study



The occurrence of relapse during follow-up is presented as a Kaplan-Meier curve of cumulative probability (Figure 2), where there were significant differences among the three groups by both ITT and PP analysis (both overall p<0.001).



Changes of IgG4(a), IgG (b), IgG4-RD RI (3c), PGA (figure 3d) at baseline of the study and the endpoints by intention-to-treat analysis. RI, Responder index; PGA, physician's global assessment.

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Abstract Number: L17

Safety, Tolerability, and Exploratory Efficacy of Afimetoran, a TLR7/8 Inhibitor, in Patients with Cutaneous Lupus Erythematosus: A Phase 1b Randomized, Double-Blind, Placebo-Controlled Study

Fareeda Hosein[1], Stanislav Ignatenko[2], Kristina Chadwick[1], Lin Zhu[1], Frédéric Baribaud[1], Thanh Bach[1], Hazem Karabeber[1], Michelle Dawes[1], Leon Carayannopoulos[1] and Gopal Krishna[1], [1]Bristol Myers Squibb, Princeton, NJ, [2]Charité Research Organisation GmbH, Berlin, Germany

SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 7:30AM–9:00AM

Background/Purpose: Over 50 years have passed since the last therapy was approved for cutaneous lupus erythematosus (CLE).[1] Parenteral administration, off-label use, or toxicity with long-term use of some existing therapies illustrate a key unmet need to identify novel treatments for CLE. Toll-like receptors (TLR) are implicated in SLE pathobiology, which make these receptors candidate targets for CLE therapies.[2] Afimetoran is a first-in-class, orally bioavailable, potent, and selective small molecule inhibitor of TLR7 and TLR8. This phase 1b, randomized, double-blind, placebo-controlled study (NCT04493541) investigated the safety, tolerability, and exploratory efficacy of afimetoran in patients with CLE.

Methods: Patients were aged 18–65 years, diagnosed with either SLE according to EULAR/ACR 2019 classification criteria[3] or had biopsy-proven CLE, had a modified CLE Disease Area and Severity Index-Activity (CLASI-A) score of ≥ 6, were antinuclear antibody positive, and had no evidence of retinal toxicity. Stable doses of oral corticosteroids and/or antimalarials at baseline were permitted. Patients were randomized 2:1 to once-daily oral afimetoran (30 mg) or placebo for 16 weeks and monitored for 4 weeks after stopping treatment. The primary endpoints were safety and tolerability; efficacy was an exploratory endpoint.

Results: 13 patients were randomized (afimetoran, n = 8; placebo, n = 5); 12 patients completed 16 weeks of treatment and 1 discontinued from the afimetoran arm due to an adverse event (AE) of symptomatic COVID-19 infection. Baseline patient characteristics were generally balanced, though the patients in the afimetoran arm had higher baseline CLASI-A scores and a higher proportion of current smokers vs placebo (**Table 1**). The primary objective was met: afimetoran demonstrated a favorable safety profile and was well tolerated vs placebo. Further, there were no serious AEs or safety signals among laboratory tests, vital signs, or electrocardiography. Overall, AEs were mild or moderate and resolved by the end of the study without intervention (**Table 2**). The proportion of patients with reported AEs was lower for patients treated with afimetoran vs placebo (62.5% vs 80.0%, **Table 2**). Compared with placebo, patients treated with afimetoran showed a greater reduction in CLASI-A scores as early as week 4 (first CLASI-A assessment point) which continued through the 16 weeks of active treatment and persisted for 4 weeks after end of treatment (**Figure 1**).

Table 1. Baseline demographics and clinical characteristics

	Afimetoran (n = 8)	Placebo (n = 5)	Total (n = 13)
Age, mean (SD), years	46.0 (11.1)	51.2 (12.4)	48.0 (11.4)
Female sex, n (%)	7 (87.5)	4 (80.0)	11 (84.6)
Body mass index, mean (SD), kg/m²	26.6 (4.8)	25.4 (4.1)	26.1 (4.4)
Weight, mean (SD), kg	77.0 (16.6)	74.3 (14.5)	76.0 (15.3)
Race, n (%)			
White	8 (100.0)	5 (100.0)	13 (100.0)
Smoking status (tobacco), n (%)			
Former	1 (12.5)	1 (20.0)	2 (15.4)
Current	6 (75.0)	2 (40.0)	8 (61.5)
Primary diagnosis, n (%)			
Cutaneous lupus erythematosus	5 (62.5)	2 (40.0)	7 (53.8)
Systemic lupus erythematosus	3 (37.5)	3 (60.0)	6 (46.2)
Anti-dsDNA antibody or anti-Smith antibody, n (%)	3 (37.5)	4 (80.0)	7 (53.8)
CLASI-A score, mean (min, max)	15.0 (6, 25)	11.6 (9, 16)	13.7 (6, 25)

dsDNA, double stranded deoxyribonucleic acid; CLASI-A, Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity.

Table 2. Safety summary for placebo vs afimetoran

Event, n (%)	Afimetoran (n = 8)	Placebo (n = 5)
Deaths	0	0
AE	5 (62.5)	4 (80.0)
Serious AEs	0	0
AEs leading to discontinuation[a]	1 (12.5)	0
Drug-related AE[b,c]	2 (25.0)	2 (40.0)
Non-serious AE	5 (62.5)	4 (80.0)
Infections and infestations	3 (37.5)	1 (20.0)
Nervous system disorders	1 (12.5)	2 (40.0)
Injury/procedural complications	1 (12.5)	2 (40.0)
General and administration site disorders	2 (25.0)	0
Gastrointestinal disorders	1 (12.5)	1 (20.0)
Psychiatric disorders	1 (12.5)	0
Respiratory, thoracic, and mediastinal disorders	1 (12.5)	0
Blood and lymphatic system disorder	0	1 (20.0)
Musculoskeletal and connective tissue disorders	0	1 (20.0)

Data (n) represent the number of patients within the afimetoran or placebo arm with an event.

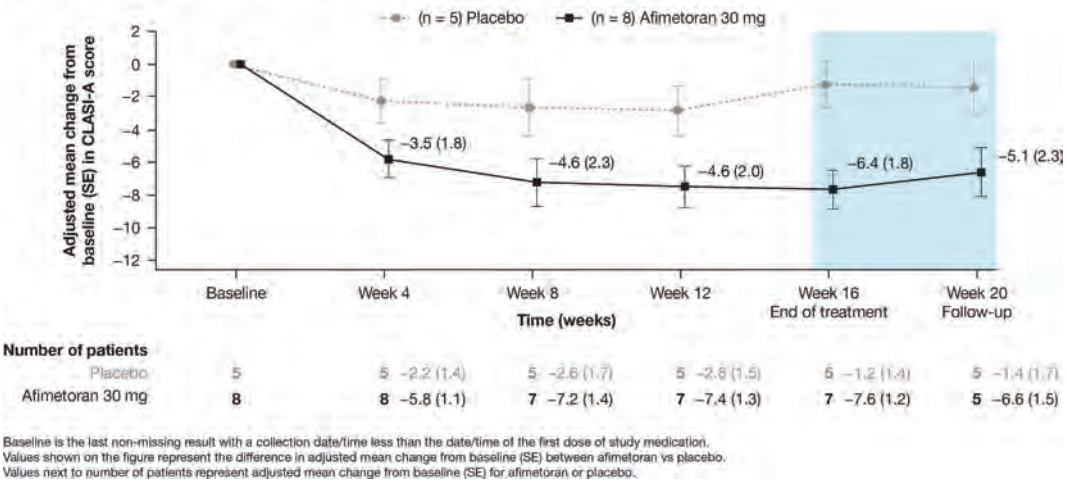
[a]Patient discontinuation at week 8 attributed to symptomatic COVID-19.

[b]Drug-related AEs were investigator assessed at each site.

[c]Drug related AEs were reported during the blinded treatment period, however after unblinding those patients were in the placebo group.

AE, adverse event.

Figure 1. Mean change from baseline in CLASI-A with afimetoran vs placebo



Baseline is the last non-missing result with a collection date/time less than the date/time of the first dose of study medication.
Values shown on the figure represent the difference in adjusted mean change from baseline (SE) between afimetoran vs placebo.
Values next to number of patients represent adjusted mean change from baseline (SE) for afimetoran or placebo.

Conclusion: Afimetoran demonstrated a favorable safety profile and was well tolerated vs placebo in patients with CLE. These results provide the first clinical evidence to suggest that afimetoran may offer a clinical benefit as indicated by an early and sustained clinical response vs placebo as measured by CLASI-A. As such, these results support the continued clinical investigation of afimetoran in lupus, including the ongoing phase 2b study in SLE (NCT04895696).

References:

1. Guo LN, et al. *Lupus Sci Med* 2021;8:e000529.
2. Ishizaka ST, et al. *Eur J Pharmacol* 2023;957:175962.
3. Aringer M, et al. *Arthritis Rheumatol* 2019;71:1400–1412

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Disclosure: F. Hosein: Bristol Myers Squibb, 3; **S. Ignatenko**: None; **K. Chadwick**: Bristol Myers Squibb, 3, 11; **L. Zhu**: Bristol Myers Squibb, 3; **F. Baribaud**: Bristol Myers Squibb, 3, 10; **T. Bach**: Bristol Myers Squibb, 3; **H. Karaberber**: Bristol Myers Squibb, 3; **M. Dawes**: Bristol Myers Squibb, 3; **L. Carayannopoulos**: Bristol Myers Squibb, 3; **G. Krishna**: Bristol Myers Squibb, 3, 11.

Abstract Number: L18

Immune-metabolic Heterogeneity and Clinical Implications in Primary Sjogren's Syndrome Revealed by Molecular Classification of Salivary Glands

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SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 7:30AM–9:00AM

Background/Purpose: Primary Sjögren's syndrome (pSS) is a complex autoimmune disease with significant heterogeneity. Our study aimed to clarify the etiology and molecular variation of the target organ, salivary glands (SGs), in pSS by stratifying them into distinguishable subgroups, which could inform treatment choices in pSS.

Methods: Large-scale transcriptomic profiling of SGs was conducted on 396 pSS, 87 non-pSS, and 44 early-pSS individuals from a multicenter consecutive Chinese cohort. Unsupervised clustering methods were used for molecular classification and integrated analyses were performed to elucidate comprehensive clinical and biological features, immune-metabolic and genetic characteristics. Lymphoma risk and treatment response for pSS subgroups was also predicted for pSS subtypes.

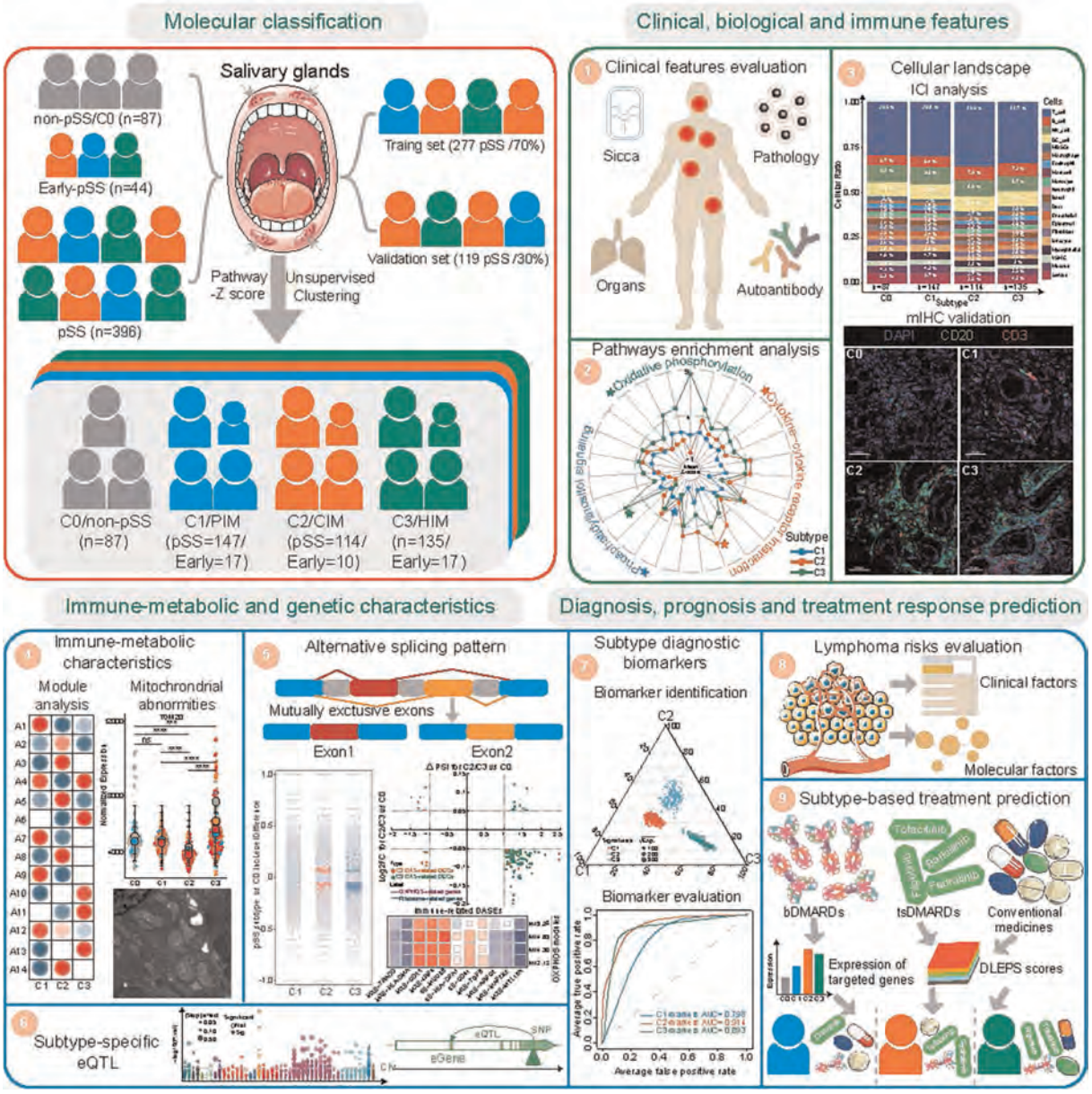
Results: Three distinct subtypes were identified both in established and early-pSS, including "pauci-immune/C1", "cold-immune/C2", and "hot-immune/C3". Pauci-immune/C1 exhibited a similar biologic pattern to non-pSS. The cold-immune/C2 displayed dramatic activation of classical adaptive immune and depressed metabolism, along with mitochondrial dysfunction and cGAS-STING-NFkB signaling overactivity. "Hot-immune/C3" had an innate immune inclination and

Table 1. Clinical characteristics of study populations and pSS subtypes

Table1. Clinical characteristics of study populations and pSS subtypes

Characteristic	non-pSS (n=87)	Early-pSS(n=44)	pSS (n=396)	P values	pSS Subtypes			P values
					C1/PIM (n=147)	C2/CIM (n=114)	C3/HIM (n=135)	
Age (year), mean ± sd	50.4±13.3	53.3±14.7	49.0±13.3	0.104	46.7 ± 12.4	53.9 ± 12.6	47.5 ± 13.9	<0.001***
Gender (female), n (%)	75 (86.21%)	35 (79.55%)	358(90.40%)	0.067	130 (88.44%)	108 (94.74%)	120 (88.89%)	0.175
Xerostomia, n (%)	44 (50.57%)	11 (25.00%)	191(48.23%)	0.010*	64 (43.54%)	65 (57.02%)	62 (45.93%)	0.078
Xerophthalmia, n (%)	53 (60.92%)	19 (43.18%)	197(49.75%)	0.093	89 (60.54%)	57 (50.00%)	51 (37.78%)	<0.001***
Focus score ≥1, n (%)	0 (0.00%)	14 (31.82%)	303(76.52%)	<0.001***	100 (68.03%)	101 (88.60%)	102 (75.56%)	<0.001***
GC-positive, n (%)	-	-	208/391 (53.20%)	-	55/144 (38.19%)	83/114 (72.81%)	70/133 (52.63%)	<0.001***
OSS-positive, n (%)	35/71 (49.30%)	14/30 (46.67%)	193/303 (63.70%)	0.019*	75/125 (60.00%)	53/83 (63.86%)	65/95 (68.42%)	0.437
Schiemer's test-positive, n (%)	38/72 (52.78%)	21/31 (67.74%)	224/307 (72.96%)	0.003**	93/127 (73.23%)	63/83 (75.90%)	68/97 (70.10%)	0.680
ANA-positive (≥1:320), n (%)	0 (0.00%)	19/43 (44.19%)	213/387 (55.04%)	<0.001***	54/142 (38.03%)	82/112 (73.21%)	77/133 (57.89%)	<0.001***
Anti-SSA/Ro60-positive, n (%)	0 (0.00%)	6/42 (14.29%)	335/390 (85.90%)	<0.001***	123/143 (86.01%)	98/113 (86.73%)	114/134 (85.07%)	0.932
Anti-Ro52-positive, n (%)	16/80 (20.00%)	27/42 (64.29%)	255/387 (65.89%)	<0.001***	81/142 (57.04%)	83/113 (73.45%)	91/132 (68.94%)	0.015*
Anti-La/SSB-positive, n (%)	2/80 (2.50%)	6 (13.64%)	146/389 (37.53%)	<0.001***	39/142 (27.46%)	49/113 (43.36%)	58/134 (43.28%)	0.008**
Hyper-IgG, n (%)	27/71 (38.03%)	25/43 (58.14%)	218/371 (58.76%)	0.005**	70/135 (51.85%)	74/111 (66.67%)	75/125 (60.00%)	0.061
Hyper-ESR, n (%)	19/60 (31.67%)	13/35 (37.14%)	144/309 (46.60%)	0.074	44/105 (41.90%)	62/98 (63.27%)	48/106 (45.28%)	0.005**
ESSDAI score, median (Q1-Q3)	-	-	4.0 (1.0-9.0)	-	4.0 (1.0-9.0)	4.0 (2.0-8.75)	3.0 (0.75-8.0)	0.335

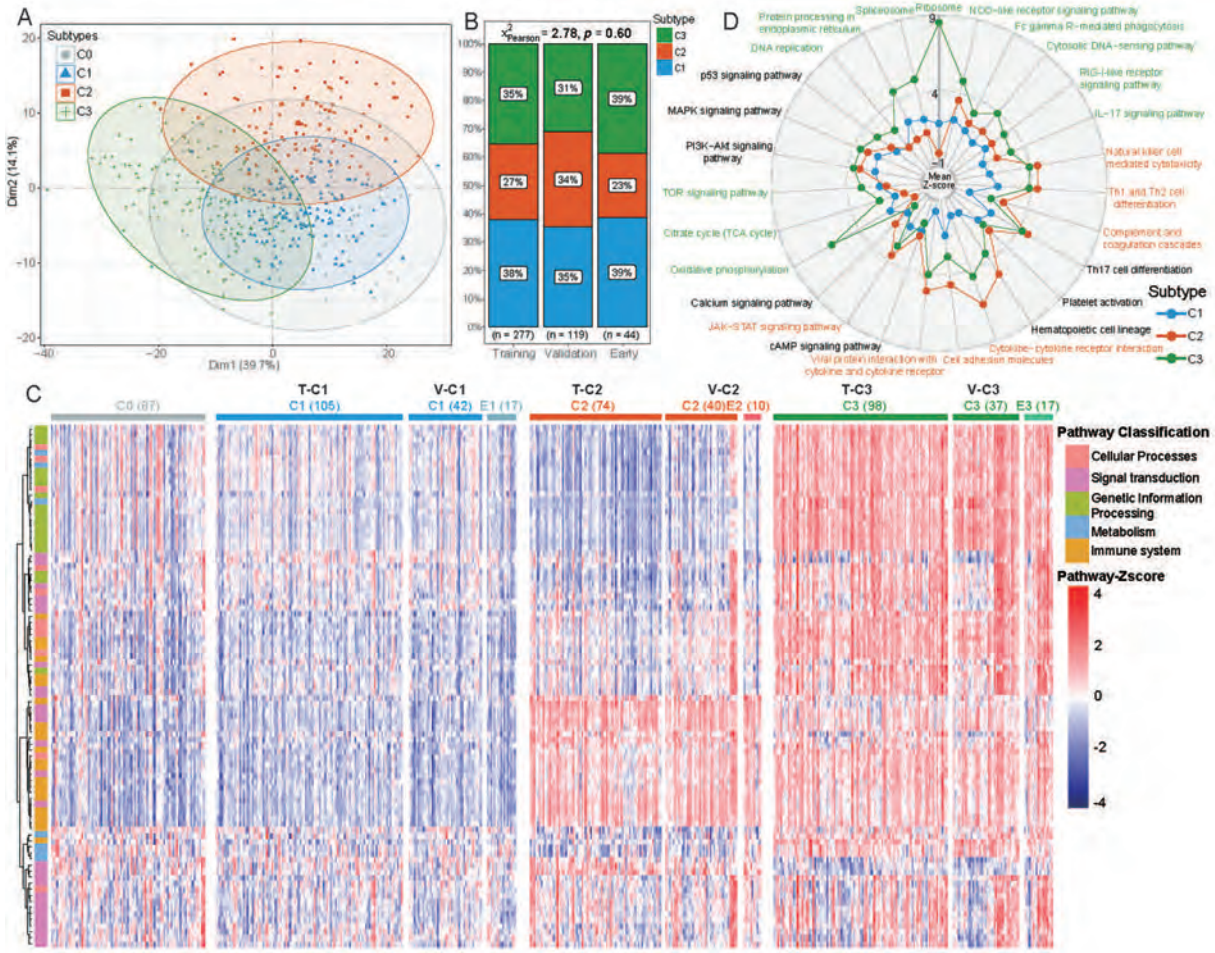
Note: GC, germinal center; OSS, ocular staining score; ANA, antinuclear antibodies; IgG, immunoglobulin G, Hyper-IgG, IgG > 16g/L; ESR, erythrocyte sedimentation rate, Hyper-ESR, ESR> 20mm/H, ESSDAI, EULAR Sjogren's Syndrome Disease Activity Index; sd, standard deviation; PIM, pauci-immune; CIM, cold-immune; HIM, hot-immune; *, $p<0.05$; **, $p<0.01$; ***, $p<0.001$



Overview of this study We recruited 527 participants based on respective criteria, including 87 non-pSS (C0), 44 early-pSS, and 396 pSS. Using an unsupervised clustering approach on the transcriptomic data of SGs, we identified three distinct molecular subtypes in pSS and early-pSS. We then conducted extensive downstream analysis on their clinical and biological and immune features, immune-metabolic and genetic characteristics, and disease diagnosis, prognosis, and treatment response prediction. pSS, primary Sjogren's syndrome; PIM, pauci-immune; CIM, cold-immune; HIM, heat-immune; ICI, immune cell infiltration; mIHC, multiplex immunohistochemistry; eQTL, expression quantitative trait loci; bDMARDs, biologic disease-modifying anti-rheumatic drugs; tsDMARDs, targeted synthesis disease-modifying anti-rheumatic drugs.

predominantly active metabolism processes, especially for oxidative phosphorylation (OXPHOS). Among the three subtypes, C2 had a higher lymphoma risk with the highest immune cell and endothelial cell infiltration in SGs. Based on the distinct features of each group, we matched them with approved or exploratory treatment options the patient most likely would benefit from, including conventional medicine, JAK inhibitors, and biologics.

Conclusion: Overall, our findings provide a comprehensive and in-depth molecular landscape of SGs in pSS, shedding light on the disease heterogeneity and promoting the development of precise clinical intervention strategies for pSS patients.



Molecular classifications and biological features of pSS subtypes (A) A PCA plot to show 3 groups of pSS patients (C1, C2, C3) by hierarchical pathway-based clustering. Non-pSS cases were overlaid using the same algorithm (C0, grey dots). (B) The scale map showing the distribution of 3 pSS subgroups in the Training set, Validation set and early-pSS cohorts without significant difference (Chi-Square test, p =0.60). (C) A heatmap generated from transcriptomic information via hierarchical pathway-based clustering based on z-score levels, including pSS Training set: 277/70%, pSS Validation set: 119/30%, 44 early-pSS patients, and 87 non-pSS cohorts, illustrating the distribution of five categories of pathways across the ten subtypes (non-pSS/C0 (87), T-C1(105), V-C1(42), E1(17), T-C2(74), V-C2 (40), E2(10), T-C3(98), V-C3(37) and E3(17)). T-C represents the clustering pSS subtypes in the Training set; V-C represents the clustering pSS subtypesthe in the Validation set; E represents the clustering early-pSS subtypes. (D) Representative significant pathways for each cluster. A radar plot showing the mean pathway z-scores in three pSS subtypes; C1 (blue), C2 (red), and C3 (green).

Disclosure: X. Wang: None; **J. Luo**: None; **S. Ying**: None; **J. Hong**: None; **H. Cheng**: None; **P. Wang**: None; **Y. He**: None; **W. Ye**: None; **X. Zhu**: None; **C. Zhu**: None; **L. Yang**: None; **Z. Li**: None; **S. Lin**: None; **D. Chen**: None; **X. Wu**: None; **Z. Xie**: None; **J. Wu**: None; **H. Xu**: None.

Abstract Number: L19

A Phase 3 Study of Repeat Injection of TLC599 in Osteoarthritis of the Knee: Benefits to 52 Weeks

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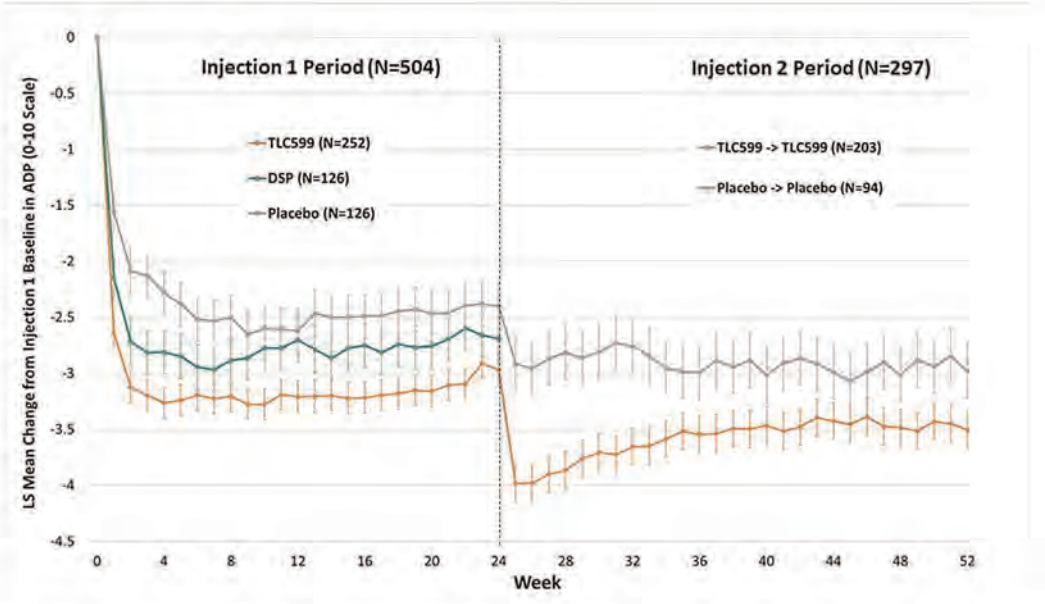
SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 7:30AM–9:00AM

Background/Purpose: In osteoarthritis (OA) of the knee, intraarticular injections of corticosteroids can relieve pain, reduce inflammation, and improve mobility, but the effect is not predictable, and the duration of pain relief can be short. The benefit of repeat injection has not been established. TLC599 is a liposomal formulation of dexamethasone sodium phosphate (DSP) intended for administration by local injection to provide sustained relief of pain of OA of the knee. The current study was conducted to confirm earlier phase 2 results demonstrating pain relief in OA patients over 24 weeks (*Hunter et al., 2022*), and to study the benefit of repeat injection over one year.

Methods: The study was a Phase 3, randomized, double-blinded, 3-armed, placebo- and active-controlled study to evaluate the efficacy and safety of TLC599 in single or repeat doses, in patients with K-L Grade 2-3 OA of the knee and average daily pain (ADP) from screening diary completion in the index knee of 5-9 (on a scale of 0-10). A total of 506 patients were randomized in a 2:1:1 ratio to receive an injection of TLC599 12 mg, DSP 4 mg, or saline placebo. At Week 24, eligible patients in the TLC599 and placebo arms received a second blinded injection of the same treatment, while patients in the DSP arm received a blinded injection of TLC599. Efficacy and safety were assessed through Week 52. Among other efficacy parameters, ADP and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain were assessed using Mixed Models for Repeated Measures (MMRM) and Analysis of Covariance (ANCOVA), respectively.

Results: With respect to WOMAC pain, TLC599 was numerically superior to placebo at all time points through week 24, and statistically superior ($p < 0.05$) at Week 12, the primary endpoint. For ADP, TLC599 was numerically and statistically superior ($p < 0.05$) to placebo at all time points during Injection 1 period (Figure). Additionally, at Week 12, the reduction in ADP for

Change from Injection 1 Baseline in Average Daily Pain (ADP) Score of Patients Who Received the First Injection through Week 24 (N=504) and Patients Who Received a Repeat Injection from Week 24 through Week 52 (N=297)



Note: Observed data are used. LS Mean (SE) was calculated using MMRM.

Change from Injection 1 Baseline in Average Daily Pain (ADP) Score of Patients Who Received the First Injection through Week 24 (N=504) and Patients Who Received a Repeat Injection from Week 24 through Week 52 (N=297)

TLC599 was superior to DSP ($p< 0.05$). A total of 203 patients who received an initial injection of TLC599 and 94 patients who received an initial injection of placebo were eligible and received repeat doses of TLC599 or placebo. The mean reduction in ADP from the injection 1 baseline for TLC599 was numerically superior to placebo at all time points through Week 52 and statistically superior through Week 34. TLC599 was generally well tolerated, with the number and type of adverse events similar among all three treatment groups. At Weeks 1 and 25 (after the second injection), there was a transient reduction in mean morning serum cortisol levels in patients who received TLC599, but this returned to normal by Weeks 2 and 26. There were no signs or symptoms of adrenal insufficiency in any patient.

Conclusion: TLC599 demonstrated a benefit over placebo in ADP and WOMAC pain in patients with OA of the knee after a single injection that was sustained to 24 weeks. A second injection of TLC599 at Week 24 provided further benefit to Week 52. These results provide additional information about the benefits of repeat steroid injection in OA of the knee and suggest that TLC599 may provide prolonged benefit and offer an alternative treatment for the management of OA knee pain.

Disclosure: G. Spencer-Green: Taiwan Liposome Company, 3; **D. Hunter**: None; **T. Schnitzer**: AstraZeneca, 1, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Horizon, 1, IBSA, 2, KolonTissueGeme, 5, Merck, 2, Moebius, 2, Orion, 2, Paradigm, 2, 5, Pfizer, 2, Regeneron, 2, 5, TLC, 5, Xalud, 2; **S. Shih**: Taiwan Liposome Company, 3, 10, 11; **T. Tai**: Taiwan Liposome Company, 3, 10, 11; **C. Kao**: Taiwan Liposome Company, 3; **S. Huang**: Taiwan Liposome Company, 3.

Abstract Number: L20

Telitacicept, a Human Recombinant Fusion Protein Targeting and Neutralizing B Lymphocyte Stimulator (BlyS) and a Proliferation-Inducing Ligand (APRIL), in Rheumatoid Arthritis (RA) Patients with an Inadequate Response to Methotrexate (MTX): A Randomized, Double-Blind, Phase 3 Study

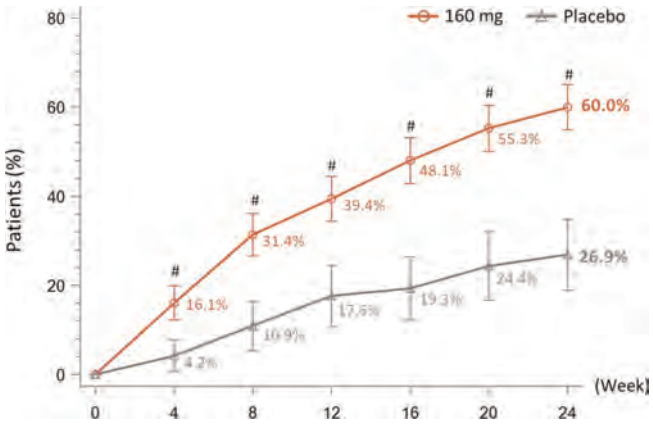
Li Wang[1], Dong Xu[2], Jianmin Fang[3], **Qing Zuraw**[4] and Fengchun Zhang[1], [1]Peking Union Medical College Hospital, Beijing, China, [2]Peking Union Medical College Hospital, Dong Cheng District, China, [3]RemeGen Co, Ltd., Yantai, China, [4]RemeGen Biosciences, Inc., San Francisco, CA

SESSION INFORMATION
Session Date: Wednesday, November 15, 2023
Session Title: Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 7:30AM–9:00AM

Background/Purpose: Telitacicept is a recombinant fusion protein targeting and neutralizing BLyS and APRIL. This phase 3, randomized, double-blind study evaluated the efficacy and safety of telitacicept 160 mg versus placebo in RA patients with an inadequate response to MTX.

Methods: This was a 24-week, randomized, double-blind, placebo-controlled, phase 3 study with an open label treatment follow up period from week 25 to 48 (NCT03016013). Patients with moderate-to-severe RA with an inadequate response to MTX were randomized 3:1 to receive either telitacicept 160 mg or placebo QW for 24 weeks. After Week 24, patients in the placebo arm were switched to telitacicept 160 mg QW for an additional 24 weeks. The primary efficacy endpoint was the proportion of patients achieving an ACR20 response at Week 24. Secondary efficacy endpoints included response rates for ACR50 and ACR70, individual components of the ACR response, DAS28-ESR, and radiographic joint damage as measured by the mTSS at Week 24.

Results: A total of 479 patients were randomized to receive telitacicept 160 mg (N=360) or placebo (N=119). Baseline demographics and disease characteristics were similar between the two groups, with the exception of CRP level which was higher for telitacicept versus placebo (22.856 mg/L vs. 17.287 mg/L). The primary endpoint was met with significantly more patients in the telitacicept 160 mg group achieving an ACR20 response at Week 24 compared with the placebo group



ACR20 Response Rate Through Week 24 (NRI, FAS). #P<0.001 vs. Placebo. NRI, missing data were imputed as non-response. FAS, full analysis set.

Secondary Efficacy Endpoints	**Telitacicept 160 mg (N=360)**	**Placebo (N=119)**	**P-Values**
ACR50 Response Rate#, n (%) % Difference [95% CI] Odds Ratio [95% CI]	77 (21.4) 15.5 [9.5-21.5] 4.305 [1.921-9.646]	7 (5.9)	<0.001
DAS28-ESR* LS Mean change from baseline (SE)	-1.58 (0.065)	-0.97 (0.114)	<0.001
HAQ Score* LS Mean change from baseline (SE)	-0.39 (0.023)	-0.29 (0.041)	0.041
Patient's Assessment of Pain*, mm LS Mean change from baseline (SE)	-19.04 (0.986)	-9.41(1.717)	<0.001
Patient's Global Assessment of Disease Activity*, mm LS Mean change from baseline (SE)	-19.57 (1.002)	-9.23 (1.743)	<0.001
Physician's Global Assessment of Disease Activity*, mm LS Mean change from baseline (SE)	-18.14 (0.905)	-11.24 (1.574)	<0.001
ESR*, mm/hour LS Mean change from baseline (SE)	-14.47 (1.079)	-5.15 (1.878)	<0.001
Radiographic Endpoints	**Telitacicept 160 mg (N=357)**	**Placebo (N=119)**	
△mTSS≤0#, n (%) % Difference [95% CI] Odds Ratio [95% CI]	322 (90.2) 23.8 [14.8-32.8] 4.845 [2.852-8.228]	79 (66.4)	<0.001
mTSS* LS Mean change from baseline (SE)	0.16 (0.065)	0.64 (0.114)	<0.001
Joint Space Narrowing Score+ LS Mean change from baseline (SE)	0.07 (0.025)	0.30 (0.043)	<0.001
Erosion Score+ LS Mean change from baseline (SE)	0.09 (0.052)	0.34 (0.091)	0.019

Secondary Efficacy Endpoints and Radiographic Endpoints at Week 24 (FAS).#Missing data were imputed by non-responder imputation (NRI). *Missing data were imputed by last observation carried forward method (LOCF). +Missing data were not imputed, the observed values were analyzed. FAS, full analysis set.

AE, n (%)	Telitacicept 160 mg (N=360)	Placebo (N=119)
TEAE	287 (79.7)	92 (77.3)
SAE	23 (6.4)	8 (6.7)
TEAE leading to discontinuation from study treatment	14 (3.9)	4 (3.4)
Death	0 (0)	0 (0)
Infections and infestations* (SOC)	148 (41.1)	50 (42.0)
Upper respiratory tract infection	88 (24.4)	28 (23.5)
Urinary tract infection	26 (7.2)	10 (8.4)
Bronchitis	12 (3.3)	1 (0.8)
Herpes zoster	2 (0.6)	4 (3.4)
Serious infections	8 (2.2)	4 (3.4)

Summary of Adverse Events Through Week 24 AE, adverse event; TEAE, treatment-emergent adverse event; SAE, serious adverse event; SOC, system organ class. *AEs with an incidence of ≥3% in any group were listed.

(60.0% vs 26.9%, P< 0.001) (Figure 1). At Week 24, the proportion of patients achieving an ACR50 response was significantly higher in the telitacicept 160 mg group compared with placebo (21.4% vs. 5.9%, P< 0.001) and the reductions from baseline in the DAS28-ESR as well as the individual components of the ACR criteria were significantly greater for patients receiving telitacicept compared with placebo (Table 1). Significantly more patients in the telitacicept 160 mg group showed no radiographic progression (△mTSS ≤0) at Week 24 compared with placebo (90.2% vs 66.4%, P< 0.001). Additionally, patients in the telitacicept 160 mg group showed significantly less progression of joint damage (as measured by mTSS, joint space narrowing score, erosion score) from baseline to Week 24 (Table 1). The incidences of treatment-emergent adverse events (TEAEs), serious adverse events (SAEs), TEAEs leading to discontinuation from study treatment, and infections were similar between the telitacicept 160 mg group and placebo group (Table 2). No patient deaths occurred during the study.

Conclusion: These phase 3 study results demonstrate the efficacy (e.g., responses in the ACR20, ACR50, and DAS28-ESR; and no radiographic progression measured by mTSS) and safety of telitacicept in treating moderate-to-severe RA patients with an inadequate response to MTX.

Disclosure: L. Wang: None; **D. Xu**: None; **J. Fang**: RemeGen, Ltd., 3, 4, 8, 10, 11; **Q. Zuraw**: RemeGen, 3, 11; **F. ZHANG**: None.

Patient Perspectives

Number: PP01

You Can't Get This from a Doctor: The Role of Support Groups for Adults Aged 25-55 Living with Arthritis

Eileen Davidson, Global Healthy Living Foundation, Burnaby, BC, Canada

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Living with a rheumatic condition comes with unique concerns specific to mental and social health like struggling with fatigue, anxiety, depression, and isolation, all while experiencing chronic pain and complications from being immunocompromised. Since my rheumatoid arthritis (RA) diagnosis eight years ago, I am no stranger to such feelings. The Covid-19 pandemic heightened these concerns, and had a large impact on my well-being and the well-being of many other people living with arthritis.

Intervention: Peer support groups for people with arthritis to meet with each other in person is an effective approach to combating anxiety and loneliness. With support from the Arthritis Society Canada's Community Action Grant, and using my skills and connections as a patient advocate to create a support group, I created an in-person support group to be held at a Vancouver, Canada arthritis clinic. "The Arthritis Social Hour" was designed for people with any form of arthritis between the ages of 25-55, an age group often without programs designed for them. The aim of this group was to provide a safe space for patients to express their concerns, share their journey, and learn from each other and qualified professionals in a fun, easy to understand and engaging environment.

Maintenance: Across ten in-person support group sessions held from February 8 to April 5, eighteen unique patients attended, many attending multiple sessions. Some patients reported never having met another person with arthritis in their age range, including someone who had been living with RA for 30 years. Patients new to Canada, who did not know anyone living with the condition and were newly diagnosed without current medical help, were able to receive guidance on where to seek care for their arthritis. Some patients met with an occupational therapist or physiotherapist for the first time at the in-person sessions. These providers offered long-term advice on how to exercise or self-manage arthritis.

Quality of Life: As people with lived experience, we speak a unique language together that can often not be provided elsewhere. Connecting with others living through similar experiences can foster transformative moments in our disease journeys. Such encounters lead us to feeling part of a community that understands and relates to the struggles that come with living with arthritis, especially as younger to middle-aged adults.

Hosting a support group reminded me how important it is for patients to connect with each other, to support each other, and learn together.

Since hosting the event, I have been able to reduce my own feelings of isolation and loneliness as a person living with arthritis.

THEMES	SPEAKERS
Medications Sleep Mental Health Work Diet Nordic Walking Poles Fatigue Relationships Covid-19 Art Exercise Yoga Advocacy	Physiotherapist Researchers Occupational Therapists Rheumatologists Patient Advocates Certified Yoga Therapist Kinesiologists Expressive Arts Therapist

The majority of my appointments are no longer than 20 minutes, which is not enough time for deep conversations on topics important to me. The opportunity to sit for two hours talking with other patients and professionals provided me with an incredibly invaluable amount of information and resources from my local community, which has broadened my abilities to self-manage my condition.

The Arthritis Social Hour continues to meet once a month to connect more people. The group's size and popularity is growing, along with my skills as a leading patient advocate.

Disclosure: E. Davidson: None.

Number: PP02

Patient Centered Care: The Complete Picture

Chisa Nosamiefan, South Weymouth, MA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: My recollection is that in l997 there about, I began to feel sick and I experienced these symptoms, night sweats, pain in my chest, breathlessness, always being tired, and I was loosing weight. This persisted over a span of five years. My doctor's interpretation of my symptoms was unexplained fevers, pericarditis, pleurisy, fatigue, unintentional weight loss. Initially, the diagnosis was unclear, and the treatment focused on managing the symptoms. Eventually, I was diagnosed with mixed connective tissue disorder and later with lupus.

Intervention: My healthcare team headed by my exceptional rheumatologist was able to step me down from clinically critical to medically stable but lupus continued to ravage other areas of my life which kept me unwell.

To address this, I applied a patient-centered therapy approach to my non-clinical symptoms of lupus. I identified and addressed various issues that didn't necessarily show up in my blood work but still impacted their health and well-being.

Maintenance: The first four issues I addressed were as follows:

1. Stress factors: By listing my assumed or real stresses, I was able to alleviate a significant level of stress. I made adjustments in my lifestyle and eliminated unnecessary sources of stress, considering my reduced income due to not being able to work.
2. Diet and Exercise: Educating myself about nutrition and eating habits led to changes in my diet, gradually reducing sugar, salt, and fried food. This change in diet resulted in reduced fatigue and enabled me to start exercising. Water aerobics, a low-impact exercise, became a fun activity for I began.
3. Support system: I recognized that relying solely on my family for support and care was not feasible, as my family members were also affected by lupus in a secondary sense. I intentionally built a support system that included emotional, spiritual, instrumental, informational, and appraisal support. I found a network of caring and knowledgeable individuals, including fellow patients, doctors, friends, and empaths, who provided the support I needed.
4. Hobby, Interest, or Amusement: Lupus had taken away my enjoyment in life, so I decided to explore new hobbies. I began visiting different neighboring towns and cities, engaging in sightseeing, taking pictures of historic architecture and water views, and people-watching from my car. This allowed me to find amusement and have fun without requiring extensive physical activity.

Quality of Life: Gradually over time there was a significant change in the quality of my life. I learned how to distress, I was going to the gym for the first time in my adult life, I had a new social community and I was out and about. More importantly I believe that the application of precision patient centered therapy to my non clinical lupus symptoms impacted my clinical symptoms. I had fewer flares and no more lupus related hospitalization.

The Labalaba Foundation inspired by my approach, adapted this patient centered approach in their programs for lupus patients self care management.

Disclosure: C. Nosamiefan: None.

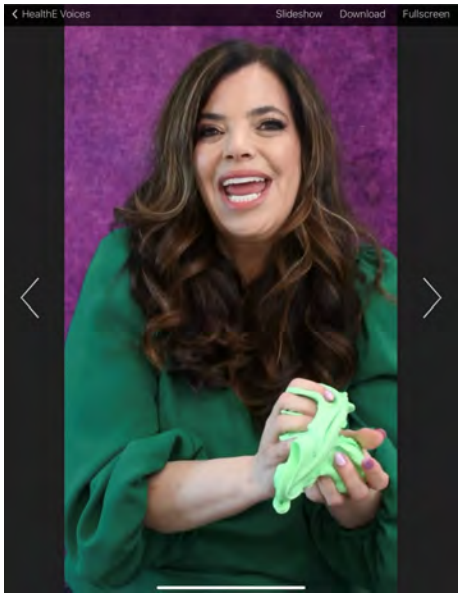
Number: PP03

Lupus with Slime: Improve QOL and Increase ROM in SLE with Slime

Amanda Greene, Los Angeles, CA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In 1983, over forty years ago, I was diagnosed with Systemic Lupus Erythematosus (SLE). I was immediately prescribed high dose corticosteroids. My body and disease flared. After 16 months, the rheumatologist and internist decided to start to taper my medication dosage. I was stabilized at 20, 15, 12.5 and 10m milligram daily doses. However, the side effects were still drastic, and I wanted to see how well I would do at a lower dose. So together with my doctors, I started a slow (super slow) taper process. Eventually, I was taking 2.5 milligrams of steroids a day. After three months, we discussed another tapering. It took another three months, in 1989 I took my last dose of corticosteroids. At the



While living with Lupus using slime has a positive impact on both my physical and mental health.

Stepping into slime requires strength, stability and balance.

time, my doctors thought I would have a potential future need for another round of corticosteroids, as most people living with lupus do. My prognosis at the time of diagnosis was a life expectancy of 5-7 years based on my symptoms and lab work.

Intervention: During the intervention, and while I was in lockdown, I was struggling to balance my mental and physical health, when I discovered how slime could help me stretch my mind and body. I quickly realized how much I needed the tactile sensation and distraction; the slime had helped me regain my sense of play and I was captivated by the autonomous sensory meridian response (ASMR) that popping slime provided. With some practice, I was doing tricks and I saw my outstretched arms and shoulders above my head, even better I was not wincing in agony. My Range Of Motion (ROM) was increasing with each session and I was thoroughly enjoying my self, while the slime was providing me with quality occupational therapy, I was improving my Quality of Life (QOL) and the impact on my state of mind which is evident in the "countless smiles that smile has brought to my face." Slime has had a such positive impact on my life that I am using less prescription pain and anxiety medication to help maintain my healthy "flare free" state while living and thriving with SLE for 40 years and still striving.

Stretching slime, opens up my ROM and I have discovered countless smiles and reduced anxiety due to the essential oils that enhance the sensations and tactile joy.

Maintenance: Due to my use of slime as a tool for my mental and physical health, I am using less prescription pain and anxiety medication to maintain a healthy state of aging with while living with SLE and I am a proud "adult slimer" who has found a way to quantify my playtime as being truly good for my health.

Quality of Life: Due to my use of slime as a tool for my mental and physical health, I am using less prescription pain and anxiety medication to maintain a healthy state of aging with while living with SLE and I am a proud "adult slimer" who has found a way to quantify my playtime as being truly good for my health.

Disclosure: A. Greene: None.

Number: PP04

Bouncing Back: How I Found My Running Shoes Using a Rebounder for My Psoriatic Arthritis

Ashley Krivohlavek, University of Oklahoma, Claremore, OK

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: When I was diagnosed with psoriatic arthritis (PsA) nine years ago, I thought my running days were behind me. Since high school, I have loved exercising. Cardio, specifically running, had always been my favorite because it cleared my head and invigorated me, preparing me mentally and physically for the day ahead. I built a running routine that fits my life well. I started by getting up ten minutes earlier than normal to ensure I had enough time to work out. Once I established the routine of getting up earlier, I gradually increased the minutes (five to ten minutes at a time) to where I am now. I also find that laying out workout clothes and shoes the night before helps keep me from missing my workout. I have also found that rewarding myself before and/or after my workout with something like coffee keeps me interested and excited about doing it. Given that my family has a history of heart disease and diabetes, I was proud that I was establishing a lifelong habit of and love for exercise. However, when my joints started becoming inflamed and painful from PsA about nine years ago, it looked like my running days were over. My rheumatologist recommended light workouts such as yoga and tai chi, so I incorporated them into my new routine, but I really missed running and runner's high. I began researching how I could run without further trauma to my joints.

Intervention: I began by researching workouts online and found several that included run-in-place examples. These run-in place examples were on a rebounder (mini trampoline). The constant impact on my feet, ankles, knees, and hips prevented me from running as I had before my PsA diagnosis. I was interested to try running on the rebounder and see if it gave me the

Table 1. Example HIIT Routine Using a Rebounder

Time in Seconds	Exercise Example
10	Rest
30	Run-In-Place
10	Rest
30	Run-In-Place
10	Rest
30	Run-In-Place
10	Rest
30	Ski Hop (Hop Keeping Your Knees together, Like Skiing)
10	Rest
30	Run-In-Place
10	Rest
30	Run-In-Place
10	Rest
30	Run-In-Place
10	Rest
30	Elow-Knee Cross (Right Elbow Touches the Left Knee and the Left Elbow Touches the Right Knee)
10	Rest
30	Run-In-Place
10	Rest
30	Run-In-Place
10	Rest
30	Run-In-Place
10	Rest
30	Jumping Jacks
10	Rest
30	Run-In-Place
10	Rest
30	Run-In-Place
10	Rest
30	Run-In-Place
10	Rest
30	Run-In-Place
10	Rest
30	Ballerina (Raising Arms Above the Head & Crossing Legs In the Middle of the Rebounder)
10	Rest
Time in Seconds	**Exercise Example**
30	Run-In-Place
10	Rest
30	Run-In-Place
10	Rest
30	Run-In-Place
10	Rest
30	Twist (Twist Your Body at the Abdomen)
10	Rest
30	Run-In-Place
10	Rest
30	Run-In-Place
10	Rest
30	Run-In-Place
10	Rest
30	Jump Rope (Act as Though You Are Jumping Rope)
10	Rest
30	Run-In-Place
10	Rest
30	Run-In-Place
10	Rest
30	Run-In-Place
10	Rest
30	Leg Cross (Wide Leg Cross Spanning the Diameter of the Rebounder In Front of the Body)
10	Rest
50	Run-In-Place
20	Rest
20 Minutes Total	To Increase Intensity, Add Weight Such as Dumbbells or Ankle Weights

Table 2. My Weekly Exercise Schedule

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
Rest	Weight & Core Training HIIT Routine (Table 1)	Yoga, Pilates, & Strengthening	Weight & Core Training HIIT Routine (Table 1)	Yoga, Pilates, & Strengthening	Weight & Core Training HIIT Routine (Table 1)	Rest

same benefits as regular running. I bought a rebounder and began practicing. Once I got comfortable running in place, I started doing other things on the rebounder, such as jumping jacks and squats. I also found a free Tabata timer app and created a high-intensity interval training (HIIT) routine (Table 1). I showed it to my rheumatologist, who approved my routine and reminded me to wear running shoes while on the rebounder, hydrate before and after, listen to my body, and slow down if needed. I had found my way back to running without adding more trauma to my joints.

Maintenance: Since starting my HIIT routine, I have added weights and core training to my regimen. In addition, I have increased my endurance by doing a longer HIIT routine and added a day of yoga and Pilates to my weekly schedule (Table 2). I plan to continue increasing the amount of time I do my HIIT routine and gradually adding heavier weights.

Quality of Life: I like to say that rebounding gave me back my running shoes. It fosters the same love of running I had before PsA and builds my physical strength while providing mental clarity. My rebounder helped teach me that I could still have autonomy over my body, even when PsA continues to occasionally surprise me with new physical and mental disruptions.

Disclosure: A. Krivohlavek: None.

Number: PP05

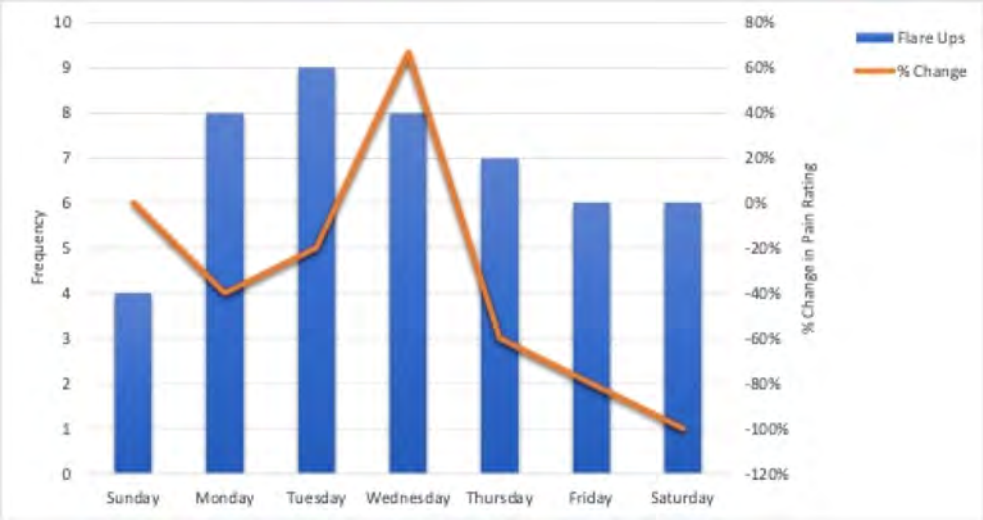
Relief Redefined: A Patient's Journey to Reducing the Impact of Her PsA Flare Ups

Caitlin West, Advocate, Coatesville, PA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: I was diagnosed with Psoriatic Arthritis (PsA) ten years ago, at 25. I had been dealing with stiffness and chronic fatigue for most of my life. Growing up I was actively accident prone (falling off horses, rock climbing falls, a skiing accident or two). I didn't think much of my pain growing up as I was so tough on my body. However, the pain I was experiencing, at 25, was unnatural. Approximately a couple months after my relocation from Santa Monica, CA to Houston, TX, I was unable to move my hands and morning inflammation lead to stiffness which severely limited my mobility for 1.5 hours. I was taking 6 Advil (200 mg) around 3x a day. A couple months later psoriasis' began to appear all over my face, neck, shoulders, and chest.

My primary doctor thought I had stressed induced eczema and possibly lupus. She was able to help expediate my dermatologist appointment. By the time I had my dermatology appointment my fingers swelled to the point of looking like sausage links, my face was swollen and bloated, and I had a hard time standing up or sitting down. The dermatologist was confident that I



Average daily flare ups and the % change in pain rating

had psoriasis and naturally with the visibility of my joint inflammation + chronic pain, she was also confident that I had PsA. Within a month I was able to get into a rheumatologist and time to diagnosis was relatively short. I was on Remicade infusions within a couple weeks after my visit. My dosage was 500 mg every 4 weeks and eventually reducing the frequency to every 8 weeks (present day). I do not pair Remicade with other drugs, outside of steroid injections and meloxicam 15mg (as needed).

Intervention: Novel therapy circuit inspired by over-the-counter therapeutic devices

1 out of 4 arthritis individuals experience daily debilitating pain and +80% are dissatisfied with their pain management options during these times (MEDSurvey April 2023). Therapeutic devices mainly encompass one technology (i.e. infrared light, TENS, PEMF), bulky and obvious (i.e. wires, straps, and gadgets to keep the device in place), and expensive! Personally, I spent ~$300 / device and have four devices. I was determined to create a better solution; obtaining flare up relief had to be easier and less frustrating.

Through experimentation, I found using infrared light, electric stimulation, and hot/cold therapies in a specific manner + routines resulted in a reduction of intensity of my flare ups. For 84 days (42 pre and 42 test period) I tracked my: back spasms and sharp pain (back, knees and hips). In the pretest and test period I continued my workout routine which includes swimming and biking 4x a week. During the test period I created a routine of 3 days /week (min.) where I utilized the novel therapy combination: 5 mins infrared light, 10 mins electric simulation, 5 mins hot/cold therapy with reduced intensity of infrared light.

Maintenance:

The Result: -45% reduction in flare up intensity (95% CI $p < 0.03$)

Reference chart

Quality of Life: I have noticed a significant improvement in my quality of life since the introduction of my novel therapy. The pain and discomfort which used to interfere with my daily routine has significantly reduced. My mood has lifted considerably, and I find myself feeling more optimistic and energetic.

Disclosure: C. West: None.

Number: PP06

Dana's Data Dashboard: Applying a Familiar Framework for Efficient and Effective Health Management

Dana Guglielmo, Los Angeles, CA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: As a researcher and data analyst, I enjoy the meticulous attention to detail that my work requires. I love the process of collecting, analyzing, and interpreting data to find patterns to ultimately improve population health. My passion for public health comes from my own health battles: I have rheumatoid arthritis and several other chronic conditions. These require ongoing maintenance, including doctor appointments, medications, labs, prior authorizations, referrals, and more. I started seeing more specialists in my 20s, and with each new specialist it became increasingly challenging to remember all of the complex and intricate details of my health management plan. I felt overwhelmed trying to stay on top of all of the moving parts, and I realized I needed to make a change.

Intervention: I applied a familiar framework to my health management by turning it into a research project! The first step was getting organized, so I created a spreadsheet to manage my health information. Although it accomplished my immediate goal of getting organized, the spreadsheet was very plain and I did not use it often. I decided to turn it into a Dashboard (Figure 1). In the research world, a "Dashboard" is any data visualization platform that distills large amounts of complex information into a user-friendly data snapshot. I'm a fun and vibrant person, and the design needed to match this. I added colors, icons, clickable dropdown buttons, and optimized it for use on a computer or mobile device. I embedded links to different apps - for example, clicking an address pulls up real-time directions.

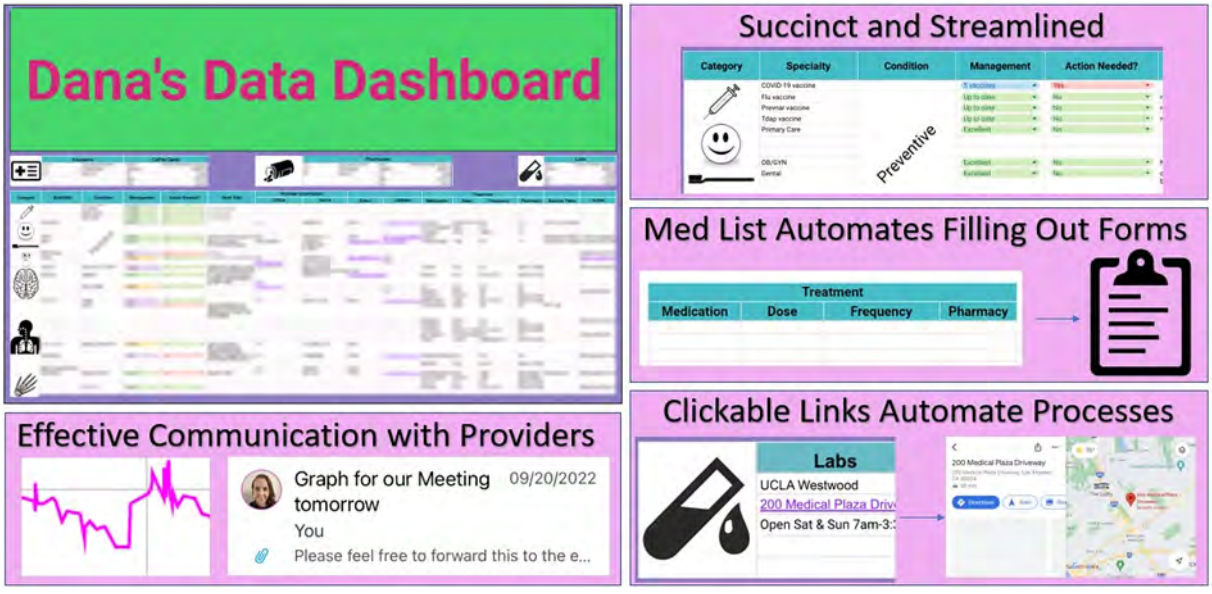


Figure 1. Dana's Data Dashboard: a snapshot of the numerous features and benefits of my dashboard.

Figure 2. Proactive instead of reactive health management: finally getting my routine rheumatology labs completed on schedule!

Figure 3. Portable, adaptable, and user-friendly: demonstrating that I can manage my health anytime and anywhere (even in a tree!) at Santa Ynez Falls, Los Angeles California.

Maintenance: My dashboard greatly improved my health management in several ways: (1) My approach changed from reactive to proactive (Figure 2). I now stay on top of appointments, medication refills, labs, prior authorizations, etc. long before they are due. (2) My communication with my health care team substantially improved. I can communicate large amounts of accurate health data efficiently, concisely, and effectively. I can articulate my thoughts much more clearly. For example, if I want to demonstrate a pattern I've noticed, I present it in a graph. (3) I am significantly more confident about my health management. Visualizing my progress allows me to come up with creative ideas and solutions to problems efficiently - just like a research project! (4) Most importantly, these changes have led to reduced stress levels and a decrease in symptoms of my arthritis and other chronic conditions.

Quality of Life: Dana's Data Dashboard transformed my health management. Not only can I manage my health anytime and anywhere (Figure 3), but it has enabled me to "zoom out on the graph." Instead of focusing on the day-to-day never-ending list of tasks, I can see the bigger picture: I am finally managing my health effectively. The final piece of any research project is disseminating findings in a way that can help others - hence this abstract! My hope is that this abstract will provide inspiration for others to work with their medical team to utilize their own strengths and interests to translate their health management into an area of their life in which they can excel and thrive.

Disclosure: D. Guglielmo: None.

Number: PP07

How "Coming Out" About My Lupus Diagnosis Allowed Me to Connect With Patients, Get Involved With Research, and Spread Awareness

Jamie Chieh Lo, School of Medicine, I-Shou University, Keelung, Taiwan

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Ever since I started medical school, I have been advised to not talk about my experiences with SLE. Family, friends, and even professors have warned me that discussing such topics may have negative implications on my future career.

Initially, I was skeptical. However, I soon found out that many young people, particular physicians, are extremely reluctant to openly discuss their chronic conditions, because they were worried about employers viewing them as a liability.

Intervention: In order to spread awareness about lupus, I ventured out of the private patient support groups and started with a Facebook post explaining my diagnosis to family and friends, more than 4 years after my first rheumatologist visit.

I also started to post regularly about both my personal journey and educational content about lupus on my Instagram account with more than 13000 followers. Friends and strangers alike messaged me to exchange experiences (as well as morbid jokes that will make healthy peers quite uncomfortable). I was also able to convince a few who were experiencing mysterious symptoms to see a rheumatologist. In one case, lupus nephritis was diagnosed early, and treatment was initiated before any further damage occurred!

The author presenting at the HBV Patient Session, AASLD The Liver Meeting 2022

Encouraged by the response I received, I felt empowered to go further in my advocacy and started sharing my experiences with another stigmatized condition: CHB. With CHB, managing lupus is more challenging since the treatments I am on, like steroids and rituximab, carry a high risk of causing HBV reactivation.

However, as a young "healthy" carrier, I was ineligible for costly antiviral medications under Taiwanese National Health Insurance (NHI), even though I had an off-the-charts viral load, mildly abnormal liver function, and was at risk of infecting my patients. I shared my story at multiple international hepatitis meetings, and with the effort of fellow advocates, eventually NHI agreed to start covering antivirals for immunosuppressed patients like me.

Maintenance: In recent years, Taiwan has seen an upsurge of patient-led advocacy efforts. As a result, many new drugs are now available for oncology and rare disease patients, and we are beginning to see the same trend in rheumatology. Patients have also become more health-literate, thanks to improved access to high-quality educational materials in Mandarin.

As a bilingual medical student, I also joined the translation task force of the COVID-19 Global Rheumatology Alliance. Over the past 3 years, we have translated the adult and pediatric versions of our vaccine survey into dozens of languages and disseminated them worldwide. I am also working on several other projects in autoimmunity and viral hepatitis, and was able to present my research at several international conferences.

Quality of Life: Inspired by the feedback I've received and progress that has been made, I no longer view myself as a "liability". Instead, I strongly believe that my lived experience as both a medical student and a patient are valuable assets when it comes to patient care, research, and advocacy.

In the future, I hope to become a rheumatologist who conducts research that meets patients' needs, as well as an advocate for a more inclusive workplace environment for young professionals living with chronic illness.

Disclosure: J. Lo: None.

Number: PP08

Finding Gratitude in Adversity: The Impact of Finding the Right Rheumatologist

Yaideliz Acevedo, Global Healthy Living Foundation, Newark, NJ

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: I recall sitting in the doctor's office with my one-month-old baby in his stroller, hearing the words "You have rheumatoid arthritis." At 21, I had no understanding of this condition, and my primary care doctor didn't take the time to talk to me about it. I didn't perceive it as too serious, but after my first visit with a rheumatologist, I felt worse than before. He assured me that I would be fine, but left the room before I could ask any questions or seek comfort in understanding my disease. This made me feel frustrated because I felt I would receive the same standard care as everyone else.

Because of this, I decided not to take the prescribed medication, hoping the condition would pass.. However, my condition deteriorated to the point where I couldn't care for myself, let alone my son.

Intervention: This realization prompted me to seek answers and take control of my health. I started on my own research journey and found a rheumatologist who took me seriously and took the time to answer my questions. She emphasized the importance of adhering to the treatment plan. This marked a turning point for me, igniting a desire to be proactive in my care.

Around that time I also found CreakyJoints. CreakyJoints is an international digital community for people living with arthritis who seek education, support, advocacy, and patient-centered research. The articles and personal stories available on the CreakyJoints.org website provided invaluable insights and answered questions I thought no one could address. To this day, I keep a 'bucket list' of ideas to try from those articles. Whenever doubts, concerns, or questions arose, I turned to CreakyJoints for guidance. It became my go-to resource and has prompted many great conversations about integrative treatments with my rheumatologist.

Through CreakyJoints, I discovered patient advocacy opportunities and ArthritisPower, a patient-centered research registry. Inspired to be a voice for others facing similar challenges, I embraced the chance to advocate for the rheumatoid arthritis (RA) community. By fostering a closer relationship with my doctor, I gained better control over my flares and realized that a fulfilling life with this disease was possible. Lifestyle changes and the insights I gained from my experiences allowed me to manage my RA effectively.

Maintenance: I'm still navigating how to thrive with the disease. Currently employed as a certified medical assistant at a cancer center, I cherish the open line of communication and trust I've developed with my rheumatologist. Participating in various projects with CreakyJoints has been transformative. Connecting with individuals across the world who share similar conditions has provided immense support and learning opportunities. We help one another while gaining insights into our conditions and sharing ideas that may work for some but not others. Being part of this community has given me a voice and the chance to advocate for those who may feel unheard.

Quality of Life: Finding the right rheumatologist inspired me to become an active member of the chronic disease community and explore integrative treatments. Embracing this journey has led to a significantly improved quality of life, and I am profoundly grateful for the experiences I have gained.

Disclosure: Y. Acevedo: None.

Number: PP09

Practicing Mindfulness to Improve Quality of Life

Vanessa Patino-Lydia, Global Healthy Living Foundation, Hallandale, FL

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: I've been living with symptoms of PSA and fibromyalgia for over 15 years. Four years ago, after flareup that severely impacted my mobility where I was unable to walk up/down stairs, get in/out of car, I was diagnosed with non-radial axial spondylarthritis. My quality of life was compromised and my future outlook felt grim.

Intervention: I began learning about spondylarthritis: what to expect, treatments, prognosis and ways to ease the pain. In the past my approach to rheumatic disease has been to just deal with the pain, ignore it, and keep pushing through, but this time I knew I had to do something drastically different. I needed to build a better relationship with my body. I tried complementary strategies to medical treatment such as meditation, reading, journaling, resting, leaving job, reducing commitments, massage, walking/movement, aqua therapy, and gluten- and sugar-free diets. Certainly all of these complementary approaches helped, but the real change occurred when I made a mental shift from thinking of my condition as "something I have to fix or change" to "something that I have to make peace with."

My rheumatologist recommended mindfulness training and a trusted friend recommended the Mindfulness Based Stress Reduction (MBSR) class, specifically. Over the course of six months, I began doing it in a self-directed way by watching videos, reading, reflecting, and practicing mindfulness activities, specifically:

- Body scanning and breathwork

- Building Awareness and slowing down
- Perspective changing
- Responding vs. reacting
- Not judging, self-love (loving kindness)
- Individualized choice
- Asking for what I need from family, from doctors

Maintenance: I still wake up tired with neck, hip, and back pain from my inflammatory arthritis. Mornings tend to be slow moving for me, and I don't commit to doing too much in the first two hours after I wake up. But now I have built awareness of this into my life. I look forward to my internal body scan as part of my daily mindfulness meditation routine. Fatigue is something I still experience, but what I tell myself about such things is different. These don't make me less than. They are my body's way of communicating with me. Am I going to listen? Am I going to advocate for myself? It is an ongoing process of befriending my body.

Quality of Life: I am much more aware of how I engage with my life and with stressors. My nervous system feels more relaxed, my heart rate is lower and I'm living with increased ease of wellbeing. This means more movement, presence with nature, getting outside, engaging in social activities and feeling more connected, less isolated. I am even planning a family trip overseas and working with my rheumatologist to have medications with me in case I have a flare up. Mindfulness helps me experience less suffering over pain (Table). I am less focused on needing to find a solution and instead focused on knowing that healing is within me.

Table. Observed Shifts in Quality of Life as a Result of Practicing Mindfulness

Shifting from this... **Focus on Emotional and Physical Toll of Living with Rheumatic Disease**	*To this...* **Mindful Adaptations to Healing**
Suffering: fearful of future and unknown, fearful of pain and loss of mobility	Listening to body and giving it what it needs: heat, cold, rest, stretching. Better sleep equals rest equals better mood and a feeling of having internal resources to cope with whatever comes up
Feeling defeated: depressed about what can't do anymore	Awareness of intrusive thoughts. Accepting what is, what's changed, showing love to myself.
Working harder: feeling behind not good enough which increased stress response	Mindful adaptation: shifting goals, realistic expectations, releasing judgement and having patience
Feeling guilty: Saying no to extra activities, social activities	More choice: Being intentional about time and energy and saying no to what I don't want to do.
Limited movement: Saying no to physical activity time and car travel	Knowing I am worth making adjustments: using back rest, heated seats for road trips, preparing medications, building in recovery time
Not making plans because can't commit	Being OK with change of plans
Grieving loss of self.	Living life even if it looks different: Freedom of Beginner's mind and trusting self Renewed personal outlook/sense of self

Disclosure: V. Patino-Lydia: None.

Number: PP10

Saved by Plants: How a Necessary Lifestyle Change Led to a Happier Life with Decreased Rheumatoid Arthritis Pain and Fatigue

Shelley Fritz, Global Healthy Living Foundation, Nyack, NY

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: After my RA diagnosis over eleven years ago, I was optimistic that the first biologic DMARD I took would slow the progression of my RA and ease symptoms. I spent the next decade switching medications to find better options, all while taking steroids between biologics to continue to have a decent quality of life. Weight gain came quickly and stayed. I began having gastrointestinal problems like microscopic colitis, but the moment that sent me racing for a healthier lifestyle was when I was diagnosed with non-alcoholic fatty liver disease (NAFLD).

Intervention: After a doctor told me I had fatty liver in 2022, I began exercising more regularly. I still had pain and fatigue, but my lab work showed low inflammation levels. Since 2015, I've been tracking my pain, sleep, and fatigue using patient-reported outcome measures available in the ArthritisPower app. Beginning in 2020, when I felt more isolated after a big move away from family and friends and the pandemic began, I also started tracking my satisfaction in social activities. I've been gluten-free and dairy-free for over a decade, but in January of 2023, I added one more change to determine how my diet might have an impact on my pain, fatigue, and sleep. This was because I always seemed to feel worse after eating processed foods and red meat, which are considered high-inflammatory foods.

Because I needed more information first, I researched low-inflammatory foods and diet plans. It was important for me to find a plan I could easily adhere to while keeping my meals free of gluten and dairy. I read that the Mediterranean diet is plant-based at its core, and I wondered if this diet plan would help me minimize inflammation and feel better. So, I made the decision to fully implement the Mediterranean diet and try it for four months (Table).

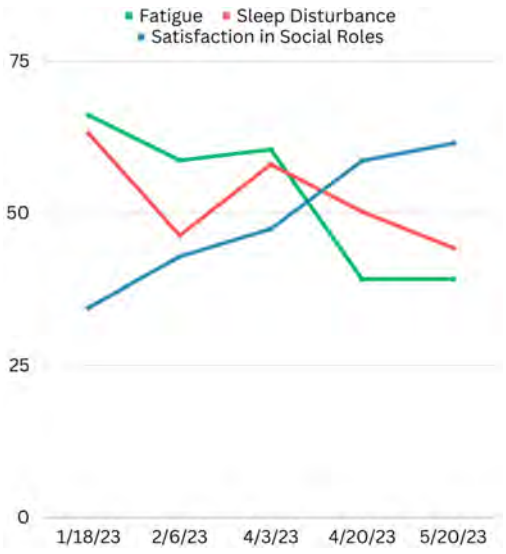


Figure 1: ArthritisPower data shows decreases in fatigue and sleep disturbance and increase in satisfaction with social roles.

Figure 2: Data from ArthritisPower app shows decrease in social isolation from January-May 2023

Within the first week of my Mediterranean diet, I felt major changes in my body. I had more energy and less fatigue. I continued tracking my symptoms over four months and found that my pain, fatigue, and sleep disturbance decreased noticeably on my ArthritisPower Health Picture (Figures 1 and 2). In addition, my desire to reach out to friends and socialize improved.

Table. My Mediterranean Diet

	Meal Examples			
Day	Breakfast	Lunch	Dinner	Snacks
1	Berries	Salad: asparagus, walnuts,	Salmon, artichokes, green beans	Roasted pistachios
2	Scrambled eggs with asparagus	Edamame hummus almond wrap	Roasted cauliflower with pistachios	Carrots with hummus
3	Fresh fruit bowl	Spaghetti squash with cannellini beans	Edamame pasta with chicken	Cashews
4	Omelet with spinach	Salad of vegetables and beans	Mahi Mahi with olives, capers, Greek-style potatoes	Apricot
5	Spinach and eggs with berries	Lentil soup	Black bean quinoa bowl	Celery and hummus
6	Berries and non-dairy yogurt	Roasted eggplant with non-dairy yogurt sauce	Shrimp with tomatoes and feta	Almonds
7	Frittata with red pepper and broccoli	Sauteed zucchini with lemon-basil dressing	Grilled chicken kebobs with Greek salad	Papaya

Maintenance: Eating healthy fats and avoiding foods that increase inflammation have been key to helping me feel better. I learned that blood work never tells the whole story. Before implementing the diet, I felt terrible even though my C-reactive protein (CRP) and erythrocyte sedimentation rate were lower than ever. Having a visual to represent how I feel helps me to communicate to my doctor that my medications are indeed working well now and that my dietary changes have helped me to feel as good as my blood work looked. The slight increase in fatigue and sleep disturbance in April reflects the two weeks I paused the new diet.

Quality of Life: Adhering to the diet helped me to make major improvements in my well-being. Today I have normal liver levels, more energy, less fatigue, less pain, and more inclination to socialize with family and friends. Managing RA is not only about effective medications; patients may need to also make lifestyle changes to support their treatment plan. There are limitations to the diet as it is high in healthy fats and may not help with weight loss, so continuing daily exercise and using portion control are essential.

Disclosure: S. Fritz: None.

Number: PP11

We Suffered For Decades, But Then She Was Born

Ian Stedman[1] and Barbara Stedman[2], [1]Canadian Autoinflammatory Network, Vaughan, ON, Canada, [2]Canadian Autoinflammatory Network, Turkey Point, ON, Canada

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: I was born in 1981; my mother in 1949; and my grandmother in 1926. Our story runs at least four generations deep, that we know of.

I began visiting my family doctor at 2 years of age for various issues, including swollen joints, bloodshot eyes, unexplained rashes, fevers, and debilitating headaches. My symptoms lasted from a half day to three days, with no patterns or triggers. My mother had the same challenges, as did her mother.

My childhood was defined by an endless search for answers. We rushed from specialist to specialist and spent long hours in waiting rooms to endure never-ending tests. I was prescribed anti-inflammatories, antihistamines, pain meds, but never accurately diagnosed. Doctors treated my symptoms, yet never suggested they might be connected.

By my late teens I lost interest in continuing the "specialist shuffle". I took the medicines I was prescribed and adjusted my lifestyle as needed. I missed school. I missed sports. I missed activities with friends. I accepted that my normal was not everyone's.

Intervention: Everything changed in 2012 when our first daughter was born. Like many babies, she had a rash at birth. Hers was different though. Like mine, it would go away and come back. It covered her body and sometimes her face, and she even experienced joint problems. Although I had given up looking for answers ten years earlier, it became clear that I didn't have that right anymore.

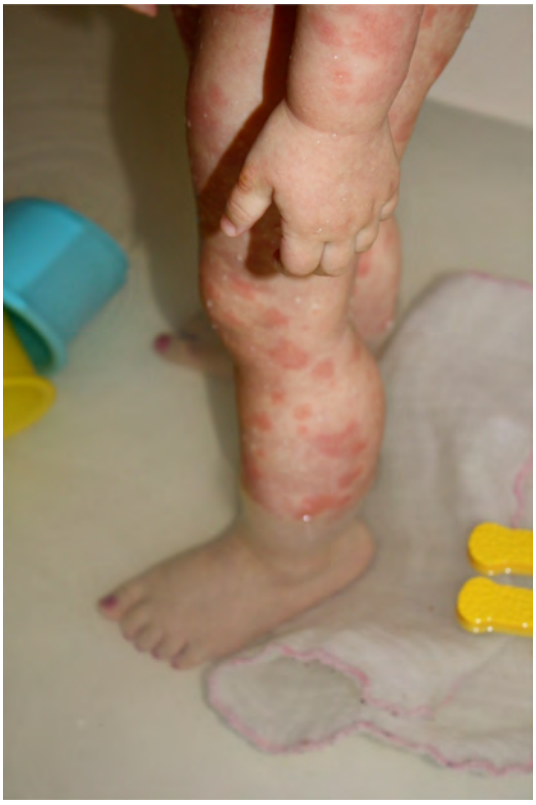


Image of skin on daughter's legs and left arm.

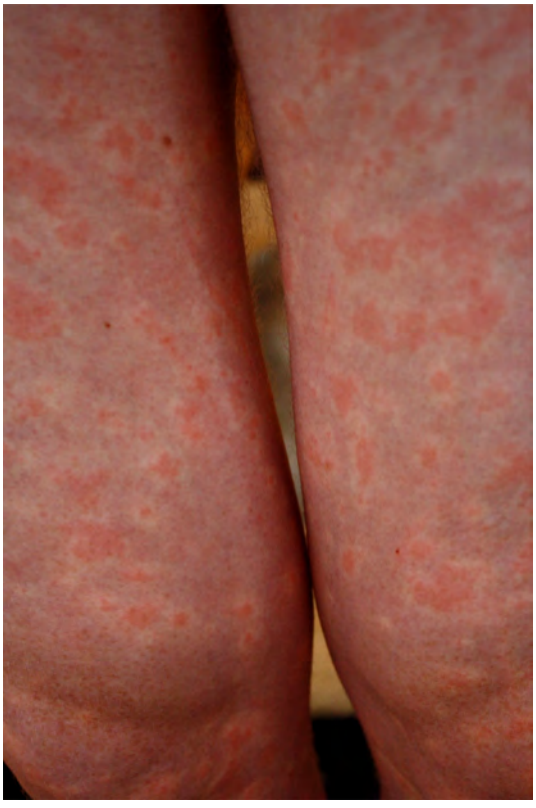


Image of author's legs.

My diagnostic odyssey re-started, I spent nights reading medical journals to no avail. Desperate, I searched online for images of rashes and found a blog. The blogger described his diagnosis and posted pictures of his rash. It looked like ours! I headed back to the journals, made a plan, visited more specialists, then had my eureka moment - I think we have Muckle Wells Syndrome! I searched for physicians who knew this rare disease and cold emailed a rheumatologist at our children's hospital. That rheumatologist responded within hours and asked me to obtain a referral.

Back to the hospital for more questions and tests. This time our blood was sent for genetic analysis and three months later we confirmed that we have Muckle Wells Syndrome (MWS). We learned that if left untreated, MWS can cause amyloidosis and sometimes lead to death.

Maintenance: Luckily, effective therapies were available. My mother, daughter and I now take an anti-IL-1b monoclonal antibody every 8 weeks. Our symptoms went away overnight and my daughter does have to live the same life that we did. I was in complete disbelief after that first dose and struggled for months to accept our "new normal". I feared it might be temporary, so I took nothing for granted.

Quality of Life: Treatment has changed our lives. It transformed my sense of what I am capable of and inspired me to think deeply about what I am responsible for. I am lifted each morning knowing that I am no longer limited by my health. I joined the board of a national rare disease advocacy group, which broadened my perspectives. I went back to University, earned my PhD in law and became a professor. I have testified before Canada's House of Commons Committee on Health and even co-founded a not-for-profit to help bring awareness to these diseases. MWS is merely one of 60+ gene mutations that have been described in the field of autoinflammation. Everyone should know them!

Disclosure: I. Stedman: None; **B. Stedman**: None.

Number: PP12

Sjögren's-Fatigue: Non-Therapeutic Lifestyle Adjustments to Help Manage My Most Problematic Symptom

Lisa Rubenstein, Sjögren's Foundation, Los Angeles, CA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: I was diagnosed with Sjögren's disease in 2015. I sought help from a rheumatologist after experiencing hand pain. I also had dry eyes and dry mouth but thought the level of dryness was "normal." At the time, my health was so good that I did not even have a primary care provider. Since then, my disease has progressed to include comorbidities of orthostatic hypotension, Raynaud's phenomenon, and peripheral neuropathy. I now see five specialists on a regular basis. My Sjögren's symptoms have also worsened and fatigue is the symptom that affects my quality of life the most.

My fatigue takes different forms. I never feel rested and always wake up feeling tired. There are times when I feel as if I've literally hit a wall and need to immediately sit down and take a break. At times I can't even lift my arms.

Intervention: Unfortunately, at this time there is no medicine approved for Sjögren's that treats fatigue. I knew I had to do something to manage my fatigue to maintain and improve my quality of life. I started keeping a journal of when the fatigue worsened. I tracked the level of fatigue, frequency, time of day, activities during that day and the previous day, and level of stress. I tried to identify what activities would increase fatigue and what activities might lessen it. I found that my peak energy is early in the day and decreases significantly by midday. Stress definitely increases all of my Sjögren's symptoms, including fatigue. Debilitating fatigue occurs most often when my schedule is overloaded. As long as the fatigue is not debilitating, I found that exercise can temporarily make the fatigue go away.

Maintenance: Based on my analysis, I now schedule all appointments for the morning. I limit errands to 1-2 each day and do them in the morning. For the first time in my life, I hired house cleaners. I would rather save my energy for more fun activities! I stay active and exercise regularly, where I again try to schedule this for the morning. I also know that I should not plan other activities like laundry or errands on days with a heavy workout. I take a 1-2 hour break midday, then decide what else to accomplish the rest of the day based on my energy level after the break. I rarely go out in the evening.

Quality of Life: Despite my Sjögren's, I still do quite a bit of traveling, both in the United States and internationally. I understand that a trip will result in an enormous amount of fatigue. I do not schedule any appointments or events for a week after I return. I accept this as the price I pay to pursue my interests and continue to travel.

Although fatigue is still my most challenging symptom, scheduling my activities to minimize fatigue has reduced its impact on my life to a more tolerable level. I've accepted that I have a constant level of fatigue. I continue to do the activities I enjoy most – running and traveling among them. I'm not going to let my Sjögren's and fatigue stop me from living a fulfilling life.

Disclosure: L. Rubenstein: None.

Number: PP13

My Four Pillars of Wellness: How Sleep, Diet, Exercise and Stress Reduction Enable Me to Define My Life and not let Sjögren's Define Me

Susan Barajas, Sjögren's Foundation, Los Angeles, CA

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Being diagnosed with Sjögren's has been a life changing event for me.I was diagnosed in 2013 after suffering from various odd ailments. Ultimately, extreme fatigue, muscle pain and weakness led to my diagnosis. I spent 6 weeks with my legs feeling like I had just run a marathon. I was always on the move, played competitive tennis and had a corporate full-time career. I was a woman on-the-go…until I wasn't. My internist confirmed something was amiss and that I had positive ANA and SSB antibodies, and, subsequently sent me for a lip biopsy and to a rheumatologist for further evaluation, which confirmed my Sjögren's diagnosis.

Intervention: I was fortunate to have connected with a rheumatologist who was well-versed in Sjögren's and is deeply involved in rheumatic disease research. She immediately started me on 300mg of plaquenil, which took several weeks to kick in. In an effort to stay on top of things I began making adjustments based on the 4 main pillars of my wellness: sleep, diet, exercise and stress reduction. I developed a strict sleep routine and equipped my bedroom with the essentials for

restful sleep. I began working with a nutritionist and, on my doctor's recommendation, went gluten free and reduced my dairy and sugar intake, though I still love dark chocolate M&M's! It has been amazing to see the impact my diet changes have had on my inflammation. Keeping my body moving is key, even when I just want to curl up under a blanket. My exercise of choice is walking, and my preference is to be outdoors as much as possible. Lastly, I transitioned from my full-time corporate career to a more fulfilling career where I can manage my own calendar and stress. We call it Lisa 2.0.

Maintenance: Being diagnosed with a progressive disease only stressed the importance of keeping my health at the forefront of everything I do. With this in mind, those same pillars are my playbook – every single day. Maintenance for me is staying ahead of my disease. Sjögren's is truly a game of whack-a-mole. Sjögren's affects my bladder, nerves, eyes, and digestive tract. As these issues pop up, they need to be addressed immediately and I've had to endure numerous treatments as part of these processes. I don't let my guard down and I am open and honest about what I can and cannot do. I've become comfortable accepting that "no" is a complete and acceptable sentence and I'm intentional with my energy and how I use it throughout the day. I'm aware of my productive times of the day and how to operate in low gear when I need to. I've been intentional in choosing doctor's that are familiar with Sjögren's and are compassionate to the complexities of this disease. Being surrounded by an amazing team of doctors has been critical to my health.

Quality of Life: I'm not going to lie and say this is all easy. I've completely adjusted my life to accommodate this disease. It affects everyone around you, and, let's face it, it's an invisible disease which makes it hard for people to understand that you feel sick when you look fine. I try not to focus on what I can't do, and instead put my energy into the things I can do. When something new pops up, I allow myself a little time to mourn and move on. Life has changed and I need to keep moving forward. I have confidence in my medical team and my 4 pillars have served me well. I don't allow Sjögren's to define me.

Disclosure: S. Barajas: None.

Number: PP14

Putting Lived Experience into Action: Flipping the Script on Living with a Chronic Disease

Natasha Trehan[1] and Naomi Abrahams[2], [1]University of Ottawa, Take a Pain Check Foundation, Toronto, ON, Canada, [2]University of Ottawa, Ottawa, ON, Canada

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives
Session Type: Patient Perspectives
Session Time: 4:00PM–5:00PM

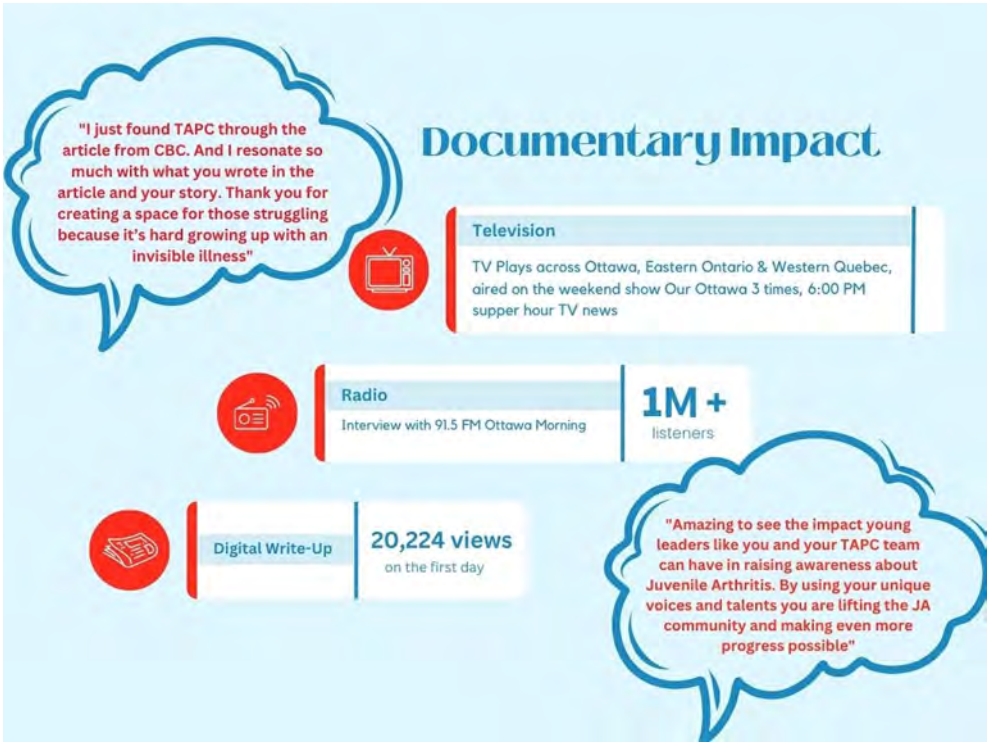
Background/Purpose: Naomi was diagnosed with Juvenile Idiopathic Arthritis (JIA) at the age of 18, after enduring 3 years of misdiagnoses. Similarly, Natasha received a diagnosis of the same condition at the age of 13. Despite their distinct timelines, they lived with the challenges of chronic autoimmune disease. To seek support, they sought out communities where they could connect with others who shared similar lived experiences. However, this proved difficult at times, prompting them to take the initiative in creating their own inclusive and supportive spaces.

Intervention: Recognizing a gap in the chronic illness community, Natasha decided to create an online platform for youth with rheumatic diseases. "I wanted to make sure other young people would never have to feel alone and go through the experience I had." This led her to create Take a Pain Check (TAPC), a non-profit organization which supports, empowers,

and provides an inclusive space where youth with rheumatic diseases feel understood. They run ambassador programs, chronic illness-related events, host podcasts, and monthly hangouts. TAPC has brought together a global network of healthcare professionals and patients to raise awareness and advocate for young people with invisible disabilities. To combine their passion for research and experiences with JIA, they joined the Choice Research Lab as patient partners. The lab focuses on patient engagement, valuing patient voices in research and shared decision-making. As patient partners, they represent young people's perspectives within the healthcare system, from diagnosis in adolescence into adulthood, influencing knowledge translation. Naomi emphasized the value of her role in a TAPC podcast episode, "Being a patient partner enables me to use both my knowledge and experience as a researcher and respondent to participate in research promotion that values lived experience."

Maintenance: Their commitment to raising awareness about arthritis has garnered recognition from the broadcaster Canadian Broadcasting Corporation (CBC) leading them to produce a documentary "If it weren't for my friends, I wouldn't have survived". The documentary emphasizes the importance of self-advocacy, finding and building a community, patient engagement and the role of friendship during one's diagnosis. Having a friend who has a similar condition can alleviate the burden of navigating it alone. This resource provides insight on obtaining support, advocating and raising awareness. Following the documentary, TAPC saw a 20% increase in followers.

Quality of Life: Arthritis is often wrongly perceived as a disease that only affects older individuals. They are determined to challenge this misconception and break down the associated stigma. Through their advocacy work, they aim to create positive change and increase awareness. They are committed to advocating for themselves and others in the chronic disease community. They hope to inspire others and expand inclusive advocacy measures in both research and social media. Their ultimate goal is to empower those affected by chronic conditions and to foster a more understanding and accepting society.



The Impact

Disclosure: N. Trehan: None; **N. Abrahams**: None.

Number: PP15

Toward a Frontier Beyond the Barriers of Position and Prejudice

Noriko Okochi[1], Eiji Oishi[2], Yuki Kojima[3], Noro Takashi[3], Mika Ishiguro[3], Toshiko Ito-Ihara[4] and YOSHIHIRO ARIMURA[5], [1]Rheumatic Disease and Vasculitis Support Network Japan, Institute of Neuropsychiatry, Tokyo, Japan, [2]Rheumatic Disease and Vasculitis Support Network Japan, UBE Frontier University, Yamaguchi, Japan, [3]Rheumatic Disease and Vasculitis Support Network Japan, Shinagawa-Ku, Tokyo, Japan, [4]Kyoto Prefectural University of Medicine, Rheumatic Disease and Vasculitis Support Network Japan, Kyoto, Japan, [5]Kyorin University School of Medicine, Kichijoji Asahi Hospital, Rheumatic Disease and Vasculitis Support Network Japan, Mitaka-Shi, Tokyo, Japan

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives
Session Type: Patient Perspectives
Session Time: 4:00PM–5:00PM

Background/Purpose: In Japan, firm boundaries exist between people from different walks of life surrounding diseases.

【Patients】

Some patients are unable to assert themselves before doctors who are knowledgeable and socially authoritative, and they are treated as they are told. It appears as if it is taboo to express to a medical professional one's desire for self-fulfillment by putting off treatment. They feel sorry for their family members, lower their self-esteem, and are unable to say what they want to prioritize in their lives.

【Caregivers of children with illnesses】

In Japan, where interaction with neighbors is decreasing, many families are isolated in child-rearing. This is even more difficult when the child has an incurable disease. Only the caregiver is responsible for the child's protection. The caregiver's personal feelings, history, and life are rarely shared with the patients themselves or with health professionals.

【Health care professionals】

It is difficult to fully interact with patients in the small amount of time available for consultation. Doctors experience many conflicts during treatment and feel helpless if their patients' conditions worsen. They may have to deal with complaints from patients because they are frustrated by their lack of success in treatment.

【Researcher】

There is a delay in the practice of patients actively participating in research. Patients have a victimized sense of being "experimented on" when asked to cooperate in drug development. Researchers and pharmaceutical companies are seen as the bad guys. Communication is not open and transparent.

The strong boundaries created by these positions have caused divisions within our society.

Intervention: It was against this cultural background that we launched the non-profit organization named Rheumatic Disease and Vasculitis Support Network in Japan. We had to resolve a number of conflicts in order to create a framework that was different from the previous Japanese patient associations.We were encouraged by many people's comments when we presented our work at the ACR in 2021.

Activities created by people from many perspectives

Maintenance: Patients, Caregivers, Health care professionals, and researchers know each other, accept each other, and work hand in hand together on various projects.

In April 2022, we exhibited a booth at the Japan College of Rheumatology. There, many doctors and researchers who support the organization joined the group. Occupational therapists and psychologists joined the group when making a video on rehabilitation.While conducting awareness-raising activities, we were contacted from overseas and exchanged views with an Indonesian patient group. I feel empowered, hopeful, and joyful by the expansion of encounters.

Quality of Life: Although patient association activities are not active in Japan, we believe that many people are encouraged by these activities.In fact, in the course of our activities to date, we have received hopeful responses from many patients and caregivers. We are working to overcome the divisions created by the strong boundaries of position. We hope that this organization will be a beacon of hope in the area of rheumatic diseases and vasculitis.

Disclosure: N. Okochi: None; **E. Oishi**: None; **Y. Kojima**: None; **N. Takashi**: None; **M. Ishiguro**: None; **T. Ito-Ihara**: None; **Y. ARIMURA**: None.

Number: PP16

Peer Health Coaches Help Scleroderma Patients Cope with Isolation

Mary Alore[1], Yen Chen[2] and Susan Murphy[3], [1]Troy, MI, [2]University of Michigan, Ann Arbor, MI, [3]University of Michigan, Plymouth, MI

SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives
Session Type: Patient Perspectives
Session Time: 4:00PM–5:00PM

Background/Purpose: In 2011, I felt extremely isolated with my new diagnosis of diffuse systemic sclerosis and sought support online and in support groups. In addition to being confusing, the misinformation I found about the disease was even scarier and more isolating than my diagnosis. I then sought social support through my rheumatologist at the University of Michigan who put me in contact with a few other patients who had asked him for similar social support. Since then, my focus

has been on supporting and educating fellow scleroderma patients as a mentor. I have worked one-on-one with over 100 scleroderma patients and concluded that patients need peer support for their mental and physical wellbeing.

Intervention: In my work as a Peer Mentor with the Michigan Medicine Scleroderma Program, I received the opportunity to become a Peer Health Coach for the RENEW study. After meeting with 45 participants, I learned that almost all patients were lonely and isolated in their disease, just like I was ten years ago.

In addition to being diagnosed with scleroderma, you receive a new status – isolated. You've never heard of scleroderma prior to the diagnosis, nor has anyone you know. Also, the physicians you have been trying to get a diagnosis from over the last year are not familiar with scleroderma either. Plus, you get the reaction, "But you don't look sick!" Through the RENEW study, health coaches met with patients virtually nine times over 12 weeks. Coaches led patients through goal-focused health-related learning modules and provided guidance, experience, and social support. As a health coach, I could offer real-life, lived experience and provide the support that was unavailable from family, friends, physicians, or therapists.

Maintenance: Patients need support and are seeking it. A trained health coach with a goal-setting framework helps them be less isolated and feel that they are not alone. Peer support is crucial for helping individuals change behaviors, like improving mental clarity and outlook, as well as motivating them to achieve health goals.

Quality of Life: I am able to discuss the health coaching experience from both the health coach and patient perspective to help reinforce the positive outcomes of peer social support. This is a valuable part of patient care that is missing in health systems.

RENEW Study logo

Disclosure: M. Alore: None; **Y. Chen**: None; **S. Murphy**: None.

Number: PP17

Utilizing Support Networks to Improve Patient Outcomes

Brian Vogel, Lupus and Allied Diseases Association, Inc., San Diego, CA

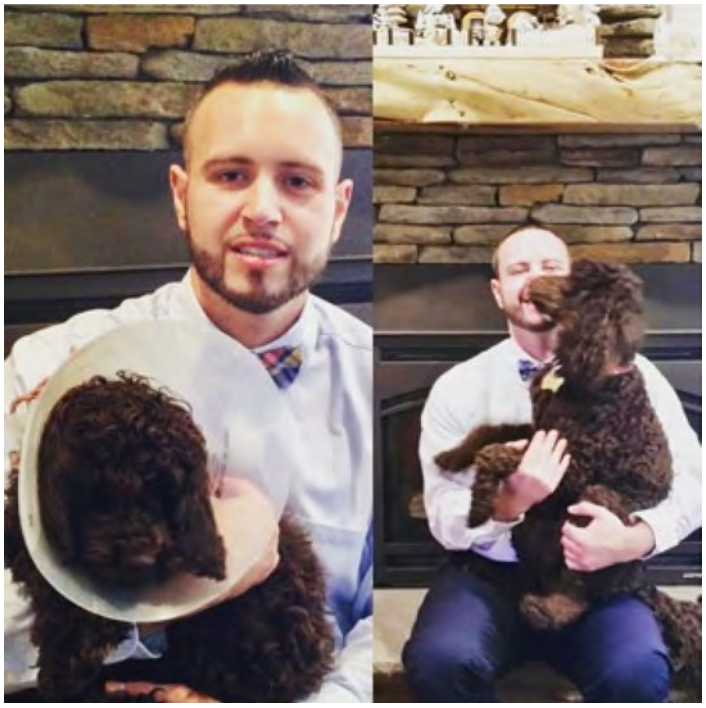
SESSION INFORMATION
Session Date: Sunday, November 12, 2023
Session Title: Patient Perspectives
Session Type: Patient Perspectives
Session Time: 4:00PM–5:00PM

Background/Purpose: In 2006, I realized I was gay and identified as LGBTQIA but did not come out. In 2008, I began experiencing chronic widespread pain, fatigue, and joint inflammation. I was referred to a rheumatologist due to a positive antinuclear antibody (ANA) test and misdiagnosed with juvenile rheumatoid arthritis. I began a medication regimen but no improvement. I consulted another rheumatologist and started a hydroxychloroquine (HCQ) and prednisone regimen. In 2010, I was diagnosed with Idiopathic Thrombocytopenia (ITP) and consulted with an oncologist when my platelets dropped dangerously low. After several failed intravenous immunoglobulin therapy (IVIG) infusions, I consulted a new oncologist and received a ten-week rituximab infusion treatment that raised my platelets. In 2011, I was formally diagnosed with Systemic Lupus Erythematosus (SLE). In 2013, I came out to my family and friends. I've tried numerous treatments between 2011-2022. SLE stabilized since February 2022 on current treatment.

Intervention: In 2017, my mom reached out to LADA and I volunteered at LADA's Annual Lupus Charity Golf Classic. I met other people with lupus and other autoimmune diseases for the first time. I then participated in LADA's Lupus Education Symposium. We learned a lot about the importance of clinical trials, patient empowerment, and care partnering from experts in the field. We then attended Annual Awareness Day at the State Capitol, as constituents of LADA, to meet with various legislators in the Senate and Assembly. I told my own story for the first time and shared my story with SLE. I will never forget the feeling of validation when seeing my story resonate with others. This feeling sparked a sense of empowerment and passion for advocating. I now share more on social media along with details of my story. When I moved to San Diego, I joined gay sports leagues to meet other gay men. It's allowed me to make new friends and connections that are essential parts of my support networks. They significantly improve my SLE outcomes regarding my social, physical, and psychological well-being. Support networks became an essential component of coping with my SLE.

Maintenance: Through joining gay sports leagues, I've cultivated a tribe of friends in San Diego that are lifelong friends and connections. LADA has indeed steered me down a road to advocacy and self-empowerment as well as amplified my support networks. I've made lifelong friends and connections around the country that have become part of support network and certainly improved my outcomes coping with SLE. They've created a close-knit Lupus community that I can rely on when I need support and questions answered. In April 2020, I became LADA Board Member. I continue my advocacy efforts alongside LADA working with people with Lupus through raising my voice and sharing my journey.

My family at the 19th Annual Lupus Charity Golf Classic 2019



My care partner poodle "Charlie" and I

Our golf team "Don't Drink and Drive"

Quality of Life: In 2013, I earned my Bachelor of Science degree. In November of 2020, I relocated to warmer climate and now live in San Diego. I've since changed careers and team of doctors. I've established strong healthy support networks in San Diego while maintaining LADA relationships. I'm eating healthier and exercising regularly. As a result of these things, I'm experiencing reduced disease activity and better quality of life.

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#

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